

W. Theilheimer

Synthetic Methods of Organic Chemistry

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W. Theilheimer

Synthetic Methods of Organic Chemistry

An Annual Survey

Synthetische Methoden der Organischen Chemie

Jahresbericht

Vol. 6

Mit deutschem Register-Schlüssel



19

52

BASEL (Schweiz)

S. KARGER

NEW YORK

For the Western Hemisphere: Interscience Publishers, Inc., New York

For Great Britain: Interscience Publishers, Ltd., London

<i>English Translation</i>		<i>Deutsche Ausgabe</i>
1948 Interscience Publishers	<i>Vol. I</i>	1946 1. Auflage 1948 2. unveränderte Auflage 1950 3. unveränderte Auflage
1949 Interscience Publishers	<i>Vol. II</i>	1948
	<i>Vol. III</i>	1949 Deutsche Ausgabe with English Index Key
	<i>Vol. IV</i>	1950 Deutsche Ausgabe with English Index Key
<i>English Edition</i>	<i>Vol. V</i>	1951 With Reaction Titles Vol. I-V and Cumulative Index. Mit deutschem Register- Schlüssel

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Printed in Switzerland

Druck: Friedrich Reinhardt AG., Basel

The following firms sponsored the editorial preparation of this work. The author gratefully acknowledges their generosity and interest in the promotion of chemical literature.

Abbott Laboratories, North Chicago, Ill., USA
Carbide & Carbon Chemicals Co., New York, N.Y., USA
Ciba Aktiengesellschaft, Basel, Switzerland
Ciba Pharmaceutical Products, Inc., Summit, N.J., USA
The Dow Chemical Company, Midland, Mich., USA
The Givaudan Corporation, Delawanna, N.J., USA
Hercules Powder Company, Inc., Wilmington, Del., USA
Heyden Chemical Corporation, New York, N.Y., USA
F. Hoffmann-La Roche & Co. AG., Basel, Switzerland
Hoffmann-La Roche, Inc., Nutley, N.J., USA
Eli Lilly Co., Indianapolis, Ind., USA
Mallinckrodt Chemical Works, St. Louis, Mo., USA
Merck & Co., Inc., Rahway, N.J., USA
The Wm. S. Merrell Company, Cincinnati, Ohio, USA
Monsanto Chemical Co., Dayton, Ohio, USA
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Sharp & Dohme, Inc., Philadelphia, Pa., USA
E. R. Squibb & Sons, New York, N.Y., USA
Standard Oil Development Co., New York, N.Y., USA
The Upjohn Co., Kalamazoo, Mich., USA

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From the Prefaces to the Preceding Volumes

New methods for the synthesis of organic compounds, improvements of known methods, and also old proved methods scattered in periodicals, are being recorded continuously in this book series.

An attempt has been made to develop the system of Weygand (Organic Preparations, Interscience Publishers, Inc., New York, 1945), and to group the reactions on a simple, although purely formal, basis. This has led to the invention of reaction symbols that can be classified systematically so that the methods can be treated without knowledge of the current trivial and author names (e.g., "Oxidation" and "Friedel-Crafts reaction").

Readers accustomed to the common notations will find these in the subject index. In many cases, particularly in searching for complex reactions, use of the classification system may be avoided by consulting the subject index. It is thought that the volumes should be used for immediate reference in the laboratory. They should provide a quick survey of the situation at hand, and obviate the necessity of first searching the entire literature. Syntheses are therefore recorded in the subject index by starting materials and end products, along with the systematic arrangement for the methods. This makes possible a sub-classification within the reaction symbols by reagents, a further methodical criterion. Starting with Volume 5, a table indicating the sequence of the reagents has been included. It may help the reader to locate reactions in the body of the text, particularly within large chapters. This table also contains such frequently used reagents as NaOH and HCl, which are not included in the subject index. Another innovation is the indexing of complex compounds with cross references under the related simpler compounds. General terms, such as synthesis, replacement, heterocyclic compounds, may also be brought to the special attention of the reader.

The abstracts are limited to the information needed for an appraisal of the applicability of a desired synthesis. This includes the number and nature of the reaction steps, the yield, and the important literature in question. In order to carry out a particular synthesis it is therefore still necessary to have recourse to the original papers or, at least, to an abstracting journal. In order to avoid repetition, selections are made on the basis of most detailed description and best yields, whenever the same method is used in similar cases. Continuations of

papers already included will not be abstracted, unless they contain essentially new information. They may, however, be quoted at the place corresponding to the abstracted papers. These brief literature references were newly introduced in the 3rd volume.

Furthermore, to avoid a "jungle" of references, the following limitations have been decided on: Papers are not included, if their content does not fit the subject matter of "Synthetic Methods" and if they can be found easily in the indices of the abstract journals. Less accessible and readable papers, such as the Russian ones, are only abstracted, as a rule, if the method in question is described nowhere else.

Syntheses that are split into their various steps, which are recorded in different places, can be followed with the help of the notations *startg. m. f.* (starting material for the preparation of ...) and *prepn. s.* (preparation, see).

Aus den Vorworten zu den vorhergehenden Bänden

In dieser Buchreihe sollen neue Methoden zur Synthese organischer Verbindungen, Verbesserungen bekannter und auch bewährte ältere Methoden, die sich in den in Fachzeitschriften veröffentlichten Originalarbeiten verstreut vorfinden, laufend registriert werden.

Aufbauend auf der Weygandschen Systematik wurde versucht, alle Reaktionen an Hand weniger einfacher, wenn auch rein formaler Richtlinien zu ordnen. Dies führte zur Ausarbeitung von Reaktions-Formelzeichen, die sich im Gegensatz zu den bisherigen Trivial- bzw. Autorennamen, wie Oxydation, Friedel-Crafts-Synthese, systematisch anordnen lassen. Man kann so die Methoden, ohne ihren Namen zu kennen, mittels des Formelzeichens auffinden.

Benutzer, die an die alten Bezeichnungen gewöhnt sind, finden diese im alphabetischen Register, das in vielen Fällen den Gebrauch der Systematik entbehrlich machen und besonders zum Aufsuchen komplizierter Reaktionen mit Vorteil benutzt werden dürfte. Da die Sammlung für die Handbibliothek am Arbeitsplatz im Laboratorium gedacht ist, soll sie eine rasche Orientierung gestatten, ohne daß fürs erste die Literatur der Instituts- oder Werkbibliothek herangezogen werden muß. Neben der systematischen Registrierung der Methoden werden deshalb im alphabetischen Register auch Synthesen durch ihre Ausgangs- und Endprodukte registriert. Dies ermöglicht es, im Text, innerhalb der Reaktionszeichen, nach einem weiteren methodischen Kriterium, nämlich den Hilfsstoffen einzuteilen. Beginnend mit Band 5 ist eine Tafel aufgenommen worden, die die Reihenfolge der Hilfsstoffe angibt. Sie

dürfte zum Aufsuchen von Reaktionen im Text, besonders in großen Kapiteln, nützlich sein. Sie enthält auch so häufig gebrauchte Hilfstoffe wie NaOH und HCl, die im alphabetischen Register nicht aufgeführt sind. Neuartig ist ferner die Registrierung der komplizierten Verbindungen. Auf Sammelbegriffe wie Aufbau, Austausch, Heterocyclen sei noch besonders hingewiesen.

Die Referate beschränken sich auf das zur Beurteilung der Zweckmäßigkeit einer Synthese Notwendige, wie Zahl und Art der Reaktionsstufen, die Ausbeute, wichtige, die Methode betreffende Literatur usw. Vor Ausführung einer bestimmten Synthese ist es deshalb erforderlich, das Chemische Zentralblatt oder ein anderes Referatenblatt und, wenn möglich, auch die Originalarbeit zu Rate zu ziehen. Zur Vermeidung von Wiederholungen wurden bei der Anwendung einer Methode in ähnlichen Fällen diejenigen ausgewählt, die am ausführlichsten beschrieben sind und die besten Ausbeuten geben. Fortsetzungen bereits aufgenommener Arbeiten, die nichts wesentlich Neues bringen, werden nicht mehr referiert, evtl. aber an der Stelle der aufgenommenen Arbeit zitiert. Diese kurzen Literaturzitate wurden im 3. Band neu eingeführt.

Um ferner das Material nicht zu sehr auf Kosten der Uebersicht anschwellen zu lassen, werden Veröffentlichungen, die nicht ganz in den Rahmen der «Synth. Meth.» passen und die in den Sachregistern der Referatenblätter leicht aufgefunden werden können, nicht aufgenommen. Arbeiten aus schwerer zugänglichen und lesbaren Zeitschriften, wie z. B. den russischen, werden im allgemeinen nur dann referiert, wenn die betreffende Methode sonst nirgends beschrieben ist.

Synthesen, die in ihre Stufen zerlegt und an verschiedenen Stellen eingeordnet sind, können mit Hilfe der Vermerke *startg. m. f.* (Ausgangsmaterial für die Darstellung von ...) und *prepn. s.* (Darstellung siehe) zusammengesetzt werden

Preface to Volume 6

Volume 6 continues the collection of organic synthetic methods over the period of one year. It consists of abstracts from papers published mostly in 1949 and 1950, with supplementary references from 1951.

This volume is meant to be the first one of a second series. New references to material in the preceding volumes have, however, been included in the text. The index also contains a few additional or revised entries to former volumes.

Since publications dealing with organic chemistry are increasing from year to year, some omissions may have occurred. The author will,

therefore, be grateful if important methods not yet included are brought to his attention.

Grants from the chemical industry once again made possible the continuation of this book series. They are acknowledged on a separate page. Thanks are due again to Dr. J. A. Aeschlimann, Director of Chemical Research, Hoffmann-La Roche, Inc., for liberally providing me with library and office facilities, and to Professor H. Erlenmeyer, Basle, Switzerland, for his continued interest in this enterprise. Finally, I want to thank Dr. John T. Plati for having read the text and giving me valuable advice, and again to Dr. and Mrs. Sorkin-Brügger, Basle, Switzerland, for their thorough proof-reading.

Nutley (New Jersey/USA), June 1952.

W. Th.

Vorwort zu Band 6

Der vorliegende 6. Band setzt die Sammlung organisch-synthetischer Methoden über den Zeitraum eines Jahres fort. Er enthält hauptsächlich Referate von Arbeiten aus den Jahren 1949 und 1950 mit Ergänzungen aus dem Jahre 1951.

Dieser Band ist als der erste einer zweiten Serie gedacht. Jedoch enthält der Text auch neue Zitate zu Referaten aus früheren Bänden. Im Register finden sich ebenfalls einige zusätzliche und revidierte Schlagworte zu diesen Bänden.

Da die Zahl der Veröffentlichungen auf dem Gebiete der organischen Chemie in den letzten Jahren sehr angewachsen ist, konnten Lücken nicht vermieden werden. Wir wären deshalb dankbar, wenn wir auf wichtige Methoden aufmerksam gemacht würden, die in unserer Sammlung noch nicht enthalten sind.

Nutley (New Jersey/USA), im Juni 1952.

W. Th.

Method of Classification

The following directions serve to explain the system of Classification.

1. Reaction Symbols.

The first part of the symbol refers to the chemical bonds formed during the reaction. These bonds appear in the reaction symbols as the symbols for the two elements that have been linked together (e.g., the bond between hydrogen and nitrogen, as HN). The order of the elements is the same as in *Chemisches Zentralblatt* and in Beilstein's *Handbuch der organischen Chemie*: H, O, N, Hal (Halogen), S, and the remaining elements (Rem). C is always placed last.

The "principle of the latest position" determines the order of the element symbols, and is used whenever possible.

The methods of obtaining a particular chemical bond are subdivided according to methods of formation. Four types are distinguished: addition ($\Downarrow$), rearrangement ($\frown\Downarrow$), exchange ($\nleftrightarrow$), and elimination ($\Uparrow$). The next part of the symbol refers to the types of bond which are destroyed in the reaction. Of the elements which form these bonds, in general two appear in the reaction symbols of addition and rearrangement and one appears in the reaction symbols of exchange and elimination.

The use of the reaction symbols will be made clearer by the following simplifying stipulations. (1) The chemical bond is rigidly classified according to structural formula, with no consideration of the mechanism of the reaction. (2) Double or triple bonds are treated as being equivalent to two or three single bonds, respectively. (3) Generally speaking, only stable organic compounds are taken into consideration. Intermediary compounds, such as Grignard compounds and sodiomalonic esters, and anorganic reactants, such as nitric acid, are therefore not expressed in the reaction symbols.

Examples:

see Volume II, page viii (Interscience Publishers)

Systematic Survey

see page 393.

2. Reagents.

A further subdivision, not expressed by the reaction symbols, is made on the basis of the reagents characteristic of the reaction. The order usually follows that of the periodic system. Reagents made up of several components are arranged according to the significant element for the reaction (e.g., KMnO_4 under Mn, NaClO under Cl). When a constituent of the reagent goes into the products of the reaction, the remainder of the reagent, which acts as a carrier of this constituent, is the criterion for the classification; for example, phosphorus is the carrier in a chlorination with PCl_5 and sodium in a nitrosation with NaNO_2 . A table indicating the sequence of the reagents may be found on page 395.

3. The material between the listings of the reagents is arranged with the simple examples first and the more complicated ones following.

4. When changes in more than one chemical bond occur during a reaction, as, for example, in the formation of a new ring, or if the reaction can be carried out in different ways, these reactions are introduced in several places when necessary. The main entry in such cases will usually follow according to the "principle of the latest position"; the other entries will be cross-referenced back to it.

Systematik

Für die Reihenfolge der Methoden gelten folgende Richtlinien:

1. Reaktionszeichen.

Die Einteilung erfolgt zuerst nach den Bindungen, die bei einer Reaktion entstehen. Diese erscheinen im Reaktions-Formelzeichen in Gestalt ihrer beiden Elementsymbole, z. B. die Bindung zwischen Wasserstoff und Stickstoff als HN. Die Reihenfolge der Elemente ist die gleiche wie im Chemischen Zentralblatt und in Beilsteins Handbuch der organischen Chemie: H, O, N, Hal (Halogen), S, Rem (Uebrige Elemente), C steht an letzter Stelle.

Das «*Prinzip der letzten Stelle*» bestimmt die Reihenfolge der Elementsymbole und ist auch sonst nach Möglichkeit immer angewandt worden.

Die Methoden zur Herstellung einer bestimmten Bindung werden nach ihrer Bildungsweise eingeteilt. Es werden 4 Fälle unterschieden: Aufnahme ($\downarrow$), Umlagerung ($\curvearrowright$), Austausch ($\nleftrightarrow$) und Abgabe ($\uparrow$).

Die weitere Einteilung ergibt sich aus den Bindungen, die bei der Reaktion gelöst werden. Von den Elementen, die an diesen Bindungen beteiligt sind, werden im allgemeinen bei Aufnahme und Umlagerung zwei, bei Austausch und Abgabe eines in das Reaktionszeichen aufgenommen.

Die Bildung des Reaktionszeichens wird durch folgende vereinfachende Annahmen erleichtert:

1. Die Bindungen für die Registrierung ergeben sich rein formal aus den Strukturformeln, ohne daß auf Reaktionsmechanismen Rücksicht genommen wird.

2. Doppel- und Dreifachbindungen werden 2 bzw. 3 Einfachbindungen gleichgesetzt.

3. Es werden in der Regel nur stabile organische Verbindungen berücksichtigt, Zwischenprodukte, wie z. B. Grignard-Verbindungen, Na-Malonester und anorganische Reaktionspartner, wie z. B. Salpetersäure, werden deshalb nicht zur Bildung des Reaktionszeichens herangezogen.

Beispiele

siehe Band 2, Seite VI

Systematische Uebersicht

siehe Seite 393

2. Hilfsstoffe.

Eine weitere Unterteilung, die im Reaktionszeichen nicht mehr zum Ausdruck kommt, wird nach den für die Reaktion charakteristischen Hilfsstoffen vorgenommen. Ihre Reihenfolge richtet sich im wesentlichen nach dem periodischen System. Hilfsstoffe, die sich aus mehreren Bestandteilen zusammensetzen, werden nach demjenigen eingeteilt, der für die Reaktion verantwortlich ist, z. B. steht KMnO_4 bei Mn, NaClO bei Cl. Geht ein Bestandteil des Hilfsstoffs in das Reaktionsprodukt ein, dann ist der Rest als Träger dieses Bestandteils für die Einordnung maßgebend; das ist z. B. bei einer Chlorierung mit PCl_5 Phosphor, bei einer Nitrosierung mit NaNO_2 Natrium. Eine Tafel der in diesem Band verwendeten Reihenfolge der Hilfsstoffe befindet sich auf Seite 395.

3. Innerhalb dieser Unterteilung sind die einzelnen Referate von einfachen zu komplizierten Beispielen fortschreitend angeordnet.

4. Treten bei einer Reaktion Veränderungen an mehreren Bindungen ein, wie z. B. bei Ringschlüssen, oder kann sie auf verschiedene Art durchgeführt werden, dann wird sie, falls notwendig, an mehreren Stellen eingeordnet. Das Hauptzitat steht in diesen Fällen in der Regel an der letzten Stelle; an den übrigen Stellen befinden sich Hinweise auf dieses.

Formation of H—O Bond

Uptake

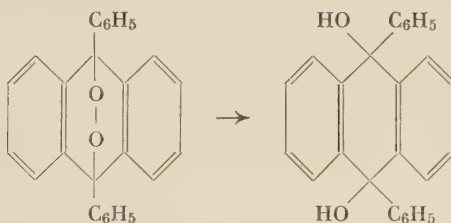
Addition to Oxygen

HO $\downarrow$ O*Phenyl magnesium bromide* C_6H_5MgBr

Hydroxy compounds from peroxides

←

1.



9,10-Diphenylanthracene peroxide and benzene added to an ethereal soln. of phenyl-MgBr, refluxed 2 hrs., and kept overnight at room temp. $\rightarrow$ 9,10-dihydroxy-9,10-diphenyldihydroanthracene. Y: 85%. F. e. s. A. Mustafa, Soc. 1949, 1662.

Addition to Oxygen and Carbon

HO $\downarrow$ OC*Potassium hydroxide/alcohol*

KOH

γ -Pyrone ring opening

C

s. 6, 128

Sulfuric acid/acetic acid H_2SO_4/CH_3COOH

Hydroxycarboxylic acids from lactones

←

2.

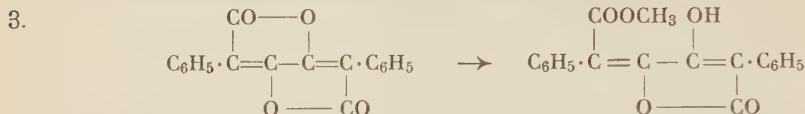


A soln. of α,α -diphenyl- β -propiolactone in H_2SO_4 -acetic acid-water heated 7 hrs. on a steam bath $\rightarrow$ α -phenyltropic acid. Y: 83%. H. E. Zaugg, Am. Soc. 72, 3001 (1950).

Hydrochloric acid

HCl

Hydroxycarbalkoxylactones from dilactones

 $\leftarrow$ 

A suspension of pulvinic acid lactone in methanol and some concd. HCl refluxed 15 min. $\rightarrow$ vulpinic acid. Y: 90%. F. e. s. R. L. Frank, G. R. Clark, and J. N. Coker, *Am. Soc.* 72, 1824 (1950).

Rearrangement

Hydrogen/Carbon Type

HO $\curvearrowright$ HC

Sodium/pyridine

Na/C₅H₅N

Acetylene derivatives from benzofurans

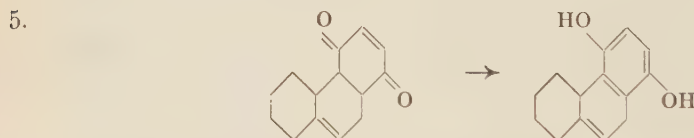
 $\curvearrowright$ 

Coumarone refluxed 4 hrs. with Na in pyridine at an oil bath temp. of 180-190° $\rightarrow$ o-hydroxyphenylacetylene. Y: 84%. V. Prey and G. Pieh, *M.* 80, 790 (1949).

Stannous chloride

SnCl₂

Quinols from endiones

 $\leftarrow$ 

SnCl₂ and HCl added to a soln. of 1,4-diketodecahydrophenanthrene in ethanol under N₂, and refluxed 1 hr. on a water bath $\rightarrow$ 1,4-dihydroxy-4b,5,6,7,8,10-hexahydrophenanthrene. Y: 96%. C. A. Grob, W. Jundt, and H. Wicki, *Helv.* 32, 2427 (1949).

Exchange

Halogen $\nleftrightarrow$ HO $\nleftrightarrow$ Hal

Sodium

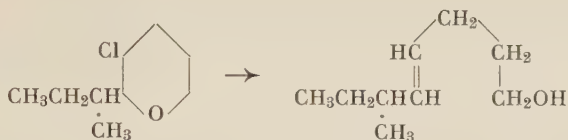
Na

Ethylenealcohols from cyclic halogenoethers

 $\curvearrowright$

Synthesis with addition of 4 and 5 C-atoms

6.



Crude mixed ($\pm$) *cis-trans*-2-*sec*-butyl-3-chlorotetrahydropyran added dropwise to a stirred suspension of powdered Na in dry ether and allowed to stand overnight $\rightarrow$ ($\pm$) *-trans*-6-methyl-4-octen-1-ol. Y: 85%.—By using tetrahydrofuran derivatives as intermediates, a chain extension by 4 C-atoms can be achieved. F. e. s. L. Crombie and S. H. Harper, Soc. 1950, 2685, 1707, 1714; s. a. R. C. Brandon, J. M. Derfer, and C. E. Boord, Am. Soc. 72, 2120 (1950).

Sodium sulfide

Na₂S

Sulfinic acids from sulfonic acid chlorides

SO₂Cl $\rightarrow$ SO₂H

7.

Na₂S·9H₂O gradually added with stirring below 40° to a suspension of 1,5-anthraquinonedisulfonyl chloride (from the di-K salt and PCl₅), and stirring continued for 30 min. $\rightarrow$ 1,5-anthraquinonedisulfinic acid. Y: 83.5% based on disulfonic acid. F. e. s. V. V. Kozlov and D. D. Smolin, Ж 19, 740 (1949); C. A. 44, 3479a.

Sulfur †

HO † S

Potassium hydroxide

KOH

Selective detosylation

OTs $\rightarrow$ OH

8.



1-p-Toluenesulfonmethylamido-2-naphthyl p-toluenesulfonate (prepn. s. 410) refluxed 2 hrs. in alc. KOH $\rightarrow$ 1-p-toluenesulfonmethylamido-2-naphthol. Y: 94%. F. e. s. F. Kurzer, Soc. 1949, 3434.

Nickel

Ni

Cleavage of sulfonic acid esters

ROSO₂R' $\rightarrow$ ROH

Hydrocarbons from sulfonic acid esters

ArOTs $\rightarrow$ ArH

9.

Alkyl esters of p-toluenesulfonic acid yield the corresponding alcohols on treatment with H₂ and Raney-Ni catalysts (but not with Pd-BaSO₄ or Adams' PtO₂); *aryl esters* give the aromatic hydrocarbons. Alkyl and aryl esters of benzyisulfonic acid are rapidly reduced to the hydroxy

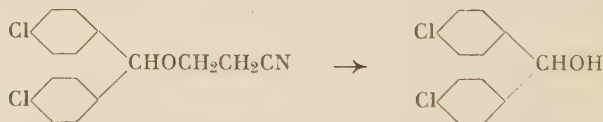
compounds, and benzylsulfonic anilides give (with lower yields) anilines.—E: 3-Benzylsulfonyl-1:2,5:6-diisopropylidene-D-glucose hydrogenated in ethanol with Raney-Ni at atmospheric pressure and room temp. for $\frac{1}{4}$ hr. $\rightarrow$ 1:2,5:6-isopropylidene-D-glucose. Y: 100%.—Similarly: p-Tosyl-m-acetamidophenol $\rightarrow$ acetanilide. Y: 90%. F.e.s. G.W.Kenner and M.A.Murray, Soc. 1949, S178.

Remaining elements ∇ **HO ∇ Rem***Hydrochloric acid**HCl***Hydrolysis of phosphoric acid esters** $\cdot\text{OPO}(\text{OH})_2 \rightarrow \cdot\text{OH}$

10. Inositol-5-phosphoric acid (prepn. s. 912) with 2 N HCl heated in a sealed tube at 130° for 24 hrs. $\rightarrow$ *meso*-inositol. Crude Y: 91%. B. M. Iselin, Am. Soc. 71, 3822 (1949).

Carbon ∇ **HO ∇ C***Sodium hydroxide**NaOH***Cleavage of ethers** $\text{ROR} \rightarrow \text{ROH}$

11.



p,p'-Dichlorobenzhydryl- β -cyanoethyl ether refluxed 4 hrs. with 25%-NaOH $\rightarrow$ p,p'-dichlorobenzhydrol. Y: 97%. O. Grummitt and D. Marsh. Am. Soc. 71, 4156 (1949); s. a. H. E. Ungnade and K. T. Zilch, J. Org. Chem. 15, 1108 (1950).

Selective hydrolysis $\leftarrow$

s. 6, 137

*Sodium hydroxide/potassium hydroxide**NaOH/KOH***Cleavage of ethers** $\text{ROR} \rightarrow \text{ROH}$

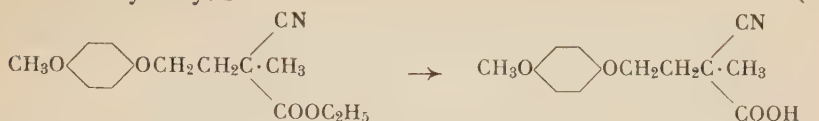
s. 6, 160

*Potassium hydroxide**KOH***Carboxylic acids from carboxylic acid esters** $\text{COOR} \rightarrow \text{COOH}$

s. 6, 136, 689

Selective hydrolysis

12.



Ethyl α -cyano- α -methyl- γ -(p-methoxyphenoxy)butyrate (prepn. s. 802) allowed to stand with 1 equivalent of KOH in alcohol-water at room temp. for 6 hrs. $\rightarrow$ α -cyano- α -methyl- γ -(p-methoxyphenoxy)-butyric acid. Y: 89.3%. N. J. Leonard and W. C. Wildman, Am. Soc. 71, 3089 (1949).

Sodium hydroxide/alcohol

s. 6, 466

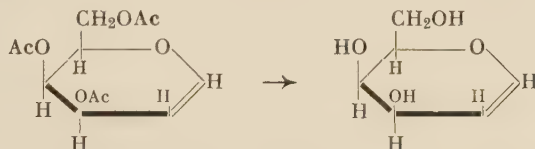
Sodium alkoxide

NaOR

Deacetylation

OAc $\rightarrow$ OH

13.



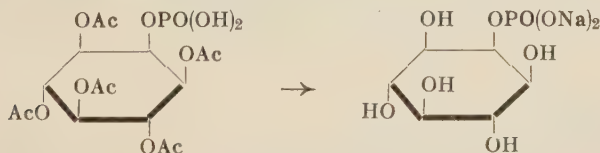
Na added to a soln. of 3,4,6-triacetyl-D-galactal, kept 48 hrs., then solid CO_2 added $\rightarrow$ D-galactal. Y: 81%.—Deacetylation with $\text{Ba}(\text{OH})_2$ gave only 59% yield. W. G. Overend, F. Shafizadeh, and M. Stacey, Soc. 1950, 671.

of glycosides

s. 1, 1; s. a. E. L. May, E. Mosettig, and H. G. Latham, Jr., J. Org. Chem. 15, 890, 884 (1950).

Hydroxyphosphoric acid esters from acetoxyphosphoric acid esters

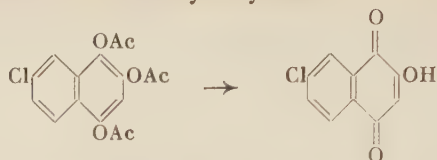
14.



2.5 moles of Na-methoxide in dry methanol added to a methanolic soln. of 1,2,3,4,6-pentaacetyl-D-inositol-5-phosphoric acid (prepn. s. 158), and allowed to stand at 0° overnight $\rightarrow$ Na-inositol-5-phosphate (startg. m. f. 912). Y: 97%. B. M. Iselin, Am. Soc. 71, 3822 (1949).

Hydroxyquinones from triacetoxyisocyclics

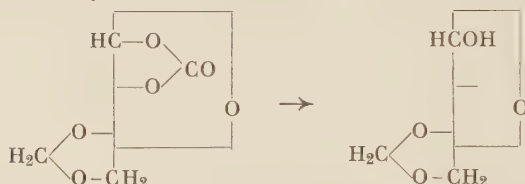
15.



7-Chloro-1,2,4-triacetoxynaphthalene added within 10 min. to a suspension of Na-methoxide in methanol, and stirred 1 hr. in an ice bath in the presence of air $\rightarrow$ 7-chloro-2-hydroxy-1,4-naphthoquinone. Y: 91%. F. e. s. L. F. Fieser and R. H. Brown, Am. Soc. 71, 3615 (1949).

Cleavage of carbohydrate carbonates

16.



3,5-Monomethylene-D-xylose carbonate in *N*/20 Na-methoxide shaken for 3 hrs., then allowed to stand at room temp. for 3 additional hrs. $\rightarrow$ 3,5-monomethylene-D-xylose. Y: 92.5%. O. T. Schmidt and G. Nieswandt, B. 82, 1 (1949).

Sodium chloride/aluminum chloride *s.*

Aluminum chloride/sodium chloride

NaCl/AlCl₃

Piperidine

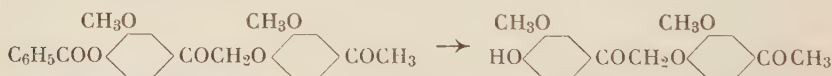
C₅H₁₁N

Selective hydrolysis

Debenzoylation

OBz $\rightarrow$ OH

17.

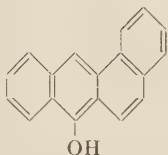


Magnesium hydroxide $Mg(OH)_2$ **Aldehydes from 1,1-di(acoxy)compounds** $CH(OAc)_2 \rightarrow CHO$

19. p-Nitrobenzylidene diacetate refluxed 2 hrs. with a 2.5% suspension of $Mg(OH)_2 \rightarrow$ p-nitrobenzaldehyde. Y: 90-95%. W. Davey and J. R. Gwilt, Soc. 1950, 204.

Alkyl magnesium halide $RMgHal$ **Deacetylation** $OAc \rightarrow OH$

20.



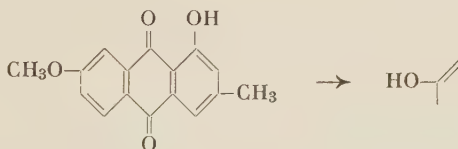
1,2-Benzanthranyl-10-acetate followed by benzene added to an ethereal soln. of n-butyl-MgBr, the ether allowed to distill, then refluxed for 1 hr. $\rightarrow$ 1,2-benz-10-anthranol. Y: 84%. L. F. Fieser and E. B. Hersherg, Am. Soc. 59, 1028 (1937).

Barium methoxide $Ba(OR)_2$ **Deacylation of glycosides**

s. 1, 4; 6, 291; s. a. C. Sannié and H. Lapin, Bl. 1950, 1234

Aluminum chloride/sodium chloride $AlCl_3/NaCl$ **Cleavage of ethers** $ROR \rightarrow ROH$

21.



0.4 gm. 1-hydroxy-3-methyl-7-methoxyanthraquinone ground with $AlCl_3$ and NaCl, then heated at a bath temp. of 170° for 2 hrs. $\rightarrow$ 0.3 gm. 1,7-dihydroxy-3-methylanthraquinone.—Demethylation with HBr in glacial acetic acid was not successful. H. Mühlemann, Pharm. Acta Helv. 24, 356 (1949).

Aluminum bromide $AlBr_3$

s. 1, 234; 4, 14; selective cleavage s. E. H. Ungnade et al., J. Org. Chem. 16, 64, 70 (1951)

Chymotrypsin $\leftarrow$ **Carboxylic acids from carboxylic acid esters** $COOR \rightarrow COOH$ **Enzymatic resolution of racemates**

s. 5, 670; s. a. H. T. Huang and C. Niemann, Am. Soc. 73, 1541 (1951)

Formic acid**Carboxylic acids from carboxylic acid esters****Acidolysis**

22. A mixture of methyl acrylate, 98-100%-formic acid, some hydroquinone, and a little H_2SO_4 refluxed 1-3 hrs., then distilled $\rightarrow$ acrylic acid. Y: 74-78%. C. E. Rehberg, *Org. Synth.* 29, 5 (1949).

Sulfuric acid**Carboxy-sulfonic acid amides**

s. 5, 14; s. a. Am. Soc. 72, 2458 (1950)

Hydrochloric acid**Enols from enolethers**

s. 6, 320

Cleavage of acetals

s. 6, 575

**of alkyleneacetals**

s. 6, 216

Selective hydrolysis

23. $C_6H_5CH_2CONHCH_2CH(OC_2H_5)_2 \rightarrow C_6H_5CH_2CONHCH_2CHO$

An ethereal soln. of phenylacetyl aminoacetal vigorously stirred with aq. NaCl-HCl at room temp. for 4 hrs., neutralized with solid Na-carbonate, and treated with solid CO_2 to chill the soln. and drive off the remaining ether $\rightarrow$ phenylacetyl aminoacetaldehyde hemihydrate. Y: 86%. F. e. s. E. V. Brown. *Chemistry of Penicillin* 1949, 482.

24. A soln. of methyl 2,6-dimethanesulfonyl-3,4-isopropyliden- α -D-galactoside in methanol containing some 5 N HCl refluxed 2 hrs. $\rightarrow$ methyl 2,6-dimethanesulfonyl- α -D-galactoside. Y: ca. 100 % A.B.Foster et al., *Soc.* 1949, 2542.

Deacetylation

s. 6, 51

**Partial deacetylation
of steroid-3-acetoxy groups**

s. 2, 29; s. a. L. F. Fieser and S. Rajagopalan, *Am. Soc.* 72, 5530 (1950)

Carboxylic acids from carboxylic acid esters

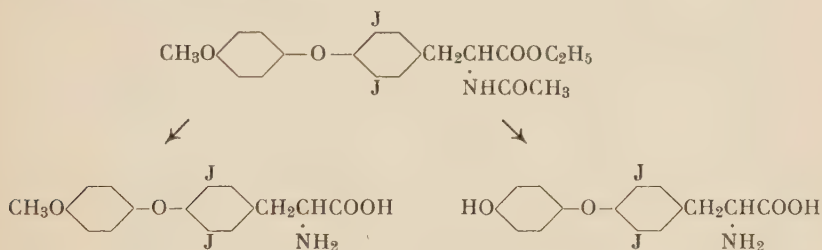
25. Concd. HCl added to a soln. of methyl β -ketopalmitate in glacial acetic acid until the soln. becomes slightly turbid, and allowed to stand at room temp. for 48 hrs. $\rightarrow$ β -ketopalmitic acid. Y: 93%. F. e. s. M. A. Mitz, A. E. Axelrod, and K. Hofmann, *Am. Soc.* 72, 1231 (1950).

Hydrobromic acid**Cleavage of ethers**

Demethylation s. 1, 11/2; 2, 31; 4, 18; debenzylation s. E. D. Amstutz, *Am. Soc.* 72, 3420 (1950)

Hydrochloric and hydriodic acids**Selective hydrolysis****Optically active compounds**

26.



3,5-Diiodo-4-p-methoxyphenoxy-N-acetyl-L-phenylalanine ethyl ester
(prepn. s. 592)

refluxed 2 hrs. with a 1:1 mixture of concd. HCl and glacial acetic acid $\rightarrow$ 3,5-diiodo-4-p-methoxyphenoxy-L-phenylalanine. Y: ca. 100 %.

refluxed 4 hrs. in a mixture of 57 % -HI and glacial acetic acid $\rightarrow$ 3,5-diiodo-L-thyronine. Y: 90%.

To avoid racemization, it is preferable to protect the amino group by acetylation and the carboxyl group by esterification rather than by formation of a hydantoin ring. J. R. Chalmers et al., *Soc.* 1949, 3424

Hydriodic acid**Cleavage of ethers**

27. 3,5-Dimethoxyethylbenzene boiled with HI-acetic acid at 130° for 35 min. $\rightarrow$ 5-ethylresorcinol. Y: almost 100%. F. e. s. J. P. Brown et al., *Soc.* 1949, 859; without acetic acid s. S. V. Sunthakar and H. Gilman, *J. Org. Chem.* 16, 8 (1951).

Enols from enolethers

s. 6, 320

*Platinum oxide* PtO_2 **Hydrogenolysis of phosphoric acid esters**

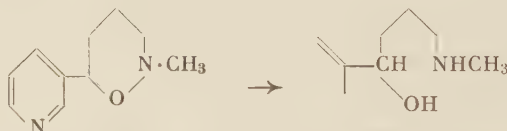
s. 6, 158

←

Formation of H—N Bond**Uptake****Addition to Oxygen and Nitrogen****HN ∇ ON***Zinc**Zn***Reductive oxazine ring opening**

C

28.

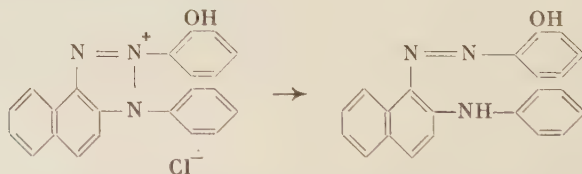


Zn-dust added in small amounts with stirring to a soln. of 2-methyl-6-(3-pyridyl)tetrahydro-1,2-oxazine (prepn., s. 195), in 10%-acetic acid and worked up after 4 hrs. $\rightarrow$ 4-methylamino-1-(3-pyridyl)-1-butanol. Y: 84.5%. C. H. Rayburn, W. R. Harlan, and H. R. Hanmer. Am. Soc. 72, 1721 (1950).

Addition to Nitrogen**HN ∇ NN***Sodium hyposulfite* $\text{Na}_2\text{S}_2\text{O}_4$ **o-Aminoazo compounds from 1,2,3-triazolium salts**

C

29.



Crude 1-phenyl-2-(o-hydroxyphenyl)naphtho[1,2]triazolium chloride in methanol and some aq. NaOH reduced with Na-hyposulfite at 20° $\rightarrow$ 1-(o-hydroxyphenyl)azo-2-phenylaminonaphthalene. Y: 73%. R. Kuhn and E. Ludolphy, A. 564, 35 (1949).

Rearrangement

Hydrogen/Oxygen Type



Sulfur/sulfuric acid



α,β -Ethylenecarboxylic acid amides from cyanohydrins



Acetone cyanohydrin added with rapid stirring at 75-80° during 25 min. to 98%-H₂SO₄ containing a small quantity of flowers of sulfur, then the temp. raised within 5 min. to 150° with continued stirring, and maintained for 15 min. at this temp. $\rightarrow$ methacrylamide. Y: 61-70%. R. H. Wiley and W. E. Wadley, Org. Synth. 29, 61 (1949).

Exchange

Oxygen $\dagger$



Aluminum amalgam



Amines from nitro compounds



s. 5, 20; s. a. C. A. Grob and F. Reber, Helv. 33, 1776 (1950)

Lithium aluminum hydride



Amines from nitroethylene derivatives

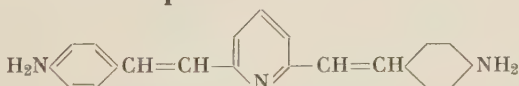


s. 6, 87

Tin

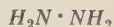


Amines from nitro compounds



A mixture of 2,6-di-(p-nitrostyryl)pyridine, Sn, and 10%-HCl gently refluxed until the metal has disappeared completely $\rightarrow$ 2,6-di-(p-aminostyryl)pyridine. Y: 100%.—Hydrogenation with Raney-Ni gave only 49% yield. E. D. Bergmann and S. Pinchas, J. Org. Chem. 15, 1184 (1950); amino- γ -pyrones s. E. L. Shimmin and F. Challenger, Soc. 1949, 1185 who found electrolytic and catalytic reduction methods unsuitable and proceeded according to Ost, J. pr. 19, 189 (1879); α -amino- β -(allythio)carboxylic acid esters s. 621.

Hydrazine



s. 3, 14; 4, 71; s. a. L. P. Kuhn, Am. Soc. 73, 1510 (1951).

Ammonium sulfide



Amino-oximes from nitro-oximes

32.



Aq. $(\text{NH}_4)_2\text{S}$ added to a soln. of 2-nitroanisaldoxime in ethanol, and heated 1 hr. on a water bath $\rightarrow$ 2-aminoanisaldoxime (startg. m. s. 477). Y: 80%. W. R. Boon, Soc. 1949, S 230.

Hyposulfite



s. 1, 360; s. a. M. D. Soffer et al., Am. Soc. 72, 3704 (1950)

Iron



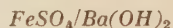
s. 3, 17; 6, 820; aliphatic compounds s. G. Tsatsas. Bl. 1949, 884

simultaneously:

amines from N-oxides

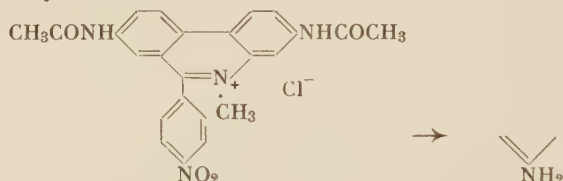
s. 6, 389

Ferrous sulfate/barium hydroxide



Quaternary aminoammonium salts from quaternary nitroammonium salts

33.



An aq. suspension of $\text{Fe}(\text{OH})_2$, prepared from hot aq. soln. of FeSO_4 and $\text{Ba}(\text{OH})_2$, added to a stirred suspension of 3,8-diacetamido-6-(p-nitrophenyl)-5-methylphenanthridinium chloride in water at 90-95°, heated 30 min. on a steam bath, filtered, the filtrate subjected to further interaction with $\text{Fe}(\text{OH})_2$ for 30 min., filtered, and the filtrate treated with $\text{NaCl} \rightarrow$ 3,8-diacetamido-6-(p-aminophenyl)-5-methylphenanthridinium chloride. Y: ca. 100%.— This method proved to be better suited for the reduction of quaternary nitroammonium salts than the reduction with Fe powder. F. e. s. L. P. Walls et al., Soc. 1950, 41, 311, 2698.

Nickel



s. 1, 28/9; 2, 48, 77; 3, 18/9; aliphatic compounds s. G. B. Butler and F. N. McMillan, Am. Soc. 72, 2978 (1950)

Aminoacetals from nitroacetals

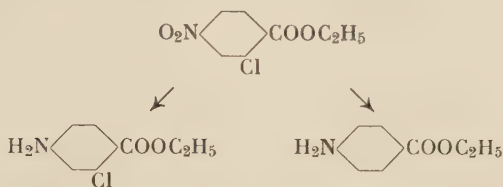
34.

m-Nitrobenzaldehyde dimethylacetal hydrogenated with Raney-Ni at 1000-1500 lbs. below 85° $\rightarrow$ m-aminobenzaldehyde dimethylacetal. Y: 67-78%. R. N. Icke et al., Org. Synth. 29, 6 (1949).

*Palladium-barium sulfate**Pd-BaSO₄*

also with simultaneous replacement
of chlorine by hydrogen

35.



In the catalytic reduction of 4-nitro-2-chlorobenzoic acid and its esters the chlorine was lost in hydroxylic solvents, but not in ethyl acetate:

Ethyl 4-amino-2-chlorobenzoate hydrogenated with 5 %-Pd-BaSO₄
at room temp. and atmospheric pressure

in ethyl acetate for 3 hrs. →	ethyl 4-amino-2-chlorobenzoate.
Y: ca. 100%.	

in isopropyl alcohol for 5 hrs. →	ethyl 4-aminobenzoate hydro-
	chloride. Y: ca. 100%.

F. e. and side reactions s. A. Weizmann. Am. Soc. 71, 4154 (1949).

*Palladium-barium sulfate/oxalic acid**Pd-BaSO₄/(COOH)₂*

**Aliphatic hydroxylamines from
aliphatic nitro compounds**

NO₂ → NHOH

36.



A soln. of 1-nitro-2-pentanol and oxalic acid in 95 %-alcohol hydrogenated with 5 %-Pd-BaSO₄ → 1-hydroxylamino-2-pentanol oxalate. Y: 81%. F. e. s. E. Schmidt, A. Ascherl, and L. Mayer, B. 58, 2430 (1925); s. a. A. Allais, Bl. 1949, 536.

*Platinum**Pt*

Amines from oximes

C : NOH → CHNH₂

s. 5, 27; s. a. Bl. 1950, 627

*Platinum and platinum oxide**Pt and PtO₂*

Amines from nitro compounds

NO₂ → NH₂

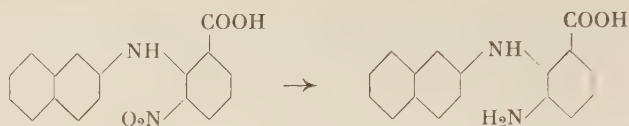
37.



β-(4-Nitrophenyl)ethanol in 95 % alcohol hydrogenated with Pt-black at an initial pressure of 50 lbs./sq.in. with intermittent shaking until the calculated amount of H₂ has been absorbed → β-(4-aminophenyl) ethanol. Y: 85%. F. e. s. H. M. Woodburn and C. F. Stuntz, Am. Soc. 72, 1361 (1950); with PtO₂ s. A. Dornow and F. Boberg, B. 83, 261 (1950).

Platinum oxide PtO_2

38.



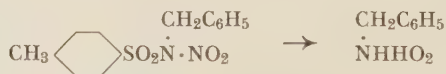
2-(2-Naphthylamino)-3-nitrobenzoic acid hydrogenated with PtO_2 in 96%-alcohol for ca. 2 hrs. $\rightarrow$ 2-(2-naphthylamino)-3-aminobenzoic acid. Y: 82%.—Phenazine ring closure takes place in the reduction with SnCl_2 . R. Huisgen and G. Sorge, A. 566, 162 (1950).

Nitrogen $\nleftrightarrow$ $\text{HN} \nleftrightarrow \text{N}$ *Without additional reagents**w.a.r.***Nitroguanidines from
N-nitroso-N'-nitroguanidines** $\leftarrow$

s. 5, 28; s. a. R. A. Henry, Am. Soc. 72, 3287 (1950)

Sulfur $\nleftrightarrow$ $\text{HN} \nleftrightarrow \text{S}$ *Sodium hydroxide* NaOH **Cleavage of sulfonic acid amides** $\text{N} \cdot \text{SO}_2\text{R} \rightarrow \text{NH}$ **N-Nitramines**

39.



N-Nitro-N-benzyltoluene-p-sulfonamide refluxed with 0.1 N NaOH until complete solution was obtained $\rightarrow$ benzylnitramine. Y: ca. 90%. F. e. s. M. I. Gillibrand and A. H. Lamberton, Soc. 1949, 1883.

Carbon $\nleftrightarrow$ $\text{HN} \nleftrightarrow \text{C}$ *Without additional reagents**w.a.r.* **α -Aminocarboxylic acid amides
from oxazolidines** $\curvearrowright$

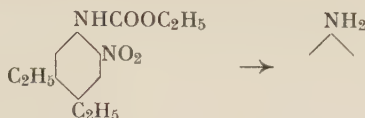
s. 6, 347

Sodium hydroxide $\sim \text{NaOH}$ **α -Aminocarboxylic acids from
 α -formamidomalonic esters** $\leftarrow$

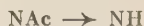
s. 6, 127, 789

Elimination of N-carbethoxy groups

40.



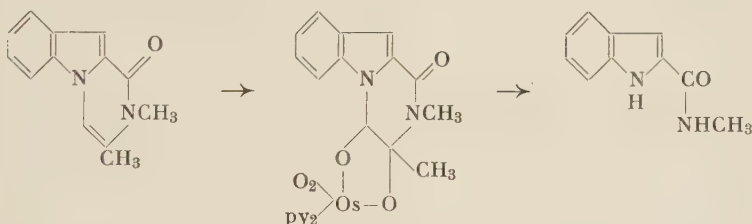
4,5-Diethyl-2-nitrocarbethoxyanilide added to aq.-alc. NaOH, the temp. raised to 70° with stirring, and held at this temp. for 1 hr. → 4,5-diethyl-2-nitroaniline. Y: 81%. J. P. Lambooy, Am. Soc. 71, 3756 (1949).

Potassium hydroxide**Amines from acylamines**

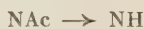
s. 6, 502

Sodium sulfite**Pyrazine ring degradation**

41.



A soln. of 3'-keto-4',5'-dimethyl-1',2',3',4'-tetrahydropyrazino(1',2',1,2)-indole in anhydrous benzene containing pyridine treated with OsO₄, worked up after 3 days, and the pyridine osmate (Y: high) refluxed 1 hr. with Na-sulfite in alcohol-water → indole-2-carboxymethylamide (Y: 77%). J. A. Elvidge and F. S. Spring, Soc. 1949, 2935.

Hog kidney enzyme**Resolution of racemates by enzymic hydrolysis****Amines from acylamines**

42.



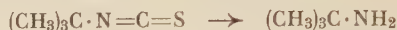
A suspension of hog kidney enzyme preparation (see original paper) added to a mixture of acetyl-DL-alanine in dil. aq. NH₃ at pH 7.9, and kept at 37° for 12 hrs. → L-alanine. Y: 73%. F. e. s. V. E. Price et al., J. Biol. Chem. 178, 503 (1949); 179, 1169 (1949); s. a. J. P. Greenstein et al. Am. Soc. 72, 2812 (1950); J. Biol. Chem. 182, 452 (1950); C. G. Baker and A. Meister, Am. Soc. 73, 1336 (1951).

Formic acid

HCOOH

Amines from isothiocyanatesN : C : S $\rightarrow$ NH₂

43.



tert-Butyl isothiocyanate refluxed with 94%-formic acid on a water bath for 80-120 hrs. until the escaping vapors fail to darken Pb-acetate paper $\rightarrow$ *tert*-butylamine. Y: 79.3%. E. Schmidt et al., A. 568, 192 (1950).

Formic acid/hydrochloric acid

HCOOH/HCl

**α -Aminocarboxylic acids from
 α -cyanourethans**

 $\leftarrow$

s. 3, 189; s. a. Can. J. Research 28 B, 207 (1950)

Acetic acid

CH₃COOH **β -Aminoalcohols from oxazolidines**

C

s. 6, 73

Hydrazine

H₂N · NH₂**Prim. amines from phthalimides**

s. 6, 342



Phosphonium iodide

PH₄I**Amines from urethans**

**Cleavage of carbalkoxy derivatives
of amines**

NHCOOR $\rightarrow$ NH₂

s. 2, 138; 3, 25; s. a. C. M. Stevens and R. Watanabe, Am. Soc. 72, 725 (1950); F. W. Dunn and K. Dittmer, J. Biol. Chem. 188, 263 (1951)

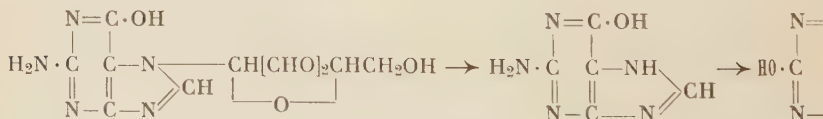
Sulfuric acid

H₂SO₄

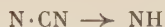
**Cleavage of nucleosides
with subsequent replacement of
amino groups by hydroxyl**

 $\leftarrow$

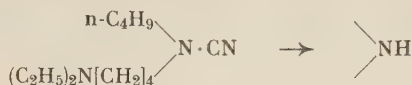
44.



Guanosine boiled 15 min. with H₂SO₄-water, cooled to 85°, and treated dropwise with aq. NaNO₂ at 70-80° over a period of 2-3 hrs. $\rightarrow$ xanthine (startg. m. f. 485). Y: 97%. H. Bredereck, H.-G. v. Schuh, and A. Martini, Chem. B. 83, 201 (1950).

Amines from cyanamides

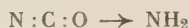
45.



N-Butyl- δ -diethylaminobutylcyanamide refluxed 15 hrs. with H_2SO_4 -water $\rightarrow$ 1-diethylamino-4-butylaminobutane. Y: 80%.—The cyano group can also be removed by hydrogenolysis with Raney-Ni. F. e. s. R. C. Elderfield and H. A. Hageman, J. Org. Chem. 14, 605 (1949).

*Hydrochloric acid**HCl***Elimination of the N-carbethoxy group**

s. 6, 465

Amines from isocyanates

s. 6, 381

*Hydrochloric and hydroiodic acids**HCl and HI***Amines from acylamines****Selective hydrolysis**

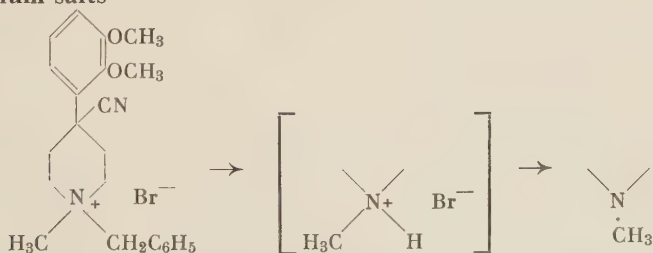
s. 6, 26

*Nickel**Ni***Amines from cyanamides**

s. 6, 45

*Palladium**Pd***Tert. amines from quaternary ammonium salts** $\leftarrow$

46.



1-Methyl-1-benzyl-4-o,m-dimethoxyphenyl-4-cyanopyridinium bromide hydrogenated in 50%-alcohol with Pd-black until 1 mole of H_2 is absorbed, the hydrobromide so obtained dissolved in water, and the free base precipitated with Na-carbonate $\rightarrow$ 1-methyl-4-o,m-dimethoxyphenyl-4-cyanopiperidine. Y: almost 100%. F. e. s. H. Kägi and K. Miescher, Helv. 32, 2489 (1949).

*Palladium-carbon**Pd-C***Debenzylation**

s. 6, 364

Formation of H—S Bond

Exchange

Halogen ∇

HS ∇ Hal

Lithium aluminum hydride

LiAlH₄

Reduction of sulfur compounds

SO₂Cl → SH

Mercaptans from thiocyanates, disulfides, and sulfonic acid chlorides

SCN → SH

RSSR → 2 RSH

Sym. disulfides from sulfenyl chlorides and thiosulfonates

2 RSCl → RSSR

RSO₂SR → RSSR

Hydrocarbons from sulfonic acid esters

ROSO₂R' → RH

47. Cholesteryl thiocyanate allowed to react with LiAlH₄ in ether → 3-mercapto-5-cholestene. Y: 81%.—Similarly: Dicholesteryl disulfide → 3-mercapto-5-cholestene. Y: 88%.—p-Tolyl sulfenylchloride → di-p-tolyl disulfide. Y: 88%.—p-Toluenesulfonyl chloride → p-thiocresol. Y: 90%.—p-Tolyl p-toluenethiosulfonate → di-p-tolyl disulfide. Y: 75%.—3-Cholesterol p-toluenesulfonate → cholestane. Y: 80%.—The reduction of disulfides is very slow. Sulfonamides (in contrast to carbonamides), thioethers, sulfoxides, and sulfones could not be reduced. F. e. s. J. Strating and H. J. Backer, R. 69, 638, 909 (1950).

Sulfur ∇

HS ∇ S

Sodium sulfide

Na₂S

Mercaptans from sym. disulfides

RS·SR → 2 RSH

s. 6, 660

Zinc

Zn

48. Conc'd. HCl and Zn-dust added in portions to a soln. of 2,2'-dichlorodibenzyl disulfide so as to maintain a rapid evolution of H₂, and worked up when a diluted sample formed a clear soln. with aq. NaOH → o-chlorobenzyl mercaptan. Y: ca. 100%. F. e. s. J. W. Boenigk, J. E. Christian, and G. L. Jenkins, J. Am. Pharm. Assoc. 38, 357 (1949).

Lithium aluminum hydride

LiAlH₄

s. 6, 47; s. a. R. C. Arnold, A. P. Lien, and R. M. Alm, Am. Soc. 72, 731 (1950)

Carbon ∇

HS ∇ C

Sodium hydroxide/alcohol

NaOH

Mercaptans from thiolic acid esters

SCOR → SH

s. 6, 51

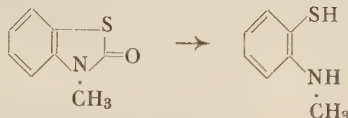
Potassium hydroxide/alcohol

KOH

C

Thiazole ring opening

49.



3-Methyl-2(3H)-benzothiazolone boiled 10-20 min. with KOH in alcohol $\rightarrow$ o-(methylamino)phenyl mercaptan. Y: 84%. F. e. s. A. I. Kiprianov and Z. N. Pazenko, *Ж.* 19, 1523 (1949); *C. A.* 44, 3487g.

Ammonia

 NH_3 **Mercaptans from xanthates**

s. 6, 656



Lithium aluminum hydride

 LiAlH_4 **Mercaptans from thiocyanates**

s. 6, 47

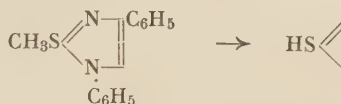
 $\text{SCN} \rightarrow \text{SH}$

Phosphorus/iodine

P/I

Mercaptans from thioethers $\text{RSR} \rightarrow \text{RSH}$

50.



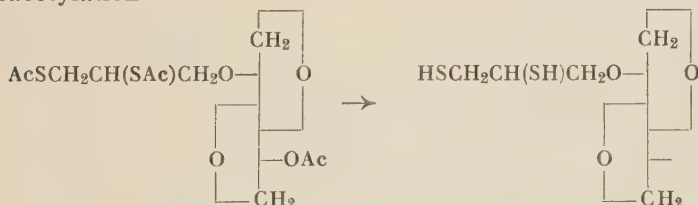
Red P added to iodine in glacial acetic acid, refluxed 20 min., 2-methylthio-1,4-diphenylimidazole added, and refluxed 3.5 hrs. $\rightarrow$ 1,4-diphenyl-2-thiolimidazole (startg. m. f. 142). Y: 76%. F. e. s. R. M. Dodson and F. Ross, *Am. Soc.* 72, 1478 (1950); method, s. *Am. Soc.* 70, 2753 (1948).

Hydrochloric acid

HCl

Mercaptans from thiolic acid esters $\text{SCOR} \rightarrow \text{SH}$ **Deacetylation**

51.



Triacetyl-2-(2,3-dimercaptopropyl)-1,4:3,6-dianhydromannitol refluxed 4 hrs. under N_2 with 2% methanolic HCl $\rightarrow$ 2-(2,3-dimercaptopropyl)-1,4:3,6-dianhydromannitol. Y: 83%. P. Bladon and L. N. Owen, *Soc.* 1950, 591; f. e. s. *Soc.* 1950, 579; with NaOH/methanol s. *Soc.* 1950, 2943.

Formation of H—Rem Bond

Exchange

Halogen ∇

HRem ∇ Hal

Lithium aluminum hydride

LiAlH_4

Silanes from halogenosilanes

$\text{SiHal} \rightarrow \text{SiH}$

52.



A soln. of chlorotri(cyclohexyl)silane in anhydrous ether added dropwise to an excess of LiAlH_4 in ether, and refluxed 0.5 hr. $\rightarrow$ tri(cyclohexyl)silane. Y: 90%. W. H. Nebergall and O. H. Johnson, *Am. Soc.* 71, 4022 (1949); 72, 4702 (1950).

Formation of H—C Bond

Uptake

Addition to Oxygen and Carbon

HC $\downarrow$ OC

Sodium amalgam

Na, Hg

Prim. alcohols from aldehydes

$\text{CHO} \rightarrow \text{CH}_2\text{OH}$

s. 2, 55; 3, 32; hydroxycarboxylic acids s. A. S. Elina and O. Y. Magidson, *Ж21*, 780 (1951); C. A. 45, 9531 d

Lithium boron hydride

LiBH_4

Lactones from ketocarboxylic acids, nitroalcohols from nitroketones, and other reductions

$\leftarrow$

53. LiBH_4 in ether is a more powerful reducing agent than NaBH_4 (in water or alcohol) but is milder than LiAlH_4 . Oxo compounds are reduced rapidly at room temp. in exothermic reactions, whereas esters react slowly and the mixtures must be refluxed for periods up to 6 hrs. In the selective reduction of the carbonyl group ice-bath cooling is employed to enhance selectivity.—E: β -Benzoylpropionic acid $\rightarrow$ γ -phenylbutyrolactone. Y: 78%.—m-Nitroacetophenone $\rightarrow$ α -(m-nitrophenyl)ethanol. Y: 93%. F. e. s. R. F. Nystrom, S. W. Chaikin, and W. G. Brown, *Am. Soc.* 71, 3245 (1949).

Sodium boron hydride

NaBH_4

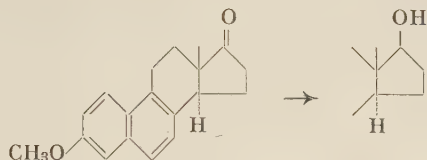
Alcohols from oxo compounds

$\text{CO} \rightarrow \text{CHOH}$

s. 5, 40; s. a. J. H. Biel, *Am. Soc.* 73, 847 (1951)

Lithium aluminum hydride LiAlH_4 **Sec. alcohols from ketones**

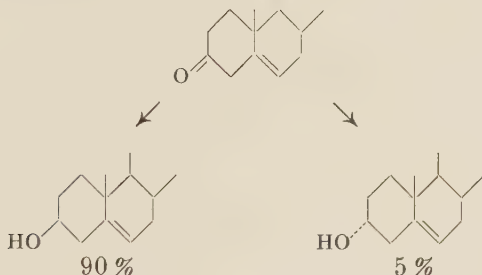
54.



A mixture of d-equilenin methyl ether and LiAlH_4 in ether refluxed 3 hrs. $\rightarrow$ β -dihydroequilenin methyl ether. Y: 97%. W. Bachmann and A. S. Dreiding, *Am. Soc.* 72, 1323 (1950); α, β -diaminoalcohols s. N. H. Cromwell and Kwan-Chung Tsou, *J. Org. Chem.* 15, 1219 (1950); alcohols from hindered ketones s. E. L. May and E. Mosettig, *Am. Soc.* 73, 1301 (1951).

Stereoisomeric steroids

55.



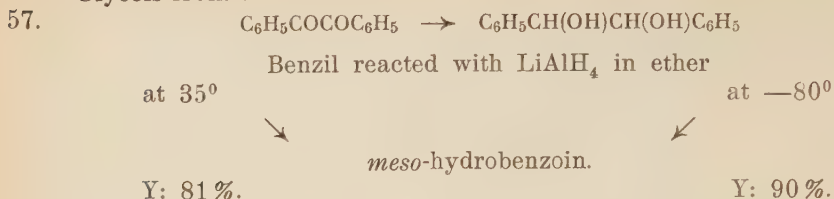
An ethereal soln. of cholest-5-en-3-one added during 25 min. to a vigorously stirred ethereal soln. of LiAlH_4 , and stirring continued for 2 hrs. with addition of ether from time to time $\rightarrow$ cholesterol (Y: ca. 90%) and epicholesterol (Y: ca. 5%). F. e. s. C. W. Shoppee and G. H. R. Summers, *Soc.* 1950, 687.

Sec. ethylenealcohols from ethyleneketones

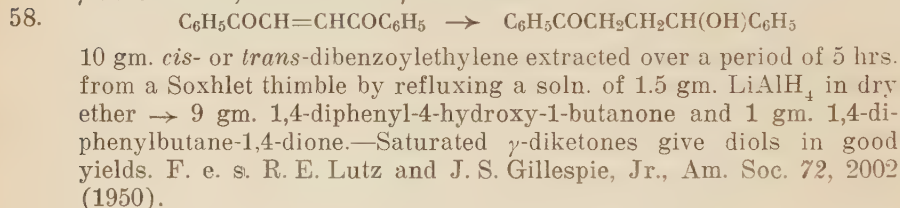
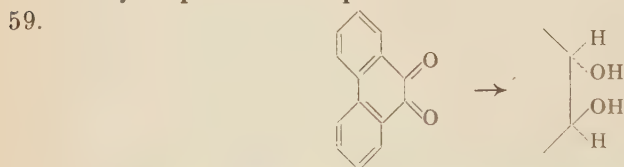
56.



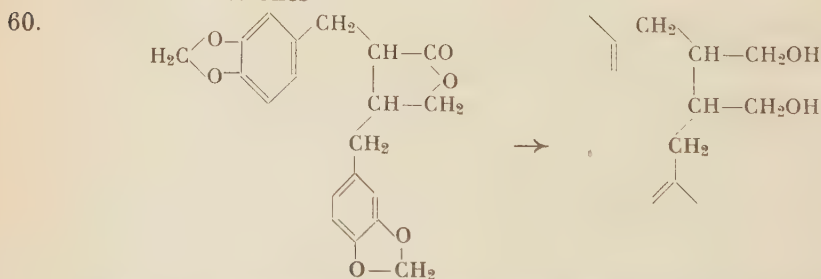
β -Ionone in abs. ether dropped into a soln. of LiAlH_4 in abs. ether with stirring and ice-cooling over a period of 10 min., and stirring continued at 0° for 1 hr. $\rightarrow$ β -ionol. Y: almost 100%.—The double bond is not affected at low temp. H. H. Inhoffen, F. and M. Bohlmann, *A.* 565, 35 (1949); s. a. V. Boekelheide and C. E. Larrabee, *Am. Soc.* 72, 1245, 1240 (1950).

Glycols from α -diketones

The isomeric composition obtained by this reaction resembles that in catalytic hydrogenation. F. e. s. L. W. Trevoy and W. G. Brown, Am. Soc. 71, 1675 (1949).

 γ -Hydroxyketones from α,β -ethylene- γ -diketones 1,4-Diols from γ -diketones**Dihydroquinols from quinones**

9,10-Phenanthrenequinone extracted in a Soxhlet apparatus with ether containing $\text{LiAlH}_4 \rightarrow (\pm)$ -*trans*-9,10-dihydroxy-9,10-dihydrophenanthrene. Y: over 80%. F. e. s. J. Booth, E. Boyland, and E. E. Turner. Soc. 1950, 1188.

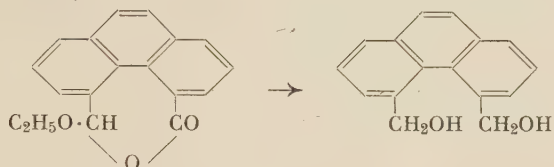
Diols from lactones

1 gm. (—)-hinokinin in benzene mixed with a soln. of LiAlH_4 in ether, and worked up after 2 hrs. $\rightarrow$ 0.93 gm. (—)-1,4-di-(3,4-methy-

lenedioxyphenyl)-2,3-di(hydroxymethyl)butane. F. e. s. R. D. Hawthorth and L. Wilson, *Soc.* 1950, 71; s. a. C. O. Guss and L. H. Jules, *Am. Soc.* 72, 3462 (1950); 73, 608 (1951); N. L. Drake and E. H. Price, *Am. Soc.* 73, 201 (1951).

Diols from alkoxy lactones

61.



A warm soln. of pseudo ethyl 5-formyl-4-phenanthrenecarboxylate in benzene added with stirring to an ethereal soln. of $\text{LiAlH}_4 \rightarrow$ 4,5-phenanthrenedimethanol (startg. m. f. 302). Y: 90%. M. S. Neuman and H. S. Whitehouse, *Am. Soc.* 71, 3664 (1949).

Aluminum alkoxide

Al(OR)_3

Meerwein-Ponndorf reduction

Prim. alcohols from aldehydes

$\text{CHO} \rightarrow \text{CH}_2\text{OH}$

62.



Abs. ethanol added slowly at reflux temp. to coarsely powdered Al, some Al-ethoxide, and xylene, decanted when almost all of the Al is dissolved, the soln. treated with furanacrolein, and heated 2.5 hrs. on a steam bath $\rightarrow$ 3-(2-furyl)allyl alcohol. Y: 60-70%. M. V. Likhoshershtov et al., *Ж* 20, 627 (1950); *C. A.* 44, 7823d.

Sec. alcohols from ketones

$\text{CO} \rightarrow \text{CHOH}$

63.



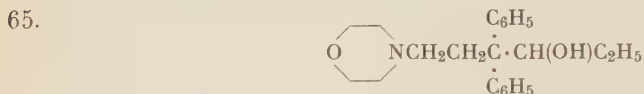
Salts of ω -dialkylaminoacetophenones may be reduced directly instead of reducing the free base.—E.: p-Bromo- ω -piperidinoacetophenone hydrochloride, Al-isopropoxide, and benzene slowly distilled with addition of isopropanol until the distillate no longer gives a test for acetone $\rightarrow$ 2-piperidino-1-(p-bromophenyl)ethanol hydrochloride. Y: 89%. F. e. s. D. W. Mathieson and G. Newbery, *Soc.* 1949, 1133.

s. a. D. S. Noyce and D. B. Denney, *Am. Soc.* 72, 5743 (1950); Ph. Buu-Hoi and H. Khôi, *Soc.* 1951, 255

Benzohydrols s. J. P. Picard and C. W. Kearns, *Can. J. Research* 28B, 56 (1950)

Modified Meerwein-Ponndorf reduction

Improved yields of alcohols are obtained from aldehydes and unstable ketones, when the oxo compound is added dropwise during the reaction, so that its concentration is always low.—In certain cases, reductions without solvent may be conveniently employed.—E: A soln. of benzylideneacetone in isopropanol added dropwise within 4.25 hrs., to a refluxing soln. of Al-isopropoxyde distillate collected during the addition at the same rate, and worked up after additional 70 min. $\rightarrow$ 1-phenylbut-1-en-3-ol. Y: 96%. F. e. s. A. K. Macbeth and J. A. Mills, Soc. 1949, 2646.

Sec. alcohols from ketones difficult to reduce

1-(4-morpholinyl)-3,3-diphenylhexan-4-one and Al-isopropoxide heated in dry toluene at a bath-temp. of 140—150°, with slow distillation at intervals and addition of more toluene as required, until after ca. 100 hrs. the Na-nitroprusside test for acetone is negative $\rightarrow$ 1-(4-morpholinyl)-3,3-diphenylhexan-4-ol. Y: 80-90%. A. H. Beckett and W. H. Linnell, J. Pharm. Pharmacol. 2, 418 (1950).

Stereoisomeric cyclic alcohols from cyclic ketones

66. When cyclic ketones are reduced with Al-alkoxides, the proportion of *cis*-isomer is greatest from ketones and reducing alcohols in which steric hindrance is greatest. L. M. Jackman, A. K. Macbeth, and J. A. Mills, Soc. 1949, 2641.

Copper chromite

 CuCr_2O_4 **Alcohols from oxo compounds** $\text{CO} \rightarrow \text{CHOH}$

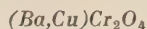
s. 6, 108

Prim. alcohols from aldehydes $\text{CHO} \rightarrow \text{CH}_2\text{OH}$

s. 6, 107; s. a. E. R. Shepard and J. F. Noth, Am. Soc. 72, 4364 (1950)

Sec. alcohols from ketones $\text{CO} \rightarrow \text{CHOH}$

s. 3, 36; large batches s. D. T. Mowry and E. L. Ringwald, Am. Soc. 72, 2037 (1950)

Barium copper chromite

67.



Methyl cyclopropyl ketone hydrogenated with Ba-promoted copper chromite catalyst at 100° and an initial pressure of 1750 p. s. i./room temp., for ca. 9 hrs., the H₂-absorption beginning after an induction period of ca. 5 hrs. → methylcyclopropylcarbinol. Y: 90%.—Other methods gave lower yields. V. A. Slabey and P. H. Wise, *Am. Soc.* 71, 3252 (1949).

Nickel

Ni

Prim. alcohols from aldehydes

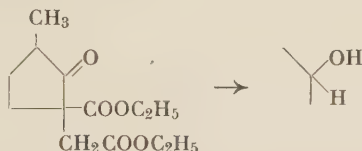
68.



100 gm. α-diethylaminomethylisobutyraldehyde hydrogenated with Raney-Ni in aq. HCl at pH 3-6, 150 lbs. pressure, and 79-80° → 80-90 gm. γ-diethylamino-β,β-dimethylpropanol.—Other reaction conditions and catalysts were unsatisfactory. F. e. s. W. Wenner, *J. Org. Chem.* 15, 301 (1950), s. a. E. L. Eliel, *Am. Soc.* 73, 43 (1951).

Sec. alcohols from ketones

69.



5.5 gm. ethyl 2-carbethoxy-5-methylcyclopentan-1-one-2-acetate in ethanol stirred under H₂ with Raney-Ni at 100°/50 atm. for 6 hrs. → 5.0 gm. ethyl 2-carbethoxy-5-methylcyclopentan-1-ol-2-acetate.—The reduction with Al₂Hg and Al-isopropoxide did not succeed. L. N. Owen, *Soc.* 1949, 1582.

Cyclic sec. alcohols from cyclic ketones**Elimination of the induction period**

70.

Cyclopentanone hydrogenated at 100 atm. and 130-140° with Raney-Ni for 1 hr. → cyclopentanol. Y: 90%. An induction period of 6-7 hrs. is avoided by adding a little cyclopentanol at the start. G. E. McCasland and D. A. Smith, *Am. Soc.* 72, 2190 (1950).

γ-Hydroxypiperidines from γ-pyridones

s. 6, 90

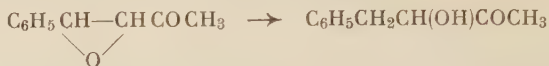
Nickel/palladium

Ni/Pd

α-Hydroxyketones from α,β-oxidoketones

←

71.



Benzylideneacetone oxide hydrogenated with Ni (activated by PdCl_2) in ethanol at atmospheric pressure and room temp. for ca. 0.5 hr. → benzyl acetyl carbinol. Y: 80%. T. I. Temnikova and V. A. Kropachev, *Ж* 19, 2069 (1949); C. A. 44, 3941c; *Ж* 21, 501 (1951); C. A. 45, 8447c.

Palladium/sulfuric acid or sodium hydroxide

 $\text{Pd}/\text{H}_2\text{SO}_4$ or Pd/NaOH **Sec. alcohols from ketones** $\text{CO} \rightarrow \text{CHOH}$

72.



Conditioning of catalysts. Catalysts, e. g. palladium and platinum, can be activated by treating with acids and again deactivated by addition of bases. Certain hydrogenations can best be performed by such an activated-deactivated catalyst. E: Acetophenone with Pd-black, prepared according to Willstätter and Waldschmidt-Leitz, B. 54, 123 (1921) and treated with H_2SO_4 , hydrogenated in methanol in the presence of a trace of NaOH at 2.5 atm. and room temp. → α-phenylethyl alcohol. Y: 93%. K. Kindler, E. Schärfe, and P. Henrich, A. 565, 51 (1949).

Palladium-carbon

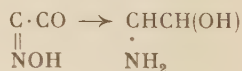
Pd-C

s. 4, 55; correction s. W. R. Nes and A. Burger, Am. Soc. 72, 5409 (1950)

Platinum dioxide

 PtO_2 **α-Aminoalcohols from α-isonitrosoketones**

s. 6, 79

**Addition to Nitrogen and Carbon**

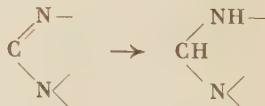
HC↓NC

Aluminum amalgam

Al,Hg

1,1-Diamines from amidines

s. 6, 237



Lithium aluminum hydride

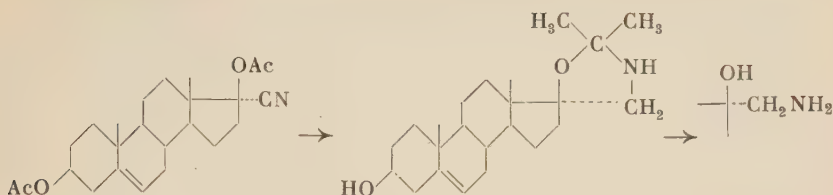
 LiAlH_4 **Amines from nitriles** $\text{CN} \rightarrow \text{CH}_2\text{NH}_2$

s. 4, 60; s. a. L. H. Amundsen and L. S. Nelson, Am. Soc. 73, 242 (1951)

**β-Aminoalcohols from cyanohydrin acetates
via oxazolidines**



73.



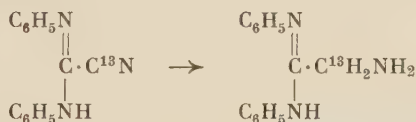
LiAlH_4 in ether added dropwise with good stirring to a soln. of $\Delta^{5,6}$ - $3\beta,17\beta$ -diacetoxy-17-isoetiocholenic acid nitrile, stirring continued for 0.5 hr. at room temp. and for an additional 0.5 hr. at 40° , and worked up whereby the reaction product is extracted with acetone $\rightarrow$ oxazolidine derivative (Y: over 90%), 100 mg. of which in glacial acetic acid treated with water $\rightarrow$ 93 mg. $\Delta^{5,6}$ - $3\beta,17\beta$ -dihydroxy-17 α -aminomethylandrosterone.—Side reactions are avoided by reducing the cyanohydrin acetate in place of the free cyanohydrin. H. Heusser et al., *Helv.* 33, 1093 (1950).

Aminoacetamidines from cyanoformamidines

←

Labeled compounds

74.

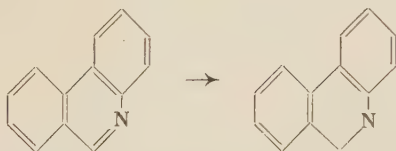


A soln. of crude, but alcohol-free N,N' -diphenylcyanoformamidine (prepn. s. 824) in anhydrous ether added to LiAlH_4 in anhydrous ether in a slow N_2 stream during ca. 2 hrs., at a rate to maintain gentle refluxing $\rightarrow$ (N,N' -diphenyl)aminoacetamidine (startg. m. s. 230). Y: 65-70%. G. Ehrensvärd and R. Stjernholm, *Acta Chem. Scand.* 3, 971 (1949).

Selective ring hydrogenation

←

75.



Phenanthridine introduced by use of a Soxhlet extractor into a well-stirred soln. of LiAlH_4 in anhydrous ether over a period of 10 hrs $\rightarrow$ 5,6-dihydrophenanthridine. Y: 74%. W. C. Wooten and R. L. McKee, *Am. Soc.* 71, 2946 (1949).

Sodium

Na

Cyclic ketones from phenolethers

←

83.



Na added during 35 min. to a soln. of 225 gm. crude 1,6-dimethoxynaphthalene in boiling alcohol, after addition of more alcohol refluxing continued for ca. 40 min. until the metal has disappeared → 5-methoxy-2-tetralone. Y: ca. 75%. J. W. Cornforth and R. Robinson, Soc. 1949, 1855; s. a. M. D. Soffer et al., Am. Soc. 72, 3704 (1950).

Hydrogenation of N-heterocyclic rings

s. 2, 71; s. a. W. Gruber and K. Schlögl, M. 80, 499 (1949)

Sodium amalgam

Na,Hg

Hydrogenation of ethylene derivatives

C : C → CHCH

s. 3, 610; s. a. J. Org. Chem. 14, 915 (1949); L. J. Owen and F. F. Nord, J. Org. Chem. 15, 988 (1950)

Lithium/N-methylaniline

Li/C₆H₅NHCH₃**Partial reduction of dienes to ethylene derivatives**

84. Cycloöcta-1,3-diene, N-methylaniline, and Li in abs. ether mechanically shaken for 1 day → *cis*-cycloöctene. Y: almost 100%. K. Ziegler and H. Wilms, A. 567, 1 (1950); s. a. A. 511, 83 (1934); 528, 111 (1937).

Sodium/liq. ammonia

Na/NH₃**Hydrocarbons from α,β-ethylenealcohols**

←

s. 6, 138

Sodium/liq. ammonia/alcohol

Reduction by dissolving metals

←

Partial ring hydrogenation

s. 5, 47; s. a. Soc. 1950, 1551

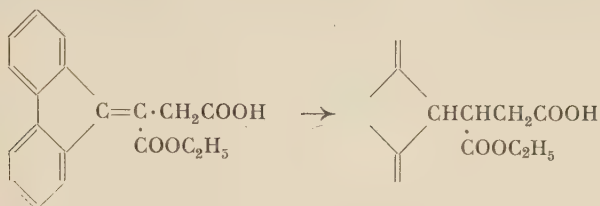
Zinc

Zn

Hydrogenation of ethylene derivatives

C : C → CHCH

85.

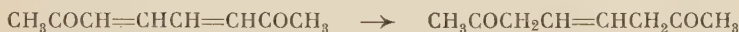


A soln. of 1 gm. β -carbethoxy- β -fluorenylidene propionic acid in glacial acetic acid refluxed with Zn dust for 1 hr. $\rightarrow$ 0.91 gm. β -carbethoxy- β -9-fluorenylpropionic acid. F. e. s. N. Campbell and A. E. S. Fairfull, Soc. 1949, 1102; s. a. L. J. Owen and F. F. Nord, J. Org. Chem. 15, 988 (1950).

Zinc/pyridine/acetic acid

Zn/C₅H₅N/CH₃COOH**Partial reduction of dienes to ethylene derivatives**

86.



3,5-Octadiene-2,7-dione dissolved with warming in dry pyridine, Zn-dust added, followed by glacial acetic acid, and shaken vigorously $\rightarrow$ 4-octene-2,7-dione. Y: 70-75%. P. Karrer and C. H. Eugster, Helv. 32, 1934 (1949).

Lithium aluminum hydride

LiAlH₄ **γ -Hydroxyketones from α,β -ethylene- γ -diketones**

←

s. 6, 58

Amines from nitroethylene derivatives

←

Soxhlet extractor technique

87.



4-Hydroxy-3-methoxy- β -nitrostyrene (prepn. s. 754) added by the Soxhlet extractor technique (cf. Nystrom and Brown, Am. Soc. 69, 1197 (1947); Synth. Meth. 6, 58, 75) to a well-stirred mixture of LiAlH₄ and abs. ether over a period of 59 hrs., and the reaction product isolated as picrate $\rightarrow$ 4-hydroxy-3-methoxyphenylethylamine. Y: 80%. F. e. s. F. A. Ramirez, A. Burger, and M. Erne, Am. Soc. 72, 2781 (1950); Helv. 33, 912 (1950); s. a. J. Finkelstein, Am. Soc. 73, 550 (1951); cf. R. T. Gilsdorf and F. F. Nord, J. Org. Chem. 15, 807 (1950).

*Formic acid**HCOOH***Amines from enamines**

C : C → CHCH

88.



87%-formic acid added dropwise with stirring to 1-octenyldimethylamine, then warmed 1-2 hrs. at 50-70° → octyldimethylamine. Y: 92%. F. e. s, P. L. DeBenneville and J. H. Macartney. Am. Soc. 72, 3073 (1950).

*Phosphorus**P***Hydrogenation of ethylene derivatives**

s. 6, 762

*Phosphorus/hydriodic acid**P/HI*

α-Aminocarboxylic acids from thiazolidones

s. 6, 269

*Copper chromite**CuCr₂O₄***Alcohols from ethylene ketones**

←

Selective hydrogenation

s. 5, 491; s. a. Am. Soc. 72, 5506 (1950)

Alcohols from ethylenecarboxylic acid esters

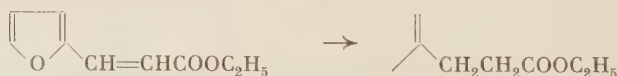
←

s. 6, 109

*Dicobalt octacarbonyl**Co₂(CO)₈***Hydrogenation of ethylene derivatives**

C : C → CHCH

89.



Co₂(CO)₈-catalyst is effective for the hydrogenation of the carbon carbon double bond in certain α,β-ethylenic carbonyl compounds. The yields with the aldehydes were 40-50% while with the ketones and esters they were in the range of 70-90%.—E: 37 gm. ethyl β-(2-furan)-acrylate and dicobalt octacarbonyl in benzene, under a pressure of 4700 p. s. i. of equal parts of H₂ and CO at 125° rocked for 6.5 hrs. → 34.3 gm. ethyl β-(2-furan)propionate.—Hydroformylation of other ethylene derivatives with the same reagent s. Synth. Meth. 4, 667. H. Akins and G. Krsek, Am. Soc. 71, 3051 (1949).

Nickel

Ni

Selective hydrogenation of the carbon carbon double bond

s. 6, 761; s. a. E. and F. Berliner, Am. Soc. 72, 222 (1950)

cis-trans-Isomeric ethylene derivatives from acetylene derivatives

s. 1, 59/60; s. a. W. R. Taylor and F. M. Strong, Am. Soc. 72, 4263 (1950); C. S. Marvel and C. H. Young, Am. Soc. 73, 1066 (1951)

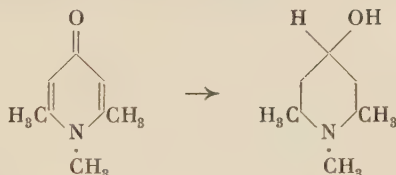
Ring hydrogenation

←

s. 4, 98; of amines s. M. Métayer, A. ch. 4, 196 (1949)

Hydrogenation of N-heterocyclic rings **γ -Hydroxypiperidines from γ -pyridones**

90.



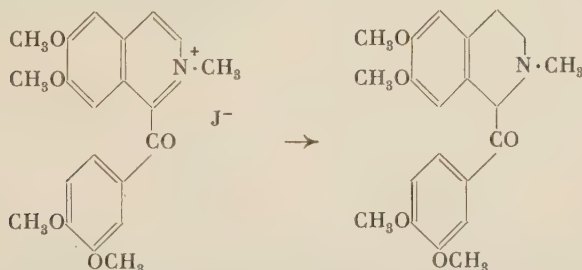
A mixture of 1,2,6-trimethyl-4-pyridone, abs. alcohol, and Raney-Ni hydrogenated at 130 atm. and 125° for 4 hrs. $\rightarrow$ 1,2,6-trimethyl-4-piperidinol. Y: 85%. F. e. s. K. N. Campbell, J. F. Ackerman, and B. K. Campbell, J. Org. Chem. 15, 337 (1950).

Piperidones from pyridones

s. 6, 95

Selective hydrogenation of cyclic quaternary ammonium salts

91.



1-(4,5-Dimethoxybenzoyl)-6,7-dimethoxyisoquinoline methiodide hydrogenated with Raney-Ni in abs. alcohol at 19° until 2 moles of

H_2 are absorbed $\rightarrow$ 1-(4,5-dimethoxybenzoyl)-6,7-dimethoxy-2-methyl-1,2,3,4-tetrahydroisoquinoline. Y: 78%. F. e. s. E. Schlittler and A. Lindemann, *Helv.* **32**, 1880 (1949); in the presence of a base s. J. A. Barltrop and D. A. H. Taylor, *Soc.* **1951**, 108; with PtO_2 s. D. R. Howton and D. R. V. Golding, *J. Org. Chem.* **15**, 1 (1950).

Nickel/alkalis

Carboxylic acids from ethylenecarboxylic acids

$C:C \rightarrow CHCH$

s. **2**, 74; s. a. R. G. Jones, E. C. Kornfeld, and K. C. McLaughlin, *Am. Soc.* **72**, 3539 (1950)

Palladium-carbon

Pd-C

Selective hydrogenation

s. **4**, 81; **5**, 56; s. a. H. Moreu et al., *Bl.* **1949**, 475

Palladium-calcium carbonate/pyridine

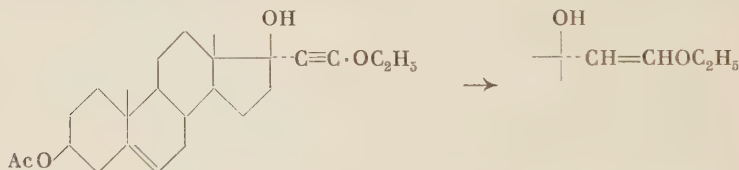
Pd-CaCO₃/C₅H₅N

Selective and partial hydrogenation

Ethylene from acetylene derivatives

$C:C \rightarrow CH:CH$

92.



A soln. of 300 mg. 3 β -acetoxy-17 β -hydroxy-17 α -ethoxyethynyl- Δ^5 -androstene in pyridine shaken under H_2 with 2.5% $-Pd-CaCO_3$ for ca. 17 min. until the calculated amount of H_2 is absorbed $\rightarrow$ 250 mg. 3 β -acetoxy-17 β -hydroxy-17 α -ethoxyvinyl- Δ^5 -androstene. H. Heusser, K. Eichenberger, and P. A. Plattner, *Helv.* **33**, 370 (1950); s. a. C. Djerassi, R. Yashin, and G. Rosenkranz, *Am. Soc.* **72**, 5750 (1950).

Palladium hydroxide-calcium carbonate

Pd(OH)₂-CaCO₃

Hydrogenation of enolacetates

$C:C(OAc) \rightarrow CHCH(OAc)$

93.



$\Delta^{\alpha,\beta}$ - α -Acetoxy- β -methylbutenolide hydrogenated in alcohol with 2% $-Pd(OH)_2-CaCO_3$ for 1 hr. after reduction of the catalyst $\rightarrow$ α -acetoxy- β -methylbutanolide. Y: ca. 100%. F. e. s. F. Fleck et al., *Helv.* **33**, 130 (1949).⁷ (1950)

Platinum oxide PtO_2 **Hydrocarbons from enolesters
trans-Hydrogenation**

←

94.



Cholestenone enol acetate hydrogenated with prehydrogenated PtO_2 in alcohol $\rightarrow$ cholestane. Y: 90%. F. e. s. H. H. Inhoffen et al., A. 568, 52 (1950).

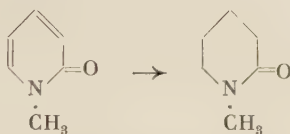
Hydrogenation of N-heterocyclic rings

←

s. 4, 86; s. a. G. R. Clemons et al., Soc. 1950, 1140

Piperidones from pyridones

95.



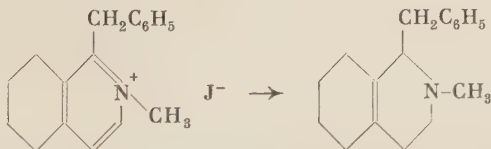
1-Methyl-2-pyridone hydrogenated 17 hrs. with PtO_2 in glacial acetic acid at 2-3.5 atm. and $26^\circ \rightarrow$ 1-methyl-2-piperidone. Y: 87.5%. N. J. Leonard and E. Barthel, Jr., Am. Soc. 71, 3098 (1949); with Raney-Ni s. J. A. Gautier and J. Renault, R. 69, 421 (1950).

**Selective hydrogenation of cyclic
quaternary ammonium salts**

s. 6, 91

Platinum oxide/sodium hydroxide/iodine $PtO_2/NaOH/I$ **Partial hydrogenation of cyclic
quaternary ammonium salts**

96.



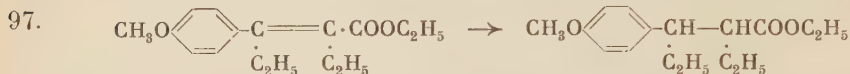
1-Benzyl-5,6,7,8-tetrahydroisoquinoline methiodide in aq.-methanolic NaOH hydrogenated ca. 2 hrs. with Adams catalyst (PtO_2) in the presence of a little iodine $\rightarrow$ 2-methyl-1-benzyl-1,2,3,4,5,6,7,8-octahydroquinoline (isolated as picrate). Y: 82%. F. e. s. R. Grewe, A. Mondon, and E. Nolte, A. 564, 161 (1949).

Platinum oxide/palladium

PtO₂/Pd

Hydrogenation of ethylene derivatives

C : C → CHCH



Ethyl (α,β -diethyl-*p*-methoxy) cinnamate in ethanol hydrogenated with PtO₂ and Pd black in a Parr hydrogenator at 60 lbs./sq. in. until the H₂-uptake is complete in ca. 4 hrs. → ethyl (2-ethyl-3-anisyl) valerate. Y: 97%. A. J. Shukis and J. J. Ritter, Am. Soc. 72, 1488 (1950).

Rearrangement

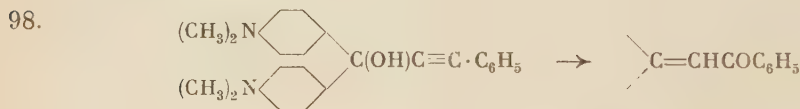
Hydrogen/Oxygen Type

HC↘HO

Sulfuric acid

H₂SO₄ α,β -Ethyleneketones from

←

 α,β -acetylenecohols

Bis-(*p*-dimethylaminophenyl) (phenylethynyl) carbinol refluxed 10 min. in alc. H₂SO₄ → 1,1-bis-(*p*-dimethylaminophenyl)-3-phenyl-1-propen-3-one. Y: 90%. C. Dufraisse, J. Lefrancq, and P. Barbieri, R. 69, 380 (1950).

Exchange

Oxygen ↕

HC↗O

Sodium

Na

β -Hydroxyketones from β -ketocarboxylic acid esters

←

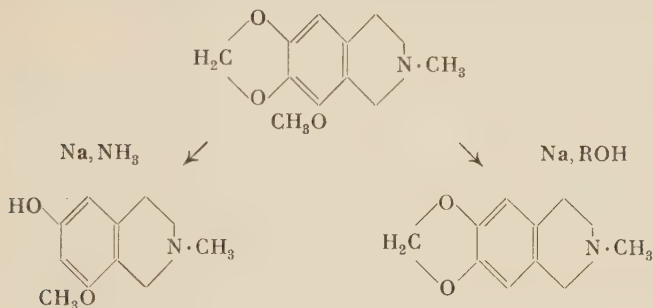
s. 6, 216

Sodium and sodium/liq. ammonia

Na and Na/NH₃**Reductive cleavage of ethers**

←

99.



Hydrocotarnine (prepn., s. 112)

dissolved in ether, added to liq. NH₃ containing NH₄Cl, then Na added cautiously with stirring until a permanent blue color is obtained → 6-hydroxy-8-methoxy-2-methyl-1,2,3,4-tetrahydroisoquinoline. Y: 96%.

D. B. Clayson, Soc. 1949, 2016.

and 6 atoms Na in xylene boiled with vigorous stirring until the Na was finely dispersed, then isoamyl alcohol run in, and stirring continued for 20 min. after the first vigorous reaction has subsided → hydrohydrastinine Y: 60%.

Zinc and stannous chloride s. Stannous chloride and zinc

Zn/SnCl₂

Zinc amalgam

Zn,Hg

Amines from α -aminoketones with rearrangement

←

Clemmensen reduction**Ring contraction and enlargement**

100.



A soln. of 1-methyl-2-ethyl-3-piperidone in concd. HCl added cautiously to Zn-amalgam, after the vigorous reaction has subsided refluxed 12 hrs. with repeated additions of concd. HCl → 1-methyl-2-n-propylpyrrolidine. Y: 65-71%. F. e. s. N. J. Leonard et al., Am. Soc. 71, 3094, 3098, 3100 (1949); 72, 3632 (1950); ring enlargement s. G. R. Clemo and H. Vipond, Chemistry and Industry 1949, 856.

Lithium boron hydride LiBH_4 **Lactones from ketocarboxylic acids**

○

s. 6, 53

Lithium aluminum hydride LiAlH_4 **Hydrocarbons from sulfonic acid esters** $\text{ROSO}_2\text{R}' \rightarrow \text{RH}$

s. 6, 47

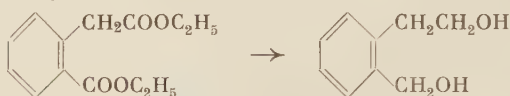
Alcohols from carboxylic acids and esters

←

s. 3, 52; 5, 60; s. a. S. P. Ligthelm, E. v. Rudloff, and D. A. Sutton, Soc. 1950, 3187

from carboxylic acid esters $\text{COOR} \rightarrow \text{CH}_2\text{OH}$

101.

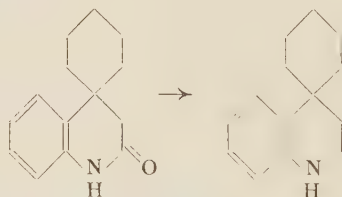


A soln. of ethyl homophthalate in dry ether added to ethereal LiAlH_4 at such a rate that gentle refluxing is maintained, and allowed to stand overnight $\rightarrow$ o-2-hydroxyethylbenzyl alcohol. Y: 91%. E. L. Anderson and F. G. Holliman, Soc. 1950, 1037; steroids s. D. Magrath et al., Soc. 1950, 2393.

Cyclic amines from lactams

←

102.



Spiro(cyclohexane-1,4'-dihydrocarbostyryl) in dry benzene added dropwise over 1 hr. to a soln. of 100% excess LiAlH_4 in ether, which is then distilled off, finally refluxed 24 hrs. $\rightarrow$ spiro(cyclohexane-1,4'-1',2',3',4'-tetrahydroquinoline). Y: 96%. L. H. Schwartzman, J. Org. Chem. 15, 517 (1950); s. a. O. E. Edwards and L. Marion, Am. Soc. 71, 1694 (1949); R. B. Moffett, J. Org. Chem. 14, 862 (1949); indoles from oxindoles s. P. L. Julian and A. Magnani, Am. Soc. 71, 2307 (1949).

Pyridine ring from dicarboxylic acid imides

103.



Anhydrous ether and LiAlH_4 stirred and refluxed for 2 hrs., then the condenser replaced by a Soxhlet extraction apparatus with N-(β -acet-

oxyethyl)naphthalimide in the extraction thimble, and refluxing continued for 20 hrs. $\rightarrow$ 2,3-dihydro-1-benz[de]isoquinoline-2-ethanol. Y: 68.5%. W. L. Garbrecht, J. H. Hunter, and J. B. Wright, *Am. Soc.* **72**, 1359 (1950); s. a. R. B. Moffett, *J. Org. Chem.* **14**, 862 (1949).

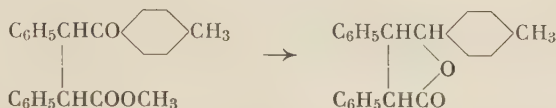
Aluminum alkoxide



Lactones from ketocarboxylic acid esters

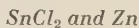


104.



Methyl α,β -diphenyl- β -p-tolylpropionate heated with Al-isopropoxide and isopropanol $\rightarrow$ α,β -diphenyl- γ -p-tolyl- γ -butyrolactone. Y: 82%. J. A. McRae, R. A. B. Bannard, and R. B. Ross, *Can. J. Research* **28 B**, 73 (1950); s. a. J. English, Jr., and J. E. Dayan, *Am. Soc.* **72**, 4187 (1950); method s. F. Bergmann, H. E. Eschinazi, and D. Schapiro, *Am. Soc.* **64**, 557 (1942).

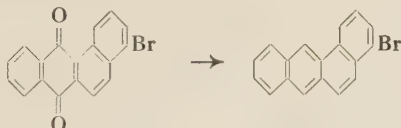
Stannous chloride and zinc



Anthracenes from anthraquinones



105.



1.5 gm. 4'-bromo-1,2-benzanthraquinone refluxed 1 hr. with $SnCl_2$ in acetic acid-concd. HCl, and the crude product reduced further by boiling with Zn-dust in 2 N NaOH for 3 hrs. $\rightarrow$ 1.4 gm. 4'-bromo-1,2-benzanthracene. F. e. s. G. M. Badger and A. R. M. Gibb, *Soc.* **1949**, 799.

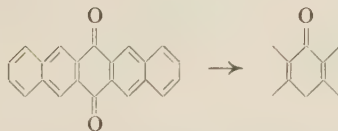
Hyposulfite



Anthrones from anthraquinones



106.

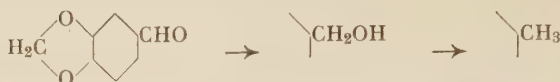


7 gm. pentacene-6,13-quinone, NaOH, and $Na_2S_2O_4$ in water heated almost to boiling for 1 hr. with exclusion of air $\rightarrow$ 6 gm. 6-pentacenone. E. Clar, *B.* **82**, 495 (1949).

Copper chromite

 CuCr_2O_4 **Hydrocarbons from aldehydes via prim. alcohols** $\text{CHO} \rightarrow \text{CH}_2\text{OH} \rightarrow \text{CH}_3$

107.



Piperonal hydrogenated in dioxane with CuCr_2O_4 at 300 atm. and 160-175° for 1¼ hrs. $\rightarrow$ piperonyl alcohol (Y: 98%) hydrogenated with CuCr_2O_4 at 375 atm. and 280° for 2 hrs. $\rightarrow$ 3,4-methylenedioxytoluene (Y: 84.5%). W. Reeve and J. D. Sterling, Jr., *Am. Soc.* **71**, 3657 (1949).

Hydrocarbons from ketones $\text{CO} \rightarrow \text{CH}_2$

s. 4, 97; carboxylic acids from ketocarboxylic acids s. F. C. Novello and M. E. Christy, *Am. Soc.* **73**, 1267 (1951)

Alcohols and hydrocarbons from oxo compounds $\leftarrow$

108. Ar. ketones and methoxy ar. aldehydes may be hydrogenated over CuCr_2O_4 at an initial H_2 -pressure of 220-340 atm. to the corresponding carbinol at 110-130° or the alkylbenzene or cresol at 185-250° in nearly 100% yields.—The o- and p-hydroxybenzaldehydes are reduced to o- and p-cresol at 110-130° with yields of 86 and 73% respectively. while m-hydroxybenzaldehyde gives a 84% yield of m-hydroxybenzyl alcohol at this temp.—Both o- and p-hydroxyketones are reduced to alkylphenols at 110-130° with yields of 75-90%. E. s. D. Nightingale and H. D. Radford, *J. Org. Chem.* **14**, 1089 (1949).

Alcohols from ethylenecarboxylic acid esters $\leftarrow$

109.



Ethyl 3-methylnonenoate hydrogenated with CuCr_2O_4 at 250° and an initial maximum pressure of 3490 p. s. i./20° for 7 hrs. $\rightarrow$ 3-methyl-1-nonanol. Y: 86%. J. Cason et al., *J. Org. Chem.* **15**, 135 (1950).

Nickel

Ni

Hydrocarbons from sulfonic acid esters $\text{ArOTs} \rightarrow \text{ArH}$

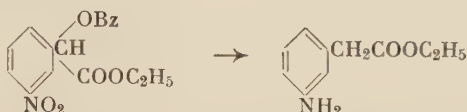
s. 6, 9

Nickel/sodium carbonate

Ni/Na₂CO₃

Carboxylic acid esters from α -acoxycarboxylic acid esters, simultaneously: amines from nitro compounds

110.



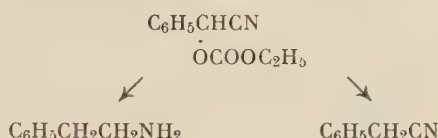
A suspension of ethyl m-nitro-O-benzoylmandelate (prepn. s. 239). Na-carbonate, and Raney-Ni in abs. alcohol hydrogenated at 150-200 atm. and, during the last 50 min., at 120-130° $\rightarrow$ ethyl m-aminophenylacetate. Y: 87%. M. W. Cronyn, J. Org. Chem. 14, 1013 (1949).

Palladium-carbon

Pd-C

**Amines and nitriles from cyanocarboxates
Directing the hydrogenation by acids**

111.



O-Carbethoxymandelonitrile hydrogenated

with Pd-C in methanol-concd. H₂SO₄ at 2 atm. and room temp. $\rightarrow$ β -phenylethylamine. Y: 92%.

ca. 4 hrs. in benzene with Pd-black in a H₂-stream to remove the CO₂ formed $\rightarrow$ benzyl cyanide. Y. 90%

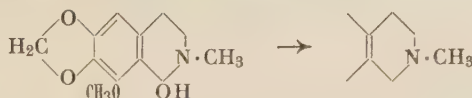
K. Kindler and K. Schrader, A. 564, 49 (1949).

Oximes from α -nitroethylene derivatives CH:CHNO₂ $\rightarrow$ CH₂CH:NOH
s. 5, 65; s. a. B. Reichert and H. Marquardt, Pharmazie 5, 10 (1950)

Platinum oxide

PtO₂**Replacement of hydroxyl by hydrogen**OH $\rightarrow$ H

112.



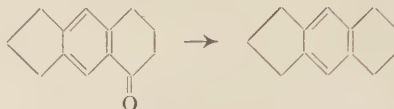
Cotarnine hydrochloride hydrogenated in water with PtO₂ (Adams') catalyst at room temp. and 2 atm. until the theoretical amount of H₂ has been absorbed after 60-90 min. $\rightarrow$ hydrocotarnine (startg. m. f. 99). Y: 95%. D. B. Clayson, Soc. 1949, 2016.

Hydrocarbons from enolesters

s. 6, 94

Hydrocarbons from ketonesCO $\rightarrow$ CH₂

113.



1-Keto-1,2,3,4-tetrahydro-6,7-cyclopentenonaphthalene in glacial acetic acid-concd. HCl shaken with PtO₂ (Adams' catalyst) in a H₂ atmosphere for 40 hrs. until the absorption of H₂ ceases $\rightarrow$ 1,2,3,4-tetrahydro-6,7-cyclopentenonaphthalene. Y: 94%. P. A. Plattner, A. Fürst, and W. Keller, *Helv.* 32, 2464 (1949).

Ethylene derivatives from enol acetatesC:C(OAc) $\rightarrow$ C:CH

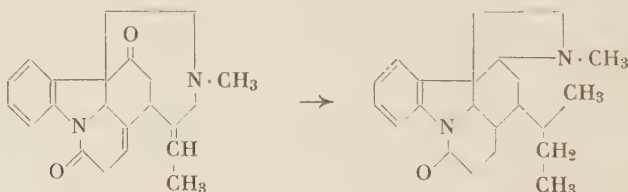
114.



3,6-Diacetoxy-4-methoxycoumarone hydrogenated with PtO₂ in glacial acetic acid until, after 22 min., the theoretical quantity of H₂ has been absorbed, filtered, and acetic acid split off by distillation in vacuo $\rightarrow$ 4-methoxy-6-acetoxycoumarone. Y: 91%. F. e. s. W. Gruber and K. Horváth, *M.* 80, 563 (1949).

Reductive ring contraction

115.



Desoxy-N-methylisopseudostrychnine hydrogenated in 0.25 N acetic acid with PtO₂ at room temp. for 4 hrs. $\rightarrow$ desoxy-N-methylhexahydrochano-isostrychnine. Y: 65%. F. e. s. H.-G. Boit, *B.* 83, 217 (1950).

*Via intermediates**v.i.***Hydrocarbons from oxo compounds via hydrazones according to Wolff-Kishner**CO $\rightarrow$ CH₂**Simplified procedures**s. 2, 96; s. a. *Oesterr. Chem.-Ztg.* 50, 5 (1949)

Huang-Minlon modification

s. 3, 57; s. a. Ng. Ph. Buu-Hoï and Ng. Hoán, *Am. Soc.* **73**, 98 (1951); W. E. Bachmann and E. J. Fornefeld, *Am. Soc.* **73**, 51 (1951)

116. In the case of steroids the reduction of the keto groups proceeds normally at positions C₃, C₇, C₁₂, C₁₇ and C₂₀, but the C₁₁-keto group remains unattacked. Huang-Minlon, *Am. Soc.* **71**, 3301 (1949).

steric hindrance s. J. Cason, G. Sumrell, and R. S. Mitchell, *J. Org. Chem.* **15**, 850 (1950)

Wolff-Kishner reduction with migration of a carbon carbon double bond

117.



In the Wolff-Kishner reduction of α,β -ethyleneoxo compounds, migration of the double bond can occur, permitting synthesis of compounds not otherwise available, e.g. compounds with a semi-cyclic methylene group.—E: 3 gm. β -cyclocitral allowed to stand at room temp. for 1 hr. with hydrazine hydrate in alcohol, refluxed 30 min., a soln. of Na in abs. alcohol added, and heated at 200-210° in a sealed tube overnight $\rightarrow$ 2.28 gm. 1,1,3-trimethyl-2-methylene-cyclohexane. F. e. s. G. Lardelli and O. Jeger, *Helv.* **32**, 1817 (1949).

Nitrogen ∇ **HC ∇ N**

Sodium carbonate

Na_2CO_3

Hydrocarbons from sulfonic acid hydrazides

$\text{NHNHSO}_3\text{R} \rightarrow \text{H}$

s. 6, 121

Sodium nitrite

NaNO_2

Replacement of amino groups by hydrogen

$\text{NH}_2 \rightarrow \text{H}$

s. 2, 103; s. a. R. B. Carlin and W. O. Forshey, Jr., *Am. Soc.* **72**, 793 (1950)

Sulfuric acid

H_2SO_4

Aldehydes from

1-acyl-1,2-dihydroquinaldonitriles

(Reissert compounds)

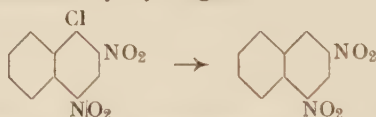
s. 6, 122

Copper chromite CuCr_2O_4 **Hydrocarbons from tert. amines** $\text{NR}_2 \rightarrow \text{H}$ **Hydrogenolysis of Mannich bases**

s. 6, 730

*Hydriodic acid**HI***Methyl ketones from α -diazoketones** $\text{COCHN}_2 \rightarrow \text{COCH}_3$ s. 3, 60; s. a. R. B. Wagner and J. M. Tone, *Am. Soc.* 72, 3477 (1950)**Halogen †****HC†Hal***Copper**Cu***Replacement of chlorine by hydrogen** $\text{Cl} \rightarrow \text{H}$

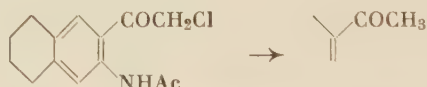
118.



Ar. nitrochloro compounds containing a nitro group ortho to the chlorine undergo dechlorination when heated with Cu-powder and an organic acid at 150-200°.—E: Cu-powder added in several portions over a period of 5 min. at 150-200° to a manually stirred mixture of benzoic acid and 1-chloro-2,4-dinitronaphthalene $\rightarrow$ 1,3-dinitronaphthalene. Y: 74%. F. e. s. W. T. Smith, Jr., *Am. Soc.* 71, 2855 (1949).

*Zinc**Zn*

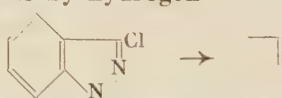
119.



10 gm. 6-acetamido-7-chloroacetyltetralin. Zn (etched with dil. H_2SO_4 and washed with water). and alcohol refluxed with vigorous stirring for 8 hrs. $\rightarrow$ 8.42 gm. 6-acetyl-7-methyltetralin. F. e. s. K. Schofield, T. Swain, and R. S. Theobald, *Soc.* 1949, 2399.

Stannous chloride SnCl_2 **Methyl ketones from α -bromoketones** $\text{Br} \rightarrow \text{H}$ s. 3, 63; s. a. J. Siegle and B. E. Christensen, *Am. Soc.* 72, 4186 (1950)*Phosphorus/hydriodic acid**P/HI***Replacement of chlorine by hydrogen** $\text{Cl} \rightarrow \text{H}$

120.



3-Chloroindazole, red P. and constant-boiling HI (d. 1.7) refluxed 24 hrs. $\rightarrow$ indazole. Y: 82-86%. E. F. M. Stephenson, *Org. Synth.* 29, 54 (1949); s. a. W. R. Boon, W. G. M. Jones, and G. R. Ramage, *Soc.* 1951, 96.

Chromous chloride CrCl_2 **Replacement of halogen by hydrogen** $\text{Hal} \rightarrow \text{H}$

s. 4, 112; s. a. Am. Soc. 72, 4077, 4081 (1950)

Palladium-barium sulfate Pd-BaSO_4 **simultaneously:****amines from nitro compounds**

s. 6, 35

Aldehydes from carboxylic acid chlorides $\text{COCl} \rightarrow \text{CHO}$

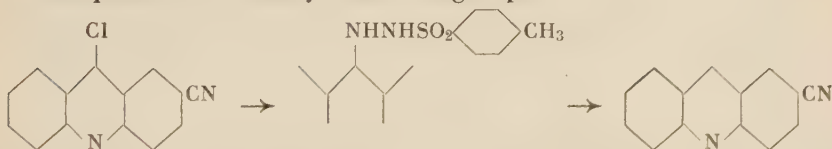
s. 1, 99, 101; s. a. W. K. Detweiler and E. D. Amstutz, Am. Soc. 72, 2882 (1950); H. Rapoport, A. R. Williams, and M. E. Cisney, Am. Soc. 73, 1414 (1951)

Palladium-carbon Pd-C **Replacement of halogen by hydrogen** $\text{Hal} \rightarrow \text{H}$

s. 6, 731

*Via intermediates**v.i.***Replacement of active chlorine by hydrogen** $\text{Cl} \rightarrow \text{H}$ **via sulfonic acid hydrazides****in compounds with easily reducible groups**

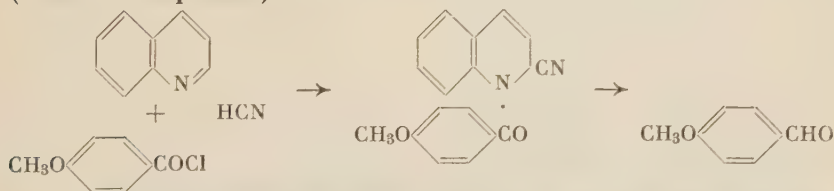
121.



Cold satd. chloroform solutions of p-toluenesulfonylhydrazide and 9-chloro-2-cyanoacridine mixed, and set aside for 1-2 days $\rightarrow$ crude 9-[N'-(p-toluenesulfonyl)hydrazino]-2-cyanoacridine hydrochloride (Y: ca. 100%) decomposed with $\text{Na}_2\text{CO}_3 \rightarrow$ 2-cyanoacridine (Y: 65%). —In other cases the hydrazides were prepared in the presence of dry HCl, and decomposed with NaOH. F. e. s. A. Albert and R. Royer, Soc. 1949, 1148.

Aldehydes from carboxylic acid chlorides $\text{COCl} \rightarrow \text{CHO}$ **via 1-acyl-1,2-dihydroquinaldonitriles****(Reissert compounds)**

122.



Anhydrous HCN poured at about -5° into freshly distilled quinoline, under further cooling a soln. of 4-methoxybenzoyl chloride in abs.

benzene dropped in over a period of 10 min., and allowed to stand at room temp. for ca. 16 hrs. $\rightarrow$ 1-(p-methoxybenzoyl)-1,2-dihydroquinol-donitrile (Y: 88%) steam-distilled with 10 N $\text{H}_2\text{SO}_4 \rightarrow$ p-methoxybenzaldehyde (Y: 98%). F. e., also without isolation of the intermediate, s. J. M. Grosheintz and H. O. L. Fischer, *Am. Soc.* **63**, 2021 (1941).

Sulfur †

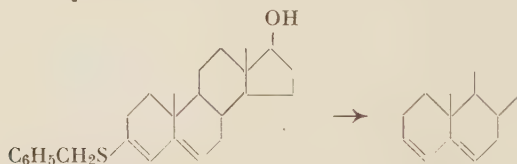
HC † S

Nickel

Ni

Replacement of sulfhydryl by hydrogenSH $\rightarrow$ H**Imidazoles from 2-mercaptoimidazoles**s. **5**, 77; s. a. R. A. Turner, *Am. Soc.* **71**, 3476 (1949)**Desulfuration of thioenolethers**C:C(SR) $\rightarrow$ C:CH**Deactivated catalyst**

123.



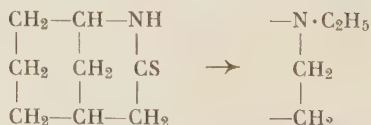
Benzyl enethiolether from testosterone refluxed 4 hrs. in acetone with Raney-Ni, which has been partially deactivated by refluxing 1 hr. in acetone (cf. *Synth. Meth.* **4**, 118) $\rightarrow$ $\Delta^{3,5}$ -androstadien-17 β -ol. Y: 87%. —If the catalyst is not deactivated, the double bonds are hydrogenated. F. e. s. G. Rosenkranz, S. Kaufmann, and J. Romo, *Am. Soc.* **71**, 3689 (1949).

Hydrocarbons from mercaptalsC(SR)₂ $\rightarrow$ CH₂

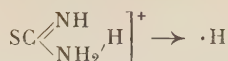
s. **3**, 72; carbohydrates s. M. L. Wolfrom et al., *Am. Soc.* **71**, 4057 (1949); **73**, 1528 (1951).

Amines from carboxylic acid thioamidesCSN $\rightarrow$ CH₂N**Cyclic amines from thiolactams****N-Alkylation**

124.



A soln. of *cis*-3-aminocyclohexanecarboxylic acid thiolactam (prepn. s. 636) in abs. ethanol, protected with a soda-lime tube, refluxed for 3 hrs. with Raney-Ni $\rightarrow$ 2 ethyl-2-azabicyclo[3.3.1]nonane. Y: 76%. Also without alkylation s. M. W. Cronyn, *J. Org. Chem.* **14**, 1013 (1949); noncyclic amines s. E. C. Kornfeld, *J. Org. Chem.* **16**, 131 (1951).

Hydrocarbons from thiuronium salts

s. 2, 111; s. a. G. M. Badger et al., Soc. 1950, 2326

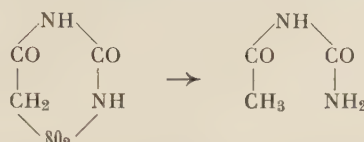
Thiophene ring opening

C

s. 5, 79; s. a. Am. Soc. 71, 4010 (1949); E. J. Modest and J. Szmuszkowicz, Am. Soc. 72, 577 (1950)

1,2,4-Thiadiazine ring opening

125.



Trimethylene-1,2,4-thiadiazine-3,5-dione-1,1-dioxide refluxed 4 hrs. with Raney-Ni according to Mazingo in 75%-ethanol $\rightarrow$ acetylurea. Y: 79%. F. e. s. P. N. Rylander and E. Campaigne, J. Org. Chem. 15, 249 (1950).

*Nickel/sodium carbonate*Ni/Na₂CO₃**Hydrocarbons from thioethers**SR $\rightarrow$ H**Carboxymethyl thioethers as intermediates**

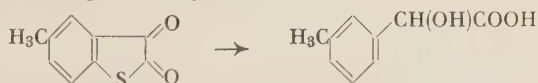
s. 6, 482

Nickel/aluminum

Ni/Al

Reductions of sulfur compounds $\leftarrow$ **with nickel aluminum alloy****Thianaphthene ring opening**

126.



In general, this reaction proceeds smoothly, and good yields of desulfurized products are obtained.—E: 15 gm. 5-methylthianaphthenequinone (prepn. s. 818) in 10%-NaOH reacted with Ni, Al-alloy $\rightarrow$ 9.8 gm. m-methylmandelic acid. F. e. s. D. Papa, E. Schwenk, and H. F. Ginsberg, J. Org. Chem. 14, 723 (1949).

Carbon $\uparrow$

HC≡C

Sodium hydroxide

NaOH

Subst. glutaric acids from $\leftarrow$ **arylmethylene-bis-acetoacetates**

s. 6, 759

**α -Aminocarboxylic acids from
 α -formamidomalonic esters**

←



Diethyl propargylformamidomalonate refluxed 4 hrs. with 8% NaOH, diluted with water, passed first through a column of Duolite C-10H to remove the base, then through a column of Duolite A-2 to remove the formic acid produced $\rightarrow$ propargylglycine. Y: 88.5%. H. Gershon, J. S. Meek, and K. Dittmer, *Am. Soc.* **71**, 3573 (1949).

s. a. 6, 789

Potassium hydroxide

KOH

Replacement of C-acyl by hydrogen

COR $\rightarrow$ H

s. 5, 80; s. a. P. J. Pollak and D. Y. Curtin, *Am. Soc.* **72**, 961 (1950)

**Carboxylic acids from cyanocarboxylic
acid esters**

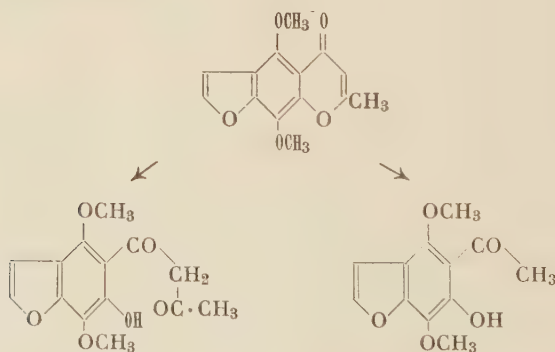
←

s. 6, 700; s. a. K. Pettersson, *Acta Chem. Scand.* **4**, 395 (1950)

γ -Pyrone ring opening

C

128.



A soln. of KOH in abs. alcohol at 70° poured onto 10 g. khellin, and shaken for 15 min. without further heating $\rightarrow$ 8.5 g. ω -aceto-khellinone.

Khellin boiled with aq. KOH for 1 hr. $\rightarrow$ khellinone. Y: ca. 90%.

A. Schönberg and A. Sina, *Am. Soc.* **72**, 1611 (1950).

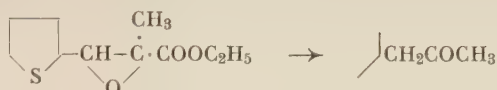
Sodium alkoxide

NaOR

Ketones from glycidic acid esters

←

129.



Ethyl α -methyl-2-thiopheneglycidate refluxed with a slight excess of alc. NaOH, most of the alcohol evaporated, the Na-salt dissolved in water, acidified with HCl, extracted with ether, and the ether residue heated 5 min. at 120° $\rightarrow$ α -thienylacetone. Y: 87%. P. Cagniant, Bl. 1949, 847.

 β -Ketocarboxylic acid esters fromCOR $\rightarrow$ H **β,β' -diketocarboxylic acid esters**

s. 1, 649, 770; 4, 122; s. a. D. Libermann, J. Himbert, and L. Hengl. Bl. 1950, 486

Sodium amide

NaNH₂**Replacement of cyano groups by hydrogen**CN $\rightarrow$ H

s. 5, 81; s. a. M. Jackman, F. C. Nachod, and S. Archer, Am. Soc. 72, 716 (1950)

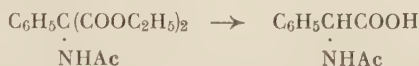
Sodium carbonate

Na₂CO₃ **α -Acetamidocarboxylic acids from**

←

acetamido-malonic esters and **α -cyanocarboxylic esters**

130.



Alkylacetamidomalonic esters are refluxed overnight (ca. 16 hrs.) with an equal weight of Na-carbonate dissolved in 10 volumes of water. Alkylacetamidocyanoacetic esters are refluxed ca. 60 hrs. until evolution of NH₃ has practically ceased.—E: Benzylacetamidomalonic ester $\rightarrow$ acetyl-DL-phenylalanine. Y: 75%.—3-Indolemethyl-acetamidocyanoacetic ester $\rightarrow$ acetyl-DL-tryptophan. Y: 81%. F. e. s. N. F. Albertson, Am. Soc. 72, 1396 (1950).

Sodium cyanide

NaCN

Reverse Mannich reactionCH₂N < $\rightarrow$ H

s. 5, 82; cf. G. Zigeuner, M. 80, 801 (1949)

Ammonia

NH₃**Carboxylic acids from barbituric acids**

C

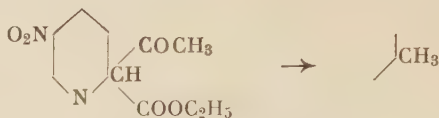
s. 6, 228

Sulfuric acid

 H_2SO_4 **Hydrocarbons from β -ketocarboxylic acid esters**

←

131.

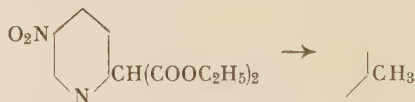


Ethyl (5-nitro-2-pyridyl)acetoacetate heated in 10% H_2SO_4 on a water bath for 5 hrs. $\rightarrow$ 2-methyl-5-nitropyridine. Y: 81%.—The methyl ketone could not be obtained. W. Gruber and K. Schlögl, M. 80, 499 (1949).

Hydrocarbons from malonic acid esters

←

132.

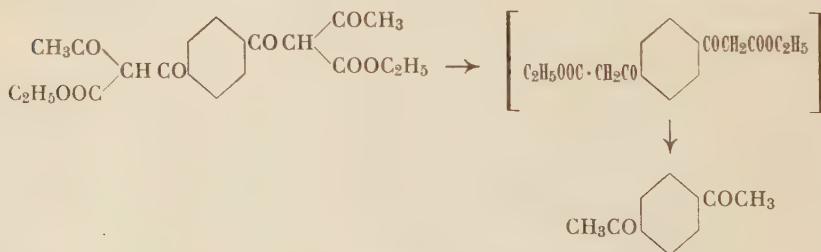


(5-Nitro-2-pyridyl)malonic acid ester heated 4 hrs. at 120-130° with 1:2 H_2SO_4 -water $\rightarrow$ 5-nitro-2-methylpyridine. Y: 90%. W. Gruber and K. Schlögl, M. 81, 473 (1950).

Methyl ketones from β,β -diketocarboxylic acid esters

←

133.



Terephthaloyldiacetoacetic ester, alcohol, and concd. H_2SO_4 refluxed 14 hrs., water added, concentrated to its original volume, then refluxed for 8 hrs. more $\rightarrow$ p-diacetylbenzene. Y: 60%. Also isolation of the intermediates s. K. Schofield and R. S. Theobald, Soc. 1949, 2404; method, see Kermack and Smith, Soc. 1929, 814.

Methyl ketones from acylmalonic acid esters

s. 6, 285



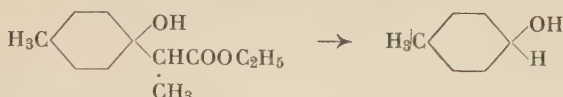
Hydrochloric acid

HCl

Hydrogenolysis of the carbon carbon bond

←

134.



A soln. of ethyl α -(4-methyl-1-hydroxycyclohexyl)propionate in dioxane hydrogenated with Cu-chromite at 270° and an initial pressure of 3400 lbs./sq. in./25° $\rightarrow$ 4-methylcyclohexanol. Y: 60-70%. R. L. Frank and R. E. Berry, *Am. Soc.* 72, 2985 (1950); s. a. R. Connor and H. Adkins, *Am. Soc.* 54, 4678 (1932).

Copper chromite

 CuCr_2O_4 **Dicarboxylic acids from dicyanocarboxylic acid esters**

←

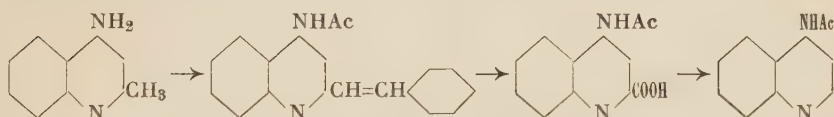
s. 6, 705; s. a. E. C. Horning and A. F. Finelli, *Org. Synth.* 30, 81 (1950)

Via intermediates

v.i.

Replacement of methyl groups by hydrogen Styrylheterocyclics $\text{CH}_3 \rightarrow \text{H}$ **Carboxylic acids from hydrocarbons****Decarboxylation**

135.



4-Aminoquinoline, benzaldehyde, and acetic anhydride heated 3 hrs. at 155-160° $\rightarrow$ 4-acetamido-2-styrylquinoline (Y: 91%) in pyridine-water treated at 18-20° with KMnO_4 during 1 hr., and stirring continued for 30 min. $\rightarrow$ 4-acetamidoquinoline-2-carboxylic acid (Y: 82%) added during 5 min. to paraffin at 290°, and worked up after a further 5 min. $\rightarrow$ 4-acetamidoquinoline (Y: 89%). F. e. s. R. Royer, *Soc.* 1949, 1803.

Hydrocarbons from carboxylic acid esters via carboxylic acids $\text{COOR} \rightarrow \text{H}$

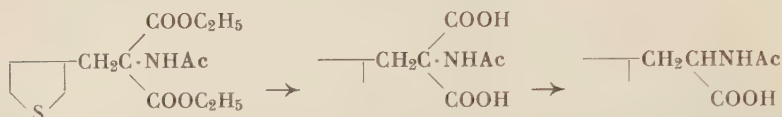
136.



Ethyl 3,5-dichloro-4-hydroxybenzoate hydrate (prepn. s. 572) heated 1 hr. on a steam bath with Claisen's alkali (KOH in methanol-water) $\rightarrow$ 3,5-dichloro-4-hydroxybenzoic acid (Y: 93-97%) heated slowly with dimethylaniline to 190-200°, then ca. 2 hrs. at this temp., until the evolution of gas has ceased $\rightarrow$ 2,6-dichlorophenol (Y: 80-91%). D. S. Tarbell, J. W. Wilson, and P. E. Fanta, *Org. Synth.* 29, 35 (1949).

**α -Acylaminocarboxylic acids from
acylaminomalonic acid esters
Selective hydrolysis
Decarboxylation**

137.



Diethyl 3-thenylacetamidomalonate and 10% NaOH mixed to a paste, let stand at room temp. for 24 hrs., or until soln. takes place, filtered, cooled in ice, and neutralized with 12 *N* HCl below 20° to prevent decarboxylation $\rightarrow$ 3-thenylacetamidomalonic acid (Y: 84%) boiled 2 hrs. with water, then evaporated to near dryness on a steam bath $\rightarrow$ N-acetyl- β -3-thienylalanine (Y: 84%).—The process can be performed in one step, but in this case no excess acid must be used to neutralize the alkali before boiling to prevent loss of the acid-labile thiophene derivative. R. G. Garst, E. Campaigne, and H. G. Day, *J. Biol. Chem.* **180**, 1013 (1949).

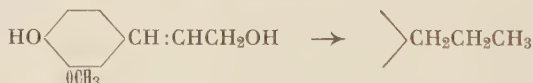
Elimination

Oxygen $\downarrow$ HC $\uparrow$ O

Sodium/liq. ammonia

Na/NH₃Hydrocarbons from α,β -ethylenecohols

138.

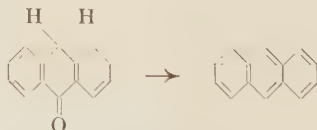


Na added to a soln. of coniferyl alcohol in liq. NH₃, and kept 5 days with Dry-Ice cooling $\rightarrow$ dihydroeugenol. Y: 86%. N. N. Shorygina, T. Y. Kefeli, and A. F. Semechkina, *Ж.* **19**, 1558 (1949); *C. A.* **44**, 3919 c.

Zinc/copper sulfate/alkali hydroxide

Anthracenes from anthrones

139.



2 *N* NaOH, toluene, and anthrone added to Zn-dust activated with aq. CuSO₄, and refluxed 12 hrs. $\rightarrow$ anthracene. Y: 93%. E. L. Martin, *Am. Soc.* **58**, 1438 (1936); with KOH s. E. Clar and D. G. Stewart, *Soc.* **1951**, 687.

Copper chromite

 CuCr_2O_4 **Hydrocarbons from alcohols**OH $\rightarrow$ H

s. 6, 107

Hydriodic acid/phosphorus

HI/P

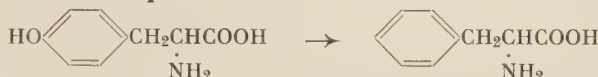
s. 5, 91; s. a. A. W. Ruddy and J. S. Buckley, Jr., Am. Soc. 72, 718 (1950)

Nickel

Ni

Hydrocarbons from phenols

140.



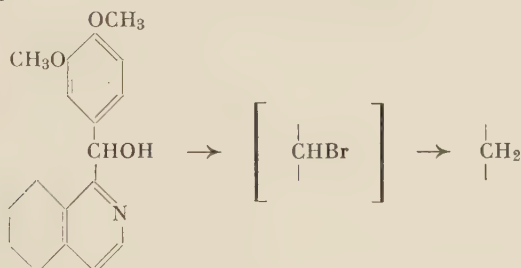
Tyrosine hydrogenated in aq. K-carbonate with Raney-Ni at 92 atm. and 196-200° $\rightarrow$ phenylalanine. Y: ca. 100%. M. Metayer, A. ch. [12] 4, 212 (1949).

Via intermediates

v.i.

Replacement of hydroxyl by hydrogen via bromides

141.



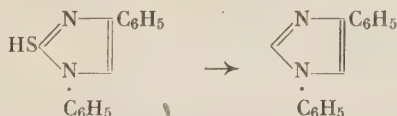
1-(α -Hydroxyveratryl)-5,6,7,8-tetrahydroisoquinoline dissolved in HBr-glacial acetic acid, allowed to stand for 24 hrs., and treated with Zn-dust at 25-30° over a period of 2 hrs. with stirring $\rightarrow$ 1-veratryl-5,6,7,8-tetrahydroisoquinoline. Y: 83%. F. e. s. R. Grewe, A. Mondon, and E. Nolte, A. 564, 161 (1949).

Sulfur $\downarrow$ HC $\uparrow$ S

Nitric acid/nitrous acid

 $\text{HNO}_3/\text{HNO}_2$ **Replacement of sulfhydryl by hydrogen**SH $\rightarrow$ H

142.



A soln. of NaNO_2 in dil. (1:3) HNO_3 added with stirring below 35° to an ice-cooled soln. of 1 gm. 1,4-diphenyl-2-thiolimidazole (prepn. s. 50)

in glacial acetic acid, and stirring continued for 15 min. → 0.8 gm. crude 1,4-diphenylimidazole. R. M. Dodson and F. Ross. *Am. Soc.* 72, 1478 (1950).

Carbon ↑**HC ↑ C***Without additional reagents**w.a.r.***Decarboxylation**

COOH → H

s. 6, 135, 137

Dimethylaniline $C_6H_5N(CH_3)_3$

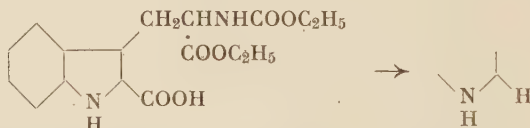
s. 6, 136

*Copper (II) carbonate, basic*s. 1, 113; s. a. J. W. Cook and J. S. Moffatt, *Soc.* 1950, 1160*Calcium hydroxide* $Ca(OH)_2$

s. 6, 796

Resorcinol

143.

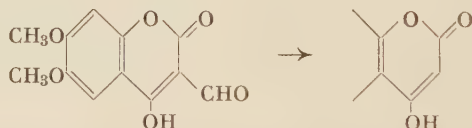


Ethyl β -(2-carboxy-3-indolyl)- α -(carbethoxyamino)propionate heated in resorcinol at 235° for 10 min. → ethyl β -(3-indolyl)- α -(carbethoxyamino)propionate. Y: 75%. H. Pleninger, *B.* 83, 268 (1950).

Sulfuric acid H_2SO_4 **Deformylation**

CHO → H

144.



1 gm. 4-hydroxy-6,7-dimethoxy-3-formylcoumarin refluxed 5 hrs. with H_2SO_4 in acetone → 0.7 gm. 4-hydroxy-6,7-dimethoxycoumarin. G. W. K. Cavill, A. Robertson, and W. B. Whalley, *Soc.* 1950, 1031.

Nickel-silica $Ni-SiO_2$ **Hydrocarbons from prim. alcohols**CH₂OH → H**Degradation with loss of 1 C-atom**

145.



n-Butyl alcohol hydrogenated in the presence of Ni-kieselguhr catalyst at 239° and atmospheric pressure → propane. Y: 98-99%. F. e. s. V. N. Ipatieff et al., *Ind. Eng. Chem.* 41, 1802 (1949).

Formation of O—N Bond

Uptake

Addition to Nitrogen



Perphthalic acid



N-Oxides



as intermediates s. 6, 389

Hydrogen peroxide



s. 3, 95a; from aliphatic tert. amines s. A. C. Cope and P. H. Towle, Am. Soc. 71, 3423 (1949)

Formation of O—S Bond

Uptake

Addition to Hydrogen and Oxygen



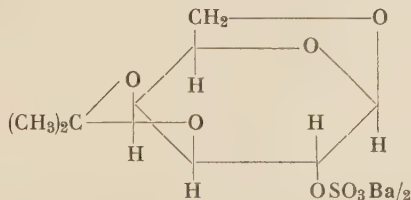
Pyridine



Carbohydrate sulfuric acid esters



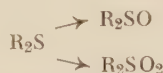
146.



Pyridine- SO_3 added with shaking to a soln. of 3,4-isopropylidene-1,6-anhydro- β -D-galactose in dry pyridine, stirred with a vigorous current of N_2 and heated at 50° for 2.5 hrs., then poured with stirring into excess of a suspension of Ba-carbonate in water $\rightarrow$ Ba-3,4-isopropylidene-1,6-anhydro- β -D-galactose-2-sulfate. Y: 89%.—This process avoids the use of large volumes of Ag_2SO_4 , necessary, when ClSO_3H is used, cf. Synth. Meth. 2, 133. F. e. s. R. B. Duff, Soc. 1949, 1597.

Steroid sulfuric acid esters

s. 1, 122

Addition to Sulfur**OS ↓ S***Hydrogen peroxide* H_2O_2 **Sulfoxides and sulfones from thioethers**

s. 5, 101; s. a. C. G. Overberger, S. P. Ligthelm, and E. A. Swire, Am. Soc. 72, 2856 (1950); P. Block, Jr., and J. L. Balmat, Am. Soc. 72, 5638 (1950)

Sulfones from thioethers $R_2S \rightarrow R_2SO_2$

s. 1, 117; 2, 542, 558; 3, 502; 5, 101; 6, 148; s. a. A. C. Cope, D. E. Morrison, and L. Field, Am. Soc. 72, 59 (1950)

Iodosobenzene C_6H_5IO **Sulfoxides from thioethers** $R_2S \rightarrow R_2SO$ 

12 gm. thiodiglycol in water heated on a steam bath, iodosobenzene added, and worked up after 15 min. $\rightarrow$ 11 gm. 2,2'-dihydroxydiethyl sulfoxide.—Iodosobenzene is a useful reagent for this reaction. F. e. s. A. H. Ford-Moore, Soc. 1949, 2126.

Potassium permanganate $KMnO_4$ **Sulfones from thioethers** $R_2S \rightarrow R_2SO_2$

148. H_2O_2 -oxidation of diphenyl sulfides with no substituents in o-position takes place smoothly at 50° in excellent yield. With one substituent, the oxidation gives lower yields, and with substituents in 0,0'-positions, the H_2O_2 -oxidation fails completely as preparative method. The oxidation of 0,0'-disubst. compounds can, however, successfully be carried out by the use of $KMnO_4$ in dil. acetic acid, E. s. B. R. Baker, M. V. Querry, and A. F. Kadish, J. Org. Chem. 15, 402 (1950).

Exchange**Hydrogen †****OS † H***Thionyl chloride* $SOCl_2$ **Sulfurous acid esters** $(RO)_2SO$

s. 4, 144; cf. W. Gerrard, A. Neehvatat, and B. M. Wilson, Soc. 1950, 2088

Halogen †**OS † Hal***Without additional reagents**w.a.r.***Chlorosulfinic acid esters** $ROSOCI$

s. 4, 144; s. a. E. M. Fry, J. Org. Chem. 14, 887 (1949)

Sodium hydroxide

NaOH

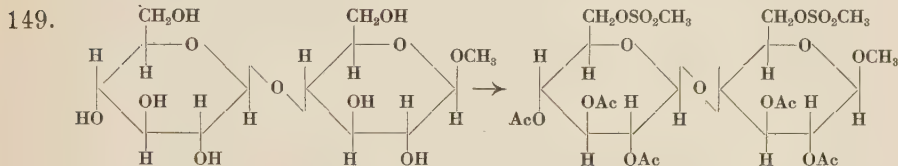
Sulfonic acid esters from sulfonic acid chlorides $\text{SO}_2\text{Cl} \rightarrow \text{SO}_2\text{OR}$

s. 4, 212; aryl esters s. H. R. Slagh and E. C. Britton, *Am. Soc.* 72, 2808 (1950)

Pyridine

 $\text{C}_5\text{H}_5\text{N}$ **Methanesulfonic acid esters from alcohols**
Selective acylation

←



A soln. of 11.7 gm. methyl β -cellobioside in pyridine treated at 0° with 2 moles of methanesulfonyl chloride for 12 hrs., followed by acetic anhydride for 4 hrs. at room temp. $\rightarrow$ 19 gm. methyl 6,6'-bis (methanesulfonyl)pentaacetyl β -cellobioside. F. H. Newth et al., *Soc.* 1949, 2550.

Sulfonyloximes $\text{C} : \text{NOSO}_2\text{R}$

s. 4, 143; s. a. *Am. Soc.* 72, 2738 (1950)

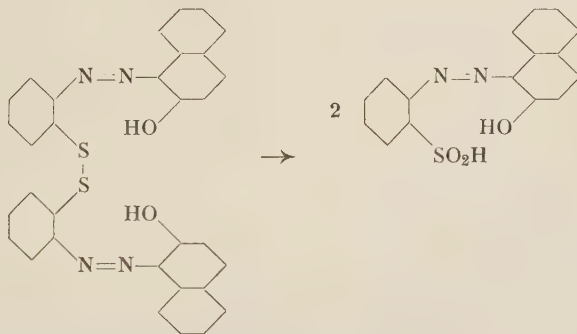
Sulfur †**OS † S**

Sodium hydroxide

NaOH

Sulfinic acids from disulfides $\text{RSSR} \rightarrow 2 \text{RSO}_2\text{H}$

150.



Bis-*o*-(2-hydroxy-1-naphthylazo)phenyl disulfide refluxed 3 hrs. with NaOH in aq. ethanol (1 : 1) $\rightarrow$ *o*-(2-hydroxy-1-naphthylazo)benzenesulfinic acid. Y: 80%. A. Burawoy and C. Turner, *Soc.* 1950, 469.

Elimination

Oxygen $\uparrow$ OS $\uparrow$ O

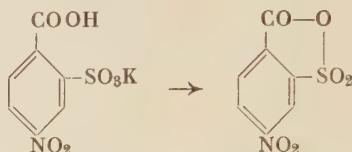
Thionyl chloride

SOCl₂

Carboxylic sulfonic acid anhydrides

 $\leftarrow$

151.



Mono-K-salt of 4-nitro-2-sulfobenzoic acid and SOCl₂ refluxed for 18 hrs. on a water bath $\rightarrow$ 4-nitro-2-sulfobenzoic acid endoanhydride. Y: 72%. F. methods s. C. A. Grob and M. W. Goldberg, *Helv.* 32, 172 (1949).

Formation of O—Rem Bond

Uptake

Addition to Oxygen and Carbon|

ORem $\downarrow$ OC

Without additional reagents

w.a.r

Phosphoric acid esters from oxido compounds

 $\leftarrow$

152.



Di-p-nitrobenzyl hydrogen phosphate and cyclohexene oxide dissolved in dioxane, and heated on a water bath for 2 hrs. $\rightarrow$ 2-hydroxycyclohexyl di-p-nitrobenzyl phosphate. Y: 95%. F. e. s. J. Baddiley et al., *Soc.* 1949, 815.

Addition to Remaining Elements

ORem $\downarrow$ Rem

Hydrogen peroxide

H₂O₂

Arsine oxides from arsines

 $\leftarrow$

153.



30% -H₂O₂ added dropwise with stirring over a period of 20-30 min. at 25-30° to a soln. of triphenylarsine (prepn. s. 673) in acetone, and stirring continued for 30 min. $\rightarrow$ triphenylarsine oxide (startg. m. f. 670). Y: 84-87%. R. L. Shriner and C. N. Wolf, *Org. Synth.* 30, 95 (1950).

Exchange

Hydrogen ∇

ORem ∇ H*Without additional reagents**w.a.r.*

Dithiophosphoric acids

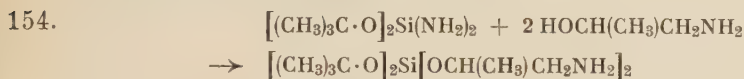
 $(RO)_2 \rightarrow PSSH$

s. 6, 156

Nitrogen ∇

ORem ∇ N*Without additional reagents**w.a.r.*

Silicates from aminosilanes

 $\leftarrow$ 

Di-t-butoxydiaminosilane and 1-amino-2-propanol refluxed 1 hr. $\rightarrow$ di-t-butyl-di-(2-amino-1-methylethyl) silicate. Y: 72%. F. e. s. P. A. Di Giorgio, L. H. Sommer, and F. C. Whitmore, *Am. Soc.* **71**, 3254 (1949).

Halogen ∇

ORem ∇ Hal*Without additional reagents**w.a.r.*

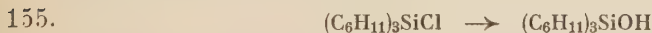
Siloxanes from halogenosilanes

 $\leftarrow$

s. 6, 543

*Potassium hydroxide**KOH*

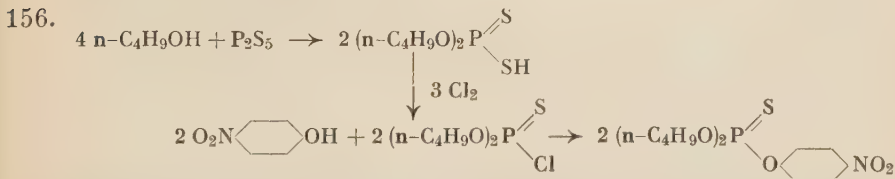
Silanols from halogenosilanes

 $SiCl \rightarrow SiOH$ 

Chlorotri(cyclohexyl)silane dissolved in boiling 5%-alc.-KOH, and worked up after a few min. $\rightarrow$ tri(cyclohexyl)silanol. Y: 87%. W. H. Nebergall and O. H. Johnson, *Am. Soc.* **71**, 4022 (1949).

Sodium carbonate Na_2CO_3

Monothiophosphoric acid esters via dithiophosphoric acids and chlorothiophosphoric acid esters

 $\leftarrow$ 

n-Butanol added over a period of 1.5-2.5 hrs. to a refluxing suspension of P_2S_5 in benzene, refluxing continued for 2 hrs., Cl_2 introduced at

25-30° over a period of ca. 1.5 hrs., stirred 15-20 min. more, and added to water with vigorous stirring during 30-45 min. at 25-35° 0,0-dibutyl chlorothiophosphate (Y: 64% based on P_2S_5), p-nitrophenol, and anhydrous Na-carbonate in methyl ethyl ketone refluxed 3-5 hrs. with stirring $\rightarrow$ 0,0-dibutyl-0-(p-nitrophenyl)thiophosphate (Y: 89%). F. e., using also acetone in the second step, s. J. H. Fletcher et al., Am. Soc. 72, 2461 (1950).

Sodium salt

Na^+

Monothiophosphoric acid esters

$\leftarrow$

s. 4, 147; addition of tert. amines and phosphines as catalysts s. A. D. F. Toy and T. M. Beck, Am. Soc. 72, 3191 (1950)

Dialkylaniline

$C_6H_5NR_2$

Phosphites

$\leftarrow$

157.



PCl_3 added dropwise with ice-cooling and stirring to a mixture of 1-ethoxy-2-hydroxypropane, dimethylaniline, and dry ether, stirring continued for 0.5 hr. $\rightarrow$ 1-ethoxy-2-propyl phosphite. Y: 70%. F. e. s. V. S. Abramov and E. N. Nikolaeva, *Ж.* 20, 100 (1950); C. A. 44, 5799 h; cf. W. Gerrard, A. Nechvatal, and B. M. Wilson, Soc. 1950, 2088; with diethylaniline s. A. H. Ford-Moore and B. J. Perry, Org. Synth. 31, 111 (1951).

Pyridine

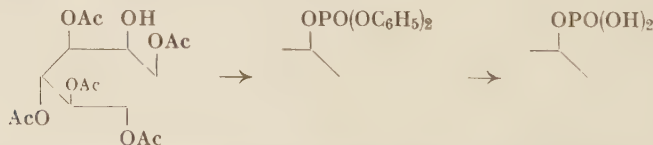
C_5H_5N

Phosphorylation of hydroxy compounds

$\leftarrow$

Hydrogenolysis of phosphoric acid esters

158.



3 moles of diphenylchlorophosphonate added to a soln. of 1,2,3,4,6-pentaacetylinsitol in anhydrous pyridine, and the mixture kept at 80° for 20 hrs. $\rightarrow$ 1,2,3,4,6-pentaacetylinsitol-5-diphenylphosphate (Y: 64%) hydrogenated in anhydrous ethanol with PtO_2 at room temp. and atmospheric pressure for 90 min. until the absorption of H_2 ceases $\rightarrow$ 1,2,3,4,6-pentaacetylinsitol-5-phosphoric acid (startg. m. f. 14) (Y: 80%). B. M. Iselin, Am. Soc. 71, 3822 (1949); s. a. K. R. Farrar, Soc. 1949, 3131; K. M. Mann and H. A. Lardy, J. Biol. Chem. 187, 339 (1950).

Phosphorylcholines

←

s. 5, 108; s. a. Am. Soc. 72, 942 (1950)

Sulfur ∇ **ORem ∇ S***Hydrogen peroxide* H_2O_2 **Seleninic acids and sulfonic acids
from selenylsulfides**

←

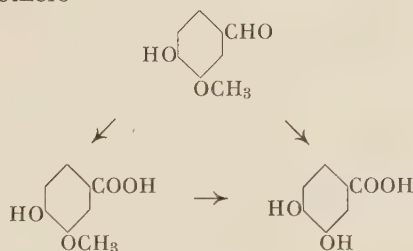
159.



Excess 30% $-H_2O_2$ added to a soln. of o-nitrophenylselenenyl phenyl sulfide (prepn. s. 602) in glacial acetic acid allowed to stand 2 hrs. at room temp. and evaporated on a water bath until the odor of acetic acid disappears $\rightarrow$ o-nitrobenzeneseleninic acid (Y: 91.9%) and benzenesulfonic acid (Y: 91.7%). H. Reinboldt and E. Giesbrecht, A. 568, 198 (1950).

Formation of O—C Bond**Uptake****Addition to Hydrogen and Carbon****OC ∇ HC***Sodium hydroxide/potassium hydroxide* $NaOH/KOH$ **Carboxylic acids from aldehydes,
also cleavage of ethers** $CHO \rightarrow COOH$

160.



Vanillin added slowly with stirring at 165–200° to a mixture of $NaOH$ and KOH in some water

and stirred an additional 5 min.
 $\rightarrow$ vanillic acid. Y: 98%.

and heated at 250° for 1 hr. $\rightarrow$
 protocatechuic acid. Y: 99%.

F. more details s. I. A. Pearl and D. L. Beyer. Ind. Eng. Chem. 42, 376 (1950); s. a. Org. Synth. 29, 85 (1949); 30, 103 (1950)

Sodium nitrite/nitric acid s. Nitric acid/sodium nitrite $NaNO_2/HNO_3$ *Copper acetate/nickel acetate s. Nickel acetate/copper acetate*

←

Silver nitrate/sodium hydroxide

AgNO₃/NaOH**Carboxylic acids from aldehydes**

CHO → COOH

s. 3, 112; s. a. J. C. Sheehan and C. A. Robinson, Am. Soc. 73, 1207 (1951)

Nitric acid/sodium nitrite

HNO₃/NaNO₂**Carboxylic acids from aldehydes**

s. 6, 170

Persulfate

S₂O₈²⁻**Replacement of hydrogen by hydroxyl**

H → OH

Elbs oxidation

s. 1, 131; s. a. J. Forrest and V. Petrow, Soc. 1950, 2340

Bromine

Br

Aldonic acids from carbohydrates

CHO → COOH

161.



Br₂ added to an aq. soln. of D-arabinose, kept for 2 hrs., excess Br₂ removed by aeration, the HBr formed removed by Ag₂O, any Ag⁺ in soln. precipitated with H₂S and the soln. boiled 15 min. with Ca-carbonate → Ca-D-arabonate. Y: 85.2%. L. F. Wiggins et al., Soc. 1949, 1358; also in the presence of CaCO₃ s. Soc. 1949, 1879

Nickel acetate/copper acetate

←

Carboxylic acids from aldehydes

←

s. 6, 292

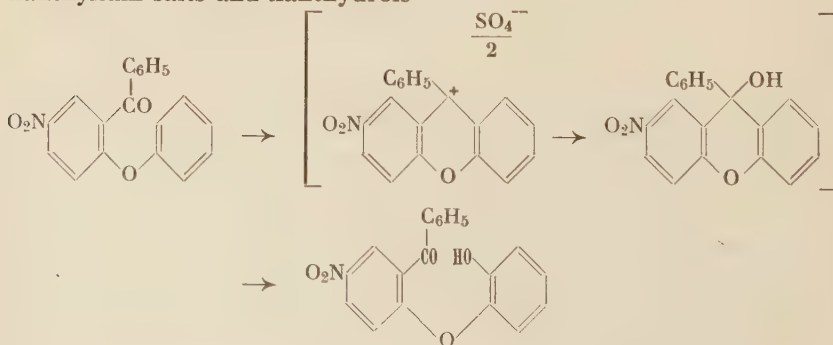
Via intermediates

v.i.

o-Hydroxyethers from ethers via xanthylium salts and xanthiols

←

162.



5-Nitro-2-phenoxybenzophenone dissolved in cold concd. H_2SO_4 , after 30 min. acetic acid added, then H_2O_2 added during 5 min. with vigorous stirring but without external cooling, and kept at room temp. for 3 hrs. $\rightarrow$ 5-nitro-2-o-hydroxyphenoxybenzophenone. Y: almost 100%. F. e., also with isolation of the intermediates, s. J. D. Loudon et al., Soc. 1950, 55.

Addition to Oxygen and Carbon

OC $\downarrow$ OC

Without additional reagents

w.a.r.

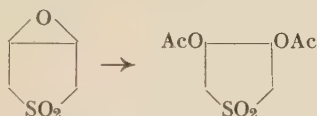
Partial and mixed dicarboxylic acid derivatives

C

s. 3, 114; s. a. F. E. King, B. S. Jackson, and D. A. A. Kidd, Soc. 1951, 243

Glycol esters from oxido compounds

163.



Butadiene sulfone epoxide and acetic acid heated 12 hrs. at $210^\circ \rightarrow$ 3,4-diacetoxythiacyclopentane 1,1-dioxide. Y: 83%. O. E. van Lohuizen and H. J. Backer, R. 68, 1137 (1949).

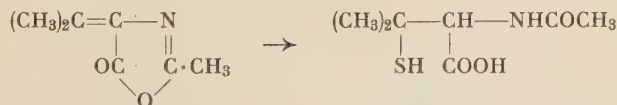
Oxazolone ring opening

164.



A mixture of 2-benzyl-4-hydroxymethylene-5-oxazolone, benzyl alcohol, and dry benzene refluxed for ca. 45 min. $\rightarrow$ benzyl benzylpenaldate. Y: 90%. F. e. s. E. V. Brown, Chemistry of Penicillin 1949, 508; s. a. Synth. Meth. 4, 804.

165.



Methanol satd. at 0° with H_2S in a pressure bottle, freshly distilled 4-isopropylidene-2-methyl-5(4H)-oxazolone added, stoppered, allowed to stand overnight at room temp., evaporated in vacuo, and the residue heated with water at 90° for 15 min. $\rightarrow$ N-acetyl-DL-penicillamine. Y: 80%. H. M. Crooks, Jr., Chemistry of Penicillin 1949, 455.

Coumarin ring opening

166.



3-Phenylcoumarin treated with NaOH and excess Na-chloroacetate $\rightarrow$ α -phenylcoumarinic acid-O-acetic acid. Y: 93%. F. e. s. C. F. Koelsch and C. R. Stephens, Jr., Am. Soc. 72, 2209 (1950).

Sodium hydroxide

NaOH

Oxazole ring opening

167.



2 gm. 2-phenyloxazole-4-aldehyde boiled 2 min. with 2 N NaOH until dissolved $\rightarrow$ 2 gm. benzamidomalondialdehyde. F. e. s. J. W. Cornforth et al., Soc. 1949, 1549; cf. Synth. Meth. 6, 197.

Sodium alkoxide

NaOR

Oxazolone ring opening

s. 6, 757

Boron fluoride

BF₃**Triacoxisocyclics from quinones** $\leftarrow$ **Thiele reaction**

s. 5, 121; s. a. D. J. Cram, Am. Soc. 71, 3953 (1949)

Peracetic acid/cobalt(II)-acetate

s. Cobalt(II)-acetate/peracetic acid

 $\text{CH}_3\text{COO}_2\text{H}/(\text{CH}_3\text{COO})_2\text{Co}$

Nitrous acid/nitric acid

 $\text{HNO}_2/\text{HNO}_3$ **Oxidative furan ring opening**

168.

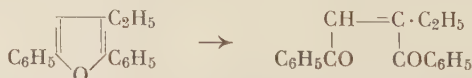


Tetrahydrofuran and 10.5 N HNO₃, containing a little NaNO₂, kept at 8° for 15 hrs. $\rightarrow$ succinic acid. Y: 84%. F. details s. H. Schmid, A. Maschka and H. Frauenschill, M. 80, 670 (1949).

Nitric acid

HNO₃

169.

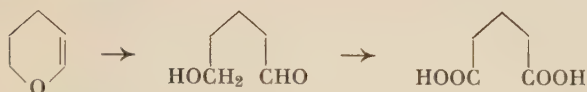


A suspension of 3-ethyl-2,5-diphenylfuran in glacial acetic acid treated with a soln. of HNO₃ in glacial acetic acid, and worked up after 20 min. $\rightarrow$ 1,2-dibenzoyl-1-butene. Y: 74%. F. e. s. P. S. Bailey and W. W. Hakki, Am. Soc. 71, 2886 (1949).

s. 5, 122; s. a. P. S. Bailey and J. D. Christian, Am. Soc. 71, 4122 (1949)

Glutaric acids
Pyran ring opening

170.



A mixture of dihydropyran and 0.2 *N* HNO₃ heated 0.5-1 hr. on a steam bath with swirling after 25-45 min. to aid dissolution, the δ-hydroxyvaleraldehyde soln. so obtained added with cooling to concd. HNO₃ containing NaNO₂, stirring continued for 90 min. with cooling, then the temp. allowed to rise to 25-30°, and worked up when the color has turned light yellow after 2-3 hrs. → glutaric acid. Y: 70-80%. J. English, Jr., and J. E. Dayan, *Org. Synth.* 30, 48 (1950).

p-Toluenesulfonic acid

TsOH

**Dicarboxylic acid esters from
 dicarboxylic acid anhydrides**

171.



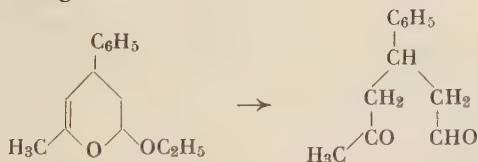
cis-4^A-Tetrahydrophthalic anhydride, commercial abs. ethanol, and some *p*-toluenesulfonic acid monohydrate refluxed 12-16 hrs. at an oil bath temp. of 95-105°, toluene added, distilled; when the vapor temp. begins to drop, more ethanol added, and refluxing with subsequent azeotropic distillation repeated → diethyl *cis*-4^A-tetrahydrophthalate. Y: 83-86%. F. e. s. A. C. Cope and E. C. Herrick, *Org. Synth.* 30, 29 (1950); *Am. Soc.* 72, 983 (1950); s. a. E. C. Schreiber and E. J. Becker, *Am. Soc.* 72, 4829 (1950).

Hydrochloric acid

HCl

Pyran ring opening

172.



2-Ethoxy-6-methyl-4-phenyl-3,4-dihydro-2H-pyran (prepn. s. 696) and HCl in acetone-water warmed at 35° until it becomes homogeneous and thereafter at 40° for 1 hr. → 5-oxo-3-phenylhexanal. Y: 85%. F. e. s. R. I. Longley, Jr., and W. S. Emerson, *Am. Soc.* 72, 3079 (1950).

Cobalt(II)-acetate/peracetic acid

 $(\text{CH}_3\text{COO})_2\text{Co}/\text{CH}_3\text{COO}_2\text{H}$ **Oxidative ring opening**

173.



A soln. of peracetic acid in glacial acetic acid added at 0-10° with stirring and cooling to a soln. of pyrocatechol in glacial acetic acid, after 10 min. a soln. of Co(II)-acetate in glacial acetic acid added, and worked up after 4-5 days → muconic acid. Y: 65-85%.—With more peracetic acid muconyl acetyl peroxide is formed in a yield of 60-66%. A. Wacek and R. Fiedler, M. 80, 170 (1949).

Addition to Nitrogen and Carbon

OC↓NC

Without additional reagents

w.a.r.

Acylcarbamates from isocyanates

NCO → NHCOOAc



50 gm. glacial acetic acid added dropwise at 8-15° to a soln. of 50 gm. hexamethylene di-isocyanate in benzine, and filtered by suction after $\frac{3}{4}$ hrs. → 80 gm. diacetyl hexamethylenedicarbamate. F. e. s. S. Petersen, A. 562, 205 (1949).

Sodium hydroxide

NaOH

Pseudobases

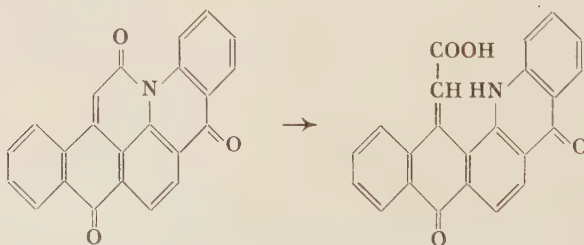
←

s. 6, 820

Pyridone ring opening

C

175.



Anthrapyridonacridone boiled in 10% aq.-alc. (1 : 1) NaOH for 5 min. → 9-methyleneanthronacridone- ω -carboxylic acid. Y: 84.6%. F. e. s. A. M. Lukin and P. M. Aronovich, Ж. 19, 362 (1949); C. A. 44, 1080c.

Sodium/alcohol

NaOR

Isoureas from cyanamides

←

176.



12.1 gm. methylisopropylecyanamide added to a soln. of Na in methanol, and stirred 2 hrs. at 50-55° → 10.4 gm. O,N-dimethyl-N-isopropylisourea. F. e. s. F. H. S. Curd, D. G. Davey, and D. N. Richardson, Soc. 1949, 1732.

Triethylamine

(C₂H₅)₃N**Urethans from phenols**

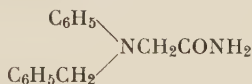
OH → OCONHR

s. 5, 125; s. a. J. M. Lyons and R. M. Thomson, Soc. 1950, 1971

Sulfuric acid

H₂SO₄**Carboxylic acid amides from nitriles**CN → CONH₂

177.



Cold N-benzyl-N-phenylglycinonitrile added dropwise to concd. H₂SO₄ cooled to -8°, and allowed to stand 72 hrs. at room temp. → N-benzyl-N-phenyl-glycinamide. Y: 90%. F. e. s. R. A. Turner and C. Djerassi, Am. Soc. 72, 3081 (1950).

Potassium ferricyanide

K₃[Fe(CN)₆]**2-Pyridone ring from N-alkylpyridinium ring**

←

s. 2, 264; 3, 226; s. a. V. Petrow and W. R. Wragg, Soc. 1950, 3516

Addition to Sulfur and Carbon

OC↓SC

Hydrochloric acid

HCl

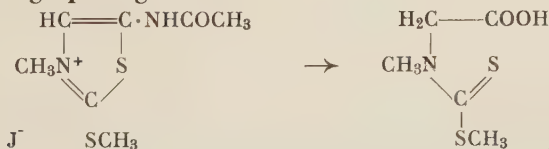
Piperidone ring opening

C

s. 4, 159; s. a. R. Gaudry and L. Berlinguet, Can. J. Research 28 B, 245 (1950)

Thiazole ring opening

178.



2-Methylmercapto-3-methylthiazolium iodide (prepn. s. 378) refluxed 1 hr. with 2 N HCl → N-dithiocarbomethoxy-N-methylglycine. Y: 86%. F. e. s. A. H. Cook and S. F. Cox, Soc. 1949, 2337.

Addition to Carbon**OC ↓ CC***Sodium**Na***Ethers from ethylene derivatives** $C:C \rightarrow CHC(OR)$

179. cf. Synth. Meth. 3, 128.

The order of activity in the addition of hydroxy compounds to alkyl acrylates is phenols > prim. alcohols > sec. alcohols. Tert. alcohols did not react. E. s. C. E. Rehberg and M. B. Dixon, Am. Soc. 72, 2205 (1950).

s. a. D. D. Coffman et al., J. Org. Chem. 14, 747 (1949); fluoro compounds s. A. L. Henne and M. A. Smook, Am. Soc. 72, 4378 (1950)

Alkali hydroxide

←

Dicarboxylic acids and cyclic ketones from β-ketocarboxylic acid esters

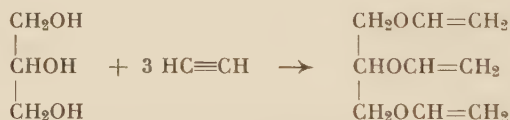
←

s. 2, 160; s. a. R. Fusco and R. Trave, G. 80, 496 (1950)

*Potassium hydroxide**KOH***Vinyl ethers**

←

180.



Glycerol, powdered KOH, and acetylene heated at 180-190° and 10 atm. in a rotating autoclave, with repeated addition of acetylene until absorption stops → glyceryl trivinyl ether. Y: 90.3%. M. F. Shostakovskii and E. P. Gracheva, Ж. 19, 1250 (1949); C. A. 44, 3439a.

*Potassium hydroxide in alcohol***3-Alkoxythianaphthene 1,1-dioxides, 2,3-dihydro- from thianaphthene 1,1-dioxides** $C:C \rightarrow CHC(OR)$

181.



The 2-3 bond in thianaphthene 1,1-dioxide has no aromatic character and gives reactions typical of an α,β-unsatd. sulfone.—E: A soln. of thianaphthene 1,1-dioxide, KOH, and ethanol refluxed 24 hrs. → 3-ethoxy-2,3-dihydrothianaphthene 1,1-dioxide. Y: 94%. F. e. s. F. G. Bordwell and W. H. McKellin, Am. Soc. 72, 1985 (1950).

Sodium/alcohol

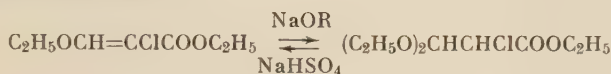
NaOR

Acetals from enolethers

←

 α -Halogenacetals**Enolethers from acetals**

182.



A soln. of a small amount of Na in anhydrous ethanol added to an alc. soln. of ethyl α -chloro- β -ethoxyacrylate, warmed to 60°, and held at 50-60° for 1 hr. $\rightarrow$ ethyl α -chloro- β,β -diethoxypropionate (Y: 69.7 to 77%) distilled from NaHSO₄ $\rightarrow$ ethyl α -chloro- β -ethoxyacrylate (Y: 66.5%). W. J. Croxall and M. F. Fegley, Am. Soc. 72, 2888 (1950).

Pyridine

C₅H₅N**Lactolesters from hydroperoxides**

←

s. 5, 133; also isolation of the intermediate acyl peroxide s. A. C. Cope and G. Holzman, Am. Soc. 72, 3062 (1950)

Silver benzoate/iodine

C₆H₅COOAg/I**Glycols from ethylene derivatives**C:C $\rightarrow$ C(OH)C(OH)**Stereoisomers**

183. **Stereoisomers.** The reaction of ethylene derivatives with Prévost reagent (Ag-benzoate, iodine) is stereospecific and yields the *trans*-isomer. M. Sletzing and C. R. Dawson, J. Org. Chem. 14, 849 (1949); cf. Synth. Meth. 1, 146.

Performic acid

HCOO₂H

s. 5, 138; s. a. L. F. Fieser and S. Rajagopalan, Am. Soc. 71, 3938 (1949); J. B. Brown, H. B. Henbest, and E. R. H. Jones, Soc. 1950, 3634

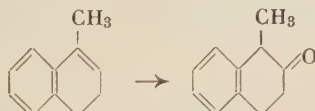
Peracetic acid/ozone s. Ozone/peracetic acid

CH₃COO₂H/O₃

Perbenzoic acid

C₆H₅COO₂H**Ketones from ethylene derivatives**C:CH $\rightarrow$ CHCO

184.



A soln. of 4-methyl-1,2-dihydronaphthalene in chloroform added with ice-cooling to a soln. of perbenzoic acid in chloroform, and worked up after 3 hrs. $\rightarrow$ 4-methyl-3-tetralone. Y: 84%. H. Hock, Shon Lang, and G. Knaul, B. 83, 227 (1950); s. a. H. E. Zaugg, M. Freifelder, and B. W. Horrom, J. Org. Chem. 15, 1197 (1950).

Carboxylic acid esters from ketones ←

s. 4, 169; modification and simultaneous protection of a carbon carbon double bond s. P. Wieland and K. Miescher, *Helv.* 32, 1768, 1922 (1949); stereoisomers s. R. B. Turner, *Am. Soc.* 72, 878 (1950)

Red lead oxide Pb_3O_4 **via glycol diacetates**

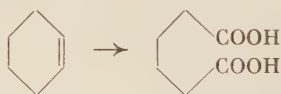
Anethole reacted with Pb_3O_4 in glacial acetic acid below 40° , and the glycol acetate so obtained boiled 4 hrs. with 20% $H_2SO_4 \rightarrow$ anisylacetone. Y: 65%. A. Buzas and C. Dufour, *Bl.* 1950, 139.

Lead tetraacetate/potassium carbonate $(CH_3COO)_4Pb/K_2CO_3$ **Oxidative ring opening** C

s. 6, 842

*Ammonium vanadate*s. 4, 170; s. a. J. Golé, *Bl.* 1949, 894.*Ozone* O_3 **of indoles**s. 2, 168; s. a. C. Mentzer, D. Molho, and Y. Berguer, *Bl.* 1950, 782*Ozone/peracetic acid* O_3/CH_3COO_2H **Oxidative ring opening****Cleavage of ozonides**

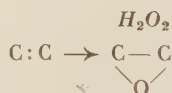
186.



Cyclohexene ozonized at -50° in methyl acetate, then peracetic acid in glacial acetic acid added, the low boiling solvent distilled off at 50° under slightly reduced pressure, more peracetic acid added, kept 12 hrs. at $50-60^\circ$, finally refluxed 1 hr. $\rightarrow$ adipic acid. Y: 86.2-90.3%. F. e. s. H. Wilms, *A.* 567, 96 (1950).

Hydrogen peroxide **α,β -Oxidoketones from chalcones**

s. 6, 192, 901

**o-Hydroxyethers from xanthidols** ←

s. 6, 162

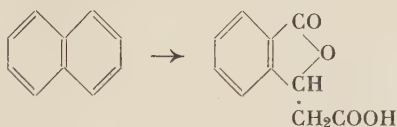
Hydrogen peroxide/ammonium molybdate

 H_2O_2/NH_4MoO_4 **Phthalides from naphthalene ring**

C

Oxidative ring opening

187.

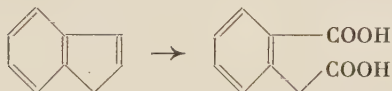


30% H_2O_2 slowly added over a period of 4 hrs. to a gently refluxing soln. of naphthalene and NH_4 -molybdate in glacial acetic acid $\rightarrow$ β -hydroxy- β -o-carboxyphenylpropionic acid lactone. Y: 69% (43% without molybdate). I. D. Raake-Fels et al., *J. Org. Chem.* **15**, 627 (1950).

Chromic acid

 CrO_3 **Oxidative ring opening**

188.



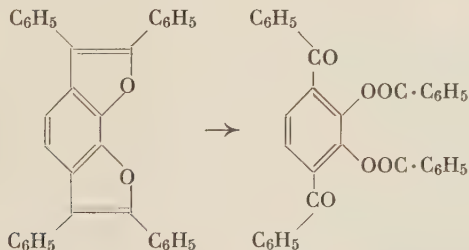
Technical ca. 90%-indene added dropwise at $65 \pm 2^\circ$ to an aq. soln. of $K_2Cr_2O_7$ and H_2SO_4 , then stirred 2 hrs. more at the same temp. $\rightarrow$ homophthalic acid (startg. m. f. 297). Y: 66-77%. O. Grummitt, R. Egan, and A. Buck, *Org. Synth.* **29**, 49 (1949); acenaphthene ring opening s. H. E. Nürsten and A. T. Peters, *Soc.* **1950**, 729.

Ketocarboxylic acids

s. 4, 173; s. a. J. R. Schaeffer and A. O. Snoddy, *Org. Synth.* **31**, 3 (1951)

Furan ring opening

189.



10% excess CrO_3 added to a boiling suspension of tetraphenyl-o-benzodifuran in glacial acetic acid over a period of 1 hr., and boiling continued for 15 min. $\rightarrow$ 2,3-bis(benzoxy)-1,4-dibenzoylbenzene. Y: almost 100%. Also partial ring opening s. O. Dischendorfer et al., *Ж.* **80**, 741 (1949); **81**, 725 (1950); **82**, 1 (1951).

*Pertungstic acid*W₂O₃**Glycols from ethylene derivatives**

C:C → C(OH)C(OH)

cis-trans-Isomers

190. Whereas OsO₄ gives *cis*-glycols, W₂O₃, V₂O₅, and SeO₂ give *trans*-glycols.—E: A mixture of cyclohexene, 30% -H₂O₂, W₂O₃, and glacial acetic acid stirred 5-6.5 hrs. at 50° → *trans*-1,2-cyclohexanediol. Y: 74% (77% in the presence of 2 drops H₂SO₄). F. e. s. M. Mugdan and D. P. Young, Soc. 1949, 2988.

*Iodine/silver benzoate s. Silver benzoate/iodine*I/C₆H₅COOAg*Hydrochloric acid*

HCl

β-Alkoxyacetals from α,β-ethylene aldehydes

←

s. 6, 220

*Potassium permanganate*KMnO₄**α-Diketones from acetylene derivatives**

C:C → COCO

191.
$$\begin{array}{ccccccc} (\text{CH}_3)_2\text{C} \cdot \text{C} \equiv \text{C} \cdot \text{C}(\text{CH}_3)_2 & \rightarrow & (\text{CH}_3)_2\text{C} \cdot \text{COCO} \cdot \text{C}(\text{CH}_3)_2 \\ \text{OAc} & & \text{OAc} & & \text{OAc} & & \text{OAc} \end{array}$$

2,5-Dimethyl-3-hexyne-2,5-diol diacetate and KMnO₄ in water stirred ca. 2 hrs. with ice-water cooling → 2,5-dimethylhexane-3,4-dione-2,5-diol diacetate. Y: 67%. G. Dupont, R. Dulou, and D. Lefort, Bl. 1949, 789.

*Osmium tetroxide*OsO₄**Pyrazine ring degradation**

↻

s. 6, 41

Rearrangement

Hydrogen/Oxygen Type

OC↷HO

Hydrogen halides

HHal

Lactones from ethylenecarboxylic acids

←

s. 5, 149; s. a. Am. Soc. 72, 514 (1950)

Hydrogen/Carbon Type

OC↷HC

Potassium hydroxide

KOH

α-Diketones from chalcones via

COCO

α,β-oxidoketones

192.
$$\text{C}_6\text{H}_5\text{CH}=\text{CHCO} \begin{array}{c} \text{H}_3\text{C} \quad \text{NO}_2 \\ \diagdown \quad \diagup \\ \text{---} \text{C} \quad \text{C} \text{---} \\ \diagup \quad \diagdown \\ \text{H}_3\text{C} \end{array} \text{CH}_3 \rightarrow \text{C}_6\text{H}_5\text{CH}-\overset{\text{O}}{\text{CHCO}} \lt \rightarrow \text{C}_6\text{H}_5\text{CH}_2\text{COCO} \lt$$

15% -H₂O₂ added at 20° to a soln. of benzal-3-nitroacetomesitylene in alcohol containing an equivalent amount of 6 N KOH, and stirring

continued for 1.5 hrs. $\rightarrow$ 1-(3-nitromesityl)-2-phenylethylene oxide (Y: 86%) dissolved in alcohol, and boiled 1.5 hrs. with 1.5 mole *N* KOH $\rightarrow$ 3-nitromesityl benzyl ketone (Y: 75%). F. e. s. R. P. Barnes and L. A. Gist, Jr., Am. Soc. 72, 2509 (1950).

Zinc

Zn

Ketones from glycol acetates $\leftarrow$ **Serini reaction**

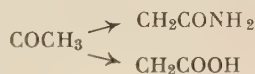
from monoacetates s. 5, 150; from diacetates s. C. Djerassi and C. R. Scholz, Am. Soc. 71, 3962 (1949)

Titanium tetrachloride $TiCl_4$ **Change of configuration of carbohydrates** $\leftarrow$

193. Cyclohexyl tetraacetyl- β -glucoside and $TiCl_4$ in abs. chloroform gently refluxed for not more than 75 min. $\rightarrow$ cyclohexyl tetraacetyl- α -glucoside. Y: 80%. E. Pascu, Am. Soc. 52, 2568 (1930); s. a. B. Lindberg, Acta Chem. Scand. 3, 151 (1949).

Ammonium polysulfide $(NH_4)_2S_x$

**Carboxylic acid amides and
carboxylic acids from
methyl ketones**

**Willgerodt reaction**

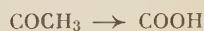
s. 1, 151/2; 2, 180/a; s. a. E. V. Brown and J. A. Blanchette, Am. Soc. 72, 3414 (1950)

Sulfuric acid H_2SO_4 **Ketones from glycol acetates**

s. 6, 185

*Via intermediates**v.i.*

**Carboxylic acids from methylketones
via thioamides**

**Willgerodt-Kindler reaction**

s. 2, 181; 3, 141; s. a. C. C. Price and B. D. Halpern, Am. Soc. 73, 818 (1951)

Interconversion via oxazolines $\leftarrow$

s. 5, 154; s. a. Am. Soc. 73, 1216 (1951); trans-cis rearrangement s. S. Winstein and R. Boschan, Am. Soc. 72, 4669 (1950)

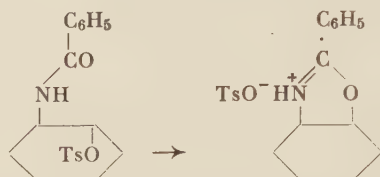
Oxygen/Carbon Type*Acetic acid*

OC ↷ OC

CH₃COOH**Oxazoline ring**

○

194.



trans-2-Benzamidocyclohexyl p-toluenesulfonate heated several min. in glacial acetic acid $\rightarrow$ 2-phenyl-4,5-tetramethylenesoxazolinium p-toluenesulfonate. Y: 95%. S. Winstein, L. Goodman, and R. Boschan. Am. Soc. 72, 2311 (1950).

Nitrogen/Carbon Type*Without additional reagents*

OC ↷ NC

*w.a.r.***Aminocarboxylic acid esters from betaines**

←

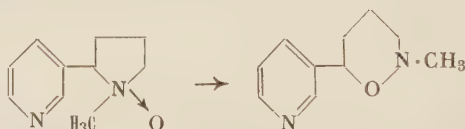
s. 6, 222

1,2-Oxazines from pyrrole N-oxides

←

Ring enlargement

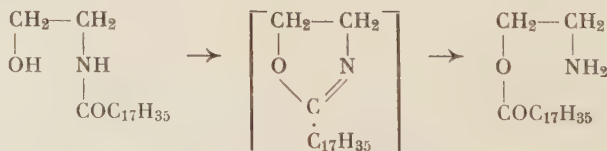
195.



Nicotine oxide distilled at an oil bath temp. of 190-200° and 1 mm. pressure, and the reaction product isolated as dihydrochloride $\rightarrow$ 2-methyl-6-(3-pyridyl)tetrahydro-1,2-oxazine (startg. m. f. 28). Y: 57%. C. H. Rayburn, W. Harlan, and H. R. Hanmer. Am. Soc. 72, 1721 (1950).

*Thionyl chloride*SOCl₂**Acyl migration**NAc $\rightarrow$ OAc**O-Acyl from N-acyl**

196.



Oxazolines as intermediates. N-Stearoyl-2-ethanolamine warmed at 50° with 1.25 mole SOCl₂ for ca. 1 hr., SOCl₂ distilled off in vacuo, the residue dissolved in water, and heated 0.5 hr. on a water bath $\rightarrow$ O-stearoyl-2-ethanolamine (isolated as hydrochloride). Y: ca. 100%. P. Desnuelle, M. Naudet, and E. Sambuc, Bl. 1949, 650.

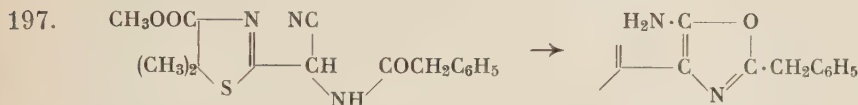
Hydrochloric acid

HCl

s. 1, 154; s. a. L. H. Welsh, Am. Soc. 71, 3500 (1949); H. Bretschneider et. al., M. 81, 31 (1950)

Oxazoles from α -acylaminonitriles

○



19.8 gm. methyl 5,5-dimethyl-2-[(phenylacetamino)cyanomethyl]-thiazoline-4-carboxylate in ethyl acetate and ether containing HCl allowed to stand for 20 hrs. $\rightarrow$ 21.3 gm. 5-amino-2-benzyl-4-(4-carbomethoxy-5,5-dimethyl-2-thiazolin-2-yl)oxazole hydrochloride.—This isomerization can be reversed with bases. F. e. s. A. H. Cook, G. Harris, and A. L. Levy, Soc. 1949, 3227.

Carbon/Carbon Type

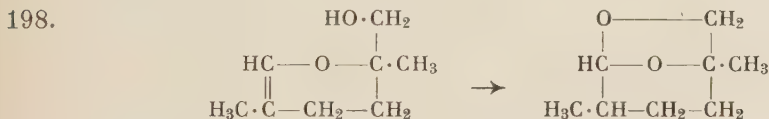
OC $\curvearrowright$ CC

Without additional reagents

w.a.r.

m-Dioxane ring

○

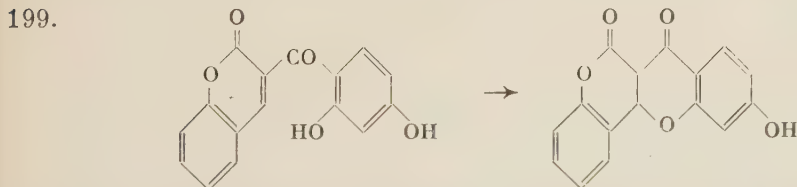


3,4-Dihydro-2,5-dimethyl-2H-pyran-2-methanol refluxed 90 min. until the boiling point has decreased to a constant value $\rightarrow$ 1,4-dimethyl-6,8-dioxabicyclo[3.2.1]octane. Y: 86%. G. G. Stoner and J. S. McNulty, Am. Soc. 72, 1531 (1950).

Acetic acid

CH₃COOH

Chromono(3',2',3,4)coumarin ring



2',4'-Dihydroxy-3-benzoylcoumarin dissolved in boiling acetic acid, and allowed to cool $\rightarrow$ 7'-hydroxy-3,4-dihydrochromanono(3',2',3,4)-coumarin. Y: almost 100%. F. e. s. G. Parker and A. Robertson, Soc. 1950, 1121.

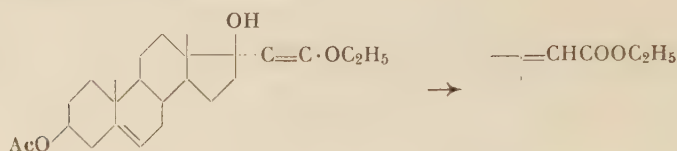
Sulfuric acid

 H_2SO_4

α, β -Ethylenecarboxylic acid esters
from alkoxyacetylenealcohols

←

200.



A soln. of 300 mg. Δ^5 - 3β -acetoxy- 17β -hydroxy- 17α -ethoxyethynylandrosterone in dioxane shaken 25 min. with 10%-aq.- H_2SO_4 at room temp. $\rightarrow$ 210 mg. ethyl $\Delta^{5,17(20)}$ - 3β -acetoxypregnadiene-21-carboxylate. H. Heusser, K. Eichenberger, and P. A. Plattner, *Helv.* **33**, 1088 (1950); s. a. A. Caliezi and H. Schinz, *Helv.* **33**, 1129 (1950).

Exchange

Hydrogen $\uparrow$ $\text{OC} \uparrow \text{H}$

Sodium polysulfide

 Na_2S_x

Aminoaldehydes from nitrohydrocarbons

←

s. 1, 162; s. a. E. Campaigne, W. M. Budde, and G. F. Schaeffer, *Org. Synth.* **31**, 6 (1951)

Nitric acid/sodium nitrite

 $\text{HNO}_3/\text{NaNO}_2$

Carboxylic acids from alcohols

 $\text{CH}_2\text{O} \rightarrow \text{COOH}$

s. 6, 170

Selenium dioxide

 SeO_2

Ketones from hydrocarbons

 $\text{CH}_2 \rightarrow \text{CO}$

s. 1, 164; 2, 186; s. a. A. G. Caldwell, F. C. Copp, and L. P. Walls, *Soc.* **1950**, 2698

 α -Diketones from ketones $\text{COCH}_2 \rightarrow \text{COCO}$

s. 4, 190; s. a. W. van der Haar, R. C. Voter, and C. V. Banks, *J. Org. Chem.* **14**, 836 (1949)

Chromic acid

 CrO_3

Carboxylic acids from alcohols

 $\text{CH}_2\text{OH} \rightarrow \text{COOH}$

s. 6, 233

*Hydrobromic acid**HBr***Oxidation of hydrocarbons
Ketones and hydroperoxides from
hydrocarbons**

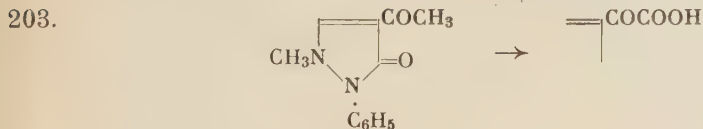
←



The gas phase O_2 -oxidation of the lower hydrocarbons is greatly modified by the presence of HBr . Straight-chain paraffins are converted mainly to ketones, and branched-chain compounds to stable peroxides. The character of the product is determined principally by the most reactive C-H linkage. The reactivity of this linkage increases markedly in the order—primary, secondary, and tertiary. The oxidation is accompanied by a low degree of C-C bond scission, the operating temp. is low, and the conversions and yields are high.—Propane at $189^\circ \rightarrow$ acetone. Y: 71.6%.—Isobutane at $163^\circ \rightarrow$ tert-butyl hydroperoxide. Y: 69.5%. F. e. s. F. F. Rust, W. E. Vaughan et al., *Ind. Eng. Chem.* 41, 2595-2612 (1949).

*Potassium permanganate**KMnO₄***Ketones from hydrocarbons** $\text{CH}_2 \rightarrow \text{CO}$ 

KMnO_4 added in portions at 70° to a stirred aq. suspension of 2-benzylpyridine, then the temp. raised to 100° until all the KMnO_4 has reacted $\rightarrow$ 2-benzoylpyridine. Y: 86%. E. H. Huntress and H. C. Walter, *Am. Soc.* 70, 3702 (1948); method, see K. E. Crook and S. M. McElvain, *Am. Soc.* 52, 4006 (1930); s. a. K. Schofield, *Soc.* 1949, 2408.

 α -Ketocarboxylic acids from methyl ketones $\text{COCH}_3 \rightarrow \text{COCO}_2\text{H}$ 

A satd. soln. of KMnO_4 slowly added at 40° to an aq. soln. of 1-phenyl-2-methyl-4-acetyl-5-pyrazolone and KOH , and worked up after the color has disappeared $\rightarrow$ 1-phenyl-2-methyl-5-pyrazolone-4-glyoxylic acid. Y: 80%. F. e. s. K. Bodendorf and A. Popelak, *A.* 566, 84 (1950).

Carboxylic acid amides from amines $\text{CH}_2\text{NR}_2 \rightarrow \text{CONR}_2$

s. 2, 190; s. a. *Soc.* 1951, 303

*Via intermediates**v.i.***Carboxylic acids from alcohols
via aldehydes** $\text{CH}_2\text{OH} \rightarrow \text{COOH}$

s. 6, 292

Oxygen †**OC H O***Without additional reagents**w.a.r.***Carboxylic acid esters from carboxylic acids** $\text{COOH} \rightarrow \text{COOR}$

s. 5, 166; under a slight vacuum s. J. Colonge and P. Stuchlik, *Bl.* 1950, 586; azeotropic removal of the water formed s. E. E. Burgoyne and F. E. Condon, *Am. Soc.* 72, 3276 (1950); R. N. Smith and W. V. Bolliger, *J. Chem. Education* 27, 369 (1950)

*Potassium hydroxide***KOH****Nitronates**

←

204.



A. soln. of 6-nitro-4-hydroxycinnoline in the minimum quantity of 2%-aq.-KOH treated with dimethyl sulfate at 50° with stirring, and worked up after 15 min. → methyl 4-cinnolone-6-nitronate. Y: 55%. F. e. s. J. R. Keneford et al., *Soc.* 1950, 1104.

*Sodium acetate***CH₃COONa****Acetylation****OH → OAc**

s. 2, 193; 3, 158; carbohydrates s. M. L. Wolfson, W. L. Shilling, and W. W. Binkley, *Am. Soc.* 72, 4544 (1950)

Diene synthesis via enolesters

←

s. 6, 695

*Potassium acetate***CH₃COOK****Enol acetates from aldehydes** $\text{CHCHO} \rightarrow \text{C:CH(OAc)}$

s. 6, 214, 575

*Ammonia***NH₃****6-Alkoxy-5,6-dihydrophenanthridines****OH → OR**

s. 6, 820

Pyridine C_5H_5N **Propionates** $OH \rightarrow OAc$

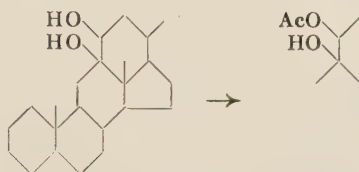
s. 2, 198; of carbohydrates s. V. Deulofeu and F. Giménez, *J. Org. Chem.* 15, 460 (1950)

Unsatd. esters of sucrose $OH \rightarrow OCOCH:CHCH_3$

205. Crotonic anhydride added slowly with rapid stirring at 70-75° to a mixture of sucrose and pyridine, heated 5 hrs. at 80-90°, and left overnight at room temp. $\rightarrow$ octacrotonylsucrose. Y: 95%. F. e., also with carboxylic acid chlorides, s. M. Zief, *Am. Soc.* 72, 1137 (1950).

Selective acylation

206.



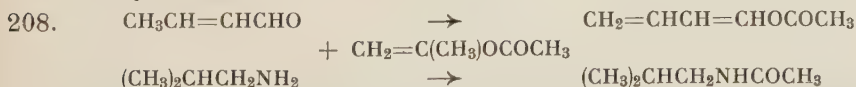
Acetic anhydride added to a soln. of 12,23-dihydroxydehydronorcholane in pyridine, and allowed to stand 24 hrs. at room temp. $\rightarrow$ 23-acetoxy-12-hydroxydehydronorcholane. Y: 90%.—Only the sec. hydroxyl group is esterified. A. Butenandt and H. Dannenberg, *A.* 568, 83 (1950).

Enol esters

207.

 $C:CH(OAc)$

Acetic anhydride added to a soln. of 0.5 gm. 2-hydroxy-3-phenyl-2-cyclohexeneglyoxylic acid γ -lactone (prepn. s. 746) in pyridine, and refluxed 3 min. $\rightarrow$ 0.52 gm. enol acetate. F. e. s. W. E. Bachmann, G. I. Fujimoto, and L. B. Wick, *Am. Soc.* 72, 1995 (1950); s. a. R. Kuhn and K. Dury, *A.* 571, 44 (1950).

Cupric acetate $(CH_3COO)_2Cu$ **Reactions with isopropenyl acetate****Acetylation, enol acetates****Acetylaminines**

Isopropenyl acetate is an excellent acetylating agent, which is decomposed into the original components, ketene and acetone, by heating in

the presence of acid catalysts. It is superior to ketene and acetic anhydride for enol acetylation and it reacts with all enolizable carbonyl compounds. It is particularly useful for acetylation under mild conditions.—E: Crotonaldehyde added to isopropenyl acetate containing some p-toluenesulfonic acid and a little Cu-acetate over a period of 2-3 hrs., while the acetone formed is distilled off $\rightarrow$ 1-acetoxy-1,3-butadiene. Y: 90%.—Similarly: Isobutylamine added to isopropenyl acetate $\rightarrow$ N-isobutylacetamide. Y: 94%. F. e. and reactions s. H. J. Hagemeyer, Jr., and D. C. Hull, *Ind. Eng. Chem.* **41**, 2920 (1949).

Boron fluoride**Acylation**

s. **1**, 177; **2**, 202; s. a. L. F. Fieser and S. Rajagopalan, *Am. Soc.* **71**, 3938 (1949); T. W. Campbell and G. M. Coppinger, *Am. Soc.* **73**, 2708 (1951).

Carboxylic acid esters from carboxylic acids

209. BF_3 -ethyl ether complex added slowly below 40° to a suspension of 4-amino-2-hydroxybenzoic acid in anhydrous isopropanol, and allowed to stand at room temp. for several days $\rightarrow$ isopropyl 4-amino-2-hydroxybenzoate. Y: 75%.—Other methods gave very low yields, the primary product being m-aminophenol. F. e. s. J. J. Schaefer and L. Doub, *Am. Soc.* **71**, 3564 (1949).

Bauxite

s. **6**, 420

Acetic anhydride

210.
$$C_6H_5CH(CH_3)C_6H_4OH + HOOC \cdot CH_2CH_3 \rightarrow C_6H_5CH(CH_3)C_6H_4OOC \cdot CH_2CH_3$$

A mixture of p-(α -phenylethyl)phenol, propionic acid, and acetic anhydride refluxed ca. 0.5 hr., then the acetic acid formed distilled off $\rightarrow$ p-(α -phenylethyl)phenyl propionate. Y: 93%. F. e. s. K. C. Frisch, *J. Org. Chem.* **15**, 587 (1950).

Trifluoroacetic anhydride

211. **Acylation of hydroxy compounds.** Esters can be produced from alcohols and phenols by treatment with carboxylic acids in the presence of trifluoroacetic anhydride. The method can be used to esterify carboxylic acids in both the aliphatic and the aromatic series. In many cases the reaction proceeds spontaneously and is essentially complete within a few minutes. The general conditions of the reaction are relatively mild and enable, for example, acyl derivatives to be prepared

in good yield from acid-labile glycosides. The method is particularly convenient for the acylation of polysaccharides and also for the production of poly-esters.—E: Trifluoroacetic anhydride introduced into a mixture of D-mannitol and glacial acetic acid, and allowed to cool slowly $\rightarrow$ D-mannitol hexaacetate. Y: 80%.—Palmitic acid and trifluoroacetic anhydride mixed, kept at room temp. for 30 min., β -naphthol added, and worked up after 45 min. at room temp. and 5 min. at 50° $\rightarrow$ β -naphthyl palmitate. Y: 85%. F. e. s. E. J. Bourne et al., Soc. 1949, 2976.

Methyl iodide

CH₃I

Ketals with simultaneous formation of sulfonium salts

←

212.



Thiacyclohexan-4-one in refluxing methanol treated with methyl iodide, and refluxing continued for 2.5 hrs. $\rightarrow$ 4,4-dimethoxythiacyclohexane methiodide. Y: 78%.—The ketomethiodide can be obtained at room temp. F. ketals s. H. M. E. Cardwell, Soc. 1950, 1059.

Ammonium nitrate

NH₄NO₃

α,β -Ethyleneacetals from

CHO $\rightarrow$ CH(OR)₂

α,β -ethylenealdehydes

s. 6, 220

Phosphorus pentoxide

P₂O₅

Carboxylic acid esters from carboxylic acids

COOH $\rightarrow$ COOR

213. Methacrylic acid (prepn. s. 292) refluxed 4 hrs. with excess methanol in the presence of P₂O₅ $\rightarrow$ methyl methacrylate. Y: ca. 100%. J. M. Church and L. Lynn, Ind. Eng. Chem. 42, 768 (1950).

Ozone

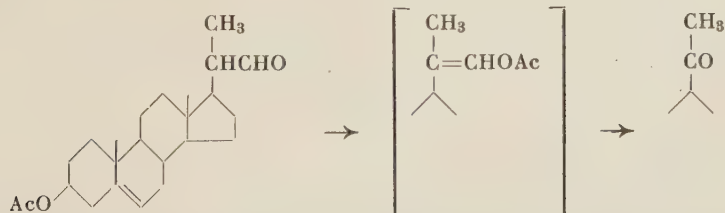
O₃

Ketones from aldehydes via enolesters

←

Degradation with loss of 1 C-atom

214.



A mixture of 3 β -acetoxybisnor-5-cholenaldehyde, acetic anhydride, and freshly fused Na-acetate refluxed 8 hrs. under N₂, evaporated to

dryness under reduced pressure, redissolved in chloroform, the insoluble Na-acetate removed by filtration, ozonized with ice-cooling for 22 min., chloroform removed in vacuo, and the ozonide decomposed with Zn-dust and glacial acetic acid in the presence of ether $\rightarrow$ 5-pregnene-3 β -ol-20-one acetate. Y: 57%. F. e. s. F. W. Heyl and M. E. Herr, Am. Soc. 72, 2617 (1950).

p-Toluenesulfonic acid

TsOH

Enolethers

C:C(OR)

215.



A mixture of methone, abs. ethanol, benzene, and a small amount of *p*-toluenesulfonic acid refluxed under a continuous water separator until no more water was formed $\rightarrow$ 5,5-dimethyl-3-ethoxy-2-cyclohexenone. Y: 83%. F. e. s. R. L. Frank and H. K. Hall, Jr., Am. Soc. 72, 1645 (1950).

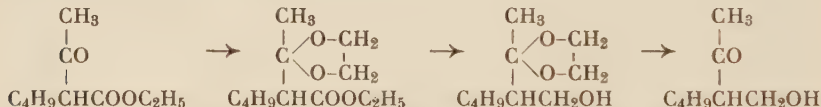
β -Hydroxyketones from β -ketocarboxylic acid esters

$\leftarrow$

Protection of the carbonyl group

Alkylene acetals

216.



Ethyl α -butylacetoacetate, ethylene glycol, benzene, and a trace of *p*-toluenesulfonic acid refluxed 10 hrs. with separation of the water formed $\rightarrow$ ethyl α -butylacetoacetate ethyleneketal (Y: 84%) reduced with Na in abs. alcohol at an oil bath temp. of ca. 160° $\rightarrow$ 2-butyl-2-acetylethanol ethylene ketal (Y: 77%) heated 1 hr. with water-alcohol and a drop of concd. HCl on a water bath $\rightarrow$ 2-butyl-2-acetylethanol (Y: 89%).—Alkylene acetals are more stable than dialkyl acetals and can easily be prepared by the above method, which is not limited to enolizable carbonyl groups. F. e. s. L. Willmann and H. Schinz, Helv. 32, 2151 (1949); preparation of steroid ketals with toluene in place of benzene, and hydrolysis by *p*-toluenesulfonic acid s. C. A. Grob, W. Jundt, and H. Wicki, Helv. 32, 2427 (1949).

Acetylation of alcohols by azeotropic distillation

OH $\rightarrow$ OAc

217.



A mixture of trimethylene chlorohydrin, glacial acetic acid, benzene, and *p*-toluenesulfonic acid monohydrate refluxed for 7-9 hrs. with

distillation of the benzene-water azeotrope $\rightarrow$ γ -chloropropyl acetate. Y: 93-95%. C. F. H. Allen and F. W. Spangler, *Org. Synth.* 29, 33 (1949).

Sulfuric acid



Ethers from alcohols



s. 4, 201; s. a. R. C. Fuson and H. L. Jackson, *Am. Soc.* 72, 351 (1950)

Ethylidene derivatives of carbohydrates



s. 2, 205; s. a. R. C. Hockett, D. V. Collins, and A. Scattergood, *Am. Soc.* 73, 599 (1950)

Carboxylic acid esters from carboxylic acids



Azeotropic distillation

218.



A mixture of tiglic acid, abs. ethanol, benzene, and some concd. H_2SO_4 refluxed 24 hrs. in a Soxhlet extraction apparatus, the thimble of which contains $CaC_2 \rightarrow$ ethyl tiglate. Y: 74-80%. R. E. Buckles and G. V. Mock, *J. Org. Chem.* 15, 680 (1950).

with $MgSO_4$ in the thimble s. 3, 168; s. a. W. Baker and W. D. Ollis, *Soc.* 1951, 556.

Perchloric acid



Acetylation



s. 3, 171; s. a. H. Burton and P. F. G. Praill, *Soc.* 1950, 1203

of carbohydrates

Acetobromosugars

s. 6, 582

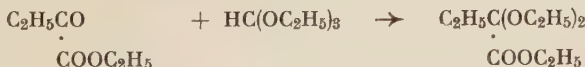
Hydrochloric acid



Acetals with orthoformate



219.



Ethyl α -ketobutyrate, orthoformate, and abs. alc. HCl allowed to stand overnight in a closed flask $\rightarrow$ ethyl α -ketobutyrate diethylketal. Y: 89%. F. e. s. E. Vogel and H. Schinz, *Helv.* 33, 116 (1950); method, s. Claisen, *B.* 29, 1005 (1896); 40, 3903 (1907).

**α,β -Ethyleneacetals and β -alkoxyacetals
from α,β -ethylenealdehydes**

←

220.



A warm soln. of NH_4 -nitrate in dry alcohol added to a mixture of acrolein and ethyl orthoformate, then refluxed 8–10 min. $\rightarrow$ acrolein diethyl acetal. Y: 73%. H. O. L. Fischer and E. Baer, *Helv.* 18, 514 (1935).



A mixture of acrolein, ethyl ortho-silicate, and abs. ethanol containing anhydrous HCl allowed to stand at room temp. for 2 weeks $\rightarrow$ β -ethoxypropionaldehyde diethyl acetal. Y: 76%. C.E. Feazel and W.G. Berl, *Am. Soc.* 72, 2278 (1950); s.a. F. Krausz, *Ann. chim.* [12] 4, 811 (1949).

Dehydration with simultaneous esterification

←

s. 6, 689; cf. L. F. Fieser and S. Rajagopalan, *Am. Soc.* 72, 5530 (1950)

Nitrogen †

OC † N

Without additional reagents

w.a.r.

**Cleavage of nitramines
Steric hindrance**

←

221.

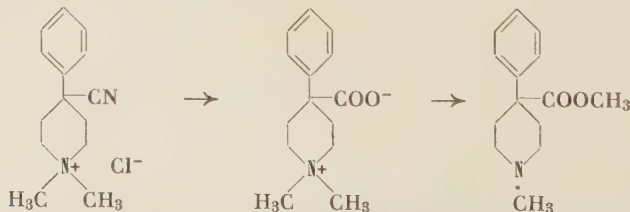


Certain sterically hindered nitramines exhibit marked instability in the presence of water.—E: N-(2-Nitroisobutyl)isopropylamine distilled with water $\rightarrow$ isopropylamine (conversion 83%) and 2-nitro-2-methyl-1-propanol (conversion 62%). F. e. s. M. Senkus, *Am. Soc.* 72, 2069 (1950).

**Aminocarboxylic acid esters
from quaternary cyanoammonium salts
via betaines**

←

222.



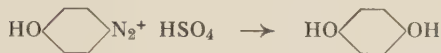
1,1-Dimethyl-4-phenyl-4-cyanopiperidinium chloride refluxed 3.5 hrs. with 1 mole of aq. NaOH $\rightarrow$ 1,1-dimethyl-1-hydroxy-4-phenylpiperidi-

nium-4-carboxylic acid betaine heated in vacuo $\rightarrow$ methyl 1-methyl-4-phenylpiperidine-4-carboxylate. Y: 81.5%.—Cyanopiperidinium salts, like the above mentioned, are quite reactive, particularly their cyano group. F. e. s. H. Kägi and K. Miescher, *Helv.* 32, 2489 (1949).

Phenols from diazonium salts

←

223.



A cooled aq. soln. of p-hydroxybenzenediazonium hydrogen sulfate irradiated with a mercury lamp $\rightarrow$ hydroquinone. Y: 88%.—Side reactions are largely avoided by irradiation of a very dilute soln. at a temp. slightly above 0° and by using a high light intensity. F. e. s. J. de Jonge and R. Dijkstra, *R.* 68, 426 (1949).

Sodium hydroxide

NaOH

Carboxylic acids from barbituric acids

C

s. 6, 290

α -Aminocarboxylic acids from hydantoins

s. 6, 761/2

Potassium hydroxide

KOH

Carboxylic acids from cyanocarboxylic acid esters

←

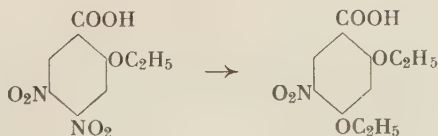
s. 6, 700

Potassium hydroxide/alcohol

Replacement of mobile nitro groups by alkoxyl

NO₂ $\rightarrow$ OR

224.

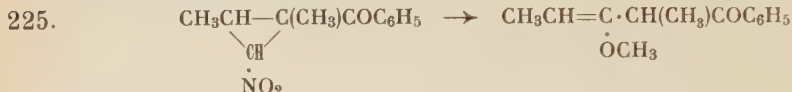


A soln. of 4,5-dinitro-2-ethoxybenzoic acid in abs. alcohol added to a soln. of KOH in abs. alcohol, and warmed at 50° for 0.5 hr. $\rightarrow$ 5-nitro-2,4-diethoxybenzoic acid. Y: 82%. H. Goldstein and R. Brochon, *Helv.* 32, 2334 (1949).

Sodium/alcohol

 $NaOR$

Nitrocyclopropane ring opening

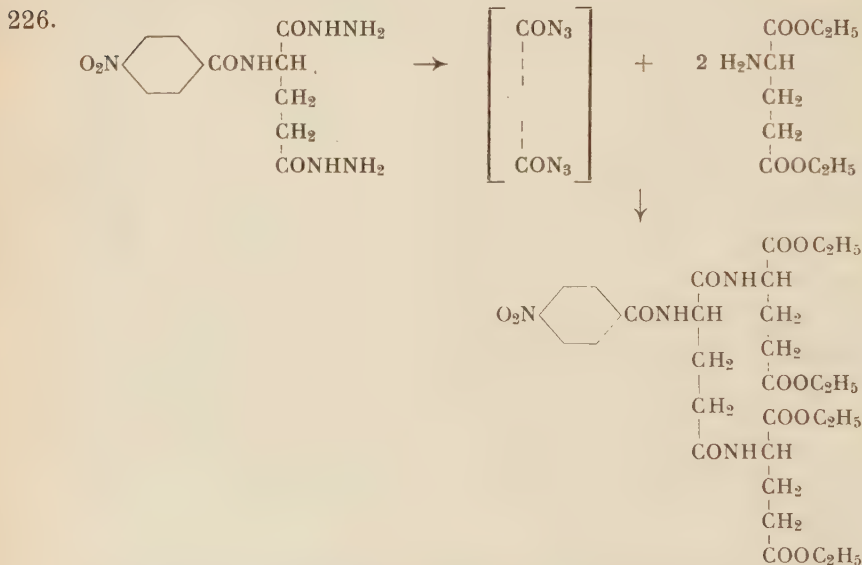
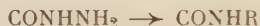


1,3-Dimethyl-2-nitro-1-cyclopropyl phenyl ketone added with stirring to a soln. of Na in dry methanol, and stirring continued for 2.5 hrs. $\rightarrow$ β -methoxy- α -methyl- β -pentenophenone. Y: 77%. F. e. s. L. I. Smith and V. A. Engelhardt, Am. Soc. 71, 2671 (1949).

Sodium hydrogen carbonate

 NaHCO_3

Subst. carboxylic acid amides from carboxylic acid hydrazides via carboxylic acid azides



A cold aq. soln. of NaNO_2 added with vigorous stirring below 5° during 25 min. to a mixture of p-nitrobenzoylglutamic acid dihydrazide, aq. HCl , and ethyl acetate, stirring continued for 40 min., the soln. in ethyl acetate of the diazide obtained added to a well stirred soln. of diethylglutamate hydrochloride in a mixture of water and NaHCO_3 , and stirring continued at room temp. for ca. 5 hrs. $\rightarrow$ p-nitrobenzoyl- α,γ -glutamylidiglutamic acid tetra ethyl ester. Y: 61%. F. e. s. J. H. Mowat et al., *Am. Soc.* 71, 2308, 2304, 2310 (1949); cf. H. Adkins, R. M. Ross, and D. C. Schroeder, *Am. Soc.* 72, 5401 (1950).

Sodium acetate CH_3COONa **Carboxylic acids from prim. nitro compounds** $CH_2NO_2 \rightarrow COOH$

227.



Na-acetate added to a soln. of phenylnitromethane in acetic anhydride, and refluxed 30 min. $\rightarrow$ triacetylhydroxylamine (startg. m. f. 387) (Y: 56%) and benzoic acid (Y: 84%). F. e. s. T. Urbanski, Soc. 1949, 3374.

Sodium nitrite $NaNO_2$

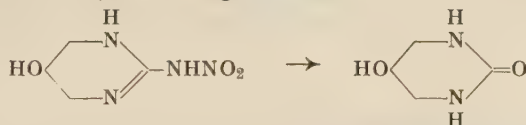
**Cleavage of nucleosides
with subsequent replacement of
amino groups by hydroxyl**
s. 6, 44

 $NH_2 \rightarrow OH$ *Ammonia* NH_3 **Carboxylic acids from barbituric acids** $\begin{array}{c} \diagup \\ \diagdown \end{array}$

228. 5-Phenyl-5-ethylbarbituric acid hydrolized with 10% aq. $NH_3 \rightarrow$ phenyl-ethylacetic acid. Y: 80%. B. Samdahl and B. Berg, Bl. 1949, 461; C. r. 228, 1894 (1949).

Benzylamine $C_6H_5CH_2NH_2$ **Cyclic ureas from cyclic nitroguanidines** $\leftarrow$

229.



2-Nitramino-5-hydroxy-1,3-diaza-2-cyclohexene refluxed 14 hrs. in water containing a small quantity of benzylamine $\rightarrow$ 4-hydroxy-2,6-diaza-1-cyclohexanone. Y: 98%. F. e. s. A. F. McKay, J. R. Coleman, and G. A. Grant, Am. Soc. 72, 3205 (1950); cf. 72, 3659.

Silver oxide Ag_2O

**Malonic acid esters from
carboxylic acid bromides via
diazo compounds**

 $\leftarrow$

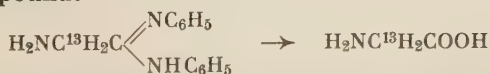
s. 6, 795

Barium hydroxide $Ba(OH)_2$

**Carboxylic acids from nitriles
Labeled compounds**

 $CN \rightarrow COOH$

230.



Methylene-labeled (N,N-diphenyl)aminoacetamidine (prepn. 74) refluxed with a 10% soln. of $Ba(OH)_2$ at an oil bath temp. of 130° for 1 hr. $\rightarrow$ methylene-labeled glycine. Y: almost 100%. G. Ehrensward and R. Stjernholm, Acta Chem. Scand. 3, 971 (1949).

Pyruvic acid $\text{CH}_3\text{COCO}_2\text{H}$ **Cleavage of hydrazones** $\text{C:N'NHR} \rightarrow \text{C:O}$

s. 6, 290, 891

Cleavage of semicarbazones $\text{C:N'NHCONH}_2 \rightarrow \text{C:O}$

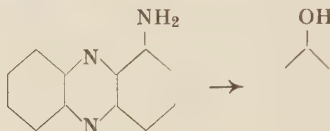
s. 6, 891

Acetic anhydride $(\text{CH}_3\text{CO})_2\text{O}$ **Acoxy compounds from tert. amines** $\text{NR}_2 \rightarrow \text{OAc}$

s. 6, 731; s. a. E. L. Eliel, Am. Soc. 73, 43 (1951)

Phosphoric acid H_3PO_4 **Replacement of amino groups by hydroxyl** $\text{NH}_2 \rightarrow \text{OH}$

231.



1-Aminophenazine heated with 3 N H_3PO_4 at 150-160° in a sealed tube for 36 hrs. $\rightarrow$ 1-hydroxyphenazine. Y: 53%.—Refluxing in an open vessel is almost without effect. B. Hegedüs, Helv. 33, 766 (1950).

Sulfur dioxide SO_2 **Replacement of amino groups by hydroxyl** $\text{NH}_2 \rightarrow \text{OH}$ **Modified Bucherer reaction**

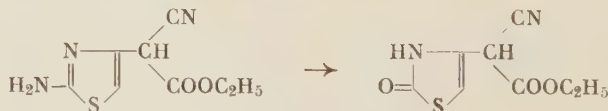
s. 4, 224; s. a. H. Rapoport, A. R. Williams, and M. E. Cisney, Am. Soc. 73, 1414 (1951)

Sulfuric acid H_2SO_4 **Carboxylic acid esters from nitriles** $\text{CN} \rightarrow \text{COOR}$

s. 3, 196; s. a. H. F. Piepenbrink, A. 572, 83 (1951)

Sulfuric acid/alcohol $\text{H}_2\text{SO}_4/\text{C}_2\text{H}_5\text{OH}$ **2-Thiazolones from 2-aminothiazoles** $\leftarrow$

232.

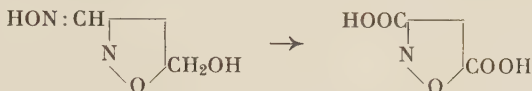


A mixture of ethyl (2-amino-4-thiazolyl)cyanoacetate, concd. H_2SO_4 , and abs. alcohol heated on a water bath for ca. 2-3 hrs. until the ester is dissolved $\rightarrow$ ethyl (thiazol-2-on-4-yl)cyanoacetate. Y: ca. 80%. H. Beyer and H. Höhn, B. 83, 14 (1950).

Chromic acid CrO_3 **Carboxylic acids from aldoximes and alcohols**

←

233.



5-Hydroxymethyl-3-isoxazolecarboxaldehyde oxime and a soln. of $\text{K}_2\text{Cr}_2\text{O}_7$ in 10% H_2SO_4 refluxed ca. 1 hr. $\rightarrow$ 3,5-isoxazoledicarboxylic acid. Y: almost 100%. F. e. s. A. Quilico and G. Stagno D'Alcontres, G. 79, 654 (1949).

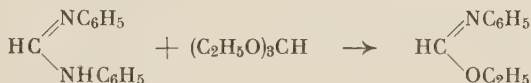
Hydrochloride

←

Iminoesters from amidines and orthoformic acid esters

←

234.



A mixture of N,N'-diphenylformamidine, ethyl orthoformate, and aniline hydrochloride refluxed 1 hr., distilled for 15 min., anhydrous K-carbonate added, shaken, and allowed to stand for 2 hrs. $\rightarrow$ ethyl N-phenylformimidate (startg. m. f. 808). Y: 96%. F. e. s. R. M. Roberts. Am. Soc. 71, 3848 (1949).

Hydrochloric acid HCl **Oxo compounds from imines** $\text{C:NH} \rightarrow \text{C:O}$

s. 6, 483

Isatins from 2-iminoisatins

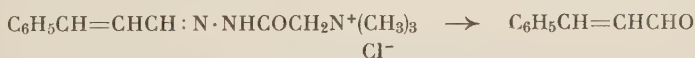
s. 6, 871

Cleavage of azomethines $\text{C:NR} \rightarrow \text{C:O}$

235. 2-Methyl-2-pentenylidene-isobutylamine (prepn. s. 741) refluxed in HCl with stirring for $\frac{3}{4}$ hr. $\rightarrow$ 2-methyl-2-pentenal. Y: 86%. F. e. s. A. M. Paquin, B. 82, 316 (1949).

Aldehydes from hydrazones $\text{CH:N}\cdot\text{NHR} \rightarrow \text{CHO}$ **Cleavage of Girard derivatives**

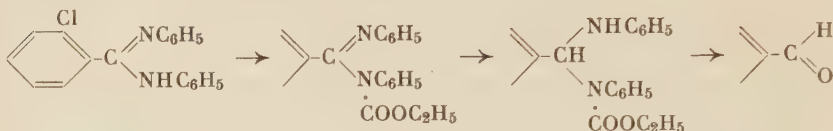
236.



Aldehyde derivatives of Girard reagents T (acetylhydrazide-trimethylammonium chloride) and P (acetylhydrazide-pyridinium chloride) are as easily hydrolyzed by 0.5-2 N HCl as the ketone derivatives.—E: Cinnamic aldehyde. Recovery: 90%. F. e. s. E. Lederer and G. Nachmias, Bl. 1949, 400.

Aldehydes from amidines**via 1,1-diamines****N-Carbethoxyamidines****Preparation of aluminum amalgam**

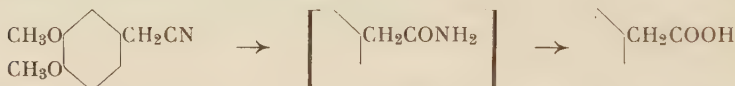
237.



4.8 gm. ethyl chloroformate slowly added with cooling to a soln. of 15 gm. *N,N'*-diphenyl-*o*-chlorobenzamidine in dry benzene containing NaHCO_3 , and kept overnight at $0^\circ \rightarrow$ 8 gm. *N,N'*-diphenyl-*N*-carbethoxy-*o*-chlorobenzamidine, reduced with Al,Hg (prepn. given in detail in the original paper) in moist ethyl acetate or ether $\rightarrow$ *N,N'*-diphenyl-*N*-carbethoxydihydro-*o*-chlorobenzamidine (Y: good), 2 gm. of which hydrolyzed with concd. $\text{HCl} \rightarrow$ 0.4 gm. *o*-chlorobenzaldehyde.—This method can be used to convert ar. carboxylic acids into aldehydes. M. V. Shirsat and R. C. Shah, *J. Indian Chem. Soc.* **27**, 13 (1950).

Carboxylic acids from nitriles

238.

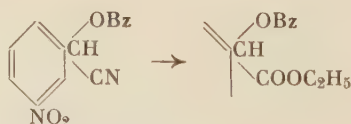


Vigorous stirring with aq. concd. HCl at low temp. converts aryl-acetonitriles into the corresponding amides. These amides are easily saponified to the acids by heating with dil. HCl .—E: 3,4-Dimethoxytolunitrile stirred with concd. HCl below 40° for ca. 3 hrs. until the nitrile is dissolved, warmed at 50° for 2 hrs., water added, and refluxed 7 hrs. with stirring $\rightarrow$ homoveratric acid. Y: 95%. F. e. s. W. Wenner, *J. Org. Chem.* **15**, 548 (1950).

Carboxylic acid esters from nitriles

s. 3, 200; s. a. R. A. Cutler, A. R. Surrey, and J. B. Cloke. *Am. Soc.* **71**, 3375 (1949).

239.



α -Acoxycarboxylic acid esters. *m*-Nitro-*o*-benzoylmandelonitrile added to a soln. of dry HCl in abs. ethanol, heated to refluxing, water added in several portions with swirling, and filtered hot after refluxing for 30 min. $\rightarrow$ ethyl *m*-nitro-*o*-benzoylmandelate (startg. m. f. 110). Y: 90%. M. W. Cronyn, *J. Org. Chem.* **14**, 1013 (1949).

Dicarboxylic acids from dicyanocarboxylic acid esters

s. 6, 705

←

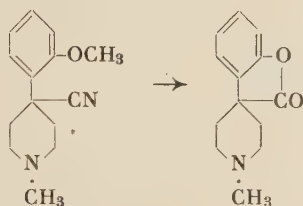
Hydrobromic acid

HBr

Lactones from alkoxy nitriles

○

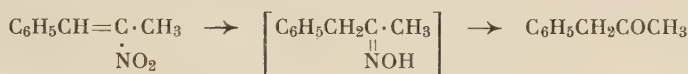
240.



1-Methyl-4-(4-methoxyphenyl)-4-cyanopiperidine refluxed 6 hrs. with 10 N HBr → 1-methyl-4-(4-hydroxyphenyl)piperidine-4-carboxylic acid lactone hydrobromide (startg. m. f. 687). Y: 80%. F. e. s. H. Kägi and K. Miescher, *Helv.* 32, 2489 (1949).

*Iron/ferric chloride*Fe/FeCl₃**Ketones from α-nitroethylene derivatives**CH: C(NO₂) → CH₂CO

241.



Concd. HCl added dropwise at a bath temp. of 85-95° over a period of 5-6 hrs. to 1-phenyl-2-nitropropene (prepn. s. 755), cast iron turnings, and a little FeCl₃ in water → phenylacetone. Y: 77%.—With less HCl, the ketoxime can be obtained in fair yield. F. e. s. H. B. Hass, A. G. Susie, and R. L. Heider, *J. Org. Chem.* 15, 8 (1950); s. a. J. A. Pearl and D. L. Beyer, *J. Org. Chem.* 16, 221 (1951).

*Ferric sulfate*Fe₂(SO₄)₃**Quinones from aminophenols**

←

s. 1, 173

Halogen †

OC † Hal

Without additional reagents

w.a.r.

Glycosides from benzoylated halogenosugars

←

s. 5, 192; s. a. *Am. Soc.* 72, 4173 (1950).**β-Dialkylaminoethyl esters**

COCl → COOR

s. 2, 238; s. a. R. Fusco et al., *G.* 79, 129 (1949).

Chloroformates

OCOCI

s. 3, 368; without solvent s. A. C. Farthing, Soc. 1950, 3213

Sodium

Na

Disaccharides from monosaccharides

ROR

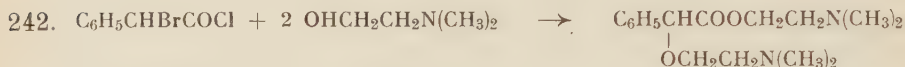
s. 3, 203; in air s. Soc. 1951, 285

Potassium

K

 **α -Alkoxy-carboxylic acid esters from
 α -bromocarboxylic acid chlorides**

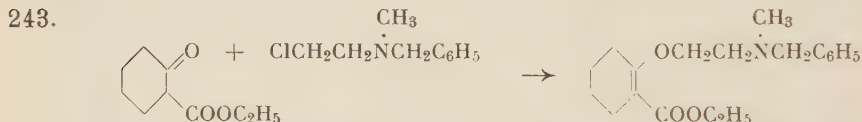
←



K added to a soln. of β -dimethylaminoethanol in toluene, after reaction of all of the K a soln. of freshly distilled α -bromophenylacetyl chloride in dry toluene added dropwise with stirring, and refluxed 4-10 hrs. with continuous stirring $\rightarrow$ 2-dimethylaminoethyl α -(2-dimethylaminoethoxy)phenylacetate. Y: 77%. F. e. s. P. Truitt et al., Am. Soc. 71, 3479 (1949).

**Carbalkoxyenoleters from
 β -ketocarboxylic acid esters**

←



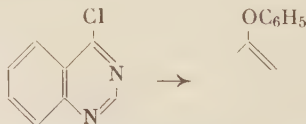
Two alkylating agents, bromoacetaldehyde diethylacetal and methylbenzyl- β -chloroethylamine, were found to O-alkylate 2-carbethoxycyclohexanone.—E: 2-Carbethoxycyclohexanone added dropwise with stirring to a suspension of K sand in toluene, refluxed ca. 20 min. until a clear soln. results, cooled to room temp., a soln. of methylbenzyl- β -chloroethylamine in toluene added, and refluxed 7 hrs. $\rightarrow$ ethyl-2-(β -methylbenzylaminoethoxy)-1-cyclohexenecarboxylate. Y: 48.4%. F. e. s. J. C. Sheehan and C. E. Mumaw, Am. Soc. 72, 2127 (1950).

Potassium hydroxide

KOH

Phenol ethers from halidesHal $\rightarrow$ OR

244.



4-Chloroquinazoline added during 10 min. to a soln. of KOH in phenol at ca. 50°, and kept at this temp. for 1 hr. $\rightarrow$ 4-phenoxyquinazoline (startg. m. f. 500). Y: 90%. J. S. Morley and J. C. E. Simpson, Soc. 1949, 1354; s. a. A. Sadykov, Zh. 19, 143 (1949); C. A. 43, 6210 b.

Benzofurans via 3-chlorocoumarins

Perkin transformation

←

s. 6, 784

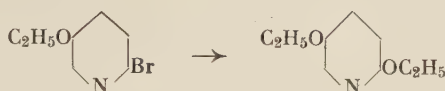
Sodium/alcohol

NaOR

Ethers from halides

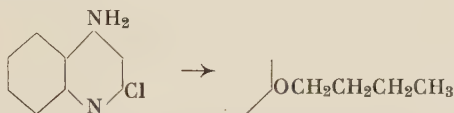
Hal → OR

245.



2-Bromo-5-ethoxypyridine heated 5 hrs. with a soln. of Na in ethanol at 160° in a sealed tube → 2,5-diethoxypyridine. Y: 90%. F. e. s. H. J. den Hertog, J. P. Wibaut et al., R. 69, 700, 673 (1950).

246.



2-Chloro-4-aminoquinoline heated with a soln. of Na in abs. n-butanol in a sealed tube at 150° for 24 hrs. → 2-n-butoxy-4-aminoquinoline. Y: 88%. F. e. s. J. Büchi, H. Hurni, and R. Lieberherr, Helv. 32, 1806 (1949).

Selective replacement of chlorine by alkoxyl

Cl → OR

247.



trans-1,3-Dichloropropene stirred with a soln. of 1 mole Na in ethanol for 2 hrs. without cooling, whereby the temp. rises to 75° → *trans*-3-ethoxy-1-chloro-1-propene. Y: 76%.—Similarly: *cis*-Isomer. Y: 71%. L. F. Hatch, H. E. Alexander, and J. D. Randolph, J. Org. Chem. 15, 654 (1950).

Sodium methoxide

←

α,β-Ethylenecarboxylic acid esters from methyl α,β-dibromoketones

←

248.



2 moles of 3,4-dibromo-3-methyl-2-butanone added with stirring and ice-salt cooling at 20° over a 1.5 hr. period to a suspension of 4 moles of Na-methoxide in anhydrous ether, and stirring continued for an additional hr. → methyl β,β-dimethylacrylate. Y: 64%. F. e. s. R. B. Wagner, Am. Soc. 71, 3214 (1949).

Sodium amide

NaNH₂

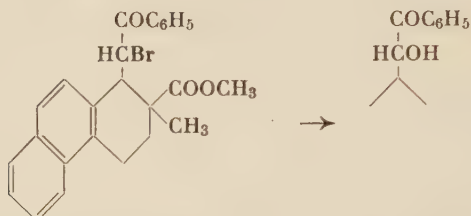
s. 5, 198; s. a. D. Papa, N. Sperber, and M. Sherlock, Am. Soc. 73, 1279 (1951)

Potassium carbonate K_2CO_3 **Ethers**

ROR

s. 2, 248; 3, 208; in methyl ethyl ketone s. H. Erdtman and B. Leopold, *Acta Chem. Scand.* 3, 1358 (1949); J. H. Barnes et al., *Soc.* 1950, 2824*Sodium formate* $HCOONa$ **Replacement of bromine by hydroxyl** $Br \rightarrow OH$

249.



cis-1-Benzoylbromomethyl-2-carbomethoxy-2-methyl-1,2,3,4-tetrahydronaphthalene refluxed 24 hrs. with anhydrous Na-formate in anhydrous methanol, the solvent removed, and the residue stirred with water $\rightarrow$ *cis*-1-benzoylhydroxymethyl-2-carbomethoxy-2-methyl-1,2,3,4-tetrahydronaphthalene. Y: 90%. W. E. Bachmann and F. Ramirez. *Am. Soc.* 72, 2525 (1950).

Potassium acetate CH_3COOK **Acetates from halides** $Hal \rightarrow OAc$ from bromides s. 1, 211; 3, 227; from chlorides s. W. Oroshnik and R. A. Mallory, *Am. Soc.* 72, 4608 (1950)*Pyridine* C_5H_5N **Ethers from halides** $Hal \rightarrow OR$

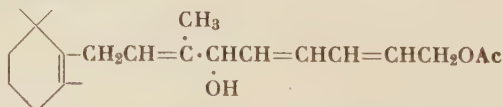
s. 6, 264

Benzoylation of carbohydrates $OH \rightarrow OAc$

s. 6, 291, 296

Selective acetylation

250.



A soln. of acetyl chloride in benzene added during 10 min. with stirring to a soln. of 11.7 gm. 9-(2',6',6'-trimethylcyclohex-1'-enyl)-7-methylnona-2,4,7-triene-1,6-diol in dry benzene-pyridine, and stirred for a further 14 hrs. at room temp. $\rightarrow$ 12.9 gm. 9-acetoxy-1-(2',6',6'-trimethylcyclohex-1'-enyl)-3-methylnona-2,5,7-trien-4-ol. I. Heilbron et al., *Soc.* 1949, 1516.

Pyridine/silver nitrate *s.* Silver nitrate/pyridine $C_5H_5N/AgNO_3$

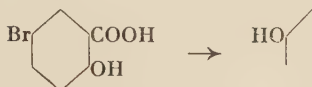
Copper

Cu

Phenols from halides

Hal $\rightarrow$ OH

251.



5-Bromosalicylic acid and Cu-powder in 8%-NaOH heated 1.5 hrs. at 140-150° in an autoclave $\rightarrow$ gentisic acid. Y: 72%. J. Lowenthal and J. M. Pepper, *Am. Soc.* 72, 3292 (1950).

Copper/calcium oxide

Cu/CaO

252.



4-Nitro-2-chlorobenzoic acid, carbonate-free CaO, water, and some Cu-powder heated with shaking at 155-160° under 1000 lbs. N_2 pressure in an autoclave for 6 hrs. $\rightarrow$ 4-nitrosalicylic acid. Y: 80-86%. E. Wenis and T. S. Gardner, *J. Am. Pharm. Assoc.* 38, 9 (1949).

Silver oxide

 Ag_2O

Glycosides

ROR

s. 1, 217; *s. a.* N. M. Ferguson and I. H. Gardner, *Am. Soc.* 72, 2877 (1950)

Silver carbonate

 Ag_2CO_3

Methyl glycosides

Königs-Knorr reaction

s. 1, 218; *s. a.* H. G. Fletcher, Jr., and C. S. Hudson, *Am. Soc.* 72, 4173 (1950)

Steroid glycosides

s. 1, 219/20; *s. a.* E. Hardegger and F. G. Robinet, *Helv.* 33, 456, 1871 (1950)

Silver acetate

 CH_3COOAg

Replacement of bromine by acetoxy groups

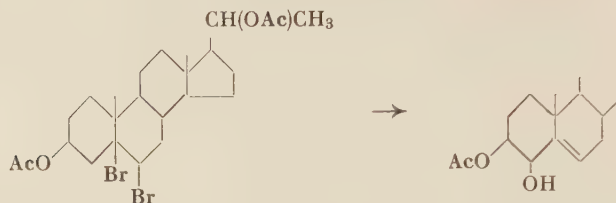
Br $\rightarrow$ OAc

s. 1, 221; 2, 261; *s. a.* A. C. Cope and S. W. Fenton, *Am. Soc.* 73, 1668 (1951)

Silver nitrate/pyridine

 $\text{AgNO}_3/\text{C}_5\text{H}_5\text{N}$ **Ethylenealcohols from 1,2-dibromides**

253.

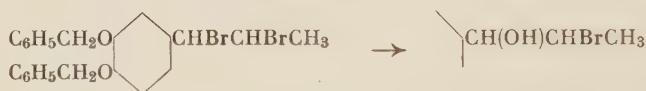


Δ^5 -Pregnene-3,20-diol 3,20-diacetate dibromide and AgNO_3 in anhydrous pyridine allowed to stand in the dark for 3-5 days with occasional stirring $\rightarrow$ Δ^5 -pregnene-3,4,20-triol 3,20-diacetate. Y: 60%. F. e., with lower yields, s. M. Pesez and A. Petit, *Bl.* 1949, 632.

Calcium carbonate

 CaCO_3 **Bromohydrins from 1,2-dibromides** $\text{CBrClBr} \rightarrow \text{C}(\text{OH})\text{CBr}$

254.



Precipitated CaCO_3 added to a soln. of 1-(3,4-dibenzoyloxyphenyl)-1,2-dibromopropane in acetone-water, and heated on a steam bath for 1 hr. $\rightarrow$ 1-(3,4-dibenzoyloxyphenyl)-2-bromo-1-propanol. Y: nearly 100%. J. Kovács and T. Horváth, *J. Org. Chem.* 14, 306 (1949).

Hexamethylenetetramine

 $\text{C}_6\text{H}_{12}\text{N}_4$ **Aldehydes from halides** $\text{CH}_2\text{Hal} \rightarrow \text{CHO}$ **Sommelet reaction**

255. o-Iodobenzyl bromide and hexamethylenetetramine in chloroform allowed to stand overnight, the salt (Y: 95%) separated, and refluxed in 50%-acetic acid for 2 hrs. $\rightarrow$ o-iodobenzaldehyde. Y: 76%.—Two substituents in the o-position hinder the reaction, electron-attracting and -repelling groups acting in the same way (*Soc.* 1949, 2704). Electron-attracting substituents decrease the rate of the reaction and the yield, even when electron-releasing substituents are also present.—50%-Acetic acid proved to be the best solvent (*Soc.* 1950, 2141). F. e. s. S. J. Angyal et al., *Soc.* 1949, 2704, 2700; 1950, 2141; *Org. Synth.* 30, 67 (1950); dialdehydes s. J. H. Wood et al., *Am. Soc.* 72, 2992 (1950).

Isopropane nitronate

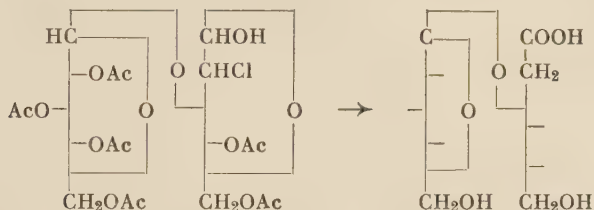
s. 5, 202; s. a. *Am. Soc.* 71, 3482 (1949); in acetone-water s. G. Dupont, R. Dulou, and V. Léon, *Bl.* 1950, 1313

Stannic chloride SnCl_4 **Hydroperoxides from halides**Hal $\rightarrow$ OOH

256. 90% H_2O_2 added at 0° to ethereal p-nitrotriphenylmethyl chloride, then SnCl_4 added dropwise with stirring and ice-cooling, and allowed to stand 2 or more hrs. in an ice bath $\rightarrow$ p-nitrotriphenylmethyl hydroperoxide (startg. m. f. 319). Y: 61-80%. P. D. Bartlett and J. D. Cotman, Jr., Am. Soc. 72, 3095 (1950).

Lead oxide PbO **Carboxylic acids from halogenhydrins** $\leftarrow$

257.



2-Chlorohexaacetate heated with Pb oxide in water at a gradually rising temp. of $60-100^\circ$ for 30-35 hrs., and the reaction product isolated as Ca salt $\rightarrow$ Ca-glucosido-3-glucosaccharinate. Y: 79%. A. M. Gakhokidze, Ж. 19, 2082 (1949); C. A. 44, 3914 b.

Sulfur dioxide SO_2 **Selective O-acylation**OH $\rightarrow$ OAc

s. 4, 244; s. a. M. 81, 647 (1950)

Sulfuric acid H_2SO_4 **Carboxylic acids from 1,1,1-trihalides** $\text{CHal}_3 \rightarrow \text{COOH}$

258. A mixture of benzotrifluoride and 100% H_2SO_4 heated cautiously until the benzotrifluoride layer disappears $\rightarrow$ benzoic acid. Y: 94%. F. e. s. G. M. LeFave, Am. Soc. 71, 4148 (1949); with $\text{H}_2\text{SO}_4/\text{ClSO}_3\text{H}$ s. Am. Soc. 72, 3308 (1950).

Carboxylic acid esters from 1,1,1-trihalides $\text{CHal}_3 \rightarrow \text{COOR}$

259.



A mixture of benzotrichloride and 100% H_2SO_4 heated with a smoky flame until the reaction ensues, frequently agitated over a 1 hr. period until the reaction is completed, cooled, poured cautiously with stirring into n-propanol, and gently refluxed for 0.5 hr. $\rightarrow$ n-propyl benzoate. Y: 81%. F. e. with trifluorides s. G. M. LeFave and P. G. Scheurer, Am. Soc. 72, 2464 (1950).

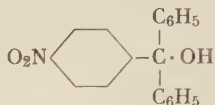
Chlorosulfonic acid/sulfuric acid $\text{HSO}_3\text{Cl}/\text{H}_2\text{SO}_4$ **Carboxylic acids from 1,1,1-trihalides** $\text{CHal}_3 \rightarrow \text{COOH}$

s. 6, 258

*Perchloric acid**HClO₄***Replacement of chlorine by hydroxyl**

Cl → OH

260.



HClO₄ added to a soln. of p-nitrotriphenylmethyl chloride in glacial acetic acid, then poured into a large excess of water → p-nitrotriphenylcarbinol. Y: 78%. P. D. Bartlett and J. D. Cotman, Jr., Am. Soc. 72, 3095 (1950).

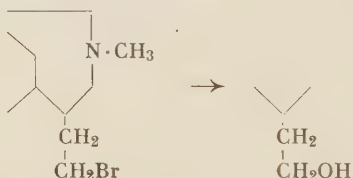
*Hydrochloric acid**HCl***partial replacement**

s. 3, 220; s. a. S. J. Childress and R. L. McKee, Am. Soc. 72, 4271 (1950)

*Hydrobromic acid/sulfuric acid**HBr/H₂SO₄***Replacement of bromine by hydroxyl**

Br → OH

261.

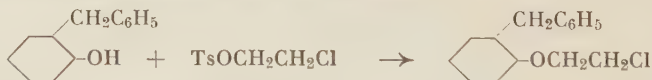


0.5 gm. bromodesoxy-N-methyldihydroisopseudostrychnine hydrobromide (prepn. s. 583) boiled with aq. HBr-H₂SO₄ for 2.5 hrs. → 0.34 gm. N-methyldihydroisopseudostrychnine. F. e. s. H.-G. Boit, B. 83, 217 (1950).

Sulfur †**OC † S***Sodium hydride**NaH***Ethers from p-toluenesulfonic acid esters**

OH → OR

262.



A soln. of o-benzylphenol in toluene added dropwise to a stirred suspension of NaH in toluene under N₂, refluxed 30 min., β-chloroethyl p-toluenesulfonate added dropwise with stirring and refluxing, and worked up after 16 hrs. of refluxing → β-(o-benzylphenoxy)ethyl chloride. Y: 89%. F. e. s. W. B. Wheatley et al., Am. Soc. 72, 1655 (1950).

Alkali hydroxide

←

Replacement of sulfonic acid groups by hydroxyl $\text{SO}_3\text{H} \rightarrow \text{OH}$

s. 3, 229; s. a. M. F. Clarke and L. N. Owen, Soc. 1950, 2108

Sodium hydroxide

NaOH

Hydroxy compounds from sulfones $\text{SO}_2\text{R} \rightarrow \text{OH}$

s. 6, 484

Sodium hydroxide/potassium hydroxide

NaOH/KOH

Replacement of sulfonic acid groups by hydroxyl $\text{SO}_3\text{H} \rightarrow \text{OH}$

s. 2, 268; s. a. R. N. Shreve and F. R. Lloyd, Ind. Eng. Chem. 42, 811 (1950)

Sodium acetate

 CH_3COONa **Acetates from tosylates Epimerization**

←

263.



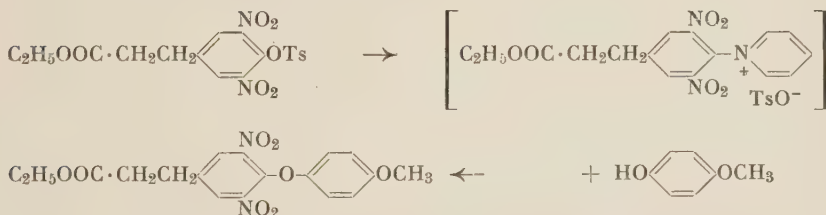
A mixture of *trans*- α -tosyloxy- β -methyl- γ -lactone, freshly fused Na-acetate, glacial acetic acid, and acetic anhydride refluxed 7 hrs. $\rightarrow$ *cis*- α -acetoxy- β -methyl- γ -lactone. Y: 70%. F. Fleck and H. Schinz, Helv. 33, 140 (1950).

Pyridine

 $\text{C}_5\text{H}_5\text{N}$ **Ethers from tosylates and halides via quaternary pyridinium salts**

←

264.



Ethyl β -(3,5-dinitro-4-p-tolylsulfonxyloxyphenyl)propionate and quinol monomethyl ether refluxed in pyridine for 1 hr. $\rightarrow$ ethyl β -(3,5-dinitro-4-p-methoxyphenoxyphenyl)propionate. Y: 95%.—Similarly, other quaternary salts, e.g. from halides, yield the ethers. F. c. s. E. T. Borrowes et al., Soc. 1949, S190, S199.

Phosphorus/hydroiodic acid s. Hydroiodic acid/phosphorus

P/HI

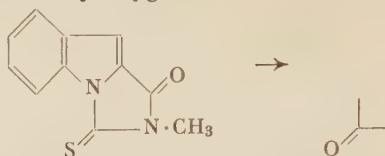
Hydrogen peroxide



Replacement of sulfur by oxygen



265.



A hot alc. soln. of 0.3 gm. 2-thio-3-methylindolo(1',2',1,5)hydantoin treated with 30% H_2O_2 , then with methanolic KOH $\rightarrow$ 0.25 gm. 3-methylindolo(1',2',1,5)hydantoin. J. A. Elvidge and F. S. Spring, Soc. 1949, S135; C^{14} -compounds s. C. Heidelberger and R. B. Hurlbert, Am. Soc. 72, 4704 (1950).

Sulfuric acid

Carbohydrate acetates from
carbohydrate sulfuric acid esters

266. Acetic anhydride added during 5–8 hrs. below -10° in a CO_2 -atmosphere to a mixture of 0.85 g. Na D-glucose 6-sulfate and abs. H_2SO_4 , then kept tightly stoppered at -15 to -20° for 14–16 hrs., and ca. 4 hrs. at room temp. $\rightarrow$ 0.90 g. α -D-glucopyranose pentaacetate.—The reaction takes place without Walden inversion but with some glycosidic hydrolysis. F. e. s. M. L. Wolfrom and R. Montgomery, Am. Soc. 72, 2859 (1950).

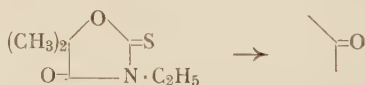
Chlorine



Replacement of sulfur by oxygen



267.



2-Thio-5,5-dimethyl-3-ethyloxazolid-4-one in CCl_4 stirred with water, Cl_2 passed through for $\frac{3}{4}$ hr. below 10° , and excess Cl_2 removed by a current of air $\rightarrow$ 5,5-dimethyl-3-ethyloxazolid-2,4-dione. Y: 90%. F. e. s. J. S. H. Davies, W. H. Hook, and F. Long, Soc. 1950, 36.

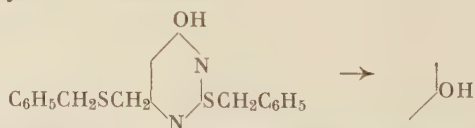
Hydrochloric acid



Partial hydrolysis of thioethers



268.



A soln. of 2-benzylthio-4-benzylthiomethyl-6-hydroxypyrimidine in HCl-acetic acid-water heated 2.5 hrs. on a steam bath $\rightarrow$ 2,6-dihydroxy-4-benzylthiomethylpyrimidine. Y: 98.7%. F. e. s. R. M. Dodson, E. R. Peterson, and J. K. Seyler, Am. Soc. 72, 3281 (1950).

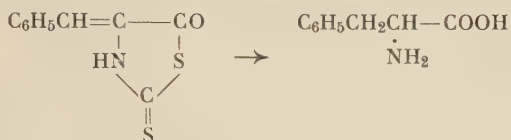
Hydroiodic acid/phosphorus

HI/P

 α -Aminocarboxylic acids from thiazolidones

C

269.



Red P, followed by 40%-aq.-HI added to a suspension of 2-thio-4-benzylidenethiazolid-5-one in glacial acetic acid, and refluxed 1.5 hrs. $\rightarrow$ β -phenylalanine. Y: 70%. F. e. s. J. D. Billimoria and A. H. Cook, Soc. 1949, 2323.

Remaining Elements †

OC † Rem

Sodium salt

Na⁺**Carboxylic acid esters from carboxylic acids**COOH $\rightarrow$ COOR**Labeled compounds**

270. A mixture of Na-acetate-2-C¹⁴ and n-butyl phosphate refluxed 1 hr. at 140-220° $\rightarrow$ n-butyl acetate-2-C¹⁴. Y: 82%.—Alkyl phosphates have been found to be somewhat superior to the use of the corresponding alkyl sulfates which boil slightly lower and are much less stable at temp. near 200°. F. e. s. G. A. Ropp, Am. Soc. 72, 2299 (1950).

Carbon †

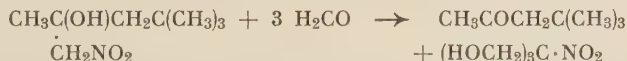
OC † C

Sodium hydroxide

NaOH

Ketones from nitroalcohols $\leftarrow$

271.



1-nitro-2,4,4-trimethylpentan-2-ol treated with paraformaldehyde in alcohol with the addition of a small pellet of NaOH, and the volatile material distilled off at 25° in vacuo $\rightarrow$ nitrotri(hydroxymethyl)-methane (Y: 92.7%) and 4,4-dimethylpentan-2-one (Y: 73.2%). H. Baldock, N. Levy, and C. W. Scaife, Soc. 1949, 2627.

Carboxylic acids from α -halogenoketones via pyridinium saltsCOCH₂Br $\rightarrow$ COOH**Degradation with loss of 1 C-atom**

s. 1, 789; 2, 833; s. a. R. B. Wagner and J. M. Tome, Am. Soc. 72, 3477 (1950); R. T. Arnold, K. Murai, and R. M. Dodson, Am. Soc. 72, 4193 (1950)

Potassium hydroxide

KOH

Transesterification of activated ethers

OR → OR'

272.



2,4-Dinitroanisole added to a soln. of KOH in isobutyl alcohol, and refluxed 10 hrs. → 2,4-dinitrophenyl isobutyl ether. Y: 77%. F. e. s. Y. Ogata and M. Okano, *Am. Soc.* **71**, 3211 (1949).

Pyridine

C₅H₅N**1,1-Di(acylperoxy) compounds from hydroxy hydroperoxy peroxides**

←

273.



1-Hydroxy-1'-hydroperoxydicyclohexyl peroxide added with ice-cooling to a mixture of benzoyl chloride and abs. pyridine, then allowed to stand overnight → 1,1-di(benzoperoxy)cyclohexane. Y: 91%. R. Criegee, W. Schnorrenberg, and J. Becke, *A.* **565**, 7 (1949).

Zinc/ozone s. Ozone/zinc

Zn/O₃

Mercuric acetate

(CH₃COO)₂Hg**Carboxylic acid esters from carboxylic acids**

COOH → COOR

Transacylation

274. Caprylic acid, vinyl acetate, a trace of Cu-resinate, and mercuric acetate added in that order, then stirred vigorously, a little H₂SO₄ added, stirring continued until a homogeneous soln. results, allowed to stand at 30° for 72 hrs., Na-acetate added with good stirring, and distilled → vinyl caprylate. Y: 95% based on recoverable material. Conversion: 72.5%.—By keeping the temp. low (20–30°) the formation of ethylidene diesters is avoided. F. e. s. R. L. Adelman, *J. Org. Chem.* **14**, 1057 (1949); s. a. D. Swern and E. F. Jordan, *Org. Synth.* **30**, 106 (1950).

Peracetic acid/*p*-toluenesulfonic acid s.*p*-Toluenesulfonic acid/peracetic acidCH₃COO₂H/TsOH

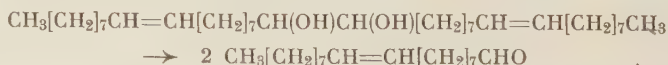
Lead tetraacetate

(CH₃COO)₄Pb**Oxidative cleavage**

←

Oxo compounds from glycols

275.



Hexatriaconta-9,27-diene-18,19-diol and the theoretical quantity of Pb-tetraacetate in abs. benzene under dry N₂ shaken at room temp. for

0.5 hr. $\rightarrow$ olealdehyde. Y: above 90%. F. e. s. F. Bouquet and C. Paquot, *Bl.* 1949, 440; ketones s. J. D. Roberts and C. W. Sauer, *Am. Soc.* 71, 3925 (1949).

Sodium azide

NaN_3

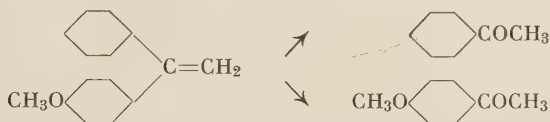
Ketones from 1,1-diarylethylenes

$\leftarrow$

Schmidt reaction

Migration aptitude

276.



Concd. H_2SO_4 added dropwise with stirring and ice-cooling to a suspension of NaN_3 in chloroform, then a soln. of 1-p-anisyl-1-phenylethylene in chloroform added at 25° dropwise, with stirring, in the course of several hrs., stirring continued for another hr., and allowed to stand overnight $\rightarrow$ acetophenone (Y: 49%) and p-methoxyacetophenone (Y: 8%).—The reaction involves a migration of an aryl group from a carbon to a nitrogen atom. The order of migratory aptitude follows the sequence p-anisyl > p-tolyl > p-biphenyl > phenyl > p-chlorophenyl > methyl, and is in qualitative agreement with the sequence found in the pinacol-pinacolone rearrangement of sym. pinacols. F. e. s. W. E. McEwen, M. Gilliland, and B. I. Sparr, *Am. Soc.* 72, 3212 (1950); s. a. L. P. Kuhn and J. D. Domenico, *Am. Soc.* 72, 5777 (1950).

p-Toluenesulfonic acid

TsOH

Transesterification

$\text{COOR} \rightarrow \text{COOR}'$

s. 4, 263; s. a. W. S. Emerson and R. A. Heimsch, *Am. Soc.* 73, 1297 (1951)

Sodium bismuthate

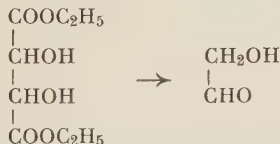
NaBiO_3

Oxidative cleavage and degradation

$\leftarrow$

Oxo compounds from glycols, acyloins, and α -hydroxycarboxylic acids

277.



Na-bismuthate in an acid medium smoothly and selectively effects oxidations similar to those brought about by Pb-tetraacetate and HIO_4 ; 1,2-glycols undergo fission to aldehydes or ketones, acyloins to the derived carbonyl compounds and carboxylic acids, and α -hydroxycarboxylic acids to the lower aldehyde or ketone, all in good yield.

Aldehydes are not further oxidized.—E: Ethyl tartrate and Na-bismuthate in aq. H_3PO_4 shaken 3.5 hrs. at $17-18^\circ \rightarrow$ glycolaldehyde (isolated as phenylhydrazone). Y: 94%. F. e. s. W. Rigby, Soc. 1950, 1907.

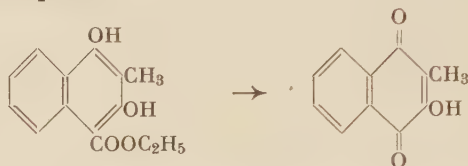
Oxygen

O_2

Hydroxynaphthoquinones

$\leftarrow$

278.



Ethyl 1,3-dihydroxy-2-methylnaphthalene-4-carboxylate and 6% -NaOH shaken with O_2 for 2 hrs. $\rightarrow$ phthiocol (3-hydroxy-2-methylnaphthoquinone). Y: 75%. O. Neunhoeffer and H. v. Hörner, Chem. B. 83, 99 (1950).

Ozone

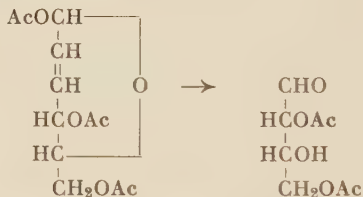
O_3

Aldehydes from ethylene derivatives

$\leftarrow$

Degradation of carbohydrates

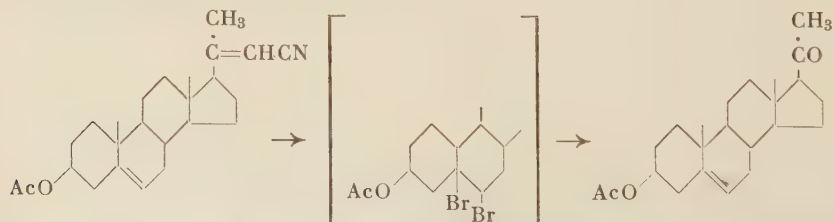
279.



A stream of O_2-O_3 passed through a soln. of 1,4,6-triacetyl pseudo-glucal at 12° until it no longer decolorized a soln. of Br_2 in CCl_4 , after dilution with ether, Zn-dust added, and the mixture refluxed until the soln. failed to color starch-iodide paper $\rightarrow$ 2,4-diacetyl-D-erythrose. Y: 95.4%. W. G. Overend, M. Stacey, and L. F. Wiggins, Soc. 1949, 1358.

Ketones from ethylene derivatives with protection of a double bond

280.



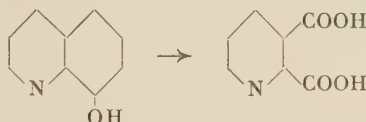
A soln. of Br_2 in chloroform added dropwise with stirring to an ice-cooled soln. of 0.5 gm. 22-cyanobisnor-5,20;22-choladiene-3 β -ol acetate

(m. p. 182°), a stream of O_3-O_2 passed through for 26 min., the solvent removed in vacuo, the residue taken up in glacial acetic acid-ether, then shaken and refluxed with Zn dust for 10 min. $\rightarrow$ 0.46 gm. crude 5-pregnene-3 β -ol-20-one acetate. M. E. Herr and F. W. Heyl, Am. Soc. 72, 1753 (1950); protection of a double bond s. a. P. Wieland and K. Miescher, Helv. 32, 1922 (1949).

Oxidative ring opening

C

281.



A soln. of 8-hydroxyquinoline in glacial acetic acid subjected to a stream of 9-10% ozonized oxygen at 20 l. per hr., for 48 hrs. at room temp., then 30% H_2O_2 added cautiously, and refluxed 2 hrs. $\rightarrow$ quino-
linic acid. Y: 92%. F. e. with lower yields s. A. F. Lindenstruth and C. A. VanderWerf, Am. Soc. 71, 3020 (1949).

Ozone/zinc

 O_3/Zn

Aldehydes from ethylene derivatives

 $\leftarrow$

Degradation of carbohydrates with loss of 1 C-atom

282. Oxygen containing 3-5% ozone introduced into a soln. of hexaacetyl-
glucosido-3-glucal (prepn. s. 887) in glacial acetic acid, after com-
pletion of the reaction diluted with ether, Zn dust added, and heated
on a water bath with shaking $\rightarrow$ hexaacetyl- α -glucosido-2-arabinose.
Y: 69%. A. M. Gakhokidze, Ж. 19, 2082 (1949); C. A. 44, 3914b.

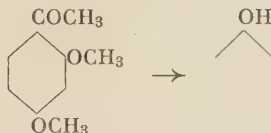
p-Toluenesulfonic acid/peracetic acid $TsOH/CH_3COO_2H$

Hydroxy compounds from ketones

COR $\rightarrow$ OH

Oxidative degradation

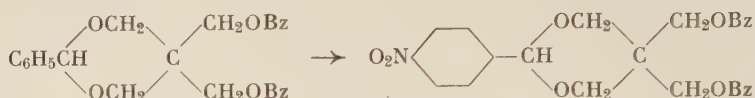
283.



A soln. of 2,4-dimethoxyacetophenone, 20-22%-peracetic acid, and a
trace of *p*-toluenesulfonic acid in glacial acetic acid warmed 0.5 hr. at
35°, then 3 hrs. at 60–65°, more peracetic acid added, and allowed to
stand 24 hrs. $\rightarrow$ 1-hydroxy-2,4-dimethoxybenzene. Y: 54%. A. Ballio,
G. 79, 924 (1949); cf. W. v. E. Doering and L. Speers, Am. Soc. 72,
5515 (1950).

α-Naphthalenesulfonic acid ←**Transacetalization** ←

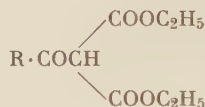
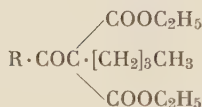
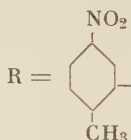
284.



A mixture of benzalpentaaerythritol dibenzoate, p-nitrobenzaldehyde, *α*-naphthalenesulfonic acid, and benzene refluxed for 6 hrs. → (p-nitrobenzal)pentaaerythritol dibenzoate. Y: 93%. F. e. s. E. Bograchov, Am. Soc. 72, 2268 (1950).

*Sulfuric acid**H₂SO₄***Carboxylic acids and methyl ketones from acylmalonic acid esters** ←

285.



Diethyl 2-methyl-5-nitrobenzoyl-n-butylmalonate

Diethyl 2-methyl-5-nitrobenzoylmalonate

heated with a 2:1:6 mixture of concd. H_2SO_4 -water-acetic acid in an oil bath at 105–110° for 3 hrs.

2-methyl-5-nitrobenzoic acid.

Y: 91%.

2-methyl-5-nitroacetophenone.

Y: 95%.

M. E. Blumer and E. Sorkin, Helv. 32, 2547 (1949).

*Hypohalites**HalO⁻***Carboxylic acids from ketones** $\text{COR} \rightarrow \text{COOH}$ **Oxidative degradation**

286. If alkaline hypobromite soln. is to be used successfully for the oxidation of the higher alkyl aryl ketones to acids, the ketone should have 2 H-atoms on the C-atom adjacent to the carbonyl group. E. s. R. Levine and J. R. Stephens, Am. Soc. 72, 1642 (1950).

*Hypochlorites**ClO⁻***Haloform reaction****Carboxylic acids from methyl ketones** $\text{COCH}_3 \rightarrow \text{COOH}$ **Degradation with loss of 1 C-atom**

s. 1, 237; large batches s. D. T. Mowry and E. L. Ringwald, *Am. Soc.* 72, 2037 (1950)

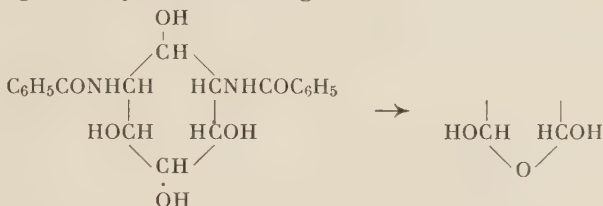
*Periodate**IO₄⁻***Oxidative cleavage of the carbon chain**

s. 3, 238; s. a. C. F. Huebner and K. P. Link, *Am. Soc.* 72, 4812 (1950)

Pyran ring from cyclohexane ring

←

287.



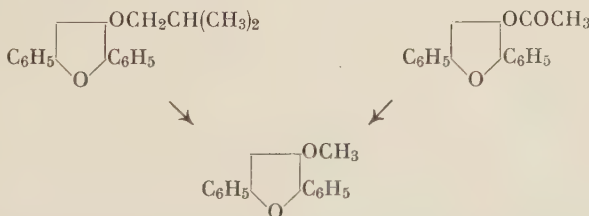
N,N'-Dibenzoylstreptamine and Na-metaperiodate (NaIO_4) in 50%-methanol allowed to stand at room temp. for 12-15 hrs. until ca. 2 moles of periodate per mole of sample have been consumed, then the excess periodate and the iodate formed removed by precipitation with Pb-nitrate $\rightarrow$ 2,4,6-trihydroxy-3,5-dibenzamidotetrahydropyran. Y: 83.5%. H. E. Carter, Y. H. Loo, and J. W. Rothrock, *J. Biol. Chem.* 179, 1027 (1949).

Triethylamine hydrochloride $(\text{CH}_3)_3\text{N}\cdot\text{HCl}$ **Transetherification**

←

Ethers from carboxylic acid esters**3-Alkoxyfurans**

288.



3-Isobutoxy-2,5-diphenylfuran

3-Acetoxy-2,5-diphenylfuran

refluxed 30 hrs. with methanol containing HCl
and triethylamine hydrochloride at a pH of 2-3 $\rightarrow$
3-methoxy-2,5-diphenyl-furan

Y: 76% with 20% recovery of
starting material.

Y: 96%

F. e. s. P. S. Bailey and J. D. Christian, *Am. Soc.* 71, 4122 (1949).

*Potassium permanganate**KMnO₄***Aldonic acids from glycals**

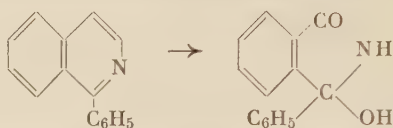
←

s. 6, 322

3-Hydroxyphthalimidines from isoquinolines

←

289.



Aq. KMnO_4 gradually added during 2 hrs. to a stirred refluxing suspension of 1 gm. 1-phenylisoquinoline in water $\rightarrow$ 0.7 gm. 3-hydroxy-3-phenylphthalimidine. W. Davies, T. H. Ramsay, and E. R. Stove, *Soc.* 1949, 2633.

*Potassium permanganate/pyridine**KMnO₄/C₅H₅N***Carboxylic acids from ethylene derivatives** $\text{CH}_2\text{C} \rightarrow \text{COOH}$

s. 6, 135

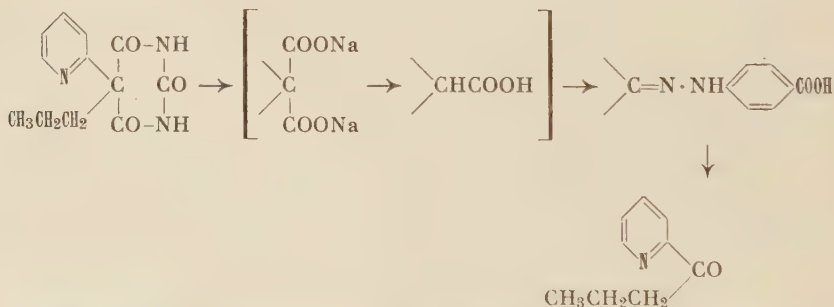
Via intermediates

v.i.

Ketones from barbituric acids
via carboxylic acids and hydrazones
Japp-Klingemann reaction

←

290.



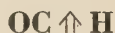
5-n-Propyl-5-(2'-pyridyl)barbituric acid heated in 20% aq. NaOH on a steam cone for 1 hr., evaporated to dryness, redissolved in water, acidified with concd. HCl just before the addition of a p-carboxybenzene-diazonium chloride soln. from p-aminobenzoic acid, followed by aq. Na-acetate below 5°, and allowed to stand 96 hrs. at 4° $\rightarrow$ 2-n-butrylpyridine p-carboxyphenylhydrazone (Y: 94%) refluxed 1 hr. with pyruvic acid in aq. acetic acid $\rightarrow$ 2-n-butrylpyridine (Y: 81%).—F. e. for the Japp-Klingemann reaction s. R. L. Frank and R. R. Phillips, *Am. Soc.* 71, 2804 (1949).

Carboxylic acids from hydrocarbons

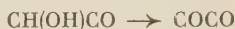
s. 6, 135

Transacylation of glycosides

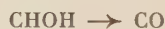
291. A soln. of methyl β -D-mannopyranoside tetraacetate in anhydrous methanol treated with 2 *N* Ba-methoxide, after 21 hrs. at room temp. concentrated in vacuo at 35° to a syrup which is then dissolved in dry pyridine, cooled in an ice bath, slowly treated with benzoyl chloride, and held at 60° for 2.5 hrs. $\rightarrow$ methyl β -D-mannopyranoside tetrabenzoate. Y: 81%. R. K. Ness, H. G. Fletcher, Jr., and C. S. Hudson, *Am. Soc.* 72, 2200 (1950); deacylation s. a. 72, 4173.

Elimination**Hydrogen $\uparrow$** *Copper**Cu***Carboxylic acids from alcohols
via aldehydes**

292. Methallyl alcohol and O_2 passed at 300-350° over a copper gauze catalyst $\rightarrow$ methacrolein (Y: 95.3% based on alcohol consumed; conversion 71%) kept ca. 5 hrs. in a rocking bomb under a pressure of 210 lbs. of oxygen in the presence of a mixture of Cu- and Ni-acetates $\rightarrow$ methacrylic acid (startg. m. f. 213) (Y: over 96%; conversion ca. 61%). J. M. Church and L. Lynn, *Ind. Eng. Chem.* 42, 768 (1950).

Cupric acetate**Oxidation of acyloins**

s. 2, 287; s. a. N. R. Campbell, J. H. Dunsmuir, and M. E. H. Fitzgerald, *Soc.* 1950, 2743

Aluminum alkoxide**Oxo compounds from alcohols****Oppenauer oxidation**

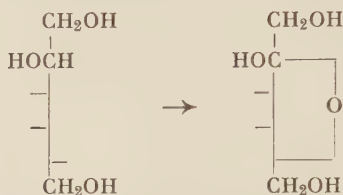
s. 1, 157/8; 2, 286; stability of β -aminoalcohols toward the oxidation s. R. E. Lutz and R. L. Wayland, Jr., *Am. Soc.* 73, 1639 (1951)

Acetobacter suboxydans

Carbohydrates from polyalcohols

Biochemical oxidation

293.



Talitol, Difco yeast extract, and some glycerol in water kept 6 days at 30° in the presence of a culture of *Acetobacter suboxydans*, and worked up using Pb-acetate to remove the proteins and IR-100 ion exchange resin to remove the Pb-ions $\rightarrow$ D-tagatose. Y: 75–84%. E. L. Totton and H. A. Lardy, *Am. Soc.* **71**, 3076 (1949).

N-Bromoacetamide

$$CH_3CONHBr$$

Ketones from sec. alcohols

$$\text{CHOH} \rightarrow \text{CO}$$

s. 4, 269; s. a. B. A. Koechlin, T. H. Kritchevsky, and T. F. Gallagher, *J. Biol. Chem.* 184, 393 (1950)

N-Bromosuccinimide

$$\begin{array}{c} \text{CH}_2\text{CO} \\ | \\ \text{CH}_2\text{CO} \end{array} \text{NBr}$$

294.



Selective oxidation. Cholestane-3 β ,5 α ,6 β -triol, N-bromosuccinimide, ether, methanol, and water shaken a few min. until dissolved $\rightarrow$ cholestane-3 β ,5 α -diol-6-one. Y: 96,5%. F.e.s. L. F. Fieser and S. Rajagopalan, *Am. Soc.* **71**, 3938, 3935 (1949).

Lead tetraacetate

$$(CH_3COO)_4Pb$$

Benzoxazoles from azomethines

○

S. 6, 503

Chromic acid

 CrO_3

Ketones from sec. alcohols

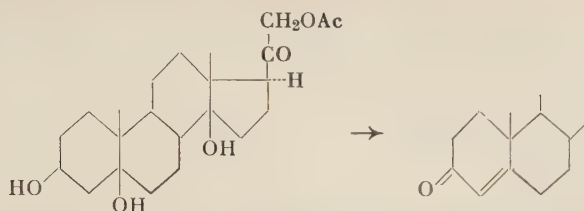
$$\text{CHOH} \rightarrow \text{CO}$$

s. 1, 167; 4, 129; s. a. W. A. Mosher und E. O. Langerak, *Am. Soc.* 73, 1302 (1951)

α,β -Ethyleneketones from 1,3-diols

←

295.



505 mg. 21-acetoxy-3 β ,5,14-trihydroxy-14-isopregnan-20-one and CrO_3 in glacial acetic acid allowed to stand at 18° for 16 hrs. $\rightarrow$ 370 mg. 14-hydroxy-14-iso-11-desoxycorticosterone acetate. F. e. s. A. Lardon, *Helv.* 32, 1517 (1949).

Oxygen ↑

OC ↑ O

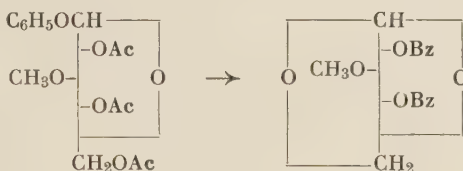
Sodium hydroxide

NaOH

Anhydrosugars from glycosides

○

296.



Phenyl 3-methyltriacetate- β -D-glucoside in 2.6 *N*ethanolic NaOH refluxed for 40 hrs., neutralized, the solvent evaporated, the residue and benzoyl chloride in anhydrous pyridine kept at 60° for 2 hrs., then at room temp. overnight $\rightarrow$ 3-methyl-2,4-dibenzoyllevoglucosan. Y: 82%. M. P. Bardolph and G. H. Coleman, *J. Org. Chem.* 15, 169 (1950).

Acetic anhydride

 $(\text{CH}_3\text{CO})_2\text{O}$ **Dicarboxylic acid anhydrides from dicarboxylic acids**

297. A mixture of dry homophthalic acid (prepn., s. 188) and acetic anhydride refluxed for 2 hrs. $\rightarrow$ homophthalic anhydride. Y: 85-88%. O. Grummitt, R. Egan, and A. Buck, *Org. Synth.* 29, 49 (1949); s. a. E. C. Horning and A. F. Finelli, *Org. Synth.* 30, 81 (1950); J. C. Roberts and B. Shaw, *Soc.* 1950, 2842.

3,1,4-Benzoxazones (Acylantranils)

298.



0.05 mole of N-propionylantranilic acid and 90-100%-acetic anhydride refluxed 1 hr., then slowly distilled below 139° until ca. 25 ml. is col-

lected, and the remaining acetic anhydride removed under reduced pressure $\rightarrow$ 2-ethyl-3,1,4-benzoxazone (startg. m. f. 406). Y: 74.7%. F. e. s. D. T. Zentmyer and E. C. Wagner, *J. Org. Chem.* 14, 967 (1949).

Acetyl chloride

CH_3COCl

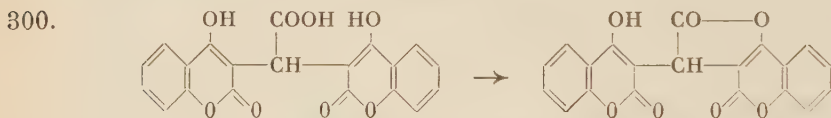
Dicarboxylic acid anhydrides from dicarboxylic acids

299. α,α' -Diphenylsuccinic acid refluxed with glacial acetic acid and acetyl chloride until all of the acid is dissolved, then distilled in vacuo $\rightarrow$ α,α' -diphenylsuccinic acid anhydride. Y: 80-87%. J. A. McRae, R. A. B. Bannard, and R. B. Ross, *Can. J. Research* 28B, 73 (1950); s. a. J. Cason, G. Sumvell, and R. S. Mitchell, *J. Org. Chem.* 15, 850 (1950).

Thionyl chloride

SOCl_2

Lactones from hydroxycarboxylic acids

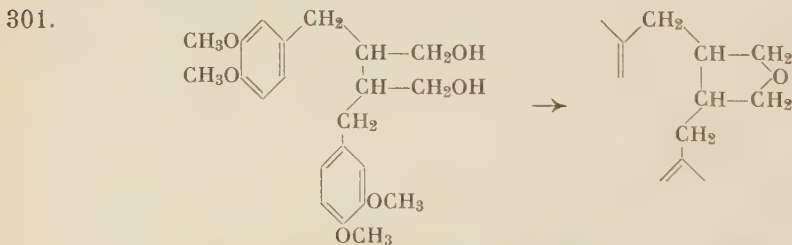


1 gm. di-(4-hydroxycoumarinyl-3)-acetic acid boiled with SOCl_2 for several min. $\rightarrow$ 0.93 gm. lactone. K. Fučík et al., *Bl.* 1949, 609.

Potassium hydrogen sulfate

KHSO_4

Tetrahydrofurans



0.06 gm. *meso*-1,4-di-(3,4-dimethoxyphenyl)-2,3-di(hydroxymethyl)-butane heated 0.5 hr. with KHSO_4 at 180° $\rightarrow$ 0.05 gm. *meso*-3,4-di-(3,4-dimethoxybenzyl)tetrahydrofuran. R. D. Haworth and L. Wilson, *Soc.* 1950, 71.

Sulfuric acid

H_2SO_4

Furan ring closure

s. 3, 169; s. a. R. Kuhn and K. Dury, *A.* 571, 44 (1951)

Morpholines

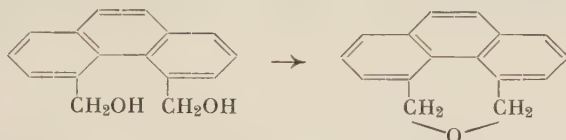
s. 6, 345

Hydrochloric acid

HCl

Cyclic ethers from diols

302/3.



Anhydrous HCl passed into a suspension of 4,5-phenanthrenedimethanol (prepn. s. 61) in benzene at room temp. for 15 min. $\rightarrow$ cyclic ether. Y: 90%. M. S. Newman and H. S. Whitehouse, *Am. Soc.* 71, 3664 (1949).

Chromone rings. 1, 546; s. a. J. S. H. Davies et al., *Soc.* 1950, 3195, 3206

Hydrobromic acid

HBr

s. 6, 868

Ferrous sulfate

FeSO₄**Ketones from hydroperoxides****Free-radical decomposition**

s. 1, 246; s. a. M. S. Kharasch, A. Fono, and W. Nudenberg, *J. Org. Chem.* 16, 128 (1951)

Nitrogen $\downarrow$ OC $\uparrow$ N

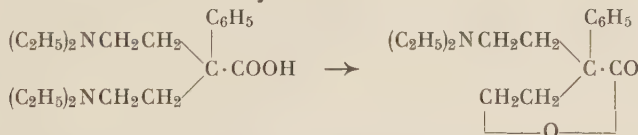
Without additional reagents

w.a.r.

Lactones from aminocarboxylic acids

○

304.

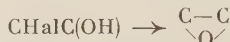


γ -N,N-Dialkylamino acids are converted on pyrolysis to γ -lactones with simultaneous elimination of dialkylamine unless decarboxylation becomes the predominating reaction.—E: α,α -Bis-(β -Diethylaminoethyl)- α -phenylacetic acid heated 30 min. at 210–222° $\rightarrow$ α -diethylaminoethyl- α -phenylbutyrolactone. Y: 84%. F. e. s. R. L. Clarke and A. Mooradian, *Am. Soc.* 71, 2825 (1949).

Halogen $\downarrow$ OC $\uparrow$ Hal

Sodium hydroxide

NaOH

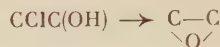
Oxido compounds from halogenhydrins

305. Iodohydroxystearic acid treated with excess cold 0.1 N NaOH for 1 hr. $\rightarrow$ elaidic acid oxide. Y: almost 100%.—Some dihydroxystearic acid also results when concd. alkali at 100° is used. F. e. s. G. King, *Soc.* 1949, 1817.

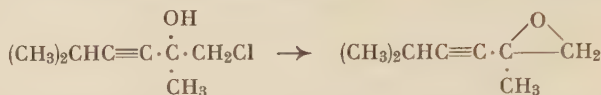
Potassium hydroxide

KOH

Oxido compounds from chlorohydrins



306.



Powdered KOH added portionwise with stirring and cooling to a soln. of 2,5-dimethyl-6-chloro-3-hexyn-5-ol in abs. ether $\rightarrow$ 1,2-epoxy-2,5-dimethyl-3-hexyne. Y: 80-85%. F. Y. Perveev, *Ж.* 19, 1309 (1949); f. e. s. 19, 1303 (1949); C. A. 44, 1008e/a.

O-Heterocyclics from halogenhydrins

○

307.



2'-Chloro-2,5-dihydroxydiphenyl heated with aq. ca. 40%-KOH and Na-hydrosulfite in an autoclave at 230° for 1 hr. $\rightarrow$ 3-hydroxydiphenylene oxide. Y: 94.5%. F. e. s. K. Schimmelschmidt, A. 566, 184 (1950).

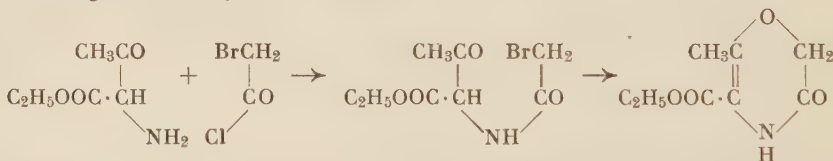
Sodium/alcohol

NaOR

1,4-Oxazines

 α -Halogenocarboxylic acid amides

308.



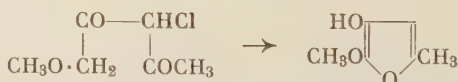
N-Methylmorpholine in dry chloroform added dropwise during 30 min. at 0° to a mixture of ethyl α -amino- β -ketobutyrate hydrochloride and α -bromoacetyl chloride in dry chloroform, and stirring continued for 1 hr. at 0° $\rightarrow$ ethyl α -bromoacetamido- β -ketobutyrate (Y: 83%) in dry ethanol treated with a soln. of Na in ethanol at 15°, and kept at this temp. for 16 hrs. $\rightarrow$ ethyl 5-hydroxy-2-methyl-1,4-oxazine-3-carboxylate (Y: 54.5%). F. e. s. G. T. Newbold, F. S. Spring, and W. Sweeny, Soc. 1950, 909.

Potassium acetate

CH₃COOK

Furans

309.



α -Chloro- γ -methoxyacetylacetone added to a soln. of K-acetate and a little acetic anhydride in glacial acetic acid, and warmed at 80° for

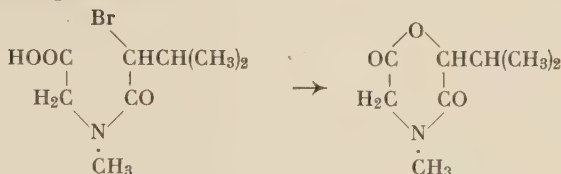
5 hrs. $\rightarrow$ 3-hydroxy-2-methoxy-5-methylfuran. Y: 71.4%. F. e. s. H. Henecka, Chem. B. 82, 32 (1949).

Sodium salt

Na⁺

2,5-Diketomorpholines

310.



N- α -Bromoisovalerylsarcosine dissolved in 2 N NaOH, evaporated to dryness in vacuo, then distilled at 150°/10⁻⁵ mm. $\rightarrow$ 3,6-diketo-4-methyl-2-isopropylmorpholine. Y: 73%.—The ring is formed with varying ease depending on substitution and steric configuration. A. H. Cook and S. F. Cox, Soc. 1949, 2347.

Via intermediates

v.i.

α -Bromo- γ -lactones from α,γ -dibromocarboxylic acid bromides

s. 6, 569

Sulfur $\uparrow$

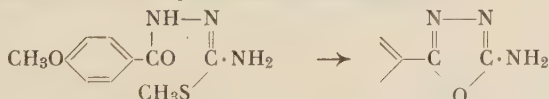
OC $\uparrow$ S

Without additional reagents

w.a.r.

1,3,4-Oxadiazoles from acylthiosemicarbazides

311.



1.2 gm. p-methoxybenzoyl-S-methylisothiosemicarbazide heated $\frac{1}{4}$ hr. at 190° $\rightarrow$ 0.85 gm. 2-amino-5-p-methoxyphenyl-1,3,4-oxadiazole. F. e. s. E. Hoggarth, Soc. 1949, 1918.

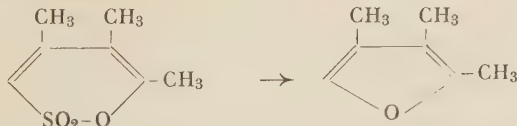
Calcium oxide/quinoline

$\leftarrow$

Furans from sultones

$\leftarrow$

312.

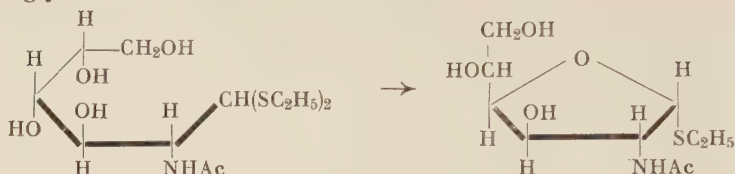


An intimate mixture of 2,3-dimethyl-4-hydroxy-1,3-pentadiene 1-sulfonic acid sultone, CaO-powder, and quinoline distilled at 200-250° $\rightarrow$ 2,3,4-trimethylfuran. Y: 76%. F. e. s. T. Morel and P. E. Verkade, R. 70, 35 (1951).

Mercuric oxide/mercuric chloride

HgO/HgCl₂**Thioglycosides**

313.



Yellow HgO added to an aq. soln. of 4.65 g. N-acetyl-D-glucosamine diethyl thioacetal, this suspension treated dropwise with vigorous stirring over a period of 20 min. an aq. soln. of HgCl₂, stirring maintained for 15 min. after the addition, pyridine added, and filtered $\rightarrow$ 2.01 g. ethyl 2-acetamido-2-desoxy- α -D-gluciothiofuranoside. M. L. Wolfrom, S. M. Olin, and W. J. Polglase, *Am. Soc.* 72, 1724 (1950).

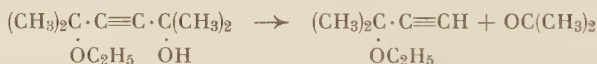
Carbon $\downarrow$ OC $\uparrow$ C

Potassium hydroxide

KOH

**Hydrolytic cleavage of the carbon chain
Hydrocarbons and ketones from alcohols**

314.

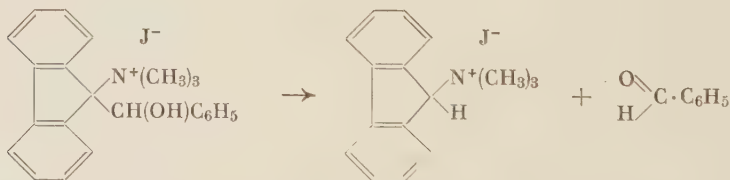


A mixture of tetramethylbutynediol monoethyl ether and powdered KOH distilled $\rightarrow$ dimethylethynylcarbinol ethyl ether. Y: 71.8%. F. e. s. Y. S. Zal'kind and L. P. Chigogidze-Chanturishvili, *Ж.* 20, 719 (1950); *C. A.* 44, 7764h.

Sodium/alcohol

NaOR

315.



The decomposition of certain organic alkali compounds into their components is the reason why some condensations ordinarily promoted by alkali do not occur (83, 110). E: Trimethyl-[9-(hydroxyphenyl)-methyl]-9-fluorenyl]ammonium iodide mixed with a soln. of Na in ethanol, then a little water and the equivalent amount of phenylhydrazine added $\rightarrow$ benzaldehyde phenylhydrazone (Y: 90%) and trimethyl-9-fluorenylammonium iodide (Y: 80%). G. Wittig and K. Nagel, *Chem. B.* 83, 106, 110 (1950).

Red lead oxide

 Pb_3O_4 **Ketones from α -hydroxycarboxylic acids**

←

s. 6, 901

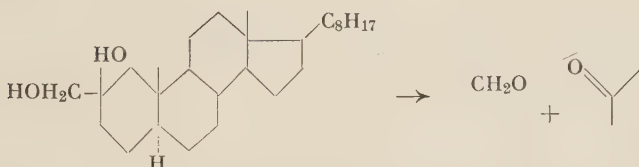
Lead tetraacetate

 $(CH_3COO)_4Pb$ **Ketones from glycols**

←

Degradation

316.



200 mg. crude 2-hydroxymethyl-2-hydroxycholestan-3-ol allowed to stand with Pb-tetraacetate in glacial acetic acid at 20° for 5 hrs. $\rightarrow$ 150 mg. 2-ketocholestan-3-ol. F. e. s. G. Lardelli and O. Jeger, *Helv.* 32, 1817 (1949); s. a. C. Dorée, J. F. McGhie, and F. Kurzer, *Soc.* 1949, S167.

Oxygen

 O_2 **Isatin ring**

○

s. 6, 775

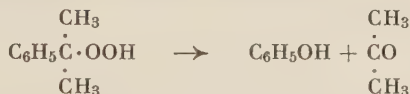
Sulfuric acid

 H_2SO_4 **Hydrolytic cleavage of the carbon chain**

←

Ketones and phenols from hydroperoxides

317.



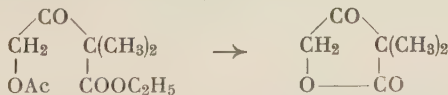
A mixture of aq. H_2SO_4 and a soln. of isopropylbenzene hydroperoxide in isopropylbenzene refluxed 90 min. with vigorous stirring $\rightarrow$ phenol (Y: 82%) and acetone (Y: 74%). G. P. Armstrong, R. H. Hall, and D. C. Quin, *Soc.* 1950, 666.

Lactones from acoxycarboxylic acid esters

○

 β -Keto- γ -lactones (Tetronic acids)

318.



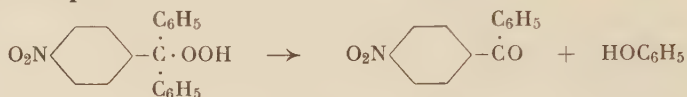
Ethyl α, α -dimethyl- γ -acetoxyacetoacetate added dropwise below 8° to rapidly stirred concd. H_2SO_4 , and kept 48 hrs. in a closed container at refrigerator temp. $\rightarrow$ 3,3-dimethyltetronic acid. Y: 89.4%. F. tetronic acids s. E. B. Reid, R. B. Fortenbaugh, and H. R. Patterson, *J. Org. Chem.* 15, 572 (1950).

Perchloric acid

HClO₄

Hydrolytic cleavage of the carbon chain
Ketones and phenols from hydroperoxides
Migration aptitude

319.



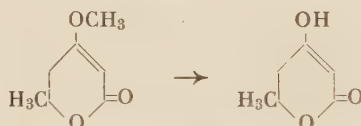
HClO₄ added with cooling to a soln. of p-nitrotriphenylmethyl hydroperoxide (prepn. s. 256) in glacial acetic acid, then water added → p-nitrobenzophenone. Y: 94%.—In the free-radical mechanism of thermal decomposition, the p-nitrophenyl group has a greater migration aptitude than the phenyl group. P. D. Bartlett and J. D. Cotman, Jr., *Am. Soc.* 72, 3095 (1950); s. a. M. S. Kharasch et al., *J. Org. Chem.* 15, 775, 748 (1950); free-radical mechanism s. *J. Org. Chem.* 15, 753, 763 (1950).

Hydrochloric acid

HCl

Hydrolysis of enolethers
Ketones and enols from enolethers

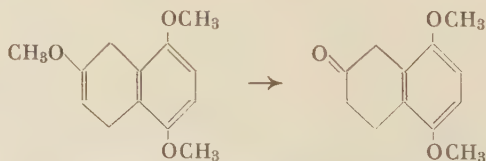
320.



An ethereal soln. of 4-methoxy-6-methyl-5,6-dihydro-2-pyrone treated with a carefully controlled quantity of concd. HCl. and kept at 20° for 48 hrs. with occasional stirring → 4-hydroxy-6-methyl-5,6-dihydro-2-pyrone. Y: 75%. E. R. H. Jones and M. C. Whiting, *Soc.* 1949, 1419; with HI s. E. B. Reid and W. R. Ruby, *Am. Soc.* 73, 1054 (1951).



Concd. HCl added at 0° to a suspension of β-methoxysorbic acid in dry ether, and kept 2.5 hrs. at the same temp. with occasional shaking → crotonylacetic acid. Y: 80%. *Soc.* 1949, 1419.

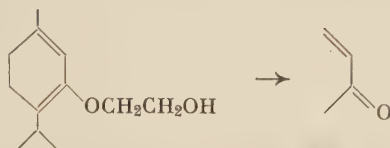


2 N HCl added dropwise to an alc. soln. of 1,4,6-trimethoxy-5,8-dihydronaphthalene, and most of the alcohol distilled off in vacuo at 30°

→ 5,8-dimethoxy-2-tetralone. Y: almost 100%. C. A. Grob and H. Wicki, *Helv.* 31, 1706 (1948).

Ketones from enolethers

321.



17.5 gm. 2-(2-hydroxyethoxy)-4-methyl-1-isopropyl-1,4-cyclohexadiene refluxed 20 min. with 5% -HCl → 14 gm. piperitone.—Because of the high boiling point of hydroxylated ethers compared with that of the ketone produced, the latter can be readily purified by distillation. F. e. s. A. J. Birch and S. M. Mukherji, *Soc.* 1949, 2531.

Ferric sulfate/hydrogen peroxide/barium carbonate

$\text{Fe}_2(\text{SO}_4)_3/\text{H}_2\text{O}_2/\text{BaCO}_3$

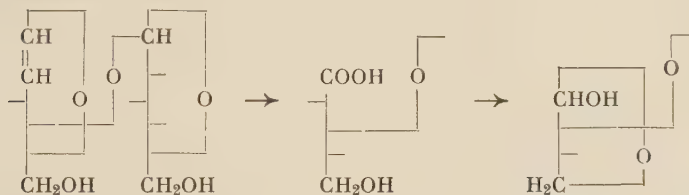
Ruff degradation of carbohydrates

Elimination of carbon monoxide

←

Degradation of glycals via aldonic acids

322.

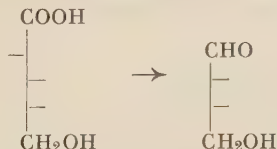


Maltal in aq. K-carbonate treated slowly at 30-50° with 4% -KMnO₄ until the color persists, and the product isolated as Ca salt → Ca glucosido-3-arabonate (Y: 60%) boiled 10 min. with Ba-carbonate and $\text{Fe}_2(\text{SO}_4)_3$ in water, filtered, cooled, the stirred soln. treated with 30% -H₂O₂ followed by an additional portion after 3 hrs., and warmed gently on a water bath → glucosido-2-erythrose (Y: 79%). A. M. Gakhokidze, *Ж.* 20, 116 (1950); f. e. s. *Ж.* 20, 120, 289; C. A. 44, 5819c/g, 6822c.

Ferric sulfate/hydrogen peroxide/barium acetate $\text{Fe}_2(\text{SO}_4)_3/\text{H}_2\text{O}_2/(\text{CH}_3\text{COO})_2\text{Ba}$

Aldehydes from α -hydroxycarboxylic acids

323.



Ca-D-arabonate slowly added to a gently boiling aq. soln. of Ba-acetate and $\text{Fe}_2(\text{SO}_4)_3$, boiling continued for 20 min., filtered

through a carbon pad, H_2O_2 added in 2 portions at 40° , and allowed to stand overnight $\rightarrow$ D-erythrose. Y: 46%. W. G. Overend, M. Stacey, and L. F. Wiggins, Soc. 1949, 1358; method, see Hockett and Hudson, Am. Soc. 56, 1632 (1934); s. a. Am. Soc. 72, 4546 (1950).

Formation of N—N Bond

Rearrangement

Nitrogen/Carbon Type

NN $\curvearrowright$ NC

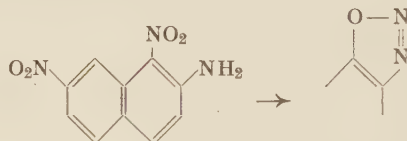
Sodium nitrite

 NaNO_2

Diazo oxides from o-nitramines

○

324.



A soln. of 0.5 gm. 1,7-dinitro-2-naphthylamine in H_2SO_4 (d. 1.84) treated below 10° with a soln. of NaNO_2 in H_2SO_4 (d. 1.84), and the mixture stirred into a suspension of Cu-carbonate in glacial acetic acid $\rightarrow$ 0.45 gm. 7-nitronaphthalene-2,1-diazo oxide. H. H. Hodgson and R. E. Dean, Soc. 1950, 818.

Exchange

Hydrogen $\nmid$

NN $\nmid$ H

Sodium acetate

 CH_3COONa

Azo compounds by coupling

N:N

s. 6, 325

Sodium nitrite

 NaNO_2

Triazenes

 $\leftarrow$

s. 1, 607; s. a. D. E. Pearson, W. C. Holland, and H. P. Midgett, Am. Soc. 72, 2303 (1950)

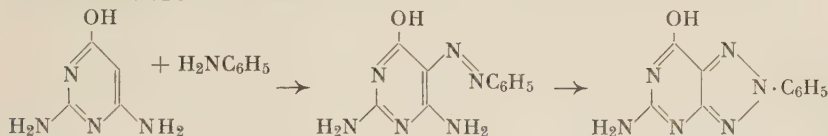
1,2,3-Triazoles

○

s. 1, 262-4; s. a. K. Eiter and A. Nezval, M. 81, 404 (1950)

Cupric sulfate CaSO_4 **1,2,3-Triazole ring via azo compounds**
v-Triazolo(d)pyrimidines

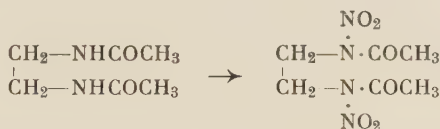
325.



Aniline in HCl diazotized with aq. NaNO_2 below 3° , excess HNO_2 destroyed with urea, the diazonium salt soln. so obtained added slowly to a stirred soln. of 2,4-diamino-6-hydroxypyrimidine sulfate in aq. Na-acetate, and stirred for 10 min. $\rightarrow$ 2,4-diamino-5-phenylazo-6-hydroxypyrimidine sesquihydrate (Y: ca. 100%) added to a refluxing mixture of CuSO_4 , water, and pyridine, and refluxing continued for 3 hrs. with vigorous stirring $\rightarrow$ 2-phenyl-5-amino-7-hydroxy-v-triazolo(d)pyrimidine (Y: 70.5%). F. e. s. F. R. Benson, L. W. Hartzel, and W. L. Savell, *Am. Soc. 72*, 1816 (1950).

Acetic anhydride $(\text{CH}_3\text{CO})_2\text{O}$ **Nitration****Nitramines** $\text{N} \cdot \text{NO}_2$

326.



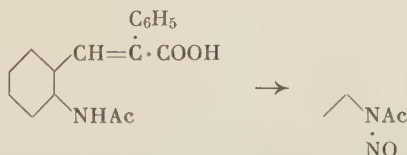
A mixture of acetic anhydride and 98% HNO_3 may be able to nitrate compounds which remain unchanged in 98% HNO_3 alone or mixed with concd. H_2SO_4 .—E: Ethylenebisacetamide added portionwise below 5° to the above mixture, and worked up after 6 hrs. at $5^\circ \rightarrow$ N,N'-dinitroethylenebisacetamide. Y: 83%. F. e. s. W. E. Bachmann et al., *Am. Soc. 72*, 3132 (1950); s. a. A. F. McKay and J. E. Milks, *Am. Soc. 72*, 1616 (1950).

Stannous chloride SnCl_2 **Hydrazines from amines** $\text{NH}_2 \rightarrow \text{NHHN}_2$

s. 2, 304; s. a. P. P. T. Sah, *R. 69*, 1025 (1950)

Nitrosyl chloride NOCl **N-Nitrosamines** $\text{N} \cdot \text{NO}$

327.



A soln. of NOCl in glacial acetic acid added dropwise at 0° with stirring to a mixture of 5 gm. o-acetamido- α -phenylcinnamic acid, freshly fused

K-acetate, P_2O_5 , glacial acetic acid, and acetic anhydride, then stirred for a further 30 min. $\rightarrow$ 4.47 gm. o-nitrosoacetamido- α -phenylcinnamic acid. D. H. Hey and J. M. Osbond, Soc. 1949, 3164; f. e. s. Soc. 1949, 3181.

Sulfur dioxide

SO_2

Hydrazines from amines

$NH_2 \rightarrow NHNH_2$

s. 1, 261; s. a. R. L. Barker et al., J. Soc. Chem. Ind. 68, 277 (1949)

Hydroxylamine-O-sulfonic acid

NH_2OSO_3H

Hydrazines from amines

$NH_2 \rightarrow NHNH_2$

328.



An aq. soln. of hydroxylamine-O-sulfonic acid added dropwise over a period of 8 min. to a refluxing mixture of n-butylamine and water, cooled, acidified with glacial acetic acid, warmed 10 min. to 50° with benzaldehyde, cooled, extracted with ether, added to aq. oxalic acid, and steam-distilled until no more benzaldehyde comes over $\rightarrow$ n-butylhydrazine oxalate. Y: 60%. F. e., with lower yields, s. G. Gever and K. Hayes, J. Org. Chem. 14, 813 (1949).

Chlorine ion

Cl^-

N-Nitramines

$N \cdot NO_2$

s. 4, 290; s. a. Am. Soc. 72, 341 (1950)

Oxygen †

NN † O

Zinc

Zn

Sym. azo compounds from nitro compounds

$2RNO_2 \rightarrow RN:NR$

s. 3, 251; s. a. R. B. Carlin and W. O. Forshey, Jr. Am. Soc. 72, 793 (1950)

Arsenic trioxide

As_2O_3

Azoxy compounds from nitro compounds

$2RNO_2 \rightarrow RN:NR$
 $\downarrow$
 O

s. 4, 292; s. a. R. Gaudry and K. F. Keirstead, Can. J. Research 27 B, 890 (1949)

Elimination

Hydrogen $\uparrow$

NN $\uparrow$ H*Alkyl nitrite*

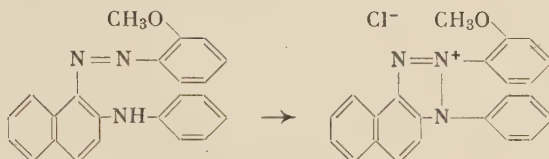
RONO

○

1,2,3-Triazolium salts from o-aminoazo compounds

Tetrazolium salts from formazans

329.



5 gm. o-methoxybenzeneazo-N-phenyl- β -naphthylamine in chloroform dehydrogenated with isoamyl nitrite and HCl-gas $\rightarrow$ 6.8 gm. 2-phenyl-3-(o-methoxyphenyl)-3H-naphtho[1,2]triazolium chloride. F. e., also with $K_2Cr_2O_7$, s. R. Kuhn and E. Ludolphy, A. 564, 35 (1949); tetrazolium salts from formazans s. D. Jerchel and H. Fischer, A. 563, 200, 208 (1949); S. W. Fox and E. Hemmingson Atkinson, Am. Soc. 72, 3629 (1950).

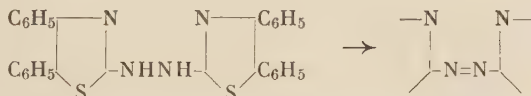
Nitric acid HNO_3

Azo compounds from hydrazo compounds

 $\cdot NHH \cdot \rightarrow \cdot N:N \cdot$

s. 6, 869

330.



Azothiazoles. A suspension of 4,4',5,5'-tetraphenylhydrazothiazole-2,2' in dil. HNO_3 gradually heated until the material suddenly turns deep red $\rightarrow$ 4,4',5,5'-tetraphenylazothiazole-2,2'. Y: ca. 100%. F. e. s. H. Beyer et al., Chem. B. 82, 148, cf. 143 (1949).

Formation of N—S Bond

Uptake

Addition to Sulfur and Carbon

NS $\downarrow$ SC*Sodium hydroxide*

NaOH

Dithiocarbamic acids from amines

NH $\rightarrow$ NCSSH

s. 6, 332

Exchange

Hydrogen †

NS † H

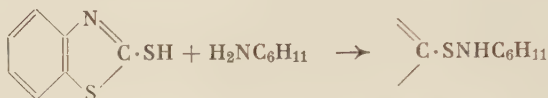
Chlorine

Cl

Sulfenamides from amines

NH → NSR

331.



A mixture of Cl_2 and air introduced at 25–32° and a pH of 13.1–12.5 to a rapidly stirred aq. soln. of benzothiazole-2-thiol, NaOH, and cyclohexylamine over a period of 4–5 hrs. → N-cyclohexylbenzothiazole-2-sulfenamide. Y: 96.5%. F. e. and methods s. E. L. Carr, G. E. P. Smith, and G. Alliger, J. Org. Chem. 14, 921 (1949).

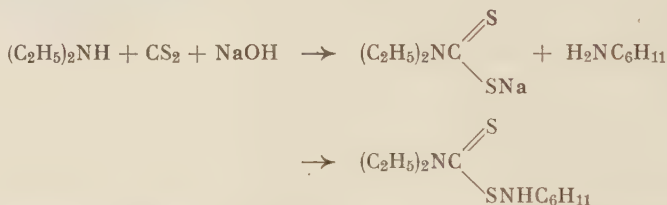
Iodine

I

Thiocarbamylsulfenamides from amines
via dithiocarbamic acids

←

332.



Cyclohexylamine added to a soln. of Na-N,N-diethylthiocarbamate, prepared from diethylamine, CS_2 , and NaOH in water, then an aq. soln. of iodine and KI slowly added at 15–31° over a period of 1.5 hrs. → N,N-diethylthiocarbamyl-N-cyclohexylsulfenamide. Y: 82%. F. e. and methods s. G. E. P. Smith et al., J. Org. Chem. 14, 935 (1949).

Halogen †

NS † Hal

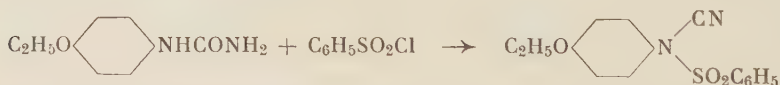
Pyridine

 $\text{C}_5\text{H}_5\text{N}$

N-Sulfonylcyanamides from ureas

←

333.



By treating a soln. or suspension of a subst. arylurea in pyridine with a sulfonyl chloride below 60°, and working up after 12–15 min., N-sulfonylcyanamides are obtained. The velocity of the reaction is affected noticeably by the choice of the sulfonyl chloride.—E: p-Ethoxyphenylurea and benzenesulfonyl chloride → benzenesulfonyl-p-ethoxyphenylcyanamide. Y: 80%. F. e. s. F. Kurzer, Soc. 1949, 3029.

Elimination

Hydrogen

NS † H

Iodine

I

Tetrahydro-1,2,5-thiadiazine-6-thiones
from amino-dithiocarbamic acids

○

s. 6, 363

Sulfur

NS † S

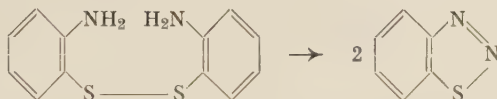
Cuprous chloride

CuCl

1,2,3-Benzothiadiazoles from
0,0'-diaminodisulfides

○

334.



An ice-cold soln. of 2,2-diaminodiphenyl disulfide in concd. H_2SO_4 slowly added during ca. 30 min. to nitrosylsulfuric acid (from NaNO_2 and concd. H_2SO_4) kept in a freezing mixture, the tetrazonium salt soln. so obtained poured into an ice-cold soln. of CuCl in concd. HCl , then NaOH added $\rightarrow$ 1,2,3-benzothiadiazole. Y: 85%. F. reactions of the tetrazonium salt s. A. Burawoy and C. Turner, Soc. 1950, 469.

Formation of N—Rem Bond

Exchange

Oxygen †

NRem † O

Without additional reagents

w.a.r.

Organo lead compounds

←

N-(Trialkylplumbi)sulfonamides

335.

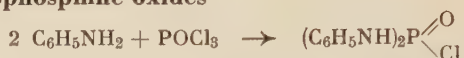


An alc. soln. of benzenesulfonamide added to an alc. soln. of tri(n-propyl)-Pb hydroxide, and water added after 10 min. $\rightarrow$ N-(tri-n-propylplumbi)benzenesulfonamide. Y: almost 100%. F. e. s. B. C. Saunders, Soc. 1950, 684.

Halogen †**NRem †† Hal***Without additional reagents**w.a.r.***Diaminochlorophosphine oxides**

←

336.

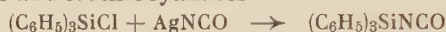


An ethereal soln. of aniline added slowly to an ice-cooled ethereal soln. of the calculated quantity of POCl_3 , and allowed to stand overnight $\rightarrow$ dianilinochlorophosphine oxide. Y: almost 100%. F. e. s. H. G. Cook et al., Soc. 1949, 2921.

*Silver and lead salts**Ag⁺ and Pb⁺⁺***Silyl isocyanates and isothiocyanates**

←

337.

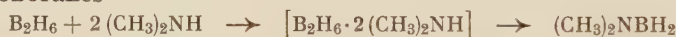


Triphenylsilyl chloride and Ag-isocyanate refluxed 1 hr. in benzene under $\text{N}_2 \rightarrow$ triphenylsilyl isocyanate. Y: 82-85%.—Similarly with Pb-isothiocyanate: Triphenylsilyl isothiocyanate. Y: 97%. F. methods s. H. Gilman, B. Hofferth, and H. W. Melvin, Am. Soc. 72, 3045 (1950).

Remaining elements †**NRem †† Rem***Without additional reagents**w.a.r.***Aminoboranes**

←

338.

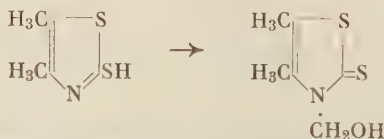


Diborane passed into dry liq. dimethylamine at -42° , the excess dimethylamine pumped off in a high vacuum at room temp., dry N_2 admitted to bring the pressure to 400 mm., and the addition compound obtained heated at 130° with sublimation of the reaction product $\rightarrow$ dimethylaminoborane. Y: ca. 100%. F. e. s. A. B. Burg and C. L. Randolph, Jr., Am. Soc. 71, 3451 (1949).

Formation of N—C Bond**Uptake****Addition to Oxygen and Carbon****NC ↓ OC***Without additional reagents**w.a.r.***N-Hydroxymethylation**

←

339.

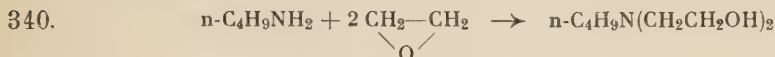


4,5-Dimethyl-2-mercaptothiazole and 37%-formaldehyde agitated and heated together at $93-95^\circ$ for 2 hrs. $\rightarrow$ 3-hydroxymethyl-4,5-dimethyl-

2-thiono-4-thiazoline. Y: 89%. F. D. Stewart and R. A. Mathes, *J. Org. Chem.* 14, 1111 (1949).

Di(hydroxyalkyl)amines from oxido compounds

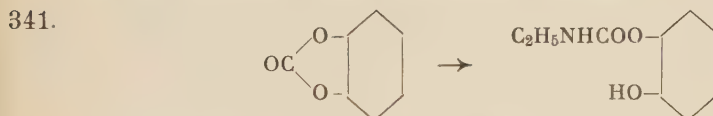
←



1.21 moles ethylene oxide bubbled into a stirred aq. soln. of 0.526 mole n-butylamine over a period of 6.5 hrs. → bis-(β-hydroxyethyl)-n-butylamine, Y: 85%. F. e. s. A. F. McKay and H. H. Brownell, *J. Org. Chem.* 15, 648 (1950); s. a. J. Lecocq, *Bl.* 1950, 188.

Hydroxyurethans from carbonic acid esters

C



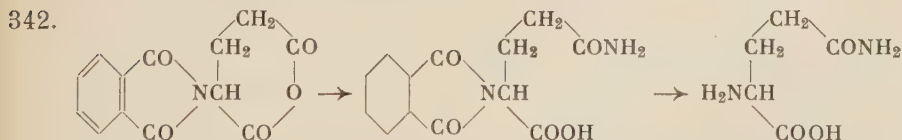
A soln. of ethylamine in alcohol-water added to a suspension of 40.8 gm. pyrocatechol carbonate in ice-cold alcohol → 35 gm. pyrocatechol mono(ethylcarbamate) (startg. m. f. 504). F. e. s. S. Petersen, *A.* 562, 205 (1949).

Dicarboxylic acid monoamides from dicarboxylic acid anhydrides

s. 4, 308; s. a. R. Adams and J. B. Campbell, *Am. Soc.* 72, 128, 153 (1950); G. A. Swan, *Soc.* 1950, 1534

Glutamines

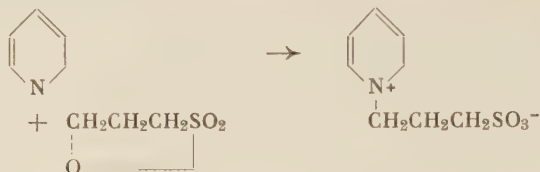
Prim. amines from phthalimides; mild hydrolysis in the cold



A soln. of phthalyl-L-glutamic anhydride in dioxane treated with small quantities of dry ethereal NH_3 in excess, and worked up when the precipitation is complete → phthalyl-L-glutamine (Y: 77%) dissolved in aq. Na-carbonate, treated with 50%-hydrazine hydrate, and allowed to stand at room temp. for 2 days → L-glutamine (Y: 67%).—The phthalyl derivative differs from the carbobenzoxy derivative in combining with ammonia and amines to form γ-amides instead of α-amides. F. e., also N-subst. glutamines, s. F. E. King and D. A. A. Kidd, *Soc* 1949, 3315.

Aminosulfonic acid inner salts from sultones

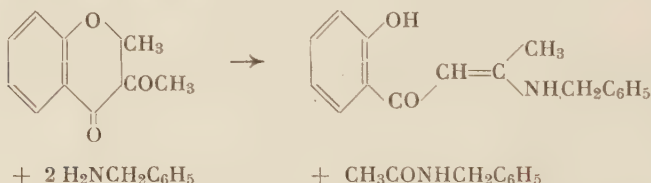
343.



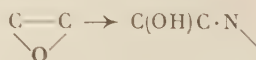
Propane sultone dissolved in pyridine, and heated 1 hr. on a water bath after the initial vigorous reaction has subsided $\rightarrow$ 1-(N-pyridyl)-propane sulfonic acid betaine. Y: ca. 100%. F. e. and adducts of sultones s. J. H. Helberger, G. Manecke, and R. Heyden, *A.* 565, 22 (1949).

Chromone ring opening

344.

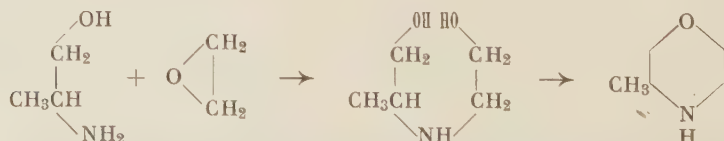


A soln. of 3-acetyl-2-methylchromone and benzylamine in benzene allowed to stand at room temp. for 24 hrs. $\rightarrow$ 2- β -benzylaminocrotonylphenol (Y: ca. 90%) and acetobenzylamide (Y: ca. 100%) (1949, 2142).—Treatment of 3-aroyleflavones with benzylamine results in all cases in the loss of the 3-aroyle group as an aroylebenzylamide and formation of an unsatd. benzylamino compound; this general reaction may be used for orientation purposes (1950, 2759). F. e. s. W. Baker, V. S. Butt, and F. Glockling, *Soc.* 1949, 2142; 1950, 2759.

N-Subst. aminoalcohols from oxido compounds

s. 1, 277/8; 2, 317/8; 3, 362; s. a. N. G. Barker and N. H. Cromwell, *Am. Soc.* 73, 1051 (1951)

345.



Morpholines. Ethylene oxide in alcohol added with cooling and stirring to β -hydroxyisopropylamine in alcohol $\rightarrow$ α -methyl- β , β' -dihydroxy-

diethylamine (Y: 95%) heated with concd. H_2SO_4 (d. 1.84) at 170–180° for 8 hrs., and isolated as hydrochloride $\rightarrow$ 3-methylmorpholine hydrochloride (Y: 93%).—The reaction with olefin oxides proceeds as well in abs. as in moist alcohol, i. e. 95%-ethanol.—F. e. s. A. Y. Berlin and T. P. Sycheva, *Ж.* 20, 640 (1950); *C. A.* 44, 7853f.

Oxazolidines from aminoalcohols

○

346.



(β -Hydroxyethyl)aniline rubbed with excess 40%-formaldehyde until, after 1-2 min., a clear soln. is formed $\rightarrow$ 3-phenyloxazolidine. Y: ca. 100%. F. e. s. G. A. R. Kon and J. J. Roberts, *Soc.* 1950, 978; s. a. L. H. Goodson and H. Cristopher, *Am. Soc.* 72, 358 (1950); E. L. Engelhardt, F. S. Crossley, and J. M. Sprague, *Am. Soc.* 72, 2718 (1950); s. a. L. W. Daasch and U. E. Hanninen, *Am. Soc.* 72, 3673 (1950).

Oxazolidines from cyanohydrin acetates

s. 6, 73

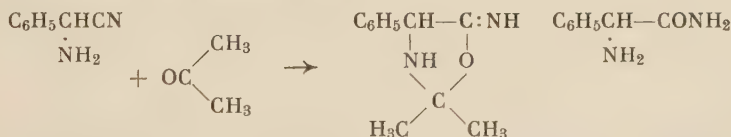
Sodium/alcohol

NaOR

α -Aminocarboxylic acid amides from
 α -aminonitriles via oxazolidines

 $\leftarrow$

347.



A soln. of Na in methanol added to a soln. of 20 gm. α -aminobenzyl cyanide in cold acetone $\rightarrow$ 23 gm. 5-imino-4-phenyl-2,2-dimethyloxazolidine, 15 gm. of which refluxed with water $\rightarrow$ 13 gm. α -aminophenylacetamide. J. D. Billimoria and A. H. Cook, *Soc.* 1949, 2323.

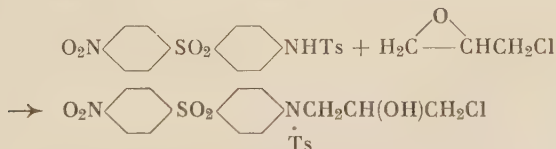
Pyridine

 $\text{C}_5\text{H}_5\text{N}$

Aminoalcohols from oxido compounds

C

348.



A mixture of 4-tosylamino-4'-nitrodiphenyl sulfone, pyridine, and epichlorohydrin heated on a steam bath for 1 hr. $\rightarrow$ 4-(N-tosyl- γ -chloro- β -hydroxypropylamino)-4'-nitrodiphenyl sulfone. Y: 85%. F. e. s. B. R. Baker, M. V. Querry, and A. F. Kadish, *J. Org. Chem.* 15, 402 (1950).

Hydrochloric acid

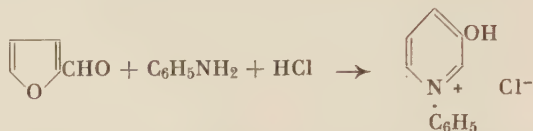
HCl

Ring enlargement

 $\leftarrow$

N-Heterocyclics from O-heterocyclics

349.



Furfural in alcohol added at 15° to a soln. of aniline and concd. HCl in alcohol, kept in an ice-bath for 3 hrs., steam-distilled, and the residue worked up $\rightarrow$ 1-phenyl-3-hydroxypyridinium chloride. Y: 49%. C. F. Koelsch and J. J. Carney, *Am. Soc.* **72**, 2285 (1950).

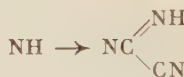
Addition to Nitrogen and Carbon

NC $\Downarrow$ NC

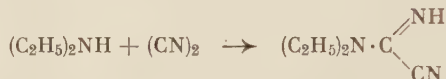
Without additional reagents

w.a.r.

Cyanoforamidines from amines



350.

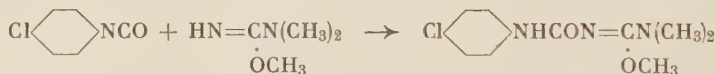


A soln. of diethylamine in anhydrous ethyl acetate cooled in an ice-bath, and saturated with cyanogen $\rightarrow$ N-diethylcyanoforamidine. Y: 70%. F. e. s. H. M. Woodburn, B. A. Morehead, and W. H. Bonner, *J. Org. Chem.* **14**, 555 (1949).

Isobiurets from isoureas

 $\leftarrow$

351.



A soln. of 7.5 gm. O,N,N-trimethylisourea in dry ether added to a soln. of 10 gm. p-chlorophenyl isocyanate in dry ether, and worked up after a few min. $\rightarrow$ 10.25 gm. 1-(p-chlorophenyl)-4.5.5-trimethyl-4-isobiuret. F. e. s. F. H. S. Curd, D. G. Davey, and D. N. Richardson, *Soc.* **1949**, 1732.

Thiosemicarbazides from isothiocyanates and hydrazines

 $\leftarrow$

352.



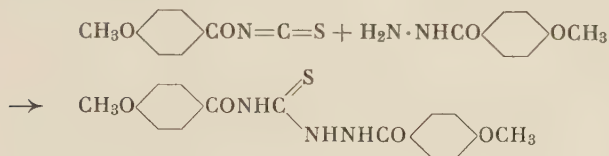
A soln. of 1.3 gm. methyl isothiocyanate and 1.9 gm. phenylhydrazine in ethanol warmed for several min., then evaporated under reduced pressure $\rightarrow$ 2 gm. 2-phenyl-4-methylthiosemicarbazide. J. S. Elvidge

and F. S. Spring, Soc. 1949, S135; s. a. J. Druey and B. H. Ringier, *Helv.* 34, 195 (1951); cf. J. D. Brooks et al., Soc. 1950, 452; in aq. soln. s. E. Schmidt et al., A. 568, 192 (1950).

Acylthiosemicarbazides from acylisothiocyanates

←

353.

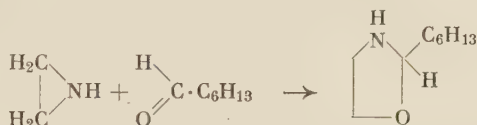


1.9 gm. p-methoxybenzoyl isothiocyanate (prepn. s. 480) added during 5 min. to a stirred soln. of 1.7 gm. p-methoxybenzoylhydrazide in warm alcohol, and worked up after 1 hr. $\rightarrow$ 2.8 gm. 1,4-di-p-methoxybenzoylthiosemicarbazide. F. e. s. E. Hoggarth, Soc. 1949, 1160.

Oxazolidines from oxo compounds

←

354.



Ethyleneimine added dropwise at 5-10° over a period of 1.5-2 hrs. to a soln. of heptaldehyde in ethyl or isopropyl ether, and refluxed ca. 24 hrs. $\rightarrow$ 2-hexyloxazolidine. Y: 95%. F. e., with lower yields, s. J. B. Doughty, C. L. Lazzell, and A. R. Collett, Am. Soc. 72, 2866 (1950).

Sodium hydroxide

NaOH

Ureas from amines and isocyanates

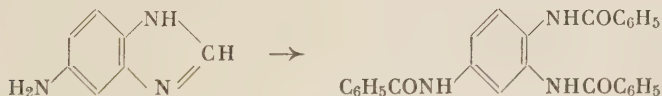
 $\text{NH}_2 \rightarrow \text{NHCONHR}$

s. 3, 267; s. a. K. Zeile and M. Oetzel, Z. physiol. Chem. 284, 1 (1949)

Imidazole ring opening

C

355.



Benzoyl chloride added with vigorous stirring to a soln. of 12 gm. 5-aminobenzimidazole in 10%-NaOH, and heated 15 min. at 90-95° $\rightarrow$ 31 gm. 1,2,4-tribenzamidobenzene. F. e. s. M. Stäuble, *Helv.* 32, 135 (1949).

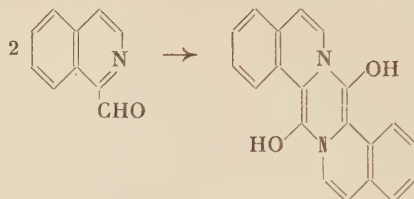
Potassium cyanide

KCN

Quinocolls

○

356.



A hot soln. of 1 gm. isoquinoline-1-aldehyde in aq. alcohol treated with aq. KCN, and refluxed 15 min. $\rightarrow$ 1 gm. crude dihydroisoquinocoll. F. e. s. B. R. Brown and D. L. Hammick, Soc. 1950, 628.

Alkali salt

 $\leftarrow$

Ureas from amines

 $\text{NH}_2 \rightarrow \text{NHCONH}_2$

s. 4, 460; s. a. F. Kurzer, Org. Synth. 31, 8 (1951)

Pyridine

 $\text{C}_5\text{H}_5\text{N}$

Ureas from amines and isocyanates

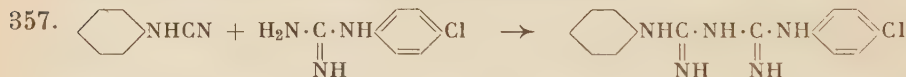
 $\text{NH}_2 \rightarrow \text{NHCONHR}$

s. 6, 508

Magnesium

Mg

Biguanides from cyanamides and guanidines

 $\leftarrow$ 

Ethereal ethyl-MgI gradually added to a stirred suspension of p-chlorophenylguanidine in anisole, refluxed 15-30 min., cooled to room temp., a soln. of cyclohexylcyanamide in anisole added, refluxed 18-24 hrs. with stirring, ice-cooled, and decomposed with HCl-ice water $\rightarrow$ N¹-p-chlorophenyl-N⁵-cyclohexyldiguanide (isolated as hydrochloride). Y: 69%. F. e. s. S. Birtwell, F. H. S. Curd, and F. L. Rose, Soc. 1949, 2556.

Acetic acid

 CH_3COOH

Sulfonylguanidines from sulfonylcyanamides

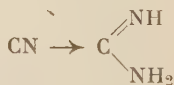
 $\leftarrow$

s. 6, 529

Sulfonates

 RSO_3^-

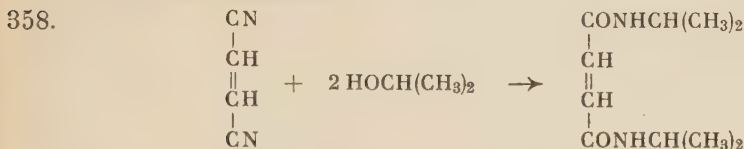
Amidines from nitriles



s. 2, 326; s. a. L. Bauer and J. Cymerman, Soc. 1950, 1826, 2078

Dihydroglyoxalines ○

s. 4, 316; s. a. L. Bauer and J. Cymerman, Soc. 1950, 2078

Sulfuric acid H_2SO_4 **Subst. carboxylic acid amides from nitriles and alcohols**CN $\rightarrow$ CONHR

Isopropanol added below 45° to a soln. of fumaronitrile in concd. H_2SO_4 over a period of 20 min., and worked up after 2 hrs. $\rightarrow$ N,N'-diisopropylfumaramide. Y: 80%. F. e. s. J. J. Ritter et al., Am. Soc. 71, 4128, 4130 (1949); 72, 5577 (1950).

*Hydrochlorides***Ureas from amines** $NH_2 \rightarrow NHCONH_2$ 

A warm aq. soln. of KCNO added in one portion to an aq. soln. of glycine ethyl ester hydrochloride, and warmed 15 min. on a steam bath $\rightarrow$ ethyl hydantoate. Y: 93%. W. E. Bachmann and C. E. Maxwell, 3rd., Am. Soc. 72, 2880 (1950).

Guanidines from amines

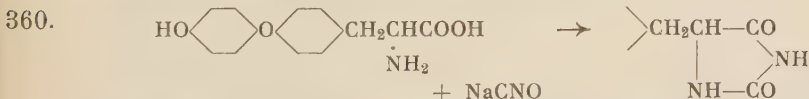
s. 5, 346; s. a. E. L. May, E. Mosettig, and H. G. Latham, Jr., J. Org. Chem. 15, 890, 884 (1950)

Hydrochloric acid HCl **Thioureas from amines** $NH_2 \rightarrow NHCSNH_2$

s. 1, 363; s. a. F. Kurzer, Org. Synth. 31, 21 (1951)

Carbamylmercaptoacetamides from amines $NH_2 \rightarrow NHCOCH_2SCONH_2$

s. 4, 397; s. a. Am. Soc. 72, 1687 (1950)

Hydantoins from α -aminocarboxylic acids ○

A suspension of 2 gm. thyronine in water containing Na-cyanate refluxed until all solid has dissolved, concd. HCl added, and refluxed for a further 30 min. $\rightarrow$ 1.9 gm. 5-(4-p-hydroxyphenoxybenzyl)hydantoin. F. e. s. J. C. Clayton and B. A. Hems, Soc. 1950, 840.

2-Mercaptoimidazoles from aminoacetals

s. 5, 252; with KSCN s. Am. Soc. 71, 4000 (1949)

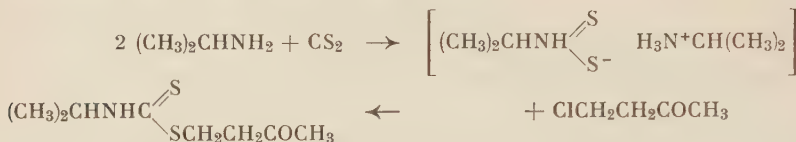
Addition to Sulfur and Carbon

NC ↓ SC

*Without additional reagents**w.a.r.***Dithiocarbamic acid esters from amines**

←

361.

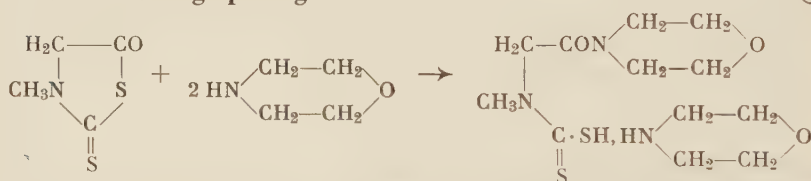


CS_2 added to a well-stirred soln. of isopropylamine in alcohol, methyl 2-chloroethyl ketone added to the resulting suspension over a period of 0.5 hr., and allowed to stand at room temp. for 2 days → 3-keto-butyl isopropylidithiocarbamate. Y: 84%. J. W. Batty and B. C. L. Weedon, Soc. 1949, 786.

Thiazolidine ring opening

C

362.

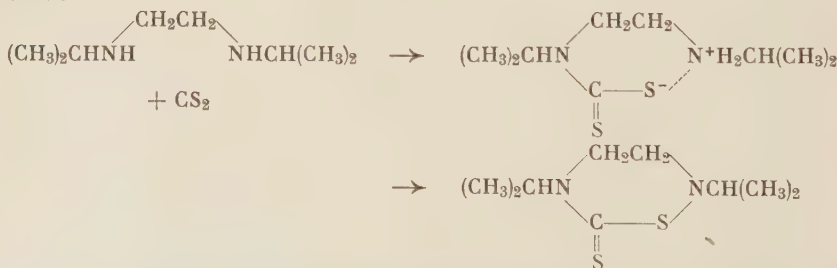


2-Thio-3-methylthiazolid-5-one (prepn., s. 610) in acetone treated with 2 equivalents of morpholine → morpholinium salt of N-dithiocarboxy-N-methylaminoacetomorpholide. Y: 90%. A. H. Cook et al., Soc. 1949, 2337; f. e. s. Soc. 1949, 2323.

Tetrahydro-1,2,5-thiadiazine-6-thiones from diamines via amino-dithiocarbamic acids

O

363.



CS_2 in acetone added dropwise at 10-15° with vigorous stirring and cooling to a soln. of N,N'-diisopropylethylenediamine in acetone →

N-isopropyl-N-(β -isopropylaminoethyl)dithiocarbamic acid inner salt (Y: 90%) dissolved in 1.4 N aq. NaOH, then stirred vigorously, while aq. iodine KI-soln. is added dropwise, and worked up after precipitation is complete $\rightarrow$ 2,5-diisopropyltetrahydro-1,2,5-thiadiazine-6-thione (Y: 71%). F. e. s. R. A. Donia et al., *J. Org. Chem.* 14, 946 (1949).

Addition to Carbon

NC $\downarrow$ CC

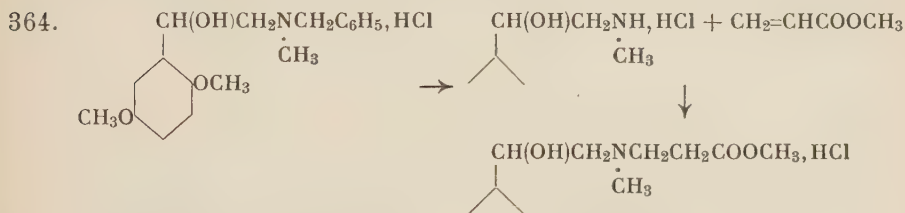
Without additional reagents

w.a.r.

Amines from ethylene derivatives

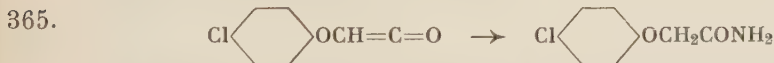
C:C $\rightarrow$ CHCN $\leftarrow$

s. 2, 328/9; 4, 539; s. a. A. P. Phillips, *Am. Soc.* 72, 3298 (1950)



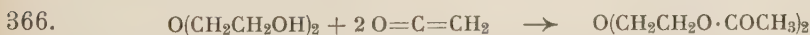
Preceding debenzoylation. A soln. of β -(2,5-dimethoxyphenyl)- β -hydroxyethyl-benzyl-methylamine hydrochloride in methanol hydrogenated with palladized charcoal $\rightarrow$ β -hydroxy- β -(2,5-dimethoxyphenyl)ethyl-methylamine hydrochloride, the liberated base in benzene added to methyl acrylate, allowed to stand at room temp. for 3 days, warmed to ca. 50° for 3 hrs., and isolated as hydrochloride $\rightarrow$ N-methyl-N-(β -hydroxy- β -(2,5-dimethoxyphenyl)ethyl)- β -alanine methyl ester hydrochloride. Y: 90%. F. e. s. R. Baltzly and A. P. Phillips, *Am. Soc.* 71, 3419, 3421 (1949).

Carboxylic acid amides from ketenes

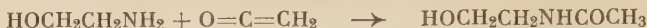
 $\leftarrow$ 

Dry NH_3 -gas passed into an ethereal soln. of 4-chlorophenoxyketene (prepn. s. 883) until precipitation is complete $\rightarrow$ 4-chlorophenoxyacetamide. Y: 73%. F. e., also anilides, s. C. M. Hill, G. W. Senter, and M. E. Hill, *Am. Soc.* 72, 2286 (1950).

Acetylation with ketene Selective N-acetylation

 $\leftarrow$ 

Ketene introduced into diethyleneglycol in the presence of Na-acetate below 63° for 1.5 hrs. $\rightarrow$ diethyleneglycol diacetate. Y: 85%.—Only mixtures of mono- and diacetate are obtained in the absence of Na-acetate.



Ketene introduced into an aq. soln. of monoethanolamine $\rightarrow$ N-acetyl-aminoethanol. Y: 81.4%. Also diacetylation s. A. A. Ponomarev and Y. B. Isaev, *Ж.* 20, 1079 (1950); C. A. 44, 9349d.

1,2,3-Triazoles from acetylene

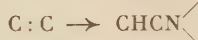
○

derivatives
s. 1, 290; s. a. J. C. Sheehan and C. A. Robinson, *Am. Soc.* 73, 1207 (1951)

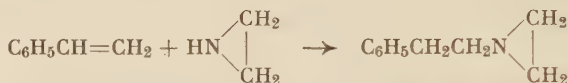
Sodium

Na

Amines from ethylene derivatives



367.



Anhydrous ethyleneimine treated with Na, then with styrene at 25-45°, and stirring continued at room temp. for 5 hrs. $\rightarrow$ N-(β -phenylethyl)-ethyleneimine. Y: 89%. F. e. and reactions of ethyleneimine s. H. Bestian, *A.* 566, 210 (1950).

368.



Phenylethylamines. 1-3% Na dissolved in refluxing piperidine, then styrene added dropwise over a period of 2 hrs., and refluxed for 3-5 hrs. more $\rightarrow$ N-(phenylethyl)piperidine. Y: 81%. F. e. with lower yields s. R. Wegler and G. Pieper, *Chem. B.* 83, 1 (1950).

Bases

N-Cyanoethylation of α -aminocarboxylic acids



369.



By adding 1 equivalent of aq. NaOH, KOH, or Ba(OH)₂ followed by 1-1.1 equivalents of acrylonitrile below 30° to an aq. suspension of an α -amino acid, shaking until homogeneous, keeping overnight at 5° or room temp., and, if necessary, warming 2 hrs., at 50—60° to complete the reaction, N-monocyanoethyl- α -amino acids are obtained in good yields.—E: N-(2-Cyanoethyl)-DL-alanine. Y: 82.5%.—N-(2-Cyanoethyl)-L-leucine. Crude Y: 91%.—Racemization does not occur during the reaction. F. e. s. L. L. McKinney et al., *Am. Soc.* 72, 2599 (1950); dicyano-ethylation s. *Am. Soc.* 73, 1641 (1951).

Borax**Carboxylic acid amides from
 α,α -dihalogenoethylene derivatives**

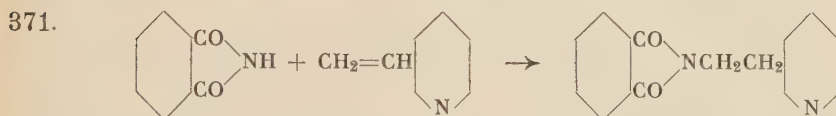
←



A mixture of aniline, borax ($\text{Na}_2\text{B}_4\text{O}_7 \cdot 10 \text{H}_2\text{O}$), and tetrafluoroethylene heated 8 hrs. with shaking at $130^\circ \rightarrow$ difluoroacetanilide. Y: 71%. F. e. s. D. D. Coffman et al., J. Org. Chem. 14, 747 (1949).

*Triton B***Phthalimides from ethylene derivatives**

←



Phthalimide, 2-vinylpyridine, and a little Triton B refluxed ca. 2 hrs. until the bath temp. reaches 188° without appreciable refluxing $\rightarrow$ N-[2-(2-pyridylethyl)]phthalimide. Y: 75%. F. K. Kirchner et al., J. Org. Chem. 14, 388 (1949); method, see A. Galat, Am. Soc. 67, 1414 (1945).

*Salts of org. bases***N-Cyanoethylation** **β -(Arylamino)propionitriles**

←



Aniline, aniline acetate, and acrylonitrile heated in an oil bath at 120 – 140° for 14 hrs. $\rightarrow$ β -anilinopropionitrile. Y: 98%. F. e. s. A. F. Bekhli and A. G. Serebrennikov, Ж. 19, 1553 (1949); C. A. 44, 3448d.

Hydrazoic acid**Carboxylic acid amides from ketones**

←

s. 4, 326; s. a. D. V. Nightingale and R. M. Brooker, Am. Soc. 72, 5539 (1950)

Sulfuric acid**Subst. carboxylic acid amides from
nitriles and ethylene derivatives**

←

s. 5, 258; s. a. Am. Soc. 71, 4128, 4130 (1949); J. Heyboer and A. J. Staverman, R. 69, 787 (1950)

Chlorosulfonic acid/sodium azide

ClSO₃H/NaN₃**Tetrazoles from oximes**

←

Ring enlargement

373.



Chlorosulfonic acid added below 35° to a vigorously stirred suspension of NaN₃ in ethylene dichloride, then 4-isopropylcyclohexane oxime in ethylene dichloride added dropwise at 35-45°, and stirring continued until the reaction mixture has cooled to room temp. → 8-isopropyl-pentamethylenetetrazole. Y: 67%. F. e. s. E. K. Harvill, C. W. Roberts, and R. M. Herbst, *J. Org. Chem.* 15, 58, 671 (1950).

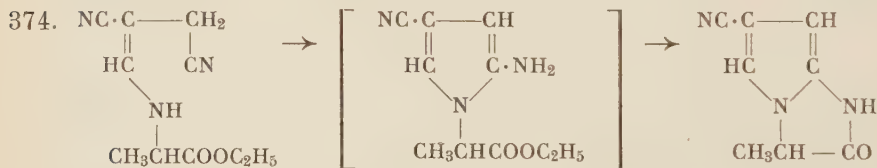
Rearrangement**Hydrogen/Nitrogen Type**NC $\Downarrow$ HN

Potassium/alcohol

KOR

1,2-Dihydroimidazo[1,2-a]pyrroles

○

via α -aminopyrroles from α -aminomethylene compounds

A soln. of α -(1-carbethoxyethylamino)methylene|succinonitrile in abs. benzene added with stirring to a soln. of K in a mixture of abs. *tert*-amyl alcohol and benzene under N₂, and allowed to stand at room temp. for 3 hrs. → 2-oxo-3-methyl-6-cyano-1,2,3,4-tetrahydroimidazo[1,2-a]pyrrole. Y: 81%. F. e., also α -aminopyrroles, s. C. A. Grob and P. Ankli, *Helv.* 33, 273 (1950).

Oxygen/Carbon TypeNC $\Downarrow$ OC

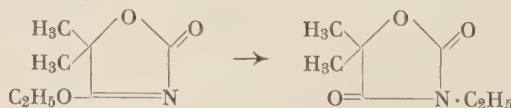
Without additional reagents

w.a.r.

N-Alkyl from O-alkyl

OR → NR

375.



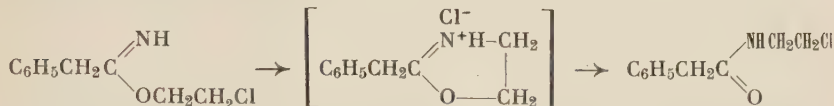
4-Ethoxy-5,5-dimethyloxazol-2-one heated at 180° for 24 hrs. → 5,5-dimethyl-3-ethyloxazolid-2,4-dione. Y: almost 100%. J. S. H. Davies and W. H. Hook, *Soc.* 1950, 30; s. a. G. A. Wiese and J. W. Jones,

J. Am. Pharm. Assoc. 39, 286 (1950); R. F. Rekker, H. Verleur, and W. T. Nauta, R. 70, 5 (1951).

Subst. carboxylic acid amides from iminoesters via oxazolines

←

376.



Phenylacetimino 2-chloroethyl ether (from the hydrochloride) heated 1 hr. at 130° → N-2-chloroethylphenylacetamide. Y: 75%. F. e. s. M. W. Partridge and H. A. Turner, Soc. 1949, 1308.

Bases

←

Acyl migration

OAc → NAc

N-Acyl from O-acyl

s. 1, 292; s. a. H. Bretschneider et al., M. 81, 31 (1950)

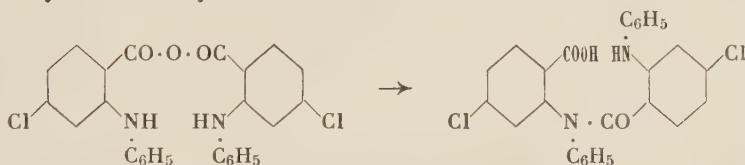
Acetic acid

CH₃COOH

Carboxylic acid amides from carboxylic acid anhydrides

←

377.



5-Chlorodiphenylamine-2-carboxylic acid anhydride in glacial acetic acid gently boiled for 1 hr. → (N-phenyl-p-chloroanthranoyl)-N-phenyl-p-chloroanthranilic acid. Y: 90%. F. e. s. A. M. Grigorovskii, Ж. 19, 1744 (1949); C. A. 44, 2953c.

Sulfur/Carbon Type

NC $\curvearrowright$ SC

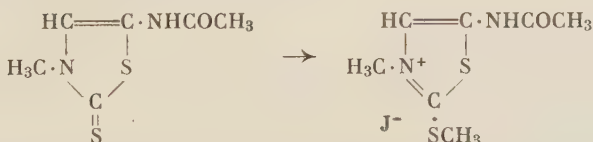
Without additional reagents

w.a.r.

Thiazolium salts from thiazolines

←

378.



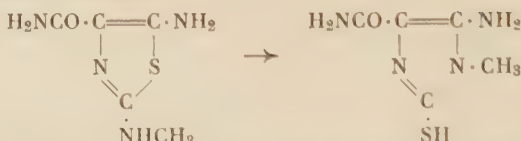
A suspension of 5-acetamido-2-thio-3-methylthiazoline (prepn. s. 610) in methanol refluxed 1 hr. with methyl iodide → 5-acetamido-2-methylmercapto-3-methylthiazolium iodide (startg. m. f. 178). Y: 80%. A. H. Cook and S. F. Cox, Soc. 1949, 2337.

Sodium carbonate

 Na_2CO_3

Imidazoles from thiazoles

379.



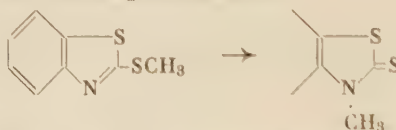
1.2 gm. 5-amino-2-methylaminothiazole-4-carboxamide refluxed 1 hr. with 1 *N* aq. Na-carbonate $\rightarrow$ 0.9 gm. 5-amino-2-mercapto-1-methylglyoxaline-4-carboxamide. A. H. Cook, I. Heilbron, and E. Smith, *See* 1949, 1440, 3001.

Iodine

L

Thiazolethiones from mercaptothiazoles

380.



2-(Methylmercapto)benzothiazole heated with a little iodine at 210-220° for 4 hrs. in a sealed tube $\rightarrow$ 3-methyl-2 (3H)-benzothiazolethione. Y: 80%. A. I. Kiprianov and Z. N. Pazenko. *Ж. 19*, 1523 (1949); C. A. 44, 3487g.

Carbon/Carbon Type

NC  CC

Without additional reagents

w, q, r.

Isocyanates from carboxylic acid azides

$$\text{CON}_3 \rightarrow \text{C}:\text{C}:\text{O}$$

s. 6, 470

Sodium nitrite

 NaNO_3

2-Oxazolidones from hydroxycarboxylic acid hydrazides

○

s. 5, 263; s. a. E. D. Bergmann and M. Sulzbacher, *J. Org. Chem.* **16**, 84 (1951)

Sodium hypobromite

 NaOBr

Amines from carboxylic acid amides via isocyanates



tert-Carbinamines

Hofmann degradation

381.



Br₂ added slowly with rapid stirring to ice-cold aq. NaOH, then finely powdered tributylacetamide added in one portion, and stirred vigor-

ously for 4 hrs. at 0° $\rightarrow$ 1,1-dibutylamyl isocyanate (Y: 90%) heated 5 hrs. with 20%—HCl on a steam bath with stirring $\rightarrow$ 1,1-dibutylamylamine (Y: 72%). F. e. s. N. Sperber and R. Fricano, *Am. Soc.* 71, 3352 (1949).

Exchange

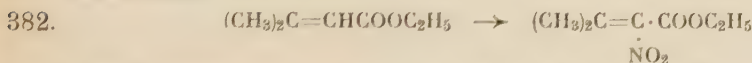
Hydrogen $\downarrow$

NC $\nmid$ H

Without additional reagents

w.a.r.

α -Nitro- α,β -ethylenecarboxylic acid esters from α,β -ethylenecarboxylic acid esters

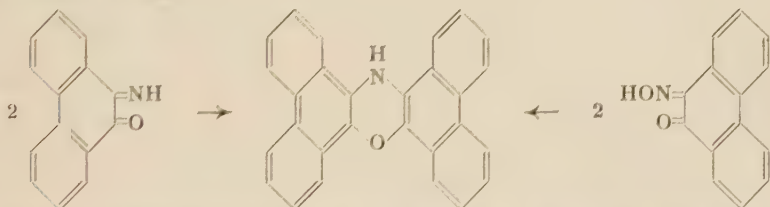
H $\rightarrow$ NO

Ethyl dimethylacrylate added with slow stirring below 5° to red HNO_3 (d. ca. 1.44) containing nitrogen oxides, and slow stirring continued at 20° for 5-6 hrs. $\rightarrow$ ethyl α -nitrodimethylacrylate (startg. m. f. 621). Y: 70-75%. R. Trave, *G.* 79, 233 (1949); cf. O. Süss, W. Schäfer, and M. Grundkötter, *A.* 571, 201 (1951).

Photoreduction 1,4-Oxazine ring

O

383.



Phenanthrenequinone-monoxime or -imine in isopropanol exposed to sunlight for 20 weeks $\rightarrow$ diphenanthroxazine. Y: ca. 100%. F. e. s. A. Schönberg et al., *Soc.* 1950, 374.

Sodium acetate

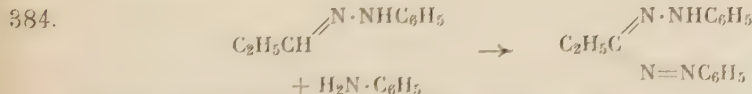
 CH_3COONa

Aliphatic azo compounds by coupling

N:N

s. 6, 519

Formazans from hydrazones

 $\leftarrow$ 

Aniline diazotized with aq. NaNO_2 in HCl, the diazonium salt soln. so obtained added at 0° to 3.2 gm. propionaldehyde phenylhydrazone and

Na-acetate in methanol, and worked up after 14 hrs. $\rightarrow$ 3.5 gm. C-ethyl-N,N'-diphenylformazan. F. e. s. D. Jerchel et al., Chem. B. 82, 515 (1949); A. 563, 200, 208 (1949); with KOH s. S. W. Fox and E. Hemmingson Atkinson, Am. Soc. 72, 3629 (1950).

Sodium cyanide

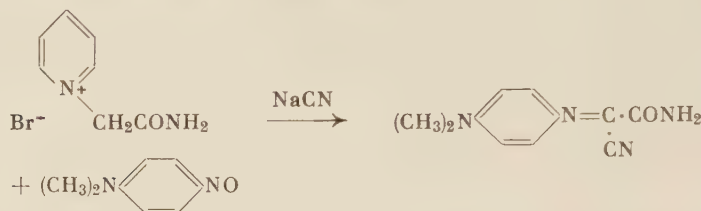
NaCN

1,1-Cyanoimines from pyridinium salts

C=N·

CN

385.



An aq. soln. of NaCN added below 20° to (aminoformylmethyl)pyridinium bromide and nitrosodimethylaniline in alcohol $\rightarrow$ aminoformylglyoxylic acid nitrile p-dimethylaminoanil. Y: ca. 100%. F. e. s. F. Kröhnke, Chem. B. 83, 50, 60 (1950).

Sodium nitrite

NaNO₂

Nitrosation

H $\rightarrow$ NO

s. 2, 342; in dioxane s. R. F. Milligan and L. Koch, Am. Soc. 72, 3811 (1950)

Nitration

H $\rightarrow$ NO₂

s. 1, 330; C. E. Clarkson, J. G. Holden, and T. Malkin, Soc. 1950, 1556

Indazoles

○

s. 1, 321; s. a. P. Petitcolas and R. Sureau, Bl. 1950, 466

Alkali nitrate

Nitration

H $\rightarrow$ NO₂

with KNO₃ s. 3, 291; 4, 337; with NaNO₃ s. H. Diaz de Arce, J. L. Greene, Jr., and J. D. Capps, Am. Soc. 72, 2971 (1950)

Cupric nitrate

Cu(NO₃)₂

386.



Powdered hydrated Cu(II)-nitrate added in small portions at 25-30° to a stirred, water-cooled suspension of 4-acetamido-3,2'-ditolyl in acetic anhydride, and worked up after 1 hr. $\rightarrow$ 5-nitro-4-acetamido-

3,2'-ditolyl. Y: 90%. M. C. Ford, W. A. Waters, and H. T. Young, Soc. 1950, 833; isomers by different nitration procedures s. W. Davey and J. R. Gwilt, Soc. 1950, 204; nitroaldehydes s. Soc. 1950, 3348.

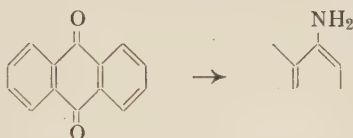
Vanadium pentoxide

V_2O_5

Replacement of hydrogen by amino groups

$H \rightarrow NH_2$

387.



Triacetylhydroxylamine (prepn. s. 227) added to a soln. of anthraquinone in concd. H_2SO_4 containing V_2O_5 , and heated with stirring at 130-140° for 8 hrs. $\rightarrow$ 5.9 gm. 1-aminoanthraquinone (from 6.1 gm. anthraquinone converted). T. Urbanski, Soc. 1949, 3374.

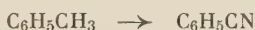
Molybdenum trioxide-alumina

$MoO_3-Al_2O_3$

Nitriles from hydrocarbons

$CH_3 \rightarrow CN$

388.



Toluene and NH_3 passed over MoO_3 on activated Al_2O_3 at atmospheric pressure and 525-550° $\rightarrow$ benzonitrile. Y: 60-85%, based on toluene consumed; conversion 5-10% per pass. F. e. s. W. I. Denton et al., Ind. Eng. Chem. 42, 796 (1950).

Sulfuric acid

H_2SO_4

Nitration

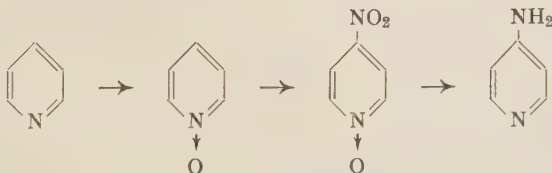
$H \rightarrow NO_2$

s. 6, 593

Replacement of hydrogen by amino groups via nitro compounds

N-Oxides as intermediates

389.



The N-oxide is used to make the pyridine nucleus accessible for substitution in positions 2 and 4.—E: Pyridine reacted with perchthalic acid in ether according to B. Bobranski, L. Kochanska, and A. Kowalewska, B. 71, 2385 (1938) $\rightarrow$ pyridine-N-oxide phthalate (Y: ca. 100%) dissolved in H_2SO_4 , added dropwise to a mixture of fuming HNO_3 and H_2SO_4 , and heated 1.5 hrs. at 90° $\rightarrow$ 4-nitropyridine-N-oxide

(Y: 80-85%) heated 1 hr. at 100° with a mixture of Fe-powder and acetic acid → 4-aminopyridine (Y: ca. 100%). F. e. s. H. J. den Hertog and J. Overhoff, R. 69, 468 (1950).

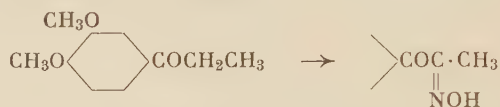
Hydrochloric acid

HCl

α -Isonitrosoketones from ketones

$\text{COCH}_2 \rightarrow \text{COC}:\text{NOH}$

390.



20% -HCl in abs. ether added to a soln. of ethyl 3,4-dimethoxyphenyl ketone in benzene, then isobutyl nitrite in abs. ether added portionwise with ice-cooling during 1 hr., and allowed to stand in ice overnight → isonitrosoethyl 3,4-dimethoxyphenyl ketone. Y: 95%. F. e. s. E. Karg, Arch. Pharm. 282, 49 (1944); with dry HCl-gas and isomyl nitrite s. J. A. Barltrop, A. J. Johnson, and C. D. Meakins, Soc. 1951, 181.

Via intermediates

v.i.

Aminophenols from phenols

$\text{H} \rightarrow \text{NH}_2$

via azophenols

s. 5, 267; s. a. D. Wasserman and C. R. Dawson, Am. Soc. 72, 4994 (1950)

Oxygen †

NC † O

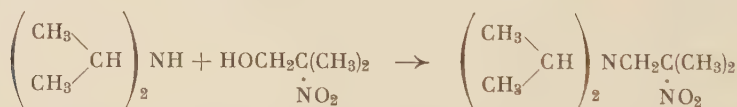
Without additional reagents

w.a.r.

Nitramines from nitroalcohols

$\text{OH} \rightarrow \text{N} \begin{array}{c} \diagup \\ \diagdown \end{array}$

391.

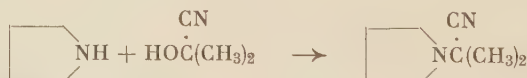


A mixture of diisopropylamine and 2-nitro-2-methyl-1-propanol refluxed whereby the water formed is removed as an azeotrope with the excess diisopropylamine, and rectified after the formation of water has ceased → N-(2-nitroisobutyl)diisopropylamine. Conversion 87%. Reverse reaction s. 221. F. e. s. M. Senkus, Am. Soc. 72, 2069 (1950).

α -Aminonitriles from cyanohydrins

←

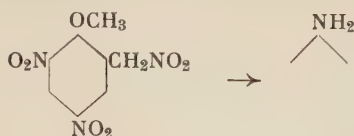
392.



Pyrrolidine added slowly to acetone cyanohydrin, with slight cooling to keep the temp. below the boiling point → α -(1-pyrrolidyl)isobutyronitrile. Y: 88.7%. R. B. Moffett, J. Org. Chem. 14, 862 (1949).

Prim. amines from ethersOR $\rightarrow$ NH₂

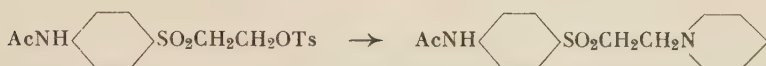
393.



A soln. of 4,6-dinitro-2-nitromethylanisole in concd. aq. NH₃ kept at room temp. for 3 hrs. $\rightarrow$ 4,6-dinitro-2-nitromethylaniline. Y: 91%. G. Bendz et al., Soc. 1950, 1130.

Amines from tosylatesOTs $\rightarrow$ N

394.



Piperidine added to 4-acetamidophenyl β -(p-toluenesulfonyloxy)ethyl sulfone, then heated on a steam bath for 2 hrs. $\rightarrow$ 4-acetamidophenyl β -piperidinoethyl sulfone. Y: 99%. F. e. s. B. R. Baker and M. V. Querry, J. Org. Chem. 15, 413 (1950).

Prim. enamines from ketonesCHCO $\rightarrow$ C:C·NH₂

395.

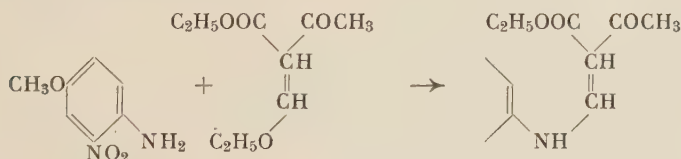


NH₃-gas introduced into ethyl α -(β -cyanoethyl)acetoacetate at 80-90° for 6 hrs. $\rightarrow$ ethyl β -amino- α -(β -cyanoethyl)crotonate. Y: 77.5%. H. Henecka, Chem. B. 82, 104 (1949); s. a. Ng. Ph. Buu-Hoi et al., J. Org. Chem. 14, 802 (1949).

Enamines as intermediates in the quinoline ring synthesis

C:C·N

396.



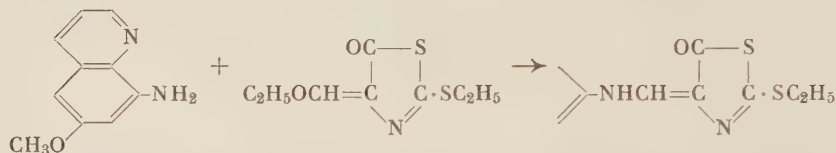
Equimolecular quantities of m-nitroanisidine and ethyl ethoxymethyleneacetoacetate heated 15 min. at 150° $\rightarrow$ ethyl α -acetyl- β -(o-nitro-p-methoxyanilino)acrylate. Y: ca. 100%.—Direct combination of the nitroanisidine, ethyl orthoformate, and acetoacetic ester is simpler but gives poorer yields. R. H. Baker et al., Am. Soc. 71, 3060 (1949).

Enamines from α -hydroxymethylene compounds

s. 2, 725a; s. a. A. Cohen, Soc. 1950, 3005

Enamines from α -alkoxymethylene compounds

397.



0.22 gm. 2-ethylmercapto-4-ethoxymethylene-5-thiazolone and 0.17 gm. 8-amino-6-methoxyquinoline mixed in ethanol $\rightarrow$ 0.35 gm. 2-ethylmercapto-4-(6'-methoxy-8'-quinolylaminomethylene)-5-thiazolone. A. H. Cook, G. Harris, and G. Shaw, Soc. 1949, 1435.

s. a. 3, 715; 5, 269

Azomethines from amines and oxo compounds

s. 6, 741

Reaction of nitroso compounds with active methylene groups

s. 1, 298; cf. Helv. 33, 1648 (1950)

**Reactions with isopropenyl acetate
Acetylaminos**

s. 6, 208

Carboxylic acid amides from carboxylic acids**Subst. carboxylic acid amides**

s. 1, 305; 5, 276; s. a. G. Tsatsas, Bl. 1949, 884

Carbalkoxycarboxylic acid amides from dicarboxylic acid esters

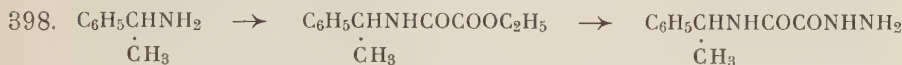
s. 6, 844

Carboxylic acid imides from dicarboxylic acids

s. 2, 363; s. a. R. B. Moffett, J. Org. Chem. 14, 862 (1949)

Carboxylic acid amide hydrazides
from dicarboxylic acid esters
via dicarboxylic acid amide esters

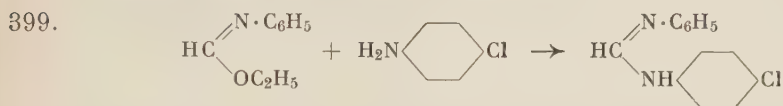
←



0.25 mole ethyl oxalate added slowly with stirring at room temp. to 0.12 mole α -phenylethylamine in abs. ethanol, and allowed to stand for 24 hrs. $\rightarrow$ ethyl N-(α -phenylethyl)oxamide (Y: 91%), dissolved in abs. ethanol, and 85%-hydrazine hydrate added with stirring $\rightarrow$ 5-(α -phenylethyl)semioxamazide (Y: 93%). N. J. Leonard and J. H. Boyer, *J. Org. Chem.* 15, 42 (1950).

Formamidines from N-subst. iminoesters

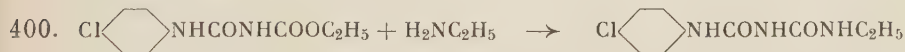
NHCH:NR



A mixture of p-chloroaniline and ethylisoxanilide heated 2 hrs. on a steam bath under slightly reduced pressure $\rightarrow$ N-phenyl-N'-p-chlorophenylformamidine. Y: ca. 100%. F. e. s. E. B. Knott and R. A. Jeffreys, *J. Org. Chem.* 14, 879 (1949).

Biurets from carbalkoxyureas

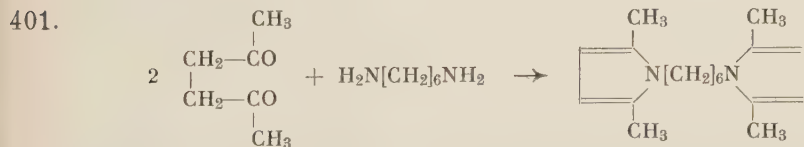
←



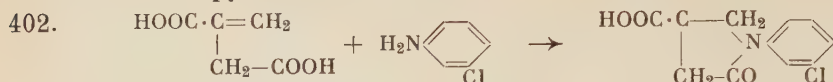
5 gm. N-carbethoxy-N'-p-chlorophenylurea and 33%-aq.-ethylamine heated 1 hr. at 100° in a closed vessel $\rightarrow$ 4.1 gm. 1-(p-chlorophenyl)-5-ethylbiuret. F. e. s. F. H. S. Curd, D. G. Davey, and D. N. Richardson, *Soc.* 1949, 1732.

Pyrrole ring

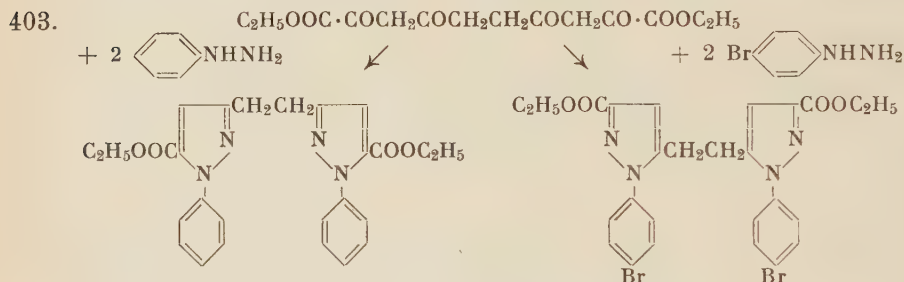
○



A mixture of 1,6-diaminohexane and acetonylacetone refluxed 15 min. $\rightarrow$ 1,1-hexamethylenebis-(2,5-dimethylpyrrole). Y: almost 100%.—The reaction with ar. amines does not appear to be sensitive to steric hindrance when it is performed at high temp. without a solvent. F. e. s. Ng. Ph. Buu-Hoi, *Soc.* 1949, 2882.

N-Subst. 2-pyrrolidones

m-Chloroaniline and itaconic acid maintained at the fusion point for 10-20 min. $\rightarrow$ 4-carboxy-1-(m-chlorophenyl)-2-pyrrolidone. Y: 84%. F. e. and limitations s. P. L. Paytash, E. Sparrow, and J. C. Gathe, *Am. Soc.* 72, 1415 (1950); s. a. G. L. Evans, H. W. Gray, and H. W. Jacobson, *Am. Soc.* 72, 2727 (1950).

Pyrazoles from β -diketones**Diethyl α,γ,ξ,θ -tetraketosebacate**

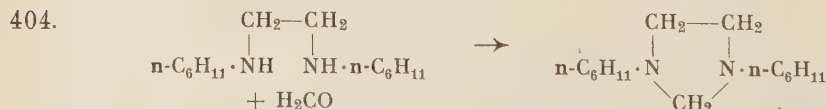
(7.2 g.) reacted with phenylhydrazine in alcohol or glacial acetic acid $\rightarrow$ 5.5 g. 1,2-bis-(1-phenyl-5-carbethoxy-3-pyrazolyl)ethane.

(2.32 g.) reacted with p-bromophenylhydrazine in alcohol $\rightarrow$ 1.9 g. 1,2-bis-[1-(p-bromophenyl)-3-carbethoxy-5-pyrazolyl]ethane.

The reactivity of the carbonyl group depends on the arylhydrazine. With phenylhydrazine, the α -carbonyl group is the more reactive, whereas with p-bromophenyl and p-nitrophenyl-hydrazine the γ -carbonyl group is the more reactive. F. e. s. C. Musante and R. Beretti, *G.* 79, 666 (1949).

Imidazole ring

s. 4, 357; s. a. C. A. Saleminck and G. M. van der Want, *R.* 68, 1013 (1949); P. Mamalis, V. Petrow, and B. Sturgeon, *Soc.* 1950, 1600

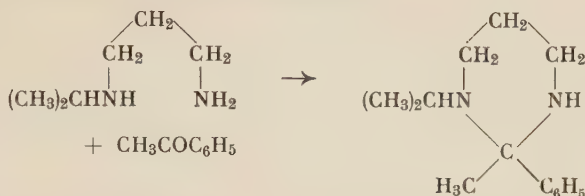
Imidazolidines

35—40% formalin added below 50° to 10% excess of N,N-dicyclohexylethylenediamine $\rightarrow$ 1,3-dicyclohexylimidazolidine (startg. m. f. 616). Y: 79%. F. e. s. R. A. Donia et al., *J. Org. Chem.* 14, 952 (1949); s. a.

J. L. Riebsomer, *J. Org. Chem.* **15**, 237 (1950); J. L. Boivin and G. F. Wright, *Can. J. Research* **28 B**, 213 (1950).

Hexahydropyrimidines from 1,3-diamines

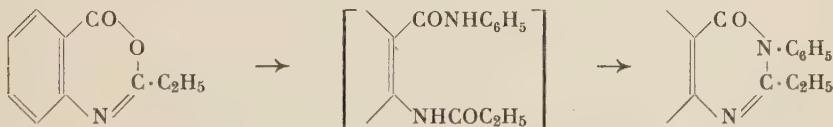
405.



N-Isopropyl-1,3-propanediamine, acetophenone, and a little benzene heated from 120° to 180° during a 6-hr.-period with distillation of the benzene-water azeotropic mixture $\rightarrow$ 1-isopropyl-2-methyl-2-phenylhexahydropyrimidine. Y: 57%. F. e. with higher yields s. J. L. Riebsomer and G. H. Morey, *J. Org. Chem.* **15**, 245 (1950).

Quinazolones from 3,1,4-benzoxazones

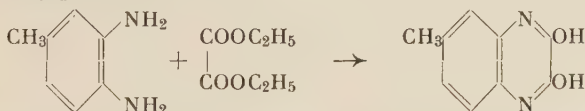
406.



A mixture of 2-ethyl-3,1,4-benzoxazone (prepn. s. 298) and aniline heated at 150—160° for 30 min. $\rightarrow$ 2-ethyl-3-phenyl-4-quinazolone. Y: 67.8%. F. e., also isolation of the intermediate, s. D. T. Zentmyer and E. C. Wagner, *J. Org. Chem.* **14**, 967 (1949).

2,3-Dihydroxyquinoxalines

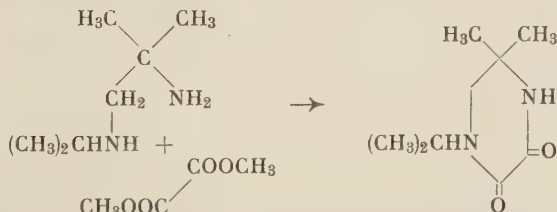
407.



Crude 4-methyl-1,2-phenylenediamine and ethyl oxalate heated at 170 to 180° for 3 hrs. $\rightarrow$ crude 2,3-dihydroxy-6-methylquinoxaline. Y: 94%. F. e. s. F. H. S. Curd, D. G. Davey, and G. J. Stacey, *Soc.* **1949**, 1271.

2,3-Piperazinediones

408.



A mixture of N-(2-aminoisobutyl)isopropylamine and dimethyl oxalate heated with distillation of the methanol formed, so that the temp.

of the reaction flask is slowly increased during 4 hrs. to a maximum of $180^\circ \rightarrow$ 5,5-dimethyl-1-isopropyl-2,3-piperazinedione. Y: 63%. F. e. s. J. L. Riebsomer, *J. Org. Chem.* 15, 68 (1950).

Photoreduction

1,4-Oxazine ring

s. 6, 383

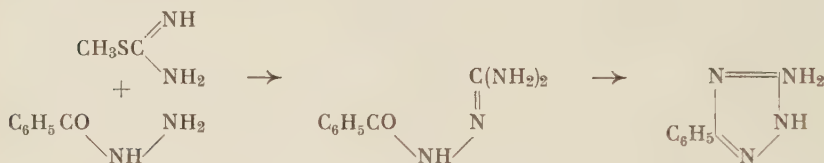
1,2,4-Triazoles

from carboxylic acid hydrazides

and isothioureas

via acylaminoguanidines

409.



13.9 gm. S-methylisothiourea sulfate added with stirring to ice-cold N NaOH, followed by 13.5 gm. benzhydrazide, kept at room temp. 3-4 days, slowly warmed to 50° , and kept at this temp. for 3 hrs. $\rightarrow$ 12.2 gm. benzamidoguanidine, 5 gm. of which heated 5 min. just below its melting point at $220^\circ \rightarrow$ 3.8 gm. 5-amino-3-phenyl-1,2,4-triazole. F. e., also without isolation of the intermediate, s. E. Hoggarth, *Soc.* 1950, 612.

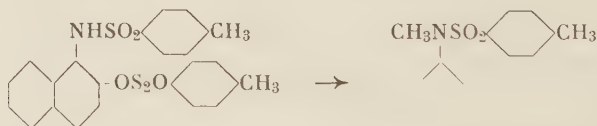
Sodium hydroxide

NaOH

N-Alkylation

NH $\rightarrow$ NR

410.

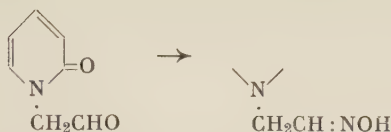


A soln. of 1-p-toluenesulfonamido-2-naphthyl p-toluenesulfonate in acetone treated with vigorous stirring at $65-75^\circ$ alternately with small portions of 30% NaOH soln. and dimethyl sulfate over a period of 20 min., and refluxing continued for 0.5 hr. with addition of more NaOH soln. to keep the mixture alkaline $\rightarrow$ 1-p-toluenesulfonmethylamido-2-naphthyl p-toluenesulfonate (startg. m. f. 8). Y: almost 100%. F. Kurzer, *Soc.* 1949, 3434.

Aldoximes



411.



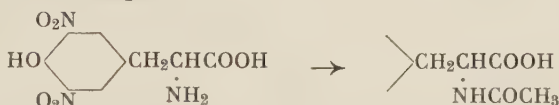
A soln. of N-2-pyridone acetaldehyde hydrochloride and hydroxylamine hydrochloride in 95%-ethanol made just basic to litmus with 10%-aq.-NaOH, and evaporated to dryness on a steam-cone $\rightarrow$ N-2-pyridone acetaldoxime. Y: 85%. R. Adams and V. V. Jones, *Am. Soc.* **71**, 3826 (1949).

Acylamines from amines



Optically active compounds

412.

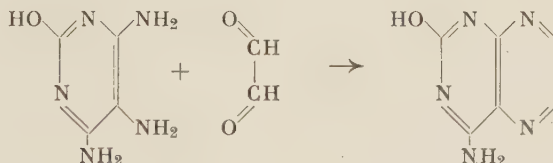


A soln. of 3,5-dinitro-L-tyrosine in 2 N NaOH treated with stirring below 20° with acetic anhydride, stirring continued at room temp. for 1 hr., then warmed 30 min. at 40° in order to decompose excess acetic anhydride $\rightarrow$ 3,5-dinitro-N-acetyl-L-tyrosine. Y: 82%. J. R. Chalmers et al., *Soc.* **1949**, 3424; s. a. L. J. Reed, A. R. Kidwal, and V. du Vigneaud, *J. Biol. Chem.* **180**, 571 (1949).

Pyrimido[4,5-b]pyrazines



413.



Glyoxal bisulfite added to a soln. of 4,5,6-triamino-2-hydroxypyrimidine sulfate in water adjusted to pH 5 with dil. NaOH, heated to boiling, the pH adjusted to 9, and boiled 15 min. $\rightarrow$ 4-amino-2-hydroxypyrimidine. Y: 80%.—Because of the ready hydrolysis of the 4-amino group, it is necessary to effect the condensation in neutral or slightly alkaline soln. F. e. s. E. C. Taylor, Jr., and C. K. Cain, *Am. Soc.* **71**, 2538 (1949); cf. N. R. Campbell, J. H. Dunsmuir, and M. E. H. Fitzgerald, *Soc.* **1950**, 2743.

Potassium hydroxide

KOH

 α -Aminomethylene compounds from
 α -hydroxymethylene compounds

s. 6, 511

Oximes

s. 2, 372; s. a. F. J. Villani and D. Papa, Am. Soc. 72, 2722 (1950)

3,4-Dihydro-1,3,2H-benzoxazines

s. 5, 288; cf. Am. Soc. 72, 4691 (1950)

Sodium/alcohol**Alkoximes from isomeric oximes**

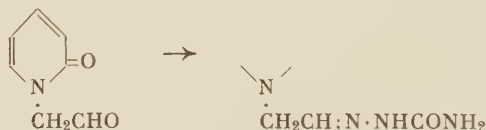
s. 6, 462

Carboxylic acid amides from carboxylic acids

414. Ethyl ethylmalonate in a soln. of NH_3 and a little Na in methanol allowed to stand in a stoppered flask at room temp. for 96 hrs. $\rightarrow$ ethylmalondiamide. Y: 91%. F. e. s. P. B. Russell, Am. Soc. 72, 1853 (1950).

Sodium acetate**Semicarbazones**

415.



An aq. soln. of N-2-pyridone acetaldehyde hydrochloride, semicarbazide hydrochloride, and Na-acetate heated 5 min. on a steam-cone $\rightarrow$ N-2-pyridone acetaldehyde semicarbazone. Y: ca. 100%. R. Adams and V. V. Jones, Am. Soc. 71, 3826 (1949).

Ammonia**Dihydropyrazines from α -aminoketones**s. 4, 367; with NH_3 s. G. Muller, G. Amiard, and J. Mathieu, Bl. 1949, 533*Aniline***Osazones**

416. The osazone-formation velocity of aldoses with phenylhydrazine in dil. acetic acid is considerably increased in the presence of aniline and can be used for the differentiation between aldoses and ketoses. F. Weygand and M. Reckhaus, Chem. B. 82, 442 (1949).

Pyridine C_5H_5N **Diacylamines** $N(Ac)_2$

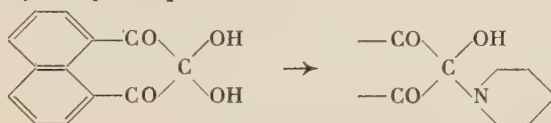
417.



A mixture of acetylglycine ethyl ester, acetic anhydride, and pyridine gently refluxed with stirring for 6.5 hrs. $\rightarrow$ N,N-diacetylglycine ethyl ester. Y: 88%. F. e. s. R. H. Wiley and O. H. Borum, Am. Soc. 72, 1626 (1950).

Piperidine $C_5H_{11}N$ **1,1-Aminohydroxy compounds from 1,1-dihydroxy compounds** $\leftarrow$

418.



1 gm. *peri*-naphthindane-1,2,3-trione hydrate in water and piperidine in alcohol mixed together, and worked up after 0.5 hr. $\rightarrow$ 1.2 gm. 2-hydroxy-2-(1'-piperidino)-*peri*-naphthindane-1,3-dione. F. e. s. R. Moubasher and W. I. Awad, Am. Soc. 1949, 1137.

Calcium oxide CaO **Hydrazones from ketones** $C:O \rightarrow C:NNH \cdot$

s. 6, 450

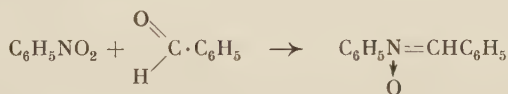
Zinc/acetic acid Zn/CH_3COOH **Nitrones from aldehydes and nitro compounds**

$$C=NR$$

$$\downarrow$$

$$O$$
Isaldoximes

419.



A mixture of nitrobenzene and benzaldehyde reacted with Zn-dust in alcohol-water-acetic acid at -8° over a period of 2 hrs. $\rightarrow$ phenyl-isobenzaldoxime. Y: 90%. F. e. s. J. Wiemann and C. Glacet, Bl. 1950, 176.

Bauxite Al_2O_3 **Sec. from prim. amines and alcohols** $\leftarrow$ **Carboxylic acid esters and nitriles from carboxylic acids**

420. Activated bauxite is an abundant and relatively inexpensive catalyst for drying and for dehydration reactions in organic chemistry. It has been found to be equal or superior to the various forms of activated

alumina. The yield obtained in dehydration reactions is affected by such variables as reaction temp., activation temp., and iron content of the bauxite.—E: Aniline and ethanol at 275° → ethylaniline. Y: 83.9%.—Capryl alcohol refluxed 2 hrs. with acetic acid → capryl acetate. Y: 82%.—Acetic acid and NH₃ at 425° → acetonitrile. Y: 95%. F. e. s. H. Heinemann, R. W. Wert, and W. S. W. McCarter, *Ind. Eng. Chem.* 41, 2928 (1949).

Formamide**Amines from ketones****Leuckart reaction**

s. 2, 390; s. a. M. Métayer, P. Mastagli, and A. Bricard, *Bl.* 1950, 1054

Papain**Enzymatic resolution of stereoisomers****Carboxylic acid anilides from carboxylic acids**

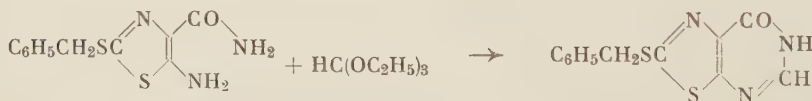
s. 3, 330; s. a. L. J. Reed, A. R. Kidwal, and V. du Vigneaud, *J. Biol. Chem.* 180, 571 (1949); W. E. Hanby et al., *Soc.* 1950, 3239

Acetic anhydride**Formylation of amines**

s. 2, 391; s. a. H. R. Snyder and F. X. Werber, *Am. Soc.* 72, 2962 (1950); with 90%-formic acid s. A. Stoll and E. Seebeck, *Helv.* 34, 481 (1951)

Pyrimidine ring closure

421.



0.7 gm. 5-amino-2-benzylmercaptothiazole-4-carboxamide and ethyl orthoformate in acetic anhydride refluxed 2 hrs. → 0.8 gm. 6-keto-2'-benzylmercapto-1,6-dihydrothiazolo(5',4',4,5)pyrimidine. F. e. s. A. H. Cook and E. Smith, *Soc.* 1949, 2329; pyrimido[4,5-b]pyrazines s. A. Albert, D. J. Brown, and G. Cheeseman, *Soc.* 1951, 474.

Oxazole ring synthesis

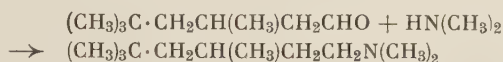
s. 4, 370; without Na-acetate s. C. Sannié and H. Lapin, *Bl.* 1950, 322

Formic acid**Leuckart-Wallach reaction**

422. **Alkylation of amines with oxo compounds.** The alkylation is promoted by conditions which favor condensation. Formylation of the amine retards but does not prevent alkylation. E. and further results of a study of

this reaction s. E. Staple and E. C. Wagner, J. Org. Chem. 14, 559 (1949). The advantage of using Na-formate in acetic acid lies probably in the diminished acidity of the medium and is apparent only when the starting amine is very feebly basic or has little tendency to add to the carbonyl group. The Leuckart-Wallach reaction is of some utility for the preparation of sec. amines when alkyl halides are unreactive (cyclohexyl halides) or react in undesired fashion (anisyl halides). E. s. R. Baltzly and O. Kauder, J. Org. Chem. 16, 173 (1951); s. a. P. A. S. Smith and A. J. Macdonald, Am. Soc. 72, 1037 (1950).

423.



Amines from aldehydes. The alkylation of sec. amines with aliphatic aldehydes is initiated and completed at a generally lower temp. and under milder conditions than in other known instances of this reaction.—Procedure: The amine formate is first prepared by addition of the amine, as gas or liquid, to formic acid in 1 : 1 mole ratio. The temp. is then raised to ca. 60°, the aldehyde added dropwise over a 1-hr.-period, and the mixture generally heated on a steam bath for ca. 1 hr. until CO₂ evolution ceases.—E: 3,5,5-Trimethylhexaldehyde and dimethylamine → dimethyl-(3,5,5-trimethylhexyl)amine. Y: 84%. F. e. with lower yields and 2 step procedure (cf. 88) s. P. L. DeBenneville and J. H. Macartney, Am. Soc. 72, 3073 (1950).

*Acetic acid*CH₃COOH

Azo compounds from quinones and hydrazines

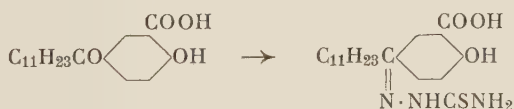
←

s. 2, 392; s. a. P. P. T. Sah, R. 69, 1025 (1950)

Thiosemicarbazones



424.



Alc. thiosemicarbazide and some glacial acetic acid added to alc. 5-lauroylsalicylic acid, and refluxed 3.5 hrs. on a steam bath → 5-lauroylsalicylic acid thiosemicarbazone. Y: 98%. H. Bretschneider and H. Haas, M. 81, 524 (1950).

Phthalazines from o-ketocarboxylic acids

○

s. 3, 335; s. a. Buu-Hoï, Hoán, and Xuong, R. 69, 1083 (1950)

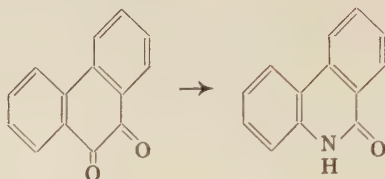
Sodium azide

 NaN_3

Phenanthridines from quinones

←

425.



A soln. of 208 mg. phenanthrenequinone in concd. H_2SO_4 treated with finely powdered NaN_3 at $0-10^\circ$, then kept at room temp. for 2-3 hrs. until gas evolution has subsided and the original deep green color has faded $\rightarrow$ 180 mg. phenanthridone. E. F. M. Stephenson, Soc. 1949, 2620.

Phosphorus trichloride

 PCl_3

Subst. carboxylic acid amides

 $\text{COOH} \rightarrow \text{CONHR}$

from carboxylic acids

Peptides



A mixture of 0.9 gm. methyl 5,5-dimethylthiazolidine-4-carboxylate, 1 gm. phenacetic acid, and PCl_3 in abs. benzene refluxed 2 hrs. with stirring $\rightarrow$ 1.4 gm. methyl 3-phenacetyl-5,5-dimethylthiazolidine-4-carboxylate. F. e. s. O. Süss, A. 564, 54 (1949); peptides s. O. Süss and H. Hoffmann, A. 572, 96 (1951).

s. a. 6, 884

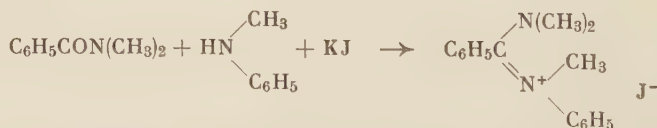
Phosphorus oxychloride

 POCl_3

Amidinium salts from carboxylic acid amides

←

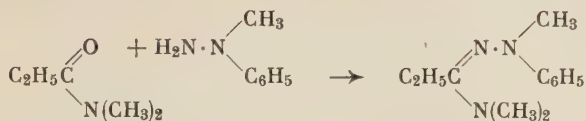
427.



Benzodimethylamide, methylaniline hydrochloride, and POCl_3 heated 5 hrs. at $120-130^\circ$, and worked up with addition of KI $\rightarrow$ N'-phenyl-N,N,N'-trimethylbenzamidinium iodide. Y: 90%. F. e. s. C. G. Raison, Soc. 1949, 3319.

Amidrazones from carboxylic acid amides and hydrazines

428.



A soln. of α -methyl- α -phenylhydrazine and N,N-dimethylpropionamide in dry benzene added to a stirred, refluxing soln. of POCl_3 in benzene, stirring and refluxing continued for 5 hrs. $\rightarrow$ $\text{N}^1, \text{N}^3, \text{N}^3$ -trimethyl- N^1 -phenylpropionamidrazone. Y: 82%. F. e. s. H. Rapoport and R. M. Bonner, Am. Soc. 72, 2783 (1950).

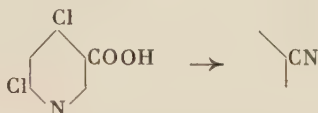
Phosphorus oxychloride/phosphorus pentachloride

$\text{POCl}_3/\text{PCl}_5$

Nitriles from carboxylic acids

$\text{COOH} \rightarrow \text{CN}$

429.



A mixture of 2,4-dichloropyridine-5-carboxylic acid and POCl_3 heated to 100° , PCl_5 gradually added, heated 0.5 hr. at 140° , POCl_3 distilled off in vacuo, the residue dissolved in benzene, and NH_3 -gas passed into the soln. $\rightarrow$ 2,4-dichloropyridine-5-carbonitrile (startg. m. f. 532). Y: 95%. H. J. den Hertog et al., R. 69, 673 (1950).

Phosphorus pentachloride/p-toluenesulfonic acid amide

$\text{PCl}_5/\text{TsNH}_2$



PCl_5 added with stirring to a mixture of p-nitrobenzoic acid and p-toluenesulfonamide, warmed gently in a hot-air bath to initiate the reaction, after subsiding of the first reaction gradually heated to ca. 205° , and maintained at this temp. until no more material distils $\rightarrow$ p-nitrobenzonitrile. Y: 85-90%.—Aliphatic acids give low yields and, in some cases, chlorinated by-products. F. e. s. C. S. Miller, Org. Synth. 29, 75 (1949).

Sulfamide/pyridine

$\text{SO}_2(\text{NH}_2)_2/\text{C}_5\text{H}_5\text{N}$

Carboxylic acid amides from carboxylic acids

$\text{COOH} \rightarrow \text{CONH}_2$

431. Benzoic acid, sulfamide, and pyridine heated on a steam bath for 3 hrs. $\rightarrow$ benzamide. Y: 84.3%. F. e. s. A. V. Kirsanov and Y. M. Zolotov, Ж. 19, 2201 (1949); C. A. 44, 4446g; cf. 20, 1637 (1950); C. A. 45, 1950c

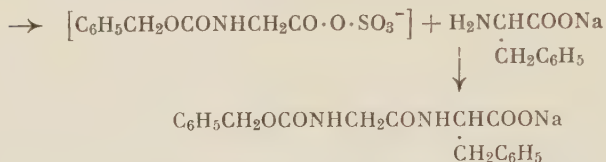
Dimethylformamide-sulfur trioxide complex

 $HCON(CH_3)_2 \cdot SO_3$

Peptides

 $COOH \rightarrow CONHR$

432.



A soln. of carbobenzoxyglycine in dimethylformamide neutralized with methanolic phenyltrimethylammonium methoxide, a portion of the solvent distilled off at 50° in vacuo whereby methanol and traces of water are removed, the homogeneous soln. of the phenyltrimethylammonium salt of carbobenzoxyglycine cooled to 0°, an equivalent of SO_3 in dimethylformamide added, followed after 1 min. by an aq. soln. of Na-L-phenylalanine and sufficient NaOH to restore the pH to 9 $\rightarrow$ carbobenzoxyglycyl-L-phenylalanine. Y: 72%. F. e. s. G. W. Kenner, *Chemistry and Industry* 1951, 15.

Sulfuric acid

 H_2SO_4

Monosubst. ureas from alcohols

 $OH \rightarrow NHCONH_2$

433.



Finely powdered urea added slowly at 20-25° to concd. H_2SO_4 , then *tert*-butyl alcohol added dropwise at the same temp., stirred for an additional 0.5 hr., and allowed to stand at room temp. for ca. 16 hrs. $\rightarrow$ *tert*-butylurea (startg. m. f. 494). Y: 31-33%. F. e. s. L. I. Smith and O. H. Emerson, *Org. Synth.* 29, 18 (1949).

Perchloric acid

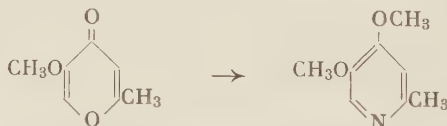
 $HClO_4$

Pyridine ring from pyrone ring

 $\leftarrow$

Baeyer reaction

434.



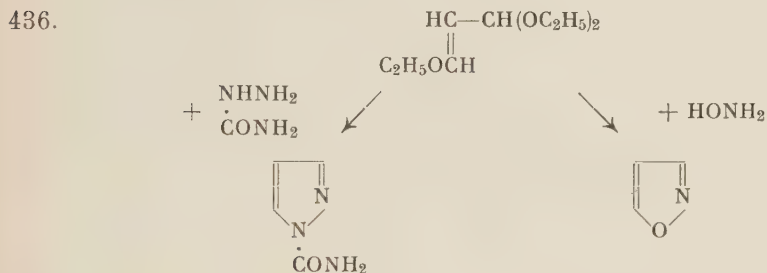
A mixture of 30 gm. 2-methyl-5-methoxy-4-pyrone and dimethyl sulfate heated 2 hrs. at 50°, cooled in an ice bath, added to a twofold excess of cold 20% $HClO_4$, allowed to stand for 2 hrs., filtered, the crystalline methoperchlorate added in portions to cold 10% NH_4 -carbonate soln., and allowed to come to room temp. $\rightarrow$ 20 gm. crude 2-methyl-4,5-dimethoxypyridine. K. N. Campbell, J. F. Ackerman, and B. K. Campbell, *J. Org. Chem.* 15, 221 (1950).

Ammonium chloride

 NH_4Cl **Carboxylic acid amides
from carboxylic acid esters** $COOR \rightarrow CONH_2$ 

A mixture of diethyl fumarate, concd. aq. NH_3 , and NH_4Cl stirred 7 hrs. at 25–30° with slight cooling $\rightarrow$ fumaramide. Y: 80–88%. D. T. Mowry and J. M. Butler, *Org. Synth.* 30, 46 (1950).

Hydrochlorides

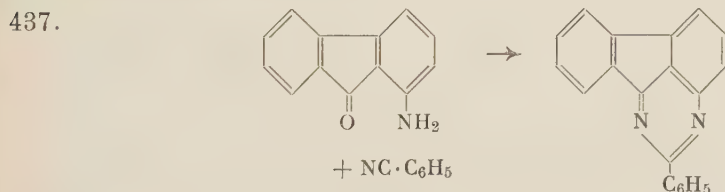
**Pyrazoles and isoxazoles
from enolether acetals***β*-Ethoxyacrolein diethylacetal

shaken with aq. semicarbazide hydrochloride for 15 min. $\rightarrow$ pyrazole-1-carboxylic acid amide. Y: 87%.

refluxed 1 hr. with aq. hydroxylamine hydrochloride in a water bath $\rightarrow$ isoxazole. Y: 67%.

F. e. s. A. Dornow and K. Peterlein, *Chem. B.* 82, 257 (1949); pyridine ring with *β*-ethoxyacrolein diethylacetal s. 735.

Hydrochloric acid

 HCl **2,4-Diazafluoranthenes**

Dry HCl passed at 180–185° into a mixture of 1 gm. 1-aminofluorenone and 5 c.c. benzonitrile during 11 hrs. $\rightarrow$ 0.9 gm. 3-phenyl-2,4-diazafluoranthene. F. e. s. J. W. Cook and J. S. Moffatt, *Soc.* 1950, 1160.

Nickel

Ni

Amines from oxo compounds

←

s. 3, 350; 4, 401; 5, 313; also from unsatd. oxo compounds s.
P. Mastagli, M. Metayer, and A. Bricard, *Bl.* 1950, 1045

Palladium-barium sulfate/aluminum chloride

Pd-BaSO₄/AlCl₃**Tert. from prim. and sec. amines**

NH → NR



By hydrogenation of a mixture of certain amines and an oxo compound with Pd-BaSO₄ in the presence of an activator, e.g. AlCl₃, ZnCl₂, HCl, tert. amines can be obtained from prim. and sec. amines. In the absence of an activator, sec. amines are obtained only. E: A soln. of 10.5 gm. *iso*-α-hydroxy-β-amino-α,β-diphenylethane in methanol treated with acetaldehyde and AlCl₃·6H₂O, and hydrogenated with Pd-BaSO₄ at room temp. and 3.4 atm. until the theoretical amount of H₂ has been absorbed → 6.5 gm. *iso*-α-hydroxy-β-diethylamino-α,β-diphenylethane. F. e. s. W. Stühmer and W. Neumann, *Chem. B.* 83, 66 (1950).

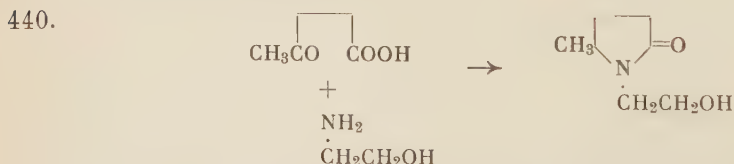
Platinum oxide

PtO₂
Sec. from prim. amines and oxo compounds
Aminoalcohols

439. cf. 4, 406. When the aminoalcohol contains a catechol nucleus, only ketones can be employed. A nuclear amino group may be alkylated simultaneously if an excess of carbonyl compound is used. F. s. E. L. Engelhardt, F. S. Crossley, and J. M. Sprague, *Am. Soc.* 72, 2718 (1950).

2-Pyrrolidones from
γ-ketocarboxylic acids

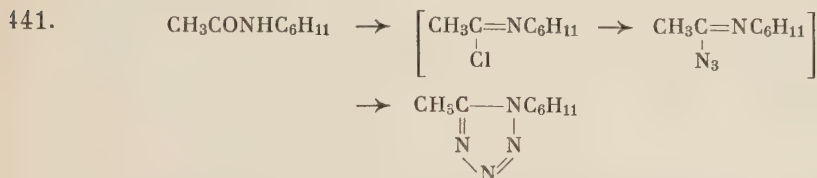
○



A suspension of PtO₂ in abs. ethanol hydrogenated to Pt. a soln. of levulinic acid and ethanolamine in abs. alcohol added, and hydrogenated ca. 4 hrs. at 50 lbs./sq.in. and room temp. until the theoretical quantity of H₂ is absorbed → 1-(2-hydroxyethyl)-5-methyl-2-pyrrolidone. Y: 95%. F. e. s. R. B. Moffett, *J. Org. Chem.* 14, 862 (1949).

Via intermediates

v.i.

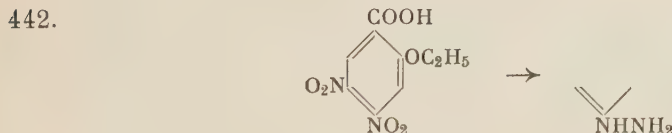
Amidines from subst. carboxylic acid amidess. 1, 351; s. a. A. C. Hontz and E. C. Wagner, *Org. Synth.* 31, 48 (1951)**Tetrazoles from carboxylic acid amides via iminochlorides**

PCl_5 added portionwise to a stirred and cooled soln. of N-cyclohexylacetamide in benzene, HN_3 in benzene added after PCl_5 has disappeared, the mixture allowed to stand 1 hr. at room temp. after the vigorous reaction has subsided, then gradually warmed to the boiling point on a water bath, and maintained at this temp. ca. 3 hrs. until the HCl evolution has ceased $\rightarrow$ 1-cyclohexyl-5-methyltetrazole. Y: 51%. F. e. s. E. K. Harvill et al., *J. Org. Chem.* 15, 662 (1950).

Nitrogen ∇ NC ∇ N

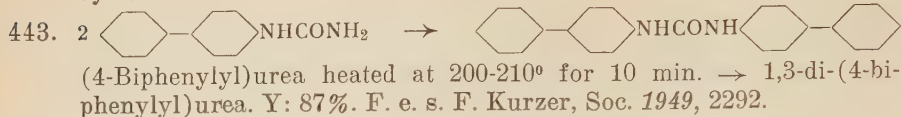
Without additional reagents

w.a.r.

Replacement of mobile nitro groups by hydrazino groups $\text{NO}_2 \rightarrow \text{NHNH}_2$ 

A soln. of 4,5-dinitro-2-ethoxybenzoic acid and hydrazine hydrate in alcohol heated 0.5 hr. on a steam bath $\rightarrow$ 5-nitro-4-hydrazino-2-ethoxybenzoic acid (startg. m. f. 509). Y: 85%.—Similarly with phenylhydrazine: 5-nitro-4-phenylhydrazino-2-ethoxybenzoic acid. Y: 78%. H. Goldstein and R. Brochon, *Helv.* 32, 2334 (1949); f. e. s. *Helv.* 34, 146 (1951).

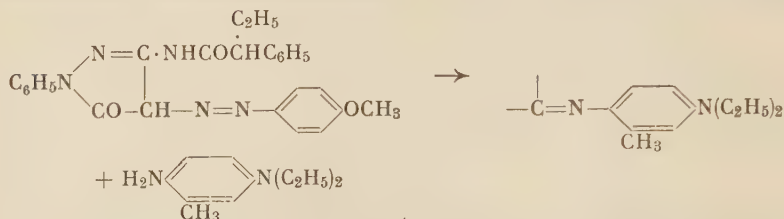
Ureas from amines $\text{NH}_2 \rightarrow \text{NHCONH}_2$ s. 4, 413; s. a. W. E. Bachmann et al., *Am. Soc.* 72, 3132 (1950)

Sym. ureas from monosubst. ureas

Silver nitrate

 AgNO_3 **Azomethines from azo compounds** $\text{CHN:NR} \rightarrow \text{C:NR}'$

444.



A soln. of 1-phenyl-3-(α -phenylbutyramido)-4-(p-anisylazo)-5-pyrazolone in ethyl acetate stirred with a soln. of Ag-nitrate in aq. NH_3 , an aq. soln. of 2-amino-5-diethylaminotoluene hydrochloride added dropwise, and stirring continued for 30 min. $\rightarrow$ azomethine dye. Y: 66%. F. e. s. P. W. Vittum et al., Am. Soc. 72, 1533 (1950).

Zinc

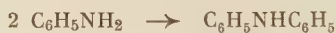
 Zn **Formamides from azo compounds** $\cdot\text{N:NR} \rightarrow \cdot\text{NHCHO}$

s. 6, 519

Alumina

 Al_2O_3 **Selfcondensation** $2 \text{RNH}_2 \rightarrow \text{R}_2\text{NH}$

445/6.

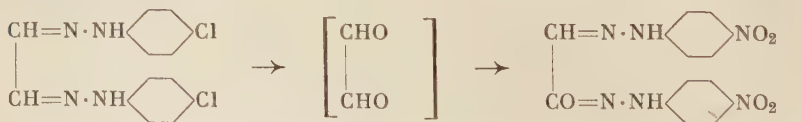


Aniline passed at 460° over activated alumina $\rightarrow$ diphenylamine. Conversion: ca. 35%. Under optimum conditions, because of the absence of side reactions, yields after recycling should approach 100%. H. E. Hoelscher and D. F. Chamberlain, Ind. Eng. Chem. 42, 1558 (1950); correction s. 43, 1828 (1951).

Acetic acid

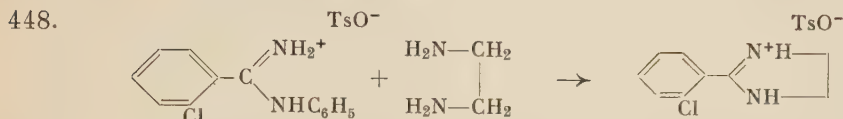
 CH_3COOH **Transosazonation**

447.



A soln. of p-nitrophenylhydrazine in dil. acetic acid added to a soln. of glyoxal p-bromophenylosazone in methyl cellosolve, and refluxed 2.5 hrs. on a water bath $\rightarrow$ glyoxal p-nitrophenylosazone. Y: 87%. F. e. s. I. Mandl, Arch. Biochem. 25, 109 (1950).

Sulfonates

Imidazolines and other 1,3-diazacyclo-
alkenes from subst. amidines

An equimolecular mixture of N-phenyl-o-chlorobenzamidine p-toluene-sulfonate and ethylenediamine heated 30 min. at 140° → 2-(o-chloro-phenyl)-4,5-dihydroglyoxalinium p-toluenesulfonate. Y: 88%. F. e. s. P. Oxley and W. F. Short, Soc. 1950, 859.

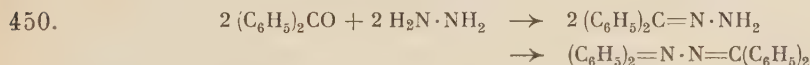
Δ²-Oxazolines from α-aminoalcohols

N-Phenyl-p-(methylsulfonyl)benzamidine benzenesulfonate and 2-hydroxyethylamine heated 4 hrs. on a steam bath → 2-p-methyl-sulfonylphenyl-Δ²-oxazoline. Y: 82%. F. e. s. P. Oxley and W. F. Short, Soc. 1950, 1100.

Sulfuric acid



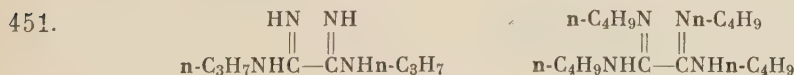
Azines from ketones via hydrazones



The reaction of hydrazine with carbonyl compounds proceeds with increasing difficulty as the carbonyl compound varies in the order aldehyde < dialkyl ketone < alkaryl ketone < diaryl ketone.—E: Benzophenone and hydrazine hydrate in 95%-ethanol refluxed 16-24 hrs. in a Soxhlet extractor, the extraction thimble of which is filled with freshly heated CaO → benzophenone hydrazone (Y: 88%) mixed with 95%-ethanol, treated with a few drops of concd. H₂SO₄ until the mixture remains acidic to methyl orange indicator, and allowed to stand 12-15 hrs. → benzophenone azine (Y: 85%). F. e. s. H. H. Szmant and C. McGinnis, Am. Soc. 72, 2890 (1950).

Hydrochlorides

Subst. oxamidines



sym-Di-*n*-propyloxamidine dihydrochloride refluxed 5 hrs. with excess

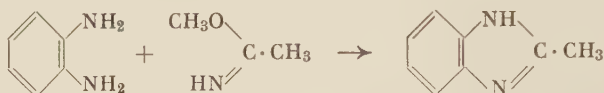
n-propylamine $\rightarrow$
sym-tetra-*n*-propyloxamidine.
 Y: 80%.

n-butylamine $\rightarrow$
sym-tetra-*n*-butyloxamidine.
 Y: 90%.

In other cases, only the alkyl groups are exchanged, a second disubst. oxamidine resulting thereby. F. e. s. H. Woodburn, B. A. Morehead, and Chen Ming Chih, *J. Org. Chem.* **15**, 541 (1950).

Imidazole ring from iminoesters

452.



A mixture of o-phenylenediamine and acetimino methyl ester hydrochloride in methanol warmed 10 min. on a steam bath $\rightarrow$ 2-methylbenzimidazole. Y: 91%. F. e. s. F. E. King and R. M. Acheson, *Soc.* **1949**, 1396; s. a. J. Walker, *Soc.* **1949**, 2002.

Via intermediates

v.i.

**Subst. carboxylic acid amides from
 carboxylic acid hydrazides via
 carboxylic acid azides**



s. **6**, 226; s. a. **1**, 359; *Helv.* **33**, 57, 108 (1950)

Halogen ∇

NC ∇ Hal

Without additional reagents

w.a.r.

Sec. from prim. amines and halides



453.

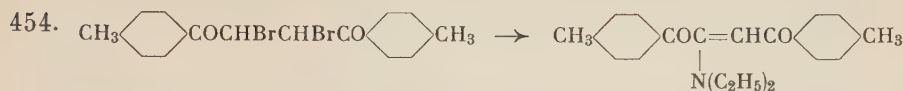


Twice the theoretical amount of β -chloroethyldiethylamine added to a warm soln. of p-aminophenyl p-chlorophenyl sulfone in p-dichlorobenzene, and boiled 1 hr. $\rightarrow$ p-(2-diethylaminoethyl)aminophenyl p'-chlorophenyl sulfone. Y: 75%.—p-Dichlorobenzene was found to be the most suitable of several solvents. F. e., also via sulfonic acid amides, s. E. Knüsli, *G.* **79**, 621 (1949).

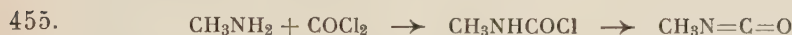
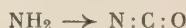
Diamines from halogenamines

Rearrangement of halogenamines

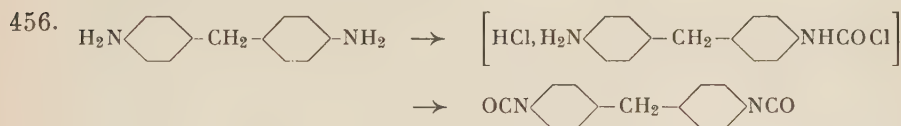
s. **5**, 325; s. a. R. C. Elderfield and C. Ressler, *Am. Soc.* **72**, 4059 (1950)

Enamines from 1,2-dibromides

A suspension of 1,2-di-(p-methylbenzoyl)ethylene dibromide in ethanol containing a large excess of diethylamine kept 20-25 min. at 50-65° → 1-diethylamino-1,2-di-(p-methylbenzoyl)ethylene. Y: 90%. F. e. s. R. E. Lutz et al., *J. Org. Chem.* 15, 181 (1950).

**Isocyanates from amines
via carbamyl chlorides**

Methylamine passed with 1.3 mole COCl_2 through a Pyrex tube at ca. 275° → crude methylcarbamyl chloride stirred and treated slowly with a soln. of dry pyridine and toluene → methyl isocyanate. Y: 88%. F. e. also without using a tert. amine in the second step, s. R. J. Slocombe et al., *Am. Soc.* 72, 1888 (1950).

Di-isocyanates from diamines

A hot soln. of 4,4'-diaminodiphenylmethane in o-dichlorobenzene added to an ice-salt cooled soln. of COCl_2 in o-dichlorobenzene so that the temp. does not exceed 0°, the suspension formed slowly heated to 130°, and treated with more COCl_2 until dissolved → 4,4'-diphenylmethane diisocyanate. Y: 84%. F. e., also with carbamic acids, s. W. Siefken, *A.* 562, 75 (1949).

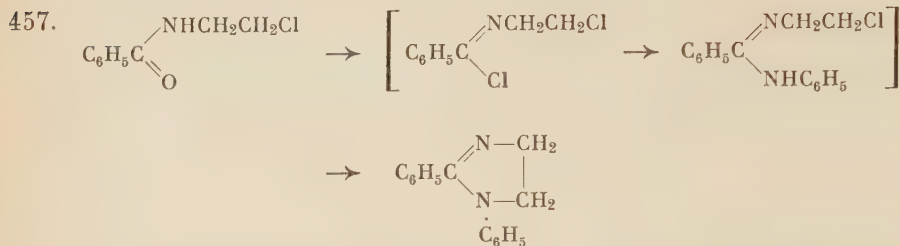
Peptides

s. 1, 426; s. a. F. W. Dunn and K. Dittmer, *J. Biol. Chem.* 188, 263 (1951)

**Sulfonic acid hydrazides
from chlorides**

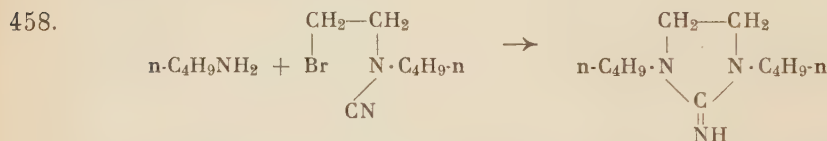
s. 6, 121

Imidazolines from carboxylic acid amides via iminochlorides and amidines



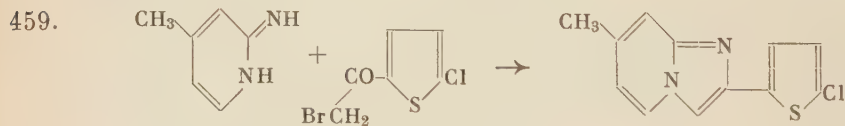
N-2-Chloroethylbenzamide added to a soln. of PCl_5 in dry benzene, to the resulting soln. aniline, dissolved in benzene, added slowly, refluxed for 3 hrs., then the solvent and POCl_3 evaporated in vacuo $\rightarrow$ 1,2-diphenyl-4,5-dihydroglyoxaline. Y: 92%. F. e. s. M. W. Partridge and H. A. Turner, Soc. 1949, 1308, 3043; amidines from iminochlorides s. a. C. G. Raison, Soc. 1949, 3319.

Cycl. guanidines from halogenocyanamides

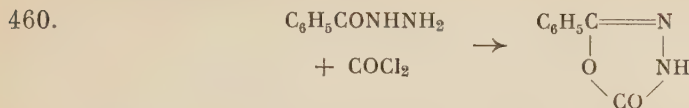


Equimolecular quantities of butyl- β -bromoethylcyanamide and n-butylamine in abs. ethanol refluxed 3-4 hrs. $\rightarrow$ 1,3-di-n-butyl-2-iminoimidazolidine hydrobromide. Y: 86%. F. e. s. R. C. Elderfield and H. A. Hageman, J. Org. Chem. 14, 605 (1949).

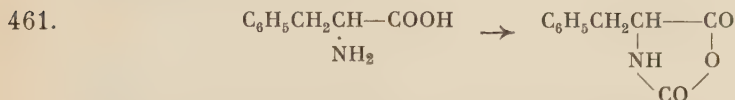
Pyrimidazoles



A mixture of 8 gm. 5-chloro-2-bromoacetylthiophene, 4 gm. 4-methyl-2-aminopyridine, and abs. alcohol warmed at 45-50° overnight $\rightarrow$ 8 gm. 2-(5'-chloro-2'-thienyl)-7-methylpyrimidazole. F. e. s. Ng. Ph. Buu-Hoï and Nguyen-Hoán, R. 68, 441 (1949).

1,3,4-Oxadiazolones

Benzhydrazide in chlorobenzene heated to boiling, then treated with phosgene for 30 min. $\rightarrow$ 2-phenyl-1,3,4-oxadiazol-5-one. Y: 98%. F. e. and limitations s. T. Lieser and G. Nischk, Chem. B. 82, 527 (1949).

2,5-Oxazolidiones from α -aminocarboxylic acids

DL- β -Phenylalanine refluxed with a soln. of phosgene in toluene until dissolved $\rightarrow$ anhydro-N-carboxy-DL- β -phenylalanine. Y: 70%. A. L. Levy, Nature 165, 152 (1950); Soc. 1950, 404; s. a. A. C. Farthing, Soc. 1950, 3213; D. Coleman, Soc. 1950, 3222; J. L. Bailey, Soc. 1950, 3461.

Sodium hydroxide

NaOH

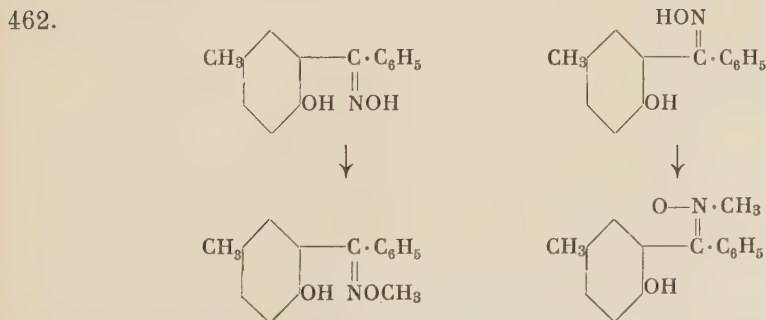
Carbalkoxy derivatives of amines

NHCOOR

s. 3, 368; s. a. H. L. Yale et al., Am. Soc. 72, 3710 (1950); carballyloxy derivatives s. C. M. Stevens and R. Watanabe, Am. Soc. 72, 725 (1950); carbobenzoxy derivatives s. S. W. Fox et al., Am. Soc. 72, 1862 (1950); W. E. Bachmann et al., Am. Soc. 72, 3132 (1950)

Sodium/alcohol

NaOR

Alkoximes from isomeric oximes $\leftarrow$ 

syn- and *anti*-Phenyl 2-hydroxy-5-methylphenyl ketoxime respectively dissolved in 1 mole 1-1.3 *N* Na-methoxide, 1.5-2 mole methyl iodide added, and left stoppered for 18-24 hrs. at room temp.

syn-Ketoxime $\rightarrow$ *syn*-phenyl
2-hydroxy-5-methylphenyl ket-
oxime O-methyl ether. Y: 77–83%.

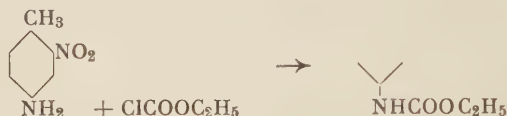
anti-Ketoxime $\rightarrow$ *anti*-phenyl
2-hydroxy-5-methyl-phenyl ket-
oxime N-methyl ether. Y: 83–90%.

The difference in the behavior is caused by the H-bond in the *syn*-isomer.
A. H. Blatt and S. Archer, Am. Soc. 71, 3021 (1949).

Carbethoxy derivatives of amines

NHCOOR

463.



Ethyl chloroformate added slowly with stirring and cooling to a cold soln. of 2-nitro-p-toluidine in abs. alcohol, then Na-ethoxide added so that the mixture is always kept faintly alkaline $\rightarrow$ N-carbethoxy-2-nitro-p-toluidine. Y: 95%. M. Viscontini and J. Pudles, Helv. 33, 591 (1950).

Sodium carbonate

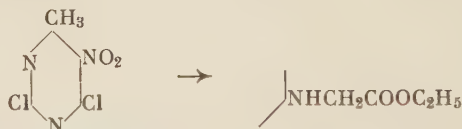
Na_2CO_3

Amines from chlorides

Hal $\rightarrow$ NHR

Partial replacement

464.



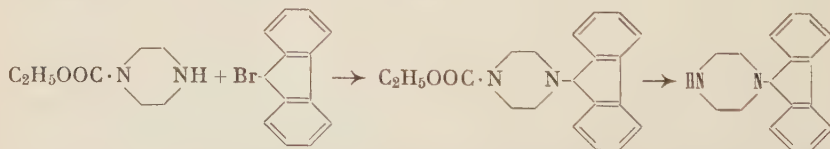
An alc. suspension of glycine ethyl ester hydrochloride added to an alc. suspension of 2,4-dichloro-5-nitro-6-methylpyrimidine, kept 30 min. at 4°, aq. Na-carbonate added with stirring, which is continued for 1.5 hrs. $\rightarrow$ 4-carbethoxymethylamino-2-chloro-5-nitro-6-methylpyrimidine. Y: 76%.—This partial replacement is made possible by esterification of the carboxylic group of glycine. M. Polonovski and H. Jérôme, C. r. 230, 392 (1950).

Substitution of piperazines

NH $\rightarrow$ NR

Elimination of N-carbethoxy groups

465.



A mixture of 1-carbethoxypiperazine, 9-bromofluorene, and Na-carbonate in butanol heated 4 hrs. on a steam bath $\rightarrow$ 1-(9-fluorenyl)-4-carbethoxypiperazine (Y: 70%) refluxed 60 hrs. in concd. HCl $\rightarrow$ 1-(9-fluorenyl)piperazine (Y: 89%). F. e., also disubstitution, and methods, s. K. E. Hamlin et al., Am. Soc. 71, 2734, 2731 (1949).

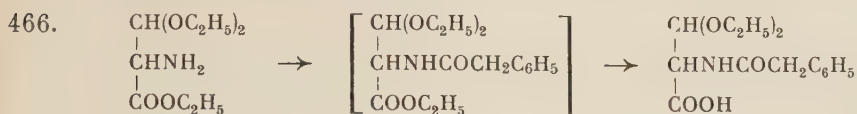
Sodium hydrogen carbonate

NaHCO₃

Acylamines from amines

NH₂ → NHAc

Selective hydrolysis



Phenylacetyl chloride slowly added at 5° to a vigorously stirred mixture of β,β-diethoxyalanine ethyl ester, NaHCO₃, water, and chloroform, stirred 1 hr. at room temp., the crude ester obtained added to ethanolic NaOH, and allowed to stand for 5 hrs. → benzylpenaldic acid diethyl-acetal. Y: 90.7%. F. e. s. E. V. Brown, *Chemistry of Penicillin 1949*, 512.

N-Carboethoxyamidines

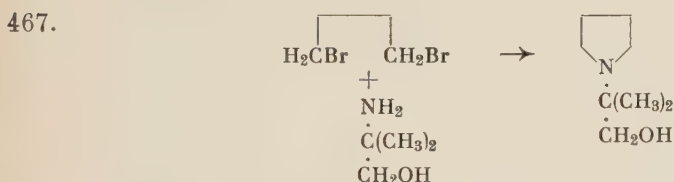
←

s. 6, 237

Pyrrolidines from γ-dihalides

○

N-Pyrrolidylalkanols



A mixture of 2-amino-2-methylpropanol, tetramethylene dibromide, and toluene refluxed 3 hrs. with stirring, NaHCO₃ added, and refluxed with vigorous stirring for an additional 15 hrs. → 2-(1-pyrrolidyl)-2-methylpropanol. Y: 75.5%. F. syntheses of pyrrolidylalkanols s. R. B. Moffett, *J. Org. Chem.* 14, 862 (1949).

Potassium hydrogen carbonate

KHCO₃

Cyanohydrazides

CONHNHCN



Aq. BrCN added to an aq. soln. of adipic acid dihydrazide and KHCO₃, and allowed to stand overnight → adipic acid di-(N^β,N'^β-cyano-hydrazide). Y: 88%. F. e. s. H. Gehlen, *A.* 563, 185 (1949).

Sodium acetate

CH₃COONa

α,β-Ethylenehydrazones from α-bromoketones

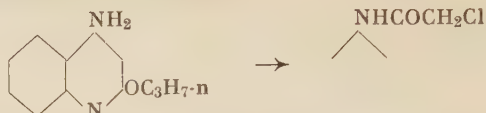
←

s. 4, 852; 6, 891

α -Halogenocarboxylic acid amides

CHalCONHR

469.



2-n-Propoxy-4-aminoquinoline in acetone treated with anhydrous Na-carbonate, cooled, treated dropwise with chloroacetyl chloride, and boiled 2 hrs. on a water bath $\rightarrow$ 2-n-propoxy-4-(chloroacetylamino)-quinoline. Y: 90%. F. e. s. J. Büchi, L. Ragaz, and R. Lieberherr, *Helv.* 32, 2310 (1949).

Sodium azide NaN_3 **Isocyanates from carboxylic acid chlorides via carboxylic acid azides** $\text{COCl} \rightarrow \text{N:C:O}$ **Activation of sodium azide**

470.



3-Isothiocyanatobenzoyl chloride refluxed with finely powdered NaN_3 in chlorobenzene for 24 hrs. $\rightarrow$ 3-isothiocyanatophenyl isocyanate. Y: 90%. W. Siefken, *A.* 562, 75 (1949); f. activation of NaN_3 s. R. F. Reker et al., *R.* 70, 113 (1951).

Diethylaniline $\text{C}_6\text{H}_5\text{N}(\text{C}_2\text{H}_5)_2$ **Urethans from amines** $\text{NH} \rightarrow \text{NCOOR}$

s. 6, 586

N-Methylmorpholine $\leftarrow$ **α -Halogenocarboxylic acid amides**

CHalCONHR

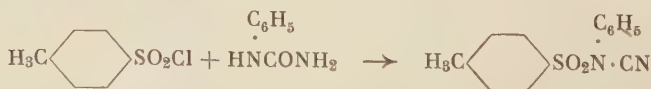
s. 6, 308

Acylamines from amines and carboxylic acid chlorides $\text{NH}_2 \rightarrow \text{NHAc}$

s. 1, 374/5; also modified procedure s. P. E. Verkade, B. M. Wepster, and P. H. Witjens, *R.* 70, 127 (1951)

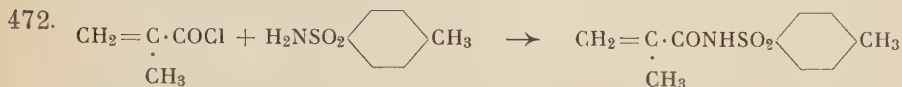
Pyridine $\text{C}_5\text{H}_5\text{N}$ **Sulfonylcyanamides from sulfonic acid chlorides** $\text{SO}_2\text{Cl} \rightarrow \text{SO}_2\text{NRCN}$

471.



6 mols. p-toluenesulfonyl chloride added with cooling below 30° to a soln. of 1 mol. phenylurea in pyridine, and allowed to stand for 10 min.

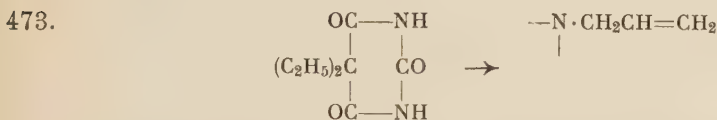
→ N-(p-toluenesulfonyl)-N-phenylcyanamide. Y: 95%.—Sulfonyl-ureas, synthesized by alternative methods, are not dehydrated by sulfonyl chlorides under these conditions. F. e. s. F. Kurzer, *Soc.* 1949, 1034.

*Copper**Cu***N-Acylsulfonic acid amides**SO₂NHAc

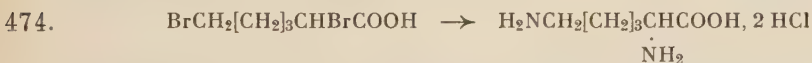
Methacrylyl chloride (prepn. s. 578), p-toluenesulfonamide, and some Cu-powder refluxed $\frac{3}{4}$ hr. until the HCl-evolution ceases → N-methacrylyl-p-toluenesulfonamide. Y: 75%. F. e. s. J. Heyboer and A. J. Staverman, *R.* 69, 787 (1950).

*Silver hydroxide**AgOH***N-Alkylbarbituric acids**

NH → NR



Na-Barbital and allyl chloride refluxed with stirring for 4 hrs. in the presence of AgOH → N-allylbarbital. Y: 87%. A. Halpern and J. W. Jones, *J. Am. Pharm. Assoc.* 37, 333 (1948); f. e. s. 38, 352 (1949).

*Cuprous chloride**CuCl***Prim. amines from halides**Hal → NH₂

A mixture of 2,6-dibromohexanoic acid, aq. NH₃, NH₄-carbonate, and a little CuCl heated 18-20 hrs. at 125-150° in a closed vessel → lysine dihydrochloride. Y: 81%. F. e. s. D. C. Sayles and E. F. Degering, *Am. Soc.* 71, 3161 (1949).

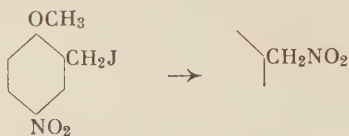
Sec. from prim. amines and halidesNH₂ → NHR

A mixture of 4-amino-4'-chlorodiphenyl sulfone, isopropanolamine, and CuCl stirred and refluxed at 165-175° for 15 hrs., and worked up whereby the copper is removed by treating with H₂S → 4-amino-4'-(β-hydroxypropylamino)diphenyl sulfone. Y: 85%. F. e. s. J. Weijlard and E. F. Swanezy, *Am. Soc.* 71, 4134 (1949); s. a. E. C. Hughes, F. Veatch, and V. Elersich, *Ind. Chem.* 42, 787 (1950).

Silver nitrite

 AgNO_2 **Aliphatic nitro compounds from iodides** $\text{I} \rightarrow \text{NO}_2$

476.

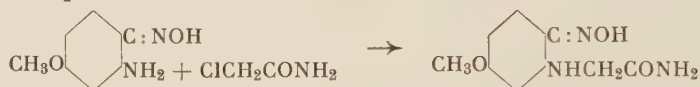


4-Nitro-2-(iodomethyl)anisole in benzene-ether treated with powdered AgNO_2 , and kept at room temp. for 3 days with occasional shaking $\rightarrow$ 4-nitro-2-(nitromethyl)anisole. Y: 81%.— HgNO_2 gives more hydroxymethyl compound as by-product. G. Bendz et al., Soc. 1950, 1130.

Calcium carbonate

 CaCO_3 **Sec. from prim. amines and halides** $\text{NH}_2 \rightarrow \text{NHR}$

477.

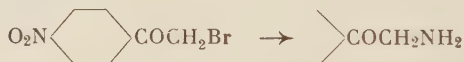


2-Aminoanisaldoxime (prepn. s. 32), Ca carbonate, chloroacetamide, and water refluxed 3 hrs. $\rightarrow$ 2-formyl-5-methoxyphenylglycineamide oxime. Y: 89%. W. R. Boon, Soc. 1949, S230.

Hexamethylenetetramine

 $\leftarrow$ **Prim. amines from halides** $\text{Hal} \rightarrow \text{NH}_2$

478.



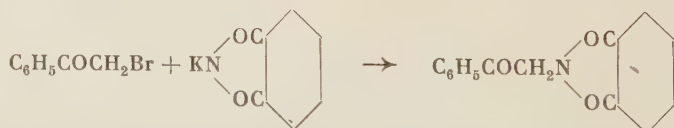
A soln. of p-nitro- α -bromoacetophenone in chlorobenzene added with stirring in one portion at room temp. to a mixture of hexamethylenetetramine and dry chlorobenzene, warmed 4 hrs. at 50-52°, the salt obtained (Y: 95%) added at 25° to a mixture of 95%-ethanol and concd. HCl, and stirred 16 hrs. at room temp. $\rightarrow$ p-nitro- α -aminoacetophenone hydrochloride. Y: 74%. L. M. Long and H. D. Troutman, Am. Soc. 71, 2473 (1949); s. a. Ng. Ph. Buu-Hoi et al., Soc. 1950, 2766.

Dimethylformamide

 $\text{HCON}(\text{CH}_3)_2$ **Phthalimides from halides****Gabriel synthesis****Improved procedure**

$$\text{Hal} \rightarrow \begin{array}{c} \text{CO} \\ | \\ \text{N} \\ | \\ \text{CO} \end{array}$$

479.



The use of dimethylformamide as solvent for K-phthalimide gives improved yields of the phthalimides.—E: K-phthalimide added to a soln.

of phenacyl bromide in dimethylformamide, and stirring continued for 30 min. → phthalimidoacetophenone. Y: 92%. F. e. s. J. C. Sheehan and W. A. Bolhofer, *Am. Soc.* 72, 2786 (1950).

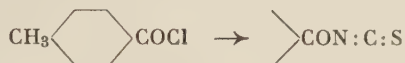
Lead salts

Pb++

Acylisothiocyanates from carboxylic acid chlorides

COCl → CON:C:S

480.



51 gm. p-methoxybenzoyl chloride, benzene, and Pb-thiocyanate boiled with good stirring for 1 hr. → 43 gm. p-methoxybenzoyl isothiocyanate (startg. m. f. 353). F. e. s. E. Hoggarth, *Soc.* 1949, 1160.

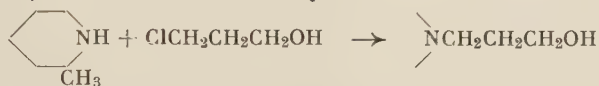
Alkali iodides

I⁻

(tert-Amino)alcohols from chlorohydrins

Hal → N<

481.



A mixture of 2-methylpiperidine, trimethylene chlorohydrin, abs. alcohol, and Na- or K-iodide refluxed with stirring for 24 hrs., cooled, and the stirred mixture treated with a soln. of Na in abs. alcohol → 3-(2-methylpiperidyl-1)-propanol. Y: 92% based on recovered 2-methylpiperidine. F. e. s. R. O. Clinton, U. J. Salvador, and S. C. Laskowski, *Am. Soc.* 71, 3366 (1949).

Hydrochlorides

←

Isocyanates from amines

NH₂ → N:C:O

s. 1, 385; s. a. T. Lieser and G. Nischk, *A.* 569, 59 (1950); M. W. Farlow, *Org. Synth.* 31, 62 (1951)

Sulfur †

NC † S

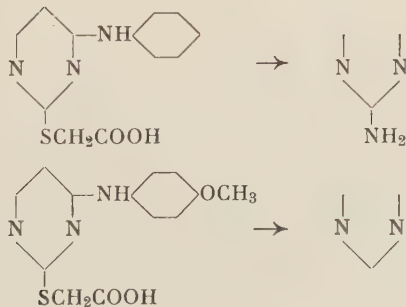
Without additional reagents

w.a.r.

Carboxymethyl thioethers as intermediates

←

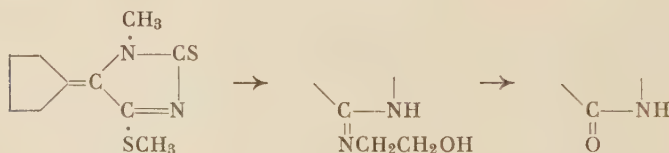
482.



In certain cases replacement of the sulfhydryl group may be best effected via the carboxymethyl derivatives.—E: 4-Anilino-2-(carboxymethylthio)pyrimidine heated with NH_3 -soln. (d. 0.9) in a sealed tube at 140-150° for 24 hrs. $\rightarrow$ 2-amino-4-anilino-2-pyrimidine. Y: 80%.—4-Anilino-2-mercaptopyrimidine gave no reaction under these conditions.—2.2 gm. 4-p-methoxyanilino-2-(carboxymethylthio)pyrimidine refluxed 3 hrs. with Raney-Ni and Na_2CO_3 in abs. alcohol $\rightarrow$ 1.7 gm. 4-p-methoxyanilino-2-pyrimidine.—The better solubility of the carboxymethyl derivatives may facilitate the desulfuration. F. e. s. G. H. Hitchings and P. B. Russell, Soc. 1949, 2454.

Oxo compounds from thioenolethers via imines

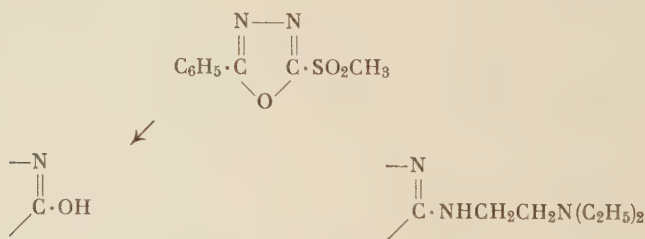
483.



2-Thio-4-methylthio-1-methyl-5,5-pentamethylene-2,5-dihydroglyoxaline and 2-amino-ethanol heated 15 min. at 110-120° $\rightarrow$ 4-(2'-hydroxyethylimino)-1-methyl-5,5-pentamethylene-2-thiohydantoin (Y: ca. 100 per cent) boiled with 20% -HCl $\rightarrow$ 1-methyl-5,5-pentamethylene-2-thiohydantoin (Y: 31%). F. e. s. H. C. Carrington and W. S. Waring, Soc. 1950, 354.

Sec. amines and hydroxy compounds from sulfones

484.



2-Methanesulfonyl-5-phenyl-1,3,4-oxadiazole

(1 g.) ground with *N* NaOH $\rightarrow$ 0.65 g. 2-hydroxy-5-phenyl-1,3,4-oxadiazole.

(3.3 g.) cautiously added to dry 2-diethylaminoethylamine at 80° during 10 min., so that the temp. does not rise above 100° $\rightarrow$ 3.1 g. 2-(2'-diethylaminoethylamino)-5-phenyl-1,3,4-oxadiazole.

F. e. s. E. Hoggarth, Soc. 1949, 1918, 3311.

Sodium

Na

Alkylation of acylaminesNHAc $\rightarrow$ NRAc

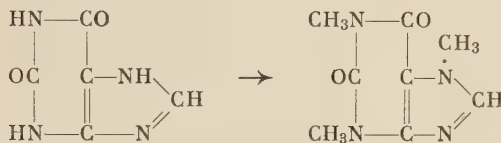
s. 6, 502

Sodium hydroxide

NaOH

Methylation of purinesNH $\rightarrow$ NR

485.



Dimethyl sulfate and NaOH added simultaneously at 35° and pH 8-9 to an aq. suspension of xanthine (prepn. s. 44) over a period of 70 min., and stirring continued for 30 min. at the same pH with addition of a little more aq. NaOH $\rightarrow$ caffeine. Y: 86-90%.—Depending on the pH, different methylation products are obtained. F. e. s. H. Bredereck, H.-G. v. Schuh, and A. Martini, Chem. B. 83, 201 (1950).

**Acylaminoguanidines from
carboxylic acid hydrazides
and isothiureas**
 $\leftarrow$

s. 6, 409

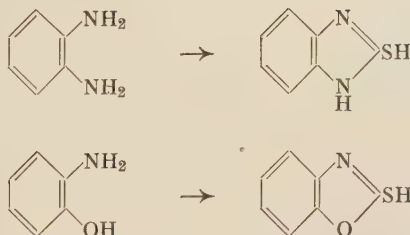
Potassium hydroxide

KOH

**2-Mercaptobenzimidazoles and
2-mercaptobenzoxazoles**

○

486.



A mixture of o-phenylenediamine, K ethyl xanthate (or KOH and CS₂), ethanol, and water refluxed 3 hrs. $\rightarrow$ 2-mercaptobenzimidazole. Y: 84 to 86.5%.—Similarly with o-aminophenol $\rightarrow$ 2-mercaptobenzoxazole. Y: 80%. J. A. Van Allan and B. D. Deacon, Org. Synth. 30, 56 (1950).

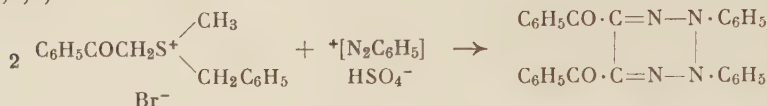
Sodium acetate

 CH_3COONa **Coupling diazonium salts with sulfonium salts**

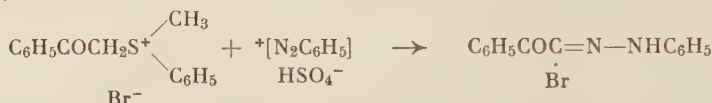
←

1,2,3,4-Tetrazines

487.



A soln. of methylbenzylphenacylsulfonium bromide and Na-acetate treated with phenyldiazonium sulfate, and allowed to stand overnight → 2,3-diphenyl-5,6-dibenzoyl-2,3-dihydro-1,2,3,4-tetrazine. Crude-Y: 77%.



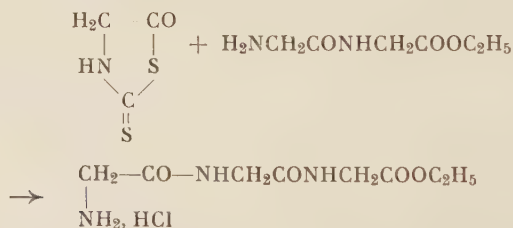
A soln. of 22.7 gm. methylphenylphenacylsulfonium bromide and Na-acetate in 50% methanol treated with phenyldiazonium sulfate, and worked up after 15 min. → 14 gm. crude α -bromo- β -phenylglyoxal α -phenylhydrazone. F. Krollpfeiffer and H. Hartmann, Chem. B. 83, 90 (1950).

Triethylamine

 $(\text{C}_2\text{H}_5)_3\text{N}$ **Peptides from 2-thiazolidinethiones**

C

488.



2-Thio-5-thiazolidone added to a mixture of glycylglycine ethyl ester hydrochloride and 2 equivalents of triethylamine in ethanol, and the clear soln. acidified with 5 N ethanolic HCl → triglycine ethyl ester hydrochloride. Y: 86%. F. e., methods, and catalysts s. A. H. Cook and A. L. Levy, Soc. 1950, 646, 651.

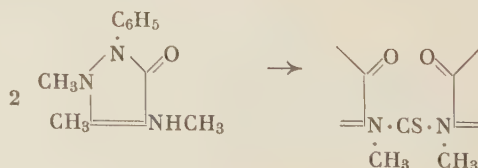
Sulfur

S

Sym. thioureas from amines

←

489.



Imidazole ring from imidazolone ring**Purines**

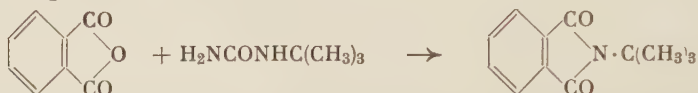
493.



15 gm. uric acid boiled 2 hrs. with 300 gm. acetamide $\rightarrow$ 12 gm. 8-methylxanthine. F. e., also with formamide, s. H. Brederick, H. v. Schuh, and A. Martini, Chem. B. 83, 201 (1950).

N-Subst. phthalimides from ureas

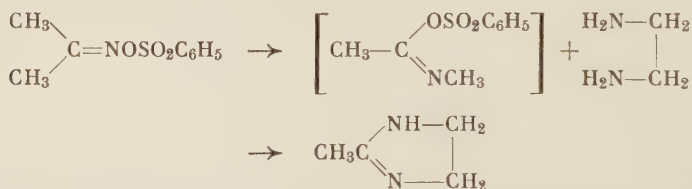
494.



A mixture of *tert*-butylurea (prepn. s. 433) and phthalic anhydride heated 10 min. at 200°, then 5 min. at 220-240° $\rightarrow$ *tert*-butylphthalimide. Y: 72-76%. F. e. s. L. I. Smith and O. H. Emerson, Org. Synth. 29, 19 (1949).

Imidazolines from ketoxime sulfonates

495.



Acetoxime benzenesulfonate, ethylenediamine, and toluene refluxed 0.5 hr. $\rightarrow$ 2-methyl-4,5-dihydroglyoxaline. Y: 74.5%, isolated as picrate. F. e. s. P. Oxley and W. F. Short, Soc. 1950, 859.

Amino-dithiocarbamic acids from imidazolines

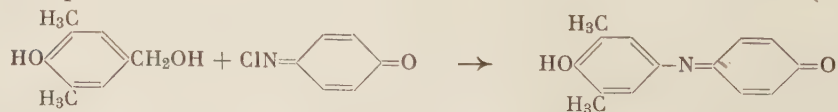
s. 6, 616

Sodium hydroxide

NaOH

Indophenols

496.



The formation of indophenols may occur even when the position para to the hydroxyl group is substituted.—E: 10%-aq.-NaOH added with

stirring at 0° to a suspension of 4-hydroxy-3,5-dimethylbenzylalcohol and p-quinoneimine chloride, and the Na-salt obtained decomposed with CO₂ → 3',5'-dimethylindophenol. Y: ca. 100%. F. e. s. E. Ziegler and K. Gartler, M. 80, 759 (1949).

Japp-Klingemann reaction

Hydrazones from diazonium salts

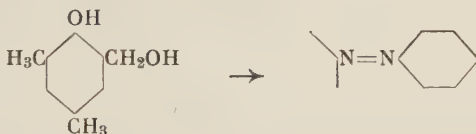
α-Ketocarboxylic acid ester phenylhydrazones from β-ketocarboxylic acid esters

s. 2, 426; s. a. V. Boekelheide and C. Ainsworth, Am. Soc. 72, 2132 (1950)

Azo compounds by coupling with elimination of formaldehyde



497.



Benzenediazonium sulfate soln. added with ice-cooling to a soln. of 1.52 gm. 2-hydroxy-3,5-dimethylbenzyl alcohol in 10%-NaOH → 1.6 gm. crude 2-hydroxy-3,5-dimethylazobenzene. F. e. s. E. Ziegler and G. Zigeuner, M. 79, 42, 89, 358 (1948).

Sodium/alcohol

NaOR

α-Oximinocarboxylic acid esters from malonic acid esters



s. 6, 823

Sodium acetate

CH₃COONa

Hydrazones from diazonium salts

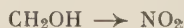
Japp-Klingemann reaction

s. 6, 290

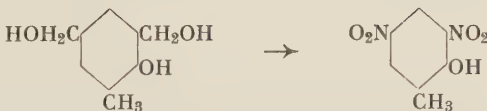
Sodium nitrite

NaNO₂

Replacement of hydroxymethyl by nitro groups



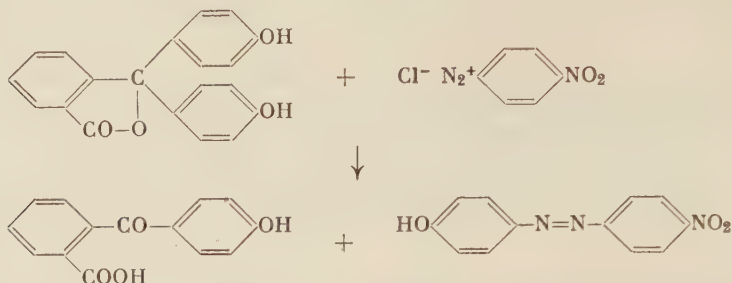
498.



1.68 gm. o-cresoldialcohol allowed to stand 24 hrs. in a soln. of NaNO₂ in aq. HCl, then steam-distilled → 1.42 gm. 2,4-dinitro-o-cresol. F. e., also partial replacement, s. E. Ziegler and K. Gartler. M. 80, 634 (1949).

Cleavage of di- and tri-arylmethane derivatives to azo compounds

499.



A soln. of phenolphthalein in aq. NaOH slowly treated with an equimolecular quantity of p-nitrobenzenediazonium chloride (prepared from p-nitroaniline, NaNO_2 , and HCl), then neutralized cautiously with dil. $\text{H}_2\text{SO}_4 \rightarrow$ 2-(4'-hydroxybenzoyl)benzoic acid (Y: 80%) and 4-(4'-nitrobenzeneazo)phenol (Y: 80%). G. Zigeuner and E. Ziegler, M. 79, 371 (1948); cleavage of diarylmethane derivatives s. M. 79, 363 (1948); 80, 295 (1949).

Hydrazoic acid

HN_3

Schmidt reaction

$\text{COOH} \rightarrow \text{NH}_2$

Amines from carboxylic acids

Degradation with loss of 1 C-atom

s. 1, 338/9; 5, 354; diamines s. D. M. Hall, S. Mahboob, and E. E. Turner, Soc. 1950, 1842

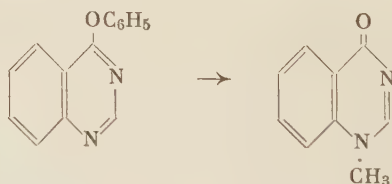
Tosylates

TsOR

1-Subst. quinazolones from 4-alkoxyquinazolines

$\leftarrow$

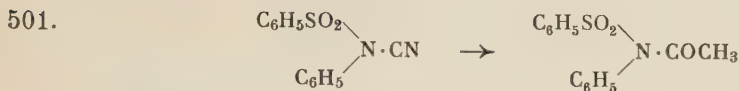
500.



A mixture of 4-phenoxyquinazoline (prepn. s. 244) and methyl p-toluenesulfonate fused at 150° for $\frac{1}{4}$ hr. $\rightarrow$ 1-methyl-4-quinazolone (isolated as picrate). Y: 87%. J. S. Morley and J. C. E. Simpson, Soc. 1949, 1354.

Sulfuric acid H_2SO_4 **N-Sulfonylcarboxylic acid amides
from N-sulfonylcyanamides**

←



A soln. of benzenesulfonylphenylcyanamide in acetic anhydride treated with 6 drops of H_2SO_4 , and refluxed 2 hrs. → N-acetylbenzenesulfonanilide. Y: 80%. F. e. s. F. Kurzer, Soc. 1949, 3029.

Hydrochlorides

←

Subst. oxamidines

←

s. 6, 451

Via intermediates

v.i.

Sec. amines from acylamines $\text{NHAc} \rightarrow \text{NHR}$ 

Pure dry m-benzyloxyacetanilide added with rapid stirring at 61° to Na-sand in xylene, the temp. raised to $100-110^\circ$, held at this temp. for 1 hr., dry dimethyl sulfate added in small portions without external heating, when the exothermic reaction has subsided stirred an additional 15 min., and worked up, whereby the anilide is hydrolyzed by refluxing with KOH in 90%-alcohol for 48 hrs. → N-methyl-m-benzyl-oxyaniline. Crude Y: 94%. A. A. Morton and W. R. Slaunwhite, Jr., J. Biol. Chem. 179, 259 (1949).

**Shortened Curtius degradation
Amines from carboxylic acids
via carboxylic acid chlorides
and azides** $\text{COOH} \rightarrow \text{NH}_2$

s. 1, 390; 2, 466; 3, 402; 4, 451; s. a. A. McCoubrey, Soc. 1950, 1833; H. Rapoport, A. R. Williams, and M. E. Cisney, Am. Soc. 73, 1414 (1951); compounds with isotopes s. E. M. Gal, R. E. Spenger, and D. M. Greenberg, J. Org. Chem. 15, 1261 (1950)

Elimination

Hydrogen $\downarrow$ NC $\uparrow$ H*Mercuric oxide**HgO*

Subst. oximes

 $\leftarrow$

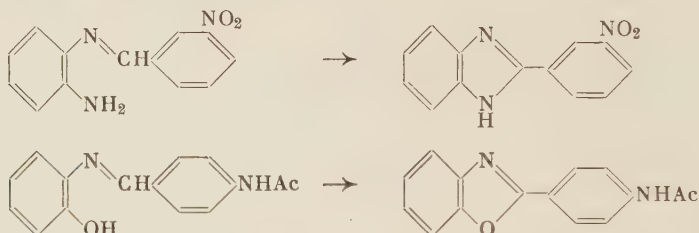
from subst. hydroxylamines

s. 3, 403; s. a. A. C. Cope and A. C. Haven, Jr., *Am. Soc.* 72, 4896 (1950)

Lead tetraacetate $(\text{CH}_3\text{COO})_4\text{Pb}$ Benzimidazoles and benzoxazoles
from azomethines

O

503.



Benzimidazoles and benzoxazoles are obtained in excellent yields by treatment of the corresponding Schiff's base, in benzene or acetic acid, with 1 molecular equivalent of Pb-tetraacetate.—E: N-m'-Nitrobenzylidene-o-phenylenediamine $\rightarrow$ 2-m-nitrophenylbenzimidazole. Y: 95%. —2-(p-acetamidobenzylideneamino)phenol $\rightarrow$ 2-p-acetamidophenylbenzoxazole. Y: 95%. F. e. s. F. F. Stephens and J. D. Bower, *Soc.* 1949, 2971. Other reagents, particularly chloranil, N-bromosuccinimide, and benzoyl peroxide, can be used as well. *Soc.* 1950, 1722.

Hydrogen peroxide H_2O_2

Quinoxalines from

 $\leftarrow$

1,2,3,4-tetrahydroquinoxalines

s. 6, 514

Oxygen $\downarrow$ NC $\uparrow$ O*Without additional reagents**w.a.r.*Low molecular isocyanates
from urethans $\text{NHCOOR} \rightarrow \text{N:C:O}$

504.

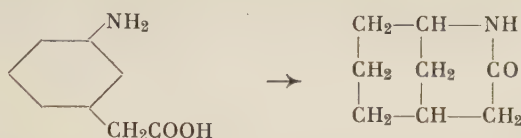


Pyrocatechol mono(ethylcarbamate) (prepn. s. 341) distilled at 210 to 250° $\rightarrow$ ethyl isocyanate. Y: 40-55%. F. e. s. S. Petersen, *A.* 562, 205 (1949).

m-Ring closure of N-heterocyclics

○

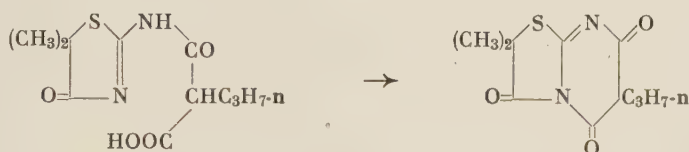
505.



cis-3-Aminocyclohexanecarboxylic acid heated in an N_2 -atmosphere for 30 min. at $260^\circ \rightarrow$ *cis*-3-aminocyclohexanecarboxylic acid lactam (startg. m. s. 636). Y: 90%. F. e. s. M. W. Cronyn, J. Org. Chem. 14, 1013 (1949).

Thiazolo[3.2-a]pyrimidines, 2,3,6,7-tetrahydro-

506.



0.5 gm. 2-(α -carboxy-*n*-valerylamido)-5,5-dimethyl-4-thiazolone heated 2 hrs. at $185^\circ/0.001$ mm. $\rightarrow$ 0.4 gm. 3,5,7-triketo-2,2-dimethyl-6-*n*-propyl-2,3,6,7-tetrahydro-5*H*-thiazolo[3.2-a]pyrimidine. F. e. s. P. J. Heald and T. K. Walker, Soc. 1950, 1127.

Sodium hydroxide

NaOH

Cyclic imines from
aminosulfuric acid esters

507.



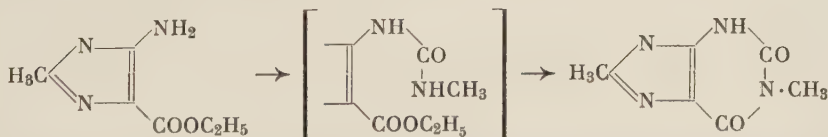
A mixture of β -aminoethylsulfuric acid and 40% NaOH heated to boiling with a free flame, and after the reaction has subsided, heating resumed, and the mixture distilled as quickly as possible $\rightarrow$ ethyleneimine. Y: 34-37%. C. F. H. Allen, F. W. Spangler, and E. R. Webster, Org. Synth. 30, 38 (1950).

Pyrimidine ring

New synthesis of purines from imidazoles

Thiazolo[5.4-d]pyrimidines

508.

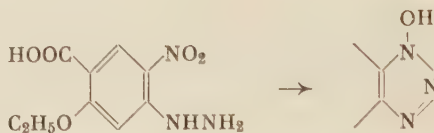


4-Amino-5-carbethoxy-2-methylglyoxaline and a large excess of methyl isocyanate in pyridine refluxed 2 hrs., pyridine removed in vacuo, and

the residue boiled with 10% -NaOH $\rightarrow$ 1,8-dimethylxanthine. Y: 67%. F. e., also isolation of the intermediate, s. A. H. Cook et al., Soc. 1949, 1071; thiazolo[5,4-d]pyrimidines from thiazoles s. Soc. 1949, 1064, 1069.

1,2,3-Triazoles

509.



5-Nitro-4-hydrazino-2-ethoxybenzoic acid (prepn. s. 442) dissolved in 2 N NaOH, and heated 1 min. on a steam bath $\rightarrow$ 6-ethoxy-3-hydroxybenzotriazole-5-carboxylic acid. Y: 96%. H. Goldstein and R. Brochon, Helv. 32, 2334 (1949); with Na-carbonate s. Helv. 34, 146 (1951).

Sodium/alcohol

NaOR

1,2,4-Triazoles from acylthiosemicarbazides

510.



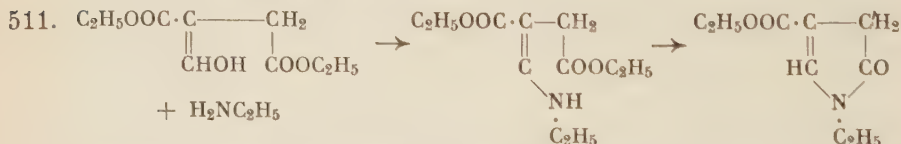
3.9 gm. 1-benzoylthiosemicarbazide added to a soln. of Na in alcohol, then gently refluxed for 12 hrs. $\rightarrow$ 2.8 gm. 3-phenyl-1,2,4-triazole-5-thiol. F. e. s. E. Hoggarth, Soc. 1949, 1163, 1160; 1950, 614, 1579.

Potassium/alcohol

KOR

2-Pyrrolines

α -Aminomethylene compounds from α -hydroxymethylene compounds



An ethereal soln. of ethylamine, obtained from the hydrochloride with concd. aq. KOH, mixed with diethyl formylsuccinate, and allowed to stand for 2 hrs. $\rightarrow$ diethyl ethylaminomethylenesuccinate (Y: 91%) dissolved in abs. benzene, then dropped under anhydrous conditions in a stream of N_2 into a cold soln. of K in tert.-amyl alcohol-benzene with swirling, and allowed to stand overnight $\rightarrow$ 1-ethyl-4-carbethoxy-2-pyrrolone (Y: 75%). F. e. s. C. A. Grob and P. Ankli, Helv. 32, 2010 (1949); α -aminomethylene from α -hydroxymethylene compounds s. a. A. H. Cook et al., Soc. 1950, 1947.

1,2-Dihydroimidazo[1.2-a]pyrroles
via α -aminopyrroles from
aminomethylene compounds

s. 6, 374

Sodium carbonate

Na_2CO_3

1,2,3-Triazoles

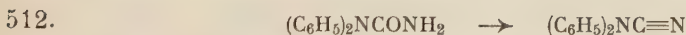
s. 6, 509

Pyridine

$\text{C}_5\text{H}_5\text{N}$

Disubst. cyanamides from ureas

$\text{R}_2\text{NCONH}_2 \rightarrow \text{R}_2\text{NCN}$



A soln. of *as*-diphenylurea in pyridine treated with excess *p*-toluenesulfonyl chloride, and heated 2 hrs. on a steam bath $\rightarrow$ diphenylecyanamide. Y: 97%. F. Kurzer, Soc. 1949, 3033.

N-Sulfonylcyanamides from ureas

$\leftarrow$

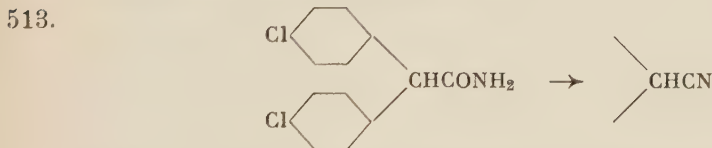
s. 6, 333

Acetic anhydride

$(\text{CH}_3\text{CO})_2\text{O}$

Nitriles from carboxylic acid amides

$\text{CONH}_2 \rightarrow \text{CN}$



1,1-Bis-(*p*-chlorophenyl)acetamide refluxed 4 hrs. with acetic anhydride $\rightarrow$ 1,1-bis-(*p*-chlorophenyl)acetonitrile. Y: 89%. P. Weiss, M. G. Cordasco, and L. Reiner, Am. Soc. 71, 2650 (1949).

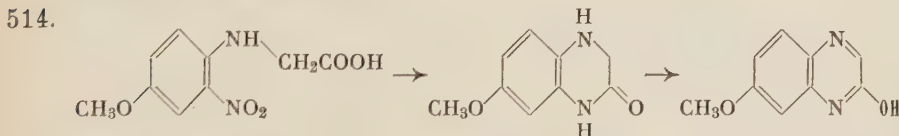
Tin

Sn

Quinoxalines via 1,2,3,4-tetra-
hydroquinoxalines

$\bigcirc$

Reductive ring closure



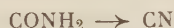
Concd. HCl added in small portions to a mixture of N-(2-nitro-4-methoxyphenyl)glycine, Sn, and ethanol, then refluxed 2 hrs. $\rightarrow$ 1,2,3,4-tetrahydro-2-keto-7-methoxyquinoxaline (Y: 85%) and H_2O_2 in aq.

NaOH heated 2 hrs. on a steam bath $\rightarrow$ 2-hydroxy-7-methoxyquin-oxaline (Y: ca. 100%). F. e. s. R. L. Wear and C. S. Hamilton, *Am. Soc.* 72, 2893 (1950).

Phosphorus oxychloride



Nitriles from carboxylic acid amides

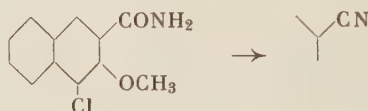


s. 3, 407; s. a. E. J. Skerrett and D. Woodcock, *Soc.* 1950, 2718

Phosphorus pentachloride

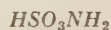


515.



4-Chloro-3-methoxynaphthoic acid amide heated with an equal amount of PCl_5 in a water bath until the evolution of HCl ceases $\rightarrow$ 4-chloro-3-methoxy-2-naphthonitrile. Y: 90%. F. e. s. H. Richtzenhain and P. Nippus, *Chem. B.* 82, 408 (1949).

Sulfamic acid



516. An intimate mixture of p-nitrobenzamide and sulfamic acid heated to 220° during 20 min., and kept at this temp. for 5 min. $\rightarrow$ p-nitrobenzonitrile. Y: 94%. F. e. s. A. V. Kirsanov and Y. M. Zolotov, *Ж.* 20, 284 (1950); *C. A.* 44, 6384i.

Hydroxylaminedisulfonate



Oximes from nitro compounds



517.



35% $-NaHSO_3$ added slowly to $NaNO_2$ and crushed ice. SO_2 passed in at $0-2^\circ$ until the soln. is acid to Congo red, the soln. of hydroxylamine-disulfonate thus formed treated with 20% $-H_2SO_4$ at $4-5^\circ$, immediately followed by nitrocyclohexane in a slight excess of aq. $NaOH$ at $6-8^\circ$, and stirred 1 hr. $\rightarrow$ cyclohexanone oxime. Y: 85-90%. S. S. Nametkin, G. I. Zyabreva, and B. A. Krentsel, *Doklady Akad. Nauk S. S. S. R.* 72, 711 (1950); *C. A.* 44, 9362d.

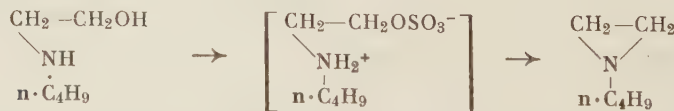
Chlorosulfonic acid/potassium hydroxide



Cyclic imines from aminoalcohols



518.



Chlorosulfonic acid added portionwise with shaking to crude N-(n-butyl)ethanolamine hydrochloride, after the initial reaction has sub-

sided heated 40 min. on a steam bath, then at 80° under water pump vacuum, finally at 140-145° for 1.5 hrs., dissolved in cold water, then added portionwise with vigorous agitation below 70° to aq. KOH, and steam-distilled $\rightarrow$ N(n-butyl)ethyleneimine. Y: 74%. F. e. s. R. C. Elderfield and H. A. Hageman, *J. Org. Chem.* **14**, 605 (1949).

Copper chromite

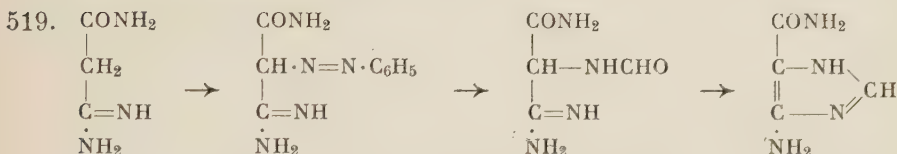
CuCr_2O_4

Pyrrolizidines

s. 4, 390; s. a. *Am. Soc.* **72**, 2537, 2543 (1950)

Hydrochlorides

Imidazoles via azo compounds and formamides



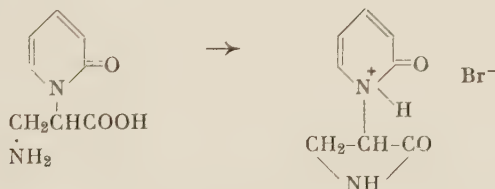
A soln. of aniline in 6 N HCl gradually treated below 5° with aq. NaNO_2 , excess HNO_2 decomposed with urea, the diazonium salt soln. obtained poured into an aq. soln. of malonamidine hydrochloride, and the pH brought to ca. 4 by addition of concd. aq. Na-acetate $\rightarrow$ phenylazomalonomamidine hydrochloride (Y: 90%) added in portions with occasional agitation during 1 hr. to a suspension of Zn-dust in 98%-formic acid, and warmed on a hot plate until the residual azo color is discharged $\rightarrow$ formamidomalonomamidine hydrochloride (Y: 63%) heated ca. 10 min. at an oil-bath temp. of ca. 170° $\rightarrow$ 4-amino-5-imidazolecarboxamide hydrochloride (Y: 89%). E. Shaw and D. W. Woolley, *J. Biol. Chem.* **181**, 89 (1949).

Hydrobromic acid

HBr

β -Lactams

520.



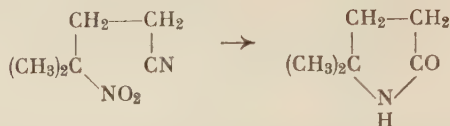
Dry HBr passed into a suspension of α -(N-2-pyridone)- β -aminopropionic acid in abs. ethanol until a clear soln. results, and allowed to stand overnight in a refrigerator $\rightarrow$ α -(N-2-pyridone)- β -aminopropiolactam hydrobromide. Y: 89%. R. Adams and V. V. Jones, *Am. Soc.* **71**, 3826 (1949).

Nickel

Ni

2-Pyrrolidones from nitriles

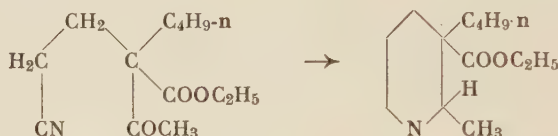
521.



γ -Methyl- γ -nitrovaleronitrile in abs. alcohol hydrogenated with Raney-Ni at 170-240° and an initial pressure of 2200 lbs./sq.in. with final shaking $\rightarrow$ 2,2-dimethyl-5-pyrrolidone. Y: 58-61%. R. C. Elderfield and H. A. Hageman, *J. Org. Chem.* **14**, 605 (1949).

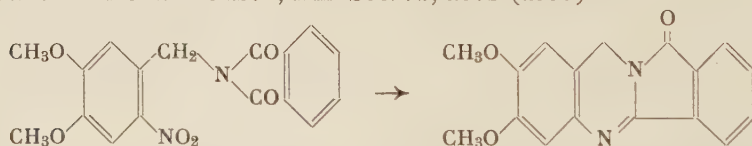
Reductive ring closure

522.



Piperidines. An alc. soln. of ethyl 3-n-butyl-1-cyano-4-pentanone-3-carboxylate hydrogenated 0.5 hr. with 16% Ni-on-fuller's earth at 100° and 80 atm. $\rightarrow$ ethyl 2-methyl-3-n-butylpiperidine-3-carboxylate. Y: 83%. F. e. s. H. Henecka, *Chem. B.* **82**, 104 (1949); s. a. N. F. Albertson and J. L. Fillman, *Am. Soc.* **71**, 2818 (1949); **72**, 2594 (1950); C. F. Koelsch and S. T. Rolfson, *Am. Soc.* **72**, 1871 (1950).

523.

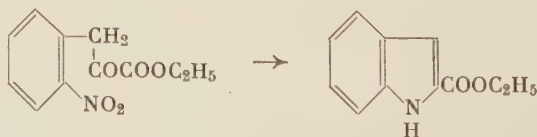


Pyrrolo [2,1-b] quinazoline ring. N-(2-Nitro-4,5-dimethoxybenzyl)phthalimide suspended in hot alcohol and hydrogenated with Raney-Ni at a few hundred mm. pressure $\rightarrow$ 7,8-dimethoxy-12-keto-10,12-dihydroisoindolo[1,2-b]quinazoline. Y: 75%. F. e. s. A. M. Downes and F. Lions, *Am. Soc.* **72**, 3053 (1950).

Platinum oxide

PtO₂

524.

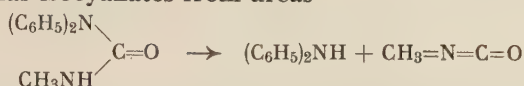


Indoles. A soln. of crude ethyl o-nitrophenylpyruvate in glacial acetic acid hydrogenated with PtO₂ at 3 atm., whereby reduction occurs very rapidly $\rightarrow$ ethyl indole-2-carboxylate. Y: 80%. W. J. Brehm, *Am. Soc.* **71**, 3541 (1949).

Nitrogen $\uparrow$ NC $\uparrow$ N*Without additional reagents**w.a.r.***Low molecular isocyanates from ureas**

←

525.

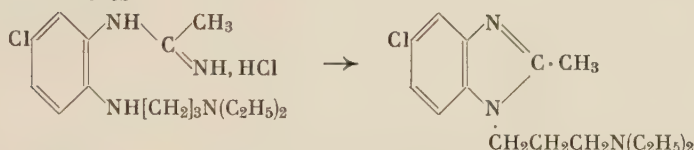


226 gm. N,N-diphenyl-N'-methylurea heated to 240-290° $\rightarrow$ 57 gm. methylisocyanate and 169 gm. diphenylamine. W. Siefken, A. 562, 75 (1949).

*Acetyl chloride*CH₃COCl**Benzimidazoles**

○

526.

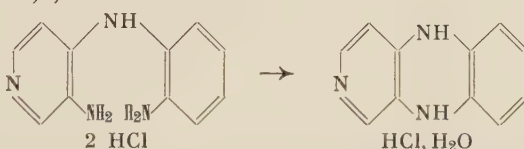


N-[5-Chloro-2-(3-diethylaminopropylamino)phenyl]acetamidine hydrochloride and acetyl chloride refluxed 3 hrs. $\rightarrow$ 5-chloro-2-methyl-1-(3-diethylaminopropyl)benzimidazole. Y: 92%. F. e. s. F. E. King and R. M. Acheson, Soc. 1949, 1396.

*Hydrochlorides***9,10-Dihydro-2,9,10-triaza-anthracenes**

←

527.



3-Amino-4-o-aminoanilinyridine dihydrochloride heated 2 min. at its decomposition point (283-284°) $\rightarrow$ 9,10-dihydro-2,9,10-triaza-anthracene hydrochloride monohydrate. Y: 58%. V. Petrow, J. Saper, and B. Sturgeon, Soc. 1949, 2540.

Halogen $\uparrow$ NC $\uparrow$ Hal*Without additional reagents**w.a.r.***Imidazolines from guanidines**

○

528.



β -Chloroethylnitroguanidine refluxed with 2-pentanol $\rightarrow$ 1-nitro-2-amino-2-imidazoline hydrochloride. Y: ca. 100%. F. e. s. A. F. McKay and J. E. Milks, Am. Soc. 72, 1616 (1950).

Pyridine

 C_5H_5N **Isocyanates** $NHCOCl \rightarrow N:C:O$ **from carbamyl chlorides**

s. 6, 455

Sulfur $\uparrow$ **NC $\uparrow$ S**

Sodium hydroxide

 $NaOH$ **Guanidines from sulfonylguanidines** $\leftarrow$

s. 4, 465; s. a. R. 68, 595 (1949)

Lead acetate

 $(CH_3COO)_2Pb$ **Cyanamides from thioureas** $NHCSNH_2 \rightarrow NHCN$

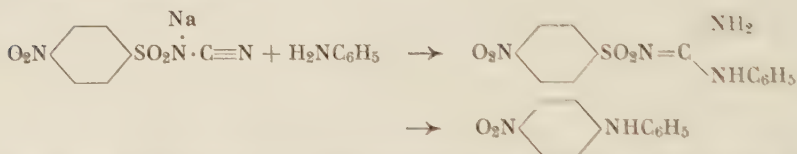
s. 4, 466; s. a. F. Kurzer, Org. Synth. 31, 19 (1951)

Carbon $\uparrow$ **NC $\uparrow$ C**

Sodium hydroxide

 $NaOH$ **Sec. from prim. amines and** $\leftarrow$ **N-sulfonylcyanamides****via sulfonylguanidines**

529.



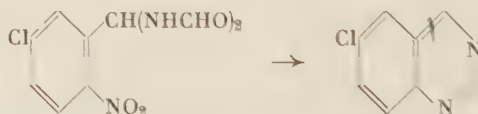
Na salt of p-nitrophenylsulfonylcyanamide and aniline dissolved in glacial acetic acid and boiled 10 min. $\rightarrow$ N-p-nitrophenylsulfonyl-N'-phenylguanidine (Y: 78%) boiled several min. with 2 N NaOH $\rightarrow$ 4-nitrodiphenylamine (Y: 97%). F. e. s. H. J. Backer et al., R. 68, 595 (1949); 69, 1348 (1950).

Zinc

Zn

Quinazolines $\bigcirc$

530.



5-Chloro-2-nitrobenzylidenebisformamide and Zn-dust treated with acetic acid and crushed ice during 10 min., shaken for 0.5 hr., then stirred with addition of small amounts of Zn for 1.5 hrs. $\rightarrow$ 6-chloro-quinazoline. Y: 84%. F. e. s. K. Schofield and T. Swain, Soc. 1949, 1367.

Acetic anhydride $(CH_3CO)_2O$ **Nitriles from
 α -oximinocarboxylic acids** $C(:NOH)COOH \rightarrow CN$

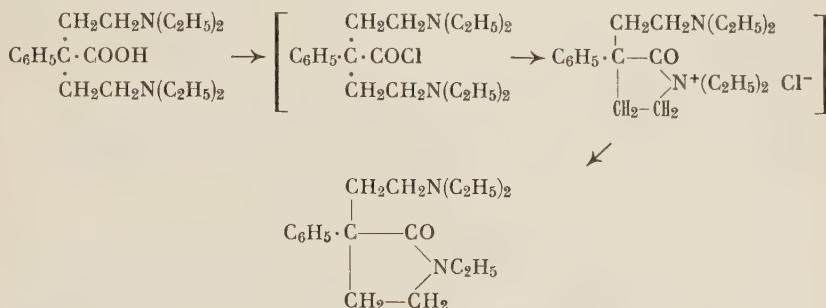
s. 6, 823

Thionyl chloride $SOCl_2$ **Lactams**

O

s. 5, 374; s. a. A. L. Morrison, M. Königstein, and A. Cohen, *Soc.* 1950, 2887

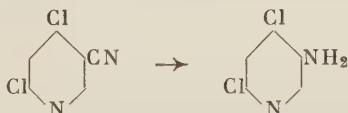
531.



N-subst. 2-Pyrrolidones and 2-piperidines. An intramolecular reaction between acid chlorides and tert. amines, with the simultaneous elimination of alkyl halides can be applied to the synthesis of pyrrolidones and piperidones.—E: α, α -Bis-(β -diethylaminoethyl)phenylacetic acid added slowly with vigorous stirring at 5-10° to $SOCl_2$, warmed, whereby acid chloride-formation occurs between 25 and 60° and ethyl chloride evolution between 70 and 80°, finally refluxed at 85-88° for 1.5 hrs. $\rightarrow$ 1-ethyl-3-(β -diethylaminoethyl)-3-phenyl-2-pyrrolidone. Y: 70%.—This reaction can also be used for the opening of N-hetero rings. F. e. s. R. L. Clarke et al., *Am. Soc.* 71, 2821 (1949).

Alkali hypohalites $\leftarrow$ **Hofmann degradation** $CONH_2 \rightarrow NH_2$ s. 2, 464, 475/6; s. a. R. G. Jones, E. C. Kornfeld, and K. C. McLaughlin, *Am. Soc.* 72, 3539 (1950)**Amines from nitriles** $CN \rightarrow NH_2$

532.



2,4-Dichloropyridine-5-carbonitrile (prepn. s. 429) shaken with a soln. of Br in 7%-KOH at room temp. for a few hrs., then warmed on a water bath at 70° for a few more hrs. $\rightarrow$ 5-amino-2,4-dichloropyridine. Y: 30-40%. H. J. den Hertog et al., *R.* 69, 673 (1950).

Formation of Hal—Hal Bond

Exchange

Halogen †

HalHal ↔ Hal

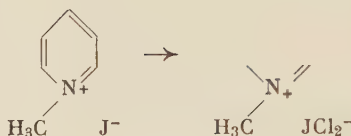
Thionyl chloride

SOCl_2

Chloroiodates

←

533.



SOCl_2 added to dry methylpyridinium iodide $\rightarrow$ methylpyridinium chloroiodate. Y: 73%. F. e. s. W. B. Brownell and L. C. King, *Am. Soc.* 71, 2926 (1949).

Formation of Hal—S Bond

Exchange

Hydrogen †

HalS ↔ H

Cupric chloride

CuCl_2

**Sulfonic acid chlorides from
sulfinic acids**

$\text{SO}_2\text{H} \rightarrow \text{SO}_2\text{Cl}$

534.



A soln. of Na-p-toluenesulfinate in HCOOH added to a soln. of CuCl_2 in HCOOH -water $\rightarrow$ p-toluenesulfonyl chloride. Y: ca. 100%. E. Pfeil and O. Velten, *A.* 565, 183 (1949).

Chlorine

Cl

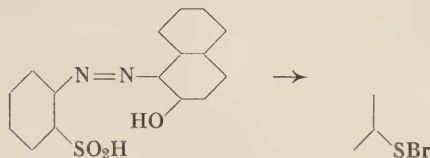
**Sulfonic acid chlorides from
mercaptans**

$\text{SH} \rightarrow \text{SO}_2\text{Cl}$

s. 3, 418; s. a. R. O. Roblin, Jr., and J. W. Clapp, *Am. Soc.* 72, 4890 (1950)

Oxygen ∇ **HalS ∇ O***Acetic acid* CH_3COOH **Sulfenyl bromides from sulfinic acids** $\text{SO}_2\text{H} \rightarrow \text{SBr}$

535.



A suspension of o-(2-hydroxy-1-naphthylazo)benzenesulfonic acid in glacial acetic acid containing 48% -HBr shaken for 48 hrs. at room temp. $\rightarrow$ o-(2-hydroxy-1-naphthylazo)phenylsulfenyl bromide (startg. m. f. 644). Y: ca. 100%. A. Burawoy and C. Turner, Soc. 1950, 469.

Thionyl chloride SOCl_2 **Sulfonic acid chlorides from sulfonic acids** $\text{SO}_3\text{H} \rightarrow \text{SO}_2\text{Cl}$

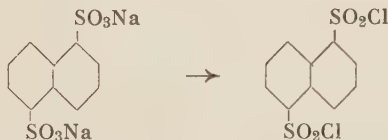
536.



SOCl_2 added at 95° to methanesulfonic acid over a period of 4 hrs., and heating continued at the same temp. for 3.5 hrs. $\rightarrow$ methanesulfonyl chloride. Y: 71-83%. P. J. Hearst and C. R. Noller, Org. Synth. 30, 58 (1950).

Chlorosulfonic acid ClSO_3H **Sulfonic acid chlorides from sodium sulfonates** $\text{SO}_3\text{Na} \rightarrow \text{SO}_2\text{Cl}$

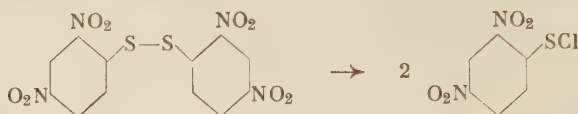
537.



Dry di-Na-1,5-naphthalenedisulfonate heated 2 hrs. with chlorosulfonic acid at 98° $\rightarrow$ naphthalene-1,5-disulfonyl dichloride. Y: 93.7%.—At higher temp., the yield declines sharply. F. reaction conditions s. A. A. Spryskov and N. V. Apar'eva, Ж. 19, 1576 (1949); 20, 1818 (1950); C. A. 44, 1082i; 45, 2434a; s. a. B. A. Everard and J. A. Mills, Soc. 1950, 3386.

Sulfur †**HalS †† S***Fuming sulfuric acid* H_2SO_4, SO_3 **Sulfenylhalides from disulfides** $RSSR \rightarrow 2 RSCl$

538.



Cl_2 introduced into a suspension of 2,4-dinitrophenyl disulfide in ethylene chloride in the presence of 3 drops of fuming H_2SO_4 at an initial temp. of ca. 25° for 30-35 min. $\rightarrow$ 2,4-dinitrobenzenesulfenyl chloride. Y: ca. 86%. F. e., catalysts, and inhibitors s. N. Kharasch, G. J. Gleason, and C. M. Buess, Am. Soc. 72, 1796 (1950).

Formation of Hal—Rem Bond**Uptake****Addition to Remaining Elements****HalRem †† Rem***Without additional reagents**w.a.r.***Selenium dibromides from selenides** $R_2Se \rightarrow R_2SeBr_2$

539.



A soln. of Br_2 in CS_2 added quickly to a soln. of di-*p*-methoxyphenyl selenide in the same solvent $\rightarrow$ di-*p*-methoxyphenyl selenium dibromide. Y: ca. 100%. G. V. Boyd, M. Doughty, and J. Kenyon. Soc. 1949, 2196.

Exchange**Hydrogen †****HalRem †† H***Without additional reagents**w.a.r.***Halogenosilanes from silanes** $SiH \rightarrow SiHal$

540.



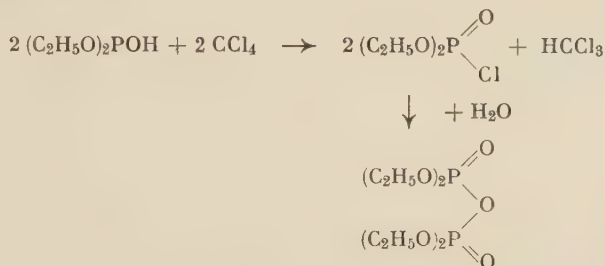
Triethylsilane added dropwise during $\frac{1}{4}$ hr. to iodine, then refluxed 0.5 hr. in a dry N_2 -stream to carry off HI while more triethylsilane is added to remove the remaining iodine, a little Mg-powder added, and

fractionated $\rightarrow$ triethyliodosilane. Y: 85%. C. Eaborn, Soc. 1949, 2755; also bromosilanes s. W. H. Nebergall and O. H. Johnson, Am. Soc. 71, 4022 (1949); 72, 4702 (1950); chlorosilanes s. J. W. Jenkins and H. W. Post, J. Org. Chem. 15, 552 (1950).

Triethylamine/polyhalogenalkane ←

**Chlorophosphoric acid esters and
pyrophosphoric acid esters from
dialkylphosphites** ←

541.



Triethylamine added slowly at 0° to a stirred mixture of diethyl phosphite and CCl_4 , the temp. maintained at 0° for 15 min., then allowed to rise to room temp., and stirred for 3 hrs. $\rightarrow$ diethyl chlorophosphate. Y: 81%.—In the presence of water, tetraethyl pyrophosphate (Y: 73%) is formed. F. e. s. G. M. Steinberg, J. Org. Chem. 15, 637 (1950).

Oxygen †

HalRem †† O

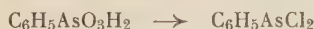
Sulfur dioxide/iodine

SO_2/I

Dichloroarsines from arsonic acids

$\text{AsO}_3\text{H}_2 \rightarrow \text{AsCl}_2$

542.



A little iodine added to a soln. of phenylarsonic acid in concd. HCl , then SO_2 passed in with efficient stirring below 50° for 1.75 hrs. $\rightarrow$ phenyldichloroarsine (startg. m. f. 676). Crude Y: 91%. R. L. Barker et al., J. Soc. Chem. Ind. 68, 289 (1949).

Halogen †

HalRem †† Hal

Aluminum iodide

AlI_3

**Siloxanes from fluorosilanes
via iodosilanes** ←

543.



Tri-n-propylfluorosilane boiled with AlI_3 for 0.5 hr. $\rightarrow$ tri-n-propyl-iodosilane (Y: 70%) shaken several times with water, dried, and distilled $\rightarrow$ hexa-n-propyldisiloxane (Y: 76%). F. e. s. C. Eaborn, Soc. 1949, 2755.

Sulfur †**HalRem †† S***Without additional reagents**w.a.r.***Chlorothiophosphoric acid esters
from dithiophosphoric acids**

s. 6, 156

**Selenyltribromides and sulfenylbromides
from selenylsulfides**

←

544.

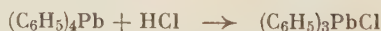


Br_2 added dropwise with ice-water cooling and shaking to a soln. of phenylselenyl o-nitrophenyl sulfide in chloroform, and worked up after 2 hrs. at room temp. $\rightarrow$ phenyl selenyltribromide (Y: 96.1%) and o-nitrophenyl sulfenylbromide (Y: 98.3%). H. Rheinboldt and E. Giesbrecht, A. 568, 198 (1950).

Carbon †**HalRem †† C***Without additional reagents**w.a.r.***Halogeno-lead compounds, organo**

←

545.

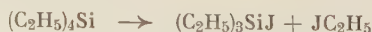


A stream of dry HCl passed into a boiling soln. of tetraphenyl-Pb in chloroform for 55 min. $\rightarrow$ triphenyl-Pb chloride (startg. m. f. 674). Y: 75%. H. Gilman and D. S. Melstrom, Am. Soc. 72, 2953 (1950); s. a. R. Heap and B. C. Saunders, Soc. 1949, 2983.

Aluminum iodide AlI_3 **Iodosilanes from silanes**

←

546.



Tetraethylsilane refluxed $\frac{3}{4}$ hr. in the presence of AlI_3 while iodine is added repeatedly $\rightarrow$ triethyliodosilane (Y: 77%) and ethyl iodide (Y: 90%). F. e. s. C. Eaborn, Soc. 1949, 2755.

Formation of Hal—C Bond

Uptake

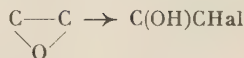
Addition to Oxygen and Carbon

HalC $\downarrow$ OC

Without additional reagents

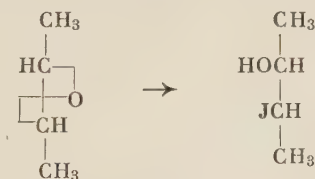
w.a.r.

Halogenhydrins from oxido compounds



s. 4, 475; s. a. O. E. van Lohuizen and H. J. Baker, R. 68, 1137 (1949);
steroids s. D. H. R. Barton and E. Miller, Am. Soc. 72, 370, 1066 (1950)

547.

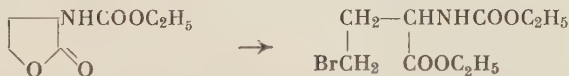


Walden inversion. 55%-aq.-HI added dropwise with vigorous stirring at -10 to 0° to D(+)-2,3-epoxybutane over a period of ca. 40 min., and stirring continued for ca. 10 Min. $\rightarrow$ L(+)-erythro-3-iodo-2-butanol. Y: 75%.—A single Walden inversion accompanies the opening of the ring. F. e. s. H. J. Lucas and H. K. Garner, Am. Soc. 72, 2145 (1950).

Halogenocarboxylic acid esters from lactones

C

548.



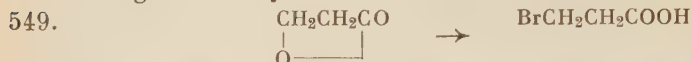
Carbethoxyaminobutyrolactone dissolved at 0° in satd. alc. HBr, and allowed to stand below 10° for 24 hrs. $\rightarrow$ ethyl γ -bromo- α -carbethoxyaminobutyrate. Y: 80%. H. Pleninger, B. 83, 268 (1950).

Potassium iodide/phosphoric acid

KI/H₃PO₄

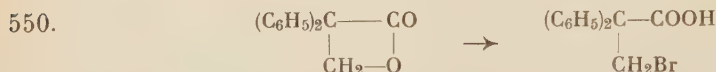
s. Phosphoric acid/potassium iodide

Magnesium bromide

MgBr₂**Halogenocarboxylic acids from lactones**

β -Propiolactone added to MgBr₂-dietherate in anhydrous ether $\rightarrow$ β -bromopropionic acid. Y: 83%. T. L. Gresham et al., Am. Soc. 71, 2807 (1949).

Acetic acid

CH₃COOH

α,α -Diphenyl- β -propiolactone added to glacial acetic acid (satd. with dry HBr), and allowed to stand 20 hrs. at room temp. $\rightarrow$ 2,2-diphenyl-3-bromopropanoic acid. Y: 93% F. e. s. H. E. Zaugg, Am. Soc. 72, 2998 (1950).

Phosphorus

P

 α,γ -Dibromocarboxylic acid bromides from γ -lactones

s. 6, 569

Phosphoric acid/potassium iodide

H₃PO₄/KI**Tetrahydrofuran ring opening**

s. 6, 584

Phosphorus oxychloride/sulfuric acid

POCl₃/H₂SO₄

POCl₃ followed by concd. H₂SO₄ added with cooling to dry tetrahydrofuran, and the reaction allowed to proceed at 90-100° $\rightarrow$ 4,4'-dichlorodibutyl ether. Y: 52-54%. K. Alexander and H. V. Towles, Org. Synth. 30, 27 (1950).

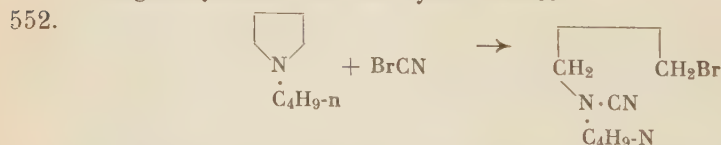
Addition to Nitrogen and CarbonHalC $\downarrow$ NC

Without additional reagents

w.a.r.

Halogenocyanamides from cyclic imines

C



1-n-Butylpyrrolidine in dry benzene added with stirring during 2.5 hrs. to a soln. of cyanogen bromide in dry benzene, and allowed to

stand overnight $\rightarrow$ *n*-butyl- δ -bromobutylecyanamide. Y: ca. 100%. F. e. s. R. C. Elderfield and H. A. Hageman, J. Org. Chem. 14, 605 (1949).

Addition to Carbon

HalC $\downarrow$ CC

Without additional reagents

w.a.r.

Halides from ethylene derivatives

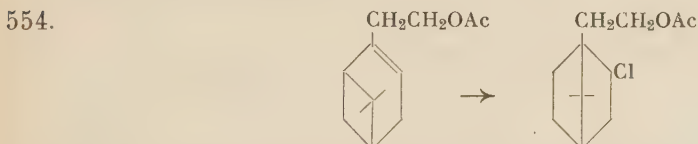
C : C $\rightarrow$ CHCHal



A vigorous stream of HBr passed for 20 min. into a soln. of β -benzoylacrylic acid in glacial acetic acid with ice cooling, then allowed to stand at room temp. for 3 hrs. $\rightarrow$ α -bromo- β -benzoylpropionic acid. Y: 90%.—Similarly: α -Chloro- β -benzoylpropionic acid. Y: 81%. E. Buchta and S. Danner, Chem. B. 82, 63 (1949).

Chlorides from ethylene derivatives with rearrangement

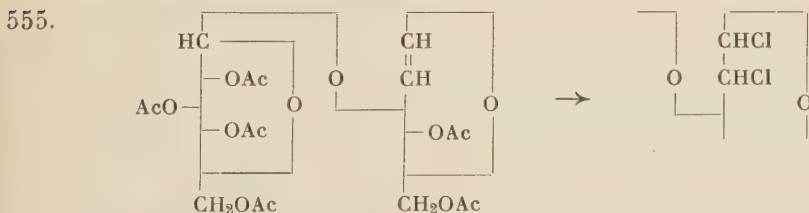
$\leftarrow$



HCl passed at 2-10° into a soln. of nopyl acetate in ethylene chloride until absorption is complete, and allowed to warm to room temp. overnight $\rightarrow$ 2-chloro-1-apocamphane- β -ethyl acetate. Y: 70-75%. J. P. Bain et al., Am. Soc. 72, 3124 (1950).

1,2-Dihalides from ethylene derivatives

C : C $\rightarrow$ CHalCHal



A dry stream of chlorine introduced with cooling into a soln. of hexaacetylglucosido-3-glucal in dry chloroform until a test with bromine water indicates the end of the reaction $\rightarrow$ 1,2-dichlorohexaacetylglucosido-3-glucose. Y: 79%. Similarly: Dibromo derivative. Y: 73%. A. M. Gakhokidze, Zh. 19, 2082 (1949); C. A. 44, 3914b; chlorination s. a. M. Jacobson, Am. Soc. 72, 1489 (1950).

s. a. 6, 575

Protection of a double bond

s. 6, 280

Light

556.



1,2-Dibromides. Crotonic acid in CCl_4 treated with Br_2 below 60° with illumination over a period of 4.5 hrs. $\rightarrow \alpha, \beta$ -dibromobutyric acid. Y: 90%.—Illumination allows working at lower temp. Substitution can thus be avoided. F. e. s. P. Seifert et al., *Helv.* 33, 725 (1950); α, β -dibromonitro compounds s. W. K. Noyce, C. H. Coleman, and J. T. Barr, *Am. Soc.* 73, 1295 (1951).

*Potassium iodide/phosphoric acid**KI/H₃PO₄**s. Phosphoric acid/potassium iodide**Calcium hypochlorite**Ca(OCl)₂***Chlorohydrins from ethylene derivatives** $\text{[C:C]} \rightarrow \text{C(OH)CCl}$

557.

CO_2 bubbled into a stirred cooled mixture of diallyl ether, water, and Ca(OCl)_2 until after ca. 4 hrs. titration indicates that the reaction is complete $\rightarrow$ diallyl ether di(chlorohydrin). Crude Y: 94.4%. H. Wittcoff, J. R. Roach, and S. E. Miller, *Am. Soc.* 71, 2666 (1949).

*Stannic chloride**SnCl₄***Chlorides from ethylene derivatives** $\text{C:C} \rightarrow \text{CHCCl}$

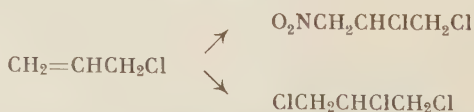
s. 5, 389; s. a. Bl. 1949, 396

*Nitrosyl chloride**NOCl***Reaction of nitrosyl chloride with ethylene derivatives**

←

1,2-Nitrohalides and 1,2-dihalides

558.



24 gm. allyl chloride in 3 equal portions allowed to stand in a sealed tube with NOCl at room temp. for 12-24 hrs. until the red color disappears $\rightarrow$ 18.4 gm. 1,2-dichloro-3-nitropropane, 4 gm. 1,2,3-trichloropropane, and 9 gm. starting material. F. e. s. A. Y. Yakubovich and A. L. Lemke, *Ж.* 19, 649 (1949); *C. A.* 44, 1011b.

Phosphoric acid/potassium iodide

 H_3PO_4/KI **Iodides from ethylene derivatives** $C:C \rightarrow CHCl$

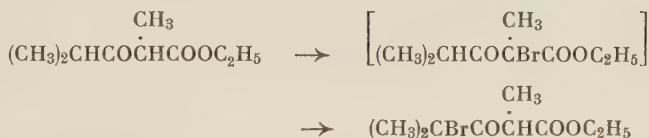
s. 6, 584

Hypochlorite ClO^- **Chlorohydrins from ethylene derivatives** $C:C \rightarrow C(OH)CCl$ with NaOCl s. 4, 484; s. a. M. Naudet, *Bl.* 1950, 842; with $Ca(OCl)_2$ s. 6, 557

Rearrangement

Hydrogen/Carbon TypeHalC $\curvearrowright$ HC*Hydrobromic acid**HBr***Bromination with migration of bromine** $\leftarrow$

559.



Br_2 in CCl_4 added dropwise below 5° to a rapidly stirred soln. of ethyl α -isobutyrylpropionate in CCl_4 , and allowed to stand in the cold-room to complete the rearrangement to the γ -bromoester $\rightarrow$ ethyl γ -bromo- α -isobutyrylpropionate. Y: 95%. E. B. Reid, R. B. Fortenbaugh, and H. R. Patterson, *J. Org. Chem.* 15, 572 (1950); 16, 33 (1951); s. a. A. Becker, *Helv.* 32, 1584 (1949).

Exchange

Hydrogen $\downarrow$ HalC $\Uparrow$ H*Without additional reagents**w.a.r.***Bromination** $H \rightarrow Br$

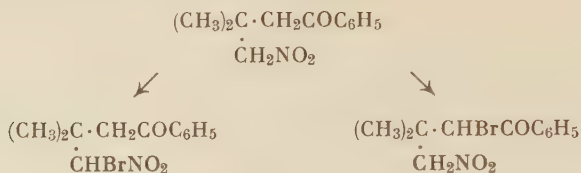
560.



Br_2 added in portions during ca. $\frac{3}{4}$ hr. to p-chlorotoluene at $140\text{--}150^\circ$ in a pressure bottle, which is opened at each addition of Br_2 , finally heated at $140\text{--}150^\circ$ for an additional 0.5 hr. $\rightarrow$ p-chlorobenzyl bromide. Y: 89%. F. Kröhnke, *Chem. B.* 83, 35 (1950).

Aliphat. nitrohalides from aliphat. nitro compounds

561.



β,β -Dimethyl- γ -nitrobutyrophenone

treated slowly below 5° with a soln. of Na in dry methanol, after 15 min. the soln. of the *aci*-nitro compound so obtained added dropwise with stirring at 0° to a soln. of Br_2 in dry chloroform, cooling discontinued, and stirred 35 min. more $\rightarrow$ β,β -dimethyl- γ -bromo- γ -nitrobutyrophenone startg. m. f. 881. Crude Y: 92.5%.

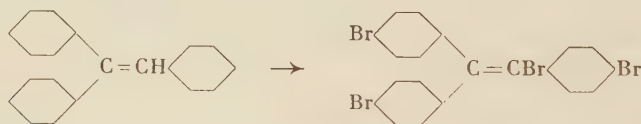
dissolved in dry chloroform, treated dropwise with liq. Br_2 over a period of 45 min., then stirred for 1 hr. $\rightarrow$ β,β -dimethyl- α -bromo- γ -nitrobutyrophenone. Y: 96%.

F. e. for the γ -bromination in alkaline medium s. L. I. Smith and V. A. Engelhardt, Am. Soc. **71**, 2671, 2676 (1949).

Reaction of bromine vapor with solid compounds

α,β -Ethylenebromides from ethylene derivatives

562.



When solid aryl olefins are treated with bromine vapor, p-positions of unsubst. phenyl groups are brominated. Highly subst. double bonds do not add bromine but undergo substitution of bromine for hydrogen. —E: Triphenylethylene treated 17 hrs. with bromine vapor $\rightarrow$ bromotri-(p-bromophenyl)ethylene. Y: 77%. F. e. s. R. E. Buckles, E. A. Hausman, and N. G. Wheeler, Am. Soc. **72**, 2494 (1950); bromination in p-position s. a. Org. Synth. **31**, 29 (1951).

Bromination with migration of bromine

s. 6, 559

Sodium acetate

 CH_3COONa **Bromination**

s. 3, 155; 4, 489; α -bromoketones s. V. R. Mattox and E. C. Kendall, J. Biol. Chem. 188, 287 (1951)

Sodium acetate/phosphoric acid

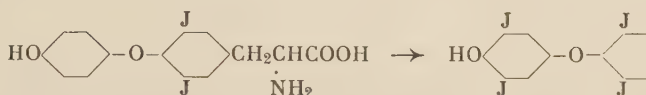
 $\text{CH}_3\text{COONa}/\text{H}_3\text{PO}_4$

s. Phosphoric acid/sodium acetate

Ethylamine/potassium iodide

 $\text{C}_2\text{H}_5\text{NH}_2/\text{KI}$ **Iodination** $\text{H} \rightarrow \text{I}$

563.

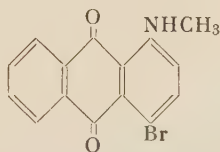


A soln. of iodine in KI-soln. added dropwise to a stirred soln. of 3,5-diiodothyronine in aq. ethylamine soln., and stirring continued for 10 min. $\rightarrow$ thyroxine. Y: 90%.—The use of aq. or alc. prim. or sec. aliphatic amine soln. is preferable to the use of aq. NH_3 , which may form explosive nitrogen iodides. J. C. Clayton and B. A. Hems, Soc. 1950, 840; cf. Soc. 1950, 2824; J. A. Goodson et al., Brit. J. Pharmacol. 3, 49 (1948); with NaOH s. D. Papa et al., Am. Soc. 72, 2619, 4906 (1950).

Pyridine

 $\text{C}_5\text{H}_5\text{N}$ **Bromination** $\text{H} \rightarrow \text{Br}$

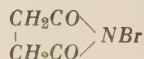
564.



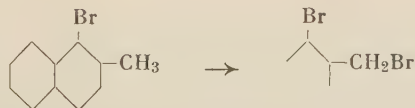
Br_2 added with stirring to 1-methylaminoanthraquinone (prepn. s. 491) and pyridine over a period of 9-10 min., then heated on a steam bath for 6 hrs. $\rightarrow$ 1-methylamino-4-bromoanthraquinone. Y: 70-74%. C. V. Wilson, Org. Synth. 29, 68 (1949).

s. a. 5, 395; R. Kuhn and K. Dury, A. 571, 44 (1951)

N-Bromosuccinimide

**Bromination**

565.



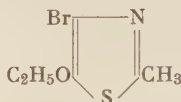
A mixture of 1-bromo-2-methylnaphthalene, N-bromosuccinimide, a little benzoylperoxide, and CCl_4 refluxed 2.5 hrs. $\rightarrow$ 1-bromo-2-bromo-

methylnaphthalene. Y: 85%.—High temp. bromination at 230-240° gave yields which never exceeded 59%. W. S. Newman and A. I. Kosak, J. Org. Chem. 14, 375 (1949); s. a. A. C. Cope and S. W. Fenton, Am. Soc. 73, 1668, 1673 (1951).

s. a. 6, 840

N-Bromosuccinimide/benzoyl peroxide

566.

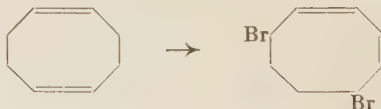


Isosters. *N*-Bromosuccinimide and benzoyl peroxide added to 2-methyl-5-ethoxythiazole (prepn. s. 638) in dry CCl_4 , and refluxed 1 hr. after the spontaneous reaction has subsided $\rightarrow$ 2-methyl-4-bromo-5-ethoxythiazole. Y: 81%.—The 5-ethoxyl group promotes electrophilic attack in the 4-position, just as the 3-ethoxyl group of the isosteric pyridine favors electrophilic attack in the 2-position of the pyridine ring. D. S. Tarbell, H. P. Hirschler, and R. B. Carlin, Am. Soc. 72, 3138 (1950).

**Bromination of unsatd. compounds
in the allyl position with rearrangement**

←

567.



A mixture of 1,5-cyclooctadiene, *N*-bromosuccinimide, benzoyl peroxide, and CCl_4 refluxed 3 hrs. with stirring $\rightarrow$ 5,8-dibromo-1,3-cyclooctadiene. Y: 86%. A. C. Cope, C. L. Stevens, and F. A. Hochstein, Am. Soc. 72, 2510 (1950).

Nitric acid

HNO_3

Iodination

$\text{H} \rightarrow \text{I}$

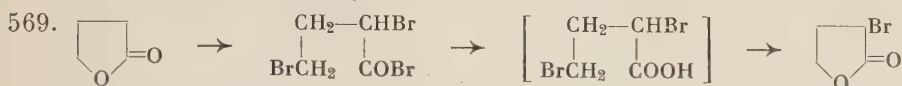
568.



HNO_3 added slowly with vigorous stirring to thiophene and iodine, with slight heating to start the reaction and occasional cooling to control it, then refluxed on a water bath for 30 min. after all the HNO_3 has been added $\rightarrow$ 2-iodothiophene. Y: 68-72%. H. Y. Lew and C. R. Noller, Org. Synth. 30, 53 (1950); Am. Soc. 72, 5715 (1950).

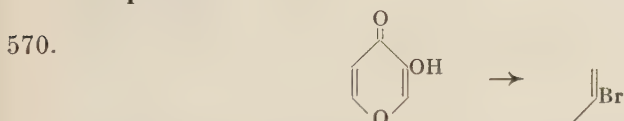
Phosphorus

P

 **α -Bromo- γ -lactones from γ -lactones
via α,β -dibromocarboxylic acid bromides**H $\rightarrow$ Br

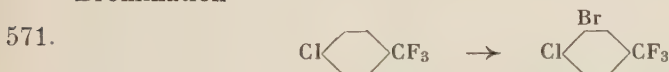
Br added with stirring to 100 gm. butyrolactone and red P, first at 20-30° with cooling, then at 70°, finally heated 3 hrs. at 80°, and excess Br blown off with air $\rightarrow$ 345 gm. α,γ -dibromobutyric acid bromide treated with water at 80° with vigorous stirring, and the acid so obtained heated 3 hrs. at 130-140° in vacuo until the gas evolution ceases $\rightarrow$ α -bromobutyrolactone (Y: 94%). H. Pleninger, B. 83, 265 (1950).

Phosphoric acid/sodium acetate

 H_3PO_4/CH_3COONa **Bromination of acid-sensitive
compounds**

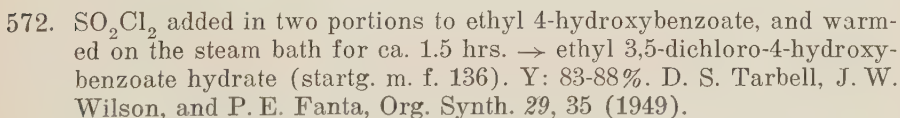
A soln. of pyromeconic acid in orthophosphoric acid treated at 0° with a soln. of Br_2 in saturated aq. Na-acetate $\rightarrow$ 2-bromopyromeconic acid. Y: up to 85%. High yields are obtained by using butter soln. to adjust the pH. E. L. Shimmin and F. Challenger, Soc. 1949, 1185.

Antimony pentachloride

 $SbCl_5$ **Bromination**

A soln. of Br_2 in 4-chloro(trifluoromethyl)benzene added slowly at 20° with cooling to $SbCl_5$, and Cl_2 introduced after the initial reaction has subsided $\rightarrow$ 3-bromo-4-chloro(trifluoromethyl)benzene. Y: 74.2%; conversion 31.1%.— Cl_2 reconverts Sb(III) salts into Sb(V)-chloride. Hydrolysis of the trifluoromethyl group to carboxyl occurs in the presence of Fe at 60°. F. e. s. E. T. McBee, R. A. Sanford, and P. J. Graham, Am. Soc. 72, 1651 (1950).

Sulfuryl chloride

 SO_2Cl_2 **Chlorination**H $\rightarrow$ Cl

s. 1, 417; s. a. D. F. Walker, J. Am. Pharm. Assoc. 39, 396 (1950)

**α -Chloro- β -ketocarboxylic acid esters
from β -ketocarboxylic acid esters**

573.



SO_2Cl_2 added dropwise with stirring during 15 min. at $0-5^\circ$ to ethyl 2-keto-6-cyanoheptanoate in dry benzene, and after a further 15 min. refluxed 0.5 hr. $\rightarrow$ ethyl 3-chloro-2-keto-6-cyanoheptanoate. Y: 87%. F. e. s. G. Swain, Soc. 1949, 2898.

Sulfuric acid

 H_2SO_4 **Iodination** $\text{H} \rightarrow \text{I}$

s. 4, 492; s. a. D. Twiss and R. V. Heinzelmann, J. Org. Chem. 15, 496 (1950)

Iodine monochloride

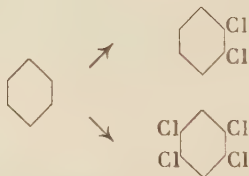
 ICl

s. 1, 419; 2, 493; 3, 443; s. a. S. C. J. Olivier and W. P. Combé, R. 69, 22 (1950)

Iodine trichloride

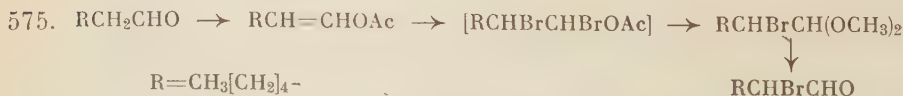
 ICl_3 **Vicinal dichlorination** $\text{CHCH} \rightarrow \text{CCICCI}$

574.



Benzene and ICl_3 allowed to react in $\text{CCl}_4 \rightarrow$ o-dichlorobenzene (Y: 67%) and 1,2,4,5-tetrachlorobenzene (Y: 32%). F. e. s. E. Campaigne and W. Thompson, Am. Soc. 72, 629 (1950).

Via intermediates

v.i. **α -Bromoaldehydes from aldehydes** $\text{H} \rightarrow \text{Br}$ **General method****Enol acetates from aldehydes** **α -Bromoacetals from enol acetates****via α,β -bromoacetates****Cleavage of acetals**

A mixture of heptaldehyde, acetic anhydride, and powdered K-acetate heated 1 hr. at an oil-bath temp. of $155-160^\circ \rightarrow$ heptaldehyde enol acetate

(Y: 45-50%) dissolved in CCl_4 , treated with shaking below 10° with a mixture of Br_2 and CCl_4 until the Br_2 is no longer decolorized, the brominated mixture added to anhydrous methanol, and allowed to stand for at least 48 hrs. $\rightarrow$ α -bromoheptaldehyde dimethyl acetal (Y: 80-85%) boiled gently with concd. HCl with distillation of the methanol liberated until the vapor temp. reaches 90° , the residue and distillate combined, and worked up $\rightarrow$ α -bromoheptaldehyde (Y: 90-95%). P. Z. Bedoukian, *Org. Synth.* 29, 14 (1949).

Oxygen ∇

HalC ∇ O

Without additional reagents

w.a.r.

Chlorides from alcohols

$\text{OH} \rightarrow \text{Cl}$

s. 1, 421; 4, 497; s. a. E. Ziegler, *M.* 79, 142 (1948)

Replacement of acoxy groups by bromine

$\text{OAc} \rightarrow \text{Br}$

s. 6, 731

Lithium chloride

LiCl

Chlorides from sulfonates

$\text{OSO}_2\text{R} \rightarrow \text{Cl}$

s. 5, 402; s. a. M. F. Clarke and L. N. Owen, *Soc.* 1950, 2108; G. Eglinton and M. C. Whiting, *Soc.* 1950, 3650

Sodium iodide

NaI

Iodides from sulfonates of carbohydrates

$\text{OSO}_2\text{R} \rightarrow \text{I}$

576. 6-Methanesulfonyl-1,2,3,4-diisopropylidene-D-galactose and NaI in acetone heated 40 hrs. at 130 - $135^\circ \rightarrow$ 1,2,3,4-diisopropylidene-6-iodo-6-desoxy-D-galactose. Y: 93%.—Other groups attached to the sugar molecule exercise a shielding effect on the tosyl and mesyl residues; this effect is greater for the latter smaller group. F. e. s. A. B. Foster et al., *Soc.* 1949, 2542.

577. of **glycols**. The ethylene bond confers lability on a tosyloxy or mesyloxy group of the adjacent C-atom, so that a sec. tosyloxy group may be exchanged before a prim. one, which latter is usually more reactive. E. s. S. Laland, W. G. Overend, and M. Stacey, *Soc.* 1950, 738.

Potassium iodide/phosphoric acid

KI/H₃PO₄

s. Phosphoric acid/potassium iodide

Pyridine/phosphorus tribromide

C₅H₅N/PBr₃

Bromides from alcohols

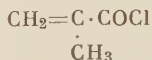
$\text{OH} \rightarrow \text{Br}$

s. 3, 458; s. a. G. M. Badger et al., *Soc.* 1950, 2326

Pyridine/benzenesulfonic acid chloride

 $C_5H_5N/C_6H_5SO_2Cl$ **Carboxylic acid chlorides from carboxylic acids** $COOH \rightarrow COCl$

578.

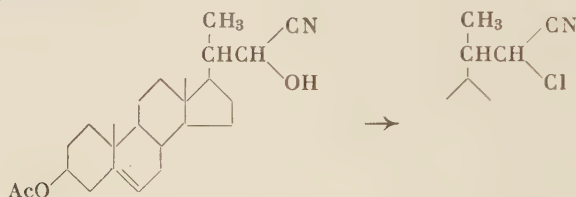


A mixture of methacrylic acid and pyridine added with continuous shaking and cooling to benzenesulfonyl chloride, and distilled immediately $\rightarrow$ methacrylyl chloride (startg. m. f. NC ∇ Hal. 6720). Y: 86%. J. Heyboer and A. J. Staverman, R. 69, 787 (1950).

Lutidine/phosphorus oxychloride

 α -Halogenonitriles from α -hydroxynitriles $OH \rightarrow Hal$

579.

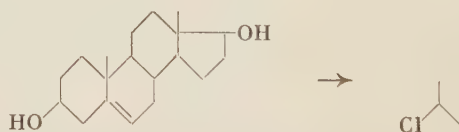


A mixture of 250 mg. 3 β -acetoxybisanor-5-cholenaldehyde cyanohydrin and $POCl_3$ in lutidine gently refluxed for 10 min. $\rightarrow$ 250 mg. 22-cyano-22-chlorobisanor-5-cholen-3 β -ol acetate. F. e. s. M. E. Herr and F. W. Heyl, Am. Soc. 72, 1753 (1950).

Calcium carbonate/thionyl chloride

 $CaCO_3/SOCl_2$ **Partial replacement of hydroxyl by chlorine** $OH \rightarrow Cl$

580.



500 mg. 15-androstene-3 β ,17 β -diol, dry $CaCO_3$, and a soln. of $SOCl_2$ in abs. benzene refluxed 1 hr. $\rightarrow$ 460 mg. 15-3-chloroandrosten-17 β -ol. C. A. Grob and W. A. Goldberg, Helv. 32, 184 (1949).

Calcium chloride

 $CaCl_2$ **Chlorides from alcohols**

s. 6, 812

Acetic acid

 CH_3COOH **Acylhalogenosugars** $OAc \rightarrow Hal$

s. 5, 405; s. a. Am. Soc. 72, 4173 (1950)

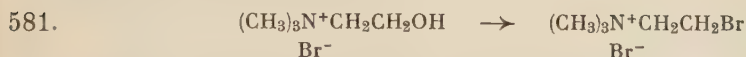
Benzoyl bromide

 C_6H_5COBr **Carboxylic acid bromides**

COBr

C¹⁴-Compounds

s. 5, 566; s. a. C. Heidelberger and R. B. Hurlbert, Am. Soc. 72, 4704 (1950)

 α -Bromoisovaleryl bromide $(CH_3)_2CHCHBrCOBr$ **Bromides from alcohols**OH $\rightarrow$ Br

Choline bromide heated with α -bromoisovaleryl bromide to 110°, then the temp. raised to 140° during 2-3 hrs. $\rightarrow$ bromocholine bromide. Y: 75%. G. Kubiczek and L. Neugebauer, M. 80, 395 (1949).

Phosphorus

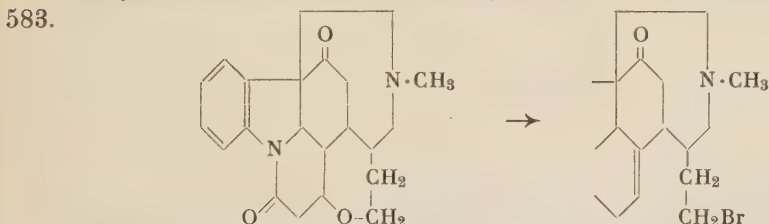
P

Acetobromosugars $\leftarrow$

582. Glucose added at 30-40° in the course of 0.5 hr. to acetic anhydride and a small amount of $HClO_4$, then amorphous P, and, gradually, below 20°, Br added, followed by 90% of the stoichiometric amount of water during 0.5 hr. with stirring, the flask closed, and left at room temp. for 1.5-2 hrs. $\rightarrow$ acetobromoglucose. Y: 85%. F. e. s. M. Bárczai-Martos and F. Körösy, Nature 165, 369 (1950).

Ethylenebromides from O-heterocyclics

C



N-Methyldihydropseudostrychnine refluxed 5 hrs. at 130-140° with glacial acetic acid, red P, and fuming HBr $\rightarrow$ bromodesoxy-N-methyldihydroisopseudostrychnine hydrobromide (startg. m. f. 261). Y: ca. 100%. F. e. s. H.-G. Boit, B. 83, 217 (1950); s. a. B. 84, 16 (1951).

Phosphoric acid/potassium iodide

 H_3PO_4/KI **Iodides from ethers, alcohols, and ethylene derivatives** $\leftarrow$ **Tetrahydrofuran ring opening**

Tetrahydrofuran and KI in 95% H_3PO_4 refluxed 3 hrs. with stirring 1,4-diiodobutane. Y: 92-96%.—Similarly: Diisopropyl ether $\rightarrow$ iso-

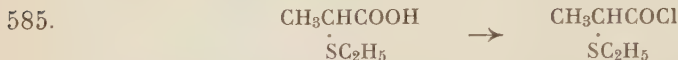
propyl iodide. Y: 90%.—1,6-Hexanediol $\rightarrow$ 1,6-diiodohexane. Y: 83 to 85%.—2,3-Dimethyl-2-butene $\rightarrow$ 2,3-dimethyl-2-iodobutane. Y: 91.4%.—Excellent yields were obtained from various prim., sec., and tert. alcohols; phenols, however, were not converted into iodides. F. e. s. H. Stone and H. Shechter, *Org. Synth.* **30**, 33 (1950); **31**, 31, 66 (1951); *J. Org. Chem.* **15**, 491 (1950).

Phosphorus trichloride

PCl_3

Carboxylic acid chlorides from carboxylic acids

$\text{COOH} \rightarrow \text{COCl}$

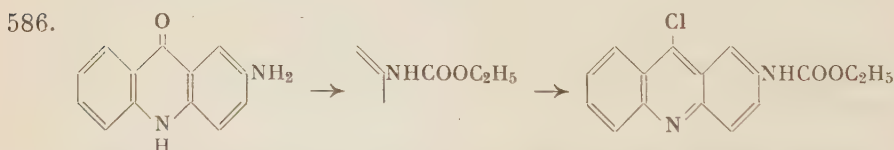


A mixture of 2-ethylmercaptopropionic acid and PCl_3 allowed to stand overnight, then heated 1 hr. on a steam bath $\rightarrow$ 2-ethylmercaptopropionyl chloride. Y: 64%.— PCl_3 possesses the advantage that a colorless product is almost always obtained, and, in some instances, it gives a fair yield, when the use of SOCl_2 results in tar formation. From the viewpoint of yield, however, SOCl_2 is usually to be preferred. F. e. s. A. Mooradian et al., *Am. Soc.* **71**, 3372 (1949).

Phosphorus oxychloride

POCl_3

9-Chloroacridines from acridones with protection of an amino group
Urethans from amines



Freshly distilled ethyl chloroformate added to 2-aminoacridone and diethylaniline in boiling abs. alcohol, refluxed 30 min., concentrated to $\frac{1}{3}$ of its volume, and poured into N HCl $\rightarrow$ 2-urethanoacridone (Y: 95%) refluxed with POCl_3 for 1 hr. $\rightarrow$ 9-chloro-2-urethanoacridine (Y: 87%). A. Albert and R. Royer, *Soc.* **1949**, 1148.

Phosphorus pentachloride

PCl_5

Ethylene chlorides from ketones

$\text{COCH}_2 \rightarrow \text{CCl}_2\text{CH}$

s. **3**, 470; s. a. M. Mousseron and R. Jacquier, *Bl.* **1950**, 648; E. A. Braude and C. J. Timmons, *Soc.* **1950**, 2014

1,1-Dichlorides from ketones

$\text{C}\ddot{\text{O}} \rightarrow \text{CCl}_2$



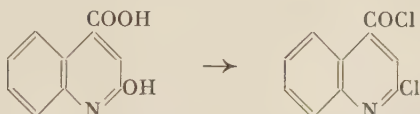
Trifluoroacetophenone and 50% excess PCl_5 refluxed 21 hrs. at an oil-bath temp. of 175° , acetone added to convert excess PCl_5 into POCl_3 for

easier separation, and fractionated $\rightarrow$ α,α -dichloro- β,β,β -trifluoroethylbenzene. Y: 90%. F. e. s. S. G. Cohen, H. T. Wolosinski, and P. J. Scheuer, Am. Soc. 71, 3439 (1949); 72, 3952 (1950); s. a. L. J. Andrews and W. W. Kaeding, Am. Soc. 73, 1007 (1951).

Carboxylic acid chlorides from carboxylic acids with simultaneous replacement of hydroxyl by chlorine



588.



A mixture of 2-hydroxyquinoline-4-carboxylic acid (prepn. s. 723) and PCl_5 refluxed 1 hr. at $140\text{--}145^\circ \rightarrow$ 2-chloroquinoline-4-carboxylic acid chloride. Y: 98.5%. J. Büchi, H. Hurni, and R. Lieberherr, Helv. 32, 1806 (1949); 33, 858 (1950).

Iminochlorides from carboxylic acid amides

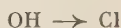


s. 6, 441, 457

Thionyl chloride



Chloramines from aminoalcohols

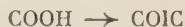


589.



A soln. of pure N-methyldiethanolamine in trichloroethylene added with stirring during 1 hr. to a mixture of SOCl_2 and trichloroethylene at 50° , and refluxed for 2 hrs. $\rightarrow$ N-methyl-2,2'-dichlorodiethylamine. Y: 95%, purity 96%. Variation of reaction conditions and solvents s. J. T. Abrams et al. J. Soc. Chem. Ind. 68, 280 (1949); s. a. J. H. Burckhalter, V. C. Stephens, and L. A. R. Hall, J. Am. Pharm. Assoc. 39, 271 (1950).

Carboxylic acid chlorides from carboxylic acids

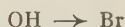


s. 6, 585; s. a. O. T. Schmidt and A. Schach, A. 571, 29 (1951)

Sulfuric acid



Replacement of hydroxyl by bromine



s. 1, 437; s. a. S. Bezzi and P. Lanza, G. 80, 180 (1950)

Fluorosulfonic acid

FSO₃H

Sulfonic acid fluorides

SO₂F

590. A mixture of dry crude Na-p-chlorobenzenesulfonate, fluorosulfonic acid, and CCl₄ stirred and heated at 70-75° for 24 hrs. → p-chlorobenzenesulfonyl fluoride. Y: 85%. F. e. s. M. Kulka, Am. Soc. 72, 1215 (1950).

Nitrogen †

HalC † N

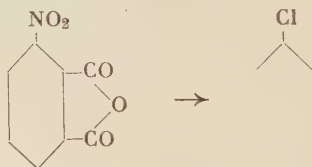
Without additional reagents

w.a.r.

Replacement of nitro groups by chlorine

NO₂ → Cl

591.



22 gm. 3-nitrophthalic anhydride treated with Cl₂ at 230-250° for 6-7 hrs. → 15-15.5 gm. 3-chlorophthalic anhydride. F. e. s. A. A. Ponomarenko, Ж. 20, 469 (1950); C. A. 44, 7810b.

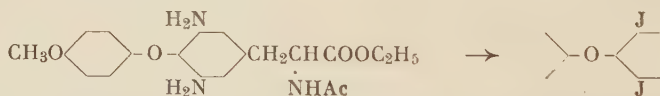
Sodium nitrite

NaNO₂

Iodides from amines

NH₂ → I

592.



A soln. of 3,5-diamino-4-p-methoxyphenoxy-N-acetyl-L-phenylalanine ethyl ester in acetic acid-H₂SO₄ added dropwise during ca. 2 hrs. with stirring and cooling to a soln. of NaNO₂ in glacial acetic acid-H₂SO₄, stirring continued for 1 hr. at 0°, added fairly rapidly without cooling to a well stirred soln. of NaI, iodine, and urea in water over a layer of chloroform, and stirring continued for 1 hr. → 3,5-diiodo-4-p-methoxyphenoxy-N-acetyl-L-phenylalanine ethyl ester (startg. m. f. 26). Y: 82%.—The chloroform, which extracts the reaction product, avoids the formation of solid or semi-solid matter during the reaction. J. R. Chalmers et al., Soc. 1949, 3424.

Potassium iodide

KI

s. 1, 438; 2, 522; s. a. S. C. J. Olivier and W. P. Combé, R. 69, 22 (1950)

Copper

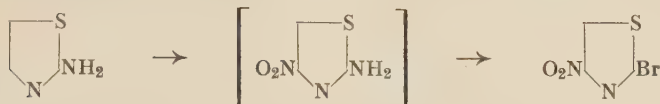
Cu

Nitration

←

with subsequent replacement
of amino groups by halogen

593.



HNO₃ (d.1.51) added dropwise with stirring to a soln. of 30 gm. 2-aminothiazole in concd. H₂SO₄, after 12 hrs. the mixture and Gattermann-Cu added simultaneously at 15° to aq. NaBr, then diazotized with aq. NaNO₂ at 10-15° over a period of 20 min. with stirring — 33 gm. 2-bromo-5-nitrothiazole. H. v. Babo and P. Prijs. *Helv.* 33, 306 (1950).

Fluoboric acid

HBF₄

Fluorides from amines
Schiemann reaction

NH₂ → F

s. 3, 478; 4, 509; s. a. G. C. Finger. *Am. Soc.* 73, 149 (1951) and other papers of this series

Halogen ∇ **HalC ∇ Hal**

Without additional reagents

*w.a.r.***Chlorides from bromides**

Br → Cl

s. 5, 413; s. a. G. Fawaz and L. F. Fieser, *Am. Soc.* 72, 996 (1950); H. J. den Hertog and J. de Bruyn, *R.* 70, 182 (1951); F. Arndt et al., *B.* 84, 319 (1951)

Sodium iodide

NaI

Iodides from other halides
Finkelstein reaction

Hal → I

s. 1, 450; 4, 512; in ethyl methyl ketone s. 6, 906; E. Klingsberg, *Am. Soc.* 72, 1031 (1950)

Antimony pentachloride

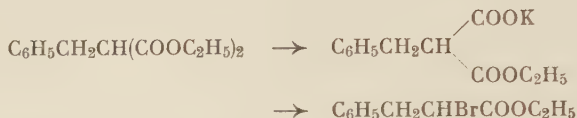
SbCl₅**Fluorides from chlorides**

Cl → F

s. 4, 514; s. a. E. T. McBee and R. A. Sanford, *Am. Soc.* 72, 5574 (1950)

Carbon ∇ **HalC ∇ C***Potassium salt* K^+ **α -Bromocarboxylic acid esters
from malonic esters** $\leftarrow$

594.



A soln. of KOH in abs. alcohol added with stirring to a soln. of diethyl benzylmalonate, allowed to stand several hrs. at room temp., filtered, the alcohol distilled off, the remaining K ethyl benzylmalonate dried, finely pulverized, mixed with CCl_4 , and the stirred ice-cold mixture treated with a soln. of Br_2 in CCl_4 during 2-4 hrs. $\rightarrow$ ethyl α -bromo- β -phenylpropionate. Y: 80%. F. e. with lower yields s. J. R. Dice and J. N. Bowden, Am. Soc. 71, 3107 (1949).

Silver salt Ag^+ **Halides from carboxylic acids** $\text{COOH} \rightarrow \text{Hal}$ **Degradation with loss of 1 C-atom**

s. 1, 453/4; 3, 489; 4, 517; s. a. A. L. Henne and W. G. Finnegan, Am. Soc. 72, 3806 (1950); A. C. Cope and M. E. Synerholm, Am. Soc. 72, 5228 (1950); M. Heintzeler, A. 569, 102 (1950); R. N. Haszeldine, Soc. 1951, 584; pure sec. bromides s. J. Cason and R. H. Mills, Am. Soc. 73, 1354 (1951); in trichloroethylene s. M. Stoll and A. Rouvé, Helv. 34, 98 (1951)

595. **Effect of nitro groups.** Competing reactions, i.e. nuclear and side chain bromination, can be minimized by introduction of nitro groups into the nucleus. E. s. R. A. Barnes and R. J. Prochaska, Am. Soc. 72, 3188 (1950); W. G. Dauben and H. Tilles, Am. Soc. 72, 3185 (1950).

Sodium hypobromite NaOBr **Halides from α -ketocarboxylic
acid esters** $\text{COCOOR} \rightarrow \text{Hal}$

596.



An ice-cold mixture of Br_2 , NaOH, and water added at 0° to a soln. of ethyl phenylcyanopyruvate in aq. NaOH $\rightarrow$ phenylbromoacetonitrile. Y: 82%. F. e. s. S. Wideqvist, Am. Soc. 71, 4152 (1949).

Formation of S—S Bond

Exchange

Hydrogen ∇

SS ∇ H

Potassium ferricyanide

$K_3[Fe(CN)_6]$

Sym. disulfides from mercaptans



597.



A soln. of thiophenol in aq. NaOH oxidized with K-ferricyanide $\rightarrow$ diphenyl disulfide. Y: almost 100%. V. O. Lukashevich and M. M. Sergeeva, *Ж.* 19, 1493 (1949); *C. A.* 44, 3451i.

Oxygen ∇

SS ∇ O

Hydrochloric acid

HCl

Sym. disulfoxides from sulfinic acids



598.



An aq. soln. of Na-p-cyanobenzenesulfinate cooled to 0°, acidified strongly with concd. HCl, and kept 2 days at 0° $\rightarrow$ di-p-cyanophenyl disulfoxide. Y: 70%. L. Bauer and J. Cymerman, *Soc.* 1950, 109.

Halogen ∇

SS ∇ Hal

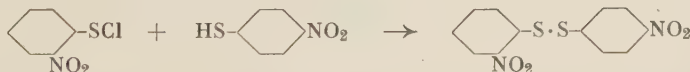
Without additional reagents

w.a.r.

Disulfides from sulfenylchlorides

$\leftarrow$

599.



o-Nitrophenyl sulfenylchloride mixed with p-nitrophenylmercaptan in ether, and worked up on the next day $\rightarrow$ 2,4'-dinitrophenyl disulfide. Y: 88%. F. e. s. V. O. Lukashevich and M. M. Sergeeva, *Ж.* 19, 1493 (1949); *C. A.* 44, 3451i. In the presence of NaOH s. F. D. Stuart and R. A. Mathes, *J. Org. Chem.* 14, 1111 (1949).

Lithium aluminum hydride

LiAlH_4

Sym. disulfides from sulfenylchlorides

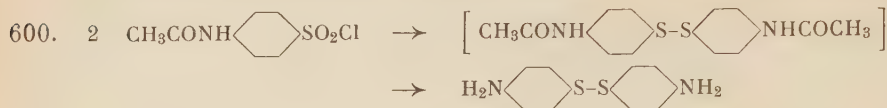


s. 6, 47

Hydriodic acid

HI

Sym. disulfides from sulfonic acid chlorides



p-Acetamidobenzenesulfonyl chloride and HI (d. 1.72) in glacial acetic acid allowed to stand at room temp. for 22 hrs., diluted with Na-thiosulfate soln., and worked up, whereby the amino group is deacylated by refluxing 1.5 hrs. with concd. HCl-alcohol $\rightarrow$ di-p-amino-phenyl disulfide. Y: 77.5%. F. e. s. L. Bauer and J. Cymerman, Soc. 1949, 3434.

Sulfur †

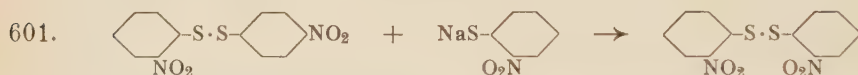
SS † S

Sodium salt

Na⁺

Reactions with di- and tri-sulfides

←



A suspension of 2,4'-dinitrodiphenyl disulfide in methanol treated with a soln. of Na-2-nitrophenylmercaptide in methanol, and shaken 1 hr. at room temp. $\rightarrow$ 2,2'-dinitrodiphenyl disulfide. Y: 82.3%. F. e. s. V. O. Lukashevich and M. M. Sergeeva, Ж 19, 1493 (1949); C. A. 44, 3451i.

Formation of S—Rem Bond

Exchange

Halogen †

SRem † Hal

Without additional reagents

w.a.r.

Selenysulfides from selenylhalides

←



o-Nitrophenyl selenylbromide triturated with thiophenol, then allowed to stand 24 hrs. at room temp. $\rightarrow$ o-nitrophenylselenyl phenyl sulfide (startg. m. f. 159, 666). Y: 97.4%. F. methods and e. s. H. Rheinboldt and E. Giesbrecht, A. 568, 198 (1950).

Potassium salt

 K^+ **Selenylthiocyanates from selenylhalides** $\text{SeHal} \rightarrow \text{SeSCN}$

603.



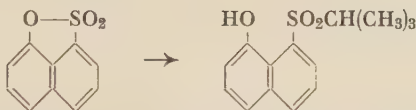
A soln. of *o*-nitrophenylselenyl bromide in dry benzene agitated 3 hrs. at room temp. with K -thiocyanate and some glass beads $\rightarrow$ *o*-nitrophenylselenyl thiocyanate. Y: ca. 100%. F. e. and reactions s. H. Reinholdt and M. Perrier, *Bl.* 1950, 245.

Formation of S—C Bond**Uptake****Addition to Oxygen and Sulfur** $\text{SC} \nabla \text{OS}$

Magnesium

 Mg **Hydroxysulfones from sultones** C

604.



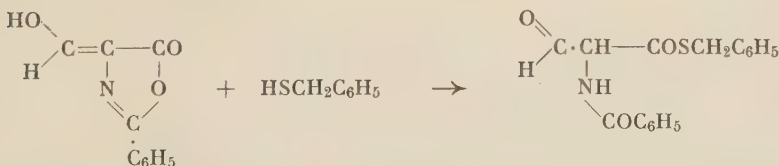
Naphthosultone in dry benzene added to an ethereal soln. of *tert*-butyl-MgBr, refluxed for 4 hrs., then set aside overnight $\rightarrow$ 8-*tert*-butylsulfonyl-1-naphthol. Y: ca. 75%. F. e. s. A. Mustafa, *Soc.* 1949, 2151.

Addition to Oxygen and Carbon $\text{SC} \nabla \text{OC}$

Sodium

 Na **Oxazolone ring opening** C

605



2-Phenyl-4-hydroxymethylene-5-oxazolone heated at 100° with benzyl mercaptan and a small piece of Na for 0.5 hr. $\rightarrow$ benzyl phenylthio-

penaldate. Y: ca. 100%. E. V. Brown, *Chemistry of Penicillin* 1949, 516.

Sodium salt

Na^+

Hydroxythioethers from oxido compounds

Carbohydrates

s. 2, 532; s. a. F. H. Newth, G. N. Richards, and L. F. Wiggins, *Soc. 1950*, 2356

Addition to Nitrogen and Carbon

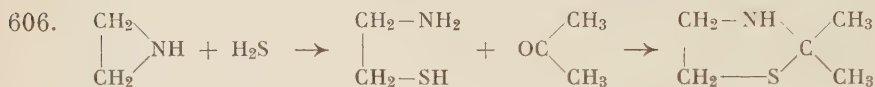
SC ↓ NC

Without additional reagents

w.a.r.

Aminomercaptans and thiazolidines from cyclic imines

←



Ethyleneimine added at -70 to -60° to a soln. of H_2S in methanol, and allowed to warm gradually to room temp. $\rightarrow$ β -mercaptoethylamine. Y: 70–80%.

H_2S introduced at $10\text{--}20^\circ$ with stirring into a soln. of ethyleneimine in acetone over a period of 3 hrs., and stirring continued at room temp. for several hrs. $\rightarrow$ 2,2-dimethylthiazolidine. Y: 90%.

F. e. and reactions with ethyleneimine s. H. Bestian, *A. 566*, 210 (1950); aminomercaptans s. a. G. J. Braz, *Ж. 21*, 688 (1951); *C. A. 45*, 9473e.

Sodium/alcohol

NaOR

Carboxylic acid thioamides from nitriles

$\text{CN} \rightarrow \text{CSNH}_2$

s. 6, 608

Ammonia

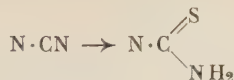
NH_3



N-Benzyl-N-phenylglycynonitrile, NH_3 , and H_2S in methanol heated 1 hr. at 70° in a pressure bottle $\rightarrow$ N-benzyl-N-phenylaminoacetothioamide. Y: 97%. F. e. s. R. A. Turner and C. Djerassi, *Am. Soc. 72*, 3081 (1950).

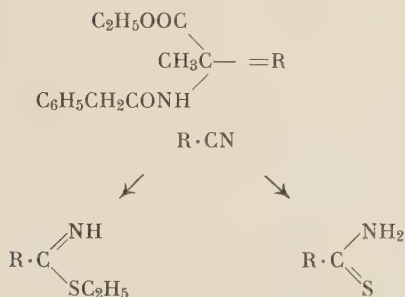
Thioureas from cyanamides

s. 4, 532; s. a. F. Kurzer, Soc. 1950, 3269

*Hydrochloric acid**HCl***Iminothiolic esters and
carboxylic acid thioamides
from nitriles**

←

608.

 **α -Phenylacetamido- α -carbethoxypropionitrile**

(4.6 g.) in dry ether and ethylmercaptan saturated at 0° with dry HCl, kept 24 hrs. at the same temp., evaporated, redissolved in chloroform, and shaken with aq. $\text{NaHCO}_3 \rightarrow$ 3 g. $\rightarrow$ α -phenylacetamido- α -carbethoxypropionimino ethyl thioether.

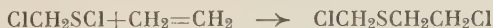
(1 g.) added to a soln. of Na in ethanol, which has been saturated at -10° with H_2S , and heated 6 hrs. at 50-60° in a closed vessel $\rightarrow$ 0.85 g. α -phenylacetamido- α -carbethoxypropionothioamide.

A. H. Cook et al., Soc. 1949, 3220; thioamides s. a. R. Dahlbom, Acta Chem. Scand, 4, 744 (1950).

Addition to Halogen and SulfurSC $\Downarrow$ HalS*Without additional reagents**w.a.r.***Chlorothioethers from sulfenylchlorides**

←

609.



A slow stream of ethylene introduced into chloromethyl sulfenylchloride below 50° until the soln. is colorless $\rightarrow$ chloromethyl β -chloroethyl sulfide. Y: ca. 100%. H. Brintzinger et al., Chem. B. 83, 87 (1950).

Addition to Sulfur and Carbon

SC ↓ SC

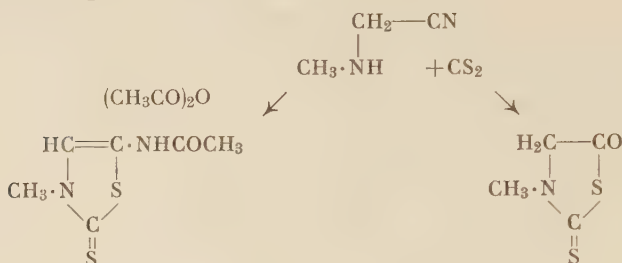
Without additional reagents

w.a.r.

Thiazole ring from α -aminonitriles

○

610.



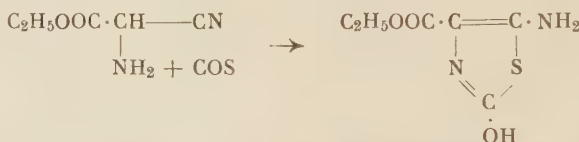
Methylaminoacetonitrile

in ethyl acetate added under N_2 with cooling and stirring to CS_2 , then treated with acetic anhydride $\rightarrow$ 5-acetamido-2-thio-3-methylthiazoline (startg. m. f. 378). Y: 74%.

in methanol added under N_2 with cooling and stirring to CS_2 in methanol, after 30 min. treated with KOH in methanol, kept at 0° for 24 hrs., evaporated in vacuo, dissolved in water, and treated with concd. HCl $\rightarrow$ 2-thio-3-methylthiazolid-5-one (startg. m. f. 362). Y: 78%.

A. H. Cook and S. F. Cox, Soc. 1949, 2337.

611.



5-Amino-2-hydroxythiazoles. Ethyl aminocynoacetate in ether treated with excess carbon oxysulfide, which is bubbled into the soln. during 6 hrs. $\rightarrow$ 5-amino-2-hydroxy-4-carbethoxythiazole. Y: 96%. F. e. s. A. H. Cook, I. Heilbron, and G. D. Hunter, Soc. 1949, 1443.

Potassium hydroxide/alcohol

KOH

s. 6, 610

Addition to Carbon

SC ↓ CC

Without additional reagents

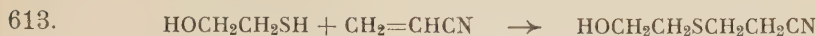
w.a.r.

Thioethers from ethylene derivatives

C:C $\rightarrow$ CHCSR

612. The highest rate of addition of ethyl mercaptan to 1-hexadecene is obtained by using ultraviolet light of the proper wave length. Catalysts and inhibitors, s. J. T. Hackmann and R. Berkenbosch, R. 68, 745 (1949).

Cyanoethyl hydroxyalkyl thioethers from vinyl cyanides



Acrylonitrile added with stirring to 2-mercaptoethanol, a small portion added at first, then warmed at 35-40° for 5 min., a second portion added dropwise during 10 min. at 55-60°, and a final portion added all at once, then stirred 16 hrs. at room temp. $\rightarrow$ β -(2-hydroxyethylmercapto)propionitrile. Y: 92-94%. L. L. Gershbein and C. D. Hurd, *Org. Synth.* 29, 52 (1949).

β -Ketosulfones from α,β -ethyleneketones C: C $\rightarrow$ CHCSO_2R
s. 4, 535; cf. H. Gilman and L. F. Cason, *Am. Soc.* 72, 3469 (1950)

Addition of thiolic acids to carbon double and triple bonds

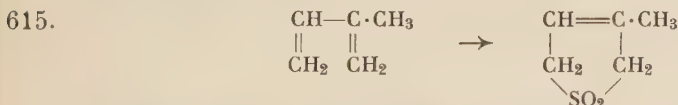
←



Thioacetic acid added dropwise to cyclohexylacetylene on a water bath, then heated 2 hrs. more $\rightarrow$ 2-cyclohexylvinyl thiolacetate. Y: 96%. F. e., also addition of 2 mole thiolic acid, s. H. Behringer, *A.* 564, 219 (1949).

Sulfones from dienes

○



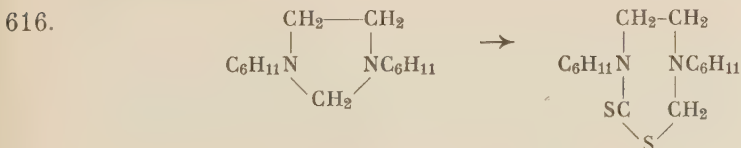
A precooled autoclave charged with isoprene, liq. SO_2 , methanol, and some hydroquinone, sealed, heated slowly to 85°, and maintained at that temp. for 4 hrs. $\rightarrow$ 3-methyl-2,5-dihydrothiophene-1,1-dioxide. Y: 77-87% depending on the purity of isoprene. F. e. s. R. L. Frank and R. P. Seven, *Org. Synth.* 29, 59 (1949).

s. a. 1, 459, 713; O. Grummitt, A. E. Ardis, and J. Fick, *Am. Soc.* 72, 5167 (1950)

Hexahydro-1,3,6-thiadiazepine-2-thiones and amino-dithiocarbamic acids from imidazolines

←

Ring enlargement



Addition to Sulfur and Carbon

SC $\downarrow$ SC

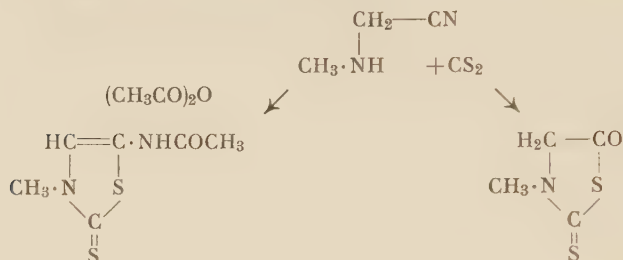
Without additional reagents

w.a.r.

Thiazole ring from α -aminonitriles

○

610.



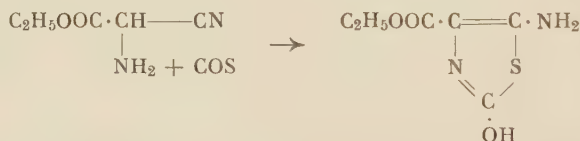
Methylaminoacetonitrile

in ethyl acetate added under N_2 with cooling and stirring to CS_2 , then treated with acetic anhydride $\rightarrow$ 5-acetamido-2-thio-3-methylthiazoline (startg. m. f. 378). Y: 74%.

in methanol added under N_2 with cooling and stirring to CS_2 in methanol, after 30 min. treated with KOH in methanol, kept at 0° for 24 hrs., evaporated in vacuo, dissolved in water, and treated with concd. HCl $\rightarrow$ 2-thio-3-methylthiazolid-5-one (startg. m. f. 362). Y: 78%.

A. H. Cook and S. F. Cox, Soc. 1949, 2337.

611.



5-Amino-2-hydroxythiazoles. Ethyl aminocynoacetate in ether treated with excess carbon oxysulfide, which is bubbled into the soln. during 6 hrs. $\rightarrow$ 5-amino-2-hydroxy-4-carbethoxythiazole. Y: 96%. F. e. s. A. H. Cook, I. Heilbron, and G. D. Hunter, Soc. 1949, 1443.

Potassium hydroxide/alcohol
s. 6, 610

KOH

Addition to Carbon

SC $\downarrow$ CC

Without additional reagents

w.a.r.

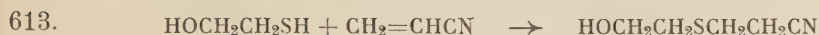
Thioethers from ethylene derivatives

C:C $\rightarrow$ CHCSR

612.

The highest rate of addition of ethyl mercaptan to 1-hexadecene is obtained by using ultraviolet light of the proper wave length. Catalysts and inhibitors, s. J. T. Hackmann and R. Berkenbosch, R. 68, 745 (1949).

Cyanoethyl hydroxyalkyl thioethers from vinyl cyanides



Acrylonitrile added with stirring to 2-mercaptoethanol, a small portion added at first, then warmed at 35-40° for 5 min., a second portion added dropwise during 10 min. at 55-60°, and a final portion added all at once, then stirred 16 hrs. at room temp. $\rightarrow$ β -(2-hydroxyethylmercapto)propionitrile. Y: 92-94%. L. L. Gershbein and C. D. Hurd, *Org. Synth.* 29, 52 (1949).

β -Ketosulfones from α,β -ethyleneketones C:C $\rightarrow$ CHCSO_2R
s. 4, 535; cf. H. Gilman and L. F. Cason, *Am. Soc.* 72, 3469 (1950)

Addition of thiolic acids to carbon double and triple bonds

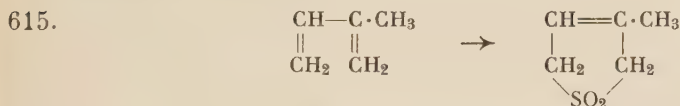
←



Thioacetic acid added dropwise to cyclohexylacetylene on a water bath, then heated 2 hrs. more $\rightarrow$ 2-cyclohexylvinyl thiolacetate. Y: 96%. F. e., also addition of 2 mole thiolic acid, s. H. Behringer, *A.* 564, 219 (1949).

Sulfones from dienes

○



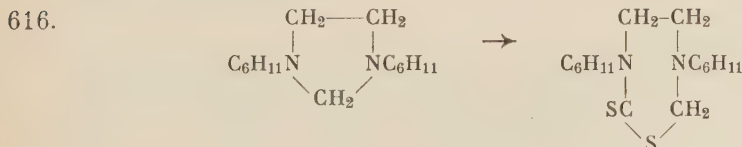
A precooled autoclave charged with isoprene, liq. SO_2 , methanol, and some hydroquinone, sealed, heated slowly to 85°, and maintained at that temp. for 4 hrs. $\rightarrow$ 3-methyl-2,5-dihydrothiophene-1,1-dioxide. Y: 77-87% depending on the purity of isoprene. F. e. s. R. L. Frank and R. P. Seven, *Org. Synth.* 29, 59 (1949).

s. a. 1, 459, 713; O. Grummitt, A. E. Ardis, and J. Fick, *Am. Soc.* 72, 5167 (1950)

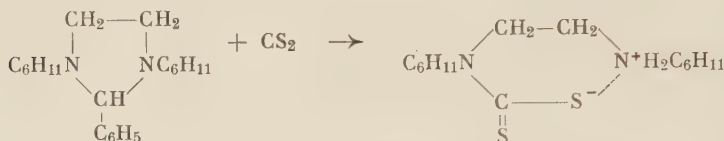
Hexahydro-1,3,6-thiadiazepine-2-thiones and amino-dithiocarbamic acids from imidazolines

←

Ring enlargement



CS_2 added to a soln. of 1,3-dicyclohexylimidazolidine (prepn. s. 404) in alcohol, and allowed to stand at room temp. for 2 hrs. $\rightarrow$ 3,6-dicyclohexyl-hexahydro-1,3,6-thiadiazepine-2-thione. Y: 97%.



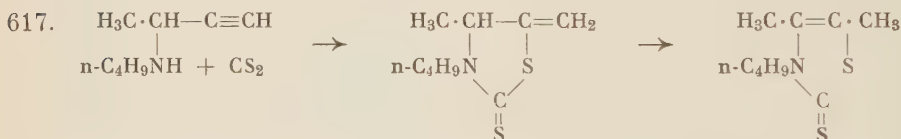
2.5 gm. CS_2 added slowly to an agitated soln. of 9.8 gm. 1,3-dicyclohexyl-2-phenylimidazolidine in alcohol, and worked up after 2 hrs. $\rightarrow$ 8.9 gm. N-cyclohexyl-N-(β -cyclohexylaminoethyl)dithiocarbamic acid inner salt.—The different course of the reaction is caused by substitution in position 2. F. e. s. R. A. Donia et al., J. Org. Chem. **14**, 952 (1949).

Sodium hydroxide

NaOH

5-Methyl-2(3H)-thiazolethiones from acetyleneamines via 5-methylene-2-thiazolidinethiones

←



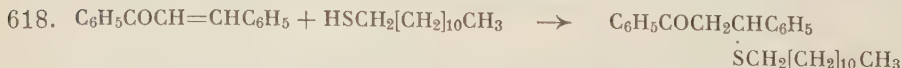
CS_2 added dropwise during 1 hr. to a well-stirred mixture of NaOH, water, and 2-n-butylamino-3-butyne at 50° , and stirring continued for a further 2 hrs. $\rightarrow$ 4-methyl-3-n-butyl-5-methylene-2-thiazolidinethione (Y: 87%) dissolved in concd. H_2SO_4 , and poured on crushed ice $\rightarrow$ 4,5-dimethyl-3-n-butyl-2(3H)-thiazolethione (Y: 86%). F. e. s. J. W. Batty and B. C. L. Weedon, Soc. **1949**, 786.

Sodium/alcohol

NaOR

β -Ketothioethers from α,β -ethyleneketones

C : C $\rightarrow$ CHCSR



A little 2 N Na-ethoxide added to a mixture of benzylideneacetophenone, n-dodecyl mercaptan, and benzene, vigorously shaken, and allowed to stand for 12 hrs. $\rightarrow$ benzylacetophenone β -n-dodecyl sulfide. Y: 95%. F. e. s. F. Kipnis and J. Ornfelt, Am. Soc. **71**, 3554 (1949).

Sodium acetate

 CH_3COONa **Sym. thioethers from ethylene derivatives**

←

619.

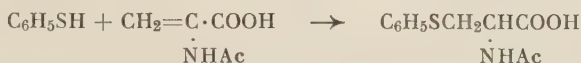


H_2S introduced over a period of 25 hrs. into a boiling soln. of methyl acrylate, Na-acetate trihydrate, and 95%-ethanol $\rightarrow$ methyl β -thiodi-propionate. Y: 71-81%. E. A. Fehnel and M. Carmack, *Org. Synth.* **30**, 65 (1950).

Piperidine

 $C_5H_{11}N$ **Thioethers from ethylene derivatives**C : C $\rightarrow$ CHCSR**Mercapturic acids**

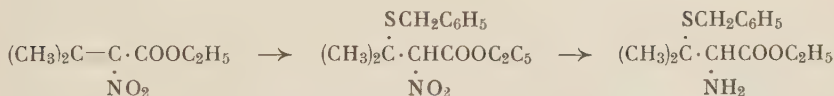
620.



Acetaminoacrylic acid, thiophenol, and piperidine in dioxane refluxed 1 hr. $\rightarrow$ rac. phenylmercapturic acid. Y: 86%. F. e. s. H. Behringer and E. Fackler, *A.* **564**, 73 (1949); cyanosulfides s. R. M. Ross, H. L. Bushey, and R. J. Rolih, *Am. Soc.* **73**, 540 (1951).

 β -Alkylthio- α -aminocarboxylic acid esters from **α -nitro- α,β -ethylenecarboxylic acid****esters via** **β -alkylthio- α -nitrocarboxylic acid esters**

621.



A soln. of benzylmercaptan in abs. methanol treated with piperidine, cooled to 0° , ethyl α -nitrodimethylacrylate (prepn. s. 382) added during 1 hr., allowed to stand 6 hrs. at 0° , then 48 hrs. at 20° , then 48 hrs. at 20° , neutralized with acetic acid, methanol distilled off in vacuo, the residue, containing ethyl α -nitro- β -(benzylmercapto)isovalerate, dissolved in ethanol, powdered Sn added, then treated slowly with 37%-HCl at 20 - 25° with vigorous stirring during 4-6 hrs., stirring continued until the Sn has disappeared, and worked up via the chlorostannate $\rightarrow$ ethyl α -amino- β -(benzylmercapto)isovalerate. Y: ca. 70%. R. Trave, *G.* **79**, 233 (1949).

Hydroquinone

←

Sulfones from dienes

○

s. 6, 615

Hydrochloric acid

HCl

1,6-Addition

←

s. 6, 655

Exchange

Hydrogen $\blacktriangle$ SC ∇ H

Without additional reagents

w.a.r.

Sulfochlorination

H $\rightarrow$ SO₂Cl

s. 2, 538; 3, 511; s. a. H. Y. Lew and C. R. Noller, *Am. Soc.* 72, 5715 (1950); J. A. Solov'eva and G. J. Arbuzov, *Ж.* 21, 765 (1951); C. A. 45, 9524i

1,2-Dithioles from ethylene derivatives

○

622.



2-Methyl-1-phenylpropene heated with S to 190°, and kept 10 hrs. at 190-210° $\rightarrow$ 4-methyl-5-phenyl-1,2-dithiole-3-thione. Y: 80%. F. e. s. M. G. Voronkov, A. S. Broun, and G. B. Karpenko, *Ж.* 19, 1927 (1949); C. A. 44, 1955g.

Potassium thiocyanate

KSCN

2-Aminobenzothiazoles

623.



A soln. of Br₂ in glacial acetic acid added dropwise with stirring below 35° to a soln. of p-anisidine and K-thiocyanate in 96% acetic acid, then stirred for 10 hrs. $\rightarrow$ 2-amino-6-methoxybenzothiazole. Y: 87%. C. G. Stuckwisch, *Am. Soc.* 71, 3417 (1949).

Pyridine-sulfur trioxide

C₅H₅N·SO₃

Sulfonation

H $\rightarrow$ SO₃H

of heterocyclics s. 3, 508; of dienes s. *Ж.* 21, 704; C. A. 45, 8969f

Mercuric sulfate

HgSO₄

s. 2, 540; s. a. S. Maffei, *G.* 80, 651 (1950)

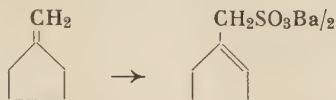
Dioxane/sulfur trioxide

←

Replacement of hydrogen by sulfonic acid groups with rearrangement

←

624.



A soln. of methylenecyclopentane in ethylene chloride added with vigorous stirring at -5 to 0° over a period of 40 min. to a suspension of dioxane- SO_3 complex in ethylene chloride, the following day decomposed with ice-water, and the aq. phase neutralized by careful addition of Ba-carbonate $\rightarrow$ Ba-1-cyclopentenylmethanesulfonate. Y: 97%. F. reactions with migration of the double bond into the ring s. R. T. Arnold, R. W. Amidon, and R. M. Dodson, Am. Soc. 72, 2871 (1950); without rearrangement s. R. Sperling, Soc. 1949, 1925; oxo compounds s. W. E. Truce and C. C. Alfieri, Am. Soc. 72, 2740 (1950).

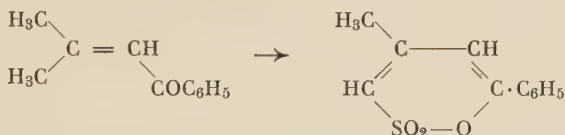
Acetic anhydride

 $(\text{CH}_3\text{CO})_2\text{O}$

Sultones from ethylene ketones

○

625.



H_2SO_4 (d. 1.84) followed by isopropylideneacetophenone added dropwise with ice-salt cooling and vigorous stirring below 0° to acetic anhydride, then kept at -5° for 24 hrs. and at room temp. for another 24 hrs. $\rightarrow$ 2-methyl-4-phenyl-4-buta-1,3-dien-4-ol-1-sulfonic acid sultone. Crude: Y: 84%. F. e. s. T. Morel and P. E. Verkade, R. 68, 619 (1949).

Oxygen ∇ SC ∇ O

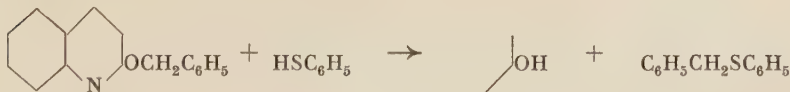
Without additional reagents

w.a.r.

Cleavage of ethers by mercaptans

←

626.

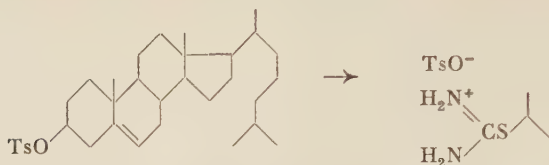


A mixture of 2-benzyl-2-oxo-1,2,3,4-tetrahydroquinoline and thiophenol stirred at $150-170^\circ$ in a dry N_2 -atmosphere for 52 hrs. $\rightarrow$ 2-hydroxyquinoline (Y: 96%) and benzyl phenyl sulfide (Y: 75%). F. e. s. G. Illuminati and H. Gilman, Am. Soc. 71, 3349 (1949).

Isothiureas from tosylates

←

627.

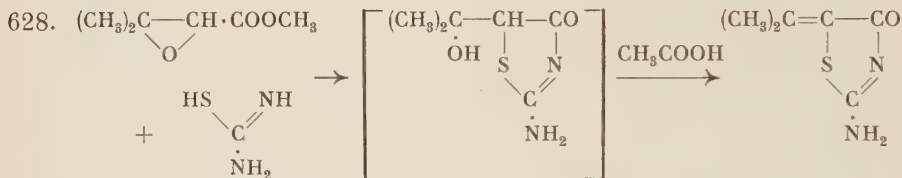


A mixture of 3 β -p-toluenesulfonyl-5-cholestene, thiourea, and 99% 2-propanol refluxed 4 hrs. with addition of water $\rightarrow$ cholesterylisothiuronium p-toluenesulfonate. Y: 96%. J. W. Ralls, R. M. Dodson, and B. Riegel, *Am. Soc.* **71**, 3320 (1949).

Thiazolines from glycidic acid esters

○

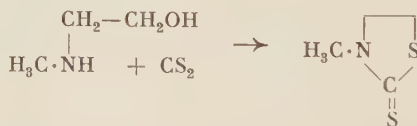
Dehydration



A soln. of methyl dimethylglycidate and thiourea in methanol allowed to stand at 35° for 10 weeks, filtered, evaporated to dryness, and the residue boiled with glacial acetic acid $\rightarrow$ 2-amino-4-keto-5-isopropylidene-2-thiazoline. Y: 92%. F. e. s. C. C. J. Culvenor et al., *Soc.* **1949**, 2573.

2-Thiazolidinethiones from aminoalcohols

629.



A soln. of 5 gm. 2-methylaminoethanol in CS_2 heated in a steel autoclave at 120-140° for 3.5 hrs. $\rightarrow$ 5.8 gm. 3-methyl-2-thiazolidinethione. J. W. Batty and B. C. L. Weedon, *Soc.* **1949**, 786.

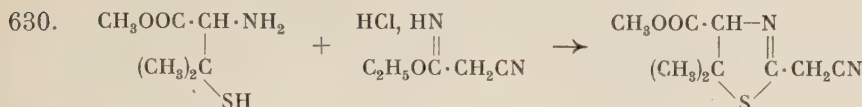
Thiazolidines from cyclic imines

←

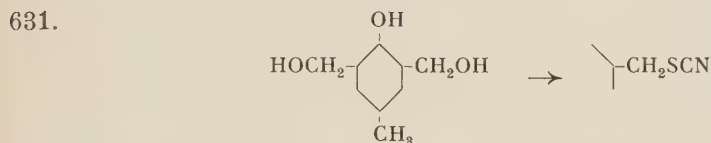
s. 6, 606

Potassium acetate CH_3COOK **Thiazolines from iminoesters**

○



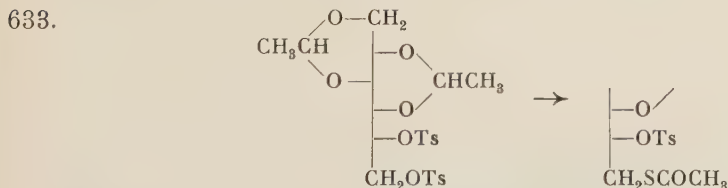
13.8 gm. penicillamine methyl ester hydrochloride, cyanoacetimino ethyl ester hydrochloride, ether, and an aq. K-acetate soln. shaken for 2 hrs. $\rightarrow$ 13.2 gm. methyl 5,5-dimethyl-2-cyanomethylthiazoline-4-carboxylate. F. e. s. A. H. Cook, G. Harris, and A. L. Levy, Soc. 1949, 3227.

Potassium thiocyanate KSCN **Thiocyanates from alcohols** $\text{OH} \rightarrow \text{SCN}$ 

p-Cresoldialcohol and K-thiocyanate in dil. HCl warmed at 70° for 1-2 min. $\rightarrow$ 2-thiocyanomethyl-4-methyl-6-hydroxymethylphenol. Y: 85%.—Heating for a longer period in addition gives the 2,6-di(thiocyanomethyl) derivative. E. Ziegler and H. Lüdde, M. 79, 316 (1948).

Sodium sulfide Na_2S **Sym. thioethers from sulfuric acid esters** $\leftarrow$ 

Dimethyl sulfate rapidly dropped into a boiling aq. soln. of Na_2S so that a vigorous reaction takes place and the reaction product distills $\rightarrow$ dimethyl sulfide. Y: 70%. H. Böhme and W. Krause, Chem. B. 82, 426 (1949).

Potassium salt K^+ **Thiolic acid esters from tosylates** $\text{OTs} \rightarrow \text{SCOR}$ 

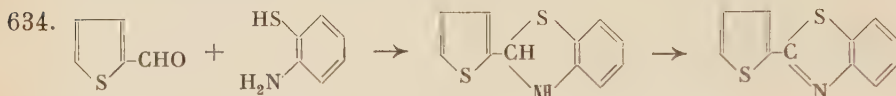
The reaction of prim. p-toluenesulfonates with K-thiolacetate in ethanol or acetone provides a useful method for the preparation of

thiolacetates, and, thence, by hydrolysis, of thiols. Sec. p-toluene-sulfonates show wide differences in behavior. Methanesulfonates generally react in the same way, but the yields are lower.—E: 5,6-Ditosyl-1,3:2,4-diethylidenesorbitol refluxed 6 hrs. with K-thiolacetate in acetone $\rightarrow$ 5-tosyl-6-acetyl-1,3:2,4-diethylidene-6-thiosorbitol. Y: 87%. F. e. s. L. N. Owen, J. H. Chapman, and P. Bladon, *Soc.* 1950, 579, 585.

Pyridine

 C_5H_5N Thiazole ring from o-aminomercaptans
via thiazoline ring

○



2-Thiophenealdehyde added in a thin stream to a soln of o-aminothiophenol in pyridine, and stirred 0.5 hr. at 85-95° $\rightarrow$ crude 2-(2'-thienyl)benzothiazoline (Y: 92%) dissolved in warm ethanol, a soln. of $FeCl_3$ in ethanol added, and warmed for another 0.5 hr. $\rightarrow$ 2-(2'-thienyl)benzothiazole (Y: 74%). W. S. Emerson and T. M. Patrick, Jr., *J. Org. Chem.* 14, 790 (1949); method of the thiazoline ring synthesis s. Lankelma and Sharnoff, *Am. Soc.* 53, 2654 (1931).

Zinc chloride/sodium sulfate

 $ZnCl_2/Na_2SO_4$

Steroid mercaptans

 $C(SR)_2$

s. 5, 430; s. a. D. K. Fukushima, S. Lieberman, and B. Praetz, *Am. Soc.* 72, 5205 (1950)

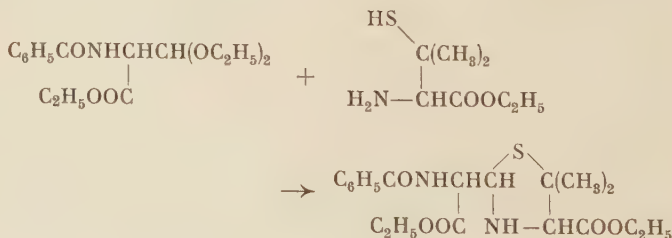
Acetic acid

 CH_3COOH

Thiazolidines

○

635.



A mixture of DL-penicillamine ethyl ester hydrochloride, ethyl phenylpenaldate diethylacetal, and glacial acetic acid warmed on a steam bath for 30 min. $\rightarrow$ diethyl DL-phenylpenicilloate. Y: 90%. F. e. s. E. V. Brown, *Chemistry of Penicillin* 1949, 528.

Phosphorus pentasulfide

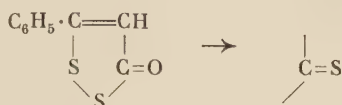
 P_2S_5

Replacement of oxygen by sulfur

←

636. in **N-heterocycles**. A suspension of *cis*-3-aminocyclohexaneacetic acid lactam (prepn. s. 505) and P_2S_5 in xylene heated with vigorous stirring at 125-130° for 1 hr. in an oil bath → *cis*-3-aminocyclohexaneacetic acid thiolactam (startg. m. f. 124). Y: 77%. M. W. Cronyn, J. Org. Chem. 14, 1013 (1949); thiohydantoin s. H. C. Carrington and W. S. Waring, Soc. 1950, 354.

637.



1,2-Dithioles. 5-Oxo-3-phenyl-1,2-dithiole refluxed 7 hrs. with P_2S_5 in CS_2 → 5-thio-3-phenyl-1,2-dithiole. Y: 80%. F. e. s. B. Böttcher and F. Bauer, A. 568, 227 (1950).

Thiazoles from α -acylaminocarboxylic acid esters

○

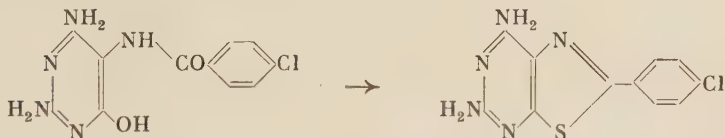
638.



P_2S_5 added in small portions to N-acetylglycine ethyl ester, heated on a steam bath with stirring, chloroform added, when the mixture becomes too viscous to stir, and heating continued for several hrs. after the addition → 2-methyl-5-ethoxythiazole (startg. m. f. HalC4H.6794). Y: 65%, isolated as picrate. D. S. Tarbell, H. P. Hirschler, and R. B. Carlin, Am. Soc. 72, 3138 (1950).

Thiazolo [5.4-d]pyrimidines

639.

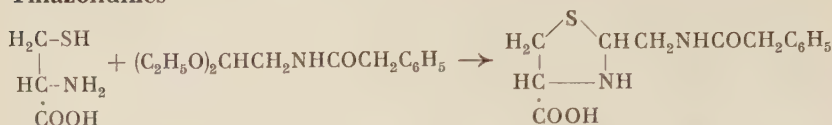


A suspension of 5-(p-chlorobenzamido)-2,4-diamino-6-hydroxypyrimidine and 3 parts of P_2S_5 in tetralin heated with stirring at 150-200° for 2 hrs. → 2-(p-chlorophenyl)-5,7-diaminothiazolo[5.4-d]pyrimidine. Y: 76%. F. e. s. E. A. Falco and G. H. Hitchings, Am. Soc. 72, 3203 (1950).

Hydrochlorides

Thiazolidines

640.

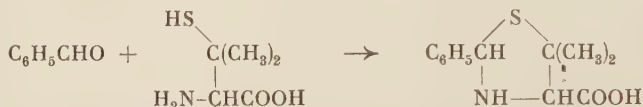


A mixture of phenylacetylaminioacetal and cysteine hydrochloride in water shaken for 1 day, and allowed to stand overnight $\rightarrow$ 2-(phenylacetylaminomethyl)thiazolidine-4-carboxylic acid. Y: 86% (p. 485). F. e. s. E. V. Brown, *Chemistry of Penicillin* 1949, 473.

Hydrofluoric acid

HF

641.



D-Penicillamine and benzaldehyde in anhydrous dioxane containing HF stirred in a copper flask for 3 hrs. $\rightarrow$ D-2-phenyl-4-carboxy-5,5-dimethylthiazolidine. Y: 77% (p. 938). F. e. and reactions s. A. H. Cook and I. M. Heilbron, *Chemistry of Penicillin* 1949, 921.

Hydrochloric acid

HCl

Thioethers from acoxy compounds

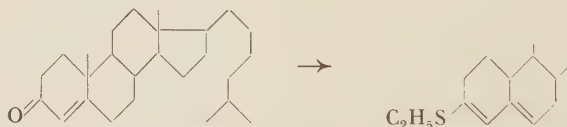
OAc $\rightarrow$ SR

s. 6, 655

Thioenolethers of steroids

C : C(SR)

642.

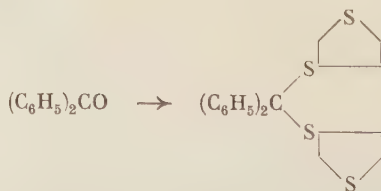


10 drops of concd. HCl added to a mixture of acetic acid, ethyl mercaptan, and cholestenone, then cooled for 0.5 hr. $\rightarrow$ 3-ethyl-mercapto-3,5-cholestadiene. Y: 78%. J. W. Ralls, R. M. Dodson, and B. Riegel, *Am. Soc.* 71, 3320 (1949).

Mercaptals

C(SR)₂

643.



Anhydrous HCl bubbled through a mixture of benzophenone, 3-thiophenethiol, and xylene at 10-15° for 2 hrs., and kept in a refrigerator overnight $\rightarrow$ benzophenone di-3-thienyl mercaptal. Y: 80%. F. e. s.

J. W. Brooks, E. G. Howard, and J. J. Wehrle, Am. Soc. 72, 1289 (1950); also cyclic mercaptals s. H. Hauptmann and B. Wladislaw, Am. Soc. 72, 707 (1950).

of carbohydrates

s. 1, 469; s. a. E. Hardegger, E. Schreier, and Z. El Heweihi, Helv. 33, 1159 (1950)

Nitrogen ∇

SC ∇ N

Cuprous thiocyanate

CuSCN

Thiocyanates from amines

NH₂ $\rightarrow$ SCN

s. 1, 470; s. a. C. van der Stelt, W. van der Lugt, and W. T. Nauta, R. 70, 285 (1951)

Halogen ∇

SC ∇ Hal

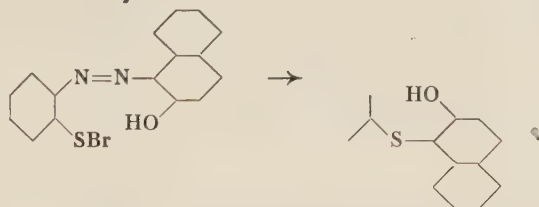
Without additional reagents

w.a.r.

Thioethers from sulfenylbromides

SBr $\rightarrow$ SR

644.



A mixture of o-(2-hydroxy-1-naphthylazo)phenylsulfenyl bromide (prepn. s. 535) and β -naphthol heated at 110-115° for 15 min. $\rightarrow$ o-(2-hydroxy-1-naphthylazo)phenyl 2-hydroxy-1-naphthyl sulfide. Y: 93%. A. Burawoy and C. Turner, Soc. 1950, 469; α -ketothioethers s. P. Truitt et al., Am. Soc. 71, 3511 (1949).

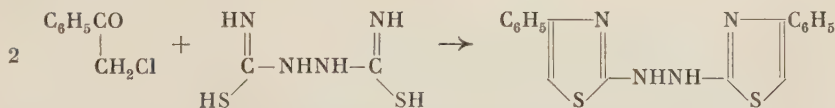
Thiazole ring with thioamides

○

s. 1, 472/3; 2, 552-4; s. a. R. G. Jones, E. C. Kornfeld, and K. C. McLaughlin, Am. Soc. 72, 4526 (1950)

Hydrazothiazoles

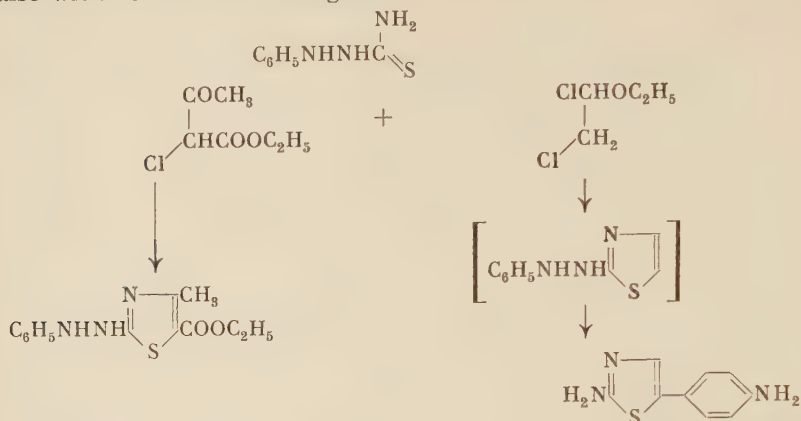
645.



Hydrazine-N,N'-bis(carboxylic acid thioamide) and ω -chloroacetophenone in 96%-alcohol refluxed 0.5 hr. on a water bath $\rightarrow$ 4,4'-diphenylhydrazothiazole-2,2'. Y: 80%. F. e. s. H. Beyer et al., Chem. B. 82, 143, 148 (1949).

**Thiazoles from thiosemicarbazides,
also with benzidine rearrangement**

646.



1-Phenylthiosemicarbazide in abs. alcohol refluxed 20–30 min. with α -chloroacetoacetic ester $\rightarrow$ 2-phenylhydrazino-4-methyl-5-carboethoxythiazole. Y: almost 100%.

α,β -dichloroether $\rightarrow$ 2-amino-5-(p-aminophenyl)thiazole dihydrochloride. Y: almost 100%.

F. e. s. H. Beyer and G. Henseke, B. 83, 247 (1950).

Sodium hydroxide

NaOH

Sulfones

$\text{R}\cdot\text{SO}_2\cdot\text{R}$

Sulfonylcarboxylic acids

s. 2, 556; cf. C. S. Marvel, R. S. Johnson, and N. A. Meinhardt, J. Org. Chem. 13, 822 (1948); Am. Soc. 73, 859 (1951)

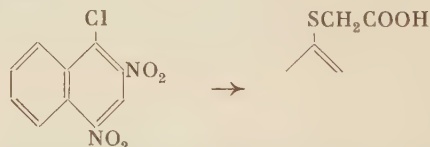
Sodium hydrogen carbonate

NaHCO₃

Thioethers from halides

$\text{Hal} \rightarrow \text{SR}$

647.



A soln. of thioglycolic acid in a little alcohol, then NaHCO_3 added to a boiling suspension of 1-chloro-2,4-dinitronaphthalene in alcohol, stirred and boiled until dissolved $\rightarrow$ (2,4-dinitro-1-naphthyl)mercaptoacetic acid (startg. m. f. 889). Y: 60%.—Temp. and pH are very important, and if not correct, 2,4-dinitro-1-naphthol is chiefly obtained. G. Leandri, G. 79, 50 (1949); α -ketothioethers s. S. Teich and D. Y. Curtin, Am. Soc. 72, 2481 (1950).

Sodium sulfide Na_2S **Sym. thioethers from halides** $2RHal \rightarrow RSR$

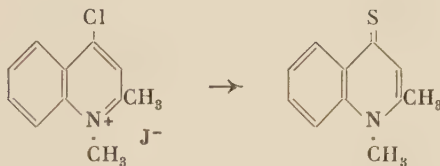
s. 5, 442; s. a. C. G. Overberger, S. P. Ligthelm, and E. A. Swire, *Am. Soc.* 72, 2856 (1950)

Sodium hydrogen sulfide $NaHS$

Tert. amines from quaternary ammonium salts with simultaneous replacement of chlorine by sulfur

←

648.



A mixture of 4-chloroquinaldine methiodide and NaHS (containing 28% water of crystallization) in ethanol refluxed 12 hrs. $\rightarrow$ N-methyl-4-thioquinaldone. Y: 83%.—The nature of the substituent in position 2 has a definite influence, both on the synthesis and the properties of the thiones, depending upon the electron-attracting or -releasing character of the group. F. e. s. E. Campaigne, R. E. Cline, and C. E. Kaslow, *J. Org. Chem.* 15, 600 (1950).

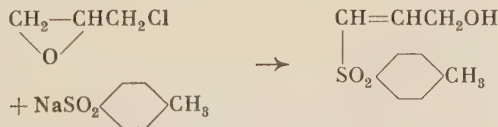
Sodium sulfite Na_2SO_3 **Sulfonic acids** $Hal \rightarrow SO_3H$

s. 1, 488/9; 3, 523; s. a. P. Petitcolas and R. Sureau, *Bl.* 1950, 466

Sodium salt Na^+ **Hydroxyethylenesulfones from oxidohalides**

←

649.



Epichlorohydrin and Na-p-toluenesulfinate in water-alcohol kept at 32° for 24 hrs. $\rightarrow$ 3-p-toluenesulfonyl-2-propen-1-ol. Y: 90%. F. e. s. C. C. J. Culvenor, W. Davies, and W. E. Savage, *Soc.* 1949, 2198.

Thiolic acid esters from carboxylic acid chlorides

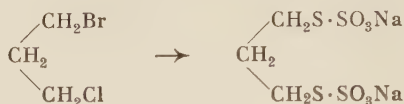
650.



Benzoyl chloride added to a suspension of Na-4,5-dimethylthiazole-2-mercaptide in benzene, and the soln. formed refluxed for 1 hr. $\rightarrow$ 4,5-dimethyl-2-benzoylmercaptothiazole. Y: 99%. F. e. s. F. D. Stewart and R. A. Mathes, J. Org. Chem. 14, 1111 (1949).

Alkylthiosulfates from halides

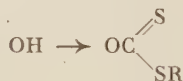
651.



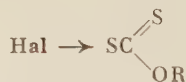
1-Chloro-3-bromopropane added with stirring to aq. Na-thiosulfate, stirring continued at 40-45° for 60-80 hrs. $\rightarrow$ Na trimethylene dithiosulfate (startg. m. f. 659). Y: 86%. F. e. s. Ya. G. Mazover, Ж. 19, 843, 849 (1949); C. A. 44, 3436a, f; s. a. U. Weiss and S. Sokol, Am. Soc. 72, 1687 (1950).

Potassium salt**Xanthates****from alcohols**

s. 6, 841

**from halides**

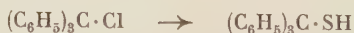
s. 6, 656

*Ammonia***Thioethers from halides**

652. A slow stream of NH_3 introduced at ca. 50° for 30 min. into a mixture of p-nitrobenzyl chloride and benzylmercaptan in abs. alcohol $\rightarrow$ p-nitrobenzyl benzyl sulfide. Y: 95%. C. G. Overberger, S. P. Lichtelm, and E. A. Swire, Am. Soc. 72, 2856 (1950).

Alumina**Mercaptans from halides**

653.



Dry H_2S passed into a mixture of triphenylmethyl chloride and activated Al_2O_3 (Alcoa F-20) in dry dioxane for 15 hrs. at such a rate as to agitate the suspended Al_2O_3 gently and to keep the soln. saturated with the gas $\rightarrow$ triphenylmethyl mercaptan. Y: 75-80%. N. Kharasch and H. R. Williams, Am. Soc. 72, 1843 (1950).

Ammonium thiocyanate

 NH_4SCN **Thiocyanates from chlorides** $\text{Cl} \rightarrow \text{SCN}$

s. 5, 448; s. a. E. Szarvasi, Bl. 1950, 463

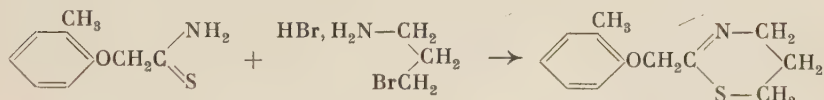
Hydribromides

 $\leftarrow$ **1,3-S,N-Heterocyclics**

○

1,3-Thiazines

654.

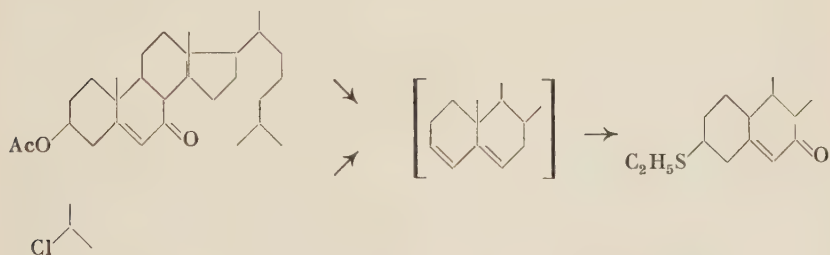


o-Toloxymethylacetothioamide and 3-bromopropylamine hydrobromide heated 5 min. at $160^\circ \rightarrow$ 2-(o-toloxymethyl)penthiazoline. Y: 69%. F. e. s. C. Djerassi and C. R. Scholz, J. Org. Chem. 15, 694 (1950).

Hydrochloric acid

 HCl
Thioethers from
acyo compounds and chlorides
1,6-Addition
 $\leftarrow$

655.



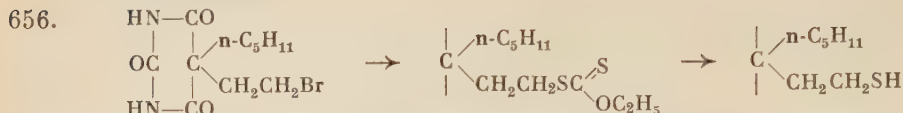
Ethylmercaptan added to a soln. of 7-ketocholesteryl acetate or 3 β -chloro-5-cholesten-7-one in glacial acetic acid containing concd. HCl , and worked up after 30 min. $\rightarrow$ 3-ethylmercapto-5-cholesten-7-one. Y: 83% and 80% respectively. J. W. Ralls, R. M. Dodson, and B. Riegel, Am. Soc. 71, 3320 (1949).

Via intermediates

*v.i.***Mercaptans from halides** $\text{Hal} \rightarrow \text{SH}$ **via isothiureas**

s. 1, 493-5; mercaptopyrimidines s. M. Polonovski and H. Schmitt, Bl. 1950, 616

via xanthates



A soln. of 5-n-amyl-5-β-bromoethylbarbituric acid and freshly prepared K-ethylxanthate in abs. alcohol kept 5 hrs. at ca. 45° → crude 5-n-amyl-5-(β-ethylxanthoethyl)barbituric acid (Y: 85%) dissolved in 10%-NaOH, aq. NH₃ added with stirring, and allowed to stand at room temp. for 7 hrs. → 5-n-amyl-5-β-mercaptoethylbarbituric acid (Y: 79%). F. e. s. G. S. Skinner and J. B. Bicking, *Am. Soc.* 72, 1140 (1950).

Carboxymethylthioethers from halides

Hal → SCH₂COOH

A soln. of thiourea in 95%-alcohol refluxed 4 hrs. with n-butyl bromide, most of the alcohol distilled off, aq. NaOH added, refluxing continued for an additional 2 hrs., more aq. NaOH added until the mercaptan which has separated is dissolved, cooled to ca. 0°, neutral aq. Na-chloroacetate added, allowed to warm to room temp., finally refluxed 1 hr. → n-butylthioacetic acid. Y: 90%. S. Chodroff and W. F. Whitmore, *Am. Soc.* 72, 1073 (1950).

Sulfur †

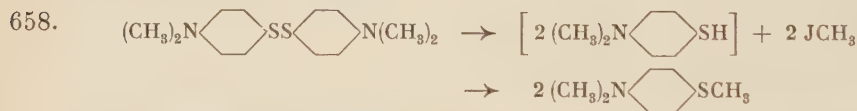
SC †† S

Sodium/liq. ammonia

Na/NH₃

Thioethers from disulfides

←



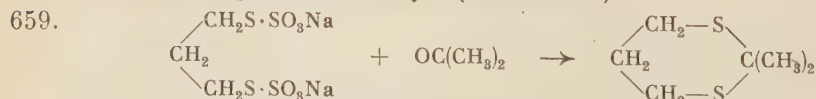
Bis-(p-dimethylaminophenyl) disulfide added slowly with stirring to a soln. of Na in liq. NH₃ until the color of the soln. has turned from blue to pink, then methyl iodide added dropwise → p-dimethylaminophenyl methyl sulfide. Y: 79%. H. Gilman and F. J. Webb, *Am. Soc.* 71, 4062 (1949).

Hydrochloric acid

HCl

Cyclic mercaptals from alkyldi(thiosulfates)

○



15%-alc. HCl added with cooling and frequent shaking to Na trimethylene dithiosulfate (prepn. s. 651) and acetone over a period of

6 hrs., then allowed to stand overnight $\rightarrow$ acetone trimethylene mercaptal. Y: 58%. F. e. s. Ya. G. Mazover, *Ж.* 19, 843, 849 (1949); C. A. 44, 3436a, f.

Via intermediates

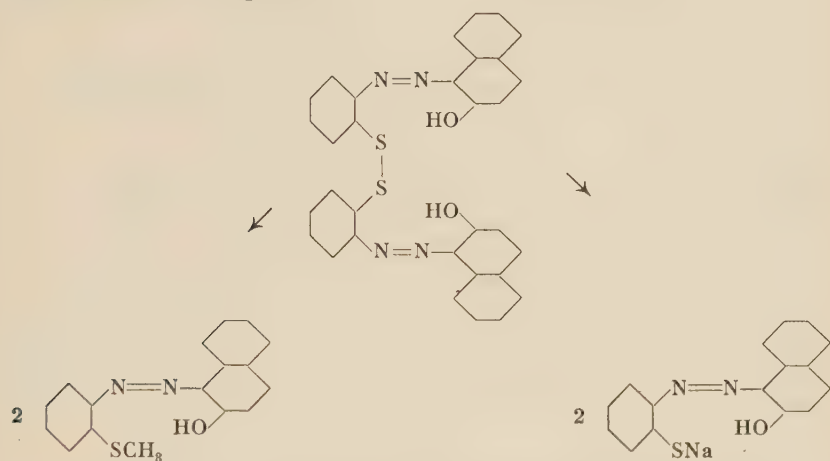
v.i.

Thioethers and mercaptans from disulfides

$\leftarrow$

o-Mercaptoazo compounds

660.



A suspension of di-o,o'-(2-hydroxy-1-naphtylazo) phenyl disulfide

in methanol shaken 2 hrs. at room temp. with aq. Na_2S , water added followed by 4 additions of aq. NaOH and dimethyl sulfate with vigorous shaking $\rightarrow$ 1-(o-methylmercaptophenylazo)-2-naphthol. Y: ca. 100%.

in ethanol shaken 4 hrs. at room temp. with aq. Na_2S , then water added $\rightarrow$ Na salt of 1-(o-mercaptophenylazo)-2-naphthol. Y: 88%.

A. Burawoy and C. Turner, *Soc.* 1950, 469.

Carbon ∇

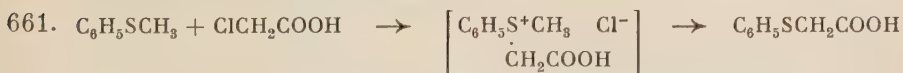
SC ∇ C

Without additional reagents

w.a.r.

Transetherification of thioethers

SR $\rightarrow$ SR'



A mixture of thioanisole and 3-4 parts of chloroacetic acid heated 8-10 hrs. in a boiling water bath $\rightarrow$ phenylthioglycolic acid. Y: ca. 80%. F. e. s. F. Krollpfeiffer et al., A. 566, 139 (1950); B. 83, 90 (1950).

Elimination

Hydrogen $\uparrow$ SC $\uparrow$ H

Without additional reagents

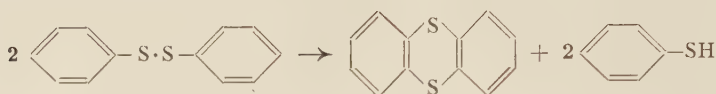
w.a.r.

Thianthrenes from disulfides

○

Disproportionation

662.



Diphenyl disulfide heated in a CO_2 -atmosphere at 270° for 6 hrs. $\rightarrow$ thianthrene. Y: 60%. A. Schönberg and A. Mustafa, *Soc.* 1949, 889.

Oxygen $\uparrow$ SC $\uparrow$ O

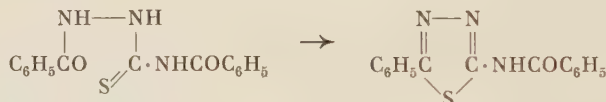
Phosphoric acid

 H_3PO_4

1,3,4-Thiadiazoles from acylthiosemicarbazides

○

663.



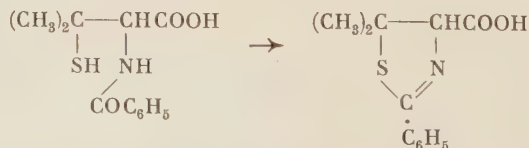
3 gm. 1,4-dibenzoylthiosemicarbazide allowed to react with syrupy H_3PO_4 at $120^\circ \rightarrow$ 2.4 gm. 2-benzamido-5-phenyl-1,3,4-thiadiazole. F. e. s. E. Hoggarth, *Soc.* 1949, 1163.

Hydrochloric acid

HCl

Thiazolines

664.



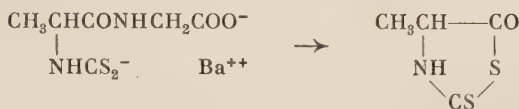
N-Benzoylpenicillamine refluxed with dil. HCl under N_2 for 16 hrs. $\rightarrow$ 2-phenyl-4-carboxy-5,5-dimethylthiazoline. Y: 91% (p. 471). F. e. s. H. M. Crooks, Jr., *Chemistry of Penicillin* 1949, 455.

Nitrogen $\downarrow$ *Hydrochloric acid***Thiazolidones****Elimination of terminal moieties from peptides**SC $\uparrow$ N

HCl

○

665.



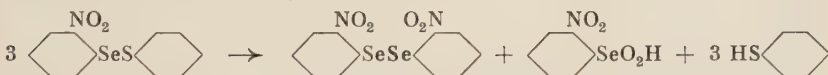
Ba-(N-dithiocarboxyalanyl)glycine in water acidified with *N* HCl $\rightarrow$ 2-thio-4-methylthiazolid-5-one. Y: 75%. F. e. s. A. L. Levy, Soc. 1950, 404.

Formation of Rem—Rem Bond**Exchange****Sulfur $\downarrow$** *Potassium hydroxide*RemRem $\uparrow\downarrow$ S

KOH

Diselenides from selenylsulfides $\leftarrow$

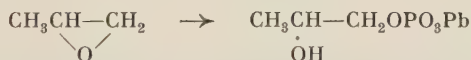
666.



o-Nitrobenzeneselenyl phenyl sulfide (prepn. s. 602) refluxed with aq.-alc. (1 : 1) KOH until the soln. is almost colorless $\rightarrow$ *o,o'*-dinitrodiphenyl diselenide (Y: 97.8%) *o*-nitrobenzeneseleninic acid (Y: 87.2%), and thiophenol (Y: 90.8%). H. Reinboldt and E. Giesbrecht, A. 568, 198 (1950).

Formation of Rem—C Bond**Uptake****Addition to Oxygen and Carbon***Potassium salt*RemC $\downarrow$ OCK⁺**Phosphoric acid esters from oxido compounds** $\leftarrow$

667.



Propylene oxide and K₂HPO₄ in water heated 12 hrs. in a pressure bottle on a steam bath, and the reaction product isolated as Pb-salt $\rightarrow$

Pb-propane-1,2-diol- α -phosphate. Y: 87%.—This procedure is especially adaptable to syntheses involving radioactive phosphorus. G. P. L. Lampson and H. A. Lardy, *J. Biol. Chem.* **181**, 697 (1949); f. e. s. **181**, 693.

Addition to Carbon

RemC ↓ CC

Without additional reagents

w.a.r.

Organo mercury compounds from ethylene derivatives



s. **1**, 498-500; s. a. G. A. Wiese and J. W. Jones, *J. Am. Pharm. Assoc.* **39**, 286 (1950); D. E. Pearson, M. V. Sigal, Jr., and R. H. Krug, *J. Org. Chem.* **15**, 1048, 1055 (1950)

Acyl peroxides



Silanes from ethylene derivatives

←

s. **3**, 534; with benzoyl peroxide s. G. N. Gadsby, *Research* **3**, 338 (1950)

Exchange

Hydrogen †

RemC †† H

Lithium

Li

Silanes



s. **3**, 535; s. a. H. Gilman and H. W. Melvin, Jr., *Am. Soc.* **71**, 4050 (1949); influence of the solvent s. W. H. Nebergall, *Am. Soc.* **72**, 4702 (1950)

Organo tin compounds



668.



Triphenyltin hydride treated with phenyl-Li, then benzyl chloride added to react with any triphenyltinlithium that might have been formed → tetraphenyltin. Y: 91%. G. Gilman and H. W. Melvin, Jr., *Am. Soc.* **71**, 4050 (1949).

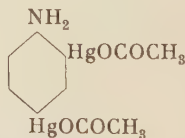
Sodium hydrogen carbonate



Mercuriation



669.



Aniline added with stirring at pH 4.25 to a mixture of glacial acetic acid, NaHCO_3 , and mercuric acetate → 2,4-diacetoxymercurianiline. Y: 93.5%.—Careful adjustment of the pH is essential for obtaining high yields. T. C. Bruice, *Am. Soc.* **72**, 1398 (1950).

Oxygen †**RemC † O***Magnesium**Mg***Arsonium salts from arsine oxides**

←



Phenyl-MgBr from bromobenzene and Mg in ether added with vigorous stirring to a soln. of triphenylarsine oxide (prepn. s. 153) in hot benzene, stirring continued for 15 min., then refluxed and stirred for 30 min., the addition product hydrolyzed with dil. HCl, and crystallized from concd. HCl $\rightarrow$ tetraphenylarsonium chloride hydrochloride. Y: 74-80%. R. L. Shriner and C. N. Wolf, *Org. Synth.* 30, 95 (1950).

Nitrogen †**RemC † N***Cuprous oxide**Cu₂O***Cyanoarsines from hydrazines
via chloroarsines**

←



Phenylhydrazine added slowly with stirring at 75° to a mixture of 25% excess technical grade arsenic acid and Cu₂O, extracted with CCl₄, and the extract shaken with concd. HCl $\rightarrow$ crude diphenylchloroarsine (Y of pure product 69-73%) treated during 0.5 hr. with ca. 10% excess of aq. 33%-NaCN at 60° with stirring, which is continued at the same temp. for 0.5 hr. $\rightarrow$ diphenylcyanoarsine (Y: ca. 85%; purity 87%). Overall Y: 60%. R. L. Barker et al., *J. Soc. Chem. Ind.* 68, 277 (1949).

Halogen †**RemC † Hal***Without additional reagents**w.a.r.***Phosphonic acid esters from
phosphites**

←

Arbusov rearrangement

s. 4, 597; s. a. F. W. Mitchell, Jr., and H. J. Lucas, *Am. Soc.* 72, 5779 (1950); A. H. Ford-Moore and B. J. Perry, *Org. Synth.* 31, 33 (1951)

*Lithium**Li***Silanes**

←

s. 3, 542; s. a. H. Gilman and G. N. R. Smart, *J. Org. Chem.* 15, 720 (1950)

Organo lead compounds

←



A soln. of methyl-Li in ether added during 20 min. to a suspension of PbI_2 in ether containing methyl iodide $\rightarrow$ ethereal soln. of tetramethyl-Pb (Y: ca. 100%) washed with dil. HCl and water, dried, cooled to -60° , and a soln. of Br in chloroform added with stirring $\rightarrow$ dimethyl-Pb-dibromide (Y: 92%). H. Gilman and R. G. Jones, Am. Soc. 72, 1760 (1950).

Sodium

Na

Tert. arsinesAsR₃

A mixture of AsCl_3 and chlorobenzene added dropwise with stirring over a period of 1.5-2 hrs. to powdered Na covered with benzene and heated on a steam bath, which is removed when the reaction mixture begins to boil, then stirred and refluxed 12 hrs. $\rightarrow$ triphenylarsine (startg. m. f. 153). Y: 88-97%. R. L. Shriner and C. N. Wolf, Org. Synth. 30, 95 (1950).

Sodium cyanide

NaCN

Cyanoarsines from chloroarsinesAsCl $\rightarrow$ AsCN

s. 6, 671

Sodium salt

Na⁺**Phosphonic acid esters
from phosphites**

s. 4, 604; s. a. B. A. Arbusov and B. P. Lugovkin, Ж. 21, 99 (1951); C. A. 45, 7002e

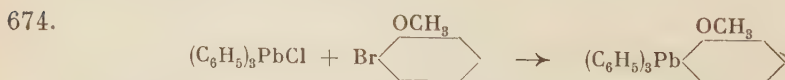
Potassium salt

K⁺**Selenocyanates from halides**Hal $\rightarrow$ SeCN

s. 3, 544; s. a. H. Reinboldt and H. Vieira de Campos, Am. Soc. 72, 2784 (1950)

Magnesium

Mg

Organo lead compounds $:\text{PbH} \rightarrow :\text{PbR}$ 

Triphenyllead chloride (prepn. s. 545) added to o-anisyl-MgBr (from o-bromoanisole and Mg in ether), diluted with ether and toluene after

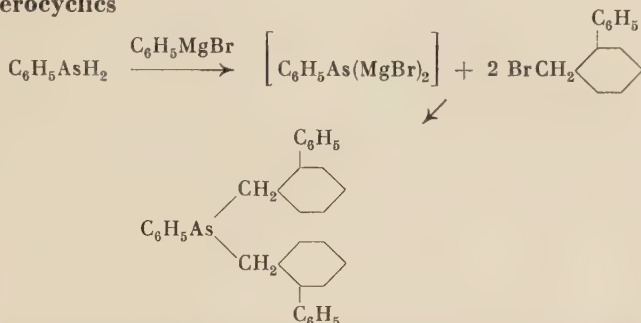
an initial brief period of vigorous refluxing, and heating continued under reflux for 1 hr. $\rightarrow$ (o-anisyl)triphenyllead. Y: 81%. F. e. s. H. Gilman and D. S. Melstrom, *Am. Soc.* 72, 2953 (1950).

Arsines via arsenic magnesium compounds

←

As-Heterocyclics

675.



A soln. of phenylarsine in benzene added with cooling to phenyl-MgBr, from bromobenzene and Mg in ether, refluxed 30 min., cooled, a soln. of o-phenylbenzyl bromide in benzene added during 20 min., refluxed 1 hr., cooled, and hydrolyzed with aq. $\text{NH}_4\text{Cl} \rightarrow$ phenylbis-(o-phenylbenzyl)arsine. Crude Y: 94%. G. H. Cookson and F. G. Mann, *Soc.* 1949, 2888; As-heterocyclics s. *Soc.* 1950, 1917, 1923.

Remaining Elements †

RemC † Rem

Zinc oxide

ZnO

Chloroarsines

←

676.



ZnO added in small portions to a 3 : 1 mixture of phenyldichloroarsine (prepn. s. 542) and phenylarsenoxide, placed in a mild steel flask, with stirring at 60°, then the temp. raised rapidly to 120°, and maintained at this temp. with stirring for 2.5 hrs. $\rightarrow$ diphenylchloroarsine. Y: 93.6%. R. L. Barker et al., *J. Soc. Chem. Ind.* 68, 295 (1949).

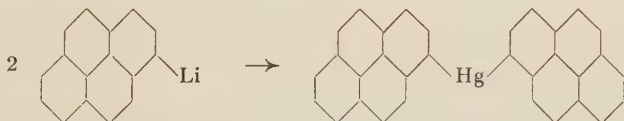
Mercuric chloride

 HgCl_2

Diaryl mercury from aryl lithium

←

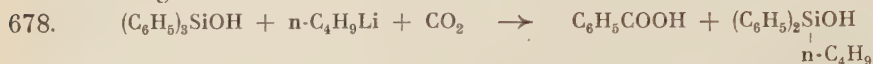
677.



Finely powdered HgCl_2 added to an ethereal suspension of 3-pyrenyl-Li, and shaken for 12 hrs. after the initial vigorous reaction subsides $\rightarrow$ di-3-pyrenyl-Hg. Y: 80.4%. A. Berg, *Acta Chem. Scand.* 3, 655 (1949).

Carbon †**RemC † C***Lithium**Li***Cleavage of silanes and silanols**

←



An ethereal soln. of *n*-butyl-Li added slowly with vigorous agitation to an ethereal soln. of triphenylsilanol in an atmosphere of dry N_2 , refluxed 24 hrs., and poured on crushed Dry Ice $\rightarrow$ benzoic acid (Y: 76%) and diphenyl-*n*-butylsilanol (Y: 86%).—*n*-Butyl-Li attacks the C-Si bond rather than the C-H bond as in triphenylcarbinol where metalation of the ar. nucleus occurs. F. e. and limitations s. H. Gilman, R. A. Benkeser, and G. E. Dunn, Am. Soc. 72, 1689 (1950).

Formation of C—C Bond**Uptake****Addition to Hydrogen and Carbon****CC ↓ HC***Potassium amide**KNH₂***Carboxylic acids from hydrocarbons** $\text{H} \rightarrow \text{COOH}$ **Synthesis with addition of 1 C-atom**

s. 4, 614; s. a. Am. Soc. 72, 3290 (1950); M. C. Kloetzel and H. E. Mer-tel, Am. Soc. 72, 4786 (1950)

Kolbe synthesis of**phenolcarboxylic acids from phenols**

s. 4, 615; s. a. M. 81, 1071 (1950)

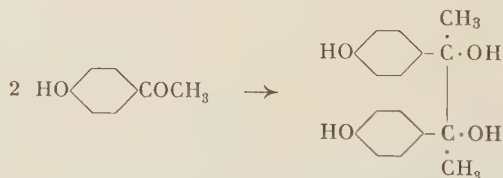
Addition to Oxygen and Carbon**CC ↓ OC***Electrolysis*

↘

Pinacols

←

679.



A soln. of *p*-hydroxyacetophenone in 2 *N* NaOH electrolyzed with Hg-cathode, Pt-anode, — 2.2 v, and an initial current of 3.5 amp., at 35°,

under N_2 , for 20 min. $\rightarrow$ 2,3-bis-(p-hydroxyphenyl)-2,3-butanediol (startg. m. f. 719). Y: 77%. F. e. s. M. J. Allen, *J. Org. Chem.* 15, 435 (1950); *Am. Soc.* 72, 114, 117, 3797 (1950).

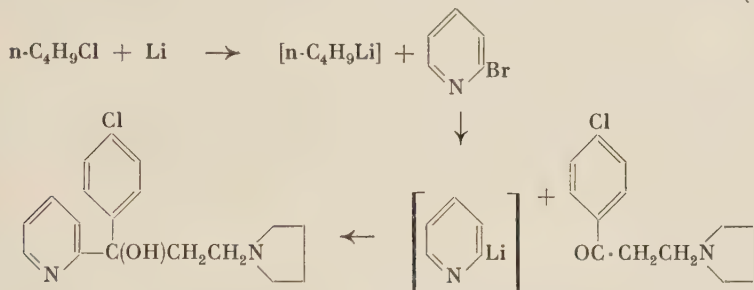
Lithium

Li

Tert. alcohols from ketones

CO $\rightarrow$ C(OH)R

680.



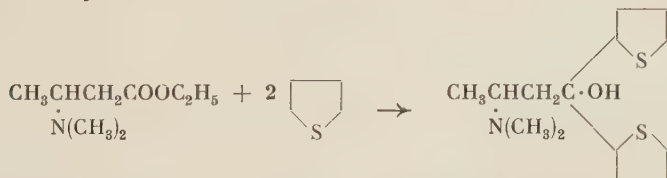
n-Butyl chloride in anhydrous ether added dropwise with stirring under N_2 to freshly sliced Li mixed with a few glass beads, the reaction initiated by warming, and thereafter the rate of addition adjusted to maintain gentle reflux, after the addition (ca. 30 min.) refluxed with stirring for 1 hr., excess Li removed by filtration, the filtrate cooled to -45° , 2-bromopyridine in anhydrous ether added during 15 min., stirring continued for 6 min., p-chlorophenyl- β -pyrrolidinopropiophenone in anhydrous ether added dropwise during 20 min., the temp. allowed to rise to -15° , and stirring continued for 30 min. $\rightarrow$ 3-pyrrolidino-1-(p-chlorophenyl)-1-(2-pyridyl)propan-1-ol. Y: 69%.—Omitting to remove excess Li reduced the yield of carbinols from p-chlorophenyl ketones, but those from the unsubst. phenyl ketones were not affected. F. e. s. D. W. Adamson and J. W. Billingham, *Soc.* 1950, 1039.

s. a. J. D. Sculley and N. H. Cromwell, *J. Org. Chem.* 16, 94 (1951).

Amino-tert.-alcohols from aminocarboxylic acid esters

COOR $\rightarrow$ C(OH)R₂

681.



Thiophene in ether added under N_2 to an ethereal soln. of phenyl-Li, prepared from bromobenzene and Li in ether, refluxed 2 hrs., ethyl β -dimethylaminobutyrate in ether added gradually with stirring at -20° , stirring continued for 1 hr. at room temp., and kept overnight $\rightarrow$ 3-dimethylamino-1,1-di-2'-thienylbutan-1-ol. Y: 71%. F. e. s. D. W. Adamson, *Soc.* 1950, 885.

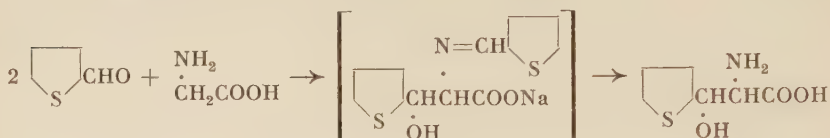
Sodium hydroxide

NaOH

α-Aminoalcohols from aldehydes

←

682.



2-Thiophenecarboxaldehyde added in one portion at room temp. to a soln. of glycine in aq. NaOH, stirring continued ca. 0.5 hr., allowed to stand 24 hrs., and the Schiff base obtained macerated with concd. HCl in a mortar → 2-thiopheneserine. Y: 79%. G. Weitnauer, G. 81, 162 (1951); f. e. s. G. 79, 856 (1949).

Potassium hydroxide

KOH

Acetylenealcohols from ketones

CO → C(OH)C:CR

s. 3, 552; s. a. P. Cadot and A. Willemart, Bl. 1951, 100; vinyl ethynyl derivatives s. I. N. Nazarov et al., Ж. 20, 2009, 2021 (1950); C. A. 45, 5636i, 5637f

α-Nitroalcohols from aldehydesCHO → CH(OH)CH(NO₂)R

s. 6, 772

Haloform condensationCO → C(OH)CCl₃

s. 4, 623; s. a. Am. Soc. 72, 5012 (1950)

Sodium/alcohol

NaOR

Synthesis of lactones from oxido compounds

←

s. 3, 554; s. a. E. E. Van Tamelen, G. Van Zyl, and G. D. Zuidema, Am. Soc. 72, 488 (1950)

Potassium alkoxide

KOR

Ethynylalcohols from oxo compounds

CO → C(OH)C≡CH

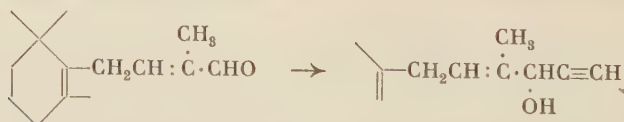
s. 2, 593; with K-tert-butoxide s. C. Djerassi, R. Yadin, and G. Rosenkranz, Am. Soc. 72, 5750 (1950)

Lithium/liq. ammonia

Li/NH₃**Ethynylalcohols from aldehydes**

CHO → CH(OH)C:CH

683.



A rapid stream of dry acetylene passed through a stirred suspension of Li in liq. NH₃, cooled in a CO₂-alcohol bath; when all the Li had

reacted γ -(2,6,6-trimethylcyclohex-1-enyl)- α -methylcrotonaldehyde in ether added dropwise, and stirred overnight, a slow stream of acetylene being passed in throughout $\rightarrow$ 6-(2',6',6'-trimethylcyclohex-1'-enyl)-4-methylhex-4-en-1-yn-3-ol. Y: 75% (33% with Na-acetylide). I. Heilbron et al., Soc. 1949, 1516; s. a. N. A. Milas et al., Am. Soc. 70, 1584 (1948); from α,β -ethyleneketones, also with Ca, s. W. Oroshnik and A. D. Mebane, Am. Soc. 71, 2062 (1949).

Sodium hydrogen carbonate

NaHCO_3

Hydroxymethylation of ketones

$\text{H} \rightarrow \text{CH}_2\text{OH}$

s. 6, 749

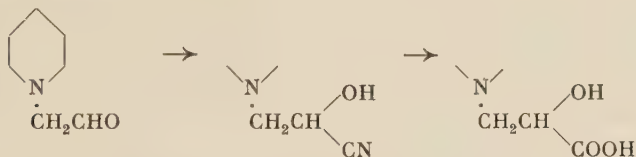
Sodium cyanide

NaCN

α -Hydroxycarboxylic acids from aldehydes via cyanohydrins

$\leftarrow$

684.



An aq. soln. of piperidinoacetaldehyde hydrochloride added slowly to an ice-cold aq. soln. of $\text{NaCN} \rightarrow \alpha$ -hydroxy- β -piperidinopropionitrile (Y: 95%) refluxed 4 hrs. with concd. HBr , the excess acid removed by distillation at atmospheric pressure until a solid separated, then further concentrated by evaporation on a steam-cone aided by a stream of air $\rightarrow \alpha$ -hydroxy- β -N-piperidinopropionic acid (Y: 92%). R. Adams and V. V. Jones, Am. Soc. 71, 3826 (1949).

Sodium hydrogen sulfite

NaHSO_3

Cyanohydrins from oxo compounds

$\text{CO} \rightarrow \text{C}(\text{OH})\text{CN}$

from aldehydes s. 4, 625; s. a. H. Rapoport, A. R. Williams, and M. E. Cisney, Am. Soc. 73, 1414 (1951); from ketones s. M. Stoll, L. Ruzicka, and C. F. Seidel, Helv. 33, 1245 (1950)

Diethylamine

$(\text{C}_2\text{H}_5)_2\text{NH}$

α -Nitroalcohols from aldehydes

$\text{CHO} \rightarrow \text{CH}(\text{OH})\text{CH}(\text{NO}_2)\text{R}$

s. 3, 559; s. a. D. J. Cook, D. Dock, and R. Shrontz, Am. Soc. 72, 4989 (1950)

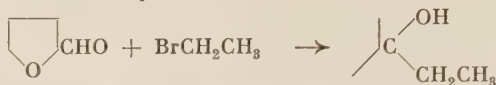
Magnesium

Mg

Sec. alcohols from aldehydes



685.

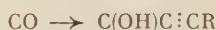


Furfural in ether added with stirring at ca. -15° to ethereal ethyl-MgBr, heated 0.5 hr. on a steam bath, cooled, decomposed with water, the ether extract washed with 40% NaHSO_3 , and distilled in the presence of 10-12 drops of aniline to eliminate traces of acid → ethyl-2-furylcarbinol. Y: 89%. F. e. with lower yields s. Y. K. Yur'ev and I. P. Gragerov, *Ж.* 19, 724 (1949); C. A. 44, 1092c.

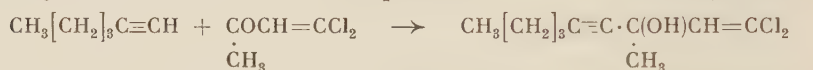
 α,β -Ethylenealcohols

s. 6, 764

Acetylenealcohols from oxo compounds



686.



An ethereal soln. of 1-hexyne added with ice-cooling during 2 hrs. to ethereal ethyl-MgBr, refluxed 3 hrs., then methyl 2,2-dichlorovinyl ketone (prepn. s. 814) in dry ether added slowly with cooling, and allowed to stand overnight → 1,1-dichloro-3-methylnon-1-en-4-yn-3-ol. Y: 85%.—The condensation with Na-acetylide in liq. NH_3 was not successful in this case. F. e. s. I. M. Heilbron, E. R. H. Jones, and M. Julia, *Soc.* 1949, 1430; s. a. P. Karrer and P. Schneider, *M.* 81, 111 (1950).

Amino-tert.-alcohols from aminoketones



s. 1, 679; s. a. A. W. Ruddy and J. S. Buckley, Jr., *Am. Soc.* 72, 718 (1950); J. J. Denton et al., *Am. Soc.* 72, 3795 (1950)

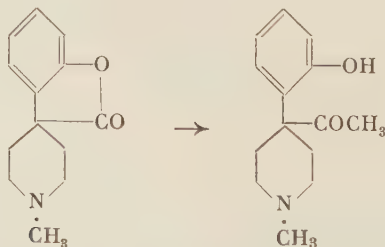
Diols from lactones

C

s. 5, 477; s. a. W. Baker, R. F. Curtis, and J. F. W. McOmie, *Soc.* 1951, 76

Hydroxyketones from lactones

687.



1-Methyl-4-o-hydroxyphenylpiperidine-4-carboxylic acid lactone hydrobromide (prepn. s. 240) added to ice-cold ethereal methyl-

MgBr, stirred 1/2 hr. in the cold, then 10 min. under reflux → 1-methyl-4-o-hydroxyphenyl-4-piperidyl methyl ketone. Y: 82%. F. e. s. H. Kägi and K. Miescher, *Helv.* 32, 2489 (1949).

Magnesium/magnesium iodide

Mg/MgI₂

Pinacols

←

s. 1, 689; s. a. R. Moubasher, *Soc.* 1950, 2243

Calcium/liq. ammonia

Ca/NH₃

Ethynylalcohols from aldehydes

CHO → CH(OH)C≡CH

s. 6, 683

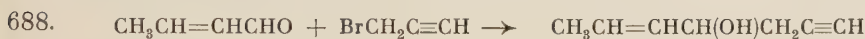
Zinc

Zn

Reformatskii synthesis

CO → C(OH)C≡CH

of acetylenalcohols from oxo compounds

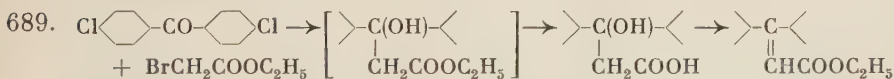


A mixture of freshly distilled crotonaldehyde and propargyl bromide in dry ether added to Zn wool covered with benzene, a part of which has been distilled off to remove traces of water, and refluxed 5 min. → 5-hepten-1-yn-4-ol. Y: 67%.—Occasionally, when the reaction is difficult to start, addition of a little HgCl₂ proves effective. F. e. s. H. B. Henbest, E. R. H. Jones, and I. M. S. Walls, *Soc.* 1949, 2696; 1950, 3634; s. a. R. Golse, J. Gavaret, and G. Demange, *Bl.* 1950, 285; P. Karrer and C. H. Eugster, *Helv.* 34, 28 (1951).

Reformatskii synthesis of carboxylic acid esters

←

Dehydration with simultaneous esterification



Excess 30-mesh Zn, activated according to Fieser and Johnson, *Am. Soc.* 62, 575 (1940), and a crystal of iodine added to a soln. of 4,4'-dichlorobenzophenone and excess ethyl bromoacetate in anhydrous benzene-toluene, refluxed with stirring for ca. 30 min. until the exothermic reaction starts, cooled with cold water during the next 20 min., refluxed 2 more hrs. after the reaction has subsided, and the ester, so obtained, hydrolyzed by refluxing with KOH in ethanol-water for 2 hrs. → β,β-bis-(p-chlorophenyl)hydraacrylic acid (Y: 92.3%) dissolved in abs. alcohol, anhydrous HCl passed through for 4 hrs., and refluxed during the last hr. → ethyl β,β-bis-(p-chlorophenyl)acrylate (Y: 83.5%). J. F. Freeman and E. D. Amstutz, *Am. Soc.* 72, 1522 (1950); Reformatskii synthesis s. a. R. C. Gilmore, Jr., and W. J. Horton, *Am. Soc.* 73, 1411 (1951).

Aluminum chloride

 $AlCl_3$ **Ketocarboxylic acids from dicarboxylic acid anhydrides** $\leftarrow$

s. 1, 519; 2, 601; 3, 566; 4, 635 a; s. a. J. A. McRae, R. A. B. Bannard, and R. B. Ross, *Can. J. Research* 28B, 73 (1950); in s-tetrachloroethane s. R. R. Burtner and J. M. Brown, *Am. Soc.* 73, 897 (1951)

690.



with migration of a carbon double bond. A soln. of itaconic anhydride in dry benzene treated with finely powdered anhydrous $AlCl_3$, the reaction started by slight warming, and after subsiding refluxing continued for 3 hrs. $\rightarrow$ β -benzoyl- α -methylacrylic acid. Y: 78%. S. Dixon, H. Gregory, and L. F. Wiggins, *Soc.* 1949, 2139.

Addition to Nitrogen and CarbonCC $\downarrow$ NC

Without additional reagents

w.a.r.

1-Acyl-1,2-dihydroquinaldonitriles $\leftarrow$

(Reissert compounds)

from carboxylic acid chlorides

s. 6, 122

Pyridine

 C_5H_5N **Cyanoformamides from isocyanates**N:C:O $\rightarrow$ NHCOCN

691.



Anhydrous HCN added to a soln. of 252 gm. hexamethylene diisocyanate in toluene, cooled, pyridine added, and allowed to stand overnight $\rightarrow$ 290 gm. N,N'-dicyanoformylhexamethylenediamine. F. e. s. S. Petersen, A. 562, 205 (1949).

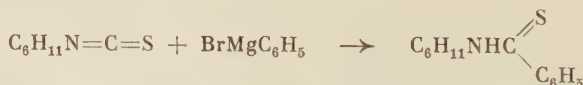
Magnesium

Mg

Subst. carboxylic acid thioamidesN:C:S $\rightarrow$ $\text{NHC} \begin{array}{c} \text{S} \\ \diagup \quad \diagdown \\ \text{R} \end{array}$

from isothiocyanates

692.



Cyclohexyl isothiocyanate in ether added below 5° with stirring to ethereal phenyl-MgBr, stirring continued at 5° for 1 hr., then allowed to come to room temp. $\rightarrow$ N-cyclohexylthiobenzamide. Y: 88%. F. e. s. G. Alliger et al., *J. Org. Chem.* 14, 962 (1949).

Zinc chloride

ZnCl₂**Hoesch synthesis of ketones**CN $\rightarrow$ COR

s. 1, 618; 2, 606/7; s. a. W. B. Whalley, Soc. 1951, 665

Aluminum chloride

AlCl₃**Aminoketones from aminonitriles**CN $\rightarrow$ COR**Hoesch synthesis**

693.



Aminoketones from aminonitriles. Phenol and methylaminoacetonitrile hydrochloride added all at once with shaking to a soln. of AlCl₃ in nitrobenzene, then a current of dry HCl passed through at 20-30° with stirring for 3 hrs. $\rightarrow$ p-hydroxy- ω -(methylamino)acetophenone. Y: 75%. F. e. s. M. Asscher, R. 68, 960 (1949).

Addition to Sulfur and CarbonCC $\downarrow$ SC

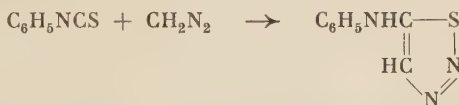
Without additional reagents

w.a.r.

1,2,3-Thiadiazoles from isothiocyanates and diazomethane

○

694.



Cold ethereal diazomethane added to ethereal phenylisothiocyanate, then allowed to stand at room temp. for 1 hr. and at 0-5° overnight $\rightarrow$ 5-anilino-1,2,3-thiadiazole. Y: 60%. J. C. Sheehan and P. T. Izzo, Am. Soc. 71, 4059 (1949).

Addition to CarbonCC $\downarrow$ CC

Without additional reagents

w.a.r.

Subst. succinic acid anhydrides from maleic acid anhydride $\leftarrow$

s. 5, 487; s. a. R. T. Arnold, R. W. Amidon, and R. M. Dodson, Am. Soc. 72, 2871 (1950); C. S. Rondestvedt, Jr., Org. Synth. 31, 85 (1951)

Diene synthesis

○

Diels-Alder reaction

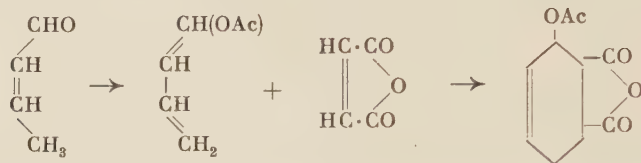
s. 1, 526-9; 2, 609-11; 3, 576; s. a. G. O. Schenck, B. 82, 123 (1949); with unsym. addends s. K. Alder et al., A. 564, 79, 120 (1949); with naphthalenes s. M. C. Kloetzel, R. P. Dayton, and H. L. Herzog, Am. Soc.

72, 273, 1991 (1950); with $\alpha,\beta,\gamma,\delta$ -unsatd. carboxylic acids s. N. C. Deno, Am. Soc. 72, 4057 (1950)

Diene synthesis via enolesters

Polymerization inhibitors

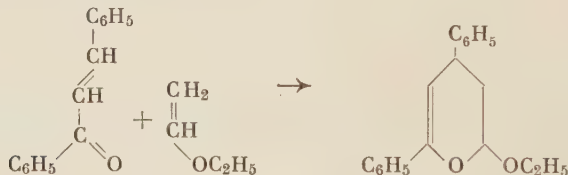
695.



Crotonaldehyde, acetic anhydride, and anhydrous Na-acetate heated 5 hrs. under reflux at 160°, cooled, filtered, distilled, a little thionine as polymerization inhibitor and maleic anhydride in acetone added, and heated 0.5 hr. on a water bath $\rightarrow$ 3-acetoxy-1,2,3,6-tetrahydropthalic anhydride (startg. m. f. 864). Y: up to 95% based on reacted maleic anhydride. F. e. and inhibitors s. W. Flaig, A. 568, 1 (1950).

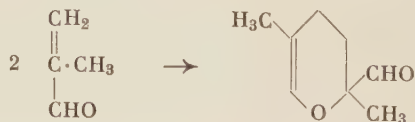
Pyrans, dihydro- from α,β -ethyleneoxo compounds

696.



Benzalacetophenone, ethyl vinyl ether, and a small amount of hydroquinone (as polymerization inhibitor) heated 13 hrs. at 180° in an autoclave $\rightarrow$ 2-ethoxy-4,6-diphenyl-3,4-dihydro-1,2-pyran (startg. m. f. 172). Y: 74%. F. e. s. R. I. Longley, Jr., and W. S. Emerson, Am. Soc. 72, 3079 (1950).

697.

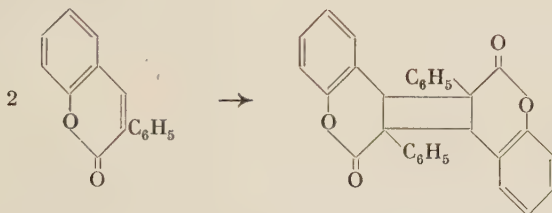


Dimers by polymerization reaction. Freshly distilled methacrylaldehyde containing a little hydroquinone heated in a sealed tube at 140-150° for 44 hrs. $\rightarrow$ 3,4-dihydro-2,5-dimethyl-2H-pyran-2-carboxaldehyde. Y: 89%. G. G. Stoner and J. S. McNulty, Am. Soc. 72, 1531 (1950).

Light

**Cyclobutane ring from
ethylene derivatives
Photodimerization**

698.



3-Phenylcoumarin in benzene exposed to sunlight for 1 month $\rightarrow$ photodimer. Y: ca. 90%. F. e. s. A. Schönberg et al., Soc. 1950, 374.

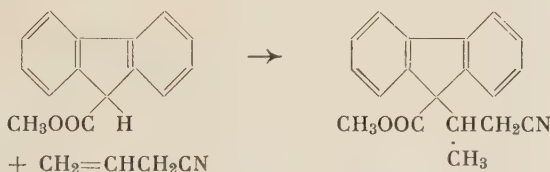
Potassium hydroxide

KOH

C-Cyanoethylation

H $\rightarrow$ CH₂CH₂CN

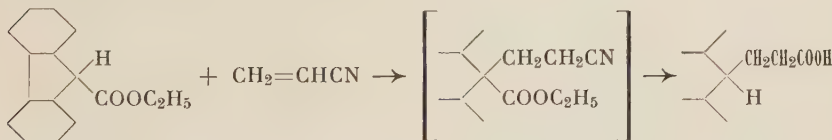
699.



Dioxane, KOH, allyl cyanide, and methyl fluorene-9-carboxylate mixed in that order, and allowed to stand at room temp. for 4 days $\rightarrow$ 2-(9'-carbomethoxy-9'-fluorenyl)propyl cyanide. Y: 73%.—2-Methoxyethanol can be used in place of dioxane as a solvent. Other reaction conditions (s. original paper) were not successful. S. H. Tucker, Soc. 1949, 2182.

**Subst. propionic acids from
carboxylic acid esters via
 α -(2-cyanoethyl)carboxylic acid esters**

700.

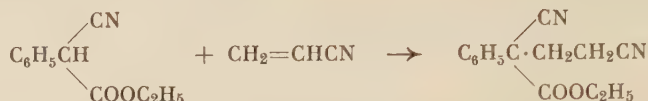


Ethyl 9-fluorencarboxylate, then vinyl cyanide added to a soln. of KOH in 2-methoxyethanol, after 15 min. treated with aq. 10 N KOH, then with more 2-methoxyethanol, and boiled 30 min. $\rightarrow$ β -9-fluorene-propionic acid. Y: 90%. Also isolation of the intermediates s. A. Campbell and S. H. Tucker, Soc. 1949, 2623; with Triton B s. T. Holbro and E. Tagmann, Helv. 33, 2178 (1950).

Potassium hydroxide/alcohol

**C-Cyanoethylation of
α-cyanocarboxylic acid esters**

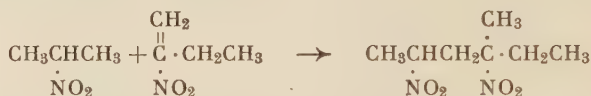
701.



A soln. of acrylonitrile in *tert*-butanol added dropwise to a soln. of ethyl phenylcyanoacetate in *tert*-butanol at 40-45°, while some methanolic 30%-KOH is added in 2 portions; when the exothermic reaction subsides, warmed in a water bath at 40-45° for 1 hr., then allowed to stand overnight → α-phenyl-α-carbethoxyglutaronitrile. Y: 69-83%. E. C. Horning and A. F. Finelli, *Am. Soc.* **71**, 3204 (1949); *Org. Synth.* **30**, 80 (1950).

β-Dinitro compounds, aliphatic

702.



Fresh 2-nitro-1-butene added at 18-20° in small portions with vigorous stirring over a period of 30 min. to the K-salt of 2-nitropropane, prepared with alc. KOH, dil. with water, and acidified with acetic acid → 3,5-dinitro-3-methylhexane. Crude Y: 90%. F. e. s. C. T. Bahner and H. T. Kite, *Am. Soc.* **71**, 3597 (1949).

Sodium/alcohol

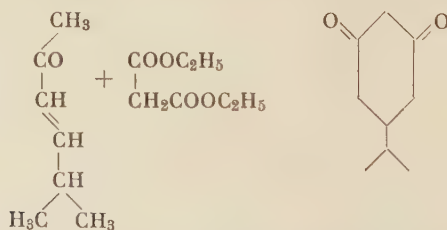
NaOR

Michael addition

←

s. 5, 494; s. a. D. Ginsburg and R. Pappo, *Soc.* **1951**, 938; D. L. Turner, *Am. Soc.* **73**, 1284 (1951)

703.



Cyclohexanediones. Ethyl malonate and isobutyrideneacetone added to a soln. of Na in abs. ethanol, refluxed 1 hr., additional abs. ethanol added, refluxing continued for 2 more hrs., aq. KOH added, and refluxed an additional 6 hrs. → 5-isopropyl-1,3-cyclohexanedione. Y: 80%. R. L. Frank and H. K. Hall, Jr., *Am. Soc.* **72**, 1645 (1950).

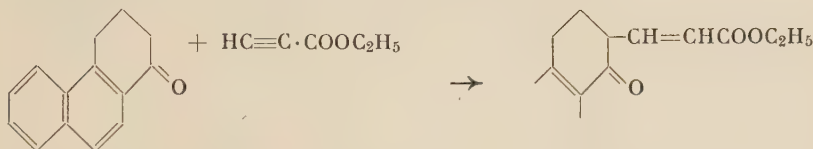
Sodium amide

NaNH₂

**α,β-Ethylene-δ-ketocarboxylic
acid esters**
from ketones and propiolic esters

←

704.



Semiaromatic ketones, in the presence of NaNH₂, undergo a Michael reaction with propiolic esters, whereas these esters are added to the carbonyl group of purely alicyclic ketones to form α,β-acetylenic γ-hydroxyesters.—E: 1-Keto-1,2,3,4-tetrahydrophenanthrene allowed to react with ethyl propiolate and NaNH₂ in liq. NH₃ → ethyl β-(1-keto-1,2,3,4-tetrahydro-2-phenanthrene)acrylate. Y: 83%. F. e. s. W. E. Bachmann, E. K. Raunio, and G. I. Fujimoto, *Am. Soc.* 72, 2533, 2530 (1950).

Potassium cyanide

KCN

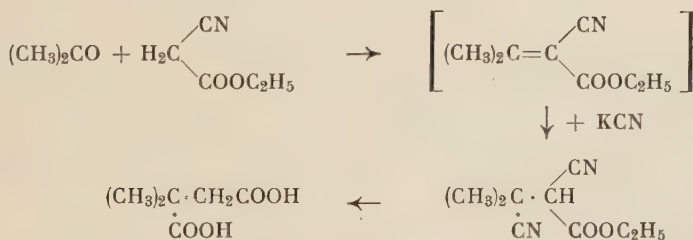
Nitriles from ethylene derivatives

C:C → CHC(CN)

s. 3, 583; s. a. P. Kurtz, *A.* 572, 23 (1951); A. C. Cope and S. W. Fenton, *Am. Soc.* 73, 1668 (1951)

Unsym. subst. succinic acids
Dicarboxylic acids from
dicyanodicarboxylic acid esters

705.



A mixture of dry acetone, ethyl cyanoacetate, pyridine, and glacial acetic acid refluxed 1 hr., abs. ethanol added; as soon as active boiling subsides, KCN added, and refluxed ca. 1 hr. more → ethyl α,β-dicyano-β-methylbutyrate (Y: 70%) refluxed with concd. HCl for 8 hrs. → α,α-dimethylsuccinic acid (Y: 76%). F. e. s. P. A. S. Smith and J. P. Horwitz, *Am. Soc.* 71, 3418 (1949); s. a. E. J. Cragoe, Jr., C. M. Robb, and J. M. Sprague, *J. Org. Chem.* 15, 381 (1950).

Triton B

←

C-CyanoethylationH → CH₂CH₂CN

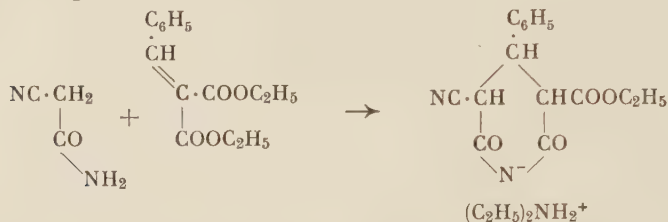
s. 5, 497; s. a. N. A. Acara and R. Levine, *Am. Soc.* **72**, 2864 (1950);
W. E. Bachmann and L. B. Wick, *Am. Soc.* **72**, 3388 (1950)

Diethylamine

(C₂H₅)₂NH**Pyridine ring from cyanoacetamides**

○

706.



A suspension of 0.8 gm. cyanoacetamide in 2.5 gm. ethyl benzylidene-malonate treated with diethylamine, after 3 days dissolved in alcohol by heating, some fresh diethylamine added, and worked up on the following day → 2.8 gm. diethylammonium salt of 3-carbethoxy-5-cyano-2,6-diketo-4-phenylpiperidine. F. e. s. N. Palit, *J. Indian Chem. Soc.* **26**, 501 (1949).

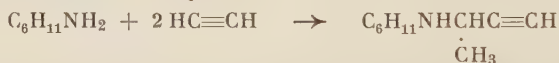
Cuprous chloride

CuCl

Synthesis of 3-amino-1-butyne

←

707.



Cyclohexylamine and CuCl in tetrahydrofuran treated at 106° with acetylene-N₂ under pressure → 3-cyclohexylamino-1-butyne. Y: 70%. F. e. s. J. D. Rose et al., *Soc.* **1949**, 780, 792.

Cuprous iodide/magnesium

CuI/Mg

tert-Alkyl-α-cyanoacetic esters from alkylidene-α-cyanoacetic esters

←

s. 2, 616; cf. E. R. Alexander, J. D. McCollum, and D. E. Paul, *Am. Soc.* **72**, 4791 (1950)

Magnesium

Mg

Synthesis of hydrocarbons from ethylene derivatives

C:C → CHCR

708.



The presence of a mesityl radical in the β-position of an α,β-ethylene ester or unhindered ketone does not prevent conjugate addition of

mesityl-Mg-bromide.—E: A soln. of mesitalacetophenone (prep. s. 740) in dry benzene-ether added to a Grignard reagent, prepared from bromomesitylene, Mg, and dry ether, then stirred and refluxed 2 hrs., and hydrolyzed by a satd. soln. of $\text{NH}_4\text{Cl} \rightarrow \beta, \beta$ -dimesitylpropiofenone. Y: 84%. R. C. Fuson and H. L. Jackson, *Am. Soc.* 72, 1637 (1950).

Alumina/silica

$\text{Al}_2\text{O}_3/\text{SiO}_2$

Alkylation of the nucleus with ethylene derivatives

s. 3, 585; s. a. V. N. Ipatieff, E. E. Meisinger, and H. Pines, *Am. Soc.* 72, 2772 (1950)

Aluminum chloride

AlCl_3

Polyhalides

$\text{C}:\text{C} \rightarrow \text{CHalCR}$

Prins reaction

s. 3, 586; 4, 660; s. a. H. J. Prins, *R.* 69, 1003 (1950)

Acyl peroxides

$(\text{RCOO})_2$

Addition of polyhalides

←

to unsaturated carbon carbon bonds

addition to double bonds s. 3, 587; 4, 665; G. Dupont, R. Dulou, and P. Guantin, *Bl.* 1951, 59; addition to triple bonds s. M. S. Kharasch, J. J. Jerome, and W. H. Urry, *J. Org. Chem.* 15, 966 (1950)

Acetic acid

CH_3COOH

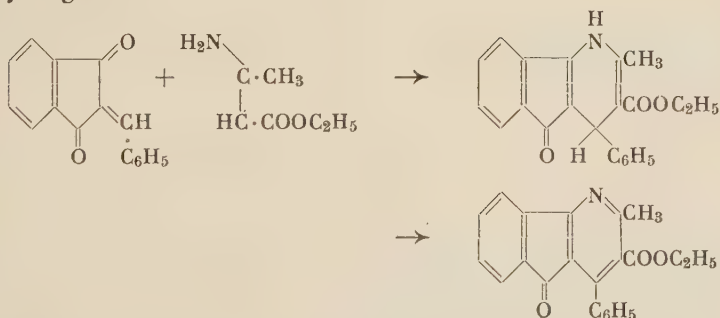
Pyridine ring synthesis

○

4-Azafluorenones

Dehydrogenation

709.



A soln. of benzylideneindane-1,3-dione in acetic acid treated at the boiling point with ethyl β-aminocrotonate $\rightarrow$ ethyl 1-phenyl-3-methyl-1,4-dihydro-4-azafluorenone-2-carboxylate (Y: 87%) dissolved in warm acetic acid and treated with aq. CrO_3 for 5 min. $\rightarrow$ ethyl 1-phenyl-3-methyl-4-azafluorenone-2-carboxylate (Y: 88%). F. e. s. V. Petrow et al., *Soc.* 1949, 2134, 2128.

Sulfuric acid H_2SO_4 **Synthesis of hydrocarbons from ethylene derivatives** $C:C \rightarrow CHCR$ **Isocyclics**s. 5, 506; s. a. R. Truffault and Y. Monteils, *Bl.* 1951, 97**Alkylation of thiophenes with olefins**s. 5, 507; cf. H. Pines, B. Kvetinskas, and J. A. Vesely, *Am. Soc.* 72, 1568 (1950)**m-Dioxanes from ethylene derivatives**

○

s. 4, 637

Hydrofluoric acid HF **One-step indanone ring synthesis**

s. 6, 819

Cobalt carbonyl $Co(CO)_4$ **Aldehydes from ethylene derivatives** $C:C \rightarrow CHC(CHO)$ **Synthesis with addition of 1 C-atom**s. 4, 667; s. a. W. E. Parham and H. E. Holmquist, *Am. Soc.* 73, 913 (1951)*Nickel carbonyl* $Ni(CO)_4$ **α,β -Ethylenecarboxylic acids from acetylene derivatives** $C:C \rightarrow CH:C \cdot COOH$

710.



The reaction between monosubst. acetylene derivatives, Ni-carbonyl, and water in the presence of acids leads to the formation of α -subst. acrylic acids. The products from β,γ -acetylenic carbinols cyclize spontaneously to lactones. With α,β -acetylenic carbinols, it is preferable to employ the acetates rather than the free alcohols.—E: Phenylethynylcarbinyl acetate, ethanol, glacial acetic acid, and water allowed to react at 70° with $Ni(CO)_4$ in ethanol $\rightarrow$ 3-acetoxy-3-phenylprop-1-ene-2-carboxylic acid. Y: 50%. F. e. s. E. R. H. Jones, T. Y. Shen, and M. C. Whiting, *Soc.* 1950, 230; *Soc.* 1951, 48; cf. E. D. Bergmann and E. Zimkin, *Soc.* 1950, 3455.

Rearrangement

Hydrogen/Carbon Type

CC $\curvearrowright$ HC

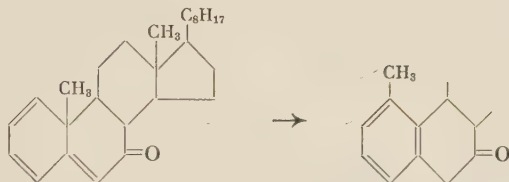
Without additional reagents

w.a.r.

Aromatization

←

711.



200 mg. $\Delta^{1,3,5(6)}$ -cholestatrien-7-one slowly heated to 160° , and kept at this temp. for 15 min. $\rightarrow$ 130 mg. 1-methyl- $\Delta^{1,3,5(10)}$ -nor 10 -cholestatrien-7-one. P. Karrer and A. R. Naik, *Helv.* **32**, 2392 (1949).

Sodium hydroxide

NaOH

Migration of carbon double bonds

←

Prototropic change

712.



0.82 gm. α -ethoxy- β -methylenebutyric acid heated 24 hrs. with aq. 5 N NaOH at $100^\circ \rightarrow$ 0.7 gm. α -ethoxy- β,β -dimethylacrylic acid. F. e. s. L. N. Owen and M. U. S. Sultanbawa, *Soc.* **1949**, 3089.

Sodium/alcohol

NaOR

Nitrocyclopropane ring opening

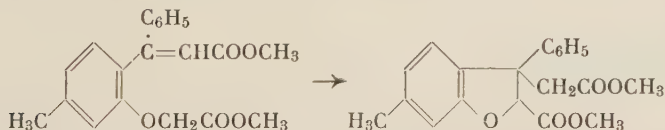
C

s. 6, 225

Heterocyclics by internal Michael addition

O

713.



A mixture of methyl 4-methyl- β -phenylcoumarinate 0-acetic acid methyl ester with 4 drops of a concd. soln. of Na-methoxide in methanol warmed to 60° , after which the temp. rises spontaneously to ca. 90° during 4 min. $\rightarrow$ methyl 3-carbomethoxymethyl-6-methyl-3-phenyl-2,3-dihydrocoumarilate. Y: 80%. F. e. s. C. F. Koelsch and C. R. Stephens, Jr., *Am. Soc.* **72**, 2209 (1950).

Sodium amide

NaNH₂**4-Amino-2-hydroxypyridine ring
from β -acyliminonitriles**

s. 5, 511; s. a. G. A. Reynolds et al., J. Org. Chem. 16, 165 (1951)

Boron fluoride/sulfuric acid

BF₃/H₂SO₄**Cycloisomerization**

714.



A soln. of benzyl 2-methylpropenyl sulfone in 95% -H₂SO₄ containing ca. 12% BF₃ heated 3 hrs. at 70° → 5,5-dimethyl-3,4-benzothiacyclohexane 1,1-dioxide. Y: 75%. F. e. s. H. J. Backer and N. Dost, R. 68, 1143 (1949).

Aluminum chloride

AlCl₃**Migration****of carbon double bonds**

s. 6, 690

←

Aluminum chloride/hydrochloric acid

AlCl₃/HCl**of alkyl groups**

s. 6, 833

Hydrazine/sodium/alcohol

H₂N·NH₂/NaOR**of carbon double bonds**

s. 6, 117

Phosphoric acid

H₃PO₄**Ring closure to isocyclics**

○

s. 5, 515; without H in the vinyl radical of the starting material s. Ж. 20, 1441 (1950); C. A. 45, 1964f

p-Toluenesulfonic acid

TsOH

cis-trans Rearrangement

←

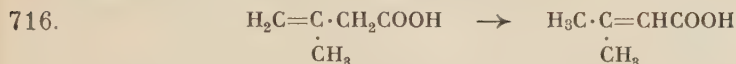
715.



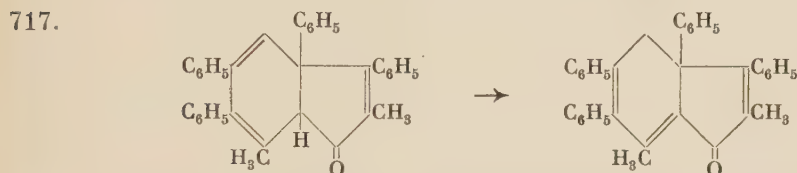
13.5 gm. *cis*-2-phenyl-2-butene slowly fractionated at 29.5 mm in the presence of a small amount of *p*-toluenesulfonic acid → 11.4 gm. *trans*-2-phenyl-2-butene.—The lower boiling *trans*-isomer can be distilled from the continually equilibrating mixture. D. J. Cram, Am. Soc. 71, 3883 (1949).

Sulfuric acid H_2SO_4 **Migration of carbon double bonds**

←



A mixture of 3-methyl-3-butenic acid, dry ether, and 90% H_2SO_4 allowed to stand at room temp. for 48 hrs. $\rightarrow$ β,β -dimethylacrylic acid. Y: 97%. R. B. Wagner, Am. Soc. 71, 3214 (1949).



to conjugated double bonds. 3,3a,5,6-Tetraphenyl-2,7-dimethyl-3a,7a-dihydroindenone and a little concd. H_2SO_4 in acetic acid warmed 2 hrs. on a steam bath $\rightarrow$ 3,3a,5,6-tetraphenyl-2,7-dimethyl-3a,4-dihydroindenone. Y: 92%. C. F. H. Allen and J. A. VanAllan, J. Org. Chem. 14, 1051 (1949).

Phenols from cyclic ketones with migration of alkyl groups

←

s. 5, 517; s. a. Am. Soc. 73, 364 (1951)

5-Methyl-2(3H)-thiazolethiones from 5-methylene-2-thiazolidinethiones

s. 6, 617

Iodine

I

cis-trans Rearrangement

←

s. 4, 669; s. a. J. A. Elvidge et al., Soc. 1950, 2235

Hydrochloric acid HCl **Chlorides from ethylene derivatives with rearrangement**

←

s. 6, 554

Palladium-carbon $Pd-C$ **Epimerization**

←

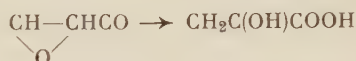
s. 6, 838

Oxygen/Carbon Type

CC↵OC

Sodium hydroxide

NaOH

 α -Hydroxycarboxylic acids from α,β -oxidoketones

s. 6, 901

Potassium hydroxide or ethyl sodium acetoacetate/pyridine

←

Baker-Venkataraman transformation

←

s. 6, 868

Dialkylaniline $\text{C}_6\text{H}_5\text{NR}_2$ **Allylphenols from allyl ethers**

←

Claisen rearrangement

s. 4, 674; s. a. Ng. Ph. Buu-Hoï, Soc. 1950, 2096

Aluminum chloride AlCl_3 **Unusual Fries rearrangement**

←

718.



In a few exceptional cases, the acyl group migrates to the m-position. —E: A soln. of 1-acetoxy-2,4-dimethoxybenzene in dry nitrobenzene added with cooling to AlCl_3 , and allowed to stand at 25° for 2 days $\rightarrow$ 2,4-dimethoxy-5-hydroxyacetophenone. Y: 50%. A. Ballio. G. 79, 924 (1949).

Sulfuric acid H_2SO_4 **Rearrangement to conjugated double bonds**

←

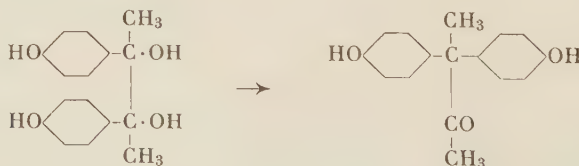
s. 2, 624/5; s. a. E. A. Braude and C. J. Timmons, Soc. 1950, 2007

Pinacol rearrangement

←

Deacetylation

719.



A few drops of concd. H_2SO_4 added to a suspension of 2,3-bis-(p-hydroxyphenyl)-2,3-butanediol (prepn. s. 679) in acetic anhydride,

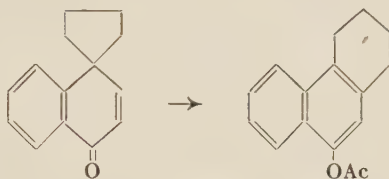
shaken until dissolved, poured on ice, and the diacetate so obtained hydrolyzed by heating with aq.-alc. KOH on a steam bath until all the alcohol has evaporated $\rightarrow$ 3,3-bis-(p-hydroxyphenyl)-2-butanone. Y: 80%. M. J. Allen, J. Org. Chem. 15, 435 (1950); pinacol rearrangement without acetic anhydride s. H. E. Zaugg, M. Freifelder, and B. W. Horrom, J. Org. Chem. 15, 1191 (1950).

Phenol acetates from dienones

←

s. 3, 597; s. a. R. B. Woodward and T. Singh, Am. Soc. 72, 494 (1950)

720.

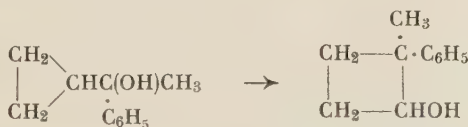


Ring enlargement. A soln. of 1-keto-4,4-tetramethylene-1,4-dihydronaphthalene in acetic anhydride treated with a soln. of H_2SO_4 in acetic anhydride, and allowed to stand 4 hrs. at room temp. $\rightarrow$ 1,2,3,4-tetrahydro-9-phenanthryl acetate. Y: 95%.—The rearrangement of *spiro*-dienones represents a new method, free of inhibiting steric factors, for the preparation of rings containing 6 or more C-atoms. R. T. Arnold, J. S. Buckley, Jr., and R. M. Dodson, Am. Soc. 72, 3153 (1950).

Cyclobutanes from cyclopropanes

←

721.



Methylphenylcyclopropylcarbinol boiled 5 hrs. with 25% H_2SO_4 $\rightarrow$ 1,1-methylphenyl-2-cyclobutanol. Y: 47%. T. A. Favorskaya and Sh. A. Fridman, Ж. 20, 581 (1950); C. A. 44, 7784f.

Nitrogen/Nitrogen Type

CC $\curvearrowright$ NN

Without additional reagents

w.a.r.

Thiazoles from thiosemicarbazides with benzidine rearrangement

←

s. 6, 646

Nitrogen/Carbon Type

CC ↙ NC

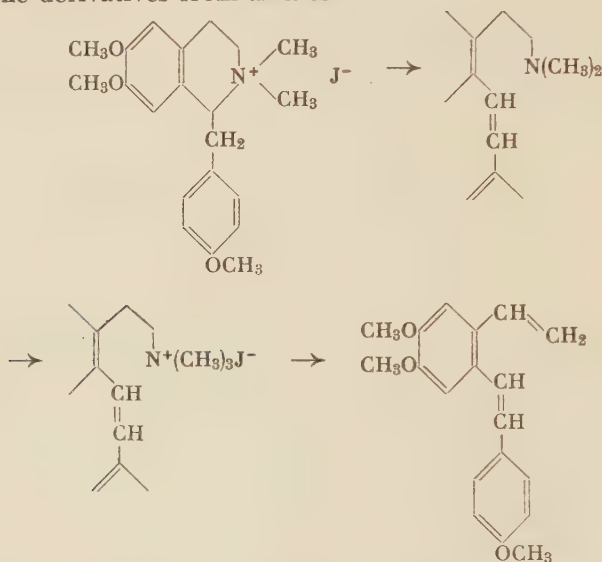
Sodium hydroxide

NaOH

Hofmann degradation
of quaternary ammonium salts
Ring opening
Ethylene derivatives from amines

←

722.

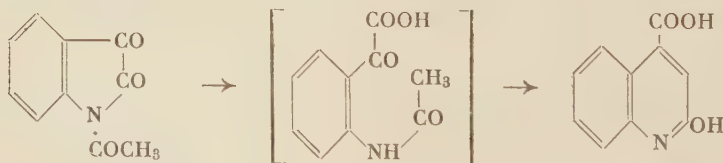


O-Methyl-dl-armepavine methiodide added to methanolic NaOH, and heated on a steam bath for 90 min. → des-O,N-dimethylarmepavine (Y: ca. 100%), 90 mg. of which refluxed 90 min. with methanol and methyl iodide → 95 mg. des-O,N-dimethylarmepavine methiodide added to methanolic KOH, and heated on a steam bath for 1¼ hrs. → 4,4',5-trimethoxy-2-vinylstilbene (Y: 95%). L. Marion, L. Lemay, and V. Portelance, *J. Org. Chem.* 15, 216 (1950).

Quinoline ring from isatin ring

←

723.



N-Acetylisatin added to boiling aq. NaOH, and vigorous boiling continued for 1 hr. → 2-hydroxyquinoline-4-carboxylic acid (startg. m. f. 588). Y: 87% based on converted N-acetylisatin. J. Büchi, H. Hurni, and R. Lieberherr, *Helv.* 32, 1806 (1949).

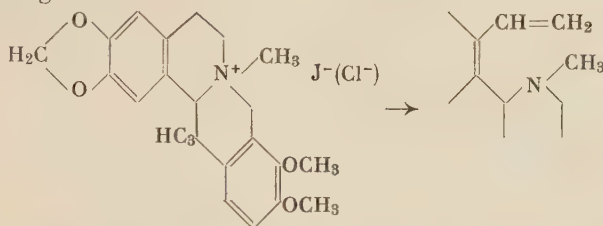
Potassium hydroxide

KOH

**Hofmann degradation
of quaternary ammonium salts
Ring opening**

←

724.



3 gm. 4-methyltetrahydroberberine methiodide converted into the methochloride with AgCl, KOH added, and concentrated until no more oil is formed $\rightarrow$ 1.5 gm. desbase.—The presence of *cis* H-atoms on the C-atoms α and β to the N is a condition for the occurrence of a smooth Hofmann degradation. F. e. s. H.-W. Bersch, Arch. Pharm. 283, 36 (1950).

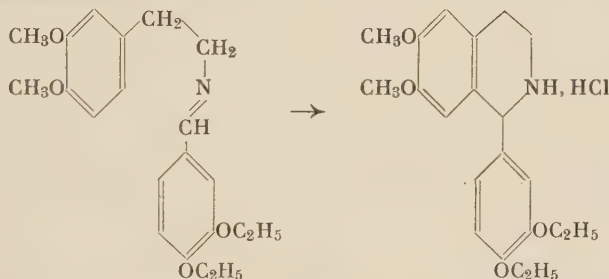
Hydrochloric acid

HCl

**1,2,3,4-Tetrahydroisoquinolines
from azomethines**

○

725.



24% -HCl added with vigorous stirring to N-(3,4-diethoxybenzylidene)-homoveratrylamine, and heated 40-60 min. on a water bath with continued stirring $\rightarrow$ 6,7-dimethoxy-3',4'-diethoxy-1-phenyltetrahydroisoquinoline hydrochloride. Y: 81%. F. e. s. E. C. Weinbach and W. H. Hartung, J. Org. Chem. 15, 676 (1950).

Sulfur/Carbon Type

CC $\curvearrowright$ SC

Sodium/alcohol

NaOR

**Thioethers from sulfonium salts
with rearrangement**

←

726.



Methyl benzyl phenacyl sulfonium bromide added to a soln. of Na in methanol, and refluxed 1 hr. on a water bath $\rightarrow$ methyl α -benzyl-

phenacyl sulfide. Y: 81%. F. e. s. F. Krollpfeiffer and H. Hartmann, Chem. B. 83, 90 (1950).

Carbon/Carbon Type

 $\text{CC} \downarrow \text{CC}$

Potassium/alcohol

KOR

**Carboxylic acid esters from
 α -halogenoketones
with rearrangement**

←

s. 4, 683; s. a. Helv. 33, 2243 (1950)

Exchange

Hydrogen †

 $\text{CC} \nmid \text{H}$

Mercuric fulminate

 $\text{Hg}(\text{ONC})_2$

Replacement of hydrogen by cyano groups

 $\text{H} \rightarrow \text{CN}$

727.



A satd. aq. soln. of 2.13 gm. barbituric acid added to a mixture of $\text{Hg}(\text{II})$ -fulminate and KI in water, refluxed 1.5 hrs., then treated with $\text{H}_2\text{S} \rightarrow$ 1.85 gm. K-5-cyanobarbituric acid. F. e. s. M. Ridi and G. Feroci, G. 78, 932 (1948).

Chloranil

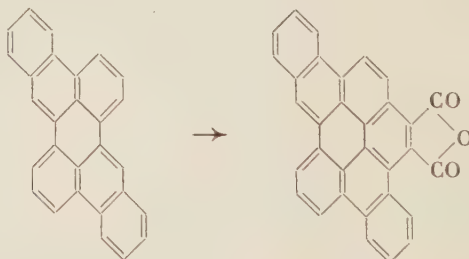
←

Benzene ring synthesis

○

Condensed isocyclics

728.



Chloranil or bromanil added portionwise to a boiling mixture of 2,3,8,9-dibenzoperylene and maleic anhydride $\rightarrow$ 1,12,2,3,8,9-tribenzoperylene-1',2'-dicarboxylic anhydride. Y: ca. 100%. E. Clar and H. Frömmel, Chem. B. 82, 46 (1949).

Oxygen †

CC + O

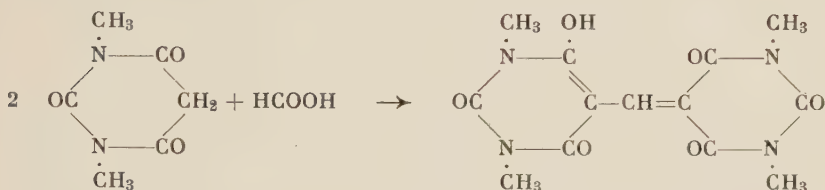
Without additional reagents

w.a.r.

Methine condensation

·CH:

729.



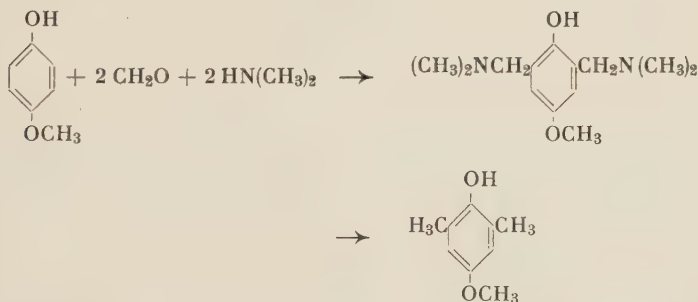
A soln. of N,N'-dimethylbarbituric acid in anhydrous formic acid heated at 120° for 20 hrs. → methinebis-(1,3-dimethylbarbituric acid). Y: 78%. F. e. s. H. Gysling and G. Schwarzenbach, *Hely.* 32, 1484 (1949); s. a. M. Ridi, *G.* 80, 533 (1950).

Mannich reaction**Aminomethylation**H → CH₂NR₂

Replacement of hydrogen by methyl
via tert. amines

Hydrogenolysis of Mannich bases

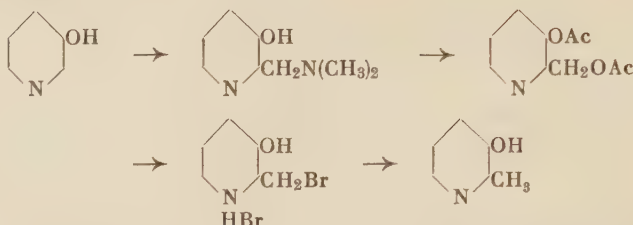
730.



37%-formaldehyde added at 15-20° over a period of 1 hr. to hydroquinone monomethyl ether and a 25% soln. of dimethylamine, stirred another hr. without cooling, then refluxed gently with stirring for 45 min., while more formaldehyde is added dropwise → 2,6-bis-(dimethylaminomethyl)-4-methoxyphenol (Crude Y: 77%) hydrogenated ca. 2 hrs. with Cu-chromite in dioxane at 235° and an initial pressure of 275 atm./room temp. → 2,6-dimethyl-4-methoxyphenol (Crude Y: 90%). W. Reeve and A. Sadle, *Am. Soc.* 72, 3252 (1950); cf. R. B. Carlin and H. P. Landerl, *Am. Soc.* 72, 2762 (1950); hydrogenolysis of Mannich bases s. a. *Synth. Meth.* 2, 106.

**Replacement of hydrogen by methyl
via tert. amines, acoxy compounds
and halides**

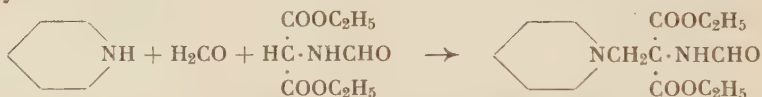
731.



35%-formalin added to an aq. soln. of 3-pyridol and dimethylamine, then heated 2 hrs. on a steam bath $\rightarrow$ 2-dimethylamino-3-pyridol (Y: 70%) refluxed 1.5 hrs. in acetic anhydride $\rightarrow$ 2-hydroxymethyl-3-pyridol diacetate dissolved in 48%-HBr, and refluxed 0.5 hr. $\rightarrow$ 2-bromomethyl-3-pyridol hydrobromide (Y: 82%) dissolved in methanol, and shaken with 3%-Pd-on-charcoal at room temp., until, after a short time, the theoretical quantity of H_2 is absorbed $\rightarrow$ 2-methyl-3-pyridol hydrobromide (Y: 90%). Overall Y: 45%. A. Stempel and E. C. Buzzi, *Am. Soc.* 71, 2969 (1949); acoxy compounds from tert. amines s. a. S. R. Finn and W. G. Musty, *J. Applied Chem.* 1, 182 (1951).

**Mannich reaction with
acylaminomalonate esters**

732.



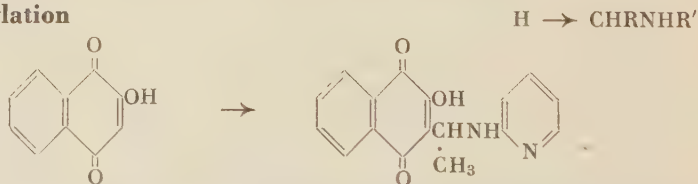
Diethyl formamidomalonate dissolved in piperidine without warming, treated with 40%-formalin, and stirred rapidly for ca. 1 min. until the mixture solidifies $\rightarrow$ diethyl (1-piperidylmethyl)formamidomalonate (startg. m. f. 789). Y: 93%. F. e. s. A. Butenandt and H. Hellmann, *Z. physiol. Chem.* 284, 168 (1949).

Aminomethyl-N-heterocyclics

s. 3, 608; s. a. H. Bader, J. D. Downer, and P. Driver, *Soc.* 1950, 2775.

Aminoalkylation

733.



Acetaldehyde added at 25-30° with shaking to a mixture of 2-hydroxy-1,4-naphthoquinone and 2-aminopyridine, then allowed to stand for

ca. 24 hrs. $\rightarrow$ 2-hydroxy-3- α -(2'-pyridylamino)ethyl-1,4-naphthoquinone. Y: 96%. F. e. s. C. E. Dalglish, Am. Soc. 71, 1697 (1949).

Aldimines from hydrocarbons



734.



2 gm. thiobarbituric acid and NH_4 -formate gradually heated to 190° , then 1 hr. at the same temp. $\rightarrow$ 2.1 gm. thiobarbituric aldimine. M. Ridi, G. 79, 175 (1949).

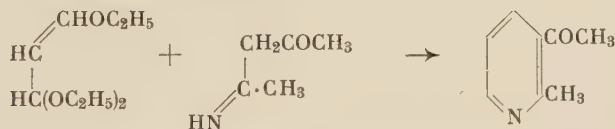
4-Hydroxycoumarins

○

s. 2, 635; improved procedure s. Bl. 1950, 1248

Pyridine ring from enolether acetals

735.



β -Ethoxyacrolein diethylacetal and acetylacetone imine refluxed 24 hrs. at 105 – $110^\circ \rightarrow$ 2-methyl-3-acetylpyridine. Y: 90-95%. A. Dornow et al., Chem. B. 82, 117, 216 (1949).

Lithium

Li

Ketones from carboxylic acids



s. 5, 532; cf. W. G. Dauben and E. Hoerger, Am. Soc. 73, 1504 (1951)

Hantzsch pyridine ring synthesis

s. 1, 542; s. a. A. P. Phillips, Am. Soc. 71, 4003 (1949)

Sodium

Na

Acyloins from carboxylic acid esters

←

s. 1, 545; s. a. N. R. Campbell, J. H. Dunsmuir, and M. E. H. Fitzgerald, Soc. 1950, 2743

4-Hydroxycoumarins

○

s. 4, 698; s. a. P. Vercier, D. Molho, and C. Mentzer, Bl. 1950, 1248

Chromone synthesis

s. 2, 642; cf. A. Schönberg and S. Sina, Am. Soc. 72, 3396 (1950)

Sodium/copper

Na/Cu

Guerbet condensation of alcohols

←



148 gm. butyl alcohol, Na, and a little Cu heated in an autoclave to 300°, the pressure released to 50-60 atm., and heating continued for 6 hrs. → 79 gm. 2-ethylhexanol, 50 gm. butyric acid, and 10 gm. 2-ethylhexoic acid. F. e. s. C. Weizmann, E. Bergmann, and M. Sulzbacher, *J. Org. Chem.* 15, 54 (1950); s. a. W. M. Bruner, *Ind. Eng. Chem.* 41, 2860 (1949).

Sodium hydride

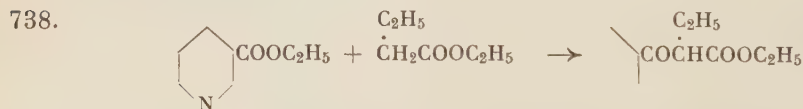
NaH

β-DiketonesCOCH₂CO

In acylations (and carbethoxylations) of ketones. NaH generally produces as good yields as NaNH₂ and usually better yields than Na-ethoxide or Na.—E: Acetone in dry ether added during 30-60 min. at 30-40° to a stirred mixture of ethyl laurate and NaH, and stirring continued at 40-55° with addition of more ether until at least 80% of the H₂ has been evolved → lauroylacetone. Y: 83%. F. e. s. F. W. Swamer and C. R. Hauser, *Am. Soc.* 72, 1352 (1950); s. a. T. A. Geissman, *Am. Soc.* 71, 1498 (1949).

β-Ketocarboxylic acid esters from carboxylic acid esters

←

Mixed ester condensation**Ball mill reactor**

In the self-condensation of methyl and ethyl esters and especially in certain mixed ester condensations, NaH is superior to Na-ethoxide. Na, or NaNH₂.—The use of a ball mill reactor may be advantageous in several cases, generally resulting in higher yields in less reaction time.—E: Ethyl *n*-butyrate in dibutyl ether added dropwise at 100° over a period of 30-60 min. to a stirred mixture of ethyl nicotinate and NaH, and stirring continued at 100-110° with addition of more dibutyl ether until gas evolution stops and for 1 hr. thereafter → ethyl α-nicotinyl-*n*-butyrate. Y: 68%. F. e. s. F. W. Swamer and C. R. Hauser, *Am. Soc.* 72, 1352 (1950).

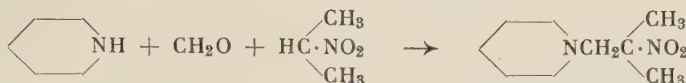
Sodium hydroxide

NaOH

Mannich reaction
Aminomethylation
Nitramines

H → CH₂NR₂

739.



A mixture of 37%-formaldehyde and 2%-NaOH added below 10° to piperidine, 2-nitropropane, and dioxane, stirred 1 hr. after completion of the addition, then heated 1 hr. on a steam bath → N-(2-nitro-2-methylpropyl)piperidine. Y: 76.5%. F. e. s. G. B. Butler and F. N. McMillan, Am. Soc. 72, 2978 (1950).

α,β-Ethyleneketones from aldehydes

CHO → CH:CHCOR

s. 1, 549; s. a. P. T. Mora and T. Széki, Am. Soc. 72, 3009 (1950); K. Alexander et al., Am. Soc. 72, 5506 (1950)

740.



Chalcones. Acetophenone added with stirring to a soln. of NaOH in ethanol, cooled to 0°, mesitaldehyde added with stirring, and, after 3 hrs., stirring continued at 15-20° for 15 hrs. → mesitalacetophenone startg. m. f. 708). Y: 87%. R. C. Fuson and H. L. Jackson, Am. Soc. 72, 1637 (1950).

Benzene ring synthesis

○

2,6-Polymethylene-4-nitrophenols

s. 4, 701; s. a. Helv. 33, 1937 (1950)

Potassium hydroxide

KOH

Aldol condensation with subsequent
formation of azomethines

←

741.



Propionaldehyde stirred 10 hrs. at 5-8° with dil. KOH, neutralized, and isobutylamine added over a period of 1 hr. at 40-45° → 2-methyl-2-pentylideneisobutylamine (startg. m. f. 235). Y: 91%. F. e. of the reaction of aldehydes with amines s. A. M. Paquin, Chem. B. 82, 316 (1949).

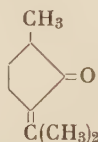
*Potassium hydroxide/alcohol***Cyclopentadienones**

○

s. 3, 618; s. a. C. F. H. Allen and J. A. Van Allan, *Am. Soc.* **72**, 5165 (1950)*Sodium/alcohol**NaOR* **α -Hydroxymethyleneketones from ketones** $\text{CH}_2 \rightarrow \text{C:CHOH}$ s. 2, 643; 4, 756; s. a. C. H. Shunk and A. L. Wilds, *Am. Soc.* **71**, 3946 (1949)**Synthesis of α,β -ethyleneketones from ketones**

←

742.

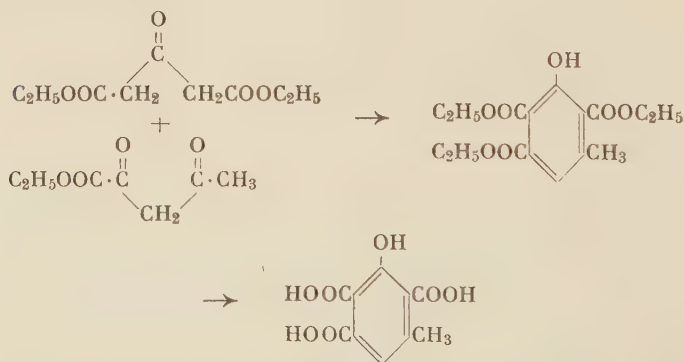


A soln. of Na in alcohol added at -10° to α -methylcyclopentanone and acetone, and allowed to stand at room temp. for 5 days $\rightarrow$ camphorone.
Y: 85%. *J. Golé, Bl. 1949, 894.*

 α -Cyanoketones from nitriles $\text{CH}_2\text{CN} \rightarrow \text{CH}(\text{CN})\text{COR}$ s. 2, 645; s. a. W. R. Nes and A. Burger, *Am. Soc.* **72**, 5409 (1950)**Benzene ring synthesis**

○

743.

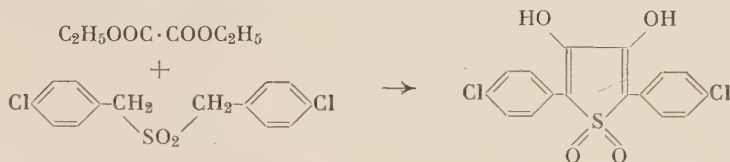


Ethyl Na-acetopyruvate, obtained from ethyl oxalate, acetone, and Na in abs. alcohol according to C. S. Marvel and E. E. Dreger, *Org. Synth.*, Coll. Vol. I, 2nd ed., p. 238, without isolation treated with diethyl

acetonedicarboxylate with vigorous stirring, gently warmed until dissolved, allowed to stand in a closed flask for 48 hrs., treated with aq. KOH, the alcohol distilled off on a water bath as completely as possible, then refluxed for 2 hrs. $\rightarrow$ mono-K-isocochenillate. Y: 76%. H. Mühlemann, *Pharm. Acta Helv.* 24, 351, 356 (1949).

3,4-Dihydroxythiophene 1,1-dioxides

744.



p,p'-Dichlorobenzyl sulfone and a large excess of diethyl oxalate in a soln. of Na in abs. alcohol refluxed 2 hrs. with stirring $\rightarrow$ 2,5-(p,p'-dichlorophenyl)-3,4-dihydroxythiophene 1,1-dioxide. Y: 91.1%.—The use of NaH or powdered Na gave lower yields. F. e. s. C. G. Overberger, S. P. Ligthelm, and E. A. Swire, *Am. Soc.* 72, 2856 (1950).

Sodium alkoxide

β -Diketones

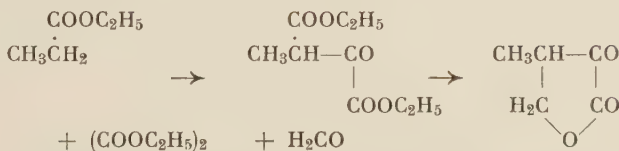
COCH₂CO

s. 1, 556; with Na-methoxide s. J. C. Reid and M. Calvin, *Am. Soc.* 72, 2948 (1950)

α -Keto- γ -lactones

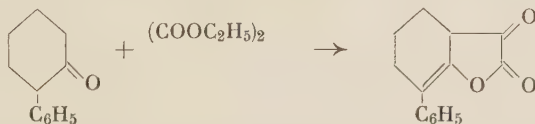
○

745.



Simplified procedure. Diethyl oxalate, followed by ethyl propionate, added dropwise to a suspension of Na-ethoxide in abs. ether, refluxed 3 hrs., the solvent removed in vacuo, the residue dissolved in water, 35%-formalin added portionwise with water-cooling, warmed at 50° for 1 hr., the alcohol formed removed in vacuo, acidified with HCl, and refluxed 4 hrs. in the presence of hydroquinone $\rightarrow$ α -keto- β -methyl- γ -lactone. Y: 82.5%. F. e. s. F. Fleck et al., *Helv.* 33, 130 (1950).

746.



from ketones. A mixture of powdered Na-methoxide, diethyl oxalate, and benzene refluxed 10 min. with shaking, cooled, a soln. of 2-phenyl-

cyclohexanone in benzene added, shaken for 15 min., and allowed to stand 4 hrs. at room temp. $\rightarrow$ 2-hydroxy-3-phenyl-2-cyclohexene-glyoxalic acid γ -lactone (startg. m. f. 207). Y: 79%. F. e. s. W. E. Bachmann, G. I. Fujimoto, and L. B. Wick, *Am. Soc.* 72, 1995 (1950).

Potassium alkoxide (Potassium/alcohol)

KOR

Oxalic ester synthesis

H $\rightarrow$ COCOOR

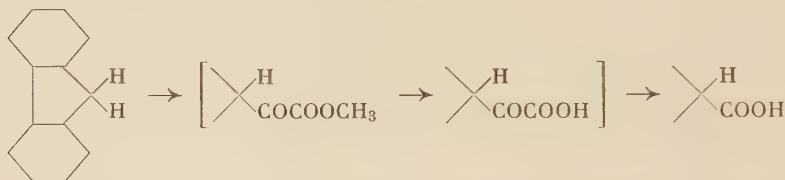
Carboxylic acids from hydrocarbons

via α -ketocarboxylic acid esters

and α -ketocarboxylic acids

Synthesis with addition of 1 C-atom

747.



Fluorene and methyl oxalate added to a soln. of K in anhydrous methanol, heated and shaken until homogeneous, methanol and excess of methyl oxalate slowly distilled off, the residue boiled 1 hr. in acetic acid- H_2SO_4 -water, cooled, 30%- H_2O_2 added in portions, and allowed to stand with occasional swirling for 4 hrs. $\rightarrow$ 9-fluorene-9-carboxylic acid. Y: 76%. Also isolation of the intermediates s. A. Campbell and S. H. Tucker, *Soc.* 1949, 2623.

α,β -Ketodicarboxylic acid esters

s. 3, 622; 4, 707; 6, 858; C^{14} -compounds s. C. Heidelberger and R. B. Hurlbert, *Am. Soc.* 72, 4704 (1950)

Subst., unsatd. succinic acid monoesters

$\leftarrow$

Stobbe condensation

s. 2, 647; s. a. W. S. Johnson and V. L. Stromberg, *Am. Soc.* 72, 505 (1950); also use of NaH s. J. G. Burr, Jr., W. F. Holton, and C. N. Webb, *Am. Soc.* 72, 4903 (1950); with aldehydes s. G. Tschudi and H. Schinz, *Helv.* 33, 1865 (1950)

Sodium amide

NaNH_2

α,β -Ethylenenitriles from ketones

$\text{CO} + \text{H}_2\text{C} \cdot \text{CN} \xrightarrow{\text{Na}} \text{C} : \text{C} \cdot \text{CN}$

s. 4, 711; s. a. S. Wawzonek and E. M. Smolin, *Org. Synth.* 31, 52 (1951)

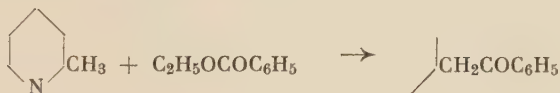
β -Diketones from carboxylic acid estersCOCH₂CO

s. 4, 713; relative reactivity of the esters s. J. K. Sneed and R. Levine, Am. Soc. 72, 5219 (1950)

Potassium amide

KNH₂**Ketones from carboxylic acid esters**COOR $\rightarrow$ COR'

748.

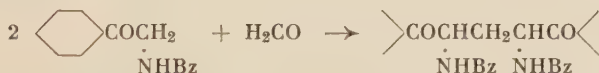


α -Picoline added with stirring during 6 min. to a KNH₂ soln. (from K, liq. NH₃, and FeCl₃ catalyst), ethyl benzoate added over a period of 8 min., stirred for 20 min., diluted with ether, stirring continued for 6 hrs., during which time the mixture was allowed to come to room temp., and the reaction product isolated as hydrobromide $\rightarrow$ α -phenacylpyridine hydrobromide. Y: 44%. D. R. Howton and D. R. V. Golding, J. Org. Chem. 15, 1 (1950); also with NaNH₂ s. M. J. Weiss and C. R. Hauser, Am. Soc. 71, 2023 (1949).

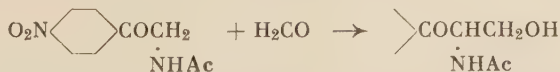
Potassium carbonate

K₂CO₃**Methylene bridging and hydroxymethylation** $\leftarrow$

749.



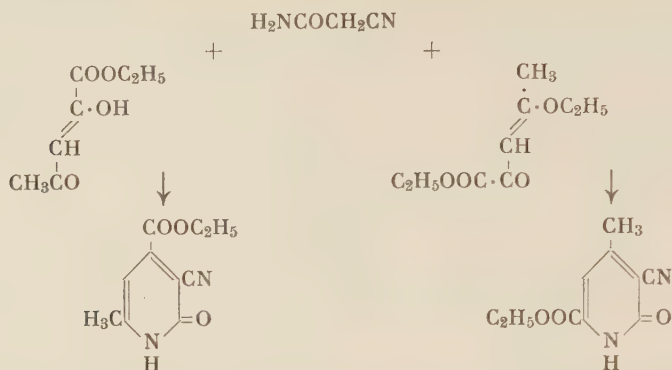
α -Benzamidoacetophenone, paraformaldehyde, K₂CO₃, and methanol shaken at room temp. for 20 min. $\rightarrow$ 1,5-diphenyl-2,4-dibenzamido-1,5-pentadione. Y: 90%. (Am. Soc. 71, 2469.)



A mixture of p-nitro- α -acetamidoacetophenone, 95%-ethanol, excess 36-38% aq. formaldehyde, and a small amount of NaHCO₃ stirred 2 hrs. at 35° $\rightarrow$ p-nitro- α -acetamido- β -hydroxypropioacetophenone. Y: 86%. (Am. Soc. 71, 2473.) L. M. Long and H. D. Troutman, Am. Soc. 71, 2469, 2473 (1949); hydroxy methylation s. a. Am. Soc. 72, 4445 (1950); Ph. Buu-Hoï and H. Khôi, C. r. 229, 1343 (1949); Soc. 1950, 2766; 1951, 255; cf. G. Carrara and G. Weitnauer, G. 81, 142 (1951).

β -Cyanopyridones

750.



Anhydrous K-carbonate gradually added to a soln. of cyanoacetamide in acetone, then

acetynyloxalic ester

O-ethyl acetynyloxalic ester

dropped in with vigorous stirring, boiling and stirring continued for

6 hrs. $\rightarrow$ ethyl 2-methyl-5-cyano-6(1H)-pyridone-4-carboxylate.

Y: 82.2%.

for ca. 14 hrs. $\rightarrow$ ethyl 4-methyl-5-cyano-6(1H)-pyridone-2-carboxylate. Y: 73%.

F. e. s. H. Henecka, Chem. B. 82, 36 (1949).

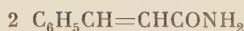
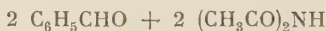
Sodium acetate and potassium acetate

CH_3COONa and CH_3COOK

α,β -Ethylenecarboxylic acid amides
and unsym. 1,1-di(acylamino)
compounds
from aldehydes and diacylamines
Cation specificity

$\leftarrow$

751.



Benzaldehyde and diacetimide heated

with fused Na-acetate at 220° for 8 hrs. $\rightarrow$
cinnamamide. Y: 81.2%.

with K-acetate at 180° for 5 hrs. $\rightarrow$
cinnamamide (Y: 37.5%) and benzylidene-
N-acetyl-N'-cinnamoyldiamine (Y: 36.2%).

F. e. s. J. B. Polya and T. M. Spotswood, R. 70, 269, 146 (1951).

Sodium cyanide

NaCN

**Sym. hydrazodinitriles
from ketones**

←

s. 6, 869

Potassium cyanide

KCN

 α -Aminonitriles from ketonesCO $\rightarrow$ C(CN)NHR

752.



p-Acetamido-o-toluidine and cyclopentanone in acetic acid treated with aq. KCN, and left at room temp. for 36 hrs. $\rightarrow$ 1-(p-acetamido-o-toluidino)-1-cyanocyclopentane. Y: 75%. F. e. s. A. E. Bond, T. Deegan, and S. G. P. Plant, Soc. 1949, S160.

Hydantoins from oxo compounds

○

s. 4, 715; s. a. J. Org. Chem. 15, 901 (1950)

Sodium hydrogen sulfite

NaHSO₃ **α -Aminonitriles from aldehydes**CHO $\rightarrow$ CH(CN)NHR

753.



n-Butyraldehyde added with cooling and stirring to an aq. soln. of Na-pyrosulfite (Na₂S₂O₅), after 30 min. 1.5 equivalents of 33% aq. methylamine run in rapidly, after a further 30 min. finely powdered KCN added, and stirring continued for 1 hr. $\rightarrow$ α -methylamino-n-valeronitrile. Y: 80%. F. e. s. A. H. Cook and S. F. Cox, Soc. 1949, 2334.

Sodium compound

←

Phenol ring from β -dioxo compounds

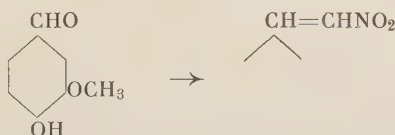
○

s. 4, 705; s. a. Helv. 34, 258 (1951)

Methylamine

CH₃NH₂ **α -Nitroethylene derivatives
from aldehydes**CHO $\rightarrow$ CH:C·NO₂

754.



A mixture of methylamine hydrochloride, Na-carbonate, and methanol stirred well, filtered, added to a soln. of vanillin and nitromethane in

methanol, and kept at room temp. in the dark for 72 hrs. $\rightarrow$ 4-hydroxy-3-methoxy- β -nitrostyrene (startg. m. f. 87). Y: 81%. F. e. s. F. A. Ramirez and A. Burger, Am. Soc. 72, 2781 (1950).

n-Butylamine

Benzaldehyde, nitroethane, and some *n*-butylamine in abs. ethanol refluxed 8 hrs. $\rightarrow$ 1-phenyl-2-nitropropene (startg. m. f. 241). Y: 86.5%, conversion 64%. F. e. s. H. B. Hass, A. G. Susie, and R. L. Heider, J. Org. Chem. 15, 8 (1950); method, s. Knoevenagel and Walter, B. 37, 4502 (1904); with *n*-amylamine s. R. T. Gilsdorf and F. F. Nord, J. Org. Chem. 15, 807 (1950).

tert. Amines ← α -Acylamidoketones from ← α -aminocarboxylic acids

Dakin-West reaction

756. cf. Synth. Meth. 3, 170.

3-Picoline and 1-methylpiperidine were found to be somewhat better catalysts than pyridine. S. Searles and G. J. Cvejnovich, Am. Soc. 72, 3200 (1950); f. mechanism s. a. C. S. Rondestvedt, Jr., B. Manning, and S. Tabibian, Am. Soc. 72, 3183 (1950).

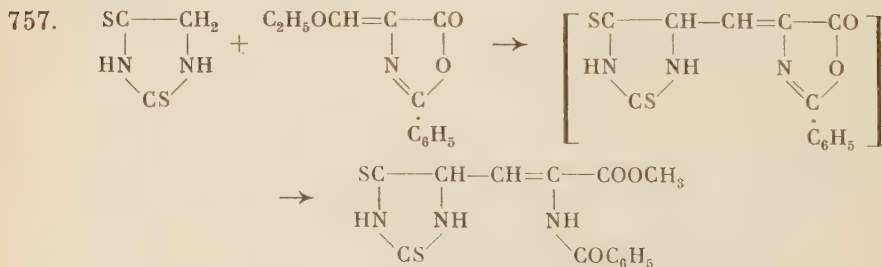
Triethylamine

 α,β -Ethylenecarboxylic acids from aldehydes $\text{CHO} \rightarrow \text{CH}:\text{CRCOOH}$

s. 4, 717; s. a. H. Rapoport, A. R. Williams, and M. E. Cisney, Am. Soc. 73, 1414 (1951)

Methine condensation ←

Oxazolone ring opening



Dithiohydantoin and 2-phenyl-4-ethoxymethyleneoxazolone treated with methanol and triethylamine, whereupon the temp. rises almost to the boiling point, after 0.5 hr. at room temp. 2 *N* methanolic Na-methoxide added with ice-cooling, and the soln. kept at 0° for 12 hrs.

→ methyl α -benzamido- β -(2,4-dimercapto-5-glyoxalanyl)acrylate. Y: 93.5%.—The intermediate product can be isolated. F. e. s. A. C. Davis and A. L. Levy, Soc. 1949, 2179.

Piperidine

 $C_5H_{11}N$

Methylene bridge with formaldehyde

 $2 RH \rightarrow R \cdot CH_2 \cdot R$

s. 4, 720; s. a. H. B. Henbest and E. R. H. Jones, Soc. 1950, 3628

α,β -Ethylenecarboxylic acids from aldehydes Doebner modification of the Perkin reaction

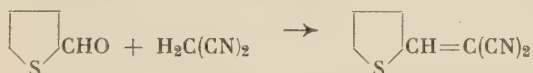
 $CHO \rightarrow CH:CHCOOH$

s. 1, 570; 2, 657; s. a. J. Koo et al., Org. Synth. 31, 35 (1951); M. Sulzbacher, J. Applied Chem. 1, 95 (1951)

α,α -Ethylenedinitriles from aldehydes

 $CHO \rightarrow CH:C(CN)_2$

758.



A mixture of 2-thiophenealdehyde, malononitrile, and abs. ethanol heated to boiling, 2 drops of piperidine added, and heating continued for an additional 5 min. → 2-thenalmalononitrile. Y: 97%. W. S. Emerson and T. M. Patrick, Jr., J. Org. Chem. 14, 790 (1949).

Alkylideneacetoacetic esters from aldehydes

 $CHO \rightarrow CH:C(COCH_3)COOR$

s. 1, 400, 571; s. a. Ng. Ph. Buu-Hoï, Ng. Hoán, and D. Lavit, Soc. 1950, 2130

α,β -Ethylene- β -dicarboxylic acid esters from aldehydes

 $CHO \rightarrow CH:C(COOR)_2$

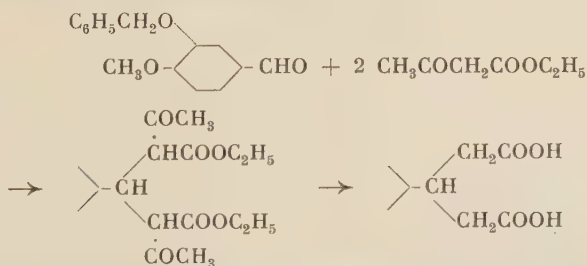
Knoevenagel synthesis

s. 3, 632; s. a. J. Jaques and A. Horeau, Bl. 1950, 512

β -Subst. glutaric acids from aldehydes via arylmethylene-bis-acetoacetates

←

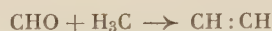
759.



A mixture of benzylisovanillin, 2 moles of ethyl acetoacetate, and piperidine in 95%-ethanol allowed to stand at room temp. for 19 hrs.

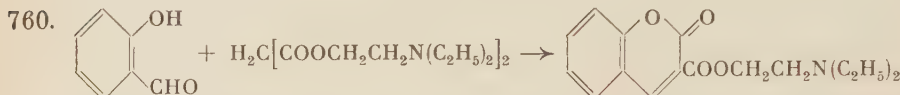
→ ethyl benzylvanillal-bis-acetoacetate (Y: 70%) refluxed vigorously for 3 hrs. in aq.-alc. NaOH → β -(3-benzoxo-4-methoxyphenyl)glutaric acid (Y: 95%). F. e. s. W. T. Smith, Jr., and P. G. Kort, *Am. Soc.* 72, 1877 (1950).

Styrylheterocyclics



s. 5, 541; thiophene derivatives s. Ng. Ph. Buu-Hoï, Ng. Hoán, and D. Lavit, *Soc.* 1950, 2130

Coumarin ring



A mixture of salicylaldehyde and crude bis-(2-diethylaminoethyl)-malonate heated 3 hrs. on a steam bath in the presence of piperidine and the reaction product isolated as hydrochloride → 2-diethylaminoethyl coumarin-3-carboxylate hydrochloride. Y: excellent.—In certain cases it is necessary to force the reaction by heating and thorough use of increased amounts of piperidine catalyst. F. e. s. R. O. Clinton and S. C. Laskowski, *Am. Soc.* 71, 3602 (1949); s. a. F. M. Dean, A. Robertson, and W. B. Whalley, *Soc.* 1950, 895.

Morpholine

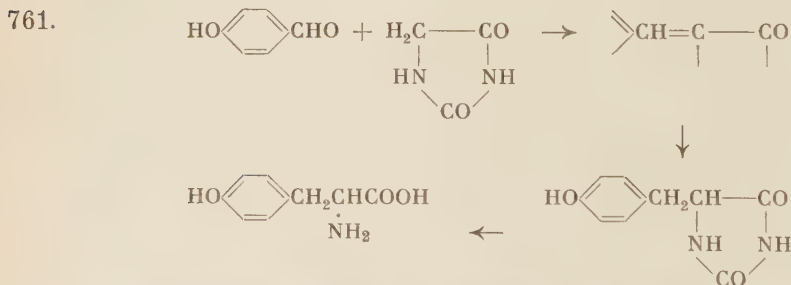
α -Aminocarboxylic acids from aldehydes

via hydantoin

Synthesis with addition of 2 C-atoms

Ethylenheterocyclics

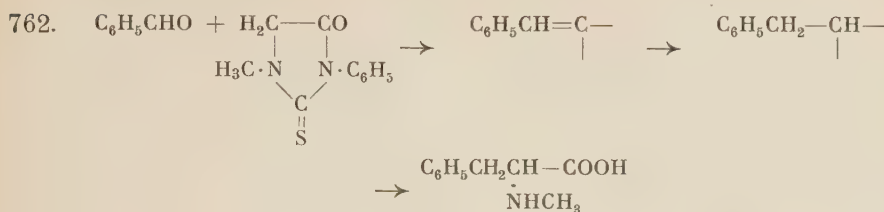
Hydrogenation of ethylene derivatives



Also hydrogenation of ethylene derivatives. Hydantoin, p-hydroxybenzaldehyde, and morpholine in glycerol heated 3.5 hrs. at 160° → 5-(4'-hydroxybenzylidene)hydantoin (Y: 80%) hydrogenated in alcohol with Raney-Ni at 130° and 50 atm. for 5 hrs. until absorption ceases → 5-(4'-hydroxybenzyl)hydantoin (Y: 94%) refluxed with 2 N NaOH for 24 hrs. → DL-tyrosine (Y: 84%). E. F. Borrows, J. C. Clayton, and B. A. Hems, *Soc.* 1949, S185.

Morpholine/pyridine

←



2-Thio-3-phenyl-1-methylhydantoin in pyridine containing morpholine and benzaldehyde refluxed 1 hr. $\rightarrow$ 2-thio-3-phenyl-5-benzylidene-1-methylhydantoin (Y: 92%) dissolved in acetic acid containing red P, and refluxed 5 hrs. $\rightarrow$ 2-thio-3-phenyl-5-benzyl-1-methylhydantoin (Y: 90%) refluxed 24 hrs. with aq.-alc. NaOH $\rightarrow$ β -phenyl-N-methylalanine (Y: 82%).—Morpholine in pyridine is more effective as condensing agent than Na-acetate in acetic acid.—Other heterocyclic intermediates may be preferred in some cases for sterical or other reasons. F. e. s. A. H. Cook and S. F. Cox, Soc. 1949, 2342.

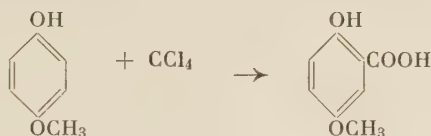
Copper

Cu

Introduction of carboxylic acid groups into ar. rings

H $\rightarrow$ COOH

763.



A mixture of hydroquinone monomethyl ether, CCl_4 , 50% aq. NaOH, and Cu-powder refluxed 8 hrs. with stirring $\rightarrow$ 2-hydroxy-5-methoxybenzoic acid. Y: 74%. F. J. Villani and J. Lang, Am. Soc. 72, 2301 (1950).

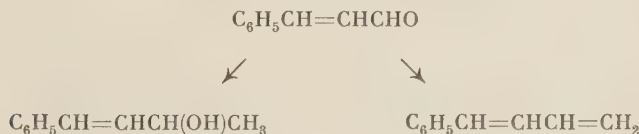
Magnesium

Mg

Synthesis of α,β -ethylenalcohols and dienes from α,β -ethylenaldehydes

←

764.



A soln. of cinnamaldehyde in abs. ether added below 10^0 with the

passage of a slow
 N_2 -stream to a 1.5-2 *N* ethereal soln. of methyl-MgBr,
 stirred 30 min., a satd. soln.
 of NH_4Cl (neutralized to
 litmus with concd. aq. NH_3)
 added dropwise at 5-10°
 over a period of 1-1.5 hrs.
 → *trans*-methylstyrylcar-
 binol. Y: 88-90%.

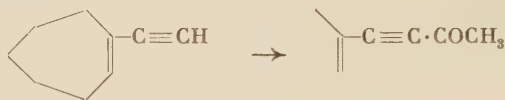
this mixture added rapidly during 5-7
 min. with efficient stirring to 30%- H_2 -
 SO_4 , gentle refluxing continued, and
 worked up after 20 min., using phenyl-
 β -naphthylamine as a polymerization
 inhibitor → *trans*-1-phenyl-1,3-buta-
 diene. Y: 72-75%.

O. Grummitt and E. I. Becker, Org. Synth. 30, 75 (1950).

**Ketones from carboxylic acid
 anhydrides**
Acetylene ketones

$C \equiv C'COR$

765.



1-Ethynylcycloheptene in ether added dropwise to an ethereal soln. of ethyl-MgCl, refluxed for 2 hrs., the cooled suspension slowly added with stirring to a soln. of acetic anhydride in dry ether at -60°, stirred for 1 hr., then the temp. allowed to rise to 20° during 2 hrs. → 4-(1-cyclohepten-1-yl)-3-buten-2-one. Y: 70%. F. e. s. I. Heilbron et al., Soc. 1949, 1827.

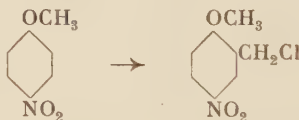
Zinc chloride

$ZnCl_2$

Chloromethylation

$H \rightarrow CH_2Cl$

766.



A mixture of *p*-nitroanisole, di(chloromethyl) ether, $ZnCl_2$, and CS_2 refluxed 9 hrs. → 4-nitro-2-chloromethylanisole. Y: 74%.—The procedure using paraformaldehyde and HCl gave a poor yield. G. Bendz et al., Soc. 1950, 1130.

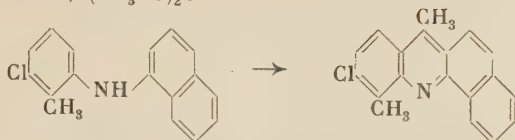
**Ketones from carboxylic acid
 anhydrides**

$CO \cdot O \cdot OC \xrightarrow{\quad} COR$

s. 3, 651; s. a. H. Burton and P. F. G. Praill, Soc. 1951, 726

Acridine ring Modified Bernthsen reaction

○

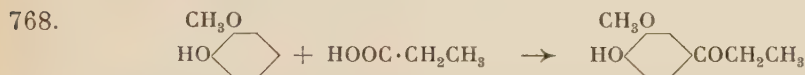
767. $+ (\text{CH}_3\text{CO})_2\text{O}$ 

4 gm. N-(3-chloro-2-methylphenyl)- α -naphthylamine heated with acetic anhydride and ZnCl_2 at $190\text{--}200^\circ$ for 20 hrs. $\rightarrow$ 3.5 gm. 10-chloro-7,11-dimethylbenzo[ghi]perylene. F. e., also with acids in place of anhydrides, s. Ng. Ph. Buu-Hoi, Soc. 1950, 1146.

Boron fluoride

 BF_3

Ketones from carboxylic acids

 $\text{COOH} \rightarrow \text{COR}$ 

A soln. of guaiacol in propionic acid saturated with BF_3 while cooling with ice, after 5 hrs. heated at 70° for 90 min. in a water-bath, then poured with stirring into aq. Na-acetate $\rightarrow$ 3-methoxy-4-hydroxypropiophenone. Y: 77.4%. G. Fodor, J. Kiss, and M. Szekerke, J. Org. Chem. 15, 227 (1950); s. a. G. Fawaz and L. F. Fieser, Am. Soc. 72, 996 (1950).

Ketones from carboxylic acid anhydrides

 $\text{CO}\cdot\text{O}\cdot\text{OC} \rightarrow \text{COR}$

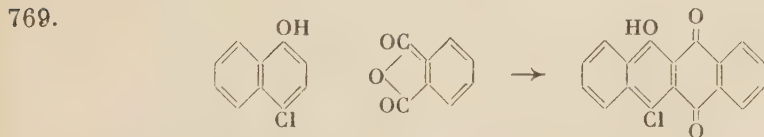
s. 4, 725; furan- and thiophene derivatives s. a. M. W. Farrar and R. Levine, Am. Soc. 72, 3695, 4433 (1950)

Aluminum chloride/sodium chloride

 $\text{AlCl}_3/\text{NaCl}$

Annulization Hydroxyquinones

○



A mixture of phthalic anhydride and 4-chloro-1-hydroxynaphthalene added at 150° to an $\text{AlCl}_3\text{--NaCl}$ melt, and heated 2 hrs. at 210° $\rightarrow$ 4-chloro-1-hydroxy-2,3-benzanthraquinone. Y: 90%. F. e. s. H. Waldmann and E. Ulsperger, Chem. B. 83, 178 (1950); s. a. A. M. Lukin and K. K. Mozgova, Ж. 20, 1504 (1950); C. A. 45, 2460c.

Ammonium acetate

 $\text{CH}_3\text{COONH}_4$ **Alkylidene-cyanoacetic and
-malonic esters**

←

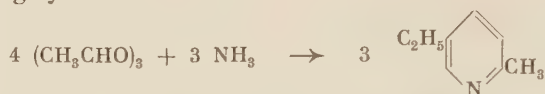
s. 1, 586; s. a. S. M. McElvain and R. E. Lyle, Jr., *Am. Soc.* **72**, 384 (1950)

770. **Alkylidenecyanoacetic esters.** NH_4 -acetate was found to be a satisfactory catalyst for the condensation of diaryl ketones and certain hindered ketones with ethyl cyanoacetate. The yields of alkylidenecyanoacetates were improved by the portionwise addition of the NH_4 -acetate to prevent its conversion into the ineffective acetamide. E. s. E. J. Cragoe, Jr., C. M. Robb, and J. M. Sprague, *J. Org. Chem.* **15**, 381 (1950).

Pyridine ring synthesis

○

771.



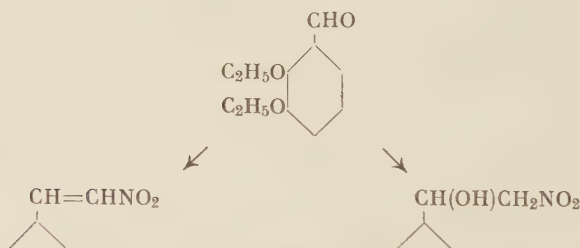
Paraldehyde, 28% aq. NH_3 , and NH_4 -acetate heated in an autoclave to 230° with continuous agitation, and maintained at this temp. for 1 hr. $\rightarrow$ 5-ethyl-2-methylpyridine. Y: 50-70% depending on the ratio NH_3 : paraldehyde. R. L. Frank, F. J. Pilgrim, and E. F. Riener, *Org. Synth.* **30**, 41 (1950).

Benzylamine/acetic acid

 $\text{C}_6\text{H}_5\text{CH}_2\text{NH}_2/\text{CH}_3\text{COOH}$ **α -Nitroethylene derivatives and
 α -nitroalcohols from aldehydes**

←

772.



To a soln. of 2,3-diethoxybenzaldehyde and nitromethane in alcohol added

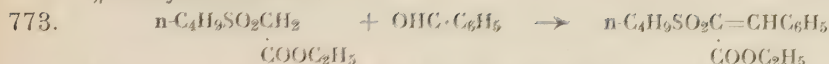
benzylamine and glacial acetic acid, then warmed at 50° with stirring for 10 hrs. $\rightarrow$ 2,3-diethoxy- α -nitrostyrene. Y: 86.8%,

aq.-alc. KOH in small portions below 0° , and the soln. of the salt of the pseudoacid so obtained added in small portions with stirring to ice-cooled 50%-acetic acid $\rightarrow$ 2-(2,3-diethoxyphenyl)-2-hydroxy-1-nitroethane. Y: 92.8%.

F. nitroethylene derivatives s. G. Tsatsas, *Bl.* **1949**, 884.

Piperidinium acetate

←

 α,β -EthylenesulfonesC : C · S₂OR

A mixture of ethyl *n*-butylsulfonyleacetate, benzaldehyde, benzene, piperidine, and acetic acid refluxed 2 hrs. with separation of the water formed $\rightarrow$ α -*n*-butylsulfonyl α -carbethoxy- β -phenylethylene. Y: 83%. F. e. s. S. Chodroff and W. F. Whitmore, Am. Soc. 72, 1673 (1950)

Acetic anhydride

 $(\text{CH}_3\text{CO})_2\text{O}$

Styrylheterocyclics

 $\text{CHO} + \text{H}_2\text{C} \rightarrow \text{CH}:\text{CH}$

s. 6, 135

Acetic acid

 CH_3COOH

Aminomethylation

 $\text{H} \rightarrow \text{CH}_2\text{NR}_2$

Mannich reaction

s. 2, 670; s. a. H. Hellmann, Z. physiol. Chem. 284, 163 (1949)

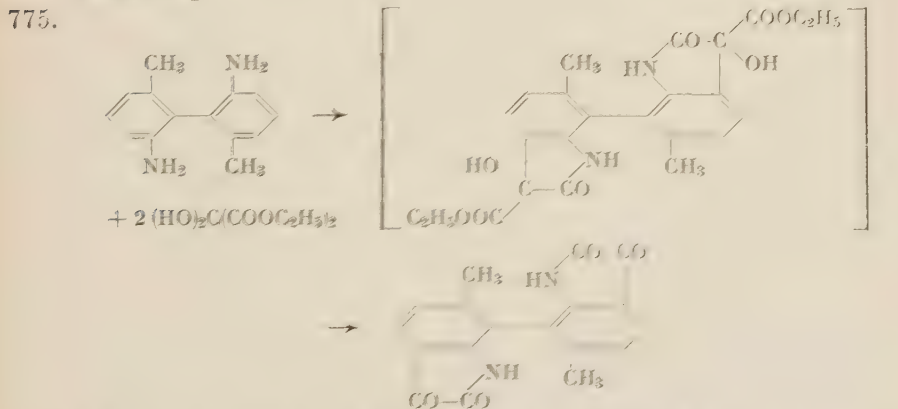
Oxo condensation

←



2-Mercapto-5(4H)-thiazolone and 4(5)-formylglyoxaline dissolved in glacial acetic acid, heated to boiling, which maintains itself for several min. by the exothermic reaction $\rightarrow$ 2-mercapto-4-(5'-glyoxalinylmethylene)thiazol-5-one. Y: 80%. A. C. Davis, A. L. Levy, and G. F. Woods, Soc. 1949, 2179.

Isatin ring

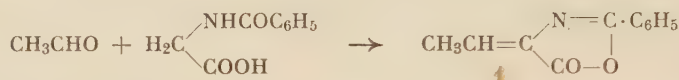


6,6'-Diamino-2,2'-dimethyl-1,1'-biphenyl in boiling glacial acetic acid treated with mesoxalic ester hydrate in glacial acetic acid, heated 1 hr.

more, steam-distilled, and the residual diethyl bis(dioxindolecarboxylate) heated 2-3 hrs. in 3% -NaOH on a water bath, while air is being passed through $\rightarrow$ 6,6'-dimethyl-7,7'-biisatin. Y: 90%. W. Dethloff and H. Mix, Chem. B. 82, 534 (1949); method, see M. J. Martinet, A. ch. [9] 11, 15 (1949).

Lead acetate**4-Alkylideneoxazol-5-ones**

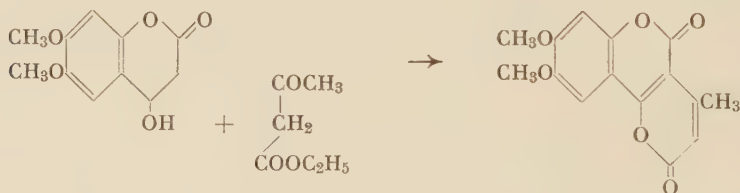
776.



Acetic anhydride, hippuric acid, and Pb-acetate (or basic Pb-acetate) added successively to acetaldehyde, shaken at room temp. for 15 hrs., and kept for a further 33 hrs. with occasional shaking $\rightarrow$ 2-phenyl-4-ethylideneoxazol-5-one. Y: 58%.—Other catalysts gave lower yields. F. e. s. I. L. Finar and D. D. Libman, Soc. 1949, 2726.

Phosphorus pentoxide **α -Pyrono(5',6',3,4)coumarins**

777.



A mixture of 1 gm. 4-hydroxy-6,7-dimethoxycoumarin, P_2O_5 , ethyl acetoacetate, and acetic acid heated 20 min. on a steam bath $\rightarrow$ 0.9 gm. 6,7-dimethoxy-4'-methyl- α -pyrono(5',6',3,4)coumarin.— POCl_3 gave a yield of only 0.35 gm., and concd. H_2SO_4 gave a very small amount. G. G. Badcock et al., Soc. 1950, 903.

Phosphoric acid**Alkylation of isocyclics with alcohols**

s. 3, 643; naphthol derivatives s. Ng. Ph. Buu-Hoï, H. Le Bihan, and F. Binon, J. Org. Chem. 16, 185 (1951)

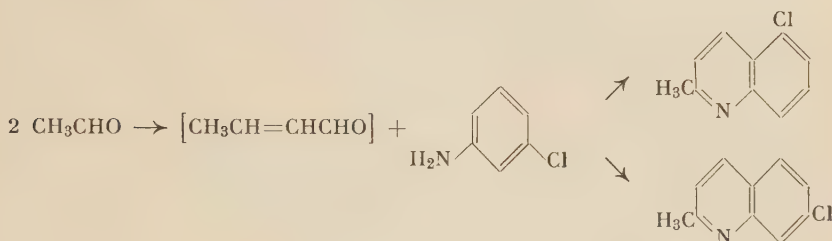
Na-m-nitrobenzenesulfonate

←

Quinolines

Modified Döbner-Miller synthesis

778.



Paraldehyde added dropwise with stirring at 120-130° to m-chloroaniline, 60% H_2SO_4 , and Na-m-nitrobenzenesulfonate, stirring and refluxing continued for 1.5 hrs., and worked up, whereby any unchanged m-chloroaniline is decomposed by boiling 0.5 hr. with excess $\text{NaNO}_2 \rightarrow$ mixture consisting of ca. 75% 7- and 25% 5-chloroquinoline. Y: 60%.—The proportion of 7-subst. isomer increases with decrease of acid concentration. A. M. Spivey and F. H. S. Curd, *Soc.* 1949, 2656.

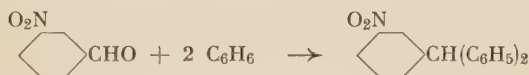
Sulfuric acid

 H_2SO_4

Triarylmethanes from arylaldehydes

 $\text{CHO} \rightarrow \text{CHR}_2$

779.



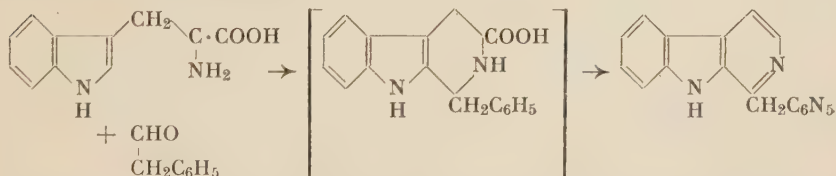
A mixture of m-nitrobenzaldehyde, concd. H_2SO_4 , and benzene shaken at 25° for 24 hrs. in a closed bottle $\rightarrow$ m-nitrotriphenylmethane. Y: 76%. F. e. s. C. N. Wolf and R. L. Shriner, *J. Org. Chem.* 15, 367 (1950).

Aromatization

○

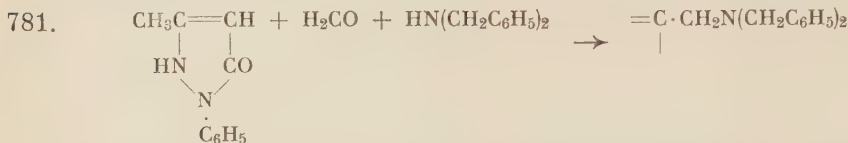
9(H)-Pyrid[3.4-b]indoles

780.



Alc. phenylacetaldehyde added to a soln. of tryptophan in $N \text{ H}_2\text{SO}_4$, refluxed 4.5 hrs., more alcohol added, heated another 4 hrs., the crude tetrahydronorybyrincarboxylic acid so obtained dissolved in hot water, the boiling soln. treated with 10% aq. $\text{K}_2\text{Cr}_2\text{O}_7$ and acetic acid, then boiled 2 min. more $\rightarrow$ norybyrine. Y: 56%. J. Keufer, *Bl.* 1950, 109.

Ammonium chloride

 NH_4Cl **Aminomethylation
Mannich reaction** $\text{H} \rightarrow \text{CH}_2\text{NR}_2$ 

Antipyrine, dibenzylamine, formalin, and a little NH_4Cl in 95% ethanol refluxed 2 hrs. $\rightarrow$ 4-(dibenzylaminomethyl)antipyrine. Y: 89%. F. e., reaction conditions, and mechanism s. S. V. Lieberman and E. C. Wagner, *J. Org. Chem.* 14, 1001 (1949).

Hydrochlorides

 $\leftarrow$ **Tetraarylmethanes from triarylcarbinols** $\text{C} \cdot \text{OH} \rightarrow \text{C} \cdot \text{R}$ 

Technical grade triphenylcarbinol, dry aniline hydrochloride, and glacial acetic acid refluxed 3 hrs. $\rightarrow$ p-aminotetraphenylmethane. Y: 70 to 74%. B. Witten and E. E. Reid, *Org. Synth.* 30, 5 (1950).

C-Alkylation of ar. amines $\leftarrow$

s. 1, 592; s. a. B. M. Dubinin and N. E. Kozhevnikova, *Ж.* 21, 662 (1951); *C. A.* 45, 9500c

Hydrofluoric acid

HF

One-step indanone ring synthesis

○

s. 6, 819

Hydrochloric acid

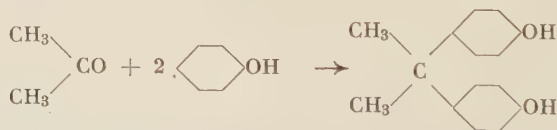
HCl

Methylene bridging with formaldehyde $2 \text{RH} \rightarrow \text{R} \cdot \text{CH}_2 \cdot \text{R}$

s. 3, 163; s. a. L. J. Smith and W. J. Dale, *J. Org. Chem.* 15, 832 (1950)

1,1-Disubst. alkanes from ketones $\text{CO} \rightarrow \text{CR}_2$

783.



A mixture of acetone, phenol, and concd. HCl saturated with dry HCl-gas once a day during a week $\rightarrow$ 2,2-di-(p-hydroxyphenyl)propane. Y: 90%. P. W. Vittum and G. H. Brown, *Am. Soc.* 71, 2287 (1949).

Chloromethylation

s. 1, 593-5, 597; 3, 653; bis-chloromethylation s. J. H. Wood, M. A. Perry, and C. C. Tung, *Am. Soc.* **72**, 2989 (1950)

N-Cyanomethylation

s. 3, 656; modified procedure s. R. A. Turner and C. Djerassi, *Am. Soc.* **72**, 3081 (1950)

Einhorn amidomethylation**Condensation with hydroxymethylamides**

s. 3, 657; 5, 562; s. a. A. M. Downes and F. Lions, *Am. Soc.* **72**, 3053 (1950); R. D. Haworth, R. MacGillivray, and D. H. Peacock, *Soc.* **1950**, 1493

 α,β -Ethylenketones

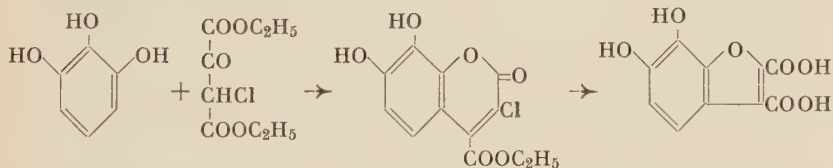
s. 5, 563; s. a. J. Schläger and W. Leeb, *M.* **81**, 714 (1950)

Benzopyrylium salts

s. 1, 603; s. a. D. A. Collins et al., *Soc.* **1950**, 1876; R. R. Otter and R. L. Shriner, *Am. Soc.* **73**, 887 (1951)

Benzofurans via 3-halogenocoumarins**Perkin transformation**

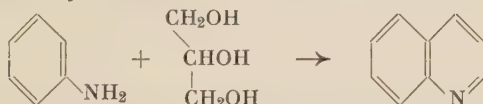
784.



6 gm. pyrogallol and 10.6 gm. ethyl β -chloro- β -carbethoxypyruvate in alcohol with excess of HCl allowed to stand for 3 days $\rightarrow$ 11.5 gm. ethyl 3-chloro-7,8-dihydroxycoumarin-4-carboxylate, 3 gm. of which heated on a steam bath with oxygen-free aq. 10% -KOH in a N_2 -atmosphere for 45 min. $\rightarrow$ 2 gm. 6,7-dihydroxycoumarone-2,3-dicarboxylic acid. F. e. s. G. W. Holton, G. Parker, and A. Robertson, *Soc.* **1949**, 2049; transformation s. a. V. J. Dalvi and S. Sethna, *J. Indian Chem. Soc.* **26**, 359, 467 (1949).

Ferrous sulfate/nitrobenzene**Skraup quinoline synthesis**

785.



Moderation of violence and increase in yield are obtained by adding the amine followed by glycerol to the concd. H_2SO_4 with cooling at

70-90°. This premix is then added portionwise to the nitro compound and FeSO_4 .—E.: A mixture of aniline, glycerol, and concd. H_2SO_4 added portionwise to nitrobenzene and $\text{FeSO}_4 \cdot 7\text{H}_2\text{O}$ preheated to 100 to 120°, at such a rate that the exothermic reaction proceeds at 160 to 170°, and refluxed 4 hrs. $\rightarrow$ quinoline. Y: ca. 100%. F. e. s. R. H. F. Manske, A. E. Ledingham, and W. R. Ashford, *Can. J. Research* 27F, 359 (1949).

Via intermediates

v.i.

Nitriles from alcohols via chlorides

OH $\rightarrow$ CN

s. 6, 812

Gränacher synthesis via rhodanine

CHO $\rightarrow$ CH_2CN

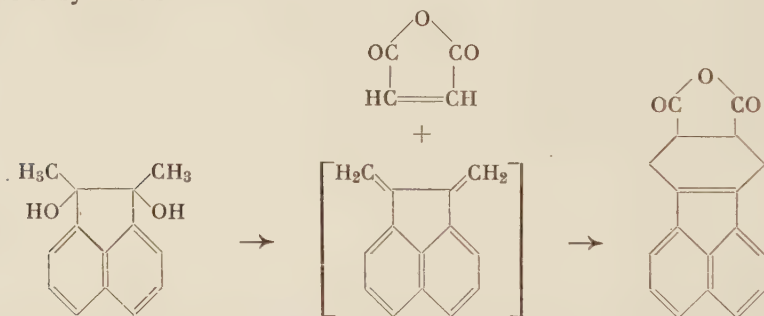
Nitriles from aldehydes

s. 3, 662; s. a. F. E. King and M. F. Grundon, *Soc.* 1950, 3547; J. C. Sheehan and C. A. Robinson, *Am. Soc.* 73, 1207 (1951)

Diene synthesis

○

786.



trans-7,8-Dimethylacenaphthene-7,8-diol, maleic anhydride, and acetic anhydride refluxed 15 min. $\rightarrow$ 10,11,12,13-tetrahydro-11,12-fluoranthenedicarboxylic anhydride. Y: 70%.—Less reactive dienophiles give only polymeric products. F. e. s. N. Campbell and R. S. Gow, *Soc.* 1949, 1555, 1513 (1949).

Nitrogen †

CC#N

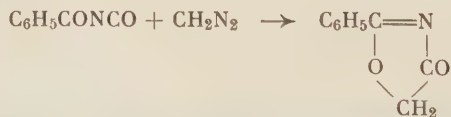
Without additional reagents

w.a.r.

Oxazolones from acylisocyanates and diazomethane

○

787.



Ethereal diazomethane added slowly to ethereal benzoyl isocyanate, then allowed to stand at room temp. for 1 hr. and at 0-5° overnight

→ 2-phenyl-4-oxazolone. Y: 68%. J. C. Sheehan and P. T. Izzo, Am. Soc. 71, 4059 (1949).

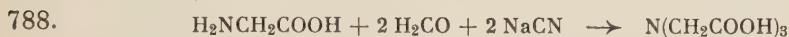
Ring enlargement of cyclic ketones

s. 5, 571; s. a. Bl. 1949, 392

Sodium hydroxide

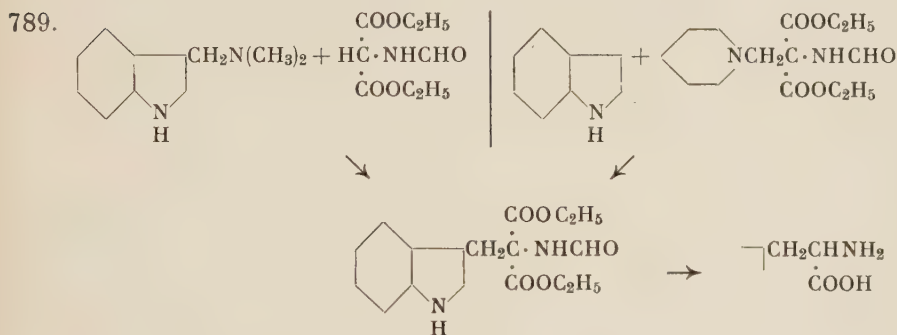
NaOH

N-Carboxymethylation



A soln. of glycine in aq. NaOH treated alternately with a soln. of NaCN in NaOH and 37%-formaldehyde at 80° with vigorous stirring over a period of 8 hrs., allowed to stand overnight, then heated to 100° on a water bath, and stirred for 2 hrs. → triglycine. Y: 93%. A. E. Martell and F. C. Bersworth, J. Org. Chem. 15, 46, 255 (1950).

Syntheses with tert. amines



3-(Diethylaminomethyl)indole and diethyl formamidomalonate added to boiling dry toluene containing powdered NaOH, and refluxed 0.5–1 hr. in a vigorous N_2 -stream → Y: 98%

A mixture of indole, diethyl (1-piperidylmethyl)formamidomalonate (prepn. s. 732), and powdered NaOH refluxed 5 hrs. in anhydrous xylene in an N_2 -stream → Y: 76%

diethyl (skatyl)formamidomalonate

and aq. NaOH heated 6 hrs. at an oil-bath temp. of 120–130°, acetic acid added, and heating continued at 130° for 1–2 hrs. → DL-tryptophan (Y: 96%).

H. Hellmann et al., Z. physiol. Chem. 284, 163, 175 (1949).

Sodium/alcohol

NaOR

s. 3, 665; 4, 754; s. a. N. J. Leonard and E. H. Burk, Jr., Am. Soc. 72, 2543 (1950)

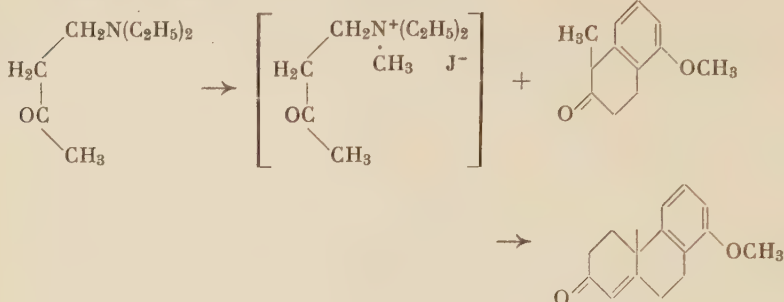
Potassium/alcohol

KOR

Synthesis of isocyclics with tert. amines

O

790.



Methyl iodide added with swirling and ice-cooling during 0.5 hr. to 4-diethylamino-2-butanone, when all has solidified kept in ice for 0.5 hr., then under the tap for 45 min., a soln. of 5-methoxy-1-methyl-2-tetralone in dry, thiophene-free benzene added, the air expelled by dry N_2 , a soln. of K in dry ethanol added with ice-cooling during 5 min., swirling continued until the methiodide has all dissolved after ca. 30 min., kept in ice for another hr., and boiled gently for 25 min. $\rightarrow$ 7-keto-1-methoxy-13-methyl-5,6,7,9,10,13-hexahydrophenanthrene. Y: 71%.—This procedure is suitable for large scale preparations. J. W. Cornforth and R. Robinson, *Soc.* 1949, 1855.

Potassium cyanide

KCN

von Richter reaction

 $\leftarrow$

Position shift of substituents of isocyclics

Carboxylic acids from nitro compounds

791.



p-Nitrobenzene heated at 145–155° with KCN in 48%-alcohol in a sealed tube for 1 hr. $\rightarrow$ m-bromobenzoic acid. Y: 22%. F. e. s. J. F. Bunnett, J. F. Cormack, and F. C. McKay, *J. Org. Chem.* 15, 481 (1950).

Sodium nitrite

 $NaNO_2$

Carboxylic acids from aminosulfonic acids

Replacement of amino groups

by cyano groups

s. 4, 757; s. a. Bl. 1950, 757

Union of aryl nuclei



s. 1, 608; arylquinols s. G. B. Marini-Bettolo, O. A. Polla, and J. H. Abril, *G.* 80, 76 (1950)

*Cuprous cyanide**CuCN***Replacement of amino by cyano groups** $\text{NH}_2 \rightarrow \text{CN}$

s. 3, 666; s. a. C. A. Grob and H. U. Schmid, *Helv.* 33, 1955 (1950); in strongly acid soln. s. H. Bretschneider and H. Rager, *M.* 81, 970 (1950)

*Cupric sulfate**CuSO₄***Diaryls from arylamines** $2 \text{RNH}_2 \rightarrow \text{R} \cdot \text{R}$ **Dimerization**

s. 2, 701; s. a. E. R. Atkinson, D. M. Murphy, and J. E. Lufkin, *Org. Synth.* 31, 96 (1951)

*Cupric chloride**CuCl₂***Diazo coupling** $\leftarrow$

792. $\text{C}_6\text{H}_5\text{N}_2\text{Cl} + \text{CH}_2=\text{CHCN} \rightarrow \text{C}_6\text{H}_5\text{CH}_2\text{CHClCN}$

A soln. of CuCl_2 in a small amount of water added to acrylonitrile, Na-acetate, benzenediazonium chloride soln., and acetone, and worked up after 1.5 hrs. at 10–11° $\rightarrow$ α -chloro- β -phenylpropionitrile. Y: 81%. F. e. s. W. H. Brunner et al., *M.* 79, 187 (1948); 82, 100 (1951).

1,4-Addition

s. 4, 760; s. a. *Am. Soc.* 72, 3960 (1950); *Org. Synth.* 31, 80 (1951)

Hexamethylenetetramine/boric acid $\text{C}_6\text{H}_{12}\text{N}_4/\text{HBO}_2$ **Introduction of the aldehyde group into ar. nuclei** $\text{H} \rightarrow \text{CHO}$ **Hydroxy aldehydes from phenols**

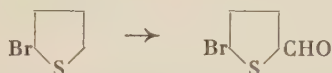
o-Hydroxyaldehydes s. 1, 621; 3, 667; *p*-hydroxyaldehydes s. C. F. H. Allen and G. W. Leubner, *Org. Synth.* 31, 92 (1951)

*Phosphorus oxychloride**POCl₃***Aldehyde synthesis with methylformanilide** $\text{H} \rightarrow \text{CHO}$ **Heterocyclic aldehydes**

s. 3, 668; formylthiophenes s. Ng. Ph. Buu-Hoï, Ng. Hoán, and D. Lavit, *Soc.* 1950, 2130; A. W. Weston and R. J. Michaels, Jr., *Org. Synth.* 31, 108 (1951); carbazole aldehydes s. *Am. Soc.* 73, 98 (1951)

*Phosphorus oxybromide**POBr₃*

793.



2-Bromothiophene added dropwise to a soln. of POBr_3 and *N*-methylformanilide in chlorobenzene at 50°, and stirred 18 hrs. at room temp.

→ 5-bromo-2-thiophenecarboxaldehyde. Y: 70%.—This reaction proceeds well at room temp.—Halogen interchange can be avoided by using POBr_3 in place of POCl_3 . F. e. with POCl_3 s. A. W. Weston and R. J. Michaels, Jr., *Am. Soc.* **72**, 1422 (1950).

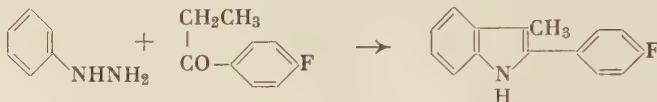
Hydrochloric acid

HCl

Fischer indole ring synthesis

○

794.



A mixture of p-fluoropropiophenone and phenylhydrazine heated to 200° with evaporation of the water formed, allowed to cool, acetic acid saturated with HCl gas added, and cautiously refluxed several min. → 2-(4'-fluorophenyl)skatole. Y: ca. 75%. F. e. s. Ng. Ph. Buu-Hoi, Ng. Hoán, and P. Jacquignon, *R.* **68**, 781 (1949); *Soc.* **1949**, 2882. When the hydrazines used are decomposed at elevated temp., the hydrazones must be isolated before the cyclization. *R.* **68**, 441 (1949).

Halogen †

CC † Hal

Without additional reagents

w.a.r.

Condensation



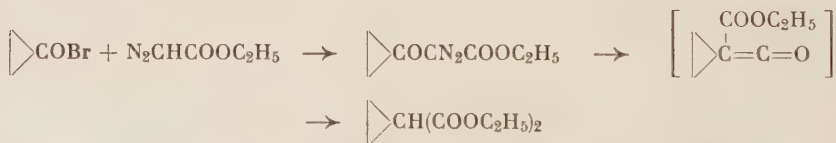
with elimination of hydrogen halides

s. **5**, 577; s. a. E. Ziegler, *M.* **79**, 142 (1948); H. Hart and J. H. Simons, *Am. Soc.* **71**, 345 (1949)

Malonic acid esters from carboxylic acid bromides via diazo compounds



795.

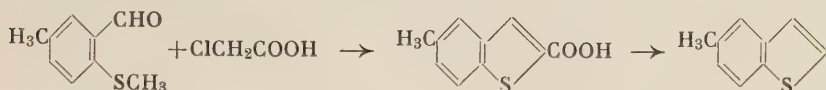


Cyclopropanecarboxyl bromide added with stirring to an ethereal soln. of ethyl diazoacetate, cooled for a few moments until the N_2 -evolution subsides somewhat, allowed to stand 1 day at room temp., then refluxed gently for 2 days → ethyl cyclopropanecarboxyldiazoacetate (Y: 72%) refluxed 3-4 hrs. with Ag_2O and toluene under CO_2 until the N_2 -evolution ceases, the toluene removed, and the residue distilled in vacuo into cooled ethanol → ethyl cyclopropylmalonate (Y: 43%). L. I. Smith and S. McKenzie, Jr., *J. Org. Chem.* **15**, 74 (1950).

Thianaphthenes Decarboxylation

○

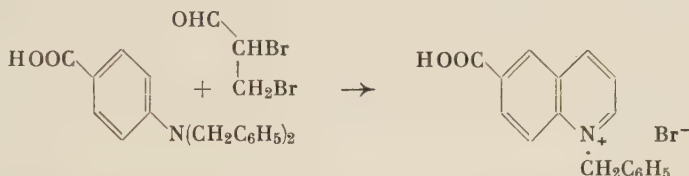
796.



2-Methylmercapto-5-methylbenzaldehyde and chloroacetic acid heated 10 hrs. in a boiling water bath $\rightarrow$ 5-methylthianaphthene-2-carboxylic acid (Y: 88%) mixed intimately with $\text{Ca}(\text{OH})_2$, and distilled $\rightarrow$ 5-methylthianaphthene (Y: 90%). F. e. with ketones s. F. Krollpfeiffer, K. L. Schneider, and A. Wissner, A. 566, 139 (1950).

Synthesis of quinolinium salts

797.



N,N-Dibenzyl-p-aminobenzoic acid and acrolein dibromide in dioxane boiled 75 min. in an oil bath $\rightarrow$ 1-benzyl-6-carboxyquinolinium bromide. Y: 75%. F. e. s. F. Weygand and W. Rupp, Chem. B. 83, 455 (1950).

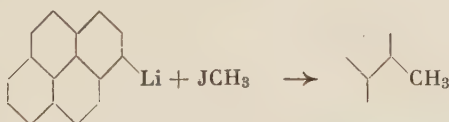
Lithium

Li

Synthesis of hydrocarbons from halides

RHal $\rightarrow$ R · R

798.



Crystalline 3-pyrenyl-Li allowed to react with methyl iodide in ether, and worked up after 15 min. $\rightarrow$ 3-methylpyrene. Y: 83%. F. e. s. A. Berg, Acta Chem. Scand. 3, 655 (1949); s. a. V. Boekelheide and C. E. Larrabee, Am. Soc. 72, 1245 (1950); G. Wittig et al., A. 566, 101 (1950); B. 83, 359 (1950).

o-Alkylation and o-arylation of N-heterocyclics

isoquinolines s. 4, 768; pyridines s. E. Doering and V. Z. Pasternak, Am. Soc. 72, 143 (1950); quinolines s. J. P. Philipps, R. L. Elbinger, and L. L. Merritt, Jr., Am. Soc. 71, 3986 (1949)

Sodium

Na

Synthesis of hydrocarbons from halides

s. 2, 710b; s. a. D. Bryce-Smith and E. E. Turner, Soc. 1950, 1975

Wurtz-Fittig synthesis

s. 1, 633; 2, 710/a; 3, 669; ring closure s. A. C. Cope and S. W. Fenton, Am. Soc. 73, 1668 (1951)

Synthesis of hydrocarbons from ethers

←

s. 5, 581; optically active compounds s. Am. Soc. 72, 849 (1950)

Sodium hydroxide

NaOH

Introduction of the aldehyde group into ar. nuclei according to Reimer-Tiemann

s. 2, 714; 3, 670; s. a. G. S. Kolesnikov, V. V. Korshak, and J. P. Krakovnaya, Ж. 21, 397 (1951); C. A. 45, 7553c

Sodium/alcohol

NaOR

Alkylation of β -ketocarboxylic acid esters

s. 1, 637; 2, 717/8, 827; s. a. G. Tschudi and H. Schinz, Helv. 33, 1865 (1950)

Alkylation of acylaminomalonic esters **α -Aminocarboxylic acids from halides****Synthesis with addition of 2 C-atoms**

s. 3, 674; s. a. J. H. Burckhalter and V. C. Stephens, Am. Soc. 73, 56 (1951)

Alkylation of α -cyanocarboxylic acid esters

s. 6, 802

Sodium-tert-amylate

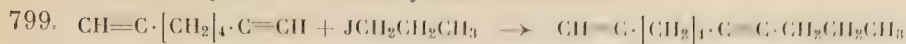
Alkylation of ketones

s. 3, 671; s. a. Bl. 1950, 533, 537

Sodium/liq. ammonia

Na/NH₃**Acetylenehalides from dihalides**

s. 5, 588; from iodochlorides s. W. R. Taylor and F. M. Strong, Am. Soc. 72, 4263 (1950)

Partial alkylation of diacetylene derivatives

Octa-1,7-diyne in dry ether added during 10 min. with stirring and alcohol- CO_2 -cooling to a suspension of 1.1 moles of NaNH_2 in liq. NH_3 (prepared from Na with $\text{Fe}(\text{NO}_3)_3$ catalyst according to Vaughan, Vogt, and Nieuwland, *Am. Soc.* 56, 2120 (1934)), stirred 2 hrs., propyl iodide in ether gradually added, and stirring continued for another 6 hrs. at ca. $-40^\circ \rightarrow$ undeca-1,7-diyne. Y: 86%; conversion 49%. Propyl bromide gives a much lower yield. F. e. s. R. A. Raphael and F. Sondheimer, *Soc.* 1950, 115, 120.

Sodium amide

 NaNH_2 **Aminoalkylation of ketones** $\text{COCH} \rightarrow \text{COCR}$

s. 3, 679; s. a. W. G. Stoll, C. Frey, and C. J. Morel, *Helv.* 33, 1208 (1950); cf. N. Sperber, R. Fricano, and D. Papa, *Am. Soc.* 72, 3068 (1950)

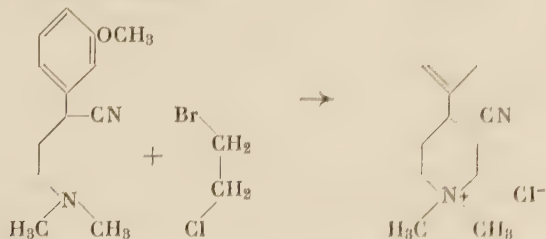
Alkylation of nitriles $\text{CHCN} \rightarrow \text{CRCN}$

s. 1, 656; 3, 680; 4, 774; s. a. R. Paul and S. Tschelitcheff, *Bl.* 1949, 470

Piperidinium ring synthesis

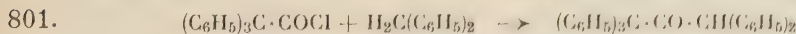
O

800.



Dimethylaminoethyl-m-methoxybenzyl cyanide added dropwise at 20° to powdered NaNH_2 in toluene with stirring and water cooling, stirring continued for 5 hrs. at the same temp., cooled to 10° , ethylene chlorobromide added at $8-10^\circ$, and worked up after $\frac{1}{4}$ hr. $\rightarrow$ 1,1-dimethyl-4-m-methoxyphenyl-4-cyanopiperidinium chloride. Y: 70%. F. e. s. H. Kägi and K. Miescher, *Helv.* 32, 2489 (1949).

Potassium amide

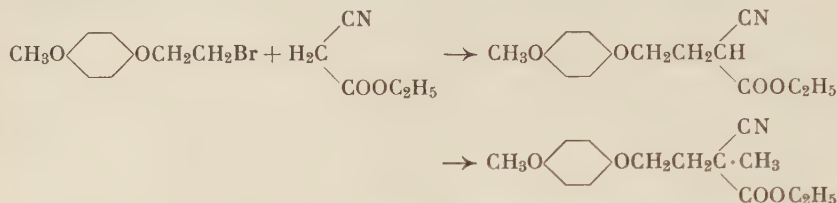
 KNH_2 **Ketones from carboxylic acid chlorides** $\text{COCl} \rightarrow \text{COR}$ 

A soln. of triphenylacetyl chloride in dry benzene added rapidly to a suspension of K-diphenylmethide (prepared from diphenylmethane and KNH_2) in ether cooled in a Dry Ice acetone bath, then refluxed 24 hrs. $\rightarrow$ pentaphenylacetone. Y: 70-87%. F. e. s. S. W. Kantor and C. R. Hauser, *Am. Soc.* 72, 3290 (1950).

Potassium carbonate

Alkylation of α -cyanocarboxylic acid esters

802.

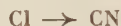


A mixture of 1-bromo-2-(p-methoxyphenoxy)ethane, anhydrous K-carbonate, and ethyl cyanoacetate refluxed 22 hrs. at 130°/120 mm. $\rightarrow$ ethyl- α -cyano- γ -(p-methoxyphenoxy)butyrate (Y: 81%) added to a soln. of Na in abs. ethanol, stirred and treated at reflux temp. with methyl iodide over a period of 0.5 hr., and refluxing continued for 5 hrs. $\rightarrow$ ethyl α -cyano- α -methyl- γ -(p-methoxyphenoxy)butyrate (startg. m. f. 12) (Y: 91%). N. J. Leonard and W. C. Wildman, Am. Soc. 71, 3089 (1949).

Potassium cyanide



Nitriles from chlorides



803.



2-(Chloromethyl)thiophene and KCN in acetone refluxed 6 hrs. $\rightarrow$ 2-thienylacetonitrile. Y: 80%.—In alcohol-water 30% of α -(ethoxymethyl)thiophene are formed as by-product. P. Cagniant, Bl. 1949, 847 (1949).

Triethylamine



Ketenedimers from carboxylic acid chlorides



s. 4, 779; cf. C. M. Hill et al., Am. Soc. 73, 1660 (1951)

Copper



Dimerization

Diaryls from arylhalides



s. 1, 660-2; s. a. H. Brockmann, R. Neeff, and E. Mühlmann, B. 83, 467 (1950)

Ethylene derivatives from 1,1-dihalides



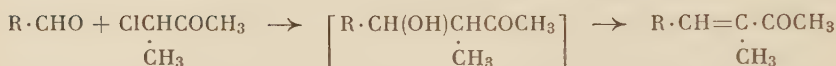
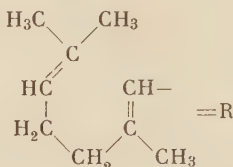
s. 5, 594; s. a. R. E. Buckles and G. M. Matlack, Org. Synth. 31, 104 (1951)

Dimerization of halides

of chlorides s. 1, 668; 4, 780; of bromides s. E. H. Farmer and C. G. Moore, Soc. 1951, 131

Ethylene derivatives from aldehydes

807.



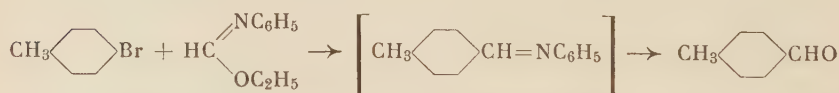
α,β -Ethyleneketones. A vigorously reacting mixture of Mg, ethyl bromide, and dry ether added to a mixture of Mg (etched by a trace of iodine) and 3-chlorobutan-2-one, free of HCl, then a mixture of citral, more 3-chlorobutan-2-one, and dry ether added under N_2 and gentle refluxing, stirring and refluxing continued until the visible reaction has stopped, thereafter an additional hr., and the product distilled quickly, whereby water is split off $\rightarrow$ pseudoisomethylionone. Y: up to 48%.—By using chloroketone in place of bromoketone, the yield could be considerably improved. M. G. J. Beets, R. 69, 307 (1950).

Aldehydes from halides**with orthoformic acid esters**

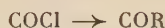
s. 1, 683; s. a. Y. Hirshberg, E. and F. Bergmann, Am. Soc. 72, 5120 (1950)

with N-phenylformimide

808.



N-Phenylformimide (prepn. s. 234) added dropwise at room temp. to p-tolyl-Mg-bromide (prepared from p-bromotoluene and Mg in ether in the presence of ethyl bromide and a crystal of iodine), refluxed 30 min., decomposed with ice-HCl, and refluxed another 30 min. to hydrolyze the anil $\rightarrow$ p-tolualdehyde. Y: 82.2% as bisulfite compound. F. e. s. L. I. Smith and J. Nichols, J. Org. Chem. 6, 489 (1941).

Ketones from carboxylic acid chlorides
Steric hindrance in Grignard reactions


809.



A certain amount of steric hindrance is necessary to obtain ketones from carboxylic acid chlorides and Grignard compounds. Certain mono-ortho subst. Grignard compounds give ketones with equimolecular proportions and reverse order of addition.—E: An ethereal soln. of 1-naphthyl-MgBr added slowly with stirring and ice-cooling to an ethereal soln. of benzoyl chloride, and heated for 5 hrs. → phenyl 1-naphthyl ketone. Y: 69%. F. e. s. I. I. Lapkin and A. V. Lyubimova, *Ж. 19*, 707 (1949); C. A. 44, 1058a.

Ketocarboxylic acids from
dicarboxylic acid anhydrides

←

810. This method is superior to the Friedel-Crafts' in those cases where nitrobenzene or tetrachloroethane must be used as a solvent, and may also serve for the determination of the orientation of the acids produced by the Friedel-Crafts method. E. s. J. A. McRae, R. A. B. Bannard, and R. B. Ross, *Can. J. Research* 28B, 73 (1950).

1-Subst. 1,2-dihydroisoquinolines

←

s. 5, 600; s. a. G. Wittig et al., A. 572, 15 (1951)

Magnesium/cuprous chloride

Mg/CuCl

Highly branched ketones from
carboxylic acid chlorides


811. $(\text{CH}_3)_3\text{C} \cdot \text{MgCl} + \text{ClCOC}(\text{CH}_3)_3 \rightarrow (\text{CH}_3)_3\text{C} \cdot \text{CO} \cdot \text{C}(\text{CH}_3)_3$

A filtered 3 M soln. of *tert*-butyl-MgCl added at reflux temp. over a 1 hr. period to a soln. of trimethylacetyl chloride and CuCl in anhydrous ether, most of the solvent distilled off, then heated at 100° for 3 days → hexamethylacetone. Y: 71.6%.—Reactions in glass without CuCl gave only a yield of 1-2%. Yields with straight chain reactants are not as markedly improved as with highly branched ones. N. C. Cook and W. C. Percival, *Am. Soc.* 71, 4141 (1949).

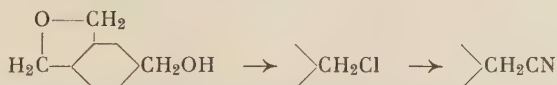
Mercuric cyanide

Hg(CN)₂

Nitriles from alcohols via chlorides

Synthesis with addition of 1 C-atom

812.



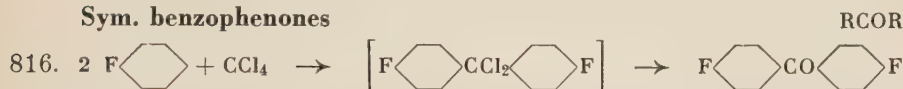
Piperonyl alcohol allowed to react with concd. HCl and sufficient CaCl_2 to saturate the aq. layer → 3,4-methylenedioxybenzyl chloride

1,2-Diaroylthylenes



Fumaryl chloride added slowly with stirring to a mixture of finely powdered AlCl_3 and benzene, stirring continued for 1 hr. at room temp. $\rightarrow$ *trans*-dibenzoylthylene. Y: 74%. F. e. s. J. B. Conant and R. E. Lutz, Am. Soc. 45, 1303 (1923); s. a. N. Campbell and N. M. Khanna, Soc. 1949, S33.

Sym. benzophenones

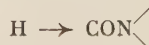


p-Fluorobenzene added to a mixture of dry CCl_4 , anhydrous AlCl_3 , and CS_2 , kept 3 hrs. at room temp., ice added, excess CS_2 removed by steam distillation, and heating continued for 2 hrs. to hydrolyze the 4,4'-difluorobenzophenone dichloride $\rightarrow$ 4,4'-difluorobenzophenone. Y: 85%. F. e. s. J. P. Picard and C. W. Kearns, Can. J. Research 28B, 56 (1950).

 α -Ketocarboxylic acids

AlCl_3 added gradually with stirring at 0° to a soln. of 2-ethyl-4-methylresorcinol and ethyl oxalyl chloride in nitrobenzene, allowed to stand 24 hrs. at room temp., decomposed with ice-HCl, and the nitrobenzene removed by steam distillation $\rightarrow$ 2,4-dihydroxy-3-ethyl-5-methylphenylglyoxylic acid. Y: 70%. F. e. s. R. D. Sprenger, P. M. Ruoff, and A. H. Frazer, Am. Soc. 72, 2874 (1950).

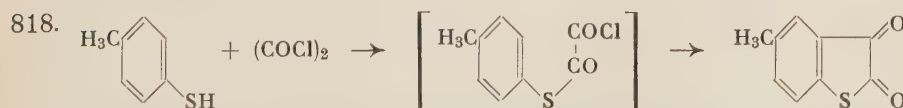
Carboxylic acid amides from hydrocarbons



Synthesis with addition of 1 C-atom

s. 5, 607; subst. carboxylic acid amides s. J. H. Saunders, R. J. Slocombe, and E. E. Hardy, Am. Soc. 72, 3312 (1950)

Thianaphthenequinones



48 gm. of oxalyl chloride in dry ether added dropwise to 31 gm. p-thiocresol in ether, warmed on a steam bath, the ether evaporated, excess

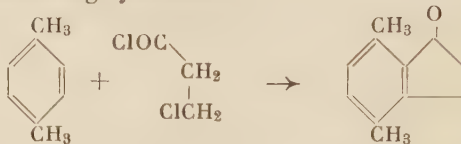
oxalyl chloride removed in a vacuum desiccator over KOH, the residue dissolved in CS_2 , cooled to 0° , AlCl_3 added, the temp. allowed to rise to room temp., then refluxed 0.5 hr. $\rightarrow$ 30 gm. 5-methylthianaphthenequinone (startg. m. f. 126). F. e. s. D. Papa, E. Schwenk, and H. F. Ginsberg, *J. Org. Chem.* **14**, 723 (1949).

Aluminum chloride/sulfuric acid

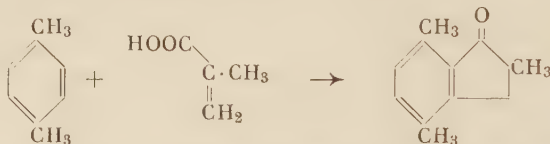
$\text{AlCl}_3/\text{H}_2\text{SO}_4$

One-step indanone ring synthesis

819.



A soln. of β -chloropropionyl chloride and p-xylene in CS_2 added over 45 min. to AlCl_3 covered with CS_2 , stirred 3 hrs. at room temp., CS_2 removed at the water-pump, concd. H_2SO_4 added, and heated 45 min. at $90^\circ \rightarrow$ 4,7-dimethyl-1-indanone. Y: 72.5%.



A mixture of p-xylene and aq. 40%-methacrylic acid added to cold anhydrous liq. HF in a pressure reactor, shaken to aid in soln., and heated 6 hrs. at $90^\circ \rightarrow$ 2,4,7-trimethyl-1-indanone. Y: 62.1%. F. e. s. R. T. Hart and R. F. Tebbe, *Am. Soc.* **72**, 3286 (1950).

Stannic chloride

SnCl_4

Shortened phenanthridine ring closure

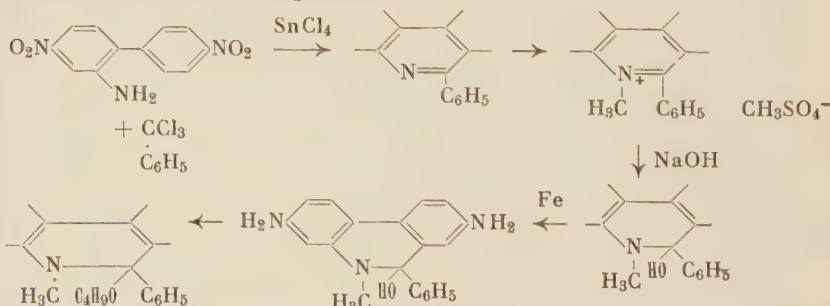
6-Alkoxy-5,6-dihydrophenanthridines

from phenanthridinium salts

Pseudobases

Amines from nitro compounds

820.



A mixture of benzotrichloride and SnCl_4 added during 40 min. to a boiling soln. of 4,4'-dinitro-2-aminodiphenyl in dry nitrobenzene, re-

fluxing continued for 1 hr., part of the nitrobenzene and SnCl_4 removed by distillation, dimethyl sulfate added at 190° during 2 min., kept 45 min. at ca. 180° , the residual nitrobenzene removed by steam distillation over a period of 7 hrs., partially neutralized at the boiling point with 2 *N* NaOH, filtered hot, added at ca. 80° during 7 min. to a boiling, vigorously stirred suspension of reduced Fe in water, stirred 45 min. at the boiling point, filtered, the filtrate treated with aq. NH_3 , reboiled, on the next day filtered again, the filtrate stirred with butanol, then aq. NaOH added $\rightarrow$ 3,8-diamino-6-butoxy-6-phenyl-5-methyl-5,6-dihydrophenanthridine. Y: 67%. Limitations of the method for the ring closure s. H. J. Barber et al., *J. Soc. Chem. Ind.* 69, 82 (1950); pseudobases s. a. B. Skinner, *Soc.* 1950, 823.

Chromium sulfate

CrSO_4

Dimerization

$2 \text{ RHal} \rightarrow \text{R} \cdot \text{R}$

821.

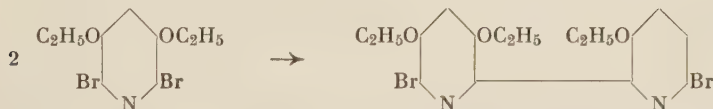


A soln. of CrSO_4 in 0.1 *N* H_2SO_4 added, in an atmosphere of H_2 , to a soln. of 5-chloroacridine in acetic acid at 20° , after 30 min. concd. H_2SO_4 and $\text{K}_2\text{Cr}_2\text{O}_7$ added, and boiled for 20 min. $\rightarrow$ 9,9'-biacridine. Y: 96%. R. Royer, *Soc.* 1949, 1663.

Ferric bromide

FeBr_3

822.



Dipyridyls. 2,6-Dibromo-3,5-diethoxypyridine shaken 6 hrs. in sunlight at 0° with a mixture of FeBr_3 and $\text{Br}_2 \rightarrow$ 6,6'-dibromo-3,3',5,5'-tetraethoxy-2,2'-dipyridyl. Y: 95-100%. H. J. den Hertog and B. Mulder, *R.* 68, 433 (1949).

Via intermediates

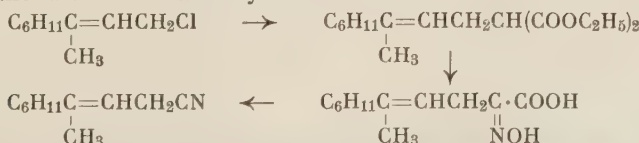
v.i.

β, γ -Ethylenenitriles from

$\leftarrow$

β, γ -ethylenehalides via malonic esters and α -oximinocarboxylic acids

823.



Ethyl geranylmalonate from geranyl chloride and ethyl malonate (Y: 50%) added slowly at 0° to a soln. of Na in ethanol, *n*-amyl nitrite

added dropwise with vigorous stirring, ethanol removed under reduced pressure at 30°, mixed with crushed ice, acidified with aq. 25% -H₂SO₄, extracted with ether, washed with 10% -NaOH until colorless, and the aq. soln. thus obtained heated 15 min. on a steam bath, the dissolved ether being distilled off → crude α -oximinogeranyl-acetic acid (Y: 90%) suspended in light petroleum, acetic anhydride added slowly with stirring, and the resulting soln. stirred with water for 2 hrs. → geranyl cyanide (Y: 70%).—Other methods were inefficient. F. e. s. D. Barnard and L. Bateman, Soc. 1950, 926.

Sulfur †

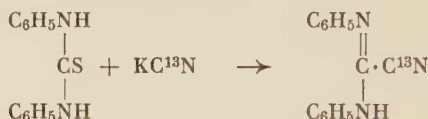
CC †† S

Basic lead carbonate $Pb(OH)_2 \cdot PbCO_3$ **Cyanoformamidines from thioureas**

←

Labeled compounds

824.



Basic Pb-carbonate, N,N'-diphenylthiourea, and 95%-alcohol added to aq. KC¹³N, and warmed at 50-55° with stirring for ca. 1 hr., until a sample does not discolorize Pb-carbonate on short boiling → N,N'-diphenylcyanoformamidine (startg. m. f. 74). Crude Y: 90%. G. Ehrens-värd and R. Stjernholm, Acta Chem. Scand. 3, 971 (1949).

Carbon †

CC †† C

*Without additional reagents**w. a. r.***Allyl-aminomethane derivatives**

←

825.



A mixture of α -allylbenzylamine, 36-38%-formalin, and methanol refluxed 10 hrs., 6 N H₂SO₄ added, and steam-distilled → benzaldehyde (Y: 81%) and 3-butenylamine (crude Y: 56%). F. e. s. R. M. Horowitz and T. A. Geissman, Am. Soc. 72, 1518 (1950).

Electrolysis

↘

Ketones from carboxylic acids according to Kolbe $RCOOH + HOOCR' \rightarrow R \cdot R'$

s. 1, 715/6; s. a. R. P. Linstead et al., Soc. 1950, 3326, 3331; retention of optical activity s. Soc. 1950, 3333

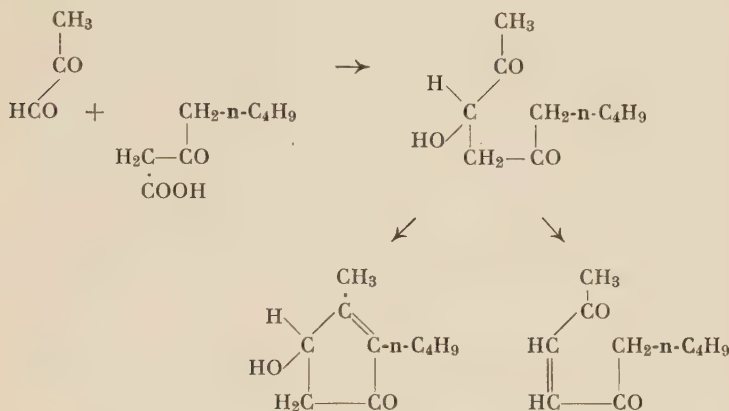
Sodium hydroxide

NaOH

**α,β -Ethylene- γ -diketones and
cyclopentenones from α -ketoaldehydes
and β -ketocarboxylic acids
via α -hydroxy- γ -diketones**

←

826.



Na- β -oxocaprylate and pyruvaldehyde kept in very dil. aq. NaOH of pH 8 at room temp. for 2 days $\rightarrow$ 3-hydroxy-2,5-decanedione (Y: 65%)

shaken overnight with 2%-NaOH soln. under $\text{N}_2 \rightarrow$ d,l-dihydrocinerolone (Y: 63%).

treated with acetic anhydride and a little anhydrous Na-acetate, and heated 10 min. at 100° on the following day $\rightarrow$ 3-decene-2,5-dione (Y: ca. 100%).

F. e. s. M. S. Schechter, N. Green, and F. B. LaForge, Am. Soc. 71, 3165 (1949).

Boron fluoride

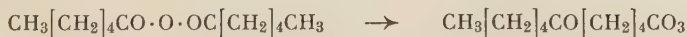
 BF_3

**Sym. ketones from
carboxylic acid anhydrides**



**Self-condensation of
carboxylic acid anhydrides**

827.



Caproic acid anhydride allowed to react with BF_3 at ca. 0° $\rightarrow$ di-n-amyl ketone. Y: 64%. F. e. s. E. H. Man and C. R. Hauser, Am. Soc. 72, 3294 (1950).

Aluminum chloride

 $AlCl_3$

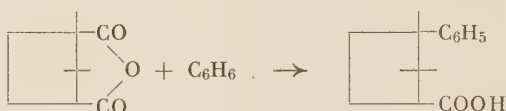
**Synthesis of hydrocarbons
from carboxylic acid chlorides
and of carboxylic acids from
carboxylic acid anhydrides**

←

828. In certain cases, arylation with loss of CO rather than ketone formation occurs in the presence of $AlCl_3$, e.g. with derivatives of tert. acids and benzene. However, derivatives of arylated tert. acids give cyclic ketones predominantly.



Methyl 1-chlorocarbonylcyclopentylacetate added to $AlCl_3$ and benzene below $10^\circ \rightarrow$ methyl 1-phenylcyclopentylacetate. Y: 78.9%. (Soc. 1949, 1953).



$AlCl_3$ added in small portions to a vigorously stirred soln. of camphoric anhydride and benzene $\rightarrow$ 2-phenyl-1,1,2-trimethylcyclopentane-5-carboxylic acid. Y: 67% (Soc. 1949, 1961). F. e. s. E. Rothstein and R. W. Saville, Soc. 1949, 1946-61.

**Aminoketones from
N-carboxyaminocarboxylic
acid anhydrides**

←

829.



Powdered $AlCl_3$ added gradually with stirring at -10° to a suspension of anhydro-N-carboxyglycine in methylene dichloride, benzene added, the temp. allowed to rise to $10-20^\circ$, where it is maintained until gas evolution ceases $\rightarrow$ ω -aminoacetophenone. Y: 79% (isolated as picrate).—Similarly: Anhydro-N-carboxy-DL- β -phenylalanine $\rightarrow$ 2-aminoindanone. Y: 54% (isolated as picrate). F. e. s. F. S. Statham, Soc. 1951, 213.

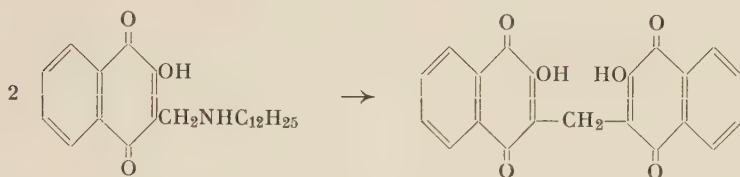
Acetic acid

 CH_3COOH

Methylene condensation

←

830.



2-Hydroxy-3-dodecylaminomethyl-1,4-naphthoquinone warmed with glacial acetic acid $\rightarrow$ 3,3'-methylenebis-2-hydroxy-1,4-naphthoquinone. Y: 90%. C. E. Dalglish, Am. Soc. 71, 1697 (1949).

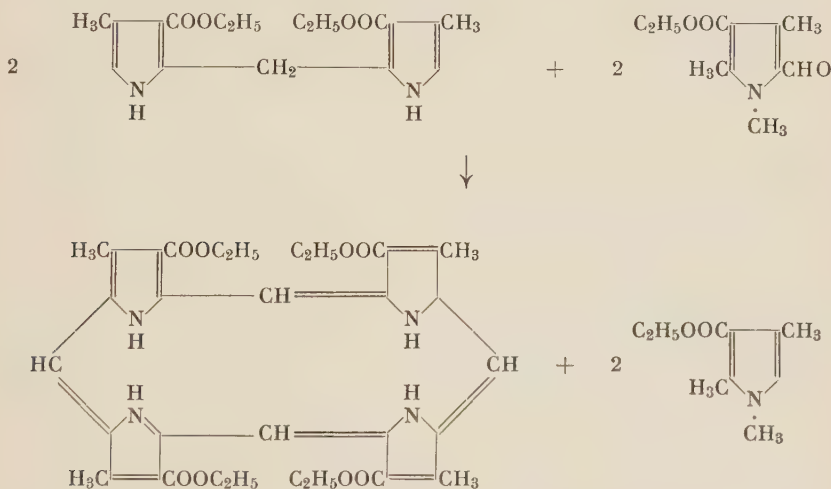
Hydrochloric acid

HCl

New synthesis of porphyrins

←

831.



A soln. of 3,3'-dicarbethoxy-4,4'-dimethyldipyrromethane and 1,2,4-trimethyl-3-carbethoxy-5-formylpyrrole in ether saturated with dry HCl at 0° , stoppered tightly, and allowed to stand 10 days in the dark at room temp. $\rightarrow$ 1,4,5,8-tetramethyl-2,3,6,7-tetracarboxyporphyrin. Y: up to 40%.—The pyrrole aldehyde appears to serve solely as the source of the methin groups. J. S. Andrews, A. H. Corwin, and A. G. Sharp, Am. Soc. 72, 491 (1950).

Elimination

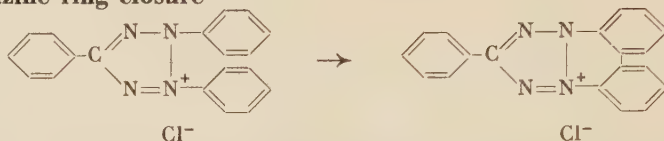
Hydrogen $\downarrow$ CC $\uparrow$ H

Without additional reagents

w.a.r.

Pyridazine ring closure

832.



A soln. of triphenyltetrazolium chloride in abs. alcohol exposed to UV-light during 14 hrs. $\rightarrow$ 2,3-diphenylene-5-phenyltetrazolium chloride. Y: almost 100%. I. Hausser, D. Jerchel, and R. Kuhn, Chem. B. 82, 195 (1949).

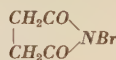
Aluminum chloride/hydrochloric acid

 $AlCl_3/HCl$

Scholl ring closure

Migration of alkyl groups

833. HCl catalyzes the Scholl reaction and the intramolecular migration of alkyl groups in phenol homologues, ar. ketones, and ar. hydroxyketones, in the presence of $AlCl_3$. These reactions do not occur, or occur at greatly reduced rates, when a stream of dry O_2 or N_2 is passed through the reaction mixture. E. s. G. Baddeley, Soc. 1950, 994.

N-Bromosuccinimide

Dehydrogenation

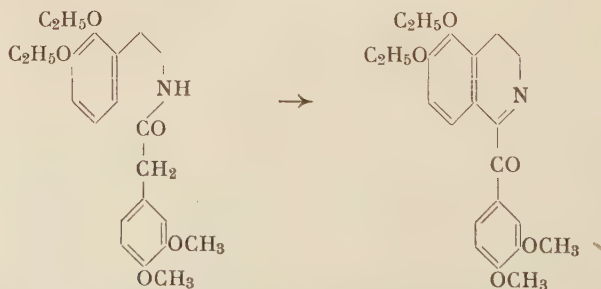
CHCH $\rightarrow$ C:C

s. 1, 726; 2, 757/8; O-heterocyclics s. T. A. Geissman, T. G. Halsall, and E. Hinreiner, Am. Soc. 72, 4326 (1950); 73, 782 (1951)

Phosphorus oxychloride

 $POCl_3$ Bischler-Napieralski ring closure
with simultaneous oxidation

834.



$POCl_3$ added to a soln. of 3,4-dimethoxyphenylacetyl- β -(2,3-diethoxyphenyl)ethylamide in xylene, and refluxed 20 min. $\rightarrow$ 1-(3,4-dimethoxy-

benzoyl)-5,6-diethoxy-3,4-dihydroisoquinoline. Crude Y: 87.9%. F. e., without oxidation, s. G. Tsatsas, Bl. 1949, 884.

Oxygen

O₂

Dehydrogenation

CHCH → C:C

s. 3, 705; s. a. G. T. Gmitter and F. L. Benton, Am. Soc. 72, 4586 (1950)

Sulfur

S

s. 6, 858; s. a. W. E. Bachmann and G. D. Johnson, Am. Soc. 71, 3463 (1949)

Selenium dioxide

SeO₂

α,β-Ethyleneketones from ketones

s. 4, 807; s. a. L. F. Fieser and S. Rajagopalan, Am. Soc. 72, 5530 (1950)

Chromic acid

CrO₃

s. 6, 709

9(H)-Pyrid[3.4-b]indoles

s. 6, 780

Bromine

Br

835.



Br₂ added dropwise to a soln. of 6-phenyl-4-methyl-pyridazinone in hot glacial acetic acid, then heated at 100° for 15 min. → 6-phenyl-4-methyl-3-pyridazone. Y: 83%. S. Dixon, H. Gregory, and L. F. Wiggins, Soc. 1949, 2139; s. a. V. R. Mattox and E. C. Kendall, J. Biol. Chem. 185, 601 (1950).

Cobalt-silica

Co-SiO₂

836.



2-Benzyl-4,5-dihydroglyoxaline heated 45 min. at 250° with 40%-Cokieselguhr catalyst until the H₂-evolution is complete, and the reaction product isolated as hydrochloride → 2-benzylglyoxalinium chloride. Y: 72%. P. Oxley and W. F. Short, Soc. 1950, 859.

Nickel-chromium oxide

Ni-Cr₂O₃**Benzene as hydrogen acceptor**

s. 4, 811; also with other catalysts, preferably platinum s. Am. Soc. 71, 2956-2964 (1949)

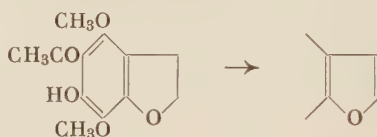
Palladium-carbon

Pd-C

s. 1, 729-31, 761; 2, 765; 4, 853; s. a. M. C. Kloetzel and F. L. Chubb, Am. Soc. 72, 150 (1950); G. F. Woods, A. L. Van Artsdale, and F. T. Reed, Am. Soc. 72, 3221 (1950); H. H. Günthard et al., Helv. 34, 959 (1951)

Dehydrogenation in the vapor phase

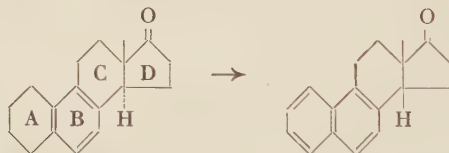
837.



1 gm. 6-hydroxy-4,7-dimethoxy-5-acetylcoumaran sublimed at 150°/10⁻⁴ mm. through a column of 30% Pd-norit on glass wool, and the sublimation repeated with fresh catalyst → 0.8 gm. 6-hydroxy-4,7-dimethoxy-5-acetylcoumarone.—The success of the dehydrogenation depends on the nature of the catalyst. R. A. Baxter, G. R. Ramage, and J. A. Timson, Soc. 1949, S30.

Dehydrogenation and epimerization
The action of palladium-on-charcoal
catalyst on steroids

838.

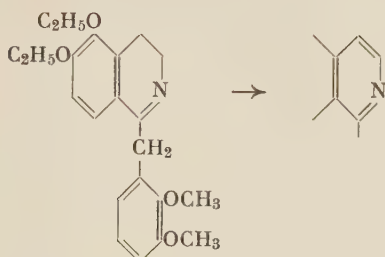


At 250°, three effects are obtained, depending on the compounds: (1) When the C-D ring juncture has the *trans*-configuration epimerization takes place at C₁₄. When the C-D ring juncture is *cis*, and when ring D is open in compounds of both configurations, no epimerization is observed. (2) When ring A (and/or B) is alicyclic it is aromatized. (3) A C₁₇ hydroxyl group is dehydrogenated to a keto group.—At 350°, rings A, B, and C are dehydrogenated, and a cleavage of ring D occurs with loss of a carbon atom as CO₂ in such a manner that a 1-ethyl-2-methylphenanthrene structure results.—E: dl-1,2,3,4-Tetrahydrodesoxyequilenin and an equal weight of 5%-Pd-on-charcoal heated 8 min. at ca. 250° → dl-desoxyisoequilenin. Y: 86%. F. e. s. W. E. Bachmann and A. S. Dreiding, Am. Soc. 72, 1323 (1950).

Palladium-pumice

Dehydrogenation

839.



10% -Pd-on-pumice (prepn. s. original paper) added to a soln. of 1-(2,3-dimethoxybenzyl)-5,6-diethoxy-3,4-dihydroisoquinoline in tetralin, and boiled under CO_2 for 3 hrs. $\rightarrow$ 1-(2,3-dimethoxybenzyl)-5,6-diethoxy-3,4-dihydroisoquinoline. Y: 90%. F. e. s. G. Tsatsas, Bl. 1949, 884.

Via intermediates

v.i.

Ethylene derivatives from hydrocarbons via bromides

840.



A mixture of 2-n-butyl-naphthalene, N-bromosuccinimide, and CCl_4 refluxed 6 hrs., and the crude bromo derivative heated 2 hrs. with quinoline at $150\text{--}160^\circ \rightarrow$ 1-(2-naphthyl)-1-butene. Y: 81%. G. B. Pickering and J. C. Smith, R. 69, 535 (1950).

Oxygen $\uparrow$ CC $\uparrow$ O

Without additional reagents

w.a.r.

Thermal cleavage

Ethylene derivatives from acetates

CHC(OAc) $\rightarrow$ C:C

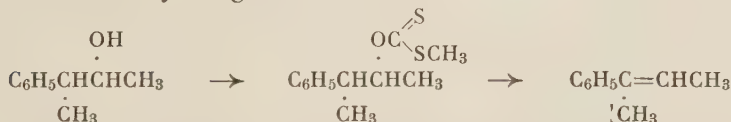
s. 2, 768; 4, 814; s. a. K. N. Campbell, J. O. Knobloch, and B. K. Campbell, Am. Soc. 72, 4380 (1950); to 4, 814 s. a. Am. Soc. 72, 839 (1950)

Dehydration via xanthates

CHC(OH) $\rightarrow$ C:C

cis-Elimination by Chugaev reaction

841.



The Chugaev reaction is predominantly a *cis*-elimination reaction in an acyclic system.—3-Phenyl-2-butanol, K, and dry toluene refluxed 16 hrs., cooled, excess K removed, a large excess of CS_2 added, refluxed with stirring overnight, again cooled, methyl iodide added, and

refluxed 4 hrs. $\rightarrow$ 3-phenyl-2-butyl xanthate (Y: 85%) heated at 180° with distillation of the olefin formed $\rightarrow$ 2-phenyl-2-butene (Y: 91%). D. J. Cram, *Am. Soc.* 71, 3883 (1949); s. a. E. R. Alexander and A. Mudrak, *Am. Soc.* 72, 3194 (1950).

Quinoline ring from enamines

s. 3, 713; 5, 614; optimum conditions s. W. J. Adams and D. H. Hey, *Soc.* 1950, 3254

Naphthyridines from aminopyridines

s. 5, 355; s. a. C. R. Hauser and G. A. Reynolds, *J. Org. Chem.* 15, 1224 (1950)

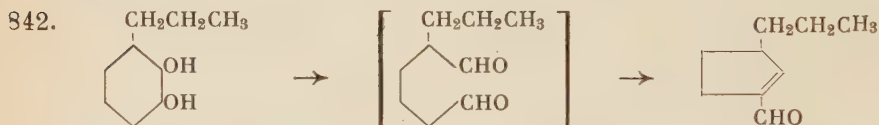
Quinoline ring via enamines

EMME method

s. 3, 715; s. a. G. R. Loppin, *J. Chem. Education* 28, 126 (1951)

1-Cyclopentenealdehydes

Ring contraction



Pb-tetraacetate added over a period of 1 hr. under N_2 to a vigorously stirred mixture of 3-n-propylcyclohexane-1,2-diol and anhydrous K-carbonate in benzene, then stirred for an additional hr., the isolated, undistilled 2-propyladipic aldehyde (Y: 68% when distilled) heated 5 hrs. with distilled water at 110° in a bomb $\rightarrow$ 3-n-propyl-1-cyclopentenealdehyde. Y: 52%. F. e. s. J. English, Jr., and G. W. Barber, *Am. Soc.* 71, 3310 (1949); s. a. E. B. Reid and J. F. Yost, *Am. Soc.* 72, 5232 (1950).

Sodium

Na

Acyloin condensation

COCH(OH)

s. 4, 816; s. a. F. Bouquet and C. Paquot, *Bl.* 1949, 440; A. C. Cope and E. C. Herrick, *Am. Soc.* 72, 983 (1950); J. C. Sheehan, R. C. O'Neill, and M. A. White, *Am. Soc.* 72, 3376 (1950)

Sodium hydroxide

NaOH

Cyclopentenones from α -hydroxy- γ -diketones

s. 6, 826

Anthrapyridones

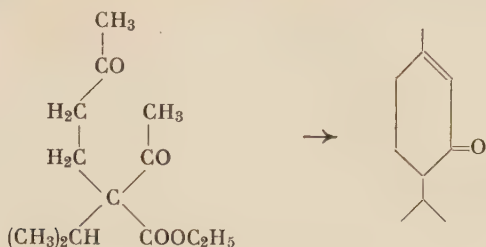
s. 6, 859

Potassium hydroxide/alcohol

KOH

Cyclohexenones

843.



Ethyl 3-isopropylheptane-2,6-dione-3-carboxylate dropped into a 20% soln. of KOH in methanol, then boiled for 7 hrs. → piperitone. Y: 84.8%. F. e. s. H. Henecka, Chem. B. 82, 112 (1949).

Sodium/alcohol

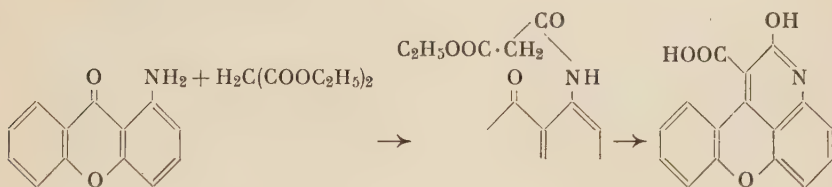
NaOR

Dieckmann condensation

4-Piperidones s. 3, 717; 3-piperidones s. A. W. D. Avison and A. L. Morrison, Soc. 1950, 1471

Camps pyridone ring closure**Dicarboxylic acid amide esters from dicarboxylic acid esters**

844.



A soln. of 1-xanthoneamine and ethyl malonate boiled 20 min., then most of the ester removed by rapid distillation → 1-(carbethoxyacetamido)xanthone (Y: 86%), a suspension of this compound in alcohol treated at the boiling point during 15 min. with a soln. of Na in alcohol, then boiled for an additional 15 min. → ethyl 2-hydroxy[1]benzopyrano[4,2-de]quinoline-1-carboxylate (Y: 90%). F. e. s. C. F. Koelsch and F. J. Lucht, Am. Soc. 71, 3556 (1949).

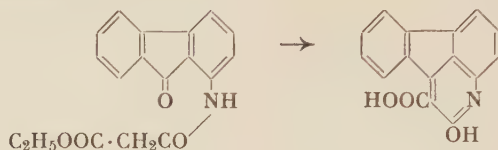
Azaindoles

s. 2, 817; s. a. J. C. Clayton and J. Kenyon, Soc. 1950, 2952

Sodium methoxide

4-Azafluoranthenes

845.



A mechanically stirred soln. of 5 gm. 1-carbethoxyacetamidofluorenone in anhydrous nitrobenzene treated with powdered Na-methoxide, then heated 11 hrs. at 135-140° $\rightarrow$ 3.4 gm. 3-hydroxy-4-azafluoranthene-2-carboxylic acid. F. e. s. J. W. Cook and J. S. Moffatt, Soc. 1950, 1160.

Sodium hydrogen carbonate

 NaHCO_3 **N-Heterocondensed rings**

s. 3, 726; pyrrolo 2.1-b thiazoles s. W. Traupel, M. Erne, and E. Sorokin, Helv. 33, 1960 (1950)

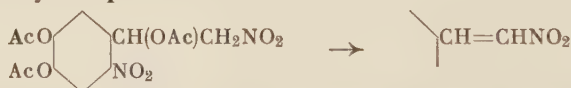
Sodium acetate

 CH_3COONa **α,β -Ethylene- γ -diketones from α -hydroxy- γ -diketones** $\text{CHC}(\text{OH}) \rightarrow \text{C}:\text{C}$

s. 6, 826

1,1-Nitroethylene derivatives from 1,2-nitroacetoxy compounds $\text{CHC}(\text{OAc}) \rightarrow \text{C}:\text{C}$

846.

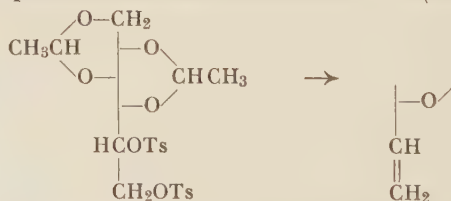


A mixture of 2-nitro-1-(2-nitro-4,5-diacetoxyphenyl)ethyl acetate, anhydrous Na-acetate, and acetic anhydride boiled 1-2 min. $\rightarrow$ β ,2-dinitro-4,5-diacetoxystyrene. Y: 96%. F. e. s. H. Burton, J. A. Duffield, and P. F. G. Prail, Soc. 1950, 1062.

Sodium iodide

 NaI **Glycols from di-p-toluenesulfonic acid esters** $\text{C}(\text{OTs})\text{C}(\text{OTs}) \rightarrow \text{C}:\text{C}$

847.



5,6-Ditosyl-1,3:2,4-diethylidenesorbitol, anhydrous NaI, and pure acetone heated 6 hrs. in a pressure bottle at 100° $\rightarrow$ 1,3:2,4-diethylidene-5,6-sorbitoleen. Y: 73%. F. e. s. P. Bladon and L. N. Owen, Soc. 1950, 598.

Pyridine

 C_5H_5N **Ethylene derivatives from acoxy compounds** $CHC(OAc) \rightarrow C:C$

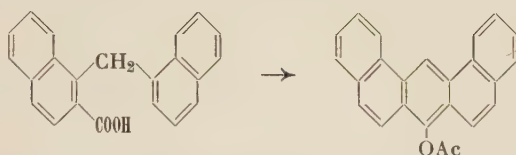
s. 6, 864

Zinc chloride

 $ZnCl_2$ **Anthracene ring**

○

848.



A mixture of 1,1'-dinaphthylmethane-2-carboxylic acid, glacial acetic acid, acetic anhydride, and a little anhydrous $ZnCl_2$ refluxed for ca. 1 hr. $\rightarrow$ 10-acetoxy-1,2,7,8-dibenzanthracene. Y: 85%. J. W. Cook and E. F. M. Stephenson, *Soc.* 1949, 842; method, see L. F. Fieser and E. B. Hershberg, *Am. Soc.* 59, 1032 (1937); 60, 1895 (1938).

Enediolethers from α -alkoxyacetals

←

849.



Ethoxyacetal dropped onto alumina pellets at 190° under a slight N_2 -pressure $\rightarrow$ 1,2-diethoxyethylene. Y: 70%. S. M. McElvain and C. H. Stammer, *Am. Soc.* 73, 915 (1951).

Alumina

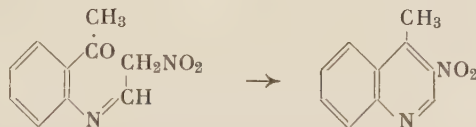
 Al_2O_3 **Dehydration** $CHC(OH) \rightarrow C:C$

s. 1, 744; 3, 730/1; s. a. D. T. Mowry and E. L. Ringwald, *Am. Soc.* 72, 2037 (1950); I. A. Goodman and P. H. Wise, *Am. Soc.* 72, 3076 (1950); V. N. Ipatieff, H. R. Appell, and H. Pines, *Am. Soc.* 72, 4260 (1950)

3-Nitroquinolines

○

850.



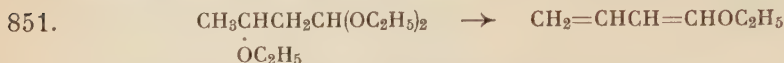
o-(2-Nitroethylideneamino)acetophenones and their oximes are quantitatively cyclized by activated alumina, except in a few cases.—E: An acetone soln. of 2-(2-nitroethylideneamino)acetophenone treated with 10 parts of activated Al_2O_3 , and left overnight $\rightarrow$ 3-nitrolepidine. F. e. s. K. Schofield and R. S. Theobald, *Soc.* 1950, 395.

Aluminum phosphate water glass

←

Alkoxydienes from alkoxyacetals

←



1,1,3-Triethoxybutane distilled through AlPO_4 -water glass at $300^\circ/10$ mm. over a period of 1 hr. $\rightarrow$ 1-ethoxy-1,3-butadiene. Y: 82%. F. e., catalysts, and reaction conditions s. W. Flaig, A. 568, 1 (1950).

Acetic acid

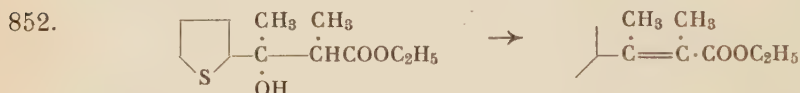
 CH_3COOH

Dehydration

 $\text{CHC}(\text{OH}) \rightarrow \text{C}:\text{C}$

s. 6, 628

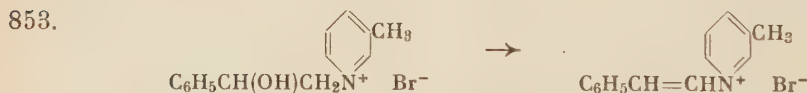
Oxalic acid

 $(\text{COOH})_2$ 

Ethyl α,β -dimethyl- β -hydroxy- β -(2-thienyl)propionate refluxed with 6% aq. oxalic acid for 3-6 hrs. $\rightarrow$ ethyl α,β -dimethyl- β -(2-thienyl)-acrylate. Y: almost 100%. Other dehydration reagents caused the formation of tarry by-products. F. e. s. R. E. Miller and F. F. Nord, J. Org. Chem. 15, 89 (1950); s. a. E. D. Bergmann, R. Pappo, and D. Ginsburg, Soc. 1950, 1369.

s. a. 3, 734; C. C. Price and J. A. Pappalardo, Am. Soc. 72, 2613 (1950)

Benzoyl chloride

 $\text{C}_6\text{H}_5\text{COCl}$ 

A mixture of 1-(2-phenyl-2-hydroxyethyl)-3-picolinium bromide and benzoyl chloride heated 1 hr. at $190\text{--}200^\circ \rightarrow$ 1-styryl-3-picolinium bromide. Y: 83%. F. e. s. L. C. King and W. B. Brownell, Am. Soc. 72, 2507 (1950).

Phosphorus pentoxide

 P_2O_5

s. 2, 783; s. a. R. L. Frank and R. E. Berry, Am. Soc. 72, 2985 (1950); styrenes E. T. McBee and R. A. Sanford, Am. Soc. 72, 4053 (1950)

Phosphorus pentoxide/phosphoric acid

 $\text{P}_2\text{O}_5/\text{H}_3\text{PO}_4$

Cyclic ketones from carboxylic acids

O

s. 5, 622; s. a. R. C. Gilmore, Jr., and W. J. Horton, Am. Soc. 73, 1411 (1951)

Phosphoric acid

 H_3PO_4 **Dehydration of stereoisomeric cyclic alcohols** $CHC(OH) \rightarrow C:C$

s. 6, 867

Polyphosphoric acid

 $H(PO_3H)_xOH$ **Cyclic ketones from carboxylic acids**

○

854.

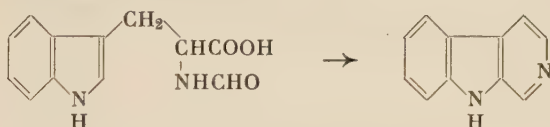


A mixture of 2-bromo-5-methoxyhydrocinnamic acid and polyphosphoric acid heated with vigorous stirring at 90-105° for 5 min. $\rightarrow$ 4-bromo-7-methoxy-1-indanone. Crude Y: 76%. F. e. s. H. R. Snyder and F. X. Werber, *Am. Soc.* 72, 2965 (1950).

Polyphosphoric acid/phosphorus oxychloride

 $H(PO_3H)_xOH/POCl_3$ **Bischler-Napieralski ring closure**

855.



A mixture of N-formyl-d,l-tryptophan, polyphosphoric acid, and $POCl_3$ heated 80 min. in an oil-bath at 125° with vigorous stirring $\rightarrow$ norharman. Y: 36%.—In certain cases, the mixture of polyphosphoric acid and $POCl_3$ is the only catalyst to effect cyclization. F. e. s. H. R. Snyder and F. X. Werber, *Am. Soc.* 72, 2962 (1950).

Phosphorus oxychloride

 $POCl_3$ **3,4-Dihydroisoquinolines**

s. 2, 788; s. a. L. Marion, L. Lemay, and R. Ayotte, *Can. J. Research* 28B, 21 (1950); E. R. Shepard and J. F. Noth, *Am. Soc.* 72, 4364 (1950); W. Reese and W. M. Eareckson, 3rd, *Am. Soc.* 72, 5195 (1950)

Oxazoles from oxazolidones

←

856.



Crude 2 gm. 2,5-diphenyl-4-oxazolidone warmed with $POCl_3$ for 0.5 hr. at 85-90°, $POCl_3$ removed at low pressure, the residue triturated with

ethereal 1%-HCl, collected, and shaken with water and ether $\rightarrow$ 1.5 gm. 2,5-diphenyloxazole. F. e. s. J. W. and R. H. Cornforth, Soc. 1949, 1028.

Sodium hydrogen sulfate

NaHSO_4

Enolethers from acetals

$\text{CHC(OR)}_2 \rightarrow \text{C:C(OR)}$

s. 6, 182; s. a. M. G. Voronkov, Ж. 20, 2060 (1950); C. A. 45, 5607h

Sulfuric acid

H_2SO_4

Dehydration of alcohols

$\text{CHC(OH)} \rightarrow \text{C:C}$

s. 5, 627; with 85% H_2SO_4 s. D. W. Adamson and J. W. Billingham, Soc. 1950, 1039; with 30% H_2SO_4 s. E. D. Bergmann, Am. Soc. 73, 1218 (1951)

Isoacyclics from alcohols

O

857. Tert. alcohols are cyclized more easily than sec. alcohols. E. for both types s. J. Colonge and L. Pichat, Bl. 1949, 855; s. a. H. W. D. Stubbs and S. H. Tucker, Soc. 1950, 3288.

Cyclic ketones from carboxylic acids

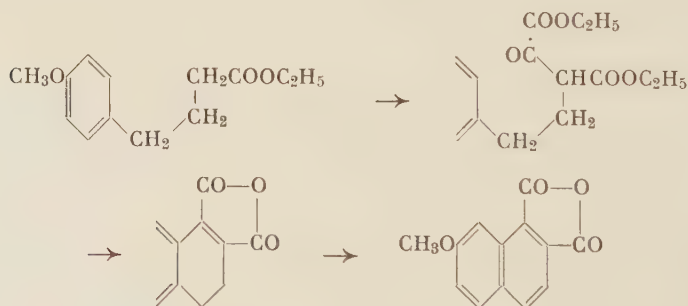
s. 2, 796/7; s. a. M. C. Kloetzel, R. P. Dayton, and H. L. Herzog, Am Soc. 72, 273 (1950)

**Dicarboxylic acid anhydrides
from carboxylic acid esters via
 α -keto- β -dicarboxylic acid esters**

Bougault ring closure

Dehydrogenation

858.



The K salt of ethyl α -(ethoxalyl)- γ -(p-methoxyphenyl) butyrate, prepared from ethyl γ -(p-methoxyphenyl)butyrate and ethyl oxalate in the presence of K-ethoxide in ether, added in small portions with stirring to ice-salt-cooled 60% H_2SO_4 , heated 15 min. on a steam bath.

cooled, treated with 80% H_2SO_4 , and heated 15 min. longer $\rightarrow$ 7-methoxy-3,4-dihydronaphthalene-1,2-dicarboxylic acid anhydride. Y: 77%. —By using H_2SO_4 just strong enough to effect the cyclization, aromatization in some cases can be prevented or at least minimized. Aromatization can be effected easily and in good yields with sulfur. F. e. s. L. F. Fieser and E. B. Hershberg, *Am. Soc.* 58, 2314 (1936); s. a. W. G. Dauben and M. Tanabe, *Am. Soc.* 71, 2877 (1949).

Xanthylum salts

s. 6, 162

Quinoline ring from azomethines according to Combes

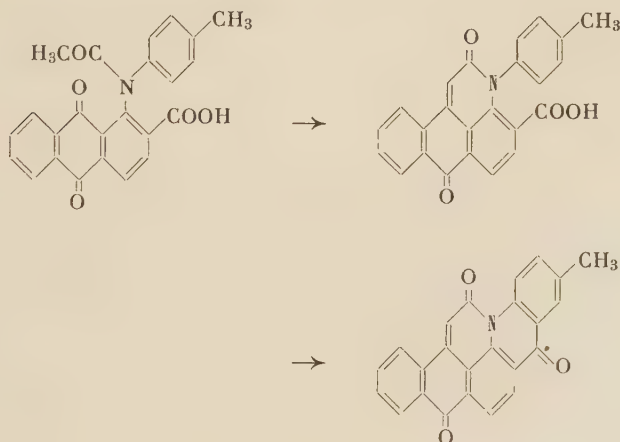
s. 4, 835; s. a. D. H. Hey and J. M. Williams, *Soc.* 1950, 1678; R. Adams and J. Campbell, *Am. Soc.* 72, 1021 (1950)

Chlorosulfonic acid

ClSO_3H

Anthrapyridonacridones via anthrapyridones

859.



1-(N-Acetyl-p-tolylamino)anthraquinone-2-carboxylic acid boiled 10 hrs. with 0.8% $\text{NaOH} \rightarrow$ N-(p-tolyl)-1,9-anthrapyridone-2-carboxylic acid (Y: 96%) warmed at 40-45° with chlorosulfonic acid for 2 hrs. $\rightarrow$ 4'-methyl-1,9-anthrapyridonacridone (Y: 98%). F. e. s. A. M. Lukin and P. M. Aronovich, *Ж.* 19, 358 (1949); *C. A.* 44, 1079h.

Iodine

I

Dehydration of alcoholsCHC(OH) $\rightarrow$ C:C

860.



3,4,5-Trimethoxyphenylethylcarbinol heated with a crystal of iodine under distillation conditions at diminished pressure $\rightarrow$ isoelemicin. Y: 85-87%.—Other methods (s. original paper) were less satisfactory. J. W. Cook, T. Y. Johnston, and J. D. Loudon, Soc. 1950, 537.

Hydrofluoric acid

HF

Cyclic ketones from carboxylic acids

O

s. 1, 758-61; 2, 801; s. a. M. F. Ansell and D. H. Hey, Soc. 1950, 2874

Cyclic ketones from carboxylic acids and carboxylic acid chlorides

861. The formation of cyclic ketones from carboxylic acids with HF or their chlorides with AlCl_3 can give markedly contrasting results. Syntheses of indan-1-one-carboxylic acids from β -arylsbst. glutaric acids. s. D. H. Hey and D. H. Kohn, Soc. 1949, 3177; s. a. C. D. Gutsche, Am. Soc. 73, 786 (1951).

Hydrochloric acid

HCl

DehydrationCHC(OH) $\rightarrow$ C:C

862.



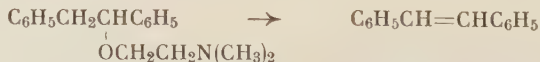
Perinaphthanol-7 in HCl-abs. alcohol refluxed 15 min. $\rightarrow$ perinaphthene. Y: 65-85%. — Other methods were not successful. V. Boekelheide and C. E. Larrabee, Am. Soc. 72, 1245 (1950); f. e. s. Am. Soc. 72, 1240 (1950).

with simultaneous esterification

s. 6, 689

Ethylene derivatives from ethersCHC(OR) $\rightarrow$ C:C

863.

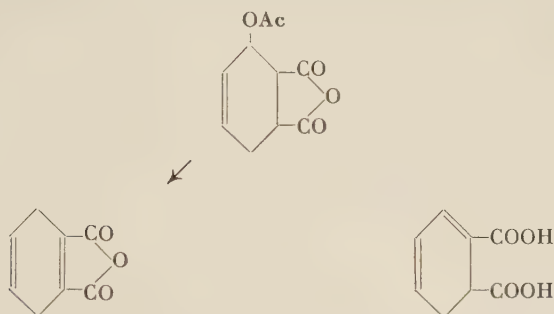


A soln. of β -dimethylaminoethyl 1,2-diphenylethyl ether in 20%-HCl heated 1 hr. on a steam bath $\rightarrow$ stilbene. Crude Y: ca. 95%. N. Sperber, R. Fricano, and D. Papa, Am. Soc. 72, 3068 (1950).

Ethylene derivatives from acoxy compounds with rearrangement

←

864.



3-Acetoxy-1,2,3,6-tetrahydrophthalic anhydride (prepn. s. 695)

heated with pyridine on a water bath for 10 min. → 3,6-dihydrophthalic anhydride. Y: almost 100%.

(50 gm.) refluxed with concd. HCl → 33 gm. 2,3-dihydrophthalic acid.

Also one-step syntheses of 3,6-dihydrophthalic anhydride from crotonaldehyde and maleic anhydride (cf. 695) s. W. Flaig, A. 568, 1 (1950).

Ar. amines from hydroaromatic oximes

←

Dehydroisomerization

s. 2, 778; s. a. H. E. Zaugg, M. Freifelder, and B. W. Horrom, J. Org. Chem. 15, 1197 (1950)

Isocyclics from ketones

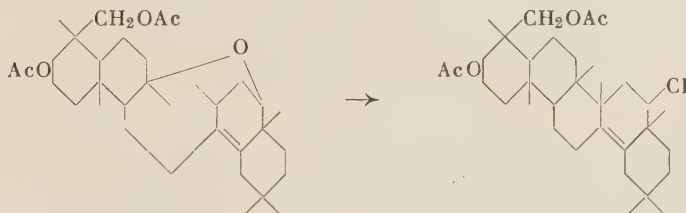
○

s. 2, 697; s. a. A. C. Cope, F. S. Fawcett, and G. Munn, Am. Soc. 72, 3399, 3405 (1950)

Isocyclics from O-heterocyclics

←

865.



HCl-gas introduced at 95° into a soln. of soysapogenol-D diacetate in acetic anhydride for 2 hrs. → pentacyclic diacetoxychloro derivative. Y: 91%. A. Meyer, O. Jeger, and L. Ruzicka, Helv. 33, 687 (1950).

Hydrochloric acid/acetic acid

HCl/CH₃COOH**Dehydration**CHC(OH) $\rightarrow$ C:C

s. 1, 534, 764; ethylene amines s. D. W. Adamson, P. A. Barrett, and S. Wilkinson, Soc. 1951, 52

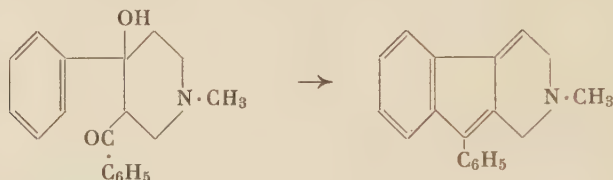
Hydrobromic acid

HBr

1H-Indeno[2.1-c]pyridines

○

866.



750 gm. 1-methyl-3-benzoyl-4-hydroxy-4-phenylpiperidine and 48% HBr distilled over a period of ca. 1 hr., then the residue worked up $\rightarrow$ 700-720 gm. 2-methyl-9-phenyl-2,3-dihydro-1-pyridindene hydrobromide. F. e. s. J. T. Plati and W. Wenner, J. Org. Chem. 15, 209 (1950).

Hydrobromic acid/acetic acid

HBr/CH₃COOH**Isocyclics from ketones**

s. 5, 642; s. a. Am. Soc. 72, 277 (1950)

Via intermediates

v.i.

Dehydration of stereoisomeric cyclic alcoholsCHC(OH) $\rightarrow$ C:C

867. In contrast to the H₃PO₄-catalyzed dehydration of *cis*- and *trans*-2-phenylcyclohexanols, the thermal decomposition of their acetates or methyl xanthates involves the preferential elimination of a *cis*- β -H-atom. E. s. E. R. Alexander and A. Mudrak, Am. Soc. 72, 1810 (1950).

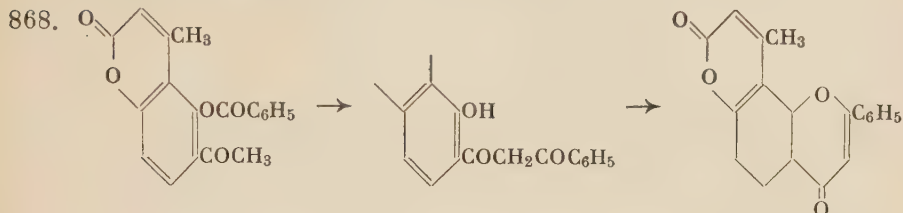
Cyclic ketones from carboxylic acids

○

s. 1, 778-80; 2, 808; 4, 841; 5, 652/3

Naphtho[1.8-bc]thiapyrans

s. 6, 889

o-Hydroxy- β -diketones from o-acoxyketones**Baker-Venkataraman transformation****Chromone ring**

A mixture of 5-benzoyloxy-6-acetyl-4-methylcoumarin, ethyl Na-acetoacetate, and pyridine refluxed 20 min., and kept at room temp. for 12 hrs. $\rightarrow$ 5-hydroxy-6-benzoylacetyl-4-methylcoumarin (Y: almost 100%) dissolved in acetic acid containing 50% HBr, then diluted with water $\rightarrow$ 2'-phenyl-4-methylchromone[7',8',6,5]-2-pyrone (Y: almost 100%). F. e., also one-step preparation, s. T. S. Wheeler et al., Soc. 1949, 1915; also transformation with KOH/pyridine and ring closure with HCl and H_2SO_4 s. Soc. 1950, 340, 1252, 1925; W. Baker and F. Glockling, Soc. 1950, 2759.

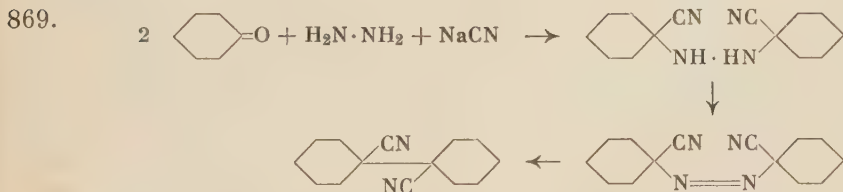
Nitrogen †**CC ↑ N**

Without additional reagents

w.a.r.

Sym. α -dinitriles from ketones**via sym. hydrazodinitriles and****sym. azodinitriles****Dimerization**

←



Cyclohexanone, hydrazine sulfate, and NaCN in water shaken at room temp. for 2 days $\rightarrow$ 1,1'-hydrazobis(cyclohexanecarbonitrile) (Y: 95%) dissolved in HCl-alcohol-water, and Br_2 -water added until a permanent yellow color results $\rightarrow$ 1,1'-azobis(cyclohexanecarbonitrile) (Y: 92%) heated in small quantities at 120° in a N_2 -stream for 1 hr. $\rightarrow$ 1,1'-dicyanobicyclohexyl (Y: 98%). F. e. s. C. G. Overberger, M. T. O'Shaughnessy, and H. Shalit, Am. Soc. 71, 2661 (1949).

Potassium hydroxide

KOH

Hofmann degradation

←

Ethylene derivatives from amines

s. 6, 722

Sodium nitrite

NaNO₂**Ring closure by diazo coupling**

○

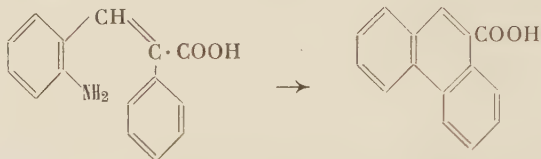
s. 2, 810; discussion s. DeLos F. DeTar and S.V. Sagmanli, Am. Soc. 72, 965 (1950)

Copper

Cu

Pschorr ring closure

870.

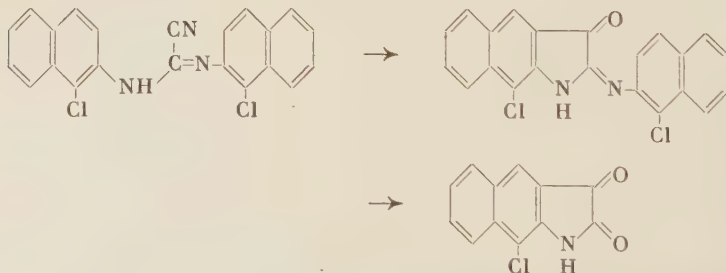


Isoamyl nitrite added dropwise with shaking at 0° to a suspension of o-amino- α -phenylcinnamic acid hydrochloride (from the acid and dry HCl) in alcohol, allowed to stand for 0.5 hr., ether added, filtered, and the solid diazonium chloride decomposed in the course of 1 min. under acetone in the presence of a small amount of Cu-powder $\rightarrow$ phenanthrene-9-carboxylic acid. Y: 81%. F. methods, discussion, and e. s. D. H. Hey and J. M. Osbond, Soc. 1949, 3164, 3172; s. a. E. Schlittler and A. Lindemann, Helv. 32, 1880 (1949); P. Block, Jr., Am. Soc. 72, 5641 (1950).

Aluminum chloride/sodium chloride

AlCl₃/NaCl**Isatins from amidines via 2-iminoisatins**

871.

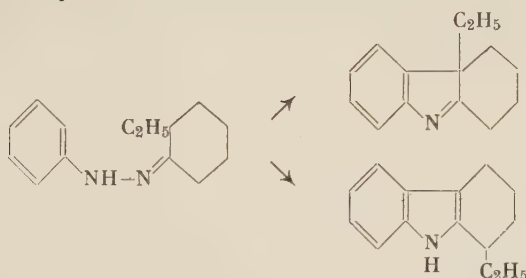


A mixture of N,N'-bis-(1-chloro-2-naphthyl)- α -cyanoformamidine, AlCl₃ and NaCl heated in a boiling xylene bath until pasty, then 5 min. longer $\rightarrow$ 2-(1'-chloro-2'-naphthylimino)-7-chloro-5,6-benzisatin (Y: 75%) heated 20 min. in HCl-acetic acid-water $\rightarrow$ 7-chloro-5,6-benzisatin (Y: 89%). A. Etienne, Bl. 1949, 515.

Acetic acid

 CH_3COOH **Fischer indole synthesis**

872.



2-Ethylcyclohexanone phenylhydrazone refluxed 0.5 hr. in glacial acetic acid $\rightarrow$ 11-ethyltetrahydrocarbazolenine (Y: 76%) and 1-ethyltetrahydrocarbazole (Y: 13%).—Whereas H_2SO_4 favors the formation of the neutral 1-subst. tetrahydrocarbazoles, the basic 11-subst. tetrahydrocarbazolenines are the principal products formed when glacial acetic acid is used. F. e. s. K. H. Pausacker, Soc. 1950, 621.

Phosphorus pentoxide

 P_2O_5 **Ethylene derivatives from acylamines** $\text{CHC}(\text{NHAc}) \rightarrow \text{C}:\text{C}$

873.

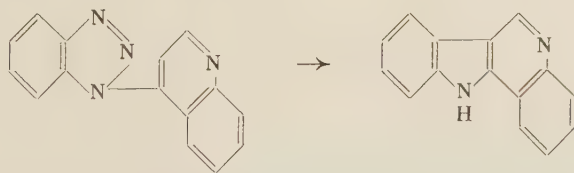


Aceto-1,2-diphenylethylamide and P_2O_5 in xylene refluxed 20 min. $\rightarrow$ stilbene. Y: 70%. F. e. s. J. W. Cook et al., Soc. 1949, 1074.

Phosphoric acid

 H_3PO_4 **Carbazoles from 1,2,3-triazoles according to Graebe-Ullmann** $\leftarrow$

874.



4-(1H-Benzotriazol-1-yl)quinoline heated in syrupy H_3PO_4 until the evolution of N_2 ceases $\rightarrow$ 2,3-benz- γ -carboline. Y: 77%. F. e. s. W. O. Kermack and N. E. Storey, Soc. 1950, 607.

Hydrochlorides

 $\leftarrow$ **Ethylene derivatives from tert. amines** $\text{CHC}(\text{NR}_2) \rightarrow \text{C}:\text{C}$

s. 5, 648; s. a. A. F. Bekhli, Ж. 21, 86 (1951); C. A. 45, 7540g

Halogen $\downarrow$ **CC $\uparrow$ Hal***Lithium**Li***Dihydrophenanthrene ring**

○

875.



An ethereal soln. of 2,2'-di(bromomethyl)biphenyl added as rapidly as possible to phenyl-Li from Li and bromobenzene in ether $\rightarrow$ 9,10-dihydrophenanthrene. Y: 86%. D. M. Hall, M. S. Lesslie, and E. E. Turner, *Soc.* 1950, 711.

*Sodium hydroxide**NaOH***Cyclopropane ring from halides**

s. 3, 748; cyclopropylketones s. G. W. Cannon, R. C. Ellis, and J. R. Leal, *Org. Synth.* 31, 74 (1951)

*Potassium hydroxide**KOH***Acetylene derivatives from** $\text{CH}:\text{CHal} \rightarrow \text{C}:\text{C}$ **α,β -ethylenehalides****Selective dehydrohalogenation**

876.



3,3,3-Trifluoro-1-iodopropene added to a large excess of dried, powdered KOH, and the bath temp. gradually raised from 120° to 150° during 6 hrs. $\rightarrow$ 3,3,3-trifluoropropyne. Y: 68-75%. R. N. Haszeldine, *Soc.* 1951, 588.

**Acetylene derivatives from
1,2-dichlorides** $\text{CHClCHCl} \rightarrow \text{C}:\text{C}$

877.



KOH in alcohol-water added dropwise during 1 hr. at 95° to 2 gm. 5-chloro-2-nitrostilbazole dichloride in alcohol, and refluxed for a further hr. $\rightarrow$ 1.36 gm. 5-chloro-2-nitrotolazole. F. e. s. K. Schofield and T. Swain, *Soc.* 1949, 2393.

Phenyl lithium $\sim \text{C}_6\text{H}_5\text{Li}$ **Acetylene derivatives from** $\text{CH}:\text{CHal} \rightarrow \text{C}:\text{C}$ **α,β -ethylenehalides**

s. 6, 880

Sodium amide

 NaNH_2

Acetylene derivatives from 1,2-dihalides

 $\text{CHHalCHHal} \rightarrow \text{C}\equiv\text{C}$

Acetyleneamines

Preparation of sodium amide

878.



Finely powdered, dry styrene dibromide added gradually with vigorous stirring to NaNH_2 (prepared by adding Na to liq. NH_3 in the presence of $\text{Fe}(\text{NO}_3)_3$) in liq. NH_3 containing some aniline, and stirring continued for 2 hrs. $\rightarrow$ phenylacetylene. Y: 45-52%. K. N. Campbell and B. K. Campbell, *Org. Synth.* 30, 72 (1950); acetylene amines s. R. F. Parcell and C. B. Pollard, *Am. Soc.* 72, 2385 (1950).

Mild dehydrobromination

879.



1,2,5,6-Tetrabromohexane added dropwise during 2 hrs. to an alcohol- CO_2 -cooled, stirred suspension of NaNH_2 in liq. NH_3 (prepared from Na with $\text{Fe}(\text{NO}_3)_3$ -catalyst), stirred another 3 hrs., and allowed to stand overnight at room temp., whereby NH_3 evaporates $\rightarrow$ dipropargyl. Y: 56%. R. A. Raphael and F. Sondheimer, *Soc.* 1950, 120; method s. Vaughn, Vogt, and Nieuwland, *Am. Soc.* 56, 2120 (1934).

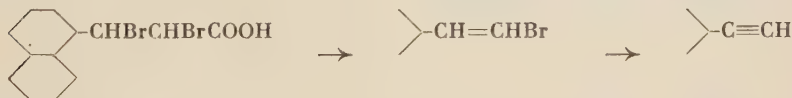
Potassium carbonate

 K_2CO_3

Acetylene derivatives from
 α,β -dihalogenocarboxylic acids
 via α,β -ethylenahalides

 $\leftarrow$

880.



α,β -Dibromo-1-naphthalenepropionic acid treated with cold aq. 10%-K-carbonate $\rightarrow$ 1-bromo-2-(1-naphthyl)ethylene (Y: 90%) treated with phenyl-Li, then decomposed with water $\rightarrow$ 1-naphthylacetylene (Y: 90%). D. Bertin, *C. r.* 229, 660 (1949).

Sodium acetate

 CH_3COONa

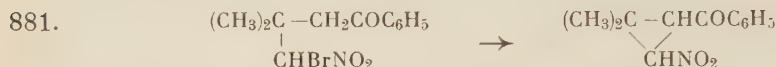
Ethylene derivatives from halides

 $\text{CHCHal} \rightarrow \text{C}\equiv\text{C}$

s. 6, 891

Potassium acetate CH_3COOK **Cyclopropane ring from halides**

○



β,β -Dimethyl- γ -bromo- γ -nitrobutyrophenone (prepn. s. 561) dissolved in a soln. of freshly fused K-acetate in dry methanol, allowed to stand at room temp. for 15 hrs., KBr removed, and the filtrate refluxed 13 hrs. until no more KBr separates $\rightarrow$ 3,3-dimethyl-2-nitro-1-cyclopropyl phenyl ketone. Y: 75%. F. e. s. L. I. Smith and V. A. Engelhardt, Am. Soc. 71, 2671, 2676 (1949).

Alkali iodides

←

Ethylene bromides from tribromides $CBr_2CBr \rightarrow C:C$

s. 4, 812; with NaI s. Helv. 33, 2229 (1950)

*Sodium iodide**Nal***Ethylene iodides from 1,2,4-tribromides**

←



A soln. of 4-phenyl-1,3,4-tribromo-2-butanone in acetone added to a soln. of NaI in acetone, and allowed to stand at room temp. for 3 hrs. $\rightarrow$ iodomethyl styryl ketone. Y: 90%. P. L. Southwick, L. A. Pursglove, and P. Numerof, Am. Soc. 72, 1604 (1950).

Diethylamine $(C_2H_5)_2NH$ **Enamines from 1,2-dibromides** $CHBrCHBr \rightarrow CH:CN \diagup$

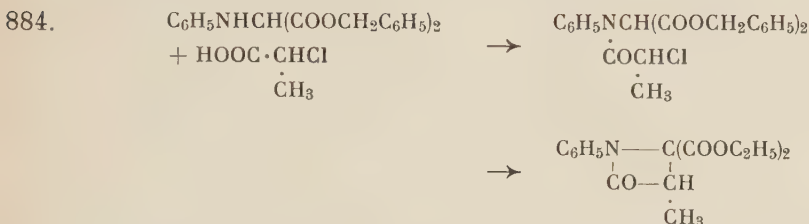
s. 6, 454

Triethylamine $(C_2H_5)_3N$ **Ketenes from carboxylic acid chlorides** $CHCOCl \rightarrow C:C:O$ 

4-Chlorophenoxyacetyl chloride allowed to react with a small excess of triethylamine $\rightarrow$ 4-chlorophenoxyketene (startg. m. f. 365). Y: 77.5%. F. e. s. C. M. Hill, G. W. Senter, and M. E. Hill, Am. Soc. 72, 2286 (1950).

Azetidinones**Subst. carboxylic acid amides
from carboxylic acids**

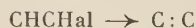
○



A soln. of dibenzyl anilinomalonate, α -chloropropionic acid, and PCl_3 in benzene refluxed 2 hrs. $\rightarrow$ dibenzyl N-(α -chloropropionyl)-anilinomalonate (Y: 86.3%) and triethylamine in benzene kept at 50 to 60° overnight $\rightarrow$ 1-phenyl-3-methyl-4,4-dicarbobenzyloxy-2-azetidinone (Y: 97.6%). F. e. s. J. C. Sheehan and A. K. Bose, *Am. Soc.* **73**, 1761 (1951); **72**, 5158 (1950).

Quinoline

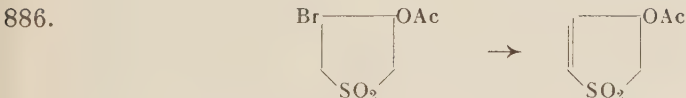
←

Ethylene derivatives from halides

s. 6, 840

Calcium carbonate

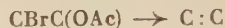
100 gm. 2,2'-dichlorodiethyl sulfone, precipitated CaCO_3 , and water heated with stirring at 85-90° for 4 hrs. $\rightarrow$ divinyl sulfone. Y: 79-85%. A. H. Ford-Moore, R. A. Peters, and R. W. Wakelin, *Soc.* **1949**, 1754.

Barium carbonate

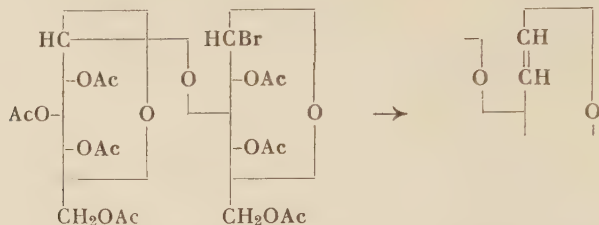
Ethylenesulfones. 3-Bromo-4-acetoxythiacyclopentane, 1,1-dioxide heated with aq. BaCO_3 at 85° for 2 hrs. $\rightarrow$ 4-acetoxythiacyclopent-2-ene 1,1-dioxide. Y: 90%. O. E. van Lohuizen and H. J. Backer, *R.* **68**, 1137 (1949).

Zinc

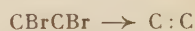
Zn

Glycols from acetobromosugars

887.

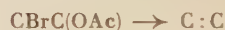


Acetobromoglucosido-3-glucose shaken 2 hrs. with Zn dust in 60%-acetic acid $\rightarrow$ hexaacetylglucosido-3-glucal (startg. m. f. 282). Y: 80%. A. M. Gakhokidze, *Ж.* 19, 2100 (1949); *C. A.* 44, 3913f.

Ethylene derivatives from 1,2-dibromides

protection of a carbon double bond s. 6, 280; selective dehalogenation s. A. L. Henne and M. Nager, *Am. Soc.* 73, 1042 (1951)

Zinc/hexachloroplatinic acid

**Glycols from acetobromosugars**

888.



A soln. of pure β -acetobromo-L-arabinose in glacial acetic acid added at -10° during 10 min. to a stirred mixture of Zn-dust and 50%-acetic acid containing a few drops of chloroplatinic acid soln., which is further added dropwise at intervals of 30 min. to maintain a vigorous reaction, stirring continued for 3 hrs., and kept overnight at $0^\circ \rightarrow$ 3,4-diacetyl-L-arabinal. Y: 65%. R. E. Deriaz et al., *Soc.* 1949, 1879.

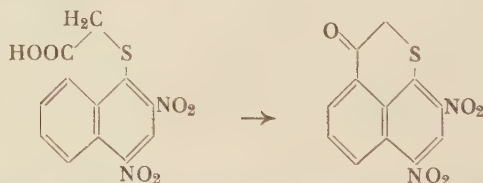
Aluminum chloride

**Cyclic ketones from carboxylic acid chlorides**

s. 6, 861

Naphtho[1.8-bc]thiapyrans

889.



PCl_5 added to a suspension of (2,4-dinitro-1-naphthylmercapto)acetic acid (prepn. s. 647) in CS_2 , refluxed until dissolved, cooled to room temp., an ethereal soln. of AlCl_3 added, and refluxed for 2 hrs. with

frequent shaking $\rightarrow$ 2,4-dinitronaphtho-1,8-thioindoxyl. Y: 90%.—Other dehydrating agents, e.g. H_2SO_4 and P_2O_5 , do not give good results. Solvents other than CS_2 gave poorer yields. G. Leandri, G. 79, 50 (1949).

Stannic chloride

SnCl_4

Cyclic ketones from carboxylic acids

s. 1, 778-80; 2, 808; 4, 841; s. a. R. C. Gilmore, Jr., and W. J. Horton, Am. Soc. 72, 733 (1950); D. L. Turner et al., Am. Soc. 72, 5654 (1950)

Sulfuric acid

H_2SO_4

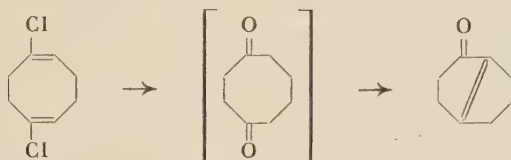
Isocyclics from γ -chlorocrotyl compounds

s. 5, 654; s. a. M. O. Melikyan and G. T. Tatevosyan, Ж. 21, 696; C. A. 45, 9489c

Bicyclo[3.3.0]octane ring from cyclooctane ring

$\leftarrow$

890.



1,6-Dichloro-1,5-cyclooctadiene added dropwise with stirring during 25 min. to ice-cooled concd. H_2SO_4 , stirring continued at room temp. for 5 min. and at 70° for 30 min., whereby the HCl evolved is swept from the flask with $\text{N}_2 \rightarrow$ bicyclo[3.3.0]-1(5)-octen-2-one. Y: 70-77%. A. C. Cope and W. R. Schmitz, Am. Soc. 72, 3056 (1950).

Via intermediates

v.i.

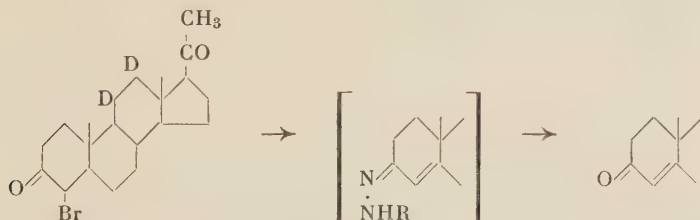
α,β -Ethylene ketones from α -bromoketones via α,β -ethylenehydrazones

$\text{CHCHal} \rightarrow \text{C:C}$

Mattox-Kendall reaction

s. 4, 852; s. a. J. Biol. Chem. 188, 287 (1951)

891.



Modified procedure. Deutero compounds. Pure 4-bromo-11,12- d_2 -pregnane-3,20-dione dissolved in glacial acetic acid at 60° , Na-acetate, followed by 2,4-dinitrophenylhydrazine, added, dissolved under a N_2 -stream, kept at 60° for 20 min., during which the mono-2,4-dinitrophenyl-

hydrazone crystallizes, chloroform, Na-acetate, pyruvic acid, and water added, and refluxed 3 hrs. at ca. 70° under a N₂-stream, with repeated additions of pyruvic acid and water until the color changes from red to yellow → 11,12-d₂-progesterone. Y: 80%.—The cleavage is performed without addition of HBr. F. e., also procedure via semicarbazones, s. B. A. Koechlin, T. H. Kritevsky, and T. F. Gallagher, J. Biol. Chem. 184, 393 (1950).

Remaining elements †

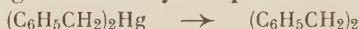
CC ↑ Rem

Without additional reagents

w.a.r.

Photoreactions of organo mercury compounds

892.



Dibenzyl-Hg irradiated in methanol for 50 hrs. → bibenzyl. Y: 80%. F. e. s. G. Razuvaev et al., Ж. 19, 1487, 1483 (1949). 20, 175. 181 (1950); C. A. 44, 3450h, 5832h, 5833b.

Aluminum chloride

AlCl₃

Cyclopropanes from 1,3-halogenosilanes

○

γ-Elimination

893.



A few crystals of AlCl₃ added to γ-bromopropyltrimethylsilane, and warmed to 70° after most of the reaction has taken place → cyclopropane (Y: 92%) and trimethylbromosilane (Y: 82%). L. H. Sommer, R. E. VanStrien, and F. C. Whitmore, Am. Soc. 71, 3056 (1949).

Carbon †

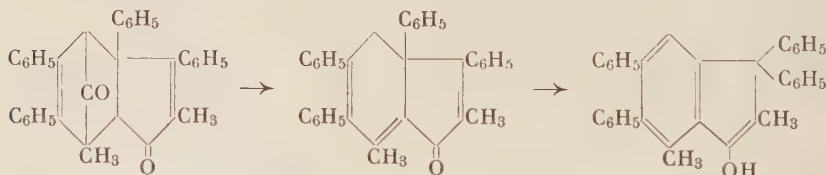
CC ↑ C

Without additional reagents

w.a.r.

Benzene ring from endocarbonyl compounds

894.



4,7-Endocarbonyl-3,3a,5,6-tetraphenyl-2,7-dimethyl-3a,4,7,7a-tetrahydroindenone heated at 240°

for a maximum of 10 min. until the evolution of gas ceased → 3,3a,5,6-tetraphenyl-2,7-dimethyl-3a,4-dihydroindenone. Y: 85%.

for 3 hrs. → 1,1,5,6-tetraphenyl-2,4-dimethyl-3-hydroxyindene. 7.8 gm. from 10 gm.

C. F. H. Allen and J. A. VanAllan, J. Org. Chem. 14, 1051 (1949).

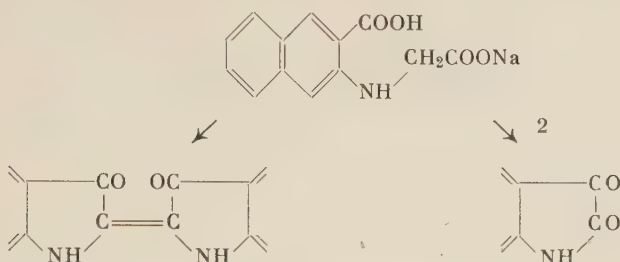
Sodium amide/potassium hydroxide

NaNH₂/KOH

Isatins and indigo compounds

○

895.



Na (3-carboxy-2-naphthylamino)acetate added to a mixture of fused KOH and NaNH₂

in a porcelain crucible at 200°, heated 15 min. at 210°, dissolved in ice-water, and air passed through → 5,6,5',6'-dibenzindigo. Y: 60%.

in a copper crucible, kept at 190 to 200° for 15 min., dissolved cautiously in ice-water with exclusion of air, warmed to 80°, and treated dropwise with aq. NH₄-persulfate → 5,6-benzisatin. Y: 85%.

W. Dethloff and K. Schreiber, Chem. B. 83, 157 (1950).

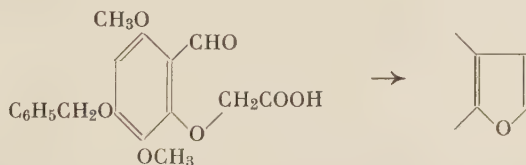
Sodium acetate

CH₃COONa

Benzofurans

with simultaneous decarboxylation

896.



9.7 gm. 5-benzyloxy-3,6-dimethoxy-2-formylphenoxyacetic acid and anhydrous Na-acetate dissolved in acetic anhydride, then refluxed 1 hr. → 6.7 gm. 6-benzyloxy-4,7-dimethoxycoumarone. R. A. Baxter, G. R. Ramage, and J. A. Timson, Soc. 1949, S30; f. e. s. A. Robertson et al., Soc. 1948, 2254; 1950, 2381.

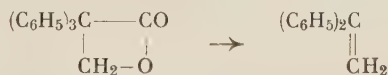
Sodium iodide

NaI

Ethylene derivatives from lactones

C

897.



A soln. of α,α -diphenyl- β -propiolactone in 95% ethanol treated with aq. NaI, and kept at 40° for 112 hrs. → crude 1,1-diphenylethylene. Y: 86%. H. E. Zaugg, Am. Soc. 72, 2998 (1950).

Ammonia and alkali hydroxide

←

 α -Halogen- α,β -ethylenecarboxylic acid esters and acids from β -halogeno- α -keto- γ -lactones

C

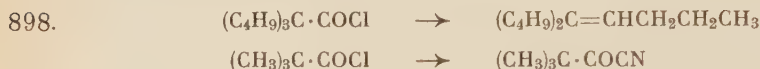
s. 4, 855; cf. A. ch. 6, 247, 322 (1951)

Cuprous cyanide

CuCN

Acylecyanides and ethylene derivatives from carboxylic acid halides

←



A mixture of tributylacetyl chloride and dry CuCN refluxed 8 hrs. by means of a metal bath at 220-240° → 5-butyl-4-nonene. Y: 81%.—Trimethylacetyl chloride and CuCN refluxed 20 hrs. → trimethylacetyl cyanide. Y: 87%. N. Sperber and R. Fricano. Am. Soc. 72, 2792 (1950).

*Aluminum chloride*AlCl₃**Cyclic aminoketones from N-carboxyaminocarboxylic acid anhydrides**

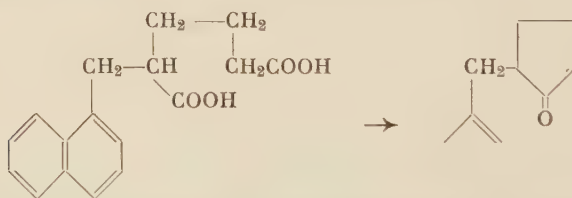
←

s. 6, 829

Acetic anhydride $(CH_3CO)_2O$ **Cyclic ketones from dicarboxylic acids according to Blanc**

○

899.



Asoln. of α -(1'-naphthylmethyl)adipic acid in acetic anhydride distilled slowly, after distillation of the acetic anhydride the apparatus filled with N₂, the temp. raised to 300° in the course of 5 min., then the pressure lowered to 30 mm. in order to complete the distillation → 2-(1'-naphthylmethyl)cyclopentanone. Y: 71%. F. e. s. W. E. Bachmann and N. C. Deno. Am. Soc. 71, 3540 (1949); s. a. P. Pfeiffer and E. Enders. B. 84, 247 (1951).

*Hydrogen peroxide*H₂O₂**Carboxylic acids from α -ketocarboxylic acids**COCO₂H → CO₂H

s. 6, 747

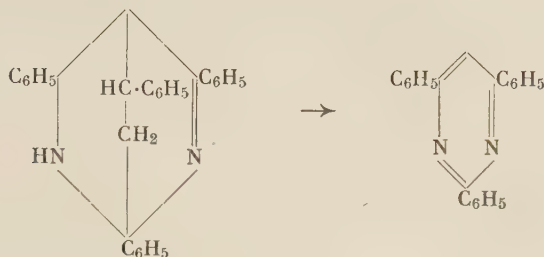
Sulfur

S

Aromatization

←

900.



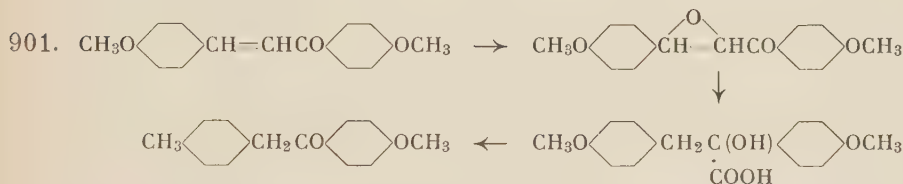
A mixture of 2,4,6-triphenyl-2,5-endo-(2'-phenylethylene)-2,3,4,5-tetrahydropyrimidine and S heated 8 hrs. at 180-190°/8 mm. → 2,4,6-triphenylpyrimidine. Y: 88%. F. e. s. D. E. Piper and G. F. Wright, Am. Soc. 72, 1669 (1950).

Via intermediates

v.i.

Desoxybenzoins from chalcones
via α,β -oxidoketones and
 α -hydroxycarboxylic acids

←



4 N NaOH and 28% H_2O_2 added at 40° to a soln. of anisyl p-methoxystyryl ketone in ethanol-acetone, and kept an additional 40 min. at 40° → p-anisyl α,β -epoxy-p-anisylethyl ketone (Y: 92%) refluxed 1.5 hrs. with aq.-alc. NaOH → p-anisyl p-methoxybenzylglycolic acid (Y: 90%), a thick paste of which with glacial acetic acid treated with red Pb-oxide in small portions below 65-70°, at the end of the reaction a few drops of glycerol in water added to destroy any excess Pb-tetraacetate → desoxyanisoin (Y: 98%). E. Rohrmann, R. G. Jones, and H. A. Shonle, Am. Soc. 66, 1856 (1944); f. e. s. E. R. Bockstahler and D. L. Wright, Am. Soc. 71, 3760 (1949); E. J. Collins and O. K. Neville, Am. Soc. 73, 2471 (1951).

2-Step Hooker oxidation

←

Degradation with loss of 1 C-atom

s. 5, 660; s. a. G. Fawaz and L. F. Fieser, Am. Soc. 72, 996 (1950); M. Paulshok and C. M. Moser, Am. Soc. 72, 5073 (1950)

Formation of Electron Pair on Nitrogen

Elimination

Hydrogen $\downarrow$

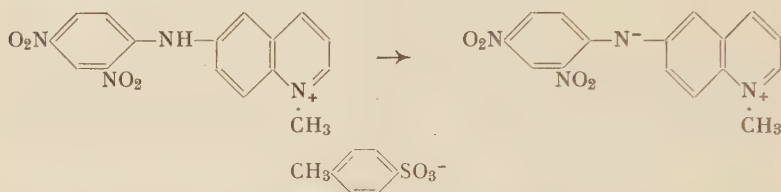
E1N $\uparrow$ H

Sodium hydroxide

NaOH

Betaine azeniates

902.



Aq.-alc. NaOH added dropwise at 50-60° to an aq.-alc. soln. of 6-(2,4-dinitroanilino)quinoline metho-p-toluenesulfonate $\rightarrow$ 6-(2,4-dinitroanilino)-1-methylquinoline betaine azeniate. Y: almost 100%. F. e. s. A. M. Simonov, *Ж.* 20, 320, 1802 (1950); *C. A.* 44, 6863a; 45, 2460i.

Alkylamines

Bases from their hydrochlorides

903.



Triethylamine dropped slowly with good stirring into a suspension of proline hydrochloride in dry chloroform, and stirring continued for 1-2 hrs. $\rightarrow$ DL-proline. Y: 78.5%.—The use of Amberlite resin is less satisfactory. N. F. Albertson and J. L. Fillman, *Am. Soc.* 71, 2818 (1949); with diethylamine s. F. E. King and D. A. A. Kidd, *Soc.* 1949, 3315.

Oxygen $\downarrow$

E1N $\uparrow$ O

Carbon oxide

CO

High pressure reductions with carbon monoxide

Azo compounds from azoxy compounds

904.



Nitro-, nitroso-, and azoxy-benzene are reduced to azobenzene, N-phenylhydroxylamine to aniline, and N-phenylbenzaldoxime to benzyl-

ideneaniline at 150-250° and 3000 atm. CO-pressure without catalyst. In the presence of Raney-Co, certain α -phenylalcohols are reduced to the corresponding hydrocarbons. Phenols, ethers, esters, amides, ketones, and purely aliphatic alcohols are not reduced by anhydrous CO.—E: 15 gm. azoxybenzene treated with CO at 200° and 3000 atm. for 20 hrs. $\rightarrow$ 13 gm. azobenzene. F. e. s. G. D. Buckley and N. H. Ray, Soc. 1949, 1154.

Iron

Fe

**Amines from N-oxides,
simultaneously amines
from nitro compounds**

 $\leftarrow$

s. 6, 389

Formation of Electron Pair on Sulfur

Elimination

Oxygen $\downarrow$ EIS $\uparrow$ O*Lithium aluminum hydride**LiAlH₄*

**Sym. disulfides from
thiosulfonic acid esters**

 $2 \text{R} \cdot \text{SO}_2\text{SR} \rightarrow \text{R} \cdot \text{SS} \cdot \text{R}$

s. 6, 47

Formation of Electron Pair on Remaining Elements

Elimination

Oxygen $\downarrow$ ElRem $\uparrow$ O*Sulfur dioxide/potassium iodide**SO₂/KI*

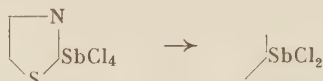
**Arsenoso compounds from
arsonic acids**

 $\text{AsO}_3\text{H}_2 \rightarrow \text{AsO}$

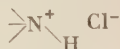
s. 3, 763; s. a. F. E. Ray and R. J. Garascia, J. Org. Chem. 15, 1233 (1950)

Halogen $\uparrow$ **ElRem $\uparrow$ Hal***Stannous chloride* SnCl_2 **Antimony(III)- from antimony(V)-
compounds** $\leftarrow$

905.



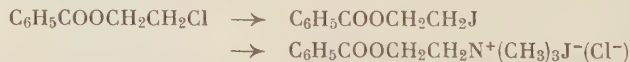
Ethanol, satd. with dry HCl, added to an intimate mixture of thiazole-2-stibinic tetrachloride and SnCl_2 , and, after 15 min., placed in the cold for crystallization $\rightarrow$ thiazole-2-stibinous chloride hydrochloride. Y: 80%. F. reactions of organo antimony compounds s. D. B. Meyers and J. W. Jones, J. Am. Pharm. Assoc. 39, 401 (1950); also reduction with SO_2/HJ s. G. O. Doak and H. H. Jaffé, Am. Soc. 72, 3025 (1950).

Heteropolar Bond**Uptake****Addition to Nitrogen****Het $\downarrow$ N***Without additional reagents**w.a.r.***Hydrochlorides**

s. 2, 829; s. a. M. W. Farlow, Org. Synth. 31, 62 (1951)

Quaternary ammonium salts

906.



A mixture of anhydrous NaI and methyl ethyl ketone heated 1 hr. on a steam bath with occasional shaking, 2-chloroethyl benzoate added, and heating continued for 22-24 hrs. with occasional shaking $\rightarrow$ 2-iodoethyl benzoate (Y: 78-81%) allowed to stand with trimethylamine in acetone for 24 hrs. in a closed flask $\rightarrow$ benzoylcholine iodide (Y: 85 to 90%) added with stirring over a period of 1 hr. at 50-60° to an aq. suspension of AgCl, and stirring continued for a further 30 min. $\rightarrow$ benzoylcholine chloride (Y: 82-87%). A. H. Ford-Moore, Org. Synth. 30, 10 (1950).

s. a. H. M. Wuest and E. H. Sakal, Am. Soc. 73, 1210 (1951)

from dibromides

907. When alkylene dibromides are added to heterocyclic bases, bis-salts are formed in most cases. With glycerol- α,γ -bromohydrin and sterically hindered bases, mono-salts are formed. In several instances, no addition occurred but the alkylene dibromide lost HBr. E. s. J. L. Hartwell and M. A. Pogorelskin, *Am. Soc.* 72, 2040 (1950).

Alkyl sulfates

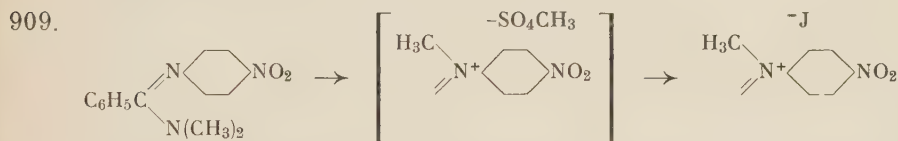
908. In the N-alkylation of tert. amines by unsym. dialkyl sulfates, the smaller alkyl group migrates to the N of the tert. amine. E. s. J. B. Niederl, M. E. McGreal, and W. F. Hart, *J. Org. Chem.* 14, 579 (1949).

Methosulfates

s. 6, 820

Via intermediates

v.i.

Acridinium salts

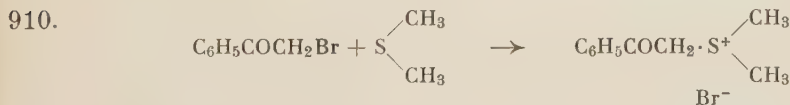
N'-p-Nitrophenyl-N,N-dimethylbenzamidinium and acid-free dimethyl sulfate heated at 115-120° until the exothermic reaction ceases, washed with benzene, dissolved in water, and KI added $\rightarrow$ N'-p-nitrophenyl-N,N,N'-trimethylbenzamidinium iodide. Y: 93%.—The influence of the nitro group was such that no reaction occurred with boiling methyl iodide. E. with methyl iodide, s. C. G. Raison, *Soc.* 1949, 3319.

Addition to Sulfur

Het $\Downarrow$ S

Without additional reagents

w.a.r.

Sulfonium salts

Dimethyl sulfide added to a soln. of ω -bromoacetophenone in acetone-water, and allowed to stand ca. 0.5 hr. $\rightarrow$ dimethyl phenacyl sulfonium

bromide. Y: 85%. F. e. s. H. Böhme and W. Krause, Chem. B. 82, 426 (1949).

**with simultaneous formation
of ketals**
s. 6, 212

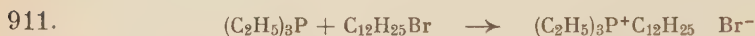
Addition to Remaining Elements

Het $\Downarrow$ Rem

Without additional reagents

w.a.r.

Phosphonium salts



Triethyl phosphine and dodecyl bromide heated 12 hrs. at 90° in a sealed tube $\rightarrow$ dodecyltriethylphosphonium bromide. Y: 80%. F. e. s. D. Jerchel and J. Kimmig, B. 83, 277 (1950); arylphosphonium salts s. K. Kröhnke, B. 83, 291 (1950).

Exchange

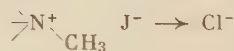
Het $\Updownarrow$

Silver chloride

AgCl

Methochlorides from methiodides

s. 6, 724, 906



Amberlite

$\leftarrow$

Acids from their salts

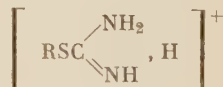
$\leftarrow$

An aq. soln. of Na-inositol-5-phosphate (prepn. s. 14) passed through a column containing moist Amberlite-IR-100AG $\rightarrow$ inositol-5-phosphoric acid (startg. m. f. 10). Y: 82%. B. M. Iselin. Am. Soc. 71, 3822 (1949).

Halides

Hal-

**Thiuronium salts
as used for the characterization
of carboxylic acids**



s. 1, 791; s. a. H. M. E. Cardwell, Soc. 1950, 1207

Index

Cumulative Index, Volumes 1–5, see Volume 5, page 503

The subject index lists the names of the methods, types of compounds, reagents, etc. For specific compounds and for authors (when a method is not named after them) the reader may be referred to the indexes of abstract journals. Complex compounds, as those with several functional groups, are referred to under the related simpler compounds, under *special s.* E.g. *aminocarboxylic acids* are found under *carboxylic acids*. Only compounds beginning with letters other than those of the parent or main compounds are listed under this subentry, and entry numbers are omitted because they are specified when the compound is given as a main entry. Methods of synthesis for a given substance are indexed under the name of this substance and the subentry *from*, e.g. carboxylic acids from alcohols, hydrocarbons. Syntheses carried out from a particular starting material are indexed under the starting material and the subentry *startg. m. f.* (starting material for the preparation of . . .), e.g. alcohols, startg. m. f. carboxylic acids, ketones.

Classes of compounds may be designated merely by the functional group that is changed during the reaction. Ring compounds may also refer to the corresponding hydrogenated rings, unless the latter are listed specifically. If that be the case, then, as in several other cases, the *inversion* has been made use of that is customary in the indexes of Chemical Abstracts. Dihydrofurans, e.g., may be found under Furans, dihydro-. All single letters, which are separated from the name by a hyphen, are being ignored in regard to alphabetic arrangement, e.g., 'O-Acetyl derivatives' are listed under A.

Register

Generalregister, Band 1—5, siehe Band 5, Seite 503

Im alphabetischen Register finden sich als Schlagworte Methoden, Verbindungsklassen, Reagenzien u. dgl.; Einzelverbindungen und Autoren, soweit nicht eine Methode nach ihnen benannt ist, sind, wie bisher, in den Registern der Referatenblätter zu suchen. Auf kompliziertere Verbindungen, z. B. mit mehreren funktionellen Gruppen, ist

bei den entsprechenden einfacheren Verbindungen unter *special s.* (spezielle siehe) hingewiesen, z. B. bei Carbonsäuren auf Aminocarbonsäuren. Es wird hier jedoch nur auf Verbindungen hingewiesen, die einen anderen Wortanfang haben und deshalb an anderer Stelle im Register stehen. Methoden zur Synthese eines bestimmten Endprodukts findet man beim Schlagwort dieses Endprodukts unter *from* (aus) registriert, z. B. Carbonsäuren aus Alkoholen, Kohlenwasserstoffen. Synthesen, die sich mit einem bestimmten Ausgangsmaterial ausführen lassen, sind bei dem Schlagwort des Ausgangsmaterials unter *startg. m. f.* (Ausgangsmaterial für die Darstellung von . . .) zu suchen, z. B. Alkohole, Ausg. f. Ketone, Carbonsäuren.

Die Bezeichnung der Verbindungsklassen kann sich auf funktionelle Gruppen beschränken, die bei der Reaktion verändert werden. Ringbezeichnungen können sich auch auf die entsprechenden hydrierten Ringe beziehen. Sind hydrierte Ringe aber besonders aufgeführt, dann ist bei ihnen, wie auch in einigen anderen Fällen, von der Inversion Gebrauch gemacht worden, wie sie in den Sachregistern der «Chemical Abstracts» üblich ist. Z. B. stehen Dihydrofurane unter Furane, Dihydro-. Griechische Buchstaben und Einzelbuchstaben, die vom eigentlichen Namen durch Bindestrich getrennt sind, werden bei der alphabetischen Anordnung nicht berücksichtigt, z. B. stehen «O-Acetyl-derivate» unter A.

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 - from
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- α, β -Ethyleneoxy compounds
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α -Formamidomalonic esters

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- from
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Glycols

- , degradation 6, 322
- from
 - acetoalogenosugars 6, 887/8
 - di-p-toluenesulfonic acid esters 6, 847

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- startg. m. f.
 - oxo compounds 6, 129
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Glycol acetates

- startg. m. f.
 - ketones 1, 139; 5, 150; 6, 185

Glycol esters

- from
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Glycolic acids

s. α -Hydroxycarboxylic acids

Glycols (s. a. Diols)

- from
 - α -diketones 6, 57
 - ethylene derivatives 6, 183, 190
- special s.
 - pinacols
- startg. m. f.
 - ketones, degradation 6, 316
 - oxo compounds, oxidative cleavage 6, 275, 277

Glycosides (s. a. Ethers, Carbohydrates)

- special s.
 - thioglycosides

 α -Glycosides

- from
 - β -glycosides 6, 193
- Glyoxalines* s. Imidazoles

Glyoxals s. α -Ketoaldehydes

Glyoxylic acids

s. α -Ketocarboxylic acids

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— special s.

acylaminoguanidines

biguanides

nitroguanidines

— startg. m. f.

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imidazolines 6, 528

—, *cyclic*

— from

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Halides (s. a. Replacement)

— from

alcohols HalC ∇ O

carboxylic acids, degradation

with loss of 1 C-atom 6, 595

ethers 6, 584

ethylene derivatives HalC ∇ CC

α -ketocarboxylic acids, degradation

with loss of 2 C-atoms 6, 596

sulfonic acid esters 6, 576/7

p-toluenesulfonic acid esters (iodides) 6, 577

— special s.

acetohalogenosugars

alkoxyhalides

chlorides

dihalides

ethylene-halides

hydroxy-

nitro-

oxido-

poly-

tri-

— startg. m. f.

aldehydes 6, 255

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— addition HalC ∇ CC

— elimination CC ∇ Hal

— replacement s. under Replacement

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— from

enolesters 6, 575

— startg. m. f.

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α -Halogenaldehydes

— from

aldehydes 6, 575

Halogenamines

— from

aminoalcohols 1, 421, 432; 6, 589

Halogenation HalC ∇ H

γ -Halogenation 6, 559, 561

α -Halogen- α,β -ethylenecarboxylic acids and — esters

— from

β -halogeno- α -keto- γ -lactones 4, 855

Halogenethers (s. a. Alkoxyhalides)

—, *cyclic*

— startg. m. f.

ethylenalcohols 2, 770; 3, 2

Halogenhydrins

— from

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oxido compounds 6, 547

— startg. m. f.

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Halogenocarboxylic acid esters

— from

lactones 6, 548

α -Halogenocarboxylic acid esters (s. a. α -Halogen- α,β -ethylenecarboxylic acid esters)

Halogenocarboxylic acids

— from

lactones 6, 549, 550

α -Halogenocarboxylic acids s.

α,β -Dihalogenocarboxylic acids

Halogenocyanamides

- from imines, cyclic 6, 552
- startg. m. f. guanidines, cyclic 6, 458

Halogeno-O-heterocyclics s.

Halogenethers, cyclic

Halogenohydrins s. Halogenhydrins *α -Halogeno- β -ketocarboxylic acid esters*

- from β -ketocarboxylic acid esters 6, 573

 β -Halogeno- α -keto- γ -lactones

- startg. m. f. α -halogeno- α,β -ethylenecarboxylic acids and — esters 4, 855

 α -Halogenoketones

- special s. dihalogenoketones
- startg. m. f. α,β -ethylenehydrazones 4, 852; 6, 891
- α,β -ethyleneketones 6, 891

 α -Halogeno- γ -lactones

- from α,γ -dihalogenocarboxylic acid halides 6, 569
- γ -lactones 6, 569

*Halogenolead compounds, organo 6, 545**Halogenomethylation s. Chloromethylation* *α -Halogenonitriles*

- from cyanohydrins 6, 579

Halogenosilanes

- from silanes 6, 540, 546
- special s. fluoro-silanes
- iodo-
- startg. m. f. silanes 6, 52
- silanols 6, 155
- siloxanes 6, 543

1,3-Halogenosilanes

- startg. m. f. cyclopropane ring 6, 893

Halogenosulfones

- startg. m. f. ethylenesulfones 6, 886

*Halogenothioethers s. Chlorothioethers**Halogenothiophosphoric acid esters*

- from dithiophosphoric acids 6, 156
- startg. m. f. monothiophosphoric acid esters 6, 156

*Halogenoxido compounds s. Oxidohalides**Heterocyclics (s. a. Ethyleneheterocyclics)*

- , by internal Michael addition 6, 713
- special s.

with 1 O-atom

benzofurans
chromones
coumarins
furans
pyrans
xanthenes

with 1 N-atom

acridines
anthrapyridonacridones
anthrapyridones
4-azafluoranthenes
azafluorenes
carbazoles
1H-indeno[2.1-c]pyridines
indoles
isoquinolines
phenanthridines
(9-azaphenanthrenes)
pyridines
pyrroles
quinolines

with 1 hetero atom other than O and N

naphtho[1.8-bc]thiapyrans
thianaphthenes
(benzothiophenes)
thiophenes

with 2 O-atoms

benzo-1,3-dioxanes
chromono(3',2',3,4) coumarins
m-dioxanes
 α -pyrono(5',6',3,4) coumarins

with 2 N-atoms

2,4-diazafluoranthenes
1,3-diazacycloalkenes
imidazoles (glyoxalines)
imidazo[1.2-a]pyrroles
indazoles
naphthyridines
(diazanaphthalenes)
phenazines
(5,10-diazaanthracenes)
phthalazines
(2,3-diazanaphthalenes)
pyrazines
pyrazoles
pyridazines
9(H)-pyrid[3.4-b]indoles

pyrimidazoles
 pyrimidines
 pyrrolo[2.1-b]quinazolines
 quinazolines
 (1,3-diazanaphthalenes)
 quinoxalines
 (1,4-diazanaphthalenes)
*with 2 hetero atoms other than
 O and N*
 1,2-dithioles
with 2 different hetero atoms
 benz-3,1-oxazines
 benzoxazoles
 isoxazoles
 1,2-oxazines
 1,4-oxazines (morpholines)
 oxazoles
 thiazoles
with 3 or more hetero atoms
 benzothiadiazoles
 1,3,4-oxadiazoles
 porphyrins
 purines
 pyrimido 4.5-b pyrazines
 (1,3,5,8-tetraazaphthalenes)
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— *chloride* OC $\uparrow\uparrow$ O; CC $\uparrow\uparrow$ Hal;

CC $\uparrow\uparrow$ O

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Deutscher Schlüssel zum Register (Index)

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Alkohole
Alkylidenacetessigester
Alkylierung
Allylumlagerung
Ameisensäure
Anhydrozucker
Anlagerung
Arylierung
Asparaginsäuren
Aufbau
Austausch

Benzolringsystem
Benzopersäure
Bernsteinsäure
Bimsstein
Blei
Bor
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Borsäureanhydrid
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Brom
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Sulfur monochloride
Chromium
Quin
Coumarin

	<i>siehe unter</i>
Dehydratisierung	Dehydration
Dehydrierung	Dehydrogenation
Diazokupplung	Diazo coupling
Einführung von funktionellen Gruppen	Replacement of hydrogen
Eisen	Iron
Erdalkalien	Earths, alkaline
Erden, seltene	Earths, rare
Fluorwasserstoffsäure	Hydrogen fluoride
Gallensäurederivate	Bile acid derivatives
Glycerine	Glycerols
Halbacetale	Hemiacetals
Halogenide	Halides
Halogenwasserstoff	Hydrogen halide
Harnsäuren	Uric acids
Harnstoff	Urea
Heterocyclen	Heterocyclics
Holzkohle	Charcoal
Hydrierung	Hydrogenation
Hypohalogenite	Hypohalites
Isocyclen	Isocyclics
Isothioharnstoffe	Isothioureas
Jod	Iodine
Jod-	Iodo-
Jodwasserstoffsäure	Hydrogen iodide
Kalium	Potassium
Kern	Nucleus
Kettenverlängerung	Chain lengthening
Kohlehydrate	Carbohydrates
Kohlendioxyd	Carbon dioxide
Kohlensäure	Carbonic acid
Kohlenwasserstoffe	Hydrocarbons
Kunstharz-Base	Resin base
Kupfer	Copper
Kupplung	Coupling
Mangan	Manganese
Molekülverbindungen	Molecular compounds
Natrium	Sodium
Natriumäthylat	Sodium ethoxide
Oxy-	Hydroxy-
Oxydation	Oxidation
Peressigsäure	Peracetic acid
Phosphinsäuren	Phosphonic acids
Polymerisierung	Polymerization

	<i>siehe unter</i>
Quecksilber	Mercury
Razemate	Racemates
Reduktions-Tropfverfahren	Dropping reduction
Ringerweiterung	Ring enlargement
Ringöffnung	Ring opening
Ringschluß	Ring closure
Ringverengung	Ring contraction
Salpetrigsäureester	Nitrous acid esters
Salpetersäure	Nitric acid
Schutz	Protection
Schwefel	Sulfur
Schwefelchloride	Sulfur chlorides
Schwefelwasserstoff	Hydrogen sulfide
Seitenketten	Side chains
Senföle	Isocyanates
Silicium	Silicon
Siliciumdioxyd	Silica
Spaltung	Cleavage
Stellungswechsel	Position shift
Stickstoff	Nitrogen
Stickstoffwasserstoffsäure	Hydrazoic acid
Sulfaminsäuren	Sulfamic acids
Sulfopersäure	Peroxymonosulfuric acid
Thiohalogenide	Sulphenylhalides
Thioharnstoff	Thiourea
Thiokohlensäuredisulfide	Disulfurdicarbthionates
Tschitschibabin	Chichibabin
Tschugaeff	Chugaeff
Umacylierung	Transacylation
Umesterung	Transesterification
Umkehrung	Inversion
Umlagerung	Rearrangement
Unterphosphorigsäure	Hypophosphorous acid
Verbindungen	Compounds
Veresterung	Esterification
Verseifung	Hydrolysis
Wanderung	Migration
Wasserstoffperoxyd	Hydrogen peroxide
Wismutverbindungen	Bismuth compounds
Zinn	Tin
Zuckersäuren	Saccharic acids

Abbreviations - Abkürzungen

abs. . . .	absolute	absolut
alc. . . .	alcoholic	alkoholisch
aq. . . .	aqueous	wäßrig
ar. . . .	aromatic	aromatisch
atm. . . .	atmosphere(s)	Atmosphäre(n)
cf. . . .	compare	vergleiche
concd. . . .	concentrated	konzentriert
d. . . .	density	Dichte
dil. . . .	diluted	verdünnt
et al. . . .	and others	und andere
E. . . .	example	Beispiel
e.g. . . .	for example	zum Beispiel
F.e.s. . . .	Further example(s) see	weitere(s) Beispiel(e) siehe
hr(s). . . .	hour(s).	Stunde(n)
liq. . . .	liquid	flüssig
min. . . .	minutes	Minuten
N. . . .	normal	normal
prepn. . . .	preparation	Darstellung
prim. . . .	primary	primär
s. . . .	see	siehe
s.a. . . .	see also	siehe auch
satd. . . .	saturated	gesättigt
sec. . . .	secondary	sekundär
soln. . . .	solution	Lösung
startg. m. f.	starting material for	Ausgangsmaterial
	(the preparation of...)	für die Darstellung von...
subst. . . .	substituted	substituiert
sym. . . .	symmetrical	symmetrisch
temp. . . .	temperature(s)	Temperatur(en)
tert. . . .	tertiary	tertiär
v.i. . . .	via intermediates	über Zwischenprodukte
w.a.r. . . .	without additional reagents	ohne Hilfsstoffe
Y*)	yield	Ausbeute

*) When yields are listed in parentheses, the yields so designated refer to the immediately preceding step of a multi-step reaction.

Bei mehrstufigen Synthesen beziehen sich eingeklammerte Ausbeuteangaben auf die unmittelbar vorhergehende Stufe.

Symbols - Zeichen

(on the right half of the page)

(auf der rechten Hälfte der Seite)

Electrolysis	↗	Elektrolyse
Ring closure	○	Ringschluß
Ring opening	↶	Ringöffnung
'see title on the left half of the page'	←	«siehe Titel auf der linken Hälfte der Seite»

Journal Abbreviations - Zeitschriften-Abkürzungen

A.	Liebig's Annalen der Chemie
A. ch.	Annales de Chimie
Am. Soc.	Journal of the American Chemical Society
Ar.	Archiv der Pharmazie und Berichte der Deutschen Pharmazeutischen Gesellschaft
Ark. Kemi	Arkiv för Kemi, Mineralogi och Geologi
B.	Chemische Berichte
Bl.	Bulletin de la Société Chimique de France
C. A.	Chemical Abstracts
C. r.	Comptes rendus (Paris)
G.	Gazzetta Chimica Italiana
H.	Hoppe Seyler's Zeitschrift für physiologische Chemie
Helv.	Helvetica Chimica Acta
J. Org. Chem.	Journal of Organic Chemistry
J. pr.	Journal für praktische Chemie
M.	Monatshefte für Chemie
Org. Synth.	Organic Syntheses
R.	Recueil des Travaux Chimiques des Pays-Bas
Ж	Journal of General Chemistry (Russia)
Soc.	Journal of the Chemical Society
Synth. Meth.	Synthetische Methoden der Organischen Chemie

For other journal abbreviations see Beilstein, Handbuch der organischen Chemie or Chemical Abstracts.

Die übrigen Zeitschriften-Abkürzungen siehe Beilsteins Handbuch der organischen Chemie oder Chemical Abstracts

Systematic Survey - Systematische Uebersicht

Reaction symbol Reaktionszeichen	page Seite	Reaction symbol Reaktionszeichen	page Seite	Reaction symbol Reaktionszeichen	page Seite
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HO $\downarrow$ OC	1	OS $\uparrow$ O	58	NS ∇ Hal	124
HO $\curvearrowright$ HC	2	O Rem $\downarrow$ OC	58	NS $\uparrow$ H	125
HO ∇ Hal	2	O Rem $\downarrow$ Rem	58	NS $\uparrow$ S	125
HO ∇ S	3	O Rem ∇ H	59	N Rem ∇ O	125
HO ∇ Rem	4	O Rem ∇ N	59	N Rem ∇ Hal	126
HO ∇ C	4	O Rem ∇ Hal	59	N Rem ∇ Rem	126
HN $\downarrow$ ON	10	O Rem ∇ S	61	NC $\downarrow$ OC	126
HN $\downarrow$ NN	10	OC $\downarrow$ HC	61	NC $\downarrow$ NC	130
HN $\curvearrowright$ HO	11	OC $\downarrow$ OC	63	NC $\downarrow$ SC	134
HN ∇ O	11	OC $\downarrow$ NC	66	NC $\downarrow$ CC	135
HN ∇ N	14	OC $\downarrow$ SC	67	NC $\curvearrowright$ HN	138
HN ∇ S	14	OC $\downarrow$ CC	68	NC $\curvearrowright$ OC	138
HN ∇ C	14	OC $\curvearrowright$ HO	72	NC $\curvearrowright$ SC	139
HS ∇ Hal	18	OC $\curvearrowright$ HC	72	NC $\curvearrowright$ CC	140
HS ∇ S	18	OC $\curvearrowright$ OC	74	NC ∇ H	141
HS ∇ C	18	OC $\curvearrowright$ NC	74	NC ∇ O	144
H Rem ∇ Hal	20	OC $\curvearrowright$ CC	75	NC ∇ N	161
HC $\downarrow$ OC	20	OC ∇ H	76	NC ∇ Hal	164
HC $\downarrow$ NC	26	OC ∇ O	78	NC ∇ S	173
HC $\downarrow$ SC	29	OC ∇ N	84	NC ∇ C	177
HC $\downarrow$ CC	29	OC ∇ Hal	91	NC $\uparrow$ H	182
HC $\curvearrowright$ HO	36	OC ∇ S	98	NC $\uparrow$ O	182
HC ∇ O	36	OC ∇ Rem	101	NC $\uparrow$ N	189
HC ∇ N	43	OC ∇ C	101	NC $\uparrow$ Hal	189
HC ∇ Hal	44	OC $\uparrow$ H	109	NC $\uparrow$ S	190
HC ∇ S	46	OC $\uparrow$ O	111	NC $\uparrow$ C	190
HC ∇ C	47	OC $\uparrow$ N	113	Hal Hal ∇ Hal	192
HC $\uparrow$ O	52	OC $\uparrow$ Hal	113	Hal S ∇ H	192
HC $\uparrow$ S	53	OC $\uparrow$ S	115	Hal S ∇ O	193
HC $\uparrow$ C	54	OC $\uparrow$ C	116	Hal S ∇ S	194
ON $\downarrow$ N	55	NN $\curvearrowright$ NC	120	Hal Rem $\downarrow$ Rem	194
OS $\downarrow$ HO	55	NN ∇ H	120	Hal Rem ∇ H	194
OS $\downarrow$ S	56	NN ∇ O	122	Hal Rem ∇ O	195
OS ∇ H	56	NN $\uparrow$ H	123	Hal Rem ∇ Hal	195
OS ∇ Hal	56	NS $\downarrow$ SC	123	Hal Rem ∇ S	196

Reaction symbol Reaktionszeichen	page Seite	Reaction symbol Reaktionszeichen	page Seite	Reaction symbol Reaktionszeichen	page Seite
HalRem $\uparrow\uparrow$ C	196	SC $\uparrow\uparrow$ Hal	231	CC $\cap$ SC	265
HalC $\downarrow$ OC	197	SC $\uparrow\uparrow$ S	236	CC $\cap$ CC	266
HalC $\downarrow$ NC	198	SC $\uparrow\uparrow$ C	237	CC $\uparrow\uparrow$ H	266
HalC $\downarrow$ CC	199	SC $\uparrow$ H	238	CC $\uparrow\uparrow$ O	267
HalC $\cap$ HC	201	SC $\uparrow$ O	238	CC $\uparrow\uparrow$ N	290
HalC $\uparrow\uparrow$ H	201	SC $\uparrow$ N	239	CC $\uparrow\uparrow$ Hal	294
HalC $\uparrow\uparrow$ O	207	RemRem $\uparrow\uparrow$ S	239	CC $\uparrow\uparrow$ S	306
HalC $\uparrow\uparrow$ N	212	RemC $\downarrow$ OC	239	CC $\uparrow\uparrow$ C	306
HalC $\uparrow\uparrow$ Hal	213	RemC $\downarrow$ CC	240	CC $\uparrow$ H	310
HalC $\uparrow\uparrow$ C	214	RemC $\uparrow\uparrow$ H	240	CC $\uparrow$ O	313
SS $\uparrow\uparrow$ H	215	RemC $\uparrow\uparrow$ O	241	CC $\uparrow$ N	325
SS $\uparrow\uparrow$ O	215	RemC $\uparrow\uparrow$ N	241	CC $\uparrow$ Hal	328
SS $\uparrow\uparrow$ Hal	215	RemC $\uparrow\uparrow$ Hal	241	CC $\uparrow$ Rem	334
SS $\uparrow\uparrow$ S	216	RemC $\uparrow\uparrow$ Rem	243	CC $\uparrow$ C	334
SRem $\uparrow\uparrow$ Hal	216	RemC $\uparrow\uparrow$ C	244	ElN $\uparrow$ H	338
SC $\downarrow$ OS	217	CC $\downarrow$ HC	244	ElN $\uparrow$ O	338
SC $\downarrow$ OC	217	CC $\downarrow$ OC	244	ElS $\uparrow$ O	339
SC $\downarrow$ NC	218	CC $\downarrow$ NC	250	ElRem $\uparrow$ O	339
SC $\downarrow$ HalS	219	CC $\downarrow$ SC	251	ElRem $\uparrow$ Hal	340
SC $\downarrow$ SC	220	CC $\downarrow$ CC	251	Het $\downarrow$ N	340
SC $\downarrow$ CC	220	CC $\cap$ HC	259	Het $\downarrow$ S	341
SC $\uparrow\uparrow$ H	224	CC $\cap$ OC	262	Het $\downarrow$ Rem	342
SC $\uparrow\uparrow$ O	225	CC $\cap$ NN	263	Het $\uparrow\uparrow$	342
SC $\uparrow\uparrow$ N	231	CC $\cap$ NC	264		

Additional Reagents - Hilfsstoffe

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<i>w.a.r.</i> (heat, light, ζ)	Na^+ , Sodium compound,	Ba(OR)_2
Li, Na, Na/K, K	K^+	CaCO_3 , BaCO_3
LiH, NaH	NH_3	$(\text{CH}_3\text{COO})_2\text{Ba}$
Na, Hg	Organic bases	CaSO_4
Bases	Resin base	CaCl_2 , $\text{BaCl}_2\text{-C}$
Alkalies	Triton B, BTAB	Mg, Mg, Hg, Mg/MgI ₂
Alkali hydroxide	Alkylamines	Zn, Zn, Cu, Zn, Hg
Aq. alkali hydroxide	Methylamine, n-Butyl-	Cd, Hg
NaOH, KOH	amine	HgO, MgO
Alkali in water a. alcohol	Benzylamine	Mg(OH)_2
NaOH/alcohols	Diethylamine,	Mg(OR)_2
KOH/alcohols	Aliphatic tert. amines	CH_3MgI
Alkali alkoxide	Triethylamine	$\text{C}_6\text{H}_5\text{MgBr}$
Na/alcohol, NaOR	Piperidine, Morpholine	Zinc alkyls, Zinc alkyl
K/alcohol, KOR,	N-Methylmorpholine	halides
K-tert-butoxide	Aniline	$(\text{CH}_3\text{COO})_2\text{Hg}$
$\text{C}_6\text{H}_5\text{Li}$	Dialkylaniline	Zn(CN)_2 , Hg(CN)_2
$(\text{C}_6\text{H}_5)_3\text{C}\cdot\text{Na}$	Dimethylaniline,	Hg(ONC)_2 (fulminate)
LiNH_2 , Li-methylanilide	Diethylaniline	$\text{Mg(NO}_3)_2$
Na/liq. NH_3 , NaNH_2 ,	Pyridine, Lutidine,	BeSO_4 , MgSO_4 , HgSO_4
Na-anilide	Collidine, Quinoline	MgBr_2
Alkali in pyridine	Cu, Ag, Ag-Cu, Cu, Mg	ZnCl_2 , $\text{ZnCl}_2\cdot 2\text{NH}_3$
Na_2O_2	Copper oxide, Cu_2O , CuO	HgCl/CdCO_3
Na_2CO_3 , NaHCO_3 ,	Ag_2O	HgCl_2 , HgBr_2
K_2CO_3 , KHCO_3	Ag_2CO_3	Mg^{++} , Ca^{++} , Zn^{++} , Hg^{++}
HCOONa	CH_3COOAg	Al, Al, Cu, Al, Hg
CH_3COONa , CH_3COOK	Cupric carbonate, basic	NaBH_4 , LiAlH_4
Na-citrate	$(\text{CH}_3\text{COO})_2\text{Cu}$	B_2O_3 , HBO_2
NaCN, KCN	Fehling solution	Al_2O_3
NaNO_2	Copper borate	Al(OR)_3
KNO_3	CuCN	Al isopropoxide, Al tert-
KH_2PO_4	CuSCN	butoxide
K-xanthate	Cu(I,II) sulfite	Al phenoxide
Na_2S , Na_2S_2 , Na_2S_x ,	CuCl , CuBr/Mg , CuI/Mg ,	Al silicate
NaHS	Cu_2Cl	Pumice
Na_2Se_x	Cu^+ , Cu^{++}	Glass powder
KHS	AgCN	$\text{AlPO}_4/\text{water glass}$
$\text{Na}_2\text{S}_2\text{O}_3$	AgN_3	BF_3
Na_2SO_3 , NaHSO_3	AgNO_2	HBF_4
NaF, KF, KHF_2	AgNO_3	AlCl_3 , AlBr_3
Alkali iodides	AgF-Cu	Al^{+++}
NaI, KI	$\text{C}_6\text{H}_5\text{COOAg}$	Ce and rare earths
Alkali salts	Ag^+	C
Alkaloid-alkali salts	CaO , BaO , BaO-SiO_2	Alkoxides
	Ca(OH)_2 , Ba(OH)_2	CH_3OH

<i>Hydroquinone</i>	<i>CH₃I</i>	<i>Phenylphosphoryl</i>
<i>Oxo compounds</i>	<i>Polyhalogenoalkanes</i>	<i>dichloride</i>
<i>Benzophenone</i>	<i>CCl₃H, CCl₃Br</i>	<i>POCl₃, POBr₃</i>
<i>Quinone</i>	<i>Benzotrichloride</i>	<i>PSCl₃</i>
<i>Ketene</i>	<i>Iodobenzene dichloride</i>	<i>PHal₅, PCl₅</i>
<i>D-Lactose hydrate</i>	<i>BrCN</i>	<i>As₂O₃, As₂O₅</i>
<i>Pyruvic acid</i>	<i>Bromoacetamide</i>	<i>AsCl₃</i>
<i>(NH₄)₂CO₃</i>	<i>Chlorourea</i>	<i>SbF₃, SbCl₃, SbCl₅</i>
<i>HCOONH₄, CH₃COONH₄</i>	<i>Bromosuccinimide,</i>	<i>Bi</i>
<i>NH₄SCN</i>	<i>Bromophthalimide</i>	<i>BiO₃⁻</i>
<i>Salts of organic bases</i>	<i>Chloramin-T</i>	<i>NH₄ vanadate</i>
<i>Acetates of organic bases</i>	<i>Chloranil</i>	<i>V₂O₅, Al₂O₃</i>
<i>Piperidinium acetate</i>	<i>COCl₂</i>	<i>O₂, O₃</i>
<i>Diazomethane</i>	<i>CH₃COCl, (COCl)₂</i>	<i>H₂O₂</i>
<i>Hexamethylenetetramine</i>	<i>C₆H₅COCl, C₆H₅COBr</i>	<i>Peroxide</i>
<i>HCONH₂</i>	<i>(CH₃)₂CHCHBrCOBr</i>	<i>S</i>
<i>HCON(CH₃)₂</i>	<i>SiO₂, SiO₂-Al₂O₃</i>	<i>S⁻, SH⁻, SH₂</i>
<i>CO(NH₂)₂</i>	<i>TiO₂/HCOOH</i>	<i>(NH₄)₂S_x</i>
<i>Phenyl isocyanate</i>	<i>SiCl₄</i>	<i>Na formaldehyde</i>
<i>Emulsin</i>	<i>Sn</i>	<i>sulfoxylate</i>
<i>Hog kidney enzyme</i>	<i>SnCl₂, SnCl₄</i>	<i>S₂O₄⁻</i>
<i>Chymotrypsin</i>	<i>PbR₄</i>	<i>Tetrathionate</i>
<i>Papain</i>	<i>PbO, Pb₃O₄, PbO₂</i>	<i>SO(NH₂)₂</i>
<i>Acetobacter suboxydans</i>	<i>Pb(OH)₂</i>	<i>Sulfonamide</i>
<i>Nitrosobenzene</i>	<i>(CH₃COO)₂Pb</i>	<i>SOCl₂, SOBr₂</i>
<i>Nitrosodimethylaniline</i>	<i>(CH₃COO)₄Pb</i>	<i>Sulfonic acid chlorides</i>
<i>Isonitrosocynoacetic ester</i>	<i>Pb⁺⁺</i>	<i>Arylsulfonyl chloride</i>
<i>Isopropane nitronate</i>	<i>ThO₂</i>	<i>p-Toluenesulfonic acid</i>
<i>Nitrobenzene</i>	<i>Dicyanodiamide</i>	<i>chloride</i>
<i>(CH₃CO)₂O</i>	<i>Phenylhydrazine</i>	<i>SO₂Cl₂</i>
<i>Ascaridole</i>	<i>H₂N·NH₂</i>	<i>SO₂</i>
<i>Acyl peroxides</i>	<i>N₃⁻, HN₃</i>	<i>S₂O₃⁻</i>
<i>Acetyl-, Benzoyl peroxide</i>	<i>NH₂OH</i>	<i>SO₃</i>
<i>Phenol, Pyrogallol</i>	<i>Nitrogen oxides</i>	<i>(NH₄)₂SO₃</i>
<i>HCOOH, CH₃COOH,</i>	<i>N₂O₃, N₂O₄, N₂O₅</i>	<i>(NH₄)₂SO₄</i>
<i>CH₃CH₂COOH</i>	<i>NH₄NO₃</i>	<i>Pyridine·SO₃</i>
<i>Thioacetic acid</i>	<i>Alkyl nitrite</i>	<i>HCON(CH₃)₂·SO₃</i>
<i>ClCH₂COOH, CCl₃COOH</i>	<i>Butyl-, Amyl nitrite</i>	<i>Sulfonates</i>
<i>(COOH)₂, CH₂(COOH)₂,</i>	<i>NO₂⁻</i>	<i>Na-m-nitrobenzene-</i>
<i>Phthalic acid</i>	<i>NOCl, NOBr</i>	<i>sulfonate</i>
<i>CO₃⁻</i>	<i>HNO₃</i>	<i>NaHSO₄, KHSO₄,</i>
<i>Peroxy acids</i>	<i>P</i>	<i>NH₄HSO₄</i>
<i>HCOO₂H, CH₃COO₂H</i>	<i>Phosphorus compounds</i>	<i>Ethanesulfonic acid</i>
<i>C₆H₅COO₂H, Perphthalic acid</i>	<i>PH₄I</i>	<i>Benzene-, p-Toluene-,</i>
<i>Thioureas</i>	<i>Phosphazo compounds</i>	<i>Naphthalene-β-sulfonic acid</i>
<i>Thiocyanates</i>	<i>P₂O₅</i>	<i>HSO₃NH₂</i>
<i>Dimethyl sulfate</i>	<i>H₂PO₂⁻</i>	<i>NH₂OSO₃H (Hydroxyl-</i>
<i>Sulfonamides</i>	<i>H₃PO₂</i>	<i>amine-O-sulfonic acid)</i>
<i>Amyl disulfide</i>	<i>Quinoline phosphate</i>	<i>H₂SO₄</i>
<i>Methyl tetrasulfide</i>	<i>H₃PO₄</i>	<i>H₂SO₅</i>
	<i>P₂S₃, P₂S₅</i>	<i>S₂O₃⁻</i>
	<i>PHal₃, PCl₃, PBr₃</i>	<i>(NH₄)₂S₂O₈</i>

$S_2O_8^{--}$	IO_4^-	Co
FSO_3H , $ClSO_3H$	Cl^- , I^-	Co/Al_2O_3
Sulfur chlorides	NH_4F , NH_4Cl , NH_4I	$Co(CO)_4$
S_2Cl_2	Hydrochlorides	Cr_2O_3 -cobalt hydrate-
Se	Pyridine hydrochloride	$CaCO_3$
SeO_2	Acetylpyridinium	Co nitrite
Chromite	chloride	$CoCl_2$
$CuCr_2O_4$, $CuCr_2O_4 \cdot C$	Hydrobromides	CoF_3
$(Ca,Cu)Cr_2O_4$,	$(CH_3)_4NBr \cdot Br_2$	Ni
$(Ba,Cu)Cr_2O_4$	Pyridine hydrobromide-	Ni-Al
Cr_2O_3, Al_2O_3	perbromide	Ni/Pt , $Ni/PtCl_4$
MoO_x , MoO_3	Acids/metal chlorides	Ni, Cr_2O_3
CrO_4^- , $Cr_2O_7^{--}$, CrO_3	Mineral acids	Nickel-zinc chromite
MoS_2	Hydrogen halides	$Ni(CO)_4$
CrO_2Cl_2	HF , HCl , HBr , HI	$NiSO_4$
$CrCl_2$	MnO_2	RuO_2
I_3^-	MnO_4^-	Pd
Halogen	$NaMnO_4$, $KMnO_4$,	$Pd-CaCO_3$, $Pd-SrCO_3$,
Cl, Br, I	$Ba(MnO_4)_2$	$Pd-BaCO_3$
BrCN	Fe	$Pd-BaSO_4$
IF_5 , ICl , ClI , BrI	Fe/Fe^{++}	$Pd-C$
Alkyl hypochlorite	FeS/Al_2O_3	Pd -pumice
$HalO^-$, ClO^-	$FeSO_4$	PdO
$NaOCl$, $KOBr$, KOI	$Fe_2(SO_4)_3$	OsO_4
$Ca(OCl)_2$, $Ba(OI)_2$	$FeCl_3$	Pt
ClO_3^- , BrO_3^-	Fe^{+++}	$Pt-C$
$KClO_3$, $NaBrO_3$, KIO_3	$Na_3[Fe(CN)_5NH_3]$	PtO_2
$HClO_4$	$K_3[Fe(CN)_6]$	<i>v.i.</i>

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81	34	413	161	707	274
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97	40	460	132	713	275
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129	110	489	203	725	283
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201	83	535	221	780	300
212	57	539	135	807	311
224	88	597	241	811	312
244	97	604	242	812	330
263	103	607	303	814	313
269	110	614/5	244	816	314
290	122	623	246	835	321
292	122	625	247	841	333
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497	256	577	294	654	333
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515	260	594	298		
517	261	600	301		

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6	7	226	164	705	51
47	18	280	332	731	88
107	24	585	211	761	33
148	56	689	84	820	12
182	320	700	48	858	274, 311

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