CHAPTER XII

SEMIMICRO TECHNIQUE

XII,1. INTRODUCTION AND GENERAL CONSIDERATIONS

ORGANIC preparations in the laboratory are sometimes divided into three categories :—

(1) *Macro scale* : Usually from 1 g. to 200+ g. for solids and 5 g. to 200+ g. for liquids.

(2) *Semimicro scale* : From *ca.* 100 mg. to 1,000 mg. for solids and 1 g. to 5 g. for liquids.

(3) *Micro scale* : Below 100 mg. for solids and 1 g. for liquids.

It must be pointed out that the division is entirely arbitrary and the categories overlap ; they are, however, useful for purposes of rough classification.

The proper training for the organic chemist must be based upon a correct interpretation and wide practice of the technique on the macro scale. A knowledge of, and experience in, semimicro technique is a valuable *supplement* to that training. It is the purpose of this Chapter to provide an outline of semimicro technique, which the student may utilise when the opportunity arises. Thus when only small quantities of organic material are available (as occurs frequently in qualitative organic analysis, in research problems or when dealing with very expensive compounds), their manipulation must of necessity be performed on a correspondingly small scale.

There are no serious difficulties in working with small quantities of solids (say, of the order of 100 mg.) ; full experimental details will be given in a later Section. For liquids special attention must be given to losses which may occur as a result of :—

(*a*) Surface effects (drainage from spherical vessels).

(*b*) Transference from one spherical vessel to another.

(*c*) Absorption by corks and retention by filter papers.

It must be appreciated that one drop, say, of 0·05 ml. weighs 50–75 mg., hence manipulation with quantities of less than 1 ml. presents new problems involving a specialised technique (micro technique), which will not be discussed here.

As a general rule, when working with semimicro quantities, it is best to employ pear-shaped vessels (Fig. *XII*, *1*, 1, *a*) and centrifuge tubes (Fig. *XII*, *1*, 1, *b*) as containers for liquids ; convenient capacities are 5, 10 and 20 or 25 ml. for flasks, and 1, 3, and 5 ml. for centrifuge tubes. Round-bottomed vessels of similar volumes

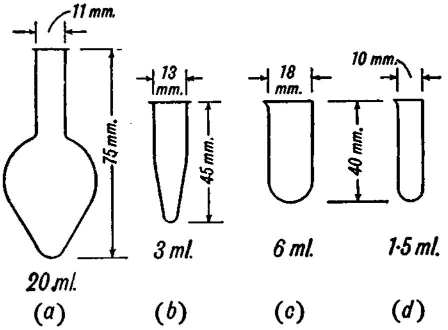


Fig. *XII*, *1*. 1.

may be used, but the losses may be significant if the volume of liquid is less than about 5 ml. Small test-tubes with lips are shown in *c* and *d*.

A liquid may be transferred from one vessel to another with a dropper pipette (Fig. *XII*, *1*, 2, *a* or *b*). If the dropper pipette is calibrated, it may be employed for measuring out a definite volume of liquid.

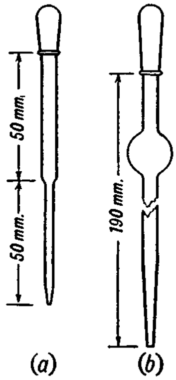


Fig. *XII*, *1*, 2.

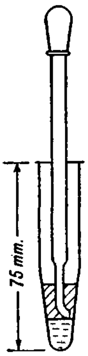


Fig. *XII*, *1*, 3.

A cylindrical or, preferably, a pear-shaped separatory funnel (Fig. *II*, *1*, 5, *e* and *d*) of 10–15 ml. capacity is usually employed for the separation of immiscible liquids. For separations on a smaller scale, a dropper pipette may be used ; the upper layer is best removed with a " bent " pipette as in Fig. *XII*, *1*, 3. For liquids which tend to emulsify, centrifugation (a hand centrifuge is satisfactory) will usually produce a clean line of demarcation between two immiscible liquids.

Single pieces of apparatus are used wherever possible in order to reduce to a minimum the absorption of liquids by corks.

As a general rule flasks and similar vessels should be heated in an air bath (compare Fig. *II*, *5*, 3). A glycerol bath may be employed for temperatures up to 140° ; the glycerol is subsequently removed from the outside of the vessel by washing with water. Medicinal liquid paraffin may be used for temperatures up to about 220° ; " hard hydrogenated " cotton seed oil, " Silicone " fluids or fusible metal may be employed when higher temperatures are required. Small test-tubes and centrifuge tubes may be heated by a semimicro Bunsen burner, but great care must be taken that the liquid does not " bump " ; it is preferable to heat these small open vessels in a water (or other liquid) bath.

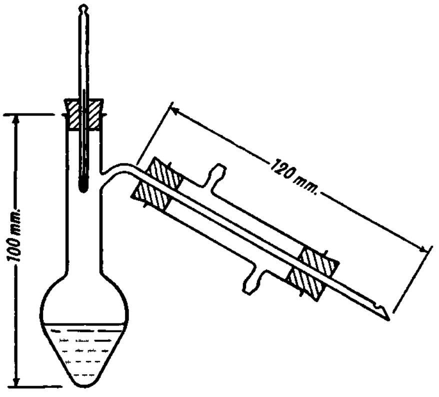


Fig. *XII*, *2*, 1.

XII,2. SOME TYPICAL OPERATIONS ON THE SEMIMICRO SCALE

1. **Distillation at atmospheric pressure.**—A simple apparatus is shown in Fig. *XII*, *2*, 1 ; the pear-shaped distilling flask with long side arm is employed for liquids of b.p. above 140°. For liquids of lower b.p., the side arm is surrounded for a large proportion of its length by a glass jacket held in position by rubber stoppers. The distillate is collected in a centrifuge tube or other small vessel (test-tube, conical flask, etc.). In an alternative set-up, a "distillation tube" (Fig. *XII*, *2*, 2) and a "cold finger" condenser (Fig. *XII*, *2*, 3 ; this may be constructed entirely of glass, if desired) are assembled as shown in Fig. *XII*, *2*, 4. All thermometers employed in small-scale work must have very small bulbs.

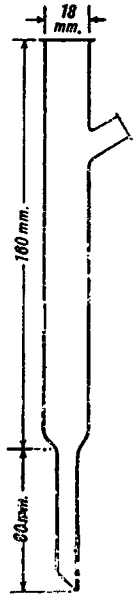


Fig. *XII*, *2*, 2.

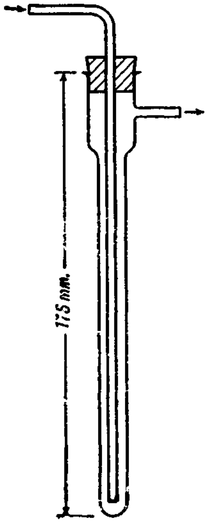


Fig. *XII*, *2*, 3.

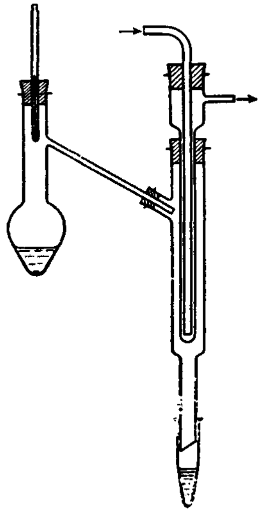


Fig. *XII*, *2*, 4.

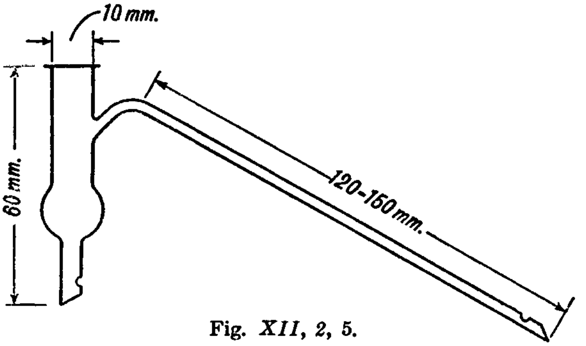


Fig. *XII*, *2*, 5.

It is sometimes necessary to remove the products of a reaction in a flask (Fig. *XII*, *1*, 1, *a*) by distillation. The still head depicted in Fig. *XII*, *2*, 5 may be used for this purpose ; the side arm may be fitted with a water condenser, if required.

The simple spring clamps shown in Fig. *XII*, *2*, 6 are recommended for the rapid assembly and dismantling of semimicro apparatus. These clamps have hardwood stems about 15 cm. long, which are slotted and can accommodate "Terry clips" of suitable sizes; they may be used in conjunction with ordinary stands and bossheads.

2. **Distillation under diminished pressure.**—A simple apparatus is illustrated in Fig. *XII, 2,* 7. The Claisen flask with pear-shaped bulb is attached to a "distillation tube" and a "cold finger" condenser. The receiver consists of a centrifuge tube or test-tube supported inside a large test-tube to which a side arm is fused.

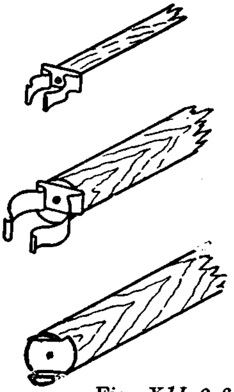


Fig. *XII, 2,* 6.

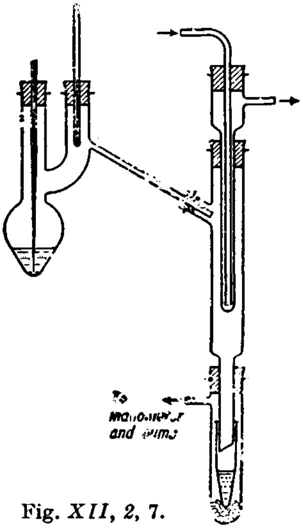


Fig. *XII, 2,* 7.

Alternatively, the apparatus shown in Fig. *II, 19,* 1 with obvious modifications (small flask with pear-shaped bulb, etc.) may be used. The set-up of Fig. *II, 20,* 1, utilising, say, a 10 or 20 ml. Claisen flask with pear-shaped bulb, a Perkin triangle (capacity of bulb *ca.* 10 ml.) and a small test-tube receiver, is recommended; it may be employed for fractional distillation under reduced pressure.

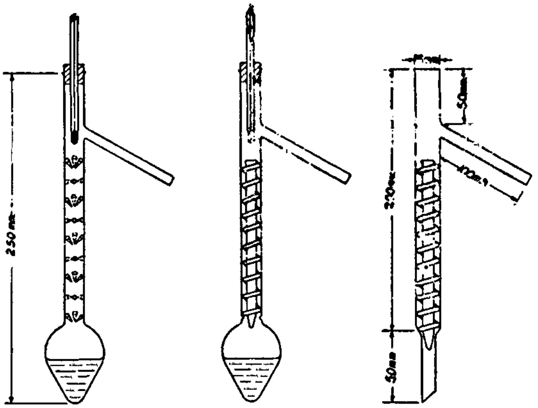


Fig. *XII, 2,* 8.

3. **Fractional distillation at atmospheric pressure.**—The flask may have the fractionating column attached (compare Figs. *II, 24,* 4–5): the latter may be:—

(i) of the Vigreux type (Fig. *XII*, 2, 8, *a*) ;

(ii) of the Widmer type (Fig. *XII*, *2*, 8, *b*)—a central glass rod or sealed tube is wound with copper or nichrome wire (16 gauge : about 24 turns) or with glass yarn ; or

(iii) it may be filled with hollow glass rings ($\frac{1}{8}''$ diameter) or, preferably, with single turn glass helices or with Dixon gauze rings (see Section **II,17**).

Alternatively, an independent column (Fig. *XII*, *2*, 8, *c*) may be inserted into a flask; the column may be of the Vigreux, Widmer or Hempel form. The fractionating column should be lagged with asbestos cloth or string for distillation temperatures above 100° : for the best results the column should be heated electrically (compare Section **II,15**) to a temperature 5–10° below the b.p. of the fraction being collected. The side arm of the flask or fractionating column may be attached to a " cold spot " condenser and receiver as in Fig. *XII*, *2*, 4 or to a Liebig's condenser and receiver as in Fig. *XII*, *2*, 1.

4. **Fractional distillation under diminished pressure.**—A 5–25 ml. Claisen flask (with pear-shaped bulb) provided with a fractionating side arm (Fig. *II*, *24*, 4–5) and attached to a Liebig's condenser and a Perkin triangle (Fig. *II*, *20*, 1 or *II*, *20*, 2 ; volume of receiver *ca.* 10 ml.) will be found to have wide application.

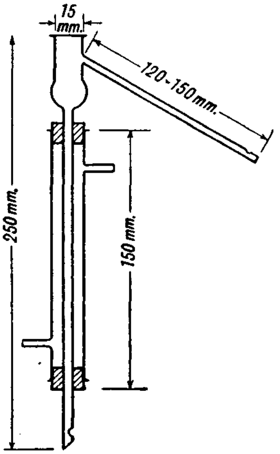


Fig. *XII*, *2*, 9.

5. **Heating under reflux.**—A water condenser of total length 25 cm. (cooling jacket 15 cm.) may be used. If the upper end is provided with a long side arm as in Fig. *XII*, *2*, 9, refluxing may be followed by distillation without transferring the contents of the flask : it may be necessary to surround part of the side arm with a short water condenser (compare

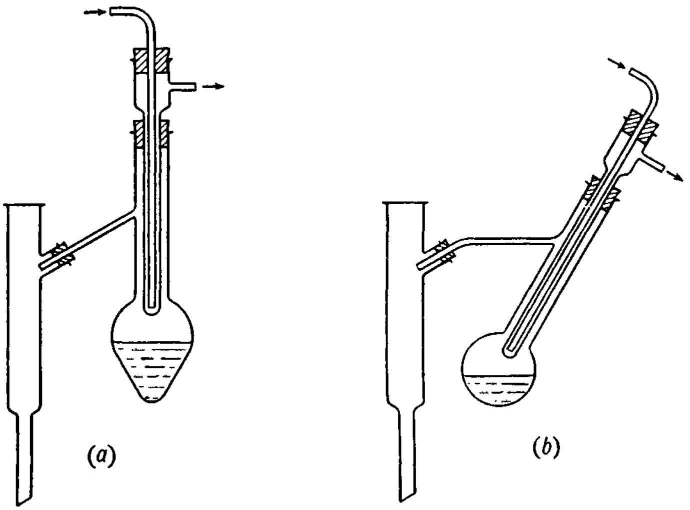

(*a*) (*b*)

Fig. *XII*, *2*, 10.

Fig. *XII, 2,* 1). For very small volumes of liquid either of the apparatus depicted in Fig. *XII, 2,* 10, incorporating a " cold finger " condenser may be employed; subsequent distillation (or steam distillation) is a facile operation as it merely involves moving the condenser as in Fig. *XII, 2,* 4 and Fig. *XII, 2,* 11. (Some of the Figures are not strictly to scale; this is in order to assist clarity of representation.)

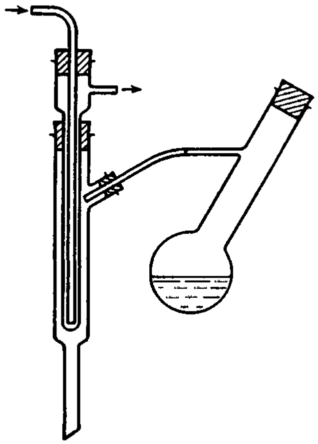


Fig. *XII, 2,* 11.

6. **Steam distillation.**—For small quantities of compounds, which are readily volatile in steam, water may be added to the contents of the reaction flask (*e.g.* Figs. *XII, 2,* 4 and *XII,* 2, 11) and the flask heated in an air bath or with a small flame. Alternatively, if preferred, steam may be passed into the reaction flask from a separate generator: this may consist of a small conical flask provided with the usual safety tube (compare Fig. *II, 40,* 1).

A compact apparatus is depicted in Fig. *XII, 2,* 12. It is designed to be fitted into a standard 100 ml. Pyrex Kjeldahl flask: if desired, the dimensions may be reduced proportionately for use with a 50 ml. flask. A screw clip is attached by rubber tubing to the side arm E; the latter may be replaced by a thin glass tube (3–4 mm. external diameter) inserted through the upper cork, thus permitting the use of a Kjeldahl flask without modification. The liquid to be steam distilled is placed in the tube A and water in the outer vessel B. Upon heating the latter, steam passes through the inlet tube C and steam-volatile compounds pass out through D; a condenser is attached at D and the steam distillate is collected in a suitable receiver. The functions of the bulb in the inlet tube C are to reduce the danger of spurting and also the " sucking back " of the liquid in A; the latter can be prevented by the timely opening of the screw clip on E.

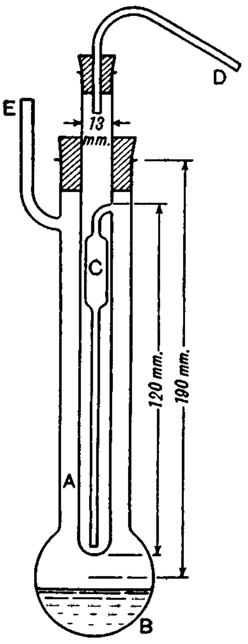


Fig. *XII, 2,* 12.

7. **Recrystallisation and filtration.**—Recrystallisation is carried out in apparatus of conventional type but reduced in size. Operations involving hot inflammable solvents should preferably be performed under reflux: when semimicro test-tubes (75 × 10 mm. or 100 × 12 mm.) or centrifuge tubes (1–5 ml.) are employed, they must be heated in a water bath and not directly by a semimicro burner. The crystals, which separate on cooling, are removed by filtration using a small Hirsch funnel (*i.e.*, a conical, porcelain Buchner funnel) or a small Pyrex funnel with sintered glass filtration plate; it is often advantageous to place a small filter paper upon the sintered glass plate since complete removal of the crystals is thereby facilitated. The filtration assembly is shown in Fig. *XII*, *2*, 13. It includes a boiling tube (150 × 25 mm.) having a side arm for attachment to the pump ; the filtrate is collected in a centrifuge tube or in a semimicro test-tube resting upon a pad of cotton wool.

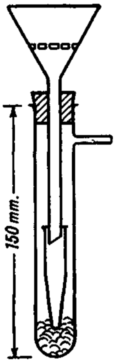


Fig. *XII*, *2*, 13.

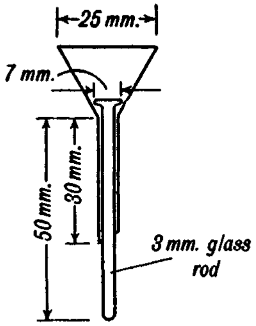


Fig. *XII*, *2*, 14.

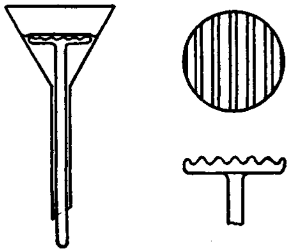


Fig. *XII*, *2*, 15.

An apparatus for the filtration of small to moderate quantities of crystals incorporates the so-called **Willstätter "filtration nail."** The latter consists of a thin glass rod flattened at one end. It is readily constructed by heating the end of a short glass rod in the blowpipe flame and pressing vertically upon an asbestos board. The "nail" is fitted into small glass funnel; it is covered by a circle of a filter paper cut with the aid of a cork borer of appropriate size. A "filtration nail" and funnel, capable of handling up to 1 g. of solid is depicted in Fig. *XII*, *2*, 14. It is convenient to make several "nails" of different size head for a single funnel so that a filter paper of diameter appropriate to the amount of solid to be collected may be employed. For the larger sizes of "nail," accommodating filter papers of 15–25 mm. diameter, it is advisable to corrugate the head of the "nail," as shown (somewhat exaggerated) in Fig. *XII*, *2*, 15, in order to permit drainage of filtrate over the entire area of the paper : these corrugations are easily produced by pressing the hot glass on the surface of an old single-cut file of coarse grade. The method of use of the glass filtration "nail" is similar to that for the conical Buchner funnel (Fig. *XII*, *2*, 13). By employing a slightly modified funnel, the glass "nail" can be utilised, in conjunction with a drying tube packed with desiccant, for drying the product by suction ; this assembly is illustrated in Fig. *XII*, *2*, 16.

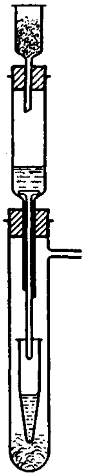


Fig. *XII*, *2*, 16.

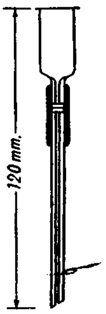


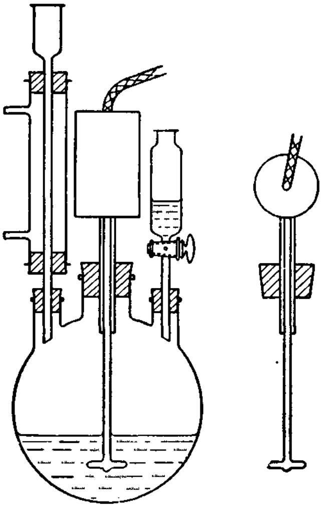
Fig. *XII*, *2*, 17.

The **Schwinger filter**, shown in Fig. *XII*, *2*, 17, finds application when dealing with very small quantities of crystals. The solid collects as a pellet above the small filter paper disc at the throat of the filter : after dismantling, the pellet may be expelled by a snugly fitting glass rod.

A Pyrex micro filter (Fig. *XII*, *2*, 18) of 8 ml. capacity and furnished with a sintered glass disc is useful for the filtration of hot or boiling liquids. The long cylindrical tube reduces evaporation. The filter may be inserted into a test-tube with side arm (Fig. *XII*, *2*, 13) and the filtrate collected in a centrifuge tube or semimicro test-tube receiver.

8. **Stirring.**—It is frequently necessary to stir organic reaction mixtures for comparatively long periods. Magnetic stirrers (see Fig. *II*, *7*, 15) are useful for this purpose provided the viscosity of the reaction mixture is not too high. Inexpensive magnetic stirrers, suitable for semimicro vessels, are available commercially, as are also combined hot plate and magnetic stirring apparatus.

Fig. *XII*, *2*, 18.



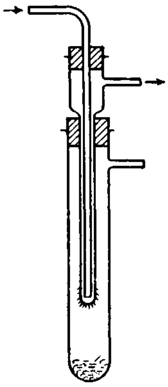


Fig. *XII*, *2*, 20.

When the curvature of the reaction vessel is too great for the efficient operation of the bar-type magnetic stirrer, a miniature solenoid-operated reciprocating stirrer may be employed (Fig. *XII*, *2*, 19). This stirrer may be easily constructed from a telephone relay or electric bell. It is advisable to have a control for adjusting the stroke while running.

In those cases where stirring for short periods is necessary, this may usually be accomplished by gentle rotation of the vessel thus imparting a swirling motion to its contents. If the vessel cannot conveniently be moved, a hand-operated stirrer constructed entirely of glass (compare Fig. *II*, *10*, 4 and Fig. *II*, *10*, 2) will be found satisfactory provided the glass loop is not too large.

9. **Sublimation.**—This is a valuable means for the purification of many organic substances and is admirably adapted for small-scale work since losses are generally small. Sublimation may be carried out either at atmospheric pressure or under reduced pressure. The apparatus shown in Fig. *XII*, *2*, 20 is simple and effective : the sublimate is collected on the " cold finger " condenser.

XII,3. SEMIMICRO APPARATUS WITH INTERCHANGEABLE GROUND GLASS JOINTS

Small scale apparatus with interchangeable ground glass joints (compare Section **II,56**) are available commercially.* One set of apparatus (*A) is based largely upon *B*10 and *B*14 joints, although occasionally a larger size joint is used as in the steam distillation apparatus shown in Fig. *XII*, *3*, 1.

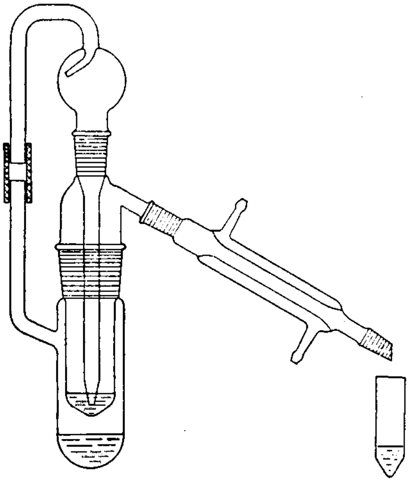


Fig. *XII*, *3*, 1.

Another set of apparatus (*B) adopts the $ 19 joint as standard (apart from $ 7/12 for thermometers) but connexions to condensers, etc., incorporate internal glass seals. A typical assembly for distillation is depicted in Fig. XII, *3*, 2.

In a third set of commercial apparatus (*C and D), the $ 14/20 joint is standard. In the basic assembly, shown in Fig. *XII*, *3*, 3, the flask (50 or 100 ml.) is equipped with a spherical 65/40 or a $ 45/50 joint ; the head is fabricated with three outer $ 14/20 joints surrounding the centre opening, which is $ 19/38 ; the central neck usually carries a precision ground stirrer. The flask may be heated by an electric heating mantle.

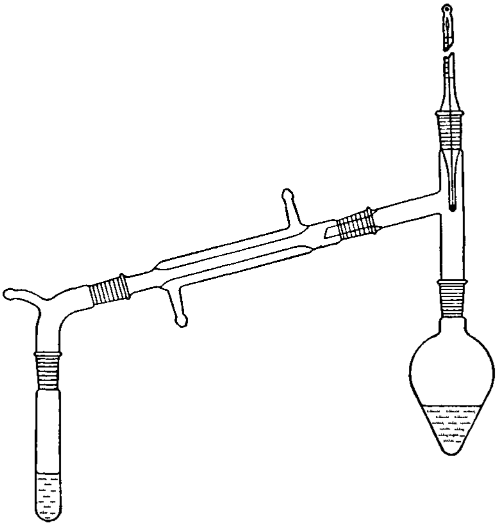


Fig. *XII*, *3*, 2.

A semimicro assembly, suitable for precision fractionation, used in the author's laboratory is illustrated in Fig. *XII*, *3*, 4; the mode of heating the fractionating column is not shown for reasons of clarity (compare Fig. *II*, *17*, 2).

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* For example, from :—

A. Quickfit and Quartz Ltd., Heart of Stone, Staffs., England.
B. Metro Industries, 29–28 41st Avenue, Long Island City 1, New York.
C. Ace Glass Incorporated, Vineland, New Jersey.
D. Scientific Glass Apparatus Co. Inc., Bloomfield, New Jersey.

The catalogues of these manufacturers contain full details of assemblies and individual items.

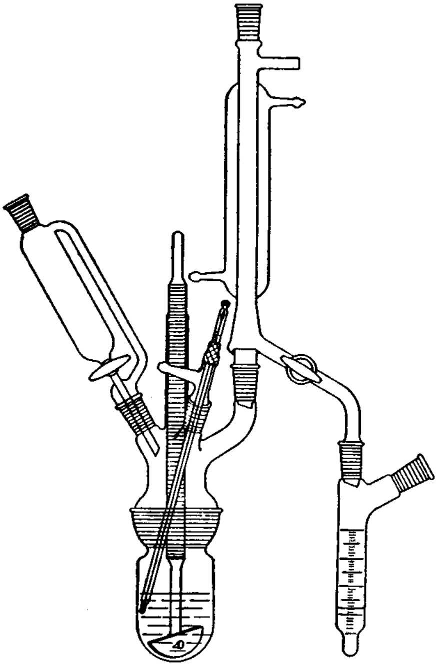

Fig. *XII*, *3*, 3.

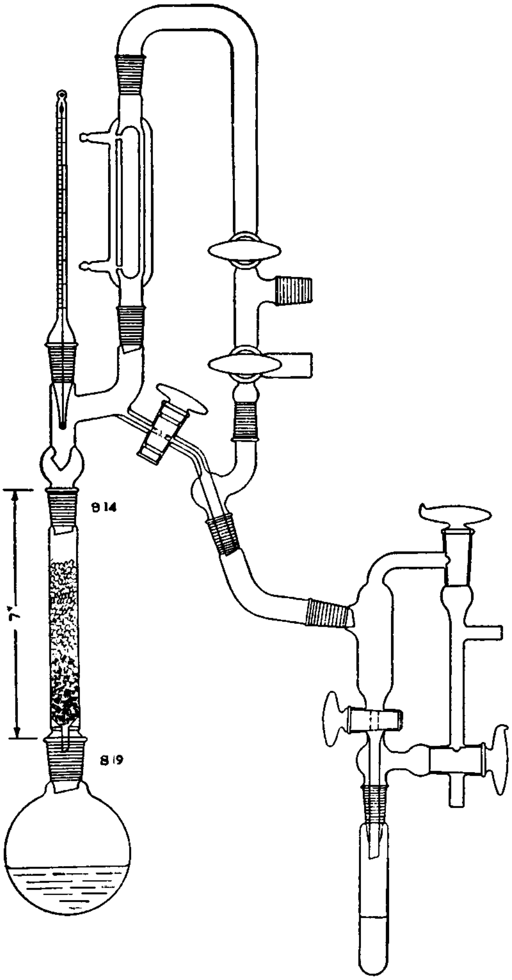

Fig. *XII*, *3*, 4.

XII,4. SMALL-SCALE PREPARATIONS*

Experienced students may carry out some typical preparations described in the text, but on a considerably reduced scale and employing the modifications described in Section **XII,2** wherever these seem suitable.

Beginners may also undertake small-scale preparations on a slightly larger scale than can be strictly classified as semimicro : the resulting saving in time, chemicals and in bench and fume cupboard space are such as to commend the reduced scale of working to all. Some advantages of small scale working may be amplified further :—

(i) Saving of time in setting up apparatus, in periods of refluxing, in filtration and washing of solids, and in recrystallisation of solids.

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* This subject is dealt with *ab initio* in the author's book entitled *Elementary Practical Organic Chemistry*. Part I. *Small Scale Preparations*. (Longmans, Green and Co. Ltd., 1957.) The treatment is comprehensive and includes a detailed account of small scale apparatus of novel design.

(ii) Economy in bench and fume cupboard space.
(iii) Economy in initial cost of apparatus and of chemicals.
(iv) Reduced cost of breakages.
(v) Reduced hazard in handling dangerous chemicals, such as bromine.
(vi) The small-scale preparation of organic compounds provides invaluable experience for subsequent training in qualitative organic analysis.

Much can be done with such standard apparatus in borosilicate glass as :—

Round-bottomed flasks ; 5 ml., 10 ml. and 25 ml.
Pear-shaped flasks (" boiling flasks, conical form ") ; 5 ml., 10 ml. and 25 ml.
Distilling flasks ; 10 ml., 25 ml. and 50 ml.
Claisen flasks ; 25 ml. and 50 ml.
Liebig's condenser (16 cm. jacket held in position by rubber stoppers, inner jacket 7 mm. in diameter ; *or* condenser, 20 cm. body with inner tube fused to outer tube).
Separatory funnels ; 10 ml. and 25 ml.
Conical flasks ; 5 ml., 10 ml. and 25 ml.
Funnels for above conical flasks.
Buchner funnel ; 2 cm.
Semimicro test-tubes ; 75 × 10 mm. or 100 × 12 mm.
Filter tubes ; 55 × 7 mm. or 100 × 12 mm.
Semimicro boiling tubes ; 60 × 25 mm.
Conical centrifuge tubes ; 1 ml., 2 ml., 3 ml., and 5 ml.

Although the yields with the above simple apparatus may not be quite so high as can be obtained with the purely semimicro apparatus described in Sections **XII,1** and **XII,2**, the numerous advantages attending the purchase of standard (and therefore comparatively inexpensive) apparatus usually outweigh the small reduction in yield.

The following list of experiments is suggested as the basis of an elementary course :

1. Determination of melting points (α-naphthylamine, α-naphthol, benzoic acid, succinic acid and *p*-nitrobenzoic acid). Use the apparatus shown in Fig. *II*, *10*, 2, *a*. Construction of calibration curve for thermometer. Determination of m.p. of " unknown " compound.

2. Determination of boiling points. Distillation method (Fig. *II*, *12*, 1) for carbon tetrachloride (25 ml. distillation flask and small water condenser), and Siwoloboff's method (Fig. *II*, *12*, 2) for carbon tetrachloride, aniline and nitrobenzene. Calibration curve for thermometer. Determination of b.p. of " unknown " liquid.

3. Purification of solid by recrystallisation : acetanilide from water ; naphthalene from methylated spirit (**III,5**). Use 1 g. of solid, 25 ml. flask and short water condenser.

4. *n*-Butyl acetate (**III,95**, $\frac{1}{10}$ scale ; use 25 ml. round-bottomed flask, water condenser ; reflux for 30 minutes).

5. *tert.*-Butyl chloride (**III,33**, $\frac{1}{10}$ scale ; if 0·5–1 g. of anhydrous zinc chloride is dissolved in the concentrated HCl, the *tert.*-butyl chloride forms almost immediately).

6. *n*-Butyl bromide (**III,36,** $\frac{1}{5}$ scale ; use 50 ml. conical flask ; reflux 30–45 minutes).
7. *n*-Butyl iodide (**III,40,** $\frac{1}{10}$ scale).

If a small-scale special apparatus is not available, proceed as follows : Place 1·5 g. (1·9 ml.) of *n*-butyl alcohol and 0·28 g. of purified red phosphorus in a 25 ml. round-bottomed flask, and add 2·5 g. of iodine in 2 portions. Allow to stand for 2–3 minutes, heat on a boiling water bath under reflux for 30 minutes, add 5 ml. of water and distil. Separate the lower layer of the distillate. Work up the product as described in **III,40.**

8. Di-*n*-butyl ether (**III,57,** $\frac{1}{2}$ scale ; use 100 ml. Pyrex bolt-head flask).
9. Chloroform (**III,43** ; $\frac{1}{10}$ scale ; use 250 ml. round-bottomed flask).
10. Iodoform (**III,45,** $\frac{1}{6}$ scale ; use 50 ml. conical flask ; recrystallise product in 25 ml. flask with short water condenser).
11. Acetyl chloride (**III,86,** $\frac{1}{5}$ scale ; use 25 ml. distilling flask ; PCl_3 may be added all at once and mixture then heated for 15 minutes at 40–50°).
12. Acetic anhydride (**III,89,** $\frac{1}{5}$ scale ; use 25 ml. distilling flask).
13. Reactions of acetic anhydride (**III,94,** $\frac{1}{2}$ scale).
14. Acetamide (**III,108,** $\frac{1}{5}$ scale ; use a 50 ml. distilling flask for the initial reaction).
15. Acetonitrile (**III,111,** $\frac{1}{5}$ scale ; use a 50 ml. distilling flask for the initial reaction).
16. Reactions of aldehydes (**III,70,** (i), (ii), (iii) and (vi), and 1 in **III,74** on $\frac{1}{2}$ scale ; use *n*-butyraldehyde).
17. Reactions of ketones {use acetone ; reactions (i), (ii), (iii) and (vi) as for aldehydes ; *cyclo*hexanone oxime ($\frac{1}{2}$ scale), *cyclo*hexanone phenylhydrazone, and acetone semicarbazone ($\frac{1}{4}$ scale) as in **III,74**}.
18. Hydrolysis of esters (**III,106**) ; *n*-butyl acetate.
19. Nitrobenzene (**IV,10,** $\frac{1}{5}$ scale ; use a 100 ml. flask ; heat at 60° for 20 minutes).
20. Aniline (**IV,34,** *Method A*, $\frac{1}{5}$ scale).

The following additional experimental details may be regarded as illustrative of a typical small-scale preparation. Place 5·0 g. (4·2 ml.) of nitrobenzene and 9 g. of granulated tin in a 100 ml. bolt-head or round-bottomed flask fitted with a short reflux water condenser. Add 10 ml. of concentrated HCl down the condenser and shake the contents of the flask steadily ; cool in a beaker of cold water if the reaction becomes unduly vigorous. When the reaction slackens, add a further 10 ml. of concentrated HCl and shake the flask to ensure good mixing. Heat on a boiling water bath for 30 minutes. Cool the flask and add gradually, with shaking, a solution of 15 g. of NaOH in 25 ml. of water ; the initial precipitate should dissolve almost completely. Add 20 ml. of water. Fit the flask with a wide bent tube (" knee " tube) and water condenser (Fig. *II, 13,* 3 but with thermometer omitted), add a few small fragments of broken porcelain, heat over a wire gauze and collect the distillate in a small flask. The aniline passes over with the steam and the distillate suddenly becomes clear after about 25 ml. have been collected ; collect a further 15 ml. of distillate.

Saturate the distillate with sodium chloride (*ca.* 8 g.) and extract four times with 5 ml. portions of ether. Dry the combined ethereal extracts with a little anhydrous potassium carbonate or a few pellets of potassium hydroxide. Remove the ether (Fig. *II, 13,* 4), using a 20–25 ml. distilling flask. When all the ether has distilled over, run the water out of the condenser, and distil the residue either by direct heating over a wire gauze or, better, with the aid of an air bath. The yield of aniline, b.p. 180–184°, is 3·0 g.

21. *m*-Dinitrobenzene (**IV,12**, $\frac{1}{5}$ scale; use a 50 or 100 ml. round-bottomed flask; a water condenser is not essential; heat on a boiling water bath for 10–15 minutes after all the nitrobenzene has been added).

22. *m*-Nitroaniline (**IV,44**, $\frac{1}{10}$ scale; use a 100 ml. conical flask; add the sodium polysulphide solution from a test-tube during 5 minutes; shaking and swirling the contents of the flask by hand may replace mechanical stirring; boil gently for 5 minutes and maintain the original volume by the addition of water, if necessary).

23. Acetanilide (**IV,45**, *Method 2*, $\frac{1}{5}$ scale; boil reaction mixture for 15 minutes). Use product for preparations 24 and 25.

24. *p*-Bromoacetanilide (**IV,48**, $\frac{1}{10}$ scale; allow reaction mixture to stand for 10 minutes).

25. *p*-Nitroacetanilide (**IV,50**, $\frac{1}{10}$ scale; allow reaction mixture to stand at room temperature for 10 minutes instead of 1 hour, then for 5 minutes after addition of crushed ice).

26. *p*-Nitroaniline (**IV,51**, $\frac{1}{10}$ scale; heat mixture in test-tube or small conical flask for 5 minutes).

27. *o*- and *p*-Nitrophenols (**IV,108**, $\frac{1}{10}$ scale; add phenol solution to acid mixture in 100 ml. conical flask during 5 minutes, keeping thoroughly mixed by swirling contents of flask; do not permit temperature to rise above 20–30°; allow to stand for 2 hours with frequent shaking during first hour when temperature may rise to, but must not be permitted to exceed, 50–55°; it is best to allow to stand overnight).

28. Bromobenzene and *p*-dibromobenzene (**IV,18**, $\frac{1}{10}$ scale; when reaction slackens, heat on a water bath at 65–70° for 30 minutes).

29. Chlorobenzene (**IV,61**, $\frac{1}{10}$ scale).

30. *p*-Tolunitrile and *p*-toluic acid (**IV,66**, $\frac{1}{5}$ scale; convert all *p*-tolunitrile into acid).

31. Diazoaminobenzene (**IV,81**, $\frac{1}{10}$ scale; reduce periods of standing to one third).

32. *p*-Amino-azobenzene (**IV,82**, $\frac{1}{5}$ scale; heat at 40–45° for 30 minutes; allow to stand for 5 minute periods in lieu of 15 minutes).

33. Benzyl alcohol and benzoic acid (**IV,123**); $\frac{1}{5}$ scale.

34. Benzoin (**IV,125**); $\frac{1}{10}$ scale.

35. Benzil (**IV,126**); $\frac{1}{10}$ or $\frac{1}{5}$ scale.

36. Cinnamic acid (**IV,124**); $\frac{1}{5}$ scale.

Alternatively, use the following procedure in which triethylamine replaces potassium acetate as the basic catalyst. Place 2·1 g. (2·0 ml.) of purified benzaldehyde, 2·0 ml. of anhydrous triethylamine and 5·0 ml. of A.R. acetic anhydride in a 200 ml. round-bottomed flask, equipped with a short reflux condenser and a calcium chloride drying tube. Boil the solution gently for 24 hours—heating may be interrupted. Incorporate a steam distillation apparatus in the flask and steam distil until the distillate is no longer cloudy (about 100 ml.) and then collect a further 50 ml. of the distillate; discard the steam distillate. Transfer the residue in the flask to a 400 ml. beaker, add water until the volume is about 200 ml., then 0·2 g. of decolourising carbon, and boil for a few minutes. Filter the hot solution, and acidify the hot filtrate with 1 : 1-hydrochloric acid to Congo red paper. Cool and filter. Recrystallise the crude cinnamic acid from hot water. The yield of pure acid, m.p. 133°, is 1·5 g.

37. Sulphanilic acid (**IV,55**, $\frac{1}{10}$ scale; heat reaction mixture in oil bath at 180–190° for 30 minutes).

38. Methyl orange (**IV,78**; $\frac{1}{10}$ or $\frac{1}{5}$ scale).

39. Triphenylcarbinol (**IV,202**, procedure for elementary students, $\frac{1}{10}$ or $\frac{1}{5}$ scale).