Purification of Substances by a Process of Freezing and Fractional Melting Under Equilibrium Conditions [1] [2]

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A purification technique has been developed whereby a mass of well-defined crystals, formed by slow crystallization of a liquid, is melted under equilibrium conditions into a series of fractions. In this process the entire mass of the substance is fractionated into its gross impurities and high-purity material. This offers distinct advantages over conventional fractional crystallization techniques. The apparatus provides for conducting the fractionating process in a closed inert system and is well adapted for purifying compounds that are corrosive, toxic, or reactive with air. Details of construction and operation of the apparatus, including experimental results on 2,5-dichlorostyrene, are included in the report.

1. Introduction

Many compounds of commercial and scientific importance may be toxic, repulsive in odor, hygroscopic, corrosive, or reactive with air. Further, thermally unstable compounds, such as monomers or weakly bound compounds, are often susceptible to heat, and polymerize, dissociate, or isomerize at elevated temperatures.

Purification of the above materials requires that the fractionation process be conducted in a closed, inert system at low temperatures. These objectives are largely attained by the combined sequence of equilibrium freezing and melting: (1) crystals of a single component (pure substance) are segregated from the other components (impurities) by cooling the sample from its liquid state until crystallization is substantially complete, and (2) the entire mass of crystallized material is then slowly melted under equilibrium conditions to obtain successive fractions (fractional melts) of increasingly higher degrees of purity. This process is so analogous to fractional distillation that the authors have suggested the term "fractional melting" to define the combined equilibrium freezing and melting process.

The technique of fractional crystallization has, of course, long been used in purification [1].[3] Fractional melting of a crystalline mass formed by slow equilibrium freezing is more effective than crystallization alone in separating the entire mass of the substance into its gross impurities and high-purity material. A fractional-melting apparatus embracing the above principles has been developed and successfully used for the past several years.

2. Fractional Melting of Ideal Systems

Ideal conditions for the separation of a crystalline phase containing only a single component include (1) that the impurities do not participate in solid solution, (2) that crystals grow very slowly in order to avoid occlusion of impurities, and (3) that the crystals be large in order to minimize the volume of liquid retained on their surfaces.

In the crystallization of a single component from its impure melt, it is a general practice to attempt the induction of crystal growth when the solution is at a temperature slightly below the freezing point. With many substances, initiation of the liquid-solid transformation cannot be accomplished until the liquid has cooled well below the freezing point. In such cases, when crystallization occurs there is a rapid growth of very small crystals, which results in contamination by occlusion in the crystal. In particular, compounds with poor symmetry tend to supercool. After the onset of this initial crystallization, which starts with the solution far from thermal equilibrium, the latent heat of fusion rapidly raises the temperature and closer approach to thermodynamic equilibrium is realized. On continued slow freezing of the system, crystallization then proceeds in a more orderly fashion. In systems containing impurities conforming to the ideal conditions enumerated in the first paragraph of this section, the crystals preferentially select the pure component and reject the impurities. During this slow crystallization the crystals successively formed from the solution are progressively less pure because of the difficulty of growing crystals of the pure component from solutions in which the impurities are concentrated. Although each system of crystallization has unique features, in general, very slow freezing produces crystals larger in size and with minimum occlusion.

Optimum melting conditions, using the apparatus described in this paper, are realized when the crystalline mass contains large crystals of a single component and the impurities are segregated into a separate liquid or a solid phase of smaller crystals melting well below the freezing point [4] of the single component. During the period of equilibrium melting, the mass of small crystals containing the impurities is melted before the bulk of the large crystals.

[4] Thermodynamically, "melting point" and "freezing point" refer to the same equilibrium temperature and define the temperature at which an infinitesimal amount of crystals of the pure component is in equilibrium with liquid.

To summarize, the fractional-melting technique of solid-liquid fractionation uses equilibrium freezing to obtain closer approach to ideal conditions for the segregation of the impurities from a crystalline phase of the pure substance during the crystallization process. Equilibrium melting of this crystallized mass into fractions is then used to remove successively impure material and finally the pure substance.

3. Procedure and Apparatus

In the crystallization of a compound from its impure melt, using the fractional-melting apparatus described in this paper, crystal growth starts at the bottom of the container and proceeds slowly up through the liquid. The crystals near the bottom of the tube are of high purity, with the bulk of the impurity concentrated near the top. After crystallization the container is inverted and heat is introduced into the system so as to produce slow melting. The first material collected is the least pure and the last portion most pure. In its downward flow, the liquid [5] from the melted crystals bathes and washes each succeeding crystal surface. The less pure material wetting the crystal surface is progressively displaced by liquid of higher purity. In addition to

the purification accomplished by progressive liquid displacement at the solid-liquid interface, any recrystallization of the liquid to solid results in added purification.

The apparatus used for the purification of a volatile sample by fractional melting of the substance under its own vapor pressure is shown in figure 1. A detailed drawing of the fractional-melting tube is shown in figure 2. Identical parts are designated by the same letters in both figures. The chamber of fractional-melting tube J, distributor R, and receiving ampoules W, are exhausted to a low pressure (10^{-5} mm Hg) by attaching the ground glass joint C to a high vacuum system consisting of a mercury diffusion pump and a forepump. The evacuated system is then isolated from any stopcock lubricant by fusing the constriction at B in the glass manifold. In this way the sample to be fractionated is exposed only to glass. The breakoff tip of ampoule E is then broken by hammer D, and the sample is distilled into the chamber of the fractional-melting tube. The manifold is then removed by sealing at A.

Nonvolatile samples are transferred as liquids. They are sealed under their own vapor pressure in inverted breakoff tip ampoules [5], which are attached to an opening into the chamber below N in

[5] If the viscosity of the liquid containing the impurities is high, separation by gravity flow will be impracticable. Such systems will require addition of a solvent to lower the viscosity.
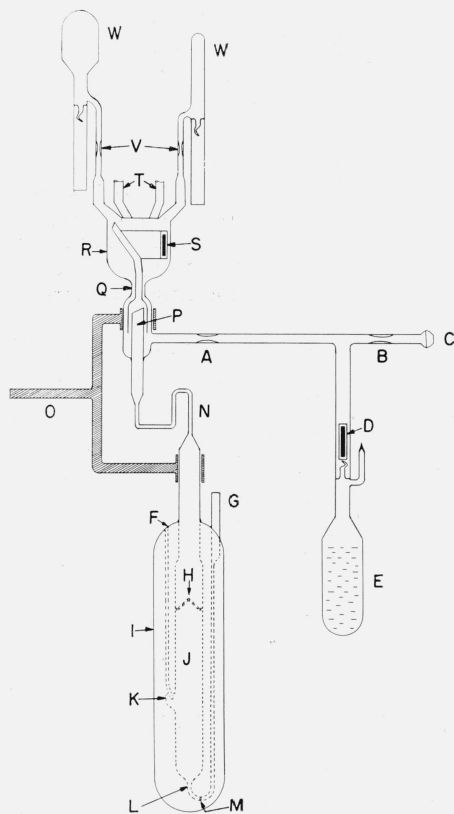
FIGURE 1. *Assembly of fractional-melting tube, distributor and receivers, and manifold for introducing volatile samples.*
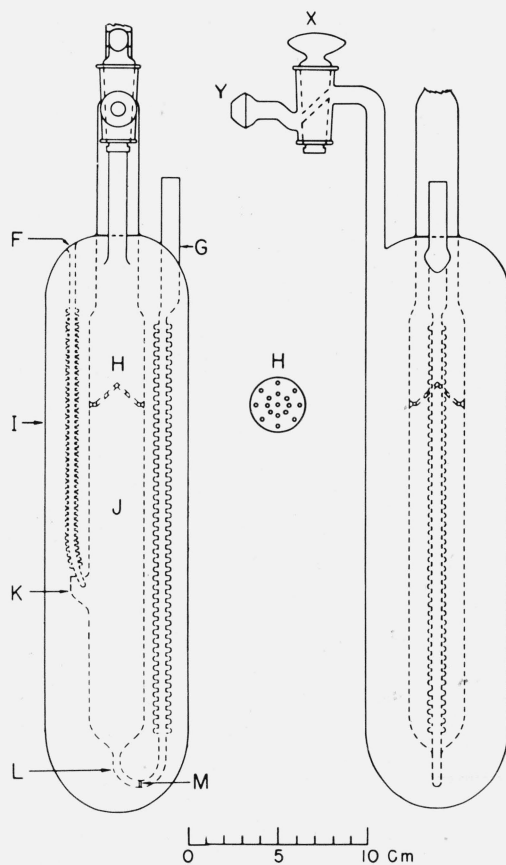

FIGURE 2. *Fractional-melting tube.*

the figure. The evacuation and subsequent removal of the empty ampoule and the manifold are similar to that described for the volatile samples.

The fractional-melting tube is placed in a Dewar flask containing the freezing bath. A solid-liquid slurry of a substance freezing at the desired temperature may be placed directly in the Dewar flask to obtain a constant-temperature bath. Ice and water are used for a temperature of 0° C, solid carbon dioxide refrigerant for −78° C, and liquid nitrogen for −196° C.

The temperature of the freezing bath required for nearly complete crystallization of the sample will depend upon the freezing point, purity, and heat of fusion of the compound being purified. For samples of high purity (98 mole percent or greater) and heats of fusion from about 2 to 4 kcal/mole, a freezing bath about 5 to 20 deg C lower than the freezing point of the sample is used. A cooling rate of the liquid near the freezing point of the sample of 1 deg in 10 to 15 min is normally used. This thermal head and cooling rate for such samples will allow substantially complete crystallization in an overnight period of 16 hr. Samples of lower purity (80 to 98 mole percent), in which a large temperature range is required for crystallization, will require the use of several baths and a longer time for the crystallization.

Transfer of energy across the space from the outer wall, I, to or from the sample contained in the chamber, J, is controlled by the degree of evacuation of this space. In order to prevent energy transfer by radiation, the inner glass surfaces confining this space are silvered. The stopcock, X, in figure 2 is connected to a high-vacuum system through a spherical joint, Y, and is used to adjust the pressure for a satisfactory rate of cooling or warming.

The temperature of the sample is measured with a thermocouple inserted in the closed tube, F, which protrudes into the sample at K. An amorphous high-melting wax is used to fill the space between the thermocouple wire and the inner glass wall to a depth of several inches above the thermocouple junction. When the sample has reached a temperature slightly below its freezing point, crystallization is induced by cooling the small amount of the sample in the constricted portion, L, of the sample tube appreciably below its freezing point. Coolant is added through the glass tube, G, which is separated from part L of the sample tube by the glass partition, M. Samples freezing above −50° C are cooled by adding powdered carbon dioxide, and samples freezing below −50° C are cooled with liquid nitrogen [2].

When the crystallization process is complete, the fractional-melting tube is inverted. It is then inserted in the special Dewar-type vessel shown in figure 3. The brass clamp, O, supports the fractional-melting tube and distributor. The small-diameter tube, N, allows some movement between these parts without breakage. For higher-purity samples (98 mole percent or higher), the outer wall of the fractional-melting tube is maintained at a temperature
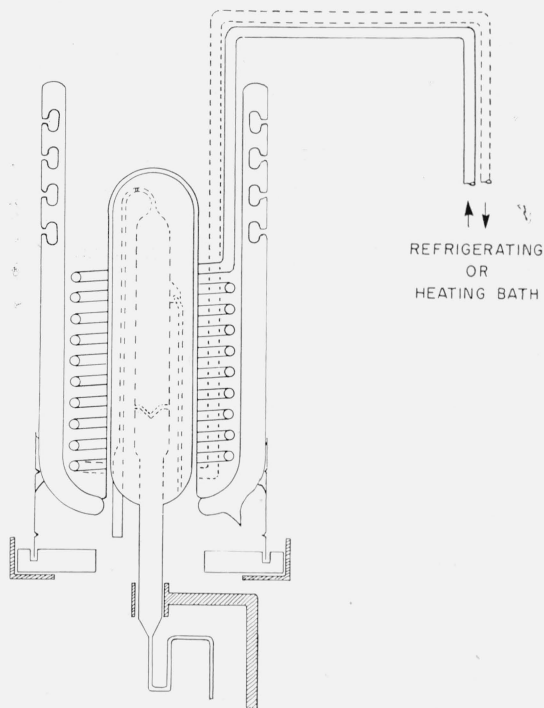

REFRIGERATING
OR
HEATING BATH

FIGURE 3. *Assembly for melting operation.*

several degrees above the freezing point of the sample. For lower-purity samples (80 to 98 mole percent), the outer wall is allowed to warm slowly from a temperature near the lowest crystallization temperature to a temperature above the freezing point of the sample. With samples of higher purity the melting operation is normally performed in a 6- to 7-hour period during the regular hours of the working day. With samples of lower purity, progressive melting of the sample requires a longer time. Because the equipment was nonautomatic, the temperature of the bath during the melting process was varied during the day, and a constant-temperature bath was used at night.

Inorganic salts and ice have been used to obtain baths of high heat capacities for retaining samples overnight without appreciable melting. These baths have been used for samples of low purity that are melted over a period longer than 1 day. Such mixtures are conveniently frozen by inserting a powdered carbon dioxide "cold finger" into the appropriate salt-water solution.

Constant-temperature baths described previously for freezing the sample may also be used as melting baths. The selection of the appropriate freezing and melting baths will depend upon the range of temperature required for solidification and complete melting of the sample. When such baths are used, the coils shown in figure 3 are removed from the special Dewar-type vessel. If the melting operation is performed during the working day, intermediate temperature baths between 0° C and solid carbon dioxide at −78° C can be maintained manually by periodically adding just enough solid carbon dioxide to a suitable solvent to keep the bath at a given

temperature. An alternate procedure is to circulate a liquid from a constant-temperature bath or refrigerating unit through coils placed in the Dewar, as shown in figure 3. For substances freezing above room temperature the outer wall of the fractional-melting tube may be heated electrically.

Crystals are retained in the chamber of the fractional-melting tube by the conical perforated glass disk, H. The liquid from melted crystals is directed into the distributing funnel, R, by the dropping tip, P. This funnel is ground at Q to a bearing surface, upon which it is rotated. It was found in practice that the friction of this bearing was sufficient to hold the funnel in a fixed position, and did not interfere with its rotation. A permanent magnet acting upon the iron rod, encased in glass at S, is used to rotate the funnel to the various positions for transferring melted fractions of the sample into the receiving ampoules, W. A U-bend, N, in a glass (4-mm outside diameter) tube serves as a stopcock between the fractional-melting tube and the distributor. This U is allowed to fill with liquid, which is then frozen with a suitable cooling bath, while a filled ampoule, also frozen, is sealed off and removed from the system at point V. In this manner the solid plug in the U acts as a closed stopcock.[6] After melting, liquid passes freely through the U. Four additional ampoules (not shown) are sealed at points T on the distributor and are filled in the same manner with subsequent fractional melts.

4. Substances Purified by Fractional Melting

This method has been applied to the purification of 2,5-dichlorostyrene. A sample of this compound, which had an original purity of 98.68 mole percent and a freezing point of 8.058° C [3], was frozen in an ice bath at 0° C. The fractional-melting tube was then placed in a 4½ liter Dewar packed with ice water. This system, when insulated with glass wool, held its temperature over the weekend to within 1 deg C. The space between the walls (unsilvered in these experiments to permit visible observation) was pumped to a high vacuum to achieve a low heat transfer. Crystallization did not occur until the

6 We are indebted to R. T. Leslie of the Bureau for this technique.

sample was cooled about 3 deg C below its freezing point.

In figure 4 the freezing and melting stages for this sample are shown. In the first stage of freezing the liquid was thermally shock-seeded at M with some powdered solid carbon dioxide. The first crystals formed quite rapidly and contained much occluded and entrapped material. This portion is shown as the hatched area in stage 1. As crystallization continued slowly up through the tube, the crystals that were formed, after the initial effects of supercooling had been overcome, contained less occluded, or entrapped, material. In the latter stages of freezing the purity of the liquid had dropped to such a point that the last crystals were formed in intimate contact with the bulk of the impurity. In the case of 2,5-dichlorostyrene, at least some of the impurities were colored, so that when the entire mass (100 ml) was allowed to crystallize slowly overnight (16 hr) it froze with the mass of impurities concentrated in a highly colored cone at the top. This is shown at Z in stage 4.

It was also noted that as crystallization proceeded in stages 2 and 3, the crystals became larger and were embedded in a matrix of smaller crystals. Crystallization with a constant-temperature bath, 0° C, became progressively slower throughout the freezing part of the experiment because of the decrease in thermal head as freezing proceeded. Progressively slower freezing was very desirable in the present apparatus as no stirring was employed and the migration of the impurity away from the crystallized mass was due to diffusion alone.

After crystallization the tube was inverted and, utilizing air at room temperature as a warming bath, the crystalline mass was slowly melted during a period of 6 to 7 hr. The complete freezing and melting experiment thus required about 24 hr. Various degrees of melting are shown in stages 5, 6, 7, and 8. Melting took place in accordance with the purity pattern obtained in crystallization. Fractions of 10 ml each were collected. Nearly all of the colored material was collected in the first fraction. The first portion melted contained the material in the core at Z and the material near M, which was first crystallized by shock-seeding. The rate of melting of subsequent fractions became progressively smaller. In this melting operation, the
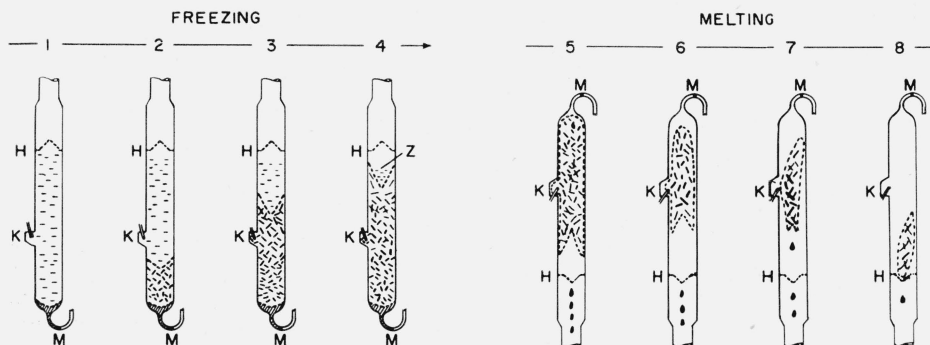

FREEZING — 1 — 2 — 3 — 4 →   MELTING — 5 — 6 — 7 — 8 →

FIGURE 4. *Freezing and melting stages of 2,5-dichlorostyrene.*

Fractional melting number	Volume increment melted	Purity	Impurity	Impurity for perfect separation ᵇ	Efficiency per stage	Total impurity—		
						Present at beginning of melting stage	Removed in the fraction	Remaining
	%	*Mole %*	*Mole %*	*Mole %*	*%*	*Mole %*	*Mole %*	*Mole %*
FM–1	0 to 20	94.98	5.02	ᶜ 6.82	73.6	ᵇ 1.364	1.004	0.360
FM–2	20 to 40	99.32	0.68	ᶜ 1.80	37.8	0.360	0.136	.224
FM–3	40 to 60	99.46	.54	ᶜ 1.12	48.2	.224	.108	.116
FM–4	69 to 80	99.65	.35	ᶜ 0.58	60.3	.116	.070	.046
FM–5	80 to 100	99.77	.23	ᶜ .23		.046		

ᵃ Purity on original sample 98.68 mole percent.
ᵇ Purity from summation of fractional melts 98.64 mole percent.
ᶜ On basis of individual fractional melts.

principal transfer of energy into the freezing chamber is through the thermocouple well, K, the seeding well, G, and the inner glass tube containing the sample, rather than across the space between the inner and outer walls (see fig. 2).

Table 1 gives a summary of the fractionation data. The purity values were determined from freezing points obtained from melting curves [3]. This purity pattern was obtained on blends of the fractions separated from 30 experiments on fractional melting, using 100-ml samples of the same stock material of 2,5-dichlorostyrene [6]. Similar increments of volume of the sample melted from the different experiments were blended. Three determinations of the purity were made by using different experimental groupings. These values of the purity checked those shown in the table. The separation was therefore considered representative of this compound under these conditions.

Figure 5 gives the total amount of impurity present at the various stages of melting (shaded bar) and the amount of impurity removed during the melting stage (open bar). FM–1, –2, –3, –4, and –5 refer to the fractions collected when 20, 40, 60, 80, and 100 percent, respectively, of the substance had melted.

In figure 6, the percentages of impurity removed, based upon the total amounts of impurity present at the various stages of melting, are shown. The numbers 1, 2, 3, 4, and 5 refer to the fractions melted. In the first fraction (C in the figure), 73.6 percent of the total impurity was removed. This initial removal of impurity is attributed to the slow crystallization [7] of the material and is not part of the improvement that occurs on fractional melting (M in the figure). The blocked lines represent the percentage of the total impurity (expressed in terms of the total impurity in the system before each successive melt) removed in the fraction. The circles are drawn at the midpoint in volume percent of these fractions. The curve for the increase in efficiency of separation during the melting operation is drawn through these circles and clearly indicates the successive improvement obtained in the fractional melting. On fraction 5 the block and curve (broken lines) are the expected course of separation of im-

[7] Schwab and Wichers point out in their work on benzoic acid [4] the importance of slow crystallization.
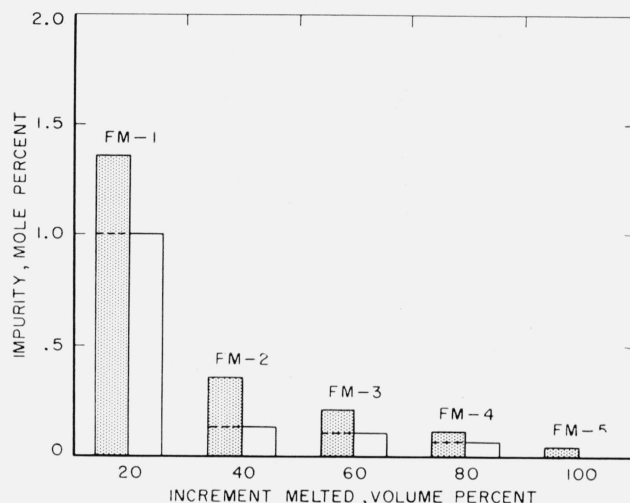

FIGURE 5. *Separation of impurities from 2,5-dichlorostyrene as a function of volume percentage of sample melted.*

Shaded bar, total impurity in system at beginning of melting. Open bar, total impurity removed in fractional melt.
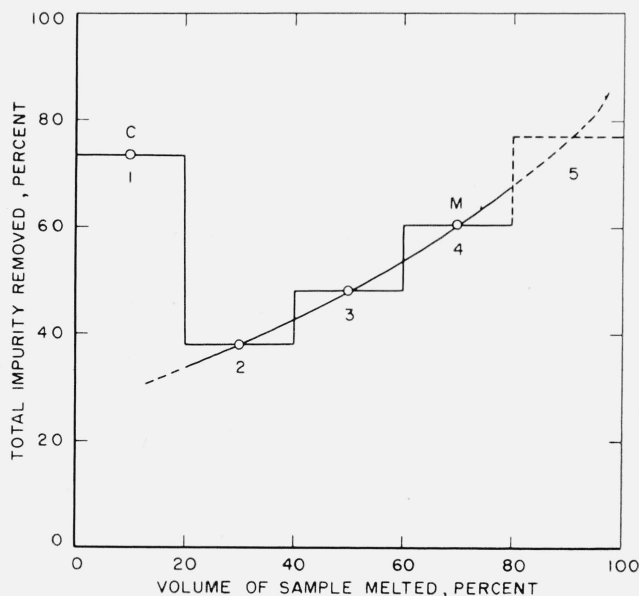

FIGURE 6. *Efficiency of separation of impurities from 2,5-dichlorostyrene by fractional melting.*

purities if this fraction had been collected in smaller volume increments. This extrapolation was made on the basis of the progressive changes that took place between fractions FM–2, FM–3, and FM–4, as shown in table 1 under efficiency per stage.

Two toxic compounds that decomposed rapidly in air were also purified by this method.[8] Each compound had an original purity of about 99.7 mole percent. The last 50 percent to melt had a purity of 99.95 mole percent. Titanium tetrachloride, which hydrolyzes rapidly in air and is reactive toward stopcock greases, was successfully processed by using the assembly shown in figure 1.

5. Summary and Conclusions

Fractional melting consists in slow equilibrium melting of a crystalline mass of a substance formed by slow equilibrium freezing. In general, for compounds that varied in purity from 98.5 to 99.5 mole percent, about 75 percent of the total impurity was separated in the first 20 percent of the melt. This technique of fractionally melting a mass of well-defined crystals into a series of fractions of increasingly higher purity offers the following distinct advantages over conventional fractional crystallization techniques:

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[8] This work was performed by Milton Tenenbaum, who also assisted in the design of the distributor shown in figure 1.

(1) The entire mass of the substance is fractionated into its gross impurities and high-purity material.

(2) This method is adaptable to the purification of small samples frequently encountered in research problems.

(3) Fractional melting is more efficient than fractional crystallization alone.

(4) Many compounds because of their toxicity and reactivity require that the solid-liquid fractionation be conducted in closed inert systems. The fractional-melting apparatus described in this paper is well adapted to such compounds.

6. References

[1] R. S. Tipson, Crystallization and recrystallization, A. Weissberger, Technique of Organic Chemistry, vol. III (Interscience Publishers, Inc., New York, N. Y., 1950).
[2] A. R. Glasgow, Jr., N. C. Krouskop, and F. D. Rossini, Anal. Chem. **22,** 1921 (1950).
[3] A. R. Glasgow, Jr., A. J. Strieff, and F. D. Rossini, J. Research NBS **35,** 355 (1945) RP1676.
[4] F. W. Schwab and E. Wichers, J. Research NBS **32,** 253 (1944) RP1588.
[5] A. R. Glasgow, Jr., and M. Tenenbaum, Cryoscopic determination of purity of highly reactive substances, Anal. Chem. (to be published).
[6] G. S. Ross and A. R. Glasgow, Jr. (NBS, unpublished work).