

Stability of *cis* Isomers.—Hindered *cis* isomers have a much lower thermodynamic stability (*i.e.*, a higher free energy) than unhindered *cis* forms.¹⁵ Until recently, it has therefore been thought that they are in fact highly unstable. A number of stable hindered *cis* forms have now been isolated.^{4,5,8,13,16} The isomerization data presented above bear out the fact that the actual (kinetic) stability of a compound does not necessarily reflect its thermodynamic stability. In terms of free energy content, the neo-a (13-*cis*) isomer of retinene and retinene oxime is probably much closer to iso-a (9-*cis*) than to neo-b (11-*cis*). Yet, kinetically it behaves more like the neo-b isomer.

Course of Isomerization.—The course of isomerization is governed by the fact that the individual double bonds appear to retain their rates of isomerization irrespective of the stereochemical configuration of the rest of the molecule.⁸ Mono-*cis* compounds often have smooth isomerization

(15) L. Pauling, *Fortschr. Chem. org. Naturst.*, **3**, 203 (1939); *Helv. Chim. Acta*, **32**, 2241 (1949).

(16) W. Oroshnik, G. Karmas and A. D. Mebane, *THIS JOURNAL*, **74**, 295, 3807 (1952); **75**, 1050 (1953).

curves.⁸ But when in a mono-*cis* compound, the *cis* linkage isomerizes slowly to *trans*, while the *trans* linkages isomerize much faster to *cis*, the extinction first falls and then rises (*cf.* iso-a (9-*cis*) retinene). Conversely, if the isomerization from *cis* to *trans* is much more rapid than the isomerization of the all-*trans* isomer, the extinction first rises and then falls (*cf.* neo-b (11-*cis*) retinene oxime). If a mono-*cis* isomer therefore has a discontinuous isomerization curve, it will display a *reversal* in the change of extinction. A discontinuous isomerization curve in which the change in extinction continues upward, implies that one is dealing with a di-*cis* compound (*cf.* iso-b (9,13-di-*cis*) retinene). A di-*cis* compound could isomerize smoothly, if the rates of isomerization of both double bonds were sufficiently similar. Its isomerization would, however, differ from that of a mono-*cis* compound since the change in extinction in the *cis* peak region would almost surely be discontinuous,⁸ as the mono-*cis* intermediate of isomerization would be expected to show increased absorption at the *cis* peak.

Structure of the Neo-b Isomer.—Robeson, *et al.*,⁴ have postulated that neo-b is the 11,13-di-*cis* isomer. We have shown that it is a hindered mono-*cis* isomer (11-*cis*).⁵ The data presented above conform with this assignment of configuration.

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Polymorphic Behavior of 1,3,5-Tridodecyl- and 1,3,5-Trioctadecylhexahydro-*sym*-triazines

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Two high molecular weight 1,3,5-trialkylhexahydro-*sym*-triazines have been prepared by the reaction of primary amines with formaldehyde in aqueous methanol. The products were characterized by their infrared absorption spectra and by the preparation of their oxalate salts. The solubilities of these representative alkyl-triazines were determined in hexane, benzene, chloroform, ethyl acetate, acetone and 95% ethanol over wide ranges of concentration and temperature. The C₁₂ derivative exhibited three polymorphic modifications in its purified state, whereas the C₁₈ derivative exhibited corresponding polymorphic behavior only in the presence of certain solvents. The highly polar solvents tend to promote precipitation of the higher melting polymorphs; non-polar and slightly polar solvents appear to stabilize the lower melting forms by inhibiting transformation.

The reaction between formaldehyde and various primary amines has been the subject of considerable study.¹ Henry² was among the earliest workers to investigate this reaction and much confusion has resulted from misinterpretation of his work. Although he was able to isolate benzylaminomethanol from the reaction of formaldehyde with benzylamine³ inferences that methylol derivatives of this type or their dehydration products, the Schiff bases, are the usual end-products of the reaction of formaldehyde with primary amines must be discounted in view of later work.

In a series of papers Graymore⁴ reported on the

(1) I. Walker, "Formaldehyde," 2nd Ed., Reinhold Publ. Corp., New York, N. Y., 1953, p. 281.

(2) L. Henry, *Bull. acad. roy. Belg.*, **29**, 355 (1895).

(3) L. Henry, *ibid.*, **28**, 359 (1894).

(4) J. Graymore, *J. Chem. Soc.*, **125**, 2283 (1924); 1490 (1931); 1490 (1932); 865 (1935); 1311 (1938); 39 (1941).

reaction of formaldehyde with methyl, ethyl, butyl and other lower primary amines and demonstrated conclusively that the reaction products were trimers of the hypothetical alkylmethyleneimine postulated by Henry.² The 1,3,5-trialkylhexahydro-*sym*-triazine structure was assigned to these products upon the basis of early speculations regarding the nature and mode of formation of hexamethylenetetramine from formaldehyde and ammonia.⁵ Raman spectra of many of these compounds confirm this widely accepted structure.⁶

The present paper reports the preparation of 1,3,5-tridodecylhexahydro-*sym*-triazine and its trioctadecyl homolog in high yield by treating the appropriate highly purified alkylamines with aqueous formaldehyde in methanol. The solubilities of the

(5) P. Duden and M. Scharff, *Ann.*, **288**, 218 (1895).

(6) L. Kahovec, *Z. physik. Chem.*, **B43**, 364 (1939).

polymorphic forms of these triazines in *n*-hexane, benzene, chloroform, ethyl acetate, acetone and 95% ethanol are reported.

Experimental

Preparation of 1,3,5-Tridodecylhexahydro-*sym*-triazine (Compound I).—A mixture of 185 g. (1.0 mole) of dodecylamine (f.p. actual 28.0°; best lit. value⁷ 28.32°), 100 g. (1.2 moles) of 36% aqueous formaldehyde (formalin), 80 cc. of water and 160 cc. of methanol was stirred for 6 hr. at 65–75°. At the conclusion of this period the mixture was cooled and 300 cc. of petroleum ether, b.p. 60–71°, was added. The upper organic phase was separated and washed with water. The light yellow solution was dried over sodium sulfate and the solvent was removed under vacuum. The yellow-colored residual liquid was 1,3,5-tridodecylhexahydro-*sym*-triazine (180 g.) which was obtained (crude) in 92% yield. The material was purified by any one of the following procedures: recrystallization from ethyl acetate at –20°; adsorption of the impurities from a hydrocarbon solution on an alumina column; washing the liquid with methanol; recrystallization at 0° from petroleum ether, b.p. 29–38°.

*Anal.*⁸ Calcd. for (C₁₃H₂₇N)₃: C, 79.11; H, 13.79; N, 7.10; neut. equiv., 197. Found: C, 79.04; H, 13.99; N, 6.99; neut. equiv., 202.

A sample of the material was dissolved in glacial acetic acid and titrated to a sharp end-point with perchloric acid using crystal violet as the indicator.

The monoöxalate of 1,3,5-tridodecylhexahydro-*sym*-triazine was readily prepared by the addition of a stoichiometric quantity of oxalic acid dissolved in ethanol to a hot ethanol suspension of the triazine. The salt (sintered 171°, m.p. 190–193°) is insoluble and is immediately precipitated. It is conveniently recrystallized from aqueous ethanol.

*Anal.*⁸ Calcd. for (C₁₃H₂₇N)₃H₂C₂O₄: N, 6.16. Found: N, 6.07.

Preparation of 1,3,5-Trioctadecylhexahydro-*sym*-triazine (Compound II).—This substance was prepared from octadecylamine (f.p. actual 52.5°; best lit. value⁷ 53.06°) in the same manner as was the homolog described above.

*Anal.*⁸ Calcd. for (C₁₈H₃₉N)₃: C, 81.06; H, 13.96; N, 4.98; neut. equiv., 282. Found: C, 81.21; H, 14.06; N, 4.86; neut. equiv., 287.

The monoöxalate sintered at 185° and melted 195–198°. Although its solubility is limited even in polar organic solvents, the monoöxalate was recrystallized from dilute solution in aqueous ethanol.

*Anal.*⁸ Calcd. for (C₁₈H₃₉N)₃H₂C₂O₄: N, 4.50. Found: N, 4.48.

Preparation of Tributyl and Trioctyl Homologs.—The tributyl and trioctyl homologs of the above triazines were prepared in the same manner. The tributyl derivative distilled at 110–115° at 0.8 mm., and the trioctyl derivative at 185–190° at 0.5 mm.

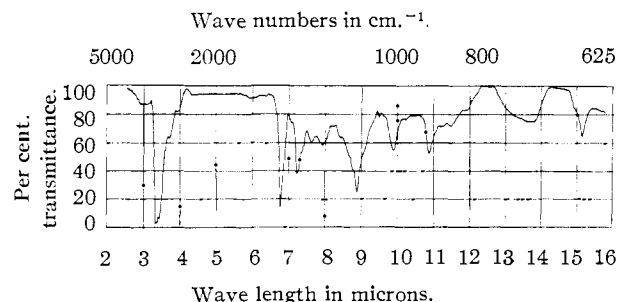


Fig. 1.—Infrared absorption spectrum of 1,3,5-tridodecylhexahydro-*sym*-triazine; 10% solution in chloroform in 0.1 mm. cell.

(7) A. W. Ralston, C. W. Hoerr, W. O. Pool and H. J. Harwood, *J. Org. Chem.*, **9**, 102 (1944).

(8) C and H determinations by Galbraith Laboratories, Knoxville, Tennessee; N determinations by L. D. Metcalf, Research Division, Armour and Company.

Infrared Analyses.—The infrared absorption spectrum of I is shown in Fig. 1. This spectrograph was obtained from a 10% solution in chloroform using a 0.1 mm. cell in a Baird Associates Spectrophotometer.

The spectrum reveals marked differences from the spectra of related *N*-methyl and dimethylalkylamines. The secondary and tertiary amines usually absorb characteristically at about 3.1, 7.8, 8.7, 9.2, 10.3 and 11.2 μ with minor variations which serve to distinguish secondary from tertiary amines. No absorptions which can be attributed to *N*-H stretching or bending vibrations occur in either the 3 or 8 μ regions of the triazines and their 9, 10 and 11 μ absorptions are shifted from their usual positions in related amines. Three bands at 8.9, 9.9 and 10.9 μ , respectively, were found to be characteristic of the triazines.⁹ The same array was observed in the spectra of similarly prepared derivatives of butyl-, octyl- and octadecylamines, which were established as 1,3,5-trialkylhexahydro-*sym*-triazines by the methods described in the Experimental section above.

Determination of Freezing Points.—The freezing points of these compounds were determined by means of cooling curves obtained by cooling 6–10 g. samples in jacketed Pyrex tubes immersed in acetone- or water-baths. The samples were agitated by means of a motor-driven Nichrome-wire stirrer until freezing was well under way. Temperatures were measured by mercury thermometers which were graduated in 0.1° intervals and which had been calibrated by the National Bureau of Standards. Appropriate emergent-steam corrections were added to the readings.

By varying the rate of cooling and the rate of stirring, and by alternately heating and cooling the samples in the appropriate temperature ranges, the existence of three polymorphic forms of I was demonstrated and their freezing points were determined. With similar treatment, II failed to exhibit more than one crystalline form. Under certain conditions in the presence of solvents, however, the latter exhibited two lower melting, metastable polymorphs.

In order to ascertain whether the difference in behavior of the triazines was related to degree of purification, I was subjected to two additional alumina adsorption treatments, alternated with recrystallization from ethyl acetate, followed by repeated heating under vacuum. A high degree of purity is indicated by the cooling curve shown in Fig. 2. No change in the polymorphic behavior was observed. Likewise, the addition of various amounts of homologous impurity to II failed to produce any effect beyond the expected proportional depression of the freezing point.

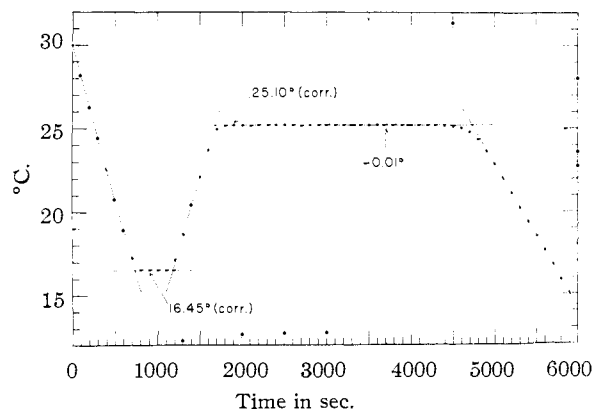


Fig. 2.—Cooling curve of 6-g. sample of 1,3,5-tridodecylhexahydro-*sym*-triazine showing transformation from intermediate to higher melting form during freezing. The latter held its freezing temperature for 33 min.

The compounds used for the solubility determinations possessed the following freezing points: compound I, H (high melting) form, 25.10°, M (intermediate melting) form, 16.45°, L (low melting) form, 8.80°. Compound II, H form, 57.61°. Extrapolation of the solubility curves of the latter indicated that, if isolation were possible, its L form would freeze at about 46.5°, and its M form at 52.5°. The

(9) C. Grundmann and A. Kreutzberger, *THIS JOURNAL*, **76**, 5646 (1954).

observed freezing points were reproducible within 0.01°, and are probably accurate within 0.02°.

Determination of Solubilities.—The solubilities of these compounds were determined by observing visually the temperatures at which known concentrations precipitated upon cooling and dissolved upon heating in the manner and with the equipment used in similar previous studies.¹⁰

In contrast to many of the previous studies in this Laboratory, the solubilities of the various polymorphs of the triazines were determined quite readily without special manipulation. Mixtures in which more than one crystalline modification was observed systematically exhibited the following sequence of events when given concentrations of solute were heated until clear isotropic solution was obtained and then cooled until precipitation occurred: upon heating slowly, the crystals dissolved gradually until the mixture was essentially clear, at which point the next higher melting polymorph precipitated abruptly, and as heating continued, the dissolving and precipitating phenomena were repeated, yielding the highest melting form in the usual manner of monotropic transformations.

However, contrary to the usual behavior of monotropic polymorphs, wherein compounds have generally been observed to crystallize in their lowest melting forms before transforming to higher melting modifications, the triazines, at certain concentrations in various organic solvents, precipitated directly in either the M or H forms. In such instances, neither extremely rapid cooling rates nor "seeding" by sharp-chilling a portion of the solution with Dry Ice effected precipitation of the L form. Other solvents appeared to have a stabilizing influence on the L and M forms. In such cases, neither seeding with stable (H form) crystals, holding at low temperatures for extended periods of time, nor very gradual rates of heating, induced transformation to the H form.

The solvents employed were reagent grade or equivalent, freshly distilled before use. The *n*-hexane (Phillips "pure" grade) was 99 mole % minimum. The benzene was thiophene-free, dried over sodium. The aqueous ethanol was commercial "absolute" diluted to 95.0% by weight with conductivity water, the ethanol content being determined by density measurement.

Solution temperatures were measured by means of the calibrated thermometers used for the freezing point determinations. Solution temperatures are considered accurate within about 0.2°.

Results and Discussion

The solubility curves of I and II in six representative organic solvents are shown graphically in Figs. 3-8. The pronounced influence of the polarity of the solvent upon the solubility of the triazines is readily apparent. In the non-polar and slightly polar solvents these compounds possess a surprisingly high degree of solubility for long-chain molecules containing 39 and 54 carbon atoms. The solubility is markedly limited, particularly at lower temperatures, in solvents of moderate polarity. In the highly polar solvents the solubility is limited to the extent that even at relatively high temperatures the systems exist as immiscible, conjugate solutions over a wide range of concentrations.

With respect to the specific influence of different solvents in preferentially promoting the formation of certain forms at certain concentrations, the behavior of both the triazines resembles that of the alkylbenzothiazoles.^{10,11} In contrast to the latter, however, the triazines generally tend to precipitate from non-polar and slightly polar solvents in their L or M forms. These forms appear to be stabilized to such an extent that transformation to the H form was not observed over wide ranges of

(10) F. K. Broome, C. W. Hoerr and H. J. Harwood, *THIS JOURNAL*, **73**, 3350 (1951); P. L. DuBrow, C. W. Hoerr and H. J. Harwood, *ibid.*, **74**, 6241 (1952).

(11) See also C. W. Hoerr, R. A. Reck, Geraldine Corcoran and H. J. Harwood, *J. Phys. Chem.*, **59**, 457 (1955).

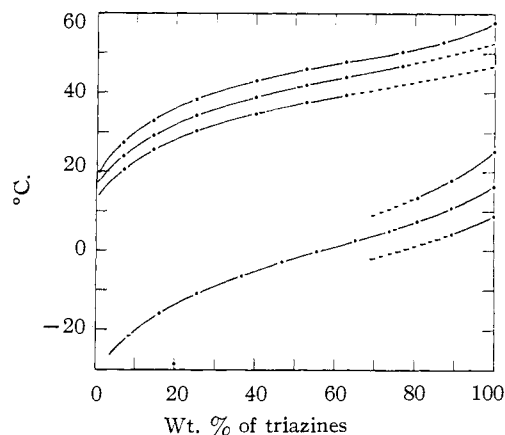


Fig. 3.—The solubilities of 1,3,5-tridodecyl- and 1,3,5-octadecylhexahydro-*sym*-triazines in *n*-hexane. The three upper curves refer to the C₁₈ derivative and the lower three to the C₁₂ derivative.

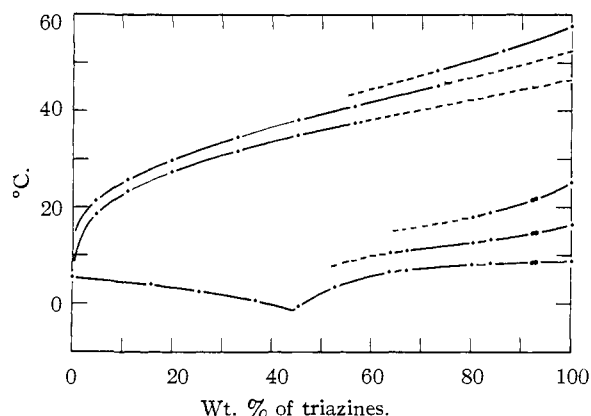


Fig. 4.—The solubilities of 1,3,5-tridodecyl- and 1,3,5-trioctadecylhexahydro-*sym*-triazines in benzene. Same order as in Fig. 3.

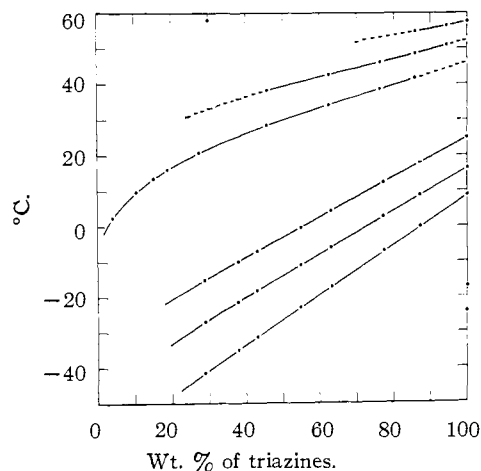


Fig. 5.—The solubilities of 1,3,5-tridodecyl- and 1,3,5-trioctadecylhexahydro-*sym*-triazines in chloroform. Same order as in Fig. 3.

concentration in most of the systems shown in Figs. 3-5. The polar solvents, on the other hand, are quite specific in promoting precipitation of the M and H forms almost exclusively. As shown by

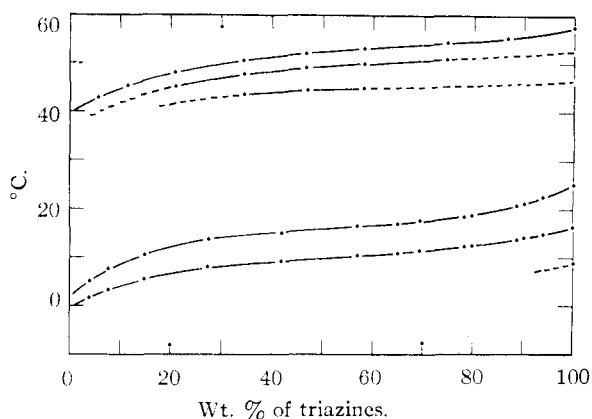


Fig. 6.—The solubilities of 1,3,5-tridodecyl- and 1,3,5-trioctadecylhexahydro-*sym*-triazines in ethyl acetate. Same order as in Fig. 3.

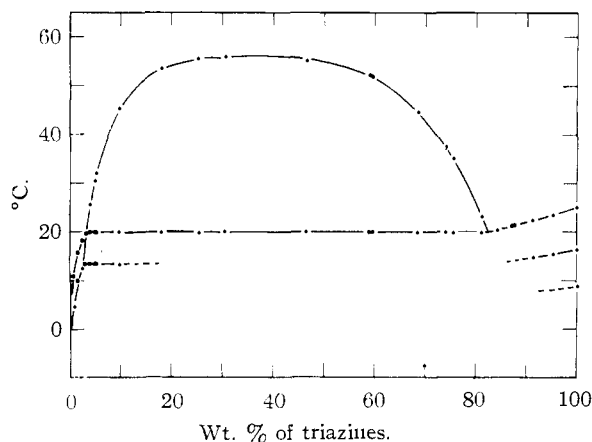


Fig. 7.—The solubility of 1,3,5-tridodecylhexahydro-*sym*-triazine in acetone. The enclosed area above the isotherm represents a two-phase immiscible liquid system.

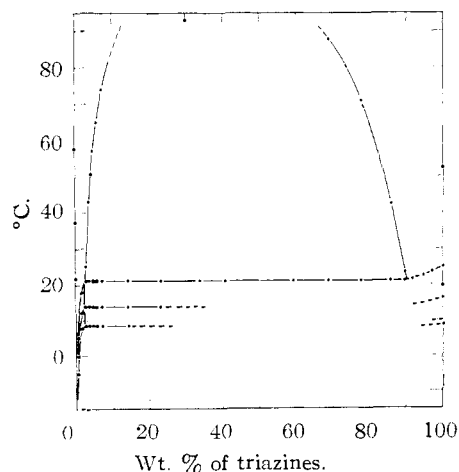


Fig. 8.—The solubility of 1,3,5-tridodecylhexahydro-*sym*-triazine in 95.0% ethanol. The area above the isotherm represents a two-phase immiscible liquid system.

Figs. 6–8, the L form was observed only in a few isolated concentrations, and in these instances

transformation to the M and H forms occurred extremely rapidly.

As mentioned above (Experimental section), the triazines do not strictly conform to the usual behavior of monotropic polymorphs. At some concentrations in most of the solvents investigated the triazines precipitate in their L or M forms, and as the temperature is increased they transform irreversibly to their H form in the manner of typical monotropes. However, other solvents in certain concentration ranges readily effect the precipitation of the triazines in their M or H forms at temperatures at least 6–7° above those at which the L form exists.

The polymorphs of long-chain compounds are usually characterized by definite angles of tilt of the molecules in the crystal lattice. Polymorphic transformations are brought about by shifts in the angle of tilt which result in substantial differences in the lattice constants. Such alterations in crystal structure are generally independent of the solvent environment.

It is possible that the differences between the polymorphs of the triazines and other long-chain compounds exhibiting similar behavior may be attributed to structural changes similar to those recently observed¹² in the higher hydrocarbons, wherein only a slight alteration in the lateral arrangement of the molecules permits some degree of rotation of the paraffin chains about their long axes. Inasmuch as the van der Waals forces between paraffin chains are effective only within a very small range, quite inappreciable variations in the degree of proximity of the chains may have a profound effect upon the physical properties of the crystal.

If the triazine polymorphs and other compounds which behave in a similar manner differ by only minor dissimilarities in the lateral arrangements of their molecules in the crystal lattice, the attractive and repulsive forces of the various solvents could conceivably be an important factor influencing the degree of approximation of the solute molecules, and thereby the nature of the solvent would determine which crystal form will precipitate. This would explain, for example, the occurrence of only the higher melting polymorphs in the presence of polar solvents. The stable (H) crystal lattice is that in which the molecules are packed in the configuration of highest density. In view of the limited solubility of the triazines in acetone and ethanol, it appears that, in repulsing the triazine molecules, the polar solvents, in effect, force the triazine molecules into their closest approximation with each other, thereby inducing precipitation of the higher melting crystalline forms.

Other solvents would have varying degrees of influence on the triazines, depending on such factors as polarity, hydrogen-bonding tendencies, concentration, temperature, etc. Verification of such postulations must await accurate determinations of the molecular configuration of the triazine crystal lattices.

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(12) J. D. Hoffman and B. F. Decker, *J. Phys. Chem.*, **57**, 520 (1953).