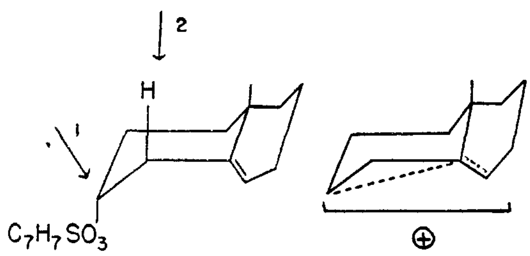
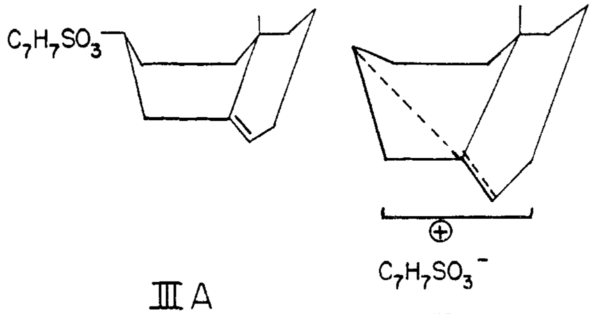


III V

Fig. 4.

diagram of III, shown in Fig. 4. Attack of a nucleophilic group along the arrow 1 gives replacement with inversion of configuration. This reaction should be slow compared to the formation of the same product from VI. Attack of any base on the polar hydrogen at 4 would cause elimination, in view of the configuration of groups, polar-polar, this reaction should be faster than the corresponding reaction with VI.[12] In principle this idea accounts for the different over-all rates of reaction and the different ratio of products obtained when reactions of III and VI are compared.

(2)—The possibility that III might slowly give the mesomeric ion V and the β-replacement product then be formed from V cannot be eliminated on the basis of the data described herein. It is considered unlikely.



IIIA IIIB

Fig. 5.

(3)—The possibility that III might exist in the boat configuration IIIA and give the inverse mesomeric ion IIIB was considered. This is considered unlikely since the mesomeric ion IIIB would give 3-α-substituted products in the replacement reaction and no such products were isolated. This process cannot be eliminated completely since our isolation experiments do not account for 100% of the reactants.

EVANSTON, ILLINOIS

[12] The steric requirement for the elimination reaction has been adequately discussed. See for example: S. J. Cristol, THIS JOURNAL, **69**, 338 (1947); M. L. Dhar, E. D. Hughs, C. K. Ingold, A. M. M. Mandour, G. A. Maw and L. I. Woolf, *J. Chem. Soc.*, 2093 (1948); D. H. R. Barton and E. Miller, THIS JOURNAL, **72**, 1006 (1950).

[CONTRIBUTION FROM THE RESEARCH DIVISION OF ARMOUR AND COMPANY]

Polymorphic Behavior of 2-Undecyl- and 2-Heptadecylbenzothiazoles in Organic Solvents[1,2]

BY P. L. DUBROW, C. W. HOERR AND H. J. HARWOOD

RECEIVED MAY 10, 1952

Preparation of higher 2-alkylbenzothiazoles has been described and their physical behavior investigated. These compounds present a greater number of polymorphic modifications than is generally observed among the aliphatic nitrogen compounds; the polymorphic behavior appears to be influenced profoundly by the nature of the solvent. In general, the non-polar solvents appear to promote the precipitation of the higher-melting modifications, whereas the highly polar solvents result in an apparent stabilization of the lower-melting forms. Impurities in the higher alkylbenzothiazoles further complicate their polymorphic behavior, both in the presence and absence of organic solvents.

The extensive investigations of Smith[3] and of Timmermans and Deffet[4,5] have demonstrated the common occurrence of polymorphism among aliphatic compounds, particularly those possessing long carbon chains. This phenomenon has been observed in connection with studies on the nitrogen-containing fatty acid derivatives, such as the higher nitriles,[6] the secondary amines[7,8] and the primary amine salts.[9-14] Of these nitrogen-containing compounds, only the didodecyl- and

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[1] Presented before the Division of Organic Chemistry at the Milwaukee Meeting of the American Chemical Society, March, 1952.

[2] Original data are available as Document 3668 from the American Documentation Institute, 1719 N Street, N.W., Washington 6, D. C. Remit $1.00 for microfilm (images 1 inch high on standard 35 mm. motion picture film) or $1.35 for photocopies (6 × 8 inches) readable without optical aid.

[3] J. C. Smith, "Fatty Acids and Other Long-Chain Compounds," Annual Reports on the Progress of Chemistry in 1938, Vol. XXXV, The Chemical Society, London, 1939.

[4] J. Timmermans and L. Deffet, "Le Polymorphisme des Composes Organiques," Vol. XLII, Memorial des Sciences Physiques, Gauthier-Villars, Paris, 1939.

[5] L. Deffet, "Répertoire des Composes Organiques Polymorphes," Desoer, Liege, 1942.

[6] E. J. Hoffman, C. W. Hoerr and A. W. Ralston, THIS JOURNAL, **67**, 1542 (1945).

[7] C. W. Hoerr, H. J. Harwood and A. W. Ralston, *J. Org. Chem.*, **9**, 201 (1944).

[8] C. W. Hoerr, H. J. Harwood and A. W. Ralston, *ibid.*, **11**, 199 (1946).

[9] H. J. Harwood, A. W. Ralston and W. M. Selby, THIS JOURNAL, **63**, 1916 (1941).

[10] C. W. Hoerr and A. W. Ralston, *ibid.*, **64**, 2824 (1942).

[11] W. O. Pool, H. J. Harwood and A. W. Ralston, *ibid.*, **67**, 775 (1945).

[12] R. S. Sedgwick, C. W. Hoerr and A. W. Ralston, *J. Org. Chem.* **10**, 498 (1945).

[13] F. K. Broome and H. J. Harwood, THIS JOURNAL, **72**, 3257 (1950).

[14] F. K. Broome, C. W. Hoerr and H. J. Harwood, *ibid.*, **73**, 3350 (1951).

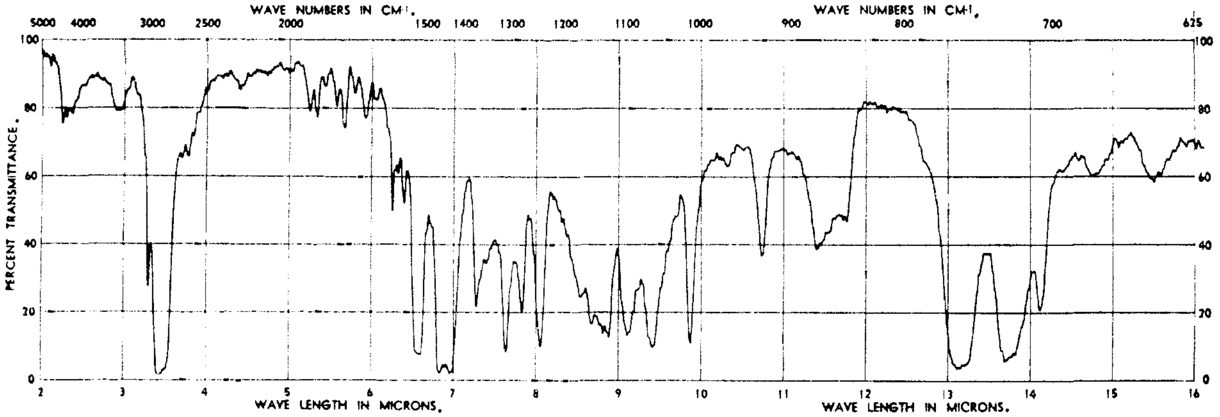

Fig. 1.—Infrared absorption spectrum of 2-undecylbenzothiazole. Liquid in 0.10 mm. cell.

ditridecylamines and dodecylammonium chloride exhibited more than one crystalline form in their pure state. The other compounds reported evidence of polymorphic behavior only in the presence of solvents or in admixture with their homologs. The phase diagram of the binary system palmitonitrile–stearonitrile shows that as little as one mole per cent. of homolog results in the occurrence of a second crystalline modification of either constituent, although the pure components exist in only one form. The behavior of these nitriles is at variance with that reported by Deffet[5] who has published two melting points for several of the higher aliphatic nitriles. As Ralston has observed,[15] the profound influence of traces of impurity on the polymorphic behavior of long-chain compounds suggests that some of the reported observations may possibly relate to mixtures. The behavior of the higher alkylbenzothiazoles seems to confirm this implication.

The preparation of the lower alkylbenzothiazoles is known, and the melting points of the dimorphs[5] of several alkyl- and aryl-substituted benzothiazoles have been reported. There is, however, no reference in the literature to any higher alkylbenzothiazoles. This paper reports the preparation of 2-undecyl- and 2-heptadecylbenzothiazoles, presents their solubilities in hexane, benzene, carbon tetrachloride, chloroform, ethyl acetate, acetone, methanol, 95% ethanol, 2-propanol and acetonitrile, and discusses the behavior of their polymorphic forms.

Experimental

The 2-alkylbenzothiazoles were prepared by the reaction of fatty acids with 2-aminobenzenethiol at elevated temperatures, using catalytic amounts of hydrochloric acid. The reaction involves the loss of two molecules of water and cyclization of the intermediate compound.

Preparation of 2-Undecylbenzothiazole.—To 100 g. of highly purified lauric acid (f.p. 44.04°) and 92 g. (50% excess) of 2-aminobenzenethiol (American Cyanamid Co.) was added one cc. of concd. hydrochloric acid and the mixture was heated in an atmosphere of carbon dioxide. During the course of heating 5 hours at 170–250°, 17 cc. of water was collected (calcd. 17.8 cc.). The mixture was stripped under reduced pressure and distilled in a Vigreux column at 0.1 mm. pressure. The distillate was further purified chromatographically in petroleum ether (boiling range 60–90°) solution, using aluminum oxide as the adsorbent. The eluting mixture was the same petroleum ether containing 3% ethyl acetate. Repetition of the chromatography, using the same petroleum ether with 2% ethyl acetate, gave a colorless product freezing at 18.20 ± 0.02°.

Anal.[16] Calcd. for $C_{18}H_{27}NS$: C, 74.68; H, 9.40; N, 4.83; S, 11.07. Found: C, 74.46; H, 9.13; N, 4.79; S, 10.88.

Infrared Analyses by A. E. Brake.—The infrared absorption spectrum of 2-undecylbenzothiazole is shown in Fig. 1. This spectrogram was obtained on a Baird Associates model B instrument.

The absence of absorption bands in the C=O stretching vibration region (5.8 μ) was viewed as first evidence of the success of the indicated reaction and this spectrogram of 2-undecylbenzothiazole was found to compare favorably with that of 2-methylbenzothiazole.[17] The close correspondence of the wave lengths of some fourteen band centers in these spectra was taken as confirmation of the structure of this reaction product as a 2-alkylbenzothiazole. These band centers were also in agreement with those reported by Metzger.[18]

In order to observe the effect of impurities, a similar preparation using Neo-Fat No. 11[19] yielded a product with the f.p. 2.0 ± 0.1°. On the basis of the composition of the fatty acid employed in its preparation, this product was assumed to consist of about 90% 2-undecylbenzothiazole with 10% adjacent homologs.

Preparation of 2-Heptadecylbenzothiazole.—This compound was prepared by the above procedure, using highly purified stearic acid (f.p. 69.61°). The distilled product was crystallized three times from 5% solution in ethanol (Formula 3A) at room temperature. After air-drying, the final product had the f.p. 39.60 ± 0.02°.

Anal.[16] Calcd. for $C_{24}H_{39}NS$: C, 77.14; H, 10.52; N, 3.74; S, 8.58. Found: C, 77.02; H, 10.44; N, 3.66; S, 8.31.

A similar preparation using Neo-Fat No. 1-65[20] yielded a product with the f.p. 51.0 ± 0.5°. On the basis of the starting material and the subsequent treatment, this product was estimated to consist of about 95% 2-heptadecylbenzothiazole and 5% 2-pentadecylbenzothiazole. This estimate is based on the assumption that recrystallization would have removed some of this saturated homolog and most of the heptadecenyl derivative.

Repeated attempts to isolate the highest-melting form of purified 2-heptadecylbenzothiazole (see below) were unsuccessful. Precipitation of this compound at −20° from 10% solution in chloroform, with subsequent filtration and removal of solvent under reduced pressure at the same tem-

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[15] A. W. Ralston, "Fatty Acids and Their Derivatives," John Wiley and Sons, Inc., New York, N. Y., 1948, pp. 332, 333.

[16] Analyses by Clark Microanalytical Laboratory, Urbana, Ill.

[17] H. M. Randall, R. G. Fowler, N. Fuson and J. R. Dangl, "Infrared Determination of Organic Structures," D. Van Nostrand Co., Inc., New York, N. Y., 1949, p. 213.

[18] J. Metzger and C. Cherrier, *Compt. rend.*, **228**, 239 (1949).

[19] A product of Armour and Company, Chemical Division, Chicago, Ill., consisting of about 90% lauric acid, the remainder being chiefly myristic acid.

[20] A product of Armour and Company, consisting of about 90% stearic acid, 6% palmitic aicd and 4% oleic acid.

TABLE I

SOLUBILITIES OF PURIFIED 2-UNDECYL- AND 2-HEPTADECYLBENZOTHIAZOLES IN VARIOUS SOLVENTS

Solvent	No. C atoms	G. solute per 100 g. solvent									
		−40.0°	−30.0°	−20.0°	−10.0°	0.0°	10.0°	20.0°	30.0°	40.0°	50.0°
Hexane	11	...	...	15.9	45	120	375	∞	∞	∞	∞
	17	...	...	...	...	...	<1	5.5	48.5	∞	∞
Benzene	11[a]	...	...	...	...	...	690	∞	∞	∞	∞
	17[b]	...	...	...	...	...	67	135	375	∞	∞
Carbon tetrachloride	11	...	...	45.0	89	190	535	∞	∞	∞	∞
	17	...	...	6.3	12.0	21.4	45	82	230	∞	∞
Chloroform	11	1.7	7.1	19.2	45.5	100	235	∞	∞	∞	∞
	17	...	<1	1.9	6.1	13.9	28.5	56	115	280	∞
Ethyl acetate	11	...	<1	5.2	27.1	88	305	∞	∞	∞	∞
	17	...	...	<2	2.0	4.7	11.2	32.	14.0	∞	∞
Acetone	11	...	<1	2.7	14.3	65	260	∞	∞	∞	∞
	17	...	...	...	...	...	<1	3.4	83	∞	∞
Methanol	11[c]	...	...	...	<1	4.5	6.7	9.4	13.0	18.6	30.3
	17[d]	...	...	...	...	...	...	0.6	0.7	0.9	1.2
95% ethanol	11	...	...	<1	1.8	12.3	245	∞	∞	∞	∞
	17[e]	...	...	...	...	...	...	...	<1	8.3	10.4
2-Propanol	11	...	...	<1	7.7	41	200	∞	∞	∞	∞
	17	...	...	...	...	...	<1	11.2	750	∞	∞
Acetonitrile	11[f]	...	...	...	...	0.1	2.6	7.2	10.1	14.0	19.2
	17[g]	...	...	...	...	...	...	...	...	<1	1.0

[a] Eutectic at 58.0 wt. % and −9.3°. [b] Eutectic at 28.5 wt. % and +1.0°. [c] Miscible above 56°. [d] Not miscible below 65°. [e] Not miscible below 80°. [f] Miscible above 79°. [g] Not miscible below 82°.

perature, yielded crystals which melted sharply at 39.60° (polarizing microscope). Evaporation of the solvent from concentrated solutions by maintaining the heated stage of the microscope just below the solution temperature gave the same results. As the last few per cent. of solvent was being removed, the solute dissolved abruptly in the neighborhood of 40°.

It was found that the highest-melting form of 2-heptadecylbenzothiazole could be produced experimentally by the addition of homolog here discussed. Upon the addition of 1–4% of 2-undecylbenzothiazole to the heptadecyl derivative, the mixtures exhibit both the intermediate and the higher melting points. At temperatures between the melting points, the mixtures existed in varying proportions of solid and liquid. Addition of 5% or more homolog to 2-heptadecylbenzothiazole gave mixtures which solidified and melted only at the higher temperature, no lower melting points being observed in the absence of solvent.

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. The procedures used in this experimentation have been described elsewhere.[13,14]

The solvents employed were reagent grade or equivalent, and were freshly distilled before using. The aqueous ethanol was commercial "absolute" which had been diluted to 95.0% by weight with conductivity water, the ethanol content being determined by comparing the density with the values in the "International Critical Tables."

Known amounts of solute were weighed into test-tubes equipped with Nichrome stirrers and thermometers, and the solution temperatures were observed upon successive dilutions with known amounts of solvent. After determination of the temperature at which precipitation occurred upon cooling, the temperature was raised immediately and the temperature at which the precipitate redissolved was observed. A few repetitions were sufficient to arrive at the temperature at which precipitation and solution coincided within 0.1°.

In the mixtures which exhibited polymorphism, transformation could be observed by a visual change in the crystals during precipitation. The solution temperatures of the higher-melting modifications were then determined by slowly heating the mixtures. In the cases where only the lower-melting polymorphs were obtained, the mixtures were seeded with a few crystals of the stable form to promote transformation.

Temperatures were measured by means of mercury thermometers which were graduated in 0.1° intervals and had been calibrated by the National Bureau of Standards. The freezing points of the purified alkylbenzothiazoles were considered accurate to ±0.02° and the solution temperatures to ±0.1°. The melting points of the various polymorphs, obtained by graphical extrapolation of their respective solubility curves, are probably accurate to about ±0.5°.

Results and Discussion

The solubilities of purified 2-undecyl- and 2-heptadecylbenzothiazoles are listed in Table I in terms of g. of solute per 100 g. of solvent. These values refer to the solubility of the crystalline form most stable in each solvent at the given temperatures. These data were obtained by plotting the experimentally observed solution temperatures[2] against concentrations on large scale graphs and reading therefrom the solubilities at the temperatures listed in Table I.

Solubilities in terms of mole fraction of solute permit a more accurate evaluation of the effects of the solvents. The solubilities of 2-undecylbenzothiazole at 10° are listed on this basis on Table II. The values in this table refer to the solubility of the same crystalline modification in each instance, namely, that of the form which freezes at 18.20° in the absence of solvent.

These compounds present a considerable variation in behavior ranging from moderate solubility in the non-polar and slightly polar solvents to quite limited solubility in even the moderately polar solvent. In the highly polar solvents, solubility becomes so limited as to result in two-phase liquid systems over considerable ranges of concentration.

Comparison of the solubilities of 2-undecylbenzothiazole with the relative internal pressures of the solvents (Table II) shows a general correlation between decreasing order of solubility and increasing internal pressure of the solvent. The relatively high solubilities in benzene, carbon tetrachloride, and chloroform are probably attributable to some form of dipole–dipole interaction with these solvents. The relatively low solubilities in even the

Table II

Mole Fraction Solubility of 2-Undecylbenzothiazole in Various Solvents at 10°

Solvent	N_2	Relative internal pressure of solvent[21]
Chloroform	0.33	1.6
Carbon tetrachloride	.32	1.5
Benzene	.30	1.6
Hexane	.12	1.00
Ethyl acetate	.076	1.4
Acetone	.035	1.7
2-Propanol	.016	1.9
95% ethanol	.0028	2.3
Acetonitrile	< .0002	2.6
Methanol	< .0002	3.2

moderately polar solvents are characteristic of molecules possessing low internal pressure and low polarity. The limited solubility in the polar solvents suggests that there is little, if any, intermolecular association between solvent and solute. This behavior demonstrates the overshadowing influence of the paraffin chain even on substituent groups possessing potentially highly polar characteristics.

The solubilities of these compounds in benzene, chloroform, acetone and 95% ethanol are shown graphically in Figs. 2–5, respectively. The solid portions of these curves represent the concentrations over which the most stable crystalline form was obtained in each given solvent. The broken lines represent the solubilities of forms which were metastable in the given solvents. These diagrams illustrate the pronounced influence of impurity on the polymorphic behavior and the remarkable specificity of the influence of the solvents with regard to the respective crystalline forms of the alkylbenzothiazoles.

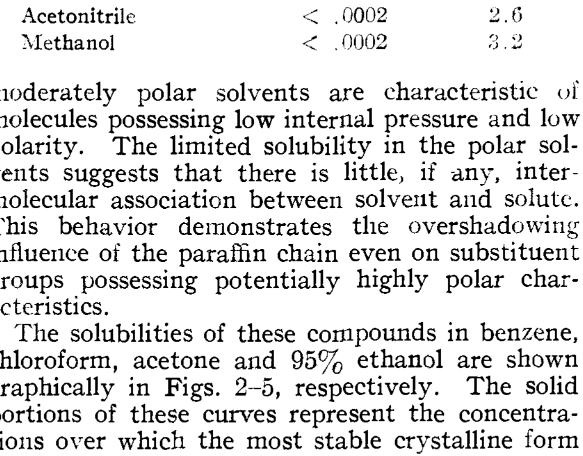

Fig. 2.—Solubilities of alkylbenzothiazoles in anhydrous benzene: ●, purified undecyl derivative; ●, impure undecyl; ▲, purified heptadecyl; ⊥, impure heptadecyl. The solid lines refer to stable modifications, the long dashes refer to metastable forms, and the short dashes refer to extrapolated curves. The Roman numerals refer to the various crystalline forms listed in Table IV.

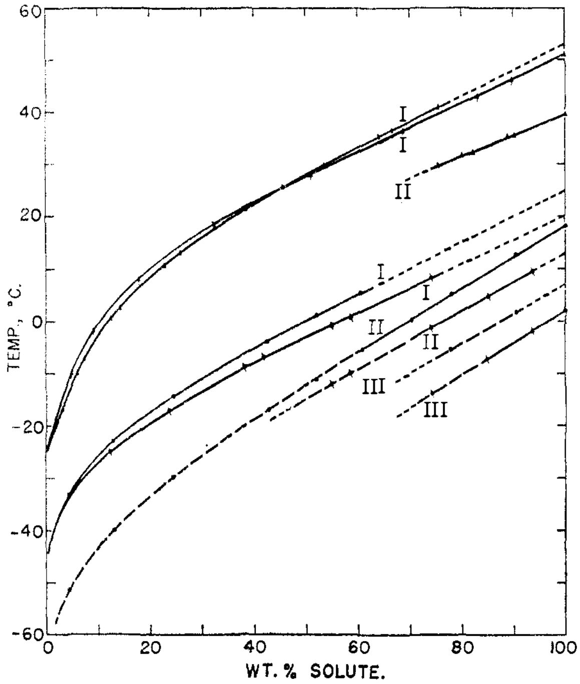

Fig. 3.—Solubilities of alkylbenzothiazoles in chloroform. Symbols and numerals as in Fig. 2.

In the subsequent discussion of the solubility curves, the crystalline modifications which possess the freezing points always obtained in the absence of solvent will be referred to as the *normal* forms. All of the solutes investigated precipitate from benzene and carbon tetrachloride in this form. Both the purified and the impure 2-undecylbenzothiazoles also precipitate from hexane, ethyl acetate, acetone, 95% ethanol, 2-propanol and acetonitrile in the normal form. The undecyl derivatives crystallize from chloroform in two additional modifications, whereas methanol promotes the precipitation of only the lower melting forms of these solutes. Behavior similar to that in chloroform was observed in a few experiments using commercial grade 1,2-dichloroethane. As shown by Tables III and IV and by the representative systems in the diagrams, 2-heptadecylbenzothiazole exhibits more diversified polymorphic behavior in that this compound appears to exist in four different modifications.

Table III

Melting Points of Polymorphic Modifications of Alkylbenzothiazoles

Alkylbenzothiazole	I	II	III	IV
Purified 2-undecyl-	25	18.2[a]	7	..
Impure 2-undecyl-	20	13	2.0[a]	..
Purified 2-heptadecyl-	53	39.6[a]	29	19
Impure 2-heptadecyl-	51[a]	37	26	..

[a] Freezing point obtained in the absence of solvent (*normal* form).

By extrapolating the solubility curves of the various forms to 100% solute, it is possible to estimate with reasonable accuracy the apparent melting

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(21) Calculated from the absolute values listed by J. H. Hildebrand and R. L. Scott, "The Solubility of Non-Electrolytes," 3rd Ed., Reinhold Publishing Corp., New York, N. Y., 1950. These computations are referred to the internal pressure of hexane as 1.00.

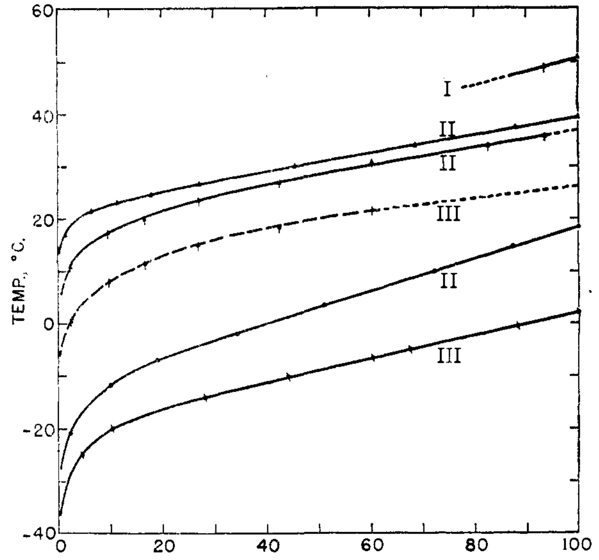

Fig. 4.—Solubilities of the alkylbenzothiazoles in acetone. Symbols and numerals as in Fig. 2.

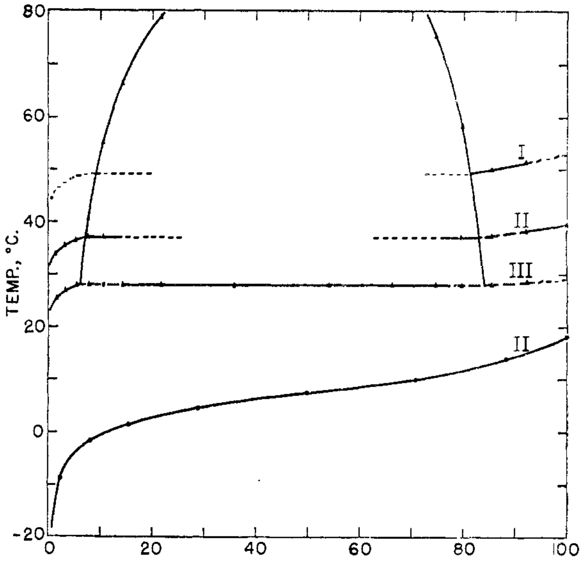

Fig. 5.—Solubilities of purified alkylbenzothiazoles in 95.0% ethanol. Symbols and numerals as in Fig. 2.

points of the crystalline modifications which cannot be realized in the absence of solvent. The melting points thus obtained are listed in Table III. This tabulation shows that the observed freezing points of the corresponding purified and impure compounds were not those of the same crystalline modification. With both of the purified compounds the apparently stable forms possessed intermediate melting and freezing points.

The results of this investigation seem to indicate general tendencies of the non-polar and slightly polar solvents, particularly some of the lower haloalkanes, to promote the precipitation of the higher melting crystalline forms of the solutes, the solvents of intermediate polarities to result in crystallization of most of the modifications of the solutes over at least some portion of the concentration range, and the highly polar solvents to bring about formation of only the lower melting forms. There are, however, some exceptions to this general behavior, as shown in Table IV.

Table IV

Crystal Forms of Alkylbenzothiazoles Precipitated from Various Solvents

Solvent	Purified undecyl-	Impure undecyl-	Purified heptadecyl-	Impure heptadecyl-
n-Hexane	II	III	II, III	I, II, III
Benzene	II, III	III	II	I
Carbon tetrachloride	II	III	II	I
Chloroform	I, II, III	I, II, III	I, II	I
Ethyl acetate	II	III	II	I, II
Acetone	II	III	II	I, II, III
Methanol	II, III	III	III, IV	II, III
95% ethanol	II	III	I, II, III	I, II, III
2-Propanol	II	III	II, III	I, II, III
Acetonitrile	II	III	III, IV	. .

Explanation of the effects of impurities is lacking. Impurity appears to bring about the stabilization of a higher melting form of 2-heptadecylbenzothiazole, whereas the opposite behavior is exhibited by 2-undecylbenzothiazole. Behavior similar to that of the heptadecyl derivative has been observed in only one other instance, namely, with the symmetrical dialkylamines containing chains of 10 or less carbon atoms.[8] The stabilization of a lower-melting form has been observed in numerous studies on a wide variety of binary mixtures of higher aliphatic compounds, for example, nitriles,[6] methyl ethyl esters of fatty acids,[22] alcohols,[23] haloalkanes[23] and hydrocarbons.[23] The effect of impurity was regarded by Ferguson and Lutton[24] as being responsible for retarding the rate of transition of the metastable form, thereby resulting in its apparent stability.

Chicago 9, Ill.

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(22) J. C. Smith, *J. Chem. Soc.*, 802 (1931); P. C. Carey and J. Smith, *ibid.*, 635 (1933); J. B. Guy and J. C. Smith, *ibid.*, 615 (1939); J. W. C. Phillips and S. A. Mumford, *Rec. trav. chim.*, **52**, 175 (181) (1933).

(23) J. C. Smith, *J. Chem. Soc.*, 737 (1932).

(24) R. H. Ferguson and E. S. Lutton, *Chem. Revs.*, **29**, 355 (1941).