Another annulation series is given in Fig. 9. Here the methylene group in the former series is substituted by the carbonyl group. The π-electrons in the latter contribute to the aromatic resonance system so that an additional red shift equivalent to half a benzene ring is produced. The wave lengths of the first p-bands of diphenyl (2500 Å.), benzanthrone (3950 Å.) and coeranthrone (4970 Å.) are thus proportional to 6^2, $(7\frac{1}{2})^2$ and $(8\frac{1}{2})^2$. Only small distortion of the molecular plane in coeranthrone could be deduced from the deviation of the annulation principle.

Experimental

9-(*o*-Carboxyphenyl)-anthracene.—This was prepared from benzophenone-2,2'-dicarboxylic acid dilactone (20 g.) following the synthesis of Scholl and Donat.[6] Crystallization from acetic acid gave 6 g. of yellow needles, m.p. 241–242° (lit. m.p. 242–243.5°).

Coeranthrone.—The procedure followed was a modification of that used by Bradsher and Vingiello.[7] 9-(*o*-Carboxyphenyl)-anthracene (6 g.) in 100% orthophosphoric acid (250 cc.) was heated at 200° for two hours, and a dark green solution obtained, which, after cooling was poured into water. The red precipitate, after thorough extraction with hot dilute ammonium hydroxide solution, was sublimed and recrystallized from acetic acid to give 4.5 g. (80%) of dark red needles, m.p. 175–176° (lit. m.p. 178–179°).

Coeranthrene.—Coeranthrone (3 g.) and zinc dust (15 g.) were added to a 10% sodium hydroxide solution (100 cc.) covered with a layer of octyl alcohol (15 cc.). After refluxing for six hours, the octyl alcohol was distilled off, and the hot solution filtered into concentrated hydrochloric acid. The precipitate was collected, washed with hot water and dried in a vacuum. The powdered product was decomposed by heating in a vacuum (0.5 mm.) and the orange-red sublimate obtained was dissolved in benzene and chromatographed (alumina). On developing the chromatogram with a benzene–petroleum ether (b.p. 40–60°) mixture, a clear yellow eluate with a blue fluorescence was obtained, which after concentration and cooling yielded large orange-yellow plates (1 g.), m.p. 138–139°. Coeranthrene dissolved readily in concentrated sulfuric acid to give a yellow solution which rapidly changed to green on standing.

Anal. Calcd. for $C_{21}H_{14}$: C, 94.70; H, 5.30. Found: C, 94.66; H, 5.23.

1,10-Trimethylene-3,4-benzphenanthrene.—The coeranthrone (0.75 g.), red phosphorus (1 g.) and 55% hydroiodic acid (10 cc.) were covered with xylene (10 cc.) and after refluxing for 48 hours, the mixture was diluted with water and filtered, the excess phosphorus being well washed with hot xylene. The xylene layer after drying and concentration was passed through a chromatographic column (alumina), a benzene–petroleum ether (b.p. 40–60°) mixture being used as eluant. A colorless, violet-blue fluorescent eluate was obtained, which on concentration and cooling gave long flat colorless prisms (0.5 g.), m.p. 116–117°, which did not dissolve readily in concentrated sulfuric acid. On warming however a green solution was obtained.

Anal. Calcd. for $C_{21}H_{16}$: C, 93.99; H, 6.01. Found: C, 94.08; H, 6.13.

Acknowledgment.—The authors wish to thank Prof. J. W. Cook, F.R.S., for a sample of 3,4,5,6-dibenzphenanthrene, and Dr. C. L. Hewett for samples for 1,2-benzchrysene, 5,6-benzchrysene and 1,2-benztetraphene.

GLASGOW, SCOTLAND

(6) Scholl and Donat, *Ann.*, **512**, 1 (1934).

(7) Bradsher and Vingiello, *J. Org. Chem.*, **13**, 786 (1948).

[CONTRIBUTION FROM THE CHEMICAL LABORATORIES OF NORTHWESTERN UNIVERSITY]

Preparation, Reactions and Kinetics of Reactions of Epicholesteryl *p*-Toluenesulfonate[1]

BY L. CARROLL KING AND M. JEROME BIGELOW

RECEIVED JULY 11, 1952

Epicholesteryl *p*-toluenesulfonate was prepared and its reactions with pyridine, piperidine, methanol and ethanol were studied. Kinetic studies were made of the solvolysis of epicholesteryl *p*-toluenesulfonate in ethanol and in methanol.

Epicholesterol (I) was prepared from cholesterol in over-all yield of 37%. Cholesterol was converted to 3-β-5-α-cholestandiol (II) by a modification of the method of King and Campbell.[2] Compound II was then converted to I by a modification of the procedure of Plattner and Lang.[3] Epicholesteryl *p*-toluenesulfonate (III) was then prepared from I. A description of these preparations, and evidence as to identity and homogeneity of products is given in the Experimental part of this paper.

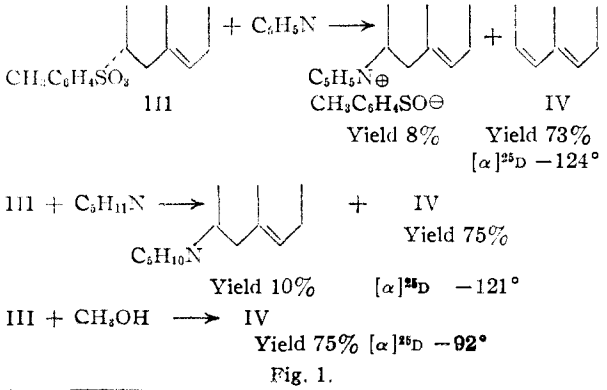


Fig. 1.

Epicholesteryl *p*-toluenesulfonate (III) reacted with pyridine to give cholestadiene (IV) in 80% yield and 6–10% of 3-β-cholesterylpyridinium *p*-toluenesulfonate.[4] With piperidine III gave a 75% yield of IV and 10% of 3-β-cholesterylpiperidine (VI).[4] When III was allowed to react with methanol or ethanol, or with ethanol containing ethoxide ion, a 75% yield of a cholestadiene was obtained. These reactions are summarized in the diagram.

Details for preparation, separation and identification are given in the Experimental part.

A kinetic study was made of the solvolysis of III

(1) Paper No. 22, Organic Division American Chemical Society, Chicago Meeting, 1950.

(2) L. C. King and J. A. Campbell, THIS JOURNAL, **71**, 3566 (1949).

(3) P. A. Plattner and W. Lang, *Helv. Chim. Acta*, **27**, 1872 (1944); P. A. Plattner, T. Petrzilka and W. Lang, *ibid.*, **27**, 518 (1944).

(4) The 3-β-structure for this compound is discussed in a recent paper; L. C. King and M. J. Bigelow, THIS JOURNAL, **74**, 3336 (1952).

in methanol, ethanol and ethanol containing ethoxide ion. A summary of the results of this investigation is given in Table I. Data for the solvolysis of cholesteryl *p*-toluenesulfonate in methanol are given for comparison.[5]

TABLE I

SOLVOLYSIS OF EPICHOLESTERYL *p*-TOLUENESULFONATE(III)

Concn. of III	Solvent	*T*, °C.	Added	k_1, min.$^{-1}$ × 10^4	k_2, l. × mole^{-1} × min.$^{-1}$
0.00425	Methanol	25.4	.....	1.99	....
.00425	Methanol	34.8	.....	6.70	....
.00440	Ethanol	34.8	.....	1.05	....
.00449	Ethanol	34.8	0.009 *M* $NaClO_4$	1.52	....
.00457	Ethanol	34.8	.00461 *M* NaOEt	2.12	0.0584
.00426	Ethanol	34.8	.00785 *M* NaOEt	2.60	.0363
.00427	Ethanol	34.8	.01179 *M* NaOet	2.66	.0302
.00427	Ethanol	34.8	.01091 *M* NaOEt		.0306
Cholesteryl *p*-toluenesulfonate					
0.00425	Methanol	34.8	.....	46.0	....

Experimental

3-β,5-α-Cholestanediol-6-isothiuronium *p*-Toluenesulfonate.—This substance was prepared by a modification of the method of King and Campbell.[1] A solution of 40 g. of cholesterol in 600 cc. of 0.38 *M* peroxyphthalic acid in ether[6] was refluxed one hour. The ether was removed and the residue leached with chloroform. Evaporation of the chloroform gave a water-white oil. To this crude oxide a solution of 25 g. of thiourea and 35 g. of *p*-toluenesulfonic acid monohydrate in 800 cc. of ethanol was added and the solution was refluxed for one hour. The product separated on cooling. The yield was 39 g. (57%), m.p. 227–229°.

3-β,5-α-Cholestanediol.—A solution consisting of 20 g. (0.03 mole) of the salt described above and 1.2 g. (0.03 mole) of sodium hydroxide in 2 l. of methanol was treated with 100 g. of standard Raney nickel catalyst.[7] The suspension was kept at reflux on the steam-bath with vigorous stirring for one hour; it remained basic to phenolphthalein. It was then cooled below reflux and filtered quickly through celite. The filtrate was concentrated to a volume of 800 cc., acidified with a few drops of acetic acid, and water (100 cc.) was added. The product separated upon cooling; the yield was 11.3 g. (91%), m.p. 219–223°. Some preparations gave a lower yield of poorer quality, probably due to a less active Raney nickel preparation. Crystallization from acetone–methanol was usually sufficient to purify the product in this case.

3-β,5-α-Diacetoxycholestane.—This substance was prepared by the method of Plattner and Lang.[3] From 8.5 g. of the diol was obtained 9.35 g. of needles (91%), m.p. 139–140°, $[\alpha]^{25}D$ 31.8° (in chloroform); reported[3] m.p. 140–141°, $[\alpha]D$ 31.5°.

3-β-Hydroxy-5-α-acetoxycholestane.—To a solution of 10 g. of sodium hydroxide in 300 cc. of methanol was added 9.35 g. of the diacetoxycholestane. After five minutes shaking, solution was complete. The solution was allowed to stand for six hours at room temperature; it was then heated to boiling, filtered, and water was added until cloudiness developed. Upon cooling, 8.5 g. of a product was obtained which was slightly contaminated with inorganic material. This was purified by dissolving in acetone, filtering and then recrystallizing from acetone–water. By this method 8.3 g. (98%) of fine needles, m.p. 161–162.5°, was obtained, $[\alpha]^{25}D$ 27.0° (in chloroform); reported[3] m.p. 158–159°, $[\alpha]D$ 30.3°.

Epicholesterol (I).—In 30 ml. of pyridine was dissolved 9.2 g. of 3-β-hydroxy-5-α-acetoxycholestane and 10 g. of *p*-toluenesulfonyl chloride. The solution was allowed to stand overnight, then refluxed for one hour. During this time it turned dark brown. The pyridine was removed under vacuum, leaving a viscous brown residue. A solution of 20 g. of potassium hydroxide in 300 cc. of methanol was added, and the solution was refluxed for two hours. Water was then added until cloudiness developed, and upon cooling brownish crystals deposited. The yield was 6.6 g., m.p. 135–138°. The product could not be purified conveniently by crystallization: it was dissolved in 200 cc. of 1:1 ether–Skellysolve B and chromatographed on a six-inch column containing 200 g. of alumina.

Fraction	Eluant	Obtained
1	400 cc. 1:8 $CHCl_3$–ether	Trace brown oil
2	400 cc. 1:1 $CHCl_3$–ether	6.5 g.

Fraction 2, 6.5 g., was epicholesterol (I), m.p. 140–141°, $[\alpha]^{25}D$ −46.5° (in chloroform); reported[3] m.p. 140–141°, $[\alpha]D$ −44°.

To a solution of 40 mg. of I, prepared as above, in 10 cc. of 95% ethanol, 100 mg. of digitonin in 10 cc. of 90% ethanol was added. No precipitate was observed, even after cooling overnight. A solution of 1 mg. of cholesterol in 10 cc. of 95% ethanol gave a visible precipitate when treated with digitonin under similar conditions.

Epicholesteryl *p*-Toluenesulfonate (III).—Three grams of I and 3 g. of *p*-toluenesulfonyl chloride were dissolved in the minimum amount of dry pyridine and allowed to stand overnight at 0°. One ml. of water was then added to the solid mass and an exothermic reaction was observed as the excess *p*-toluenesulfonyl chloride hydrolyzed. Excess water was then added, and the solution was cooled and filtered. The residue was washed with water, then taken up in chloroform. The chloroform solution was washed with water, then dried with sodium sulfate and evaporated under vacuum. After two crystallizations from Skellysolve B, 3.1 g. (74%) of white needles was obtained. This compound decomposed to a red liquid in the range 110–115°, $[\alpha]^{25}D$ −3.5°, −3.7° (in chloroform).

Anal. Calcd. for $C_{34}H_{53}O_3S$: C, 75.50; H, 9.69. Found: C, 75.31; H, 9.33.

Reaction of III with Piperidine.—Five hundred mg. of III dissolved in 20 cc. of piperidine was heated 20 hours on the steam-bath. The solution was then poured into 200 g. of ether. Upon filtration 200 mg. (35%) of piperidine tosylate was obtained. The ether solution was evaporated, then steam distilled to remove the excess piperidine. A yellow oil remained. This was taken up in ether and washed twice with water, the ether solution was dried with anhydrous sodium sulfate and evaporated to dryness. The residual oil was taken up in 20 cc. of acetone: upon cooling and filtering 44 mg. (10%) white crystals, m.p. 162–164°, was obtained. Mixed m.p. with an authentic sample of 3-β-cholesterylpiperidine[8] was 164–166°.

Dry HCl was passed into the acetone solution. Upon filtration 5 mg. of an acetone-insoluble hydrochloride was obtained. This substance was converted to 3-β-cholesteryl-piperidine, m.p. 160–164°.

The filtrate from the HCl treatment was evaporated to dryness and leached with Skellysolve B. The Skellysolve B solution was evaporated and the residue was crystallized from acetone–water. The product was cholestadiene; yield 245 mg. (75%), m.p. 79–80°, $[\alpha]^{25}D$ −121° (in chloroform).

Reaction of III with Pyridine.—One and one-tenth grams of III was heated with 3 cc. of pyridine on the steam-bath overnight. The solution was cooled and 100 cc. of ether was added. Upon filtration a white solid was obtained; this was dissolved in chloroform. The chloroform solution was washed twice with 10% ethanol in water solution (water alone gave emulsions), then dried with anhydrous sodium sulfate and evaporated to a white solid which was crystallized from acetone. One hundred mg. (8%) of a salt, m.p. 210–220°, was obtained; after recrystallization from acetone, 50 mg., m.p. 226–228°, was obtained. The mixed m.p. with an authentic sample of 3-β-cholesterylpyridinium *p*-toluenesulfonate,[8,9] m.p. 230–232°, was 227–229°.

The ether-soluble fraction from above was evaporated to dryness and the residue was recrystallized from acetone: 550 mg. (73%) of cholestadiene was obtained, m.p. 78–80°, $[\alpha]^{25}D$ −124° (in chloroform).

(5) R. G. Pearson, L. C. King and S. H. Langer, *ibid.*, **73**, 4149 (1951).

(6) H. Bohme, *Org. Syntheses*, **20**, 70 (1950).

(7) H. Adkins, "Reactions of Hydrogen with Organic Compounds," The University of Wisconsin Press, Madison, Wisc., 1937, p. 20.

(8) Prepared in this Laboratory by hydrogenation of 3-β-chloesteryl-pyridinium *p*-toluenesulfonate, L. C. King and M. J. Bigelow, THIS JOURNAL, **74**, 3338 (1952).

(9) L. C. King, R. M. Dodson and L. A. Subluskey, *ibid.*, **70**, 1176 (1948).

TABLE II

Reagents	Products	Yield, %	$[\alpha]_D$	k_1 at 34.8°, min.$^{-1}$
Cholesteryl *p*-toluenesulfonate[a] and pyridine	3-β-Cholesterylpyridinium *p*-toluenesulfonate	71		.....
	3,5-Cholestadiene	21	−114°	.....
Epicholesteryl *p*-toluenesulfonate and pyridine	3-β-Cholesterylpyridinium *p*-toluenesulfonate	8		
	3,5-Cholestadiene	71	−121	
Cholesteryl *p*-toluenesulfonate[b] and methanol	Methyl 3-β-cholesteryl ether	90		4.60×10^{-3}
Epicholesteryl *p*-toluenesulfonate, methanol	Cholestadiene	80	− 90	6.7×10^{-4}
	Ethers	10		

[a] L. C. King and B. Regan, THIS JOURNAL, **74**, 5617 (1952). [b] R. G. Pearson, L. C. King and S. Langer, *ibid.*, **73**, 4149 (1951).

Reaction of III with Methanol.—Four hundred milligrams of III was refluxed with 20 cc. of methanol for two days. The mixture was treated with ether–water and the ether extract was washed with water, dried and evaporated. The oil residue was dissolved in 50 cc. of Skellysolve B and chromatographed on an 18-inch alumina column.

Fraction	Eluant	Obtained	
1	50 cc. SK-B	95 mg., m.p. 77–80°	$[\alpha]^{25}D$ −92°
2	50 cc. Sk-B	110 mg., m.p. 76–79°	
3	100 cc. Sk-B	Small amt. oil	
4	50 cc. MeOH	Small amt. oil	

The total yield of cholestadiene, fractions 1 and 2, was 205 mg. (75%).

Fractions 3 and 4 were combined, dissolved in methanol, and cooled. A small amount of gummy yellow solid, m.p. 40–70°, was obtained. Further characterization was not accomplished.

Solvolysis of III.—The epicholesteryl *p*-toluenesulfonate was dissolved in chloroform and the reaction initiated by addition of 10 volumes of methanol. The rate of solvolysis was found by measuring the change in conductance.[10] Log $(R/(R - R_\infty))$ was plotted against time to get the first order rate constant. The value for R_∞ was determined by direct measurement. Figure 2 shows some of the results.

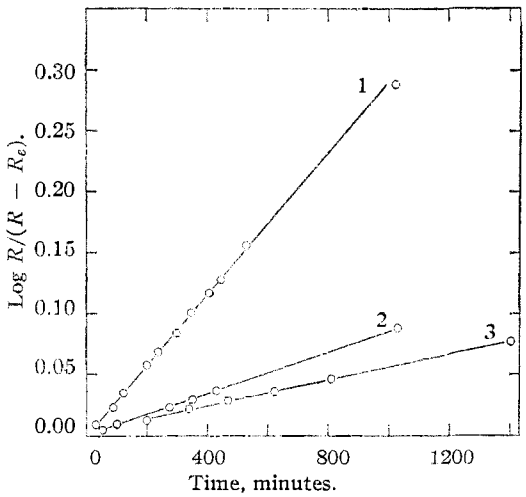


Fig. 2.—Curve 1, epicholesteryl *p*-toluenesulfonate, 0.00425 *M* in methanol at 34.8°; curve 2, epicholesteryl *p*-toluenesulfonate, 0.00425 *M* in methanol at 25.8°; curve 3, epicholesteryl *p*-toluenesulfonate, 0.00440 *M* in ethanol at 34.8°.

In the ethanolysis experiments III was dissolved in ethanol at the operating temperature. Zero time was taken when solution was complete. For the experiments on ethanolysis in the presence of ethoxide, zero time was taken when the measured volume of 0.1298 *M* sodium ethoxide was added. These data fit better a second-order plot, indicating that ethoxide as well as ethanol can react with III. See Fig. 3, for typical data.

(10) R. G. Pearson, THIS JOURNAL, **69**, 3100 (1947).

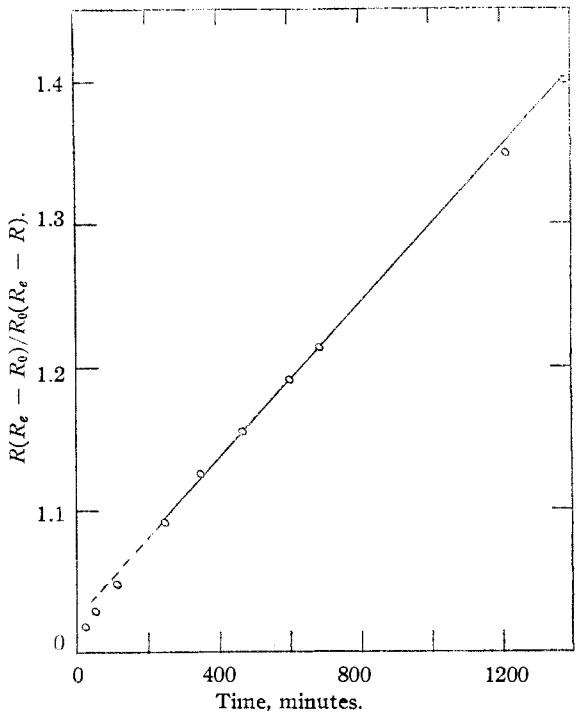


Fig. 3.—Epicholesteryl *p*-toluenesulfonate, 0.00457 *M* in ethanol containing 0.00461 ethoxide.

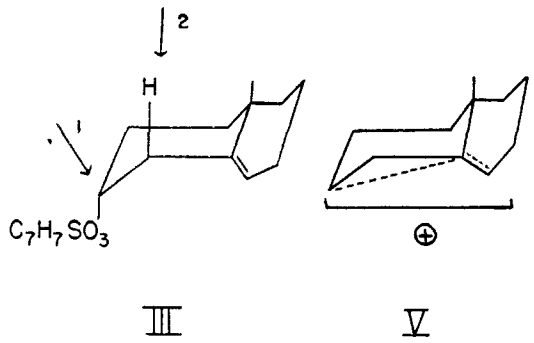
Discussion

Cholesteryl *p*-toluenesulfonate (VI) and epicholesteryl *p*-toluenesulfonate (III) react with pyridine to give identical products but in different amounts. The rates of the reactions of III and VI with methanol are different. VI reacts about 7 times as fast as III and gives 3-β-cholesteryl methyl ether as the principal product whereas III gives cholestadiene as the principal product. These observations are summarized in Table II.

The reactions of cholesteryl *p*-toluenesulfonate (VI) have been rationalized in terms of formation of the mesomeric ion V which is capable of reaction in a stereospecific manner[11] at position 3.

The reactions of epicholesteryl *p*-toluenesulfonate III may be rationalized as follows: (1)—The replacement reactions occur in the normal manner. The nucleophilic group replaces with inversion. The elimination reaction occurs readily since the hydrogens at 2 and 4 and the *p*-toluenesulfonate group at 3 are polar. These simultaneous competing reactions may be visualized by examining the

(11) E. W. Meyer, Ph.D. Thesis, Northwestern University, 1943; S. Winstein and R. Adams, THIS JOURNAL, **70**, 838 (1948); R. G. Pearson, L. A. Sublusky and L. C. King, *ibid.*, **70**, 3779 (1948).



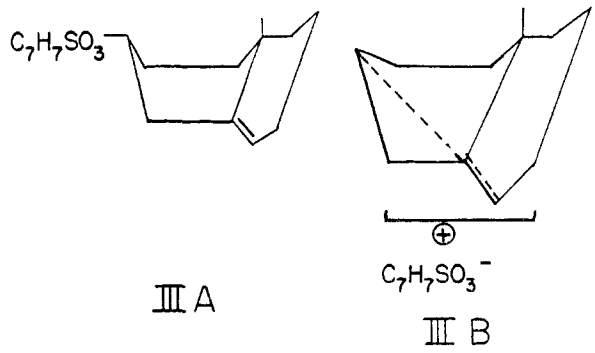
III V

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.

(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).

(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.



III A III B

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

[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

(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, "Repertoire 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).