filtered from the catalyst and spotted on Whatman No. 1 paper using 3% ammonium chloride as solvent. Two spots were obtained, one corresponding to hypoxanthine and the other corresponding to unchanged hypoxanthine-1-*N*-oxide, thus indicating that reduction was incomplete. Fresh catalyst (0.29 g.) was therefore added to this solution, which was again hydrogenated at 60 p.s.i. at 80° for 2.5 days. After removal of the catalyst from the hot reduction mixture, the filtrate was again spotted on Whatman No. 1 paper, using 3% ammonium chloride as developing solvent. Only one absorption spot, corresponding to hypoxanthine, was obtained. This was confirmed by a simultaneous run with authentic hypoxanthine. Evaporation of this solution to dryness followed by recrystallization of the residue from water yielded a light tan solid which, although it still gave a positive ferric chloride test (indicating the presence of a small amount of unreduced hypoxanthine-1-*N*-oxide) apparently was essentially hypoxanthine, since it gave only one spot on paper chromatography (corresponding precisely in R_f value with authentic hypoxanthine) and its ultraviolet absorption spectrum in 0.1*N* NaOH was identical with the spectrum given by authentic hypoxanthine. It is interesting to note that the ferric chloride test in this instance is considerably more sensitive in detecting a small amount of hypoxanthine-1-*N*-oxide in the product than is paper chromatography.

Attempted reduction of hypoxanthine-1-*N*-oxide using Raney nickel under the conditions previously described for the reduction of adenine-1-*N*-oxide to adenine[3] was completely unsuccessful. No hypoxanthine could be detected in the reduction product.

Frick Chemical Laboratory
Princeton University
Princeton, N. J.

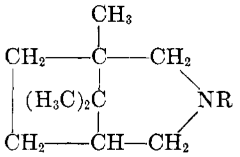
3-Substituted 1,8,8-Trimethyl-3-azabicyclo-[3.2.1]octanes

Edgar A. Steck[1] and R. Pauline Brundage

Received May 11, 1959

Recent publications[2–6] lead us to report certain aspects of our work on 3-substituted 1,8,8-trimethyl-3-azabicyclo[3.2.1]octanes, I. The 1,8,8-trimethyl-3-azabicyclo[3.2.1]octanes have been known as camphidines because of the mode of preparation from imides of camphoric acid.[7] We have made the several compounds from camphidine rather than through the imides; the method of Schmidt and Klavehn[8] provided a convenient route from camphene to camphidine.

The compounds showed only moderate activities as depressants on automatic ganglia and the central nervous system.



I

R

a. $-CH_2CH_2N(CH_3)_2$
b. $-(CH_2)_6-$

EXPERIMENTAL[9]

1,8,8-Trimethyl-3-azabicyclo[3.2.1]octane (*Camphidine*). The procedure was essentially that outlined by Schmidt and Klavehn,[8] wherein a ring expansion of camphene with hydrazoic acid[10] gave a mixture of 1,8,8-trimethyl-3-azabicyclo[3.2.1]octene-2 with the related octene-3 (α- and β-dehydrocamphidine) which was reduced catalytically to camphidine.

Camphene (260 g., 1.9 mol.) was dissolved in 2.8 l. of benzene which contained hydrazoic acid (160 g., 3.7 mol.).[10] The stirred solution was kept at 5 to 12° during the addition of tin (IV) chloride (1075 g., 4.12 mol.) over a 2 hr. period. It was warmed to room temperature for 0.5 hr. and allowed to stir for an hour longer before cooling to 15° and basified (*p*H 9–10) with sodium carbonate solution. Stirring was rendered difficult by the separation of white solid. The tin salt was collected after chilling and extracted well with benzene, giving a total of *ca.* 7 l. benzene solution which was then extracted with 2*N* hydrochloric acid. The dehydrocamphidines were liberated from the acidic extracts with 35% sodium hydroxide and taken up in benzene. Concentration of the dried extracts *in vacuo* was done with use of a column and a Dry Ice trap. The mixed bases were obtained in total yield of 80% (240 g.) by reworking the distillates.

A solution of 240 g. (1.58 mol.) of the mixed 1,8,8-trimethyl-3-azabicyclo[3.2.1]octenes in 500 cc. of methanol was treated with 1 g. of Adams' catalyst and 5 g. of charcoal for reduction at 25° under 1500 p.s.i. The temperature rose to 43° during the reduction, which was completed in 3 hr. Careful removal of solvent left a quantitative yield of camphidine (243 g.). The camphoraceous base was distilled with some difficulty because of its volatility b.p. *ca.* 150° (200 mm.); small quantities were purified by sublimation, m.p. 168–170°.

Anal. Calcd. for $C_{10}H_{19}N$: N,[11] 9.14. Found: N,[11] 8.84.

3-(2-Dimethylaminoethyl)-1,8,8-trimethyl-3-azabicyclo-[3.2.1]octane. A mixture of 7.7 g. (0.05 mol.) of camphidine and 5.5 g. (0.05 mol.) of 2-dimethylaminoethyl chloride was heated on the steam bath for 0.5 hr., an additional 7.7 g. of camphidine was added (because some camphidine had deposited in the condenser), and the mixture was heated for 3 hr. The cooled material was diluted with ether and a quantitative recovery (9.5 g.) of camphidine hydrochloride was obtained. The product was left as a golden oil (9.4 g., 84%) when the filtrates were concentrated. It passed over as a colorless oil at 64–65° (0.3 mm.).

---

[1] Present address: McNeil Laboratories, Inc., Philadelphia 32, Pennsylvania.

[2] G. Bilecki, *Med. Klinik*, **51**, 1516 (1956).

[3] Dr. Karl Thomae G.m.b.H., Belgian Patent **554,694**.

[4] L. M. Rice and C. H. Grogan, *J. Org. Chem.*, **22**, 185 (1957).

[5] L. M. Rice and C. H. Grogan, U. S. Patents **2,786,834**; **2,803,631**.

[6] C. H. Grogan and L. M. Rice, *J. Org. Chem.*, **22**, 1223 (1957).

[7] J. Tafel and K. Eckstein, *Ber.*, **34**, 3275 (1901).

[8] K. F. Schmidt and H. Klavehn, German Patent **583,565**, Frdl., **20**, 953 (1935).

[9] Analyses were performed in the Analytical Laboratories of this Institute, under the direction of Mr. M. E. Auerbach and Mr. K. D. Fleischer.

[10] Prepared according to H. Wolff, Organic Reactions (R. Adams, editor-in-chief), J. Wiley and Sons, New York, 1946, Vol. 3, p. 327.

[11] Basic nitrogen determined by acetous-perchloric acid method of G. Toennies and T. P. Callan, *J. Biol. Chem.*, **125**, 259 (1938).

Anal. Calcd. for $C_{14}H_{28}N_2$: C, 74.94; H, 12.58; N,[11] 12.59. Found: C, 74.71; H, 12.70; N,[11] 12.12.

Methobromide was formed in 90% yield when the camphidine derivative was treated with methyl bromide in hot acetone. It crystallized from ethanol-acetone as long needles, m.p. 246–247° dec.

Anal. Calcd. for $C_{15}H_{31}BrN_2$: Br, 25.03; N, 8.77. Found: Br, 25.2; N, 8.72.

1,6-Bis 1,8,8-trimethyl-3-azabicyclo[3.2.1]octan-3-yl hexane. Camphidine (7.7 g., 0.05 mol.), 1,6-dibromohexane (6.1 g., 0.025 mol.), anhydrous potassium carbonate (5.8 g., 0.04 mol.) and toluene (80 cc.) were stirred and refluxed for 20 hr., more camphidine (1.5 g., 0.01 mol.) and potassium carbonate (2.0 g., 0.015 mol.) were added and refluxing was resumed for 20 hr. longer. It was filtered and the filtrates extracted well with 4*N* hydrochloric acid. The base was liberated from the extracts, extracted with ether, and fractionated. 1,6-Bis 1,8,8-trimethyl-3-azabicyclo[3.2.1]octan-3-yl hexane was obtained as a golden oil (7.1 g., 73% yield) which boiled at 155–160° (0.22 mm.); n_D^{25} = 1.5010.

Anal. Calcd. for $C_{26}H_{28}N_2$: C, 80.34; H, 12.45; N, 7.21. Found: C, 80.33; H, 12.35; N, 7.17.

The *dihydrochloride* was prepared in ether and separated from ethanol-ether as a chalky solid, m.p. >300°.

Anal. Calcd. for $C_{26}H_{48}N_2 \cdot 2HCl$: C, 67.65; H, 10.92; Cl, 15.36. Found: C, 67.77; H, 10.61; Cl, 14.99.

STERLING-WINTHROP RESEARCH INSTITUTE
RENSSELAER, N. Y.

Dithiol Diesters of Long-Chain Acids[1]

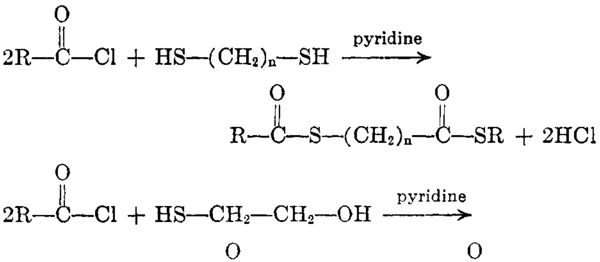
GEORGE S. SASIN, FREDERICK R. LONGO, ORESTES T. CHORTYK, PAUL A. GWINNER, AND RICHARD SASIN

Received May 20, 1959

Glycol diesters of long-chain acids are well known and useful compounds. A literature search revealed that the corresponding dithiol diesters, however, apparently are not known.

Continuing our systematic study[2] of thiol esters, this paper describes the preparation and some of the properties of 1,2-ethanedithiol, 1,3-propanedithiol, 1,4-butanedithiol, and 1,5-pentanedithiol diesters of decanoic, dodecanoic tetradecanoic, hexadecanoic, and octadecanoic acids, as well as the 2-mercaptoethanol diesters of the above mentioned acids. Also prepared were 1,2-ethanedithiol and 1,4-butanedithiol dioctanoates.

The esters were prepared by the action of dithiols or 2-mercaptoethanol on acyl halides in the presence of pyridine.



$$2R{-}\overset{O}{\overset{\|}{C}}{-}Cl + HS{-}(CH_2)_n{-}SH \xrightarrow{\text{pyridine}} R{-}\overset{O}{\overset{\|}{C}}{-}S{-}(CH_2)_n{-}\overset{O}{\overset{\|}{C}}{-}SR + 2HCl$$

$$2R{-}\overset{O}{\overset{\|}{C}}{-}Cl + HS{-}CH_2{-}CH_2{-}OH \xrightarrow{\text{pyridine}} R{-}\overset{O}{\overset{\|}{C}}{-}S{-}CH_2{-}CH_2{-}O{-}\overset{O}{\overset{\|}{C}}R + 2HCl$$

n = 2–5 R = C_9H_{19}, $C_{11}H_{23}$, $C_{13}H_{27}$, $C_{15}H_{31}$, $C_{17}H_{35}$

The properties of the esters, yields obtained and analytical data are summarized in Tables I and II.

When the reaction was carried out in the absence of pyridine, impure products were obtained and repeated recrystallizations of these products failed to purify them. Traces of unreacted acids were removed from the crude esters by chromatography on Florisil.

The dithiol diesters prepared are white crystalline solids. The lower members are sparingly soluble in ethanol and very soluble in acetone. Their solubility decreases in these solvents with increasing molecular weight. The lower members have a distinct mercaptan-like odor while the higher members are odorless.

Each of the five series of the dithiol diesters shows an alternation in melting points. Figure 1 represents the plot of the melting points of dithiol diesters against the number of carbon atoms in thiols. As in most homologous series, the even members melt at a higher temperature than the odd members. The reverse is true for alkanethiol esters.[3]

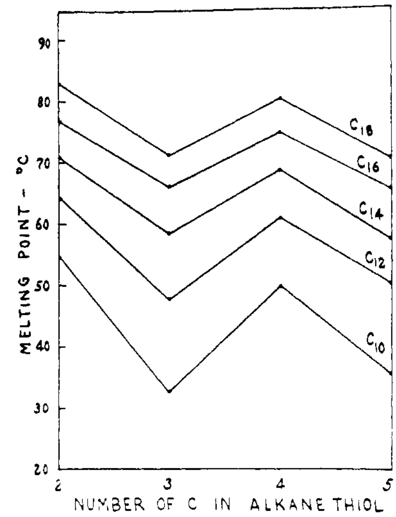


Fig. 1. Melting points of dithiol diesters

It is interesting to note that the 2-mercaptoethanol diesters melt at a lower temperature than either the corresponding 1,2-ethanedithiol or 1,2-ethane diesters.[4]

1,2-Ethanedithiol and 1,5-pentanedithiol dioctadecanoates reacted with methanol in the presence of a trace of sodium methoxide to form methyl octadecanoate by heating the reaction mixture on a steam bath for 12 hr.

---

(1) Taken in part from Senior Theses submitted by Paul A. Gwinner and Orestes T. Chortyk.

(2) Previous paper in this series is: *J. Org. Chem.*, **24**, 1143 (1959).

(3) R. Sasin, W. F. Ashley, J. W. Manning, Jr., A. Paolini, Jr., and G. S. Sasin, *J. Am. Oil Chem. Soc.*, **35**, 192 (1958).

(4) Ralston, A. W., *Fatty Acids and Their Derivatives*, John Wiley & Sons, New York, 1948, p. 528.