appropriate anthranilic acid[5] with phosgene.[6] The physical data for the various anthranilamides and 1,2,3-benzotriazin-4(3H)ones prepared are listed in tables I and II, respectively. These compounds were found to be essentially devoid of biological activity[1] on pharmacological evaluation in experimental animals.

EXPERIMENTAL[7]

The following examples are given to illustrate the methods used to prepare the compounds listed in Tables I and II. In general the experimental details varied very little from preparation to preparation.

4-Chloroisatoic anhydride. Phosgene was bubbled at room temperature through a solution of 85.8 g. (0.500 mole) of 4-chloroanthranilic acid[8] and 33.5 g. (0.316 mole) of sodium carbonate in 1750 ml. of water. The *p*H of the reaction mixture was maintained at 6–7 by a steady addition of an aqueous solution of 19.5 g. (0.184 mole) of sodium carbonate. After all of the carbonate was consumed, phosgene bubbling was continued until the *p*H dropped to about 2. The solid was filtered, washed with two 250-ml. portions of cold water, and air dried to yield 78.4 g. (79.5%) of white solid decomposing at 217°. A twice recrystallized sample from ethanol melted at 278–282° dec.

Anal. Calcd. for $C_8H_4ClNO_3$: C, 48.6; H, 2.01; Cl, 17.9; N, 7.09. Found: C, 48.7; H, 2.50; Cl, 18.2; N, 7.30.

The following two compounds were prepared by the above procedure.

5-Chloroisatoic anhydride[9] m.p. 278–281°; yield (87%).

Anal. Calcd. for $C_8H_4ClNO_3$: C, 48.6; H, 2.01; Cl, 17.9; N, 7.09. Found: C, 48.6; H, 2.23; Cl, 18.3; N, 7.33.

3,5-Dichloroisatoic anhydride, m.p. 251–253° dec.; lit.[9] m.p. 254–256°; yield (68%).

4-Chloroanthranilamide. A mixture of 12.0 g. (0.0608 mole) of 4-chloroisatoic anhydride and 304 ml. (0.608 mole) of 2*N* ammonium hydroxide was mechanically stirred for 4 hr. The solid was filtered and air-dried to yield 3.3 g. (32%) of crystalline, white product melting at 182–184°. An analytical sample was prepared by recrystallizing the crude twice from ethanol. The analytical data for this compound and the other substituted anthranilamides prepared similarly is given in Table I.

7-Chloro-1,2,3-benzotriazin-4(3H)one (Method A). To an ice-cold suspension of 3.12 g. (0.0183 mole) of 4-chloroanthranilamide in 20 ml. of water and 5.6 ml. of concd. hydrochloric acid was added a solution of 1.32 g. (0.0193 mole) of sodium nitrite in 10 ml. of water over 45 min. while maintaining the reaction temperature between 0–5°. The resultant orange mixture was treated with 7 ml. of 10*N* sodium hydroxide. The mixture changed to an orange solution, which was stirred for 10 min. and then acidified to *p*H 2 with concd. hydrochloric acid to give an orange solid which was filtered, washed with ice-water and air-dried; yield, 1.57 g. (47.3%), m.p. 179–181°. A sample recrystallized twice from ethanol afforded white needles melting at 215–216° dec.

The analytical data for this compound and the other analogous compounds is given in Table II. The dialkylaminoalkyl benzotriazinones, because of their amphoteric nature, were extracted from the reaction mixtures at neutral *p*H with chloroform.

7-Chloro-3-(γ-dimethylamino)propyl-1,2,3-benzotriazin-4(3H)one (Method B). To a solution of 0.75 g. (0.014 mole) of sodium methoxide in 50 ml. of anhydrous ethanol, was added 2.40 g. (0.0132 mole) of 7-chloro-1,2,3-benzotriazin-4(3H)one. After refluxing the mixture for 10 min., it was treated with 1.60 g. (0.0132 mole) of 3-dimethylaminopropyl chloride and then refluxed for 40 hr. The mixture was filtered hot, and the filtrate was concentrated *in vacuo* to a yellow sirup which solidified on cooling to a waxy solid melting at 43–46°. This solid was converted to the hydrochloride with ethanolic hydrochloric acid. The crystalline hydrochloride weighed 2.2 g. (57%) and melted at 256° dec.

7-Chloro-3-(β-dimethylamino)ethyl-1,2,3-benzotriazin-4(3H)one (Method C). A suspension of 7.0 g. (0.032 mole) of methyl-4-chloroanthranilate[8] hydrochloride in 35 ml. of water was treated gradually with a solution of 2.6 g. (0.038 mole) of sodium nitrite in 15 ml. of water at 0–5° over 20 min. The resultant diazonium salt solution was diluted to 350 ml. with ice water and then 5.0 g. (0.57 mole) of β-dimethylaminoethylamine was added over 10 min. The reaction mixture was stirred for 45 min. longer, and the resulting orange-yellow suspension was extracted thoroughly with ether. The pooled extracts were dried over anhydrous magnesium sulfate, and then concentrated *in vacuo* to a brown sirup. An alcoholic solution of this sirup in 15 ml. of solvent was treated with ethanolic hydrochloric acid and the precipitated hydrochloride was filtered and dried; yield, 4.4 g. (47%); m.p. 241–245° dec. The analytical sample was recrystallized from 95% ethanol, m.p. 267–270° dec.

Acknowledgment. We wish to express our appreciation to Mr. L. Brancone and his staff for the microanalytical results, to Dr. J. H. Clark and his staff for certain large scale preparations of intermediates, and to Mrs. J. L. Frederick for technical assistance on a part of this work.

ORGANIC CHEMICAL RESEARCH SECTION
LEDERLE LABORATORIES DIVISION
AMERICAN CYANAMID CO.
PEARL RIVER, N. Y.

---

[5] The substituted anthranilic acids were either purchased from a commercial source or prepared by known methods.

[6] In the case of 3,5-dichloroanthranilamide the best method of preparation was found to be that of F. E. Shiebley, *J. Org. Chem.*, **3**, 414 (1938).

[7] All melting points are uncorrected.

[8] R. E. Lutz, G. Ashburn, J. A. Freek, R. H. Jordan, N. H. Leake, T. A. Martin, R. J. Rowlett, Jr., and J. W. Wilson, *J. Am. Chem. Soc.*, **68**, 1285 (1946).

[9] R. Dorsch, *J. prakt. Chem.*, [2] **33**, 45–51 (1886).

Synthesis of the Sulfur Analogs of Batyl and Chimyl Alcohols

D. DAVID LAWSON, HORACE R. GETZ,
AND DONALD A. MILLER

Received June 6, 1960

The occurrence of α-glyceryl ethers in the nonsaponifiable residues of oils from various marine animals[1,2] has been reported especially in those of the elasmobranch group. Recently batyl alcohol (I) has been isolated also from sources other

---

[1] M. Tsujimoto and Y. Toyama, *Chem. Umschau Gebiete Fette, Öle, Wachse u. Harze*, **29**, 27 (1922); *Chem. Umschau Gebiete Fette, Öle, Wachse u. Harze*, **31**, 13, 135, 153 (1924); *Chem. Zentr.*, I, 878 (1922).

[2] I. M. Heilbron and W. M. Owens, *J. Chem. Soc.*, 942 (1928).

TABLE I

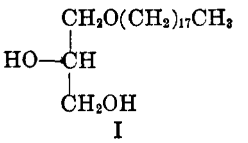
2,3-Dihydroxypropyl Alkyl Sulfide $CH_2(OH)CH(OH)CH_2S—R$

Alkyl R	Yield, %	M.P.	Formula	Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found	Sulfur, % Calcd.	Sulfur, % Found
Decane	60	44–45	$C_{13}H_{28}SO_2$	62.48	63.00	11.35	11.32	12.90	12.76
Dodecane	68	50–51	$C_{15}H_{32}SO_2$	65.15	65.09	11.66	11.77	11.59	11.52
Hexadecane	82	76–77	$C_{19}H_{40}SO_2$	68.61	68.46	12.12	12.21	9.64	9.53
Octadecane	91	74–75	$C_{21}H_{44}SO_2$	69.93	70.10	12.29	12.45	8.89	8.81

TABLE II

2,3-Dihydroxypropyl Alkyl Sulfone $CH_2(OH)CH(OH)CH_2SO_2R$

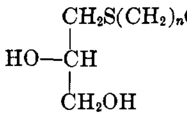
Alkyl R	Yield, %	M.P.	Formula	Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found	Sulfur, % Calcd.	Sulfur, % Found
Decane	70	92–93	$C_{13}H_{28}SO_4$	55.67	55.74	10.06	10.07	11.43	11.28
Dodecane	74	93–94	$C_{15}H_{32}SO_4$	58.39	58.36	10.45	10.49	10.39	10.25
Hexadecane	85	103–104	$C_{19}H_{40}SO_4$	62.76	62.57	10.81	11.01	8.82	8.70
Octadecane	95	105–106	$C_{21}H_{33}SO_4$	64.23	64.45	11.29	11.32	8.16	8.00



$$\begin{array}{l} \quad CH_2O(CH_2)_{17}CH_3 \\ \quad | \\ HO—CH \\ \quad | \\ \quad CH_2OH \end{array}$$

I

than marine in nature.[3,4] This indicates that the α-glyceryl ethers are fairly widespread components of animal lipid systems. This has led us to prepare the sulfur analogs of chimyl alcohol (II) and batyl alcohol (III) and related compounds as part of our search of potential tuberculostatic agents.



$$\begin{array}{l} \quad CH_2S(CH_2)_nCH_3 \\ \quad | \\ HO—CH \\ \quad | \\ \quad CH_2OH \end{array}$$

II. $n = 15$

III. $n = 17$

The synthesis used is a modification of the Williamson reaction. The potassium mercaptide of α-thioglycerine is formed *in situ* and the alkylation is effected by the appropriate long chain alkyl iodide or bromide in high yield, giving the required sulfides[5] as excellent crystalline compounds. The sulfides were then oxidized to the sulfones by the use of peracetic acid, the course of the oxidation being followed by infrared spectra.

Due to the very insoluble nature of the thiochimyl alcohol (2,3-dihydroxypropylhexadecane sulfide) and thiobatyl alcohol (2,3-dihydroxypropyloctadecane sulfide) and their sulfones, we have also prepared the shorter chain alkane derivatives which have more desirable solubility properties. The results of the biological testing will be reported elsewhere.

EXPERIMENTAL

Starting materials. The alkyl iodides were prepared by treating the appropriate alcohol with red phosphorus and iodine.[6] The alkyl bromides were obtained from Humphrey Wilkinson, Inc., North Haven, Conn., and were used without any further purification. The α-thioglycerol was generously furnished by Evans Chemetics, Inc., Waterloo, N. Y., and assayed 89.4% thioglycerol; it was used without any further purification. All melting points were obtained on Fisher-Johns melting point apparatus and all compounds reported are racemic.

General procedure for preparation of 2,3-dihydroxypropyl alkyl sulfides. A mixture of 11.2 g. of α-thioglycerine 0.1 mole of an alkyl iodide or bromide was dissolved in 200 ml. of 95% ethyl alcohol. With stirring under a nitrogen atmosphere 105 ml. of 1*N* alcoholic potassium hydroxide solution was added dropwise over a 30-min. period. The reaction mixture was allowed to stand for 10 hr., then diluted with 1 l. of water and cooled. The crystalline sulfide was collected and washed with water (10°) and recrystallized from methanol.

General procedure for preparation of 2,3-dihydroxypropylalkyl sulfones. To a mixture of 0.05 mole of 2,3-dihydroxypropyl alkyl sulfide in 150 ml. acetic acid was added dropwise 30 ml. of 30% hydrogen peroxide with stirring over a 2-hr. period. The reaction mixture was allowed to stand for 20 hr. at room temperature. The acetic acid solution was then diluted with 500 ml. water and cooled. The crystalline sulfone was collected and washed with water (10°) and recrystallized from methanol. The infrared spectra have a strong band at 1300–1350 cm.$^{-1}$ with a much weaker band at 1160–1140 cm.$^{-1}$ The sulfones tended to have higher melting points than their corresponding sulfides.

The Hastings Foundation
Altadena, Calif.

---

(3) E. Hardigger, L. Ruzicka, and E. Tagmann, *Helv. Chim. Acta,* **26,** 2205 (1943).

(4) H. N. Holmer, R. E. Corbet, W. B. Berger, N. Kornblum, and W. Alexander, *J. Am. Chem. Soc.,* **63,** 2607 (1941).

(5) R. L. Shriner, H. C. Struck, and W. J. Jorison, *J. Am. Chem. Soc.,* **52,** 2066 (1930).

(6) R. Smith, *J. Chem. Soc.,* 738 (1932).