Evidence for α-Sulfonation in the Reaction of Palmitic Acid with Sulfur Trioxide[1]

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The reaction of sulfur trioxide or chlorosulfonic acid with the lower molecular weight normal saturated fatty acids has been reported to give sulfonation at the α-carbon atom,[2–4] Hemilian[2a] prepared a sulfobutyric acid from chlorosulfonic acid and butyric acid. Comparison of physical form, degree of hydration and solubility of several salts with those from the reaction of ammonium sulfite with ethyl α-bromobutyrate and ethyl β-chlorobutyrate showed α-sulfonation. A sulfopropionic acid, apparently the product of direct sulfonation, has been resolved into optical antipodes, proving α- rather than β-substitution.[5] Further evidence[6] for α- rather than β- or γ-sulfonation exists in the values for the solubility of the barium sulfobutyrates (α-isomer, 7.11% at 16°; β-isomer, 22.7% at 29.8°), the melting point of the acid aniline salt (α-isomer, 175°; β-isomer, 162°) and the molecular rotation of the neutral barium salts (d,α-isomer, $-32.2°$; d-β-isomer $+18.5°$). The mechanism of the α-sulfonation of the lower fatty acids has been discussed recently.[7]

α-Sulfonation has been assumed[8] but has not been established in the case of the higher fatty acids. We present data here, based on X-ray diffraction patterns, on the structure of disodium sulfopalmitate prepared from liquid sulfur trioxide and palmitic acid. This compound and some of its homologs have been shown to have detergent properties.[9] The evidence for α-sulfonation involves the Hell–Volhard–Zelinskiĭ reaction, which has been shown by Hell and Jordanoff to give only α-bromination. The bromine atom of ethyl α-bromopalmitate was replaced by CN, and the hydrolysis and decarboxylation products were identified.[10] Still further evidence for α-bromination is in the fact that fatty acids which have no α-hydrogen atom cannot be brominated[11] and that bromopalmitic acid can be hydrolyzed and oxidized to pentadecanoic acid.[12]

As a reference standard, sodium α-sulfopalmitic acid was prepared from α-bromopalmitamide by the Strecker reaction[13] and from α-bromopalmitic acid by conversion to α-mercaptopalmitic acid and oxidation. The latter method was preferred. Although both the monosodium and disodium salts formed well-defined crystalline platelets, X-ray diffraction patterns of salts prepared by direct sulfonation and by indirect methods could not be compared because the diffraction lines were relatively few and somewhat diffuse. Reaction of sodium sulfopalmitic acid with phosphorus pentabromide and ammonia gave bromopalmitamide, which was suitable for X-ray comparison.

The decomposition of secondary alkyl sulfonyl halides to the corresponding halide has been reported,[2a,14] but it is not a well-known reaction. α-Bromopalmitic acid was converted to the mercaptan, oxidized to the sulfonic acid, and then allowed to react with phosphorus pentabromide and ammonia as shown by the equations

$$C_{14}H_{29}CHBrCO_2H \xrightarrow[2,\ NaOH]{1,\ SC(NH_2)_2}$$

$$C_{14}H_{29}CHSHCO_2Na \xrightarrow[Na_2CO_3]{Br_2} C_{14}H_{29}CH(SO_3Na)CO_2Na$$

$$C_{14}H_{29}CH(SO_3Na)CO_2H \xrightarrow{PBr_5} C_{14}H_{29}CHBrCOBr \xrightarrow{NH_3} C_{14}H_{29}CHBrCONH_2$$

Table I presents the chemical analyses and melting points for bromopalmitamide samples obtained by (A) α-bromination, (B) sulfonation of palmitic acid to form sodium sulfopalmitic acid and reaction with phosphorus pentabromide and ammonia, and (C) α-bromination, conversion to mercaptan, oxidation to sodium α-sulfopalmitic acid and reaction with phosphorus pentabromide and ammonia. The small amount of impurity indicated by the lower bromine content of sample (C) had no effect on the X-ray pattern. The melting points of a mixture of A with B, B with C, and A with C showed no depression.

TABLE I

ANALYSES AND MELTING POINTS OF BROMOPALMITAMIDES

	A Hell–Volhard–Zelinskiĭ reaction	B Sulfonated palmitic acid $+PBr_5+$ NH_3	C Oxidation of sodium α-mercaptopalmitate $+PBr_5+$ NH_3	Calculated for $C_{16}H_{32}$-BrNO
Nitrogen	4.04	4.16	4.11	4.19
Bromine	24.07	23.95	23.21	23.90
Carbon	57.20	57.40	57.91	57.48
Hydrogen	9.47	9.43	9.83	9.64
Melting point, °C.	84.6–84.9	82.7–83.7	83.9–84.6	85[a] 88[b]

[a] G. Ponzio, *Gazz. chim. ital.*, **41**, I, 781 (1911). [b] See text footnote 13.

Table II shows the interplanar spacings and relative intensities of the three compounds. The structure is the same within the limits of experimental error. Although the structure might not change with the position of the bromine atom along the chain, a marked change in the relative intensities of some of the diffraction lines would be expected, as was observed in the case of the isomeric dihydroxy fatty acids.[15] However, comparison of

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[1] From one of the laboratories of the Bureau of Agricultural and Industrial Chemistry, Agricultural Research Administration, U. S. Department of Agriculture. Article not copyrighted. This paper was presented at the 5th meeting-in-miniature of the Philadelphia section, American Chemical Society, January 29, 1953.

[2] (a) W. Hemilian, *Ann.*, **176**, 1 (1875); (b) H. J. Backer and J. V. Dubsky, *Rec. trav. chim.*, **39**, 694 (1920).

[3] H. J. Backer and J. H. de Boer, *ibid.*, **43**, 297, 420 (1924).

[4] H. J. Backer and M. Toxopéus, *ibid.*, **45**, 890 (1926).

[5] A. P. N. Franchimont and H. J. Backer, *ibid.*, **39**, 689, 751 (1920).

[6] H. J. Backer and A. Bloemen, *ibid.*, **45**, 100, 110 (1926).

[7] J. H. de Boer, *ibid.*, **71**, 814 (1952).

[8] Günther, PB 30081 (1932).

[9] A. J. Stirton, J. K. Weil, Anna A. Stawitzke and S. James, *J. Am. Oil Chemists' Soc.*, **29**, 198 (1952).

[10] C. Hell and C. Jordanoff, *Ber.*, **24**, 987 (1891).

[11] S. Reformatzky, *ibid.*, **23**, 1594 (1890).

[12] H. Mendel and J. Coops, *Rec. trav. chim.*, **58**, 1133 (1939).

[13] T. N. Mehta and D. M. Trivedi, *Melliand Textilber.*, **21**, 288 (1940).

[14] M. H. Gold and L. J. Druker, *J. Org. Chem.*, **16**, 1510 (1951).

[15] E. S. Lutton, W. F. Huber, A. J. Mabis and C. B. Stewart, THIS JOURNAL, **73**, 5206 (1951).

the relative intensities of diffraction lines of the three substances showed no differences. The three bromopalmitamides are therefore identical. The sulfonation of palmitic acid with sulfur trioxide appears to be as specific as the Hell–Volhard–Zelinskiĭ reaction. Only monosubstitution seems to occur and only at the α-carbon atom.

Experimental[16]

α-Bromopalmitic Acid and Amide.—α-Bromopalmitoyl bromide was prepared as described by Hell and Jordanoff.[17] Bromine was added to a mixture of palmitic acid (neut. equiv. 257.7, m.p. 61.0–61.3°) and red phosphorus over a period of one hour. The mixture was heated from 40 to 95° for five hours.

α-Bromopalmitoyl bromide was hydrolyzed with ice to give α-bromopalmitic acid. After purification by two crystallizations from acetone and three crystallizations from petroleum ether, the yield was 85%, m.p. 49.4–49.8°.

Anal. Calcd. for $C_{16}H_{31}O_2Br$: neut. equiv., 335.3. Found: neut. equiv., 336.4.

α-Bromopalmitamide was prepared by pouring α-bromopalmitoyl bromide into an excess of aqueous ammonia and ice. It was purified by three crystallizations from alcohol and one crystallization from petroleum ether to give a 50% yield. Table I, Column A, lists the chemical analyses and melting points.

α-Mercaptopalmitic Acid.—The method of Nicolet and Bate[18] was followed in preparing α-mercaptopalmitic acid from α-bromopalmitic acid without purification of the tetradecyl pseudothiohydantoin. Three crystallizations from 95% ethanol gave the required α-mercaptopalmitic acid in a 47% yield based on α-bromopalmitic acid, m.p. 71.6–71.8°.

Anal. Calcd. for $C_{16}H_{32}O_2S$: neut. equiv., 288.5. Found: neut. equiv., 289.3.

TABLE II

DIFFRACTION PATTERNS OF BROMOPALMITAMIDES

A Hell–Volhard–Zelinskiĭ reaction		B Sulfonated palmitic acid + PBr_5 + NH_3		C Oxidation of Na α-mercaptopalmitate + PBr_5 + NH_3	
I, obsd.	*d*, Å.	*I*, obsd.	*d*, Å.	*I*, obsd.	*d*, Å.
M	15.5	M	15.7	M	15.6
W^{++}	10.30	W^{++}	10.35	W^{++}	10.32
M^{-}	7.71	M^{-}	7.73	M^{-}	7.74
W^{+++}	6.18	W^{+++}	6.21	W^{+++}	6.20
W^{-}	5.73	W^{-}	5.73	W^{-}	5.73
M	5.13	M	5.16	M	5.17
W^{-}	4.58	W^{-}	4.60	W^{-}	4.58
W^{++}	4.41	W^{++}	4.43	W^{++}	4.42
S^{-}	4.16	S^{-}	4.17	S^{-}	4.17
W	4.03	W	4.03	W	4.02
M^{++}	3.77	M^{++}	3.78	M^{++}	3.79
W^{++}	3.67	W^{++}	3.67	W^{++}	3.68
W	3.44	W	3.44	W	3.44
W^{+}	3.35	W^{+}	3.35	W^{+}	3.35
W^{+++}	3.15	W^{+++}	3.16	W^{+++}	3.16
W	3.07	W	3.06	W	3.07
W^{+}	2.90	W^{+}	2.91	W^{+}	2.90
W^{-}	2.82	W^{-}	2.83	W^{-}	2.82
W^{+}	2.67	W^{+}	2.67	W^{+}	2.67
W	2.60	W	2.61	W	2.60
W	2.48	W	2.49	W	2.49
W	2.43	W	2.43	W	2.43
W^{+++}	2.26	W^{+++}	2.26	W^{+++}	2.26

Sodium α-Sulfopalmitic Acid from Sodium α-Mercaptopalmitate.—The oxidation was a modification of the method of Levene, Mori and Mikeska.[19] Sodium α-mercaptopalmitate was treated with sodium hypobromite in an aqueous solution buffered with excess sodium carbonate. After being acidified to form the monosodium salt, it was purified by two crystallizations from water and one extraction with hot acetone; the yield was 43%.

Anal. Calcd. for $C_{16}H_{31}O_5SNa$: S, 8.95; neut. equiv., 358.5. Found: S, 8.98; neut. equiv., 358.1.

Direct Sulfonation of Palmitic Acid.—A 60% excess of sulfur trioxide was added slowly to palmitic acid in tetrachloroethylene.[9] The product was neutralized to form the monosodium salt, twice extracted with hot acetone and crystallized from water four times, giving a 61% yield. Yields of 80–90% of the monosodium salt of monosulfonated palmitic or stearic acid can be obtained with less rigorous purification.

Anal. Calcd. for $C_{16}H_{31}O_5SNa$: S, 8.95; neut. equiv., 358.5. Found: S, 8.92; neut. equiv., 358.9.

Bromopalmitamide from Sodium Sulfopalmitic Acid.—Phosphorus pentabromide, 0.10 mole, freshly prepared from phosphorus tribromide and bromine,[20] was intimately mixed with 0.04 mole of sodium sulfopalmitic acid and warmed on the steam-bath for two hours. The resultant viscous liquid was stirred into 60 ml. of 29% aqueous ammonia and 200 g. of cracked ice. The crude product was purified by two crystallizations from 95% ethanol and one crystallization from petroleum ether. The yield of purified product was 40%. Table I lists the chemical analyses and the melting points of bromopalmitamides made by the reaction of phosphorus pentabromide and ammonia with sulfonated palmitic acid (B), and from the mercaptan oxidation product (C).

X-Ray Technique.—The X-ray diffraction patterns were recorded with a powder camera of 14.32 cm. diameter; CuKα radiation, λ = 1.5405 Å. was used. Specimens were prepared for the camera by passing a finely ground sample on a glass slide and cutting from it a narrow section 0.3 mm. thick. Table II reports interplanar spacings and relative diffraction intensities for α-bromopalmitamide prepared by the three methods.

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[16] All melting points corrected.

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Studies on the Mucohalic Acids. III. The Chlorobromo Acids. Mechanism of Formation of the Mucohalic Acids

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In the course of investigations on halogenated furoic acids, Hill and Jackson[1] reported that a mucohalic acid, $C_4H_2BrClO_3$ (I), containing both bromine and chlorine atoms could be formed by the action of excess aqueous bromine on what was considered to be 3-chloro-2-furoic acid. Vander Wal[2] later showed that Hill's chlorofuroic acid was actually the 4-chloro-isomer but the "mucochlorobromic" acid derivable therefrom was never completely characterized. Our interest in replacement reactions involving the halogens of the mucohalic acids and esters has led us to study this product.

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[2] R. J. Vander Wal, *Iowa State Coll. J. Sci.*, **11**, 128 (1936).