CXXIV.—*The Unsaponifiable Matter from the Oils of Elasmobranch Fish. Part IV. The Establishment of the Structure of Selachyl and Batyl Alcohols as Monoglyceryl Ethers.*

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THE fact that selachyl and batyl alcohols, either together or associated with squalene, are common constituents of the unsaponifiable matter of many shark- and ray-liver oils was first demonstrated by Tsujimoto and Toyama (*Chem. Umschau*, 1922, **29**, 27, 35, 43), who showed that batyl alcohol is the saturated dihydro-derivative of selachyl alcohol, is dihydric, and has a molecular formula corresponding to either $C_{20}H_{42}O_3$ or $C_{21}H_{44}O_3$.

In a further important contribution to the subject, Toyama (*Chem. Umschau*, 1924, **31**, 61, 153) concluded that the latter formula was in better agreement with the analytical results of a carefully purified specimen of the alcohol (m. p. 70·4—71°) regenerated from its diacetyl derivative. The discovery of another saturated alcohol of formula $C_{19}H_{40}O_3$, to which the name chimyl alcohol (m. p. 60·5—61·5°) was given, was also reported, and attention was directed to an interesting and possibly important relationship between the alcohols present in sperm oil (Tsujimoto, *Chem. Umschau*, 1925, **32**, 127) and those under discussion. For instance, a compound of the composition of batyl alcohol would result from octadecyl alcohol in the following manner :

$$C_{18}H_{38}O + C_3H_8O_3 - H_2O = C_{21}H_{44}O_3.$$

In a similar way, selachyl alcohol would be related to oleyl alcohol, and chimyl alcohol to cetyl alcohol.

It is curious that, in spite of the above far-sighted implication, the structures of these alcohols, to which so much attention has recently been directed in connexion with work on vitamin-*A* (Drummond, Channon, and Coward, *Biochem. J.*, 1925, **19**, 1047), have not up to the present been worked out. The only definite observations hitherto made regarding their constitutions deal with selachyl alcohol, the acetate of which Toyama (*loc. cit.*) found yielded nonoic acid on oxidation with potassium permanganate, and its dry distillation led to the isolation of a fraction identical with oleyl alcohol. These results permit of the formula of selachyl acetate being expressed as $CH_3{\cdot}[CH_2]_7{\cdot}CH{:}CH{\cdot}C_{11}H_{21}O(O{\cdot}CO{\cdot}CH_3)_2$. The present communication deals with the structure of batyl alcohol which we isolated from the liver oil of *Centrophorus granulosus* (compare Chapman, *Analyst*, 1927, **52**, 622), in which it occurs in small quantity associated with selachyl alcohol and squalene. Our first inquiry was directed towards elucidation of the nature of the groups associated with the third oxygen atom. According to Weidemann (*Biochem. J.*, 1926, **20**, 685), this is present as a methoxy-group, a result deduced apparently from a Zeisel determination and calculation of the precipitated silver iodide as methoxyl. It seemed to us, however, from *a priori* reasoning extremely unlikely that such a grouping would exist in a substance obviously related to the natural fats, and, as detailed in the experimental part, repetition of this work speedily convinced us that, although the molecule certainly contained an ether oxygen atom, it was not present as methoxyl. On the other hand, we have been able definitely to establish the formation of octadecyl iodide by the action of hydriodic acid on batyl alcohol, and have verified this by conversion of the iodide into octadecyl alcohol, which was identified both by a mixed melting-point determination with an authentic specimen, and also through the preparation of its characteristic phenylurethane. Unfortunately, owing to the small amount of material at our disposal, we have been unable to detect the presence of *iso*propyl iodide, but there can be absolutely no doubt that batyl alcohol is in effect a monoglyceryl ether of octadecyl alcohol to which one or other of the following formulæ may be ascribed :

(I.) $C_{18}H_{37}{\cdot}O{\cdot}CH_2{\cdot}CH(OH){\cdot}CH_2{\cdot}OH$ $C_{18}H_{37}{\cdot}O{\cdot}CH(CH_2{\cdot}OH)_2$ (II.)

From the ease of formation of the diacetyl derivative and the phenylurethane, which we have now prepared and which, owing to its definite crystalline character and sharp melting point, is an excellent derivative for the identification of the alcohol, we rather favour formula (II).

We are at present engaged in attempted syntheses of both types of compound, and also other derivatives. It follows from the above that formulæ can also be ascribed to both selachyl alcohol and chimyl alcohol, and that the connexion referred to above on which Toyama (*loc. cit.*) focussed attention is real in all respects.

The occurrence of these glyceryl ethers in nature, forming as they do a link between the fats and waxes, is a matter of much biological interest. The following expression clearly indicates the three types and their inter-relation :

Fat $(R{\cdot}CO{\cdot}O{\cdot})_3C_3H_5$
Wax $R{\cdot}CO{\cdot}OR'$
Ethers $R'O{\cdot}C_3H_5(OH)_2$.

EXPERIMENTAL.

The residual liver oil (2500 g.) obtained from *Centrophorus granulosus*, after removal of the bulk of the squalene by distillation at 3 mm. (compare Heilbron, Kamm, and Owens, J., 1926, 1638), was saponified by refluxing with boiling alcoholic sodium hydroxide (90 g. in 2500 c.c. of industrial alcohol) for 5 hours. The alcohol was removed as far as possible by evaporation in a vacuum and the semi-solid residue was mixed with silver sand and thoroughly dried by stirring at 70°, after which it was thinned out with glass beads and extracted with hot acetone in a large Soxhlet extractor until the runnings were colourless. After removal of the acetone, the solid material was extracted with ether, the solution repeatedly washed with water to remove soap and dried over sodium sulphate, and the ether distilled. A solution of the residue in pentane, when vigorously stirred at —10°, deposited a very fine crystalline solid, which was collected on kieselguhr. After all oily matter had been washed away with ice-cold pentane, the material was dissolved out of the kieselguhr with dry ether. The crude solid obtained after removal of the ether gave, after one crystallisation from alcohol, lustrous plates, m. p. 60—63° (40 g.). This method of working up the batyl alcohol is preferred to the one described by Tsujimoto and Toyama (*Chem. Umschau*, 1922, **29**, 28), whereby the alcohol is obtained by freezing an acetone solution of the unsaponifiable matter. The solid material prepared as above failed to show the presence of cholesterol when tested with digitonin.

The pure alcohol was obtained, after repeated fractional crystallisation from alcohol, in colourless laminæ, m. p. 69—70° (27 g.) (Found : C, 72·8, 72·8, 72·9; H, 12·8, 12·6, 12·9. Calc. for $C_{21}H_{44}O_3$: C, 73·2; H, 12·9%).

The *phenylurethane* was prepared by heating the alcohol (1 g.) to boiling with an excess of phenylcarbimide (3 c.c.) and then refluxing the mixture with dry benzene (15 c.c.) for 3 hours. After the solvent and the excess of phenylcarbimide had been removed at 15 mm., the residue was extracted with cold dry ether, the solution filtered, and the ether evaporated. The urethane was first crystallised three times from benzene and finally from either alcohol or aqueous acetone, from which it separated in tufts of long, irregular needles, m. p. 98° (Found : C, 71·9; H, 9·3; N, 5·2. $C_{35}H_{54}O_5N_2$ requires C, 72·2; H, 9·3; N, 4·8%).

Batyl p-*nitrobenzoate*. The alcohol (3·4 g.), dissolved in cold pyridine (25 c.c.), was slowly treated with *p*-nitrobenzoyl chloride (3·6 g.). Some heat was evolved and the whole set to a dark red, crystalline mass, which was warmed for 1 hour at 50°. After

12 hours, the reaction mixture was poured into ice-cold dilute hydrochloric acid, and the precipitated solid dissolved in ether. The ethereal solution was washed with dilute sodium carbonate solution and with water and dried over sodium sulphate, and the ether allowed to evaporate. By repeated extraction of the resinous product with dry methyl alcohol, the p-*nitrobenzoate* was obtained in pale yellow, fern-like clusters, m. p. 53—54°, which darkened somewhat on exposure to sunlight [Found : C, 63·2, 63·2; H, 7·9, 8·1; N, 4·3. $C_{21}H_{42}O(O{\cdot}CO{\cdot}C_6H_4{\cdot}NO_2)_2,2CH_3{\cdot}OH$ requires C, 62·9; H, 8·2; N, 4·0%].

Examination of Batyl Alcohol for the Presence of Alkyloxy-radicals.—A qualitative experiment by the Pregl–Zeisel method gave a precipitate of silver iodide, showing the presence of an ether oxygen atom in the molecule (Weidemann, *loc. cit.*). That the ether, however, was not easily ruptured was evidenced by the fact that the decomposition was not complete in the ordinary time (20 minutes) and that variable values, calculated as –OMe, were obtained : 20 minutes, 6·22, 8·8; 25 minutes, 7·4; 30 minutes, 8·2%.

Test for methoxyl. The testing solution consisted of aqueous trimethylamine (24 drops of 33%) in 2 c.c. of absolute alcohol (compare Willstätter and Utzenger, *Annalen*, 1911, **382**, 148). Batyl alcohol (15 mg.) was treated with hydriodic acid (3·2 c.c., *d* 1·7) for 30 minutes, but no precipitate appeared in the absorbing liquid. On removal of the alcohol under reduced pressure, a small amount of an oil having a garlic-like odour (possibly allyl iodide) was obtained. As vanillin (8 mg.) on similar treatment gave in two consecutive experiments a copious crystalline precipitate of tetramethylammonium iodide, it can be inferred that no methoxyl group is present in batyl alcohol, and this probably also applies to ethoxyl and propoxyl.

Formation of Octadecyl Iodide.—Batyl alcohol (10 g.) was refluxed with hydriodic acid (30 c.c., *d* 1·7) for 1 hour. The reaction mixture was taken up in ether, and the solution washed successively with dilute aqueous sodium bisulphite, sodium carbonate solution, and water. After drying, the ether was removed and the residual pale yellow oil poured into alcohol, from which needles immediately separated. These were thrice recrystallised from alcohol–acetone, from which the octadecyl iodide separated in lustrous needles, m. p. 33°. Gascard gives 33·5° (*Ann. Chim.*, 1921, **15**, 340) [Found : (micro) C, 56·8; H, 9·8; I, 32·3, 34·2; *M*, 415. Calc. for $C_{18}H_{37}I$: C, 56·8; H, 9·7; I, 33·5%; *M*, 380].

Preparation of Octadecane.—The iodide (2 g.) was dissolved in a mixture of acetic acid (20 c.c.), previously saturated with hydrogen chloride, and ether (10 c.c.). Zinc dust (5 g.) was then added during

½ hour. The reaction, which was at first rapid but gradually abated, was completed by warming on the water-bath and allowing the ether to evaporate. The mixture was boiled for a further ½ hour, the solvent was then removed by distillation under diminished pressure, and the residue was poured into water and extracted with ether. The ethereal solution was washed with dilute aqueous sodium carbonate and with water, dried, and evaporated. The residual low-melting solid still contained a small amount of halogen, which was removed by repeating the above process. The crude hydrocarbon was repeatedly crystallised from ether–methyl alcohol, from which it separated in long, colourless needles, m. p. 28—29° (Gascard, *loc. cit.*, gives 27—28°), very readily soluble in ether, hexane, and acetone [Found : (micro) C, 84·7 ; H, 15·0 ; *M*, 274, 264. Calc. for $C_{18}H_{38}$: C, 85·0 ; H, 15·0% ; *M*, 254]. The reduction of the iodide to octadecane can also be carried out by Stephen's method (J., 1914, **105**, 1050) with zinc in an alcohol–acetic acid solution.

Octadecyl Methyl Ether.—The iodide (2 g.) was refluxed for 2 hours with an excess of alcoholic sodium methoxide (2 g. of sodium in 20 c.c. of methyl alcohol) and the reaction mixture was diluted with water and extracted with ether. The extract was thoroughly washed with water and dried over anhydrous sodium sulphate. *Octadecyl methyl ether* crystallised from ether–methyl alcohol in very fine laminæ, m. p. 30—31° [Found : (micro) C, 80·3 ; H, 13·9. $C_{19}H_{40}O$ requires C, 80·3 ; H, 14·1%].

Octadecyl Alcohol.—The iodide (4 g.) together with silver acetate (4 g.) was refluxed with absolute alcohol (100 c.c.) for 6 hours. The supernatant liquid was decanted, the residue well washed with acetone, and the combined liquids were worked up as described in the preparation of octadecane. The acetate, obtained as a colourless, low-melting solid, was without further purification heated under reflux with methyl-alcoholic potassium hydroxide. The hydrolysed product was diluted with water and extracted with ether and, after drying and removal of solvent, the crude octadecyl alcohol was crystallised from acetone and finally from 92% alcohol. It formed colourless crystals, m. p. 57—58°, alone or mixed with an authentic specimen. The alcohol was also characterised by the preparation of its phenylurethane, which crystallised from alcohol in feathery needles, m. p. 77—78° (André and Francis give 79—80° ; *Compt. rend.*, 1926, **183**, 663) [Found : (micro) C, 76·9 ; H, 11·2 ; N, 3·7. Calc. for $C_{25}H_{43}O_2N$: C, 77·1 ; H, 11·1 ; N, 3·6%].

Detection of Selachyl Alcohol.—The presence of this alcohol in the liver oil of *Centrophorus granulosus* has already been detected by Chapman (*loc. cit.*), whose statement regarding the impossibility of separating it entirely from squalene (spinacene) we fully confirm.

Chapman hydrogenated it to batyl alcohol by means of platinum-black, and we have obtained the same result using a nickel catalyst at 150°, and working on the residues obtained after removal of as much solid batyl alcohol as possible.

In conclusion, we desire to thank the Food Investigation Board for a grant which has enabled this research to be carried out.

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