[CONTRIBUTION FROM THE DEPARTMENT OF APPLIED CHEMISTRY, FACULTY OF ENGINEERING, TOKYO IMPERIAL UNIVERSITY]

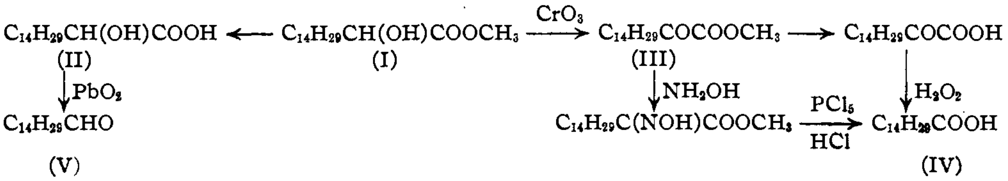
Studies on Wool Wax. I. Lanopalmic Acid

BY TSUTOMU KUWATA

Though lanopalmic acid, $C_{16}H_{32}O_3$, a hydroxy acid found by Darmstaedter and Lifschütz,[1] has been considered a characteristic acid constituent of wool wax, there have been some ambiguous points yet to be cleared. Drummond and Baker[2] stated that they could obtain no evidence of such a high hydroxy acid in wool fat. Abraham and Hilditch[3] assumed the formula of $C_{15}H_{30}O_3$ instead of $C_{16}H_{32}O_3$ for lanopalmic acid. The author has succeeded, while studying the acid constituents of wool wax from Merino sheep, in isolating pure lanopalmic acid and proved it to be a stereoisomer of synthetic α-hydroxypalmitic acid.

Lanopalmic acid (II) is readily soluble in 90% methanol and separates out from aqueous methanol or chloroform as a magma of radiated needle structure. The properties of the acid are similar to those reported by Darmstaedter and Lifschütz. The acid resembles in some respects α-hydroxypalmitic acid but differs markedly in the crystallizability from organic solvents. The methyl ester of lanopalmic acid (I) crystallizes in foliate fine needles from ligroin and melts at 45–46°, whereas synthetic α-hydroxypalmitic acid methyl ester crystallizes in stout needles melting at 58–59°.

Lanopalminonic acid methyl ester (III) which was produced by the oxidation of I with chromic acid is identical with α-ketopalmitic acid methyl ester. By the cleavage of the oxime of III through Beckmann rearrangement or by the oxidation of lanopalminonic acid with hydrogen peroxide, *n*-pentadecylic acid (IV) has been produced. Direct oxidation of II with lead peroxide has given *n*-pentadecyl aldehyde (V).



$$\begin{tikzcd}
\mathrm{C_{14}H_{29}CH(OH)COOH}\ \mathrm{(II)} \arrow[d, "\mathrm{PbO_2}"] & \mathrm{C_{14}H_{29}CH(OH)COOCH_3}\ \mathrm{(I)} \arrow[l] \arrow[r, "\mathrm{CrO_3}"] & \mathrm{C_{14}H_{29}COCOOCH_3}\ \mathrm{(III)} \arrow[r] \arrow[d, "\mathrm{NH_2OH}"] & \mathrm{C_{14}H_{29}COCOOH} \arrow[d, "\mathrm{H_2O_2}"] \\
\mathrm{C_{14}H_{29}CHO}\ \mathrm{(V)} & & \mathrm{C_{14}H_{29}C(NOH)COOCH_3} \arrow[r, "\mathrm{PCl_5}", "\mathrm{HCl}"'] & \mathrm{C_{14}H_{29}COOH}\ \mathrm{(IV)}
\end{tikzcd}$$

It is of much interest, not only from a chemical point of view but from a biochemical, that a stereoisomer of higher α-hydroxy acid as lanopalmic acid is present in wool wax secreted from the skin organ of the sheep.

Experimental Part

Lanopalmic Acid Methyl Ester (I).—Wool wax which was separated from the scouring liquor of Merino sheep's wool with DeLaval centrifuge was saponified with 3 *N* alcoholic potash, and the mixed wool acids were obtained from the soap solution by the usual method. The mixed acids contained a non-acidic resinous substance soluble in dilute alcohol and showed saponification no. 168.2 and neutralization no. 141.6. By means of 90% aqueous methanol, lanopalmic acid, together with lower acids and resinous substance, was extracted from the mixed acids and then converted to methyl ester by reacting potassium hydroxide and dimethyl sulfate. In order to remove the resinous substance, the crude ester was dissolved in low boiling ligroin in which the resinous substance is insoluble. The extract, after distilling off the solvent, was distilled under reduced pressure. The distillate 225–235° (5 mm.) gave pure lanopalmic acid methyl ester by one crystallization from low boiling ligroin. The content of lanopalmic acid in the mixed acids was found to be about 7%.

Lanopalmic acid methyl ester had b. p. 230–231° (5 mm.), m. p. 45–46°, $[\alpha]_D$ −1.5° (*c*, 10.0 in alcohol) and was soluble in most organic solvents.

Anal. Calcd. for $C_{16}H_{31}O_3CH_3$: C, 71.26; H, 11.97; saponification no., 196.2. Found: C, 71.64; H, 11.34; saponification no., 197.3.

Lanopalmic acid (II) prepared by the saponification of I had m. p. 86–87°, $[\alpha]_D$ −1.0° (*c*, 5.2 in alcohol). Its magnesium salt was insoluble in boiling alcohol and melted above 280°.

Anal. Calcd. for $C_{16}H_{32}O_3$: C, 70.52; H, 11.85. Found: C, 70.90; H, 11.94.

Lanopalminonic Acid Methyl Ester (III).—Three grams of lanopalmic acid methyl ester dissolved in 50 cc. of glacial acetic acid was oxidized with 0.8 g. of chromic anhydride in 10 cc. of 50% acetic acid at ordinary temperatures. After standing overnight, the oxidized ester was precipitated by adding water and crystallized from petroleum ether; yield 2.8 g. Lanopalminonic acid methyl ester was small plates of silky luster and melted at 47–47.5°. No depression was observed in the melting point on admixture with synthetic α-ketopalmitic acid methyl ester.

Anal. Calcd. for $C_{16}H_{29}O_3CH_3$: C, 71.76; H, 11.36. Found: C, 71.80; H, 11.15.

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(1) L. Darmstaedter and J. Lifschütz, *Ber.*, **29**, 2891 (1896); **31**, 97 (1898).

(2) J. C. Drummond and L. C. Baker, *J. Soc. Chem. Ind.*, **48**, 234T (1929).

(3) E. Abraham and T. P. Hilditch, *ibid.*, **54**, 398T (1935).

Synthesis of α-Ketopalmitic Acid Methyl Ester.—α-Hydroxypalmitic acid (m. p. 86°) was prepared from α-bromopalmitic acid as described by Le Sueur.[4] On treating 5 g. of silver salt of α-hydroxypalmitic acid with 4 g. of methyl iodide in benzene solution on a water-bath for five hours, 3.5 g. of α-hydroxypalmitic acid methyl ester was obtained which melted at 58–59°. The ester dissolved less in cold petroleum ether or benzene in comparison with lanopalmic acid methyl ester. The oxidation of α-hydroxypalmitic acid methyl ester to α-ketopalmitic acid methyl ester was carried out in a manner similar to the preparation of lanopalminonic acid methyl ester, and the resulting product was purified by recrystallization from aqueous methanol and then from low boiling ligroin; glistening laminas melting at 47°.

Anal. Calcd. for $C_{14}H_{29}COCO_2CH_3$: C, 71.76; H, 11.36. Found: C, 71.54; H, 11.10.

Cleavage of the Oxime of III.—For the oximation of III, 3 g. of the substance was added to 10 cc. of aqueous–alcoholic solution containing 0.74 g. of hydroxylamine hydrochloride and 1.1 g. of sodium carbonate, and allowed to stand for three days at room temperature. Dilution with water precipitated the oxime, which was filtered, washed and dried. It weighed 3.1 g. and showed a m. p. of 92° after recrystallization from petroleum ether.

Anal. Calcd. for $C_{17}H_{32}O_2NOH$: N, 4.68. Found: N, 4.62.

In order to carry out a Beckmann rearrangement, 2 g. of the oxime was treated with excess of phosphorus pentachloride in ethereal solution at −5°. The acid amide purified by the crystallization from petroleum ether melted at 111–112°.

Anal. Calcd. for $C_{17}H_{33}O_3N$: N, 4.68. Found: N, 4.41.

One gram of the acid amide obtained above was hydrolyzed at 150–160° for six hours in a sealed tube containing 20 cc. of concentrated hydrochloric acid yielding 0.6 g. of pentadecylic acid which melted at 52–52.5° and showed no depression of m. p. on addition of *n*-pentadecylic acid. The amide of the acid melted at 102°, the m. p. of *n*-pentadecylic acid amide.

Anal. Calcd. for $C_{15}H_{30}O_2$: C, 74.31; H, 12.48; mol. wt., 242. Found: C, 74.52; H, 12.60; mol. wt. (from neutralization no.), 243. Calcd. for acid amide ($C_{15}H_{31}ON$): N, 5.81. Found: N, 5.87.

Oxidation of Lanopalminonic Acid with Hydrogen Peroxide.—Lanopalminonic acid obtained by the saponification of III with dilute alcoholic potash is flat needles from ligroin melting at 69°. On mixing the keto acid (1.6 g.) with 30% hydrogen peroxide solution (10 cc.), the evolution of gas was observed. After the stirring was continued as long as any gas was evolved, the oxidized acid (1.4 g.) was collected on filter paper, washed and crystallized from methanol; laminas of silky luster, m. p. 52°. The acid did not depress the m. p. of *n*-pentadecylic acid.

Oxidation of Lanopalmic Acid with Lead Peroxide.—A mixture of 0.5 g. of lanopalmic acid and 5 g. of lead peroxide was distilled in a current of steam. An oily substance distilling over and having an odor of higher aldehyde is treated with hydroxylamine and the oxime was recrystallized, after removing acid substances, from aqueous methanol; yield 1.3 g. The oxime obtained was small needles and melted at 83–84°.

Anal. Calcd. for $C_{15}H_{30}NOH$: N, 5.81. Found: N, 5.88.

Acknowledgment.—It is a pleasant duty of the author to thank Prof. Y. Tanaka for kind advice and encouragement.

Summary

Lanopalmic acid has been isolated from the mixed acids of Merino sheep wool wax, and the acid has been proved to be a stereoisomer of α-hydroxypalmitic acid.

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[4] Le Sueur, *J. Chem. Soc.*, **87**, 1895 (1905).

[CONTRIBUTION FROM THE DEPARTMENT OF BIOLOGICAL AND COLLOIDAL CHEMISTRY, THE HEBREW UNIVERSITY]

The Behavior of Peptides when Heated in β-Naphthol

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When **dipeptides** are heated in β-naphthol at a temperature of 135–150°, they dissolve and form diketopiperazines which may be separated in good yield on cooling by removing the β-naphthol with ether. By this method the respective anhydrides of the following dipeptides were obtained: *d,l*-leucyl-*d,l*-leucine, *d,l*-leucylglycine, glycyl-*d,l*-leucine, *d,l*-valylglycine, *d,l*-alanyl-*d,l*-leucine, glycyl-*d,l*-phenylalanine.

Benzoylated dipeptides, such as benzoyl-*d,l*-leucylglycine, benzoylglycylglycine and benzoylglycyl-*d,l*-phenylalanine dissolve, but suffer no ring closure and may be recovered unchanged. Glycylglycine which is insoluble in hot β-naphthol also remains unchanged.

If **tripeptides** are treated in the same manner, the terminal amino acid in the free form and the diketopiperazine corresponding to the first amino acid, which contains the free amino group, and to the second adjacent amino acid of the peptide, are obtained.

In this fashion glycine and *d,l*-alanyl-*d,l*-leucine