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10(S)-HYDROXY-6(R),9(S)-OXIDOHEXADECANOIC ACID, A NEW ACID IN WOOL FAT

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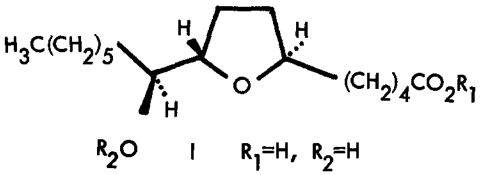
One of the most remarkable features of wool fat is that it contains a number of unusual fatty acids in large quantity (2). In our effort to characterize these acids, we have isolated a new homologous series of fatty acids containing a hydroxyl group and a tetrahydrofurane ring. The present paper deals with the elucidation of the structure of the major constituent.

Wool fat obtained from either corriedale or merino wool was saponified and the resulted acid fraction was chromatographed on silica gel. A more polar fraction was methylated and further chromatographed on silica gel which yielded a polar ester fraction (ca. 1%) (3). The main component which amounted to ca. 85% of the ester fraction was obtained by chromatography using deactivated silica gel and its alkaline hydrolysis yielded a crystalline acid (I), $C_{16}H_{30}O_4$, m.p. 43.5°, $[\alpha]_D^{18}$ +10.8° (4), methyl ester (II), liquid, $[\alpha]_D$ +9.8°, ν 3600, 1730 cm^{-1}, δ 0.90 (3H, br.t, $-C\underline{H}_3$), 2.25 (1H, s, $-O\underline{H}$), 3.25 (1H, m, $-C\underline{H}-OH$), 3.63 (3H, s, $-OC\underline{H}_3$), 3.75 (2H, m, $-C\underline{H}O-$), methyl ester acetate (III), ν 1735 cm^{-1}, br. (no ν_{OH}), δ 0.90 (3H, t, $-C\underline{H}_3$), 2.00 (3H, s, $-CO-C\underline{H}_3$), 3.62 (3H, s, $-OC\underline{H}_3$), 3.90 (2H, m, $-C\underline{H}-O-$), 4.75 (1H, m, $-C\underline{H}OAc$). The formation of these derivatives revealed the presence of a hydroxyl and a carboxyl groups accounting for three oxygen atoms out of four in the molecule. Thus the remaining oxygen atom is present as a cyclic ether, since II resists to catalytic hydrogenation and peracid oxidation.

Oxidation (CrO_3/Py) of II yielded the ketoester (IV), liquid, $[\alpha]_D^{18}$ +17.8°, $[\theta]_{302}$ +745°, ν 1725 cm^{-1}, δ 3.60 (3H, s, $-OC\underline{H}_3$), 3.90 (1H, br.m, $-C\underline{H}O-$), 4.20 (1H, t, J=7.0, $-O-C\underline{H}-CO-$), m/e 298 (M^+), which, on prolonged oxidation, afforded n-heptanoic acid (V) and the γ-lactonic ester (VI), liquid, ν 1770, 1730 cm^{-1}, δ 4.38 (1H, m, $-C\underline{H}O-$), m/e 200 (M^+), 169 (M-31), 85 ($C_4H_5O_2^+$)(5). The compounds IV was also cleaved to give V and VI by perbenzoic acid or even by air. These observations established the planer structure of I.

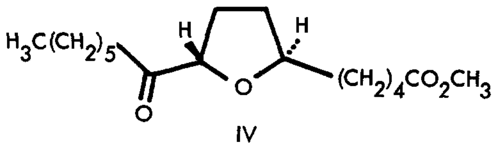


I R_1=H, R_2=H

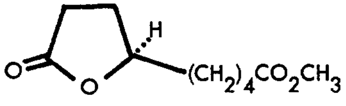
II R_1=CH_3, R_2=H

III R_1=CH_3, R_2=Ac

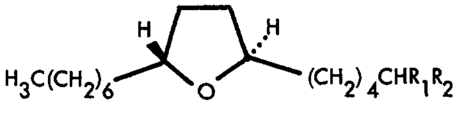
VII R_1=CH_3, R_2=COC_6H_5



IV



VI



VIII R_1=H, R_2=OH

IX R_1, R_2=O

X R_1=H, R_2=CH_2CH_3

The stereochemistry of I, with three asymmetric centers, was determined in the following way. The positive Cotton effect $[\theta]_{216}$ +440° of the lactonic ester VI revealed the R-configuration at C_6 following the Klyne's lactone sector rule (6,7). For the elucidation of absolute stereochemistry at $C_{10'}$, the methyl-ester benzoate (VII), liquid, $[\alpha]_D$ +13.0°, m/e 404 (M^+), was prepared and the benzoate rule (8) was applied. The molecular rotation difference due to benzoylation was dextrorotatory, $\Delta[M]_D$= +23.5°, $\Delta[M]_{400}$=+62.4° establishing S-configuration at the asymmetric center. The stereochemistry at C_9 was elucidated in relation to that of C_6. Thus, tosylation of II (product, liquid) followed by LAH reduction yielded the oxido alcohol (VIII), liquid, $[\alpha]_D^{23}$ +7.7°, ν 3450 cm^{-1}, δ 0.90 (3H, t, $-C\underline{H}_3$), 3.47 (3H, m, $-C\underline{H}_2-O\underline{H}$), 3.87 (2H, m, $-C\underline{H}-O-$), which was oxidized by CrO_3-pyridine complex (9) to the corresponding aldehyde (IX), liquid, ν 2750, 1730 cm^{-1}, δ 0.91 (3H, t, $-C\underline{H}_3$), 3.83 (2H, m, $-C\underline{H}-O-$), 9.83 (1H, br.s, $-C\underline{H}O$). IX was subjected to Grignard reaction using ethyl magnesium bromide and the product, liquid, δ 0.90 (6H, t, $-C\underline{H}_3$), 3.50 (1H, m, $-C\underline{H}-OH$), 3.80 (2H, m, $-C\underline{H}-O-$) was tosylated and, without isolation of product, reduced with LAH to yield the ether (X) with the same side chains, liquid, δ 0.88 (6H, t, $-C\underline{H}_3$), 3.77 (2H, m, $-C\underline{H}-O-$), m/e 268 ($\overset{+}{M}$). Since X clearly shows optical activity, $[\alpha]_D$ +20.2°, $[\alpha]_{270}$ +570°, the two identical side chains should be trans to each other.

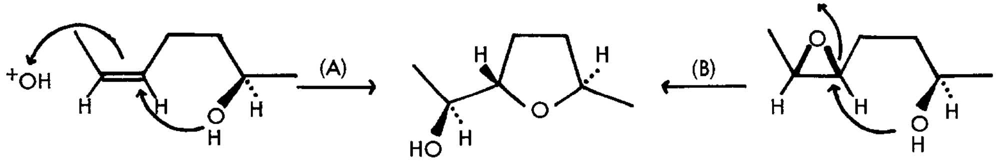
As was mentioned before, the polar ester fraction is a mixture of at least five components composition of which is listed in the TABLE. After acetylation of the fraction, each component was separated by glc. and identified by their mass spectra. The principal ions observed in MS are also listed in the TABLE.

<u>TABLE</u>. Methyl 10-Hydroxy-6,9-oxidoalkanoates in Polar ester Fraction of Wool Fat.

$R-CHOH-C_8H_{14}O-CO_2Me$	Contents	Mass Fragments of Methyl Ester Acetate (m/e)				
R	(%)	M-OMe	 $C_4H_8CO_2Me$	$185-H_2O$	185-MeOH	167-MeOH $153-H_2O$
$CH_3(CH_2)_3$	5.7	283	185 (b.p.)	167	153	135
$CH_3(CH_2)_4$	3.4	297	185 (b.p.)	167	153	135
$CH_3(CH_2)_5$	85.0	311	185 (b.p.)	167	153	135
$CH_3(CH_2)_6$	1.5	325	185 (b.p.)	167	153	135
$CH_3(CH_2)_7$	4.4	339	185 (b.p.)	167	153	135

Although the molecular ions are not observed in all cases, the ion $(M-CH_3O)^+$ being the largest fragment, all compounds exhibits a base peak at m/e 185 (10) and this ion eliminates MeOH and H_2O. The lower fragment regions (m/e < 185) are almost superimposable for all compounds.

The consequential structural details suggest the plausible biogenesis of these fatty acids. The precursors, 6(R)-hydroxy-cis-alk-9-enoic acids of $C_{14}-C_{18}$ (11), are converted to I and its homologs either by the direct addition of $H\overset{+}{O}$ and C_6-OH to the double bond in a concerted manner (A) or through the intervening 9,10-epoxides (B) (5b, 12). It is of interest that the oxygen atoms attack the molecule only from the same side in the two separate oxygenation processes (those at C_6 and C_{10}).



The further separation of wool fat is in progress.

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References and Footnotes

1) On leave of absence from Tokyo Research Laboratory, Kao Soap Co. Ltd., 2-1-3, Bunka, Sumida-ku, Tokyo, Japan.

2) T. Kuwada and Y. Ishii, J. Soc. Chem. Ind. Japan, 39, suppl. 317 (1935), T. Nozoe, S. Katsura and S.L. Lin, J. Chem. Soc. Japan, 60, 486 (1939), T. Nozoe, Japanese patent, 147111 (1941), 147677, 153628-9, 153634 (1942) (cf. C.A., 43, 3219 (1949)), A.W. Weitkawp, J. Amer. Chem. Soc., 67, 447 (1945).

3) Although the ester fraction gives a single spot on TLC (SiO_2), it exhibits 5 peaks on glc (carbowax).

4) All new compounds described in this paper gave satisfactory elemental analyses as well as physico-chemical data.

5) For similar cleavage, see a) C.M.M. Halls and E.W. Warnhoff, Canad. J. Chem., 43, 3311 (1965). b) A. Chawla and S. Dev, Tetrahedron Letters, 4837 (1967).

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