62. *Tricosanoic and Tetracosanoic Acids and Certain Derivatives.*

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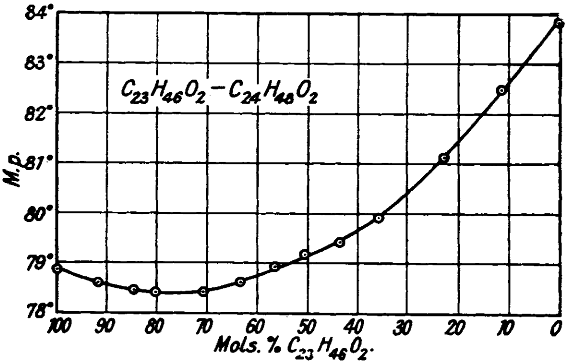
The identity of the acid obtained by the oxidation of cerebronic acid (Thierfelder, *Z. physiol. Chem.*, 1904, **43**, 21) has been the subject of considerable discussion (Klenk, *ibid.*, 1928, **174**, 214; Taylor and Levene, *J. Biol. Chem.*, 1929, **84**, 23; Klenk and Diebold, *Z. physiol. Chem.*, 1933, **215**, 79; Levene and Heymann, *J. Biol. Chem.*, 1933, **102**, 1); it is agreed that the substance is either *tricosanoic acid* or a mixture containing tetracosanoic acid. We have accordingly synthesised these acids by the method of Robinson and Robinson (J., 1925, **127**, 175; 1930, 745) and carefully characterised the pure substances by determinations of freezing and melting points with the thermometer immersed in the liquid.



The melting-point curve for the system tricosanoic acid–tetracosanoic acid shows that these acids form a continuous series of solid solutions with a minimum (type III, Roozeboom, *Z. physikal. Chem.*, 1899, **30**, 385), there being less than 0·5° difference in melting point between mixtures containing from 0 to 40% of tetracosanoic acid. Mixtures of acids containing an even number of carbon atoms, for example, tetracosanoic and hexacosanoic acids (Piper, Chibnall, and Williams, *Biochem. J.*, 1934, **28**, 2182; compare de Visser, *Rec. trav. chim.*, 1897, **17**, 182), show considerable depressions of melting point. But it has been shown that heptadecoic acid forms type III systems with either palmitic or stearic acid (Shriner, Fulton, and Burks, *J. Amer. Chem. Soc.*, 1933, **55**, 1494), and moreover there is no evidence in the " odd-even " systems of the non-congruent melting points which in the " even-even " systems indicate the existence of some " crystal compound " between the two acids. Thus the " even-odd " acid systems resemble the alcohol and the hydrocarbon systems (Smith, J., 1931, 802; 1932, 737). A specimen of the oxidation product of cerebronic acid was supplied by Professor Dr. E. Klenk, to whom our warmest thanks are due, but in view of the cryoscopic behaviour of tricosanoic and tetracosanoic acid mixtures it was found impossible to reach a definite conclusion in regard to its identity. It is hoped that an *X*-ray examination will throw more definite light on the matter.

In view of the frequent use of the method of mixed melting points in capillary tubes for the identification of long-chain compounds, it is necessary to point out that the method is often quite unreliable; the present is a clear case in point.

EXPERIMENTAL.

Lauryl Chloride.—Lauric acid was purified by fractionation of its ethyl ester, b. p. 140°/15 mm., followed by crystallisation of the acid recovered after hydrolysis of the middle fraction, to constant m. p. 43·7° (m. p. in a capillary tube, 44·8°). The chloride, b. p. 134°/9—10 mm., was obtained by the use of thionyl chloride.

Ethyl 11-*Bromoundecoate.*—This ester, b. p. 174°/10 mm., was obtained by esterification of the acid prepared by the method of Ashton and Smith (J., 1934, 1308); the difficulties reported by Walker and Lumsden (J., 1901, **79**, 1196) were not encountered.

13-*Ketotetracosanoic Acid.*—Acetoacetic ester (19 g.) was added to a cooled solution of sodium (2·7 g.) in the minimum quantity of alcohol. Ethyl 11-bromoundecoate (34 g.) was then added, and the mixture refluxed for 10 hours. The isolated product distilled at 197°/1·1 mm. (yield, 26·5 g. or 66%) (cf. G. M. Robinson, J., 1930, 745).

Sodium (3·5 g.) was granulated and mixed with a solution of the above ester (51 g.) in ether. When the sodium had disappeared, an ethereal solution of lauryl chloride (33 g.) was added. After being kept for 24 hours at room temperature, the mixture was refluxed for 1 hour. The precipitated sodium chloride was removed by washing with water, and the ether evaporated. The residue (75 g.) was shaken for 24 hours with 2·5% sodium hydroxide solution (300 c.c.), and the product isolated by acidification and extraction with ether. After the ether had been removed, 5% sulphuric acid (375 c.c.) was added, and the mixture boiled for 24 hours. The product was isolated in the same manner as before, 5% sodium hydroxide solution (375 c.c.) added, and the mixture boiled for 24 hours, a clear solution being obtained. On acidification an oil separated; this solidified on cooling and was collected (57·5 g.). After four crystallisations from alcohol and two from light petroleum, the *acid* had a constant m. p. 95° (yield, 16 g. or 33%) (Found: C, 75·9; H, 12·0. $C_{24}H_{46}O_3$ requires C, 75·4; H, 12·0%).

Tetracosanoic Acid.—13-Keto-*n*-tetracosanoic acid (5 g.) was reduced by Clemmensen's method (*Ber.*, 1913, **46**, 1837; cf. Le Sueur and Withers, J., 1915, **107**, 736). The product was extracted with boiling benzene. On cooling, the solution deposited crystals (flat plates), m. p. 83° (yield, 4·5 g. or 95%). Two crystallisations from acetone brought the m. p. to 84° (capillary tube) and this was not changed by two further recrystallisations from benzene (Meyer, Brod, and Soyka, *Monatsh.*, 1913, **34**, 1113, give m. p. 85·5—86°; Taylor, *J. Biol. Chem.*, 1931, **91**, 541, gives m. p. 84—85°). With the thermometer in the liquid, the acid froze at 82·7° and melted at 82·8°. This specimen was used in preliminary experiments in the system $C_{23}H_{46}O_2$–$C_{24}H_{28}O_2$.

Another specimen, synthesised in the same way, was purified as follows: (1) crystallised from benzene, it softened at 81°, m. p. 82—83° (capillary tube); (2) recrystallised from benzene, it softened and melted 0·5° higher (3 g.); (3) recrystallised from acetone, it softened at 83·5°, m. p. 83—84° (2·55 g.); (4) recrystallised from acetone, no change, m. p. 83·25° (Beckmann apparatus); (5) recrystallised from acetone; (6) recrystallised from acetone, f. p. 83·37°, m. p. 83·70° (2·2 g.); (7), (8) recrystallised from acetone, m. p. 83·8°; (9) recrystallised from *n*-propyl alcohol; (10) recrystallised from acetone, f. p. 83·5°, m. p. 83·8°, m. p. 83·5—84·5° (capillary tube). The acid behaved like a polymorphous substance, a transition occurring near the m. p. (Found: C, 78·4; H, 13·2. Calc. for $C_{24}H_{48}O_2$: C, 78·3; H, 13·0%).

2-*Bromotetracosanoic Acid.*—Dry bromine (4·9 g.) was slowly added to a mixture of molten tetracosanoic acid (3·1 g.) and red phosphorus (0·2 g.). Heating on the steam-bath was continued for 6 hours; an excess of bromine was then still present. The bromo-acid bromide was hydrolysed to the acid, which was collected by means of ether. The product, m. p. 71·5—72°, was recrystallised from light petroleum (yield, 3·2 g. of m. p. 72°, or 85%) (Taylor and Levene, *J. Biol. Chem.*, 1928, **80**, 609, give 69·5—70° as the m. p. of α-bromolignoceric acid).

2-*Hydroxytetracosanoic Acid.*—2-Bromotetracosanoic acid (3 g.) was heated with fused potassium acetate (1·5 g.) and acetic acid (6 c.c.) at 120° for 30 hours. The product was poured into water, collected, washed, and refluxed for 1½ hours with potassium hydroxide (1·5 g.) in alcoholic solution. The acid was precipitated by means of dilute hydrochloric acid and collected. Crystallisation from acetone gave colourless plates, m. p. 96° (yield, 2·2 g. or 85%). Two more crystallisations raised the m. p. to 99·5—100°, unaltered by further recrystallisation from benzene, ethyl alcohol and again from benzene (Taylor and Levene, *loc. cit.*, give 94—95° as the m. p. of α-hydroxylignoceric acid) (Found: C, 75·0; H, 12·5. Calc. for $C_{24}H_{48}O_3$: C, 75·0; H, 12·5%).

Undecoyl Chloride.—Pure undecenoic acid (50 g. of f. p. 24·5°), dissolved in alcohol, was reduced at room temperature in the presence of palladised charcoal. The product (50 g.), crystallised from light petroleum, had m. p. 28·5—29° (Levene and West, *J. Biol. Chem.*, 1914, **18**, 464, give m. p. 29°; Chuit, Boelsing, Hausser, and Malet, *Helv. Chim. Acta*, 1927, **10**, 113, give m. p. 29·5—30·5°). The acid was converted into the acid chloride, b. p. 130°/15 mm., by means of thionyl chloride.

Tricosanoic Acid.—Crude 13-ketotricosanoic acid (19 g.), prepared by substituting undecoyl chloride for lauryl chloride in the above-described synthesis of ketotetracosanoic acid, was reduced by Clemmensen's method, yielding a mixture of tricosanoic and myristic acids (14·5 g.). After three crystallisations from benzene the *tricosanoic acid* had m. p. 78·7° (m. p. in capillary tube, 79·5°) (Found: C, 78·1; H, 12·9. $C_{23}H_{46}O_2$ requires C, 78·0; H, 13·0%). After further crystallisations from benzene and acetone the acid (2·5 g.) had m. p. 79—80·5° (capillary tube), f. p. 78·5°, m. p. 78·6—78·8° (Beckmann apparatus, corr.). It was then recrystallised from pure benzene (100 c.c.) and again from 60 c.c., f. p. 78·60°, m. p. 78·80° (2·3 g.); recrystallised from benzene, m. p. 78·86°; and again from benzene and toluene, f. p. 78·75°, m. p. 78·86° (1·9 g.). The final purifications did not raise the m. p. to a large extent, but the gap between the f. p. and the m. p. was closed and the rate of crystallisation was increased.

Mixtures of Tricosanoic and Tetracosanoic Acids.—The m. p.'s were determined in the Beckmann-type apparatus (cf. Smith, *loc. cit.*), a short Anschütz thermometer being used; in the same apparatus, the f. p.'s were usually 0·05—0·1° lower than the m. p.'s. All the mixtures crystallised readily, and if portions were heated in capillary tubes of the usual size, the whole process of shrinking, softening, and melting occurred over a range of 1·5°.

The m. p.'s observed (see figure) were the following, in which the first figure of each pair recorded shows the mols. % of tricosanoic acid: 100, 78·85°; 91·8, 78·6°; 84·5, 78·45°; 80·1, 78·4°; 70·9, 78·4°; 63·3, 78·6°; 56·5, 78·9°; 50·5, 79·15°; 43·7, 79·4°; 36·0, 79·9°; 22·8, 81·1°; 11·5, 82·45°; 0·0 (100% $C_{24}H_{48}O_2$), 83·8°.

Only a small amount of the oxidation product of cerebronic acid (Klenk) was available and it was not possible to make a comparison with the synthetic acids by the Beckmann technique. A micro-method, however, gave the following results: synthetic tricosanoic acid, m. p. 78·6—78·7°; oxidation product (Klenk), m. p. 77·4—77·8°; a mixture of the foregoing (1 : 1), m. p. 78·0—78·4°. Synthetic tetracosanoic acid, m. p. 82·8°; oxidation product (Klenk), m. p. 77·4—77·8°; a mixture of 2 parts of tetracosanoic acid and 3 parts of the oxidation product had m. p. 78·2—78·5°.

It is not possible to draw definite conclusions from these results, but the oxidation product may be tricosanoic acid still contaminated with an acid of lower molecular weight.

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