

61. 15-Phenylpentadecoic Acid and 22-Phenylbehenic Acid.

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RAPER and WAYNE (*Biochem. J.*, 1928, **22**, 188) prepared 10-phenyldecoic acid * (cf. Borsche, *Ber.*, 1919, **52**, 2077) and found that when it was administered to dogs the amount recovered in the form of phenaceturic acid was less than that anticipated on the theory of quantitative β -oxidation of the fatty acid chain. The longer the chain in the acids of this series, the closer is the approximation to a normal fatty acid and hence we synthesised the *substances* named in the title with the object of studying the end products of their katabolism.

The synthetic method of Robinson and Robinson (*J.*, 1925, **127**, 175) was employed and the condensation products of ethyl sodio-13-keto-12-carbethoxymyristate with β -phenylpropionyl chloride and 10-phenyldecoyl chloride were hydrolysed in stages. The resulting keto-acids, 13-keto-15-phenylpentadecoic acid and 13-keto-22-phenylbehenic acid, respectively, were reduced by Clemmensen's method.

• The carboxyl group of the fatty acids is numbered 1.

Experiments with rabbits were carried out with the assistance of Dr. C. P. Stewart in the Department of Chemistry Applied to Medicine of Edinburgh University, and the authors are grateful to Professor G. Barger, F.R.S., for kindly providing the necessary facilities. The physical properties of the sodium salts of the acids, however, rendered them unsuitable for injection, and no evidence for the metabolism of the acids was obtained after feeding by stomach tube. The order of magnitude of the solubility of sodium 15-phenylpentadecate in water was: 35°, 0.8; 40°, 1.7; 65°, 17.0 g./1000 c.c. Sodium 22-phenylbehenate gave no true aqueous solutions, but formed metastable emulsions containing up to 10–15% of the salt. The p_H was near 10, but could be reduced to about 8 by the addition of bile salt. The more concentrated emulsions set to a translucent gel when kept at room temperature.

EXPERIMENTAL.

13-Keto-15-phenylpentadecic Acid, $\text{CH}_2\text{Ph}\cdot\text{CH}_2\cdot\text{CO}\cdot[\text{CH}_2]_{11}\cdot\text{CO}_2\text{H}$.—Ethyl sodio-13-keto-12-carbethoxymyristate (from 34.5 g. of the ester and 2.3 g. of granulated sodium) was prepared in boiling ethereal solution (300 c.c.) and, after cooling, β -phenylpropionyl chloride (17 g.) in ether (20 c.c.) was added. The mixture was kept for 24 hours and then refluxed for an hour; sodium chloride was removed by washing with water, and the solvent evaporated. The residue was shaken with 3% aqueous potassium hydroxide (1000 c.c.) for 12 hours and the products were collected after acidification and refluxed with 5% sulphuric acid (750 c.c.) for 24 hours. The organic products were again isolated and boiled with 3.5% aqueous potassium hydroxide (650 c.c.) for 12 hours. The material now precipitated by acid (air-dried, 32.5 g.) had m. p. 45–52°. Repeated crystallisation of a small specimen from light petroleum, benzene–light petroleum, carbon disulphide, and aqueous methyl alcohol gave a product, m. p. 67°, the carbon content of which was 3% lower than expected. The crude material (45 g.) was therefore crystallised once from light petroleum, affording 31 g., m. p. 61–64°, and phenylpropionic acid (7 g.). The ethyl ester was then prepared and fractionated, yielding (a) 0.5 g., b. p. 130–150°/12 mm., consisting of ethyl β -phenylpropionate; (b) 18 g., b. p. 145–160°/0.5 mm., consisting of ethyl 13-ketomyristate (see below); (c) 12.5 g. of residue, m. p. 33–35°. After saponification the crude acid from the residue had m. p. 60–63° (12 g.) and it separated from benzene eventually as white plates, m. p. 76–77° (Found: C, 75.8; H, 9.7. $\text{C}_{21}\text{H}_{32}\text{O}_3$ requires C, 75.9; H, 9.7%). The yield of ethyl ketomyristate was 46% and that of the *ketophenylpentadecic acid*, once crystallised from benzene, m. p. 72–74°, was 20%. The *semicarbazone* crystallised from alcohol in irregular prisms, m. p. 87–88° (Found: C, 67.7; H, 8.9; N, 10.6. $\text{C}_{22}\text{H}_{35}\text{O}_3\text{N}_3$ requires C, 67.8; H, 9.1; N, 10.8%).

Ethyl 13-ketomyristate (above) gave the same semicarbazone as the impure ester obtained by Ruzicka and Stoll (*Helv. Chim. Acta*, 1927, **10**, 691). The ester crystallised from chilled light petroleum in narrow prisms, m. p. 28–29° (Found: C, 71.5; H, 11.1. $\text{C}_{16}\text{H}_{30}\text{O}_3$ requires C, 71.1; H, 11.2%).

15-Phenylpentadecic Acid, $\text{CH}_2\text{Ph}\cdot[\text{CH}_2]_{13}\cdot\text{CO}_2\text{H}$.—Reduction of the foregoing keto-acid was effected by Clemmensen's method as modified by Le Sueur and Withers (J., 1915, **107**, 736): amalgamated zinc filings (20 g.) and concentrated hydrochloric acid (100 c.c.) were used to reduce 1 g. of the acid in 70–80 hours at the b. p., and the yield was 94%. The zinc was added in two portions, and the hydrochloric acid in many portions; occasionally the liquid was filtered through glass wool (which was later added to the zinc), and fresh hydrochloric acid employed. The *acid* crystallised from alcohol or light petroleum in white irregular prisms, m. p. 60–61° (Found: C, 79.1; H, 10.9. $\text{C}_{21}\text{H}_{34}\text{O}_2$ requires C, 79.2; H, 10.8%).

13-Keto-22-phenylbehenic Acid, $\text{CH}_2\text{Ph}\cdot[\text{CH}_2]_8\cdot\text{CO}\cdot[\text{CH}_2]_{11}\cdot\text{CO}_2\text{H}$.—10-Phenyldecoic acid (Raper and Wayne, *loc. cit.*) was converted into the chloride, b. p. 204°/14 mm. (some decomp.), by means of thionyl chloride. The *anilide*, obtained from the chloride and aniline, crystallised from aqueous alcohol in colourless needles, m. p. 71–72° (Found: C, 81.8; H, 9.0; N, 4.3. $\text{C}_{23}\text{H}_{29}\text{ON}$ requires C, 81.7; H, 9.0; N, 4.3%). Ethyl phenyldecoate, from the chloride and alcohol, had b. p. 199°/13 mm., 171°/0.3 mm.

The synthesis of the keto-acid followed exactly the lines of that already described, the β -phenylpropionyl chloride being replaced by 10-phenyldecoyl chloride (from 24.8 g. of the acid). The yield of crude acids was 40 g. and the related ethyl esters (32.5 g.) were fractionated, yielding 19 g. of a mixture of ethyl ketomyristate and ethyl phenyldecoate, b. p. 154–162°/0.45 mm., and 8.5 g. of a residue. The latter was hydrolysed, and the *ketophenylbehenic acid*

isolated; it separated from alcohol in white crystals, m. p. 81° (Found: C, 78.2; H, 10.5. $C_{28}H_{46}O_2$ requires C, 78.3; H, 10.8%).

22-Phenylbehenic Acid.—The keto-acid (4 g.) was reduced in the same way as ketophenylpentadecanoic acid; the product crystallised from acetone in irregular prisms, m. p. 81° (Found: C, 80.7; H, 11.5. $C_{28}H_{48}O_2$ requires C, 80.7; H, 11.6%). Mixed with the keto-acid, m. p. 81° , the depression was only 2° . This acid is readily soluble in alcohol, benzene, and warm ethyl acetate, sparingly soluble in cold ethyl acetate, and very sparingly soluble in boiling light petroleum. On a larger scale the crude products of hydrolysis of the $\beta\beta'$ -diketonic ester were reduced by means of amalgamated zinc and hydrochloric acid, and the products esterified and distilled. In this way ethyl myristate, b. p. $140-155^{\circ}/0.5$ mm., and ethyl phenyldecoate, b. p. $170-190^{\circ}/0.5$ mm., could be readily separated and purified by refractionation; the residual *ethyl phenylbehenate* crystallised from alcohol in white prisms, m. p. 53° (Found: C, 80.8; H, 11.8. $C_{30}H_{52}O_2$ requires C, 81.0; H, 11.8%). The yield of crude phenylbehenic acid was about 30%.

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