39. *Synthetic Long-chain Aliphatic Compounds. Part II. Erucic and Brassidic Acids. A New Olefin Synthesis.*

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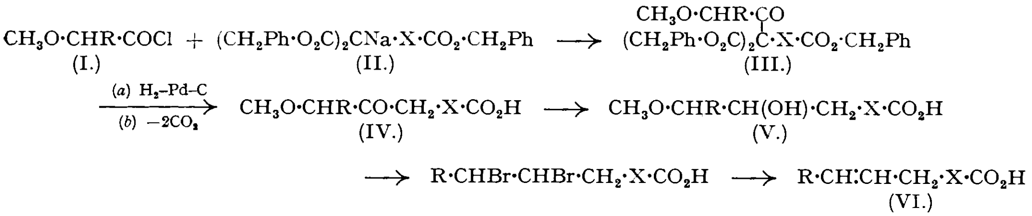
A new olefin synthesis, whereby methoxy-ketones (IV) are converted into the corresponding methoxy-alcohols (V) and thence, by successive treatment with hydrogen bromide and zinc, into the olefin (VI), has led to the total synthesis of erucic and brassidic acids (for a preliminary account of this work, see *Nature*, 1949, **163**, 95).

Concurrently with the synthesis of saturated acids (Part I, preceding paper), we were interested in developing a new and general method of synthesis of the corresponding unsaturated compounds, particularly since, at the time when these experiments were begun, the only general syntheses of olefinic acids (Noller and Bannerot, *J. Amer. Chem. Soc.*, 1934, **56**, 1563) were based on the method of Boord (*ibid.*, 1930, **52**, 3396). This synthesis, however, suffers from the disadvantage that the starting materials, αω-chloro-aldehydes, are difficult of access, although a later modification due to Baudart (*Compt. rend.*, 1943, **217**, 399; 1945, **220**, 404) has, to some extent, eased this situation.

Ruzicka, Plattner, and Widmer (*Helv. Chim. Acta*, 1942, **25**, 604, 1086) have recently developed a new method employing a symmetrical acyloin as intermediate. This method has since been modified by Baudart (*Bull. Soc. chim.*, 1946, [v], **13**, 87) to allow of the synthesis of the asymmetrical monobasic unsaturated acids. When this work was nearing completion, Ahmud and Strong (*J. Amer. Chem. Soc.*, 1948, **70**, 1699) reported a new general method based on the semi-hydrogenation of the corresponding acetylenic acid (cf. Bhattacharya, Saletore, and Simonsen, *J.*, 1928, 2678).[*]

Two routes, both employing our new ketone synthesis (*J.*, in the press), were available, one using the acyloin $R{\cdot}CH(OH){\cdot}CO{\cdot}[CH_2]_n{\cdot}CO_2H$ and starting from the appropriate α-acetyl-acid chloride, the other using the α-alkoxy-acid chloride (I) and the α-alkoxy-ketone (IV) in the following general manner:



$$\underset{(I.)}{CH_3O{\cdot}CHR{\cdot}COCl} + \underset{(II.)}{(CH_2Ph{\cdot}O_2C)_2CNa{\cdot}X{\cdot}CO_2{\cdot}CH_2Ph} \longrightarrow \underset{(III.)}{\overset{CH_3O{\cdot}CHR{\cdot}CO}{(CH_2Ph{\cdot}O_2C)_2C{\cdot}X{\cdot}CO_2{\cdot}CH_2Ph}}$$

$$\xrightarrow[(b)\ -2CO_2]{(a)\ H_2\text{-}Pd\text{-}C} \underset{(IV.)}{CH_3O{\cdot}CHR{\cdot}CO{\cdot}CH_2{\cdot}X{\cdot}CO_2H} \longrightarrow \underset{(V.)}{CH_3O{\cdot}CHR{\cdot}CH(OH){\cdot}CH_2{\cdot}X{\cdot}CO_2H}$$

$$\longrightarrow R{\cdot}CHBr{\cdot}CHBr{\cdot}CH_2{\cdot}X{\cdot}CO_2H \longrightarrow \underset{(VI.)}{R{\cdot}CH{:}CH{\cdot}CH_2{\cdot}X{\cdot}CO_2H}$$

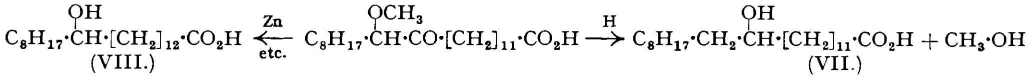
The experiments now described herein had as their objective the realisation of the second route as applied to the synthesis of erucic and brassidic acids (VI; $R = C_8H_{17}$, $X = [CH_2]_{10}$).

The early experiments were concerned with the preparation of 2-methoxydecanoic acid [*] from the corresponding methyl bromo-ester by treatment with methanolic sodium methoxide.

$$CH_2R{\cdot}CO_2H \longrightarrow Br{\cdot}CHR{\cdot}CO_2CH_3 \longrightarrow CH_3O{\cdot}CHR{\cdot}CO_2CH_3 \longrightarrow CH_3O{\cdot}CHR{\cdot}CO_2H$$

Considerable difficulty was encountered in obtaining the α-methoxy-acid free from a small amount of impurity, but eventually by careful fractionation of the crude methyl 2-methoxydecanoate through a Fenske column, the pure *ester* was obtained and thence, by hydrolysis, pure 2-*methoxydecanoic acid*. The acid was converted into the corresponding chloride (I; $R = C_8H_{17}$) with thionyl chloride without rearrangement (as shown by its hydrolysis by dilute alkali to give the original acid in a pure state). Condensation with tribenzyl sodioundecane-1 : 1 : 11-tricarboxylate (II; $X = [CH_2]_{10}$) furnished the keto-ester which, on hydrogenolysis and decarboxylation according to the general method, yielded 13-*keto*-14-*methoxydocosanoic acid* (IV; $R = C_8H_{17}$, $X = [CH_2]_{10}$) as a low-melting solid.

Before proceeding with the olefin synthesis, the action of a number of reducing agents on this methoxy-ketone was examined. Sodium and ethanol furnished an oil and a small amount of a crystalline solid, m. p. 87—87·5°, which is formulated as 13-*hydroxydocosanoic acid* (VII)



$$\underset{(VIII.)}{C_8H_{17}{\cdot}\overset{OH}{CH}{\cdot}[CH_2]_{12}{\cdot}CO_2H} \xleftarrow[etc.]{Zn} C_8H_{17}{\cdot}\overset{OCH_3}{CH}{\cdot}CO{\cdot}[CH_2]_{11}{\cdot}CO_2H \xrightarrow{H} \underset{(VII.)}{C_8H_{17}{\cdot}CH_2{\cdot}\overset{OH}{CH}{\cdot}[CH_2]_{11}{\cdot}CO_2H} + CH_3{\cdot}OH$$

[cf. the reduction of ethoxyacetone by sodium amalgam and acid to give acetone and ethanol (Fittig and Erlenbach, *Annalen*, 1892, **269**, 22), and a similar reduction of an acyloin by sodium and ethanol to give some of the corresponding monohydroxy-compound (Ruzicka *et al.*, *loc. cit.*)]. Reductions with zinc and acid under a variety of conditions gave rise, in high yield, to an isomeric hydroxy-acid, m. p. 90°, depressed to 78—82° by admixture with the previous product, and formulated as 14-*hydroxydocosanoic acid* (VIII.). A sample of this material was oxidised to the corresponding keto-acid, m. p. 85° (lit., 85°) which raised the m. p. of a sample of 14-keto-docosanoic acid, m. p. 83°, obtained previously by the hydration of behenolic acid with sulphuric acid (Holt and Baruch, *Ber.*, 1893, **26**, 838), a reaction unlikely to result in unidirectional addition (Robinson and Robinson, *J.*, 1925, **127**, 175; 1930, 745).

Attempts to reduce the methoxy-ketone catalytically with Adams's catalyst were not successful. Reduction with aluminium *iso*propoxide, however, furnished a solid product which was separated by light petroleum into a solid 13-*hydroxy*-14-*methoxydocosanoic acid* (V; $R = C_8H_{17}$, $X = [CH_2]_{10}$) and a liquid product containing some unchanged methoxy-acid. The liquid fraction, on treatment with hydrogen bromide followed by zinc dust in alcohol, gave a

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[*] Geneva nomenclature is used in this paper.—Ed.

solid from which brassidic and erucic acids were isolated. Both acids were obtained pure and shown to be identical with materials obtained from natural sources, by mixed melting points of the parent acids, their *p*-bromophenacyl esters, and the derived dihydroxy-acids obtained by the action of peracetic acid (Dorée and Pepper, *J.*, 1942, 477).

Conversion of the solid hydroxy-methoxy-acid into the dibromide proved more difficult. We were, at that time, unaware of Baudart's technique (*loc. cit.*) which has since been used with success, but finally by treatment with gaseous hydrogen bromide at 150—160° for 6 hours followed by zinc dust, a moderate yield of brassidic acid was obtained.

It is realised that the method for conversion of the hydroxy-methoxy-acids into the olefinic acid used in this work is far from satisfactory. Experiments are in hand on the development of a technique suitable for general application and will be reported later.

EXPERIMENTAL.

The equipment and techniques employed were as described in Part I.

Decanoic Acid.—A sample of commercial ethyl decanoate (Messrs. A. Boake, Roberts & Co., Ltd.) was fractionated through the Fenske column (total-reflux head) and the fraction, b. p. 118°/10 mm., collected. The acid obtained by hydrolysis was distilled (Vigreux column) and the fraction, b. p. 118—119°/1·5 mm., m. p. 31° (thermometer in liquid), was used.

Methyl 2-Bromodecanoate.—Decanoic acid (110 g.) was converted into its chloride with thionyl chloride (75 ml.). After removal of excess of the latter *in vacuo*, the mass was heated to 110° and treated with bromine (40 ml.) in the usual manner and finally poured into methanol (300 ml.) and left overnight. Isolated as usual the ester was distilled through a column (Vigreux), and the fraction (140 g.), b. p. 89°/0·5 mm., collected.

2-Methoxydecanoic Acid.—The foregoing ester was added with stirring to a solution of sodium methoxide (from 17 g. of metal) in methanol (300 ml.; magnesium-dried), and the mixture boiled under reflux for 4 hours, whereafter most of the solvent was removed by distillation. The cooled residue was diluted with water, and the product isolated with light petroleum (b. p. 40—60°). The oil thus obtained was treated with a mixture of silver oxide (10 g.) and methyl iodide (15 ml.) in acetone solution (100 ml.) under reflux for 6 hours. After removal of solid material by filtration, the product was carefully distilled through the Fenske column to give fractions, (i) b. p. 86—97°/12 mm. (15 ml.) and (ii) pure *methyl 2-methoxydecanoate*, b. p. 97°/2 mm., n_D^{20} 1·4312 (70 g.) (Found: C, 66·7; H, 10·9. $C_{12}H_{24}O_3$ requires C, 66·7; H, 11·1%).

The ester (70 g.) was hydrolysed by treatment with sodium hydroxide (50 ml. of 10N.) in methanol (70 ml.) for ¼ hour, dilution with water (300 ml.), and boiling with escape of methanol (1 hour). Acidification of the cooled solution with sulphuric acid (50 ml. of 20N.) furnished the acid which was isolated with light petroleum (b. p. 40—60°). *2-Methoxydecanoic acid* was obtained as a colourless oil, b. p. 118°/0·5 mm., which solidified immediately and then had m. p. 42·5° (thermometer in liquid). A sample crystallised from light petroleum (b. p. 40—60°) at −10° in colourless slender needles, m. p. 43—43·5° (capillary) (Found: C, 65·5; H, 10·7. $C_{11}H_{22}O_3$ requires C, 65·34; H, 10·9%). It was characterised as the *tribromoanilide*: the acid chloride (see below; 1·7 g.) was added to a solution of tribromoaniline (2 g.) and pure dimethylaniline (2 g.) in dry, purified dioxan (10 ml.), and the mixture refluxed for 0·5 hour; the cooled solution was poured into excess of dilute hydrochloric acid, and the solid removed by filtration; after being washed with water and triturated with alkali and then with water, the product crystallised from aqueous alcohol (norite) in rosettes of slender needles, m. p. 81—82° (Found: C, 39·8; H, 4·7. $C_{17}H_{24}O_2NBr_3$ requires C, 39·7; H, 4·8%).

2-Methoxydecanoyl Chloride (I; R = C_8H_{17}).—A mixture of the foregoing acid (61 g.) and purified thionyl chloride (50 ml.) was kept successively at room temperature for 1 hour, at 30° for 2 hours, and finally at 60° for the same period. Distillation gave the *acid chloride* as a colourless liquid with a characteristic odour and b. p. 83—84°/0·4 mm. (62 g., 93%). It was characterised as the tribromoanilide (as above) and by mild hydrolysis at room temperature with aqueous sodium hydrogen carbonate whence acidification at 0° gave the original acid, m. p. 42° (air-dried) undepressed by admixture with the original material.

Ethyl ω-Bromoundecanoate.—The bromo-acid (Ashton and Smith, *J.*, 1934, 438; m. p. 51°) was esterified azeotropically in the manner described for the corresponding bromoheptoic acid in Part I (*loc. cit.*). The ester was thus obtained as a colourless oil (98%), b. p. 118—119°/0·15 mm.

Ethyl n-*Undecane*-1 : 1 : 11-*tricarboxylate.*—The above bromo-ester (154 g., 0·53 mol.) was treated with sodiomalonic ester (0·75 mol.) in absolute ethanol (300 ml.) under reflux for 6 hours. Isolated in the usual manner, the triester was carefully distilled and, after rejection of a fore-run (b. p. 80—180°), was collected at 180—182°/0·15 mm., m. p. 0—1° (150 g., 76%).

13-*Keto*-14-*methoxydocosanoic Acid* (IV; R = C_8H_{17}, X = $[CH_2]_{10}$).—The foregoing triethyl ester (93 g., 0·25 mol.) was converted into the sodium salt of its enol in benzene (300 ml.) with powdered sodium (5·75 g., 0·25 mol.) and treated with benzyl alcohol (81 g., 0·75 mol.) according to the general procedure to give the corresponding tribenzyl sodio-ester (II; X = $[CH_2]_{10}$). The latter was treated with 2-methoxydecanoyl chloride (55 g., 0·25 mol.), and the product in ethanol (200 ml.) containing ethyl acetate (100 ml.) was debenzylated and decarboxylated as usual. The residue obtained after removal of solvent was treated with light petroleum (b. p. 40—60°; 500 ml.) at 0° and filtered from solid material. Solvent and unchanged 2-methoxydecanoic acid were removed by distillation up to 200° (bath temperature) at 0·2 mm. pressure to give the crude *keto-methoxy-acid* (68 g., 71%) which solidified at room temperature and was used directly for future experiments. A sample was crystallised from light petroleum (b. p. 40—60°) at −25° and furnished the pure acid in colourless plates, m. p. 32—33° (Found: C, 71·2; H, 11·2. $C_{23}H_{44}O_4$ requires C, 71·9; H, 11·4%).

Reduction Experiments.—Sodium and ethanol. The crude keto-methoxy-acid (2 g.) was dissolved in boiling ethanol (25 ml.) and treated with sodium (2 g.) in portions. Dilution with water and acidification afforded a gummy product which was dissolved in boiling methanol (15 ml.). On cooling, 13-*hydroxydocosanoic acid* (0·4 g.), m. p. 86—87°, separated. It crystallised from ethyl acetate in tiny colourless prisms, m. p. 87—87·5° (Found: C, 74·3; H, 11·9. $C_{22}H_{44}O_3$ requires C, 74·2; H, 12·3%).

Zinc. The keto-methoxy-acid (2 g.) was submitted to the following procedures. (*a*) Clemmensen reduction with amalgamated zinc (15 g.) in hydrochloric acid (5N.) for 6 hours. (*b*) Refluxing with zinc dust (12 g.) in 70% acetic acid containing hydrochloric acid (3 drops of 10N.) for 0·5 hour. (*c*) Its solution in ethanol (40 ml.) mixed with amalgamated zinc dust (10 g.) with periodic addition of hydrochloric acid (20 ml. of 10N.) over 2 hours, the temperature being kept below 15°, and finally, hydrolysis of the crude product with alkali. In all cases, a high yield (90%) of 14-*hydroxydocosanoic acid* was obtained. Crystallisation from acetone furnished the hydroxy-acid in colourless prisms, m. p. 90°, depressed to 78—82° by admixture with the 13-isomer (Found: C, 73·9; H, 12·5. $C_{22}H_{44}O_3$ requires C, 74·2; H, 12·3%).

A sample was oxidised in warm acetic acid solution with chromic acid (20N.) to give the 14-ketodocosanoic acid which separated from aqueous alcohol in plates, m. p. 85°. A mixture of this keto-acid and a sample of 14-ketodocosanoic acid, m. p. 83° (prepared from behenolic acid and sulphuric acid), melted at 83—84°.

Aluminium iso*propoxide.* The crude keto-methoxy-acid (26 g.) was added to *iso*propanol (250 ml.) in which aluminium (4·5 g.) had been dissolved, and the mixture slowly distilled through the Fenske column until the distillate was free from acetone (7 hours). Treatment of the residue with warm dilute sulphuric acid (1 l. of N.) until decomposition of the aluminium complex was complete afforded an oil which solidified and was collected by filtration. By crystallisation from light petroleum (b. p. 40—60°) at room temperature and at 0°, it was separated into a yellow, viscous oil (A) and solid 13-*hydroxy*-14-*methoxydocosanoic acid* (B) in the form of colourless prisms, m. p. 50—51° (Found: C, 71·4; H, 11·6. $C_{23}H_{46}O_4$ requires C, 71·5; H, 11·9%).

Brassidic and Erucic Acids.—(*a*) The foregoing oily reduction product (A; 6 g.) was dissolved in toluene (100 ml.), and the solution saturated with dry hydrogen bromide and left overnight. The mixture was then heated to 80° and kept at this temperature with passage of hydrogen bromide for 6 hours. The oil, obtained after removal of solvent, was dissolved in ethanol (25 ml.), and the solution added to zinc dust (10 g.). The mixture was boiled under reflux with periodic addition of alcoholic hydrogen chloride (5 ml. of 4N. in all) for 3 hours. Decantation of the solution from zinc and dilution with water furnished an oil which was isolated with benzene. The combined organic extracts were washed with aqueous sodium hydrogen carbonate and distilled to give, after a small fore-run, an unsaturated ester, b. p. 178—182°/0·3 mm., n_D^{20} 1·4530 (3 g.). Hydrolysis of the latter with aqueous alcoholic sodium hydroxide afforded a crude acid, m. p. *ca.* 50°, which was dissolved in boiling ethanol (9 ml.). Cooling of this solution to 20° gave crop (A) (1·2 g.), to 0° crop (B) (0·2 g.), and to −50° crop (C) (0·15 g.). Crop (A) had m. p. 60° and was substantially pure brassidic acid; it separated from ethanol in colourless, lustrous plates, m. p. 60·5°, undepressed by admixture with authentic material (Found: C, 77·8; H, 12·4. Calc. for $C_{22}H_{42}O_2$: C, 78·1; H, 12·4%). It furnished a *p*-bromophenacyl ester which crystallised from ethanol in plates, m. p. 74,° undepressed by admixture with authentic material, and gave, on treatment with peracetic acid (Dorée and Pepper, *loc. cit.*), the corresponding dihydroxybehenic acid, m. p. and mixed m. p. 131°. Crop (B) was a mixture of (A) and (C) and was not investigated further. Crop (C) (m. p. 28—30°) was dissolved in ethanol (5 ml.), and excess of aqueous lithium hydroxide added at the b. p. On cooling, the beautifully crystalline lithium salt of erucic acid (150 mg.) separated. Decomposition with acid in the presence of light petroleum (b. p. 40—60°) furnished almost pure erucic acid (85 mg.) (Found: equiv., 337. Calc. for $C_{22}H_{42}O_2$: equiv., 338), m. p. 31°, raised to 31—32° by admixture with a specimen of the natural material. It formed a *p*-bromophenacyl ester, m. p. 62°, and a dihydroxybehenic acid, m. p. 98°, both undepressed by admixture with samples prepared from the natural material.

(*b*) A stream of hydrogen bromide was passed through the molten 13-hydroxy-14-methoxydocosanoic acid (B) (1·2 g.) at 150—160° for 6 hours. The residue was treated with ethanol and zinc as before and, in view of the small quantity available, was hydrolysed directly with alkali to give crude brassidic acid (0·4 g.), m. p. 58—59°. Crystallisation from ethanol furnished pure brassidic acid in plates, m. p. 60°, undepressed by authentic material.

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