239. *Synthetic Long-chain Aliphatic Compounds. Part IV. Some Methyl-substituted Oleic Acids.*

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Further applications of the alkoxy-ketone unsaturated acid synthesis (see Part III, preceding paper) have yielded 12-methyl- and 5 : 7 : 13 : 17-tetramethyl-octadec-9-enoic acids * of high purity. An attempt to use the acyloin route for the preparation of 7 : 11-dimethyloctadec-9-enoic acid failed, and the former route is thus to be preferred for the synthesis of branched-chain unsaturated acids. Preliminary experiments on the synthesis of olefinic acids bearing an alkyl group on the double bond have yielded 9-methyloctadec-9-enoic acid of moderate purity.

As described in Part III (preceding paper), efficient methods have now been developed for the synthesis of straight-chain unsaturated acids from either α-alkoxy-ketones or acyloins. The experiments now described were undertaken to examine the suitability of both methods for the preparation of the branched-chain analogues of oleic acid. No particular significance, however, is to be attributed to the choice of final products, which have been chosen primarily from the point of view of ease of preparation of starting materials.

The alkoxy-ketone route was first applied to the synthesis of a mono- and a tetra-methyloleic acid. 4-Methyldecanoic acid,* obtained from *n*-hexylmagnesium bromide and ethyl lævulate (Cason *et al.*, *J. Amer. Chem. Soc.*, 1944, **66**, 1764), was converted *via* the α-bromo-ester into 2-methoxy-4-methyldecanoic acid (I) in the manner used for the preparation of the unmethylated acid (Bowman, *J.*, 1950, 175). The acid chloride from (I) and ethyl heptane-1 : 1 : 7-tricarboxylate were then subjected to the debenzylation ketone synthesis to give 9-keto-10-methoxy-12-methyloctadecanoic acid, isolated as its ethyl ester (II) in 45% yield.

$$\underset{\text{(I.)}}{CH_3{\cdot}[CH_2]_5{\cdot}CHMe{\cdot}CH_2{\cdot}CH(OMe){\cdot}CO_2H} \qquad \underset{\text{(II.)}}{CH_3{\cdot}[CH_2]_5{\cdot}CHMe{\cdot}CH_2{\cdot}CH(OMe){\cdot}CO{\cdot}[CH_2]_7{\cdot}CO_2Et}$$

Catalytic reduction of (II) by means of Raney nickel W7 at room temperature and pressure in ethanol readily gave the pure hydroxy-methoxy-ester, converted by hydrogen bromide–acetic acid–sulphuric acid followed by esterification into the corresponding dibromo-ester. Debromination of the latter with zinc and ethanol then gave the unsaturated ester, which was hydrolysed to give an oily product consisting of the *cis*- and *trans*-12-methyloctadec-9-enoic acids (III); both ester and derived acid had almost the theoretical iodine values.

$$CH_3{\cdot}[CH_2]_5{\cdot}CHMe{\cdot}CH_2{\cdot}CH{:}CH{\cdot}[CH_2]_7{\cdot}CO_2H \qquad \text{(III.)}$$
$$CH_3{\cdot}CHMe{\cdot}[CH_2]_3{\cdot}CHMe{\cdot}[CH_2]_2{\cdot}CH(OEt){\cdot}CO_2H \qquad \text{(IV.)}$$

The intermediates chosen for the second acid (VIII) were (IV) and (VI). The former was readily obtained by the usual malonic ester synthesis employing dihydrocitronellyl bromide and potassio-ethoxymalonic ester, and the latter from the readily accessible ethyl 7-keto-5-methyloctanoate (V) (Ames and Bowman, *J.*, 1950, 329) in the following manner :

$$\underset{\text{(V.)}}{CH_3{\cdot}CO{\cdot}CH_2{\cdot}CHMe{\cdot}[CH_2]_3{\cdot}CO_2Et} \xrightarrow[\text{(b) } H_2\text{–}Pd]{\text{(a) } CN{\cdot}CH_2{\cdot}CO_2Et} CN{\cdot}CH(CO_2Et){\cdot}CHMe{\cdot}CH_2{\cdot}CHMe{\cdot}[CH_2]_3{\cdot}CO_2Et$$
$$\xrightarrow{\text{Alcoholysis}} \underset{\text{(VI.)}}{CH(CO_2Et)_2{\cdot}CHMe{\cdot}CH_2{\cdot}CHMe{\cdot}[CH_2]_3{\cdot}CO_2Et}$$

Thionyl chloride converted (IV) into the acid chloride, which on reaction with the tribenzyl sodio-derivative of (VI) gave a keto-ester which on debenzylation and decarboxylation furnished the ethoxy-keto-acid, isolated as its ethyl ester (VII); the yield (29%), however, was the lowest yet encountered in this synthesis and is attributed to difficulties in completing the ester interchange of (VI) with benzyl alcohol owing to steric factors.

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* Geneva numbering, $CO_2H = 1$.

The ester (VII) then yielded, by way of the usual stages (reduction, conversion into dibromides, debromination, and hydrolysis), an oily mixture of the stereoisomers of *cis*- and *trans*-5 : 7 : 13 : 17-tetramethyloctadec-9-enoic acids (VIII); again, the product was exceptionally pure as judged by its nearly theoretical iodine value. A sample of the corresponding saturated acid was also prepared by catalytic hydrogenation of (VIII).

$$\mathrm{CH_3{\cdot}CHMe{\cdot}[CH_2]_3{\cdot}CHMe{\cdot}[CH_2]_2{\cdot}CH(OEt){\cdot}CO{\cdot}CH_2{\cdot}CHMe{\cdot}CH_2{\cdot}CHMe{\cdot}[CH_2]_3{\cdot}CO_2Et}$$

(VII.)

$$\mathrm{CH_3{\cdot}CHMe{\cdot}[CH_2]_3{\cdot}CHMe{\cdot}[CH_2]_2{\cdot}CH{:}CH{\cdot}CH_2{\cdot}CHMe{\cdot}CH_2{\cdot}CHMe{\cdot}[CH_2]_3{\cdot}CO_2H}$$

(VIII.)

Attention was next directed to the use of the acyloin synthesis for the preparation of 7 : 11-dimethyloctadec-9-enoic acid. Heptyl methyl ketone was converted by reaction with cyanoacetic ester and hydrogenation of the product (Cope *et al.*, *J. Amer. Chem. Soc.*, 1941, **63**, 3452), followed by hydrolysis and decarboxylation, into 3-methyldecanoic acid (IX). Bromination by Papa and Schwenk's method (*ibid.*, 1948, **70**, 3627) gave the α-bromo-acid, and reaction with potassium acetate and hydrolysis with alkali afforded crude 2-hydroxy-3-methyldecanoic acid; this separated as a gel from light petroleum at low temperatures, and was purified by careful vacuum-fractionation of its ethyl ester through a Fenske column. Hydrolysis furnished an oily acid, converted by successive treatment with acetyl chloride and thionyl chloride into the acetoxy-acid chloride (X).

$\mathrm{CH_3{\cdot}[CH_2]_6{\cdot}CHMe{\cdot}CH_2{\cdot}CO_2H}$ (IX.)

$\mathrm{CH_3{\cdot}[CH_2]_6{\cdot}CHMe{\cdot}CH(OAc){\cdot}COCl}$ (X.)

The requisite malonic ester (XII) was next prepared by starting from trimethylene glycol :

$$\mathrm{HO{\cdot}[CH_2]_3{\cdot}OH} \xrightarrow{\mathrm{S_2Cl_2}} \mathrm{HO{\cdot}[CH_2]_3Cl} \xrightarrow[\text{(2) HBr–HOAc–H}_2\text{SO}_4]{\text{(1) Malonation}} \mathrm{Br{\cdot}[CH_2]_4{\cdot}CO_2H} \xrightarrow[\substack{\text{(2) CH}_3\text{·CO·CHNa·CO}_2\text{Et} \\ \text{(3) Hydrolysis}}]{\text{(1) Esterification}}$$

$$\mathrm{CH_3{\cdot}CO{\cdot}[CH_2]_5{\cdot}CO_2Et} \xrightarrow[\substack{(b)\ \text{H}_2\text{–Pd} \\ (c)\ \text{Alcoholysis}}]{(a)\ \text{CN·CH}_2\text{·CO}_2\text{Et}} \mathrm{CH(CO_2Et)_2{\cdot}CHMe{\cdot}[CH_2]_5{\cdot}CO_2Et}$$

(XII.)

The only noteworthy step in these reactions is the preparation of ω-bromovaleric acid (XI) by a method analogous to that used for ω-bromoheptanoic acid (Ames, Bowman, and Mason, *J.*, 1950, 174); the yields were not so good but could probably be improved. Condensation of (X) and the sodio-tribenzyl derivative of (XII) appeared to proceed normally to give a keto-ester, which was submitted to catalytic debenzylation and subsequent decarboxylation in the usual manner. The product, however, was heterogeneous and was not obtained in sufficient yield for further investigation.

This example makes it evident that the difficulties likely to be associated with the preparation of branched-chain α-hydroxy-acids in a pure condition, and anomalies occurring at the later stages of the synthesis, render the acyloin method, as applied above, unsuitable for the synthesis of branched-chain unsaturated acids. On the other hand, the alkoxy-ketone route is particularly convenient for the synthesis of these acids in a high state of purity on account of the ease of preparation of the starting materials and of the ease of the subsequent stages of the synthesis.

$\mathrm{CH_3{\cdot}O{\cdot}[CH_2]_5{\cdot}CH(CO_2Et)_2}$ (XIV.)

$\mathrm{CH_3{\cdot}[CH_2]_7{\cdot}CH(OMe){\cdot}CO{\cdot}[CH_2]_6{\cdot}OMe}$ (XV.)

$\mathrm{CH_3{\cdot}[CH_2]_7{\cdot}CH(OMe){\cdot}CMe(OH){\cdot}[CH_2]_6{\cdot}OMe}$ (XVI.)

Finally, we record some preliminary experiments on the synthesis of unsaturated acids bearing an alkyl substituent on the double bond. Subjection of 2-methoxydecanoyl chloride and ω-methoxyamylmalonic ester (XIV) to the debenzylation ketone synthesis furnished, in satisfactory yield, 7-keto-1 : 8-dimethoxyhexadecane (XV), which was converted by reaction with methylmagnesium iodide into the tertiary alcohol (XVI). Conversion of this into the corresponding tribromide proved difficult. Reaction with hydrogen bromide–acetic acid at 100° gave a dibromide in which, presumably, the terminal methoxy-group remained intact, but the presence of sulphuric acid brought about extensive decomposition. Rather surprisingly, however, the dibromide itself was sufficiently stable to sulphuric acid to permit further reaction with hydrogen bromide to be carried out in its presence. The resulting crude tribromide (XVII) was then treated as follows :

$$\underset{\text{(XVII.)}}{\mathrm{CH_3\cdot[CH_2]_7\cdot CHBr\cdot CMeBr\cdot[CH_2]_6\cdot Br}} \xrightarrow{\mathrm{Zn}} \mathrm{CH_3\cdot[CH_2]_7\cdot CH{:}CMe\cdot[CH_2]_6\cdot Br}$$

$$\xrightarrow{\text{Malonation; hydrolysis; decarboxylation.}} \mathrm{CH_3\cdot[CH_2]_7\cdot CH{:}CMe\cdot[CH_2]_7\cdot CO_2H} \qquad \text{(XVIII.)}$$

Although the resulting 9-methyloctadec-9-enoic acid (XVIII) and its precursors had unsatisfactory analyses, the acid itself had a fairly satisfactory iodine value (89; theory, 86) and on hydrogenation furnished the known 9-methyloctadecanoic acid.

EXPERIMENTAL.

The following general techniques have been used throughout this work and are collected here for present and future reference.

Esterifications.—(1) *Methyl esters.* The procedure is similar to that used by Brown *et al.* (*J. Org. Chem.*, 1947, **12**, 163) in which a mixture of the acid (0·25 mol.), chloroform (130 ml.), methanol (100 ml.), and sulphuric acid (1 ml.) is refluxed in an apparatus fitted with a Soxhlet thimble containing anhydrous magnesium or copper sulphate for 12 hours. The cooled solution is then washed successively with water, sodium hydrogen carbonate solution, and water, dried ($MgSO_4$), and distilled. The yield exceeded 90%.

(2) *Ethyl esters.* A mixture of the acid (1 mol.), benzene (500 ml.), ethanol (250 ml.), and sulphuric acid (1 ml.) is refluxed through a Fenske column (35 mm. of packing) fitted with a Dean and Stark separator, until no further phase separation takes place. The product is then worked up as in the previous example; the yield was >95%. For small quantities of acid (0·01 mol.) the phase separator is replaced by a reflux-head of the Whitmore–Lux pattern, and very slow distillation, under a high reflux-ratio, is allowed to take place until the temperature of the vapours rises to 68°.

Ketone Syntheses.—The method is that described in the preceding paper and elsewhere.

Reduction of Ketones.—The following procedure is, in our experience, far superior to any other catalytic method. The ester (0·05 mol.) is added to pre-reduced Raney nickel W7 (*ca.* 5 g.) (Adkins and Billica, *J. Amer. Chem. Soc.*, 1948, **70**, 698) in ethanol (250 ml.) in an atmosphere of hydrogen, and stirring is continued at room temperature (or up to 40°) until absorption of gas ceases. The catalyst is then filtered off and most of the solvent removed by distillation *in vacuo*. The residue is dissolved in light petroleum (b. p. 40—60°) and after being washed with water, dilute sulphuric acid, sodium hydrogen carbonate solution, and water, is distilled in the usual manner; the yield was ~95%.

Preparation of αβ-Dibromides.—The dihydroxy- or hydroxymethoxy-acid (1 vol.) is mixed with acetic acid containing dry hydrogen bromide (25%, *d* 1·2) (10 vols.), and sulphuric acid (2·5 vols.) added. After 8 hours at room temperature, the mixture is heated to 100° during 1 hour and kept at that temperature for a further 4 hours, whereafter more hydrogen bromide reagent (1 vol.) is added, and the mixture kept at 100° for 4 hours, cooled, poured into water, and extracted with benzene. The organic extract is then subjected to azeotropic esterification with ethanol, and the crude, undistilled ester, dissolved in light petroleum (b. p. 40—60°; 200 ml. per 10 g.), is passed slowly through a column of activated alumina (15 cm. × 1·5 cm.). After being washed with the same solvent (400 ml.), the combined eluates are distilled; the yield exceeds 70%.

Unsaturated Acids.—Zinc dust (1 g.) in ethanol (5 ml.) containing hydrobromic acid (0·1 ml. of 50%) is boiled in an atmosphere of nitrogen for 5 minutes, and the dibromide (0·6 g.) added. After the ensuing exothermic reaction is complete, the solution is refluxed for 1 hour, and the zinc is filtered off and washed with light petroleum (b. p. 40—60°). The combined filtrates are then diluted with water, and the unsaturated ester isolated as usual and distilled (nitrogen leak). Hydrolysis of the ester is effected by refluxing it with excess of ethanolic sodium hydroxide ((N.) in an atmosphere of nitrogen. Ethanol is then removed by steam-distillation, and the unsaturated acid liberated by addition of dilute mineral acid and isolated in the usual manner.

4-*Methyldecanoic Acid.*—Following exactly the procedures used by Cason *et al.* (*loc. cit.*), the Grignard reagent from *n*-hexyl bromide (145 g.) and magnesium (21·5 g.) was allowed to react with ethyl lævulate (117 g.) in benzene, and the crude lactone (b. p. 140—150°/7 mm.) thus obtained was converted through the chloro-ethyl ester into the unsaturated ester. The latter (b. p. 103—108°/2 mm.; 62 g.) was dissolved in ethanol (150 ml.) and hydrogenated in the presence of palladised strontium carbonate (5 g. of 7%) and platinum oxide (0·7 g.) until absorption ceased (1 mol.). Hydrolysis of the product and isolation with benzene yielded 4-methyldecanoic acid as a colourless oil, b. p. 153—155°/10 mm. (49 g., 33% yield overall). The *p*-bromophenacyl ester separated from ethanol in needles, m. p. 43° (Polgar and Robinson, *J.*, 1945, 389, give m. p. 42°).

Methyl 2-*Bromo*-4-*methyldecanoate.*—The foregoing acid (48 g.) was converted into the chloride with thionyl chloride (60 ml.) and brominated (45 g. of bromine) by Papa and Schwenk's procedure (*loc. cit.*). After removal of excess of thionyl halides *in vacuo*, the product was gradually added to methanol (150 ml.), and the mixture set aside at room temperature for 48 hours. Addition of water, followed by extraction with chloroform and distillation through a Vigreux column, furnished the *methyl* ester as a pale yellow oil, b. p. 89°/0·1 mm. (62 g., 84%) (Found: C, 51·1; H, 8·4. $C_{12}H_{23}O_2Br$ requires C, 51·6; H, 8·3%).

2-*Methoxy*-4-*methyldecanoic Acid* (I).—Sodium (8·0 g.) was dissolved in dry methanol (150 ml.) and the foregoing ester (58 g.) was then added. After refluxing for 1 hour (bath, 110°) methanol (70 ml.) was distilled off, the residue poured into dilute sulphuric acid, and the product isolated with benzene. The crude product was then fractionated through a Fenske column fitted with a reflux-head, the separations being followed by refractive-index observations. A fore-run (5 g.) was rejected, and then *methyl* 2-*methoxy*-4-*methyldecanoate* (b. p. 91°/0·7 mm., n_D^{20} 1·4340; 30 g., 62%) was collected (Found: C, 67·6; H, 10·7. $C_{13}H_{26}O_3$ requires C, 67·8; H, 11·4%). It (30 g.) was hydrolysed with methanolic sodium hydroxide in the usual manner to give the *acid*, which distilled as a colourless oil, b. p. 112°/0·2 mm., n_D^{20} 1·4458 (Found: C, 66·9; H, 10·7. $C_{12}H_{24}O_3$ requires C, 66·6; H, 11·2%).

Ethyl 9-*Keto*-10-*methoxy*-12-*methyloctadecanoate* (II).—Thionyl chloride (25 ml.) was added to the foregoing acid (21 g.), and the whole was warmed at 30° for 2 hours and then at 60° for 1·5 hours; the excess of thionyl chloride was removed *in vacuo*, and 2-*methoxy*-4-*methyldecanoyl chloride* distilled as a colourless oil, b. p. 80/0·2 mm. (21 g.) (Found: Cl, 15·4. $C_{12}H_{23}O_2Cl$ requires Cl, 15·1%). This acid chloride (20 g.; 0·085 mol.) was condensed with tribenzyl sodioheptane-1 : 1 : 7-tricarboxylate (0·13 mol.) [from sodium (3·0 g.), the triethyl ester (41 g.), and benzyl alcohol (52 g.)]. The condensation products were isolated, debenzylated, and decarboxylated in the usual manner. Light petroleum (250 ml.; b. p. 40—60°) was added, and heptane-1 : 1 : 7-tricarboxylic acid removed by washing with aqueous ethanol (3 × 30 ml., 1 : 1 v/v) and then water (30 ml.). After drying ($MgSO_4$) and evaporation, the crude residue was esterified azeotropically. Distillation yielded crude methoxy-ester and then *ethyl* 9-*keto*-10-*methoxy*-12-*methyloctadecanoate* as a pale yellow oil, b. p. 184°/0·3 mm., n_D^{20} 1·4523 (14 g., 45%) (Found: C, 72·2; H, 11·5. $C_{22}H_{42}O_4$ requires C, 71·3; H, 11·4%).

12-*Methyloctadec*-9-*enoic Acid*.—The latter ester was reduced catalytically to give *ethyl* 9-*hydroxy*-10-*methoxy*-12-*methyloctadecanoate* as a colourless oil, b. p. 180°/0·15 mm., n_D^{20} 1·4549 (Found: C, 70·8; H, 11·6. $C_{22}H_{44}O_4$ requires C, 70·9; H, 11·9%), and by the general procedures this afforded *ethyl* 9 : 10-*dibromo*-12-*methyloctadecanoate*, a pale yellow oil, b. p. 212°/0·4 mm., n_D^{20} 1·4866 (Found: C, 52·3; H, 7·9; Br, 33·2. $C_{21}H_{40}O_2Br_2$ requires C, 52·1; H, 8·3; Br, 33·0%), *ethyl* 12-*methyloctadec*-9-*enoate*, a colourless oil, b. p. 154°/0·3 mm., n_D^{20} 1·4532 (Found: C, 77·4; H, 12·2%; I.V., 77·7. $C_{21}H_{40}O_2$ requires C, 77·7; H, 12·4%; I.V., 78·2), and finally, 12-*methyloctadec*-9-*enoic acid*, a colourless oil, b. p. 176°/0·4 mm., n_D^{20} 1·4620 (Found: C, 77·2; H, 12·0%; I.V., 85·0. $C_{19}H_{36}O_2$ requires C, 76·8; H, 12·2%; I.V., 85·6).

(−)-1-*Bromo*-3 : 7-*dimethyloctane*.—Purified (+)-citronellol (n_D^{20} 1·4569, $[\alpha]_D^{18}$ +3·60°) was hydrogenated by means of Adams's catalyst in the usual manner in ethanolic solution at atmospheric pressure, and the product converted into the bromide by use of hydrobromic–sulphuric acids followed by steam-distillation (Kamm and Marvel, *Org. Synth.*, 1921, **1**, 7). The product, (−)-1-bromo-3 : 7-dimethyloctane, was a colourless oil, b. p. 84°/6 mm., n_D^{20} 1·4554; $[\alpha]_D^{22}$ −4·97° (pure liquid).

(−)-2-*Ethoxy*-5 : 9-*dimethyldecanoic Acid*.—To a solution of potassium *tert.*-butoxide (0·35 mol.) in *tert.*-butanol (from 13·5 g. of metal and 250 ml. of the alcohol) were added ethyl ethoxymalonate (71·5 g., 0·35 mol.) and then the foregoing bromide (78 g., 0·35 mol.). After 12 hours' stirring under reflux (bath, 110°), dilute sulphuric acid was added to the cooled mixture, and the products were isolated with benzene and distilled.

(−)-*Ethyl ethoxy*-4 : 8-*dimethylnonane*-1 : 1-*dicarboxylate* was thus obtained as a colourless oil, b. p. 133—134°/0·5 mm., n_D^{20} 1·4386, $[\alpha]_D^{22}$ −2·11° (pure liquid) (92 g., 78%) (Found: C, 66·4; H, 11·0. $C_{19}H_{36}O_5$ requires C, 66·2; H, 10·5%). This ester (84 g.) with sodium hydroxide solution yielded the crude dicarboxylic acid, which was isolated with ethyl acetate–benzene (1 : 1) and decarboxylated by being heated at 180—190° (bath) till gas evolution ceased (30 mins.). To ensure complete conversion, the product was then resubmitted to the same procedures. Distillation then furnished (−)-2-*ethoxy*-5 : 9-*dimethyldecanoic acid* as a colourless, viscous oil, b. p. 136°/0·7 mm., n_D^{20} 1·4426, $[\alpha]_D^{20}$ −0·17° (54 g., 85%) (Found: C, 68·9; H, 11·8%; equiv., 243. $C_{14}H_{28}O_3$ requires C, 68·8; H, 11·5%; equiv., 244).

Triethyl 2 : 4-*Dimethylheptane*-1 : 1 : 7-*tricarboxylate* (VI).—Ethyl 7-keto-5-methyloctanoate (62 g.; Ames and Bowman, *loc. cit.*) was heated with ethyl cyanoacetate (32 g.), acetic acid (3 g.), ammonium acetate (2 g.), and benzene (35 ml.) according to Cope's method (*loc. cit.*) until no further water was collected. The cooled mixture was washed with water and distilled to give unchanged keto-ester (b. p. 80—90°/0·3 mm.; 25 g.) and the crude cyano-diester (b. p. 150—155°/0·4 mm.; 61 g.); the former fraction was then submitted to the same process again (total yield: 79 g., 87%). Hydrogenation of the product (79 g.) in ethanol (150 ml.) at 40—50° by aid of palladised strontium carbonate (3 g. of 10% Pd) proceeded readily and ceased when 1·05 mols. of hydrogen had been taken up. The filtered solution was concentrated *in vacuo* (130 ml.) and saturated with hydrogen chloride at 0°. After being kept at room temperature for 12 days, the mixture was gradually added to water (500 ml.) stirred with benzene (200 ml.); the separated benzene solution was evaporated under reduced pressure, and ethanol (200 ml.) and sulphuric acid (50 ml., 98%) were added to the residue. The solution was then refluxed for 8 hours and cooled, and the products were isolated as previously. The *triethyl* ester was obtained as a colourless, somewhat viscous oil, b. p. 144—145°/0·1 mm., n_D^{20} 1·4453 (70 g., 77%) (Found: C, 63·2; H, 9·5. $C_{18}H_{32}O_6$ requires C, 62·8; H, 9·4%).

Ethyl 10-*Ethoxy*-9-*keto*-5 : 7 : 13 : 17-*tetramethyloctadecanoate*.—A mixture of 2-ethoxy-5 : 9-dimethyldecanoic acid (50 g.) and thionyl chloride (50 ml.) was treated exactly as before to give the *chloride* as a colourless mobile oil, b. p. 120°/1 mm. (48 g.) (Found: Cl, 14·0. $C_{14}H_{27}O_2Cl$ requires Cl, 13·5%). This (36 g.) was added to a solution of tribenzyl sodio-2 : 4-dimethylheptane-1 : 1 : 7-tricarboxylate prepared from the triethyl ester (65 g.), benzyl alcohol (61 g.), and sodium (4·3 g.). The procedures then followed exactly those of the previous example, eventually yielding the *ethoxy-keto*-ester as an almost colourless oil, b. p. 190°/0·1 mm., n_D^{20} 1·4520 (17 g., 29%) (Found: C, 72·7; H, 11·8. $C_{26}H_{50}O_4$ requires C, 73·2; H, 11·8%).

5 : 7 : 13 : 17-*Tetramethyloctadec*-9-*enoic Acid*.—Reduction of the above ester furnished *ethyl* 10-*ethoxy*-9-*hydroxy*-5 : 7 : 13 : 17-*tetramethyloctadecanoate*, a colourless oil, b. p. 198—202°/0·5 mm., n_D^{20} 1·4550 (Found : C, 73·0; H, 12·0. $C_{26}H_{52}O_4$ requires C, 72·8; H, 12·2%), converted according to the general procedure into the corresponding dibromide. A portion of the latter was distilled, yielding a yellow oil, b. p. 225—230°/0·3 mm., n_D^{20} 1·4847 (slight decomposition occurred during the distillation) (Found : C, 54·4; H, 8·3; Br, 30·8. $C_{24}H_{46}O_2Br_2$ requires C, 54·7; H, 8·7; Br, 30·4%). The remainder was debrominated in the usual manner, furnishing *ethyl* 5 : 7 : 13 : 17-*tetramethyloctadec*-9-*enoate* as a colourless oil, b. p. 185°/0·5 mm., n_D^{20} 1·4555 (Found : C, 78·8; H, 12·6%; I.V., 69·0. $C_{24}H_{46}O_2$ requires C, 78·6; H, 12·7%; I.V., 69·2), converted by hydrolysis into the *acid*, a colourless oil, b. p. 185°/0·2 mm., n_D^{20} 1·4638 (Found : C, 78·4; H, 12·5%; I.V., 75·5. $C_{22}H_{44}O_2$ requires C, 78·0; H, 12·5%; I.V., 74·9). A sample of this acid (0·6 g.) in ethyl acetate (40 ml.) was shaken in hydrogen in the presence of palladised strontium carbonate for 2 hours. The filtered solution was then distilled, giving 5 : 7 : 13 : 17-*tetramethyloctadecanoic acid*, a colourless, somewhat viscous oil, b. p. 180°/0·1 mm., n_D^{20} 1·4566 (Found : C, 77·4; H, 12·8. $C_{22}H_{44}O_2$ requires C, 77·6; H, 13·0%).

3-*Methyldecanoic Acid*.—Nonan-2-one (b. p. 84°/20 mm.; 110 g.) was condensed with ethyl cyanoacetate by Cope's method (*loc. cit.*), and the crude product (b. p. 120—130°/0·5 mm.; 136 g.) hydrogenated in ethanol (200 ml.) in the presence of palladised strontium carbonate until absorption ceased (1·08 mols.). The filtered solution was evaporated under reduced pressure, and the residue hydrolysed by boiling for 25 hours with potassium hydroxide (130 g.), water (150 ml.), and ethylene glycol (100 ml.). After acidification with excess of dilute sulphuric acid, the product was extracted with benzene–ethyl acetate (1 : 1), and the solution washed with water, dried (Na_2SO_4), and evaporated. The residue was heated (bath, 180—190°) until decarboxylation ceased, and then distilled, yielding 3-methyldecanoic acid as a colourless oil, b. p. 125°/0·3 mm., n_D^{20} 1·4411 (87 g., 60%).

Ethyl 2-*Hydroxy*-3-*methyldecanoate*.—The foregoing acid was converted in exactly the same manner as used for the 4-isomer into *ethyl* 2-*bromo*-3-*methyldecanoate*, a colourless oil, b. p. 110°/0·5 mm., n_D^{20} 1·4592 (98% yield) (Found : C, 54·0; H, 9·0. $C_{13}H_{25}O_2Br$ requires C, 53·2; H, 8·6%). The latter (135 g.) was added in portions to a solution of potassium acetate (128 g.) in glacial acetic acid, and the mixture refluxed for 10 hours. Acetic acid was removed by distillation under reduced pressure, and water (500 ml.) added, the product being extracted with benzene. After removal of solvent, the residue was hydrolysed with boiling ethanolic sodium hydroxide, and ethanol distilled off in steam. The cooled solution was acidified with excess of dilute acid, and the product extracted with benzene–ethyl acetate (1 : 1); the extracts were washed three times with water, dried (Na_2SO_4), and evaporated *in vacuo*. The viscous, oily residue could not be induced to crystallise and was therefore esterified azeotropically, and the ester fractionated through a short Fenske column. After low-boiling products (7 g.) had been removed, the *hydroxy*-ester was collected as a colourless oil, b. p. 100—101°/0·5 mm., n_D^{20} 1·4405 (57 g., 54%) (Found : C, 68·1; H, 11·3. $C_{13}H_{26}O_3$ requires C, 67·8; H, 11·4%).

2-*Acetoxy*-3-*methyldecanoic Acid*.—Hydrolysis of the foregoing ester in the usual manner afforded the oily hydroxy-acid, which was treated with acetyl chloride (75 ml.) in portions, and the mixture set aside at room temperature for 15 hours. Distillation under reduced pressure yielded the *acid* as an almost colourless, viscous oil, b. p. 148°/0·2 mm., n_D^{20} 1·4451 (30 g., 50%) (Found : C, 64·5; H, 10·0%; equiv., 243. $C_{13}H_{24}O_4$ requires C, 63·9; H, 10·0%; equiv., 244).

2-*Acetoxy*-3-*methyldecanoyl Chloride*.—The preceding acid (25 g.) was warmed with thionyl chloride (30 ml.) at 35° for 2 hours and then at 45° for 1 hour. Distillation of the mixture under reduced pressure yielded the *chloride* as a colourless oil, b. p. 95°/0·2 mm. (22 g.) (Found : Cl, 13·8. $C_{13}H_{23}O_3Cl$ requires Cl, 13·5%).

5-*Bromopentanoic Acid*.—3-Chloropropanol (Gough and King, *J.*, 1928, 2439) was treated with sodiomalonic ester in the manner used for 7-bromoheptanoic acid (Ames, Bowman, and Mason, *loc. cit.*) to give 5-bromopentanoic acid (f. p. 36°; 21%).

Ethyl 7-*Keto-octanoate*.—The foregoing acid (70 g.) was esterified azeotropically, and the crude, undistilled ester treated with ethyl sodioacetoacetate (0·75 mol.) in dioxan (200 ml.) for 8 hours under reflux, the products being isolated in the usual manner. The crude residue was then boiled with glacial acetic acid (120 ml.) and concentrated sulphuric acid (1·5 g.) for 6 hours; sodium acetate (3·4 g.) was added, and after removal of acetic acid *in vacuo*, the residue was subjected to azeotropic esterification to give ethyl 7-keto-octanoate as a colourless oil, b. p. 113—115°/2 mm. (39 g., 54%).

Triethyl 6-*Methylheptane*-1 : 1 : 7-*tricarboxylate*.—A mixture of the aforementioned ester (39 g.), ethyl cyanoacetate (20 g.), ammonium acetate (1·5 g.), glacial acetic acid (2·0 g.), and benzene (25 ml.) was refluxed in a flask fitted with a Dean and Stark separator until no more water separated (Cope *et al.*, *loc. cit.*). The solution was washed with water, dried, and distilled to give the crude cyano-diester (37 g.; b. p. 160—170°/0·5 mm.) which was hydrogenated as previously. The crude product was then dissolved in ethanol–benzene (40 ml. each) and the solution saturated with dry hydrogen chloride at 0°; the mixture was kept at room temperature for 10 days and poured into water (250 ml.). The product was isolated with benzene and distilled to give the *triethyl* ester as a colourless, somewhat viscous oil, b. p. 157—159°/0·2 mm., n_D^{20} 1·4460 (33 g., 47%) (Found : C, 62·1; H, 9·2. $C_{17}H_{30}O_6$ requires C, 61·8; H, 9·2%).

Attempted Synthesis of Ethyl 10-*Hydroxy*-9-*keto*-7 : 11-*dimethyloctadecanoate*.—The foregoing triethyl ester (27·5 g.) was converted by reaction with sodium (1·9 g.) and benzyl alcohol (27 g.) in the usual manner into the corresponding tribenzyl ester, which was condensed with 2-acetoxy-3-methyldecanoyl chloride (21 g.). The product was isolated, debenzylated, and decarboxylated by the general procedure and then esterified azeotropically with methanol. Isolated in the usual manner, the ester was distilled under reduced pressure, but persistent decomposition occurred and a considerable residue which could not be distilled was obtained. The total distillate was redistilled and furnished a fraction of wide boiling range (160—210°/0·1 mm.; 8 g.) which could not be purified.

Diethyl 6-*Methoxyhexane*-1 : 1-*dicarboxylate*.—5-Bromo-1-methoxypentane (b. p. 81—82°/30 mm., n_D^{20} 1·4550) was prepared the method of Drake *et al.* (*J. Amer. Chem. Soc.*, 1946, **68**, 1537) and purified by fractional distillation through a Fenske column. The product (70 g.) was added to a solution of ethyl sodiomalonate (0·38 mol.) in ethanol (250 ml.), and the mixture refluxed for 1·5 hours and then poured into water. After isolation in the usual manner, the product was fractionated through a Fenske column fitted with a reflux-head, furnishing the *diethyl* ester as a colourless oil, b. p. 117—118°/0·7 mm., n_D^{20} 1·4346 (63 g., 63%) (Found : C, 60·2; H, 9·4. $C_{13}H_{24}O_5$ requires C, 60·0; H, 9·4%).

7-*Keto*-1 : 8-*dimethoxyhexadecane*.—The dibenzyl sodio-ester prepared from the foregoing ethyl ester (63 g.), sodium (5·5 g.), and benzyl alcohol (52 g.) was condensed with 2-methoxydecanoyl chloride (51 g.), and the product isolated, debenzylated, and decarboxylated by the general procedures. The resulting oil was shaken with light petroleum (b. p. 80—100°; 50 ml.) and water (200 ml.), and the mixture basified to phenolphthalein with sodium hydroxide (2N.) and heated to 50°; the aqueous layer was separated and extracted with fresh solvent, and the combined organic extracts were washed with water, dried, and distilled to give the *ketone* as a colourless oil, b. p. 138—140°/0·1 mm., n_D^{20} 1·4472 (47 g., 68%) (Found : C, 71·7; H, 11·9. $C_{18}H_{36}O_3$ requires C, 72·0; H, 12·0%).

7-*Hydroxy*-1 : 8-*dimethoxy*-7-*methylhexadecane*.—The foregoing ketone (15 g.) was added during 10 minutes to the Grignard reagent prepared from magnesium (2·4 g.) and methyl iodide (14 g.) in ether (50 ml.), the mixture being stirred at 0° during the addition and for a further 10 minutes and then refluxed for 30 minutes. The reaction mixture was cooled to 0° and decomposed with ammonium chloride (25 g.) in water (50 ml.) containing ice, the product being taken up in light petroleum (b. p. 40—60°). After being washed with water and dried (K_2CO_3), the solution was distilled, giving 7-*hydroxy*-1 : 8-*dimethoxy*-7-*methylhexadecane* as a colourless, slightly viscous oil, b. p. 157—158°/0·4 mm., n_D^{20} 1·4520 (14 g., 88%) (Found : C, 72·3; H, 12·6. $C_{19}H_{40}O_3$ requires C, 72·1; H, 12·7%).

Attempts to prepare 1 : 7 : 8-*Tribromo*-7-*methylhexadecane*.—(*a*) The foregoing alcohol (8 g.) was dissolved in hydrogen bromide–acetic acid (*d* 1·25, 80 ml.) at room temperature, and after 1 hour, concentrated sulphuric acid (20 ml.) was added in portions with cooling and shaking. After 20 hours, the mixture was reddish-orange and an oily layer has settled out; the mass was heated to 100° during 1 hour, kept at that temperature for 7 hours, and poured into water. The product was a black resinous material which was not examined further.

(*b*) Hydrogen bromide in acetic acid (*d* 1·25; 50 ml.) was mixed with the *tert.*-alcohol (15 g.) at room temperature, and after 60 hours the mixture was heated at 100° for 10 hours. After addition of water, the products were taken up in light petroleum (b. p. 40—60°; 400 ml.), and the solution was decolorised by passage through a 40-cm. column of kieselguhr–activated charcoal, the same solvent (500 ml.) being used for elution. Evaporation of the total eluates yielded crude 7 : 8-*dibromo*-1-*methoxy*-7-*methylhexadecane*, a pale yellow oil, n_D^{20} 1·4944 (16 g.) (Found : Br, 39·4. $C_{18}H_{36}O_2Br_2$ requires Br, 37·4%).

(*c*) This product (15 g.) was treated with hydrogen bromide–acetic acid–sulphuric acid as in (*a*) to give a dark red oil (18 g.; n_D^{20} 1·5265) which was probably crude 1 : 7 : 8-tribromo-7-methylhexadecane (Found : Br, 56·4. Calc. for $C_{17}H_{33}Br_3$: Br, 50·3%).

1-*Bromo*-7-*methylhexadec*-7-*ene*.—Debromination of the crude tribromide (18 g.) by activated zinc in the usual manner furnished a dark red oil, which was distilled, giving impure bromo-olefin as a yellow oil, b. p. 140—170°/0·2 mm., n_D^{20} 1·4875 (6·5 g.) (Found : Br, 28·0. Calc. for $C_{17}H_{33}Br$: Br, 25·2%).

9-*Methyloctadec*-9-*enoic Acid*.—The foregoing bromide was treated with excess of sodiomalonic ester (4 mols.) in ethanol in the usual manner to give *diethyl* 8-*methylheptadec*-8-*ene*-1 : 1-*dicarboxylate*, an almost colourless oil, b. p. 198—202°/0·5 mm., n_D^{20} 1·4613 (Found : C, 70·7; H, 10·2%; I.V., 62·2. $C_{24}H_{44}O_4$ requires C, 72·7; H, 11·2%; I.V., 64·0). This was hydrolysed in the usual manner, and the product isolated, decarboxylated at 190° and then distilled. 9-*Methyloctadec*-9-*enoic acid* was thus obtained as a colourless oil, b. p. 178—180°/0·4 mm., n_D^{20} 1·4710 (Found : C, 75·2; H, 11·4%; I.V., 87·9. $C_{19}H_{36}O_2$ requires C, 76·8; H, 12·2%; I.V., 85·6).

A portion of the unsaturated acid was hydrogenated in the same manner as for the tetramethyloleic acid, furnishing a crude product which solidified at room temperature and crystallised from acetone at −20°, yielding colourless plates of 9-methyloctadecanoic acid, m. p. 37·5—38·5° (Found : C, 75·9; H, 12·5. Calc. for $C_{19}H_{38}O_2$: C, 76·4; H, 12·8%). Cason and Winans (*J. Org. Chem.*, 1950, **15**, 139) recorded m. p. 38·5—39·1°.

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