96. *Synthetical Experiments bearing on the Constitution of Phthioic Acid.*

By N. Polgar and Sir Robert Robinson.

Previous investigations (Polgar and Robinson, J., 1943, 615) indicated that a structure with two or three long chains is not compatible with the relatively small area of the compressed monolayers of phthioic acid. A number of long-chain acids containing several methyl substituents have therefore been synthesised. It is found that such acids with at least three methyl branches, exemplified by 2 : 13 : 17 : 21-*tetramethyldocosanoic acid*, exhibit film properties corresponding to those of phthioic acid, thus indicating an analogous structure for the latter. This represents a return in a modified form to views expressed by Spielman and Anderson.

In the course of further studies designed to identify a C_{11}-acid obtained by oxidation of phthioic acid (Spielman and Anderson, *J. Biol. Chem.*, 1935—36, **112**, 759) six methyl-substituted C_{11}-acids, one of them also in optically active form, have been synthesised and characterised. Evidence is presented that the oxidation product is 5- or 6-methyldecoic acid and most probably the latter.*

These results are shown to indicate that the sequence $\cdot CH_3 \cdot [CH_2]_3 \cdot CHMe \cdot [CH_2]_5 \cdot CHMe \cdot$ is present in phthioic acid; hence azelaic acid, which is another oxidation product of phthioic acid (Wagner-Jauregg, *Z. physiol. Chem.*, 1937, **247**, 135), must be derived from the remainder of the molecule. This, on the basis of the empirical formula $C_{26}H_{52}O_2$, limits the structural possibilities for phthioic acid to formula (IX) or (X), of which the latter is preferred.

The structure (X) has been shown to be feasible by the synthesis of the substance, namely, 3 : 13 : 19-*trimethyltricosanoic acid*, which is found to exhibit properties tallying with those of phthioic acid.

A method is described for the synthesis of methyl-substituted long-chain acids which depends on the addition of hydrogen bromide to a diene (III) under peroxide-catalysed conditions and leads, by condensation of the resulting dibromide (IV) with ethyl sodiomalonate or sodiomethylmalonate, to acids of type (VII) and (VIII) respectively. In a modification, involving treatment with hydrogen iodide (no peroxide effect) in place of hydrogen bromide, acids of type (X) are obtained.

Phthioic acid is a liquid saturated fatty acid, $C_{26}H_{52}O_2$, which has been isolated from the lipoids of tubercle bacilli by Anderson and associates (*J. Biol. Chem.*, 1929—30, **85**, 77; 1935—36, **112**, 759; and other papers). Its constitution presents a problem of considerable interest, because it has been claimed to be the specific cellular stimulant responsible for the tubercle, the characteristic lesion of tuberculosis (Sabin *et al.*, *J. Exp. Med.*, 1930, **52**, Suppl. 3; and later papers). Moreover, analogous acids occur in other acid-fast bacteria and recently attention has been drawn to the fact that the lipoids extracted from the crown-gall bacillus *Phytomonas tumefaciens*, which stimulates in plants an abnormal cell growth resembling malignant animal neoplasia, also contain fatty acids similar in several respects to the branched-chain fatty acids of the tubercle bacillus (Velick and Anderson, *J. Biol. Chem.*, 1944, **152**, 523).

Previous investigations afford no conclusive evidence from which the constitution of phthioic acid can be deduced; the principal facts are summarised below.

Spielman and Anderson (*loc. cit.*) isolated as an oxidation product a C_{11}-acid not identical with *n*-undecoic acid; Wagner-Jauregg (*loc. cit.*) later found azelaic acid among the oxidation products.

Side-chain methyl estimation by the Kuhn–Roth method gave according to Wagner-Jauregg (*loc. cit.*) 2·4 molecules of acetic acid from phthioic acid, as compared with a value of 1·4 in the case of tuberculostearic acid with two methyl groups, thus indicating for phthioic acid the presence of at least three, and not more than four, methyl groups.

In view of the probable analogy with tuberculostearic acid, which has been found by Spielman (*J. Biol.*

* The carboxyl group is numbered 1 in this communication.

Chem., 1934, **106**, 87) to be a 10-methylstearic acid, Spielman and Anderson suggested that phthioic acid is probably a polymethylated fatty acid. Strong arguments against such a structure were, however, presented by Stenhagen and Ställberg (*J. Biol. Chem.*, 1941, **139**, 345) partly on account of the long crystal spacings found on examination of multilayers of barium phthioate by *X*-ray reflection, which indicated that the length of the molecule was that of a chain not exceeding 15 carbon atoms, and partly in view of the properties exhibited by monolayers of phthioic acid, which could not be compressed below an area of about 38 A.^{2}, whereas the area of one compressed chain is about 18—20 A.^{2} They concluded that phthioic acid is a trisubstituted acetic acid with one short hydrocarbon chain and two long chains of unequal lengths, probably ethyl-*n*-decyl-*n*-dodecylacetic acid.

Later Schneider and Spielman (*J. Biol. Chem.*, 1942, **142**, 345) expressed the view that the chemical evidence is consistent with the above formula of Stenhagen and Ställberg, but taking account of the oxidation products of phthioic acid, isolated by Spielman and Anderson and by Wagner-Jauregg, they suggested a modification of this formula such that at least one of the long chains is methylated or otherwise branched.

A similar suggestion has been made recently by Buu-Hoi and Cagniant (*Ber.*, 1943, **76**, 689), based on a comparison of the m. p. of phthiamide (45°; Spielman and Anderson, *loc. cit.*) with that of a synthetic product, supposed to be ethyldecyldodecylacetamide, which had a higher m. p. (87°). These authors did not prepare, however, the corresponding acid and it may be mentioned that we obtained from ethyldecyldodecylacetic acid, after extensive purification, an amide which was a viscous oil (Polgar and Robinson, *loc. cit.*).

In the last-mentioned communication the formulation of phthioic acid as a trisubstituted acetic acid was proved to be incorrect by the synthesis of ethyldecyldodecylacetic acid and similar substances and by comparison of their monolayer films. Moreover, we have shown that any structure with two long chains is inconsistent with the smaller area of the compressed films of phthioic acid. Hence we reached the conclusion that phthioic acid probably contains only one long chain, which must have a greater length than previously thought possible on the *X*-ray evidence.

This view has been fully confirmed in the course of the present investigation.

Constitution of Phthioic Acid.—With the above results in mind we have prepared a number of long-chain acids containing several methyl substituents for comparison. The synthetic method is illustrated by the following examples.

2-Keto-Δ^{11}-dodecene (I), obtained from undecenoyl chloride and methylzinc iodide, was caused to react with a Grignard reagent to give the carbinol (II; where R is *n*-alkyl or methyl-substituted alkyl, see below) which was dehydrated to the diene (III). This by treatment with hydrogen bromide in benzene or toluene solution in the presence of air, *i.e.*, under peroxide-catalysed reaction conditions (cf. Smith, *Chem. and Ind.*, 1937, **15**, 833; 1938, **16**, 461, where earlier literature is reviewed), gave the dibromide (IV). On condensation of the latter with ethyl sodiomalonate or sodiomethylmalonate (in excess of the calculated amount for reaction of both bromine atoms) replacement of the primary bromine and, simultaneously, elimination of hydrogen bromide at the tertiary carbon atom occurred with formation of (V) and (VI) respectively, which by hydrogenation, followed by hydrolysis and decarboxylation, afforded the corresponding acids (VII) and (VIII).

$CH_3{\cdot}CO{\cdot}[CH_2]_8{\cdot}CH{:}CH_2$ (I.) $\quad$ $R{\cdot}C(OH)Me{\cdot}[CH_2]_8{\cdot}CH{:}CH_2$ (II.) $\quad$ $R{\cdot}CMe{:}CH{\cdot}[CH_2]_7{\cdot}CH{:}CH_2$ (III.)

$R{\cdot}CMeBr{\cdot}[CH_2]_{10}{\cdot}Br$ (IV.) $\quad$ $R{\cdot}CMe{:}CH{\cdot}[CH_2]_9{\cdot}CH(CO_2Et)_2$ (V.) $\quad$ $R{\cdot}CMe{:}CH{\cdot}[CH_2]_9{\cdot}CMe(CO_2Et)_2$ (VI.)

(VII.) $R{\cdot}CHMe{\cdot}[CH_2]_{11}{\cdot}CO_2H$ $\quad$ $R{\cdot}CHMe{\cdot}[CH_2]_{10}{\cdot}CHMe{\cdot}CO_2H$ (VIII.)

The overall yields from (I) to (III) were 73—80%, and from (III) to (V) usually 72—75%. Somewhat lower yields (50—60%) were, however, obtained in some of the earlier experiments.

13 : 16-*Dimethyltricosanoic acid* (VII; R = $CH_3{\cdot}[CH_2]_6{\cdot}CHMe{\cdot}[CH_2]_2{\cdot}$), 2 : 13-*dimethylpentacosanoic acid* (VIII; R = n-$C_{12}H_{25}{\cdot}$), and 2 : 13 : 17 : 21-*tetramethyldocosanoic acid* (VIII; R = $CH_3{\cdot}CHMe{\cdot}[CH_2]_3{\cdot}CHMe{\cdot}[CH_2]_3{\cdot}$) have been synthesised in this way, and also 7-*methyldecoic acid*, which will be discussed later, by employing allylacetone in place of the ketone (I). The correctness of the structure assigned in the last example has been proved by oxidation of an intermediate product to adipic acid.

14 : 17-*Dimethyltetracosanoic acid* has been obtained from 13 : 16-dimethyltricosanoic acid by the homologation reaction of Arndt and Eistert (*Ber.*, 1935, **68**, 200; 1936, **69**, 1074).

In a preliminary experiment an attempt was made to reverse the direction of addition of hydrogen bromide by treating the diene (III; R = $CH_3{\cdot}CHMe{\cdot}[CH_2]_3{\cdot}CHMe{\cdot}[CH_2]_3{\cdot}$) with a solution of hydrogen bromide in glacial acetic acid in the presence of quinol as an antioxidant. Comparison of the resulting acid with those previously described indicated, however, that it was 13 : 17 : 21-*trimethyldocosanoic acid* (VII; R = $CH_3{\cdot}CHMe{\cdot}[CH_2]_3{\cdot}CHMe{\cdot}[CH_2]_3{\cdot}$), and not 3 : 12 : 16 : 20-tetramethylheneicosanoic acid which should have been produced if the addition of hydrogen bromide to the intermediate had given the normal result of antioxidant conditions. This may be due to the fact that the diene (III) was very sparingly soluble in the reaction medium and formed a separate layer on the surface. It may be mentioned, however, that the addition of hydrogen halide according to Markownikow's rule (peroxide-free reaction conditions) was achieved for another example, which will be discussed later, by employing hydrogen iodide instead of hydrogen bromide.

Monolayer film measurements of the above acids will be described in detail in a later paper. It may be briefly stated that monolayers of 2 : 13 : 17 : 21-tetramethyldocosanoic acid have a limiting area of about

61 A.^{2} and collapse on compression at 39 A.^{2}, thus closely resembling monolayers of phthioic acid (limiting area 62 A.^{2}, collapsing at about 38 A.^{2}; Stenhagen and Ställberg, *loc. cit.*), whereas all acids having only two methyl branches gave more compressible films collapsing at 34—35 A.^{2}. Monolayers of 13 : 17 : 21-trimethyldocosanoic acid showed an analogous behaviour to those of 13 : 16-dimethyltricosanoic acid and 14 : 17-dimethyltetracosanoic acid, thus indicating that the 21-Me has little or no effect upon the minimum area of the film.

From these results it is evident that a structure such as that of 2 : 13 : 17 : 21-tetramethyldocosanoic acid, with or without the 21-Me, is in full harmony with the characteristic properties exhibited by monolayers of phthioic acid. This, in conjunction with our previous results excluding certain other structures, suggested that phthioic acid is analogously constituted to the above methyl-substituted acid. Hence, the way now seemed clear to consider the details of branching in the phthioic acid molecule.

As already mentioned, Spielman and Anderson isolated a saturated C_{11}-acid as an oxidation product of phthioic acid; they characterised it as the *p*-bromophenacyl ester and tribromoanilide and found both derivatives to have lower m. p.'s than those of *n*-undecoic acid. Our results, as mentioned above, indicated that this oxidation product must be a methyl-substituted C_{11}-acid and it was desirable to attempt to identify it by synthesising a series of such acids.

3-Methyl-, 4-methyl-, and 5-methyl-decoic acid have been prepared from the appropriate alkyl halides by chain lengthening according to standard methods. 6-*Methyldecoic acid* was obtained from ethyl 6-ketoheptoate (Blaise and Koehler, *Bull. Soc. chim.*, 1910, **7**, 215) and *n*-butylmagnesium bromide by use of the method of Schneider and Spielman (*loc. cit.*), which depends on the reaction of a Grignard reagent with a keto-ester to give a hydroxy-ester, followed by dehydration and hydrogenation. For the synthesis of 7-*methyldecoic acid* the method described in this paper for branched long-chain acids was adapted by employing allylacetone and *n*-propyl bromide for the Grignard reaction.

All acids were converted in the usual manner into their p-*bromophenacyl* esters and *tribromoanilides* for comparison with the oxidation product of phthioic acid. Since phthioic acid is optically active and the same had to be assumed for its oxidation product [*e.g.*, α-tocopherol or phytol giving by oxidation an optically active 4 : 8 : 12-trimethyltridecoic acid with a *p*-xenylamide melting about 5° higher than a synthetic specimen (cf. Fernholz, *J. Amer. Chem. Soc.*, 1938, **60**, 700; Karrer *et al.*, *Helv. Chim. Acta*, 1944, **27**, 1006)], p-*bromophenacyl* esters and *tribromoanilides* of *d*-4 : 8-dimethylpelargonic acid and *dl*-4 : 8-dimethylpelargonic acid were also prepared for comparison, both acids being accessible by standard methods from *d*-citronellal and citral respectively.

The m. p.'s are listed below.

	M. p. of *p*-bromophenacyl ester.	M. p. of tribromoanilide.
3-Methyldecoic acid	39°	111·5°
4-Methyldecoic acid	42	89·5
5-Methyldecoic acid	50	95·5
6-Methyldecoic acid	51	104·5
7-Methyldecoic acid	56	118
dl-4 : 8-Dimethylpelargonic acid	36	99
d-4 : 8-Dimethylpelargonic acid	36	85
Oxidation product of phthioic acid	49—50	111

Comparison of the optically active and the racemic specimen of 4 : 8-dimethylpelargonic acid indicates that the *p*-bromophenacyl esters of such acids, contrary to the tribromoanilides, show no difference in m. p. for the active form. Hence it is possible to compare the synthetic acids with the oxidation product by the m. p.'s of their *p*-bromophenacyl esters. From this comparison it follows that the oxidation product is either 5- or 6-methyldecoic acid with *p*-bromophenacyl esters melting at 50° and 51° respectively, as compared with the m. p. of 49—50° for the oxidation product.

Taking into consideration the process of isolation of the oxidation product under difficult conditions, and the small quantities available for recrystallisation, it is difficult to believe that its *p*-bromophenacyl ester melting at 49—50° should be identical with the pure synthetic product having the sharp m. p. 50° in the case of 5-methyldecoic acid, whereas for 6-methyldecoic acid the slightly higher m. p. 51° is thus accounted for. This view is confirmed by the fact that there is a discrepancy of 15·5° between the m. p.'s of the tribromoanilides of 5-methyldecoic acid and the oxidation product, whereas in the case of 6-methyldecoic acid the m. p. of the tribromoanilide is only 6·5° lower than that of the oxidation product. Larger differences are not to be anticipated (*e.g.*, cf. *dl*-4-methyldecoic acid and *d*-4 : 8-dimethylpelargonic acid); moreover, the tribromoanilide of 7-methyldecoic acid melts only 11° lower than that of *n*-undecoic acid (m. p. 129°), thus indicating that the active form of the tribromoanilides of such acids cannot melt much higher than the racemic form.

These facts justify a provisional identification of the oxidation product as 6-methyldecoic acid; however, the validity of the further conclusions below is unaffected by the question as to whether the oxidation product is 6- or 5-methyldecoic acid, except for the slight modification of formula (X) by transferring a methyl group from C-19 to C-18 if the oxidation product is eventually found to be 5-methyldecoic acid.

In view of the general structural features of phthioic acid as a long-chain acid with several methyl substituents, the formation of a C_{11}-acid as an oxidation product indicates that the sequence $C_{10}H_{21}\cdot\overset{*}{C}H_2\cdot CHMe\cdot$ is present in the molecule, the attack of oxygen having taken place at the asterisked carbon atom (cf. oxidation

of tuberculostearic acid; Spielman, *loc. cit.*). If the oxidation product is regarded as 6-methyldecoic acid for the reasons already advanced, the full structure of the above sequence is $CH_3{\cdot}[CH_2]_3{\cdot}CHMe{\cdot}[CH_2]_5{\cdot}CHMe{\cdot}$.

This having been recognised, it is clear that azelaic acid (Wagner-Jauregg, *loc. cit.*) must be derived from the remainder of the molecule, since its formation requires either a sequence of nine methylene groups at the middle of the chain, or eight methylenes adjoining the carboxyl. This leaves only the alternatives (IX) and (X) for the full structure of phthioic acid. Formula (IX) is not compatible with the high molecular rotation of phthioic acid (+50°), which requires the presence of a methyl substituent near to the carboxyl (cf. Spielman and Anderson, *loc. cit.*). Hence phthioic acid must have the structure (X), representing it as 3 : 13 : 19-trimethyltricosanoic acid.

(IX.) $CH_3{\cdot}[CH_2]_3{\cdot}CHMe{\cdot}[CH_2]_5{\cdot}CHMe{\cdot}[CH_2]_2{\cdot}CHMe{\cdot}[CH_2]_8{\cdot}CO_2H$

(X.) $CH_3{\cdot}[CH_2]_3{\cdot}CHMe{\cdot}[CH_2]_5{\cdot}CHMe{\cdot}[CH_2]_9{\cdot}CHMe{\cdot}CH_2{\cdot}CO_2H$

Spielman and Anderson (*loc. cit.*) favoured a methyl group in the α-position, mainly because, by a Wieland degradation of methyl phthioate, they obtained a neutral substance thought to be a methyl ketone, but they stated that the substance was undoubtedly a mixture and considered this evidence inconclusive. That there is no methyl substituent in the α-position, is, however, confirmed by the fact that the amide of 2 : 13 : 17 : 21-tetramethyldocosanoic acid has m. p. 66°, which is considerably higher than that of phthiamide (45°) and also higher than those of the synthetic amides not bearing a methyl group in the α-position, *e.g.*, 13 : 16-dimethyltricosanamide, m. p. 57°, and 14 : 17-dimethyltetracosanamide, m. p. 62°.

The formation of azelaic acid as an oxidation product requires, as already mentioned, branching of the chain at C-3; its formation is also in full harmony with the formation of a methyldecoic acid as a further oxidation product, both confirming the presence of another branch at C-13. Hence the positions of the methyl substituents in phthioic acid are either determined correctly, or if not so, subject to small modification.

Synthesis of 3 : 13 : 19-*Trimethyltricosanoic Acid* (X).—The general method described in this paper was adopted with the main modification that hydrogen iodide was employed in place of hydrogen bromide, in which case there is no peroxide effect (cf. Kharasch and Hannum, *J. Amer. Chem. Soc.*, 1934, **56**, 1782; Abraham and Smith, J., 1936, 1605). The requisite ketone, 2-keto-Δ^{12}-tridecene, was obtained by a Grignard process, using Δ^{11}-dodecenonitrile and methyl iodide. Reaction of the ketone with a Grignard-reagent from 6-methyldecyl bromide gave the carbinol (XI), which was converted by treatment with hydrogen iodide into (XII) and thence by condensation with ethyl sodiomalonate, followed by the usual stages, into 3 : 13 : 19-*trimethyltricosanoic acid* (X).

(XI.) $CH_3{\cdot}[CH_2]_3{\cdot}CHMe{\cdot}[CH_2]_5{\cdot}C(OH)Me{\cdot}[CH_2]_9{\cdot}CH{:}CH_2$

(XII.) $CH_3{\cdot}[CH_2]_3{\cdot}CHMe{\cdot}[CH_2]_5{\cdot}CIMe{\cdot}[CH_2]_9{\cdot}CHIMe$

The acid is a viscous oil which forms an amide melting at 37°, as compared with 45° in case of phthiamide. The difference is in harmony with the optical activity of the latter, *e.g.*, *dl*-tetrahydrogeranamide (asymmetric centre also at C-3) having m. p. 101—102° (Cahn, Penfold, and Simonsen, J., 1931, 3134) and its active form, dihydrocitronellamide, melting at 108—109° (Wallach, *Annalen*, 1897, **296**, 128; Trikojus and White, *J. Proc. Roy. Soc. New South Wales*, 1932, **66**, 284).

The synthetic acid also exhibits all the characteristic properties of phthioic acid, *e.g.*, it forms a lead salt easily soluble in ether and gives monolayers collapsing on compression at 38—39 A.^{2}. The latter minimum area, compared with that of 18—20 A.^{2} for one compressed normal chain, indicates a considerable tilting of the molecule; hence the smaller apparent length found on *X*-ray examination of barium phthioate multilayers (Stenhagen and Ställberg, *loc. cit.*) is also accounted for.

The structure advanced for phthioic acid is thus confirmed by the synthesis of a stereoisomeride. It remains to complete the proof by synthesis of optically active forms and direct comparison of these with phthioic acid.

The extent to which our conclusions may be invalidated by stereoisomerism and the production of mixtures of stereoisomerides is admittedly unknown; the dubiety exists and we fully recognise it. However, the consideration is certainly less important in the long-chain fatty acid series than in many other groups and we attach significance to the film results especially. Pure isomerides will now be synthesised in order to assess the influence of stereoisomerism.

Certain other points arising in connexion with this investigation may be briefly mentioned.

Choucroun (*Compt. rend.*, 1940, **210**, 749) claims to have obtained phthioic acid by distillation of a high molecular toxic acid extracted from tubercle bacilli, but gives m. p. 85° for the substance supposed to be phthioic acid. This high m. p. indicates that the substance is *n*-hexacosanoic acid (m. p. 87—88°), which according to Anderson and associates (*J. Biol. Chem.*, 1929—30, **85**, 351; 1938, **126**, 505; and other papers) is formed by pyrolysis of mycolic acid, the principal ether-soluble constituent of the wax isolated from tubercle bacilli. Mycolic acid has, apart from its acid-fastness, no outstanding physiological properties (Sabin, *Amer. Rev. Tuberc.*, 1941, **44**, 415); neither has *n*-hexacosanoic acid, which produces in experimental animals a foreign body giant cell reaction (Gerstl and Tennant, *Yale J. Biol. Med.*, 1943, **15**, 347).

Though the separation of phthioic acid from the normal unsaturated acids with which it occurs required catalytic hydrogenation of the crude mixture of fatty acids, the low iodine values of the original mixture mentioned repeatedly by Anderson and associates and also the amount of stearic acid formed on hydrogenation (*e.g.*, cf. Anderson, *J. Biol. Chem.*, 1927, **74**, 537) indicate that phthioic acid was present, doubtless as a derivative, but in saturated form in the bacterial cells. In view of its possible dehydrogenation in the organism

(cf. enzymatic dehydrogenation of phytanic acid and related compounds; Karrer and Koenig, *Helv. Chim. Acta*, 1941, **24**, 304) the study of unsaturated acids with the carbon skeleton of phthioic acid is, however, desirable. Moreover, such unsaturated acids are also of interest for comparison of their physiological properties with those of arachidonic acid and related substances (normal chain, non-conjugated double bonds), considered to be essential for the formation of new tissue, and also with vitamin A (methyl-branched long chain, conjugated double bonds). The investigation will be continued.

Experimental.

3-*Methyldecoic Acid.*—This acid has been mentioned by Keil (*Z. physiol. Chem.*, 1942, **274**, 175) but no details are given. Methylheptylcarbinol (75 g.; obtained by the Grignard reaction from *n*-heptyl bromide and acetaldehyde), b. p. 91°/13 mm., was converted by means of red phosphorus and iodine into its iodide (113 g.), b. p. 101—102°/12 mm., which, by interaction with ethyl sodiomalonate (from 210 g. of ethyl malonate and 17·6 g. of sodium) in alcohol (210 c.c.), afforded ethyl (1-methyloctyl)malonate (116 g.), b. p. 163—164°/14 mm. Hydrolysis of the latter with alcoholic potassium hydroxide, followed by acidification and decarboxylation, gave 3-methyldecoic acid as a colourless viscous liquid (61 g.), b. p. 153—154°/14 mm., $n_D^{17.5°}$ 1·4395. It was converted in the usual way into its p-*bromophenacyl* ester, which formed colourless needles from alcohol, m. p. 39° (Found: C, 59·9; H, 7·2. $C_{19}H_{27}O_3Br$ requires C, 59·5; H, 7·1%). Its *tribromoanilide* was obtained as a white crystalline powder, m. p. 111·5°, after crystallisation from alcohol (Found: C, 41·1; H, 4·9. $C_{17}H_{24}ONBr_3$ requires C, 41·0; H, 4·8%).

4-*Methyldecoic Acid.*—Ethyl *sec.*-octylmalonate, prepared from *sec.*-octyl iodide and ethyl malonate, was converted in the usual manner into 3-methylpelargonic acid, b. p. 136—137°/10 mm., $n_D^{16°}$ 1·4360 [*tribromoanilide*, colourless plates from alcohol and light petroleum, m. p. 111·5° (Found: C, 39·8; H, 4·8. $C_{16}H_{22}ONBr_3$ requires C, 39·7; H, 4·6%)]. The butyl ester (52 g.) of this acid was reduced by means of sodium (32 g.) and butyl alcohol (500 c.c.) to give 3-methylnonan-1-ol (25·6 g.), b. p. 117—118°/14 mm. The latter was transformed by means of 48% hydrobromic acid and sulphuric acid into the bromide (29 g.), b. p. 98—99°/10 mm., and thence, by refluxing the bromide with alcoholic potassium cyanide, into the nitrile (22 g.), b. p. 121—122°/13 mm. Hydrolysis with a mixture of sulphuric acid, acetic acid and water (18 c.c. of each) afforded 4-methyldecoic acid (20·4 g.) as a colourless oil, b. p. 150—151°/10 mm., $n_D^{19°}$ 1·4403 (Staudinger and Ruzicka, *Helv. Chim. Acta*, 1924, **7**, 245, obtained this acid from a dicarboxylic acid in the course of experiments to synthesise tetrahydropyrethrone and give b. p. 150—152°/12 mm.). p-*Bromophenacyl* ester, m. p. 42°, from alcohol (Found: C, 59·4; H, 7·0. $C_{19}H_{27}O_3Br$ requires C, 59·5; H, 7·1%). *Tribromoanilide*, shiny plates from alcohol, m. p. 89·5° (Found: C, 41·1; H, 4·8. $C_{17}H_{24}ONBr_3$ requires C, 41·0; H, 4·8%).

5-*Methyldecoic Acid.*—Ethyl 1-methylhexylidenecyanoacetate [92 g.; obtained from methyl amyl ketone and ethyl cyanoacetate in 88% yield by the method of Cope *et al.* (*J. Amer. Chem. Soc.*, 1941, **63**, 3452)], b. p. 158—159°/22 mm., $n_D^{19°}$ 1·4682, was hydrogenated in alcoholic solution in the presence of palladised strontium carbonate at room temperature/normal pressure, and the reduced product converted, by alkaline hydrolysis with decarboxylation of the isolated acidified product, followed by acid hydrolysis (sulphuric acid, acetic acid and water, 80 c.c. of each), into 3-methyloctoic acid (56·5 g.), b. p. 139—141°/20 mm. (Found: C, 68·7; H, 11·4. Calc. for $C_9H_{18}O_2$: C, 68·3; H, 11·4%). The overall yield was 82%, based upon ethyl 1-methylhexylidenecyanoacetate.

The ethyl ester (55 g.) of the foregoing acid gave by reduction with sodium in butyl alcohol 3-methyloctanol (28·8 g.), b. p. 108°/22 mm., $n_D^{19°}$ 1·4350, which was converted into its bromide (33·8 g.), b. p. 96°/17 mm., and the latter by reaction with ethyl sodiomalonate in the usual manner into *ethyl (3-methyloctyl)malonate* (35·5 g.), b. p. 176—177°/19 mm. (Found: C, 66·7; H, 10·35. $C_{16}H_{30}O_4$ requires C, 67·1; H, 10·5%). On hydrolysis with alcoholic potassium hydroxide, followed by acidification and decarboxylation, 5-methyldecoic acid (20·5 g.) was obtained as a colourless oil, b. p. 167—168°/20 mm., $n_D^{16°}$ 1·4418 (Found: C, 71·3; H, 12·0. Calc. for $C_{11}H_{22}O_2$: C, 71·0; H, 11·8%). Levene and Marker (*J. Biol. Chem.*, 1932, **95**, 153) give b. p. 135°/3 mm. The p-*bromophenacyl* ester crystallised from alcohol as white plates, m. p. 50° (Found: C, 59·65; H, 7·0. $C_{19}H_{27}O_3Br$ requires C, 59·5; H, 7·1%). The *tribromoanilide* formed a white crystalline powder from alcohol, m. p. 95·5° (Found: C, 41·5; H, 5·0. $C_{17}H_{24}ONBr_3$ requires C, 41·0; H, 4·8%).

6-*Methyldecoic Acid.*—The method of Schneider and Spielman (*loc. cit.*) has been adapted. The requisite keto-ester, ethyl 6-ketoheptoate, was obtained from 5-carbethoxyvaleryl chloride in 93% yield by the procedure of Blaise and Koehler (*loc. cit.*) with the following slight modification in detail: methyl iodide (99 g.; 0·7 mol.) was added to a mixture of toluene (47 c.c.), ethyl acetate (20·2 g.; 0·23 mol.), and zinc–copper couple (90 g., prepared according to Gladstone and Tribe, J., 1879, **35**, 567) in small quantities during 2 hours while the mixture was heated under reflux at 70—75° (bath); the temperature was then slowly raised to 100° during 2 hours and maintained there for 1 hour more. The mixture was then cooled with ice, a further quantity of toluene (47 c.c.) added, and the ice-cold solution decanted. 5-Carbethoxyvaleryl chloride (47 g.; 0·24 mol., obtained from ethyl hydrogen adipate by means of thionyl chloride) in toluene (45 c.c.) was immediately introduced during 15 minutes with cooling, accompanied by vigorous stirring, which was continued for a further 5 minutes; the mixture was then decomposed at once by pouring it on ice. The keto-ester, isolated in the known manner, distilled as a colourless liquid (39 g.), b. p. 132—133°/22 mm., $n_D^{17°}$ 1·4340. A sample purified through the semicarbazone, m. p. 107° (from alcohol) (Blaise and Koehler, *loc. cit.*, give the same m. p.), had b. p. 129—130°/20 mm., $n_D^{18°}$ 1·4333 (Found: C, 62·5; H, 9·6. Calc. for $C_9H_{16}O_3$: C, 62·8; H, 9·3%). It may be mentioned that ketones readily undergo self-condensation in the presence of acid chlorides and zinc halides (cf. Descudé, *Ann. Chim. Phys.*, 1903, **29**, 486; Colonge and Mostafavi, *Bull. Soc. chim.*, 1938, **5**, 1478).

A Grignard solution, prepared from *n*-butyl bromide (34 g.) and magnesium (6 g.) in ether (85 c.c.), was gradually added to a solution of ethyl 6-ketoheptoate (33 g.) in ether (250 c.c.) during 1 hour with stirring at room temperature; a white precipitate at once formed. After refluxing for 1 hour, the mixture was kept overnight, decomposed by treatment with dilute hydrochloric acid (ice), and the product worked up by the normal procedure. Several batches prepared in this way were combined and substances, b. p. >140°/20 mm., dehydrated by heating at 160—180° in the presence of iodine. The product was then hydrogenated (alcoholic solution, palladised calcium carbonate), and the reduced ester (b. p. 127—128°/15 mm.) hydrolysed by refluxing with alcoholic potassium hydroxide. On acidification 6-*methyldecoic acid* was obtained as a colourless oil, b. p. 164—165°/18 mm., $n_D^{20°}$ 1·4403 (Found: C, 70·6; H, 11·9. $C_{11}H_{22}O_2$ requires C, 71·0; H, 11·8%). The average yields of the pure acid, calculated on the keto-ester employed, were about 25%. Its p-*bromophenacyl* ester crystallised from alcohol in white plates, m. p. 51° (Found: C, 59·7; H, 7·1. $C_{19}H_{27}O_3Br$ requires C, 59·5; H, 7·1%). The *tribromoanilide* formed minute white plates from alcohol, m. p. 104·5° (Found: C, 41·1; H, ·9. $C_{17}H_{24}ONBr_3$ requires C, 41·0; H, 4·8%).

7-*Methyldecoic Acid.*—Allylacetone was prepared in the known manner by condensation of allyl bromide with ethyl sodioacetoacetate, followed by hydrolysis; it had b. p. 128° and formed a semicarbazone, m. p. 101—102° (from alcohol), in agreement with the literature (*e.g.*, von Braun and Stechele, *Ber.*, 1900, **33**, 1472). The foregoing ketone (37 g.) in ether (40 c.c.) was added to a Grignard solution from *n*-propyl bromide (63 g.) and magnesium (10·9 g.) in ether (60 c.c.)

during 1 hour with stirring at room temperature. Next day the Grignard complex was decomposed by treatment with ice and dilute hydrochloric acid, and the crude carbinol isolated in the usual manner. Dehydration over iodine (160°, bath) gave a mobile liquid (37 g.), b. p. 140—141°. This was dissolved in toluene (370 c.c.), and the solution saturated with hydrogen bromide at 0° while, simultaneously, a slow stream of air was passed continuously through the liquid. After the mixture had been kept overnight, excess of hydrogen bromide was expelled by means of a brisk stream of air; the solvent was then removed under diminished pressure (bath temperature, 40—45°), and the residue used without further purification for condensation with ethyl sodiomalonate. This was effected by keeping it overnight with a large excess of ethyl sodiomalonate (from 20·7 g. of sodium and 214 g. of ethyl malonate) in alcohol (250 c.c.); the mixture was then refluxed with stirring for 4 hours. *Ethyl* (5-*methyl*-Δ^5-*octenyl*)*malonate* (61 g.) was obtained as an almost colourless oil, b. p. 176—178°/18 mm., $n_D^{22°}$ 1·4480 (Found: C, 66·8; H, 9·8. $C_{16}H_{28}O_4$ requires C, 67·6; H, 9·9%).

A sample of the foregoing product (4 g.) was converted by hydrolysis with subsequent decarboxylation into 7-*methyl*-Δ^7-*decenoic acid*, which distilled as a viscous oil (2·1 g.), b. p. 165—166°/17 mm., $n_D^{22°}$ 1·4552 (Found: C, 71·9; H, 10·9. $C_{11}H_{20}O_2$ requires C, 71·7; H, 10·9%). Its identity was proved by oxidation with potassium permanganate, which gave an acid, m. p. 149° alone or mixed with adipic acid.

The substituted malonic ester (5·6 g.) in alcohol (30 c.c.) was hydrogenated in the presence of palladised calcium carbonate. Hydrolysis of the saturated material, followed by decarboxylation of the free acid, afforded 7-*methyldecoic acid* as a colourless oil (2·3 g.), b. p. 161—162°/15 mm., $n_D^{20°}$ 1·4408 (Found: C, 70·7; H, 12·0. $C_{11}H_{22}O_2$ requires C, 71·0; H, 11·8%). Its p-*bromophenacyl* ester crystallised in white plates from alcohol, m. p. 56° (Found: C, 59·2; H, 7·0. $C_{19}H_{27}O_3Br$ requires C, 59·5; H, 7·1%). The *tribromoanilide* was obtained as minute, white plates from alcohol, m. p. 118° (Found: C, 41·2; H, 4·9. $C_{17}H_{24}ONBr_3$ requires C, 41·0; H, 4·8%).

dl-4 : 8-*Dimethylpelargonic Acid.*—The starting point was citral which had been purified by means of sodium sulphite (Tiemann, *Ber.*, 1899, **32**, 812), thus affording an optically inactive material. This was hydrogenated in the presence of Raney nickel (140°/100 atms.), and the resulting saturated alcohol (tetrahydrogeraniol) converted in the known manner into the bromide, b. p. 103°/17 mm., $n_D^{16°}$ 1·4541, and thence into the nitrile, b. p. 113—114°/15 mm., $n_D^{14°}$ 1·4377. On refluxing the latter with a mixture of sulphuric acid, acetic acid and water (1 : 1 : 1) for 3 hours, *dl*-4 : 8-dimethylpelargonic acid was obtained as a colourless oil, b. p. 156—157°/15 mm., $n_D^{17·5°}$ 1·4400 (Found: C, 70·7; H, 11·85. Calc. for $C_{11}H_{22}O_2$: C, 71·0; H, 11·8%). Its amide had, after recrystallisation from alcohol and light petroleum (b. p. 60—80°), m. p. 81—81·5° (Found: N, 7·4. Calc. for $C_{11}H_{23}ON$: N, 7·6%) (Heilbron and Thompson, J., 1929, 883, give m. p. 77—79° and for another specimen 80—81°; Späth and Klager, *Ber.*, 1934, **67**, 859, give m. p. 79—81°). The p-*bromophenacyl* ester separated from alcohol as a crystalline powder, m. p. 36° (Found: C, 59·8; H, 7·0. $C_{19}H_{27}O_3Br$ requires C, 59·5; H, 7·1%). The *tribromoanilide* formed a crystalline powder from alcohol, m. p. 99° (Found: C, 41·3; H, 4·7. $C_{17}H_{24}ONBr_3$ requires C, 41·0; H, 4·8%).

d-4 : 8-*Dimethylpelargonic Acid.*—This was prepared in the same way as the previous compound except that the starting point was *d*-citronellal. The acid had b. p. 147°/9 mm., $n_D^{18°}$ 1·4408 (von Braun and Kaiser, *Ber.*, 1923, **56**, 2268, give b. p. 151—153°/14 mm.). d-*Amide*, m. p. 83° after recrystallisation from alcohol and light petroleum (Found: N, 7·6. $C_{11}H_{23}ON$ requires N, 7·6%). Its p-*bromophenacyl* ester formed white plates from alcohol, m. p. 36° (Found: C, 59·3; H, 7·1. $C_{19}H_{27}O_3Br$ requires C, 59·5; H, 7·1%). The *tribromoanilide* was obtained in plates from alcohol, m. p. 85° (Found: C, 41·0; H, 4·7. $C_{17}H_{24}ONBr_3$ requires C, 41·0; H, 4·8%).

The butyl ester of this acid on reduction with sodium and butyl alcohol gave *d*-4 : 8-dimethylnonanol, the rotation of which (+0·93° in a 0·5-dm. tube) was in agreement with the values reported by von Braun and Kaiser (*loc. cit.*), thus indicating that no racemisation has taken place in the previous operations.

13 : 16-*Dimethyltricosanoic Acid* (VII; R = $CH_3{\cdot}[CH_2]_6{\cdot}CHMe{\cdot}[CH_2]_2{\cdot}$).—2-Keto-$\Delta^{11}$-dodecene (I) was obtained by the action of undecenoyl chloride on methylzinc iodide as a mobile liquid, b. p. 114—115°/9 mm., which gave a crystalline *semicarbazone*, m. p. 112—113°, from alcohol (Found: C, 65·4; H, 10·4. $C_{13}H_{25}ON_3$ requires C, 65·3; H, 10·45%). The ketone (15 g.) in ether (25 c.c.) was caused to react with a Grignard solution from 3-methyldecyl bromide (23·5 g.; obtained from 3-methyldecanol prepared by reducing butyl 3-methyldecoate with sodium and butyl alcohol), magnesium (2·3 g.), and ether (40 c.c.). After isolation in the usual way the crude carbinol was dehydrated with a trace of iodine (180—190°, 30 minutes), to give 11 : 14-*dimethylheneicosa*-1 : 11-*diene* (18·9 g.) as a mobile liquid, b. p. 162—163°/0·2 mm. (Found: C, 86·3; H, 13·6. $C_{23}H_{44}$ requires C, 86·3; H, 13·7%). Air and hydrogen bromide were then passed during 2 hours into a solution of the diene in benzene (180 c.c.) and the resulting crude bromide, isolated in the manner already described (see section on 7-methyldecoic acid), was condensed with ethyl sodiomalonate (large excess, from 50 g. of ethyl malonate and 5·9 g. of sodium in 70 c.c. of alcohol), the mixture being kept overnight and then refluxed with stirring for 6 hours. *Ethyl* (11 : 14-*dimethyl*-Δ^{11}-*heneicosenyl*)*malonate* (20·8 g.) was obtained as a viscous oil, b. p. 229—230°/0·4 mm., $n_D^{20°}$ 1·4590 (Found: C, 75·1; H, 11·5. $C_{30}H_{56}O_4$ requires C, 75·0; H, 11·7%). This substance (17·8 g.) was hydrogenated in alcoholic solution in the presence of palladised strontium carbonate, and the reduced ester hydrolysed by means of alcoholic potassium hydroxide. Decarboxylation of the free acid furnished 13 : 16-*dimethyltricosanoic acid*, b. p. 212—213°/0·2 mm.; it was a viscous oil at room temperature, $n_D^{25°}$ 1·4572, but solidified on cooling with ice and melted at 14—15° (Found: C, 78·1; H, 13·2. $C_{25}H_{50}O_2$ requires C, 78·5; H, 13·1%). Its *amide* had m. p. 57° (from methanol) (Found: C, 78·2; H, 13·3. $C_{25}H_{51}ON$ requires C, 78·7; H, 13·4%).

14 : 17-*Dimethyltetracosanoic Acid.*—13 : 16-Dimethyltricosanoic acid (0·5 g.) was converted into its chloride by means of thionyl chloride, and this treated with an ethereal solution of diazomethane. The resulting diazo-ketone was dissolved in dioxan (40 c.c.), and the solution heated on a steam-bath with addition of aqueous ammonia (5 c.c. of 35%) and a 10% solution of silver nitrate (3 c.c.); when the vigorous reaction had subsided (a few minutes), the mixture was refluxed for 1 hour. The solution was then filtered and diluted with water. On cooling, 14 : 17-*dimethyltetracosanamide* separated in small plates, m. p. 62° after recrystallisation from methanol (Found: C, 78·8; H, 13·1; N, 3·6. $C_{26}H_{53}ON$ requires C, 79·0; H, 13·4; N, 3·5%).

In another experiment the diazo-ketone was converted by treatment with silver oxide and methanol into the homologous methyl ester. This furnished by hydrolysis with alcoholic potassium hydroxide and subsequent acidification the required *acid* as a viscous oil, which distilled from a bath at 215—225°/0·1 mm. and, on redistillation, had b. p. 221—222°/0·2 mm., $n_D^{25°}$ 1·4589; it solidified on cooling and melted at about 20° (Found: C, 78·7; H, 12·7. $C_{26}H_{52}O_2$ requires C, 78·8; H, 13·1%).

2 : 13-*Dimethylpentacosanoic Acid* (VIII; R = n-$C_{12}H_{25}$·).—2-Keto-Δ^{11}-dodecene (18·5 g.) was treated with n-dodecylmagnesium bromide (from 2·4 g. of magnesium), and the product worked up as described in previous experiments. Dehydration of the crude carbinol gave a mobile liquid (18·7 g.), b. p. 170—172°/0·1 mm., $n_D^{19°}$ 1·4610. This substance (7·5 g.) in benzene solution (50 c.c.) was treated in the usual way with hydrogen bromide in the presence of air, and the product condensed with an excess of the sodio-compound of ethyl methylmalonate (2 g. of sodium, 19·3 g. of ethyl methylmalonate). *Ethyl* (11-*methyl*-Δ^{11}-*tricosenyl*)*methylmalonate* (7·25 g.) was thus obtained as a pale yellow oil, b. p. 242—243°/0·2 mm., $n_D^{18°}$ 1·4596 (Found: C, 75·6; H, 11·8. $C_{32}H_{60}O_4$ requires C, 75·6; H, 11·8%). This was reduced with hydrogen (alcohol solution, 15 c.c.) in the presence of palladised strontium carbonate, and the saturated material

hydrolysed by means of alcoholic potassium hydroxide. On decarboxylation of the free acid 2 : 13-*dimethylpentacosanoic acid* (3·9 g.) was obtained as a viscous oil, b. p. 226—227°/0·1 mm., which soon solidified and melted at 36—37° after recrystallisation from acetone (Found : C, 78·9; H, 13·1. $C_{27}H_{54}O_2$ requires C, 79·0; H, 13·2%). Its *amide* had m. p. 85° (from alcohol) (Found : N, 3·6. $C_{27}H_{55}ON$ requires N, 3·4%).

2 : 13 : 17 : 21-*Tetramethyldocosanoic Acid* (VIII, R = CH_3·CHMe·$[CH_2]_3$·CHMe·$[CH_2]_3$·).—Reaction between 2-keto-Δ^{11}-dodecene (25 g.) and a Grignard solution from *d*-4 : 8-dimethylnonyl bromide (35 g.; obtained from the corresponding alcohol by means of 48% hydrobromic acid and sulphuric acid), magnesium (3·7 g.), and ether (45 c.c.), followed by the usual dehydration in the presence of iodine (0·05 g.; 160—180°, 1 hour), gave 11 : 15 : 19-*trimethyleicosa*-1 : 11-*diene* as a mobile liquid (26·4 g.), b. p. 162—163°/0·3 mm., $n_D^{19°}$ 1·4595 (Found : C, 86·2; H, 13·7. $C_{23}H_{44}$ requires C, 86·3; H, 13·7%). The foregoing compound (12·7 g.) was dissolved in benzene (80 c.c.) and subjected to the action of hydrogen bromide in the presence of air as in previous examples. On reaction of the resulting crude bromide with a large excess of ethyl sodiomethylmalonate (from 35 g. of ethyl methylmalonate and 3·6 g. of sodium in 45 c.c. of alcohol) *ethyl* (11 : 15 : 19-*trimethyl*-Δ^{11}-*eicosenyl*)*methylmalonate* was obtained as a viscous oil (10·4 g.), b. p. 217—218°/0·1 mm., $n_D^{18°}$ 1·4601 (Found : C, 75·0; H, 11·8. $C_{31}H_{58}O_4$ requires C, 75·3; H, 11·7%). This on hydrogenation (palladised strontium carbonate), followed by the normal procedure (hydrolysis, decarboxylation), furnished 2 : 13 : 17 : 21-*tetramethyldocosanoic acid* as a colourless viscous oil (6·9 g.), b. p. 221—222°/0·1 mm., $n_D^{19°}$ 1·4584 (Found : C, 78·7; H, 13·0. $C_{26}H_{52}O_2$ requires C, 78·8; H, 13·1%). It formed an *amide* which was extremely soluble in organic solvents and separated from minimum quantities of ice-cold alcohol as a tallow-like, white solid, m. p. 66° (Found : N, 3·35. $C_{26}H_{53}ON$ requires N, 3·5%).

Attempted Preparation of 3 : 12 : 16 : 20-*Tetramethylheneicosanoic Acid.*—A modification of the foregoing experiment by adding hydrogen bromide to 11 : 15 : 19-trimethyleicosa-1 : 11-diene under antioxidant conditions was explored in a preliminary fashion. A mixture of the diene (13·5 g.) with quinol (0·05 g.) and a solution of hydrogen bromide in glacial acetic acid (75 c.c.; 50 w/v %) was kept for 19 days with occasional shaking (both the diene and quinol seemed practically insoluble in the mixture). It was then poured into ice-water, and the bromide isolated by means of ether and dried with calcium chloride. After removal of the ether dry benzene was repeatedly added to the residue and removed at 40° (bath temperature) under reduced pressure. The residual heavy oil was then caused to react with ethyl sodiomalonate (from 35 g. of ethyl malonate and 3·9 g. of sodium) according to the usual procedure; the *product* was a viscous oil (10·6 g.) b. p. 220—221°/0·3 mm., $n_D^{19°}$ 1·4588 (Found : C, 74·3; H, 11·5. $C_{30}H_{56}O_4$ requires C, 75·0; H, 11·7%). After being reduced catalytically with palladised strontium carbonate in alcohol (25 c.c.), and the hydrolysed product decarboxylated as previously described, the *acid* distilled as an almost colourless oil (7 g.), b. p. 218—219°/0·2 mm., $n_D^{17°}$ 1·4595, which solidified on cooling and melted at 19—20° (Found : C, 78·6; H, 12·7. $C_{25}H_{50}O_2$ requires C, 78·5; H, 13·1%). Its *amide* had m. p. 55° (from alcohol) (Found : N, 3·6. $C_{25}H_{51}ON$ requires N, 3·7%). Comparison of these m. p.'s with those of 13 : 16-dimethyltricosanoic acid and 14 : 17-dimethyltetracosanoic acid suggests that the acid formed is 13 : 17 : 21-*trimethyldocosanoic acid* (VII; R = CH_3·CHMe·$[CH_2]_3$·CHMe·$[CH_2]_3$·), resulting from addition of hydrogen bromide by peroxide catalysis. This is confirmed by the fact that its monolayer film gives a pressure/area curve similar to those of the afore-named acids, whereas an additional methyl branch at C-3 (from addition of hydrogen halide under antiperoxide reaction conditions; see following preparation) was found to cause a larger minimum area of the film.

3 : 13 : 19-*Trimethyltricosanoic Acid* (X).—2-Keto-Δ^{12}-tridecene was prepared by the reaction between Δ^{11}-dodecenonitrile (24·5 g.; b. p. 145—146°/15 mm., obtained from Δ^{10}-undecenol *via* the chloride) and methylmagnesium iodide (from 14 g. of magnesium); it distilled as a colourless liquid (19 g.), b. p. 133—135°/13 mm., and formed a *semicarbazone*, m. p. 113—114° (from alcohol) (Found : C, 66·2; H, 10·35. $C_{14}H_{27}ON_3$ requires C, 66·4; H, 10·7%).

The above ketone (9·4 g.) was brought to reaction with a Grignard solution from 6-methyldecyl bromide (13·5 g.; obtained from ethyl 6-methyldecoate by the normal procedure), magnesium (1·34 g.), and ether (45 c.c.) as described in previous examples. Distillation of the crude product furnished 12-*hydroxy*-12 : 18-*dimethyl*-Δ^1-*docosene* (8·6 g.) as a colourless oil, b. p. 175—179°/0·1 mm. (Found : C, 81·2; H, 13·3. $C_{24}H_{48}O$ requires C, 81·8; H, 13·6%). This substance (8·4 g.) was dissolved in benzene (30 c.c.), and a slow current of hydrogen iodide (generated by dropping hydriodic acid on phosphoric oxide and passed over a column of red phosphorus on glass wool before admission to the reaction vessel) passed into the solution, cooled with ice-water, until saturation (about 1 hour). Next day the solution was decanted from small quantities of water produced, dried over anhydrous sodium sulphate, and the solvent slowly evaporated at 30° (bath) under diminished pressure. The residual oil gave on reaction with ethyl sodiomalonate (from 2·7 g. of sodium and 35 g. of ethyl malonate) in alcohol (35 c.c.), the mixture being refluxed for 3 hours, *ethyl* (1 : 11 : 17-*trimethyl*-Δ^{11}-*heneicosenyl*)*malonate* (7·7 g.) as a viscous oil, b. p. 222—223°/0·2 mm., $n_D^{19°}$ 1·4610 (Found : C, 75·1; H, 11·6. $C_{31}H_{58}O_4$ requires C, 75·3; H, 11·7%). This ester (4·6 g.) in alcohol (40 c.c.) was hydrogenated in the presence of palladised charcoal, and the saturated material hydrolysed by refluxing with alcoholic potassium hydroxide. When the free acid was heated at 100° under diminished pressure, decarboxylation occurred, which was completed by heating at about 120—130°/1 mm. 3 : 13 : 19-*Trimethyltricosanoic acid* distilled as an almost colourless viscous oil (2 g.), b. p. 206—208°/0·1 mm., $n_D^{17°}$ 1·4620 (Found : C, 78·7; H, 12·9. $C_{26}H_{52}O_2$ requires C, 78·8; H, 13·1%). It showed no signs of crystallisation after 2 days in the refrigerator (there are three asymmetric carbon atoms, admitting eight optical isomers). The *amide* was extremely soluble in organic solvents and distilled at 225—235° (bath temperature)/0·1 mm. as a viscous oil which soon became a tallow-like solid, m. p. 37° (Found : N, 3·5. $C_{26}H_{53}ON$ requires N, 3·5%).

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