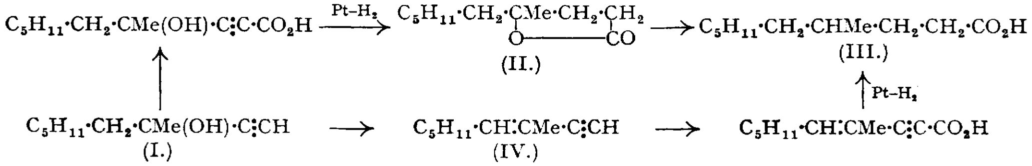
524. *The Synthesis of Long-chain Aliphatic Acids from Acetylenic Compounds. Part IV. A New Approach to the Synthesis of Branched-chain Acids.*

By C. L. Leese and R. A. Raphael.

Good methods of synthesis of monomethyl-substituted long-chain fatty acids are described which employ the easily accessible methyl ketones and readily available acetylenic compounds.

The isolation of the branched-chain fatty acids tuberculostearic acid, phthioic acid, and mycocerosic acid from tubercle bacilli and the investigation of their lesion-producing properties (for review, see Weitzel, *Angew. Chem.*, 1948, **60**, 263) have stimulated considerable study of the synthesis of such methyl-substituted compounds. The methods available for the preparation of the monomethyl acids fall into two classes, *i.e.*, the repeated homologation by classical procedures of a branched-chain starting material (Polgar and Robinson, *J.*, 1943, 615; 1945, 389; 1949, 1545; Wilson, *J. Amer. Chem. Soc.*, 1945, **67**, 2162; Stenhagen *et al.*, *Svensk Kem. Tids.*, 1942, **54**, 145; *Arkiv Kem. Min. Geol.*, 1946, **22**, *A*, No. 19; 1948, **26**, *A*, No. 12) or the condensation of the relevant branched-chain cadmium dialkyl with an ω-carbethoxyalkanoyl chloride followed by reduction of the keto-ester produced (Cason *et al.*, *J. Amer. Chem. Soc.*, 1942, **64**, 1106; 1944, **66**, 1764; 1947, **69**, 1233; 1948, **70**, 298; *J. Org. Chem.*, 1948, **13**, 227, 239; 1949, **14**, 132, 137, 147, 155; 1950, **15**, 135, 139, 148). The first of these processes is often very tedious, and the disadvantages of the latter have recently been pointed out by Ames, Bowman, and Mason (*J.*, 1950, 174).

The present interest in acetylenic compounds, resulting in the ready availability of many members of the series, suggested their use for the synthesis of branched-chain acids of this type, and examples of this are described below. In each case the branching methyl group is introduced by means of a methyl ketone reactant at the stage in which the complete carbon skeleton is formed, thus obviating the necessity of preparing a branched-chain intermediate.



$$\begin{tikzcd}
C_5H_{11}\cdot CH_2\cdot CMe(OH)\cdot C{\vdots}C\cdot CO_2H \arrow[r, "Pt\text{-}H_2"] & \underset{(II.)}{C_5H_{11}\cdot CH_2\cdot \overset{}{C}Me\cdot CH_2\cdot CH_2 \ (O\text{---}CO)} \arrow[r] & \underset{(III.)}{C_5H_{11}\cdot CH_2\cdot CHMe\cdot CH_2\cdot CH_2\cdot CO_2H} \\
\underset{(I.)}{C_5H_{11}\cdot CH_2\cdot CMe(OH)\cdot C{\vdots}CH} \arrow[u] \arrow[r] & \underset{(IV.)}{C_5H_{11}\cdot CH{:}CMe\cdot C{\vdots}CH} \arrow[r] & C_5H_{11}\cdot CH{:}CMe\cdot C{\vdots}C\cdot CO_2H \arrow[u, "Pt\text{-}H_2"']
\end{tikzcd}$$

The scheme delineates an example of a general method for preparing 3-methyl-1-carboxylic acids. 3-Methylnon-1-yn-3-ol (I; prepared from hexyl methyl ketone and sodium acetylide) was carboxylated by the method of Haynes and Jones (*J.*, 1946, 503), and the resulting acetylenic hydroxy-acid catalytically hydrogenated to the lactone (II). Fission of this lactone by the procedure of Cason *et al.* (1944, *loc. cit.*) furnished the corresponding ethylenic ester which, after hydrogenation and hydrolysis, yielded 3-methylnonane-1-carboxylic acid (III). As the lactone fission did not proceed smoothly, the following variant was adopted with considerable enhancement in the yield of the final acid. Catalytic dehydration of the carbinol (I) over aluminium phosphate (Heilbron, Jones, and Richardson, *J.*, 1949, 287) produced 3-methylnon-3-en-1-yne (IV); carboxylation of the derived Grignard complex and hydrogenation of the unsaturated acid produced gave an excellent yield of the acid (III).

$$C_4H_9\cdot CH_2\cdot COMe + CH{\vdots}C\cdot[CH_2]_2\cdot OH \longrightarrow \underset{(V.)}{C_4H_9\cdot CH_2\cdot CMe(OH)\cdot C{\vdots}C\cdot[CH_2]_2\cdot OH} \xrightarrow{KHSO_4}$$

$$\underset{(VI.)}{C_4H_9\cdot CH{:}CMe\cdot C{\vdots}C\cdot[CH_2]_2\cdot OH} \xrightarrow[(2)\ CrO_3]{(1)\ Pt\text{-}H_2} \underset{(VII.)}{C_4H_9\cdot CH_2\cdot CHMe\cdot[CH_2]_3\cdot CO_2H}$$

For the preparation of 4-methyl-1-carboxylic acids the easily obtainable but-4-yn-1-ol may be employed. Thus, in the example designated above, condensation of the Grignard complex of this carbinol with *n*-amyl methyl ketone furnished the glycol (V). Dehydration of this compound with potassium hydrogen sulphate involved only the tertiary hydroxyl group thus producing 5-methyldec-5-en-3-yn-1-ol (VI) which, after hydrogenation and oxidation, gave 4-methylnonane-1-carboxylic acid (VII). The use of pent-5-yn-1-ol (obtainable from tetrahydrofurfuryl chloride in excellent yield; Eglinton, Jones, and Whiting, forthcoming publication; cf. Jones, *J.*, 1950, 756) in a synthesis of this type provides a ready route to 5-methyl-1-carboxylic acids. Thus condensation of this carbinol with *n*-butyl methyl ketone gave eventually 5-methylnonane-1-carboxylic acid.

$$CH_3\cdot CH_2\cdot CMe(OH)\cdot C{\vdots}CH \longrightarrow \underset{(VIII.)}{CH_3\cdot CH{:}CMe\cdot C{\vdots}CH} + I\cdot[CH_2]_4\cdot Cl \xrightarrow{NaNH_2\text{-}NH_3}$$

$$\underset{(IX.)}{CH_3\cdot CH{:}CMe\cdot C{\vdots}C\cdot[CH_2]_4\cdot Cl} \xrightarrow[(2)\ KCN]{(1)\ Pt\text{-}H_2} \underset{(X.)}{CH_3\cdot CH_2\cdot CHMe\cdot[CH_2]_6\cdot CO_2H}$$

The recently perfected method of preparing long-chain αω-chloro-iodides (Ahmad and Strong, *J. Amer. Chem. Soc.*, 1948, **70**, 1699, 3391) suggested their condensation with branched-chain vinylacetylenes to provide intermediates of obvious use in this field. The above series of reactions represents an example of this procedure. Dehydration of 3-methylpent-1-yn-3-ol (prepared from ethyl methyl ketone and sodium acetylide) furnished 3-methylpent-3-en-1-yne (VIII). Condensation of the sodium salt of this hydrocarbon with 1-chloro-4-iodobutane produced the unsaturated chloride (IX); hydrogenation, nitrile formation, and hydrolysis yielded 7-methylnonane-1-carboxylic acid (X). This method is obviously capable of wide variation and applicability, and the ready availability of the starting materials is another advantage. A restricting factor, however, is the solubility of the sodium salt of the intermediate vinylacetylene, *e.g.*, (VIII), in liquid ammonia; this tends to decrease as the length of the carbon chain increases, with consequent deleterious effect on the yield of condensation product. In order to obviate this, the following series of reactions, exemplified by the synthesis of 9-methylheptadecane-1-carboxylic acid, was evolved.

$$\underset{}{C_8H_{17}\cdot CH_2\cdot COMe} + \underset{\text{(XI.)}}{CH{\vdots}C\cdot[CH_2]_5\cdot OR} \longrightarrow \underset{\text{(XII.)}}{C_8H_{17}\cdot CH_2\cdot CMe(OH)\cdot C{\vdots}C\cdot[CH_2]_5\cdot OR} \xrightarrow{KHSO_4}$$

$$\underset{\text{(XIII.)}}{C_8H_{17}\cdot CH{:}CMe\cdot C{\vdots}C\cdot[CH_2]_5\cdot OR} \xrightarrow{Pt\text{–}H_2} C_8H_{17}\cdot CH_2\cdot CHMe\cdot[CH_2]_7\cdot OR \xrightarrow{\text{(1) HBr, (2) KCN, (3) Hydrolysis.}}$$

$$\underset{\text{(XIV.)}}{C_8H_{17}\cdot CH_2\cdot CHMe\cdot[CH_2]_7\cdot CO_2H} \qquad [R = o\text{-}MeO\cdot C_6H_4\cdot]$$

Reaction of the sodium salt of guaiacol with excess of 1 : 5-dibromopentane gave 1-bromo-5-*o*-methoxyphenoxypentane which furnished the acetylenic ether (XI) on being treated with sodium acetylide in liquid ammonia. Condensation of the Grignard complex of this ether with methyl nonyl ketone gave the glycol ether (XII) which was readily dehydrated to the unsaturated ether (XIII). Obvious procedures of hydrogenation, ether fission, nitrile formation, and hydrolysis then yielded the final product, 9-methylheptadecane-1-carboxylic acid (XIV). [Guaiacol was used as a protecting agent because of the relative ease of fission of methoxylated phenyl ethers (Ziegler *et al.*, *Ber.*, 1937, **70**, 1275; 1942, **75**, 1715).]

Although all the above reactions exemplify the synthesis of compounds with a branching methyl group, they are obviously capable of extension to prepare compounds with a branching group of any size by employing the requisite ketone.

EXPERIMENTAL.

3-*Methylnon*-1-*yn*-3-*ol*.—The reaction of hexyl methyl ketone (256 g.) with sodium acetylide (from sodium, 46 g.) employing the usual procedure gave the acetylenic carbinol (232 g., 76%), b. p. 88°/15 mm., n_D^{20} 1·4409 (Petrov and Harlic, *J. Gen. Chem. Russia*, 1941, **11**, 1100, give b. p. 69°/2 mm.).

3-*Methylnon*-1-*yn*-3-*ol*-1-*carboxylic Acid*.—The Grignard complex prepared from the above carbinol (77 g.) and ethylmagnesium bromide (from Mg, 29 g.) was treated with excess of solid carbon dioxide in an autoclave by the method of Haynes and Jones (*loc. cit.*). Working up in the usual manner gave the *acid* (80 g., 80%), crystallising from benzene–light petroleum (b. p. 60—80°) in plates, m. p. 76°; a small sample was purified for analysis by high-vacuum sublimation (Found: C, 67·0; H, 9·35. $C_{11}H_{18}O_3$ requires C, 66·65; H, 9·15%). The S-*benzyl*iso*thiuronium* salt crystallised from aqueous alcohol in needles, m. p. 162° (Found: N, 7·95. $C_{19}H_{28}O_3N_2S$ requires N, 7·95%).

Lactone of 3-*Methylnonan*-3-*ol*-1-*carboxylic Acid* (II).—A solution of the above acetylenic hydroxy-acid (20 g.) in ethyl acetate (50 c.c.) was hydrogenated by use of platinic oxide as catalyst. Removal of catalyst and solvent gave an oil (18 g.), b. p. 112°/0·5 mm., n_D^{20} 1·4487 (Franck *et al.*, *J. Amer. Chem. Soc.*, 1944, **66**, 4, give b. p. 120—125°/4—5 mm. and n_D^{20} 1·4487 for this lactone).

3-*Methylnon*-3-*en*-1-*yne* (IV).—3-Methylnon-1-yn-3-ol (50 g.) was slowly distilled through porous-tile chips coated with aluminium phosphate at 300°/25 mm. in a nitrogen atmosphere; the operation was complete in 2 hours. The wet distillate was diluted with ether, and the solution dried ($MgSO_4$); evaporation of the solvent and distillation gave the *nonenyne* (IV) (32 g.) as a colourless, mobile liquid, b. p. 53°/11 mm., n_D^{22} 1·4464 (Found: C, 88·5; H, 12·2. $C_{10}H_{16}$ requires C, 88·15; H, 11·85%). Light absorption in ethanol: Maximum, 2240 A.; ε = 11,000.

3-*Methylnon*-3-*en*-1-*yne*-1-*carboxylic Acid*.—The hydrocarbon (IV) (25 g.) in an equal volume of dry benzene was added to a benzene solution of ethylmagnesium bromide (from Mg, 4·85 g.), and the stirred mixture heated by steam under nitrogen for 1 hour. The cooled Grignard complex solution was poured on excess of solid carbon dioxide in an autoclave, which was then sealed and kept for 16 hours at room temperature. Working up in the usual manner gave the *acid* as an unstable, pale yellow oil, b. p. 118°/0·05 mm., n_D^{20} 1·4901 (19 g., 58%) (Found: C, 73·1; H, 8·9. $C_{11}H_{16}O_2$ requires C, 73·3; H, 8·95%). Light absorption in ethanol: Maximum, 2420 A., ε = 8500. Inflection, 2710 A., ε = 8000. The S-*benzyl*iso*thiuronium* salt was stable and crystallised from aqueous alcohol in needles, m. p. 148° (Found: N, 8·2. $C_{19}H_{26}O_2N_2S$ requires N, 8·1%).

3-*Methylnonane*-1-*carboxylic Acid*.—(*a*) The lactone (II) (12·4 g.), thionyl chloride (24 g.), and dry benzene (15 c.c.) were heated under reflux for 3 hours, and then cooled; saturated ethanolic hydrogen chloride (50 c.c.) was added dropwise during 15 minutes, and the mixture heated under reflux for a further 15 minutes. The solvents were then removed under vacuum, and the residue heated under reflux for 3 hours; hydrogen chloride was steadily evolved. The product on being distilled gave *ethyl* 3-*methylnon*-3-*ene*-1-*carboxylate* (9·4 g.), b. p. 129°/15 mm., n_D^{21} 1·4379 (Found: C, 73·1; H, 11·7. $C_{13}H_{24}O_2$ requires C, 73·55; H, 11·4%). The ester was immediately dissolved in methanol (50 c.c.) and shaken with hydrogen in the presence of platinic oxide. When absorption was complete the catalyst was filtered off, and methanolic potash (30%; 20 c.c.) added. The mixture was heated under reflux for 30 minutes, and the solvent then removed under vacuum; the residue was dissolved in water and the non-saponified matter extracted with ether. Acidification of the aqueous phase with hydrochloric acid and isolation by means of ether furnished the required acid (III) (7 g.), b. p. 152—153°/10 mm., n_D^{20} 1·4395 (Polgar and Robinson, *J.*, 1945, 390, give b. p. 150—151°/10 mm., $n_D^{17.5}$ 1·4403). The *p*-bromophenacyl ester, m. p. 46°, and the tribromoanilide, m. p. 96°, were prepared by the usual procedures (Polgar and Robinson, *loc. cit.*, give m. p.s 42° and 89·5°; Wilson, *J. Amer. Chem. Soc.*, 1945, **67**, 2162, gives m. p.s 45—46° and 96—97°. These two references will henceforth be designated as P. and W., respectively).

An attempt was made to obtain (III) from the lactone directly by high-pressure hydrogenolysis of the aqueous sodium salt in the presence of copper chromite (Johnson, Goldman, and Schneider, *J. Amer. Chem. Soc.*, 1945, **67**, 1357) but the lactone was reovered unchanged.

(*b*) 3-Methylnon-3-en-1-yne-1-carboxylic acid (6 g.) in methanol (20 c.c.) was catalytically hydrogenated by means of platinic oxide. When uptake was complete, removal of catalyst and solvent followed by distillation yielded the saturated acid (5·4 g.), b. p. 152°/11 mm., n_D^{20} 1·4400, giving derivatives identical with those described above.

But-4-*yn*-1-*ol*.—This carbinol was prepared in 46% yield from ethylene oxide and sodium acetylide in liquid ammonia (cf. Froning and Hennion, *J. Amer. Chem. Soc.*, 1940, **62**, 653). In addition, a high-boiling by-product (7%) was obtained, b. p. 80°/11 mm., n_D^{18} 1·4650 (Found: C, 62·6; H, 8·9. $C_6H_{10}O_2$ requires C, 63·1; H, 8·85%); the compound exhibited alcoholic properties and gave a silver salt and was probably 4-2′-*hydroxyethoxybut*-1-*yne*, $CH\vdots C\cdot[CH_2]_2\cdot O\cdot[CH_2]_2\cdot OH$.

5-*Methyldeca*-3-*yne*-1 : 5-*diol* (V).—But-4-yn-1-ol (20 g.) was slowly added to a solution of ethylmagnesium bromide (from Mg, 15·2 g.) in ether (500 c.c.), and the stirred mixture heated under reflux in nitrogen for 1 hour. A solution of *n*-amyl methyl ketone (28 g.) in benzene (50 c.c.) was then added dropwise, and the whole heated and stirred under reflux for 36 hours. The complex was decomposed with ice and dilute sulphuric acid, and the product isolated by means of ether in the usual manner. Distillation yielded the *diol* (39 g.) as a viscous colourless oil, b. p. 120—122°/10⁻⁴ mm., n_D^{18} 1·4725 (Found: C, 71·75; H, 10·6. $C_{11}H_{20}O_2$ requires C, 71·7; H, 10·9%).

5-*Methyldec*-5-*en*-3-*yn*-1-*ol* (VI).—A mixture of the diol (V) (12 g.) and fused powdered potassium hydrogen sulphate (3 g.) was distilled at atmospheric pressure; the product distilled between 245° and 260°. It was dissolved in ether (30 c.c.), washed with sodium hydrogen carbonate solution, and dried ($MgSO_4$). Evaporation and distillation gave the unsaturated *carbinol* (10 g.), b. p. 128—129°/12 mm., n_D^{20} 1·4800 (Found: C, 78·95; H, 11·05. $C_{11}H_{18}O$ requires C, 79·5; H, 10·9%). Light absorption in ethanol: Maximum, 2270 A.; $\varepsilon = 13{,}000$.

5-*Methyldecan*-1-*ol*.—The unsaturated carbinol (VI) (13 g.), dissolved in ethyl acetate (50 c.c.), was catalytically hydrogenated in the presence of platinic oxide. Removal of catalyst and solvent and distillation furnished the saturated *alcohol* (11 g.), b. p. 120—122°/12 mm., n_D^{20} 1·4383 (Found: C, 76·55; H, 14·05. $C_{11}H_{24}O$ requires C, 76·7; H, 14·05%).

4-*Methylnonane*-1-*carboxylic Acid* (VII).—To a stirred solution of 5-methyldecan-1-ol (7 g.) in acetone (50 c.c.) was added slowly a solution of chromium trioxide in sulphuric acid (6N.; 40 c.c.), and stirring was continued at room temperature for 1 hour. Isolation by means of ether gave the acid (VII) (5·5 g.), b. p. 166°/18 mm., n_D^{21} 1·4416 (*p*-bromophenacyl ester, m. p. 49°; tribromoanilide, m. p. 95°) (P. give b. p. 167—168°/20 mm., n_D^{16} 1·4418; m. p.s 50° and 95·5° respectively).

6-*Methyldec*-4-*yne*-1 : 6-*diol*.—To a solution of the Grignard complex derived from pent-4-yn-1-ol (19·6 g.) and ethylmagnesium bromide (from Mg, 13·2 g.) was added a solution of *n*-butyl methyl ketone (23 g.) in benzene (50 c.c.) in a manner analogous to the cognate preparation described above. Isolation in the usual fashion gave 6-*methyldec*-4-*yne*-1 : 6-*diol* (30 g.) as a viscous, pale yellow oil, b. p. 116°/10⁻³ mm., n_D^{20} 1·4778 (Found: C, 72·2; H, 11·1. $C_{11}H_{20}O_2$ requires C, 71·7; H, 10·9%).

6-*Methyldec*-6-*en*-4-*yn*-1-*ol*.—A mixture of the above diol (10 g.) and potassium hydrogen sulphate (3 g.) was distilled under atmospheric pressure and the distillate collecting between 200° and 230° was diluted with ether (30 c.c.), washed with sodium hydrogen carbonate solution, and dried ($MgSO_4$). Evaporation and distillation gave the primary *alcohol* (7 g.), b. p. 79—82°/10⁻³ mm., n_D^{20} 1·4867 (Found: C, 79·3; H, 11·0. $C_{11}H_{18}O$ requires C, 79·5; H, 10·9%). Light absorption: Maximum, 2280 A.; $\varepsilon = 15{,}000$.

5-*Methylnonane*-1-*carboxylic Acid*.—A solution of the unsaturated carbinol (4 g.) in acetone (20 c.c.) was hydrogenated, platinic oxide being used as catalyst. After removal of the catalyst, the filtrate was treated with a solution of chromium trioxide in sulphuric acid (6N.; 22 c.c.), and the mixture warmed for 30 minutes by steam. The product was extracted with ether, from which the acidic fraction was removed by shaking with sodium hydrogen carbonate solution. Acidification and isolation by means of ether furnished the required acid (2·2 g.), b. p. 155°/12 mm., n_D^{20} 1·4406; *p*-bromophenacyl ester, m. p. 50° (P. give b. p. 164—165°/18 mm., n_D^{20} 1·4403, m. p. 51°).

3-*Methylpent*-3-*en*-1-*yne* (VIII).—3-Methylpent-1-yn-3-ol (70 g.) was slowly distilled in a stream of nitrogen through a tube containing aluminium phosphate-coated porous pot heated to 300°. Drying ($MgSO_4$) and distillation of the product yielded the hydrocarbon (22 g.), b. p. 67—70°, n_D^{20} 1·4318, and unchanged carbinol (27 g.).

1-*Chloro*-7-*methylnon*-7-*en*-5-*yne* (IX).—The hydrocarbon (VIII) (22 g.) in dry ether (50 c.c.) was added to a solution of sodamide (from Na, 11 g.) in liquid ammonia (500 c.c.), and the mixture stirred for one hour. 1-Chloro-4-iodobutane (60 g.; Ahmad and Strong, *loc. cit.*) in dry ether (100 c.c.) was then added, and the stirring continued for 24 hours with constant cooling (carbon dioxide–acetone). The reaction mixture was treated with ammonium chloride (25 g.), and the ammonia allowed to evaporate. Isolation by means of ether in the usual fashion furnished the unsaturated *chloride* (IX) (26 g.) as a pale yellow oil, b. p. 122°/20 mm., n_D^{20} 1·4882 (Found: C, 70·8; H, 9·0. $C_{10}H_{15}Cl$ requires C, 70·4; H, 8·85%). Light absorption in ethanol: Maximum, 2250 A.; $\varepsilon = 9000$.

1-*Chloro*-7-*methylnonane*.—A solution of the unsaturated chloride (IX; 23 g.) in methyl acetate (50 c.c.) was shaken with hydrogen in the presence of platinic oxide until absorption was complete. Removal of catalyst and solvent, followed by distillation, yielded the saturated *chloride* (21 g.), b. p. 113°/20 mm., n_D^{20} 1·4470 (Found: C, 67·7; H, 11·4. $C_{10}H_{21}Cl$ requires C, 67·95; H, 12·0%). The *thiuronium picrate*, prepared by the method of Brown and Campbell (*J.*, 1937, 1699), crystallised from alcohol in yellow needles, m. p. >300°, which detonated violently on rapid heating (Found: N, 15·4. $C_{17}H_{27}O_7N_5S$ requires N, 15·7%).

7-*Methylnonane*-1-*carboxylic Acid*.—The above saturated chloride (14 g.) was heated under reflux with a solution of sodium iodide (25 g.) in dry acetone (200 c.c.) for 12 hours. The precipitated sodium chloride was filtered off, and the solution evaporated; the residue was heated under reflux for 36 hours with a solution of potassium cyanide (9 g.) in aqueous alcohol (80%; 50 c.c.). A solution of potassium hydroxide (9 g.) in water (10 c.c.) was then added, and the mixture heated under reflux for a further 14 hours. Most of the alcohol was removed, and the residue diluted with water and extracted with ether to remove non-acidic material. The aqueous layer was acidified, and the precipitated oil isolated by means of ether. Distillation furnished 7-*methylnonane*-1-*carboxylic acid* (X) (9·2 g.), b. p. 175°/25 mm., n_D^{21} 1·4460 (Found: C, 70·6; H, 11·7. $C_{11}H_{22}O_2$ requires C, 70·9; H, 11·9%). The p-*bromophenacyl* ester crystallised in plates, m. p. 49°, from alcohol (Found: C, 58·9; H, 7·0. $C_{19}H_{27}O_3Br$ requires C, 59·5; H, 7·1%). Evaporation of the ethereal solution of unhydrolysed material yielded the *amide* (1·4 g.), crystallising from alcohol in plates, m. p. 82° (Found: C, 71·05; H, 12·15; N, 7·85. $C_{11}H_{23}ON$ requires C, 71·3; H, 12·5; N, 7·55%).

1-*Bromo*-5-o-*methoxyphenoxypentane* (first prepared by A. W. NINEHAM).—To a solution of sodium (11·5 g.) in absolute alcohol (250 c.c.) was added guaiacol (63 g.) in alcohol (50 c.c.), and the mixture heated by steam for 30 minutes. 1 : 5-Dibromopentane (460 g., 4 mols.) was then rapidly added, and the heating continued for 16 hours. Dilution with an equal volume of water, isolation by means of ether, and distillation furnished 1 : 5-dibromopentane (308 g.) and then 1-*bromo*-5-o-*methoxyphenoxypentane* (103 g.), b. p. 145—147°/1 mm. (Found: Br, 28·9. $C_{12}H_{17}O_2Br$ requires Br, 29·3%).

1-o-*Methoxyphenoxyhept*-6-*yne* (XI) (first prepared by A. W. NINEHAM).—The above bromo-ether (75 g.) in dry ether (50 c.c.) was slowly added to a stirred solution of sodium acetylide (from Na, 14·2 g.) in liquid ammonia (1 l.), and stirring continued for 3 hours. Ammonium chloride (25 g.) was then added, the ammonia allowed to evaporate, and the product isolated by means of ether in the usual fashion. Distillation gave 1-o-*methoxyphenoxyhept*-6-*yne* (55 g.) as a viscous oil, b. p. 122°/10^{-3} mm., which solidified, when kept, to a crystalline mass of needles, m. p. 41° (Found: C, 76·8; H, 8·4. $C_{14}H_{18}O_2$ requires C, 77·05; H, 8·3%).

1-o-*Methoxyphenoxy*-8-*methylheptadec*-6-*yn*-8-*ol* (XII).—To the solution obtained by heating under reflux for 2 hours the foregoing compound (XI) (95 g.) and ethylmagnesium bromide (from Mg, 14·5 g.) in ether (750 c.c.) was added methyl *n*-nonyl ketone (90 g.) in benzene (100 c.c.), and the mixture was heated under reflux for 36 hours. Decomposition with saturated ammonium chloride solution and isolation in the usual manner gave the acetylenic *carbinol* (XII) (112 g.), b. p. 218°/10^{-3} mm., n_D^{20} 1·5038, as a viscous oil which solidified on being cooled to 0° (Found: C, 77·6; H, 10·6. $C_{25}H_{40}O_3$ requires C, 77·3; H, 10·4%).

1-o-*Methoxyphenoxy*-8-*methylheptadec*-8-*en*-6-*yne* (XIII).—A mixture of the acetylenic carbinol (XII) (50 g.) and fused powdered potassium hydrogen sulphate (10 g.) was heated at 0·5 mm. pressure. Water was vigorously evolved when the bath-temperature reached 200°, and the product distilled between 215° and 220°. The product was diluted with ether, washed with sodium hydrogen carbonate solution, and dried ($MgSO_4$). Evaporation and distillation furnished the unsaturated ether (XIII) (34 g.), b. p. 186°/10^{-3} mm., n_D^{20} 1·5100 (Found: C, 80·8; H, 10·4. $C_{25}H_{38}O_2$ requires C, 81·05; H, 10·35%). Light absorption in ethanol: Maximum, 2260 A.; $\varepsilon = 25,000$.

1-o-*Methoxyphenoxy*-8-*methylheptadecane*.—The above ether (XIII) (9 g.) in ethyl acetate (20 c.c.) was shaken with hydrogen in the presence of platinic oxide. When absorption was complete, removal of catalyst and solvent followed by distillation gave the *heptadecane* (8 g.), b. p. 178°/10^{-2} mm., n_D^{23} 1·4878 (Found: C, 79·3; H, 11·95. $C_{25}H_{44}O_2$ requires C, 79·7; H, 11·8%).

1-*Bromo*-8-*methylheptadecane*.—To a solution of the above saturated ether (40 g.) in acetic anhydride (100 c.c.) was slowly added hydrobromic acid (48%; 200 c.c.), and the mixture heated under reflux for 72 hours. The product was cooled, diluted with an equal volume of water, and continuously extracted with light petroleum (b. p. 40—60°). The extract was washed with 2N-sodium hydroxide and dried ($MgSO_4$); evaporation and distillation gave 1-*bromo*-8-*methylheptadecane* (26 g.), b. p. 134°/10^{-3} mm., n_D^{28} 1·4630 (Found: C, 64·8; H, 11·15. $C_{18}H_{37}Br$ requires C, 64·85; H, 11·2%). The *thiuronium picrate*, prepared in the usual manner, crystallised from alcohol in needles, m. p. 111° (Found: N, 12·35. $C_{25}H_{43}O_7N_5S$ requires N, 12·55%).

8-*Methylheptadecane*-1-*carboxylic Acid* (XIV).—A mixture of 1-bromo-8-methylheptadecane (13 g.), potassium cyanide (6 g.), and aqueous alcohol (80%; 50 c.c.) was heated under reflux for 48 hours. Potassium hydroxide (6 g.) in water (10 c.c.) was added, and the solution heated under reflux for a further 36 hours. It was then diluted with an equal volume of water, and the unhydrolysed material extracted with ether ; acidification of the aqueous layer with concentrated hydrochloric acid followed by isolation by means of ether yielded 8-methylheptadecane-1-carboxylic acid (XIV) (11 g.), b. p. 168°/10^{-2} mm., n_D^{28} 1·4530, which soon solidified and crystallised from acetone in prismatic plates, m. p. 40—41° (Found : C, 76·9 ; H, 12·9. Calc. for $C_{19}H_{38}O_2$: C, 76·5 ; H, 12·85%). The amide prepared by way of the acid chloride formed plates, m. p. 70°, from alcohol (Found : N, 4·9. Calc. for $C_{19}H_{39}ON$: N, 4·7%) ; the tribromoanilide, m. p. 90°, crystallised from alcohol in plates (Found : N, 2·3. Calc. for $C_{25}H_{40}ONBr_3$: N, 2·3%) (Cason and Winans, *J. Org. Chem.*, 1950, **15**, 139, give m. p. 38·5—39·1° for the acid, m. p. 69·8—70·5° for the amide, and m. p. 90—91·6° for the tribromoanilide).

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IMPERIAL COLLEGE OF SCIENCE AND TECHNOLOGY,
S. KENSINGTON, LONDON, S.W.7.

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