352. *The Preparation of Some Branched-chain Monocarboxylic Acids.*

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A method is described for preparing monocarboxylic acids containing a quaternary carbon atom in the γ-position to the carboxyl group by condensation of vinyl cyanide with ketones of appropriate structure and the subsequent hydrolysis and reduction (mainly by the Wolff–Kishner method) of the resulting keto-cyanides.

The natural occurrence of a number of branched-chain monocarboxylic acids of physiological importance has stimulated interest in their pure chemistry. The most difficultly accessible of these acids are those containing a quaternary carbon atom, and until recently there were few general methods available for their preparation. The present communication describes a general method for the preparation of monocarboxylic acids containing a quaternary carbon atom in the γ-position to the carboxyl group, based upon the elegant cyanoethylation procedure developed more particularly by Bruson and his co-workers (*J. Amer. Chem. Soc.*, 1942, **64**, 2457 and later papers, especially *ibid.*, p. 2850). These authors have shown that vinyl cyanide condenses smoothly in the presence of alkali with compounds containing active hydrogen (*e.g.*, a methylene group activated by an adjacent carbonyl group) to give (in the example quoted) keto-cyanides which can be hydrolysed to 4-keto-carboxylic acids. When either a methyl or a methylene group is available, the methylene group as expected proves the more reactive. As is shown below, a $CH\lessdot$ group is also selectively activated. These keto-acids can be reduced to yield acids of the required type, the general course of the synthesis thus being :

$$R\cdot CO\cdot CHR'R'' + CH_2{:}CH\cdot CN \longrightarrow R\cdot CO\cdot CR'R''\cdot CH_2\cdot CH_2\cdot CN \xrightarrow{\text{(2 stages)}} R\cdot CH_2\cdot CR'R''\cdot CH_2\cdot CH_2\cdot CO_2H$$

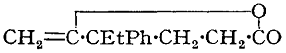
To test the generality of the method, several of the readily accessible aryl alkyl ketones were first examined. *iso*Butyrophenone reacted smoothly with vinyl cyanide to give 3-*benzoyl*-iso*amyl cyanide* which was hydrolysed with aqueous potassium hydroxide to 3-*benzoyl*-3-*methylbutanecarboxylic acid*. This was reduced in good yield by the Clemmensen process to 4-*phenyl*-3 : 3-*dimethylbutanecarboxylic acid*. Propiophenone was alkylated with sodamide and butyl iodide to give ω-*methyl*-ω-n-*butylacetophenone* which with vinyl cyanide gave 3-benzoyl-3-

methylheptyl cyanide, and this was hydrolysed to the *acid*. This could not be reduced completely by the Clemmensen process, but reduction by the modified Wolff–Kishner method (Huang-Minlon, *J. Amer. Chem. Soc.*, 1946, **68**, 2487) yielded 3-*benzyl*-3-*methylheptanecarboxylic acid*. Starting with ω-*methyl*-ω-n-*octylacetophenone* (from propiophenone, sodamide, and *n*-octyl iodide), 3-*benzoyl*-3-*methylundecanecarboxylic acid* was prepared and reduced to 3-*benzyl*-3-*methylundecanecarboxylic acid*. In an attempted preparation of 3-benzyl-3-ethylhexanecarboxylic acid, however, although the intermediate 3-*benzoyl*-3-*ethylhexanecarboxylic acid* was prepared by the cyanoethylation procedure from ω-*ethyl*-ω-*propylacetophenone* it was only partially reduced by the Wolff–Kishner method. In these examples the structures of the cyanides and keto-acids must be those assumed, since only one active position is open to attack in the ketone.

The next two examples of these acids were prepared from benzyl methyl ketone by mono-alkylation followed by reaction with vinyl cyanide, hydrolysis, and reduction. Here it has been assumed that the point of attack must be at the doubly activated position between the benzene ring and the carbonyl group. Ethylation of benzyl methyl ketone followed by cyanoethylation and hydrolysis gave 3-*acetyl*-3-*phenylpentanecarboxylic acid* (I). As expected, this proved resistant to Clemmensen reduction, and an attempted reduction with red phosphorus and hydriodic acid gave a crystalline *product*, $C_{14}H_{16}O_2$, whose structure is not apparent from its general behaviour. It liberates carbon dioxide from aqueous sodium carbonate and is unsaturated, perbenzoic-acid titration indicating the presence of one double bond. The molecular formula and unsaturation could be accommodated in a lactone structure (II),*

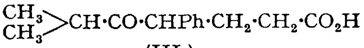
$CH_3{\cdot}CO{\cdot}CEtPh{\cdot}CH_2{\cdot}CH_2{\cdot}CO_2H$

(I).



$CH_2{=}C{\cdot}CEtPh{\cdot}CH_2{\cdot}CH_2{\cdot}CO$ (ring closed through O)

(II.)



$(CH_3)_2{>}CH{\cdot}CO{\cdot}CHPh{\cdot}CH_2{\cdot}CH_2{\cdot}CO_2H$

(III.)

and it is known that γ-keto-acids may be transformed into unsaturated lactones under the influence of such reagents as acetic anhydride, but the reaction of the above product with carbonate solution was more characteristically that of an acid than a lactone. In an attempt to prepare such a lactone, 3-acetyl-3-phenylpentanecarboxylic acid was refluxed with acetic anhydride, but no homogeneous material of the desired composition was obtained from the neutral fraction of the distilled product. For further comparison a specimen of 3-*phenyl*-3-iso-*butyrylpropanecarboxylic acid* (III), in which the carbonyl group is flanked on each side by CH groups, was prepared by cyanoethylation of benzyl *iso*propyl ketone and hydrolysis. This acid was recovered largely unchanged after being heated with syrupy phosphoric acid containing phosphoric oxide, and after being heated with acetic anhydride. Reduction of the acetyl-phenylpentanecarboxylic acid by the Wolff–Kishner method gave the required 3-*phenyl*-3-*ethylpentanecarboxylic acid*. Octylation of benzyl methyl ketone gave 3-*phenylundecan*-2-*one*, and this on cyanoethylation and hydrolysis yielded 3-*acetyl*-3-*phenylundecanecarboxylic acid*, reduced by the Wolff–Kishner process to 3-*phenyl*-3-*ethylundecanecarboxylic acid*.

Finally, some specimens of purely aliphatic acids of the type under consideration were prepared. 3-Acetyl-3-methylbutanecarboxylic acid was prepared from methyl *iso*propyl ketone, its melting point and that of its semicarbazone agreeing satisfactorily with the recorded figures and confirming the view that the CH$<$ group rather than the methyl group would be attacked by the vinyl cyanide. It was partially reduced by prolonged Clemmensen treatment, and by careful fractionation of the product a specimen of pure 3 : 3-*dimethylpentanecarboxylic acid* was obtained. 3 : 3-*Dimethylnonane*- and 3 : 3-*dimethyltridecane-carboxylic acid* were obtained in the same way from the appropriate ketones, the final reduction being achieved by the Wolff–Kishner method.

The characterisation of these acids proved difficult, and the only satisfactory crystalline derivatives prepared were the *S*-benzylthiouronium salts (Donleavy, *J. Amer. Chem. Soc.*, 1936, **58**, 1004). The acids themselves were mostly viscous liquids showing little tendency to crystallise, although some crystallised on long standing.

In the preparation of 3-benzoyl-3-methylbutanecarboxylic acid an attempt was made to hasten the slow hydrolysis of the cyanide by addition of methyl alcohol to the reaction mixture.

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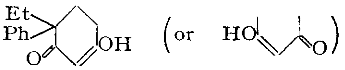
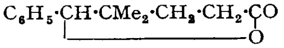
* The authors are indebted to Dr. A. J. Birch for the suggestion that the substance is probably a dihydroresorcinol derivative :



Dr. Birch has observed the formation of such a substance from a similar keto-acid by the action of sulphuric acid.

Rapid reaction occurred, but the product, a crystalline substance melting at 102—103°, was obviously not the expected acid. It proved to be the *lactone* of 4-*hydroxy*-4-*phenyl*-3 : 3-*dimethylbutanecarboxylic acid* (IV), resulting evidently from the reduction of the carbonyl group of the primary product of hydrolysis, the keto-acid, by the aqueous methyl-alcoholic potash.

(IV.)



$$C_6H_5\cdot CH\cdot CMe_2\cdot CH_2\cdot CH_2\cdot CO \quad (CH\text{—}O\text{—}CO)$$

The use of methyl alcohol as a reducing agent is familiar in some fields, but the reduction of ketones by this method may not be so well known, although the use of metal alkoxides and alcohols is now common. An early example of this type of reaction is the conversion of camphor into borneol by means of alcoholic potash (Berthelot, *Ann. Chim.*, 1859, **56**, 51), and the reduction of benzophenone to benzhydrol by alcoholic potash has been reported by several workers (*e.g.*, Saqumenny, *Annalen*, 1877, **184**, 174; Montagne, *Rec. Trav. chim.*, 1908, **27**, 334). The latter reduction proceeds well in the presence of a large excess of 30% methyl-alcoholic potassium hydroxide, but with only one molecular proportion of potassium hydroxide no reduction was observed. When *iso*propyl alcohol was used the reaction proceeded well in the presence of a moderate excess of potassium hydroxide.

EXPERIMENTAL.

3-*Benzoyl*iso*amyl Cyanide*.—Vinyl cyanide (21·2 g.) was added dropwise with stirring to a solution of *iso*butyrophenone (60 g.) in dioxan (100 g.) containing 5 c.c. of 30% methyl-alcoholic potassium hydroxide. The product was poured into water and the oil separated, dried, and distilled. After low-boiling material (including 20 g. of recovered and redistilled *iso*butyrophenone, b. p. 108°/23 mm.) had been removed, the required *cyanide* was obtained as a viscous oil (31 g.), b. p. 194—200°/23 mm. (Found : N, 7·4. $C_{13}H_{15}ON$ requires N, 7·0%).

3-*Benzoyl*-3-*methylbutanecarboxylic Acid*.—The cyanide (25·5 g.) was refluxed and stirred vigorously with a solution of potassium hydroxide (25 g.) in water (120 c.c.) until evolution of ammonia ceased. The reaction mixture was acidified, extracted with chloroform, dried, and distilled, yielding the *acid* (23 g.) as a viscous oil distilling almost entirely at 213°/18 mm. (Found : C, 70·6; H, 7·13. $C_{13}H_{16}O_3$ requires C, 70·9; H, 7·28%). The acid was characterised as the *semicarbazone* which crystallised from alcohol in small clumps of needles, m. p. 202—203° (decomp.) (Found : N, 15·0. $C_{14}H_{19}O_3N_3$ requires N, 15·2%).

4-*Phenyl*-3 : 3-*dimethylbutanecarboxylic Acid*.—The above keto-acid (22 g.) in toluene was refluxed with amalgamated zinc (100 g.) and excess of somewhat diluted hydrochloric acid for 24 hours with addition from time to time of further quantities of concentrated hydrochloric acid. The *acid* (17·5 g.) was isolated as a viscous oil, the bulk distilling at 181°/15 mm. (Found : C, 75·7; H, 8·34. $C_{13}H_{18}O_2$ requires C, 75·8; H, 8·74%). The S-*benzylthiouronium* salt had m. p. (from alcohol) 148° (Found : N, 7·3. $C_{21}H_{28}O_2N_2S$ requires N, 7·5%).

ω-*Methyl*-ω-n-*butylacetophenone*.—Propiophenone (27 g.) in benzene was alkylated with sodamide (9 g.) and *n*-butyl iodide (37 g.), and worked up to give the *ketone* (20 g.) as a viscous oil, b. p. 133—138°/15 mm. (Found : C, 81·6; H, 9·91. $C_{13}H_{18}O$ requires C, 82·1; H, 9·47%). The orange-coloured 2 : 4-*dinitrophenylhydrazone* had m. p. 74·5—75° (Found : N, 15·3. $C_{19}H_{22}O_4N_4$ requires N, 15·1%).

3-*Benzoyl*-3-*methylheptanecarboxylic Acid*.—The above ketone (18 g.) in dioxan was treated dropwise with vinyl cyanide (6 g.) in the presence of a small quantity of methyl-alcoholic potash, and the mixture kept at 50—60° for a few hours. The product was worked up to give the cyanide (5 g.) as a clear liquid, b. p. 210—215°/15 mm. A repetition of this preparation, using *tert.*-butyl alcohol as solvent, resulted in a more vigorous reaction and a better yield (6 g. of cyanide from 10 g. of ketone). The cyanide (11 g.) was hydrolysed with excess of concentrated aqueous potassium hydroxide, evolution of ammonia taking place slowly during about 12 hours' refluxing. The *acid* was obtained as a thick viscous oil (7 g.), b. p. 238°/16 mm. (Found : C, 72·5; H, 8·92. $C_{16}H_{22}O_3$ requires C, 73·3; H, 8·4%).

3-*Benzyl*-3-*methylheptanecarboxylic Acid*.—The keto-acid was only partly reduced in toluene by the Clemmensen method during 20 hours (Found, on a specimen of the distillate of b. p. 216—218°/14 mm.: C, 74·7; H, 8·86. Calc. for $C_{16}H_{24}O_2$: C, 77·4; H, 9·68%). The keto-acid was therefore reduced by the modified Wolff–Kishner method; a mixture of the acid (3 g.), 50% hydrazine hydrate (3 c.c.), and sodium hydroxide (1 g.) in 2 : 2′-dihydroxydiethyl ether (10 c.c.) was refluxed for $1\frac{1}{2}$ hours, and water then removed in a slow current of air until the temperature of the mixture rose to 195°; refluxing was then continued on the oil-bath for 4 hours. The product was worked up to give the *acid* (2 g.) as a viscous oil, b. p. 197—200°/11 mm. (Found : C, 77·7; H, 9·81%). The S-*benzylthiouronium* salt had m. p. (from alcohol) 122° (Found : N, 7·0. $C_{24}H_{32}O_2N_2S$ requires N, 6·8%).

ω-*Methyl*-ω-n-*octylacetophenone*.—Propiophenone (21 g.) in benzene was gently refluxed with sodamide (7 g.), and octyl iodide (36 g.) was then added with stirring. After an induction period a vigorous reaction took place. The mixture was refluxed for $1\frac{1}{2}$ hours, left overnight, and worked up to give the *ketone* (20 g.) as a viscous oil, b. p. 183—187° (Found : C, 83·0; H, 10·57. $C_{17}H_{26}O$ requires C, 82·9; H, 10·57%). The 2 : 4-*dinitrophenylhydrazone* crystallised from alcohol in yellow platelets, m. p. 88—89° (Found : N, 13·4. $C_{23}H_{30}O_4N_4$ requires N, 13·1%).

3-*Benzoyl*-3-*methylundecanecarboxylic Acid*.—The above ketone (19 g.) in dioxan was cyanoethylated with vinyl cyanide (5 g.) in the presence of methyl-alcoholic potash to give after distillation unchanged ketone (13 g.) and a rather poor yield (6 g.) of cyanide. By carrying out the reaction in *tert.*-butyl alcohol, however, an excellent yield was obtained (13 g. of cyanide, b. p. 190—197°/1 mm., from 13 g.

of ketone). The cyanide (12 g.) was hydrolysed (12 hours) by excess of aqueous potassium hydroxide to give the *acid*, which was obtained as a thick yellow oil (8 g.), b. p. 223—225°/1 mm. (Found: C, 75·0; H, 9·60. $C_{20}H_{30}O_3$ requires C, 75·4; H, 9·43%).

3-*Benzyl*-3-*methylundecanecarboxylic Acid*.—The keto-acid (8 g.), 50% hydrazine hydrate (10 c.c.), and sodium hydroxide (3 g.) in 2 : 2′-dihydroxydiethyl ether (40 c.c.) were refluxed for 1½ hours, and water was then removed until the temperature of the liquid reached 195°; refluxing was then continued for 4 hours. The *acid* was obtained as a white solid (4 g.), b. p. 207—208°/1 mm., which crystallised in fine needles, m. p. 81°, from methyl alcohol (Found: C, 79·2; H, 10·31. $C_{20}H_{32}O_2$ requires C, 78·9; H, 10·5%). The S-*benzylthiouronium* salt had m. p. (from alcohol) 145° (Found: N, 5·9. $C_{28}H_{42}O_2N_2S$ requires N, 6·2%).

3-*Benzoyl*-3-*ethylhexanecarboxylic Acid*.—ω-Ethyl-ω-*n*-propylacetophenone (38 g.) in dioxan was cyanoethylated to give a small high-boiling fraction together with a large amount of unchanged ketone (26 g.). The crude cyanide was slowly hydrolysed by aqueous potassium hydroxide to give the required *acid*, isolated as a thick viscous oil (4·5 g.), b. p. (redistilled) 220°/16 mm. (Found: C, 73·1; H, 8·26. $C_{16}H_{22}O_3$ requires C, 73·3. H, 8·4%). This acid underwent partial reduction under Wolff–Kishner conditions, giving a small amount (1·5 g.) of a yellow oil with a characteristic unpleasant odour of burned fat, b. p. *ca.* 175°/1 mm. (Found: C, 75·5; H, 8·99. Calc. for $C_{16}H_{24}O_2$: C, 77·4; H, 9·68%).

3-*Acetyl*-3-*phenylpentanecarboxylic Acid*.—Benzyl methyl ketone (27 g.) in benzene was alkylated with sodamide (8 g.) and ethyl iodide (33 g.) to give 3-phenylpentan-2-one as a clear mobile liquid (23 g.), b. p. 123—125°/24 mm. The semicarbazone crystallised in white platelets from aqueous acetone, m. p. 190—191° (Suter and Wilson, *J. Amer. Chem. Soc.*, 1942, **64**, 533, give m. p. 190·5—191·5°). The ketone (14 g.) in dioxan was cyanoethylated (6 g. of vinyl cyanide) to give the required cyanide as a slightly yellow viscous oil (11 g.), b. p. 205—215°/23 mm. The cyanide (27 g.) was hydrolysed to give the *acid* (27 g.), b. p. 193—197°/2—3 mm. By crystallisation from light petroleum (b. p. 60—80°) in the presence of a little chloroform it was obtained as clear diamond-shaped crystals, m. p. 78° (Found: C, 71·8; H, 7·6. $C_{14}H_{18}O_3$ requires C, 71·8; H, 7·7%). It did not give a semicarbazone or a dinitrophenylhydrazone.

3-*Phenyl*-3-*ethylpentanecarboxylic Acid*.—(*a*) After an attempted reduction of the above keto-acid by the Clemmensen method for 20 hours, almost all the starting material was recovered unchanged.

(*b*) *Reduction with red phosphorus and hydriodic acid.* The keto-acid (7 g.) was refluxed with potassium iodide (2 g.) and red phosphorus (6 g.) in phosphoric acid (70 c.c.) and water (10 c.c.) for 6 hours. The mixture was poured into water, filtered, and ether-extracted. After being washed with sodium thiosulphate solution the ethereal solution was dried and distilled, giving a syrupy yellow oil (3 g., b. p. 195—200°/2—4 mm.) which set to a glassy mass. By being warmed with ether the material was obtained in the form of white crystals, m. p. 156° [Found: C, 77·8, 77·6; H, 7·64, 7·53; *M* (Rast), 218. $C_{14}H_{16}O_2$ requires C, 77·7; H, 7·41%; *M*, 216). The *substance* liberated carbon dioxide from aqueous sodium carbonate, decolourised alkaline permanganate immediately, and reacted readily with bromine in chloroform. Perbenzoic acid titration indicated the presence of one double bond (0·0076 g. of substance reacted with 0·00608 m.e. of perbenzoic acid. Calc.: 0·00703 m.e.). By refluxing with excess of acetic anhydride the substance was partly converted into neutral material, but no pure product was isolated.

(*c*) *Wolff–Kishner reduction.* The keto-acid (7 g.), 50% hydrazine hydrate (10 c.c.), and sodium hydroxide (3 g.), after working up, gave the *acid* (3 g.) as a clear syrupy liquid, b. p. 155—165°/1—2 mm., with a characteristic smell of burned fat (Found: C, 75·8; H, 8·9. $C_{14}H_{20}O_2$ requires C, 76·4; H, 9·1%). The S-*benzylthiouronium* salt had m. p. (from alcohol) 153—154° (Found: N, 7·4. $C_{22}H_{30}O_2N_2S$ requires N, 7·3%).

3-*Phenyl*-3-iso*butyrylpropyl Cyanide*.—Vinyl cyanide (10 g.) was added slowly with shaking to benzyl *iso*propyl ketone (27 g.) in dioxan containing a small quantity of 30% methyl-alcoholic potash. The mixture became hot; after 3 hours it was poured into water, acidified, and extracted with ether. Distillation gave the *cyanide* (27 g.) as a clear mobile liquid, b. p. 218—222°/71 mm. (Found: N, 6·4. $C_{14}H_{17}ON$ requires N, 6·5%).

3-*Phenyl*-3-iso*butyrylpropanecarboxylic Acid*.—The above cyanide (26 g.) was saponified with a concentrated aqueous solution of potassium hydroxide (20 g.) by refluxing overnight. The potassium salt, which had separated as an oily layer which congealed on cooling, was dissolved in water and the acid precipitated with hydrochloric acid. On standing, it slowly solidified. It was dissolved in chloroform, and the solution dried and distilled to give a very viscous oil (25 g., b. p. 235—237°/64 mm.) which slowly crystallised. Crystallisation from light petroleum (b. p. 80—100°) gave the *acid* as clusters of needles, m. p. 71·5° (after some previous softening) (Found: C, 71·7; H, 7·6. $C_{14}H_{18}O_3$ requires C, 71·8; H, 7·7%). By heating the acid with excess of syrupy phosphoric acid containing phosphoric oxide, a dark wine-red solution was obtained; after pouring this into water and working up through the sodium salt (charcoal), a crude material was obtained which immediately decolourised alkaline permanganate, but the only pure compound isolated from it was the unchanged keto-acid. After being refluxed for several hours with excess of acetic anhydride the keto-acid was recovered largely unchanged, and more prolonged treatment gave only a small amount of neutral material from which no pure compound was isolated.

3-*Phenylundecan*-2-*one*.—Benzyl methyl ketone (32 g.) in benzene was alkylated with sodamide (10 g.) and octyl iodide (54 g.), and, after working up, the *ketone* was obtained as a clear liquid (27 g.), b. p. 173—174°/14 mm. (Found: C, 82·6; H, 10·78. $C_{17}H_{26}O$ requires C, 82·9; H, 10·57%). The *semicarbazone* separated from alcohol as a white powder, m. p. 57° (Found: N, 13·8. $C_{18}H_{29}ON_3$ requires N, 13·9%). The 2 : 4-*dinitrophenylhydrazone* crystallised from alcohol in yellow needles, m. p. 51° (Found: N, 13·6. $C_{23}H_{30}O_4N_4$ requires N, 13·1%).

3-*Acetyl*-3-*phenylundecanecarboxylic Acid*.—The above ketone (26 g.) in *tert.*-butyl alcohol was cyanoethylated with vinyl cyanide (7 g.) in the presence of methyl-alcoholic potash to give the cyanide (14 g.) as a slightly yellow viscous oil, b. p. 217°/2—3 mm. Alkaline hydrolysis of the cyanide (12 g.) with vigorous stirring and refluxing for 16 hours followed by acidification, extraction with chloroform, drying, and distillation gave the required *acid* (7 g.) as a thick liquid (b. p. 230°/1 mm.) which solidified.

It was crystallised from light petroleum, from which it separated as a white powder, m. p. 63° (Found : C, 75·9; H, 9·72. $C_{20}H_{30}O_3$ requires C, 75·4; H, 9·43%).

3-*Phenyl*-3-*ethylundecanecarboxylic Acid*.—The above keto-acid (6 g.) was reduced with 50% hydrazine hydrate (8 c.c.), sodium hydroxide (3 g.), and 2 : 2′-dihydroxydiethyl ether to give the required *acid* (3 g.) as a yellow oil, b. p. 205—210°/1 mm., with a peculiar fatty odour (Found : C, 78·2; H, 10·10. $C_{20}H_{32}O_2$ requires C, 78·9; H, 10·52%). The *S*-benzylthiouronium salt could not be prepared in a crystalline form.

3 : 3-*Dimethylpentanecarboxylic Acid*.—Vinyl cyanide (30 g.) and methyl *iso*propyl ketone (42 g.) in *tert*.-butyl alcohol (6 g.) containing 10 c.c. of 30% methyl-alcoholic potash gave 3-acetyl*iso*amyl cyanide (41 g.), b. p. 134°/18 mm., which was hydrolysed with aqueous potassium hydroxide to the corresponding acid (42 g.), b. p. 173—175°/21 mm., which solidified to a brittle solid, m. p. 40—45°, raised by 3 crystallisations to 46·5—47° (Blaise, *Bull. Soc. chim.*, 1899, **21**, 719, gives m. p. 48—49°). The semicarbazone had m. p. 186° (decomp.) (Blaise, *loc. cit.*, gives m. p. 185°). The keto-acid (10 g.), potassium iodide (2 g.), red phosphorus (6 g.), phosphoric acid (70 c.c.), and water (10 c.c.) gave, after refluxing for 5 hours and working up, a product, b. p. 150—160°/21 mm., from which unchanged keto-acid crystallised on standing. The oily residue was redistilled to give a clear liquid whose analytical figures indicated only partial reduction (Found : C, 64·5; H, 8·69. $C_8H_{16}O_2$ requires C, 66·7; H, 11·11%). By prolonged Clemmensen reduction a small amount of pure 3 : 3-*dimethylpentanecarboxylic acid* was obtained; the keto-acid (10 g.) in toluene (20 c.c.) was refluxed for 40 hours with amalgamated zinc (20 g.), water (15 c.c.), concentrated hydrochloric acid (35 c.c.), and glacial acetic acid (2 c.c.), further addition of hydrochloric acid being made at the rate of 10 c.c. every 6 hours. The toluene layer was separated and added to an ethereal extract of the aqueous layer, dried, and distilled, giving two fractions : (*a*) b. p. 130—150°/16 mm. (4 g.), (*b*) b. p. 165—170°/16 mm. (6 g., unchanged keto-acid). Fraction (*a*) was redistilled, and a portion of the middle distillate analysed (Found : C, 66·7; H, 11·23%). The acid was characterised as the S-*benzylthiouronium* salt, m. p. (from alcohol) 150° (Found : N, 9·4. $C_{16}H_{26}O_2N_2S$ requires N, 9·0%).

3-*Hexoyl*-3-*methylbutanecarboxylic Acid*.—*iso*Propyl amyl ketone (16 g.) was cyanoethylated with vinyl cyanide (7 g.) in *tert*.-butyl alcohol in the presence of a small amount of methyl-alcoholic potash to give the cyanide as a yellow oil, b. p. 156—159°/11 mm. The cyanide (9 g.) was hydrolysed by 10 hours' refluxing with concentrated aqueous potassium hydroxide and worked up to yield the corresponding acid as a yellow oil (4 g.), b. p. 181—183°/10 mm., which was not yet pure, although giving a satisfactory product on reduction in the next stage (Found : C, 66·1, 65·9; H, 10·0, 10·1. Calc. for $C_{12}H_{22}O_3$: C, 67·3; H, 10·28%).

3 : 3-*Dimethylnonanecarboxylic Acid*.—The above keto-acid was reduced by the Wolff–Kishner method (3 c.c. of 50% hydrazine hydrate, 1 g. of sodium hydroxide, 20 c.c. of 2 : 2′-dihydroxydiethyl ether) to give the *acid* (2 g.) as a liquid with a peculiar fatty odour, b. p. 157°/10 mm. (Found : C, 71·6; H, 12·1. $C_{12}H_{24}O_2$ requires C, 72·0; H, 12·0%). The S-*benzylthiouronium* salt had m. p. (from alcohol) 133° (Found : N, 7·7. $C_{20}H_{34}O_2N_2S$ requires N, 7·8%).

2-*Methyldodecan*-3-*one*.—A mixture of nonanecarboxylic acid (0·5 mol.) and *iso*butyric acid (1 mol.) was passed over a thoria catalyst supported on pumice at a furnace temperature of 450—470°. The distillate was neutralised, dried, and distilled, giving the following fractions : (*a*) di*iso*propyl ketone (20 g.), (*b*) iso*propyl nonyl ketone*, b. p. 150—151°/16 mm., m. p. −1° (16 g.) (Found : C, 78·3; H, 13·12. $C_{13}H_{26}O$ requires C, 78·8; H, 13·13%). Crystalline derivatives were obtained with 2 : 4-dinitrophenylhydrazine (orange plates, m. p. 36°) and semicarbazide (m. p. 50—51°), but in spite of repeated recrystallisations satisfactory figures for the nitrogen content of these derivatives were not obtained, Kjeldahl determinations (which had given satisfactory results in all other cases in this series) being erratic and unreproducible.

3-*Decoyl*-3-*methylbutanecarboxylic Acid*.—The above ketone (15 g.) in *tert*.-butyl alcohol was cyanoethylated with vinyl cyanide (5 g.) in the presence of methyl-alcoholic potash, a vigorous reaction taking place. The cyanide was obtained as a yellow oil (12 g.), b. p. 210—220°/10 mm., which solidified on freezing; m. p. 10°. The cyanide was slowly hydrolysed by refluxing with excess of aqueous potassium hydroxide, and the product worked up to give the corresponding *acid* (7 g.), b. p. 225—230°/10 mm., which solidified on cooling. It was recrystallised from light petroleum; m. p. 43° (Found : C, 71·4; H, 11·48. $C_{16}H_{30}O_3$ requires C, 71·1; H, 11·16%).

3 : 3-*Dimethyltridecanecarboxylic Acid*.—The keto-acid (6 g.) was reduced by the Wolff–Kishner process (using 4 c.c. of 50% hydrazine hydrate, 3 g. of sodium hydroxide, and 30 c.c. of 2 : 2′-dihydroxydiethyl ether) to give the *acid* (3 g.), b. p. 200—205°/10 mm., as a fatty-smelling liquid (Found : C, 75·3; H, 12·5. $C_{16}H_{32}O_2$ requires C, 75·0; H, 12·5%). The S-*benzylthiouronium* salt had m. p. (from alcohol) 134° (Found : N, 6·6. $C_{24}H_{42}O_2N_2S$ requires N, 6·5%).

The Lactone of 4-*Hydroxy*-4-*phenyl*-3 : 3-*dimethylbutanecarboxylic Acid*.—3-Benzoyl*iso*amyl cyanide (28 g.) was treated with excess of a concentrated aqueous solution of potassium hydroxide (30 g.), and sufficient methyl alcohol added to make the mixture homogeneous. On refluxing, a rapid evolution of ammonia took place, and when this had ceased the product was diluted with water, acidified, and extracted with chloroform. The dried extract was distilled, yielding a viscous oil (20 g.), b. p. 117—125°/26 mm., which solidified slowly. The *lactone* crystallised from light petroleum (80—100°) as felted white needles, m. p. 102—103° (Found : C, 76·5; H, 7·9. $C_{13}H_{16}O_2$ requires C, 76·5; H, 7·8%). It was not affected by dilute aqueous sodium carbonate in the cold, but reacted on heating. The resulting solution was stable to permanganate.

Reduction of Benzophenone.—Benzophenone (5 g.) was refluxed overnight with a large excess of methyl-alcoholic potash, diluted with water, and extracted with ether. Removal of the solvent yielded a residue of crude benzhydrol (5 g.) which on crystallisation from light petroleum melted at 65—66°. When benzophenone was heated with an equimolecular quantity of potassium hydroxide in excess of methyl alcohol no reduction took place. When the methyl alcohol was replaced by *iso*propyl alcohol, however (3·64 g. of ketone, 20 c.c. of alcohol), reduction took place readily in the presence of a moderate excess of potassium hydroxide (1·20 g.); the crude benzhydrol, isolated by pouring the mixture into water, was yellowish-brown, but after being dried and crystallised from light petroleum it was obtained as white needles (2·38 g.), m. p. 65—66°.

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