88. *Long-chain Acids containing a Quaternary Carbon Atom. Part I.*

By A. J. Birch and Sir Robert Robinson.

A preliminary survey has been made of the methods applicable to the synthesis of acids of varied constitution containing a quaternary carbon atom, and a number of substances of this type have been prepared. Their characteristic behaviour in mono-layer films and their biological effects will be described later.

Very few branched-chain fatty acids have been found in nature and most of those known are related to terpenoid compounds. The oils of *Hydnocarpus* and related species contain, however, a number of acids characterised by the presence of a *cyclo*pentene ring. The naphthenic acids from petroleum (cf. " The Science of Petroleum," Oxford, 1938, **2**, 1013) are mainly homologous compounds, containing a trimethyl*cyclo*pentane ring, but some are straight-chain acids with attached methyl groups. Another important series of branched-chain fatty acids has recently been isolated by Anderson and co-workers from *Mycobacterium Lepræ* and *M. Tuberculosis*, and some of the compounds were thought to be the characteristic toxins of the organisms (*J. Biol. Chem.*, 1927, **74**, 537; 1929, **83**, 169; 1930, **85**, 77; 1932, **97**, 619; 1932, **98**, 43; 1934, **106**, 87; 1936, **113**, 637; 1936, **114**, 431, 467; and later papers). Sabin (*J. Exp. Med.*, 1927, **46**, 645) showed that Anderson's phthioic acid (from *M. Tuberculosis*) produces local lesions on injection, similar in character to those produced by the living organism, but it now seems possible that it is a breakdown product of the true toxin, which is an acid $C_{60}H_{120}(CO_2H)(CH_2{\cdot}OH)$, active in doses of only 0·002 mg., and produces lesions away from the site of injection, *e.g.*, in the lungs (Chocroun, *Compt. rend.*, 1940, **210**, 749).

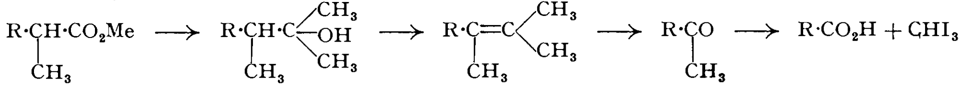
Many synthetic branched-chain acids have been synthesised, especially by Adams and his co-workers (*J. Amer. Chem. Soc.*, 1925, **47**, 2727; 1926, **48**, 1080, 1089, 2385, 2393, 2444; 1927, **49**, 2934, 2940; 1928, **50**, 1475, 1503, 1983, 2297; 1929, **51**, 1261), but since the malonic ester method was almost invariably used, the acids have been of the mono- or di-substituted-acetic acid type. Only one or two long-chain acids containing quaternary carbon atoms have been described.

Phthioic Acid.—Anderson (*loc. cit.*) isolated the branched-chain acids from *M. Tuberculosis* by first extracting fatty material with a mixture of alcohol and ether, and then separating the fraction soluble in acetone. The acids produced by saponification, when submitted to a lead salt–ether separation, gave lead palmitate with a little stearate and cerotate, and the soluble lead salts of a mixture of acids. These were hydrogenated, and again separated by solution of the lead salts in ether. The soluble portion contained the salts of a mixture of saturated fatty acids which were esterified, and fractionated, giving esters corresponding to an acid $C_{19}H_{38}O_2$, tuberculostearic acid, which had no physiological action, an acid, $C_{26}H_{52}O_2$, phthioic acid, which was toxic, and some higher acids which were not fully investigated.

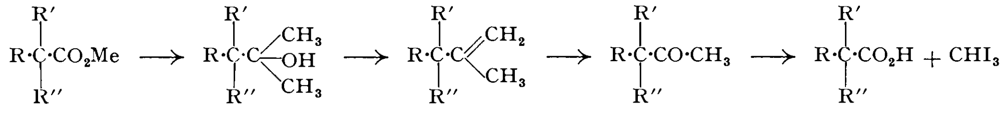
The purest specimens of phthioic acid had m. p. 20—21° and were optically active. Analysis of the acid itself, and of crystalline derivatives, established the formula $C_{26}H_{52}O_2$; it may be derived from some unsaturated precursor. The degradation of phthioic acid has not shed much light on the structure of the substance. Wagner-Jauregg (*Z. physiol. Chem.*, 1937, **247**, 135) obtained a maximum of 2·41 mols. of acetic acid in a Kuhn–Roth determination, compared with a value of 1·41 for tuberculostearic acid. Apart from the possibility of a larger number of *gem*-dimethyl groups, this demonstrated that phthioic acid has three, or at most four, chains in the molecule. Chargaff (*Ber.*, 1932, **65**, 745) synthesised a number of C_{26} acids of the form $RR'CH{\cdot}CO_2H$, and from a study of their m. p.'s arrived at the same conclusion.

Spielman and Anderson (*J. Biol. Chem.*, 1935—36, **112**, 759) oxidised phthioic acid by means of chromic acid in acetic acid solution. They obtained a saturated fatty acid, $C_{11}H_{22}O_2$, which was stated to differ from *n*-undecoic acid in that the derivatives had lower m. p.'s. They therefore concluded that it had a branched chain but in view of the small amount available, and the difficulty of separating close homologues, the identity of this C_{11} acid must still be regarded as an open question.

Spielman and Anderson also attempted to determine the nature of the alkyl groups adjacent to the carboxyl by treating methyl phthioate with methylmagnesium iodide, dehydrating the tertiary alcohol formed, and oxidising the hydrocarbon. They obtained what they thought to be a methyl ketone, and interpreted their results in the following manner :



The experimental evidence is not convincing and these results can be interpreted in other ways, for example :



Spielman and Anderson found the chlorination of the acid by phosphorus pentachloride to be gradual and progressive and no clear deduction from the experiment was possible.

These workers stated their conclusions as follows : " Phthioic acid possesses a branched chain, probably with methyl groups in the α-position, and in the neighbourhood of the eleventh carbon atom."

Since purely chemical methods had proved inconclusive, Stenhagen (private communications) turned his attention to physical methods. Chibnall and Piper (*Biochem. J.*, 1934, **28**, 2189, etc.; cf. Francis, *Proc. Roy. Soc.*, 1930, *A*, **128**, 214; Shearer, *Proc. Roy. Soc.*, 1925, *A*, **108**, 655) have used the method of *X*-ray reflection from crystalline layers with signal success in the examination of long-chain substances from waxes, but it was found that suitable layers could not be obtained from phthioic acid. Stenhagen succeeded, however, in building multilayer films of barium phthioate. Examination of these by *X*-ray reflection gave for the molecule a length of between twelve and fourteen carbon atoms.

Stenhagen next turned his attention to surface films of the substance on water, and found that it formed a monolayer film different in type from that of any known fatty acid, and in particular behaved quite differently from disubstituted acetic acids, *e.g.*, decyldodecylacetic acid, collapsing at an area of about 38 A.^{2}, compared with a value of about 60 A.^{2}, and having a considerably higher surface dipole moment. Since the area of one highly compressed chain is about 18—20 A.^{2}, he concluded that the molecule contains two long chains, and postulated in addition the presence of an ethyl or methyl group in the neighbourhood of the carboxyl, which would have the effect of causing the chains to adhere more readily. Owing to the comparatively large value of the optical rotation he considered an ethyl group more likely than a methyl, and, of course, the chains must be unequal to permit of activity at all. He considered the most likely formulation to be ethyldecyldodecylacetic acid.

The main problem has therefore been the synthesis of this, or related substances, and an examination of their film properties and physiological behaviour. Although this object has not yet been completely attained, a number of trisubstituted acetic acids and trisubstituted propionic acids have been prepared and studied. As we do not wish to anticipate unpublished results of Stenhagen, we refrain from giving full details at this stage but our results are in harmony with those of the Swedish author so far as we know them. They are, briefly, that the films of the trialkylacetic and βββ-trialkylpropionic acids collapse at a much smaller area than those of the disubstituted acids, approximating to phthioic acid in their behaviour. Stenhagen (*loc. cit.*) obtained the collapse areas of the disubstituted acetic acids by rapidly compressing the film to a pressure of some 20 dynes, when values of about 60 A.^{2} were found. We found that the films begin to collapse at about 12 dynes, and that it was impossible to obtain reproducible curves above that pressure, the area being then about 75 A.^{2}. The trisubstituted acids, however, give definite, almost flat, collapse points, at about 11 dynes and 40 A.^{2} in the case of the straight chain acids, and 60 A.^{2} in the case of β-methyl-β-(β'-*cyclo*hexylethyl)-β-decylpropionic acid. Trialkylcarbinols, such as methyldioctylcarbinol, give very similar curves, but the dialkylcarbinols do not form stable films.

All our film measurements were made on N/100-sulphuric acid, with the type of apparatus designed by Professor N. K. Adam, and modified by Dr. G. I. Jenkins, whose kind assistance the authors gratefully acknowledge.

The results of biological tests are not yet available in full. Stenhagen, however, has stated that dimethyldecylacetic acid produces toxic symptoms on injection into the peritoneum of rabbits, and that methyldioctylacetic acid produces toxic cell reactions. He also reported that 3-methyl-3-octylundecoic acid has no toxic or irritant properties on injection. It is, therefore, of interest that its antiseptic potency against *M. Tuberculosis* is at least as great as that of the C_{20} acids studied by Adams and Stanley. It is hoped that a report on the bactericidal properties of these and other similar acids that may be synthesised will be published in due course by our biological collaborators. This work is in its initial stages at the present time and all that can be said is that several of the branched-chain acids exhibit bactericidal potency which is, however, surpassed by that of certain other types of synthetic agents. This does not discourage us because it seems possible that the aliphatic compounds may be useful auxiliaries, and it is certainly necessary to explore their potentialities.

Synthetical Methods.—Variants of direct alkylation processes are available for the synthesis of trisubstituted acetic acids and the method of Hudson and Hauser (*J. Amer. Chem. Soc.*, 1940, **62**, 2457), published during the course of the present work, may prove of great value. It works best with disubstituted acetic esters, which are treated with sodium triphenylmethyl and an alkyl halide in ethereal solution (cf. Schlenk, Hillemann, and Rodoff, *Annalen*, 1931, **487**, 147).

Aliphatic nitriles can be alkylated by the method of Ziegler (G.P. 570,594 of 1931; 581,728 of 1933, cf. Bockmühl and Ehrhardt, G.P. 622,875 of 1934), and in this way we have prepared n-*octyl*-n-*nonylacetonitrile* from undeconitrile and octyl bromide in the presence of sodamide and *methyldi*-n-*decylacetonitrile* from propionitrile and decyl bromide under similar conditions. The former could be hydrolysed to an *amide*, but the latter was unchanged after having been submitted to the most vigorous of hydrolytic agents. Incidentally the lack of difficulty experienced in the hydrolysis of esters of phthioic acid is hard to explain on the basis of Stenhagen's suggestions.

Haller's method (*Compt. rend.*, 1909, **148**, 127; 1909, **149**, 5) of alkylation of acetophenone and subsequent decomposition of the ω-trialkylacetophenone by sodamide was applied by him to the synthesis of 2 : 2-dimethyllauric acid,* $CH_3\cdot[CH_2]_9\cdot CMe_2\cdot CO_2H$, but we find that the m. p. is 4°, not 27°, and the specimens of higher m. p. (which we also obtained in the first instance) contained unchanged amide.

We were able to prepare 2 : 2-*dimethylstearic acid* in a similar fashion, but all attempts to alkylate acetophenones substituted in the ω-position by two long-chain alkyls were unsuccessful. For example, we were unable to methylate *ωω-di*-n-*decylacetophenone*, itself prepared by applying the Friedel–Crafts reaction to benzene and di-*n*-decylacetyl chloride. A number of new long-chain *tert.*-alcohols have been prepared and several methods for the replacement of hydroxyl by carboxyl have been studied; none of them proved of great interest.

Whitmore and Badertscher (*J. Amer. Chem. Soc.*, 1933, **55**, 1550) prepared Grignard reagents from *tert.*-alkyl chlorides up to dimethyl-*n*-amylcarbinyl chloride. In this case the yield of carboxylic acid obtained by reaction with carbon dioxide was 22%. We were unable, however, to prepare an organo-magnesium compound from methyldi-*n*-decylcarbinyl chloride, either alone or in the presence of an equivalent of methyl iodide, or of magnesium iodide. Synthesis of nitriles from the carbinols (cf. Butlerow, *Annalen*, 1873, **165**, 323) is a process known to give poor yields and such nitriles are more easily made by direct alkylation.

Reichstein, Rosenberg, and Eberhardt (*Helv. Chim. Acta*, 1935, **18**, 721) condensed *tert.*-alkyl chlorides with methyl furoate in presence of aluminium chloride and later oxidised away the furan nucleus. The result of applying this process to methyldiheptylcarbinyl chloride and to methyldioctylcarbinyl chloride was that small quantities of acids were obtained, apparently of the anticipated nature, but in view of the possibility of isomeric change in the alkyl groups (cf. Gilman and Turck, *J. Amer. Chem. Soc.*, 1939, **61**, 473) we do not feel confident that the products are homogeneous. A specimen of 2 : 2-dimethyl-lauric acid made in this way was certainly not quite pure. Anschütz (*Annalen*, 1903, **327**, 406) obtained trimethylacetic acid by the oxidation of *tert.*-butylphenol and we tried to improve this type of method by employment of a catechol derivative.

4-*αα-Dimethylundecylveratrole* (I) was obtained in good yield by the condensation of dimethyl-*n*-decyl-

---

* The carboxyl group of the normal fatty acids is numbered 1 in this communication.

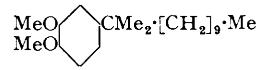
carbinyl chloride with veratrole in the presence of aluminium chloride, and the corresponding dihydric phenol was oxidised with some difficulty to 2 : 2-dimethyl-lauric acid. Methyldi-*n*-heptylcarbinyl chloride gave, however, a very mixed product in the first stage. It seems that a generally applicable procedure for the conversion of *tert.*-alcohols, including more than one long-chain group, into corresponding carboxylic acids is not yet available.

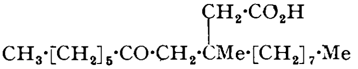
A very direct route to ethyldialkylacetic acids would be opened up if the disubstituted acetoacetic esters could be reduced. The reduction of ethyl acetoacetate to ethyl butyrate has been reported by Vavon (*Ann. Chim.*, 1914, [ix], **1**, 179; cf. Sabatier and Mailhe, *ibid.*, 1909, [viii], **16**, 78) and by Steinkopf and Wolfram (*Annalen*, 1923, **430**, 113), but we found that the *C*-di-*n*-nonyl derivative was highly resistant to reducing agents and was recovered unchanged in all our experiments. In this case there is doubtless a powerful protection of the carbonyl group by the neighbouring long chains and better success was to be anticipated if the carbonyl group were placed in the γ- or δ-position to the alkyl substituents.

The methods to which we have paid most attention are based on the use of $\alpha\alpha$-dialkylsuccinic and $\beta\beta$-dialkylglutaric acids as intermediates and also the application of the Michael reaction to appropriate $\alpha\beta$-unsaturated ketones. The preparation of the substituted succinic and glutaric acids was effected by known methods, essentially those of Higson and Thorpe (J., 1906, **89**, 1455) and Lapworth and McRae (J., 1922, **121**, 2741) for the former and of Guareschi (*Atti R. Accad. Sci. Torino*, 1900—1, **36**, 443 and later papers) and Thole and Thorpe (J., 1911, **99**, 440) for the latter. The ketones employed as starting points were *n*-hexyl, *n*-octyl, and *n*-decyl methyl ketones and it seems that these methods succeed only with methyl ketones; for instance, ethyl *n*-decyl ketone did not undergo the Guareschi reaction, nor could it be condensed with cyanoacetamide in the presence of piperidine (cf. Thole and Thorpe, *loc. cit.*). This sets a limit to the general applicability of these methods; one of the substituting groups must be methyl. The necessary modifications of detail are described in the experimental section, but mention may be made of the excellent device of Cope (*J. Amer. Chem. Soc.*, 1937, **59**, 2327), of which advantage was taken in effecting the condensation of the ketones with ethyl cyanoacetate in the presence of piperidine. The $\beta\beta$-dialkylglutaric anhydrides were converted into semi-esters by reaction with alcohol, and then into ester chlorides. The ester chlorides made from the $\alpha\alpha$-dialkylsuccinic anhydrides in this way would not be of the desired structure and in this case it was necessary to resort to partial hydrolysis of the esters (cf. Bone, Sudborough, and Sprankling, J., 1904, **85**, 534). In this way intermediates of the type $CO_2Et\cdot CRR'\cdot CH_2\cdot COCl$ were secured.

The keto-acid synthesis of Robinson and Robinson (J., 1925, **127**, 175; 1930, 745; 1934, 1543) has been used in several examples, but it did not give good results with acylacetoacetic esters in which the acyl group is derived from succinic or glutaric acid. As an example the ester chloride from β-methyl-β-octylglutaric acid was condensed with ethyl sodio-2-acetylheptoate, and the product hydrolysed to *5-keto-3-methyl-3-*n*-octyl-undecoic acid* (II). This acid was reduced by Clemmensen's method, and a small quantity of unchanged material removed by esterification and treatment with alcoholic sodium ethoxide, which converted the keto-ester into an alkali-soluble dihydroresorcinol derivative.

(I.)





$$CH_3\cdot[CH_2]_5\cdot CO\cdot CH_2\cdot \overset{CH_2\cdot CO_2H}{CMe}\cdot[CH_2]_7\cdot Me$$

(II.)

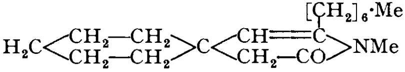
*3-Methyl-3-*n*-hexylnonoic acid*, 3 : *3-dimethylundecoic acid*, and 3 : *3-dimethyltetradecoic acid* were prepared in this way; the yields were of the order 10—15% and the recovery of the more valuable starting material was inadequate compensation.

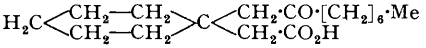
Reaction of the ester chlorides with zinc alkyls (cf. Blaise and Koehler, *Compt. rend.*, 1909, **148**, 489; *Bull. Soc. chim.*, 1910, **7**, 215) gave improved results and this method is much the more direct though also not of general applicability. The use of organo-cadmium compounds (Gilman, *Rec. Trav. chim.*, 1936, **55**, 518) was tried, also with success, but the yields were somewhat inferior to those obtained with the zinc derivatives.

The ester chloride from β-methyl-β-*n*-octylglutaric acid reacted with *n*-heptylzinc chloride, with formation of the ester of *5-keto-3-methyl-3-*n*-octyl-lauric acid* [homologue of (II)].

We were unable to employ the interaction of Grignard agents and acid anhydrides in the long-chain series (cf. Weizmann and Bergmann, J., 1936, 567; 1938, 1147; Guha, *Ber.*, 1938, **71**, 2671), but the method of Lukes (*Coll. Czech. Chem. Comm.*, 1929, **1**, 119; 1936, **8**, 223) gave more promise. This consists in the hydrolysis of the product of interaction of an *N*-substituted cyclic imide with an organo-magnesium compound, whereby keto-acids are produced. For example, cyclo*hexane-1 : 1-diacetomethylimide* and *n*-heptylmagnesium bromide furnished the intermediate (III), which on hydrolysis with concentrated hydrobromic acid was converted into the keto-acid (IV).

(III.)





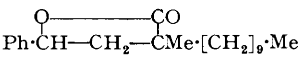
(IV.)

Since the work of Adams and Stanley (*loc. cit.*) showed that the presence of a *cyclo*hexyl group in the fatty acid molecule was consistent with antiseptic activity against *B. Leprae*, we extended the work in this direction. Phenyl-keto-acids were obtained in good yield from the substituted succinic and glutaric anhydrides in the presence of aluminium chloride under remarkably mild conditions. Examples are (V) from α-methyl-α-*n*-decylsuccinic anhydride and (VI) from β-methyl-β-*n*-hexylglutaric anhydride.

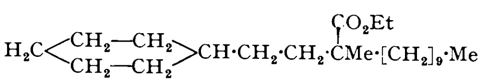
(V.) $Ph\cdot CO\cdot CH_2\cdot CMe(CO_2H)\cdot[CH_2]_9\cdot Me$ $Ph\cdot CO\cdot CH_2\cdot CMe(C_6H_{13})\cdot CH_2\cdot CO_2H$ (VI.)

The reduction of (V) by Clemmensen's method proceeded slowly and furnished a mixture of products, from which two isomeric forms of the lactone (VII) were isolated.

(VII.)



$$\begin{array}{l} \mathrm{O}\!-\!\!-\!\!-\!\!-\!\!-\!\!-\!\!-\mathrm{CO} \\ \mathrm{Ph{\cdot}CH{-}CH_2{-}CMe{\cdot}[CH_2]_9{\cdot}Me} \end{array}$$



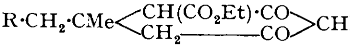
$$\mathrm{H_2C}\!<\!\begin{smallmatrix}\mathrm{CH_2{-}CH_2}\\ \mathrm{CH_2{-}CH_2}\end{smallmatrix}\!>\!\mathrm{CH{\cdot}CH_2{\cdot}CH_2{\cdot}\overset{\displaystyle CO_2Et}{\overset{|}{C}}Me{\cdot}[CH_2]_9{\cdot}Me}$$

(VIII.)

Saturated esters, *e.g.*, (VIII) from the ester of (V), were obtained directly by pressure hydrogenation over Raney nickel (cf. Adkins, " Reactions of Hydrogen," Wisconsin Univ., **1937**, p. 71).

Self-condensation products of methyl *n*-amyl ketone and methyl *n*-decyl ketone were obtained by following the noteworthy procedure of Colonge (*Bull. Soc. chim.*, 1933, [iv], **53**, 282; 1934, [v], **1**, 1101; 1938, **5**, 98, 155) in which methylanilinomagnesium bromide is used as the condensing agent in ethereal solution. The product from methyl amyl ketone was shown to be n-*amyl* β-n-*amyl*iso*propenyl ketone* (IX) and that from methyl decyl ketone is doubtless analogously constituted. Reaction with ethyl sodiomalonate in boiling alcoholic solution

(IX.) $\mathrm{Me{\cdot}[CH_2]_4{\cdot}CMe{:}CH{\cdot}CO{\cdot}[CH_2]_4{\cdot}Me}$



$$\mathrm{R{\cdot}CH_2{\cdot}CMe}\!<\!\begin{smallmatrix}\mathrm{CH(CO_2Et){\cdot}CO}\\ \mathrm{CH_2{-}\!\!-\!\!-\!\!-\!\!-CO}\end{smallmatrix}\!>\!\mathrm{CHR}$$

(X.)

furnished the substituted diketo-esters of the form (X; $\mathrm{R} = \mathrm{C_4H_9}$ or $\mathrm{C_9H_{19}}$) and these were readily hydrolysed and decarboxylated to the corresponding substituted dihydroresorcinols. The latter compounds could not be hydrolysed to keto-acids and it was therefore necessary to avoid the formation of the ring in the first place. This was accomplished by the use of sodiocyanoacetamide instead of ethyl sodiomalonate. The crystalline compounds (XI; $\mathrm{R} = \mathrm{C_5H_{11}}$ or $\mathrm{C_{10}H_{21}}$) were thus obtained and hydrolysis to the keto-acids (XII) was smoothly effected by a boiling mixture of sulphuric and acetic acids with water. Hydrolysis by alkalis (cf. Qudrat i Khuda, J., 1929, 715) was much less satisfactory; it brought about reversal of the Michael addition to some extent and the later decarboxylation stage gave ketodilactone in addition to the keto-acid.

(XI.) $\mathrm{R{\cdot}CO{\cdot}CH_2{\cdot}CMeR{\cdot}CH(CN){\cdot}CO{\cdot}NH_2}$ $\mathrm{R{\cdot}CO{\cdot}CH_2{\cdot}CMeR{\cdot}CH_2{\cdot}CO_2H}$ (XII.)

The reduction of the keto-acids, made by the foregoing methods, was usually effected by Clemmensen's method, but in certain cases no reduction occurred in 100 hours, even with the addition of toluene (Martin, *J. Amer. Chem. Soc.*, 1936, **58**, 1938). The Wolff–Kishner method and reduction by sodium and alcohol were unsuccessful in the few cases tried and a generally applicable process is still to be found; pressure hydrogenation offers the best prospects. In case *sec.*-alcohols were obtained we studied the reduction of di-*n*-decylcarbinol as a model. With hydriodic acid and phosphorus at 130° it gave the corresponding iodide, which was reduced to heneicosane, m. p. 42°, by zinc dust and alcohol.

A few preliminary experiments were made on the use of methods depending on migration of groups.

Tiffeneau and Lévy (*Bull. Soc. chim.*, 1931, **49**, 1628, 1690), basing their conclusions on the work of Meerwein (*Annalen*, 1913, **396**, 256; 1919, **419**, 121), Parry (J., 1915, **107**, 108), and Nybergh (*Ber.*, 1922, **55**, 1960), have pointed out that in pinacols of the type $\mathrm{CR_2(OH){\cdot}CMe_2{\cdot}OH}$ it is the longer chain alkyl group that possesses the greater migratory aptitude and as the chain in R grows longer the proportion of the pinacolone, $\mathrm{R{\cdot}CO{\cdot}CMe_2R}$, in the product increases.

The pinacol from ethyl α-hydroxy*iso*butyrate and *n*-amylmagnesium bromide was converted through the pinacolone into 2 : 2-dimethylheptoic acid, isolated as the amide, but the investigation was abandoned when it was found that interaction of *n*-heptylmagnesium bromide and *n*-decylmagnesium bromide with ethyl α-hydroxy*iso*butyrate afforded no *as.*-pinacols but only hydrocarbons. Moreover we were unable to obtain any significant yield of pinacol by reduction of methyl *n*-decyl ketone.

Haller and Lassieur (*Compt. rend.*, 1910, **150**, 1017) obtained a compound, $\mathrm{C_{22}H_{44}O}$, by Sabatier–Senderens reduction of methyl *n*-nonyl ketone. They formulated this as a pinacolone, $\mathrm{C_9H_{19}{\cdot}CO{\cdot}CMe_2{\cdot}C_9H_{19}}$. It seems much more probable that it is derived by reduction of a self-condensation product and is $\mathrm{C_9H_{19}{\cdot}CHMe{\cdot}CH_2{\cdot}CO{\cdot}C_9H_{19}}$.

EXPERIMENTAL.

2 : 2-*Dimethyl-lauric Acid.*—A mixture of ωω-dimethyl-ω-*n*-decylacetophenone (Haller, *loc. cit.*), twice its volume of toluene, and powdered sodamide (2 mols.) was refluxed for 6 hours. The amide was isolated (pearly plates; yield, 48%), dissolved in 10 times its weight of sulphuric acid, and sodium nitrite (1·25 mols.) gradually added. After 12 hours, the mixture was heated on the steam-bath for ½ hour. The product, b. p. 165—180°/10 mm., melted indefinitely at about 30° (Haller, *loc. cit.*, ascribes the m. p. 27° to the dimethyl-lauric acid). This material contained nitrogen and was clearly a mixture of the acid and the amide. It was esterified by means of boiling alcoholic sulphuric acid; the ester was a colourless oil, b. p. 145—150°/10 mm., with a pineapple odour. On hydrolysis the pure acid, b. p. 175—180°/10 mm., m. p. 4°, was obtained (Found: C, 73·5; H, 12·1. Calc. for $\mathrm{C_{14}H_{28}O_2}$: C, 73·7; H, 12·3%).

2 : 2-*Dimethylstearic Acid.*—A mixture of stearoylbenzene (10 g.), powdered sodamide (1·3 g.), and toluene (15 c c.) was refluxed for ½ hour, methyl iodide (5 c.c.) added, and boiling continued for 2 hours. Water was added, and the organic layer separated, dried, and distilled until a little toluene had been collected. When the water had been completely removed, the volume was made up to 25 c.c. by the addition of toluene, sodamide (3 g.) was added, and the liquid refluxed for 3 hours. On pouring into water, pearly plates (2 g.) separated from the toluene layer. These were recrystallised from light petroleum (b. p. 40—60°) and had m. p. 81°. This amide was converted into the *acid* by prolonged treatment with sulphuric acid and sodium nitrite; b. p. 215—220°/15 mm., m. p. 42° (Found: C, 76·6; H, 12·9. $\mathrm{C_{20}H_{40}O_2}$ requires C, 76·9; H, 12·8%).

The liquid (4 g.) remaining in the toluene was isolated and treated with sodium nitrite and sulphuric acid. The products were benzoic acid (from incompletely methylated material, see below) and crude dimethylstearic acid. This gave 0·5 g. of pure distilled ester, which was saponified to the acid, m. p. 42°.

*ωω-Di-*n*-decylacetophenone.*—Ethyl di-*n*-decylmalonate, b. p. 264—268°/10 mm., was obtained in 75% yield from ethyl malonate (20 g.), *n*-decyl bromide (57 g.), sodium (2·9 g.), a little sodium iodide, and alcohol (50 c.c.), the mixture being refluxed for 6 hours. On hydrolysis with aqueous alcoholic sodium hydroxide it gave di-*n*-decylmalonic acid, greasy plates, m. p. 60—61°, in almost quantitative yield, and this decomposed at 185° to 2-*n*-decyl-lauric acid, m. p. 54° after crystallisation from acetone. The acid (28 g.) and thionyl chloride (50 c.c.) were allowed to react at 60° for 5 hours; the resulting 2-*n*-decyl-lauryl chloride (22 g., b. p. 245—250°/10 mm.) furnished the amide, colourless needles, m. p. 115—116°, from alcohol, on treatment with aqueous ammonia. The chloride (21 g.) was added to a mixture of benzene (100 c.c.) and powdered aluminium chloride (8·8 g.). After 12 hours the mixture was heated at 40° for 3 hours and then decomposed by ice. *Di-*n*-decylacetophenone* was obtained as a pale yellow oil (13 g.), b. p. 275—280° (Found : C, 83·0; H, 12·6. $C_{28}H_{48}O$ requires C, 83·2; H, 12·6%). It could not be converted into a crystalline oxime, semicarbazone, or dinitrophenylhydrazone.

When it was treated with sodamide in boiling toluene, ammonia was evolved, but subsequent attempted methylation with methyl iodide under the usual conditions was unsuccessful. After decomposition of the product with sodamide, oils, b. p. 170—280°/10 mm., were isolated, but there was no evidence of the presence of a trisubstituted acetamide. When the initial product was treated with sulphuric acid and sodium nitrite, benzoic acid was produced. *iso*Butyrophenone was found to be decomposed with formation of benzoic acid under the same conditions, whereas phenyl *tert.*-butyl ketone was not changed (cf. Lapworth and Steele, J., 1911, **99**, 1886). Similar experiments were carried out with ωω-di-*n*-heptylacetophenone. 2-*n*-Heptylnonoic acid (b. p. 190—195°/12 mm.) (Stanley, Jay, and Adams, *J. Amer. Chem. Soc.*, 1929, **51**, 1261) with thionyl chloride furnished the chloride, b. p. 170—175°, in 80% yield. Condensation with benzene in presence of aluminium chloride afforded diheptylacetophenone, b. p. 210—215°/15 mm. This ketone could not be methylated by means of sodamide and methyl iodide. The crude product was decomposed by sodium nitrite and sulphuric acid to benzoic acid and a small quantity of a neutral compound, m. p. 44°. The use of *iso*amyl nitrite and alcoholic sodium ethoxide (Lapworth and Steele, *loc. cit.*) gave ethyl benzoate and the substance, m. p. 44°, which is probably di-*n*-heptyl ketone.

2-n-*Octylundecamide.*—Sodamide (8 g.) was added during 15 minutes to a mixture of undeconitrile (33 g., b. p. 145°/14 mm., from undecamide by the action of thionyl chloride), *n*-octyl bromide (39 g.), and benzene (50 c.c.). After 1 hour the whole was refluxed for 1 hour. The product was a colourless oil (15 g.), b. p. 215—220°/12 mm. This 2-*n*-octylundeconitrile could not be methylated by means of sodamide and methyl iodide. When refluxed with a mixture of acetic acid, sulphuric acid and water (4 : 2 : 1), it afforded the *amide*, m. p. 109°, from alcohol (Found : N, 4·9. $C_{19}H_{39}ON$ requires N, 4·7%). The action of syrupy phosphoric acid on the nitrile at 160° (cf. Berger and Olivier, *Rec. Trav. chim.*, 1927, **46**, 600) also gave the amide.

2-*Methyl*-2-n-*decyl-lauronitrile.*—Powdered sodamide (3·9 g.) was added to propionitrile (5·5 g.) and *n*-decyl bromide (22 g.) in toluene (20 c.c.), and the mixture kept for 15 minutes and then heated on the steam-bath for 2 hours. The product was isolated, and substances, b. p. $<$140°/14 mm., rejected. The residue was re-treated as above with sodamide, and decyl bromide in toluene, the mixture being refluxed for 5 hours. On working up, a small quantity of a low-melting base was obtained and the main product (12 g.) was a colourless, odourless oil, b. p. 230—245°/1 mm. (Found : N, 4·4. $C_{23}H_{45}N$ requires N, 4·2%). This *nitrile* was unchanged by a boiling mixture of acetic and sulphuric acids or by heating for 5 hours at 160° with syrupy phosphoric acid fortified by addition of a little phosphoric anhydride.

4-*αα-Dimethylundecylveratrole.*—1 : 1-Dimethylundecan-1-ol (35 g., b. p. 135—138°/13 mm., from 50 g. of ethyl undecoate, 75 g. of methyl iodide and 6·5 g. of magnesium) was heated with thionyl chloride (40 c.c.) at 40° for an hour. The excess of the reagent was removed under diminished pressure, and the product washed with aqueous sodium carbonate and dried. It was not distilled because it suffered some decomposition at 90°. A mixture of this dimethylundecyl chloride (25 g.), veratrole (16 g.), carbon disulphide (60 c.c.), and powdered aluminium chloride (20 g.) was stirred for 3 hours. After 4 days the *product* (18 g.) was isolated in the known manner and was obtained as a pale yellow oil, b. p. 220—225°/13 mm. (Found : C, 78·9; H, 11·4. $C_{21}H_{36}O_2$ requires C, 78·7; H, 11·2%). The corresponding dimethylundecylcatechol, b. p. 240—245°/13 mm., was prepared by refluxing the dimethyl ether (18 g.) with hydrobromic acid (40 c.c., *d* 1·5) and acetic acid (40 c.c.) for 4 hours. The pale yellow oil darkened on keeping and gave an olive-green coloration with alcoholic ferric chloride. Powdered potassium permanganate (25 g.) was added during 2 hours to a well-stirred solution of this catechol derivative (8 g.) in acetone (250 c.c.); the mixture was then refluxed for 1 hour. The isolated product did not appear to have been completely oxidised and it was accordingly dissolved in dilute aqueous sodium hydroxide and oxidised at 50° by the addition of 5% aqueous potassium permanganate until the colour of the latter persisted. The product was isolated, dissolved in aqueous sodium hydroxide (30 c.c. of 5%), hydrogen peroxide (15 c.c. of 10%) added, and the solution was kept for 12 hours. The isolated acid (2·2 g.) had b. p. 175—180°/12 mm.; a considerable residue indicated that oxidation was incomplete even after the above treatment. The acid was identified as 2 : 2-dimethyl-lauric acid (above) by conversion into the amide, m. p. 94°.

The method of Reichstein (*loc. cit.*) was also tried and a small yield of ethyl 1′ : 1′-dimethylundecylfuroate, b. p. 220—235°/12 mm., obtained. On oxidation this furnished some dimethyl-lauric acid (amide, m. p. 90°), but the process was not satisfactory.

1-*Methyl*-1-*heptyloctan*-1-*ol* (32 g., b. p. 165°/13 mm.) was obtained from ethyl acetate (20 g.), *n*-heptyl bromide (80 g.), and magnesium (5·5 g.) (Found : C, 79·5; H, 13·9. $C_{16}H_{34}O$ requires C, 79·3; H, 14·0%). The product of the condensation of the corresponding chloride with veratrole in the presence of aluminium chloride had b. p. 150—250° and could not be separated into definite fractions.

1-*Methyl*-1-n-*octyldecoic Acid.*—1-Methyl-1-*n*-octylnonan-1-ol (10 g., b. p. 190—195°/20 mm., m. p. −5°) was obtained from ethyl acetate (10 g.), *n*-octyl bromide (48 g.), and magnesium (6 g.). It was converted into the chloride by reaction with thionyl chloride. A mixture of methyloctylnonyl chloride (29 g.), methyl furoate (12·5 g.), carbon disulphide (60 c.c.), and powdered aluminium chloride (40 g.) was kept for a week and then worked up in the known manner. The material (0·8 g.), b. p. 200—260°, was redistilled, b. p. 235—260°/13 mm. (0·5 g.). The viscous acid obtained on hydrolysis could not be crystallised; it was oxidised in dilute aqueous sodium hydroxide with potassium permanganate at 35° until the oxidising agent was no longer reduced. The acidic product (0·2 g.) was a viscous oil, b. p. 220—235°/12 mm. (Found : C, 74·4; H, 13·8. $C_{19}H_{38}O_2$ requires C, 74·7; H, 13·6%).

1-Ethyl-1-*n*-octylnonan-1-ol (10 g., b. p. 190—195°, m. p. −10°, from 15 g. of ethyl propionate, 48 g. of *n*-octyl bromide, and 6 g. of magnesium) and 1-methyl-1-*n*-decylundecan-1-ol (11 g., b. p. 225—230°/12 mm., m. p. 21°, from 5 g. of ethyl acetate, 25 g. of *n*-decyl bromide, and 2·7 g. of magnesium) were converted into chlorides, but no recognisable products were obtained on attempted condensation with methyl furoate and subsequent oxidation.

Attempted Reduction of Ethyl 2-n-*Nonyl*-2-*acetoundecoate.*—The ester (b. p. 240°/18 mm.) was treated with amalgamated zinc in boiling alcoholic hydrogen chloride solution, with sodium in boiling alcohol, and with hydrogen in glacial acetic acid solution at 50° in the presence of Adams's catalyst. In no case did reduction occur and the products on hydrolysis furnished only 2-*n*-nonylundecoic acid, m. p. 45°, and dinonylacetone.

Ethyl 5-*Keto*-6-*acetyl*-6-*carbethoxy*-3 : 3-*dimethylundecoate.*—A solution of ββ-dimethylglutaric anhydride (10 g.) in alcohol (20 c.c.) was refluxed for 30 hours, and the solvent evaporated under diminished pressure. A mixture of the viscous half-ester with thionyl chloride (12 c.c.) was kept for 2 hours and then heated at 45° for 30 minutes. The product distilled as a colourless oil (9·2 g.), b. p. 110°/10 mm. The whole of this ester chloride was added to ethyl sodio-2-acetylheptoate (from 12 g. of the ester, b. p. 121°/10 mm., and 1·05 g. of sodium) in ether (25 c.c.). After the initial reaction, the mixture was refluxed for 15 minutes; the *product* was a colourless oil (6·5 g.), b. p. 200°/10 mm., with a faint pleasant odour (Found : C, 64·9; H, 9·3. $C_{19}H_{32}O_6$ requires C, 64·0; H, 9·2%).

5-*Keto*-3 : 3-*dimethylundecoic Acid*.—The above ester (5 g.) was shaken with an excess of aqueous sodium hydroxide (5%) for 15 hours and then acidified; the product, collected by means of ether, was refluxed for 15 hours with 5% sulphuric acid, again isolated, and refluxed for 10 hours with 10% aqueous sodium hydroxide. After steam distillation to remove methyl hexyl ketone, the acid was liberated and isolated (0·25 g.), b. p. 190°/10 mm. It formed a 2 : 4-*dinitrophenylhydrazone*, which crystallised from alcohol in bright orange needles, m. p. 122° (Found : N, 13·2. $C_{19}H_{28}O_6N_2$ requires N, 13·7%). Reduction by Clemmensen's method gave a colourless, viscous oil that did not react with dinitrophenylhydrazine, but the yield of the keto-acid was so unfavourable that the subject was not pursued further.

3 : 3-*Dimethyltetradecoic Acid*.—4-Carbethoxy-3 : 3-dimethylbutyryl chloride (55 g.) reacted with ethyl sodio-2-acetyldecoate (from 66 g. of the ester and 6·2 g. of sodium) to form ethyl 5-keto-6-acetyl-6-carbethoxy-3 : 3-dimethyltetradecoate (80 g.), b. p. 240—242°/9 mm. Half of this material was hydrolysed by treatment with ammonia in dry ether (cf. Bardhan, J., 1936, 1850) and subsequently with boiling 12% aqueous sodium hydroxide. The resulting acid was esterified and the yield of pure keto-ester (see below) was 6 g. The other half (40 g.) was shaken with aqueous sodium hydroxide (500 c.c. of 2·5%) for 40 hours; sodium hydroxide (20 g.) was then added, and the solution refluxed for 20 hours. The acid was then isolated and refluxed with 15% sodium hydroxide solution for 3 hours; it was again isolated and esterified by means of boiling 5% alcoholic sulphuric acid. Ethyl 5-keto-3 : 3-dimethyltetradecoic acid (9 g.), b. p. 186—188°/9 mm., was obtained. The corresponding acid is a low-melting solid; 2 : 4-dinitrophenylhydrazone, m. p. 85°. It was refluxed for 100 hours with 20% hydrochloric acid and amalgamated zinc; the reduced *acid* had b. p. 195°/10 mm., m p. 15° (Found : C, 74·8; H, 12·3. $C_{16}H_{32}O_2$ requires C, 75·0; H, 12·5%).

5-*Keto*-3-*methyl*-3-n-*hexylnonoic Acid*.—The solid that separated during 3 days from a mixture of methyl hexyl ketone (40 g.), ethyl cyanoacetate (90 g.), and saturated alcoholic ammonia (100 c.c.) was collected and treated with dilute hydrochloric acid. The resulting αα′-dicyano-β-methyl-β-hexylglutarimide (cf. Guareschi and Grande, *Atti R. Accad. Sci. Torino*, 1900, **34**, 18) was refluxed with sulphuric acid (100 c.c.), acetic acid (70 c.c.), and water (30 c.c.) for 8 hours. The methylhexylglutaric acid was collected by thorough extraction of the diluted mixture with ether and then esterified by boiling 10% alcoholic sulphuric acid; the ester (35 g.) was a pleasant smelling oil, b. p. 163—165°/9 mm. On hydrolysis the pure *β-methyl-β-*n*-hexylglutaric acid* was obtained; it crystallised from light petroleum in colourless prisms, m. p. 61° (Found : C, 62·5; H, 9·5. $C_{12}H_{22}O_4$ requires C, 62·6; H, 9·5%).

The acid was converted into its anhydride by boiling with acetic anhydride, and the mixture distilled. Methylhexylglutaric anhydride was obtained as a colourless oil, b. p. 196°/9 mm. It was converted into the semi-ester by means of slightly more than the theoretical amount of sodium ethoxide in the minimum quantity of anhydrous alcohol. The oily acid ester was isolated, dried, and mixed with an equal volume of thionyl chloride; after 3 hours the mixture was heated at 45° for 1 hour. The ester chloride had b. p. 167°/9 mm. (76% yield from the acid).

(i) After 4-carbethoxy-3-methyl-3-*n*-hexylbutyryl chloride (15 g.) had been added to ethyl sodio-2-acetylvalerate (13·5 g. of the ester and 1·9 g. of sodium) in ether (30 c.c.), the mixture was refluxed for 3 hours. Ethyl 5-keto-6-acetyl-6-carbethoxy-3-methyl-3-*n*-hexylnonoate (18 g., b. p. 200°/10 mm.) was obtained on distillation of the product.

This ester was hydrolysed by following, exactly, the second of the methods mentioned above in the section "3 : 3-dimethyltetradecoic acid." The crude acidic product was dissolved in light petroleum, and the solution washed with very dilute aqueous potassium carbonate. This removed methylhexylglutaric acid, which was recovered by acidification of the washings. The residue (0·6 g., b. p. 190—210°/14 mm.) in the organic solvent was esterified with methyl-alcoholic hydrogen chloride and distillation of the ester gave two fractions, b. p. 160—165°/10 mm. and 178—182°/10 mm. The former was shown by hydrolysis to be methyl methylhexylglutarate and the latter was mainly the required *keto-ester* (Found : C, 70·6; H, 11·0. $C_{17}H_{32}O_3$ requires C, 71·7; H, 11·2%). Owing to the small quantity (0·3 g.) available the specimen could not be freed from the lower-boiling ester ($C_{14}H_{26}O_4$ requires C, 65·1; H, 10·1%).

(ii) The above ester chloride (30 g.) was added to a solution of zinc di-*n*-butyl (9 g.) (Organic Syntheses, XII, 89) in benzene (30 c.c.), and the solution refluxed for 1 hour. On working up, a crude oil, b. p. 195—210°/9 mm., was obtained and its methyl ester, b. p. 178—182°/9 mm., was separated from some admixed methyl methylhexylglutarate, b. p. 163—168°/9 mm. The recovered keto-acid had b. p. 205—210°/9 mm. and formed a red, oily 2 : 4-dinitrophenylhydrazone.

5-*Keto*-3-*methyl*-3-n-*octylundecoic Acid*.—A mixture of methyl *n*-octyl ketone (50 g.), ethyl cyanoacetate (112 g.), and saturated alcoholic ammonia (200 c.c.) deposited in a few days *αα′-dicyano-β-methyl-β-octylglutarimide* (55 g.), which crystallised from light petroleum in pearly plates, m. p. 139° (Found : N, 14·8. $C_{16}H_{23}O_2N_3$ requires N, 14·5%). On refluxing with 50% sulphuric acid for 4 hours, practically pure *β-methyl-β-*n*-octylglutarimide* was obtained. This separated from light petroleum in plates, m. p. 91° (Found : N, 6·1. $C_{14}H_{25}O_2N$ requires N, 5·9%). The imide was hydrolysed by refluxing for 6 hours with a mixture (10 : 7 : 3) of sulphuric acid, acetic acid, and water. The crude oily acid was esterified with 10% alcoholic sulphuric acid (ester, b. p. 195°/18 mm.) and hydrolysis then afforded methyloctylglutaric acid as an oil that solidified in prisms, m. p. 58°. This was converted into the anhydride by refluxing with acetic anhydride (50 c.c.); the product (31 g.) was a colourless, viscous oil, b. p. 210—212°/13 mm.

The ester chloride (20 g., b. p. 185—187°/9 mm.) was prepared from the anhydride (18 g.) as in the analogous examples. Successive treatment with aqueous ammonia, aqueous sodium hydroxide and hydrochloric acid regenerated the imide, m. p. 91°.

Following the usual procedure, the ester chloride (14 g.) and ethyl sodio-2-acetylheptoate (12 g. of the ester; reaction mixture refluxed for 2 hours) afforded ethyl 5-keto-6-acetyl-6-carbethoxy-3-methyl-3-*n*-octylundecoate (15 g.) as a colourless, viscous oil, b. p. 255—265°/10 mm. This was shaken for 30 hours with aqueous sodium hydroxide (350 c.c. of 5%) and for 10 hours more after the addition of sodium hydroxide (15 g.) and alcohol (200 c.c.). The solution was then refluxed for 8 hours, and the acids liberated and isolated by means of ether. Analysis of the oil (8 g., b. p. 210—230°/10 mm.) obtained on distillation showed it to be a mixture. It was dissolved in light petroleum, and methyloctylglutaric acid (recovered, m. p. 58°) removed by washing with dilute aqueous potassium carbonate. The light petroleum solution was shaken with dilute hydrochloric acid and distilled. The *keto-acid* (1·0 g.) had b. p. 235—240°/10 mm. (Found : C, 73·2; H, 11·6. $C_{20}H_{38}O_3$ requires C, 73·6; H, 11·6%). The substance gave no crystalline semicarbazone and a red, oily 2 : 4-dinitrophenylhydrazone. On reduction by Clemmensen's method (refluxing for 100 hours), 3-methyl-3-*n*-octylundecoic acid, b. p. 225—230°/20 mm., was obtained; it did not react with 2 : 4-dinitrophenylhydrazine.

n-*Decyl Methyl and Ethyl Ketones*.—These ketones were conveniently prepared on a small scale by the action of undecoyl chloride on methylzinc iodide and ethylzinc iodide respectively, under the known conditions (toluene as solvent). On a larger scale the method of Pickard and Kenyon (J., 1911, **99**, 57) was adopted. Methyl *n*-decyl ketone (b. p. 245°, m. p. 20°) gives a 2 : 4-dinitrophenylhydrazone, m. p. 81°, and a semicarbazone, m. p. 125° (Pickard and Kenyon give

122—123°; Stoll, Ruzicka, and Schinz, *Helv. Chim. Acta*, 1928, **11**, 670, give 104—105°, which is probably a misprint). Ethyl *n*-decyl ketone, m. p. 31° (Pickard and Kenyon, 25°), forms a 2 : 4-dinitrophenylhydrazone, m. p. 55°, and a semicarbazone, m. p. 93° (lit., 90°). This ketone was also obtained in poor yield from the product of reaction of ethylmagnesium bromide and undeconitrile.

*αα'-Dicyano-β-methyl-β-*n*-decylglutarimide.*—A mixture of methyl decyl ketone (12 g.), ethyl cyanoacetate (15 g.), and saturated alcoholic ammonia (50 c.c.) gradually deposited the condensation *product*. It crystallised from light petroleum in pearly plates, m. p. 135° (Found : N, 13·2. $C_{18}H_{27}O_2N_3$ requires N, 13·2%). Methyl-*n*-decylglutaric anhydride (9 g.), b. p. 235—237°/18 mm., was obtained in the usual manner and on hydration gave the acid, colourless prisms, m. p. 63—64°. The anhydride prepared from the pure acid had m. p. 31°. The imide, obtained by heating the anhydride with urea and crystallised from light petroleum, had m. p. 71°.

Ethyl *n*-decyl ketone did not undergo the Guareschi reaction; it could be condensed neither with cyanoacetamide under various conditions nor with ethyl cyanoacetate in the presence of sodium ethoxide or piperidine.

*α-Methyl-α-*n*-decylsuccinic Anhydride.*—A mixture of methyl decyl ketone (92 g.), ethyl cyanoacetate (60 g.), toluene (200 c.c.), and piperidine (3 c.c.) was refluxed under a condensing system that included a water-trap. The formation of water ceased after 3 hours and, on distillation, ethyl 2-cyano-3-methyl-Δ^2-tridecenoate was obtained as a colourless oil (120 g.), b. p. 196—200°/16 mm. [A mixture of this ester (5 g.), ethyl cyanoacetate (2 g.), and saturated alcoholic ammonia (20 c.c.), kept for 8 hours, deposited 4 g. of αα'-dicyano-β-methyl-β-*n*-decylglutarimide (above), m. p. 135° after crystallisation from light petroleum.] A solution of sodium cyanide (25 g.) in the minimum quantity of water and enough alcohol to give a clear solution were added, the temperature rising. After 1 hour an equal volume of water was added, and the solution acidified. The ethyl 2 : 3-dicyano-3-methyltridecoate was collected by means of ether. It decomposed to some extent on distillation (b. p. 214—220°/15 mm.) and was used in the crude form for the next stage, which was effected by refluxing for 4 hours with sulphuric acid (100 c.c.), acetic acid (70 c.c.), and water (30 c.c.). [Refluxing with 50% sulphuric acid for 2 hours carried the hydrolysis as far as the imide.] The acid was collected by ether and esterified by boiling alcoholic sulphuric acid (150 c.c. of 10%); the ethyl α-methyl-α-*n*-decylsuccinate was a colourless oil (81 g.), b. p. 189—192°/8 mm. The acid obtained on hydrolysis was a viscous oil; it was converted by boiling acetic anhydride into the *anhydride*, b. p. 187°/8 mm., m. p. 37° (Found : C, 70·9; H, 10·3. $C_{15}H_{26}O_3$ requires C, 70·9; H, 10·2%). The ester (48 g.) was refluxed for 20 minutes with an alcoholic solution of sodium ethoxide (4·5 g. of sodium), water (5 c.c.) being gradually added. After the addition of acetic acid (5 c.c.) most of the alcohol was evaporated under diminished pressure. The residue was taken up in 3% sodium hydroxide solution (500 c.c.), the undissolved oil removed, and the acid set free and collected by means of ether. A mixture with thionyl chloride (50 c.c.) was kept for 8 hours, heated at 45° for 1 hour, and distilled. 3-Carbethoxy-3-methyltridecoyl chloride (31 g.), b. p. 160°/1 mm., was thus obtained. Successive treatment with aqueous ammonia, aqueous sodium hydroxide, and hydrochloric acid gave the *imide*, m. p. 98° (Found : C, 71·0; H, 10·8; N, 5·4. $C_{15}H_{27}O_2N$ requires C, 71·2; H, 10·7; N, 5·5%).

α-Methyl-α-hexylsuccinic acid derivatives were made in a similar way. Methyl *n*-hexyl ketone (100 g.), ethyl cyanoacetate (70 g.), and piperidine (1·5 g.), condensed in boiling toluene, gave ethyl 2-cyano-3-methyl-Δ^2-nonenoate (yield, 80%), b. p. 162—168°/14 mm. Ethyl methylhexylsuccinate, obtained by addition of hydrogen cyanide and hydrolysis of the product, had b. p. 155—158°/14 mm.; the anhydride of the corresponding acid had b. p. 160—162°/14 mm. The imide, prepared by partial hydrolysis of the dicyano-ester or by heating the anhydride with urea, crystallised from ethyl acetate–light petroleum in plates, m. p. 115°. The ethyl ester chloride had b. p. 153—155°/13 mm. Hydrolysis of the condensation product of this ester chloride with ethyl sodio-2-acetylvalerate or of the ester chloride of methyldecylsuccinic acid with ethyl sodio-2-acetylheptoate gave no new keto-acids and the starting products (acids) were regenerated.

*Methyl 5-Keto-3-methyl-3-*n*-octyl-laurate.*—A solution of fused zinc chloride (20 g.) in ether (40 c.c.) and then toluene (100 c.c.) were added to a Grignard reagent prepared from *n*-heptyl bromide (16·5 g.), magnesium (2·2 g.), and ether (50 c.c.). The liquid was distilled until the thermometer registered 108° and toluene (40 c.c.) was introduced during this process. 4-Carbethoxy-3-methyl-3-*n*-octylbutyryl chloride (21 g.) was added to the cooled solution, which was then heated on the steam-bath for 3 hours with occasional stirring. The product (13 g.) was a colourless, viscous oil, b. p. 230—240°/20 mm. It was hydrolysed by means of alcoholic potassium hydroxide, whereby some heptyl alcohol and some of the methyloctylglutaric acid were formed. The isolated acid was converted into its *methyl* ester (9 g.), b. p. 235°/19 mm. (Found : C, 74·2; H, 11·6. $C_{22}H_{42}O_3$ requires C, 74·6; H, 11·8%.) In a similar experiment with *n*-octyl bromide on the one hand and methyldecylsuccinic anhydride on the other, the formation of a new keto-acid did not occur. The higher-boiling product consisted entirely of unchanged anhydride, b. p. 187°/8 mm., m. p. 37°.

*2-Keto-1 : 3-dimethyl-3 : 5-di-*n*-decyl-2 : 3-dihydropyrrole.*—α-Methyl-α-*n*-decylsuccinic anhydride (20 g.) was heated with aqueous methylamine (6·5 c.c. of 33%), and the mixture distilled; the methylimide was a colourless, viscous oil, b. p. 205°/15 mm. It was mixed with a Grignard solution prepared from *n*-decyl bromide (35 g.), magnesium (4 g.), and ether (60 c.c.) and heated on the steam-bath for 2 hours. On working up, a very viscous oil (8 g.), b. p. 265—280°/15 mm. (Found : N, 3·6. $C_{26}H_{49}ON$ requires N, 3·6%), was obtained, along with eicosane and unchanged methylimide in the lower-boiling fractions. The *substance* resisted the action of boiling hydrobromic acid during 10 hours and other attempted methods of hydrolysis gave unchanged material, tar, or both.

5-Keto-3 : 3-dimethyl-lauric Acid.—A Grignard solution prepared from *n*-heptyl bromide (40 g.) and magnesium (5 g.) in ether (90 c.c.) was gradually added with stirring to ββ-dimethylglutaromethylimide (22 g.) dissolved in warm benzene (50 c.c.); a white precipitate at once formed. After refluxing for 3 hours, the product was isolated, b. p. 195—206°/16 mm. It was hydrolysed during 10 hours by a boiling mixture of sulphuric acid (20 c.c.), acetic acid (60 c.c.), and water (25 c.c.). The acid was isolated and esterified with ethyl alcohol, and the ester distilled (7 g.), b. p. 179—181°/14 mm. Hydrolysis afforded the pure acid, b. p. 203°/18 mm. The semicarbazone separated from methyl alcohol in prisms, m. p. 113°, and the 2 : 4-*dinitrophenylhydrazone* crystallised from alcohol in vermilion needles, m. p. 99° (Found : N, 12·9. $C_{20}H_{30}O_6N_4$ requires N, 13·2%).

*1-β-Ketononyl*cyclo*hexane-1-acetic Acid.*—cyclo*Hexane-1 : 1-diacetomethylimide* was prepared by distilling a solution of its methylammonium salt (1MeNH$_2$ suffices). It had b. p. 184°/15 mm. and crystallised from alcohol in prisms, m. p. 66° (Found : N, 7·4. $C_{11}H_{15}O_2N$ requires N, 7·3%). A solution of this methylimide (30 g.) in benzene (100 c.c.) was added, all at once, to the Grignard reagent prepared from *n*-heptyl bromide (30 g.) and magnesium (6 g.) in ether (100 c.c.). After 12 hours, the mixture was refluxed for 1 hour. The product (6 g.), b. p. 215—225°/15 mm., was obtained after a considerable amount of the unchanged material had been recovered. It was refluxed for 16 hours with hydrobromic acid (*d* 1·15), and the acid isolated and esterified. Distillation of the ester gave a fraction, b. p. 160—175°/15 mm., largely ethyl *cyclo*hexanediacetate, a fraction, b. p. 175—200°/15 mm., and material of higher b. p., possibly containing still some unchanged methylimide. Hydrolysis of the middle fraction gave an oily *acid* which partly crystallised (0·4 g., m. p. 151°) (Found : C, 72·8; H, 10·7. $C_{17}H_{30}O_3$ requires C, 72·3; H, 10·6%).

*Ethyl 3-Methyl-3-(β-*cyclo*hexylethyl)nonoate.*—A mixture of β-methyl-β-*n*-hexylglutaric anhydride (10 g.), benzene (20 c.c.), and powdered aluminium chloride (15 g.) was kept for 6 hours. The product was isolated as a viscous oil, b. p. 225—230°/10 mm. It gave a red, oily 2 : 4-dinitrophenylhydrazone, but no crystalline semicarbazone or oxime could be obtained. The ethyl ester (10 g.), b. p. 214—216°/12 mm. (ethyl 4-benzoyl-3-methyl-3-*n*-hexylbutyrate), was dissolved in an equal volume of alcohol and hydrogenated at 200°/50—60 atms. in the presence of Raney nickel. The reduced *ester*, b. p. 190—200°/14 mm. (Found : C, 77·5; H, 11·1. $C_{20}H_{38}O_2$ requires C, 77·4; H, 12·3%), furnished, on hydrolysis, the acid, b. p. 225—228°/13 mm.

2-*Phenacyl*-2-*methyl-lauric Acid*.—A mixture of α-methyl-α-*n*-decylsuccinic anhydride (10 g.), benzene (20 c.c.), and powdered aluminium chloride (15 g.) was kept for 20 hours and then heated at 40° for 1 hour. The *product*, collected by means of ether, solidified; it crystallised from light petroleum in colourless prisms (10 g.), m. p. 87° (Found : C, 75·5; H, 9·8. $C_{21}H_{32}O_3$ requires C, 75·9; H, 9·6%). Search for an isomeric product was fruitless and it is evident that the reaction proceeded almost exclusively in one of the two possible directions. It has been established in several similar cases that it is the α-substituted, sterically hindered carboxyl group that survives.

Ethyl 2-*Methyl*-2-(β-cyclo*hexylethyl*)*laurate*.—A mixture of the above acid (8 g.), alcohol (15 c.c.), and Raney nickel (*ca.* 5 g.) was shaken under hydrogen at 200°/50 atms. The product was esterified and distilled (6 g.), b. p. 245—250°/14 mm. (Found : C, 78·9; H, 12·4. $C_{23}H_{44}O_2$ requires C, 78·4; H, 12·5%).

Prolonged reduction of the keto-acid (5 g.) according to Clemmensen (using 50 g. of amalgamated zinc) gave a product, b. p. 240—280°/9 mm. This material still contained some keto-acid and was obviously a mixture. On trituration with light petroleum, it partly solidified, and by fractional crystallisation from ethyl acetate–light petroleum two substances were separated, namely, γ-*phenyl*-α-*methyl*-α-n-*decylbutyrolactone-A*, m. p. 102° (Found : C, 79·4; H, 10·2. $C_{21}H_{32}O_2$ requires C, 79·6; H, 10·1%), and the more sparingly soluble *isomeride-B*, m. p. 164° (Found : C, 79·6; H, 10·1%). The substances showed the typical behaviour of lactones and are doubtless the *r*- and the *meso*-modification produced by the presence of two asymmetric carbon atoms in the molecule.

2-*Phenacyl*-2-*methyloctoic Acid*.—(i) A mixture of α-methyl-α-*n*-hexylsuccinic anhydride (10 g.), benzene (30 c.c.), and powdered aluminium chloride (18 g.) was kept for 10 hours and decomposed with ice. Evaporation of the benzene left a crystalline residue. The *substance* crystallised from ethyl acetate–light petroleum in prisms (9 g.), m. p. 95° (Found : C, 73·6; H, 8·8. $C_{17}H_{24}O_3$ requires C, 73·9; H, 8·7%).

(ii) A mixture of 3-carbethoxy-3-methylnonoyl chloride (5 g.), benzene (15 c.c.), and powdered aluminium chloride (9 g.) was kept for 12 hours. The oily product was isolated and hydrolysed by means of 20% aqueous sodium hydroxide; the liberated acid crystallised from ethyl acetate–light petroleum in prisms (3·5 g.), m. p. 95° alone or mixed with the product of (i).

n-*Amyl* β-n-*Amyl*iso*propenyl Ketone*.—Methylaniline (35 g.) in benzene (100 c.c.) was added to a Grignard solution prepared from ethyl bromide (50 g.), magnesium (9 g.), and ether (120 c.c.), and the solution gradually added with stirring to methyl *n*-amyl ketone (75 g.) in benzene (50 c.c.). After 10 hours, dilute hydrochloric acid was added, and the *product* isolated as a pale yellow oil (55 g.), b. p. 140°/13 mm. (Found : C, 80·1; H, 12·5. $C_{14}H_{26}O$ requires C, 80·0; H, 12·4%). Oxidation with alkaline permanganate afforded methyl amyl ketone and *n*-hexoic acid.

Ethyl 5-*Keto*-3-*methyl*-3-n-*amyldecoate*.—(i) A mixture of amyl amyl*iso*propenyl ketone (20 g.), ethyl malonate (16 g.), and alcoholic sodium ethoxide (2·3 g. of sodium in 35 c.c.) was refluxed for 1 hour. Potassium hydroxide (10 g.) and water (30 c.c.) were added, and refluxing continued for 2 hours. Acidification precipitated 5-*methyl*-2-*butyl*-5-n-*amyl*cyclo*hexane*-1 : 3-*dione* (15 g.). This crystallised from acetone in colourless needles, m. p. 72—73° (Found : C, 76·1; H, 11·3. $C_{16}H_{28}O_2$ requires C, 76·2; H, 11·1%). (ii) A mixture of amyl amyl*iso*propenyl ketone (20 g.), cyanoacetamide (8·5 g.), and alcoholic sodium ethoxide (0·5 g. of sodium in 50 c.c.) was refluxed for 1 hour. The solution was poured into dilute sulphuric acid, and the solid collected (18 g., colourless plates, m. p. 215°, from alcohol). This material was refluxed for 4 hours with sulphuric acid (50 c.c.), acetic acid (100 c.c.), and water (60 c.c.), then added to water, and the acid product collected by means of ether. It was esterified by boiling for 3 hours with alcohol (100 c.c.) and sulphuric acid (5 c.c.). The *ester* was a colourless oil, b. p. 185—188°/12 mm. (Found : C, 72·3; H, 11·4. $C_{18}H_{34}O_3$ requires C, 72·5; H, 11·4%). The semicarbazone of the corresponding acid (a viscous oil) separated from alcohol in colourless prisms, m. p. 98°. An attempt to apply the Wolff–Kishner reduction process to this semicarbazone was unsuccessful. After acid hydrolysis of the product, the unchanged keto-acid was recovered as the ester, b. p. 185—190°/13 mm., hydrolysed to the keto-acid and recognised as the semicarbazone, m. p. 98°.

Some non-ketonic material was obtained by reduction of the acid according to Clemmensen (ester, b. p. 170—175°/11 mm.), but the process was unsatisfactory and was not further investigated.

5-*Methyl*-2-n-*nonyl*-5-n-*decyl*cyclo*hexane*-1 : 3-*dione*.—Methylaniline (12 g.) in benzene (25 c.c.) was added to a Grignard solution prepared from ethyl bromide (16 g.), magnesium (3 g.), and ether (40 c.c.). This mixture was gradually added during ½ hour to a cooled and stirred solution of methyl *n*-decyl ketone (32 g.) in benzene (30 c.c.). After 10 hours, dilute hydrochloric acid was added, and the product isolated and distilled after addition of a trace of iodine. The pale yellow oil (18 g.), b. p. 235°/14 mm., is assumed from close analogies to be *n*-decyl β-*n*-decyl*iso*propenyl ketone.

A mixture of this αβ-unsaturated ketone (6 g.), ethyl malonate (4 g.), and alcoholic sodium ethoxide (0·5 g. of sodium in 10 c.c.) was refluxed for 4 hours. Potassium hydroxide (10 g.) in water (15 c.c.) was then added, and refluxing continued for 2 hours. Acidification after pouring into water precipitated an oil that gradually solidified. The *substance* crystallised from a little acetone in colourless needles (4 g.), m. p. 69° (Found : C, 79·3; H, 12·2. $C_{26}H_{48}O_2$ requires C, 79·6; H, 12·2%). It gave a pale brown coloration in alcoholic ferric chloride.

Ethyl 5-*Keto*-3-*methyl*-3-n-*decylpentadecoate*.—A mixture of the decyl decyl*iso*propenyl ketone (41 g.), cyanoacetamide (9 g.), and alcoholic sodium ethoxide (2·5 g. of sodium in 100 c.c.) was refluxed for 6 hours. It was then poured into dilute sulphuric acid, and the gummy solid collected. It was refluxed with sulphuric acid (30 c.c.), acetic acid (100 c.c.), and water (40 c.c.) for 5 hours. The acidic product was isolated, converted into its *ethyl* ester, and distilled, b. p. 245—250°/13 mm. (Found : C, 76·5; H, 12·1. $C_{28}H_{34}O_3$ requires C, 76·7; H, 12·3%). Acid hydrolysis afforded the corresponding acid, b. p. 265—270°/10 mm.

Neither the ester nor the acid could be reduced by Clemmensen's method even under the most vigorous conditions and in presence of toluene and acetic acid. The unchanged material was recognised by re-esterification and cyclisation to the above dihydroresorcinol derivative.

Experiments with Pinacols.—2-Methyl-3-*n*-amyloctane-2 : 3-diol was obtained, by the action of *n*-amylmagnesium bromide on ethyl α-hydroxy*iso*butyrate in ethereal solution, as a colourless oil, b. p. 150—160°/10 mm., that solidified after a long time as a mass of fibrous crystals, m. p. *ca.* 35°. The main product, b. p. 60—65°/10 mm., appeared to be a hydrocarbon. This pinacol was converted by cold concentrated sulphuric acid into a ketonic substance (2 : 4-dinitrophenylhydrazone), a pale yellow oil having a pleasant odour, and oxidation of this pinacolone with boiling 33% nitric acid gave a mixture of acids. The fraction, b. p. 150—210°, furnished a crystalline amide, m. p. 117° (Found : N, 9·0. $C_9H_{19}ON$ requires N, 9·0%). Hence this is probably 2 : 2-*dimethylheptamide*.

The reaction between *n*-heptylmagnesium bromide and ethyl α-hydroxy*iso*butyrate (14 g.) gave as the chief product a colourless oil (22 g.), b. p. 130°/12 mm., m. p. 3° (Found : C, 86·2; H, 13·8. $C_{18}H_{34}$ requires C, 86·4; H, 13·6%). When ethyl lactate was used, the product was of similar nature, b. p. 120—130°/14 mm., m. p. 2°. In both cases very little material of higher b. p. was produced.

n-Dodecylmagnesium bromide and ethyl α-hydroxy*iso*butyrate (13·2 g.) gave dodecane (10 g., b. p. 212—215°) and a solid (21 g.) which crystallised from alcohol in plates, m. p. 53—54° (Found: C, 85·4; H, 14·5. $C_{28}H_{56}$ requires C, 85·7; H, 14·3%). The same substances were obtained by the action of magnesium on a mixture of dodecyl bromide and ethyl hydroxy*iso*butyrate in ethereal solution.

The action of amalgamated magnesium on methyl *n*-decyl ketone (20 g.) gave a poor yield of the pinacol (2 g., b. p. 240—250°/12 mm.), recognised as such by oxidation with lead tetra-acetate, whereby methyl decyl ketone was produced (semicarbazone, m. p. 121°). The action of cold concentrated sulphuric acid on this material gave a ketone (0·8 g., b. p. 200—240°/12 mm.). The reduction of methyl decyl ketone by sodium in moist ether afforded dodecan-2-ol and only traces of material of higher b. p.

The authors are grateful to the Commissioners of the Exhibition of 1851 for an Overseas Scholarship awarded to one of them.

DYSON PERRINS LABORATORY, OXFORD UNIVERSITY. [*Received, March* 19*th*, 1942.]