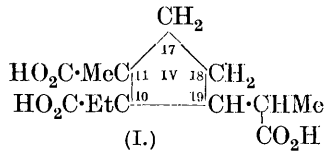
# CCXIII.—*Synthesis of Substances analogous to Bile Acid Degradation Products. Part I. Preliminary Investigation of Methods of Attachment of Carboxylated Side Chains to the* cyclo*Pentane Nucleus.*

By JOHN WILLIAM BAKER.

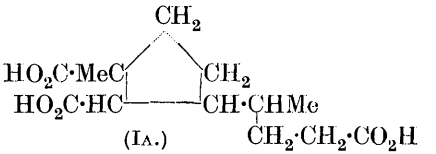
DEGRADATION of cholesterol and of acids of the cholane group has now resulted in the isolation of several relatively simple products, particularly those in which the five-membered ring (ring IV) of the nuclear skeleton remains intact. Of these, the simplest is a *cyclo*pentane acid, $C_{13}H_{20}O_6$ (Wieland and Vocke, *Z. physiol. Chem.*, 1928, **177**, 68), for which comparatively few structural forms are probable. It was therefore considered desirable to commence attack on the problem of the structure of these degradation products from another angle, and to attempt to synthesise the more probable of the structures assigned to them in an endeavour to elucidate their true constitution.

The present communication describes the results of some pre-

liminary work on the attachment of the appropriate side chains to a *cyclo*pentane nucleus, the ultimate object of which is to effect the synthesis of compounds of the structures tentatively assigned to the acids $C_{16}H_{24}O_8$ and $C_{13}H_{20}O_6$ obtained as the ultimate products of the oxidative degradation of deoxybilianic acid (*loc. cit.*). When this investigation was commenced, Wieland had reduced the number of possible alternative structures of cholanic acid to twenty, of which eleven were favoured, and of these eleven, four especially so (compare *Ann. Reports*, 1928, **25**, 162). One of these four, one which contains the quaternary methyl group, the carboxylated side chain, and an ethyl group in positions 11, 19, and 10 in ring IV, is unique in that it corresponds to a cholesterol skeleton divisible into a farnesene chain, linked end to end with two normal $C_6$ units, and this alternative would require that the acid $C_{13}H_{20}O_6$ should possess the structure (I). The same structure would be derived



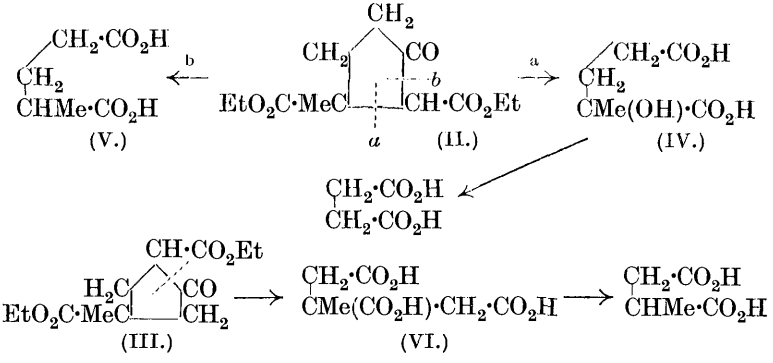

(I.)




(IA.)

from the 10-17-11 combination. Attention was therefore directed in the first instance to the synthesis of an acid of this structure.

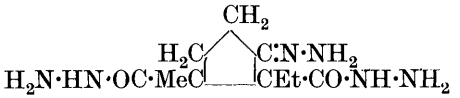
A convenient starting point for such a synthesis is found in the *cyclo*pentanone ester obtained by Ruzicka (*Ber.*, 1917, **50**, 1362) in his synthesis of fenchone. This ester is obtained by a Dieckmann condensation from ethyl β-methylbutane-αβδ-tricarboxylate. Ring closure can obviously occur in two ways, giving the *cyclo*pentanone ester (II) or (III). Ruzicka did not determine the constitution of



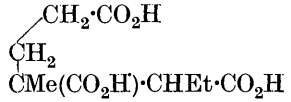

this ester, since, on acid hydrolysis, either structure would yield 2-methyl*cyclo*pentanone-2-carboxylic acid which was the required

intermediate in the fenchone synthesis. For the present purpose, however, it is essential that the ester should possess the structure (II). That this is actually the case is proved by careful oxidation with potassium permanganate. The products of this oxidation have been identified as α-methylglutaric acid (V), a liquid acid, analysis of the silver salt of which corresponds with that of α-hydroxy-α-methylglutaric acid (IV), and a trace of succinic acid. Although carefully sought for, no trace of either β-methyltricarballylic acid (VI) or of methylsuccinic acid, the products which would result from oxidation of an ester of structure (III), could be detected. Hence the ketonic ester is definitely established to be *ethyl* 3-*methyl*cyclo*pentanone*-2 : 3-*dicarboxylate* (II).

Alkylation of this ester will obviously occur at position 2, and the introduction of an ethyl group here affords a *cyclo*pentanone ester with the required arrangement of alkyl and carboxyl groups, together with a reactive carbonyl group at the desired point of attachment of the side chain. Unexpected difficulty was encountered in effecting complete ethylation of this ester. The product obtained by the action of alcoholic sodium ethoxide and ethyl iodide always contained up to 20% of the unethylated ketonic ester, which could not be removed by fractional distillation. The difficulty was finally overcome by the use of sodamide in dry ether and a large excess of ethyl iodide, any small trace of unethylated ester in the product being removed by shaking the ligroin solution with aqueous ferric chloride. The structure of the ethylated ester was confirmed by the preparation of a crystalline *hydrazone-dihydrazide* (VII) with hydrazine hydrate and by hydrolysis with alcoholic potassium hydroxide to *γ-methyl*-n-*hexane-αγδ-tricarboxylic acid* (VIII).




(VII.)




(VIII.)

It was anticipated that the required side chain, $CHMe{\cdot}CO_2H$, could be introduced (in position 1) into *ethyl* 3-*methyl*-2-*ethyl*cyclo*pentanone*-2 : 3-*dicarboxylate* by a Reformatsky reaction with ethyl α-bromopropionate. Owing to the difficulty of obtaining the parent *cyclo*pentanone ester in quantity, however, the reaction was first investigated with an analogous open-chain compound, namely, ethyl dimethylacetoacetate. This condensed with ethyl α-bromopropionate and zinc to give a moderate yield of *ethyl* β-*hydroxy-ααα'β-tetramethylglutarate* (IX), converted by boiling with concentrated hydrochloric acid and amalgamated zinc, or by treatment

with phosphorus pentachloride, followed by hydrolysis with alcoholic potassium hydroxide, into *αα*β*γ-tetramethylglutaconic acid* (X). This was reduced by hydrogen and platinum-black in acetic acid to *ααα'*β*-tetramethylglutaric acid* (XI), which is the open-chain analogue of the required *cyclo*pentane acid.

$$MeCO{\cdot}CMe_2{\cdot}CO_2Et + CHMeBr{\cdot}CO_2Et \xrightarrow{Zn} \begin{matrix} CMe(OH){\cdot}CMe_2{\cdot}CO_2Et \\ | \\ CHMe{\cdot}CO_2Et \end{matrix} \quad (IX.)$$

$$\longrightarrow (X.)\ \begin{matrix} CMe{\cdot}CMe_2{\cdot}CO_2H \\ \| \\ CMe{\cdot}CO_2H \end{matrix} \longrightarrow CHMe(CO_2H){\cdot}CHMe{\cdot}CMe_2{\cdot}CO_2H \ (XI.)$$

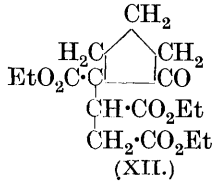
When the same condensation process was applied to the ethylated *cyclo*pentanone ester, however, most of the latter was recovered unchanged and no product containing the required side chain could be isolated.

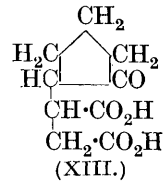
At this point in the investigation Wieland and Vocke published their paper (*Z. physiol. Chem.*, 1930, **191**, 68) in which it was clearly shown that the acid $C_{13}H_{20}O_6$ does not contain an ethyl group in the ring, but that it is most probably represented by the structure (IA). It was therefore considered advisable to postpone, for the present, further attempts to attach the side chain $CHMe{\cdot}CO_2Et$ to ethyl 3-methyl-2-ethyl*cyclo*pentanone-2 : 3-dicarboxylate, and to undertake a preliminary investigation of methods by which the longer side chain $CHMe{\cdot}[CH_2]_2{\cdot}CO_2H$, and also the side chain $CH(CO_2H){\cdot}CH_2{\cdot}CO_2H$ present in the $C_{16}H_{24}O_8$ acid (XIV) (*loc. cit.*), might be introduced into the *cyclo*pentane nucleus. The introduction of the lengthened side chain with the two extra methylene groups obviously presents greater difficulties than does the similar introduction of the shorter one originally required, and, although work in this direction is proceeding, has not yet been accomplished. An attempt to condense ethyl *γ*-bromo-*n*-valerate with the 5-sodio-derivative of ethyl 2-methyl*cyclo*pentanone-2-carboxylate obtained by the action of sodamide on the parent ester was unsuccessful.

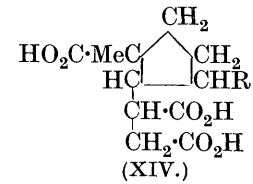
For the attachment of the succinic acid residue present in the $C_{16}$ acid, two methods suggest themselves, (1) a Michael condensation between ethyl fumarate and a *cyclo*pentanone-2-carboxylic ester, (2) condensation of the sodio-derivative of the latter with ethyl α-bromosuccinate.

Little success has been obtained with ethyl *cyclo*pentanone-2-carboxylate by the first method, but the sodio-derivative of this ester readily condenses with ethyl α-bromosuccinate to give the *ester* (XII). This is hydrolysed by hydrochloric acid to *keto*cyclo*pentyl-2-succinic acid* (XIII), which contains the appropriate side chain of the $C_{16}$ acid. This acid yields an *anhydride* when heated above its m. p. in the usual manner. A similar synthesis applied

to ethyl 3-methyl*cyclo*pentanone-2 : 3-dicarboxylate should afford a *cyclo*pentanone ester from which it should be possible to build up

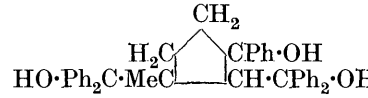

(XII.)


(XIII.)


(XIV.)

the acid $C_{16}H_{24}O_8$, or its simpler degradation products in which the side chain $CHMe\cdot[CH_2]_2\cdot CO_2H$ (R) (XIV) has been shortened by suitable oxidation processes, and work in this direction is in hand.

One further line of attack on the problem has also been initiated. Ethyl 3-methyl*cyclo*pentanone-2 : 3-dicarboxylate (II) was allowed to react with a large excess of phenylmagnesium bromide, and from the reaction product was isolated a very small amount of a crystalline substance which probably has the structure (XV) or one of its two possible internal ethers (see experimental portion). On the

(XV.) 

assumption that the acid $C_{13}H_{20}O_6$ is correctly represented by structure (IA), it should be possible to prepare this derivative by removal of the $CHMe\cdot[CH_2]_2\cdot CO_2H$ side chain from this $C_{13}$ acid by means of alternate Grignard condensations and oxidations, in a similar manner to that used by Wieland, Schlichting, and Jacobi (*Z. physiol. Chem.*, 1926, **161**, 180) in the degradation of cholanic acid to ætiocholanone, and the further action of phenylmagnesium bromide on the *cyclo*pentanone dicarboxylic ester so formed. It is hoped to extend the investigation in this direction also.

## EXPERIMENTAL.

Ethyl β-methylbutane-αββ-tricarboxylate was prepared as described by Ruzicka (*Ber.*, 1917, **50**, 1362). Ethyl lævulate was condensed with ethyl bromoacetate and zinc in benzene solution to give the lactone of ethyl β-hydroxy-β-methyladipate. The lactone (125 g.) was heated with 60 g. of potassium cyanide for 8 hours at 200—220°, and the product hydrolysed as described by Ruzicka with alcoholic sulphuric acid for 10 days at 120°. Careful control of the temperature at this stage was necessary and an attempt to shorten the time of hydrolysis by using alcoholic hydrogen chloride was unsuccessful.

*Ethyl* 3-*methyl*cyclo*pentanone*-2 : 3-*dicarboxylate* (II) was prepared

by heating 79 g. of the tricarboxylic ester with 7·3 g. of "molecular" sodium in benzene for 1 hour on a steam-bath. The product was decomposed with ice and shaken with dilute sulphuric acid, and the benzene extract washed several times with dilute sodium hydrogen carbonate solution. Fractional distillation of the residue from the dried benzene solution gave the required *ester*, b. p. 130—134°/2—2·5 mm., in 75% yield (Found: C, 59·7; H, 7·5. $C_{12}H_{18}O_5$ requires C, 59·5; H, 7·4%). Attempts to prepare a semicarbazone were unsuccessful.

*Ethyl* 3-*Methyl*-2-*ethyl*cyclo*pentanone*-2 : 3-*dicarboxylate*.—Ethylation of the *cyclo*pentanone ester was first attempted with alcoholic sodium ethoxide and ethyl iodide or ethyl sulphate. The ester (20 g.) was added to a cooled solution of 1·9 g. of sodium in 25 c.c. of anhydrous alcohol and 13 g. of ethyl sulphate were added to the yellow solution formed. The mixture was heated on the steam-bath for 1 hour, a further small quantity of ethyl sulphate being added. The reaction mixture became colourless and neutral, but when the neutral product was worked up in the usual manner the main fraction, b. p. 157—157·5°/8 mm., still gave a colour with ferric chloride. Colorimetric determinations showed the presence of about 25% of the unethylated ketonic ester in this product (Found: C, 60·5; H, 8·0. $C_{14}H_{22}O_5$ requires C, 62·2; H, 8·2%). Repeated extraction of a ligroin solution of this fraction with dilute aqueous ferric chloride removed the unethylated ester and gave a product, b. p. 165°/10 mm., which gave scarcely any coloration with ferric chloride (Found: C, 61·5; H, 8·1%). Subsequently ethylation was effected by the use of sodamide and ethyl iodide. The ester (28 g.), dissolved in an equal volume of ether, was added in small successive portions to 5·5 g. (1·2 mols.) of powdered sodamide under 30 c.c. of dry ether. A brisk evolution of ammonia set in after each addition. The mixture was heated on the steam-bath until ammonia ceased to be evolved and most of the ether had been removed. A large excess of ethyl iodide was added, and the whole gently refluxed for about 12 hours. After distillation of most of the excess of ethyl iodide, the separated sodium iodide was filtered off and washed with ligroin (b. p. 40—60°), and the ligroin extract of the product shaken with aqueous ferric chloride until no further colour was produced. Distillation of the residue from the dried ligroin solution gave the required *ester*, b. p. 135°/3 mm. (Found: C, 62·2; H, 8·2%).

The *hydrazone-dihydrazide* (VII) was obtained by heating a small quantity of the ester with a slight excess of hydrazine hydrate in alcoholic solution for 20 hours. The mixture was evaporated over sulphuric acid in a vacuum at the ordinary temperature. The

residual gum partly crystallised on keeping and, after being drained on porous porcelain, the hydrazone-dihydrazide was obtained as a crystalline powder, m. p. 163°, by crystallisation from alcohol–ethyl acetate (Found: C, 46·8; H, 7·7; N, 32·3. $C_{10}H_{20}O_2N_6$ requires C, 46·9; H, 7·8; N, 32·6%).

*γ-Methyl*-n-*hexane-αγδ-tricarboxylic Acid* (VIII).—The ethylated *cyclo*pentanone ester was refluxed for 2—3 hours with absolute-alcoholic potassium hydroxide. The crystalline potassium salt was filtered off, washed with cold alcohol and ether, and dissolved in cold dilute hydrochloric acid, and the acid extracted with ether. After keeping, the gum obtained from the dried ethereal solution solidified when rubbed with a cold mixture of ether and ligroin (b. p. 40—60°) and the *acid* crystallised from ether–ligroin in small nodules, m. p. 155° (Found: C, 52·4, 52·1; H, 7·2, 7·0; equiv., by titration, 77·5. $C_{10}H_{16}O_6$ requires C, 51·7; H, 6·9%; equiv. as tribasic acid, 77·3). From the impure residues a *silver* salt, which was not quite pure, was prepared in the usual manner (Found: Ag, 55·2. $C_{10}H_{13}O_6Ag_3$ requires Ag, 58·6%).

*Attempt to condense the Ethylated Ester with Ethyl α-Bromopropionate.*—The ester (30·5 g.) was boiled under reflux with 22 g. of ethyl α-bromopropionate and 8·2 g. of zinc in 100 c.c. of dry benzene until a brisk exothermic reaction set in, which was finally completed by heating for a further period of 1 hour. Distillation of the neutral product, isolated in the usual manner, afforded two main fractions, b. p. 156—162°/8·5 mm. and b. p. 162—174°/8·5 mm., which, however, consisted of the unchanged ethylated ester (Found: C, 62·4, 62·2; H, 8·2, 8·2%), since on hydrolysis with alcoholic potassium hydroxide they gave a specimen of γ-methyl-*n*-hexane-αγδ-tricarboxylic acid, the m. p. of which was not depressed by admixture with the specimen obtained by similar hydrolysis of the parent ester.

*Oxidation of Ethyl* 3-*Methyl*cyclo*pentanone*-2 : 3-*dicarboxylate.*—The ester (4·8 g.) was dissolved in a solution of 7·5 g. of potassium hydroxide in 20 c.c. of water, and a solution of 6·3 g. of potassium permanganate in 250 c.c. of water added in small successive portions at 30°. The reaction mixture was left for 1 hour at the ordinary temperature and then heated on the steam-bath for 2 hours. Sulphur dioxide was passed into the cooled solution, and the product extracted with ether. When the ethereal solution was extracted with aqueous sodium carbonate, the whole product passed into the aqueous layer (A), which was then re-acidified and again extracted with ether (B). The residue (0·51 g.) from the dried ethereal solution B crystallised and had m. p. 68—70° in the crude state. Crystallisation from benzene gave α-methylglutaric acid, m. p.

75—77° either alone or mixed with a genuine specimen of this acid. The aqueous liquor A was made alkaline and evaporated to dryness on the steam-bath, the residue acidified with a little concentrated hydrochloric acid and filtered, and the aqueous solution again extracted with ether (C). The solid residue was extracted with dry acetone (D). The last extract D gave only a small quantity of a brown oil, from which a few crystals, insufficient for investigation, separated. The residue (2·24 g.) from the second ethereal extract C deposited a further small quantity (0·05 g.) of a solid, m. p. 70—100°, which depressed the m. p. of α-methylsuccinic acid, m. p. 111°, and after crystallisation from ether–ligroin gave a small quantity of an acid, m. p. 182—184°, not depressed by admixture with succinic acid. The main portion of C would not crystallise. It was extracted with cold chloroform (in which β-methyltricarballylic acid is insoluble) and then with ether at 0°. Neither the insoluble residue nor the residues from the chloroform and ether extracts could be induced to crystallise, hence these fractions were united and distilled first at 50 mm. to encourage anhydride formation, and then almost completely at 180—220°/2 mm. The distillate (0·716 g.) was triturated with cold aqueous sodium carbonate to remove acid products from any anhydrides, but almost the whole product went into solution. The solution was extracted with ether to remove any non-acidic impurity, boiled to hydrolyse any anhydro-acids, acidified with hydrochloric acid, and carefully evaporated to dryness on the steam-bath. The residue was extracted with dry acetone, the solution concentrated, and benzene added. No crystallisation of β-methyltricarballylic acid occurred. The whole of the liquid acid after evaporation of the solvents was therefore converted into its *silver* salt (0·75 g.) in the usual manner (Found: C, 19·0; H, 1·9; Ag, 57·7. $C_6H_8O_5Ag_2$ requires C, 19·4; H, 2·1; Ag, 57·4%). The liquid acid is therefore, probably, α-hydroxy-α-methylglutaric acid.

*Ethyl* β-*Hydroxy*-αα*α'*β-*tetramethylglutarate* (IX).—Ethyl dimethylacetoacetate (15·8 g.), ethyl α-bromopropionate (18·2 g.), and 6·5 g. of zinc were heated in 100 c.c. of dry benzene until the exothermic reaction commenced. The reaction was finally completed by heating on a steam-bath for 1 hour, the product decomposed with ice-cold dilute sulphuric acid, and the neutral product isolated in the usual manner. Fractional distillation of this gave 10 g. of unchanged ketonic ester, b. p. 55°/4 mm., and 5 g. of the required *ester*, b. p. 125—127°/6 mm. (Found: C, 59·9; H, 9·2. $C_{13}H_{24}O_5$ requires C, 60·0; H, 9·2%). Allowing for recovered ethyl dimethylacetate, the yield is 50% of the theoretical.

αα*βγ-Tetramethylglutaconic Acid* (X).—The hydroxy-ester could

not be dehydrated to the unsaturated ester by distillation under atmospheric pressure. The unsaturated acid was obtained by several methods:

(*a*) Clemmensen reduction. The ester was refluxed with concentrated hydrochloric acid for 1—2 hours to effect hydrolysis and then amalgamated zinc was added in successive portions to the boiling solution during a further period of 1 hour. The product was extracted with ether, and the acid portion removed with sodium carbonate solution. The residue from the dried ethereal extract of the acidified sodium carbonate extract crystallised on keeping. After crystallisation from ether–ligroin the *glutaconic acid* had m. p. 128° (Found: C, 58·0; H, 7·6; equiv., by titration, 93. $C_9H_{14}O_4$ requires C, 58·0; H, 7·5%; equiv., 93).

(*b*) When the hydroxy-ester (2 g.) was warmed with phosphorus pentachloride (2 g.), conversion into the chloro-ester did not seem to be complete, but hydrolysis of the product with a warm concentrated solution of potassium hydroxide in anhydrous alcohol afforded a crystalline potassium salt from which, after washing with alcohol and ether, the same acid, m. p. 128°, was regenerated in the usual manner (Found: C, 58·2; H, 7·7%). The acid decolorised a solution of potassium permanganate in aqueous sodium hydrogen carbonate only very slowly. The *silver* salt was prepared from the ammonium salt in the usual manner (Found: Ag, 54·0. $C_9H_{12}O_4Ag_2$ requires Ag, 54·0%).

*αα'β-Tetramethylglutaric Acid* (XI).—The glutaconic acid (0·197 g.) was reduced with hydrogen and platinum-black in acetic acid. Absorption of the hydrogen was rapid, 26 c.c. being taken up in 1 hour (theoretical for 1 double linking, 24·5 c.c.). After the catalyst had been filtered off and washed with acetic acid, the solution was evaporated over potassium hydroxide in a vacuum at the ordinary temperature. The residue crystallised completely and, after crystallisation from ether–ligroin, the *glutaric acid* had m. p. 121°, depressed to 110—119° by admixture with a specimen of the original glutaconic acid (Found: C, 57·4; H, 8·5; equiv., by titration, 93·4. $C_9H_{16}O_4$ requires C, 57·4; H, 8·4%; equiv., 94).

*Ethyl 2-Carbethoxy-1-ketocyclopentyl-2-succinate* (XII).—(1) *Condensation of ethyl* cyclo*pentanone-2-carboxylate with ethyl fumarate.* The *cyclo*pentanone ester (10 g.) (Dobson, Ferns, and Perkin, J., 1909, **95**, 2015) was added to a cooled solution of 1·5 g. of sodium in 20 c.c. of anhydrous alcohol. The solid sodio-derivative separated immediately. This was refluxed on a steam-bath with 11 g. of ethyl fumarate for 2·5 hours; all the sodio-derivative had then passed into solution. After the product had been poured into water, the neutral fraction was isolated in the usual manner and

fractionally distilled. After unchanged ethyl fumarate had distilled, two fractions were collected, b. p. 110—124°/8 mm. (2 g.), and b. p. 124—126°/8 mm. (2 g.); the latter gave scarcely any colour with ferric chloride, but analysis proved that it was not the required condensation product (Found : C, 58·9; H, 8·6. $C_{16}H_{24}O_7$ requires C, 58·5; H, 7·3%). It gave adipic acid on hydrolysis with alcoholic potassium hydroxide and was not further investigated.

(2) *Condensation of ethyl* cyclo*pentanone-2-carboxylate with ethyl monobromosuccinate.* The *cyclo*pentanone ester (15·6 g.) was added to a cooled solution of 2·3 g. of sodium in 40 c.c. of anhydrous alcohol and the solid sodio-derivative which separated was refluxed with 25·3 g. of ethyl bromosuccinate for ½ hour. The bulk of the separated sodium bromide (7·8 g.) was filtered off and washed with ether, and the washings were added to an ethereal extract of the filtrate, which had been poured into a large volume of water. Fractionation of the residue from the dried ethereal solution of the neutral portion gave 22 g. of the required *ester*, b. p. 211—215°/10 mm. (Found : C, 58·3; H, 7·3. $C_{16}H_{27}O_7$ requires C, 58·5; H, 7·3%).

1-*Keto*cyclo*pentyl-2-succinic Acid* (XIII).—The ester was hydrolysed by boiling with concentrated hydrochloric acid for 2 hours under reflux; the solution was poured into water and extracted with ether, and the acid fraction separated with aqueous sodium carbonate in the usual manner. The residue from the dried ethereal extract of the acid portion partly crystallised in a vacuum desiccator. It was triturated with chloroform at 0° and drained on porous porcelain. The *acid* crystallised from acetone–chloroform or, better, ether–ligroin in small nodules, m. p. 138—139° (Found : C, 53·7; H, 6·05. $C_9H_{12}O_5$ requires C, 54·0; H, 6·0%). A further yield of the acid was obtained by evaporation of the original acid aqueous liquor to dryness on the steam-bath. A small amount of the acid was converted into the *anhydride* by gentle heating above its m. p. for a few minutes. The product, crystallised from benzene, had m. p. 116° (mixed m. p. with parent acid, 110°) and was not quite pure (Found : C, 58·8; H, 5·8. $C_9H_{10}O_4$ requires C, 59·4; H, 5·5%).

*Action of Phenylmagnesium Bromide on Ethyl* 3-*Methyl*cyclo*pentanone*-2 : 3-*dicarboxylate.*—The Grignard reagent (10 mols.) was prepared in the usual manner from 2·4 g. of magnesium, 15·7 g. of bromobenzene, and 50 c.c. of dry ether and was decanted from the slight residue. The *cyclo*pentanone ester (2·4 g.) was then added with cooling. After the initial vigorous reaction was over, the mixture was refluxed on a steam-bath for 18 hours, decomposed with ice and ice-cold dilute sulphuric acid, and extracted with

ether, and the extract washed with sodium carbonate solution; the residue from the dried ethereal solution (5 g.) set to a glass when kept in a vacuum over concentrated sulphuric acid. After some months this was extracted with boiling ligroin (b. p. 40—60°). By cooling the ligroin solution in ice, a white solid was precipitated which, however, could not be crystallised. Extraction of this solid with cold ligroin (b. p. 40—60°) and spontaneous evaporation of the solution at the ordinary temperature afforded a gum which partly crystallised. After draining on a porous plate and crystallisation from ligroin, diphenyl was isolated, m. p. 70° (alone or mixed with a genuine specimen). After further prolonged keeping over sulphuric acid, the portion insoluble in ligroin solidified to a dry amorphous powder. This was triturated with cold dry ether, which left undissolved a small quantity of crystalline material. This substance, after crystallisation from acetone–methyl alcohol, had m. p. 231° (Found : C, 86·6; H, 6·8. $C_{38}H_{36}O_3$ requires C, 84·5; H, 6·7. $C_{38}H_{34}O_2$ requires C, 87·3; H, 6·5%). Although the constitution of this substance cannot yet be stated with certainty, the high percentage of carbon present indicates that it is most probably a derivative of the type suggested.

The author desires to thank the Government Grant Committee of the Royal Society for a grant with the aid of which some of the heavy expense incurred in this investigation has been met.

THE UNIVERSITY, LEEDS. [*Received, April 16th*, 1931.]