113. *The Influence of Alkylation on the Reactions of Acid Derivatives in the Friedel–Crafts Synthesis.*

By Eugene Rothstein and M. A. Saboor.

When acids or their chlorides or anhydrides are treated under various conditions with reagents such as phosphoric oxide and anhydrous aluminium chloride, their reactions fall into two classes. The first, which includes mainly the primary and secondary acid derivatives, yields ketones (under Friedel–Crafts conditions) or ketones and carbon dioxide (Kipping, J., 1890, **57**, 532); in the second, tertiary acids always eliminate carbon monoxide and the product is an unsaturated substance or its polymeride (cf. *inter alia* Laughlin and Whitmore, *J. Amer. Chem. Soc.*, 1932, **57**, 532). In the present paper these reactions are discussed and a mechanism which explains them is suggested. Experiments have been carried out which fully confirm the hypotheses put forward, and a new application of the Friedel–Crafts synthesis is described, whereby tertiary acid anhydrides or chlorides lose carbon monoxide with replacement of a carboxyl group by an aromatic nucleus. This reaction affords an improvement on the method devised by Whitmore and his collaborators for diagnosing tertiary aliphatic acids.

Much of the work on the Friedel–Crafts synthesis deals with the function of the catalyst, comparatively little attention having been directed to the influence of substituents; the present investigation deals with the influence of alkyl groups on the course of the reaction when acid derivatives are treated with aluminium chloride or other substances having a similar catalytic action.

I. When alkylated succinic anhydrides are treated with benzene and aluminium chloride, the phenyl group tends to attach itself to the carbonyl group next to the least alkylated carbon atom (compare *inter alia*, Mayer and Stamm, *Ber.*, 1923, **56**, 1424; Haworth, J., 1932, 1128; Clemo and Dickenson, J., 1937, 255; Desai and Wali, *Proc. Indian Acad. Sci.*, 1937, **6***A*, 135). Methylsuccinic anhydride, for instance, yields a mixture of β-benzoyl-β- (I) and -α-methylpropionic acid* (II), the second being the major product. Desai and Wali (*loc. cit.*), using phenylsuccinic anhydride and toluene, isolated five times as much β-toluoyl-α-phenyl- (III) as β-toluoyl-β-phenyl-propionic acid (IV) when toluene was also the solvent, but in nitrobenzene the proportions were reversed. Both Haworth (*loc. cit.*) and Desai and Wali advance similar mechanisms which ascribe the preferential formation of (I) to the repulsion of the phenyl anion by the inductive effect of the alkyl groups. The latter authors further regard the preponderating amount of one or other of the isomerides (III) or (IV) as due to the ability of the phenyl group to act both as an electron source and as an electron sink. This, however, is not acceptable since, among other reasons, a similar explanation cannot be applied to methylsuccinic anhydride. The effect of nitrobenzene may be significant in view of its high ionising power (see below), and in this connection Desai and Wali report that when *gem*-dialkyl groups or ring structures such as *cyclo*-pentane or

(I.) $COPh{\cdot}CHMe{\cdot}CH_2{\cdot}CO_2H$ $COPh{\cdot}CH_2{\cdot}CHMe{\cdot}CO_2H$ (II.)

(III.) $C_6H_4Me{\cdot}CO{\cdot}CH_2{\cdot}CHPh{\cdot}CO_2H$ $C_6H_4Me{\cdot}CO{\cdot}CHPh{\cdot}CH_2{\cdot}CO_2H$ (IV.)

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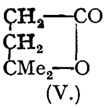
* In order to simplify comparison, in all appropriate cases the substances are regarded as derivatives of propionic acid, but systematic names also are given for new compounds.

-hexane substitute one of the methylene groups of succinic anhydride, *e.g.*, in *cyclo*pentane-1-carboxylic-1-acetic anhydride, the product is always the β-benzoyl-α-substituted propionic acid, $COPh\cdot CH_2\cdot C(:C_4H_8)\cdot CO_2H$, even in nitrobenzene solution. It is known that phenyl *tert.*-alkyl ketones, $Ph\cdot CO\cdot CR_3$, cannot be prepared by the Friedel–Crafts reaction, but are usually obtained by alkylation of the phenyl dialkyl ketone (Haller and Bauer, *Compt. rend.*, 1909, **148**, 72). Reasons for this are discussed later.

II. Kipping (J., 1890, **57**, 532, 980; 1893, **63**, 452) found that fatty acids ranging from *n*-heptoic to stearic yielded ketones when heated with excess of phosphoric oxide at 180—220°, carbon dioxide being eliminated. More recently, Laughlin and Whitmore (*J. Amer. Chem. Soc.*, 1932, **54**, 4462) and Whitmore and Crooks (*ibid.*, 1938, **60**, 2078) analysed the gases evolved when various alkylated fatty acids mixed with phosphoric oxide were heated to 155—160°. The experiments showed that primary and secondary acids yielded small quantities of carbon dioxide containing a small proportion of monoxide, but with tertiary acids such as trimethyl-, dimethylethyl-, methyldiethyl-, and methyl-*tert.*-butyl*neo*pentyl-acetic acids, the yields of carbon monoxide increased with increasing alkylation, being 55% for the first and over 90% of the theoretical for the last. Very small amounts of carbon dioxide (corresponding, presumably, to ketone formation) were also formed, but the yield never exceeded 0·6%, whereas under the same conditions for less alkylated acids the quantity was of the order of 6%. The residues were usually tars, but those from trimethylacetic acid were mainly polymerised *iso*butylene.

III. The reactions between aluminium chloride and acid chlorides and anhydrides have also in certain cases been found to lead to elimination of carbon monoxide; *e.g.*, *as*-dimethylsuccinic anhydride affords ββ-dimethylacrylic acid, $CMe_2:CH\cdot CO_2H$, and carbon monoxide when warmed with aluminium chloride in chloroform solution (Desfontaines, *Compt. rend.*, 1902, **134**, 295), and similarly αα-dimethylglutaric anhydride yields the lactone of γ-hydroxy-γ-methylvaleric acid (V) and γ-methyl-Δ^{β}-pentenoic acid (VI) with loss of carbon monoxide, the lactone obviously being derived from the unsaturated acid by subsequent hydration. This reaction does not take place with α-methylglutaric anhydride.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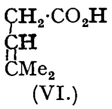
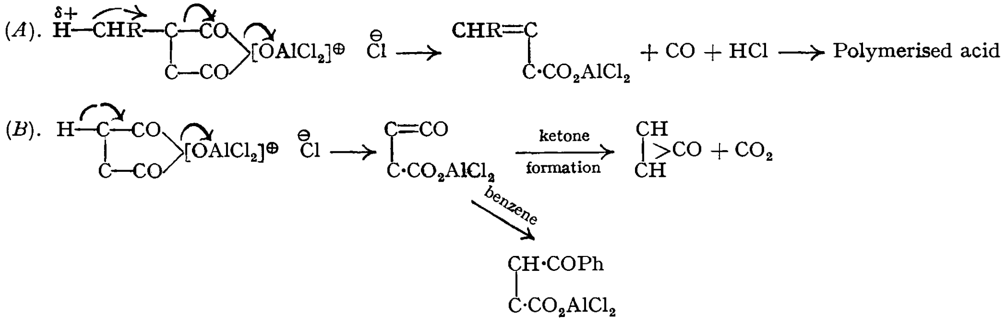

(VI.)

Two final instances of analogous reactions of importance in this connection are the formation of carbon monoxide, hydrogen chloride, and a polymerised hydrocarbon when trimethylacetyl chloride is mixed with aluminium chloride at 0°, and of carbon monoxide, hydrogen chloride, and *iso*butylenedisulphonic acid when the same substance is heated with concentrated sulphuric acid at 100° (Boëseken, *Rec. Trav. chim.*, 1910, **29**, 100).

In all the above examples it is evident that the absence of an *ionisable* α-hydrogen atom leads to formation of an unsaturated substance, usually polymerised, with loss of carbon monoxide; in other cases little of the latter is eliminated and a ketone results, and in this connection the reactions of dimethylsuccinic anhydride in the non-ionising chloroform solution may be of significance. The possible mechanisms for these reactions are outlined in (*A*) and (*B*) in which aluminium chloride is depicted as the catalyst. The corresponding reactions with other catalysts are probably essentially similar.



The interpretation (*A*) of the experiments of Whitmore and his collaborators is further illustrated in the present paper by the dry distillation of calcium β-phenyl-ααββ-tetramethylpropionate (as XI), which furnishes an unsaturated hydrocarbon with loss of carbon monoxide and water, no ketone being formed. The keten-like intermediate in (*B*) may represent a transition structure only and not a definite compound. It is envisaged that reaction with acid chlorides is precisely similar, with analogous mechanisms. This is of some importance because, though the literature does not reveal a case of cyclic ketone formation from an anhydride and aluminium chloride, diethyl ketone and di-*n*-propyl ketone are produced when propionyl and *n*-butyryl chlorides, respectively, are treated with anhydrous ferric chloride (Hamonet, *Bull. Soc. chim.*, 1888, **50**, 355).*

Two other deductions may be drawn from the above formulation of these related reactions, and we have obtained experimental confirmation for both of them.

(1) The normal reaction of acid derivatives with aluminium chloride and benzene is only possible where an

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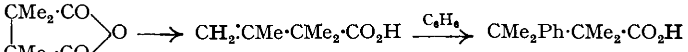
* The course of the final stage in (*B*) does not affect the arguments advanced in this paper, but the probable intermediate formation of a propiopropionyl chloride–ferric chloride complex in the formation of ketones from acid chlorides suggests an analogy with the Claisen reaction.

α-hydrogen atom is present, and in this case the aromatic nucleus will attach itself to the carbonyl group nearest to the one which is most ionised. This is again shown in that the sole product from trimethylsuccinic anhydride is β-*benzoyl*-αaβ-*trimethylpropionic acid* [β-*benzoyl*-αα-*dimethyl*-n-*butyric acid*], $COPh{\cdot}CHMe{\cdot}CMe_2{\cdot}CO_2H$ (VII). The structure assigned to this acid follows from its identity with the acid obtained by methylation of β-benzoyl-αα-dimethylpropionic acid, $COPh{\cdot}CH_2{\cdot}CMe_2{\cdot}CO_2H$ (VIII). This acid, m. p. 173° (Clemo and Dickenson; Desai and Wali), whose structure was not previously completely established, has now been directly compared with the isomeric β-benzoyl-ββ-dimethylpropionic acid, $COPh{\cdot}CMe_2{\cdot}CH_2{\cdot}CO_2H$ (IX), m. p. 101°, synthesised from sodio*iso*butyrophenone and ethyl iodoacetate (Haller and Ramart-Lucas, *Compt. rend.*, 1914, **159**, 143). Direct comparison of (VII) with β-benzoyl-αββ-trimethylpropionic acid, $COPh{\cdot}CMe_2{\cdot}CHMe{\cdot}CO_2H$, was not possible because the latter could not be prepared: attempted syntheses from sodio*iso*butyrophenone and methyl α-iodopropionate, or from (IX) by alkylation were both unsuccessful. On the other hand, alkylation of β-*benzoyl*-αβ-*dimethylpropionic acid* [β-*benzoyl*-α-*methyl*-n-*butyric acid*], $COPh{\cdot}CHMe{\cdot}CHMe{\cdot}CO_2H$, afforded (VII).

(2) As a corollary of (1), it should not be possible to obtain a ketone or a ketonic acid by the Friedel–Crafts reaction on the anhydrides or acid chlorides of tertiary acids. In these cases, the unsaturated acid first formed may be expected to condense with benzene to give β-phenyl derivatives. Experiments carried out both with tetramethylsuccinic and with trimethylacetic anhydride succeeded in illustrating this. A third experiment shows that the postulated intermediate compound (X) in (*A*) reacts in the expected manner.

When tetramethylsuccinic anhydride was condensed with benzene in the presence of aluminium chloride, carbon monoxide was immediately evolved in 60% yield in the cold. The main product (yield at least 70%) was β-*phenyl*-ααββ-*tetramethylpropionic acid* [β-*phenyl*-ααβ-*trimethyl*-n-*butyric acid*] (XI). The *methyl* ester was identical with that obtained when the methyl ester of (X) (Courtot, *Bull. Soc. chim.*, 1906, **35**, 298) was



$$CH_2{:}CMe{\cdot}CMe_2{\cdot}CO_2H \xrightarrow{C_6H_6} CMe_2Ph{\cdot}CMe_2{\cdot}CO_2H$$

(X.) (XI.)

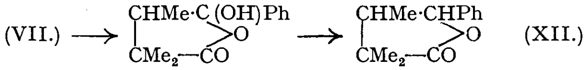
treated with benzene and aluminium chloride. Hydrolysis furnished the acid, identical with (XI). Though both β-*chloro*- and β-hydroxy-ααββ-tetramethylpropionic esters similarly yield (XI), its structure is not without ambiguity. The possible isomeric β-benzyl-ααβ-trimethylpropionic acid, $CH_2Ph{\cdot}CHMe{\cdot}CMe_2{\cdot}CO_2H$, has not been prepared and the independent synthesis of (XI) was found impracticable. The next lower homologue, methyl αα-dimethyl-β-methylenepropionate, $CH_2{:}CH{\cdot}CMe_2{\cdot}CO_2Me$, however, does afford an acid which is probably β-*phenyl*-ααβ-*trimethylpropionic acid* [β-*phenyl*-αα-*dimethyl*-n-*butyric acid*], $CHPhMe{\cdot}CMe_2{\cdot}CO_2H$, since its m. p. differs from that of β-benzyl-αα-dimethylpropionic acid obtained by the reduction of (VIII).

Exactly similar results to the foregoing were obtained with trimethylacetic anhydride: trimethylacetic acid, *tert.*-butylbenzene (yield, 55%), and carbon monoxide were isolated: $(CMe_3{\cdot}CO)_2O + C_6H_6 \longrightarrow CPhMe_3 + CMe_3{\cdot}CO_2H + CO$.

Whitmore's work was designed to obtain a suitable method for distinguishing tertiary from primary and secondary acids, but it would appear that the action of aluminium chloride on a benzene solution of the acid chloride or anhydride is a simpler test, since in all cases carbon monoxide is eliminated at room temperature and there is the added advantage that the use of phosphoric oxide is avoided.

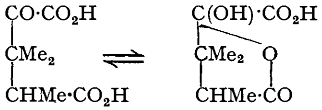
Two more points need elaborating. Attempts were made to synthesise the acid (IX) by a Friedel–Crafts reaction on the half ester chloride, $COCl{\cdot}CMe_2{\cdot}CH_2{\cdot}CO_2Me$, but only the isomeride (VIII) was isolated, although the corresponding methyl ketone, $COMe{\cdot}CMe_2{\cdot}CH_2{\cdot}CO_2Me$ has been prepared from this substance (Blanc, *Bull. Soc. chim.*, 1901, **25**, 68), but by the Grignard reaction. The acid (XI) is similarly the only product obtained from the half ester chloride of tetramethylsuccinic acid.

Both β-benzoyl-αα-dimethylpropionic acid (VIII) and its ester yield ketonic derivatives, and the former is reduced to β-benzyl-αα-dimethylpropionic acid. On the other hand, no ketonic reactions could be obtained

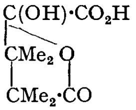


(VII.) (XII.)

from the methylated homologue (VII), and on reduction the lactone of γ-hydroxy-γ-phenyl-ααβ-trimethylbutyric acid (XII) was formed. Comparison with α-keto-ββγ-trimethylglutaric acid (XIII), which exists as a tautomeric mixture of the keto- and the keto-cyclol form (Kon, Stevenson, and Thorpe, J., 1922, **121**, 654;



(XIII.)



(XIV.)

Rothstein, Stevenson, and Thorpe, *ibid.*, 1925, **127**, 1073), and with α-keto-ββγγ-tetramethylglutaric acid (XIV), which is stable only in the keto-cyclol form (Rothstein and Shoppee, J., 1927, 531), suggests that the terminal methyl group has a greater influence in conferring stability on the ring structure than has the β-methyl group.

EXPERIMENTAL.

Derivatives of β-Benzoyl-αα-dimethylpropionic Acid (VIII).—The acid was prepared in 80% yield from *as*-dimethylsuccinic anhydride (17 g.), benzene (70 g.), and aluminium chloride (36 g.), and after decolorisation (charcoal) separated from ethyl acetate in prisms, m. p. 173° (Found: C, 69·6; H, 6·5. Calc.: C, 69·9; H, 6·8%). When titrated with potassium hydroxide it gave a sharp end-point with phenolphthalein and was reprecipitated by carbon dioxide. A solution of the acid in concentrated sulphuric acid was yellow, and on warming, the colour changed to orange, then dark blood-red. The 2 : 4-*dinitrophenylhydrazone* separated from absolute alcohol in yellow plates, m. p. 198—199° (Found: C, 55·5; H, 4·6; N, 14·4. $C_{18}H_{18}O_6N_4$ requires C, 55·9; H, 4·7; N, 14·5%). The *methyl* ester, b. p. 153°/7 mm., was prepared (i) in 85% yield by saturating a solution of the acid in twice the theoretical quantity of methyl alcohol with dry hydrogen chloride, or (ii) from the silver salt and methyl iodide; it separated from petrol (b. p. 60—80°) in plates, m. p. 46—47° (Found: C, 70·2; H, 6·9. $C_{13}H_{16}O_3$ requires C, 70·9; H, 7·3%), and furnished a 2 : 4-*dinitrophenylhydrazone* which crystallised from absolute alcohol in orange leaflets, m. p. 126° (Found: C, 56·6; H, 5·0; N, 13·6. $C_{19}H_{20}O_6N_4$ requires C, 57·0; H, 5·0; N, 14·0%).

Action of acetyl chloride. When the acid (VIII) was refluxed with excess of acetyl chloride, hydrogen chloride was evolved, and after removal of the solvent, the residual *γ-phenyl-αα-dimethyl-Δ^β-butyrolactone* was crystallised from petrol (b. p. 40—60°), and had m. p. 45° (Found: C, 76·0; H, 6·4. $C_{12}H_{12}O_2$ requires C, 76·6; H, 6·4%).

Reduction with hydriodic acid. The acid was reduced by refluxing it with excess of hydriodic acid (*d* 1·9) for 5 hours in glacial acetic acid containing a little red phosphorus. The β-benzyl-αα-dimethylpropionic acid so obtained had been previously prepared by Clemo and Dickenson (*loc. cit.*) by reduction with amalgamated zinc (Found: C, 75·0; H, 8·3. Calc.: C, 75·0; H, 8·3%).

Alkylation. Methyl β-benzoyl-αα-dimethylpropionate (5·6 g.) was added to a boiling solution of potassium (1·6 g.) in *tert.*-butyl alcohol. The mixture was boiled for a further 20 minutes, cooled somewhat, and methyl iodide (10 c.c.) added, the refluxing being continued until the solution was neutral. The product after isolation and hydrolysis with alcoholic potash afforded β-benzoyl-ααβ-trimethylpropionic acid (VII) in 80% yield. It was identical (m. p. and mixed m. p.) with that described below.

Derivatives of β-Benzoyl-αβ-dimethylpropionic Acid.—Aluminium chloride (70 g.) was gradually added to *trans*-αβ-dimethylsuccinic anhydride (43 g.) dissolved in dry benzene (250 c.c.). A fairly brisk reaction took place and the liquid boiled gently. After 15 hours, the mixture was warmed at 100° for a short time, decomposed with ice and sulphuric acid, and extracted with ether. The dried extract furnished *β-benzoyl-αβ-dimethylpropionic acid* [*β-benzoyl-α-methyl-*n*-butyric acid*], which crystallised from petrol (b. p. 60—80°) in needles, m. p. 78—79°; yield 59 g., 86% (Found: C, 69·3; H, 6·0. $C_{12}H_{14}O_3$ requires C, 69·9; H, 6·8%). This acid, unlike β-benzoyl-αα-dimethyl-, -ββ-dimethyl-, and -ααβ-trimethyl-propionic acids, (VIII), (IX), and (VII), respectively, decomposed cold sodium bicarbonate solution easily. Its *methyl* ester, b. p. 164°/14 mm., was obtained in 89% yield in the same way as the αα-dimethyl ester (Found: C, 71·0; H, 7·3. $C_{13}H_{16}O_3$ requires C, 70·9; H, 7·3%).

Alkylation. A solution of the methyl ester (17 g.) in *tert.*-butyl alcohol (45 c.c.) containing potassium (3·1 g.) was refluxed with excess methyl iodide. The resulting liquid was freed from precipitated potassium iodide by centrifuging, and fractionally distilled. Analysis showed that the methylated ester, b. p. 168°/16 mm., still contained traces of the alcohol (Found: C, 73·6; H, 7·5. Calc.: C, 71·8; H, 7·7%). It was hydrolysed by 4 hrs.' refluxing with twice the calculated quantity of alcoholic potash, the solvent distilled off, and the residue dissolved in water. After extraction of the neutral compounds with ether, the aqueous layer was acidified with 7N-sulphuric acid, and the liberated oil extracted with ether. The acid (yield, 68·5% overall) crystallised after isolation and was identical with the trimethyl acid (VII) above (Found: C, 70·5; H, 7·3. Calc.: C, 70·9; H, 7·3%). Further alkylation could not be achieved by the same method, nor was it possible to alkylate either the dimethyl or the trimethyl acid by the use of sodamide in benzene (Haller and Bauer, *loc. cit.*).

Derivatives of β-Benzoyl-ααβ-trimethylpropionic Acid (VII).—Trimethylsuccinic anhydride (47·3 g.) when condensed with benzene (235 c.c.) and aluminium chloride (85 g.) afforded *β-benzoyl-ααβ-trimethylpropionic acid* [*β-benzoyl-αα-dimethyl-*n*-butyric acid*] (VII) (or *γ-hydroxy-γ-phenyl-ααβ-trimethylbutyrolactone*) separating from ethyl acetate in clusters of needles, m. p. 135·6°. Yield, 55% (Found: C, 70·9; H, 7·2. $C_{13}H_{16}O_3$ requires C, 70·9; H, 7·3%). In a second experiment a crude yield of 85% was obtained from the anhydride mixed with twice its weight of aluminium chloride and five times its weight of benzene.

The substance was a weak acid and its potassium salt was decomposed by carbon dioxide. A yellow solution in concentrated sulphuric acid became orange on standing and a deep permanganate colour on gentle warming. When added to water, the product formed a blue solution and sulphur dioxide was evolved. The *methyl* ester (or *ether*) was obtained by the usual method in 89% yield; b. p. 151°/8 mm. (Found: C, 71·6; H, 7·9; $C_{14}H_{18}O_3$ requires C, 71·8; H, 7·7%). Neither the acid nor the ester yielded a ketonic derivative. The acid was converted into *γ-phenyl-ααβ-trimethyl-Δ^β-butyrolactone*, b. p. 145°/10 mm., when it was refluxed with excess of acetyl chloride (Found: C, 77·6; H, 6·8. $C_{13}H_{14}O_2$ requires C, 77·2; H, 6·9%). Reduction of the acid with hydriodic acid gave *γ-phenyl-ααβ-trimethylbutyrolactone* (XII), crystallising from petrol (b. p. 40—60°) in short needles, m. p. 71° (Found: C, 76·2; H, 7·8. $C_{13}H_{16}O_2$ requires C, 76·5; H, 7·8%).

Reaction between Tetramethylsuccinic Anhydride and Benzene.—The anhydride (20 g.) was dissolved in dry benzene contained in a flask connected to a gas-jar over water. Aluminium chloride (25 g.) was added gradually with shaking and ice-cooling, and after the liquid had remained at 0° for some time, the temperature was gradually raised to 100° and maintained there until the evolution of gas, which had been fairly brisk at the commencement of the reaction, had ceased. The product was decomposed by ice, the benzene distilled, and the residue treated with excess of hydrochloric acid. After filtration, the substance was dissolved in sodium hydroxide solution, and the small amount of neutral product (about 0·1 g. after crystallisation) filtered off. Acidification of the alkaline solution afforded *β-phenyl-ααββ-tetramethylpropionic acid* [*β-phenyl-ααβ-trimethyl-*n*-butyric acid*], (XI), which separated from alcohol or ethyl acetate in needles, m. p. 179°. Yield of recrystallised acid, 70% (Found: C, 75·6; H, 8·8. $C_{13}H_{18}O_2$ requires C, 75·7; H, 8·8%). The neutral *substance* crystallised from petrol (b. p. 60—80°) in long needles, m. p. 147—148° (Found: C, 81·7; H, 7·9. $C_{20}H_{22}O_2$ requires C, 81·6; H, 7·5%). Evidently it was a condensation product with two phenyl groups, but the quantity was too small for its structure to be determined. It crystallised unchanged, however, from boiling alcoholic potash and so was not an ester or a lactone.

The volume of gas collected in the above reaction was 2170 c.c. at N.T.P., and the presence of carbon monoxide was established (blue flame). A measured volume was washed with potassium hydroxide, bromine water, and potassium hydroxide again, then finally with water, and absorbed in ammoniacal cuprous chloride. The total volume of carbon monoxide at N.T.P. thus measured was 1727 c.c., *i.e.*, 60% of the amount derivable from one carboxyl group.

*β-*p*-Tolyl-ααββ-tetramethylpropionic* [*-ααβ-trimethyl-*n*-butyric*] *acid*, similarly obtained by use of toluene instead of benzene, crystallised from ethyl acetate in needles, m. p. 178° (Found: C, 76·3; H, 9·0. $C_{14}H_{20}O_2$ requires C, 76·4; H, 9·1%).

Like the potassium salts of the highly alkylated benzoylpropionic acids, potassium β-phenyl-ααββ-tetramethylpropionate is decomposed by carbon dioxide with precipitation of the original acid. The silver and the calcium salt can be obtained by addition of silver nitrate and calcium chloride respectively to solutions of the potassium salt. Dry distillation of the calcium salt yielded an unsaturated *hydrocarbon*, $C_{12}H_{16}$, b. p. 110° (Found : C, 90·4; H, 9·6. $C_{12}H_{16}$ requires C, 90·0; H, 10·0%). A second *hydrocarbon* with the same empirical formula but b. p. 154° is obtained when the phenyltetramethylpropionic acid is distilled from its mixture with soda–lime (Found : C, 89·8; H, 10·1; *M*, 133. $C_{12}H_{16}$ requires C, 90·0; H, 10·0%; *M*, 160). Bromine was rapidly absorbed by both these hydrocarbons, yielding exceedingly lachrymatory bromo-derivatives.

Methyl β-phenyl-ααββ-tetramethylpropionate [*β-phenyl-ααβ-trimethyl-*n*-butyrate*], b. p. 138°/12 mm., was prepared in nearly theoretical yield from the silver salt and methyl iodide. It had a characteristic camphoraceous odour and separated from petrol (b. p. 40—60°) in leafy plates, m. p. 24—25° (Found : C, 76·8; H, 9·4. $C_{14}H_{20}O_2$ requires C, 76·4; H, 9·1%).

β-Phenyl-ααββ-tetramethylpropionic [*β-Phenyl-ααβ-trimethyl-*n*-butyric*] *anhydride* resulted from boiling the acid with acetic anhydride. It separated from petrol (b. p. 60—80°) in small plates, m. p. 87° (Found : C, 79·6; H, 8·7; *M*, 366. $C_{26}H_{34}O_3$ requires, C, 79·2; H, 8·6%; *M*, 394). A *mononitro*-derivative of the acid was prepared by heating it with excess of concentrated nitric acid on the steam-bath for 6 hours and diluting the product with water. It crystallised from ethyl acetate–petrol (b. p. 60—80°) in faintly yellow needles, m. p. 232° (Found : C, 62·5; H, 6·6; N, 5·9; *M*, 281. $C_{13}H_{17}O_4N$ requires C, 62·2; H, 6·8; N, 5·6%; *M*, 251).

2 : 2 : 3 : 3-*Tetramethyl-α-hydrindone* was formed by dissolving the tetramethyl acid in concentrated sulphuric acid. There was a slight evolution of heat, and after warming the liquid for a few minutes, it was diluted with water and extracted with ether. This afforded in quantitative yield a highly refracting, mobile liquid, b. p. 142°/25 mm. (Found : C, 83·2; H, 8·6; *M*, 181. $C_{13}H_{16}O$ requires C, 83·0; H, 8·5%; *M*, 188). It was also obtained in small yield by the prolonged heating of the acid with concentrated hydriodic acid and red phosphorus. The tetramethylhydrindone has a camphoraceous odour and is very resistant to the attack of reagents; the usual ketonic reactions are absent, and when it was heated on the steam-bath for 3 days with concentrated nitric acid, the oily layer gradually disappeared and dilution with water yielded a *nitro*-2 : 2 : 3 : 3-*tetramethyl-α-hydrindone*, separating from petrol (b. p. 60—80°) in faint yellow needles, m. p. 130—131° (Found : C, 67·6; H, 6·1; N, 6·3; *M*, 239. $C_{13}H_{15}O_3N$ requires C, 67·0; H, 6·4; N, 6·0%; *M*, 233).

Preparation of β-Phenylpropionic Acid Derivatives.—*Methyl β-phenyl-ααβ-trimethylpropionate* [*β-phenyl-αα-dimethyl-*n*-butyrate*] was obtained in 65% yield by the action of benzene (25 c.c.) and aluminium chloride (7 g.) on methyl dimethylvinylacetate (5 g.) prepared by Courtot's method (*Bull. Soc. chim.*, 1906, **35**, 118). The impure ester had b. p. 124—126° (Found : C, 74·8; H, 8·7. $C_{13}H_{18}O_2$ requires C, 75·7; H, 8·8%). Hydrolysis with alcoholic potash yielded the *acid*, separating from petrol (b. p. 40—60°), in which it was extremely soluble, in plates, m. p. 54—57° (Found : C, 74·5; H, 8·7. $C_{12}H_{16}O_2$ requires C, 75·0; H, 8·3%). The acid did not react with sodium bicarbonate solution.

Preparation of β-Phenyl-ααββ-tetramethylpropionic Acid (XI) *from Methyl ααβ-Trimethyl-β-methylenepropionate* (*as* X).—The ester (10 g.), dissolved in dry benzene (50 c.c.), was mixed with aluminium chloride (13 g.), and the reaction completed by heating the dark solution for ½ hr. Decomposition with ice and sulphuric acid, followed by extraction with ether, afforded a 78·5% yield of methyl β-phenyl-ααββ-tetramethylpropionate identical (m. p. and mixed m. p.) with that obtained from tetramethylsuccinic anhydride. Hydrolysis yielded the acid (XI), m. p. 179°. Similarly, ethyl β-hydroxy- and β-chloro-ααββ-tetramethylpropionate both furnished *ethyl β-phenyl-ααββ-tetramethylpropionate* [*β-phenyl-ααββ-trimethyl-*n*-butyrate*], b. p. 138°/11 mm. (Found : C, 76·2; H, 9·2; *M*, 211. $C_{15}H_{22}O_2$ requires C, 76·9; H, 9·4%; *M*, 234). Hydrolysis gave the acid, m. p. 179° (Found : C, 75·4; H, 8·6%; *M*, 237. Calc. : *M*, 206).

The conversion of ethyl β-hydroxy-ααββ-tetramethylpropionate into the chloro-derivative was a matter of some difficulty since phosphorus halides and thionyl chloride led mainly to the dehydration product, but the following method was effective. The hydroxy-ester (15 g.) was mixed with an equivalent amount of pyridine and thionyl chloride (10·4 g.) added, and the crystalline mass so obtained kept overnight, mixed with water, and extracted with ether. The dried extract was repeatedly fractionally distilled. The lower-boiling fraction (3·4 g.) was mainly unsaturated ester, but this could not be entirely separated from the *chloro*-ester, b. p. 70—74°/8 mm.; yield, 6·8 g., 41% (Found : C, 56·8; H, 9·0; Cl, 17·2; *M*, 205. $C_9H_{17}O_2Cl$ requires C, 56·1; H, 8·8; Cl, 18·4%; *M*, 192·5).

Reaction between Trimethylacetic Anhydride, Benzene, and Aluminium Chloride.—The anhydride was best prepared (yield 80%) by heating equivalent quantities of the acid chloride and the fused potassium salt at 100°. The yield was slightly increased by use of the dried silver salt instead of the potassium one and by extracting the anhydride from the reaction mixture with petrol. Trimethylacetic anhydride (12 g.) was slowly added to a mixture of benzene (50 c.c.) and aluminium chloride (12 g.). Carbon monoxide was immediately liberated, followed appreciably later by hydrogen chloride. The reaction was completed on the steam-bath, and the products isolated in the usual way. Trimethylacetic acid (yield, 8 g., *i.e.*, 63·5% of the total recoverable acid) (Found : C, 58·8; H, 10·2. Calc. : C, 58·8; H, 9·8%) was removed from the mixture by extraction with sodium hydroxide, and the *tert.*-butylbenzene (b. p. 59—61°/14 mm.) extracted with ether; yield, 4·8 g., 55·5% (Found : C, 89·4; H, 10·6; *M*, 141. Calc. : C, 89·6; H, 10·4%; *M*, 134). In a second experiment, the volume of carbon monoxide at N.T.P. eliminated from trimethylacetic anhydride (4·9 g.), benzene (21 g.), and aluminium chloride (7 g.) was 499 c.c. = 84·5%.

Experiments with β-Benzoyl-ββ-dimethylpropionic Acid (IX).—This acid, prepared from the ethyl ester (obtained in 21% yield from *iso*butyrophenone, sodamide, and ethyl iodoacetate), did not crystallise well and was therefore converted into its *methyl* ester (b. p. 131—143°/8 mm.) by saturating its solution in methyl alcohol with hydrogen chloride (Found : C, 70·4; H, 7·5. $C_{13}H_{16}O_3$ requires C, 70·9; H, 7·3%). Hydrolysis of this afforded the crystalline acid, m. p. 100—102° (Found : C, 69·5; H, 6·4. Calc. : C, 69·9; H, 6·8%). The m. p. was depressed when it was mixed with the isomeric β-benzoyl-αα-dimethylpropionic acid (VIII). It was recovered unchanged when its methyl ester was refluxed with potassium *tert.*-butoxide and excess of methyl iodide.

Attempted Synthesis of β-Benzoyl-αββ-trimethylpropionic Acid.—The following condensations were unsuccessful, in most cases the original reactants being recovered unchanged : bromo*iso*butyrophenone with ethyl methylsodiomalonate or with ethyl sodiocyanoacetate; sodio*iso*butyrophenone (prepared in benzene, by use of sodamide) or the potassio-compound (from potassium *tert.*-butoxide) with ethyl bromomalonate. The product of the reaction between ethyl α-iodopropionate and potassio*iso*butyrophenone was an ester of indeterminate b. p.; the acid obtained by hydrolysis did not crystallise and was therefore re-esterified with methyl alcohol. The resulting *methyl* ester, b. p. 95°/0·3 mm. (Found : C, 71·7; H, 7·8. $C_{14}H_{18}O_3$ requires C, 71·8; H, 7·7%), was possibly the required product, but a non-crystalline acid was again formed from it.

Most of the analyses were carried out by Drs. G. Weiler and F. B. Strauss of Oxford.

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[*Received, May 28th*, 1943.]