71. *Experiments on the Synthesis of Carbonyl Compounds. Part II. A General Synthesis of Saturated Ketones,* R·CO·CH$_2$R′.

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The benzyl esters of acylmalonic acids (II) undergo hydrogenolysis with the formation of the parent keto-acids, which readily lose two molecules of carbon dioxide to give the corresponding ketones, R·CO·CH$_2$R′. The reaction appears to be of general application subject only to the absence of reducible substituents. A preliminary account of this work has already been published (*Nature*, 1948, **162**, 111).

In the preceding paper a method of converting acylmalonic esters, R·CO·CH(CO$_2$Et)$_2$, into the ketones R·CO·CH$_3$ by acidolysis was described. Failure to extend this reaction to the fully substituted compounds R·CO·CR(CO$_2$Et)$_2$ demonstrated the need of an entirely new approach to the problem. The hydrogenolytic fission of benzyl esters appeared to offer an alternative method of developing a general ketone synthesis as follows :

$$\mathrm{CH_2(CO_2{\cdot}CH_2Ph)_2} \longrightarrow \mathrm{R'{\cdot}CH(CO_2{\cdot}CH_2Ph)_2} \longrightarrow \underset{\text{(I.)}}{\mathrm{R'{\cdot}CNa(CO_2{\cdot}CH_2Ph)_2}} \xrightarrow{\mathrm{R{\cdot}COCl}}$$

$$\mathrm{R{\cdot}CO{\cdot}CR'(CO_2{\cdot}CH_2Ph)_2} \xrightarrow{\mathrm{H_2\text{-}Pd}} \mathrm{R{\cdot}CO{\cdot}CR'(CO_2H)_2} \longrightarrow \mathrm{R{\cdot}CO{\cdot}CH_2R'} + 2\mathrm{CO_2}$$

A critical examination of this route served to emphasise the difficulties likely to be encountered in the first stage of the synthesis owing, in particular, to the high boiling points (*e.g.*, benzyl malonate boils at *ca.* 170°/0·5 mm.) and low crystallising powers associated with benzyl esters in general : furthermore, there was also the possibility of some hydrogenolysis of the benzyl groups during the second stage of the process. Consideration of the possibilities involved, however, suggested that these difficulties might be avoided by forming the sodio-benzyl ester (I) *in situ* from the corresponding ethyl ester by ester interchange with benzyl alcohol in benzene solution, the sodium enol acting as catalyst for the interchange and the reaction being forced to completion by removal of the ethanol formed as its azeotrope with benzene. The next stages in the procedure would then consist of coupling of the sodio-derivative (I) with the requisite acid chloride, catalytic debenzylation of the resulting keto-ester (II), and finally thermal decarboxylation of the acid (III) to the ketone (IV):

$$\text{(I)} + \text{R·COCl} \longrightarrow \underset{\text{(II.)}}{\text{R·CO·CR}'(\text{CO}_2\text{·CH}_2\text{Ph})_2} \xrightarrow{4\text{H}} \underset{\text{(III.)}}{\text{R·CO·CR}'(\text{CO}_2\text{H})_2} \longrightarrow \underset{\text{(IV.)}}{\text{R·CO·CH}_2\text{R}'}$$

This idea was first put to test using ethyl ethane-1 : 1 : 2-tricarboxylate (I; $R' = CH_2{\cdot}CO_2Et$) which was converted into its sodio-derivative in benzene in the usual manner and treated with benzyl alcohol (3 mols.). Ester interchange was found to proceed readily as shown by the elimination of ethanol which was obtained (as azeotrope with benzene) with the aid of a fractionating column in almost theoretical yield. The resulting tribenzyl sodio-ester (I; $R' = CH_2{\cdot}CO_2{\cdot}CH_2Ph$) was then coupled with undecanoyl chloride, and the crude keto-ester (II; $R = n\text{-}C_{10}H_{21}$, $R' = CH_2{\cdot}CO_2{\cdot}CH_2Ph$) submitted to catalytic debenzylation using palladised charcoal at atmospheric pressure and temperature in ethanolic solution. Considerable difficulties were encountered at this stage owing to catalyst poisoning, but eventually most of the required hydrogen was absorbed. Decarboxylation of the product proceeded smoothly at, or just below, the boiling point of the solvent (ethanol), the expected product, 4-ketotetradecanoic acid * (IV; $R = C_{10}H_{21}$, $R' = CH_2{\cdot}CO_2H$) being obtained in 66% yield.

At this stage of the work, attention was focussed on the purely practical aspects of the problem, namely, the purification of commercial benzyl alcohol and the finding of more effective catalysts. Initially, debenzylations were carried out in alcohol with palladised charcoal (iron-free) as catalyst; later mixtures of the latter and palladised strontium carbonate were used. More recently (unpublished results) the use of palladised strontium carbonate (10% of Pd) in ethyl acetate has been found to be most effective and is now the preferred procedure. As the result of these and subsequent experiments a general technique has been evolved and is described in full in the Experimental section.

By use of this technique, *n*-octanoyl chloride and *n*-octylmalonic ester yielded *heptadecan-8-one* (IV; $R = C_7H_{15}$, $R' = C_8H_{17}$) (91%) which was characterised as the substituted *hydantoin* (Henze, *J. Amer. Chem. Soc.*, 1942, **64**, 522), and similarly *2-methylpentadecan-5-one* [IV; $R = C_{10}H_{21}$, $R' = (CH_3)_2CH{\cdot}CH_2{\cdot}CH_2$] (80%) was obtained as an oil which resisted our attempts at characterisation.

Sebacoyl chloride and *n*-octylmalonic ester (2 mols.) furnished *octacosane-10 : 19-dione* (V) in 78% yield, characterised as the *dioxime* and by reduction (Huang-Minlon, *J. Amer. Chem. Soc.*, 1946, **68**, 2487) to the saturated paraffin, *n*-octacosane, together with the product of partial reaction, the known 10-ketononadecanoic acid (VI).

(V.) $C_9H_{19}{\cdot}CO{\cdot}[CH_2]_8{\cdot}CO{\cdot}C_9H_{19}$

$C_9H_{19}{\cdot}CO{\cdot}[CH_2]_8{\cdot}CO_2H$ (VI.)

(VIII.) $C_4H_9{\cdot}CHEt{\cdot}CO{\cdot}[CH_2]_{11}{\cdot}CO_2H$

$OH{\cdot}CHPh{\cdot}CO{\cdot}C_{13}H_{27}$ (IX.)

The failure of the G. M. Robinson ketone synthesis (*J.*, 1930, 745) when applied to the preparation of α-substituted ketones (*Ann. Reports*, 1939, **36**, 300), and the low yields encountered in the use of the cadmium di-*sec.*-alkyls (Cason, *J. Amer. Chem. Soc.*, 1946, **68**, 2078), made it of interest to determine whether any such steric factors would operate in the debenzylation reaction. Accordingly 2-ethylhexanoyl chloride was condensed with benzyl sodioundecane-1 : 1 : 11-tricarboxylate, and the product debenzylated and decarboxylated to yield *13-keto-14-ethyloctadecanoic acid* (VIII) in 78% yield (crude); this acid was purified through its *ethyl* ester and characterised as the p-*phenylphenacyl* ester.

Attention was next turned to the synthesis of ketones containing groups other than alkyl or carboxy-groups. ω-Hydroxyundecanoic acid was converted by successive treatment with acetyl chloride and oxalyl chloride into the ω-acetoxy-acid chloride which, without isolation, was coupled with benzyl sodio-*n*-octylmalonate (I; $R' = C_8H_{17}$) and furnished in the same manner *11-ketoeicosanol*, $C_9H_{19}{\cdot}CO{\cdot}[CH_2]_{10}{\cdot}OH$, characterised as the *oxime* and by reduction (Clemmensen) to the known eicosanol. Acetylmandeloyl chloride and benzyl sodio-*n*-dodecylmalonate gave, by the general procedure, *1-hydroxy-1-phenylpentadecan-2-one* (IX) in 65% yield. (IX) was characterised by oxidation with chromic acid (cf. Prelog, Frenkiel, Kobelt, and Barman, *Helv. Chim. Acta*, 1947, **30**, 1741) to the *diketone* and by reaction of the latter with *o*-phenylenediamine to give a *quinoxaline*.

Finally, as an example in the aromatic series, *m*-anisoyl chloride and benzyl sodioethane-1 : 1 : 2-tricarboxylate were condensed, and the product debenzylated and decarboxylated to yield the known γ-keto-γ-*m*-methoxyphenylbutyric acid. The investigation is being continued.

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* Geneva nomenclature is used throughout this paper.

EXPERIMENTAL.

Apparatus.—All-glass apparatus fitted with ground-glass joints lubricated with silicone grease was used. The fractionating column used in the ester interchanges contained a packed section (40 × 1·8 cm.) of single-turn glass helices (Fenske) and was fitted with a total condensation–partial take-off head of the Whitmore–Lux pattern.

Reagents.—Benzene. The benzene used in these experiments was commercial AnalaR benzene which had been stored over sodium wire.

Benzyl alcohol. Commercial " pure " benzyl alcohol was mixed with Raney nickel (5% w/w) and the mixture heated on the steam-bath for 3 hours with occasional agitation. After cooling, the alcohol was decanted from the bulk of the metal and distilled under reduced pressure. The distillate usually contained benzaldehyde which was separated by careful fractionation under reduced pressure in an atmosphere of nitrogen or by oximation followed by distillation.

Palladium–charcoal catalyst. The catalyst was prepared in the manner described in *Org. Synth.*, 1946, **26**, 78 (catalyst D), with two modifications. First, the iron was removed from the charcoal with 6N-hydrochloric acid and, secondly, hydrogen was thoroughly removed by evacuation from the reduction mixture *at the final stage* of preparation before air was admitted. This procedure allows drying of the catalyst at 120° without ignition.

Palladised strontium carbonate (ca. 10% of Pd). Palladous chloride (8·9 g.) was dissolved in AnalaR concentrated hydrochloric acid (21 ml.) at the b. p., and the solution, after dilution with water (400 ml.), added with vigorous stirring to a suspension of strontium carbonate (" precipitated "; 70 g.) in water (500 ml.) during 5 minutes. The temperature of the stirred mixture was then raised to 80° during 15 minutes, and the solid allowed to settle. The supernatant liquid was removed by syphoning and washing (5 l.) carried out in the same manner. The catalyst was then removed by filtration, dried at 120°, and finely powdered.

Acid chlorides. Unless otherwise specified, acid chlorides were prepared in the usual manner from the acid and thionyl chloride, except that a considerable amount of first runnings was rejected to avoid contamination with sulphur-containing substances.

General Methods.—Preparation of benzyl sodiomalonates. The requisite ethyl sodiomalonates were prepared by two methods. (*a*) The ethyl malonate in benzene solution was added in the usual manner to sodium which had been powdered under pure toluene or xylene, the solvent decanted, and the residue washed several times with AnalaR benzene. (*b*) Clean sodium (1 mol.) was dissolved in magnesium-dried ethanol (20 × wt. of sodium), and the solution distilled from a flask fitted with tap-funnel (guard-tube) and condenser leading to a Kon rectangle, in an oil-bath heated to 190°. When most of the ethanol had distilled off and a slight crust had formed on the surface of the residue, the pressure in the flask was rapidly lowered, resulting in the rapid removal of solvent and the production of a solid foam of sodium ethoxide. The oil-bath was then removed and the ethoxide allowed to cool *in vacuo*. The system was closed by means of the appropriate taps and the malonic ester (1 mol.) in benzene solution added from the tap-funnel. Formation of the sodium enol was immediate as shown by dissolution of the sodium ethoxide; air was then admitted through the guard-tube. Benzyl alcohol (1 mol. per carbalkoxy-group in the malonic ester) was added to the foregoing solution, and the mixture distilled through the fractionating column already described, under a reflux-ratio of about 5 : 1 so that the temperature did not rise above 69°/760 mm. The distillation of benzene–ethanol azeotrope was rapid at first but gradually slowed down towards the end of the interchange when distillation was carried out under a higher reflux-ratio (20 : 1) at about 1—3 drops per minute, the temperature gradually rising to *ca.* 79°. At this stage the interchange was considered complete, and the residue which consisted of a benzene solution of benzyl sodiomalonate was allowed to cool.

Method (*a*) was used in the preliminary experiments as it allowed the interchange to be followed quantitatively but later, when this was found to be substantially complete under the conditions employed, the second method was always used since, in practice, it was more convenient and furnished a cleaner product.

Benzyl acylmalonates. The acid chloride (0·98 mol.) in benzene solution was added to the benzene solution of the benzyl sodiomalonate (1 mol.), with stirring or shaking, during a few minutes, and the mixture refluxed for a further 30 minutes. The cooled reaction mixture was then added to ice-water containing a trace of sulphuric acid, and the organic layer separated. The aqueous layer was extracted with fresh benzene and the combined benzene extracts washed with water and dried (Na_2SO_4). Removal of solvent was carried out at room temperature under reduced pressure until all water had distilled off, and was finally completed at 100°/0·5 mm. The products were yellow or yellow-brown viscous oils.

Debenzylation and decarboxylation of benzyl acylmalonates. The foregoing product (0·5 mol.) was dissolved in absolute ethanol or a mixture of ethanol and ethyl acetate (solvent volume, *ca.* 200 ml.), and stirred in an atmosphere of hydrogen in the presence of palladised charcoal (10% of Pd; 4 g.) until absorption became slow owing to poisoning of the catalyst (frequently 1 l. taken up). At this stage the catalyst was either removed by filtration and fresh charcoal catalyst added, or palladised strontium carbonate (10% of Pd; 5 g.) was added to the hydrogenation mixture, and the hydrogenation continued. If the first procedure was adopted, it was sometimes necessary to repeat the process, rates of up to 200 ml. per minute being realised; with the second method somewhat slower rates (*e.g.*, 60 ml. per minute) of hydrogen absorption occurred. The temperature of the reaction mixture was kept below 30° by external cooling. Furthermore, it was found on occasions that the hydrogenation became slow owing to premature decarboxylation, and accordingly the flask was evacuated and refilled with fresh hydrogen before the addition of fresh catalyst. When the hydrogenation was complete, the catalyst was removed by filtration, and the filtrate raised to the b. p. under a reflux condenser, whereupon brisk evolution of carbon dioxide took place. On completion of this stage (30 minutes), the solvent was distilled off and the product isolated.

4-*Ketotetradecanoic Acid.*—Undecanoyl chloride (b. p. 95°/2 mm.; 25·1 g., 0·122 mol.) was treated with the sodium enol of benzyl ethane-1 : 1 : 2-tricarboxylate (0·125 mol.) prepared from the ethyl ester (30·75 g., 0·125 mol.), sodium (2·9 g., 0·125 mol.) and benzyl alcohol (40·5 g., 0·375 mol.), and the product debenzylated and decarboxylated as described above. The product, after removal of solvent, was a semi-solid mass which was triturated with cold toluene (50 ml.). The solid (14 g.) was removed and the filtrate evaporated in an oil-bath at 170° to remove solvent and to decarboxylate any free ethanetricarboxylic acid. When cold, the residue was dissolved in ethyl acetate (100 ml.), and the solution washed with water and evaporated to dryness. Trituration of the residue with cold light petroleum (b. p. 40—60°) containing benzene (1%) furnished a further crop (6 g.). In this manner the total yield of crude keto-acid, m. p. 84—85°, was 20 g. (66%). The acid separated from benzene–light petroleum (b. p. 60—80°) in colourless plates, m. p. 87°; Robinson and Robinson (*J.*, 1926, 2206) give m. p. 87°. The oxime separated from light petroleum (b. p. 60—80°)-benzene (trace) in prisms, m. p. 74°, as described by the same authors.

Heptadecan-8-*one*.—The reactants were *n*-octoyl chloride (b. p. 81—82°/16 mm.; 19·9 g., 0·122 mol.) and benzyl sodio-*n*-octylmalonate (ethyl ester; 34 g., 0·125 mol.). The product was dissolved in light petroleum (b. p. 40—60°; 100 ml.) containing benzene (30 ml.), and the mixture treated with 2N-sodium hydroxide until alkaline. The organic layer was separated and the aqueous layer extracted again (2 × 50 ml. of same solvent mixture). The bulked extracts were washed with water and dried (Na_2SO_4), and the solvent removed by distillation, eventually, at 100°/0·2 mm. (to constant weight). The product readily solidified on cooling and was substantially pure *ketone* (28·2 g., 91%), m. p. 39—41°. It crystallised readily from methanol in colourless plates, m. p. 42° (Found: C, 80·4; H, 13·4. $C_{17}H_{34}O$ requires C, 80·3; H, 13·4%). The derived *hydantoin* (Henze, *loc. cit.*) separated from methanol in colourless tablets, m. p. 123° (Found : N, 8·3. $C_{19}H_{36}O_2N_2$ requires N, 8·6%).

2-*Methylpentadecan*-5-*one*.—The *ketone* was obtained in the same manner as in the previous experiment, from undecanoyl chloride (25·1 g., 0·122 mol.) and benzyl sodio*iso*butylmalonate, as a colourless oil, b. p. 134—136°/2 mm., m. p. 9—10°, n_D^{20} 1·4408 (23·4 g., 80%) (Found : C, 79·7; H, 13·2. $C_{16}H_{32}O$ requires C, 80·0; H, 13·3%). Attempts to prepare crystalline derivatives failed.

Octacosane-10 : 19-*dione*.—Sebacoyl chloride (b. p. 140°/1 mm.; 15 g., 0·062 mol.) was caused to react with benzyl sodio-*n*-octylmalonate (0·125 mol.) prepared as previously, and the product debenzylated and decarboxylated in the usual manner in ethanol–ethyl acetate solution (100 ml. : 50 ml.). The solution obtained after decarboxylation, furnished, on cooling, 15 g. of the ketone. Concentration of the filtrate to 25 ml. furnished a second crop (5·5 g.), the total yield of crude material, m. p. 92—94°, being 78%. *Octacosane*-10 : 19-*dione* separated from methanol as colourless plates, m. p. 95° (Found : C, 79·2; H, 12·6. $C_{28}H_{54}O_2$ requires C, 79·6; H, 12·8%). The *dioxime* crystallised from ethyl acetate in colourless prisms which melted at 68°, resolidified, and finally remelted at 78° (Found : N, 6·3. $C_{28}H_{56}O_2N_2$ requires N, 6·2%). A sample of the ketone was subjected to the modified Wolff–Kishner reduction (Huang-Minlon, *loc. cit.*), to give *n*-octacosane, colourless plates (from ethanol), m. p. 64° (lit., 64—65°).

The filtrate from the second crop of ketone was diluted with water (5 ml.) and neutralised hot with sodium hydroxide (4N.); on cooling, the sodium salt of the keto-acid separated (2·7 g.). The free acid, 10-ketononadecoic acid, obtained in the usual manner, crystallised from light petroleum (b. p. 80—100°) in colourless plates, m. p. 86—87°. Robinson and Robinson (*loc. cit.*) gave m. p. 86—87°. The oily oxime was treated with sulphuric acid to give the derived amide, m. p. 83°.

13-*Keto*-14-*ethyloctadecanoic Acid*.—A sample of 2-ethylhexanoic acid (Messrs. British Industrial Solvents, Ltd.) was converted into its acid chloride (b. p. 76°/20 mm.), and the latter (16·0 g., 0·098 mol.) treated with benzyl sodioundecane-1 : 1 : 11-tricarboxylate (0·1 mol.). The oily product obtained in the usual manner was refluxed with acetic acid (50 ml.) containing sulphuric acid (2 ml.; 20N.) for 30 minutes to decompose any keto-ester present. After dilution with water, the mixture was steam-distilled until free from steam-volatile materials, and the residual oil isolated with ether. The residue was extracted with light petroleum (b. p. 40—60°; 400 ml.) at 0°. Evaporation of the light petroleum extract furnished the crude keto-acid (25·5 g., 78%) which was substantially pure since it was solid at room temperature (22°). A sample (10 g.) was purified by conversion into its *ethyl* ester (by azeotropic esterification), which distilled as a colourless oil, b. p. 186—192°/0·2 mm., n_D^{20} 1·4480 (Found : C, 74·0; H, 11·6. $C_{22}H_{42}O_3$ requires C, 74·6; H, 11·9%).

The ester was hydrolysed with boiling aqueous-alcoholic sodium hydroxide (N.), and the free *keto-acid* isolated as a colourless oil, b. p. 203—204°/0·3 mm., m. p. 24—25·5° (thermometer in liquid; faintly cloudy melt), n_D^{25} 1·4580 (Found : C, 73·4; H, 11·7. $C_{20}H_{38}O_3$ requires C, 73·6; H, 11·7%). It formed a p-*phenylphenacyl* ester which separated from moist ethanol (norite) at 0° in interlocking colourless needles, m. p. 43° (Found : C, 78·2; H, 9·1. $C_{35}H_{50}O_4$ requires C, 78·6; H, 9·4%).

11-*Ketoeicosanol*.—11-Hydroxyundecanoic acid (24·8 g., 0·122 mol.) was dissolved in dry AnalaR benzene (50 ml.), and acetyl chloride (13 ml.) added during 10 minutes. The solution was then refluxed for a further 10 minutes, and the solvent and excess reagent were removed by distillation under reduced pressure. The residual acetoxy-acid was dissolved in fresh, dry AnalaR benzene (50 ml.), and oxalyl chloride (45 g., 0·35 mol.) added. After the vigorous reaction had subsided, the mixture was refluxed on the steam-bath for 0·5 hour, and solvent and unchanged chloride removed by distillation under reduced pressure, eventually at 90°/0·5 mm. The yield of crude acetoxyundecanoyl chloride was 33·0 g. (calc., 32·2 g.). The chloride in benzene solution was brought into reaction with benzyl sodio-*n*-octylmalonate (0·125 mol.), and the reaction product isolated as described for heptadecan-8-one. The product remaining after evaporation of the solvent was hydrolysed with boiling alcoholic potassium hydroxide (N.; 100% excess) and isolated by dilution with water. 11-*Ketoeicosanol* was thus obtained as a white solid (22·9 g., 60%), m. p. 74—76°, which crystallised from ethanol and then light petroleum (b. p. 60—80°) in interlocking needles, m. p. 77° (Found : C, 76·8; H, 12·6. $C_{20}H_{40}O_2$ requires C, 76·9; H, 12·8%). It was characterised as the *oxime* which separated from benzene–light petroleum (b. p. 40—60°) at 0° in slender needles, m. p. 38—38·5° (Found : N, 4·4. $C_{20}H_{41}O_2N$ requires N, 4·3%), and by Clemmensen reduction in the usual manner to *n*-eicosanol, prisms (from methanol), m. p. 64—65° (Levene and Taylor, *J. Biol. Chem.*, 1924, **59**, 915, reported m. p. 65—65·5°).

1-*Hydroxy*-1-*phenylpentadecan*-2-*one*.—Acetylmandelyl chloride (34·8 g., 0·163 mol.) was condensed with benzyl sodio-*n*-dodecylmalonate (0·167 mol.) as before. The residue obtained after decarboxylation and removal of solvent was dissolved in light petroleum (b. p. 40—60°)–ethyl acetate (1 : 1), and the mixture made alkaline with aqueous sodium hydroxide. Considerable difficulty in separation of the phases owing to emulsification was encountered, but eventually the extraction was completed. The combined organic extracts (500 ml.) were washed with water, and the solvent was removed by distillation. The residue was gently warmed with aqueous alcoholic sodium hydroxide (N.; 0·16 mol.) for 15 minutes, and the product isolated by dilution with water. The crude *acyloin* (35 g., 65%), m. p. 50—53°, was slightly yellow, owing presumably to the presence of the corresponding diketone. It was crystallised several times from methanol and then light petroleum (b. p. 40—60°), whence it separated as tiny colourless prisms, m. p. 60° (Found: C, 78·8; H, 10·9. $C_{21}H_{34}O_2$ requires C, 79·2; H, 10·7%).

The acyloin (1·5 g.) in acetic acid (20 ml.) containing sulphuric acid (2 ml. of 20N.) was treated dropwise at room temperature with chromic acid (10N.) until the solution assumed a permanent orange-red colour. Dilution with water afforded the product as a yellow oil which readily solidified. Crystallisation from methanol at 0° and then from light petroleum (b. p. 40—60°) furnished the *diketone* as yellow plates, m. p. 52—53° (Found: C, 79·3; H, 10·4. $C_{21}H_{32}O_2$ requires C, 79·6; H, 10·2%). The diketone (1·58 g., 0·05 mol.) and *o*-phenylenediamine (0·54 g., 0·05 mol.) were refluxed in methanolic solution (10 ml.) for 5 minutes. The solution, on cooling, deposited the *quinoxaline* (0·9 g.), m. p. 62°, which separated from methanol (norite) in colourless felted needles, m. p. 62—63° (Found: N, 7·2. $C_{27}H_{36}N_2$ requires N, 7·8%).

γ-*Keto*-γ-m-*methoxyphenylbutyric Acid*.—*m*-Anisoyl chloride (b. p. 96—97°/3 mm.; 16·3 g., 0·095 mol.) was treated with benzyl sodioethane-1 : 1 : 2-tricarboxylate (0·1 mol.) in the usual manner. The product, after debenzylation, decarboxylation, and removal of solvent, was boiled with sodium hydroxide (200 ml.; 2N.) for 30 minutes and the cooled solution acidified with excess of sulphuric acid (20N.). The acid (16·35 g., 83%; m. p. 100—102°) crystallised from aqueous alcohol (norite) in long needles, m. p. 110°. The semicarbazone separated slowly from its reaction mixture (aqueous-alcoholic solution) in needles, m. p. 177°. Thompson (*J.*, 1932, 2314) gave m. p. 111° and 177° respectively for the keto-acid and its semicarbazone.

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