

*$\beta$ -Aroylpropionic Acids. Part V.\* The Synthesis of  $\beta$ -Aroyl- $\alpha$ -methylpropionic Acids, and their Conversion into Polynuclear Compounds.*

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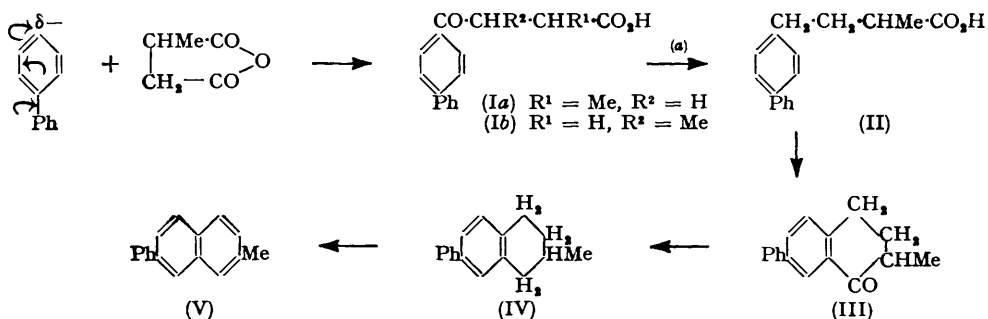
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4 : 4'- and 2 : 2'-Dimethoxydiphenyl condense with succinic anhydride in presence of aluminium chloride to give  $\beta$ -2-methoxy-5-*p*-methoxyphenyl- and  $\beta$ -4-methoxy-3-*o*-methoxyphenyl-benzoylpropionic acid, respectively. Condensation of diphenyl and the above derivatives with methylsuccinic anhydride gives two products in each case,  $\text{Ar}\cdot\text{CO}\cdot\text{CH}_2\cdot\text{CHMe}\cdot\text{CO}_2\text{H}$  and  $\text{Ar}\cdot\text{CO}\cdot\text{CHMe}\cdot\text{CH}_2\cdot\text{CO}_2\text{H}$ . Two acids of the former type are cyclised to naphthalene derivatives. 4-Methoxydiphenyl gives four products, two of each type.

Fluorene gives similarly a product of each type, and the  $\alpha$ -methyl acid is converted into 3'-methyl-2 : 3-benzofluorene.

SEVERAL investigators have reported that condensed polynuclear compounds such as naphthalene (Haworth, *J.*, 1932, 1125), phenanthrene (Cook and Haslewood, *J.*, 1934, 428; Bergmann and Blum-Bergmann, *J. Amer. Chem. Soc.*, 1937, 59, 1573),  $\alpha$ - and  $\beta$ -methyl-naphthalene (Haworth, Melvin, and Sheldrick, *J.*, 1934, 454; and Haworth and Bolam, *J.*, 1932, 2248, respectively), and some phenolic ethers such as anisole and *o*-, *m*-, and *p*-tolyl methyl ether, condense with methylsuccinic anhydride in presence of aluminium chloride to give only the  $\beta$ -aroyl- $\alpha$ -methylpropionic acid. We have studied in this investigation whether this is true for diphenyl and some of its derivatives and fluorene. The products were always mixtures of the  $\alpha$ - and the  $\beta$ -methyl acid,  $\text{Ar}\cdot\text{CO}\cdot\text{CH}_2\cdot\text{CHMe}\cdot\text{CO}_2\text{H}$  and  $\text{Ar}\cdot\text{CO}\cdot\text{CHMe}\cdot\text{CH}_2\cdot\text{CO}_2\text{H}$ , in which the former predominated. The structures of the  $\alpha$ -methyl acids were deduced from the facts that they were the less soluble isomers (*Org. Reactions*, 1949, 5, 243) and with an alcoholic solution of salicylaldehyde and dry hydrogen chloride gave precipitates of the coloured pyrylium derivatives (cf. Mitter and De, *J. Indian Chem. Soc.*, 1939, 16, 199; Desai and Wali, *Proc. Indian Acad. Sci.*, 1937, 6, A, 135). The other isomers failed to give this reaction.

Thus, diphenyl and methylsuccinic anhydride in nitrobenzene gave a mixture of the acids (Ia and b) in the ratio of 12 : 1. The yield of the latter acid increased when nitrobenzene was replaced by *s*-tetrachloroethane. The position of attack on the diphenyl nucleus was elucidated by oxidising both acids to diphenyl-4-carboxylic acid.

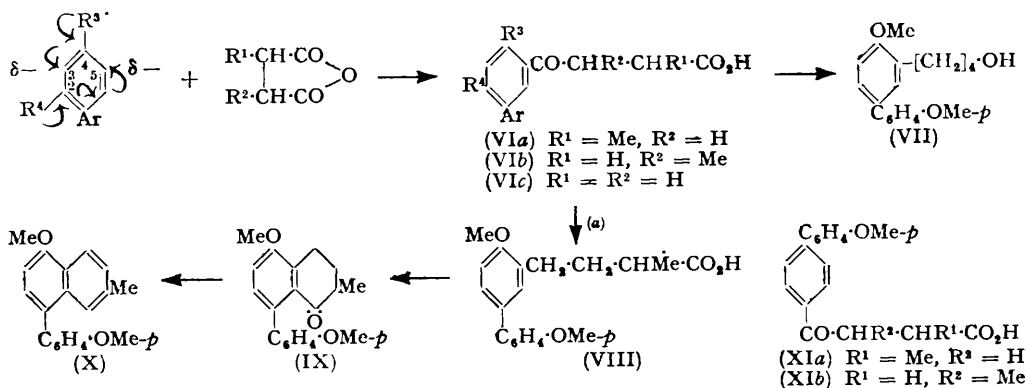


The  $\alpha$ -methyl-keto-acid (Ia) was reduced by Clemmensen's method to the butyric acid (II), which was cyclised with phosphoric oxide to the tetralone (III). This was reduced by lithium aluminium hydride to the tetralin (IV), which was dehydrogenated with selenium to 2-methyl-7-phenylnaphthalene (V).

4 : 4'- and 2 : 2'-Dimethoxydiphenyl condensed with succinic anhydride to give the acids (VIc;  $\text{Ar} = p\text{-MeO}\cdot\text{C}_6\text{H}_4$ ,  $\text{R}^3 = \text{OMe}$ ,  $\text{R}^4 = \text{H}$ ) and (VIc;  $\text{Ar} = o\text{-MeO}\cdot\text{C}_6\text{H}_4$ ,  $\text{R}^3 = \text{H}$ ,

$R^4 = \text{OMe}$ ), respectively, which were oxidised to 2-methoxy-5-*p*-methoxy- and 4-methoxy-3-*o*-methoxy-phenylbenzoic acid, respectively. Authentic specimens of the benzoic acids were prepared by condensing methyl 5-bromo-2-methoxybenzoate with *p*-iodoanisole and methyl 3-iodo-4-methoxybenzoate with *o*-iodoanisole in presence of copper bronze. This showed that electrophilic substitution in the 4 : 4'- and 2 : 2'-dimethoxydiphenyl molecules takes place at positions 3 and 5, respectively.

Attempted reduction of the acid (VIc; Ar = *p*-MeO-C<sub>6</sub>H<sub>4</sub>, R<sup>3</sup> = MeO, R<sup>4</sup> = H) by the Clemmensen method or its modifications was unsuccessful. Its reduction with excess of lithium aluminium hydride gave the butanol (VII), which gave a resin on attempted cyclisation with phosphoric oxide. With methylsuccinic anhydride 4 : 4'-dimethoxydi-



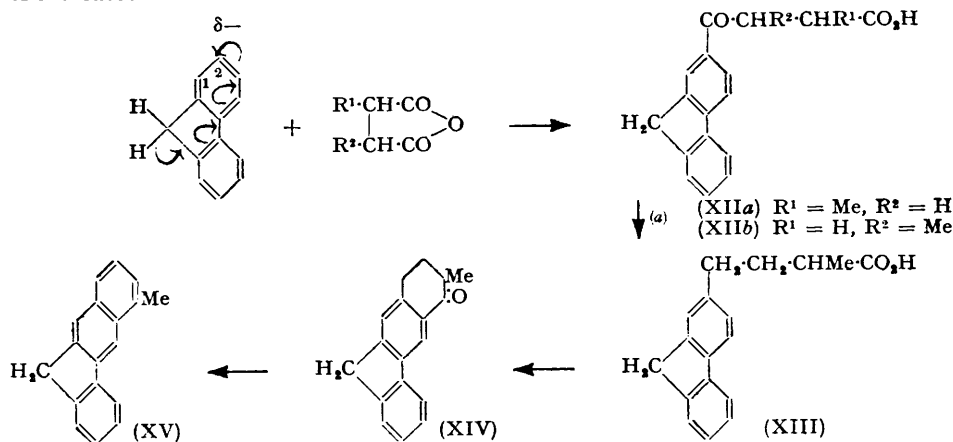
phenyl gave a mixture of the acids (VIa and b; Ar = *p*-MeO-C<sub>6</sub>H<sub>4</sub>, R<sup>3</sup> = OMe, R<sup>4</sup> = H), and 2 : 2'-dimethoxydiphenyl gave a corresponding pair (Ar = *o*-MeO-C<sub>6</sub>H<sub>4</sub>). The structures were established by the pyrylium reaction and by oxidising the first pair of acids to 2-methoxy-5-*p*-methoxyphenyl- and the latter pair to 4-methoxy-3-*o*-methoxyphenylbenzoic acid, but the acids (VIb) were rather indefinite materials and may not have been pure isomers. The  $\alpha$ -methyl-keto-acid (VIa; Ar = *p*-MeO-C<sub>6</sub>H<sub>4</sub>, R<sup>3</sup> = OMe, R<sup>4</sup> = H) was reduced by Clemmensen's method to the butyric acid (VIII), which was cyclised to the tetralone (IX). This was converted into 1-methoxy-4-*p*-methoxyphenyl-6-methylnaphthalene (X) by reduction with lithium aluminium hydride followed by dehydrogenation with selenium.

4-Methoxydiphenyl and methylsuccinic anhydride under the same conditions gave a mixture containing 2 parts of the acids (VIa and b; Ar = Ph, R<sup>3</sup> = OMe, R<sup>4</sup> = H) and 1 part of the acids (XIa and b) (cf. Fieser and Bradsher, *J. Amer. Chem. Soc.*, 1936, 58, 1738). Again the  $\alpha$ -methyl acids (VIa) and (XIa) were undoubtedly pure, but their isomers not necessarily so. Alkaline permanganate oxidation of this pair of acids (VI) gave 4-methoxydiphenyl-3-carboxylic acid, and of the acids (XI) gave 4-methoxydiphenyl-4'-carboxylic acid. Authentic specimens of 4-methoxydiphenyl-3- and -4'-carboxylic acid were prepared by unambiguous Ullmann reactions.

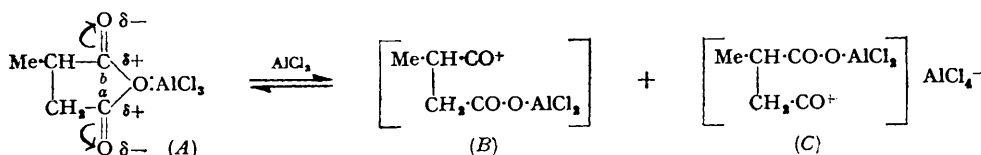
Condensation of fluorene with methylsuccinic anhydride in nitrobenzene gave a mixture of the acids (XIIa and b) in the ratio of 5 : 1. The ratio was 3 : 1 on reaction in *s*-tetrachloroethane. The oxidation of these two acids with sodium hypobromite gave 2-carboxyfluorenone, which was found to be identical with a specimen prepared by oxidation of  $\gamma$ -2-fluorenyl- $\gamma$ -oxobutyric acid (cf. Koelsch, *J. Amer. Chem. Soc.*, 1933, 55, 3885). Reduction of the  $\alpha$ -methyl-keto-acid (XIIa) by Clemmensen's method gave  $\gamma$ -2-fluorenyl- $\alpha$ -methylbutyric acid (XIII). Cyclisation of the butyric acid with phosphorus oxychloride in *s*-tetrachloroethane gave the oxobenzofluorene (XIV), converted into 3'-methyl-2 : 3-benzofluorene (XV) on reduction with lithium aluminium hydride followed by dehydrogenation with sulphur. The assignment of a 2 : 3- and not a 1 : 2-benzofluorene structure to the product was based on analogy with  $\gamma$ -2-fluorenylbutyric acid (cf. Koelsch, *loc. cit.*).

The preferential substitution of fluorene by electrophilic reagents at position 2 indicates

that this carbon atom carries the highest electron density, owing to the electronic displacements indicated.



The above results, as well as unpublished results on anisole and toluene, showed that the amount of the  $\beta$ -methyl-keto-acid ( $\beta$ -aroylbutyric acid) increased with the decrease in the dielectric constant of the medium. This may be due to the fact that in this case the complex (A) rather than (B) and (C) (cf. Groggins and Nagel, *Ind. Eng. Chem.*, 1934, **26**, 1313; Saboor, *J.*, 1945, 922) is the main constituent of the mixture. The ratio of the



$\alpha$ - to the  $\beta$ -methyl-keto-acid will be directly proportional to the electron deficiencies at carbon atoms (a) and (b), respectively. In solvents with high dielectric constant such as nitrobenzene, ion (C) is the main constituent of the mixture, thus leading predominantly to the  $\alpha$ -methyl-keto-acid.

### EXPERIMENTAL

The Friedel-Crafts reaction was carried out as follows unless otherwise stated.

A stirred and ice-cooled mixture of the reactants (1 mol. each) in nitrobenzene was treated portionwise with powdered anhydrous aluminium chloride (2 mols.) at such a rate that the temperature did not exceed 5° (30–45 min.). The mixture was allowed to come slowly to room temperature (20–30°) and kept thereat for a few days with occasional stirring, and then decomposed with ice and dilute hydrochloric acid. When methylsuccinic anhydride was used, the isomeric acids were separated by one of the following methods. (i) The nitrobenzene was removed in steam. A solution of the residue in hot sodium carbonate solution (charcoal) was filtered, and acidified, and the precipitated acids were worked up according to (a) and/or (b): (a) They were crystallised from the least amount of glacial acetic acid or ethyl alcohol: the  $\beta$ -aroyl- $\alpha$ -methylpropionic acid (series a) crystallised, leaving the crude  $\beta$ -aroylbutyric acid (series b) in the mother-liquor, which was obtained by evaporation in a vacuum to dryness. (b) The acids were dissolved in the least amount of hot 10% sodium carbonate solution, then cooled in ice, and the precipitated sodium salt was decomposed with hot dilute hydrochloric acid to give the  $\alpha$ -methylpropionic acid; the sodium carbonate mother-liquor gave the crude isomer on acidification. (ii) The insoluble  $\alpha$ -methylpropionic acid was filtered off; the nitrobenzene solution was extracted with ammonia solution, which gave on acidification the crude  $\beta$ -aroylbutyric acid (cf. Cocker *et al.*, *J.*, 1951, 926).

*Diphenyl and Methylsuccinic Anhydride.*—The mixture from methylsuccinic anhydride (cf. *Org. Synth.*, 1946, **26**, 54; Dev and Guha, *J. Indian Chem. Soc.*, 1948, **25**, 13) (8.4 g.), diphenyl (10 g.), nitrobenzene (80 ml.), and aluminium chloride (17.8 g.) (5 days) was worked up

according to method (ia). The product (15 g., 86%), m. p. 190—202°, was crystallised from the least amount of ethyl alcohol (ca. 380 ml.). The crystalline acid (7.1 g.) was recrystallised from alcohol or glacial acetic acid, to give  $\alpha$ -methyl- $\beta$ -*p*-phenylbenzoylpropionic acid (Ia) in colourless needles, m. p. 209—210° (Found : C, 75.5; H, 5.9.  $C_{17}H_{16}O_3$  requires C, 76.1; H, 6.0%), soluble in acetone, insoluble in benzene or light petroleum.

The crude isomer was repeatedly digested with light petroleum (b. p. 50—60°). The insoluble fraction (ca. 1.0 g.) proved to be the above acid. Removal of the light petroleum left a solid (0.7 g.) which was repeatedly crystallised from the same solvent, to give colourless  $\beta$ -*p*-phenylbenzoylbutyric acid (Ib), m. p. 81—82° (Found : C, 76.4; H, 6.3%), freely soluble in acetone, ethanol, and benzene. The isomers could also be separated by methods (ib) and (ii).

When nitrobenzene was replaced by *s*-tetrachloroethane, the product (60%) had m. p. 160—170°, and yielded no pure component. However, it was probably a mixture of the acids (Ia and b), since on oxidation with sodium hypobromite solution it gave pure diphenyl-4-carboxylic acid.

Each of the acids (Ia and b) (0.4 g.) was heated with 10% sodium hypobromite solution (45 ml.) on the water-bath (4 hr.) and worked up as usual (cf. Cook *et al.*, *J.*, 1953, 11) to give diphenyl-4-carboxylic acid, m. p. and mixed m. p. 224° (from dilute alcohol).

$\gamma$ -4-Diphenyl- $\alpha$ -methylbutyric Acid (II).—A mixture of the keto-acid (Ia) (20 g.), amalgamated zinc (50 g.), ethanol (120 ml.), and hydrochloric acid (120 ml.) was gently refluxed for 30 hr., during which hydrochloric acid (total, 80 ml.) was added in portions every 6 hr.  $\gamma$ -4-Diphenyl- $\alpha$ -methylbutyric acid (90%) was obtained in colourless needles, m. p. 90—91° [from light petroleum (b. p. 50—60°)] (Found : 79.7; H, 6.9.  $C_{17}H_{16}O_2$  requires C, 80.3; H, 7.1%).

2-Methyl-7-phenyl-1-tetralone (III).—The butyric acid (5 g.) was refluxed with phosphoric oxide (28.5 g.) in dry benzene (60 ml.) for 3.5 hr., the oxide being added portionwise. The product was worked up as usual and distilled, to give 2-methyl-7-phenyl-1-tetralone (64%), b. p. 178—180°/6 mm.,  $n_D^{25}$  1.6980 (Found : C, 85.8; H, 6.5.  $C_{17}H_{16}O$  requires C, 86.4; H, 6.8%). It did not give a semicarbazone or a 2 : 4-dinitrophenylhydrazone (cf. Cocker *et al.*, *J.*, 1951, 926; Cagniant and Buu-Hoi, *Bull. Soc. chim. France*, 1942, 9, 841). Cyclisation with 85% sulphuric acid or with stannic chloride (acid chloride) (4 hr. at 100°) was unsuccessful.

1 : 2 : 3 : 4-Tetrahydro-2-methyl-7-phenyl-naphthalene (IV).—The tetralone (0.5 g.) in dry ether (15 ml.) was reduced with lithium aluminium hydride (0.2 g.) in dry ether (15 ml.) (3 hours' refluxing, then left overnight). The product, b. p. 225—235°/6 mm., gave 1 : 2 : 3 : 4-tetrahydro-2-methyl-7-phenyl-naphthalene (64%) in colourless needles [from light petroleum (b. p. <40°)], m. p. 39—40° (Found : C, 91.2; H, 8.2.  $C_{17}H_{18}$  requires C, 91.9; H, 8.1%). The tetralone was recovered unchanged after treatment by Clemmensen's method or its modifications.

2-Methyl-7-phenyl-naphthalene (V).—The tetrahydronaphthalene (0.5 g.) was heated with selenium (0.6 g.) at 330—340° for 2.5 hr. The product was extracted with ether, to give 2-methyl-7-phenyl-naphthalene (40%), m. p. 141—142° [from light petroleum (b. p. 50—60°)] (Found : C, 92.8; H, 6.2.  $C_{17}H_{14}$  requires C, 93.5; H, 6.5%).

Diphenyl-4-carboxylic Acid.—Copper bronze (3.8 g.) was added portionwise during  $\frac{1}{2}$  hr. to a stirred mixture of methyl *p*-iodobenzoate (2.6 g., 1 mol.) and iodobenzene (2 g., 1 mol.) at 170°. The temperature was kept thereat for a further  $\frac{1}{2}$  hr., then gradually raised to 230—235°. More iodobenzene (4 g.) was added in two portions at hourly intervals, then the heating was continued for further 2 hr. The product was worked up as stated by Baddar and Gindy (*J.*, 1948, 1231). The acid soluble in benzene was converted into its methyl ester, b. p. 220—230°/18 mm., then hydrolysed with alcoholic sodium hydroxide to diphenyl-4-carboxylic acid (0.8 g., 40%), m. p. 226—227° (from dilute alcohol) (Found : C, 78.3; H, 5.0. Calc. for  $C_{13}H_{10}O_2$  : C, 78.75; H, 5.1%). Liebermann and Zuffa (*Ber.*, 1911, 44, 852) and Gull and Turner (*J.*, 1929, 498) gave m. p. 224° and 228°, respectively. The benzene-insoluble acid, m. p. >300°, was esterified (methyl alcohol and sulphuric acid, 5 hr.) to give dimethyl diphenyl-4 : 4'-dicarboxylate, m. p. and mixed m. p. 211—212° (from methyl alcohol) (Found : C, 71.3; H, 5.3. Calc. for  $C_{16}H_{14}O_4$  : C, 71.1; H, 5.2%). Weiler (*Ber.*, 1899, 32, 1063) and Ullmann *et al.* (*Annalen*, 1904, 332, 73) gave m. p. 212—213° and 214°, respectively.

4 : 4'-Dimethoxydiphenyl and Succinic Anhydride.—A stirred mixture of 4 : 4'-dimethoxydiphenyl (10 g.), aluminium chloride (13.4 g.), and nitrobenzene (50 ml.) was treated portionwise with a solution of succinic anhydride (5.2 g.) in nitrobenzene (200 ml.), then left overnight. The product was decomposed with ice and hydrochloric acid and treated with benzene, and the organic layer was extracted with sodium carbonate solution (charcoal), which was later acidified. The precipitated acid (14.6 g.; m. p. 123—125°) was  $\beta$ -2-methoxy-5-*p*-methoxyphenylbenzoylpropionic acid (VIc; Ar = *p*-MeO·C<sub>6</sub>H<sub>4</sub>, R<sup>s</sup> = OMe, R<sup>t</sup> = H), colourless crystals (from benzene),

m. p. 135—136° (Found : C, 68.5; H, 5.8; OMe, 19.5.  $C_{18}H_{18}O_5$  requires C, 68.8; H, 5.8; OMe, 19.7%), soluble in ethanol or acetone, and insoluble in ether and light petroleum. When the reaction was carried out as described in the first experiment, an uncrystallisable sticky material was obtained. When nitrobenzene was replaced by *s*-tetrachloroethane no reaction took place.

This acid (0.4 g.) was oxidised with 10% sodium hypobromite solution (45 ml.) in the usual manner. The precipitated acid, m. p. 133—135°, was converted into its methyl ester, m. p. 80—81° [from light petroleum (b. p. 50—60°)], undepressed on admixture with methyl 2-methoxy-5-*p*-methoxyphenylbenzoate (Found : C, 70.4; H, 5.9. Calc. for  $C_{16}H_{16}O_4$  : C, 70.6; H, 5.9%).

4-(2-Methoxy-5-*p*-methoxyphenylphenyl)butan-1-ol (VII).—A solution of the keto-acid (5 g.) in dry thiophen-free benzene (100 ml.) was reduced with lithium aluminium hydride (2.5 g.) in dry ether (200 ml.) as mentioned above. The alcohol (66%) was obtained in colourless needles, m. p. 67—68°, from light petroleum (b. p. 50—60°) (Found : C, 75.4; H, 7.5; active H, 0.35.  $C_{18}H_{22}O_3$  requires C, 75.5; H, 7.7; active H, 0.35%). The acid was recovered unchanged on treatment by Clemmensen's method. Attempts to cyclise this alcohol with phosphoric oxide in benzene on a boiling-water bath or at room temperature gave viscous uncrystallisable material.

4 : 4'-Dimethoxydiphenyl and Methylsuccinic Anhydride.—The product (15 g.; m. p. 142—150°) from 4 : 4'-dimethoxydiphenyl (10 g.), methylsuccinic anhydride (5.8 g.), nitrobenzene (80 ml.), and aluminium chloride (13 g.) (3 days) was worked up according to procedure (ia).  $\beta$ -(2-Methoxy-5-*p*-methoxyphenylbenzoyl)- $\alpha$ -methylpropionic acid (VIa; Ar = *p*-MeO-C<sub>6</sub>H<sub>4</sub>, R<sup>3</sup> = OMe, R<sup>4</sup> = H) (9.0 g. from 20 ml. of glacial acetic acid) was obtained in colourless needles, m. p. 159—160° (Found : C, 68.9; H, 5.8; OMe, 18.4.  $C_{19}H_{20}O_5$  requires C, 69.5; H, 6.1; OMe, 18.9%). The crude isomer (4 g.) failed to solidify. It was repeatedly extracted with boiling light petroleum (b. p. <40°), and the combined extracts were concentrated and kept in the ice-chest (one month) to give the aroylbutyric acid as a pale yellow solid, m. p. 80—100° not improved by recrystallisation. It failed to give a solid semicarbazone or a 2 : 4-dinitrophenylhydrazone. Both acids gave on oxidation with sodium hypobromite solution 2-methoxy-5-methoxyphenylbenzoic acid. The acids could also be separated by method (ii).

$\gamma$ -(2-Methoxy-5-*p*-methoxyphenylphenyl)- $\alpha$ -methylbutyric Acid (VIII).—The keto-acid (7 g.) was reduced with zinc amalgam (25 g.) and hydrochloric acid (100 ml.) (20 hr.) to this butyric acid (89%), colourless needles [from light petroleum (b. p. 100—120°)], m. p. 119—120° (Found : C, 72.6; H, 6.9; OMe, 19.1.  $C_{19}H_{22}O_4$  requires C, 72.6; H, 7.1; OMe, 19.7%).

5-Methoxy-8-*p*-methoxyphenyl-2-methyl-1-tetralone (IX).—A benzene solution of the acid chloride of the above butyric acid (6.4 g.) [prepared by phosphorus pentachloride (4 g.)] was cooled in ice, treated dropwise during 15 min. with a solution of stannic chloride (8 ml.) in dry thiophen-free benzene (10 ml.), left overnight, and worked up as usual. The tetralone (60%) was obtained in pale yellow crystals [from light petroleum (b. p. 100—120°)], m. p. 140—141° (Found : C, 76.6; H, 6.9.  $C_{19}H_{20}O_3$  requires C, 77.0; H, 6.8%).

1 : 2 : 3 : 4-Tetrahydro-5-methoxy-8-*p*-methoxyphenyl-2-methylnaphthalene.—A solution of the above tetralone (1 g.) in dry ether (20 ml.) and dry thiophen-free benzene (20 ml.) was reduced with lithium aluminium hydride (0.5 g.) in dry ether (15 ml.) (2 hours' refluxing), then worked up as usual. The product, b. p. 225—235°/7 mm. (75%), gave the tetrahydronaphthalene, m. p. 84—85° (from alcohol) (Found : C, 81.0; H, 7.6.  $C_{19}H_{22}O_2$  requires C, 80.8; H, 7.9%). The substance contained no active hydrogen, which proved that it was a tetralin.

1-Methoxy-4-*p*-methoxyphenyl-6-methylnaphthalene (X).—The tetrahydronaphthalene (0.5 g.) was heated with selenium (0.5 g.) at 330—340° for 2 hr. 1-Methoxy-4-*p*-methoxyphenyl-6-methylnaphthalene (40%) was obtained nearly colourless (from alcohol), m. p. 126—127° (Found : C, 81.3; H, 6.5; MeO, 22.5.  $C_{19}H_{18}O_2$  requires C, 82.0; H, 6.5; MeO, 22.3%).

5-Bromo-2-methoxybenzoic Acid.—2-Methoxybenzoic acid (5 g.) was treated with bromine in the manner adopted by Derbyshire and Waters (*J.*, 1950, 576) for benzoic acid (2 hr. at room temperature). The product (98%), m. p. 119°, was pure enough for the next step (Peratoner, *Gazzetta*, 1886, 16, 405, gave the same m. p.). The methyl ester had m. p. 39—40°. Peratoner (*loc. cit.*) gave the same m. p.

Methyl 2-Methoxy-5-*p*-methoxyphenylbenzoate.—A stirred mixture of the above ester (4 g., 1 mol.) and *p*-iodoanisole (3.7 g., 1 mol.) was treated portionwise at 180° with copper bronze (5.1 g.). The temperature was then raised to 230—235° and maintained thereat for 6 hr., and the product worked up as usual. The acid soluble in benzene was esterified, to give methyl 2-methoxy-5-*p*-methoxyphenylbenzoate, b. p. 230—240°/6 mm. (7%), needles [from light petroleum (b. p. 50—60°)], m. p. 80—81° (Found : C, 70.3; H, 5.8; OMe, 34.5.  $C_{16}H_{16}O_4$  requires C, 70.6; H, 5.9; OMe, 34.2%).

2 : 2'-Dimethoxydiphenyl and Succinic Anhydride.—The product (14 g.; m. p. 223—225°) from 2 : 2'-dimethoxydiphenyl (10 g.), succinic anhydride (5.2 g.), nitrobenzene (80 ml.), and aluminium chloride (13.6 g.) (2 days) gave  $\beta$ -(4-methoxy-3-o-methoxyphenylbenzoyl)propionic acid, colourless needles (from acetic acid), m. p. 229—230° (darkened at 200°) (Found : C, 64.1; H, 5.8; OMe, 17.1.  $C_{18}H_{18}O_5, CH_3 \cdot CO_2H$  requires C, 64.1; H, 5.9; MeO, 16.6%). The proof of the presence of acetic acid of crystallisation rested entirely on the analysis. The acid could also be purified through its insoluble sodium salt. Its *ethyl ester* had m. p. 152—153° (from ethanol) (Found : 69.7; H, 6.4.  $C_{20}H_{22}O_5$  requires C, 70.1; H, 6.5%). Attempts to reduce this keto-acid or its ester by the Clemmensen method or its modifications were not successful. Lithium aluminium hydride gave a neutral oil which failed to give a solid toluene-*p*-sulphonate or a 3 : 5-dinitrobenzoate. The keto-acid, on oxidation with 10% sodium hypobromite solution, gave 4-methoxy-3-*o*-methoxyphenylbenzoic acid, m. p. 334—336° (from acetic acid). Its methyl ester, stout monoclinic crystals (from methanol), had m. p. and mixed m. p. 171—172°.

*Methyl 4-Methoxy-3-o-methoxyphenylbenzoate*.—The reaction between methyl 3-iodo-4-methoxybenzoate (3.5 g.), copper bronze (4 g.), and *o*-iodoanisole (2.8 g.) was complete in 4 hr. (230—235°). The product was worked up as usual, and the neutral fraction proved to be 2 : 2'-dimethoxydiphenyl. 4-Methoxy-3-*o*-methoxyphenylbenzoic acid, needles (from acetic acid), m. p. 330—336°, gave a methyl ester (13%), monoclinic crystals, m. p. 171—172°, from methanol (Found : C, 69.9; H, 5.6; OMe, 33.4.  $C_{18}H_{18}O_4$  requires C, 70.6; H, 5.9; OMe, 34.2%).

2 : 2'-Dimethoxydiphenyl and Methylsuccinic Anhydride.—The product (m. p. 200—211°; 15 g.) from 2 : 2'-dimethoxydiphenyl (10 g.), methylsuccinic anhydride (5.8 g.), nitrobenzene (80 ml.), and aluminium chloride (13 g.) was worked up according to method (1; a).  $\beta$ -(4-Methoxy-3-*o*-methoxyphenylbenzoyl)- $\alpha$ -methylpropionic acid (8 g.; from 20 ml. of glacial acetic acid) was obtained in colourless needles, m. p. 234—235° (Found : C, 65.0; H, 5.9; OMe, 15.2.  $C_{19}H_{20}O_5, CH_3 \cdot CO_2H$  requires C, 64.9; H, 6.2; OMe, 16.0%). The product in the acetic acid mother-liquor failed to solidify or to give a semicarbazone or 2 : 4-dinitrophenylhydrazone. However, it was most probably the  $\beta$ -aroylbutyric acid. Both the keto-acids, on oxidation with sodium hypobromite solution and esterification, gave methyl 4-methoxy-3-*o*-methoxyphenylbenzoate, m. p. and mixed m. p. 171—172°. Attempted reduction of the  $\alpha$ -methyl acid by Clemmensen's method was unsuccessful (cf. Cook *et al.*, *loc. cit.*). Reduction with lithium aluminium hydride gave a neutral oil from which no solid toluene-*p*-sulphonate or 3 : 5-dinitrobenzoate could be obtained.

*Methylsuccinic Anhydride and 4-Methoxydiphenyl*.—The product (23 g.; m. p. 120—162°) from aluminium chloride (21 g.), 4-methoxydiphenyl (15 g.), methylsuccinic anhydride (10.2 g.), and nitrobenzene (120 ml.) (overnight) was worked according to (ib). The acids (7 g.) resulting from the acidification of the insoluble sodium salts had m. p. 180—202° and on repeated crystallisation from glacial acetic acid (*ca.* 40 ml.) gave  $\beta$ -4-*p*-methoxyphenylbenzoyl- $\alpha$ -methylpropionic acid (3.4 g.), m. p. 204—205° (Found : C, 72.7; H, 6.3; OMe, 11.3.  $C_{18}H_{18}O_4$  requires C, 72.45; H, 6.1; OMe, 10.4%). The first acetic acid mother-liquor was evaporated in a vacuum to dryness, and the residue (*ca.* 2 g.) was triturated with light petroleum (b. p. <40°). It melted at 147—165° (shrinking at 140°), and the m. p. was not improved by repeated crystallisation. It was probably impure  $\beta$ -4-*p*-methoxyphenylbenzoylbutyric acid. Both the keto-acids on oxidation with alkaline permanganate (cf. Fieser and Bradsher, *J. Amer. Chem. Soc.*, 1936, 58, 1738) gave 4'-methoxydiphenyl-4-carboxylic acid, m. p. and mixed m. p. 248—249°. The acids liberated from the soluble sodium salts gave  $\beta$ -(2-methoxy-5-phenylbenzoyl)- $\alpha$ -methylpropionic acid (*ca.* 7 g.; m. p. 132—134°), m. p. 146—147° [repeatedly crystallised from benzene-light petroleum (b. p. 50—60°)] (Found : C, 72.2; H, 5.9; OMe, 12.2.  $C_{18}H_{18}O_4$  requires C, 72.45; H, 6.1; OMe, 10.4%). The benzene-light petroleum mother-liquor left on evaporation an oil (*ca.* 3 g.), which was triturated with light petroleum (b. p. <40°), then crystallised from benzene-light petroleum (b. p. 50—60°) to give impure  $\beta$ -2-methoxy-5-phenylbenzoylbutyric acid, m. p. 105—120°. The m. p. did not improve by repeated crystallisation from the same solvent. Both acids on oxidation with alkaline permanganate gave 4-methoxydiphenyl-3-carboxylic acid, m. p. and mixed m. p. 169—170° (Fieser and Bradsher, *loc. cit.*, gave m. p. 166—167°). Oxidation of these keto-acids with alkaline hypobromite gave unsatisfactory results.

4'-Methoxydiphenyl-4-carboxylic Acid.—This was prepared from methyl *p*-iodobenzoate (7.8 g.), *p*-iodoanisole (6.9 g.), and copper bronze (11.4 g.) in the usual manner (5 hr. at 230—235°). The benzene-soluble acid (0.6 g., 9%) gave 4'-methoxydiphenyl-4-carboxylic acid, needles (from acetic acid), m. p. 248—249° (Found : C, 72.6; H, 5.1; OMe, 15.2. Calc. for  $C_{14}H_{12}O_3$  : C, 73.6; H, 5.3; OMe, 13.6%). Fieser and Bradsher (*loc. cit.*) gave the same m. p. The

benzene-insoluble acid on methylation gave dimethyl diphenyl-4 : 4'-dicarboxylate, m. p. and mixed m. p. 211—212° (from methanol).

*4-Methoxydiphenyl-3-carboxylic Acid.*—This was prepared from methyl 5-bromo-2-methoxybenzoate (4.9 g., 1 mol.), iodobenzene (12.3 g., 3 mols.), and copper bronze (7.6 g.) in the usual manner (5 hr. at 230—235°). The iodobenzene was added in portions during the first 2 hr. The benzene-soluble acid (0.5 g., 11%) gave 4-methoxydiphenyl-3-carboxylic acid, m. p. 169—170° (from ether) (Found : C, 72.9; H, 5.2; OMe, 14.6. Calc. for C<sub>14</sub>H<sub>12</sub>O<sub>3</sub> : C, 73.6; H, 5.3; OMe, 13.6%). Fieser and Bradsher (*loc. cit.*) gave m. p. 166—167°.

*Fluorene and Methylsuccinic Anhydride.*—The product from fluorene (10 g.), methylsuccinic anhydride (8.2 g.), nitrobenzene (80 ml.), and aluminium chloride (19 g.) (3 days) was worked up according to procedure (ii). The insoluble acid (14 g.; m. p. 204—206°) gave *γ*-2-fluorenyl-*α*-methyl-*γ*-oxobutyric acid (XIIIa), needles, m. p. 212—213° (from acetic acid) (Found : C, 77.2; H, 5.8. C<sub>18</sub>H<sub>16</sub>O<sub>3</sub> requires C, 77.1; H, 5.8%). It was soluble in ethanol, insoluble in benzene. The pale yellow acid (2 g.), recovered from the ammonia, gave *β*-(2-fluorenylcarbonyl)butyric acid (XIIIb), m. p. 113—116° [from light petroleum, b. p. 100—120°] (Found : C, 76.6; H, 5.7%).

The crude acids were also separated by procedure (1; b) in the ratio of 5 : 1. When nitrobenzene was replaced by *s*-tetrachloroethane, the ratio of the acids, separated by procedure (ib), was 3 : 1. Both acids on oxidation with sodium hypobromite solution gave an acid, the methyl ester of which was identical with methyl fluorenone-2-carboxylate. This was prepared by the oxidation of *γ*-2-fluorenyl-*γ*-oxobutyric acid (cf. Koelsch, *J. Amer. Chem. Soc.*, 1933, 55, 3885) with alkaline hypobromite, followed by methylation, and had m. p. and mixed m. p., 179—180°. Fortner (*Monatsh.*, 1904, 25, 443) and Koelsch (*loc. cit.*) gave m. p. 181° and 177—181°, respectively.

*γ*-2-Fluorenyl-*α*-methylbutyric Acid (XIII).—The keto-acid (XIIIa) (20 g.) was reduced with zinc amalgam (100 g.), ethanol (150 ml.), and hydrochloric acid (250 ml.) (30 hours' refluxing) in the usual manner. *γ*-2-Fluorenyl-*α*-methylbutyric acid (17 g.) was obtained in colourless needles, m. p. 124—125° [from light petroleum (b. p. 100—120°)] (Found : C, 81.4; H, 7.0. C<sub>18</sub>H<sub>18</sub>O<sub>3</sub> requires C, 81.2; H, 6.8%).

1' : 2' : 3' : 4'-Tetrahydro-3'-methyl-4'-oxo-2 : 3-benzofluorene (XIV).—The butyric acid (1.5 g.) was cyclised with phosphorus oxychloride (1.5 ml.) in dry *s*-tetrachloroethane (20 ml.) (2.5 hours' refluxing). The solvent was steam-distilled and the product, b. p. 222—226°/6 mm., gave the colourless cyclic ketone (1 g.), m. p. 53—54° [from light petroleum (b. p. <40°)] (Found : C, 86.5; H, 6.2. C<sub>18</sub>H<sub>16</sub>O requires C, 87.05; H, 6.5%). It acquired a violet colour on exposure to light. Cyclisation (acid chloride) with aluminium chloride or fuming stannic chloride gave a poor yield.

1' : 2' : 3' : 4'-Tetrahydro-3'-methyl-2 : 3-benzofluorene.—The above ketone (0.6 g.) was reduced with lithium aluminium hydride (0.5 g.) in the usual manner. The product, b. p. 225—235°/8 mm., gave 1' : 2' : 3' : 4'-tetrahydro-3'-methyl-2 : 3-benzofluorene (0.4 g.), colourless needles, m. p. 151—152° (from methanol) (Found : C, 92.8; H, 7.5. C<sub>18</sub>H<sub>18</sub> requires C, 92.3; H, 7.7%). Reduction by the modified Clemmensen method was unsuccessful.

3'-Methyl-2 : 3-benzofluorene (XV).—The tetrahydrobenzofluorene (0.5 g.) was heated with sulphur (0.3 g.) at 280—290° for 1 hr. 3'-Methyl-2 : 3-benzofluorene (0.2 g.) was obtained in pale yellow crystals, m. p. 114—115° [from benzene-light petroleum (b. p. 60—80°)] depressed to 80—87° on admixture with the tetrahydro-compound (Found : C, 92.9; H, 5.9. C<sub>18</sub>H<sub>14</sub> requires C, 93.9; H, 6.1%).