

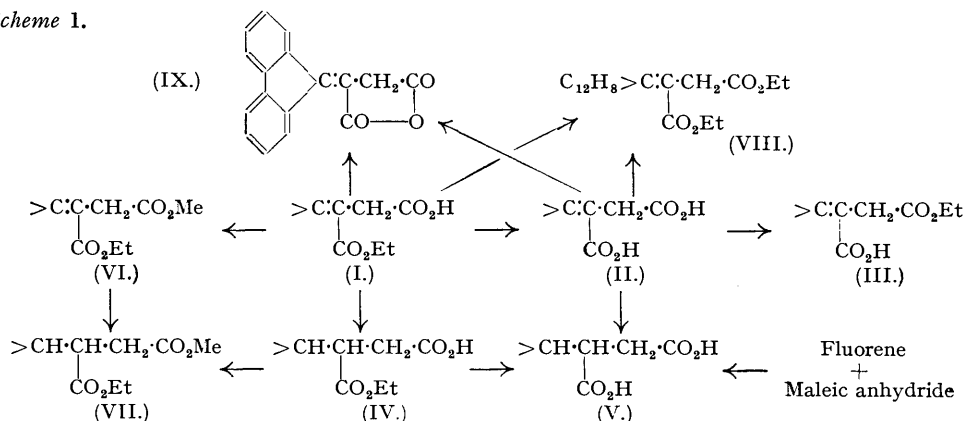
234. The Condensation of Fluorenone and Ethyl Succinate.

By NEIL CAMPBELL and A. E. S. FAIRFULL.

Fluorenone and ethyl succinate condense in presence of potassium *tert.*-butoxide or sodium hydride to give a mixture from which β -carbethoxy- β -fluorenylidenepropionic acid (I) and 1:4-difluorenylidenesuccinic acid (XIX) have been isolated. With sodium ethoxide only the latter was isolated. The chemistry of the former product and its derivatives has been investigated, and the inability of the latter to form an anhydride explained on stereochemical grounds.

THE synthetic value of 3:3-disubstituted itaconic acids (Borsche, *Annalen*, 1936, 526, 1; Cook and Preston, *J.*, 1944, 553, etc.) led us to prepare and study *fluorenylidenesuccinic acid* (3:3-*diphenylenecitraconic acid*). We first attempted to prepare the compound by condensing fluorenone with ethyl succinate by means of sodium ethoxide (Stobbe, *Annalen*, 1899, 308, 89), but later adopted the procedure of Johnson and his co-workers (*J. Amer. Chem. Soc.*, 1945, 67, 1357, 1360, 1366) in which potassium *tert.*-butoxide is used. By the latter method a mixture of products was obtained the nature of which was not completely elucidated (see below), but we isolated β -carbethoxy- β -fluorenylidenepropionic acid (I), referred to below as the "half-ester." Its constitution was suggested by the formation of the analogous ester from benzophenone and ethyl succinate (Stobbe, *Annalen*, 1894, 282, 281; 1899, 308, 98; Borsche, *loc. cit.*; Johnson *et al.*, *J. Amer. Chem. Soc.*, 1947, 69, 74) and confirmed by the reactions shown in scheme 1.

Scheme 1.



Thus, in particular, the carbon skeleton was proved by formation, in several steps, of 9-fluorenyl-succinic acid (V), which was prepared also from fluorene and maleic anhydride; the sterically hindered position of the esterified carboxyl group was proved by formation of the isomeric *monoethyl ester* (III), rather than the original ester, on esterification of the *dicarboxylic acid* (II); and the presence of the methylene group in the unsaturated compounds is shown by condensation of the *diester* (VIII) with benzaldehyde to give α -benzylidene- α -9-fluorenylidenesuccinic acid, which is also obtained from fluorenone and ethyl phenylitaconate (Stobbe *et al.*, *Annalen*, 1911, 380, 126). The structure of the isomeric *monoethyl ester* (III) is also proved by similar reactions.

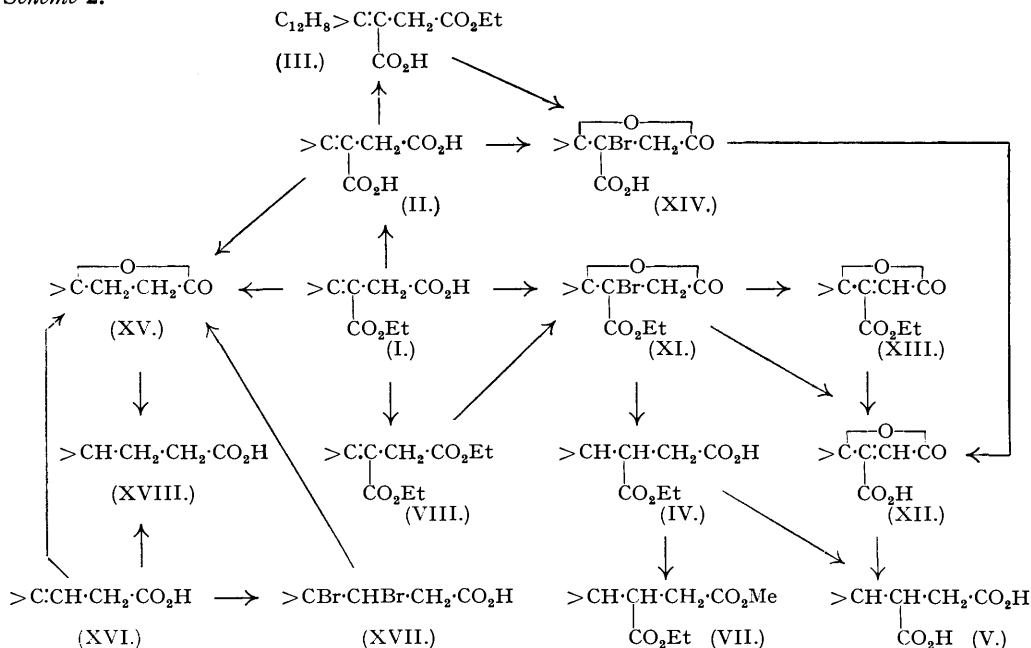
Interaction of the diacid and its esters with bromine leads to *bromo-lactones* (XI) and (XIV) (see scheme 2), formed by elimination of hydrogen bromide between CO_2H and $\geq\text{CBr}$ or of ethyl bromide between CO_2Et and $\geq\text{CBr}$ (cf. Stobbe, *Ber.*, 1911, 44, 1297).

The acid (I) with hydrobromic acid and acetic acid (cf. Johnson, *loc. cit.*) was hydrolysed and decarboxylated to the *lactone* (XV), also prepared in the same way from the acid (II) or from β -fluorenylidenepropionic acid (XVI) either by sulphuric acid or *via* its *dibromo-derivative* (XVII). The lactone was reduced by hydriodic acid and red phosphorus to β -9-fluorenyl-propionic acid (XVIII), also obtained by reduction of the acid (XVI).

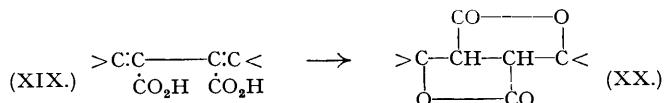
Attempts at ring-closure by refluxing the half-ester (I) with sodium acetate and acetic anhydride or by treating the dibasic acid (II) with concentrated sulphuric acid or aluminium chloride in nitrobenzene (cf. Stobbe and Gollücke, *Ber.*, 1906, 39, 1066) were unsuccessful. Failure to form an indone derivative with two contiguous five-membered rings in an aromatic system is not surprising, but failure to obtain a fluoranthene derivative was unexpected in view

of Borsche's conversion (*loc. cit.*) of 2-carbethoxy-3 : 3-diphenylvinylacetic acid into a derivative of phenyl-naphthol.

Scheme 2.



In the Stobbe condensations with sodium ethoxide a yellow product was obtained; it was also formed in the Johnson modification at the expense of the half-ester (I) when heating lasted for more than 30 minutes. A molecular-weight determination indicated that two molecules of fluorenone had condensed with one of ethyl succinate, and analysis supported the belief that the yellow compound was *difluorenylidenesuccinic acid* (XIX). This was confirmed by decarboxylation to *difluorenylidene-ethane* followed by reduction to di-9-fluorenylethane.



It was found that fluorenone and ethyl succinate with sodium hydride gave the same products as with potassium *tert.*-butoxide.

The dicarboxylic acid (XIX) when heated under reflux with acetic acid and hydrobromic acid gave a *dilactone* (XX), but all efforts to prepare the anhydride failed. This is most plausibly attributed to the *trans*-configuration of the carboxyl groups which involves slight overlapping of the fluorene residues and carboxyl groups, while the *cis*-configuration required for anhydride formation would result in heavy overlapping of the fluorene nuclei. Stobbe *et al.* (*loc. cit.*) obtained the anhydride from α -phenyl- β -diphenylene-fulgenic acid only on long boiling with acetyl chloride. It is noteworthy that Koelsch and Richter (*J. Org. Chem.*, 1939, 3, 473) easily obtained the anhydride of tetraphenylfulgenic acid. This striking difference between molecules very similar in structure is probably to be explained by the rigidity of the fluorene molecule which causes the whole molecule to be coplanar or nearly so, while in the tetraphenylfulgenic acid the phenyl rings are not necessarily coplanar and consequently the *trans*-acid can be converted into the *cis*-acid by the blocking phenyl groups tilting and then "sliding past" one another.

EXPERIMENTAL.

Aluminium oxide (Brockmann) was used for the chromatographic adsorption experiments, and a Hanovia ultra-violet lamp for the fluorescence observations. The identity of different samples was established by mixed m. p.s, and analyses were by Drs. Weiler and Strauss, Oxford.

β-Carbethoxy-*β*-fluorenylidene-*n*propionic Acid (I).—Fluorenone (9 g., 0.05 mol.) in ethyl succinate (13.05 g., 0.075 mol.) and *tert*-butanol (30 ml.) were cooled to 0° and added to a chilled solution of potassium (2.15 g., 0.055 mol.) in *tert*-butanol (45 ml.). The solution was gently heated under reflux for 35 minutes, cooled, and acidified with dilute hydrochloric acid. Dilution with water to 600 ml. gave an orange oil which was extracted with ether; the ethereal layer was washed with water and extracted with 5% sodium hydroxide. The alkaline solution yielded on acidification an orange oil, which was dissolved in ether; the ether solution was washed with water, dried (Na₂SO₄), and evaporated. The resulting yellow oil (11.7 g.) was dissolved in carbon disulphide (20 ml.) which overnight deposited crystals (4.4 g.), m. p. 120—123°. Several recrystallisations from benzene gave almost colourless crystals of the ester (I), m. p. 126—127° (Found: C, 73.6; H, 5.3. C₁₉H₁₆O₄ requires C, 74.0; H, 5.2%). The carbon disulphide was removed, and the oily residue dissolved in the minimum of boiling methanol. On cooling, yellow needles (0.6 g.) separated, m. p. 208—210°, which gave no m. p. depression with difluorenylidene-succinic acid (see below). The methanolic filtrate was added to 75 c.c. of 10% sodium hydroxide and the whole heated under reflux for 1½ hours. After dilution with water to 150 c.c., the boiling solution (charcoal) was filtered, and the filtrate acidified to give *fluorenylidene-succinic acid* (II), m. p. 202—204° (decomp.) (3.3 g.), identical with a sample obtained by the hydrolysis (NaOH) of the above half-ester (I), yellow-orange needles (benzene), m. p. 205—206° (Found: C, 72.9; H, 4.3. C₁₇H₁₂O₄ requires C, 72.9; H, 4.3%). The acid was esterified only with difficulty, 4 hours' refluxing with ethanol and concentrated sulphuric acid giving a 15% yield of the *diethyl ester* (VIII), m. p. 83—84°, yellow needles (ethanol) or prisms (light petroleum), m. p. 83—84°, identical with a sample prepared similarly from the half-ester (I) (Found: C, 74.8; H, 5.9. C₂₁H₂₀O₄ requires C, 75.0; H, 6.0%). When heated under reflux in ethanol for 24 hours, 0.5 g. of the dibasic acid yielded the ethyl ester (VIII; 0.12 g.) and *ethyl β-carboxy-β-fluorenylidene-*n*propionate* (III) (0.28 g.), soluble in potassium carbonate solution from which it was precipitated by hydrochloric acid as fine needles (benzene), m. p. 127—128° (Found: C, 73.7; H, 5.15. C₁₉H₁₆O₄ requires C, 74.0; H, 5.2%); the melt solidified at 170° and then fused at 202—204° owing to anhydride formation. The dibasic acid with methanol and sulphuric acid yielded *methyl β-carboxy-β-fluorenylidene-*n*propionate*, pale yellow needles (benzene), m. p. 125—126°, depressed by the corresponding ethyl ester (Found: C, 73.45; H, 5.0. C₁₈H₁₄O₄ requires C, 73.5; H, 4.8%). No dimethyl ester was isolated. Esterification of the half-ester (I) with methanol and sulphuric acid yielded *methyl β-carbethoxy-β-fluorenylidene-*n*propionate* (VI), compact yellow prisms (light petroleum) (70% yield), m. p. 93—94° (Found: C, 74.6; H, 5.7. C₂₀H₁₈O₄ requires C, 74.5; H, 5.6%).

Sodium methoxide (0.6 g.) was added to the ester (VIII) (1.7 g.) and benzaldehyde (1 c.c.) in sodium-dried ether (20 c.c.) and kept for 5 days. The brown precipitate was washed with ether and dissolved in water. Concentrated hydrochloric acid gave a very sticky solid which was extracted with ether. The ether was washed with water, dried (Na₂SO₄), and evaporated to a brown oil, which was dissolved in boiling benzene. From the cold solution *α*-benzylidene-*α'*-fluorenylidene-succinic acid was deposited, orange crystals (chlorobenzene), m. p. 204—206° (lit., 206—208°).

Fluorenone (9 g.) condensed with ethyl succinate (17.5 g.) in the presence of sodium hydride (2.4 g.) to give *β*-carbethoxy-*β*-fluorenylidene-*n*propionic acid (6.7 g., 42%), the corresponding dibasic acid (1.4 g., 10%), difluorenylidene-succinic acid (0.35 g., 3.2%), and 0.4 g. of a compound, m. p. 125—127° after crystallisation from benzene-light petroleum, which is probably ethyl 1:4-diketocyclohexane-2:5-dicarboxylate.

Fluorenylidene-succinic anhydride (IX) was prepared by two methods. (a) The half-ester (I) (0.7 g.) was heated under reflux in acetic anhydride (5 ml.), glacial acetic acid (5 ml.), and zinc chloride (0.01 g.) for 4 hours. On cooling, the anhydride (0.45 g.) separated in needles, which on crystallisation from glacial acetic acid had m. p. 203—205°. It gave no m. p. depression with the dicarboxylic acid, probably owing to anhydridisation of the latter. (b) The di-acid (II) (1 g.) was kept in acetyl chloride (40 ml.) for 1 hour. Benzene was then added to dissolve the precipitate, and the solution warmed gently to remove the acetyl chloride. On cooling, the anhydride separated in yellow elongated prisms, m. p. 211—212°, giving no m. p. depression with the above anhydride or the di-acid (Found: C, 77.0; H, 3.8. C₁₇H₁₀O₃ requires C, 77.8; H, 3.8%).

Fluorenylidene-succinic acid (II) (0.4 g.) was heated under reflux in glacial acetic acid (10 ml.), and zinc dust (2 g.) added. After 20 minutes the colourless solution was poured into water (90 ml.) and extracted with ether. The ethereal layer was twice extracted with aqueous potassium carbonate (5%), which on acidification yielded *9-fluorenylsuccinic acid* (V), 0.37 g., m. p. 181—184°, identical with a sample obtained from fluorene and maleic anhydride as needles (benzene-light petroleum), m. p. 185—186° (cf. Alder, Vagt, and Pascher, *Ber.*, 1942, 75, 1501) (Found: C, 72.0; H, 5.6. C₁₇H₁₄O₄ requires C, 72.3; H, 5.0%). The dimethyl esters were also identical.

*Reduction of β-Carbethoxy-β-fluorenylidene-*n*propionic Acid* (I).—The half-ester (1 g.) was dissolved in glacial acetic acid (20 ml.), zinc dust (3 g.) added, the mixture heated under reflux for 1 hour and poured into water (60 ml.), and the white precipitate extracted with ether. The ether was extracted with aqueous potassium carbonate, which on acidification gave *β-carbethoxy-β-9-fluorenylpropionic acid* (IV) (0.91 g.), needles (benzene), m. p. 168—169° (Found: C, 73.5; H, 6.0. C₁₉H₁₈O₄ requires C, 73.5; H, 5.85%). It was hydrolysed by boiling with 10% sodium hydroxide for 30 minutes; acidification gave *9-fluorenylsuccinic acid*, m. p. 182—185°, which was esterified with methanol and concentrated sulphuric acid to *methyl β-carbethoxy-β-9-fluorenylpropionate* (VII), m. p. 93—94°, needles (methanol), identical with the product obtained by reducing methyl *β*-carbethoxy-*β*-fluorenylidene-*n*propionate (VI) with zinc dust and glacial acetic acid (Found: C, 73.4; H, 6.25. C₂₀H₂₀O₄ requires C, 74.1; H, 6.2%).

β-Bromo-β-carbethoxy-β-9-hydroxy-9-fluorenylpropionic Acid Lactone (XI).—*β*-Carbethoxy-*β*-fluorenylidene-*n*propionic acid (1 g.) in glacial acetic acid (3 ml.) was treated with bromine (0.6 g.). The solution when kept deposited crystals of the *bromo-lactone* (XI), which were crystallised from benzene-light petroleum (b. p. 60—80°); needles, m. p. 149—150°; yield 0.65 g. (Found: Br, 20.5. C₁₉H₁₅O₄Br requires Br, 20.6%). A further 0.25 g. was obtained from the original solution by addition of water and

subsequent purification. It was also prepared similarly by the bromination of the di-ester (VIII). The bromo-lactone (0.5 g.) was dissolved in dry pyridine (5 c.c.) and the solution kept just below the b. p. for 1 hour. Addition of water (25 c.c.) gave the lactone of β -carbethoxy- β -9-hydroxy-9-fluorenylacrylic acid (XIII), needles (0.28 g.) (methanol), m. p. 124—125° (Found: C, 74.55; H, 4.6. $C_{19}H_{14}O_4$ requires C, 74.5; H, 4.6%). This gave with hot 10% sodium hydroxide for 30 minutes, followed by acidification, the *carboxy-lactone* (XII), also obtained as follows. The bromo-lactone (0.5 g.) was heated under reflux for 40 minutes with glacial acetic acid (5 c.c.) and hydrobromic acid (34%; 5 c.c.), and the mixture poured into water (40 c.c.). The precipitate was extracted with ether, and from the ethereal layer by shaking with aqueous potassium carbonate, followed by acidification, the *carboxy-lactone* (XII) was obtained in prisms (chlorobenzene), m. p. 230—231° (Found: C, 73.4; H, 3.75. $C_{17}H_{10}O_4$ requires C, 73.4; H, 3.6%). It was also obtained from the carbethoxy-lactone (XIII) by boiling with 10% sodium hydroxide for 30 minutes. The butenolide (XII) (0.1 g.) was heated under reflux in glacial acetic acid (5 c.c.) with zinc dust (1 g.), the solution decanted into water, and the oil extracted with ether. Extraction of the ethereal layer with aqueous potassium carbonate, followed by acidification with concentrated hydrochloric acid, gave a white precipitate (0.07 g.) of 9-fluorenylsuccinic acid (V), m. p. 185—186°.

β -Bromo- β -carbethoxy- β -9-hydroxy-9-fluorenylpropionic acid lactone (XI) (0.5 g.) was heated under reflux in glacial acetic acid (10 c.c.) with zinc dust (2 g.) and the mixture added to water (50 c.c.). The precipitate on the usual treatment gave the acid (IV), m. p. 168—169° (no m. p. depression with a sample prepared as above), which was hydrolysed to 9-fluorenylsuccinic acid, m. p. 183—184°, by 10% sodium hydroxide, and esterified with methanol and sulphuric acid to methyl β -carbethoxy- β -9-fluorenylpropionate (VII).

β -Bromo- β -carboxy- β -9-hydroxy-9-fluorenylpropionic Acid Lactone (XIV).—Bromine (0.6 g.) was added to the acid (I) (1.0 g.), dissolved in hot glacial acetic acid (3 c.c.). After heating for 5 minutes, the solution was poured into water, and the oil extracted with ether. The ethereal layer was washed with water, dried (Na_2SO_4), and evaporated. The resulting oil was triturated with benzene, and the solid lactone (XIV) crystallised from chlorobenzene; m. p. 220—224°; yield 0.5 g. (Found: Br, 22.0. $C_{17}H_{11}O_4Br$ requires Br, 22.8%). A purer product was obtained by adding bromine (0.2 g.) in glacial acetic acid (2 c.c.) to a cold solution of the ethyl ester (III) (0.2 g.) in glacial acetic acid (2 c.c.) and keeping the solution for 3 hours. Water was added, the oily precipitate extracted with ether, and the ethereal layer washed several times with water, then with sodium hydrogen sulphite solution, and dried (Na_2SO_4). Evaporation gave an oil which on trituration with benzene yielded the bromo-lactone, purified by washing with benzene (3 c.c.); m. p. 224—225°, yield 0.075 g. Heating the bromo-lactone with 10% sodium hydroxide under reflux for 20 minutes and acidifying the clear solution with concentrated hydrochloric acid gave needles of the butenolide (XII), m. p. 228—230°.

Decarboxylation of β -Carbethoxy- β -9-fluorenylidenepropionic Acid (I).—The half-ester (I) (1 g.) was heated under reflux in a mixture of glacial acetic acid (20 c.c.) and hydrobromic acid (34%, 20 c.c.) for 4 hours. The solution was slowly cooled; the precipitate on crystallisation from benzene or ethanol deposited colourless needles (0.8 g.), m. p. 197—199°, undepressed when mixed with the lactone (XV) prepared as described below, and having a blue fluorescence. A similar result was obtained with the dibasic acid (II). The lactone was heated under reflux with red phosphorus (0.4 g.) and hydriodic acid (d 1.9, 5 c.c.) for 45 minutes, and the mixture added to water. The product was extracted with ether, and the ether shaken with sodium carbonate, which on acidification gave an oily solid which was extracted five times with 30-c.c. portions of boiling light petroleum (b. p. 100—120°). Cooling gave 0.47 g. of β -9-fluorenylpropionic acid (XVIII), m. p. 141—142°.

β -9-Fluorenylidenepropionic acid (XVI) (2.4 g.), prepared from acrylonitrile and fluorenone (Campbell and Fairfull, unpublished results), was dissolved in cold glacial acetic acid, and bromine (1.6 g.) added. After 3 hours, water was added and the precipitate was extracted several times with boiling light petroleum (b. p. 100—120°). On cooling 9- β -dibromo- β -9-fluorenylpropionic acid (XVII) (1.5 g.) separated; it crystallised from benzene (twice) in elongated prisms, m. p. 165—167° (Found: Br, 40.7. $C_{18}H_{12}O_2Br_2$ requires Br, 40.3%). The dibromo-acid (1.5 g.) was boiled in glacial acetic acid (10 c.c.) with zinc dust (5 g.) for 15 minutes, and the solution filtered. Addition of water and crystallisation of the precipitate from benzene gave needles, m. p. 197—199°, with a bright blue fluorescence, identical with the lactone (XV), prepared as follows. The acid (XVI) (8 g.) was heated under reflux with 10% sulphuric acid (150 c.c.) for 2 hours and poured into ice-water (150 g.). The crude lactone (7.7 g.) separated and crystallised from benzene in needles, m. p. 200—201° (Found: C, 81.2; H, 5.0. $C_{16}H_{12}O_2$ requires C, 81.3; H, 5.1%), with a bright blue fluorescence.

The acid (XVI) (2.4 g.) was catalytically reduced with Adams' platinum oxide catalyst in glacial acetic acid. The volume was then reduced to 10 c.c., and water added. The precipitate was extracted several times with boiling light petroleum (b. p. 100—120°), which on cooling deposited β -9-fluorenylpropionic acid (XVIII), m. p. 141—142° (50% yield) after several crystallisations from benzene (no m. p. depression when mixed with a sample prepared as above) (Found: C, 80.3; H, 6.25. Calc. for $C_{16}H_{14}O_2$: C, 80.6; H, 5.9%).

Di-9-fluorenylidene-succinic Acid (XIX).—Fluorenone (9 g.) in ethyl succinate (13 g.) and sodium-dried ether (600 c.c.) was gradually stirred into a suspension of sodium methoxide (7.5 g.) in dry ether (200 c.c.) cooled in ice-salt. Stirring was continued for a further 3 hours, and the mixture kept in a refrigerator for 5 days and finally at room temperature for 1 day. The ether (containing 2.2 g. of fluorenone) was removed, water (1500 c.c.) added to the aqueous residue, and the mixture boiled. Concentrated hydrochloric acid gave a dark mass (9.5 g.) of the acid (XIX) which solidified on cooling and crystallised from methanol in yellow needles (3.5 g.), m. p. 212—213° (decomp.) (Found: C, 81.1; H, 4.3; M, 420—456. $C_{30}H_{18}O_4$ requires C, 81.45; H, 4.1%; M, 442). It was not esterified by methanol-sulphuric acid, but with diazomethane gave the *dimethyl* ester, yellow octahedra (toluene), m. p. 224—225° (Found: C, 80.9; H, 4.95. $C_{32}H_{22}O_4$ requires C, 81.7; H, 4.7%), which on hydrolysis with sodium hydroxide for 1 hour gave the original acid. Attempts to form the anhydride by boiling the acid with acetyl chloride, etc. were unsuccessful.

The acid (XIX) (0.5 g.) was heated in quinoline (20 c.c.) with copper bronze (0.05 g.) (temperature of oil-bath 180°) until evolution of carbon dioxide ceased. The solution was poured into dilute hydrochloric acid (100 c.c.), and the precipitate filtered off, washed with acetone, and crystallised from xylene. Orange-red needles of di-9-fluorenylidene-ethane separated; m. p. (uncorr.) 368—370°, sublimes just below the m. p. (lit., m. p. 372—374°) (Found: C, 94.5; H, 5.2. Calc. for $C_{28}H_{18}$: C, 94.8; H, 5.2%). This gives in nitrobenzene with aluminium chloride a red colour turning to dark green, and with cold fuming sulphuric acid a beautiful blue colour changing to green. The hydrocarbon (0.2 g.) in glacial acetic acid (30 c.c.) was heated under reflux for 1 hour with zinc dust (5 g.) until the red colour had disappeared. Di-9-fluorenylethylene (0.12 g.) separated; m. p. (uncorr.) 262—263°, after crystallisation from glacial acetic acid (lit., m. p. 267—268°). This hydrocarbon (0.1 g.) was heated under reflux with sodium amalgam in aqueous alcohol (30 c.c.) for 2 hours. The solution was decanted and filtered, and on cooling deposited di-9-fluorenylethane, which after crystallisation from benzene-light petroleum had m. p. 224—225° (lit., m. p. 224—225°).

The di-acid (XIX) (5 g.) was heated under reflux in acetic acid (600 c.c.) and 34% hydrobromic acid (400 c.c.) for 24 hours. The solution was poured into ice-water (2 l.), the precipitate dissolved in boiling ethanol (charcoal), the solution filtered, and water added until the solution became turbid. The *dilactone* (XX) separated as colourless prisms, m. p. 284—286° (Found: C, 81.5; H, 4.3. $C_{30}H_{18}O_4$ requires C, 81.45; H, 4.1%). It yielded, when heated under reflux with sodium hydroxide for 2 hours, a solution which on acidification gave the di-acid.

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THE UNIVERSITY OF EDINBURGH.

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