640. *Synthesis of Fluoranthenes. Part VI. Utilization of the Mannich Reaction.*
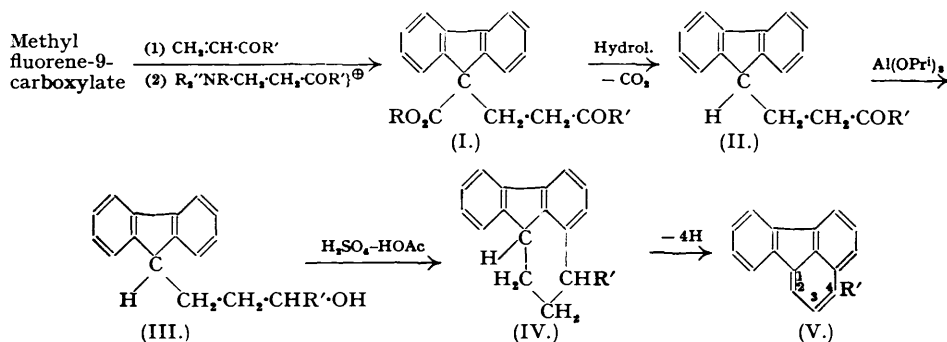
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Methyl fluorene-9-carboxylate reacts with vinyl ketones, CH_2:$CH \cdot COR$ (R = Me or Ph), or with the quaternary salts of the corresponding Mannich bases, $R_2N \cdot CH_2 \cdot CH_2 \cdot COR'$ (R' = Me or Ph), to give 2-(9-carbomethoxy-9-fluorenyl)ethyl methyl and phenyl ketones. From these two ketones 4-methyl- and 4-phenyl-fluoranthene have been synthesised.

Successful attempts have been made to prepare bis*peri*phenylenenaphthalene; these will be communicated shortly. For this work we needed 4-phenylfluoranthene, but the published method (von Braun and Manz, *Ber.*, 1937, **70**, 1610)—the action of phenylmagnesium bromide on 4-keto-1 : 2 : 3 : 4-tetrahydrofluoranthene, etc.—suffered from several disadvantages. These were overcome to some extent by an improved method of preparing the last compound (A. Campbell and Tucker, *J.*, 1949, 2623), but a more direct synthesis of 4-phenylfluoranthene has now been effected, and is described below.

Fluorene undergoes the normal Michael reaction with one molecular equivalent of an αβ-unsaturated ketone such as mesityl oxide, chalcone, or benzylideneacetone (Maitland and Tucker, *J.*, 1929, 2559; France, Maitland, and Tucker, *J.*, 1937, 1739; Tucker and Whalley, *J.*, 1949, 50; N. Campbell and Fairfull, *J.*, 1949, 1239; see also Taylor and Connor, *J. Org. Chem.*, 1941, **6**, 696; Pinck and Hilbert, *J. Amer. Chem. Soc.*, 1946, **68**, 2015); but in practice the method is not general—it has to be varied to suit each particular ketone. Employment of 9-fluorenyl-lithium extended the applicability of this reaction (Tucker and Whalley, *loc. cit.*). We have now found that the simple unsubstituted αβ-unsaturated ketones, methyl and phenyl vinyl ketone, do not combine with fluorene, the reason being that under the alkaline conditions prevailing to effect the Michael addition reaction the vinyl compound polymerises before addition can take place. This is in striking contrast to the great reactivity of vinyl cyanide, which not only undergoes the Michael addition reaction with fluorene, but reacts with both the 9-hydrogen atoms to give the di-addition product, 9 : 9-di-(2-cyanoethyl)fluorene (Bruson, *J. Amer. Chem. Soc.*, 1942, **64**, 2457). On the other hand, 2-methylvinyl cyanide (crotononitrile) combines with fluorene directly in 1 : 1 molecular proportion (Bruson, *loc. cit.*); but there is no comparable example. It was on account of these results that we turned to the use of the fluorene-9-carboxylic esters, which have—as far as the Michael reaction is concerned—two advantages : they possess only one reactive hydrogen atom, and that more reactive than either of the two hydrogen atoms at position 9 in fluorene (Tucker, *J.*, 1949, 2182; A. Campbell and Tucker, *ibid.*, p. 2623; cf. N. Campbell and Fairfull, *loc. cit.*, who showed that 9-phenyl- and 9-hydroxy-fluorene underwent the Michael reaction with vinyl cyanide). Condensation of fluorene-9-carboxylic esters with αβ-unsaturated ketones and cyanides has been uniformly successful, qualitatively and quantitatively, in providing 1 : 1 adducts uncontaminated by 1 : 2 addition products. Furthermore, this method is valuable not only on account of its wide applicability but

because the products readily give definitely oriented derivatives of fluoranthene (Tucker, *loc. cit.*; A. Campbell and Tucker, *loc. cit.*). We now find that although, as stated, methyl and phenyl vinyl ketones do not react with fluorene, they do so with methyl fluorene-9-carboxylate to give the expected products 2-(9-carbomethoxy-9-fluorenyl)ethyl methyl ketone (I; R = R′ = Me) and the corresponding phenyl ketone (I; R = Me, R′ = Ph), respectively, in good yield.

Methyl fluorene-9-carboxylate
$\xrightarrow[\text{(2) } R_3''NR \cdot CH_2 \cdot CH_2 \cdot COR']{\text{(1) } CH_2 \cdot CH \cdot COR'}$

(I.)   RO₂C   CH₂·CH₂·COR′

$\xrightarrow[-CO_2]{\text{Hydrol.}}$

(II.)   H   CH₂·CH₂·COR′

$\xrightarrow{\text{Al(OPr}^i)_3}$

(III.)   H   CH₂·CH₂·CHR′·OH

$\xrightarrow{H_2SO_4-HOAc}$

(IV.)   H   H₂C   CHR′   CH₂

$\xrightarrow{-4H}$

(V.)   R′

Vinyl compounds are, however, in general, prone to polymerise; accordingly, we turned our attention to the preparation of Mannich bases (Blicke, " Organic Reactions," 1942, I, p. 303), which, as is well known, can when appropriately treated give vinyl ketones, or, better, may be used directly in place of vinyl derivatives. For instance, it was found by du Feu, McQuillin, and Robinson (*J.*, 1937, 53) that methiodides of Mannich bases condensed with the sodio-derivatives of reactive methylene compounds to give the same ketones as those derivable by the Michael reaction of the methylene compound and the vinyl ketone corresponding to the Mannich base. We have found, in fact, that methyl 2-morpholinoethyl ketone, after conversion into the methiodide, reacted with methyl fluorene-9-carboxylate to give 2-(9-carbomethoxy-9-fluorenyl)ethyl methyl ketone (I; R = R′ = Me). In preparation of the methiodide care was taken to remove excess of methyl iodide. This was found to be necessary since use of methyl sulphate instead of methyl iodide in this reaction gave methyl 9-methylfluorene-9-carboxylate as sole product—clearly, the competitive methylation reaction of MeSO₄⁻ on the fluorene ester took place exclusively. On the other hand, the Mannich base, 2-diethylaminoethyl phenyl ketone gave a quaternary salt with methyl sulphate which reacted normally with methyl fluorene-9-carboxylate to give 2-(9-carbomethoxy-9-fluorenyl)ethyl phenyl ketone (I; R = Me, R′ = Ph). That there is no fundamental difference in mode of reaction of the two Mannich bases is shown by the fact that, as mentioned above, when the quaternary salt is free from methylating agent the methyl keto-compound reacts in the same manner as the phenyl keto-compound. It may be that the incipiently-formed vinyl compound from the latter is liberated much more rapidly than from the former, thus cutting out the competitive methylation process. It is clear that in reactions of these Mannich salts with fluorenecarboxylic esters, methyl sulphate is, in general, to be avoided.

Michael addition of the free vinyl ketones to methyl fluorene-9-carboxylate was carried out in dioxan, 0·2 mole of potassium hydroxide being used. As found in earlier researches (Tucker, *loc. cit.*; A. Campbell and Tucker, *loc. cit.*), increasing the amount of potassium hydroxide to one equivalent lowered the yield of addition product. The addition products were converted into 4-methyl- and 4-phenyl-fluoranthene by the series of reactions indicated by (I)—(V). Reduction of (II; R′ = Me or Ph) by aluminium *iso*propoxide in *iso*propanol gave (III), which readily cyclised in a mixture of concentrated sulphuric acid and glacial acetic acid to (IV; R′ = Me or Ph). Attempts to cyclise (II) by means of hydrogen bromide, so successful with analogous compounds, failed (cf. Bradsher and Smith, *J. Amer. Chem. Soc.*, 1943, **65**, 854, 1643; Bradsher and Kittila, *ibid.*, 1950, **72**, 277; France, Tucker, and Forrest, *loc. cit.*). Ring closure of (II; R′ = Me) to give (IV; R′ = Me) was effected in poor yield by boiling it in glacial acetic acid with hydriodic acid solution. We have already shown that, when there are substituents on the carbon atoms α and/or β to the keto-group, cyclisation by means of hydrogen bromide or iodide is easy.

Attempts to effect cyclisation of amines corresponding to the carbinols (III; NH₂ in place of OH) failed. The amines were prepared by hydrogenation of the oximes of (II) (Hartung, *J. Amer. Chem. Soc.*, 1928, **50**, 3370; 1931, **53**, 2248; Fodor *et al.*, *J.*, 1948, 885, 1949, 1681).

Dehydrogenation of (IV; R′ = Me or Ph) was accomplished either by boiling it with chloranil in xylene solution (Clar and John, *Ber.*, 1930, **63**, 2967; 1931, **64**, 98; Tucker, *J.*, 1949, 2182), or by heating it with sulphur.

Although fluorene-9-carboxylic acid is now readily available (Yost and Hauser, *J. Amer. Chem. Soc.*, 1947, **69**, 2326; Tucker and Whalley, *loc. cit.*; A. Campbell and Tucker, *loc. cit.*; Arnold, Parham, and Dodson, *J. Amer. Chem. Soc.*, 1949, **71**, 2439), we tried for theoretical reasons to prepare it by oxidation of 9-formylfluorene (Von and Wagner, *J. Org. Chem.*, 1944, **9**, 155; but cf. Wislicenus and Waldmüller, *Ber.*, 1909, **42**, 785; Wislicenus and Russ, *Ber.*, 1910, **43**, 2719, who claim to have isolated two forms) by hydrogen peroxide in acetic acid; but instead of fluorene-9-carboxylic acid an unidentified compound was isolated. Although 9-fluorenyl-lithium reacts with methyl carbonate to give methyl fluorene-9-carboxylate (Blum-Bergmann, *Annalen*, 1930, **484**, 47; yield not given) we were unable to obtain any ester by the corresponding action of 9-fluorenylpotassium on ethyl carbonate; but ethyl chloroformate gave ethyl fluorene-9-carboxylate (36%).

EXPERIMENTAL.

2-(9-Carbomethoxy-9-fluorenyl)ethyl Methyl Ketone (I; R = R′ = Me).—(a) Methyl fluorene-9-carboxylate (11·2 g., 1 mol.) and methyl vinyl ketone (3·5 g., 1 mol.) were dissolved in dry dioxan (55 ml.), and dry, powdered potassium hydroxide (0·56 g., 0·2 mol.) was added. The mixture was kept for 24 hours (warming was observed during the first 15 minutes), during which the potassium hydroxide went into solution. Pouring into water, extraction with ether, and evaporation of the ether gave *2-(9-carbomethoxy-9-fluorenyl)ethyl methyl ketone*, which crystallised from methanol or ethanol in leaflets (10·5 g., 71%), m. p. 101—103° (Found : C, 77·5; H, 6·2. $C_{19}H_{18}O_3$ requires C, 77·5; H, 6·2%). When the quantity of potassium hydroxide was increased to 2·8 g. (1 mol.) the product required repeated crystallisation for purification, and the yield was substantially lower. The addition of pyridine (1 ml.) had no effect on the yield.

(b) Methyl iodide (1 g., slight excess) was mixed with methyl 2-morpholinoethyl ketone (1 g.) (Harradence and Lions, *J. Proc. Roy. Soc. N. S. Wales*, 1938, **72**, 233), and the excess of methyl iodide removed from the pasty methiodide by applying water-pump vacuum for 30 minutes. The methiodide, which had a slight smell of methyl vinyl ketone, was washed with methanol (5 ml.) into a solution of methyl fluorene-9-carboxylate (1·42 g.) and sodium (0·15 g.) in methanol (5 ml.), and the resulting mixture boiled (90 minutes). On cooling, crystals (0·8 g., 45%) were deposited, the m. p. of which and of a mixture with an authentic specimen of 2-(9-carbomethoxy-9-fluorenyl)ethyl methyl ketone was 101—102°.

2-(9-Carboxy-9-fluorenyl)ethyl Methyl Ketone (I; R = H, R′ = Me).—The above methyl ester was dissolved in hot ethanol and treated with a small amount of 10N-potassium hydroxide solution. Working up in the usual manner gave 2-(9-carboxy-9-fluorenyl)ethyl methyl ketone, which crystallised from methyl cyanide in prisms, m. p. 108—113° (decomp.) (Found : C, 72·2, 72·4; H, 5·8, 5·9. Calc. for $C_{18}H_{16}O_3$: C, 77·1; H, 5·8%).

2-9′-Fluorenylethyl Methyl Ketone (II; R′ = Me).—The above acid was warmed gently with 10N-potassium hydroxide solution. When the vigorous effervescence ceased the mixture was diluted with water and the precipitated oil extracted with ether. Evaporation of the ether, after its washing with water, gave 2-9′-fluorenylethyl methyl ketone (96%), which crystallised from methanol in prisms, m. p. 75—76° (Found : C, 86·1; H, 6·8. $C_{17}H_{16}O$ requires C, 86·4; H, 6·8%). The oxime crystallised from ethanol in a mixture of sword-blades and feathery needles (possibly the two stereoisomers), m. p. 121—123° (Found : C, 81·1; H, 6·5; N, 5·4. $C_{17}H_{17}ON$ requires C, 81·2; H, 6·8; N, 5·6%).

4-9′-Fluorenylbutan-2-ol (III; R′ = Me).—The above ketone was heated with three molecules (9 equivs.) of aluminium *iso*propoxide in *iso*propanol till no more acetone was present in the distillate (*ca.* 1 hour). Most of the remaining *iso*propanol was distilled off under slightly reduced pressure and, after acidification and extraction with ether, the oily residue from evaporation of the ether crystallised at 0° from light petroleum (b. p. 60—80°) in needles, m. p. 45—49° (Found : C, 82·9, 83·1; H, 7·6, 7·4. Calc. for $C_{17}H_{18}O$: C, 85·7; H, 7·6%).

1 : 2 : 3 : 4-Tetrahydro-4-methylfluoranthene (IV; R′ = Me).—The above carbinol (1·7 g.) was dissolved in glacial acetic acid (7 ml.), and a mixture of acetic acid (7 ml.) and sulphuric acid (7 ml.) added. The mixture was warmed on the steam-bath (5 minutes) and diluted with water, the precipitated oil was extracted with ether and washed with sodium hydrogen carbonate solution and water, and the ether evaporated off. The residue distilled at 120—130° (bath-temp.) at 1 mm., yielding 1 : 2 : 3 : 4-tetrahydro-4-methylfluoranthene (1·25 g., 80%), m. p. 32—37°, which liquefied when mixed with the carbinol at room temperature. With 2 : 4 : 7-trinitrofluorenone in acetic acid it formed a *complex*, crystallising from acetic acid in orange needles, m. p. 131—133° (Found : C, 67·5; H, 4·0; N, 7·9. $C_{17}H_{16},C_{13}H_5O_7N_3$ requires C, 67·3; H, 3·95; N, 7·85%).

4-Methylfluoranthene (V; R′ = Me).—The above tetrahydro-compound (0·11 g.), chloranil (0·245 g.), and xylene (1 ml.) were boiled for 1 hour, during which the solution changed from blood-red to pale brown with deposition of pale brown needles of tetrachloroquinol. After cooling and filtration, the filtrate was diluted with ether, extracted with 5% sodium hydroxide solution, washed with water, and evaporated. The residue (0·09 g., 83%) crystallised from ethanol in pale green sword-blades of 4-methyl-fluoranthene, m. p. 65—66° (von Braun and Manz, *loc. cit.*, give m. p. 66°). It formed a picrate, crystallising as orange needles from ethanol, m. p. 171—173° (von Braun and Manz, *loc. cit.*, give m. p. 172°).

Methyl 9-Methylfluorene-9-carboxylate.—Methyl sulphate (3·15 g.) was added slowly with cooling to a solution of sodium methoxide (from 0·575 g. of sodium), methyl 2-morpholinoethyl ketone (3·925 g.), and methyl fluorene-9-carboxylate (5·6 g.) in methanol (80 ml.). Colourless crystals (2·5 g.) of *methyl 9-methylfluorene-9-carboxylate* were deposited during 4 days' storage at room temperature. Dilution of the filtrate with water gave, on crystallisation of the oily residue, a further 2·5 g. (total yield, 84%). Crystallisation from methanol gave sword-blades, m. p. 108—109° (Found : C, 80·7; H, 5·8. $C_{16}H_{14}O_2$ requires C, 80·7; H, 5·9%).

9-Methylfluorene-9-carboxylic Acid.—The above ester was hydrolysed by the addition of 10N-potassium hydroxide solution to a hot ethanolic solution. The acid crystallised from carbon tetra-chloride in needles, m. p. 168—169° (Found : C, 80·6; H, 5·2. Calc. for $C_{15}H_{12}O_2$: C, 80·3; H, 5·4%).

9-Methylfluorene.—Boiling (15 minutes) either the above ester or the acid with 2-methoxyethanol and an equal volume of 10N-potassium hydroxide solution, dilution with water, and extraction with ether gave, on evaporation of the ether, 9-methylfluorene, which, crystallised from ethanol, had m. p. 45—47°

2-(9-Carbomethoxy-9-fluorenyl)ethyl Phenyl Ketone (I; R = Me, R′ = Ph).—(a) Methyl fluorene-9-carboxylate (2·24 g., 1 mol.) and phenyl vinyl ketone (1·32 g., 1 mol.) (Young and Roberts, *J. Amer. Chem. Soc.*, 1946, **68**, 651; Leslie and Henze, *ibid.*, 1949, **71**, 3480) were dissolved in dry dioxan (11 ml.), and dry powdered potassium hydroxide (0·11 g., 0·2 mol.) was added. On being kept for 7 days with occasional shaking and worked up in the usual manner, this gave 2-*carbomethoxy-9-fluorenyl)ethyl phenyl ketone* (2 g., 56%) in prisms (from methanol), m. p. 110—111° (Found : C, 80·9; H, 5·6. $C_{24}H_{20}O_3$ requires C, 80·9; H, 5·7%).

(b) Methyl fluorene-9-carboxylate (28·4 g., 1 mol.) was added to a solution of sodium (2·92 g., 1 atom) in anhydrous methanol (125 ml.), and to this was added a mixture of 2-diethylaminoethyl phenyl ketone (26·1 g., 1 mol.) (Young and Roberts, *loc. cit.*), anhydrous methanol (64 ml.), and methyl sulphate (15·9 g., 1 mol.—added cautiously with cooling). After the mixture had been boiled (30 minutes) and then cooled in ice, prisms (34·5 g., 83%) of practically pure 2-(9-carbomethoxy-9-fluorenyl)ethyl phenyl ketone, m. p. 110—111°, were deposited.

(c) The use of 2-morpholinoethyl phenyl ketone (Harradence and Lions, *loc. cit.*) in place of 2-diethyl-aminoethyl phenyl ketone gave a lower yield of the above product.

The Mannich bases used above were prepared from their hydrochlorides immediately before use, since the hydrochlorides were stable and could be kept for several months, whereas the free bases decomposed on storage and their use after some weeks led to decreased yields.

2-(9-Carboxy-9-fluorenyl)ethyl Phenyl Ketone (I; R = H, R′ = Ph).—The above ester, dissolved in hot ethanol, was hydrolysed in the usual manner by addition of 10N-potassium hydroxide solution, to give the *ketone*, which crystallised from acetic acid in colourless sword-blades, m. p. 174—179° (Found : C, 80·1, 80·3; H, 5·1, 5·5. $C_{23}H_{18}O_3$ requires C, 80·7; H, 5·3%).

2-9′-Fluorenylethyl Phenyl Ketone (II; R′ = Ph).—The above acid (3·2 g.) was warmed with 10N-potassium hydroxide solution till the vigorous effervescence ceased (5 minutes). Dilution of the mixture with water and extraction with ether gave, on evaporation of the ether, 2-9′-*fluorenylethyl phenyl ketone* (2·7 g., 96%), which crystallised from ethanol or light petroleum (b. p. 60—80°) in needles, m. p. 80—81° (Found : C, 88·9; H, 6·3. $C_{22}H_{18}O$ requires C, 88·6; H, 6·1%). The *oxime* crystallised from light petroleum (b. p. 60—80°) in white needles, m. p. 135—140° (Found : C, 84·3; H, 6·1; N, 4·5. $C_{22}H_{19}ON$ requires C, 84·3; H, 6·1; N, 4·5%). Reduction of an ethanolic solution of the *oxime* (containing 3 equivs. of dry hydrogen chloride), with hydrogen in the presence of a palladium–charcoal catalyst gave 3-9′-*fluorenyl-1-phenylpropylamine hydrochloride*. Crystallisation from ethanol–ether yielded needles, m. p. 240—242° (Found : C, 78·7; H, 6·7; N, 4·1. $C_{22}H_{22}NCl$ requires C, 78·7; H, 6·6; N, 4·2%).

1 : 2 : 3 : 4-*Tetrahydro-4-phenylfluoranthene* (IV; R′ = Ph).—2-9′-Fluorenylethyl phenyl ketone in *iso*propanol solution was heated with 3 moles (9 equivs.) of aluminium *iso*propoxide till no more acetone was present in the distillate. Working up in the usual manner gave an uncrystallisable oily residue. Warming (5 minutes) the oil in solution in acetic acid (1 vol.) with a mixture of acetic acid (1 vol.) and sulphuric acid (1 vol.) gave, after the usual treatment, an oily solid, which, when mixed with acetone and crystallised from ethanol or acetone, gave prisms of 1 : 2 : 3 : 4-*tetrahydro-4-phenylfluoranthene*, m. p. 110—112° (Found : C 93·8; H, 6·5. $C_{22}H_{18}$ requires C, 93·6; H, 6·4%).

4-Phenylfluoranthene (V; R′ = Ph).—(1) *By use of chloranil*. The above tetrahydro-compound (0·141 g.), chloranil (0·246 g.), and xylene (1 ml.) were boiled till no more tetrachloroquinol was deposited (*ca.* 24 hours). Working up in the usual manner gave a yellow solid, m. p. 120—134°. A solution of this in light petroleum (b. p. 60—80°) was chromatographed (alumina). The first colourless eluate, fluorescing pale blue in daylight and strong green-blue in ultra-violet light, yielded 4-phenylfluoranthene, which crystallised from ethanol in pale green needles, m. p. 141—143° (von Braun and Manz, *loc. cit.*, give m. p. 144°).

(2) *By use of sulphur*. The above tetrahydro-compound (0·5 g.) and sulphur (0·12 g.) were heated at 190—200°, a vigorous evolution of hydrogen sulphide occurring. The effervescence slackened after 45 minutes, and no further evolution of gas took place when the mixture was heated to 230°. After cooling, the residue was dissolved in light petroleum (b. p. 60—80°) and chromatographed (alumina). Sulphur-containing compounds were retained as yellow and brown bands, 4-phenylfluoranthene passing through as a colourless, pale blue-fluorescent solution, evaporation of which gave 4-phenylfluoranthene (0·42 g., 84%), m. p. 142—144°. Sublimation from zinc dust in vacuum, and crystallisation, failed to separate 4-phenylfluoranthene from sulphur-containing compounds.

Oxidation of 9-Formylfluorene.—9-Formylfluorene (2·8 g.), acetic acid (10 ml.), and hydrogen peroxide (5 ml.; 30% solution) were mixed and kept (4—5 hours) at room temperature; a pale yellow solid separated, and crystallisation from benzene gave a *product* as colourless needles, m. p. 130—

135° (with reddening and decomp.). It became pink in air and was not acidic (Found : C, 77·4; H, 5·4. $C_{12}H_{10}O_2$ requires C, 77·4; H, 5·4%).

Action of 9-Fluorenylpotassium on Ethyl Chloroformate.—9-Fluorenylpotassium, prepared from fluorene (1·66 g.) and potassium (0·43 g.) in liquid ammonia, was suspended in dry ether (50 ml.), which was boiled (15 minutes) to remove all the ammonia, and ethyl chloroformate (1·1 g., theoretical quantity) added. After the boiling solution had been stirred for 30 minutes it was kept at room temperature overnight, then poured into water, and separated, and the ethereal layer evaporated. Warming of the residue with dilute sodium hydroxide in ethanol solution, dilution with water, extraction with ether, and acidification of the aqueous layer gave fluorene-9-carboxylic acid (0·34 g.); the ethereal extract gave fluorene (1 g.). (Yield, 36% of ethyl fluorene-9-carboxylate, calculated on unrecovered fluorene.)