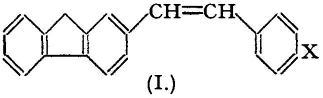
140. *Derivatives of 2-Styrylfluorene.*

By (Miss) E. F. M. Stephenson.

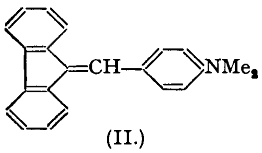
A series of derivatives of 2-styrylfluorene (type I) has been prepared by standard methods and is being tested for tumour-inhibitory action. In certain cases both geometrical isomerides have been obtained.

The tumour-inhibitory (and carcinogenic) activity of certain *trans*-stilbene derivatives containing basic substituents has been reported (*24th Annual Report of the British Empire Cancer Campaign*, 1947, p. **37**; Haddow, Harris, and Kon, *Biochem. J.*, 1945, **39**, Proc. ii). It seemed of interest, therefore, to examine analogous derivatives of 2-styrylfluorene, especially as the fluorene derivative (II) has already been found to inhibit tumour growth (Haddow, Harris, and Kon, *loc. cit.*). A number of 2-styrylfluorenes have now been synthesised and are being tested for biological activity by Professor A. Haddow. The *p*-substituents in the phenyl group were not limited to basic substituents.



(I.)

(I*a*; X = H.) (I*b*; X = NO_2.) (I*c*; X = NHAc.)
(I*d*; X = OMe.) (I*e*; X = Cl.) (I*f*; X = NMe_2.)



(II.)

For the preparation of the α-(2-fluorenyl)cinnamic acids (III) satisfactory results were obtained, where X = H, NO_2, OMe, and Cl, by using a Perkin condensation between the triethylamine salt of fluorene-2-acetic acid and the appropriate aldehyde. This led to a series of substituted cinnamic acids in all of which the two aryl groups presumably occupy *cis*-positions (compare Ruggli and Staub, *Helv. Chim. Acta*, 1936, **19**, 1288; 1937, **20**, **37**; Ruggli and Dinger, *ibid.*, 1941, **24**, 173). Similar condensation of *p*-dimethylaminobenzaldehyde gave a poor yield (<10%) of the cinnamic acid. Decarboxylation of the cinnamic acids with copper chromite and quinoline gave the 2-styrylfluorenes. It would be expected from earlier studies that in these stilbene derivatives the *cis*-configuration would be largely retained (Ruggli and Staub, *loc. cit.*; Taylor and Hobson, *J.*, 1936, 181; Zechmeister and McNeely, *J. Amer. Chem. Soc.*, 1942, **64**, 1919; *idem*, with Solyom, *ibid.*, p. 1922). This view was supported by the fact that in four cases (I*a*, I*b*, I*d*, I*e*) the pure products which were isolated were converted into higher-melting, probably *trans*-, isomerides by iodine in boiling benzene solution. Moreover, in two cases (I*a*, I*b*) the same higher-melting isomerides were synthesised by Meerwein's procedure, which is known to give *trans*-stilbenes. For this purpose, fluorene-2-diazonium chloride was allowed to react with cinnamic and *p*-nitrocinnamic acids which gave, respectively, trans-2-*styrylfluorene* (I*a*) and trans-2-p-*nitrostyrylfluorene* (I*b*) (compare Meerwein, Büchner, and van Emster, *J. pr. Chem.*, 1939, **152**, 237; Bergmann and Weinberg, *J. Org. Chem.*, 1941, **6**, 134; Bergmann, Weizman, and Schapiro, *ibid.*, 1944, **9**, 408; Bergmann and Schapiro, *ibid.*, 1947, **12**, 57).

The Friedel–Crafts reaction between *p*-nitrophenylacetyl chloride and fluorene gave 2-(p-*nitrophenylacetyl*)*fluorene* (IV). The carbonyl group in this was reduced with aluminium *iso*propoxide and the resulting *carbinol* was dehydrated to give, in small yield, *trans*-2-*p*-nitrostyrylfluorene (I*b*). This method of preparation provides additional evidence for the *trans*-configuration. Reduction of this nitro-compound with stannous chloride, followed by acetylation of the crude amine, gave trans-2-p-*acetamidostyrylfluorene* (I*c*).

$p\text{-X}\cdot C_6H_4\cdot CH{:}CR\cdot CO_2H$
(III.)

$p\text{-}NO_2\cdot C_6H_4\cdot CH_2\cdot COR$
(IV.)

(III*a*; X = H.) (III*b*; X = NO_2.) (III*c*; X = NH_2.) (III*d*; X = OMe.)
(III*e*; X = Cl.) (III*f*; X = NMe_2.)

$p\text{-OMe}\cdot C_6H_4\cdot CO\cdot CH_2R$
(V.)

$p\text{-}NH_2\cdot C_6H_4\cdot CH_2\cdot CHR\cdot CO_2H$
(VI.)

$p\text{-OMe}\cdot C_6H_4\cdot CH_2\cdot CHR\cdot NH_2$
(VII.)

[In (III—VII), R = 2-fluorenyl.]

2-p-*Dimethylaminostyrylfluorene* (I*f*) was obtained as a by-product in the Perkin reaction between fluorene-2-acetic acid and *p*-dimethylaminobenzaldehyde, using the triethylamine salt of the acid, but was more suitably prepared by condensing the acid with the aldehyde by means of piperidine. This product probably had the *trans*-configuration (compare Bachman and Hoaglin, *J. Org. Chem.*, 1943, **8**, 300).

Kuhn and Winterstein's modification (*Helv. Chim. Acta*, 1928, **11**, 103) of the Perkin reaction often favours production of the *trans*-stilbene at the expense of the cinnamic acid (compare Bachman and Hoaglin, *loc. cit.*; Bergmann *et al.*, *loc. cit.*). When, however, it was applied to *p*-nitrobenzaldehyde, (I*b*) was not formed, (III*b*) being the only product isolated.

Fluorene-2-acetyl chloride and anisole reacted in presence of aluminium chloride to give p-*methoxyphenyl* 2-*fluorenylmethyl ketone* (V). Miscellaneous compounds of related structures, including (VI), are described in the experimental section.

EXPERIMENTAL.

(All m. p.s are uncorrected.)

Perkin Condensations.—The general procedure was as follows: A mixture of fluorene-2-acetic acid (1 mol.), the aromatic aldehyde (5—20% excess), triethylamine (1 mol.), and acetic anhydride (3 or more mols.) was heated at 90—100° (oil-bath temp.) for 11—12 hours, and the still warm solution poured into water. After standing for 12 hours the mixture was heated on the water-bath until the oily product solidified (1—2 hours). The crude acid was collected, washed, and converted into its sparingly soluble sodium (or potassium) salt, and the latter was collected and washed with benzene until the washings were colourless. The residual salt was dissolved in hot water (charcoal, and a filter aid) and the acid was recovered by acidification of the filtrate. Where a comparison was made the triethylamine salt gave better yields in the Perkin condensation than the sodium or potassium salts. In the case of (III*b*) heating at 85—95° was preferable (compare Amstutz and Spitzmiller, *J. Amer. Chem. Soc.*, 1943, **65**, 367); in that of (III*f*) a red resin was obtained after heating on the water-bath but could be worked up by the usual procedure. For (III*e*) the Perkin reaction was carried out under a nitrogen atmosphere.

The α-(2-fluorenyl)cinnamic acids were then further purified as follows.

cis-p-*Nitro*-α-(2-*fluorenyl*)*cinnamic acid* (III*b*). 4·5 G. of an acid, m. p. 259—261°, were obtained from 5·6 g. of fluorene-2-acetic acid. This was sufficiently pure for decarboxylation. For analysis, the *acid* was crystallised twice from 90% acetic acid and then from alcohol, giving bright yellow platelets, m. p. 262—263° (decomp.) (Found: C, 73·9; H, 4·3; N, 3·9. $C_{22}H_{15}O_4N$ requires C, 73·9; H, 4·2; N, 3·9%).

cis-p-*Chloro*-α-(2-*fluorenyl*)*cinnamic acid* (III*e*). 8·96 G. of fluorene-2-acetic acid gave 6·9 g. of this *acid* (cream-coloured crystals, m. p. 236·5—238·5°). For analysis it was recrystallised from benzene, 3 times from 90% acetic acid, and again from benzene, giving cream-coloured needles or prisms, m. p. 245—245·5° (Found : C, 76·0; H, 4·35; Cl, 10·3. $C_{22}H_{15}O_2Cl$ requires C, 76·2; H, 4·4; Cl, 10·2%).

cis-p-*Methoxy-α-(2-fluorenyl)cinnamic acid* (III*d*). 2·24 G. of fluorene-2-acetic acid gave 1·25 g. of colourless *acid*, m. p. 271—272° (slight decomp.). After recrystallisation from 90% acetic acid and then alcohol, it formed pale cream needles or prisms, m. p. 273—274·5° (Found : C, 80·7; H, 5·2. $C_{23}H_{18}O_3$ requires C, 80·7; H, 5·3%).

cis-*α-(2-Fluorenyl)cinnamic acid* (III*a*). 2·24 G. of fluorene-2-acetic acid gave 1·89 g. of an *acid*, m. p. 217—219°. After 3 recrystallisations from 90% alcohol it formed small colourless needles, m. p. 220—222° (slight decomp.) (Found : C, 84·4; H, 5·2. $C_{22}H_{16}O_2$ requires C, 84·6; H, 5·2%).

cis-p-*Dimethylamino-α-(2-fluorenyl)cinnamic acid* (III*f*). 3·36 G. of fluorene-2-acetic acid gave 250 mg. of the *acid* (III*f*), m. p. 272—274° (decomp.). Crystallised twice from xylene, it gave bright yellow needles, m. p. 273—274° (decomp.) (Found : C, 81·2; H, 5·8; N, 3·8. $C_{24}H_{21}O_2N$ requires C, 81·1; H, 6·0; N, 3·9%).

cis-p-*Amino-α-(2-fluorenyl)cinnamic acid* (III*c*). A mixture of ferrous sulphate (22 g.) in water (50 ml.), (III*b*) (2·7 g.) in water (100 ml.) and concentrated ammonia (140 ml.) was heated on the water-bath for 2 hours and then boiled for a few minutes. The precipitate was filtered (filter aid) and washed repeatedly with hot 1% ammonia until practically free from acid. Acidification of the alkaline filtrate with acetic acid gave the crude *amino-acid*. It was collected, dissolved in hot sodium carbonate solution, and the solution filtered (filter aid). After several crystallisations from 90% alcohol, the recovered acid (2·2 g.) was obtained as dull yellow crystals, m. p. 250·5—252° (decomp.) (Found : C, 80·9; H, 5·4; N, 4·2. $C_{22}H_{17}O_2N$ requires C, 80·7; H, 5·25; N, 4·3%).

Decarboxylation of (III*a*, *b*, *d*, and *e*) was effected by heating a solution of the acid (0·005 mol.) in quinoline (20 ml.) with copper powder (Gattermann, *Ber.*, 1890, **23**, 1219; dried immediately before use) or with copper chromite, at 205—215° (metal-bath temp.) for 10—12 minutes, the initial brisk reaction then having almost ceased. The still warm mixture was poured into light petroleum (250 ml.; b. p. 60—80°; but benzene was used for I*b*), filtered, and the filtrate shaken repeatedly with dilute hydrochloric acid, and washed with water and then with sodium carbonate solution. Acidification of the sodium carbonate extract showed that decarboxylation was practically complete. The organic solution was dried (Na_2SO_4) and chromatographed on a column of alumina (B.D.H.; 10 × 2 cm.) at room temperature. For (I*a*, *d*, and *e*) a broad, homogeneous, colourless band, weakly fluorescent in ultraviolet light, passed first down the column, followed by a narrow, colourless, more strongly fluorescent band and then by miscellaneous coloured zones. [For (I*a*, *d*, and *c*) elutions were carried out with light petroleum (b. p. 60—80°).] To obtain a separation of (I*b*) it was necessary to pass the solution (in benzene, in this case) through several columns of alumina (10 × 2 cm.). No *trans*-isomeride was isolated. The substitution of copper powder by copper chromite did not noticeably increase the yields. The *cis*-2-styrylfluorenes were then further purified as follows :

cis-2-p-*Nitrostyrylfluorene* (I*b*). After crystallisation from light petroleum (b. p. 80—100°) containing a little benzene, the sticky crystalline residue from chromatography gave 150 mg. of bright yellow needles, m. p. 134—135·5°. Crystallisation from alcohol gave the *nitro*-compound in bright yellow needles, m. p. 134—136° (Found : C, 80·7; H, 4·9; N, 4·5. $C_{21}H_{15}O_2N$ requires C, 80·4; H, 4·8; N, 4·5%). Other methods of decarboxylation were tried but no improvement in yields was obtained.

cis-2-p-*Chlorostyrylfluorene* (I*e*). After chromatography there remained 0·82 g. (54% of the theoretical amount), m. p. 97—99°. Decarboxylation of larger quantities gave smaller yields. This was also the case with the other cinnamic acids. For analysis, the *chloro*-compound (I*e*) was crystallised from alcohol, giving colourless needles, m. p. 103·5—104° (Found : C, 83·5; H, 5·2; Cl, 11·6. $C_{21}H_{15}Cl$ requires C, 83·3; H, 5·0; Cl, 11·7%).

cis-2-p-*Methoxystyrylfluorene* (I*d*). 0·9 G. (60% of the theoretical amount) of a sticky, crystalline product was obtained after chromatography. After two crystallisations from alcohol, the *fluorene* was obtained as shiny plates, m. p. 91—91·5° (Found : C, 88·7; H, 6·2. $C_{22}H_{18}O$ requires C, 88·5; H, 6·1%).

cis-2-*Styrylfluorene* (I*a*). A yield of 64% of the theoretical amount of the *fluorene* was obtained after chromatography. Two crystallisations from alcohol gave shiny plates, m. p. 74·5—75·0° (Found : C, 94·2; H, 6·0. $C_{21}H_{16}$ requires C, 94·0; H, 6·0%). For the isomerisation of the *cis*-2-styrylfluorenes to their *trans*-isomerides the following procedure was adopted. The *cis*-compound was dissolved in pure, dry benzene, a crystal of iodine added, and the benzene distilled; the *trans*-isomeride usually separated from the hot solution during the distillation. The crystalline residue was maintained at 140—150° (oil-bath temp.) for a further 10—15 minutes, then cooled, stirred with sulphurous acid solution, collected, and washed. The *trans*-2-styrylfluorenes were then further purified as follows.

trans-2-p-*Nitrostyrylfluorene* (I*b*). (*a*) The isomerised *product* was crystallised from benzene–alcohol (4 : 1) and then melted at 222—223°, to an opalescent liquid which became clear at 252—253° (slight decomp.) (Found : C, 80·6; H, 4·9; N, 4·4. $C_{21}H_{15}O_2N$ requires C, 80·4; H, 4·8; N, 4·5%). The *trans*-chloro- and -methoxy-compounds also showed liquid-crystal formation (compare Weygand and Gabler, *Ber.*, 1938, **71**, 2474).

(*b*) A suspension of 2-fluorenediazonium chloride prepared from 2-aminofluorene (0·91 g., 0·005 mol.), concentrated hydrochloric acid (1·5 ml.), water (7·5 ml.), and sodium nitrite (0·4 g.) in water (2·5 ml.) was added to *p*-nitrocinnamic acid (0·97 g.; 0·005 mol.) suspended in " AnalaR " acetone (130 ml.), and solutions of sodium acetate (2 g. in 6·5 ml. of water) and cupric chloride (0·86 g. in 2·5 ml. of water) were immediately added. The temperature was then adjusted so that steady evolution of gas took place (30—40°). After 1—1·5 hours reaction was complete. The reaction mixture was steam-distilled to remove acetone, chloroacetone, fluorene, and 2-chlorofluorene, and the brown solid residue was collected, extracted with hot sodium carbonate solution, and again filtered. Acidification of the combined filtrates gave 0·85 g. of *p*-nitrocinnamic acid. The dry carbonate-insoluble material was shaken with benzene, and the solution chromatographed on alumina; a bright yellow zone separated first and yielded a slightly sticky, yellow crystalline residue (15—20 mg.) which after washing with alcohol had m. p. 218·5—219·5° (to an opalescent liquid). After crystallisation from benzene–alcohol (4 : 1), the product had m. p. 221·5—222·5° to an opalescent liquid which became clear at 252—253° (slight decomp.). A mixed m. p. with the product obtained by method (*a*) gave no depression.

(*c*) Pure 2-(*p*-nitrophenylacetyl)fluorene (IV) (see below) was mixed with excess of a M-solution of aluminium *iso*propoxide in dry, thiophen-free benzene, and the benzene slowly distilled through a rod-and-disc fractionating column (20 cm.) until no further test for acetone was obtained in the distillate (about 10 hours). (Benzene was added during the distillation to maintain the volume constant.) The reaction mixture was decomposed with ice-cold hydrochloric acid, and the benzene distilled. The residual suspension of a yellow crystalline solid was filtered. The product had m. p. 172—175°, raised to 175—176·5° by crystallisation from alcohol (Found : C, 76·2; H, 5·3; N, 4·25. $C_{21}H_{17}O_3N$ requires C, 76·1; H, 5·2; N, 4·2%). The *carbinol* was dehydrated by boiling its solution in acetic anhydride containing dry hydrogen chloride for 3½ hours. After decomposition of the acetic anhydride the product was recovered as a bright yellow solid, which after crystallisation from benzene–alcohol (4 : 1) melted at 222—223° to an opalescent liquid which cleared at 253·5—254·5°. A mixed m. p. with the product from (*a*) gave no depression.

trans-2-p-*Acetamidostyrylfluorene* (Ic). A mixture of *trans*-(I*b*), stannous chloride, and equal volumes of acetic acid and concentrated hydrochloric acid was heated on the water-bath until reduction of the nitro-group was complete (*ca.* 4 hours). After cooling, the reddish precipitate was collected and worked up by standard procedures, but the amine did not crystallise well and was converted into its acetyl derivative by heating with acetic anhydride. After two crystallisations from acetic acid the *acetyl* compound was obtained as pale straw-coloured crystals, m. p. 278—280° (decomp.) (Found : C, 85·0; H, 5·8; N, 4·7. $C_{23}H_{19}ON$ requires C, 84·9; H, 5·9; N, 4·3%).

trans-2-p-*Chlorostyrylfluorene* (I*e*). The isomerised *product* had m. p. 220—222° (to an opalescent liquid). It was thrice crystallised from benzene containing 15% of alcohol, giving colourless, opalescent plates, m. p. 224·5—225° to an opalescent liquid clearing at 239—240° (Found : C, 83·2; H, 5·0; Cl, 11·5. $C_{21}H_{15}Cl$ requires C, 83·3; H, 5·0; Cl, 11·7%).

trans-2-p-*Methoxystyrylfluorene* (I*d*). The isomerised *product* after two crystallisations from benzene containing 10% of alcohol gave colourless, shiny plates, m. p. 226—227° to an opalescent liquid clearing at 264—265° (slight decomp.) (Found : C, 88·6; H, 6·0. $C_{22}H_{18}O$ requires C, 88·5; H, 6·1%).

trans-2-*Styrylfluorene* (I*a*). (*a*) The isomerised product was crystallised from alcohol, giving small, silky plates, m. p. 218—219°.

(*b*) A suspension of 2-fluorenediazonium chloride, prepared from 2-aminofluorene (2·6 g.; 1/70 mol.), concentrated hydrochloric acid (4 ml.), and water (20 ml.) and sodium nitrite (1·1 g.) in water (5 ml.), was added to a solution of cinnamic acid (2·1 g.; 1/70 mol.) in " AnalaR " acetone (30 ml.), and solutions of sodium acetate (4·7 g.) in water (15 ml.) and then cupric chloride (1 g.) in water (3 ml.) were added immediately. The reaction proceeded slowly at room temperature (16°) and was complete in 24 hours. After removal of the steam-volatile substances, the insoluble residue was collected, digested with hot sodium carbonate solution, and again filtered. On acidification of the combined filtrates 0·6 g. of cinnamic acid was recovered. After drying, the alkali-insoluble residue was shaken with light petroleum (b. p. 60—80°), and the solution allowed to percolate through a column of alumina (B.D.H.; 10 × 2 cm.); the coloured impurities were strongly adsorbed and a colourless fluorescent substance was easily eluted with light petroleum (b. p. 60—80°). It had m. p. 214—216°. After two crystallisations from alcohol it gave small silky plates, m. p. 218·5—219·5° (Found : C, 94·0; H, 6·05. $C_{21}H_{16}$ requires C, 94·0; H, 6·0%). A mixed m. p. with the *fluorene* obtained under (*a*) gave no depression.

trans-2-p-*Dimethylaminostyrylfluorene* (I*f*). (*a*) A mixture of fluorene-2-acetic acid (3·36 g.), *p*-dimethylaminobenzaldehyde (2·4 g.), and piperidine (1·5 ml.) was heated to 130—140° (oil-bath temp.), whereupon a reaction set in and the mass liquefied. After 5½ hours at 130—140° the reddish-brown viscous product was digested with warm sodium carbonate solution, and the resulting yellow suspension extracted repeatedly with chloroform, in which the bulk of the alkali-insoluble material dissolved. The combined chloroform extracts were washed once with water, and the chloroform removed, leaving a dark tarry residue which was digested with 50 ml. of hot alcohol and the solution allowed to cool. The yellow solid which separated was collected and washed well with alcohol (yield 0·85 g.). After three recrystallisations from benzene–alcohol (4 : 1) the *dimethylamino*-compound formed pale yellow, shiny crystals, m. p. 259—261° (decomp.) (Found : C, 88·8; H, 6·9; N, 4·55. $C_{23}H_{21}N$ requires C, 88·7; H, 6·8; N, 4·5%). 0·9 G. of crude fluorene-2-acetic acid was recovered from the alkaline solution (see above).

(*b*) The neutral red resinous material from the Perkin reaction was digested with benzene–alcohol, and a yellow solid (150 mg.) separated. After two crystallisations from benzene–alcohol (4 : 1) it had m. p. 259—262° (decomp.) undepressed on admixture with the product obtained under (*a*).

β-p-*Aminophenyl*-α-(2-*fluorenyl*)*propionic Acid* (VI).—Attempts to reduce the ethylenic bond and the nitro-group of (III*b*) by shaking its alcoholic or acetic acid solution with hydrogen (atmospheric pressure) and palladium-black did not give a satisfactory product. Satisfactory reduction was obtained when an alcoholic suspension of the acid was shaken with Raney nickel and hydrogen (20—25 atm.) at 40—60°. After separation of the catalyst and removal of the alcohol a slightly discoloured crystalline *acid* remained which was purified through its sparingly soluble sodium salt, and then crystallised from alcohol giving cream-coloured crystals, m. p. 250—251·5° (decomp.) (Found : C 80·3; H, 5·9; N, 4·3. $C_{22}H_{19}O_2N$ requires C, 80·2; H, 5·8; N, 4·25%).

p-*Methoxyphenyl* 2-*Fluorenylmethyl Ketone* (V).—Fluorene-2-acetic acid (2·24 g.) was converted into its chloride by heating with thionyl chloride, the excess of the latter being removed under reduced pressure. A solution of the acid chloride in carbon disulphide (" AnalaR "; 30 ml.) was mixed with anisole (1·25 ml.) and cooled in an ice-bath. Finely powdered anhydrous aluminium chloride (1·5 g.) was added; a brisk reaction took place but subsided in 1—2 hours. After standing for 5 hours in the ice-bath and overnight at room temperature, the mixture was decomposed with ice and hydrochloric acid. The unchanged anisole was removed in steam and the insoluble residue was washed, dried, and sublimed in a vacuum, giving 1·6 g. of a product, m. p. 172—177°. Crystallised from 90% acetic acid, the *ketone* formed colourless needles, m. p. 183—184° (Found : C, 84·4; H, 5·9. $C_{22}H_{18}O_2$ requires

C, 84·0; H, 5·8%). The *oxime* was prepared by heating the ketone (0·74 g.), hydroxylamine hydrochloride (0·35 g.), sodium acetate (0·68 g.), alcohol (75 ml.), and water (3 ml.) under reflux for 4½ hours. After two recrystallisations from alcohol the product formed colourless crystals, m. p. 197·5—199° (slight decomp.) (Found : C, 80·3; H, 5·9; N, 4·4. $C_{22}H_{19}O_2N$ requires C, 80·2; H, 5·8; N, 4·25%).

Reduction of the oxime. The oxime was suspended in a mixture of alcohol and acetic acid at 50—60° and treated with 2·5% sodium amalgam, sufficient acetic acid being added to keep the solution acid (cf. Dodds, Lawson, and Williams, *Proc. Roy. Soc.*, 1944, *B*, **132**, 119). It was not found possible to purify the colourless product (no unchanged oxime was recovered), and in an attempt to prepare an acetyl derivative of the desired amine (VII) the product was refluxed for 10 minutes with acetic anhydride containing a few drops of concentrated sulphuric acid. After decomposition of the acetic anhydride the product was crystallised 5 times from benzene containing 10% of alcohol and gave shiny plates, m. p. 226—227·5° to an opalescent liquid clearing at 262—262·5° (slight decomp.) (Found : C, 88·5; H, 5·9. Calc. for $C_{22}H_{18}O$: C, 88·5; H, 6·1%). A mixed m. p. with *trans*-2-*p*-methoxystyrylfluorene gave no depression. Presumably ammonia had been split out of the crude amine, giving the ethylene derivative.

1-p-*Methoxyphenyl*-2-2′-*fluorenylethane*.—A solution of (I*d*) (0·298 g.) in acetic acid (50 ml.) was shaken with hydrogen (at 1 atm. pressure) and palladium–charcoal; absorption ceased when the theoretical amount of hydrogen for one double bond had been taken up. After removal of the catalyst the filtrate was diluted with water, and a colourless precipitate, m. p. 154—155°, separated. After crystallisation from alcohol, this substituted *ethane* gave colourless prisms of the same m. p. (Found : C, 87·8; H, 6·7. $C_{22}H_{20}O$ requires C, 88·0; H, 6·7%).

2-(p-*Nitrophenylacetyl*)*fluorene* (IV).—Dry, powdered *p*-nitrophenylacetic acid (18·1 g.) was added with shaking, during 10—15 minutes, to a mixture of phosphorus pentachloride (23 g.) and dry, thiophen-free benzene (30 ml.). After the initial reaction had subsided, the mixture was heated at 80—85° for 20 minutes and the benzene and phosphorus oxychloride were then removed under reduced pressure at temperatures not exceeding 85°. Fluorene (16·6 g.) and carbon disulphide (" AnalaR ", 45 ml.) were then added, and when the mixture had cooled to room temperature finely powdered, anhydrous aluminium chloride (19 g.) was added gradually (30—40 minutes). A brisk reaction took place and after 4 hours the mixture had solidified. It was decomposed in the usual way and unchanged fluorene was removed in steam. The insoluble residue was collected, digested with warm sodium carbonate solution, and again filtered. From the combined filtrates 2 g. of *p*-nitrophenylacetic acid were recovered. The brown alkali-insoluble residue underwent much decomposition when sublimed at 0·1 mm., and a preliminary purification was effected by passing its benzene solution through a column of silica. Removal of the solvent and washing the residue with benzene left a yellow crystalline *product* (*ca.* 50% recovery) which, after crystallisation from benzene, then from acetic acid, and finally from benzene, formed cream-coloured plates, m. p. 210·5—211·5° (Found : C, 76·8; H, 4·7; N, 4·3. $C_{21}H_{15}O_3N$ requires C, 76·6; H, 4·6; N, 4·3%).

p-*Diacetylaminobenzyl* 2-*Fluorenyl Ketone*.—The ketone (IV) was reduced by Pfeiffer and Sergiewskaja's method (*Ber.*, 1911, **44**, 1110). Dry hydrogen chloride was passed into a suspension of stannous chloride (20 g.) in acetic acid (60 ml.) until a clear solution was obtained; (IV) (5·7 g.) was then added, and the passage of hydrogen chloride continued for a further 15 minutes. After standing overnight, the mixture was heated on the water-bath until reduction of the nitro-group was complete (<3 hours; a purple colour was no longer obtained with alcoholic sodium hydroxide; compare Rubin and Wishinsky, *J. Amer. Chem. Soc.*, 1944, **66**, 1948). After dilution of the mixture with concentrated hydrochloric acid, the amine salt was collected and converted into the free base. The latter was not purified but was boiled with excess of acetic anhydride. The brown *ketone* (6 g.) was crystallised from light petroleum (b. p. 80—100°)-benzene (3 : 1) (charcoal), giving slightly discoloured crystals. Repeated crystallisations from the same mixture gave colourless, shiny plates, m. p. 201—202·5° (Found : C, 78·7; H, 5·5; N, 4·0. $C_{25}H_{21}O_3N$ requires C, 78·3; H, 5·5; N, 3·65%).

The author is indebted to the Finney-Howell Research Foundation for a Fellowship, to the Director of the Chemical Research Laboratory, Teddington, for a gift of fluorene, and to Professor J. W. Cook, F.R.S., for his interest in this work. Microanalyses were carried out by Mr. J. M. L. Cameron and Miss R. H. Kennaway.

UNIVERSITY OF GLASGOW. [*Received, July 28th*, 1948.]