

*The Friedel-Crafts Reaction on 2-Methoxyfluorene and the Preparation of 7-Methoxyfluorenone-2-carboxylic Acid.*

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In the Friedel-Crafts reaction with acetyl chloride in carbon disulphide solution 2-methoxyfluorene yields a mixture from which pure 2-acetyl-7-methoxyfluorene has been isolated. The orientation of the acetyl group has been confirmed by oxidation of the ketone to 7-methoxyfluorene- and thence to 7-methoxyfluorenone-2-carboxylic acid, which was synthesised from 2-amino-7-nitrofluorenone.

7-METHOXYFLUORENE-2-CARBOXYLIC ACID and 7-methoxyfluorenone-2-carboxylic acid were required for examination of their possible mesomorphic behaviour. Since the two-stage oxidation of 2-acetyl-7-methoxyfluorene should afford both acids, the Friedel-Crafts reaction on 2-methoxyfluorene was undertaken.

The preparation of 2-methoxyfluorene starts with nitration of technical fluorene (Kuhn, *Org. Synth.*, 1933, **13**, 74). The scale of the reduction to 2-aminofluorene (78—80%) by calcium chloride and zinc dust (Kuhn, *loc. cit.*) is limited by the large volume of the reactants. Much larger quantities of 2-nitrofluorene may be reduced in high yield by iron pin dust and hydrochloric acid, in alcohol. Ruiz (*Anal. Asoc. Quim. Argentina*, 1928, **16**, 225), Ray and Hull (*J. Org. Chem.*, 1949, **14**, 394), and Lothrop (*J. Amer. Chem. Soc.*, 1939, **61**, 2115) describe the preparation of 2-hydroxyfluorene in yields ranging from 20—90%, but in our hands the methods were not satisfactory.

When applied to 2-methoxyfluorene, the procedure adopted to prepare 4'-acetyl-4-methoxydiphenyl from 4-methoxydiphenyl (Gray, Hartley, and Brynmor Jones, *J.*, 1955, 1412) gave a mixture and isolation of 2-acetyl-7-methoxyfluorene was difficult: of thirty such reactions, twenty-five gave an average yield of 27% of the 7-acetyl derivative, but in five no pure product was isolatable. Attempts to obtain the other possible isomeric

ketones (1- and 3-acetyl-2-methoxyfluorene) from the mother-liquors gave impure fractions and yielded impure 2:4-dinitrophenylhydrazones. Fieser and Bradscher (*J. Amer. Chem. Soc.*, 1936, **58**, 1738), who first prepared 4-acetyl-4'-methoxydiphenyl from 4-methoxydiphenyl, isolated the isomeric 3-acetyl derivative, in unspecified yield, only after hydrolysis of its purified semicarbazone.

The constitution of 2-acetyl-7-methoxyfluorene was proved by oxidation to 7-methoxyfluorene-2-carboxylic acid which was then oxidised to 7-methoxyfluorenone-2-carboxylic acid. 2-Amino-7-methoxyfluorenone was then prepared, with some modification to the original methods (Gouldon and Kon, *J.*, 1945, 930; Eckert and Langecker, *J. prakt. Chem.*, 1928, **118**, 263). 2-Amino-7-methoxyfluorenone, whose constitution is established, was then converted into 2-cyano-7-methoxyfluorenone which on hydrolysis yielded the keto-acid and thence, by Wolff-Kishner reduction, the fluorene-carboxylic acid, both identical with the acids from the Friedel-Crafts product.

#### EXPERIMENTAL

M. p.s are corrected.

**2-Nitrofluorene.**—Technical fluorene (180 g.) was nitrated by Kuhn's method (*loc. cit.*), and the product crystallised from acetic acid, to give pale yellow needles, m. p. 158° (55–65%).

**2-Aminofluorene.**—To 2-nitrofluorene (62 g., 1 mol.), 90% ethanol (500 ml.), and concentrated hydrochloric acid (29 ml.), stirred on a boiling-water bath, iron pin dust (58 g., 3 atom-equiv.) was added gradually during 30 min. Heating was continued for at least 12 hr., then sodium carbonate (17 g.) was added, followed by a few drops of concentrated aqueous ammonia to alkalinity. Heating and stirring were continued for a further 45 min., the mixture was filtered hot (Whatman 541 paper), and the filtrate evaporated until crystallisation commenced. The light grey crystals of 2-aminofluorene, m. p. 127° (75%), were collected. This can be done on twice the above scale, but the yield is 67% owing to higher losses in the hot filtration. Kuhn (*loc. cit.*) records the m. p. 127·5°.

**2-Hydroxyfluorene.**—2-Aminofluorene (11 g., 1 mol.) was dissolved in boiling glacial acetic acid (240 ml.), the solution was allowed to cool to 80°, and boiling 40% w/w sulphuric acid (50 ml.) added quickly with stirring. Rapid cooling gave the very finely divided amine sulphate, which was diazotised in suspension by the dropwise addition of sodium nitrite (5 g., 1·2 mole) in water (50 ml.) during 20 min. Stirring was continued for a further 1·5 hr., at 0–5°. The excess of nitrite was destroyed by sulphamic acid. The suspension was diluted with water (70 ml.) and added in a thin stream to boiling 40% w/w sulphuric acid (250 ml.). Tar was produced, and, after 10 minutes' boiling, charcoal was added and the mixture filtered hot. 2-Hydroxyfluorene which crystallised from the filtrate was washed with dilute aqueous sodium hydrogen carbonate, dried, and crystallised from glacial acetic acid. The light brown crystals, m. p. 170·5°, were obtained in average yield of 45%. Ray and Hull (*loc. cit.*) give m. p. 169–171°.

**2-Methoxyfluorene.**—2-Hydroxyfluorene (30·2 g., 1 mol.) was stirred with a solution of sodium hydroxide (20·5 g., 3 mols.) in water (500 ml.), and heated to 70°. Methyl sulphate (42 g., 2 mols.) was added to the suspension of the sodium salt, and the temperature maintained at 70° for 30 min. The cooled alkaline suspension was filtered and the ether washed with water. Crystallisation from absolute ethyl alcohol gave nearly colourless plates of 2-methoxyfluorene, m. p. 109° (80%). Ruiz (*loc. cit.*) records the m. p. 108°.

**2-Acetyl-7-methoxyfluorene.**—To 2-methoxyfluorene (9·8 g., 1 mol.), dissolved in redistilled carbon disulphide (100 ml.), finely sieved, anhydrous aluminium chloride (8·1 g., 1·17 mol.) was added quickly. The mixture was stirred and the temperature kept at 3–4° during addition of redistilled acetyl chloride (4 ml., 1·1 mol.). The temperature was then raised to 45° for 45 min.; an orange-brown complex separated. The mixture was cooled and the complex decomposed by ice and concentrated hydrochloric acid (100 ml.). The solvent was removed by passing steam over the surface of the stirred mixture, whereafter the whole was cooled, and the grey solid mixture of ketones (11·3 g.; m. p. 64–110°) was collected. The solid was stirred twice for 10 min. with ether (40 ml.). After filtration and washing with ether (10 ml.), the solid crystallised from isopropyl alcohol (50 ml.), giving a pale yellow ketone, m. p. 98–114° (4·3 g.). The crystals passed in chloroform through activated alumina (10 ×  $\frac{3}{4}$ "). Elution with chloroform gave a narrow band (dark) at the top of the column, followed by a broad yellow

band (green fluorescence), and a nearly colourless band (blue fluorescence). Elution was continued until the middle band reached the end of the column, the eluent was evaporated, and the colourless solid crystallised from isopropyl alcohol (then having m. p. 123—125°) and finally from methyl alcohol to give colourless plates (3.2 g.), m. p. 129.5—130.5° (27%). No other pure compound could be isolated from the column. Repeated crystallisation of the 2-acetyl-7-methoxyfluorene from the above solvents gave a maximum m. p. of 134.5° (Found: C, 80.5; H, 5.6.  $C_{16}H_{14}O_2$  requires C, 80.7; H, 5.9%). The deep red 2:4-dinitrophenylhydrazone (Found: C, 63.0; H, 4.5; N, 13.4.  $C_{22}H_{18}O_5N_4$  requires C, 63.15; H, 4.3; N, 13.4%) has m. p. 222°.

If the orange-brown complex is filtered directly from the cooled reaction mixture, sucked dry, and added with stirring to ice-cold concentrated hydrochloric acid, then triturated and crystallised from isopropyl alcohol as above, the 2-acetyl derivative (m. p. 123—125°) is obtained without chromatographic purification. The yield is however only 11%.

**7-Methoxyfluorene-2-carboxylic Acid.**—2-Acetyl-7-methoxyfluorene (8 g.) was dissolved in dioxan (200 ml.) at 45° and cooled quickly to 20° and treated during 10 min. with sodium hypobromite [from bromine (8 ml.), and sodium hydroxide (22.5 g.) in water (110 ml.)]. The temperature rose to about 30°, whereafter the mixture was warmed at 35—40° for 15 min. Sodium dithionite was added and the whole boiled 30 min. to steam-distil off most of the bromoform and dioxan. Sufficient water was added to dissolve the sodium salt at the b. p., and the solution was filtered hot, and acidified. The precipitate was collected, dried, sublimed at 170—180°/ <1 mm., and crystallised twice from xylene. 7-Methoxyfluorene-2-carboxylic acid was obtained in 75% yield as slightly yellow needles, m. p. 267.5° (Found: C, 75.1; H, 4.9.  $C_{15}H_{12}O_3$  requires C, 75.0; H, 5.0%). The acid is mesomorphic, exhibiting a nematic phase which becomes isotropic at 294° with slight decomposition.

**7-Methoxyfluorenone-2-carboxylic Acid.**—7-Methoxyfluorene-2-carboxylic acid (0.4 g.), sodium dichromate (5 g.), and acetic acid (100 ml.) were refluxed for 4 hr. The solution was cooled and diluted with an equal volume of water, and the orange precipitate collected. The 7-methoxyfluorenone-2-carboxylic acid was dissolved in warm, dilute sodium hydroxide and the solution filtered hot. The filtrate was acidified and the orange gelatinous precipitate filtered off and dried. Two crystallisations from nitrobenzene gave orange prisms (0.35 g., 83%), m. p. 344° (decomp.) (Found: C, 71.0; H, 4.0.  $C_{15}H_{10}O_4$  requires C, 70.9; H, 3.9%). The amide crystallised from nitrobenzene as orange needles, m. p. 291—292° (Found: C, 71.0; H, 4.5; N, 5.5.  $C_{15}H_{11}O_3N$  requires C, 71.1; H, 4.3; N, 5.5%).

**2-Nitrofluorenone.**—Oxidation of 2-nitrofluorene by Diels's method (*Ber.*, 1901, 34, 1760) gave 2-nitrofluorenone, m. p. 225° (72%), after crystallisation from nitrobenzene.

**2-Aminofluorenone.**—2-Nitrofluorenone (60 g.), hydrated stannous chloride (240 g.), concentrated hydrochloric acid (300 ml.), and acetic acid (600 ml.) were stirred for 30 min. on a boiling-water bath. The reaction is exothermic. The mixture was cooled, and the hydrochloride collected, washed with water, and stirred with 2N-sodium hydroxide (600 ml.) for 10 min. The solid was filtered off when cold, and crystallised from ethanol, giving deep red prisms of 2-aminofluorenone, m. p. 160.5° (41 g., 78%). Diels (*loc. cit.*), who used ammonium polysulphide, records m. p. 160°.

**2-Amino-7-nitrofluorenone.**—2-Aminofluorenone was nitrated on a 30-g. scale by Gouldon and Kon's method (*loc. cit.*), but it was beneficial to the yield to keep the reaction mixture at room temperature for at least 24 hr. Highly efficient cooling is necessary when the nitration mixture is poured on ice. Crystallisation from nitrobenzene gave blue-black needles, m. p. 287—288° (80—85%). Eckert and Langecker (*loc. cit.*) record m. p. 279°.

**2-Hydroxy-7-nitrofluorenone.**—2-Amino-7-nitrofluorenone (30 g.) was readily diazotised and hydrolysed by Gouldon and Kon's method (*loc. cit.*). The product crystallised from nitrobenzene in 68—74% yield as red plates, m. p. 305—306°.

**2-Methoxy-7-nitrofluorenone.**—Methylation must be effected in weak alkali. 2-Hydroxy-7-nitrofluorenone (38.5 g., 1 mol.), sodium hydroxide (8 g., 1 mol.), and water (770 ml.) were heated to 70—80°, and methyl sulphate (20 g., 1 mol.) was added with stirring. After 30 min. at 80°, more methyl sulphate (1 mol.) and aqueous sodium hydroxide were added alternately in small portions, the mixture being kept just alkaline. When cold, the brown solid was separated, dried, and crystallised from nitrobenzene-chlorobenzene (250 : 50 ml.). The brown crystals, m. p. 247.5—249.5°, were obtained in 70% yield. Eckert and Langecker (*loc. cit.*) record m. p. 248.5—249.5°.

**2-Amino-7-methoxyfluorenone.**—2-Methoxy-7-nitrofluorenone (33 g.), acetic acid (330 ml.), concentrated hydrochloric acid (165 ml.), and hydrated stannous chloride (132 g.) were stirred

on a boiling-water bath for 1 hr. When cold, the red solid was collected, washed with concentrated hydrochloric acid, boiled for 10 min. with 2*N*-potassium hydroxide (330 ml.), and cooled. The product, m. p. 193—195° (92%), crystallised from chlorobenzene as permanganate-coloured needles, m. p. 194.5° (21.5 g., 71%). Eckert and Langecker (*loc. cit.*), who used sodium polysulphide, record m. p. 195—196°.

*2-Cyano-7-methoxyfluorenone*.—2-Amino-7-methoxyfluorenone (2.25 g., 1 mol.) was dissolved in boiling glacial acetic acid (25 ml.), and hot 2*N*-sulphuric acid (30 ml.) added, and the whole rapidly cooled to 0°. Sodium nitrite (0.8 g., 1.15 mol.) in water (5 ml.) was added at 0—5°, and the mixture stirred for 30 min. After the first 10 min., a dark red solution was obtained, and then the crystalline, purple-red diazo-sulphate separated. This was collected and added in small portions to a solution of potassium nickelocyanide [potassium cyanide (3.6 g.) in water (40 ml.) was added to a solution of nickel sulphate (3 g.) in water (40 ml.)] at 90°. A light brown solid separated, and the suspension was boiled until nitrogen evolution was complete. The crude *2-cyano-7-methoxyfluorenone* was collected, dried, and sublimed at 170—180°/1 mm. Crystallisation from chlorobenzene yielded orange, felt-like needles, m. p. 205° (1.2 g., 50%) (Found: C, 76.5; H, 4.0; N, 5.8. C<sub>15</sub>H<sub>9</sub>O<sub>2</sub>N requires C, 76.6; H, 3.8; N, 5.95%).

Initially the more soluble amine hydrochloride was diazotised and treated as above. Crystallisation of the sublimate from glacial acetic acid gave orange needles, m. p. 156° (50%). Analysis showed this material to be 2-chloro-7-methoxyfluorenone (Found: 68.7; H, 3.4; Cl, 13.8. Calc. for C<sub>14</sub>H<sub>9</sub>O<sub>2</sub>Cl: C, 68.7; H, 3.7; Cl, 14.5%), containing 3—4% of the nitrile, from which it could not be completely separated.

*7-Methoxyfluorenone-2-carboxylic Acid*.—The nitrile (1 g.), in a hot mixture of acetic acid (40 ml.), concentrated sulphuric acid (40 ml.), and water (30 ml.), was refluxed for 3 hr. The acid which separated was washed with water and crystallised from nitrobenzene in orange prisms, m. p. 344° (decomp.) (0.95 g., 86%) (Found: C, 71.0; H, 4.0%).

*7-Methoxyfluorene-2-carboxylic Acid*.—7-Methoxyfluorenone-2-carboxylic acid (1 g.), 5% sodium ethoxide in absolute ethyl alcohol (16 ml.), and 100% hydrazine (2 ml.) were heated at 170° for 8 hr. Care must be taken not to allow the reactants to splash on to the walls while filling the tube, as this causes evaporation and formation of an orange solid which is not reduced out of contact with the reaction mixture. When cold, the colourless solid was filtered off and washed with a little warm water. The sodium salt was dissolved in boiling water (200 ml.) and filtered hot, and the filtrate acidified. The colourless precipitate was collected, dried, sublimed at 170—180° at <1 mm., and crystallised twice from xylene. Pale straw needles of 7-methoxyfluorene-2-carboxylic acid, m. p. 167.5° (80%), were obtained (Found: C, 75.1; H, 5.1%). The upper transition point of the nematic phase was again 294°, with slight decomposition.

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