470. *The Preparation of Some Substituted 9-Carboxy-, 9-Hydroxy-, and 9-Halogeno-fluorenes.*

By J. D. Dickinson and C. Eaborn.

Several 2- and 3-substituted fluorenes, 9-carboxyfluorenes, 9-hydroxyfluorenes, and 9-halogenofluorenes have been prepared, some by new or improved methods. Zinc in alcoholic calcium chloride satisfactorily reduces fluorenones to fluorenols.

This paper describes the preparation of a range of fluorene derivatives required for kinetic studies to be reported later.

The 2-substituted 9-carboxylic acids, 2-R-9-$HO_2C{\cdot}C_{13}H_8$, where R = Me, Et, HO, MeO, and Br, were prepared by carboxylation of the 9-lithio-derivatives obtained by metallation of the 2-$RC_{13}H_9$ compounds with n-butyl-lithium in ether. There was no interference from cross-metallation at the 2-position in the reaction involving 2-bromofluorene.

In recent years aluminium isopropoxide [1] and lithium aluminium hydride [2] have been recommended for reducing fluorenones to fluorenols. In 1901 Diels [3] observed that treatment of 2-nitrofluorenone with zinc dust and alcoholic calcium chloride gives 2-aminofluoren-9-ol, reduction of the carbonyl group accompanying the expected reduction of the nitro-group. We have found that this simple method can be used with other fluorenones, fluoren-9-ol and its 2-methyl, 3-methyl, and 2-methoxy-derivatives being obtained in 65—67% yield from the corresponding fluorenones. 3-Methoxyfluorenone gave a product from which we could not obtain pure 3-methoxyfluorenol, but which was similar to the material we obtained on using Arcus and Coombs's method [1] of reduction.

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[1] Arcus and Coombs, *J.*, 1954, 3977.

[2] Bergmann, Bertier, Fischer, Hirshberg, Lavie, Loewenthal, and Pullman, *Bull. Soc. chim. France*, 1952, **19**, 73.

[3] Diels, *Ber.*, 1901, **34**, 1760.

The use of *N*-bromosuccinimide to brominate the 9-position [4] has been extended to the preparation of 2-bromo-, 2,7-dibromo-, 2-cyano-, and 9-bromo-2-methoxy-fluorene. 2-Methyl-, 2-ethyl-, and 2-amino-9-bromofluorene could not be prepared in this way, but the 2-methyl and 3-methyl compounds were obtained by treating corresponding fluoren-9-ols with acetyl bromide.[2]

Several of the 9-bromo-compounds were converted into the corresponding iodides by treatment with potassium iodide in acetone. 2-Ethyl- and 2-cyano-fluorene were prepared by improved methods, and a new route was found to 2-methylfluorenone.

EXPERIMENTAL

2-*Aminofluorene*.—This, m. p. 130°, was prepared by Kuhn's method from 2-nitrofluorene.[5]

2-*Hydroxy- and* 2-*Methoxy-fluorene*.—In conversion of 2-aminofluorene into the 2-hydroxy-compound,[6] decomposition of the diazonium salt with 20% instead of 40% sulphuric acid gave less tar. The hydroxy-compound, m. p. 170·5°, was obtained in 50% yield, and some was converted [6] into the 2-methoxy-compound, m. p. 109°.

2-*Cyanofluorene*.—2-Aminofluorene (42 g.) was dissolved in boiling glacial acetic acid (600 ml.). The solution was allowed to cool to 80° and boiling 40% w/w sulphuric acid solution (195 ml.) was added. The mixture was cooled to 0—5°, sodium nitrite (19 g.) in water (195 ml.) was added during 1 hr. with vigorous stirring, and the mixture was stirred for 1½ hr. at 0—5°. The diazonium salt was filtered off, and its suspension in water (100 ml.) was added slowly to a solution of potassium cyanide (95 g.) and nickel sulphate (70 g.) in water (2 l.) at 85—90°. The crude 2-cyanofluorene which separated on cooling was filtered off, dried, and taken up in light petroleum (b. p. 100—120°) in a Soxhlet apparatus. The solution was decolorized with charcoal, and the solvent was removed. Recrystallization from light petroleum gave material of m. p. 94° (previously reported,[7] 88°) in 30—80% yield. In experiments giving low yields, vacuum-distillation of the residues gave additional 2-cyanofluorene, b. p. 194—200°/9—10 mm., which gave pure product on recrystallization from methanol.

2-*Acetylfluorene*.—Ray and Rieveschl's method [8] was used, except that vacuum-distillation (188°/4 mm.) was used to purify the product before recrystallization from ethanol. This gave material of m. p. 132°.

2-*Methylfluorene*.[9]—2-Acetylfluorene was converted into 2-fluorenylacetic acid, some of which (55 g.) was decarboxylated with calcium oxide to give 2-methylfluorene (23 g.), m. p. 101·5—102·5°.

2-*Ethylfluorene*.—As previously observed,[10] Clemmensen reduction of 2-acetylfluorene gave a material difficult to purify. Much better results were obtained by use of the Huang-Minlon modification [11] of the Wolff–Kishner reduction, as follows.

A mixture of 2-acetylfluorene (12 g.), powdered potassium hydroxide (5 g.), 60% hydrazine hydrate solution (18 ml.), and ethylene glycol (125 ml.) was boiled under reflux for 8 hr., water being taken off intermittently during the first 2 hr. until the mixture was boiling at 185—195°. The solution was poured into water, and the solid which separated was purified by sublimation at reduced pressure to give 10 g. (90%) of material of m. p. 99·5—100° (previously reported,[10] 81—82°) (Found: C, 92·7; H, 7·2. Calc. for $C_{15}H_{14}$: C, 92·7; H, 7·3%).

Fluorene-9-*carboxylic Acids*.—n-Butyl-lithium (usually 1 mol., but 2 mol. with the 2-hydroxy-compound) in ether was added slowly to the appropriate 2-substituted fluorene in ether, and the mixture was boiled for 1½ hr. before carboxylation was carried out in the usual way. The following 9-carboxylic acids were obtained: 2-*methoxy*- (94%), m. p. 186° (from benzene, then aqueous methanol) (Found: C, 74·5; H, 4·9. $C_{15}H_{12}O_3$ requires C, 75·0; H, 5·0%); 2-*methyl*- (89%), m. p. 205° (but 185° with decomposition on slow heating) (from aqueous methanol) (Found: C, 80·1; H, 5·3. $C_{15}H_{12}O_2$ requires C, 80·3; H, 5·4%); 2-*ethyl*- (91%), m. p. 165° (from aqueous methanol) (Found: C, 80·6; H, 5·9. $C_{16}H_{14}O_2$ requires C,

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[4] Eaborn and Shaw, *J.*, 1955, 1420.

[5] Kuhn, *Org. Synth.*, 1933, **13**, 74.

[6] Gray, Hartley, and Ibbotson, *J.*, 1955, 2687.

[7] Fortner, *Monatsh.*, 1904, **25**, 443.

[8] Ray and Rieveschl, *Org. Synth.*, Coll. Vol. III, 1955, p. 23.

[9] Bergmann, Berthier, Hirshberg, Loewenthal, Pullman, and Pullman, *Bull. Soc. chim. France*, 1951, **18**, 669.

[10] Campbell and Wang, *J.*, 1949, 1513.

[11] Huang-Minlon, *J. Amer. Chem. Soc.*, 1946, **68**, 2487.

80·6; H, 5·9%); 2-*hydroxy*- (86%), m. p. 229—230° (from aqueous methanol) (Found: C, 74·3; H,4·4. $C_{14}H_{10}O_3$ requires C, 74·3; H, 4·45%); 2-*bromo*- (80%), m. p. 226° (from aqueous propan-2-ol, then aqueous methanol) (Found: C, 57·6; H, 3·1; Br, 27·9. $C_{14}H_9O_2Br$ requires C, 58·1; H, 3·1; Br, 27·6%).

Fluorene 9-carboxylic acid, m. p. 229—230° (from propan-2-ol), was obtained in 85% yield by the above procedure but in lower yield when the fluorene in ether was added to the n-butyllithium solution.

2-*Acetamidofluorene*-9-*carboxylic Acid*.—2-Nitrofluorene-9-carboxylic acid, prepared by Rose's method [12] except that a reaction time of 1 hr. was used, had m. p. 191° (decomp.) (previously reported,[12] 186—187°) after 6 recrystallizations from 1 : 1 acetone–chloroform (Found: C, 65·8; H, 3·5; N, 5·3. Calc. for $C_{14}H_9O_4N$: C, 65·9; H, 3·6; N, 5·5%). It was reduced to the 2-amino-compound (m. p. 207—208°),[12] 0·7 g. of which was treated in 2N-hydrochloric acid with acetic anhydride and sodium acetate to give the 2-*acetamido-compound* (0·83 g., 70%), m. p. 195° (from ethanol) (Found: N, 5·25. $C_{16}H_{13}O_3N$ requires N, 5·24%).

2-*Methylfluorenone*.—Potassium (2·5 g.) was dissolved in ethanol (10 ml.) and anhydrous ether (40 ml.). To the solution was added a solution of 2-methylfluorene (10 g.) and pentyl nitrite (6·8 g.) in anhydrous ether (70 ml.). The orange mixture was boiled under reflux for ½ hr. and set aside for 18 hr. A little solid which separated was removed, the ethereal solution was extracted several times with water and then with dilute potassium hydroxide solution, and the aqueous extracts were acidified. The several samples of crude 2-methylfluorenone oxime were combined and steam-distilled from 20% sulphuric acid (200 ml.) to give 2-methylfluorenone (9·2 g., 85%), m. p. 91—92°.

2-*Nitro- and* 2-*Amino-fluorenone*.—2-Nitrofluorenone, m. p. 222—223° (from acetic acid), was prepared in 97% yield by oxidation of 2-nitrofluorene with sodium dichromate in glacial acetic acid.[3] Reduction [1] gave 2-aminofluorenone, m. p. 158°, in 79% yield.

2-*Bromofluorenone*.—This, m. p. 149° (from light petroleum, then ethanol), was obtained in 95% yield from 2-bromofluorene by the method used for the 2-nitro-compound.

2-*Hydroxyfluorenone* (cf. Diels [3]).—2-Aminofluorenone (58·5 g.) was dissolved in boiling glacial acetic acid (1200 ml.), the solution was cooled to 80°, and 40% w/w sulphuric acid (250 ml.) was added. The solution was cooled rapidly to 0° to give the amine sulphate in fine particles. The suspension was diazotized at 0° by adding sodium nitrite (25 g.) in water (250 ml.) during ½ hr. and stirring for a further 1½ hr. at 0—5°. The yellow solution was diluted with water (350 ml.) and added in a thin stream to boiling 10% sulphuric acid (1250 ml.). Charcoal was added, boiling was continued for 10 min., and the mixture was filtered hot. Red crystals separated on cooling and were washed with water and dried to give 2-hydroxyfluorene (37·5 g., 64%), m. p. 211°.

2-*Methoxyfluorenone*.—This, m. p. 77—78° (from ethanol), was prepared in 76% yield by methylation [6] of the 2-hydroxy-compound.

2-*Acetamidofluorenone*.—2-Aminofluorene was boiled with acetic anhydride and acetic acid (1 : 1 molar ratio) for 1½ hr. The solution was added to water, and the solid obtained was recrystallized from glacial acetic acid to give the 2-acetamido-derivative, m. p. 227—228°, in 75% yield.

3-*Methyl- and* 3-*Methoxy-fluorenone*.—These were prepared from 2-amino-4′-methyl- and -4′-methoxy-benzophenone, respectively.[13] Recrystallization from light petroleum gave yellow products, m. p. 68° and 100°, respectively, with a daffodil odour.

3-*Bromofluorenone*.—2-Aminofluorenone (20 g.) was treated with bromine (17 g.) in glacial acetic acid (500 ml.) to give 2-amino-3-bromofluorenone (25·3 g., 90%), m. p. 215—216° (from benzene). Diazotization and treatment with hypophosphorous acid [14] gave 3-bromofluorenone (10·6 g., 45%), m. p. 165·5—166° (from ethanol).

2-*Cyanofluorenone*.—2-*Cyanofluorenone*, m. p. 173° (from light petroleum), was prepared in 35% yield from 2-aminofluorenone by a method similar to that described above for 2-cyanofluorene (Found: C, 81·9; H, 3·5; N, 7·0. $C_{14}H_7ON$ requires 81·9; H, 3·4; N, 6·8%).

9-*Bromofluorenes*.—The appropriate ring-substituted fluorenes were treated with *N*-bromosuccinimide in carbon tetrachloride in presence of a little benzoyl peroxide to give the following 9-bromofluorenes: 2-bromo- (88%), m. p. 127° (from benzene); 2-*cyano*- (81%), m. p. 163·5—164° (yellow crystals from ethanol, then carbon tetrachloride) (Found: C, 62·3; H, 3·2; N,

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[12] Rose, *J.*, 1932, 2361.

[13] Ullmann and Mallet, *Ber.*, 1898, **31**, 1694.

[14] Kornblum, " Organic Reactions," John Wiley and Sons, Inc., New York, 1944, Vol. II, p. 262.

5·4; Br, 29·0. $C_{14}H_8NBr$ requires C, 62·2; H, 3·8; N, 5·2; Br, 29·6%); 2-*methoxy*- (65%), m. p. 112·5—113° (from benzene, then ether) (Found: C, 61·2; H, 4·2; Br, 29·3. $C_{14}H_{11}OBr$ requires C, 61·1; H, 4·0; Br, 29·1%); also 2,7,9-tribromofluorene, m. p. 195—196° (from ethyl acetate). (The 2-methoxy-compound, m. p. 112—113°, was also prepared from 2-methoxyfluoren-9-ol by the method described below for 9-bromo-2-methylfluorene.)

Bromination with *N*-bromosuccinimide was unsatisfactory with 2-methylfluorene (which underwent side-chain bromination), and with 2-ethyl- and 2-amino-fluorene (both of which gave material containing bromine but inert to alcoholic silver nitrate).

2-*Aminofluorenol*.—This amine, m. p. 195°, was prepared in 63% yield by Diels's method.[3]

Reduction of Fluorenones.—Fluorenone (5 g.), calcium chloride (2 g.), zinc dust (60 g.), and 78% ethanol (200 ml.) were boiled together for 4 hr. The solution was filtered hot and added to water. The precipitated solid was dried and recrystallized from light petroleum, to give fluoren-9-ol, m. p. 154° (3·3 g., 65%).

In the same way 2-methyl-, m. p. 144—145° (from light petroleum), 2-methoxy-, m. p. 157·5° (from ethanol), and 3-methyl-fluoren-9-ol, m. p. 143·5—144·5° (from ethanol), were prepared from the corresponding fluorenones in 65—67% yield.

When 3-methoxyfluorenone was treated in this way a green plastic material was obtained. Extraction with light petroleum left a white solid of m. p. 155—170°, but attempted recrystallization of this from ethanol reproduced the original green plastic material, and a sharp-melting solid could not be obtained. Very similar material was obtained when 3-methoxyfluorenone was reduced with aluminium isopropoxide by Arcus and Coombs's method.[1]

9-*Bromo*-x-*methylfluorenes*.—2-Methylfluoren-9-ol was converted into 9-bromo-2-methylfluorene (from ethanol, then hexane), m. p. 104° (previously reported,[2] 100—103°) in 90% yield, by treatment with acetyl bromide.[2]

The 3-methyl isomer, m. p. 89° (from ethanol, then hexane), was prepared analogously in 85% yield.

9-*Iodofluorenes*.—Interaction of potassium iodide and 9-bromo-, 9-bromo-2-nitro-, 9-bromo-2-methoxy-, and 2,9-dibromo-fluorene in dry acetone gave, respectively, 9-iodofluorene, m. p. 125° (decomp.) (from light petroleum), 9-*iodo*-2-*nitrofluorene*, m. p. 165—166° (from ethanol) (Found: C, 46·9; H, 2·5; I, 36·6; N, 4·2. $C_{13}H_8O_2NI$ requires C, 46·3; H, 2·4; I, 37·6; N, 4·2%), 9-*iodo*-2-*methoxyfluorene*, m. p. 94° (decomp.) (from light petroleum) (Found: C, 53·0; H, 3·5; I, 38·4. $C_{14}H_{11}OI$ requires C, 52·2; H, 3·4; I, 39·4%), and 2-*bromo*-9-*iodofluorene*, m. p. 145—147° (decomp.) (from light petroleum) (Found: C, 43·2; H, 2·3. $C_{13}H_8IBr$ requires C, 42·1%; H, 2·2%. The microanalysis gave 98% of the calculated quantity of silver halide).

THE UNIVERSITY, LEICESTER.

[*Received, March 9th*, 1959.]