63. *The Ring-closure of Derivatives of 2-Aminofluorene.*

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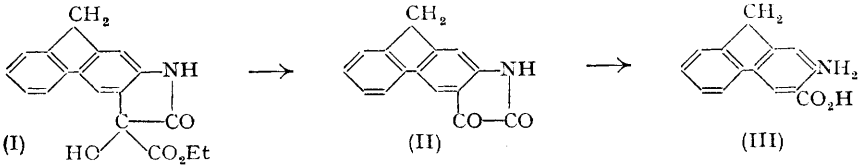
The product obtained from 2-aminofluorene and ethyl mesoxalate (Neish, *Rec. Trav. chim.*, 1948, **67**, 349) is shown to be ethyl indeno(3′ : 2′-5 : 6)-dioxindole-3-carboxylate (I). Spectroscopic evidence suggests that the product obtained by the Skraup reaction on 2-aminofluorene is indeno-(3′ : 2′-6 : 7)quinoline. The mercuration of fluorene is described and the results of previous workers are criticised. Fluorene-3-carboxylic acid is synthesised.

Exact information of the ring closure of 2-aminofluorene derivatives is lacking. 2-Aminofluorene with ethyl ethoxymethylenemalonate gives a product which was proved by Bremer and Hamilton (*J. Amer. Chem. Soc.*, 1951, **73**, 1844) to be ethyl 1-hydroxyindeno(3′ : 2′-7 : 8)quinoline-2-carboxylate, thereby showing that ring-closure had occurred at position 1 of the fluorene molecule. On the other hand, 2-aminofluorene undergoes the Skraup reaction to give an indenoquinoline (Diels and Staehlin, *Ber.*, 1902, **35**, 3275), and forms with mesoxalic ester an indenoisatin (Martinet reaction) (Neish, *Rec. Trav. chim.*, 1948, **67**, 349) neither of which has been orientated. We have studied both these products in an attempt to determine their chemical constitutions.

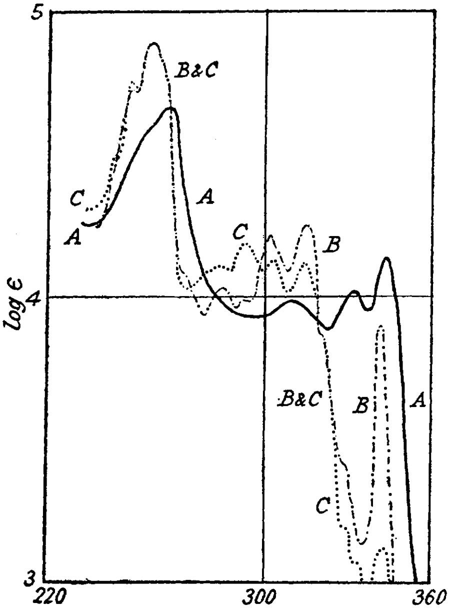
Neish's substance is undoubtedly ethyl indeno(3′ : 2′-5 : 6)dioxindole-3-carboxylate (I) since it gives indeno(3′ : 2′-5 : 6)isatin (II) which can be oxidised to 2-aminofluorene-3-carboxylic acid (III). The structure of this acid follows from its deamination to fluorene-3-carboxylic acid, m. p. 231°, which gave a m. p. depression when admixed with fluorene-1-carboxylic acid, m. p. 245°, but gave no m. p. depression with the 3-acid; on oxidation it yielded fluorenone-3-carboxylic acid, m. p. 300—301°. This value differs considerably from the 285—286° and 283—284° cited respectively by Sieglitz and Schatzkes (*Ber.*, 1921, **54**, 2070) and by Kruber (*Ber.*, 1932, **65**, 1382). We therefore synthesised the keto-acid and purified it *via* the methyl ester. The acid thus obtained had m. p. 304°, and it appears that the acid of the earlier workers was impure. Although it is evident that Kruber would encounter difficulties in purifying the product obtained by oxidising a mixed crystallate of methylfluorenes, it is not so easy to account for the results of Sieglitz and Schatzkes (*loc. cit.*) who oxidised pure 3-methylfluorenone.



To synthesise fluorenone-3-carboxylic acid we first cleaved fluorenone-1-carboxylic acid with alkali. No trace of diphenyl-2 : 3-dicarboxylic acid was found, the only products being diphenyl-2 : 3′-dicarboxylic acid and unchanged fluorenone-1-carboxylic acid; ring closure of the 2 : 3′-diacid by means of sulphuric acid yielded both fluorenone-1- and -3-carboxylic acids. Our results thus differ from those of Mayer and Freitag (*Ber.*, 1921, **54**, 347) who isolated only the 1-acid in 12% yield.

Other attempts to synthesise fluorene- or fluorenone-3-carboxylic acid were unsuccessful. 2-Amino-3-nitrofluorene on deamination gave as the main product a red substance of unknown constitution. The aminonitro-compound was therefore converted into 2-bromo-3-nitrofluorene by a modification of the method of Campbell *et al.* (*J.*, 1940, 446). Reduction gave 3-aminofluorene, but the yield was so poor that further work on these lines was abandoned.

Attempts to prepare 3-bromo-fluorene or -fluorenone from mercurated fluorene were completely unsuccessful. Miller and Bachman (*J. Amer. Chem. Soc.*, 1935, **57**, 2447) claimed by the action of mercuric acetate on fluorene followed by suitable treatment to have prepared two monobromofluorenes, m. p. 90—91° and 165° respectively, the former of which was stated to be 3-bromofluorene, identical with the product, m. p. 94°, obtained by Clemmensen reduction of 3-bromofluorenone. We have repeated the mercuration of fluorene following closely the directions of the American workers but could find no trace of a monobromofluorene, m. p. 88—94°, and we think it probable that the product with this m. p. was a mixture of fluorene and dibromofluorenes. We isolated a product, m. p. 163°, but found it is a dibromofluorene which on oxidation gives a dibromofluorenone, m. p. 140°. It may be pointed out that the four monobromofluorenones are now known, and the highest m. p. is that of 3-bromofluorenone, *viz.*, 161° (Heilbron and Hey, *J.*, 1938, 1364). This nullifies Miller and Bachman's claim to have oxidised their "monobromofluorene," m. p. 165°, to a bromofluorenone, m. p. 185—187°. From our own work and that of Huntress *et al.* (*J. Amer. Chem. Soc.*, 1942, **64**, 2845) we conclude that Miller and Bachman's results on the mercuration of fluorene are not reliable.



A. *Product of Skraup synthesis.*
B. 2 : 3-*Benzofluorene.*
C. 1 : 2-*Benzofluorene.*

An attempt was made to orientate the indenoquinoline obtained by the Skraup reaction on 2-aminofluorene (Diels and Staehlin, *loc. cit.*) by comparing its ultra-violet absorption spectrum with those of 1 : 2- and 2 : 3-benzofluorenes (Orchin and Friedel, *J. Amer. Chem. Soc.*, 1949, **71**, 3002). It is apparent from the figure that the spectrum of the indenoquinoline resembles that of 2 : 3- rather than that of 1 : 2-benzoquinoline, thereby suggesting that its structure is indeno(3′ : 2′-6 : 7)quinoline. The spectral differences of the benzofluorenes, however, are not sufficient to make the proof final.

Fluorenone-1-carboxylic acid reacts with hydrazine hydrate to give 4-hydroxy-2 : 3-diazafluoranthene which is a useful derivative for the identification and characterisation of the acid. The acid on nitration gives a dinitrofluorenone-1-carboxylic acid of unknown structure.

In studying the effect of hydrazoic acid on fluorene derivatives, we found that sodium azide and sulphuric acid with fluorene yielded chiefly unchanged hydrocarbon and a little 2 : 7-diaminofluorene.

EXPERIMENTAL

Structure of Ethyl Indeno(3′ : 2′-5 : 6)*dioxindole*-3-*carboxylate.*—The indenodioxindole, m. p. 247—249°, was obtained by Neish's method (*loc. cit.*) in 40—50% yields. The substance (0·25 g.) was dissolved in ethanol (5 ml.) and 4N-sodium hydroxide (5 ml.) and treated with perhydrol (2 ml.). The solution was warmed until evolution of oxygen ceased and was then diluted with water (30 ml.) containing sufficient acetic acid to make the solution slightly acid. The precipitated amino-acid was extracted with ether (4 × 25 ml.) and the volume of the dried extract (Na_2SO_4) was reduced to 15 ml. Dry hydrogen chloride was passed through the solutions and the precipitated amino-acid hydrochloride was washed with ether. The hydrochloride in water (5 ml.) gave with saturated sodium acetate solution 2-*aminofluorene*-3-*carboxylic acid* (0·12 g.), plates (from glacial acetic acid), m. p. 256° (Found : C, 74·3; H, 4·3; N, 6·3. $C_{19}H_{11}O_2N$ requires C, 74·7; H, 4·9; N, 6·2%). The amino-acid (0·1 g.) was dissolved in warm 6N-hydrochloric acid (4 ml.). The solution, cooled to 0°, was treated with a slight excess of saturated sodium nitrite solution and the temperature allowed to rise to 10°. Calcium hypophosphite (2 g.) in concentrated hydrochloric acid (4 ml.) and ethanol (4 ml.) was added, and after 2 hours the temperature was raised during $\frac{1}{2}$ hour to 85°. The solution was poured into water (50 ml.) and extracted with ether (2 × 25 ml.). The dried extract (Na_2SO_4) on evaporation gave *fluorene*-3-*carboxylic acid* (0·042 g.), rhombic prisms, m. p. 231°, after crystallisation from acetic acid (charcoal) and sublimation (Found : C, 79·2; H, 4·8. $C_{14}H_{10}O_2$ requires C, 80·0; H, 4·8%). The acid (0·05 g.) was oxidised by boiling it in 4N-sodium hydroxide (2 ml.) with potassium permanganate (0·2 g.). Acidification gave fluorenone-3-carboxylic acid (0·02 g.), yellow needles (from acetic acid), m. p. 300—301°, not depressed when mixed with a sample prepared as below.

Indeno(3′ : 2′-5 : 6)isatin was prepared in excellent yield from the carbethoxyindenodioxindole by Neish's method (*loc. cit.*) and was characterised by oxidation to 2-aminofluorene-3-carboxylic acid and by the isolation of the *quinoxaline* derivative by treatment with *o*-phenylenediamine in ethanol. The quinoxaline separated from acetic acid in yellow needles, m. p. $>350°$ (Found : C, 81·6; H, 3·5; N, 13·5. $C_{21}H_{13}N_3$ requires C, 82·1; H, 4·2; N, 13·7%).

Synthesis of Fluorenone-3-carboxylic Acid.—Fluorenone-1-carboxylic acid (10 g.) was added in portions to the emulsion obtained by adding potassium hydroxide (30 g.) to diphenyl ether (125 ml.) and stirring vigorously while the temperature was raised to 200° (bath-temp. 230°). The cooled solution was poured into water (100 ml.), and the flask rinsed with water (50 ml.). Carbon tetrachloride (150 ml.) was added and the aqueous layer which separated was washed with carbon tetrachloride (50 ml.) and on acidification gave a mixture of acids. The acids were extracted for 5 minutes with boiling water (1 l.), and the extract was boiled for 5 minutes with charcoal (2 g.) and filtered. The filtrate on cooling deposited diphenyl-2 : 3′-dicarboxylic acid. The filtrate was used to extract the residue of the first extraction, and the cycle was continued until no further extraction occurred. The residue was fluorenone-1-carboxylic acid, and the acid from the combined filtrates was diphenyl-2 : 3′-dicarboxylic acid (yield variable), m. p. 216—217° (Found : C, 69·6; H, 4·2. Calc. for $C_{14}H_{10}O_4$: C, 69·4; H, 4·2%). The methyl ester, prepared from the acid and diazomethane and crystallised from light petroleum (b. p. 40—60°), had m. p. 71—72° (Found : C, 71·3; H, 5·2. Calc. for $C_{16}H_{14}O_4$: C, 71·1; H, 5·2%). Diphenyl-2 : 3′-dicarboxylic acid (2·5 g.) was warmed in concentrated sulphuric acid (25 ml.) to 140° and kept at this temperature for 1 minute. The solution was poured into water (100 ml.) and boiled. The yellow precipitate was dissolved in boiling ethanol (300 ml.), and the cooled solution deposited a solid (1·3 g.) which was boiled in ethanol (50 ml.) for 10 minutes; one-third to one-half dissolved and the residue was substantially fluorenone-3-carboxylic acid. This acid (0·5 g.) was boiled in methanol (20 ml.) and sulphuric acid (2 ml.) and poured into water. Extraction with ether (4 × 50 ml.), followed by evaporation, gave *methyl fluorenone-3-carboxylate* (0·4 g.), pale yellow needles (from methanol–light petroleum), m. p. 145° (Found : C, 75·4; H, 4·3. $C_{15}H_{10}O_3$ requires C, 75·6; H, 4·2%). Hydrolysis of the ester by 30% sodium hydroxide solution, followed by acidification, gave the acid, m. p. 304° (Found : C, 74·8; H, 3·6. Calc. for $C_{14}H_8O_3$: C, 75·0; H, 3·5%).

Clemmensen reduction of the acid was unsatisfactory owing to the coating of the zinc with a yellow insoluble gum, but the following modification gave good results. The acid (0·2 g.), dioxan (5 ml.), acetic acid (5 ml.), concentrated hydrochloric acid (2 ml.), and a large excess of amalgamated granulated zinc, previously washed with acid, were boiled with periodic additions of concentrated hydrochloric acid (4 × 1 ml.) until the solution became colourless (*ca.* 2 hours). The solution was decanted from the zinc, concentrated to 3—4 ml., and diluted with water (20 ml.). Fluorene-3-carboxylic acid (0·16 g.) was obtained, having m. p. 230° after crystallisation from acetic acid. Fluorene-1-carboxylic acid was similarly obtained from the corresponding keto-acid.

Synthesis of 3-Aminofluorene.—The mixture of 2-amino-3- and -7-nitrofluorenes (Diels, *Ber.*, 1902, **35**, 328) was partly separated by means of the different basicities of the isomers. The crude 3-compound was chromatographed on alumina (30 g. per g. of crude product), with sulphur-free xylene as developer and eluant. The crimson zone gave an orange-yellow eluate which when concentrated yielded crimson plates of 2-amino-3-nitrofluorene, m. p. 203°, which on crystallisation from acetic acid reverted to the prisms described by Diels (*loc. cit.*). The solution of 2-amino-3-nitrofluorene (3 g.) in boiling glacial acetic acid (30 ml.) was rapidly cooled to give a mass of small crystals which was added to a mixture of sodium nitrite (1·4 g.), concentrated sulphuric acid (10 ml.), and glacial acetic acid (30 ml.), cooled to 10°. The temperature was allowed to rise to 15° and a solution of cuprous bromide (3·5 g.) in concentrated hydrobromic acid (50 ml.) was then rapidly added. The solution was warmed until after 90 minutes the temperature had reached 100°, and the suspension was poured into water (250 ml.). The greenish-yellow solid was filtered off and dried by azeotropic distillation with benzene before being chromatographed on alumina (100 g.). The eluate was collected until it became tinged with red. Removal of the benzene gave 2-bromo-3-nitrofluorene (1·25 g.), pale yellow laths [from light petroleum (b. p. 100—120°) or acetic acid], m. p. 119° (cf. Campbell *et al., loc. cit.*). The mother-liquors yielded a further 0·25 g. of material. 2-Bromo-3-nitrofluorene (1·2 g.), stannous chloride (" AnalaR ") (4·5 g.), acetic acid (10 ml.), and concentrated hydrochloric acid (10 ml.) were boiled for 2½ hours, further additions of hydrochloric acid (5 ml.) being made every ½ hour. The solution was poured into an equal volume of cold concentrated hydrochloric acid, whereupon the stannichloride crystallised. This was treated with 20% aqueous sodium hydroxide, and the mixture extracted with ether (2 × 50 ml.). The dried extract (Na_2SO_4) on evaporation gave 3-aminofluorene (0·49 g.), yellow needles, m. p. 149—150° (Found : N, 7·2. Calc. for $C_{13}H_{11}N$: N, 7·6%), from light petroleum (b. p. 80—100°).

Mercuration of Fluorene.—A ground mixture of fluorene (80 g.) and mercuric acetate (160 g.) was fused at 140—145° and the acetic acid produced was condensed and weighed. Miller and Bachman (*loc. cit.*) claim completion of the reaction after 25 minutes, but we found that after 45 minutes only 65% of the required amount of acetic acid was evolved. The mercurichloride was formed by Miller and Bachman's method and was well washed with hot ethanol, acetic acid, and benzene. The pink powder after prolonged drying at 70° weighed 145 g. The mercurichloride (80 g.) was brominated by Miller and Bachman's procedure. Hydrogen sulphide gave a buff-coloured precipitate which was filtered off and extracted several times with hot glacial acetic acid. The combined filtrates were concentrated and yielded crystals, which after crystallisation from light petroleum (b. p. 80—100°), benzene–methanol, and acetic acid gave irregular plates of a *dibromofluorene*, m. p. 163° (Found : Br, 49·2. $C_{13}H_8Br_2$ requires Br, 48·8%). No trace of a lower-melting substance possessing the solubilities reported by Miller and Bachman could be found. The dibromofluorene (0·5 g.) was oxidised in 5 minutes by chromic oxide (" AnalaR ; " 0·5 g.) in boiling acetic acid to a *dibromofluorenone* (0·47 g.), elongated prisms (from light petroleum), m. p. 140° (Found : Br, 47·3. $C_{13}H_6OBr_2$ requires Br, 47·3%). It forms a 2 : 4-*dinitrophenylhydrazone*, orange needles (from chlorobenzene), m. p. 340° (Found : N, 10·4. $C_{19}H_{10}O_4N_4Br_2$ requires N, 10·4%). The dibromofluorene with fuming nitric acid in boiling acetic acid gave a *dibromonitrofluorenone*, m. p. 192—193°, after crystallisation from glacial acetic acid (Found : N, 4·1; Br, 44·4. $C_{13}H_7O_2NBr_2$ requires N, 3·8; Br, 43·2%).

Miller and Bachman's second method for preparing fluorene mercurichlorides was also repeated. The product was free from fluorene since it yielded none on steam-distillation. Bromination was effected as before, and the mixture was filtered hot. The filtrate was concentrated in stages, and the first crystalline fraction after being washed with benzene was crystallised first from chlorobenzene and then from nitrobenzene. The product contains both bromine and mercury and is probably a *bromomercuridibromofluorene* (Found : Br, 39·8. $C_{13}H_7Br_3Hg$ requires Br, 39·7%). The filtrate was distilled to remove all the acetic acid and the residue was added to that obtained from the above benzene washings. Steam-distillation gave fluorene, but no bromo-product. The residue from the steam-distillation was distilled up to 250° (bath-temp.)/0·1 mm. The main product was a mixture of dibromofluorenes, principally that of m. p. 163°, and a little 2 : 7-dibromofluorene.

*Properties of Fluorenone-*1-*carboxylic Acid.*—The acid (0·20 g.) was boiled with dioxan (5 ml.) and 90% hydrazine hydrate (1 ml.) for 2 hours. 4-*Hydroxy*-2 : 3-*diazafluoranthene* (0·18 g.) separated; crystallised from glacial acetic acid, it had m. p. 267—268° (Found : C, 76·2; H, 3·5. $C_{14}H_8ON_2$ requires C, 76·4; H, 3·6%). Potassium nitrate (1 g.) was added to fluorenone-1-carboxylic acid (1 g.) dissolved in sulphuric acid, and the mixture was warmed on a water-bath to 80° and then poured into water (100 ml.); 2 : 7(?)-*dinitrofluorenone*-1-*carboxylic acid* (0·5 g.) separated and was crystallised from acetic acid; it had m. p. 267° (Found : N, 8·9. $C_{14}H_6O_7N_2$ requires N, 8·9%).

Ultra-violet Absorption Spectrum of Indenoquinoline.—The absorption spectrum was measured by means of a Hilger Barfit medium spectrograph. Absorption maxima occurred at 265 (log ε 4·66), 310 (log ε 3·99), 328 (log ε 4·02), and 342 mμ (log ε 4·14), and minima at 235 (log ε 4·25), 296 (log ε 3·93), 321 (log ε 3·89), and 336 mμ (log ε 3·95).

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