552. *Synthesis of Fluoranthenes. Part II. Michael Addition of Vinyl Cyanide to Fluorene-9-carboxylic Esters.*

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Mono-addition of vinyl cyanide to the 9-position of the fluorene structure has been achieved with fluorene-9-carboxylic esters. The adducts have been hydrolysed directly, or in stages, to *β*-9′-fluorenylpropionic acid (II), which has been cyclised to 4-keto-1 : 2 : 3 : 4-tetrahydrofluoranthene (improved yield).

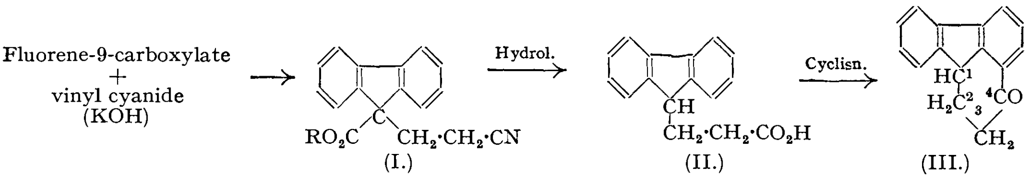
A new method of preparing fluorene-9-carboxylic acid from fluorene is described.

VINYL CYANIDE can undergo Michael addition to compounds possessing only weakly activated hydrogen atoms. Bruson (*J. Amer. Chem. Soc.*, 1942, **64**, 2459, 2850) found that even fluorene adds two molecules to form 9 : 9-di-2′-cyanoethylfluorene. No method has hitherto been found whereby mono-addition, to the exclusion of di-addition, can be achieved. Bruson and Riener (*J. Amer. Chem. Soc.*, 1943, **65**, 23) and Bruson (U.S.P. 2,361,259) found similarly that vinyl cyanide can react with all available reactive hydrogen atoms of aliphatic nitro-compounds; although mono-adducts could be isolated when certain primary nitro-paraffins, $R\cdot CH_2\cdot NO_2$, were used. Buckley, Elliott, Hunt, and Lowe (*J.*, 1947, 1505) improved the preparation of mono-adducts in these reactions by using a molecular proportion of alkali as condensing agent.

On the other hand, Bruson (1942, *loc. cit.*) effected exclusive mono-addition of propenyl cyanide (crotononitrile) to fluorene. Mono-addition of substituted vinyl cyanides seems to be the general rule (see also Buckley *et al.*, *loc. cit.*; Neil Campbell *et al.*, this vol., p. 1239).

To ensure mono-addition, not only of substituted vinyl cyanides, but of vinyl cyanide itself to the 9-position of fluorene one of us (Tucker, this vol., p. 2182) utilised alkyl fluorene-9-carboxylates in Michael addition with substituted vinyl cyanides since the fluorene-9-carboxylates have, in respect to the Michael reaction, only one replaceable hydrogen atom—and that a more reactive one than those in fluorene. Wislicenus and Mocker (*Ber.*, 1913, **46**, 2789) and von Braun and Anton (*Ber.*, 1929, **62**, 149) had previously used ethyl fluorene-9-carboxylate in reaction with β-iodo- (or β-chloro-)propionate, to prepare ultimately fluoranthene and its 4-substituted derivatives (von Braun and Manz, *Ber.*, 1937, **70**, 1609); but as a synthetic method this process is of limited scope.

We now record the Michael reaction of fluorene-9-carboxylates with vinyl cyanide, the products of which, 9-carbalkoxy-9-2′-cyanoethylfluorenes (I), without isolation, give on hydrolysis directly β-9-fluorenylpropionic acid (II).



Stepwise hydrolysis of (I) to (II) readily gives intermediates. Mild hydrolysis of the ester-cyanide (I) led to the acid-cyanide, *9-2′-cyanoethylfluorene-9-carboxylic acid*, which by decarboxylation gave *9-2′-cyanoethylfluorene*. This or the ester-cyanide (I) by vigorous alkaline hydrolysis gave β-9-fluorenylpropionic acid. Hydrolysis of (I) by water–sulphuric–acetic acid gave the dicarboxylic acid, β-(9-carboxy-9-fluorenyl)propionic acid (I; R = H; CO_2H for CN), readily decarboxylated to β-9-fluorenylpropionic acid (II). Von Braun and Anton (*loc. cit.*) by cyclisation of this acid obtained 4-keto-1 : 2 : 3 : 4-tetrahydrofluoranthene, but the yield was poor. This is rather surprising since β-9-fluorenylbutyric acid has been readily cyclised to 2-methyl-4-keto-1 : 2 : 3 : 4-tetrahydrofluoranthene (Tucker, *loc. cit.*). Cyclisation of β-9-fluorenylpropionic acid (II) has now been improved, however, by using phosphorus pentachloride followed by stannic chloride in benzene (yield, 44%). A comparison of cyclisation methods is given in the experimental portion. Hydrogen fluoride gave a pure product, but the yield was surprisingly low.

Owing to the greater ease of preparation of the 9-glyoxylates than of the 9-carboxylates of fluorene the former were at first used in this work (cf. Wislicenus and Densch, *Ber.*, 1902, **35**, 76; Wislicenus and Mocker, *ibid.*, p. 2790) but were found to be less reactive, and, owing to the possibility of undesirable ring formation, were unsuitable. The older methods of preparing fluorene-9-carboxylic acid involve synthesis of the fluorene skeleton, and give products which are difficult to purify; more recent methods proceed from fluorene and give high yields of pure material but involve specialised preparative techniques (Tucker and Whalley, this vol., p. 50; Yost and Hauser, *J. Amer. Chem. Soc.*, 1947, **69**, 2326). We have now found a simple method of preparation of fluorene-9-carboxylic acid, eminently suitable on the laboratory scale, which gives the acid directly, without isolation of any intermediate. It is represented by: fluorene $\xrightarrow[\text{KOMe–MeOH}]{Me_2C_2O_4} C_{13}H_9CO{\cdot}CO_2Me \xrightarrow{\text{acid}} C_{13}H_9CO{\cdot}CO_2H \xrightarrow{H_2O_2} C_{13}H_9CO_2H$ (for details see the Experimental section). Since ethyl fluorene-9-carboxylate oxidises extremely easily in *alkaline* solution to ethyl 9-hydroxyfluorene-9-carboxylate, it was possible that hydrogen peroxide in acid solution, as used above, might also cause formation of this by-product. There was no evidence, however, of this: the crude product when warmed with concentrated sulphuric acid gave a clear green colour, due to fluorene-9-carboxylate: the 9-hydroxy-derivative gives an indigo-blue colour under these conditions (Wislicenus and Mocker, *loc. cit.*) and, if it had been present, would certainly have masked the green coloration. It was found necessary to use the proportion, fluorene: methyl oxalate : sodium = 1 mol. : 2 mols. : 2 atoms. This is reminiscent of the advantageous use of two molecular proportions of ethylmagnesium bromide in the preparation of 9-fluorenylmagnesium bromide (Tucker and Whalley, *loc. cit.*). Methyl fluorene-9-glyoxylate was stable and therefore used in synthetic work in preference to the ethyl ester, which even in the course of a few days softens, eventually oxidising to fluorenone. Moreover, experiments in which the fluorene-9-glyoxylic esters were isolated showed that with ethyl oxalate the yield rarely exceeded 60%, whereas with the dimethyl ester it was >80%. The intermediate fluorene-9-glyoxylic acid has also been isolated in high yield. Failure attended attempts to convert methyl fluorene-9-glyoxylate into methyl fluorene-9-carboxylate by heating it alone or in presence of a catalytic amount of boric acid (Prelog and Hinden, *Helv. Chim. Acta*, 1944, **27**, 1854); evolution of carbon monoxide occurred at ~220°, and red crystalline products were obtained, but not identified.

Attempts to convert 9 : 9-di-2′-cyanoethylfluorene into 9-2′-cyanoethylfluorene by heating it alone or with a trace of solid potassium hydroxide failed (cf. Buckley *et al.*, *loc. cit.*). Hydrolysis converted the dicyano-compound into 9 : 9-di-2-carboxyethylfluorene. On two occasions this compound was isolated as sole product in attempted preparations of β-fluorenylpropionic acid by the direct method from methyl fluorene-9-carboxylate; it was recognised by its relatively high melting point (265—269°). It is conceivable that in these exceptional experiments methyl fluorene-9-carboxylate failed to react initially with the vinyl cyanide and was subsequently hydrolysed to fluorene which then reacted with the vinyl cyanide to give 9 : 9-di-2-cyanoethylfluorene, which in turn was hydrolysed to 9 : 9-di-2-carboxyethylfluorene.

ADDENDUM. After this paper had been written, a preprint of a paper by Neil Campbell and Fairfull (this vol., p. 1239) was received. They describe the condensation of vinyl cyanide with 9-phenyl- and with 9-hydroxy-fluorene, and its failure to condense with 9-chloro-, 9-ethyl-, or 9-benzyl-fluorene. They confirm the low yields obtained by von Braun and Anton (*loc. cit.*) in the cyclisation of β-9-fluorenylpropionic acid (II) to 4-keto-1 : 2 : 3 : 4-tetrahydrofluoranthene (III).

EXPERIMENTAL.

Fluorene-9-carboxylic Acid.—Potassium (1·95 g., 2 atoms) was dissolved in anhydrous methanol (20 ml.; Baker and Holdsworth, *J.*, 1947, 724), fluorene (4·15 g., 1 mol.) and methyl oxalate (5·9 g., 2 mols.) were added, and the whole was rendered homogeneous by heating and shaking it in a distilling flask (250 ml.). The flask was then immersed in water which was heated so that methanol slowly distilled (18 ml. in 30—45 minutes). The water was finally boiled, and the pressure in the flask slowly reduced, care being taken that as residual methanol and excess of methyl oxalate distilled the yellow pasty mass did not froth over (15 minutes) (cf. McElvain *et al.*, *J. Amer. Chem. Soc.*, 1929, **51**, 3124; 1933, **55**, 1697; 1937, **59**, 2007; Floyd and Miller, *J. Amer. Chem. Soc.*, 1947, **69**, 2354). Glacial acetic acid (35 ml.) was added, and the yellow solid dissolved by warming and swirling. A mixture of concentrated sulphuric acid (5 ml.) and water (25 ml.) was added; a voluminous yellow precipitate separated, but on boiling the mixture the precipitate liquefied, and after ½ hour a clear yellow solution was obtained. Boiling was continued for a further ½ hour, the solution cooled, and hydrogen peroxide (10 ml.; 30%) added in portions. The mixture became warm and maintained its temperature for some time, whilst the suspended solid became pale yellow (cf. Holleman, *Proc. K. Akad. Wetensch. Amsterdam*, 1904, **6**, 715; *Rec. Trav. chim.*, 1904, **23**, 169). After occasional swirling during 4 hours (or overnight) the solid was filtered off, washed, dried (4·5 g.), and recrystallised from acetic acid diluted at its b. p. with water, or from methyl cyanide, giving fluorene-9-carboxylic acid, m. p. 220—225° (4·0 g., 76%). Use of sodium (1·15 g., 2 atoms) instead of potassium in the above preparation gave a slightly lower yield of fluorene-9-carboxylic acid. Further, when the proportions were reduced so that the ratio, fluorene : methyl oxalate : sodium, was 1 mol. : 1·1 mols. : 1·1 atoms, the yield of fluorene-9-carboxylic acid was greatly reduced (2·43 g., crude) and, correspondingly, fluorene was recovered (1·32 g.). The latter was also recoverable when the proportions were 1 mol. : 1·5 mols. : 1·5 atoms.

Stepwise Preparation of Fluorene-9-carboxylic Acid from Fluorene.—Methyl fluorene-9-glyoxylate was prepared as above, except that after removal of methanol the yellow solid residue was dissolved in cold 5% sodium hydroxide solution by shaking, with occasional swirling, filtered from a small amount of solid which contained fluorene, and treated with excess of concentrated hydrochloric acid. The washed and dried precipitate (5·40 g.), crystallised from carbon tetrachloride, gave methyl fluorene-9-glyoxylate (5·18 g., 82%), m. p. 115—120° (Kuhn and Levy, *Ber.*, 1928, **61**, 2240, give 117·5°). This ester is stable (cf. the instability of the ethyl ester, described below). The use of relatively less sodium or of potassium (1·25 atoms) and of methyl oxalate (1·25 atoms) gave lower yields of the glyoxylate with higher recovery of fluorene. The use of benzene to entrain the last traces of methanol during distillation was found to be of no advantage.

Preparation of the corresponding ethyl fluorene-9-glyoxylate gave uncertain results, yields rarely exceeding 60%. It was best crystallised by dissolving it in boiling carbon tetrachloride and adding twice the volume of boiling light petroleum (b. p. 60—80°) to give the ester, m. p. 75—78° (softening at 72°) (cf. von Braun and Anton, *Ber.*, 1929, **62**, 148, footnote, who give 89—90°). The preparation of this ethyl ester was abandoned since, even when kept in stoppered bottles, it readily liquefies (within a few weeks), eventually giving mainly fluorenone.

Fluorene-9-glyoxylic acid was prepared by boiling a mixture of methyl fluorene-9-glyoxylate (2·52 g.), glacial acetic acid (10 ml.), concentrated sulphuric acid (1 ml.), and water (5 ml.) for 1 hour. The clear yellow solution was treated with excess of concentrated hydrochloric acid and set aside overnight. The separated, bright yellow solid (~100% yield) recrystallised from toluene in pale greenish-yellow rosettes of needles, a second crop being obtained by addition of light petroleum (b. p. 60—80°) (1·72 g., 72%). The m. p. was indefinite—from shrinkage at 140° to clear melt at 165° (Wislicenus and Densch, *loc. cit.*, report peculiarities).

Fluorene-9-carboxylic acid was obtained by hydrolysis of methyl fluorene-9-glyoxylate (2·52 g.) as above; then, instead of precipitation by adding hydrochloric acid, the cooled solution of the glyoxylic acid was treated with hydrogen peroxide (5 ml.; 30%), occasionally shaken, and set aside (4 hours). The white precipitate (2·0 g., 95%) consisted of fluorene-9-carboxylic acid. This acid was also obtained by treating fluorene-9-glyoxylic acid (1·72 g.) in glacial acetic acid (10 ml.) with hydrogen peroxide (5 ml.) and setting the mixture aside overnight (1·29 g., 79%).

Synthesis of β-9-Fluorenylpropionic Acid from Ethyl (or Methyl) Fluorene-9-carboxylate without Isolation of Intermediates.—Ethyl fluorene-9-carboxylate (Tucker, *loc. cit.*) (5·95 g., 1 mol.) and then vinyl cyanide (1·33 g., 1 mol.) were added to a solution of potassium hydroxide (0·28 g., 0·2 mol.) in 2-methoxyethanol (25 ml.). The mixture became warm, and after 15 minutes was treated with aqueous 10N-potassium hydroxide (37 ml.) and then with 2-methoxyethanol (25 ml.), and the mixture boiled (30 minutes). On pouring into water a slightly milky solution was obtained; it was mixed with charcoal, filtered, and treated with excess of concentrated hydrochloric acid. The pure white, crystalline precipitate, after drying and crystallisation from methyl cyanide, gave large prisms (5·4 g., 90%) of β-9-fluorenylpropionic acid, m. p. 140—145° (Wislicenus and Mocker, *loc. cit.*, p. 2790, give 148—149°; Neil Campbell and Fairfull, *loc. cit.*, give m. p. 143—144°) (Found : C, 80·6; H, 5·9. Calc. for $C_{16}H_{14}O_2$: C, 80·7; H, 5·9%).

Changing the order of addition of alkali and 2-methoxyethanol used in the hydrolysis seemed to have no effect : no 9 : 9-di-2′-carboxyethylfluorene was obtained.

Preparation of Intermediates in the Synthesis of β-9-Fluorenylpropionic Acid from Fluorene 9-Carboxylates and Vinyl Cyanide.—*Methyl 9-2′-cyanoethylfluorene-9-carboxylate* (I; R = Me). Methyl fluorene-9-carboxylate (1·12 g., 1 mol.) and vinyl cyanide (0·265 g., 1 mol.) were added to a warm mixture of dioxan (3 ml.) and potassium hydroxide (0·056 g., 0·2 mol., powdered; or 0·1 ml. of 50% aqueous solution). After 15 minutes the mixture was treated with excess of dilute hydrochloric acid; the precipitated oil solidified, and crystallised from methanol in large prisms, m. p. 84—86° (1·30 g., 94%), of *methyl 9-2′-cyanoethylfluorene-9-carboxylate* (Found : C, 78·2; H, 5·6; N, 5·0. $C_{18}H_{15}O_2N$ requires C, 78·0; H, 5·4; N, 5·0%). The alkali used may be replaced by sodium hydroxide or by 35% aqueous trimethylbenzylammonium hydroxide.

Ethyl fluorene-9-carboxylate, similarly employed, gave a pale yellow oil (ether extraction) which became solid after several days (refrigerator; scratch). *Ethyl 9-2′-cyanoethylfluorene-9-carboxylate* (I; R = Et) crystallised from light petroleum (b. p. 40—60°) in prisms, m. p. 45—46° (a mixture with ethyl fluorene-9-carboxylate was molten at room temperature) (Found: C, 78·5; H, 5·8; N, 4·9. $C_{19}H_{17}O_2N$ requires C, 78·35; H, 5·8; N, 4·8%). It was more difficult to isolate than the methyl homologue (yield, high).

9-2′-Cyanoethylfluorene-9-carboxylic Acid (I; R = H).—The foregoing methyl ester, dissolved in warm ethanol, was treated with 10N-potassium hydroxide and set aside until a drop gave no precipitate with water (a few minutes). Acidification gave a solid which from ethanol gave hexagonal plates, softening at 98°, m. p. 115° (effervescence). Crystals from methanol similarly separated with solvent of crystallisation; after drying in a vacuum at 60° these gave the pure *acid* (Found : C, 77·8; H, 5·1; N, 5·1. $C_{17}H_{13}O_2N$ requires C, 77·6; H, 4·9; N, 5·3%).

9-2′-Cyanoethylfluorene.—The acid (I; R = H) was gently heated in suspension in aqueous 10N-potassium hydroxide (2—2·5 ml.) until effervescence just ceased (~1 minute). The oily suspension, poured into water, gave *9-2′-cyanoethylfluorene* which crystallised in rods (from methanol), m. p.

73—75° (Found: C, 87·7; H, 5·85; N, 6·3. $C_{16}H_{13}N$ requires C, 87·7; H, 5·9; N, 6·4%). After several days it slowly liquefied. It was also prepared by acting as above on the methyl ester (I; R = Me).

β-9-*Fluorenylpropionic Acid* (II).—The ester (II; R = Me) (2·77 g.), 2-methoxyethanol (25 ml.), and 10N-potassium hydroxide (25 ml.) were boiled together for 15 minutes and then poured into water, and the clear solution was treated with excess of concentrated hydrochloric acid to give β-9-fluorenylpropionic acid (~100%). When the amount of 2-methoxyethanol and alkali were halved relative to the amount of the ester-cyanide, the solution, poured into water as above, gave β-9-fluorenylpropionic acid and a small amount of β-9-*fluorenylpropionamide*, crystallising from ethanol in long, nacreous laminæ, m. p. 185—186° (softening at 180°) (Found: C, 81·2; H, 6·3; N, 5·9. $C_{16}H_{15}ON$ requires C, 81·0; H, 6·4; N, 5·9%). β-9-Fluorenylpropionic acid (II) was also obtained (84% yield) by hydrolysis of the ethyl ester (I; R = Et) (0·53 g.) in 2-methoxyethanol (4 ml.) and aqueous 10N-potassium hydroxide (5 ml.) (boiling; 15 minutes). This acid (II) was also prepared by acid hydrolysis of the methyl ester (I; R = Me) by boiling it for 3 hours in glacial acetic–concentrated sulphuric acid–water (2 : 1 : 1, by volume) (Reichstein, *Helv. Chim. Acta*, 1937, **20**, 1418), giving rise in the usual manner after crystallisation from aqueous methanol to β-(9-carboxy-9-fluorenyl)propionic acid (I; R = H; CO_2H for CN) (yield, 71%), m. p. 192° (softening at 115°) (cf. Wislicenus and Mocker, *loc. cit.*, p. 2789, who give m. p. 195—196°) (Found: C, 72·1; H, 4·9. Calc. for $C_{17}H_{14}O_4$: C, 72·3; H, 5·0%). When heated to 260° it smoothly gave β-9-fluorenylpropionic acid (68%).

β-(9-*Carbomethoxy*-9-*fluorenyl*)*propionamide* was obtained by the action of a slightly alkaline ethanolic solution of hydrogen peroxide on the methyl ester (I; R = Me) (Radziszewski, *Ber.*, 1885, **18**, 355). It crystallised from ethanol in diamond-shaped crystals, m. p. 207° (softening at 190°) (Found: C, 73·4; H, 5·7; N, 4·6. $C_{18}H_{17}ON$ requires C, 73·2; H, 5·8; N, 4·75%).

Hydrolysis of 9 : 9-*Di*-2′-*cyanoethylfluorene*.—This was effected by boiling the dicyanide (0·27 g.) with aqueous 10N-potassium hydroxide (1·5 ml.) in 2-methoxyethanol (3 ml.) for ½ hour. 9 : 9-*Di*-2′-*carboxyethylfluorene* (0·17 g.) recrystallised from glacial acetic acid in prisms, m. p. 265—269° (softening at 240°) (Found: C, 73·3; H, 5·8. $C_{19}H_{18}O_4$ requires C, 73·5; H, 5·85%).

Cyclisation of β-9-*Fluorenylpropionic Acid* (II) *to* 4-*Keto*-1 : 2 : 3 : 4-*tetrahydrofluoranthene* (III).—(*a*) (II) (2·38 g.) in benzene (10 ml.) was treated with phosphorus pentachloride (2·3 g., 10% excess), and after 15 minutes was heated on the water-bath for 5 minutes. After cooling, stannic chloride (2·33 ml., 100% excess) was added and rinsed in with benzene (2 ml.). The mixture became purple almost immediately and was apparently unchanged after being kept overnight. It was poured into concentrated hydrochloric acid and extracted with methylene dichloride [since (III) is only slightly soluble in ether], and the green-yellow, strongly fluorescent liquid washed well with acid and then with water, and evaporated to dryness. Since the pale green residue contained no acid it was boiled in ethereal solution with charcoal, filtered, and evaporated, and the residue crystallised in cream-coloured balls of (III), m. p. 92—96° (0·96 g., 44%), from methanol.

(*b*) The use of thionyl chloride (10 ml.; distilled from quinoline and then from boiled linseed oil) similarly gave (III) (0·78 g., 35%).

(*c*) Dissolution of the acid (II) (1·19 g.) in hydrogen fluoride (25 ml.) gave (III) (0·24 g., 22%), slightly cream-coloured, m. p. 98—99° (softening at 96°) (cf. von Braun and Anton, *loc. cit.*, who give 98°, and Neil Campbell and Fairfull, *loc. cit.*, who give 94—97°). Unchanged acid was recovered.

Cyclisations, by known methods, using phosphoric acid + phosphoric oxide, aluminium chloride + sodium chloride, or acetic acid + acetic anhydride + zinc chloride, gave (III), but in relatively low and variable yields. (II) was recovered unchanged from boiling stannic chloride; it was sulphonated by sulphuric acid.

4-Keto-1 : 2 : 3 : 4-tetrahydrofluoranthene (III) gave a 2 : 4-dinitrophenylhydrazone in orange, feathery crystals (from dioxan or toluene), m. p. 255—259° (decomp.) (cf. Neil Campbell and Fairfull, *loc. cit.*, who give m. p. 234—236°, possibly a typographical error for 254—256°) (Found: C, 65·9; H, 4·35; N, 13·9. Calc. for $C_{22}H_{16}O_4N_4$: C, 66·0; H, 4·0; N, 14·0%). The oxime of (III) crystallised from methanol in cream-coloured, minute crystals, m. p. 178° (softening at 174°) (von Braun and Anton, *loc. cit.*, p. 149, give 170—171°) (Found: C, 81·7; H, 5·2; N, 6·0. Calc. for $C_{16}H_{13}ON$: C, 81·7; H, 5·6; N, 6·0%).

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