3. *The Condensation of Fluorene with Acetone. Part III. Formation of Fluoranthene Derivatives.*

By HAROLD FRANCE, S. HORWOOD TUCKER, and (in part) JAMES FORREST.

Methyl β-9-fluorenyl-β-methyl-*n*-propyl ketone (I) has been cyclised to 2 : 2 : 4-trimethyl-1 : 2-dihydrofluoranthene (III) * by the action of hydrogen bromide.

The ketone (I) has been converted into 2 : 2 : 4-trimethyl-1 : 2 : 3 : 4-tetrahydrofluoranthene (IV) either by cyclisation by means of hydrogen iodide or by conversion with aluminium *iso*propoxide into the intermediate alcohol, δ-9-*fluorenyl*-δ-*methylpentan*-β-*ol* (V), followed by elimination from the latter compound of the elements of water.

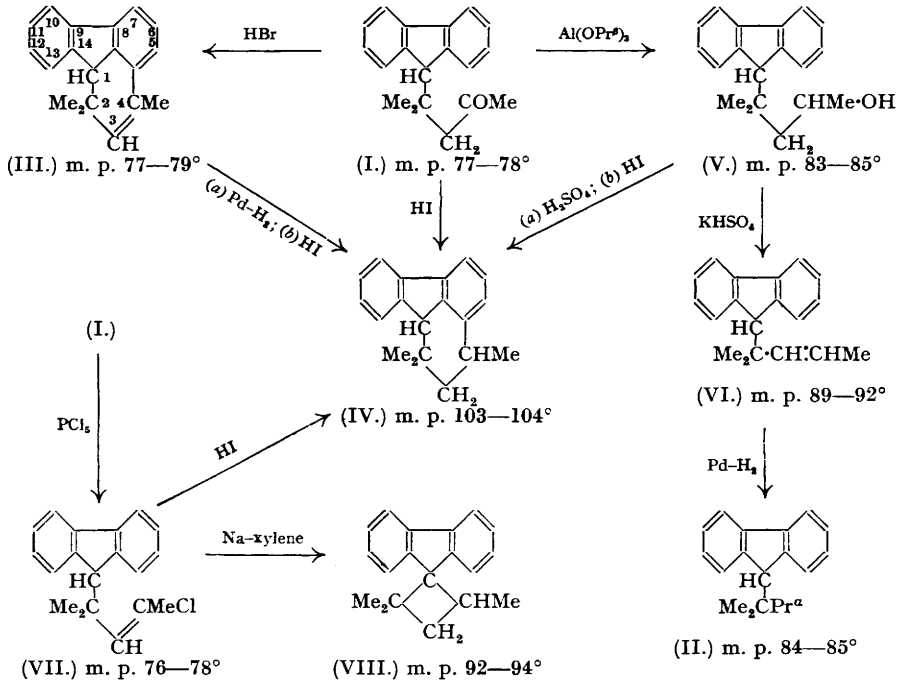
The ketone (I) has been treated with phosphorus pentachloride to form β-*chloro*-δ-9-*fluorenyl*-δ-*methyl*-Δ$^{\beta}$-*pentene* (VII), which, by reaction with sodium in boiling xylene, has given *fluorene*-9-spiro-2′ : 2′ : 4′-*trimethyl*-cyclo*butane* (VIII).

Oxidation of the compounds (III) and (IV) to 1-*acetylfluorenone* and thence to fluorenone-1-carboxylic acid furnishes proof that they are derivatives of fluoranthene.

IT has been shown [Maitland and Tucker, J., 1929, 2559 (Part I); France, Maitland, and Tucker, J., 1937, 1739 (Part II)] that fluorene and acetone in presence of potassium hydroxide combine to give methyl β-9-fluorenyl-β-methyl-*n*-propyl ketone (I). Reduction of (I) gave rise to several products, depending on the reducing agent used; *e.g.*, reduction by either the Kishner–Wolff or the Clemmensen method gave

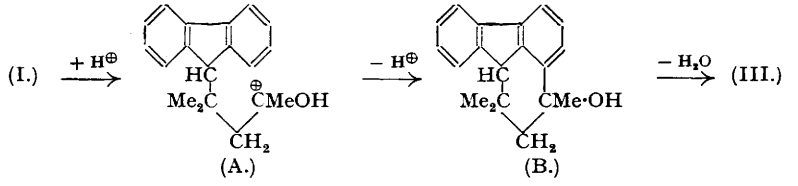
* The numbering follows von Braun and Anton (*Ber.*, 1934, **67**, 1051; cf. *idem*, *ibid.*, 1929, **62**, 147).

β-9-fluorenyl-β-methylpentane (II); but in the latter reaction a substance, $C_{19}H_{20}$, m. p. 103—104°, was also obtained. This substance was also prepared by the action of hydriodic acid in boiling acetic acid on the ketone



(I). Furthermore, by the action of hydrobromic acid in acetic acid, the ketone (I) gave a substance, $C_{19}H_{18}$, m. p. 77—79°, which by catalytic hydrogenation gave the above substance, $C_{19}H_{20}$.

We have now established that oxidation of these substances, of formulæ $C_{19}H_{18}$ and $C_{19}H_{20}$ respectively, by sodium dichromate in boiling glacial acetic acid gives an intermediate compound, 1-*acetylfluorenone*, and finally fluorenone-1-carboxylic acid (maximum yield, 53%). It is therefore evident that the two hydrocarbons are derivatives of fluoranthene, *viz.*, 2 : 2 : 4-trimethyl-1 : 2-dihydrofluoranthene (III) ($C_{19}H_{18}$) and 2 : 2 : 4-trimethyl-1 : 2 : 3 : 4-tetrahydrofluoranthene (IV) ($C_{19}H_{20}$), being produced by ring-closure involving the 1-position in the fluorene nucleus. Presumably (see Berliner, *J. Amer. Chem. Soc.*, 1942, **64**, 2894; Bradsher and Smith, *ibid.*, 1943, **65**, 854) the reaction of the ketone (I) with hydrogen bromide may be formulated thus :



The solution of hydrobromic acid converts the ketone (I), by addition of a proton to the carbonyl group, into the hypothetical intermediate compound (A), which by virtue of its carbonium atom and an electrophilic attack on the carbon atom in position 1 in the fluorene nucleus effects ring closure, a proton being liberated. Facile dehydration of the tertiary alcohol (B) produces 2 : 2 : 4-trimethyl-1 : 2-dihydrofluoranthene (III).

Attempts to cyclise the ketone (I) to give (III) by means of acetic anhydride containing a few drops of concentrated sulphuric acid failed (cf. Bradsher, *J. Amer. Chem. Soc.*, 1943, **65**, 451).

When the ketone (I) was boiled with hydriodic acid (*d* 1·7) in acetic acid, as previously reported (France, Maitland, and Tucker, *loc. cit.*), the substance $C_{19}H_{20}$, m. p. 103—104°, was obtained : it is undoubtedly 2 : 2 : 4-trimethyl-1 : 2 : 3 : 4-tetrahydrofluoranthene (IV). It has not yet been established whether its formation is to be interpreted as (*a*) analogous to that suggested for the action of hydrobromic acid on (I), followed by reduction of (III) to (IV), or (*b*) as reduction of (I) to δ-9-fluorenyl-δ-methylpentan-β-ol (V), which then, instead of undergoing normal reduction to the hydrocarbon (II), eliminates water and cyclises to the fluoranthene derivative (IV) in the usual manner.

That the second mechanism is probable is substantiated by the following : Reduction of the ketone (I) by aluminium *iso*propoxide in *iso*propyl alcohol gave δ-9-*fluorenyl*-δ-*methylpentan*-β-*ol* (V), which (*a*) by boiling with hydriodic acid (*d* 1·5) in acetic acid for 20 minutes, or (*b*) by the action of concentrated sulphuric acid in glacial acetic acid at room temperature, at once gave (IV). Furthermore, attempts to reduce (III) to (IV) by

boiling with hydriodic acid (*d* 1·7) in acetic acid for 4 hours—the conditions under which (I) gives (IV) (France, Maitland, and Tucker, *loc. cit.*, p. 1742; and this communication)—gave only a very small yield of (IV).

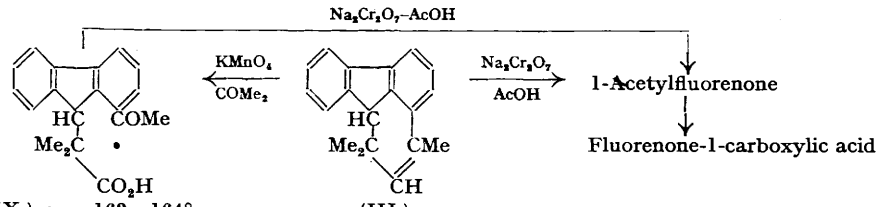
Heating the alcohol (V) with potassium hydrogen sulphate gave an olefin which is probably *δ-9-fluorenyl-δ-methyl-Δ$^{\beta}$-pentene* (VI) (or possibly δ-9-fluorenyl-δ-methyl-Δ$^{\alpha}$-pentene). Catalytic hydrogenation (palladium–acetic acid) of the olefin (VI) gave the expected pentane (II).

The original ketone (I) reacted with phosphorus pentachloride in chloroform to give probably *β-chloro-δ-9-fluorenyl-δ-methyl-Δ$^{\beta}$-pentene* (VII) (or the corresponding Δ$^{\alpha}$-derivative), which, by the action of hydriodic acid (*d* 1·7) in boiling acetic acid, gave the fluoranthene derivative (IV); oxidation of (VII) with sodium dichromate in glacial acetic acid gave fluorenone, thus proving that the chlorine atom is in the open chain and not in the fluorene nucleus.

The chloro-compound (VII), on boiling with sodium in xylene, gave *fluorene*-9-spiro-2′ : 2′ : 4′-*trimethyl*-cyclo*butane* (VIII). Oxidation of this compound gave an unidentifiable oil: neither fluorenone nor any acidic product could be obtained. The oil did not react with hydroxylamine.

Oxidation of 2 : 2 : 4-trimethyl-1 : 2-dihydrofluoranthene (III) by sodium dichromate solution in boiling glacial acetic acid for 1½ hours gave rise to 1-*acetylfluorenone*, m. p. 114—116° (yield, 10%), and fluorenone-1-carboxylic acid (yield, 31%), which softened at 188° and melted at 191—194° (Ray and Rieveschl, *J. Amer. Chem. Soc.*, 1943, **65**, 836, give m. p. 193—194°; Fieser and Seligman, *ibid.*, 1935, **57**, 2174, m. p. 191—193°; Huntress, Pfister, and Pfister, *ibid.*, 1942, **64**, 2845, m. p. 188—190°). When the oxidation mixture was boiled for 24 hours, fluorenone-1-carboxylic acid only was obtained (crude, 64%; pure, 53%) [cf. 52% obtained by the oxidation of fluoranthene (Ray and Rieveschl, *loc. cit.*)]. 1-Acetylfluorenone gives a dioxime, but the substance obtained by the action of 2 : 4-dinitrophenylhydrazine on 1-acetylfluorenone gave inexplicable analytical results; the constitution of 1-acetylfluorenone was, however, established by the above oxidation, and by oxidation by means of sodium hypochlorite solution to fluorenone-1-carboxylic acid. Oxidation of 2 : 2 : 4-trimethyl-1 : 2 : 3 : 4-tetrahydrofluoranthene (IV) by dichromate as above (25 hours) gave 1-acetylfluorenone (4%) and fluorenone-1-carboxylic acid (28%).

It is now clear that the substance $C_{19}H_{18}O_3$, m. p. 163—164°, obtained by permanganate–acetone oxidation of 2 : 2 : 4-trimethyl-1 : 2-dihydrofluoranthene (III) (France, Maitland, and Tucker, *loc. cit.*, p. 1743) is 1-*acetylfluorene*-9-iso*butyric acid* (IX); and since it has now been shown that this acid is oxidised by dichromate–acetic acid to 1-acetylfluorenone and fluorenone-1-carboxylic acid, the course of oxidation is probably as shown :



(IX.) m.p. 163—164°. (III.)

(III) and (IV) have no growth-inhibitory effect (Badger, Elson, Haddow, Hewett, and Robinson, *Proc. Roy. Soc.*, 1942, *B*, **130**, pp. 268, 270) and no carcinogenic activity (Badger, Cook, Hewett, Kennaway, Kennaway, and Martin, *ibid.*, 1942, *B*, **131**, 170).

Experimental.

2 : 2 : 4-*Trimethyl*-1 : 2-*dihydrofluoranthene* (III).—The method formerly adopted for the preparation of (III) (France, Maitland, and Tucker, *loc. cit.*, p. 1743) has been improved: Hydrogen bromide (prepared by the action of bromine on boiling tetralin) was passed into a solution of the ketone (I) (10 g.) in glacial acetic acid (100 ml.) for 1 hour. Crystals separated; these were removed an hour later and washed with cold glacial acetic acid. The acid washings were added to the filtrate and after 3—4 hours a second crop of crystals was removed. Addition of water to the filtrate, whether otherwise untreated or previously boiled to remove hydrogen bromide, gave only a small amount of oil. The crystalline deposits were dissolved in glacial acetic acid, the solution boiled to expel hydrogen bromide, and, after cooling, the deposited material was crystallised from methanol, giving 2 : 2 : 4-trimethyl-1 : 2-dihydrofluoranthene (III), m. p. 77—79° (5·9 g.; yield, 63%).

Passage of hydrogen bromide until the acetic acid solution of (I) was merely saturated (15 mins.), followed by standing or boiling, gave lowered yields of (III).

2 : 2 : 4-*Trimethyl*-1 : 2 : 3 : 4-*tetrahydrofluoranthene* (IV).—(a) Catalytic hydrogenation of (III) by means of palladium-black–hydrogen–acetic acid gave the hydrocarbon $C_{19}H_{20}$, m. p. 103—104°, now known to be (IV) (yield, 95%) (France, Maitland, and Tucker, *loc. cit.*, p. 1743).

(b) *Action of hydriodic acid on* (I) (France, Maitland, and Tucker, *loc. cit.*, p. 1742). Improved method: The ketone (I) (25 g.) in glacial acetic acid (300 ml.) and hydriodic acid (*d* 1·7, 60 ml.) were boiled together for 5 hours, and the product isolated as before (12 g.; yield, 50%). (IV) was similarly obtained from (III) (very small yield), from the alcohol (V)—boiling for 20 minutes (yield, 50%)—and from the chloro-compound (VII).

(c) *Action of sulphuric acid on the alcohol* (V). The alcohol (V) was dissolved in glacial acetic acid, and an equal volume of a mixture of concentrated sulphuric acid and glacial acetic acid (1 : 1 by vol.) added. The mixture became warm, turned faintly brown, and in a few seconds deposited crystals of (IV) (excellent yield).

An attempt to prepare (IV) by ring closure of the olefin (VI) by using anhydrous aluminium chloride in cold carbon disulphide gave an uncrystallisable oil.

(IV) does not form a picrate (acetic acid solution).

δ-9-Fluorenyl-δ-methylpentan-β-ol (V).—The ketone (I) (5·28 g.) was boiled with a molar solution of aluminium *iso*propoxide in *iso*propyl alcohol 25 ml.) with slow distillation of the alcohol, the volume of the reaction mixture being kept

at 25 ml. by periodical additions of *iso*propyl alcohol, until the distillate became free from acetone (2 : 4-dinitrophenylhydrazone test) (5 hours). The reaction mixture became gelatinous. The pale yellow solid precipitated by dilute sulphuric acid crystallised from light petroleum (b. p. 60—80°) in colourless rosettes, m. p. 83—85° (4·4 g.; yield, 85%), of δ-9-*fluorenyl*-δ-*methylpentan*-β-*ol* (V) (Found : C, 85·7; H, 8·3. $C_{19}H_{22}O$ requires C, 85·7; H, 8·3%).

The *phenylurethane* of (V), obtained by standing and heating its benzene solution with phenyl *iso*cyanate, gave thick-set rosettes from glacial acetic acid, m. p. 157—159° (Found : C, 81·3; H, 7·0; N, 3·6. $C_{26}H_{27}O_2N$ requires C, 81·0; H, 7·0; N, 3·6%).

The 3 : 5-*dinitrobenzoate* prepared by boiling a solution of (V) with 3 : 5-dinitrobenzoyl chloride in pyridine for 1 minute crystallised from glacial acetic acid in pale green prisms, m. p. 164—165° after softening at 161° (Found : C, 67·7; H, 5·2; N, 6·0. $C_{26}H_{24}O_6N_2$ requires C, 67·8; H, 5·2; N, 6·1%).

The alcohol (V) (1 g.) was heated with potassium hydrogen sulphate (1 g.) for 10 minutes at 180°. The product, isolated in the usual way, was crystallised from acetic acid diluted with a trace of water, then from methanol, and gave δ-9-*fluorenyl*-δ-*methyl*-Δ^{β}-*pentene* (VI) in colourless needles, m. p. 92° after softening at 89° (0·28 g.; yield, 33%) (Found : C, 91·8; H, 8·0. $C_{19}H_{20}$ requires C, 91·9; H, 8·1%). Microhydrogenation, with palladium-black in acetic acid, gave a value corresponding to 1·2 double bonds. The reduction product alone, or mixed with (II) obtained by the Clemmensen method of reduction of the original ketone (I), melted at 84—85°, thus proving that (VI) has an open chain and on hydrogenation gives (II).

β-*Chloro*-δ-9-*fluorenyl*-δ-*methyl*-Δ^{β}-*pentene* (VII).—The ketone (I) (5 g.) was heated with phosphorus pentachloride (20 g.) in chloroform (50 ml.) for 1 hour. After the chloroform had been removed by steam-distillation, the residue crystallised from glacial acetic acid in colourless plates, m. p. 76—78° (1·9 g., yield, 30%) (Found : C, 80·7; H, 7·0; Cl, 12·9. $C_{19}H_{19}Cl$ requires C, 80·7; H, 6·7; Cl, 12·6%).

When phosphorus pentabromide was used instead of the chloride in the above process, the dibromo-derivative $C_{19}H_{18}OBr_2$ previously isolated (France, Maitland, and Tucker, *loc. cit.*, p. 1744) was obtained.

Fluorene-9-spiro-2′ : 2′ : 4′-*trimethyl*cyclo*butane* (VIII).—The chloro-compound (VII) (2·82 g.) was boiled in xylene (5 ml.) with finely divided sodium (0·5 g.) for 1 hour; the xylene solution, separated from the purple precipitate, was evaporated; the residue so obtained crystallised from methanol in long colourless prisms (0·94 g.). Treatment of the purple precipitate with ethanol and then with excess of water, followed by extraction with and crystallisation from methanol, gave more of this product (0·15 g.) (total, 1·09; yield, 44%), *fluorene*-9-spiro-2′ : 2′ : 4′-*trimethyl*cyclo*butane*, m. p. 92—94° (Found : C, 91·8; H, 8·1; *M*, 198. $C_{19}H_{20}$ requires C, 91·9; H, 8·1%; *M*, 248).

Oxidation of Fluoranthene Derivatives to 1-*Acetylfluorenone and to Fluorenone*-1-*carboxylic Acid.—Oxidation of* 2 : 2 : 4-*trimethyl*-1 : 2-*dihydrofluoranthene* (III). The compound (III) (2·46 g.), sodium dichromate (13 g.), and glacial acetic acid (90 ml.) were boiled together for 1½ hours; then more dichromate (10 g.) was added, and boiling continued for 1½ hours. Half the bulk of acetic acid was removed by distillation, and the residual liquor poured into a large excess of dilute sulphuric acid. The washed precipitate was extracted with potassium hydroxide solution; the residue crystallised from methanol to give 1-*acetylfluorenone* in golden sword-blades, m. p. 114—116° (crude, 0·51 g.; pure 0·25 g.; yield, 10%) (Found : C, 80·9; H, 4·4. $C_{15}H_{10}O_2$ requires C, 81·1; H, 4·5%). The alkaline extract on acidification with dilute sulphuric acid gave the characteristic salmon-coloured precipitate of fluorenone-1-carboxylic acid (0·99 g.; yield, 45%). Purification was difficult; repeated crystallisation from glacial acetic acid gave eventually orange-red needles, m. p. 191—193° after softening at 189° (0·7 g.; yield, 31%). A sample of the acid prepared from fluoranthene by oxidation with chromic acid in aqueous acetic acid melted similarly.

2 : 2 : 4-Trimethyl-1 : 2-dihydrofluoranthene (III) under the latter conditions of oxidation gave no acid but appeared to be completely destroyed.

Increasing the period of heating and the amount of dichromate used in the above-described experiment caused increase in the yield of fluorenone-1-carboxylic acid (18 hours; yield, 46%) at the expense of 1-acetylfluorenone : thus when (III) (1·23 g.) was boiled with sodium dichromate (14 g.) in acetic acid (50 ml.) for 24 hours, and the liquor treated as above, only a trace of 1-acetylfluorenone was obtained but an increased yield of fluorenone-1-carboxylic acid (crude, 0·72 g.; pure, 0·60 g.; yield, 53%).

1-Acetylfluorenone gave a *dioxime* which, crystallised from dilute acetic acid and then from toluene, formed pale green nodules, m. p. 197° after softening at 180° (Found : C, 71·2; H, 4·8: $C_{15}H_{12}O_2N_2$ requires C, 71·4; H, 4·8%).

A *derivative* of 1-acetylfluorenone prepared by the action of 2 : 4-dinitrophenylhydrazine in methanol containing a drop of sulphuric acid crystallised from dioxan, then from toluene, in hairy, orange-yellow crystals, m. p. 251° (decomp.) after softening at 248°, and is of doubtful composition (Found : C, 61·4, 61·5; H, 3·6, 3·6; N, 12·8. A monohydrazone, $C_{21}H_{14}O_5N_4$, would require C, 62·7; H, 3·5; N, 13·9%).

1-Acetylfluorenone (0·12 g.) in warm methanol (5 ml.) was treated with aqueous sodium hypochlorite (5 ml.) and sodium hydroxide solution (10%, 1 ml.) and left for a short time. After filtration, sulphurous acid and dilute sulphuric acid were added to the filtrate. The orange-red precipitate, crystallised from acetic acid, consisted of fluorenone-1-carboxylic acid (0·07 g.; yield, 55%).

1-Acetylfluorenone, dissolved in dioxan containing a drop of benzyltrimethylammonium hydroxide solution, when treated with acrylonitrile and warmed, gave brown crystals from acetic anhydride, m. p. >280°. It was not further characterised (cf. Bruson *et al.*, *J. Amer. Chem. Soc.*, 1942, **64**, 2457).

Oxidation of 2 : 2 : 4-*Trimethyl*-1 : 2 : 3 : 4-*tetrahydrofluoranthene* (IV).—The substance (1·24 g.) was boiled in glacial acetic acid (50 ml.) containing sodium dichromate (12 g.) for 25 hours. The above method of isolation gave 1-acetylfluorenone (4%) and fluorenone-1-carboxylic acid (28%).

Oxidation of 1-*Acetylfluorene*-9-iso*butyric acid* (IX).—Oxidation with dichromate–acetic acid for 5 hours gave 1-acetylfluorenone (5%) and fluorenone-1-carboxylic acid (22%).

The ketone (I), heated with an ethanol–dilute sulphuric acid solution of 2 : 4-dinitrophenylhydrazine, gave the 2 : 4-*dinitrophenylhydrazone*, which crystallised from glacial acetic acid in orange prisms, m. p. 200—202° (Found : C, 67·7; H, 5·4; N, 12·5. $C_{25}H_{24}O_4N_4$ requires C, 67·6; H, 5·4; N, 12·6%).

We are grateful for the award of Carnegie Scholarships to two of us (H. F. and J. F.), for a grant from the Department of Scientific and Industrial Research to one of us (J. F.), and for financial assistance from the Chemical Society. We must again express our thanks to Mr. J. M. L. Cameron, who carried out the micro-analyses.

UNIVERSITY OF GLASGOW. [*Received, September 1st*, 1944.]