

SUBSTITUTION IN POLYCYCLIC SYSTEMS*

Part II. The Nitroderivatives of Fluoryl 9-Trimethylammonium Compounds

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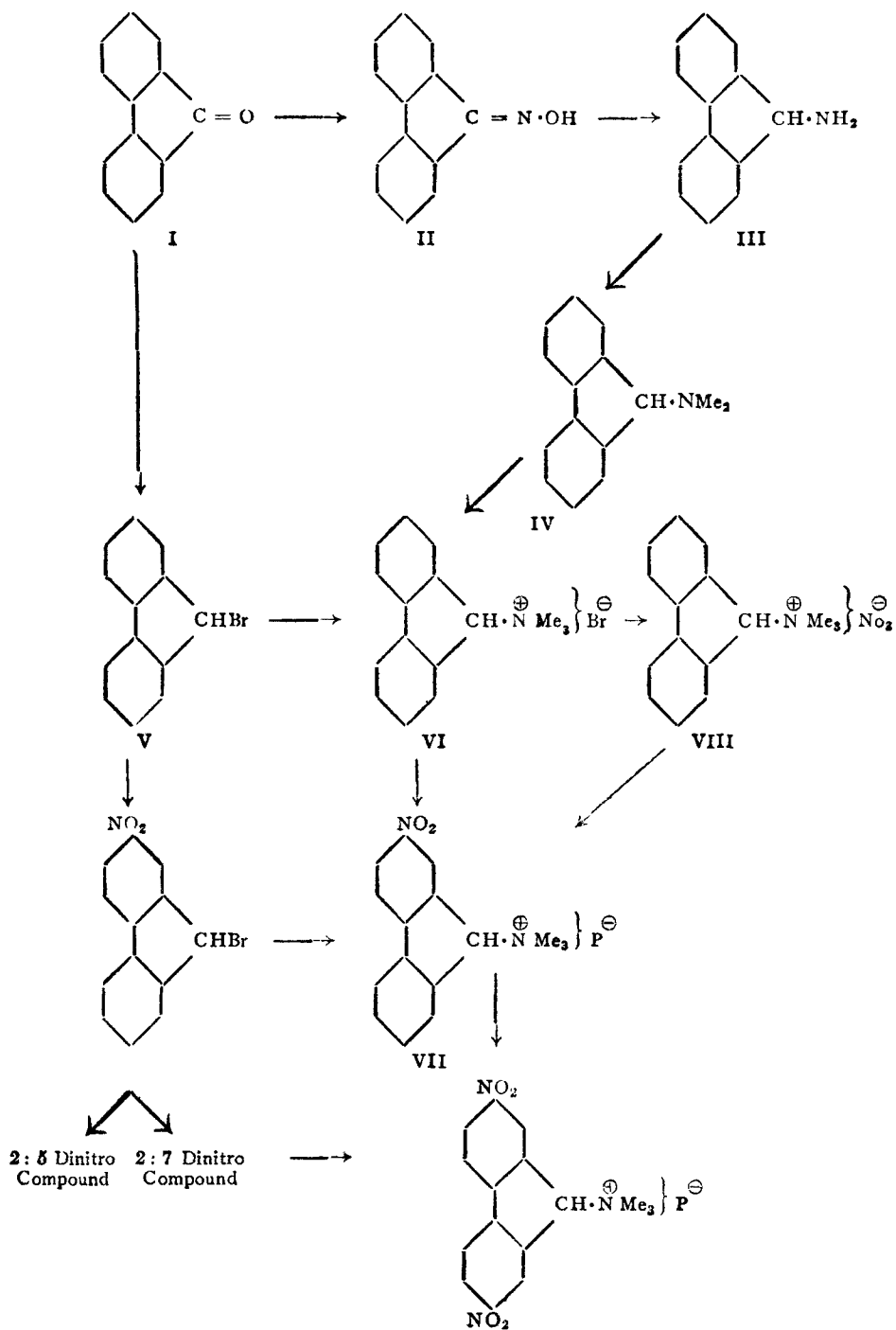
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IN the nitrations of 9-substituted fluorene compounds, it has been found that generally the introduction of substituent groups in the 9-position does not affect the general orientation in the nucleus even though the relative proportions of the isomers might vary. In the case of 9-bromofluorene it was noticed that the introduction of a second nitro group was predominantly in the 7-position while a small amount of the 2 : 5 compound and a number of other products were obtained, the dinitro product being obtained as easily as with the unsubstituted fluorene though the nitration conditions had to be kept under greater control; with an average room temperature in our laboratories of 30° C., a rigid control of temperature below 15° C. was found necessary to minimise side reactions.

With a closed system of mobile electrons involving the two benzene nuclei and the cyclopentadiene system, a 9-substituent may be expected to disturb substitution in other positions especially if a strong electron attracting group (class—I of Ingold's classification) is in that position. The present paper deals with studies involving quaternary ammonium compounds which were needed by the authors in another investigation. A report on the studies on 9-nitro and 9-carbonyl derivatives will form the subject of a later communication.

The experimental investigation was carried out according to the following scheme:—

* For Part I see Anantakrishnan and Hughes, *J.C.S.*, 1935, 1607.



Schmidt and Stutzel⁶ reported the production of two compounds by reducing II, both being considered stereoisomeric forms of 9-aminofluorene. Kuhn and Jacob⁵ also report several forms. Ingold and Wilson,⁴ however, find that only one form of III is obtained along with some acetyl derivative. We have carried out the reduction several times and in all cases obtained only one form of 9-aminofluorene confirming the observations of Ingold and Wilson (*loc. cit.*).

For the conversion of III into its dimethyl derivative (IV), Stevens⁸ uses formaldehyde as the methylating agent carrying out the reaction in a pressure bottle at 130°. We find that without recourse to high temperature or pressure, this methylation could be smoothly carried out with dimethyl sulphate and excess alkali, the reaction taking a shorter time.

For the preparation of the quaternary ammonium compound, the method involving 9-bromofluorene was found more convenient and has been adopted in the experiments.

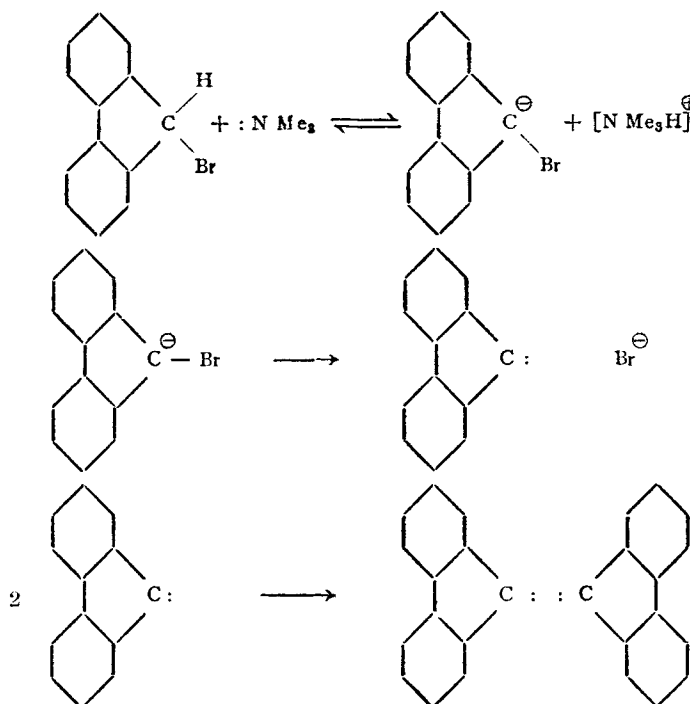
The mono-nitro 'Onium compound could be easily prepared either by nitrating the unsubstituted salt or by reacting 2-nitro 9-bromofluorene with trimethylamine in acetonitrile. Here also the entrance of the nitro group in the 2-position shows that a 9-substituent does not materially affect the orientation. It must be borne in mind that in the nitration of the salt it is only the cation that is concerned and the ease of nitration is independent of the nature of the anion.

The preparation of the corresponding dinitro compounds by direct nitration of the salt under mild conditions, however, gave very unsatisfactory results. The isomeric 2:5 and 2:7 dinitrofluoryl 9-trimethyl ammonium compounds could be obtained by dinitration of 9-bromofluorene and controlled reaction of these with trimethylamine. Boiling of the salt with fuming nitric acid appears to be necessary for the introduction of a second nitro group which goes predominantly in the 7-position.

Here we have a striking illustration of the difference between the corresponding sulphonium and ammonium compounds. Under conditions which yield directly the dinitrosulphonium compound (Hughes and Kuriyan¹), the fluoryl 9-trimethyl ammonium salts give only a mononitro product. From *a priori* considerations it can be shown that the quaternary ammonium "pole" exerts a greater deactivating influence than the corresponding sulphonium "pole" and it is also well known that the mechanism of elimination is more complex in the case of sulphonium compounds. With a powerful electron attracting group, the deactivating influence is only to be

expected. A substituent in the side chain usually exerts a comparatively feeble influence on the reactivity of the nucleus but the 9-position in fluorene has to be considered differently. The electronic structure of fluorene and the fluoryl radical visualises the cyclopentadiene ring as part of the system of mobile electrons and consequently one has to expect transmission of group influences when these are sufficiently powerful as in the present case. Consequently both benzene nuclei are deactivated and slow nitration is the result. With the introduction of the first nitro group, this deactivating influence is greatly augmented and further nitration becomes very difficult, the conditions approximating to that of trinitration of 2:7 dinitro fluorene. Here again, is noticed the similarity between diphenyl and fluorene. In both classes polynitro compounds are obtained only by indirect means.

The present series of compounds also illustrate the converse of this influence, substituents in other positions affecting reactivity in the 9-position. The facile transmission of electromeric and inductive effects by the cyclopentadiene system is noticed here also. As is well known, the nitro group (-I-T) promotes reactivity towards nucleophilic reagents and retards reactivity towards electrophilic reagents. In benzene this influence is most noticeable in the ortho and para-positions by electromeric relay. In the present studies this same effect is noticed with 9-substituents in fluorene. Taking substituted 9-bromo-fluorenes, the two reactions that may be envisaged involve either elimination of bromine as an anion or that of hydrogen as a cation. In one case we have the disruption of a C-Br linkage and in the other a C-H linkage. When a substituted 9-bromo compound reacts with trimethylamine, two reactions are therefore possible the formation of an 'Onium compound which will be considered in a later paper and the formation of a bis-fluorenylidine:



The evidence for this ionic *cum* free radical mechanism is at present purely circumstantial and it is hoped at a later stage to adduce more definite experimental proof. The series of colour changes that is invariably noticed in this reaction together with the necessity for an excess of the base render this scheme plausible. It must be pointed out here that the introduction of solvents in which ionisation may not be expected, considerably slows down the reaction giving the halogen-free compound. The introduction of a nitro group in the nucleus facilitates the egress of the proton and the bis-fluorenylidene compound is readily obtained. A second nitro group in the nucleus makes this reaction almost quantitative (Table I). It is

TABLE I

Compound	% Halogen-free compound formed with NMe_3
9-Bromofluorene	0
2-Nitro-9-Bromofluorene .. .	10-20
2:7-Dinitro-9-Bromofluorene .. .	80
2:5-Dinitro-9-Bromofluorene .. .	99

significant that the stabilisation of a negative charge on the ter-covalent 9-carbon atom is facilitated by the presence of nitro groups in the nucleus.¹

The influence of the nitro group is felt not only in the chemical behaviour but also on the physical properties of the compounds studied as may be seen from an examination of the table (Table II).

TABLE II
Melting points of some derivatives of fluorene

	Unsubstituted	Substituents in Nucleus		
		2-Nitro	2: 7-Dinitro	2: 5-Dinitro
Fluorene	114·5°	156-57	295-300	207
Fluorenone	85	221	292	241
9-Bromofluorene	103-104·5	145	260	199
Fluoryl 9-trimethyl-ammonium bromid	189-90	198-200	225	..
Fluoryl 9-trimethyl-ammonium picrate	170-75	226	235-36	209-10
Fluoryl 9-dimethyl sulphonium bromide	133	130-35	230	..
Fluoryl 9-dimethyl sulphonium picrate	149-50	185	255-60	..

In all the series the 2: 7 compounds, like the para derivatives in benzene, the 2: 6 or 1: 5 derivatives in naphthalene and 4, 4' derivatives of diphenyl exhibit the highest melting point. Any systematic correlation between structure and melting point in the present series has, however, to meet the limitations set by the chemical behaviour of the compounds. In a number of cases of the substituted compounds, especially those in the last three columns, the "melting points" really represent the temperature of decomposition of the compounds as it has often been found that the rate of heating appeared to modify the melting point. The values given refer to results obtained under comparable rates of heating. We can then readily understand the very close range in the 'Onium series. It is interesting to note in this connection that corresponding sulphonium compounds also present a similar anomalous position. In both cases, we have the "electron sink" nitro groups reinforcing the 'Onium pole so as to facilitate the easy removal of the proton which represents the first step in the elimination reaction.

Experimental

Oxidation of fluorene.—A modification of the method of Schmidt and Wagner⁷ was adopted. The reaction was allowed to proceed at or below

100° C. Higher temperatures were found to give more of by-products. The vigorous reaction in the early stages had to be controlled by cooling. The yield (90%) was better than that of Huntress and Cliff,² m.p. 85° C.

The oxime [m.p. 195° C. (yellow needles from dilute alcohol)] was prepared by the usual methods.

Reduction of Fluorenone Oxime.—9-Aminofluorene was obtained by a modification of earlier methods⁴ using diluted (92%) acetic acid to minimise the formation of the acetyl derivative. The hydrochloride was crystallised from dilute hydrochloric acid in long needles melting with decomposition at 255° C. The amine liberated from this crystallized from n. hexane, m.p. 64°–65° C. Only one amino compound was obtained in all experiments.

Methylation of 9-Aminofluorene.—The free amine was shaken up with an excess of sodium hydroxide and dimethyl sulphate, the excess of the latter compound being destroyed at the end of the reaction. The mixture was cooled, extracted with benzene, washed free from alkali and a stream of dry hydrogen chloride was passed. The hydrochloride of the base which was thrown down was recrystallised from an alcohol ether mixture. The free base was obtained by basification and ether extraction. The residual oil after removing ether was purified by distillation under ordinary pressure, the distillate readily solidifying to fine long needles, m.p. 49–50° C. Picrate m.p. 203–04° (yield 10·20%) (*cf.* Ingold and Jessop³). The identity of this compound was established by comparison with a specimen prepared by Steven's method.⁸

The tertiary base was converted to the quaternary ammonium compound with methyl iodide and the picrate from this had a melting point 170–75° (*c.f.* next preparation).

Preparation of Fluoryl 9-Trimethyl Ammoniumbromide.—9-Bromofluorene was dissolved in the minimum quantity of acetonitrile and treated with an excess of tri-methylamine, the reaction being carried out at 0° and left overnight. The solution was diluted with ether. An oily substance separated which on keeping overnight at 0° C. solidified in cubical crystals. The salt was filtered, washed with dry ether and appeared pure m.p. 189–90°; Picrate 170–75° C. (yield nearly quantitative).

Nitration of Fluoryl 9-Trimethyl Ammoniumbromide.—Nitration of the bromide invariably led to products with nuclear bromine and the nitro derivatives could be obtained only after conversion of the bromide into other salts.

The bromide (3.04 g.) was converted into the nitrate by reacting with an equivalent amount of silver nitrate, filtered off from the bromide and evaporated to a syrupy consistency when the nitrate crystallised in feathery hygroscopic needles* (m.p. 194° C.). This nitrate was suspended in acetic anhydride (15 c.c.) and treated with 2.5 c.c. concentrated nitric acid (1.42 s.g.) the temperature being maintained below -10° C. and the acid being added dropwise. The reaction mixture was kept at the same temperature for two hours, gradually allowed to rise to room temperature (30° C.) and then heated on the water-bath for one hour. The hot solution was poured into a large volume of water. Small quantities of a white precipitate insoluble in water (fluorenol?) were filtered off and the clear filtrate treated with sodium picrate. A yellow precipitate was obtained. Purified by recrystallisation from aqueous acetone (with animal charcoal) containing a trace of picric acid, m.p. 225-26° C. (Found: C, 53.1%; H, 4.0%. $C_{22}H_{19}N_5O_9$ requires C, 53.1%; H, 3.8%.)

The same product was obtained by treating the corresponding picrate (1.0 g.) with 5 c.c. of fuming nitric acid, the addition being carried out slowly and the temperature maintained below -10° C. for about two and a half hours. The reaction mixture was allowed to rise slowly to 0° C. and then poured into a large volume of water. No dinitro compound could be isolated (yield > 80%).

The method of Hughes and Kuriyan (*loc. cit.*) for dinitration of sulphonium analogue resulted only in the mono-nitration product.

The position of the nitro group in all these cases was established by comparison with the compound prepared with definitely oriented starting material as follows: 2-nitro 9-bromofluorene was prepared by the method of Anantakrishnan and Hughes (*loc. cit.*) dissolved in acetonitrile and treated with excess trimethyl amine also in acetonitrile solution. The reaction was very rapid (*cf.* Hughes and Kuriyan, *loc. cit.*, for the sulphonium compound). After three quarters of an hour, the quaternary ammonium bromide contaminated with a coloured product crystallised out on addition of a large volume of dry ether. The precipitate was filtered, and washed with ether in which the impurity appeared to dissolve, m.p. 198-200°. (Found: Br, 21.4%. $C_{16}H_{17}N_2O_2$ Br requires Br, 22.9%.) A solution of the bromide in water was treated with an aqueous solution of sodium picrate when the 'Onium picrate separated in fine golden needles (m.p. and mixed melting point with compound obtained above 225-26°).

* Note added in proof.—Slow evaporation of concentrated solutions give tabular prismatic crystals.

Dinitration of Fluoryl 9-Trimethyl Ammonium Salts.—Ordinary conditions of nitration led invariably to mononitro products irrespective of the nitric acid concentration. Only the strongest nitrating agents combined with a moderately high temperature lead to dinitro derivatives.

Fluoryl 9-trimethyl ammonium picrate was treated with a large excess of fuming nitric acid (1 mol. of salt to 70 mols. acid) at room temperature. The temperature shot up to 60° C. and was gradually allowed to cool down. After a few hours, the mixture was cautiously boiled for a short time over the free flame. The clear solution which was somewhat pale in colour was poured into a large volume of water. The picrate separated out as a yellow crystalline powder which was filtered off, washed with water, and recrystallized from dry acetone to which a little picric acid was added. Only one dinitro compound could be isolated, the proportion of the isomer if formed being very low.

The orientation of this was carried out as before. 2:5 and 2:7 Dinitro 9-bromo fluorenes were obtained by the method of Anantakrishnan and Hughes (*loc. cit.*). Reactions of these with trimethyl amine in acetonitrile or nitromethane led to a variety of products. The 'Onium compounds could be obtained in small yields by carrying out the reaction in benzene solution. The coloured products obtained were repeatedly extracted with hot water. The aqueous solutions were evaporated on the water-bath to small bulk. On addition of ether to the concentrated solution, the bromides crystallised out (m.p. of 2:7 Dinitro 9-trimethyl ammonium bromide 225°). (Found: Br, 19.2%. $C_{16}H_{16}N_3O_4$ Br requires Br, 20.3%.) The solutions of the bromides were treated with *neutral* sodium picrate solution. The products were recrystallised from acetone as before. The 2:5 Dinitrofluorenyl 9-trimethyl ammonium picrate was obtained as heavy yellow crystals, m.p. 209–10°.

The 2:7 Dinitro compound was obtained as brownish yellow crystals, m.p. 235–36° C. Mixed m.p. with compound obtained by drastic nitration of unsubstituted salt 236°. (Found: C, 48.7%; H, 3.3%. $C_{22}H_{18}N_6O_{11}$ requires C, 48.7%; H, 3.2%.)

Summary

The nitration of fluoryl-9-trimethylammonium compounds and the orientation of the products is described. It has been found that the best method of obtaining the unsubstituted 'Onium salt is from 9-bromo luorene. The 9-substituent does not appear to have any marked influence on the position of new entrant groups but exerts a noticeable one on the activity

of the nuclear positions. The converse influence of nuclear substituents on the activity of the 9-position is evident.

REFERENCES

1. Hughes and Kuriyan .. *J.C.S.*, 1935, 1610.
2. Huntress and Cliff .. *J. Amer. Chem. Soc.*, 1931, **53**, 2720.
3. Ingold and Jessop .. *J.C.S.*, 1929, 2361.
4. ——— and Wilson .. *Ibid.*, 1933, 1499.
5. Kuhn and Jacob .. *Ber.*, 1925, **58**, 1432.
6. Schmidt and Stutzel .. *Ibid.*, 1908, **41**, 1243.
7. ——— and Wagner .. *Ibid.*, 1910, **43**, 1797.
8. Stevens .. *J.C.S.*, 1930, 2115.