430. *Substitution Products of 2-Aminofluorene.*

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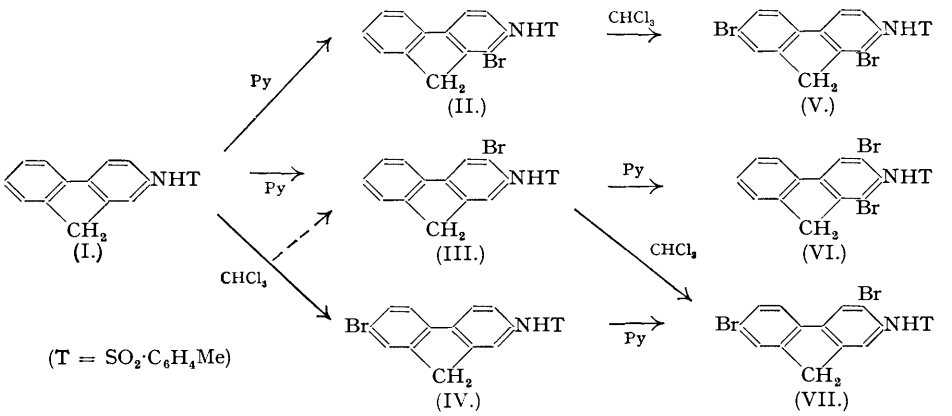
The bromination and nitration of derivatives of 2-aminofluorene have been studied. The position entered is determined by both the entering group and the directing group (especially as modified by the nature of the solvent).

2-Aminofluorene is one of the most readily available derivatives of fluorene (*Org. Synth.*, Coll. Vol. II, 447), and several papers have already appeared on its substitution products. Eckert and Langecker (*J. pr. Chem.*, 1928, **118**, 263) by bromination of the base in acetic acid isolated a tribromo-derivative which could be oxidised to a tribromoaminofluorenone. It is, therefore, most probably 1 : 3 : 7-tribromo-2-aminofluorene. The nitration of 2-acetamidofluorene has been studied by Diels, Schill, and Tolson (*Ber.*, 1902, **35**, 3286), Eckert and Langecker (*loc. cit.*), and Koshits and Nikiforova (*J. Appl. Chem. U.S.S.R.*, 1940, **13**, 215). These authors agree that mononitration occurs at both positions 3 and 7 in the ratio of approximately 2·5 : 1. This result may be compared with the nitration of the closely related 4-acetamidodiphenyl entirely at position 3 (Fichter and Sulzberger, *Ber.*, 1904, **37**, 878).

Campbell, Anderson, and Gilmore (*J.*, 1940, 446), wishing to obtain fluorenes with a bromo-group in position 1, examined the bromination of both 2-toluene-*p*-sulphonamido- and 2-acetamido-fluorene. In each case only one product was isolated and this, by analogy with the nitro-derivative of 2-acetamidofluorene, was assumed to be the 3 : 7-dibromo-compound.*



In the present experiments we first re-examined the bromination of 2-aminofluorene in acetic acid solution and found that it was possible to isolate both a *monobromo-* and a *dibromo-*base, most probably the 3-bromo- and 1 : 3-dibromo-derivatives. Bromination of 2-acetamidofluorene gave a mixture of products from which it was possible to isolate 7-bromo- (70% yield) and 3 : 7-dibromo-2-acetamidofluorene. The position of entry of the bromine atom into 2-toluene-*p*-sulphonamidofluorene (I) is largely governed by the choice of chloroform or pyridine as a solvent. With one molecular proportion of bromine in chloroform there was produced a 60% yield of 7-bromo-2-toluene-*p*-sulphonamidofluorene (IV) (together with a small amount of 7-bromo-2-aminofluorene produced by hydrolysis) and impure 3-*bromo*-2-*toluene*-p-*sulphonamidofluorene* (III). With 2 molecular proportions of bromine in chloroform there was obtained a 70% yield of the 3 : 7-dibromo-derivative (VII), identified by hydrolysis to the base and acetylation of this to 3 : 7-dibromo-2-acetamidofluorene. With 1 molecular proportion of bromine in pyridine there was obtained as the main product the 3-bromo-derivative and with 2 molecular proportions 1 : 3-*dibromo*-2-*toluene*-p-*sulphonamidofluorene* (VI). A small amount of 1-bromo-2-toluene-*p*-sulphonamidofluorene (II) must be present in the crude 3-bromo-derivative, for on further bromination in chloroform it gave the 3 : 7-dibromo-derivative (main) together with 1 : 7-*dibromo*-2-*toluene*-p-*sulphonamidofluorene* (V) (trace).

* The structure of derivatives of 2-aminofluorene has seldom been established with complete certainty. In particular, ring closures with 2-aminofluorenes which are usually assumed to occur at position 1 (see, *e.g.*, Diels and Staehlin, *Ber.*, 1902, **35**, 3275; Hughes, Lions, and Wright, *J. Proc. Roy. Soc. N.S. Wales*, 1938, **71**, 449; Neish, *Rec. Trav. chim.*, 1948, **67**, 349) might on general grounds be expected to occur at position 3.

Further bromination of (VII) gave 1 : 3 : 7-*tribromo*-2-*toluene*-p-*sulphonamidofluorene*, which was smoothly hydrolysed to the tribromo-base previously described by Eckert and Langecker.

Next, it was found that 2-*dimethylaminofluorene* behaved exactly as 4-dimethylaminodiphenyl (*J.*, 1926, 2709). With sodium nitrite in acetic acid it readily yielded the 3-*nitro*-derivative, which on further nitration gave a *dinitro*-2-*nitrosomethylaminofluorene*.

The nitration of 2-toluene-*p*-sulphonamidofluorene proceeded less smoothly than that of 4-toluene-*p*-sulphonamidodiphenyl (*J.*, 1926, 2708). Although the main product was the 3-*nitro*-derivative, it was accompanied by a small amount of a *trinitro*-derivative, which was alternatively prepared by the nitration of both 3- and 7-*nitro*-2-*toluene*-p-*sulphonamidofluorene*. It was not possible to prepare a dinitro-derivative and, further, since the nitro-toluene-*p*-sulphonamido-derivatives cannot be smoothly hydrolysed this gives a bad route to nitro-2-aminofluorenes.

Experimental.

(Analyses by Drs. Weiler and Strauss.)

2-Toluene-*p*-sulphonamidofluorene, prepared by interaction of 2-aminofluorene with toluene-*p*-sulphonyl chloride in pyridine, crystallised from acetic acid in needles, m. p. 161°. 7-*Nitro*-2-*toluene*-p-*sulphonamidofluorene*, from 7-nitro-2-aminofluorene (Diels, Schill, and Tolson, *loc. cit.*), crystallised from acetic acid in very pale yellow, glistening needles, m. p. 202° (Found : C, 62·9; H, 4·2. $C_{20}H_{16}O_4N_2S$ requires C, 63·2; H, 4·2%). 3-*Nitro*-2-*toluene*-p-*sulphonamidofluorene*, obtained in poor yield from 3-nitro-2-aminofluorene, formed a bright yellow crystalline powder, m. p. 198—201° (Found : N, 7·8. $C_{20}H_{16}O_4N_2S$ requires N, 7·4%).

Nitration of 2-*Toluene*-p-*sulphonamidofluorene*.—5 G. were dissolved in acetic acid (50 c.c.) by warming to 90° and the solution was rapidly cooled to 40°. Concentrated nitric acid (4 c.c.) in acetic acid (10 c.c.) was added to the resultant paste which rapidly dissolved to a clear solution that almost immediately began to fill with a bright yellow crystalline deposit of crude 3-nitro-2-toluene-*p*-sulphonamidofluorene (5 g.), m. p. 185—190°. This was filtered off and the mother-liquor poured into water. The resultant sticky mass was rubbed with acetic acid to dissolve away soluble impurities, and the residual solid recrystallised from bromobenzene. In this way 1 : 3 : 7-*trinitro*-2-*toluene*-p-*sulphonamidofluorene* was obtained as prisms, m. p. 233° with vigorous decomposition (Found : N, 12·1. $C_{20}H_{14}O_8N_4S$ requires N, 11·9%). It is almost insoluble in chloroform, toluene, or glycol, is sparingly soluble in acetone, dissolves in pyridine to yield a black solution, and recrystallises from acetic acid in needles containing solvent of crystallisation. It was alternatively prepared as follows.

(*a*) 3-Nitro-2-toluene-*p*-sulphonamidofluorene (1 g.), mixed with acetic acid (10 c.c.) and fuming nitric acid (2 c.c.), was heated on a steam-bath for 1 hour. The pasty mass was cooled and filtered, and the product (0·8 g.) purified by recrystallisation from bromobenzene.

(*b*) 7-Nitro-2-toluene-*p*-sulphonamidofluorene (1 g.) in hot acetic acid (15 c.c.) was treated with fuming nitric acid (1 c.c.) in acetic acid (2 c.c.). The liquid almost immediately became filled with a pale yellow precipitate (1 g.) of almost pure trinitro-derivative.

3-Nitro-2-toluene-*p*-sulphonamidofluorene was recovered unchanged after being boiled for 6 hours with an alcoholic solution of hydrogen chloride. It dissolved rapidly in cold concentrated sulphuric acid. The solution, on being poured into water and subsequently neutralised with aqueous ammonia furnished an orange-red product, separated by acetic acid into a sulphur-containing product (insoluble) and 3-nitro-2-aminofluorene, m. p. 202° (soluble in the hot acid but crystallising out on cooling). The base was readily acetylated by acetic anhydride containing a trace of sulphuric acid, to give 3-nitro-2-acetamidofluorene, glistening plates, m. p. 200°, in agreement with Hayashi and Nakayama (*J. Soc. Chem. Ind. Japan*, 1933, **36**, 127).

7-Nitro-2-aminofluorene is readily acetylated by acetic anhydride alone, yielding 7-nitro-2-acetamidofluorene, m. p. 250° [Aslak and Hamilton, *J. Amer. Chem. Soc.*, 1931, **53**, 746, give m. p. 250—253° (corr.)].

2-*Dimethylaminofluorene*.—This was expeditiously prepared in 50—60% yield by the methylation of 2-aminofluorene with dimethyl sulphate in the presence of sodium hydroxide. It crystallised from alcohol in lustrous plates, m. p. 179° (Found : C, 85·7; H, 7·2. $C_{15}H_{15}N$ requires C, 86·1; H, 7·2%), and dissolved readily in dilute hydrochloric acid. Interaction of this solution with sodium nitrite led to the precipitation of crude 3-nitro-2-dimethylaminofluorene, which was more conveniently prepared in the following way. Excess of sodium nitrite was added to a cooled solution of 2-dimethylaminofluorene (2 g.) in acetic acid (20 c.c.). The precipitated 3-*nitro*-2-*dimethylaminofluorene* (2·05 g.) recrystallised from alcohol in compact orange-red prisms, m. p. 100—103° (Found : C, 71·3; H, 5·7. $C_{15}H_{14}O_2N_2$ requires C, 70·9; H, 5·5%).

Dinitro-2-*nitrosomethylaminofluorene*.—Nitric acid (*d* 1·5; 1 c.c.) in acetic acid (2 c.c.) was added to a warm solution of 3-nitro-2-dimethylaminofluorene (1·5 g.) in acetic acid (10 c.c.). The liquid almost immediately began to deposit yellow needles (1·2 g.), m. p. 162° (decomp.). Recrystallisation from benzene gave *dinitro*-2-*nitrosomethylaminofluorene* as small, pale yellow needles, m. p. 165° (decomp.) (Found : C, 53·7; H, 3·3. $C_{14}H_9O_7N_5$ requires C, 53·5; H, 3·2%). This compound underwent partial decomposition on attempted recrystallisation from boiling acetic acid.

Bromination of 2-*Acetamidofluorene*.—Various solvents (acetic acid, chloroform, and carbon tetrachloride) and proportions of bromine (1—3 mols.) were tried, but in no case was it found possible to isolate a uniform product. The following is a typical experiment. Bromine (7 g., 2 mols.) was added to a warm solution of 2-acetamidofluorene (5 g.) in chloroform (60 c.c.). The liquid immediately became filled with a greenish-yellow precipitate which after 1 hour was filtered off (8·6 g.) and decomposed with aqueous ammonia. Repeated crystallisation from alcohol and then acetic acid gave a 70% yield of

7-bromo-2-acetamidofluorene, which formed needles, m. p. 228° alone or mixed with an authentic specimen prepared from 7-bromo-2-aminofluorene by acetylation (Found : C, 59·4; H, 4·0. Calc. for $C_{15}H_{12}ONBr$: C, 59·6; H, 4·0%). The chloroform mother-liquor, on evaporation, gave crude 3 : 7-dibromo-2-acetamidofluorene, which was obtained in snow-white glistening needles, m. p. 265° (decomp.), from bromobenzene (Found : C, 47·6; H, 2·9. Calc. for $C_{15}H_{11}ONBr_2$: C, 47·2; H, 2·9%). This compound was obtained in good yield by the further bromination of 3-bromo-2-acetamidofluorene in hot chloroform solution.

Bromination of 2-*Toluene*-p-*sulphonamidofluorene*.—(*a*) To 6·7 g. of this compound, dissolved in warm chloroform (50 c.c.), was added bromine (3·3 g., 1 mol.) in chloroform (3 c.c.), and the whole gently boiled until evolution of hydrogen bromide ceased. The hot solution was filtered from 7-bromo-2-aminofluorene hydrobromide (0·3 g.) and on cooling deposited needles (3·7 g.) of 7-bromo-2-toluene-*p*-sulphonamidofluorene, which formed feathery needles, m. p. 210°, from acetic acid (Found : Br, 19·6. Calc. for $C_{20}H_{16}O_2NBrS$: Br, 19·3%). This compound gave 7-bromo-2-aminofluorene, m. p. 144° (alone or mixed with an authentic sample), on dissolution in cold concentrated sulphuric acid. The chloroform mother-liquor from the bromination on evaporation furnished a brown plastic residue which on crystallisation from acetic acid furnished 3 g. of crude 3-bromo-2-toluene-*p*-sulphonamidofluorene (below).

(*b*) The experiment (*a*) was repeated with use of 2 mols. of bromine. After removal of a small amount of a hydrobromide, the crop, m. p. 195—201°, furnished 3 : 7-dibromo-2-toluene-*p*-sulphonamidofluorene in stellate clumps of fine needles, m. p. 203° (from acetic acid) (Found : Br, 31·9. Calc. for $C_{20}H_{15}O_2NBr_2S$: Br, 32·4%). Yield, 71%. This compound was alternatively prepared by the addition of bromine (1 mol.) to 7-bromo-2-toluene-*p*-sulphonamidofluorene dissolved in pyridine. Hydrolysis by dissolution in cold concentrated sulphuric acid gave 3 : 7-dibromo-2-aminofluorene, which crystallised from alcohol in needles, m. p. 148° (Campbell, Anderson, and Gilmore give 135°) (Found : C, 46·2; H, 3·0. Calc. for $C_{13}H_9NBr_2$: C, 46·0; H, 2·7%). Dissolution of this base in warm acetic anhydride gave 3 : 7-dibromo-2-acetamidofluorene (above).

(*c*) A solution of 3·35 g. of the sulphonamide in pyridine (*ca.* 15 c.c.) rapidly set to a semi-solid mass of the pyridine salt. To this was added, drop by drop, bromine (1 mol.) diluted with light petroleum (5 c.c.). The mixture was set aside for 3 hours and then decomposed with hydrochloric acid. The pasty product was filtered off and dissolved in hot ethanol. The pale yellow 3-*bromo*-2-*toluene*-p-*sulphonamidofluorene* (1·6 g.), m. p. 140—147°, after repeated crystallisation from benzene or acetic acid formed prisms, m. p. 155—156° (Found : Br, 19·6. $C_{20}H_{16}O_2NBrS$ requires Br, 19·3%). The alcoholic mother-liquor furnished only resinous material. This compound was readily brominated in chloroform to give 3 : 7-dibromo-2-toluene-*p*-sulphonamidofluorene in good yield.

(*d*) Experiment (*c*) was repeated with use of 2 mols. of bromine. The plastic product was freed from most of a non-crystallisable impurity (1·8 g.) by extraction with acetic acid. The residue, a brown powder, m. p. *ca.* 185° (2·8 g.), was fairly soluble in acetic acid and almost insoluble in ethanol, and was best crystallised from benzene. It then gave 1 : 3-*dibromo*-2-*toluene*-p-*sulphonamidofluorene* as prismatic needles, m. p. 214—215° (Found : Br, 31·8. $C_{20}H_{15}O_2NBr_2S$ requires Br, 32·4%). Dissolution in cold concentrated sulphuric acid gave 1 : 3-*dibromo*-2-*aminofluorene* in poor yield. The base crystallised from benzene in needles, m. p. 176—179° (Found : Br, 48·0. $C_{13}H_9NBr_2$ requires Br, 47·2%), and could be recovered unchanged from acetic anhydride or after treatment with toluene-*p*-sulphonyl chloride in pyridine.

Bromination of 2-*Aminofluorene*.—(*a*) The process of Eckert and Langecker (*loc. cit.*) gave tribromo-2-aminofluorene, which crystallised from xylene in colourless needles, m. p. 205°. This base did not react with toluene-*p*-sulphonyl chloride in pyridine, but with acetic anhydride gave 1 : 3 : 7-*tribromo*-2-*diacetamidofluorene*, which crystallised from acetic acid as a cotton-wool-like mass of needles, m. p. 241° (Found : C, 41·0; H, 2·6. $C_{15}H_{10}ONBr_3$ requires C, 40·6; H, 2·4%).

(*b*) Bromination in acetic acid with bromine (1 mol.) gave material from which it was impossible to isolate any pure individual.

(*c*) Bromine (6·4 g.; 2 mols.) in acetic acid (8 c.c.) was added to a cooled solution of 2-aminofluorene (3·6 g.) in acetic acid (72 c.c.). After 1 hour the separated material was filtered off, triturated with ammonia solution, filtered, and dried. It was then extracted with hot alcohol (70 c.c.). The residue (3·9 g.) was slightly impure 1 : 3-dibromo-2-aminofluorene [(*d*) above]. From the alcoholic extract was obtained a small amount of 3-(or 1-)*bromo*-2-*aminofluorene* as lustrous plates, m. p. 143° (Found : Br, 29·9. $C_{13}H_{10}NBr$ requires Br, 30·8%), greatly depressed in m. p. on admixture with 7-bromo-2-aminofluorene. It readily gave 3-(or 1-)*bromo*-2-*acetamidofluorene*, needles, m. p. 206—207°, from acetic acid (Found : C, 59·3; H, 4·0. $C_{15}H_{12}ONBr$ requires C, 59·6; H, 4·0%).

1 : 3 : 7-*Tribromo*-2-*toluene*-p-*sulphonamidofluorene*.—This was readily prepared by the bromination of 3 : 7-dibromo-2-toluene-*p*-sulphonamidofluorene in cold pyridine, although this compound was unaffected by bromine in chloroform. It crystallised from acetic acid in compact needles, m. p. 215° (Found : C, 42·3; H, 2·6. $C_{20}H_{14}O_2NBr_3S$ requires C, 41·8; H, 2·4%), and was readily hydrolysed to the tribromo-base [(*a*) above] by dissolution in cold concentrated sulphuric acid.

Crude 3-bromo-2-toluene-*p*-sulphonamidofluorene (6 g.) in chloroform (30 c.c.) was treated with bromine (1 mol.) and heated until evolution of hydrogen bromide ceased. The solution was filtered from 1 : 3 : 7-tribromo-2-aminofluorene hydrobromide (0·5 g.) and evaporated to dryness. The residue on crystallisation from acetic acid furnished 3 : 7-dibromo-2-toluene-*p*-sulphonamidofluorene (3·7 g.) [(*b*) above]. The mother-liquor, on fractional crystallisation, gave stout needles of 1 : 7-*dibromo*-2-*toluene*-p-*sulphonamidofluorene*, m. p. 202—203° depressed by admixture with either the 1 : 3- or 3 : 7-isomeride (Found : Br, 32·8. $C_{20}H_{15}O_2NBr_2S$ requires Br, 32·4%).

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