Synthesis and Reactions of 2,2′-Hydrazofluorene and Related Compounds

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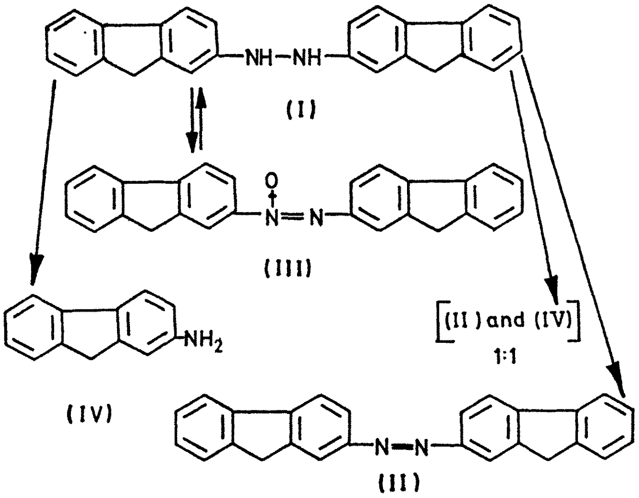
Summary Methods are described for synthesis of the hitherto unknown 2,2′-hydrazofluorene, and 2,2′-azofluorene, compounds of possible importance in elucidation of carcinogenic mechanisms.

BECAUSE of interest in possible metabolic intermediates of the carcinogen *N*-2-fluorenylacetamide, and because the title compound (I) and 2,2′-azofluorene (II) have never been reported, we undertook the synthesis of these and related compounds. Several methods, successful with many other such substances, did not work in this series, and we therefore devised the methods described below.

Compound (I) was of additional interest because, when heated in alcoholic HCl, quantitative disproportionation occurs without side-reactions. Recently,[1] a "clean" disproportionation reaction of this type was studied; however, it was found that side-reactions occurred. Compound (I) would appear to be an excellent substance for the study of a "clean" reaction.



Smooth reduction of simple aromatic azo- or azoxy-compounds to the corresponding hydrazines has been reported, using hydrazine hydrate and Pd on C.[2] These reagents, with 2,2′-azoxyfluorene (III),[3] gave a quantitative yield of fluoren-2-ylamine (IV). We next tried to reduce 2-nitrofluorene with hydrazine hydrate, Ru on C, and alcoholic KOH, which had been successful in another case,[4] but the nitro-compound was insufficiently soluble. To increase the solubility while maintaining basicity, we used pyridine instead of alcoholic KOH. In this case 2-nitrofluorene gave a mixture of (III) and impure (I).

When (III), however, is reduced in the following way, pure (I) is obtained: to a hot (80°) solution of 7·5 g. of (III) in 250 ml. of pyridine, 30 mg. of Ru on C (5%) in an alcoholic slurry and 6 ml. of hydrazine hydrate (100%) are added and the mixture is heated on a steam bath for 1 hr. The brown solution becomes green and begins to decolorize. Further catalyst (20 mg.) is added and the heating is continued for 30 min. The catalyst is removed by filtration and the filtrate is boiled down to *ca.* 30 ml. and cooled to room temperature. The reddish-brown precipitate is filtered off, washed with benzene, and dried, giving 5·5 g. (77%) of (I), m.p. 183—234°.†

Compound (I) passed through Al_2O_3 in C_6H_6 is converted into (II), m.p. 297—299°. Oxidation of (I) with an excess of *m*-chloroperbenzoic acid in toluene gives (III); when an equivalent amount of the reagent is used, (II) is formed. In an earlier attempt‡ to make (II), 2-nitrosofluorene§ was condensed with (IV). The product, even when obtained under nitrogen, was a mixture of (II) and (III) as revealed by mass spectroscopy. Reduction of (I) with hydrazine hydrate and Pd on C gives (IV) quantitatively.

An attempted semidine-type rearrangement of (I) in alcoholic HCl resulted in quantitative disproportionation to give (II) and (IV).

With brief boiling in acetic anhydride, (I) gives the monoacetyl derivative, m.p. 212—236°† (analysis C, H, N) which is split quantitatively by Pd on C and hydrazine hydrate to give equivalent amounts of (IV) and *N*-2-fluorenylacetamide.

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† Melting points were taken on a Fisher–Johns apparatus and are corrected to standards. The wide ranges on these m.p.s indicate that the melting range depends on where the substance is put on the plate. If put on within a degree of the top figure the melting range is 1°, melting instantaneously at a higher temperature. If put on at the lower figure, melting begins but is spread over a somewhat wider range.

‡ This condensation was carried out by Miss C.-A. Cole of this laboratory.

§ 2-Nitrosofluorene was kindly furnished by Drs. J. A. and E. C. Miller of the University of Wisconsin.

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