

An Oxidation-Reduction Reaction Involving Triphenylcarbinol

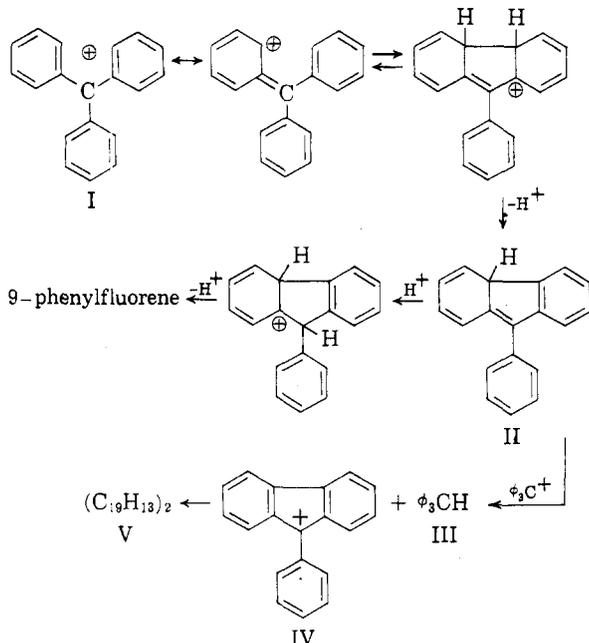
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The recent report¹ that a 90% yield of triphenylmethane can be realized by heating a solution of triphenylcarbinol with sulfuric and glacial acetic acids was of considerable interest to us. The uncertainty expressed¹ as to the path of this reaction is indeed justified when one considers that the excellent yield of triphenylmethane reported is evidence for a reduction in the absence of any conceivable reducing agent.

We therefore undertook a reinvestigation of this reaction and found that contrary to the original report, the product is a mixture of at least three different hydrocarbons. Chromatographic separation of the crude product afforded triphenylmethane, 9-phenylfluorene and an unidentified amorphous hydrocarbon with an approximate formula of $(C_{19}H_{13})_2$.

Although it is apparent that reduction is indeed taking place, the isolation of these products allows a rational picture for the over-all process:



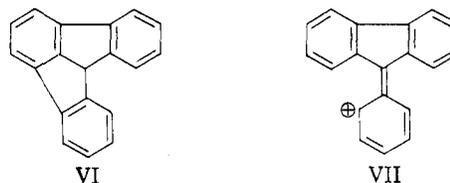
The triphenylcarbonium ion (I) generated in the strongly acid medium can rearrange in an *intramolecular* oxidation-reduction, to form 9-phenylfluorene from intermediate II as shown above. Intermediate II could also participate in an *intermolecular* process whereby a hydride ion is transferred to the triphenylcarbonium ion, in what would probably be a concerted process, to

(1) C. A. MacKenzie and G. Chuchani, *J. Org. Chem.*, **20**, 342 (1955).

form triphenylmethane III and a new carbonium ion IV. This new carbonium ion then can proceed to give the third hydrocarbon V whose structure is problematical. The infrared spectrum of V was complex and indicated that it may well be a mixture, but there was an over-all similarity to the spectrum of hydrindene.²

Cryoscopic molecular weight determinations of V gave an average value in the vicinity of 500, possibly indicating some type of dimeric structure of 9-phenylfluorene. Such a structure could conceivably arise by the intermolecular attack of IV on another molecule of 9-phenylfluorene. Such an attack would probably result in a mixture consisting of several closely related isomeric structures, which would account for the difficulties encountered in the purification of this material.

At first it was thought that V might be the strained hydrocarbon indeno[1.2.3-*jk*]fluorene (VI). Such a compound could conceivably arise from



ion VII in a manner analogous to the formation of 9-phenylfluorene. However the molecular weight obtained for V, together with the isolation of a small amount of benzoic acid from the chromic acid oxidation of this material would argue against the presence of any of VI in the mixture.

Confirmatory evidence for the formation of carbonium ion IV can be obtained from earlier work by Kovache³ who treated 9-phenyl-9-hydroxyfluorene with hot formic acid. Although the product was not adequately characterized it was reported as an amorphous material with solubility characteristics similar to those of V and with a melting range (165–170°) which corresponded closely to that of our material before purification.⁴

EXPERIMENTAL

A mixture of 2.6 g. (.01 mole) of triphenylcarbinol, 5 ml. of concentrated sulfuric acid, and 30 ml. of glacial acetic acid was heated to reflux. The carbinol dissolved to give a deep yellow-orange solution which began to deposit an oil after a few moments. After refluxing for 2 hr. the orange-brown mixture was cooled and the liquid was decanted from a heavy yellow gum.

The gum was taken up in benzene and this solution washed with base and water and dried over magnesium sulfate.

(2) Infrared Spectral Data—American Petroleum Institute Research Project 44. Spectrum 1147.

(3) A. Kovache, *Ann. chim. (Paris)* [9], **10**, 206 (1918).

(4) It should also be noted that Schorigin [*Ber.*, **60**, 2375 (1927)] also observed the formation of triphenylmethane in low yield from triphenylcarbinol. While he conjectured that oxidation products like 9-phenylfluorene might also be formed, he did not characterize such products.

After removing most of the solvent on the steam plate, the solution was poured onto an alumina column (Merck). Development and elution with 15% benzene in petroleum ether (60-70°) gave 2 fractions which were subsequently recrystallized from ethanol. The first afforded 400 mg. (17%) of triphenylmethane melting at 92° and not depressed by an authentic sample. The second gave 210 mg. of 9-phenylfluorene melting at 147-148° and not depressed by an authentic sample.⁵

Elution of the column with benzene gave a colorless gum which solidified on treatment with ethanol. The yield of material melting at 160-180° was 700 mg. After several reprecipitations from benzene with ethanol, the melting point of this white amorphous solid was 200-203°. Further efforts at purification or crystallization were fruitless. The material was soluble in all of the common organic solvents except alcohols and acetic acid. It did not dissolve in concentrated sulfuric acid. Oxidation of 900 mg. of the hydrocarbon with chromic acid in acetic acid afforded a few milligrams of benzoic acid melting at 121-122° and undepressed by admixture with an authentic sample.

Anal., Calcd. for (C₁₅H₁₃)₂: C, 94.6; H, 5.4. Found: C, 95.03; H, 5.2.

Three cryoscopic molecular weight determinations of V in benzene gave values of 510, 498, and 530. Calcd. for (C₁₅H₁₃)₂: mol. wt., 482.6.

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(5) A. Kliegl, *Ber.*, **38**, 287 (1905).

4-(4-Aminostyryl)quinolines¹

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A series of analogs of 4-(4-dimethylaminostyryl)quinoline (I)^{2,3} have been prepared in which other groups have the place of the dimethylamino group. 4-(4-Aminostyryl)quinoline, prepared by two different methods, was a convenient intermediate for the preparation of a variety of derivatives through reactions of the primary amino group. The effectiveness of oral administration of the compounds in causing regression or inhibition of growth of Lymphoma 8 tumors in rats is being tested at the Wistar Institute of Anatomy and Biology through the cooperation of Dr. Margaret Reed Lewis, Dr. Boland Hughes, and Mr. Aubrey L. Bates, and the financial assistance of a grant-in-aid from the National Institutes of Health. Effectiveness of intraperitoneal injection of arachis oil solutions of the compounds in preventing growth of Walker 256 tumors is being tested by Professor Alexander Haddow and his associates at the Chester Beatty

(1) This research was aided by a grant from the American Cancer Society.

(2) H. Gilman and G. Karmas, *J. Am. Chem. Soc.*, **67**, 342 (1945).

(3) M. A. Clapp and R. S. Tipson, *J. Am. Chem. Soc.*, **68**, 1332 (1946).

Research Institute. Most of the compounds reported here were less active than I against the tumors, in that larger doses were necessary in order to produce a given response, but the toxic side effects varied with the compound and method of administration. Some of the compounds had the advantage of being much less toxic than I. A more detailed report of the biological observations is to be made elsewhere.

EXPERIMENTAL

4-(4-Diethylaminostyryl)quinoline (II) did not crystallize as readily as I from the still residue obtained by the general method of Clapp and Tipson.³ Isolation of the product through the zinc salt⁴ was more convenient. II was found to be as active as I against Lymphoma 8.⁵ The hydrochloride, administered intravenously to leukemic rats, was reported to produce a prompt return of the white blood cell count to normal.⁶

4-(4-Diethylaminostyryl)-3-methylquinoline. Fifty-six grams (0.376 mole) of *p*-diethylaminobenzaldehyde was added to a molten mixture of 10.65 g. (0.078 mole) of zinc chloride and 25 g. of 3-methyllepidine (0.159 mole). After heating 8 hr. in an oil bath at 175-180°, the tarry reaction mixture was dissolved partially in methanol. Red crystals weighing 13.9 g. were separated from the solution. These were ground thoroughly with two portions of ammonium hydroxide, and washed with water. The tar thus produced was dissolved in hot isohexane. The yellow solution was decanted from the red oil that separated on cooling slightly. Cooling the solution to room temperature then precipitated 2.3 g. of solid which was recrystallized from 65 ml. of isohexane to yield 1.9 g., (4%) of yellow crystals, m.p. 104.6-107.1°.⁷

Anal. Calcd. for C₂₂H₂₄N₂: C, 83.50, H, 7.65. Found: C, 83.66, 83.60; H, 7.72, 7.56.⁸

The *picrate* of this base was obtained as dark red crystals; m.p. 270.0-270.8°.

Anal. Calcd. for C₂₈H₂₇N₅O₇: C, 58.10, H, 3.60, N, 14.73. Found: C, 58.33, 57.89; H 3.47, 3.75.⁸

4-[4-(*N*-Ethyl-*N*-methylamino)styryl]quinoline. By the method of Leese⁹ a mixture of 27.3 g. (0.21 mole) 4-(*N*-ethyl-*N*-methylamino)benzaldehyde and 30 g. (0.21 mole) of lepidine hydrochloride was heated 30 min. in an oil bath at 150°. The dark purple mass solidified on cooling, and was dissolved in 400 ml. of hot methanol; then 200 ml. of distilled water and 100 ml. of concentrated ammonium hydroxide were added. The yellow-brown crystals that appeared on chilling were triturated with ammonium hydroxide in a mortar, washed with water, and dried; weight, 42.3 g., m.p. 96-99°; after 8 additional recrystallizations from methanol, m.p. 123.7-124.8°, yield 4.4 g. (8.7%).

Anal. Calcd. for C₂₀H₂₀N₂: C, 83.29, H, 6.99. Found: C, 83.27, 83.44, H, 6.97, 7.17.

4-[4-(*N*-Benzyl-*N*-ethylamino)styryl]quinoline. A mixture of 10 g. (0.07 mole) of lepidine, 16 g. (0.067 mole) of 4-(*N*-benzyl-*N*-ethylamino)benzaldehyde, and 4.8 g. of zinc chloride was heated 24 hr. at 110-120°. The reaction mixture was dissolved in chloroform, washed with ammonium hydroxide, and dried over sodium sulfate. The chloroform

(4) C. T. Bahner, Clarence Cook, John Dale, John Fain, Edgar Franklin, J. C. Goan, William Stump, and Joan Wilson, *J. Org. Chem.*, **22**, 682 (1957).

(5) M. R. Lewis, B. Hughes, and A. L. Bates, *Growth*, **19**, 323 (1955).

(6) B. Hughes, M. R. Lewis, and A. L. Bates, *Nature*, **177**, 331 (1956).

(7) All melting points are corrected.

(8) Analyses by Weiler and Strauss.

(9) C. L. Leese, private communication.