The Behavior of 3,4′-Diaminobiphenyl in the Skraup Reaction. Synthesis of 6,7′-Biquinoline[1]

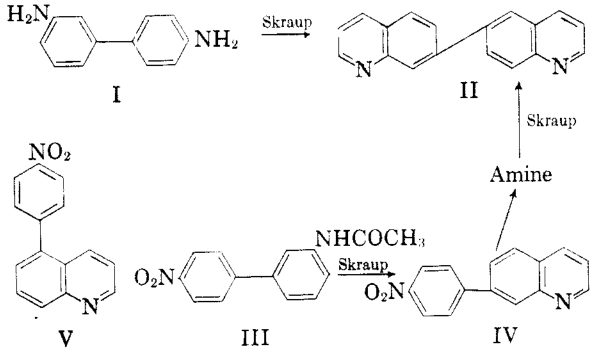
FRANCIS H. CASE AND CARL J. BUCK

Received February 9, 1956

Of the six possible heteronuclear diaminobiphenyls, three (4,4′, 2,4′, and 2,2′) have been converted to the corresponding biquinolines (6,6′[2] 6,8′,[3] and 8,8′[4] respectively) by the use of the Skraup reaction. In each of these three cases, only a single product could theoretically be formed. In the remaining three (2,3′, 3,3′, and 3,4′-diaminobiphenyls) two or three possible biquinolines might result in each case. In the present investigation, the Skraup reaction on 3,4′-diaminobiphenyl (I) was studied.

The preparation of 3,4′-diaminobiphenyl,[5] previously prepared by a very indirect method, was effected by catalytic reduction of 3,4′-dinitrobiphenyl.[6] In the Skraup reaction a yield of 40% of 6,7′-biquinoline (II) was obtained, but none of the isomeric 5,6′-biquinoline could be found.

The proof of the identity of the biquinoline obtained was as follows. 3-Acetamido-4′-nitrobiphenyl (III),[7] subjected to a Skraup reaction, yielded a single product, which must have been either 7-(*p*-nitrophenyl)quinoline (IV) or the 5-isomer, (V). Catalytic reduction followed by deamination yielded a phenylquinoline whose picrate depressed the melting point of the picrate of 5-phenylquinoline[8] and which was identical with the picrate of 7-phenylquinoline, prepared from *m*-acetamidobiphenyl by a modification of the method of Hey and Walker.[9] From this picrate, 7-phenylquinoline, hitherto undescribed, was obtained. The result of the Skraup reaction on 3-acetamido-4′-nitrobiphenyl was therefore IV. The amine resulting from the reduction of IV yielded in a second Skraup reaction, 6,7′-biquinoline which proved to be identical with the biquinoline obtained from 3,4′-diaminobiphenyl.



EXPERIMENTAL

3,4′-Diaminobiphenyl. Catalytic reduction of 30 g. of 3,4′-dinitrobiphenyl using Adams' catalyst yielded 20.7 g. of diamine, m.p. 85–86° (lit.[5] 85.5–86.5°).

Skraup reaction on 3,4′-diaminobiphenyl. A mixture of 10 g. of 3,4′-diaminobiphenyl, 16 g. of arsenic acid, 32 g. of concentrated sulfuric acid, and 32 g. of glycerol was refluxed for 3 hours. The reaction mixture was poured on ice and made alkaline with sodium hydroxide. The resulting precipitate was filtered, dried, and crystallized from benzene. The yield of biquinoline was 5.6 g. (40%), m.p. 132–133°.

Anal. Calc'd for $C_{18}H_{12}N_2$: C, 84.35; H, 4.72. Found: C, 84.33; H, 5.00.

7-(p-Nitrophenyl)quinoline. A mixture of 24.6 g. of 3-acetamido-4′-nitrobiphenyl,[7] 9.5 g. of arsenic acid, and 37.8 g. of concentrated sulfuric acid was heated to 105° and treated with 31.8 g. of glycerol at such a rate that the temperature never exceeded 135°. The reaction mixture was heated for two hours at 130–135°, then poured on ice and made alkaline with sodium hydroxide. The resulting precipitate was filtered, dried, and crystallized from petroleum ether (b.p. 90–100°). The yield was 6.8 g. (28%), m.p. 183–184°.

Anal. Calc'd for $C_{15}H_{10}N_2O_2$: C, 71.99; H, 4.03. Found: C, 72.11; H, 3.79.

7-(p-Aminophenyl)quinoline. This substance was prepared by catalytic reduction of 7-(*p*-nitrophenyl)quinoline. The pure product, crystallized from petroleum ether (b.p. 90–100°), melted at 122–123°.

Anal. Calc'd for $C_{15}H_{12}N_2$: C, 81.79; H, 5.49. Found. C, 81.87; H, 5.42.

Deamination of the above amine by means of hypophosphorous acid[10] yielded a product whose picrate melted at 208–209° (m.p. undepressed on admixture with 7-phenylquinoline picrate prepared by the method of Hey and Walker,[9] but depressed by admixture with 5-phenylquinoline picrate.)[8,9]

6,7′-Biquinoline. The procedure of Yale and Bernstein[11] was used. A stirred mixture of 10.3 g. of 7-(*p*-aminophenyl)-quinoline, 14.1 g. of arsenic acid, and 60 ml. of 85% phosphoric acid was heated to 100°, and treated at this temperature with 3.9 g. of acrolein. After 30 minutes at 100°, the reaction mixture was poured on ice and made alkaline with potassium hydroxide solution. The precipitate was removed by filtration, dried, and crystallized from petroleum ether (b.p. 90–100°). The yield of pure product melting at 131–132° was 4.4 g., or 37%. This melting point was undepressed on admixture of the above compound with the biquinoline obtained by the Skraup reaction on 3,4′-diaminobiphenyl.

7-Phenylquinoline. A stirred mixture of 22 g. of 3-acetamidobiphenyl, 14.4 g. of arsenic acid, 22 ml. of concentrated sulfuric acid, and 7 ml. of water was heated to 100° and treated with 34 g. of glycerol at such a rate that the temperature did not exceed 140°. It was kept at this temperature for two more hours. The reaction mixture was then poured on ice, and neutralized with sodium hydroxide solution. The resulting tarry mass was extracted with hot benzene. Removal of the benzene, extraction with petroleum

---

(1) This work was supported by a grant from the Committee on Research and Publications of Temple University, Philadelphia 22, Pa.

(2) Ostermayer and Henrichsen, *Ber.*, **17**, 2444 (1884).

(3) Fischer, *Monatsh.*, **6**, 546 (1885).

(4) Niementowski and Seifert, *Ber.*, **38**, 762 (1905).

(5) Carlin and Swakon, *J. Am. Chem. Soc.*, **77**, 966 (1955).

(6) Blakey and Scarborough, *J. Chem. Soc.*, 3000 (1927).

(7) Case, *J. Am. Chem. Soc.*, **61**, 767 (1939).

(8) Case, *J. Org. Chem.*, **16**, 1541 (1951).

(9) Hey and Walker, *J. Chem. Soc.*, 2220 (1948).

(10) Kornblum, *Org. Reactions*, Coll. Vol. 2, 294 (1944).

(11) Yale and Bernstein, *J. Am. Chem. Soc.*, **70**, 254 (1948).

ether (b.p. 90–100°), and removal of solvent left an oil (8 g.) which was dissolved in 100 ml. of ethanol and treated with a solution of 11 g. of picric acid in 200 ml. of ethanol. The alcoholic solution was heated to boiling, and the insoluble picrate was separated by filtration. Crystallization from acetone yielded 5.9 g. of picrate, m.p. 210–211°. This product was refluxed with 13 ml. of water, 15 ml. of concentrated hydrochloric acid, and 50 ml. of benzene until solution was complete. The aqueous layer was then separated, extracted five times with hot benzene, and made alkaline with sodium hydroxide solution. Extraction with ether and crystallization from petroleum ether (b.p. 60–70°) yielded 2 g. of 7-phenylquinoline, m.p. 59–60°.

Anal. Calc'd for $C_{15}H_{11}N$: C, 87.78; H, 5.40. Found: C, 88.05; H, 5.78.

No attempt was made to isolate the picrate of 5-phenylquinoline from the picrate filtrate.

CHEMISTRY DEPARTMENT
TEMPLE UNIVERSITY
PHILADELPHIA 22, PENNA.

4-Nitrofluorene-5-carboxylic Acid

ELIZABETH K. WEISBURGER

Received February 10, 1956

It has been demonstrated by Moore and Huntress[1] that nitration of fluorenone-4-carboxylic acid leads to substitution of the nitro group mostly in the 7 position and to a lesser extent in the 5 position. In a recent paper we have shown that the main product in the nitration of fluorene-4-carboxylic acid is 2-nitrofluorene-5-carboxylic acid.[2]

During the process of preparing a large quantity of the latter compound, several hundred grams of fluorene-4-carboxylic acid was nitrated. After removal of the main product, the mother liquors from the nitration afforded material with a melting point a few degrees higher than the melting point of 2-nitrofluorene-5-carboxylic acid. However, examination of the infrared and ultraviolet absorption spectra showed it to be an entirely different compound. By analogy with the findings of Moore and Huntress[1] and our own observations[2] this substance was suspected to be 4-nitrofluorene-5-carboxylic acid. This assumption was confirmed by oxidation of the material to a bright yellow compound with a melting point identical to that reported for 4-nitrofluorenone-5-carboxylic acid.[1]

A Schmidt reaction on 4-nitrofluorene-5-carboxylic acid produced a dark red low-melting nitro amine which had a greater solubility and different ultraviolet and infrared spectra than the isomeric 2-nitro-5-aminofluorene.[2] Deamination of this nitroamine gave 4-nitrofluorene,[3] thus definitely proving the structures of 4-amino-5-nitrofluorene and of 4-nitrofluorene-5-carboxylic acid.

Reduction of 4-amino-5-nitrofluorene to 4,5-diaminofluorene was best effected by catalytic hydrogenation. The use of various chemical reducing agents gave very low yields of the pure diamine.

EXPERIMENTAL

Microanalyses by Mr. Robert Koegel and staff. The ultraviolet absorption spectra were determined on a Cary instrument using 5×10^{-5} *molar* solutions in ethanol. Infrared spectra were recorded on a Perkin-Elmer spectrophotometer, using the solid potassium bromide disk method. All spectra were determined by Mr. P. H. Grantham.

4-Nitrofluorene-5-carboxylic acid (I). Fluorene-4-carboxylic acid was nitrated in six 50-g. batches as was described previously.[2] After removal of the 2-nitrofluorene-5-carboxylic acid, wt. 180 g., the mother liquor from the nitration was poured into water. A dark yellow precipitate mixed with some red oil formed. After standing overnight the oil had solidified. The precipitate, m.p. 255°, weighed 147 g. It was crystallized from acetic acid-water (2:1) to give 71 g. of I, m.p. 285°, or a 19% yield. A further crystallization from ethanol raised the m.p. to 292°. Nitration of 10–20 g. batches of fluorene-4-carboxylic acid gave better yields of 2-nitrofluorene-5-carboxylic acid and only 8% yields of I. The ultraviolet absorption spectrum in ethanol showed maxima at 250 (ϵ 19,300) and 335 mμ (ϵ 7,600) and minima at 233.5 (ϵ 14,160) and 289 mμ (ϵ 3,700).

Anal. Calc'd for $C_{14}H_9NO_4$: C, 65.88; H, 3.55; N, 5.49. Found: C, 65.43; H, 3.91; N, 5.33.

Oxidation of I. A solution of 1 g. of chromic trioxide in 3 ml. of dilute acetic acid was added to a solution of 0.2 g. of I in 40 ml. of acetic acid and was refluxed for 2 hours. The product obtained melted at 232–233°. After crystallization from ethanol the bright yellow needles had m.p. 232.5–233.5°. Moore and Huntress[1] reported m.p. 232–233° for 4-nitrofluorenone-5-carboxylic acid.

4-Amino-5-nitrofluorene (II). A Schmidt reaction on I, according to the procedure used for the isomer,[2] gave the crude dark red amine, m.p. 96°, in a 67% yield. Purification by chromatography on alumina and crystallization from ethanol (2 g./25 ml.) or benzene (2 g./5 ml.) yielded red needles, m.p. 100–101°. The spectrum had maxima at 259 (ϵ 12,300) and 319 mμ (ϵ 5,000) with minima at 255 (ϵ 12,200) and 308 mμ (ϵ 4,800) and an inflection point at 235 mμ (ϵ 18,000).

Anal. Calc'd for $C_{13}H_{10}N_2O_2$: C, 69.01; H, 4.46; N, 12.39. Found: C, 69.38; H, 4.62; N, 12.05.

The *acetyl derivative* of II formed yellow plates, m.p. 229–230°. Its spectrum showed maxima at 259 (ϵ 16,000) and 317 mμ (ϵ 4,400) with minima at 243.5 (ϵ 14,000) and 292 mμ (ϵ 3,900).

Anal. Calc'd for $C_{15}H_{12}N_2O_3$: C, 67.15; H, 4.51; N, 10.44. Found: C, 67.28; H, 4.62; N, 10.62.

Deamination of II. The amine (0.45 g.) was dissolved in 10 ml. of acetic acid. After the addition of 10 ml. of 18 *N* sulfuric acid, the mixture was cooled to 10°. Diazotization was effected by adding 0.16 g. of sodium nitrite in 2 ml. of water and stirring for 0.5 hour. Then 15 ml. of cold hypophosphorous acid was added and the mixture was stirred in the cold overnight. The precipitate obtained was extracted with hot benzene and the benzene solution was percolated through an alumina column. Evaporation of the eluate gave 100 mg. of 4-nitrofluorene, m.p. 69–71°. Crystallization from cyclohexane yielded light tan needles, m.p. 73–74°, shown to be authentic 4-nitrofluorene by mixture m.p. and infrared spectrum.

4,5-Diaminofluorene (III). A solution of 2 g. of II in 50 ml. of ethanol was hydrogenated for 1 hour at room temperature under 50 lbs. pressure, using 50 mg. of platinum

---

(1) Moore and Huntress, *J. Am. Chem. Soc.*, **49**, 1324 (1927).

(2) Weisburger and Weisburger, *J. Org. Chem.*, **20**, 1396 (1955).

(3) Weisburger, Weisburger, and Morris, *J. Am. Chem. Soc.*, **74**, 4540 (1952).