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3,4-DICYANOBIPHENYL AND RELATED COMPOUNDS[1]

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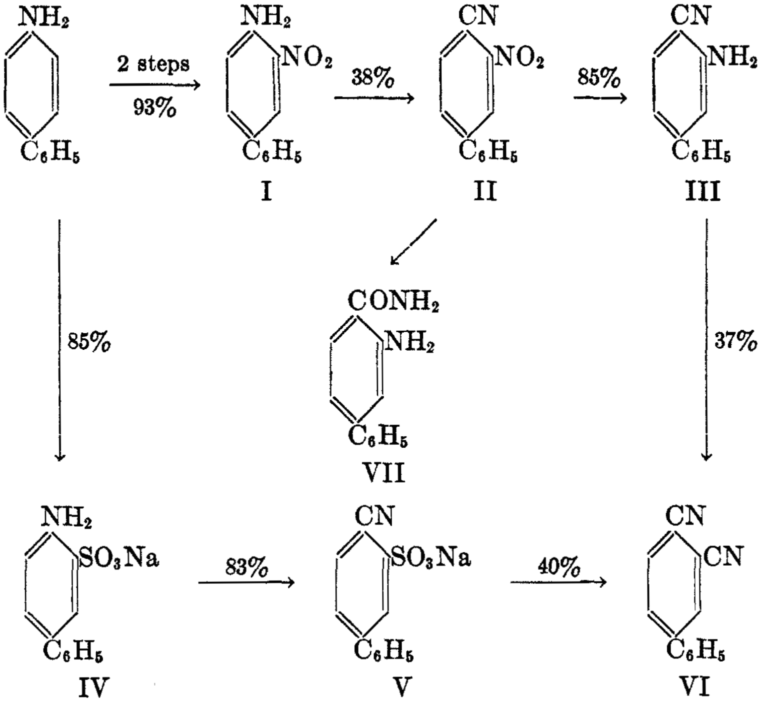
Since 3-amino-4-cyanobiphenyl (III) and 3,4-dicyanobiphenyl (VI) were required in connection with another problem, it was found necessary to work out procedures for their preparation. Both compounds are mentioned in the patent literature (1, 2) but useful experimental details for their synthesis are lacking.

The 3-amino-4-cyanobiphenyl was prepared in 30% over-all yield from 4-aminobiphenyl through the 3-nitro derivative (I). Diazotization of 3-nitro-4-aminobiphenyl by Hodgson's method (3) proceeded smoothly, but after the diazonium salt had been separated by precipitation with ether and added to cuprous cyanide, the cyano derivative (II) was obtained in a rather poor yield.



The reduction of the 3-nitro-4-cyanobiphenyl (II) with stannous chloride in concentrated hydrochloric acid afforded the desired 3-amino-4-cyanobiphenyl (III) in a yield of 85%; but, in accordance with Reissert's observations in the case of *o*-nitrobenzonitrile, the use of ethanol as the solvent in the reaction caused

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[1] After this paper was submitted, a paper by Haworth, Heilbron, Hey, Wilkinson and Bradbrook appeared [*J. Chem. Soc.*, 409 (1945)], in which 3,4-dicyanobiphenyl was synthesized from 4-aminophthalonitrile by the Gomberg reaction.

partial hydrolysis of the cyano group with the production of the corresponding amino-amide (VII) (4).

It was possible to prepare 3,4-dicyanobiphenyl from 3-amino-4-cyanobiphenyl by a procedure very similar to that used for the preparation of 3-nitro-4-cyanobiphenyl, but the low yield (37%) made the over-all yield from 4-aminobiphenyl only 11%.

A more convenient process (2) for the production of this compound in better over-all yields (28%) involves the cyanide fusion of sodium 4-cyanobiphenyl-3-sulfonate (V), prepared from the 4-amino derivative (IV) by Bradbrook and Linstead's method (5).

The "bake" process for preparing the amine sulfonic acid was preferred over the method using chlorosulfonic acid in *o*-dichlorobenzene, as suggested in the patent (2), since the product obtained by the latter method often contained some of the 4′-sulfonic acid which could not be removed easily. Attempts to prevent the formation of the isomeric acid by cooling the reaction mixture were not very successful, since the thick paste which formed on adding chlorosulfonic acid to the amine solution interfered with the stirring unless excessive amounts of *o*-dichlorobenzene were used.

The 80% yield claimed in the patent (2) on the fusion step could not be duplicated, but the 36% over-all yield on the Sandmeyer reaction and fusion was more in accord with that obtained by Linstead in the naphthalene series (50%) (5). It is quite probable that differences in the apparatus used for the fusion cause some variation in the yield, as we have been unable to repeat the preparation of 1,2-dicyanonaphthalene in yields greater than 40%, using our apparatus.

EXPERIMENTAL

3-Nitro-4-aminobiphenyl (I) was prepared in 93% yield by refluxing a solution of 500 g. of 4-aminobiphenyl in 400 cc. of glacial acetic acid and 275 cc. of acetic anhydride for thirty minutes, pouring the mixture on ice, and nitrating and hydrolyzing the crude dry acetyl derivative according to the procedure of Campbell, Anderson, and Gilmore (6).

3-Nitro-4-cyanobiphenyl (II). A solution of 58 g. of 3-nitro-4-cyanobiphenyl in a boiling mixture of 210 cc. of glacial acetic acid and 19 cc. of concentrated sulfuric acid was stirred vigorously and cooled to 15°, during which time the amine sulfate crystallized. To the stirred, smooth paste was added, dropwise, 41 cc. of *n*-butyl nitrite over a period of forty-five minutes, the temperature being maintained at 18–20°. After the reddish-yellow solution had stood for thirty minutes longer, 1 liter of ice-cold ether was added and rapid stirring was continued until the oil which separated had solidified. The ether solution was decanted, the residue was dissolved in 1 liter of ice-water, and the solution was added rapidly to a stirred solution of cuprous cyanide cooled to 20–25° (prepared by adding 180 g. of potassium cyanide to a warm stirred solution of 160 g. of copper sulfate in 800 cc. of water). The decomposition of the diazonium salt started immediately and was completed by heating the mixture to 70° on the steam-bath. The cooled mixture was filtered and the residue was extracted by four 50-cc. portions of boiling ethanol. Removal of the ethanol and distillation of the residue *in vacuo* gave 6.8 g. of a fore-run, b.p. 170–185°/5 mm., and 28 g. (46%) of crude 3-nitro-4-cyanobiphenyl, b.p. 230–250°/5 mm., m.p. 112–116°. Crystallization from 300 cc. of ethanol and cooling in ice afforded 23.1 g. (38%) of yellow needles, m.p. 117–119°. The product forms plates, needles, or blades, depending on the rate of cooling.

Anal. Calc'd for $C_{13}H_8N_2O_2$: N, 12.5. Found: N, 12.3.

The yellow forerun, after redistillation and crystallization from methanol, was identified as 3-nitrobiphenyl by its melting point, 58–59.5°, and analysis.

3-Amino-4-cyanobiphenyl (III). To a stirred solution of 134.4 g. of crystalline stannous chloride in 240 cc. of concentrated hydrochloric acid was added slowly 44.8 g. of the nitro compound, the temperature of the reaction mixture being kept below 40°. As the reduction proceeded, the solid dissolved and gave a pale yellow solution. After there was no further tendency to warm up, the solution was stirred for two hours and then was added slowly to 1100 cc. of 40% sodium hydroxide, the temperature of which was kept below 10° by the addition of ice. The suspension was filtered, after being allowed to stand for four hours, and the residue was washed with water and dried. There was obtained 39.7 g. of a yellow powder, m.p. 96–101°, suitable for use in the next step without further purification. One crystallization from ethanol (Norit) by cooling in ice afforded 32.9 g. (85%) of pale yellow plates, m.p. 101–103°, in two crops. Further recrystallizations from ethanol and ligroin (70–90°) gave colorless, diamond-shaped plates, m.p. 103–104°.

Anal. Calc'd for $C_{13}H_{10}N_2$: N, 14.4. Found: N, 14.4.

2-Amino-4-phenylbenzamide (VII). To a solution of 12 g. of stannous chloride in 50 cc. of absolute ethanol was added 4 g. of the nitro compound, the temperature being kept below 40°. The reaction mixture was worked up in the manner described previously. The product (2.9 g., 76%) crystallized from ethanol in pale yellow blades, m.p. 218–219°. Repeated crystallizations did not raise the melting point.

Anal. Calc'd for $C_{13}H_{12}N_2O$: C, 73.6; H, 5.7; N, 13.2.
Found: C, 73.6; H, 5.5; N, 13.2.

The amide was hydrolyzed by refluxing it with constant-boiling hydrochloric acid. The hydrochloride of 2-amino-4-phenylbenzoic acid separated from the cooled mixture and crystallized from dilute hydrochloric acid in colorless needles, m.p. 221° desiccated. Since the analysis indicated that it was partially hydrolyzed, it was converted to the sodium salt which crystallized from water in fine, pale yellow plates.

Anal. Calc'd for $C_{13}H_{10}NNaO_2$: N, 6.0; Na, 9.8. Found: N, 6.0; Na, 9.8.

Sodium 4-aminobiphenyl-3-sulfonate (IV). A mixture of 200 g. of 4-aminobiphenyl, 65 cc. of concentrated sulfuric acid, and 1400 cc. of water was stirred thoroughly for thirty minutes and then evaporated to dryness on the steam-bath. The colorless solid was powdered finely, placed in a 2-l. flask, and heated in an oil-bath under a water-pump vacuum at 200–220° for forty-eight hours. From time to time the flask was rotated to ensure complete heating of the powder and to prevent excessive carbonization. The product was cooled and dissolved in 3.5 l. of hot water containing 82 g. of sodium carbonate. The solution was treated with Darco and evaporated to dryness. Most of the salt was nearly colorless, but it contained traces of brown impurities. After being dried at 100°, it weighed 272 g. (84.5%).

A small sample was recrystallized twice from water by cooling the solution in ice. It formed colorless needles.

Anal. Calc'd for $C_{12}H_{10}NNaO_3S$: C, 53.1; H, 3.7; Na, 8.5.
Found: C, 53.3; H, 3.9; Na, 8.5.

3,4-Dicyanobiphenyl (VI). (a) *From 3-amino-4-cyanobiphenyl.* A stirred suspension of 3-amino-4-cyanobiphenyl sulfate in 75 cc. of acetic acid (prepared from 11 g. of the amine and 4 cc. of concentrated sulfuric acid in the manner described previously) was cooled to 15° and 8 cc. of *n*-butyl nitrite was added dropwise. The brown suspension turned yellow as the diazotization proceeded. After all the nitrite had been added, the mixture was stirred for thirty minutes and 400 cc. of ice-cold absolute ether was added. The solid was filtered and added to a well-stirred solution of cuprous cyanide warmed to 30–40° (prepared from 33 g. of potassium cyanide, 30 g. of copper sulfate, and 150 cc. of water). A vigorous evolution of nitrogen resulted, and the reaction mixture had to be cooled externally to prevent the temperature from rising above 40°. After the evolution of nitrogen had ceased, the mixture was heated to 75° for fifteen minutes, cooled, and filtered. The residue was extracted with three 100-cc. portions of boiling ethanol and the solution was evaporated to dryness. Sublimation of the residue at 300–320° at 20 mm. produced 4.5 g. of a pale green product, m.p. 155–157°. One crystallization from ethanol (Darco) by cooling the solution in ice gave 3.8 g. (37%) of colorless needles, m.p. 157–158°. Repeated crystallization from ligroin (70–90°) produced colorless plates melting at 159–160° (Lit., 161–162°) (2).

Anal. Calc'd for $C_{14}H_8N_2$: N, 13.7. Found: N, 13.5.

(b) *From sodium 4-aminobiphenyl sulfonate.* A solution of 136 g. of the amine sulfonate and 38 g. of sodium nitrite in 8 l. of water was divided into two equal parts and each was added in a steady stream to a vigorously stirred mixture of 130 cc. of concentrated hydrochloric acid and ice over a period of fifteen minutes. Ice was added as needed to maintain the temperature of the mixture below 0°. After all the reagents had been mixed, the pale yellow suspension was stirred for twenty minutes at 0°, filtered, and the residue was washed with a little ice-water. The pale yellow solid was added in small portions to a stirred solution of cuprous cyanide (prepared from 210 g. of potassium cyanide, 190 g. of copper sulfate, and 1 l. of water). During the addition of the diazonium salt, the temperature of the solution was maintained at 50–60° by heating it intermittently on the steam-bath. After the reaction was complete, 180 g. of salt was added and the solution was cooled to 0° overnight. A dirty brown crystalline product was obtained which, after being filtered and dried at 100°, weighed 109.5 g. (83%). It was used in the next step without purification.

A finely powdered mixture of 25 g. of the crude cyano sulfonate and 50 g. of anhydrous potassium ferrocyanide was heated at 260–300° at 30 mm. in an electric tube furnace (7) for one hour. The temperature was raised gradually to 360° and the product sublimed to the cooler portions of the tube. The solid was crystallized from ethanol (Darco) by cooling the solution in ice. The yield of slightly green product, m.p. 155–158°, was 8.2 g. (45%). Recrystallization gave 7.3 g. (40%), of colorless needles, m.p. 159–160°.

SUMMARY

Detailed procedures for the synthesis of 3-amino-4-cyanobiphenyl and 3,4-dicyanobiphenyl are described.

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