N-(9-Carbazolyl)-*o*-haloanilines from the Decompositions of *o*-Carboxybenzenediazonium Halides Involving Benzyne Intermediates

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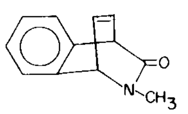
Introduction.

It has been reported that the 1,4-cycloaddition of 1-methyl-2-pyridone with benzyne produced **1** (2), irrespective of whether benzyne was generated from benzenediazonium-*o*-carboxylate (**2**) (3,4) or more conveniently, from either the corresponding hydrochloride or hydrobromide, **3** or **4**.



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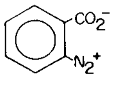
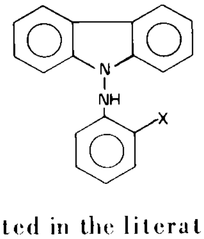


2

3 Hydrochloride of **2**
4 Hydrobromide of **2**

When **3** or **4** were used in conjunction with propylene oxide to generate benzyne (4-6), in the presence or absence of 1-methyl-2-pyridone, there was isolated also **5** or **6**, respectively. The isolation and structure proof of **5** and **6** are the main subject of this paper, particularly since few benzyne decomposition products containing nitrogen have been isolated (7,8). Indeed, few *N*-(carbazolyl)anilines have been reported in the literature (8,9) and the method described below presents facile access to this system, although in low yields. Furthermore, several chlorine-containing products were reported recently when **3** was used as a benzyne precursor (10).



5 X Cl
6 X Br

Structure Proof of 5 and 6.

The similarity of their spectra and chemical behavior attested to the close structural similarity of **5** and **6**. Pertinent details for the structure proof of **6** are discussed. Its proton magnetic resonance (pmr) spectrum presented a complex pattern between δ 6.0 and 8.2 (deuteriochloroform) consisting of a series of overlapping multiplets which were not simplified even at 220 MHz or effected by several chemical shift reagents. One of the signals (δ 6.7) disappeared upon deuterium oxide exchange and was due to an NH proton (ir, ν (NH) 3360 cm^{-1}). Methylation of **6** furnished an *N*-methyl derivative which substantiated this part of the structure. Catalytic reduction of either **6**, or its *N*-methyl derivative, furnished carbazole as the only recognizable product. These experiments established the presence of a carbazole nucleus for **6**, but did not pinpoint the location of the bromine atom in the parent compound. Pyrolysis of the *N*-methyl derivative of **6** produced carbazole which established that the bromine atom in **6** had to be associated with the remaining fragment, C_6H_5BrN. Combined gas chromatography and mass spectrometry established that **6** decomposed readily in the gas chromatograph to give only two products, carbazole and *o*-bromoaniline, while the *N*-methyl derivative yielded carbazole and *N*-methyl-*o*-bromoaniline. This facile cleavage under pyrolysis or upon catalytic reduction suggested cleavage of a nitrogen-nitrogen bond and indicated that the anilino fragment was attached to the carbazole nucleus as shown in **5** and **6**.

Mechanism of Decomposition of 3 and 4.

A number of experiments carried out on **4** produced some interesting observations. When **4** was heated in 1,2-dichloroethane at 95° for a short time, no gas evolution was observed and the salt was recovered virtually, unchanged. After 32 hours, a large quantity of **4** was recovered and during this time no significant carbon dioxide evolution was noted. Some of **4** had been transformed to a mixture of acids which were found in the 1,2-dichloroethane soluble portion of this reaction mixture. Conversion of these acids to esters by diazomethane and subsequent gc-analysis revealed a mixture of methyl benzoate, methyl *o*-chloro- and *o*-bromobenzoates, in the ratio of 1:1:3. It had been reported that pyrolysis of **4** had yielded benzoic and *o*-bromobenzoic acids but this reaction was not conducted in 1,2-dichloroethane (7). Several mechanisms leading to these acids were proposed involving either *o*-

carboxyphenyl cations or *o*-carboxyphenyl free radical intermediates (7).

It was not possible to distinquish between mechanisms involving either intermediates, since either could account for the formation of benzoic or *o*-halobenzoic acids by abstraction of hydrogen or halogen from the solvent (11). Thus, the formation of *o*-chlorobenzoic acid from **4** could be explained since 1,2-dichloroethane was the solvent for the reaction.

It became evident that propylene oxide was essential for the formation of **6** from **4**. As a matter of fact, addition of propylene oxide to a warm suspension of **4** in 1,2-dichloroethane led to an instant and copious evolution of carbon dioxide with simultaneous disappearance of solid **4**, almost like a titration. For the formation of **6**, it would appear that **4** loses carbon dioxide first to yield *o*-diazoniumphenylcarbanion, which then utilizes two equivalents of benzyne and one of hydrogen bromide to produce **6**. No detailed mechanisms are presented at this time.

EXPERIMENTAL

Materials and Methods.

Melting points were determined on a Mel-Temp apparatus and are uncorrected. Analyses for *N* were determined by Mr. Richard Dvorak using a Coleman Nitrogen Analyser, Model 29, those for C and H, by Micro-Tech Labs, Skokie, Illinois. Ir and uv spectra were recorded using either the Perkin-Elmer 337 (or 700) and UV-Visible Model 202 recording spectrophotometer, respectively. Pmr spectra were obtained on a Varian A-60 spectrometer. Mass spectra were obtained by Mr. Richard Dvorak using a Hitachi Perkin-Elmer RMU-6D Mass Spectrometer. In general, relative abundances are reported for fragments over 5% of base peak, except for the molecular ion.

Column chromatography utilized alumina (Alcoa F-20) and analytical grade solvents were used for elution; petroleum ether (b.p. 30-60°). Each fraction was spotted and developed with benzene on a commercially prepared thin layer chromatographic plate (2.5 x 8 cm., alumina containing a fluorescent indicator, Eastman Chromagram, No. 6063). Spots were detected using iodine vapor or uv light.

o-Carboxybenzenediazonium Bromide (**4**).

To a stirred ice-cold solution of anthranilic acid (21.9 g., 0.16 mole) and concentrated hydrobromic acid (48.8%, 30 ml.) in ethanol (220 ml.) was added isopentyl nitrite (12) (40 ml.) in small portions (20 minutes). The temperature was maintained below 20°. The hydrobromide began to precipitate after 15 minutes. Dry ether (170 ml.) was added and the solution was stirred for an additional 30 minutes. The product was collected, washed with ether and pressed somewhat dry at the pump (5 minutes) and was used immediately before it had a chance to dry.

Reaction of **4** in the Presence of Propylene Oxide.

A number of reactions were performed varying the amounts of solvent, quantity and mode of addition of propylene oxide. Each reaction was monitored for the evolution of carbon dioxide (aqueous barium hydroxide solution) and pure **6** was isolated by repeated chromatography. With one or more equivalent of propylene oxide, **4** readily dissolved with copious and fast evolution of carbon dioxide. With lesser quantities of the epoxide, some remained after the mixture was heated at 95°. The best experiment is described.

A suspension of **4** in 1,2-dichloroethane (175 ml.) containing propylene oxide (16.26 g.) was heated on a steam bath. At 75°, gas evolution was rapid and ceased after 0.75 hour. Solvents were removed, *in vacuo*, and the residue dissolved in benzene (50 ml.) and this solution washed with 5% sodium hydroxide solution (5 x 30 ml.), and then, water (5 x 30 ml.). The benzene extract was concentrated, *in vacuo*, and chromatographed on alumina (200 g.). Elution with 50 ml. portions of benzene (2nd and 3rd fractions) furnished **6** as was evidenced by tlc (R_f = 0.74) and its pmr spectrum. The brown gum (3 g.) which was obtained from the first column was dissolved in petroleum ether and was rechromatographed on alumina (30 g.) which had been prepared in petroleum ether. The product, (0.36 g., 2.0%) was eluted with petroleum ether (200 ml.) petroleum ether in benzene (9:1, 150 ml. and 1:1, 300 ml.), m.p. 154-157°, unchanged after sublimation at 110° (0.5 Torr); uv max (ethanol): nm (log ϵ) 204, (5.06), 233 (5.09), 289 (4.62), 336 (3.08); mass spectrum (70 eV), m/e (relative intensity): 339 (6), 338 (25), 337 (7), 336 (26), 258 (5), 257 (19), 256 (13), 255 (7), 167 (19), 166 (100), 165 (5), 140 (18), 139 (11), 91 (8), 62 (5).

Anal. Calcd. for $C_{18}H_{13}BrN_2$: C, 64.11; H, 3.88; N, 8.38. Found: C, 64.44; H, 4.01; N, 8.41.

When this experiment was conducted on the same scale in the presence of 1-methyl-2-pyridone, (7.26 g., 0.07 mole) the crude product was chromatographed in benzene. The bromo compound, **6** (0.2 g., (1.1%) was eluted by benzene (900 ml.) and then **1** [1.0 g., 7%, m.p. 100-102°, lit (2) m.p. 100-102°] was eluted by ether-chloroform (9:1, 600 ml.; 1:1, 600 ml.) and chloroform (600 ml.).

Reaction of *o*-Carboxybenzenediazonium Chloride, **3** with Porpylene Oxide in 1,2-Dichloroethane.

When **3** was prepared from anthranilic acid (21.9 g.) by literature methods (4,5; Note: hazard warning) and reacted with propylene oxide in 1,2-dichloroethane, as described for the synthesis of **6** from **4**, there was obtained, after chromatography by elution with benzene, **5** (0.17 g., 1.3%) m.p. 148-150°, unchanged after recrystallization from cyclohexane-petroleum ether; R_f = 0.74; uv max (ethanol): nm (log ϵ) 204 (5.05), 233 (5.11), 289 (4.62), 336 (3.08); mass spectrum (70 eV), m/e (relative intensity): 295 (3), 294 (17), 293 (11), 292 (50), 258 (3), 257 (15), 256 (7), 255 (6), 167 (17), 166 (100), 164 (3), 140 (18), 139 (8), 128 (3), 99 (4), 63 (3).

Anal. Calcd. for $C_{18}H_{13}ClN_2$: C, 73.85; H, 4.44; N, 9.57. Found: C, 73.90; H, 4.42; N, 9.63.

Reaction of **4** in 1,2-Dichloroethane.

When a suspension of **4** (prepared as above) in 1,2-dichloroethane (175 ml.) was heated at 95°, very little evolution of carbon dioxide was observed. After 32 hours, the solid was filtered, washed several times with cold chloroform, and dried between filter papers. It weighed 15 g. (40%, based on starting anthranilic acid) and was shown to be **4** by its ir spectrum (Nujol). The spectrum was obtained after drying a small amount of the solid by pressing gently between filter papers.

The 1,2-dichloroethane filtrate was evaporated to dryness, *in vacuo*, and yielded a brown solid (7.63 g.). A portion of the solid (0.70 g.) was sublimed at 90° (0.5 Torr). The sublimate (0.35 g.), after recrystallization from water was shown by its ir and mass spectra to consist mainly of benzoic acid.

The residue from the sublimation, was recrystallized from water, and consisted primarily of *o*-bromobenzoic acid. The impurities could not be removed from either fraction although ir, pmr and mass spectra data compared well with those from authentic samples.

The acids (0.1 g.) were dissolved in ether and treated with diazomethane (estimated to be about 3.0 g.), which was generated from *N*-nitroso-*N*-methyl-*p*-toluenesulfonamide (13). Gc analysis (14) (injection temperature 230°, oven temperature 120°, isothermally) indicated 3 peaks, relative retention times, 3.4, 6.5 and 8.8 minutes, in the ratio of *ca.* 1:1:3. Enrichment with methyl benzoate identified the peak at 3.4 minutes. The mass spectrum at 70 eV of the 6.5 minute peak identified this substance as methyl *o*-chlorobenzoate, m/e (relative intensity): 172 (14), 171 (6), 170 (43), 169 (4), 142 (5), 141 (50), 140 (16), 139 (100), 113 (17), 112 (5), 111 (47), 85 (5), 84 (3), 77 (5), 76 (11), 75 (34), 74 (11), 51 (8), 50 (19), 45 (3).

The peak at R_t 8.8 minutes was methyl *o*-bromobenzoate, with the following mass spectrum (70 eV); m/e (relative intensity): 217 (3), 216 (35), 215 (6), 214 (37), 213 (3), 186 (10), 185 (100), 184 (14), 183 (99), 158 (4), 157 (36), 156 (5), 155 (33), 104 (5), 92 (4), 77 (11), 76 (39), 75 (37), 74 (16), 51 (9), 50 (39), 49 (4), 44 (6).

N-Methyl-*N*-(9-carbazolyl)-*o*-bromoaniline.

Methyl iodide (1.3 g., 0.009 mole) was added to a solution of the **6** (0.05 g., 0.0015 mole) and sodium hydride (50% in oil, 0.192 g., 0.0004 mole) in freshly-distilled *N,N*-dimethylformamide (30 ml.) and the mixture was heated for 24 hours at 55-60°. Solvents were removed, *in vacuo*, the residue diluted with water and extracted with benzene (5 x 20 ml.). The benzene solution was washed with water (8 x 30 ml.) and dried (sodium sulfate). Solvents were removed, *in vacuo*, and the black residue (0.60 g.) was triturated with benzene (10 ml.). The solid which separated, m.p. 137-139° (R_f = 0.48) was identified by its uv and mass spectrum at 70-eV as carbazole, m/e (relative intensity): 168 (17), 167 (100), 166 (17), 164 (3), 140 (10), 139 (13), 113 (3), 83.5 (10), 71 (5), 69 (5).

The filtrate was chromatographed on a column of alumina (15 g., prepared in benzene) and was eluted with 25 ml. of benzene. A white gum crystallized after trituration with petroleum ether, to furnish the product, (0.165 g., 32%) m.p. 120-121°, R_f = 0.74; uv max (ethanol): nm (log ϵ), 208 (5.19), 233 (5.31), 290 (4.81), 336 nm (4.00); pmr (see discussion); mass spectrum (70 eV), m/e (relative intensity): 353 (9), 352 (45), 351 (11), 350 (46), 272 (4), 271 (19), 254 (8), 255 (11), 186 (15), 184 (17), 168 (15), 167 (96), 166 (100), 160 (4), 140 (19), 139 (19), 128 (6), 105 (10), 104 (7), 77 (15), 63 (5), 51 (4), 39 (5).

Anal. Calcd. for $C_{19}H_{15}BrN_2$: N, 7.97. Found: N, 8.01.

Hydrogenation of this compound (0.165 g., 0.0005 mole) in acetic acid (20 ml.) with hydrogen (3 atmospheric pressure) in presence of 5% palladium on charcoal was carried out initially at 25° for 24 hours. Tlc shows two spots, R_f = 0.74 and 0.48. The reduction was continued at 50-60° for 24 hours longer. Solvents were removed, *in vacuo*, the residue was dissolved in water (30 ml.) and neutralized with sodium carbonate. Extraction with benzene (3 x 15 ml.) produced carbazole (0.05 g., 64%).

Pyrolysis, under GC Conditions (14).

(i) of **5**.

An acetone solution of **5** was injected at 200° and the 2 minute post injection period was programmed from 100-200° at 10°/minute and held for 14 minutes. Under these conditions, two different peaks, other than the one for acetone, were observed. The peak, with a relative retention time of 15.3 minutes, corresponded to carbazole. The other peak after 5.7 minutes, arose from *o*-chloroaniline (enrichment and mass spectrum; *m*- and *p*-chloroanilines were eluted at 6.7 and 6.5 minutes, respectively).

(ii) of **6**.

Using the conditions described above, injection of an acetone solution of **6**, gave rise to two peaks, relative retention times, 6.3 and 15.1 minutes. Enrichment with *o*-bromoaniline, enhanced the peak at 6.3 minutes and carbazole was identified by enrichment as the peak at 15.1 minutes.

(iii) *N*-Methyl Derivative of **6**.

Pyrolysis gave rise to two peaks, relative retention times 7.9 and 15.2 minutes. The latter was shown to be carbazole. The mass spectrum of the first peak at 70 eV, [m/e, (relative intensity): 188 (11), 187 (94), 186 (84), 185 (100), 184 (80), 106 (9), 105 (40), 103 (18), 92 (11), 91 (23), 90 (8), 79 (12), 78 (22), 77 (75), 76 (14), 75 (11), 74 (13), 73 (6), 65 (20), 64 (22), 63 (29), 62 (11), 61 (6), 58 (14), 53 (17), 52.5 (31), 52 (26), 51 (40), 50 (36), 46 (6), 44 (31), 43 (44), 42 (5), 41 (9), 40 (6), 39 (31), 38 (21), 37 (10), 32 (31), 30 (15), 29 (6)] is compatible with an *N*-methyl-*o*-bromoaniline.

Conversion of **4** to *o*-Iodobenzoic Acid.

o-Carboxybenzenediazonium bromide (15 g., 0.065 mole), was dissolved in water (75 ml.). Potassium iodide (20 g., 0.12 mole) and 6*N* hydrochloric acid (5 ml.) were added. The mixture was heated in a steam bath for 0.5 hour, cooled, filtered and washed with 6*N* hydrochloric acid, and then with water. Recrystallization from water-ethanol (8:1) gave 14 g., (87.5%) *o*-iodobenzoic acid, m.p. 157-159°, lit. m.p. 163°; its mass spectrum was identical to that of an authentic sample.

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(6) Presumably propylene oxide reacted with HX accompanying **2** and is converted to propylene chlorohydrins. The addition of alcohols to benzyne has been discussed by J. F. Bunnett, D. A. R. Happer, M. Patsch, C. Pyun and H. Takayama [*J. Am. Chem. Soc.*, 88, 5250 (1966)].

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(10) When 2-biphenylenediazonium-3-carboxylate was decomposed in boiling 1,2-dichloroethane, 2-chlorobiphenylene was obtained in 9% yield [E. N. Losey and E. LeGoff, *J. Org. Chem.*, 37, 3812 (1972)]. The reaction of 1,1-dicyclopropylethene with **3**

afforded, among other products, 2-cyclopropyl-3-phenyl-5-chloro-1-pentene in 21% yield. Apparently here, the HCl associated with **3** opened one of the cyclopropyl groups during the reaction. [V. Usieli and S. Sarel, *ibid.*, 38, 1703 (1973)].

(11) In a related report, J. I. G. Cadogan and G. A. Molina [*J. Chem. Soc., Perkins I*, 541 (1973)] described the reduction of aromatic amines by diazotization with pentyl nitrite in boiling tetrahydrofuran.

(12) W. A. Noyes, *Org. Syn., Coll. Vol., II*, 108 (1943).

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(14) A Perkin-Elmer Model 800 chromatograph was used for all gc determinations. It was equipped with a 50 ft. 0.02-inch support-coated open tubular stainless steel column, coated with OV-101, as the liquid phase. The sample size was 1 μl. and He was used as carrier gas at 9 lb gauge pressure. The gc was connected to the mass spectrometer for direct gc-mass spectra determination.