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The Bamberger-Ham condensation of 4-substituted nitrosobenzenes in concentrated sulfuric acid reported as a method of synthesis for phenazine *N*-oxides has been found to be limited to electron donating substituents. Methyl 4-nitrosobenzoate has been found to react under these conditions to give dimethyl 2-nitrodiphenylamine-4',5-dicarboxylate (**2**). Compounds of unknown structure previously reported to arise from acid treatment of 4-bromo- and 4-chloro-nitrosobenzene have been shown to be 4',5-dibromo-2-nitrosophenylamine (**10**) and the analogous dichloro compound. Treatment under stronger acidic conditions (oleum) converted **10** but not **2** into the corresponding phenazine *N*-oxide. Mechanistic implications are discussed.

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Bamberger and Ham reported the acid catalyzed conversion of a number of 4-substituted nitrosobenzenes into substituted phenazines and phenazine *N*-oxides (1,2). More recently this method has been employed in the dye field and methyl 4-nitrosobenzoate (**1**) has been reported (3,4) to form phenazine-2,7-dicarboxylic acid *N*-oxide under acidic conditions. Unfortunately, no physical data on this compound was included in the report. In connection with other studies, we needed phenazine-2,7-dicarboxylic acid *N*-oxide and the sulfuric acid condensation of methyl 4-nitrosobenzoate was repeated.

The compound isolated from this reaction, in 70% yield, has been found to be dimethyl 2-nitrodiphenylamine-4',5-dicarboxylate (**2**). Elemental analysis and mass spectral data are consistent with the molecular formula $C_{16}H_{14}N_2O_6$. The carbon-13 nmr data supports the diphenylamine structure assignment since 10 lines are observed in the atomic region, whereas 12 would be expected for the phenazine *N*-oxide.

The diethyl ester analog (diethyl 2-nitrodiphenylamine-4',5-dicarboxylate **3**) of **2** was also prepared in a 76% yield from ethyl 4-nitrosobenzoate under similar conditions. Compounds **2** and **3** were hydrolyzed to the same dicarboxylic acid (**4**), which was converted to the corresponding dicarbonyl chloride (**5**), and the latter was reacted with diethylamine to form its diethylamide (**6**) all of which gave physical data consistent with the diphenylamine structure. Reduction of **3** with iron/acetic acid gave diethyl 2-aminodiphenylamine-4',5-dicarboxylate (**7**).

Indirect evidence exists which confirms the structural assignment of **2**. The only other reasonable structure for **2** is its isomer 2,4'-dicarbomethoxy-5-nitrodiphenylamine. Its dicarboxylic acid analog has been prepared by the condensation of 4-aminobenzoic acid and 2-chloro-4-nitrobenzoic acid, and the reported (5) physical data differs from that of **4**.

The earlier report (3) also describes the conversion of

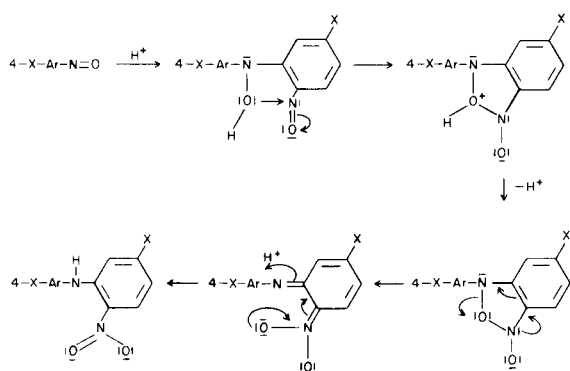
"phenazine-2,7-dicarboxylic acid *N*-oxide" into phenazine-2,7-dicarboxylic acid. The sequence involved reduction with stannous chloride to form a dihydrophenazine which was oxidized with nitric acid to reportedly form phenazine-2,7-dicarboxylic acid (no physical data given). Reduction of 2-nitrodiphenylamines with several reagents have been reported (6) to form phenazines, and consequently **4** was subjected to reduction by sodium hydrosulfite, stannous chloride and sodium borohydride/sodium ethoxide. The latter reagent has found rather general use in reductive cyclization of 2-nitrodiphenylamines into phenazines (6a,b). 2-Aminodiphenylamine-4',5-dicarboxylic acid (**8**) was the only product isolated from these reduction experiments.

One interpretation of these results is that a 2-nitrodiphenylamine is an intermediate in the conversion of 4-substituted nitrosobenzenes into phenazine *N*-oxides in the Bamberger-Ham phenazine *N*-oxide synthesis. These early workers reported that acid treatment of 4-bromo-nitrosobenzene formed 2,7-dibromophenazine *N*-oxide (**9**) and an unknown compound which melted at 174° and analyzed for C_6H_2BrNO . We have repeated this reaction and found that the compound melting at 174° is 4',5-dibromo-2-nitrodiphenylamine (**10**). Its structure was established by synthesis from 4-bromoaniline and 3,4-dinitrochlorobenzene (7). Bamberger and Ham also report a compound from the acid treatment of 4-chloronitrosobenzene which analyzed for C_6H_4ClNO . In view of our results and the concordance of the literature melting point of the unknown C_6H_4ClNO with that reported for the compound formed from the reaction between 4-chloroaniline and 3,4-dinitrochlorobenzene, we conclude that the unknown C_6H_4ClNO is 4',5-dichloro-2-nitrodiphenylamine (8,9).

When the diphenylamines **10** and **3** are subjected to sulfuric acid according to the Bamberger-Ham method, they are recovered unchanged. This result suggests that 2-nitrodiphenylamines are not intermediates in phenazine *N*-oxide formation under Bamberger-Ham conditions and are formed in a competing process. Interestingly, when

dibromonitrodiphenylamine **10** is subjected to more drastic conditions (oleum) reported to convert 2-nitrodiphenylamines into phenazine *N*-oxide (**8**), 2,7-dibromophenazine *N*-oxide (**9**) is formed. Similar treatment of **3** produced unidentified sulfur containing products. The failure of diethyl 2-nitrodiphenylamine-4',5-dicarboxylate **3** to cyclize to the corresponding *N*-oxide is probably associated with the electron attracting properties of the carboethoxy groups which deactivate the ring to electrophilic attack in a ring closure step. Alternatively, an electron withdrawing group could enhance the rate of formation of 2-nitrodiphenylamine at the expense of phenazine *N*-oxide formation. This suggestion is consistent with the mechanism postulated below to account for the formation of the 2-nitrodiphenylamine from nitrosobenzenes. Since in the cases studied by Bamberger-Ham, and Cross and co-workers, all the substituents were electron donors (halogens and methyl) and in view of the results reported here, it would appear that electron withdrawing groups have a deleterious effect on phenazine *N*-oxide formation under both types of acidic conditions.

It is well documented that nitrosobenzenes form *N,N*-diphenylhydroxylamines on treatment with strong acid (**10**). We offer below a plausible mechanism for the conversion of the presumed intermediate hydroxylamine into the corresponding 2-nitrodiphenylamine. The first step in this postulated mechanism for the intramolecular redox process is nucleophilic attack on the nitroso function for which there is ample precedent (**11**). As alluded to earlier the electron withdrawing effect of the carboethoxy group would be expected to facilitate this step and might be contributory to the failure to form a phenazine in the case of the reaction of **1**. The remaining steps in the proposed mechanism are straightforward and do not warrant further comment.



EXPERIMENTAL

Dimethyl 2-Nitrodiphenylamine-4',5-dicarboxylate (**2**).

Methyl *p*-nitrosobenzoate (**1**) (5 g., 0.03 mole) was added gradually and with vigorous stirring to concentrated sulfuric acid

(25 ml.) during a period of 15 minutes. The temperature during this period was maintained between 18 and 23° by external cooling. The mixture was stirred for another 15 minutes at 20° and then poured onto ice (250 g.). The solid which separated was collected, washed with water and dried. It was shaken with chloroform (50 ml.) and filtered from a black residue. The solvent was removed from the filtrate and the residual solid crystallized twice from ethanol, m.p. 172-174°, yield 3.3 g. (70%); ms: M^+ at *m/e* 330; ir (potassium bromide): 3375, 1730, 1710, 1600, 1490, 1250, 1200, 1105, 840, 765, 745 cm^{-1} ; ^{13}C nmr (deuteriochloroform): 52.1, 52.8, 118.6, 119.1, 121.4, 126.4, 127.0, 131.5, 136.2, 136.5, 140.3, 143.0, 165.1, 166.2 ppm; ^1H nmr (deuteriochloroform): δ 3.95 (d, 6, 2CH₃), 7.25-8.4 (m, 7, aromatic Hs), 9.5 (broad NH).

Anal. Calcd. for C₁₆H₁₄N₂O₆: C, 58.18; H, 4.27; N, 8.48. Found: C, 58.14; H, 4.27; N, 8.51.

Diethyl 2-Nitrodiphenylamine-4',5-dicarboxylate (**3**).

A similar procedure using ethyl *p*-nitrosobenzoate with the reaction temperature maintained between 10 and 15° yielded **3** in 76% yield, m.p. 94-5° after recrystallization from ethanol. If the reaction temperature was maintained at 20°, the yield was 50%; ms: M^+ at *m/e* 358; ir (potassium bromide): 3375, 2980, 1745, 1720, 1610, 1500, 1250, 1195, 1170, 765, 740 cm^{-1} ; ^{13}C nmr (DMSO-*d*₆): 13.8, 14.0, 60.2, 61.4, 119.4, 120.2, 120.7, 124.1, 126.7, 130.6, 135.2, 138.2, 129.1, 144.9, 164.0, 165.1 ppm; ^1H nmr (DMSO-*d*₆): δ 1.3 (2 sets of t, 6, 2CH₃), 4.15 (q, 4, 2 CH₂), 7.1-8.0 (m, 7, aromatic Hs), 9.1 (s, 1, NH disappears on deuterium oxide shake).

Anal. Calcd. for C₁₈H₁₈N₂O₆: C, 60.35; H, 5.03; N, 7.82. Found: C, 60.41; H, 5.12; N, 7.80.

2-Nitrodiphenylamine-4,5-dicarboxylic Acid (**4**).

Ethyl 2-nitrodiphenylamine-4',5-dicarboxylate (**3**) (6.8 g., 0.02 mole) was dissolved in ethanol (70 ml.) by heating. To this solution was added with stirring, a 10% sodium hydroxide solution (80 ml.) and the resulting dark red solution boiled gently under reflux for 1 hour. Ethanol was removed by distillation under reduced pressure and the residual mixture diluted with water (200 ml.). It was heated to 100° and then acidified by adding acetic acid with vigorous stirring. The acid **4** precipitated out as a dark orange colored solid. The mixture was heated for another 30 minutes and acetic acid was added as necessary to keep the mixture slightly acidic. The solid was filtered hot, washed with water, dried and crystallized from DMF/water, m.p. 338-340° dec. The dimethyl ester was hydrolyzed in a similar manner and the acid obtained had m.p. 340-342° dec. The mixture melting point with the two samples was underpressed and the ir spectra of the two samples were superimposable; ir (potassium bromide): 3350, 3100, 3020, 2900, 2690, 2575, 1740, 1700, 1620, 1590, 1515, 1440, 1255, 845, 775, 740, cm^{-1} . ^{13}C nmr (DMSO-*d*₆): 120.0, 125.3, 126.7, 130.9, 136.5, 138.6, 138.8, 144.5, 165.6, 166.7 ppm.

Anal. Calcd. for C₁₄H₁₀N₂O₆: C, 55.63; H, 3.34; N, 9.27. Found: C, 55.62; H, 3.36; N, 9.23.

2-Nitrodiphenylamine-4',5-dicarbonyl Chloride (**5**).

2-Nitrodiphenylamine-4',5-dicarboxylic acid (**4**) (3 g., 0.01 mole) was suspended in dry benzene (10 ml.) and redistilled thionyl chloride (3.5 ml.) was added to this slurry followed by a solution of DMF (0.5 g.) in dry benzene (2 ml.). The mixture was warmed and the reaction started with the evolution of hydrogen chloride gas. When the initial reaction had subsided, the mixture

was refluxed for 2 hours (the acid dissolved within 15 minutes of start of refluxing). On cooling to room temperature, the red colored crystals began to separate. After 2 hours, the solid was filtered off with suction, washed with petroleum ether (b.p. 40-50°) dried and crystallized from benzene, m.p. 156-157°, yield 2.5 g. (80%); ir (potassium bromide): 3350, 3120, 1750, 1695, 1610, 1510, 1275, 1170, 850, 800, 700, 650 cm^{-1} .

Anal. Calcd. for $\text{C}_{14}\text{H}_8\text{Cl}_2\text{N}_2\text{O}_4$: Cl, 20.71. Found: Cl, 20.91.

2-Nitrodiphenylamine-4',5-diethylamide (6).

2-Nitrodiphenylamine-4',5-dicarbonyl chloride (5) (1.13 g., 0.003 mole) was dissolved in benzene (50 ml.) by warming. The cooled solution was then added to a solution of diethylamine (3 ml.) in benzene (20 ml.) gradually and with stirring. The mixture was allowed to stand overnight and then refluxed for 1 hour. After cooling, the precipitated diethylamine hydrochloride was filtered and benzene distilled from the filtrate. The residual yellow solid was treated with a sodium carbonate solution, filtered, washed with water, dried and crystallized from 50% ethanol, m.p. 128-129°, yield 1 g. (73%); ir (potassium bromide): 3320, 2280, 1625, 1560, 1480, 1315, 1260, 1165, 740 cm^{-1} . ^{13}C nmr (DMSO- d_6): 13.3, 114.3, 116.3, 122.8, 126.7, 127.6, 133.3, 134.0, 139.9, 141.0, 143.6, 167.7, 169.3 ppm (methylene peaks masked by DMSO- d_6).

Anal. Calcd. for $\text{C}_{22}\text{H}_{28}\text{N}_4\text{O}_4$: C, 64.08; H, 6.79; N, 13.59. Found: C, 63.98; H, 6.87; N, 13.59.

Reaction of *p*-Nitrosobromobenzene with Concentrated Sulfuric Acid.

p-Nitrosobromobenzene (42 g., in three portions of 14 g. each) was treated with concentrated sulfuric acid according to the procedure of Bamberger and Ham (1). The material after extraction with 2*N* sodium hydroxide was 21 g. This was extracted with hexane, acetic acid and xylene according to the published procedure. The final isolation of the products was, however, better achieved by chromatography.

The residue obtained after evaporating the hexane extract was dissolved in benzene and chromatographed over alumina and eluted with the same solvent. The light yellow band which eluted first contained impure compound $\text{C}_6\text{H}_4\text{BrNO}$, an intense yellow band eluted next. The residue from this fraction was crystallized from ethanol three times and 1.6 g., m.p. 172-174°, of material was obtained; ir (potassium bromide): 3340, 1600, 1550, 1480, 1470, 1250, 1200, 1065, 915, 805, 745 cm^{-1} ; ^{13}C nmr (deuteriochloroform): 118.2, 119.4, 121.2, 126.2, 128.0, 131.3, 133.1, 137.0, 143.2 ppm. The compound was identical with 4',5-dibromo-2-nitrodiphenylamine (10) obtained below. A mixed melting point with compound 10 obtained below was undepressed and the ir spectra of the two samples were superimposable.

The material obtained from the xylene extract was dissolved in chloroform and passed over an alumina column and eluted with chloroform. The yellow band was collected, solvent removed and the residue crystallized from xylene which afforded 2,7-dibromophenazine *N*-oxide 9, m.p. 239-240° (lit. (1) m.p. 240°); ir (potassium bromide): 3120, 1610, 1475, 1415, 1375, 840 cm^{-1} ; ^{13}C nmr (deuteriochloroform): 120.3, 121.3, 124.8, 126.0, 131.5, 132.1, 133.6, 135.3, 145.4 ppm.

4',5-Dibromo-2-nitrodiphenylamine (10).

A solution of 3,4-dinitrobromobenzene (7) (6.2 g., .025 mole) and *p*-bromoaniline (10 g., 0.06 mole) in ethanol (50 ml.) was refluxed on a steam bath for 4 hours and then left at room temperature overnight. This solid which crystallized was filtered,

washed with cold ethanol, digested with 3*N* hydrochloric acid and then recrystallized from ethanol, m.p. 171-173°, yield 2.5 g. (28%). The mixed melting point with the sample obtained by method of Bamberger and Ham was undepressed and the ir spectra of the two samples were superimposable.

Preparation of 2,7-Dibromophenazine *N*-Oxide (9) from 4',5-Dibromo-2-nitrodiphenylamine (10).

4',5-Dibromo-2-nitrodiphenylamine (10) (0.7 g.) was dissolved in concentrated sulfuric acid (2 ml.) and cooled to 20°. Fuming sulfuric acid (2.5 ml.) was then added dropwise with stirring while the temperature was maintained at ca. 20°. After five minutes of stirring at 20°, the reaction mixture was poured into a vigorously stirred solution of sodium bicarbonate (15 g.) in water (250 ml.) and ethanol (30 ml.). A yellowish solid separated; the aqueous suspension was extracted with methylene chloride, washed with water, dried over calcium sulfate and the solvent removed. The residue was crystallized from ethanol, m.p. 235-236°, yield 0.2 g. (30%). Crystallization from xylene did not raise the melting point. It was dissolved in chloroform and passed over an alumina column and the residue from this solution was crystallized from xylene, m.p. 237-238°. The mixed melting point of the sample obtained above was undepressed and ir spectra of the two samples were identical.

Diethyl 2-Aminodiphenylamine-4',5-dicarboxylate (7).

The ester 3 (1 g., 0.003 mole), iron powder (2 g.) and glacial acetic acid (30 ml.) were heated together on a steam bath for one hour, cooled and filtered. The filtrate was diluted with water and a white semi-solid mass separated. It was washed with water, dried in vacuum and crystallized from benzene/hexane, m.p. 122-123°, yield 0.3 g.; ir (potassium bromide): 3425, 3320, 2975, 1685, 1600, 1520, 1290, 1185, 1120, 1040, 865, 785 cm^{-1} ; ^{13}C nmr (deuteriochloroform): 14.4, 60.4, 113.3, 114.7, 120.4, 120.8, 124.9, 129.0, 129.3, 131.4, 147.6, 149.5, 166.3, 166.6 ppm.

Anal. Calcd. for $\text{C}_{18}\text{H}_{20}\text{N}_2\text{O}_4$: C, 65.83; H, 6.13; N, 8.53. Found: C, 65.52; H, 6.03; N, 8.70.

2-Aminodiphenylamine-4',5-dicarboxylic Acid (8).

The acid 4 (1 g., 0.0033 mole) was dissolved in 5% sodium carbonate solution (30 ml.) resulting in a red solution. Sodium hydrosulfite (2 g.) was added in small portions with stirring and the color changed to light yellow. After stirring for one hour the mixture was made acidic with dilute hydrochloric acid. The white solid which separated was filtered, washed with water, dried and crystallized from ethylene glycol monomethyl ether/water, m.p. 287-288°; ir (potassium bromide): 3490, 3400, 2050, 2650, 1675, 1600, 1520, 1410, 1275, 1240, 1175, 1150, 845, 770, 660 cm^{-1} ; ^{13}C nmr (DMSO- d_6) 113.0, 114.1, 117.9, 119.3, 124.5, 127.1, 127.9, 131.1, 148.2, 150.3, 167.3 ppm.

Anal. Calcd. for $\text{C}_{14}\text{H}_{12}\text{N}_2\text{O}_4$: C, 61.76; H, 4.44; N, 10.29. Found: C, 61.54; H, 4.50; N, 10.17.

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