[Contribution from the Chemical Laboratories of the University of Buffalo and the Johns Hopkins University]

THE NITRATION OF SUBSTITUTED ANILINES[1]

By E. Raymond Riegel, Howard W. Post and E. Emmet Reid[2]

Received September 17, 1928 Published February 5, 1929

As is well known, it is customary to acetylate an aromatic amine to protect it during nitration. In acetanilide and in its substitution products, the nitrogen is trivalent and probably remains so even in the presence of strong acids. It directs an entering group to the ortho or para position. In the case of aniline in sulfuric acid solution, the nitrogen is pentavalent and orients an entering group chiefly to the meta position. The yield of *m*-nitraniline is only moderate.

The object of the present investigation was to determine the effect of various substituents on the stability of aniline, *i. e.*, the resistivity toward the oxidizing action of nitric acid, during nitration in sulfuric acid solution. Certain substituted anilines give good yields of nitranilines, while others are entirely destroyed by the same nitration mixture. The substituents that have been used are the hydroxyl, carboxyl and sulfonic acid groups, with the nitro group in one case. In all, fourteen substituted anilines were studied. These are arranged in order of decreasing "persistence" of amino. The figures given represent the percentage of original amino present after nitration. We have taken no account of possible formation of nitrous acid during nitration and consequent conversion of amino to hydroxyl. The formulas given are those of probable nitration products, determined by formation of derivatives.

	Compound	%		Compound	%
1	*p*-Aminophenol	72.6	8	*m*-Amino-*p*-hydroxybenzoic acid	0.0
2	*m*-Aminosalicylic acid	42.5	9	*m*-Amino-*p*-hydroxytoluene	.0
3	*m*-Amino-*p*-hydroxybenzenesulfonic acid	40.0	10	*o*-Amino-*p*-nitrophenol	.0
4	Sulfanilic acid	34.0	11	Anthranilic acid	.0
5	Metanilic acid	26.7	12	1-Amino-4-phenol-6-sulfonic acid	.0
6	*p*-Amino-*m*-hydroxybenzenesulfonic acid	4.8	13	*m*-Aminophenol	.0
7	*o*-Aminophenol	0.0	14	1-Amino-2-hydroxy-4-naphthalenesulfonic acid	49.0

Method of Nitration.—The amine was dissolved in 13 to 18 parts by weight of concentrated sulfuric acid (sp. gr., 1.84) and cooled to below 5° and the nitrating mixture of fuming nitric and concentrated sulfuric acids added, drop by drop from a buret. The

---

[1] Presented at the Detroit meeting of the American Chemical Society, September 1927.

[2] Submitted by the second author to the Board of University Studies of the Johns Hopkins University in conformity with the requirements for the degree of Doctor of Philosophy, June, 1927. The work was begun at the University of Buffalo.

acid mixture was added in 10% excess based on the amount required to yield a mono-nitro derivative. It was made up to contain 0.0083 mole of nitric acid per cc. The system was stirred constantly. The mixture of acids and amine was kept for one hour at 0°, one hour at room temperature and then poured over ice. The resulting precipitate was filtered off and analyzed. Water solutions of nitration products were titrated against standard sodium nitrite in the presence of hydrochloric acid for amino contents, using starch iodide paper as indicator. Nitro groups were determined by titration against standard titanous chloride[3] and chlorine was determined whenever necessary by the Carius method.

Discussion of Results.—Nitrating aniline itself, by our method, gave a nitration product which probably consisted of a number of dinitro derivatives. After repeated extraction with alcohol and ether the product melted between 180 and 200° with decomposition. Further investigations are now being carried on to determine the identity of this material.

As regards the substitution products of aniline, the presence of hydroxyl ortho to amino seems to make the compound extremely susceptible to oxidation, while the same group in the para position gives a molecule which can be nitrated with good yield. This holds true with respect to the pairs above: 1 and 7, 2 and 8, 3 and 6. Again, the effect of the hydroxyl group in the ortho position can be overcome by the introduction of the sulfonic acid group, as witness 3 and 7, but this sulfonic acid group is a better protecting agent, in one case para to the amino (4 and 5) and in another meta (3 and 6). Evidently this is due to the presence of the hydroxyl, as Nos. 4 and 5 are sulfanilic and metanilic acids, respectively, and 3 and 6 are *m*-amino-*p*-hydroxybenzenesulfonic acid and *m*-hydroxy-*p*-aminobenzenesulfonic acid. It should be noted that *p*-hydroxy-aniline sulfonated spontaneously, during the reaction, and its resistance to decomposition may be due in part, at least, to the introduction of the sulfonic acid group.

The question arises as to why there should be such a difference in resistance toward the oxidizing action of nitric acid between ortho and para aminophenols and their derivatives.

Conclusions.—*o*-Aminophenol and its derivatives are unstable in the presence of a strong oxidizing agent such as fuming nitric acid, *o*-aminophenol itself going to pieces. *p*-Aminophenol is capable of giving a good yield of nitro-aminophenolsulfonic acid under the conditions holding in our work. Assuming the most stable configuration of the benzene ring to be that in which alternate carbons are similarly polarized, an electronegative group can be said to direct an entering group to the ortho or para position, while an electropositive group directs meta. This holds qualitatively. *p*-Aminophenol directs both sulfonic acid and nitro to the positions ortho to hydroxyl, thus giving evidence that hydroxyl is the determining factor. The amino tends in this case to adopt an electro-

---

[3] Thornton and Wood, *Ind. Eng. Chem.*, 19, 150 (1927).

positive character, at least in a relative sense. We assume that the resistivity of the ring in this case is due to the coincidence between the directive effects of the two groups, at least in part, and that the two groups when ortho to each other do not succeed in adopting such distinctly opposite polarity because of their proximity to each other.

Materials

p-**Aminophenol** was obtained from the Eastman Kodak Co.; NH_2, 14.34%.

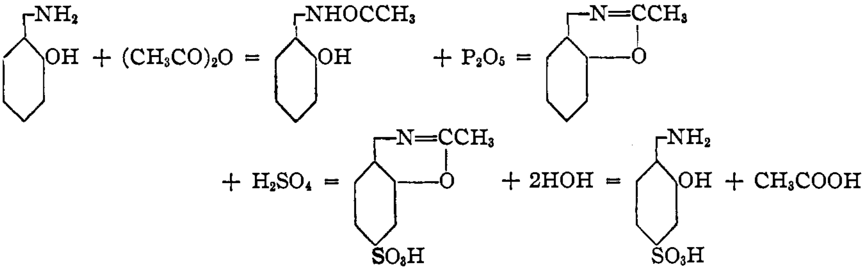
m-**Aminosalicylic** acid was made by coupling salicylic acid with benzene diazo chloride and reducing the azo compound with stannous chloride and hydrochloric acid.[4] The hydrochloride melted at 236°; Cl, 18.61. The free amine melted at 250–260°; acetyl derivative at 218°.[5]

m-**Amino**-*p*-**hydroxybenzenesulfonic** acid was obtained from the National Aniline and Chemical Co., and from the Wilbur White Chemical Co.; NH_2, 8.52%, S, 15.93; the anilide melted at 203°.[6]

Sulfanilic acid was obtained from the Eastman Kodak Company; NH_2, 9.42%.

Metanilic acid was obtained from the Eastman Kodak Company; NH_2, 9.16%.

1-Amino-6-hydroxy-4-benzenesulfonic acid was made by a method which is outlined in the literature but not in detail. *o*-Aminophenol, 85 g., was treated with 190 g. of acetic anhydride and the cooled product sucked dry and desiccated. This acetylaminophenol (40 g.) was then distilled off at 200° with phosphorus pentoxide. There was about 20 cc. of oily product.[7] This gave us ethenyl-*o*-aminophenol, of which 20 g. was placed in a ten-inch test-tube and treated with 24 g. of fuming sulfuric acid ("163%") drop by drop, the test-tube being immersed in a freezing mixture of ice and salt and the system stirred. The entire sulfonation mixture was allowed to stand for one hour and then thrown into ice water. The resulting solid was sucked dry and hydrolyzed by boiling water (400 cc.); yield, 13 g. of blue-black needles, melting after recrystallization from water at 205–210° with decomposition; NH_2, 8.66%.



o-**Aminophenol** was made by nitrating phenol and reducing, checking with material from the Eastman Kodak Company.

1-Amino-6-hydroxy-3-benzoic acid was made by coupling *p*-hydroxybenzoic acid with benzene diazo chloride and reducing with tin and hydrochloric acid, then comparing the product with one made by nitrating *p*-hydroxybenzoic acid and reducing with tin and hydrochloric acid; melting point, 226°; NH_2, 10.72%. In only one run

---

[4] Fischer, *Ber.*, **32**, 81 (1899).

[5] Grandmougin, *ibid.*, **39**, 3930 (1906).

[6] Post, *Ann.*, **205**, 51 (1880).

[7] Friedländer, Vol. IX, p. 148 (German Patent 197,496); Bücherer, "Lehrbuch der Farbenchemie."

were we able to do this with the free acid; all subsequent runs were made with the methyl ester.[8]

1-Amino-3-methyl-6-hydroxybenzene was made by dissolving 21.6 g. of *p*-cresol in 36 g. of sodium hydroxide and 60 cc. of water. To this was added benzene diazo chloride made by titrating a solution of 18.6 g. of aniline in 150 cc. of hydrochloric acid (1:1) with 13.8 g. of sodium nitrite in 35 cc. of water. The precipitated azo compound was reduced by covering with a solution of 113 g. of stannous chloride in 119 g. of hydrochloric acid and gently warming. The product was precipitated by pouring into concentrated hydrochloric acid solution, the process being repeated to eliminate aniline hydrochloride. The free base was obtained by boiling with water; m. p. 129°; NH_2, 12.58%.

1-Amino-3-nitro-6-phenol was made by the reduction of dinitrophenol; m. p. 136°.[9]

***o*-Aminobenzoic acid** was purchased from the Eastman Kodak Company; NH_2, 11.71%.

1-Amino-4-phenol-2-sulfonic acid was made by treating phenol with nitrous acid and then with sodium bisulfite; m. p. 270°.[10]

***m*-Aminophenol** was purchased from the Eastman Kodak Company.

1-Amino-4-naphthol-2-sulfonic acid was purchased from the National Aniline and Chemical Co.

Identification of Nitration Products.—*p*-Aminophenol gave $C_6H_2(1)NH_2(3)SO_3H(4)OH(5)NO_2$; derivative with dinitrochlorobenzene a red powder;[11] nitration product: NH_2, 6.82%; NO_2, 19.06%.

1-Amino-4-hydroxy-3-benzoic acid gave $C_6H_2(1)NH_2(3)COOH(4)OH(5)NO_2$; NH_2, 8.91%; NO_2, 21.81%.

1-Amino-6-phenol-3-sulfonic acid gave $C_6H_2(1)NH_2(3)SO_3H(6)OH(5)NO_2$; derivative with β-naphthol a brown powder;[12] nitration product: NH_2, 6.79%; NO_2, 18.37%.

***p*-Aminobenzenesulfonic acid** gave $C_6H_3(1)NH_2(4)SO_3H(5)NO_2$($NH_2$, 7.34%); derivative with salicylic acid a yellow-green material.

***m*-Aminobenzenesulfonic acid** gave probably mostly unchanged amine and some *m*-phenolsulfonic acid (NH_2, 8.38%); derivative with diazotized benzidene and Gamma Acid a trace of black powder.[13]

1-Amino-6-phenol-4-sulfonic acid gave $C_6H_2(1)NH_2(3)NO_2(4)SO_3H(6)OH$; NH_2, 6.71%; NO_2, 18.87%.

Summary

Fourteen substituted anilines have been nitrated with mixed acids under the same conditions. Great differences in stability have been found; some groups seem to stabilize the molecule, *i. e.*, render it more resistant to the oxidizing action of the nitric acid, while others bring about its destruction. The influence of the groups depends on their position—two electronegative groups para to each other seem to make the resultant molecule more resistant to oxidation.

BALTIMORE, MARYLAND

---

[8] Friedländer, Vol. VI, p. 1153 (German Patent 111,932).

[9] Auwers and Röhrig, *Ber.*, **30**, 992 (1897); Laurent and Gerhardt, *Ann.*, **75**, 68 (1850).

[10] Schultz and Stäble, *J. prakt. Chem.*, (2) **69**, 334 (1904); Friedländer, Vol. III, p. 57 (German Patent 71,368).

[11] *Chem. Centr.*, II, 656 (1900); German Patent 113,337.

[12] Friedländer, Vol. VII, p. 419.

[13] Friedländer, Vol. XI, p. 419.