gen under a hood. The pale yellow product was recrystallized from an ethanol–water mixture; m.p. 219–220°.

Anal. Calcd. for $C_{14}H_{21}O_2N_1$: O, 13.60; N, 5.95. Found: O, 13.43; N, 5.39.

2,4-Dinitrophenylhydrazone of 2,6-Di-*t*-butyl-1,4-benzoquinone.—Fifty mg. of I was dissolved in 10 ml. of 95% alcohol and to this solution was added 2 ml. of a freshly prepared sulfuric acid solution of 2,4-dinitrophenylhydrazine in alcohol. The red precipitate separated almost immediately and after recrystallization had m.p. 198–200°.

Anal. Calcd. for $C_{20}H_{24}O_5N_4$: C, 59.98; H, 6.04; N, 13.99; O, 19.98. Found: C, 60.79; H, 6.30; N, 13.90; O, 19.42.

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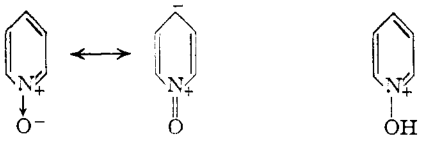
The Sulfonation of Pyridine-N-Oxide[1]

BY HARRY S. MOSHER AND FRANK J. WELCH

RECEIVED DECEMBER 27, 1954

Although pyridine undergoes nitration with considerable difficulty to give 3-nitropyridine,[2,3] pyridine-N-oxide (I) reacts with comparative ease to give a product substituted in the 4-position.[4–6] Ochiai[4,5] has attributed the susceptibility to nitration of the 4-position of the pyridine-N-oxide ring to the contribution of the resonance structure II to the activated state of the molecule. Linton[7] has shown by comparing the dipole moments of several tertiary amine-N-oxides that structures of the type II which increase the electron densities at the 2- and 4-positions of the ring are important to the activated state of the pyridine-N-oxide molecule. If the resonance structure II is responsible for the location of the entering nitro group, it is to be expected that other electrophilic reagents as well will attack pyridine-N-oxide in the 4-position. However, there has been no report in the literature of the substitution of pyridine-N-oxide by electrophilic reagents other than in the case of the nitration reaction.[8] Formulas I and II, however, are an oversimplification of the states of the molecule under the conditions of the reaction since the nitration is conducted in sulfuric acid solution in which the pyridine-N-oxide must exist primarily as the salt form, $\overset{+}{\mathrm{III}}$. This form, because of its positive charge, can hardly be readily susceptible to electrophilic attack. Thus if II is in reality the form of pyridine-N-oxide responsible for its ready nitration, then it must be formed from III on the approach of the nitronium ion with the simultaneous expulsion of a proton. Because of these considerations, an investigation of the action of other electrophilic reagents on this compound was undertaken.



I II III

The sulfonation of aromatic nuclei by fuming sulfuric acid is established as an electrophilic substitution.[9] When the conditions necessary for the sulfonation of pyridine-N-oxide were investigated, it was found that pyridine-N-oxide gave 3-pyridine-N-oxidesulfonic acid when treated with 20% fuming sulfuric acid in the presence of mercuric sulfate at 220–240°.[10] The structure of the product was determined by reducing it to 3-pyridinesulfonic acid and comparing this material with an authentic sample prepared by the sulfonation of pyridine. When the sulfonation was attempted at a temperature of 150° using the same reactants, no sulfonated product was isolated and 60% of the pyridine-N-oxide was recovered as the picrate. When the reaction was carried out at 220–240° in the absence of the mercuric sulfate, no sulfonated product was obtained. The conditions under which the sulfonation of pyridine-N-oxide was successful were the same as those necessary for the sulfonation of pyridine[11] and in both cases the 3-substituted derivative was obtained.

The action of several other electrophilic reagents on pyridine-N-oxide or on a suitably substituted pyridine-N-oxide was investigated, but in every case under the conditions employed no substituted product was isolated. Thus after treatment of pyridine-N-oxide with bromine at 110° in the presence of iron powder, the starting material was recovered as the picrate and no substitution product was isolated. Chlorosulfonation at 100° also failed to give a substituted product and 90% of the starting material was recovered as the picrate. The treatment of 3-methoxypyridine-N-oxide with *p*-nitrobenzoyl chloride and anhydrous aluminum chloride in refluxing carbon disulfide or in nitrobenzene at 90° was unsuccessful. Previous experiments[12] had shown that pyridine-N-oxide failed to undergo substitution with benzoyl chloride and aluminum chloride in nitrobenzene solvent at 190°; 75% of the pyridine-N-oxide was recovered as the picrate. Treatment of 3-hydroxypyridine-N-oxide with diazotized picramide failed to give a coupling product.

The results of these experiments seem to indicate that with the exception of nitration, pyridine-N-oxide is as resistant to electrophilic substitution as pyridine itself. The relative inertness of pyridine-N-oxide to electrophilic substitution is to be expected since the compound is basic and must exist

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[1] Abstracted from the M.S. Thesis of Frank J. Welch, Stanford University, 1952.

[2] F. Friedl, *Ber.*, **45**, 428 (1912).

[3] A. Kirpal and E. Reiter, *ibid.*, **58**, 699 (1925).

[4] E. Ochiai and M. Ishikawa, *Proc. Imp. Acad.* (*Tokyo*), **18**, 561 (1942).

[5] E. Ochiai, *J. Org. Chem.*, **18**, 534 (1953).

[6] H. J. Den Hertog and J. Overhoff, *Rec. trav. chim.*, **69**, 468 (1950).

[7] E. P. Linton, THIS JOURNAL, **62**, 1945 (1940).

[8] Substitution does occur with sulfuryl chloride, but this presumably is not a simple electrophilic substitution reaction (B. Bobranski, L. Kochanska and A. Kowalewska, *Ber.*, **71**, 2385 (1938)). Since this investigation was completed, the mercuration of pyridine N-oxide in the 4-position has been reported by T. Ukai, Y. Yamamoto and S. Hirano, *J. Pharm. Soc. Japan*, **73**, 821 (1953); *C. A.*, **48**, 9946 (1954).

[9] C. M. Suter and A. W. Weston, "Organic Reactions," Vol. III, 1946, p. 142.

[10] Dr. T. Cislak in a private communication has reported that similar results have been obtained in the laboratories of Reilly Tar and Chemical Co.

[11] S. M. McElvain and M. A. Goese, THIS JOURNAL, **65**, 2233 (1943).

[12] These experiments were performed by Mr. Allen Carlsmith.

in acid solution in the form of a positive ion, III, similar to that found in the case of pyridine.

Experimental

The Sulfonation of Pyridine-N-oxide.—A mixture of 20 g. of fuming sulfuric acid (20%), 2 g. of pyridine-N-oxide[13] and 0.2 g. of mercuric sulfate was heated at 220–240° for 22 hours. The reaction mixture was poured into 20 ml. of water and neutralized with a hot saturated solution of barium hydroxide and finally with powdered barium carbonate. The mixture was cooled and filtered through Celite and the filtrate was treated with Norit and evaporated to a volume of 50 ml. The Norit was removed and the filtrate was evaporated to dryness leaving a solid residue. The residue was stirred with 10 ml. of ethanol, cooled overnight and filtered giving 3.5 g. of a white crystalline solid. The salt was dissolved in a minimum of water, the barium was precipitated with an equivalent amount of sulfuric acid and the mixture was filtered. Evaporation of the filtrate left 1.9 g. (51%) of solid which on recrystallization from methanol melted at 237–238°. The ammonium salt melted 261–263°.

Anal. Calcd. for $C_5H_5NO_4S$: C, 34.28; H, 2.88; equiv. wt., 175. Found: C, 34.35, 34.48; H, 2.90, 3.02; equiv. wt., 176.

A mixture of 12 g. of fuming sulfuric acid (20%) and 2 g. of pyridine-N-oxide was heated at 220–240° for 24 hours in the absence of mercuric sulfate. Upon working up the mixture as described above, an oil was obtained from the neutral solution which gave a picrate, m.p. 178–181°, which represented a 90% recovery of the pyridine-N-oxide.

A mixture of 40 g. of fuming sulfuric acid (20%), 10 g. of pyridine-N-oxide and 0.3 g. of mercuric sulfate was heated at 150–170° for 18 hours. After working up the mixture as described, an oil, 7.3 g., was obtained which gave the picrate of pyridine-N-oxide, m.p. 178–180°.

The Reduction of 3-Pyridine-N-oxidesulfonic Acid.—A solution of 3.5 g. of 3-pyridine-N-oxidesulfonic acid, prepared by the sulfonation of pyridine-N-oxide, in 200 ml. of 95% ethanol was treated with hydrogen at 60–70° in the presence of Raney nickel at three atmospheres pressure. The theoretical pressure drop was observed after one hour. The hot mixture was filtered and the filtrate was evaporated to dryness leaving 2.2 g. of pale green solid. The residue was dissolved in water and the solution was made basic with a saturated solution of barium hydroxide. The mixture was filtered and the barium was precipitated from the filtrate with an equivalent quantity of sulfuric acid. The mixture was filtered and the filtrate was evaporated to a volume of 5 ml. and cooled. The crystals which separated were removed, m.p. 338–339°; mixture melting point with a sample of 3-pyridinesulfonic acid, m.p. 330–334°, prepared by the sulfonation of pyridine[10] was 332–336°.

Anal. Calcd. for $C_5H_5NO_3S$: equiv. wt., 159. Found: equiv. wt., 160.

The ammonium salt was prepared from the reduction product, m.p. 217–233° dec. An authentic sample of ammonium 3-pyridinesulfonate melted at 217–233° dec. either alone or when mixed with the above sample.

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[13] H. S. Mosher, L. Turner and A. Carlsmith, *Org. Syntheses*, **33**, 79 (1953).

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2,2,2-Trifluoroethylnitroguanidine[1]

BY VIRGIL MILANI, SOL SKOLNIK AND ROBERT EVANS

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2,2,2-Trifluoroethylnitroguanidine has been obtained by the amination of N-nitro-S-methylpseudothiourea[2] with 2,2,2-trifluoroethylamine. This compound was used as an intermediate in the preparation of the picrate and nitrate salts of 2,2,2-trifluoroethylguanidine.

Experimental[3]

2,2,2-Trifluoroethylnitroguanidine.—To 10.1 g. (0.0747 mole) of N-nitro-S-methylpseudothiourea was added 15.0 g. (0.151 mole) of 2,2,2-trifluoroethylamine diluted with 1.0 g. of water. The mixture was heated at the reflux temperature for six hours, 2.2 g. (0.022 mole) of the amine added and then refluxed for an additional seven hours. The water and excess amine were removed under a vacuum and the residual crystalline material recrystallized from 90 ml. of hot water adjusted to a *p*H of 6 with sulfuric acid. The product was recovered in 94% yield based on the N-nitro-S-methylpseudothiourea and melted at 147–148°.

Anal. Calcd. for $C_3H_5O_2N_4F_3$: N, 30.1; F, 30.62; NO_2-N, 7.52. Found: N, 29.75; F, 30.51; NO_2-N, 7.45.

2,2,2-Trifluoroethylguanidine Picrate.—A mixture of 2.5 g. (0.0134 mole) of 2,2,2-trifluoroethylnitroguanidine, 0.125 g. of palladium black and 62 ml. of 15% acetic acid was placed in a modified Skita[4] hydrogenation apparatus and subjected to hydrogenolysis[5] overnight at slightly above atmospheric pressure and room temperature. The palladium black was removed and the filtrate treated with 3.07 g. (0.0134 mole) of picric acid in 25 ml. of hot absolute ethanol. The solution was allowed to crystallize overnight at room temperature. The yellow needle-like crystals began decomposing at 183° and were completely liquid at 193°.

Anal. Calcd. for $C_9H_9O_7N_6F_3$: N, 22.70; F, 15.40. Found: N, 22.7; F, 15.32.

2,2,2-Trifluoroethylguanidine Nitrate.—The picrate of 2,2,2-trifluoroethylguanidine (2.0 g., 0.0054 mole) was treated with 10 ml. of 20% nitric acid, the precipitated picric acid removed, and the filtrate extracted with ether until colorless. The remaining aqueous solution was evaporated to dryness, the residue dissolved in ethanol, and ether added until the crystalline precipitate of 2,2,2-trifluoroethylguanidine nitrate appeared. The nitrate salt melted at 134–136°.

Anal. Calcd. for $C_3H_7O_3N_4F_3$: N, 27.45; F, 27.94. Found: N, 27.40; F, 27.85.

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[1] Publication approved by the Bureau of Ordnance, Navy Department. The conclusions and opinions are those of the authors and are not to be construed as representing an official statement of the Navy Department.

[2] L. Fishbein and J. A. Gallaghan, THIS JOURNAL, **76**, 1877 (1954).

[3] All melting points were measured on a Kofler micro hot-stage.

[4] A. Skita and W. A. Meyer, *Ber.*, **45**, 3589 (1912).

[5] Procedure of Dr. J. A. Gallaghan of this Laboratory.

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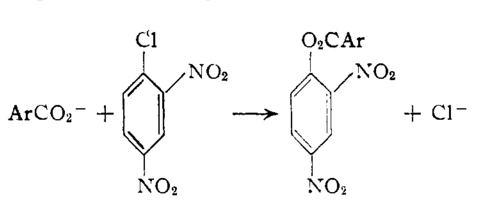
Substituent Effects on the Reactions of Benzoate Ions with 2,4-Dinitrochlorobenzene and Methyl Iodide

BY LAWRENCE R. PARKS, GEORGE S. HAMMOND AND M. FREDERICK HAWTHORNE

RECEIVED DECEMBER 6, 1954

In a continuation of our studies designed to cast light upon the transition state configurations[1] involved in aromatic nucleophilic displacements we have investigated the effects of substituents on the nucleophilic reactivity of benzoate ions in reaction 1.



(1)

As is indicated by the data in Table I, the rates of reaction of benzoate, *p*-methoxybenzoate and *p*-

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[1] For general discussion and references see G. S. Hammond and L. R. Parks, THIS JOURNAL, **77**, 340 (1955).