[CONTRIBUTION NO. 2084 FROM THE KODAK RESEARCH LABORATORIES]

The Hydrogenation of Nitrophthalic Acids

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Received April 20, 1960

Aminophthalic acids can be prepared by catalytic hydrogenation of the disodium salts of 3- and 4-nitrophthalic acids in water. Certain amino and nitro aromatic carboxylic acids function as accelerators in the hydrogenation of otherwise unreceptive nitro acids. The corresponding isomeric azidophthalic acids are described.

Chemical reduction of 3- and 4-nitrophthalic acids to aminophthalic acid using stannous chloride,[1] tin-acid,[2] or zinc-acid[3] gives as products metal double salts or materials which are difficult to separate from metal residues. The 4-isomer gives particularly poor yields because of its high solubility and the ensuing problems of isolating either the amine or its hydrochloride. Hydrogenation of nitrophthalic anhydride[4] in acetone or ester[5] in alcohol has given good yields, but hydrogenation of the free acids in alcohol gives a large quantity of unidentified by-products.[5b,6]

In the present investigation, both 3- and 4-nitrophthalic acids have been converted to the corresponding amines in essentially quantitative yields by hydrogenation of the disodium salts in water solution. With Raney nickel catalyst, hydrogenation at moderate pressure was complete in about fifteen minutes at 70°. Low-pressure reduction on the Parr apparatus required several hours. After removal of the catalyst and acidification, the colorless, amino acid solution was used directly for a subsequent diazotization reaction. The amine could be isolated as the hydrochloride if desired.

The yields were estimated by diazotization and conversion to the azide which precipitated as crystalline material. Inasmuch as the diazotization always consumed the calculated amount of sodium nitrite, the small loss in yield probably occurred in the formation and recovery of the azide.

In the low-pressure hydrogenation of the nitrophthalic acids over platinum, the hydrogen pressure (range, 3–1.5 atmospheres) fell at a constant rate during the course of the reduction. When the theoretical amount of hydrogen had been consumed, the pressure remained constant. This signifies a zero-order reaction with respect to both hydrogen and nitro compound. This conclusion is valid only if equilibrium conditions exist at the catalyst.[7] No experiments were made to verify this. Furthermore, there may have been an autocatalytic or accelerator effect of the product, as was noted for the moderate-pressure hydrogenation of 4-nitrophthalic acid using Raney nickel. The moderate-pressure hydrogenations over nickel proceeded so rapidly that rate observations were not feasible. Raney nickel would not catalyze the reduction at low pressure.

Though both 3- and 4-nitrophthalic acids could be reduced with platinum at low pressure, only the 3-isomer would reduce with Raney nickel at moderate pressure. The 4-nitrophthalic acid was recovered unchanged in repeated attempts. However, if a small amount of the 3-isomer was added to the nitrophthalate salt solution, hydrogenation occurred at a rate comparable to that of the pure 3-isomer. Further examination revealed that a number of nitro and amino aromatic carboxylic acids would promote the hydrogenation of 4-nitrophthalic acid with Raney nickel. The results of hydrogenation at 1500 p.s.i. at 70° of 0.1 mole of 4-nitrophthalic acid with 5 mole % of the indicated accelerator and the time (in minutes) required for complete reduction are: 3-nitrophthalic acid, 15; 3-aminophthalic acid, 15; 4-aminophthalic acid, 60; *o*-nitrobenzoic acid, no reduction; anthranilic acid, 75; *m*-nitrobenzoic acid, no reduction; *m*-aminobenzoic acid, 35; *p*-nitrobenzoic acid, 45; *p*-aminobenzoic acid, 45; and aniline, no reduction. About 2 g. of commercially prepared Raney nickel was used. No perceptible pressure drop after three hours was considered as no reduction. The times given here for complete reduction should be considered as only gross approximations because of the difficulty of controlling the temperature and the amount of effective catalyst present.

The conclusion is drawn from these results that the amino compounds are actually the accelerators. Nitro compounds are first reduced; the amines then serve as accelerators. If this is true, *o*- and *m*-nitrobenzoic acids by themselves should not be reduced under these conditions, for they do not

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[1] (1a) M. T. Bogert and F. L. Jouard, *J. Am. Chem. Soc.*, **31**, 485 (1909); (b) M. T. Bogert and R. R. Renshaw, *J. Am. Chem. Soc.*, **30**, 1135 (1908); (c) W. A. Lawrance, *J. Am. Chem. Soc.*, **42**, 1871 (1920).

[2] (2a) J. G. F. Druce, *Chemical News*, **119**, 74 (1919); (b) C. S. Hamilton and R. Frazier, *J. Am. Chem. Soc.*, **48**, 2415 (1926).

[3] (3a) A. Bernthsen and A. Semper, *Ber.*, **19**, 164 (1886); (b) J. Kenner and A. M. Mathews, *J. Chem. Soc.*, **105**, 2471 (1914).

[4] (4) E. L. Eliel, A. W. Burgstahler, D. E. Rivard, and L. Haefele, *J. Am. Chem. Soc.*, **77**, 5092 (1955).

[5] (5a) F. F. Blicke and F. D. Smith, *J. Am. Chem. Soc.*, **51**, 1865 (1929); (b) D. Twiss and R. V. Heinzelmann, *J. Org. Chem.*, **15**, 496 (1950); (c) O. Exner and M. Protiva, *Chem. listy*, **48**, 1550 (1954)(*Chem. Abstr.*, **49**, 11569[b]).

[6] (6) O. Gisvold, *J. Am. Pharm. Assoc.*, **31**, 202 (1942).

[7] (7) H. A. Smith in *Catalysis*, Vol. V, Reinhold Publishing Corp., New York, N. Y., 1957, p. 181.

serve as accelerators, while the corresponding amino acids do. Actually, both of these nitro acids do reduce slowly, requiring three hours for complete reduction. But the addition of 5% *p*-isomer to each of them diminished the time required for reduction of *o*-nitrobenzoic acid to 45 min., and to 90 min. for *m*-nitrobenzoic acid. Thus, the *p*-isomer is capable of promoting the reduction of *o*- and *m*-nitrobenzoic acids, and as an impurity, it may account for the three-hour reduction of these two acids. When these two nitrobenzoic acids were tried as accelerators for the 4-nitrophthalic acid in the amount of 5 mole %, no reduction occurred because the amount, if any, of the *p*-nitrobenzoic acid present as impurity was too small to have a detectable effect.

Infrared spectroscopy of the original *o*-nitrobenzoic acid sample revealed a shoulder at 13.9 μ, probably indicative of *p*-isomer present to the extent of 1.5% maximum. From the spectrum of the *m*-nitrobenzoic acid, no conclusion could be drawn as to the presence of *p*-isomer. More exact interpretation of these spectra was difficult, owing to the lack of isomer samples of known purity.

EXPERIMENTAL

The organic acids were Eastman White Label grade. Melting points are corrected.

3-Aminophthalic acid hydrochloride. a. *By hydrogenation over platinum oxide.* In a solution of 8.2 g. (0.205 mole) of sodium hydroxide in 75 ml. of water was dissolved 21.0 g. (0.100 mole) of 3-nitrophthalic acid. The *p*H of the mixture was adjusted to 8–9 with dilute acetic acid. Reduction on the Parr low-pressure hydrogenation apparatus with 0.1 g. of platinum oxide at 3 atm. initial pressure required 4 hr. at 45°. The pressure fell at a constant rate during that period. The clear, colorless solution which remained after filtration to remove the catalyst was treated with 50 ml. of concd. hydrochloric acid, with cooling to avoid decarboxylation. This precipitated the amine hydrochloride in high purity. However, it was not isolated; the suspension was used for the diazotization which followed.

b. *By hydrogenation over Raney nickel.* A solution of 0.1 mole of disodium 3-nitrophthalate at *p*H 8–9 was prepared as just described. It was hydrogenated in a 300-ml. bomb at about 100 atm. with 2 g. of commercially prepared Raney nickel.[8] The reduction required about 15 min. at 70°. The product was handled as before.

3-Azidophthalic acid. The amine hydrochloride from either of these preparations was diazotized with a 25% solution of the calculated amount of sodium nitrite (6.9 g.) and converted to the azide by the addition in portions of an excess of 20% sodium azide solution, the temperature being kept below 15°. Cooling for several hours completed the crystallization of 19 g. (95%) of the product which melted, with decomposition, at 167–169°. A sample recrystallized from ethanol-water melted, with decomposition, at 171°.

Anal. Calcd. for $C_8H_5O_4N_3$: C, 46.3; H, 2.4; N, 20.3. Found: C, 46.2: H, 2.6; N, 20.6.

4-Aminophthalic acid hydrochloride. The sodium salt of 4-nitrophthalic acid was hydrogenated with platinum oxide at 3 atm., as described for the 3-isomer.

4-Azidophthalic acid. Conversion of the amine to the azide was accomplished as before in an over-all yield of 88%. The lower yield was probably due to the greater solubility in water of this azide isomer. Recrystallization from water gave a product which melted, with decomposition, at 170–171°.

Anal. Found: C, 46.8; H, 3.0; N, 20.6.

Hydrogenation of 4-nitrophthalic acid at 100 atmospheres with Raney nickel to evaluate accelerators. The acids which were tested for their ability to promote hydrogenation were added with the 4-nitrophthalic acid in the amount equal to 5 mole % of the latter to the sodium hydroxide solution, and the *p*H was adjusted to 8–9. When aniline was used, it was charged directly into the bomb with the nitrophthalate solution. The proper drop in hydrogen pressure was taken as an indication of reduction to amine.

Acknowledgment. The author wishes to express his debt to Mr. J. F. Stenberg, for performing many of the hydrogenations; and to Miss T. J. Davis, for interpretation of spectrograms.

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[8] No. 28 Active Raney Catalyst in water. Raney Catalyst Co., Chattanooga, Tenn.