

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, PURDUE UNIVERSITY]

The Alkaline Reduction of Aromatic Nitro Compounds with Glucose¹

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The conditions affecting the reduction of aromatic nitro compounds to azoxy compounds with glucose and alkali have been studied and a procedure evolved which has been applied to a variety of nitro compounds. Twenty-two compounds have been successfully reduced with conversions ranging from 40 to 100%. Fifteen nitro compounds were tested which could not be reduced under the conditions employed. Conspicuous in this class are ortho- and para-nitroanilines and their substitution products, although the meta-nitroanilines reduce smoothly. The sugar acids formed by the breakdown of glucose are probably largely of the saccharinic type, but have not been definitely identified.

The fact that aromatic nitro compounds may be reduced by glucose in alkaline solution was apparently first discovered in 1865 by Braun,² who found that on heating an alkaline glucose solution with picric acid a red color developed, which he believed was due to the formation of picramic acid. Since that time the reaction has been occasionally employed in the reduction of aromatic nitro compounds to yield azoxy compounds although azo compounds have been reported in a few cases and both the isolation of hydrazo and hydroxylamine compounds have been recorded. Thus, Wacker³ was able to reduce 1-nitronaphthalene-5-sulfonic acid and 1-nitronaphthalene-3,5-disulfonic acid to the corresponding azoxy compounds and 1-nitroanthraquinone-2-sulfonic acid to 1-hydroxylaminoanthraquinone-2-sulfonic acid.⁴

Sawdust⁵ and molasses⁶ in strong sodium hydroxide solution with heat and pressure have been used to reduce nitrobenzene to azoxybenzene, but glucose is usually the carbohydrate employed. Jansen⁷ was able to convert 2-amino-4-nitrotoluene to 3,3'-diamino-4,4'-dimethylazoxybenzene with glucose and alkali, and Bacharach and Weinstein⁸ successfully reduced *p*-nitrobenzoic acid to the azoxydicarboxylic acid. A series^{9,10,11} of studies at Fordham University on the reduction of nitrobenzene with glucose and sodium hydroxide culminated in a paper by Opolonick¹² which contains the only detailed study which has been made of the reaction.

In our studies we have been interested in testing the applicability of the glucose-alkali reducing mixture with a wide variety of aromatic nitro compounds and in studying the effects of substituents upon the aromatic ring. We have limited the investigation to the preparation of azoxy compounds, since these compounds show a remarkable stability in alkali and the glucose-alkali combination has been so little studied in their preparation that Bigelow¹³ in his review of azoxy compounds

does not even list the use of glucose as a means of preparation.

The work of Opolonick¹² was taken as the starting point as it offered the most complete investigation of the conversion of nitrobenzene to azoxybenzene with glucose and alkali. By a study of the variables involved, however, we were able to reduce the reaction time from 3 hours to approximately 30 minutes while maintaining the same yield (80-85%).

In general, the results of our studies have indicated that most simple aromatic nitro compounds, such as the nitrotoluenes, can be reduced quickly and easily to the corresponding azoxy compounds in good yield. 1-Nitronaphthalene, however, was not reduced. In this we confirm the results of Wacker.³ Contrary to the findings of Landau¹⁰ who obtained a 90% yield of 3,3'-dinitroazoxybenzene from *m*-dinitrobenzene, we were unable to convert either *m*-dinitrobenzene or 3,5-dinitrobenzoic acid to an azoxy compound, in spite of the fact that the *o*-, *m*- and *p*-nitrobenzoic acids were reduced in high yield.

No difficulty was experienced in reducing the nitroaryl halides, 3-nitrophthalic acid, or various nitrosulfonic acids, although the purification of the latter compounds was difficult. A surprising finding was the fact that while *m*-nitroaniline and substituted *m*-nitroanilines reduced smoothly, in only one case could a clean-cut reduction be found when a compound contained an amino group ortho or para to a nitro group. Five compounds of this type were tested with negative results. The sole exception occurred with sodium 3-nitro-6-aminobenzenesulfonate. The negative results in these cases might be due to the activating influence of the nitro group on the ortho and para positions, causing hydrolysis of the amino group.

Nitroketones and nitroethers, as exemplified by *m*-nitroacetophenone and the *o*- and *p*-anisoles, respectively, gave good yields of the corresponding azoxy compounds while a series of three nitroazo compounds failed to yield any recognizable product. *p*-Nitrosodimethylaniline and two nitrophenylhydrazines also gave negative results.

A series of studies on the variables affecting the reduction of *p*-nitrotoluene were made and provided the basis for determining the conditions under which the various other nitro compounds were reduced.

A few studies have been made on replacing sodium hydroxide with sodium ethoxide, but as no particular advantages were found, the sodium ethoxide was abandoned. Likewise, it was found feasible to reduce nitrobenzene with sucrose and

(1) Abstracted from a thesis by Harry W. Galbraith, submitted to the Faculty of the Graduate School of Purdue University in partial fulfillment of the requirements for the degree of Doctor of Philosophy, June, 1949.

(2) Braun, *Z. anal. Chem.*, **4**, 185 (1865).

(3) Wacker, *Ann.*, **321**, 61 (1902).

(4) Wacker, *Ber.*, **35**, 667 (1902).

(5) Griesheim, German Patent 225,245 (April 24, 1908).

(6) Griesheim, German Patent 228,722 (May 1, 1908).

(7) Jansen, *Z. Farbenind.*, **12**, 181 (1913).

(8) Bacharach and Weinstein, *Rec. trav. chim.*, **54**, 933 (1935).

(9) Hynes, Ph.D. Thesis, Fordham University, June, 1927.

(10) Landau, Ph.D. Thesis, Fordham University, March, 1929.

(11) Weber, Ph.D. Thesis, Fordham University, April, 1930.

(12) Opolonick, *Ind. Eng. Chem.*, **27**, 1045 (1935).

(13) Bigelow, *Chem. Revs.*, **9**, 147 (1931).

TABLE I
 NITRO COMPOUNDS SUCCESSFULLY REDUCED TO AZOXY COMPOUNDS

Nitro compound	Conversion, %	M.p., °C.	Formula of azoxy compound	Nitrogen, %	
				Calcd.	Found
<i>p</i> -Nitrotoluene	83	69-70	C ₁₄ H ₁₄ ON ₂	12.38	12.27
<i>o</i> -Nitrotoluene	44	58-59	C ₁₄ H ₁₄ ON ₂	12.38	12.30
<i>m</i> -Nitrotoluene	61	Oil	C ₁₄ H ₁₄ ON ₂	12.38	12.43
Nitrobenzene	83	35-35.5	C ₁₄ H ₁₀ ON ₂	14.14	14.16
<i>o</i> -Chloronitrobenzene	65	54-55	C ₁₂ H ₉ ON ₂ Cl ₂	10.48	10.58
<i>p</i> -Chloronitrobenzene	93	154-155	C ₁₂ H ₉ ON ₂ Cl ₂	10.48	10.38
2-Nitro-4-chlorotoluene	71 ^d	126-127	C ₁₄ H ₁₂ ON ₂ Cl ₂	9.50	9.57
<i>p</i> -Nitrobenzoic acid	91 ^e	Dec. 240	C ₁₄ H ₁₀ O ₃ N ₂	9.78	9.88
<i>m</i> -Nitrobenzoic acid	84 ^e	Dec. 320	C ₁₄ H ₁₀ O ₃ N ₂	9.78	9.80
<i>o</i> -Nitrobenzoic acid	100	Dec. 248	C ₁₄ H ₁₀ O ₃ N ₂	9.78	9.70
3-Naphthalic acid	68 ^f	360	C ₁₈ H ₁₀ O ₃ N ₂ ^e	7.48	7.59
<i>m</i> -Nitrobenzene sulfonic acid	78	^a	C ₁₂ H ₉ O ₇ N ₂ S ₂ Na ₂	6.96	6.62
3-Nitro-4-bromobenzenesulfonic acid	71 ^g	360	C ₁₂ H ₈ O ₇ N ₂ Br ₂ S ₂	5.42	5.63
3-Chloro-5-nitrobenzenesulfonic acid	62 ^g	^a	C ₁₂ H ₈ O ₇ N ₂ S ₂ Cl ₂ Na ₂ ^e	5.94	5.80
Sodium 3-nitro-6-aminobenzenesulfonate	90 ^h	^b	C ₁₂ H ₁₄ O ₇ N ₄ S ₂ Cl ₂ ^e	12.13	12.30
<i>m</i> -Nitroaniline	70	146-148	C ₁₂ H ₁₂ ON ₄	24.55	24.50
4-Nitro-2-aminotoluene	79 ^e	155-155.5	C ₁₄ H ₁₆ ON ₄	21.84	21.62
<i>o</i> -Nitroanisole	69	80-81	C ₁₄ H ₁₆ ON ₄	10.84	10.62
<i>p</i> -Nitroanisole	64 ⁱ	Melts 118, clears 135	C ₁₄ H ₁₄ O ₃ N ₂	10.84	10.66
<i>m</i> -Nitroacetophenone	81 ^j	131-131.5	C ₁₆ H ₁₄ O ₃ N ₂	9.94	10.01
6-Nitroquinoline	40 ^{e,k}	260-262	C ₁₈ H ₁₂ ON ₄ ^e	18.68	18.78
<i>o</i> -Nitrophenol	87	153-154	C ₁₂ H ₁₀ O ₃ N ₂	12.18	12.32

^a Sodium salt. ^b Dihydrochloride. ^c New compound. ^d Glucose to ArNO₂ ratio of 3:2. ^e Twenty per cent. sodium hydroxide. ^f Glucose to ArNO₂ ratio of 3:1. ^g Glucose to ArNO₂ ratio of 2:1. ^h Sixty per cent. sodium hydroxide. ⁱ 50%. ^j Ten per cent. sodium hydroxide. ^k 90%.

sodium hydroxide, but only with high temperatures and a long reaction time.

The fate of the glucose consumed in the reaction was investigated briefly. It was found that a little more than two equivalents of organic acids was formed per mole of glucose destroyed. About 17% of these acids were volatile, presumably acetic acid since formic acid was absent. Among the remainder, a little lactic acid and a trace of oxalic was found but the bulk of the acids were not identified although it was demonstrated that gluconic, glucuronic, saccharic, 5-ketogluconic and tartaric acids were apparently absent. The unidentified acids were probably of the saccharinic type.

Experimental

In a preliminary survey, some of the variables affecting the reduction of *p*-nitrotoluene were studied. The variables examined were temperature, time, concentration of reactants (separately and collectively), the rate of stirring and the effect of emulsifying agents. A set of standard conditions were set up as follows:

A mixture of 100 ml. of 30% sodium hydroxide and 23 g. (0.167 mole) of *p*-nitrotoluene is heated to 80° in a 500-ml. three-necked flask with stirring and 23 g. (0.128 mole) of glucose added at a rate sufficient to maintain the temperature. After addition of all the sugar (usually 30 minutes), the mixture is steam distilled to remove any unreacted nitrotoluene and the residue chilled. The *p*-azoxytoluene is filtered off, washed with water, air-dried and weighed. These preliminary experiments indicate that: (1) The temperature of the reaction is not of critical importance between 70 and 100°. (2) Prolonging the reaction beyond 35 minutes had no effect on the yield, which dropped with shorter reaction times. (3) Twenty per cent. sodium hy-

droxide appeared to be the optimum concentration. The conversions drop off slightly with higher concentrations of base and fall rapidly with less than thirteen per cent. sodium hydroxide. (4) Under the conditions studied, increasing the concentration of the glucose increases the conversion up to the point where 1.5 moles of glucose were used per mole of nitrotoluene. (5) Within the range of 100 to 500 ml. the concentration had little effect on the conversion. (6) The importance of adequate mixing is shown by a linear relationship between the rate of stirring and the conversion. (7) As might be expected from 6, emulsifying agents increase the conversion for a given rate of stirring.

These results were used as guides to indicate the probable effects of variations in the basic procedure as applied to various nitro compounds. The procedure used is to heat one-tenth mole of the nitro compound with one-half ml. of Tergitol 08 detergent in 100 ml. of 30% sodium hydroxide solution to 60°. One-tenth mole of glucose is added with vigorous stirring (1,000 r.p.m.) at a rate sufficient to maintain the temperature at 60°, which takes about 30 minutes. The reaction mixture is worked up in a way appropriate for the azoxy compound being prepared, usually by chilling and filtering off the crude azoxy compound which is then purified by recrystallization. In cases where the compound contained acidic groups, it is of course necessary to acidify the alkaline solution to obtain precipitation. For some of the compounds studied, it is necessary to alter some of the conditions to obtain satisfactory yields. The results of successful reductions are shown in Table I, while the nitro compounds whose attempted reduction was unsuccessful include: α -nitronaphthalene, *m*-dinitrobenzene, 3,5-dinitrobenzoic acid, *p*-nitroaniline, *o*-nitroaniline, 2-nitro-4-methylaniline, 2-methyl-4-nitroaniline, 2-nitro-4-chloroaniline, 2-chloro-4-nitroaniline, *p*-nitrosodimethylaniline, *p*-nitrophenylhydrazine, 3,5-dinitrophenylhydrazine, 2-(2-nitrophenylazo)-2-nitropropane, 2-(2-nitro-4-methylphenylazo)-2-nitropropane and *p*-nitrobenzeneazoresorcinol.

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