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## THE HYDROXYLATION OF AROMATIC NITRO COMPOUNDS BY ALKALIES

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The oldest work of this kind (Dusart 1855) reported the formation of 4-nitro-1-naphthol from 1-nitronaphthalene by 6 hours heating with potassium hydroxide and calcium hydroxide below 100°. Merz and Coray (1871) noted a vigorous reaction when nitrobenzene was heated with solid potassium hydroxide, but Wohl (1899) first studied the products of this interaction. Whether the reaction occurs at room temperature or at 60-70°, the main product is *o*-nitrophenol in 33 to 50 percent yield, based on the amount of nitrobenzene used up; *p*-nitrophenol is formed only in traces. The reaction (hereinafter called the Wohl reaction) does not involve oxygen from the air, for it proceeds in a stream of inert gas or in solution in ligroin or other organic solvent. Lepsius (1899), without giving any experimental evidence, suggested the mechanism  $5C_6H_5NO_2 + 3KOH \rightarrow 3C_6H_4(NO_2)OK + C_6H_5N(O)NC_6H_5 + 3H_2O$  but Wohl was unable to detect any azoxybenzene or other reduction product of nitrobenzene. Later Wohl (1901) converted *m*-dinitrobenzene to 2,4-dinitrophenol, 1-nitronaphthalene to 1-nitro-2-naphthol, *m*-nitrochlorobenzene to 2-chloro-6-nitrophenol, and *m*-nitrotoluene to 3-nitro-2-hydroxytoluene. These reactions could be produced with solid sodium hydroxide, which did not affect nitrobenzene itself. Lewis and Thiessen (1924) proved that the hydroxylation of nitrobenzene does not involve hydrolysis, by obtaining a negative test for nitrites and nitrates in the used alkali.

Hepp (1880) had previously shown that the presence of an oxidizing agent facilitates the Wohl reaction; in boiling alkaline solutions potassium ferricyanide changes *m*-dinitrobenzene to 2,4- and 2,6-dinitrophenols, and *sym*-trinitrobenzene to picric acid.

Colbert, Meigs, and Jenkins (1937) used the Wohl reaction to prepare 4-nitro-3-hydroxybiphenyl from *p*-nitrobiphenyl; they also obtained a nitrophenol from *o*-nitrobiphenyl.

Reactions similar to the Wohl reaction, but differing from it in producing *para*-substituted products, are the several aminations of nitrobenzene described by de Montmollin and de Montmollin (1923), Bradley and Robinson (1932), and Bergstrom, Granara, and Erickson (1942).

In work of which the authors learned only after the completion of the present research, Hall (1939) devoted some study to the Wohl reaction.

He found that dryness and fineness of grinding of the alkali was essential. By using a heated steel ball mill with stainless steel balls, the whole arranged so that it could be heated while being rotated, and a large excess of sodium hydroxide, Hall obtained a yield (not deducting recovered nitrobenzene) of 37 per cent of *o*-nitrophenol and a trace of the *para* compound. With barium hydroxide he obtained no isolable products. He also studied the effect of sodium sulfide, sodium phenoxide, and alkali thiophenoxides upon aromatic compounds, chiefly nitrobenzene, but the results were inconclusive.

The reaction of 3,5-dinitrobenzoic acid with strong alkali to produce 2,3-dihydroxy-5-nitrobenzoic acid (Bollinger and Reuter, 1939a) and 3,3'-dinitro-5,5'-dicarboxyazoxybenzene (Shukoff 1895, Bolliger and Reuter 1939b) evidently involves a Wohl reaction and the hydrolytic loss of one nitro group.

The present work is a continuation of Wohl's study, with particular view toward improving the yields; this seemed feasible since more than half of both reagents remained unattacked in his work. To this end a considerable number of variations in procedure was tested, but without conspicuous success. Motor-stirring of powdered potassium hydroxide (25 g) with excess nitrobenzene (50 ml) for various times and at several temperatures showed five hours and 60° to 80° to give the best yield of *o*-nitrophenol (3 g). Stirring in the presence of glass beads, to secure a ball-mill effect, improved the yield to 4 g, evidently by increasing the reacting surface. Chemical purity of the potassium hydroxide had no observable effect, but the presence of more than two percent of water in it lowered the yield markedly. Intensive drying was therefore tried, but neither precautions taken in grinding, nor preliminary fusion of the alkali, nor the addition of barium oxide as a desiccant<sup>1</sup> proved of any advantage. Use of the potassium dioxide, KO<sub>2</sub>, made from 10 g of metallic potassium by burning in air, along with 10 ml of nitrobenzene, produced 2 g of *o*-nitrophenol; this represents the most efficient conversion attained, both reagents considered. The activity of the dioxide is attributed to its ability to remove water by undergoing hydrolysis rather than to its oxidizing power, since sodium peroxide does not improve yields at all, either alone or along with potassium hydroxide.

Wohl (1899) stated that nitrobenzene does not react with sodium hydroxide, but in the work here reported small yields of *o*-nitrophenol (up to 0.5 g) were obtained from 25 g of alkali and 35 ml of nitrobenzene, best at 130°. Although sodium hydroxide and nitrobenzene undergo violent decomposition at 190°, sodium peroxide refluxed with nitrobenzene for a half hour merely produced a small amount (0.5 g) of *o*-nitrophenol. Alkalies that proved completely inactive even in boiling nitrobenzene include barium oxide, barium hydroxide, calcium oxide, calcium hydroxide, silver oxide, potassium carbonate, and sodium carbonate.

Technical xylene or pyridine employed as diluents for the nitrobenzene in the Wohl reaction do not alter the yield. Neither do mercuric or cupric salts, added to the reaction mixture as possible catalysts, nor potassium chlorate, potassium permanganate, potassium ferricyanide, and ferric chloride, all potential oxidizing agents.

To test whether the accumulation of a reduction product of nitrobenzene was preventing further reaction, the used nitrobenzene from a run was stirred with fresh powdered potassium hydroxide. The yield of

<sup>1</sup> Chichibabin (1924, 1930), in the comparable hydroxylation of quinolines with potassium hydroxide, found that barium oxide served as a powerful dehydrating agent. However, the work was carried out at or above 225°.

*o*-nitrophenol was the same as with fresh nitrobenzene, proving the absence of any such effect. Again, if equilibrium were established in the reaction, the initial presence of an excess of potassium *o*-nitrophenoxide should diminish the yield; but no such diminution occurs. The only remaining product is water; and this is now believed to render the potassium hydroxide incapable of further reaction by coating the surface.

Wohl's statement that the hydroxylation proceeds in the absence of air is true, but then the yield is unaccountably only half its usual value. The unreacted steam-distilled nitrobenzene from such runs gives a red color with anhydrous aluminum chloride and benzene (Shriner and Fuson 1940, p. 34) identical with that produced by a known nitrobenzene-azoxybenzene mixture. More convincing proof that azoxybenzene was present was obtained by rearranging it to *p*-hydroxyazobenzene, m.p. 155-156°, with concentrated sulfuric acid (the Wallach (1880) rearrangement). In one run made under natural gas, 25 g of potassium hydroxide and 25 ml of nitrobenzene allowed to stand together for a week produced 1.20 g of *o*-nitrophenol and 0.38 g of *p*-hydroxyazobenzene. This ratio of products indicates that Lepsius' equation is substantially correct; that only about seven-tenths of the calculated amount of *p*-hydroxyazobenzene was obtained may be attributed to air oxidation of the azoxybenzene during its isolation and to the non-quantitative nature of its rearrangement.

No pure products could be isolated when *m*-dinitrobenzene was warmed with alkalis, but it was observed that when the reaction mixture was acidified, oxides of nitrogen were evolved. If *o*- and *p*-dinitrobenzenes were present in the *m*-dinitrobenzene, as they well might be in a product made by nitration, hydrolysis would be expected; but these impurities are not solely responsible for the formation of nitrites, for re-treating the unreacted *m*-dinitrobenzene with alkali gave the same effect. Lobry de Bruyn (1894) reported this hydrolysis of nitrobenzene, but at least one major reference book on organic chemistry (Whitmore 1937, p. 730) states that a nitro group in the meta position does not activate a second nitro group on a benzene ring.

No chemical individuals were obtained by applying the Wohl reaction to *o*- and *p*-nitrotoluenes; the reaction became dangerously violent even without external heating unless a solvent was used. It probably involves the known intramolecular oxidation of the methyl group. In an analogous case Chichibabin (1924) was unable to hydroxylate quinaldine.

When 15 g of 1-nitronaphthalene was stirred mechanically with 25 g of potassium hydroxide and 50 ml of benzene for five hours at 70°, 1 g of 1-nitro-2-naphthol, m.p. 103°, was obtained.

Ten g of 2-nitrobiphenyl was stirred with 100 g of potassium hydroxide and 100 ml of benzene for five hours at 80°. When the benzene layer was discarded and the aqueous one acidified and steam-distilled for a long time, 6 g of a phenol were collected. Isolating it as the potassium salt instead of by distillation (Colbert, Meigs and Jenkins 1937) gave a similar but less pure product. It exhibits a peculiar melting-point behavior; samples crystallized from water are cream-colored, and as soon as dry they melt at about 64-65°. Upon keeping the crystals or warming them in air they rapidly turn bright yellow and the melting point rises to 81-82°; Colbert and Jenkins (1936) found the value 82.6°. If the yellow form is again recrystallized from water, it yields the same low-melting form, whereas recrystallization from alcohol or ligroin gives the yellow form immediately. The latter gives theoretical analytical values for 2-nitro-3-hydroxybiphenyl.

Calcd. for  $C_{12}H_9O_2N$  : N, 6.51. Found : N, 6.41. (Analyses by Kjeldahl method as modified by Eckert 1913).

This suggests that the low-melting form is an unstable hydrate, but it would be difficult to get it pure enough for analysis.

The melting point of the benzoate, made by the Schotten-Baumen method, was 131-132.5°.

*Anal.* Calcd. for  $C_{19}H_{11}O_4N$  : N, 4.39. Found : N, 4.30.

The acetate, made with acetic anhydride, melted at 61.5-62.5°.

*Anal.* Calcd. for  $C_{17}H_{11}O_4N$  : N, 5.44. Found : N, 5.40.

The benzenesulfonate melted at 130-131°.

*Anal.* Calcd. for  $C_{12}H_9O_4NS$  : N, 3.94. Found : N, 3.83. This compound yielded no recognizable aromatic acids when oxidized with either acid or alkaline permanganate or with chromic acid.

The most powerful evidence for assigning the phenol the structure of 2-nitro-3-hydroxybiphenyl is its volatility in steam, plus the fact that upon nitration by the method of Colbert, Meigs and Jenkins (1937) it produced a new compound, m.p. 169-170°, evidently identical with their *x*,4-dinitro-3-hydroxybiphenyl, m.p. 169-171°.

When 14 g of *4-nitrobiphenyl* was heated with 25 g of potassium hydroxide and 25 ml of benzene as usual, 2 g of 4-nitro-3-hydroxybiphenyl resulted, m.p. 103°. The melting point is in agreement with that of the compound prepared by Colbert, Meigs, and Jenkins by essentially the same method.

When *o-nitroanisole* was stirred with potassium hydroxide without diluent for five hours at 80°, a nitrophenol, m.p. 46-47°, was produced. The structure of this compound, believed to be the monomethyl ether of 2-nitroresorcinol, was not proved because the amount available was insufficient.

Five g of *p-nitrophenetole* was stirred with 25 g of pulverized potassium hydroxide and 50 ml of benzene for five hours at 80°. Five-tenths g of a phenol, m.p. 76-77°, was obtained; this is evidently the expected 1-ethyl ether of 4-nitroresorcinol, m.p. 79° (Weselsky and Benedikt 1880).

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