Mechanism for Reaction of *p*-Nitrotoluene with Sodium Polysulfide to Form *p*-Aminobenzaldehyde

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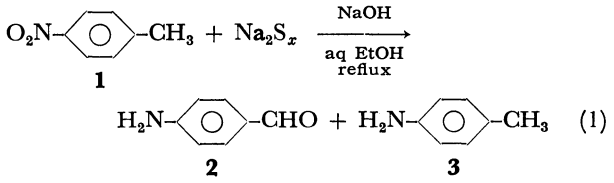
The conversion of *p*-nitrotoluene to *p*-aminobenzaldehyde was found to be most effectively done by a mixture of Na_2S_4 and *ca.* two equivalents of NaOH to *p*-nitrotoluene. After examination of probable intermediates, toluidine, *p*-nitrobenzaldehyde and *p*-nitrosotoluene were discarded as the intermediate. The reaction of carbanion $ArCO\bar{C}HAr$ with the sulfide and the effect of some nitrobenzenes as an electron accepter were examined. These results suggest a mechanism involving a simultaneous oxidation-reduction in a nitrotoluene molecule.

Sulfur frequently shows a unique ability by which the substrate is oxidized at one site but reduced at another site. A typical example is the conversion of *p*-nitrotoluene to *p*-aminobenzaldehyde. In aqueous ethanolic solution of sodium polysulfide, *p*-nitrotoluene is converted to *p*-aminobenzaldehyde. This reaction is known to be the best route for synthesis of *p*-aminobenzaldehyde. But the reaction mechanism is still obscure and unconvincible.[2,3] We wish to clarify it by examining the effects of reaction conditions and substrate structure and by isolating intermediates, since the kinetic study was difficult.

Results and Discussion

Effect of Na_2S_x and NaOH. *p*-Nitrotoluene was allowed to react with polysulfide (Na_2S–Na_2S_5). It was found that Na_2S_4 was the best reagent (Table 1) and that elemental sulfur itself was not always essential for this reaction.



(1)

With 1.9 mol of NaOH for one mol of *p*-nitrotoluene, the highest yield of *p*-aminobenzaldehyde was obtained. If a less amount of NaOH was used, the yield of *p*-toluidine increased, but that of *p*-aminobenzaldehyde decreased remarkably. This may be due to the Eq. 2[4] which consumes NaOH, decreasing the concentration of benzyl anion (Table 2).

Table 1. Yield of products in a reaction of *p*-nitrotoluene (**1**) with Na_2S_x in aqueous ethanol by refluxing for 3 h[a]

Na_2S_x	Yield	
	2 (%)	**3** (%)
$x=1$	6.1	60.1
2	9.3	94.3
3	35.4	21.5
4	43.5	16.4
5	24.4	43.3

a) **1** (0.037 mol), NaOH (0.068 mol).

Table 2. Effect of NaOH on the yields of *p*-aminobenzaldehyde (**2**) and *p*-toluidine (**3**) in the reaction of *p*-nitrotoluene (**1**) with Na_2S_4 in 3 h refluxing

1 (g)	Na_2S_4 (g)	NaOH (g)	**2** (%)	**3** (%)
5.00	3.40	0	0	101.5
5.00	3.40	0.74	6.8	48.1
5.00	3.40	1.37	24.7	35.3
5.00	3.40	2.74	37.4	16.1
5.00	3.40	4.04	34.0	16.6

$$6NaOH + 1/2S_8 \longrightarrow 2Na_2S + Na_2S_2O_3 + 3H_2O \quad (2)$$

Time Conversion. Figure 1 shows the consumption of *p*-nitrotoluene and the yields of *p*-toluidine and *p*-aminobenzaldehyde. The formation of *p*-toluidine stopped after 30 min.

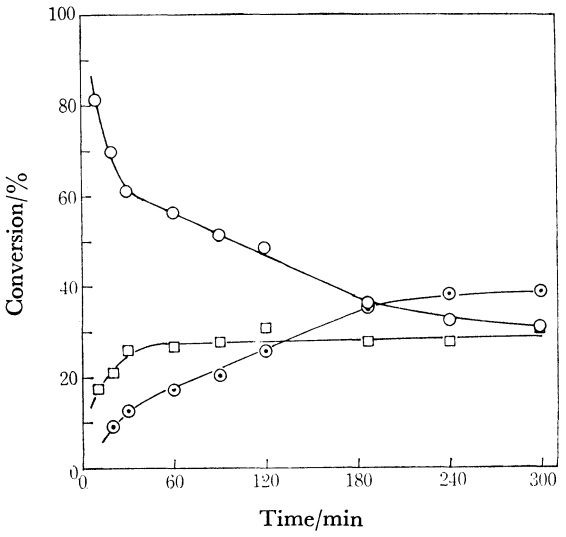
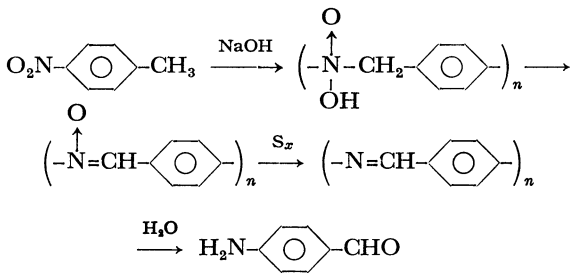


Fig. 1. Reaction of *p*-nitrotoluene with Na_2S_4 in 90% aqueous ethanol at 80 °C. The initial amount of reagents were: *p*-nitrotoluene 0.037 mol; Na_2S_4 3.30 g; NaOH 0.068 mol: (○) *p*-nitrotoluene, (□) *p*-toluidine, (⊙) *p*-aminobenzaldehyde. (*p*-Aminobenzaldehyde was estimated by subtracting the sum of the amount of *p*-nitrotoluene and *p*-toluidine from 0.037 mol.)

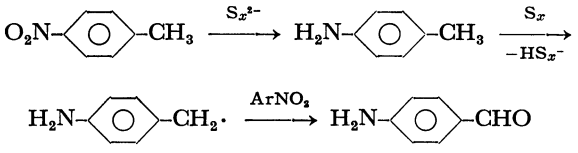
Discussion of Mechanisms. Information thus far obtained suggests several mechanisms which will be discussed below.

(I) Mechanism via *Anthranil Nitrone*: Shchukina *et al.*[3]



Scheme 1.

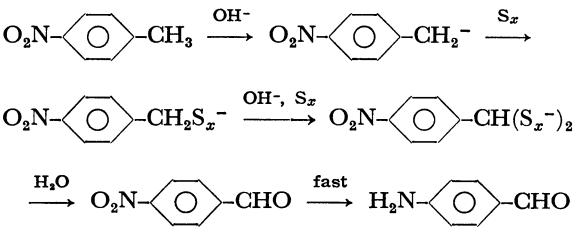
proposed a mechanism involving polynitrone formation (Scheme 1). This mechanism employs sulfur as a reducing agent. So that we replaced sulfur with triphenylphosphine which is known to be a strong reductant for nitrone,[5] but no *p*-aminobenzaldehyde was obtained. Hence this mechanism is of doubt.



Scheme 2.

(II) Mechanism via p-*Toluidine*: Polysulfenyl radicals are electrophilic,[6] and therefore an amino group would increase the rate of attacks of these radicals on the benzylic position, if the oxidation involved hydrogen abstraction by sulfenyl radicals. But the reaction of *p*-toluidine with Na_2S_x gave no *p*-aminobenzaldehyde even in the presence of a strong electron-accepter such as *m*-dinitrobenzene. Hence, this mechanism can also be eliminated.

(III) Mechanism via p-*Nitrobenzaldehyde*: Hodgson *et al.*[2] proposed a mechanism *via p*-nitrobenzaldehyde. Indeed, substitution of electron-attracting *p*-NO_2 group stabilizes benzyl anion and increases its concentration in a basic solution. The *p*-nitrobenzyl anion may attack



Scheme 3.

the S–S bonds as a nucleophile[7] or it may be converted to a radical by loss of one electron, and then links with polysulfenyl radical to form benzylpolysulfide, which is hydrolyzed to *p*-nitrobenzaldehyde (Scheme 3). The electron-attracting formyl group should accelerate the reduction of nitro group as apparent from our reported Hammett's ρ value of $+3.55$.[8] But our attempt for detection of *p*-nitrobenzaldehyde itself by UV spectrum and trapping *p*-nitrobenzaldehyde by phenylhydrazine were unsuccesful, but in view of its low concentration this mechanism *via p*-nitrobenzaldehyde cannot completely be excluded.

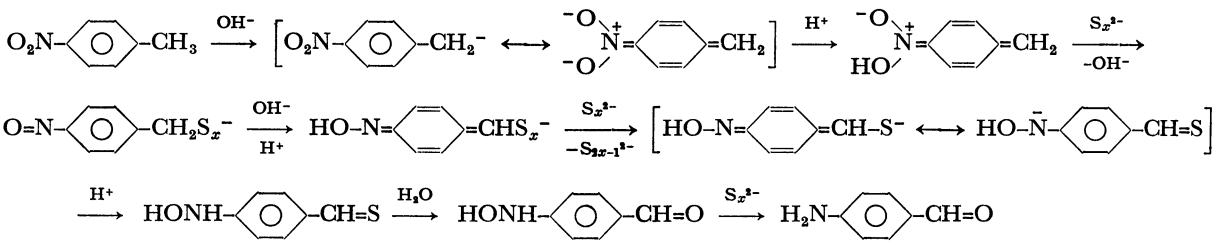
To test the possibility of oxidation of another carbanion with sulfur, *p*-chlorodeoxybenzoin, which loses proton easily with base, was reacted with polysufides but no *p*-chlorobenzil was obtained. Moreover, an attempted reaction of *p*-chlorodeoxybenzoin in the presence of nitrobenzene and Na_2S_x gave virtually no reaction. Hence, a nitro group is necessary for this type of reaction.

(IV) A Probable Mechanism: There are still left two mechanisms as probable candidates. One is the intramolecular direct migration of oxygen and hydrogens, and another is the concurrent oxidation and reduction in a molecule.

The reaction of 4-nitro-*m*-xylene with Na_2S_x gave 3-methyl-4-aminobenzaldehyde (7%) and 4-amino-*m*-xylene (*ca.* 8%), but no 5-methyl-2-aminobenzaldehyde. Therefore, the direct internal migration of oxygen to the nearest ortho position is disfavored. The very low yield of oxidation product (aldehyde) may be due to the electron-releasing methyl group, which lowers the concentration of benzyl anion.

In conclusion, a plausible mechanism which does not contradict with our observations described above may be as shown in Scheme 4.

This tentative mechanism involves conversion of *p*-nitrotoluene to the benzyl anion with hydroxide ion and protonation at the nitro group resulting in the formation of quinonoid isomer of *p*-nitrotoluene. This is a kind of olefin, which may undergo a Michael type addition of polysulfide ion[9] assisted by the electron-attracting *p*-NO_2 group with simultaneous or subsequent elimination of hydroxide ion, giving a hypothetical nitrosobenzyl polysulfide intermediate. Analogous base-catalyzed prototropy would give its quinonoid isomer, whose sulfur atom at the β-position to the benzylic carbon atom would be attacked by polysulfide ion, giving thiobenzaldehyde derivative. The thiolate ion attacks more easily on sulfur atom than on carbon atom, the reaction rate being fast.[10] Further, formation



Scheme 4.

of thiocarbonyl as an intermediate of Willgerodt reaction of acetophenone with ammonium polysulfide has been reported.[11] The *p*-hydroxyaminothiobenzaldehyde is easily hydrolyzed[11a] and reduced to *p*-aminobenzaldehyde[12] as apparent from the literature.

Another evidence for supporting this mechanism is that *o*-nitrotoluene can give *o*-aminobenzaldehyde,[13] but *m*-nitrotoluene cannot give *m*-aminobenzaldehyde albeit the simple discussion as an unpublished data.[14] Further, no effect of bubbling air (oxygen) on the conversion of *p*-nitrotoluene was observed, and also neither 4,4'-dinitrobibenzyl nor 4,4'-dinitrostilbene can be detected in the reaction products. Therfore, a mechanism *via* radical, $p\text{-}NO_2\text{–}C_6H_4\text{–}CH_2\cdot$, is less probable.

Experimental

Melting points were measured by a Yanagimoto micro melting point apparatus and were not corrected. IR and NMR spectra were recorded on a Perkin-Elmer 337 spectrophotometer and a Hitachi R-24B NMR spectrometer using Me_4Si as an internal standard. The GLC analysis was performed with a Yanagimoto 550-F gas chromatograph with a flame ionization detecter.

Materials. Sodium polysulfide were prepared by the method of Gabel *et al.*;[15] a yellow hygroscopic solid. Melting points and boiling points of principal reactants were: *p*-nitrotoluene, mp 53—54 °C; *p*-toluidine mp 44—45 °C; 4-nitro-*m*-xylene bp 125—127 °C/15 Torr.

Reaction of p-*Nitrotoluene (1) with* Na_2S_x.[16] A hot aqueous solution (90 ml) of $Na_2S\cdot 9H_2O$ (0.013 mol), S (0.047 g atom), and NaOH (0.067 mol) was poured into a 300 ml round-bottomed flask containing a hot ethanolic solution (30 ml) of **1** (0.036 mol). The mixture was heated under reflux for 3 h and then steam-distilled. The distillate was extracted with ether and the extract was analyzed by GLC. GLC analysis was conducted at 80—250 °C using two sorts of columns (1 m): PEG 20 M, 10% on Chromosorb WAW; Silicon OV 17, 5% on Simalite 201D. The residue was filtered while hot, and then chilled in an ice bath. The crystals of *p*-aminobenzaldehyde (**2**) were collected and washed with ice water. The product was identified by the NMR and IR in comparison with the authentic specimen. The yield of **2** was 52%.

Reaction of **1** *with* Na_2S *to* Na_2S_5. According to the procedure of the reaction of **1** with Na_2S_x, we used Na_2S–Na_2S_5 instead of $Na_2S\cdot 9H_2O$ and S.

Conversion of **1**. A mixture of **1** (0.037 mol), NaOH (0.068 mol), Na_2S_4 (3.3 g), ethanol (90 ml), and water (10 ml) was placed in a 200 ml two-necked flask and refluxed. One ml of sample was pippetted out at appropriate time intervals. Ethanol (5 ml) was added, and the solution was analyzed by GLC (PEG 20 M).

Reaction of p-*Toluidine (3) with* Na_2S_x. According to the procedure of the reaction of **1** with Na_2S_x, a mixture of **3** (0.035 mol), $Na_2S\cdot 9H_2O$ (0.015 mol), S (0.046 g atom), and NaOH (0.071 mol) was allowed to react. The recovery of **3** was 50%. Similarly, a mixture of same reactions as above and *m*-dinitrobenzene (0.036 mol) was allowed to react. The recovery of **3** was 63% and the yield of *p*-nitroaniline was 23%.

Attempted Trap of p-*Nitrobenzaldehyde.* A hot aqueous solution (12 ml) of NaOH (0.013 mol) and Na_2S_4 (0.70 g) was added to a hot ethanolic solution (6 ml) of **1** (7.3×10^{-3} mol) and phenylhydrazine (7.4×10^{-3} mol), refluxed for 1 h and cooled rapidly. The extract with ether was hydrolyzed with 4 N HCl (100 ml), and the ether extract was analyzed by GLC (PEG 20 M).

*Reaction of 4-Nitro-*m-*xylene (6) with* Na_2S_x. Similar work up for the reaction of **1** with Na_2S_x was applied to **6**; *i.e.*, a mixture of **6** (0.036 mol), $Na_2S\cdot 9H_2O$ (0.014 mol), S (0.055 g atom), and NaOH (0.068 mol) was allowed to react. The yield of 3-methyl-4-aminobenzaldehyde was 70%; mp 104—107 °C (lit,[17] 92 °C); NMR ($CDCl_3$): δ 2.18 (s, 3H, CH_3), 4.19 (s, 2H, NH_2) 6.65 (d, 1H, ArH, J=9 Hz), 7.55 (d, 1H, ArH, J=9 Hz), 7.57 (m, 1H, ArH), 9.70 (s, 1H, CHO).

Reaction of m-*Nitrotoluene (7) with* Na_2S_x. According to the procedure for **1** with Na_2S_x, a mixture of **7** (0.037 mol), $Na_2S\cdot 9H_2O$ (0.013 mol), S (0.050 g atom), and NaOH (0.069 mol) was allowed to react. The recovery of **7** was 30% and the yield of *m*-toluidine was 65%, but no trace of *m*-aminobenzaldehyde was detected with NMR.

Effect of Oxygen on p-*Nitrotoluene Conversion.* A mixture of **1**, NaOH (0.051 mol), Na_2S_4 (3.1 g), ethanol (90 ml), and water (10 ml) was placed in a 200 ml two-necked flask. After the flask had been thermostated at 50±0.5 °C, air was bubbled into the reaction mixture during the run. Two ml of the sample was pippetted out at appropriate time intervals. An ethanolic solution (1 ml) of biphenyl as an internal standard was added, and the solution was analyzed by GLC (PEG 20 M). The similar work up without bubbling of air was also carried out. The conversions (%) at various times were as follows, where figures in parenthesis indicate the conversion without air bubbling; 5 min: 12 (9), 10 min: 30 (24), 15 min: 41 (35), 20 min: 46 (46), 25 min: 47 (47), 30 min: 48 (52).

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