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Studies on the Baudisch Reaction. III. A Possible Intermediate in the Reaction[1)]

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The Baudisch reaction was applied to 1- and 2-naphthols, and 2-nitroso-1-naphthol was obtained as the sole product in both reactions. In a reinvestigation of the products obtained from phenols, it was also found that in some cases the nitroso group replaced the hydroxy group and a hydroxy group was newly introduced into the position *ortho* to the nitroso group. These results indicate that a copper(II)-hydroxylamine-catechol complex will be a possible intermediate of the reaction of phenol. The product studies on the reaction of catechols support the assumption. Kinetically, the formation of the complex seems to be the rate-determining step in the reaction of phenols.

Baudisch[2)] and Cronheim[3)] obtained various *o*-nitrosophenols from phenols by the reaction with hydroxylamine hydrochloride, hydrogen peroxide and copper(II) salt. At first we intended to extend this reaction to naphthols. However, the reaction of 2-naphthol gave an unexpected product, and it became necessary to reinvestigate the products from some substituted phenols. In the present paper, a possible intermediate of the Baudisch reaction is discussed on the basis of experimental results.

Results and Discussion

The Reactions of Naphthols. In methanol, 1- and 2-naphthols reacted with copper(II) nitrate, hydroxylamine hydrochloride and hydrogen peroxide at room temperature, though the reactions proceeded slower than that of phenol. The reaction mixture was poured into water, then the copper salt of the product precipitated. Nitrosonaphthol was liberated from precipitate by an acid. The product from 1-naphthol was 2-nitroso-1-naphthol. Unexpectedly, however, 2-naphthol also gave 2-nitroso-1-naphthol; the hydroxy group of 2-naphthol was replaced by the nitroso group and a hydroxy group was introduced into position 1. Identification of the products was carried out by means of elementary analysis, determination of mixed melting point with the authentic sample and measurement of the NMR spectrum.

Reexamination of the Products from Some Phenols. It was accepted without proof that the position of the hydroxy group does not change in the reactions of phenols.[2,3)] However, the results in the preceding section required reinvestigation of the configurations of *o*-nitrosophenols which were produced from substituted phenols. As *o*-nitrosophenols are volatile, *o*-nitrophenols obtained by oxidation of the products were identified. The results are tabulated in Table 1. Obviously the hydroxy groups of *p*-cresol and 3,5-dimethylphenol were replaced by nitroso groups.

Reactions of Catechols. It was demonstrated in a previous paper that catechol was found when the reaction of phenol was performed under higher pH and that the production of catechol would also be controlled by the copper-hydroxylamine complex.[1b)] However, the mechanistic relationship between the formation of catechol and that of *o*-nitrosophenol has not yet been established. A mixture of catechol, hydroxylamine hydrochloride and copper(II) nitrate in a buffered aqueous solution (pH 2.5) was blue and showed no change in color under a nitrogen atmosphere, but with the addition of a hydrogen peroxide solution the reaction started and proceeded very fast. The red reaction mixture was acidified and the product was extracted with petroleum ether. The product was oxidized and the resulting *o*-nitrophenol was identified. Thus it was confirmed that the reaction product from catechol under the Baudisch reaction conditions was *o*-nitrosophenol. Under the same conditions, 3,4-dihydroxytoluene selectively changed into 5-methyl-2-nitrosophenol which was the sole reaction product from both *m*- and *p*-cresols (Table 1).

Kinetic Measurements for Catechols. In Fig. 1, the kinetic plot for the reaction of catechol is shown, together with that for phenol. The concentration of catechol at any time was assumed

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1) a) Part I: K. Maruyama, I. Tanimoto and R. Gotō, *J. Org. Chem.*, **32**, 2516 (1967); b) Part II: I. Tanimoto, This Bulletin, **43**, 139 (1970).

2) a) O. Baudisch and S. H. Smith, *Naturwissenschaften*, **27**, 769 (1939); b) O. Baudisch, *Science*, **92**, 336 (1940).

3) G. Cronheim, *J. Org. Chem.*, **12**, 7 (1947).

TABLE 1. PRODUCTS FROM PHENOLS IN THE BAUDISCH REACTION[a]

Materials	Products	Oxidized products[b]	Mp of Nitrophenols[c] (lit, mp)(°C)
o-Cresol	6-Methyl-2-nitrosophenol	6-Methyl-2-nitrophenol	68[d] (69—70)
m-Cresol	5-Methyl-2-nitrosophenol	5-Methyl-2-nitrophenol	54[e] (56)
p-Cresol	5-Methyl-2-nitrosophenol	5-Methyl-2-nitrophenol	55[e] (56)
2,4-Dimethylphenol	4,6-Dimethyl-2-nitrosophenol	4,6-Dimethyl-2-nitrophenol	70[f] (71—72)
3,5-Dimethylphenol	4,6-Dimethyl-2-nitrosophenol	4,6-Dimethyl-2-nitrophenol	69[f] (71—72)
Catechol	2-Nitrosophenol	2-Nitrophenol	46 (45)
3,4-Dihydroxytoluene	5-Methyl-2-nitrosophenol	5-Methyl-2-nitrophenol	54[e] (56)

a) Conducted in aqueous medium at 30°C.
b) Oxidized by hydrogen peroxide in acetic acid.
c) Undepressed by admixture with authentic samples.
d) Depressed by admixture with authentic 3-methyl-2-nitrophenol (mp 41°C).
e) Depressed by admixture with authentic 4-methyl-2-nitrophenol (mp 32°C).
f) Depressed by admixture with authentic 3,5-dimethyl-2-nitrophenol(mp 63—64.5°C).

TABLE 2. KINETIC DATA FOR THE BAUDISCH REACTION OF CATECHOL AND PHENOL[a]

	$k \times 10^5$, sec^{-1}				E, kcal. mol^{-1}	$\Delta S^{\neq}$,[b] e.u.
	0.0°C	10.0°C	20.0°C	30.0°C		
Catechol	4.09	7.54	32.3	50.0	14.8±1.5	−27.0
Phenol	2.39	3.56	14.0	29.8	14.9±1.5	−28.2

a) All reactions were conducted under a nitrogen atmosphere. Catechol (1×10^{-3} mol), copper(II) nitrate (1×10^{-3} mol) and hydroxylamine hydrochloride (2×10^{-3} mol) were stirred in 198 m*l* of a Walpole buffer (pH 2.50) after addition of a hydrogen peroxide solution (1.0M)(2 m*l*). Temperature was controlled within ±0.1°C.
b) Entropy of activation was calculated at10.0°C.
c) The data was taken from that shown in Part II of this series.[1b]

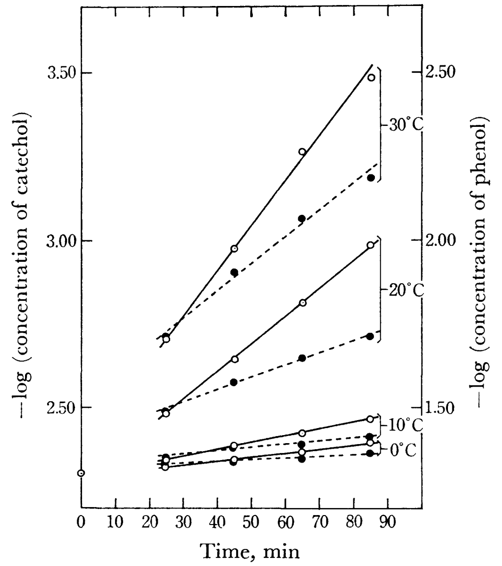


Fig. 1. First-order plots for the Baudisch reaction of catechol and of phenol.

The plot for the reaction of phenol was based on the data shown in the Part II of this series.[1b]

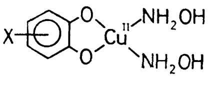
Initial concentration of catechol (—○—): 5×10^{-3}M.

Initial concentration of phenol (—●—): 5×10^{-2}M.

to be given by the difference between its initial concentration and the concentration of *o*-nitrosophenol. Apparently the reaction of catechol is first-order in catechol, and from this plot the rate constants and thermodynamic quantities can be calculated. The results of the calculation are shown in Table 2, together with the data for the reaction of phenol. The rate constants for catechol are about twice those for phenol.

The reaction of 3,4-dihydroxytoluene proceeded much faster than that of both *m*- and *p*-cresols, but reliable kinetic data could not be obtained.

Discussion. The copper-hydroxylamine complex combined with the phenoxy group plays an important role in the reaction of phenol.[1b] If the complex is responsible for the direct nitrosation of benzene ring, the position of the hydroxy group in the resulting *o*-nitrosophenol should not change from that of the hydroxy group in phenol. However, the formation of 5-methyl-2-nitrosophenol from 3,4-dihydroxytoluene, *m*- and *p*-cresols rejects this mechanism. A reasonable explanation for this may be given by the assumption that complex I is formed in each of the reactions as a common intermediate, because the isokinetic plots shown in the previous paper indicated a constant mechanism for the related series of reactions.[1b] In Table 2, it is shown that catechol has a higher reaction rate



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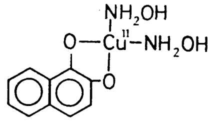

II

than phenol. Since catechol easily changes into complex I, it may be concluded that the kinetic data shown in Table 2 indicate the high reactivity of complex I. Thus the rate-determining step in the reaction of phenol would be the formation of complex I. In the reactions of naphthols, complex II will be formed as a common intermediate. This explains the production of 2-nitroso-1-naphthol from both 1- and 2-naphthols. There are two possible mechanisms by which complex I changes into *o*-nitrosophenol; the one involves the cleavage of the C–O bond and the attack of hydroxylamine moiety on the carbon atom, and the other the formation of *o*-quinone and subsequent oximation. Studies are in progress to establish the mechanism.

Experimental

Materials. Reagent grade 30% hydrogen peroxide solution and *p*- and *m*-cresols were the same as described.[1b)] Other reagents were of the best available grade and, if necessary, were used after further purification. Some of the authentic samples were prepared according to directions in literature and others were of the best commercially available grade (Table 3).

TABLE 3. AUTHENTIC SAMPLES

Samples	Mp °C	Lit, mp °C
3-Methyl-2-nitrophenol[a)]	41.0	41
4-Methyl -2-nitrophenol[b)]	32.0	34
5-Methyl-2-nitrophenol[c)]	55.0	56
6-Methyl-2-nitrophenol[d)]	71.5—72.5	69—70
3,5-Dimethyl-2-nitrophenol[e)]	63—64.5	66
4,6-Dimethyl-2-nitrophenol[b)]	72	71—72
2-Nitrophenol[f)]	45	45
2-Nitroso-1-naphthol[f)]	160—162	162—164
1-Nitroso-2-naphthol[f)]	109.5	109.5

a) G. P. Gibson, *J. Chem. Scc.*, **123**, 1269 (1923).
b) Obtained by the nitration of *p*-cresol and2, 4-dimethylphenol.
c) K. G. Blaikie and W. H.Perkin, *ibid.*, **125**, 307 (1924).
d) G. P. Gibson, *ibid.*,**127**, 42 (1925).
e) K. V. Auwers and E. Borsche, *Ber.* **48**, 1698 (1915).
f) Commercial guaranteed reagent.

2-Nitroso-1-naphthol. In a 1 *l* round-bottomed, threenecked flask provided with a stirrer, 12 g (0.05 mol) of copper(II) nitrate was dissolved with 100 m*l* of methanol, and the solution was mixed with a solution of 8 g (0.12 mol) of hydroxylamine hydrochloride in 100 m*l* of methanol. The flask was then well cooled with ice and stirred at 0°C under a nitrogen atmosphere. After 30 min, 4 g (0.028 mol) of 2-naphthol was added to the solution and stirring was continued for 10 min. A dilute solution of hydrogen peroxide which was obtained from 10 m*l* of 30% hydrogen peroxide solution and 30 m*l* of hydrochloric acid-sodium acetate buffer (pH 2.5) was added to the reaction mixture in about 1 hr. The mixture was then warmed to 20°C gradually and the reaction was continued for 4 hr. After the reaction was completed, the mixture was poured into 200 m*l* of water and allowed to stand in an ice-box overnight. The precipitate was filtered, washed twice with a small amount of ether, and suspended in a mixture of methanol (100 m*l*) and concentrated hydrochloric acid (100 m*l*). The suspension was added to chloroform in a 1 *l* separatory funnel, shaken well, and then separated into two layers by addition of water. The aqueous layer was repeatedly extracted with fresh chloroform. All of the chloroform extract was washed with 6N hydrochloric acid and twice-distilled water. The extract was dried over anhydrous sodium sulfate and the solvent was removed under reduced pressure. By recrystallization of the residue from ethanol-water, 1.6 g of 2-nitroso-1-naphthol of mp 160—162°C (lit, mp 162—164°C) was obtained. The yield was *ca.* 35% of the theoretical value.

Found: C, 69.64; H, 4.02; N, 7.84%. Calcd for $C_{10}H_7O_2N$: C, 69.36; H, 4.07; N, 8.09%.

With the same procedure 1-naphthol gave 0.3—0.4 g of 2-nitroso-1-naphthol, mp 166—167°C.

Found: C, 69.64; H, 4.07; N, 8.05%.

Nitrosophenols from Phenols and Catechols. As *o*-nitrosophenol is very volatile and difficult to identify, the product of the reaction was oxidized to nitrophenol and its identification was conducted. As a typical example of the procedure, the formation of 5-methyl-2-nitrosophenol from *p*-cresol will be described.

In a 1 *l* three-necked flask, equipped with a stirrer, was placed copper(II) nitrate (7.2 g, 0.03 mol) and 200 m*l* of hydrochloric acid-sodium acetate buffer (pH 2.5). To this was added a mixture of hydroxylamine hydrochloride (4.2 g, 0.06 mol) and *p*-cresol (3.24 g, 0.03 mol) dissolved in 400 m*l* of water. The solution was stirred for 6 hr at 30°C after the addition of 6 m*l* of hydrogen peroxide solution. The reaction mixture was acidified and extracted with petroleum ether. *o*-Nitrosophenol in the petroleum ether was extracted with aqueous solution of copper(II) sulfate as a copper salt. The red solution was acidified and extracted with petroleum ether. The petroleum ether solution of pure *o*-nitrosocresol was added with 40 m*l* of glacial acetic acid and evaporated at about 50°C. To the resulting acetic acid solution of *o*-nitrosocresol was added a mixture of glacial acetic acid (15 m*l*) and 30% hydrogen peroxide (15 m*l*) and the solution was allowed to stand at 70—80°C for about 20 min. Completion of oxidation was confirmed by observing that a drop of the acetic acid solution did not turn red with the addition of methanolic copper(II) nitrate solution. To the acetic acid solution was then added a large amount of ice-water and extraction was carried out with ethyl ether. The ether extract was washed with water and extracted with 2N sodium hydroxide solution. Steam distillation of the solution after acidification gave 75 mg of yellow crystalline needles with mp of

49.5—52°C. Recrystallization from aqueous ethanol gave 5-methyl-2-nitrophenol, mp 55°C (lit, mp 56°C), undepressed by admixture with an authentic sample.

Kinetic Studies. The general procedure for phenols was used.[1b)]

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