

Kinetic Studies of the Acid-catalyzed Amination of *p*-Nitrosoanisole with Anilines in Methanol

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The allelotrope of *p*-nitrosophenol¹⁾ and/or another keto-enol tautomers^{2,3)} are easily etherified with an alcohol in the presence of inorganic acid, even at room temperature. Furthermore, the methoxy group of the methyl ether of the allelotrope, *p*-nitrosoanisole, can readily be replaced by an electro-negative atom with an unshared electron pair, such as the N-atom of amines. Thus, *p*-nitrosodiphenylamines are obtained by the title reaction in a favorable yield.⁴⁾

In the present paper, we should like to propose a new reaction mechanism, though a mechanism has previously been speculated on the basis of the synthetic data.⁴⁾

Experimental

Materials. The *p*-nitrosoanisole (abbreviated as PNA) was prepared by the reaction of the allelotrope of *p*-nitrosophenol (abbreviated as PNP) with methanol in the presence of sulfuric acid.⁵⁾ The blue crystals obtained by subsequent steam distillation were recrystallized twice from petroleum ether; yield, 50%; mp 23°C (lit, 23°C⁶⁾). The product was kept at 0°C in a dark place for safe storage. Commercial *p*-nitrosodiphenylamine (abbreviated as PNDA) was recrystallized three times from benzene; mp 143—145°C (lit, 143°C,⁷⁾ 144—145°C⁴⁾). The *p*-nitroso-*p*'- or -*m*'-substituted diphenylamines were prepared by the acid-catalyzed amination of *p*-nitrosoanisole with the corresponding *p*- or -*m*-substituted anilines and were recrystallized from benzene and/or methanol; *p*-nitroso-*p*'-methoxydiphenylamine, mp 163—165°C (lit, 164—166°C⁴⁾); *p*-nitroso-*p*'-methyldiphenylamine, mp 172—173°C (lit, 172—173°C⁴⁾); *p*-nitroso-*p*'-chlorodiphenylamine, mp 158—159°C (lit, 157—160°C⁴⁾); *p*-nitroso-*m*'-chlorodiphenylamine,⁸⁾ mp 148.5—149.5°C. Found: C, 62.04; H, 3.93; N, 12.05%. Calcd for C₁₂H₉ClN₂O: C, 61.95; H, 3.93; N, 12.04%. Commercial aniline, *p*-toluidine, *m*-chloroaniline, and *p*-chloroaniline were distilled twice under reduced pressure; aniline, bp 83°C/23 mmHg; *p*-toluidine, bp 95—95.5°C/22 mmHg; *m*-chloroaniline, bp 114—114.5°C/20 mmHg; *p*-chloroaniline, bp 115—116°C/21 mmHg. The *p*-anisidine was recrystallized from water and methanol—

water; mp 58°C. Methanol as a medium was rectified; bp 65—65.5°C. The methanolic solution of hydrogen chloride was prepared by bubbling hydrogen chloride well dried with phosphorus pentoxide into the rectified methanol.

Reaction Product Criterion. A mixture (50 ml) of PNA (0.2M), aniline (0.5M), and hydrogen chloride (0.05N) in methanol was kept at 30°C for 11 hr, and then neutralized with methanolic potassium hydroxide. The mixture was filtered after adding water. PNDA was thus obtained; mp and mmp 143—145°C; yield 90%.

Ultraviolet Spectrophotometry and Chemical Analysis. The conversion percentages were calculated from the calibration curve which has been prepared by plotting the difference in extinction at 260, 290, and 340 nm, ($E_{260} - E_{340}$) vs. ($E_{290} - E_{340}$), and at 0 and 100% conversions. The difference between the conversion percentage obtained from the curve and that obtained from the composition of the mixture was within 1% at each attempted conversion percentage.

A Typical Run for the Rate Measurements. A two ml portion of methanolic solution of 1M PNA was poured into 8 ml of a methanolic solution containing 0.625M aniline and 0.0625N hydrogen chloride in order to start the reaction after both the solutions had attained the temperature equilibrium at 30°C. Aliquots (0.1 ml, each) were taken out at appropriate intervals of time and then diluted with methanol to a 4×10^{-5} M total concentration of PNA and PNDA. The conversion percentage was calculated graphically.

Results and Discussion

When the reaction product, PNDA, was kept at 30°C for 48 hr in methanol containing 0.01N hydrogen chloride, a slight side reaction tends to occur,⁹⁾ but the reverse reaction does not take place at all. There-

TABLE I. THE RATE DATA FOR THE ACID-CATALYZED AMINATION OF *p*-NITROSOANISOLE WITH ANILINE IN THE PRESENCE OF 0.05 N HYDROGEN CHLORIDE IN METHANOL

[PNA] ₀ M	[Aniline] ₀ M	Temp. °C	$k_{2008} \times 10^4$ M ⁻¹ sec ⁻¹
0.2	0.2	30	4.81
0.2	0.3	30	4.88
0.2	0.4	30	4.82
0.2	0.5	30	4.85
0.2	0.6	30	4.80
0.1	0.5	30	4.80
0.3	0.5	30	4.85
0.4	0.5	30	4.89
0.2	0.5	20	3.12
0.2	0.5	25	3.79
0.2	0.5	35	6.16

$$E_a, 8.69 \text{ kcal mol}^{-1} \quad \Delta S^\ddagger, -47.01 \text{ e.u.}$$

9) It is considered that azophenine is formed after a prolonged reaction; O. Fischer and E. Hepp, *Ber.*, **20**, 2479 (1887); **21**, 679, 2617 (1888).

1) Y. Furuya, I. Urasaki, K. Itoho, and A. Takashima, *This Bulletin*, **42**, 1922 (1969).

2) Y. Furuya, I. Urasaki, K. Itoho, and S. Miyazaki, *ibid.*, **42**, 1769 (1969).

3) Y. Furuya, K. Itoho, and K. Mori, Presented at the 21st Symposium of the Organic Reaction Mechanisms, Hiroshima, October, 1970.

4) J. T. Hays, H. L. Young, and H. H. Espy, *J. Org. Chem.*, **32**, 158 (1967).

5) See, for example, Y. Furuya, and R. Oda, *Kogyo Kagaku Zasshi*, **65**, 214 (1962).

6) A. Rising, *Ber.*, **37**, 44 (1904).

7) O. Fischer and E. Hepp, *Ber.*, **19**, 2991 (1886).

8) *m*-Chloroaniline was detected paper chromatographically in an ethereal solution extracted from an alkaline hydrolyzed mixture of this compound.

fore, the amination reaction follows the irreversible second-order rate equation with PNA and aniline:

$$v = k_{2\text{obs}}[\text{PNA}][\text{Aniline}] \quad (1)$$

The rate was affected by the acidity. The plots of $k_{2\text{obs}}$ vs. the square root of the concentration of hydrogen chloride gave a straight line passing through the point of origin, as is shown in Fig. 1. Therefore, the rate constant, $k_{2\text{obs}}$, may be expressed as follows:

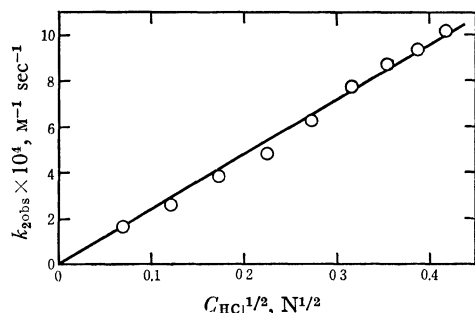


Fig. 1. The plot of $k_{2\text{obs}}$ vs. square root of the concentration of hydrogen chloride in methanol for the amination of PNA with aniline at 30°C.

Initial concn. of PNA: 0.2M, Initial concn. of aniline: 0.5M

$$k_{2\text{obs}} = k_2 C_{\text{HCl}}^{1/2} \quad (2)$$

Here, $C_{\text{HCl}}^{1/2}$ is expressed as:

$$C_{\text{HCl}}^{1/2} = C_{\text{H}^+}/K^{1/2} \quad (3)$$

where K is the dissociation constant of hydrogen chloride in methanol. Therefore, the following relationship is obtained:

$$k_{2\text{obs}} = k_2 K^{-1/2} C_{\text{H}^+} \quad (4)$$

The $\text{p}K_{\text{BH}^+}$ values of aniline, methanol, and the allelotype of PNP in water are 4.6,¹⁰ -2.5,¹¹ and -3.4,¹ respectively. As the σ_p value of the hydroxyl group (-0.357) is smaller than that of the methoxy group (-0.268), the $\text{p}K_{\text{BH}^+}$ value of PNA may be smaller than that of the allelotype of PNP. Thus, the order of ease for the protonation may be expressed as: aniline \gg methanol $>$ PNA. In other words, the protonated aniline exists in the medium predominantly.

On the other hand, the reaction was accelerated by the introduction of an electron-releasing group into the phenyl group of aniline, and retarded by the introduction of an electron-attracting group, as is shown in Table 2 and Fig. 2. The plot of the logarithm of the rate constant ratio, $\log k_2/k_{20}$, against Deno's σ^+ gives a straight line with a slope of -0.95 ($r=0.994$), as is

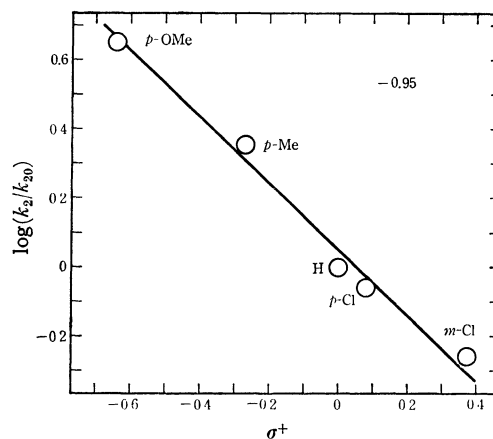
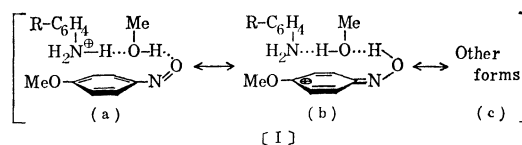


Fig. 2. Hammett plots for the acid-catalyzed amination of PNA with anilines at 25°C. Concn. of HCl: 0.05N.

shown in Fig. 2.¹² These results suggest the participation of the anilinium ion in the formation of transition state of this reaction.

Moreover, the value of the activation entropy of the reaction (-47.01 e.u.) is much smaller than that in the ordinary protonation. Therefore, the transition state having a hydrogen-bonding annular construction of the protonated aniline, PNA, and a solvent molecule such as is illustrated below might be involved.¹³ The over-all rate may be controlled by this step.



It is considered that the contribution of the Ib structure may be important because of the increase in the stability of the positive charge by diffusion into the benzene ring of PNA; hence, the nucleophilic attack of the N-atom of aniline on the positive C-atom of Ib may occur predominantly in the following step.

From these findings and considerations, a probable mechanism may be charted as below:

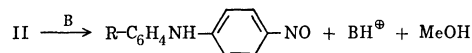
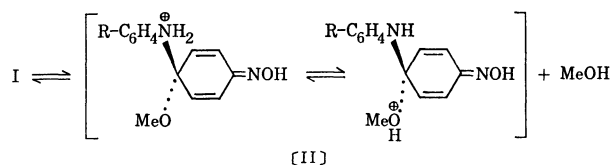
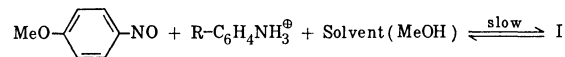
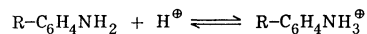


TABLE 2. SUBSTITUENT EFFECT OF THE HYDROGEN CHLORIDE-CATALYZED AMINATION OF PNA WITH ANILINES IN METHANOL AT 25°C
Concn. of HCl: 0.05 N

Anilines	Deno's σ^+	$k_{2\text{obs}} \times 10^4$ $\text{M}^{-1}\text{sec}^{-1}$
<i>p</i> -Anisidine	-0.64	16.95
<i>p</i> -Toluidine	-0.27	8.50
Aniline	0	3.79
<i>p</i> -Chloroaniline	+0.08	3.27
<i>m</i> -Chloroaniline	+0.373	2.09

10) S. Patai, "The Chemistry of the Amino Group," Interscience Publishers, New York (1968), p. 182.

11) N. C. Deno and J. O. Turner, *J. Org. Chem.*, **31**, 1969 (1966).

12) If the direct nucleophilic attack of aniline on the protonated PNA⁴ occurs, σ values should be used in Hammett plot of this reaction.

13) See, for example, L. M. Litvimenko, D. M. Aleksandrova, and N. I. Pilyuk, *Ukrain. Khim. Zhur.*, **25**, 81 (1959); *Chem. Abstr.*, **53**, 21782i (1959).