January, 1974] BULLETIN OF THE CHEMICAL SOCIETY OF JAPAN, VOL. 47(1), 193—196 (1974) 193

N-Alkylideneanilines. III.[1] Behavior of *N*-Isopropylideneanilines in Methanol-d_4

Hiizu Iwamura,* Michiko Tsuchimoto,** and Shigeo Nishimura**
Department of Chemistry, Faculty of Science, The University of Tokyo, Hongo, Tokyo 113
***Department of Industrial Chemistry, Tokyo University of Agriculture and Technology, Koganei, Tokyo 184*

(Received August 6, 1973)

When *N*-isopropylideneanilines are dissolved in methanol-d_4, three types of reactions, exchange of protons in isopropylidene moiety, formation of carbinolamine ethers, and liberation of anilines with formation of acetone dimethyl acetal take place as revealed by NMR spectra of the solutions. The H–D exchange reaction is favored by electron-releasing ring substituents and yet is considerably slower than the rates of the E–Z isomerization of the corresponding imines. The carbinolamine ethers are formed when the substituents are strongly electronegative. Formation of acetone dimethyl acetal occurs additionally with imines carrying halogen atoms as the ring substituents. The competitive reaction mechanism is proposed.

Recently Jennings and Boyd pointed out the intermediacy of enamine tautomers for the E–Z isomerization of imines containing HCC=N moiety.[2] To test the role of this mechanism in the E–Z isomerization of a series of *N*-isopropylideneanilines with various ring substituents, we have examined their rates of H–D exchange reaction by the NMR spectroscopy and found that the above mechanism is not operative in these imines and that they behave quite differently in methanol-d_4, depending on the nature of the ring substituents. Specifically the following three types of reactions were observed for *N*-isopropylideneanilines.

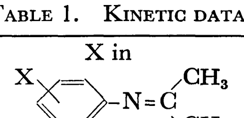
1) Exchange of protons in isopropylidene moiety.
2) Formation of adducts of *N*-isopropylideneanilines with methanol-d_4.
3) Liberation of anilines with formation of acetone dimethyl acetal-d_6.

Experimental

NMR spectra were obtained on a JEOL C-60 HL (Japan Electron Optics Lab. Co., Ltd.) high resolution NMR instrument (60 MHz). *N*-Isopropylideneanilines (0.25 mmol) were dissolved in 0.5 ml of CD_3OD (99.5%). The measurement was carried out at time intervals on the growth and decay of resonance signals by recorder integration (the accuracy of each integration is about ±4%). The chemical shifts were read relative to TMS as the internal reference at 25 °C.

General procedure of the preparation of *N*-isopropylideneanilines:[3] 30 g of molecular sieve 4A were added to a solution of 0.1 mol of acetone and 0.05 mol of aniline in anhydrous ether. The mixture was kept at 10 °C for 9 to 10 days, by renewing the molecular sieve 2—3 times. After removing the molecular sieve by filtration and the solvent by application of a rotary evaporator, the residue was fractionaly distilled.

Table 1. Kinetic data of H–D exchange reactions

X in 	k/sec
p-OCH_3	2.80×10^{-5}
p-CH_3	1.69×10^{-5}
H	6.60×10^{-6}
p-F	3.70×10^{-6}
p-I	2.59×10^{-6}
p-Cl	5.66×10^{-6}
p-Br	5.38×10^{-6}
m-CF_3	1.19×10^{-6}

N-Isopropylidene-*p*-iodoaniline was obtained as a yellow oil (bp 127 °C/8 mmHg, n_D^{25} 1.5732); NMR spectrum ($CDCl_3$, 25 °C): *syn* CH_3, s, 1.80 ppm; *anti* CH_3, s, 2.18 ppm;[4] 2,6 ring protons, d, 6.55 ppm; 3,5 ring protons, d, 7.66 ppm. Found: C, 41.67; H, 3.70; N, 5.37%. Calcd for $C_9H_{10}NI$: C, 41.72; H, 3.89; N, 5.41%.

N-Isopropylidene-*p*-fluoroaniline; a colorless oil (bp 54—56 °C/5 mmHg, n_D^{25} 1.5081; NMR spectrum ($CDCl_3$, 25 °C): *syn* CH_3, s, 1.80 ppm; *anti* CH_3, s, 2.18 ppm;[4] ring protons, centered at 6.88 ppm. Found: C, 71.34; H, 6.53; N, 9.34%. Calcd for $C_9H_{10}NF$: C, 71.50; H, 6.67; N, 9.27%.

N-Isopropylidene-*m*-trifluoromethylaniline: a yellow oil (bp 52 °C/5 mmHg, n_D^{25} 1.4712); NMR spectrum ($CDCl_3$, 25 °C): *syn* CH_3, s, 1.82 ppm; *anti* CH_3, s, 2.20 ppm;[4] 2,6 ring protons, d, 7.01 ppm; 3,4 ring protons, d, 7.42 ppm. Found: C, 59.73; H, 5.02; N, 7.14%. Calcd for $C_{10}H_{10}$-NF_3: C, 59.70; H, 5.01; N, 6.96%.

Results and Discussion

The H–D Exchange Reaction. The isopropylidene methyl protons of *N*-isopropylideneanilines carrying electron-releasing *p*-substituents exchange with deuterium in methanol-d_4 solution at ambient temperature. The rate of the reaction can readily be followed by measuring the decrease of their proton signals or the

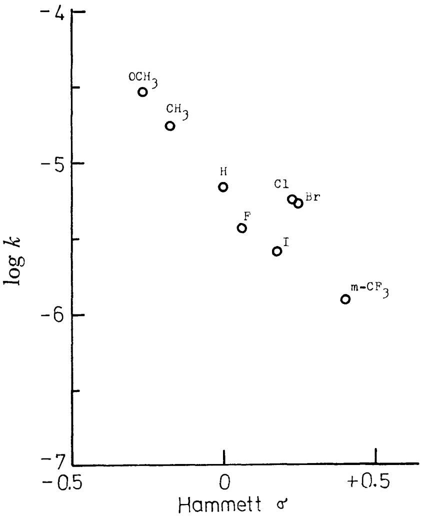


Fig. 1. The Hammett plots of the rates of H–D exchange reaction.

increase of the OH protons[5] due to CD_3OH produced. The pseudo-first-order rate constants for the exchange reaction in a large excess of CD_3OD are calculated and given in Table 1. Note that the rates of exchange increase with increasing electron-donating ability of the substituents. This relation is demonstrated more clearly by the Hammett expression as shown in Fig. 1. The trend indicates that the exchange reaction is nucleophilic and that protonation either to the imines or to the enamines is the rate-determining step. The values for *p*-Cl and *p*-Br deviate from the straight line. This might be due to inaccuracy of the determination of the rates because of the concurrent occurrence of the addition reaction (*vide infra*). In those having more electron-withdrawing substituents than the halogenes, the exchange is not observed to detectable extent and the addition reaction is the exclusive one.

We recall that the rates of E–Z isomerization [$k(s^{-1}) = 4.0 \times 10^{-2}$ for *m*-CF_3 and 2.5×10^{-3} for *p*-OCH_3 at 25 °C][6] are faster by order of magnitude than the rates of exchange in Table 1 and are subject to reverse substituent effects; the electron-withdrawing groups enhance while the electron-releasing substituents retard the isomerization. It is concluded from these results that formation of enamine is slower and cannot be the contributing mechanism for the E–Z isomerization.

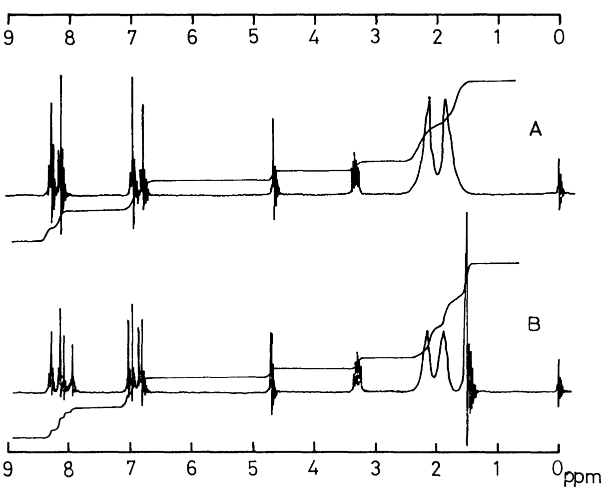


Fig. 2. NMR spectra of *N*-isopropylidene-*p*-nitroaniline (0.25 mmol) in CD_3OD (0.5 ml), 25 °C.
A: At the beginning of the reaction.
B: After 212 min with 32% adduct formation.

The Addition Reaction. When *N*-isopropylidene-*p*-nitroaniline is allowed to stand in CD_3OD, the signals due to the *syn*- and *anti*-methyl protons (δ 1.87 and 2.21) as well as A_2X_2 type aromatic protons (δ 6.93 and 8.23) diminish their intensity with a corresponding increase of a new singlet at δ 1.51, as shown in Fig. 2. The new A_2X_2 type multiplets start to develop in the aromatic region (δ 6.98 and 8.07). No increase in the OH proton signal was detected. The diamagnetic shift of the singlet signal suggests that the carbon atom to which the methyl groups are attached has changed its hybridization from sp^2 to sp^3. The chemical shifts of the aromatic protons are now more like those of *p*-nitroaniline.[7]

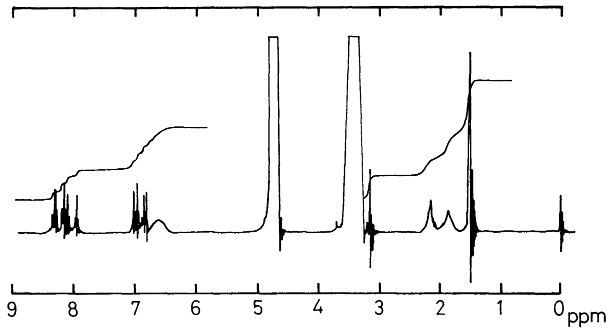
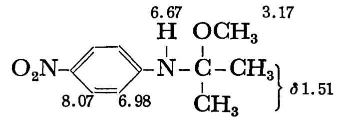


Fig. 3. NMR spectra of *N*-isopropylidene-*p*-nitroaniline (0.25 mmol) in CH_3OH (0.5 ml), 25 °C, taken at 300 min after the start of the reaction. 40% conversion.

While we have not succeeded in isolating the product, these spectral changes can be fully explained in terms of the formation of the adduct of the *N*-isopropylideneaniline with methanol. The carbinolamine ether structure is further supported by the change in the NMR signals when the *N*-isopropylidene-*p*-nitroaniline is dissolved in CH_3OH (Fig. 3). Thus the additional singlets at δ 6.67 and 3.17 are consistent with the N$\underline{H}$ and OC$\underline{H}_3$ protons in structure



In Table 2 are given the equilibrium constants K_c, which are defined for the addition reactions by equation

$$K_c = X_e/[(a-X_e)(b-X_e)]$$

where a and b are the stoichiometric molar concentrations of *N*-isopropylideneanilines (2.50×10^{-4}) and CD_3OD (1.09×10^{-2}) and X_e is the molar concentration of the adduct in equilibrium. The pseudo-first-order rate constants for the addition reaction of various substituted *N*-isopropylideneanilines are also calculated

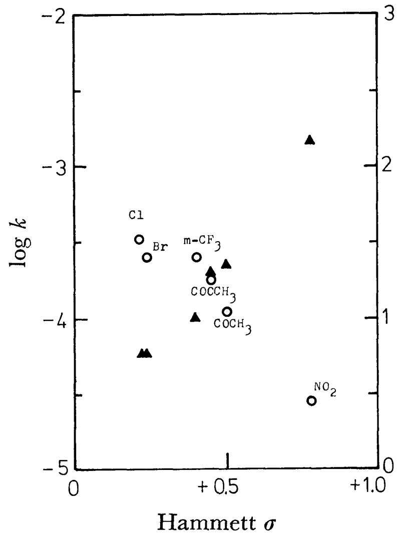
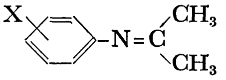
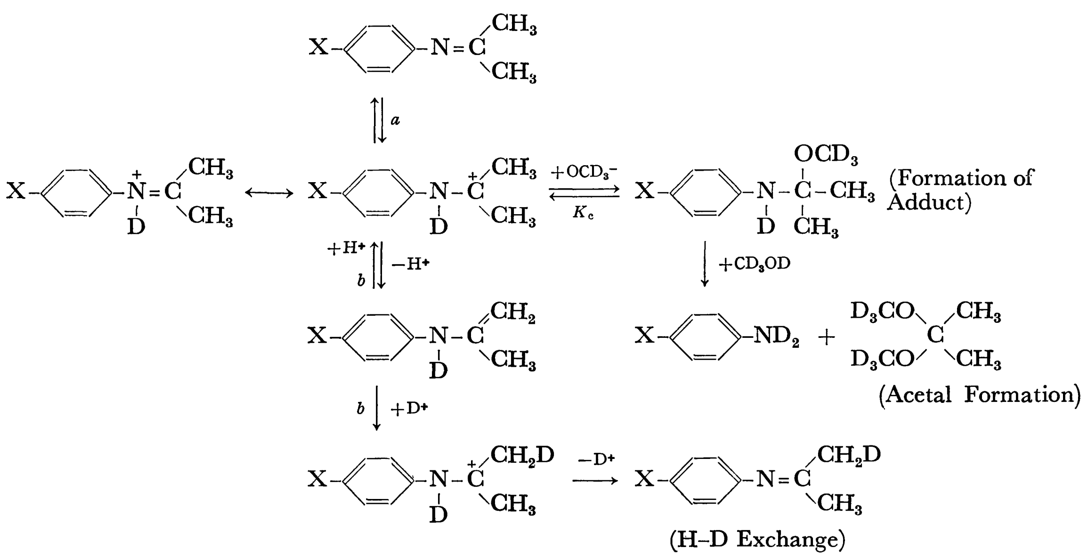


Fig. 4. The Hammett plots of the equilibrium constant K_c and the rate of adduct formation.
(○) for log k, (▲) for log K_c.

Table 2. Kinetic data of addition reactions

X in 	k/sec	X_e/%	X_e/mol	K_c	Time to equiribrium (min)
p-Cl	3.31×10^{-4}	6.1	1.53×10^{-5}	5.97	18
p-Br	2.34×10^{-4}	6.1	1.53×10^{-5}	5.97	14
m-CF_3	2.63×10^{-4}	9.0	2.25×10^{-4}	9.07	25
p-$COOCH_3$	2.29×10^{-4}	17.9	4.48×10^{-5}	20.1	36
p-$COCH_3$	1.41×10^{-4}	19.3	4.83×10^{-5}	22.0	74
p-NO_2	3.20×10^{-5}	61.7	1.54×10^{-4}	1.49×10^{2}	24 hr



Scheme 1

and shown in the same Table. At 25 °C, the equilibrium is attained for the addition reaction in approximately 20—70 min. Especially p-NO_2 compound requires 24 hr before the equilibrium state is obtained. We note that, with increasing electronegativity of the ring substituents, the rate of formation of the adduct decreases, but the equilibrium constant for formation of the adduct increases. The effects of the ring substituents obey the Hammett relationship as shown in Fig. 4.

Relevant to the mechanism is the fact that there is no incorporation of deuterium observed in the methyl groups of the carbinolamine ether adducts.

The Acetal Formation. In the N-isopropylideneanilines having p-Cl, p-Br, p-I, and m-CF_3, it has been found that the formation of the carbinolamine ether is followed by the slow formation ($k \simeq 10^{-6}$—10^{-7}) of acetone dimethyl acetal which is identified by the appearance of the signal at δ 1.30, independent of the ring substituents. The assignment is confirmed by comparison of the chemical shift with that of an authentic sample.[8] The reactions are practically complete in 2 weeks at ambient temperature with *ca.* 11% conversion.

It is of interest that the formation of the acetal is seen only in these N-isopropylideneanilines. In those having more electron-releasing substituents the formation of the intermediate adduct is very small, while in those having more electronegative substituents the intermediate adduct seems too stable to undergo further reaction into the acetal.

The Mechanism of the Reaction. As seen from the results described above, the course and rates of the reac tions of N-isopropylideneanilines in CD_3OD are characteristically dependent on the nature of ring substituents. The reaction scheme and probable mechanisms for the whole reactions are summarized in Scheme 1.[9] Whereas the substituent effects on the rates of H–D exchange and formation of carbinolamine ethers have the same trend, the fact that the latter without H–D exchange has larger rate constants rules out the possibility that protonation or deuteration of the imines (step a) is rate-determining step in both cases. Step a may well be the rate-determining step for adduct formation, but protonation of enamines (step b) is more likely to be slower than step a and rate-determining for exchange reactions. The extent of formation of the carbinolamine ethers is governed by the electrophilicity of the conjugate acid of the imines.

References

1) For Part II see: H. Iwamura, M. Tsuchimoto, and S. Nishimura, *Chem. Lett.*, **1972**, 1073.

2) W. B. Jennings and D. R. Boyd, *J. Amer. Chem. Soc.*, **94**, 7187 (1972).

3) M. Tsuchimoto, S. Nishimura, and H. Iwamura,

This Bulletin, **46**, 675 (1973).

4) See Ref. 1 for the signal assignment.

5) Divided by six to obtain the rate constant per proton of the two methyl groups.

6) M. Tsuchimoto, S. Nishimura, and H. Iwamura, The 5th Symposium on Structural Organic Chemistry, October 11, Nagoya (1972), p. 63 of the Proceedings; to be published elsewhere.

7) *p*-Nitroaniline shows the A_2X_2 multiplets at δ 6.60 and 7.97 in methanol-d_4.

8) The *O*-methyl protons which should appear at δ 3.09 cannnot be detected for the reactions in methanol-d_4.

9) For the mechanism of analogous hydrolysis of the imines see: E. H. Cordes and W. P. Jencks, *J. Amer. Chem. Soc.*, **85**, 2843 (1963); E. F. Pratt and M. J. Kamlet, *J. Org. Chem.*, **26**, 4029 (1961); and papers cited therein.