N-Alkylideneanilines. IV.[1] Kinetics and Mechanism for Site-Exchange of the Methyl Groups in *N*-Isopropylideneanilines

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*

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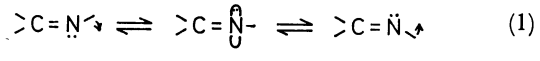
The kinetics of the site-exchange of the methyl groups in twelve *N*-isopropylideneanilines have been studied by the coalescence point analysis of their proton NMR spectra. The free energies of activation at the coalescence temperature were found to be in the range 16.5 (at 53.5 °C for *p*-nitro) ~22.4 (at 161 °C for *p*-amino derivative) kcal/mol. They give a Hammett σ^- ρ plot with $\rho=2.83$ ($r=0.976$). The results are interpreted in terms of an in-plane inversion about the imine nitrogen for the site-exchange. Noticeable deviation of the points representing *p*-chloro and *p*-bromo compounds from the linearity indicates the destabilization of the transition state by the electron-releasing resonance effect of the substituents and is consistent with the inversion mechanism.

Of recent years the mechanism of interconversion of (*Z*)- and (*E*)-*N*-arylimines has been the subject of considerable debate, and has been considered in terms of either an in-plane inversion (1) or a torsional mechanism (2).[2,3] The rate of isomerization is characteristically dependent on substituents at either side of the carbon-nitrogen bond of *N*-arylimines. The application of the Hammett linear free energy relationship to the process has shown that the rate is generally less sensitive to the nature of the *C*-aryl substituents. In *N*-benzylideneanilines, for example, substituents on the phenyl rings bound to nitrogen have a much larger effect on the isomerization rate, being correlated by $\rho=2.0$, while the ρ-value for substitution on the aldehyde ring is only +0.4 (at 30 °C).[2c] Since the torsional mechanism is favored by contribution of a dipolar transition state (I), there should be appreciable substituent effects at both the carbon and nitrogen rings as in the rotation of amide groups. On the other hand, an inversion transition state (II) should be stabilized by resonance interaction with the electron-withdrawing *N*-substituents as in amine inversion, but may be affected to a lesser extent by the *C*-aryl substituents. Thus an inversion mechanism appears in many cases to be preferred.[3] In hexafluoroacetone *N*-arylimines, however, a Hammett plot gives the ρ value of −0.98.[2n] The result is interpreted as being the consequence of a torsional mechanism, in which the single bond character of the imine bond is considered to be favored by contribution of electron-releasing substituents (III). All of these studies concern with *N*-arylimines which carry at the imine carbon atom groups with strong inductive and/or resonance interaction with the imine moiety.

As only limited information is available for the



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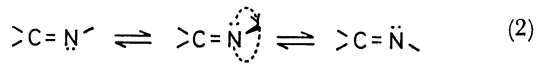

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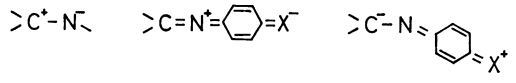


(I) (II) (III)

imines with the *C*-substituents of only moderate electronic effects, we wish to report here the kinetic study on the *N*-isopropylideneanilines.

Results

The temperature-dependent NMR spectra of a series of acetone *N*-arylimines[4] as dilute solutions in bromobenzene were examined. The two characteristic signals due to the (*Z*)- and (*E*)-methyl groups which are separated by 22 (for the *p*-NH_2) to 28.5 Hz (for the *m*-CF_3 derivative) were taken into account. The chemical shift differences between these two methyl signals for each imine change very little in the temperature range of −40 °C to +20 °C (in the case of *N*-isopropylidene-*p*-nitroaniline the range is −40 °C to −10 °C). As the temperature is raised, the two lines first start to broaden and then coalesce to a singlet. The coalescence temperature depends heavily on the nature of ring substituents. In a lower extreme of *N*-*p*-nitrophenylimine, it is only at 54 °C. In the other extreme it is as high as 161 °C for the *p*-amino derivative. One-point interconversion rate constants, k_c, at the coalescence temperature were obtained from the spectra using the relationship in Eq. (3) where ν_{ab} refers to the chemical shift difference of the two methyl singlets.[5] From the values of k_c and T_c thus determined, the free energy of activation at T_c, denoted $\Delta G_c^{\ddagger}$, was calculated using the Eyring equation and assuming as usual a value of unity for the transmission coefficient (Eq. (4)).

$$k_c = \pi \cdot \nu_{ab}/\sqrt{2} = 2.22\nu_{ab} \tag{3}$$

$$\ln(k/T) = \ln(k/h) - \Delta G^{\ddagger}/RT = \ln(k/h) + \Delta S^{\ddagger}/R - (\Delta H^{\ddagger}/RT) \tag{4}$$

The pertinent NMR and kinetic data are summarized in Table 1. Although it is difficult to estimate the error in such one-point rate constants, it can be shown that the value of $\Delta G_c^{\ddagger}$ is rather insensitive to the exact choice of k_c.[2e] It is desirable for the following discussion to compare the rates of interconversion at the same temperature. Strictly speaking, this can be done only with a knowledge of $\Delta S^{\ddagger}$ for each compound as seen in Eq. (4). Therefore the $\Delta G_c^{\ddagger}$ values are compared to show the substituent effects.

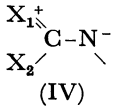
Table 1. NMR and kinetic data of *N*-isopropylideneanilines

X	T_c, °C	$\Delta\nu_{ab}$, Hz	k_c, s^{-1}	ΔG_c^*, kcal/mol	k_{25}, s^{-1} [a]
p-NH_2	161.1	22.0	48.9	22.4	2.36×10^{-4}
p-OCH_3	138.8	23.5	52.2	21.1	1.98×10^{-3}
p-CH_3	133.8	24.0	53.3	20.9	3.92×10^{-3}
H	127.1	25.5	56.7	20.5	6.06×10^{-3}
	126			20.3 [2b]	
p-F	124.4	25.0	55.5	20.3	7.68×10^{-3}
p-I	122.3	26.0	57.5	20.2	9.70×10^{-3}
p-Cl	130.8	26.5	58.9	20.6	4.71×10^{-3}
p-Br	128.3	26.5	58.9	20.5	5.92×10^{-3}
m-CF_3	110.2	28.5	63.2	19.5	3.22×10^{-2}
p-$COOCH_3$	99.7	27.0	59.9	19.0	7.76×10^{-2}
p-$COCH_3$	87.7	26.5	58.8	18.3	2.21×10^{-1}
p-NO_2	53.5	27.5	61.1	16.5	4.78×10^{-1}

a) The rate constants at 25 °C estimated on assuming a similar entropy of activation.

Discussion

The site-exchange of the methyl groups in *N*-isopropylideneanilines can be achieved either by an in-plane inversion at the nitrogen center or by rotation of the carbon-nitrogen bond (Eqs. (1) and (2), respectively). Both mechanisms are found to be actually operative in lower analogues; typical examples are the inversion in methyleneimine CH_2=NH and the rotation in carbodiimide HN=C=NH.[6] Attempts to choose between these mechanisms have been made by the application of the Hammett free energy relationship to the ΔG_c^* data in Table 1. On assuming a similar entropy of activation for the series of *N*-isopropylideneanilines, we note the results correspond to 10^3-fold enhancement of the rates at 25 °C on going from the *p*-amino to *p*-nitro derivatives. The increased facility of isomerization with electron-withdrawing groups on *N*-phenyl rings, as indicated by the positive slope, is consistent with a transition state of type II. A better linear correlation (ρ=2.83, r=0.976) is found when σ^- values are used in place of σ. The result suggests that the para-substituents capable of stabilizing a negative charge by resonance are especially favorable, thus providing further support for the transition state structure II. It may be argued that the same trend of $\sigma^-\rho$ correlation could also have been predicated for a rotational transition state I.[2k] However, two methyl groups are considered not to be strong enough to stabilize the positive charge on the imine carbon. In contrast to the groups such as dimethylamino, methoxy and methylthio which have unshared electron pairs on the heteroatoms that permit resonance stabilization of I, hyperconjugative effect of methyl groups are limited. The ΔG^* values for a series of *N*-phenylimines summarized in the first column of Table 2 afford an excellent insight into the effect of *C*-substituents. We note that the trasition state for the site-exchange in the acetone *N*-phenylimine under discussion is among the least stabilized. The lower free energies of activation for other *N*-phenylimines might suggest contribution of torsional character in the transition state which is stabilized as in IV, especially when the *C*-substituents X_1 and X_2 are Me_2N, MeO, and MeS. Since analyses of the *C*-aryl substituent effects,[2c,7] MO calculations,[8] and other arguments[9] have favored an inversion mechanism for the site-exchange process in these *N*-phenylimines, a torsional mechanism finds the remotest possibility in *N*-isopropylideneanilines.



(IV)

Further inspection of the Hammett plot reveals that the points for the *p*-chloro and *p*-bromo substituents deviate considerably from the linear correlation (see Fig. 1). The errors involved in the approximation used in the coalescence point method can be a responsible factor. However, they are expected to be systematic and may not be a reason for deviation of a particular point or two. It has been shown by the results of more elaborate procedure, *e.g.*, a total line shape analysis, on the similar quinoneanils and ketimines that the relative rates of interconversion are not a sensitive function of the choice of ΔS^* which is furthermore found not to be much different from zero.[2g,2j] It is well-documented that the increase in resonance release of electron density and in inductive electron withdrawal is effective in raising the barrier to inversion of amines.[3] The observed deviation suggests that

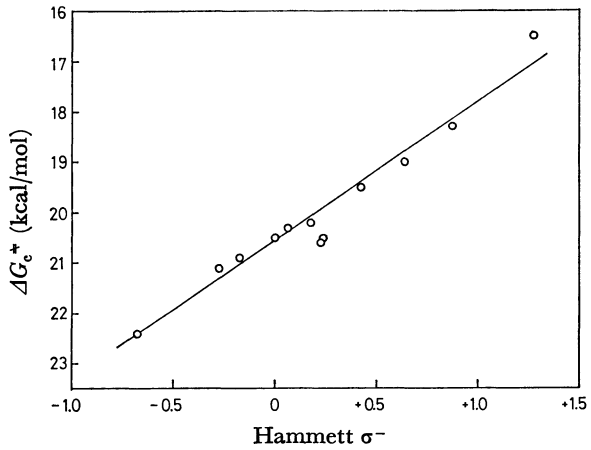
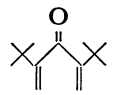


Fig. 1. The Hammett σ^- plots of $-\Delta G_c^*$ values for the site-exchange reaction.

Table 2. Hammett correlations in *N*-arylimines $X_1X_2C{=}NAr$

X_1	X_2	$\Delta G^{\ddagger}$ (T °C)	$\rho_{25°}$	Reference
Me_2N	Me_2N	12.1 (−35)	2.11	2h, 2l, 2m
Ph	H	16.5 (30)	2.04	2c, 2l
		22.2 (140)	1.90	2g, 2l
p-Me-OC_6H_4	*p*-Me-OC_6H_4	18.1 (62)	1.88	2e, 2l
CH_3	CH_3	20.5 (127)	1.71[a]	this work
MeO	MeO	14.3 (0)	1.44	2h
CF_3	CF_3	15.5 (25)	−0.98	2n
CH_3S	CH_3S	13.7 (−22)		2f

a) The rate constants at 25 °C estimated on assuming a similar entropy of activation.

both electronic substituent effects are not adequately represented by the Hammett σ^- constants. The standard Hammett σ values of 0.227 and 0.232 for the *p*-Cl and *p*-Br substituents, respectively, reflect the interplay of the electron-withdrawing inductive (σ_i; 0.348 and 0.337, respectively) and electron-donating resonance effects (σ_π; −0.070 and −0.054, respectively).[10] The fact that the rates of interconversion in *p*-Cl and *p*-Br compounds are slower than in the parent *N*-isopropylideneanilines, *i.e.*, $k_{Cl}/k_H=0.78$ and $k_{Br}/k_H=0.98$,[11] means that resonance substituent effect dominates the stability of the transition state. Precedent for the prevalence of the resonance substituent effect can be found in the pyramidal inversion of aryl *p*-tolyl sulfoxides.[12] Electronic effects on the inversion process for both series of compounds, namely, acetone *N*-arylimines and aryl *p*-tolyl sulfoxides, are quite similar.

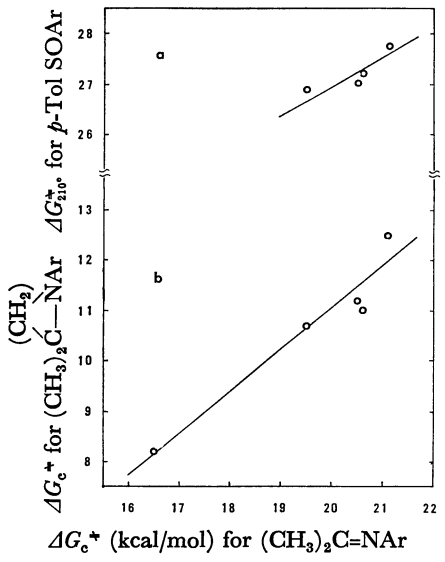
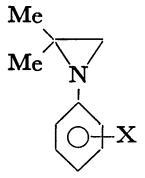


Fig. 2. Correlation of $\Delta G_c^{\ddagger}$ values for inversion of (a) aryl *p*-tolyl sulfoxides and (b) 2,2-dimethyl-1-arylaziridines *vs.* *N*-isopropylideneanilines.

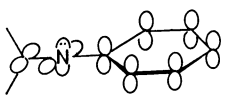
While the Hammett plots against σ^- give positive slopes as a whole, the relative rates k_{Cl}/k_H are equally less than unity (0.78, at 25 °C in the former and 0.81 at 210 °C in the latter). As a result, the $\Delta G^{\ddagger}$ values correlate very nicely between the two series as shown in Fig. 2a.

Of related interest to the inversion of *N*-arylimine nitrogen is the pyramidal inversion of 1-aryl-2,2-dimethylaziridines (V).[13] When we consider the structural similarity with respect to the unit Me_2C–N–Ar between *N*-isopropylideneanilines and V, it is not unexpected that plots of $\Delta G^{\ddagger}$ values of V *vs.* those of the former show good linear correlation (Fig. 2b). This is taken as another support for an inversion mechanism in the *N*-arylimines. The slope of the line, 0.84, may be regarded as a measure of the sensitivity of the *N*-isopropylideneanilines relative to the aziridines to electronic substituent effects. Furthermore the point for the *N*-*p*-chlorophenylaziridine conforms to the Hammett correlation defined by the other aziridines V; $k_{Cl}/k_H=1.7$ at −60 °C.[13] Thus resonance substituent effects appear not to be dominant in V. These two points, slightly diminished sensitivity to ring substituents and reduced resonance substituent effects in V, indicate that the structural analogy between *N*-arylimines and *N*-arylaziridines for inversion at the

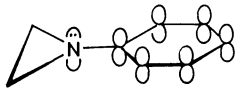


(V)

nitrogen center is only superficial. We propose as one of a number of possible origins of the more effective transmission of substituent effects in the *N*-arylimines relative to *N*-arylaziridines the difference in the nitrogen hybridization in the transition state for inversion, In the *N*-arylimines, the nitrogen center is sp hybridized and the lone pair of electrons reside in a purely *p*-charactered AO which is most favorably situated to conjugate with the benzene ring (VI). The carbon-nitrogen bonds of aziridine rings are rich in *p*-character as approximated by $sp^{4.1}$ hybridization for the cyclopropane ring orbitals in the Coulson-Moffit model.[14] As a result, the hybridized orbital in which lone pair of electrons reside has some s character to effect reluctance to delocalize into the aromatic ring (VII).

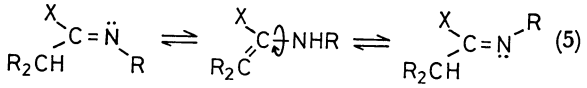


VI



VII

Recently a third mechanism in which tautomerization to the enamine (Eq. 5) has been proposed for the imines which contain a *C*-alkyl-substituent with at least



(5)

one α-hydrogen atom.[7] The mechanism has been

shown to be operative in some *N*-alkylimines in which barriers to inversion can often be high ($\Delta G^{\ddagger}\sim25$ kcal/mol).[7] The tautomerism has been shown by the deuterium incorporation experiments in methanol-d_4 to be considerably slower(10^{-5}—10^{-6} s^{-1})[1] than inversion (10^{-1}—10^{-4} s^{-1})[11] in *N*-isopropylideneanilines. Therefore the site-exchange of the methyl groups *via* imine-enamine tautomerism can be ruled out in the case of *N*-isopropylideneanilines.

Experimental

General procedure for the preparation of *N*-isopropylideneanilines:[4] 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 2 to 3 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.

NMR spectra were obtained on a JEOL C-60HL (Japan Electron Optics Lab. Co., Ltd.) spectrometer (60 MHz), equipped with a variable temperature probe. Solutions of 0.25 mmol of *N*-isopropylideneanilines in 0.5 ml bromobenzene (25 °C——40 °C) containing TMS as internal references were employed. Temperature were calibrated by 1,3-propanediol in the region of 25 °C—160 °C, and by methanol in the region 25 °C——40 °C, and are believed to be accurate to ±1 °C. In the recording of spectra, care was taken to avoid saturation of the signal especially when the height intensity is weak near the coalescence point. Three or more spectra were recorded in the vicinity of each coalescence temperature.

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