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Kinetics and Mechanism of Reactions of Benzhydryl Chlorides with Anilines

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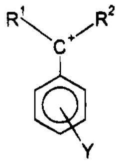
Nucleophilic substitution reactions of substituted benzhydryl chlorides with anilines in acetonitrile and methanol are investigated. The reactions are found to proceed by the attack of nucleophile on the preformed carbocation, **I**, within the ion pair. The cross-interaction constants, ρ_{XY}, are relatively large in both acetonitrile ($\rho_{XY} = -2.47$) and methanol ($\rho_{XY} = -1.46$). The isokinetic points ($\hat{\sigma}_Y^+$) where ρ_X (ρ_{nuc}) is zero and the sign of ρ_X changes, are observed at positive substrate substituent constants, $\hat{\sigma}_Y^+ = 0.13$ and 0.22 in acetonitrile and methanol, respectively. The isokinetic phenomenon ($\rho_X = 0$) has been shown to occur when the thermodynamic driving force, $\Delta G°$, is practically completely compensated for by the intrinsic barrier, $\Delta G_o^{\ddagger}$. The two change in a compensatory manner; the intrinsic barrier becomes higher when resonance electron delocalization of the Y substituent to C_α is stronger, which in turn results when the thermodynamic driving force becomes higher by stronger electron-withdrawing α-substituents, R^1 and/or R^2.

Introduction

Recently, the effects of α-substituents, R^1 and R^2, on the reactivity and mechanism of nucleophilic substitution at the carbocations, **I**, have attracted considerable interest.[1−6] The rate of nucleophilic substitution at a benzylic carbocation, **I**, has been shown to be relatively constant for a wide variety of α-substituents, R^1 and/or R^2, with a strongly electron-donating ring substituent, e.g., Y = p-CH_3O.[4e] For example, carbocation **I** (Y = CH_3O) is more stable with $R^1 = R^2 = CH_3$ (by 23 kcal mol^{-1} experimentally[4e] and by 27 kcal mol^{-1} MO theoretically with the AM1 method)[6e] than that with $R^1 = R^2 = CF_3$, but the solvolysis rate was found to be similar.[4e] This was attributed to (i) a more efficient resonance electron delocalization from Y to C_α when strong electron-withdrawing substituents, R^1 and/or R^2, are substituted on the α-carbon and (ii) an imbalance in the expression of polar and resonance substituent effects in the transition state (TS) leading to a more advanced loss, and hence a greater contribution, of the resonance interaction than the polar interaction in the TS.[1a,4e] Thus, a thermodynamically more unstable, and hence more reactive due to a greater thermodynamic driving force, compound (e.g., **I** with $R^1 = R^2 = CF_3$) is kinetically (or intrinsically) more unfavorable due to the rate retardation caused by a greater loss or destruction of resonance structure required in the TS, which in effect increases the intrinsic barrier.



I

On the other hand, addition of a nucleophile to a resonance-stabilized carbocation center, **I**, is characterized by a manifestation of the observable sign reversal of ρ_X (ρ_{nuc}) to $\rho_X > 0$ from the normal $\rho_X < 0$ with a relatively large magnitude of the cross-interaction constant,[4e,6a] ρ_{XY} in eq 1,[7] where X and Y denote the

$$\log (k_{XY}/k_{HH}) = \rho_X^\circ\sigma_X + \rho_Y^\circ\sigma_Y + \rho_{XY}\sigma_X\sigma_Y \qquad (1)$$

substituents in the nucleophile and substrate, respectively, and the degree symbol in ρ_i° (i, j = X or Y) indicates the ρ_i value for j = H or $\sigma_j = 0$. The isokinetic (noninteractive[8] or isoparametric[9]) point $\hat{\sigma}_Y$, at which the ρ_X becomes zero (and hence the reaction becomes isokinetic with no cross-interaction[8]) can be derived by transforming eq 1.[6] In the reaction of 1-phenylethyl chloride with aniline in methanol, an isokinetic point of $\hat{\sigma}_Y^+ = -0.23$ was observed at which $\rho_X = 0$ and ρ_X changed

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$$\log (k_{XY}/k_{HH}) = \rho^\circ_Y \sigma_Y + (\rho^\circ_X + \rho_{XY}\sigma_Y)\sigma_X$$

$$= \rho^\circ_Y \hat{\sigma}_Y = -\frac{\rho^\circ_X \rho^\circ_Y}{\rho_{XY}} = \text{constant} \quad (2)$$

$$\text{where } \hat{\sigma}_Y = -\frac{\rho^\circ_X}{\rho_{XY}} \quad (3)$$

sign from $\rho_X < 0$ for $\hat{\sigma}_Y{}^+ < \sigma_Y{}^+$ to $\rho_X > 0$ for $\hat{\sigma}_Y{}^+ > \sigma_Y{}^+$.[6] This reaction has been shown to proceed by a nucleophilic attack of 1-phenylethyl carbocation (R^+) in the tight ion pair (R^+Cl^-) by the aniline nucleophile. It has been suggested that the isokinetic phenomenon with the sign reversal of ρ_X is related to the TS imbalance associated with the nucleophilic addition of a neutral molecule to a stable carbocation.[6c]

In this work, we carried out kinetic studies on the nucleophilic addition reaction at another stable benzylic carbocation to demonstrate further the isokinetic phenomenon using the reaction of monosubstituted benzhydryl chlorides with anilines in acetonitrile at 65.0 °C and methanol at 35.0 °C, eq 4.

$$YC_6H_4CR^1R^2Cl + 2XC_6H_4NH_2 \xrightarrow[CH_3OH\text{ at }35.0\text{ °C}]{CH_3CN\text{ at }65.0\text{ °C}} YC_6H_4CR^1R^2NHC_6H_4X + XC_6H_4NH_3{}^+ + Cl^- \quad (4)$$

$R^1 = H, R^2 = C_6H_5$

$X = p\text{-}CH_3O, p\text{-}CH_3, H, p\text{-}Cl, m\text{-}NO_2, \text{ or } p\text{-}NO_2$

$Y = p\text{-}CH_3, H, p\text{-}Cl, m\text{-}Cl, m,p\text{-}(Cl)_2, \text{ or } p\text{-}NO_2$

Results

Aminolyses of benzhydryl chlorides in both acetonitrile and methanol under pseudo-first-order conditions obey a simple second order rate law, eq 5.

$$k_{obsd} = k_1 + k_2[\text{aniline}] \quad (5)$$

where $k_1 = 0$ in MeCN while k_1 in MeOH obtained as an intercept in eq 5 was found to agree within experimental error with the methanolysis rate constant determined independently.

The chloride common ion effect was examined by adding KCl in the methanolysis reaction systems. The results in Table 1 indicate that there is very small common ion rate depression at relatively low KCl concentration. As the KCl concentration is increased, however, the normal salt effect of increasing rate is observed.

In order to examine the isotope effects in the methanolysis, the solvent kinetic isotope effects, k_{SOH}/k_{SOD}, were determined as shown in Table 2. The isotope effects are near unity, but for Y = p-NO$_2$ the value is less than 1. A similar trend in the solvent kinetic isotope effects has been observed in the methanolysis of 1-phenylethyl chloride.[10]

Aniline possesses two equivalent mobile protons on its nitrogen, one of which is transfered to another molecule when the aniline reacts to form an anilide, whereas pyrrolidine has one proton on its nitrogen which is to be transfered in the reaction. We determined kinetic isotope effects in acetonitrile with deuterated anilines and pyrrolidine. The isotope effects with deuterated aniline nucleophiles (Table 3) are inverse-type secondary isotope effects (k_H/k_D < 1.0) while they are greater than unity (k_H/k_D > 1.0) with deuterated pyrrolidine (Table 4). The magnitude of the latter are similar to those obtained by Menger et al. for the reactions of p-nitrophenyl acetate with deuterated primary and secondary amines.[11]

Table 1. Solvolysis Rate Constants, k_1, for the Reactions of p-Methyl- and p-Nitrobenzhydryl Chlorides with KCl (M) Added in Methanol at 35.0 °C

	[KCl] (M)				
Y	0.00	0.01	0.02	0.03	0.04
p-CH$_3$ k_1 ($\times 10^2$)	5.52	5.34	5.16	5.37	5.63
p-NO$_2$ k_1 ($\times 10^6$)	2.19	1.46	0.97	1.04	1.86

Table 2. First-Order Rate Constants for the Solvolysis of Y-Benzhydryl Chlorides in Methanol and Deuterated Methanol at 35.0 °C

Y	MeOH (s^{-1})	MeOD (s^{-1})	k_{SOH}/k_{SOD}
p-CH$_3$	$(5.52 \pm 0.03)^a \times 10^{-2}$	$(4.71 \pm 0.02) \times 10^{-2}$	$1.17_2 \pm 0.00_8{}^b$
H	$(2.61 \pm 0.01) \times 10^{-3}$	$(2.47 \pm 0.02) \times 10^{-3}$	$1.05_7 \pm 0.00_6$
p-Cl	$(9.88 \pm 0.02) \times 10^{-4}$	$(8.36 \pm 0.05) \times 10^{-4}$	$1.18_2 \pm 0.00_9$
m-Cl	$(7.50 \pm 0.05) \times 10^{-5}$	$(6.92 \pm 0.02) \times 10^{-5}$	$1.08_4 \pm 0.00_8$
p-NO$_2$	$(2.19 \pm 0.02) \times 10^{-6}$	$(2.27 \pm 0.03) \times 10^{-6}$	$0.96_5 \pm 0.00_1$
	$\rho_Y{}^+{}_{(H)} = -3.98$	$\rho_Y{}^+{}_{(D)} = -3.91$	

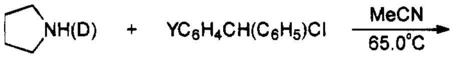
[a] Standard deviation. [b] Standard error: Crumpler, T. B.; Yoh, J. H. *Chemical Computations and Error*; Wiley: New York, 1940; p 178.

Table 3. Kinetic Isotope Effects for the Reactions of Y-Benzhydryl Chlorides with Deuterated X-Anilines in Acetonitrile at 65.0 °C

X	Y	k_H ($\times 10^5$) (M^{-1} s^{-1})	k_D ($\times 10^5$) (M^{-1} s^{-1})	k_H/k_D
p-CH$_3$O	p-CH$_3$	50.2 ± 0.9^a	55.4 ± 0.8	$0.90_6 \pm 0.00_8{}^b$
p-CH$_3$O	m-Cl	2.14 ± 0.02	2.52 ± 0.07	$0.84_9 \pm 0.00_9$
p-Cl	p-CH$_3$	127 ± 2	131 ± 2	$0.97_0 \pm 0.01_2$
p-Cl	m-Cl	1.29 ± 0.02	1.46 ± 0.08	$0.88_4 \pm 0.00_8$

[a] Standard deviation. [b] Standard error: Crumpler, T. B.; Yoh, J. H. *Chemical Computations and Error*; Wiley: New York, 1940; p 178.

Table 4. Kinetic Isotope Effects for the Reactions of Y-Benzhydryl Chlorides with Deuterated Pyrrolidine in Acetonitrile at 65.0 °C



Y	k_H ($\times 10^4$) (M^{-1} s^{-1})	k_D ($\times 10^4$) (M^{-1} s^{-1})	k_H/k_D
p-CH$_3$	11.8 ($\pm$0.1)^a	10.6 ($\pm$0.2)	$1.11_3 \pm 0.00_8{}^b$
H	4.21 ($\pm$0.05)	4.10 ($\pm$0.02)	$1.02_7 \pm 0.00_6$
p-Cl	1.78 ($\pm$0.02)	1.74 ($\pm$0.01)	$1.02_3 \pm 0.00_9$

[a] Standard deviation. [b] Standard error: Crumpler, T. B.; Yoh, J. H. *Chemical Computations and Error*; Wiley: New York, 1940; p 178.

The salt effects on the rate of nucleophilic substitution reaction of benzhydryl chloride with aniline were investigated using low concentrations of NaClO$_4$. The results are summarized in Table 5. For Y = p-CH$_3$ with X = p-CH$_3$O, the initial increase in the rate is relatively large (ca. 20% increase in k$_2$ at [NaClO$_4$] = 0.01 M) as can be seen in Figure 1. Since the concentration of substrate, benzhydryl chloride, used was ca. 5.0×10^{-4} mol dm^{-3},

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Table 5. Second-Order Rate Constants, k_2 ($\times 10^5$) ($dm^3\ mol^{-1}\ s^{-1}$),[a] for the Reactions of Y-Benzhydryl Chlorides with X-Anilines, wth $NaClO_4$ (M) Added in Acetonitrile at 65.0 °C

X	Y	[NaClO4] (M)								
		0.0	0.0015	0.002	0.003	0.006	0.01	0.02	0.03	0.04
p-CH_3O	*p*-CH_3	50.2	53.1	54.0	56.3	58.1	60.3	62.2	63.5	64.3
p-CH_3O	*m*-Cl	2.14	2.29	2.38	2.52	2.66	2.69	2.74	2.79	2.84
H	H	8.71	10.2	10.7	11.2	11.7	12.2	12.6	12.9	13.3

[a] Average of three to five determinations.

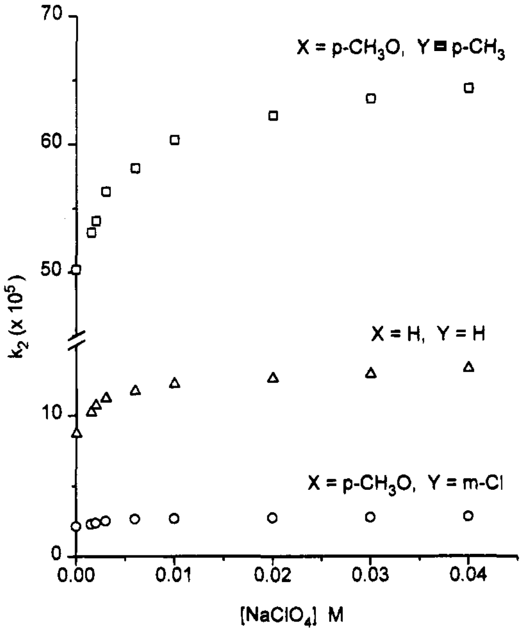


Figure 1. Plots of second-order rate constants *vs* [$NaClO_4$] (M) for the reactions of Y-benzhydryl chlorides with X-anilines, with $NaClO_4$ added in acetonitrile at 65.0 °C.

Table 6. Second-Order Rate Constants, k_2 ($\times 10^5$) ($dm^3\ mol^{-1}\ s^{-1}$), for the Reactions of Y-Benzhydryl Chlorides with X-Anilines in Acetonitrile at 65.0 °C

X	Y				
	p-CH_3	H	*p*-Cl	*m*-Cl	*p*-NO_2
p-CH_3O	5.02	7.59	4.46	2.14	1.82
p-CH_3	57.5	7.94	4.57	2.01	1.29
H	83.2	8.71	4.75	1.65	0.955
p-Cl	127	11.0	4.90	1.29	0.550
p-NO_2	447	15.8	5.43	0.661	
ρ_X[a]	0.92	0.32	0.08	−0.50	−1.01
β_X[b]	−0.23	−0.07	−0.02	0.12	0.40

[a] The correlation coefficients were better than 0.995 in all cases.
[b] The correlation coefficients were better than 0.979 in all cases.

Table 7. Second-Order Rate Constants, k_2 ($\times 10^5$) ($dm^3\ mol^{-1}\ s^{-1}$), for the Reactions of Y-Benzhydryl Chlorides with X-Anilines in Methanol at 35.0 °C

X	Y					
	p-CH_3	H	*p*-Cl	*m*-Cl	*m*,*p*-Cl_2	*p*-NO_2
p-CH_3O	1652	164	84.4	8.43	6.81	2.17
p-CH_3	2040	166	90.6	8.30	6.20	1.73
H	2829	199	94.2	8.25	5.50	1.28
p-Cl	5456	240	101	7.95	4.54	0.906
m-NO_2	13435	325	119	7.79	3.08	0.380
ρ_X[a]	0.95	0.32	0.14	−0.04	−0.35	−0.76
β_X[b]	−0.32	−0.11	−0.059	0.01	0.12	0.25

[a] The correlation coefficients were better than 0.968 in all cases.
[b] The correlation coefficients were better than 0.960 in all cases.

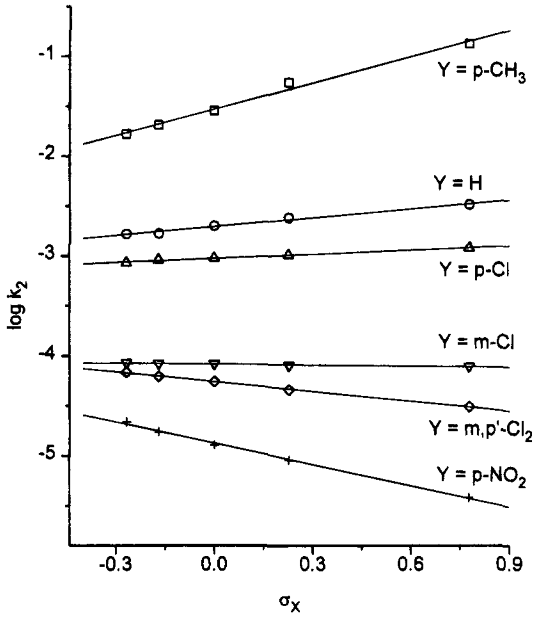


Figure 2. Hammett plots (ρ_X) for the reactions of Y-benzhydryl chlorides with X-anilines in methanol at 35.0 °C.

the salt effect due to the reaction product ions formed during the reaction on the rate can be considered insignificant at this substrate concentration.

The second-order rate constants, k_2 ($dm^3\ mol^{-1}\ s^{-1}$), *obtained by eq 5 for the reactions of monosubstituted* (Y) benzhydryl chlorides with substituted (X) anilines in acetonitrile at 65.0 °C and in methanol at 35.0 °C, are summarized in Tables 6 and 7, respectively. We note that the rate is much faster in methanol than in acetonitrile. The methanolysis rate constants, k_1 (s^{-1}), determined independently, are given in Table 2. The rates of methanolysis are in general of a similar order of magnitude with those for the aminolysis in methanol, Table 7. The two reactions, methanolysis and aminolysis, compete but do not interfere each other in any way. The Hammett and Brönsted plots for the substituent changes in the nucleophile (σ_X) were linear with sign reversals in ρ_X (ρ_{nuc}) and β_X (β_{nuc}) as listed in Tables 6 and 7. The Hammett plots for the reactions in methanol are shown in Figure 2. The Hammett plots involving substituent changes in the substrate (σ_Y^+) are curvilinear for both reactions in MeCN and MeOH; an example is shown in Figure 3 for the reactions in acetonitrile. The cross-interaction constants, ρ_{XY}, determined by subjecting the rate constants in Tables 6 and 7 to multiple linear regression using eq 1, were $\rho_{XY} = -2.47$ and -1.46 in MeCN and MeOH, respectively. The calculated isokinetic points, $\hat{\sigma}_Y^+$, using eq 3 were $\hat{\sigma}_Y^+ = 0.13$ and 0.22 for the reactions in MeCN and MeOH, respectively. There is a good agreement between the calculated $\hat{\sigma}_Y^+$ value (using eq 3) and the isokinetic point obtained in the log k_2 versus σ_Y^+ plots as shown in Figure 3 for the reactions in MeCN.

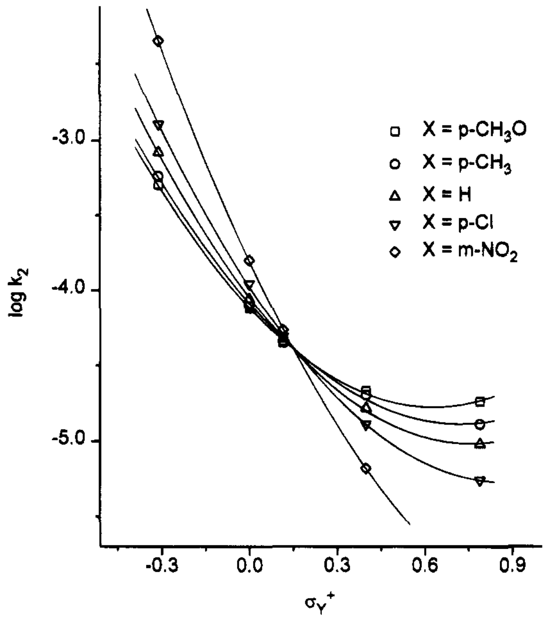
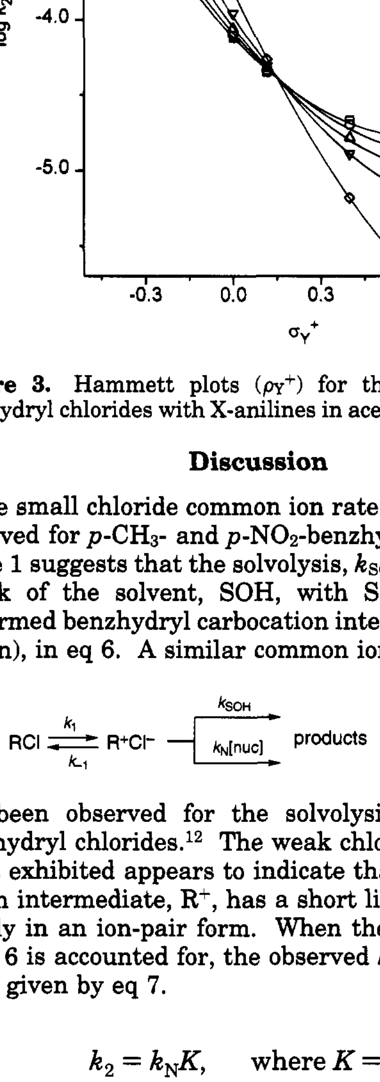


Figure 3. Hammett plots (ρ_Y^+) for the reactions of Y-benzhydryl chlorides with X-anilines in acetonitrile at 65.0 °C.

Discussion

The small chloride common ion rate depression effect observed for p-CH$_3$- and p-NO$_2$-benzhydryl chlorides in Table 1 suggests that the solvolysis, k_{SOH}, takes place by attack of the solvent, SOH, with S = CH$_3$, on the preformed benzhydryl carbocation intermediate, R$^+$ (not shown), in eq 6. A similar common ion rate depression



(6)

has been observed for the solvolysis of substituted benzhydryl chlorides.[12] The weak chloride common ion effect exhibited appears to indicate that the free carbocation intermediate, R$^+$, has a short lifetime and exists mostly in an ion-pair form. When the pre-equilibrium in eq 6 is accounted for, the observed k_2 values from eq 5 are given by eq 7.

$$k_2 = k_N K, \qquad \text{where } K = \frac{k_1}{k_{-1}} \qquad (7)$$

The kinetic solvent isotope effects, KSIE = k_{SOH}/k_{SOD}, in Table 2 are very similar to those for the reactions of 1-phenylethyl carbocations with methanol.[10] The k_{SOH}/k_{SOD} value decreases from 1.17$_2$ for Y = p-CH$_3$ to 0.96$_5$ for Y = p-NO$_2$, and the $\Delta\rho_Y^+$ value defined in eq 8[13] is

$$\frac{\Delta \log \text{KSIE}}{\Delta\sigma_Y} = \rho_Y{}^+{}_{(SOH)} - \rho_Y{}^+{}_{(SOD)} = \Delta\rho_Y{}^+ \qquad (8)$$

small negative, $\Delta\rho_Y{}^+ = -0.07$. For normal S$_N$1 and S$_N$2 reactions at neutral substrates, $\Delta\rho_Y{}^+$ is found to be either zero or positive.[13] The negative $\rho_Y{}^+$ and $\Delta\rho_Y{}^+$ values observed are again an indication of the ion-pair mechanism, eq 6.[13]

The secondary kinetic isotope effects involving deuterated nucleophiles are not affected by using k_2 rather than k_N since K in eq 7 is independent of the nucleophile (X) (vide infra). The values summarized in Tables 3 and 4 are consistent with the ion-pair mechanism, eq 6. For the nucleophilic attack at a relatively stable carbocation by a nucleophile, general base catalysis is often observed.[1b,c,6a,14] For one proton system, pyrrolidine, partial deprotonation due to general base catalysis requires a primary kinetic isotope effect with $k_H/k_D > 1.0$ as observed. However, for the two-proton system, aniline, frequencies of one N−H vibration will increase greatly due to a considerable steric crowding in the TS by a bulky α-ring with a strong inverse secondary kinetic isotope effect, $k_H/k_D < 1.0$, in addition to a partially deprotonated N−H bond with $k_H/k_D > 1.0$. The sum result is the predominance of the former, i.e., the inverse secondary kinetic isotope effect ($k_H/k_D < 1.0$) of the nondeprotonating N−H bond. The more stabilized carbocation with Y = CH$_3$ has a greater k_H/k_D value, which is consistent with the fact that the more stable carbocation requires a greater degree of deprotonation due to general base catalysis, i.e., $k_H/k_D > 1.0$.[1b,c,6a,14]

The salt effects in Table 5 are relatively small. However a rather steep initial rise in the rate of Y = CH$_3$ may be attributed to a special salt effect, which is considered to arise due to extra stabilization of the benzhydryl carbocation, R$^+$, within the solvent-separated ion pair by the perchlorate anion added.[15] This effect is stronger with the more stable carbocation (with Y = p-CH$_3$) rather than a more unstable carbocation (with Y = m-Cl) which may be short lived.

In general, ρ_X (ρ_{nuc}) is negative (or β_X (β_{nuc}) is positive) in the nucleophilic substitution reactions[7] at a neutral carbon center, and hence, the observation of positive ρ_X (or negative β_X) in Tables 6 and 7 is highly unusual. One may cast doubt about the reality of such a positive ρ_X based on the following two arguments:

(i) The positive ρ_X (or negative β_X) in Tables 6 and 7 is the result of a desolvation effect. Such unusual negative β_X (β_{nuc}) values that can be ascribable to the desolvation of nucleophile have indeed been observed.[16]

It can be shown, however, that this argument is false and is not applicable: The solvent, MeOH, has a higher solute hydrogen bond basicity[17] ($\beta^H{}_2 = 0.47$) than the aniline nucleophiles used ($\beta^H{}_2 = 0.30-0.45$) (except p-MeO-aniline, $\beta^H{}_2 = 0.65$) so that the H-bonds between MeOH molecules are stronger than those between MeOH and aniline nucleophile. Moreover, excellent linearities found for the plots of log k_2 versus σ_X suggest that the desolvation of any aniline nucleophile before or during the rate-determining step cannot affect the rate constant, k_2. This is also supported by the similar trends observed for ρ_X in MeOH and in MeCN, since solvation of the aniline nucleophile should be negligible in MeCN.[16d,18] For example, in Tables 6 and 7

$$\rho_X = 0.95\ (\beta_X = -0.32) \text{ in MeOH at 35.0 °C} \quad \text{for } Y = p\text{-Me}$$

$$\rho_X = 0.92\ (\beta_X = -0.23) \text{ in MeCN at 65.0 °C} \quad \text{for } Y = p\text{-Me}$$

In this example, the negative β_X (β_{nuc}) values exceed the

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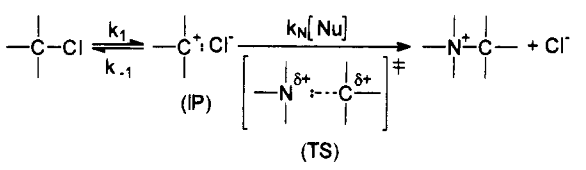
[12] Bailey, T. H.; Fox, J. R.; Jackson, E.; Kohnstam, G.; Queen, A. *Chem. Commun.* **1966**, 122.

[13] Lee, I.; Koh, H. J.; Park, Y. S.; Lee, H. W. *J. Chem. Soc., Perkin Trans. 2* **1993**, 1575.

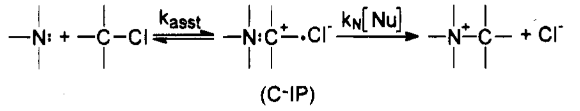
[14] Bentley, T. W.; Ryu, Z. H. *J. Chem. Soc., Perkin Trans. 2* **1994**, 761.

[15] Lowry, T. H.; Richardson, K. S. *Mechanism and Theory in Organic Chemistry*, 3rd ed.; Harper and Row: New York, 1987; p 345.

Scheme 1



Scheme 2



$\beta_X = -0.2$[16] suggested for the equilibrium desolvation for nucleophiles of much higher basicity, $pK_a(RNH_3^+) > 8$, than the aniline nucleophiles used in our work ($pK_a = 3.5-5.3$).[19] The lower values of ρ_X and β_X in MeCN are undoubtedly due partly to the higher temperature in MeCN, since the numerical values of all first derivative susceptibility parameters are known to decrease with a rise in the reaction temperature.[20]

(ii) The positive ρ_X (and negative β_X) values are obtained because macroscopic rate constants, k_2, are used instead of microscopic rate constants, k_N, in the determination in Scheme 1; in other words, it is due to neglect of K in $k_2 = Kk_N$.

This argument can also be shown to be untenable: (a) Although there is evidence that nucleophilic assistance by nucleophile to ionization, k_{asst} in Scheme 2, is insignificant,[4c] let us nevertheless *assume* that there is such an assistance (Scheme 2). A stronger, or more basic, nucleophile ($\delta\sigma_X < 0$) will form more stabilized encounter complex between nucleophile and ion pair (C-IP) leading to an increase in K. As a result, $\rho_X(K)$ will become negative, eq 9. The negative $\rho_X(K)$ will in turn result in

$$\rho_X(K) = \frac{\partial \log K}{\partial \sigma_X}\left(= \frac{(+)}{(-)}\right) < 0 \qquad (9)$$

a more negative $\rho_X(k_2)$ than $\rho_X(k_N)$, i.e., $\rho_X(k_2) < \rho_X(k_N)$. This means that the positive value observed, $\rho_X(k_2) > 0$, is in fact less positive than the true microscopic $\rho_X(k_N)$ if we assume K is not independent of σ_X, eq 10. It is

$$\rho_X(k_2) = \rho_X(K) + \rho_X(k_N)\ (= (-) + (+)) \qquad (10)$$

therefore concluded that the positive ρ_X (and negative β_X) values observed are not due to the neglect of the effect of nucleophile on K.

(b) Since the concentration or amount of the encounter complex, [C-IP], will be greater for the more stabilized cation with a stronger donor Y, $\delta\sigma_Y < 0$, $\rho_X(K)$ and, hence, $\rho_X(k_2)$ will become more negative as a result of the shift of the equilibrium to the right, $\delta\rho_X(K) < 0 \rightarrow \delta\rho_X(k_2) < 0$. This is an opposite trend to what we observe, i.e., a more positive $\rho_X(k_2)$ is obtained for a stronger donor Y. This analysis also leads to a positive sign for $\rho_{XY}(K)$, eq 11.

$$\rho_{XY}(K) = \frac{\delta \rho_X(K)}{\delta \sigma_Y}\left(= \frac{(-)}{(-)}\right) > 0 \qquad (11)$$

(c) The observed $\rho_{XY}(k_2)$ should be a small negative quantity assuming nucleophilic assistance by nucleophile to ionization, since $\rho_{XY}(K)$ is positive, eq 11, and $\rho_{XY}(k_N)$ is negative (vide infra, eq 15).

$$\rho_{XY}(k_2) = \rho_{XY}(K) + \rho_{XY}(k_N)\ (= (+) + (-)) = \text{small negative}$$

However, this expectation is not fulfilled, since we obtain a relatively large negative $\rho_{XY}(k_2)$ value. For normal S_N2 processes, the ρ_{XY} values are smaller with $\rho_{XY} = -0.6$ to -0.8.[7]

$$\rho_{XY}(k_2) = -2.47 \text{ in MeCN at } 65.0\ ^\circ\text{C for } Y = H$$

$$\rho_{XY}(k_2) = -1.46 \text{ in MeOH at } 35.0\ ^\circ\text{C for } Y = H$$

We conclude that the effect of σ_X on K is insignificant, and hence, the macroscopic ρ_X ($\rho_X(k_2)$) is equal to the microscopic ρ_X ($\rho_X(k_N)$) and the observed positive $\rho_X(k_2)$ values are not due to neglect of the effect of σ_X on K.

Further support for the ion-pair mechanism, Scheme 1, is provided by the trends in the plots of $\log k_2$ against σ_Y^+. Scheme 1 omits the differentiation of initially formed ion pairs and solvent-separated ion pairs, since our data do not directly elucidate the respective roles of the two types of ion pairs. Moreover, there is evidence that nucleophilic additions to a free carbocation and its ion pair occur with similar rate constants.[4a,21]

The observed macroscopic $\rho_Y(k_2)$ can be expressed as a sum of the two component ρ_Y terms, eq 12.

$$\rho_Y(k_2) = \rho_Y(K) + \rho_Y(k_N) \qquad (12)$$

The signs of each ρ_Y can be determined: (a) A more resonance-stabilized carbocation by a stronger electron donor Y, $\delta\sigma_Y < 0$, will result in a greater equilibrium constant, $\delta \log K > 0$, leading to a negative $\rho_Y(K)$, $\rho_Y(K) = \delta \log K/\delta\sigma_Y$ $(= (+)/(-)) < 0$. Experimentally, in solution[1a,2c] and in gas phase,[5] large negative $\rho_Y(K)$ values are indeed observed ranging -10 to -14.

(b) A more positive benzylic carbon, C_α, by a stronger electron acceptor Y, $\delta\sigma_Y > 0$, will induce a more facile cation–nucleophile combination, $\delta \log k_N > 0$, leading to a positive $\rho_Y(k_N)$, $\rho_Y(k_N) = \delta \log k_N/\delta\sigma_Y$ $(= (+)/(+)) > 0$. Again, positive $\rho_Y(k_N)$ values are observed experimentally.[16d]

(c) The observed $\rho_Y(k_2)$ value is given by the sum of the two component terms; a negative value is expected since $\rho_Y(K)$ is large negative but $\rho_Y(k_N)$ is moderately positive. This means that the macroscopic ρ_Y, ($\rho_Y(k_2)$), is not the same as the microscopic, ρ_Y ($\rho_Y(k_N)$), $\rho_Y(k_2) \neq \rho_Y(k_N)$. The observed slopes of the plots of $\log k_2$ versus σ_Y,

$$\rho_Y(k_2) = \rho_Y(K) + \rho_Y(k_N)\ (= (-\,-) + (+)) < 0 \qquad (13)$$

$$|\rho_Y(K)| > |\rho_Y(k_N)|$$

$\rho_Y(k_2)$, were all negative. However, the negative slopes

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[16] (a) Jencks, W. P.; Haber, M. T.; Herschlag, D.; Nazaretian, K. I. *J. Am. Chem. Soc.* **1986**, *108*, 479. (b) Richard, J. P. *J. Chem. Soc., Chem. Commun.* **1987**, 1768. (c) Jencks, W. P. In *Nucleophilicity*; Harris, M., McManus, S., Eds.; Adv. in Chem. Series; *American Chemical Society*: Washington, DC, 1987; p 155. (d) McClleland, R. A.; Kanagasabaphathy, V. M.; Banait, N. S.; Steenken, S. *J. Am. Chem. Soc.* **1992**, *114*, 1816.

[17] Abraham, M. H. *Chem. Soc. Rev.* **1993**, *22*, 73.

[18] Johnson, C. D.; Roberts, I.; Taylor, P. G. *J. Chem. Soc., Perkin Trans. 2* **1981**, 409.

[19] pK_a values for anilinium ion: Dean, J. A. *Handbook of Organic Chemistry*; McGraw-Hill: New York, 1987; Table 8.

[20] Klumpp, G. W. *Reactivity in Organic Chemistry*; Wiley: New York, 1982; p 224.

[21] Ritchie, C. D.; Hoeflich, T. C. *J. Am. Chem. Soc.* **1980**, *102*, 7039.

of $\rho_Y(k_2)$ tend to be lower for the nucleophile with a stronger donor X, e.g., X = *p*-MeO, and steeper for the nucleophile with a stronger acceptor X, e.g., X = *m*-NO$_2$: −3.5 to −5.5, −2.3 to −4.5 (nonlinear) and −4.8 to −5.3 for 1-phenylethyl,[6a] benzhydryl, and cumyl systems,[22] respectively. This is in line with the ion-pair mechanism shown in Scheme 1: A stronger nucleophile with a stronger donor X, $\delta\sigma_X < 0$, will stabilize the TS more and charge transfer to carbocation will be greater so that $\rho_Y(k_N)$ will be more positive, $\delta\rho_Y(k_N) > 0$. Since K is independent of σ_X, i.e., there is no nucleophilic assistance by the nucleophile to ionization, $\delta\rho_Y(K)$ will be zero (vide supra). Thus

$$\delta\rho_Y(k_2) = \delta\rho_Y(K) + \delta\rho_Y(k_N)\,(= 0 + (+)) > 0 \quad (14)$$

This means that $\rho_Y(k_2)$ becomes less negative for a stronger nucleophile so that the negative slope will be less steep, as experimentally observed. Conversely, a weak nucleophile with a strong acceptor X, $\delta\sigma_X > 0$, will lead to a less positive $\rho_Y(k_N)$, $\delta\rho_Y(k_N) < 0$, so that observed negative slope will become steeper, $\delta\rho_Y(k_2) < 0$, as observed experimentally.[6a,22] The curvilinear plot of log k_2 vs σ_Y^+ (Figure 3) resembles those for bimolecular substitution reactions at benzyl derivatives. However, it can be ascribed to a symbiotic effect of rate increase for the electron-withdrawing Y and electron-donating X due to greater thermodynamic driving force; benzhydryl cation has two rings so that the Y substituted ring can play the role of an α-substituent, R^1 or R^2 in **1**, when Y is an electron acceptor which will increase thermodynamic driving force symbiotically together with a strong electron-donor X.[6c]

Since $\rho_Y(k_N)$ increases with a stronger nucleophile, and alternatively $\rho_Y(k_N)$ decreases with a weaker nucleophile, $\rho_{XY}(k_N)$ is negative, eq 15. Again, $\rho_Y(K)$ is independent

$$\rho_{XY}(k_N) = \frac{\partial\rho_Y(k_N)}{\partial\sigma_X}\left(= \frac{(+)}{(-)} \text{ or } \frac{(-)}{(+)}\right) < 0 \quad (15)$$

of σ_X, and hence, the overall, observed $\rho_{XY}(k_2)$ is also negative, as experimentally found.[6a,22]

$$\rho_{XY}(k_2) = \rho_{XY}(K) + \rho_{XY}(k_N)\,(= 0 + (-)) < 0$$

Thus, $\rho_{XY}(k_N) = \rho_{XY}(k_2) < 0$, since $\rho_{XY}(K) = 0$.

On the other hand, if reactions of anilines with the carbocation are diffusion-limited, k_N will be insensitive to changes in substituent at the aniline. Thus, if k_N is diffusion-limited and invariant, ρ_Y will be dependent upon only the change in K with changing substituent Y and will be independent of the aniline nucleophile so that ρ_X will be zero and ρ_{XY} will also be zero. Since our results show that ρ_X changes with Y and $\rho_{XY}(k_2) = \rho_{XY}(k_N)$ is large negative, we can conclude that the aniline combination with the carbocation is not diffusion limited.

In conclusion, the trends found in the plots of log k_2 versus σ_Y and the signs predicted and observed for $\rho_{XY}(k_2)$ are consistent with the proposed mechanism involving rate-limiting attack by the nucleophile, aniline, on a preformed carbocation in the ion pair, in Scheme 1.

We have attempted a rough estimate of the second-order rate constants, k_2, for the reactions of 1-phenylethyl carbocations using the literature data and compared them with our experimental results.

$$k_2\,(\mathrm{H_2O}) \cong 10^4 k_2\,(\mathrm{MeOH}) \text{ at temperatures ranging between 25 and 50 °C}^{23}$$

$$k_2\,(\mathrm{H_2O}) \cong 30 k_2\,(50\%\ \mathrm{TFE}) \text{ at 25 °C}^{1a}$$

These relations lead to

$$k_2\,(50\%\ \mathrm{TFE}) \cong 330 k_2\,(\mathrm{MeOH})$$

On the other hand,

$$k_2\,(\mathrm{MeOH, 65\ °C}) \cong 10^2 k_2\,(\mathrm{MeOH, 25\ °C})^{23}$$

Thus,

$$k_2\,(50\%\ \mathrm{TFE, 25\ °C}) \cong 3k_2\,(\mathrm{MeOH, 65\ °C}) \quad (16)$$

The data in Table 8 reveal that the agreements between the observed k_2(MeOH, 65 °C) and *ca.* three times (eq 16) of the estimated k_2 values based on the ion-pair mechanism, i.e., $k_2 = Kk_N$ (50% TFE, 25 °C), are reasonable. We also note that the agreements are fair for the reactions of other carbocations. The k_2 values observed for the reactions with aniline are in general somewhat greater than the corresponding values with MeOH due to a greater nucleophilicity of aniline. A better agreement is, however, noted for k_2 with MeOH for cumyl cation: 5×10^{-4} M^{-1} s^{-1} at 25 °C by $k_2 = Kk_N$[1a] and 6.1×10^{-4} M^{-1} s^{-1} observed at 35 °C.[22] The k_2 value for the reaction of benzhydryl cation with CF$_3$CH$_2$NH$_2$ (pK_a = 5.7) at 25 °C in 50% TFE is in fair agreement with the observed k_2 value with C$_6$H$_5$NH$_2$ (pK_a = 4.6) at 35 °C in MeOH. One notable disagreement in Table 8 is the reaction of the benzyl system: $k_2 = Kk_N$ at 25 °C in 50% TFE is $\sim10^{-9}$, whereas k_2 observed with MeOH at 65 °C is $\sim10^{-6}$. The large difference of $\sim10^3$ results most probably from the assumption of the ion-pair mechanism; benzyl chloride is not likely to react with MeOH by the ion-pair mechanism.

In summary, these analyses shown in Table 8 provide additional support for the ion-pair mechanism proposed in Scheme 1 for the benzhydryl carbocation in methanol reacting with nucleophiles, anilines, and MeOH.

The rate ratios, k_2/k_1 (eq 5), are low for this reaction, indicating that the methanolysis rate is relatively high compared with the aminolysis rate. The selectivity plots, log (k_2/k_1) *vs* σ_Y^+, gave curves crossing at $\sigma_Y^+ \cong 0.25$ as shown in Figure 4. The slope, $\Delta\rho_Y^+$, changes from negative to positive for weak nucleophile X = *m*-NO$_2$ while it is positive for the relatively strong nucleophiles. The trends of changes in the curves depending on the nucleophile (X) are remarkably similar to those found for the 1-phenylethyl carbocation reactions with anilines in methanol.[13] The similarity of the plots seems to support the similarity in the mechanisms involved in the two reactions, i.e., ion-pair mechanisms apply to both 1-phenylethyl and benzhydryl carbocation reactions with anilines.

In the reactions with anilines, the cross-interaction constants ρ_{XY} are both negative in MeCN and MeOH with relative large magnitude. The magnitude is greater in MeCN, indicating that the TS involved in MeCN is tighter than that in MeOH, which is again consistent with our previous results.[24] Since ρ_X and ρ_{XY} are independent of K (vide supra), the isokinetic point, $\bar{\sigma}_Y^+$, is also

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(22) Lee, I.; Koh, H. J.; Hong, S. N.; Lee, B. S. *Gazz. Chim. Ital.*, in press.

(23) Fainberg, A. H.; Winsteien, S. *J. Am. Chem. Soc.* **1957**, *79*, 1579.

Table 8. Comparison of Observed and Estimated ($k_2 = Kk_N$) Rate Constants for the Reactions of Benzylic Carbocations with Nucleophiles

	cation	K_{eq} (25 °C)[a]	k_{H_2O}[c]	$k_2 = K_{eq}k_N$ (25 °C)[f]	k_2 (obsd)[g]
1	$4\text{-}CH_3C_6H_4CH(CH_3)^+$	6.5×10^{-12}	1.3×10^8	8×10^{-4}	3.6×10^{-4} (7.0×10^{-3}) (65 °C)
2	$C_6H_5CH(CH_3)^+$	1×10^{-14}	3×10^9	3×10^{-5}	9.3×10^{-6} (3.8×10^{-4}) (65 °C)
3	$4\text{-}NO_2C_6H_4CH(CH_3)^+$	1×10^{-20}	4×10^{11}	5×10^{-9}	3.5×10^{-9} (2.0×10^{-5}) (65 °C)
4	$C_6H_5C(CH_3)_2^+$	1.5×10^{-11} [b]	5×10^8 [b] (3×10^7)[d]	7.3×10^{-3} (5×10^{-4})[d]	6.1×10^{-4} [h] (6.6×10^{-3}) (35 °C)
5	$(C_6H_5)_2CH^+$	5.4×10^{-11} [b]	9×10^6 [b] (2×10^8)[e]	4.9×10^{-4} (1×10^{-2})[e]	1.1×10^{-4} [i] (2.0×10^{-3}) (35 °C)
6	$C_6H_5CH_2^+$	$\leq 2 \times 10^{-19}$	$\geq 1 \times 10^{10}$	$\leq 2 \times 10^{-9}$	$\geq 1 \times 10^{-6}$ [j] (65 °C)

[a] $K_{eq} = k_H/k_{H_2O}$[c] for

$$ROH + H^+ \underset{k_{H_2O}}{\overset{k_H}{\rightleftharpoons}} R + H_2O$$

in 50:50 (v/v) TFE/H_2O at 25.0 °C with $I = 0.5$ ($NaClO_4$). Richard, J. P.; Rothenberg, M. E.; Jencks, W. P. *J. Am. Chem. Soc.* **1984**, *106*, 1361. [b] Amyls, T. L.; Richard, J. P.; Novak, M. *J. Am. Chem. Soc.* **1992**, *114*, 8032. [c] k_{H_2O} values ($M^{-1}\ s^{-1}$) obtained by combining the azide:solvent selectivity values with an estimated value of $5 \times 10^9\ M^{-1}\ s^{-1}$ for the diffusional reaction of azide.[a] [d] Second-order rate constant ($M^{-1}\ s^{-1}$) with MeOH in 50:50 TFE/H_2O solution. Richard, J. P. *J. Org. Chem.* **1994**, *59*, 25. [e] Second-order rate constant ($M^{-1}\ s^{-1}$) for the reaction of $(C_6H_5)_2CH^+$ with $CF_3CH_2NH_2$ ($pK_a = 5.7$) in H_2O estimated from data in MeCN. McClelland, R. A.; Kanagasabapathy, V. M.; Banait, N. S.; Steeken, S, *J. Am. Chem. Soc.* **1992**, *114*, 1816. [f] Estimated by the relation $k_2 = K_{eq}k_N$ at 25 °C. [g] The second-order rate constants ($M^{-1}\ s^{-1}$) for the reactions with MeOH and with aniline (in parentheses) at respective temperatures. The data for 1-phenylethyl cations are from: Lee, I.; Lee, W. H.; Lee, H. W. *J. Phys. Org. Chem.* **1993**, *6*, 361. Lee, I.; Lee, W. H.; Lee, H. W.; Bentley, T. W. *J. Chem. Soc., Perkin Trans. 2* **1993**, 141. [h] Lee, I.; Koh, H. J.; Hong, S. N.; Lee, B. S. *Gazz. Chim. Ital.*, in press. [i] This work. [j] Estimated from the methanolysis rate constant. Lee, I.; Koh, H. J.; Park, Y. S.; Lee, H. W. *J. Chem. Soc., Perkin Trans. 2* **1993**, 1575.

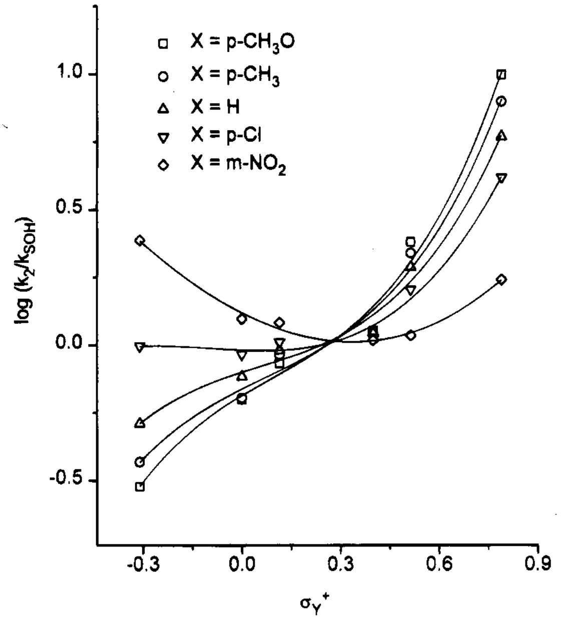

Figure 4. Plots of log (k_2/k_{SOH}) *vs* σ_Y^+ for the reactions of Y-benzhydryl chlorides with X-anilines in methanol at 35.0 °C.

not affected by the use of k_2 (eq 3) rather than k_N. The isokinetic points, $\hat{\sigma}_Y^+$, correspond to the Y substituent with positive σ_Y^+, and $\hat{\sigma}_Y^+$ is more positive in MeOH ($\hat{\sigma}_Y^+ = 0.22$) than in MeCN ($\hat{\sigma}_Y^+ = 0.13$).[25] Since the ion pair, R^+Cl^- (or carbocation R^+), will be more stable in a protic solvent, MeOH, than in an aprotic solvent, MeCN, the manifestation of the isokinetic point, at which ρ_X vanishes and sign reversal from $\rho_X < 0$ for $\hat{\sigma}_Y^+ < \sigma_Y^+$ to $\rho_X > 0$ for $\hat{\sigma}_Y^+ > \sigma_Y^+$ occurs, seems to be related to the stability of the carbocation.

The stability of a carbocation, **I**, can be achieved in two ways: Thermodynamically more stable carbocation is obtained when α-substituents, R^1 and/or R^2, are more electron-donating, e.g., $R^1 = CH_3$, OCH_3, etc. However, in this case, the electron delocalization from the substituent Y will be smaller, and hence, kinetic (or intrinsic) stability is lower than for R^1 (and/or R^2) is an electron acceptor.[4e] *Kinetically (or intrinsically)* more stable carbocation can be obtained with stronger electron-withdrawing α-substituents, e.g., $R^1 = CF_3$. In this case, due to a stronger electron resonance delocalization from Y to C_α, the intrinsic barrier to the addition of the nucleophile on a carbocation will be higher, i.e., intrinsically more stable, although the system is thermodynamically more unstable so that thermodynamic driving force is higher.[4e]

For the 1-phenylethyl carbocation, an electron donating α-substituent, α-CH_3, required a Y-donor, a substituent with $\sigma_Y^+ = -0.23$,[6a] whereas for the benzhydryl carbocation, an electron acceptor α-C_6H_5 required an electron acceptor Y, $\sigma_Y^+ = 0.22$, at the isokinetic point, $\hat{\sigma}_Y^+$.

How can we rationalize this phenomenon of isokinetic or isoparametric behavior with $\rho_X = 0$ at $\hat{\sigma}_Y^+$ for the benzylic carbocation–nucleophile combination reactions? In order for the rate to be invariant, the energy compensation is required.[6c,22] In the nucleophilic addition of an aniline with a stronger electron donor at the para position, *e.g.*, X = *p*-OMe, to the carbocation, **I**, the N atom of the aniline will experience a stronger repulsive electronic interaction as it approaches the partly-filled π-orbital of the benzylic carbon atom, **II**. This will cause elevation of the intrinsic barrier, $\delta\Delta G_0^{\ddagger}(X) > 0$, and the rate will be depressed accordingly; *i.e.*, the overall activation barrier is raised, $\delta\Delta G^{\ddagger}(X) > 0$. On the other hand, however, a stronger electron-donating X substituent will raise the basicity of the aniline. This will increase the thermodynamic driving force, $\delta\Delta G^\circ(X) < 0$, leading to an increase in the rate, *i.e.*, to a decrease in the overall activation barrier, $\delta\Delta G^{\ddagger}(X) < 0$. These two factors, the increasing intrinsic barrier and thermodynamic driving

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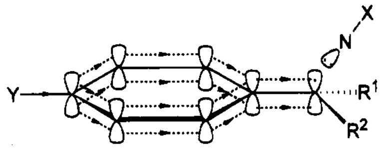
(24) Lee, I.; Choi, Y. H.; Rhyu, K. W.; Shim, C. S. *J. Chem. Soc., Perkin Trans. 2* **1981**, 1881.

(25) There is 30° temperature difference between the two $\hat{\sigma}_Y^+$ values determined in MeCN and MeOH. However the temperature effect on $\hat{\sigma}_Y^+$ will be negligible since the effect on ρ_X and ρ_{XY} cancels out in eq 3.



Substituents
α (R¹, R²), X, Y

II

force, are mutually canceling and reduce substituent effects on the rate. When σ_Y is relatively large negative, *e.g.*, Y = *p*-MeO, resonance delocalization of Y toward the carbocationic center will be large so that the intrinsic effect may become dominant. The net result becomes a lower rate ($\delta \log k_2 < 0$) for the aniline with a stronger electron-donating X substituent ($\delta\sigma_X < 0$), leading to a positive ρ_X. This means that in the region where σ_Y is more negative than $\hat{\sigma}_Y^+$ a thermodynamically more stable derivative with a more electron withdrawing X substituent (a less basic aniline, $\delta\sigma_X > 0$, is thermodynamically more stable) leads to a greater kinetic reactivity, $\delta \log k_2 > 0 \rightarrow \rho_X > 0$; thus, an inverse thermodynamic stability/reactivity relationship holds in this region. This sort of situation will be favored when the substituent in the ring, Y, is a rather strong electron donor ($\delta\sigma_Y^+ < 0$) so that the cationic center is rich in π-electrons to effectively repel initial approach of the nucleophile and in the subsequent disruption of the π-system there is a large energy requirement for electronic reorganization on going from ground to transition state.

In contrast, when Y is a weak electron donor or electron acceptor, the approaching nucleophile will not experience enough repulsion; in this case, the changes in the intrinsic barrier as the nucleophile is varied will be small and the changes in the thermodynamic driving force will become dominant. An aniline with a stronger electron-donating X substituent ($\delta\sigma_X < 0$) will lead to a greater rate ($\delta \log k_2 > 0$), and a negative ρ_X is obtained as in the normal S_N2 reactions. In this region of σ_Y^+, $\sigma_Y^+ > \hat{\sigma}_Y^+$, a thermodynamically more stable derivative leads to a lower reactivity and a normal thermodynamic stability/reactivity relationship holds.

In between the two extreme cases, at an intermediate σ_Y^+, $\hat{\sigma}_Y^+$, there is a balancing point at which the change in the intrinsic barrier is effectively compensated for nearly completely by the change in the thermodynamic driving force resulting in the isokinetic relation, $\rho_X = 0$ [$\delta\Delta G^{\ddagger}(X) = 0$], as we change the substituent X in the nucleophile.

Simplification of the Marcus equation[26] by neglecting the second-order term leads to eq 17a. For the isokinetic condition, the two component energy terms in this expression cancel out as X is varied, eq 17b. Thus, the

$$\delta\Delta G^{\ddagger} = \delta\Delta G^{\circ} + \delta\Delta G_0^{\ddagger} \qquad (17a)$$

$$\delta\Delta G^{\circ}(X) = -\delta\Delta G_0^{\ddagger}(X) \qquad (17b)$$

effect of the intrinsic barrier on the rate is dominant for the more electron-donating Y, whereas the effect of the thermodynamic driving force on the rate is dominant for the less electron-donating Y than $\hat{\sigma}_Y^+$, at which the two effects cancel out.

The invariant rate constants for the addition of substituted anilines to a benzylic carbocation with a vanishing ρ_X can therefore be ascribed to the cancellation of the two effects. However, the stabilizing equilibrium resonance effect, $\delta\Delta G_R^{\circ} < 0$, of electron delocalization from substituent Y in the ring toward the cationic center, C_α, which increases the intrinsic barrier, $\delta\Delta G_0^{\ddagger} > 0$, is in general small compared to the destabilizing equilibrium polar effect of substituent α, $\delta\Delta G_P^{\circ} > 0$,[3b] which increases the thermodynamic driving force, $\delta\Delta G^{\circ} < 0$. This is why we observe the normal thermodynamic stability/reactivity relationship with a lower kinetic reactivity for a thermodynamically more stable derivative more often than the inverse relationship. In order to rationalize the nearly complete cancellation of the two effects, the concept of an imbalance in the expression of the destabilizing inductive and stabilizing resonance interactions in the transition state[4e] may be invoked. The fractional expression, or selectivity, of the small resonance effect, ρ^R, is larger than that of the large polar effect, ρ^P, and this imbalance in the expression of the two opposing polar and resonance effects leads to the nearly complete cancellation;[4e] in other words, cancellation of the two energy terms, eq 17b, occurs due to the larger ρ^R than ρ^P ($\rho^R > \rho^P$) despite the smaller equilibrium resonance effect, $\delta\Delta G_R^{\circ} < \delta\Delta G_P^{\circ}$, eqs 18. This concept of nonsynchronization in the development of polar and resonance interactions[4e] is therefore useful for the interpretation of the cancellation of the two opposing effects (eq 17b) which in turn provides qualitative explanation for the isokinetic behaviors observed in the benzylic carbocation–nucleophile addition reactions.

$$\delta\Delta G^{\circ} = \rho^P \delta\Delta G_P^{\circ} \qquad (18a)$$

$$\delta\Delta G_0^{\ddagger} = \rho^R \delta\Delta G_R^{\circ} \qquad (18b)$$

Conclusion

Benzhydryl chlorides react with anilines in acetonitrile and methanol by the ion-pair mechanism in which the nucleophile attacks on the preformed carbocation, R^+, within a solvent-separated ion pair. This reaction manifests an observable isokinetic point, $\hat{\sigma}_Y^+$ (where Y is a substituent in the substrate), at which ρ_X (ρ_{nuc}) vanishes the changes sign from a normal $\rho_X < 0$ for $\sigma_Y^+ > \hat{\sigma}_Y^+$ to $\rho_X > 0$ for $\sigma_Y^+ < \hat{\sigma}_Y^+$. At the isokinetic point, $\hat{\sigma}_Y^+$, the rate becomes constant irrespective of the substituent in the nucleophile (X), and this point is dependent on the α-substituents in the benzylic carbocation, R^1 in **I**; $\hat{\sigma}_Y^+ = -0.23$ for R^1 = H with $R^2 = CH_3$, and $\hat{\sigma}_Y^+ = 0.22$ for R_1 = H with $R^2 = C_6H_5$, in methanol. Thus, the isokinetic point is a function of X, Y, and R^1 (and/or R^2) in a fixed solvent. Marcus equation predicts that at an isokinetic point, $\hat{\sigma}_Y^+$, the intrinsic barrier ($\Delta G_0^{\ddagger}$) and thermodynamic driving force (ΔG°) are practically completely compensating each other as X is varied. Here, the TS imbalance plays a key role by increasing the intrinsic barrier to compensate for an increase in the thermodynamic driving force or alternatively decreasing $\Delta G_0^{\ddagger}$ to compensate for a decrease in ΔG°.

Experimental Section

Materials. Merck analytical grade methanol was used without further purification. Merk G.R. acetonitrile was used after three distillations. The nucleophiles, aniline, were

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(26) Marcus, R. A. *J. Phys. Chem.* **1968**, *72*, 891.

Aldrich G.R. purchased, which were redistilled or recrystallized before use. Preparation of deuterated anilines and pyrrolidine were as described previously.[27] The analysis (NMR spectroscopy) of the deuterated nucleophiles showed more than 99% deuterium content, so no corrections to kinetic isotope effects for incomplete deuterium were made. Substrates, benzhydryl chlorides, were prepared by reacting benzhydryl alcohols with thionyl chloride or hydrogen chloride gas.[28]

Kinetic Procedure. Rates were measured conductometrically at 35.0 ± 0.05 °C in methanol and at 65.0 ± 0.05 °C. The conductivity bridge used in this work was a self-made computer interface automatic A/D converter conductivity bridge. Substrates were injected with a syringe. Pseudo-first-order rate constants, k_{obs}, were determined by the Guggenheim method[29] with a large excess of aniline; [benzhydryl chloride] = 10^{-4} mol dm^{-3} and [aniline] = 0.05–0.50 mol dm^{-3}. Second-order rate constants, k_2, are obtained from the slope of a plot of k_{obs} vs [aniline] with more than four concentrations of aniline. The k_2 values in Tables 6 and 7 are the averages obtained by more than triplicate runs and were reproducible to within ±3%.

Product Analysis. Benzhydryl chloride was reacted with excess toluidine with stirring for more than 15 half-lives at 65.0 °C in acetonitrile and 35.0 °C in methanol, and the products were isolated by evaporating the solvent under reduced pressure. The TLC analysis of the product mixture gave four spots (silica gel, glass plate, 10% ethyl acetate/*n*-hexane).

R_f values: 0.56 ($C_6H_5CH(C_6H_5)OCH_3$), 0.46 ($C_6H_5CH(C_6H_5)NHC_6H_4$-*p*-CH_3), 0.24 (*p*-$CH_3C_6H_4NH_2$), 0.05 (*p*-$CH_3C_6H_4NH_3^+Cl^-$). The product mixture was treated with column chromatography (silica gel, 10% ethyl acetate/*n*-hexane). Analysis of the products, $C_6H_5CH(C_6H_5)OCH_3$, $C_6H_5CH(C_6H_5)NHC_6H_4$-*p*-CH_3, *p*-$CH_3C_6H_4NH_2$, and *p*-$CH_3C_6H_4NH_3^+Cl^-$ gave the following results. $C_6H_5CH(C_6H_5)OCH_3$: $\delta_H(CDCl_3)$ 3.2 (OCH_3, 3H, s), 4.3 (CH, 1H, s), 7.2 (phenyl, 10H, s). $C_6H_5CH(C_6H_5)NHC_6H_4$-*p*-CH_3: $\delta_H(CDCl_3)$ 2.2 (CH_3, 3H, s), 3.8 (NH, 1H, s), 4.3 (CH, 1H, s), 6.3–7.2 (phenyl, 14H, m). *p*-$CH_3C_6H_4NH_2$: mp 45 °C; $\delta_H(CDCl_3)$ 2.2 (CH_3, 3H, s), 3.5 (NH_2, 2H, broad) 6.5–7.0 (phenyl, 4H, m). *p*-$CH_3C_6H_4NH_3^+Cl^-$: mp 243 °C; δ_H(DMSO-d_6) 2.3 (CH_3, 3H, s), 7.2 (phenyl, 4H, s), 9.4–10.6 (NH_3^+, 3H, broad).

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