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REVIEW COMMENTARY

ISOKINETIC BEHAVIORS IN THE ADDITION REACTIONS OF ANILINE NUCLEOPHILES WITH BENZYLIC CARBOCATIONS

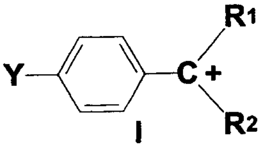
IKCHOON LEE

Department of Chemistry, Inha University, Inchon 402-751, Korea

In the addition reactions of aniline nucleophiles with a benzylic carbocation, isokinetic behavior is often observed: $\rho_X (\rho_{nuc})$ vanishes and the rate becomes constant irrespective of the substituent, X, in the nucleophile when α and Y substituents on the benzylic carbon and on the ring, respectively, are kept constant ($\hat{\sigma}_\alpha$ and $\hat{\sigma}_Y$). This means that there is a region ($\sigma_Y < \hat{\sigma}_Y$)where thermodynamically more stable derivatives ($\delta\sigma_X > 0$) are kinetically more labile ($\delta \log k_{XY} > 0$) so that ρ_X is positive, i.e. an inverse thermodynamic stability–reactivity relationship holds. The observable isokinetic point at $\hat{\sigma}_Y$ is rationalized by the compensation effect of the intrinsic barrier, $\Delta G_0^{\ddagger}$, and thermodynamic driving force, ΔG°, for the specified α and Y substituents. Moreover, the two substituents, α and Y, that satisfy the condition of vanishing ρ_X are found to be related in a compensating manner to preserve the condition of nearly complete cancellation between the two energy terms for the vanishing ρ_X. The cancellation of the two energy terms is made possible by an imbalance or non-synchronization of the expression of destabilizing polar and stabilizing resonance interactions in the transition state.

INTRODUCTION

There has been considerable interest in the reactions of the benzylic carbocation intermediate I with nucleophiles. Depending on the stability or lifetime of the carbocation intermediate, solvent or added nucleophiles react with the contact ion pair, solvent-separated ion pair or free ion intermediate.[1] The thermodynamic stability of the intermediate has been shown to be strongly dependent on the α-substituent, R^1 and/or R^2 in I.[1f,2]



I

An interesting aspect of the carbocation–nucleophile addition reactions is the isokinetic behaviors observed. The reactivity of I (for Y = MeO) with methanol[3] or with a solvent of 50 : 50 (v/v) trifluoroethanol–water at 25 °C[2] was found to be nearly independent of very wide variations in the thermodynamic stability of I caused by a wide range of α-substituents.

More interestingly, in the reactions of aniline nucleophiles with benzyl carbocations I with various α-substituents, the isokinetic behaviors have been observed with a constant reactivity irrespective of the substituent, X, in the nucleophile, leading to a vanishing ρ_X (ρ_{nuc}) at a substituent Y in the ring of I, $\hat{\sigma}_Y$.[4,5] The isokinetic point, $\hat{\sigma}_Y$, at which ρ_X vanishes, falls within the observable range of ρ_Y depending on the α-substituents. The isokinetic point is observable only when there is an observable region ($\sigma_Y < \hat{\sigma}_Y$) where the thermodynamically more stable derivatives (a less basic aniline with a more electron-withdrawing substituent, $\delta\sigma_X > 0$, is thermodynamically more stable) are kinetically more reactive ($\log k_{XY} > 0$) so that ρ_X is positive. In such a region, an inverse thermodynamic stability–reactivity relationship holds.

It has been shown that at the isokinetic point there is a compensatory relationship between the thermodynamic driving force and intrinsic barrier as the substituent, X, is varied. The compensation is established between the thermodynamic driving force, ΔG°, which is largely determined by the polar effect of α-substituents, R^1 and R^2 in I, and the intrinsic barrier, $\Delta G_0^{\ddagger}$, which is dominantly influenced by resonance effect of substituent Y in the ring.[2,3,5]

The observable isokinetic point provides important mechanistic information for carbocation–nucleophile addition reactions. Moreover, it must be taken as a caveat against the failure of the Hammett coefficient, ρ, as a measure of nucleophile selectivity, since at $\hat{\sigma}_Y$, ρ_X changes sign and in the σ_Y ranges above and below this

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isokinetic point the selectivities of the nucleophile become inverted.

In this review, the isokinetic behaviors observed in the benzylic carbocation–nucleophile addition reactions are discussed in the light of the cancellation effect between thermodynamic driving force, $\Delta G°$, and the intrinsic barrier, $\Delta G_0^{\neq}$.

THEORY

The rate constant, k, is a function of structural and environmental factors such as σ, pK_a, Y, N, T and P, where σ, pK_a, Y, etc., have the usual meanings of Hammett substituent constant, basicity, ionizing power, etc. Let us assume that k is dependent only on the two of these rate variables, m and n, with all the rest being kept constant.

A Taylor series expansion of log k around $m = n = 0$ with the assumption of negligible pure second-order and higher order terms leads to a simple second-order expression [equation (1)].[6] Let $k = k(m, n)$ and $k_0 = k$ $(m = n = 0)$, where $m, n = \sigma_i, \sigma_j, \ldots, pK_i, pK_j, \ldots, Y, T, P$, etc. Then,

$$\log(k/k_0) = M_m^0 m + N_n^0 n + Q_{mn} mn \tag{1}$$

where

$$M_m^0 = \left(\frac{\partial \log k}{\partial m}\right)_{n=0} \qquad N_n^0 = \left(\frac{\partial \log k}{\partial n}\right)_{m=0}$$

$$Q_{mn} = \left(\frac{\partial^2 \log k}{\partial m\, \partial n}\right) = \frac{\partial N_n^0}{\partial m} = \frac{\partial M_m^0}{\partial n}$$

provided

$$Q_{mm} = Q_{nn} = Q_{lmn} \cdots \approx 0$$

We can now define an arbitrary constant, $\hat{m}$, for one of the two rate variables, at which the cross term, Q_{mn}, vanishes, and the two variables become no longer interactive, i.e. *non-interactive*.[7] Moreover, the reactivity becomes constant at this point and the reaction is therefore *isokinetic*. Since at $\hat{m}$ the members of the other variables, $n_1, n_2, \ldots, n_n$, do not cause any reactivity change and all have the same value, it can be termed *isoparametric*.[8]

$$\begin{aligned} \log(k/k_0) &= M_m^0 m + N_n^0 n + Q_{mn} mn \\ &= M_m^0 m + (N_n^0 + Q_{mn} m) n \\ &= M_m^0 m + N_n n \\ &= M_m^0 \hat{m} \qquad \text{(2a)} \\ &= -\frac{M_m^0 N_n^0}{Q_{mn}} = \text{constant} \qquad \text{(2b)} \end{aligned}$$

where

$$N_n = N_n^0 + Q_{mn} m$$

and

$$N_n = 0 \quad \text{at} \quad \hat{m} = -\frac{N_n^0}{Q_{mn}} \tag{2c}$$

$$M_n = 0 \quad \text{at} \quad \hat{n} = -\frac{M_m^0}{Q_{mn}} \tag{2d}$$

As a special case, if the two variables m and n are the substituent constants in the two reactants, we obtain an isokinetic substituent or reactant, $\hat{\sigma}$, for which the reactant does not cause reactivity change and isokinetic condition is attained. For example, at $\hat{\sigma}_i\, \rho_j = 0$ and all σ_j values, $\sigma_{j1}, \sigma_{j2}, \ldots, \sigma_{jn}, \ldots$, have the same effect on the reactivity, ie. isokinetic and isoparametric.

$$\log(k/k_0) = \rho_i^0 \sigma_i + \rho_j^0 \sigma_j + \rho_{ij} \sigma_i \sigma_j \tag{3a}$$

$$= \rho_i^0 \hat{\sigma}_i = -\frac{\rho_i^0 \rho_j^0}{\rho_{ij}} \tag{3b}$$

where

$$\rho_j = 0 \quad \text{at} \quad \hat{\sigma}_i = -\frac{\rho_j^0}{\rho_{ij}} \tag{3c}$$

Since at $\hat{\sigma}_i$, $\rho_j = 0$ and ρ_j changes sign, the mechanistic interpretation of the magnitude of ρ_j, as a measure of the extent of bond making or breaking becomes difficult; an exactly opposite trend will be obtained in the regions above and below the non-interactive point, $\hat{\sigma}_i$.

Likewise, if $m, n = \sigma$ and T, we obtain an isokinetic temperature, $\hat{T}$, at which ρ vanishes. This is fairly well-known in physical organic chemistry.[9] Since at $\hat{T}$, ρ changes sign, the mechanistic interpretation of ρ becomes exactly opposite above and below $\hat{T}$.

In a similar manner, it is possible to define an isokinetic pressure $\hat{P}$, medium or ionizing power $\hat{Y}$, etc.

For $m, n = \sigma, T$,

$$\log(k/k_0) = \rho^0 \sigma + N_T^0 T + Q_{\sigma T} \sigma T$$

$\rho = 0$ at $\hat{T}$, isokinetic temperature

Likewise,

$\rho = 0$ at $\hat{P}$, isokinetic pressure

$\rho = 0$ at $\hat{Y}$, isokinetic medium, or solvent, etc.

APPLICATIONS

Let us now consider nucleophilic substitution reactions of benzyl chlorides with anilines in methanol:[4,5,10]

$$2XC_6H_4NH_2 + YC_6H_4CR^1R^2Cl \longrightarrow XC_6H_4NHCR^1R^2C_6H_4Y + XC_6H_4NH_3^+ + Cl^- \tag{4}$$

If this reaction were to proceed by a normal S_N2 mechanism, ρ_X (ρ_{nuc}) should be negative and β_X (β_{nuc})

should be positive for all substituent Y. In contrast, if the reaction were of a limiting S_N1 type, ρ_X and β_X should all vanish since nucleophiles do not participate in the transition state.[6]

However, it was found that for this type of reaction the isokinetic or isoparametric phenomena are observed at $\hat{\sigma}_{Y^+}$, where ρ_X vanishes and changes sign from negative at $\sigma_Y{}^+ > \hat{\sigma}_{Y^+}$ to positive at $\sigma_Y{}^+ < \hat{\sigma}_{Y^+}$. These kinds of isokinetic phenomena are observable only through cancellation effects of changes in the thermodynamic driving force, $\delta\Delta G°$, and intrinsic barrier, $\delta\Delta G_0^{\ddagger}$, in the reactions of benzylic carbocations, $YC_6H_4CR^1R^{2\,+}$ (**I**) with nucleophiles, aniline [equation (5)]. The reactions are believed to proceed through ion-pair mechanism (Scheme 1) so that the observed second-order rate constant, k_2, is a complex quantity: $k_2 = (k_1/k_{-1})k_N = Kk_N$.

$$YC_6H_4CR^1R^{2\,+} + 2XC_6H_4NH_2 \longrightarrow YC_6H_4CR^1R^2NHC_6H_4X + XC_6H_4NH_3{}^+ \qquad (5)$$

There are three kinds of substituents, α (R^1 and/or R^2 on C_α), X (on the nucleophile) and Y (at the *para* position of the ring). The three rate variables, σ_α, σ_X and σ_Y, can be independently varied, and hence the rate constant, k_{ij}, is given by equation (6), where two variables i and j can be any two among the three, α, X or Y, keeping the third constant.

$$k_{ij} = k(\sigma_\alpha, \sigma_X, \sigma_Y) \qquad (6)$$

We have three choices for application of equation (3).

(i) Let us choose σ_X and σ_Y as independent variables [i.e. $i, j = X, Y$ in equation (3a)] and σ_α a constant ($\hat{\sigma}_\alpha$). We then have the following equation:

$$\log(k_{XY}/k_{HH}) = \rho_X^0\sigma_X + \rho_Y^0\sigma_Y + \rho_{X,Y}\sigma_X\sigma_Y \qquad (7)$$

This leads to either

$$\rho_X = 0 \text{ at constant } \sigma_Y\ (\hat{\sigma}_\alpha \text{ and } \hat{\sigma}_Y) \qquad (8a)$$

or

$$\rho_Y = 0 \text{ at constant } \sigma_X\ (\hat{\sigma}_\alpha \text{ and } \hat{\sigma}_X) \qquad (8b)$$

(ii) By fixing σ_X ($\hat{\sigma}_X$) we arrive at similar equations:

$$\rho_\alpha = 0 \text{ at constant } \sigma_Y\ (\hat{\sigma}_X \text{ and } \hat{\sigma}_Y) \qquad (9a)$$

$$\rho_Y = 0 \text{ at constant } \sigma_\alpha\ (\hat{\sigma}_X \text{ and } \hat{\sigma}_\alpha) \qquad (9b)$$

(iii) By fixing σ_Y ($\hat{\sigma}_Y$), the following equations are obtained:

$$\rho_X = 0 \text{ at constant } \sigma_\alpha\ (\hat{\sigma}_Y \text{ and } \hat{\sigma}_\alpha) \qquad (10a)$$

$$\rho_\alpha = 0 \text{ at constant } \sigma_X\ (\hat{\sigma}_Y \text{ and } \hat{\sigma}_X) \qquad (10b)$$

We note that equations (8a) and (10a) are identical, and so are equations (8b) and (9b) and equations (9a) and (10b). The conditions $\rho_\alpha = 0$ [equations (9a) and (10b)] indicate that for fixed substituents X in the nucleophile and Y in the ring the rate constant k_2 in equation (5) does not change and stays constant as we vary substituent α, R^1 and/or R^2. Examples of this type of reaction were reported by Richard and co-workers.[2,3]

Examples

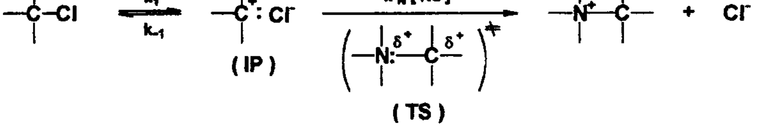
Fixing the nucleophile (X) as MeOH[3] or to 50 : 50 (v/v) $CF_3CH_2OH-H_2O$[2] and Y as 4-MeO, the microscopic rate constants corresponding to k_N in Scheme 1 were found to be approximately constant at $(2-6) \times 10^7$, despite the widely varying stability of the carbocation I depending on the α substituent.

What we are really interested in in this work is the case when $\rho_X = 0$ [equations (8a) and (10a)]. In this case, variations of σ_X with fixed α and Y substituents to $\hat{\sigma}_\alpha$ and $\hat{\sigma}_Y$ do not cause rate changes, and the observed k_2 values are the macroscopic rate constants which are complex quantities given by $k_2 = Kk_N$ in Scheme 1. The rates are constant irrespective of X when α and Y are kept constant. Such combinations of $\hat{\sigma}_\alpha$ and $\hat{\sigma}_Y$ leading to $\rho_X = 0$ are experimentally observed for the reactions of benzylic carbocations with anilines in methanol [equation (5)].

(i) Keeping α constant to $\{R^1 = H \text{ and } R^2 = CH_3\}$, ρ_X vanishes and changes sign at $\hat{\sigma}_{Y^+} = -0{\cdot}23$ in methanol; $\rho_X = 0$ at $\sigma_Y{}^+ = -0{\cdot}23$, while $\rho_X > 0$ at $\sigma_Y{}^+ < -0{\cdot}23$ and $\rho_X < 0$ at $\sigma_Y{}^+ > -0{\cdot}23$. The constant k_{XY} (k_2) value was estimated to be $6 \times 10^{-4}\ l\,mol^{-1}\,s^{-1}$ at 35·0 °C.[4]

(ii) Similarly, fixing α to $\{R^1 = H \text{ and } R^2 = C_6H_5\}$, $\rho_X = 0$ at $\hat{\sigma}_{Y^+} = 0{\cdot}22$ in methanol with the rate constant k_{XY} $(= k_2) = 9 \times 10^{-5}\ l\,mol^{-1}\,s^{-1}$ at 35·0 °C.[5]

(iii) For fixed α to $\{R^1 = R^2 = CH_3\}$, $\rho_X = 0$ at the estimated [using equation (3c)] $\hat{\sigma}_{Y^+}$ of 0·72 in methanol with k_{XY} $(= k_2) = 2 \times 10^{-6}\ l\,mol^{-1}\,s^{-1}$ at 35·0 °C.[10] For this system, the ρ_X values were all positive, ranging



Scheme 1

from $+0{\cdot}51$ ($Y = p-\mathrm{Ph}$) to $+0{\cdot}28$ ($Y = m-\mathrm{Cl}$); corresponding β_X values varied from $-0{\cdot}17$ to $-0{\cdot}07$.

(iv) For fixed α to $\{R^1 = R^2 = H\}$, extrapolation of the kinetic results led to $\rho_X = 0$ at $\bar{\sigma}_{Y^+} = -2{\cdot}15$ in methanol with k_{XY} $(= k_2) = 1 \times 10^{-3}\,\mathrm{l\,mol^{-1}\,s^{-1}}$ at 35·0 °C.[11] For this system, no positive ρ_X or negative β_X were actually observed.

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

First, the positive ρ_X (or negative β_X) is the results of desolvation effect. Such unusual negative β_X (β_{nuc}) values that can be ascribable to the desolvation of nucleophile have indeed been observed.[12]

It can be shown, however, that this argument is false and is not applicable. The solvent, MeOH, has a higher solute hydrogen bond basicity[13] ($\beta_2^{\mathrm{H}} = 0{\cdot}47$) than the aniline nucleophiles used ($\beta_2^{\mathrm{H}} = 0{\cdot}30$–$0{\cdot}45$)(except *p*-MeO-aniline, $\beta_2^{\mathrm{H}} = 0{\cdot}65$), so that the H-bonds between MeOH molecules are stronger than those between MeOH and the 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.[12d,14] For example,[5]

$\rho_X = 0{\cdot}95$ ($\beta_X = -0{\cdot}32$) in MeOH
at 35·0 °C for *p*-Me-benzhydryl cation;

$\rho_X = 0{\cdot}92$ ($\beta_X = -0{\cdot}23$) in MeCN
at 65·0 °C for *p*-Me-bezhydryl cation.

In this example, the negative β_X (β_{nuc}) values exceed the $\beta_X = -0{\cdot}2$[12] suggested for the equilibrium desolvation for nucleophiles of much higher basicity, $\mathrm{p}K_a(\mathrm{RNH_3^+}) > 8$, than the aniline nucleophiles used in our work ($\mathrm{p}K_a = 3{\cdot}5$–$5{\cdot}3$). 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.[15]

Second, 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 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 the nucleophilic assistance by nucleophiles to ionization, k_{asst} in Scheme 2, is insignificant,[16] let us nevertheless *assume* that there is such an assistance (Scheme 2). A stronger, or more basic, nucleophile ($\delta\sigma_X < 0$) will form a more stabilized encounter complex between a nucleophile and an ion pair (C–IP), leading to an increase in K. As a result, $\rho_X(K)$ will become negative:

$$\rho_X(K) = \frac{\partial \log K}{\partial \sigma_X}\left[= \frac{(+)}{(-)}\right] < 0 \tag{11}$$

The negative $\rho_X(K)$ will in turn result in 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 that K is not independent of σ_X [equation (12)].

$$\rho_X(k_2) = \rho_X(K) + \rho_X(k_N)\ (= (-) + (+)) \tag{12}$$

It is 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 ($\delta \log K > 0$) for the more stabilized cation with a stronger donor Y, $\delta\sigma_Y < 0$, and with a stronger donor X, $\delta\sigma_X < 0$, $\rho_{XY}(K)$ should be positive [equation (13a)]. This means that $\rho_X(K)$ [and hence $\rho_X(k_2)$] will become more negative [$\delta\rho_X(K) < 0$] as a result of the shift of the equilibrium to the right for a stronger donor Y ($\delta\sigma_Y < 0$), $\delta\rho_X(K) < 0$ [equation (13b)]$\longrightarrow \delta\rho_X(k_2) < 0$. This is the opposite trend to what we observe, i.e. a more positive $\rho_X(k_2)$ is obtained for a stronger donor Y.

$$\rho_{XY}(K) = \frac{\partial^2 \log K}{\partial\sigma_X\,\partial\sigma_Y} = \frac{(+)}{(-)(-)} > 0 \tag{13a}$$

$$\rho_{XY}(K) = \frac{\delta\rho_X(K)}{\delta\sigma_Y}\left[= \frac{(-)}{(-)}\right] > 0 \tag{13b}$$

(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 [equations (13)]:

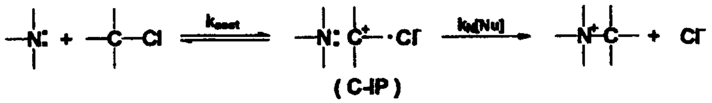
$$\rho_{XY}(k_2) = \rho_{XY}(K) + \rho_{XY}(k_N)\ [= (+) + (-)] = \text{small negative.}$$

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 $\rho_{XY} = -0{\cdot}6$ to $-0{\cdot}8$.[6]

$\rho_{XY}(k_2) = -2{\cdot}47$ in MeCN at 65·0 °C
for benzhydryl cation;[5]

$\rho_{XY}(k_2) = -1{\cdot}46$ in MeOH at 35·0 °C
for benzhydryl cation.[5]

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.



Scheme 2

Further support for the ion-pair mechanism (Scheme 1) is provided by the trends in the plots of log k_2 against $\sigma_Y{}^+$. 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.[1d,17]

The observed macroscopic $\rho_Y(k_2)$ can be expressed as a sum of the two-component ρ_Y terms:

$$\rho_Y(k_2) = \rho_Y(K) + \rho_Y(k_N) \qquad (14)$$

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,c] and in the gas phase,[18] large negative $\rho_Y(K)$ values are indeed observed ranging from -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.[12d,19]

(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 $[\rho_Y(k_N)]$, $\rho_Y(k_2) \neq \rho_Y(k_N)$:

$$\rho_Y(k_2) = \rho_Y(K) + \rho_Y(k_N)\ [= (-) + (+)] < 0$$
$$|\rho_Y(K)| > \rho_Y(k_N)|$$

The observed slopes of the plots of log k_2 versus σ_Y, $\rho_Y(k_2)$, were all negative:[4,5,10] $-3{\cdot}5$ to $-5{\cdot}5$, $-2{\cdot}3$ to $-4{\cdot}5$ (non-linear) and $-4{\cdot}8$ to $-5{\cdot}3$ for 1-phenylethyl, benzhydryl and cumyl systems, respectively. However, the negative slopes tend to be lower for a stronger donor X, e.g. X = p-MeO, and steeper for a stronger acceptor X, e.g. X = m-NO_2. This is in line with the ion-pair mechanism shown in Scheme 1: a stronger nucleophile with a stronger donor X, $\delta\sigma_X < 0$, and a stronger acceptor Y, $\delta\sigma_Y > 0$, will stabilize the TS more, $\delta \log k_N > 0$, and hence $\rho_{XY}(k_N)$ will be negative [equation (15a)]. This means that for a stronger donor X, $\delta\sigma_X < 0$, $\rho_Y(k_N)$ will be more positive, $\delta\rho_Y(k_N) > 0$ [equation (15b)]. 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 (see above). Thus,

$$\delta\rho_Y(k_2) = \delta\rho_Y(K) + \delta\rho_Y(k_N)\ [= 0 + (+)] > 0$$

This means that $\rho_Y(k_2)$ becomes less negative (or more positive) for a stronger nucleophile so that the negative slope will be less steep, as observed experimentally. Conversely, a weak nucleophile with a strong acceptor X, $\delta\sigma_X > 0$, will lead to a less positive $\rho_Y(k_N)$, $\delta\rho_Y(k_N) < 0$ [equation (15b)], so that the observed negative slope will become steeper, $\delta\rho_Y(k_2) < 0$, as observed experimentally.[4,5,10]

$$\rho_{XY}(k_N) = \frac{\partial^2 \log k_N}{\partial\sigma_X\,\partial\sigma_Y} = \frac{(+)}{(-)(+)} < 0 \qquad (15a)$$

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

Again, $\rho_Y(K)$ is independent of σ_X, and hence the overall, observed $\rho_{XY}(k_2)$ is also negative, as found experimentally.[4,5,10]

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

Thus,

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

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 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 with our experimental results:

$$k_2\ (H_2O) \approx 10^4 k_2\ (\text{MeOH}) \text{ at } 25\text{–}50\ °\text{C}^{20}$$
$$k_2\ (H_2O) \approx 30 k_2\ (50\%\ \text{TFE}) \text{ at } 25\ °\text{C.}^{1a}$$

These relationships lead to

$$k_2\ (50\%\ \text{TFE}) \approx 330 k_2\ (\text{MeOH})$$

On the other hand,

$$k_2\ (\text{MeOH}, 65\ °\text{C}) \approx 10^2 k_2\ (\text{MeOH}, 25\ °\text{C})^{20}$$

Thus,

$$k_2\ (50\%\ \text{TFE}, 25\ °\text{C}) \approx 3 k_2\ (\text{MeOH}, 65\ °\text{C}) \qquad (16)$$

The data in Table 1 reveal that the agreements between the observed k_2(MeOH, 65 °C) and about three times [equation (16)] 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 greater than the corresponding values with MeOH owing to a greater nucleophilicity of aniline. Better agreement is noted, however, for k_2 with MeOH for cumyl cation: $5 \times 10^{-4}\ \mathrm{l\,mol^{-1}\,s^{-1}}$ at 25 °C by $k_2 = Kk_N$[1a] and $6{\cdot}1 \times 10^{-4}\ \mathrm{l\,mol^{-1}\,s^{-1}}$ observed at 35 °C.[10] The k_2 value for the reaction of benzhydryl cation with $CF_3CH_2NH_2$ (p$K_a = 5{\cdot}7$) at 25 °C in 50% TFE is in fair agreement with the observed k_2 value with $C_6H_5NH_2$ (p$K_a = 4{\cdot}6$) at 35 °C in MeOH. One notable disagreement in Table 1 is the reaction of benzyl system: $k_2 = Kk_N$ at 25 °C in 50% TFE is *ca* 10^{-9} whereas k_2 observed with MeOH at 65 °C is *ca* 10^{-6}. The large difference of *ca* 10^3 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. There is also a large difference of *ca* 10^3 for the reaction of the *p*-nitro-1-phenylethyl system with aniline, which suggests that aniline reacts by the S_N2 mechanism with the neutral *p*-nitro-1-phenylethyl chloride.[1e]

In summary, the analyses shown in Table 1 provide additional support for the ion-pair mechanism proposed in Scheme 1 for the 1-phenylethyl, cumyl and bezhydryl carbocations in methanol reacting with nucleophiles, anilines and MeOH.

Table 1. 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]
$4\text{-}CH_3C_6H_4CH(CH_3)^+$	$6{\cdot}5 \times 10^{-12}$	$1{\cdot}3 \times 10^8$	8×10^{-4}	$3{\cdot}6 \times 10^{-4}$ $(7{\cdot}0 \times 10^{-3})$ (65 °C)
$C_6H_5CH(CH_3)^+$	1×10^{-14}	3×10^9	3×10^{-5}	$9{\cdot}3 \times 10^{-6}$ $(3{\cdot}8 \times 10^{-4})$ (65 °C)
$4\text{-}NO_2C_6H_4CH(CH_3)^+$	1×10^{-20}	4×10^{11}	5×10^{-9}	$3{\cdot}5 \times 10^{-9}$ $(2{\cdot}0 \times 10^{-5})$ (65 °C)
$C_6H_5C(CH_3)_2{}^+$	5×10^{-11}[b]	5×10^8[b] (3×10^7)[d]	$7{\cdot}3 \times 10^{-3}$ (5×10^{-4})[d]	$6{\cdot}1 \times 10^{-4}$[h] $(6{\cdot}6 \times 10^{-3})$ (35 °C)
$(C_6H_5)_2CH^+$	$5{\cdot}4 \times 10^{-11}$[b]	9×10^6[b] (2×10^8)[e]	$4{\cdot}9 \times 10^{-4}$ (1×10^{-2})[e]	$1{\cdot}1 \times 10^{-4}$[i] $(2{\cdot}0 \times 10^{13})$ (35 °C)
$C_6H_5CH_2{}^+$	$\leqslant 2 \times 10^{-19}$	$\geqslant 1 \times 10^{10}$	$\leqslant 2 \times 10^{-9}$	$\geqslant \times 10^{-6}$[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 $I = 0{\cdot}5$ ($NaClO_4$). J. P. Richard, M. E. Rothenberg and W. P. Jencks, *J. Am. Chem Soc.* **106**, 1361 (1984).

[b] T. L. Amyls, J. P. Richard and M. Novak, *J. Am. Chem. Soc.* **114**, 8032 (1992).

[c] k_{H_2O} values ($\mathrm{l\,mol^{-1}\,s^{-1}}$) obtained by combining the azide solvent selectivity values with an estimated value of $5 \times 10^9\ \mathrm{l\,mol^{-1}\,s^{-1}}$ for the diffusional reaction of azide.[a]

[d] Second-order rate constant ($\mathrm{l\,mol^{-1}\,s^{-1}}$) with MeOH at 25 °C in 50:50 TFE–H_2O solution. J. P. Richard, *J. Org. Chem.* **59**, 25 (1994).

[e] Second-order rate constant ($\mathrm{l\,mol^{-1}\,s^{-1}}$) for the reaction of $(C_6H_5)_2CH^+$ with $CF_3CH_2NH_2$ (p$K_a = 5{\cdot}7$) in H_2O (20 °C) estimated from data in MeCN. R. A. McClelland, V. M. Kanagasabapathy, N. S. Banait and S. Steenken, *J. Am. Chem. Soc.* **114**, 1816 (1992).

[f] Estimated by the relation $k_2 = K_{eq}k_N$ at 25 °C.

[g] The second-order rate constants ($\mathrm{l\,mol^{-1}\,s^{-1}}$) for the reactions with MeOH and with aniline at the respective temperatures. The data for 1-phenylethyl cations are from I. Lee, W. H. Lee and H. W. Lee, *J. Phys. Org. Chem.* **6**, 361 (1993) and I. Lee, W. H. Lee and H. W. Lee and T. W. Bentley, *J. Chem. Soc., Perkin Trans 2* 141 (1993).

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DISCUSSION

How can we rationalize this phenomenon of isokinetic or isoparametric behavior for the benzylic carbocation–nucleophile combination reactions? In order for the rate to be invariant, the energy compensation is required.[5]

The stabilities of the carbocations can be calculated using the AM1 method as the enthalpies of formation, ΔH° in kcal mol^{-1}, from the neutral compounds with Y = MeO:[21]

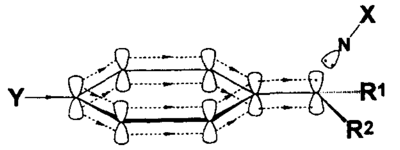
$$\mathrm{MeOC_6H_4CR^1R^2Cl} \longrightarrow \mathrm{MeOC_6H_4CR^1R^{2\,+}} + \mathrm{Cl^-} \quad (17)$$

The data calculated reveal that as the electron-withdrawing power of the α-substituents increases ($\delta\sigma_\alpha > 0$) carbocations become unstable ($\delta\Delta H^\circ > 0$) so that the thermodynamic driving force should increase accordingly ($\delta\Delta G^\circ < 0$). In contrast, the increment of positive charge when the carbocation is formed [equation (17)] decreases ($\delta\Delta q(\mathrm{C}_\alpha{}^+) < 0$), reflecting an increase in the resonance delocalization of electrons from substituent Y (= MeO) with the increase in the electron-withdrawing power of the α-substituents; this should in turn result in an increase in the intrinsic barrier ($\delta\Delta G_0^\ddagger > 0$). Thus there is an energy compensation between $\delta\Delta G^\circ$ and $\delta\Delta G_0^\ddagger$ reducing the effects of α-substituents on the rate. The nearly complete cancellation of the activation barrier ($\delta\Delta G^\ddagger \approx 0$) in the simplified Marcus equation[22] [equation (18a)] by neglecting the second-order term should lead to an isokinetic condition of constant reactivity irrespective of the α-substituent, i.e. $\rho_\alpha = 0$, at $\hat{\sigma}_\mathrm{Y}$ and $\hat{\sigma}_\mathrm{X}$ corresponding to the nucleophiles of MeOH and 50% TFE solution.

$$\delta\Delta G^\ddagger \approx \delta\Delta G^\circ + \delta\Delta G_0^\ddagger \quad (18a)$$

$$\delta\Delta G^\circ(\alpha) \approx -\delta\Delta G_0^\ddagger(\alpha) \quad (18b)$$

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 fully developed π-orbital charge of the benzylic carbon atom, **II**. This will cause an elevation of the intrinsic barrier, $\delta\Delta G_0^\ddagger(\mathrm{X}) > 0$, and the rate will be depressed accordingly, i.e., the overall activation barrier is raised, $\delta\Delta G^\ddagger(\mathrm{X}) > 0$. 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, $\delta\Delta G^\circ(\mathrm{X}) < 0$, leading to an increase in the rate, i.e. to a decrease in the overall activation barrier, $\delta\Delta G^\ddagger(\mathrm{X}) < 0$.



II

Substituents

α (R¹, R²) , X, Y.

These two factors, the increasing intrinsic barrier and thermodynamic driving 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 ($\delta \log k_\mathrm{XY} < 0$) for the aniline with a stronger electron-donating X substituent ($\delta\sigma_\mathrm{X} < 0$), leading to a positive ρ_X. This means that in the region where σ_Y is more negative than $\hat{\sigma}_\mathrm{Y}$ a thermodynamically more stable derivative with a more electron-withdrawing X substituent (a less basic aniline, $\delta\sigma_\mathrm{X} > 0$, is thermodynamically more stable) leads to a greater kinetic reactivity, $\delta \log k_\mathrm{XY} > 0 \longrightarrow \rho_\mathrm{X} > 0$; 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 fairly strong electron donor in the carbocation ($\delta\sigma_\mathrm{Y} < 0$) so that the cationic center is rich in π-electrons, effectively repeling the 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 the 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 ($\delta\sigma_\mathrm{X} < 0$) will lead to a greater rate ($\delta \log k_\mathrm{XY} > 0$), and a negative ρ_X is obtained as in the normal $S_\mathrm{N}2$ reactions. In this region of σ_Y, $\sigma_\mathrm{Y} > \hat{\sigma}_\mathrm{Y}$, 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, $\hat{\sigma}_\mathrm{Y}$, 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, $\rho_\mathrm{X} = 0$ [$\delta\Delta G^\ddagger(\mathrm{X}) = 0$], as we change the substituent X in the nucleophile.

For the isokinetic condition, the two component energy terms in the Marcus equation [equation (18a)] are approximately equal as X is varied:

$$\delta\Delta G^\circ(\mathrm{X}) \approx -\delta\Delta G_0^\ddagger(\mathrm{X}) \quad (18c)$$

Thus the 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 $\hat{\sigma}_\mathrm{Y}$, 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, $\delta\Delta G_\mathrm{R}^\circ < 0$, 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 with the destabilizing equilibrium polar effect of substituent α, $\delta\Delta G_P^\circ > 0$,[23] 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[2] 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;[2] in other words, cancellation of the two energy terms [equation (18c)] occurs due to the larger ρ^R than ρ^P ($\rho^R > \rho^P$) despite the smaller equilibrium resonance effect, $\delta\Delta G_R^\circ < \delta\Delta G_P^\circ$ [equations (19)].

$$\delta\Delta G^\circ = \rho^P\ \delta\Delta G_P^\circ \qquad (19a)$$

$$\delta\Delta G_0^{\ddagger} = \rho^R\ \delta\Delta G_R^\circ \qquad (19b)$$

This concept of non-synchronization in the development of polar and resonance interactions[2] is therefore useful for the interpretation of the cancellation of the two opposing effects [equation (18c)], which in turn provides a qualitative explanation for the isokinetic behaviors observed in the benzylic carbocation–nucleophile addition reactions.

It should be noted that in the normal S_N2 reactions at a neutral carbon center the positive charge develops at C_α only partially in the TS. Developing resonance structure lags behind this developing positive charge ($\rho^R < \rho^P$) so that only a minor fraction of π charge is present at C_α; repulsive interaction between N and C_α is therefore minimal and the intrinsic barrier is negligible relative to the thermodynamic driving force, $\delta\Delta G_0^{\ddagger} \ll \delta\Delta G^\circ$. Thus the normal S_N2 reactions are controlled mostly by the thermodynamic driving force so that ρ_X is always negative, and hence isokinetic behavior is not observed.

The addition of an alcohol or water (ROH) [or any weak nucleophile with mobile proton(s)] to a carbocationic center requires the removal of a proton before, during or after the addition step; it is well known, however, that deprotonation before or during the reaction, i.e. base catalysis, becomes more significant as ROH becomes more acidic and/or the carbocationic center becomes less reactive as a result of a stronger resonance stabilization by a stronger electron-donating Y substituent.[1b]

In the intrinsic barrier dominated region, i.e. in the region where ρ_X is positive, a large repulsive electronic interaction is expected and the aniline nucleophile requires base catalysis as has been known for the nucleophilic addition to a resonance stabilized carbocation center.[24] In this catalysis, partial deprotonation of aniline occurs, which should elevate the HOMO level of the nucleophile, aniline, to enhance the FMO orbital interactions.[25] There is a small primary kinetic isotope effect for the attacking nucleophile, as observed experimentally[5,25] and theoretically predicted.[27,28]

The results of experimental studies on the kinetic solvent isotope effects, k_{SOH}/k_{SOD}, reveal that the values are normal, $k_{SOH}/k_{SOD} > 1{\cdot}0$, in the region where carbocation is resonance stabilized ($\sigma_Y < \hat{\sigma}_Y$) due to partial deprotonation occuring in the base catalysis. In contrast, however, when σ_Y is electron withdrawing no base catalysis occurs and the values become inverted, $k_{SOH}k_{SOD} < 1{\cdot}0$, owing to an increase in the vibrational frequencies associated with desolvation of the nucleophile.[26]

Similarly, α-deuterium kinetic isotope effects involving deuterated nucleophiles are normal, $k_H/k_D > 1{\cdot}0$, due to partial deprotonation in the base catalysis when a nucleophile with a single mobile proton is used.[5] When, however, a nucleophile with two mobile protons (anilines) is used, the values become inverted since bending vibrational frequencies of the other, non-cleaving, N–H bond are increased owing to an increase in the steric crowding in the nucleophilic attack on the cationic center. In this case, the secondary kinetic isotope effect resulting in the inverted value of k_H/k_D ($<1{\cdot}0$) is dominant over the normal ($k_H/k_D > 1{\cdot}0$) primary effect due to base catalysis.[5,10] This is supported by the relatively large normal k_H/k_D ($>1{\cdot}0$) values for the 1-phenylethyl system for which the steric effect should be relatively small.[4]

The trends of change in the k_H/k_D values are consistent with this interpretation: for reactions involving an electron-donor Y, i.e. with a resonance-stabilized cationic center, and/or an electron acceptor X, i.e. with a nucleophile having an acidic proton, the k_H/k_D values are greater, regardless of whether they are greater or less than one. This is because the deprotonation process before or during the reactions involving such substituents are facilitated[1b] and the contribution of the normal-effect fraction increases.

Theoretically, *ab initio* self-consistent reaction-field (SCRF) MO results[27] predicted the partial deprotonation required for a benzylic type carbocation with an electron donor Y, and in contrast a simple desolvation is required for the cation with no substituent (or with an electron acceptor Y).[27] If, on the other hand, the reaction were of the normal S_N2 type occurring at a neutral compound, $YC_6H_4CR^1R^2Cl$, instead of the carbocation–nucleophile combination at **I**, an inverse effect, $k_H/k_D < 1{\cdot}0$, would have been observed in all cases including the value for the nucleophile with one mobile proton.[28]

The balancing point, $\hat{\sigma}_Y$, is also dependent on $\hat{\sigma}_\alpha$ according to equations (8a) and (10a). Thus,

$$\rho_X = f(\hat{\sigma}_\alpha, \hat{\sigma}_Y) = 0 \qquad (20)$$

The two variables in equation (20) cannot be mutually independent since the two must vary, satisfying the condition of vanishing ρ_X. Thus $\hat{\sigma}_\alpha$ and $\hat{\sigma}_Y$ are functionally dependent to maintain the compensating relation between $\delta\Delta G^\circ$ and $\delta\Delta G_0^\ddagger$ [equation (18d)], leading to the vanishing ρ_X.

$$\delta\Delta G^\circ(\alpha, \mathrm{Y}) = -\delta\Delta G_0^\ddagger(\alpha, \mathrm{Y}) \qquad (18d)$$

Since the effects of α substituents, R^1 and/or R^2, are polar and hence thermodynamic in nature, using thermodynamic stability of carbocations, ΔH°, instead of $\hat{\sigma}_\alpha$, we may test the compensating relation between the two. Since an increase in ΔH° by changing it to a more electron-withdrawing α substituent, i.e. by decreasing the stability of benzylic carbocation, $[\delta\Delta H^\circ(\alpha) > 0]$, will lead to an increase in the thermodynamic driving force of the carbocation $[\delta\Delta H^\circ(\alpha) > 0 \longrightarrow \delta\Delta G^\circ(\alpha) < 0]$ and an increase in $\hat{\sigma}_{Y^+}$ $(\delta\sigma_Y{}^+ > 0)$ should lead to a lower degree of resonance delocalization of the positive charge away from C_α, i.e. lowers the intrinsic barrier $[\delta\hat{\sigma}_{Y^+} > 0 \longrightarrow \delta\Delta G_0^\ddagger < 0]$, the slope, A in equation (21) is expected to be negative in order to preserve the compensation between $\delta\Delta G^\circ$ and $\delta\Delta G_0^\ddagger$ [equation (18b)].

$$\delta\Delta H^\circ = A\delta\hat{\sigma}_{Y^+} \qquad (21)$$

The plot of ΔH° versus $\hat{\sigma}_{Y^+}$ using the relevant data in Table 2 indeed gave a negative slope, $A = -6{\cdot}7$, with a correlation coefficient $r = 0{\cdot}986$.[10] This means that an increased stabilizing polar effect of the electron-donating α substituent $[\delta\sigma_\alpha < 0 \longrightarrow \delta\Delta H^\circ < 0 \longrightarrow \delta\Delta G^\circ > 0]$ is compensated for nearly completely by a decreased resonance delocalization effect of electron-withdrawing Y substituent $[\delta\hat{\sigma}_{Y^+} > 0 \longrightarrow \delta\Delta G_0^\ddagger < 0]$, leading to no rate change, $\delta\Delta G^\ddagger(\alpha, \mathrm{Y}) \approx 0$,as we move down from benzyl to cumyl in Table 2.

We note in Table 2 that the constant rate, k_{XY}, decreases as we move down the column because the isokinetic point, $\hat{\sigma}_{Y^+}$, lies successively in a lower rate region, i.e. $\log(k_{XY}/k_{HH})$ changes to a lower value, from positive to negative, down the column. This is again a result of compensating relation between the intrinsic barrier and thermodynamic driving force; the compensation of a greater stabilizing polar effect of the electron-donating α substituent $(\delta\sigma_\alpha < 0)$ requires a lower stabilizing resonance effect of a weaker electron donating or electron-withdrawing Y substituent $(\delta\hat{\sigma}_{Y^+} > 0)$. Since $\hat{\sigma}_{Y^+}$ becomes successively more positive, the rate at $\hat{\sigma}_{Y^+}$, k_{XY}, becomes successively lowered, as the rate decreases in general with a more positive σ_{Y^+} [since $\rho_Y(k_2)$ is negative] for the addition reactions of carbocation with nucleophiles.[4,5,10]

In the above discussion, we neglected steric effects of the α-substituents on the observed rate constants, $k_2 = Kk_N$. There will be increasing differences in ground-state strain in substrates with α-substituents of different bulk, which favors ionization for the substrate with large α-substituents owing to the larger relief of strain energy in the TS for departure of the nucleofuge. The rate increase expected from the increase in K will be partially offset, however, by a similar steric rate retarding effect on the k_N step. Thus, any steric effect on K will have a similar but opposite effect on k_N and hence the two cancel out so that the steric effect on the observed rate constant, k_2 is expected to be small.

Moreover, steric effects in the TS (on k_N) for the carbocation–nucleophile combination reactions are found to be small or negligible.[29] Since steric effects are certain to be present in the addition products, this implies that the nucleophile and the carbocation are separated by large distances at the TS,[29] i.e. the TS is formed at a relatively early stage in the reaction.

This implification is contradicted, however, by the observation of fairly large magnitude of ρ_{XY}, which suggests that the TS is rather tight with a relatively strong nucleophile–carbocation interaction. This discrepancy can be rationalized by the concept of imbalance in the transition-state expression of the equilibrium polar and resonance substituent effects. For example, addition of water to p-MeO-1-phenylethyl carbocation indicated *ca* 36% bond formation based on the change in inductive interaction. In contrast, the fractional expression of the resonance substituent effect was close to 53% of the equilibrium value.[30] This example reveals that although the TS is actually earlier (ca 36%), the loss of resonance interaction corresponds to the value for a later TS with 53% bond formation.

Table 2. Relevant data for estimation of and observed isokinetic points, $\hat{\sigma}_{Y^+}$

Compounds	$[R^1, R^2]$	ρ_X^0	$\rho_Y^0(\rho_Y^{+0})$	ρ_{XY}	$\hat{\sigma}_{Y^+}(= -\rho_X^0/\rho_{XY})$	k_{XY}[a] $(\mathrm{l\,mol^{-1}\,s^{-1}})$	ΔH° $(\mathrm{kcal\,mol^{-1}})$
Benzyl chlorides	[H, H]	−1·61	−0·63	−0·75	(−2·15)	1×10^{-3}	166·7
1-Phenylethyl chlorides	$[H, CH_3]$	−0·47	−4·19	−2·05	−0·23	6×10^{-4}	156·6
Benzhydryl chlorides	$[H, C_6H_5]$	0·32	−2·78	−1·46	+0·22	9×10^{-5}	150·4
Cumyl chlorides	$[CH_3, CH_3]$	0·39	−4·87	−0·54	(+0·72)	2×10^{16}	147·5

[a] Isokinetic rate constant at 35·0 °C $(k_{XY} = k_2 = Kk_N)$.

Conversely, in the carbocation formation from the neutral substrate, a similar but exactly opposite effect is observed since the resonance interaction develops slowly compared with the polar interaction when the TS is approached from the neutral substrate; thee development of resonance structure lags behind the expression of a polar effect in the TS for carbocation formation from the neutral substrate. This means that steric effects in the TS for the carbocation formation step should also be small.

The difference in the fractional expression of equilibrium polar and resonance substituent effects on the rate constants will become greater as the resonance stabilization is greater in the benzylic carbocation. This is reflected in the decreasing magnitude of ρ_{XY} with the increasing stabilizing polar effects of the α-substituents or alternatively with the decreasing resonance delocalization from the Y-substituted bezene ring; the magnitude of ρ_{XY} decreases successively from $-2{\cdot}05$, through $-1{\cdot}46$ to $-0{\cdot}54$ for 1-phenylethyl, benzhydryl and cumyl cations, respectively. This change is consistent with the decreasing trend in the intrinsic barrier at the isokinetic point, $\hat{\sigma}_{Y^+}$, $-0{\cdot}23$, $+0{\cdot}22$ and $+0{\cdot}72$, respectively. This means that when the cation is stabilized by an electron-donor α-substituent, resonance electron delocalization from the Y-substituted benzene ring is small, which should lead to a lesser extent of the TS imbalance. When the resonance delocalization is sufficiently small, the TS imbalance may become so small that the fractional expression of the polar and resonance effects may become nearly identical. This could be the reason why the magnitude of ρ_{XY} for the cumyl cation–aniline combination is smaller ($-0{\cdot}54$) than that for the benzyl chloride reactions with anilines ($-0{\cdot}75$), which is believed to occur by a normal S_N2 process. Thus the TS for the cumyl cation–aniline combination could be looser than the S_N2 TS for the benzyl chloride reactions with anilines. The greater magnitude of ρ_{XY} for the 1-phenylethyl cation is an indication of rather greater TS imbalance resulting from a strong resonance electron delocalization to the cationic center from the Y-substituted ring.

CONCLUSION

The isokinetic behaviors observed in the benzylic carbocation–nucleophile addition reactions are the results of cancellation effect between thermodynamic driving force and intrinsic barrier as one rate variable, e.g. substituent X in the nucleophile, is varied while the other two, α (on C_α) and Y (on the ring) substituents, are kept constant. However, in order to satisfy the compensation requirement, the two constant variables must also be themselves mutually related in a compensating manner.

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