



The Isoparametricity Phenomenon in the Reactions of Benzoyl Halides and Benzyl Bromides with Anilines

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Experimental evidence for the isoparametricity phenomenon has been obtained: at critical values of $\hat{\sigma}_x$ constants of substituents X in anilines, the rate of nucleophilic displacement does not change with variation in substituents Y in benzoyl halides and benzyl bromides; after passing through the critical values of $\hat{\sigma}_x$ the order of reactivity for both substrates is reversed.

During studies of the reaction kinetics of Y-substituted benzoyl and benzyl halides with X-substituted anilines, significant cross-interaction between the substituents Y and X was found, *i.e.* their effects were non-additive.^{1–4} This provided experimental evidence for the existence of a unique isoparametricity phenomenon⁵ in a number of reaction series studied. A quantitative measurement (ρ_{XY}) of this interaction is given by eqn. (1), using multiple regression analysis of the second-order rate constants k_{XY} ($\text{mol}^{-1} \text{dm}^3 \text{s}^{-1}$). Eqn. (1) is an example of a two-parameter relationship based on the principle of polylinearity⁵ and is characterized by isoparametricity. The term means

that at critical values of the structural parameters $\hat{\sigma}_Y = -\rho_{Y=H}\rho_{YX}^{-1}$ or $\hat{\sigma}_X = -\rho_{Y=H}\rho_{YX}^{-1}$, called isoparametric points (IPPs), the magnitude of $\lg k_{YX}$ in eqn. (1) is the same. *I.e.* $\lg k_{XY} = \lg k_{HH} - \rho_{Y=H}\rho_{X=H}\rho_{YX}^{-1}$, and remains constant when either the substituents Y in the substrate at the IPP $\hat{\sigma}_X$ ($\rho_X = 0$), or the substituents X in the nucleophile at the IPP $\hat{\sigma}_Y$ ($\rho_Y = 0$), are varied. Another striking feature of eqn. (1) emerges when it is presented in the form of eqn. (2). If one of the substituents is fixed, *e.g.* X in aniline, then σ_X becomes a constant; accordingly, eqn. (2) is transformed into a one-factor correlation [eqn. (3)], where $\lg k_{HX} = \lg k_{HH} + \rho_{Y=H}\sigma_X$,

Table 1 Coefficients $\rho_{X=H}$, $\rho_{Y=H}$ and ρ_{YX} [eqn. (1)] for reactions of benzoyl halides and benzyl bromides with anilines in aprotic solvents

No.	Solvent	Reagents (temp./°C)	$\rho_{X=H}$	$\rho_{Y=H}$	ρ_{YX}	$\hat{\sigma}_Y$	$\hat{\sigma}_X$	CC ^a	Refs.
1	PhCl–C ₆ H ₁₂ ^b (1:1, v/v)	Benzoyl chlorides + anilines (25.0)	1.09 ± 0.06	– 3.35 ± 0.03	– 0.77 ± 0.08	– 4.35 ^c	1.41 ^c	0.997	^e
2	PhCl–C ₆ H ₁₂ ^b (1:1, v/v)	Benzyl bromides + anilines (25.0)	0.58 ± 0.12	– 3.16 ± 0.04	– 0.62 ± 0.13	– 5.10	0.94 ^d	0.998	2
3	PhNO ₂	Benzyl bromides + anilines (40.0)	– 0.29 ± 0.03	– 1.82 ± 0.02	– 0.42 ± 0.05	– 4.33	– 0.69 ^c	0.998	^e
4	1 mol dm ^{–3} Me ₂ SO in PhNO ₂	Benzyl bromides + anilines (40.0)	0.22 ± 0.04	– 1.40 ± 0.04	– 0.57 ± 0.07	– 2.46	0.39 ^d	0.998	3

^a Multiple correlation coefficient. ^b C₆H₁₂: cyclohexane. ^c Experimentally observed IPP. ^d IPP has been crossed through. ^e This work.

$\rho_X = \rho_{X=H} + \rho_{YX}\sigma_H$. The sign and value of ρ_X in eqn. (3) are determined by the value of the constant σ_X of the fixed substituent X. Since $\rho_X = 0$ in IPP, $\hat{\sigma}_X = -\rho_{X=H}\rho_{YX}^{-1}$, the sign of the sensitivity coefficient ρ_X in correlation (3) is reversed after passing through this IPP value when, on the one hand, $\sigma_X > -\rho_{X=H}\rho_{YX}^{-1}$, and on the other hand, $\sigma_X < -\rho_{X=H}\rho_{YX}^{-1}$. The sign inversion for the sensitivity coefficient ρ_Y in the respective one-factor correlations upon passing through the IPP, $\hat{\sigma}_Y$, is predicted in an analogous way.

$$\lg k_{YX} = \lg k_{HH} + \rho_{X=H}\sigma_Y + \rho_{Y=H}\sigma_X + \rho_{YX}\sigma_Y\sigma_X \quad (1)$$

$$\lg k_{YX} = \lg k_{HH} + \rho_{Y=H}\sigma_X + (\rho_{X=H} + \rho_{YX}\sigma_X)\sigma_Y \quad (2)$$

$$\lg k_{YX} = \lg k_{HX} + \rho_X\sigma_Y \quad (3)$$

Thus, analysis of the formal isoparametric equation (1) provides for reversal of the order of reactivity for either the substrate or the nucleophile within the framework of a single cross-reaction series. Since the isoparametricity paradox is a challenge to the traditional concepts of organic chemistry, we sought experimental proof of the presence of IPPs in nucleophilic substitution reactions at benzoyl and benzyl carbon atoms, these being most appropriate for this purpose. This communication presents the results for reactions of benzoyl halides and benzyl bromides with anilines in aprotic solvents. Table 1 adduces the values of the coefficients in eqn. (1) and the values $\hat{\sigma}_Y$ and $\hat{\sigma}_X$ calculated on the basis of these data for reactions in which the isoparametricity phenomenon has been proved experimentally. In four reaction series the IPP $\hat{\sigma}_X$ was realized, with two (*i.e.* Nos. 2 and 4) actually passing through the IPP. An obvious manifestation of isoparametricity is presented in Table 2, in which the values ρ_X for the one-factor correlation (3) are shown to vary for a series of fixed substituents X in aniline. Thus, if the calculated value for $\hat{\sigma}_X$ coincides with that of the σ_X constant of the substituent X, then $\rho_X = 0$, and after passing through the isoparametric value of $\hat{\sigma}_X$ the sign of ρ_X , *i.e.* the order of reactivity of the substrate is reversed in all cases.

The experimental transition through the isoparametric values of $\hat{\sigma}_X$ has a direct bearing on the reactivity–selectivity

principle (RSP).⁶ Our results convincingly demonstrate that RSP is a particular case of the isoparametricity phenomenon. This principle is fulfilled only in one of the two IPP-divided parts of a cross-section series and is not fulfilled in its other part (see Table 2).

The isoparametricity phenomenon in the reactions in question can be interpreted in terms of the concept of variable transition state (TS) structure of a direct concerted S_N2 displacement. Upon mutual cross-interaction of the structural factors the ratio between bond-making and bond-breaking in the activation process in the TS is changed. At the IPP $\hat{\sigma}_X$ the TS must be symmetrical ($\rho_X = 0$), and after passing through the isoparametric values of $\hat{\sigma}_X$ it is either bond-making (associative TS, $\rho_X > 0$), or bond-breaking (dissociative TS, $\rho_X < 0$) that predominates.

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Table 2 Values of ρ_X in one-factor correlations (3) for reactions of benzoyl halides and benzyl bromides with anilines

X	σ_X^a	$\rho_X [\hat{\sigma}_X]$			
		No. 1 ^b	No. 2	No. 3	No. 4
4-NH ₂	– 0.66			0	
H	0	1.03 ± 0.03	0.63 ± 0.09	– 0.23 ± 0.03	0.22 ± 0.04
3-Cl	0.37	0.78 ± 0.04	0.42 ± 0.03	– 0.46 ± 0.03	0
3-NO ₂	0.71	0.53 ± 0.06	0.16 ± 0.02	– 0.62 ± 0.02	– 0.14 ± 0.01
5-NO ₂ -3-CO ₂ Me	0.96	0.15 ± 0.01	0		– 0.35 ± 0.06
3,5-(NO ₂) ₂	1.42	0	– 0.37 ± 0.04		
		[1.41]	[0.94]	[– 0.69]	[0.39]

^a The value of 0.96 for the constant σ_X with the substituent X = 5-NO₂-3-CO₂Me was determined as reported elsewhere,¹ whereas for other substituents X normal Hammett constants were used. ^b Numbers correspond to the reaction series in Table 1.