

# Separation of Ring Polar and Resonance Effects on the Rate and Equilibrium Constants for Methoxide Ion-Promoted Addition of Methanol to *N*-Benzylideneanilines Substituted at the Benzylidene Moiety

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Rate and equilibrium constants for the title reaction ( $\alpha$ -amino ether formation) at 25 °C in methanol are reported for 16 *N*-benzylideneanilines (BAs) substituted at the benzaldehyde moiety. In contrast to a previous report dealing with BAs substituted at the aniline residue, it is shown that an uncatalyzed pathway competes with the methoxide ion-catalyzed reaction, these two processes corresponding to rate-limiting attachment of the lyate ion to the C=N bond of iminium ion and free imine, respectively. For the latter reaction pathway, the lifetimes of the amide-ion intermediates are long enough to allow a stepwise mechanism. The equilibrium constants for the overall reaction are correlated by the two-parameter Young-Jencks (YJ) equation [ $\log K$  or  $\log k = \rho^n \sigma^n + \rho^r (\sigma^+ - \sigma^n) + C$ ] allowing separation of the overall polar effect of the substituted ring ( $\rho^n = 0.87$ ), including resonance-induced polar (RP) effects, from the direct resonance (DR) effect due to conjugation with the C=N group ( $\rho^r = 0.54$ ). For the forward methoxide ion-catalyzed process, the polar and DR contributions to the substituent effects on the second-order rate constant have the same sign ( $\rho^n = 1.79$  and  $\rho^r = 0.28$ , respectively), but these have opposite signs ( $\rho^n = 0.92$  and  $\rho^r = -0.25$ ) for the reverse reaction. The contribution of the DR effects for the reverse rate constants, which make the points lie above the  $\log k - \sigma^n$  line, stems from gain in resonance at the negatively charged transition state. The validity and significance of the YJ treatment are discussed.

## Introduction

Separation of polar and resonance effects on rate and equilibrium constants for the reactions of aromatic compounds is usually based on two-parameter free energy relationships.<sup>1</sup> The most popular treatment is that suggested by Taft and co-workers ca. 30 years ago,<sup>2</sup> rate or equilibrium constants being expressed by the dual-substituent parameter (DSP) eq 1. In this equation,  $\sigma_I$  is

$$\log K \text{ or } \log k = \rho_I \sigma_I + \rho_R \sigma_R + C \quad (1)$$

the polar effect parameter of the substituent and  $\sigma_R$  an appropriate resonance parameter depending on the electron demand. Since, in the case of reactions at side chains conjugated with the ring, this  $\pi$ -electron demand of the central atom depends on the changes in orbital hybridization on going from the initial state to the transition state or to the products, a single set of  $\sigma_R$  parameters cannot account for the various situations. This led Taft and co-workers to suggest the use of four different scales: (1) the  $\sigma_R^0$  parameters, derived from the  $\sigma^0$  set (primarily based on  $pK_a$  data for substituted phenylethanoic acids), should be valid when there is no resonance interaction between the ring and the side chain, (ii and iii) the  $\sigma_R^+$  and  $\sigma_R^-$  parameters are expected to be appropriate when the

reaction site is either strongly  $\pi$ -electron-demanding (by reference to what happens in  $\alpha$ -aryl carbenium ion formation) or strongly  $\pi$ -electron-demanding (as in the case of phenate ions or substituted anilines), and finally, (iv) the  $\sigma_R^{BA}$  parameter, based on the original Hammett values, should account for situations when the  $\pi$ -electron demand is weak, as in the case of benzoic acids. However, whereas the physical meaning of the  $\sigma_R^0$  scale is clear, since these parameters account for the changes in the polar effect of the substituted ring due to resonance of the substituent with the ring [hereafter called resonance-induced polar (RP) effect<sup>3</sup>], the three latter sets of parameters correspond to two different resonance contributions, namely the RP and direct resonance (DR) contributions. The DR effect is due to changes in resonance interactions between the substituted ring and the reaction center in the course of the reaction; it depends on the electron demand. It follows that the four  $\sigma_R$  sets cannot account for situations where the relative contributions of the RP and DR effects do not coincide with what they are in the case of the reference reactions. Moreover, since these two resonance effects can contribute differently to energy along the reaction path, the Taft treatment does not provide any information on their relative variations.

The other type of two-parameter treatment is that suggested by Young and Jencks.<sup>4</sup> These authors rewrote the Yukawa-Tsuno-Sawada equation (eq 2)<sup>5,6</sup> as shown in eq 3, where  $\Delta\sigma_R^+ = \sigma^+ - \sigma^n$ . Here,  $\sigma^+$  and  $\sigma^n$  parameters

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$$\log k \text{ or } \log K = \rho^n(\sigma^n + r\Delta\sigma_R^+) + C \quad (2)$$

$$\log k \text{ or } \log K = \rho^n\sigma^n + \rho^r\Delta\sigma_R^+ + C \quad (3)$$

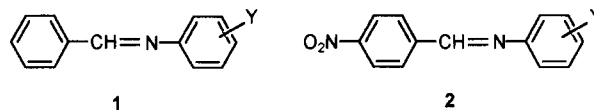
are the Brown–Okamoto<sup>10</sup> and Wepster<sup>8</sup> substituent parameters which, respectively, account for situations when the overall polar and  $\pi$ -electron-donating DR effects coexist and when the latter effect is suppressed by the presence of a methylene group between the ring and the reaction center. When rate or equilibrium constants are expressed by eq 3, the  $\rho^r\Delta\sigma_R^+$  term is assumed to correspond to  $\pi$ -electron-donating DR effects and  $\rho^n\sigma^n$  (analogous to  $\rho^0\sigma^0$ ) to the substituent-induced changes in the polar effect of the substituted ring. In the case of mesomeric interactions between the substituent and the  $\pi$ -system of the nucleus, the  $\rho^n\sigma^n$  term includes not only the polar effect of the substituent but also the RP effects. A similar equation involving  $\sigma$  can also be derived in the case of  $\pi$ -electron-accepting contributions. A three-parameter equation can be used if both  $\pi$ -electron-accepting and  $\pi$ -electron-donating DR effects are involved.

The main disadvantage of the YJ equation stems from the fact that it does not allow any separation of the substituent polar effect from the RP effect. These two effects are assumed to contribute to the same relative extent in the reaction under study as in those which have served to define  $\sigma^n$ . This assumption is questionable in many cases since it has been shown that the  $\rho_R^0/\rho_I$  ratio is not constant but depends on the reaction.<sup>2c,11</sup> Moreover, it is noteworthy that the RP effect is not related only to the conjugation of the substituent with the ring but that it can depend also on conjugation interactions with the reacting side chain. This can be considered as a fundamental drawback in the case of significant through-ring (cross) resonance (e.g., between a  $\pi$ -electron-donating substituent and a  $\pi$ -electron-accepting function). It follows that the interpretation of the second term of eq 3 in terms of resonance energy variations on going from the ground state to the transition state or to the products is generally questionable. Equation 2 was even considered as a mathematical artifact of a three-parameter equation involving  $\sigma_I$ ,  $\sigma_R^+$ , and  $\sigma_R^-$ .<sup>11</sup> Nevertheless, eq 3 was shown to be suitable and informative when the substituent effects on the forward ( $k_f$ ) and reverse ( $k_r$ ) rate constants for reversible systems were examined.<sup>4,12</sup> One important advantage lies in the fact that the differences in the  $\rho^n$  and  $\rho^r$  coefficients for  $k_f$  and  $k_r$  coincide with those for full

equilibrium. These complementary coefficients make it possible to compare the polar and resonance (DR) contributions to the energy of the transition with what happens in the initial and final states.

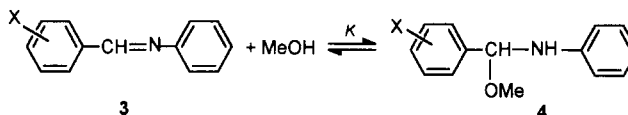
In this and the following paper, we examine situations which cannot be dealt with by eq 1 because the relative RP and DR contributions need to be separated. In the case of the title reaction ( $\alpha$ -amino ether formation) the RP and DR effects on  $k_r$  are of opposite signs; in that of *N*-arylidenealkylamine formation, the DR effects largely predominate with only a very small contribution of the polar plus RP effects which results in a very low  $\rho^n$  value. The situation for these two reactions is too different from what happens for the  $\sigma_R$ -defining reactions to make it possible to use eq 1.

The addition of alcohols to Schiff bases is analogous both to hemiacetal formation from aldehydes and to  $\alpha$ -amino alcohol formation, the first stage of imine hydrolysis, but has not received much attention. The addition of methanol and other aliphatic alcohols to *N*-benzylideneanilines, 1, or to *N*-(4-nitrobenzylidene)-



anilines, 2, both substituted at the aniline residue, was examined by Ogata and Kawasaki.<sup>13</sup> These authors showed that the reaction is induced by methoxide ion attachment to the C=N group and, for meta and  $\pi$ -electron-releasing Y substituents, that  $\log K$  depends linearly on  $\sigma_Y^+$  because of the conjugation between the C=N and C<sub>6</sub>H<sub>4</sub>Y groups. In contrast, the second-order rate constant for the forward reaction depends on Hammett's  $\sigma$  with large and positive  $\rho$  values. Following this work, we studied the addition of methanol to similar compounds 3 substituted on the benzaldehyde residue (Scheme 1) in order to examine the polar and resonance

Scheme 1



3/4a: X = 4-OMe; b: X = 4-OPh; c: 4-Me; d: X = H;  
e: X = 3-OMe; f: X = 4-F; g: X = 3-F; h: X = 4-Cl;  
i: X = 3-Cl; j: X = 4-Br; k: X = 3-Br; l: X = 4-CF<sub>3</sub>;  
m: X = 4-CN; n: X = 3-CN; o: X = 3-NO<sub>2</sub>; p: X = 4-NO<sub>2</sub>

effects on rate and equilibrium constants. This reaction is interesting because of its analogies with nucleophile-induced additions to the carbonyl group. For most of these reactions it was observed that the rate and equilibrium constants are accounted for by eq 3,<sup>12</sup> this allowing separation of the polar and resonance effects. Although mainly focused on LFER treatments, this paper also deals with some mechanistic aspects of the reaction. A significant point is the observation of an uncatalyzed pathway unnoticed by Ogata and Kawasaki and analogous to that reported for the hydrolysis of the same compounds.

## Results

The equilibrium and rate constants for the reaction shown in Scheme 1 were determined in the same experi-

(6) Modified Taft  $\sigma^0$  parameters<sup>7</sup> were originally used in the Yukawa–Tsuno–Sawada equation instead of Wepster's  $\sigma^n$  parameters.<sup>8</sup> Although the  $\sigma^n$  and  $\sigma^0$  parameters have basically the same physical meaning, the  $\sigma^n$  constants were used throughout this work since they were based on a large set of reactions and since a theoretical examination of the interaction energies between a point charge and substituted benzene rings has shown that the relationship between the  $\sigma$  values and the interaction energies is better when the  $\sigma^n$  set is used.<sup>9</sup>

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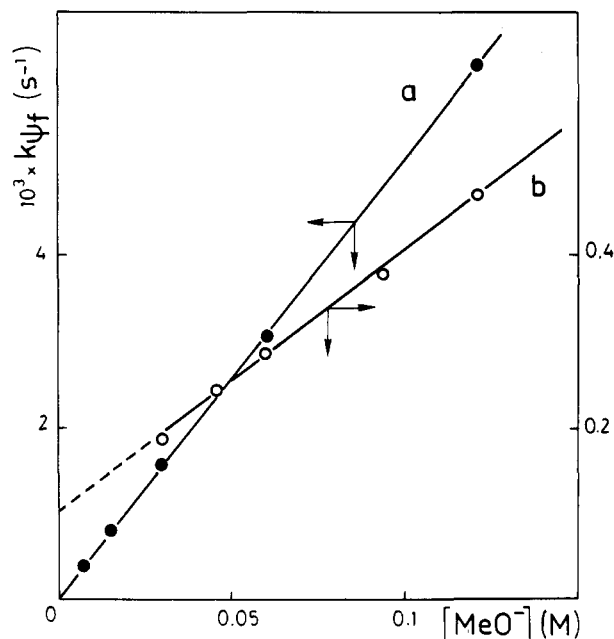
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**Figure 1.** Dependence of the first-order rate constant ( $k_{\psi f} = [k_{\psi}K/(1+K)]$ ) for the addition of methanol to **3o** (a) and **3d** (b) on methoxide ion concentration (25 °C).

ments by following the decrease in UV absorbance at 330 nm (370 nm for **3o** and **3p**) in methoxide ion solutions. Under these conditions the  $\alpha$ -amino ethers **4a-p** formed are expected not to absorb, this because their absorbance spectra should roughly correspond to the sums of those for aniline and the corresponding substituted benzenes. The experimental curves observed following benzaldehyde addition were shown to agree with eq 4, where  $A_0$ ,  $A_{\infty}$ , and

$$A_t - A_{\infty} = (A_0 - A_{\infty})e^{-k_{\psi}t} \quad (4)$$

$A_t$  are the initial and final absorbances and the absorbance at time  $t$ , respectively, and where  $k_{\psi}$  is the sum of the forward,  $k_{\psi f}$ , and reverse,  $k_{\psi r}$ , rate constants of the incomplete  $\alpha$ -amino ether formation reaction. The  $k_{\psi}$ ,  $A_0$ , and  $A_{\infty}$  data were derived as described in the Experimental Section and the equilibrium constants,  $K$ , calculated by eq 5. The rate constants  $k_{\psi f} [= k_{\psi}K/(1+K)]$

$$K = (A_0 - A_{\infty})/A_{\infty} \quad (5)$$

and  $k_{\psi r} [= k_{\psi}/(1+K)]$  were plotted against methoxide ion (NaOMe) concentration. Good straight lines were observed with slopes corresponding to the second-order catalytic rate constants,  $k_f$  and  $k_r$ , up to  $[MeO^-] = 0.2-0.3$  M. In the case of **3l-3p** the lines went through zero (see Figure 1a in the case of **3o**). In contrast, nonzero intercepts were observed for **3a-3k** (see Figure 1b in the case of **3d**). The rate constants for  $\alpha$ -amino ether formation are therefore accounted for by eq 6, the intercept  $k_f^0$  cor-

$$k_{\psi f} = k_f[MeO^-] + k_f^0 \quad (6)$$

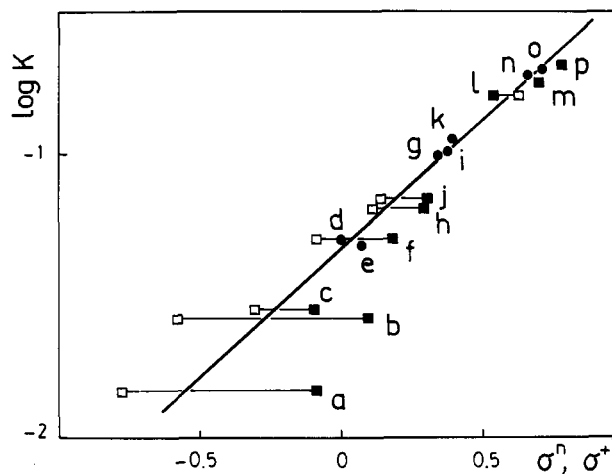
responding to the uncatalyzed reaction, being negligible only for the most electron-withdrawing substituents.

Table 1 lists the experimental values of  $k_f$  and  $k_r$  ( $= k_f/K$ ), the second-order rate constants for the methoxide ion-induced forward and reverse reactions, and  $k_f^0$  for the uncatalyzed forward process. Figure 2 shows the plot of

**Table 1.** Equilibrium and Rate Constants for the Addition of Methanol to *N*-Arylideneanilines **3a-p**<sup>a</sup>

compd	$K^b$	$10^3 k_f^c$ (M <sup>-1</sup> s <sup>-1</sup> )	$10^2 k_r^d$ (M <sup>-1</sup> s <sup>-1</sup> )	$10^4 k_f^0^e$ (s <sup>-1</sup> )
<b>3a</b>	0.0146 ± 0.0017	1.16 ± 0.20	7.9 ± 0.9	3.95 ± 0.55
<b>3b</b>	0.0266 ± 0.0017	2.75 ± 0.24	10.3 ± 0.4	1.92 ± 0.21
<b>3c</b>	0.0282 ± 0.0017	1.80 ± 0.09	6.37 ± 0.25	1.87 ± 0.19
<b>3d</b>	0.0492 ± 0.0008	3.01 ± 0.24	6.11 ± 0.36	1.00 ± 0.14
<b>3e</b>	0.0472 ± 0.0012	3.28 ± 0.16	7.04 ± 0.20	0.50 ± 0.30
<b>3f</b>	0.0495 ± 0.0020	4.81 ± 0.27	9.71 ± 0.16	0.73 ± 0.10
<b>3g</b>	0.0970 ± 0.0024	11.5 ± 0.4	11.8 ± 0.2	ca. 0
<b>3h</b>	0.0661 ± 0.0018	8.66 ± 0.38	13.1 ± 0.3	0.50 ± 0.10
<b>3i</b>	0.101 ± 0.003	13.3 ± 0.5	13.2 ± 0.1	0.16 ± 0.10
<b>3j</b>	0.0682 ± 0.0034	9.06 ± 0.35	13.3 ± 0.1	0.26 ± 0.10
<b>3k</b>	0.112 ± 0.002	13.9 ± 0.4	13.1 ± 0.1	0.20 ± 0.10
<b>3l</b>	0.161 ± 0.004	27.5 ± 0.9	17.1 ± 0.2	ca. 0
<b>3m</b>	0.175 ± 0.007	50.4 ± 3.0	28.8 ± 0.6	ca. 0
<b>3n</b>	0.189 ± 0.002	45.8 ± 1.0	24.2 ± 0.3	ca. 0
<b>3o</b>	0.197 ± 0.002	53.3 ± 2.0	26.9 ± 0.7	ca. 0
<b>3p</b>	0.200 ± 0.005	68.3 ± 2.4	34.2 ± 0.4	ca. 0

<sup>a</sup> In methanol at 25 ± 0.1 °C. Numbers after the ± signs are standard deviations. <sup>b</sup>  $K = [4]/[3]$ , calculated by eq 5. <sup>c</sup> Catalytic rate constants for MeO-catalyzed addition of methanol. <sup>d</sup> Catalytic rate constants for MeO-catalyzed methanol elimination from **4**. <sup>e</sup> Rate constants for uncatalyzed addition of methanol to **3**.



**Figure 2.** Plots of the logarithm of the equilibrium constant for the addition of methanol to **3a-3p** against the  $\sigma^n$  (Wepster) and  $\sigma^+$  (Brown) substituent parameters. The closed circles correspond to the meta substituents ( $\sigma^n = \sigma^+$ ) and the squares to the log  $K$  values for para substituents plotted against  $\sigma^n$  (■) or  $\sigma^+$  (□).

$\log K$  against  $\sigma^n$ ,<sup>14</sup> which accounts for the overall polar effects of the substituted ring (including the RP effects). It is clear that the points corresponding to the meta substituents or to the  $\pi$ -electron-withdrawing para substituents (except 4-CF<sub>3</sub>) are on the straight line ( $\rho^n = 0.88 \pm 0.05$ ;  $r^2 = 0.979$ ) but that the other points deviate. On the other hand, a plot of  $\log K$  against  $\sigma^{+10}$  shows that the  $\pi$ -electron-donating resonance contribution is overestimated when these parameters are used. This situation is usually dealt with by the Yukawa-Tsuno-Sawada or Young-Jencks equations (eqs 2 and 3). A least-squares treatment based on eq 3 gives  $\rho^n = 0.87 \pm 0.04$  and  $\rho^+ = 0.54 \pm 0.05$  ( $r^2 = 0.990$ ).<sup>14,15</sup> To these figures corresponds a  $r$  value of 0.62 in eq 2. Table 2 makes it possible to compare the statistical parameters for the latter treatment

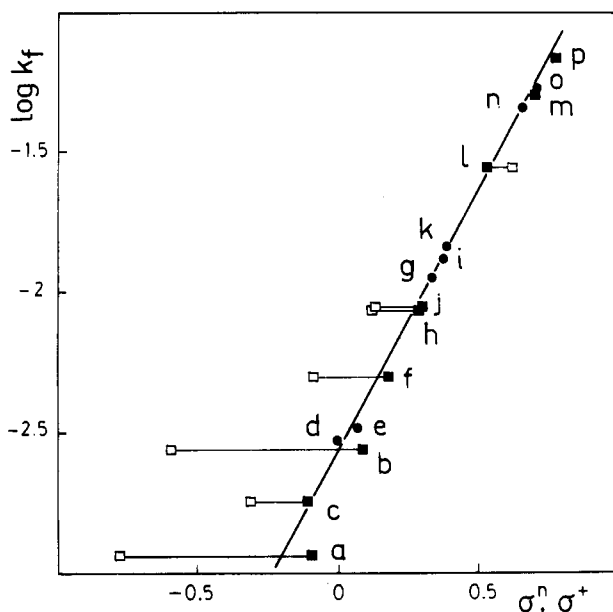
(14) The  $\sigma^n$  values are those given in ref 8a, except for X = 4-OMe (-0.09), 4-OPh (0.09), 4-Me (-0.10), 4-F (0.18), 4-Cl (0.29), and 4-Br (0.30) (ref 8b).

(15) For the para substituents, the following  $\Delta\sigma_n^+$  values, based on Wepster's compilation,<sup>8b</sup> were used: -0.71 (4-OMe), -0.68 (4-OPh), -0.22 (4-Me), -0.26 (4-F), -0.19 (4-Cl), -0.16 (4-Br), and 0.09 (4-CF<sub>3</sub>). A value of 0.04 was used for X = 4-NO<sub>2</sub> to account partially for small deviations for this point. This corresponds to  $\sigma^+ = 0.82$ , the value of  $\sigma^0$ .

**Table 2. Correlation Coefficients of the Young-Jencks and Ehrenson-Taft Equations Calculated from Rate and Equilibrium Constants for  $\alpha$ -Amino Ether Formation<sup>a</sup>**

parameters used	Young-Jencks (eq 3) <sup>b</sup> $\sigma^n, \Delta\sigma_R^+$	Ehrenson-Taft (eq 1) <sup>c</sup>		
		$\sigma_I, \sigma_R^0$	$\sigma_I, \sigma_R^{BA}$	$\sigma_I, \sigma_R^{+b}$
$K$	$\rho^n = 0.87 \pm 0.04$ $\rho^r = 0.54 \pm 0.05$ $C = 1.33 \pm 0.02$ $r^2 = \underline{0.990}$	$\rho_I = 0.87 \pm 0.13$ $\rho_R = 1.35 \pm 0.15$ $C = 1.33 \pm 0.07$ $r^2 = 0.930$	$\rho_I = 0.91 \pm 0.09$ $\rho_R = 1.10 \pm 0.08$ $C = 1.34 \pm 0.04$ $r^2 = \underline{0.969}$	$\rho_I = 0.90 \pm 0.07$ $\rho_R = 0.69 \pm 0.69$ $C = 1.33 \pm 0.04$ $r^2 = \underline{0.981}$
$k_f$	$\rho^n = 1.79 \pm 0.03$ $\rho^r = 0.28 \pm 0.04$ $C = -2.55 \pm 0.02$ $r^2 = \underline{0.998}$	$\rho_I = 1.71 \pm 0.09$ $\rho_R = 1.97 \pm 0.10$ $C = -2.49 \pm 0.04$ $r^2 = 0.988$	$\rho_I = 1.78 \pm 0.06$ $\rho_R = 1.56 \pm 0.05$ $C = -2.52 \pm 0.03$ $r^2 = \underline{0.994}$	$\rho_I = 1.81 \pm 0.16$ $\rho_R = 0.92 \pm 0.09$ $C = -2.53 \pm 0.08$ $r^2 = 0.960$
$k_r$	$\rho^n = 0.92 \pm 0.03$ $\rho^r = -0.25 \pm 0.04$ $C = -1.21 \pm 0.01$ $r^2 = \underline{0.988}$	$\rho_I = 0.84 \pm 0.09$ $\rho_R = 0.62 \pm 0.10$ $C = -1.16 \pm 0.04$ $r^2 = 0.936$	$\rho_I = 0.88 \pm 0.10$ $\rho_R = 0.46 \pm 0.09$ $C = -1.18 \pm 0.05$ $r^2 = 0.912$	$\rho_I = 0.90 \pm 0.13$ $\rho_R = 0.23 \pm 0.07$ $C = -1.20 \pm 0.06$ $r^2 = 0.850$

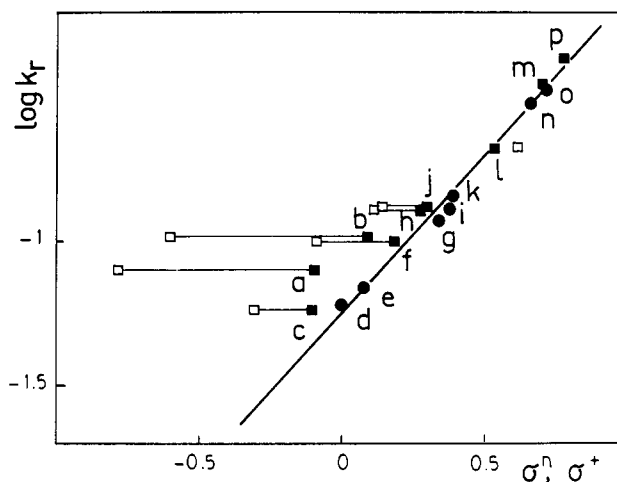
<sup>a</sup> Figures after the sign  $\pm$  are standard deviations.  $r^2$  = square of the correlation coefficient. The  $r^2$  value is underlined when the relationship is considered as satisfactory from a statistical point of view. <sup>b</sup> For the  $\sigma^n$  and  $\Delta\sigma_R^+$  used, see refs 14 and 15. <sup>c</sup> The  $\sigma_I, \sigma_R^0, \sigma_R^{BA}$ , and  $\sigma_R^{+b}$  were taken from ref 2c, except for X = 4-OPh. In this case,  $\sigma_I$  was taken as 0.40 from ref 1a;  $\sigma_R^{BA}$  (= 0.40) was calculated as  $(\sigma_p - \sigma_I)$  with  $\sigma_p$  (Hammett) = -0.08 (ref 1a);  $\sigma_R^0$  = -0.31 was estimated as  $\sigma^n - \sigma_I$ ;  $\sigma_R^{+b}$  = -0.99 (=  $\sigma^+ - \sigma_I$ ). Similar calculations using an improved set of  $\sigma_I$  substituent parameters<sup>1a</sup> did not give significant differences in the coefficients and in the goodness of fit.



**Figure 3.** Plots of the logarithm of the second-order rate constant for methoxide ion-promoted addition of methanol to 3a-p against the  $\sigma^n$  (Wepster) and  $\sigma^+$  (Brown) substituent parameters. For the meaning of the different signs, see the caption of Figure 2.

with those calculated when the Taft DSP equation is used with  $\sigma_R^0, \sigma_R^+$ , and  $\sigma_R^{BA}$ . Although the two-parameter equation can be considered as satisfactory with the  $\sigma_R^{BA}$  or  $\sigma_R^+$  sets, the goodness-of-fit is a little poorer than when the YJ equation is used. This is because none of the  $\sigma_R$  scales accounts for the relative amounts of the polar and DR effects. A  $\sigma_R$  set intermediate between  $\sigma_R^0$  and  $\sigma_R^+$  would be necessary for a better fitting of the data by eq 1.

Figure 3 shows the plots of the logarithm of the second-order rate constant  $k_f$  for methoxide ion-promoted addition of methanol to 3a-p versus the Wepster  $\sigma^n$  parameters.<sup>14</sup> The relationship observed is excellent ( $r^2 = 0.997$ ) for the meta and  $\pi$ -electron-withdrawing para substituents ( $\rho^n = 1.83 \pm 0.04$ ). Small, negative deviations for the  $\pi$ -electron-donating para substituents are accounted for by eq 3 with  $\rho^n = 1.79 \pm 0.03$  and  $\rho^r = 0.28 \pm 0.04$  ( $r^2 = 0.997$ ).<sup>15</sup> On the other hand, Figure 4 shows that the rate constants for the methoxide ion-promoted

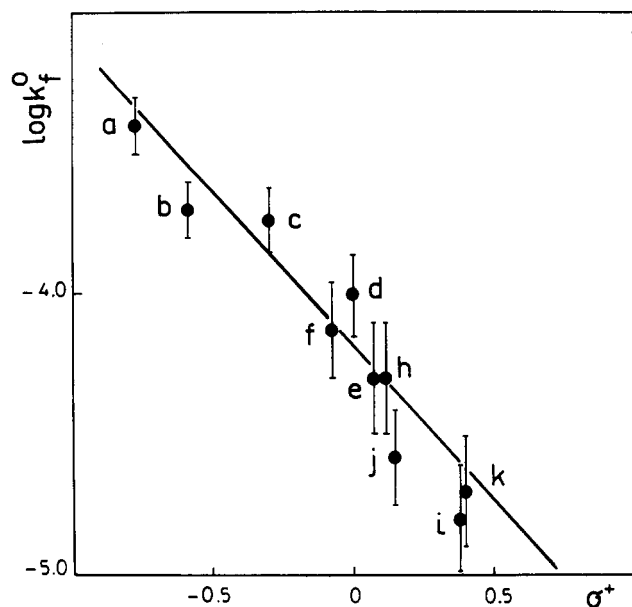


**Figure 4.** Plots of the logarithm of the second-order rate constant for methoxide ion-catalyzed elimination of methanol from 4a-p against the  $\sigma^n$  (Wepster) and  $\sigma^+$  (Brown) substituent parameters. For the meaning of the different signs, see the caption of Figure 2.

reverse reaction,  $k_r$ , are also accounted for by the  $\sigma^n$  parameters ( $\rho^n = 0.94 \pm 0.02$ ;  $r^2 = 0.996$ ) for meta substituents but that more significant positive deviations are observed for the para substituents. The points lie above the line for the  $\pi$ -electron-donating groups and that corresponding to 4-CF<sub>3</sub> is slightly below. This substituent is known to make the aryl groups less  $\pi$ -electron-donating.<sup>16</sup> Quantitatively, the variations of  $k_r$  are well accounted for by eq 3 ( $r^2 = 0.988$ ). The polar effect coefficient ( $\rho^n = 0.92 \pm 0.03$ ) is positive, but that for the DR effects is negative ( $\rho^r = -0.25 \pm 0.04$ ). This means that the  $r$  value of eq 2 is negative ( $r = -0.27$ ), i.e., outside of the usual range of magnitude of this parameter ( $0 < r < 1$ ). On the other hand, the DSP treatment clearly cannot account for such a situation, this because the RP and DR contributions to the four scales of  $\sigma_R$  parameters have the same sign.

As mentioned above, the plots of  $k_{\psi f}$  against [MeO<sup>-</sup>] indicate that an uncatalyzed pathway is partially followed when the substituent is  $\pi$ -electron donating or weakly electron withdrawing. Figure 5 shows, despite the low

(16) This is illustrated by the  $\sigma_R^+$  (0.15) value for the 4-CF<sub>3</sub> group.<sup>1a,b</sup>



**Figure 5.** Plot of the logarithm of the first-order rate constant for uncatalyzed addition of methanol to 3a–3k. The approximate standard deviations are shown by the vertical segments.

accuracy of the data, that  $\log k_f^0$  depends linearly on  $\sigma^+$  with  $\rho^+ = \text{ca. } -1.2$ .

### Discussion

#### Substituent Effects on the Equilibrium Constants.

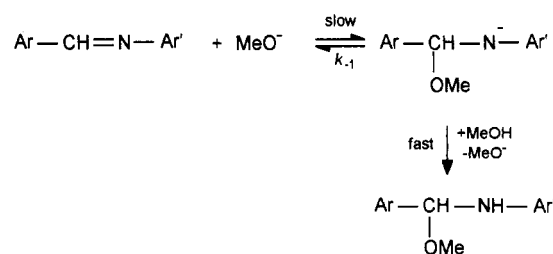
The substituent effects on the equilibrium constants are reminiscent of those observed for the addition of methanol to benzaldehydes<sup>17,18</sup> or acetophenones<sup>12b</sup> (hemiacetal formation) and for similar reactions yielding uncharged species. In these cases, it was shown that eq 3 is valid whatever the solvent.<sup>12b</sup> The  $\rho^n$  and  $\rho^r$  coefficients are both always close to unity in water, corresponding to satisfactory relationships when only the  $\sigma^+$  parameters are used, whereas they are different in methanol or in dodecane. Under these latter conditions, the DR effect coefficient,  $\rho^r$ , remains equal to 1.0 whatever the reaction; the polar effect coefficient,  $\rho^n$ , is larger and in the 1.8–2.0 range. These data were explained in terms of solvent dependence of the resonance and polar effects on the stability of the starting materials. Benzaldehydes or acetophenones are destabilized by polar electron-withdrawing substituents but stabilized by  $\pi$ -electron donation, this because of the partial carbenium ion character of the central atom. A similar explanation is evident in the case of methanol addition to *N*-arylideneanilines:  $\pi$ -electron-donating substituents stabilize the starting material,<sup>19</sup> this being destabilized by polar electron-withdrawing effects.

(17) Arota, M.; Cox, B. G.; Sørensen, P. E. *J. Chem. Soc., Perkin Trans. 2* 1979, 103.

(18) Crampton, M. R. *J. Chem. Soc., Perkin Trans. 2* 1975, 185.

(19) There is a considerable body of experimental and theoretical data about the molecular structure of *N*-arylideneanilines in relation with resonance (for recent papers, see ref 20). All these data agree with a nonplanar *E* configuration with the ring of the benzaldehyde moiety roughly in the plane of the C=N, but with the nucleus of the anilino group rotated. The dihedral angle,  $\theta$ , between the plane of the latter benzene ring and the C=N nodal plane was shown to depend markedly on substituents. It is the result of the balance between two resonance-dependent contributions to the energy of the molecule, resonance between the  $\pi$ -orbitals of the ring and those of the C=N bond and overlap between the former orbitals and the lone pair of N. Substituents which are  $\pi$ -electron donating make  $\theta$  small;  $\theta$  is close to 90° for strongly  $\pi$ -electron-demanding groups.

### Scheme 2



**Table 3.** Estimated Rate Constants for the Cleavage of the Amide Anions of the  $\alpha$ -Amino Ethers 4

comps	$p(K_{a})_{\text{Ae}}^a$	$k_f^b$ ( $\text{M}^{-1} \text{s}^{-1}$ )	$10^9 k_{-1}^c$ ( $\text{s}^{-1}$ )
4a	26.5	0.0790	5.0
4d	26.4	0.0611	3.1
4i	25.9	0.132	2.1
4o	25.5	0.269	2.1
4p	25.4	0.342	1.7

<sup>a</sup>  $pK_a$  values for amide ion formation from 4, estimated as described in ref 29. <sup>b</sup> Data from Table 1. <sup>c</sup> First-order rate constants for the cleavage of amide ions (see Scheme 2).

The fact that the  $\rho^n$  and  $\rho^r$  coefficients are half those for hemiacetal formation is due to the weaker polarity of the C=N group.<sup>21</sup> The central atom is less  $\pi$ - and  $\sigma$ -electron demanding.

Oakes and Stacy<sup>25</sup> determined the equilibrium constants for the addition of 1-butanethiol to the same substrates in methanol yielding  $\alpha$ -amino thioethers. They observed similar substituent effects, the LFER being better when the  $\sigma^+$  parameters are used instead of  $\sigma$ . The  $\rho^+$  coefficient, 0.86, is close to the  $\rho^n$  value observed here for the formation of 4. Because of the small number of substituents, a two-parameter treatment of the data is questionable. Nevertheless, a better fit is observed with  $\rho^n = 0.93$  and  $\rho^r = 0.69$ . Clearly, the origin of the substituent effects is the same, namely the dependence of the energy of the starting material on polar and resonance interactions.

**Mechanism of Methoxide Ion Catalysis.** Ogata and Kawasaki<sup>13</sup> assumed the mechanism shown in Scheme 2. This is supported by the large effects of the substituents on the aniline residues of 1 and 2<sup>26</sup> and by the significant kinetic solvent isotope effects attributed to methoxide ion desolvation. In order to examine whether this mechanism is plausible, we calculated the  $k_{-1}$  values for 4a–4p, the rate constant for first-order amide ion cleavage. In a stepwise mechanism  $k_{-1}$  should be smaller than  $k_{\text{diff}}$  (ca.  $10^{11} \text{ s}^{-1}$ ), the first-order rate constant for a process controlled by diffusional separation of the methoxide ion from the Schiff base moiety.<sup>27</sup> Table 3 lists some of the  $k_{-1}$  rate constants estimated as  $k_f K_{\text{auto}} / (K_a)_{\text{Ae}}$ , where  $K_{\text{auto}}$

(20) Norinder, U. *Mol. Cryst. Liq. Cryst.* 1987, 149, 195. Russo, N. *THEOCHEM* 1988, 41, 403. Meic, Z.; Baranovic, G. *Pure Appl. Chem.* 1989, 61, 2129.

(21) The dipole moment of  $\text{H}_2\text{C}=\text{O}$  (2.33 D) is much larger than that the corresponding methylimine  $\text{H}_2\text{C}=\text{NCH}_3$  (1.53 D).<sup>22</sup> The weight of the C–O<sup>+</sup> valence-bond structure is 0.404.<sup>23</sup> Generalized valence-bond calculations show that the  $\pi$ -electron distribution for methylimine is +0.10 on C and –0.09 on N.<sup>24</sup>

(22) *CRC Handbook of Chemistry and Physics*, 68th ed.; Weast, R. C., Astle, M. J., Beyer, W. H., Eds.; CRC Press: Boca Raton, FL, 1987; p E59.

(23) Berthier, G.; Serre, J. In *The Chemistry of the Carbonyl Group*; Patai, S., Ed.; Wiley-Interscience: London, 1966; p 1.

(24) López-Garriga, J. J.; Hanton, S.; Babcock, G. T.; Harrison, J. F. *J. Am. Chem. Soc.* 1986, 108, 7251.

(25) Oakes, T. R.; Stacy, G. W. *J. Am. Chem. Soc.* 1972, 94, 1594.

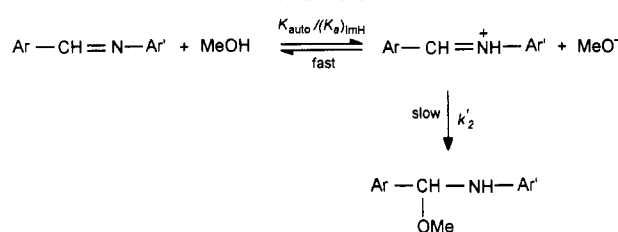
(26) Hammett  $\rho$  values of 1.7 and 2.65 have been reported for 1 and 2, respectively, at 25 °C.<sup>13</sup>

(27) Sayer, J. M.; Jencks, W. P. *J. Am. Chem. Soc.* 1973, 95, 5637.

(10<sup>-16.7</sup>)<sup>28</sup> is the autoprotolysis equilibrium constant for methanol and ( $K_a$ )<sub>Ae</sub> the acid dissociation constants of the  $\alpha$ -amino ethers **4a–4p**. These rate constants are always at least 20-fold smaller than  $k_{diff}$ . Moreover, since Figure 2 does not exhibit any curvature, the mechanism does not change gradually from stepwise to concerted.

The fairly large  $\rho^n$  value (1.79) calculated from the  $k_f$  data for the *N*-benzylideneanilines substituted at the Ar ring is in agreement with what is expected from the mechanism shown in Scheme 2: since the methoxide attachment step is strongly endergonic the transition state can be expected to be late. A late transition state is consistent with the  $\rho^n$  values observed for methoxide ion-catalyzed addition of methanol to **1** and **2**,<sup>26</sup> i.e., when Ar' was changed. It is also consistent with the solvent isotope effect [( $k_f$ )<sub>MeOH</sub>/( $k_f$ )<sub>MeOD</sub> = 0.60] observed for *N*-(*p*-nitrobenzylidene)-*m*-chloroaniline,<sup>13</sup> which means that there is extensive desolvation of the methoxide ion on going from the initial to the transition state.<sup>33</sup> It is therefore a little surprising that  $k_f$  does not depend more on the DR effects and that, in contrast,  $k_r$  does. Compared to the  $\rho^r$  value of 0.54 observed for equilibrium, the figure of  $\rho^r = 0.28$ , which accounts for the DR contribution to the substituent effects on the forward rate constant, suggests that the resonance energies at the transition state are about half those in the starting material. On the other hand, the negative  $\rho^r$  value (-0.25) for the reverse reaction means that resonance between C=N and Ar is about half-established at the transition state on the way back to the imino compound. The interpretation of the difference in signs of the  $\rho^n$  and  $\rho^r$  coefficients for  $k_r$  is straightforward:  $\rho^n$  is positive because the transition state is negatively charged and stabilized by substituents which increase the electron-withdrawing properties of the aromatic ring; the negative value of  $\rho^r$  is due to the fact that  $\pi$ -electron-donating substituents make the Ar ring more able to conjugate with the partially formed C=N bond. It is clear in this case that the RP effect of a substituent, e.g., the

Scheme 3



methoxy group which renders the ring less  $\sigma$ -electron-withdrawing, should be distinguished from the DR effect.

The reaction of alkoxide ion-catalyzed addition of alcohols to arylideneanilines is analogous to that to substituted benzaldehydes<sup>17</sup> or other aldehydes, the rate-limiting step of base-catalyzed hemiacetal formation,<sup>35,36</sup> amide ions (*N*-deprotonated  $\alpha$ -amino ethers) being formed instead of hemiacetal anions. Marked similarities in behavior are expected. For substituted benzaldehydes, the  $\rho^n$  value calculated from the rate constants for methoxide ion-catalyzed addition of methanol can be calculated as 2.4 from Arota's data.<sup>17</sup> This can be interpreted in terms of a transition state resembling the hemiacetal anion. In contrast, when the reverse hydrolysis reaction was examined, the large dependence of rate on the  $pK_a$  of the leaving alcohol ( $\beta_{1g} = 1.1$  and 0.92 for formaldehyde<sup>35</sup> and acetaldehyde,<sup>36</sup> respectively), as well as the secondary kinetic isotope effects,<sup>37</sup> show that the transition state resembles the (aldehyde + alkoxide ion) system. It was suggested that this apparent inconsistency can be accounted for by imbalance between the alkoxide-ion desolvation/solvation and C–O bond formation/cleavage processes.<sup>37,38</sup> In the forward reaction, C–O bond formation lags behind desolvation. A similar explanation seems to be valid here in the case of  $\alpha$ -amino ether formation. Despite the instability of the amide ion intermediate, prior desolvation of the methoxide ion makes the degree of C–O bond formation relatively low. In a forthcoming publication,<sup>39</sup> we shall show that the  $\pi$ -electron-withdrawing effects of substituents on the aniline residue are surprisingly of relatively minor significance. These small effects suggest a fairly small negative charge development on nitrogen.

**Mechanism of the Uncatalyzed Pathway.** The existence of the  $k_f^0$  term in eq 6 is reminiscent of what was observed for the hydrolysis of the same compounds,<sup>40,41</sup> a reaction which proceeds via  $\alpha$ -amino alcohol formation. By analogy, the mechanism of Scheme 3 can be assumed, and  $k_f^0$  can be expressed by eq 7, where ( $K_a$ )<sub>ImH</sub> and  $K_{\text{auto}}$

$$k_f^0 = K_{\text{auto}}k'_2/(K_a)_{\text{ImH}} \quad (7)$$

(28) Rondinini, S.; Londhi, P.; Mussini, P. R.; Mussini, T. IUPAC Commission on Electroanalytical Chemistry (Anal. Chem. Div., IUPAC, Oxford, UK). *Pure Appl. Chem.* 1987, 59, 1693 and references cited therein. Values slightly different from 10<sup>-16.7</sup> are also listed.

(29) The  $pK_a$  values for deprotonation of **4a–p** were calculated from the aniline  $pK_a$  in water<sup>30</sup> corrected for the change in solvent and for the polar effect of the XC<sub>6</sub>H<sub>4</sub>CH(OMe) group. The effect of the latter group was estimated from the relationship  $pK_a = -33.3(\sigma)_{\text{YC}_6\text{H}_4} + 31.2$ , which we observed by plotting the  $pK_a$  values for meta-substituted anilines against Charton  $\sigma_1$  parameters<sup>1a</sup> of the YC<sub>6</sub>H<sub>4</sub> groups. It was assumed that this relationship is also valid for **4** [ $pK_a = -33.3[(\sigma)_{\text{Ph}} + (\sigma)_{\text{XC}_6\text{H}_4\text{CHOMe}}] + 31.2$ ]. The  $\sigma_1$  parameter for XC<sub>6</sub>H<sub>4</sub>CH(OMe) (0.132 for X = H) was calculated from the relationship  $(\sigma)_{\text{Z}_1\text{Z}_2\text{CH}} = 0.297[(\sigma)_{\text{Z}_1} + (\sigma)_{\text{Z}_2}] + 0.0482$ ,<sup>1a</sup> which accounts for the additivity of the polar effects of Z<sub>1</sub> and Z<sub>2</sub> within the Z<sub>1</sub>Z<sub>2</sub>CH group [( $\sigma$ )<sub>Ph</sub> = 0.12 and ( $\sigma$ )<sub>OMe</sub> = 0.31]. To take the change of solvent into account, we assumed that the differences in  $pK_a$  between water and methanol are equal to that observed between the  $pK_a$  of 2,4,6-trinitroaniline in water (12.25<sup>30,31</sup>) and in methanol (15.84<sup>32</sup>). This assumption is supported by the fact that a difference of 2–4  $pK_a$  units is usually observed between methanol and water for acids yielding unit-charged conjugated bases. Since the negative charge in the trinitroaniline anion is more delocalized than in deprotonated **4**, the difference due to solvent can be larger, but the error is not expected to be more than one  $pK_a$  unit.

(30) Dolman, D.; Stewart, R. *Can. J. Chem.* 1967, 45, 911. Stewart, R.; Dolman, D. *Can. J. Chem.* 1967, 45, 925.

(31) Schaal, R. *J. Chim. Phys., Phys. Chim. Biol.* 1955, 52, 784.

(32) Crampton, M. R.; Gibson, B. *J. Chem. Soc., Perkin Trans. 2* 1980, 752.

(33) The expected maximum solvent isotope effect for complete desolvation of the methoxide ion at the transition state and negligible solvation of the amide ion moiety can be calculated as  $\Phi_{\text{OMe}}^{\delta} = 0.37$ , where  $\Phi_{\text{OMe}} = 0.734$  is the fractionation factor of deuterium within the three methanol molecules which are expected to solvate the methoxide ion.<sup>34</sup>

(34) Gold, V.; Grist, S. *J. Chem. Soc. B* 1971, 1665. Gold, V.; Grist, S. *J. Chem. Soc. B* 1971, 2282.

(35) Funderburk, L. H.; Aldwin, L.; Jencks, W. P. *J. Am. Chem. Soc.* 1978, 100, 5444.

(36) Sørensen, P. E.; Jencks, W. P. *J. Am. Chem. Soc.* 1987, 109, 4675.

(37) Palmer, J. L.; Jencks, W. P. *J. Am. Chem. Soc.* 1980, 102, 6472.

(38) Hupe, D. J.; Jencks, W. P. *J. Am. Chem. Soc.* 1977, 99, 451. Jencks, W. P.; Brant, S. R.; Gandler, J. R.; Fendrich, G.; Nakamura, C. *J. Am. Chem. Soc.* 1982, 104, 7045. Hupe, D. J.; Pohl, E. R. *J. Am. Chem. Soc.* 1984, 106, 5634. Imbalance between alkoxide ion desolvation and proton transfers is also well documented (for a recent report, see: Cassamassina, T. E.; Huskey, W. P. *J. Am. Chem. Soc.* 1993, 115, 14).

(39) Toullec, J.; Bennour, S. Manuscript in preparation.

(40) Jencks, W. P. *Catalysis and Enzymology*; McGraw-Hill: New York, 1969; Chapter 10.

(41) Do Amaral, L.; Sandstrom, W. A.; Cordes, E. H. *J. Am. Chem. Soc.* 1966, 88, 2225. Willi, A. V. *Helv. Chim. Acta* 1956, 39, 1193. Reeves, R. L. *J. Am. Chem. Soc.* 1962, 84, 3332. Mesli, A. *Bull. Soc. Chim. Fr.* 1975, 1745.

are the iminium ion acidity constant and the methanol autoprotolysis equilibrium constant, respectively. As in the case of imine hydrolysis, the negative  $\rho^+$  value (-1.2) obtained by plotting  $\log k_f^0$  for different substituents at the Ar group can be attributed to predominant effects on  $(K_a)_{\text{imH}}$ . An electron-withdrawing substituent makes the intermediate more acidic and slows down the overall reaction even though  $k_2'$  is increased. However, the fact that  $k_f^0$  depends on  $\sigma^+$ , instead of on  $\sigma$  as observed for hydrolysis of the same substrates, and that  $\rho$  ( $\rho^+$ ) is more negative (-1.2 instead of ca. -0.5) than for this latter reaction indicates that the transition state is more iminium ion-like for methoxide ion attachment in methanol than for hydroxide ion attachment in water. This is in agreement with what is expected: iminium ions are less stable in alcohol which is less polar and less hydrogen bond-donating than water.

The stepwise mechanism shown in Scheme 3 is likely because the  $k_2$  values, calculated by rearranged eq 7 from  $k_f^0$  and estimated  $\text{p}K_a$ s, are below the diffusion limit (ca.  $10^{10} \text{ M}^{-1} \text{ s}^{-1}$ ).<sup>42</sup> A  $\text{p}K_a$  value of 2.8 in water was estimated for protonated *N*-(3-chlorobenzylidene)aniline (**3i**),<sup>43</sup> making  $\text{p}K_a = 2.8 + (6.0 - 4.6) = 4.2$  in methanol if it is assumed that the difference in  $\text{p}K_a$  between the two solvents is the same as for the anilinium ion (6.0 and 4.63 in methanol and water, respectively<sup>44</sup>). It follows that, by means of eq 7,  $\log k_2'$  can be calculated from the  $k_f^0$  data in Table 1 as  $[\log (0.16 \times 10^{-4}) - 4.2 + 16.7] = 7.7$ . Similar calculations can be performed by considering the  $\text{p}K_a$  estimates for protonated *N*-[4-(trimethylammonio)benzylidene]-4-methylaniline in water, 1.93,<sup>45</sup> and correcting this value for the  $\text{NMe}_3^+$  and Me group effects. To do so, it can be assumed that the  $\rho^+$  values for the effects of substituents on the benzaldehyde and aniline residues, -2.4 and -3.9, respectively, are the same in methanol as those observed in nitromethane.<sup>46</sup> Taking into account  $\sigma^+$  values of 0.82 and -0.31 for the two groups, the  $\text{p}K_a$  of the unsubstituted *N*-benzylideneanilinium ion ( $3\text{d}\cdot\text{H}^+$ ) can be calculated as  $[1.93 + (0.82 \times 2.4) - (0.31 \times 3.9)] = 2.69$  in water and  $(2.69 + 6.0 - 4.6) = 4.09$  in methanol, and  $\log k_2'$  is  $(\log 10^{-4} - 4.09 + 16.7) = \text{ca. } 8.7$ . When the  $\rho^+$  value of -1.2 for the  $k_f^0$  variations is considered, it is noteworthy that this coefficient is much smaller than that expected for  $\text{p}K_a$  variations of protonated **3**, i.e., that expected if  $k_2$  were diffusion-controlled. As indicated above, the  $\text{p}K_a$  in nitromethane depends on  $\sigma^+$  with a slope of -2.4; for *N*-arylidene-2,2-dimethylethylamine in water  $\rho^+$  is -1.6.<sup>43</sup> Since the former value is probably close to that governing  $\text{p}K_a$  variations in methanol (because of the similarities in dielectric properties), it follows that the  $\log k_f^0$  variations ( $\rho^+ = -1.2$ ) are only half of those on  $\text{p}K_a$ .

**Relevance of the Young-Jencks Dual-Parameter Relationships.** When the YJ equation (eq 3) is used instead of eq 1 it is implicitly assumed that two different substituent effects can be separated, namely (i) the DR effects due to the substituent-induced changes in resonance interactions between the aromatic ring and the reaction

center and (ii) the polar effect of the substituted ring, this latter including the inductive (and/or field) effect of the substituent itself and the resonance-induced polar (RP) effect. The substituted phenyl group,  $\text{C}_6\text{H}_4\text{X}$ , is therefore considered as a group that influences the reactivity of the side-chain reaction center both by polar and resonance effects, whatever happens within this group. The signs and absolute values of  $\rho^a$  and  $\rho^r$  indicate how the polar and resonance effects of  $\text{C}_6\text{H}_4\text{X}$  contribute to the changes in the energy difference between the transition state or products and the reactants. For instance, the positive  $\rho^a$  values observed from the  $k_f$  and  $k_r$  variations mean that an increase in the  $\sigma$ -electron-withdrawing properties of  $\text{C}_6\text{H}_4\text{X}$  stabilizes the negatively charged transition state relative to the starting materials, the Schiff base or the  $\alpha$ -amino ether, respectively; the negative  $\rho^r$  coefficient calculated from the  $k_r$  data is typical of a transition state stabilized by  $\pi$ -electron donation by  $\text{C}_6\text{H}_4\text{X}$ . The fact that  $\rho^a$  and  $\rho^r$  are of opposite signs suggests some independence of the two contributions. In contrast, Taft's DSP equation (eq 1) allows a different separation of the substituent effects, the inductive (or field) effect of the *substituent* on one hand and the overall resonance contribution on the other. This latter is free from direct resonance only if there is no conjugation between the reaction center and the ring. It follows that these two equations can be considered as simplified forms of a three-parameter equation (eq 8), similar to that put forward by other

$$\log k \text{ or } \log K = \rho_I \sigma_I + \rho_{\text{RP}} \sigma_{\text{RP}} + \rho_{\text{DR}} \sigma_{\text{DR}} + C \quad (8)$$

authors,<sup>47</sup> and where the  $\rho_{\text{RP}} \sigma_{\text{RP}}$  and  $\rho_{\text{DR}} \sigma_{\text{DR}}$  terms account for the RP and DR effects, respectively.<sup>48</sup> The work reported here and other previous data handled by the YJ equation suggest that it is often convenient and informative to assume that the  $\rho_I / \rho_{\text{RP}}$  ratios are close to unity, making it licit to merge the first two terms, even though this is not rigorously valid<sup>49</sup> in view of a compilation by Ehrenson<sup>2b</sup> of  $\rho_I$  and  $\rho_R$  data for various reactions. It is noteworthy that in the absence of DR effects a one-parameter relationship of rate or equilibrium constants vs  $\sigma^a$  or  $\sigma^o$  is generally observed and that this means that the  $\rho_{\text{R}}^o / \rho_I = 1$  condition is then satisfied.

As stressed in the Introduction, a major disadvantage of the Taft equation lies in the difficulty of dealing with different situations in electron demand of the reactive or examined site. We believe that this is an important drawback when the electron demand changes gradually along the reaction path and when the polar and resonance effects influence the energies of both transition state (or

(47) (a) Nieuwdorp, G. H. E.; De Ligny, C. L.; Van Houwelingen, H. C. *J. Chem. Soc., Perkin Trans. 2* 1979, 537. (b) de Ligny, C. L.; Van Houwelingen, H. C. *J. Chem. Soc., Perkin Trans. 2* 1987, 559.

(48) Equation 8 implies that the direct resonance effects can be accounted for by a single term,  $\rho_{\text{DR}} \sigma_{\text{DR}}$ . This should be true when the reaction center is either  $\pi$ -electron demanding or  $\pi$ -electron donating. In the first case  $\sigma_{\text{DR}}$  can be expressed by the  $(\sigma^+ - \sigma^a)$  difference; in the latter  $(\sigma - \sigma^a)$  can be thought to account for the  $\pi$ -electron-accepting effects of the substituents. However, in other cases rate and equilibrium constants can depend on both  $\pi$ -electron-donating and  $\pi$ -electron-demanding DR effects, especially when resonance occurs at different states of the reactions or when resonance involves two localized molecular orbitals of the reacting side chain. In these cases, it can be expected that two  $\rho_{\text{DR}} \sigma_{\text{DR}}$  terms [ $(\rho^+)(\sigma^+ - \sigma^a)$  and  $(\rho^-)(\sigma - \sigma^a)$ ] should be included in an expanded eq 8. It was suggested in ref 47 that a single  $\rho_{\text{DR}} \sigma_{\text{DR}}$  term (called  $\rho_{\text{DR}} \sigma_{\text{DR}}$ ) is sufficient to deal with most situations whatever the  $\pi$ -electron demand. However, although the fit of the data can be judged satisfactory, we believe that this hypothesis, which means that resonance does not depend on the electron demand, is chemically misleading.

(49) For a detailed discussion of this point, see also ref 47a.

(42) This rough value is that calculated from the Smoluchowski-Debye equation when the electrostatic contribution is taken into account. For a review, see: Ridd, J. H. *Adv. Phys. Org. Chem.* 1978, 16, 1.

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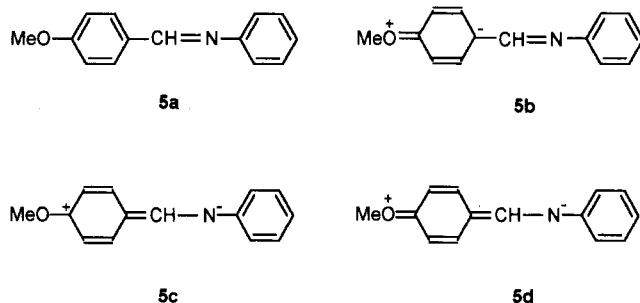


products) and reactants. Happer and Wright<sup>50</sup> suggested a two-parameter equation analogous to eq 1, but with a  $\sigma_R$  parameter varying continuously with  $\epsilon$ , an adjustable parameter characterizing the electron demand, and Bromilow et al.<sup>51</sup> used "dual-substituent parameter nonlinear resonance relationships",  $\sigma_R$  in eq 1 being replaced by  $\sigma_R^0/(1 - \epsilon\sigma_R^0)$ . More recently, Charton claimed that a triparametric equation (named the "LDR equation") (eq 9)<sup>52</sup> can represent the full spectrum of electrical effects

$$\log k \text{ or } \log K = L\sigma_I + D\sigma_d + R\sigma_e + C \quad (9)$$

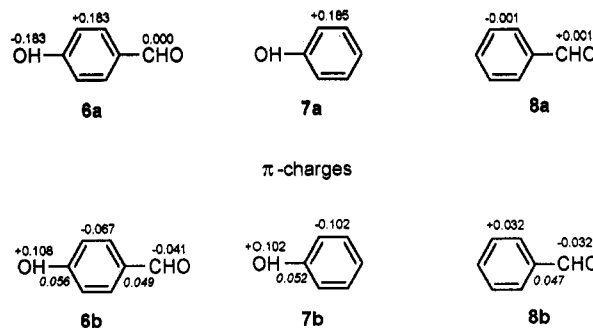
exerted by substituents bonded to carbon. In this equation,  $\sigma_I$  is the localized (field and/or inductive) effect parameter,  $\sigma_d$  characterizes the intrinsic delocalized (resonance) electrical effect, and  $\sigma_e$  represents the sensitivity of the substituent to change in electronic demand by the active or reactive site. It is noteworthy that none of these equations introduces any distinction between the RP and DR effects.

Because both the C=N and X groups in 3 are conjugated with the phenylene (Pn) ring, with possible through-ring conjugation between  $\pi$ -electron-donating X and  $\pi$ -electron-demanding C=N, it can be argued that the above dissection of the resonance effects is not valid. Through-conjugation between X and C=N, as well as resonance between Pn and C=N, can be thought to change the  $\pi$ -electron charge on the ring and its distribution on the different atoms. The RP effect would be dependent on the reacting side chain. This can be seen in the case of the *p*-methoxy derivative if one considers some of the contributing structures 5a–5d. The assumption that the

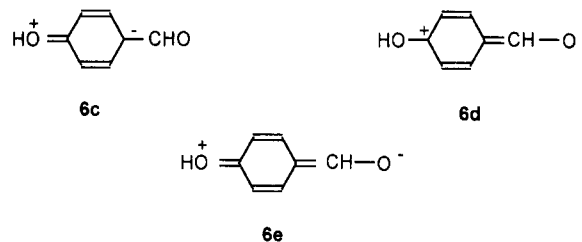


RP and DR effects can be separated implies that the contribution of 5d is of minor importance. This is, at first sight, in disagreement with the simple view of resonance within the valence-bond theory. However, for XPnY molecules, where X and Y are  $\pi$ -electron-donating and demanding groups, respectively, ab initio MO calculations at the STO-3G level and using standard model geometries show that the charge transfers from X to Pn or from Pn to Y are fairly independent of the other group present in the molecule.<sup>53</sup> For instance, let us consider the ab initio data for 4-hydroxybenzaldehyde 6 (Scheme 4), where the OH and CHO groups are analogous to OMe and CH=NPh,

**Scheme 4**  
 $\sigma$ -charges



respectively, compared with those for phenol 7 and benzaldehyde 8. [In 6, 7, and 8, the upper figures correspond to the net  $\sigma$  and  $\pi$  charges; below the bonds and italicized are the  $\pi$ -bond characters (data from refs 53 and 54)]. These comparisons clearly show that the negative charge on CHO is only a little increased on going from 8 to 6 and that the  $\pi$ -bond character of the C(H)=O bond is almost unchanged after substitution by the OH group. Moreover, these data show that the  $\pi$ -charge on the ring of 6b (-0.067) is close to that expected (0.032–0.102) when additivity of the OH and CHO group effects is assumed. It follows that the contributing structure 6e



can be considered as being of less significance than 6c and 6d as far as charge distribution is concerned.<sup>55</sup> In this case it is valid to assume that the RP and DR effects are additive. However, this assumption should usually be considered as a crude approximation. The dependence of the RP effect on cross resonance is certainly more significant when the  $\pi$ -electron-demanding effect of the reacting sidechain increases.

The additivity assumption for charge transfer and charge localization on the ring is certainly not valid for the substituted  $\alpha,\alpha$ -dimethylbenzyl cations (9a), which rates



of formation have served to define the  $\sigma^+$  parameters.<sup>10</sup> The weight of the through-conjugation contributing structure 9b should be large, making the separation of the RP and DR effects questionable. Moreover, it was shown that the ability of a substituent to provide resonance stabilization depends on the electronic demand.<sup>52</sup> Because of differences in polarizability, two substituents may have the same ability to provide  $\pi$ -electrons when the electron

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(55) Similar conclusions can be drawn when one considers the CN or NO<sub>2</sub> groups instead of CHO.



demand is weak and different ones when they are conjugated with a very electron-deficient center. Notwithstanding, it is noteworthy that equilibrium constants for many addition reactions to carbonyl compounds correlate perfectly with the  $\sigma^+$  parameters<sup>12b</sup> despite the relatively low electron demand as compared with carbenium ions. This seems to indicate that the above reservations are probably not very serious.

### Experimental Section

**Reagents.** **3a-3p** were prepared by the previously described<sup>56</sup> condensation of the substituted benzaldehydes (from Aldrich or Janssen Chimica) (0.1 mol) with aniline (Aldrich) (0.1 mol) dissolved in heptane. Water was removed by azeotropic distillation by means of a Dean-Stark tube. The use of heptane makes the reaction complete in less than 1 h. Crystallization was usually observed on cooling and **3a-3p** were recrystallized twice, usually from *n*-pentane or *n*-hexane. In the case of **3e**, **3f**, and **3i**, which are liquid at rt, filtration was performed at low temperature. They were identified by <sup>1</sup>H-NMR. For the other compounds, the melting points were observed to correspond, when available, to literature data [all mps (uncorrected) in °C] [**3a**, 63.5–64 (lit.<sup>56-58</sup> 63–64); **3b**, 47.5–48; **3c**, 44–45 (lit.<sup>59</sup> 45.5–47, lit.<sup>60</sup> 43.5–44.5); **3d**, 51.5–52 (lit.<sup>58</sup> 52, lit.<sup>57</sup> 52–53, lit.<sup>59</sup> 51–52, lit.<sup>60</sup> 50.5–51.5); **3f**, 42.5–43 (lit.<sup>60</sup> 42–43); **3g**, 30–30.5; **3h**, 63.5–64 (lit.<sup>57,59</sup> 63.5–64.5, lit.<sup>56,60</sup> 64–65); **3j**, 72–72.5 (lit.<sup>59</sup> 72.5–73.5, lit.<sup>57,58</sup> 73–74, lit.<sup>60</sup> 73.5–74); **3l**, 77.5–78; **3m**, 93.5–94.5 (lit.<sup>60</sup> 97–98); **3n**, 42–42.5; **3o**, 64.5–65; and **3p**, 91–92 (lit.<sup>59</sup> 91–92, lit.<sup>57</sup> 92–93)]. "Analyzed Baker Reagent" methanol was used as received. Methoxide ion solutions, prepared by the addition of sodium to methanol, were protected against moisture and carbon dioxide. Concentrations of the stock solutions were measured by acid titration. Low concentration solutions were obtained by volume-to-volume dilutions, and [MeO<sup>-</sup>] was corrected for the fall in concentration due to reactions with small amounts of dissolved carbon dioxide and/or formic acid. This uptake of methoxide ion (ca. 10<sup>-4</sup> M) was determined from the linear plot of  $k_{\psi}$  for **3p** against the calculated methoxide concentration. Contrary to what is expected in the absence of carbon dioxide or formic acid in methanol, the lines observed did not pass exactly through the

origin but crossed the abscissa coordinate at a point corresponding to the small amount of methoxide ion which had reacted.

**Kinetic and Equilibrium Measurements.** UV-vis absorption spectra were recorded with a Varian/Cary 118 spectrophotometer, whereas rate and equilibrium measurements were performed on a Cary 16 spectrophotometer. The contents of the thermostated 1-cm cell were stirred by means of a Teflon-coated magnet rotated by a motor located beneath the cell holder. Temperature (25 ± 0.05 °C) was checked in the cell by a Yellow Springs Instrument 45 CU cuvette thermometer (thermistor detector YSI 4502). Kinetic runs observed at 330 nm (**3a-3s**) or 370 nm (**3o-3p**) were followed on a pen recorder after microsyringe addition of ca. 10 μL of a solution of Schiff base in dioxane. Rate constants, as well as the initial,  $A_0$ , and final,  $A_{\infty}$ , extrapolated absorbances, were calculated by the Guggenheim method, which consists of expressing the absorbance by eq 10, where  $A_t$  and  $A_{t'}$

$$A_t - A_{t'} = (A_0 - A_{\infty})(1 - e^{-k_{\psi}\theta})e^{-k_{\psi}t} \quad (10)$$

are the absorbances at times  $t$  and  $t' = t + \theta$  ( $\theta = \text{constant}$ ). The linear plots of  $\ln(A_t - A_{t'})$  against time  $t$  yield  $-k_{\psi}$  as the slopes and  $[\ln(A_0 - A_{\infty}) + \ln[1 - \exp(-k_{\psi}\theta)]]$  as the intercepts. The  $A_0 - A_{\infty}$  values can then be calculated by combining the intercept and slope data. In practice,  $N$  points ( $N$  even) were taken from the absorbance-time curve, starting from an arbitrary first point at time  $t_i$ , with a data time interval  $h$ . The constant  $\theta$  was always chosen as  $Nh/2$ . The differences  $A_i - A_{\infty}$  were calculated from a modified eq 10 with  $t - t_i$  and  $A_i - A_{\infty}$  replacing  $t$  and  $A_0 - A_{\infty}$ , respectively. The differences ( $\pm 0.2$  s) between time zero, corresponding to aldehyde addition, and times  $t_i$  were estimated from the absorbance curves since the former corresponded to abrupt jumps in absorbance. The  $A_0$  values were calculated as  $(A_i - A_{\infty}) \exp(k_{\psi}t_i) + A_{\infty}$ . The calculations were usually repeated for various  $A_i$  starting points along the curves, and final average  $A_0$ ,  $A_{\infty}$ , and  $k_{\psi}$  values were deduced. Comparisons between this method and the alternative one, which consists in measuring final  $A_{\infty}$  values, calculating  $A_0$  from the amount of aldehyde added, and deducing  $k_{\psi}$  as the slopes of the  $\ln(A_t - A_{\infty})$ -time plots, showed that the former is safer and more accurate. This is because direct  $A_{\infty}$  determinations are sometimes difficult, especially when the reaction is slow, and because small errors in  $A_{\infty}$  determination have dramatic consequences on the  $k_{\psi}$  and  $K$  values. Moreover, the method used does not require the initial benzaldehyde concentration to be exactly known.

Equilibrium constants, calculated by eq 5, were not corrected for the small amounts of dioxane introduced in methanol (<1%). It was checked that the extrapolated  $A_0$  absorbance values corresponded to those expected from absorptivity data. This and the absence of any deformation of the first-order curve at the beginning of the reaction make it possible to rule out any slow *E*-to-*Z* isomer transformation parallel to the addition reaction.

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