Nucleophilic Attacks on Carbon–Nitrogen Double Bonds. 2.[1] Diversity of Mechanisms for the Substitution of Diarylimidoyl Chlorides by Amines in Benzene

Rachel Ta-Shma and Zvi Rappoport*

Contribution from the Department of Organic Chemistry, The Hebrew University, Jerusalem, Israel. *Received May 24, 1976*

Abstract: The reactions of diarylimidoyl chlorides $ArC(Cl)=NC_6H_4Y$ with piperidine, morpholine, and diethylamine which form the corresponding amidines were studied in benzene. Either only first-order term in the amine (mostly with piperidine) or both first- and second-order terms in the amine (mostly with morpholine) were found. The Hammett plots show a minimum when Y = *p*-Cl with piperidine and when Y = *m*-Cl with morpholine, and the element effect $k(PhC(Br)=NPh)/k(PhC(Cl)=NPh)$ for the reaction with piperidine is 440. Analysis of the substituent effects, the Hammett-type correlations, the catalyzed route, the effect of the nucleophile and the element effect, and the activation parameters suggest that the bimolecular substitution proceeds via the $S_N2(IP)$ mechanism for electron-donating substituents and via nucleophilic addition–elimination for electron-attracting substituents. Superimposed on these routes are less important variants of third-order amine-catalyzed routes, where the amine may serve as a basic, electrophilic, or bifunctional catalyst.

Nucleophilic attacks on carbon–oxygen,[2] carbon–nitrogen,[3] and activated carbon–carbon[4] double bonds leading to addition, substitution and isomerization reactions are common, and some of them were extensively studied.[2-4] The carbon–nitrogen double bond is intermediate in properties (bond length and energy, dipole moment)[5] between the C=O and the C=C double bonds, and the mechanisms of nucleophilic reactions at the C=N bond are therefore expected to be analogous to those established for reactions at these bonds. Two such routes are nucleophilic attack on the double bond to form an intermediate carbanion or zwitterion which gives substitution, addition, and cleavage products, and a cleavage of the C–X bond to form a cationoid species when X is a leaving group (Scheme I).

Much mechanistic work was devoted to the substitution of activated vinyl halides[6] and acyl halides.[2a,7] However, the mechanisms of the corresponding reactions of simple azomethine systems were much less investigated,[3] although more data are available for systems where the nitrogen is substituted by an heteroatom.[8]

Ugi, Beck, and Fetzer[9] found that the solvolysis of *C*-chloroazomethine systems RC(Cl)=NR′ (R, R′ = alkyl, aryl) in aqueous acetone shows common ion rate depression by Cl^-, rate enhancement by increasing the solvent polarity, by addition of several amines, and by increase in the bulk of the N-substituent, and rate reduction on increase in the bulk of the C-substituent. Electron-withdrawing substituents reduced the hydrolysis rate, and the reaction was more sensitive to a change in the substituent on the nitrogen than to a change in the substituent on carbon. For *N*-phenylbenzimidoyl chlorides we calculated from Ugi's data[9] a ρ^+ value of −1.2.[10]

The hydrolysis was discussed in terms of ionization to an ion pair which either returns to the imidoyl chloride or forms the product.[9] Surprisingly, the intervention of free ions was not invoked, although the common ion rate depression indicates[11] that free ions lead to a large fraction of the product (Scheme II).

Scheme II

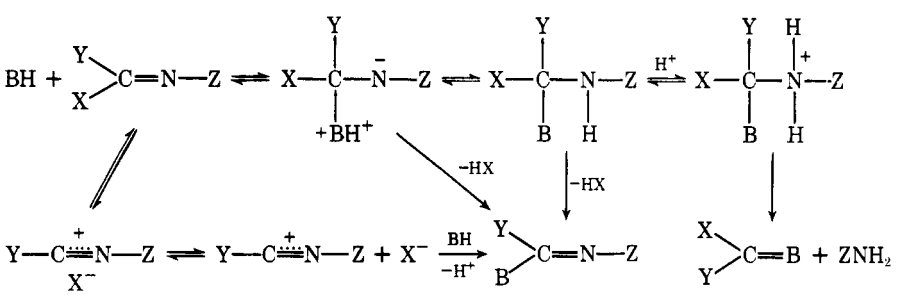
$$RC(Cl)=NR' \underset{k_{-1},\,Cl^-}{\overset{k_1}{\rightleftharpoons}} R-C^{+}\equiv N-R' + Cl^- \xrightarrow{k_2,\ H_2O} RCONHR'$$

Hegarty, Cronin, and Scott[12] showed that the hydrolysis of compounds RC(Cl)=NAr′ (R = Ar, ArO, ArS, and ArNMe) in 90% dioxane proceeds via the S_N1 mechanism as evidenced by common ion, salt, and substituent effects. Most of the other information on substitution at the C=N bond comes from the work of Scott, Hegarty, and co-workers[8] on the hydrolysis of hydrazonyl halides $R^1C(X)=NNR^2R^3$ and the related halodiazabutadienes. The S_N1 mechanism is substantiated by the negative ρ or ρ^* values for a change in R^1, R^2, and R^3,[8i,h,o] by the high Winstein–Grunwald *m* values,[8h,m] by the positive salt effect,[8m] and by the common ion rate depression.[8i,m,l] The configurational instability of the azomethine systems[13] prevented the study of the stereochemistry of the substitution of most of the azomethine systems.

When R^3 = H an alternative mechanism was observed: the reaction is initiated by elimination of HX with the formation of a dipolar intermediate.[8i]

Much less is known about the bimolecular substitution mechanism at the C=N bond compared with the analogous reactions at C=C[4] and C=O[2,7] centers. An example is the basic hydrolysis of the diarylchloroimidates ArOC(Cl)=NAr′

Scheme I



X, Y, Z = R, Ar, H, OR, SR, NR_2, halogen
BH = H_2O, ROH, RSH, RNH_2, R_2NH, HCN

Table I. Second-Order Rate Constants k_{II} for the Reaction of Diarylimidoyl Chlorides **1** with Amines in Benzene

Compd	Amine[a]	10^2[Amine], M	10^4k_{II}, M^{-1} s^{-1} at 30 °C	Compd	Amine[a]	10^2[Amine], M	10^4k_{II}, M^{-1} s^{-1} at 45 °C
1a	Pip	2.42	20.9	**1a**	Pip	5.01	52.9
1a	Pip	7.26	21.0	**1a**	Pip	16.7	55.4
1a	Pip	13.6	21.3	**1a**	Pip	33.4	49.4
1a	Pip	19.1	20.8				
1b	Pip	9.55	39.9	**1b**	Pip	3.34	96.8
1b	Pip	28.7	37.7	**1b**	Pip	6.68	92.3
1b	Pip	47.8	37.8	**1b**	Pip	10.0	85.8
1c	Pip	17.5	2.82	**1c**	Pip	16.7	6.92
1c	Pip	52.6	2.78	**1c**	Pip	50.1	6.99
				1c	Pip	100.0	7.35
1d	Pip	15.1	2.02	**1d**	Pip	16.7	6.34
1d	Pip	45.2	2.02	**1d**	Pip	50.1	5.71
1d	Pip	90.3	2.36	**1d**	Pip	100.0	6.45
1e	Pip	19.1	2.36				
1e	Pip	49.5	2.88				
1e	Pip	76.5	2.87				
1f	Pip	5.10	6.98	**1f**	Pip	5.10	16.7
1f	Pip	10.2	7.30	**1f**	Pip	20.4	16.3
1f	Pip	15.3	7.46	**1f**	Pip	30.5	16.3
1f	Pip	20.4	7.85				
1f	Pip	30.6	7.95				
1g	Pip	7.7	14.2	**1g**	Pip	33.4	32.2
1g	Pip	11.5	14.7	**1g**	Pip	133.4	34.3
1g	Pip	17.6	15.8	**1g**	Pip	200.0	35.4
1g	Pip	26.3	16.2				
1g	Pip	32.0	17.4				
1g	Pip	40.0	18.3				
1g	Pip	47.9	19.4				
1h	Pip	9.83	12.4	**1h**	Pip	1.48	29.2
1h	Pip	25.6	12.7	**1h**	Pip	5.92	28.4
1h	Pip	59.0	11.1	**1h**	Pip	17.85	29.0
1i	Pip	27.5	2.50				
1i	Pip	68.7	2.53				
1i	Pip	96.2	2.72				
1j	Pip	20.0	2.95	**1j**	Pip	49.5	6.73
1j	Pip	39.9	3.32	**1j**	Pip	198.0	6.90
1j	Pip	59.8	3.89	**1j**	Pip	297	7.07
1j	Pip	79.7	4.23				
1j	Pip	99.7	4.56				
1j	Pip	119.6	4.79				
1k	Pip	19.7	2.56	**1k**	Pip	20.1	6.31
1k	Pip	39.3	2.67	**1k**	Pip	80.5	6.69
1k	Pip	58.9	2.78	**1k**	Pip	120.8	6.93
1k	Pip	98.2	3.01				
1k	Pip	118.0	3.08				
1l	Pip	3.03	622	**1l**	Pip	2.95	135
1l	Pip	6.06	674	**1l**	Pip	11.8	132
1l	Pip	8.35	699	**1l**	Pip	17.7	144
1l	Pip	8.35[b]	677				
1l	Pip	12.1	729				
1l	Pip	18.2	798				
1l	Pip	24.7	874				
1a	Mor	12.0	20.3				
1a	Mor	18.3	21.9				
1a	Mor	24.0	23.2				
1a	Mor	27.5	24.9				
1a	Mor	30.0	25.7				
1a	Mor	36.0	26.8				
1c	Mor	19.7	2.05				
1c	Mor	29.6	2.34				
1c	Mor	39.5	2.18				
1c	Mor	59.2	2.45				
1d	Mor	79.8	0.840				
1d	Mor	99.8	0.923				
1d	Mor	119.6	1.026				
1d	Mor	139.5	1.105				
1d	Mor	159.5	1.141				
1d	Mor	179.4	1.272				
1e	Mor	40.1	0.416				
1e	Mor	60.2	0.488				
1e	Mor	80.2	0.519				

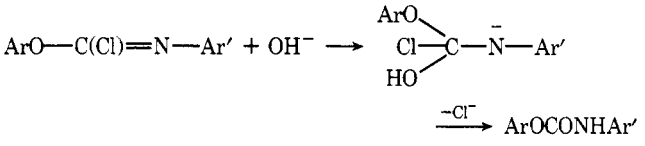
Table I (*Continued*)

Compd	Amine[a]	10^2[Amine], M	$10^4k''$, M^{-1} s^{-1} at 30 °C	Compd	Amine[a]	10^2[Amine], M	$10^4k''$, M^{-1} s^{-1} at 45 °C
1e	Mor	100.2	0.574				
1e	Mor	120.2	0.637				
1f	Mor	60.3	0.716				
1f	Mor	80.4	0.837				
1f	Mor	100.5	0.982				
1f	Mor	120.5	1.090				
1f	Mor	140.6	1.185				
1f	Mor	181.0	1.438				
1g	Mor	39.9	1.086	**1g**	Mor	10.1	1.59
1g	Mor	49.8	1.148	**1g**	Mor	40.2	2.31
1g	Mor	59.8	1.271	**1g**	Mor	60.3	2.74
1g	Mor	69.7	1.356				
1g	Mor	79.7	1.510				
1g	Mor	8.96	1.628				
1c	Et_2NH	118.0	0.176				
1c	Et_2NH	148.0	0.165				
1c	Et_2NH	177.0	0.158				
1g	Et_2NH	39.0	0.118	**1g**	Et_2NH	80.3	0.331
1g	Et_2NH	118.0	0.119	**1g**	Et_2NH	160.5	0.324
1g	Et_2NH	235.0	0.119	**1g**	Et_2NH	241.0	0.318
1l	Et_2NH	59.8	0.464				
1l	Et_2NH	95.6	0.516				
1l	Et_2NH	119.5	0.544				
1l	Et_2NH	143.5	0.574				
1l	Et_2NH	179.2	0.621				

[a] Pip, piperidine; Mor, morpholine. [b] In the presence of 0.15 M *N*-methylpiperidine.

which is first order in the imidate and in OH^- and gives $\rho(Ar) = 1.41$ and $\rho(Ar') = 2.39$, suggesting reaction via a tetrahedral intermediate (Scheme III) with negative charge dispersal over the aryl groups.[12]

Scheme III



Johnson et al.[14] found exclusive or predominant inversion of configuration in the substitution of *Z*- and *E*-*O*-methylbenzohydroximoyl chlorides (and the *p*-nitro derivatives) by methoxide ion in methanol, and a nucleophilic addition-elimination mechanism (Scheme III) seems likely since the k_{Br}/k_{Cl} ratio for the *E* isomers is only 1.9. In contrast, McCormack and Hegarty[15] found retention of configuration in the substitution of several *Z*-hydrazonyl halides RC(X)=NN(Me)Ar by methoxide ion. These stereochemical differences are not easily rationalized.

The mechanism of substitution at the C=N bond by nucleophiles other than those derived from the solvent were not studied kinetically. As a part of a project to delineate the various mechanistic routes for substitution at the C=N bond and to compare them with those at C=C bonds,[6,16] we report now the effect of the substituents, the leaving group, and the amine on the substitution of diarylimidoyl chlorides by amines in benzene—a solvent with low dielectric constant. The diversity of mechanisms found was extended by studying the reactions in acetonitrile[1,17]—a solvent with higher dielectric constant, as reported in a recent publication.[17a]

Results

The substitution of the diarylimidoyl chlorides **1a–1m** by piperidine, morpholine, and diethylamine which gives quantitatively the corresponding amidines (eq 1) was followed spectrophotometrically in benzene in the presence of excess amine. The reaction was first order in the imidoyl chloride at 0.00005–0.0005 M concentrations with pseudo-first-order constants (k_{obsd}),[18] and in most of the systems it was also first order in the amine. In several cases the overall second-order constants $k'' = k_{obsd}/[R_2NH]$[18] were linear in the amine concentration:

$$\underset{\mathbf{1}}{XC_6H_4C(Cl)=NC_6H_4Y} + 2R_2NH \rightarrow R_2NH_2^+Cl^- + \underset{\mathbf{2}}{XC_6H_4C(NR_2)=NC_6H_4Y} \quad (1)$$

a, X = H, Y = *p*-MeO
b, X = H, Y = *m*-Me
c, X = H, Y = H
d, X = H, Y = *p*-Cl
e, X = H, Y = *m*-Cl
f, X = H, Y = *p*-CN
g, X = H, Y = *p*-NO_2
h, X = *p*-MeO, Y = H
i, X = *p*-Cl, Y = H
j, X = *p*-NO_2, Y = H
k, X = *p*-NO_2, Y = *p*-MeO
l, X = *p*-NO_2, Y = *p*-NO_2
m, X = H, Y = *p*-Br

$$k'' = k' + k''[R_2NH] \quad (2)$$

Equation 2 applies mostly with morpholine, and the second-order term in the amine becomes more pronounced with the increase in the electron-withdrawing ability of Y. With piperidine and Et_2NH it applies only when either X or Y are strongly electron withdrawing.

The data are collected in Table I. Only typical k'' values are given when k'' is constant, and a larger number of k'' values are given when eq 2 is obeyed. Table II summarizes the k', k'', and k''/k' values and the activation parameters for systems obeying eq 2. When k'' is constant, its average value which is based on larger amount of data than in Table I is given under k'.

Table II. Second-Order (k') and Third-Order (k'')[a] Rate Constants and Activation Parameters for the Reaction of p-$XC_6H_4C(Cl)=NC_6H_4Y$ with Amines in Benzene

Amine	X	Y	$10^4k'$ in M^{-1} s^{-1} 30 °C	$10^4k'$ in M^{-1} s^{-1} 45 °C	$10^4k''$ in M^{-2} s^{-1} at 30 °C	k''/k', M^{-1} at 30 °C	$\Delta H^{\ddagger}$, kcal/mol[b]	$\Delta S^{\ddagger}$, eu[b]
Piperidine	H	p-MeO	20.8 ± 0.8	52.7 ± 1			11.5 ± 0.9	−35 ± 3
	H	m-Me	3.80 ± 0.07	9.26 ± 0.4			10.8 ± 0.8	−41 ± 3
	H	H	2.74 ± 0.1	7.17 ± 0.15			11.5 ± 0.7	−39 ± 2
	H	p-Cl	2.12 ± 0.08	5.97 ± 0.3			12.5 ± 1.0	−36 ± 4
	H	m-Cl	2.84 ± 0.2					
	H	p-CN	6.78 ± 0.02	16.5 ± 0.2	4.8 ± 0.3	0.71	10.6 ± 0.2	−40 ± 0.6
	H	p-NO_2	13.2 ± 0.3	34.2 ± 1	12.8 ± 0.8	0.97	11.4 ± 0.7	−36 ± 2
	MeO	H	12.0 ± 0.8	28.7 ± 0.3			10.4 ± 1.0	−40 ± 3
	Cl	H	2.54 ± 0.09					
	NO_2	H	2.62 ± 0.08	6.86 ± 0.2	1.92 ± 0.06	0.73	11.5 ± 0.8	−39 ± 3
	NO_2	p-MeO	2.46 ± 0.02	6.67 ± 0.23	0.55 ± 0.02	0.22	12.0 ± 0.5	−38 ± 2
	NO_2	p-NO_2	59.8 ± 0.5	136.0 ± 5	111.0 ± 4	1.86	9.8 ± 0.6	−38 ± 2
Morpholine	H	p-MeO[c]	16.8 ± 0.5		28.0 ± 2	1.66		
	H	H	2.2 ± 0.2					
	H	p-Cl	0.51 ± 0.03		0.42 ± 0.02	0.82		
	H	m-Cl	0.32 ± 0.01		0.26 ± 0.02[d]	0.81		
	H	p-CN	0.37 ± 0.02		0.59 ± 0.015	1.60		
	H	p-NO_2	0.62 ± 0.04	1.40 ± 0.1[e]	1.11 ± 0.06[e]	1.80	9.7 ± 0.6	−48 ± 2
							7.4 ± 2[f]	−54 ± 6[f]
Et_2NH	H	H	0.17 ± 0.01					
	H	p-NO_2	0.118 ± 0.0005	0.323 ± 0.005			12.2 ± 0.2	−43 ± 0.8
	NO_2	p-NO_2	0.39 ± 0.01		0.13 ± 0.01	0.33		

[a] The correlation coefficients of the k'' vs. $[R_2NH]$ plots are >0.99. [b] Calculated for the k' process. The errors in $\Delta H^{\ddagger}$ and in $\Delta S^{\ddagger}$ were calculated according to R. C. Peterson, J. H. Markgraf, and S. D. Ross, *J. Am. Chem. Soc.*, **83**, 3819 (1961). [c] With aniline k'' ~7.5×10^{-4} M^{-1} s^{-1} at room temperature. [d] The change in the dielectric constant contributes ca. half of the change in k''. [e] At 45 °C, $k'' = 2.1 \pm 0.2$ M^{-2} s^{-1}; $k''/k' = 1.5$ M^{-1}. [f] Calculated for the k'' process.

Table III. Solvent Effect on the Reaction of $XC_6H_4C(Cl)=NC_6H_4Y$ with Amines in Benzene at 30 °C

X	Y	Amine	[Amine], M	[PhCl], M	$10^5k''$, M^{-1} s^{-1}
H	H	Morpholine	0.51		24.9
			0.51	0.49	32.0
			0.51	0.99	37.8
H	m-Cl	Morpholine	0.80		5.2
			0.80	0.40	5.4
			0.80	0.81	5.9
H	p-NO_2	Morpholine	0.99		19.4
			0.99	0.34	19.8
			0.99	0.69	20.2
H	p-NO_2	Piperidine	0.30		165
			0.30	0.42	175

Although the second-order term in the amine is interpreted below as due to amine catalysis in the substitution, it may also result from dimerization of the amine in benzene or from an increase in the dielectric constant of the solvent (ϵ 2.28)[19] by the amine (piperidine, ϵ 5.8; morpholine, ϵ 7.33).[19] However, since the effect was not found for systems where the highest amine concentrations were used, explanation in terms of catalysis is more likely. The effect of the dielectric constant was evaluated by conducting several of the reactions in the presence of chlorobenzene whose dielectric constant (5.71) resembles that of piperidine. The pronounced rate enhancement (Table III) indicates that when the change in k'' is small or nonsystematic or when it is important only at low $[R_2NH]$, it may be due to a dielectric constant effect. Even for systems (e.g., **1g**) where k'' is relatively large, ca. 20% of the change may be due to this effect.

Element Effect. In order to study the effect of the leaving group we tried to synthesize several imidoyl bromides with the same substituents as in compounds **1**. Although the intermediacy of imidoyl bromides in the degradation of amides by PBr_5 was suggested a long time ago,[20a] they were not isolated until recently.[20b] Attempts to prepare *N*-arylbenzimidoyl bromides from the aldimine and *N*-bromosuccinimide gave only black oils or tars. Thionyl bromide or PBr_5 did not react with *N*-*p*-nitrophenylbenzanilide, while *N*-phenylbenzanilide and thionyl bromide gave a disubstitution product on the aniline ring, probably an *N*-*o*,*p*-dibromophenylbenzanilide. Likewise, *N*-*p*-methoxyphenylbenzanilide gave ring bromination with PBr_5. Finally, bromination of benzanilide with PBr_5 gave a mixture of *N*-phenylbenzimidoyl bromide (**3a**) and *N*-*p*-bromophenylbenzimidoyl bromide (**3b**), which could not be separated by distillation and which decomposed during separation by other methods. Hence, the kinetics of the substitution of two mixtures, (i) 80% **3a**:20% **3b** and (ii) 73% **3a** and 27% **3b** with piperidine (eq 3 and 4), was followed by the increase of the optical density at 295 nm.

$$\underset{\mathbf{3a}}{PhC(Br)=NPh} + C_5H_{10}NH \rightarrow \underset{\mathbf{2c}}{PhC(NC_5H_{10})=NPh} \quad (3)$$

$$\underset{\mathbf{3b}}{PhC(Br)=NC_6H_4Br\text{-}p} + C_5H_{10}NH \rightarrow \underset{\mathbf{2m}}{PhC(NC_5H_{10})=NC_6H_4Br\text{-}p} \quad (4)$$

The molar absorption coefficients of pure **3a** and **3b** could not be measured. However, the absence of conjugation between the substituent Y and the C=N bond[21] results in a very similar spectral change at 280–400 nm when **1** is converted to **2** for different Y's, e.g., ϵ(**2c**) − ϵ(**1c**) = 2200 ± 200 and ϵ(**2m**) − ϵ(**1m**) = 2500 ± 300. If we assume that this is also true for the ϵ(**2c**) − ϵ(**3a**) and the ϵ(**2m**) − ϵ(**3b**) differences, the increase of the absorption at λ 295 nm could be treated as due to increased concentration of the same component C, formed independently with first-order constants k_a and k_b from the starting materials A and B. The rate is given by:[22]

$$\ln (C_\infty - C) = \ln(A + B) = \ln (A_0e^{-k_at} + B_0e^{-k_bt}) \quad (5)$$

Table IV. Calculated Values for **3b**[a] for the Reaction of 4:1 Mixture of **3a** to **3b** with Piperidine in Benzene at 30 °C

10^3[Piperidine], M	6.73	8.72	11.2	14.5	17.6	
% of **3b** in the mixture	35	37	28	22	29	
$10^2k''$ for **3b**, M^{-1} s^{-1} [b]	3.5	3.5	2.6	2.8	2.7	3.0 ± 0.4[c]

[a] [RBr] = 0.0003–0.0004 M. [b] Calculated from the linear portion of the line ($r > 0.998$) at >80% reaction. [c] Average value.

Table V. Second-Order Constants for the Reaction of Piperidine with **3a–3b** in Benzene

	(A) 80% of **3a** and 20% of **3b**[a]								
10^3[Piperidine], M	2.90	4.48	5.81	6.73	8.72	11.6	14.5	17.6	
$10^2k''$ for **3a**, M^{-1} s^{-1} at 30 °C[b]	10.6	10.4	10.6	10.6	10.1	9.88	10.2	9.4	10.2 ± 0.3[c]
10^3[Piperidine], M	3.13	4.18	5.22						
$10^2k''$ for **3a**, M^{-1} s^{-1} at 45 °C[b]	18.0	17.7	16.7		17.5 ± 0.5[c]				
	(B) 73% of **3a** and 27% **3b**[a]								
10^3[Piperidine], M	2.83	3.26	5.64	6.52	8.47	8.77			
$10^2k''$ for **3a**, M^{-1} s^{-1} at 30 °C[b]	8.66	8.80	8.49	8.71	8.82	8.73		8.70 ± 0.01[c]	

[a] [RBr] = 0.00026–0.0004 M. [b] $r \geq 0.999$ for the first 30–50% of the first-order plot. [c] Average value.

where A_0, B_0 are the initial concentrations and $C_\infty = A_0 + B_0$. If $B_0 > A_0$ and $k_b < k_a$ (i.e., the mixture is richer in the slow component) the curved plot of ln $(C_\infty - C)$ vs. t should become linear (eq 6) during the reaction since the fast component will be completely consumed. Both B_0 and k_b could be then eliminated, and A_0 and k_a will be obtained from eq 5.

$$\ln (C_\infty - C) = \ln B_0 - k_b t \qquad (6)$$

Unfortunately, our mixtures are richer in the fast component, and since the rate difference between **3a** and **3b** is not large, linearity of the ln $(C_\infty - C)$ vs. t plot was obtained only after 80% reaction when the reaction was followed up to 90–95%. Table IV gives the percentage of **3b** and k'' for **3b** as calculated for mixture i from the linear portion of the line, at several piperidine concentrations. The values are not constant, and the percentage of **3b** differs from the value of 20% obtained from the elemental analysis. Nevertheless, considering the error involved, the average k'' value of 0.03 ± 0.004 M^{-1} s^{-1} is a rough estimate for the rate constant of **3b** with piperidine in benzene at 30 °C.

On the other hand, since the fast compound is the major component of the mixtures, the plot of ln $(C_\infty - C)$ vs. t shows good linearity up to 40–50% reaction. This is due to the following reason: by inserting the values $A = A_0e^{-k_at}$, $B = B_0e^{-k_bt}$ into the following equation:

$$dc/dt = k_aA + k_bB = k_T(C_\infty - C) \qquad (7)$$

we obtain

$$k_T = \frac{k_aA_0e^{-k_at} + k_bB_0e^{-k_bt}}{A_0e^{-k_at} + B_0e^{-k_bt}} \qquad (8)$$

for k_T, the apparent first-order constant. The k_T value which depends on the A_0/B_0 ratio, on the magnitude and the ratio of k_a and k_b, and on the time t decreases with the progress of the reaction when the mixture becomes richer in the slow component. However, when we apply our conditions (i.e., $A_0/B_0 \geq 3$; $k_a/k_b \leq 4$) to eq 8 we find that k_T should decrease by ≤9% up to 50% reaction, as was indeed observed. Equation 8 therefore enables the calculation of the initial pseudo-first-order constants and of the k'' values. These were found to decrease during the reaction, as expected (Table V).

By using the average k'' for mixture i, the average k'' for **3b** and the **3a**/**3b** ratio, an approximate k'' value of 0.12 ± 0.01 M^- s^{-1} for the reaction of *N*-phenylbenzimidoyl bromide (**3a**) with piperidine in benzene at 30 °C was estimated. This gave a k_{Br}/k_{Cl} ($= k_{3a}/k_{1c}$) ratio of 440 ± 40. A very rough k_{Br}/k_{Cl} ratio of 140 can be estimated from the k'' values for the reactions of piperidine with *N*-*p*-bromobenzimidoyl bromide (**3b**) and *N*-*p*-chlorobenzimidoyl chloride (**1d**).

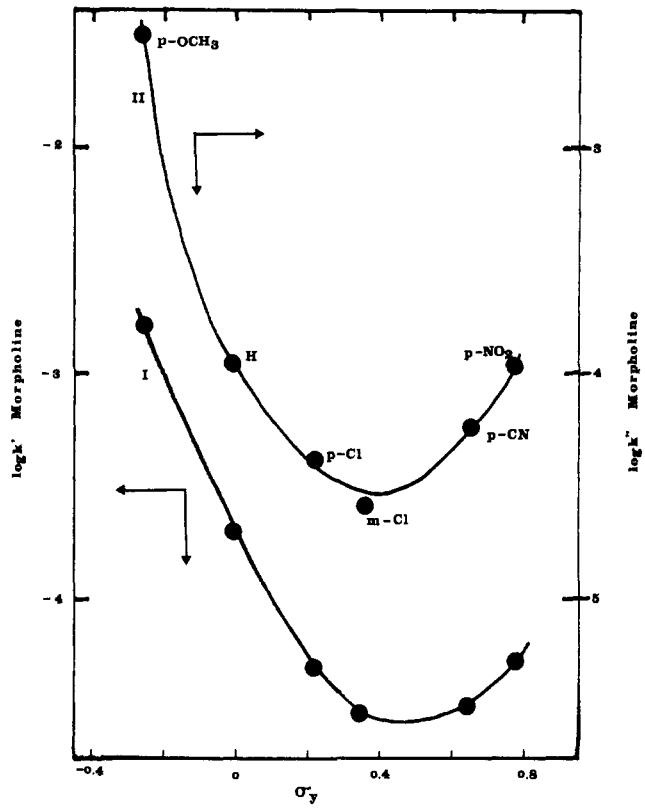


Figure 1. Hammett plot for the reaction of PhC(Cl)=NC_6H_4Y with morpholine in benzene at 30 °C; (I) log k' vs. σ_Y; (II) log k'' vs. σ_Y.

Hammett-Type Correlations. The Hammett plots for the substituents Y when X = H are parabola-shaped both for the second-order and for the third-order process (Figures 1 and 2). If the curvature results from a combination of two mechanisms, then when X = H the k_Y value (k' or k'') will be the sum of $k_Y(1)$ and $k_Y(2)$ which are the rate constants for the mechanisms with negative and positive ρ value, respectively. Equation 9 gives the relationship between k_Y and the Hammett parameters [$\sigma_Y(1)$, $\rho(1)$, $\sigma_Y(2)$, and $\rho(2)$] for the two mechanisms:

$$k_Y = k_Y(1) + k_Y(2) = [k_H(1)]10^{\sigma_Y(1)\rho(1)} + [k_H(2)]10^{\sigma_Y(2)\rho(2)} \qquad (9)$$

Table VI. $\rho(1)$, $\rho(2)$, $k_H(1)$, and $k_H(2)$ Values for the Reaction of Compounds **1** with Piperidine and Morpholine in Benzene

Set	R_2NH	k	T, °C	$\sigma(1)$	$\sigma(2)$	$\rho(1)$	$\rho(2)$	$10^4k_H(1)$	$10^4k_H(2)$	δ, %[a]
1	Piperidine	k'	30	σ	σ	−3.71	1.77	2.02	0.517	9.6
				σ^+	σ	−1.11	2.30	2.77	0.191	7.9
				σ^+	σ^-	−1.16	1.09	2.48	0.533	9.7
2	Piperidine	k'	45	σ	σ	−3.63	2.06	5.58	0.794	13.7
				σ^+	σ	−1.10	2.62	7.30	0.282	2.4
				σ^+	σ^-	−1.14	1.26	6.78	0.829	2.9
3	Morpholine	k'	30	σ	σ	−3.33	1.27	2.15	0.058	4.6
				σ^+	σ	−1.29	5.07	1.67	0.000046	34.7
				σ^+	σ^-	−1.29	2.50	1.67	0.00031	34.8
3a[b]	Morpholine	k'	30	σ^+	σ	−1.69	1.74	0.81	0.024	5.1
				σ^+	σ^-	−1.70	0.81	0.79	0.054	6.0
4	Morpholine	k''	30	σ	σ	−3.84	2.07	2.61	0.025	1.6
				σ^+	σ	−2.05	2.16	0.71	0.021	1.8
				σ^+	σ^-	−2.08	1.02	0.67	0.055	3.3

[a] $\delta = (100/n)\Sigma(k_Y - k_{obsd,Y})/k_{obsd,Y}$ (when n is the number of points), i.e., δ is the average deviation (in %) of the observed from the calculated rate constants. [b] Based on the same data as series 3, except for k' for **1c**.

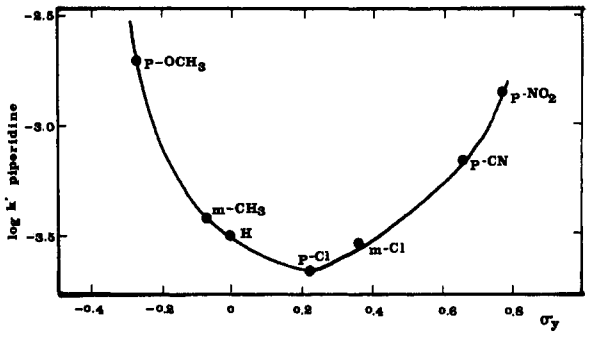


Figure 2. Log k' vs. σ_Y plot for the reaction of $PhC(Cl)=NC_6H_4Y$ with piperidine in benzene at 30 °C.

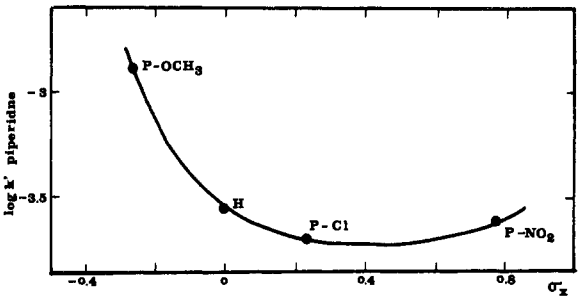


Figure 3. Log k' vs. σ_X plot for the reaction of $XC_6H_4C(Cl)=NPh$ with piperidine in benzene at 30 °C.

We searched for the best fit of the experimental k_Y values to eq 9 for three combinations of $\sigma(1)$ and $\sigma(2)$ values: (a) $\sigma(1) = \sigma^+$; $\sigma(2) = \sigma$; (b) $\sigma(1) = \sigma^+$; $\sigma(2) = \sigma^-$; (c) $\sigma(1) = \sigma(2) = \sigma$. We used the computer program CURVEFIT for calculating the best values of $k_H(1)$, $k_H(2)$, $\rho(1)$, and $\rho(2)$. The results and the average deviation of the experimental from the calculated values (in %) are given in Table VI.

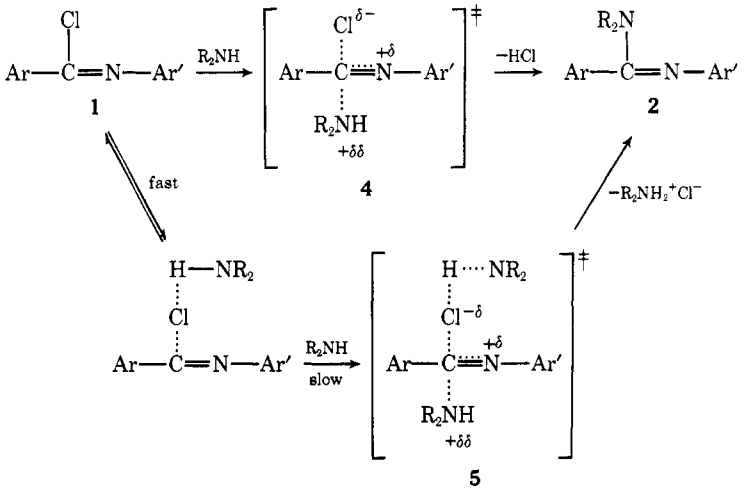
Discussion

The most characteristic features of our results are the substituent effects (Table II and Figures 1-3). The rate decreases ($\rho < 0$) from the fastest compound when Y = *p*-MeO to a minimum value when Y = *p*-Cl or *m*-Cl in the reactions with piperidine and morpholine, respectively, and then increases more moderately ($\rho > 0$) with σ_Y.

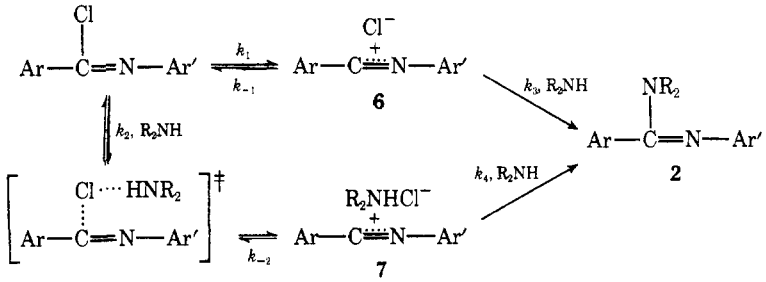
Curved Hammett plots with minima are usually ascribed to competition of two mechanisms with opposite electronic demands,[23] where each one predominates in a different range of σ values. Several such mechanisms should be considered for our system.

There are two possibilities for the mechanism with a negative ρ value. (a) A dissociative bimolecular S_N2 reaction where bond cleavage appreciably precedes bond formation will have a partial positive charge on the nitrogen in the transition state **4** and consequently a negative ρ for the substituents Y. The second-order dependence in the reaction of morpholine with

Scheme IV



Scheme V



1a suggests a variant via a termolecular transition state **5**: the expulsion of the chlorine is electrophilically assisted by the hydrogens of a second amine molecule which may either first associate with **1** or react in concert with the nucleophilic amine molecule. These possibilities are shown in Scheme IV.

(b) Reaction via an ion pair **6** whose reaction with the amine is slower than its return to the covalent material. This is Sneen's ion pair mechanism,[24] which is designated here as $S_N2(IP)$. A similar mechanism designated $S_N2(C^+)$, where a free carbonium ion which is formed in a preequilibrium process is attacked slowly by the nucleophile, was suggested by Ingold.[25] Both cationoid species (the ion pair and the free ion) may be involved in the reaction as suggested for the substitution of acetyl chloride and bromide by phenols in acetonitrile and nitromethane.[26] Since we did not observe common ion rate depression by the formed Cl^- within a run and high concentrations of external free Cl^- ion could not be used due to solubility reasons and the low ion pair dissociation constants of salts in benzene, there is no evidence for the intervention of free ions. However, we prefer the ion pair mechanism since ion pair dissociation is unfavored in benzene. The second order in the morpholine requires again a variant where the second amine molecule assists in the C–Cl bond heterolysis to form the ion pair. Scheme V summarizes these pathways.

A steady-state treatment of Scheme V gives eq 10 for the pseudo-first-order rate constant k_{obsd}:

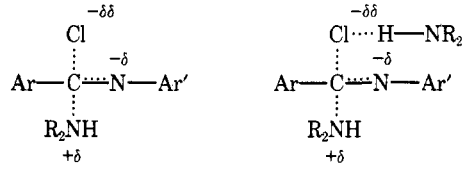
$$k_{obsd} = \frac{k_1k_3[R_2NH]}{k_{-1} + k_3[R_2NH]} + \frac{k_2k_4[R_2NH]^2}{k_{-2} + k_4[R_2NH]} \quad (10)$$

By assuming a relative rapid return of the ion pairs **6** and **7** to the covalent material, i.e., $k_{-1} \gg k_3[R_2NH]$; $k_{-2} \gg k_4[R_2NH]$, the second-order rate constant is given by

$$k'' = \frac{k_1k_3}{k_{-1}} + \frac{k_2k_4}{k_{-2}}[R_2NH] \quad (11)$$

This is similar to the experimentally observed eq 2, with $k' = k_1k_3/k_{-1}$ and $k'' = k_2k_4/k_{-2}$, and consequently Scheme V accounts for the results.

When X = H and $\sigma_Y > 0.227$ (for piperidine) and >0.373 (for morpholine), the reaction is bimolecular with a positive ρ value. A mechanistic possibility is an associative S_N2 reaction where bond formation precedes bond cleavage. This will be analogous to Scheme IV except that in the corresponding transition states **8** and **9** a negative charge is formed on the



azomethine nitrogen and partial cleavage of the C=N bond takes place.

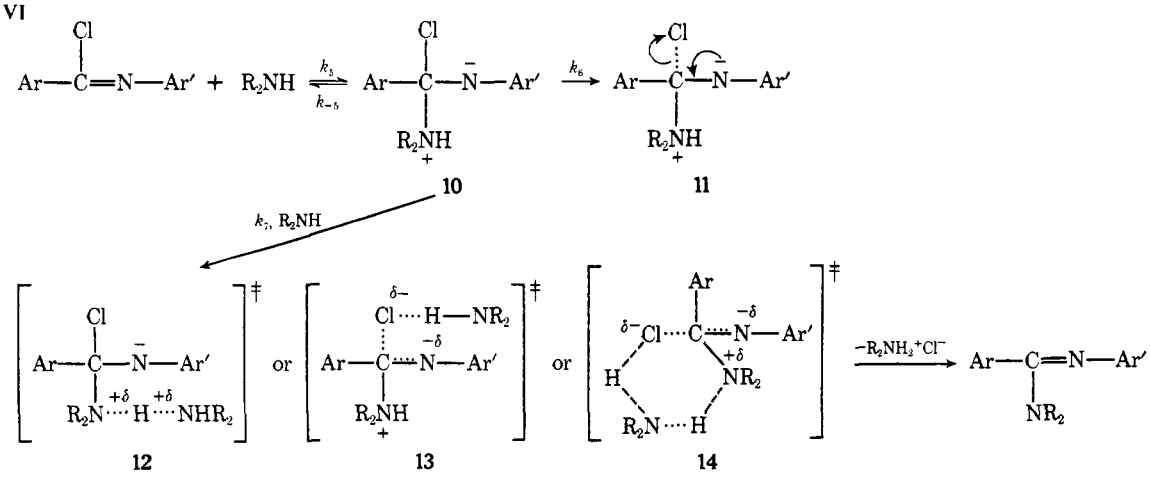
An alternative is a nucleophilic addition–elimination (Ad_N–E), via intermediate **10.** The transition state for the elimination step may be either noncatalyzed (cf. **11**), base catalyzed (cf. **12**), acid catalyzed (cf. **13**) or bifunctional catalyzed (cf. **14**) (Scheme VI) as found for catalyzed nucleophilic attacks by amines on aromatic,[27-29] vinylic,[30] and carbonyl[31] systems. As suggested for nucleophilic aromatic[28c] and vinylic[30c] substitutions, the base catalysis may be more complex, when a rapid preequilibrium deprotonation of **10** is followed by the ammonium ion ($R_2NH_2^+$)-assisted expulsion of the chloride ion (Scheme VII). However, recent work for systems carrying good leaving groups in S_NAr reactions points to a scheme similar to Scheme VII via transition state **12**,[29b] without electrophilic assistance to leaving group expulsion.

For either case of catalysis the steady-state treatment combined with the assumption of a rate-determining elimination gives rate equations which are identical with the experimental rate eq 2. For Scheme VI, assuming $k_{-5} \gg k_6 + k_7[R_2NH]$, eq 12 is obtained and $k' = k_5k_6/k_{-5}$, $k'' = k_5k_7/k_{-5}$. For Scheme VII with rate-determining k_8' eq 13 is obtained with $k' = k_5k_6/k_{-5}$ and $k'' = k_5k_7'k_8'/k_{-5}k_{-7}'$.

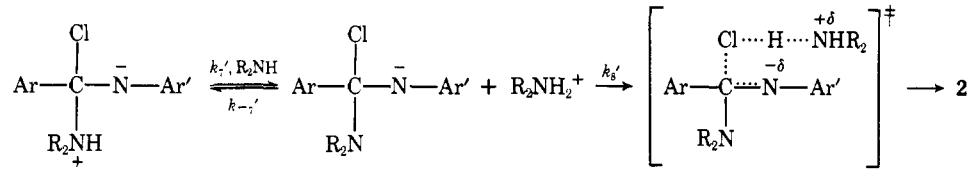
$$k' = \frac{k_5k_6}{k_{-5}} + \frac{k_5k_7}{k_{-5}}[R_2NH] \quad (12)$$

$$k' = \frac{k_5k_6}{k_{-5}} + \frac{k_5k_7'k_8'}{k_{-5}k_{-7}'}[R_2NH] \quad (13)$$

Scheme VI



Scheme VII



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Although the addition-elimination route is the only one invoked up to now for the bimolecular reaction at azomethine systems, the curved log k–σ plots could be also ascribed to a single S_N2 mechanism whose transition state gradually changes from a dissociative (i.e., via **4**) for electron-donating Y's to an associative (i.e., via **8**) for electron-withdrawing Y's. This interpretation for our "substituted benzyl halides" is similar to that given by Hudson and Klopman for the log k–σ plots with minima obtained for the reaction of thiophenoxide ions with substituted benzyl bromides.[32] A decrease of the electron density at the benzylic carbon on increasing σ_Y results in a more difficult C–Cl bond cleavage and an easier C–N bond formation, and correspondingly in a change from a dissociative to an associative S_N2 mechanism.

The possibility of an S_N2C^+, an addition-elimination, and a synchronous displacement with variable transition-state structure was recently discussed by Kevill et al.[33] for the analogous reaction of the ethanolysis of acyl chlorides. They concluded that the synchronous mechanism alone or in combination with the addition-elimination route accounts for their results. However, we believe that in our systems a combination of the S_N2(IP) route for electron-donating substituents with a nucleophilic addition-elimination route for electron-withdrawing substituents is the most plausible, although the synchronous mechanism cannot be unequivocally excluded. As discussed below, we base this suggestion on analysis of the amine-catalyzed route, on quantitative analysis of the substituent effects, on the effects of the nucleophile and the leaving group, and on the values of the activation parameters.

Catalyzed Route. The contribution of the second-order ("amine-catalyzed") route in the amine is small as reflected by the k''/k' ratios of Table II. The catalysis is not due to formation of a stronger nucleophilic anion by self-protonation of the amine (eq 14) since it does not fit the increase of the k''/k' ratios with σ_X and σ_Y and their higher values for morpholine, as well as the absence of catalysis of the reaction of piperidine with **11** by the stronger base *N*-methylpiperidine. Several possibilities for the transition state were suggested above.

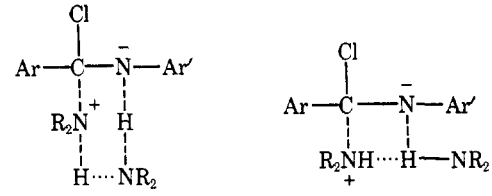
$$2R_2NH \rightleftharpoons R_2NH_2^+ + R_2N^- \qquad (14)$$

If we assume that direct formation of a termolecular transition state from the reactant is less likely than its formation by a multistep reaction, the catalysis is more in line with a combination of the multistep S_N2(IP) and Ad_N–E routes. However, it should be noted that reservations were raised concerning structurally related transition states to those described above for our catalyzed route. In discussing the rate acceleration by bases in the analogous S_NAr reactions, Bunnett and Garst[28b] raised doubt whether even k''/k' values higher than ours can be regarded as a good evidence for the intervention of base-catalyzed routes via transition states analogous to **12.** Likewise, Jencks' "libido rule" [34] cast doubt on the intermediacy of species involved in electrophilic catalysis by protonation of the leaving group (the conjugate base of a strong acid) by the weakly acidic amine.

However, contrary to the cases studied by Bunnett and Garst,[28b] the k''/k' values in our systems change systematically with the substrate and the amine: the values increase with σ_X or σ_Y due to increasing difficulty in the expulsion of Cl^- from **10.** The importance of steric effects may be reflected by the ineffectiveness of *N*-methylpiperidine as a catalyst and by the lower k''/k' for the reaction of **11** with Et_2NH (0.33) compared with that with piperidine (1.86). Unfortunately, unhindered tertiary bases such as γ-picoline could not be used to determine the nature of the catalysis since they reacted with the imidoyl chlorides.

The stronger catalysis with the weaker base (morpholine) favors electrophilic catalysis via S_N2(IP) for electron-donating substituents (Scheme V, **1** → **7**). It also fits an electrophilic or bifunctional catalysis for chloride ion expulsion for electron-withdrawing substituents (transition states **13** and **14**), although base catalysis via Scheme VII is also possible, since k_8' for morpholinium ion will be higher than that for piperidinium ion. Such interpretation was given for the catalyzed reactions of these amines with 1-*p*-dimethylaminophenyl-1-ethoxy-2,2-dicyanoethylene.[30c] Since hydrogen bonding to the leaving group is an important contributor to the enhanced heterolytic cleavage rate for S_N1 reactions, and since this factor should be important especially in low dielectric solvent such as benzene, the electrophilically catalyzed routes seem plausible for our system. Moreover, it is not at all clear that the "libido rule" is applicable for the process $RCl + HNR_2 \rightarrow R\cdots Cl\cdots HNR_2 \rightarrow R^+ + Cl^-\cdots HNR_2$ in an aprotic solvent.

In analogy with the mechanisms suggested for nucleophilic substitution in cyclic azomethine systems[35a] and for addition of HCN to benzalanilines[35b] an electrophilic or bifunctional catalysis in the addition step via the intermediates or the transition states **15** or **16** also account for the inefficiency of



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N-methylpiperidine as a catalyst and for the preferred catalysis by morpholine. However, the k''/k' ratios are then expected to decrease on increasing σ_Y, and Scheme VI seems more likely.

Substituent Effects. The nature of the different mechanisms for electron-attracting and for electron-donating substituents is probed by analysis of the curved Hammett plots in term of different combinations of σ values (Table VI).

The values of the average deviation suggest that the assumption of competing two mechanisms is correct. The best fit for the reaction of 7-*N*-arylbenzimidoyl chlorides with piperidine at 30 and at 45 °C is with the σ^+ values for the mechanism with negative ρ and with σ values for the mechanism with positive ρ. When σ is replaced by σ^- the deviation increases slightly. The fit with σ^+ corroborates the S_N2(IP) mechanism for systems with electron-donating Y's. The resulting ρ^+ of −1.1 is lower than the values for formation of benzhydryl ($\rho^+ = -3$ to -5)[36] or vinyl cations ($\rho^+ = -3$ to -6.6),[16,37] where the charge dispersal on the α-aryl group is resonative, since in our system the main effect of the anilino-ring substituents is inductive. Our ρ value is lower than $\rho = -2.75$ found for compounds **1** with electron-withdrawing

Table VII. β Values, Based on k' for Piperidine and Morpholine for $PhC(Cl)=NC_6H_4Y$ at 30 °C

Y	*p*-MeO	H	*p*-Cl	*m*-Cl	*p*-CN[a]	*p*-NO_2[b,c]
σ[d]	−0.268	0	0.227	0.373	0.66	0.78
β	0.028	0.083	0.22	0.34	0.45	0.48

[a] For k'', $\beta = 0.33$. [b] For k'', $\beta = 0.38$. [c] For k' (45 °C), $\beta = 0.50$. [d] From H. H. Jaffe, *Chem. Rev.*, **53**, 191 (1953).

substituents in dioxane–water[12] and is similar to $\rho \sim -1$ which was calculated from Ugi's data[9] for compounds **1a** and **1c** in aqueous acetone. The difference may be due to the fact that the ρ's in Ugi's and in our case are probably complex and involve also the ρ for the reaction of the nucleophile with the ion pair, while for Hegarty's system in aqueous dioxane ρ is only for the C–Cl bond ionization step.[12] The better fit of the "positive ρ" mechanism to σ than to σ^- supports an associative S_N2 mechanism, but it cannot exclude an addition–elimination route, since a better correlation with σ than with σ^- was found in the isomerization via nucleophilic addition–elimination of α-cyanostilbenes PhCH=C(CN)Ar.[38] The ρ values of 1.7–2.6 resemble the value of 2.39 for the hydrolysis of *N*-aryl-*C*-chloroformimidates in aqueous dioxane at pH >13 which was ascribed to an addition–elimination,[12] or the value of 1.9 for the base-catalyzed addition of methanol to benzalaniline.[39] Both the ρ values and the ρ^- values of 1.1–1.3 are lower than $\rho = 3.35$ and $\rho^- = 2.2$–2.6 found for substitution in vinylic systems,[40] and this again may be due to the complex nature of our rate constant.

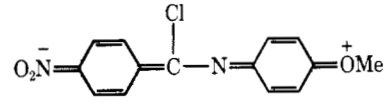
Both the second- and third-order constants of six compounds **1** with morpholine show the best fit with σ values for both mechanisms, with ρ values of −3.3 and +1.3. This may indicate that morpholine reacts via S_N2 rather than by S_N2(IP), but it may also be due to the exceptional k' value for the reaction of **1c** where a clear second-order dependence on the amine was not observed. When this value was discarded, a good correlation with a combination of either σ^+ and σ or of σ^+ and σ^- was observed. The ρ values of the catalyzed reaction (Table VI, series 4) are higher than those for the uncatalyzed reaction (series 3 and 3a), but it should be noted that the k'' values probably involve some contribution from dielectric constant effects.

For each set of σ values the ρ values (for k') for morpholine are lower than those for piperidine, and the minimum of the curve is shifted from *p*-Cl for piperidine to *m*-Cl for morpholine. This behavior fits either an S_N2 route with increasing associative character with the increase in the basicity of the nucleophile, or a mixture of addition–elimination and S_N2(IP) processes, where the contribution of the former is apparent earlier for the stronger nucleophile.

The dependence of log k on σ_X when Y = H (Figure 3) is also concave, but the rates are almost the same when X = H, *p*-Cl, and *p*-NO_2 and only when X = *p*-MeO the reaction is substantially faster. The negligible effect of the electron-attracting substituents fits the addition–elimination route since resonative negative charge dispersal by the α-aryl group is impossible in the intermediate **10** and the inductive effect is canceled. A similar behavior was observed for the addition of methanol to similarly substituted benzalanilines.[39] When X = *p*-MeO the reaction probably proceeds via initial ionization, and the effect of the substituent on the carbon-substituted ring is smaller than that in the nitrogen-substituted ring [(k'(**1h**)/k'(**1a**) = 0.6], as already found for the hydrolysis of *N*-arylbenzimidoyl halides.[9,12]

In contrast, when *Y* = *p*-MeO, a change of X from H to *p*-NO_2 reduces the rate eightfold since the ground-state stabilization (cf. **17**) is lost either in the zwitterion or in the nitrilium ion.

Effect of the Nucleophile. The sensitivity of the reaction to the basicity and steric effects of the nucleophile is deduced



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from comparison of the reactivities of piperidine (pK_a (H_2O) 11.12),[41] morpholine (pK_a (H_2O) 8.33),[41] and diethylamine (pK_a (H_2O) 11.04).[41] The basicities of piperidine and Et_2NH are similar but attack by the latter is sterically more hindered, while the steric effects of piperidine and morpholine are similar but morpholine is much less basic. Table II shows that piperidine is faster than morpholine, and the Bronsted "β" 's, calculated from the k' and the pK_a (H_2O) values for the two amines only, are substituent dependent (Table VII) and reflect the nucleophile basicity.

Literature β values for S_N2 reactions on alkyl and benzyl systems are 0.15–0.43;[42] for addition to activated double bonds or substitution via rate-determining addition, $\beta = 0.4$–0.46,[43] and for attack on C=O bonds, $\beta = 0.65$–0.9.[42b,44] In comparison, our β values of <0.1 for Y = H or *p*-MeO are very low, especially for a reaction in a nonpolar aprotic solvent. These values point to a mechanism with a very low extent of carbon–nucleophile bond formation in the transition state and are consistent with the S_N2(IP) route since early transition state is expected for combination of amine with the positively charged carbon atom. The β values for systems **1d–1g** with electron-attracting substituents are consistent both with an S_N2 reaction and with the addition–elimination route.

The k'(piperidine)/k'(Et_2NH) values depend on the electron-attracting ability of the system and increase from 16 for **1c** to 112 for **1g** to 153 for **1l.** Catalysis was observed with Et_2NH only for **1l,** where k''(piperidine)/k''(Et_2NH) = 853. These values are understood in terms of an addition–elimination mechanism, where steric effects in the nucleophile are of great importance.[30] It is noteworthy that compound **1l** is both more reactive and more selective, in contrast to the expectation from the Hammond principle.[45]

Activation Parameters. The activation parameters (Table II) for piperidine ($\Delta H^{\ddagger} \sim 11$ kcal/mol, $\Delta S^{\ddagger} \sim -38$ eu) show small dependence on the substituents. In view of the caution which should be exercised in interpreting these parameters, only analogies which may have bearing on the mechanism are presented. Thus, in the S_N2 reactions of anilines with arylsulfonyl chlorides, $\Delta H^{\ddagger}$ is appreciably dependent on the substituents,[46] while $\Delta H^{\ddagger}$ for the ionization of triphenylmethyl chloride to an ion pair is 12 kcal/mol in benzene.[47] The importance of the $\Delta H^{\ddagger}$ term is shown by the low value of 6.2 kcal/mol ($\Delta S^{\ddagger} = -45$ eu) for bromide as the leaving group, in the reaction of a 4:1 mixture of **3a** to **3b** with piperidine.

The change of the nucleophile from piperidine to Et_2NH resulted in higher $\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$, as expected for steric reasons. In the reaction with **1g** the change from piperidine to morpholine is accompanied by a decrease of 2 kcal/mol in $\Delta H^{\ddagger}$ and 12 eu in $\Delta S^{\ddagger}$. We ascribe these changes to stronger internal hydrogen bonds in the zwitterion **18** when R_2N^+ is the

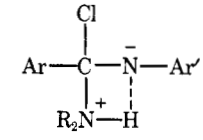

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Table VIII. Diarylimidoyl Chlorides $XC_6H_4C(Cl)=NC_6H_4Y$

X	Y	Color, crystalline form	Mp, °C	Analysis: Calcd, % C	H	N	Cl	Formula	Found, % C	H	N	Cl
H	*m*-Me	yellow, oil	*a*	73.24	5.23	6.10	15.47	$C_{14}H_{12}NCl$	72.72	5.28	5.79	15.17
H	*p*-Cl	white, solid	62	62.40	3.60	5.61	28.35	$C_{13}H_9NCl_2$	62.41	3.94	5.70	28.70
H	*p*-Br	white, solid	70.5	52.90	3.25	4.76	12.03	$C_{13}H_9NBrCl$	52.91	3.15	4.90	11.60
H	*p*-CN	white, solid	88	69.85	3.74	11.63	14.72	$C_{14}H_9N_2Cl$	70.08	4.06	11.71	12.80
p-Cl	H	white, solid	68	62.40	3.60	5.61	28.35	$C_{13}H_9NCl_2$	62.68	3.79	5.59	28.69
p-NO_2	*p*-MeO	yellow-orange, solid	134	57.80	3.79	9.65	12.20	$C_{14}H_{11}N_2O_3Cl$	57.96	3.97	9.66	12.31
H	*m*-Cl	yellow, oil	*b*	62.40	3.60	5.61	28.35	$C_{13}H_9NCl_2$	62.13	3.92	5.28	28.80

[a] Bp 146–149 °C (2–3 mm). [b] Bp 164 °C (4 mm).

Table IX. UV and NMR Spectra of Diarylimidoyl Chlorides $XC_6H_4C(Cl)=NC_6H_4Y$

X	Y	λ_{max}(MeCN), nm (ϵ)	λ_{max}(C_6H_6), nm (ϵ)	$\delta_{Ar\text{-}C}$($CDCl_3$)	$\delta_{Ar\text{-}N}$($CDCl_3$)	δ_{Me}($CDCl_3$)
H	*p*-MeO	242 (21 100), 323 (5700)	328 (6900)	6.9 (3 H, m), 7.6 (2 H, m)[a]	6.83 (4 H, q)[a]	3.23 (s)
H	*m*-Me	244 (19 200), 305 (3200)	314 (3400)	8.1 (2 H, m)	6.9–7.4 (7 H, m)	2.26 (s)
H	*p*-Cl	245 (20 700), 306 (3600)	314 (4800)	7.55 (3 H, m), 8.2 (2 H, m)	7.03, 7.42 (4 H, q)	
H	*m*-Cl	249 (18 500), 302 (3000)	305 (3500)	8.2 (2 H, m)[b]	6.9–7.5 (7 H, m)[b]	
H	*p*-CN	254 (31 000), 295 sh (7100)	310 sh (5300)	7.65 (3 H, m), 8.25 (2 H, m)	7.10, 7.55 (4 H, q)	
H	*p*-NO_2	254 (11 200), 305 (15 100)	292 (15 500)	7.5–8.3 (9 H, m)[c]		
p-MeO	H	283 (26 700)		6.95, 8.15 (4 H, q)	6.9–7.5 (5 H, m)	3.90 (s)
p-NO_2	H	268 (17 000), 333 (4400)	340 sh (5000)	9.0 (4 H, m)	7.0–7.53 (5 H, m)	
H	H	282 (22 200)	284 (19 300)	7.65 (2 H, m)	6.50–6.95 (7 H, m)	
p-NO_2	*p*-MeO		368 (7700)			
p-Cl	H	254 (21 300), 304 (4000)	311 (3800)			
H	*p*-Br	247 (23 000), 305 (4500)	313 (5700)	7.5 (3 H, m), 8.15 (2 H, m)	7.0–7.4 (4 H, q)	

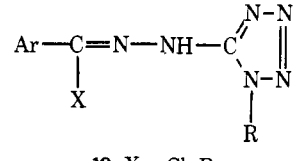
[a] In CCl_4. [b] In neat solution. [c] In $(CD_3)_2SO$.

more acidic morpholinium entity as compared with **18** when R_2N^+ is piperidinium, in analogy to the interpretation in vinylic substitution via addition–elimination.[30b] A similar entropy effect was found for the addition of amines to acrylamide.[43]

Activation parameters for the catalyzed reaction are available only for system **1g** with morpholine. As expected $\Delta S^{\ddagger}(k'') - \Delta S^{\ddagger}(k') = -6$ eu, while $\Delta H^{\ddagger}(k') - \Delta H^{\ddagger}(k'') = 2$ kcal/mol. Such differences explain the absence of apparent catalysis for other systems at 45 °C. Examples for reduced catalysis at a higher temperature are known.[30a]

Element Effect. Additional criterion for distinguishing between mechanistic alternatives is the $k(RBr)/k(RCl)$ reactivity ratio (the "element effect"). The k_{Br}/k_{Cl} ratios are 30–450 when R = alkyl or benzyl,[48] but they cannot always clearly distinguish between mechanisms with and without partial bonding of the nucleophile to the reaction center as shown by the following examples: the ratios are 425 for the S_N2 reaction of chloride ion with the MeX system in acetone and 450 for the S_N1 reaction of the *t*-BuX system in dimethylformamide.[48] The values are also high for substitution in the RCOX system.[26,49,50] The value of 25 found for the reaction of morpholine with PhCOX was ascribed to a rate-determining elimination from a tetrahedral intermediate;[50] the ratio of 80 for the reaction of acyl halides with phenols was ascribed to a bimolecular rate-determining attack on a cationoid species,[26] and the ratio of 75 for the reaction of acyl halides with *p*-nitroaniline was discussed in terms of an S_N2 mechanism with an appreciable bonding to the nucleophile in the transition state.[51]

On the other hand, the element effect in vinylic systems is capable of distinguishing between the addition–elimination mechanism (where k_{Br}/k_{Cl} ratios are 1–2,[6,52] and the highest ratio is 6.7[53]) and the S_N1 mechanism (where the ratios are 20–80).[54] It seems that the same also applies for azomethine systems. The bimolecular reactions of hydroxamoyl halides with MeO^- give a k_{Br}/k_{Cl} ratio of 1.9,[14] while the hydrolysis of compounds **19** which proceed via the intermediacy of ni-



19, X = Cl, Br

trilium ions give ratios of 30–400.[8g] Our (approximate) k_{Br}/k_{Cl} ratios of 440 and 140 for $PhC(X)=NC_6H_4Y$ (Y = H, *p*-Br) support our suggested mechanism of an initial ionization to an ion pair when the Y's are not strongly electron withdrawing although they do not exclude some contribution from a competitive mechanism via rate-determining nucleophilic addition. In analogy with the reactions of acyl halides they cannot exclude an Ad_N–E mechanism with a rate-determining C–X bond cleavage, but this is excluded by the substituent effects described above and by the lower k_{Br}/k_{Cl} ratio when Y is more electron attracting.

Table X. Analytical Data for the Amidines p-$XC_6H_4C(Z)=NC_6H_4Y$

X	Y	Z[a]	Mp, °C	Color, crystalline form	Crystallization solvent	Analysis								
						Calcd, %					Found, %			
						C	H	N	Cl	Formula	C	H	N	Cl
H	p-MeO	$C_5H_{10}N$		Yellow, oil		77.52	7.54	9.52		$C_{19}H_{22}N_2O$	77.32	7.61	9.52	
H	p-Me	$C_5H_{10}N$	56	Colorless	EtOH–H_2O	81.95	7.98	10.05		$C_{19}H_{22}N_2$	81.15	7.94	10.01	
H	H	$C_5H_{10}N$	51	Colorless	EtOH–H_2O	81.75	7.62	10.59		$C_{18}H_{20}N_2$	82.08	7.94	10.63	
H	p-Cl	$C_5H_{10}N$	84	Colorless	EtOH–H_2O	72.28	6.36	9.37	11.86	$C_{18}H_{19}N_2Cl$	72.49	6.67	9.19	12.18
H	m-Cl	$C_5H_{10}N$		Oil		72.28	6.36	9.37	11.86	$C_{18}H_{19}N_2Cl$	72.19	6.41	8.67	11.54
H	p-Br	$C_5H_{10}N$	87	Colorless	EtOH–H_2O	63.05	5.54	8.17	23.35[b]	$C_{18}H_{19}N_2Br$	62.76	5.82	8.60	24.40[b]
H	p-CN	$C_5H_{10}N$	110	Yellow, powder	CCl_4	78.90	6.58	14.53		$C_{19}H_{19}N_3$	79.15	6.96	14.27	
H	p-NO_2	$C_5H_{10}N$	84.5	Yellow, needles	EtOH	69.90	6.14	13.57		$C_{18}H_{19}N_3O_2$	70.08	6.11	13.41	
MeO	H	$C_5H_{10}N$	86	Colorless	EtOH	77.52	7.54	9.52		$C_{19}H_{22}N_2O$	77.80	7.25	9.09	
Cl	H	$C_5H_{10}N$	102	Colorless, needles	EtOH–H_2O	72.28	6.36	9.37	11.86	$C_{18}H_{19}N_2Cl$	72.16	6.38	9.53	11.36
p-NO_2	H	$C_5H_{10}N$		Red, oil		69.90	6.14	13.57		$C_{18}H_{19}N_3O_2$	69.47	6.31	13.25	
p-NO_2	p-NO_2	$C_5H_{10}N$	134	Yellow, needles	EtOH–H_2O	61.05	5.08	15.81		$C_{18}H_{18}N_4O_4$	60.84	5.07	16.00	
p-NO_2	p-MeO	$C_5H_{10}N$	146	Orange, needles	EtOH–H_2O	67.35	6.19	12.32		$C_{19}H_{21}N_3O_3$	66.67	6.25	12.45	
H	p-MeO	C_4H_8NO	95.5	Colorless, plates	Ether	72.95	6.80	9.45		$C_{18}H_{20}N_2O_2$	73.35	6.87	9.52	
H	H	C_4H_8NO	88	Colorless, plates	Ether	76.66	6.81	10.53		$C_{17}H_{18}N_2O$	76.37	7.10	10.61	
H	p-Cl	C_4H_8NO	113.5	Colorless, plates	Ether	67.88	5.65	9.31	11.78	$C_{17}H_{17}N_2OCl$	67.96	5.55	9.33	11.32
H	m-Cl	C_4H_8NO	119	Colorless, plates	Ether	67.88	5.65	9.31	11.78	$C_{17}H_{17}N_2OCl$	67.84	5.89	9.02	11.95
H	p-CN	C_4H_8NO	133	Colorless, needles	EtOH–H_2O	74.30	5.85	14.40		$C_{18}H_{17}N_3O$	74.53	6.08	14.32	
H	p-NO_2	C_4H_8NO	135	Yellow, plates	Ether	65.58	5.50	13.50		$C_{17}H_{17}N_3O_3$	65.55	5.71	13.24	
H	m-Me	C_4H_8NO	111	Colorless, plates	Ether	77.11	7.19	9.99		$C_{18}H_{20}N_2O$	77.00	7.11	10.34	
H	H	Et_2N		Oil		81.00	7.95	11.10		$C_{17}H_{20}N_2$	81.17	8.11	11.08	
H	p-NO_2	Et_2N	91	Yellow, needles	EtOH–H_2O	67.80	6.40	14.13		$C_{17}H_{19}N_3O_2$	68.78	6.50	13.94	
H	p-MeO	PhNMe	94.5	White, powder	EtOH–H_2O	79.50	6.32	8.87		$C_{21}H_{20}N_2O$	78.80	6.34	8.81	

[a] $C_5H_{10}N$, piperidino; C_4H_8NO, morpholino. [b] Data for Br.

Table XI. UV and NMR Spectra of the Amidines $XC_6H_4C(Z)=NC_6H_4Y$

X	Y	Z	λ_{max}(MeCN), nm (ϵ)	δ ($CDCl_3$), ppm[a]				
				α-CH_2	β- and γ-CH_2	Ar–C	Ar–N	Me
H	*p*-MeO	$C_5H_{10}N$	242 (14 700), 288 sh (6400)	3.33 (4 H, m)	1.60 (6 H, m)	7.2 (5 H, m)	6.5 (4 H, m)	3.65 (3 H, s)
H	*m*-Me[b]	$C_5H_{10}N$	244 (12 700)	3.35 (4 H, m)	1.60 (6 H, m)	6.10–7.15 (9 H, m)		2.10 (3 H, s)
H	H	$C_5H_{10}N$	246 (13 000)	3.41 (4 H, m)	1.69 (6 H, m)	6.30–7.20 (9 H, m)		
H	*p*-Cl[b]	$C_5H_{10}N$	254 (13 600)	3.38 (4 H, m)	1.63 (6 H, m)	7.22 (5 H, s)	6.64 (4 H, q)	
H	*m*-Cl	$C_5H_{10}N$	250 (10 400)	3.45 (4 H, m)	1.65 (6 H, m)	6.5–7.5 (9 H, m)		
H	*p*-CN[b]	$C_5H_{10}N$	297 (16 600)	3.43 (4 H, m)	1.70 (6 H, m)	7.25 (5 H, m)	6.87 (4 H, q)	
H	*p*-NO_2	$C_5H_{10}N$	368 (16 500)	3.44 (4 H, m)	1.66 (6 H, m)	7.22 (5 H, m)	7.19 (4 H, q)	
p-MeO	H	$C_5H_{10}N$	238 (17 600)	3.40 (4 H, m)	1.53 (6 H, m)	6.4–7.1 (9 H, m)		3.65 (3 H, s)
p-Cl	H	$C_5H_{10}N$	231 (20 400)	3.43 (4 H, m)	1.70 (6 H, m)	6.5–7.45 (9 H, m)		
p-NO_2	H	$C_5H_{10}N$	276 (10 000)	3.43 (4 H, m)	1.70 (6 H, m)	6.5–8.4 (9 H, m)		
p-NO_2	*p*-MeO[d]	$C_5H_{10}N$	236 (10 200), 271 (17 600)	3.37 (4 H, m)	1.65 (6 H, m)	6.55 (4 H, q)	7.79 (4 H, q)	3.65 (3 H, s)
p-NO_2	*p*-NO_2	$C_5H_{10}N$	257 (13 300), 355 (14 600)					
H	*p*-MeO	C_4H_8NO	240 (14 000), 280 sh (6200)	3.57 (8 H, m)		7.23(5 H, m)	6.60 (4 H, m)	3.65 (3 H, m)
H	*m*-Me	C_4H_8NO	238 (14 000)	3.60 (8 H, m)		6.1–7.25 (9 H, m)		2.13 (3 H, m)
H	H	C_4H_8NO	237 (13 500)	3.58 (8 H, m)		6.47–7.25 (10 H, m)		
H	*p*-Cl	C_4H_8NO	248 (14 400)	3.60 (8 H, m)		7.30 (5 H, m)	7.78 (4 H, q)	
H	*m*-Cl	C_4H_8NO	244 (12 300)					
H	*p*-NO_2	C_4H_8NO	356 (15 900)	3.66 (8 H, m)		7.30 (5 H, m)	7.30 (4 H, q)	
H	*p*-NO_2	Et_2N	368 (15 700)	3.30 (4 H, q)		7.20 (5 H, m)	7.28 (4 H, q)	1.1 (6 H, t)
H	H	Et_2N	242 (13 300)	3.30 (4 H, q)		6.3–7.15 (10 H, m)		1.1 (6 H, t)
p-NO_2	*p*-NO_2	Et_2N	368 (15 500)					
H	*p*-MeO	PhNMe	244 (17 500), 289 sh (7700)			6.25–7.30 (15 H, m)		3.58 (3 H, s, N–Me) 3.68 (3 H, s, OMe)

[a] For AA'BB' quartets the center of the quartet is given. [b] NMR in CCl_4. [c] In EtOH. [d] NMR in CD_3CN.

In conclusion, all the mechanistic criteria fit a bimolecular substitution which proceeds by two mechanisms: an $S_N2(IP)$ for electron-donating substituents, and nucleophilic addition-elimination for electron-attracting substituents.

Experimental Section

Melting points were determined with a Beckman apparatus and are uncorrected. UV spectra were recorded with a Perkin-Elmer 450 or with a Unicam S.P. 800 spectrometer, and the kinetics were followed by using a Gilford 2400 S instrument. IR spectra were recorded with a Perkin-Elmer 337 instrument and NMR spectra were taken with Varian HA-100 and T-60 instruments, and the signal positions are given in ppm downfield from internal tetramethylsilane.

Diarylimidoyl Chlorides. The diarylimidoyl chlorides were prepared by the reaction of the corresponding benzanilides with a slight molar excess of phosphorus pentachloride in benzene.[55] The reaction is immediate, but the mixtures were refluxed for 2 additional hours in order to ensure completion. The solvent and the phosphorus oxychloride were distilled in vacuo, and the imidoyl chlorides which were either oils or low-melting solids were distilled at 1-4 mm. Compounds **1a, 1b, 1c, 1h,** and **1g** are known and had the literature melting points.[9] The analytical data for the new imidoyl chlorides are given in Table VIII.

The compounds, especially those which do not carry strong electron-withdrawing substituents, are unstable and hydrolyze relatively rapidly in air to he corresponding benzanilides. In the dark at argon atmosphere and at low temperature they remain stable for several weeks. The UV spectra in dry benzene remain stable for 2 days, but in dry acetonitrile at 30 °c the UV spectra show that the compounds decompose to the amides at a rate of 2-10% per h. Most of the chloride is converted to the amide during its dissolution in dry ethanol.

The λ_{max} and ϵ values of all the imidoyl chlorides studied are summarized in Table IX. The spectra strongly resemble one another and in acetonitrile they show two absorption maxima, one at 295-306 nm with ϵ of several thousands and one at 248-268 nm with ϵ of ca. 20 000. These bands parallel those of benzanilide in acetonitrile [262 nm (16 500), 305 nm (7700)]. *N-p*-Nitrophenylbenzimidoyl chloride is exceptional by having a high intensity absorption band at 305 nm. The imidoyl chlorides show absorptions at ν_{max} 3060-3070 cm^{-1} (C-H, Ar), 1580 cm^{-1} (ring C=C), and 1660-1670 cm^{-1} [C(Cl)=N—]. The increase in the C=N absorption compared with PhCH=NPh (ν_{max} 1627 cm^{-1})[56] parallels the corresponding increase on α substitution in acyl halides.

The NMR shows the presence of aromatic protons whose positions and splitting depend on the nature of the substituents. The hydrogens at the ortho positions of the carbon-substituted ring usually appear at a lower field compared with the other hydrogens.

***N*-Arylbenzimidoyl Bromides (3a + 3b).** To a moisture-protected ($CaCl_2$) flask containing phosphorus tribromide (20.7 g, 76 mM) in dry petroleum ether (30 mL), bromine (12.8 g, 80 mM) was added dropwise under argon atmosphere. The brown liquid was decanted from the powdered yellow phosphorus pentabromide, and the solid was washed thrice with petroleum ether. Carbon tetrachloride (50 mL) and benzanilide (15 g, 76 mM) were added, and the mixture was gently heated until the evolution of hydrogen bromide was started and then refluxed for 6 h under argon. The solid obtained was identified as a monobromo- or a mixture of monobromobenzanilides by the bromine analysis and the UV and IR spectra. The solvent and the phosphorus oxychlorides were distilled at 65-70 °C (90 mm), and a viscous yellow-orange oil (5 g, 25%) boiling at 140-160 °C at 0.01-0.5 mm was collected: λ_{max} (CCl_4) 249 nm (ϵ 10 000), 313 nm (ϵ 2600); λ_{max} (C_6H_6) 314 nm (ϵ 2800); ν_{max} 3060 (C-H), 1660 [conjugated C(Br)=N], 1580 (ring C=C) cm^{-1}; *m/e* 341, 339, 337 (M for **3b**), 261, 259 (M for **3a**), 258, 260 ($PhC{=}^{+}NC_6H_4Br$), 180 ($PhC{=}^{+}NPh$), 157, 155 ($C_6H_4Br^{+}$), 103 ($C_6H_5CN^{+}$), 77 (Ph^{+}).

Anal. Calcd for a mixture of 80% of **3a** ($C_{13}H_{10}NBr$) and 20% of **3b** ($C_{13}H_9NBr_2$): C, 57.22; H, 3.61; N, 34.06. Found: C, 56.95; H, 3.81; N, 33.87.

Repeated distillation did not change the composition of the mixture.

When the experiment was repeated by using half of the quantities of the reactants and the shortest reaction time (90 min), a 20% yield of a mixture consisting of 73% of **3a** and 27% of **3b** was obtained.

The imidoyl bromides were stable when kept at 0 °C in the dark at argon atmosphere. On dissolution in polar solvents (e.g., "dry" acetonitrile), a very rapid hydrolysis to the benzanilides took place. However, in dry benzene the absorption decreased by only 2% per day, enabling kinetic measurements.

Substituted Benzamidines. The substituted benzamidines were prepared by mixing the corresponding imidoyl chlorides with the amines in dry ether at room temperature.[57] At the end of the reaction the amine hydrochloride was filtered, and the ether was evaporated. The solid amidines were crystallized twice from ether or from aqueous ethanol, and the oils were distilled. The analytical data are given in Table X and the spectral properties in Table XI.

Acknowledgment. We are indebted to Dr. Frank Hegarty for enlightening comments.

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Absence of Intramolecular Charge-Transfer Quenching in Photoexcited 4-Benzoylpiperidines[1]

Peter J. Wagner* and B. J. Scheve

Contribution from the Department of Chemistry, Michigan State University, East Lansing, Michigan, 48824. *Received September 28, 1976*

Abstract: The photochemistry of *N*-methyl- and *N*-benzyl-4-methyl-4-benzoylpiperidine (**1** and **2**) has been compared with that of 1-methyl-1-benzoylcyclohexane (**3**). Like **3**, **1** and **2** undergo competitive α cleavage (yielding benzaldehyde) and cyclization to bicyclo[3.1.1]heptan-6-ols. Sensitization and quenching studies both reveal that **1**, like **3**, forms two kinetically distinct triplets. These are assigned to separate chair conformers with the benzoyl group axial (**1**-a) or equatorial (**1**-e). Low-temperature ^{13}C NMR indicates a **1**-a/**1**-e ratio comparable with that for **3**. **1**-e has the same triplet lifetime as **3**-e and cleaves with the same quantum efficiency. The lack of intramolecular CT quenching in **1**-e indicates that such quenching requires through-space orbital overlap. Triplet decay of **1**-a is 100 times faster than in **3**-a. The enhancement is ascribed to stabilization of the γ-radical site by the nitrogen lone pair.

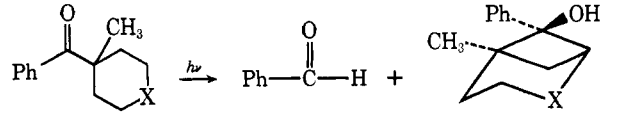
Some years ago we reported rates of intramolecular charge-transfer (CT) quenching of the electronically excited benzoyl group in several α-benzoyl-ω-dialkylaminoalkanes.[2] We assumed that CT quenching occurs in conformations in which the amino group has rotated close enough to the carbonyl for significant overlap of the nitrogen lone-pair orbital with the carbonyl n orbital. Therefore we were surprised to read a major annual review describing our results in terms of through-bond coupling![3] In this case differentiating between through-space and through-bond electronic coupling is far more important than usual because of the kinetics boundary conditions involved. Bimolecular CT quenching of triplet phenyl ketones by tertiary amines occurs at rates close to those of diffusion control.[2,4] Consequently the analogous intramolecular reaction should be rotation controlled provided that through-bond effects are negligible.[5] That is, the rate-determining step for intramolecular quenching may be rotation into proper conformations. Eisenthal was among the first to point out that the rapid intramolecular exciplex formation in an (ω-aminoalkyl) anthracene must be rotationally controlled[6] and picosecond spectroscopists are now well aware of this aspect of kinetics.[7]

If we can demonstrate that CT quenching in amino ketones involves only through-space interactions, then the kinetics of CT quenching in flexible amino ketones will provide valuable information regarding rates of bond rotations in large molecules. Consequently we have investigated the photochemistry of two *N*-alkyl-4-methyl-4-benzoylpiperidines, in which the nitrogen lone pair is fixed some 5–6 Å away from the carbonyl group. We find no evidence for any intramolecular CT quenching in these molecules.

Results

N-Methyl- and *N*-benzyl-4-methyl-4-benzoylpiperidine (**1** and **2**) were prepared as described in the Experimental Section and outlined in Scheme I. Each of these ketones undergoes two

Scheme I



1, X = N–CH_3
2, X = N–CH_2Ph
3, X = CH_2

4, X = N–CH_3
5, X = N–CH_2Ph
6, X = CH_2

competitive photoreactions, as might be anticipated from Lewis' work on the carbocyclic analogue **3**.[8] Benzaldehyde, formed by an α cleavage reaction, was identified by its characteristic odor and gas chromatographic (GC) retention time. No attempt was made to characterize the piperidine fragments which accompany the benzaldehyde. The bicyclic alcohol **4**,