

## KINETICS AND MECHANISM OF THE AMINOLYSIS OF BENZOIC ANHYDRIDES

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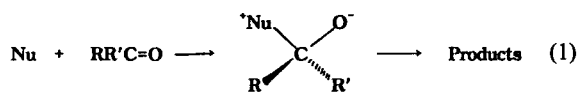
AND

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**Nucleophilic substitution reactions of benzoic anhydrides, in which one of the rings is substituted, with anilines were investigated in methanol. The product-formation step coincides with the rate-limiting step so that the two rate constants,  $k_{XY}$  and  $k_{XZ}$ , for the competitive reaction pathways can be dissected. The two cross-interaction constants,  $\rho_{XY}$  and  $\rho_{XZ}$ , especially an unusually large magnitude of the latter, indicate that the reaction proceeds by a frontside  $S_N2$  attack on either one of the carbonyl carbon with a strong interaction between the nucleophile (X) and the leaving group (Z). The mechanism is also supposed by the trends in the activation parameters.**

Nucleophilic substitution at a carbonyl carbon is of great importance in chemistry and biochemistry, and its mechanism has been widely studied both experimentally and theoretically. It has been generally accepted that a tetrahedral species is formed in such a process and the formation of the tetrahedral species is normally the rate-determining step, equation (1):<sup>1</sup>



Results of extensive solution-phase experimental work have been interpreted in favour of a two-step mechanism involving the tetrahedral species as an intermediate in equation (1).<sup>1,2</sup> However, recent gas-phase experiments<sup>3</sup> and gas-phase<sup>4</sup> and solution phase<sup>5</sup> theoretical studies have predicted a concerted mechanism, with the tetrahedral species as a transition state (TS) instead of a stable intermediate, in equation (1).

Extensive work on the reactions of aryloxide ions with aryl acetates by Williams,<sup>6</sup> has indicated that the

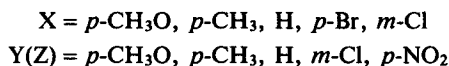
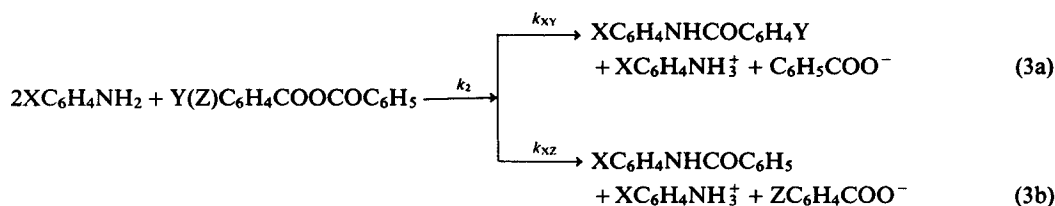
reactions proceed by a concerted mechanism. Similarly the reactions of benzoyl fluorides with primary amines in aqueous solution have been shown to be consistent with a concerted mechanism.<sup>7</sup>

In our recent studies of the aminolysis of *S*-phenyl thiobenzoates<sup>8</sup> [Nu = XC<sub>6</sub>H<sub>4</sub>NH<sub>2</sub>, R = YC<sub>6</sub>H<sub>4</sub> and R' = SC<sub>6</sub>H<sub>4</sub>Z, where X, Y and Z are substituents in the nucleophile, substrate and leaving group (LG), respectively], we reached the conclusion that the reaction proceeds by a concerted process with a tetrahedral TS based on various cross-interaction constants,  $\rho_{ij}$  where  $i, j = X, Y$  or  $Z$  in equation (2):<sup>9</sup>

$$\log(k_{ij}/k_{HH}) = \rho_i\sigma_i + \rho_j\sigma_j + \rho_{ij}\sigma_i\sigma_j \quad (2)$$

In order to gain further information about the mechanism of the nucleophilic substitution at a carbonyl carbon, we investigated the aminolysis of benzoic anhydrides (BA), **I**, in which one of the two phenyl groups is substituted, YC<sub>6</sub>H<sub>4</sub>C(O)OC(O)C<sub>6</sub>H<sub>5</sub>. This reaction system is of particular interests since the nucleophile, XC<sub>6</sub>H<sub>4</sub>NH<sub>2</sub>, can attack either of the two carbonyl carbons competitively, [equations (3a) and (3b)]. In process (3a), substituent Y is in the substrate, but it is in the LG in process (3b), so that it becomes Z in the LG.

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## EXPERIMENTAL

**Materials.** Merck GR-grade methanol and Aldrich GR-grade anilines were used without further purification. The benzoic anhydrides were prepared by a well known method,<sup>10</sup> by reaction of Y-benzoic acid with benzoyl chloride. Solid anhydrides were recrystallized from benzene and light petroleum. The analytical data for the compounds,  $YC_6H_4C(O)OC(O)C_6H_5$ , are as follows.  $p\text{-CH}_3OC_6H_4COOCOC_6H_5$ : IR,  $\nu_{\max}$ (KBr), 3050 (aromatic, CH), 2900 (CH, str.), 1750 (C=O, two peaks); NMR,  $\delta$  (60 MHz,  $CDCl_3 + DMSO-d_6$ ), 7.0–8.3 (9H, ring), 3.9 (3H,  $p\text{-CH}_3$ ); analysis, found, C 70.0, H 4.6;  $C_{15}H_{12}O_4$  requires C 70.3, H 4.7%.  $p\text{-CH}_3C_6H_4COOCOC_6H_5$ : IR,  $\nu_{\max}$ (KBr), 3050 (aromatic, CH), 2950 (CH, str.), 1730, 1760 (C=O, two peaks); NMR,  $\delta$  (60 MHz,  $CDCl_3 + DMSO-d_6$ ), 7.3–8.3 (9H, ring), 2.5 (3H,  $p\text{-CH}_3$ ); (analysis, found, C 74.9, H 5.0;  $C_{15}H_{12}O_3$  requires C 75.0, H 5.0%.  $C_6H_5COOCOC_6H_5$ : m.p. 40 °C (lit.<sup>10b</sup> m.p. 40–42 °C); IR,  $\nu_{\max}$ (KBr), 3060 (aromatic, CH), 1730, 1750 (C=O, two peaks); NMR,  $\delta$  (60 MHz,  $CDCl_3 + DMSO-d_6$ ), 7.5–8.3 (10H, ring).  $m\text{-ClC}_6H_4COOCOC_6H_5$ : IR,  $\nu_{\max}$ (KBr), 3050 (aromatic, CH), 1730, 1750 (C=O, two peaks); NMR,  $\delta$  (60 MHz,  $CDCl_3 + DMSO-d_6$ ), 7.5–8.3 (9H, ring); analysis, found, C, 64.2, H 3.4;  $C_{12}H_9ClO_3$  requires C 64.5, H 3.5%.  $p\text{-NO}_2C_6H_4COOCOC_6H_5$ : m.p. 128 °C (lit.<sup>10b</sup> m.p. 130 °C); IR,  $\nu_{\max}$ (KBr), 3100 (aromatic, CH), 1730, 1760 (C=O, two peaks); NMR,  $\delta$  (60 MHz,  $CDCl_3 + DMSO-d_6$ ), 7.4–8.5 (9H, ring).

**Kinetic procedures.** Rates were measured conductimetrically. Pseudo-first-order rate constants,  $k_{\text{obs}}$ , were determined by the Guggenheim method<sup>11</sup> and second-order rate constants,  $k_2$ , were then obtained from the slope of a plot of  $k_{\text{obs}}$  versus aniline concentration with a greater than tenfold excess of aniline:

$$k_{\text{obs}} = k_1 + k_2[\text{aniline}] \quad (4)$$

The substrate concentrations were kept at  $ca\ 10^{-3}$  M. The intercepts in the plot corresponding to methanolysis rate constants,  $k_1$ , were normally less than one tenth of the  $k_2$  values, and agreed well with  $k_1$ , values determined independently.

**Product analysis.** The analyses of reaction products were carried out using a Hewlett-Packard HP 5890A gas chromatograph, the operating conditions of which are given in Table 1. The product anilides were recrystallized from 95% ethanol, and melting points were determined as given in Table 2. The two anilides detected by GC were identified using the retention times for the standard compounds prepared independently. The relative amounts of the two anilides were determined from

Table 1. GC operating conditions

Parameter	Condition
Column	HP-1 (2.65 $\mu\text{m}$ ) (5 m $\times$ 0.53 mm i.d.)
Detector	Flame ionization 350 °C
Injector temperature	250 °C
Column temperature: Programme	
Initial temperature	100 °C
Rate	10 °C min <sup>-1</sup>
Intermediate temperature	140 °C
Rate	2 °C min <sup>-1</sup>
Final temperature	200 °C
Carrier gas (N <sub>2</sub> ) flow rate	20 ml min <sup>-1</sup>

Table 2. Melting points (°C) of the anilides ( $XC_6H_4NHCOC_6H_4Y$ )<sup>a</sup>

Y	X				
	$p\text{-CH}_3\text{O}$	$p\text{-CH}_3$	H	$p\text{-Br}$	$m\text{-Cl}$
$p\text{-CH}_3\text{O}$	184	148	168 (169)	212	128
$p\text{-CH}_3$	166	160 (160)	146 (146)	228	118
H	155	158 (158)	164 (162)	208	119
$m\text{-Cl}$	164	124	126 (124)	142	117
$p\text{-NO}_2$	198	198 (203)	214 (211)	240	152

<sup>a</sup> Values in parentheses from Ref. 12.

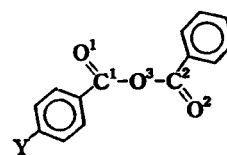
Table 3. Ratios (*R*) of the reaction products, anilides, for the reactions of  $YC_6H_4COOCOC_6H_5$  and  $XC_6H_4NH_2$  in methanol at 25.0, 35.0 and 45.0 °C ( $R = [YC_6H_4CONHC_6H_4X] / [C_6H_5CONHC_6H_4X]$ )

X	<i>R</i>											
	Y = <i>p</i> -CH <sub>3</sub> O			Y = <i>p</i> -CH <sub>3</sub>			Y = <i>m</i> -Cl			Y = <i>p</i> -NO <sub>2</sub>		
	25.0 °C	35.0 °C	45.0 °C	25.0 °C	35.0 °C	45.0 °C	25.0 °C	35.0 °C	45.0 °C	25.0 °C	35.0 °C	45.0 °C
<i>p</i> -CH <sub>3</sub> O	0.78	0.69	0.69	1.23	1.19	1.20	1.05	1.05	1.02			
<i>p</i> -CH <sub>3</sub>	0.72	0.67	0.69	1.17	1.16	1.21	1.02	1.05	1.04			
H	0.72	0.70	0.71	1.22	1.20	1.22	0.97	0.95	0.93			
<i>p</i> -Br	0.74	0.71	0.72	1.26	1.15	1.22	0.92	0.96	0.95	0.42	0.47	0.47
<i>m</i> -Cl	0.75	0.73	0.68	1.21	1.21	1.23	0.86	0.95	0.95	0.43	0.49	0.50

the relative areas of the two corresponding GC peaks, which were calibrated by a linear correlation between concentration and peak area. The product ratios obtained are summarized in Table 3.

### RESULTS AND DISCUSSION

The overall second-order rate constants,  $k_2$ , are summarized in Table 4. The rates are faster with a more electron-withdrawing substituent (EWS), Y, in the substrate and with a stronger nucleophile (X = *p*-CH<sub>3</sub>O); the former trend suggests that negative charge develops at the reaction centre carbon, either C-1 or C-2, in the TS (I). This means that the reactivity of a more electron-donating substituent (EDS) Y is lower on account of the lower electrophilicity of both C-1 (due to the higher negative charge at C-1) and C-2 (due to a lower leaving ability of the  $YC_6H_4C^1O^1O^3$



(BA), I

group). In contrast, the reactivity of a more EWS Y will be higher owing to the higher electrophilicity of both C-1 (due to the lower negative charge at C-1) and C-2 (due to the higher leaving ability of the  $YC_6H_4C^1O^1O^3$  group). On the other hand, the potential energy surface<sup>9</sup> (or More O'Ferrall-Jencks<sup>9</sup>) diagram predicts that a weaker nucleophile with a more EWS in the nucleophile (e.g. X = *m*-Cl) will lead to a greater degree of bond making and breaking. Hence the reactivity will be lower as a closer approach and a greater degree of

Table 4. Second-order rate constants,  $k_2$  ( $\times 10^2$  l mol<sup>-1</sup> s<sup>-1</sup>) for the reactions of benzoic anhydrides with anilines in methanol at 45.0, 35.0 and 25.0 °C

Temperature (°C)	X	Y				
		<i>p</i> -CH <sub>3</sub> O	<i>p</i> -CH <sub>3</sub>	H	<i>m</i> -Cl	<i>p</i> -NO <sub>2</sub>
45.0	<i>p</i> -CH <sub>3</sub> O	21.0 <sup>a</sup>	38.6	56.7	144	
	<i>p</i> -CH <sub>3</sub>	7.96	15.9	24.8	71.2	
	H	2.22	4.10	6.94	23.3	
	<i>p</i> -Br	0.372	0.826	1.29	5.58	26.7
	<i>m</i> -Cl	0.110	0.292	0.572	2.48	12.0
35.0	<i>p</i> -CH <sub>3</sub> O	14.4 <sup>a</sup>	27.0	41.0	103	
	<i>p</i> -CH <sub>3</sub>	5.48	10.4	17.6	49.6	
	H	1.62	3.11	5.25	18.0	
	<i>p</i> -BR	0.244	0.526	1.04	4.14	18.5
	<i>m</i> -Cl	0.0558	0.181	0.331	1.36	8.16
25.0	<i>p</i> -CH <sub>3</sub> O	10.4 <sup>a</sup>	16.2	27.2	70.5	
	<i>p</i> -CH <sub>3</sub>	3.60	6.41	12.0	31.7	
	H	0.800	1.45	3.09	11.0	
	<i>p</i> -Br	0.110	0.192	0.464	2.17	10.3
	<i>m</i> -Cl	0.0298	0.0570	0.151	0.750	4.32

<sup>a</sup> The  $k_2$  values are averages of at least two determinations.

bond cleavage are both energetically unfavourable. A stronger nucleophile should therefore lead to a greater reactivity, as observed.

An attack of C-2 by a nucleophile, when Y is an EDS, is favoured on account of lower negative charge at C-2 (relative to C-1) but is disfavoured owing to the lower leaving ability of the  $YC_6H_4C^1O^1O^3$  group (relative to  $C_6H_5C^2O^2O^3$  group). In contrast, for Y = EWS, an attack of C-1 by a nucleophile is favoured (relative to C-2) but is disfavoured owing to the lower leaving ability of the  $C_6H_5C^2O^2O^3$  group.

These trends show that the effects of nucleophile on the selectivity, i.e. on the product ratio, are compensatory, so that unless either of the two effects, i.e. nucleophilic vs leaving ability, is dominant, the product ratio should not depend much on the nucleophile. This conclusion is true, of course, if the rate-limiting step and the product-forming step is the same. This is indeed borne out by the product ratio values in Table 3. Table 3 reveals that the selectivity,  $R$ , changes very little between nucleophiles for Y =  $p$ -CH<sub>3</sub> and  $p$ -CH<sub>3</sub>O, but a decreasing trend in  $R$  for Y =  $m$ -Cl and  $p$ -NO<sub>2</sub> is noted as the nucleophile becomes weaker, X =  $p$ -CH<sub>3</sub>O → X =  $m$ -Cl; this means that for Y = EWS, the formation of a product with substituent in the LG, i.e. an attack on C-2, becomes more favoured with a weaker nucleophile, which leads to a greater degree of bond making and breaking. Preference for the product with substituent in the LG should therefore indicate that in the rate-determining step the leaving ability (attack at C-2) becomes more important than the nucleophilicity (attack at C-1) when the nucleofugicity of the LG is stronger (Y = EWS) and the extent of bond cleavage is relatively greater (with X = EWS). This is

reasonable since an increase in the amount of product in the  $k_{XZ}$  process with the substituent in the LG is expected when the bond cleavage process becomes more important in the rate-determining step.

On the other hand, a strong electron-donating group, Y =  $p$ -CH<sub>3</sub>O, in the substrate appears to render a significant activation barrier for the attack on C-1 owing to the relatively high negative charge, lowering the  $R$  values, i.e. yielding less amount of the product resulting from the C-1 attack compared with the product given by displacement at C-2. This is in contrast to the selectivity trend of other Y-substituted anhydrides, for which the leaving group ability of the substituted benzoates with cleavage of the C-2—O-3 bond has been shown to be more important.

Since the product-forming step coincides with the rate-determining step, the product ratio can be given by the two competing rate ratios, [equation (5b)], and the rate constants for the two separate processes,  $k_{XY}$  [equation (3a)] and  $k_{XZ}$  [equation (3b)], can now be calculated using equations (5a) and (5b), with the experimentally observed values of  $k_2$  (Table 4) and  $R$  (Table 3).

$$k_2 = k_{XY} + k_{XZ} \quad (5a)$$

$$R = k_{XY}/k_{XZ} \quad (5b)$$

The calculated values of  $k_{XY}$  and  $k_{XZ}$  are summarized in Tables 5 and 6, respectively. The simple Hammetts coefficients  $\rho_X$ ,  $\rho_Y$  and  $\rho_Z$ , were then determined using these rate constants, and are shown in Tables 7 and 8. It is notable that the  $\rho_X$  values for the process  $k_{XY}$  differ very little from the corresponding values for the process  $k_{XZ}$ . The sign of  $\rho_Y$  is positive, which is consistent with

Table 5. Second-order rate constants,  $k_{XY}$  ( $\times 10^2$  l mol<sup>-1</sup> s<sup>-1</sup>) for the reactions of benzoic anhydrides with anilines in methanol at 45.0, 35.0 and 25.0 °C

Temperature (°C)	X	Y				
		$p$ -CH <sub>3</sub> O	$p$ -CH <sub>3</sub>	H	$m$ -Cl	$p$ -NO <sub>2</sub>
45.0	$p$ -CH <sub>3</sub> O	8.59	21.1	28.4	72.7	
	$p$ -CH <sub>3</sub>	3.25	8.70	12.4	36.2	
	H	0.919	2.25	3.47	11.2	
	$p$ -Br	0.156	0.454	0.645	2.72	8.54
	$m$ -Cl	0.0446	0.161	0.286	1.21	3.98
35.0	$p$ -CH <sub>3</sub> O	5.89	14.7	20.5	52.7	
	$p$ -CH <sub>3</sub>	2.19	5.59	8.80	25.3	
	H	0.666	1.70	2.63	8.77	
	$p$ -Br	0.101	0.281	0.520	2.02	5.96
	$m$ -Cl	0.0236	0.0990	0.166	0.661	2.68
25.0	$p$ -CH <sub>3</sub> O	4.56	8.93	13.6	36.2	
	$p$ -CH <sub>3</sub>	1.50	3.46	6.00	16.0	
	H	0.334	0.798	1.55	5.40	
	$p$ -Br	0.0466	0.106	0.230	1.04	3.03
	$m$ -Cl	0.0128	0.0312	0.0750	0.301	1.31

Table 6. Second-order rate constants,  $k_{XZ}$  ( $\times 10^2 \text{ l mol}^{-1} \text{ s}^{-1}$ ) for the reactions of benzoic anhydrides with anilines in methanol at 45.0, 35.0 and 25.0 °C

Temperature (°C)	X	Y				
		<i>p</i> -CH <sub>3</sub> O	<i>p</i> -CH <sub>3</sub>	H	<i>m</i> -Cl	<i>p</i> -NO <sub>2</sub>
45.0	<i>p</i> -CH <sub>3</sub> O	12.4	17.5	28.4	71.3	
	<i>p</i> -CH <sub>3</sub>	4.71	7.20	12.4	35.0	
	H	1.30	1.85	3.47	12.1	
	<i>p</i> -Br	0.216	0.372	0.645	2.86	18.2
	<i>m</i> -Cl	0.0654	0.131	0.286	1.27	8.02
35.0	<i>p</i> -CH <sub>3</sub> O	8.51	12.3	20.5	50.3	
	<i>p</i> -CH <sub>3</sub>	3.29	4.81	8.80	24.3	
	H	0.954	1.41	2.63	9.23	
	<i>p</i> -Br	0.143	0.245	0.520	2.12	12.5
	<i>m</i> -Cl	0.0322	0.0820	0.166	0.699	5.48
25.0	<i>p</i> -CH <sub>3</sub> O	5.84	7.27	13.6	34.3	
	<i>p</i> -CH <sub>3</sub>	2.10	2.95	6.00	15.7	
	H	0.466	0.652	1.55	5.60	
	<i>p</i> -Br	0.0634	0.0842	0.230	1.13	7.27
	<i>m</i> -Cl	0.0170	0.0258	0.0750	0.449	3.01

the negative charge development at the action centre carbon in the TS. The size of  $\rho_Z$  is also considerable, indicating a relatively large degree of bond cleavage in the TS.

The rate data in Tables 7 and 8 were then subjected to multiple linear regression using equation (2)<sup>9</sup> with appropriate substituent notations for  $i$  and  $j$  (i.e.,  $i, j = X, Y$  or  $Z$ ). The cross-interaction constants obtained,  $\rho_{XY}$  and  $\rho_{XZ}$ ,<sup>9</sup> are given in Table 9. The magnitude of  $\rho_{XY}$  is well within the range of those observed for typical  $S_N2$  processes,  $|\rho_{XY}| = 0.5-0.8$ .<sup>9</sup> However the large  $\rho_{XZ}$  values ( $\rho_{XZ} = 1.2-1.5$ ) obtained are unusual; in fact, they are the largest ever observed so

far in our series of studies. Our experience has shown that whenever frontside nucleophilic attack is involved in  $S_N2$  reactions, the magnitude of  $\rho_{XZ}$  becomes exceptionally large, as we have reported for  $S_N2$  reactions involving the frontside attack of 1-phenylethyl arenuesulphonates ( $\rho_{XZ} = -0.56$ )<sup>13</sup> and cumyl arenuesulphonates ( $\rho_{XZ} = -0.75$ ).<sup>14</sup> These are in contrast to the smaller  $\rho_{XZ}$  values observed for the processes involving normal rearside  $S_N2$  attack, e.g. reactions of benzyl arenuesulphonates with anilines gave  $\rho_{XZ} = -0.10$ ,<sup>9</sup> and for an  $S_N1$  reaction  $\rho_{XZ} = 0$ .<sup>15</sup>

It has been shown theoretically<sup>4</sup> that in the TS for nucleophilic displacement on acyl system the

Table 7. Simple Hammett  $\rho_i$  values from  $k_{XY}$  for the reactions of benzoic anhydrides with anilines in methanol at 45.0, 35.0 and 25.0 °C

Temperature (°C)	$\rho_X^a$ (YC <sub>6</sub> H <sub>4</sub> COOCOC <sub>6</sub> H <sub>5</sub> )				
	Y = <i>p</i> -CH <sub>3</sub> O	<i>p</i> -CH <sub>3</sub>	H	<i>m</i> -Cl	<i>p</i> -NO <sub>2</sub>
45.0	-3.50	-3.27	-3.14	-2.78	-2.37
35.0	-3.63	-3.35	-3.20	-2.91	-2.48
25.0	-3.92	-3.82	-3.53	-3.18	-2.60
Temperature (°C)	$\rho_Y^b$ (XC <sub>6</sub> H <sub>4</sub> NH <sub>2</sub> )				
	X = <i>p</i> -CH <sub>3</sub> O	<i>p</i> -CH <sub>3</sub>	H	<i>p</i> -Br	<i>m</i> -Cl
45.0	1.01	1.17	1.31	1.39	1.49
35.0	1.04	1.21	1.34	1.41	1.53
25.0	1.13	1.22	1.43	1.54	1.68

<sup>a</sup> Correlation coefficients  $\geq 0.999$ .

<sup>b</sup> Correlation coefficients  $\geq 0.997$ . For  $\rho_Y$  values, Y = *p*-CH<sub>3</sub>O is excluded.

Table 8. Simple Hammett  $\rho_i$  values from  $k_{XZ}$  for the reactions of benzoic anhydrides with anilines in methanol at 45.0, 35.0 and 25.0 °C

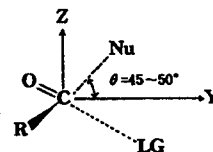
Temperature (°C)	$\rho_x^a$ ( $C_6H_4COOCOC_6H_4Z$ )				
	Z = <i>p</i> -CH <sub>3</sub> O	<i>p</i> -CH <sub>3</sub>	H	<i>m</i> -Cl	<i>p</i> -NO <sub>2</sub>
45.0	-3.47	-3.29	-3.14	-2.73	-2.54
35.0	-3.58	-3.37	-3.20	-2.84	-2.56
25.0	-3.91	-3.84	-3.53	-2.92	-2.74

Temperature (°C)	$\rho_x^b$ ( $XC_6H_4NH_2$ )				
	X = <i>p</i> -CH <sub>3</sub> O	<i>p</i> -CH <sub>3</sub>	H	<i>p</i> -Br	<i>m</i> -Cl
45.0	1.17	1.33	1.51	1.81	1.93
35.0	1.19	1.34	1.53	1.82	1.96
25.0	1.22	1.36	1.71	1.98	2.16

<sup>a</sup> Correlation coefficients  $\geq 0.999$ .<sup>b</sup> Correlation coefficients  $\geq 0.997$ .Table 9. Cross-interaction constants,  $\rho_{ij}$ , values by multiple linear regression for the reactions of benzoic anhydrides with anilines in methanol at 45.0, 35.0 and 25.0 °C

Parameter	Temperature (°C)	$\rho_x$	$\rho_y$	$\rho_{xy}$	$r^a$
$k_{XY}$	45.0	-3.12	1.24	0.54	0.990
	35.0	-3.21	1.28	0.53	0.990
	25.0	-3.59	1.38	0.64	0.990
$k_{XZ}$		$\rho_x$	$\rho_z$	$\rho_{xz}$	$r^a$
	45.0	-3.14	1.52	1.19	0.999
	35.0	-3.23	1.54	1.25	0.998
	25.0	-3.54	1.64	1.46	0.999

<sup>a</sup> Correlation coefficient.

OCY is coplanar

 $\angle Nu-C-Y = 45-50^\circ$ 

C-Z is perpendicular to the OCY plane

Figure 1

Table 10. Activation parameters,  $\Delta H^\ddagger$  (kcal mol<sup>-1</sup>) and  $\Delta S^\ddagger$  (cal K<sup>-1</sup> mol<sup>-1</sup>) for aminolysis of benzoic anhydrides in methanol

Type	X	Y									
		<i>p</i> -CH <sub>3</sub> O		<i>p</i> -CH <sub>3</sub>		H		<i>m</i> -Cl		<i>p</i> -NO <sub>2</sub>	
		$\Delta H^\ddagger$	$-\Delta S^\ddagger$	$\Delta H^\ddagger$	$-\Delta S^\ddagger$	$\Delta H^\ddagger$	$-\Delta S^\ddagger$	$\Delta H^\ddagger$	$-\Delta S^\ddagger$	$\Delta H^\ddagger$	$-\Delta S^\ddagger$
$k_{XY}$	<i>p</i> -CH <sub>3</sub> O	5.4	47	7.5	38	6.4	41	6.0	40		
	<i>p</i> -CH <sub>3</sub>	6.7	45	8.1	38	6.2	43	7.1	38		
	H	9.0	40	9.2	37	7.0	43	6.3	43		
	<i>p</i> -Br	11.0	37	13.1	28	9.3	40	8.5	39	9.2	35
	<i>m</i> -Cl	11.2	39	14.9	25	12.2	32	12.5	28	9.9	34
$k_{XZ}$	<i>p</i> -CH <sub>3</sub> O	6.5	42	7.7	38	6.4	41	6.3	40		
	<i>p</i> -CH <sub>3</sub>	7.0	43	7.8	39	6.2	43	7.0	39		
	H	9.1	39	9.3	37	7.0	43	6.7	42		
	<i>p</i> -Br	10.7	37	13.4	28	9.3	40	8.2	40	8.1	37
	<i>m</i> -Cl	12.0	36	14.7	26	12.2	32	9.2	39	8.7	37

<sup>a</sup> Calculated values at 25.0 °C.

nucleophile approaches at an angle of *ca* 45–50° above the acyl plane along the carbon end of the C=O  $\pi^*$  orbital ( $\pi_{C=O}^*$ ), which is the lowest unoccupied MO (LUMO) (Figure 1). In this type of TS, the nucleophile (Nu) can come very close to the LG, unlike in the rear-side attack  $S_N2$  processes; the two form *ca* 90° in Scheme 1, which should be *ca* 180° in the rear-side attack. We therefore conclude that in the aminolysis of benzoic anhydrides a frontside nucleophilic attack is involved and as a result the nucleophile is situated very close to the LG, causing a strong interaction between them with a large  $\rho_{XZ}$  value.

Finally, calculated activation parameters,  $\Delta H^\ddagger$  and  $\Delta S^\ddagger$ , are summarized in Table 10. The data that the  $\Delta H^\ddagger$  values are relatively low whereas the  $\Delta S^\ddagger$  values are large and negative, which are consistent with those for the  $S_N2$  reaction.<sup>16</sup> Close examination of Table 10 also reveals that the reactions are in general enthalpy controlled, except for the reactions of compounds with Y = *p*-CH<sub>3</sub>O. This is in line with our conclusion above that the bond cleavage (endoergic)<sup>16b</sup> is dominant in general except for the reactions of compounds with Y = *p*-CH<sub>3</sub>O, for which bond making (less endoergic but entropic)<sup>15b</sup> is important in controlling the rate and product ratios.

### CONCLUSIONS

The reaction of benzoic anhydrides with anilines proceeds by a frontside  $S_N2$  attack on either one of the carbonyl carbon. The frontside approach in the TS causes a strong interaction between the nucleophile and LG with an unusually large  $\rho_{XZ}$  value. In this reaction, the product-forming step coincides with the rate-determining step, so that the two rate constants,  $k_{XY}$  and  $k_{XZ}$ , for the competitive attack on C-1 and C-2 can be determined. The use of these two constants permits the determination of the cross-interaction constants  $\rho_{XY}$  and  $\rho_{XZ}$ . The magnitude of these is consistent with the frontside attack  $S_N2$  mechanism. The activation parameters also support the proposed mechanism, and especially the anomalous product ratios exhibited by the compounds with Y = *p*-CH<sub>3</sub>O can be accommodated by the reversal in the trends of activation par-

ameters from the normal enthalpy-controlled processes for all other compounds.

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