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# **Basic Methanolysis of Anilides. Evidence for the Mechanism Applying** to the Special Case of N-Methyl-4'-nitroanilides

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Evidence from activation parameters, solvent effects on rate, and solvent activity coefficients suggests that Nmethyl-4'-nitroanilides undergo basic methanolysis by way of rate-determining methoxide addition to the amide. For other ring-substituted N-methyl and all NH anilides, decomposition of the tetrahedral intermediate is rate determining. Hammett data are discussed in terms of these mechanisms and an explanation of the behavior of the N-methyl-4'-nitroanilides is proposed.

The details of the mechanisms of basic anilide hydrolysis and alcoholysis are of current interest. To summarize (using methanolysis as the example and referring to eq 1), formation of 1 (mechanism A) or its decomposition to

$$\begin{array}{c}
\text{OMe} \\
\text{R-C-NR'Ar} + \text{MeO} \xrightarrow{k_{1}} \text{R-C-NR'Ar} \xrightarrow{k_{2}} \\
\text{O} \\
\text{O} \\
\text{O} \\
\text{OMe} \\
\text{R-C} + \text{NHR'Ar} + \text{MeO} \\
\text{O} \\
\text{OMe} \\
\text{R-C} + \text{NHR'Ar} + \text{MeO} \\
\text{O} \\
\text{OMe} \\
\text{R-C} \\
\text{OMe} \\
\text{NHR'Ar} + \text{MeO} \\
\text{OH} \\
\text{OH}$$

products can be rate determining. In the latter case, two. extreme transition states are possible.<sup>1</sup> Where NR'Ar is a poor leaving group (mechanism B), protonation of the nitrogen is rate determining (transition state 2) while for better leaving groups (mechanism C) solvent-assisted C-N cleavage is rate determining (transition state 3).



It appears that the mechanism is affected by many aspects of the structure of the anilide. For example, in acetanilides (R = Me<sup>2</sup> or CF<sub>3</sub>;<sup>1</sup> R' = H or Me) a gradual change from B to C occurs when the substituent on the benzene ring is changed from methoxy through to nitro. On the other hand, N-methylbenzanilides have been stated<sup>3</sup> to follow C irrespective of the nature of Ar.

Discussion of the possible occurrence of mechanism A has been limited to compounds containing the 4'-nitro substituent, the best leaving group studied to date, where decomposition of 1 to products might be so favored that A operates. It is our purpose here to summarize previous results, provide new data, and hopefully clarify the situation regarding this possibility.

### **Results and Discussion**

pH-Rate Profiles in Basic Hydrolysis. Hydrolysis and methanolysis reactions are closely related and information about one can be related to the other with fair confidence.

Decomposition of the hydrolysis intermediate analogous to 1 can proceed via a dianionic intermediate (4). At high



pH, this route is fast and dominates for 4'-nitro-NH-anilides, formation of 1 becomes rate determining, and  $k_{obsd}$ tends to level off.<sup>4,5</sup> This behavior is not observed for analogous N-methyl compounds<sup>4-6</sup> and here the pH-rate profile is linear over the entire pH range. This has been variously interpreted as  $consistent^6$  or  $not^5$  consistent with mechanism A operating in this pH range for the N-methyl compounds.

Activation Parameters. Though N-methyl-4'-nitroacetanilide undergoes basic methanolysis only 1.5 times faster than the NH compound at 373 K, activation parameter measurements revealed a major difference between the two.7 The much higher activation energy but more favorable entropy for the NH compound was ascribed to a predominant ground state solvation effect, it being assumed that both compounds reacted by mechanism C.

New rate data for reactions in methanol are collected in Table I. Activation parameters for other anilides have been calculated from some of the results and these, with the literature values for the 4'-nitro compounds, are listed in Table II.

*	RUONR AF IN Methanol							
Registry no.	R	R'	Ar	Temp, K	10 <sup>3</sup> k <sub>obsd</sub> M <sup>-1</sup> sec <sup>-1</sup>			
122-28-1	Ме	Н	3'-NO <sub>2</sub> C <sub>6</sub> H <sub>4</sub>	373	1.75			
				390	7.59			
				399	18.0			
2963-34-0	Me	Н	$3'-C1-5'-NO_2C_6H_3$	353	3.31			
38802-18-5	Me	Н	$3', 5' - (NO_2)_2 C_6 H_3$	334	3.45			
				353	30.3			
				363	67.9			
21353-89-9	Me	Me	$3'-NO_2C_6H_4$	352	2.32			
				374	15.5			
				387	38.5			
54338-36-2	Me	Me	$3', 5' - (NO_2)_2 C_6 H_3$	300	20.9			
				309	47.4			
				319	104			
33672-82-1	$\mathbf{Ph}$	Me	$4'-NO_2C_6H_4$	310	7.00			
				321	16.3			
				339	62.1			
55975-43-4	Ph	Me	$3', 5' - (NO_2)_2 C_6 H_3$	298	24.5			
•				310	65.1			
				333	349			
55975-44-5	$\mathbf{Ph}$	Ħ	$3', 5' - (NO_2)_2 C_6 H_3$	373	$462^{a}$			
3393-96-2			$4'-NO_2C_6H_4$	373	260			
55975-45-6			$4'-MeSO_2C_6H_4$	373	20.4			
5411-13-2			$4'$ -COMeC $_6$ H $_4$	373	7.08			
4771-08-8			$3'-NO_2C_6H_4$	373	3.93			
6004-21-3			$3'-ClC_6H_4$	373	0.40			

Table I Rate Data for the Basic Methanolysis of RCONR'Ar in Methanol

<sup>a</sup> Calculated from plot of  $1/k_{exp}$  vs.  $1/MeO^-$ . See ref 11.  $10^3 k_{exp}$  = 0.97 (0.003 M MeO<sup>-</sup>), 1.36 (0.005 M), 1.80 (0.01 M) sec<sup>-1</sup>.  $k_{exp}$  is the observed pseudo-first-order rate constant.

In the case of the 4'-nitro substituted compounds, the values obtained for benzanilides and acetanilides are very similar and it is likely that any discussion regarding acetanilides will also apply to benzanilides. It is apparent that, in the acetanilides, the values for the N-methyl-4'-nitro compound are anomalous when compared with those for other members of the series. The appreciably negative entropy for this compound is of the same order as that found<sup>8</sup> in ester hydrolysis (AcOEt;  $E_a = 14.9 \text{ kcal}, \Delta S^{\ddagger}_{298} = -20 \text{ cal}$  $mol^{-1} K^{-1}$  in 80% ethanol), where rate-determining formation of the tetrahedral intermediate occurs. A consequence of the activation energy order is that, in any Hammett treatment of data, the effective  $\sigma$  value for the 4'-nitro substituent in the N-methyl series will be temperature dependent. For example, the N-methylacetanilide plot in Figure 1 gives  $\bar{\sigma}_{4'-NO_2} = 1.16$  at 373 K, while analogous treatment of rate data at 318 K gives  $\rho = 4.3$  and  $\bar{\sigma}_{4'-NO_2} = 1.24$ .

Solvent Effect on Rate. Gani and Viout showed<sup>9</sup> that the rate of hydrolysis of N-methyl-4'-nitroacetanilide was markedly increased by the addition of Me<sub>2</sub>SO. Using the analogy of ester hydrolysis where the same effect is observed, they concluded that the anilide hydrolyzed by mechanism A. Substituted N-methylacetanilides reacting by way of mechanism B showed a negligible solvent effect. We measured the rate of basic methanolysis of 3'-nitro-Nmethyltrifluoroacetanilide in Me<sub>2</sub>SO-MeOH, a reaction which appeared<sup>1</sup> to satisfy the requirements of mechanism C, and also obtained a large rate increase.<sup>10</sup> Thus, either both compounds reacted by the same mechanism or the effect of Me<sub>2</sub>SO on rate could not be used to differentiate between C and A.

We have now carried out further studies on the effect of

 
 Table II

 Activation Parameters for Basic Methanolysis of Anilides RCONR'Ar in Methanol

		R <b>ʻ</b>	'≕ Me	R' = H	
R	Ar	E <sub>a</sub> , kcal	$\Delta S^{\pm}_{298},$ cal mol <sup>-1</sup> K <sup>-1</sup>	E <sub>a</sub> , kcal	$\frac{\Delta S^{\dagger}_{298}}{\text{cal mol}^{-1}}$ $\kappa^{-1}$
Me Me Me Ph	$3' - NO_2C_6H_4$ $4' - NO_2C_6H_4$ $3', 5' - (NO_2)_2C_6H_3$ $4' - NO_2C_6H_4$	21.4 $14.6^{a}$ 15.0 15.7	-12 -23 <sup>a</sup> -18 -20	27.8 $25.3^{a}$ 24.7 $22.5^{b}$	$+1 + 5^a + 2 - 3^b$

<sup>a</sup> From ref 7. <sup>b</sup> From ref 11.

added Me<sub>2</sub>SO on basic methanolysis of nitroacetanilides and the results are given in Table III. No results were obtained for N-methyl-3',5'-dinitroacetanilide or for 3'-nitroacetanilide. For the former, complications due to probable methoxide addition to the aromatic ring were evident, while product instability occurred at the higher temperatures necessary for reaction of the latter compound. Extensive ionization was observed for 4'-nitroacetanilide in this solvent and the quoted rate constants have been corrected<sup>11</sup> to allow for this.

The addition of Me<sub>2</sub>SO produces a rate increase for each compound but it is an order of magnitude less for the *N*-methyl-4'-nitro compound, which once again shows anomalous behavior. Thus, while a rate increase with addition of Me<sub>2</sub>SO cannot in itself be used as evidence for a particular mechanism, the magnitude of the rate increase may be a useful mechanistic indicator. It is of interest that a solvent effect of 91 at 288 K ( $k_{obsd}^{Me_2SO-MeOH} = 10.7$ ;  $k_{obsd}^{MeOH} = 0.118 M^{-1} \sec^{-1}$ ) was obtained for reaction of *N*-4'-nitrophenylazetidinone (formation of the tetrahedral intermediate is rate determining)<sup>6</sup> and similar solvent changes in ester hydrolysis produce rate increases of ~100<sup>12</sup>.

It is worthy of note that the NH anilide solvent effect would be smaller at higher temperatures. This is because of the much smaller activation energy for reaction of this compound in Me<sub>2</sub>SO-MeOH (Table III) than in methanol.

Gani and Viout have recently reported<sup>13</sup> the effect of methanol on the hydrolysis of N-methylnitroacetanilides and have shown that the 4'-nitro and 3'-nitro compounds respond quite differently to solvent change. This is presented as favoring mechanism A for reaction of N-methyl-4'-nitroacetanilide.

Solvent Activity Coefficients. It became obvious that our original interpretation<sup>7</sup> of the differences in activation parameters for the NH and NMe 4'-nitroacetanilides in terms of ground-state effects was too simplified. Solvent activity coefficients,<sup>14</sup> determined from rate measurements and solubilities, can provide information about the effect of solvent on both ground and transition states. We have determined these for some nitroacetanilides (Table IV) for the system 80% Me<sub>2</sub>SO–MeOH relative to methanol from

$$\log \frac{\kappa_{\rm DM}}{k_{\rm M}} = \log^{\rm M} \gamma_{\rm MeO}^{\rm DM} + \log^{\rm M} \gamma_{\rm anilide}^{\rm DM} - \log^{\rm M} \gamma_{\rm \ddagger}^{\rm DM}$$
(2)

Ŀ

eq 2. Solubility values are listed in Table IV and the required rate data are from Table III.

Large differences are apparent within the series. It is evident that the NH anilide is rather better solvated by  $Me_2SO$  relative to methanol than are the *N*-methyl analogs. This is reasonable if hydrogen bond donation by the anilide is important. However, major differences also occur in transition state values, though interpretation of these

<sup>a</sup> Calculated from Table I. <sup>b</sup>  $E_a = 15.2 \text{ kcal}$ ;  $\Delta S^{\ddagger}_{298} = -12 \text{ cal mol}^{-1} \text{ K}^{-1}$ . <sup>c</sup>  $E_a = 16.7 \text{ kcal}$ ;  $\Delta S^{\ddagger}_{298} = -10 \text{ cal mol}^{-1} \text{ K}^{-1}$ . <sup>d</sup> Calculated from plot of  $1/k_{\text{exp}}$  vs.  $1/\text{MeO}^-$ . See ref 11. <sup>e</sup> 10<sup>5</sup>  $k_{\text{exp}} = 8.13$  (0.001 *M* MeO<sup>-</sup>), 11.4 (0.002 *M*), 16.0 (0.01 *M*) sec<sup>-1</sup>. / 10<sup>5</sup>  $k_{\text{exp}} = 16.2$  (0.001 *M* MeO<sup>-</sup>), 23.3 (0.002 *M*), 30.5 (0.01 *M*) sec<sup>-1</sup>. <sup>g</sup> 10<sup>5</sup>  $k_{\text{exp}} = 35.5$  (0.001 *M* MeO<sup>-</sup>), 48.0 (0.002 *M*), 63.8 (0.01 *M*).



		Solubility	', M		
R	NO <sub>2</sub> position	80% Me2 <mark>SO—</mark> MeOH	MeOH	Log <sup>M</sup> 7 anilide <sup>DM</sup>	Log M <sub>γ</sub> +DM
н	4'	1.356	0.079	-1.23	-0.26
Me	4'	0.613	0.265	-0.37	+1.57
Me	31	1.42	0,984	-0.16	+0.41
<sup>a</sup> Log	$g^M\gamma_{anilide}$	$DM = \log S^M -$	$\log S^{\rm DM};$	$\log M \gamma_{MeO} - DM =$	4.0 (ref 14).

must be made with caution. It may be noted from Table III that the activation parameters for reaction of both 4'-nitroanilides are quite similar, unlike the situation in methanol. The details of the effect of solvent on this reaction have not yet been fully investigated, but the mechanism

applicable to the NH compound in particular may be dif-

ferent in Me<sub>2</sub>SO and methanol. In such a case, solvent activity values would not give a true picture. Nevertheless, the fact that each compound gives such different values is a useful indication of their fundamentally different behavior, and the result for N-methyl-4'-nitroacetanilide is probably valid. Pollack<sup>15</sup> has shown that  $k_2/k_{-1}$  (Me<sub>2</sub>SO) >  $k_2/k_{-1}$  (H<sub>2</sub>O) for hydrolysis of 4'-nitroacetanilide. Thus, if this also applies to the N-methyl compound and if this compound undergoes methanolysis by mechanism A in methanol, then it no doubt does so in Me<sub>2</sub>SO-methanol also. The solvent activity coefficients are reasonable if this is so. The nearest analogy for which results are available<sup>14</sup> is the reaction of *p*-nitrophenylacetate with azide in DMF, with values of log  $(k_{\text{DMF}}/k_{\text{MeOH}}) = 1.4$ ,  $\log M_{\gamma_{ester}} DMF = -0.9$ , and  $\log M_{\gamma_{\ddagger}} DMF = 2.6$ . A transition state such as 3, where the charge is diffuse, might not be expected to be so much better solvated by methanol.

Hammett Treatment. The entire results from activation parameters, solvent effects on rate, and solvent activity coefficients are most reasonably accommodated on the basis that of all compounds studied to date, N-methyl-4'nitroanilides alone react by mechanism A.

If one accepts the different mechanism for this group of compounds, it is necessary to see if an analysis of substituent effects on rate is consistent with this interpretation.

From various Hammett studies,  $\rho$  values of  $\sim 1.3^6$  (mechanism A),  $\sim 0^1$  (B), and  $\sim 3^{1,3}$  (C) have been found. Thus, for acetanilides a change from B (4'-methoxy) to C (3'-nitro) results<sup>1</sup> in a concave upward plot while a change from C to A would result in the opposite curvature. This latter has never been observed and, for N-methylbenzanil-

**Figure 1.** Hammett plots for methanolysis:  $\Box$ , *N*-methylacetanilides (353 K) (1 + log k);  $\times$ , *N*-methylbenzanilides (373 K): O, benzanilides (373 K);  $\triangle$ , acetanilides (373 K).

ides which give a linear plot,<sup>3</sup> the point for the 4'-nitro substituent fitted this line satisfactorily.

We have now measured rates of basic methanolysis in NH benzanilides and have extended measurements in three other series to compounds more reactive than the 4'nitro substituted ones to seek evidence for downward curvature in the Hammett plots. New rate data are listed in Table I.

The appropriate Hammett plots are shown in Figure 1. The lines are drawn taking particular account of points for meta substituents and neglecting 4'-nitro values. There is clearly no sign of a decrease in slopes beyond the 3'-nitro point in any series. The  $\rho$  values are all similar (allowing for temperature differences, and a two-point line in one case) and are compatible with the operation of mechanism C. The 4'-nitro points have been placed using the standard  $\sigma^$ value of 1.27.<sup>16</sup> It is of interest that the 4'-nitro point lies below the line in both N-methyl plots and above it in the NH ones. In the case of the NH acetanilides, the 4'-nitro substituted compound in fact reacts faster than does the 3',5'-dinitro one.

If mechanism A operates for N-methyl-4'-nitroanilides, then the fair correlation of these points may be a chance result. As mentioned above, activation energies are such that

 $Table \, III \\ Rate \, Data \, for the \, Basic \, Methanolysis \, of \, CH_3 CONR' C_6 H_4 NO_2 \, in \, 80\% \, Me_2 SO-MeOH \\$ 

Begistary ag		NO2 position	Temp K	10 <sup>3</sup> k <sub>obsd</sub> ,	10 <sup>3</sup> kobsd <sup>298</sup>	<sup>k</sup> Me <sub>2</sub> SO-MeOH <sub>298</sub> K <sup>a</sup>	
Registry no.	K.			M · Sec ·	cared	~MeOH	
	Me	3'	298	27.3	27.3	2680	
121-95-9	Me <sup>b</sup>	4'	281	79.9	380	115	
			288	161			
			294	273			
			298	402			
			305	667			
104-04-1	$H^{c}$	4'	307	139 <sup>d</sup> · e	63.1	1070	
			315	289 <sup><i>d</i>, <i>f</i></sup>			
			326	694 <sup>d</sup> • <sup>g</sup>			



Table V Hammett ρ Data for the Basic Methanolysis of Ar<sub>1</sub>CONRAr<sub>2</sub> in Methanol

Series	Ar <sub>1</sub>	Ar2	R	. •1	°2	Temp, K	Ref
a	Ph	V <sup>a</sup>	Me		2.83	373	3, b
b	$\mathbf{P}\mathbf{h}$	V	н		2.95	373	b
с	V	Ph	Me	1.76		373	3
d	V	$4'-NO_2C_6H_4$	$\mathbf{Me}$	1.73		339	3
е	v	$4'-NO_2C_6H_4$	Н	1.88		333	11
a V =	= vario	us substituents.	<sup>b</sup> This	work.			

the effective  $\sigma$  value for the 4'-nitro substituent is temperature dependent, if the 3'-nitro and 3',5'-dinitro points are taken as defining the correlation line. In addition, though differences are small, the opposite trend in  $\sigma$  values for the 4'-nitro substituent in NH and N-methyl series is probably real and might not be expected if the two sets reacted via very similar rate-determining transition states. The evidence to date on anilide hydrolysis<sup>4,17</sup> suggests that, for N-methyl-4'-nitro compounds, breakdown of the intermediate to products or reactants is about equally likely, i.e.,  $k_2/k_{-1} \sim 1$ . This means that there is no one clearly ratedetermining step. In this complicated situation, minimal deviation from the Hammett plot might be reasonable. In other words, the Hammett treatment is not sensitive enough in this case to pick up the mechanistic change.

The lack of curvature or change of slope in the Hammett plots in the N-methyl series is explicable if meta and para compounds are considered separately. This requires thinking in terms of the dual parameter Hammett equation<sup>18</sup> (eq

$$\log k_2 / k_2^0 = \rho_{\mathbf{I}} \sigma_{\mathbf{I}} + \rho_{\mathbf{R}} \sigma_{\mathbf{R}}$$
(3)

3) where the blend of resonance and inductive effects can be different for meta and para substituents.

The  $k_2$  step in mechanism C (transition state 3, with developing charge on the nitrogen) would be powerfully aided by strong resonance-withdrawing substituents in the para position. Thus,  $\rho_{\rm R}$  would be greater for a para series than for a meta one. Of the compounds measured to date in the *N*-methyl series, it may well be that only in the case of the strongest para withdrawing substituent is the stabilization sufficient to make this step so fast that formation of 1 (mechanism A) is rate determining. While  $3',5'-({\rm NO}_2)_2 >$  $4'-{\rm NO}_2$  in total  $\sigma$ , the mechanism for the  $3',5'-({\rm initro}\ com$  $pound\ could\ still\ be\ C\ since\ \rho_{\rm R}$  is relatively small and  $\sigma_{\rm R}$ rather than  $\sigma_{\rm R}^-$  would be applicable.

On the basis of mechanism A operating for N-methyl-4'-nitroanilides (but not the NH analogs), some of the Hammett data for benzanilide reactivity published previously<sup>3</sup> requires reinterpretation to be consistent with this picture.

In Table V are collected the various  $\rho$  values now available for basic benzanilide methanolysis. The first point requiring explanation is why the three  $\rho_1$  values are very similar if series d has a different rate-determining step from the other two.

The observed second-order rate constant for conversion of reactants to products can be expressed as

$$k_{\text{obsd}} = \frac{k_1 k_2}{k_{-1} + k_2} = \frac{k_1}{k_{-1}/k_2 + 1}$$

Now, it is a reasonable assumption that there will be little substituent effect from Ar<sub>1</sub> on the *relative* ease of loss of methoxide or amine from the tetrahedral intermediate, i.e.,  $k_{-1}/k_2$  would be effectively constant. Thus, for c and e, while the rate-determining step is breakdown of 1 to prod-

ucts, the effect of a substituent on  $k_{obsd}$  is essentially governed by its effect on  $k_1$ , the rate of formation of 1. It is therefore not inconsistent that for series d, where the ratedetermining step is formation of 1, the  $\rho$  value is very similar to that for the other two series.

In the previous paper,<sup>3</sup> the analogy of the hydrolysis of Ar<sub>1</sub>COOEt and CH<sub>3</sub>COOAr<sub>2</sub> was used to illustrate that, for rate-determining bond formation, substituent effects in the acyl aryl ring are more pronounced and  $\rho_1 > \rho_2$ . This analogy is wrong since it cannot apply where substituent effects in various series are mainly on different steps. The anilide  $\rho_1$  values all represent a substituent effect essentially only on the formation of 1, while the  $\rho_2$  values arise from a presumably smaller substituent effect on  $k_1$  together with a substantial additional effect on the breakdown of 1 to products. This occurs because the partitioning ratio  $(k_{-1}/k_2)$  will be markedly affected by substituents in Ar<sub>2</sub>. Thus  $\rho_1 < \rho_2$  is compatible with the proposed mechanisms.

The Hammett  $\rho$  data are therefore not inconsistent with the following mechanistic summary: series d and the compound PhCONMeC<sub>6</sub>H<sub>4</sub>NO<sub>2</sub>-4' react via rate-determining formation of 1; all other benzanilides studied to date react via rate-determining decomposition of 1 to products.

The Origin of the Special Effect. The unique effect in the N-methyl-4'-nitroanilides must involve contributions from both the N-methyl (to distinguish from NH behavior) and 4'-nitro (to distinguish from 3'-nitro behavior) groups, i.e., a combination of steric and electronic effects, and we tentatively offer the following explanation.

In anilides, steric effects cause twisting of the aromatic ring out of the amide plane, especially in N-alkylanilides.<sup>19</sup> This twisting is minimized when the aromatic ring contains a para withdrawing substituent. In intermediate 1, conjugation between the nitrogen lone pair and a 4'-nitro substituent will be more important than in the amide itself and one can envisage the aromatic ring coplanar with the nitrogen  $\sigma$  bonds as being the most stable configuration in the intermediate from the electronic point of view. This configuration would be retained during C–N bond cleavage. However, planarity in this part of the molecule increases steric interactions which, in the N-methyl case, cannot be removed by rotation about the C–N bond (5  $\rightarrow$  7).



In a *m*-nitro compound, the equivalent to 6 would not be important since there is no through conjugation to produce planarity, while in an NH compound the equivalent of 7 would not be a source of strong interaction. The *N*-methyl system can apparently gain more relief from this situation by loss of amine to give products than by loss of methoxide to revert to reactants, relative to the analogous NH compound.

It is clear from the total results available at this stage that the detailed mechanism by which an anilide can undergo basic methanolysis (and no doubt hydrolysis) is affected by many structural features in the anilide, and probably by the solvent in some cases.<sup>31</sup> The system is obviously finely balanced and provides a fascinating field for investigating the subtle effects of structural changes on mechanism.

### **Experimental Section**

Amines. 3,5-Dinitroaniline, mp 159° (lit.<sup>20</sup> mp 162–163°), and N-methyl-3',5'-dinitroaniline, mp 160° (lit.<sup>21</sup> mp 158–159°), were prepared by literature methods. Nitration of N-methylaniline at <10° with concentrated sulfuric-nitric acids gave N-methyl-3-nitroaniline, mp 64° (lit.<sup>20</sup> mp 68°). Chlorosulfonation of acetanilide,<sup>22</sup> followed by reduction to the sulfinic acid with sodium sulfite<sup>23</sup> and methylation with methyl iodide,<sup>24</sup> gave 4'-methylsulfonylacetanilide. Hydrolysis gave 4'-methylsulfonylaniline.

3-Chloro-5-nitroaniline. A solution of sodium nitrite (4.2 g) in water (5 ml) was added dropwise, with stirring, to a suspension of 3,5-dinitroaniline (10 g) in 20% fluoroboric acid (100 ml) at 0°. The mixture was stirred for 15 min and the precipitated diazonium salt was filtered and washed with fluoroboric acid, ethanol, and ether. Cuprous chloride [prepared from cupric sulfate (25 g), sodium chloride (6.5 g), sodium metabisulfite (5 g), sodium hydroxide (3.5 g), and water (120 ml)] was dissolved in 5 M hydrochloric acid (50 ml). The diazonium salt in 5 M hydrochloric acid (20 ml) was added to this solution with stirring at 0°. Vigorous gas evolution occurred. Water (200 ml) was added, the mixture was heated at 80° for 10 min, and the 1-chloro-3,5-dinitrobenzene, mp 53° (lit.25 mp 55°), was isolated by steam distillation. Reduction of this compound with aqueous sodium sulfide<sup>26</sup> gave 3-chloro-5-nitroaniline, mp 132° (lit.<sup>27</sup> mp 133–136°), after column chromatography (silica gel-1:1 chloroform-light petroleum).

Acetanilides. 3'-Nitro-, mp 152° (lit.20 mp 155°); 3',5'-dinitro-, mp 188° (lit.<sup>28</sup> mp 191°); N-methyl-3',5'-dinitro-, mp 133-134° (EtOH) (Anal. Calcd for  $C_9H_9N_3O_5$ : C, 45.2; H, 3.8; N, 17.6. Found: C, 45.2; H, 3.7; N, 17.9); 3'-chloro-5'-nitro-, mp 173-174° (after chromatography on alumina-1:1 chloroform-light petroleum) (lit.<sup>29</sup> mp 175°); and N-methyl-3'-nitro-, mp 93-95° (lit.<sup>20</sup> mp 95°), acetanilides were prepared from the appropriate amine by standard treatment with acetic anhydride-acetic acid.

Benzanilides. The appropriate amine was treated with benzoyl chloride in acetone (A), pyridine (B), or under Schotten-Baumann conditions (C). The following benzanilides were prepared: 3',5'dinitro-, (A), mp 254–256° (Anal. Calcd for  $C_{13}H_9N_3O_5$ : C, 54.4; H, 3.1; N, 14.6. Found: C, 54.4; H, 3.35; N, 14.8); 4'-nitro-, (A), mp 200-201° (lit.<sup>20</sup> mp 199°); 4'-methylsulfonyl-, (A), mp 208-209° (Anal. Calcd for  $C_{14}H_{13}NO_3S$ : C, 61.1; H, 4.7; N, 5.1; S, 11.6. Found: C, 61.3; H, 5.1; N, 5.3; S, 11.4); N-methyl-3',5'-dinitro- (B), mp 126° (lit.<sup>21</sup> mp 124–125°); 4'-acetyl- (C), mp 201–202° (lit.<sup>30</sup> mp 204–206°); 3'-chloro- (C), mp 122° (lit.<sup>20</sup> mp 122°); 3'-nitro-(C), mp 155–156° (lit.<sup>20</sup> mp 157°).

Rate Measurements. These were carried out as described previously.3 In the few cases where ionization of the anilide was significant (noted in Tables I and III) the data were treated by a known method.11

Solubilities.<sup>14</sup> Saturated solutions were analyzed spectrophotometrically.

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