Energetics of Carbonyl Addition and Elimination. Kinetic Manifestations of Acyl Substituent Effects in Anilide Hydrolysis[1]

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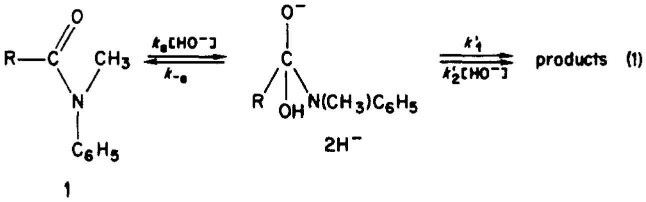
A variation in the acyl substituent R seems to produce very deep-seated kinetic effects in the basic hydrolysis of $RCON(CH_3)C_6H_5$. For R = CF_3, the major rate-limiting process in the range of hydroxide concentrations $\sim 10^{-3}$ to $\sim 10^{-1}$ M changes from (a) rate-limiting water-catalyzed leaving-group elimination from the tetrahedral intermediate at low base to (b) hydroxide-catalyzed elimination and then to (c) rate-limiting addition of hydroxide to substrate carbonyl at high base. For the same range of hydroxide concentrations, other R groups show more restricted kinetics. For R = CCl_3, only hydroxide addition can be observed, with elimination being apparently rapid. For R = $CHCl_2$, only the two elimination processes are kinetically significant, with addition being rapid. For R = CH_2Cl, addition and hydroxide-catalyzed elimination are kinetically significant but water-catalyzed elimination is unobservable. Construction of approximate free energy relationships based on the observable rate constants, and interpolation or extrapolation to unobserved values, leads to a simple and rational model for this behavior, in terms of electronic and steric effects.

Anilides 1 undergo hydrolysis in basic solution by initial addition of hydroxide to generate the tetrahedral adduct $2H^-$, with subsequent elimination occuring in parallel water-catalyzed, hydroxide-catalyzed, and general acid–base catalyzed processes.[2-5] In unbuffered solution, the reaction proceeds as in eq 1 with the steady-state kinetic



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$2H^-$

law shown in eq 2, where $k_1 = k_a k_1'/k_{-a}$; $k_2 = k_a k_2'/k_{-a}$. All three processes are kinetically significant for the highly

$$k_0 = k_a[HO^-](k_1 + k_2[HO^-])/(k_a + k_1 + k_2[HO^-]) \qquad (2)$$

reactive trifluoroacetyl substrates (**1**, R = CF_3), and the kinetic law of eq 2 is based principally on experimental evidence from these compounds.[6] In this paper we report results with three other acyl substituents: R = CCl_3, $CHCl_2$, and CH_2Cl.

Results

Kinetics. The observed rate constants at various base concentrations and at various temperatures for the three substrates examined are available as supplementary material. None of the data sets can be satisfactorily fit to eq 2 to produce positive values of k_a, k_1, and k_2 with acceptable standard deviations. Most give small intercepts k_w at $[HO^-] = 0$, but even when k_0 is corrected to $k_0 - k_w$, eq 2 is still not required in its full form. Rather, restricted versions of eq 2 describe the data.

For example, plots of k_0 vs. $[HO^-]$ for R = CCl_3 are linear; thus either k_a or k_1 or both are kinetically significant but k_2 is not. We believe the second-order rate constant obtained from these linear plots is k_a, as we discuss below.

Table I. Rate Constants from Fitting of k_0 for Hydrolysis of $RCON(CH_3)C_6H_5$ to Equations 3, 4, and 5

		rate constants (s^{-1} for k_w,[b] M^{-1} s^{-1} for k_a and k_1, M^{-2} s^{-1} for k_2), SD (μ = 0.1, KCl)				
temp,[a] °C	solvent	10^6k_w[b]	10^5k_a	10^4k_1	10^3k_2	10^2k_a
		R = CCl_3				
25	H_2O					49, 1
25	D_2O					60, 1
30	H_2O					66, 1
35	H_2O					95, 2
40	H_2O					108, 3
		R = $CHCl_2$				
27	H_2O	33.3		35, 2	97, 2	
25	D_2O	16.7		21, 1	92, 1	
35	H_2O	66.7		41, 3	128, 3	
45	H_2O	100.0		68, 5	170, 4	
		R = CH_2Cl				
27	H_2O	8.3	150, 3		66, 4	
25	D_2O	4.2	111, 4		51, 1	
35	H_2O	15.0	211, 2		134, 7	
45	H_2O	20.0	317, 4		358, 32	
50	H_2O	26.7	392, 4		507, 44	

[a] Reliable to 0.1 °C. [b] Values were zero for R = CCl_3; otherwise these were read from plots of k_0 vs. $[HO^-]$ and treated as constants.

Plots of $(k_0 - k_w)$ vs. $[HO^-]$ are nonlinear for R = $CHCl_2$ but not in the full sense implied by eq 2. Instead, they are quadratic and plots of $([k_0 - k_w]/[HO^-])$ vs. $[HO^-]$ are linear with non-zero intercept. This shows that only the k_1 and k_2 processes are kinetically significant here.

Finally, $(k_0 - k_w)$ vs. $[HO^-]$ is also nonlinear when R = CH_2Cl but again not in the full sense of eq 2. The reaction is second order in $[HO^-]$ at low base concentrations but the order falls toward first at higher concentrations. A plot of $([HO^-]/[k_0 - k_w])$ is now linear in $(1/[HO^-])$. Therefore here the kinetically significant processes are the k_a and k_2 steps.

Rate constants were determined by general least-squares[7] fitting to the simplified kinetic laws of eq 3–5, where k_w represents the apparent solvent-catalyzed reaction and is not well-determined. The results are shown in Table I. Although we have not illustrated the fit of the

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[1] This research was supported by the National Institutes of Health and the National Science Foundation.

[2] Talbot, R. J. E. *Compr. Chem. Kin.* **1972**, *10*, 287.

[3] Kershner, L. D.; Schowen, R. L. *J. Am. Chem. Soc.* **1971**, *93*, 2014.

[4] Drake, D.; Schowen, R. L.; Jayaraman, H. J. *J. Am. Chem. Soc.* **1973**, *95*, 454.

[5] Eriksson, S. D. *Acta. Pharm. Suec.* **1969**, *6*, 139. De Wolfe, R. E.; Newcomb, R. C. *J. Org. Chem.* **1971**, *36*, 3870.

[6] Schowen, R. L.; Jayaraman, H.; Kershner, L. D. *J. Am. Chem. Soc.* **1966**, *88*, 3373.

[7] Program PAR, BMDP-81, University of California Press, Berkeley and Los Angeles, 1981.

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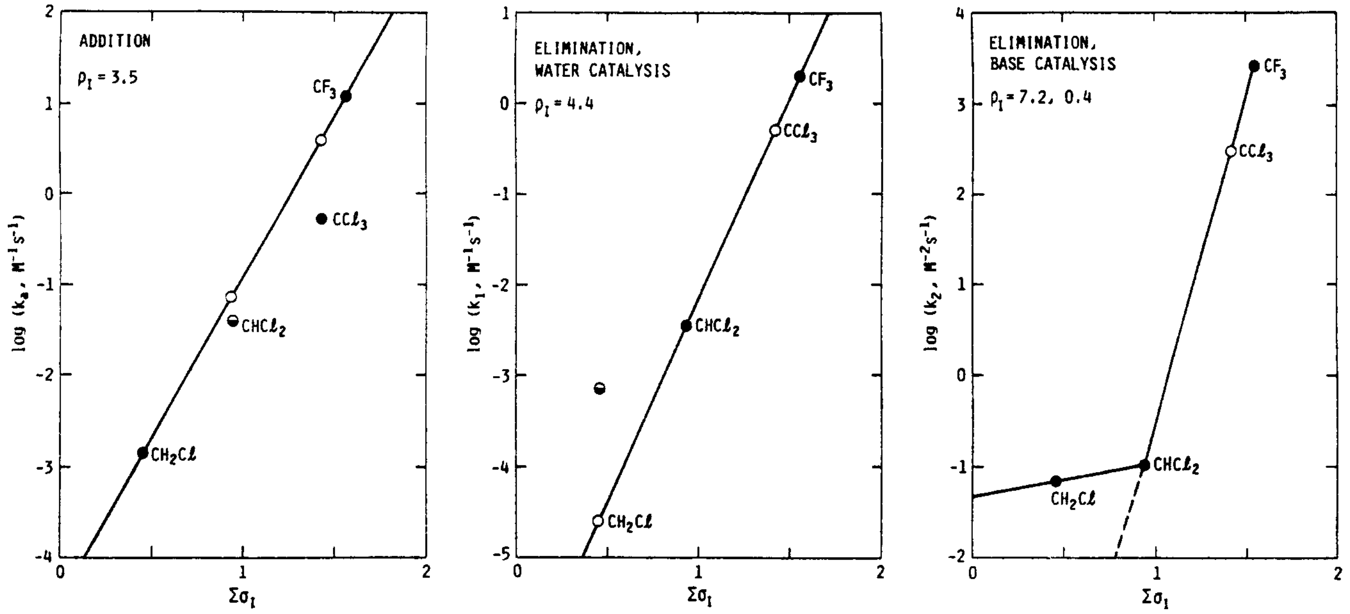

Figure 1. Hypothetical free energy relationships for (a) addition, k_a; (b) water-catalyzed elimination, k_1; and (c) hydroxide-catalyzed elimination, k_2. The filled circles are experimental values. The half-filled values are experimental values of low reliability. The open circles are extrapolated or interpolated in accordance with postulates I–III.

Table II. Activation Parameters[a] and Solvent Isotope Effects for Experimentally Available Rate Constants in the Basic Hydrolysis of $RCON(CH_3)C_6H_5$ in Water

R	rate constants	ΔH^*, kcal mol^{-1}	ΔS^*, cal K^{-1} mol^{-1}	k_{HOH}/k_{DOD}
CF_3[b]	k_a	6	-36	0.79 ± 0.05
	k_1	6	-37	2.3 ± 1.7
	k_2	7	-21	1.22 ± 0.06
CCl_3	k_a	10	-28	0.82 ± 0.03
$CHCl_2$	k_1	6	-49	1.62 ± 0.14
	k_2	5	-46	1.06 ± 0.03
CH_2Cl	k_a	7	-47	1.36 ± 0.06
	k_2	17	-8	1.31 ± 0.27

[a] Enthalpies reliable to about 1 kcal mol^{-1}, entropies to about 3 cal K^{-1} mol^{-1}. Standard states 1 M. [b] Activation parameters from ref 6, solvent isotope effects from ref 3.

data to eq 3–5 in graphical form, the reader can evaluate the quality of the fits by examining the standard deviations of the parameters k_a, k_1, and k_2. These are given in Table I and are relatively small in most cases.

$$R = CCl_3\colon\ k_0 = k_w + k_a[HO^-] \tag{3}$$

$$R = CHCl_2\colon\ k_0 = k_w + k_1[HO^-] + k_2[HO^-]^2 \tag{4}$$

$$R = CH_2Cl\colon\ k_0 = k_w + (k_ak_2[HO^-]^2/[k_a + k_2[HO^-]]) \tag{5}$$

Activation Parameters and Solvent Effects. Enthalpies and entropies of activation, along with solvent isotope effects at 25 °C, are shown in Table II; values of ΔH^* and ΔS^* were obtained by least-squares fits to the Eyring equation.

Discussion

These data present, at first glance, a complex and disturbing picture. For four different acyl substituents, we have four different versions of the kinetic law. An analysis by means of free energy relationships, however, leads to a reasonably satisfying semiquantitative resolution of the apparent anomaly. The conclusions thus reached are strengthened by the activation parameters and solvent isotope effects.

Approximate Free Energy Relationships. Figure 1 portrays log k vs. σ_I plots (σ_I taken[8] as 0.47 for Cl and 0.52 for F and assumed additive for polyhalo compounds) for each of the rate constants k_a, k_1, and k_2. None of the plots has more than two experimental points (filled circles) in a linear range, so the construction of the lines shown must be regarded as a part of the mechanistic hypothesis rather than a conclusion from experiment. The open circles shown on the plots represent interpolated or extrapolated estimations of rate constants which could not be experimentally observed. The half-filled circles represent points which can be determined only at 25 °C, where more abundant data are available. They are not of high reliability but can be regarded as guides in interpretation and will be considered in the discussion below.

With three postulates about these free energy relationships, it is possible to generate a coherent model of the kinetic behavior of these compounds. These postulates are as follows.

I. For k_a (Figure 1a) the line shown ($\rho_I = 3.5$) represents the "normal" electronic effect; all the R groups except CCl_3 fit on this line; CCl_3 exhibits a negative deviation of about 10-fold because of a steric effect. An alternative hypothesis, which we will not pursue and which would not alter the general conclusions, is that CF_3 shows a positive deviation (from a *lack* of steric effect) from a line of even smaller ρ_I drawn through the points for CCl_3 and CH_2Cl.

II. For k_1, the line shown ($\rho_I = 4.4$) represents the "normal" electronic effect; steric effects are relatively unimportant and no steric deviations occur.

III. For k_2, the steep line shown ($\rho_I = 7.2$) gives the electronic effect (steric effects assumed unimportant) for the CF_3, CCl_3, and $CHCl_2$ compounds; for the CH_2Cl compound a different mechanism enters, with smaller electronic effect ($\rho_I = 0.4$).

A critique of these postulates is given below. First we show how they account for the kinetic observations. For this purpose, we want a simple way to convey pictorially which of the rate processes of eq 1 dominates the rate in a given range of base concentrations and to what degree

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[8] Hansch, C.; Leo, A. "Substituent Constants for Correlation Analysis in Chemistry and Biology"; Wiley: New York, 1979.

Table III. Calculated[a] and Estimated[b] Values of Rate Constants for the Basic Hydrolysis of $RCON(CH_3)C_6H_5$ in Water at 25 °C

rate constant	R = CF_3[c]	R = CCl_3	R = $CHCl_2$	R = CH_2Cl
k_a, M^{-1} s^{-1}	11	0.5	(0.13)	0.0015
k_1, M^{-1} s^{-1}	2	(0.6)	0.0035	(2.5×10^{-5})
k_2, M^{-2} s^{-1}	2500	(320)	0.10	0.066

[a] Obtained by least-squares fitting to eq 3 (R = CCl_3); eq 4 (R = $CHCl_2$); eq 5 (R = CH_2Cl); uncertainties around 10–20%. [b] In parentheses; estimated from the free energy relationships of Figure 1. [c] Reference 3.

this dominance is exercised. A useful approach is the virtual transition-state, or weighting factor, concept of Stein.[9]

Analysis by Stein's Method. In this approach, we first invert eq 2 to dissect it into a term for addition to substrate carbonyl and a term for elimination from the tetrahedral adduct:

$$(1/k_0) = (1/k_a[HO^-]) + (1/[k_1 + k_2[HO^-]][HO^-]) \quad (6)$$

Multiplying both sides by k_0, we have eq 7. Each of the two terms on the right-hand side of eq 7 is a *weighting*

$$1 = (k_0/k_a[HO^-]) + (k_0/[k_1 + k_2[HO^-]][HO^-]) \quad (7)$$

factor (they sum to unity); the first measures the kinetic significance of the addition step, the second the kinetic significance of the elimination steps. Since elimination proceeds by two parallel pathways, we may further subdivide its weight into contributions from the k_1 process (weight $[k_1/(k_1 + k_2[HO^-])]$) and the k_2 process (weight $[k_2[HO^-]/(k_1 + k_2[HO^-])]$). For each of the kinetic processes, we thus obtain a weighting factor which measures its relative kinetic significance at a given value of $[HO^-]$:

$$w_a = (k_0/k_a[HO^-]) \quad (8a)$$

$$w_1 = k_1k_0/[HO^-][k_1 + k_2[HO^-]]^2 \quad (8b)$$

$$w_2 = k_2k_0/[k_1 + k_2[HO^-]]^2 \quad (8c)$$

Figure 2 exhibits plots of these three weighting factors as functions of log $[HO^-]$. Figure 2a refers to the CF_3 substrate for which all rate constants k_a, k_1, and k_2 are well-known from ref 3. These are given in Table III. The plot accurately portrays the actual situation. At low $[HO^-]$, the elimination routes (w_1 and w_2) dominate slightly and about equally. As $[HO^-]$ increases, both become faster, the w_2 process (second order in $[HO^-]$) more so, so that it temporarily dominates. Then elimination through the w_2 route becomes so fast that addition becomes rate limiting (w_a dominance) and this continues as $[HO^-]$ rises further.

In Figure 2b, a hypothetical circumstance for the CCl_3 compound is considered in which only the electronic effects of acyl substitution are considered. If this were so, the ρ_I values of 3.5 (k_a), 4.4 (k_1), and 7.2 (k_2) would apply exactly. To simulate this, we read off values of the three rate constants, shown as open circles in Figure 1 (k_a = 4 M^{-1} s^{-1}; k_1 and k_2 given in Table III). The corresponding weighting factors are plotted in Figure 2b. The resemblance to Figure 2a is strong, with differences in the expected direction. The chief difference is a more effective competition of k_1 and k_2 against k_a in determining the rate. This is because their ρ_I values are larger (the elimination transition states, particularly the dinegative transition state for k_2, are more greatly destabilized by electron donation) and the elimination steps have become relatively slower.

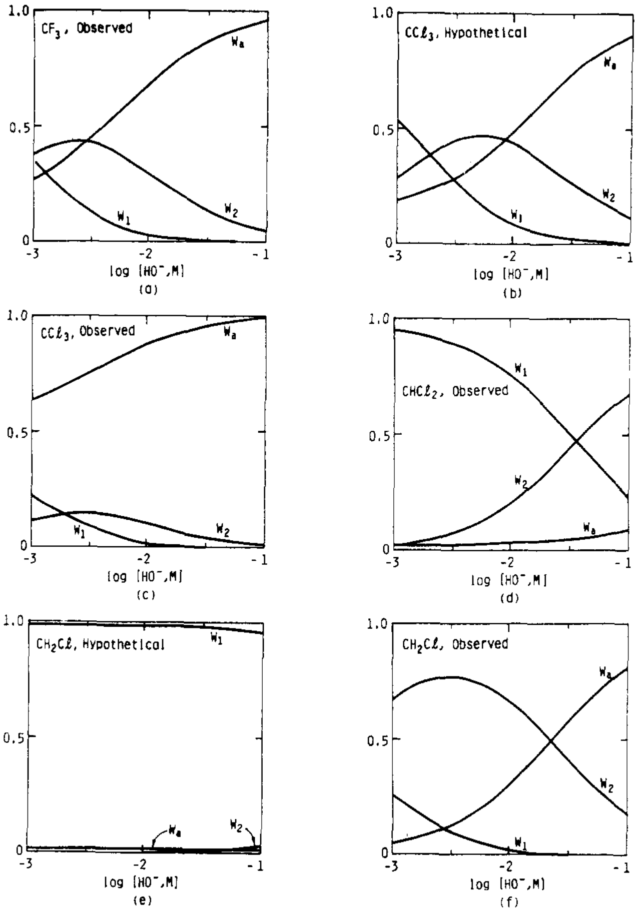

Figure 2. Weighting factors vs. $[HO^-]$ for hypothetical and observed situations with various R groups.

The facts, however, are not in accord with this simple hypothetical picture. For the CCl_3 compound, the value of k_a is not 4 M^{-1} s^{-1} as read from Figure 1a; rather the observed value is 0.5 M^{-1} s^{-1}, about 8-fold slower. We attribute this to a steric effect. If we make no *other* assumption, we can then account for the observations with this compound. Figure 2c shows the weighting factors calculated from the observed k_a and values of k_1 and k_2 taken from the plots of Figures 1b and 1c. It indicates that k_a determines the rate to more than 60% at all $[HO^-]$ and to more than 90% above $[HO^-]$ = 10^{-2} M. Thus the effective rate law is simply that of eq 3.

For the $CHCl_2$ compound, the observed values of k_1 and k_2 lie on the lines drawn in Figures 1b and 1c. Further, the approximate value of k_a obtained at 25 °C only (half-filled circle in Figure 1a) lies very close to the hypothetical line. We therefore introduce no further assumptions and plot Figure 2d. This shows directly that elimination is heavily rate limiting because the larger substituent effects have now slowed elimination substantially compared to addition. Thus the observed rate law of eq 4, with contributions only from k_1 and k_2, is directly accounted for.

Proceeding to the CH_2Cl compound, we find nothing remarkable for k_a (Figure 1a) but a strong positive deviation for k_2 (Figure 1c). If this latter deviation had *not* occurred, k_2 would have been 10^{-5} M^{-2} s^{-1} whereas it is actually 0.066 M^{-2} s^{-1}. In fact, if the deviation had not occurred, the situation would have been as portrayed in Figure 2e, for which k_2 was taken as 10^{-5} M^{-2} s^{-1} and k_a and k_1 as the observed values. This would correspond to the trend of the other compounds having continued, with k_1 now fully rate determining. However, the fact of the

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[9] Stein, R. L. *J. Org. Chem.* 1981, *46*, 3328.

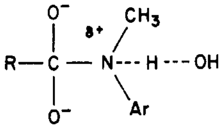
positive deviation produces Figure 2f: the greater value of k_2 means, first, that it takes over from k_1 in parallel competition and, second, that the more rapid elimination now yields to some extent in rate determination to addition: the result is a rate law depending on only k_a and k_2 (eq 5).

The positive deviation of the k_2 point presumably corresponds to a change in mechanism, from a process with $\rho_I = 7.2$ to one with $\rho_I = 0.4$. An acceptable mechanism for $\rho_I = 0.4$ will then have to have far less negative charge near the substituent R in the transition state than the mechanism for $\rho_I = 7.2$. A hypothesis to this effect is considered below.

This completes the rationale of the diversity of kinetic laws observed for various acyl substituents, based on the three postulates given above and reasonable chemical ideas. If this rationale is correct, it entails certain mechanistic conclusions. These are first presented and then a critique of the postulates is given.

Conclusions. The main conclusion from the rationale just presented is that the k_2 process must involve two parallel mechanisms (one for R relatively electron withdrawing, with $\rho_I = 7.2$; one for R relatively electron releasing, with $\rho_I = 0.4$). We have previously postulated[3] that parallel mechanisms are involved in this process with R = CF_3, where the indication of their presence is a nonlinear Hammett plot for substituents X in the leaving-group aryl ring. For relatively electron-releasing X ($\sigma < 0$), $\rho \sim 0.3$; for relatively electron-withdrawing X ($\sigma > 0$), $\rho \sim 2.4$.

Two possibilities for the transition states along these routes are those previously discussed.[3] Structure 3 is for



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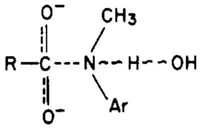

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a rate-limiting proton transfer (R electron withdrawing, X electron releasing: $\rho_I = 7.2$, $\rho = 0.3$). Structure 4 is for C–N bond fission with solvation catalysis[3] by water (catalytic proton not moving in reaction coordinate). It should prevail for R electron releasing, X electron withdrawing ($\rho_I = 0.4$, $\rho = 2.4$).

The observed solvent isotope effects are not in conflict with structures 3 and 4 but do not test strongly for them. The values of k_2^{HOH}/k_2^{DOD} for R = CF_3 and $CHCl_2$ are 1.22 ± 0.06 and 1.06 ± 0.03. The fact that two hydroxide ions are consumed in reaching either 3 or 4 means that these observed values are products of $K_{HOH}/K_{DOD} \sim {}^1/_4$ for formation of the dinegative adduct[3] and k_{HOH}/k_{DOD} for its decomposition. The latter is therefore in the range $k_{HOH}/k_{DOD} \sim 4$–5. This is fully acceptable for 3 and of borderline acceptability for 4. The value of 4–5 involves not only the proton-transfer or solvation-bridge isotope effect but also contributions from solvation of the forming HO^- and other anionic centers. The values of k_a^{HOH}/k_a^{DOD} for R = CF_3 and CCl_3 are, as expected, inverse. This is strong evidence that k_a and not k_1 is the rate constant being measured for R = CCl_3. A somewhat surprising result is the normal value of around 1.4 for R = CH_2Cl.

One would certainly expect that a changeover from 3 to 4 would give rise to a large release of solvating water, with an accompanying rise in both ΔH^* and ΔS^*. Indeed this is observed for k_2 with R = $CHCl_2$ (presumably 3) and CH_2Cl (presumably 4): ΔH^* rises by 12 kcal mol^{-1} and ΔS^* by 38 cal K^{-1} mol^{-1}.

In Figure 1b for the k_1 process, it may be noted that a major discrepancy is that the half-filled circle for CH_2Cl falls far above the line for $\rho_I = 4.4$. This implies that a second mechanism is coming in for the CH_2Cl compound along the k_1 route as well as along the k_2 route. Probably the two transition states involved are protonated versions of 3 and 4.

Critique of the Postulates. The first postulate (steric effect of CCl_3 in k_a reaction) is not in itself remarkable, since carbonyl addition is well-known to be sensitive to steric effects, but it seems difficult to understand why the k_a reaction should be more sensitive to steric effects than the k_1 and k_2 reactions. One relevant point is that the steric effect on carbonyl addition/elimination rates may *not* be maximal when the transition state most resembles the tetrahedral adduct. The steric effect doubtless arises from repulsions between the "test substituent" (R in this case) and the other three ligands on the carbonyl carbon. If we consider the decomposition of a tetrahedral adduct, then the distance from R to the two ligands which remain attached to the carbonyl carbon will increase steadily as the carbonyl–carbon hybridization changes from sp^3 to sp^2. On the other hand, the distance from R to the *leaving group* Z may or may not increase monotonically: this is because the bond to Z is breaking, which tends to increase the R–Z distance, at the same time that the carbonyl ligands are moving into the carbonyl plane, which tends to decrease the R–Z distance. Whether the R–Z distance increases monotonically or instead decreases at first and then increases depends on the "balance" between reaction progress in breaking the C–Z bond and in making the carbonyl group and its substituents coplanar. If these are exactly balanced (dynamically and kinetically coupled[11]) in the sense that the out-of-plane angle of a carbonyl substituent has changed by the same fraction as the bond order of the C–Z bond has changed, then a simple calculation suggests that the R–Z distance increases monotonically.[12] This would indeed place the maximum steric effect of R at the tetrahedral structure. However, if the change in the out-of-plane angle runs ahead of the bond stretching (as its smaller force constant might allow[11]) in the sense the angle has changed by the square of the change in bond order, then the R–Z distance is minimal[12] at a C–Z bond order of about ${}^3/_4$. Steric effects would then be smaller for *either* earlier or later transition states. It is therefore entirely possible that steric effects should be more pronounced in the k_a transition state than in the k_1 and k_2 transition states, regardless of their structure.

That steric effects should be absent or less important for CF_3, $CHCl_2$, and CH_2Cl is reasonable because of the smaller effective size of all of these. The CF bonds are shorter, while the large atoms can be turned away in the other two groups.

The second postulate requires that the substituent R "see" more negative charge in the k_1 than in the k_a transition state. This is consistent with a structure like 3, but

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(10) Bell, R. P. *Adv. Phys. Org. Chem.* **1966**, *4*, 1.

(11) Maggiora, G. M.; Schowen, R. L. In "Bioorganic Chemistry"; van Tamelen, E. E., Ed.; Academic Press: New York, 1977; Vol. 1.

(12) If a tetrahedral adduct with all bonds of equal length R_1 decomposes, the distance from a carbonyl ligand R to the leaving group Z, R_{RZ}, is given by $R_{RZ}{}^2 = R_1{}^2 + R_n{}^2 - 2R_1R_n \cos A$, where R_n is the bond distance for the breaking bond or bond order n and A is the angle between a bond to a ligand and the breaking bond. We take $\rho = R_{RZ}/R_1$ and $n = \exp[(R_1 - R_n)/0.3]$ (Pauling's rule[13]). For "exact balance" between bond-breaking and angle bending, $A = (90°)(1 - n) + (109.5°)(n)$. Then ρ begins at 1.633 ($n = 1$) and increases steadily, with $\rho = 1.694$ at $n = 0.5$, for example. To simulate the angle bending "running ahead", we let $A = (90°)(1 - n)^2 + (109.5°)(n^2)$. Then again $\rho = 1.633$ at $n = 0$ (of course) but now decreases to $\rho = 1.610$ at $n = 0.75$, 0.70, and then rises; $\rho = 1.632$ at $n = 0.50$, $\rho = 1.663$ at $n = 0.40$.

(13) Burton, G. N.; Sims, L. B.; Wilson, J. C.; Fry, A. *J. Am. Chem. Soc.* **1977**, *99*, 3371.

bearing an extra proton: the k_a transition state has a negative ligand only partially attached, while the k_1 transition state has a fully attached negative ligand. As already noted, the half-filled circle for CH_2Cl in Figure 1b indicates weakly that a shift to a transition state resembling 4 (plus a proton) is occurring here; this was not taken into account in postulate II. The main effect of this error would be to change Figure 2f so as to increase the importance of w_1 compared to w_2, while somewhat decreasing the importance of both compared to w_a. Nevertheless, the kinetic law would continue to depend chiefly on the k_a and k_2 processes.[14]

Postulate III has in effect already been defended in terms of structures **3** and **4** for the two k_2 transition states. The main requirement is that they should have, respectively, large and small ρ_I values, and this seems reasonable in terms of their structures, which place more and less negative charge, respectively, near R.

Experimental Section

Materials. Sodium hydroxide (Matheson, Coleman and Bell analytical reagents), potassium hydrogen phthalate (Fisher Chemical Co., dried at 110 °C before use), potassium chloride (Mallinkrodt Analytical Reagent; dried at 110 °C before use), and deuterium oxide (Bio-Rad Laboratories) were used without further purification.

Anilides. The mono-, di-, and trichloro-*N*-methylacetanilides were prepared by first allowing the corresponding acid to react with sulfuryl chloride to form the acid chloride and then treating the latter with *N*-methylaniline in ethyl ether solvent. The precipitated product was recrystallized from an ethanol–water mixture. The melting points of mono-, di-, and trichloro-*N*-methylacetanilide were 67.5–69.0 °C (lit.[15] mp 69 °C), 69.4–70.0 °C (lit.[16] mp 69.9 °C), and 72.0–73.0 °C (lit.[17] mp 72.5–73 °C), respectively.

Kinetics. The hydrolysis reactions were carried out under pseudo-first-order conditions (anilide concentrations typically about 10^{-4} M while the hydroxide ion concentrations varied from 10^{-2}–10^{-1} M) at constant ionic strength (0.1 M in KCl). The reaction was followed by monitoring the production of *N*-methylaniline at 285 nm or at 235 nm, by use of a Beckman DU-2 spectrophotometer equipped with temperature-controlled cell compartments. The pseudo-first-order rate constants were evaluated by the Guggenheim method for each hydroxide ion concentration employed. The kinetic law best describing each set of data was identified by nonlinear least-squares regression analysis.

Registry No. 1 (R = CF_3), 345-81-3; 1 (R = CCl_3), 36558-96-0; 1 (R = $CHCl_2$), 23496-29-9; 1 (R = CH_2Cl), 2620-05-5; DOD, 7789-20-0; D_2, 7782-39-0; HO^-, 14280-30-9.

Supplementary Material Available: Observed rate constants on which Table I is based (5 pages). Ordering information is given on any current masthead page.

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[14] The deviation of the half-filled circle for CH_2Cl above the open circle corresponds to about 40-fold in the value of k_1. In Table III, the ratio of k_2 to k_1 is 2640, so that their contributions are equal at $[HO^-] = {}^1/_{2640} = 3.8 \times 10^{-4}$ M. The corrected ratio is 66, so that the crossover point is now $[HO^-] = 1.5 \times 10^{-2}$ M. At the same time, the relative importance of k_a will be increased. Since the experimental measurements were all at $[HO^-] > 0.027$ M, the dominant terms will remain k_a and k_2.

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Micellar Effects on the Reaction of (Arylsulfonyl)alkyl Arenesulfonates with Hydroxide Ion. 1. Microenvironmental and Substituent Effects in the Stern Layer of Cationic Micelles[1]

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The reaction of the sulfonates p-$XC_6H_4SO_2CH(R)OSO_2C_6H_4Y$-$p$ **1a–g** with hydroxide ion (involving nucleophilic attack at sulfonate sulfur) is accelerated (7–25 times) in the presence of CTAB micelles (32.1 °C). The kinetic data are analyzed in detail by using the pseudophase ion-exchange (PPIE) model, taking into account partitioning of the reactants between the micellar and aqueous pseudophases and competition between hydroxide ions and detergent counterions for binding to the micelles. Binding constants obtained from the kinetic analysis are compared with those from ultrafiltration experiments. Generally, the PPIE model reproduces the experimental rate constants quite well, except at low detergent concentration (around the cmc). The second-order rate constants for reaction in the micellar pseudophase are 4–12 times *smaller* than those for reaction in bulk water. Therefore the observed catalysis is purely the result of the high local concentration of both reactants in the micellar pseudophase. The substituent effects for the reaction in the micelles reveal an increased susceptibility for variation of Y. No evidence for orientational effects was found. It is shown that the binding of the sulfonates with the micelles is mainly determined by the presence of the aryl groups. Based on a comparison with kinetic solvent effects on the reaction in 1,4-dioxane–water, it is suggested that the rates in the micellar pseudophase reflect a decrease in micropolarity at the binding sites of the substrate molecules.

Bimolecular micellar-catalyzed processes have been the subject of intensive research during the last 2 decades.[2] It is now firmly established that the bringing together or the separation of the reagents by the micelle are the dominant factors in the micellar rate effects. Several kinetic treatments have been advanced to rationalize the micellar rate effects, including the enzyme,[3] cooperativity,[4] pseudophase,[5] and the pseudophase ion-exchange (PPIE)[6]

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