References and Notes

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Acid-Catalyzed Hydrolysis of *N*-Vinylacetamides (Enamides). Substituent Effects of the Acetamido and Amino Groups and Linear Free Energy Correlations of Cyclohexene Reactivities

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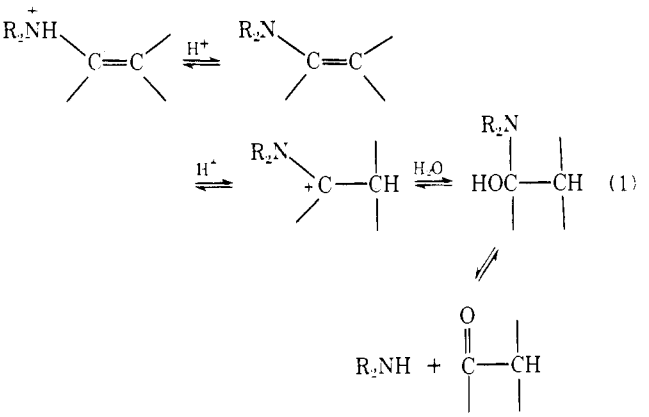
Abstract: The rates of acid-catalyzed hydration of *N*-vinylacetamide (**1**), *N*-(2-propenyl)acetamide (**2**), *N*-(1-phenylvinyl)-acetamide (**3**), and *N*-(1-cyclohexenyl)acetamide (**4**) have been measured. These compounds react through rate-limiting protonation on carbon (the $A_{SE}2$ mechanism) as evidenced by the observation of general acid catalysis for **2**, the solvent isotope effect $k_{H_3O^+}/k_{D_3O^+}$ for **1**, **3**, and **4**, and the correlation of the reactivity of **1**–**3** with the substituent effect-rate correlation established for this mechanism. A contrary mechanism previously proposed for 2-arylenamides is not substantiated. A new linear free energy correlation of the rates of hydration of 1-substituted cyclohexenes is established and also supports the $A_{SE}2$ mechanism for **4**. A σ_p^+ of −0.65 for the acetamido substituent is most compatible with these hydration results and data on various chemical processes available in the literature. Hydration rates of *p*-acetamidostyrene (**5**) and *p*-acetamido-α-methylstyrene (**6**) define a value of σ_p^+ for acetamido of −0.33 applicable to substituted styrenes. Literature data for the effect of amino substituents on the hydration of alkenes and styrenes are also analyzed and all of the data are satisfactorily accommodated by our previously proposed relationship $\log k_2 = -10.5\Sigma\sigma_p^+ - 8.92$. Over 110 compounds spanning 23 powers of ten in reactivity are included, with only modest curvature suggesting minimal saturation of the substituent effects.

The amide function is arguably the most important group for the linking of different organic subunits, so it is not surprising that the hydrolysis of amides has been a topic of continuing interest in a number of different laboratories.[1] Similarly the *N*-vinylamines (enamines) are of great practical use in organic synthesis,[2] and the mechanism of their hydrolysis has been studied in some detail.

In aqueous solution enamines have been found to react by the scheme shown in eq 1.[3] General-acid-catalyzed protonation on carbon is rate limiting near pH 10 but in more acidic solution protonation is very fast and decomposition of the intermediate immonium ion or carbinolamine becomes rate determining.[3b] The hydration of *p*-aminostyrene in aqueous acid at 80 °C has also been studied.[4] This compound is in equilibrium with the anilinium ion in acid, and below 5 M $HClO_4$ undergoes hydration by rate-determining protonation on carbon of the free amine, whereas in more acidic media protonation of the anilinium ion is rate limiting (eq 2).



(1)

We have been engaged in a study of substituent effects on electrophilic reactions of alkenes, especially acid-catalyzed hydrations.[5] This effort has been highly informative as to the nature of both the interactions of the substituents and the mechanisms of electrophilic additions. Together with studies in other laboratories our efforts have established the $A_{SE}2$ mechanism of rate-limiting protonation on carbon (eq 3) for practically all acid-catalyzed alkene hydrations which have

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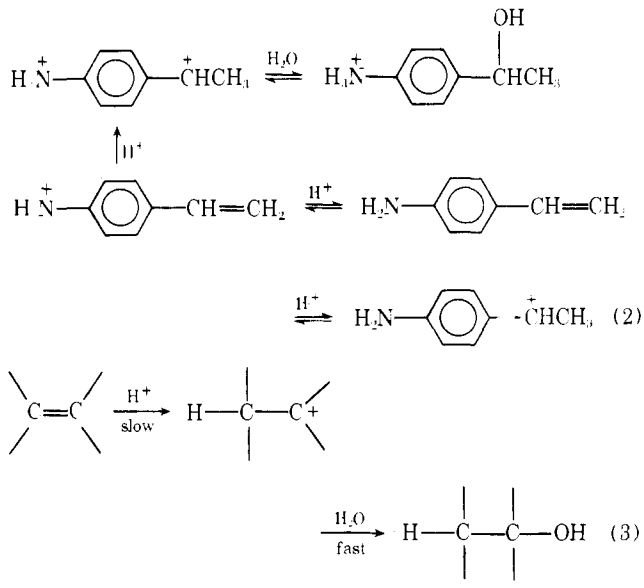


(2)

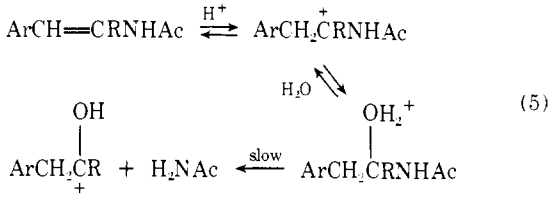
(3)

been studied. Most recently we have examined[5f] styrenes substituted with the extremely strongly electron withdrawing group CF_3, and some of these compounds were less reactive than ethylene itself. Nevertheless all of the rates were adequately correlated by eq 4

$$\log k_2 = -10.5\Sigma\sigma_p^+ - 8.92 \quad (4)$$

which has been previously established to correlate the rates of reactions proceeding by eq 3.[5]

N-Vinylamides (enamides) possess the interesting C=C–N–C=O structural unit and have become increasingly important synthetic intermediates.[6,7] A study has appeared on the reactivity in acid-catalyzed hydrolysis of 2-arylacetamidoalkenes,[8] but in contrast to the mechanism established[5] for other alkenes it was proposed that these compounds react by equilibrium protonation on carbon and hydration followed by rate-limiting dissociation to the protonated ketone (eq 5).



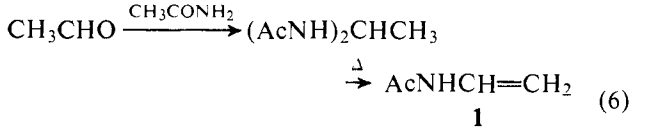
(5)

Despite strenuous efforts to observe such changes in mechanism in alkene hydrations,[9a] this phenomenon is rarely observed.[3,9b]

Because of the importance of the enamide function and the interesting mechanistic possibilities implicit in its hydrolysis we have undertaken a study of the reactivity of this group. In addition the existing knowledge on the influence of amino groups on alkene protonations has been critically reexamined, and the results have been used as a test of the value of eq 4 as a guide to mechanistic interpretations.

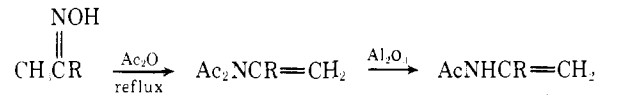
Results

N-Vinylacetamide (**1**) was prepared by the reported[7a] pyrolysis of 1,1-diacetamidoethane obtained from acetaldehyde and acetamide (eq 6). *N*-(2-Propenyl)acetamide (**2**),[7b] *N*-

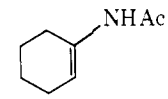


(6)

(1-phenylvinyl)acetamide (**3**),[7c] and *N*-(1-cyclohexenyl)-acetamide (**4**)[7b] were prepared by the treatment of the corresponding oximes with refluxing acetic anhydride to give the *N*,*N*-diacetylaminoalkenes as reported by Barton et al.[7d] These were converted to the *N*-alkenylacetamides by chromatography on alumina,[7d]



2 (R = Me), **3** (R = Ph)



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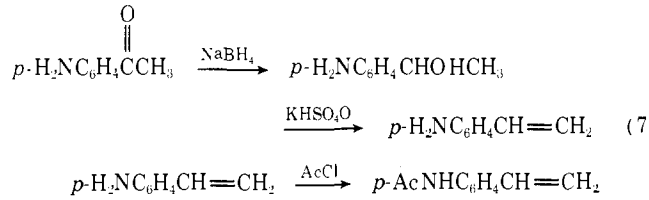
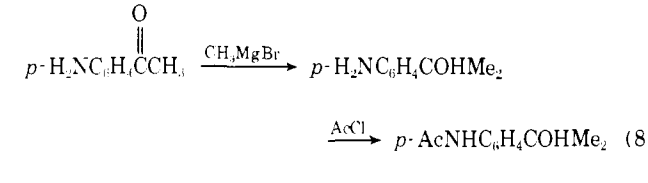
p-Acetamidostyrene (**5**)[10a,b] was prepared by acetylation of *p*-aminostyrene, which was obtained from *p*-aminoacetophenone by reduction and dehydration (eq 7). *p*-Acetamido-



(7)

5

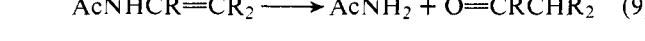
α-methylstyrene (**6**)[10c] was obtained by dehydration of *p*-acetamidocumyl alcohol prepared from *p*-aminoacetophenone by treatment with methylmagnesium bromide and then acetylation (eq 8).



(8)

6

The enamides showed strong UV maxima between 225 and 245 nm and their rates of acid-catalyzed hydrolysis in aqueous acid were conveniently monitored by observing the change of this alkene chromophore. These alkenes showed excellent first-order kinetics with complete disappearance of the alkene absorption. Enamides are known to undergo hydrolysis to acetamide and carbonyl compounds (eq 9)[7b,8] and this was

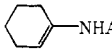


(9)

confirmed in the present investigation in the case of **1** and **3**. The hydrolyses of **1**, **3**, and **4** were monitored in dilute H_2SO_4 and the rates were correlated with the H_0 acidity function for this medium. These data are summarized in Table I. For rate studies on **2** acetic acid buffers were used. The compound showed both specific and general acid catalysis. The rate date for **2** are summarized in Table II.

Rates of hydration of the *p*-acetamidostyrenes were observed by the disappearance of the styrene chromophores by UV spectroscopy. The absorbance decreased to less than 5% of the original value indicating that the hydration was essentially complete. Good first-order rate behavior was observed in all cases. However, for *p*-acetamidostyrene the slopes of log k_{obsd} vs. the acidity function H_0 were −0.73 in $HClO_4$ and −0.84 in H_2SO_4. The magnitude of these slopes is much less than the normally observed values for hydration of styrenes in acid (−1.0 to −1.3).[5f,11-14] The origin of this effect is evidently the competitive equilibrium protonation of this styrene

Table I. Rates of Hydration of *N*-Vinylamides in Aqueous Sulfuric Acid at 25 °C

amide	$[H_2SO_4]$, M[a]	H_0[b]	k_{obsd}, s^{-1}
 4	0.0117	1.73	2.97×10^{-3}
	0.005 25	2.05	1.44×10^{-3}
	0.004 67	2.09	1.235×10^{-3}
	0.003 50	2.21	9.71×10^{-4}
	0.002 33	2.36	6.29×10^{-4}
	0.001 17	2.67	3.27×10^{-4}
	0.007 06[d]		5.35×10^{-4}
	0.007 06[e]	1.93	1.85×10^{-3}
$AcNHCH{=}CH_2$[f] **1**	0.0117	1.73	7.65×10^{-4}
	0.004 67	2.09	3.43×10^{-4}
	0.001 17	2.67	8.08×10^{-5}
	0.0156[d]		2.76×10^{-4}
	0.0156[e]	1.61	1.04×10^{-3}
$AcNHCPh{=}CH_2$[g] **3**	0.105	0.92	3.17×10^{-2}
	0.0117	1.73	3.50×10^{-3}
	0.005 25[h]	2.05	1.65×10^{-3}
	0.001 17	2.67	3.59×10^{-4}
	0.0132[d]		1.02×10^{-3}
	0.0132[e]	1.67	4.43×10^{-3}

[a] Concentration determined by titration. [b] K. N. Bascombe and R. P. Bell, *J. Chem. Soc.*, 1096 (1959). [c] Log $k = -1.03H_0 - 0.74$ ($r = 0.999$), $k_2 = 0.181\ M^{-1}\ s^{-1}$; $k_{H^+}/k_{D^+} = 3.46$. [d] D_2SO_4. [e] Interpolated for H_2SO_4 from the plot of log k vs. H_0. [f] Log $k = -1.04H_0 - 1.30$ ($r = 1.000$), $k_2 = 0.500 \times 10^{-1}\ M^{-1}\ s^{-1}$; $k_{H^+}/k_{D^+} = 3.77$. [g] Log $k = -1.11H_0 - 0.50$ ($r = 0.999$), $k_2 = 0.318\ M^{-1}\ s^{-1}$; $k_{H^+}/k_{D^+} = 4.34$. [h] One run only at this acidity.

Table II. Hydrolysis of $AcNHCMe{=}CH_2$ in HOAc-NaOAc Buffers at 25 °C[a,b]

pH	[HOAc], M	[HOAc]/[NaOAc]	k_{obsd}, s^{-1}
3.93	0.0500	5.0	1.86×10^{-3}
4.04	0.0400	4.0	1.53×10^{-3}
4.20	0.0300	3.0	1.17×10^{-3}
4.65	0.002 50	1.0	2.75×10^{-4}
4.65	0.005 00	1.0	3.13×10^{-4}
4.65	0.0100	1.0	3.90×10^{-4}
4.65	0.0200	1.0	5.30×10^{-4}
4.65	0.0300	1.0	6.70×10^{-4}
4.95	0.005 00	0.5	1.94×10^{-4}

[a] Ionic strength kept at 0.1 M with NaCl; reported rates are averages of duplicate runs. [b] At pH 4.65 $k_{obsd} = k_{H^+}[H^+] + k_{HOAc}[HOAc]$, $k_{H^+} = 10.8\ M^{-1}\ s^{-1}$, and $k_{HOAc} = 1.42 \times 10^{-2}\ M^{-1}\ s^{-1}$.

on nitrogen (eq 10). The basicities of acetanilides in H_2SO_4 have been studied,[15a] and from the observed correlation of

$$p\text{-}Ac\overset{+}{N}H_2C_6H_4CH{=}CH_2 \underset{H^+}{\overset{K_{eq}}{\rightleftharpoons}} \underset{\mathbf{5}}{p\text{-}AcNHC_6H_4CH{=}CH_2} \xrightarrow{H^+} p\text{-}AcNHC_6H_4\overset{+}{C}HCH_3 \quad (10)$$

pK_{BH^+} of substituted acetanilides with σ parameters and the σ_p value of the vinyl group of −0.02 a pK_{BH^+} of −1.57 may be calculated for *p*-acetamidostyrene (**5**). Using this value the equilibrium concentrations of **5** at the various acidities used in the hydration measurements were derived and the rate constants k_{hyd} for protonation of the neutral styrene calculated. These values are reported in Table III. The slopes of log k_{hyd} vs. H_0 were −1.20 and −1.22 for H_2SO_4 and $HClO_4$ solutions, respectively, with intercepts of −5.53 and −5.69. The close agreement of both sets of values is reassuring, but it is clear that slopes of H_0 plots should only be used with great caution as a criterion of mechanism.

Table III. Rates of Hydration of *p*-Acetamidostyrenes *p*-$AcNHC_6H_4CR{=}CH_2$ in Aqueous Acids at 25 °C

reactant	[acid], M	H_0	k_{obsd}, s^{-1}	k_{hyd},[a] s^{-1}
5 (R = H)[b,c] in $HClO_4$	8.10	−4.32	1.00×10^{-2}	0.408
	6.98	−3.47	2.41×10^{-3}	3.57×10^{-2}
	5.58	−2.65	6.98×10^{-4}	3.47×10^{-3}
	4.40	−1.99	1.94×10^{-4}	4.95×10^{-4}
	3.73	−1.67	1.21×10^{-4}	2.31×10^{-4}
	3.23	−1.43	7.87×10^{-5}	1.27×10^{-4}
5 (R = H)[d,e] in H_2SO_4	6.04	−2.77	1.29×10^{-3}	6.79×10^{-3}
	4.90	−2.25	5.00×10^{-4}	1.52×10^{-3}
	4.03	−1.86	2.08×10^{-4}	4.31×10^{-4}
	3.65	−1.69	1.38×10^{-4}	2.50×10^{-4}
	3.03	−1.39	8.82×10^{-5}	1.30×10^{-4}
	2.58	−1.17	6.32×10^{-5}	8.38×10^{-5}
	2.39	−1.06	4.76×10^{-5}	6.05×10^{-5}
6 (R = Me)[f] in H_2SO_4	1.58	−0.66	5.27×10^{-3}	
	1.35	−0.54	3.92×10^{-3}	
	1.10	−0.36	2.44×10^{-3}	
	0.887	−0.23	1.55×10^{-3}	
	0.619	0.01	8.86×10^{-4}	

[a] $k_{hyd} = k_{obsd}([B] + [BH^+])[B]^{-1}$, where [B] is the concentration of free acetamide and $[BH^+]$ is the concentration of protonated acetamide. [b] Log $k_{hyd} = -1.22H_0 - 5.69$ ($r = 1.000$), $k_2 = 0.206 \times 10^{-5}$. [c] Log $k_{obsd} = -0.73H_0 - 5.14$ ($r = 0.999$). [d] Log $k_{hyd} = -1.20H_0 - 5.53$ ($r = 0.997$), $k_2 = 0.293 \times 10^{-5}$. [e] Log $k_{obsd} = -0.84H_0 - 5.22$ ($r = 0.998$). [f] Log $k_{obsd} = -1.18H_0 - 3.05$ ($r = 1.000$), $k_2 = 0.887 \times 10^{-3}$.

The extraction of the rate constants k_{hyd} for **5** from the observed rates is strictly analogous to the procedure used by Schubert and Jensen[4a] for *p*-amino- and *p*-dimethylaminostyrene. These authors also provide a detailed discussion of the interrelation of the medium dependence of the activity coefficients and the acidity functions in systems of this type.

The potential complication of competitive amide hydrolysis and alkene hydration does not interfere under our conditions. Acetanilide[15b] and acetanilides comparably substituted to **5**[15c] are known to undergo amide hydrolysis at rates rather lower than the hydration rate of **5** at comparable acidities.

Discussion

Assignment of the mechanism of alkene hydration as rate-determining protonation on carbon (the $A_{SE}2$ mechanism) normally depends[11-14,16-18] on the criteria of a linear dependence of log k on H_0, solvent isotope effects $k_{H_3O^+}/k_{D_3O^+}$ greater than 1.0, general acid catalysis, and a dependence of rate on the substituent parameters σ_p^+ of the groups R in $R_1R_2C{=}CH_2$ indicated by eq 4.[5] In the present series this route (eq 11) is supported by the rate dependence on acidity

$$AcNHCR{=}CH_2 \xrightarrow[\text{slow}]{H^+} AcNH\overset{+}{C}RCH_3 \xrightarrow{H_2O} AcNHC(^+OH_2)RCH_3 \quad (11)$$
$$\downarrow$$
$$AcNH_2 + O{=}CRCH_3$$

for **1**-**4**, the values of $k_{H_3O^+}/k_{D_3O^+}$ of 3.8, 4.3, and 3.5 for **1**, **3**, and **4**, respectively, and the observation of general acid catalysis for **2**.

In order to test the correlation of these reactions by eq 4 a suitable σ_p^+ parameter for the acetamido (AcNH) group must be defined. A number of values reported for this parameter are summarized in Table IV, including for comparison the values obtained by using the rates observed in this investigation by eq 4. The most reliable values are assumed to be the two aromatic halogenation values (−0.76 and −0.64), the IR value

Table IV. σ_p^+ Constants for the AcNH Group

reaction (X = AcNH)	σ_p^+
hydration $XC_6H_4CH{=}CH_2$, $HClO_4$[a]	−0.35
hydration $XC_6H_4CH{=}CH_2$, H_2SO_4[b]	−0.30
hydration $XC_6H_4CMe{=}CH_2$, H_2SO_4[c]	−0.35
hydration $XCR{=}CH_2$[d,e]	−0.66
hydration 1-cyclohexenyl-X[e]	−0.58
bromination, ArX[f]	−0.76
IR of $XC_6H_4COCH_3$[g]	−0.59
chlorination, ArX[h]	−0.64
calculation[i]	−0.25
charge transfer spectra[j]	−0.60
Ar_3COH ionization[k]	−0.47
ester pyrolysis[l]	−0.62

[a] Reference 13. At 3.53 M $HClO_4$ ($H_0 = -1.57$) $\log k_{obsd} = -3.58\sigma_p^+ - 5.02$ ($r = 0.999$). For AcNH $\log k$ at $H_0 = -1.57$ is interpolated to be −3.994. [b] Reference 14, omitting the point for *m*-NO_2 which seriously deviates from the line; at $H_0 = 0$ $\log k_{obsd} = -2.90\sigma_p^+ - 6.42$ ($r = 0.993$). [c] References 11 and 14a: at 20.2% H_2SO_4 ($H_0 = -1.03$) $\log k_{obsd} = -2.87\sigma_p^+ - 2.85$ ($r = 0.981$). [d] Calculated from $\log k_2 = -10.5\Sigma\sigma_p^+ - 8.92$. Value given is average of those for R = H (**1**), R = Me (**2**), and R = Ph (**3**), of −0.73, −0.64, and −0.62, respectively. [e] This work. [f] Reference 19b. [g] T. G. Traylor and J. C. Ware, *J. Am. Chem. Soc.*, **89**, 2304 (1967). [h] P. B. D. de la Mare and M. Hassan, *J. Chem. Soc.*, 1519 (1958); P. B. D. de la Mare, private communication. [i] C. G. Swain and E. C. Lupton, Jr., *J. Am. Chem. Soc.*, **90**, 4328 (1968). [j] W. Hanstein, H. J. Berwin, and T. G. Traylor, *ibid.*, **92**, 829 (1970). [k] Reference 19a. [l] R. Taylor, *J. Chem. Soc., Perkin Trans. 2*, 755 (1978).

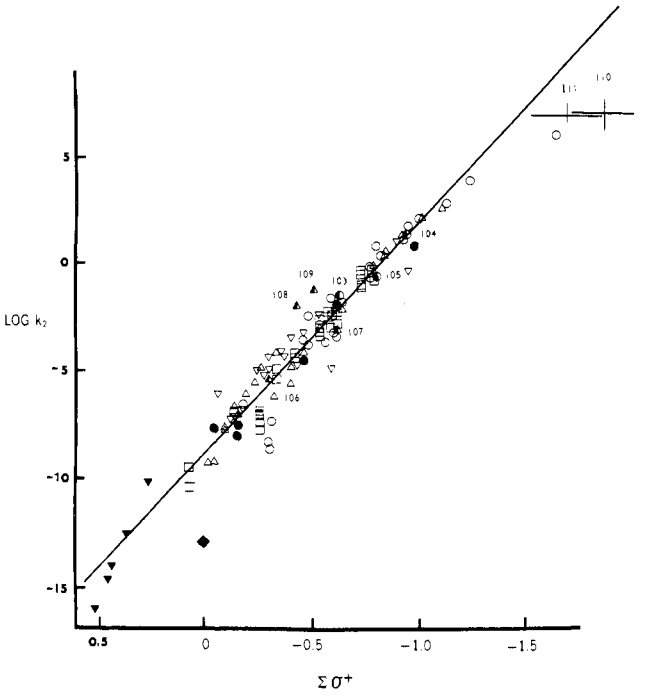
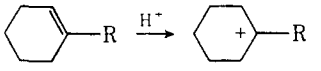


Figure 1. Correlation of the acid-catalyzed hydration of *N*-vinylacetamides $AcNHCR{=}CH_2$ (●), **103–105**, *p*-acetamidostyrenes (▲) **106–107**, *p*-aminostyrenes (△) **108–109**, and enamines (+) **110–111**.

(−0.59), and the value from charge transfer spectra (−0.60). The average of these values (−0.65) is almost exactly the average calculated from eq 4 from the rates of hydration of **1–3**. This agreement lends credence to the validity of the value and further supports eq 11 as the mode of hydration of these alkenes.

The values excluded from the derivation of the σ_p^+ value for acetamido are that of −0.47 from Ar_3COH ionization, suspected to be unreliable by the original authors,[19a] and the value of −0.25 calculated from the Swain and Lupton treatment, a method that has been shown to be imprecise for the prediction of σ_p^+ in another example.[18a]

Heretofore the hydrations of 1-substituted cyclohexenes (eq 12) have not been correlated by a linear free energy correlation.



(12)

Rates of hydration are available for R = H,[16] Me,[16] OMe,[17] and OEt[17] in this series and these are correlated by the new equation

$$\log k_2 = -11.2\sigma_p^+(R) - 7.21 \qquad (13)$$

with $r = 0.999$. This correlation is much more precise than that obtained for the acyclic alkenes (eq 4) and covers a reactivity range of more than 10^9. The origin of this better correlation is an item of interest. Part of the scatter in the acyclic cases may arise from different conformational preferences of the substituents, whereas the substituted cyclohexenes might adopt a more constant geometry in the ground and transition states throughout the series. This would reduce variable effects due to substituent conformation and also variable solvation.

The σ_p^+ value for AcNH derived from the newly established correlation (13) for substituted cyclohexene reactivities is −0.58, which is in satisfactory agreement with that of −0.66 from the acyclic cases. The fit of the data for compounds **1–3** to eq 4 is shown in Figure 1, and the correlation of eq 13 plus the value for **4** is shown in Figure 2.

Thus the $A_{SE}2$ mechanism (eq 11) is securely established

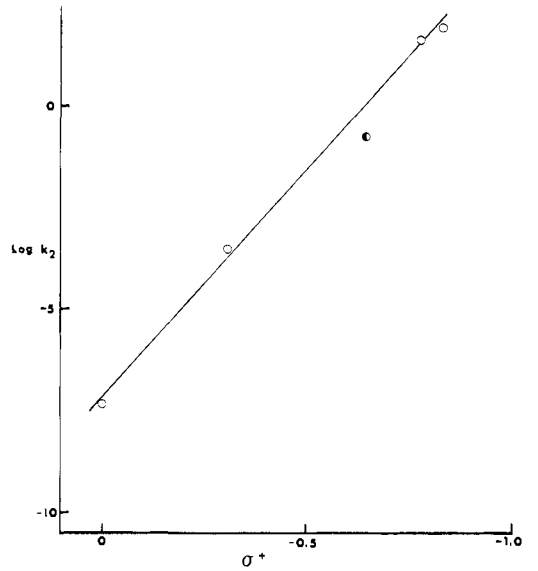


Figure 2. Correlation of the acid-catalyzed hydration of 1-substituted cyclohexenes by substituent parameters (1-acetamidocyclohexene, ●).

for **1–4**. The proposal[8] that β-arylenamides hydrolyze by reversible protonation and hydration followed by rate-determining dissociation to a carbonium ion (eq 5) was based on the observed acid catalysis and the accelerating effect of electron-donating substituents R. However, these effects are also compatible with the $A_{SE}2$ mechanism. The rates were measured in partly aqueous mixed solvents so quantitative comparisons with rates in water are not feasible but qualitative comparisons between these solvents can be made[18] and the reported[8] rates clearly show large (~10^3) decelerations due to β-phenyl substitution. This is the expected result for the $A_{SE}2$ mechanism.[21] There is no reason to expect the β-aryl compounds, which are less reactive than **1–4**, to react by a different mechanism, so in the absence of any contrary evi-

dence we conclude that the β-arylenamides also react by the $A_{SE}2$ route.

Examination of the σ_p^+ values for AcNH in Table IV reveals an average value of −0.33 for the styrene hydration, as contrasted to the value of −0.65 derived above. There is frequently some dispersion in σ_p^+ values obtained from different reaction series and the variability of resonance electron donation by acetamido has been commented upon elsewhere;[20] however, it is not obvious why the styrene hydration rates give distinctly lower σ_p^+ values for AcNH. As summarized in the footnotes to Table IV two of the styrene correlations have rather poor correlation coefficients, but this should not have such a drastic effect on the σ_p^+ values. Resolution of this anomaly must await the results of further studies. Nevertheless the rates of the compounds are adequately predicted by eq 4 using the σ_p^+ values for aryl groups,[18b] The fit for compounds **1-6** is shown in Figure 1.

The value of −0.65 for the σ_p^+ value of acetamido may be compared to the average value of −1.3 for amino.[19b] This diminution is due to the familiar resonance and inductive electron withdrawal from nitrogen by the acetyl group. In comparison the σ_p^+ value of −0.92 of hydroxy is reduced to −0.06 by acetylation.[18a]

To extend the range of Figure 1 still further we may utilize reported rate data for the hydration of (*E*)-MeCH=C(Ph)-NMe_2 (**110**),[3b,22] which tests the ability of eq 4 to predict the rate of an alkene substituted with the strongly electron-donating Me_2N group. From the observed rates of buffer-catalyzed hydrolysis of **110** between pH 7 and 14 a k_{H^+} value of 3.0×10^6 M^{-1} s^{-1} was derived, which is corrected to 1.02×10^7 M^{-1} s^{-1} when multiplied by a factor of 3.4 to account for the anticipated rate retardation by the β-methyl.[21] A rate of 8.4×19^6 M^{-1} s^{-1} may also be derived from the reported rate for Me_2C=CH(NC_5H_{10}) (**111**)[3d,e,22] after correction for the rate-retarding effect of 30 expected for β,β-dimethyl substitution[21] and by the Me_2N/piperidino rate ratio of 2.[3b] The σ_p^+ value of −1.7 for Me_2N is an average of values ranging from −1.49 to 1.87 from various reactions.[19] The fit of the data for the two alkenes substituted with the Me_2N group by eq 4 is shown in Figure 1. Within the uncertainties of the σ_p^+ parameter for Me_2N and the rates for these compounds the fit to the correlation appears rather satisfactory.

Rates of protonation of the olefinic bond of *p*-aminostyrene (**108**)[22] and *p*-dimethylaminostyrene (**109**)[22] have been obtained[4] which permit calculation of the rates of these compounds at 25 °C. Values of k_2 (M^{-1} s^{-1}) are 5.0×10^{-2} (**108**) and 0.25 (**109**). The fit of these points to eq 4 using the σ_p^+ parameters for the aryl groups as previously discussed[18b] is illustrated in Figure 1. These rates for **108** and **109** also provide an excellent extension of the Brown-Hammett correlation for substituted styrenes reported by Schubert and Keeffe[13] (at $H_0 = 0$, $\log k = -3.72\sigma^+ - 6.77$; $r = 0.994$).

With the inclusion in the rate correlation of the very reactive acetamido- and amino-substituted compounds examined in this study and the very unreactive trifluoromethyl-substituted alkenes considered in our recent work[5f] the total range of reactivity covered by eq 4 is now more than 23 powers of ten. The plot of Figure 1 is essentially linear over that entire range, with at most modest curvature. The possibility of variable electron donation by substituents during large changes in electron demand has been a topic of intense recent interest.[23] This behavior has been described as "capricious"[23a] but our results emphasize that practical additivity of substituent effects is possible over enormous changes in reactivity.

Experimental Section

p-Aminoacetophenone, acetone oxime, and acetophenone oxime were obtained from Aldrich. NMR spectra were run using a Varian T-60 instrument with tetramethylsilane (Me_4Si) as an internal standard. Kinetics were carried out using Cary 14 and 118 and Unicam 1800 instruments. Duplicate runs were made in all cases except as noted.

N-Vinylacetamide (**1**) was prepared from a reported procedure.[7a] *N*-(2-Propenyl)acetamide (**2**),[7b] *N*-(1-phenylvinyl)acetamide (**3**),[7c] and *N*-(1-cyclohexenyl)acetamide (**4**)[7b] were prepared according to a published procedure[7d] which involved refluxing the oximes with acetic anhydride to give the crude *N,N*-diacetylaminoalkenes which were converted to the *N*-alkenylacetamides by chromatography on alumina.[7d]

The NMR spectra and melting points of the enamides agreed with those reported.[7] They showed UV maxima in water as follows: **1**, 225 nm, ε 13 700; **2**, 227 nm, ε 5060; **3**, 245 nm, ε 20 560; **4**, 230 nm, ε 5250.

p-Acetamidostyrene (**5**)[10a] was obtained from the reaction of *p*-aminostyrene with acetyl chloride and triethylamine at 0 °C. *p*-Aminostyrene was prepared by distillation from $KHSO_4$ of *p*-aminophenyl-1-ethanol obtained from $NaBH_4$ reduction of *p*-aminoacetophenone: NMR **5** (CCl_4) δ 2.10 (s, 3, Me), 5.0-7.0 (m, 3, vinyl H), 7.3 (m, 4, Ar), 8.4 (broad s, 1, NH). The crude product, mp 135 °C (lit.[10a,b] 134, 135-136 °C), was used directly in kinetic experiments.

p-Acetamido-α-methylstyrene (**6**)[10c] was obtained by distillation from $KHSO_4$ of *p*-acetamidocumyl alcohol using an Aldrich Kugelrohr apparatus at 150-180 °C and 0.2-10 mm pressure: NMR (CCl_4) δ 2.16 (broad s, 6, CH_3CO and CH_3C=C), 5.12 (m, 1, (*E*)-C*H*=CMe), 5.40 (broad s, 1, (*Z*)-C*H*=CMe), 7.52 (s, 4, Ar), and 7.6 (very broad s, 1, NH). The *p*-acetamidocumyl alcohol was obtained from the reaction of acetyl chloride and triethylamine with *p*-aminocumyl alcohol, obtained from twice reacting methylmagnesium bromide with *p*-aminoacetophenone. The crude **6** was used directly in kinetic measurements.

Kinetic measurements on **1**, **2**, and **4** were carried out by injecting 10-μL samples of 0.1 M solutions of the substrate in H_2O into 3 mL of acid solution thermostated in the cell compartment of the UV spectrophotometer. The decrease of the UV absorption at the maximum was then monitored as a function of time; except in the case of **3** the increase in acetophenone absorption at 245 nm was observed. The hydrations of **5** and **6** were followed in a comparable manner by following the absorption at 272 and 280 nm, respectively.

The observed rates for **5** in H_2SO_4 were converted to hydration rates of the neutral styrene by the relation $k_{hyd} = k_{obsd}([B]/([B] + [BH^+])^{-1}$ where B refers to the neutral styrene and BH^+ to the corresponding N-protonated form, and $[B]/([B] + [BH^+])^{-1} = (1 + [BH^+]/[B])$ and $\log [BH^+]/[B] = pK_{BH^+} - H_A$. The appropriate amide acidity functions H_A for H_2SO_4[24a] and $HClO_4$[24b] were used.

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(22) Numbering of compounds in our total compilation of alkene reactivities[5] is **1 (103), 2 (104), 3 (105), 5 (106), 6 (107),** (*E*)-MeCH=C(Ph)NMe$_2$ **(110),** Me$_2$C=CH(NC$_5$H$_{10}$) **(111)** (NC$_5$H$_{10}$ = 1-piperidino), *p*-H$_2$NC$_6$H$_4$CH=CH$_2$ **(108),** and *p*-Me$_2$NC$_6$H$_4$CH=CH$_2$ **(109).**
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Structures and Mass Spectral Behavior of the Inositol Cyclic Boronic Esters

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Abstract: The structures of the cyclic tris(boronic) esters of each of the inositols have been examined by electron ionization mass spectrometry. Structural assignments have been made from mass spectral features and from mixed boronic ester experiments. The structures appear to fall into three related groups: *myo*- and *muco*-inositol, the former with two α,γ- and one α,β-cyclic ester, the latter with two α,γ- and one α,δ-cyclic esters: *cis*- and *allo*-inositol, each with two α,β- and one α,δ-ester; *neo*-, *chiro*-, and *epi*-inositol each with three α,β-cyclic boronates, one of which is trans in each case. *scyllo*-Inositol, which does not form a triboronate, was found to produce, after sequential butaneboronation and trimethylsilylation, a bis(trimethylsilyl)bis-(butaneboronate) derivative.

The inositols (Figure 1) are useful candidates for studying the effects of stereochemical features on fragmentation following electron ionization in the mass spectrometer. We have noted earlier that trimethylsilyl ethers of the inositols show much larger variations in the intensities of ions in their mass spectra than do the inositol acetates.[1] We attributed this to an expression of the stereochemistry of each isomer, enhanced by the effect of bulky trimethylsilyl groups. In the present study we report the behavior of each of the inositols when they are reacted with boronic acids, derivatizing reagents which themselves have steric requirements for the formation of stable cyclic esters. As previously reported,[2] *myo*-, *muco*-, *neo*-, and *chiro*-inositols form derivatives, on reaction with butaneboronic acid, which readily undergo gas chromatography. *scyllo*-Inositol does not form volatile products under these conditions. We have found that the remaining isomers (*epi*-, *allo*-, and *cis*-inositols) also react readily with butaneboronic acid. Methane-, octane-, and benzeneboronates were examined as well.

Results and Discussion

Each of the inositols, except *scyllo*-inositol, which is discussed below, on reaction with butaneboronic acid, gives a product which gas chromatographs as a single peak. Eisenberg[3] first reported that *myo*-inositol forms a tributaneboronate and we find that the rest of the inositols, with the exception noted, also form triesters.

The structures of these cyclic boronates can be divided into three groups on the basis of similarities in their mass spectra: first, the butaneboronate derivatives of *myo*-inositol (Figure 2) and *muco*-inositol have comparatively simple mass spectra with an abundant ion at *m/e* 139 and a much less intense ion at *m/e* 126 (the structurally diagnostic usefulness of these two ions is discussed below); second, *cis*-inositol (Figure 2) and *allo*-inositol cyclic butaneboronates have complex spectra with an ion $[M - C_4H_9]^+$ (*m/e* 321) as base peak; and third, *neo*-inositol (Figure 2), *chiro*-inositol, and *epi*-inositol butaneboronates have spectra with the *m/e* 126 ion approximately three times more intense than the ion *m/e* 139.

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