Kinetics of Acid-Catalyzed Hydration of Acetylene. Evidence for the Presence in the Solution Phase of Unsubstituted Vinyl Cation[†]
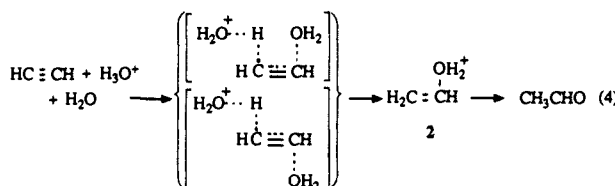
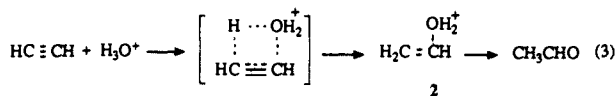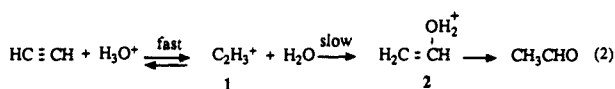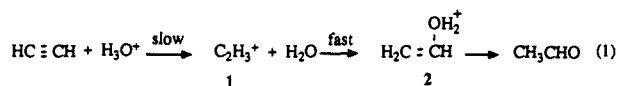## Vittorio Lucchini[*,‡] and Giorgio Modena[*,§]

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Abstract: The rates of acetylene hydration in the convenient range of aqueous sulfuric acid (and those of propyne, *tert*-butylacetylene, ethylene, propene, and *tert*-butylethylene, for comparative purposes) have been measured at 25 °C with an NMR technique. The correlation of the kinetic data with the excess acidity function X gives a value of 1.12 for the slope parameter m^*, which suggests that the intermediate is protonated acetylene, $C_2H_3^+$ (probably as vinyl cation 3 rather than as hydrogen-bridged ion 4). The comparison with the m^* value for the hydration of ethylene (1.50) indicates that protonated acetylene possesses stronger susceptibility to solvation than ethylium ion $C_2H_5^+$. The deuteration patterns in the products (acetaldehyde and crotonaldehyde) obtained in deuteriosulfuric acid rule out the reversibility of the protonation process and also the conversion between 3 and 4.

The acid-catalyzed hydration of acetylene to acetaldehyde, followed by condensation to crotonaldehyde, is a well-known reaction, first studied by Berthelot in 1862.[1] For synthetic purposes, this practice has been superseded by more efficient procedures, which require much milder conditions and a catalyst (generally a metallic ion).[2] Nevertheless the hydration of acetylene, within the research realm of electrophilic addition to carbon–carbon double and triple bonds,[3] remains a much debated argument,[4] with many uncertainties still unresolved concerning fundamental mechanistic details, such as the following: (i) the relative reactivities of acetylene and ethylene toward protonation;[5] (ii) the actual presence of protonated acetylene ($C_2H_3^+$ ion) along the reaction path; and (iii) the structure of this ion under solvating conditions.

Regarding point ii, four limiting mechanistic hypotheses (eq 1–4) may be proposed. Hypotheses 1 and 2, which are indeed

$$HC \equiv CH + H_3O^+ \xrightarrow{\text{slow}} C_2H_3^+ + H_2O \xrightarrow{\text{fast}} H_2C = \overset{\overset{+}{O}H_2}{CH} \longrightarrow CH_3CHO \quad (1)$$
$$\phantom{HC \equiv CH + H_3O^+ \xrightarrow{\text{slow}}} 1 \phantom{+ H_2O \xrightarrow{\text{fast}}} 2$$

$$HC \equiv CH + H_3O^+ \underset{\text{fast}}{\rightleftharpoons} C_2H_3^+ + H_2O \xrightarrow{\text{slow}} H_2C = \overset{\overset{+}{O}H_2}{CH} \longrightarrow CH_3CHO \quad (2)$$
$$ 1 \phantom{+ H_2O \xrightarrow{\text{slow}}} 2$$

$$HC \equiv CH + H_3O^+ \longrightarrow \left[\begin{array}{c} H \cdots \overset{+}{O}H_2 \\ \vdots \quad \vdots \\ HC \equiv\!\equiv CH \end{array} \right] \longrightarrow H_2C = \overset{\overset{+}{O}H_2}{CH} \longrightarrow CH_3CHO \quad (3)$$
$$ 2$$

$$HC \equiv CH + H_3O^+ + H_2O \longrightarrow \left\{ \begin{array}{c} \left[\begin{array}{cc} H_2\overset{+}{O}\cdots H & OH_2 \\ \vdots & \vdots \\ H\overset{}{C} \equiv\!\equiv CH \end{array}\right] \\ \left[\begin{array}{c} H_2\overset{+}{O}\cdots H \\ \vdots \\ H\overset{}{C} \equiv\!\equiv CH \\ \vdots \\ OH_2 \end{array}\right] \end{array} \right\} \longrightarrow H_2C = \overset{\overset{+}{O}H_2}{CH} \longrightarrow CH_3CHO \quad (4)$$
$$ 2$$

variations of the same Ad$_E$2 mechanism, require the intermediacy of protonated acetylene 1, but only in the former is proton transfer the rate-determining step. This mechanism has been proposed for the trifluoroacetic acid addition to dialkylacetylenes,[6] for the acid-catalyzed hydration[7] or the photohydration of phenylacetylenes,[8] and for the fluorosulfonic acid addition to these same

substrates.[9] The predominant syn addition observed for the addition of fluorosulfonic acid to terminal alkylacetylenes[9] and for the addition of hydrogen halides to phenylacetylenes[10] was explained by the intermediacy of an ion pair. For the sake of completeness, we will also consider mechanism 3, where, as for the ion pair case, the electrophilic and nucleophilic moieties originate from the same molecule. Although a concerted 2σ–2π syn addition would be a forbidden thermal reaction, it has been argued that this mechanism may actually occur when the two partners have greatly different polarities.[11] Ad$_E$3 mechanism 4, with the anti transition state, was proposed for the predominantly anti addition of hydrogen halides to dialkylacetylenes.[12] Both mechanisms 3 and 4 lead directly to protonated vinyl alcohol 2.

As for point iii, two alternative structures, either the linear vinyl cation 3 or the nonclassical proton-bridged cyclic species 4, may be proposed for protonated acetylene. The existence of protonated

$$\begin{array}{cc} \overset{H}{\underset{H}{\diagdown}} C = \overset{+}{C} - H & \overset{H^+}{\overset{\diagup\diagdown}{H - C = C - H}} \\ 3 & 4 \end{array}$$
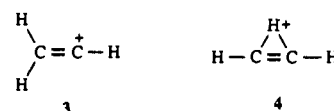
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acetylene in the gas phase is firmly established.[13] The structure of this species could until recently be investigated only by quantum mechanical methodologies.[14] The most sophisticated ab initio calculations[14d] suggest that the bridged structures 4 is more stable by about 5.0 kcal mol^{-1} than the linear isomer 3. The theoretical results recently have been confirmed by the Coulomb explosion imaging technique, which has provided the first experimental evidence for the gas-phase bridged structure of protonated acetylene.[15] More recently, an alternative model has been proposed,[16] in which the hydrogens of $C_2H_3^+$ tunnel through the energy barrier and rotate in the molecular plane around the C–C skeleton, thus becoming equivalent. The gas-phase infrared spectrum of $C_2H_3^+$ in the 3150-cm^{-1} region was reported to agree with this model.[17]

The solvation energies for the two structures are at least one order of magnitude greater[18] than the computed structural energy difference, and therefore the computational or the experimental gas-phase evidence cannot be a trustworthy indication for the ground-state structure of protonated acetylene in solution. In the case of protonation of substituted acetylenes, both calculations[19] and experimental findings[7,20] favor the linear vinylic structure. Linear vinyl cations, strongly stabilized by proper substituents, have been spectroscopically detected in solution.[21]

The difficulty in obtaining experimental evidence for the hydration of acetylene is a consequence of the lack of a suitable technique for monitoring the primary step of the process. The hydration of higher homologues of acetylene may be conveniently followed by means of UV spectroscopy.[7,22] The same technique has been extensively used for studying the acid-catalyzed hydrations of ethylene and of its higher homologues.[23] On the other hand the UV spectra of unsubstituted acetylene exhibit a single absorption at the hypsochromic end of the transparent region (below 230 nm). In the strongly acidic range where the hydration of acetylene occurs at a convenient rate, acetaldehyde quickly dimerizes and the triple bond absorption is readily overwhelmed by that of protonated crotonaldehyde, which possesses a much stronger chromophore.[24]

The monitoring by means of NMR spectroscopy is possible in principle, but not easily accomplished in practice, because of the intrinsic poor sensitivity of the technique, which makes substrates

of exceedingly low solubility (as it is acetylene in aqueous solutions) hardly detectable, and because of the low precision associated with the integration of the resonance signal. As a matter of fact, only one report has appeared[25] describing a semiquantitative NMR investigation of the behavior of acetylene in concentrated sulfuric acid. The problem can only be tackled with a high-field high-sensitivity FT instrument and the adoption of the instrumental suppression of the solvent peak. Still, even with these instrumental facilities, the integration of the signals of acetylene and of the standard remains affected by unacceptable errors (usually greater than 10%). The overall error is significantly reduced when the first-order kinetics is calculated from the greatest possible number of observations. In our work, between 50 and 300 points (from spectra swiftly aquired with a small number of scans) have been collected for each kinetic run, except in the case of the faster kinetics. More details for the integration procedure are presented in the Experimental Section.

With this methodology we could measure the rates of disappearance of acetylene, both in protio and deuteriosulfuric acid. To assess the reliability of our measurements, we have also followed the hydration of propyne, ethylene, and propene, investigated by means of UV spectroscopy.[22b,23c] We have extended the investigation to *tert*-butylacetylene and *tert*-butylethylene. A preliminary report of this investigation has appeared.[26]

The hydration rate constants, obtained under greatly different acid conditions, may be compared within themselves or with LFER substituent parameters only if they are extrapolated to a common standard state by means of an appropriate correlation function.[22c,27] This highly debated problem, which goes back to the early thirties, has found only in recent times a satisfactory solution, with the formulation of the appropriate equations[28–30] and reference scales.[31] These equations have been thoroughly tested with consistent results. One general formulation is based on the excess acidity function X, which correlates the observables of the acid–base equilibria (the ionization ratios I) or of the acid-catalyzed reactions (the rate coefficients k_{obs}) with the acidity of the medium through eq 5 and 6, respectively.[29,30]

$$\log I - \log c_{H^+} = m^*_{eq}X - \log K_{BH^+} \qquad (5)$$

$$\log k_{obs} - \log c_{H^+} = m^*X + \log k_0 \qquad (6)$$

If one ($n = 1$) or more water molecules are involved before the rate-limiting step, as in mechanism 4, the correlation becomes

$$\log k_{obs} - \log c_{H^+} - n \log a_w = m^*X + \log k_0 \qquad (7)$$

In the framework of the older treatment by Bunnett and Olson[28a,b] X corresponds to $-(H_0 + \log c_{H^+})$ and m^*_{eq} and m^* to ($1 - \phi_e$) and ($1 - \phi_r$), respectively. When the c_{H^+} term is considered as the conglomerated concentration of all species capable of transferring a proton (H_3O^+, H_2SO_4, $H_3SO_4^+$, and, in diluted solutions, HSO_4^-), the state described by $X = 0$ is the ideal state of infinite dilution in water.[32]

The slope parameter m^*_{eq} may be related to the susceptibility of the protonated base to stabilization by the solvent, mainly through hydrogen bonding, in comparison to the stabilization of the conjugated base and with reference to the stabilization of the acid–base pairs utilized for the construction of the H_0 acidity function.[30,33] Each grand class of bases is associated with m^*_{eq}

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Table I. Rate Constants of Acid-Catalyzed Hydration of Alkynes and Alkenes at 25 °C

compd	mol of H_2SO_4 or D_2SO_4	k_{obs}, s^{-1}
	H_2SO_4	
CH≡CH	15.07	5.48×10^{-6}
	16.09	2.56×10^{-5}
	16.76	7.67×10^{-5}
	17.32	2.01×10^{-4}
	17.96	7.51×10^{-4}
MeC≡CH	7.07	5.06×10^{-6}
	7.78	1.53×10^{-5}
	8.49	4.48×10^{-5}
	8.86	8.00×10^{-5}
	9.31	1.81×10^{-4}
	9.84	4.30×10^{-4}
t-BuC≡CH	6.93	9.31×10^{-6}
	7.64	4.79×10^{-5}
	8.06	7.41×10^{-5}
	8.60	2.15×10^{-4}
	9.19	5.28×10^{-4}
CH_2=CH_2	12.11	5.24×10^{-6}
	12.68	1.83×10^{-5}
	13.05	4.01×10^{-5}
	13.64	1.23×10^{-4}
	14.38	7.21×10^{-4}
MeCH=CH_2	5.46	1.07×10^{-5}
	6.03	2.97×10^{-5}
	6.54	6.26×10^{-5}
	6.93	1.50×10^{-4}
	7.64	4.63×10^{-4}
t-BuCH=CH_2	5.46	1.71×10^{-5}
	6.03	5.25×10^{-5}
	6.54	9.03×10^{-5}
	6.93	2.16×10^{-4}
	7.64	7.31×10^{-4}
	D_2SO_4	
CH≡CH	16.28	1.62×10^{-5}
	17.04	4.82×10^{-5}
	17.51	1.22×10^{-4}
	18.07	3.38×10^{-4}

values that span a relatively small interval. Relevant for the sake of the following discussion are the equilibria involving carbonium ions (with m^*_{eq} values between 1.85 and 1.41, denoting that they are weakly affected by the solvent) and protonated alcohols (exhibiting m^*_{eq} values between 0.13 and 0.15, and therefore strongly stabilized by hydrogen bonding). The smallest value, $m^*_{eq} = 0$, is associated with the reference solvent, the H_3O^+/H_2O acid-base pair. The correlation is so safe that the parameter m^*_{eq} gives a confident indication of the site of protonation of substrates with more basic centers.[30]

The thermodynamic and kinetic slope parameters for the same reaction define a Brønsted-type coefficient α_A:[28b,30]

$$\alpha_A = m^*/m^*_{eq} \qquad (8)$$

As for the conventional Brønsted coefficient, α_A is an indicator of the transition-state position along the reaction coordinate from the reagents (B + H_3O^+, and $m^* = 0$) to the products (BH$^+$ + H_2O, and $m^* = m^*_{eq}$).

Results

The rates of hydration of acetylene, propyne, *tert*-butylacetylene, ethylene, propene, and *tert*-butylethylene in the proper sulfuric acid concentration range at 25 °C have been followed with the NMR technique outlined in the Introduction and detailed in the Experimental Section by monitoring the unique or most convenient (methyl doublet or *tert*-butyl singlet) reagent signal. The hydration of acetylene was also investigated in deuteriosulfuric acid. The observed rate constants are collected in Table I.

The application of eq 6, which describes the mechanistic hypotheses 1, 2, and 3, gives excellent linear plots (see Figure 1).
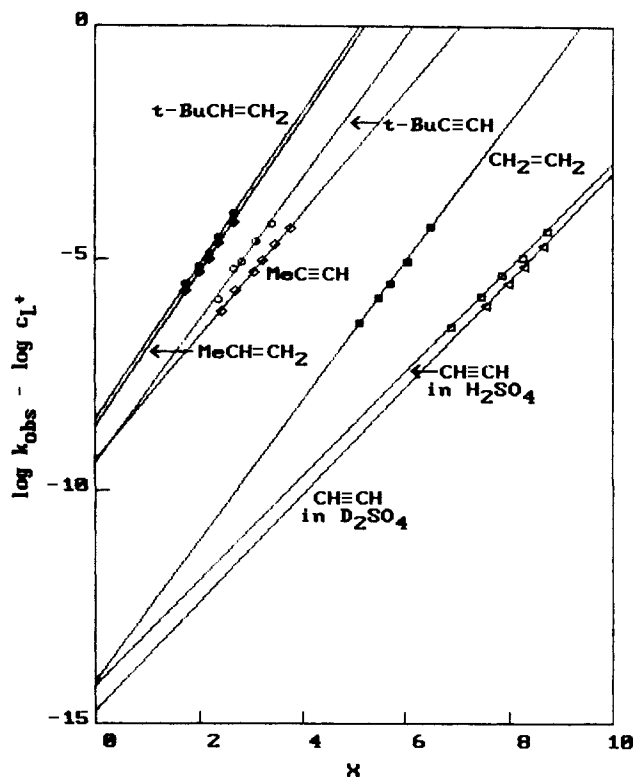
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Figure 1. Effect of acid concentration on the rate constants for the hydration of the given hydrocarbons in protio [L = H, $X = -(H_0 + \log c_{H^+})$] and deuteriosulfuric acid [L = D, $X = -(D_0 + \log c_{D^+})$] at 25 °C.

Table II. Correlation with Acidity of the Rate Constants of Hydration of Alkynes and Alkenes

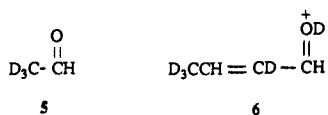| compd	$\log k_0$	m^*	r
	Equation 6		
CH≡CH in H_2SO_4	-14.19 ± 0.07	1.12 ± 0.01	0.9998
CH≡CH in D_2SO_4	-14.71 ± 0.23	1.15 ± 0.03	0.9988
MeC≡CH	-9.34 ± 0.05	1.33 ± 0.02	0.9996
t-BuC≡CH	-9.38 ± 0.27	1.52 ± 0.09	0.9904
CH_2=CH_2	-14.07 ± 0.16	1.50 ± 0.03	0.9991
MeCH=CH_2	-8.62 ± 0.10	1.65 ± 0.04	0.9982
t-BuCH=CH_2	-8.45 ± 0.12	1.65 ± 0.06	0.9971
	Equation 7		
CH≡CH in H_2SO_4	-18.79 ± 0.23	2.18 ± 0.03	0.9995

For the sake of the following discussion, eq 7, describing mechanism 4, was also tested in the case of acetylene, yielding again a good linear plot. The slope m^* and the intercept $\log k_0$ parameters, together with the correlation coefficients r, are listed in Table II.

The primary kinetic solvent isotope effect $k_{obs}(H_2SO_4)/k_{obs}(D_2SO_4)$ for acetylene in the experimentally accessible range is between 2.22 and 2.47, in agreement with determinations on other carbon bases.[7,34] The isotope effect on the slope parameter, $m^*(H_2SO_4)/m^*(D_2SO_4) = 0.97$, is within experimental error (the parameter m^*, as an indicator of the interaction with solvent, is to be considered an equilibrium term).

The low-field region in the NMR spectra taken in undeuterated sulfuric acid is heavily perturbed by the presaturation of the solvent (see Experimental Section), but it may be adequately examined in the spectra taken in deuteriosulfuric acid. In a typical case (hydration monitored in 16.28 mol D_2SO_4), a signal at δ 9.85, due to methyl-deuterated acetaldehyde 5, is observed in the early stages of the reaction. Before the end of the hydration process, it converts to two broad 1:1 singlets at δ 8.75 and 9.27.[35] The

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$$\begin{array}{cc} \overset{O}{\underset{\|}{D_3C-CH}} & \overset{\overset{+}{O}D}{\underset{\|}{D_3CCH=CD-CH}} \\ \mathbf{5} & \mathbf{6} \end{array}$$

conversion is complete in a period about four times longer than that required by the hydration process. At the end the cumulated intensity of these signals corresponds to half the initial intensity of acetylene. The two final singlets correspond fairly well with those reported (but measured in a different acidic medium)[36] for the H-1 and H-3 resonances of protonated crotonaldehyde. No other signals could be detected, and the final product is therefore protonated crotonaldehyde 6, deuterated at C-2 and C-4.

Discussion

The intermediacy of α-substituted vinyl cations in the acid-catalyzed hydration of higher homologues of acetylenes is generally accepted.[7,8] On the other hand, the existence of unsubstituted protonated acetylene is documented in the gas phase only.[13] More recently,[37] the formation of this ion in the solution phase was attained by nuclear decay of tritiated ethylene, i.e. by an unconventional nonchemical process. So far no evidence has been provided for the intermediacy of protonated acetylene in more conventional acid-catalyzed reactions.

The Irreversibility of the Hydration Process. The results for the hydration in deuteriosulfuric acid, and in particular the detection of the NMR resonances of the aldehydic proton in the primary product 5 and of H-1 and H-3 in the secondary product 6, reveal that these hydrogens do not undergo isotope exchange. Furthermore, the measured kinetic isotope effect is consistent with proton transfer in the rate-determining step. These experimental results rule out mechanistic hypothesis 2.

The rapid interconversion between the isomeric structures 3 and 4 and the consequent hydrogen scrambling around the C–C skeleton may also cause isotope exchange. The persistency of the signals of 5 and 6 indicates that this process does not occur in the condensed phase, either because only one isomer is present or because the interconversion, which may require an energetically costly solvent reorganization, is slower than the nucleophilic attack by water. Therefore also the hypothesis of hydrogen tunneling[16] for the $C_2H_3^+$ structure is to be ruled out, at least in the condensed phase.

The Parameter m^*_{eq} as an Indicator of the Structure of the Protonated Intermediate. In the few cases of carbon bases sufficiently strong to allow the determination of the protonation rates as well as of the ionization ratios I,[38] Brønsted-type α_A coefficients of about 0.5 have been found, indicating that the transition state falls roughly halfway between the reagent system and the product system. The bases we are discussing in this work are much weaker, and the corresponding transition states certainly lie closer to the protonated intermediates.[7b] This should be more so for the hydration process of acetylene (possessing a gas-phase basicity, GB, of 146.1 kcal mol^{-1}) than for that of ethylene (with a GB of 155.6 kcal mol^{-1}).[39] Thus we may attribute to protonated acetylene a m^*_{eq} value not much greater than the m^* value of 1.12, while that of protonated ethylene (ethylium ion) should be somewhat greater than the m^* value of 1.50.

When properly analyzed, the results for the hydration of acetylene (and of the other bases that we present in this paper)
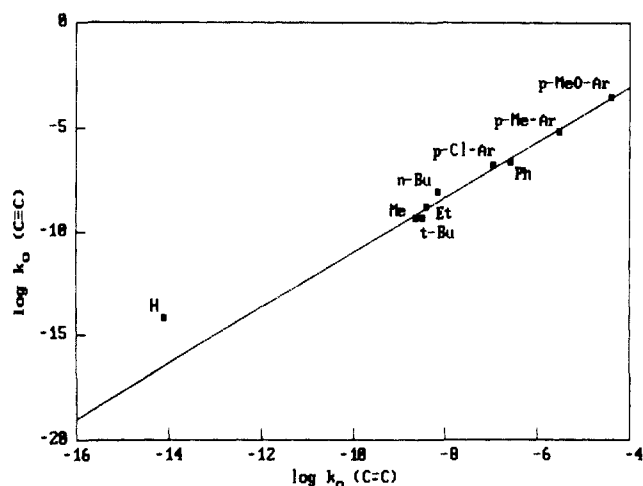
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Figure 2. Comparison of the log k_0 values for the hydration in sulfuric acid of acetylene and some higher homologues RC≡CH with those of ethylene and the corresponding homologues RCH=CH$_2$.

may give reliable indication of the structure of the intermediate. Three approaches may be proposed: (i) the inspection of the linearity of the plots obtained from the application of either eq 6 or eq 7 to the experimental reaction rate coefficients; (ii) the systematic comparison of the hydration rates of a series of alkynes with those of the corresponding alkenes; and (iii) the careful consideration of the slope parameter m^*.

The first approach, which has been successfully applied in other instances,[40] does not give a straightforward answer in the present case; in fact, in the narrow acidity ranges where the kinetic measurements are experimentally accessible, the log a_W term is practically linear with the X term, so that also eq 7 gives linear plots.

Regarding the second approach, we present in Figure 2 a comparison of the log k_0 values for the hydration of a series of alkynes RC≡CH with those of the corresponding alkenes RCH=CH$_2$. The log k_0 values are calculated with eq 6 from our own data and from all other base pairs for which rate constants at 25 °C are available from the literature.[7,22,23] The least-squares analysis of all points, omitting that for the acetylene–ethylene point, gives a very good correlation (slope, 1.32; r, 0.9913), with a significant improvement over a previous report.[22c] Such a good correlation is strong evidence for the similarity, if not for the identity, of the mechanism for the two reactions. The deviation of the acetylene–ethylene point is large, but it is not large enough to acquire a mechanistic meaning. As the log k_0 values depend on the slope, the deviation may be attributed, also within the hypothesis of an identical mechanism for the two substrates, to a different position of the transition states along the reaction coordinate, to different solvation of the transition states, or even to larger errors as a consequence of the longer extrapolations.

The third approach appears to be more reliable. In the same manner that the magnitude of the m^*_{eq} parameter gives confident indications concerning the nature of the protonated base,[30] the structure of the transition state and, by extention, that of the protonated intermediate may be inferred from examination of the m^* parameter. As equilibrium measurements for the proton-transfer step in hydration reactions of alkenes and alkynes are not available, we have to resort to comparisons with other appropriate acid–base pairs.

The value of the m^*_{eq} parameter for the protonation of primary alcohols is not greater than 0.15.[41] Even though the steric hindrance to solvation may shift the m^*_{eq} parameter to higher values,[30] the protonated vinyl alcohol 2, intermediate for mechanisms 3 and 4, is certainly not more hindered than primary alcohols. Therefore the m^* value for the transition state leading to this

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Kinetics of Acid-Catalyzed Hydration of Acetylene

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intermediate should vary between 0 and about 0.15. The values of the slope parameter m^* for eq 6, describing mechanism 3, and for eq 7, describing mechanism 4, are 1.12 and 2.18, respectively, thus ruling out the hypothesis of 2 as an intermediate.

Typical m^*_{eq} values for protonation equilibria of organic carbon bases lie between 1.41 and 1.85.[30] This suggests that the parameter m^* for the transition state leading to protonated acetylene 1 should vary between 0 and a value of this magnitude. The m^* value of 1.12, from the application of eq 6 to mechanism 1, is well within this interval.

We think that this analysis provides the first evidence for the presence in the condensed phase of a $C_2H_3^+$ species (either with structure 3 or structure 4), generated by a conventional chemical route.

The Parameters m^* or m^*_{eq} as Indicators of the Solvent Affinity of the Transition State or the Protonated Intermediate. As discussed above, the slope parameters m^*_{eq} or m^* describe the "external" stabilization through solvation of the conjugated acid or of the transition state. The intercept parameters $\log K_{BH^+}$ or $\log k_0$ are complex terms, which measure both the "internal" stabilization induced by charge delocalization inside the molecule and the "external" stabilization by solvation. The magnitude of the latter depends also on the residual charge density at the protonated center, and it has to be affected by the former quantity. Therefore slope and intercept parameters should compensate to a certain extent, but actually only poor correlations are found.[30] As the parameter m^* depends also on the position of the transition state along the reaction coordinate, the correlation between the kinetic parameters m^* and $\log k_0$ is even poorer. Nevertheless, some compensation is observed for alkylated alkynes and alkenes. Alkynes, which are constantly more resistant to protonation than the corresponding alkenes, are also characterized by smaller m^* values, i.e. the transition states are subjected to a greater "external" stabilization in less acidic and more solvating solutions. Thus, the $\log k_0$ values span a shorter interval than the $\log k_{obs}$ values measured in the region where the protonations are actually observed. A similar behavior already has been described for more reactive carbon bases such as substituted phenylacetylenes and styrenes.[22]

This compensation is particularly evident for the acetylene–ethylene pair: the hydration of acetylene occurs in a much more acidic region than that of ethylene (this resistance to protonation in such a poorly solvating medium is paralleled by the smaller gas-phase basicity of acetylene in comparison to that of ethylene[39]), but the greater solvent affinity of the transition state leading to protonated acetylene makes the $\log k_0$ values for the two carbon bases almost identical. It therefore confirms the hypothesis already advanced[5,42] that the basicities of double and triple bonds are very similar in good solvating media. As a matter of fact, the relevantly greater basicity of ethylene with respect to that of acetylene in the gas phase ($\Delta\Delta G^\circ = 9.5$ kcal mol^{-1}) is reduced in 15 mol H_2SO_4 (the center of the accessible protonation range for both bases) to $\Delta\Delta G^\circ \simeq \Delta\Delta G^\ddagger = 3.9$ kcal mol^{-1}, and further to $\Delta\Delta G^\circ \simeq \Delta\Delta G^\ddagger = 0.2$ kcal mol^{-1} in water.[43] The differences in the solvent affinities of the charged species may cause a substantial modification or even a reversal of the gas-phase basicities of the corresponding precursors. This topic has been the subject of many investigations, which have recently led to the description of some exemplary cases.[33,38,44]

In all protonation processes of organic bases, alkyl substitution brings about a shift of the m^*_{eq} parameter toward higher values, as a consequence of the following factors: (i) the increased "internal" stabilization of the protonated species; (ii) the reduced number of hydrogens at the site bearing the positive charge; and

(iii) the increased steric hindrance to solvation.[30] Accordingly, the hydration of alkyl-substituted alkynes and alkenes is characterized by m^* values that are higher and also level off. A similar trend is observed for the corresponding gas-phase basicities, which are higher and compressed in a relatively small interval.[39] The precision of measurement of the m^* values and the gas-phase basicities allows only these qualitative comparisons.

As already stated,[30,44a,45] the solvent affinity of the protonated base is also determined by the number of hydrogens bound at the charged atom, which may participate in hydrogen bonding with water. We think that a simple counting does not suffice and that every single hydrogen bond should be properly weighed. The inconsistency of the estimated m^*_{eq} values for vinyl cation (with one hydrogen at the charged carbon) and ethylium ion (with two such hydrogens) with the counting criterion is revealing. We would suggest that the affinity of a hydrogen at charged carbon toward a basic solvent such as water parallels the acidity of this same hydrogen and is therefore in the order C_{sp}-H > C_{sp^2}-H > C_{sp^3}-H. This picture is not altered when charge delocalization onto β-carbon is considered: the delocalization in the vinyl cation (through conjugation of the vacant p orbital at α-carbon with the antisymmetric combination of the C–H bonds at β-carbon[34a,46,47]) is likely similar or even larger than that in the ethylium ion (through hyperconjugation[46,48]). Thus the vinyl cation 3, with one C_{sp} and two C_{sp^2} hydrogens bound at a C–C system with delocalized charge, should possess a relatively high susceptibility to solvation. The bridged structure 4 does not seem so well suited for hydrogen bonding: the bridging hydrogen contributes to the "internal" stabilization of the cation and also, because of the already high coordination, cannot interact so much with the solvent.

Experimental Section

Protio and deuteriosulfuric acid–water mixtures were prepared by dilution of commercial 98% sulfuric acid and titrated with standard NaOH. As only weighed amounts were used in the titrations, the resulting w/w % values were converted to molarities by means of published density data.[49]

Acetylene, ethylene, propyne, and propene are commercial gases. They have been dried and freed from other gases by being passed through concentrated sulfuric acid and then bubbled into the NMR tube already containing the proper acid solvent. A small volume of solvent is further added, in order to avoid saturation. *tert*-Butylethylene and *tert*-butylacetylene are commercial low-boiling liquids that can be added to the proper acid solution directly in the NMR tube, avoiding the formation of a hydrocarbon layer, which may enter the solution in the course of the hydration process.

Dried tetramethylammonium sulfate may be added as an integration standard.

NMR Measurements. The spectra were run at 25 °C on a Bruker WP200SY instrument equipped with a variable-temperature control (estimated error ±1 °C). The low hydrocarbon solubility commands the maximization of instrumental receiver gain, which in turn requires the presaturation of the solvent signal (in protic acid solutions) by gated homonuclear decoupling with the highest available power. When the monitored signal is not far enough from the decoupling resonance, this practice introduces severe baseline distortions that should be manually corrected for proper integration. The best integration procedure, although rather demanding for the operator, is the internal comparison of one selected hydrocarbon resonance by differential spectroscopy: a pivot spectrum is selected at about half reaction time, and the time variations are given by the multipliers that bring the resonance of choice to an exact matching with the same resonance in the pivot spectrum. A prerequisite

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for this procedure is the rigorous control of instrumental conditions, which is only possible when the whole kinetic run is monitored without removing the sample from the instrument. A more automatic alternative is the recording of absolute peak heights (on baseline-corrected spectra), while the instrumental integration (either graphic or numerical) is as a rule more prone to error. When the instrument is properly controlled, the calibration against an integration standard is useless or even error enhancing.

Data Processing. The log c_{H^+} and log c_{D^+} terms as a function of analytical molar concentration c_0 of protio or deuteriosulfuric acid were evaluated by numerical root-finding[50] of eq 7 in ref 32 (using literature

values[52] for the dissociation constants K_a of HSO_4^- and DSO_4^- and for the autoprotolysis constants K_w of H_2O and D_2O). The corresponding H_0 and D_0 values were interpolated from tabulated acidity functions.[52] The water activity, a_w, values are derived from published data.[53]

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Predicting the Stability of Cyclic Disulfides by Molecular Modeling: "Effective Concentrations" in Thiol–Disulfide Interchange and the Design of Strongly Reducing Dithiols
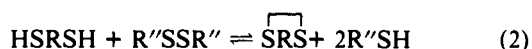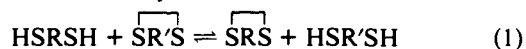
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Abstract: We have tested molecular mechanics calculations at the level of MM2(85) for their capacity to rationalize relationships between structure and equilibrium constants for thiol–disulfide interchange reactions. With 20 α,ω-dithiols taken from the literature, equilibrium constants for thiol–disulfide interchange with 1,2-dithiane were calculated: $HSRSH + \overline{S(CH_2)_4S} \rightleftharpoons \overline{SRS} + HS(CH_2)_4SH$. The relation between experimental values of ΔG and calculated differences in strain energy was $\Delta G = 0.41\Delta SE + 0.5$ kJ/mol with a correlation coefficient of 0.93 (excluding one anomalous point). Results from molecular mechanics correlate well with experimental results, but they cannot give absolute values of energies. Results of molecular mechanics calculations are used to discuss the physical interpretation of the concept of "effective concentration" as it is used for the thiol–disulfide interchange reaction.

Introduction

We have studied two aspects of the relations between molecular structures and stabilities of α,ω-dithiols (HSRSH) and of cyclic disulfides ($\overline{SRS}$) derived from them by oxidation. First, we have explored the capacity of molecular mechanics to rationalize relative stabilities using equilibrium constants for thiol–disulfide interchange reactions as measures of these stabilities (eqs 1 and 2). Second, we applied these computational methods to the design of disulfides whose stability had not been determined.

$$HSRSH + \overline{SR'S} \rightleftharpoons \overline{SRS} + HSR'SH \qquad (1)$$

$$HSRSH + R''SSR'' \rightleftharpoons \overline{SRS} + 2R''SH \qquad (2)$$

This work had four objectives. *First, we intended to evaluate the capability of molecular mechanics[1] to rationalize and predict equilibrium constants for thiol–disulfide interchange.* The absolute accuracy of the calculations was particularly relevant to their use in molecular design: Was their accuracy sufficient to give absolute values of energies, or only high enough to be useful in correlations? *Second, we wished to disentangle the various enthalpic contributions to these equilibria.* Estimating the importance of torsional strain in the C–S–S–C group of the disulfide relative to strain in other parts of the disulfide and in the thiol was important in interpreting the influence of structure on energy.

Third, we needed to evaluate the efficacy of molecular mechanics calculations as a guide to design and synthesis. We use thiol–disulfide interchange both as a model system for studies in physical-organic chemistry[2–6] and as a reaction useful in synthesis. A computational method that would increase the effectiveness of molecular design would improve the efficiency of both activities. *Fourth, we wished to understand the origin, utility, and significance of values of "effective concentration" (EC)[7,8] derived from measurements of equilibrium constants for thiol–disulfide interchange.*[9] The EC—a number characterizing the advantage in rate or equilibrium constant for an intramolecular reaction relative to a closely analogous intermolecular one—has come to be widely used in physical-organic chemistry and biochemistry

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