Isotope Effects in the Acid-Catalyzed Hydration of Phenylacetylene[1-3]

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Abstract: The rate of the acid-catalyzed hydration of phenylacetylene, and of four substituted phenylacetylenes, is smaller in deuterated media, k_{H_2O}/k_{D_2O} being about 2. This result is in accord with a rate-limiting proton transfer. The rate of hydration of ethynyl-*d*-benzene is decreased by 10% by a combination of secondary isotope effects. The relation of these results to mechanism and to other related reactions is discussed.

In recent years several studies have shown that the acid-catalyzed reactions of unsaturated systems involve rate-limiting addition of a proton to give a carbonium ion intermediate.[5] In the previous paper[3] we reported that the acid-catalyzed hydration of phenylacetylene likewise involves rate-determining proton transfer to the terminal carbon, which results in the formation of a benzylic vinyl cation. Evidence supporting this conclusion included the fact that the reaction is subject to general acid catalysis in a series of buffers, that the reaction is characterized by a very negative ρ, and that consistency of behavior among phenylpropiolic acid,[6] phenylbenzoylacetylene,[7] and phenylacetylene is observed with regard to the entropy of activation and acidity dependence.

It is the purpose of the present paper to present the results of a study of isotope effects in the hydration of phenylacetylenes.

Experimental Section[8]

Preparation of Materials. Ethynyl-*d*-benzene was prepared by adapting a procedure used by Hogeveen and Drenth[9] for the preparation of ethylthioethyne-*d*. Ethynylbenzene (10 g) was equilibrated with 5 ml of a solution comprised of 0.16 g of sodium metal dissolved in 5 ml of deuterium oxide for 24 hr at room temperature in a 25-ml flask. This process was repeated four times using fresh sodium deuterioxide–deuterium oxide solution. Intimate contact in this two-phase system was assured by using a vibrating shaker. The organic layer was separated and distilled giving 5.1 g of deuterated alkyne, bp 47.0–47.3° (21 mm). This material was purified by preparative gas chromatography under the conditions described earlier.[3] There was no evidence of an acetylenic hydrogen signal in the nmr or any acetylenic C–H stretch in the infrared spectrum. Mass spectral analysis showed the sample to be 96.5 ± 1% deuterated. Infrared analysis using the C–H stretching band at 3380 cm^{-1} in relatively concentrated solution showed the sample was 99.3% deuterated.

4-Ethynyl-*d*-anisole was prepared similarly. The sample thus obtained after four exchanges was isolated in the usual manner and purified by sublimation at atmospheric pressure at room temperature, mp 26°. There was no evidence of an acetylenic hydrogen signal in the nmr spectrum. A sample of 4-ethynylanisole subjected to only two 24-hr equilibrations was 93% deuterated as shown by mass spectral analysis. The nmr spectrum of this sample still showed a small proton signal at 2.9 ppm at 60 Mc.

Kinetic Measurements. The kinetic methods have been described previously.[3] The rates of hydration of ethynylbenzene and ethynyl-*d*-benzene in sulfuric acid were measured at different times. The hydration rates of 4-ethynylanisole and 4-ethynyl-*d*-anisole, on the other hand, were measured simultaneously. This matched run technique involved using the same acid solution for dilution of the stock solutions and placing the uv cells in the thermostated cell compartment of the Beckman DU spectrometer simultaneously. Therefore, adventitious errors would tend to be minimized. Some matched runs were later performed on ethynylbenzene and ethynyl-*d*-benzene at several acidities, and these results were in complete agreement with the earlier determinations. All systems studied gave excellent pseudo-first-order kinetics beyond 95% reaction. No induction periods or other consistent deviations from first-order behavior were detected. Rate constants were independent of the wavelength at which they were determined.

The standard deviations calculated by a least-squares computer program showed the precision of the measurements to be good, the error limits obtained generally being less than ±1% in the observed rate constant.

For solutions in D_2SO_4, H_0 values used were those corresponding to the same mole fraction of sulfate, and rate comparisons were made at the same mole fraction of sulfate. The advantages of this method for comparing acidity in H_2SO_4 and D_2SO_4 have been discussed by Noyce, Avarbock, and Reed.[5c]

Results and Discussion

Solvent Isotope Effects. The rate of hydration of phenylacetylene and of selected substituted phenylacetylenes was measured in deuteriosulfuric acid solution. The rate data are given in Table I. In all cases excellent linear correlations with the acidity function H_0 are observed, and the best least-squares slope of a plot of the logarithm of the observed rate *vs.* H_0 is given in Table II. These slopes are similar to those obtained in sulfuric acid,[3] but not identical. Thus, the calculated solvent isotope effect, k_{H_2O}/k_{D_2O}, shows some variation with acidity, generally being larger for the more acidic solutions. Values of the solvent isotope effect are summarized in Table III.

For the most reactive of the substituted phenylacetylenes, *p*-methoxyphenylacetylene, data have been obtained in very dilute acid solutions. It is interesting to note that the solvent isotope effect is less than the predicted maximum value suggested by Bunton and

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[2] A portion of this material has been published in preliminary form: D. S. Noyce, Sr. M. A. Matesich, M. D. Schiavelli, and P. E. Peterson, *J. Amer. Chem. Soc.*, **87**, 2295 (1965).

[3] Previous paper: D. S. Noyce and M. D. Schiavelli, *ibid.*, in press.

[4] National Science Foundation Predoctoral Fellow, 1964–1966; National Institutes of Health Predoctoral Fellow, 1966–1967.

[5] *Cf., inter alia* (a) A. J. Kresge and Y. Chiang, *J. Amer. Chem. Soc.*, **84**, 3976 (1962); (b) J. Schulze and F. A. Long, *ibid.*, **86**, 231 (1964); (c) D. S. Noyce, H. S. Avarbock, and W. L. Reed, *ibid.*, **84**, 1647 (1962).

[6] D. S. Noyce, M. A. Matesich and P. E. Peterson, *ibid.*, **89**, 6225 (1967).

[7] D. S. Noyce and K. E. DeBruin, *ibid.*, **90**, 372 (1968).

[8] Melting points were determined using a Buchi melting point apparatus. Boiling points and melting points are uncorrected. Nmr spectra were obtained using a Varian A-60 or HA-100 instrument. Infrared analyses were carried out using a Perkin-Elmer Model 421 spectrophotometer; mass spectral analyses were obtained using a CEC 103 or CEC 130 instrument.

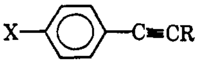
[9] H. Hogeveen and W. Drenth, *Rec. Trav. Chim.*, **82**, 375 (1963).

Table I. Hydration of Phenylacetylenes in Deuteriosulfuric Acid at 24.9°

Compd	Wt % D_2SO_4	10^4k_{obsd}, sec^{-1}	D_0[a]	$-$Log k_{obsd}
p-CH_3O	1.18	0.198	+0.73	4.704
	3.07	0.571	+0.30	4.243
	4.78	0.935	+0.09	4.029
	6.62	1.62	−0.07	3.790
	10.21	3.48	−0.37	3.458
	13.58	6.45	−0.63	3.190
p-Me	16.62	0.234	−0.85	4.631
	21.78	0.617	−1.18	4.210
	25.88	1.42	−1.46	3.847
	31.30	4.36	−1.87	3.361
	34.99	9.27	−2.15	3.033
	38.57	21.03	−2.46	2.677
H	37.30	0.924	−2.34	4.034
	40.78	2.12	−2.66	3.673
	40.92	1.975	−2.67	3.704
	45.46	7.570	−3.14	3.121
	47.23	11.34	−3.33	2.945
	48.24	14.67	−3.43	2.834
	49.03	21.40	−3.53	2.670
p-Cl	26.05	0.0275	−1.48	5.561
	29.28	0.0533	−1.71	5.273
	34.95	0.198	−2.15	4.704
	38.47	0.402	−2.45	4.396
	41.56	0.857	−2.74	4.067
	46.11	2.81	−3.21	3.551
Ethynyl-*d*-benzene	36.76	0.756	−2.28	4.121
	40.26	1.77	−2.60	3.751
	41.94	2.56	−2.75	3.591
	43.40	3.84	−2.93	3.415
	45.37	6.41	−3.15	3.193
	46.20	7.63	−3.24	3.117
	48.12	13.8	−3.44	2.859
	48.16	13.3	−3.45	2.877

[a] See Experimental Section.

Table II. Least-Squares Treatment of Acidity Dependence Data for Phenylacetylenes



Arylacetylene X	R	Temp, °C	Acidity range[a]	$-d \log k/dH_0$[b]	$-$Log k_0[c]	r[d]	Solvent	λ, mμ[e]
CH_3O	H	25.00	1.18–13.58	1.128 ± 0.023	3.893 ± 0.010	0.9992	D_2SO_4	296
CH_3O	D	24.88	0.49–14.10	1.185 ± 0.015	3.453 ± 0.008	0.9995	H_2SO_4	296
		44.93	0.12–5.92	1.033 ± 0.010	2.677 ± 0.010	0.9998	H_2SO_4	296
CH_3	H	25.00	16.62–38.57	1.212 ± 0.014	5.641 ± 0.025	0.9997	D_2SO_4	265
H	H	24.92	37.30–49.03	1.133 ± 0.023	6.699 ± 0.070	0.9990	D_2SO_4	256
H	D	24.92	5.98–48.77	1.237 ± 0.011	6.565 ± 0.027	0.9994	H_2SO_4	256
		24.85	36.76–48.16	1.055 ± 0.017	6.511 ± 0.050	0.9992	D_2SO_4	256
Cl	H	25.00	26.05–46.11	1.160 ± 0.023	7.249 ± 0.033	0.9992	D_2SO_4	266

[a] Weight per cent sulfuric acid. [b] Slope of log k_{obsd} *vs.* H_0 plot as determined by least squares. [c] Extrapolated rate at $H_0 = 0$, *i.e.*, intercept of log k_{obsd} *vs.* H_0 plot. [d] Correlation coefficient. [e] Wavelength at which rate of appearance of ketone was measured.

Shiner.[10] This fact is in accord with the suggestion that the proton is largely transferred from the solution to the acetylenic carbon at the transition state, a suggestion which results from a consideration of the magnitude of the Brønsted catalysis constant, α[3]. Extrapolation from the very dilute sulfuric acid range to the midrange (about 40% sulfuric acid) predicts a solvent isotope effect which is slightly above the suggested[10] maximum value of 3.6. Clearly other influences of the medium are important as well in this region of acidity.

The values of the solvent isotope effect for the other compounds studies generally fall in the range of 2 to 3.

These relatively large isotope effects compare favorably with those observed for a number of other acid-catalyzed reactions in which the rate-limiting step is the proton transfer. These values are not in agreement with solvent isotope effects observed for compounds which react by other possible mechanisms such as one involving equilibrium formation of the vinyl cation followed by slow attack by water.

Drenth and Hogeveen[11] have reported that the hydration of ethylthioethyne to ethyl thiolacetate exhibits a solvent isotope effect, k_{H_2O}/k_{D_2O}, of 2.1. Similarly, the hydration of the triple bond in *cis*-1-propenyl propynyl ether in 5×10^{-3} *M* $HClO_4$ proceeds 1.8 times more slowly in $DClO_4$.[12] Previous reports from these laboratories have shown that the hydration of phenylpropiolic acids[6] and phenylbenzoylacetylenes[7] also proceeds more slowly in deuterated media. These reactions all involve an A–SE2 mechanism, *i.e.*, a slow proton transfer.

In contrast, a mechanism which involves the rate-limiting addition of water to a vinyl cation would be expected to exhibit an inverse solvent isotope effect. Perhaps the most pertinent example of such a reaction is the *cis–trans* isomerization of chalcone which has been shown by Noyce and coworkers[13] to proceed by a rate-limiting addition of water. *cis*-Chalcone isomerizes twice as rapidly in D_2SO_4 as in H_2SO_4.

Secondary Isotope Effects. The demonstration[3] that the exchange of the acetylenic hydrogen with the acid, though observable, proceeds only to a very minor extent makes it possible to examine the rate of hydration of ethynyl-*d*-benzene. Such studies provide valuable information regarding the nature of secondary isotope effects in the hydration of phenylacetylene.

Two compounds have been examined in some detail. Rate data are given in Table IV. The hydration of ethynyl-*d*-benzene in sulfuric acid is slower than its protium analog. The slope of a plot of the logarithm of the observed rates *vs.* H_0 is the same (-1.24) as for the protium analog. Hence, each determination of the secondary isotope effect at different acidities constitutes one point in a multiple determination. The value of k_H/k_D is thus 1.11 ± 0.005.

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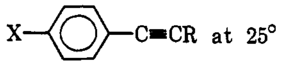
(10) C. A. Bunton and V. J. Shiner, Jr., *J Amer. Chem. Soc.*, **83**, 3214 (1961).

(11) W. Drenth and H. Hogeveen, *Rec. Trav. Chim.*, **79**, 1002 (1960).

(12) E. J. Stamhuis and W. Drenth, *ibid.*, **82**, 394 (1963).

(13) D. S. Noyce, G. L. Woo, and M. J. Jorgenson, *J. Amer. Chem. Soc.*, **83**, 1160 (1961).

Table III. Solvent Deuterium Isotope Effects for the Hydration of Phenylacetylenes



X	R	$-H_0$ range	$(k_{H_2SO_4}/k_{D_2SO_4})^a$	$(k_{H_2SO_4}/k_{D_2SO_4})^b$
CH_3O	H	−0.73–0.60	2.67–3.18	3.82
CH_3	H	0.85–2.12	2.39–2.74	2.70
H	H	2.34–3.24	2.67–3.32	2.46
H	D	2.28–3.26	2.30–3.47	2.04
Cl	H	1.91–3.21	2.97–3.10	2.98

[a] Range of values observed. [b] Isotope effect at $H_0 = -2.0$.

Table IV. Hydration of Deuteriophenylacetylenes in H_2SO_4

Compound	Wt % H_2SO_4	10^4k_{obsd}, sec^{-1}	H_0	$-\text{Log}\ k_{obsd}$
	At 24.9°			
Ethynyl-*d*-benzene	5.98	0.00251	+0.02	6.600
	31.78	0.402	−1.77	4.396
	33.94	0.629	−1.93	4.201
	33.95	0.624	−1.93	4.204
	34.53	0.752	−1.97	4.124
	37.34	1.43	−2.18	3.845
	39.80	2.64	−2.38	3.579
	41.89	4.21	−2.57	3.375
	41.89	4.45	−2.57	3.352
	43.50	6.91	−2.72	3.160
	43.69	6.67	−2.76	3.176
	43.77	6.73	−2.76	3.172
	43.98	8.26	−2.78	3.083
	44.90	9.94	−2.86	3.003
	46.48	15.3	−3.03	2.815
	48.73	27.5	−3.26	2.560
	48.77	24.8	−3.26	2.606
4-Ethynyl-*d*-anisole	0.49	0.179	+1.11	4.746
	1.55	0.584	+0.65	4.234
	3.04	1.30	+0.34	3.887
	6.00	3.28	+0.02	3.484
	6.06	3.34	+0.01	3.476
	9.64	7.34	−0.25	3.134
	9.73	7.63	−0.26	3.118
	14.10	17.7	−0.60	2.752
	At 44.9°			
Ethynyl-*d*-benzene	32.54	3.97	−1.83	3.401
	32.56	3.78	−1.83	3.422
4-Ethynyl-*d*-anisole	0.12	0.320	+1.74	4.494
	0.34	0.918	+1.34	4.037
	0.47	1.25	+1.19	3.093
	1.48	3.99	+0.70	3.399
	2.98	8.15	+0.39	3.089
	5.92	17.8	+0.06	2.751
	5.92	18.7	+0.06	2.728

For 4-ethynyl-*d*-anisole the situation is much the same. The value of the secondary isotope effect k_H/k_D is 1.07 ± 0.005. At higher temperatures the secondary isotope effect is substantially less, dropping at 45° to about 1%.

Noyce and coworkers[2] pointed out that the enhanced reactivity of phenylacetylene relative to 1-phenylpropyne parallels the difference in heats of hydrogenation of propyne and 2-butyne. A major factor contributing to this difference seems to be the difference in rehybridization energies involved in going from a C_{sp}–H bond to C_{sp^2}–H bond in the transition state for phenylacetylene as compared to the change from C_{sp}–C_{sp^3} to C_{sp^2}–C_{sp^3} for 1-phenylpropyne.

These bond-rehybridization changes are intimately involved in the origin of α secondary isotope effects for such changes result in a marked change in C–H bending frequencies. The direction of such an effect is predictable from the direction of the rehybridization change in terms of the p character of a C–H bond. Numerous examples of α isotope effects which arise from rehybridization changes in the direction of less p character in the C–H bond are recorded in the literature; the prime examples are unimolecular solvolysis reactions.

Fewer examples are found of α isotope effects for reactions which involve changes toward more p character in the substituted C–H bond. Denney and Tunkel[14] have observed that the isotope effect for addition of a number of reagents across the double bond in *trans*-stilbene is less than unity and varies only slightly from 0.88 over a wide range of temperatures and solvent polarities. A similar situation obtains in the Diels–Alder reaction of maleic-d_2 anhydride with cyclopentadiene[15] where the α isotope effect observed is also less than unity.

The hydration reaction studied here involves a hybridization change toward more p character in the C–H bond. The calculated isotope effect for phenylacetylene using Streitwieser's[16] simplified equation is 0.57.[17] This model takes into account only changes in carbon–hydrogen stretching and bending frequencies. However, Drenth and coworkers[9] have pointed out in the case of the hydration of $C_2H_5SC{\equiv}CH(D)$ that the substitution of deuterium affects the carbon–carbon triple bond stretching frequency. This effect is not counterbalanced by a corresponding change in the carbon–carbon double bond stretching frequency upon isotopic substitution. The triple bond stretching frequency is 2115 cm^{-1} [18] in phenylacetylene and is 1989 cm^{-1} in ethynyl-*d*-benzene, whereas the corresponding values for $CH{=}CH_2$ and $CH{=}CHD$ are 1620 and 1637 cm^{-1}, respectively.[9] From this more elaborate treatment, the α isotope effect is predicted to be 0.74.

The secondary isotope effect in the hydration reaction is not solely dependent upon the α effect for its origin. In the transition state, the isotopically substituted C–H bond is ideally situated for overlap with the developing, vacant p orbital, as shown in Figure 1. This hyperconjugative interaction is normally designated as a β secondary isotope effect. The combination of these two effects then gives rise to the observed isotope effects which are compiled in Table V. The hybridization of the terminal carbon atom gives rise to an α effect predicted to be less than unity. Secondly, any hyperconjugative interaction in the transition state lowers the bending frequency of the C–H bond in the transition state and results in a β contribution to the isotope effect greater than unity.

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(14) D. B. Denney and N. Tunkel, *Chem. Ind.* (London), 1383 (1959).

(15) D. E. Van Sickle, *Tetrahedron Letters*, 687 (1961).

(16) A. Streitwieser, Jr., R. H. Jagow, R. C. Fahey, and S. Suzuki, *J. Amer. Chem. Soc.*, 80, 2326 (1958).

(17) C–H frequencies used in calculating α effect:

	Initial state	Transition state
Stretching	3315 cm^{-1}	3085 cm^{-1}
Bending	648 cm^{-1}	"In plane" 1451 cm^{-1}
	648 cm^{-1}	"Out of plane" 990 cm^{-1}

(18) A. D. Allen and C. D. Cook, *Can. J. Chem.*, 41, 1084 (1963).

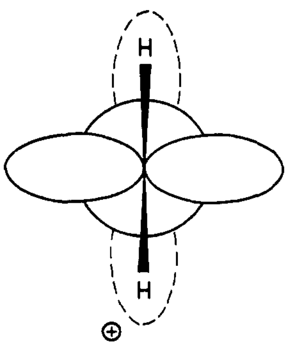

Figure 1. Hyperconjugative overlap in vinyl cation.

That contribution to the secondary isotope effect which arises through hyperconjugative interaction in the transition state should show some dependence on the relative amount of positive charge at the carbon atom adjacent to the ring, as Streitwieser and coworkers[15] have suggested. This hypothesis is supported by the work of Shiner and coworkers[19] on the variation of the β secondary isotope effect with the degree of carbonium ion character in the transition state of a number of solvolysis reactions. They note that the apparent demand for hyperconjugation decreases as the degree of carbonium ion character decreases.

Table V. Observed Secondary Isotope Effects

Compound	k_H/k_D at 25°	k_H/k_D at 45°
p-$CH_3OC_6H_4C{\equiv}CH$	1.07 ± 0.005	1.11–0.98[a]
$C_6H_5C{\equiv}CH$	1.11 ± 0.005	—

[a] Decreases with increasing acidity in the range 0.12 to 5.92% acid.

Recently, Shiner and coworkers[20] have examined the effect of ring substitution on the α and β secondary isotope effects in the solvolysis of α-phenethyl halides. While the α effect remains constant with substituent, the β effect decreases as more electron-releasing substituents are placed in the ring.

The results of the study of such a dependence by varying the *para* substituent in phenylacetylene hydration can be seen in Table V. Although the α effect probably remains constant,[21] the hyperconjugative effect should become less important when a methoxy group is placed in the ring.

Assuming then that the α secondary isotope effect is constant and equal to 0.74, the β secondary isotope effects are 1.50 and 1.44 for the phenylacetylene and *p*-methoxyphenylacetylene, respectively. These values are in good agreement with the values reported by Shiner and coworkers[22] in the solvolysis of *cis*-4-*t*-butylcyclohexyl brosylate-*trans*-2-*d* where the dihedral angle between the developing p orbital and the bond of the hydrogen isotope is also 180°. The value they observed is 1.44. Furthermore, the relative order of these values in acetylene hydration constitutes firm evidence of hyperconjugative stabilization in the vinylic cations formed in the hydration reaction of phenylacetylenes.

Analogously, Drenth and coworkers[9] have reported that ethylthioethyne hydrates 0.97 times as rapidly as ethylthioethyne-*d*. They suggest that this result may be due to the cancelling of two effects as described above. In this case the cation I is substantially stabilized by resonance interaction with the sulfur atom II which also accounts for the higher rates of hydration of such ethers compared to phenylacetylenes. It would

$$\underset{\text{I}}{C_2H_5S\overset{+}{C}{=}CH_2} \longleftrightarrow \underset{\text{II}}{C_2H_5\overset{+}{S}{=}C{=}CH_2}$$

be expected, therefore, that the need for hyperconjugative interaction might be substantially lowered leading to an observed isotope effect closer to unity, *i.e.*, in the direction of a greater relative α contribution than in phenylacetylene.

Finally, attention should be called to the interplay of these two influences in two other situations. In the hydration of styrene and styrene-β,β-d_2, k_H/k_D is reported by Schubert and Lamm[23] to be 1.02. Here the activated complex has the two deuteriums much more nearly in the nodal plane, and hyperconjugative interaction is suppressed.

Similar considerations apply in aromatic hydrogen exchange, and have been discussed by Streitwieser, *et al.*,[16] and Schulze and Long.[5b]

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(19) V. J. Shiner, Jr., J. W. Wilson, G. Heineman, and N. Salliday, *J. Amer. Chem. Soc.*, **84**, 2408 (1962).

(20) V. J. Shiner, Jr., W. E. Buddenbaum, B. L. Murr, and G. Lamaty, 154th National Meeting of the American Chemical Society, Chicago, Ill., Sept 1967, Abstract 7S.

(21) The α effect is dependent upon the degree of hybridization change at the reaction center. This in turn is related to the degree to which the proton has been transferred in the transition state. Since the solvent isotope effects for ethynylbenzene and 4-ethynylanisole do not differ substantially, it appears that the degree of hybridization change is very similar in the two transition states.

(22) V. J. Shiner, Jr., and J. G. Jewett, *J. Amer. Chem. Soc.*, **86**, 945 (1964).

(23) W. M. Schubert and B. Lamm, *ibid.*, **88**, 120 (1966).