A modification of the usual Volhard procedure was required to determine the amount of hydrogen bromide liberated as a function of time, since excess silver ion strongly catalyzes the solvolysis of alkyl halides. Samples were removed periodically from the constant-temperature bath, quenched in a Dry Ice–acetone bath, and opened. The contents were transferred quantitatively to a 250-ml erlenmeyer flask containing a cold solution of 1.000 ml of 0.1752 *N* potassium thiocyanate (delivered by buret), 20 ml of chloroform, and 20 ml of a solution consisting of 2.5 ml of concentrated nitric acid, 2.0 ml of a saturated aqueous solution of ferric ammonium sulfate, and distilled water. The cold mixture was stirred vigorously with the aid of a magnetic stirring bar and titrated with 0.1783 *N* silver nitrate to a colorless end point. After two half-lives, the remaining samples were removed from the constant-temperature bath and added to another constant-temperature bath at 94° for an additional 10 half-lives; the infinity point was then determined in triplicate. Control experiments indicated that analysis of a known amount of sodium bromide in the presence of *exo*-norbornyl bromide under the conditions described above could give results accurate to within 0.1%.

C. Conductometric Solvolyses of *endo*-Norbornyl Bromides. The solvent used in all kinetic studies was 50 vol % aqueous ethanol. The constant-temperature bath was maintained at 60.21 ± 0.01°. The conductance cells were of the Freas type with shiny platinum electrodes 1 cm^2 in area and spaced 1 cm apart. Several cells were used for the kinetic studies and rate constants were independent of the cell used. The conductance cells were filled almost to capacity with solvent and equilibrated in the bath before introduction of 4 μl of bromide. After ten solvolysis half-lives for the *exo* isomer (about 700 min), conductivity measurements for the *endo* isomer were begun. Measurements were recorded over a period of five half-lives. No systematic deviations from the first-order rate law were observed and the rate constants were independent of the initial concentration of bromide in the concentration ranges which we employed. Rate constants were reproducible to $\pm\sim 1\%$ and are summarized in Table II.

Acknowledgments. M. J. D. and D. S. W. wish to express their gratitude to the National Science Foundation for cooperative fellowships that they held during their tenures as graduate students. We also wish to thank the California Research Corp. for a research grant used to support a large portion of these studies.

The Decarboxylation of *p*-Methoxy-β-methylcinnamic Acid. Solvent Isotope Effects and Acid Catalysis[1]

Donald S. Noyce, Leon M. Gortler, Fred B. Kirby, and Melvyn D. Schiavelli[2]

Contribution from the Department of Chemistry, University of California, Berkeley, California 94720. *Received July 24, 1967*

Abstract: In dilute aqueous sulfuric acid, *p*-methoxy-β-methylcinnamic acid undergoes decarboxylation by a reaction which shows strong acid catalysis. In the region of 10–25% sulfuric acid, this reaction is characterized by a rate-determining proton transfer as shown by the fact that the solvent kinetic isotope effect, k_{H_2O}/k_{D_2O}, is 3. In more concentrated sulfuric acid (above 40%), the rate-limiting process changes as shown by the abrupt change in the solvent isotope effect, k_{H_2O}/k_{D_2O} decreasing to 1.7.

Recent studies from these laboratories have examined the complex interrelations among hydration and dehydration reactions, racemization processes, and the synchronous decarboxylation–dehydration reaction of variously substituted cinnamic acids and related β-hydroxy acids. It was shown[3] that β-phenyl-β-hydroxybutyric acid (**1**) undergoes dehydration in moderately concentrated sulfuric acid to give both the conjugated isomer, β-methylcinnamic acid (**2**), and the nonconjugated isomer, 3-phenyl-3-butenoic acid (**3**), at comparable rates. However, the acid-catalyzed hydration of **3** is very rapid and hence little **3** accumulates; the major product of acid-catalyzed dehydration is therefore **2**. Additionally it was shown that racemization of β-hydroxybutyric acids is more rapid than dehydration[4] in 1 *M* sulfuric acid.

In a related study,[1] of the decarboxylation of β-phenylcinnamic acid in sulfuric acid, a complex rate–acidity profile was observed. It was shown that this complex rate *vs.* acidity profile could be satisfactorily interpreted on the basis of a change in the rate-limiting process. At low mineral acid concentrations the rate-limiting process is acid-catalyzed hydration of β-phenylcinnamic acid and at high mineral acid concentrations the rate-limiting process is the synchronous decarboxylation–dehydration of an equilibrium low concentration of β,β-diphenyl-β-hydroxypropionic acid.

It is the purpose of the present report to examine further predictions from this group of conclusions about the pathways of these reactions.

Experimental Section

Materials. The preparation of β-(*p*-methoxyphenyl)-β-hydroxybutyric acid (**5**) and of β-(*p*-methylphenyl)-β-hydroxybutyric acid (**7**) has been described previously[4] as has the preparation of sulfuric acid-d_2.[5]

Kinetic Methods. Rate measurements were made by following the change in absorbance at 290–300 mμ, a region of the ultraviolet spectrum where the only strongly absorbing species is the substituted cinnamic acid. Solutions were generally 10^{-5} *M* in organic substrate; at this concentration carbon dioxide (bubble formation) generally caused no difficulty.

For preparation of kinetic solutions a weighed sample of β-(*p*-methoxyphenyl)-β-hydroxybutyric acid was dissolved in a measured small quantity of water. An aliquot of this solution was diluted with sulfuric acid of the requisite strength, rapidly mixed, and

---

[1] Previous paper: D. S. Noyce, S. K. Brauman, and F. B. Kirby, *J. Am. Chem. Soc.*, **87**, 4335 (1965).

[2] National Science Foundation Predoctoral Fellow, 1964–1966.

[3] D. S. Noyce and R. A. Heller, *J. Am. Chem. Soc.*, **87**, 4325 (1965).

[4] D. S. Noyce, L. Gortler, M. J. Jorgenson, F. B. Kirby, and E. C. McGoran, *ibid.*, **87**, 4329 (1965).

[5] D. S. Noyce, H. S. Avarbock, and W. L. Reed, *J. Am. Chem. Soc.*, **84**, 1647 (1962).

placed in the thermostated cell compartment of a Beckman DU spectrophotometer. Readings were initiated immediately. To determine the final sulfuric acid concentration, weighed aliquots of the kinetic solution were titrated.

The rate data were treated in two different ways depending upon the initial starting material used. The decomposition of *p*-methoxy-β-methylcinnamic acid (**6**) follows good pseudo-first-order kinetics in dilute sulfuric acid solutions and the observed kinetics at high acidities also fit a first-order rate law well. In high acidities measurement of the first few per cent reaction is precluded by the rapidity of the reaction. These data are recorded in Table IV.

Starting with **5** the absorbance due to **6** rapidly builds up, reaches a maximum, and slowly decays. From the early increase in absorbance a preliminary rate constant may be calculated. The final decline in absorbance matches that observed starting with **6** and the rate constant may be identified with the pseudo-first-order rate constant discussed above. Finally the maximum which is reached allows calculation of the fraction of **5** which initially goes to **6** and thus the ratio of rate constants k_2 and k_3 may be set.

These preliminary values for k_1, k_2, and k_3 were used to calculate time–concentration curves for all species and particularly to compare the time–concentration curves for **5**. Adjustments were made in the values of k_1, k_2, and k_3 and the computed curve (calculated with the aid of the IBM 7094 and an *x-y* plotting routine) was adjusted for the best match with the experimental data. The first approximations were within 10–15% of the finally accepted values, which were obtained by one or two adjustments of the values of k_1, k_2, and k_3. Further iteration did not seem warranted.

Results and Discussion

Dehydration of β-Anisyl-β-hydroxybutyric Acid (5). In 30–40% sulfuric acid, β-anisyl-β-hydroxybutyric acid (**5**) reacts very rapidly; straightforward dehydration to *p*-methoxy-β-methylcinnamic acid (**6**) competes with synchronous decarboxylation and dehydration. This situation is analogous to the behavior of β-phenyl-β-hydroxybutyric acid[3] which has been studied in detail. Those studies allow the following simplifications to be invoked for the present study. Even though the formation of a small fraction of 3-phenyl-3-butenoic acid (**3**) occurs rapidly, the fraction of **3** present is always extremely small.[3] In the present instance, therefore, the extraneous formation of small amounts of 3-anisyl-3-butenoic acid may be ignored without in any way vitiating the results obtained. Thus a kinetic investigation which discards the first very small amount of reaction will yield meaningful results. Further the very rapidity of the reactions of β-anisyl-β-hydroxybutyric acid in 30–40% sulfuric acid precludes an examination of the initial few per cent reaction.

Measurement of the absorption increase at 300 mμ as a function of time permits determination of both the rate of formation of *p*-methoxy-β-methylcinnamic acid (**6**) and the fraction of **5** converted to **6**. The total rate of disappearance of **5** can readily be determined as other compounds formed concurrently are essentially transparent in this region of the spectrum. The absorbancy at 300 mμ first reaches a maximum and then slowly decreases. Associating the decrease in absorbancy with the acid-catalyzed destruction of *p*-methoxy-β-methylcinnamic acid shows that the two stages in the change of optical absorbancy can be treated almost independently. For the first stage the

$$\begin{array}{l} \text{hydroxy acid} \xrightarrow{k_{-\mathrm{H_2O}}} \text{cinnamic acid} \\ \quad \lfloor\!\xrightarrow{k_{-\mathrm{CO_2}}} \text{styrene} + \mathrm{CO_2} + \mathrm{H_2O} \end{array} \qquad (1)$$

schematic situation in (1) then allows for determination of both the rate of dehydration, $k_{-\mathrm{H_2O}}$, and the rate of synchronous decarboxylation, $k_{-\mathrm{CO_2}}$, once the fraction of *p*-methoxy-β-methylcinnamic acid formed in the initial stages of the reaction is determined. Values obtained graphically were adjusted to give the best fit to the exact equation by computer techniques.

Tables I and II give the relevant results. A plot of the logarithm of the rate of dehydration *vs.* the acidity function, H_0, gives the typical result of a slope somewhat greater than unity; the slope of the plot of the rate of synchronous decarboxylation *vs.* H_0 gives the shallow rate–acidity profile observed previously.[3]

Table I. Extent of Dehydration of β-(*p*-Methoxyphenyl)-β-hydroxybutyric Acid in Aqueous Sulfuric Acid at 25°

H_2SO_4, %	H_0	OD_{max}[a]	Dehydn, %
33.00	−1.92	0.265 0.262	31 ± 1
37.10	−2.21	0.330 0.336	40 ± 1
42.21	−2.60	0.445 0.440 0.426	53 ± 2
48.03[b]	−3.17	0.530	64 ± 3[b]

[a] For a solution originally 5.75×10^{-6} *M* measured in 10-cm cells, λ 290 mμ. [b] Less precise.

Table II. Rates of Reaction of β-(*p*-Methoxyphenyl)-β-hydroxybutyric Acid in Aqueous Sulfuric Acid at 25°

H_2SO_4	H_0	$k_{-\mathrm{H_2O}} \times 10^3$ sec^{-1}	$k_{-\mathrm{CO_2}} \times 10^3$ sec^{-1}
30.60	−1.76	1.16	2.66
33.00	−1.92	2.02	3.37
35.10	−2.06	3.24	4.38
37.10	−2.21	5.00	5.80
40.00	−2.41	9.59	7.91
42.21	−2.60	16.1	10.9

Brief examination of the behavior of β-(*p*-methylphenyl)-β-hydroxybutyric acid (**7**) under comparable conditions likewise allows determination of the rates for dehydration and for synchronous decarboxylation (Table III).

Table III. Rate of Reaction of β-(*p*-Methylphenyl)-β-hydroxybutyric Acid at 24.92°

H_2SO_4, %	H_0	$k_{\mathrm{total}} \times 10^4$ sec^{-1}	Dehydn, %	$k_{-\mathrm{H_2O}} \times 10^5$ sec^{-1}	$k_{-\mathrm{CO_2}} \times 10^5$ sec^{-1}
32.72	−1.91	1.17	31	3.63	8.07
34.40	−2.02	1.54	34	5.24	10.2
39.56	−2.38	3.30	47	15.5	17.4
39.58	−2.38	3.30	47	15.5	17.4
40.92	−2.49	4.48	50	22.4	22.4
41.01	−2.50	4.57	50	22.8	22.8
41.15	−2.51	5.33		26.6	26.6
42.41	−2.62	6.72	54	36.3	30.9
43.85	−2.75	8.52	57	48.6	36.6
45.32	−2.88	13.30	60	79.8	53.2

Patterns which emerge from these data are the following: the relative rates of formation of the three substituted cinnamic acids from the respective β-hydroxybutyric acids, **1**, **5**, and **7**, are correlated by a ρ value of

-3.9, using σ^+ substituent constants, a ρ similar to that for other carbonium ion reactions.[6]

The conditions under which dehydration to the cinnamic acid competes equally with synchronous decarboxylation and dehydration are very similar for the three hydroxy acids. This shows that the decarboxylative dehydration involves a charge distribution pattern and resonance involvement of the aromatic ring to an extent similar to that in simple dehydration. The involvement of a carbonium ion intermediate is naturally suggested by this similarity. However, the differences in H_0 slopes clearly suggest a difference in mechanism. These differences will be discussed later.

With the factual data in hand on the behavior of **5** and with a general pattern for the correlation of reactivities for these compounds, it is now interesting to turn to the behavior of *p*-methoxy-β-methylcinnamic acid. The destruction of *p*-methoxy-β-methylcinnamic acid in aqueous sulfuric acid is a relatively facile reaction. The course of the reaction can be followed by CO_2 evolution, but much more expeditiously and easily by the loss of optical absorbance in the region of 300 mμ.

The data over an extended range of mineral acid concentrations and at two different temperatures are given in Table IV. The decarboxylation of *p*-methoxy-β-methylcinnamic acid shows a complex rate profile when plotted against the acidity function H_0. It is most lucid to discuss these results in sections. In the range of low acidity, 0.1–3 *M* sulfuric acid, the observed rate is in fact the rate of hydration of β-methyl-*p*-methoxycinnamic acid. Justification for this assertion comes from the following lines of evidence.

Table IV. Decarboxylation of *p*-Methoxy-β-methylcinnamic Acid in Aqueous Sulfuric Acid

H_2SO_4, %	$-H_0$	$k_{obsd} \times 10^5$ sec^{-1}	Log *k*	Log *k* + H_0
		A. At 25.00°		
2.49	−0.55	0.200	−5.70	−5.15
9.67	0.24	0.966	−5.00	−5.24
16.51	0.76	2.66	−4.58	−5.32
23.03	1.23	7.00	−4.15	−5.38
23.50	1.26	7.45	−4.13	−5.39
28.33	1.60	15.4	−3.81	−5.41
29.77	1.70	17.8	−3.75	−5.45
32.66	1.90	26.3	−3.58	−5.48
37.00	2.20	42.8	−3.37	−5.57
38.38	2.30	48.1	−3.32	−5.62
39.78	2.40	56.3	−3.25	−5.65
43.39	2.71	60.8	−3.22	−5.93
43.80	2.74	61.9	−3.21	−5.95
47.91	3.16	74.5	−3.13	−6.29
54.85	3.89	121.0	−2.91	−6.80
		B. At 45.00°		
5.24	−0.07	3.10	−4.51	−4.44
6.36	0.05	4.28	−4.37	−4.42
12.10	0.50	10.3	−3.99	−4.49
16.64	0.81	20.3	−3.69	−4.50
19.57	1.01	32.5	−3.49	−4.50
22.39	1.21	45.3	−3.34	−4.55

Ample evidence has been accumulated to demonstrate that the hydration reaction of substituted cinnamic acids is acid catalyzed and that the rate-limiting step is the proton attack upon the olefinic system. From the studies of the conversion of *cis*-cinnamic acid into *trans*-cinnamic acid,[7] a ρ–σ^+ correlation was developed for such a hydration reaction.

In the study of the reaction of β-phenyl-β-hydroxybutyric acid, the rate of hydration (*i.e.*, the rate of proton attack) of 3-phenyl-2-butenoic acid (β-methylcinnamic acid) was measured. It is thus possible to extrapolate from these data to estimate very closely the rate of hydration of *p*-methoxy-β-methylcinnamic acid. In Table V is collected relevant information and these extrapolated rates. Thus the predicted rate for the hydration reaction in fact corresponds very closely (within a factor of 2) to the observed rate of loss of carbon dioxide in the more dilute acid region. The steps following hydration are fast under these conditions. This has been clearly demonstrated in the preceding paper.[1] The synchronous decarboxylation and dehydration is the exclusive reaction of the hydroxy acid under these conditions (dilute mineral acid) and moreover it is fast compared to the acid-catalyzed hydration discussed above. These conclusions parallel in all respects the situation observed with β-phenylcinnamic acid.

Table V. Rates of Hydration of Substituted Cinnamic Acids at 25.00°

	Log *k*			
Compound	H_0 = 0	H_0 = −2	H_0 = −3.39	H_0 = −4.00
cis-Cinnamic acid[a]	−9.79	−7.79	−6.40	−5.79
cis-*p*-Methoxycinnamic acid[b]	−6.44	−4.44	−3.05	−2.44
β-Methylcinnamic acid (**2**)[c]	−7.66	−5.66	−4.27	−3.66
p-Methoxy-β-methylcinnamic acid[d]	−4.94	−2.94	−1.55	−0.94
3-Anisyl-2-butenoic acid[e]	−5.24	−3.48	−3.04	−2.89

[a] Extrapolated using log $k + H_0 = -9.79$: D. S. Noyce, P. A. King, F. B. Kirby, and W. L. Reed, *J. Am. Chem. Soc.*, **84**, 1632 (1962). [b] Extrapolated from data in ref 7. [c] Extrapolated from data in ref 3, using log $k + H_0 = -7.66 \pm 0.05$. [d] Predicted from data for **2** using $\rho = -3.5$; log $k + H_0 = -4.94$. It is to be noted that a similar value of ρ for the hydration of 2-arylpropenes is reported by N. C. Deno, F. A. Kish, and H. J. Peterson, *J. Am. Chem. Soc.*, **87**, 2157 (1965). [e] Observed rate of decarboxylation interpolated from Table IV.

Shifting now to the behavior of *p*-methoxy-β-methylcinnamic acid in the highest concentrations of sulfuric acid in which measurements were made, the conclusions are very sharply reversed. Predicted rates of both hydration and dehydration are extremely fast and the extrapolated rate of decarboxylation from the hydroxy acid is also quite rapid. However, assuming a steady-state concentration of the hydroxy acid leads to a most satisfying picture, consistent in all respects. Again this conclusion is completely analogous to, and in accord with, the results reported for β-phenylcinnamic acid.

With these two extremes in hand the limiting slopes of the observed rate of decarboxylation are easily determined. At the extreme of low sulfuric acid concentrations the slope of log *k* *vs.* H_0 will be unity. At

---

(6) H. C. Brown and Y. Okamoto, *J. Am. Chem. Soc.*, **80**, 4979 (1958).

(7) D. S. Noyce and H. S. Avarbock, *ibid.*, **84**, 1644 (1962).

the limiting high sulfuric acid concentration the slope will be the sum of the slopes (*vs.* H_0) of log K (equilibrium constant for the hydration reaction) and log $k_{-\mathrm{CO}_2}$ (for the decarboxylation process proceeding from the hydroxy acid), as more fully discussed previously.[1]

Further, the region of sulfuric acid concentration in which the observed rate of decarboxylation for **6** sharply departs from the predicted rate of hydration of **6** is precisely the region (*ca.* 40% sulfuric acid) in which simple dehydration now competes favorably with synchronous decarboxylation and dehydration in the reactions of **5**. Thus the observed rate pattern for **5** and **6** is entirely explicable.

Solvent Kinetic Isotope Effects. A particularly useful test of this picture for the decarboxylation of *p*-methoxy-*β*-methylcinnamic acid is provided by a study of the solvent kinetic isotope effect. The results of kinetic measurements on the decarboxylation of **6** at four different acidities and at two different temperatures are summarized in Table VI.

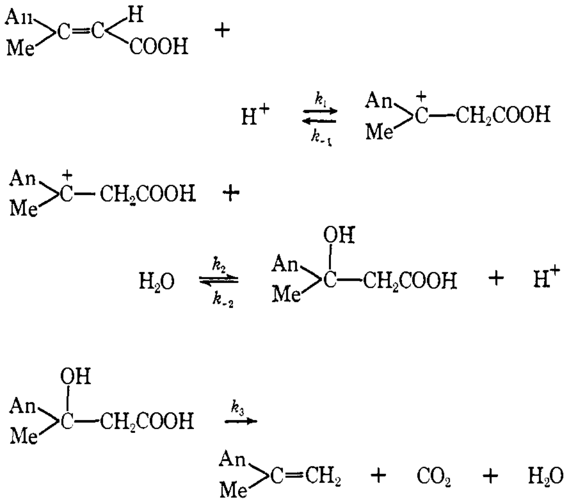
Table VI. Solvent Isotope Effects for the Acid-Catalyzed Decarboxylation of *p*-Methoxy-*β*-methylcinnamic Acid

D_2SO_4, wt %	Temp, °C	N_{SO_4}[a]	$k_{D_2O} \times 10^5$ sec^{-1}	$k_{H_2O} \times 10^5$ sec^{-1} [b]	k_{H_2O}/k_{D_2O}
13.10	45.0	0.02929	4.53	13.8	3.04
15.55	45.0	0.03554	6.95	20.5	2.96
26.11	25.00	0.06604	3.88	13.6	3.51
43.07	25.00	0.1315	38.2	66.0	1.72

[a] Mole fraction of sulfate. [b] Interpolated from the data in Table IV for comparisons at common mole fractions of SO_4.

At low mineral acid concentrations, the rate of decarboxylation is less in deuteriosulfuric acid, k_{H_2O}/k_{D_2O} being about 3. This result clearly shows that in 10–25% sulfuric acid, the reaction sequence is properly characterized by a rate-determining proton transfer. That this is proton transfer to the olefinic α carbon is amply justified by consideration of the substantial body of information regarding the *cis* and *trans* isomerizations of cinnamic acids which we have studied. Values of k_{H_2O}/k_{D_2O} for a variety of rate-determining proton additions to olefins have been measured; in the acid-catalyzed isomerization of *cis*-cinnamic acids, values between 3 and 6 were observed.[5] Similar results have been obtained from more recent studies of the acid-catalyzed isomerization of *cis*-stilbenes[8] and in the acid-catalyzed hydration of styrenes.[9]

Hence the following applies in more dilute sulfuric acid (eq 2–4), with step 1 rate limiting



$$\mathrm{An(Me)C{=}CH{-}COOH} + \mathrm{H^+} \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} \mathrm{An(Me)\overset{+}{C}{-}CH_2COOH} \quad (2)$$

$$\mathrm{An(Me)\overset{+}{C}{-}CH_2COOH} + \mathrm{H_2O} \underset{k_{-2}}{\overset{k_2}{\rightleftharpoons}} \mathrm{An(Me)C(OH){-}CH_2COOH} + \mathrm{H^+} \quad (3)$$

$$\mathrm{An(Me)C(OH){-}CH_2COOH} \xrightarrow{k_3} \mathrm{An(Me)C{=}CH_2} + \mathrm{CO_2} + \mathrm{H_2O} \quad (4)$$

but with little reversal (k_{-1} very small) and step 4 fast.

At increased sulfuric acid concentrations there is a marked change in the solvent kinetic isotope effect. The solvent kinetic isotope effect drops abruptly in going to 43% sulfuric acid.

These results are taken as an overwhelming indication of a change in the rate-limiting process. Solvent kinetic isotope effects for a variety of acid-catalyzed reactions do vary somewhat as the concentration of the catalyzing acid is changed; however, in more concentrated acid k_{H_2O}/k_{D_2O} tends to increase slightly,[5] not decrease abruptly.

In accord with this, the conclusion is drawn that the rate-limiting process has shifted to a later step in the reaction sequence and step 4 has become rate limiting.

Acknowledgments. This investigation was supported in part by grants from the National Science Foundation, G-13125 and GP-1572 and supported in part also by a grant from the Petroleum Research Fund administered by the American Chemical Society. Grateful acknowledgment is made to the donors of these funds. This investigation was also supported in part by a Public Health Service Fellowship (No. 1-Fl-GM-33805-01 to M. D. S. for 1966–1967) from the National Institute of General Medical Sciences.

---

(8) D. S. Noyce, D. R. Hartter, and F. B. Miles, *J. Am. Chem. Soc.*, **86**, 3583 (1964).

(9) W. M. Schubert, B. Lamm, and J. R. Keefe, *ibid.*, **86**, 4727 (1964).