

benzene is very short and is virtually independent of viscosity.²⁵ This implies that f_{\parallel} is near 0. Experiments also show that f_{\perp} is greater than 0.²⁵ The observed ratio $f_{\parallel}/f_{\perp} \approx 0$ for benzene cannot be predicted by any plausible configuration of beads in a scalar bead model, including the so-called shell models.^{45,46} Similar arguments may be made to show that bead models are inadequate for describing a number of other molecular rotations about axes of high symmetry, such as those of methane or methyl groups.

Physically, the low value of the rotational friction coefficient in small spherical molecules such as methane, or the sixfold ro-

tation of benzene, arises from the fact that no fluid is displaced as the molecule rotates freely within a cage of its neighbors. Caution is advised when modeling such systems with bead approximations; alternative approaches such as those of Hu and Zwanzig²⁴ or of Youngren and Acrivos⁴⁷ or an explicitly anisotropic bead treatment⁴⁸ may be more appropriate.

Registry No. Benzene, 71-43-2; toluene, 108-88-3; bromobenzene, 108-86-1; butane, 106-97-8; cyclohexane, 110-82-7; neopentane, 463-82-1; carbon tetrachloride, 56-23-5; chloroform, 67-66-3; ethyl iodide, 75-03-6; propyl iodide, 107-08-4; ethyl bromide, 74-96-4; hexafluorobenzene, 392-56-3; mesitylene, 108-67-8; *p*-xylene, 106-42-3; acetonitrile, 75-05-8; propyne, 74-99-7; methyl iodide, 74-88-4.

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Estimation of Malonic Acid and Methylmalonic Acid Enolization Rate Constants by an Isotopic-Exchange Reaction Using ¹H NMR Spectroscopy

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In the oscillatory Belousov-Zhabotinsky (BZ) reaction, bromination of the organic substrate is an important component process. Because bromination of the organic substrate in the BZ reaction occurs via an enolization mechanism, which generally is considered to be rate determining, the enolization rate constants are important parameters. In this paper, we report enolization rate constants of malonic and methylmalonic acid in 1 M sulfuric acid by following with ¹H NMR spectroscopy the isotopic substitution of enol-exchangeable hydrogen atoms by deuterium. We find for the first enolization step of malonic acid a rate constant of $(1.066 \pm 0.003) \times 10^{-3} \text{ s}^{-1}$ and for the second enolization step a rate constant value of $(4.2 \pm 0.2) \times 10^{-4} \text{ s}^{-1}$. The corresponding value for methylmalonic acid is $(5.7 \pm 0.1) \times 10^{-5} \text{ s}^{-1}$. While earlier literature data for malonic acid are difficult to compare with our present results, the determined enolization rate constant for methylmalonic acid is in excellent agreement with two other experimental determinations performed in 1 M sulfuric acid. When the sulfuric acid activity is taken into account, then methylmalonic acid enolization rates can be extrapolated to other sulfuric acid concentrations.

Introduction

The Belousov-Zhabotinsky^{2,3} (BZ) reaction is one of the most studied and best understood chemical oscillating reactions. Even in a closed system the reaction exhibits an unexpected wealth of dynamic behaviors ranging from sustained oscillations,¹⁻⁵ excitable behaviors,⁶⁻⁸ and chemical wave activity⁹⁻¹¹ to bistability.^{7,12-14} In general, a BZ reaction is the simultaneous bromination and oxidation of an organic substrate by bromate in the presence of a metal ion catalyst in aqueous acidic media.^{15,16} The basic mechanism was elucidated by Noyes and co-workers and is now known as the Field-Körös-Noyes (FKN) mechanism.⁵ An important feature of the mechanism is that bromide ion acts as a control intermediate.⁵ Recently, Field and Försterling¹⁷ revised the rate constants of the FKN mechanism and Noyes¹⁸ reviewed the subject.

Shortly after publication of the mechanism,⁵ Field and Noyes presented a simplified mathematical model of the FKN scheme, the so-called Oregonator model,¹⁹ which has been very successful in simulating and predicting various types of dynamic behaviors of BZ systems, including oscillations induced by silver ion^{20,21} or oscillations induced by other bromide ion removing reagents.²²⁻²⁴

Despite the success of the Oregonator model, criticism arose concerning to the stoichiometry of the bromide-regenerating step,²⁵

and subsequently Noyes²⁶ presented a revised version of the Oregonator model.²⁷ A characteristic feature of that model is

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its independence of the catalyst.

However, experimental results indicate that the catalyst itself has a considerable influence on the dynamics of BZ reactions.^{6b} This led Ruoff and Noyes²⁸ to propose an amplified Oregonator scheme. This model does not only omit, as in the case of the revised Oregonator, the criticized stoichiometric *f*-factor of the original¹⁹ Oregonator, but is also able to model excitability of a reduced steady state induced by silver ions and excitability of an oxidized steady state induced by bromide ions. The amplified Oregonator also simulates how oscillations in batch conditions during a single run might change from reduction pulses to oxidation pulses. Finally, this model is even able to simulate temporary bistability in a closed system.²⁸

The amplified Oregonator model implies that for almost every BZ system it should be possible to do semiquantitative simulations by considering only (i) the attack of the oxidized form of the catalyst on the organic substrate and (ii) the bromination rate of the organic substrate via enolization, as long as no considerable amount of bromine (Br₂) builds up.²⁸

Because bromination of the organic substrates used in BZ reactions proceeds via an enolization mechanism, the knowledge of enolization rate constants is necessary to simulate the dynamic behavior of BZ systems with different organic substrates.²⁸

This paper describes a relatively simple NMR procedure by which the enolization rate constants of various organic substrates can be estimated in strong aqueous acidic solutions by following the isotopic substitution of enol-exchangeable hydrogen atoms by deuterium. As an example, we have determined the enolization rate constants of malonic acid and methylmalonic acid in 1 M D₂SO₄. Although the first observation of such an isotopic exchange has qualitatively been described by Halford and Anderson²⁹ and Münzberg and Oberst³⁰ as early as 1936, to our knowledge no kinetic investigation of malonic and methylmalonic enolization rates exists in strongly acid aqueous media at 25 °C.

Methods of extracting enolization rate constants directly from NMR records of a complete BZ system will be the subject of another paper.³¹

Experimental Section

The ¹H NMR spectra were obtained on a Bruker CXP 200 pulse Fourier transform NMR spectrometer, operating at a frequency of 200 MHz. Sixteen scans for each record were accumulated over a bandwidth of 1.5 kHz with 16K data points and a 35° pulse angle.

All chemicals were of analytical grade, except methylmalonic acid (MeMA) which was of purum quality (>99%, Fluka, Switzerland). All chemicals were used without further purification.

The experiments were performed directly in the spectrometer at 25 ± 2 °C. The reaction volume was 0.75 mL (the spectrometer was equipped with a 5-mm probe), and all spectra were obtained with sample spinning under a nitrogen atmosphere and continuous stirring of the reaction medium. Peak areas in the spectrum were determined by using a mechanical integrating device ("PLANIX

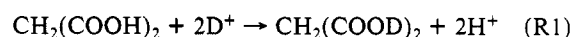
7", Tamaya, Japan) by taking the average of three area measurements for each peak. The estimated uncertainty of this procedure was less than 1%.

There was a time delay of approximately 10 min between mixing of the reagents and the start of NMR measurements, resulting from inserting the stirring equipment into the sample tube and fine shimming (i.e., improving the magnetic field homogeneity) of the sample. Although during these 10 min the concentration of nondeuteriated malonic acids may be reduced by up to 40%, there was no difficulty in extrapolating the observed exponential decay back to the initial conditions (*t* = 0). The extrapolated intensity at *t* = 0 is then equivalent to the initial amount of undeuteriated malonic acid, and all other concentrations are calculated from this reference intensity.

The reproducibility of our measurements was found to be within 10–15%, which we believe is due to temperature changes inside the NMR instrument.

Results

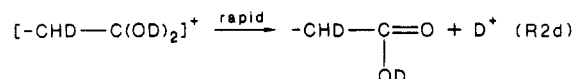
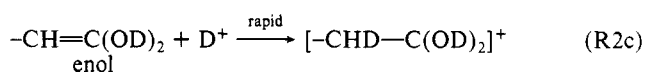
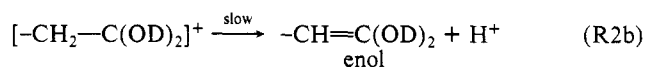
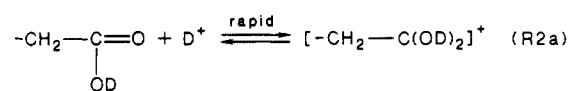
Malonic Acid. When malonic acid or 2-substituted malonic acids are dissolved in D₂SO₄ with D₂O as a solvent, two isotopic-exchange reactions occur where hydrogen atoms are replaced by deuterium. The first reaction is the very rapid exchange of the carboxylic protons by D⁺³²



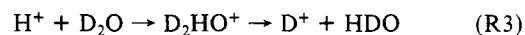
while the second process (R2) is the much slower exchange of the hydrogens attached to the central carbon:



The overall process R2 proceeds via two steps with the enol form of the malonic acid as an intermediate.³³ The sequence R2a–d illustrates the incorporation of deuterium (only one carboxyl group of the malonic acid is shown). Reaction R2a is a rapid pre-



equilibrium followed by the slow expulsion of H⁺ with formation of the enol. Although all steps are potentially reversible, reaction R2b is practically irreversible because any formed H⁺ is rapidly "absorbed" in the D₂SO₄/D₂O medium



and only approximately 1% of the total available hydrogen is ¹H⁺.

In substitution reactions, where a central malonic acid hydrogen is replaced by deuterium or a bromine atom, the rate-determining step is the formation of an enol intermediate.^{34–36}

Figure 1A shows a ¹H NMR spectrum of malonic acid dissolved in 1 M D₂SO₄/D₂O. We observe a single peak due to the two hydrogens attached to the central carbon.

Figure 1B shows the change of the malonic acid peak against reaction time. The appearance of the triplet is caused by the spin-spin coupling between the incorporated deuterium (a spin

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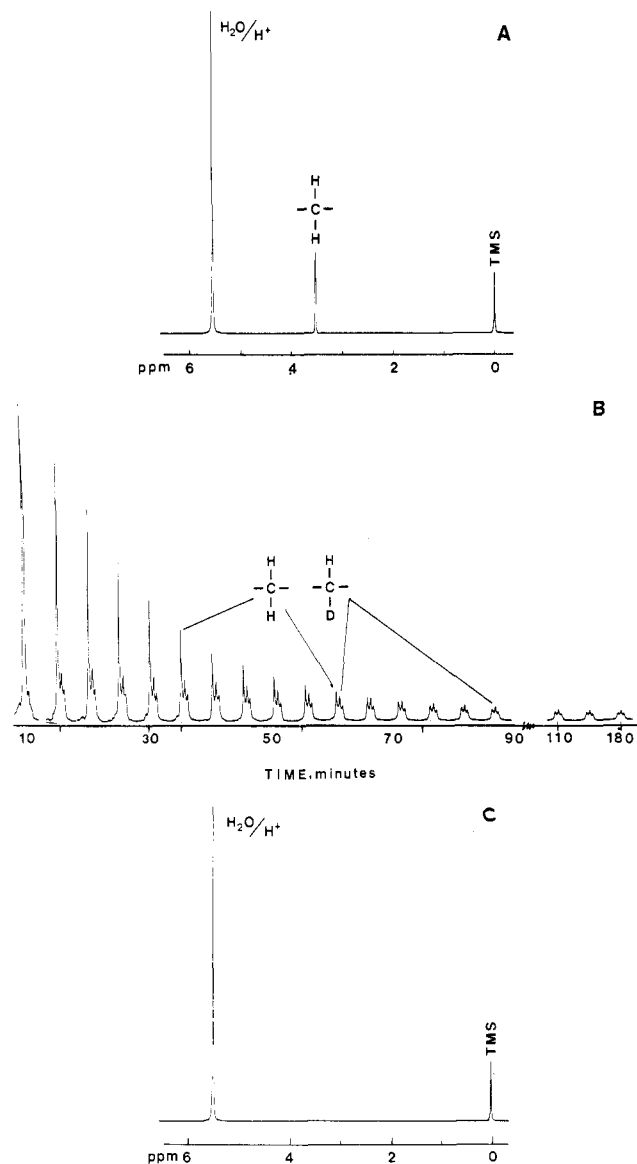
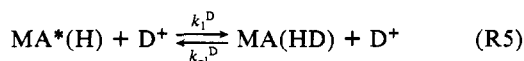


Figure 1. (A) ^1H NMR spectrum of malonic acid in 1 M D_2SO_4 . The single left peak is due to residual water protons from the solvent and the acidic protons from malonic acid. The singlet in the middle is due to the two protons in the undeuteriated malonic acid. (B) Time behavior of NMR composite signal from $\text{MA}(\text{H}_2)$ and $\text{MA}(\text{DH})$. The signal is composed of the $\text{MA}(\text{H}_2)$ singlet peak and the $\text{MA}(\text{DH})$ triplet. The triplet peak is caused by a coupling between the spin 1 nucleus, deuterium, and the spin $1/2$ nucleus, ^1H . (C) Final NMR spectrum when the two central hydrogen atoms have been replaced completely by deuterium. $\text{MA}(\text{D}_2)$ is not observable in the ^1H NMR spectrum.

1 nucleus) and the remaining hydrogen (a spin $1/2$ nucleus) in $\text{CHD}(\text{COOD})_2$.

Figure 1C shows the final ^1H NMR spectrum of malonic acid at the end of the reaction when both hydrogens have been replaced by deuterium: the malonic acid peaks have disappeared.

The simplified reaction scheme that describes the exchange of the central hydrogens by deuterium is



where R4 is the sum of processes R2a and R2b and R5 is the sum of processes R2c and R2d, and with the assignments

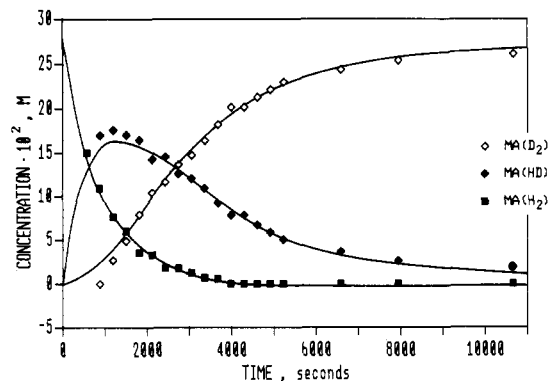
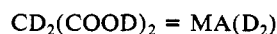
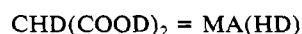
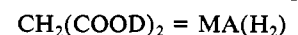
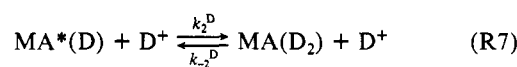


Figure 2. Concentration of different isotopic species of malonic acid vs time determined from NMR peak intensities. The concentration of $\text{MA}(\text{D}_2)$ is calculated from the material balance equation 1. The solid lines are calculated from eq 7-9.

The species with an asterisk are the enol forms.

Similarly, equations R6 and R7



describe the exchange of the second methylene hydrogen by deuterium in malonic acid. R4 and R6 are practically irreversible due to the proton "absorption" in the $\text{D}_2\text{SO}_4/\text{D}_2\text{O}$ medium (R3).

The species $\text{MA}(\text{D}_2)$ cannot be observed by ^1H NMR, but its concentration can be calculated by the mass-balance equation:

$$[\text{MA}(\text{H}_2)]_0 = [\text{MA}(\text{H}_2)] + [\text{MA}(\text{HD})] + [\text{MA}(\text{D}_2)] \quad (1)$$

The concentrations of the enol forms $\text{MA}^*(\text{H})$ and $\text{MA}^*(\text{D})$ are too low to be taken into consideration in the mass balance equation (1).

By assuming that the intermediate enol forms of malonic acid are in a steady state, i.e.

$$d[\text{MA}^*(\text{H})]/dt = 0 \quad (2)$$

$$d[\text{MA}^*(\text{D})]/dt = 0 \quad (3)$$

eq R4-R7 generate the rate equations

$$d[\text{MA}(\text{H}_2)]/dt = -k_1^{\text{H}}[\text{D}^+][\text{MA}(\text{H}_2)] \quad (4)$$

$$d[\text{MA}(\text{HD})]/dt = k_1^{\text{H}}[\text{D}^+][\text{MA}(\text{H}_2)] - k_2^{\text{H}}[\text{D}^+][\text{MA}(\text{HD})] \quad (5)$$

$$d[\text{MA}(\text{D}_2)]/dt = k_2^{\text{H}}[\text{D}^+][\text{MA}(\text{HD})] \quad (6)$$

Equations 4-6 can be solved analytically and have the solutions

$$[\text{MA}(\text{H}_2)] = [\text{MA}(\text{H}_2)]_0 \exp(-K_1^{\text{H}}t) \quad (7)$$

$$[\text{MA}(\text{HD})] = \frac{([\text{MA}(\text{H}_2)]_0 / (K_1^{\text{H}} - K_2^{\text{H}})) (\exp(-K_2^{\text{H}}t) - \exp(-K_1^{\text{H}}t))}{1} \quad (8)$$

$$[\text{MA}(\text{D}_2)] = \left\{ ([\text{MA}(\text{H}_2)]_0 K_1^{\text{H}} / (K_1^{\text{H}} - K_2^{\text{H}})) \exp(-K_1^{\text{H}}t) \right\} - \left\{ ([\text{MA}(\text{H}_2)]_0 K_1^{\text{H}} / (K_1^{\text{H}} - K_2^{\text{H}})) \exp(-K_2^{\text{H}}t) \right\} + [\text{MA}(\text{H}_2)]_0 \quad (9)$$

where $K_i = k_i[\text{D}^+]$.

Figure 2 shows the experimental concentrations of $\text{MA}(\text{H}_2)$, $\text{MA}(\text{HD})$, and $\text{MA}(\text{D}_2)$ as a function of time in 1 M D_2SO_4 . The solid curves in Figure 2 were obtained by first determining K_1^{H} from eq 7 by a nonlinear least-squares fit, inserting K_1^{H} into eq 8, and then determining K_2^{H} . This analysis yields K_1^{H} and K_2^{H} values of $(1.066 \pm 0.003) \times 10^{-3} \text{ s}^{-1}$ and $(4.18 \pm 0.2) \times 10^{-4} \text{ s}^{-1}$, respectively. The $\text{MA}(\text{D}_2)$ concentration was obtained by inserting the calculated rate constant values into eq 9.

Methylmalonic Acid. In methylmalonic acid there is only one exchangeable hydrogen atom on the central carbon atom.

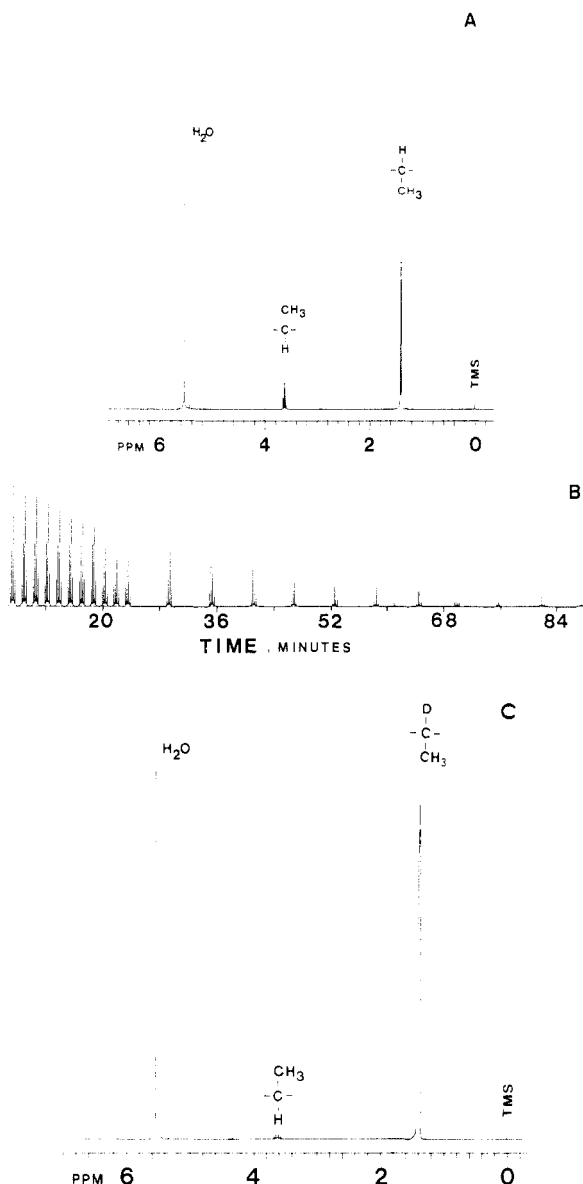


Figure 3. (A) ^1H NMR spectrum of methylmalonic acid (MeMA) dissolved in 1 M D_2SO_4 . (B) Intensity of the quartet peak (2.17 ppm) representing nondeuteriated methylmalonic acid (MeMA(H)) vs. time. (C) Final ^1H NMR spectrum of MeMA in 1 M D_2SO_4 .

Figure 3A shows the ^1H NMR spectrum of methylmalonic acid in 1 M D_2SO_4 . The quartet peak (next to the water peak) arises because the single proton attached at the central carbon couples with the three equivalent methyl protons. This quartet gives a unique and quantitative measure of the undeuteriated methylmalonic acid (MeMA(H)) concentration in the system. Figure 3B shows the quartet peak versus reaction time, and Figure 4 shows the logarithm of the peak area against time for three different D_2SO_4 concentrations.

In a similar way the deuteriated compound can be indirectly identified by the coupling between the deuterium nucleus and the methyl protons. Theoretically, the methyl protons in the deuteriated methylmalonic acid (MeMA(D)) should be seen in the spectrum as a triplet peak, but because of the quadrupole properties of the deuterium nucleus, we observe only a broad "singlet". Although there is a substantial overlap between the CH_3 doublet in MeMA(H) and the CH_3 "singlet" in MeMA(D), it has been possible to resolve the two peaks and to calculate the intensity of each of them.

We have confirmed experimentally that, within our experimental error, a mass balance holds:

$$[\text{MeMA(H)}]_0 = [\text{MeMA(H)}] + [\text{MeMA(D)}] \quad (10)$$

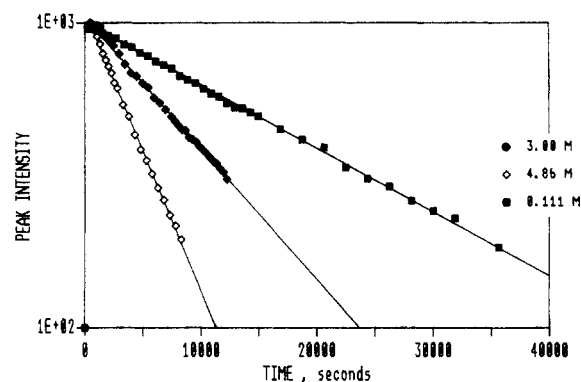
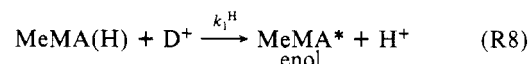


Figure 4. Logarithm (base 10) of quartet peak intensity of MeMA(H) vs. time for three different D_2SO_4 concentrations. The solid lines are calculated from eq 11.

As we have done for MA, we can also here describe the incorporation of deuterium into MeMA by the reaction scheme



with the corresponding first-order rate equation for $[\text{MeMA(H)}]$:

$$d[\text{MeMA(H)}]/dt = -K_1^{\text{H}}[\text{MeMA(H)}] \quad (11)$$

where $K_1 = k_1[\text{D}^+]$. Equation 11 can be solved analytically with the solution

$$[\text{MeMA(H)}] = [\text{MeMA}]_0 \exp(-K_1^{\text{H}}t) \quad (12)$$

where $[\text{MeMA(H)}]_0$ is the initial MeMA concentration.

The enolization rate constant K_1^{H} is calculated by finding the best least-squares fit of eq 12 to our experimentally observed peak areas. K_1^{H} was found to be $(5.7 \pm 0.1) \times 10^{-5} \text{ s}^{-1}$, and the solid lines in Figure 4 show the calculated fit.

Figure 5A shows K_1^{H} as a function of the D_2SO_4 concentration. We observe that this rate constant is a concave function of the sulfuric acid concentration. However, when taking into consideration the activity of the deuteriated sulfuric acid (Figure 5B),^{37,38} we observe a linear relationship between K_1^{H} and the sulfuric acid activity (Figure 5C). We have not incorporated the activity of the methylmalonic acid in our treatment, because this is of marginal significance.

Discussion

It is well-known that halogenation of compounds containing a reactive C-H group is usually kinetically of zero order with respect to halogen. The interpretation of Lapworth³⁴ is now generally accepted^{35,36} that the rate-determining step is the formation of a reactive enol, and enolization rates of malonic acid can therefore be determined indirectly from halogenation experiments. For malonic acid, however, only a few quantitative bromination^{39,40} and deuteriation⁴¹ experiments have been reported; but the experimental conditions under which these experiments were performed are so different from our experimental conditions that it is very difficult to make a quantitative comparison.

Also, for MeMA the few existing halogenation experiments⁴² differ very much from our experimental conditions so that a direct comparison of estimated enolization rate constants is almost im-

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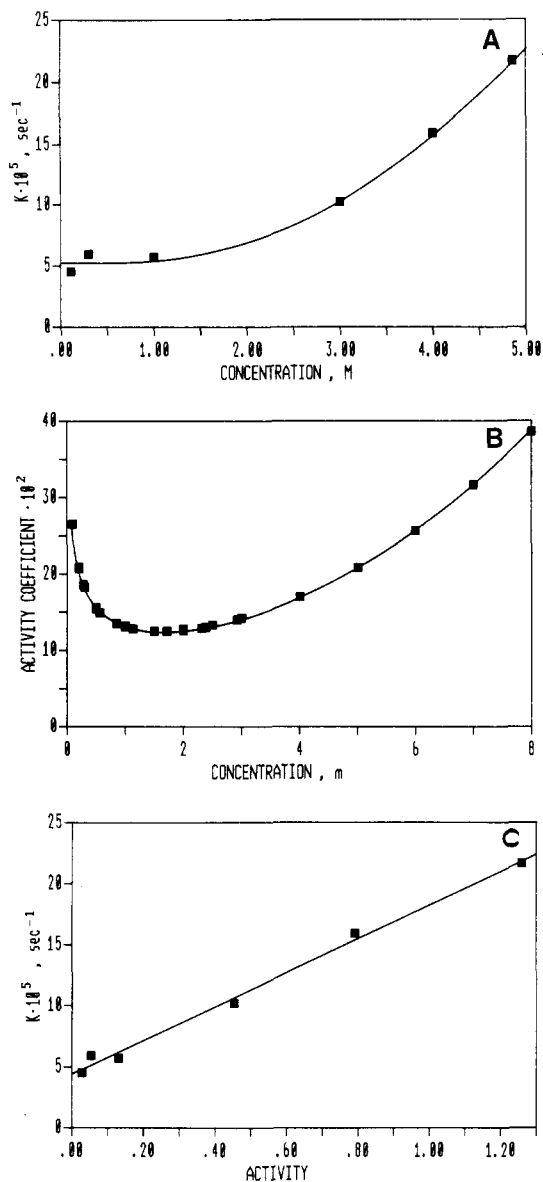


Figure 5. (A) K_1^H of MeMA as a function of D_2SO_4 concentration. (B) Activity coefficient of H_2SO_4 as a function of concentration. The data were taken from ref 34 and 35. (C) K_1^H of MeMA vs D_2SO_4 activity.

possible. However, in the case of MeMA, Ruoff and Schwitters⁴³ estimated the enolization rate constant in 1 M H_2SO_4 using induction-period-length data in the corresponding cerium-catalyzed BZ reaction. These results are in excellent agreement with the enolization data presented in this and in another³¹ paper.

In general, if a hydrogen transfer from the solvent or some acid solute is rate-determining, a normal isotope effect will arise in this particular reaction step. If, on the other hand, there is a rapid preequilibrium, in which the reactant is converted to its conjugate acid, as in step R2a, the (enol) intermediate will be present in a higher steady-state concentration in the heavy medium, because the dissociation of weak acids is generally smaller in the deuterated solvent system.^{44,45} Therefore, the rate of the subsequent (rate-determining) formation of the enol should be faster in the heavy system, provided this last step does not show an isotope

effect.^{44,45} Most of the accelerations of rate due to the use of D_2O as a solvent are on the order of 1.3–3.0.⁴⁴ We therefore expect that enolization rates performed by this technique might be faster by a factor of 1.3–3.0 compared to rates observed in H_2SO_4 . However, for MeMA, comparison with enolization rates in H_2SO_4 ⁴³ indicate that in this case the expected increase in enolization rate in the heavy medium is negligible.

For malonic acid no previous experimental data of enolization rates in 1 M sulfuric acid exist. However, from our methylmalonic acid results we expect that for the first malonic acid enolization step the measured rates in 1 M D_2SO_4 should be very close to rates one would obtain in 1 M H_2SO_4 . In the second enolization step of malonic acid, however, one deuterium atom has already been incorporated, such that K_2^H is subject to a secondary kinetic isotope effect. Therefore this rate constant may vary (at room temperature) by a factor of about 1.2, which generally is expected to arise from changes in the carbon hybridization. The secondary isotope effect may generally affect the rate constant in either direction.⁴⁶ Because of the statistical constraints K_1^H would be precisely twice as large as K_2^H if there were no isotope effects. Our observed K_1^H/K_2^H ratio of 2.55 shows that in this case the secondary kinetic isotope effect retards K_2^H by a factor of about 1.3 ($=2.55/2$).

In acid media, enolization is known to show general acid catalysis.⁴⁷ Taking, for example, methylmalonic acid, K_1^H can in principle be expressed as a sum of separate contributions:^{46,47}

$$K_1^H = k_1 + k_2[D^+] + k_3[D_2SO_4] + k_4[HSO_4^-] \quad (13)$$

where the first term often arises because of the catalysis by undissociated water.⁴⁶ Figure 5C shows that K_1^H is in fact expressed as

$$K_1^H = k_1 + k(a(D_2SO_4)) \quad (14)$$

where $a(D_2SO_4)$ is the activity of D_2SO_4 . The advantage of such a formulation is that methylmalonic acid enolization rates can be estimated for other sulfuric acid concentrations than those investigated by us, by simple extrapolation of the experimental data of Figure 5C, and by use of the activity coefficients of sulfuric acid of Figure 5B.

Conclusion

We have used a relatively simple NMR procedure to estimate enolization rate constants of organic compounds containing a reactive CH group. The experiments have been performed in 1 M D_2SO_4 at 25 °C but are expected to apply also to 1 M H_2SO_4 . As an example we have determined the rate constant of the first enolization step of malonic acid and methylmalonic acid, with the values $(1.066 \pm 0.003) \times 10^{-3} s^{-1}$ and $(5.7 \pm 0.1) \times 10^{-5} s^{-1}$, respectively. The second enolization step of malonic acid ($(4.18 \pm 0.19) \times 10^{-4} s^{-1}$) is subject to a secondary kinetic isotope effect, which decreases the rate constant by a factor of about 1.3. Finally, the observed methylmalonic acid enolization rate constant increases linearly with sulfuric acid activity. This makes it possible to obtain enolization rate constants for other sulfuric acid concentrations by simple linear extrapolation and use of the sulfuric acid activity-concentration relationship.

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