

## Kinetics and Mechanisms of the Acid-Catalyzed Cleavage of 1,3-Dioxoles and Isomeric 4-Alkylidene-1,3-dioxolanes

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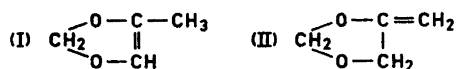
It is shown by kinetic methods that 4-methyl-1,3-dioxole (I) and its methyl-substituted derivatives are cleaved in their acid-catalyzed hydrolysis mainly as acetals (A-1 mechanism; ring atom 2 the carbonium ion center), whereas their isomers, 4-methylene-1,3-dioxolane (II) and the methyl derivatives of the latter, display vinyl ether hydrolysis (proton transfer rate-determining; carbon atom 4 the carbonium ion center). These conclusions are based on considerations of structural effects, deuterium solvent isotope effects, and the influence of Brønsted acids.

Thermochemical measurements indicate that I and its derivatives are energetically more stable than II and the corresponding derivatives by almost 10 kcal/mole. This is probably largely due to the stabilization of the  $p$ - $\pi$  electrons in the ring in the former compounds, as the number of these electrons is six. On the basis of this energy difference and the kinetic data, free energy profiles have been constructed for the possible routes of cleavage of I and II and their derivatives, from which it can be seen that the mechanistic differences largely originate from different initial state stabilities.

In earlier studies of the acid-catalyzed hydrolysis of a number of vinyl ethers,<sup>1,2</sup> the reaction was shown to be subject to general acid catalysis, on the basis of which and other experimental evidence it was concluded that the reaction involves as its rate-determining stage a proton transfer from the catalyst acid. The same conclusion has been also reached by Kresge and Chiang<sup>3</sup> in their recent investigation of ethyl vinyl ether.

Except for the hydrolyses of 2,3-dihydrofuran<sup>1</sup> and furans,<sup>4</sup> the investigations have been thus far limited to open-chain vinyl ethers. In the present study of cyclic vinyl ethers, the main interest was focused on the relation between the *endo* or *exo* position of the double bond and the kinetics of the ring rupture reaction. As examples of *endo-exo* isomeric vinyl ethers, 4-methyl-1,3-dioxole (I) and its 2-methyl-substituted derivatives were subjected to kinetic investigation along with their isomers, 4-methylene-1,3-dioxolane (II) and

its methyl derivatives. The kinetics and mechanisms of hydrolysis of the corresponding saturated compounds have been investigated in detail earlier.<sup>5-7</sup>



## EXPERIMENTAL

**Syntheses.** The preparation and physical data of 4-methylene-1,3-dioxolane, 2-methyl-4-methylene-1,3-dioxolane, and their isomers, 4-methyl-1,3-dioxole and 2,4-dimethyl-1,3-dioxole, have been described previously.<sup>8</sup> 2,2-Dimethyl-4-methylene-1,3-dioxolane was synthesized by the same methods. The following constants were determined for the last-mentioned compound: b.p. 49–51°C/95–98 torr,  $n_D^{20}$  1.4247,  $d_4^{20}$  0.9511.

**Kinetic measurements.** The course of the hydrolytic decomposition of most of the vinyl ethers studied was followed kinetically by measuring the increase of the carbonyl absorption by a spectrophotometric method using the same technique as in the previous study of vinyl ethers.<sup>1</sup> In the case of 2,2-dimethyl-4-methylene-1,3-dioxolane, however, it was more advantageous to follow the rate of disappearance of the carbon-carbon double bond absorption at approximately 232  $\mu$ , because it was found that the final carbonyl readings showed a tendency to decrease slightly with time, which was probably due to a slow subsequent reaction of the products formed in the hydrolysis. First-order kinetics was strictly obeyed in all cases, the standard errors of the rate coefficients being less than 1 % in each run.

Owing to the slowness of the hydrolysis of 4-methyl-1,3-dioxole, accurate kinetic data could not be obtained for this compound by the spectrophotometric method, and therefore the reactions were carried out in sealed glass ampoules,<sup>9</sup> which were broken at suitable time intervals and the unchanged 1,3-dioxole was analyzed by gas chromatography, following the procedure used when studying the hydrolysis of 2,3-dihydropyran.<sup>1</sup> The standard errors of the rate coefficients did not exceed 1 % in any run conducted by this method.

**Thermochemical measurements.** In order to obtain information about the relative stabilities of 4-methyl-1,3-dioxoles and the isomeric 4-methylene-1,3-dioxolanes, the *endo* and *exo* forms were equilibrated with acid catalysts in a variety of solvents and the equilibrium mixtures were subjected to gas-chromatographic analysis. It was found, however, that the quantities of the *exo* forms at equilibria were so minute that they could not be detected by gas chromatography. Therefore, the heats of isomerization were determined by combustion calorimetry, the entropies of isomerization being estimated by approximate methods.

The heats of combustion were measured employing a Parr Adiabatic Oxygen Bomb Calorimeter. Great care was paid to the purity of the compounds under study. The vinyl ethers were always freshly fractionated in a Todd precision fractionation assembly and their purities were confirmed by gas chromatography. Each combustion experiment was repeated 6–8 times. The standard errors of the values of the heats of combustion varied from 0.2 to 0.6 kcal/mole.

## RESULTS AND DISCUSSION

**Hydrolysis of 4-methylene-1,3-dioxolanes.** The rate coefficients at different temperatures and the least-square values of the parameters of the Arrhenius equation for the hydronium ion-catalyzed cleavage of 4-methylene-1,3-dioxolanes are collected in Table 1. The Arrhenius equation was satisfactorily obeyed in all cases.

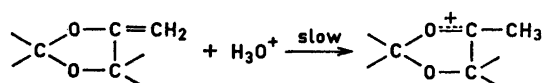
Table 1. Rate coefficients and derived kinetic quantities for the hydronium ion-catalyzed hydrolysis of 4-methylene-1,3-dioxolane and its 2-methyl derivatives in water.

1,3-Dioxolane	°C	$k_{\text{H}_3\text{O}^+}$ , $\text{M}^{-1}\text{s}^{-1}$	$E$ , kcal	$\log A$	$\Delta S^\ddagger$ , e.u.
4-Methylene-	25	$3.39 \pm 0.01$			
»	35	$7.15 \pm 0.01$	13.00	10.07	-14.5
»	45	$13.43 \pm 0.06$			
2-Methyl-4-methylene-	25	$7.58 \pm 0.02$			
»	35	$16.30 \pm 0.08$	13.67	10.90	-10.6
»	45	$32.33 \pm 0.18$			
2,2-Dimethyl-4-methylene-	10	$6.030 \pm 0.006$			
»	25	$18.02 \pm 0.03$			
»	35	$34.15 \pm 0.06$	12.05	10.08	-14.4
»	45	$63.9 \pm 0.1$			

The kinetic values of Table 1 may be compared with those measured earlier<sup>5,7</sup> for the corresponding saturated compounds, 4-methyl-1,3-dioxolane and its derivatives. It is seen that 4-methylene-1,3-dioxolane hydrolyzes faster than its saturated analog by a factor of  $10^6$ . Additional methyl substitutions at carbon atom 2 greatly increase the rate of hydrolysis of the saturated dioxolanes, in accordance with the postulated A-1 mechanism with the 2-carbon as the carbonium ion center, whereas in the case of the unsaturated dioxolanes, the influence of 2-methyl substitution is rather small.

The above facts clearly demonstrate that the hydrolysis mechanisms of the both series of compounds are different. This is also reflected by the values of the derived kinetic quantities. The activation entropies for the saturated dioxolanes are more positive by 10–20 e.u. and the energies of activation 7–12 kcal/mole higher than the corresponding values for 4-methylenedioxolanes.

The above facts are readily understood, if it is assumed that 4-methylene-1,3-dioxolanes are cleaved as vinyl ethers with proton transfer from the catalyst to the double bond as the rate-determining step<sup>1</sup> and with carbon atom 4 as the center of the intermediate alkoxy-carbonium ion:



This conclusion is supported by the fact that the reaction, unlike the hydrolysis of acetals, exhibits general acid catalysis. Table 2 gives values of the catalytic coefficients of undissociated acetic acid calculated from the rates in acetate buffers of varying acetic acid concentration. A comparison of these values with the respective catalytic coefficients for the hydronium ion (Table 1) shows that the value of the Brønsted constant  $\alpha$  is approximately of the same magnitude as for other vinyl ethers,<sup>1</sup> viz. about 0.5.

Table 2. Catalytic coefficients of undissociated acetic acid in the protolytic cleavage of 4-methylene-1,3-dioxolane and its 2-methyl derivatives in water at 25°C. Ionic strength = 0.24 M.

1,3-Dioxolane	No. of points in the plot	$10^3 \times k_{\text{CH}_3\text{COOH}} \text{ M}^{-1} \text{ s}^{-1}$
4-Methylene-	4	$3.52 \pm 0.12$
2-Methyl-4-methylene-	3	$7.88 \pm 0.34$
2,2-Dimethyl-4-methylene-	4	$41.1 \pm 0.8$

Table 3. Deuterium solvent isotope effect on the lyonium ion-catalyzed hydrolysis of 4-methylene-1,3-dioxolanes in water at 25°C.

1,3-Dioxolane	$k_{\text{D}_3\text{O}^+}$ (in $\text{D}_2\text{O}$ ), $\text{M}^{-1} \text{ s}^{-1}$	$k_{\text{D}}/k_{\text{H}}$
4-Methylene-	$1.304 \pm 0.004$	$0.385 \pm 0.002$
2-Methyl-4-methylene-	$2.530 \pm 0.006$	$0.334 \pm 0.001$
2,2-Dimethyl-4-methylene-	$5.51 \pm 0.01$	$0.307 \pm 0.001$

Table 3 shows values determined for the  $\text{D}_3\text{O}^+$ -catalyzed hydrolysis of the 4-methylene-1,3-dioxolanes studied in deuterium oxide, and the deuterium solvent isotope effects calculated from these values. Whereas in the case of the *A*-1 hydrolysis of acetals, the values of  $k_{\text{H}}$  are higher than those of  $k_{\text{D}}$  by factors of about 2.5,<sup>10</sup> the isotope effect is the inverse for the present compounds as for other vinyl ethers.<sup>1</sup>

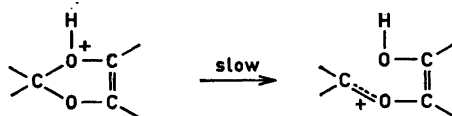
*Hydrolysis of 4-methyl-1,3-dioxoles.* Table 4 gives the values of the rate coefficients and Arrhenius parameters for 4-methyl-1,3-dioxoles, which are the *endo* isomers of the 4-methylene-1,3-dioxolanes discussed above. It is seen that the hydrolysis rate is lower by several powers of ten when the double bond is between the ring atoms (*cf.* Table 1).

Table 4. Rate coefficients and derived kinetic quantities for the hydronium ion-catalyzed hydrolysis of 4-methyl-1,3-dioxole and its 2-methyl derivatives in water solution.

1,3-Dioxole	°C	$10^4 \times k_{\text{H}_3\text{O}^+}$	<i>E</i> , kcal	log <i>A</i>	$\Delta S^\ddagger$ , e.u.
4-Methyl-	52.4	$0.996 \pm 0.010$			
»	66.7	$3.24 \pm 0.04$	24.92	12.70	-2.4
»	76.9	$14.92 \pm 0.15$			
2,4-Dimethyl-	25	$131.4 \pm 0.3$			
»	35	$451 \pm 1$	22.03	14.27	+4.8
»	45	$1360 \pm 5$			
2,4-Dimethyl- (in $\text{D}_2\text{O}$ )	25	$354.0 \pm 0.5^a$		$k_{\text{D}}/k_{\text{H}} = 2.69$	

<sup>a</sup>  $10^4 \times k_{\text{D}_3\text{O}^+}$

The results for the 1,3-dioxoles distinctly show that these compounds display *A-1* hydrolysis of acetals with the ring atom 2 as the carbonium ion center, *i.e.*, their hydrolysis involves a fast pre-equilibrium protonation followed by the subsequent rate-determining stage:



First, the values of the rate coefficients are almost the same as those of the corresponding saturated compounds, 1,3-dioxolanes. The following values (in  $M^{-1} s^{-1}$ ) were measured earlier<sup>5,7</sup> for the hydronium ion-catalyzed hydrolysis of 1,3-dioxolanes at 25°C: 4-methyl-1,3-dioxolane,  $3.24 \times 10^{-6}$ , 2,4-dimethyl-1,3-dioxolane,  $1.95 \times 10^{-2}$  (*cis* form),  $0.507 \times 10^{-2}$  (*trans* form), 2,2,4-trimethyl-1,3-dioxolane, 0.146. The value for 4-methyl-1,3-dioxole, at 25°C calculated by the Arrhenius equation from the data at other temperatures given in Table 4 is  $2.76 \times 10^{-6} M^{-1} s^{-1}$ . Second, the values of the entropies of activation for the hydrolysis of 1,3-dioxoles are of the same magnitude as those of their saturated analogs.<sup>5,7</sup> Third, the deuterium solvent isotope effect differs from that for 4-methylene-1,3-dioxolanes (see above) and is in the same direction and of the same magnitude as that for the hydrolysis of acetals in general.<sup>10</sup> Fourth, as no general acid catalysis was detected in experiments with buffer solutions the reaction is specifically hydronium ion-catalyzed.

*Relative thermodynamic stabilities of the isomeric compounds.* In order to gain an insight into the various factors which are responsible for the mechanistic differences between the *exo* and *endo* forms of the compounds studied,



the thermochemistry of the isomerization reaction was investigated. As mentioned in the experimental part, the amounts of the *exo* forms in the equilibrium mixtures were so minute that it was not possible to derive any values for the free energy differences,  $\Delta G^\circ$ , between the two forms from equilibrium studies. The difference in enthalpy could, however, be easily determined from the heats of combustion. The following values were obtained for the heats of combustion of the 2-methyl-substituted isomers at 25°C:

*Exo*, 4-methylene-2-methyl-1,3-dioxolane,  $-\Delta H^\circ (l) = 642.95 \pm 0.62$  kcal/mole. *Endo*, 2,4-dimethyl-1,3-dioxole,  $-\Delta H^\circ (l) = 633.92 \pm 0.27$  kcal/mole. Thus, as measured by the enthalpy difference, the *endo* form is more stable than the *exo* form by  $9.0 \pm 0.7$  kcal/mole.

The relative stabilities of the *endo* and *exo* forms of unsaturated cyclic hydrocarbons have recently been the subject of several investigations.<sup>11-12</sup> In the case of five-membered homocycles,<sup>11</sup> methylene cyclopentane (*exo*) and 1-methyl-cyclopentene (*endo*), the enthalpy difference is 3.9 kcal/mole

in favor of the *endo* form. This enthalpy difference is about 5 kcal/mole smaller than the corresponding differences between 4-methylene-1,3-dioxolanes and 4-methyl-1,3-dioxoles. The greater difference in stability in the latter case must largely be a consequence of additional stability of the 1,3-dioxoles due to the six *p*- $\pi$  electrons in the ring,<sup>13</sup> in principle similar to that in the furan ring,<sup>4</sup> although much smaller in magnitude. The empirical value for the "resonance energy" of furan is about 17 kcal/mole.<sup>14</sup>

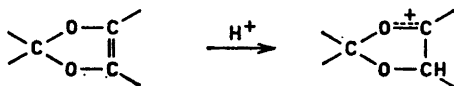
Although the free energy differences of the isomers cannot be measured directly, it can be concluded that the contribution of the entropy term to  $\Delta G^\circ$  is very small in magnitude in comparison with that of the enthalpy term. First, one can estimate by the group increment method of Franklin<sup>15</sup> that the  $T\Delta S^\circ$  term is about 0.5 kcal/mole for our *endo-exo* isomer pairs and acts in the same direction as the enthalpy term. Second, the measurements of Cope *et al.*<sup>12</sup> indicate that, for the corresponding pair of isomeric cyclic olefins,  $\Delta S^\circ$  for the change *exo*  $\rightarrow$  *endo* is 0.9 e.u. at 25°C, which gives 0.3 kcal/mole for  $T\Delta S^\circ$ . Thus, the standard free energy differences between 4-methylene-1,3-dioxolanes and 4-methyl-1,3-dioxolanes are approximately -9.5 kcal/mole with an accuracy of 1 kcal/mole. This means that the equilibrium ratio  $K = (\textit{endo})/(\textit{exo})$  is of the order of  $10^7$ .

*General considerations.* It is interesting to compare the actual magnitudes of the rate coefficients measured for 4-methylene-substituted 1,3-dioxolanes with those reported earlier for aliphatic vinyl ethers,<sup>1</sup> because the mechanisms of hydrolysis are similar for both classes of compounds. It is seen, *e.g.*, that the rate coefficients of 4-methylene-1,3-dioxolane and ethyl vinyl ether (25°C,  $\text{H}_3\text{O}^+$  as the catalyst) do not differ grossly in magnitude:



This is in good accord with the fact that the influence of the alkyl component of the ether on the rate of vinyl ether hydrolysis is relatively small, whereas the rate is greatly dependent on the nature of the group attached directly to the carbon atom which will become the center of the carbonium ion in the rate-determining stage.<sup>1</sup> As to the effect of the former type of substituent, it may be noted that the polarity of an alkoxyethyl group is almost the same as that of a hydrogen atom,<sup>16</sup> which accounts for the similar rates of the above compounds. By similar arguments it can be concluded that all 4-methylene-1,3-dioxolanes investigated are hydrolyzed at "normal" rates, *i.e.*, at rates expected by the proton transfer mechanism of vinyl ether hydrolysis.

Turning to the isomers of 4-methylene-1,3-dioxolanes, 4-methyl-1,3-dioxoles, it is seen that the situation is different owing to the great initial stabilization of the ring system. Protonation of the double bond would destroy this stabilization by reducing the number of *p*- $\pi$  electrons in the ring from six to four:



which renders the proton transfer mechanism very difficult for these compounds. The main reason for the fact that another hydrolysis mechanism becomes operative is therefore the initial state stability, which is about 10 kcal/mole greater than in 4-methylene-1,3-dioxolanes (see above).

An idea about the hydrolysis rates of 4-methyl-1,3-dioxoles by the vinyl ether mechanism (proton transfer rate-determining) may be gained in the following way. It is shown in a study of the corresponding furan derivatives,<sup>17</sup> 2-methylenetetrahydrofuran and the isomeric 2-methyl-4,5-dihydrofuran, that the transition states of the proton transfer mechanism of vinyl ether hydrolysis have almost the same free energy levels, the rate differences being thus virtually due to the differences in the initial state free energies. As the same must be approximately true for the isomers of the present study, when proton transfer to the ethylenic linkage takes place, one can estimate the free energy of activation at 25°C for the vinyl ether hydrolysis of 2,4-dimethyl-1,3-dioxole to be  $26.2 \pm 1.0$  kcal/mole, which corresponds to a rate coefficient of about  $10^{-7} \text{ M}^{-1} \text{ s}^{-1}$ . This is smaller by five powers of ten than the experimental value for 2,4-dimethyl-1,3-dioxole (Table 4) and therefore it is easily understood that an alternative reaction mechanism, the A-1 hydrolysis of acetals, is greatly favored in this case. The same applies also to 4-methyl-1,3-dioxole, although in this case, owing to the relatively low rates of hydrolysis of formaldehyde acetals, the hydrolysis rate by the vinyl ether mechanism is slower only by about two powers of ten.

An additional inference may be drawn from the kinetic data for 4-methyl-1,3-dioxoles in relation to the initial stability of the ring system. It was pointed out above that the rate coefficients for these compounds are virtually the same as those for the corresponding saturated compounds, 4-methyl-1,3-dioxolanes. As the latter compounds lack the stabilization of the six  $p$ - $\pi$  ring electrons present in the former compounds, it can be concluded that with the former compounds the initial stabilization is largely maintained in the transition state.

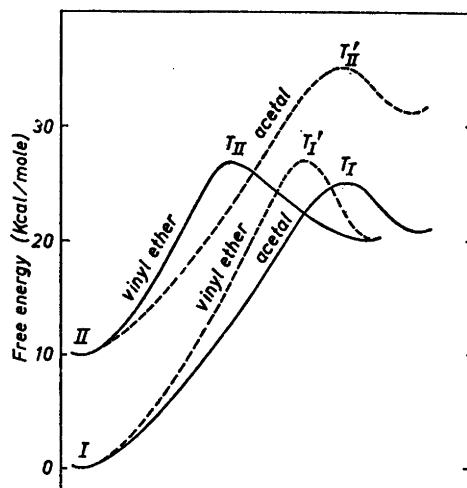


Fig. 1. Free energy profiles for possible routes of hydrolytic cleavage of 4-methyl-1,3-dioxoles (I) and the isomeric 4-methylene-1,3-dioxolanes (II). The solid curves refer to the actual mechanisms and the dashed curves to the alternative mechanisms discussed in the text.

In Fig. 1 are drawn the free energy profiles for the hydrolysis mechanisms discussed above. I and II are the initial states for the hydrolysis of 4-methyl-1,3-dioxoles and 4-methylene-1,3-dioxolanes, respectively, and the  $T$ 's are the corresponding transition states. The notation "acetal" refers to the acetal hydrolysis mechanism (A-1; carbon atom 2 as the carbonium ion center) and "vinyl ether" to the proton transfer mechanism of vinyl ether hydrolysis (carbon atom 4 as the carbonium ion center). For simplicity, the preliminary proton uptake equilibrium of acetal hydrolysis has been omitted from the profiles. In constructing the solid curves, the experimental values of 4-methyl-1,3-dioxole and 4-methylene-1,3-dioxolane at 25°C were used. The hypothetical profile for the vinyl ether mechanism of I has been drawn on the basis that the transition states of this mechanism must be at about the same free energy level for I and II.<sup>17</sup> The height of the transition state of II in the case of the acetal hydrolysis mechanism,  $T_{II}'$ , is based on the above discussion of structural effects, according to which the hydrolysis rate by this mechanism must be virtually the same as that reported earlier<sup>5,7</sup> for the corresponding saturated compound.

*Acknowledgements.* The authors wish to thank Mr. Jussi Heikkilä for the measurement of the heats of combustion, and the *National Research Council for Sciences* for financial support.

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Received June 7, 1967.