Determination of Relative Rates. Mixtures of 200 μL of a reference allene (1-ethylallene or 1-ethyl-1-methylallene), 200 μL of the allene whose relative rate was to be determined, and 100 μL of an internal standard (heptane) were prepared and analyzed by GLC on a 12-ft 10% Apiezon L on firebrick column. Allene to internal standard area ratios were determined by electronic integration of peak areas and were averaged over several analyses.

A 100-μL aliquot of each mixture (approximately 0.7 mmol of total allene) was added to individual NMR tubes containing 0.17 mmol of NPMI and 1 mL of xylene. The tubes were triply freeze degassed and sealed under a vacuum and were then heated in a sand bath at 160 °C until NMR analysis indicated the complete disappearance of the NPMI. The tubes were opened and the contents were analyzed by GLC to determine the allene-to-internal standard area ratios. The area ratios were converted to moles of each allene consumed (by density conversions), and the relative rates were calculated by an iterative computer program using competitive second-order reactions. The relative rate data appear in Table IV.

Measurement of Kinetic Isotope Effects. k_{H_2}/k_{D_2}. In an NMR tube was placed 0.0492 g (0.284 mmol) of NPMI, 0.0512 g of a mixture of 1,1-dimethylallene and its 3,3-d_2 analogue (32.94 ± 0.22% d_2, total of 0.746 mmol of allene), and 0.4 mL of xylene. The contents of the tube were triply freeze degassed, and the tube was sealed under vacuum. The tube was placed in a sand bath at 160 °C for 22 h, at which time analysis by NMR showed the absence of 1,1-dimethylallene with the formation of the 1:1 and 1:2 adducts in a 75.4:24.6 ratio. The tube was opened and the unreacted 1,1-dimethylallene was removed on a vacuum line. Analysis of the 1,1-dimethylallene by mass spectrometry[10b] showed the presence of 32.67 ± 0.28% d_2 isomer. The deuterium content of the 1:1 and 1:2 adducts was determined by mass spectrometric techniques[10b] on the reaction mixture with direct injection probe techniques. At temperatures <250 °C with partial lowering of the probe only peaks of the 1:1 adduct were present. The peaks of the 1:2 adduct became apparent after the 1:1 adduct had vaporized from the probe, the probe was fully lowered, and the temperature was raised to 300 °C. The 1:1 adduct contained 33.61 ± 0.37% d_2 (average of three analyses) and the 1:2 adduct contained 35.16 ± 0.16% d_2. The overall deuterium balance showed an excess of 0.4% d_2 in the products and recovered allene.

k_{H_6}/k_{D_6}. A mixture of 0.0490 (0.283 mmol) of NPMI and 0.0396 g of a mixture of 1,1-dimethylallene and 1,1-bis(trideuteriomethyl)allene (33.59 ± 0.36% d_6, total of 0.566 mmol of allene) in 0.4 mL of xylene was treated as described above. The ratio of the 1:1 to 1:2 adducts was 79:22. The recovered 1,1-dimethylallene contained 36.33 ± 0.13% d_6, the 1:1 adduct contained 32.36 ± 0.38% d_6, and the 1:2 adduct contained 27.57 ± 0.53% d_6. The overall deuterium balance showed an excess of d_6 of 2.0% in the products and recovered allene.

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Registry No. 4a, 591-95-7; **4b**, 13865-36-6; **4c**, 13643-05-5; **4d**, 29681-77-1; **5a**, 81624-56-8; **5b**, 81624-57-9; **5c**, 81624-58-0; **6a**, 81655-08-5; **6b**, 81655-09-6; **6c**, 81655-10-9; **6d**, 81624-59-1; **7a**, 81702-82-1; **7b**, 81624-60-4; **7c**, 81624-61-5; **7d**, 81624-62-6; **8a**, 81624-63-7; **8b**, 81655-11-0; **8c**, 81655-12-1; **8d**, 81655-73-2; **9a**, 81624-64-8; **9b**, 81624-65-9; **9c**, 81624-66-0; **9d**, 81624-67-1; **10a**, 81624-68-2; **10b**, 81624-69-3; **10c**, 81624-70-6; **10** (R = CH_3), isomer 1, 81624-71-7; **10** (R = CH_3), isomer 2, 81624-72-8; **11a**, 598-25-4; **11b**, 4717-48-3; **11c**, 7417-50-7; **12a**, 81624-73-9; **12b**, 81624-74-0; **13b**, 81655-14-3; **13c**, 81624-75-1; **14a**, 81624-76-2; **16a**, 81624-77-3; **16b**, 81624-78-4; **16c**, 81624-79-5; **17**, 81624-80-8; **18**, 81624-81-9; **19**, 81624-82-0; **20**, 81624-83-1; **34**, 29212-09-7; **36**, 81624-84-2; **37**, isomer 1, 81624-85-3; **37**, isomer 2, 81624-86-4; (*E*)-**38**, 20626-38-4; (*Z*)-**38**, 65150-07-4; (*E*)-**39**, 32763-68-1; (*Z*)-**39**, 32763-69-2; NPMI, 941-69-5.

Hydrolysis of Trimethyl Orthocyclopropanecarboxylate: A Change in Rate-Determining Step

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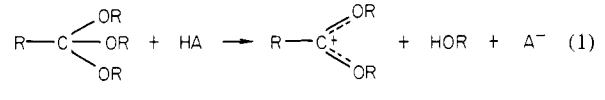
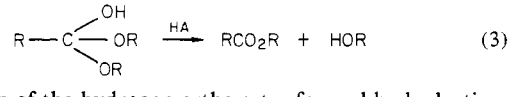
Abstract: The rate constant for the hydronium ion catalyzed hydrolysis of trimethyl orthocyclopropanecarboxylate measured in dilute aqueous HCl, k_{H^+} = 5300 M^{-1} s^{-1}, was found to be different from that measured in buffer solutions at pH 6-8, k_{H^+} = 81 000 M^{-1} s^{-1}. This difference is similar to that observed before for cyclic ortho esters and is taken as evidence for a change in reaction mechanism from rate-determining conversion of ortho ester to a dialkoxycarbonium ion intermediate at high pH to rate-determining decomposition of the hydrogen ortho ester formed by hydration of this ion at low pH. Discovery of this mechanistic change in this acyclic system suggests that this is a general phenomenon common to all ortho esters substituted with carbocation-stabilizing groups at their *pro*-acyl carbon atoms.

We recently discovered that the rate-determining step in the hydrolysis of certain ortho esters in aqueous solution changes from generation of a dialkoxycarbonium ion intermediate, eq 1, to





decomposition of the hydrogen ortho ester formed by hydration of this ion, eq 3.[2] Through suitable choice of reaction conditions, we were consequently able to measure rate constants for both of these reaction steps. These measurements showed that at low pH where acids are the only effective catalytic species, step 3 (eq 3) is slower than step 1 (eq 1). As the pH is raised, however, an especially effective base catalysis of step 3 comes into operation; since step 1 is not subject to base catalysis, the rate of step 3 quickly overtakes that of step 1, and step 1 then becomes rate determining.

Such a change in reaction mechanism can occur only if step 1 is faster than step 3 in the absence of base catalysis. It is significant therefore that the ortho esters for which we first ob-

(1) (a) University of Toronto. (b) Marquette University.

(2) (a) Ahmad, M.; Bergstrom, R. G.; Cashen, M. J.; Kresge, A. J.; McClelland, R. A.; Powell, M. F. *J. Am. Chem. Soc.* **1977**, *99*, 4827-4829. (b) Ahmad, M.; Bergstrom, R. G.; Cashen, M. J.; Chiang, Y.; Kresge, A. J.; McClelland, R. A.; Powell, M. F. *Ibid.* **1979**, *101*, 2669-2677; (c) *Ibid.* **1982**, *104*, in press.

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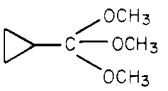
served this change, and all substrates with which further examples of this phenomenon were subsequently found,[3] possess electron-donating substituents at their *pro*-acyl carbon atoms. These substituents stabilize the positive charge generated in forming the dialkoxycarbonium ion intermediates produced in step 1, thus accelerating this reaction step; they have less, or perhaps no, accelerative effect on the rate of step 3, probably because this reaction step can occur by a concerted mechanism that avoids a cationic intermediate.

Each of the substrates for which this change in rate-determining step had been observed was also a cyclic ortho ester, i.e., a substance in which two, or all three, of the alkoxy groups were incorporated into five- or six-membered rings. It seems unlikely that this structural feature is a necessary requirement for the mechanistic change, and we have therefore examined the behavior of a simple acyclic ortho ester. We used trimethyl orthocyclopropanecarboxylate, **1**, for this purpose because of the strong



cation-stabilizing ability of the cyclopropyl group, and we used comparison of rates at low and high pH as a criterion of mechanistic change.

Experimental Section

Materials. Trimethyl orthocyclopropanecarboxylate was prepared from cyclopropanecarbonyl chloride (Aldrich Chemical Co.) via the anilide acetal by an adaptation of a method recently reported for the synthesis of aryl ortho esters.[4] We found that the anilide acetal intermediate could be converted to the desired ortho ester by simple heating in vacuo and that treatment with acetic acid and methanol was therefore not necessary. The anilide acetal was consequently heated to 150 °C at 0.1-mm pressure and the products, ortho ester, methyl cyclopropanecarboxylate, and *N*-methylaniline, were trapped at 0 °C. Preliminary separation of this mixture was effected by distillation, and final purification of ortho ester was accomplished by gas chromatography. The product was identified by its NMR spectra [($CDCl_3$) ^1H: δ 0.5 (m, 4 H, $-CH_2CH_2-$), 1.0 (s, 1 H, -CH-), 3.3 (s, 9 H, $-OCH_3$), ^{13}C: δ 0.9 ($-CH_2-$), 12.5 (-CH-), 49.2 ($-OCH_3$), 113.3 [$-C(OMe)_3$]] and its mass spectrum (electron inpact gave an ion at m/e 115 corresponding to loss of OCH_3 from the unobserved M^+ parent ion, while chemical ionization gave an MH^+ ion at m/e 147).

All other materials were best available commercial grades. Solutions were prepared by using deionized water purified further by distillation in an all-glass apparatus.

Kinetics. Rate measurements were made spectroscopically by monitoring the appearance of methyl cyclopropanecarboxylate absorbance at 202 or 210 nm. For the slower runs (buffer solution, 202 nm) a Cary Model 118C spectrometer with cell compartment thermostated at 25.1 ± 0.05 °C was used, and observed first-order rate constants were evaluated by visual determination of slopes of plots of ln ($A_\infty - A$) vs. time using final absorbances, A_∞, measured after ten half-lives. The faster runs (HCl solution, 210 nm) were conducted in a Durrum–Gibson stopped-flow apparatus whose output was fed directly through an analog-to-digital converter into a transient recorder; the information was then transferred to a Tektronix Model 4051 minicomputer, which calculated observed first-order rate constants by linear least-squares analysis and also provided visual displays. In all cases, the data conformed to the first-order rate law within the experimental accuracy.

Results

Rate measurements at low pH were performed in dilute HCl solutions. The data so obtained gave first-order rate constants that were accurately proportional to acid concentration (Table SI);[5] linear least-squares analysis produced the second-order catalytic coefficient $k_{H^+} = (5.3 \pm 0.2) \times 10^3\ M^{-1}\ s^{-1}$ and an uncatalyzed term smaller than its experimental uncertainty, $k_0 = 1.7 \pm 2.2\ s^{-1}$.[6]

Rate measurements were also carried out at pH 6.5–8.2 in buffer solutions of the acid–base pairs, $H_2PO_4^-/HPO_4^{2-}$ and Tris·H^+/Tris [Tris = tris(hydroxymethyl)methylamine]; the data are summarized in Table S2.[5] Buffer catalysis was not strong in these solutions, especially in the Tris buffers where observed first-order rate constants barely changed with buffer concentration at constant buffer ratio.[7] Nevertheless, least-squares analysis of the relationship between observed rate constants and buffer acid concentration gave concordant values of catalytic coefficients for a series of solutions of rather different buffer ratio; this shows that the buffer catalysis, though weak, was of the general acid type, as expected.

These data could be extrapolated to zero buffer concentration with good precision. The intercepts thus obtained represent hydronium ion and uncatalyzed components of the hydrolysis rates, and hydronium ion catalytic coefficients were estimated from them. The hydronium ion concentrations of the buffer solutions required for this purpose were calculated from literature pK_a's, 7.20 for $H_2PO_4^-$[9] and 8.07 for Tris·H^+,[10] and activity coefficients recommended by Bates[11] for H_3O^+, $H_2PO_4^-$, and HPO_4^{2-} plus a value for Tris·H^+ calculated by using the Debye–Huckel equation with an ion-size parameter of 6 Å;[12] the activity coefficient of Tris was taken to be unity. In all cases these calculated hydronium ion concentrations agreed well with those deduced from directly measured pH values. Linear least-squares analysis of the relationship between hydronium ion concentration and rate constants extrapolated to zero buffer concentration gave the hydronium ion catalytic coefficient $k_{H^+} = (8.12 \pm 0.07) \times 10^4\ M^{-1}\ s^{-1}$ and an uncatalyzed term again smaller than its experimental uncertainty, $k_0 = (0.20 \pm 1.55) \times 10^{-4}\ s^{-1}$; the latter is nevertheless consistent with a direct determination made in 2×10^{-4} M NaOH solution: $k_0 = 1.02 \times 10^{-4}\ s^{-1}$.

Discussion

Our measurements show that the overall rate of hydrolysis of trimethyl orthocyclopropanecarboxylate catalyzed by the hydronium ion is decidedly different at low pH than at high pH: $k_{H^+} = 5\,300\ M^{-1}\ s^{-1}$ in 0.004–0.014 M HCl solutions, whereas $k_{H^+} = 81\,000\ M^{-1}\ s^{-1}$ in buffers at pH 6–8. This difference is similar both in kind and in magnitude to that observed for certain cyclic ortho esters whose hydrolysis is known to undergo a change in rate-determining step between low and high pH,[2,3] and it can therefore be taken to indicate that a similar change is taking place here. This mechanistic assignment then allows the rate constant measured in buffer solutions to be identified as the specific rate of dialkoxycarbonium ion formation, eq 1, $k^1_{H^+} = 81\,000\ M^{-1}\ s^{-1}$, and the rate constant measured in HCl solutions to be identified as the specific rate of hydrogen ortho ester decomposition, eq 3, $k^3_{H^+} = 5300\ M^{-1}\ s^{-1}$.

In the cyclic systems for which this change in rate-determining step was first observed, it could be attributed to the accelerating

(3) McClelland, R. A.; Ahmad, M.; Bohonek, J.; Gedge, S. *Can. J. Chem.* **1979**, *57*, 1531–1540. McClelland, R. A.; Gedge, S.; Bohonek, J. *J. Org. Chem.* **1981**, *46*, 896–891.

(4) McClelland, R. A.; Patel, G.; Lam, P. W. K. *J. Org. Chem.* **1981**, *46*, 1011–1012.

(5) Tables S1 and S2 are available as supplementary material; see paragraph at the end of this paper.

(6) It will be shown later that these rate constants refer to step 3 of the reaction scheme (eq 3), for which measurable values of k_0 and a saturation of the H^+ catalytic effect, and consequent nonlinear dependence of first-order rates of hydrolysis upon [H^+], have usually been observed.[2b] In the present case, however, the reaction was especially rapid, and low acid concentrations, below the expected region of marked nonlinear dependence, had to be used. At the low wavelength employed (210 nm), moreover, the signal to noise ratio of our Durrum–Gibson stopped-flow spectrometer deteriorates and the precision with which rate constants can be determined is consequently lowered; since k_0 could not have been more than a few percent of most of the observed rate constants, this increased scatter probably masked its appearance.

(7) In a proton transfer reaction of this kind, electrostatic effects will make a positively charged acid such as Tris·H^+ a less effective catalyst than a negatively charged species such as $H_2PO_4^-$.[8]

(8) Kresge, A. J.; Chiang, Y. *J. Am. Chem. Soc.* **1973**, *95*, 803–806. Chwang, W. K.; Eliason, R.; Kresge, A. J. *Ibid.* **1977**, *99*, 805–808.

(9) Grybowski, A. K. *J. Phys. Chem.* **1958**, *62*, 555–559.

(10) Datta, S. P.; Grybowski, A. K.; Weston, B. A. *J. Chem. Soc.* **1963**, 792–796.

(11) Bates, R. G. "Determination of pH"; Wiley–Interscience: New York, 1973; p 49

(12) Roy, R. N.; Robinson, R. A.; Bates, R. G. *J. Am. Chem. Soc.* **1973**, *95*, 8231–8235.

effect of carbocation-stabilizing substituents at the *pro*-acyl carbon atom on the rate of dialkoxycarbonium ion formation (eq 1). The situation is quite the same here: the cyclopropyl group in trimethyl orthocyclopropanecarboxylate raises the rate of this reaction by a factor of 310,[13] which is closely similar to the 290-fold acceleration shown by a cyclopropyl group in the cyclic 1,3-dioxolane series.[2] It seems likely, therefore, that this kind of change in rate-determining step will prove to be a general phenomenon that will appear in the hydrolysis of all ortho esters, cyclic or not, substituted with carbocation-stabilizing groups at the *pro*-acyl carbon atom.

Acknowledgment. We are grateful to the Natural Sciences and Engineering Research Council of Canada and to the donors of the Petroleum Research Fund, administered by the American Chemical Society, for their financial support of this research.

Registry No. 1, 54917-76-9.

Supplementary Material Available: Tables of rate constants (3 pages). Ordering information is given on any current masthead page.

(13) This comparison is based on $k^1_{H^+}$ = 263 M^{-1} s^{-1} for trimethyl orthoformate.[14]

(14) Chiang, Y.; Kresge, A. J.; Salomaa, P.; Young, C. I. *J. Am. Chem. Soc.* **1974**, *96*, 4494–4499.

Hydrolysis of Bicyclic Ortho Esters in the 2,6,7-Trioxabicyclo[2.2.1]heptane Series. Confirmation of the Absence of Strain-Relief Rate Acceleration

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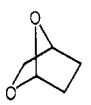
Abstract: The hydrolysis of 2,6,7-trioxabicyclo[2.2.1]heptane and its 1-phenyl derivative in aqueous solution was found to undergo a change in reaction mechanism from rate-determining formation of a dialkoxycarbonium ion intermediate from starting ortho ester at high pH to rate-determining decomposition of the hydrogen ortho ester formed by hydration of this ion at low pH. The initial ring-opening reactions of these bicyclic substrates proved to be not markedly faster than the corresponding reactions of monocyclic and acyclic models, which is consistent with the results obtained in an earlier more limited study. This behavior stands in marked contrast to the appreciable rate accelerations found in the hydrolysis of bicyclic acetals belonging to the same [2.2.1]heptane system; possible reasons for this difference are discussed.

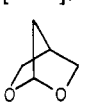
Bicyclic acetals in which the ether oxygen atoms are incorporated into small rings are unusually reactive toward acid-catalyzed hydrolysis.[2] For example, 2,7-dioxabicyclo[2.2.1]heptane (**1**) is



1

$CH_3CH(OCH_3)_2$

2



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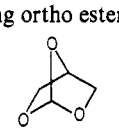
hydrolyzed in aqueous acetone containing dichloroacetic acid 25 000 times faster than its simple acyclic analogue, dimethyl acetal (**2**), and 2,6-dioxabicyclo[2.2.1]heptane (**3**) is more reactive still: its rate of hydrolysis is 6900 000 times that of dimethyl acetal.[2b] Small bicyclic ring systems of this kind are known to be strained,[3] and these rate accelerations have been attributed to partial relief of this strain upon ring-opening hydrolysis.

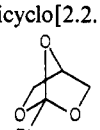
This unusual reactivity, however, appears not to extend to the corresponding ortho esters: 2,6,7-trioxabicyclo[2.2.1]heptane (**4**)



4

$HC(OCH_3)_3$

5



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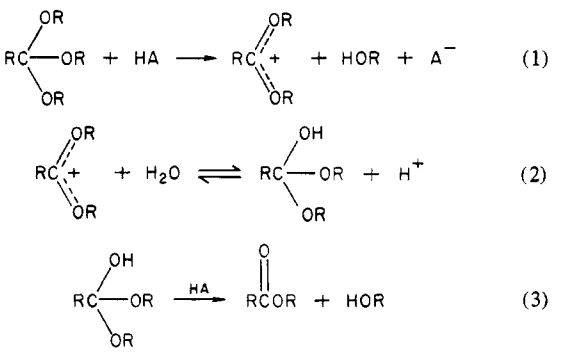
is actually hydrolyzed more slowly, by some 50%, than its acyclic analogue, trimethyl orthoformate (**5**).[4] This behavior, though unexpected, was rationalized in terms of an early hydrolysis transition state with very little ring opening and consequently little strain relief.

It is possible, however, that the situation may have been complicated by a change in the rate-determining step. Recent studies of ortho ester hydrolysis have shown that changes from a mechanism in which the first step of this reaction, eq 1, is rate determining to one in which the third step, eq 3, is slower can be effected by making structural changes that accelerate the rate of the first step.[5] Introduction of strain, as in a bicyclic system, is just such a structural change, and the rate constant measured for the bicyclic substrate, 2,6,7-trioxabicyclo[2.2.1]heptane, might



(1)

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(1) (a) University of Toronto. (b) University of Arizona.

(2) (a) Hall, H. K., Jr.; Carr, L. J.; Kellman, R.; De Blauwe, F. *J. Am. Chem. Soc.* **1974**, *96*, 7265–7269. (b) Hall, H. K., Jr.; De Blauwe, F. *Ibid.* **1975**, *97*, 655–656. Hall, H. K., Jr.; De Blauwe, F.; Carr, L. J.; Rao, V. S. *J. Polym. Sci., Polym.* **1976**, *56*, 101–115.

(3) See, for example: Greenberg, A.; Liebman, J. F. "Strained Organic Molecules"; Academic Press: New York, 1978; pp 70–77.

(4) Hall, H. K.; De Blauwe, F.; Pyriadi, T. *J. Am. Chem. Soc.* **1975**, *97*, 3854.

(5) (a) Ahmad, M.; Bergstrom, R. G.; Cashen, M. J.; Kresge, A. J.; McClelland, R. A.; Powell, M. F. *J. Am. Chem. Soc.* **1977**, *99*, 4827–4829. (b) Ahmad, M.; Bergstrom, R. G.; Cashen, M. J.; Chiang, Y.; Kresge, A. J.; McClelland, R. A.; Powell, M. F. *Ibid.* **1979**, *101*, 2669–2677. (c) McClelland, R. A.; Ahmad, M.; Bohonek, J.; Gedge, S. *Can. J. Chem.* **1979**, *57*, 1531–1540. (d) McClelland, R. A.; Gedge, S.; Bohonek, J. *J. Org. Chem.* **1981**, *46*, 896–891. (e) Burt, R. A.; Chiang, Y.; Kresge, A. J.; McKinney, M. A. *J. Am. Chem. Soc.* **1982**, *104*, preceding paper in this issue.

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