II; IR (Nujol) 1670 (strong), 1710 (medium) cm^{-1}. Anal. Calcd for $C_{14}H_{13}O_3P$: C, 64.62; H, 5.05; P, 11.90. Found: C, 64.66;, H, 4.95; P, 11.90.

3,8-Bis(trimethylsiloxy)-1-phenyl-1*H*-phosphonin 1-Oxide (7). To a solution of crude monobromide 6 (1.2 mmol) in CDCl$_3$ (2 mL) at 0 °C was added triethylamine (0.24 g, 2.4 mmol) and the mixture stirred at 0 °C for 48 h. The reaction mixture was centrifuged and the supernatant solution carefully removed (avoiding exposure to moisture) and concentrated under high vacuum. The resulting dark oil consisted of a 1:1 mixture of 7

and 8, which could not be separated without hydrolysis occuring. Spectral properties of 7 were determined by deleting the signals due to 8: ^{1}H NMR (CDCl$_3$) δ 4.5–5.7 (complex m, 6 H), 7.4–7.9 (m, 5 H, phenyl H); ^{31}P NMR (CDCl$_3$) δ +30.3; ^{13}C NMR (CDCl$_3$), Table I.

Registry No. 2 (isomer 1), 80794-96-3; 2 (isomer 2), 80794-95-2; 3, 75531-99-6; 4 (isomer 1), 90991-51-8; 4 (isomer 2), 91050-47-4; 5, 90991-52-9; 6a, 90991-49-4; 6b, 91050-46-3; 7, 90991-53-0; 8, 91002-47-0; 9, 90991-50-7; BSTFA, 21149-38-2.

Transition-State Structures for the Hydrolysis of Cyclic and Acyclic Carbonates[1]

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The hydrolysis of *o*-(4-nitrophenylene) carbonate (1) is third order in water while the hydrolysis of bis(4-nitrophenyl) carbonate (2) is second order in water. Proton inventories for both are downwardly curved indicating contributions by more than one proton to the observed kinetic solvent deuterium isotope effects of k_{H_2O}/k_{D_2O} = 2.46 and 2.20 for 1 and 2, respectively. The transition-state structure appears to involve a cyclic array of three water molecules in the case of 1, the cyclic carbonate. The transition-state structure for hydrolysis of the acyclic carbonate 2 involves only two water molecules with one acting as a general base to remove a proton from the nucleophilic water molecule. This has been referred to as a catalytic proton bridge transition state. Deslongchamp's theory of stereoelectronic control has been applied to an analysis of the proton inventories for the water-catalyzed hydrolysis of a cyclic and an acyclic carbonate ester.

Introduction

In order to fully delineate the mechanism of biological hydrolytic reactions it is necessary to understand their nonbiological analogues in extreme detail. Study of the hydrolytic ring opening of certain cyclic esters and comparison of the results with those for the hydrolytic cleavage of the corresponding acyclic esters may provide additional insight into the mechanisms which can serve as models for many biological systems.[3] With this in mind, Fife and McMahon[4] have extensively investigated the hydrolysis of *o*-(4-nitrophenylene) carbonate (1) and bis(4-nitrophenyl) carbonate (2). We report here a study of the pH
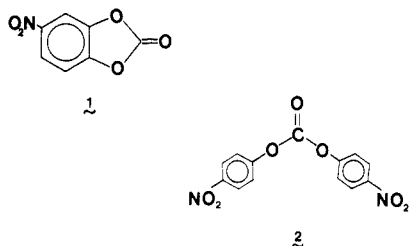
independent, water-promoted hydrolysis of 1 and 2 in mixtures of protium oxide and deuterium oxide. Such a study constitutes a proton inventory and allows us to suggest likely roles for the water molecules in the transition states for these hydrolysis reactions.

Results

The hydrolysis of 1 and 2 has been studied at pH 3.0, or the equivalent point on the pH(D) rate profile, in pro-

Table I. First-Order Rate Constants for the Water-Catalyzed Hydrolysis of *o*-(4-Nitrophenylene) Carbonate (1) in H$_2$O–D$_2$O Mixtures of Atom Fraction Deuterium (*n*) at 25.05 ± 0.05 °C at pH(D) 3[a]

n	no. of runs	$10^6 k_n$, s^{-1} obsd	calcd[b]
0.000	5	8038 ± 11[c]	8038
0.247	5	6612 ± 34	6629
0.494	5	5390 ± 22	5369
0.741	5	4235 ± 17	4253
0.988[d]	4	3273 ± 13	3271

[a] The pH(D) was maintained at 3.0 by using HCl or DCl. The ionic strength was kept at 0.2 M with potassium chloride. The volume percentage of acetonitrile for each run was 0.83%. [b] Calculated on the basis of eq 6 with ϕ_a* = 0.565 and ϕ_b* = 0.843. [c] Error limits are standard deviations. [d] Atom fraction of deuterium in "pure" 10^{-3} M DCl in D$_2$O as determined by Josef Nemeth.[43]

Table II. First-Order Rate Constants for the Water-Catalyzed Hydrolysis of *o*-(4-Nitrophenylene) Carbonate (1) in Acetonitrile Containing 8 M H$_2$O–D$_2$O Mixtures of Atom Fraction of Deuterium (*n*) at 50.05 ± 0.05 °C at pH(D) 3[a]

n	no. of runs	$10^7 k_n$, s^{-1} obsd	calcd[b]
0.000	5	5194 ± 35[c]	5194
0.247	5	4351 ± 22	4311
0.494	5	3492 ± 12	3506
0.741	5	2783 ± 9	2775
0.988	5	2125 ± 9	2116

[a] The pH(D) was maintained at 3.0 by using HCl or DCl. The ionic strength was not maintained constant. [b] Calculated on the basis of eq 6 with ϕ_a* = 0.515 and ϕ_b* = 0.883. [c] Error limits are standard deviations.

tium oxide, deuterium oxide, and mixtures of the two. Table I and Figure 1 show the dependence of the observed first-order rate constants for the hydrolysis of 1 on the isotopic composition of the solvent system of atom fraction

(1) Support of this work by the Robert A. Welch Foundation is gratefully acknowledged.
(2) On leave from Presidency College, Madras, India.
(3) Kaiser, E. T.; Kezdy, F. J. In "Progress in Bioorganic Chemistry"; Kaiser, E. T.; Kezdy, F. J., Eds.; Wiley: New York, 1979; Vol. 4.
(4) (a) Fife, T. H.; McMahon, D. M. *J. Am. Chem. Soc.* 1969, *91*, 7481. (b) Fife, T. H.; McMahon, D. M. *J. Org. Chem.* 1970, *35*, 3699.
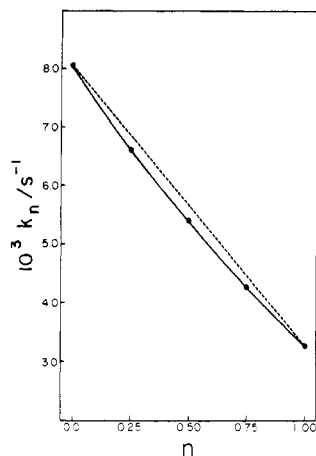
Figure 1. Proton inventory plot of the first-order rate constants for the water-catalyzed hydrolysis of o-(4-nitrophenylene) carbonate (1) vs. the atom fraction of deuterium n in the solvent at pH(D) 3.0 at 25.05 ± 0.05 °C. The data are taken from Table I.

Table III. First-Order Rate Constants for the Water-Catalyzed Hydrolysis of Bis(4-nitrophenyl) Carbonate (2) in H_2O-D_2O Mixtures of Atom Fraction of Deuterium (n) at 50.05 ± 0.05 °C at pH(D) 3[a]

| | | 10^6 k_n, s^{-1} | |
n	no. of runs	obsd	calcd[b]
0.000	5	2808 ± 5[c]	2808
0.247	5	2376 ± 19	2371
0.494	4	1970 ± 8	1969
0.741	4	1608 ± 8	1603
0.988	5	1274 ± 15	1269

[a] The pH(D) was maintained at 3.0 by using HCl or DCl. The ionic strength was maintained at 0.2 M with potassium chloride. The volume percentage of acetonitrile for each run was 3.2%. [b] Calculated on the basis of eq 6 with ϕ_a* = 0.565 and ϕ_b* = 0.889. [c] Error limits are standard deviations.

of deuterium n at 25.05 ± 0.05 °C. Visual inspection reveals the proton inventory of Figure 1 exhibits significant downward curvature, implicating the involvement of more than one proton in the transition state for the water-catalyzed hydrolysis. The kinetic solvent isotope effect of k_{H_2O}/k_{D_2O} = 2.46 in 10^{-3} M HCl(DCl) (25.05 °C) compares favorably with the literature value of 2.35 in 10^{-1} M HCl (30.0 °C).[4b]

Table II lists the rate constants for the water-catalyzed hydrolysis of 1 in acetonitrile containing 8 M protium oxide, deuterium oxide, or mixtures of the two of atom fraction of deuterium, n. The ionic strength was not maintained constant. This was not possible due to a salting-out influence at such a high acetonitrile concentration. The observed kinetic solvent isotope effect of 2.46 shows that the ionic strength has little influence on the solvent isotope effect.

Table III shows the dependence of the observed first-order rate constants for the hydrolysis of 2 on the atom fraction of deuterium, n, of the solvent system at 50 °C. A plot of the data would again reveal significant downward curvature. The observed solvent isotope effect of 2.20 differs considerably from one literature value of 2.88 in 10^{-1} M HCl (30 °C)[4b], but agrees very well with that of 2.24 (50 °C) reported by Menger and Venkatasubban.[5]

The hydrolysis of 1 and 2 has also been studied in acetonitrile containing low concentrations of water and the first-order rate constants are collected in Table IV. The

(5) Menger, F. M.; Venkatasubban, K. S. *J. Org. Chem.* 1976, 41, 1868.

Table IV. First-Order Rate Constants for the Water-Catalyzed Hydrolysis of 1 and 2 as a Function of Water Concentration in Acetonitrile at 50.05 ± 0.05 °C[a]

| | 10^5 k_1, s^{-1} | |
[H_2O], M	1	2
3	2.78 ± 0.02[b]	
4	6.32 ± 0.10	
5	12.81 ± 0.20	1.10 ± 0.03[b]
6	22.48 ± 0.33	1.60 ± 0.02
7	35.34 ± 0.30	2.45 ± 0.06
8	51.88 ± 0.31	2.86 ± 0.02
9	70.52 ± 0.15	3.63 ± 0.09
10	94.17 ± 0.13	4.42 ± 0.07

[a] Ionic strength and pH were not maintained constant. [b] Mean of two determinations with standard deviation shown.
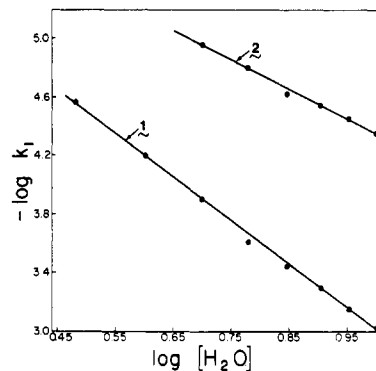

Figure 2. Plot of -log k_1 for the water-catalyzed hydrolysis of 1 or 2 vs. the log of water concentration in acetonitrile. The data are taken from Table IV.

plot of log k vs. log [H_2O] produces a straight line in each case as shown in Figure 2. The slope of the straight line is 2.96 with a correlation coefficient (r) of 0.9997 in the case of 1 and 2.13 (r = 0.9949) in the case of 2. These results suggest a third-order dependence on water in the hydrolysis of 1 and a second-order dependence on water in the hydrolysis of 2.

Discussion

The theory of the proton inventory technique is well documented in the literature.[6] This technique has recently been used to help elucidate transition-state structures for a number of organic[7-15] and enzyme-catalyzed reactions.[16-23] This technique involves the measurement

(6) (a) Gold, V. *Adv. Phys. Org. Chem.* 1969, 7, 259. (b) Kresge, A. J. *Pure Appl. Chem.* 1964, 8, 243. (c) Schowen, R. L. *Prog. Phys. Org. Chem.* 1972, 9, 275. (d) Albery, W. J. In "Proton-Transfer Reactions"; Caldin, E., Gold, V., Eds.; Chapman and Hall: London, 1975.

(7) Minor, S. S.; Schowen, R. L. *J. Am. Chem. Soc.* 1973, 95, 2279.

(8) Gandour, R. D.; Schowen, R. L. *J. Am. Chem. Soc.* 1974, 96, 2231.

(9) Hogg, J. L.; Phillips, M. K.; Jergens, D. E. *J. Org. Chem.* 1977, 42, 2459.

(10) Hogg, J. L.; Phillips, M. K. *Tetrahedron Lett.* 1977, 3011.

(11) Venkatasubban, K. S.; Davis, K. R.; Hogg, J. L. *J. Am. Chem. Soc.* 1978, 100, 6125.

(12) Patterson, J. F.; Huskey, W. P.; Venkatasubban, K. S.; Hogg, J. L. *J. Org. Chem.* 1978, 43, 4935.

(13) Karzijn, W., Engberts, J. B. F. N. *Tetrahedron Lett.* 1978, 1787.

(14) Venkatasubban, K. S.; Hogg, J. L. *Tetrahedron Lett.* 1979, 4335.

(15) Hegazi, M.; Mata-Segreda, J. F.; Schowen, R. L. *J. Org. Chem.* 1980, 45, 307.

(16) Pollock, E.; Hogg, J. L.; Schowen, R. L. *J. Am. Chem. Soc.* 1973, 95, 968.

(17) Harmony, J. A. K.; Himes, R. H.; Schowen, R. L. *Biochemistry* 1975, 14, 5379.

of reaction rates (k_n) in mixtures of protium oxide and deuterium oxide of varying atom fraction of deuterium, n, and relates k_n to the rate constant in pure protium oxide (k_0) by the Gross–Butler equation (eq 1).

$$k_n = k_0 \prod_i^{TS} (1 - n + n\phi_i^*) / \prod_j^{RS} (1 - n + n\phi_j) \quad (1)$$

This means that all exchangeable transition-state protons, i, and exchangeable reactant-state protons, j, that contribute to the observed solvent isotope effect contribute a term of the form shown in parentheses in the numerator and denominator of eq 1, respectively. In the present case, the reactants are the substrate and water. Neither substrate 1 or 2 has an isotopically exchangeable proton. Since water protons have unit fractionation factors the denominator of eq 1 is unity in the present study.

The fractionation factors of the exchangeable protons in the transition state can be evaluated from the experimental data either by polynomial regression analysis[24] or by the "gamma method".[6d] They can also be evaluated from the Brønsted coefficient of the reaction if available and if the water point falls on the Brønsted plot.[9] Our analysis will center on the use of the γ method with comments on the use of the Brønsted β value as an aid in interpreting the proton inventories.

Albery's γ method requires the calculation of the curvature parameter γ, defined by eq 2.[6d]

$$\gamma = 8 \frac{\ln (y_{0.5}/y_{1.0}^{1/2})}{(\ln y_1)^2} \quad (2)$$

in which

$$y_n = \frac{k_n}{k_0} \prod_j^{RS} (1 - n + n\phi_j) = \prod_i^{TS} (1 - n + n\phi_i^*) \quad (3)$$

The γ value calculated from the experimental data for the water-catalyzed, neutral hydrolysis of 1 is 0.46 ± 0.03. This value suggests three things: (1) The observed solvent isotope effect is caused only by the transition-state exchangeable protons. (2) The reaction does not involve parallel transition states. (3) The transition state of the rate-limiting step of the reaction involves at least two, most probably three, and perhaps four active protons (i.e., protons contributing to the observed solvent isotope effect).

The probable transition states involving two active protons are 3, 4, and 5. The H_c protons in 4 and 5 are expected to have fractionation factors of unity and should not contribute to the observed solvent isotope effect. The H_a protons will each contribute a primary solvent isotope effect. Hence, the form of the Gross–Butler equation corresponding to transition states 3, 4, and 5 is eq 4 in which ϕ_a^* is the fractionation factor of the H_a protons.
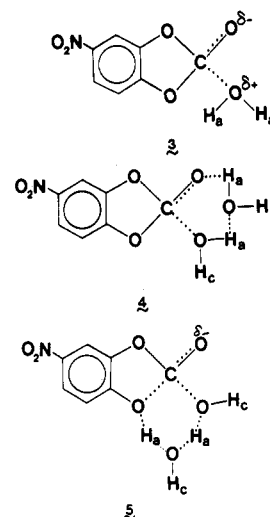
These models, 3, 4, and 5, are unacceptable, however, for the following reasons. (1) None accounts for the observed third-order dependence of the reaction on water concentration. (2) Model 3 fails to justify the additional function of water as a general base suggested by the presence of the water point on the Brønsted plot.[4] (3) Equation 4 does a very poor job of duplicating the experimental data.

$$k_n = k_0(1 - n + n\phi_a^*)^2 \quad (4)$$

The most reasonable transition-state models which involve three active protons are 6, 7, and 8. Of these, 6 and
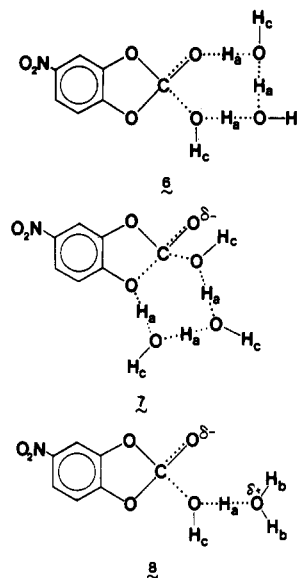
7 are consistent with the observed third-order dependence on water concentration. Further, 6 and 7 involve eight atoms in the cyclic transition state and, thus, have proton donor–acceptor arrangements much closer to linearity in accord with the preferred requirement for intramolecular proton transfer postulated by Gandour.[25] The H_c protons in models 6 and 7 should each have a fractionation factor of unity as mentioned earlier. If we assume that the H_a protons in 6 and 7 have equal fractionation factors and contribute equally to the observed solvent isotope effect, then the form of eq 1 corresponding to the models 6 and 7 is eq 5. The value of $\phi_a^* = 0.704$ calculated from the

$$k_n = k_0(1 - n + n\phi_a^*)^3 \quad (5)$$

experimental data and the calculated γ value when used

(18) Hunkapiller, M. W.; Forgac, M. D.; Richards, J. H. *Biochemistry* 1976, *15*, 5581.

(19) Konsowitz, L. M.; Cooperman, B. S. *J. Am. Chem. Soc.* 1976, *98*, 1993.

(20) Wang, M. S.; Gandour, R. D.; Rodgers, J. L.; Schowen, R. L. *Bioorg. Chem.* 1975, *4*, 392.

(21) Elrod, J. P.; Gandour, R. D.; Hogg, J. L.; Kise, M.; Maggiora, G. M.; Schowen, R. L.; Venkatasubban, K. S. *Symp. Faraday Soc.* 1975, No. 10, 145.

(22) Hogg, J. L.; Elrod, J. P.; Schowen, R. L. *J. Am. Chem. Soc.* 1980, *102*, 2082.

(23) Elrod, J. P.; Hogg, J. L.; Quinn, D. M.; Venkatasubban, K. S.; Schowen, R. L. *J. Am. Chem. Soc.* 1980, *102*, 3917.

(24) Schowen, K. B. J. In "Transition States of Biochemical Processes"; Gandour, R. D., Schowen, R. L., Eds.; Plenum: New York, 1978.

(25) Gandour, R. D. *Tetrahedron Lett.* 1974, 295.

with eq 5 fail to regenerate the proton inventory curve. However, if we assume that one of the H_a protons has a different fractionation factor ($\phi_a{}^*$) from the other two which have equal fractionation factors ($\phi_b{}^*$), then eq 1 becomes eq 6. When the values of $\phi_a{}^* = 0.565$ and $\phi_b{}^*$

$$k_n = k_0(1 - n + n\phi_a{}^*)(1 - n + n\phi_b{}^*)^2 \qquad (6)$$

= 0.843, calculated from the experimental data and the γ value, are used in eq 6 they reproduce the proton inventory data (Table I) very well.

In general, the magnitude of the fractionation factors which regenerate successfully the proton inventory data also provides information about the nature of the transfer of the corresponding protons. If ϕ is less than 0.3, the proton transfer is simple; if it is between 0.4 and 0.7, the proton transfer is concerted; and if it is greater than 0.7, the proton is not transferring in the transition state.[6d] The values of the fractionation factors (i.e., $\phi_a{}^* = 0.565$ and $\phi_b{}^* = 0.843$) used in eq 6 indicate that one proton is in flight and the other two are not moving along the reaction coordinate.

Transition state 6 is identical with that proposed for the hydration of a carbonyl group by Bell and Critchlow.[26] A semiempirical theoretical analysis of such a transition state by Critchlow[27] suggested that the three proton transfers were not all synchronous with heavy atom reorganization but that transfer of only one proton was coupled with heavy atom reorganization in an intimate stepwise mechanism.[26] Further, the proton in flight was identified as the one that undergoes transfer from a water molecule to the carbonyl oxygen.[26,27,6d]

If model 6 is the correct transition state for the hydrolysis of 1, the observed rate constant for the water-catalyzed reaction of 1 should be on the Brønsted line for general acid catalysis. However, it is present only on the Brønsted line for general base catalysis by carboxylate anions that cannot act as bifunctional catalysts.[4] Further, a transition state such as 6 is not suggested for the hydrolysis of 2 based on our data.

The hydrolysis of 1 is faster than that of 2. The angle strain present in 1 is released on forming the tetrahedral intermediate but this favorable effect is presumably balanced by the developing unfavorable torsional strain in 6. Release of strain on cleavage of the ring cannot be an accelerating factor because this step is post-rate limiting. Thus, model 6, in spite of its success in accounting for the observed order in water and the proton inventory data, fails to explain (1) the presence of the water point on the Brønsted line for the general base catalysis or (2) the enhanced reactivity of 1 over its acyclic analogue 2.

Model 7 involves the cleavage of the ring and could account for the enhanced reactivity of 1 over 2. However, it also fails to account for the presence of the water point on the Brønsted line for general base catalysis. Further, if cleavage of the C–O bond between the carbonyl carbon and the leaving group is responsible for such a cyclic transition state we would expect the same cyclic transition state in the case of 2. But such is not observed as will be seen below.

In model 8 one water molecule functions as a general base to remove a proton from the attacking water molecule. This model has three protons (one H_a and two H_b) which could contribute to the overall solvent isotope effect. The H_c proton will have a unit fractionation factor and will not contribute to the solvent isotope effect. The "in flight"

proton H_a will contribute a primary solvent effect and the two H_b protons will contribute secondary solvent isotope effects. Thus, the equation corresponding to this model is also eq 6 and the fractionation factors of the H_a protons are $\phi_a{}^* = 0.565$ and $\phi_b{}^* = 0.843$. These values, as we saw earlier, were calculated by using the proton inventory data. Similar values are obtained by using the Brønsted β value to estimate the fractionation factor.[6c] Thus, model 8 is successful in reproducing the proton inventory data and in justifying the presence of the water point on the Brønsted line for general base catalysis. However, it also fails to account for (1) the observed third-order dependence of the reaction rate on water concentration and (2) the enhanced reactivity of 1 over 2.

At this point it is worthwhile to discuss the reliability of the order determination for water since it was done in acetonitrile. Eigen,[28] Bell, et al.,[29] and Jencks and Hand[30] have determined the order dependence on water concentration in the same way in similar reactions in the absence of other methods of determination. Langford and Tong[31] have recently considered the meaning of such information in considerable detail. In the present investigation, the order with respect to water was determined under identical conditions for both the hydrolysis of 1 and 2. However, the observed order is three in the case of 1 and two in the case of 2.

Further, the proton inventories of the hydrolysis of 1 in simple H_2O–D_2O mixtures and in 0.9 volume fraction of acetonitrile are observed to be identical as evidenced by the magnitude of the solvent isotope effects and the calculated γ values. Because of this we paid considerable attention to the observed order with respect to water concentration in formulating the transition-state structure.

Another acceptable model (9) which successfully accounts for (1) the observed third-order dependence on water, (2) the enhanced reactivity of 1 over 2, and (3) the presence of the water point on the Brønsted line in general base catalysis is only a minor modification of structure 6. In 6 the proton is actually transferred to the carbonyl oxygen. One can imagine that the water molecule interacting with the carbonyl oxygen in 6 could do so in a different way. This water molecule could become merely a solvating water molecule to bridge the other water molecules to the developing negative charge on the carbonyl oxygen. This would then be essentially equivalent to the cyclic, one-encounter, concerted, nonbifunctional mechanism proposed by Jencks et al.[32] for the uncatalyzed hydration of formaldehyde proceeding by the equivalent general base catalysis. Critchlow's theoretical calculations based on a simplified potential energy surface for single processes also suggest the presence of a highly associated water molecule in the cyclic transition state for the hydration of 1,3-dichloroacetone.[27] Such an associated water molecule would contribute to the observed order because it would be part of the transition state but it would make no contribution to the solvent isotope effect because it would be isotopically equivalent to a solvent water molecule with unit fractionation factors. Such a model (9) would have only three protons actually contributing to the solvent isotope effect with the appropriate form of the Gross–Butler equation being eq 6 which was seen earlier to successfully regenerate the proton inventory data.

(26) Bell, R. P.; Critchlow, J. E. *Proc. R. Soc. London, Ser. A.* 1971, *325*, 35.
(27) Critchlow, J. E. *J. Chem. Soc., Faraday Trans. 1*, 1972, *68*, 1773.
(28) Eigen, M. *Discuss. Faraday Soc.* 1965, *39*, 7.
(29) Bell, R. P.; Mellington, J. P.; Pink, J. M. *Proc. R. Soc. London, Ser. A* 1968, *303*, 1.
(30) Hand, E. S.; Jencks, W. P. *J. Am. Chem. Soc.* 1975, *97*, 6221.
(31) Langford, C. H.; Tong, J. P. K. *Acc. Chem. Res.* 1977, *10*, 258.
(32) Funderbunk, L. H.; Aldwin, L. L.; Jencks, W. P. *J. Am. Chem. Soc.* 1978, *100*, 5444.

Fife and McMahon have studied the hydrolysis of 2.[4] They have shown that the reaction is pH independent above pH 1.0, subject to general base catalysis, and that the water point lies on the Brønsted line (β = 0.33). They suggested model 10 for the transition state. This model
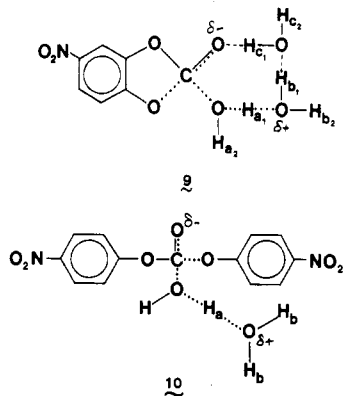
involves three "active" protons (H_a and H_b protons). Thus, the proton inventory curve sould exhibit a downward bowing.[24] Menger and Venkatasubban determined the proton inventory for this reaction at pH 2.0 and observed a linear plot of k_n vs. n.[5] This is indicative of the involvement of only one proton in the transition state. However, they also argued in favor of transition-state model 10 and attributed the linearity of the proton inventory plot to the early transition state suggested by the Brønsted coefficient of 0.33.

The rate constants for the pH independent water-promoted hydrolyses of 1-acetylimidazolium ion,[33] ethyl trifluorothioacetate,[34] 1-acetyl-1,2,4-triazole,[35] N-acetyl benzotriazole,[36] and phthalic anhydride[37] are all present on the Brønsted lines with slopes of 0.34, 0.33, 0.34, 0.38, and 0.33, respectively. In all these cases, the proton inventory plots exhibit a significant downward bowing.[9,11,13,38,39] We repeated the proton inventory studies of Menger and Venkatasubban under almost identical conditions. Our observed plot of k_n vs. n showed significant downward curvature in contrast with the earlier report.[5] We suspect that solubility problems may have led to their results. Increasing the volume of the initial acetonitrile stock solution injection from 20–100 μL solved the problem. The information we seek is essentially contained in how far $k_{0.5}$ (i.e., k_n at n = 0.5) deviates from a value interpolated between k_0 and $k_{1.0}$ (i.e., k_n at n = 0 and 1.0), respectively.[6d] The γ value calculated from the experimental data for the neutral water-catalyzed hydrolysis of 2 is 0.54 ± 0.05. This suggests a transition state involving two or three protons. The possible two proton models are similar to 3, 4, and 5 proposed for 1 but involve 2. Arguments similar to those put forth earlier disfavor these transition states for compound 2.

The three proton models similar to 6, 7, and 9 can be rejected on the basis of the observed second-order dependence on water. This leaves only model 10 that is similar to 8 for the cyclic compound. Transition state 10 is in accordance with the observed order in water. In 10 the H_a and H_b protons contribute primary and secondary

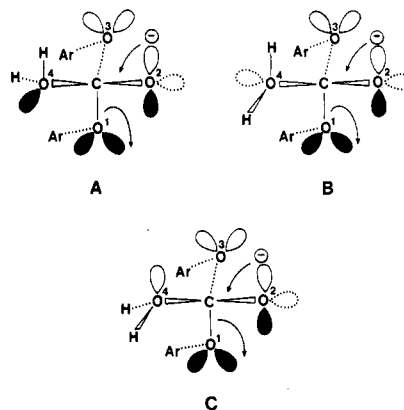**Figure 3.** Possible conformations for breakdown of the tetrahedral intermediate resulting from attack of water on 1. For expulsion of the O^1-Ar leaving group only C has the requisite two lone pairs antiperiplanar to the C–O bond. Expulsion of the O^3-Ar group, an identical reaction, could occur from A but the arrows drawn depict only loss of O^1-Ar.
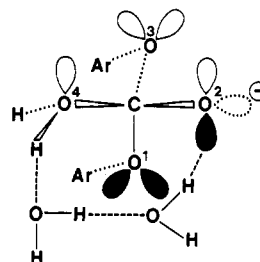

Figure 4. The hydrogen-bonded network of water molecules between the attacking water and the suitably situated lone pair on carbonyl oxygen is shown for 1.

solvent isotope effects, respectively, and H_c contributes nothing to the observed effect. The Gross–Butler equation corresponding to this model is eq 6.

The calculated γ value of 0.54 and the experimental k_n values enable us to calculate $\phi_a{}^*$ and $\phi_b{}^*$ values in eq 6 for model 10. The values thus found are: $\phi_a{}^*$ = 0.565 and $\phi_b{}^*$ = 0.889. The experimental value of β = 0.33 also enables us to calculate $\phi_b{}^*$ in a different manner by using the literature procedure.[6c] The value thus found, 0.885, is in good agreement with the $\phi_b{}^*$ obtained from the γ value. Substitution of the values $\phi_a{}^*$ = 0.565 and $\phi_b{}^*$ = 0.889 and various values of n allow one to calculate k_n values. The values of k_n thus calculated are included in Table III for comparison with experimental values. This model accurately describes the nonlinear nature of the experimental inventory.

The hydrolysis of 1 and 2 proceeds through the formation of tetrahedral intermediates and the transition states 9 and 10, respectively. Both involve cleavage of the bond between the carbonyl carbon and the leaving group oxygen. Thus, the conformation of the tetrahedral intermediate is an important parameter which should allow us to better understand the cleavage.[40] Theoretically, there are three important conformers for the tetrahedral complex. These are shown in Figure 3. The stereoelectronic theory of Deslongchamps predicts that the precise conformation of the tetrahedral intermediate directly influences the product of the reaction and cleavage of a C–O alkyl bond is allowed only if the other two oxygens of this transition state each have a lone pair orbital oriented antiperiplanar to the C–O alkyl bond to be broken.[40] Consequently, a

(33) Oakenfull, D. G.; Jencks, W. P. *J. Am. Chem. Soc.* **1971**, *93*, 178.
(34) Fedor, L. R.; Bruice, T. C. *J. Am. Chem. Soc.* **1965**, *87*, 4138.
(35) Fox, J. P.; Jencks, W. P. *J. Am. Chem. Soc.* **1974**, *96*, 1436.
(36) Reboud-Ravaux, M.; *J. Am. Chem. Soc.* **1980**, *102*, 1039.
(37) Gandour, R.; Coyne, M.; Stella, V. J.; Schowen, R. L. *J. Org. Chem.* **1980**, *45*, 1733.
(38) Patterson, J. F.; Huskey, W. P.; Hogg, J. L. *J. Org. Chem.* **1980**, *45*, 4675.
(39) Gopalakrishnan, G.; Hogg, J. L. *Bioorg. Chem.* **1981**, *10*, 243.

(40) Deslongchamps, P. *Tetrahedron* **1975**, *31*, 2463; *Heterocycles* **1977**, 1271. Deslongchamps, P. "Stereoelectronic Effects in Organic Chemistry"; Pergamon Press: New York, 1983.
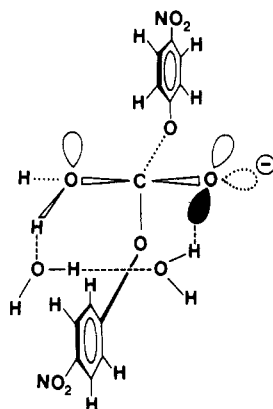
Figure 5. The unfavorable steric and hydrophobic interaction that would result if 2 employed the same hydrogen-bonded network of molecules as 1 is shown.

close visual examination of each conformer of Figure 3 shows that A and B are readily eliminated because these do not have proper orbital orientation on any two of three oxygen atoms (O_2, O_3, or O_4) to permit the cleavage of the $C-O_1$ bond. Hence, it seems the cyclic carbonate 1 is hydrolyzed via conformer C in Figure 3. A detailed examination of C in Figure 3 reveals that one of the hydrogens on the nucleophilic water molecule and one of the lone pair orbitals on the carbonyl oxygen (i.e., O_3) are properly oriented to form a cyclic chain of water molecules as shown in Figure 4. Further, it reveals that the plane of the water ring is totally away from and perpendicular to the approximate molecular plane of 1. Thus, it is away from the hydrophobic influence of the benzene ring and heterocyclic rings. This and the greater accessibility of the carbonyl group in the rigid ring system[41] are probably responsible for the existence of the ring of water molecules in 9.

In 2 the two aryl oxide groups exist in the s-cis conformation.[42] In the tetrahedral complex formed by the nucleophilic attack of water on the carbonyl carbon, the lone pair orbitals on an aryl oxygen will not be antiperiplanar to the leaving aryl oxygen group. But, if we consider the lone pair orbitals of the carbonyl oxygen and the nucleophilic water, there will be three different conformers,

similar to A, B, and C in Figure 3, for the tetrahedral complex. Of these A and B may readily be excluded because they do not have proper orbital orientation for stereoelectronic control. Hence, it is clear that the acyclic ester 2 is also hydrolyzed via conformer C. But, in this case the ring of water molecules expected to be formed as shown in Figure 5 will be subjected to severe hydrophobic and steric repulsion by the benzene ring because of the close proximity between the two (Figure 5). Hence, the population of the species similar to that in Figure 5 will be small. Further, it would be greatly deformed and thus it would have a greater energy barrier for proton transfer since a smooth, low-energy linear proton transfer is not possible. Consequently, the other proton on the nucleophilic water will move only under the influence of a general base water as shown in 10.

Experimental Section

Materials. o-(4-Nitrophenylene) carbonate (1) and bis(4-nitrophenyl) carbonate (2) were prepared from 4-nitrocatechol and 4-nitrophenol, respectively, by the literature method.[4] Deuterium oxide (99.75% atom percent deuterium, Bio-Rad) and deuterium chloride (20% solution in D_2O, Aldrich) were used as obtained. Potassium chloride was oven-dried and dessicator cooled before use. Water was twice glass distilled before use.

Kinetics. The hydrolyses of o-(4-nitrophenylene) carbonate (1) and bis(4-nitrophenyl) carbonate (2) were monitored by following the appearance of the products, 4-nitrocatechol and 4-nitrophenol, at 335 and 320 nm, respectively, on a Cary 118C UV–vis spectrophotometer equipped with a constant temperature cell compartment and holder.

Concentrated hydrochloric acid was used to prepare 10^{-3} M HCl in H_2O. Deuterium chloride was used to prepare 10^{-3} M DCl in D_2O. The ionic strength was maintained at 0.2 M with potassium chloride. Reactions in H_2O-D_2O mixtures were done by using appropriate volumes of HCl in H_2O and DCl in D_2O stock solutions.

Reactions were initiated by injecting 25 μL of stock solution which was 6.0×10^{-3} M of 1 in acetonitrile into 3.00 mL of the appropriate HCl, DCl, or HCl–DCl solution. In the case of 2, 100 μL of stock solution of concentration 1.68×10^{-3} M of 2 in acetonitrile was injected.

Reactions were followed for more than 3 half-lives. Absorbance values at 5- or 10-s intervals were collected by using a Micromation computer interfaced to the Cary 118C spectrophotometer. The data were then analyzed by using a nonlinear least-square computer program. Plots of log $(A_t - A_\infty)$ vs. time were used in a confirmatory fashion. γ values and fractionation factors were calculated by using the computer programs GAMISO1 and FRACFAC provided by Dr. John Albery.

Registry No. 1, 25859-54-5; 2, 5070-13-3; deuterium, 7782-39-0.

(41) Kaiser, E. T.; Kezdy, F. J. *Prog. Bioorg. Chem.* **1976**, *4*, 240.
(42) (a) Katon, J. E.; Cohen, M. D. *Can. J. Chem.* **1975**, *53*, 1378. (b) Byrne, J. S.; Jackson, P. F.; Morgan, K. J. *J. Chem. Soc. Perkin Trans 2*, **1976**, 1800.
(43) Urbana, IL 61801.