Decarboxylation of Monosubstituted Derivatives of Carbonic Acid. Comparative Studies of Water- and Acid-Catalyzed Decarboxylation of Sodium Alkyl Carbonates[1] in H₂O and D₂O[2]

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Abstract: The decomposition rates of HCO_3^- and of three alkyl carbonates, $CH_3OCO_2^-$, $C_2H_5OCO_2^-$, and $sec\text{-}C_4H_9OCO_2^-$, have been measured in aqueous solution using a pH stat technique at 25.0 °C in the pH range 6.7 to 10.8. Confirmatory studies on the behavior of $CH_3OCO_2^-$ in the high pH region have also been carried out using an NMR technique. The decarboxylation reactions of HCO_3^-, $CH_3OCO_2^-$, $EtOCO_2^-$, and $sec\text{-}C_4H_9OCO_2^-$ are predominantly catalyzed by H_3O^+, and to a much lesser extent by $H_2PO_4^-$ and H_2O ("spontaneous" decomposition). The acid-catalyzed decarboxylation of all four anions exhibits an inverse solvent deuterium isotope effect, $k_{H_3O^+}/k_{D_3O^+}$, of around 0.60 ± 0.1, indicating either a preequilibrium protonation of, or an advanced proton transfer to, the bicarbonate as well as the alkyl carbonate anions. Rates obtained in phosphate buffers of high ionic strength, $I = 0.5$ and 1.0, reveal that these decarboxylation reactions are also mildly catalyzed by dihydrogen phosphate. The solvent deuterium isotope effects associated with the "spontaneous" decarboxylation, $k_0^{H_2O}/k_0^{D_2O}$, exhibit values of ca. 1.8 for all alkyl carbonates studied indicating that solvent involvement is an integral part of these decompositions. The potential utility of the alkyl carbonates as substrate analogues for the carbonic anhydrase catalyzed dehydration of bicarbonate is discussed.

Carbonic anhydrase (carbonate hydro-lyase, EC 4.2.1.1) from erythrocytes is a remarkably versatile enzyme,[3] catalyzing not only the reversible hydration of CO_2 but also that of numerous aldehydes,[4,5] as well as that of α-keto acids[6] and their esters.[7] Mammalian carbonic anhydrases also act as esterases with respect to monoesters of carboxylic acids[8-12] as well as diesters of carbonic acid.[13a,b]

The great majority of these unnatural substrates are catalyzed by carbonic anhydrase in a manner formally similar to the hydration of CO_2, i.e., nucleophilic attack of hydroxide on a carbonyl moiety. Model compounds for the dehydration reaction are restricted to preliminary results in these laboratories regarding the decomposition of methyl carbonate anion, **2**, formed via the bovine carbonic anhydrase catalyzed hydrolysis of methyl 4-nitrophenyl carbonate (**1**).[13b]
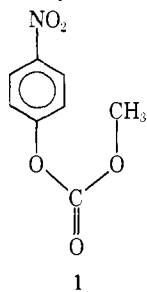
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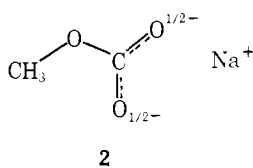
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The mechanism of the carbonic anhydrase catalyzed dehydration of HCO_3^- remains controversial. Appropriate model compounds could clarify the role of the labile bicarbonate proton and the possibility of a proton relay in carbonic anhydrase catalysis.

We present detailed decarboxylation parameters for methyl, ethyl, and *sec*-butyl carbonate monoanions in H₂O and D₂O, which are closely analogous to those of HCO_3^-. The close mechanistic analogy suggests the interaction of the alkyl carbonates with carbonic anhydrase may model important features of the catalytic action of carbonic anhydrase on bicarbonate. A forthcoming paper will detail these enzymatic interactions.

Experimental Section

Materials. Reagent grade methyl and ethyl alcohol were dried with magnesium activated with I₂ and then distilled. Reagent grade *sec*-

butyl alcohol was refluxed for 4 h over freshly ignited calcium oxide, decanted, refluxed for 4 h over magnesium, and fractionally distilled (bp 99.0–99.5 °C).[14] Neat solutions of all anhydrous alcohols showed no significant exchange broadening of the hydroxyl proton in their NMR spectra.

Metal alkoxide solutions were prepared immediately prior to use by addition of freshly cut metal to an 80-fold molar excess of anhydrous alcohol. The sodium salts of methyl and ethyl carbonate precipitated immediately upon introduction of CO_2 (Airco, research grade, 99.99%) to the corresponding anhydrous alcohol solution of the alkoxide. Potassium *sec*-butyl carbonate was similarly precipitated from a solution of potassium *sec*-butyl alkoxide in *sec*-butyl alcohol, diluted approximately fivefold with anhydrous diethyl ether (refluxed 48 h over LiAlH₄).[15]

When no further precipitation was evident, the precipitate was collected by filtration on sintered glass, washed with 2 vol of the corresponding anhydrous alcohol followed by 4 vol of anhydrous ethyl ether,[16] and dried in vacuo over CaSO₄. Great care must be taken at all stages to exclude moisture, as the precipitate must be dried and used with no further purification.[17]

Purity was indirectly checked by decomposing weighed quantities of precipitate with standardized HCl, scrubbing the resulting solution with N₂ to remove CO_2 formed, and back-titrating to a pH 7 end point with standardized NaOH. The alkyl carbonates yielded apparent equivalent weights of 98.4 ± 0.6 (calcd 98.0), 112.3 ± 0.5 (calcd 112), 155.8 ± 0.4 (calcd 156) for methyl, ethyl, and *sec*-butyl carbonate, respectively. Within the precision of the titration, contamination by HCO_3^- of more than 3 molar % should be detectable.

The buffer components, potassium dihydrogen phosphate (Matheson Coleman and Bell), disodium hydrogen phosphate (M.C.B.), boric acid (Baker), sodium sulfate (Baker), and sodium bicarbonate (Baker), were of analytical quality and were used without further purification. 1,2-Dimethylimidazole (Aldrich) was twice distilled under reduced pressure. *N,N*-Dimethylglycine was prepared from *N,N*-dimethylglycine hydrochloride (Nutritional Biochemicals Corp.) according to the method outlined by Pocker and Guilbert.[13a] Diethyl malonic acid was recrystallized from benzene 3 times (mp 126.0–127.5 °C).

D₂O, purchased from Bio-Rad (99.87% D₂O), was twice distilled through all-glass apparatus prior to use. *N,N*-Dimethylglycine (DMG) buffers in D₂O were prepared by titrating 0.05 M stock DMG solutions to the desired pD with NaOD. Use of the mono- and dihydrogen salts in the preparation of phosphate buffers in D₂O involved minor depletions in percent D₂O present in the reaction mixture which were ignored. The pD values were derived from the pH meter readings by employing the relation pD = pH meter reading + 0.41 noted by Glasoe and Long[18a] and by Li et al.[18b] Prior to taking meter and rate

measurements in D_2O buffers, electrodes were equilibrated 2 h in D_2O.

Apparatus. All pH measurements were taken at 25.0 °C with Radiometer automatic titrator (type TTT 1C) equipped with a scale expander (type PHA 630 T) and a glass calomel electrode pair (Radiometer G2222C and K4112), such that pH values were accurate to within ±0.005 pH unit. The pH meter was frequently standardized against pH reference buffer solutions (Haleco). The modified pH-stat technique of Magid and Turbeck[19] employed in this study involved the coordination of the automatic titrator with a titrigraph recorder (Radiometer, type SBR 2C) and an autoburet (Radiometer, type ABU 1B, alternately equipped with 2.5 or 0.25-mL burets), enabling decarboxylation rate constants as large as 0.030 s^{-1} to be calculated with a consistency of approximately 4% between rates monitored under identical conditions.

The reaction cell, consisting of a jacketed 30-mL, 30 M sintered glass filter (Kimax), was thermostated at 25.0 ± 0.1 °C with a precision bath pump (Forma Temp., Model 2095). Samples were added to the reaction chamber by employing syringe injection of buffer through a mixing chamber containing an appropriate aliquot of dry alkyl carbonate. The chamber consisted of a glass tube approximately 3 mm i.d. × 20 mm, capped at both ends with rubber septa, with a syringe needle outlet. Dissolution of the alkyl carbonate and evacuation of the chamber into the reaction mixture could be accomplished in 1–2 s.

By careful adjustment of titrant normality, autoburet titrant injection speed, and titragraph proportional band setting, the pH of the reaction mixture was maintained constant within 0.06 pH unit throughout an experimental run.

Methods. All kinetic data involving pH-stat work, unless otherwise stated, were obtained at 25 ± 0.1 °C employing 0.02 M buffers (phosphate, 1,2-dimethylimidazole, boric acid, diethyl malonate, and N,N-dimethylglycine) throughout the entire pH range studied (6.7–10.8). The total ionic strength of the reaction medium was maintained at 0.10 by addition of sodium sulfate.

Rates were initiated by the syringe addition of approximately 15% of the buffer for a given run through a mixing chamber containing an appropriate aliquot of dry alkyl carbonate (0.003 g average) directly into the reaction chamber, establishing a typical initial reactant concentration of 5×10^{-3} M. Rates were followed to their experimental infinities yielding plots of ln $[V_\infty - V_t]$ vs. time (where V is titrant volume) which were consistently linear past 2 half-lives. Plots of rate data were analyzed by weighted linear least-squares analysis. Data points represent at least four duplicate runs with correlation coefficients $(r) \geq 0.999$. The individual coefficients k_0, $k_{H_3O^+}$, and k_{BH} comprising the observed first-order rate constants, $k_{obsd}^{ROCO_2}$, were resolved by the method of Bell and Darwent.[20]
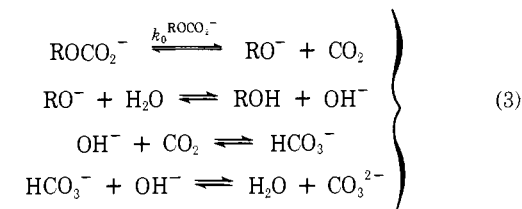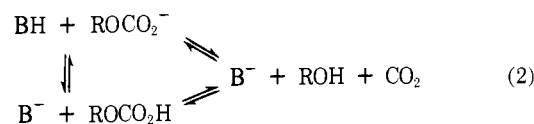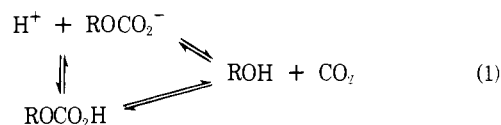
Three techniques of obtaining rate data were used. In technique I, a flow of H_2O-saturated N_2 was maintained through the glass frit of the pH-stat reaction chamber at a rate of 1400 cm^3/min, monitored by a gas flowmeter (Gilson, No. 12), to obviate interference from proton production caused by the hydration of CO_2 produced during the decomposition of the alkyl carbonates.

Some rates at pH values greater than 8.5 were followed by technique II, employing the pH stat under conditions which suppressed CO_2 evolution,[13b] to monitor the net release of protons accompanying the decomposition of the alkyl carbonates to the carbonate–bicarbonate equilibrium system ($K_{HCO_3^-} = 1.14 \times 10^{-10}$ M at 25 °C, ionic strength 0.10).
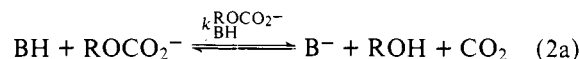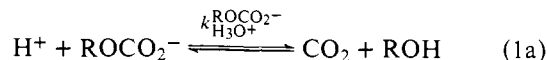
As a further check, a method completely independent of the pH stat was developed. Technique III involved simultaneous integration of the areas as a function of time of the methyl proton NMR singlets of CH_3OD ($\delta = 3.35$) and $CH_3CO_3^-$ ($\delta = 3.55$). First-order rate constants could be calculated based on the decreasing area of the $CH_3CO_3^-$ singlet or the increasing area of the CH_3OD singlet with time; constants calculated by both methods were identical. Measurements were performed at 37 °C in D_2O at ionic strength 0.10 with a Varian NMR spectrometer (Model T60) employing initial methyl carbonate concentrations of 0.05 M. No added buffers were used under these conditions since the buffering effect of the bicarbonate, formed in the decomposition process, confined changes in pD during the course of the reaction to <0.3 pD unit.

Results

Earlier workers have already established some facts about this system.[21,22] Analysis of eq 1–5 representing possible kinetic

$$H^+ + ROCO_2^- \rightleftharpoons ROH + CO_2 \quad (1)$$
$$ROCO_2H$$

$$BH + ROCO_2^- \rightleftharpoons B^- + ROH + CO_2 \quad (2)$$
$$B^- + ROCO_2H$$

$$\left. \begin{array}{l} ROCO_2^- \xrightleftharpoons{k_0^{ROCO_2^-}} RO^- + CO_2 \\ RO^- + H_2O \rightleftharpoons ROH + OH^- \\ OH^- + CO_2 \rightleftharpoons HCO_3^- \\ HCO_3^- + OH^- \rightleftharpoons H_2O + CO_3^{2-} \end{array} \right\} \quad (3)$$

$$H_2O + ROCO_2^- \underset{k_{-4}}{\overset{k_4}{\rightleftharpoons}} ROH + HCO_3^- \quad (4)$$

$$HO^- + ROCO_2^- \underset{k_{-5}}{\overset{k_5}{\rightleftharpoons}} ROH + CO_3^{2-} \quad (5)$$

schemes for the decomposition of monoalkyl carbonates in aqueous solution affords several conclusions, the first being that if direct hydrolysis steps, k_4 and k_5, are disregarded, the resulting schemes are nearly identical with those proposed by Faurholt.[21,22] Another conclusion apparent from the above schemes is that for pH values above 6, where $[ROCO_2^-] \gg [ROCO_2H]$, eq 1 can be written as eq 1a and eq 2 as eq 2a:

$$H^+ + ROCO_2^- \xrightleftharpoons{k_{H_3O^+}^{ROCO_2^-}} CO_2 + ROH \quad (1a)$$

$$BH + ROCO_2^- \xrightleftharpoons{k_{BH}^{ROCO_2^-}} B^- + ROH + CO_2 \quad (2a)$$

Furthermore, employment of technique I at N_2 flow rates above 1000 mL per min enables the $[CO_2]$ to be taken as zero, thereby making it possible to represent the overall decomposition process by the relatively simple integrated rate eq 6, involving the first-order rate coefficient $k_{obsd}^{ROCO_2}$:

$$\frac{V_{obsd}}{[ROCO_2^-]} = k_{obsd}^{ROCO_2^-} = k_0^{ROCO_2^-}$$
$$+ k_{H_3O^+}^{ROCO_2^-}[H_3O^+] + k_{BH}^{ROCO_2^-}[BH] \quad (6)$$

(This expression neglects contributions from k_4 and k_5.) It is apparent from Figure 1a that the chemical decomposition of sodium methyl carbonate exhibits a substantial pH dependence. The hydronium ion assisted reaction pathway incorporating a $k_{H_3O^+}^{CH_3OCO_2^-} = 53.6 \times 10^3$ M^{-1} s^{-1} appears to involve a rapid preequilibrium protonation as evidenced by an inverse solvent deuterium isotope effect, $k_{D_3O^+}^{CH_3OCO_2^-}/k_{H_3O^+}^{CH_3OCO_2^-} = 1.9$. Furthermore, the intercepts of plots of k_{obsd} vs. $[L_3O^+]$, corresponding to $k_0 + k_{BL}[BL]$,[23] reflect an isotopic dependency in the opposite direction. Points taken by techniques I and II in H_2O (Figure 1b, upper line) in the high pH region where H_3O^+ catalysis is negligible are in complete agreement. Furthermore, the value obtained by techniques I and II in D_2O (Figure 1b, lower line), averaging 1×10^{-3} s^{-1}, is in accord with the rate constant obtained by technique III (2.2×10^{-3} s^{-1} at 37 °C)[24] in approximately the same high pH region.

It has been shown that the breakdown of methyl and ethyl monocarbonates is not significantly dependent on $[OH^-]$ at high pH where these alkyl monocarbonates would be completely in the ionized form. Clearly the second-order process represented by k_5 can be disregarded.

In considering the relative importance of eq 4 above it is

Table I. Decarboxylation of Alkyl Carbonates at 25.0 °C in Water at Ionic Strength 0.10

Alkyl carbonates	$k_{H_3O^+} \times 10^{-4}$, $M^{-1} s^{-1}$	$k_0^{H_2O} \times 10^3$, s^{-1}	$k_{H_2PO_4^-} \times 10$, $M^{-1} s^{-1}$	$k_{H_3O^+}/k_{D_3O^+}$	$k_0^{H_2O}/k_0^{D_2O}$
HCO_3^-	5.09	0.2	1.00^b	0.62	e
$CH_3OCO_2^-$	5.36	$1.70,^c 1.55^d$	0.80^a	0.54	1.8
$C_2H_5OCO_2^-$	8.94	0.77	0.40^a	0.65	1.8
sec-$C_4H_9OCO_2^-$	12.56	0.15	0.58^a	0.62	~ 1.8

^{a} Ionic strength 0.50, at 25.0 °C. ^{b} Ionic strength 1.00, at 25.0 °C (Y. Pocker and D. Bjorkquist).[26,27] ^{c} Determined by technique I. ^{d} Determined by technique II. ^{e} This ratio is currently under study using technique I.[36]
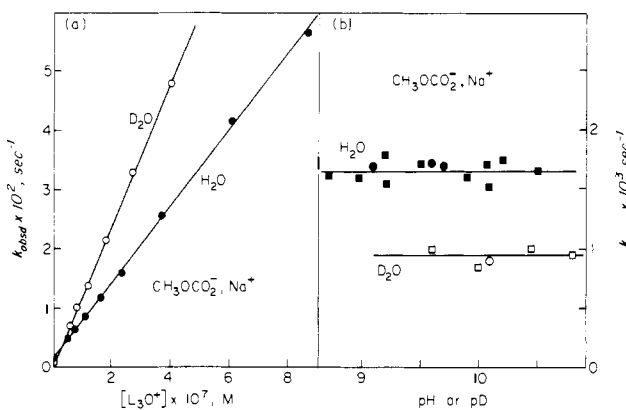

Figure 1. (a) L_3O^+-catalyzed decomposition of sodium methyl carbonate at 20 °C, ionic strength 0.10, and [phosphate] = 0.02 M (assayed by technique I): (●) H_2O; (○) D_2O. (b) High pH decomposition of sodium methyl carbonate at 25.0 °C, ionic strength 0.10, and [N,N-dimethylglycine] = 0.02 M: (●) H_2O, technique I; (■) H_2O, technique II; (○) D_2O, technique I; (□) D_2O, technique II. The points at pH 8.7 and 9.0 were measured in 1,2-dimethylimidazole buffers. 0.02 M; 1,2-dimethylimidazole and N,N-dimethylglycine had no detectable effect on the rate at the concentrations utilized. Refer to Table I for values of the pertaining parameters.

appropriate to note that Pocker and Guilbert[13b] have pointed out that a major question in regard to the interpretation of alkyl carbonate decomposition data is whether one is observing hydrolysis (such as that represented by k_4 followed by the dehydration of bicarbonate) or decarboxylation. In this respect they noted that at neutral pH (employing technique I) the rate of proton uptake by methyl carbonate was faster than that of bicarbonate, indicating that around physiological pH bicarbonate could not be involved as an intermediate.

The above results indicate that the rate-limiting steps monitored by techniques I and II are identical and, furthermore, correspond to the rate at which $CH_3OCO_2^-$ methyl protons are converted to CH_3OD methyl protons. This congruency, combined with the fact that the $k_0^{CH_3OCO_2^-}$ (obtained by technique I in both high and low pH regions) is significantly larger than the value of $k_0^{HCO_3^-}$ determined under identical conditions, clearly indicates that the measured value for $k_0^{CH_3OCO_2^-}$ is indeed a real and intrinsic decomposition parameter and that over the entire pH region investigated bicarbonate is not produced by the direct hydrolysis of $CH_3OCO_2^-$ in the manner indicated by k_4 in eq 4.

Support for this conclusion can also be found by analogy in [18]O exchange data for bicarbonate decomposition in aqueous alkali.[25] The first-order rate constant for [18]O depletion of labeled bicarbonate at pH 9.4 and 25 °C is identical with the k_0 value for the decarboxylation of bicarbonate. Therefore, depletion by a mechanism such as

$$HC^{18}O_3^- + H_2O \rightleftharpoons HCO_3^- + H_2{}^{18}O$$
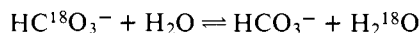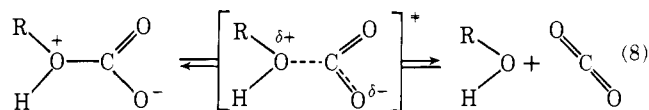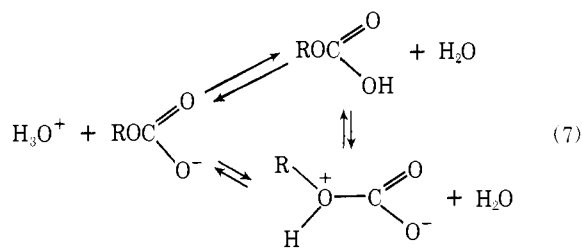
is insignificant.

Results for all four of the carbonate species studied are listed in Table I along with coefficients for dihydrogen phosphate

catalysis. Substantial inverse deuterium isotope effects appear to be a common feature among these compounds, thus confirming the existence of the protonated intermediate depicted in eq 1 of the general decomposition scheme. (A comparable value for $k_{H_3O^+}^{HCO_3^-}/k_{D_3O^+}^{DCO_3^-}$ of 0.56 was obtained by Pocker and Bjorkquist,[26,27] in these laboratories utilizing a stopped-flow technique.) In order to accurately determine the magnitude of the catalytic coefficients for dihydrogen phosphate listed in Table I it was necessary to work at elevated ionic strengths (i.e., high phosphate concentrations) whereby it was observed that the $k_{H_3O^+}$ coefficients were reduced by a factor of 0.60 (±0.05 among the various species) in going from ionic strength 0.10 to 0.50. This effect is in accord with that predicted by the Brönsted-Bjerrum-Christiansen equation for a reaction between singly charged ions of opposite sign.[28,29]

The magnitudes of the k_0 values for ethyl and sec-butyl carbonate are closer to that of bicarbonate and, within experimental error, do not permit as certain an assignment of a mechanism as does the k_0 of methyl carbonate. Likewise, while the ratios $k_0^{H_2O}/k_0^{D_2O}$ for the alkyl carbonates are comparable, the experimental error inherent in the ratio for bicarbonate must make such data suggestive, but not conclusive. Nonetheless, the suggestion of a close kinetic analogy to bicarbonate is quite strong.

Discussion

Acid Catalysis. The observed inverse solvent deuterium isotope effects $k_{H_3O^+}^{ROCO_2^-}/k_{D_3O^+}^{ROCO_2^-}$ of ca. 0.6 for the acid-catalyzed decarboxylation of alkyl carbonates indicate the involvement of a protonated intermediate resulting from a preequilibrium proton transfer, eq 7 and 8. An identical result for

bicarbonate emphasizes the kinetic similarity of the alkyl carbonates and bicarbonate.

The existence of a small but significant general acid catalysis term, $k_{H_2PO_4^-}$, in both the alkyl carbonates and bicarbonate is, however, indicative of a rate-determining proton transfer, eq 9, for which one anticipates a solvent isotope effect significantly greater than 1, rather than the observed value of 0.6.

The apparently contradictory kinetic and isotopic data may be resolved by postulating a transition-state intermediate between that of eq 8 and 9. If the proton transferred to the alkyl carbonate is nearly, though not completely, transferred in the

$$(9)$$
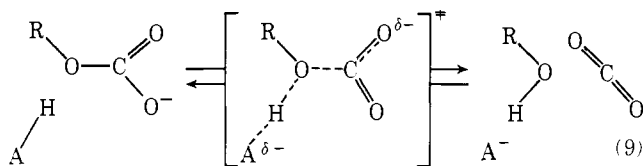
transition state, the primary isotope effect would be considerably reduced, to a value near 1. Since $(k_H/k_D)_{net} = (k_H/k_D)_{pri}(k_H/k_D)_{sec}$ the inverse secondary isotope effect would be expressed in the observed net isotope effect, while catalytic participation could still be evident.

Such an interpretation is congruent with that postulated by Kresge for the hydrolysis of alkyl orthocarbonates,[30] and would also provide an explanation of Bender's data on the dehydration of carbinolamines to oximes,[31] which represents a third example of reactions exhibiting both general acid catalysis and an inverse solvent deuterium isotope effect.

We would then conclude that the monoester of carbonic acid, ROCOOH, or its zwitterion, RO^+HCOO^- (with proton transfer nearly complete in the transition state), is the intermediate in the acid-catalyzed decarboxylation of alkyl carbonates.

Water Catalysis. Values of $k_{H_2O}^{ROCO_2^-}/k_{D_2O}^{ROCO_2^-}$ for the decarboxylation of methyl, ethyl, and sec-butyl carbonates are near 1.8, consistent with solvent involvement in the transition state for the spontaneous reaction. The reverse reaction for bicarbonate, the hydroxide-catalyzed hydration of CO_2, shows a solvent deuterium isotope effect of 0.6,[32] indicating nucleophilic attack by hydroxide in the transition state.

In view of the high degree of kinetic similarity evidenced among these species, it may be profitable to combine this information with results for the alcohol–bicarbonate–water equilibrium system from a study spanning a considerable range in pK_a of the alcohol.[33] A Bronsted plot of log $k_{RO^-}^{CO_2}$ vs. pK_a^{ROH} yielded a β_{nuc} of 0.3 for the attack of alkoxide on CO_2, implying a transition state early along the reaction coordinate. The reverse reaction is then expected to have a late transition state, by microscopic reversibility.[34]

As in the acid-catalyzed mechanism, then, a late transition state in the spontaneous decarboxylation of the alkyl carbonates would provide for the effective nucleophilic involvement of RO^- while permitting solvent involvement consistent with $k_{H_2O}^{ROCO_2^-}/k_{D_2O}^{ROCO_2^-}$, eq 10.[35,36]

$$(10)$$
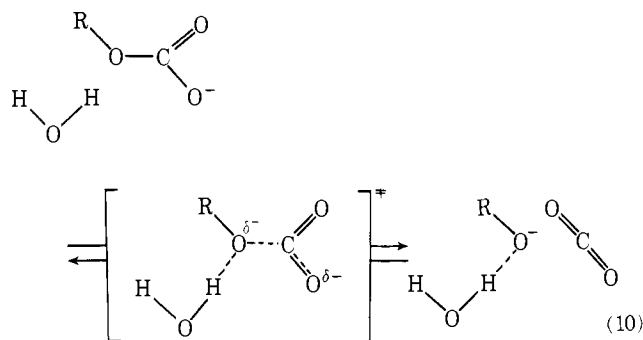
The alkyl carbonates examined in this study show considerable kinetic analogy to bicarbonate. We then reasonably anticipate a comparable mechanistic similarity. The alkyl carbonates should serve as illustrative models for the interaction of bicarbonate with carbonic anhydrase and possibly clarify the role of the labile bicarbonate proton in its enzymatic decomposition.

References and Notes

(1) The nomenclature sodium alkyl carbonate was chosen by analogy with the ACS recommendations for esters of carboxylic acids (J. H. Fletcher, O. C. Dermer, and R. B. Fox, Ed., Adv. Chem. Ser., **No. 126** (1974)). Chemical Abstracts uses carbonic acid, monoalkyl ester. We suggest that other terms be avoided to establish some consistency in the literature.

(2) Support of this work by grants from the National Institute of Arthritis, Metabolism and Digestive Diseases of the U.S. Public Health Service (AM 09221) and the National Science Foundation (BMS-74-21859) is gratefully acknowledged. B.L.D. was an Undergraduate Research Participant (1974–1975).

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(12) Of considerable interest are the carbonic anhydrase catalyzed hydrolyses of 2-hydroxy-5-nitro-α-toluenesulfonic acid sultone [K. W. Lo and E. T. Kaiser, Chem. Commun., 834 (1966); E. T. Kaiser and K. W. Lo, J. Am. Chem. Soc., **91**, 4912 (1969)] and of dimethyl 2,4-dinitrophenyl phosphate triester [Y. Pocker and S. Sarkanen, Abstracts, Northwestern Meeting of the American Chemical Society, Vol. 28, 1973, p B27; Fed. Eur. Biochem. Soc. Meet. [Proc.], **10**, 782 (1975)].

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(14) G. Jones and S. M. Christian, J. Am. Chem. Soc., **61**, 82 (1939).

(15) The addition of ether to the alcohol–alkoxide solution prior to the introduction of CO_2 was necessary in order that viscosity difficulties, resulting from the increased solubility of CO_2 in this alcohol, be avoided. The potassium salt was chosen in this case to give a more flocculent precipitate.

(16) The washing procedure was employed to minimize any possible contamination of the sodium alkyl carbonate by residual sodium alkoxide.

(17) The alkyl carbonates are stable at room temperature under desiccation. All are somewhat hygroscopic, and sec-butyl carbonates, both sodium and potassium salts, are particularly sensitive to atmospheric moisture.

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(23) Values of k_0 were deduced from data obtained in dilute buffer and an ionic strength of 0.1 where the term $k_{BL}[BL]$ is negligible.

(24) As previously stated, the NMR work was performed at 37 °C; hence, it was necessary to apply a temperature compensation factor based upon the activation parameter of HCO_3^- (our own work has suggested that the activation energies for HCO_3^-, $MeOCO_2^-$, and $EtOCO_2^-$ are nearly identical). The above argument involves a compensation factor of 2.2 which seems quite reasonable.

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(34) This study bears on another aspect of the problem. It is conceivable that the observed general acid catalysis results from a parallel, competing mechanism with rate-determining proton transfer, with the expected isotope effect masked by the dominant inverse effect due to a principal preequilibrium mechanism. The fact that H_2O falls fairly closely on the line defined for alcohols in a Bronsted plot of K_{eq}' vs. pK_a^{ROH} suggests that water does not represent a special case. Water does deviate strongly from plots of k_{nuc} vs. pK_a^{ROH} and k_{decomp} vs. pK_a^{ROH}, the forward and reverse reactions of the equilibrium, but differential solvent effects (ROH equilibria were determined in solutions up to 4 M in alcohol) might be expected to be more evident in the individual rate constants.

(35) Using the method of R. L. Schowen (Prog. Phys. Org. Chem., **9**, 275 (1972)) a net isotope effect of 1.9 was estimated for the indicated mechanism with a degree of reaction advancement in the transition state of 0.9. The close agreement with experiment is undoubtedly somewhat fortuitous. The predicted isotope effect for the acid-catalyzed reaction is 0.95, in qualitative agreement with experiment.

(36) Using the method of J. T. Edsall (NASA SP-188, 1969, p 15) for estimating k_0 it can be shown that a ratio $k_0^{H_2O}/k_0^{D_2O}$ of between 1 and 2 for the decarboxylation of bicarbonate is reasonable.