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Carbon Kinetic Isotope Effects on the Hydrolysis of Aryl Carbonates

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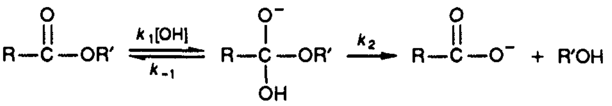
Abstract: Carbon kinetic isotope effects on the hydrolysis of aryl carbonates in 1:1 (v/v) dioxane–water at 25 °C at various pHs were used to calculate isotope effects on the reactions with hydroxide ion and with water. For diphenyl carbonate $k_{OH}^{12}/k_{OH}^{13} = 1.0482$ and $k_w^{12}/k_w^{13} = 1.0509$. For bis(*p*-methoxyphenyl)carbonate $k_{OH}^{12}/k_{OH}^{13} = 1.0493$ and $k_w^{12}/k_w^{13} = 1.0518$. For bis(*p*-nitrophenyl)carbonate $k_{OH}^{12}/K_{OH}^{13} = 1.0476$. The small change in the isotope effect with substituent group for both alkaline and neutral hydrolysis is in contrast to the large substituent effect on the rate constants for both reactions. The nearly constant isotope effect indicates that transition-state structures are similar for all substrates.

Carboxylate esters are believed to react with nucleophiles by a stepwise mechanism involving a tetrahedral intermediate[1] (eq 1). This conclusion is based on the results of a variety of experiments, including structure–reactivity relationships, isotope exchange, and isotope effects. Isotopes of carbon and oxygen have played a major role in defining the tetrahedral intermediate mechanism. Early experiments, employing ^{18}O in the ether oxygen position, indicated that hydrolysis occurs with acyl–oxygen bond cleavage.[2] Experiments with ^{18}O in the carbonyl oxygen by Bender[3] and Kirsch[4] and collaborators established that exchange of the carbonyl oxygen with solvent occurs during hydrolysis. The ratio of the rates of hydrolysis to exchange (k_h/k_{ex}) can be used to calculate a partitioning ratio (k_2/k_1, eq 1). This partitioning ratio is usually greater than unity for alkaline hydrolysis. For example, the partitioning ratio is 44 for the alkaline hydrolysis of methyl benzoate[4] in 33% dioxane–water at 25 °C. However, the ratios so derived are correct only if the tetrahedral intermediate is sufficiently long lived that proton transfers within the intermediate are at equilibrium, and Jencks has suggested that proton-transfer equilibria may not be attained in some cases.[5] The extent of oxygen exchange is frequently less than that expected on the basis of the leaving tendencies of various groups within the tetrahedral intermediate. Williams et al.[6] have recently offered evidence for a concerted mechanism for reactions of *p*-nitrophenyl acetate with certain nucleophiles. Nevertheless, the exchange data suggest that most reactions occur via a tetrahedral intermediate (eq 1), and the first step is rate determining for the majority of cases.



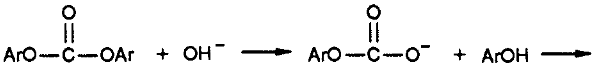
$$R{-}\overset{\overset{\displaystyle O}{\|}}{C}{-}OR' \underset{k_{-1}}{\overset{k_1[OH]}{\rightleftharpoons}} R{-}\underset{\underset{\displaystyle OH}{|}}{\overset{\overset{\displaystyle O^-}{|}}{C}}{-}OR' \xrightarrow{k_2} R{-}\overset{\overset{\displaystyle O}{\|}}{C}{-}O^- + R'OH \quad (1)$$

Substituent groups affect the rates of alkaline hydrolysis of benzoate and acetate esters. Hammett ρ-values are +1.2–1.5 for the leaving group and +2.0 for the acyl group in the alkaline hydrolysis of phenyl benzoates.[7,8] The corresponding ρ-value is +1.1 for the leaving group in the alkaline hydrolysis of phenyl acetate.[9] These results are consistent with a stepwise mechanism with a rate-determining first step (eq 1), but taken alone do not rule out a concerted mechanism.

Kinetic isotope effects have provided additional information about mechanisms of ester hydrolysis. Acyl–oxygen isotope effects are invariably small. For the alkaline hydrolysis of methyl formate[10] $k^{16}/k^{18} = 1.009$ in water at 25 °C and for methyl benzoate[11] $k^{16}/k^{18} = 1.005$ in water at 25 °C, indicating very little carbon–acyl oxygen bond breaking at the transition state. This agrees with the oxygen exchange results, indicating a rate-determining first step (eq 1). The small observed isotope effect is thought to reflect a small isotope effect due to loss of resonance in the first step. The carbonyl oxygen isotope effect for the alkaline hydrolysis of methyl benzoate ($k^{16}/k^{18} = 1.006$) is small.[11]

Carbonyl carbon isotope effects on ester hydrolysis are large. For ethyl benzoates,[12] $k^{12}/k^{14} = 1.06$ for ethyl *m*-nitrobenzoate and $k^{12}/k^{14} = 1.08$ for ethyl *p*-chlorobenzoate, both in 90% ethanol–water at 25 °C. For methyl benzoate,[11] $k^{12}/k^{13} = 1.04$ in water at 25 °C. These values indicate substantial changes in bonding to carbon on going to the transition state, as expected for a rate-determining first step in which the structure of the transition state resembles that of the tetrahedral intermediate. However, the carbon isotope effects do not distinguish between rate-determining formation and rate-determining breakdown of the tetrahedral intermediate.

The few examples available indicate that carbonyl carbon isotope effects in carbonyl groups reactions are generally likely to be large; thus, they may be a particularly useful criterion of transition-state structure. Unfortunately, measurement of carbon isotope effects usually requires conversion of the isotopic site to CO_2 for isotopic analysis; this is difficult to achieve for benzoate and acetate esters. Carbonate esters offer a solution to this problem. Reaction with the first equivalent of hydroxide liberates an equivalent of alkoxide and a carbonate monoester (eq 2), presumably via the stepwise tetrahedral mechanism discussed above for carboxylate esters.[13] Since reaction with the first equivalent of hydroxide is irreversible and the intermediate monoester does not accumulate, any isotope effect on consumption of the second and subsequent molecules of hydroxide is invisible and the observed isotope effect reflects only the first hydrolysis reaction. The product, carbon dioxide, is suitable for direct



$$ArO{-}\overset{\overset{\displaystyle O}{\|}}{C}{-}OAr + OH^- \longrightarrow ArO{-}\overset{\overset{\displaystyle O}{\|}}{C}{-}O^- + ArOH \longrightarrow CO_2 + 2ArOH \quad (2)$$

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(1) Johnson, S. L. *Adv. Phys. Org. Chem.* **1967**, *5*, 237.

(2) Polyanyi, M.; Szabo, A. L. *Trans. Faraday. Soc.* **1934**, *30*, 508.

(3) (a) Bender, M. L.; Thomas, R. J. *J. Am. Chem. Soc.* **1961**, *83*, 4189; *83*, 4193. (b) Bender, M. L.; Heck, H. d'A. *Ibid.* **1967**, *89*, 1211. (c) Bender, M. L.; Ginger, R. D.; Unik, J. P. *Ibid.* **1958**, *80*, 1044.

(4) Shain, S. A.; Kirsch, J. F. *J. Am. Chem. Soc.* **1968**, *90*, 5848.

(5) Jencks, W. P. *Acc. Chem. Res.* **1980**, *13*, 161.

(6) Ba-Saif, S.; Luthra, A. K.; Williams, A. *J. Am. Chem. Soc.* **1987**, *109*, 6362.

(7) Kirsch, J. F.; Clewell, W.; Simon, A. *J. Am. Chem. Soc.* **1968**, *33*, 127.

(8) Washkuhn, R. J.; Patel, U. K.; Robinson, J. R. *J. Pharm. Sci.* **1971**, *60*, 736.

(9) (a) Ryan, J. J.; Humffray, A. A. *J. Chem. Soc. B* **1966**, 842. (b) Bruice, T. C.; Mayahi, M. F. *J. Am. Chem. Soc.* **1960**, *82*, 3067.

(10) Sawyer, C. B.; Kirsch, J. F. *J. Am. Chem. Soc.* **1973**, *95*, 7375.

(11) O'Leary, M. H.; Marlier, J. F. *J. Am. Chem. Soc.* **1979**, *101*, 3300. ^{14}C isotope effects are approximately twice as large as ^{13}C ones.

(12) Ropp, A. G.; Raaen, V. F. *J. Chem. Phys.* **1952**, *20*, 1823.

(13) Fife, T. H.; Hutchins, J. E. C. *J. Am. Chem. Soc.* **1981**, *103*, 4194.

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analysis by isotope ratio mass spectrometry. In addition, the carbonyl carbon can serve as a remote label for the carbonyl and acyl oxygen isotope effects. In the present study we use aryl carbonates to correlate transition-state structure with classical structure–reactivity relationships.

Experimental

Materials. Spectrophotometric grade dioxane was obtained from Aldrich and used without further purification. Water was purified with a Millipore Super Q water purification system. Buffers were prepared from boric acid and KOH; pH measurements were made on a Radiometer Model 26 pH meter. The pH was calibrated by the two buffer method using water without cosolvent. Next, the pH was measured before and after the addition of cosolvent. The measured pH in the dioxane–water mixtures was corrected for the effect of cosolvent (pH*).[14] Rates of reactions were determined on a Cary 118 spectrophotometer. Isotope ratios were obtained on a Finnigan Delta-E isotope ratio mass spectrometer.

Carbonate Esters. Diphenyl carbonate was obtained from Eastman and recrystallized from absolute ethanol (mp 78.5–79 °C, lit.[15] mp 78–80 °C). Bis(*p*-nitrophenyl)carbonate was purchased from Aldrich Chemical Co. and recrystallized from $CHCl_3$ (mp 141–141.5 °C, lit.[15] mp 140–142 °C). Bis(*p*-methoxyphenyl) carbonate was synthesized from phosgene iminium chloride[16a] and recrystallized from absolute ethanol (mp 95.5–96 °C, lit.[16b] mp 93–93.5 °C). All esters were stored desiccated.

Kinetics. Rates of reaction were followed spectrophotometrically by measuring the increase in absorbance due to appearance of the various phenols: at 270 nm for phenol, at 290 nm for *p*-methoxyphenol, and at either 315 nm (low pH) or 405 nm (high pH) for *p*-nitrophenol.

All experiments were conducted at 25 °C with either phosphate or borate buffers and 1:1 (v/v) dioxane. Reactions were initiated by addition of 40 μL of 8.0 mM substrate in dioxane to a cuvette containing 500 μL of the appropriate buffer and 460 μL of dioxane. Infinity points were generated independently by reaction with excess KOH, followed by quenching with the buffer at the appropriate pH. Wherever practical, the reactions were monitored for at least one half-life. All runs were done in triplicate. No significant buffer catalysis or ionic strength effects were observed under the above conditions, in agreement with previous investigations.[15]

Isotope Effects in Borate Buffer. A 65-mL sample of 0.30 M borate buffer at the appropriate pH was sparged overnight with CO_2-free N_2. The N_2 was passed through a water trap containing dilute H_2SO_4 prior to passing through the sample of buffer. This was done to minimize the loss of water (and a resultant change in buffer concentration) during the long sparging times. A 75-mL sample of dioxane was sparged for 1 h with CO_2-free N_2. A 65-mL aliquot of sparged dioxane was added to the borate solution with a syringe through a septum while under continuous sparge. After mixing, a 30-mL sample was withdrawn and added to a smaller reaction flask.

After the larger sample was equilibrated to 25 °C, a 1.5-mL sample of 0.20 M substrate (in dioxane) was added. A small sample was removed and monitored spectrophotometrically. At the appropriate time this low conversion sample was quenched by addition of 1.0 mL of concentrated H_2SO_4 through a septum in the sidearm of the reaction vessel. The CO_2 was collected and analyzed as previously described.[17] The smaller 100% conversion sample was treated in an identical manner except 0.45 mL of 0.2 M substrate in dioxane was added and the reaction was incubated at 37 °C for at least 10 half-lives.

Isotope Effects in KOH–H_2O. A 50-mL sample of water was sparged for 2 h with CO_2-free N_2 as described above. A 47-mL sample of sparged dioxane was added to the H_2O, and the resulting solution was incubated at 25 °C. A 15–20 μL-sample of saturated KOH (CO_2-free) was added, followed by 3.0 mL of 0.10 M substrate in dioxane and the solution was stirred. After a few minutes 0.5 mL of concentrated H_2SO_4 was added and the CO_2 collected in the usual manner. These reaction mixtures contained a limiting amount of KOH, and the reaction effectively stopped after this KOH was consumed. The 100% samples were generated as described in the borate buffer experiments.

Control Experiments. To ensure that the CO_2 analyzed originated from the substrate molecule, samples containing only sparged buffer (or KOH–H_2O) and dioxane, but no substrate were carried through the entire procedure. Less than one micromole of CO_2 was present in these samples.

Table I. Rate Constants for the Neutral and Alkaline Hydrolysis of Aryl Carbonates in 51% Dioxane–H_2O at 25 °C

compound	$10^2\ k_W$, min^{-1}	k_{OH}, $M^{-1}\ min^{-1}$
diphenyl carbonate	1.2 ± 0.2	1.63 ± 0.02
bis(*p*-methoxyphenyl) carbonate	0.94 ± 0.33	0.92 ± 0.03
bis(*p*-nitrophenyl) carbonate	5.5 ± 2.6	5010 ± 113

Table II. Carbon Isotope Effects on the Hydrolysis of Aryl Carbonates in 51% Dioxane–H_2O at 25 °C

substrate	conditions	k^{12}/k^{13}	no. of determinations
diphenyl carbonate[a]	0.15 M borate, pH* 11.32	1.0503 ± 0.0005	5
	KOH, no buffer[b]	1.0482 ± 0.0004	4
bis(*p*-methoxyphenyl) carbonate	0.15 M borate, pH* 11.32	1.0514 ± 0.0003	5
	KOH, no buffer[b]	1.0493 ± 0.0005	4
bis(*p*-nitrophenyl) carbonate	0.2 M borate, pH* 9.95	1.0476 ± 0.0005	5

[a] Two runs were also done for this substrate at pH 10.44 (k^{12}/k^{13} = 1.0506). [b] Initial pH* was greater than 13.5.

Table III. Carbon Isotope Effects on the Hydrolysis of Diphenyl Carbonates in 51% Dioxane–H_2O at 25 °C

substrate	percent water pathway	k_{OH}^{12}/k_{OH}^{13}	k_W^{12}/k_W^{13a}
diphenyl carbonate	78 ± 4	1.0482 ± 0.0004	1.0509 ± 0.0010
bis(*p*-methoxyphenyl) carbonate	83 ± 9	1.0493 ± 0.0005	1.0518 ± 0.0010
bis(*p*-nitrophenyl) carbonate	11 ± 5	1.0476 ± 0.0005	

Results

Rates of hydrolysis of aryl carbonates were measured in 51% dioxane–water (v/v) at a variety of pH values and were plotted as the log of the observed first-order rate constants versus pH*. pH* values used were those for the dioxane-containing mixtures. The hydrolysis rates were assumed to follow eq 3, and individual rate constants were calculated from a plot of k_{obs} vs hydroxide concentration. The derived rate constants are summarized in Table I. This calculation assumes a pK_w for water of 14 in the 1:1

$$k_{obs} = k_{OH}[OH^-] + k_w \tag{3}$$

dioxane–water mixtures. Although it is likely that this pK_w is shifted upwards in the cosolvent mixtures, this will have no effect on the substituent effects and subsequent calculations.

Carbon isotope effects on the hydrolysis were measured at high pH in unbuffered KOH solutions and at lower pH in borate buffers. The measured values are summarized in Table II. Isotopic compositions for all 100% conversions were in good agreement for each substrate. The reaction shows a small but significant change in carbon isotope effect on going from low pH (buffered conditions) to high pH (reaction with alkali). The rate constants given in Table I were used to derive the proportions of the two pathways for the reactions in borate buffer, and the reactions were assumed to proceed exclusively via the hydroxide pathway in unbuffered KOH solution. This is a reasonable assumption since the pH* of these unbuffered reactions was >13.5 at the start and >12.2 at quenching. With these assumptions and the data in Table II, separate isotope effects for each substrate for each pathway could be calculated (Table III). Calculation of similar values was not possible for bis(*p*-nitrophenyl) carbonate because the reaction at high pH was too fast and presented mixing problems. The measured isotope effect is believed to reflect exclusively the OH^- reaction.

Discussion

Like carboxylate esters,[1] carbonate esters are expected to undergo hydrolysis by a stepwise mechanism.[13] At high pH, the attacking nucleophile is hydroxide, and the tetrahedral interme-

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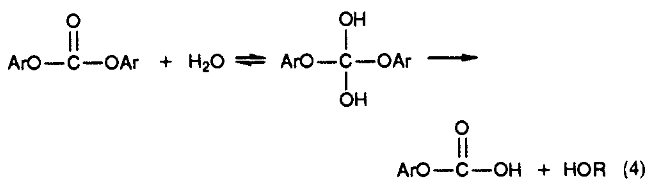
(14) Douheret, G. *Bull. Soc. Chim. Fr.* **1967**, 1412.

(15) Tillett, J. G.; Wriggins, D. E. *J. Chem. Soc.* (*B*) **1970**, 1359.

(16) (a) Viehe, H. G.; Janousek, Z. *Angew. Chem., Int. Ed. Engl.* **1973**, *12*, 806. (b) Cooper, G. D.; Johnson, H. T.; Williams, B. *J. Org. Chem.* **1965**, *30*, 3989.

(17) O'Leary, M. H. *Methods Enzymol.* **1980**, *64*, 83.

diate is negatively charged (eq 1). At neutral pH, the attacking nucleophile is water, and the intermediate is neutral (eq 4).



$$\mathrm{ArO{-}\overset{\overset{O}{\|}}{C}{-}OAr + H_2O \rightleftharpoons ArO{-}\overset{OH}{\underset{OH}{C}}{-}OAr \longrightarrow ArO{-}\overset{\overset{O}{\|}}{C}{-}OH + HOR} \quad (4)$$

Alkaline Hydrolysis. The alkaline hydrolysis of diaryl carbonates, like the alkaline hydrolysis of other esters, is expected to occur by a mechanism involving a tetrahedral intermediate in which formation of the intermediate is rate-determining. Substituent effects for hydrolysis of meta-substituted diphenyl carbonates (ρ = 2.7 for two substituents[16b]) are like those seen for leaving groups in the alkaline hydrolysis of phenyl acetates[10] (ρ = +1.1) and phenyl benzoates[7,8] (ρ = +1.2 to +1.5). Rate-determining addition of hydroxide is logical for aryl carbonates, since the tetrahedral intermediate should eliminate phenoxide more easily than hydroxide and no proton transfers are required within the tetrahedral intermediate.

The three substituents studied in this work (H, p-OCH_3, p-NO_2) span a range of 1.1 in σ values[18] and a range of 5000-fold in alkaline hydrolysis rates. However, the carbon isotope effects are large and span only a small range. The isotope effect increases slightly with decreasing reactivity. This small variation with substituent suggests that, whereas transition-state energy (and thus, reaction rate) is substantially affected by substituent, transition-state structure (and thus, isotope effect) is not; instead, the degree of C–O bond formation at the transition state seems to be nearly constant.

Neutral Hydrolysis. The substituent effects on reaction rates observed in the present study are consistent with those reported previously for the neutral hydrolysis of meta-substituted aryl carbonates.[16b] The range of substituents studied here causes only a 6-fold change in the hydrolysis rate. The carbon isotope effects are slightly larger than those for the alkaline hydrolysis, suggesting that the transition state is later for the alkaline hydrolysis, as expected from structure–reactivity considerations.[19] Isotope effects are available for only two substituents, and no experimentally significant trend with substituent is apparent. It is not clear whether in this case the formation of the tetrahedral intermediate is entirely rate-determining.

Throughout our discussion we have ignored the possibility of a concerted mechanism in favor of the widely accepted stepwise mechanism. Future planned experiments to measure the acyl oxygen and carbonyl oxygen isotope effects by the remote label procedure will afford the opportunity to consider the importance of the concerted mechanism and will allow a more complete characterization of the transition states for these reactions.

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[18] March, J. *Advanced Organic Chemistry*; John Wiley and Sons: New York, 1985; p 244.

[19] Hammond, G. S. *J. Am. Chem. Soc.* **1959**, *77*, 334.

On the Mechanism of Metal Colloid Catalyzed Hydrosilylation: Proposed Explanations for Electronic Effects and Oxygen Cocatalysis

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Abstract: Several aspects of the platinum-catalyzed hydrosilylation reaction, $R_3SiH + R'CH{=}CH_2$, are described and a mechanism based on the intermediacy of colloids is proposed. New features of this mechanism include (1) formation of a Pt colloid/R_3SiH intermediate **2** from the reaction of the Pt colloid **1** and R_3SiH, (2) consideration of the olefin as a nucleophile and thus intermediate **2** being an electrophile in this reaction, (3) hydrosilylation dependence on cocatalysis by dioxygen where no O–O bond breakage occurs and dioxygen action to electronically modify **2** by making it more electrophilic, (4) hydrosilylation being but one case of the reactivity of **2** with nucleophiles; the reaction with R″OH where R″ = H or alkyl is discussed. The effect of the electronic nature of the substituents on the rate of hydrosilylation was measured. Electron withdrawing substituents, R, on R_3SiH accelerate the rate of addition to olefins, e.g. the rate of addition of $(EtO)_3SiH$ to olefins proceeds at a higher rate than the addition of Et_3SiH to olefins. Electron donating groups, R′, on $R'CH{=}CH_2$ greatly accelerate the rate of R_3SiH to olefins, e.g. the Et_3SiH addition occurs at a faster rate to $Me_3SiCH{=}CH_2$ than to $Cl_3SiCH{=}CH_2$. The relative rate of addition of $(EtO)_3SiH$ to a series of para-substituted styrenes was studied which confirmed the trend that higher rates of addition of R_3SiH occurs to olefins, $R'CH{=}CH_2$ with more electron donating substituents, R′. The origin of the cocatalytic effect of dioxygen in hydrosilylation was studied by generating Pt colloid under an atmosphere containing $^{16}O_2$ and $^{18}O_2$ and noting that the O–O bond is not broken and reformed under these conditions. It was demonstrated that the proposed intermediate **2** behaves as an electrophile by showing that $Me_3SiCH_2CH{=}CH_2$ exchanges with Et_3SiH in the presence of Pt to give trapped products based on the rearranged products Me_3SiH and $Et_3SiCH_2CH{=}CH_2$ in the presence of an electrophile (in this case Pt/Et_3SiH). The reaction of water with R_3SiH in the presence of a Pt catalyst in commercial silicone foams produces H_2, and this reaction is described in the context of hydrosilylation where the water nucleophile replaces the olefin.

Introduction

In 1986 we reported that the key event in the Pt-catalyzed hydrosilylation reaction, eq 1, was formation of Pt colloid.[1] The well-known induction period and formation of the characteristic yellow color in this reaction were directly linked to the formation of the colloid. No evidence for molecular species was found and

$$R_3SiH + H_2C{=}CHR' \xrightarrow{\text{catalyst}} R'CH_2CH_2SiR_3 \quad (1)$$

direct evidence for colloid formation was presented; thus colloids were implicated as the catalytic species in this reaction. Since

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[1] Lewis, L. N.; Lewis, N. *J. Am. Chem. Soc.* **1986**, *108*, 7228.