J. Am. Chem. Soc. 1990, 112, 8873-8878 8873

Cyclization of Alkynyl Benzoates and Generation of Dioxolenylium Ions

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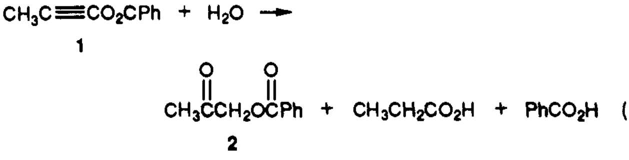
Received March 30, 1990

Abstract: Reactions of 1-ethynyl benzoates $RC{\equiv}CO_2CC_6H_4X$ in H_2O and CH_3OH have been studied. In neutral H_2O, reaction rates for $CH_3C{\equiv}CO_2CC_6H_4X$ depend on σ_p of X with ρ of 1.3. Reaction of $CH_3C{\equiv}CO_2CPh$ (**1**) in ^{18}O-labeled H_2O gives $CH_3CH_2CO_2H$ and $PhCO_2H$ in 54% relative yield with 90 and 83%, respectively, incorporation of a single ^{18}O in the acids and $CH_3COCH_2O_2CPh$ (**2**) in 46% relative yield with 100% incorporation of ^{18}O in both carbonyl oxygens. These results are explained by the hypothesis that at least 46% of **1** reacts by cyclization to an intermediate 2-hydroxy-1,3-dioxolene **18**. Methanolysis of **1** and other alkynyl benzoates gives 2-methoxy-1,3-dioxolenes, confirming the cyclization pathway. Reaction in 44% H_2SO_4 of 2-methoxy-2-phenyl-4-*tert*-butyl-1,3-dioxol-4-ene (**8**), prepared in this way, gives the 2-phenyl-4-*tert*-butyl-1,3-dioxol-4-enylium cation (**16**), directly observable by UV, which hydrolyzes to $t\text{-}BuCOCH_2O_2CPh$ (**12**).

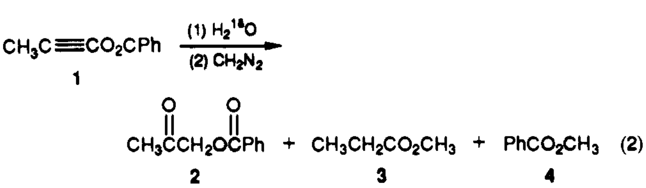
Recently, we reported[1a] that the reaction of the newly available 1-propynyl benzoate (**1**)[1b] in neutral $H_2O\text{-}CH_3CN$ led to the formation of 1-(benzoyloxy)-2-propanone (**2**), propanoic acid, and benzoic acid in relative yields of 54% of the latter two products and 46% of the former (eq 1). We now report studies that clarify the pathway of this reaction and also elucidate the structure and behavior of the novel reactive intermediates involved in this interconversion of **1** and other members of this structurally interesting family.[1c]



$$\underset{\mathbf{1}}{CH_3C{\equiv}CO_2CPh} + H_2O \longrightarrow \underset{\mathbf{2}}{CH_3\overset{O}{\overset{\|}{C}}CH_2O\overset{O}{\overset{\|}{C}}Ph} + CH_3CH_2CO_2H + PhCO_2H \quad (1)$$

Results

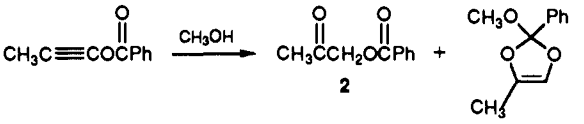
Reaction of **1** in 3/1 v/v $CH_3CN/H_2{}^{18}O$ (94 atom % ^{18}O) at 65 °C for 22 h followed by treatment with CH_2N_2 and separation of the products by vapor phase chromatography (VPC) led to the isolation of 1-(benzoyloxy)-2-propanone (**2**), methyl propanoate (**3**), and methyl benzoate (**4**) (eq 2). The identification of **2** was confirmed by NMR comparison to an authentic sample.[2] Mass spectral analysis of the ^{18}O distribution in the products and the fragment ions, as summarized in eq 2, revealed essentially 100% uptake of ^{18}O in each of the carbonyl groups of **2**, 90% uptake of a single ^{18}O in the methyl propionate (**3**), and 83% incorporation of a single ^{18}O in the methyl benzoate (**4**). Control experiments showed that benzoic acid and the ester carbonyl of **2** did not undergo ^{18}O exchange under the reaction conditions, whereas the keto oxygen of **2** underwent essentially complete exchange and propanoic acid became 27% monolabeled and 2.5% dilabeled.



$$\underset{\mathbf{1}}{CH_3C{\equiv}CO_2CPh} \xrightarrow[(2)\ CH_2N_2]{(1)\ H_2{}^{18}O} \underset{\mathbf{2}}{CH_3\overset{O}{\overset{\|}{C}}CH_2O\overset{O}{\overset{\|}{C}}Ph} + \underset{\mathbf{3}}{CH_3CH_2CO_2CH_3} + \underset{\mathbf{4}}{PhCO_2CH_3} \quad (2)$$

	2	3	4
$^{18}O \times 2$	100	8	2
$^{18}O \times 1$	0	90	83
$^{18}O \times 0$	0	2	15

Reaction of **1** in CH_3OH gave **2** and 2-methoxy-2-phenyl-4-methyl-1,3-dioxol-4-ene (**5**) in a 33/67 ratio (eq 3), as analyzed by ^1H NMR after evaporation of the CH_3OH. Attempts to purify completely **5** were not successful, but its structure was assigned on the basis of the distinctive spectral characteristics of the mixture, particularly signals at δ 1.90 and 6.17 in the ^1H NMR spectrum with a mutual coupling of 2 Hz assigned to the vinyl CH_3 and vinyl H of **5**, respectively. The mass spectrum of the mixture showed peaks for M^+ and $M^+ - OCH_3$ for **5** with the correct exact mass for **5**. When the reaction was carried out in CD_3OD and the reaction product examined directly by ^1H NMR, the coupling and the peak assigned to the vinyl H disappeared, indicating formation of **5**-d_4. The relative yield of **2** under these conditions was 8 ± 6%.



$$CH_3C{\equiv}CO\overset{O}{\overset{\|}{C}}Ph \xrightarrow{CH_3OH} \underset{\mathbf{2}}{CH_3\overset{O}{\overset{\|}{C}}CH_2O\overset{O}{\overset{\|}{C}}Ph} + \mathbf{5} \quad (3)$$

5

Further evidence for the structure of **5** includes several analogous reactions cited in the following text. There have been only a few previous reports of preparation of nonbenzannealated analogues of the ring system of **5**.[3]

The products from reaction of the additional alkynyl carboxylate esters **6–9** in CH_3OH were analyzed by ^1H NMR after evaporation of the solvent and gave the relative yields shown in Table I. The dioxolenes **5**, **11**, and **13** were rather sensitive and the yields were only modestly reproducible. However, the products **10–13** were isolated by chromatography and obtained in >95% purity as indicated by ^1H NMR and were unequivocally characterized by NMR and MS. The kinetics of the reactions of **6–9** were also measured in H_2O by monitoring the change in their UV spectra. Rate constants are summarized in Table II and given in detail in Tables III and IV.

Examination of the products of the reactions in CD_3OD at 60 °C of the alkynyl esters **1**, **7**, and **8** by ^1H NMR showed the dioxolenes **5**, **11**, and **13** (deuterated in the methoxy and vinyl positions) constituted 86, 44, and 83% of the products, respectively. The only other products observed were $ArCO_2CD_3$ and $RCD_2CO_2CD_3$, except for the case of $CH_3C{\equiv}CO_2CPh$ (**1**), which also gave 8 ± 6% of $CH_3COCD_2O_2CPh$. Similar reaction of **6** in CD_3OD gave only the deuterated analogues of the products in Table I, in the same ratio, while **9** gave only $CHD_2CO_2CD_3$ and $PhCO_2CD_3$.

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[1] (a) Allen, A. D.; Kitamura, T.; Roberts, K. A.; Stang, P. J.; Tidwell, T. T. *J. Am. Chem. Soc.* **1988**, *110*, 622–624. (b) Stang, P. J.; Boehshar, M.; Wingert, H.; Kitamura, T. *Ibid.* **1988**, *110*, 3272–3278. (c) Stang, P. J.; Kitamura, T.; Arif, A. M.; Karni, M.; Apeloig, Y. *Ibid.* **1990**, *112*, 374–381.

[2] (a) Tschesche, R.; Schäfer, H. *Chem. Ber.* **1955**, *88*, 81–90. (b) Adams, R.; Govindachari, T. R. *J. Am. Chem. Soc.* **1950**, *72*, 158–162.

[3] (a) Anderson, W. K.; Dewey, R. H. *J. Am. Chem. Soc.* **1973**, *95*, 7161–7162. (b) Lorenz, W.; Maas, G. *J. Org. Chem.* **1987**, *52*, 375–381.

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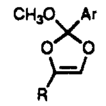
Table I. Products (Yield, %) from Methanolysis of RC≡CO$_2$CAr[a]

compd	R	Ar	$\mathrm{R\overset{O}{\overset{\|}{C}}CH_2O_2CAr}$		$ArCO_2CH_3$
1	CH_3	Ph	22 ± 8 (**2**)	44 ± 2 (**5**)	34 ± 6 (**4**)
6	CH_3	4-$CH_3OC_6H_4$	40 (**10**)	0	60 (**14**)[b]
7	CH_3	4-$O_2NC_6H_4$	0	34 ± 7 (**11**)	66 ± 7 (**15**)
8	*t*-Bu	Ph	18 ± 7 (**12**)	72 ± 5 (**13**)	12 ± 1 (**4**)
9	H	Ph	0	0	~100 (**4**)

[a] Relative yields determined by ^{1}H NMR integration, with average deviations from two or three runs. [b] Formed in 3/1 CH_3CN/H_2O followed by CH_2N_2.

Table II. Summary of Hydrolysis Rates of Alkynyl Carboxylate Esters (RC≡CO$_2$CAr), 25 °C

R	Ar	k_{H^+}[a] (M^{-1} s^{-1})	$k(H_2O)$ (s^{-1})	$k(D_2O)$ (s^{-1})	$k(H_2O)/k(D_2O)$	$k(OH^-)$ (M^{-1} s^{-1})
CH_3[b]	4-$CH_3OC_6H_4$		1.42×10^{-5}	1.01×10^{-5}	1.41	19.8[e]
CH_3[b]	Ph	3.02×10^{-5}[c]	3.42×10^{-5}	1.72×10^{-5}	1.99	73.7[e]
CH_3[b]	4-$O_2NC_6H_4$		3.69×10^{-4}	1.14×10^{-4}	3.24	1600[f]
t-Bu	Ph		6.21×10^{-5}			
H	Ph	1.86×10^{-3}[d]	2.29×10^{-4}	9.03×10^{-5}	2.54	
H	4-$CH_3OC_6H_4$		6.78×10^{-5}	3.68×10^{-5}	1.84	

[a] Rates at $H_o = 0$. [b] For CH$_3$C≡CO$_2$CAr, $\log k_{H_2O} = 1.33\sigma_p - 4.47$ and $\log k_{OH} = 1.80\sigma_p + 1.82$. [c] Reference 1a. [d] Table III. [e] Table IV. [f] Derived from rate studies with Tris buffers, [Tris] = $(0.5–2.5) \times 10^{-2}$ M, pH 8.15, $\mu = 0.1$. $k_{obs} = 1.07$ (s^{-1} M^{-1})[Tris] + 0.261×10^{-2} (s^{-1}), $r = 0.999$.

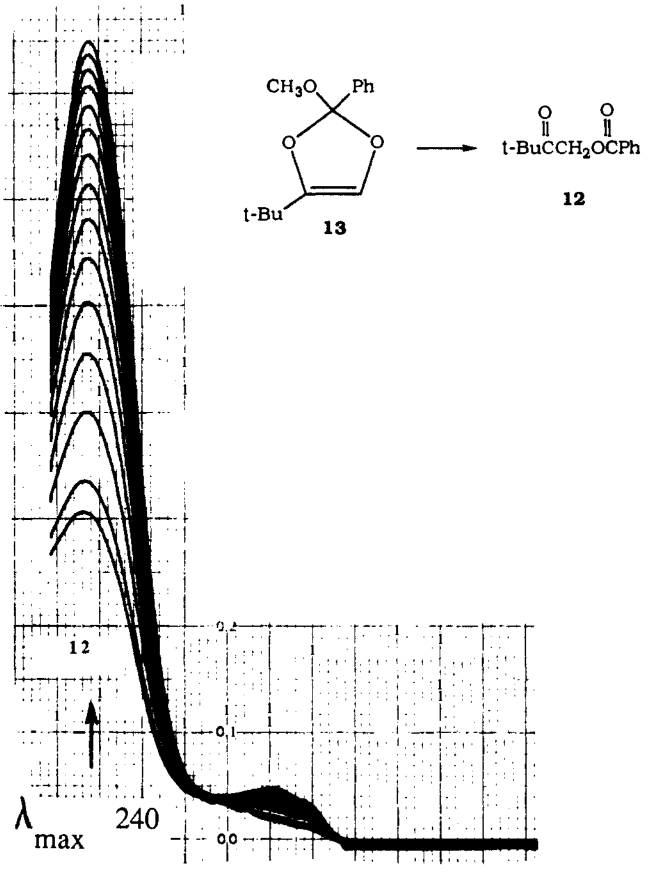


Figure 1. UV absorption of **12** forming from **13** in CH_3CO_2H buffer in 1/2 CH_3CN/H_2O, pH 5.2, 25 °C, scans every 3 min, $k_{obs} = 7.5 \times 10^{-4}$ s^{-1}.

The products from the reaction of CH$_3$C≡CO$_2$CC$_6$H$_4$OCH$_3$-4 (**6**) at 25 °C in 75% CH_3CN with 25% 10^{-3} M HCl, pH 7 buffer, and 10^{-3} M NaOH after treatment with CH_2N_2 were determined by ^{1}H NMR as 44/56, 52/48, and 54/46 mixtures of $CH_3COCH_2O_2CAr$ (**10**) and $ArCO_2CH_3$ (**14**), respectively.

Reaction of 2-methoxy-2-phenyl-4-*tert*-butyl-1,3-dioxol-4-ene (**13**) in 2/1 H_2O/CH_3CN in the presence of acetic acid buffer at pH 5.2 was monitored by the change in the UV spectrum (Figure 1) and gave *t*-$BuCOCH_2O_2CPh$ (**12**) in an acid-catalyzed process, $k_{H^+} = 120$ M^{-1} s^{-1} at 25 °C. This process evidently involves the 2-phenyl-4-*tert*-butyl-1,3-dioxol-4-enylium cation (**16**), which undergoes hydration to **17**, which opens, possibly via an enol, to form **12** (eqs 4 and 5).

Table III. Rates of HC≡CO$_2$CPh Hydrolysis in H_2SO_4, 25 °C[a]

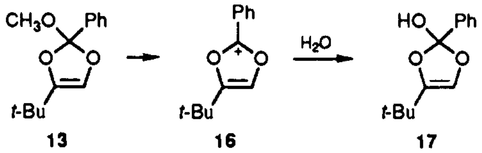
[H_2SO_4] (M)	wt %	H_o	k_{obs}[b] (s^{-1})
0.286	2.76	0.39	8.13×10^{-4}
0.557	5.31	0.06	1.57×10^{-3}
1.384	12.61	−0.57	6.26×10^{-3}
2.55	21.8	−1.16	2.68×10^{-2}
3.52	28.8	−1.63	6.68×10^{-2}

[a] Duplicate runs at each concentration, reproducible to ±5%. [b] $\log k_{obs} = -0.97H_o - 2.73$, $k_{H^+}(H_o = 0) = 1.86 \times 10^{-3}$ M^{-1} s^{-1}.

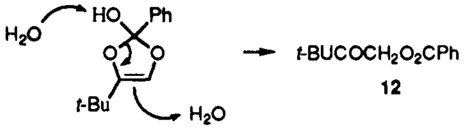
Table IV. Rates of CH$_3$C≡CO$_2$CAr Hydrolysis in NaOH Solutions, $\mu = 0.1$ (NaCl), 25 °C

Ar	[NaOH] (M)	pH[a]	k_{obs}[b] (s^{-1})
4-$CH_3OC_6H_4$[c]	4.98×10^{-3}	11.38	0.0969
	9.96×10^{-3}	11.65	0.207
	1.49×10^{-2}	11.79	0.295
	1.99×10^{-2}	11.90	0.376
	2.49×10^{-2}	11.98	0.506
C_6H_5[d]	1.14×10^{-3}	10.69	0.0805
	1.90×10^{-3}	11.00	0.151
	3.87×10^{-3}	11.31	0.311
	5.87×10^{-3}	11.49	0.429

[a] Measured. [b] Duplicate runs at each concentration, reproducible to ±5%. [c] $k_{obs} = 19.8$ (M^{-1} s^{-1})[NaOH] − 0.0052 (s^{-1}). [d] $k_{obs} = 73.7$ (M^{-1} s^{-1})[NaOH] + 0.00745 (s^{-1}).



13 **16** **17** (4)



(5)

In 90% H_2SO_4, **13** reacted to give a strong persistent maximum at 300 nm, similar to those observed for 1,3-dioxolanylium ions[5a] and ascribed to the 2-phenyl-4-*tert*-butyl-1,3-dioxol-4-enylium cation (**16**). In 44% acid this absorption decayed by first-order kinetics ($k_{obs} = 4.3 \times 10^{-3}$ s^{-1}) to give the UV spectrum of **12** (Figure 2).

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(5) (a) Santry, L. J.; Azer, S.; McClelland, R. A. *J. Am. Chem. Soc.* **1988**, *110*, 2909–2914. (b) McClelland, R. A.; Coe, M. *Ibid.* **1983**, *105*, 2718–2725.

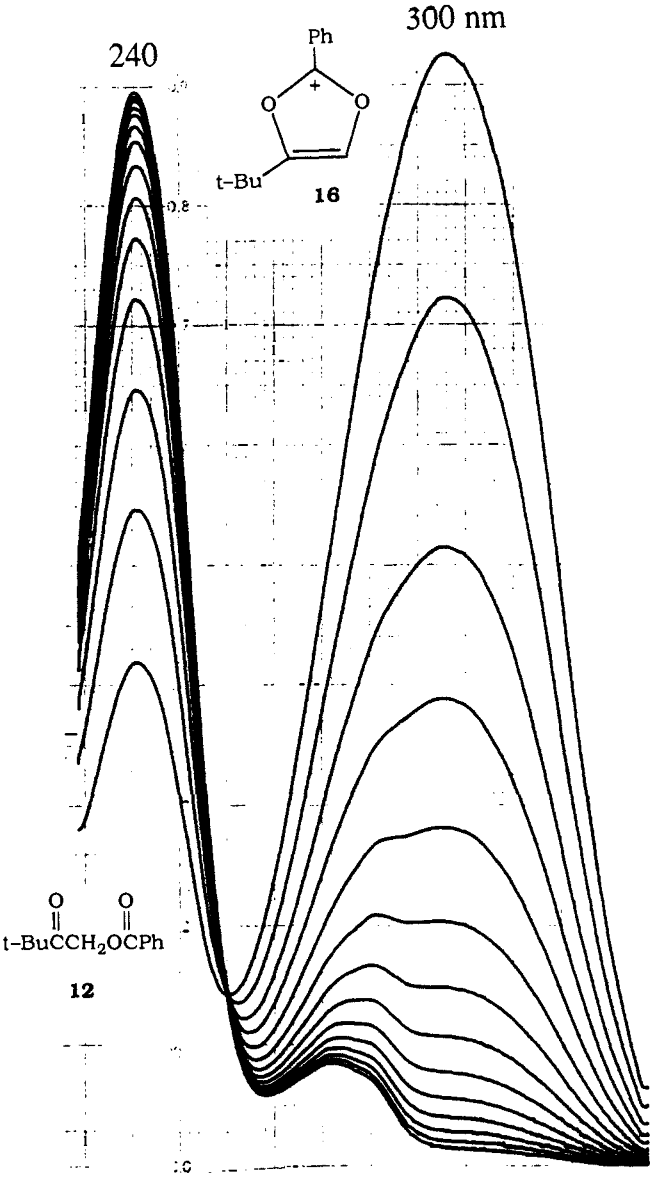
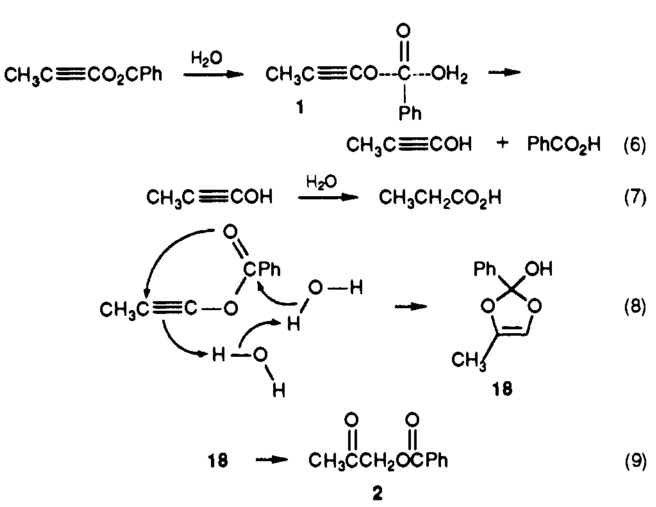


Figure 2. UV absorption of **12** forming from **16** in 44% H_2SO_4, 25 °C, $k_{\mathrm{obs}} = 4.3 \times 10^{-3}$ s^{-1}.

Discussion

The reaction of $CH_3C{\equiv}CO_2CPh$ (**1**) with neutral H_2O leads to two families of products, namely the acids $CH_3CH_2CO_2H$ and $PhCO_2H$ resulting from normal ester hydrolysis and the alkyne hydration product $CH_3COCH_2O_2CPh$ (**2**). A mechanistic scheme that explains these results involves two distinct competing pathways, one involving direct displacement of H_2O on the carbonyl carbon leading to the normal products (eqs 6 and 7) while a separate pathway leads to **2** via a cyclization process (eqs 8 and 9).

The major evidence for the cyclization pathway of eqs 8 and 9 is the complete incorporation of ^{18}O in the ester carbonyl of **2**, even though it was shown by a control experiment that this carbonyl in **2** does not exchange under the reaction conditions. The analogy of the direct observation of cyclized products in CH_3OH is also strongly supportive of the cyclization pathway. In H_2O a 2-hydroxy-1,3-dioxol-4-ene intermediate **18** is formed, which undergoes ring opening, perhaps via an enol intermediate, to give the benzoyloxy ketone **2**. Only the ester carbonyl of **2** formed in this way would be labeled by ^{18}O, but as shown by a control experiment the keto carbonyl then undergoes further exchange with the medium leading to the doubly labeled **2** observed. Our previous supposition[1a] that **2** arises from H_2O attack at C-2 of **1** is ruled out by the isotope-labeling study, as this path does not give ^{18}O label in the ester carbonyl.



$$CH_3C{\equiv}CO_2CPh \xrightarrow{H_2O} CH_3C{\equiv}CO{-}\overset{O}{\overset{\|}{\underset{Ph}{\underset{|}{C}}}}{-}OH_2 \longrightarrow CH_3C{\equiv}COH + PhCO_2H \quad (6)$$

$$CH_3C{\equiv}COH \xrightarrow{H_2O} CH_3CH_2CO_2H \quad (7)$$

(8)

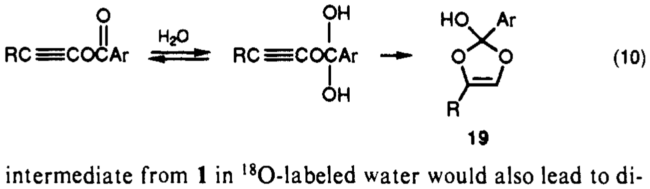
$$\mathbf{18} \longrightarrow CH_3\overset{O}{\overset{\|}{C}}CH_2O\overset{O}{\overset{\|}{C}}Ph \quad (9)$$

The neutral hydrolysis rates of **1**, **6**, and **7** are correlated with σ_p substituent parameters with a ρ value of 1.3. This is similar to the ρ of 1.7 for hydration of benzaldehydes,[5b] but is not consistent with positive charge build up at the transition state, and so is in accord with the mechanism of eqs 8 and 9. The solvent isotope effects k_{H_2O}/k_{D_2O} of 1.4–3.2 also indicate water attack, possibly with proton transfer in the transition state, and are typical of carbonyl group hydrations.[6] The reactivities of the esters $HC{\equiv}CO_2CAr$ are also correlated with σ_p with $\rho = 2.0$, although there are only two substrates in this series.

There is a distinct trend in the solvent isotope effects in that $k(H_2O)/k(D_2O)$ increases as the reactivity of the ester increases with aryl substitution (Table II). Thus, for $CH_3C{\equiv}CO_2CAr$ the relative rates for reaction with H_2O are 25, 2.3, and 1.0 for Ar = 4-$O_2NC_6H_4$, Ph, and 4-$CH_3OC_6H_4$, and the corresponding values of $k(H_2O)/k(D_2O)$ are 3.42, 1.99, and 1.41. Similarly, for $HC{\equiv}CO_2CAr$ the 4-$CH_3OC_6H_4$ derivative is 3.4 times less reactive than for phenyl, and the corresponding isotope effects are 2.54 and 1.84. The evidence suggests (vide supra) that in addition to the cyclization mechanism there is a competing pathway (eqs 6 and 7) leading to carboxylic acid products, but the aryl substituent effects on these two pathways should be similar.

The rate constant ratio k_{OH^-} (M^{-1} s^{-1})/k_{H_2O} (s^{-1}) for $CH_3C{\equiv}CO_2CAr$ is 1.4×10^6, 2.2×10^6, and 4.3×10^6 for the 4-$CH_3OC_6H_4$, Ph, and 4-$O_2NC_6H_4$ substrates, showing a small but regular increase with reactivity. These ratios may be compared to those of 1.6×10^5–1.2×10^7 found for some aldehydes and ketones,[5b,7a,b] 1.4×10^8 for 4-(nitrophenyl)-4-nitrobenzoate,[7c] and 220–4700 for α,β-unsaturated carbonyl compounds[7d] and ketenes.[6a,d] The ρ_{OH} value for the propynyl esters is 1.8, which is similar to the value of 2.0 for phenyl benzoates.[7c] The latter value is independent of substituents on the phenyl group.[7c]

A mechanistic variation to consider for the cyclization and rearrangement is one that involves addition of water to form a tetrahedral intermediate, which then undergoes cyclization to **19** (eq 10). However, equilibrium formation of such a tetrahedral intermediate from **1** in ^{18}O-labeled water would also lead to di-



(10)

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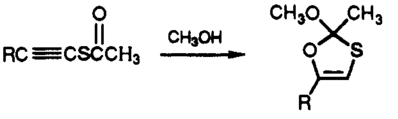
[7] (a) Ritchie, C. D. *J. Am. Chem. Soc.* **1984**, *106*, 7187–7194. (b) Funderburk, L. H.; Aldwin, L.; Jencks, W. P. *Ibid.* **1978**, *100*, 5444–5459. (c) Kirsch, J. F.; Clewell, W.; Simon, A. *J. Org. Chem.* **1968**, *33*, 127–132. (d) Bernasconi, C. F.; Stronach, M. L. *Ibid.* **1986**, *51*, 2145–2147.

labeled benzoic acid, contrary to the experimental finding, thus ruling out this process. Irreversible formation of a tetrahedral intermediate with equivalent OH groups is also excluded, as this would lead to only 50% labeling of the ester carbonyl in $CH_3COCH_2O_2CPh$ (**2**). The reactivity of **1** may be estimated to be accelerated by at least 10^2 over that of phenyl benzoate[8a] toward water. While the role of intermediates in the nucleophilic cleavage of phenyl esters in neutral water is not certain,[8b] the more rapid reaction of **1** indicates the leaving-group ability is important. The ynol $PhC{\equiv}COH$ has a pK_a less than 2.8,[9] so $CH_3C{\equiv}COH$ should also be quite acidic and would be an excellent leaving group, as in eq 6.

The intramolecular attack of the carbonyl on C-2 of the alkyne is not implausible despite the distance between these atoms in **1**. Alkynes are rather easily deformed by bending,[10a,b] are known to cyclize to 5-membered rings by nucleophilic attack[10c–e] and to react by nucleophile-promoted electrophilic attack,[10f] and are reactive at C-2 when substituted with an electronegative substituent at C-1.[10g] There is also precedent for this process in the cyclization of 1-alkynyl thioesters to **20** (eq 11).[11]



(11)

20

An example of the relative ease of angle deformation of the sp-hybridized carbon of alkynes is provided by cyclooctyne,[12a] which has C≡C—C bond angles of 154° and a C—C≡C—C torsional angle of 40°. To account for this structure, the C≡C—C bending parameter k_θ in the MM2 force field has been reduced to 0.20,[12b] which is much less than the corresponding C—C—C or C=C—C values.

For $CH_3C{\equiv}CO_2CC_6H_4OCH_3$-4 (**6**), the yield of $CH_3COCH_2O_2CAr$ (**10**) is essentially constant in 10^{-3} M HCl or NaOH or at pH 7 (44, 54, and 52%, respectively). Thus, neither protonation of C-1 of the alkyne nor hydroxide attack at the carbonyl carbon enhances the cyclization of this substrate. The transition state depicted in eq 8, in which attack of two H_2O molecules is coupled, is consistent with this absence of acid and base catalysis. A somewhat similar synchronous addition of a single H_2O molecule to an acylketene has recently been proposed.[13a] Two H_2O molecules are included in eq 8 in accord with other recent interpretations of isotope effects in carbonyl group hydrations[6] and for geometric reasons. The hydrations of ketene[13b] and formaldehyde[13c] have been proposed to occur through 6-membered-ring transition states involving two H_2O molecules.

A reaction cube[13d–h] representing the three bond-forming steps to carbon of eq 8 is shown in Figure 3. Initial formation of one of the bonds would lead to the structures A, B, or C, and formation of two bonds would give D, E, or F. The failure of the aryl CH_3O group or of added HCl or NaOH to enhance the cyclization of **6** suggests such carbanionic or cationic intermediates are not formed.

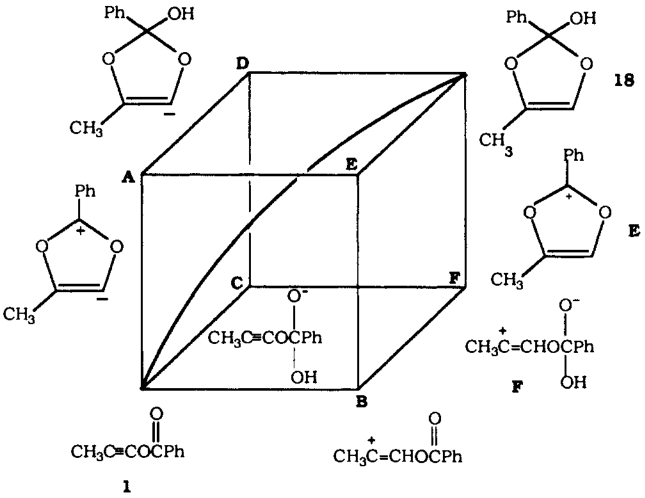
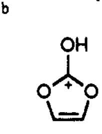


Figure 3. Reaction cube for hydration of **1** to **18**.

The ion **16** is an aromatic 6-π-electron system[14] and is related to the species **21–23** that have been reported.[14c–e] However, the degree of aromatic stabilization of these species is not settled. Capture of **23** by a nucleophile has been observed previously as shown in eq 12.[3b]



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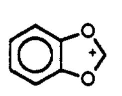

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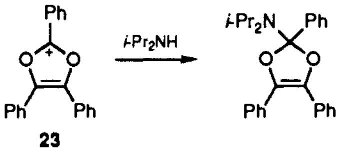
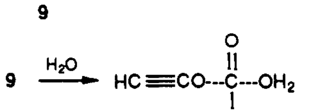


23

(12)

Ethynyl benzoate ($HC{\equiv}CO_2CPh$, **9**) is 6.7 times more reactive than $CH_3C{\equiv}CO_2CPh$ (**1**) toward neutral hydrolysis and gives no cyclization or rearrangement on methanolysis, and k_{H^+} for **9** is 62 times greater than for propynyl benzoate (**1**). Methyl substitution in some cases slows the rate of proton attack at sp carbon; for instance, the rate ratio k(1-phenylethyne)/k(1-phenylpropyne) has been reported[15] as 10 or 28, and so for **9** a higher reactivity in protonation of the alkyne is not unexpected (eq 13). In neutral water the enhanced rate evidently results from a better leaving-group ability of an ethynolate as opposed to a propynolate leaving group in a direct displacement process (eq 14). This evidence for the pathway of eq 14 for **9** lends credence

$$\underset{\mathbf{9}}{HC{\equiv}CO_2CPh} \xrightarrow{H^+} CH_2{=}\overset{+}{C}O_2CPh \qquad (13)$$



$$\mathbf{9} \xrightarrow{H_2O} HC{\equiv}CO\text{---}\underset{Ph}{\overset{O}{\overset{\|}{C}}}\text{---}OH_2 \qquad (14)$$

to the suggestion that this route and the cyclization process of

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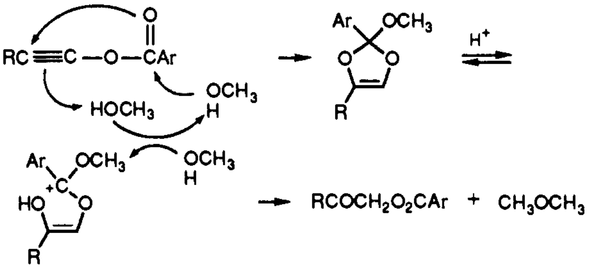
eq 8 are independent competing mechanisms for the neutral hydrolysis of α-alkynyl esters.

The direct displacement pathway of eqs 6 and 7 would lead to the singly ^{18}O-labeled benzoic acid and propanoic acid formed from $CH_3C{\equiv}CO_2CPh$ (**1**) and ^{18}O-labeled H_2O. The relative yield of these products is 54%, and they are 83 and 90% singly labeled, respectively. The greater extent of labeling of the propanoic acid probably reflects partial exchange of this product with the medium, a process we have observed. The formation of 8% dilabeled $CH_3CH_2CO_2H$ and 15% unlabeled $PhCO_2H$ from **1** could result from nucleophilic addition of H_2O to C_1 of the propyne (eq 15). The ^{18}O exchange of the product $CH_3CH_2CO_2H$ with the reaction medium is an alternate route for formation of dilabeled product.

$$CH_3C{\equiv}CO_2CPh \xrightarrow{H_2O} CH_3CH{=}C(OH)O_2CPh \rightarrow CH_3CH_2CO_2H + PhCO_2H \quad (15)$$

Formation of the 2-methoxydioxolenes **5**, **11**, and **13** from the reaction of the alkynyl benzoates **1**, **7**, and **8** in methanol can be readily explained by the first step of the process shown in eq 16,

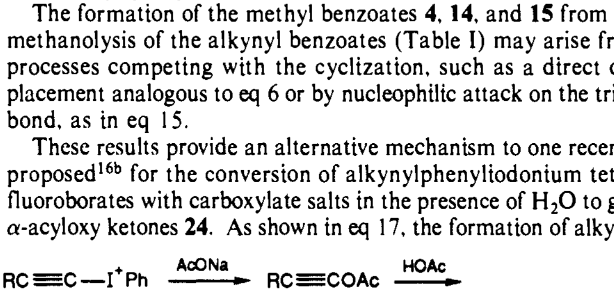


(16)

which corresponds to the hydration reaction shown in eq 8. The failure to observe the 4-anisyldioxolene (Table I) may be explained by the ring opening shown in eq 16, which would be favored by the 4-anisyl group. Such reactions of ortho esters are known.[16a]

The formation of the methyl benzoates **4**, **14**, and **15** from the methanolysis of the alkynyl benzoates (Table I) may arise from processes competing with the cyclization, such as a direct displacement analogous to eq 6 or by nucleophilic attack on the triple bond, as in eq 15.

These results provide an alternative mechanism to one recently proposed[16b] for the conversion of alkynylphenyliodonium tetrafluoroborates with carboxylate salts in the presence of H_2O to give α-acyloxy ketones **24**. As shown in eq 17, the formation of alkynyl



(17)

acetates that cyclize to acetoxydioxolenes **25** provides a route to **24**. The dioxolenes **25** would be potent acetylating agents and would provide a pathway to the observed[16b] formation of $AcOCH_2CH_2COCH_2OAc$ from $HOCH_2CH_2C{\equiv}CI^+Ph$.

In summary, the reactions of alkynyl esters show new types of chemistry not observed with other families of esters. As the study of these species progresses, other interesting developments may be anticipated.

Experimental Section

Materials and Instrumentation. The preparation of **1** and **6–9** has been reported.[1b] ^{18}O-Labeled H_2O (Aldrich) contained 94% ^{18}O by mass spectral analysis. Anhydrous CH_3OH was obtained from Aldrich. An authentic sample of 1-(benzoyloxy)-2-propanone (**2**) was prepared by the reaction of bromoacetone with potassium benzoate in toluene.[2a] Centrifugal radial thin-layer chromatographic separations were executed with a Chromatotron from Harrison Research with use of silica gel plates and 10% EtOAc/90% petroleum ether as eluent. Vapor-phase chromatographic separations (VPC) were completed with a 10 mm × 3 m OV-17 column.

Isotope Labeling. A mixture of 1-propynyl benzoate (**1**; 0.092 g, 0.55 mmol), 0.46 mL of CH_3CN, and 0.16 mL of H_2O (94% ^{18}O) formed two layers at 25 °C but was homogeneous at 65 °C. After being heated 23 h at 65 °C, the solution was cooled to 0 °C and treated with excess diazomethane in ether. After distillation of some of the ether the product was analyzed directly by GC/MS (30 m × 0.25 mm DB-1 column), showing $PhCO_2CH_3$ and $CH_3COCH_2O_2CPh$ (**2**) in relative yields of 54 and 46%, respectively. A lesser amount of $CH_3CH_2CO_2CH_3$ was also observed, and it is believed that some was lost during workup. The ^{18}O incorporation in these ions from these products, corrected to 100% ^{18}O content in the H_2O, is given below.

product	ion	$^{18}O \times 2$	$^{18}O \times 1$	$^{18}O \times 0$
$CH_3CH_2CO_2CH_3$	M^+	8.4	90.0	1.6
	$C_2H_5CO^+$	0	43.0	57.0
$PhCO_2CH_3$	M^+	2.1	83.0	14.9
	$PhCO^+$	0	44.3	55.7
$PhCO_2CH_2COCH_3$	M^+	99.6	0.4	0
	$PhCO_2CH_2^+$	1.4	98.9	0
	$PhCO^+$	0	100.0	0

To test for exchange of the products under these conditions, a mixture of $CH_3COCH_2O_2CPh$ (**2**, 0.021 g, 0.118 mmol), $PhCO_2H$ (0.016 g, 0.131 mmol), and $CH_3CH_2CO_2H$ (0.016 g, 0.22 mmol) dissolved in 0.20 mL of CH_3CN and 0.070 mL of H_2O (94% ^{18}O) was heated 23 h at 65 °C in a sealed vessel. The product was then treated with diazomethane and analyzed as above with the results below.

product	ion	$^{18}O \times 2$	$^{18}O \times 1$	$^{18}O \times 0$
$CH_3CH_2CO_2CH_3$	M^+	2.5	26.9	70.6
	$C_2H_5CO^+$	0	24.1	76.0
$PhCO_2CH_3$	M^+	0	0.4	99.6
$PhCO_2CH_2COCH_3$	M^+	0	84.6	15.4
	$PhCO_2CH_2^+$	0	0.2	99.8

Product Studies. A solution of 1-propynyl benzoate (**1**; 0.047 g, 0.27 mmol) in 0.5 mL of dry CH_3OH was heated at 60 °C in a sealed vial for 24 h. After evaporation of solvent, integration of the distinctive phenyl resonances in the ^1H NMR spectrum gave relative yields of products as 14% 1-(benzoyloxy)-2-propanone (**2**), 46% 2-methoxy-2-phenyl-4-methyl-1,3-dioxol-4-ene (**5**), and 40% methyl benzoate. Attempts to purify **5** by VPC or chromatography on silica gel were unsuccessful, so the structure assignment was based on spectral studies of the product mixture: ^1H NMR (CCl_4) δ 1.90 (d, 3, $J = 2$ Hz, $CH_3C{=}C$), 3.3 (s, CH_3OC and residual CH_3OH), 6.17 (q, 1, $J = 2$ Hz, $C{=}CH$), 7.1–8.2 (m, 5, Ph); mass spectrum, m/z (rel intens) 192 (30, M^+), 161 (54, $M^+ - OCH_3$), 105 (100, $C_6H_5CO^+$); high-resolution mass spectrum (HRMS), m/z 192.0786, calcd 192.0786. When the comparable reaction was carried out in CD_3OD, the signal at δ 1.90 in the ^1H NMR appeared as a singlet and that at δ 6.17 disappeared.

Reaction of **1-propynyl 4-methoxybenzoate** (**6**; 0.042 g, 0.22 mmol) in 1 mL of CH_3OH at 60 °C for 47 h and purification of the product by radial chromatography gave as the first fraction methyl 4-methoxybenzoate (**15**) and then 1-[(4-methoxybenzoyl)oxy]-2-propanone (**10**): ^1H NMR (CCl_4) δ 2.13 (s, 3, CH_3CO), 3.87 (s, 3, CH_3O), 4.73 (s, 2, OCH_2CO), 6.90 and 8.00 (2 d, $J = 8$ Hz, A_2B_2 of C_6H_4); mass spectrum, m/z (rel intens) 208 (28, M^+), 165 (7, $M^+ - CH_3CO$), 135 (100, $CH_3OC_6H_4CO^+$), 107 (17, $CH_3OC_6H_4^+$); HRMS, m/z 208.0746, calcd 208.0758.

Reaction of **1-propynyl 4-nitrobenzoate** (**7**; 0.0407 g, 0.198 mmol) in 1 mL of dry CH_3OH at 60 °C for 2 h and purification of the product by radial chromatography gave 2-methoxy-2-(4-nitrophenyl)-4-methyl-1,3-dioxol-4-ene (**11**): ^1H NMR (CCl_4) δ 1.92 (d, 3, $J = 2$ Hz, $CH_3C{=}C$), 3.40 (s, 3, CH_3O), 6.13 (q, 1, $J = 2$ Hz, $C{=}CH$), 7.42–8.20 (q, 4, Ar); mass spectrum, m/z (rel intens) 150 (100, $O_2NC_6H_4CO^+$), 104 (51, $C_6H_4CO^+$).

A solution of **1-(3,3-dimethyl-1-butynyl) benzoate** (**8**; 0.064 g, 0.314 mmol) in 0.8 mL of dry CH_3OH was heated at 60 °C 18 h in a sealed ampule. The solvent was distilled, and the products were separated by radial chromatography, giving 2-methoxy-2-phenyl-4-*tert*-butyl-1,3-dioxol-4-ene (**13**): ^1H NMR (CCl_4) δ 1.20 (s, 9, *t*-Bu), 3.44 (s, 3, OCH_3), 6.15 (s, 1, $C{=}CH$), 7.1–7.6 (m, 5, Ph); ^{13}C NMR ($CDCl_3$) δ 27.4, 30.3, 49.5, 119.4, 123.6, 125.3, 128.1, 129.1, 138.4, 148.0; mass spectrum, m/z (rel intens) 234 (44, M^+), 203 (44, $M^+ - CH_3O$), 105 (100, $C_6H_5CO^+$); HRMS, M^+ 234.1259, calcd 234.1256. The second band was identified as 1-(benzoyloxy)-3,3-dimethyl-2-butanone (**12**):[4] ^1H NMR (CCl_4) δ 1.23 (s, 9, *t*-Bu), 5.00 (s, 2, CH_2O), 7.2–8.2 (m, 5, Ph); mass spectrum,

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m/z (rel intens) 221 (15, M$^+$ + 1), 163 (56, M$^+$ − t-Bu), 105 (100, $C_6H_5CO^+$), 57 (91, t-Bu$^+$). Analysis of the original product mixture by ^{1}H NMR showed **12** and **13** as the only detectable products in the ratio of 28/72. Further heating of the crude reaction product in CH_3OH for 48 h led to no apparent change in the product composition as indicated by ^{1}H NMR.

Ethynyl benzoate (**9**; 0.0425 g, 0.29 mmol) was kept in 1 mL of CH_3OH at 60 °C for 4.5 h. Examination of the reaction mixture by TLC showed methyl benzoate as the only detectable product. Part of the CH_3OH was distilled, and the ^{1}H NMR spectrum showed the presence of methyl benzoate, methanol, and possibly methyl acetate. The methyl benzoate was isolated by radial chromatography and its identity confirmed by ^{1}H NMR.

Acknowledgment. Support in Toronto by the Natural Sciences and Engineering Research Council of Canada and in Utah by the National Cancer Institute of the National Institutes of Health (Grant 1ROCA16903) is gratefully acknowledged.

Equilibration of *N*-(2-Cyanoethyl)pyridinium Cations with Substituted Pyridines and Acrylonitrile. A Change in Rate-Determining Step in an E1cb Reaction

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Abstract: The rates of equilibration of *N*-(2-cyanoethyl)pyridinium cations (**1**) with the corresponding pyridines and acrylonitrile have been measured in aqueous solutions of ionic strength 0.1 at 25 °C. Second-order rate constants (k_{OH}) have been obtained for the hydroxide ion catalyzed elimination reactions of 16 ring-substituted **1** having pyridine leaving groups of pK_{BH} in the range 1.5–9.7. Brønsted plots of log k_{OH} vs pK_{BH} are "concave down" with two distinct linear regions having $\beta_{lg} = -0.30$ (for $pK_{BH} < 5.8$) and $\beta_{lg} = -0.93$ (for $pK_{BH} > 5.8$). This observation is consistent with a change in rate-determining step within an E1cb reaction mechanism from rate-determining deprotonation of **1** (i.e., (E1cb)$_{irrev}$) for $pK_{BH} < 5.8$ to rate-determining leaving-group expulsion from the carbanionic intermediate (i.e., (E1cb)$_{rev}$) for $pK_{BH} > 5.8$. This interpretation is supported by ^{1}H NMR spectral observations in basic D_2O, which show no incorporation of deuterium into the acrylonitrile product for $pK_{BH} < 5.8$ but do show D for H exchange of the methylene protons that are α to the cyano group at a rate that is faster than elimination for $pK_{BH} > 5.8$. Rates of nucleophilic attack of pyridines and pyridinone anions ($pK_{BH} > 6$) upon acrylonitrile have also been measured. These display a linear Brønsted plot of $\beta_{nuc} = 0.20$. Combination of β_{lg} and β_{nuc} gives $\beta_{eq} = 0.13$ for the Michael-type addition of pyridinium cations to acrylonitrile to produce **1**. Although the rates of the addition of pyridines of $pK_{BH} < 6$ are too slow for convenient measurement in the current study, the combination of the measured rate and equilibrium Brønsted parameters allows the demonstration of the change in rate-determining step in these addition reactions from rate-determining nucleophilic attack (carbanion formation) with $\beta_{nuc} = 0.20$ for pyridines of $pK_{BH} > 5.8$ to rate-determining protonation of the carbanionic intermediate with $\beta_{nuc} = 0.83$ for pyridine nucleophiles of $pK_{BH} < 5.8$. General-base catalysis of the elimination reactions is observable in the (E1cb)$_{irrev}$ region but is extremely weak under the current experimental conditions.

In 1972, Bordwell presented[1] a tabular summary of the variety of mechanistic possibilities that have been recognized for base-catalyzed 1,2-elimination reactions. This table and variations upon it have now been widely reproduced[2] in review articles on this important general class of organic reactions. Experimental criteria for distinguishing between most of the mechanistic possibilities are generally available; however, a simple experimental test to allow the distinction between the E2 ($A_{xh}D_HD_N$ in IUPAC mechanistic nomenclature[3]) and (E1cb)$_{irrev}$ ($A_{xh}D_H^{\ddagger} + D_N$) mechanisms remains quite elusive, although second-derivative p_{xy} cross-correlation coefficients have been used to distinguish between these two mechanistic possibilities.[4] In principle, the demonstration of the (E1cb)$_{irrev}$ mechanism should be possible by the extension of structure–reactivity relationships until a change in rate-determining step is observed. This would effectively represent the conversion of the (E1cb)$_{irrev}$ ($A_{xh}D_H^{\ddagger} + D_N$) mechanism into the (E1cb)$_{rev}$ ($A_{xh}D_H + D_N^{\ddagger}$) case and allow a distinction between the E1cb mechanism and the formal E2 concerted elimination reaction in which no change in rate-determining step is possible.

Despite the common occurrence[1,5] of the carbanionic E1cb mechanism in eliminations involving activated carbon acids, there appear to have been only relatively few demonstrations of a change in rate-determining step from deprotonation ((E1cb)$_{irrev}$) to leaving-group expulsion ((E1cb)$_{rev}$) in any one reaction series. The only clear demonstrations of such a change in rate-determining step that we have been able to locate are the data of Jencks and co-workers for eliminations from *N*-(4-nitrophenethyl)quinuclidinium cations[6] and from 2-cyanoethyl sulfides[7] in predominantly aqueous media, the study of Fedor and Glave[8a] on the elimination reactions of 4-phenoxy-2-butanones in aqueous solution, and the studies of Stirling and co-workers[8b] on the eliminations of β-activated ethylammonium cations in ethanolic solution. In these cases, the change in rate-determining step involves the demonstration of a kinetic saturation effect at high concentrations of the general-base catalyst species. A change in rate-determining step that results from structural variation in the elimination substrate itself does not seem to have been clearly demonstrated, although there was an indication of such a phe-

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