literature regarding the reasons,[5] a large body of evidence indicates that the propensity for O-alkylation increases as the electrophilic character of the alkylating agent is increased.[4a,6]

A further unusual aspect of this reaction is that alkylation occurs at an ester oxygen to form relatively high energy product **2**. This appears to be the first example of alkylation of an acetoacetic ester at the ester oxygen. Of course, alkylation at the ketone oxygen would be quite unfavorable, requiring formation of a seven-membered ring. Therefore, alkylation at carbon might be expected to be particularly favored. For this reason, the observed mode of alkylation further suggests that the reaction proceeds by an abnormal pathway in this instance.

In addition to the novel regiochemical and mechanistic possibilities afforded by these transformations, they appear to have considerable synthetic potential. Ketene acetal **2** is a precursor to 1,3-dioxygenated dienes which have proven useful in natural product synthesis via cycloaddition reactions.[7] Such dienes have generally been accessible only by laborious, low-yielding reaction schemes.[8] In contrast, **2** is easily prepared from readily available starting materials, and its preparation has been scaled-up to 0.5 mol with no apparent difficulty. Furthermore, **2** could be anticipated to be more reactive than its acyclic counterparts. Therefore, it seems possible that the enol tautomer of **2** could serve as a useful diene for Diels–Alder applications without the necessity of prior conversion to an O-acylated or silylated derivative. Precedent for such behavior was found with the dimethylketene acetal analogous to **2**.[8b] We are currently pursuing potential cycloaddition applications of **2**, and this will be the subject of a subsequent communication.

Experimental Section

Methods. Melting points were determined on a Mel-Temp apparatus (Laboratory Devices, Inc., Cambridge, MA) and are uncorrected. Proton NMR spectra were recorded at 60 MHz on a Varian T-60A instrument in $CDCl_3$ relative to tetramethylsilane as internal standard. IR spectra were obtained employing Beckman Model No. 4250 and Perkin-Elmer Model 457 spectrophotometers, either as a KBr pellet for solids or neat for liquids. Mass spectra were obtained on a Finnigan Model 1015-D spectrometer. Elemental analyses were carried out at the University of California, Berkeley microanalytical laboratory. Gas–liquid phase chromatography (GLPC) was carried out on a 6 ft, 3% OV-1 on 60/80-mesh gas Chrom Q column installed in a Varian Model 3700 gas chromatograph and employing a flame ionization detector.

2-Chloroethyl Acetoacetate (1). Prepared from diketene and 2-chloroethanol by using the organic synthesis procedure[9]. Acetoacetate **1** was obtained in a 72% yield following distillation [bp 65–67 °C (0.15 mm), lit. bp 94 °C (5mm),[10a] bp 120–121 °C (19mm)[10b]]: NMR δ 2.24 (s, 3, CH_3 CO), 3.55 (s, 2, $COCH_2CO$), 4.40 (t, 2, J = 7 Hz, OCH_2CH_2Cl), 3.63 (t, 2, J = 7 Hz, OCH_2CH_2Cl).

2-(2-Oxopropylidene)-1,3-dioxolane (2). A solution of acetoacetate **1** (20.0 g, 0.12 mol) in DMF (80 mL) was stirred under N_2 with *powdered*, anhydrous K_2CO_3 (19.3 g, 0.139 mol, Hooker). The initial reaction was mildly exothermic. Stirring was continued at ambient temperature for 5 h. Following this period, no residual **1** could be detected by GLPC. The crude product mixture was filtered and the residue was rinsed with DMF. The DMF was removed by rotary evaporation [50 °C (1 mm)] to yield a light brown oil which was taken up in 100 mL of ethyl acetate and filtered through Dicalite to remove residual salts. Rotary evaporation [50 °C (1 mm)] gave 13.3 g (85%) a dark yellow solid, mp 56–64 °C. The solid was deliquescent but could be stored for weeks in tightly capped jars without apparent change. Recrystallization from CCl_4 afforded colorless needles, mp 68–69 °C. Alternatively, sublimation at 50 °C (0.2 mm) yielded smaller hard white crystals, mp 63–69 °C: NMR δ 2.13 (s, 3, CH_3CO), 4.91 (s, 1, COCH=C), 4.35 (m, 2, OCH_2CH_2O), 4.57 (m, 2, OCH_2CH_2O); IR 2920–3000 (CH), 1660 (C=O), 1610 (C=C) cm^{-1}; MS, m/e (relative intensity) 129 (22, $M^+ + 1$), 128 (16, M^+), 113 (64), 87 (18), 69 (base peak).

Anal. Calcd for $C_6H_8O_3$: C, 56.25; H, 6.29. Found: C, 56.22; H, 6.35.

Bis(2-chloroethyl) malonate (3) was obtained from Fischer esterification[11] of malonic acid with 2-chloroethanol in 33% yield [bp 107–121 °C (0.1 mm), lit.[12] bp 150–151 °C (5 mm)].

2-[[[2-(Chloroethyl)oxy]carbonyl]methylidene]-1,3-dioxolane (4). A solution of malonate **3** (112 g, 0.49 mol) in DMF (200 mL) was stirred under N_2 with powdered, anhydrous K_2CO_3 (97 g, 0.7 mol, Hooker Chemical Company). The reaction was mildly exothermic with the temperature increasing from 22 °C to 51 °C over the first 5 min. After 15 min, GLPC analysis indicated ca. 2% residual starting **3**. Following a total of 45 min, the reaction mixture had returned to ambient temperature and the solids were removed by suction filteration. The residue was washed with 200 mL of DMF, and the combined filtrates were rotary evaporated [(60 °C (15 mm)]. The residual, nearly colorless oil was taken up in 400 mL of ethyl acetate and filtered through Dicalite. The ethyl acetate was removed by rotary evaporation [60 °C (1 mm)] to yield 99 g (105%) of a soft, white solid which was recrystallized from toluene to give 65 g (68%) of a hygroscopic white, finely crystalline solid, mp 88–97 °C. A second recrystallization from toluene gave white needles, mp 92–96 °C. Alternatively, **4** could be further purified by sublimation [(85 °C (0.1 mm)]: NMR δ 3.58 (t, 2, J = 7 Hz, $ClCH_2$), 4.21 (t, 2, J = 7 Hz, $ClCH_2CH_2O$), 4.2–4.7 (m, 5); IR 2880–3000 (CH), 1702 (C=O), 1625 (C=C) cm^{-1}; MS, m/e (relative intensity) 192 (16, M^+), 157 (30), 130 (53), 115 (54), 114 (27), 113 (48), 86 (46), 69 (base peak), 63 (22).

Anal. Calcd for $C_7H_9ClO_4$: C, 43.65; H, 4.71; Cl, 18.41. Found: C, 43.71; H, 4.68; Cl, 18.12.

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Registry No. 1, 54527-68-3; 2, 6704-30-9; 3, 1605-30-7; 4, 94844-08-3.

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Solvent Effects in A1 and AS_E2 Reactions in Water/2,2,2-Trifluoroethanol Mixtures

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The solvent effects on A1 and AS_E2 reactions have been studied in a variety of aqueous/organic solvent systems.[1–4]

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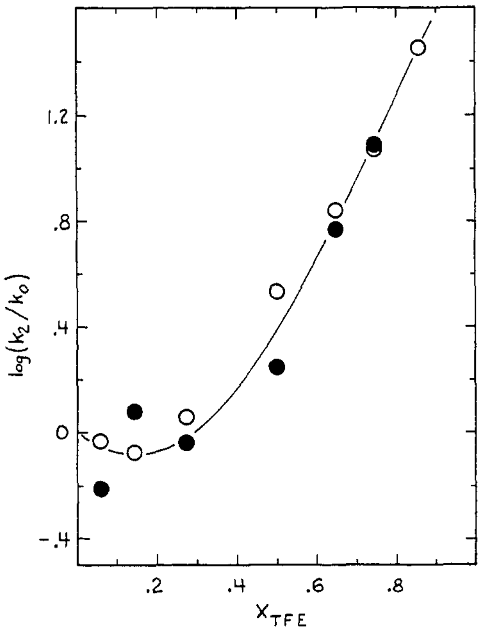

Figure 1. Solvent effects on hydrolysis reactions. The logarithm of the second-order rate constant, k_2, relative to that in pure water, k_0, is plotted vs. molar fraction of 2,2,2-trifluoroethanol in water. The open circles represent acid-catalyzed ethyl vinyl ether hydrolysis ($A_{S_E}2$ mechanism). The closed circles represent acid-catalyzed diethyl acetal hydrolysis (A1 mechanism).

In all of these cases the organic component has been a poor hydrogen bond donator and a good hydrogen bond acceptor—*N*,*N*-dimethylformamide,[1] *N*-methylpropionamide,[1] acetone,[1] dimethyl sulfoxide,[1-4] and dioxane.[4] For the A1 mechanism the solvent effect in these solvent systems follows the same pattern. The second-order rate constant decreases with increasing organic component until a minimum is reached, whereupon it increases again as the pure organic component is approached. The $A_{S_E}2$ mechanism has only been studied in dimethyl sulfoxide[3,4] and dioxane.[4] The solvent effect follows the same pattern as that found for the A1 mechanism. We decided to investigate the solvent effect on these two mechanisms using an organic component which was a poor hydrogen bond acceptor (in contrast to the previous solvents) and a good hydrogen bond donor. The solvent chosen was 2,2,2-trifluoroethanol (TFE).

The rates of the acid-catalyzed hydrolysis of diethyl acetal (A1 mechanism) and ethyl vinyl ether ($A_{S_E}2$ mechanism) have been determined in a series of water/TFE mixtures. The catalyst was perchloric acid. The pseudo-first-order rate constants were determined in at least duplicate and in most cases triplicate. The average second-order rate constant, k_2, for diethyl acetal hydrolysis in pure water was 1.47 M^{-1} s^{-1} which compares favorably to the previously obtained value[1] of 1.46 M^{-1} s^{-1}. The value of k_2 for ethyl vinyl ether hydrolysis in pure water was 1.80 M^{-1} s^{-1} which is in agreement with the previous value[5] of 1.71 M^{-1} s^{-1}.

The log (k_2/k_0) values for both substrates are plotted against the molar fraction of TFE in Figure 1 where k_0 is k_2 in pure water. It appears as if the two sets of data could be treated as a single set which exhibits deviations around a curve. This suggests that the solvent effect on these two mechanisms is not only similar but identical. Kankaanperä and Merilahti[4] studied the acid-catalyzed hydrolysis of 2-methyl-1,3-dioxolane and 2-methyl-4-methylene-1,3-dioxolane which react by Al and As_E2 mechanisms, respectively. They used water/dimethyl sulfoxide and water/dioxane solvent mixtures. The solvent effect showed the general pattern mentioned previously, but in neither solvent system was the solvent effect identical for the two mechanisms. The mechanisms in each case were distinguished from each other.

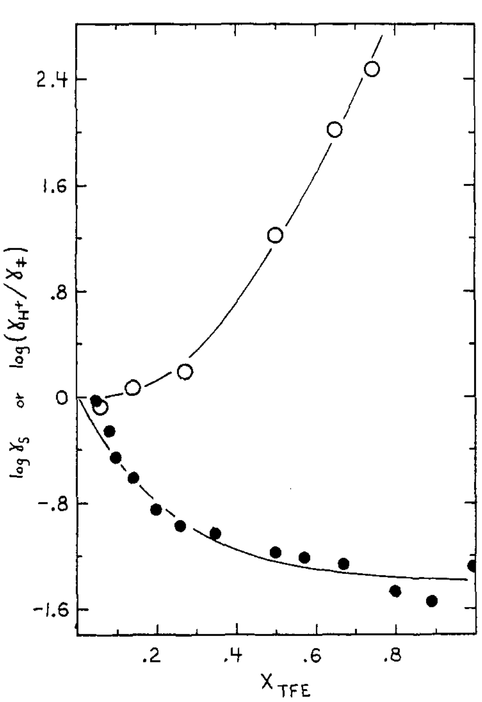

Figure 2. The logarithm of molar activity coefficients relative to pure water as the standard state vs. molar fraction of 2,2,2-trifluoroethanol in water. The open circles represent log $(\gamma_{H^+}/\gamma_{\ddagger})$ for diethyl acetal hydrolysis. The closed circles represent log γ_S for diethyl acetal.

Using the approach of Cox and McTigue[3] the relative rate constant, k_2/k_0, for the Al mechanism can be expressed as a function of activity coefficients of the substrates and transition state. The relationship is given by log (k_2/k_0) = log γ_s + log $(\gamma_{H^+}/\gamma_{\ddagger})$, which can be derived from the rate law $-d[S]/dt = k_2[H^+][S]$ where S represents diethyl acetal. We determined the acetal activity coefficients, γ_S, in a series of water/TFE mixtures and then calculated log $(\gamma_{H^+}/\gamma_{\ddagger})$ values. For example, at $\chi_{TFE} = 0.5$, log $(k_2/k_0) = 0.25$ (see Figure 1) and log $\gamma_S = -1.18$ (see Figure 2). Using the above relationship, log $(\gamma_{H^+}/\gamma_{\ddagger})$ = 1.43. The results of all these calculations are shown in Figure 2.

As can be seen the hydronium ion activity coefficient is increasing relative to the transition-state activity coefficient. If γ_{H^+} is mainly affected by solvation due to hydrogen bonding, addition of the weak hydrogen bond acceptor TFE would tend to decrease the "solvation" of H^+ relative to water because of the weak basicity of the nonbonded oxygen electrons. This explanation is supported by the increase in acidity function with increasing mole fraction TFE.[6] Thus, the prediction is that γ_{H^+} would increase with increasing χ_{TFE} causing the $\gamma_{H^+}/\gamma_{\ddagger}$ ratio to increase. The transition state has different solvation requirements than H^+, even though it carries the same charge, due to its bulkiness. It has hydrophobic groups

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which would be much better solvated by TFE through London dispersion forces than by water. Addition of TFE would decrease $\gamma_\ddagger$ relative to water causing the $\gamma_{\mathrm{H}^+}/\gamma_\ddagger$ ratio to increase. Therefore, for an A1 mechanism the solvation effect of TFE on both H^+ and the transition state is to cause $\gamma_{\mathrm{H}^+}/\gamma_\ddagger$ to increase.

The situation should be similar in the $\mathrm{AS_E2}$ case. The effect on γ_{H^+} would be identical as above. The $\mathrm{AS_E2}$ transition state for ethyl vinyl ether would be structurally related to that for diethyl acetal—the difference being a water molecule and an ethanol molecule, respectively. There is considerable charge dispersal in both cases. The expectation would be that TFE would have the same solvation effect on $\gamma_\ddagger$ for $\mathrm{AS_E2}$ as it did for A1. One would predict, therefore, that addition of TFE would increase γ_{H^+} and decrease $\gamma_\ddagger$ causing the $\gamma_{\mathrm{H}^+}/\gamma_\ddagger$ ratio to increase.

It has been argued[3] that dimethyl sulfoxide solvates H^+ better than water, giving rise to a decrease in γ_{H^+}. The same argument probably applies to dioxane which can only function as a hydrogen bond acceptor. The opposite argument was applied above for TFE. It appears that the solvent effect on both A1 and $\mathrm{AS_E2}$ reactions can be predicted qualitatively by considering the solvent effect on γ_{H^+}, and the effect on γ_{H^+} can be surmised by looking at the H^+ solvating ability of the organic solvent with respect to that of water.

Experimental Section

Diethyl acetal, ethyl vinyl ether, and 2,2,2-trifluoroethanol were obtained commercially (Aldrich Chemical Co.), were distilled once, and were used without further purification. An aqueous stock solution of perchloric acid was prepared and then standardized by the usual analytical techniques.[7] A series of water/TFE solutions of known acid concentration were then prepared.

The rate of hydrolysis of both diethyl acetal and ethyl vinyl ether was followed by monitoring the buildup of acetaldehyde at 270 nm with time. The reactions were initiated by injecting 30–50 μL of substrate into 3 mL of reaction solution contained in a spectrophotometer cell. All solutions and the spectrophotometer cell holder were thermostated at 25.0 ± 0.2 °C. All reactions were followed for at least 3 half-lives. The pseudo-first-order rate constants could be replicated with discrepancies of no more than 10%. In the case of ethyl vinyl ether the rate was also followed by monitoring the disappearance of the vinyl ether at 236 nm. Identical rate constants were obtained by whichever method was used. The second-order rate constants were calculated from the pseudo-first-order rate constants and the acid concentration.

The molar activity coefficients of diethyl acetal were determined from the distribution ratios in the two-phase system of cyclohexane/water–TFE at 25 ± 1 °C. The acetal concentration in the water–TFE layer was determined by adding acid and titrating the released aldehyde by the method of Siggia and Maxcy.[8] The concentration in the cyclohexane layer was calculated by the difference between the total amount of acetal added and the amount in the water–TFE. The activity coefficient, γ_S, relative to pure water as the standard state was then calculated by dividing the distribution ratio for cyclohexane/water by the distribution ratio for each cyclohexane/water–TFE system. This method depended on the insolubility of water and especially TFE in cyclohexane. Since TFE was the most likely candidate, its presence in cyclohexane was determined. Cyclohexane and TFE were shaken together. Gas chromatographic analysis of the cyclohexane layer using a column of 10% Carbowax on 60/80 Chrom W resulted in no detection of TFE in the cyclohexane.

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Registry No. Ethyl vinyl ether, 109-92-2; diethyl acetal, 105-57-7; proton, 12586-59-3.

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Photochemical Reactions in the Benzophenone/*tert*-Butyl Alcohol/Oxygen System. Some Unexpected Results

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tert-Butyl alcohol is often used as a solvent for photochemical reactions (especially photoreductions) due to its inertness. Its primary aliphatic hydrogen atoms are not expected to be readily abstracted by a carbonyl triplet state. However, it has been reported that aromatic ketones may be photoreduced by *tert*-butyl alcohol in the absence of any more reactive hydrogen donors.[1] Thus, irradiation of a solution of benzophenone in *tert*-butyl alcohol (0.5 g in 150 mL) for 2.5 h (Hanovia 250-W, medium pressure mercury lamp, Pyrex) in the absence of oxygen led to the complete disappearance of benzophenone.[1d] The benzophenone–*tert*-butyl alcohol adduct 1 was isolated in a 26% yield[1c] (Scheme I).

This unexpected result shows that the photoreduction of benzophenone by *tert*-butyl alcohol is a rather fast process.[2] We reported also that during long irradiations of nitrogen containing heterocycles in the presence of benzophenone and *oxygen* products derived either from benzophenone or from *tert*-butyl alcohol were formed.[3] These findings prompted us to undertake a detailed study of the mechanism of formation of these side products which could interfere with the main photochemical reaction.

Irradiation (medium pressure mercury lamp, MEDA 400-W, Pyrex) of an oxygen-saturated solution of benzophenone in *tert*-butyl alcohol (150 mL) for 168 h gave the mixture of products shown in Table I. These may be split into three groups according to their origin: (1) products of coupling reactions of radicals resulting from the photoreduction of benzophenone by *tert*-butyl alcohol, (2) products of oxidation of radicals derived from *tert*-butyl alcohol (in particular, a rather important amount of acetone was formed), and (3) products derived from benzophenone by other reactions.

(1) $\mathrm{Ph_2CO}$/*t*-BuOH Coupling Products. 1,1-Diphenylethylene is obtained even though oxygen is present, presumably by fragmentation of the 1,3-diol 1[1c,4] already

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[2] The rate constant of reduction of triplet benzophenone by *tert*-butyl alcohol has been determined in $\mathrm{CCl_4}$: $k_r = 5.35 \times 10^4$ mol^{-1} s^{-1}.[10] This value is a hundred times smaller than the rate constant of reduction of triplet benzophenone by isopropyl alcohol ($k_r = 4.10 \times 10^6$ mol^{-1} s^{-1} in the same conditions). Our observation is consistent with these values since in our[1d] and others[1c] experiments *tert*-butyl alcohol is used as a solvent in a very high concentration.

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