and concentrated under reduced pressure to give spiro alcohol **6** as the sole product (10.9 mg, 0.05 mmol, 85%). Similar reduction of pure **3b** (31 mg, 0.15 mmol) gave spiro alcohol 8 (16 mg, 0.08 mmol, 51%) as the sole product.

Aluminum Chloride Catalyzed Isomerization of 6 to 8 and 7 to 5. Aluminum chloride (6 mg, 0.05 mmol) was added to a CH_2Cl_2 (2 mL) solution of spiro alcohol **7** (27 mg, 1.3 mmol) and the resulting mixture was stirred at room temperature under N_2 while monitored by TLC on silica gel (1:1 *n*-hexane/EtOAc). After 1.5 h, the mixture was poured onto 2 N aqueous NaOH (2 mL) and the aqueous layer was extracted with CH_2Cl_2 (2×). The combined organics were washed with brine, dried (Na_2SO_4), filtered, and concentrated under reduced pressure to give **5** (24 mg, 1.2 mmol, 89%) and a trace amount of **7** (**5**:**7** > 20:1 as judged by 500-MHz ^1H NMR). Similar isomerization (0.5 equiv $AlCl_3$, 10 h) of **6** produced a >5:1 (90-MHz ^1H NMR) mixture of crude spiro alcohols **8** and **6**, respectively.

Acknowledgment. This research was supported by funds provided by the Research Corporation and the committee on Research of the University of California, Davis. We gratefully acknowledge IBM Instruments for donation of an LC/9553 ternary high-pressure liquid chromatography system and Mr. M. D. Yanuck for assistance in the X-ray structure determination.

Supplementary Material Available: A stereoplot drawing of **3a** and listings of atom coordinates, bond lengths, bond angles, and hydrogen atom coordinates (5 pages). Ordering information is given on any current masthead page.

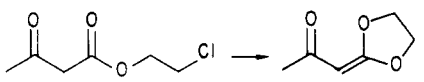
A Novel Intramolecular Ester–Enolate Alkylation: Preparation of Acylketene Acetals

Michael D. Broadhurst[1]

Stauffer Chemical Company, de Guigne Technical Center, Richmond, California 94804

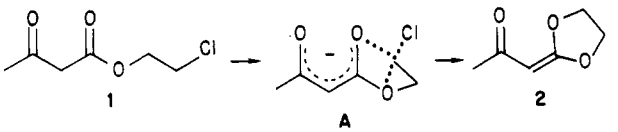
Received February 10, 1984

During an investigation directed toward potential methods for the preparation of substituted butyrolactones, a novel and synthetically useful preparation of acylketene acetals was discovered. On base treatment, 2-chloroethyl acetoacetate (**1**) exclusively gives acylketene acetal **2** in good yield. This remarkable transformation represents one of the few examples of the base-catalyzed alkylation of an ester–enolate to yield a ketene acetal.[2] In general, ester–enolates exhibit high selectivity for alkylation at carbon when carbon-based alkylating agents are employed.[2b] Competitive O-alkylation of highly acidic and hindered esters has been reported only when diazomethane was the alkylating agent.[2a] In addition, good yields of O-silylation have been obtained in a few instances.[2b,c] However, the resultant O-silylated ketene acetals have not proven as useful as their O-alkylated counterparts in some synthetic applications.[3]



1 **2**

Scheme I

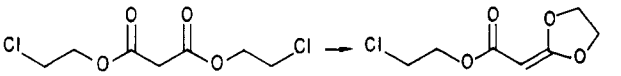


1 **A** **2**

This note provides details of the straightforward preparation of **2**, a cursory look into the generality of this chemistry, and a discussion of the origin of the unusual and highly selective O-alkylation leading to its formation.

Results and Discussion

When 2-chloroethyl acetoacetate (**1**) was treated with potassium carbonate in DMF, a mildly exothermic reaction ensued, resulting in ketene acetal **2** in good yield as a low-melting, deliquescent solid. No other products could be detected in more than trace amounts by GLPC or NMR analysis. Suprisingly, even under conditions more conducive to C-alkylation, **2** was the only significant product found. Nonaprotic dipolar solvents (acetone and dimethoxyethane) and more strongly bound counterions (sodium) were employed. good yields of **2** were obtained in all instances, even though these changes should encourage C-alkylation.[4] Furthermore, the method was found to have some generality. Malonate **3** smoothly gave ketene acetal **4** under similar conditions.



3 **4**

The anomalous propensity of acetoacetate **1** and malonate **3** to give O-alkylated products is intriguing. Consideration of the normal criteria employed to assess C- vs. O-alkylation in such systems[4] would lead one to anticipate that C-alkylation to yield the corresponding butyrolactones would be the predominant or exclusive course of the reaction in both instances. Furthermore, although the specificity of these reactions is certainly related to the intramolecular nature of the alkylation, examination of molecular models did not reveal an obvious basis for differentiating the inter- and intramolecular modes of alkylation. One might argue that additional constraints imposed due to intramolecularity could increase the steric requirements in the transition state. While steric factors have been shown to increase the proportion of O-alkylation in some instances,[4b,5] it would be unwarranted to rationalize the high degree of regioselectivity observed in these cases solely on this basis.

An unobvious alternative explanation consistent with these observations would invoke participation by the neighboring ester oxygen atom not involved in delocalization of the negative charge brought about by proton abstraction. In this case, a transition state resembling A might be envisioned (Scheme I). Although such participation by an ester oxygen has not been previously proposed, increased stability of an intermediate oxonium ion or transition states which develop some positive charge at oxygen could be rationalized on the basis of the adjacent delocalized negative charge. Regardless of the exact nature of the transition state or intermediates involved, participation by the neighboring ester oxygen would be expected to direct the akylation toward oxygen, both by increasing the reaction rate and by enhancing the S_N1 character of the reaction. Although there is not total agreement in the

(1) Present Address: Stauffer Chemical Company, Nyala Farm Road, Westport, CT 06881.

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(3) Acylketene acetals can serve as precursors too 1,3-dioxygenated dienes, useful in Diels-Alder applications. In general, the more steric bulk present at the diene terminus, the less reactive it is toward cycloaddition, e.g., see: Savard, J.; Brassard, P. *Tetrahedron Lett.* **1979**, 4911.

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0022-3263/85/1950-1117$01.50/0

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_3CO), 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.

Acknowledgment. The author is greatly indebted to Dr. R. D. Gless and Dr. D. J. Bowler for invaluable technical discussions and for the expert experimental work of Ms. M. McKenna.

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

Charles Parnell, David Binder, and Robert Eliason*

Chemistry Department, Southwest State University, Marshall, Minnesota 56258

Received May 17, 1984

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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