(Grant No. E-927). We also thank Dr. Gary E. Martin and Mr. Ed L. Ezell for their assistance with the high field NMR spectroscopy.

Registry No. 1, 94942-26-4; 2, 94859-79-7; 3, 94859-80-0; 4, 94859-81-1; 5, 94859-82-2; 6, 94859-83-3; 7, 94942-27-5; 8, 94859-84-4; **10a**, 52944-79-3; **10b**, 108-24-7; Bz-Ala-OH, 2198-64-3; Bz-Lys(Z)-OH, 1946-80-1; Boc-Ala-Lys(Z)-OH, 92073-01-3; Boc-Lys(Z)-Ala-Lys(Z)-OH, 94904-24-2; MMS, 3878-55-5.

Stereoselective Synthesis of Octahydro-3-oxospiro[benzofuran-2(3*H*),2′-[2*H*]-pyran] Systems

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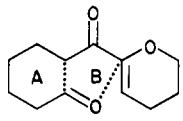
Received July 26, 1984

The dioxaspiro functional group is found in numerous structurally and biologically interesting natural products.[1] Phyllanthoside[2,3] and breynolide[4] are two prominent examples which have a common spiro[benzofuran-2-(3*H*),2′-[2*H*]pyran] skeleton. We now report a synthesis of this unique ring system which proceeds in three stereocontrolled steps (see Scheme I) from dihydropyran. In addition, a series of diastereomer interconversions is presented which demonstrate ketal equilibration and unambiguously establish stereochemistry in these dioxaspiro systems.

Two approaches to the target skeleton **3** were investigated. We first envisioned a one-pot acid-catalyzed aldol condensation/spiroketalization procedure for the construction of rings A and B. Unfortunately, all attempts to form this ring system from substrate **1**[5] under a variety of acidic conditions ($TiCl_4$, $SnCl_4$, $BF_3{\cdot}Et_2O$, PTSA) produced complicated reaction mixtures from which neither the starting material or desired spiroketal could be isolated. Similarly, treatment of **2**[6] with a variety of Lewis acids gave none of the desired 1,6-dioxaspiro[4.5]decan-4-one.



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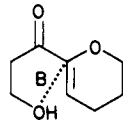

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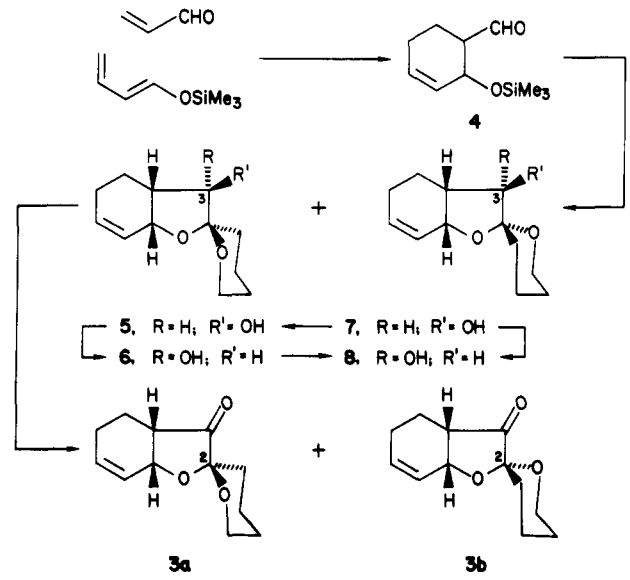
Scheme I



In light of these results, a stepwise approach to **3** was developed which is delineated in Scheme I. Diels–Alder condensation of acrolein and 1-[(trimethylsilyl)oxy]-1,3-butadiene[7] gave cyclohexenecarboxaldehyde **4** in 88% yield as a 11:1 mixture of cis and trans isomers. In a one-pot operation, this aldehyde mixture was added to a THF solution of 2-lithiodihydropyran,[8] and the resulting solution was treated with 48% hydrofluoric acid to effect concomitant desilylation and spiroketalization. Workup gave four spiro alcohols which were readily separable by MPLC on silica gel (**5**:**6**:**7**:**8** = 2.8:4.6:1.0:1.4; 50% combined yield). Parikh-modified[9] Moffatt oxidation of the carbinol mixture produced a 3:1 mixture of **3a** and **3b** in 76% yield. These spiro ketones proved inseparable by silica gel chromatography. The major diastereomer **3a** could be isolated by fractional crystallization of this mixture, while pure **3b** was available only by oxidation of previously isolated spiro alcohols **7** and **8**.

While dioxaspiro compounds **3a**, **3b**, and **5**–**8** were all readily differentiable by high-field ^1H NMR, complete structure assignments based on these differences in the proton spectra proved untenable. Therefore, the structure of **3a** was determined by single-crystal X-ray diffraction analysis and structural assignments for **3b** and **5**–**8** were then deduced by chemical correlation with **3a** as follows. Steric considerations suggested that reduction of the carbonyl in **3a** would occur via hydride addition from the β face. Indeed, lithium triethylborohydride reduction[10] of **3a** produced a single spiro alcohol which was assigned structure **6**. Likewise, reduction of **3b** produced a single spiro alcohol which was assigned structure **8**, again based on steric approach considerations.[10] Parikh-modified Moffat oxidation of either **6** or its C(3) epimer **5** produced the major spiro ketone **3a** as the sole product while similar oxidation of either **8** or its C(3) epimer **7** produced only the minor spiro ketone **3b**. In analogy with the equilibrations observed by Kozluk[11] for the diastereomers of 4-hydroxy-1,6-dioxaspiro[4.5]decane, we found that alu-

(1) The following are representative examples of dioxaspiro-containing natural products which have attracted recent synthetic investigation. (a) Olive fruit fly sex pheromone: Kocienski, P.; Yeates, C. *Tetrahedron Lett.* **1983**, *24*, 3905–6. (b) Antiparasitic agent avermectin Bla: Hanessian, S.; Ugolini, A.; Therien, M. *J. Org. Chem.* **1983**, *48*, 4427–30. (c) Antibiotic ionophore A-23187: Evans, D. A.; Sacks, C. E.; Kleschick, W. A.; Taber, T. R. *J. Am. Chem. Soc.* **1979**, *101*, 6789–91. (d) Steroidal sapogenins: Blunden, G.; Jaffer, J. A.; Jewers, K.; Griffin, W. J. *Tetrahedron* **1981**, *37*, 2911–15.

(2) Isolation of phyllanthoside: Kupchan, S. M.; LaVoie, E. J.; Branfman, A. R.; Fei, B. Y.; Bright, W. M.; Bryan, R. F. *J. Am. Chem. Soc.* **1977**, *99*, 3199–201. (d) Steroidal sapogenins: Blunden, G.; Jaffer, J. A.; Jewers, K.; Griffin, W. J. *Tetrahedron* **1981**, *37*, 2911–5.

(3) Phyllanthocin, the aglycon of **1** (R = CH_3) has been synthesized: (a) Collum, D. B.; McGuirk, P. R. *J. Org. Chem.* **1984**, *49*, 843–52. (b) Williams, D. R.; Sit, S. Y. *J. Am. Chem. Chem. Soc.* **1984**, *106*, 2949–54. (c) Smith, A. B., III; Fukui, M. "Abstracts of Papers", 187th National Meeting of the American Chemical Society, St. Louis, MO, April 1984; American Chemical Society: Washington, DC, 1984; ORGN 6.

(4) Isolation of breynolide: Sasaki, K.; Hirata, Y. *Tetrahedron Lett.* **1973**, 1439–42.

(5) Prepared in four steps from 2-lithiodihydropyran[8] and 7-[(methylthio)methoxy]heptanal.

(6) Prepared in low yield by the direct acylation of 2-lithiodihydropyran[8] with β-propiolactone.

(7) Makin, S. M.; Nguyen, P. T.; Shavrygina, O. A.; Arshava, B. M.; Romanova, I. A. *Zh. Org. Khim.* **1983**, *19*, 727–32; *Chem. Abstr.* **1983**, *99*, 88261p.

(8) Boeckman, R. K.; Bruza, K. J. *Tetrahedron* **1981**, *37*, 3997–4006.

(9) Parikh, J. R.; Doering, W. *J. Am. Chem. Soc.* **1967**, *89*, 5505–7.

(10) Wunderly, S. W.; Borchmann-Hanssen, E. *J. Org. Chem.* **1977**, *42*, 4277–8.

(11) Kozluk, T.; Cottier, L.; Descotes, G. *Tetrahedron* **1981**, *37*, 1875–80.

0022-3263/85/1950-1115$01.50/0

minum chloride in dichloromethane isomerized spiro alcohol **6** to **8** and spiro alcohol **7** to **5**. Presumably the bidentate chelation of aluminum which is available in **5** and **8**, but not **6** and **7**, promotes this equilibration. These experiments unambiguously establish the stereochemical assignments in spiro alcohols **5**–**8**[12] and spiro ketone **3b**. In addition, they demonstrate that **3a** can be converted to **3b** by a reaction sequence which involves carbonyl reduction, ketal isomerization, and carbinol oxidation (**3a** → **6** → **8** → **3b**).

Experimental Section

General Methods. Melting points were determined on a Kofler hot stage and are uncorrected. Proton magnetic resonance spectra were obtained in deuteriochloroform on Varian EM 390 (90-MHz), Nicolet NTCFT-1180 (360-MHz), and Nicolet NMCFT-1280 (500-MHz) spectrometers and are reported in ppm (δ units) downfield of internal tetramethylsilane (Me_4Si). Infrared spectra were recorded on a Beckman IR-8 spectrophotometer. Mass spectra were determined by Mr. Kei Miyano on a Dupont 21-492 instrument (electron impact, EI) through the Facility for Advanced Instrumentation, University of California, Davis. Elemental analyses were performed by the University of California, Berkeley, analytical laboratories. MPLC refers to chromatography done at 10–50 psi through EM Lobar columns packed with LiChroprep Si60 (40–63 μm) with hexane/EtOAc eluent and monitored by refractive index detection.

***cis*-(±)-2-(Trimethylsiloxy)cyclohex-3-enecarboxaldehyde[7] (4).** Acrolein (1.76 mL, 26.4 mmol), 1-(trimethylsiloxy)-1,3-butadiene (2.5 g, 17.6 mmol), and dichloromethane (20 mL) were placed in a resealable tube[13] and the vessel was sealed. The tube was heated at 50 °C for 48 h and cooled, and the resulting solution was concentrated under reduced pressure. Distillation gave **4** as a colorless oil which was an 11:1 mixture of cis and trans isomers (3.1 g, 15.7 mol, 88%) [bp 155–165 °C (40 torr); ^{1}H NMR (90-MHz, $CDCl_3$) δ 0.08 (s, 9 H, $SiCH_3$), 1.87–2.12 (m, 2 H, $2H_6$), 2.15–2.30 (m, 2 H, $2H_5$), 2.46–2.51 (m, 1 H, H_1), 4.62 (br s, 1 H, H_2), 5.75–5.79 (m, 1 H, H_3), 5.85–5.90 (m, 1 H, H_4), 9.67 (s, 1 H, *CHO*); IR (CCl_4) 3049, 2970, 1722, 1250, 1195, 1075, 1020 cm^{-1}; MS (EI), *m/e* (relative intensity) 198 (2), 183 (100), 142 (43), 127 (28), 119 (73)].

(2β,3β,3aβ,7aβ)-(±)-, (2β,3α,3aβ,7aβ)-(±)-, (2α,3β,3aβ,7aβ)-(±)-, and (2α,3α,3aβ,7aβ)-(±)-3a,4,5,7a,3′,4′,5′,6′-Octahydro-3-hydroxyspiro[benzofuran-2(3*H*),2′-[2*H*]pyran] (5, 6, 7, and 8). A 2:1 mixture of dihydropyran (670 μL, 7.38 mmol) and THF (300 μL, 3.69 mmol) was cooled to −78 °C under N_2 and treated dropwise with *tert*-butyllithium (2.6 M in pentane, 3.12 mL, 8.12 mmol). After being stirred for 10 min at −78 °C, the mixture was warmed to 0 °C and stirred for 25 min before excess THF (7.2 mL, 88.6 mmol) was added. Stirring was continued on an additional 25 min at 0 °C. The resulting 2-lithiodihydropyran[8] solution was cooled to −78 °C and treated rapidly dropwise with **4** (730 mg, 3.69 mmol) in THF (1.4 mL). After 30 min, the reaction was quenched at −78 °C by the addition of water (1 mL). The mixture was allowed to warm to room temperature, hydrofluoric acid (48%, 1.85 mL, 36.9 mmol) was added, and the two-phase mixture was stirred rapidly for 15 min and then made basic with aqueous sodium bicarbonate. The mixture was extracted with CH_2Cl_2 (2×) and the combined organic layers were dried (Na_2SO_4), filtered, and concentrated under reduced pressure. MPLC (60:10 *n*-hexane/EtOAc) gave, in order of elution, spiro alcohols **8** (39 mg, 0.19 mmol, 5.2%) [mp 49–51 °C from *n*-hexane/EtOAc; ^{1}H NMR (500-MHz, $CDCl_3$) δ 1.45–1.89 (m, 9 H), 2.11 (br d, J = 17.0 Hz, $H_{5\alpha}$), 2.34 (m (symmetrical six-line dddd), J^{14} = 7.9, 13.2, H_{3a}), 2.59 (d, J = 10.4, OH), 3.67 (br d, J = 11.7 $H_{6'eq}$), 3.93 (ddd, J = 2.8, 11.6, 11.6, $H_{6'ax}$), 3.98 (dd, J = 7.9, 10.4, H_3), 4.25 (br s, H_{7a}), 5.90 (br d, J = 9.3, H_7), 5.98 (m, H_6); IR ($CHCl_3$) 3579, 3040, 2950, 2930, 2890, 1410, 1360, 1250, 1210, 1152 cm^{-1}; MS(EI), *m/e* (relative intensity) 210 (23), 192 (12), 164 (28), 132 (46), 110 (51); calcd for $C_{12}H_{18}O_3$, 210.1256; found, 210.1229], **5** (110 mg, 0.52 mmol, 14.1% [mp 43–44 °C from *n*-hexane/EtOAc; ^{1}H NMR (500-MHz, $CDCl_3$) δ 1.53–1.89 (m, 8 H), 1.96 (br d, J = 17.5, $H_{5\beta}$), 2.10 (br d, J = 17.5, $H_{5\alpha}$), 2.23 (m (symmetrical six-line dddd), J^{14} = 5.9, 6.6, 12.1, H_{3a}), 2.57 (d, J = 9.9, OH), 3.55 (dd, J = 6.6, 9.9, H_3), 3.75 (br d, J = 11.6, $H_{6'eq}$), 3.96 (ddd, J = 2.7, 11.6, 11.6, $H_{6'ax}$), 4.44 (br d, J = 5.9, H_{7a}), 5.78 (br d, J = 10.1, H_7), 5.91 (m, H_6); IR (CCl_4) 3556, 3006, 2955, 2880, 1443, 1366, 1183, 1062 cm^{-1}. Anal. Calcd for $C_{12}H_{18}O_3$: C, 68.55; H, 8.63. Found: C, 68.41; H, 8.62], **6** (183 mg, 87 mmol, 23.6%) [mp 67–68 °C from *n*-hexane/EtOAc; ^{1}H NMR (500-MHz, $CDCl_3$) δ 1.48 (d, J = 8.3, OH), 1.49–1.88 (m, 8 H), 1.94 (m, $H_{5\beta}$), 2.22 (m, $H_{5\alpha}$), 2.53 (m (symmetrical six-line dddd), J^{14} = 7.8, H_{3a}), 3.62 (br d, J = 11.7, $H_{6'eq}$), 3.90 (ddd, J = 2.6, 11.7, 11.7, $H_{6'ax}$), 4.10 (dd, J = 7.8, 8.3, H_3), 4.29 (br s, H_{7a}), 5.92 (br d, J = 10, H_7), 6.05 (m, H_6); IR (CCl_4) 3620, 3460, 3020, 2960, 2890, 1185, 1100, 1040, 1015 cm^{-1}. Anal. Calcd for $C_{12}H_{18}O_3$: C, 68.55; H, 8.63. Found: C, 68.45; H, 8.49], and **7** (54 mg, 0.26 mmol, 7.1%) [viscous oil; ^{1}H NMR (500-MHz, $CDCl_3$) δ 1.45–1.90 (m, 10 H), 2.02 (m, $H_{5\alpha}$), 2.22 (m, H_{3a}), 3.60 (br d, J = 11.6, $H_{6'eq}$), 3.90 (ddd, J = 3.0, 11.6, 11.6, $H_{6'ax}$), 3.95 (d, J = 5.0, H_3), 4.55 (br d, J = 7.2, H_{7a}), 5.85 (br s, 2 H); IR ($CHCl_3$) 3570, 3060, 3025, 2975, 1365 cm^{-1}; MS(EI), *m/e* (relative intensity) 210 (15), 181 (11), 169 (17), 119 (28), 110 (22), 101 (100), 79 (55); calcd for $C_{12}H_{18}O_3$ 210.1256, found 210.1279].

(2β,3aβ,7aβ)-(±)- and (2α,3aβ,7aβ)-(±)-3a,4,5,7a,3′,4′,5′,6′-Octahydro-3-oxospiro[benzofuran-2(3*H*),2′-[2*H*]pyran] (3a and 3b). Sulfur trioxide–pyridine complex (2.1 g, 13.2 mmol) in Me_2SO (8.2 mL, 115 mmol) was added in one portion to a room-temperature Me_2SO (8.2 mL, 115 mmol) solution of triethylamine (3.2 mL, 23.1 mmol) and crude spiro alcohols **5**–**8** (2.8:4.6:1:1.4 = **5**:**6**:**7**:**8**, from 2.4 mmol of aldehyde **4**). After 1 h, water was added and the mixture was extracted with ether (3×). The combined organics were washed with 10% aqueous HCl (3×), water (1×), and brine (2×), then dried (Na_2SO_4), filtered, and concentrated under reduced pressure. MPLC (20:1 *n*-hexane/EtOAc) gave spiro ketones **3a** and **3b** (380 mg, 1.82 mmol, 76% from **4**) as an inseparable 3:1 mixture as judged by high-field ^{1}H NMR. The major diastereomer, **3a**, was isolated by fractional crystallization of this 3:1 mixture from *n*-hexane [mp 84–85 °C from *n*-hexane; ^{1}H NMR (360-MHz, $CDCl_3$) δ 1.38 (ddd, J = 4.9, 12.7, 12.7, 12.7, $H_{4\alpha}$), 1.45–2.08 (m, 8 H), 2.17 (m, $H_{5\alpha}$), 2.54 (ddd, J = 5.6, 5.6, 12.7, H_{3a}), 3.72 (br d, J = 11.3, $H_{6'eq}$), 3.94 (ddd, J = 2.7, 11.3, 11.3, $H_{6'ax}$), 4.66 (br s, H_{7a}), 5.9 (br d, J = 10, H_7), 6.12 (m, H_6); IR (CCl_4) 3040, 2980, 2890, 1710, 1180, 1070, 1030 cm^{-1}. Anal. Calcd for $C_{12}H_{16}O_3$: C, 69.21; H, 7.74. Found: C, 69.30; H, 7.76]. A recrystallized sample of **3a** was subjected to single-crystal X-ray diffraction analysis. Compound **3a** crystallizes from *n*-hexane with the monoclinic space group *Pn*. The crystal data at 140 K are as follows: a = 6.481 (5) Å, b = 9.991 (11) Å, c = 8.332 (6) Å; β = 104.11 (6)°; ρ(calcd) = 1.32 g cm^{-3} for Z = 2; 2θ(max) = 55°; 1211 reflections with $F > 6\sigma(|F|)$ used, Mo Kα (graphite (λ = 0.71069 Å), and ω scan, 58.6° min^{-1}; R = 0.039. SHELXTL programs were used on a DGC Eclipse S/230 computer.

Similar oxidation of previously isolated spiro alcohol **8** (151 mg, 0.72 mmol) gave a pure sample of minor spiro ketone **3b** (131 mg, 0.63 mmol, 87.4%) [mp 52–55 °C from *n*-hexene; ^{1}H NMR (500-MHz, $CDCl_3$) δ 1.45–2.05 (m, 9 H), 2.18 (m, $H_{5\alpha}$), 2.77 (ddd, J = 4.5, 4.5, 8.3, H_{3a}), 3.67 (br d, J = 11.5, $H_{6'eq}$), 3.87 (ddd, J = 2.6, 11.5, 11.5, $H_{6'ax}$), 4.85 (br d, J = 8.3, H_{7a}), 5.86 (m, H_6 and H_7); IR ($CHCl_3$) 3040, 3020, 2960, 2895, 1710, 1435, 1005 cm^{-1}; MS(EI), *m/e* (relative intensity) 208 (7), 107 (32), 101 (100), 80 (92); calcd for $C_{12}H_{16}O_3$ 208.1100, found, 208.1106.]. Spiro ketone **3b** was also prepared by oxidation of previously isolated **7** (80%).

Reduction of 3a and 3b to Spiro Alcohols 6 and 8. Lithium triethylborohydride (1 M in THF, 140 μL, 0.14 mmol) was added dropwise to a THF (370 μL) solution of spiro ketone **3a** at −78 °C under N_2. After 1 h at −78 °C and 1 h at 0 °C, the solution was diluted with 10% aqueous NaOH and extracted with CH_2Cl_2 (2×). The combined organic layers were dried (Na_2SO_4), filtered,

(12) Difference NOE experiments on spiro alcohols **5**, **6**, and **8** are also consistent with these experimental results. Thus, while irradiation of C(3a)-H in **6** and **8** caused large NOE's in both C(3)-H and C(7a)-H, similar irradiation in **5** caused a large NOE in C(7a)-H but only a very small NOE in C(3)-H.

(13) Assembled from the following components available from Fischer-Porter Co. (Lab Crest Scientific Division): flanged glass pipe ($^3/_4$ in.), stainless-steel glass coupling, Teflon-brand insert, neoprene gasket, aluminum sealing disk, and nonprene-asbestos insert strip.

(14) This is a partial listing of coupling constants for this proton.

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

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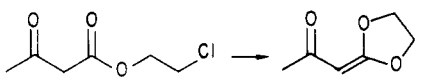
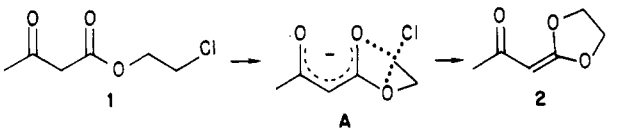
Received February 10, 1984

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

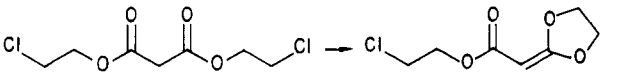


1 **A** **2**

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

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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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