A Facile, General Approach to the Synthesis of Electrophilic Acetone Equivalents

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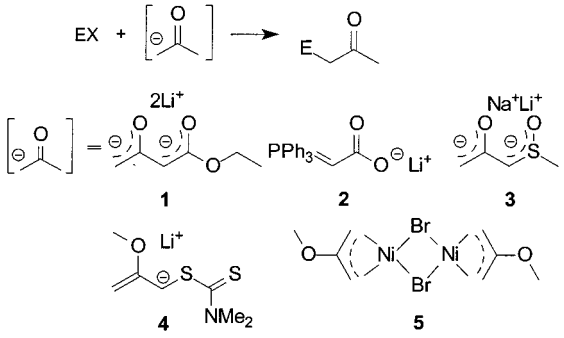
Received January 21, 1998

The facile, high-yielding, yet general synthesis of electrophilic chloroacetone equivalents **11a**−**f** is described. The enol ethers are assembled in three steps starting with trichloride **29** in overall yields of 57−93%. Nucleophilic displacement of the chloromethyl chlorine with a range of organometallic reagents generates dichlorides **30** in yields of 58−99%, which can be dehydrohalogenated with *t*-BuOK/THF in yields of 87−99% to produce enol ethers **31**. Conversion of the allyl chlorides **31** to the corresponding allyl iodides **11** with 72−99% yield completes the synthetic sequence. The entire sequence can be performed in less than 48 h on a >50 mmol scale.

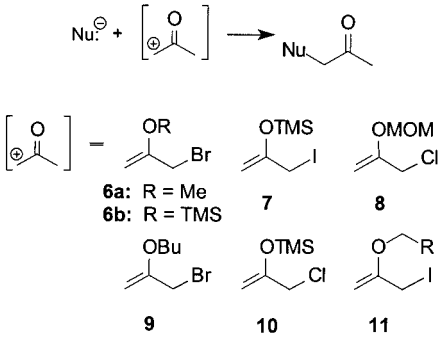
The installation of a three-carbon acetonyl group usually requires alkylation with a haloacetone or more generally a haloacetone synthetic equivalent. Halo ketones are versatile reagents for the synthesis of a wide variety of small carbocycles, α,γ-ketocarbonyl compounds, heterocycles, and their precursors and have been the subject of numerous investigations.[1,2] The parent compounds, chloroacetone and bromoacetone, introduce a three-carbon acetonyl group by nucleophilic substitution at the halogen. Despite the usefulness and well-documented success of these reagents, they are less than ideal. Selective substitution at the halogen center is often variable in the presence of the carbonyl moiety and can result in a range of side reactions, including the generation of intractable polymeric mixtures. Furthermore, both reagents exist as low-boiling liquids that are prone to polymerization and decomposition upon standing under ambient conditions or when exposed to light.

The problems associated with the unprotected carbonyl group in chloro- and bromoacetone have led to the development of numerous reagents for the introduction of an acetonyl group.[3−11] Nucleophilic, electrophilic, and free-radical-based acetonylation reagents are known, and the most common nucleophilic acetonylating reagents have been reviewed (Scheme 1).[4] While nucleophilic acetonylation reagents have proven useful in a variety of applications, the majority of uses of acetone equivalents utilize electrophilic acetonylation reagents.

Scheme 1



Scheme 2



Several electrophilic acetone equivalents have been reported, including **6**−**11** (Scheme 2).[6−11] The classic reagent methoxyallyl bromide **6a** was introduced by Horning[6a] and further developed by Jacobson.[6b] Multiple applications of this reagent include the synthesis of (+)-euphococcine,[12] methylenomycin A,[13] and precursors of ingenol.[14] Unfortunately, **6a** is difficult to prepare, prone to polymerization, and synthesized as a mixture of

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(11) Pyrolysis reactions have been used to synthesize chloroacetone equivalents. See: (a) Gu, X.-P.; Ikeda, I.; Okahara, M. *Bull. Chem. Soc. Jpn.* **1987**, *60*, 397. (b) Blanchard L. *Bull. Soc. Chim. Fr.* **1931**, *49*, 285. (c) Higgins, R. H.; Eaton, Q. L.; Worth, L.; Peterson, M. V. *J. Heterocycl. Chem.* **1987**, *24*, 255. (d) Knapp, S.; Gibson, F. S. *J. Org. Chem.* **1992**, *57*, 4802.

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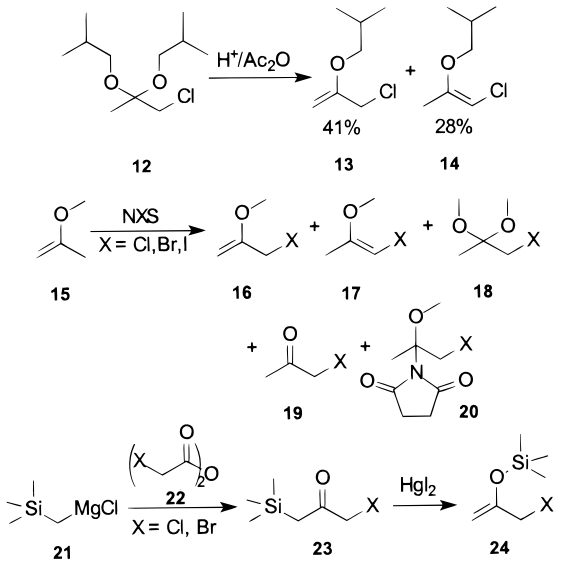
S0022-3263(98)00094-2 CCC: $15.00
Published on Web 05/08/1998

Scheme 3



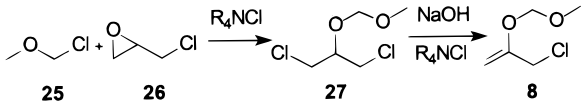
isomers.[6a] A number of other reagents have been developed,[15,16] but they are of very limited scope and synthetic utility. In general, the synthesis of electrophilic chloroacetone equivalents often requires harsh conditions that we found to be capricious, yielding product mixtures that are difficult to purify.[7]

The most often cited methods for the synthesis of electrophilic acetonylation reagents are as follows: (i) elimination of alcohols from chloroacetone ketals,[17] (ii) halogenation of ketone enol ethers at the allylic position,[8,9b,18] (iii) mercury mediated rearrangement of halomethyl ketones,[7,19,20] and (iv) base mediated elimination of hydrogen halogenide from ethers of β,β'-dihalopropanol.[9a,11a,21]

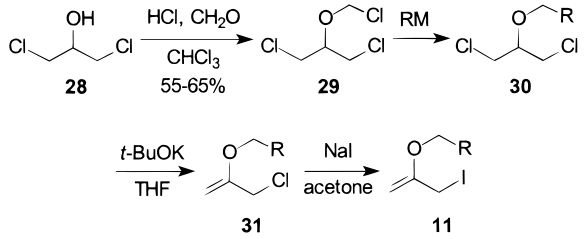
The first three methods generally afford alkoxyallyl halides with low to moderate yields, and the products are often accompanied by their isomers. For example, elimination of isobutanol from ketal **12** yields a 4:3 mixture of enol ethers **13** and **14** (Scheme 3).[17] Halogenation of enol ether **15** with NBS, NCS, or NIS leads to a mixture of five products from which **16** can be isolated by chromatography in yields of 27−54%.[8,18] Sakurai et al. utilized HgI_2 catalysis to synthesize **24** but did not elaborate on the structure of the side products of the reaction. The isolated yields were only 62% (X = Cl) and 55% (X = Br).[7,20]

By contrast, base-mediated elimination of hydrogen halogenide from ethers of β,β'-dihalopropanol can potentially lead to high yields of homogeneous products. In 1987, Gu et al. reported a synthesis of the methoxymethyl ether of chloroacetone enol **8** (Scheme 4).[11a,21] The two-step synthesis starts with the electrophilic attack of

Scheme 4



Scheme 5



methoxymethyl chloride **25** on epichlorohydrin **26** to yield the intermediate dichloroether **27** that yields **8** when treated with aqueous NaOH. Regrettably, this procedure is limited to halides that are more reactive than epichlorohydrin, like chloromethyl ethers,[11a,b,17,22] acyl chlorides,[11a,23] α-chloro esters,[11a,24] and benzyl and allyl chlorides.[25] In addition, the treatment of the analogues of the dichloride **27** with aqueous NaOH proved unsuitable for enol ethers of volatility lower than that of **8**.

We wished to create a range of protected iodides **11** in an expedient manner for the orthogonal protection of methyl ketones. In addition to its generality and efficiency, our strategy had to allow for the synthesis of chloroacetone equivalents that could be deprotected under nonacidic conditions.

Our approach (Scheme 5) starts with the commercially available dichlorohydrin **28** that is converted to the corresponding chloromethyl ether **29** by the action of anhydrous HCl in a suspension of paraformaldehyde.[19] This trichloride preferentially undergoes S_N2 displacement with organolithiums, Grignard reagents, and metal alkoxides at the (chloromethyl)acetal functionality. This is presumably the result of stereoelectronic effects that increases the electrophilicity of this carbon.[26]

The resulting ethers **30** can be dehydrohalogenated with potassium *tert*-butoxide in THF to generate the corresponding enol ethers **31** in essentially quantitative yield as determined by GC−MS and NMR spectral analysis. These chloroenol ethers are then easily converted to the iodides **11** via the Finkelstein procedure (Scheme 5). Since purification of intermediates **30** and **31** is typically not required, the entire sequence from **29** to **11** can be performed in less than 48 h. We found that **30** and **31** can be susceptible to decomposition during the purification process (FCC or vacuum distillation), although analytically pure samples can be isolated. In-

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Table 1. Synthesized Acetone Equivalents

entry	R	RM	**30**[a] (%)	**31**[a] (%)	**11**[a] (%)
a	CH_3O	CH_3ONa	98	87	76
b	$TMS(CH_2)_2O$	$TMS(CH_2)_2OLi$	>99	>99	93
c	$CH_3(CH_2)_2$	$CH_3(CH_2)_2MgCl$	98	89	83
d	Ph	PhMgBr	97	>99	83
e	p-$CH_3OC_6H_4$	p-$CH_3OC_6H_4Li$	>99	>99	72
f	$TMSCH_2$	$TMSCH_2MgCl$	58	98	>99

[a] Yields reported are averages from a minimum of three independent runs.

termediates **30** and **31** in impure form were found to be stable for weeks at −20 °C.

The purity of trichloride **29** is of paramount importance.[27] This material has reasonable shelf stability at −20 °C (stable for several months) but decomposes at room temperature over the course of several days to generate HCl and paraformaldehyde. Once prepared, the chloromethylacetal moiety can be reacted with a range of organometallic reagents.[26] In general, we observe that Grignard reagents tend to result in higher regioselectivity and in better overall yields of the dichloro ethers. The Grignard reaction products **30** are also easier to purify than those arising from the corresponding organolithiums. The reactions of **29** with propylmagnesium chloride and [(trimethylsilyl)methyl]magnesium chloride proved somewhat problematic. The latter Grignard gave variable yields with significant amounts of **29** in the crude material. In all cases, the crude chloro enol ethers **31** were also of sufficient purity to permit their direct conversion to the corresponding iodides. The iodo enol ethers **11** are most easily purified via flash column chromatography. The chloro enol ethers **31** are stable for extended periods of time at −20 °C, while the iodo enol ethers **11** must be stored at −78 °C if not used within a few days.

This methodology readily affords a variety of enol ether acetone equivalents with a range of functionality in excellent overall yields. The broad range of functionality available allows for the synthesis of acetone equivalents that can be deprotected under nonacidic conditions, e.g., **11b** and **11f** (Table 1). Classical deprotections of **6**−**10** after alkylation involve the use of aqueous acid to promote enol ether hydrolysis. To demonstrate the deprotection methods available to **11a**−**f**, we alkylated diethyl methylmalonate **32** with each of these iodides (Scheme 6). In principle, the chloro enol and iodo enol ethers can be used as alkylating agents, although we found that in most cases the iodo enol ethers **11** resulted in better yields (Table 2). The alkylation yields with the iodo enol ethers were excellent. Clean deprotection of enol ethers **33a**,**c**,**d** was accomplished using a 1% solution of aqueous oxalic acid in 1,4-dioxane. The action of ceric ammonium nitrate in 9:1 CH_3CN/H_2O cleanly deprotected the MPM enol ether **33e**, while cesium fluoride in DMF effected the conversion of **33b** and **33f** to **34**. These latter two deprotections did not occur cleanly and required a single chromatography step for purification. Attempts to convert **33b** to **34** using TBAF failed. We have found that the SEM enol ether is unusually stable and now use **11b** as our equivalent of choice.

We attempted to synthesize an acetone equivalent with a protecting group amenable to photochemical deprotection, such as **11g** or **11h** (Scheme 7). Although the formation of the *o*-nitrophenyllithium **35** has been reported, its reaction with **29** was capricious and always produced complex mixtures in which nitroso **36** was the most abundant component. The reaction of sodium alkoxide **37** appeared to proceed toward a single product, which GC−MS trace analysis showed to be **30h**. However, even upon the most careful workup, **30h** could not be isolated, and instead, the reaction yielded only an intractable red resin. The attempts to convert in situ **30h** to **11h** produced a complex mixture of products from which none of the desired enol ether could be isolated.

Scheme 6

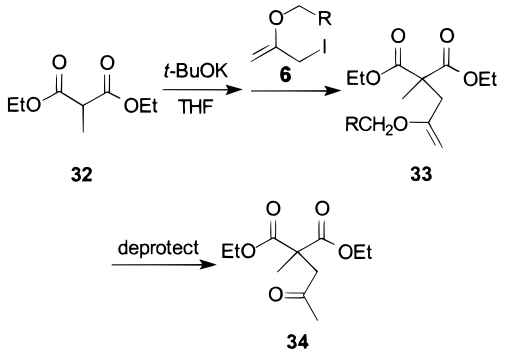
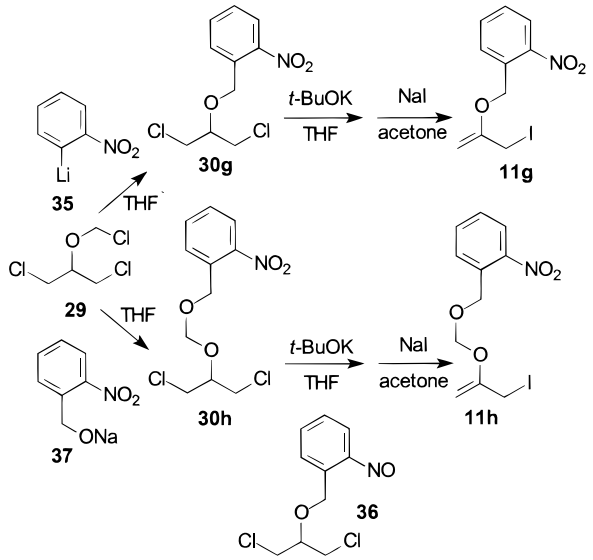


Table 2. Acetonylation Reactions and the Deprotection to Methyl Ketone 34

entry	R	**33**[a] (%)	deprotection method	**34** (%)
a	CH_3O	87	H^+	90[a]
b	$TMS(CH_2)_2O$	89	F^-	90
c	$CH_3(CH_2)_2$	87[c]	H^+	96
d	Ph	91	H^+	98[a]
e	p-$CH_3OC_6H_4$	93	CAN	96[a]
f	$TMSCH_2$	90	F^-	92

[a] Yields reported are averages from a minimum of three independent runs.

Scheme 7



Conclusion

Large amounts (>50 mmol) of chloroacetone equivalent **11** can be easily synthesized in less than 48 h.[29] In

(27) We typically fractionally distill **25** under reduced pressure at least three times. This is the rate-limiting step in the procedure. Once purified, **25** is stable for months at −20 °C and can be used without further purification.

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principle, any nucleophile capable of displacing the (chloromethyl)acetal moiety can be employed in the conversion of **29** → **30** and ultimately derivatives of **11**. Ready access to these iodides implies that a metal−halogen exchange reaction can convert **11** into a nucleophilic chloroacetone equivalent. The scope of this reaction is presently under investigation.

Experimental Section

General Methods. All reagents were purified before use. Tetrahydrofuran (THF, from Burdick-Jackson) and Et_2O (Mallinckrodt) were freshly distilled from benzophenone ketyl prior to use. *n*-BuLi in hexanes was purchased from Aldrich and titrated prior to use. Reagent-grade acetone was purchased from Mallinckrodt. Solutions of potassium *tert*-butoxide in THF were made from solid potassium *tert*-butoxide (Aldrich) dissolved in freshly distilled THF and titrated before use. Diethyl methylmalonate **32** was purchased from Aldrich. Flash column chromatography following the method of Still employed EM Science silica gel 60 (230−400 mesh). Analytical thin-layer chromatography was performed with 0.25 mm coated commercial silica gel plates (E. Merck, DC-fertigplatten Kieselgel F254 or the corresponding Altech plate). GC traces were performed on a HP OV-1 50 m capillary column. The temperature was set to 100 °C for 3 min, and then a 15 °C/min gradient was applied until 250 °C, after which the temperature was stabilized at 250 °C until the end of the run. Assignments of NMR absorptions were based on COSY, APT, and HMQC spectra.

1,3-Dichloro-2-(chloromethoxy)propane (29). Using a modified procedure of Mamedov et al.,[26] a stirred solution of dichlorohydrin (**28**, 194.3 g, 1.51 mol, Aldrich) and paraformaldehyde (102.8 g, 3.25 mol) in $CHCl_3$ (3.6 L) was cooled to 0 °C, and a stream of anhydrous HCl was passed through the mixture until all of **28** was consumed (typically 12−24 h). The solution was filtered through Celite 545, and any remaining aqueous phase was separated. The organic phase was dried (Na_2SO_4) and concentrated in vacuo to yield a light oil that was distilled under reduced pressure (1.5 mmHg). The 66−80 °C fraction was isolated (232.1 g) and was triply distilled through a 20 in. vacuum-jacketed column filled with glass helices to yield 141−162 g (52−65%) of a clear oil boiling at 70 °C: ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.75 (A in A_2B_2X, J_{AB} = −11.7 Hz, J_{AX} = 5.8 Hz, J_{BX} = 4.9 Hz, 2H, ClCH_2CH), 3.76 (B in A_2B_2X2H, (ClCH_2)$_2$CH), 4.15 (X in A_2B_2X, 2H, (ClCH_2)$_2$C*H*O), 4.76 (s, 2H, OCH_2Cl); ^{13}C NMR (100 MHz, $CDCl_3$) δ 42.97 ((ClCH_2)$_2$CH), 78.46 ((ClCH_2)$_2$*C*HO), 81.30 (O*C*H$_2$Cl). This compound was essentially pure by GC. Despite repeated attempts, no molecular ion for this compound could be observed.

1,3-Dichloro-2-(methoxymethoxy)propane (30a). A solution of **29** (14.1 g 79.4 mmol) in THF (100 mL) was cooled to −78 °C under N_2. To this was added, dropwise via cannula, 150 mL of a solution of Na^0 (3.66 g, 159 mmol) dissolved in anhydrous methanol. The stirred reaction was allowed to slowly warm to room temperature over 12 h. Water (400 mL) was slowly added to the mixture, and the solution was extracted with Et_2O (1 × 300 mL, 3 × 100 mL). The combined organic phases were dried ($MgSO_4$) and concentrated in vacuo to yield 13.5 g (78 mmol, 98.2% yield) of clear oil **30a**. This material was of suitable purity for use in the next step, although it could be further purified to >99% purity (as judged by GC) via vacuum distillation through a 6 in. Vigreux column (98−103 °C, 34 mmHg): ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.43 (s, 3H, OCH_3), 3.72 (A in A_2B_2X, J_{AB} = −11.5 Hz, J_{AX} = 5.2 Hz, J_{BX} = 5.1 Hz, 2H, ClCH_2), 3.73 (B in A_2B_2X, 2H, ClCH_2), 3.99 (X in A_2B_2X, 2H, (ClCH_2)$_2$C*H*O), 4.76 (s, 2H, OCH_2O); ^{13}C NMR (100 MHz, $CDCl_3$) δ 3.97 (Cl*C*H$_2$), 56.20 (O*C*H$_3$), 76.87 ((ClCH_2)$_2$*C*HO), 96.74 (OCH_2O); exact mass calcd for $C_5H_{10}Cl_2O_2$ 172.0058, found 170.9979 (M − 1).

1,3-Dichloro-2-[[2-(trimethylsilyl)ethoxy]methoxy]-propane (30b). A solution of 2-(trimethylsilyl)ethanol (7.30, 61.7 mmol) in anhydrous THF (150 mL) was cooled to −13 °C under N_2. To this was added 1.44 M *n*-BuLi/hexanes (52 mL, 61.7 mmol, Aldrich). The mixture stirred for 10 min and was followed by the dropwise addition of **29** (11 g, 61.7 mmol) via cannula. The stirred reaction warmed to room temperature over 12 h. Water (400 mL) was slowly added to the mixture, and the solution was extracted with Et_2O (1 × 300 mL, 3 × 100 mL). The organic phases were combined, dried ($MgSO_4$), and concentrated in vacuo to yield 16.1 g (61.7 mmol, 100.7% yield) of clear oil **30b**. This material was of suitable purity for use in the next step, although it could be further purified to >99% purity (as judged by GC) via vacuum distillation through a 6 in. Vigreux column (83−87 °C, 0.05 mmHg): ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.01 (s, 9H, Si(CH_3)$_3$), 0.93 (A in AA′XX′, J_{AX} = 10.2 Hz, $J_{A'X}$ = 6.8 Hz, $J_{AA'}$ = −2.9 Hz, $J_{XX'}$ = −2.5 Hz, 2H, CH_2Si(CH$_3$)$_3$), 3.68 (X in AA′XX′, 2H, OCH_2CH$_2$Si(CH$_3$)$_3$), 3.70 (A in A_2B_2X, J_{AB} = −11.5 Hz, J_{AX} = 5.5 Hz, J_{BX} = 4.8 Hz, 2H, ClCH_2), 3.72 (B in A_2B_2X, 2H, ClCH_2), 3.99 (X in A_2B_2X, 2H, (ClCH$_2$)$_2$C*H*O), 4.78 (s, 2H, OCH_2O); ^{13}C NMR (100 MHz, $CDCl_3$) δ −1.27 (Si(*C*H$_3$)$_3$), 18.25 (*C*H$_2$Si(CH$_3$)$_3$), 43.95 (Cl*C*H$_2$), 65.99 (O*C*H$_2$CH$_2$Si(CH$_3$)$_3$), 76.67 ((ClCH$_2$)$_2$*C*HO), 94.85 (O*C*H$_2$O); exact mass calcd for $C_9H_{20}Cl_2O_2Si$ 258.0610, found 257.0532 (M − 1).

1,3-Dichloro-2-*n*-butoxypropane (30c). A solution of **29** (11.1 g, 62.6 mmol) in Et_2O (110 mL) was cooled to −13 °C under N_2. To this was added, dropwise via cannula, 2 M propylmagnesium chloride/Et_2O (32 mL, 62.5 mmol, Aldrich). The stirred reaction warmed to room temperature over 12 h and was subsequently concentrated in vacuo. The concentrate was cooled in an ice bath, and H_2O (400 mL) was slowly added to the mixture over 1 h (CAUTION: exothermic). The solution was extracted with Et_2O (1 × 300 mL, 3 × 100 mL), and the organic phases were combined, dried ($MgSO_4$), and concentrated in vacuo to yield 11.3 g (61.7 mmol, 98.6% yield) of clear oil **30c**. This material was of suitable purity for use in the next step, although it could be further purified to >99% purity (as judged by GC) via vacuum distillation through a 6 in. Vigreux column (39−41 °C, 0.05 mmHg): ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.93 (t, J = 7.4 Hz, 3H, OCH$_2$CH$_2$CH$_2$CH_3), 1.40 (tq, J = 7.6 Hz, 7.4 Hz, 2H, O−CH$_2$CH$_2$*C*H$_2$CH$_3$), 1.58 (tt, J = 7.6, 6.7 Hz, 2H, OCH$_2$CH_2CH$_2$CH$_3$), 3.72 (t, J = 6.7 Hz, 2H, OCH_2CH$_2$CH$_2$CH$_3$), 3.62−3.77 (A_2B_2C, 5H, ClCH_2, (ClCH_2)$_2$C*H*O); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.66 (OCH$_2$CH$_2$CH$_2$*C*H$_3$), 19.02 (OCH$_2$CH$_2$*C*H$_2$CH$_3$), 31.71 (OCH$_2$*C*H$_2$CH$_2$CH$_3$), 43.06 (Cl*C*H$_2$), 70.26 (O*C*H$_2$CH$_2$CH$_2$CH$_3$), 78.57 ((ClCH$_2$)$_2$*C*HO); exact mass calcd for $C_7H_{14}Cl_2O$ 184.0421, found 183.0343 (M − 1).

1,3-Dichloro-2-(phenylmethoxy)propane (30d). A solution of **29** (12.4 g 70.2 mmol) in Et_2O (150 mL) was cooled to −13 °C under N_2. To this was added, dropwise via cannula, 1 M phenylmagnesium bromide/THF (70 mL, 70.2 mmol, Aldrich). The stirred reaction was warmed to room temperature over 12 h and was subsequently concentrated in vacuo. The concentrate was cooled in an ice bath, and H_2O (100 mL) was slowly added to the mixture over 1 h (CAUTION: exothermic). The solution was extracted with Et_2O (1 × 300 mL, 3 × 100 mL), and the combined organic phases were dried ($MgSO_4$) and concentrated in vacuo to yield 15 g (68.4 mmol, 97.4% yield) of clear oil **30d**. This material was of suitable purity for use in the next step, although it could be further purified to >99% purity (as judged by GC) via vacuum distillation through a 6 in. Vigreux column (99−101 °C, 0.05 mmHg): ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.67 (A in A_2B_2X, J_{AB} = −11.6 Hz, J_{AX} = 5.3 Hz, J_{BX} = 5.2 Hz, 2H, ClCH_2), 3.70 (B in A_2B_2X, 2H, ClCH_2), 3.82 (X in A_2B_2X, 2H, (ClCH$_2$)$_2$C*H*O), 4.66 (s, 2H, OCH_2Ph), 7.27−7.37 (AA′BB′C, 5H, C$_6H_5$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 43.08 (Cl*C*H$_2$), 72.30 (O*C*H$_2$Ph), 77.73 ((ClH$_2$C)$_2$*C*HO), 127.79 (*o*-*C*$_6$H$_5$CH$_2$), 128.02 (*p*-*C*$_6$H$_5$CH$_2$), 128.45 (*m*-*C*$_6$H$_5$CH$_2$), 137.12 (*ipso*-*C*$_6$H$_5$CH$_2$); exact mass calcd for $C_{10}H_{12}Cl_2O$ 218.0265, found 218.0265.

(29) The report on 0.5 mol scale synthesis of **6** is being prepared for publication. Chong, P. C.; Janicki, S. Z.; Petillo, P. A. *Org. Synth.* Manuscript in preparation.

1,3-Dichloro-2-[(*p*-methoxyphenyl)methoxy]propane (30e). A solution of *p*-methoxybromobenzene (6.78 g, 36.2 mmol, Aldrich) in Et_2O (100 mL) was cooled to −78 °C under N_2. To this was added, dropwise via cannula, 1.48 M *tert*-butyllithium/heptane (50 mL, 72.5 mmol, FMC). The mixture was stirred for 30 min and then warmed to −13 °C, stirred for an additional 30 min, and recooled to −78 °C. This solution was then added dropwise via cannula to a −78 °C solution of **29** (6.43 g, 36.2 mmol) in Et_2O (100 mL). The stirred reaction mixture was warmed to room temperature over 12 h and was subsequently concentrated in vacuo. The concentrate was cooled in an ice bath, and H_2O (100 mL) was slowly added to the mixture over 1 h (CAUTION: exothermic). The solution was extracted with Et_2O (1 × 300 mL, 3 × 100 mL), and the combined organic phases were dried ($MgSO_4$) and concentrated in vacuo to yield 9 g (36.1 mmol, 99.9% yield) of clear oil **30e**. This material was of suitable purity for use in the next step, although it could be further purified to >99% purity (as judged by GC) via vacuum distillation through a 6 in. Vigreux column (99−101 °C, 0.05 mmHg): ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.63 (A in A_2B_2X, $J_{AB} = -11.5$ Hz, $J_{AX} = 5.2$ Hz, $J_{BX} = 5.0$ Hz, 2H, ClCH_2), 3.66 (B in A_2B_2X, 2H, ClCH_2), 3.77 (X in A_2B_2X, 2H, $(ClCH_2)_2CHO$), 3.78 (s, 3H, OCH_3), 4.57 (s, 2H, OCH_2Ar), 6.88 (A in AA′BB′, $J_{AB} = 8.5$ Hz, $J_{AA'} = 2.7$ Hz, $J_{AB'} = 0.5$ Hz, 2H, *o*-$CH_3OC_6H_4CH_2$), 7.28 (B in AA′BB′, 2H, *m*-$CH_3OC_6H_4CH_2$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 43.37 (ClCH_2), 55.34 (OCH_3), 72.15 (OCH_2Ar), 77.53 ($(ClCH_2)_2CHO$), 114.03 (*o*-$CH_3OC_6H_4CH_2$), 129.41 (*ipso*-$CH_3OC_6H_4$), 129.67 (*m*-$CH_3OC_6H_4CH_2$), 159.63 (*ipso*-$CH_2C_6H_4$); exact mass calcd for $C_{11}H_{14}Cl_2O_2$ 248.0371, found 248.0370.

1,3-Dichloro-2-[2-(trimethylsilyl)ethoxy]propane (30f). A solution of **29** (17.6 g, 99 mmol) in Et_2O (250 mL) was cooled to −13 °C under N_2. To this was added, dropwise via cannula, 1 M [(trimethylsilyl)methyl]magnesium chloride/Et_2O (99 mL, 99 mmol, Aldrich). The stirred reaction was warmed to room temperature over 12 h and subsequently concentrated in vacuo. The concentrate was cooled in an ice bath, and H_2O (400 mL) was slowly added to the mixture over 1 h (CAUTION: exothermic). The solution was extracted with Et_2O (1 × 300 mL, 3 × 100 mL), and the organic phases were combined, dried ($MgSO_4$), and concentrated in vacuo to yield a clear oil that was fractionally distilled (93−98 °C, 2 mm Hg) to yield 13.1 g (57 mmol, 57.7% yield) of **30f**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.02 (s, 9H, Si(CH_3)$_3$), 0.96 (A in AA′XX′, $J_{AX} = 10.0$ Hz, $J_{A'X} = 6.3$ Hz, $J_{AA'} = -7.6$ Hz, $J_{XX'} = -3.9$ Hz, 2H, CH_2Si$(CH_3)_3$), 3.66 (X in AA′XX′, 2H, OCH_2CH_2Si$(CH_3)_3$), 3.61−3.76 (A_2B_2C, 5H, ClCH_2, $(ClCH_2)_2CHO$); ^{13}C NMR (100 MHz, $CDCl_3$) δ −1.18 (Si(CH_3)$_3$), 18.60 (CH_2Si$(CH_3)_3$), 43.41 (ClCH_2), 68.13 (OCH_2CH_2Si$(CH_3)_3$), 78.34 ($(ClCH_2)_2CHO$). Despite repeated attempts, no molecular ion for this compound could be observed.

General Procedure for Dehydrochlorination of 30. To a −13 °C solution of **30** (60 mmol) in anhydrous THF (100 mL) under N_2 was added via syringe 1.48 M potassium *tert*-butoxide/THF (42 mL, 63 mmol, 1.05 equiv). The stirred solution was warmed to room temperature over 12 h and then partitioned between H_2O (50 mL) and Et_2O (300 mL). The organic phase was dried ($MgSO_4$) and concentrated to yield **31** as a clear oil.

1-Chloro-2-(methoxymethoxy)-2-propene (31a): yield 87.4%. This material was of suitable purity for use in the next step, although it could be further purified to >99% purity (as judged by GC) via vacuum distillation through a 6 in. Vigreux column (65−68 °C, 35 mmHg): ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.45 (s, 3H, OCH_3), 3.99 (s, 2H, ClCH_2), 4.41 (A in ABq, J = 2.3 Hz, 1H, H_2C=C), 4.42 (B in ABq, 1H, H_2C=C), 5.02 (s, 2H, OCH_2O); ^{13}C NMR (100 MHz, $CDCl_3$) δ 56.41 (OCH_3), 45.24 (ClCH_2), 89.59 (H_2C=C), 94.10 (OCH_2O), 155.98 (H_2C=C(O)CH_2Cl); exact mass calcd for $C_5H_9ClO_2$ 136.0291, found 136.0291.

1-Chloro-2-[[2-(trimethylsilyl)ethoxy]methoxy]-2-propene (31b): yield 99.3%. This material was of suitable purity for use in the next step, although it could be further purified to >99% purity (as judged by GC) via vacuum distillation through a 6 in. Vigreux column (47−49 °C, 0.05 mmHg): ^{1}H NMR (400 MHz, $CDCl_3$) δ −0.03 (Si(CH_3)$_3$), 0.94 (A in AA′XX′, $J_{AX} = 9.7$ $J_{A'X} = 7.0$ $J_{AA'} = -3.2$ $J_{XX'} = -2.1$, 2H, CH_2Si$(CH_3)_3$), 3.70 (X in AA′XX′, 2H, OCH_2CH_2Si$(CH_3)_3$), 3.96 (s, 2H, ClCH_2), 4.37 (A in ABq, J = 2.4 Hz, 1H, (*Z*)-H_2C=C), 4.39 (B in ABq, 1H, *E*-H_2C=C), 5.04 (s, 2H, OCH_2O); ^{13}C NMR (100 MHz, $CDCl_3$) δ −1.57 (Si(CH_3)$_3$), 17.84 (CH_2Si$(CH_3)_3$), 44.97 (ClCH_2), 66.27 (OCH_2CH_2Si$(CH_3)_3$), 89.07 (H_2C=C), 92.24 (OCH_2O), 155.69 (H_2C=C(O)CH_2Cl). Despite repeated attempts, no molecular ion for this compound could be observed.

1-Chloro-2-*n*-butoxy-2-propene (31c): yield 88.9%. This material was of suitable purity for use in the next step: ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.95 (t, J = 7.4 Hz, 3H, OCH_2CH_2-CH_2CH_3), 1.44 (tq, J = 7.6, 7.4 Hz, 2H, $OCH_2CH_2CH_2CH_3$), 1.70 (tt, J = 7.6, 6.3 Hz, 2H, $OCH_2CH_2CH_2CH_3$), 3.72 (t, J = 6.3 Hz, 2H, $OCH_2CH_2CH_2CH_3$), 3.97 (s, 2H, ClCH_2), 4.08 (d, J = 2.3 Hz, 1H, (*Z*)-H_2C=C), 4.25 (d, J = 2.3 Hz, 1H, (*E*)-H_2C=C); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.67 (OCH_2CH_2-CH_2CH_3), 19.12 ($OCH_2CH_2CH_2CH_3$), 30.67 ($OCH_2CH_2CH_2CH_3$), 44.96 (ClCH_2), 67.70 ($OCH_2CH_2CH_2CH_3$), 85.19 (H_2C=C), 158.14 (H_2C=C(O)CH_2Cl); exact mass calcd for C_5H_9ClO 148.0655, found 148.0657.

1-Chloro-2-(phenylmethoxy)-2-propene (31d): yield 99.8%. This material was of suitable purity for use in the next step, although it could be further purified to >99% purity (as judged by GC) via vacuum distillation through a 6 in. Vigreux column (72−73 °C, 0.02 mmHg): ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.01 (s, 2H, ClCH_2), 4.19 (d, J = 2.7 Hz, 1H, (*Z*)-H_2C=C), 4.34 (d, J = 2.7 Hz, 1H, (*E*)-H_2C=C), 4.80 (s, 2H, OCH_2Ph), 7.27−7.38 (AA′BB′C, 5H, C_6H_5); ^{13}C NMR (100 MHz, $CDCl_3$) δ 45.09 (ClCH_2), 70.14 (OCH_2Ph), 86.78 (H_2C=C), 127.50 (*o*-$C_6H_5CH_2$), 128.11 (*p*-$C_6H_5CH_2$), 128.66 (*m*-$C_6H_5CH_2$), 136.63 (*ipso*-$C_6H_5CH_2$), 158.09 (H_2C=C(O)CH_2Cl); exact mass calcd for $C_{10}H_{11}ClO$ 182.0498, found 182.0498.

1-Chloro-2-[(*p*-methoxyphenyl)methoxy]-2-propene (31e): yield 99.1%. This material was of suitable purity for use in the next step, although it could be further purified to >99% purity (as judged by GC) via vacuum distillation through a 6 in. Vigreux column (111−113 °C, 0.03 mmHg): ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.78 (s, 3H, OCH_3), 4.00 (s, 2H, ClCH_2), 4.20 (d, J = 2.5 Hz, 1H, (*Z*)-H_2C=C), 4.33 (d, J = 2.7 Hz, 1H, (*E*)-H_2C=C), 4.73 (s, 2H, OCH_2Ar), 6.89 (A in AA′BB′, J_{AB} = 8.7, $J_{AA'} = 2.5$, $J_{AB'} = 0.7$, 2H, *o*-$CH_3OC_6H_4CH_2$), 7.30 (B in AA′BB′, 2H, *m*-$CH_3OC_6H_4CH_2$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 45.13 (ClCH_2), 55.39 (OCH_3), 69.93 (OCH_2Ar), 86.57 (H_2C=C), 114.04 (*o*-$CH_3OC_6H_4CH_2$), 128.63 (*ipso*-$CH_3OC_6H_4$), 129.26 (*m*-$CH_3OC_6H_4CH_2$), 158.10 (*ipso*-$CH_2C_6H_4$), 159.56 (H_2C=C(O)-CH_2Cl); exact mass calcd for $C_{11}H_{13}ClO_2$ 212.0604, found 212.0603.

1-Chloro-2-[2-(trimethylsilyl)ethoxy]-2-propene (31f): yield 97.9%. This material was of suitable purity for use in the next step, although it could be further purified to >99% purity (as judged by GC) via vacuum distillation through a 6 in. Vigreux column (40−43 °C, 0.025 mmHg): ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.05 (s, 9H, Si(CH_3)$_3$), 1.06 (t, J = 8.0 Hz, 2H, CH_2Si$(CH_3)_3$), 3.82 (t, J = 8.0 Hz, 2H, OCH_2CH_2Si$(CH_3)_3$), 4.07 (d, J = 2.3 Hz, (*Z*)-H_2C=C), 4.24 (d, J = 2.3 Hz, (*E*)-H_2C=C); ^{13}C NMR (100 MHz, $CDCl_3$) δ −1.18 (Si(CH_3)$_3$), 17.30 (CH_2Si$(CH_3)_3$), 45.33 (ClCH_2), 65.81 (OCH_2CH_2Si$(CH_3)_3$), 85.49 (H_2C=C), 158.37 (H_2C=C(O)CH_2Cl). Despite repeated attempts, no molecular ion for this compound could be observed.

General Procedure for the Synthesis of Iodides 11. To a solution of **31** (50 mmol) in acetone (50 mL) was added a solution of NaI (37.8 g, 250 mmol) in acetone (200 mL). The mixture was stirred overnight at room temperature under N_2 and then partitioned between CH_2Cl_2 (700 mL) and H_2O (200 mL). The aqueous phase was extracted with CH_2Cl_2 (3 × 100 mL), and the combined organic phases were dried ($MgSO_4$) and concentrated in vacuo to yield essentially pure **11**.

1-Iodo-2-(methoxymethoxy)-2-propene (11a): yield 76.4% of clear low boiling oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.48 (s, 3H, OCH_3), 3.83 (s, 2H, ICH_2), 4.34 (d, J = 2.4 Hz, 1H, H_2C=C), 4.47 (d, J = 2.4 Hz, 1H, H_2C=C), 5.01 (s, 2H, OCH_2O); ^{13}C NMR (100 MHz, $CDCl_3$) δ 4.34 (ICH_2), 56.70 (OCH_3), 87.73 (H_2C=C), 93.98 (OCH_2O), 157.08 (H_2C=

C(O)CH_2I); exact mass calcd for $C_5H_9ClO_2$ 227.9647, found 227.9647.

1-Iodo-2-[[2-(trimethylsilyl)ethoxy]methoxy]-2-propene (11b): yield 93.3%. This product was purified via flash column chromatography (SiO_2, petroleum ether/CH_2Cl_2 7:1) to give pure **11b** with 93.1% yield as a clear oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.00 (s, 9H, Si(CH_3)$_3$), 0.95 (A in AA′XX′, J_{AX} = 9.8 Hz, $J_{A'X}$ = 7.0 Hz, $J_{AA'}$ = −2.9 Hz, $J_{XX'}$ = −2.3, 2H, CH_2Si(CH_3)$_3$), 3.74 (X in AA′XX′, 2H, OCH_2CH_2Si(CH_3)$_3$), 3.81 (d, J = 0.7 Hz, 2H, ICH_2), 4.32 (dt, J = 2.4, 0.7 Hz, 1H, (*Z*)-H_2C=C), 4.44 (d, J = 2.4 Hz, 1H, (*E*)-H_2C=C), 5.04 (s, 2H, OCH_2O); ^{13}C NMR (100 MHz, $CDCl_3$) δ −1.49 (Si(CH_3)$_3$), 4.22 (ICH_2), 17.88 (CH_2Si(CH_3)$_3$), 66.46 (OCH_2CH_2Si(CH_3)$_3$), 87.24 (H_2C=C), 92.08 (OCH_2O), 155.69 (H_2C=*C*(O)CH_2I); exact mass calcd for $C_9H_{19}IO_2Si$ 314.0199, found 313.01367 (M − 1).

1-Iodo-2-*n*-butoxy-2-propene (11c). The crude product was purified by flash column chromatography (SiO_2, hexane/Et_2O 20:1) to give pure **11c** with 83.3% yield as a clear oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.96 (t, J = 7.5 Hz, 3H, OCH_2CH_2-CH_2CH_3), 1.47 (tq, J = 7.5, 7.3 Hz, 2H, OCH_2CH_2CH_2CH$_3$), 1.69 (tt, J = 7.3, 6.4 Hz, 2H, OCH_2CH_2CH$_2$CH$_3$), 3.72 (t, J = 6.4 Hz, 2H, OCH_2CH$_2$CH$_2$CH$_3$), 3.81 (d, J = 0.8 Hz, 2H, ClCH_2), 4.01 (dt, J = 2.4, 0.8 Hz, 1H, (*Z*)-H_2C=C), 4.29 (d, J = 2.4 Hz, 1H, (*E*)-H_2C=C); ^{13}C NMR (100 MHz, $CDCl_3$) δ 4.57 (ICH_2), 14.05 (OCH$_2$CH$_2$CH$_2$CH_3), 19.57 (OCH$_2$CH$_2$CH_2CH$_3$), 31.03 (OCH$_2$CH_2CH$_2$CH$_3$), 68.02 (OCH_2CH$_2$CH$_2$CH$_3$), 83.84 (H_2C=C), 159.52 (H_2C=*C*(O)CH_2I); exact mass calcd for $C_7H_{13}IO$ 240.0011, found 240.0010.

1-Iodo-2-(phenylmethoxy)-2-propene (11d). The crude product was purified by flash column chromatography (SiO_2, petroleum ether/CH_2Cl_2 10:1) to give pure **11d** in 83.3% yield as a clear oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.85 (d, J = 0.8 Hz, 2H, ICH_2), 4.11 (dt, J = 2.7 Hz, 0.8 Hz 1H, (*Z*)-H_2C=C), 4.38 (d, J = 2.7 Hz, 1H, (*E*)-H_2C=C), 4.80 (s, 2H, OCH_2Ph), 7.27−7.43 (AA′BB′C, 5H, C_6H_5); ^{13}C NMR (100 MHz, $CDCl_3$) δ 4.21 (ICH_2), 70.17 (OCH_2Ph), 85.18 (H_2C=C), 127.49 (*o*-$C_6H_5CH_2$), 128.09 (*p*-$C_6H_5CH_2$), 128.65 (*m*-$C_6H_5CH_2$), 136.74 (*ipso*-$C_6H_5CH_2$), 159.06 (H_2C=*C*(O)CH_2I); exact mass calcd for $C_{10}H_{11}IO$ 273.9855, found 274.9927 (M + 1).

1-Iodo-2-[(*p*-methoxyphenyl)methoxy]-2-propene (11e). The crude product was purified by flash column chromatography (SiO_2, hexane/CH_2Cl_2 10:1) to give pure **11e** with 72.2% yield as a clear oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.80 (s, 3H, OCH_3), 3.85 (d, J = 0.8 Hz, 2H, ICH_2), 4.13 (dt, J = 2.5, 0.8 Hz, 1H, (*Z*)-H_2C=C), 4.38 (d, J = 2.5 Hz, 1H, (*E*)-H_2C=C), 4.74 (s, 2H, OCH_2Ar), 6.90 (A in AA′BB′, J_{AB} = 8.3 Hz, $J_{AA'}$ = 2.3 Hz, $J_{AB'}$ = 0.6, 2H, *o*-$CH_3OC_6H_4CH_2$), 7.30 (B in AA′BB′, 2H, *m*-$CH_3OC_6H_4CH_2$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 4.38 (ICH_2), 55.47 (OCH_3), 70.02 (OCH_2Ar), 85.01 (H_2C=C), 114.07 (*o*-$CH_3OC_6H_4CH_2$), 128.80 (*ipso*-$CH_3OC_6H_4$), 129.25 (*m*-CH_3-$OC_6H_4CH_2$), 159.16 (*ipso*-$CH_2C_6H_4$), 159.56 (H_2C=*C*(O)CH_2I); exact mass calcd for $C_{11}H_{13}IO_2$ 303.9960, found 305.0033 (M + 1).

1-Iodo-2-[2-(trimethylsilyl)ethoxy]-2-propene (11f): yield 102.8% of a light yellow oil of low-boiling **11f**. This material was not purified, as the only contaminant observable by NMR was a minor amount of solvent, which did not affect the reactivity of the substrate: ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.06 (s, 9H, Si(CH_3)$_3$), 1.06 (A in AA′XX′, J_{AX} = 8.8 Hz, $J_{A'X}$ = 7.2 Hz, $J_{AA'}$ = −2.8 Hz, $J_{XX'}$ = −2.5 Hz, 2H, CH_2Si(CH_3)$_3$), 3.79 (d, J = 0.8 Hz, 2H, ICH_2), 3.82 (X in AA′XX′, 2H, OCH_2-CH_2Si(CH_3)$_3$), 4.07 (d, J = 2.3 Hz, (*Z*)-H_2C=C), 4.24 (d, J = 2.3 Hz, (*E*)-H_2C=C); ^{13}C NMR (100 MHz, $CDCl_3$) δ −1.06 (Si(CH_3)$_3$), 4.57 (ICH_2), 17.27 (CH_2Si(CH_3)$_3$), 65.85 (OCH_2-CH_2Si(CH_3)$_3$), 83.92 (H_2C=C), 159.43 (H_2C=*C*(O)CH_2I); exact mass calcd for $C_8H_{18}IOSi$ 284.0093, found 282.9987 (M − 1).

General Procedure for Acetonylation of 32. To a stirred solution of **32** (0.27 g, 1.56 mmol) in THF (11 mL) under N_2 was added via syringe 1.48 M potassium *tert*-butoxide/THF (1.05 mL, 1.55 mmol, 1.01 equiv). After the mixture was stirred for 20 min, **11** (1.55 mmol) was added via syringe. The mixture was stirred for 18 h and then poured into water (40 mL) and extracted with CH_2Cl_2 (4 × 40 mL). The organic phases were combined, dried ($MgSO_4$), and concentrated in vacuo to yield essentially pure oil **29**. This material was of suitable purity (>97% as judged by GC) for use in the next step although it could be purified via flash column chromatography (SiO_2, petroleum ether/EtOAc 10:1).

4,4-Dicarbethoxy-2-(methoxymethoxy)-1-pentene (33a): yield 87%; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.24 (t, 6H, J = 7.2 Hz, COOCH$_2$CH_3), 1.41 (s, 3H, OCH_3), 2.76 (s, 2H, CH_2C=CH_2), 3.38 (s, 3H, CH_3C(COOC$_2$H$_5$)$_2$), 4.04 (A in ABq, 1H, J = 1.9 Hz, (*E*)-CH_2=C), 4.17 (ABqq, 4H, J = 7.1 Hz, J_{AB} = 10.9 Hz, δ_A = 4.18, δ_B = 4.16, COOCH_2CH$_3$), 4.20 (B in ABq, 1H, (*Z*)-CH_2=C), 4.84 (s, 2H, OCH_2OCH$_3$); ^{13}C NMR (125 MHz, $CDCl_3$) δ 13.90 (COOCH$_2$*C*H$_3$), 19.23 (*C*H$_3$C(COOCH$_2$CH$_3$)$_2$), 40.63 (*C*H$_2$C=CH$_2$), 52.29 (CH$_3$*C*(COOCH$_2$CH$_3$)$_2$), 56.17 (O*C*H$_3$), 61.09 (O*C*H$_2$CH$_3$), 87.97 (*C*H$_2$=C), 93.60 (O*C*H$_2$O), 156.44 (*C*=CH$_2$), 171.79 (*C*OOCH$_2$CH$_3$); exact mass calcd for $C_{13}H_{22}O_6$ 274.1416, found 274.1412.

4,4-Dicarbethoxy-2-[[2-(trimethylsilyl)ethoxy]methoxy]-1-pentene (33b): yield 89%; ^{1}H NMR (500 MHz, $CDCl_3$) 0.03 (s, 9H, Si(CH_3)$_3$), 0.92 (A in AA′XX′, 2H, J_{AX} = 9.8 Hz, $J_{A'X}$ = 7.0, $J_{AA'}$ = −2.9 Hz, $J_{XX'}$ = −2.3 Hz, CH_2Si), 1.25 (t, 6H, J = 7.1 Hz, COOCH$_2$CH_3), 1.40 (s, 3H, CH_3C(COOC$_2$H$_5$)$_2$), 2.76 (s, 2H, CH_2C=CH$_2$), 3.62 (X in AA′XX′, 2H, OCH_2CH$_2$Si), 3.99 (A in ABq, 1H, J = 1.9 Hz, CH_2=C), 4.18 (ABqq, 4H, J = 7.1 Hz, J_{AB} = 10.8 Hz, δ_A = 4.18, δ_B = 4.16, COOCH_2CH$_3$), 4.21 (B in ABq, 1H, CH_2=C), 4.88 (s, 2H, OCH_2O); ^{13}C NMR (125 MHz, $CDCl_3$) δ −1.60 (*C*H$_3$Si), 13.86 (COOCH$_2$*C*H$_3$), 17.80 (*C*H$_2$Si), 19.15 (*C*H$_3$C(COOCH$_2$CH$_3$)$_2$), 40.62 (*C*H$_2$C=CH$_2$), 52.24 (CH$_3$*C*(COOCH$_2$CH$_3$)$_2$), 60.97 (O*C*H$_2$CH$_3$), 66.12 (O*C*H$_2$-CH$_2$Si), 87.75 (C=*C*H$_2$), 91.91 (O*C*H$_2$O), 156.48 (*C*=CH$_2$), 171.69 (*C*OOCH$_2$CH$_3$); exact mass calcd for $C_{17}H_{32}O_6Si$ 360.1968, found 361.2041 (M + 1, CI, CH_4 carrier).

4,4-Dicarboethoxy-2-*n*-butoxy-1-pentene (33c): yield 87%; ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.89 (t, 3H, J = 7.3 Hz, CH_3CH$_2$CH$_2$CH$_2$O), 1.22 (t, 6H, J = 7.2 Hz, COOCH$_2$CH_3), 1.341 (sex, 2H, J = 7.6 Hz, CH$_3$CH_2CH$_2$CH$_2$O), 1.34 (s, 3H, CH_3C(COOC$_2$H$_5$)$_2$), 1.55 (quint, J = 7.06 Hz, CH$_3$CH$_2$CH_2CH$_2$O), 2.73 (s, 2H, CH_2C=CH$_2$), 3.54 (t, 2H, J = 6.5 Hz, CH$_3$CH$_2$-CH$_2$CH_2O), 3.88 (ABq, 2H, J = 1.9 Hz, CH_2=C), 4.17 (ABqq, 4H, J = 7.1 Hz, J_{AB} = 10.9 Hz, δ_A = 4.15, δ_B = 4.12, COOCH_2CH$_3$); ^{13}C NMR (125 MHz, $CDCl_3$) δ 13.71 (OCH$_2$-CH$_2$CH$_2$*C*H$_3$), 13.89 (COOCH$_2$*C*H$_3$), 19.13 (OCH$_2$CH$_2$*C*H$_2$CH$_3$), 19.22 (*C*H$_3$C(COOCH$_2$CH$_3$)$_2$), 30.77 (OCH$_2$*C*H$_2$CH$_2$CH$_3$), 40.58 (*C*H$_2$C=CH$_2$), 52.39 (CH$_3$*C*(COOCH$_2$CH$_3$)$_2$), 61.01 (COO*C*H$_2$-CH$_3$), 67.05 (O*C*H$_2$CH$_2$CH$_2$CH$_3$), 84.37 (C=*C*H$_2$), 158.80 (*C*=CH$_2$), 171.89 (*C*OOCH$_2$CH$_3$); exact mass calcd for $C_{15}H_{26}O_5$ 286.1780, found 286.1779.

4,4-Dicarbethoxy-2-(phenylmethoxy)-1-pentene (33d): yield 91%; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.14 (t, 6H, J = 7.1 Hz, COOCH$_2$CH_3), 1.43 (s, 3H, CH_3C(COOC$_2$H$_5$)$_2$), 2.82 (s, 2H, CH_2C=CH$_2$), 4.03 (ABqq, 4H, J = 7.2 Hz, J_{AB} = 10.9 Hz, δ_A = 4.04, δ_B = 4.00, COOCH_2CH$_3$), 4.04 (A in ABq, 1H, J = 1.8 Hz, (*E*)-CH_2=C), 4.08 (B in ABq, 1H, (*Z*)-CH_2=C), 4.63 (s, 2H, OCH_2Ph), 7.25−7.4 (AA′BB′C, 5H, C_6H_5); ^{13}C NMR (125 MHz, $CDCl_3$) δ 13.73 (COOCH$_2$*C*H$_3$), 19.34 (*C*H$_3$C(COOCH$_2$CH$_3$)$_2$), 40.63 (*C*H$_2$C=CH$_2$), 52.30 (CH$_3$*C*(COOCH$_2$CH$_3$)$_2$), 60.94 (O*C*H$_2$CH$_3$), 69.94 (O*C*H$_2$C$_6$H$_5$), 85.53 (*C*H$_2$=C), 127.67 (*o*-$C_6H_5CH_2$), 127.79 (*p*-$C_6H_5CH_2$), 128.13 (*m*-$C_6H_5CH_2$), 136.56 (*ipso*-$CH_2C_6H_5$), 158.52 (*C*=CH$_2$), 171.72 (*C*OOCH$_2$CH$_3$); exact mass calcd for $C_{18}H_{24}O_5$ 320.1624, found 320.1623.

4,4-Dicarbethoxy-2-[(*p*-methoxyphenyl)methoxy]-1-pentene (33e): yield 92%; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.12 (t, 6H, J = 7.1 Hz, COOCH$_2$CH_3), 1.40 (s, 3H, CH_3C-(COOC$_2$H$_5$)$_2$), 2.78 (s, 2H, CH_2C=CH$_2$), 3.78 (s, 3H, C$_6$H$_4$OCH_3), 4.00 (ABqq, 4H, J = 7.2 Hz, J_{AB} = 10.7 Hz, δ_A = 4.02, δ_B = 3.98, COOCH_2CH$_3$), 3.99 (A in ABq, 1H, J = 2.0 Hz, (*E*)-CH_2=C), 4.06 (B in ABq, 1H, (*Z*)-CH_2=C), 4.55 (s, 2H, OCH_2C$_6$H$_4$), 6.87 (A in AA′BB′, 2H, C$_6$*H*$_4$), 7.24 (B in AA′BB′, 2H, C$_6$*H*$_4$); ^{13}C NMR (125 MHz, $CDCl_3$) δ 13.77 (COOCH$_2$*C*H$_3$), 19.36 (*C*H$_3$C(COOCH$_2$CH$_3$)$_2$), 40.69 (*C*H$_2$C=CH$_2$), 52.34 (CH$_3$*C*(COOCH$_2$CH$_3$)$_2$), 55.11 (CH$_3$OC$_6$H$_5$), 60.98 (O*C*H$_2$CH$_3$), 69.35 (O*C*H$_2$C$_6$H$_4$OCH$_3$), 85.35 (*C*H$_2$=C), 113.52 (*o*-CH$_3$-OC$_6$H$_4$CH$_2$), 128.75 (*ipso*-CH$_3$OC$_6$H$_4$), 129.49 (*m*-CH$_3$OC$_6$H$_4$CH$_2$), 158.60 (*ipso*-CH$_2$C$_6$H$_4$), 159.23 (*C*=CH$_2$), 171.79 (COOCH$_2$CH$_3$); exact mass calcd for $C_{19}H_{26}O_6$ 350.1729, found 350.1729.

4,4-Dicarbethoxy-2-[2-(trimethylsilyl)ethoxy]-1-pentene (33f): yield 90%; ^{1}H NMR (400 MHz, $CDCl_3$) 0.01 (s, 9H,

Si(CH_3)$_3$), 0.93 (A in AA′XX′, 2H, J_{AX} = 9.5, $J_{A'X}$ = 7.1 Hz, $J_{AA'}$ = −2.4 Hz, $J_{XX'}$ = −2.5 Hz, CH_2Si), 1.23 (t, 6H, J = 7.1 Hz, COOCH$_2$CH_3), 1.37 (s, 3H, CH_3C(COOC$_2$H$_5$)$_2$), 2.71 (s, 2H, CH_2C═CH$_2$), 3.64 (X in AA′XX′, 2H, OCH_2CH$_2$Si), 3.88 (ABq, 2H, J = 1.7 Hz, CH_2═C), 4.17 (ABqq, 4H, J = 7.0 Hz, J_{AB} = 10.8 Hz, δ_A = 4.17 δ_B = 4.14, COOCH_2CH$_3$); ^{13}C NMR (100 MHz, CDCl$_3$) δ −1.51 (*C*H$_3$Si), 13.97 (COOCH$_2$*C*H$_3$), 17.06 (*C*H$_2$Si), 19.34 (*C*H$_3$C(COOCH$_2$CH$_3$)$_2$), 40.73 (*C*H$_2$C═CH$_2$), 52.52 (CH$_3$*C*(COOCH$_2$CH$_3$)$_2$), 61.07 (O*C*H$_2$CH$_3$), 64.68 (O*C*H$_2$CH$_2$Si), 84.35 (C═*C*H$_2$), 158.62 (*C*═CH$_2$), 171.90 (*C*OOCH$_2$CH$_3$); exact mass calcd for $C_{16}H_{30}O_5Si$ 330.1863, found 330.1856.

Synthesis of 4,4-Dicarbethoxy-2-pentanone (34). Deprotection of 33a. To a solution of **33a** (0.175 g, 0.64 mmol) in 1,4-dioxane (2 mL) was added 1% aqueous oxalic acid (12 mL). The solution was stirred for 2 h, poured into saturated $NaHCO_3$ (30 mL), and extracted with $CHCl_3$ (4 × 30 mL). The organic layers were combined, dried ($MgSO_4$), and concentrated in vacuo to yield 0.132 g (0.573 mmol, 90% yield) of a virtually pure clear oil **34** (>98% as judged by GC): ^{1}H NMR (500 MHz, CDCl$_3$) 1.25 (t, 6H, J = 7.2 Hz, COOCH$_2$CH_3), 1.52 (s, 3H, CH_3C(COOC$_2$H$_5$)$_2$), 2.16 (s, 3H, CH_3C═O), 3.09 (s, 2H, CH_2C═O), 4.18 (q, 4H, J = 7.2, COOCH_2CH$_3$); ^{13}C NMR (100 MHz, CDCl$_3$) 13.90 (COOCH$_2$*C*H$_3$), 20.38 (*C*H$_3$C(COOCH$_2$CH$_3$)$_2$), 30.32 (*C*H$_3$C═O), 48.63 (*C*H$_2$C═O), 51.37 (CH$_3$*C*(COOCH$_2$CH$_3$)$_2$), 61.56 (O*C*H$_2$CH$_3$), 171.41 (*C*OOCH$_2$CH$_3$), 205.11 (*C*═O); exact mass calcd for $C_{11}H_{18}O_5$ 230.1154, found 230.1153.

Synthesis of 4,4-Dicarbethoxy-2-pentanone (34). Deprotection of 33b. To a solution of **33b** (0.121 g, 0.335 mmol) in DMF (2.5 mL) was added CsF (0.102 g, 0.673 mmol, 2 equiv). The solution was heated to 130 °C for 24 h, cooled, poured into water (30 mL), and extracted with $CHCl_3$ (4 × 30 mL). The organic layers were combined, dried ($MgSO_4$), and concentrated in vacuo to yield 0.050 g (0.283 mmol, 117% yield) of crude brown oil **34**. This material was purified via flash column chromatography (basic Al_2O_3, activity III, petroleum ether/ether 5:1) to yield 0.039 g (0.167 mmol, 90% yield) of pure **34**.

Synthesis of 4,4-Dicarbethoxy-2-pentanone (34). Deprotection of 33c. To a solution of **33c** (0.19 g, 0.664 mmol) in 1,4-dioxane (2 mL) was added 1% aqueous oxalic acid (11 mL). The solution was stirred for 18 h, poured into saturated $NaHCO_3$ (20 mL), and extracted with $CHCl_3$ (4 × 20 mL). The organic layers were combined, dried ($MgSO_4$), and concentrated in vacuo to yield 0.146 g (0.636 mmol, 96% yield) of an essentially pure (>96% as judged by GC) clear oil **34**.

Synthesis of 4,4-Dicarbethoxy-2-pentanone (34). Deprotection of 33d. To a solution of **33d** (0.157 g, 0.491 mmol) in 1,4-dioxane (2 mL) was added 1% aqueous oxalic acid (9 mL). The solution was stirred for 48 h and the reaction was poured into saturated $NaHCO_3$ (20 mL) and extracted with $CHCl_3$ (4 × 20 mL). The organic layers were combined, dried ($MgSO_4$), and concentrated in vacuo to yield 0.111 g (0.482 mmol, 98% yield) of an essentially (>99% as judged by GC) pure clear oil **34**.

Synthesis of 4,4-Dicarbethoxy-2-pentanone (34). Deprotection of 33e. To a solution of **33e** (0.139 g, 0.397 mmol) in 9:1 CH_3CN/H_2O (4 mL) was added ceric(IV) ammonium nitrate (0.457 g, 0.834 mmol, 2 equiv). The solution was stirred for 15 min, poured into saturated $NaHCO_3$ (30 mL), and extracted with $CHCl_3$ (4 × 20 mL). The organic layers were combined, dried ($MgSO_4$), and concentrated in vacuo to yield 0.087 g (0.379 mmol, 96% yield) of crude yellow oil **34**. This material was purified via flash column chromatography (basic Al_2O_3, activity III, petroleum ether/ether 5:1) to yield 0.083 g (0.360 mmol, 91% yield) of pure **34**.

Synthesis of 4,4-Dicarbethoxy-2-pentanone (34). Deprotection of 33f. To a solution of **33f** (0.125 g, 0.379 mmol) in DMF (1.5 mL) was added CsF (0.09 g, 0.592 mmol, 1.6 equiv). The solution was heated to 130 °C for 48 h, cooled, poured into water (30 mL), and extracted with $CHCl_3$ (4 × 20 mL). The organic layers were combined, dried ($MgSO_4$), and concentrated in vacuo to yield 0.099 g (0.429 mmol, 113% yield) of crude brown oil **34**. This material was purified via flash column chromatography (basic Al_2O_3, activity III, petroleum ether/ether 5:1) to yield 0.0491 g (0.213 mmol, 93% yield) of pure **30**.

Acknowledgment. We gratefully acknowledge financial support from the Department of Chemistry at the University of Illinois, University of Illinois Research Board and the Illinois Chapter of the American Heart Association. We wish to acknowledge members of the Petillo group for useful conversations during these studies.

Supporting Information Available: ^{1}H and ^{13}C NMR spectra for all compounds in this study in addition to GC traces where appropriate (64 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

JO980094J