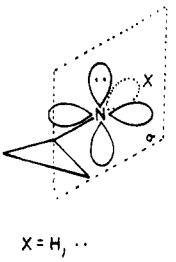


**Figure 1.**

and by cyanide ion selective electrode.[11] Kinetic analysis of the high-yielding photochemical reaction reveals that cyanide, ethylene, and $CO_2$ are formed at identical rates. First-order kinetics are observed for the direct photochemical reaction, with a rate constant of $2.2 \times 10^{-4}$ $s^{-1}$. In the presence of benzophenone, the yield is decreased with increasing concentration of triplet sensitizer, while the rate remains approximately constant. The identification of ACC in the reaction mixture suggests hydrogen abstraction as the competitive triplet reaction. Triplet quenchers (methyl pentadiene) have little effect.

The decomposition of 4 was also conducted in a 0.1-mM ethanol solution, and kinetics were determined by gas chromatography alone (flame ionization). The same rate is found in both *neutral* and basic solutions, suggesting that the reactive intermediate in the former case is the nitrene and not the alternative zwitterionic nitrenium carboxylate. This suggests that the $pK_a$ of the nitrenium ion is less than ca. 5, the $pK_a$ of cyclopropane carboxylic acid.

The acid-catalyzed decomposition of 4 was conducted under both singlet (TFA, AcOH) and triplet (TFA, $CHBr_3$) conditions. The yields are 16% and 15%, respectively, as determined by gas chromatography of the headspace and by trapping in basic solution of the hydrogen cyanide so produced. The rates are considerably faster than in the photochemical reaction ($\sim 1.5 \times 10^{-2}$ $s^{-1}$). It did not prove possible to identify any nonvolatile products of these nitrenium ion reactions.

The evidence presented above has demonstrated the competence of both singlet nitrene and nitrenium intermediates in ethylene biosynthesis. The facile conversion of these intermediates to ethylene and $CO_2$ is best explained by a concerted, chelatropic reaction to yield ethylene and cyanoformate, followed by rapid decarboxylation to give cyanide. Support for this proposals comes from the photochemical decomposition of ester iv, which yields 2-(trimethylsilyl)ethyl cyanoformate. Interestingly, an MO correlation diagram demonstrates that an orbital symmetry-allowed chelatropic reaction is possible both for singlet nitrene and nitrenium intermediates, but only when the empty nitrogen p orbital is in the "bisected" conformation (Figure 1). This situation contrasts sharply with that for the Baldwin mechanism; a retro [2 + 2] reaction to give alkene and isonitrile is symmetry disallowed.

A key aspect of nitrene and nitrenium ion proposals for ethylene biosynthesis is how the much-touted metal ion,[12] possibly manganese,[13] is involved. N-Hydroxylation through metal–oxene or –peroxide complexes appears an attractive access to the nitrenium ion, while direct M=N bond formation followed by homolysis might yield the nitrene. The former has precedent in ferrous hemes such as cytochrome P-450,[14] while the intermediacy of manganese nitrenes is inferred from a recent report.[15] Further studies as to the competence of these intermediates for ethylene biosynthesis await more detailed information regarding the natural system.

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**Registry No.** 1, 22059-21-8; 4, 82998-00-3; ii, 87831-15-0; iii, 87831-16-1; iv, 87831-17-2; ethylene, 74-85-1.

**Supplementary Material Available:** Experimental details of compounds ii–iv and 4 (4 pages). Ordering information is given on any current masthead page.

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## Highly Selective Synthesis of α-Alkylidenetetrahydrofurans and γ-Alkylidenebutyrolactones via Intramolecular Opening of Epoxysilanes[1]

*Summary:* Treatment of α-(3-hydroxypropyl)-α-(trimethylsilyl) epoxides with KH in THF cleanly provides α-alkylidenetetrahydrofurans in high yields with ≥95% retention of stereochemistry, while epoxidation of γ-(trimethylsilyl)-γ,δ-unsaturated carboxylic acids with MCPBA produces γ-(1-hydroxyalkyl)-γ-(trimethylsilyl)butyrolactones that can be converted into γ-alkylidenebutyrolactones in high yields via acetylation–fluoride treatment with ≥99% inversion of stereochemistry.

*Sir:* Stereodefined exocyclic alkenes of the types 1 and 2 (Chart I) represent a wide variety of natural products such as prostacyclin[2] (3) and freelingyne[3] (4). Their high sensitivity toward acids makes it desirable to synthesize them in a highly selective manner, preferably without having to perform isomeric separation. Although haloetherification has been successfully applied to the synthesis of prostacyclin and its *E* isomer,[2b-d] chromatographic separation of diastereomeric halo ether intermediates appears to be necessary. Stereoselective cyclic addition reactions of an acetylenic alcohol[4] or carboxylic acid[5] can produce in a stereoselective manner one stereoisomer but not the other.

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(2) (a) "Prostacyclin"; Vane, J. R., Bergström, S., Eds.; Raven Press: New York, 1979. (b) Corey, E. J.; Keck, G. E.; Székely, I. *J. Am. Chem. Soc.* **1977**, *99*, 2006. (c) Johnson, R. A.; Lincoln, F. H.; Thompson, J. L.; Nidy, E. G.; Mizsak, S. A.; Axen, U. *Ibid.* **1977**, *99*, 4182. (d) Nicolaou, K. C.; Barnette, W. E. *J. Chem. Soc., Chem. Commun.* **1977**, 331.
(3) For a nonstereoselective synthesis of freelingyne, see: Knight, D. W.; Pattenden, G. *J. Chem. Soc., Perkin Trans. 1* **1975**, 641.
(4) Riediker, M.; Schwartz, J. *J. Am. Chem. Soc.* **1982**, *104*, 5842.
(5) Krafft, G. A.; Katzenellenbogen, J. A. *J. Am. Chem. Soc.* **1981**, *103*, 5459.

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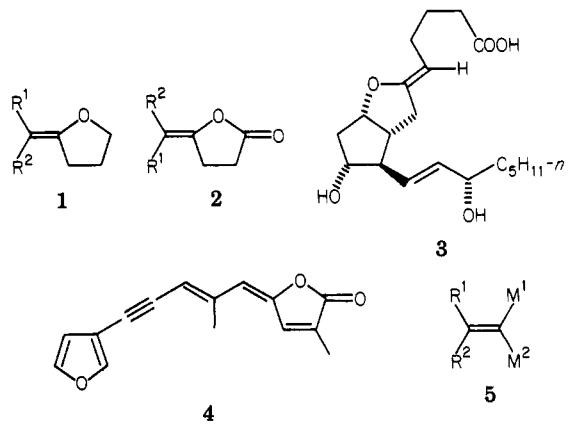
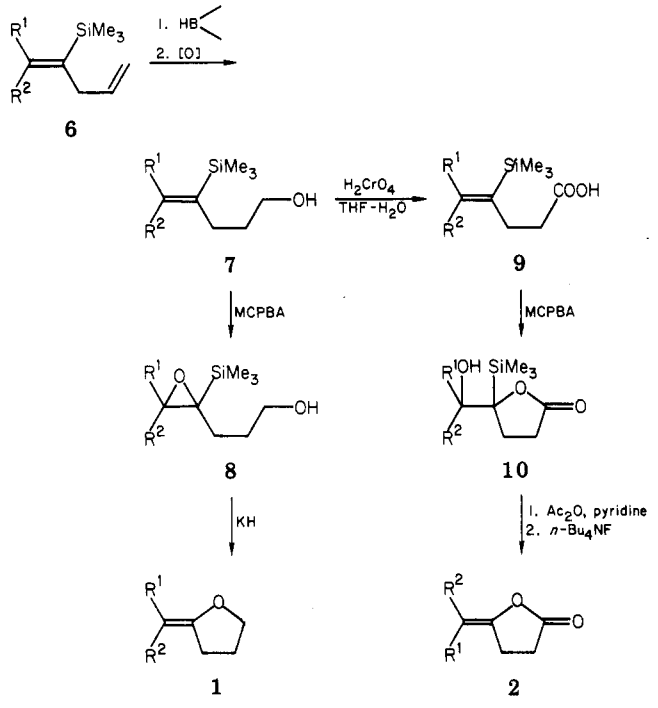
Chart I



Scheme I[a]

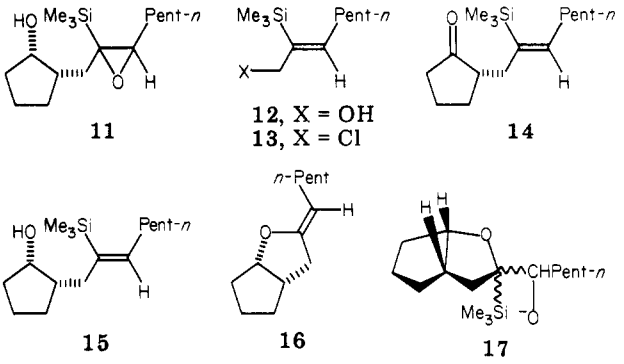


[a] a, $R^1$ = *n*-pentyl, $R^2$ = H; b, $R^1$ = H, $R^2$ = *n*-pentyl.

Stereospecific conversion of stereodefined 1,1-dimetalloalkenes (**5**) into **1** and **2** is a conceptually attractive but essentially unexplored methodology.[6] Herein we disclose one such method involving intramolecular epoxysilane-opening reactions[7] (Scheme I). One particularly attractive feature of the method reported here is that both **1** and **2**, *E* or *Z*, can be synthesized as ≥95% pure substances without any isomer separation. In fact, no chromatographic separation is used in Scheme I.

The required 1,4-dienes (**6**) are readily obtainable as described in the literature. Thus, 1-(trimethylsilyl)-1-heptyne was treated sequentially with diisobutylaluminum hydride in ether, *n*-BuLi, and allyl bromide to produce **6a** (*Z*/*E* ratio ≥99, $^{13}$C NMR) in 78% yield.[8] On the other hand, carbocupration[9] of (trimethylsilyl)ethyne with *n*-PentCu·$MgBr_2$ (*n*-Pent = *n*-pentyl) in ether in the presence of 1 equiv of $P(OEt)_3$ followed by treatment with allyl bromide[10] gave **6b** (*E*/*Z* ratio ≥99, $^{13}$C NMR) in 50–55% yield.

Chart II



Conversion of **6a** into **7a** was achieved in 93% yield by hydroboration with 9-borabicyclo[3.3.1]nonane[11] (9-BBN) in THF followed by oxidation with 3 N NaOH and 30% $H_2O_2$. The product was further oxidized with *m*-chloroperbenzoic acid (MCPBA) in $CH_2Cl_2$ at 0–25 °C to give **8a** in 89% yield. Treatment of **8a** with 1 equiv of KH suspended in THF[7b] at room temperature provided **1a** in 70% yield (95–98% stereoisomeric purity) via syn elimination: IR (neat) 1690 (s), 1170 (s), 1030 (s) $cm^{-1}$; $^1$H NMR ($CDCl_3$, $Me_4Si$) δ 2.45 (t, *J* = 7 Hz, 2 H), 3.9–4.3 (m with a t (*J* = 7 Hz) at 4.05, 3 H); $^{13}$C NMR ($CDCl_3$, $Me_4Si$) δ 13.61, 22.40, 24.80, 28.20, 29.81, 31.37, 69.23, 94.48, 154.04. In an analogous manner **6b** was converted into **7b** (84%), then into **8b** (93%), and finally into **1b** in 81% yield (≥98% stereoisomeric purity): IR (neat) 1740 (w), 1690 (s), 1150 (s), 1120 (s) $cm^{-1}$; $^1$H NMR ($CDCl_3$, $Me_4si$) δ 2.2–2.7 (m, 2 H), 4.00 (t, *J* = 7 Hz, 2 H), 4.71 (tt, *J* = 2, 7 Hz, 1 H); $^{13}$C NMR ($CDCl_3$, $Me_4Si$) δ 13.84, 22.60, 24.64, 25.32, 27.53, 30.48, 31.32, 68.69, 94.35, 155.44.

To examine the relative reactivity of a pair of diastereomeric epoxysilane intermediates in their conversion into a cyclic enol ether, we synthesized **11** (Chart II) as a pair of diastereomers in the following manner. (*Z*)-[1-(trimethylsilyl)-1-heptenyl]diisobutylalane, generated as described above, was sequentially treated with 1 equiv of *n*-BuLi and an excess of paraformaldehyde[12] to give **12** (87%), which was then converted into **13** (84%) by sequential treatment with MeLi, TsCl, and LiCl in HMPA–ether (1:3).[13] The reaction of **13** with lithium cyclopentenolate in the presence of 2 equiv of $BEt_3$ and 5 mol % of $Pd(PPh_3)_4$ in THF[14] provided **14** in 92% yield. Its treatment with 1.2 equiv of LiB(*sec*-Bu)$_3$H[15] (L-Selectride Aldrich) in THF at −78 to +25 °C gave **15** in 95% yield. The stereoisomeric purities of **12**–**15** are ≥99%, and the overall purity of each compound obtained after simple distillation is ≥98%. Treatment of **15** with MCPBA in $CH_2Cl_2$ at 0–25 °C provided **11** in 91% yield. Its $^{13}$C NMR spectrum indicated that it was a ca. 50:50 mixture of two diastereomers. The KH-induced cyclization reaction of **11** at room temperature was complete within 1–2 h, and the desired product **16**[16] was obtained in 82% yield (87%

(6) Although not closely related, a stereospecific conversion of a 1-(trimethylsilyl)-1-alkenylaluminum derivative into a bicyclic amine containing an exocyclic alkene moiety has recently been reported: Overman, L. E.; Bell, K. L. *J. Am. Chem. Soc.* **1981**, *103*, 1851.

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by GLC): IR (neat) 1690 (s), 1080 (m), 1025 (m) $cm^{-1}$; $^1H$ NMR ($CDCl_3$, $Me_4Si$) $\delta$ 4.00 (t, $J$ = 7 Hz, 1 H), 4.5–4.8 (m, 1 H); $^{13}C$ NMR ($CDCl_3$, $Me_4Si$) $\delta$ 14.07, 22.51, 24.01, 25.08, 29.92, 31.36, 32.33, 34.24, 36.30, 40.64, 87.68, 95.03, 155.03. Its stereoisomeric purity is ca. 97% by $^{13}C$ NMR analysis, and its purity by GLC is ca. 97%.

The above results point to a significant difference between this new approach to cyclic enol ethers and the base-induced $\beta$ elimination of halo ethers.[2] Namely, in contrast with the latter reaction, in which one of the two diastereomers is either inert or of low reactivity to an external base, hence requiring its chromatographic separation prior to the final elimination step, the former can proceed readily with either diastereomer, presumably because $\beta$ elimination of **17** does not require attack by an external base.

We then turned our attention to the synthesis of enol lactones **2**. Treatment of **7a** with Jones reagent gave **9a** (82%). Its treatment with MCPBA directly gave a cyclization product **10a** (ca. 80%). To our chagrin, direct treatment of **10a** with either KH suspended in THF or $BF_3{\cdot}OEt_2$ in $CH_2Cl_2$[7b] did not give the desired product **2a** in any significant amount (<2–3% by GLC). A few other bases, such as $KN(SiMe_3)_2$, were also totally unsatisfactory. On the other hand, acetylation of **10a** followed by treatment with $n$-$Bu_4NF$[17] in HMPA cleanly produced **2a**[16] (72% based on **10a**, $E/Z$ ratio of 99) presumably via anti elimination:[18] IR (neat) 1800 (s), 1700 (s), $cm^{-1}$; $^1H$ NMR ($CDCl_3$), $Me_4Si$) $\delta$ 1.8–2.1 (m, 2 H), 2.5–3.1 (m, 4 H), 5.22 (tt, $J$ = 2, 7 Hz, 1 H); $^{13}C$ NMR ($CDCl_3$, $Me_4Si$) $\delta$ 103.31, 149.51, 174.94. To our knowledge, this represents the first reported synthesis of an ($E$)-$\gamma$-alkylidene $\gamma$-lactone. In an analogous manner, **2b** was prepared in 85% yield ($Z/E$ ratio of 99) via **9b** (83%) and **10b** (92%). The spectral data for **2b**[16] are as follows: IR (neat) 1800 (s), 1700 (s) $cm^{-1}$; $^1H$ NMR ($CDCl_3$, $Me_3Si$) $\delta$ 1.9–2.3 (m, 2 H), 2.3–3.1 (m, 4 H), 4.60 (t, $J$ = 7 Hz, 1 H); $^{13}C$ NMR ($CDCl_3$, $Me_3Si$) $\delta$ 104.91, 147.70, 175.78.

The following conversion of **9a** into **2a** is representative. To **9a** (1.21 g, 5 mmol) in 10 mL of $CH_2Cl_2$ was added MCPBA (1.04 g, 6 mmol) in 30 mL of $CH_2Cl_2$ for 2 h at 0 to 25 °C. Quenching (aqueous sodium sulfite), extraction ($Et_2O$), washing (aqueous sodium sulfite), drying ($MgSO_4$), and distillation gave 1.01 g (78% yield) of **10a**, 130–135 °C (0.2 mm). Acetylation of **10a** (0.77 g, 3 mmol) was carried out with AcCl (0.35 g, 4.5 mmol) and pyridine (0.36 g, 4.5 mmol) in THF (−78 to +25 °C, 8 h). Quenching (aqueous $NH_4Cl$), extraction ($Et_2O$), drying ($MgSO_4$), and concentration under reduced pressure yielded the acetate which was ≥98% pure by GLC and $^{13}C$ NMR. Without further purification 0.60 g (2 mmol) of the acetate dissolved in HMPA was added to $n$-$Bu_4NF$ (3 mmol) in THF at 0 °C, and the mixture was stirred for 0.5 h at 25 °C. Quenching-extraction (water-pentane), drying ($MgSO_4$), and concentration provided 0.28 g (72%) of **2a**, which was stereoisomerically 99% pure but was contaminated with a minor unidentified compound (ca. 5%). The product can be further purified by low temperature distillation without being accompanied by stereoisomerization.

**Acknowledgment.** We thank the National Institutes of Health and the National Science Foundation for support. We also thank Professors P. L. Fuchs of Purdue University, P. F. Hudrlik of Howard University, and J. A. Katzenellenbogen of the University of Illinois for helpful discussions.

**Supplementary Material Available:** $^1H$ and $^{13}C$ NMR, IR, and mass spectral data as well as purity figures based on $^{13}C$ NMR and GLC (5 pages). Ordering information is given on any current masthead page.

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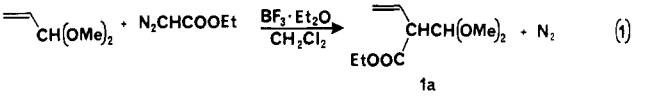
## Homologation of Acetals of $\alpha,\beta$-Unsaturated Carbonyl Compounds with Diazo Esters. Synthesis of Acetals of $\beta,\gamma$-Unsaturated Carbonyl Compounds

*Summary:* $\beta,\gamma$-Unsaturated acetals are conveniently prepared in good yields by boron trifluoride etherate catalyzed homologation of acetals of $\alpha,\beta$-unsaturated aldehydes with ethyl diazoacetate.

*Sir:* There are few preparative methodologies that utilize a specific bond migration as an integral feature of the synthetic transformation.[1] In those most useful for organic synthesis, migration takes place unidirectionally to a developing electrophilic center to produce a relatively stable carbocation.[2] Aldehyde and ketone homologation reactions by diazo compounds,[3-7] like the related pinacol rearrangement,[8] take advantage of carbocation stabilization by an adjacent oxygen. However, mixtures of products are generally obtained when two different groups can undergo migration to the developing electrophilic center, epoxide formation competes with bond migration in homologation reactions when diazomethane is employed,[3] and $\alpha,\beta$-unsaturated aldehydes and ketones are not amenable to homologation with diazo compounds.[6] We now report a new design for aldehyde and ketone homologation reactions through which acetals or ketals of $\alpha,\beta$-unsaturated carbonyl compounds are transformed into acetals or ketals of $\beta,\gamma$-unsaturated carbonyl compounds.

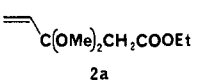
Treatment of acrolein dimethyl acetal with ethyl diazoacetate in the presence of a catalytic amount of boron trifluoride etherate results in the product (**1a**) from formal insertion of the carboethoxy carbenoid group between the vinyl and acetal carbons (eq 1). Formal acetal carbon–



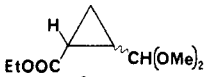
(1)

1a

hydrogen insertion (**2a**) and cyclopropane formation (**3a**)



2a



3a

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