80359-86-0; *threo*-**7d**, 80359-87-1; *erythro*-**7f**, 80359-88-2; **7g**, 80359-89-3; *erythro*-**7h**, 80359-90-6; *threo*-**7h**, 80359-91-7; **8a**, 80359-92-8; **8b**, 80359-93-9; **8d**, 70245-09-9; **8e**, 80359-94-0; **8f**, 80359-95-1; **8g**, 80359-96-2; **8h**, 80359-97-3.

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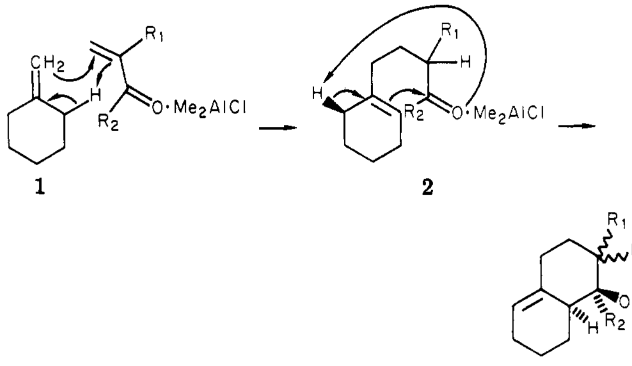
Sequential Ene Reactions. A New Annelation Procedure

Summary: Alkylidenecycloalkanes react with α,β-unsaturated carbonyl compounds in the presence of Me_2AlCl to give bicyclic alcohols resulting from two sequential ene reactions.

Sir: The use of carbon–carbon double bonds as activating groups for the formation of new carbon–carbon bonds under mild conditions is a challenge to synthetic chemists. The ene reaction provides a potential solution to this problem.[1] We have found that Lewis acid catalyzed ene reactions with acrylate esters as the enophile occur at 25 °C and that the ene reactions of α-substituted acrylate esters are regioselective and stereoselective, with the carboalkoxy group adding endo.[1b] Lewis acid catalysis offers significant advantages over the corresponding thermal ene reactions which occur at 200–300 °C. We have also shown that alkylaluminum halides are preferred catalysts for these reactions since the alkyl group functions as a proton scavenger.[2]

α,β-Unsaturated ketones and aldehydes have seen very little use as enophiles.[3] Acrolein reacts with β-pinene at 140 °C[3b] or with $ZnBr_2$ catalysis at 25 °C.[4] Methyl vinyl ketone (MVK) reacts with β-pinene at 25 °C with $ZnBr_2$ catalysis[4] and has been reported to react with limonene with $AlCl_3$ catalysis.[5]

We report here that alkylidenecycloalkanes react with β-unsubstituted α,β-unsaturated ketones or aldehydes in the presence of Me_2AlCl to give a bicyclic alcohol resulting from two sequential ene reactions. For instance, methylenecyclohexane (**1**), acrolein, and Me_2AlCl in CH_2Cl_2 at 0 °C for 20 min react to give a 63% yield of **3a**.[6,9] The initially formed ene adduct **2a** undergoes a second, intramolecular ene reaction with the complexed aldehyde functioning as the enophile. Loss of methane from the resulting alcohol–Lewis acid complex to give the aluminum alkoxide prevents proton-catalyzed side reactions or solvolysis of the alcohol. Cyclization of **2a** to **3a** is much faster than formation of **2a** since no **2a** could be detected, even when the reaction is run to low conversion at −78 °C.



1 **2** **3**

a, $R_1 = R_2 = H$
b, $R_1 = H$, $R_2 = CH_3$
c, $R_1 = \alpha\text{-}CH_3$, $R_2 = H$
d, $R_1 = \beta\text{-}CH_3$, $R_2 = H$
e, $R_1 = \alpha\text{-Br}$, $R_2 = H$
f, $R_1 = \beta\text{-Br}$, $R_2 = H$
g, $R_1 = H$, $R_2 = CH_3$, $4\alpha\text{-}CH_3$

Reaction of **1**, MVK, and Me_2AlCl at −20 °C for 2 h gives a 39% yield of **2b** and a 4% yield of **3b**. The same reaction at 25 °C for 1 h gives a 9% yield of **2b** and a 49% yield of **3b**. Thus, at different reaction times, either **2b** or **3b** can be isolated as the major product. The successful isolation of **2b**, as opposed to **2a**, results from the dimished reactivity of the ketone carbonyl as an enophile.[10] The isolation of a teritary alcohol, **3b**, from a Lewis acid catalyzed reaction is due to its protection as an aluminum alkoxide.

Reaction of **1**, methacrolein, and Me_2AlCl (0 °C, 1 h) gives a 66% yield of a 3:1 mixture of **3d** (mp 69–71 °C) and **3c** (mp 51.5–53.5 °C). The methyl group thus prefers to be equatorial, suggesting that ring formation is well ad-

---

[1] (a) Hoffmann, H. M. R. *Angew. Chem., Int. Ed. Engl.* **1969**, *8*, 556. (b) Snider, B. B. *Acc. Chem. Res.* **1980**, *13*, 426.

[2] Snider, B. B.; Rodini, D. J.; Karras, M.; Kirk, T. C.; Deutsch, E. A.; Cordova, R.; Price, R. T. *Tetrahedron* **1981**, *37*, 3927.

[3] (a) Albisetti, C. J.; Fisher, N. G.; Hogsed, M. J.; Joyce, R. M. *J. Am. Chem. Soc.* **1956**, *78*, 2637. (b) Kruk, C.; Velzen, J. C. v.; de Boer, T. J. *Recl. Trav. Chim. Pays-Bas* **1969**, *88*, 139.

[4] Snider, B. B. *J. Org. Chem.* **1974**, *39*, 255.

[5] Mehta, G.; Reddy, A. V. *Tetrahedron Lett.* **1979**, 2625. We have been unable to repeat this reaction. Professor Mehta has indicated that "the yields are somewhat erratic and decrease enormously on scale up above 10 mmole." In addition the reported yield of 75% is based on recovery of 80% of the limonene. From the spectral data reported, there is no doubt that the ene adduct was obtained. However, our results make it clear that the ene adduct will not be stable to $AlCl_3$ for 12 h in benzene. The most likely explanation is that a partially hydrated, and therefore much less active, sample of $AlCl_3$ was used.

[6] All new compounds were characterized by IR, ^1H, and ^{13}C NMR spectroscopy and gave satisfactory elemental analyses. The stereochemistry of hydroxyl and bromine substituents was established by the chemical shift and splitting pattern of the α-protons. The stereochemistry of these substituents and methyl groups could be established by ^{13}C NMR spectroscopy. The reported ^{13}C spectra of 1,2,3,4,4a,5,6,7-octahydronaphthalene and 1*H*-2,3,3a,4,5,6-hexahydroindene[7] could be assigned using the spectra of 1-methylcyclohexene and 2-(methylmethylene)cyclohexane[8] as models. With shift values for equatorial and axial substituents on cyclohexanes and the shift values for equatorial and axial methyl substituents on methylenecyclohexane,[8] the expected ^{13}C spectra could be calculated for each possible isomer. In all cases agreement between the calculated and observed spectra was very good for all carbons.

[7] Becker, K. B. *Helv. Chim. Acta* **1977**, *60*, 68.

[8] Grover, S. H.; Stothers, J. B. *Can. J. Chem.* **1975**, *53*, 589.

[9] The detailed procedure given below is typical. Methylenecyclohexane (0.53 g, 5.5 mmol) was added to a solution of acrolein (distilled from $CuSO_4$; 0.28 g, 5.0 mmol) and Me_2AlCl (4.16 mL of 1.14 M in heptane, 4.75 mmol) in 15 mL of CH_2Cl_2 at 0 °C. The mixture was stirred for 20 min at 0 °C and quenched by cautious addition of water and ether. The organic layer was removed and the aqueous layer was washed 3 times with ether. The combined organic layers were washed with brine, dried (Na_2SO_4), and evaporated to give 0.808 g of crude product. Evaporative distillation of 0.696 g (100 °C, 0.25 torr) gave 0.411 g (63%) of pure **3a**: mp 54.4–55.5 °C; NMR (CCl_4) δ 5.6 (br s, 1), 3.8 (br s, 1); ^{13}C NMR ($CDCl_3$) δ 136.0, 124.3, 71.3, 42.1, 34.8, 33.5, 26.4, 25.2, 21.9, 20.9; IR (KBr) 3370, 3050, 1670 cm^{-1}. Anal. Calcd for $C_{10}H_{16}O$: C, 78.90; H, 10.59. Found: C, 78.79; H, 10.36.

[10] Karras, M.; Snider, B. B. *J. Am. Chem. Soc.* **1980**, *102*, 7951.

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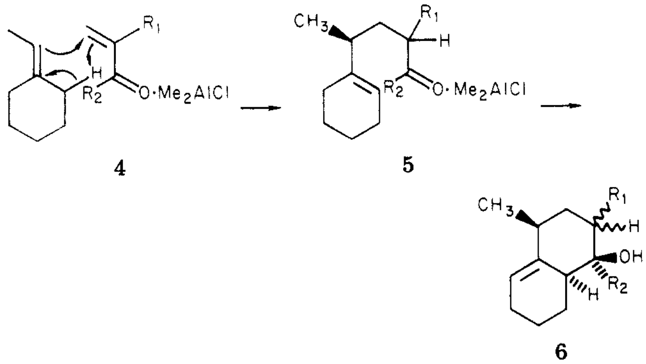
vanced in the transition state. On the other hand, **1**, α-bromoacrolein, and Me_2AlCl (0 °C, 1 h) give a 59% yield of a 14:1 mixture of **3e** (mp 85.5–86.5 °C) and **3f**.[11] The large preference for axial bromine may result from increased reactivity of the conformer of **2** with the antiperiplanar orientation of the bromine and carbonyl group. This has been previously proposed to rationalize the stereoselectivity of the Cornforth olefin synthesis.[12]

Reaction of ethylidenecyclohexane (**4**) with acrolein gives a 40% yield of **6a** (mp 61.5–62.5 °C) with an equatorial methyl group. Reaction of **4** with methacrolein can give two initial ene adducts **5c** or **5d**. If the carbonyl group adds endo as with methyl methacrylate,[13] **5d** will be the major or exclusive product. In fact, the only bicyclic alcohol which could be isolated was **6d** (38% yield), although minor unidentifiable products were formed. Similarly, α-bromoacrolein and **4** give a 42% yield of **6f** and a 5% yield of **6e**. Aldehydes **5d** and **5f** cyclize to give the adduct in which both substituents are equatorial since the transition state leading to the adduct in which both substituents are axial is very hindered.

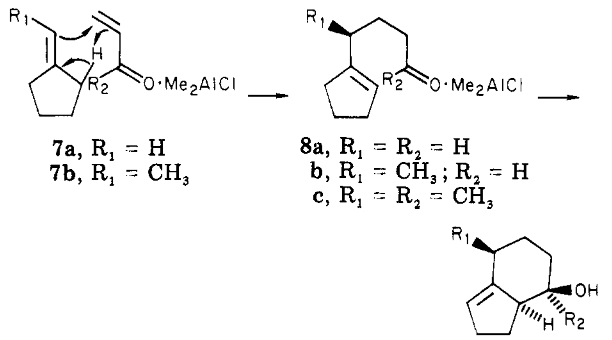


4 **5** **6**

a, $R_1 = R_2 = H$
b, $R_1 = H$, $R_2 = CH_3$
c, $R_1 = \alpha\text{-}CH_3$, $R_2 = H$
d, $R_1 = \beta\text{-}CH_3$, $R_2 = H$
e, $R_1 = \alpha\text{-Br}$, $R_2 = H$
f, $R_1 = \beta\text{-Br}$, $R_2 = H$
g, $R_1 = H$, $R_2 = CH_3$, 4α-CH_3

MVK and **4** (25 °C, 1 h) give 61% of **6b**, 4% of **6g**, 6% of a cyclobutane resulting from formal 2 + 2 cycloaddition and 9% of 5-cyclohexyl-3-hexen-2-one. The latter two products are probably formed from a zwitterionic intermediate via collapse to the cyclobutane and two 1,2-hydride shifts to give the α,β-unsaturated ketone.[10,14,15]

Methylenecyclopentane (**7a**), acrolein, and Me_2AlCl (0 °C, 20 min) give a 38% yield of **9a** (mp 41.5–42.5 °C) while ethylidenecyclopentane (**7b**), acrolein, and Me_2AlCl (0 °C, 2 h) give a 72% yield of **9b** (mp 47–48 °C). Reaction of **7b**, MVK, and Me_2AlCl at −78 °C (30 min) gives a 65% yield of **8c**. At 25 °C (30 min) 51% of **9c** is formed along with 2% of 5-cyclopentyl-3-hexene-2-one.

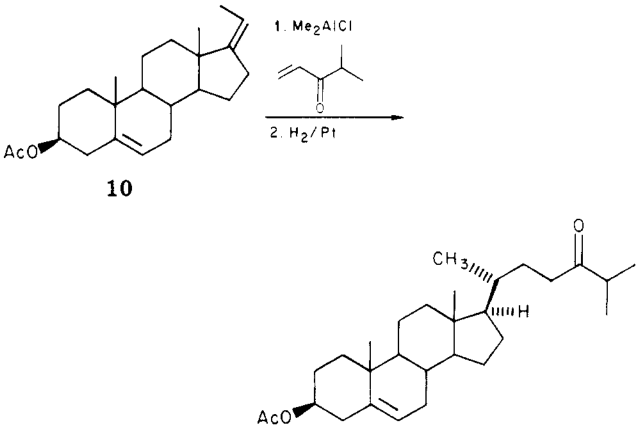


7a, $R_1 = H$
7b, $R_1 = CH_3$

8a, $R_1 = R_2 = H$
b, $R_1 = CH_3$; $R_2 = H$
c, $R_1 = R_2 = CH_3$

9a, $R_1 = R_2 = H$
b, $R_1 = CH_3$; $R_2 = H$
c, $R_1 = R_2 = CH_3$

24-Oxocholesteryl acetate (**11**) was synthesized from $\Delta^{5,17(20)}$-(*Z*)-pregnadien-3β-yl acetate (**10**) by reaction with isopropyl vinyl ketone[16] and Me_2AlCl (25 °C, 2 h) to give 46% of the ene adduct with 20-*S* stereochemistry, followed by hydrogenation of the Δ^{16} double bond of the ene adduct over Pt/C(80%).[17]



10

11

This procedure offers an attractive alternative to present annelation procedures since it allows the introduction of a variety of substituents on the newly formed cyclohexanol with control of stereochemistry.

Acknowledgment. This work was supported by the National Institutes of Health and Mobil Foundation. We thank Michael Karras for carrying out preliminary experiments.

Registry No. **1**, 1192-37-6; **2b**, 80376-43-8; **3a**, 80376-44-9; **3b**, 80376-45-0; **3c**, 80376-46-1; **3d**, 80376-47-2; **3e**, 80376-48-3; **3f**, 80387-11-7; **4**, 1003-64-1; **5c**, 80376-49-4; **5d**, 80376-50-7; **5f**, 80376-51-8; **6a**, 80376-52-9; **6b**, 80376-53-0; **6d**, 80376-54-1; **6e**, 80376-55-2; **6f**, 80376-56-3; **6g**, 80376-57-4; **7a**, 1528-30-9; **7b**, 2146-37-4; **8c**, 80376-58-5; **9a**, 80376-59-6; **9b**, 80376-60-9; **9c**, 80376-61-0; **10**, 1167-33-5; **11**, 20981-59-3; acrolein, 107-02-8; methyl vinyl ketone, 78-94-4; methacrolein, 78-85-3; α-bromoacrolein, 14925-39-4; cyclobutane, 287-23-0; 5-cyclohexyl-3-hexen-2-one, 80376-62-1; isopropyl vinyl ketone, 1606-47-9; 3β-acetoxy-5,16-cholestadien-24-one, 80376-63-2;

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(11) In addition, 2% of a cyclobutane and 21% of 1-(α-bromovinyl)-2-(1-cyclohexen-1-yl)ethanol, resulting from the carbonyl group acting as the enophile, were isolated.

(12) Morrison, J. D.; Mosher, H. S. "Asymmetric Organic Reactions"; American Chemical Society: Washington, DC, 1976; pp 98–100.

(13) Duncia, J. V.; Lansbury, P. T., Jr.; Miller, T.; Snider, B. B. *J. Am. Chem. Soc.* **1981**, manuscript submitted.

(14) Snider, B. B.; Rodini, D. J.; van Straten, J. *J. Am. Chem. Soc.* **1980**, *102*, 5872.

(15) The formation of these side products suggests that the first ene reaction is stepwise and not concerted. The second ene reaction is either concerted or stepwise with either intermolecular proton transfer or transfer of the proton directly to the methyl group of Me_2AlCl through an eight-membered-ring transition state since the proton is too far from the oxygen to be transferred directly.

(16) Seguchi, K.; Sera, A.; Otsuki, Y.; Maruyama, K. *Bull Chem. Soc. Jpn.* **1975**, *48*, 3641.

(17) For the preparation of **10**, a discussion of the stereochemistry at C-20 introduced in the ene reaction and the hydrogenation of the Δ^{16} double bond, see: Batcho, A. D.; Berger, D. E.; Uskoković, M. R.; Snider, B. B. *J. Am. Chem. Soc.* **1981**, *102*, 1293. Dauben, W. G.; Brookhart, T. *Ibid.* **1981**, *103*, 237.

(18) Fellow of the Alfred P. Sloan Foundation, 1979–1983. Address correspondence to Department of Chemistry, Brandeis University, Waltham, MA 02254.

1-(α-bromovinyl)-2-(1-cyclohexen-1-yl)ethanol, 80376-64-3.

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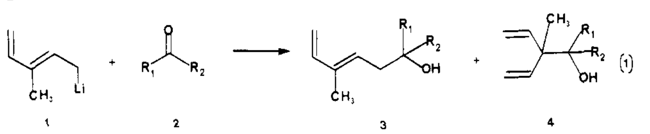
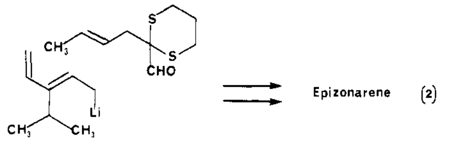
Received November 17, 1981

Acyl Silanes as Sterically Hindered Aldehydes: Additions, Oxidations, and Desilylations

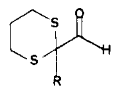
Summary: Acyl trimethylsilanes can be used as sterically hindered synthons for aldehydes, whereby the trimethylsilyl group is removed via a Brook rearrangement.

Sir: In connection with our studies of the pentadienyl anion pathway[1] to intramolecular Diels–Alder reactions we have examined several factors which control the regioisomer distributions of **3** and **4** (eq 1): (1) kinetic vs. thermodynamic control,[2] (2) solvent and cation effects,[3] and (3) steric effects. The amount of desired 1,3-diene (**3**) was usually greatest when the substrate was hindered (i.e., **2**, R_1 and R_2 large). We required a method, however, to cause an aldehyde to *temporarily* appear more hindered to the approach of an organometallic reagent (**1**). After the desired 1,3-diene was formed, the steric "blocking group" must be removed. Thus we used for this purpose a dithiane carboxaldehyde **5** in a synthesis of epizonarene (eq 2). The bulky 1,3-dithiane group could subsequently be removed with Raney nickel.

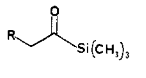




In this paper we discuss application of acyl silanes[4] such as **6a** or **6b** as sterically hindered aldehyde equivalents.



5

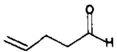
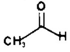
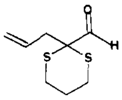
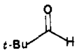
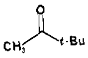
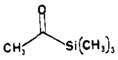
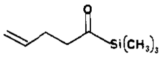


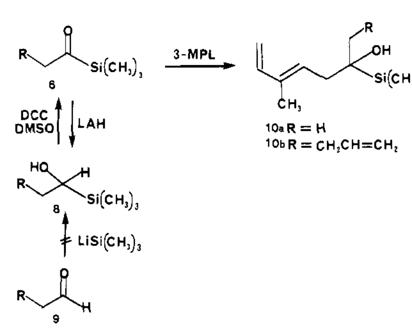
6a R = H
6b R = $CH_2CH{=}CH_2$

7a R = H
7b R = $CH_2CH{=}CH_2$

Acyl silanes **6a** or **6b** were prepared by hydrolysis[5] of the corresponding thioketals **7a** and **7b**. Acyl silanes **6a** and **6b** are stable to distillation and can be chromatographed. Compound **6b** was reduced with $LiAlH_4$ in ether to give the silyl carbinol **8**. Although we were able to oxidize **8** back to the ketone using DCC/Me_2SO methods,[6] we were not able to prepare **8** via addition of Me_3SiLi[7] to aldehyde **9**.

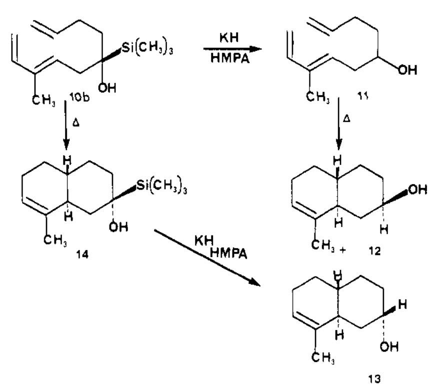
Table I. Steric Effects on the Regiochemistry of Additions of (3-Methylpentadienyl)lithium in THF (eq 1)

entry	compd 2	ratio 3/4, %
1		21/73
2		25/73
3		88/12
4		85/15
5		100/0
6		100/0
7		100/0



When 3-MPL (**1**, (3-methylpentadienyl)lithium) is allowed to react with **6a** or **6b**, only the conjugated isomers **10a** or **10b** are formed. The relative steric bulk of the Me_3Si group with respect to carbonyl additions can be seen from the regioisomer ratios in Table I. Analogy to a *tert*-butyl group seems reasonable.

The Me_3Si group, having served its purpose, could be removed by treatment of the alcohol with KH in HMPA.[8]



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(1) (a) Wilson, S. R.; Mao, D. T. *J. Am. Chem. Soc.* **1978**, *100*, 6289–6291. (b) Wilson, S. R.; Mao, D. T. *J. Org. Chem.* **1979**, *44*, 3093–3094.

(2) Wilson, S. R.; Mao, D. T.; Jernberg, K. M.; Ezmirly, S. T. *Tetrahedron Lett.* **1977**, 2559–2562.

(3) Wilson, S. R.; Misra, R. N. *J. Org. Chem.* **1980**, *45*, 5079–5081.

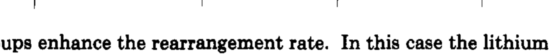
(4) Reich, H. J.; Rusek, J. J.; Olson, R. E. *J. Am. Chem. Soc.* **1979**, *101*, 2225–2227.

(5) (a) Brook, A. G.; Duff, J. M.; Jones, P. F.; Davis, N. R. *J. Am. Chem. Soc.* **1967**, *89*, 431–434. (b) Corey, E. J.; Seebach, D.; Freedman, R. *J. Am. Chem. Soc.* **1967**, *89*, 431–436.

(6) Brook, A. G. *Adv. Organomet. Chem.* **1968**, *7*, 96–155.

(7) Still, W. C. *J. Org. Chem.* **1976**, *41*, 3063–3064.

(8) The Brook arrangement has been observed for aryl-substituted α-hydroxy silanes as well as those where R = alkyl,[9] vinyl,[10] or acetylene:[11] Brook, A. G. *Acc. Chem. Res.* **1974**, *7*, 77–84. In general, anion stabilizing



R groups enhance the rearrangement rate. In this case the lithium salt of **10a** is stable, whereas the potassium salt in HMPA or in the presence of 18-crown-6 rearranges.

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