Pergamon

Tetrahedron, Vol. 53, No. 42, pp. 14235-14246, 1997

0040-4020/97 $17.00 + 0.00

PII: S0040-4020(97)00952-6

Synthesis of a *cis*-5-Cyclodecenone and Cis Fused Hydronaphthalenols through Control of the Stereochemistry of the Oxy-Cope Rearrangement with the Tri-*n*-propylsilyl Substituent

Yongliang Chu and David Colclough
Department of Chemistry and Biochemistry, Box 19065, The University of Texas at Arlington, Arlington, Texas 76019

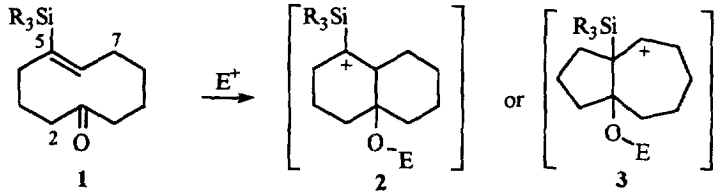
David Hotchkin, Myla Tuazon, and James B. White*
Division of Natural Science, Pepperdine University, Malibu, California 90263

Abstract: In the course of preparing a trimethylsilyl substituted 5-cyclodecenone through anionic oxy-Cope rearrangement of a *trans*-1,2-divinylcyclohexanol, it was discovered that the silyl substituent in the divinylcyclohexanol is positioned so that it destabilizes [3,3]-sigmatropic rearrangement through the normally observed chair-like transition state. In the case of the tri-*n*-propylsilyl derivative, oxy-Cope rearrangement was observed to take place exclusively through the boat-like transition state to give (*E*)-5-(tri-*n*-propylsilyl)-5-cyclodecenone with the cis double bond with respect to the ring. Acid-induced transannular cyclization of the *E* isomer led to 1,6-cyclization and generation of the cis-fused hydronaphthalenol.

INTRODUCTION

In previous work we have shown that the stereochemistry of transannular 1,5-cyclization of 5-cyclodecenones can be controlled to give either the cis or trans fused hydroazulenol via incorporation of a silyl[1] or stannyl[2,3] substituent at C7 of the ten-membered ring. We have also demonstrated that the stereochemistry of the acid-induced 1,6-cyclization of 5-cyclodecenone is dependent on the alkene geometry: the cis alkene leads to the cis ring fusion and the trans alkene leads to the trans ring fusion.[4] However, given that only *trans*-5-cyclodecenones can be readily prepared, only trans fused hydronaphthalenols are readily available from divinylcyclohexanols via sequential oxy-Cope rearrangement/transannular 1,6-cyclization. Herein we report a serendipitous discovery of a potentially general route for preparing *cis*-5-cyclodecenones and, through their cyclizations, cis fused hydronaphthalenols.

We began this study by considering the cyclization of 5-cyclodecenones functionalized with a vinylsilane moiety, e.g. **1**. For vinylsilane **1**, acid-induced cyclization could lead to either 1,6-cyclization and the secondary and α-silyl octahydronaphthalene carbocation **2**, or 1,5-cyclization and the secondary and β-silyl hydroazulene carbocation **3** (equation 1). It was not clear which carbocation would be favored as both should be relatively stabile, although the transition state leading to the hydroazulene carbocation **3** might be higher in energy as it involves C-C bond formation with the more hindered carbon of the alkene. Herein we report our work on the synthesis of 5-silyl substituted 5-cyclodecenones **1** and their transannular cyclizations.[5]

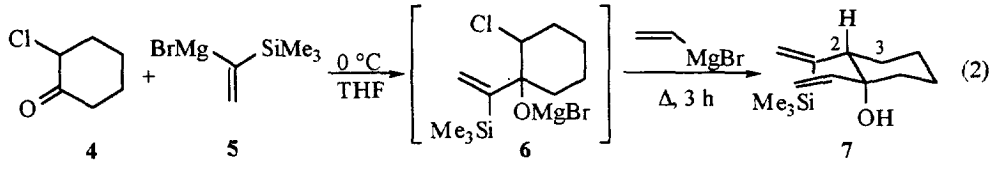


1 **2** **3** (1)

jwhite@pepperdine.edu

RESULTS AND DISCUSSION

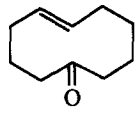
Synthesis and Cyclizations of (E)- and (Z)-5-(Trimethylsilyl)-5-cyclodecenones. The divinylcyclohexanol precursors to vinylsilanes **1** were prepared from commercially available 2-chlorocyclohexanone (**4**), using a standard methodology that involves sequential addition of two different vinyl Grignard reagents (equation 2).[6-9] Slow addition of one equivalent of 1-(trimethylsilyl)vinylmagnesium bromide (**5**)[10] in THF at 0 °C gave the intermediate **6**. Heating of this intermediate in the presence of excess vinylmagnesium bromide led to the expected pinacol-like rearrangement to give an α-vinyl ketone intermediate that reacts in situ with the second Grignard reagent to give the divinylcyclohexanol 7. The intermediate chlorohydrin from protonation of **6** was isolated when the reaction was worked-up after the first Grignard addition.



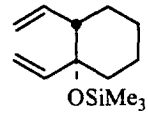
4 **5** **6** **7** (2)

The equatorial position of the trimethylsilylvinyl group of 7 is apparent from the vicinal coupling constants between the allylic hydrogen on C2 of the ring and the hydrogens on C3 (12.3 and 3.2 Hz), which are consistent with the C2 hydrogen being axial and having an axial-axial and axial-equatorial relationship with the C3 hydrogens. The assumption of a trans relationship between the two vinyl substituents of 7 is based on the general observation that nucleophiles add to 2-substituted cyclohexanones from the equatorial face.[11]

The anionic oxy-Cope rearrangement of divinylcyclohexanol 7 proved both troublesome and surprising. When treated with 18-crown-6 and an excess of potassium hydride (KH) in dimethoxyethane (DME) at room temperature, the divinylcyclohexanol 7 rearranged with loss of the TMS group and gave *trans*-5-cyclodecenone (**8**) in 55% yield. Given that when the solvent was changed from DME to diethyl ether, the TMS ether **9** was isolated, it seems likely that the TMS is migrating from the vinyl substituent to the oxyanion prior to [3,3]-sigmatropic rearrangement. Such 1,4 C(sp^2) → O silyl migrations have precedents,[12] as does the oxy-Cope rearrangement of the silyl ether of a substituted 1,2-divinylcyclohexanol under similar conditions.[13] The facility with which the TMS group in *trans*-1,2-divinylcyclohexanol 7 migrates presumably reflects the proximity of the TMS group to the oxyanion when the two vinyl appendages adopt the chair-like conformation through which the oxy-Cope rearrangement normally proceeds in such systems. The conversion of 7 into **9** also confirms the assignment of stereochemistry of 7.

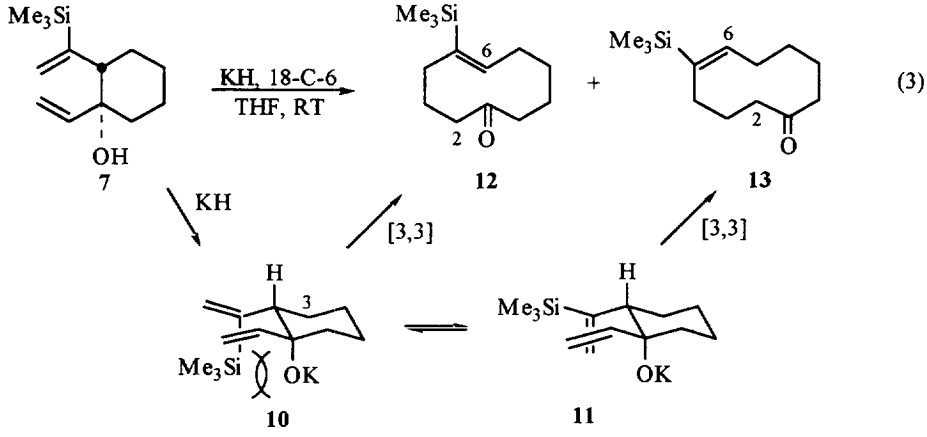


8



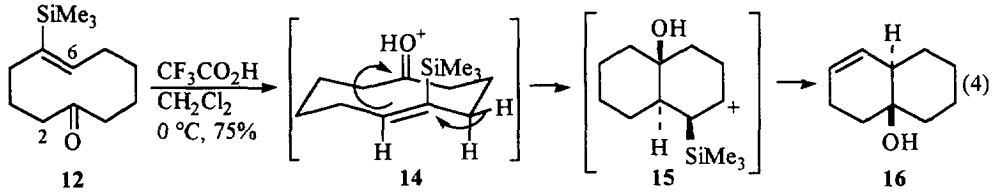
9

In attempting to effect oxy-Cope rearrangement without 1,4 C(sp^2) → O silyl migration, a variety of solvents, including pentane with and without added 18-crown-6, and bases such as sodium hydride and potassium hexamethyldisilazide (KHMDS) were used, but most conditions gave poor results. Oxy-Cope rearrangement without migration of the silyl group was best carried out with an excess of KH in the presence of 18-crown-6 (2 equiv) in THF at room temperature (equation 3). Given that all previous examples of oxy-Cope rearrangements of *trans*-1,2-divinylcyclohexanols have led exclusively to the 5-cyclodecenone with a trans double bond with respect to the ten-membered ring, we were surprised to isolate an approximately 1:1 mixture of both alkene isomers of 5-(trimethylsilyl)-5-cyclodecenone, **12** and **13**, in a combined yield of 48%. The two alkenes have nearly identical R_f values on TLC in hexane/ethyl acetate mixtures, but can be separated by HPLC. The *E* isomer **13** (cis double bond with respect to the ring) most likely arises from rearrangement through a transition state wherein the six carbon atoms comprising the four alkene carbons and C1 and C2 of the cyclohexane ring **7** adopt a boat-like conformation **11**. Apparently the chair-like transition state, which leads to the *Z* isomer **12** (trans double bond with respect to the ring), is sufficiently destabilized by the 1,3-pseudodiaxial interactions between the TMS substituent and the oxyanion (and possibly also between the TMS substituent with the axial hydrogen on C3 of **10**) to make the usually higher in energy boat-like transition state competitive.

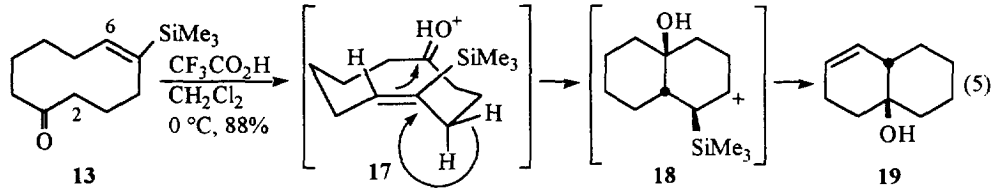


The tentative assignments[14] of alkene stereochemistry for 5-cyclodecenones **12** and **13** were confirmed through their acid-catalyzed cyclizations. We have previously demonstrated in the parent systems that 1,6-cyclization of *trans*-5-cyclodecenone leads to the trans fused hydronaphthalenol, while 1,6-cyclization of *cis*-5-cyclodecenone leads to the cis fused hydronaphthalenol.[4] Reaction of 5-cyclodecenone **12** with either a protic acid (CF_3CO_2H, CH_2Cl_2, 0 °C) or a Lewis acid ($SnCl_4$, CH_2Cl_2, -78 °C) led cleanly to the *trans*-hydronaphthalenol **16**; similar treatment of 5-cyclodecenone **13** led exclusively to the corresponding *cis*-hydronaphthalenol **19** (equations 4 and 5). No hydroazulenol products from 1,5-cyclization were observed in either reaction. It should be noted that (*E*)-5-(trimethylsilyl)-5-cyclodecenone (**13**) cyclizes much more readily than its parent compound, *cis*-5-cyclodecenone, indicating that while the TMS group does not alter the stereo- or regiochemistry of the

reaction, it does aid cyclization. The alkene position of the products can be explained by 1,6-cyclization taking place with concomitant hydride migration, i.e. **14** → **15** and **17** → **18**,[15] to give the β-silyl carbocations **15** and **18**. β-Elimination of the silyl group would then lead to the observed products **16** and **19**. (*E*)-5-cyclodecenone **13** does not cyclize in the presence of either SmI_2 or Na/naphthalene, conditions which induce cyclization of *cis*-5-cyclodecenone itself.[4]

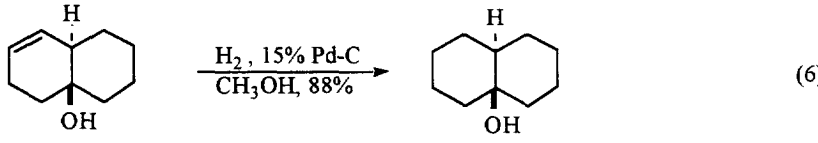


12 **14** **15** **16**

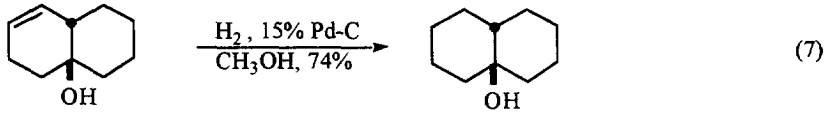


13 **17** **18** **19**

The stereochemisty of the ring fusions of *cis*- and *trans*-octahydronaphthalenols **16** and **19** were established by alkene reduction. The use of diimide ($KO_2CN{=}NCO_2K$/AcOH/CH_3OH), which successfully reduced similar double bonds in hydroazulenols,[1] failed, but catalytic hydrogenation (H_2, 15% Pd-C, CH_3OH)[16] gave the known hydronaphthalenols **20** and **21**.[17]



16 **20**



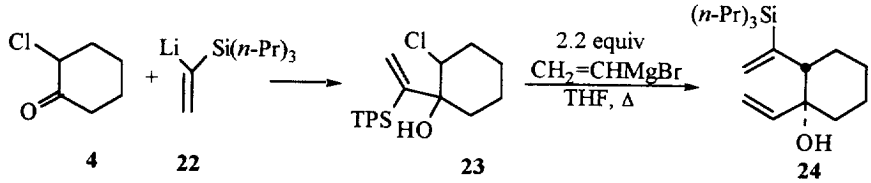
19 **21**

Synthesis and Cyclization of (Z)-5-Tri-(n-propylsilyl)-5-cyclodecenone. If steric interactions are responsible for making the boat-like transition state competitive with the chair-like transition state in the anionic oxy-Cope rearrangement of divinylcyclohexanol **7**, then a more hindered silyl group should further favor the boat-like transition state, leading to more of the *cis*-5-cyclodecenone. To this end, the triethylsilyl and tri-*n*-propylsilyl (TPS) analogs of **7** were prepared. The triethylsilyl derivative proved

difficult to make and rearrange, but the tri-*n*-propylsilyl analog **24** provided results that support the proposition that steric interactions involving the silyl substituent are altering the course of the oxy-Cope rearrangement.

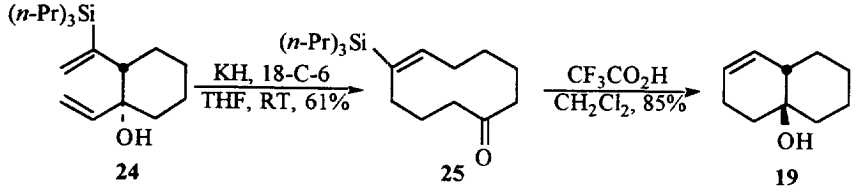
The requisite tri-*n*-propylvinylsilane[18] was prepared from trichlorovinylsilane and a slight excess of three equivalents of *n*-propylmagnesium bromide (Et_2O, Δ, 8 h, 62%). Tri-*n*-propylvinylsilane was converted into (1-bromovinyl)tri-*n*-propylsilane via the same bromination-dehydrobromination procedure used to prepare (1-bromovinyl)trimethylsilane,[10] but unlike the TMS vinyl bromide, which easily forms the Grignard reagent, the TPS vinyl bromide proved resistant to Grignard formation under a variety of conditions. However, (1-bromovinyl)tri-*n*-propylsilane did react with two equivalents of *t*-butyllithium at -78 °C, as demonstrated by quenching of the intermediate vinyllithium **22** with CH_3OH to give the debrominated product, tri-*n*-propylvinylsilane.

When a very dilute solution of the lithium reagent **22** was added to 2-chlorocyclohexanone (**4**) at -78 °C, alcohol **23** was obtained in 88% after flash chromatography. The order of addition is important as addition of the ketone to the vinyllithium reagent leads to a gross mixture of products. It also should be noted that the lithium alkoxide intermediate would not undergo in situ pinacol-like rearrangement in the presence of added vinylmagnesium bromide (cf. **6** → **7**). Instead, it proved necessary to isolate the chlorohydrin **23** and then react it with two equivalents of vinylmagnesium bromide, one to deprotonate the alcohol and induce 1,2-vinyl migration to give the α-vinyl ketone, which then underwent addition with the second equivalent of vinylmagnesium bromide to give the *trans*-1,2-divinylcyclohexan-1-ol **24** (equation 8). The coupling constants of the C2 hydrogen on the cyclohexane ring (J=12.6, 3.5 Hz) in the ^1H NMR spectrum indicate that the vinyl group at C2 of **24** is equatorial. Equatorial addition of vinylmagnesium bromide to the intermediate ketone is assumed, leading to a trans relationship between the two vinyl groups.[11]



4 **22** **23** **24** (8)

Treatment of divinylcyclohexanol **24** with excess KH and two equivalents of 18-crown-6 in THF at room temperature led to exclusive formation of (*E*)-5-(tri-*n*-propylsilyl)-5-cyclodecenone (**25**). At least for this particular substrate, it appears that the TPS group is large enough to channel all of the [3,3]-sigmatropic rearrangement through the reaction pathway with the boat-like transition state. When 5-cyclodecenone **25** was treated with trifluoroacetic acid, it, like its TMS analog **13**, gave exclusively the cis fused hydronaphthalenol **19** in good yield (equation 9).



24 **25** **19** (9)

Prior to this work, *cis*-5-cyclodecenones have not been observed as products in the oxy-Cope rearrangements of *trans*-1,2-divinylcyclohexanols; in order to make a *cis*-5-cyclodecenone via oxy-Cope rearrangement you need to start with a *cis*-1,2-divinylcyclohexanol.[19] Given that 1,2-divinyclohexanols are generally made by addition of a vinyl anion to an α-vinylcyclohexanone, which leads to a *trans*-1,2-divinylcyclohexanol, in practice only 5-cyclodecenones with a trans double bond are accessible by this methodology. Rearrangement of divinylcyclohexanol **24** to give cyclodecenone **25** is quite remarkable as it shows that both *trans*- and *cis*-5-cyclodecenones can be made from readily available *trans*-1,2-divinylcyclohexanols.

CONCLUSION

We have found that the reaction pathway of the anionic oxy-Cope rearrangement of *trans*-divinylcyclohexanols can be altered from its normally observed chair-like transition state so as to favor a boat-like transition state. To the best of our knowledge, **24** → **25** is the first and only example of an oxy-Cope rearrangement of a *trans*-1,2-divinylcyclohexanol that leads exclusively to a *cis*-5-cyclodecenone. In this rearrangement the TPS group serves several purposes: it is more resistant than the TMS group in avoiding undesired 1,4 C → O silyl migration and it alters the normally observed stereochemistry of the oxy-Cope rearrangement of *trans*-1,2-divinylcyclohexanols. Furthermore, the alkene of the 5-silyl substituted *cis*-cyclodecenone product is significantly more reactive as a nucleophile in its acid-catalyzed transannular 1,6-cyclization than is the unsubstituted cis alkene.

The incorporation of a TPS group into the synthesis of *trans*-1,2-divinylcyclohexanol represents a potentially general approach for annulation of cyclohexane derivatives to prepare cis fused hydronaphthalenols via oxy-Cope rearrangement/transannular cyclization. Studies of the use of the TPS to control the stereochemistry of oxy-Cope reactions in general, and the regiochemistry of the cyclization of 5-cyclodecenones in particular are in progress and will be reported in due course.

Acknowledgment. We thank the National Institutes of Health (GM44170-01), the Robert A. Welch Foundation, the Department of Chemistry and Biochemistry of The University of Texas at Arlington, and Pepperdine University for their generous support of this research, and Bela Derecskie for obtaining combustion analysis data. Purchase of the C,H,N analyzer through a grant from the Defense Advanced Research Projects Agency monitored by the Office of Naval Research is gratefully acknowledged. We also wish to thank the Parsons Foundation for funding both the purchase of a Bruker Avance DPX200 and a Nicolet Impact 400D IR spectrophotometer, and the construction of an organic synthesis laboratory.

EXPERIMENTAL SECTION

General. Unless otherwise noted, all starting materials were obtained from commercial suppliers and used without further purification. Diethyl ether (Et_2O) and tetrahydrofuran (THF) were distilled under nitrogen from sodium/benzophenone. Dichloromethane was distilled from P_2O_5. Reactions involving organometallic reagents were carried out under argon (balloon) in oven-dried or flame-dried glassware. Solutions of *n*-butyllithium in hexanes were titrated with 2,5-dimethoxybenzyl alcohol.[22] Unless otherwise noted, reaction mixtures were stirred using magnetic

stir bars. The organic phases from extractions were concentrated with a rotary evaporator. Reactions were monitored by thin-layer chromatography using Whatman precoated glass plates of 250 μm thickness silica gel with a fluorescent indicator. TLC plates were visualized by UV lamp and by staining with *p*-anisaldehyde/H_2SO_4/CH_3CO_2H/CH_3CH_2OH and heating on a hot plate. Flash chromatography was carried out using silica gel (32-63 micron, 60 Å pore) purchased from Scientific Adsorbents, Inc., Atlanta, Georgia. HPLC was performed with a Waters Model 590 pump (flow rate of 20 mL/min) and a Waters Differential Refractometer R403 using a Rainin Dynamax Macro-HPLC silica gel column (21.4-mm i.d.x 25-cm length). IR spectra were recorded with NaCl salt plates on either a Perkin-Elmer 1310 IR Spectrophotometer or a Nicolet Impact 400D. ^1H NMR spectra were recorded as solutions in either $CDCl_3$ or C_6D_6, at 200 MHz on either a Nicolet NT-200WB or a Bruker Avance DPX200. Chemical shifts are expressed in parts per million (δ units) relative to internal tetramethylsilane (δ 0.0) or $CHCl_3$ (δ 7.26). Data are reported as follows: chemical shift, multiplicity (s=singlet, d=doublet, t=triplet, q=quartet, m=multiplet, br=broad, gem=geminal), coupling constant(s) in Hz, and integration. ^{13}C NMR spectra were recorded as solutions using a Nicolet NT-200 WB (50.3 MHz) instrument as noted and the chemical shifts reported in parts per million (δ units) relative to the center peak of $CDCl_3$ (δ 77.0) or C_6D_6 (δ 128.0). Elemental analyses were performed on a Perkin-Elmer 2400 C,H,N analyzer. RT stands for room temperature, h for hour, min for minute, EtOAc for ethyl acetate, sat. for saturated solution, RBF for round bottom flask, and *t*-BuLi for *tert*-butyllithium.

(1R,2R*)-1-Ethenyl-2-[1-(trimethylsilyl)ethenyl]cyclohexan-1-ol (7)*

A solution of (1-bromovinyl)trimethylsilane[10] (12.5 g, 69.8 mmol) in THF (20 mL) was added to Mg turnings (1.70 g, 70.0 mg-atom) suspended in THF (5 mL). The reaction mixture was heated at reflux for 1 h before being cooled to 0 °C. This solution then was diluted in THF (20 mL) and added dropwise via cannula to a solution of 2-chlorocyclohexanone (9.28 g, 70.0 mmol) in THF (10 mL) at 0 °C. After it was determined by TLC that the ketone was consumed, the reaction mixture was warmed to RT and vinylmagnesium bromide (115 mL, 1.0 M in THF, 0.12 mole, 1.5 equiv) was added. This mixture was heated at reflux for 2.5 h before being cooled to RT, quenched with 10% NH_4Cl (50 mL) and extracted with Et_2O (3x50 mL). The combined organic layers were washed with sat. NaCl (50 mL), dried over anhydrous $MgSO_4$, filtered and concentrated. The residue was purified by flash chromatography (hexane/EtOAc=30:1) to give 6.27 g (27.9 mmol, 40% yield) of 7 as a pale yellow oil. IR (neat, cm^{-1}) 3550, 3090, 3050, 2970, 2860, 1640, 1440, 1245, 960, 910, 840; ^1H NMR (200 MHz, $CDCl_3$) δ 5.84 (d, J=2.4 Hz (gem), 1H), 5.80 (dd, J=17.2 (trans), 10.6 (cis) Hz, 1H), 5.51 (d, J=2.4 Hz (gem), 1H), 5.06 (dd, J=17.1 (trans), 1.0 (gem) Hz, 1H), 4.97 (dd, J=10.6 (cis), 1.0 (gem) Hz , 1H), 2.30 (dd, J=12.2, 3.2 Hz, 1H), 1.83-1.20 (m, 10H), 0.05 (s, 9H); ^{13}C NMR (50.3 MHz, $CDCl_3$) δ 155.4, 146.6, 125.9, 111.0, 73.1, 48.6, 38.1, 28.7, 26.3, 21.3, -0.8. Anal. Calcd for $C_{13}H_{24}OSi$: C, 69.56; H, 10.79; Found: C, 69.41; H, 11.00.

Anionic oxy-Cope rearrangement of 7 to make 8

Potassium hydride (30% dispersion in mineral oil, 637 mg, 4.7 mmol, 5 equiv) was washed with dry hexanes (3x2.5 mL) and suspended in anhydrous DME (8 mL). A solution of 18-crown-6 (496 mg, 1.88 mmol) and 7 (210 mg, 0.940 mmol) in DME (1.5 mL) was added and the mixture was stirred at RT for 7 h. Upon cooling to 0 °C, the reaction mixture was quenched with 10% aq. NH_4Cl

solution (20 mL) and the aqueous layer extracted with Et_2O (3x20 mL). The combined organic layers were washed with sat. NaCl (30 mL), dried over anhydrous $MgSO_4$, filtered and concentrated. Purification by flash chromatography (hexane/EtOAc=25:1) gave 78 mg (0.51 mmol, 55% yield) of **8**.[4]

(Z)-5-(Trimethylsilyl)-5-cyclodecenone (12) and (E)-5-(trimethylsilyl)-5-cyclodecenone (13)

Potassium hydride (7.1 g of a 26.5 % mineral oil suspension, 47 mmol, 5 equiv) was washed with dry hexanes (3x4 mL) and suspended in anhydrous THF (40 mL). A solution of 18-crown-6 (4.9 g, 19 mmol) and 7 (2.1 g, 9.4 mmol) in THF (25 mL) was added. The reaction mixture was stirred at RT for 19 h before it was cooled to 0 °C and carefully quenched with 10% aq. NH_4Cl (30 mL). The aqueous layer was extracted with Et_2O (3x40 mL), and the combined organic layers were washed with sat. NaCl (40 mL), dried over anhydrous $MgSO_4$, filtered and concentrated. The residue was purified by flash chromatography (hexane/EtOAc=30:1) to give 1.0 g (4.5 mmol, 48% yield) of a 1:1 mixture of **12** and **13**. Compounds **12** and **13** have almost same R_f value and were separated by HPLC (hexanes/EtOAc=28:1). For **12**: IR (neat, cm^{-1}) 3020, 2960, 2900, 1710, 1610, 860, 840, 760; ^1H NMR (200 MHz , $CDCl_3$) δ 5.90 (t, J=7.2 Hz, 1H), 2.4-1.5 (m, 14H), 0.15 (s, 9H); ^{13}C NMR (50.3 MHz, $CDCl_3$) d 212.7, 142.9, 142.1, 45.8, 43.5, 39.8, 32.4, 30.1, 28.1, 22.6, 0.1. Anal. Calcd for $C_{13}H_{24}OSi$: C, 69.56; H, 10.79; Found: C, 69.42; H, 11.04. For: **13**: IR (neat, cm^{-1}) 3020, 2960, 2900, 2880, 1710, 1610, 1255, 860,840, 745; ^1H NMR (200 MHz, $CDCl_3$) δ 5.71 (t, J=7.6 Hz, 1H), 2.4-1.5 (m, 14H), 0.08 (s, 9H); ^{13}C NMR (50.3 MHz, $CDCl_3$) d 214.5, 142.0, 140.3, 45.8, 34.5, 28.5, 25.9, 25.3, 23.4, 20.9, -0.8. Anal. Calcd for $C_{13}H_{24}OSi$: C, 69.56; H, 10.79; Found: C, 69.63; H, 11.02.

(1S,6R*)-Bicyclo[4.4.0]dec-4-en-1-ol (16)*

Trifluoroacetic acid (15 mg, 0.11 mL, 1.3 mmol) was added dropwise to a solution of **12** (100 mg, 0.450 mmol) in CH_2Cl_2 (5 mL) at 0 °C . After 20 min a solution of 10% aq. NH_4Cl (15 mL) was added and the aqueous layer was extracted with CH_2Cl_2 (3x15 mL). The combined organic layers were washed with sat. NaCl (20 mL), dried over anhydrous $MgSO_4$, filtered and concentrated. The residue was purified by flash chromatography (hexane/EtOAc=25:1) to afford 50.7 mg (0.335 mmol, 74% yield) of **16** as a colorless oil. IR (neat, cm^{-1}) 3500, 3050, 2940, 2860, 1640, 1445, 1090, 895; ^1H NMR (200 MHz, $CDCl_3$) δ 5.72 (ddd, J=9.6 (cis), 6.4, 3.0 Hz, 1H), 5.29 (dd, J=9.6 (cis), 1.8 Hz, 1H), 2.14 (m, 1H), 1.8-1.3 (m, 13 H); ^{13}C NMR (50.3 MHz, $CDCl_3$) δ 129.9, 127.1, 68.5, 43.5, 37.8, 35.2, 27.2, 26.4, 22.4, 21.5. Anal. Calcd for $C_{10}H_{16}O$: C, 78.88; H, 10.63; Found: C, 79.03; H, 10.86.

Cyclization of 12 with a Lewis acid (16)

To a solution of **12** (100 mg, 0.450 mmol) in dry CH_2Cl_2 (3 mL) at -78 °C was added dropwise $SnCl_4$ (1.0 M in CH_2Cl_2, 0.55 mL, 0.55 mmol). After 20 min the Dry Ice/acetone bath was replaced by an ice/water bath and then the reaction mixture was quenched with 10% aq. NH_4Cl (8 mL). The aqueous layer was extracted with CH_2Cl_2 (3x15 mL) and the combined organic layers were washed with sat. NaCl (15 mL), dried over anhydrous $MgSO_4$, filtered and concentrated. The residue was purified by flash chromatography (hexane/EtOAc=25:1) to give 43 mg (0.28 mmol, 63% yield) of **16** as a colorless oil.

(1S,6S*)-Bicyclo[4.4.0]dec-4-en-1-ol (19)*

The procedure described for the reaction of **12** with trifluoroacetic acid was repeated with **13** (120 mg, 0.540 mmol) to give 72 mg (0.47 mmol, 88% yield) of **19** as a white solid, mp 36-37 °C. IR (neat, cm^{-1}) 3500, 3025, 2905, 2840, 1640, 1440, 1010, 940, 855; ^1H NMR (200 MHz, $CDCl_3$) δ 5.62 (dm, J=10.0 (cis) Hz, 1H), 5.15 (dm, J=10.0 (cis) Hz, 1H), 2.02 (m, 1H), 1.9-1.2 (m, 13H); ^{13}C NMR (50.3 MHz, $CDCl_3$) δ 129.5, 124.8, 69.2, 42.8, 35.4, 31.2, 30.6, 22.9, 22.6, 21.7. Anal. Calcd for $C_{10}H_{16}O$: C, 78 .88; H, 10.60; Found: C, 79.18; H, 10.88.

Cyclization of 13 with a Lewis acid (19)

The procedure described for the reaction of **12** with $SnCl_4$ was repeated with **13** (100 mg, 0.450 mmol) to give 50 mg (0.33 mmol, 74% yield) of **19** as a white solid.

trans-Bicyclo[4.4.0]decan-1-ol (20)

A mixture of **16** (72 mg, 0.47 mmol), 15% Pd on C (18 mg) and CH_3OH (3.5 mL) was stirred under 1 atmosphere of H_2 for 1.2 h. The reaction mixture was filtered and the residue washed with Et_2O (3x3 mL). After evaporation the crude product was purified by flash chromatography (hexane/EtOAc=25:1) to give 58 mg (0.38 mmol, 80% yield) of **20**.[17] The product stained very weakly on TLC plates. IR (neat, cm^{-1}) 3420, 2880, 2820, 1450, 1280, 935, 900; ^1H NMR (200 MHz, $CDCl_3$) δ 1.9-1.2 (m); ^{13}C NMR (50.3 MHz, $CDCl_3$) δ 70.2, 44.1, 39.7, 28.6, 26.2, 21.6.

cis-Bicyclo[4.4.0]decan-1-ol (21)

The hydrogenation and purification described for **16** was repeated with **19** (44 mg, 0.29 mmol) to give 29 mg (0.21 mmol, 72% yield) of **21**.[17] IR (neat, cm^{-1}) 3250, 2920, 2860, 1450, 1280, 1150, 980; ^1H NMR (200 MHz, $CDCl_3$) δ 1.8-1.1 (m); ^{13}C NMR (50.3 MHz, $CDCl_3$) δ 70.78, 41.77, 35.5 (br), 27.01, 21.9.

Tri-n-propylvinylsilane

Magnesium metal turnings (14.25 g, 0.5860 g-atom) were suspended in Et_2O (300 mL) in a 2-necked, 500 mL RBF equipped with a condenser. 1-Bromopropane (80.1 g, 0.651 mol) was added by addition funnel slowly so as to keep the reaction mixture gently boiling. After all of the magnesium was consumed, trichlorovinylsilane (30.0 g, 0.186 mol) was introduced carefully and the reaction mixture then heated at reflux for 8 h before being quenched with ice water (80 mL). The aqueous layer was extracted with Et_2O (4x100 mL), and the combined organic layers were washed with sat. NaCl (70 mL), dried over anhydrous $MgSO_4$, filtered and concentrated. The residue was distilled under reduced pressure to afford 21.3 g (0.115 mol, 62% yield) of tri-*n*-propylvinylsilane[18] as a colorless oil, bp 85.0-86.5 °C/4.4 torr (lit.[18] 73 °C/3.6 torr). IR (neat, cm^{-1}) 3050, 2940, 2870, 1450, 1400; ^1H NMR (200 MHz, $CDCl_3$) δ 6.12 (dd, J=19.2 (trans), 14.6 (cis) Hz, 1H), 5.96 (dd, J=14.8 (cis), 5.2 (gem) Hz, 1H), 5.66 (dd, J=19.0 (trans), 5.4 (gem) Hz, 1H), 1.35 (m, 6H), 0.96 (t, J=7.2 Hz, 9H), 0.58 (m, 6H); ^{13}C NMR (50.3 MHz, $CDCl_3$) δ 137.6, 131.9, 18.5, 17.4, 15.2.

1-Bromo-1-(tri-n-propylvinyl)silane

To tri-*n*-propylvinylsilane (12.0 g, 65.1 mmol) was added bromine (3.5 mL, 68 mmol) slowly at -78 °C with vigorous overhead stirring. After the addition was complete the Dry Ice/acetone bath

was exchanged for an ice/water bath. After 20 min diethylamine (40.5 mL, 0.391 mol) was introduced slowly. The ice bath was removed and the reaction mixture heated at reflux for 10 h. Upon cooling to RT, the reaction mixture was quenched with water (50 mL) and the aqueous layer extracted with Et_2O (3x50 mL). The combined organic layers were washed with 10% HCl solution several times until the pH of the aqueous layer was about 2. The combined organic layers were then washed with sat. NaCl (60 mL), dried over anhydrous $MgSO_4$, filtered and concentrated. The residue was distilled under reduced pressure (bp 94 °C/1.8 torr) to give 9.8 g (37 mmol, 57%) of 1-bromo-1-(tri-*n*-propylvinyl)silane as a colorless oil. IR (neat, cm^{-1}) 3050, 2955, 2880, 1590, 1450, 1100, 1000, 910; ^1H NMR (200 MHz, $CDCl_3$) δ 6.33 (d, J=1.8 Hz (gem), 1H), 6.17 (d, J=1.6 Hz (gem), 1H), 1.35 (m, 6H), 0.97 (t, J=7.1 Hz, 9H), 0.69 (m, 6H); ^{13}C NMR (50.3 MHz, $CDCl_3$) δ 137.0, 130.6, 18.3, 17.1, 14.3.

(1R,2R*)-1-[(1-Tri-n-propylsilyl)ethenyl]-2-chlorocyclohexan-1-ol (23)*

t-BuLi (13 mmol, 8.1 mL, 1.6 M in pentane) was added dropwise over a 1 h period to a solution of 1-bromo-1-(tri-*n*-propylvinyl)silane (1.56 g, 5.92 mmol) in THF (60 mL) at -78 °C. The reaction mixture changed from colorless to bright yellow. After 20 min the reaction mixture was transferred slowly by syringe to a second RBF containing a solution of 2-chlorocyclohexanone (796 mg, 6.00 mmol) in THF (35 mL) at -78 °C. After an additional 10 min the mixture was allowed to warm to 0 °C, quenched with 10% NH_4Cl (40 mL) and extracted with Et_2O (3x40 mL). The combined organic layers were washed with sat. NaCl (60 mL), dried over anhydrous $MgSO_4$, filtered and concentrated. The residue was purified by flash chromatography (hexane/EtOAc=35:1) to give 1.65 g (5.21 mmol, 88% yield) of **23** as a yellow oil. IR (neat, cm^{-1}) 3540, 3040, 2910, 2840, 1440, 975, 925, 805, 730; ^1H NMR (200 MHz, $CDCl_3$) δ 5.77 (d, J=0.8 Hz (gem), 1H), 5.44 (d, J=0.8 Hz (gem), 1H), 4.23 (t, J=8.2 Hz, 1H), 2.29 (d, J=2.2 Hz, 1H), 2.05-1.20 (m, 14H), 0.96 (t, J=7.1 Hz, 9H), 0.70 (m, 6H); ^{13}C NMR (50.3 MHz, $CDCl_3$) δ 156.0, 124.6, 78.3, 67.9, 39.6, 33.0, 26.3, 20.7, 18.6, 17.4, 16.5.

(1R,2R*)-1-Ethenyl-2-[(1-tri-n-propylsilyl)ethenyl]cyclohexan-1-ol (24)*

A solution of vinylmagnesium bromide (18 mmol, 18 mL of a 1.0 M solution in THF) was added to a solution of **23** (1.65 g, 5.21 mmol) in THF (45 mL) at RT. The reaction mixture was heated at reflux for 4.5 h before being cooled to 0 °C and quenched carefully with 10% NH_4Cl (35 mL). The resulting aqueous layer was extracted with Et_2O (3x40 mL), and the combined organic layers were washed with sat. NaCl (50 mL), dried over anhydrous $MgSO_4$, filtered and concentrated. The residue was purified by flash chromatography (hexane/EtOAc=28:1) to afford 1.19 g (3.86 mmol, 74% yield) of **24** as an oil. IR (neat, cm^{-1}) 3500, 3050, 2930, 2870, 1440, 1060, 990, 970, 910, 810; ^1H NMR (200 MHz, $CDCl_3$) δ 5.91 (d, J=2.2 Hz (gem), 1H), 5.82 (dd, J=17.4 (trans), 10.6 (cis) Hz, 1H), 5.46 (d, J=2.2 Hz (gem), 1H), 5.11 (dd, J=17.4 (trans), 1.2 (gem) Hz, 1H), 4.93 (dd, J=10.6 (cis), 1.0 Hz (gem), 1H), 2.24 (dd, J=12.6 (anti), 3.5 Hz, 1H), 1.91-1.10 (m, 21H), 0.94 (t, J=6.5 Hz, 9H); ^{13}C NMR (50.3 Hz, $CDCl_3$) δ 152.9, 146.5, 126.9, 111.3, 73.3, 48.3, 38.3, 28.6, 26.4, 21.3, 18.6, 17.3, 15.2.

(Z)-5-Tri-n-propylsilyl-5-cyclodecenone (25)

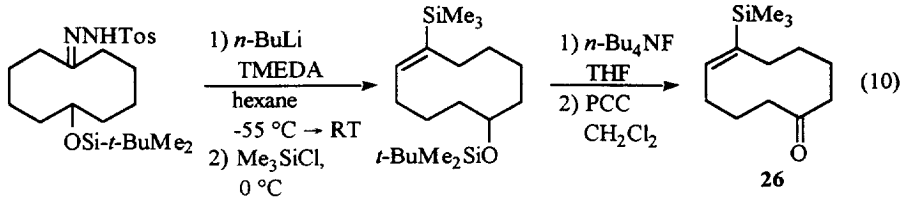
Potassium hydride (1.5 g, 11 mmol) as a 30% suspension in mineral oil was placed in a 100 mL RBF, washed with hexanes (3x5 mL) and suspended in THF (30 mL) at RT. 18-Crown-6 (1.1 g, 4.2 mmol) was added to this suspension followed by alcohol **24** (800 mg, 2.59 mmol) in THF (8 mL). After 2.5 h of stirring at RT, the flask was cooled with an ice/water bath and quenched with 10% NH_4Cl solution (25 mL). The aqueous layer was extracted with Et_2O (3x40 mL), and the combined organic layers were washed with sat. NaCl (45 mL), dried over anhydrous $MgSO_4$, filtered and concentrated. The residual oil was purified by flash chromatography (hexane/EtOAc=25:1) to afford 485 mg (1.57 mmol, 61%) of **25** as an oil. IR (neat, cm^{-1}) 2930, 2900, 2850, 1690, 1595, 1440, 1055, 995; ^1H NMR (200 MHz, $CDCl_3$) δ 5.67 (t, J=7.6 Hz, 1H), 2.50-0.52 (series of m); ^{13}C NMR (50.3 MHz, $CDCl_3$) δ 214.4, 143.2, 137.8, 45.8, 34.5, 28.6, 26.0, 25.5, 23.5, 21.0, 18.6, 17.5, 15.6. Anal. Calcd. for $C_{19}H_{36}OSi$: C, 73.95; H, 11.76; Found: C, 74.03; H, 11.54.

*Cyclization of **25** with a protic acid*

To a solution of **25** (40 mg, 0.13 mmol) in dry CH_2Cl_2 (4.5 mL) at 0 °C there was added dropwise trifluoroacetic acid (50 mL, 0.65 mmol). The reaction mixture changed from colorless to purple. After 10 min the reaction mixture was allowed to warm to RT and stirred for an additional 2 h before being diluted with CH_2Cl_2 (5 mL). The mixture then was washed with sat. Na_2CO_3 solution (10 mL) and the aqueous layer extracted with CH_2Cl_2 (3x15 mL). The combined organic layers were washed with sat. NaCl (15 mL), dried over anhydrous $MgSO_4$, filtered and concentrated. The residue was purified by flash chromatography (hexane/EtOAc=15:1) to give 17 mg (0.11 mmol, 85% yield) of **19**.

REFERENCES AND NOTES

1. Jisheng, L.; Gallardo, T.; White, J. B. *J. Org. Chem.* **1990**, *55*, 5426-5428.
2. Fan, W.; White, J. B. *Tetrahedron Lett.* **1993**, *34*, 957-960.
3. Fan, W.; White, J. B. *J. Org. Chem.* **1993**, *58*, 3557-3562.
4. Colclough, D.; White, J. B.; Smith, W. B. and Chu, Y. *J. Org. Chem.* **1993**, *58*, 6303-6313.
5. We have also prepared **26**, the *E* isomer of 6-(trimethylsiyl)-5-cyclodecenone [^{13}C NMR for **26**: (50.3 MHz, $CDCl_3$) δ 214.5, 143.1, 139.2, 46.1, 34.6, 28.2, 26.9, 24.6, 23.4, 20.5, -0.5 ppm] through modification of our method for preparing *cis*-5-cyclodecenone,[4] i.e. quenching the intermediate vinyllithium derived from the hydrazone with TMSCl instead of with CH_3OH. However, treatment of the ketone with acid (CF_3CO_2H, CH_2Cl_2, RT, two days) led to recovered starting material along with *cis*-5-cyclodecenone and the product from transannular cyclization of *cis*-5-cyclodecenone, indicating that protodesilylation is faster than cyclization for vinylsilane **26**.



6. Nishino, M; Kondo, H ; Miyake, A. *Chem. Lett.* **1973**, 667-670.
7. Kato, T.; Kondo, H.; Nishino, M.; Tanaka, M.; Hata, G.; Miyake, A. *Bull. Chem. Soc. Jpn.* **1980**, *53*, 2958-2961.
8. Holt, D. A. *Tetrahedron Lett.* **1981**, *22*, 2243-2246.
9. Wender, P. A.; Holt , D. A.; Sieburth, S. McN.; *Organic Syntheses* **1985**, *64*, 10-18.
10. Boeckman, R. K., Jr.; Blum, D. M.; Halvey, N.; Ganem, B. *Organic Syntheses* **1978**, *58*, 152-157.
11. Marvell, E. N.; Whalley, W. *Tetrahedron Lett.* **1970**, 509-512.
12. Spinazzé, P. G.; Keay, B. A. *Tetrahedron Lett.* **1989**, *30*, 1765-1768 and references therein.
13. Urabe, H. ; Kuwajima, I. *Tetrahedron Lett.* **1983**, *24*, 4241-4244.
14. Our tentative assignments of alkene geometry were based on characteristic chemical shifts we have observed in the ^{13}C NMR spectra in $CDCl_3$ of *cis*- and *trans*-5-cyclodecenones. The δ of the carbonyl carbon of cis isomers is downfield of the δ of the trans isomers (214.4-215.1 ppm versus 212.5-213.0 ppm). In addition, the cis isomers have chemical shifts at 34.6 ± 0.2 and 23.4 ± 0.2 ppm that are absent in the spectra of the trans isomers. These trends have been observed for the unsubstituted and for 5-, 6-, and 7-substituted 5-cyclodecenones.
15. We thank Professor Martin Pomerantz, Department of Chemistry and Biochemistry, The University of Texas at Arlington, for suggesting to us concurrent hydride migration with cyclization.
16. Siegel, S.; Smith, G. V. *J. Am. Chem. Soc.* **1960**, *82*, 6082-6087.
17. Molander, G. A.; Etter, J. B. *J. Org. Chem.* **1986**, *51*, 1778-1786.
18. Nagel, R.; Post, H. W. *J. Org. Chem.* **1952**, *17*, 1379-1381.
19. For examples of *cis*-1,2-divinylcyclohexanols undergoing anionic oxy-Cope rearrangement to give *cis*-5-cyclodecenones, see references 1, 20 and 21. Rearrangement of *cis*-1,2-divinylcyclohexanols can take place from either of two conformations: one in which the oxyanion is equatorial with respect to the cyclohexane ring, which leads to a *cis*-5-cyclodecenone, and one in which the oxyanion is axial, which leads to the *trans*-5-cyclodecenone. If there are no additional substituents on the cyclohexane ring, as is the case for the examples found in references 1 and 20, then anionic oxy-Cope rearrangement is observed to take place with the oxyanion in the equatorial position, which minimizes the number of axial substituents in the transition state, leading to the *cis*-5-cyclodecenone. In the one example of an anionic oxy-Cope rearrangement of a *cis*-1,2-divinylcyclohexanol with four substituents on the cyclohexane ring (reference 21), there are two substituents axial and two substituents equatorial regardless of whether the oxyanion is axial or equatorial; in this example the *cis*-1,2-divinylcyclohexanol rearranged predominantly through the pathway in which the oxyanion was axial, leading to a 97:3 ratio of the *trans*- and *cis*-5-cyclodecenones.
20. Sworin, M; Lin, K.-C. *J. Am. Chem. Soc.* **1989**, *111*, 1815-1825.
21. Clive, D. L. J.; Russell, C. G.; Suri, S. C. *J. Org. Chem.* **1982**, *47*, 1632-1641.
22. Winkle, M. R.; Lansinger, J. M.; Ronald, R. C. *J. Chem. Soc., Chem. Commun.* **1980**, 87-88.

(*Received in USA* 25 *June* 1997; *accepted* 14 *August* 1997)