Sequential Cyclization/Silylation of Enynes Catalyzed by an Organoyttrium Complex

Gary A. Molander* and William H. Retsch

Contribution from the Department of Chemistry and Biochemistry, University of Colorado, Boulder, Colorado 80309-0215

Received May 12, 1997[⊗]

Abstract: The organoyttrium complex $Cp^*_2YCH_3 \cdot THF$ ($Cp^* = C_5Me_5$) has been shown to be an effective precatalyst for the selective sequential cyclization/silylation of 1,6- and 1,7-enynes. The catalyst's ability to insert the alkyne in preference to the alkene in a regioselective manner, combined with the high diastereoselectivity of the insertion process, yields a product with only one stereochemistry about the exocyclic olefin. The reaction proceeds under extremely mild conditions with short reaction times. Cyclization of enynes functionalized in the allylic position affords silylated carbocycles with high diastereoselectivities and excellent yields.

Introduction

The use of organolanthanide and group 3 and 4 organometallic complexes as hydrosilylation catalysts of alkenes and dienes has been well established,[1] but the reactivity of silanes with enynes and other polyunsaturated systems in the presence of these various catalysts has been relatively unexplored.[2] Initial reports that organolanthanides could catalyze the regioselective hydrosilylation of terminal alkenes were soon followed by accounts of chemoselective reactions of dienes that utilized similar but more reactive organoyttrium complexes.[1c,d] Previous investigations have demonstrated that internal alkynes can also be catalytically hydrosilylated using an organoyttrium catalyst to prepare (*E*)-alkenylsilanes in a regioselective and stereoselective manner.[2a]

Organoyttrium and related catalysts have been utilized for selective carbon−carbon bond formation as well.[1e−i,3] Catalytic cyclizations of simple dienes using a variety of lanthanide and group 3 and group 4 metallocene complexes have demonstrated the ability to generate carbocycles through intramolecular insertion of a terminal olefin in conjunction with a variety of termination steps.[1e−i,3] Examples of previously reported cyclization reactions of dienes have taken advantage of the chemoselectivity of organoyttrium catalysts to cyclize substituted dienes selectively.[1e,g,i] The integration of a silylation in the termination step of this reaction provides additional functionality in the carbocyclic product.

The combination of these reports prompted us to investigate the extension of this chemistry to cyclization/silylation reactions of enynes. The focus of these efforts was to establish a protocol for this transformation utilizing a highly selective organoyttrium catalyst. Catalytic enyne cyclizations have been accomplished using a variety of palladium complexes and have provided a vast array of useful products, including intermediates in a number of natural product syntheses.[4] Intramolecular Pauson−Khand cyclizations of enynes make up a large class of processes that generate bicyclic cyclopentenones from acyclic enyne starting materials.[5] A number of stoichiometric as well as more recently reported catalytic protocols employ a variety of metal complexes to effect this transformation.[5b−g] Zirconium metallocene complexes have been utilized with enynes to mediate the formation of metallocycle intermediates that can be carried on to a Pauson−Khand-type product when reacted with carbon monoxide or protonated to yield a carbocyclic product.[6]

The process that we envisioned for the organoyttrium-catalyzed cyclization/silylation of enynes would be complementary to the previously reported methods. A viable catalytic cycle, similar to that proposed for the cyclization/silylation of dienes,[1g] is outlined in Scheme 1. At the outset, there were unknowns in several key steps of the process, and the success or failure of the sequence could only be determined effectively by experiment. The catalytic cycle would be initiated by a

[⊗] Abstract published in *Advance ACS Abstracts*, September 1, 1997.

(1) (a) Sakakura, T.; Lautenschlager, H.-J.; Tanaka, M. *J. Chem. Soc., Chem. Commun.* **1991**, 40. (b) Kesti, M. R.; Waymouth, R. M. *Organometallics* **1992**, *11*, 1095. (c) Molander, G. A.; Julius, M. *J. Org. Chem.* **1992**, *57*, 6347. (d) Molander, G. A.; Hoberg, J. O. *J. Org. Chem.* **1992**, *57*, 3266. (e) Molander, G. A.; Hoberg, J. O. *J. Am. Chem. Soc.* **1992**, *114*, 3123. (f) Sakakura, T.; Tanaka, M.; Onozawa, S. *Tetrahedron Lett.* **1994**, *35*, 8177. (g) Molander, G. A.; Nichols, P. J. *J. Am. Chem. Soc.* **1995**, *117*, 4415. (h) Marks, T. J.; Fu, P.-F.; Brard, L.; Li, Y. *J. Am. Chem. Soc.* **1995**, *117*, 7157. (i) Molander, G. A.; Nichols, P. J. *J. Org. Chem.* **1996**, *61*, 6040. (j) Molander, G. A.; Winterfeld, J. *J. Organomet. Chem.* **1996**, *524*, 275.

(2) (a) Molander, G. A.; Retsch, W. H. *Organometallics* **1995**, *14*, 4570. (b) Li, Y.; Marks, T. J. *J. Am. Chem. Soc.* **1996**, *118*, 707. (c) Heeres, H. J.; Heeres, A.; Teuben, J. H. *Organometallics* **1990**, *9*, 1508.

(3) (a) Bunel, E.; Burger, B. J.; Bercaw, J. E. *J. Am. Chem. Soc.* **1988**, *110*, 976. (b) Resconi, L.; Waymouth, R. M. *J. Am. Chem. Soc.* **1990**, *112*, 4953. (c) Piers, W. E.; Bercaw, J. E. *J. Am. Chem. Soc.* **1990**, *112*, 9406. (d) Piers, W. E.; Shapiro, P. J.; Bunel, E. E.; Bercaw, J. E. *Synlett* **1990**, 74. (e) Coates, G. W.; Waymouth, R. M. *J. Am. Chem. Soc.* **1991**, *113*, 6270. (f) Kesti, M. R.; Waymouth, R. M. *J. Am. Chem. Soc.* **1990**, *112*, 4953. (g) Shaughnessy, K. H.; Waymouth, R. M. *J. Am. Chem. Soc.* **1992**, *114*, 3563. (h) Knight, K. S.; Waymouth, R. M. *Chemtech* **1995**, *25*, 15.

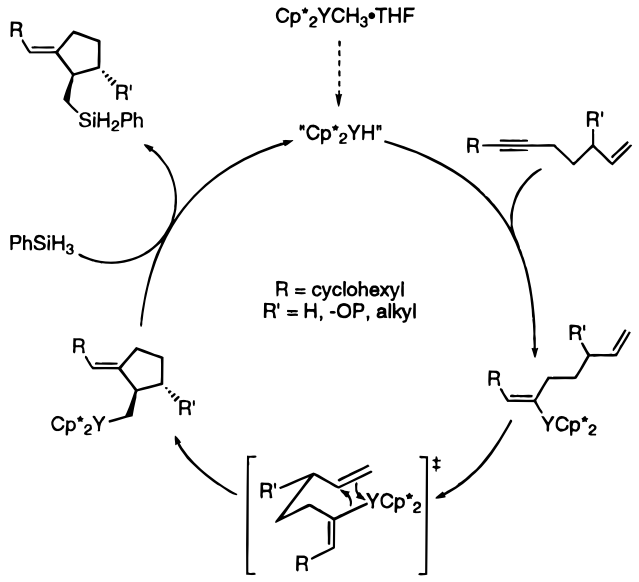
(4) (a) For a review see: Trost, B. M. *Acc. Chem. Res.* **1990**, *23*, 34 and references therein. (b) Trost, B. M.; Lautens, M.; Chan, C.; Jeberatnam, D. J.; Mueller, T. *J. Am. Chem. Soc.* **1992**, *113*, 636. (c) Villa, M.; Dumas, J.; Trost, B. M. *J. Am. Chem. Soc.* **1992**, *114*, 9836. (d) Trost, B. M.; Dumas, J. *J. Am. Chem. Soc.* **1992**, *114*, 1924. (e) Chang, V. K.; Trost, B. M. *Synthesis* **1993**, 825. (f) Phan, L. T.; Trost, B. M. *Tetrahedron Lett.* **1993**, *34*, 4735. (g) Zhu, G.; Lu, X. *J. Org. Chem.* **1995**, *60*, 1087. (h) Ji, J.; Zhang, C.; Lu, X. *J. Org. Chem.* **1995**, *60*, 1160. (i) Ji, J.; Wang, Z.; Lu, X. *Organometallics* **1996**, *15*, 2821. (j) Trost, B. M.; Fleitz, F. J.; Watkins, W. J. *J. Am. Chem. Soc.* **1996**, *118*, 5146.

(5) (a) For a general review see: Schore, N. E. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon: Oxford, 1991; Vol. 5, pp 1037−1064. (b) For a review of transition metal-catalyzed reactions see: Catellani, M.; Chivsoli, G. P.; Costa, M. *J. Organomet. Chem.* **1995**, *500*, 69. (c) Livinghouse, T.; Pagenkopf, B. L. *J. Am. Chem. Soc.* **1996**, *118*, 2285. (d) Hicks, F. A.; Kablaoui, N. M.; Buchwald, S. L. *J. Am. Chem. Soc.* **1996**, *118*, 9450. (e) Hicks, F. A.; Buchwald, S. L. *J. Am. Chem. Soc.* **1996**, *118*, 11688. (f) Hicks, F. A.; Berk, S. C.; Buchwald, S. L. *J. Org. Chem.* **1996**, *61*, 2713. (g) Zhang, M.; Buchwald, S. L. *J. Org. Chem.* **1996**, *61*, 4498.

(6) (a) For reviews see: Negishi, E.-i. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon: Oxford, 1991; Vol. 5, pp 1163−1184. (b) Negishi, E.-i.; Takahashi, T. *Acc. Chem. Res.* **1994**, *27*, 124. (c) Pagenkopf, B. L.; Lund, E. C.; Livinghouse, T. *Tetrahedron* **1995**, *51*, 4421.

S0002-7863(97)01538-2 CCC: $14.00

Scheme 1



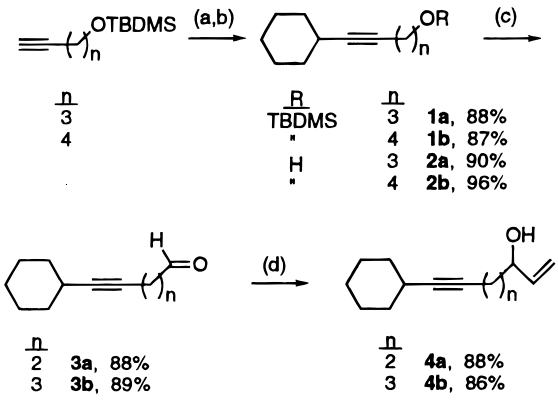
σ-bond metathesis between $Cp^*_2YCH_3$·THF and $PhSiH_3$, producing a catalytically active metal hydride species.[1c−e,g,i,2a] Next, the catalyst would have to insert one of the two sites of unsaturation of the enyne preferentially. Although evidence supported the proposition that the alkyne would be more reactive,[7] the extent to which selectivity could be achieved remained to be tested. If adequate chemoselectivity for the alkyne could be achieved, it was known that regioselectivity in this process could be dictated by steric effects to form a single alkenylyttrium intermediate.[2a] This intermediate, known to react through a σ-bond metathesis with phenylsilane to yield an alkenylsilane,[2a] might also undergo cyclization via an intramolecular olefin insertion. The intramolecular insertion of an alkene into a lanthanide sp^2 carbon bond has little precedent,[2b,c] and whether or not the insertion would occur in preference to direct σ-bond metathesis with phenylsilane was entirely unknown. Cyclization, if favored, would produce a second intermediate alkylyttrium species. This second intermediate, similar to those proposed in diene cyclizations,[1e−i] would be expected to undergo a subsequent σ-bond metathesis with silane to generate the desired product. All of these steps would have to be accomplished selectively in order to cyclize even a simple enyne, but to be truly useful a catalyst would also be required to react under mild conditions, at a reasonable rate, and tolerate a variety of functional groups as well.

We now report that the organoyttrium hydride catalyst derived from $Cp^*_2YCH_3$·THF ($Cp^* = C_5Me_5$) is indeed an effective catalyst for the selective cyclization of 1,6- and 1,7-enynes in the postulated manner, providing facile access to highly functionalized carbocycles.

Results and Discussion

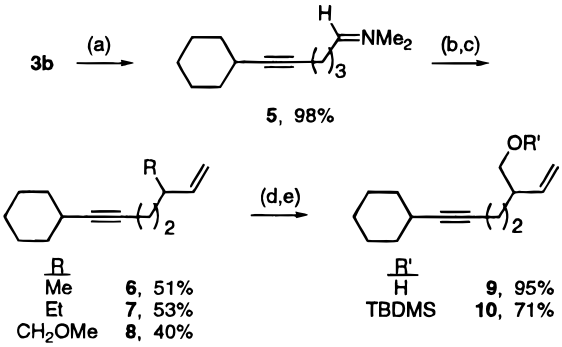
A series of 1,6-enyne substrates designed to test this new protocol was prepared according to Schemes 2−4. The substrates **20**, **22**, **24**, and **26** were all derived from **4a**. Scheme 2 outlines the synthesis of this intermediate. Commercially available 4-pentyn-1-ol was protected as the *tert*-butyldimethylsilyl ether in high yield.[8a] The cyclohexyl substituent was placed on the alkyne according to published procedures to afford **1a**.[9] Removal of the silyl protecting group with TBAF followed by oxidation via a modified Swern procedure afforded **3a**.[10] Vinylmagnesium bromide addition to the aldehyde of **3a** provided the desired allylic alcohol **4a**. The allylic alcohol was then protected according to published procedures to yield the desired substrates.[8] The tertiary amine of **26** was accessed via a Mitsunobu coupling of **4a** with phthalimide[11] followed by complete reduction of the carbonyl functionalities with LAH to afford **26**.[12]

Scheme 2



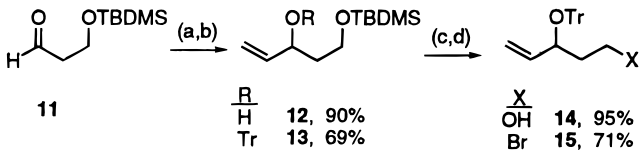
(a) 1. *n*-BuLi, $(C_6H_{11})_3B$, I_2, THF 2. $NaOH/H_2O_2$ (b) TBAF, THF (c) pyr•SO_3, DMSO, NEt_3, CH_2Cl_2 (d) vinylmagnesium bromide, THF.

Scheme 3



(a) *N,N*-dimethylhydrazine (b) 1. LDA, THF, RX 2. Amberlyst, acetone (c) CH_3PPh_3Br, *t*-BuOK, Et_2O (d) TMSI, $CHCl_3$ (e) TBDMSCl, imidazole, DMF.

Scheme 4



(a) vinylmagnesium bromide, THF (b) TrCl, DBU, CH_2Cl_2 (c) TBAF, THF (d) Ph_3PBr_2, pyridine.

(7) (a) Evans, W. J.; Meadows, J. H.; Hunter, W. E.; Atwood, J. L. *J. Am. Chem. Soc.* **1984**, *106*, 1291. (b) Jeske, G.; Lauke, H.; Mauermann, H.; Schumann, H.; Marks, T. J. *J. Am. Chem. Soc.* **1985**, *107*, 8111. (c) Jeske, G.; Lauke, H.; Mauermann, H.; Swepston, P. N.; Schumann, H.; Marks, T. J. *J. Am. Chem. Soc.* **1985**, *107*, 8091. (d) Jeske, G.; Schock, L. E.; Swepston, P. N.; Schumann, H.; Marks, T. J. *J. Am. Chem. Soc.* **1985**, *107*, 8103.

(8) (a) Corey, E. J.; Venkatesvarlu, A. *J. Am. Chem. Soc.* **1972**, *94*, 6190. (b) Corey, E. J.; Cho, H.; Rücker, C.; Hua, D. H. *Tetrahedron Lett.* **1981**, *22*, 3455. (c) Miyashita, M.; Yoshikoshi, A. *J. Org. Chem.* **1977**, *42*, 3772. (d) Colin-Messager, C.; Girard, J.-P.; Rossi, J.-C. *Tetrahedron Lett.* **1992**, *33*, 2689.

(9) Brown, H. C.; Sinclair, J. A.; Midland, M. M. *J. Am. Chem. Soc.* **1973**, *95*, 3080.

(10) Wipf, P.; Fritch, P. C. *J. Org. Chem.* **1994**, *59*, 4875.

(11) Mulzer, J.; Brand, C. *Tetrahedron* **1986**, *42*, 5961.

(12) Iriuchijima, S. *Synthesis* **1978**, 684.

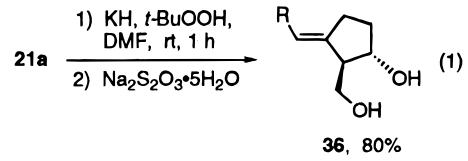
The synthesis of substrates **6**, **7**, **8**, and **10** is shown in Scheme 3. The aldehyde **3b** was prepared similarly to **3a** and then treated with *N*,*N*-dimethylhydrazine to form hydrazone **5**. Treatment of hydrazone **5** with LDA and alkylation with the appropriate electrophile was followed by removal of the hydrazone with wet Amberlyst. The resultant aldehydes were subjected directly to a Wittig reaction to yield the desired substituted enynes.[13] Some of compound **8** was used as a substrate, while a portion was treated with TMSI, cleaving the methyl ether to yield alcohol **9**.[14] Protection of **9** as the *tert*-butyldimethylsilyl ether afforded substrate **10**. Aldehyde **3b** was also subjected directly to a Wittig reaction for the preparation of **16** in 86% yield.

Substrates **32** and **34** were prepared by alkylation of the appropriate terminal alkyne with bromide **15**. The preparation of **15** is outlined in Scheme 4. Aldehyde **11** was prepared according to the literature procedure[15] and treated with vinylmagnesium bromide to provide allylic alcohol **12**. The allylic alcohol of **12** was protected as the trityl ether to provide **13**. Selective deprotection using TBAF afforded the primary alcohol **14**. Treatment with dibromotriphenylphosphorane yielded the desired bromide **15**.[16] 2,2-Dimethyl-5-ethynyl-1,3-dioxane was prepared from the literature procedure,[17] treated with *n*-BuLi to prepare the lithium acetylide, and alkylated with **15** to afford substrate **34**. Similarly, commercially available (±)-3-butyn-2-ol was protected as the *tert*-butyldimethylsilyl ether and alkylated with bromide **15** to yield substrate **32**. Substrate **18** was prepared from the lithium acetylide of commercially available 3-methyl-1-pentyne and 5-bromo-1-pentene in 75% yield.

With the substrates in hand, investigations were undertaken to determine optimum reaction conditions for the cyclization/silylation reactions and to outline the scope and limitations of the process. Compound **16** was utilized as the archetypal substrate for these studies (Table 1). The cyclization/silylation reaction of this substrate was carried out with 5 mol % of the precatalyst in the presence of an excess of phenylsilane at 25 °C for 2 h (entry 1). Compounds **17a** and **17b** were both produced in the reaction. The major cyclized product **17a** was obtained in 60% isolated yield and was formed by preferential insertion of the alkyne into the catalyst. The minor product, **17b**, was formed by initial insertion of the alkene. The latter process forms an intermediate alkyltyttrium species that undergoes σ-bond metathesis with phenylsilane to form a second intermediate, 1-cyclohexyl-7-(phenylsilyl)-1-heptyne.[18] This is transformed by another hydrosilylation reaction at the alkyne, ultimately forming **17b**.

In order to increase selectivity for the formation of the cyclized product, the catalyst's preference for initial insertion of the alkyne over the alkene was improved. The addition of a (*tert*-butyldimethylsilyl)oxy substituent in the allylic position of **20** was expected to favor the insertion of the alkyne by lowering the reactivity of the alkene by both steric and electronic effects.[1c] The reaction of substrate **20** demonstrated that higher yields of cyclized products could be obtained with no formation of uncyclized hydrosilylated products (entry 3). This suggested that the protected alcohol adequately hindered initial insertion of the alkene without compromising the intramolecular insertion required to form the cyclized products.

The formation of a new stereocenter in the cyclization reaction of **20** results in two diastereomeric products, **21a** and **21b**. The ratio of products as determined by fused silica gas chromatographic analysis was 6.5:1. The relative stereochemistry of the major product of the reaction was determined to be *trans* with respect to the ring substituents from the X-ray crystal structure of diol **36** obtained from the one-step oxidation/deprotection of **21a** (eq 1).[19] The origin of the diastereoselectivity observed



(1)

36, 80%

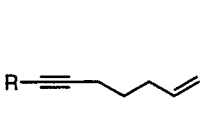
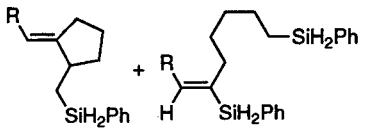
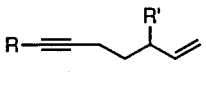
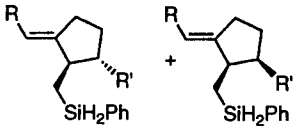
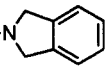
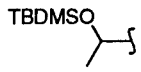
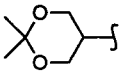
in the cyclization can be explained by the transition structure pictured in Scheme 1. If the alkenylmetallic intermediate produced by insertion of the alkyne adopts a chairlike transition structure, the allylic substituent should occupy a pseudoequatorial position about the newly forming ring. This transition structure predicts the configuration of the major cyclized product to be *trans* with respect to the ring substituents—the same as the configuration of the major product **21a**.

Some improvement in the diastereoselectivity was achieved when larger alkoxy groups were incorporated in the starting materials as depicted in entries 4 and 5. This provides further evidence for the transition structure suggested in Scheme 1 because the improved diastereomeric ratio of the products can be attributed to the bulkier allylic substituents having an increased preference to assume a pseudoequatorial orientation. Improvement of the diastereoselectivity of the reaction was also attempted by performing the reaction of **20** at 0 and −20 °C.[20] The decrease in reaction temperature had no effect on the observed diastereomeric ratio.[21] A complex incorporating a lanthanide metal with a smaller ionic radius was also utilized in an effort to improve the diastereoselectivity of the reaction. It was reasoned that if the orientation of the allylic substituent in the transition state was affected by the bulky Cp* ligands of the complex, then a smaller metal could allow for the formation of a tighter coordination environment and increase the preference for a pseudoequatorial orientation of the substituent. Thus, $Cp^*_2LuCH_3 \cdot THF$ was prepared and utilized as the precatalyst in the reaction of **20** and **22**. This precatalyst had a reactivity similar to the yttrium complex, but did not alter the observed diastereomeric ratios of the products.

The diastereoselectivities of the cyclization reactions were exceedingly high when allylic substituents with *A* values greater than that of a protected alcohol were incorporated into the enyne substrates. The tertiary amine substituent of **26** provided products in high yields and with excellent diastereoselectivity (40:1). Oxidation of the silane in this series would provide access to interesting β-amino alcohol derivatives. When alkyl substituents were incorporated in substrates **6** and **7**, formation of the minor diastereomer was not observed. Similarly, **10** reacted to give only the major diastereomer cleanly and in good yield. Substrate **8** differs from **10** only with respect to the protecting group on the primary alcohol, but was unreactive with the catalyst at 25 and 50 °C. This result was not entirely unexpected because methoxy groups have been known to inhibit

(13) Fitjer, L.; Quabek, U. *Synth. Commun.* **1985**, *15*, 855.
(14) Jung, M. E.; Lyster, M. A. *J. Org. Chem.* **1977**, *42*, 3761.
(15) Hall, D. G.; Caille, A.-S.; Drouin, M.; Lamothe, S.; Mueller, R.; Deslongchamps, P. *Synthesis* **1995**, *9*, 1081.
(16) (a) Wiley, G. A.; Hershkowitz, R. L.; Rein, B. M.; Chung, B. C. *J. Am. Chem. Soc.* **1964**, *86*, 964. (b) Borch, R. F.; Evans, A. J.; Wade, J. J. *J. Am. Chem. Soc.* **1977**, *99*, 1612.
(17) Bates, A. H.; Farina, J.; Tong, M. *J. Org. Chem.* **1986**, *51*, 2637.
(18) This compound was identified as the intermediate observed in the reaction of **16** to **17a** and **17b** from a comparison of retention times using fused silica gas chromatographic analysis. Full characterization can be found in the experimental as compound **17c**.
(19) Smitrovich, J. H.; Woerpel, K. A. *J. Org. Chem.* **1996**, *61*, 6044.
(20) Cyclopentane was used as the solvent for low-temperature reactions.
(21) Diastereomeric ratios were determined by fused silica gas chromatographic analysis.

Table 1. Cyclization/Silylation of Enynes Catalyzed by $Cp^*_2YCH_3 \cdot THF$[a]

entry	substrate	products	% isolated yield[b]	diastereomeric ratio[c]
				
1	**16** R = cyclohexyl	**17a** **(17b)**	60 (25)	
2	**18** R = *sec*-butyl	**19**	49	2:1[d]
				
3	**20** R = cyclohexyl R' = OTBDMS	**21a** **21b**	93	6.5:1
4	**22** R = cyclohexyl R' = OTIPS	**23a** **23b**	93	12:1
5	**24** R = cyclohexyl R' = OTr	**25**	84	24:1
6	**26** R = cyclohexyl R' = 	**27**	91[e]	>40:1
7	**6** R = cyclohexyl R' = Me	**28**	64	>50:1
8	**7** R = cyclohexyl R' = Et	**29**	88	>50:1
9	**8** R = cyclohexyl R' = CH_2OMe	**30**	80	20:1[f]
10	**10** R = cyclohexyl R' = $CH_2OTBDMS$	**31**	76	>50:1
11	**32** R=  R' = OTr	**33**	77	*d*
12	**34** R=  R' = OTr	**35**	88	35:1

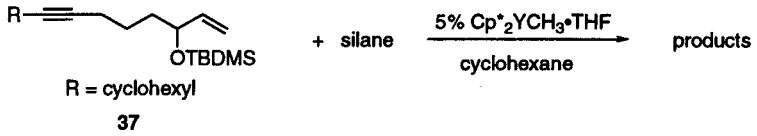
[a] Reactions were run according to the general procedure outlined in the experimental section unless otherwise indicated. [b] Refers to yields of purified materials. Overall yields reported for mixtures of diastereomers. [c] Diastereomeric ratios determined by fused silica gas chromatographic analysis on the crude reaction mixture. [d] Mixture of diastereomers owing to stereocenter in R group of substrate. [e] Reaction performed in an NMR tube with d_6-benzene as the solvent. [f] Reaction run in a sealed tube at 100 °C.

the reactivity of organolanthanide catalysts.[1j] After initial insertion of the alkyne of substrate **8** into the catalyst, a seven-membered ring chelate can form that apparently renders the catalyst unreactive until the reaction is heated to 100 °C. Presumably, at this temperature the equilibrium concentration of ligand-free organometallic is high enough that a reasonable turnover can be achieved. At this elevated reaction temperature some loss of diastereoselectivity in the cyclization was observed.

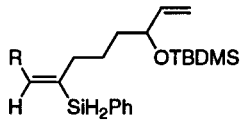
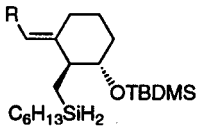
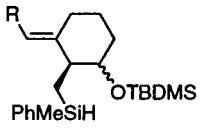
The substrates depicted in entries 1−10 possess a cyclohexyl or *sec*-butyl group as a substituent on the alkyne to provide branching in the propargyl position. This branching serves as a regiocontrol element and is required to attain complete regioselectivity in the initial alkyne insertion.[2a] Entries 11 and 12 provide examples of branched alkyne substituents containing functionalized groups that can be utilized as substituents on the alkyne without hindering reactivity. Although the addition of an allylic alkoxy group in the enyne cyclization inhibited the initial insertion of the alkene, the protected propargyl alcohol of substrate **32** had little if any effect on the alkyne in the desired transformation. Similarly, the oxygens of the acetonide-protected diol substituent of substrate **34** did not appreciably affect the reactivity of the highly electron deficient catalyst. The reaction proceeded readily at room temperature, complete selectivity in the alkyne insertion was observed, and the cyclized product was obtained in high yield and with excellent diastereoselectivity.

It was expected that the cyclization/silylation reaction of enynes could be readily extended to include the formation of six-membered rings. The reactions of **37** with various silanes were carried out with this expectation and the results are outlined in Table 2. Under conditions identical to those that allowed the cyclization/silylation of **20** to occur, **37** was reacted with the precatalyst and phenylsilane. No cyclization product was observed. Instead, the alkyne was hydrosilylated to form **38** cleanly and in high yield. This result again demonstrated the preference of the catalyst for the initial insertion of an alkyne over the terminal alkene of a protected allylic alcohol. It also demonstrated that the alkenylmetallic species produced by the initial insertion of the alkyne undergoes σ-bond metathesis with phenylsilane more readily than an intramolecular insertion of

Table 2. Effect of the Silane on the Formation of a Six-Membered Ring[a]

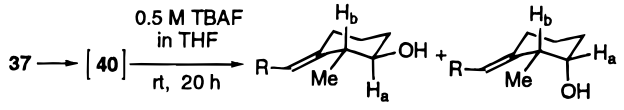


37

entry	silane	products	reaction temperature	reaction time (h)	% isolated yield[b]
1	$PhSiH_3$	 **38**	rt	21	93
2	$C_6H_{13}SiH_3$	 **39**	rt	22	47[c]
3	$PhMeSiH_2$	 **40**	50 °C	8	100[d]

[a] Reactions were run according to the general procedure outlined in the experimental section with changes in reaction times and temperatures as indicated. [b] Refers to yields of purified materials. [c] Only the major diastereomer was isolated from the reaction. [d] Crude yield of a complex mixture of diastereomers. (Structure inferred from characterization after desilylation/deprotection as shown in Scheme 5)

Scheme 5



	42 major	**43** minor
δH_a	3.25 ppm	3.75 ppm
J_{ab}	7.3 Hz	3.1 Hz

the alkene to form a six-membered ring. This suggested that if the σ-bond metathesis with the silane could be slowed down, the intramolecular insertion would occur preferentially to form a cyclized product. This was accomplished by utilizing different substituents or more than one substituent on the silane. In entry 2 hexylsilane was utilized as the silylating reagent. This terminator allowed the six-membered ring to form and to be isolated as a single diastereomer, but only in moderate yield. The minor diastereomer that was expected to have formed was inseparable and unidentifiable in the mixture of other isomers that were formed in the reaction. The relative stereochemistry of the isolated diastereomer was determined by X-ray crystallography of diol **41** obtained from the oxidation/deprotection of **39**. In entry 3 methylphenylsilane was utilized and was shown to provide the cyclized products in high yield. The formation of the additional stereocenter at silicon made characterization of the reaction products problematic. The crude reaction mixture could be deprotected and desilylated in one step to yield a mixture of **42** and **43** in 84% overall yield for the two steps (Scheme 5). Analysis of the crude reaction mixture by ^{1}H NMR indicated that a 4:1 diastereomeric mixture of products was formed. A determination of the relative stereochemistry of the diastereomers was based on the chemical shift of the proton on the carbon bearing the hydroxyl group and its vicinal coupling constant to the proton adjacent to the methyl group. The appropriate chemical shifts and coupling constants are shown in Scheme 5 and are consistent with accepted values for substituted cyclohexyl systems.[22] The relative stereochemistry of the product of entry 2 and the stereochemistry of the major product derived from entry 3 are consistent in suggesting that the major product of the cyclization of an enyne to form a six-membered ring places the ring substituents *trans* to one another.

Although methylphenylsilane allowed the formation of a six-membered ring in preference to the hydrosilylation of the alkyne, it also created more difficulties in the characterization of the reaction products because of the addition of a third stereocenter at silicon. In an effort to avoid the formation of an additional stereocenter both diphenylsilane and diethylsilane were utilized in reactions with **37**. Neither of these silanes showed any reactivity with this substrate at temperatures between 25 and 100 °C.

Conclusions

The organoyttrium complex $Cp^*_2YCH_3$•THF can be used to catalyze the cyclization/silylation of suitable 1,6-enynes with phenylsilane to form functionalized carbocycles diastereoselec-

(22) *Spectral Data for Structure Determination of Organic Compounds*; Boschke, F. L., Fresnius, W., Huber, J. F. K., Pungor, E., Rechnitz, G. A., Simon, W., West, T. S., Eds.; Springer-Verlag: Berlin, 1983; pp H185 and H195.

tively in a single step. In the sequential process, both a carbon−carbon and a carbon−silicon bond are formed selectively. The catalyst accomplishes this reaction through its ability to insert an alkyne regioselectively in preference to an alkene, proceed through an intramolecular olefin insertion that engenders high diastereoselectivity, and finally regenerate the active catalyst while at the same time placing a functional group on the product. The diastereoselectivity of the reaction can be enhanced by increasing the size of allylic substituents on the substrate. It has also been demonstrated that with an appropriate silane, a 1,7-enyne can be cyclized to provide a six-membered ring product selectively. In addition to the catalyst's ability to react selectively with the substrates, these reactions proceed at very reasonable rates under extremely mild conditions, and a variety of functional groups can be tolerated. The method complements other catalyzed cyclization reactions of enynes, and does so in a manner that is atom economical, with no byproducts formed whatsoever in the process.[23]

Experimental Section

All operations involving the organoyttrium complex were performed with rigorous exclusion of oxygen and moisture in flamed Schlenk-type glassware on an argon line connected to a vacuum system (<0.04 mmHg) or in a nitrogen-filled, Vacuum Atmospheres glovebox. The cyclohexane and benzene-d_6 used as solvents for the reactions were distilled from Na/benzophenone under argon and then stored in the glovebox. In preparation for use with the catalyst, substrates were distilled onto activated 4 Å molecular sieves and freeze/pump/thaw degassed or dried as a solution with $MgSO_4$, concentrated in vacuo, and degassed. 5-Hexyn-1-ol, 4-pentyn-1-ol, and 3-methyl-1-pentyne were purchased from Farchan Laboratories, Inc. The phenylsilane was purchased from Aldrich. Methylphenylsilane, hexylsilane, diethylsilane, and diphenylsilane were purchased from Hüls America Inc. All silanes were dried with activated 4 Å molecular sieves and degassed before use. Anhydrous YCl_3 and $LuCl_3$ were purchased from Cerac. The complexes $Cp^*_2YCH_3$·THF and $Cp^*_2LuCH_3$·THF were prepared according to published procedures for the yttrium complex.[24]

General Experimental Procedure for Cyclization/Silylation. The catalytic cyclization/silylation of **20** is representative. In the nitrogen atmosphere glovebox a solution of 0.004 g (0.009 mmol) of the precatalyst $Cp^*_2YCH_3$·THF in 1 mL of cyclohexane was added to a reaction flask equipped with a magnetic stir bar. To this solution 0.050 g (0.163 mmol) of **20** was added followed by 0.021 g (0.194 mmol) of phenylsilane. The reaction flask was sealed and stirred in the glovebox for 2 h at ambient temperature. After 2 h the reaction mixture was removed from the glovebox, diluted with 1 mL of Et_2O, and filtered through a 0.5 g column of Florisil. The Florisil was rinsed two times with 2 mL portions of Et_2O. Analysis of the crude reaction mixture by gas chromatography indicated that a 6.5:1 ratio of diastereomers was generated. The organics were combined and concentrated by rotary evaporation. The crude material was purified by flash chromatography using 6% CH_2Cl_2 in hexanes followed by Kugelrohr distillation at reduced pressure to afford 80% (0.054 g, 0.130 mmol) of **21a**, the major *trans* product, and 13% (0.009 g, 0.022 mmol) of **21b**, the minor *cis* product.

(1*E*)-1-(Cyclohexylmethylene)-2-[(phenylsilyl)methyl]cyclopentane (17a). The reaction of **16** was carried out according to the general experimental procedure for catalytic cyclization/silylation except 1.5 equiv of $PhSiH_3$ were used. A mixture of **17a** and **17b** was obtained. Purification by flash chromatography in hexanes followed by Kugelrohr distillation afforded 60% of the major product **17a** (>99% pure by GC analysis): ot 90−100 °C/0.1 mmHg; R_f 0.45 (hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.85−0.92 (m, 1H), 0.96−1.05 (m, 2H), 1.11−1.37 (m, 5H), 1.42−1.54 (m, 1H), 1.57−1.78 (m, 6H), 1.86−1.94 (m, 1H), 1.98−2.07 (m, 1H), 2.16−2.33 (m, 2H), 2.38−2.46 (m, 1H), 4.28−4.34 (m, $^1J_{^{29}Si,H}$ = 192.5 Hz, 2H), 5.02 (br dd, J = 8.8, 2.1 Hz, 1H), 7.32−7.37 (m, 3H), 7.56−7.58 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 15.09, 23.97, 26.12, 26.15, 26.20, 28.43, 33.12, 33.15, 34.74, 38.52, 40.78, 126.12, 127.94, 129.42, 133.10, 135.21, 145.79; IR (neat) 2132.8 cm^{-1}; HRMS calcd for $C_{19}H_{28}Si$ 284.1960, found 284.1955; LRMS (EI) *m*/*z* (relative intensity) 284 (26), 206 (44), 173 (47), 123 (87), 107 (100).

(1*E*)-1-Cyclohexyl-2,7-bis(phenylsilyl)-1-heptene (17b). Purification by flash chromatography in hexanes of the crude mixture of **17a** and **17b** followed by Kugelrohr distillation afforded 25% of the minor product **17b** (>99% pure by GC analysis): ot 115−125 °C/0.04 mmHg; R_f 0.29 (hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.85−0.91 (m, 2H), 1.11−1.44 (m, 11H), 1.59−1.75 (m, 5H), 2.15−2.18 (m, 2H), 2.36−2.43 (m, 1H), 4.28 (t, J = 3.5 Hz, $^1J_{^{29}Si,H}$ = 192.2 Hz, 2H), 4.28 (s, $^1J_{^{29}Si,H}$ = 194.4 Hz, 2H), 4.52 (d, J = 9.1 Hz, 1H), 7.32−7.42 (m, 6H), 7.55−7.57 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 9.87, 24.79, 25.83, 25.99, 29.40, 30.24, 32.68, 32.84, 37.68, 127.88, 127.94, 129.44, 129.47, 131.57, 132.71, 132.74, 135.18, 135.49, 152.00; IR (neat) 2130.8 cm^{-1}; HRMS calcd for $C_{25}H_{36}Si_2$ 392.2356, found 392.2329; LRMS (EI) *m*/*z* (relative intensity): 313 (26), 285 (32), 107 (100).

1-Cyclohexyl-7-(phenylsilyl)-1-heptyne (17c). The reaction of **16** was carried out a second time according to the general experimental procedure except only 0.8 equiv of $PhSiH_3$ were used and the reaction was quenched 1 min after the addition of $PhSiH_3$. Analysis of the crude reaction mixture by gas chromatography confirmed that a mixture of starting material, **17a**, **17b**, and the intermediate **17c** was obtained. Purification by flash chromatography using 8% CH_2Cl_2 in hexanes followed by Kugelrohr distillation afforded **17c** cleanly for characterization (>97% pure by GC analysis): ot 85−95 °C/0.04 mmHg; R_f 0.29 (8% CH_2Cl_2 in hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.90−0.95 (m, 2H), 1.20−1.52 (m, 12H), 1.63−1.76 (m, 4H), 2.10−2.14 (m, 2H), 2.26−2.33 (m, 1H), 4.27 (t, J = 3.8 Hz, $^1J_{^{29}Si,H}$ = 192.0 Hz, 2H), 7.32−7.40 (m, 3H), 7.54−7.56 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 9.95, 18.62, 24.61, 24.96, 25.95, 28.80, 29.15, 31.93, 33.17, 79.90, 84.74, 127.94, 129.48, 132.67, 135.19; IR (neat) 2132.6 cm^{-1}; HRMS calcd for $C_{19}H_{28}Si$ 284.1960, found 284.1959; LRMS (EI) *m*/*z* (relative intensity): 284 (3), 201 (18), 121 (35), 107 (100).

(1*E*,2*R,2′*R**/*S**)-1-(2′-Methylbutylene)-2-[(phenylsilyl)methyl]-cyclopentane (19).** Prepared from **18** according to the general experimental procedure. Analysis of the crude reaction mixture by gas chromatography indicated that a 2:1 diastereomeric ratio of products was generated. Purification by flash chromatography followed by Kugelrohr distillation afforded 49% of the title compound as a mixture of diastereomers (>96% pure by GC): R_f 0.45 (hexanes); ot 85−95 °C at 0.30 mmHg; ^{1}H NMR (400 MHz, $CDCl_3$) 0.82 (t, J = 7.4 Hz, 3H), 0.86−0.94 (m, 4H), 1.13−1.38 (m, 4H), 1.42−1.54 (m, 1H), 1.68−1.77 (m, 1H), 1.87−1.94 (m, 1H), 2.04−2.32 (m, 3H), 2.39−2.48 (m, 1H), 4.27−4.35 (m, $^1J_{^{29}Si,H}$ = 192 Hz, 2H), 4.93 (dd, J = 7.2, 3.2 Hz, 1H), 7.33−7.40 (m, 3H), 7.57−7.59 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (major diastereomer) 12.00, 15.13, 20.68, 23.96, 28.65, 30.38, 34.79, 35.74, 40.72, 126.25, 127.94, 129.42, 133.08, 135.22, 146.17; (minor diastereomer) 12.02, 15.28, 20.77, 24.04, 28.76, 30.48, 34.82, 35.74, 40.89, 126.28, 127.94, 129.42, 133.12, 135.22, 146.38; IR (neat) 2134 cm^{-1}; HRMS calcd for $C_{17}H_{26}Si$ 258.1804, found 258.1806; LRMS (EI) *m*/*z* (relative intensity) 258 (20), 201 (39), 123 (59), 107 (100).

(1*R,2*R**,3*E*)-1-[(*tert*-Butyldimethylsilyl)oxy]-3-(cyclohexylmethylene)-2-[(phenylsilyl)methyl]cyclopentane (21a).** Prepared from **20** according to the general experimental procedure. Purification by flash chromatography using 6% CH_2Cl_2 in hexanes followed by Kugelrohr distillation at reduced pressure afforded 80% of **21a** as the major diastereomer: ot 110−120 °C/0.01 mmHg; R_f 0.33 (10% CH_2Cl_2 in hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.03 (s, 3H), 0.04 (s, 3H), 0.87 (s, 9H), 0.91−1.26 (m, 7H), 1.49−1.69 (m, 6H), 1.87−1.96 (m, 1H), 1.99−2.09 (m, 1H), 2.12−2.22 (m, 1H), 2.34−2.46 (m, 2H), 3.73 (dt, J = 6.6, 6.8 Hz, 1H), 4.35 (t, J = 3.4 Hz, $^1J_{^{29}Si,H}$ = 196 Hz, 2H), 5.05 (br d, J = 9.0 Hz, 1H), 7.32−7.37 (m, 3H), 7.56−7.58 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ −4.51, −4.18, 12.22, 18.04, 25.26, 25.91, 26.08, 26.18, 32.72, 32.93, 33.03, 37.93, 49.20, 79.25, 127.91, 128.11, 129.37, 133.35, 135.24, 141.23; IR (neat) 2134.5 cm^{-1}; HRMS calcd for $C_{25}H_{41}OSi_2$ (M − H)$^+$ 413.2696, found 413.2676; LRMS (EI)

(23) (a) Trost, B. M. *Science* **1991**, *254*, 1471. (b) Trost, B. M. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 259.

(24) (a) Threlkel, R. S.; Bercaw, J. E. *J. Organomet. Chem.* **1977**, *136*, 1. (b) Den Haan, K. H.; Teuben, J. H. *J. Organomet. Chem.* **1987**, *322*, 321. (c) Den Haan, K. H.; Wielstra, Y.; Eshuis, J. J. W.; Teuben, J. H. *J. Organomet. Chem.* **1987**, *323*, 181.

m/*z* (relative intensity) 414 (0.2), 357 (41), 181 (100), 107 (30). Anal. Calcd for $C_{25}H_{42}OSi_2$: C, 72.39; H, 10.21. Found: C, 72.28; H, 10.56.

(1*R,2*S**,3*E*)-1-[(*tert*-Butyldimethylsilyl)oxy]-3-(cyclohexylmethylene)-2-[(phenylsilyl)methyl]cyclopentane (21b).** Prepared from **20** according to the general experimental procedure. Purification by flash chromatography using 6% CH_2Cl_2 in hexanes followed by Kugelrohr distillation at reduced pressure afforded 13% of **21b** as the minor diastereomer: ot 104−110 °C/0.01 mmHg; R_f 0.46 (10% CH_2Cl_2 in hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.036 (s, 3H), 0.040 (s, 3H), 0.85 (s, 9H), 0.94−1.06 (m, 3H), 1.09−1.30 (m, 4H), 1.53−1.74 (m, 7H), 1.99−2.07 (m, 1H), 2.14−2.23 (m, 1H), 2.31−2.37 (m, 2H), 4.18 (dt, J = 4.5, 4.6 Hz, 1H), 4.33−4.39 (m, $^1J_{^{29}Si,H}$ = 192 Hz, 2H), 5.01 (br dd, J = 9.1, 2.1 Hz, 1H), 7.31−7.39 (m, 3H), 7.55−7.57 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ −4.60, −4.29, 8.24, 18.20, 25.06, 25.92, 26.15, 26.23, 32.14, 33.01, 33.10, 38.22, 46.61, 74.97, 127.59, 127.94, 129.38, 133.40, 135.25, 142.45; IR (neat) 2135.2 cm^{-1}; HRMS calcd for $C_{25}H_{42}OSi_2$ $(M - H)^+$ 413.2696, found 413.2661; LRMS (EI) *m*/*z* (relative intensity) 357 (47), 181 (100), 107 (49), 73 (49). Anal. Calcd for $C_{25}H_{42}OSi_2$: C, 72.39; H, 10.21. Found: C, 72.64; H, 10.31.

(1*R,2*R**,3*E*)-3-(Cyclohexylmethylene)-2-[(phenylsilyl)methyl]-1-[(triisopropylsilyl)oxy]cyclopentane (23a)** was prepared from **22** according to the general experimental procedure. Analysis of the crude reaction mixture by gas chromatography indicated that a 12:1 diastereomeric ratio of products was generated. Purification by flash chromatography followed by Kugelrohr distillation afforded a mixture of **23a** and **23b** in 93% yield. Further purification by flash chromatography of a mixture of diastereomers using 10% CH_2Cl_2 followed by Kugelrohr distillation afforded a sample of **23a** as the major isomer for characterization (>99% pure by GC analysis): ot 120−150 °C/0.01 mmHg; R_f 0.58 (10% CH_2Cl_2 in hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.96−1.05 (m with overlapping broad singlet at 1.02, 23H), 1.10−1.29 (m, 5H), 1.59−1.69 (m, 6H), 1.90−2.07 (m, 2H), 2.16−2.24 (m, 1H), 2.36−2.45 (m, 2H), 3.91 (dt apparent quartet, J = 5.1, 5.1 Hz, 1H), 4.34 (t, J = 4.0, $^1J_{^{29}Si,H}$ = 194.6 Hz, 2H), 5.07 (dd, J = 7.3, 1.9 Hz, 1H), 7.31−7.39 (m, 3H), 7.55−7.57 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 12.43, 13.36, 18.09, 18.12, 25.09, 26.08, 26.19, 32.79, 32.86, 33.06, 38.18, 49.97, 79.56, 127.90, 128.33, 129.39, 133.10, 135.22, 142.02; IR (neat) 2136.4 cm^{-1}; HRMS calcd for $C_{28}H_{48}OSi_2$ 456.3244, found 456.3237; LRMS (EI) *m*/*z* (relative intensity) 413 (49), 237 (100), 209 (51), 167 (65). Anal. Calcd for $C_{28}H_{48}OSi_2$: C, 73.61; H, 10.59. Found: C, 74.06; H, 10.69 (sample for elemental analysis was a mixture diastereomers).

(1*R,2*S**,3*E*)-3-(Cyclohexylmethylene)-2-[(phenylsilyl)methyl]-1-[(triisopropylsilyl)oxy]cyclopentane (23b).** Purification by flash chromatography of a mixture of **23a** and **23b** using 10% CH_2Cl_2 followed by Kugelrohr distillation afforded a sample of the minor product **23b** for characterization (>98% pure by GC analysis): ot 120−150 °C/0.01 mmHg; R_f 0.62 (10% CH_2Cl_2 in hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.85−0.94 (m, 1H), 0.98−1.07 (m with overlapping broad singlet at 1.03, 23H), 1.12−1.27 (m, 2H), 1.32−1.39 (m, 1H), 1.58−1.68 (m, 6H), 1.71−1.82 (m, 2H), 1.99−2.04 (m, 1H), 2.11−2.19 (m, 1H), 2.32−2.39 (m, 1H), 2.40−2.44 (m, 1H), 4.24 (dt, J = 5.8, 6.4 Hz, 1H), 4.32−4.36 (m, $^1J_{^{29}Si,H}$ = 196 Hz, 2H), 5.05 (br d, J = 7.7 Hz, 1H), 7.30−7.38 (m, 3H), 7.54−7.56 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 7.93, 12.45, 18.11, 18.14, 24.41, 26.06, 26.17, 31.63, 32.96, 37.96, 46.79, 75.11, 127.88, 128.50, 129.30, 133.29, 135.25, 141.49; IR (neat) 2137.5 cm^{-1}; HRMS calcd for $C_{28}H_{48}OSi_2$ 456.3244, found 456.3217; LRMS (EI) *m*/*z* (relative intensity) 413 (29), 237 (100), 209 (52), 167 (65).

(1*R,2*R**,3*E*)-3-(Cyclohexylmethylene)-2-[(phenylsilyl)methyl]-1-[(triphenylmethyl)oxy]cyclopentane (25).** Prepared from **24** according to the general experimental procedure. Analysis of the crude reaction mixture by gas chromatography indicated that a 24:1 diastereomeric ratio of products was generated. Purification by flash chromatography using 5% Et_2O in hexanes followed by removal of solvents at 50 °C/0.01 mmHg afforded 88% of the desired product as a mixture of diastereomers: R_f 0.60 (5% Et_2O in hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.85 (dt, J = 7.5, 3.7 Hz, 2H), 1.00−1.37 (m, 6H), 1.45−1.77 (m, 6H), 2.07−2.15 (m, 2H), 2.38−2.50 (m, 2H), 3.68 (dt, J = 4.6, 2.3 Hz, 1H), 4.16 (t, J = 3.9, $^1J_{^{29}Si,H}$ = 194.9 Hz, 2H), 5.09 (br d, J = 9.2 Hz, 1H), 7.21−7.56 (m, 20H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.53, 25.45, 26.08, 26.19, 30.39, 32.98, 33.09, 38.52, 48.50, 81.54, 86.55, 126.83, 127.59, 127.86, 128.40, 129.04, 129.29, 133.03, 135.16, 142.57, 145.31; IR (neat) 2137.0 cm^{-1}; LRMS (EI) *m*/*z* (relative intensity) 243 (100), 165 (28), 105 (16). Anal. Calcd for $C_{38}H_{42}OSi$: C, 84.08; H, 7.80. Found: C, 84.49; H, 7.86.

(1*R,2*R**,3*E*)-3-(Cyclohexylmethylene)-1-isoindolino-2-[(phenylsilyl)methyl]cyclopentane (27). General NMR-Scale Experimental Procedure.** In the nitrogen atmosphere glovebox 0.018 g (0.068 mmol) of **26** was weighed in an NMR tube equipped with a J. Young valve. A solution of 0.002 g (0.004 mmol) of the precatalyst $Cp^*_2YCH_3$·THF in 0.6 mL of benzene-d_6 was prepared in a separate vial. This solution was added to the NMR tube followed by 0.010 g (0.092 mmol) of phenylsilane. The NMR tube was sealed and removed from the glovebox. A ^{1}H NMR taken after 0.5 h showed the reaction to be complete. The reaction mixture was diluted with 1 mL of Et_2O and filtered through a column of Florisil. The Florisil was rinsed two times with 1 mL portions of Et_2O. Analysis of the crude reaction mixture by gas chromatography indicated that a >40:1 diastereomeric ratio of products was generated. The organics were combined and concentrated by rotary evaporation followed by removal of solvents at 70 °C/0.01 mmHg to afford 91% (0.025 g, 0.062 mmol) of the desired product as a mixture of diastereomers: ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.98−1.34 (m, 7H), 1.61−1.74 (m, 6H), 1.79−1.87 (m, 1H), 2.02−2.10 (m, 1H), 2.21−2.29 (m, 1H), 2.42−2.45 (m, 1H), 2.56−2.61 (m, 1H), 2.86 (dt, J = 6.0, 7.8 Hz, 1H), 3.94 (br s, 4H), 4.34 (t, J = 3.8 Hz, $^1J_{^{29}Si,H}$ = 197.5 Hz, 2H), 5.10 (br d, J = 7.2 Hz, 1H), 7.17 (br s, 4H), 7.24−7.34 (m, 3H), 7.51−7.53 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 15.20, 24.06, 26.07, 26.11, 26.17. 26.35, 33.06, 33.09, 38.10, 44.52, 55.11, 69.56, 122.28, 126.48, 127.70, 127.78, 129.03, 134.82, 134.97, 140.05, 143.53; IR (neat) 2134.8 cm^{-1}; HRMS calcd for $C_{27}H_{35}NSi$ 401.2539, found 401.2517; LRMS (EI) *m*/*z* (relative intensity) 293 (51), 250 (51), 210 (74), 158 (100), 118 (78). Anal. Calcd for $C_{27}H_{35}NSi$: C, 80.74; H, 8.78. Found: C, 80.37; H, 8.93.

(1*E*,2*R,3*S**)-1-(Cyclohexylmethylene)-3-methyl-2-[(phenylsilyl)methyl]cyclopentane (28)** was prepared from **6** according to the general experimental procedure. Purification by flash chromatography in hexanes followed by Kugelrohr distillation afforded 69% of the desired product (>99% pure by GC analysis): ot 90−115 °C/0.25 mmHg; R_f 0.50 (hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.97−1.07 (m, 2H with overlapping d at 0.98, J = 6.5 Hz, 3H), 1.11−1.32 (m, 6H), 1.56−1.71 (m, 6H), 1.83−1.90 (m, 1H), 2.01−2.05 (m, 2H), 2.17−2.23 (m, 1H), 2.32−2.38 (m, 1H), 4.29−4.34 (m, $^1J_{^{29}Si,H}$ = 193.7 Hz, 2H), 5.04 (br d, J = 8.8 Hz, 1H), 7.32−7.40 (m, 3H), 7.56−7.59 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 13.10, 18.84, 26.11, 26.13, 26.21, 27.76, 32.78, 33.02, 33.11, 38.41, 41.46, 48.20, 127.00, 127.90, 129.32, 133.58, 135.20, 144.90; IR (neat) 2134.6 cm^{-1}; HRMS calcd for $C_{20}H_{30}Si$ 298.2117, found 298.2109; LRMS (EI) *m*/*z* (relative intensity) 298 (26), 220 (59), 137 (52), 107 (100).

(1*E*,2*S,3*R**)-1-(Cyclohexylmethylene)-3-ethyl-2-[(phenylsilyl)methyl]cyclopentane (29)** was prepared from **7** according to the general experimental procedure. Purification by flash chromatography using hexanes followed by Kugelrohr distillation to afford 88% of the desired product (>97% pure by GC analysis): ot 80−100 °C/0.02 mmHg; R_f 0.47 (hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.86 (t, J = 7.3 Hz, 3H), 0.97−1.31 (m, 9H), 1.42−1.71 (m, 7H), 1.87−1.95 (m, 1H), 2.00−2.09 (m, 1H), 2.12−2.21 (m, 2H), 2.23−2.37 (m, 1H), 4.27−4.34 (m, $^1J_{^{29}Si,H}$ = 195 Hz, 2H), 5.03 (dd, J = 9.0, 2.4 Hz, 1H), 7.32−7.40 (m, 3H), 7.55−7.58 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 12.29, 13.87, 26.12, 26.20, 26.77, 27.56, 29.77, 33.04, 33.13, 38.45, 46.28, 48.43, 126.96, 127.89, 129.31, 133.58, 135.19, 145.01; IR (neat) 2134.3 cm^{-1}; HRMS calcd for $C_{21}H_{32}Si$ 312.2273, found 312.2255; LRMS (EI) *m*/*z* (relative intensity) 312 (19), 283 (12), 234 (30), 107 (100).

(1*E*,2*R,3*S**)-1-(Cyclohexylmethylene)-3-[(methoxy)methyl]-2-[(phenylsilyl)methyl]cyclopentane (30)**. The reaction of **8** was carried out according to the general experimental procedure except the reaction was run in a sealed tube at 100 °C. Analysis of the crude reaction mixture by gas chromatography indicated that a 20:1 diastereomeric ratio of products was generated. Purification by flash chromatography using 10% Et_2O in hexanes followed by Kugelrohr distillation afforded 80% of the desired product as a mixture of diastereomers (>99% pure by GC analysis): ot 90−100 °C/0.01 mmHg; R_f 0.17 (3% Et_2O in hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.00 (br q, J = 12.0 Hz, 2H), 1.12−1.30 (m, 5H), 1.34−1.44 (m, 1H), 1.57−1.71 (m, 5H), 1.86−

1.97 (m, 2H), 1.98−2.07 (m, 1H), 2.18−2.25 (m, 1H), 2.29−2.36 (m, 2H), 3.20 (dd, J = 9.1, 7.0 Hz, 1H), 3.29 (s, 3H), 3.32 (dd, J = 9.1, 5.9 Hz, 1H), 4.28−4.33 (m, $^1J_{^{29}Si,H}$ = 195 Hz, 2H), 5.05 (dd, J = 9.1, 2.1 Hz, 1H), 7.31−7.39 (m, 3H), 7.55−7.58 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.94, 26.08, 26.17, 27.14, 27.60, 33.02, 33.09, 38.54, 43.48, 46.53, 58.77, 75.94, 127.60, 127.91, 129.36, 133.28, 135.22, 144.34; IR (neat) 2134.5 cm^{-1}; HRMS calcd for $C_{21}H_{32}OSi$ 328.2222, found 328.2218; LRMS (EI) *m*/*z* (relative intensity) 137 (31), 107 (100), 91 (37).

(1*E*,2*R,3*S**)-3-[[(*tert*-Butyldimethylsilyl)oxy]methyl]-1-(cyclohexylmethylene)-2-[(phenylsilyl)methyl]cyclopentane (31)** was prepared from **10** according to the general experimental procedure. Purification by flash chromatography using hexanes followed by Kugelrohr distillation afforded 76% of **31**: ot 90−110 °C/0.03 mmHg; R_f 0.32 (10% CH_2Cl_2 in hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.00 (s, 6H), 0.86 (s, 9H), 0.95−1.04 (m, 2H), 1.09−1.28 (m, 5H), 1.34−1.44 (m, 1H), 1.57−1.71 (m, 5H), 1.78−1.88 (m, 2H), 1.97−2.06 (m, 1H), 2.15−2.32 (m, 2H), 2.35−2.40 (m, 1H), 3.42 (B of ABX, J = 5.9, 6.2 Hz, 1H), 3.52 (A of ABX, J = 5.9, 5.2 Hz, 1H), 4.26−4.33 (m, $^1J_{^{29}Si,H}$ = 193.2 Hz, 2H), 5.03 (dd, J = 9.2, 2.0 Hz, 1H), 7.30−7.38 (m, 3H), 7.54−7.56 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ −5.35, 15.00, 18.37, 25.99, 26.11, 26.20, 26.95, 27.03, 33.06, 33.13, 38.55, 42.93, 48.97, 65.60, 127.53, 127.91, 129.34, 133.35, 135.25, 144.75; IR (neat) 2134.2 cm^{-1}; HRMS calcd for $C_{26}H_{43}OSi_2$: $(M - H)^+$ 427.2853, found 427.2823; LRMS (EI) *m*/*z* (relative intensity) 296 (22), 213 (72), 181 (44), 135 (44), 107 (53), 41 (100). Anal. Calcd for $C_{26}H_{44}OSi_2$: C, 72.83; H, 10.34. Found: C, 73.00; H, 10.41.

(1*R,2*R**,2′*R**/*S**,3*E*)-3-[2′-[(*tert*-Butyldimethylsilyl)oxy]propylene]-2-[(phenylsilyl)methyl]-1-[(triisopropylsilyl)oxy]cyclopentane (33)** was prepared from **32** according to the general experimental procedure. Purification by flash chromatography using 10% CH_2Cl_2 in hexanes followed by solvent removal at 0.04 mmHg afforded 83% (0.057 g, 0.092 mmol) of the title compound as a 1.6:1 mixture of diastereomers: R_f 0.30 (10% CH_2Cl_2 in hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.06 (d, J = 4.3 Hz, 3.6H), 0.08 (d, J = 4.8 Hz, 2.4H), 0.69−0.89 (m with 2 overlapping singlets at 0.85 and 0.89, 11H), 1.01−1.23 (m with 2 overlapping doublets at 1.10, J = 6.4 Hz and 1.23, J = 6.3 Hz, 4H), 1.34−1.55 (m, 1H), 1.99−2.16 (m, 1H), 2.24−2.47 (m, 2H), 3.63−3.65 (m, 0.6H), 3.69−3.72 (m, 0.4H), 4.05−4.10 (m, 0.8H), 4.11−4.19 (m, 1.2H), 4.34-4.43 (m, 1H), 5.24 (br d, J = 8.4 Hz, 0.4H) and 5.29 (br d, J = 8.3 Hz, 0.6H), 7.18−7.31 (m, 12H), 7.34−7.54 (m, 8H); ^{13}C NMR (100 MHz, $CDCl_3$) (major diasteromer) δ −4.73, −4.43, 14.62, 18.27, 24.37, 25.63, 25.91, 30.12, 48.59, 67.39, 81.12, 86.66, 126.88, 127.57, 127.63, 127.92, 128.98, 129.37, 132.76, 135.14, 143.84, 145.20; (minor diastereomer) −4.73, −4.24, 14.92, 18.29, 24.40, 25.32, 25.99, 30.44, 48.90, 67.42, 81.17, 86.83, 126.86, 127.63, 127.72, 127.91, 128.78, 128.98, 132.69, 135.10, 143.55, 145.18; IR (neat) 2138.0 cm^{-1}; LRMS (EI) *m*/*z* (relative intensity) 375 (11), 243 (100), 165 (64), 105 (10), 73 (28). Anal. Calcd for $C_{40}H_{50}O_2Si_2$: C, 77.69; H, 8.14. Found: C, 77.49; H, 7.95.

(1*R,2*R**,3*E*)-3-[5′-(2′,2′-Dimethyl-1′,3′-dioxanyl)methylene]-2-[(phenylsilyl)methyl]-1-[(triphenylmethyl)oxy]cyclopentane (35)** was prepared from **34** according to the general experimental procedure. Analysis of the crude reaction mixture by gas chromatography indicated that a 35:1 diastereomeric ratio of products was formed. Purification by flash chromatography using 10% Et_2O in hexanes followed by removal of solvents at 70 °C/0.01 mmHg to afford 88% of the desired product as a mixture of diastereomers (>99% pure by GC analysis): R_f 0.41 (20% Et_2O in hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.74−0.79 (m, 2H), 1.20−1.28 (m, 1H), 1.34−1.51 (m, 1H, with 2 overlapping singlets, 1.39, 3H and 1.44, 3H), 2.07−2.15 (m, 1H), 2.34−2.48 (m, 2H), 2.62−2.73 (m, 1H), 3.48−3.68 (m, 4H), 3.76−3.81 (m, 1H), 4.06 (t, J = 3.4 Hz, $^1J_{^{29}Si,H}$ = 192 Hz, 2H), 4.78 (br d, J = 9.0 Hz, 1H), 7.18−7.49 (m, 20H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.26, 19.18, 25.91, 28.95, 30.36, 36.19, 49.03, 63.94, 63.99, 81.37, 86.75, 97.37, 117.35, 127.00, 127.72, 128.01, 129.02, 129.53, 132.62, 135.15, 145.16, 149.77; IR (neat) 2136.1 cm^{-1}; HRMS calcd for $C_{37}H_{39}O_3Si$: $(M - CH_3)^+$ 559.2668, found 559.2680; LRMS (EI) *m*/*z* (relative intensity) 243 (100), 165 (86), 105 (73).

(1*R,2*R**,3*E*)-3-(Cyclohexylmethylene)-2-(hydroxymethyl)-1-cyclopentanol (36). General Procedure for the Oxidation/Deprotection of 21a.** In a 50 mL Schlenk flask purged with argon 0.245 g (2.45 mmol) of 90% *t*-BuOOH solution was weighed out and 1.2 mL of DMF was added. To this solution at 0 °C, 0.103 g (2.56 mmol) of KH was slowly added. This produced a slightly foamy pink solution which was allowed to warm to room temperature. A solution of **21a**, 105 mg, 0.25 mmol, 0.2 M in DMF was slowly added via syringe. After 3 h of stirring at room temperature, no starting material could be detected by TLC. To this solution 0.5 g of $Na_2S_2O_3\cdot 5H_2O$ was slowly added and the sides of the flask were rinsed down with hexanes. All of the volatiles were removed in vacuo. The resulting solids were extracted with $CHCl_3$, concentrated, and flashed using 1:1 EtOAc/hexanes followed by EtOAc. Concentration followed by recrystallization from $CHCl_3$ afforded 80% (0.042 mg, 0.20 mmol) of the diol **36** as white needle-like crystals (>99% pure by GC analysis): mp 107 °C; R_f 0.50 (in EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.93−1.28 (m, 5H), 1.52−1.68 (m, 6H), 1.95−2.06 (m, 2H), 2.12−2.22 (m, 2H), 2.37−2.44 (m, 2H), 2.60 (br s, 1H), 3.58 (dd, J = 10.7, 8.2 Hz, 1H), 3.80 (dd, J = 10.7, 4.9 Hz, 1H), 4.04 (dt, J = 6.8, 7.0 Hz, 1H), 4.98 (dq, J = 9.1, 2.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 25.67, 25.95, 26.01, 32.40, 32.76, 33.07, 38.06, 53.35, 64.51, 129.32, 136.99; IR (neat) 3388 cm^{-1} (br); HRMS calcd for $C_{13}H_{22}O_2$ 210.1620, found 210.1606; LRMS (EI) *m*/*z* (relative intensity) 210 (13), 192 (48), 161 (80), 81 (100). Anal. Calcd for $C_{13}H_{22}O_2$: C, 74.24; H, 10.54. Found: C, 74.09; H, 10.68.

(1*E*)-6-[(*tert*-Butyldimethylsilyl)oxy]-1-cyclohexyl-2-(phenylsilyl)-1,7-octadiene (38). The reaction of **37** was carried out according to the general experimental procedure except the reaction was stirred for 21 h. Purification by flash chromatography using 3% Et_2O in hexanes followed by Kugelrohr distillation afforded 93% of the title compound: ot 95−110 °C/0.01 mmHg; R_f 0.57 (3% Et_2O in hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.02 (s, 3H), 0.03 (s, 3H), 0.89 (s, 9H), 1.05−1.50 (m, 9H), 1.60−1.73 (m, 5H), 2.18 (br t, J = 6.5 Hz, 2H), 2.36−2.44 (m, 1H), 4.01 (br dt, J = 5.9, 5.9 Hz, 1H), 4.52 (s, $^1J_{^{29}Si,H}$ = 195 Hz, 2H), 4.99 (dd, J = 10.4, 1.2 Hz, 1H), 5.10 (dd, J = 17.2, 1.4 Hz, 1H), 5.85 (ddd, J = 17.0, 10.4, 6.0 Hz, 1H), 5.85 (br d, J = 9.2 Hz, 1H), 7.32−7.40 (m, 3H), 7.55−7.57 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ −4.83, −4.39, 18.22, 25.64, 25.76, 25.83, 25.88, 25.92, 26.00, 30.48, 32.83, 37.70, 38.02, 73.72, 113.44, 127.96, 129.44, 131.47, 132.69, 135.50, 141.69, 152.17; IR (neat) 2131.7 cm^{-1}; HRMS calcd for $C_{26}H_{43}OSi_2$ ($M - H^+$) 427.2853, found 427.2831; LRMS (EI) *m*/*z* (relative intensity) 265 (32), 181 (71), 105 (20), 75 (100). Anal. Calcd for $C_{26}H_{44}OSi_2$: C, 72.83; H, 10.34. Found: C, 72.85; H, 10.59.

(1*R,2*R**,3*E*)-1-[(*tert*-Butyldimethylsilyl)oxy]-3-(cyclohexylmethylene)-2-[(hexylsilyl)methyl]cyclohexane (39).** The reaction of **37** was carried out according to the general experimental procedure except hexylsilane was used in the place of phenylsilane and the reaction was run for 22 h. Purification by flash chromatography in hexanes afforded 47% of the title compound: R_f 0.50 (hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) δ −0.02 (s, 3H), 0.00 (s, 3H), 0.59−0.65 (m, 2H), 0.69−0.77 (m, 1H), 0.79−0.88 (m, 2H, with overlapping singlet at 0.79, 9H), 0.91−1.45 (m, 16H), 1.53−1.72 (m, 7H), 1.77−1.84 (m, 1H), 1.98−2.06 (m, 3H), 2.13−2.21 (m, 1H), 3.42−3.45 (m, 1H), 3.54−3.62 (m, $^1J_{^{29}Si,H}$ = 182.5 Hz, 2H), 4.9 (d, J = 8.9 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ −4.68, −4.51, 9.56, 10.01, 14.11, 18.05, 22.56, 23.19, 25.46, 25.82, 26.11, 26.17, 31.51, 31.55, 32.57, 33.76, 33.86, 36.44, 49.84, 75.48, 130.25, 136.46; IR (neat) 2124.5 cm^{-1}; LRMS (EI) *m*/*z* (relative intensity) 379 (35), 189 (78), 171 (95), 105 (100), 73 (82). Anal. Calcd for $C_{26}H_{52}OSi_2$: C, 71.48; H, 12.00. Found: C, 71.76; H, 11.77.

(1*R,2*R**,3*E*)-3-(Cyclohexylmethylene)-2-(hydroxymethyl)-1-cyclohexanol (41).** The oxidation of **39** was carried out according to the general procedure outlined for the oxidation of **21a** with the exception that the reaction was heated to 70 °C for 24 h. Purification by flash chromatography in 1:1 ethyl acetate/hexanes followed by recrystallization from hexanes afforded 13% of the expected diol as white needle-like crystals (>98% pure by GC analysis): mp 68 °C; R_f 0.26 (1:1 EtOAc/hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.96−1.37 (m, 6H), 1.50−1.76 (m, 7H), 1.84−1.90 (m, 2H), 2.14−2.24 (m, 2H), 2.30−2.38 (m, 2H), 2.62 (br d, J = 4.8, 1H), 3.62−3.68 (m, 1H), 3.77−3.91 (m, 2H), 4.86 (d, J = 8.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 23.78, 25.95, 27.65, 33.63, 33.78, 33.83, 36.56, 52.55, 64.15, 74.64, 130.70, 134.37; IR (neat) 3349 cm^{-1} (br); LRMS (EI) *m*/*z* (relative intensity) 206 (93), 163 (65), 135 (66), 81 (100). Anal. Calcd for $C_{14}H_{24}O_2$: C, 74.95; H, 10.78. Found: C, 75.29; H, 10.89. The relative

stereochemistry was determined by single-crystal X-ray crystal diffractometry.

(1*R,2*R**,3*E*)-3-(Cyclohexylmethylene)-2-methyl-1-cyclohexanol (42) and (1*R**,2*S**,3*E*)-3-(Cyclohexylmethylene)-2-methyl-1-cyclohexanol (43).** The reaction of **37** with $PhMeSiH_2$ was run in an NMR tube according to the general procedure outlined for the preparation of **27**. The reaction was run at 50 °C for 8 h. Standard workup procedures were employed to isolate a crude mixture of **40** as inseparable isomers. To simplify characterization the crude reaction mixture was treated with 2 equiv of 0.5 M TBAF in THF. After 20 h of stirring at room temperature, the reaction was diluted with Et_2O and washed with H_2O and brine, and the aqueous layers were extracted with Et_2O. The combined organic extracts were dried over $MgSO_4$ and concentrated in vacuo. Analysis of the crude reaction mixture by ^{1}H NMR indicated that a 4:1 diastereomeric ratio of products was generated. Purification by column chromatography using 20% EtOAc in hexanes afforded a mixture of **42** and **43** in 84% yield. The two diastereomers were isolated independently for characterization. Determination of the relative stereochemistry was based on ^{1}H NMR decoupling experiments. Alcohol **42** was isolated as the major product of the reaction (>99% pure by GC analysis): mp 74 °C; R_f 0.30 (20% CH_2Cl_2/20% Et_2O in hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.96−1.37 (m, 6H, with overlapping doublet at 1.08, J = 6.9, 3H), 1.42−1.73 (m, 8H), 1.81−1.94 (m, 2H), 2.00 (br dq, J = 7.5, 6.6 Hz, 1H), 2.12−2.22 (m, 1H), 2.31−2.37 (m, 1H), 3.24−3.30 (m, 1H), 4.98 (d, J = 8.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.97, 24.13, 26.05, 26.07, 26.08, 27.17, 32.94, 33.87, 33.88, 36.47, 46.42, 75.48, 129.42, 137.98; IR (neat) 3356 cm^{-1} (br); LRMS (EI) *m*/*z* (relative intensity) 208 (21), 190 (60), 108 (100), 95 (97). Anal. Calcd for $C_{14}H_{24}O$: C, 80.71; H, 11.61. Found: C, 80.76; H, 11.61. Alcohol **43** was isolated as the minor product of the reaction (>99% pure by GC analysis): R_f 0.36 (20% EtOAc in hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.00−1.31 (m, 6H, with overlapping doublet at 1.01, J = 6.0, 3H), 1.47−1.63 (m, 6H), 1.66−1.70 (m, 2H), 1.73−1.84 (m, 2H), 2.18−2.24 (m, 1H), 2.33 (ddq, J = 7.0, 3.1, 1.3 Hz, 1H), 2.37−2.41 (m, 1H), 3.73−3.77 (m, 1H), 4.97 (d, J = 8.7 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 13.85, 23.22, 26.06, 26.10, 27.75, 32.37, 33.72, 34.19, 36.43, 43.87, 72.82, 130.22, 137.46; IR (neat) 3382 cm^{-1} (br); HRMS calcd for $C_{14}H_{24}O$: 208.1827, found 208.1827; LRMS (EI) *m*/*z* (relative intensity) 208 (16), 190 (31), 135 (33), 111 (85), 108 (75).

Acknowledgment. We gratefully acknowledge the National Institutes of Health (GM48580) for their generous support of this research. In addition, we would also like to thank Dr. Bruce C. Noll for performing the X-ray crystal structure determinations.

Supporting Information Available: Experimental details and characterization for intermediates **1**−**10**, **12**−**16**, **18**, **20**, **22**, **24**, **26**, **32**, **34**, and **37** and crystallographic data and tables for **36** and **41** (38 pages). See any current masthead page for ordering information and Internet access instructions.

JA971538G