Sequential Cyclization/Silylation of Dienynes Catalyzed by an Organoyttrium Complex

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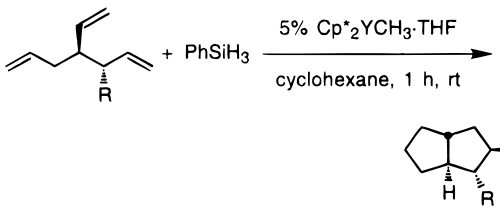
The organoyttrium complex $Cp^*_2YCH_3{\cdot}THF$ ($Cp^* = C_5Me_5$) has been shown to be an effective precatalyst for the selective sequential cyclization/silylation of dienynes. The catalyst's ability to insert the alkyne in preference to the alkenes in a regioselective manner, combined with the high diastereoselectivity of the intramolecular insertion process, leads to bicyclo[3.3.0]octane products in high yield. The stereochemistry of the exocyclic olefin, the ring fusion, and the ring substituents are all controlled in the reaction. The cyclization of dienynes thus affords silylated carbobicyclics with high diastereoselectivities in excellent yields.

Introduction

The development of novel carbon−carbon bond-forming reactions is an integral part of organic chemistry. Within this context, the cyclization of dienes and enynes represents a powerful means to convert simple, readily available substrates to more complex organic molecules. In fact, the selective conversion of readily available acyclic polyene precursors into more highly elaborated polycyclic molecules has been catalyzed by a host of metal complexes. For example, a number of recently reported protocols to effect Pauson−Khand cyclizations of enynes employ a variety of metal complexes for the preparation of bicyclic cyclopentenones.[1] A polyene cyclization catalyzed by a titanium alkoxide species[2] has been reported, as well as a variety of palladium(II)-catalyzed[3] reactions with polyenynes.

Radical[4] and organometallic cyclizations[5] of unsaturated systems terminated by a silylation reaction can also be accomplished to form functionalized carbocycles. In particular, significant progress has been made in the development of organoyttrium-catalyzed cyclization reactions.[6] The precatalyst $Cp^*_2YCH_3{\cdot}THF$ ($Cp^* = C_5Me_5$) utilized in these studies has demonstrated the ability to generate five- and six-membered rings from dienes and enynes. In addition to silylation, the cyclization reaction can be terminated by hydrogenation. Use of a silylation reaction to terminate the cyclization is of greater interest because it leads to materials that can be further functionalized by oxidation to the alcohol. The utility of this catalytic cyclization/silylation method was demonstrated through its use in the key step of a total synthesis of (±)-epilupinine.[6c] This method yielded the desired product with extremely high diastereoselectivity.

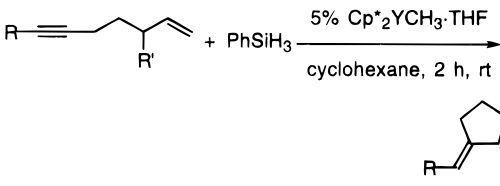
Carbobicyclics have also been synthesized from acyclic precursors using this cyclization strategy (eq 1).[7] For



(1)

example, organoyttrium catalyzed sequential cyclization/silylation reactions of trienes have been accomplished to prepare polycyclic systems. The selectivity of the catalyst for unsubstituted alkenes relative to allylically substituted alkenes permits the process to be carried out in a highly selective manner.

The organoyttrium precatalyst has also demonstrated a high degree of selectivity and stereocontrol in the catalyzed cyclization/silylation of enynes (eq 2).[6d] The



(2)

catalytic cyclization of 1,6-enynes containing allylic substituents afforded trans-substituted (phenylsilyl)methylcyclopentanes in high yields. The diastereomeric ratios generated by this protocol were in excess of 50:1 when the substrate contained an allylic alkyl substituent. The formation of the observed cyclized products was dictated

(1) (a) For a review of transition metal catalyzed reactions, see: Catellani, M.; Chiusoli, G. P.; Costa, M. *J. Organomet. Chem.* **1995**, *500*, 69. (b) Livinghouse, T.; Pagenkopf, B. L. *J. Am. Chem. Soc.* **1996**, *118*, 2285. (c) Hicks, F. A.; Kablaoui, N. M.; Buchwald, S. L. *J. Am. Chem. Soc.* **1996**, *118*, 9450. (d) Hicks, F. A.; Buchwald, S. L. *J. Am. Chem. Soc.* **1996**, *118*, 11688. (e) Hicks, F. A.; Berk, S. C.; Buchwald, S. L. *J. Org. Chem.* **1996**, *61*, 2713. (f) Zhang, M.; Buchwald, S. L. *J. Org. Chem.* **1996**, *61*, 4498.

(2) Negishi, E.-I.; Jensen, M. D.; Kondakov, D. Y.; Wang, S. *J. Am. Chem. Soc.* **1994**, *116*, 8404.

(3) (a) For a review see: Trost, B. M. *Acc. Chem. Res.* **1990**, *23*, 34 and references therein. (b) Chatani, N.; Furukawa, N.; Sakurai, H.; Murai, S. *Organometallics* **1996**, *15*, 901. (c) Trost, B. M.; Shi, Y. *J. Am. Chem. Soc.* **1993**, *115*, 9421. (d) Shi, Y.; Trost, B. M. *J. Am. Chem. Soc.* **1992**, *114*, 791.

(4) (a) Kulicke, K. J.; Giese, B. *Synlett* **1990**, 91. (b) Kraus, G. A.; Liras, S. *Tetrahedron Lett.* **1990**, *31*, 5265. (c) Kopping, B.; Chatgilialoglu, C.; Zehnder, M.; Giese, B. *J. Org. Chem.* **1992**, *57*, 3994.

(5) Ojima, I.; Donovan, R. J.; Shay, W. R. *J. Am. Chem. Soc.* **1992**, *114*, 6580.

(6) (a) Molander, G. A.; Hoberg, J. O. *J. Am. Chem. Soc.* **1992**, *114*, 3123. (b) Molander, G. A.; Nichols, P. J. *J. Am. Chem. Soc.* **1995**, *117*, 4415. (c) Molander, G. A.; Nichols, P. J. *J. Org. Chem.* **1996**, *61*, 6040. (d) Molander, G. A.; Retsch, W. H. *J. Am. Chem. Soc.* **1997**, *119*, 8817. (e) Molander, G. A.; Dowdy, E. D. *J. Org. Chem.*, in press.

(7) Molander, G. A.; Nichols, P. J. *J. Org. Chem.*, in press.

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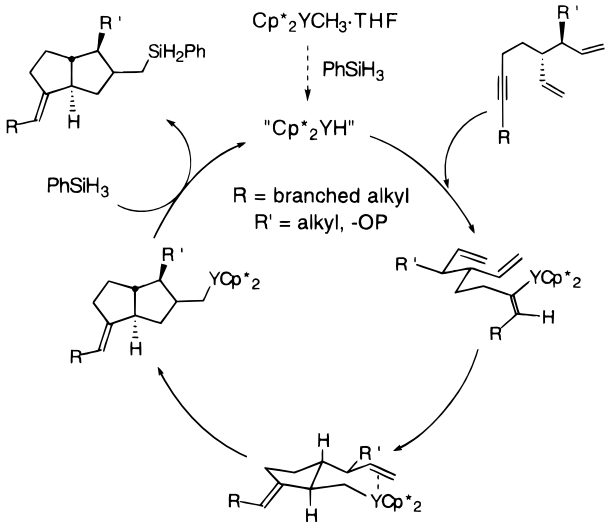
Scheme 1

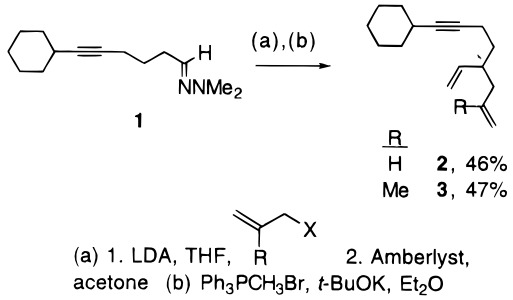


by the ability of the organoyttrium complex to selectively insert alkynes relative to allylically substituted alkenes in the first step of the reaction. The Lewis acidic organoyttrium complex tolerated ethers, acetals, and tertiary amine functionalities in the reaction.

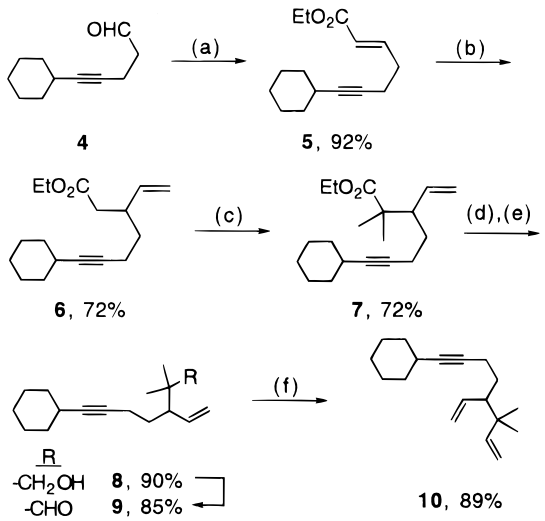
In an effort to extend the organoyttrium-catalyzed cyclization/silylation reaction of enynes to the preparation bicyclic products, a variety of dienynes were prepared and reacted under conditions similar to those used to cyclize enynes. The process envisioned for the organoyttrium-catalyzed sequential cyclization/silylation of dienynes would be complementary to the previously reported methods using other classes of catalysts. A viable catalytic cycle, similar to that proposed for the cyclization/silylation of enynes, is outlined in Scheme 1.[6d] The catalytic cycle would be initiated by a σ-bond metathesis between $Cp^*_2YCH_3$·THF and $PhSiH_3$, producing a catalytically active metal hydride species.[6a−d,8] Next, the catalyst would have to insert the alkyne selectively in preference to the two alkenes in the substrate. Evidence supports the proposition that the alkyne would be more reactive and could be inserted regioselectively in order to form a single alkenylyttrium intermediate.[6d,8b] This intermediate could undergo cyclization with either of the available alkenes. Evidence from enyne cyclizations suggested that the 5-*exo-trig* cyclization would be preferred over the 6-*exo-trig* pathway.[6d] Cyclization would provide a second intermediate alkylyttrium species. This second intermediate, similar to those proposed in prior cyclizations,[6,7] could undergo a subsequent intramolecular alkene insertion with the remaining alkene as predicted by reactions with trienes.[7] A σ-bond metathesis with silane would generate the bicyclic product and complete the catalytic cycle. All of the steps in this catalytic cycle are well precedented, and the chemo-, regio-, and diastereoselectivities demonstrated in preceding studies suggested that this reaction would also be accomplished with excellent selectivity.

We now report that the organoyttrium hydride catalyst derived from $Cp^*_2YCH_3$·THF is indeed an effective catalyst for the sequential cyclization of dienynes in the postulated manner. The reaction provides facile access to stereodefined, highly functionalized carbobicyclics from relatively simple, readily accessible acyclic starting materials.

Scheme 2



Scheme 3[a]



[a] Key: (a) (carbethoxymethylene)triphenylphosphorane, CH_2Cl_2; (b) vinylmagnesium bromide, CuI, THF; (c) (1) LDA, THF, MeI, HMPA, (2) LDA, THF, MeI, HMPA; (d) LAH, THF; (e) pyr·SO_3, DMSO, NEt_3, CH_2Cl_2; (f) Ph_3PCH_3Br, *t*-BuOK, Et_2O.

Results and Discussion

A series of dienyne substrates designed to test this new protocol was prepared according to Schemes 2−9. Scheme 2 outlines the synthesis of dienyne substrates **2** and **3**. Hydrazone **1** was prepared according to literature procedures.[6d] Treatment of the hydrazone 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 dienynes.[9]

Substrate **10** was synthesized according to the outline in Scheme 3. The aldehyde 5-cyclohexyl-4-pentynal was prepared according to a published procedure[6d] and was treated with (carbethoxymethylene)triphenylphosphorane to yield the unsaturated ester **5**.[10] Vinyl cuprate addition followed by dialkylation with iodomethane provided the substituted ester **7**. Reduction of the ester to the alcohol followed by oxidation using a modified Swern procedure afforded aldehyde **9**.[11] The aldehyde was treated with a Wittig reagent to yield the desired dienyne **10**.

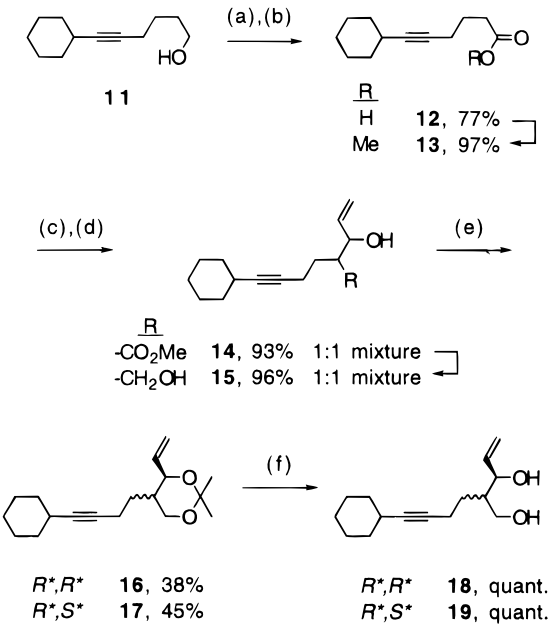
(8) (a) Molander, G. A.; Hoberg, J. O. *J. Org. Chem.* **1992**, *57*, 3266. (b) Molander, G. A.; Retsch, W. H. *Organometallics* **1995**, *14*, 4570.

(9) Fitjer, L.; Quabek, U. *Synth. Commun.* **1985**, *15*, 855.

(10) Bunce, R. A.; Dowdy, E. D.; Jones, P. B.; Holt, E. M. *J. Org. Chem.* **1993**, *58*, 7143.

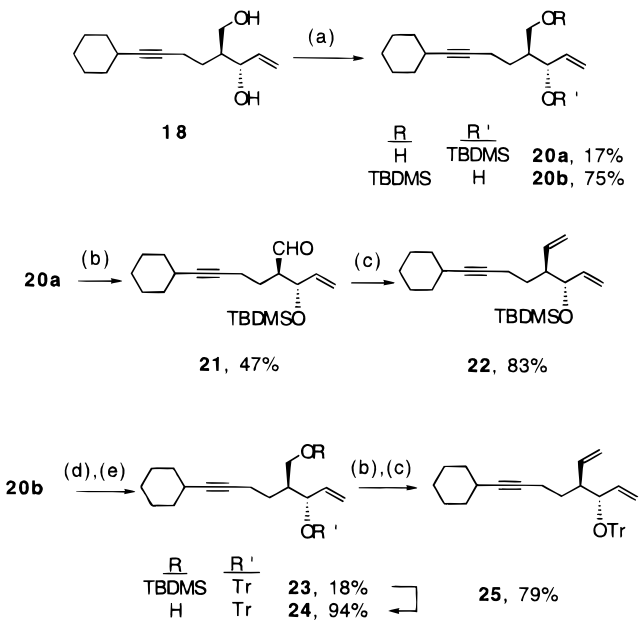
(11) Wipf, P.; Fritch, P. C. *J. Org. Chem.* **1994**, *59*, 4875.

Scheme 4[a]



[a] Key: (a) PDC, DMF; (b) DCC, DMAP, MeOH, CH_2Cl_2; (c) (1) LDA, THF, (2) acrolein; (d) LAH, THF; (e) 2,2-dimethoxypropane, cat. TsOH, acetone; (f) MeOH, cat. TsOH.

Scheme 5[a]

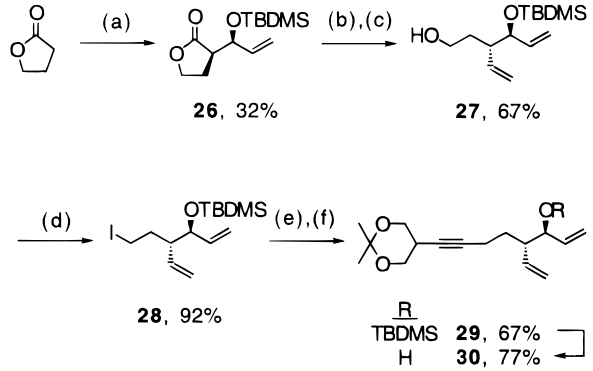


[a] Key: (a) NaH, TBDMSCl, THF; (b) cat. TPAP, NMO, molecular sieves, CH_2Cl_2; (c) Ph_3PCH_3Br, *t*-BuOK, Et_2O; (d) TrCl, DBU, CH_2Cl_2; (e) TBAF, THF.

The diastereomerically pure dienynes **22**, **25**, **56**, and **58** were prepared according to Schemes 4 and 5. Alcohol **11**[6d] was oxidized with PDC and converted to a methyl ester with DCC, DMAP, and MeOH.[12] Ester **13** was treated with LDA and acrolein in an aldol reaction to provide β-hydroxy ester **14**. Subsequent reduction with LAH provided a 1:1 mixture of the desired 1,3-diols. Treatment of **15** with 2,2-dimethoxypropane in acetone and a catalytic amount of H_2SO_4 afforded acetonides **16**

(12) Neises, B.; Steglich, W. *Organic Syntheses*; Wiley: New York, 1990; Vol. VIII, p 93.

Scheme 6[a]



[a] Key: (a) (1) LDA, THF, (2) acrolein, (3) TBDMSCl; (b) DIBALH, THF; (c) Ph_3PCH_3Br, *t*-BuOK, Et_2O; (d) PPh_3, imidazole, I_2, 3:1 Et_2O/CH_3CN; (e) alkynyllithium from 2,2-dimethyl-5-ethynyl-1,3-dioxane, HMPA, THF; (f) TBAF, THF.

and **17**, which were separable by flash chromatography. The relative stereochemistry of the acetonides was assigned on the basis of the chemical shift and coupling constants of the allylic proton. Deprotection of the acetonide provided diastereomerically pure diols **18** and **19**.

In Scheme 5, the conversion of diol **18** to the desired substituted dienynes **22** and **25** is diagrammed. A monoprotection of diol **18** yielded a separable 1:5 mixture of silyl ethers **20a** and **20b**. The minor isomer **20a** was oxidized with TPAP[13] to aldehyde **21** and treated with a Wittig reagent to provide dienyne substrate **22**. The hydroxyl group of **20b** was protected as a trityl ether, followed by TBAF deprotection of the silyl ether to yield **24**. Compound **24** was oxidized in the same manner as **21** and treated with a Wittig reagent to provide dienyne substrate **25**. An identical synthetic scheme was used for the conversion of the other diastereomer, diol **19**, to dienyne substrates **56** and **58**.

The synthesis of intermediate **30** is shown in Scheme 6. γ-Butyrolactone was treated with LDA, acrolein, and *tert*-butyldimethylsilyl chloride to yield a single diastereomer of compound **26**. Reduction of the lactone to the hemiacetal was followed by treatment with a Wittig reagent to yield **27**. The hydroxyl group of **27** was converted to an iodide[14] and displaced with the alkynyllithium derived from 2,2-dimethyl-5-ethynyl-1,3-dioxane to yield dienyne **29**.[15] The silyl ether of **29** was deprotected with TBAF to give intermediate **30**. Protection of the hydroxyl group of this intermediate provided substrates **52** and **54**.

Scheme 7 outlines the synthesis of substrate **35**. Lactone **31** was prepared according to a published procedure and treated with LDA.[16] Alkylation with benzyl bromide provided diastereomerically pure **32**. The relative stereochemistry of **32** was assigned by NOE experiments. The lactone **32** was reduced to the hemiacetal and treated directly with a Wittig reagent to provide **33**. The hydroxyl group of **33** was converted to

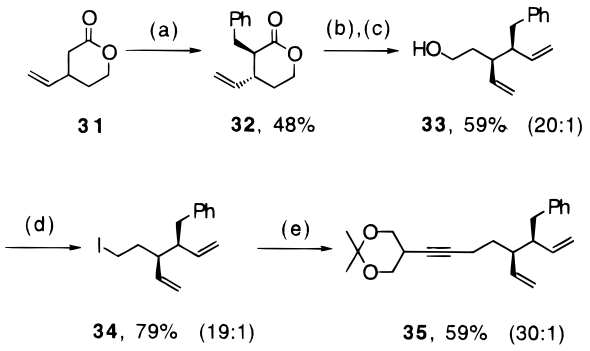
(13) Ley, S. V.; Norman, J.; Griffith, W. P.; Marsden, S. P. *Synthesis* **1994**, 639.

(14) Corey, E. J.; Pyne, S. C. *J. Org. Chem.* **1986**, *51*, 4726.

(15) To establish the relative stereochemistry of **28**, the iodide was displaced with lithium acetylide, ethylendiamine complex in DMSO to prepare a terminal alkyne. Installation of a cyclohexyl group on the alkyne afforded material identical to compound **22** by GC and NMR.

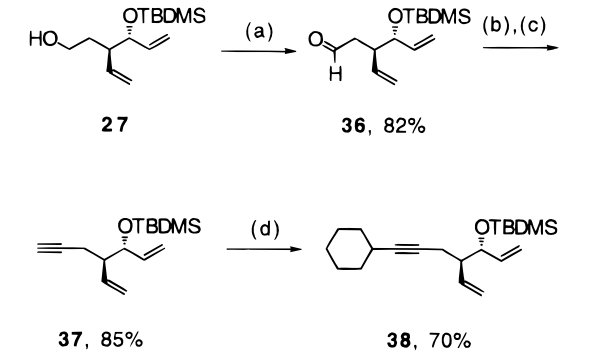
(16) Molander, G. A.; Harris, C. H. *J. Am. Chem. Soc.* **1995**, *117*, 3705.

Scheme 7[a]



[a] Key: (a) (1) LDA, THF, (2) benzyl bromide; (b) DIBALH, THF; (c) Ph_3PCH_3Br, *t*-BuOK, Et_2O; (d) PPh_3, imidazole, I_2, 3:1 Et_2O/CH_3CN; (e) alkynyllithium from 2,2-dimethyl-5-ethynyl-1,3-dioxane, HMPA, THF.

Scheme 8[a]



[a] Key: (a) pyr·SO_3, DMSO, NEt_3, CH_2Cl_2; (b) PPh_3, CBr_4, Zn, CH_2Cl_2; (c) 2 equiv of *n*-BuLi, THF; (d) (1) *n*-BuLi, $(C_6H_{11})_3B$, I_2, THF, (2) NaOH, H_2O_2.

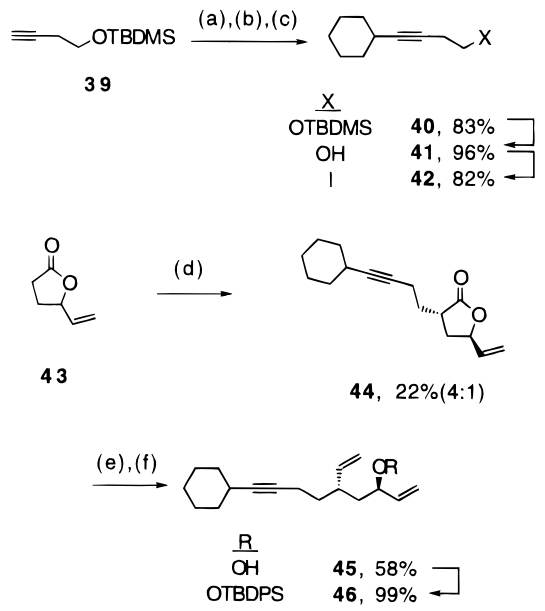
the iodide and displaced with the appropriate alkynyllithium to yield dienyne substrate **35** as a 30:1 mixture of diastereomers.

Scheme 8 depicts the synthesis of substrate **38**. Alcohol **27**, prepared in a previous synthesis, was oxidized to provide **36**. Aldehyde **36** was converted to a terminal alkyne via a Corey−Fuchs sequence.[17] A cyclohexyl group was placed on the terminal alkyne according to published procedures to yield substrate **38**.[18]

Finally, Scheme 9 provides an outline for the synthesis of compound **46**. Commercially available 3-butyn-1-ol was protected as the silyl ether and converted to iodide **42** in high yield. Lactone **43** was prepared according to the published procedure[19] and alkylated with iodide **42** to give a 4:1 mixture of diastereomers. The lactone was reduced to the hemiacetal and treated with the Wittig reagent. Flash column chromatography provided the major isomer **45** as a single diastereomer. Protection of **45** as the silyl ether provided the final dienyne substrate.

With the substrates in hand, investigations were undertaken to determine the optimum reaction conditions for the sequential cyclization/silylation reaction and to outline the scope and limitations of the process. Compound **2** was treated with 1.1 equiv of phenylsilane and 5 mol % of the precatalyst in cyclohexane for 2.5 h (entry 1, Table 1). A mixture of compounds was gener-

Scheme 9[a]



[a] Key: (a) (1) *n*-BuLi, $(C_6H_{11})_3B$, I_2, THF, (2) NaOH, H_2O_2; (b) TBAF, THF; (c) PPh_3, I_2, imidazole, 3:1 Et_2O/CH_3CN; (d) (1) LDA, THF, (2) **42**, HMPA; (e) (1) DIBALH, THF, (2) Ph_3PCH_3Br, *t*-BuOK, Et_2O; (f) TBDPSCl, imidazole, DMF.

Table 1. Sequential Cyclization/Silylation of Dienynes Catalyzed by $Cp^*_2YCH_3$·THF[a]

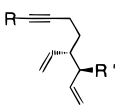
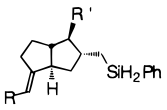
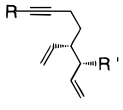
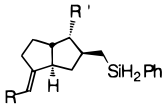
entry	substrate	products	reaction time (h)	% isolated yield
1	**2**	**47**	2.5	33
2	**3**	**48**	24	84
3	**10**	**49**	18	76 (3.9:1) [b]

[a] Reactions were run in cyclohexane with 5 mol % precatalyst and 1.1−1.3 equiv $PhSiH_3$ at rt. [b] Diastereomeric ratio was determined by fused silica gas chromatographic analysis.

ated in the reaction. Only compound **47** was isolated cleanly from the reaction mixture. The expected stereochemistry of the bicyclic product with respect to the ring fusion was predicted to be trans by comparison to the products isolated from previous enyne and polyene cyclizations.[6b−d,7,8a] The stereochemistry of the methylphenylsilyl substituent was not determined. The lack of selectivity of the catalyst for initial insertion of the alkyne over the unsubstituted alkenes was assumed to be responsible for the formation of undesirable byproducts in this reaction. To overcome this difficulty and

(17) Corey, E. J.; Fuchs, P. L. *Tetrahedron Lett.* **1972**, *36*, 3769.
(18) Brown, H. C.; Sinclair, J. A.; Midland, M. M. *J. Am. Chem. Soc.* **1973**, *95*, 3080.
(19) Annby, U.; Stenkula, M. *Tetrahedron Lett.* **1993**, *34*, 8545.

Table 2. Sequential Cyclization/Silylation of Diastereomerically Pure Dienynes Catalyzed by $Cp^*_2YCH_3 \cdot THF$[a]

entry	substrate			products	diastereomeric ratio[b]	% isolated yield
		R	R'			
1	**22**	cyclohexyl	OTBDMS	**50**	7:1	93
2	**25**	cyclohexyl	OTr	**51**	>30:1	86
3	**52**		OTr	**53**	>40:1	98
4	**54**		OTBDPS	**55**	14:1	90
		R	R'			
5	**56**	cyclohexyl	OTBDMS	**57a** (**57b**)	2:1	56 (30)
6	**58**	cyclohexyl	OTr	**59**	>60:1	97
7	**35** (30:1)		benzyl	**60**	30:1	89

[a] Reactions were run in an NMR tube according to the general procedure. [b] Diastereomeric ratios were determined by fused silica gas chromatographic analysis or by ^{1}H NMR integration of the crude reaction mixture.

increase the catalyst's preference for initial insertion of the alkyne, substrates with substituents on the alkene and in the allylic position were prepared. The presence of a methyl substituent on the alkene of dienyne **3** was expected to favor the initial insertion of the alkyne by lowering the reactivity of the alkene.[6a,20] Unfortunately, the intramolecular insertion of this 1,1-disubstituted alkene was also hindered. Only the initial cyclization occurred before the intermediate organometallic was trapped with the phenylsilane to afford compound **48** (Table 1, entry 2). Substrate **10**, prepared with a *gem*-dimethyl group allylic to the alkene, was effectively cyclized under similar reaction conditions (Table 1, entry 3). The bicyclic product **49** was isolated in 76% yield as a 3.9:1 mixture of diastereomers. This example indicated that allylic substitution at both alkenes would allow the sequential cyclization reaction to proceed cleanly. It also demonstrated that the alkenylmetallic species produced by the initial insertion undergoes a highly selective 5-*exo*-*trig* cyclization in preference to a 6-*exo*-*trig* cyclization.

The addition of an alkoxy substituent in the allylic position of alkenes has been shown to permit favorable insertion of the alkyne in preference to the alkene in enyne substrates.[6d] The allylic alkoxy substituent lowers the reactivity of the alkene by both steric and electronic effects. Entries 1−6 of Table 2 demonstrated that higher yields of bicyclic products could be obtained by the incorporation of an allylic alkoxy substituent in the substrates. The reaction of substrate **22** with an allylic (*tert*-butyldimethylsilyl)oxy substituent was carried out with 10 mol % of the precatalyst in the presence of an excess of phenylsilane at 25 °C for 2 h (Table 2, entry 1). The reaction was run in benzene-d_6 and was monitored by ^{1}H NMR. The creation of two new stereocenters in the cyclization reaction results in the formation of a mixture of two diastereomeric products in 93% isolated yield. The ratio of products as determined by fused silica gas chromatographic analysis of the crude reaction mixture was 7:1.

Results observed in the cyclization of enynes suggested that improvement of the diastereoselectivity of the cyclized products could be achieved if larger alkoxy groups were incorporated into the starting materials.[6d] The addition of a (triphenylmethyl)oxy substituent in the allylic position of substrate **25** demonstrated that higher selectivities could be achieved (Table 2, entry 2). Substrate **25** was cyclized according to the general experimental procedure to provide 86% of cyclized product **51**. The diastereoselectivity was found to be >30:1 by ^{1}H NMR of the crude reaction mixture. The enhancement of the diastereomeric ratio can be rationalized by the increased steric size of the (triphenylmethyl)oxy substituent relative to the (*tert*-butyldimethylsilyl)oxy substituent of substrate **22**. NOE data for **51** supports the relative stereochemical assignments of the products in entries 1 and 2 (Table 2).

Figure 1 suggests conformations for the expected intermediates in the sequential cyclization reaction of substrates **22** and **25**. The presence of the cyclohexyl group as a substituent on the alkyne of entries 1 and 2 (Table 2) provides branching in the propargylic position. This branching serves as a regiocontrol element in the alkyne insertion leading to the formation of proposed intermediate **I**. Intermediate **I** is drawn in a conformation that suggests a chairlike transition structure proposed for the first intramolecular alkene insertion. In this conformation, the alkyl substituent occupies a pseudoequatorial position on the ring being formed. This controls the formation of the first new stereocenter of the bicyclic ring system. A transition structure of this type was first proposed for the cyclization of enynes and is also supported by products observed in the organoyttrium-catalyzed cyclization of trienes.[6d,7] The second alkylyttrium intermediate can adopt a number of conformations. The proposed conformations designated as **IIa** and **IIb** are drawn to suggest those that lead to the transition structures for the second intramolecular insertion. Cyclization through a second chairlike transition structure, similar to the conformation of **IIa**, is proposed for the formation of the major diastereomer. Cyclization through a boatlike transition structure, as suggested by **IIb**, is expected to give rise to the minor diastereomer of the reaction.

Entries 5 and 6 of Table 2 demonstrate that the syn diastereomers of substrates **22** and **25** also cyclized in high yield to form bicyclic products. The (triphenylmethyl)oxy substituent of **58** gave rise to excellent diastereoselectivity in the formation of product **59**. The sequential cyclization/silylation reaction of **56** generated only a 2:1 ratio of diastereomers. The major products **57a** and **59** were demonstrated to have the same relative stereochemistry. This was accomplished by treatment of compound **59** with formic acid in ether[21] to liberate the alcohol, which was reprotected as the *tert*-butyldi-

(20) Molander, G. A.; Julius, M. *J. Org. Chem.* **1992**, *57*, 6347.

(21) Bessodes, M.; Komiotis, D.; Antonakis, K. *Tetrahedron Lett.* **1986**, *27*, 579.

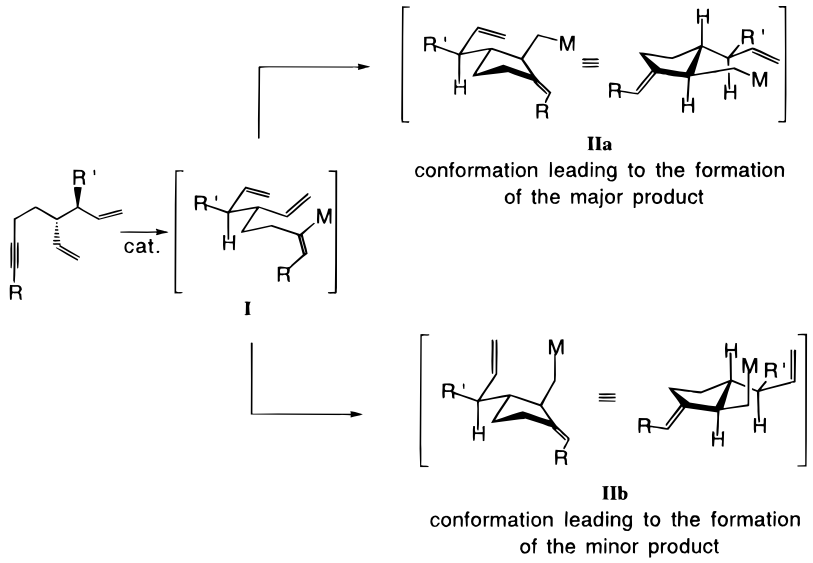


Figure 1. Intermediates in the formation of bicyclic products from *anti*-dienynes.

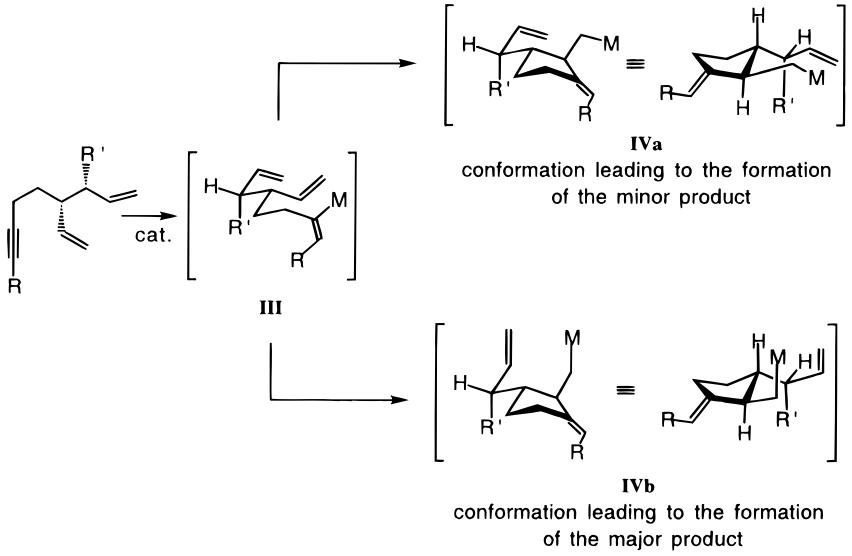


Figure 2. Intermediates in the formation of bicyclic products from *syn*-dienynes.

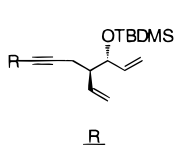
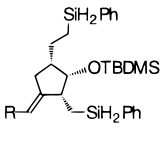
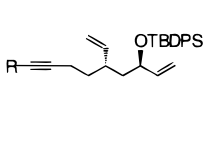
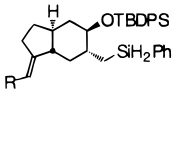
methylsilyl ether. The ^{1}H NMR of this compound matched that of **57**, the major product observed in entry 5 (Table 2). NOE Data for **59** supports the relative stereochemistry assigned to the major products of entries 5 and 6 (Table 2).

The expected intermediates formed in the cyclization reactions of **56** and **58** are shown in Figure 2. The second alkylyttrium intermediate is drawn in two conformations, **IVa** and **IVb**, to suggest possible transition-state structures. The reactions of **56** and **58** are expected to react through boatlike transition structures, as suggested by **IVb**, to give rise to the major product. This is predicted on the basis of the pseudoaxial orientation of the allylic substituent R′ in the formation of the second ring. In a chairlike conformation, allylic $A^{1,3}$-strain between R′ and vinyl protons of the alkene and steric interactions between the bulky metal ligands and the axial substituent R′ are postulated to be responsible for forcing the reaction to proceed through a boatlike transition structure. The improvement of diastereoselectivity observed when an allylic triphenylmethoxy substituent is used supports this suggestion.

Substrates in entries 1, 2, 5, and 6 (Table 2) all possess a cyclohexyl 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. Entries 3, 4, and 7 (Table 2) provide examples of functionalized alkyne substituents that can also be utilized to obtain regiocontrol without hindering reactivity. The oxygens of these alkyne substrates did not appreciably affect the reactivity of the highly electron-deficient catalyst. The reactions proceeded cleanly at room temperature, complete selectivity for the alkyne insertion was observed, and the cyclized products were obtained in high yield. The triphenylmethoxy substituent of entry 3 (Table 2) again demonstrated that excellent diastereoselectivity, >40:1, could be achieved with this bulky protecting group. NOE data supports the relative stereochemistry assigned for **53**.

A *tert*-butyldiphenylsilyl protecting group was incorporated in substrate **54** and the cyclization reaction of this substrate provided a 14:1 ratio of diastereomers in the product (Table 2, entry 4). Although not as selective

Table 3. Sequential Cyclization/Silylation Reactions Catalyzed by $Cp^*_2YCH_3 \cdot THF$[a]

entry	substrate	products	% isolated yield
1	 **38** R = cyclohexyl	 **61**	70
2	 **46** R = cyclohexyl	 **62**	90

[a] Reactions were run in an NMR tube using benzene-d_6 as the solvent according to the general procedure.

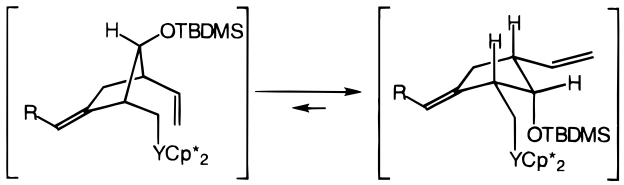


Figure 3. Conformations proposed for the intermediate in the reaction of **38**.

as the triphenylmethoxy substituent of entries 2 and 3 (Table 2), the (*tert*-butyldiphenylsilyl)oxy group of entry 4 (Table 2) achieved selectivity greater than that observed with the (*tert*-butyldimethylsilyl)oxy group utilized in substrate **22** (Table 2, entry 1).

The diastereoselectivity of enyne cyclizations was exceedingly high when allylic substituents with *A* values greater than that of a protected alcohol were incorporated into the enyne substrates.[6d] For example, substrate **35** was prepared with a benzyl group in the allylic position, and formation of the minor diastereomer was not observed (Table 2, entry 7). The 30:1 diastereomeric ratio of the product was the result of the mixture of diastereomers in the starting material (also 30:1). The cyclization of **35** demonstrated that allylic alkyl substituents are effective in achieving excellent diastereoselectivities in the cyclization of dienynes.

It was expected that the sequential cyclization/silylation reaction of dienynes could be readily extended to include the formation of other bicyclic ring structures. Substrate **38** was prepared with the expectation that it might cyclize to provide a bicyclo[3.2.0]heptane or a bicyclo[2.2.1]heptane. Under conditions identical to those that allowed the cyclization of other dienynes to occur, **38** was reacted with the precatalyst and 1.1 equiv of phenylsilane (Table 3, entry 1). No bicyclic product was identified, but a mixture of **61** and starting material was observed. By addition of excess silane the dienyne was cyclized and hydrosilylated to form the highly functionalized cyclopentane **61** cleanly and in high yield. The absence of a bicyclic product in the reaction of **38** can be explained by the intermediates depicted in Figure 3. To form a second ring, the conformation of the intermediate would be such that two of the three substituents are in pseudoaxial orientations. Presumably, the flip-chair conformation, which places the most substituents in pseudoequatorial orientation, is preferred and prohibits the second cyclization. The relative stereochemistry of compound **61** was assigned by an NOE experiment. This cyclization again demonstrated the preference of the catalyst for the insertion of an alkyne over allylically substituted alkenes. It also demonstrated that the alkenylmetallic species produced by the initial insertion undergoes a 5-*exo*-*trig* cyclization in preference to a 4-*exo*-*trig* cyclization.

Substrate **46** was prepared with the expectation that it might cyclize to provide a bicyclo[4.3.0]nonane. Under conditions identical to those that allowed the cyclization of other dienynes to occur, **46** was reacted with the precatalyst and 1.1 equiv of phenylsilane (Table 3, entry 2). The cyclization reaction readily occurred to produce a single diastereomer of the desired carbobicyclic **62** in excellent yield. An NOE experiment confirmed the relative stereochemistry as drawn.

Conclusions

The organoyttrium complex $Cp^*_2YCH_3 \cdot THF$ has been used to catalyze the sequential cyclization/silylation of suitable dienynes with phenylsilane to form functionalized bicyclic structures in a single step. In the sequential process, two carbon−carbon bonds and a carbon−silicon bond were formed selectively. The catalyst accomplishes this reaction through its ability to react selectively in each step of the reaction. In the first step, the alkyne inserts regioselectively in preference to an alkene. The second step requires that the catalyst preferentially cyclize through a 5-*exo*-*trig* pathway over a 6-*exo*-*trig* cyclization. This cyclization via intramolecular olefin insertion engenders high diastereoselectivity in the first cyclization and sets up a second intramolecular insertion that is also accomplished with a high degree of diastereoselectivity. The diastereoselectivity of the reaction can be enhanced by increasing the size of the allylic substituent in the second cyclization. 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 ether functionalities can be tolerated. This method complements and extends other catalyzed cyclization reactions of enynes and polyenes and does so in a manner that is atom economical, with no byproducts formed in the process.[22]

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 dried as a solution with $MgSO_4$, concentrated in vacuo, and freeze/pump/thaw degassed. The phenylsilane was purchased from Aldrich and was dried with activated 4 Å molecular sieves and degassed before use. Anhydrous YCl_3 was purchased from

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

Cerac. The complex $Cp^*_2YCH_3$·THF was prepared according to published procedures.[23]

General Experimental Procedure for NMR Scale Sequential Cyclization/Silylation Reactions. The catalytic sequential cyclization/silylation of **22** is representative. In the nitrogen atmosphere glovebox a solution of 6 mg (0.013 mmol) of the precatalyst $Cp^*_2YCH_3$·THF was weighed in an NMR tube equipped with a J. Young valve. Benzene-d_6 (0.6 mL) was added. To this solution was added 52 mg (0.015 mmol) of **22** followed by 21 mg (0.019 mmol) of phenylsilane. The NMR tube was sealed and removed from the glovebox. The progress of the reaction was monitored by ^{1}H NMR. After 2 h, the reaction mixture was diluted with 2 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 7:1 ratio of diastereomers was generated. The organics were combined and concentrated by rotary evaporation. The crude material was purified by flash chromatography with hexanes followed by solvent removal at 50 °C/0.04 mmHg to afford 93% (62 mg, 0.014 mmol) of **50** as a 7:1 mixture of diastereomers.

(1*E*,2*R,6*R**)-1-(Cyclohexylmethylene)-4-[(phenylsilyl)methyl]bicyclo[3.3.0]octane (47). General Experimental Procedure for Catalytic Cyclization/Silylation.** In the nitrogen atmosphere glovebox was added a solution of 6 mg (0.013 mmol) of the precatalyst $Cp^*_2YCH_3$·THF in 1 mL of cyclohexane to a reaction flask equipped with a magnetic stir bar. To this solution was added 51 mg (0.24 mmol) of **2** followed by 31 mg (0.29 mmol) of phenylsilane. The reaction flask was sealed and stirred in the glovebox for 2.5 h at ambient temperature. After 2.5 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. The organics were combined and concentrated by rotary evaporation. The crude material was purified by flash chromatography (R_f 0.51 in hexanes) followed by Kugelrohr distillation (ot 80−85 °C/0.1 mmHg) to afford 33% (26 mg, 0.08 mmol) of **47** (GC purity >97%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.84 (dt, J = 11.6, 8.6 Hz, 1H), 0.96−1.04 (m, 2H), 1.10−1.29 (m, 6H), 1.31−1.38 (m, 1H), 1.43−1.72 (m, 8H), 1.90−2.00 (m, 2H), 2.19−2.28 (m, 1H), 2.52−2.61 (m, 3H), 4.28 (t, J = 3.7 Hz, $^1J_{29Si,H}$ = 196.5 Hz, 2H), 4.82 (dd, J = 9.0, 2.3 Hz, 1H), 7.32−7.38 (m, 3H), 7.55−7.56 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.24, 26.12, 26.19, 26.82, 32.98, 33.09, 33.24, 37.85, 38.09, 40.57, 52.91, 57.09, 123.98, 127.94, 129.45, 132.79, 135.23, 139.56; IR (neat) 2136 cm^{-1}; HRMS calcd for $C_{22}H_{32}Si$ 324.2273, found 324.2271; LRMS (EI) *m*/*z* (rel intensity) 324 (4), 55 (100), 41 (97).

(1*E*,2*R,3*S**)-3-[3′-(2-Methyl-1-propenyl)]-1-(cyclohexylmethylene)-2-[(phenylsilyl)methyl]cyclopentane (48)** was prepared from **3** (99 mg, 0.43 mmol) according to the general experimental procedure outlined for the preparation of **47**. Purification by flash chromatography (R_f 0.41 in hexanes) followed by Kugelrohr distillation afforded 84% (121 mg, 0.36 mmol) of **48** (GC purity >98%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.97−1.07 (m, 2H), 1.10−1.31 (m, 6H), 1.58−1.88 (m, 8H, with overlapping singlet at 1.65, 3H), 1.89−2.09 (m, 1H), 2.12−2.24 (m, 3H), 2.28−2.36 (m, 1H), 4.29 (t, J = 4.0 Hz, $^1J_{29Si,H}$ = 197.8 Hz, 2H), 4.61 (s, 1H), 4.67 (s, 1H), 5.01−5.04 (m, 1H), 7.31−7.39 (m, 3H), 7.54−7.56 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.16, 22.31, 26.10, 26.19, 27.16, 29.84, 33.01, 33.11, 38.47, 42.86, 44.31, 46.65, 110.99, 127.34, 127.92, 129.36, 133.38, 135.21, 144.57, 144.96; IR (neat) 2134 cm^{-1}; HRMS calcd for $C_{23}H_{34}Si$ 338.2430, found 338.2425; LRMS (EI) *m*/*z* (relative intensity) 338 (3), 282 (73), 199 (64), 107 (59), 81 (71), 55 (100), 41 (90).

(1*E*,2*R,4*R*/*S*,6*R**)-1-(Cyclohexylmethylene)-5,5-dimethyl-4-[(phenylsilyl)methyl]bicyclo[3.3.0]octane (49)** was prepared from **10** (70 mg, 0.29 mmol) according to the general experimental procedure outlined for the preparation of **47**. Analysis of the crude reaction mixture by gas chromatography indicated that a 3.9:1 diastereomeric ratio of products was generated. Purification by flash chromatography (R_f 0.34 in hexanes followed by Kugelrohr distillation (ot 85−95 °C/0.02 mmHg) afforded 76% (76 mg, 0.22 mmol) of **49** as a 2.9:1 mixture of diastereomers. Major diastereomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.73 (s, 3H), 0.76−0.94 (m, 2H with overlapping singlet at 0.92, 3H), 0.95−1.07 (m, 3H), 1.10−1.31 (m, 4H), 1.34−1.44 (m, 1H), 1.48−1.54 (m, 1H), 1.57−1.71 (m, 6H), 1.92−2.12 (m, 2H), 2.39−2.55 (m, 3H), 4.25−4.35 (m, 2H), 4.81−4.83 (m, 1H), 7.33−7.41 (m, 3H), 7.56−7.58 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 12.06, 16.17, 21.64, 26.12, 26.18, 27.23, 30.32, 31.71, 33.24, 33.28, 37.74, 38.97, 51.40, 51.96, 61.99, 123.45, 127.95, 129.47, 132.82, 135.18, 140.36; IR (neat) 2134 cm^{-1}; HRMS calcd for $C_{24}H_{36}Si$ 352.2586, found 352.2579; LRMS (EI) *m*/*z* (relative intensity) 352 (1.2), 107 (65), 55 (62), 41 (100). Anal. Calcd for $C_{24}H_{36}Si_2$: C, 81.75; H, 10.29. Found: C, 81.78; H, 10.22.

(5*E*,1*R,2*R**,4*S**,8*R**)-1-[(*tert*-Butyldimethylsilyl)oxy]-5-(cyclohexylmethylene)-2-[(phenylsilyl)methyl]bicyclo-[3.3.0]octane (50)** was prepared from **22** according to the general experimental procedure. Analysis of the crude reaction mixture by gas chromatography indicated that a 7:1 diastereomeric ratio of products was generated. Flash chromatography (R_f 0.46 in hexanes) followed by removal of solvents at 50 °C/0.01 mmHg afforded 93% yield of **50** as a mixture of diastereomers: ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.01 (s, 3H), 0.02 (s, 3H), 0.85 (s, 9H), 0.93−1.05 (m, 3H), 1.07−1.28 (m, 4H), 1.32−1.42 (m, 2H), 1.55−1.82 (m, 8H), 1.89−2.01 (m, 1H), 2.26−2.36 (m, 2H), 2.49−2.54 (m, 2H), 3.46 (dd, J = 8.9, 6.0 Hz, 1H), 4.24−4.32 (m, 2H), 4.77−4.80 (m, 1H), 7.31−7.39 (m, 3H), 7.53−7.55 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ −4.49, −4.07, 16.74, 17.96, 25.81, 25.88, 25.96, 26.08, 26.15, 30.29, 32.48, 33.15, 33.19, 37.79, 49.32, 51.69, 57.83, 83.49, 124.00, 127.96, 129.49, 132.48, 135.21, 138.99; IR (neat) 2136 cm^{-1}; HRMS calcd for $C_{28}H_{46}OSi_2$ 454.3087, found 454.3038; LRMS (EI) *m*/*z* (relative intensity) 454 (7), 371 (100). Anal. Calcd for $C_{28}H_{46}OSi_2$: C, 73.94; H, 10.19. Found: C, 73.79; H, 10.37.

(5*E*,1*R,2*R**,4*S**,8*R**)-5-(Cyclohexylmethylene)-2-[(phenylsilyl)methyl]-1-[(triphenylmethyl)oxy]bicyclo[3.3.0]-octane (51)** was prepared from **25** (10 mg, 0.021 mmol) according to the general experimental procedure. Analysis of the crude reaction mixture by ^{1}H NMR indicated that >30:1 diastereomeric ratio of products was generated. Purification by flash chromatography (R_f 0.21 using 3% Et_2O in hexanes) followed by removal of solvents at 45 °C/0.01 mmHg afforded 86% (10 mg, 0.018 mmol) of **51**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.58−0.63 (m, 1H), 0.65−0.74 (m, 1H), 0.79−1.00 (m, 4H), 1.06−1.22 (m, 4H), 1.47−1.68 (m, 6H), 1.75−1.92 (m, 2H), 2.04−2.10 (m, 1H), 2.24−2.30 (m, 2H), 2.63−2.69 (m, 1H), 3.08 (dd, J = 9.0, 5.6 Hz, 1H), 4.15−4.18 (m, 2H), 4.73−4.76 (m, 1H), 7.16−7.26 (m, 9H), 7.33−7.50 (m, 11H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 16.47, 25.87, 26.08, 26.15, 30.31, 32.29, 33.16, 37.73, 48.35, 52.67, 57.69, 84.04, 86.30, 124.00, 126.82, 127.51, 127.91, 129.19, 129.46, 132.59, 135.25, 135.85, 145.36; IR (neat) 2130 cm^{-1}; HRMS calcd for $C_{41}H_{46}OSi$ 582.3318, found 582.3318; LRMS (EI) *m*/*z* (relative intensity) 350 (31), 243 (100), 165 (72).

(5*E*,1*R,2*R**,4*S**,8*R**)-5-[5′-(2′,2′-Dimethyl-1′,3′-dioxanyl)-methylene]-2-[(phenylsilyl)methyl]-1-[(triphenylmethyl)-oxy]bicyclo[3.3.0]octane (53)** was prepared from **52** (24 mg, 0.046 mmol) according to the general experimental procedure. Analysis of the crude reaction mixture by ^{1}H NMR indicated that a >40:1 diastereomeric ratio of products was generated. Purification by flash chromatography using 20% Et_2O in hexanes (R_f 0.16 using 10% Et_2O in hexanes) followed by removal of solvents at 50 °C/0.01 mmHg afforded 98% (28 mg, 0.046 mmol) of **53** as a white solid: mp 54−60 °C; ^{1}H NMR (500 MHz, C_6D_6) δ 0.57−0.64 (m, 1H), 0.66−0.75 (m, 1H), 0.81−0.90 (m, 2H), 1.28−1.32 (m, 1H), 1.37 (s, 3H), 1.42 (s, 3H), 1.61−1.67 (m, 1H), 1.78−1.85 (m, 1H), 2.05−2.11 (m, 1H), 2.26−2.36 (m, 2H), 2.51−2.59 (m, 1H), 2.64−2.70 (m, 1H), 3.09 (dd, J = 9.1, 5.7 Hz, 1H), 3.52−3.71 (m, 4H), 4.12−4.15 (m, 2H), 4.57−4.60 (m, 1H), 7.17−7.25 (m, 9H), 7.33−7.49 (m,

(23) (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.

11H); ^{13}C NMR (125 MHz, C_6D_6) δ 16.75, 19.68, 26.15, 28.98, 30.47, 32.67, 35.91, 48.73, 53.15, 57.71, 64.13, 64.16, 84.15, 86.84, 97.39, 114.00, 127.18, 127.87, 128.34, 129.56, 129.90, 132.60, 135.61, 145.26, 145.82; IR (neat) 2130 cm^{-1}; HRMS calcd for $C_{40}H_{43}O_3Si$ (M − CH_3)$^+$ 599.2981, found 599.2958; LRMS (EI) *m/z* (relative intensity) 350 (14), 243 (100), 165 (76).

(5*E*,1*R,2*R**,4*S**,8*R**)-1-[(*tert*-Butyldiphenylsilyl)oxy]-5-[5′-(2′,2′-dimethyl-1′,3′-dioxanyl)methylene]-2-[(phenylsilyl)methyl]bicyclo[3.3.0]octane (55)** was prepared from **54** (29 mg, 0.058 mmol) according to the general experimental procedure. Analysis of the crude reaction mixture by ^{1}H NMR indicated that a 14:1 diastereomeric ratio of products was generated. Purification by flash chromatography using 0−10% Et_2O in hexanes (R_f 0.43 with 20% Et_2O in hexanes) followed by removal of solvents at 50 °C/0.01 mmHg afforded 90% (32 mg, 0.052 mmol) of **55** as a 19:1 mixture of diastereomers: ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.93−0.83 (m, 2H), 1.00 (s, 9H), 1.10−1.15 (m, 1H), 1.29−1.33 (m, 1H), 1.38 (s, 3H), 1.39−1.45 (m, 1H with overlapping singlet at 1.43, 3H), 1.65−1.72 (m, 1H), 1.77−1.85 (m, 1H), 2.12−2.18 (m, 1H), 2.39−2.42 (m, 2H), 2.46−2.52 (m, 1H), 2.54−2.60 (m, 1H), 3.49 (dd, J = 9.1, 3.1 Hz, 1H), 3.54−3.72 (m, 4H), 4.18−4.20 (m, 2H), 4.58−4.61 (m, 1H), 7.31−7.41 (m, 9H), 7.46−7.47 (m, 2H), 7.62−7.65 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 16.77, 19.26, 19.30, 25.36, 26.94, 27.08, 28.65, 30.19, 32.82, 35.39, 49.41, 51.98, 57.84, 64.03, 64.06, 84.10, 97.29, 113.01, 127.43, 127.51, 127.92, 129.51, 129.55, 129.58, 132.34, 134.18, 134.26, 135.22, 135.88, 135.95, 145.81; IR (neat) 2130 cm^{-1}; HRMS calcd for $C_{38}H_{50}O_3Si_2$ 610.3299, found 610.3279; LRMS (EI) *m/z* (relative intensity) 610 (3), 305 (84), 227 (59), 199 (100), 135 (98), 91 (50). Anal. Calcd for $C_{38}H_{50}O_3Si_2$: C, 74.70; H, 8.25. Found: C, 74.86; H, 8.55.

(5*E*,1*R,2*R**,4*R**,8*S**)-1-[(*tert*-Butyldimethylsilyl)oxy]-5-(cyclohexylmethylene)-2-[(phenylsilyl)methyl]bicyclo[3.3.0]octane (57a)** was prepared from **56** 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 (R_f 0.44 in hexanes) followed by removal of solvents at 50 °C/0.01 mmHg afforded 56% of the major diastereomer **57a**: ^{1}H NMR (500 MHz, $CDCl_3$) δ −0.04 (s, 3H), −0.03 (s, 3H), 0.77−0.90 (m, 1H with overlapping singlet at 0.83, 9H), 0.94−1.04 (m, 3H), 1.09−1.29 (m, 4H), 1.45−1.62 (m, 6H), 1.64−1.70 (m, 2H), 1.92−2.05 (m, 2H), 2.30−2.36 (m, 1H), 2.49−2.59 (m, 2H), 2.64−2.71 (m, 1H), 3.64 (d, J = 3.8 Hz, 1H), 4.26−4.32 (m, 2H), 4.82−4.85 (m, 1H), 7.32−7.39 (m, 3H), 7.54−7.56 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ −4.76, −4.54, 17.94, 18.17, 21.14, 25.89, 26.13, 26.21, 32.49, 33.24, 33.26, 33.38, 37.82, 52.64, 52.75, 55.72, 78.11, 124.32, 127.97, 129.55, 132.38, 135.19, 139.68; IR (neat) 2136 cm^{-1}; HRMS calcd for $C_{28}H_{46}OSi_2$ 454.3087, found 454.3058; LRMS (EI) *m/z* (relative intensity) 454 (4.3), 305 (63), 171 (59), 73 (100).

(5*E*,1*R,2*S**,4*R**,8*S**)-1-[(*tert*-Butyldimethylsilyl)oxy]-5-(cyclohexylmethylene)-2-[(phenylsilyl)methyl]bicyclo[3.3.0]octane (57b)** was prepared from **56** according to the general experimental procedure. Purification by flash chromatography (R_f 0.54 in hexanes) followed by removal of solvents at 50 °C/0.01 mmHg afforded 10 mg (0.022 mmol) of the minor diastereomer **57b** in 30% yield: ^{1}H NMR (500 MHz, $CDCl_3$) δ −0.01 (s, 3H), 0.02 (s, 3H), 0.89 (s, 9H), 0.92−1.03 (m, 3H), 1.09−1.31 (m, 5H), 1.39−1.60 (m, 7H), 1.64−1.69 (m, 2H), 1.91−1.98 (m, 1H), 2.42−2.55 (m, 3H), 2.75−2.82 (m, 1H), 3.80 (dd, J = 4.1, 2.9 Hz, 1H), 4.26−4.32 (m, 2H), 4.81−4.84 (m, 1H), 7.32−7.39 (m, 3H), 7.54−7.56 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ −4.59, −4.36, 12.49, 18.32, 22.18, 26.04, 26.13, 26.19, 29.92, 32.16, 33.27, 37.80, 46.66, 51.56, 57.07, 72.33, 123.88, 127.94, 129.42, 132.92, 135.19, 139.89; IR (neat) 2130 cm^{-1}; HRMS calcd for $C_{28}H_{46}OSi_2$ 454.3087, found 454.3073; LRMS (EI) *m/z* (relative intensity) 454 (3.2), 171 (100), 73 (97).

(5*E*,1*R,2*R**,4*R**,8*S**)-5-(Cyclohexylmethylene)-2-[(phenylsilyl)methyl]-1-[(triphenylmethyl)oxy]bicyclo[3.3.0]-octane (59)** was prepared from **58** (15 mg, 0.032 mmol) according to the general experimental procedure. Analysis of the crude reaction mixture by ^{1}H NMR indicated that a >60:1 diastereomeric ratio of products was generated. Purification by flash chromatography (R_f 0.24 using 5% CH_2Cl_2 in hexanes) followed by removal of solvents at 45 °C/0.01 mmHg afforded 97% (18 mg, 0.031 mmol) of **59**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.51−0.61 (m, 2H), 0.60−0.69 (m, 1H), 0.94−1.05 (m, 2H), 1.09−1.28 (m, 4H), 1.47−1.71 (m, 7H), 1.91−1.97 (m, 2H), 2.08−2.14 (m, 1H), 2.41−2.48 (m, 1H), 2.56−2.61 (m, 1H), 2.91−2.97 (m, 1H), 3.69 (d, J = 4.4 Hz, 1H), 3.95−3.98 (m, 1H), 4.05−4.08 (m, 1H), 4.84−4.87 (m, 1H), 7.16−7.23 (m, 9H), 7.29−7.45 (m, 11H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 17.91, 22.27, 26.11, 26.21, 32.59, 33.06, 33.19, 37.85, 50.74, 54.09, 55.05, 80.08, 86.74, 124.80, 126.88, 127.57, 127.87, 129.24, 129.41, 132.71, 135.17, 139.48, 145.54; IR (neat) 2130 cm^{-1}; HRMS calcd for $C_{41}H_{46}OSi$: 582.3318, found 582.3282; LRMS (EI) *m/z* (relative intensity) 350 (23), 243 (100), 165 (87), 107 (68), 81 (51).

(1*E*,2*R,4*S**,5*S**,6*R**)-1-[5′-(2′,2′-Dimethyl-1′,3′-dioxanyl)-methylene]-5-[phenyl(methyl)]-4-[(phenylsilyl)methyl]-bicyclo[3.3.0]octane (60)** was prepared from **35** (22 mg, 0.065 mmol, 30:1 ratio of diastereomers) according to the general experimental procedure. Analysis of the crude reaction mixture by gas chromatography indicated that a 30:1 diastereomeric ratio of products was generated. Purification by flash chromatography (R_f 0.39 using 20% Et_2O in hexanes) followed by removal of solvents at 50 °C/0.01 mmHg afforded 89% (26 mg, 0.058 mmol) of **60**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.83−0.98 (m, 3H), 1.25−1.41 (m, 1H with overlapping singlet at 1.39, 3H), 1.45 (s, 3H), 1.47−1.53 (m, 1H), 1.84−2.00 (m, 3H), 2.16−2.24 (m, 1H), 2.32−2.43 (m, 2H), 2.46−2.68 (m, 3H), 2.74 (dd, J = 13.9, 6.7 Hz, 1H), 3.59−3.75 (m, 4H), 4.10−4.16 (m, 2H), 4.69−4.73 (m, 1H), 7.11−7.38 (m, 10H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 19.28, 23.21, 28.71, 32.72, 34.69, 35.48, 37.54, 45.92, 47.54, 53.91, 54.45, 64.10, 97.31, 113.73, 125.65, 127.89, 128.16, 129.03, 129.41, 132.30, 135.14, 141.09, 146.00; IR (neat) 2130 cm^{-1}; HRMS calcd for $C_{29}H_{38}O_2Si$ 446.2641, found 446.2644; LRMS (EI) *m/z* (relative intensity) 446 (0.8), 267 (58), 107 (100), 91 (99).

(1*E*,2*R,3*S**,4*R**)-3-[(*tert*-Butyldimethylsilyl)oxy]-1-(cyclohexylmethylene)-4-[2′-(phenylsilyl)ethyl]-2-[(phenylsilyl)methyl]cyclopentane (61)** was prepared from **38** (20 mg, 0.060 mmol) according to the general experimental procedure. Purification by flash chromatography (R_f 0.29 in hexanes) followed by removal of solvents at 50 °C/0.01 mmHg afforded 70% (23 mg, 0.042 mmol) of **61**: GC purity >99%; ^{1}H NMR (400 MHz, $CDCl_3$) δ −0.06 (s, 3H), −0.05 (s, 3H), 0.78−1.03 (m, 6H with overlapping singlet at 0.79, 9H), 1.08−1.27 (m, 3H), 1.36−1.45 (m, 1H), 1.53−1.68 (m, 6H), 1.94−2.02 (m, 3H), 2.29−2.37 (m, 1H), 2.41−2.44 (m, 1H), 3.74−3.76 (m, 1H), 4.27 (t, J = 3.7 Hz, $^1J_{29Si,H}$ = 192.0 Hz, 2H), 4.31 (t, J = 4.0 Hz, $^1J_{29Si,H}$ = 194.1 Hz, 2H), 5.02 (dd, J = 8.9, 1.1 Hz, 1H), 7.31−7.38 (m, 6H), 7.53−7.56 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ −4.71, −4.38, 8.68, 15.15, 18.02, 24.57, 25.77, 26.09, 26.22, 31.32, 32.82, 33.10, 38.50, 44.71, 49.46, 79.82, 127.94, 127.97, 128.74, 129.47, 132.74, 132.77, 135.21, 142.88; IR (neat) 2133 cm^{-1}; HRMS calcd for $C_{33}H_{51}OSi_3$ (M−H)$^+$ 547.3248, found 547.3236; LRMS (EI) *m/z* (relative intensity) 491 (30), 355 (52), 257 (70), 181 (100), 135 (66), 107 (86), 73 (77). Anal. Calcd for $C_{33}H_{52}OSi_3$: C, 72.19; H, 9.55. Found: C, 72.47; H, 9.91.

(5*E*,1*R,2*R**,4*S**,8*S**)-1-[(*tert*-Butyldimethylsilyl)oxy]-5-(cyclohexylmethylene)-2-[(phenylsilyl)methyl]bicyclo[4.430]nonane (62)** was prepared from **46** according to the general experimental procedure. Purification by flash chromatography using 10% CH_2Cl_2 in hexanes followed by removal of solvents at 50 °C/0.01 mmHg afforded **62** in 90% yield: R_f 0.34 (10% CH_2Cl_2 in hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.49−0.55 (m, 1H), 0.66 (q, J = 11.9 Hz, 1H), 0.81−1.25 (m, 7H with overlapping singlet at 1.02, 9H), 1.46−1.72 (m, 8H), 1.77−1.82 (m, 1H), 1.88−1.96 (m, 2H), 2.05−2.13 (m, 2H), 2.20−2.25 (m, 1H), 3.30 (dt, J = 10.3, 4.4 Hz, 1H), 4.30 (t, J = 4.4 Hz, $^1J_{29Si,H}$ = 191.7 Hz, 2H), 4.71−4.75 (m, 1H), 7.31−7.41 (m, 8H), 7.51−7.53 (m, 2H), 7.65−7.69 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.72, 20.21, 26.83, 26.90, 27.89, 28.43, 30.25, 33.84, 34.84, 38.57, 41.52, 42.92, 45.33, 50.06, 79.97, 124.92, 128.04, 128.23, 128.63, 130.08, 130.11, 130.20, 133.64, 134.90,

135.64, 136.00, 136.69, 136.76, 142.79; IR (neat) 2133.4 cm^{-1}; HRMS calcd for $C_{35}H_{43}OSi_2$ $(M - C_4H_9)^+$ 535.2852, found 538.2835; LRMS (EI) *m*/*z* (relative intensity) 535 (24), 305 (100), 275 (68), 201 (55).

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Supporting Information Available: Experimental details and characterization for intermediates **2**, **3**, **5**−**10**, **12**−**30**, **32**−**42**, **44**−**46**, **52**, **54**, **56**, and **58**; ^1H and ^{13}C spectra for all compounds for which elemental analysis is not reported; NOE and other spectral structural studies for compounds **16**, **17**, **32**, **51**, **53**, **59**, **61**, and **62** (175 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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