Simultaneous Discrimination of Diastereotopic Groups and Faces: The First Example in Intramolecular [3 + 2] and [2 + 2 + 1] Cycloaddition Reactions

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To explore a novel concept for controlling diastereoselectivity, systematic studies on the sense and degree of diastereotopic groups and face selections in intramolecular [3 + 2] (nitrile oxide and nitrone) and [2 + 2 + 1] (Pauson−Khand) cycloadditions have been conducted. Optically pure methyl (*S*)-3,4-*O*-isopropylidene-3,4-dihydroxybutanoate (**5**) and methyl (*S*)-2,3-*O*-isopropylidene-2,3-dihydroxypropanoate (**6**) were converted to substrate aldehydes (**1**−**4**) that bear geminal allyl groups and four types of controllers with the intention of imparting a stereochemical bias to the allylic groups and their faces. The controllers involve 1,2-bis(*tert*-butyldimethylsiloxy), 1,3-bis(*tert*-butyldimethylsiloxy), 1,2-acetonide, and 1,3-acetonide groups, which are referred to as 1,2-$(TBDMSO)_2$, 1,3-$(TBDMSO)_2$, 1,3-dioxolane, and 1,3-dioxane, respectively. Twelve runs of cycloaddition reactions as combinations between the three types of reactions and the four types of substrates were performed to provide bicyclo[4.3.0] or -[3.3.0] adducts of synthetic importance in which isoxazolidine, isoxazoline, or cyclopentenone segments were fused. For every case, high levels of diastereoselectivity have been achieved: >99% (in eight cases), 82%, and 76% for the discrimination of diastereotopic groups and 68→99% for the discrimination of diastereotopic faces. On the basis of the absolute structures of the cycloadducts, plausible stereochemical models are proposed.

Introduction

Synthetic reactions that involve the selective transformations of groups in mirror-image positions (enantiotopic groups) or in stereochemically distinct positions not related in mirror-image position (diastereotopic groups) are a powerful tool to create new stereocenters. A number of applications in this context have been demonstrated with a high level of stereocontrol.[1] With regard to diastereotopic group selection, spiro lactonization or acetalization,[2] iodolactonization,[3] radical cyclization,[4] intramolecular Michael addition,[5] and intramolecular bissilylation[6] have been reported as notable examples. In general, however, the stereochemical impact of preexisting stereogenic centers on these diastereoselective processes has been less understood and developed. Thus, those reports and such situations strongly intrigued us to apply the strategy of diastereotopic group selection to other synthetic reactions capable of inducing multiple stereogenic centers in one step relying on a preexisting single stereogenic center. At the same time, we had a strong desire to put forward a stereochemical model to account for stereochemical results as well by which we can introduce the novel concept of stereocontrol in this field. It was expected that if not only diastereotopic allyl groups but also their π-(C=C) faces are discriminated then cycloaddition reactions such as [3 + 2] (nitrone or nitrile oxide cycloaddition) or [2 + 2 + 1] (Pauson−Khand

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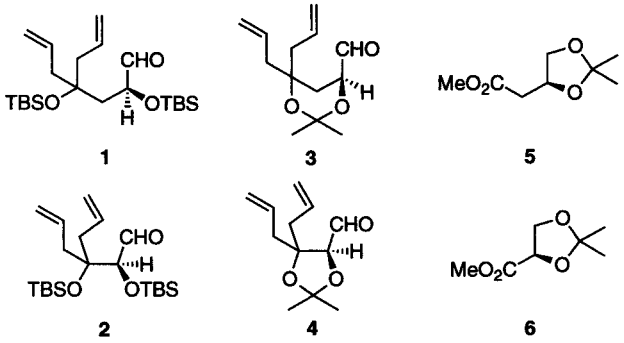
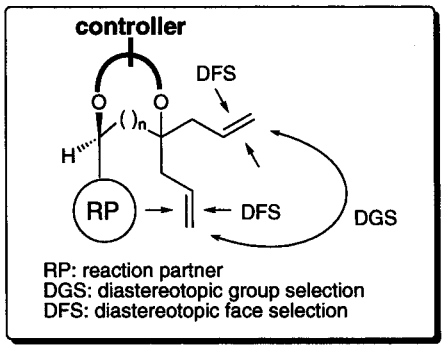
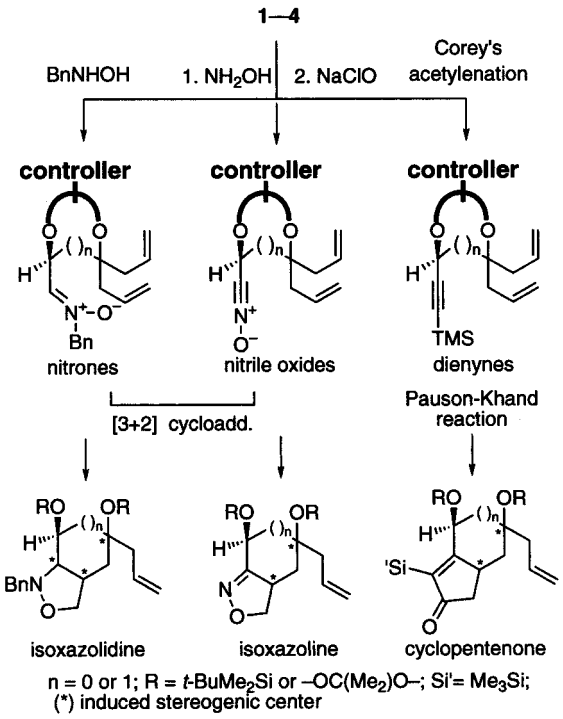
Chart 1





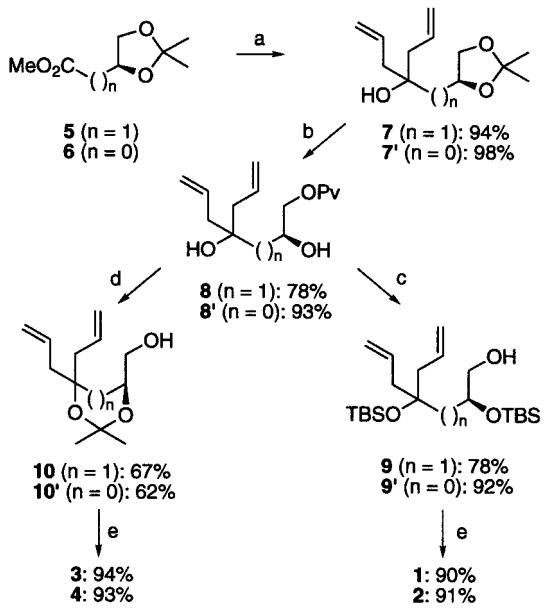
Scheme 1



reaction)[7] process should afford functionalized carbocycles with multiple stereogenic centers and functions.

Our plan is outlined in Chart 1 and Scheme 1, in which the four chiral aldehydes bearing geminal allyl groups (**1**−**4**), themselves accessible through a series of routine reactions from two common chiral hydroxy esters **5**[8] and **6**, were converted to the corresponding four sets of nitrones, nitrile oxides, and dienynes to be subjected to above-mentioned intramolecular cycloaddition reactions. One of the allyl groups can serve as a reaction partner in these cycloaddition processes to furnish isoxazolidines, isoxazolines, or cyclopentenones in a bicyclo[4.3.0] or -[3.3.0] framework. In these transformations, the 1,3- or 1,2-bis(*tert*-butyldimethylsiloxy)[9] [1,3-(TBDMSO)$_2$ or 1,2-(TBDMSO)$_2$ controller] and 1,2- or 1,3-*O*-isopropylidene groups [1,3-dioxolane or 1,3-dioxane controller] in the substrates were expected to play a pivotal role of stereocontrol by biasing the diastereotopic allylic groups and hopefully their diastereofaces as well.

Scheme 2[a]



[a] For $n = 1$ series: (a) allyl-MgBr/Et_2O/−78 °C, 50 min; (b) (1) 2 N HCl/EtOH/0 °C to rt, 2 h, (2) PcCl/Py/CH_2Cl_2/−78 °C, 4 h; (c) (1) TBSOTf/Et_3N/CH_2Cl_2/0 °C, 2 h, (2) DIBAH/toluene/−78 °C, 1 h; (d) (1) $(MeO)_2CMe_2$/THF/*p*-TsOH/rt, 36 h, (2) c-2; (e) Swern oxidation.

Results and Discussion

Synthesis of Precursors for Cycloaddition Processes. In Scheme 2 are outlined the preparations of aldehydes **1** and **3** bearing geminal allyl groups. Methyl (3*S*)-3,4-*O*-isopropylidene-3,4-dihydroxybutanoate (**5**) prepared from dimethyl (*S*)-malate[8] was reacted with an excess amount (2.5 equiv) of allylmagnesium bromide to give a diallyl alcohol (**7**: 94%). The acetonide function of this alcohol was deprotected under acidic conditions followed by acylation of the thus-generated primary hydroxy group with pivaloyl chloride in pyridine to furnish a common intermediate (**8**: 78%) for the preparation of **1** and **3**. The subsequent introduction of a *tert*-butyldimethylsilyl group or an isopropylidene group to both secondary and tertiary hydroxy groups followed by DIBALH reduction led to **9** (78%) or **10** (67%), respectively. The final Swern oxidation of the thus-generated primary hydroxy groups uneventfully gave **1** (90%) with

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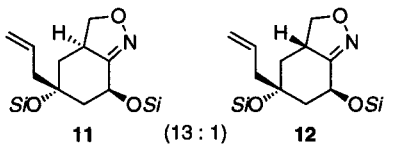
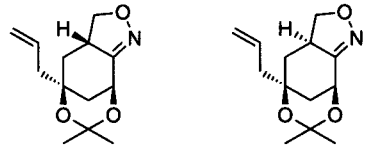
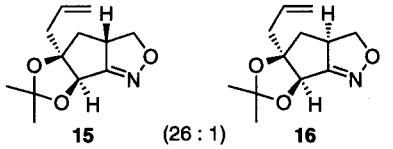
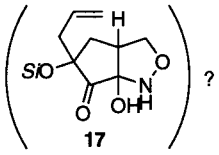
Table 1. Results of Intramolecular Cycloaddition Reactions of Nitrile Oxides Derived from Aldehydes 1−4

RCHO	RCH=NOH[a] yield/%	Cycloaddition[b] temp/°C	time/h	Products[c] yield/%	dr (group)	dr (face)	structure and composition
1	95	rt	1.5	77	>99 : 1	13 : 1	 **11** (13 : 1) **12**
3	91	0	0.7	59	>99 : 1	10 : 1	 **13** (10 : 1) **14**
4	75	rt	6	59	>99 : 1	26 : 1	 **15** (26 : 1) **16**
2	80	rt	48				 **17** ?

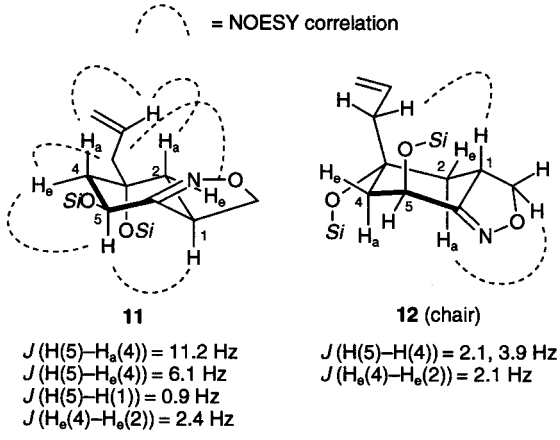
[a] Purified by silica gel column chromatography: crude oximes were prepared from **1**−**4** with hydroxylamine hydrochloride in the presence of Et_3N (0 °C to room temperature/12−20 h). [b] Nitrile oxides were in situ generated by rigorously stirring a two-phase mixture of a solution of the oximes in dichloromethane and an aqueous solution of sodium hypochlorite (5%). [c] Yields after purification by silica gel column chromatography; dr = diastereomeric ratios calculated using the weight of isolated products; dr (group) determined based on the absolute configurations of the products (*Si* = *tert*-butyldimethylsilyl).

the 1,3-bis(*tert*-butyldimethylsilyloxy) [1,3-$(TBDMSO)_2$] controller or **3** (94%) with the 1,3-acetonide (1,3-dioxane) controller.

When commercially available methyl (*R*)-2,2-dimethyl-1,3-dioxolane-4-carboxylate (**6**) was subjected to the same sequence of reactions as that for **5**, the desired diallyl aldehydes **2** and **4** with the vicinal TBDMSO [1,2-$(TBDMSO)_2$] controller and 1,2-acetonide (1,3-dioxolane) controller, respectively, were furnished in good yield: the yields of intermediates involved in these syntheses are also indicated in Scheme 2 ($n = 0$). Since the enantiomers of **5** and **6** are available, the enantiomers of **1**−**4** may be prepared by the same pathways as those in Scheme 2, if so desired.

Discrimination of Diastereotopic Groups and Faces in Intramolecular Nitrile Oxide [3 + 2] Cycloaddition Reactions. Oximes prepared from diallylaldehydes **1**−**4** were treated, after brief purification by a silica gel pad, with aqueous sodium hypochlorite in CH_2Cl_2 to generate the corresponding nitrile oxides, which immediately underwent intramolecular [3 + 2] cycloaddition reactions with perfect diastereotopic group selection, giving a mixture of two diastereomeric isoxazolines **11** + **12** (13:1), **13** + **14** (10:1), and **15** + **16** (26:1) from **1**, **3**, and **4**, respectively, indicating the degree of π-face discrimination [dr (face)], except for the case of aldehyde **2**. These cycloadducts could be separated by silica gel column chromatography, and their absolute configurations were carefully analyzed by means of NMR spectroscopy involving J_{H-H} values and NOESY correlations. These results are summarized in Table 1, and some selected NMR data are shown in Chart 2.

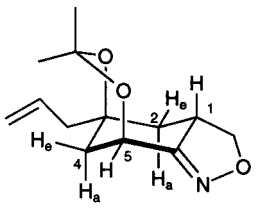
Chart 2



Both the NOESY correlations and typical coupling constants for **11** and **12** illustrated in Chart 2 unambiguously led to their absolute configurations as indicated.[10] The similar structural analysis was conducted for cy-

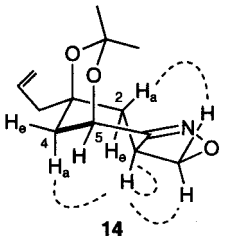
(10) The signal of H(5) appearing at 4.85 ppm as a ddd pattern with *J* values of 0.9 (long-range), 6.1, and 11.2 Hz indicated that the each TBDMSO group at the preexisting stereogenic center [C(5)] and the newly induced stereogenic center [C(3)] arrange equatorial and axial, respectively. On the other hand, the C(5)-hydrogen of the minor product **12** appeared at 4.78 ppm as a dd pattern with *J* values of 2.1 and 3.9 Hz suggested its equatorial orientation, while the NOESY data for **12** illustrated in Chart 2 clearly indicated the axial TBDMSO-group at C(5) and the axial allyl-group at C(3) in a chair conformation. The existence of long-range spin-coupling ($J = 0.9$ Hz) between H(5) and H(1) indicates a 1,3-diaxial arrangement each other intervened by C=N π-system. The w-shaped long-range spin coupling between $H_e(2)$ and $H_e(4)$ ($J = 2.4$ Hz) was also observed to support the chair conformation of **11**.

Chart 3



13

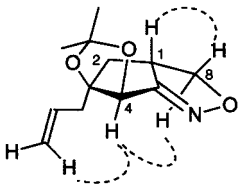
J (H(5)–H_a(4)) = 1.9 Hz
J (H(5)–H_e(4)) = 4.4 Hz
J (H_e(2)–H_e(4)) = 2.7 Hz
J (H_a(2)–H(1)) = 10.2 Hz
J (H_e(2)–H(1)) = 6.9 Hz



14

J (H(5)–H_e(4)) = 2.1 Hz
J (H(5)–H_a(4)) = 3.4 Hz
J (H_a(2)–H_e(4)) = 1.9 Hz
J (H(5)–H(1)) = 1.5 Hz
J (H_a(4)–CH_{3e})) = 0.6 Hz

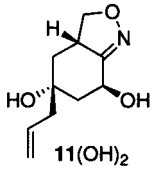
= NOESY correlation



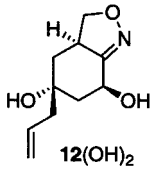
15

J ($H(8)_{convex}$–H(1)) = 7.7 Hz
J ($H(8)_{concave}$–H(1)) = 7.9 Hz
J (H(2)–H(1)) = 8.2, 10.1 Hz

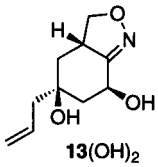
Chart 4



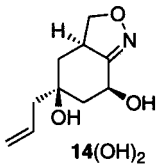
11$(OH)_2$



12$(OH)_2$



13$(OH)_2$



14$(OH)_2$

cloadducts **13** and **14**, by which their structures were elucidated as those shown in Chart 3 together with selected J_{H-H} values and NOESY correlations pertinent to these analyses. A distinctive NOESY correlation observed between H_a(4) and H(1) was the reason we determined the conformation of **14** as a boat.[11]

These results mean that we had four possible diastereomers in hand having the common preexisting C(5) stereogenic center in an enantiomerically pure form. To confirm this, the protecting groups of **11**−**14** were deprotected to give four diol derivatives **11**$(OH)_2$−**14**$(OH)_2$ as shown in Chart 4, the proton NMR spectra of which were surely not identical to each other at all. In every case, the exclusive level of diastereotopic groups selection was achieved, and quite interestingly, their senses were reversed depending whether a controller was the noncyclic 1,3-$(TBDMSO)_2$ (**1**) or the cyclic 1,3-dioxane (**3**) as we can see for **11** and **13**: the former prefers the *pro-R* allyl group as a reaction partner to the *pro-S* one, and the latter prefers the *pro-S* one to the *pro-R* one.

Although the final decision for the structure of **17** is open to further studies, the cycloaddition reaction of nitrile oxide derived from **2** bearing the 1,2-$(TBDMSO)_2$ controller was very slow (48 h) to unexpectedly result in the formation of **17** as a mixture of isomers of unknown stereochemistry (3:1): this cycloadduct probably stemmed from normal cycloadducts followed by acid-promoted tautomerization, electrophilic halogenation, and hydrolysis under the conditions.[12] On the other hand, the corresponding acetonide version (**4**) led to the formation of **15**[13] and **16**[14] (26:1) in 59% yield. In any event, it turned out that the diastereotopic group selection was perfect again in this case, and the allyl group being disposed syn to the 1,3-dipole in this 1,3-dioxolane ring system was exclusively employed as a reaction partner.

The Role of Gauche OCCC Arrangement. The absolute configurations of the cycloadducts determined as above also gave insight into transition states leading to these cycloadducts, which are summarized in Scheme 3.

The transition states TS_{11}-(chair) and TS_{12}-(boat) leading to **11** and **12** involve the axial-oriented TBDMSO group at the prostereogenic center for which the smaller *A* value (1.06 kcal mol^{-1})[15] than that of an allyl group[16] must be responsible partly at least: the difference between these *A* values, however, is not sufficiently large enough to specify one allyl group exclusively. Hence, an another stabilizing factor contributing to the preference of TS_{11}-(chair) to $TS_{11'}$ should be operating. We reasoned that this factor might be a gauche OCCC arrangement in which the electrostatic attractive interaction between the silyl-protected oxygen and the vinyl hydrogen atoms can operate as pointed out recently by Kishi[17] and Houk.[18] On the other hand, the degree (86% de) of diastereotopic faces selection can reasonably be explained on the basis of the energy difference between TS_{11}-(chair) and less stable near boatlike conformation [TS_{12} (boat)] leading to the minor product (**12**). The initial cycloadduct produced through TS_{12} (boat) should have a structure such as **12**-(boat), which, however, is thermodynamically less stable and flips to a more stable chair conformation, giving **12**-(chair) even though it contains the axially oriented TBDMSO and allyl substituents.

The transition states TS_{13} and TS_{15} leading to **13** and **15**, respectively, involve the 1,3-dioxane or 1,3-dioxolane ring system in which the cycloaddition took place between the nitrile oxide and the allyl group positioned cis to the dipole to result in the exclusive level of diastereotopic groups selection. The diastereotopic face selection was controlled by a steric factor similarly to the case of **1** to

(11) The long-range spin coupling observed between H_a(4) and lower field equatorial-methyl proton (six-bond away from each other) in the 1,3-dioxane ring also supported this structure.

(12) As far as the careful NMR analysis of **17** is concerned, we were able to assign its structure tentatively as shown.

(13) Three typical structure-supporting NOESY correlations were observed between the proton at C(4) of known absolute configuration and vinyl or one of C(8) protons, and between the C(1)-proton and the remaining C(8)-proton. These results led us to unambiguously conclude the absolute configurations of cycloadduct in this case as **15**.

(14) The absolute configurations of **16** was estimated on the basis of an idea that no chance of cycloaddition reaction was available for the *pro-R* allyl group: hence remaining possibility of isomer should be an epimer at C(1).

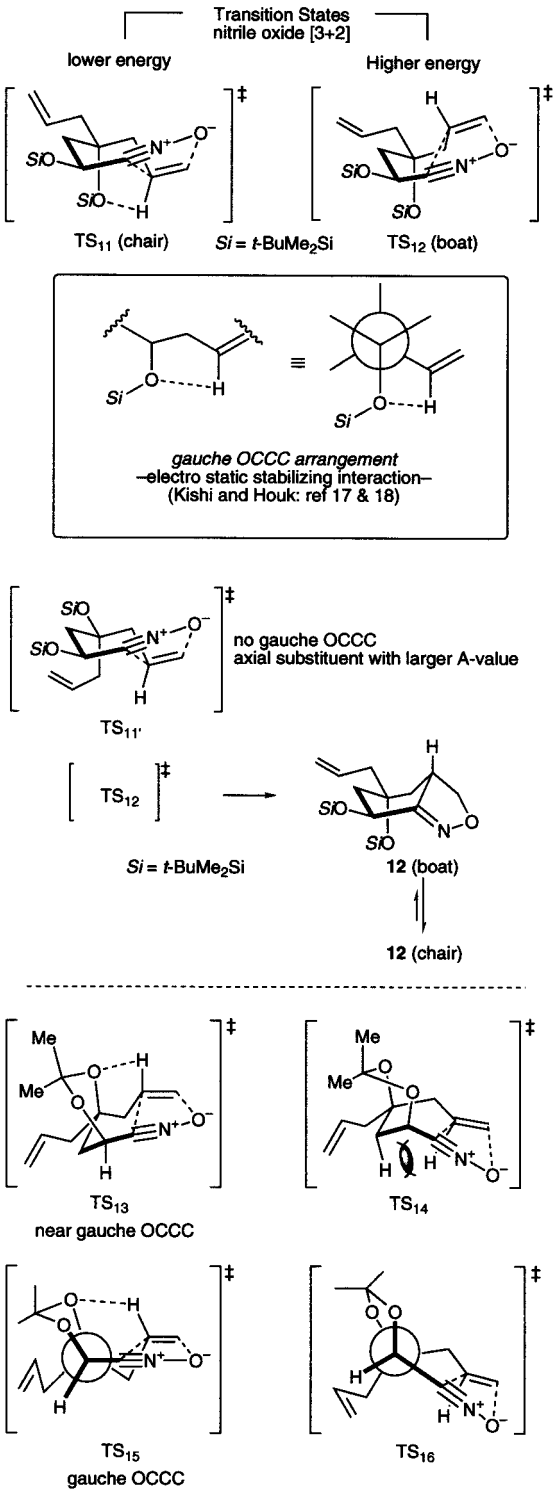
(15) Eliel, E. L.; Satici, H. *J. Org. Chem*. **1994**, *59*, 688−689.

(16) The A-value for CH_2=$CHCH_2$-group is not available from the exhaustive listing in Eliel, E. L.; Wilen, S. H.; Mander L. N. *Stereochemistry of Organic Compounds*; Wiley: New York, 1994; pp 695−698. However, we can roughly estimate it to be near that of ethyl or little more: the *A* value of CH_3CH_2-group is 1.79 kcal/mol (that of propyl group, not available).

(17) Wu, T.-C.; Goekjian, P. G.; Kishi, Y. *J. Org. Chem*. **1987**, *52*, 4819−4823.

(18) Houk, K. N.; Eksterowicz, J. E.; Wu, Y.-D.; Fuglesang, C. D.; Mitchell, D. B. *J. Am. Chem. Soc.* **1993**, *115*, 4107−4177.

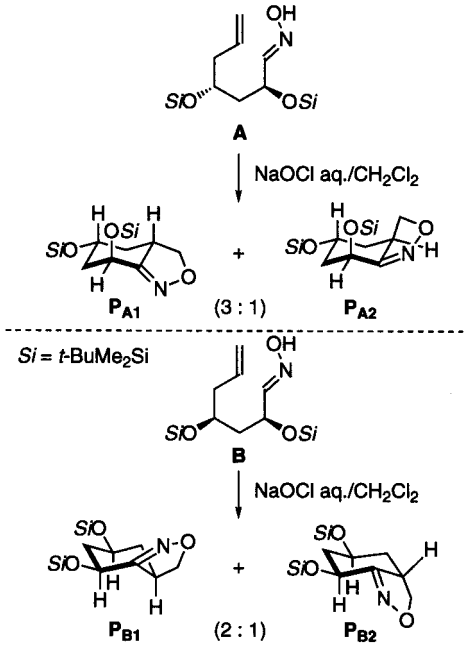
Scheme 3



result in the comparable level of diastereomeric excess (10:1 or 26:1 for **3** or **4**, respectively).

The degrees of diastereotopic faces selection observed previously in the intramolecular [3 + 2] cycloaddition reactions of nitrile oxides (**A** and **B**) were 3:1 and 2:1, respectively, as shown in Scheme 4.[19] It is of interest that the cycloaddition reaction of the nitrile oxide derived from **1** resulted in a much higher level of diastereotopic faces selection [dr (face) = 13:1, Table 1). Again, the attractive electrostatic interaction due to the gauche OCCC arrangement[17,18] should be responsible for such marked difference in the degree of diastereotopic faces selection

Scheme 4



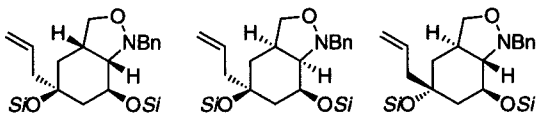
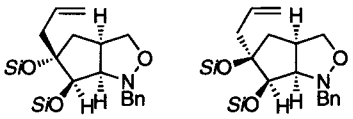
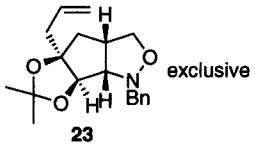
of cycloaddition reactions between the **1**-derived nitrile oxide and **A**- or **B**-derived one: the contribution of such electrostatic reinforcement to a transition state is typical for the **1**-derived nitrile oxide case [see TS_{11}-(chair)] as already mentioned.

Discrimination of Diastereotopic Groups and Faces in Intramolecular Nitrone [3 + 2] Cycloaddition Reactions. Aldehydes **1**−**4** were converted to the corresponding nitrones through a reaction with *N*-benzylhydroxylamine in a usual manner and without any purification, were subjected to the thermal cycloaddition conditions. The nitrones derived from **1** and **2** furnished a separable mixture of diastereomeric isoxazolidines **18** + **19** + **20** (5:2.4:1) and **21** + **22** (11:1), respectively, and the nitrone from **4** exclusively gave **23**. The cycloaddition reaction of the nitrone derived from **3** was not effected when a solution of the nitrone in benzene was heated at 110 °C for 48 h. These results are summarized in Table 2.

NOESY correlations used for the determination of the absolute configurations of **18**−**21** and **23** are summarized in Chart 5. To avoid an any ambiguity in the analysis of absolute configurations of **19** due to signal overlapping, the TBDMS protecting group at the preexisting stereogenic center was deprotected (TBAF/THF) followed by usual acetylation to give the corresponding acetyl derivative (**19**-(9-OAc)), in which NOESY correlations were analyzed. The J_{H-H} values including long-range cases

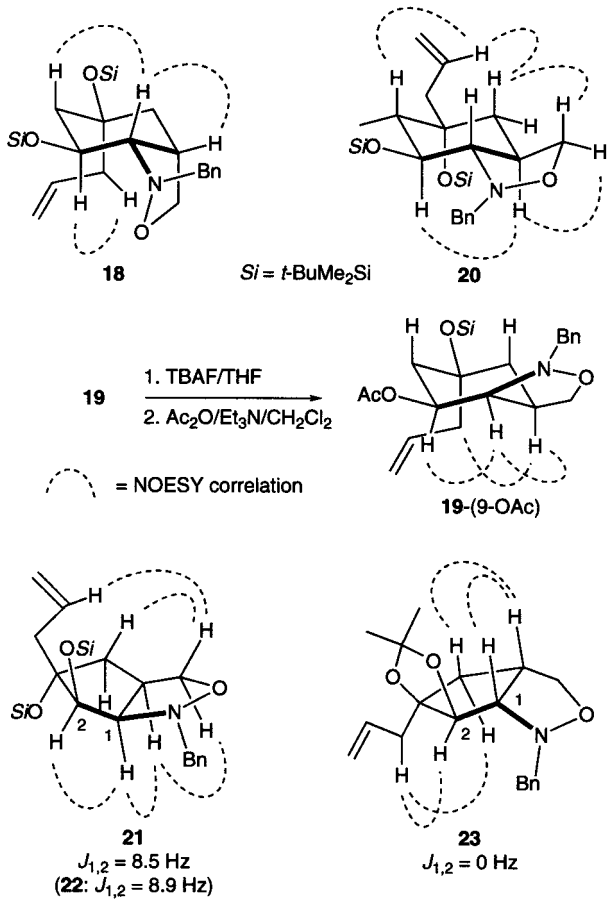
(19) (a) Ishikawa, T.; Ikeda, S.; Ibe, M.; Saito, S. *Tetrahedron* **1998**, *54*, 5869−5882. For other diastereoselective intramolecular nitrile oxide cycloaddition reactions in which one to three stereogenic centers exist, and dipolarophiles (C═C) directly link to one of such stereo centers, see: (b) Kozikowski, A. P.; Chen, Y.-Y.; Wan, B. C.; Xu, Z.-B. *Tetrahedron* **1984**, *40*, 2345−2358. (c) Nakata, M.; Akazawa, S.; Kitamura, S.; Tatsuta, K. *Tetrahedron Lett.* **1991**, *32*, 5363−5366. (d) Takahashi, T.; Shimayama, T.; Miyazawa, M.; Nakazawa, M.; Yamada, H.; Takatori, K.; Kajiwara, M. *Tetrahedron Lett.* **1992**, *33*, 5973−5976. (e) Kobayashi, Y.; Miyazaki, H.; Shiozaki, M. *J. Am. Chem. Soc.* **1992**, *114*, 10065−10066 and *J. Org. Chem.* **1994**, *59*, 813−822. (f) Takahashi, T.; Nakazawa, M.; Sakamoto, Y.; Houk, K. N. *Tetrahedron Lett.* **1993**, *34*, 4075−4078. (g) Pearson, W. H.; Lovering, F. E. *J. Am. Chem. Soc.* **1995**, *117*, 12336−12337. (h) Takahashi, T.; Iwamoto, H. *Tetrahedron Lett.* **1997**, *38*, 2483−2486. See also: (i) Irie, O.; Fujiwara, Y.; Nemoto, H.; Shishido, K. *Tetrahedron Lett.* **1996**, *37*, 9229−9232.

Table 2. Results of Intramolecular Cycloaddition Reactions of Nitrones Derived from Aldehydes 1−4

RCHO	Cycloaddition[a] temp/°C : time/h	yield/%	dr (group)	dr (face)	Products[b] structure and composition
1	50 : 18	74	7.4 : 1[c]	2.1 : 1 (**18** :**19**)[c] >99 : 1 (**20**)[d]	 **18** (5 : 2.4 : 1) **19** **20**
2	40 : 40	58	11 : 1[e]	>99 : 1 (**21**)[e] >99 : 1 (**22**)[e]	 **21** (11 : 1) **22**
4	40 : 1	91	>99 : 1[f]	>99 : 1[f]	 exclusive **23**
3	110 : 48	N.R.			

[a] Conducted using benzene as a solvent containing 1.5 equiv of *N*-benzylhydroxylamine and aldehydes **1**−**4**. [b] Yields after purification by silica gel column chromatography (*Si* = *tert*-butyldimethylsilyl). [c] dr = diastereomeric ratios calculated using the weight of isolated products. [d] >99:1 means that no isomer signals were detected in 500 MHz NMR analyses. [e] Diastereomers, inseparable by conventional silica gel column chromatography; dr determined by NMR. [f] Other diastereomers not detected at all by both silica gel column chromatography and NMR analysis.

Chart 5



obtained for these cycloadducts were also used for the analysis of absolute configurations in combination with the NOESY data.[20]

In marked contrast to the case of nitrile oxide derived from **3** in which [3 + 2] cycloaddition smoothly took place (0 °C, 0.7 h), the corresponding nitrone did not undergo the expected cycloaddition reaction at all as mentioned above. The structural difference between the nitrile oxide (linear) and nitrone parts (flat but bent plus (*Z*)-geometry in this case[21]) may be responsible for this reactivity difference: the latter should become much more demanding in terms of orbital overlapping for the [3 + 2] cycloaddition process to be effected because rotation about two carbon−carbon σ-bonds are prohibited due to the incorporation of 1,3-dioxane ring system.[22]

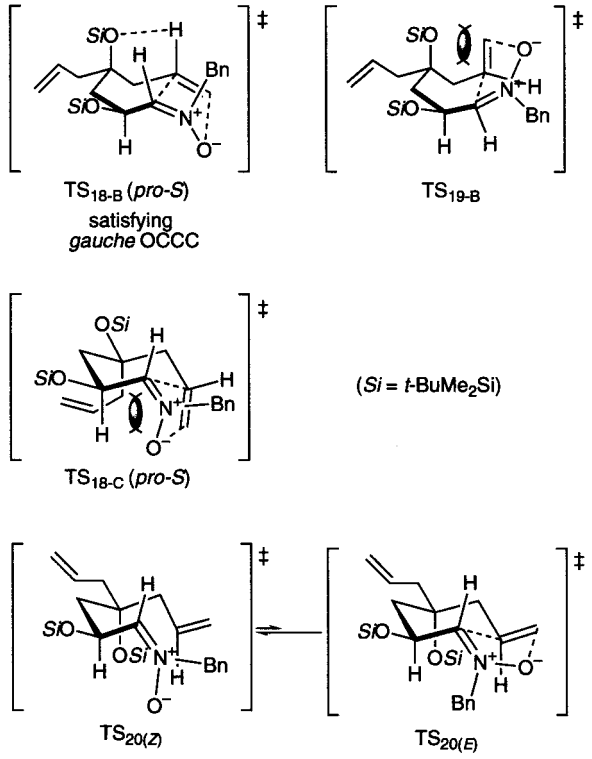
The absolute configurations of cycloadducts **18** and **19** for the nitrone prepared from **1** indicated that a reversal of diastereotopic groups selection occurred as compared to the case of the nitrile oxide derived from **1** although the same 1,3-(TBDMSO)$_2$ controller was used. On the basis of this fact, we can draw a possible transition state such as TS_{18-C} (*pro-S*) as far as a chair conformation is concerned (Scheme 5). This structure, however, is not only suffering from severe 1,3-diaxial interaction but also is bearing the axial allyl group of larger *A* value[16] than the TBDMSO group[15] and, therefore, should be ruled out. Thus, we reached the conclusion that the transition state leading to **18** might be boat in nature as TS_{18-B} (*pro-S*) bearing the axially oriented TBDMSO group in which electrostatically stabilizing interaction through the gauche OCCC arrangement[17,18] is operating similarly to the case

(20) It should be mentioned that the NMR spectrum of an inseparable mixture of **21** and **22** fortunately indicated that the $J_{1,2}$ values of **21** and **22** are 8.5 and 8.9 Hz, respectively which were crucial for the absolute configuration determination. In marked contrast to these the $J_{1,2}$ value of **23** is nearly zero indicating 1,2-trans arrangement.

(21) Saito, S.; Ishikawa, T.; Kishimoto, N.; Kohara, T.; Moriwake, T. *Synlett* **1994**, 282−284.

(22) Molecular models provided us with a more insight into this problem. We considered eight models of possible transition states, among which only two cases can make orbital overlap possible, in which, however, the olefin part is forced to be in too sterically congested space for the reaction to be effected. One remaining chance might be the isomerization of nitrone geometry from (*Z*) to (*E*), facilitating effective orbital overlapping but apparently giving rise to unfavorable torsional strain.

Scheme 5



of TS_{11} as mentioned in Scheme 3. Hence, the stereochemical outcome of **19** might also be controlled by a similar boat transition state as TS_{19-B}.

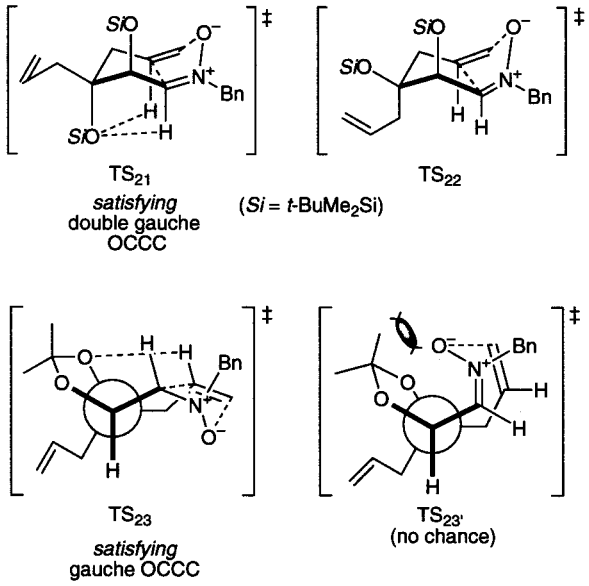
With regard to the formation of **20**, the *pro-R* allylic group was selected as a reaction partner, and therefore, the reaction should be intervened with a chair-type transition state bearing an axially oriented TBDMSO group as $TS_{20(Z)}$, in which, however, no positive orbital overlapping seems possible even though it features the gauche OCCC arrangement. Therefore, in order for the formation of **20** to be effected, the geometry of the nitrone must change from *Z* to *E* ($TS_{20(E)}$) during the reaction. The rate of such *Z* to *E* isomerization, however, is known to be slow.[23] This is the reason the thermodynamically less stable adducts **18** and **19** than **20** became major products in this case. To confirm that **18** was given under kinetically controlled conditions, a solution of **18** in toluene was heated at 110 °C for 24 h to result in the recovery of **18** and also in the formation of neither **19** nor **20**.

The 1,2-$(TBDMSO)_2$ controller system, by which the nitrile oxide cycloaddition did not proceed at all as shown above in Table 1, provided an opportunity in favor of the *pro-R* allyl group for the nitrone cycloaddition reaction. The role of 1,2-$(TBDMSO)_2$ controller has its origin in their stable anti-periplanar arrangement (anti OCCO).[9] In addition to this crucial backbone, the additional favorable structural feature such as the gauche OCCC arrangement (twice) is present in the transition state TS_{21} responsible for the formation of cycloadduct **21**, which is lacking in the transition state TS_{22} leading to the minor cycloadduct **22** (Chart 6).

The 1,3-dioxolane controller system provided an opportunity of the same sense of diastereotopic group

(23) LeBel, N. A.; Banucci, E. G. *J. Org. Chem.* **1971**, *36*, 2440−2448. See also ref 24d.

Chart 6



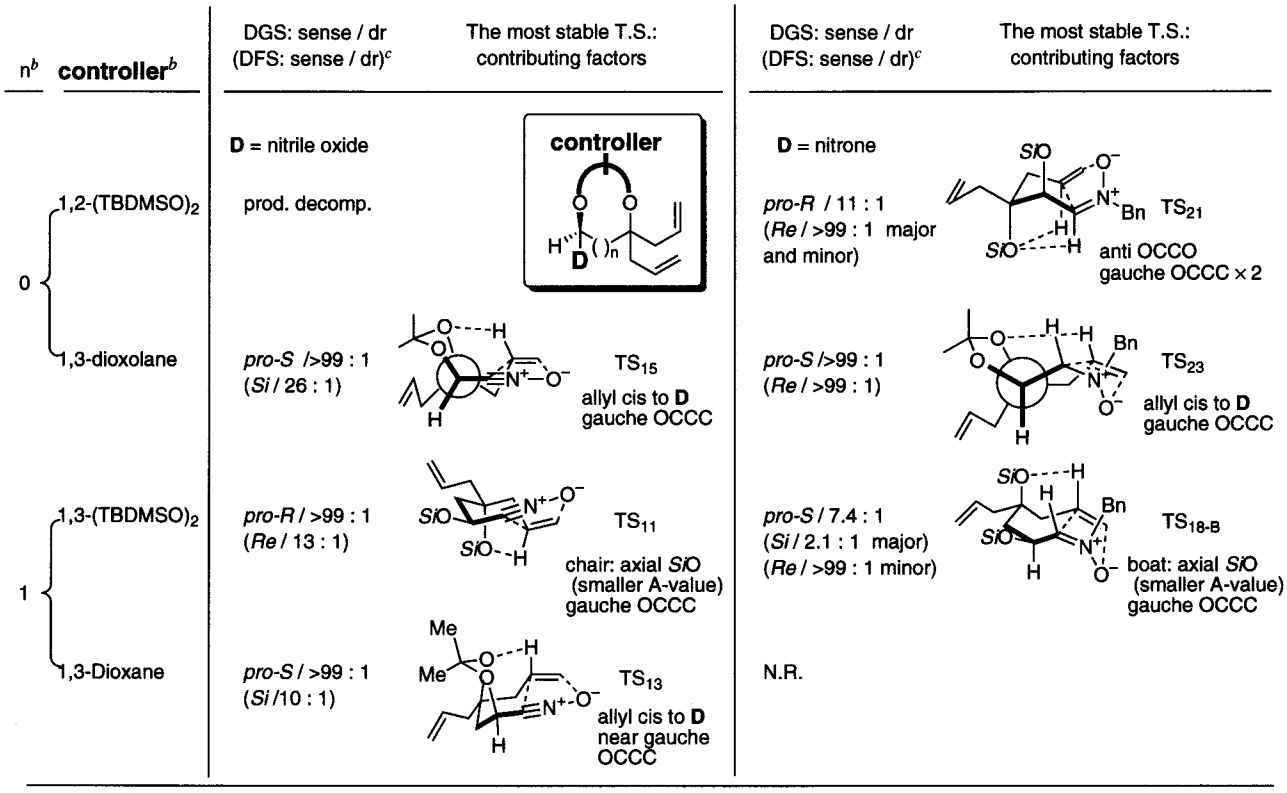
selection as the nitrile oxide case for the nitrone cycloaddition reaction with an exclusive level of diastereomeric ratio, and at the same time, the π-facial discrimination turned out to be exclusive (**23**). A model study gave more insight into this outstanding stereocontrol, which suggested that the orbital overlapping of the [3 + 2] cycloaddition process of this class became possible only when *Si-Si* face matching was achieved as in TS_{23}: *Re-Re* matching as in $TS_{23'}$ seems impossible because of extremely severe steric congestion and torsional strain.

Role of Controllers in Biasing Stereochemical Courses of Intramolecular Nitrile Oxide or Nitrone Cycloaddition Reactions. Before moving to the studies on the application of above-mentioned strategy to other classes of cycloaddition reactions such as the Pauson−Khand reaction, it seems important to summarize the steric or electronic impact of the four types of controllers on the transition-state models of the tandem stereodetermining steps involving diastereotopic groups and faces selections of this class (Chart 7).

Since the dipolar moieties are linking directly to the preexisting stereogenic centers that are incorporated into the controllers of 1,3-dioxolane or 1,3-dioxane ring system, they can nicely bias the geminal allyl groups, dictating those being disposed syn to the dipolar moieties to become a reaction partner (>99%) as shown in $TS_{13,15,23}$. These heterocyclic controllers also provide the facial bias to the allylic C=C bond imparted by steric and electronic effects. The steric effects might be evaluated positively or negatively as the result of delicate balance among various types of steric interactions, whereas the

(24) For asymmetric induction in intramolecular nitrone cycloaddition reactions, see: (a) Ihara, M.; Takahashi, M.; Fukumoto, K.; Kametani, T. *J. Chem. Soc. Chem. Commun.* **1988**, 9−10. (b) Roush, W. R.; Watts, A. E. *J. Am. Chem. Soc.* **1984,** *106*, 721−723. (c) Annunziata, R.; Cinquini, M.; Cozzi, F.; Raimondi, L. *Tetrahedron* **1987**, *43*, 4051−4056. (d) Ishikawa, T.; Kudo, T.; Shigemori, K.; Saito, S. *J. Am. Chem. Soc.* **2000,** *118*, 7633−7637; For asymmetric induction in intramolecular dipolar cycloaddition reactions other than nitrones, see: (e) Righi, P. R.; Marotta, E.; Landuzzi, A.; Rosini, G. *J. Am. Chem. Soc.* **1996,** *118*, 9446−9447. (f) Denmark, S. E.; Hurd, A. R.; Sacha, H. J. *J. Org. Chem.* **1997**, *621*, 11668-1674. (g) Garner, P.; Cox, P. B.; Anderson, J. A.; Protasiewicz, J.; Zaniewski, R. *J. Org. Chem.* **1997**, *62*, 493−498. (h) Young, D. G. J.; G.-Bengoa, E.; Hoveyda, A. H. *J. Org. Chem.* **1999**, *64*, 692−693. (i) Marrugo, H.; Dogbéavou, R.; Breau, L. *Tetrahedron Lett.* **1999**, *40*, 8979−8983.

Chart 7. Summary of the Sense and Degree of Diastereotopic Groups and Face Selections in Intramolecular Nitrile Oxide and Nitrone Cycloaddition Reactions[a]



[a] See also Tables 1 and 2: *Si* = *tert*-butyldimethylsilyl. [b] See inset for "*n*" and "**controller**". [c] DGS = diastereotopic group selection; DFS = diastereotopic face selection; dr = diastereomeric ratio.

electronic effect can operate positively through electrostatic interaction in the gauche Si−OCCC= arrangements where the oxygen atom is linking to the prostereogenic center: this kind of electrostatic effect becomes possible only in the transition states leading to major diastereoisomers ($TS_{13,15,23}$).[24]

On the other hand, we should discuss the role of the acyclic controllers individually with regard to the 1,3-(TBDMSO)$_2$ and 1,2-(TBDMSO)$_2$. The 1,3-(TBDMSO)$_2$ controller involves the equatorial TBDMSO group at the preexisting stereogenic center and the axial one at the prostereogenic center due to the generalization that a substituent of smaller *A* value arranges axial at the bicyco[4.3.0]-type transition states including the six-membered system where both TBDMSO groups are involved ($TS_{11,18-B}$). The most stable conformation attained by the 1,2-(TBDMSO)$_2$ controller should basically involve anti-OCCO arrangement[9] as shown in TS_{21}, the origin of which has been well approved so far.[25] Similar to the case of heterocyclic controllers, the gauche OCCC arrangement is commonly involved in these most stable transition states and might positively play an important role in biasing the diastereotopic faces selection again.

Mechanism of Pauson−Khand Reaction and the Preparation of Dienynes. According to the current level of mechanistic understanding of Pauson−Khand reaction,[26] we can illustrate the mechanism of this process using **24**−**27** (Scheme 6) prepared from chiral diallyl aldehydes **1**−**4** through Corey's acetylenation protocol[27] followed by trimethylsilylation of the terminal sp carbons (Scheme 7).[28] The events of both diastereotopic group and face selection of the Pauson−Khand reaction might take place during **N** → **O** conversion. Furthermore, since the first intermediate **M**, the alkyne−$Co_2(CO)_6$ complex, has two diastereotopic cobalt atoms, their subsequent complexation to the terminal olefin should affect the eventual stereochemical outcomes of Pauson−Khand reaction of **24**−**27**, in particular the degree of the diastereotopic faces selection. Thus, to achieve the high level of diastereoselectivity of this class, we expected that the TMS group introduced to the acetylenic terminus might serve as one of control elements with regard to which of the cobalt atoms is able to be involved in the complexation with the terminal olefin.

Discrimination of Diastereotopic Groups and Faces in Pauson−Khand [2 + 2 + 1] Cycloaddition Reactions. Treatment of **24**−**27** with $Co_2(CO)_8$ in dichloromethane at 0 °C to room temperature for 3 h gave the corresponding acetylenehexacarbonyldicobalt complexes (**M**) as a rather stable dark red oil, which were roughly purified by column chromatography over silica gel. A solution of these complexes in acetonitrile was heated at 65−75 °C for 11−18 h, furnishing the [2 + 2 + 1]

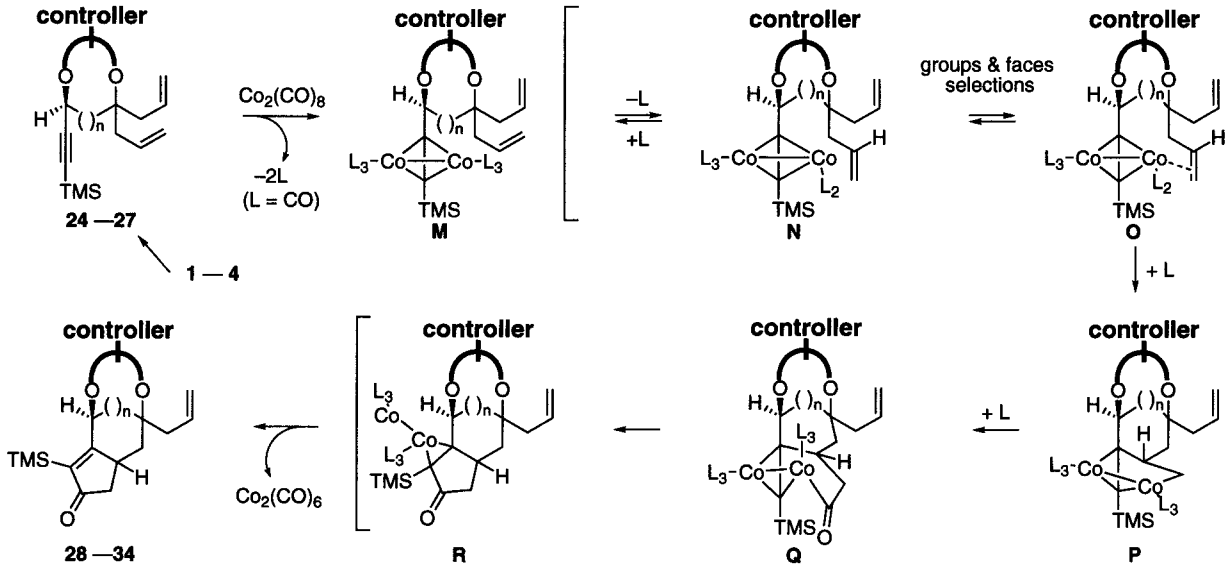
(25) Gung, B, W.; Zhu, Z.; Fouch, R. A. *J. Am. Chem. Soc.* **1995**, *122*, 1783−1788 and references therein.

(26) (a) Schore, N. E. *Org. React.* **1991**, *40*, 1−90. (b) Verdaguer, X.; Vázquez, J.; Fuster, G.; B.-Génisson, V.; Greene, A. E.; Moyano, A.; Pericas, M. A.; Riera, A. *J. Org. Chem.* **1998**, *63*, 7073−7052 and references therein.

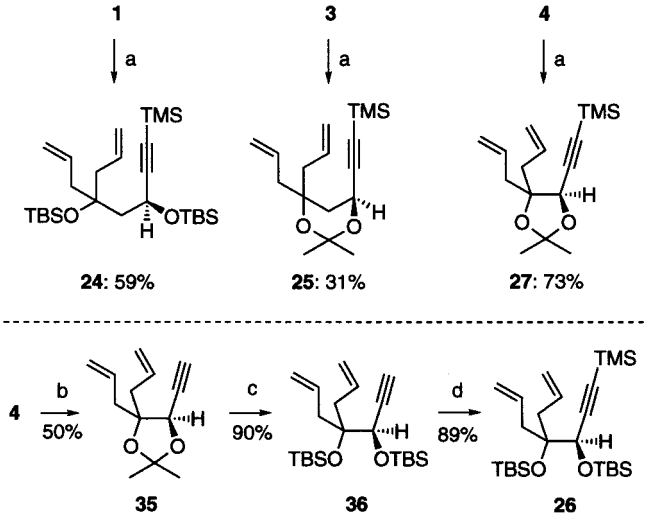
(27) Corey, E. J.; Fuchs, P. L. *Tetrahedron Lett.* **1972**, *36*, 3769−3772.

(28) Conversion of **2** to **26** through the Corey's protocol resulted in very low yield (7%). The enyne **26**, therefore, was provided from **4** through a series of reactions shown bottom in Scheme 7.

Scheme 6



Scheme 7[a]



[a] Key: (a) (1) $CBr_4/PPh_3/Zn$/0 °C to rt, (2) BuLi/THF/−78 °C, then TMS-Cl; (b) (1) (a) − 1, (2) (a) − 2 without TMS-Cl; (c) (1) 90% AcOH/MeOH/PTSA, (2) TBDMSOTf/Et_3N; (d) BuLi/TMS-Cl.

cycloadducts **28** + **29** (9:1), **30** + **31** (10:1), **32** + **33** (10:1), and **34** (exclusive) from **M** as summarized in Table 3. The Pauson−Khand reaction of additional substrate **36**, which is missing the terminal trimethylsilyl group, was carried out for comparison and resulted in a mixture of four isomers in a ratio of 2.7:1.5:1.5:1. Therefore, it seems that the terminal TMS groups tagged in **24**−**27** play an important role in the stereochemistry-determining step (**N** → **O**) of the Pauson−Khand reaction (Scheme 6) as expected.

The absolute configurations of these cycloadducts were determined not only by NOE experiments but also by appropriate derivatizations, in particular for bicyclo-[3.3.0]-type products such as **32** or **34**. It should be mentioned that, as quickly recognized from the absolute configurations shown in Chart 8, adduct **28** apparently less stable than **29** became a major product in the case of **24**. The exact reason for this result could not be given an answer at present because we have no reliable idea for the transition state structure during the **N** → **O** conversion.[29]

For **32** or **34**, NOEs between the allyl group and both C(2)−H (convex space) or C(4)−H (concave space) were clearly observed (Scheme 8), which, in turn, left behind ambiguity with regard to the sense of the diastereotopic groups selection. To make this point clear, both **32** and **34** were converted to **38** (H_2/Pd−C) and **40** [$(Ph_3P)CuH]_6$/C_6H_6], respectively, in which we observed clear-cut NOEs between C(2)-H and one of C(8)-H's and no NOE between this C(8)-H and C(5)-H, indicating that the both initial cycloadducts **32** and **34** bear the bridgehead hydrogen arranging in convex space. For **34**, since it was quite clear that the allyl group positioned cis to the trimethylsilylethynyl group became a reaction partner in this Pauson−Khand reaction, the absolute configurations at C(1) and C(3) should be those as shown in **34** in Scheme 8.

However, the absolute configuration at C(3) of **32** still remained ambiguous. Since the absolute configurations of **32** and **34** at the bridgehead centers are identical, the most simple and reliable way of solving this ambiguity is to convert **38** (+ **39**) into **41** (+ **42**), which can be examined as to whether **34** is identical with the deacetonidation product of **40**. Thus, **38** containing **39** was treated with HCl in EtOH to give **41** (+ **42**), whereas **34** was reduced (H_2/Pd−C) and deprotected (HCl/EtOH) to give a diol, the NMR of which was identical with that of **42** (Scheme 8). Thus, the absolute configuration of **32** was revealed to be those shown in Table 3 or Scheme 8.

Origin of the Diastereoselections. To determine what is responsible for the sense of the diastereotopic groups and faces selections, the results of Pauson−Khand reactions are listed in Table 4. These data together with those pertinent to this problem listed in Chart 7 clearly indicate that the levels of control for the diastereotopic

(29) Based on a model inspection we tentatively have an idea about the transition state structure leading, for instance, to **34** as shown below.

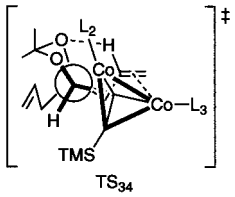
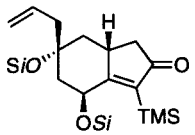
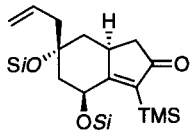
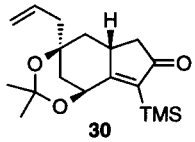
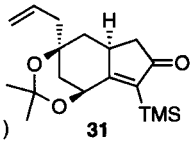
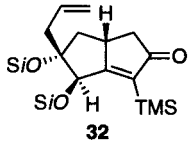
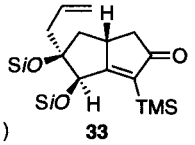
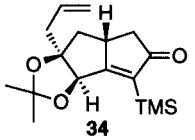
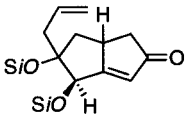


Table 3. Results of Pauson–Khand Reactions

Sub	Cycloaddition[a]		Products[b]			
	temp/°C :	time/h	yield/%	dr (group)	dr (face)	structure and composition
24	75	18	66	>99 : 1[c]	9 : 1[d]	 **28** (9 : 1)  **29**
25	70	16	21	>99 : 1[c]	10 : 1[d]	 **30** (10 : 1)  **31**
26	75	18	44	10 : 1[d]	>99 : 1 (**32**)[e] >99 : 1 (**33**)[e]	 **32** (10 : 1)  **33**
27	65	11	74	>99 : 1[e]	>99 : 1[e]	 **34** exclusive
36	60	3	60			 **37**: 4 isomers; 2.7 : 1.5 : 1.5 : 1

[a] Heating a solution of cobalt–enyne complexes, prepared from **24**–**27** (120 mol % of $Co_2(CO)_8$/CH_2Cl_2/0 °C to room temperature, 1–5 h) in acetonitrile. [b] Yields after purification by silica gel column chromatography (*Si* = *tert*-butyldimethylsilyl). [c] Determined on the basis of the absolute configurations of the products. [d] Diastereomeric ratios calculated using the weight of isolated product. [e] Other diastereomers not detected at all by both silica gel column chromatography and NMR analysis.

groups selection were uniformly high. Thus, the substrate-dependent senses of the diastereotopic groups selection were generally observed irrespective of the reaction type, suggesting that the diastereotopic bias imposed on the prostereogenic groups (*gem*-allyl groups) is the result of stereocontrol dictated by the controllers. On the other hand, the sense of the diastereotopic faces selection exhibited no controller-dependent regular change, suggesting that the diastereofacial bias was conferred on the terminal olefins as the result of the delicate balance between electrostatic and steric effects which should be determined intrinsically depending on the nature of the reaction. In any event, the degrees of the diastereotopic faces selection were uniformly acceptable.

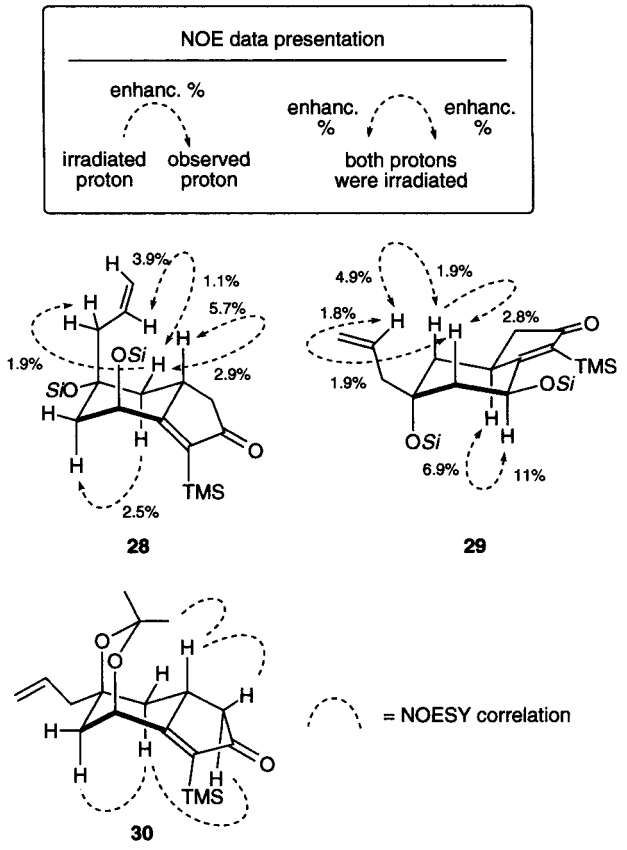
Conclusion

We have developed a novel method for realizing simultaneous discrimination of diastereotopic groups and their faces in intramolecular [3 + 2] and [2 + 2 + 1] cycloaddition reactions. The processes afforded both bicyclo[3.3.0] and bicyclo[4.3.0] adducts with three to four stereogenic centers in which isoxazolidine, isoxazoline, or cyclopentenone segments were fused. Special attention was paid to the present stereochemical models to account for how the 1,3-$(TBDMSO)_2$, 1,2-$(TBDMSO)_2$, 1,3-dioxane, and 1,3-dioxolane controllers work. The degrees of the group discriminations observed in the combinations between three types of reactions and four types of substrates were uniformly excellent (dr = >99:1 for seven cases and 7.3:1–11:1 for the remaining three cases). We have also achieved the high level of asymmetric induction in the π-facial discrimination ranging from dr = 9:1 to dr = >99:1 with only one exception (dr = 2.1:1). In the systems presented here, the multiple stereogenic centers have been constructed from a single stereogenic center in a single operation to realize the high levels of stereocontrol. The products themselves as well as these strategies will be of high value toward the synthesis of complex molecules.

Experimental Section

General Methods. ^1H NMR spectra were recorded at 300 or 500 MHz and ^{13}C NMR at 75 MHz using $CDCl_3$ as a solvent. The chemical shifts (δ) are given in parts per million relative to internal $CHCl_3$ (7.26 ppm for ^1H) or $CDCl_3$ (77 ppm for ^{13}C). The ^1H NMR spectral data are indicated in the following manner: δ value of signal (peak multiplicity, integrated number of protons, and coupling constant (if any)). Splitting patterns are abbreviated as follows: s, singlet; d, doublet; t, triplet; m, multiplet; b, broad. All the chemical shift assignments were consistent with COSY spectra, and conformational analyses were carried out on the basis of a combination of *J* values, NOE spectra, and NOESY spectra, and in every case the absolute configurations were able to be unambiguously

Chart 8



determined by means of those experiments for the cycloadducts or their derivatives. FR−IR spectra were recorded using NaCl plates. Elemental analyses were carried out by Dr. Miyoko Izawa of this laboratory. Optical rotations were measured on a digital polarimeter using a 3.5 mm × 0.5 dm Pyrex cell.

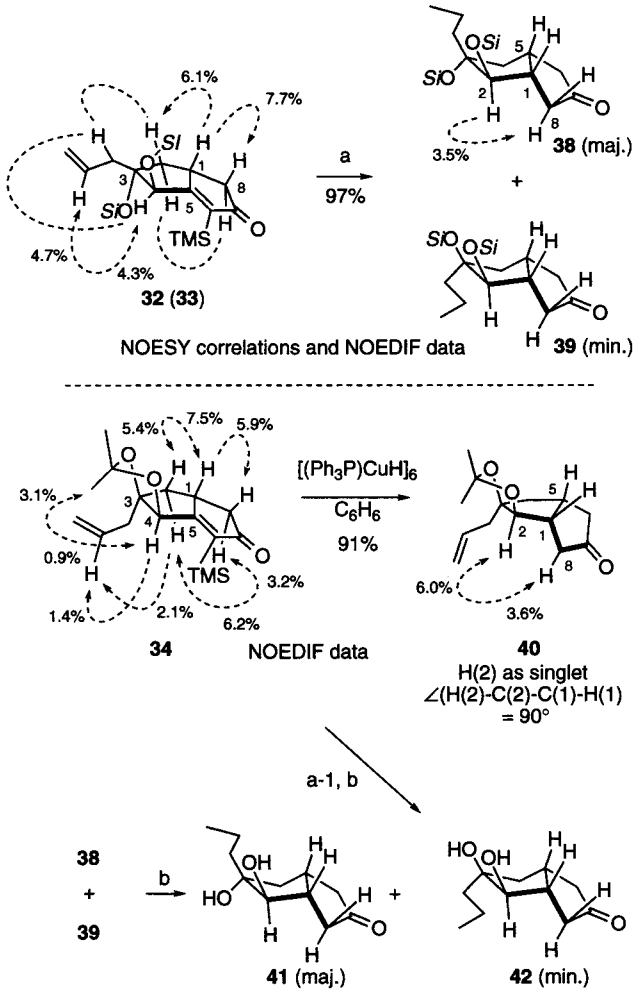
Analytical thin-layer chromatography was performed on Merck precoated silica gel 60 F-254 (0.25 mm thickness). Column chromatography was performed on Merck silica gel 60 7734 using an appropriate ratio of ethyl acetate (EtOAc)−hexane mixed solvent and abbreviated as CC. Although diastereoisomeric cycloadducts were able to be separated through flash column chromatography in many cases, it was repeatedly required in order to achieve the complete separation of the isomers.

All reactions, unless otherwise noted, were conducted under a nitrogen or an argon atmosphere. Liquid reagents were transferred via a dry hypodermic syringe and added through a rubber septum wired onto a reaction flask from which a steady stream of inert gas was flowing. Organic extracts were concentrated by evaporation with a rotary evaporator evacuated at around 60 mmHg. Unless otherwise noted, materials were obtained from commercial suppliers, and reagent grade materials were used without further purification. Toluene, triethylamine (Et_3N), dichloromethane (CH_2Cl_2), acetonitrile, and benzene were freshly distilled from CaH_2 prior to use. Methanol (MeOH) and ethanol (EtOH) were distilled from magnesium turnings under argon. Tetrahydrofuran purchased from Kanto Chemical Co., Inc., is dehydrated and stabilizer-free grade and was used as received.

(2*S*)-4-Allyl-1,2-*O*-(isopropylidene)-6-heptene-1,2,4-triol (7). To a solution of ethyl (3*S*)-3,4-dihydroxybutanoate **5** (1.0 g, 5.4 mmol) in ether (10 mL) was added allylmagnesium bromide (1.0 M, 2.5 equiv) at −78 °C. The mixture was stirred at that temperature for 50 min. The reaction was quenched by the addition of water and filtered through a Celite pad, the filter cake being thoroughly rinsed with AcOEt. The combined organic solutions were dried with Na_2SO_4 and concentrated to give an oil, which, on careful CC (50:1 hexane/EtOAc), gave **7** (1.22 g, 94%): $[\alpha]^{21}_D$ +11.9 (*c* 1.16, $CHCl_3$); ^{1}H NMR (300 MHz) δ 1.35 (s, 3H), 1.40 (s, 3H), 1.61−1.78 (m, 2H), 2.22−2.42 (m, 4H), 3.06 (s, 1H), 3.51 (dd, 1H, J = 7.6, 7.9 Hz), 4.08 (dd, 1H, J = 5.9, 7.9 Hz), 4.33−4.41 (m, 1H), 5.04−5.13 (m, 4H), 5.55−5.59 (m, 2H); ^{13}C NMR (75 MHz) δ 25.7, 26.7, 41.4, 43.8, 44.2, 70.1, 72.7, 73.0, 109.0, 118.1, 118.3, 133.7, 133.8; IR (film) 3492, 1640 cm^{-1}. Anal. Calcd for $C_{13}H_{22}O_3$: C, 68.99; H, 9.80. Found: C, 68.77; H, 9.90.

(2*S*)-4-Allyl-1-*O*-pivaloyl-6-heptene-1,2,4-triol (8). To a solution of the diallyl acetonide **7** (1.21 g, 5.3 mmol) in EtOH (6 mL) was added 2 N HCl (6 mL) at 0 °C. The mixture was stirred at room temperature for 2 h, concentrated by a rotary evaporator, and dried under high vacuum for overnight to give an oil, which, on CC (2:1 hexane/EtOAc), gave (2*S*)-4-allyl-6-heptene-1,2,4-triol (816 mg, 83%): $[\alpha]^{28}_D$ +15.7 (*c* 1.07, $CHCl_3$); ^{1}H NMR (300 MHz) δ 1.46−1.74 (m, 2H), 2.19−2.42 (m, 4H), 2.60−2.70 (b, 1H), 3.00 (b, 1H), 3.40−3.63 (m, 2H), 4.00 (b, 1H), 4.12 (m, 1H), 5.08−5.19 (m, 4H), 5.72−5.92 (m, 2H); ^{13}C

Scheme 8[a]



[a] Key: (a) (1) H_2/Pd−C/EtOH, (2) TBAF/THF; (b) 2 N HCl/EtOH.

Table 4. Summary of the Sense and Degree of Diastereotopic Groups and Face Selections in Intramolecular Pauson−Khand Reactions[a]

	group selection		face selection	
controller	sense	dr[b]	sense	dr[b]
1,2-(TBDMSO)$_2$[c]	*pro-R*	10:1	Si face	>99:1
1,3-(TBDMSO)$_2$	*pro-R*	>99:1	Si face	9:1
1,3-dioxolane	*pro-S*	>99:1	Si face	>99:1
1,3-dioxane	*pro-S*	>99:1	Si face	10:1

[a] See also Table 3. [b] dr = diastereomeric ratio. [c] dr of face selection for the major diastereomer.

NMR (75 MHz) δ 39.6, 42.7, 45.2, 67.0, 69.1, 74.2, 119.0, 119.2, 133.0, 133.2; IR (film) 3368 cm^{-1}.

To a stirred solution of the 1,2,4-triol (816 mg, 4.3 mmol) in CH_2Cl_2 (8 mL) were added pyridine (0.45 mL, 1.3 equiv) and pivaloyl chloride (0.64 mL, 1.2 equiv) at −78 °C. The mixture was stirred at −78 °C for 4 h, quenched by the addition of water, and extracted with CH_2Cl_2 (3 times). The combined extracts were dried with Na_2SO_4 and concentrated by a rotary evaporator to give an oil, which, on CC (3:1 hexane/EtOAc), gave **8** (1.09 g, 94%): $[\alpha]^{29}_D$ +8.29 (*c* 1.64, $CHCl_3$); ^{1}H NMR (300 MHz) δ 1.22 (s, 9H), 1.54−1.72 (m, 2H), 2.18−2.46 (m, 4H), 2.85 (b, 1H), 3.48 (b, 1H), 4.03 (d, 2H, J = 5.22 Hz), 4.21−4.31 (m, 1H), 5.09−5.20 (m, 4H), 5.73−5.94 (m, 2H); ^{13}C NMR (75 MHz) δ 27.1, 38.8, 40.1, 42.8, 45.1, 67.2, 68.4, 74.0, 119.0, 119.1, 133.0, 133.3, 178.6; IR (film) 3419, 1732 cm^{-1}. Anal. Calcd for $C_{15}H_{26}O_4$: C, 66.64; H, 9.69. Found: C, 66.39; H, 9.83.

(2*S*)-4-Allyl-2,4-bis-(*O*-*tert*-butyldimethylsilyl)-6-heptene-1,2,4-triol (9). To a solution of **8** (424 mg, 1.57 mmol) in CH_2Cl_2 (5 mL) was added TBDMSOTf (1.13 mL, 3.2 equiv) followed by the addition of Et_3N (0.88 mL, 3.9 equiv) at 0 °C. The reaction was continued at 0 °C for 2 h, quenched by the addition of water, and extracted with AcOEt. The combined extracts were dried with Na_2SO_4 and concentrated to give a clear colorless oil, which, on CC (10:1 hexane/EtOAc), gave (2*S*)-4-allyl-1-*O*-pivaloyl-2,4-bis-(*O*-*tert*-butyldimethylsilyl)-6-heptene-1,2,4-triol (504 mg, 83%): $[\alpha]^{21}_D$ −9.98 (*c* 1.24, $CHCl_3$); ^{1}H NMR (300 MHz) δ 0.09 (s, 3H), 0.10 (s, 3H), 0.11 (s, 3H), 0.12 (s, 3H), 0.87 (s, 18H), 1.12 (s, 9H), 1.62−1.81 (m, 2H), 2.20−2.52 (m, 2H), 3.96−4.02 (m, 2H), 4.12−4.21 (m, 1H), 4.96−5.12 (m, 4H), 5.78−5.95 (m, 2H); ^{13}C NMR (75 MHz) δ −4.2, −4.0, −1.6, −1.4, 17.9, 18.5, 25.8, 26.0, 27.2, 38.7, 43.9, 44.6, 46.0, 67.4, 69.0, 76.7, 117.5, 117.6, 134.4, 134.9, 178.3; IR (film) 1734 cm^{-1}.

To a solution of (2*S*)-4-allyl-1-*O*-pivaloyl-2,4-bis-*O*-(*tert*-butyldimethylsilyl)-6-heptene-1,2,4-triol (550 mg, 1.10 mmol) in toluene (6 mL) was added dropwise DIBALH (1.01 M in toluene, 2.0 equiv) at −78 °C. The mixture was stirred at −78 °C for 1 h and quenched by the addition of EtOH−water mixture. The precipitates were removed by filtration through a Celite pad, which was rinsed with several portions of ethyl acetate. The combined organic solutions were dried with Na_2SO_4 and concentrated to give an oil, which, on CC (50:1 hexane/EtOAc), afforded **9** (430 mg, 94%): $[\alpha]^{24}_D$ +6.36 (*c* 1.44, $CHCl_3$); ^{1}H NMR (300 MHz) δ 0.09 (s, 6H), 0.88 (s, 9H), 0.89 (s, 9H), 0.12 (s, 6H), 1.71−1.78 (m, 2H), 1.97−2.07 (m, 1H), 2.19−2.43 (m, 4H), 3.42−3.52 (m, 1H), 3.64−3.74 (m, 1H), 3.98−4.09 (m, 1H), 4.98−5.12 (m, 4H), 5.75−5.94 (m, 2H); ^{13}C NMR (75 MHz) δ -4.3, −4.2, −1.5, −1.4, 18.0, 18.5, 25.8, 26.1, 43.9, 44.6, 46.0, 67.5, 70.0, 76.5, 117.8, 117.9, 134.2, 134.4; IR (film) 3467 cm^{-1}. Anal. Calcd for $C_{22}H_{46}O_3Si_2$: C, 63.71; H, 11.18. Found: C, 63.56; H, 11.08.

(2*S*)-4-Allyl-2,4-bis-*O*-(*tert*-butyldimethylsilyl)-2,4-dihydroxy-6-heptenal (1). A solution of 1-*O*-deacylated **9** (2.77 g, 6.67 mmol) in CH_2Cl_2 (30 mL) was mixed with Swern reagent prepared from $(COCl)_2$ (1.17 mL, 13.3 mmol) and DMSO (1.89 mL, 26.7 mmol) in CH_2Cl_2 (5 mL) at −78 °C. After 15 min of stirring, Et_3N (7.45 mL, 0.053 mol) was added to the mixture at −78 °C, and stirring was continued for additional 30 min at 0 °C. The reaction was quenched by the addition of water and extracted with AcOEt. The combined organic solutions were dried with Na_2SO_4 and concentrated to give an oil, which, on CC (50:1 hexane/EtOAc), afforded **1** (2.47 g, 90%): $[\alpha]^{27}_D$ −8.66 (*c* 1.12, $CHCl_3$); ^{1}H NMR (300 MHz) δ 0.06 (s, 3H), 0.08 (s, 3H), 0.11 (s, 3H), 0.13 (s, 3H), 0.88 (s, 9H), 0.91 (s, 9H), 1.74 (dd, 1H, J = 6.6, 14.6 Hz), 1.90 (dd, 1H, J = 4.9, 14.6 Hz), 2.28−2.44 (m, 2H), 4.27−4.32 (m, 1H), 5.00−5.12 (m, 2H), 5.76−5.93 (m, 1H), 9.52 (d, 1H, J = 2.5 Hz); ^{13}C NMR (75 MHz) δ −4.7, −4.2, −1.7, −1.6, 18.1, 18.5, 25.8, 25.9, 26.1, 26.2, 41.9, 44.8, 45.8, 75.1, 76.8, 118.0, 118.1, 134.0, 134.3, 202.4; IR (film) 1737, 1472 cm^{-1}. Anal. Calcd for $C_{22}H_{44}O_3Si_2$: C, 64.02; H, 10.74. Found: C, 63.80; H, 10.99.

(2*S*)-4-Allyl-2,4-*O*-(isopropylidene)-6-heptene-1,2,4-triol (10). To a solution of **8** (54 mg, 0.20 mmol) in THF (2 mL) were added 2,2-dimethoxypropane (0.05 mL, 2 equiv) and *p*-TsOH (2.5 mg, 0.07 equiv). The mixture was stirred at room temperature for 36 h and neutralized by the addition of Et_3N (0.002 mL, 0.07 equiv). The mixture was concentrated by a rotary evaporator to give an oil, which, on CC (30:1 hexane/EtOAc), afforded (2*S*)-4-allyl-2,4-*O*-(isopropylidene)-1-*O*-pivaloyl-6-heptene-1,2,4-triol (42 mg, 68%): ^{1}H NMR (300 MHz) δ 1.21 (s, 9H), 1.39 (s, 3H), 1.44 (s, 3H), 1.40−1.56 (m, 2H), 2.18−2.60 (m, 4H), 4.07 (m, 2H), 4.10−4.18 (m, 1H), 5.00−5.14 (m, 4H), 5.75−5.90 (m, 2H).

To a solution of the triol (583 mg, 1.88 mmol) in toluene (6.0 mL) was added dropwise DIBALH (1.01 M in toluene, 5.6 mL, 5.63 mmol) at −78 °C, and the mixture was stirred at −78 °C for 40 min. The reaction was quenched by the addition of water, and the solid was removed by filtration through a Celite pad. The combined organic solutions were dried with Na_2SO_4 and concentrated to give an oil, which, on CC (2:1 hexane/EtOAc), afforded **10** (400 mg, 94%): $[\alpha]^{24}_D$ +73.7 (*c* 0.867, $CHCl_3$); ^{1}H NMR δ 1.34 (dd, 1H, J = 3.0, 13.4 Hz), 1.40 (s, 3H), 1.49 (s, 3H), 1.53 (dd, 1H, J = 11.5, 13.4 Hz), 2.01−2.07 (b, 1H), 2.19−2.33 (m, 3H), 2.55−2.64 (m, 1H), 3.50−3.68 (m, 2H), 4.02−4.11 (m, 1H), 5.00−5.15 (m, 4H), 5.73−5.91 (m, 2H); ^{13}C NMR (75 MHz) δ 25.7, 31.4, 32.6, 42.6, 45.9, 66.1, 66.4, 74.0, 98.7, 118.1, 118.2, 133.6, 133.8; IR (film) 3447 cm^{-1}. Anal. Calcd for $C_{13}H_{22}O_3$: C, 68.99; H, 9.80. Found: C, 68.75; H, 9.90.

(1*R*,3*R*,5*S*)-3-Allyl-3,5-bis-(*tert*-butyldimethylsilyloxy)-7-aza-8-oxabicyclo[4.3.0]non-6-en (11). To a solution of the aldehyde **1** (385 mg, 0.94 mmol) in EtOH (5 mL) were added NH_2OH−HCl (457 mg, 6.60 mmol) and Et_3N (0.92 mL, 6.60 mmol) at 0 °C, and the mixture was stirred at room temperature for 14 h. The reaction was diluted with water and extracted with AcOEt. The combined extracts were dried with Na_2SO_4 and concentrated to afford an oil, which, on CC (50:1 hexane/EtOAc), gave (2*R*)-4-allyl-2,4-bis-(*O*-*tert*-butyldimethylsilyl)-2,4-dihydroxy-6-heptenal oxime (381 mg, 95%). To a stirred solution of this aldoxime (381 mg, 0.90 mmol) in CH_2Cl_2 (8 mL) was added an aqueous NaOCl solution (1.5 mL), and the mixture was stirred at room temperature for 1.5 h. The reaction was diluted with water and extracted with AcOEt. The combined extracts were dried with Na_2SO_4 and concentrated to give an oil, which, on CC (125:1 hexane/EtOAc), gave **11** (more polar, 267 mg, 72%) and **12** (less polar, 20 mg, 5%). Data for the major isomer **11**: $[\alpha]^{31}_D$ −67.4 (c 1.00, $CHCl_3$); ^{1}H NMR (500 MHz) δ 0.09 (s, 6H), 0.13 (s, 3H), 0.14 (s, 3H), 0.16 (s, 3H), 0.88 (s, 9H), 0.91 (s, 9H), 1.49 (dd, 1H, J = 12.2, 13.1 Hz), 1.79 (dd, 1H, J = 11.2, 12.8 Hz), 1.91 (ddd, 1H, J = 2.4, 6.4, 13.1 Hz), 2.05 (ddd, 1H, J = 2.4, 6.1, 12.8 Hz), 2.31−2.42 (m, 2H), 3.55−3.63 (m, 1H), 3.83 (dd, 1H, J = 7.6, 10.3 Hz), 4.53 (dd, 1H, J = 7.9, 10.3 Hz), 4.85 (ddd, 1H, J = 0.9, 6.1, 11.2 Hz), 5.05−5.11 (m, 2H), 5.67−5.77 (m, 1H); ^{13}C NMR (75 MHz) δ −9.7, −9.2, −6.33, −6.31, 13.9, 14.0, 21.3, 21.4, 37.6, 40.7, 42.6, 43.2, 61.3, 69.1, 72.7, 114.5, 128.4, 157.2; IR (film) 2857, 1471 cm^{-1}. Anal. Calcd for $C_{22}H_{43}NO_3Si_2$: C, 62.06; H, 10.18; N, 3.29. Found: C, 61.87; H, 10.39; N, 3.10.

Data for the minor (1*S*,3*R*,5*S*)-isomer (**12**): $[\alpha]^{31}_D$ +2.4 (*c* 2.21, $CHCl_3$); ^{1}H NMR (500 MHz) δ 0.05 (s, 6H), 0.06 (s, 3H), 0.11 (s, 3H), 0.84 (s, 9H), 0.88 (s, 9H), 1.47 (dd, 1H, J = 12.2, 12.8 Hz), 1.78 (dd, 1H, J = 3.9, 14.0 Hz), 2.14 (dt, 1H, J = 2.1, 14.0 Hz), 2.20 (ddd, 1H , J = 2.1, 5.8, 12.2 Hz), 2.46−2.51 (m, 1H), 2.76−2.82 (m, 1H), 3.41−3.49 (m, 1H), 3.92 (dd, 1H, J = 7.9, 8.2 Hz), 4.44 (dd, 1H, J = 8.2, 10.6 Hz), 4.78 (dd, 1H, J = 2.1, 3.9 Hz), 5.04−5.10 (m, 2H), 5.91−5.99 (m, 1H); ^{13}C NMR (75 MHz) δ −5.1, −4.8, −1.8, −1.7, 17.9, 18.1, 25.6, 25.8, 43.2, 43.7, 44.7, 46.8, 63.4, 73.9, 74.5, 117.3, 134.8, 159.7; IR (film) 2857, 1472 cm^{-1}. Anal. Calcd for $C_{22}H_{43}NO_3Si_2$: C, 62.06; H, 10.18; N, 3.29. Found: C, 61.90; H, 10.22; N, 3.27.

(1*R*,3*S*,5*S*,6*S*)-3-Allyl-7-benzyl-3,5-bis-(*tert*-butyldimethylsilyloxy)-7-aza-8-oxabicyclo[4.3.0]nonane (18). To a solution of the aldehyde **1** (970 mg, 2.35 mmol) in benzene (20 mL) was added *N*-benzylhydroxylamine (435 mg, 3.53 mmol) at 0 °C. The mixture was stirred at 50 °C for 18 h. The reaction was diluted with water and extracted with AcOEt. The combined extracts were dried with Na_2SO_4 and concentrated to give an oil, which, on CC (50:1 hexane/EtOAc), afforded **19** (253 mg, 21%), **18** (537 mg, 44%), and **20** (107 mg,

8.8%), which were eluted in this order. Physical data for **18**: $[\alpha]^{28}_{D}$ −21.2 (*c* 1.56, $CHCl_3$); ^{1}H NMR (500 MHz) δ 0.09 (s, 3H), 0.10 (s, 6H), 0.12 (s, 3H), 0.88 (s, 9H), 0.89 (s, 9H), 1.49−1.57 (m, 2H), 1.61 (dd, 1H, J = 12.5, 13.4 Hz), 1.99 (dd, 1H, J = 4.6, 13.4 Hz), 2.30−2.32 (m, 2H), 2.88 (dd, 1H, J = 8.2, 9.5 Hz), 2.97−3.05 (m, 1H), 3.44 (dd, 1H, J = 5.8, 8.5 Hz), 3.70−3.76 (m, 1H), 3.88 & 4.14 (ABq, 2H, J = 14.3 Hz), 4.12 (1H, dd, J = 7.6, 8.5 Hz), 5.08−5.13 (m, 2H), 5.79−5.88 (m, 1H), 7.22−7.42 (m, 5H); ^{13}C NMR (75 MHz) δ −4.3, −4.1, −2.0, −1.9, 18.0, 18.2, 25.9, 25.9, 37.4, 39.3, 45.6, 48.4, 61.9, 70.4, 70.5, 72.2, 75.5, 118.4, 126.9, 128.2, 128.7, 133.9, 138.3; IR (film) 2858, 1472 cm^{-1}. Anal. Calcd for $C_{29}H_{51}NO_3Si_2$: C, 67.26; H, 9.93; N, 2.70. Found: C, 66.95; H, 10.13; N, 3.00.

Physical data for (1*S*,3*S*,5*S*,6*R*)-isomer (**19**): $[\alpha]^{28}_{D}$ −61.4 (*c* 1.08, $CHCl_3$); ^{1}H NMR (500 MHz) δ 0.10 (s, 3H), 0.12 (s, 9H), 0.88 (s, 9H), 0.89 (s, 9H), 1.58 (dd, 1H, J = 9.1, 13.7 Hz), 1.71−1.81 (m, 2H), 1.89 (dd, 1H, J = 3.9, 13.7 Hz), 2.31−2.35 (m, 1H), 2.41−2.46 (m, 1H), 2.74−2.83 (m, 2H), 3.72 (dd, 1H, J = 5.2, 7.3 Hz), 3.93 & 4.02 (ABq, 2H, J = 14.0 Hz), 4.04−4.08 (m, 2H), 5.03−5.12 (m, 2H), 5.84−5.93 (m, 1H), 7.23−7.42 (m, 5H); ^{13}C NMR (75 MHz) δ −4.5, −4.4, −1.8, −1.7, 18.0, 18.3, 25.9, 25.9, 26.0, 36.4, 39.8, 43.7, 47.6, 61.9, 68.6, 70.7, 71.4, 75.7, 117.6, 127.0, 128.2, 128.2, 128.6, 128.7, 134.6, 138.1; IR (film) 2857, 1472 cm^{-1}.

Physical data for (1*S*,3*R*,5*S*,6*S*)-isomer (**20**): $[\alpha]^{28}_{D}$ −50.2 (*c* 1.33, $CHCl_3$); ^{1}H NMR (500 MHz) δ 0.10 (s, 3H), 0.11 (s, 3H), 0.12 (s, 3H), 0.14 (s, 3H), 0.88 (s, 9H), 0.89 (s, 9H), 1.39 (dd, 1H, J = 12.8, 15.8 Hz), 1.45 (dd, 1H, J = 10.6, 13.4 Hz), 1.66 (dt, 1H, J = 2.1, 12.8 Hz), 1.90 (ddd, 1H, J = 2.1, 4.3, 13.4 Hz), 2.27−2.35 (m, 2H), 2.39−2.44 (m, 1H), 2.69−2.79 (m, 1H), 3.53 (dd, 1H, J = 6.4, 10.9 Hz), 3.78 & 4.48 (ABq, 2H, J = 14.2 Hz), 3.90 (t, 1H, J = 6.4 Hz), 4.16−4.22 (m, 1H), 5.05−5.13 (m, 2H), 5.76−5.84 (m, 1H), 7.22−7.44 (m, 5H); ^{13}C NMR (75 MHz) δ −4.3, −4.2, −1.8, −1.7, 18.0, 18.4, 25.9, 26.0, 37.5, 42.5, 46.7, 47.8, 64.7, 68.9, 71.3, 75.5, 77.7, 118.5, 126.8, 128.2, 128.9, 133.7, 138.4; IR (film) 2857, 1472 cm^{-1}.

(6*S*)-4-Allyl-4,6-bis-(*tert*-butyldimethylsiloxy)-8-trimethylsilyl-1-octen-7-yne (24). To a solution of aldehyde **1** (800 mg, 1.93 mmol) in CH_2Cl_2 were successively added CBr_4 (1.92 g, 5.79 mmol), PPh_3 (1.52 g, 5.79 mmol), and Zn (368 mg, 5.79 mmol) at 0 °C. The mixture was stirred at 0 °C to room temperature for 13 h. The reaction was quenched by the addition of water and filtered through a Celite pad, and the filter cake was thoroughly rinsed with AcOEt. The combined organic solutions were dried with Na_2SO_4 and concentrated to give an oil, which, on CC (hexane), afforded (3*S*)-5-allyl-1,1-dibromo-3,5-bis-(*tert*-butyldimethylsiloxy)-1,7-octadiene (940 mg, 86%): $[\alpha]^{24}_{D}$ −12.3 (*c* 1.70, $CHCl_3$); ^{1}H NMR (300 MHz) δ 0.10 (s, 3H), 0.14 (s, 3H), 0.15 (s, 3H), 0.16 (s, 3H), 0.87 (s, 9H), 0.89 (s, 9H), 1.65 (dd, 1H, J = 4.9, 14.3 Hz), 1.77 (dd, 1H, J = 7.4, 14.3 Hz), 2.23−2.38 (m, 3H), 2.42−2.50 (m, 1H), 4.58 (ddd, 1H, J = 4.9, 7.4, 8.5 Hz), 5.00−5.11 (m 2H), 5.81−5.96 (m, 1H), 6.38 (d, 1H, J = 8.5 Hz); ^{13}C NMR (75 MHz) δ −4.5, −3.9, −1.5, −1.4, 17.9, 18.5, 25.8, 26.1, 45.0, 45.7, 45.9, 70.5, 76.6, 88.5, 117.6, 117.7, 134.5, 134.8, 142.5; IR (film) 1639 cm^{-1}.

To a solution of this 1,1-dibromo olefin (940 mg, 1.65 mmol) in THF (20 mL) was added *n*-BuLi (1.5 M in hexane, 2.75 mL, 4.13 mmol) at −78 °C. The reaction mixture was stirred for 1 h before TMSCl (0.53 mL, 4.2 mmol) was added to the mixture. The mixture was stirred for 30 min at that temperature, quenched by the addition of water, and extracted with AcOEt. The combined extracts were dried with Na_2SO_4 and concentrated to give an oil, which, on CC (hexane), afforded **24** (540 mg, 69%): $[\alpha]^{25}_{D}$ −27.1 (*c* 0.80, $CHCl_3$); ^{1}H NMR (300 MHz) δ 0.11 (s, 3H), 0.12 (s, 3H), 0.14 (s, 9H), 0.15 (s, 3H), 0.16 (s, 3H), 0.88 (s, 18H), 1.92 (d, 2H, J = 6.0 Hz), 2.29−2.46 (m, 4H), 4.64 (t, 1H, J = 6.0 Hz), 4.98−5.09 (m, 2H), 5.79−5.95 (m, 1H); ^{13}C NMR (75 MHz) δ -4.7, −4.0, −1.7, −0.3, −0.2, 18.1, 18.5, 25.8, 26.0, 44.8, 45.0, 47.8, 60.0, 89.0, 108.7, 117.4, 117.6, 134.6, 134.8; IR (film) 2172 cm^{-1}.

(5*R*)-4-Allyl-4,5-isopropylidenedioxy-1-hepten-6-yne (35). The aldehyde **4** (3.55 g, 16.7 mmol) was subjected to olefination reaction to give a geminal dibromo olefin (5.50 g, 88%) in the same way as that described for **1** → **24**. (3*R*)-1,1-Dibromo-4-allyl-3,4-isopropylidenedioxy-1,6-heptadiene: $[\alpha]^{23}_{D}$ −31.2 (*c* 1.00, $CHCl_3$); ^{1}H NMR (300 MHz) δ 1.38 (s, 3H), 1.48 (s, 3H), 2.16−2.18 (m, 1H), 2.22−2.33 (m, 1H), 2.39−2.56 (m, 2H), 4.59 (d, 1H, J = 8.8 Hz), 5.06−5.22 (m, 2H), 5.78−5.94 (d, 1H, J = 8.8 Hz); ^{13}C NMR (75 MHz) δ 26.8, 28.3, 39.5, 39.8, 80.8, 84.3, 94.0, 108.6, 118.6, 118.8, 132.5, 133.0, 133.5; IR (film) 1738 cm^{-1}.

This geminal dibromo olefin (5.00 g, 13.6 mmol) was also treated in the similar way as that described for **1** → **24** employing water for quenching of the reaction in place of the trimethylchlorosilane to give **35** (1.60 g, 57%). **35**: $[\alpha]^{25}_{D}$ −31.6 (*c* 1.50, $CHCl_3$); ^{1}H NMR (300 MHz) δ 1.36 (s, 3H), 1.51 (s, 3H), 2.30−2.50 (m, 1H), 2.55−2.64 (m, 1H), 2.56 (d, 1H, J = 2.2 Hz), 4.61 (d, 1H, J = 2.2 Hz), 5.09−5.20 (m, 2H), 5.75−6.00 (m, 1H); ^{13}C NMR (75 MHz) δ 26.6, 27.8, 39.6, 39.7, 71.4, 76.3, 78.3, 83.4, 108.9, 118.1, 118.4, 132.5, 133.1; IR (film) 3313 (shoulder), 3251, 2127, 1640 cm^{-1}. Anal. Calcd for $C_{13}H_{18}O_2$: C, 75.69; H, 8.80. Found: C, 75.51; H, 9.01.

(5*R*)-4-Allyl-4,5-bis-(*tert*-butyldimethylsilyloxy)-1-hepten-6-yne (36). To a solution of **35** (200 mg, 0.969 mmol) in 90% AcOH/MeOH (1:1, 4 mL) was added *p*-toluenesulfonic acid hydrate (18 mg, 0.0969 mmol), and the mixture was stirred at 80 °C for 14 h. After the reaction was quenched by the addition of saturated aqueous $NaHCO_3$ solution, the mixture was extracted with several portions of EtOAc. The combined EtOAc solutions were dried ($MgSO_4$) and concentrated to give an oil, which, on CC (hexane), afforded deprotected diol (145 mg, 90%). (5*R*)-4-Allyl-4,5-dihydroxy-1-hepten-6-yne: $[\alpha]^{25}_{D}$ +4.90 (*c* 0.960, $CHCl_3$); ^{1}H NMR (300 MHz) δ 2.33−2.43 (m, 3H), 2.50−2.59 (m, 1H), 2.54 (d, 1H, J = 2.2 Hz), 4.28 (d, 1H, J = 2.2 Hz), 5.12−5.23 (m, 2H), 5.81−6.00 (m, 1H); ^{13}C NMR (75 MHz) δ 39.6, 39.7, 75.3, 75.5, 81.7, 119.2, 119.3, 132.8, 132.9; IR (film) 3421, 3304, 2116 (very weak), 1726 cm^{-1}.

To a solution of the diol (320 mg, 1.92 mmol) in CH_2Cl_2 (5 mL) was added TBDMSOTf (1.77 mL, 4.0 equiv) followed by the addition of Et_3N (1.34 mL, 5 equiv) at 0 °C. The reaction was continued at 0 °C to room temperature for 16 h, quenched by the addition of saturated aqueous $NaHCO_3$ solution, and extracted with CH_2Cl_2 and successively with several portions of AcOEt. The combined organic extracts were dried with $MgSO_4$ and concentrated to give a colorless oil, which, on CC (hexane), afforded **36** (720 mg, 95%). **36**: $[\alpha]^{25}_{D}$ −5.91 (*c* 1.10, $CHCl_3$); ^{1}H NMR (300 MHz) δ 0.21 (s, 3H), 0.23 (s, 3H), 0.25 (s, 3H), 0.27 (s, 3H), 0.97 (s, 9H), 1.00 (s, 9H), 2.37−2.68 (m, 4H), 2.48 (d, 1H, J = 2.2 Hz), 4.30 (d, 1H, J = 2.2 Hz), 5.10−5.22 (m, 2H), 5.90−6.08 (m, 1H); ^{13}C NMR (75 MHz) δ −5.0, −4.1, −2.9, −1.8, 18.2, 18.7, 25.7, 26.0, 40.8, 41.3, 68.8, 74.6, 79.4, 83.8, 117.4, 117.9, 133.9, 134.4; IR (film) 3310, 2154, 1640 cm^{-1}. Anal. Calcd for $C_{22}H_{42}O_2Si_2$: C, 72.07; H, 11.55. Found: C, 71.86; H, 11.63.

(5*R*)-4-Allyl-4,5-bis(*tert*-butyldimethylsilyloxy)-7-trimethylsilyl-1-hepten-6-yne (26). To a solution of **36** (450 mg, 1.13 mmol) in THF (10 mL) was added a solution of butyllithium (1.50 M in hexane, 1.13 mL, 1.71 mmol) at 0 °C, and the mixture was stirred at 0 °C for 15 min. To this solution was added TMSCl (0.29 mL, 2.26 mmol) at 0 °C, and the mixture was stirred at 0 °C for 30 min followed by the addition of AcOEt and saturated aqueous $NaHCO_3$ solution. The mixture was extracted with several portions of EtOAc, and the combined AcOEt solutions were dried ($MgSO_4$) and concentrated to give an oil, which, on CC (hexane), afforded **26** (403 mg, 89%): $[\alpha]^{26}_{D}$ −11.7 (*c* 0.93, $CHCl_3$); ^{1}H NMR (300 MHz) δ 0.11 (s, 3H), 0.13 (s, 3H), 0.15 (s, 9H), 0.16 (s, 3H), 0.17 (s, 3H), 0.89 (s, 9H), 0.91 (s, 9H), 2.24−2.58 (m, 4H), 4.18 (s, 1H), 5.01−5.10 (m, 2H), 5.80−5.97 (m, 1H); ^{13}C NMR (75 MHz) δ −4.9, −4.0, −1.8, −1.6, −0.3, 18.2, 18.7, 25.9, 26.0, 40.9, 41.4, 69.2, 79.4, 91.0, 106.1, 117.2, 117.7, 134.1, 134.6; IR (film) 2175 cm^{-1}. Anal. Calcd for $C_{25}H_{50}O_2Si_3$: C, 64.31; H, 10.79. Found: C, 64.17; H, 10.99.

(1*R*,3*S*,5*S*)-3-Allyl-3,5-bis-(*tert*-butyldimethylsilyloxy)-7-(trimethylsilyl)bicyclo[4.3.0]non-6-en-8-one (28). To a solution of **24** (190 mg, 0.36 mmol) in CH_2Cl_2 (6 mL) was added $Co_2(CO)_8$ (149 mg, 0.43 mmol) at 0 °C, and the mixture was stirred at 0 °C to room temperature for 5 h. The mixture was concentrated by a rotary evaporator to give an oil, which on

CC (hexane), afforded cobalt−enyne complex (244 mg, 83%). A solution of this complex (93 mg, 0.12 mmol) in acetonitrile (10 mL) was heated at 75 °C for 18 h. Purple precipitates were removed through a short silica gel pad, and the filtrate was concentrated to give an oil, which, on CC (30:1 hexane/EtOAc), afforded **28** (less polar, 37 mg, 59%) and **29** (more polar, 4 mg, 7%). Physical data for the major isomer **28**: $[\alpha]^{25}_D$ +28.4 (*c* 1.70, $CHCl_3$); ^{1}H NMR (500 MHz) δ 0.00 (s, 3H), 0.03 (s, 3H), 0.06 (s, 3H), 0.11 (s, 3H), 0.24 (s, 9H), 0.83 (s, 9H), 0.88 (s, 9H), 1.14 (dd, 1H, J = 11.9, 12.5 Hz), 1.68 (dd, 1H, J = 3.0, 13.7 Hz), 1.91 (dd, 1H, J = 1.8, 18.9 Hz), 2.15 (dt, 1H, J = 2.7, 13.7 Hz), 2.32 (ddd, 1H, J = 2.7, 4.8, 12.5 Hz), 2.48−2.53 (m, 1H), 2.53 (dd, 1H, J = 6.7, 18.9 Hz), 2.93 (dd, 1H, J = 9.1, 14.6 Hz), 3.05−3.11 (m, 1H), 4.98 (t, 1H, J = 3.0 Hz), 5.04−5.11 (m,2H), 5.91−6.01 (m, 1H); ^{13}C NMR (75 MHz) δ −4.3, −1.7, −0.4, 1.0, 18.0, 18.1, 25.7, 25.8, 36.1, 42.3, 45.6, 46.9, 48.1, 66.9, 74.3, 117.1, 135.3, 136.1, 188.7, 213.6; IR (film) 1699 cm^{-1}. Anal. Calcd for $C_{27}H_{52}O_3Si_3$: C, 63.72; H, 10.30. Found: C, 63.51; H, 10.19.

Physical data for the minor (1*S*,3*S*,5*S*)-isomer (**29**): $[\alpha]^{20}_D$ +8.46 (*c* 0.78, $CHCl_3$); ^{1}H NMR (500 MHz) δ 0.14 (s, 6H), 0.16 (s, 6H), 0.24 (s, 9H), 0.92 (s, 9H), 0.94 (s, 9H), 1.18 (dd, 1H, J = 12.8, 13.4 Hz), 1.55 (dd, 1H, J = 11.9, 12.2 Hz), 1.88 (dd, 1H, J = 1.8, 18.3 Hz), 2.02 (ddd, 1H, J = 2.7, 4.6, 13.4 Hz), 2.15 (ddd, 1H, J = 2.7, 4.9, 12.2 Hz), 2.21−2.27 (m, 1H), 2.39−2.44 (m, 1H), 2.51 (dd, 1H, J = 7.0, 18.3 Hz), 2.97−3.04 (m, 1H), 4.97 (dd, 1H, J = 4.9, 11.9 Hz), 5.03−5.12 (m, 2H), 5.70−5.79 (m, 1H); ^{13}C NMR (75 MHz) δ −4.0, −3.0, −1.7, −1.6, 1.4, 1.5, 18.5, 18.8, 25.7, 26.7, 38.4, 41.5, 47.1, 47.5, 49.3, 72.0, 76.8, 118, 133, 192, 212; IR (film) 1699 cm^{-1}.

(1*S*,2*R*,3*R*,5*R*)-2,3-Bis(*tert*-butyldimethylsilyloxy)-3-propylbicyclo[3.3.0]octan-7-one (38). To a solution of **32** (5 mg, 0.01 mmol: containing **33** in a 10:1 ratio) in EtOH (1 mL), placed in a hydrogenation vessel, was added a spatula tip of 10% Pd−C. The reaction vessel was flushed with hydrogen gas, and the mixture was stirred vigorously under a positive pressure of hydrogen for 16 h. The mixture was filtered through a Celite pad, and the filtrate was dried over Na_2SO_4 and concentrated to give an oil, which, on CC (30:1 hexane/EtOAc), afforded **38** + **39** (4.2 mg, 97%). The following list of physical data for the major isomer **38** was read from those recorded for the mixture: ^{1}H NMR (500 MHz) δ 0.04 (s, 3H), 0.06 (s, 6H), 0.08 (s, 3H), 0.85 (s, 9H), 0.88 (s, 9H), 0.90−0.92 (m, 3H), 1.20−1.62 (m, 5H), 2.12 (ddd, 1H, J = 1.2, 4.9, 19 Hz), 2.21 (dd, 1H, J = 8.5, 13.1 Hz), 2.29 (dd, 1H, J = 1.2, 16 Hz), 2.48−2.56 (m, 3H), 2.65−2.73 (m, 1H), 3.75 (d, 1H, J = 5.5 Hz).

(1*S*,2*R*,3*S*,5*R*)-3-Allyl-2,3-(isopropylidenedioxy)bicyclo-[3.3.0]octan-7-one (40). To a mixture of $[(Ph_3P)CuH]_6$ (191 mg, 0.097 mmol), weighted under nitrogen atmosphere, and **34** (30 mg, 0.09 mmol) was added benzene containing water, and the resulting red solution was stirred at room temperature for 14 h. The mixture was opened to air, and stirring was continued for additional 2 h. The mixture was filtered through a Celite pad and the filtrate was concentrated to give an oil, which, on CC (20:1 hexane/EtOAc), afforded **40** (21 mg, 91%): ^{1}H NMR (300 MHz) δ 1.31 (dd, 1H, J = 11.6, 14.6 Hz), 1.39 (s, 3H), 1.46 (s, 3H), 1.86 (dd, 1H, J = 11.6, 19.5 Hz), 2.14 (ddd, 1H, J = 0.9, 7.6, 14.6 Hz), 2.18 (d, 1H, J = 20 Hz), 2.34−2.46 (m, 3H), 2.61−2.65 (m, 1H), 2.74 (td, 1H, J = 7.0, 10.3 Hz), 3.06−3.14 (m, 1H), 4.29 (s, 1H), 5.10−5.16 (m, 2H), 5.80−5.88 (m, 1H); ^{13}C NMR (75 MHz) δ 27.5, 28.1, 38.1, 38.8, 42.8, 43.5, 44.7, 47.3, 89.1, 93.6, 110.3, 118.7, 133.3, 218.6.

(1*S*,2*R*,3*S*,5*R*)-2,3-Dihydroxy-3-propylbicyclo[3.3.0]-octan-7-one (42). To a solution of **34** (78 mg, 0.25 mmol) in EtOH (2 mL), placed in a hydrogenation vessel, was added a spatula tip of 10% Pd−C. The reaction vessel was flushed with hydrogen gas, and the mixture was vigorously stirred under a positive pressure of hydrogen for 2 days. The mixture was filtered through a Celite pad, and the filtrate was dried over Na_2SO_4 and concentrated to give an oil, which, on CC (30:1 hexane/EtOAc), afforded hydrogenated product (9.3 mg, 16%). To a solution of the product (9.3 mg, 0.04 mmol) in MeOH (2 mL) was added 2 N HCl (1 mL) at room temperature. The reaction was continued at room temperature for 14 h, quenched by the addition of $NaHCO_3$, and extracted with AcOEt. The combined extracts were dried with Na_2SO_4 and concentrated to give a clear colorless oil, which, on CC (EtOAc), gave **42** (3.0 mg, 28%): ^{1}H NMR (500 MHz) δ 0.96 (t, 3H), 1.35−1.66 (m, 5H), 1.76 (br, 2H), 2.16−2.26 (m, 2H), 2.34−2.43 (m, 1H), 2.49−2.62 (m, 2H), 2.67−2.77 (m, 1H), 2.90−3.01 (m, 1H), 3.75 (m, 1H); ^{13}C NMR (75 MHz) δ 14.7, 16.9, 35.2, 37.1, 43.2, 43.8, 46.4, 47.0, 84.7, 85.7, 220.6.

(1*S*,2*R*,3*R*,5*R*)-2,3-Dihydroxy-3-propylbicyclo[3.3.0]-octan-7-one (41). To a solution of the mixture of **38** and **39** (4.1 mg, 0.0096 mmol) in THF (2 mL) was added TBAF (1 mL, 1.0 M in THF) at room temperature. The reaction was continued at room temperature for 12 h, quenched by the addition of water, and extracted with AcOEt. The combined extracts were dried with Na_2SO_4 and concentrated to give a clear colorless oil, which, on CC (EtOAc), gave the product (1.5 mg, 79%) as a mixture of diastereomeric diols **41** and **42**. The following list of physical data for the major isomer **41** was read from those recorded for the mixture: ^{1}H NMR (500 MHz) δ 0.95 (t, 3H), 1.30−1.50 (m, 5H), 1.90−1.96 (m, 1H), 2.01 (br, 1H), 2.13 (br, 1H), 2.21−2.26 (dd, J = 8.5, 14.4 Hz, 1H), 2.27−2.33 (m, 1H), 2.54−2.60 (dd, J = 10.1, 19.5 Hz, 2H), 2.71−2.78 (m, 1H), 2.88−2.97 (m, 1H), 3.51 (d, J = 7.3 Hz, 1H).

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Supporting Information Available: Copies of ^{1}H and/or ^{13}C NMR spectra for compounds **1**−**4**, **11**−**16**, **18**−**23**, **28**−**32**, **34**, and **37**−**42**. Synthetic procedures and physical data for compounds **2**−**4**, **13**−**16**, **21**−**23**, **25**, **27**, and **30**−**34**. This material is available free of charge via the Internet at http://pubs.acs.org.

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