Desymmetrization of Cyclohexadienylsilanes. Regio-, Diastereo-, and Enantioselective Access to Sugar Mimics

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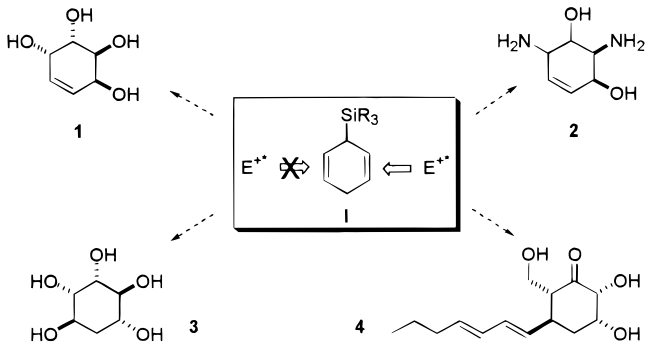
Desymmetrization of cyclohexadienylsilanes available from Birch reduction of the corresponding arylsilanes is efficiently carried out using Sharpless asymmetric dihydroxylation and aminohydroxylation. Complete diastereocontrol and reasonable enantiocontrol have been attained during the preparation of the desired diols. An excellent regiocontrol has also been observed during aminohydroxylation of dienylsilanol **6b**. The resulting diol **8** and hydroxycarbamate **27** have then been elaborated further, offering a straightforward access to various types of cyclitols, aminocyclitols, carbasugars, as well as the antibiotic palitantine **4**. The complete functionalization of the original arylsilanes **5** is thus typically achieved in fewer than eight steps with high stereoselectivities and excellent overall yield.

Introduction

Cyclitols and structurally related compounds have recently received a high degree of attention due to their wide range of biological activities.[1] Their ability to mimic the parent saccharides with respect to polarity, structure, and conformation as well as their inertness toward glycosidase-induced hydrolysis make them potential candidates as inhibitors of glycosidases, oligosaccharide-processing enzymes.[2] Small carbohydrate mimics can also bind to protein and consequently inhibit the recognition between cell surface carbohydrates and protein receptors, a crucial step in viral and bacterial infection processes.[3] These sugar mimics have recently been used as powerful probes for studying the biological function of oligosaccharides present on the cell membrane and have a considerable potential as anticancer, antidiabetic, and anti-HIV agents. This has made the discovery and the total synthesis of such inhibitors a matter of considerable interest for synthetic organic chemists.[4] Among the various synthetic strategies that have been reported, the partial oxidation of arenes into substituted cyclohexadienes is of particular interest since the six-membered ring thus obtained has resident functionalities ready for further elaboration.[5] We have recently devised a closely related approach that involves the desymmetrization of cyclohexadienylsilanes **I**, readily available through the "controlled" reduction (Birch) of the corresponding arylsilanes.[6] To our surprise, functionalization of such dienylsilanes had never been addressed before (Scheme 1).[7] Considering the double allylsilane structure of our dienylsilanes **I**, we reasoned that they could be elaborated in the same way as simple allylsilanes. It was first decided to submit substrates such as **I** to the Sharpless asymmetric dihydroxylation[8] and aminohydroxylation[9] reagents, speculating that these electrophilic reagents (E^{+}*) would be able to differentiate the two enantiotopic double bonds, affording in one step homochiral synthons with three new chiral centers. We also anticipated that *the silicon group would control the diastereofacial selec-*

Scheme 1



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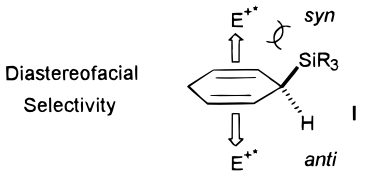
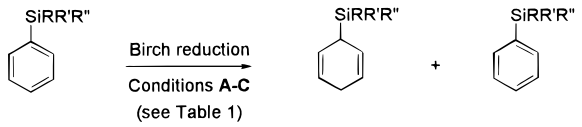


Figure 1.

Scheme 2



5a, R = R' = Me; R" = OEt — **6a**, R = R' = Me; R" = OEt — **7**

5b, R = R' = Me; R" = Cl — **6b**, R = R' = Me; R" = OH

5c, R = R' = Me; R" = *t*-Bu — **6c**, R = R' = Me; R" = *t*-Bu

5d, R = Me; R' = c-C_6H_{11}; R" = Cl — **6d**, R = Me; R' = c-C_6H_{11}; R" = OH

5e, R = R' = *i*-Pr; R" = Cl — **6e**, R = R' = *i*-Pr; R" = OH

5f, R = R' = R" = Me — **6f**, R = R' = R" = Me

tivity of the electrophilic processes, the electrophiles approaching the π-system anti relative to the SiR_3 group (Figure 1).[10] The silicon group, which is a key element in our strategy, could then be converted into a hydroxy group,[11] with *retention of configuration* at the carbon center, allowing the incorporation of a further hydroxy group onto the cyclohexane ring. The remaining double bond would then be elaborated further into the desired sugar mimics. We report here a full account of our studies on the desymmetrization of dienylsilanes and the versatility of such precursors in the total synthesis of cyclitols, such as conduritols **1**, conduramine **2**, deoxyinositols **3**, and the antibiotic palitantine **4** (Scheme 1).

Discussion

Birch Reduction of Arylsilanes 5. Cyclohexadienylsilanes **6** have been prepared through Birch reduction of the corresponding arylsilanes **5**.[12] We first extended the method originally reported by Eaborn[13] to arylsilanes possessing a silicon group that could be oxidized into a OH group through the Tamao−Kumada−Fleming oxidation.[11] The mildest oxidation conditions are generally observed with alkoxy- and fluorosilanes. We thus started our investigations by treating the phenyldimethylethoxysilane **5a** with Li and NH_3 in THF (Scheme 2). This led to a 1:1 mixture of the desired dienylethoxysilane **6a** along with the corresponding dienylsilanol **6b** in 80% overall yield after chromatography (entry 1, Table 1). The instability of the alkoxy group in the Birch reaction conditions prompted us to turn our attention to the preparation of the more stable silanol **6b** starting from the commercially available phenyldimethylchlorosilane **5b**.[14] We were pleased to find that the use of powdered lithium and neat NH_3 provided **6b** in 77% optimized yield (entry 2, Table 1). The quantity of disiloxane (10%) that is always formed upon hydrolysis may be minimized by diluting the medium prior to addition of water. The disiloxane is then easily discarded by distillation. It is worthy of note that the Birch reduction of **5b** was carried out without addition of a proton donor (usually an alcohol). As a comparison, **5c** having no chlorine substituent at the silicon center afforded trace amount of the diene **6c** in the same conditions (entry 3, Table 1). We assume that an aminosilane ($PhMe_2SiNH_2$) or a disilazane $(PhMe_2Si)_2NH$)[15] is formed upon addition of the chlorosilane onto ammonia leading to the formation of NH_4Cl,[16] the reduction then taking place on the aminosilane and not on the chlorosilane. The proton source would then be NH_4Cl or the proton of the disilazane. When increasing the steric bulk around silicon (entries 4 and 5, Table 1), we observed a low conversion of the substrate into the diene, supporting the occurrence of an aminosilane intermediate whose formation is slowed by steric hindrance. The absence in these cases of disiloxane after workup is also noteworthy and may be explained by invoking again the steric demand around silicon.

Table 1. Birch Reduction of Arylsilanes 5a−f (Scheme 2)

entry	substrate	products	condns[a]	ratio[b]	yield (%)
1	**5a**	**6a/6b**	A	50:50	80
2	**5b**	**6b/7b**	A	**100:0**	77
3	**5c**	**6c/5c**	A	2:98	88
4	**5d**	**6d/7d**	A	60:40	92
5	**5e**	**6e/7e**	A	30:70	89
6	**5c**	**6c/5c**	B	**100:0**	94
7	**5c**	**6c/5c**	C	**100:0**	87
8	**5f**	**6f/5f**	C	**100:0**	90

[a] Conditions: (A) Li, NH_3, −78 °C, 1 h; (B) Li, NH_3−THF, *t*-BuOH (96 equiv), −78 °C, 2.5h; (C) Al anode−stainless steel grid cathode, THF−HMPA 8:2, *t*-BuOH (4 equiv), LiCl, constant current (0.1 A), rt. [b] Estimated ratio from ^{1}H NMR of the crude mixture obtained after aqueous workup.

Reduction of trialkylsilane **5c** was eventually carried out in high yield (entry 6, Table 1) by using the bulky *t*-BuOH as a proton source instead of EtOH (conditions B, Table 1) to avoid the desilylation of the dienylsilane **6c** by the lithium ethanolate generated in situ.[13] Finally, the chemical Birch reduction requires a large quantity of ammonia but can be advantageously replaced by its electrochemical version using a sacrificial aluminum anode (conditions C, Table 1).[17] Under these conditions, the dienylsilanes **6c** and **6f** were obtained in yields close to that obtained using the chemical version (entries 7 and 8, Table 1).

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(14) Available from Aldrich (no. 11, 337−9). $PhMe_2SiCl$ is also easily prepared on 200−300 g scale from bromobenzene and Me_2SiCl_2: Andrianov, K. A.; Delazari, N. V. *Doklady Akad. Nauk. SSSR* **1958**, *122*, 393; *Chem. Abstr.* **1959**, *53*, 2133.

(15) Fleming, I. *Organic Silicon Chemistry*; Barton, D. H. R., Ollis, W. D., Eds.; Comprehensive Organic Chemistry Series; Pergamon Press: New York, 1979; Vol. 3, p 576 and references therein.

(16) Addition of the chlorosilane to ammonia was accompanied by the appearance of a white precipitate which is likely to be NH_4Cl.

(17) Bordeau, M.; Biran, C.; Pons, P.; Léger-Lambert, M.-P.; Dunoguès, J. *J. Org. Chem.* **1992**, *57*, 4705.

Scheme 3

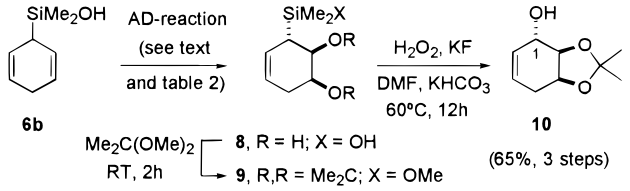


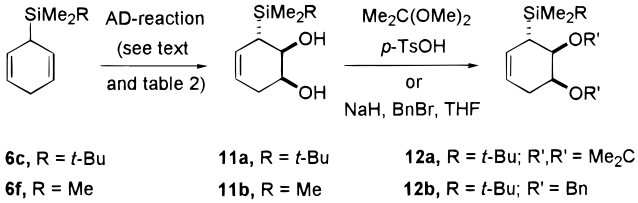
Table 2. Sharpless Asymmetric Dihydroxylation (AD Reaction) of Dienylsilanes 6 (Schemes 3 and 4)

entry	substrate	ligand[a]	product	ee (%)
1	**6b**	$(DHQD)_2Phal$	**8**	44[b]
2	**6b**	(DHQD)Ind	**8**	40[b]
3	**6b**	$(DHQD)_2Pyr$	**8**	52[b]
4	**6b**	$(DHQ)_2Pyr$	**8**	65[b]
5	**6c**	$(DHQ)_2Pyr$	**11a**	71[c]
6	**6f**	$(DHQ)_2Pyr$	**11b**	60[c]

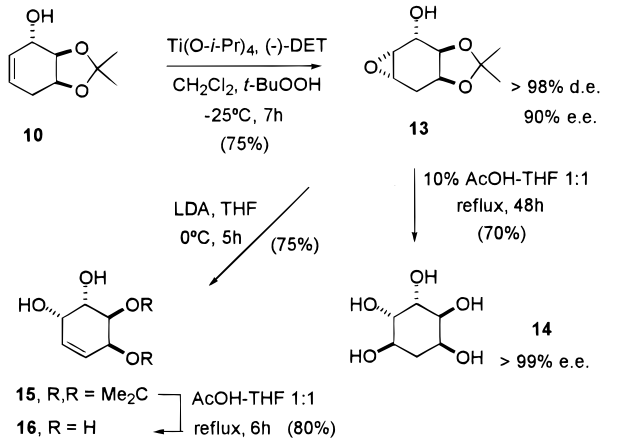
[a] AD reaction: $K_2OsO_2(OH)_4$, K_2CO_3, $K_3Fe(CN)_6$ *t*-BuOH−H_2O 1:1, $MeSO_2NH_2$, 0 °C, 12 h, ligand (see above). [b] Estimated from the ^1H NMR of the Mosher esters and ^1H NMR of **10** with $Eu(hfc)_3$. [c] Estimated from the ^1H NMR of the bis-Mosher ester of **11a**,**b**.

Asymmetric Dihydroxylation of Dienylsilanes 6. Desymmetrizations of dienylsilane **6b** using either the Sharpless[18a,b] or the Jacobsen−Katsuki epoxidations[18c] were found to be ineffective, the former leading to recovered starting material and the latter to aromatization of the substrate. We were finally pleased to find that the Sharpless asymmetric dihydroxylation (AD reaction) of **6b** led to the corresponding diol **8** in 85% crude yield (Scheme 3).[19] It is noteworthy that the reaction time had to be carefully monitored (12 h), with longer times giving reduced yield. This was attributed to the formation of bis-dihydroxylation products (tetrol), which are likely to be highly soluble in water. Modest levels of enantioselectivity[20] were attained that agree well with literature precedents on the AD reaction on cyclic and *Z*-olefins (entries-1−3, Table 2).[8] All the commercially available Sharpless ligands were tested, and the best results were obtained using $(DHQ)_2Pyr$ (entry 4, Table 2). Experiments regarding a possible kinetic amplification effect[21] have not been carried out, and therefore, such an effect toward enantioselectivity cannot be ruled out. The crude diol was then protected as its acetonide **9**, with simultaneous conversion of the $SiMe_2OH$ into an $SiMe_2OMe$ group. The C−Si bond was then oxidized using the Tamao−Kumada−Fleming[11] conditions, affording the expected allylic alcohol **10** with *retention of configuration* at the C-1 center and 50% overall yield from commercially available chlorosilane **5b**. ^1H NMR studies on **9** revealed that the process occurred, as expected, anti relative to the silicon group.[10] The AD process was also carried out on dienylsilanes **6c** and **6f** affording the desired diol **11a** and **11b** in quantitative and 85% yield, respectively, with reasonable enantioselectivities (entries 5 and 6, Table 2).

Scheme 4



Scheme 5



Protection of the diol **11a** led to the corresponding acetonide **12a** or the more robust dibenzyl ether **12b** in 85% and 52% overall yield from **6c** (Scheme 4).

Total Synthesis of Conduritol E and Deoxyinositols. We then explored the synthetic potentialities of the allylic alcohol **10** in the preparation of conduritols and analogues. It was decided to introduce the required oxygenated groups on the second double bond using the Sharpless asymmetric epoxidation[18a,b] and, thus, to take advantage of a possible kinetic resolution to improve the enantiomeric purity of the desired products. When the epoxidation was performed in the presence of (−)-DET, the *syn*-epoxide **13** was isolated after 12 h in 75% yield in diastereoisomerically pure form with 90% ee[22] (Scheme 5). The same reaction carried out with (+)-DET gave no reaction even after 2 days at −20 °C, demonstrating the high epoxidation rate difference between the "matched" and the "mismatched" pair. This result is worthy of note if one considers the poor kinetic resolution usually observed in Sharpless epoxidation of cyclic allylic alcohols. **13** was then used as a precursor of conduritols and deoxyinositols. Thus, acid-mediated epoxide ring opening and subsequent acetonide removal of **13** produced regioselectively[23] the 2-deoxy-*allo*-inositol **14**[24] in enantiomerically pure form in 26% overall yield from $PhMe_2SiCl$. In a parallel manner, treatment of **13** with an excess of LDA[25] afforded the allylic alcohol **15** through a deprotonation−epoxide ring-opening sequence. Removal of the acetonide and recrystallization finally afforded conduritol

(18) (a) Pfenninger, A. *Synthesis* **1986**, 89. (b) Gao, Y.; Hanson, R. M.; Klunder, J. M.; Ko, S. Y.; Masamune, H.; Sharpless, K. B. *J. Am. Chem. Soc.* **1987**, *109*, 5765. (c) Jacobsen, E. N. *Asymmetric Oxidation: Asymmetric Catalytic Epoxidation of Unfunctionalized Olefins* in *Catalytic Asymmetric Synthesis*; Ojima, I., Ed.; VCH: New York, 1993; p 159.

(19) It is noteworthy that when the dihydroxylation was carried out with OsO_4 and NMO in THF the fully aromatized silanol **6b** was formed as the sole product.

(20) Enantiomeric excesses were estimated from ^1H NMR of the Mosher ester and ^1H NMR of **10** with $Eu(hfc)_3$.

(21) Schreiber, S. L.; Schreiber, T. S.; Smith, D. B. *J. Am. Chem. Soc.* **1987**, *109*, 1525.

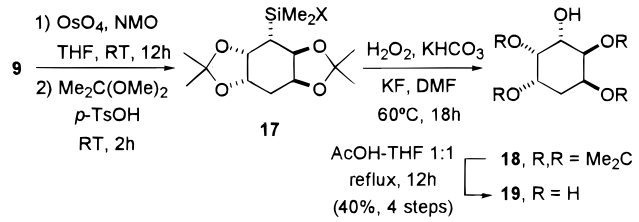
(22) The enantiomeric excess was determined using capillary GC (Cyclodex-B).

(23) The 1,2-trans-diaxial epoxide ring opening obeys the Fürst−Plattner rules; see: (a) Fürst, A.; Plattner, P. A. *Helv. Chim. Acta* **1949**, *32*, 275. (b) Hudlicky, T.; Rouden, J.; Luna, H.; Allen, S. *J. Am. Chem. Soc.* **1994**, *116*, 5099.

(24) (a) McCasland, G. E.; Furuta, S.; Johnson, L. F.; Shoolery, J. N. *J. Am. Chem. Soc.* **1961**, *83*, 2335. (b) Angyal, S. J.; Odier, L. *Carbohydr. Res.* **1982**, *101*, 209.

(25) (a) Marshall, J. A.; Audia, V. H. *J. Org. Chem.* **1987**, *52*, 1106. (b) Morgans, D. J., Jr.; Sharpless, K. B.; Traynor, S. G. *J. Am. Chem. Soc.* **1981**, *103*, 462.

Scheme 6

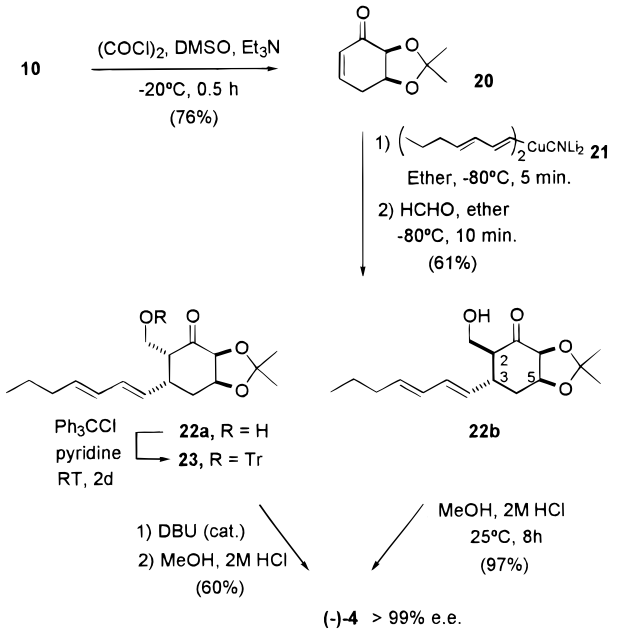


E (**16**) enantiomerically pure in 22% overall yield from **5b**.[26] It is worthy of note that this approach allows a complete functionalization of each carbon center of the original arylsilane **5b** in only six steps.

The versatility of the strategy was further illustrated with a short access to (+)-1-deoxy-*allo*-inositol **19**,[24a,27] an isomer of **14**, starting from the acetonide **9** (Scheme 6). Osmylation of **9** followed by the protection of the diol afforded the pseudo-C_2 symmetry acetonide **17** in high yield as a mixture of silanol and siloxane ($SiMe_2X$).[28] Surprisingly, it appears that the dihydroxylation occurred exclusively anti relative to the acetonide, suggesting that the two methyl groups probably hinder the top face of the allylsilane forcing the osmium reagent to approach the π-system syn relative to the silicon moiety. The C−Si bond of **17** was then oxidized as above to give the pentitol **18**, which after removal of the acetonide led to the desired deoxyinositol **19** in 40% overall yield from **9**. The optical rotation of **19** was unfortunately found not to match that of the enantiomerically pure product[27] even after several recrystallizations. Considering the different processes involved in our approach, we thus assume that **19** possesses at least the same optical purity as the starting diol **9** (65% ee).

Total Synthesis of (−)-Palitantine. (+)-Palitantine **4** is a metabolite isolated from *Penicillum palitans* that exhibits antifungal and antibiotic activities.[29] Several total syntheses of **4** have been reported to date, but only two have been carried out in the asymmetric series with overall yield not exceeding 10%.[29] The biological activity and the attractive structure of palitantine prompted us to devise a synthesis based on our desymmetrization approach. The precursor **10** was found to be particularly attractive for our purpose since a simple oxidation of the allylic alcohol would afford an α,β-unsaturated ketone that could be elaborated further into palitantine through a one-pot cupration−aldolization sequence (Scheme 7). **10** was first oxidized using Swern conditions[30] to afford the desired ketone **20** in 76% yield. 1,4-Addition of the (*E*,*E*)-dienylcyanocuprate **21** (prepared from the corresponding (*E*,*E*)-1-bromohepta-1,3-diene) onto **20** occurred anti relative to the acetonide group[31] to afford the enolate intermediate, which was directly treated with monomeric

Scheme 7



formaldehyde, leading to a 6:4 mixture of the cis isomer **22a** and trans isomer **22b**, respectively. Compounds **22a**,**b** were separated by chromatography and treated separately. The acetonide group of **22b** was cleanly removed to afford unnatural (−)-palitantine **4** in 97% yield. In a parallel manner, the primary hydroxy group of **22a** was tritylated to afford the known ether **23**,[32] which was isomerized using a catalytic amount of DBU and then converted to (−)-palitantine **4** using the reported deprotection procedure.[32] Recrystallization of the material obtained from both routes afforded enantiomerically pure unnatural (−)-**4** in 15% overall yield starting from $PhMe_2SiCl$.

Synthesis of Aminocyclitols: Asymmetric Aminohydroxylation of Cyclohexadienylsilanes. Aminocyclitols represent another class of potent glycosidase inhibitors that possess a structure close to that of cyclitols and are found as a constituent of the aglycon part of some complex antibiotics such as streptomycins and fortimycins (i.e., **2**, Scheme 1).[33] We first focused our attention on their syntheses starting from the enantiopure epoxide **13**, assuming that the ring opening of the epoxide with an amine would be as regioselective as that observed with oxygenated nucleophiles (Scheme 5).[23] Unfortunately, treatment of **13** with $BnNH_2$ in $CHCl_3$ or NaN_3 in DME−EtOH furnished a mixture of the corresponding aminocyclitols with regioselectivity not exceeding 9:1. As the regioisomers were finally found to be inseparable, we reasoned that much better regioselectivity could be achieved by tethering the nucleophile onto the allylic hydroxy group of a precursor such as **10** (Scheme 8). This was easily accomplished by treating **10** with TsNCO, which produced the desired carbamate.[34] Carbamates are known to be ambident nucleophiles, and the presence of

(26) Takano, S.; Yoshimitsu, T.; Ogasawara, K. *J. Org. Chem.* **1994**, *59*, 54. (b) Hudlicky, T.; Luna, H.; Olivo, H. F.; Andersen, C.; Nugent, T.; Price, J. D. *J. Chem. Soc., Perkin Trans. 1* **1991**, 2907.

(27) Angyal, S. J.; Odier, L. *Carbohydr. Res.* **1982**, *100*, 43.

(28) The siloxane and the silanol are probably formed through hydrolysis of the Si−OMe function during the osmylation with OsO_4−NMO·H_2O.

(29) Isolation of (+)-palitantine: Bowden, K.; Lythgoe, B.; Marsden, D. J. S. *J. Chem. Soc.* **1959**, 1662. Total asymmetric syntheses of (+)-palitantine: (a) Deruyttere, X.; Dumortier, L.; Van der Eycken, J.; Vandewalle, M. *Synlett* **1992**, 51. (b) Hanessian, S.; Sakito, Y.; Dhanoa, D.; Baptistella, L. *Tetrahedron* **1989**, *45*, 6623.

(30) Mancuso, A. J.; Swern, D. *Synthesis* **1981**, 165.

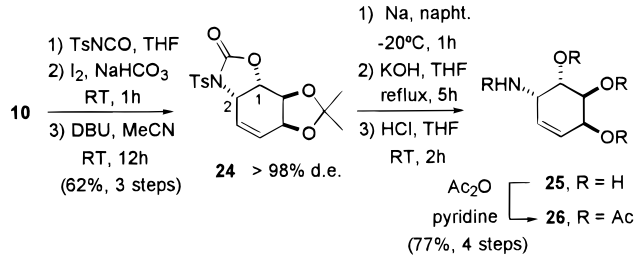
(31) Hydrolysis of the enolate directly after the cupration afforded the addition product as a unique diastereomer having the trans relationship between the acetonide and the dienyl chain at C-3.

(32) Ichichara, A.; Ubukata, M.; Sakamura, S. *Tetrahedron* **1980**, *36*, 1547.

(33) (a) Hooper, I. R. *Aminoglycoside Antibiotics*; Umezawa, U., Hooper, I. R., Eds.; Springer: Berlin, 1982; p, 7. (b) Rinehart, K. L.; Suami, T. *Aminocyclitol antibiotics*; Symposium Series no. 125; American Chemical Society: Washington D.C., 1980. (c) McAuliffe, J. C.; Hindsgaul, O. *Chem. Ind.* **1997**, 170.

(34) Hirama, M.; Iwashita, M.; Yamazaki, Y.; Ito, S. *Tetrahedron Lett.* **1984**, *25*, 4963.

Scheme 8



an *N*-tosyl group increases the nucleophilicity of the nitrogen center. Iodocarbamation then afforded the crude iodide, which on treatment with DBU led to the elimination product **24** as a unique diastereomer having the expected cis relative configuration between the C_1-O and C_2-N bonds. Having installed the amino and hydroxy groups onto the cyclohexane ring, we then removed selectively the protective groups. The tosyl function was cleanly removed using Na-naphthalene[35] leading to the free oxazolidine, which was directly saponified (KOH) to afford the amino alcohol, which on acidic treatment led to the conduramine E **25** (as its hydrochloride).[36] The latter was finally isolated as its tetraacetate **26** in 48% overall yield from **10**. Unfortunately, whereas the efficiency of the sequence was rather satisfying, the optical rotation of **26** was found not to match that of the reported enantiomerically pure material even after recrystallization of **24** and **26**.[36]

Fortunately, a more satisfactory answer to the problem of regio- and enantioselectivity described above was provided by the recent asymmetric aminohydroxylation (AA) process discovered by Sharpless et al.[9] We reasoned that the desymmetrization of dienylsilanes **6** using this new reagent would be particularly attractive, offering a more straightforward access to aminocyclitols. We assumed that, analogously to the dihydroxylation process, the aminohydroxylation reagent would approach the π-system anti relative to the silicon group. However, this AA process was even more challenging than the AD process since nothing was known at that time concerning the regioselectivity of aminohydroxylation of allylsilanes. Preliminary attempts on dienylsilane **6b** were made using the Sharpless AA mixture with chloramine T (NaClNTs) or benzylcarbamate (H_2NCO_2Bn) as nitrogen sources. Unfortunately, using these reagents, **6b** was recovered unchanged, probably owing to the steric hindrance of the groups on nitrogen. We were finally pleased to find that repeating the reaction under the same conditions with H_2NCO_2Et as the nitrogen source and $(DHQ)_2Pyr$ as a chiral ligand provided the aminohydroxylation product **27** in good yield and *more importantly with complete regio- and diastereocontrol* (to the limit of detection of ^1H NMR) (entry 1, Table 3, Scheme 9).

The oxidation of the C−Si bond with *retention of configuration* gave the diol **28**. The cis carbamate and OH groups were selectively protected as the acetonide **29**. The diastereofacial selectivity and the regioselectivity of the AA reaction on dienylsilane **6b** were finally secured with the X-ray structure determination of **29**.[6b] As

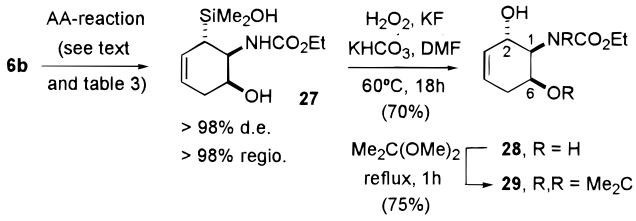
(35) Chmielewski, M.; Zegrocka, O. *Carbohydr. Res.* **1994**, *256*, 319.
(36) The optical rotation of **26**: $[\alpha]^{25}_D = +123$ (*c* 1, CH_2Cl_2) [lit. $[\alpha]^{25}_D = +151$ (*c* 1.4, CH_2Cl_2)]: Trost, B. M.; Pulley, S. R. *Tetrahedron Lett.* **1995**, *36*, 8737.

Table 3. Sharpless Asymmetric Aminohydroxylation (AA Reaction) of Dienylsilanes 6 (Schemes 9 and 11)

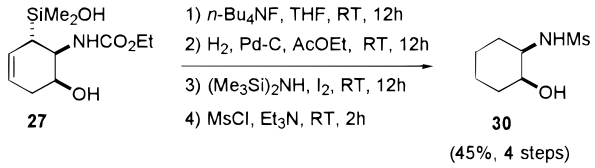
entry	substrate	ligand[a]	product	regio	ee (%)
1	**6b**	$(DHQ)_2Pyr$	**27**	>98%	68[b]
2	**6c**	$(DHQ)_2Pyr$	**31a/31b**	92:8	81[c,d]
3	**6c**	quinuclidine	**31a/31b**	7:3	
4	**6c**	*i*-Pr_2NEt	**31a/31b**	1:1	

[a] AA reaction: $K_2OsO_2(OH)_4$, *t*-BuOCl, NaOH, EtO_2CNH_2 *n*-PrOH−H_2O 1:1, rt, 1.5 h, ligand (see above). [b] Estimated from the ^1H NMR of the Mosher ester of **29**. [c] Estimated from the ^1H NMR of the Mosher ester of **31a**. [d] **31b**: ee 12% (from Mosher ester of **31b**).

Scheme 9



Scheme 10



expected, the aminohydroxylation had taken place anti relative to the bulky silicon group, with the amino group located on the carbon center the closest to the silicon group. The enantioselectivity of the process was estimated to be 68% based on the ^{19}F NMR spectrum of the Mosher ester of **29**. It is noteworthy that, owing to the presence of carbamate rotamers, this determination was achieved by recording the spectrum at 80 °C in toluene-d_8.[37] Importantly, we then found that a *single recrystallization of* **29** *in ether−hexane finally provided the allylic alcohol in optically pure form*, thus preventing the problems of enantiomeric purity encountered above. The absolute configuration of **29** (1*R*,2*S*,6*S*), determined by conversion of **27** into the known intermediate **30**,[9c] confirmed that the reaction using $(DHQ)_2Pyr$ as a chiral ligand had occurred with the same topicity as the dihydroxylation (Scheme 10). We also observed that the regioselectivity of the aminohydroxylation was substrate and ligand dependent (Table 3). AA reaction on dienylsilane **6c** thus afforded a 92:8 mixture of the chromatographically separable regioisomers **31a** and **31b**, respectively (entry 2, Table 3, Scheme 11). The enantiomeric excesses, estimated from the ^1H NMR of the corresponding Mosher esters, were found to be 81% and 12%, respectively, indicating a striking parallel between the enantio- and the regioselectivity. We also studied the influence of the nitrogen ligand structure on the regioselectivity of the AA reaction on **6c** (entries 2−4, Table 3). It was found that the best regioselectivities were encountered with chiral ligand $(DHQ)_2Pyr$ and that other

(37) ^{13}C NMR studies in $CDCl_3$ showed that at room temperature **29** is a 9:1 mixture of the *cis*- and *trans*-carbamate rotamers. ^{19}F NMR studies of the Mosher ester of **29** in toluene-d_8 produced four signals at room temperature. Upon raising the temperature to 80 °C, these signals finally coalesced into one signal for each diastereomer. For similar observations, see: Garner, P.; Park, J. M. *J. Org. Chem.* **1987**, *52*, 2361.

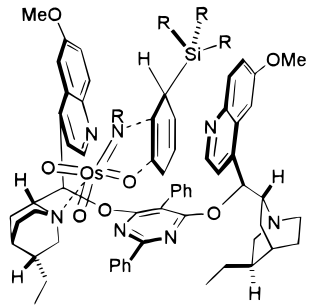
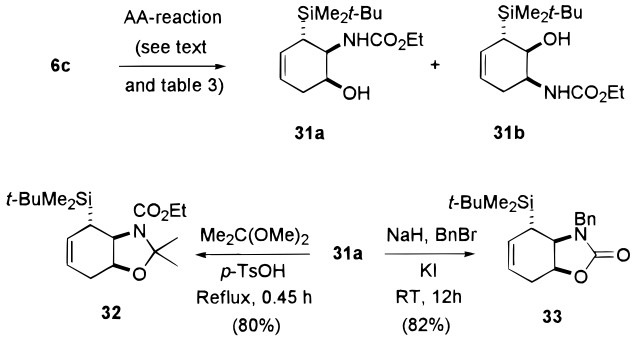


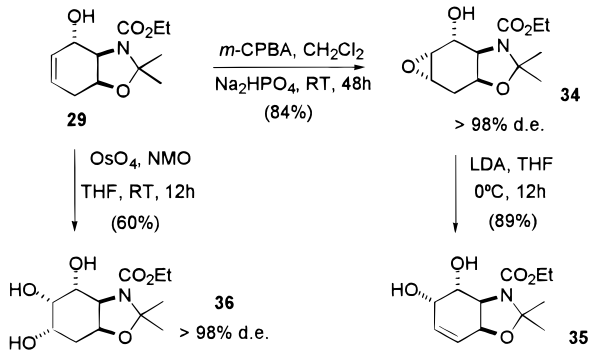
Figure 2.

Scheme 11



achiral amines led to a larger amount of the other regioisomer. This may indicate that, as suggested recently by Han and Janda,[38] the $(DHQ)_2Pyr$−osmium catalytic species adopts a binding pocket conformation that imposes the positioning of the substrate and consequently the regioselectivity of the process. The regioselectivity would thus be controlled by the way the olefin binds to the catalyst. The nitrogen atoms of the RN═ OsO_3 moiety and that of the quinuclidine ring would occupy the apical positions, the binding of the olefin then initiating the [3 + 2] cycloaddition through the axial NR groups and one of the equatorial oxygen as illustrated in Figure 2.[38] In our case, it is reasonable to assume that the more favorable diene binding mode would be that in which the sterically demanding silicon group (i.e., $SiMe_2$-*t*-Bu) is located outside the pocket (the length of a C−Si is 1.9 Å). The other regioisomer **31b** would then be formed through a nonregio- and nonenantioselective process occurring *outside* the cavity (the formation of **31b** inside the pocket would imply large steric interactions between the SiR_3 group and the spacer). Similarly, the absence of such a binding pocket in quinuclidine and *i*-$PrEt_2N$ would explain the poor regioselectivity (entries 3−4, Table 3). It is interesting to notice that in this model the polar $SiMe_2OH$ group of **6b** is ideally placed in a more hydrophilic environment outside the cavity (H_2O−*n*-PrOH), explaining the higher regioselectivity in this case (entry 1, Table 3). This parallels previous observations[9] that ligands such as $(DHQ)_2Pyr$ not only induce high enantioselectivities but also largely improve the regioselectivity of the AA process compared to that of the racemic version.[39,40] Finally, protection of the hydroxy-

Scheme 12



carbamate function allows for further elaboration of the cyclohexene skeleton. For instance, **31a** was protected in acidic conditions as an acetonide **32** and in basic conditions as an oxazolidinone **33** through nucleophilic displacement of the ethyl group of the carbamate followed by N-benzylation (Scheme 11).

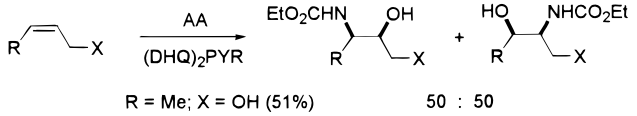
We then demonstrated that the functionalization of the enantiopure allylic alcohol **29** offered an efficient entry to a large variety of aminocyclitols. We first developed a straightforward access to an advanced precursor of fortamine,[41] the aglycon moiety of the antibiotic *fortimycins*. **29** was thus treated with *m*-CPBA, affording the epoxide **34** as a unique diastereomer. The epoxide was then treated as before with an excess of LDA to provide the fortamine precursor **35**, diastereo- and enantiomerically pure in 23% overall yield (six steps) from $PhMe_2$-SiCl (Scheme 12). It is worthy of note that the epoxidation occurred with complete diastereofacial selectivity, syn relative to the allylic hydroxy group.[42] Such a directing effect may also rationalize the stereochemical outcome of the osmylation of **29**, which provides the *syn*-diol **36** as a unique diastereomer (Scheme 12). The methyl groups of the oxazolidine that point above the plane of the olefin **29** may also force the electrophile to approach anti, thus reinforcing the syn directing effect of the allylic hydroxy group.

The versatility of our strategy was further illustrated by a straightforward access to the 1,3-aminocyclitol skeleton found in the aglycon moiety of streptomycin antibiotics.[33a] The second amino group was introduced through iodocarbamation of the allylic double bond of **29**. The carbamate intermediate easily prepared from the precursor **29** was treated with I_2 to produce the iodide **37** as a unique diastereomer (Scheme 13). As described for the preparation of conduramine E **25**, iodocarbama-

(38) For a recent study about the control of the regioselectivity of AA-process, see: Han, H.; Cho, C.-W.; Janda, K. D. *Chem. Eur. J.* **1999**, *5*, 1565 and references therein.

(39) (a) Sharpless, K. B.; Chong, A. O.; Oshima, K. *J. Org. Chem.* **1976**, *41*, 177. (b) Herranz, E.; Sharpless, K. B. *Ibid.* **1978**, *43*, 2544. (c) Herranz, E.; Biller, S. A.; Sharpless, K. B. *J. Am. Chem. Soc.* **1978**, *100*, 3596. (d) Herranz, E.; Sharpless, K. B. *J. Org. Chem.* **1980**, *45*, 2710.

(40) Investigations about the regioselectivity of the AA process were also carried out in acyclic series. As illustrated below, it appears that with terminal olefins, the bulky carbamate group prefers the less substituted end of the olefin regardless of the steric or electronic nature of the substituents at the allylic centre.With disubstituted *Z*-olefins, the picture is not so clear-cut and is more difficult to rationalize.

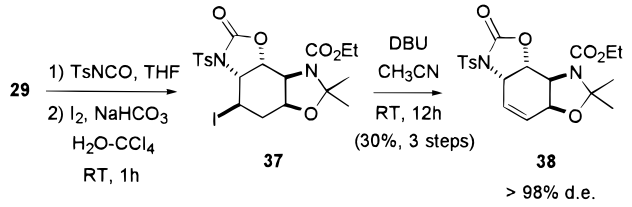


R = Me; X = OH (51%)	50 : 50
R = Me; X = $SiMe_2Ph$ (60%)	75 : 25
R = H; X = OH (83%)	100 : 0
R = H; X = $SiMe_2$(O-iPr) (60%)	100 : 0

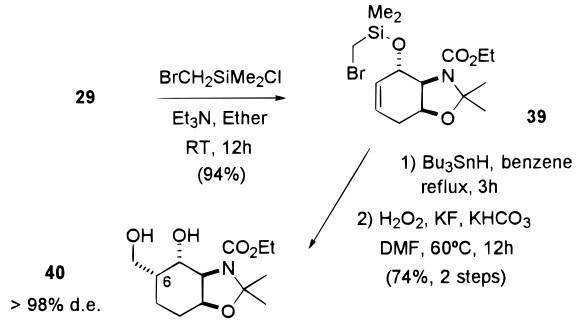
(41) Schubert, J.; Schwesinger, R.; Knothe, L.; Prinzbach, H. *Liebigs Ann. Chem.* **1986**, 2009.

(42) Hoveyda, A. H.; Evans, D. A.; Fu, G. C. *Chem. Rev.* **1993**, *93*, 1307 and references therein.

Scheme 13



Scheme 14



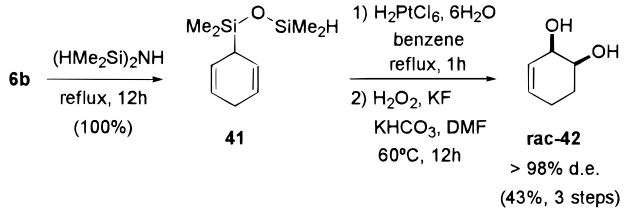
tion occurred syn relative to the allylic alcohol with the nitrogen and the iodide groups, adding anti across the double bond. **37** was then directly treated with DBU as above (Scheme 8) to afford in 30% overall yield (calculated from **29**) the 1,3-diamino cyclitol **38** possessing two orthogonally protected amino alcohol functions.

Finally, we considered a stereocontrolled access to amino carbasugar through the introduction of the CH_2-OH substituent at C-6 using a tin-mediated *5-exo-trig* radical cyclization of a bromomethylsilyl ether.[43] The silylmethyl ether precursor **39** was prepared by silylation of **29** with $ClSiMe_2CH_2Br$ (Scheme 14). The radical cyclization of **39** then led to the formation of the cyclic siloxane as one diastereomer (cis) that was directly oxidized to the desired amino carbasugar **40**. The sugar skeleton having four stereogenic centers was thus elaborated in only seven steps and 21% overall yield from chlorosilane **5b**.

Conclusion

We have described a new and efficient route to biologically relevant cyclitols, aminocyclitols, and analogues using the desymmetrization of readily available cyclohexadienylsilanes. The silicon group is a key element of our strategy that first controls the diastereofacial selectivity of the electrophilic processes before serving as a masked hydroxy group. Four to five chiral centers can thus be generated in a stereocontrolled manner in a limited number of steps (<8) from an aromatic precursor available in multigram quantities. One limitation of our approach remains the efficiency of the Sharpless dihydroxylation and aminohydroxylation processes on our substrates. Nevertheless, the enantiomeric purity of the final products has been in most cases raised through crystallization. More efficient chiral ligands are, however, required to avoid such a limitation.[44] We have so far

Scheme 15



essentially turned our attention toward electrophilic desymmetrization processes, but the scope of the utilization of such dienes can certainly be explored further. As an example, hydrosilylation was used to functionalize the diene system. A reactive silane function (i.e., $SiMe_2H$) was tethered onto the allylic hydroxy group of **6b** to give silane **41** in quantitative yield (Scheme 15). Hydrosilylation using Speier's catalyst[45] then led to the cyclic siloxane, which was directly submitted to the Tamao−Kumada oxidation affording the racemic diol **42**[46] in 43% overall yield from **6b**. Attempts to repeat this hydrosilylation in nonracemic series have failed so far, but this short sequence demonstrates that dienylsilanols may be very useful synthons for organic chemistry. Further investigations aimed at developing more in depth this chemistry are now underway in our laboratory.

Experimental Section

^1H NMR and ^{13}C NMR were recorded using $CDCl_3$ as internal reference unless otherwise indicated. The chemical shifts (δ) and coupling constants (J) are expressed in ppm and Hz, respectively. Elemental analyses were performed by the I. Beetz laboratory, W-8640 Kronach (Germany). Melting points were not corrected. Silica gel 60 (70−230 mesh) and (230−400 mesh ASTM) were used for flash chromatography. CH_2Cl_2, NEt_3, and $(i\text{-}Pr)_2NH$ were distilled from CaH_2. THF was distilled from potassium. Benzene, toluene, ether, hexane, and HMPA were distilled from sodium. Chlorosilanes were distilled over magnesium. Li powder (Fluka no. 62365) and anhydrous NH_3 (Fluka no. 09684) were used for the Birch reduction.

Birch Reduction of Siloxane (5a). In a dry 150 mL three-necked flask equipped with a magnetic stirrer, an inlet for argon, and a thermometer was condensed NH_3 (50 mL) at −80 °C under argon in THF (10 mL). **5a** (0.25 g, 1.4 mmol) was then added slowly. Lithium powder (0.3 g, 43 mmol) was then introduced, and the solution turned immediately blue. This solution was stirred at −80 °C for 1.5 h, and anhydrous NH_4-Cl was added until the blue coloration disappeared. Ether (30 mL) and water (20 mL) were then added successively, and ammonia was evaporated at room temperature. The aqueous layer was extracted with ether. The combined extracts were washed with water (2×) and brine and dried over $MgSO_4$, and the solvents were evaporated in vacuo. The residue was then purified by flash chromatography through Florisil (petroleum ether/EtOAc 98:2) to afford dienylsilane **6a** (0.11 g, 40%): ^1H NMR δ 5.85−5.52 (4H, m), 3.72 (2H, q, J = 7 Hz), 2.62 (2H, m), 2.43 (1H, m), 1.20 (3H, t, J = 7 Hz), 0.16 (6H, s). **6b** (0.09 g, 40%): ^1H NMR δ 5.75−5.57 (4H, m), 2.72 (2H, m), 2.36 (1H, m), 0.18 (6H, s); IR (film) 3300 cm^{-1}.

General Procedure for the Preparation of Dienylsilanols 6 (Conditions A): 6b. In a dry 250 mL three-necked flask equipped with a magnetic stirrer, an inlet for argon, and a thermometer was condensed NH_3 (80 mL) at −80 °C under argon. The chlorosilane **5b** (1 mL, 6 mmol) was then slowly added, and a white precipitate appeared. After 5 min, lithium powder (0.3 g, 42 mmol) was introduced, and the solution

(43) (a) Pingli, L.; Vandewalle, M. *Tetrahedron* **1994**, *50*, 7061 and references therein. (b) Bols, M.; Skrydstrup, T. *Chem. Rev.*, **1995**, *95*, 1253.

(44) Asymmetric aminohydroxylation of **6c** using recently discovered $(AQN)_2PYR$ ligand unfortunately led to recovered starting material. $(AQN)_2PYR$: Eecker, H.; Sharpless, K. B. *Angew. Chem., Int. Ed. Engl.* **1996**, *35*, 448.

(45) Benkeser, R. A.; Kang, J. *J. Organomet. Chem.* **1980**, C9.

(46) Banwell, M. G.; Lambert, J. N.; Richards, L. *Aust. J. Chem.* **1991**, *44*, 939.

turned immediately blue. This solution was then stirred at −80 °C for 45 min, and anhydrous NH_4Cl was added until the blue coloration disappeared. Ether (30 mL) and water (20 mL) were then added successively, and ammonia was evaporated at room temperature. The aqueous layer was extracted with ether. The combined extracts were washed with water (2×) and then with a saturated NaCl solution and dried over $MgSO_4$, and the solvents were evaporated in vacuo. The residue was then purified by Kugelrohr distillation (70 °C, 0.4 mbar) or by flash chromatography through Florisil (petroleum ether/EtOAc 95:5) to give dienylsilanol **6b** as a colorless oil (0.72 g, 77%). Spectroscopic data were identical in many respects with those described above.

General Procedure for the Preparation of Dienylsilanes 6 (Conditions B): **6c.** In a dry 1 L three-necked flask equipped with a magnetic stirrer, an inlet for argon, and a thermometer was condensed NH_3 (350 mL) in dry THF (80 mL) at −80 °C under argon. *t*-BuOH (182 mL, 1.95 mol) and arylsilane **5c** (3.9 g, 20.3 mmol) were then slowly added. After 2 min, lithium powder (2.84 g, 0.4 mol) was introduced, and the solution immediately turned blue. This solution was then stirred at −80 °C for 2.5 h, and anhydrous NH_4Cl was added until the blue coloration disappeared. Ether (60 mL) and water (50 mL) were then added successively, ammonia was evaporated at room temperature, and the aqueous layer was extracted with ether. The combined extracts were washed twice with water and then with a saturated NaCl solution and dried over $MgSO_4$, and the solvents were evaporated in vacuo. The residue was then purified by filtration over Celite (petroleum ether), affording the diene **6c** as a colorless oil (3.7 g, 94%): ^{1}H NMR δ 5.78−5.50 (4H, m), 2.68 (2H, m), 2.40 (1H, m), 0.93 (s, 9H), 0.00 (6H, s); IR (film) 3028 cm^{-1}. Anal. Calcd for $C_{12}H_{22}Si$: C, 74.17; H, 11.42; Si, 14.41. Found: C, 74.20; H, 11.48; Si, 14.32.

General Procedure for the Preparation of Dienylsilanes 6 (Conditions C): 6c. In a one-compartment cell fitted with a sacrificial anode of aluminum and a cylindrical stainless grid were introduced, under nitrogen, the supporting electrolyte LiCl (3.53 g, 83.3 mmol), *t*-BuOH (6 mL, 62.3 mmol), anhydrous THF (90 mL), HMPA (15 mL), and the arylsilane **5c** (4 g, 20.8 mmol). Electrolysis (constant current 0.1 A) was then initiated and was maintained until the starting material had disappeared (∼17 h) (monitored by GC). A solution of HCl 10% (50 mL) and pentane (30 mL) was then added to the reaction mixture, and the organic layer was decanted. The aqueous layer was extracted with pentane (3 × 20 mL), the combined extracts were washed with brine and dried over $MgSO_4$, and the solvents were evaporated in vacuo to afford the diene **6c** as a colorless oil used in the next step without further purifications (3.5 g, 87%). GC (5 min at 80 °C then 6 °C/min): t_R (**6c**) 12.7 min; t_R (**5c**) 11.6 min. Spectroscopic data for **6c** prepared according procedure C were identical with those described above.

Dienylsilane (6f). Following the general procedure C, the dienylsilane **6f** was obtained from arylsilane **5f** as a colorless oil (90%). Spectroscopic data were all identical in many respects with those described in the literature.[13] GC (5 min at 80 °C then 6 °C/min): t_R (**6f**) 5.13 min; t_R (**5f**) 5.05 min.

General Procedure for the Sequence Sharpless Dihydroxylation−Diol Protection−Tamao−Kumada Oxidation of Dienylsilanes 6 (10). In a 250 mL flask were placed AD-mix [(K_3FeCN_6 (12.8 g, 39 mmol), K_2CO_3 (5.4 g, 39 mmol), $(DHQ)_2Pyr$ (0.11 g, 0.13 mmol), $K_2OsO_2{\cdot}2H_2O$ (0.048 g, 0.13 mmol)], H_2O (65 mL), and *t*-BuOH (65 mL). The solution was stirred for 5 min, and methanesulfonamide (1.23 g, 13 mmol) was added. The orange solution was cooled to 0 °C, and **6b** (2 g, 13 mmol) was introduced under vigorous stirring. After 12 h at 0 °C, sodium sulfite (19.5 g) was added, and the solution was allowed to stir at room temperature for 45 min. The aqueous layer was extracted with EtOAc (5 ×), the combined extracts were washed with a 10% NaOH solution, dried over $MgSO_4$, and the solvents were evaporated in vacuo to give the crude diol **8**, which was directly protected as an acetonide following the general procedure: **8** was dissolved in acetone (20 mL) and dimethoxypropane (15 mL). A catalytic amount of *p*-TsOH was added, and the solution was stirred for 2 h at room temperature. The solvents were then evaporated in vacuo and a saturated Na_2CO_3 solution was added. The aqueous layer was extracted with ether, then the combined extracts were washed with brine and dried over $MgSO_4$. Evaporation of the solvent afforded the crude acetonide **9** (3 g) as a colorless liquid. ^{1}H NMR δ 5.74−5.67 (2H, m), 4.48−4.37 (2H, m), 3.46 (3H, s), 2.25 (2H, m), 2.02 (1H, m), 1.43 (3H, s), 1.35 (3H, s), 0.17 (3H, s), 0.16 (3H, s). **9** was then oxidized following the general Tamao−Kumada procedure: To a solution of **9** (3 g, 12.4 mmol) in DMF (5 mL) were added at 0 °C KF (2.16 g, 37.2 mmol), $KHCO_3$ (3.72 g, 37.2 mmol), and H_2O_2 (35% solution in water, 21 mL, 0.248 mol). The reaction mixture was then stirred at 60 °C overnight. The mixture was quenched with solid $Na_2S_2O_3$ and dried over $MgSO_4$ and the solvent was evaporated in vacuo. The resulting yellow oil was purified by chromatography through silica gel (petroleum ether/EtOAc 7:3) to afford **10** as a colorless oil (1.4 g, 65%, three steps) (65% ee, measured from ^{1}H NMR with Eu(hfc)$_3$): ^{1}H NMR δ 5.86−5.72 (2H, m), 4.36 (1H, ddd, J = 7.5, 5.5, 5 Hz), 4.18 (1H, br s), 4.01 (1H, dd, J = 7.5, 6 Hz), 2.65 (1H, ddd, J = 17, 5.4, 5 Hz), 2.5 (1H, br s), 2.18 (1H, dddd, J = 17, 7.9, 5.5, 2.5 Hz), 1.47 (3H, s), 1.37 (3H, s); ^{13}C NMR δ 130.5, 125.2, 108.2, 80.5, 71.6, 69.8, 28.4, 27.2, 24.8; IR (film) 3440, 1654 cm^{-1}; MS *m*/*z* 171 ($M^{\bullet+}$ + 1, 8), 112 (100); $[\alpha]^{25}_D$ + 54 (*c* 0.46, $CHCl_3$). Anal. Calcd for $C_9H_{14}O_3$: C, 63.49; H, 8.30. Found: C, 63.39; H, 8.45.

Sharpless Dihydroxylation of Dienylsilane 6f (11b). Following the general procedure described above, dienylsilane **6f** gave after Sharpless dihydroxylation and purification by chromatography through silica gel (petroleum ether/EtOAc 95:5) the diol **11b** as a colorless oil (85%) (60% ee measured from the ^{1}H NMR of the bis-Mosher's ester of the corresponding diol): ^{1}H NMR δ 5.51−5.39 (2H, m), 3.89−3.87 (1H, m), 3.77−3.70 (1H, m), 2.42 (2H, br s), 2.32−2.06 (2H, m), 1.80−1.78 (1H, m), 0.01 (9H, s); ^{13}C NMR δ 129.0, 125.2, 120.7, 70.4, 68.4, 35.8, 30.1, −2.4; IR (film) 3382, 1643 cm^{-1}; MS *m*/*z* 186 ($M^{\bullet+}$, 3), 73 (100); HRMS ($C_9H_{18}O_2Si$) calcd 186.1076, found 186.1074.

Sharpless Dihydroxylation of Dienylsilane 6c (12a). Following the general procedure described above, dienylsilane **6c** (3 g, 15.5 mmol) gave after Sharpless dihydroxylation, diol protection, and purification by chromatography through silica gel (petroleum ether/EtOAc 95:5) the acetonide **12a** as a colorless oil (3.5 g, 85%, 2 steps) (71% ee measured from the ^{1}H NMR of the bis-Mosher ester of the corresponding diol): ^{1}H NMR δ 5.77 (1H, m), 5.63 (1H, m), 4.46 (1H, m), 2.22 (2H, m), 2.09 (1H, m), 1.43 (3H, s), 1.34 (3H, s), 0.95 (9H, s), 0.04 (3H, s), −0.03 (3H, s); ^{13}C NMR δ 127.3 (d, J = 160 Hz), 120.7 (d, J = 162 Hz), 107.4, 74.5, 72.7, 28.5, 28.4, 27.3, 26.9, 25.4, 17.4, −6.0, −6.3; IR (film) 3034 cm^{-1}; MS *m*/*z* 269 ($M^{\bullet+}$ + 1, 1), 115 (12), 73 (100); $[\alpha]^{25}_D$ +132.5 (*c* 1.08, $CHCl_3$).

(1*S*,2*S*,3*S*)-1,2-Dibenzyloxy-3-*tert*-butyldimethylsilylcyclohex-4-ene (12b). Sharpless dihydroxylation of dienylsilane **6c** (4.7 g, 24.2 mmol), following the general procedure, afforded the crude diol **11a**, which was then added to a solution of NaH (2.9 g, 0.12 mol) in anhydrous THF (150 mL) at 0 °C. Benzyl bromide (6 mL, 50 mmol) and KI (8.4 g, 50 mmol) were then added successively. The solution was stirred overnight at room temperature, then quenched with an aqueous saturated solution of NH_4Cl, extracted with ether, and dried over $MgSO_4$, and the solvent was evaporated. The crude product was purified by chromatography through silica gel (petroleum ether/ EtOAc 95:5) to give **12b** as a colorless oil (5.1 g, 52%, two steps): ^{1}H NMR δ 7.43−7.25 (10H, m), 5.58−5.50 (2H, m), 4.78 (2H, 2 d, J = 12.5 Hz), 4.57 (2H, s), 3.99 (1H, m), 3.59 (1H, ddd, J = 10, 6 and 1.7 Hz), 2.55−2.32 (2H, m), 2.19 (1H, m), 0.86 (9H, s), −0.15 (3H, s), −0.19 (3H, s); ^{13}C NMR δ 139.3, 138.7, 128.3, 128.2, 127.5, 127.3, 126.2, 121.2, 75.4, 74.5, 71.5, 70.1, 31.7, 27.3, 26.8, 17.2, −6.2, −6.7; IR (film) 3063 cm^{-1}; MS *m*/*z* 426 ($M^{\bullet+}$ + 1 + NH_3, 100); $[\alpha]^{25}_D$ +68.2 (*c* 0.73, $CHCl_3$). Anal. Calcd for $C_{26}H_{36}O_2Si$: C, 76.42; H, 8.89; Si, 6.85. Found: C, 76.49; H, 8.86; Si, 6.88.

Epoxide 13. In a dry 100 mL three-necked flask equipped with a thermometer, an inlet for argon, and a septum was introduced under argon Ti(O-*i*-Pr)$_4$ (0.7 mL, 2.3 mmol) at −30

°C in CH_2Cl_2 (10 mL). (−)-Diethyl-D-tartrate (0.48 mL, 2.8 mmol) was then added under stirring. The resulting pale yellow solution was then stirred for 15 min, and allylic alcohol **10** (0.4 g, 2.3 mmol) in CH_2Cl_2 (5 mL) was added. A 3 M *t*-BuOOH solution in toluene (1.6 mL, 4.8 mmol) was then slowly introduced, and the reaction mixture was kept at −25 °C for 7 h. A saturated solution of Na_2SO_3 was then added, and a vigorous stirring was maintained for 45 min at 0 °C. The resulting orange gelatinous mixture was filtered through Celite, thoroughly washed with CH_2Cl_2, and dried over $MgSO_4$. After evaporation of the solvent under vacuum, the crude product was purified by chromatography through silica gel (petroleum ether/EtOAc 7:3) to afford the epoxide **13** as a colorless oil (0.33 g, 75%) (90% ee, GC, Cyclodex-B): ^{1}H NMR δ 4.29 (1H, ddd, J = 11.6, 11, 6.2 Hz), 4.09 (2H, m), 3.32 (2H, m), 2.61 (1H, ddd, J = 15, 11, 7.6 Hz), 2.03 (1H, ddd, J = 15, 7.5, 6.2 Hz), 1.46 (3H, s), 1.31 (3H, s); ^{13}C NMR δ 107.5, 78.9, 70.9, 70.8, 54.5, 50.7, 27.7, 27.2, 24.3; IR (film) 3447, 1267 cm^{-1}; MS m/z 187 ($M^{\bullet+}$ + 1, 5), 171 (100); $[\alpha]^{25}_D$ +67.3 (c 0.79, $CHCl_3$). Anal. Calcd for $C_9H_{14}O_4$: C, 58.04; H, 7.58. Found: C, 58.10; H, 7.41.

(−)-2-Deoxy-*allo*-inositol (14). Epoxide **13** (0.2 g, 1.07 mmol) was dissolved in a 1:1 mixture of 10% AcOH (5 mL) and THF (5 mL) and then heated under reflux for 48 h. Evaporation of the solvents under vacuum afforded the pentol **14** (0.14 g, 80%), optically pure after one recrystallization from MeOH/ether (0.12 g, 70%). Spectroscopic data were all identical in many respects with those described in the literature: mp 256−257 °C (MeOH/ether) [lit.[27] mp 254−255 °C (H_2O/EtOH)]; ^{13}C NMR (D_2O) δ 72.97, 72.74, 72.54, 68.63, 67.14, 34.30; $[\alpha]^{25}_D$ −50 (c 0.5, H_2O) [lit.[27] $[\alpha]^{20}_D$ +50 (c 1.4, H_2O)].

(+)-Conduritol E (16). In a dry 50 mL three-necked flask equipped with a thermometer, an inlet for nitrogen, and a septum was introduced **13** (0.2 g, 1.07 mmol) in THF (10 mL) under nitrogen. LDA (3.7 mmol) in THF (10 mL) was then added at −80 °C. After 5 h at 0 °C, the resulting yellow solution was quenched with a saturated solution of NH_4Cl, and the aqueous layer was extracted with EtOAc. The combined extracts were washed with brine and dried over $MgSO_4$, and the solvents were evaporated under vacuum. The crude product was purified by chromatography through silica gel (petroleum ether/EtOAc 6:4) to afford the diol **15** as a white solid (0.15 g, 75%), used directly in the next step without further purifications: mp 65 °C (hexane/ether); ^{1}H NMR δ 5.92 (2H, d, J = 2.3 Hz), 4.66 (1H, dd, J = 5.8, 1.8 Hz), 4.36 (1H, dd, J = 6.7, 1.8 Hz), 4.29 (1H, br s), 3.96 (1H, dd, J = 6.7, 3.7 Hz), 3.30 (1H, br s), 3.12 (1H, br s), 1.44 (3H, s), 1.38 (3H, s); $[\alpha]^{25}_D$ +126 (c 0.67, $CHCl_3$). The diol **15** (65 mg, 0.35 mmol) was dissolved in a 1:1 mixture of 10% AcOH (3 mL) and THF (3 mL) and then heated under reflux for 6 h. Evaporation of the solvents in vacuo afforded the (+)-conduritol E (**16**) (50 mg, 99%) obtained optically pure after one recrystallization (41 mg, 80%). Spectroscopic data were all identical in many respects with those described in the literature: mp 191−192 °C (MeOH/ether) [lit.[26] mp 192−194 °C (MeOH)]; ^{1}H NMR (D_2O) δ 5.82 (2H, br s), 4.25 (2H, br s), 3.88 (2H, br s); $[\alpha]^{25}_D$ + 327 (c 0.55, H_2O) [lit.[26] $[\alpha]^{20}_D$ +326 (c 0.22, H_2O)].

Bis-acetonide (18). Allylsilane **9** (0.8 g, 2 mmol) and NMO·H_2O (0.49 g, 2.2 mmol) were dissolved in THF (20 mL), and then a 0.05 M solution of OsO_4 in THF (2 mL, 0.1 mmol) was introduced dropwise at room temperature. The solution was stirred overnight, the solution was quenched with 10% Na_2SO_3, and the aqueous layer was extracted with EtOAc. The organic layer was dried over $MgSO_4$, and the solvents were evaporated under vacuum to afford the crude diol, which was protected as the acetonide **17** and submitted to the Tamao−Kumada oxidation following the general procedure described above. The crude mixture was purified by chromatography through silica gel (petroleum ether/EtOAc 7:3) to give the alcohol **18** as a colorless oil (0.3 g, 40%, three steps): ^{1}H NMR δ 4.53−4.47 (2H, m), 4.37 (1H, dd, J = 7.8, 3.5 Hz), 4.30 (1H, dd, J = 7.6, 6 Hz), 3.83 (1H, m), 2.49 (1H, d, J = 4.2 Hz), 2.25 (1H, ddd, J = 14.1, 6, 4.6 Hz), 1.91 (1H, ddd, J = 14.1, 7, 4.6 Hz), 1.48 (3H, s), 1.45 (3H, s), 1.35 (3H, s), 1.33 (3H, s); ^{13}C NMR δ 108.1, 75.1, 73.9, 71.5, 71.4, 29.7, 26.7, 26.1, 23.7, 23.5; IR (film) 3464, 1265 cm^{-1}; MS m/z 245 ($M^{\bullet+}$ + 1, 1); $[\alpha]^{25}_D$ +30.6 (c 0.52, $CHCl_3$). Anal. Calcd for $C_{12}H_{20}O_5$: C, 58.98; H, 8.26. Found: C, 58.86; H, 8.39.

(+)-1-Deoxy-*allo*-inositol (19). Bis-acetonide **18** (0.14 g, 0.57 mmol) was dissolved in a 1:1 mixture of 80% AcOH (5 mL) and THF (5 mL) and heated under reflux for 12 h. Evaporation of the solvents under vacuum afforded the crude pentol **19** as a white solid (0.9 g, 96%): mp 246−248 °C (EtOH) [lit.[27] mp 246−248 °C (EtOH)]; ^{13}C NMR (D_2O) δ 73.7, 71.3, 70.6, 68.7, 66.7, 33.1; $[\alpha]^{25}_D$ + 34 (c 0.75, H_2O) [lit.[27] $[\alpha]^{21}_D$ +62 (c 0.5, H_2O)].

Cyclohex-2-enone (20). To a solution of $(COCl)_2$ (0.4 mL, 4.7 mmol) in dry CH_2Cl_2 (10 mL) at −50 °C were added DMSO (0.67 mL, 9.4 mmol) and, after 5 min, the allylic alcohol **10** (0.4 g, 2.35 mmol). The solution was allowed to warm to −10 °C over 20 min, and NEt_3 (3.3 mL, 23.5 mmol) was added. Water was then added at room temperature and the organic layer extracted with CH_2Cl_2. The combined extracts were dried over $MgSO_4$ and the solvents evaporated in vacuo. The residue was purified by chromatography through silica gel (petroleum ether/EtOAc 6:4) to afford the ketone **20** as a white solid (0.3 g, 76%): mp 79 °C (hexane/ether); ^{1}H NMR δ 6.83−6.78 (1H, m), 6.09−6.05 (1H, m), 4.60 (1H, m), 4.25 (1H, d, J = 5.1 Hz), 2.88−2.73 (2H, m), 1.35 (3H, s), 1.30 (3H, s); ^{13}C NMR δ 196.2, 146.3, 128.1, 109.0, 75.4, 72.8, 27.6, 27.3, 25.8; IR ($CHCl_3$) 1690 cm^{-1}; MS m/z 186 ($M^{\bullet+}$ + NH_3, 83), 169 ($M^{\bullet+}$ + 1, 100); $[\alpha]^{25}_D$ +76.3 (c 0.94, $CHCl_3$). Anal. Calcd for $C_9H_{12}O_3$: C, 64.26; H, 7.20. Found: C, 64.31; H, 7.19.

Cupration−Aldolization of Ketone 20 (22a,b). In a dry 100 mL three-necked flask equipped with a thermometer, an inlet for nitrogen, and a septum was introduced (*E*,*E*)-1-bromohepta-1,3-diene[47] (1.04 g, 5.9 mmol) in ether (40 mL) under nitrogen. A 1.5 M solution of *t*-BuLi in pentane (7.9 mL, 11.9 mmol) was then added slowly at −90 °C. After 1.5 h at −90 °C, CuCN (0.27 g, 3 mmol) was added, and the resulting pale yellow solution was warmed to −20 °C over 40 min and then cooled to −80 °C. Ketone **20** (0.5 g, 3 mmol) in ether (10 mL) was added, and after 5 min at −80 °C, a 0.5 M solution of monomeric formaldehyde[48] in THF (24 mL, 12 mmol) was added. The black mixture was then quenched with a saturated solution of NH_4Cl, extracted with EtOAc, and dried over $MgSO_4$, and the solvents were evaporated. The crude mixture was purified by chromatography through silica gel (petroleum ether/EtOAc 6:4) to afford a 6:4 mixture of diastereomers **22a**,**b**. **22a** eluted first and was obtained as a colorless oil (0.32 g, 37%): ^{1}H NMR δ 6.08 (1H, dd, J = 14.9, 10.3 Hz), 5.97 (1H, dd, J = 14.9, 10.3 Hz), 5.64 (1H, dt, J = 14.9, 7 Hz), 5.44 (1H, dd, J = 14.9, 7.5 Hz), 4.58 (1H, m), 4.43 (1H, d, J = 5.6 Hz), 3.89−3.77 (2H, m), 3.00 (1H, m), 2.77 (1H, m), 2.20−2.00 (5H, m), 1.43−1.35 (8H, m), 0.89 (3H, t, J = 7.3 Hz); ^{13}C NMR δ 210.2, 134.8, 132.0, 129.6, 129.4, 109.8, 78.3, 76.0, 59.3, 55.8, 37.2, 34.6, 29.6, 27.1, 25.8, 22.3, 13.6; IR (film) 3485, 1726 cm^{-1}; MS m/z 295 ($M^{\bullet+}$ + 1, 15). The minor diastereomer **22b** (0.21 g, 24%) was obtained as a white solid: mp 93−95 °C (hexane/ether); ^{1}H NMR δ 6.11 (1H, dd, J = 14.9, 10.3 Hz), 5.99 (1H, dd, J = 14.9 10.3 Hz), 5.67 (1H, dt, J = 14.9 7 Hz), 5.35 (1H, dd, J = 14.9 9 Hz), 4.58 (1H, m), 4.32 (1H, d, J = 5.3 Hz), 3.76 (2H, m), 2.67 (1H, m), 2.47 (1H, t, J = 7.2 Hz), 2.36 (1H, m), 2.28 (1H, m), 2.05 (2H, q, J = 7 Hz), 1.45−1.39 (8H, m), 0.91 (3H, t, J = 7.3 Hz); ^{13}C NMR δ 210.3, 135.3, 132.7, 130.2, 129.3, 109.9, 79.1, 76.3, 59.9, 54.9, 38.6, 34.7, 33.0, 27.0, 26.0, 22.3, 13.7; IR ($CHCl_3$) 3583, 1719 cm^{-1}; MS m/z 294 ($M^{\bullet+}$, 0.3); $[\alpha]^{25}_D$ +34.8 (c 0.95, $CHCl_3$). Anal. Calcd for $C_{17}H_{26}O_4$: C, 69.34; H, 8.91. Found: C, 69.48; H, 9.01.

Trityl Ketone (23). To a solution of the alcohol **22a** (0.2 g, 0.7 mmol) in pyridine (2 mL) was added Ph_3CCl (0.28 g, 1 mmol) at room temperature. The reaction mixture was stirred for 2 days at room temperature and then quenched with a saturated solution of NH_4Cl, and the aqueous layer was extracted with ether. The combined extracts were dried over $MgSO_4$, and the solvent was evaporated in vacuo. The crude

(47) Williams, D. R.; Nishitani, K.; Bennett, W.; Sit, S. Y. *Tetrahedron Lett.* **1981**, *38*, 3745.

(48) Schlosser, M.; Jenny, T.; Guggisberg, Y. *Synlett*, **1990**, 704.

mixture was purified by chromatography through silica gel (petroleum ether/EtOAc 8:2), affording **23** (0.3 g, 80%). Spectroscopic data were all identical in many respects with those described in the literature:[32] ^{1}H NMR δ 7.40−7.18 (15 H, m), 5.96 (1H, dd, J = 15.1, 10.2 Hz), 5.84 (1H, dd, J = 15.0, 10.2 Hz), 5.57 (1H, dt, J = 15.0, 6.9 Hz), 5.20 (1H, dd, J = 15.1, 7.9 Hz), 4.45 (1H, m), 4.26 (1H, d, J = 5.5 Hz), 3.38 (1H, dd, J = 9.5, 5.8 Hz), 3.28 (1H, dd, J = 9.5, 7.4 Hz), 2.96 (1H, m), 2.82 (1H, m), 2.06−1.99 (4H, m), 1.44 (3H, s), 1.39 (2H, q, J = 7.3 Hz), 1.34 (3H, s), 0.90 (3H, t, J = 7.3 Hz).

(−)-Palitantine (4). The alcohol **22b** (0.1 g, 0.34 mmol) was dissolved in methanol (3 mL) and then treated with a 2 M solution of HCl (3 mL). The mixture was stirred for 8 h at room temperature, and the solvents were evaporated under vacuum to afford a yellow solid that was recrystallized to give (−)-palitantine **4** (88 mg, 97%): mp 162−164 °C (H_2O); $[\alpha]^{25}_{546}$ −4.33 (*c* 0.6, $CHCl_3$) [lit.[29a] $[\alpha]^{25}_{546}$ −4.4 (*c* 0.8, $CHCl_3$)]. Spectroscopic data were all identical in many respects with those described in the literature.[29a,b]

Tosyloxazolidinone (24). To a solution of alcohol **10** (0.3 g, 1.8 mmol) in dry THF (5 mL) was added tosyl isocyanate (0.28 mL, 1.8 mmol), and the mixture was stirred for 3 h at room temperature. The solvent was evaporated in vacuo and the resulting carbamate poured into CCl_4 (10 mL). A solution of $KHCO_3$ (0.7 g, 7.2 mmol) in water (10 mL) was then added followed by I_2 (0.9 g, 3.6 mmol), and the reaction mixture was stirred for 2 h at room temperature. The solution was diluted with CH_2Cl_2 and then quenched with a saturated solution of $Na_2S_2O_3$. The aqueous layer was extracted with CH_2Cl_2, and the solvents were evaporated in vacuo to afford the crude iodo intermediate, which was directly used in the next step without purification. The iodide was dissolved in CH_3CN (20 mL), and DBU (0.53 mL, 3.6 mmol) was added. The mixture was stirred overnight at room temperature, and then the solvent was evaporated in vacuo. The crude oil was diluted in ether and quenched with a saturated solution of NH_4Cl and the aqueous layer extracted with ether. The combined extracts were washed with brine and dried over $MgSO_4$, and the solvents were evaporated under vacuum to give a residue that was purified by chromatography through silica gel (petroleum ether/EtOAc 7:3) affording **24** as a white solid (0.4 g, 62%, three steps): mp 134−136 °C (petroleum ether/CH_2Cl_2); ^{1}H NMR δ 7.95 (2H, d, J = 8.4 Hz), 7.36 (2H, d, J = 8 Hz), 5.95 (2H, m), 4.93 (2H, br s), 4.53 (2H, br s), 2.45 (3H, s), 1.37 (3H, s), 1.36 (3H, s); ^{13}C NMR δ 150.3, 145.8, 135.0, 130.1, 129.8, 128.5, 121.4, 110.3, 71.5, 70.6, 68.8, 53.0, 27.8, 26.6, 21.7; IR ($CHCl_3$) 1791 cm^{-1}; MS *m*/*z* 383 ($M^{\bullet+}$ + 1 + NH_3, 100), 366 ($M^{\bullet+}$ + 1, 27); $[\alpha]^{25}_D$ +82.3 (*c* 0.48, $CHCl_3$). Anal. Calcd for $C_{17}H_{19}NO_6S$: C, 55.88; H, 5.24; N, 3.84; S, 8.76. Found: C, 55.96; H, 5.19; N, 3.89; S, 8.77.

(−)-Pentaacetylconduramine E (26). To a solution of naphthalene (0.74 g, 5.8 mmol) in anhydrous DME (0.25 mL) was added Na (0.15 g, 6.72 mmol) under argon. The green mixture was stirred for 0.5 h at room temperature and then cooled to −30 °C, and a solution of **24** (0.35 g, 0.96 mmol) in DME (1 mL) was added. After 20 min at −20 °C, the reaction mixture was quenched with H_2O and the aqueous layer extracted with EtOAc. The combined extracts were dried over $MgSO_4$, and the solvents were evaporated under vacuum. The crude product was purified by chromatography through silica gel (petroleum ether/EtOAc 1:1) to give the tosyl-free carbamate (0.2 g, 98%): ^{1}H NMR δ 6.33 (1H, br s), 5.87−5.80 (1H, m), 5.62−5.57 (1H, m), 5.01 (1H, m), 4.60 (2H, m), 4.18 (1H, m), 1.39 (3H, s), 1.36 (3H, s). The preceding carbamate was then dissolved in a 1:1 mixture of THF (15 mL) and 2 M KOH (15 mL) and then heated under reflux for 5 h. The organic layer was decanted and the aqueous layer extracted with EtOAc. The combined extracts were dried over $MgSO_4$ and the solvents evaporated in vacuo to afford a residue that was diluted in a 1:1 mixture of 2 M HCl (5 mL) and THF (5 mL) and heated under reflux for 2 h. The solution was evaporated to dryness, affording the crude conduramine E−HCl **25**, which was dissolved in pyridine (10 mL) and acetic anhydride (5 mL, 52 mmol). The reaction mixture was stirred at room temperature for 2 h, and the solvents were evaporated in vacuo. The residue was dissolved in EtOAc and the organic layer washed with a saturated solution of Na_2CO_3 and with brine then dried over $MgSO_4$. The solvent was then evaporated and the residue purified by chromatography on silica gel (petroleum ether/EtOAc 2:8), affording pure pentaacetyl conduramine E **26** (0.23 g, 77%): mp 178−180 °C (CH_2Cl_2/petroleum ether) [lit.[36] mp 182−184 °C]; ^{1}H NMR δ 6.35−6.30 (1H, m), 5.80−5.71 (2H, m), 5.54−5.53 (1H, m), 5.32−5.27 (2H, m), 5.02−5.00 (1H, m), 2.01 (3H, s), 2.00 (3H, s), 1.99 (3H, s), 1.94 (3H, s); ^{13}C NMR δ 170.2, 169.8, 130.2, 125.7, 67.3, 66.8, 66.0, 45.4, 22.8, 20.7, 20.6; $[\alpha]^{25}_D$ +123 (*c* 1, CH_2Cl_2) [lit.[36] $[\alpha]^{25}_D$ +151 (*c* 1.4, CH_2Cl_2)].

General Procedure for the Sharpless Aminohydroxylation of Dienylsilane 6 (Hydroxycarbamate 27). In a 500 mL flask equipped with a magnetic stirrer and a thermometer, H_2NCO_2Et (3.6 g, 40 mmol) was dissolved in *n*-propanol (50 mL). To this solution was added a freshly prepared solution of NaOH (1.6 g, 40 mmol) in water (100 mL), followed by *t*-BuOCl (5.8 g, 52.6 mmol) and a solution of the ligand $(DHQ)_2Pyr$ (0.57 g, 0.6 mmol) in *n*-propanol (50 mL). The flask was then immersed in a water bath (15 °C), and after the mixture was stirred for a few minutes, the osmium catalyst ($K_2OsO_2(OH)_4$, 0.12 g, 0.5 mmol) was added, followed by the diene **6b** (2 g, 12.9 mmol). The green reaction mixture was stirred for 1.5 h and then treated with sodium sulfite (5 g), followed by water (30 mL) and EtOAc (50 mL). After being stirred for 15 min, the organic layer was decanted and the aqueous layer extracted with EtOAc (4 × 50 mL). The combined extracts were dried over $MgSO_4$ and the solvent was evaporated in vacuo to give a residue that was purified by chromatography through silica gel (EtOAc/petroleum ether 8:2), affording the aminohydroxylation product **27** as a colorless oil (2.5 g, 75%): ^{1}H NMR δ 5.63−5.49 (2H, m), 5.35 (1H, m), 4.07 (4H, m), 3.09 (1H, br s), 2.41−2.10 (2H, m), 1.23 (3H, t, J = 7.1 Hz), 0.19 (3H, s), 0.16 (3H, s); ^{13}C NMR δ 155.7, 125.7, 121.3, 67.4, 61.2, 50.8, 34.2, 31.0, 14.5, −0.9, −1.7; IR (film) 3385, 1694 cm^{-1}; MS *m*/*z* 259 ($M^{\bullet+}$, 3), 75 (100); $[\alpha]^{25}_D$ +44.5 (*c* 0.47, $CHCl_3$).

(1*S*,2*S*,3*S*)-2-*N*-Ethoxycarbonylcyclohex-4-ene-1,3-diol (28). To a solution of allylsilane **27** (2.2 g, 8.5 mmol) in DMF (35 mL) were added at 0 °C $KHCO_3$ (2.6 g, 26 mmol) and KF (1.5 g, 26 mmol). A 30% H_2O_2 solution (18.6 mL, 0.27 mol) was then added dropwise over 30 min (exothermic!). After 18 h at 60 °C, the reaction mixture was cooled to 0 °C, and $Na_2S_2O_3$ was added. After filtration, the solvent was removed in vacuo to afford a pale yellow oil that was purified by chromatography through silica gel (EtOAc), affording the diol **28** as a colorless oil (1.2 g, 70%): ^{1}H NMR δ 5.75−5.66 (2H, m), 5.55 (1H, br s), 4.27 (1H, m), 4.17−4.10 (3H, m), 3.69 (1H, m), 3.34 (1H, br s), 3.00 (1H, br s), 2.51−2.22 (2H, m), 1.25 (3H, t, J = 7.2 Hz); ^{13}C NMR δ 157.8, 128.3, 125.4, 68.9, 67.6, 61.4, 57.4, 32.6, 14.5; IR (film) 3382, 1682 cm^{-1}; MS *m*/*z* 183 ($M^{\bullet+}$ − OH, 2).

Allylic Alcohol (29). The diol **28** (1 g, 5 mmol) was dissolved in dry benzene (35 mL), and then dimethoxypropane (10 mL) and *p*-TsOH (50 mg, 0.26 mmol) were added. The reaction mixture was heated under reflux for 0.5 h, cooled to room temperature, and washed with a saturated solution of Na_2CO_3. The organic layer was decanted and the aqueous layer extracted with ether. The combined extracts were dried over $MgSO_4$, and the solvent was evaporated in vacuo to give a residue that was purified by chromatography through silica gel (EtOAc/petroleum ether 8:2), affording the allylic alcohol **29** as a white solid (0.9 g, 75%), $[\alpha]^{25}_D$ −19.3 (*c* 0.71, $CHCl_3$). Recrystallization from ether/hexane gave the pure alcohol: mp 80 °C; $[\alpha]^{25}_D$ −23.3 (*c* 0.79, $CHCl_3$); ^{1}H NMR δ 5.77−5.63 (2H, m), 4.91 (1H, br s), 4.34 (1H, m), 4.19 (3H, m), 3.75 (1H, t, J = 6.3 Hz), 2.67−2.27 (2H, m), 1.58 (3H, s), 1.53 (3H, s), 1.31 (3H, t, J = 7.1 Hz); ^{13}C NMR δ 156.0, 129.0, 123.2, 92.8, 71.0, 69.9, 63.0, 62.0, 27.6, 27.5, 24.4, 14.4; IR (film) 3450, 1659 cm^{-1}; MS *m*/*z* 242 ($M^{\bullet+}$ + 1, 2). Anal. Calcd for $C_{12}H_{19}NO_4$: C, 59.72; H, 7.94; N, 5.81. Found: C, 59.60; H, 7.81; N, 5.64.

Determination of the Absolute Configuration of 27. *N*-Mesylaminocyclohexan-2-ol (30). The allylsilane **27** (0.65 g, 2.5 mmol) was dissolved in THF (10 mL), and a 1 M solution of TBAF in THF (3.8 mL, 3.75 mmol) was added dropwise.

The reaction mixture then turned red and was stirred overnight at room temperature. The solvent was evaporated in vacuo, and the residue was dissolved in EtOAc (30 mL). Pd/C (10%, 200 mg) was added to the reaction mixture, and the flask was flushed with hydrogen (3×) and then left under vigorous stirring overnight. After filtration of the catalyst, the solvent was evaporated and the residue purified by chromatography through silica gel (petroleum ether/EtOAc 4:6) to give the desired cyclohexanol (0.35 g, 75%, two steps) directly used in the next step. A mixture of hexamethyldisilazane (0.24 mL, 1.2 mmol) and iodine (0.15 g, 0.58 mmol) was refluxed until the solution became colorless. Then the preceding cyclohexanol (0.1 g, 0.53 mmol) in CH_2Cl_2 (3 mL) was added, and the yellow mixture was refluxed for 3 h and then stirred at room temperature overnight. MeOH (3 mL) was added, the solution was stirred for 10 min, and then the solvent was evaporated to give a yellow solid (0.13 g) that was dissolved in CH_2Cl_2 (5 mL). NEt_3 (0.21 mL, 1.6 mmol) and $MeSO_2Cl$ (0.038 mL, 0.53 mmol) were then added, and the reaction mixture was stirred at room temperature for 2 h. The solvent was evaporated under vacuum and the residue purified by chromatography through silica gel (petroleum ether/EtOAc 2:8) to give **30** (0.06 g, 60%, two steps): $[\alpha]^{25}_D$ +13.4 (*c* 0.8, EtOH 95%) [lit.[9c] $[\alpha]^{25}_D$ +18.8 (*c* 1, EtOH 95%)]. Spectroscopic data (^{1}H, NMR, IR) were all identical with those described in the literature.

Sharpless Aminohydroxylation of Dienylsilane 6c (31a,b). Following the general procedure described above, dienylsilane **6c** (2.2 g, 11.3 mmol) afforded after purification by chromatography through silica gel (EtOAc/petroleum ether 6:4) a 92:8 mixture of the regioisomers **31a** and **31b** (65%). **31a** (2 g): 81% ee measured from the ^{1}H NMR of the corresponding Mosher ester; ^{1}H NMR δ 5.57−5.47 (2H, m), 4.96 (1H, d, J = 6 Hz), 4.15−4.09 (3H, m), 3.92 (1H, m), 3.05 (1H, br s), 2.43−2.39 (1H, m), 2.17−2.03 (1H, m), 1.25 (3H, t, J = 6.9 Hz), 0.94 (9H, s), 0.07 (3H, s), −0.02 (3H, s); ^{13}C NMR δ 157.8, 126.4, 121.3, 67.9, 61.1, 52.4, 31.7, 30.3, 26.9, 17.3, 14.5, −6.09, −6.59; IR (film) 3439, 1698 cm^{-1}; MS *m*/*z* 299 ($M^{\bullet+}$, 11), 73 (100); $[\alpha]^{25}_D$ +108.8 (*c* 1.5, $CHCl_3$); HRMS ($C_{15}H_{29}NO_3Si$) calcd 299.1917, found 299.1912. **31b** (0.2 g): 12% ee measured from the ^{1}H NMR of the corresponding Mosher ester; ^{1}H NMR δ 5.55−5.47 (2H, m), 5.27 (1H, d, J = 8.7 Hz), 4.10−3.99 (3H, m), 3.77 (1H, m), 2.55 (1H, br s), 2.31−2.27 (1H, m), 2.05−1.98 (1H, m), 1.20 (3H, t, J = 7 Hz), 0.91 (9H, s), 0.06 (3H, br s), −0.02 (3H, s);^{13}C NMR δ 156.2, 126.0, 121.0, 69.8, 60.6, 48.8, 33.9, 27.2, 26.9, 17.2, 14.5, −6.3, −6.8; IR (film) 3396, 1703 cm^{-1}; MS *m*/*z* 299 ($M^{\bullet+}$,1), 73 (100); $[\alpha]^{25}_D$ −1.5 (*c* 0.66, $CHCl_3$).

Sharpless Aminohydroxylation of Dienylsilane 6c (32). Hydroxy carbamate **31a** (2 g, 6.7 mmol) was dissolved in dry benzene (60 mL), and dimethoxypropane (40 mL) and then *p*-TsOH (100 mg, 0.52 mmol) were added. The reaction mixture was heated under reflux for 0.75 h, cooled to room temperature, and washed with a saturated solution of Na_2CO_3. The organic layer was decanted and the aqueous layer extracted with ether. The combined extracts were washed with brine and dried over $MgSO_4$, and the solvents were evaporated in vacuo to give a crude oil that was purified by chromatography through silica gel (EtOAc/petroleum ether 95:5), affording the acetonide **32** as a pale yellow oil (1.8 g, 80%): ^{1}H NMR (toluene-d_8, 80 °C) δ 6.09−6.05 (1H, m), 5.81−5.77 (1H, m), 4.53−4.48 (2H, m), 4.31−4.23 (2H, dq, J = 7.1, 3.3 Hz), 2.43 (1H, ddd, J = 16.6, 6.9, 2 Hz), 2.16−2.09 (1H, m), 1.83 (3H, s), 1.70 (3H, s), 1.32 (3H, t, J = 7.1 Hz), 1.17 (9H, s), 0.42 (3H, s), 0.16 (3H, s); IR (film) 1703 cm^{-1}; MS *m*/*z* 339 ($M^{\bullet+}$, 10), 73 (100); $[\alpha]^{25}_D$ +62.8 (*c* 0.81, $CHCl_3$). Anal. Calcd for $C_{18}H_{33}NO_3Si$: C, 63.67; H, 9.80; N, 4.13; Si, 8.25. Found: C, 63.67; H, 9.73; N, 4.05; Si, 8.16.

Sharpless Aminohydroxylation of Dienylsilane 6c (33). Following the benzylation procedure described for **12b**, amino alcohol **31a** (1.2 g, 4 mmol) gave, after chromatography through silica gel (petroleum ether/EtOAc 8:2), the benzylated oxazolidinone **33** as a colorless oil (1.12 g, 82%): ^{1}H NMR δ 7.33−7.23 (5H, m), 5.71 (2H, m), 4.86−4.83 (1H, m), 4.72 (1H, d, J = 15.6 Hz,), 4.07−4.00 (2H, m), 2.41 (1H, dd, J = 17.5, 3.5 Hz), 2.17 (1H, dd, J = 17.5, 5.8 Hz), 2.06 (1H, m), 0.77 (9H, s), −0.12 (3H, s), −0.21 (3H, s); IR (film) 1750, 1640 cm^{-1}.

Epoxide 34. The alcohol **29** (0.27 g, 1.12 mmol) was dissolved in CH_2Cl_2 (10 mL), *m*-CPBA (0.6 g, 2.24 mmol) and Na_2HPO_4 (0.43 g, 3 mmol) were added, and the resulting white suspension was stirred for 56 h at room temperature. After addition of a saturated solution of $Na_2S_2O_3$, the aqueous layer was extracted with CH_2Cl_2. The combined extracts were washed with a saturated solution of Na_2CO_3 and dried over $MgSO_4$. The solvent was evaporated in vacuo and the crude oil purified by chromatography through silica gel (petroleum ether/EtOAc 4:6), affording the epoxide **34** as a colorless oil (0.24 g, 84%): ^{1}H NMR δ 5.29 (1H, s), 4.25−4.02 (5H, m), 3.38 (1H, m), 3.29 (1H, m), 2.65 (1H, ddd, J = 16, 8.6 and 2 Hz), 2.07 (1H, m), 1.56 (3H, s), 1.47 (3H, s), 1.30 (3H, t, J = 7.2 Hz); ^{13}C NMR δ 156.2, 92.4, 71.2, 69.6, 62.3, 60.8, 56.0, 51.0, 27.6, 24.2, 14.4; IR (film) 3392, 1662 cm^{-1}; MS *m*/*z* 258 ($M^{\bullet+}$ + 1, 13), 242 (100); $[\alpha]^{25}_D$ −44.6 (*c* 0.112, $CHCl_3$). Anal. Calcd for $C_{12}H_{19}NO_5$: C, 56.00; H, 7.45; N, 5.45. Found: C, 55.98; H, 7.42; N, 5.48.

Allylic Diol 35. To a solution of epoxide **34** (0.19 g, 0.74 mmol) in dry THF (10 mL) was added, at −80 °C, a solution of LDA (2.6 mmol) in THF (5 mL), and the resulting mixture was stirred overnight at 0 °C. The reaction mixture was then quenched with a saturated solution of NH_4Cl and the aqueous layer extracted with EtOAc. The combined extracts were washed with brine and dried over $MgSO_4$. The solvents were evaporated under vacuum, and the resulting crude oil was purified by chromatography through silica gel (petroleum ether/EtOAc 4:6), affording the diol **35** as a colorless oil (0.17 g, 89%): ^{13}C NMR δ 156.3 (s), 130.7, (d, J = 165 Hz), 126.4 (d, J = 165 Hz), 94.1 (s), 72.9 (d, J = 146 Hz), 70.7 (d, J = 147 Hz), 65.3 (d, J = 146 Hz), 62.3 (t, J = 144 Hz), 58.0 (d, J = 145 Hz), 27.5 (q, J = 128 Hz), 24.2 (q, J = 127 Hz), 14.2 (q, J = 127 Hz); IR (film) 3405, 1666 cm^{-1}; MS *m*/*z* 258 ($M^{\bullet+}$ + 1, 13); $[\alpha]^{25}_D$ +24.5 (*c* 0.67, $CHCl_3$). Anal. Calcd for $C_{12}H_{19}NO_5$: C, 56.00; H, 7.45; N, 5.45. Found: C, 55.98; H, 7.40; N, 5.36.

Triol 36. Allylic alcohol **29** (0.15 g, 0.62 mmol) was dissolved in THF (5 mL), and then $NMO{\cdot}H_2O$ (0.09 g, 0.68 mmol) and a 0.05 M solution of OsO_4 in THF (0.62 mL, 0.03 mmol) were successively added. The reaction mixture was stirred overnight at room temperature and was quenched with a 10% solution of Na_2SO_3. The organic layer was decanted and the aqueous layer extracted with EtOAc. The combined extracts were washed with brine and dried over $MgSO_4$, and the solvents were evaporated in vacuo to give the crude triol, which was recrystallized from MeOH/ether affording **36** as a white solid (0.1 g, 60%): mp 152−153 °C (MeOH/ether); ^{1}H NMR δ 4.35−4.18 (3H, m), 4.06 (1H, m), 4.01−3.88 (2H, m), 3.72 (1H, m), 2.30−2.10 (2H, m), 1.57 (3H, s), 1.51 (3H, s), 1.35 (3H, t, J = 7 Hz); IR ($CDCl_3$) 3583, 3400, 1657 cm^{-1}; MS *m*/*z* 276 ($M^{\bullet+}$ + 1, 100); $[\alpha]^{25}_D$ −7 (*c* 0.68, MeOH). Anal. Calcd for $C_{12}H_{21}NO_6$: C, 52.35; H, 7.69; N, 5.09. Found: C, 52.44; H, 7.66; N, 5.07.

1,3-Diaminocyclitol (38). To a solution of allylic alcohol **29** (0.2 g, 0.83 mmol) in dry THF (5 mL) was added tosylisocyanate (0.13 mL, 1 mmol), and the mixture was stirred for 3 h at room temperature. The solvent was evaporated under vacuum, and the crude tosyl carbamate was poured into CCl_4 (10 mL). A solution of $NaHCO_3$ (0.28 g, 3.32 mmol) in water (10 mL) was then added followed by I_2 (0.44 g, 1.7 mmol). The reaction mixture was stirred for 2 h at room temperature, diluted with CH_2Cl_2, and quenched with a saturated solution of $Na_2S_2O_3$. The organic layer was decanted and the aqueous layer extracted with CH_2Cl_2. The combined extracts were washed with brine and dried over $MgSO_4$, and the solvent was evaporated in vacuo. The crude oil was purified by chromatography through silica gel (CH_2Cl_2), affording the iodide **37** (0.28 g, 60%, two steps). This intermediate was then dissolved in CH_3CN (10 mL), and DBU (0.2 mL, 1.7 mmol) was added. The mixture was stirred overnight at room temperature and the solvent evaporated in vacuo. The crude oil was diluted in ether and quenched by a saturated solution of NH_4Cl, and the aqueous layer was extracted with ether. The combined extracts were washed with brine and dried over $MgSO_4$. The solvents were evaporated under vacuum to give an oil that was purified

by chromatography through silica gel (petroleum ether/EtOAc 6:4), affording **38** as an amorphous solid (0.11 g, 30% overall yield from **29**): ^{1}H NMR (toluene-d_8, 80 °C) δ 7.13 (2H, d, J = 8.2 Hz), 6.28 (1H, dd, J = 10.3, 2.8 Hz), 5.92 (1H, dd, J = 10.3, 4.1 Hz), 5.06 (1H, br s), 4.88 (1H, d, J = 6.8 Hz), 4.35 (1H, m), 4.27−4.15 (3H, m), 2.23 (3H, s), 1.71 (3H, s), 1.63 (3H, s), 1.29 (3H, t, J = 7.1 Hz); ^{13}C NMR (toluene-d_8, 80 °C) δ 152.9, 150.3, 95.2, 74.9, 68.2, 61.2, 55.7, 54.2, 27.5, 24.9, 20.8, 14.0; IR (film) 1800 cm^{-1}; MS m/z 437 ($M^{\bullet+}$ + 1, 1), 421 (100); $[\alpha]^{25}_D$ +81.1 (c 0.68, $CHCl_3$). Anal. Calcd for $C_{20}H_{24}N_2O_7S$: C, 55.04; H, 5.54; N, 6.42; S, 7.35. Found: C, 55.05; H, 5.63; N, 6.37; S, 7.23.

Siloxane 39. To a solution of alcohol **29** (0.3 g, 1.25 mmol) in dry ether (20 mL) were added NEt_3 (0.3 mL, 1.88 mmol) and (bromomethyl)dimethylchlorosilane (0.19 mL, 1.34 mmol). The solution was stirred at room temperature overnight. The resulting white slurry was then filtered and the solvent evaporated under vacuum. The resulting oil was purified by chromatography through silica gel (petroleum ether/EtOAc 9:1) to afford the siloxane **39** as a colorless oil (0.46 g, 94%): ^{1}H NMR δ 5.78 (2H, m), 4.39 (1H, m), 4.33−3.88 (4H, m), 2.61−2.31 (4H, m), 1.66−1.45 (6H, m), 1.29 (3H, t, J = 8 Hz), 0.28 (6H, s); IR (film) 1698 cm^{-1}; MS m/z 392 ($M^{\bullet+}$, 0.2), 171 (100). Anal. Calcd for $C_{15}H_{26}BrNO_4Si$: C, 45.92; H, 6.68; Br, 20.36; N, 3.57; Si, 7.16. Found: C, 45.99; H, 6.74; Br, 20.28; N, 3.42; Si, 7.01.

Aminocarbasugar 40. To a solution of the siloxane **39** (0.4 g, 1.02 mmol) in dry and degassed benzene (30 mL) was added via a syringe pump a mixture of Bu_3SnH (0.45 g, 1.53 mmol) and AIBN (cat.) in benzene (8 mL) under reflux over a 2 h period. The reaction mixture was then heated for an additional 1 h, and the solvent was evaporated under vacuum. The crude oil was then submitted to the general Tamao−Kumada oxidation procedure described above. The pale yellow oil thus obtained was purified by chromatography through silica gel (petroleum ether/EtOAc 2:8), affording the aminocarbasugar **40** as a colorless oil (0.25 g, 74%, two steps): ^{13}C NMR δ 155.7 (s), 92.8 (s), 75.9 (d, J = 152 Hz), 72.1 (d, J = 147 Hz), 62.3 (t, J = 140 Hz), 61.9 (t, J = 148 Hz), 61.3 (d, J = 148 Hz), 38.8 (d, J = 128 Hz), 27.2 (q, J = 127 Hz), 24.3 (q, J = 127 Hz), 21.9 (t, J = 130 Hz), 20.2 (t, J = 131 Hz), 14.2 (q, J = 127 Hz); IR (film) 3420, 1666 cm^{-1}; MS m/z 274 ($M^{\bullet+}$ + 1, 6), 258 (100); $[\alpha]^{25}_D$ −15.3 (c 0.32, $CHCl_3$). Anal. Calcd for $C_{13}H_{23}NO_5$: C, 57.13; H, 8.48. Found: C, 57.20; H, 8.52.

***cis*-Cyclohex-3-ene-1,2-diol (42).** A solution of silanol **6b** (1 g, 6.5 mmol) in tetramethyldisilazane (4 mL) was refluxed overnight. Excess disilazane was then evaporated in vacuo to give quantitatively the crude siloxane **41**, which was used in the next step without further purifications: ^{1}H NMR δ 5.70−5.55 (4H, m), 4.70 (1H, sext, J = 1.5 Hz), 2.80−2.62 (2H, m), 2.32 (1H, m), 0.19 (3H, s), 0.18 (3H, s), 0.11 (6H, s); IR (film) 3027, 2960, 2824, 2163, 1624, 1486, 1255, 1067, 911, 801, 768, 689, 661 cm^{-1}. Siloxane **41** (0.2 g, 1.3 mmol) and $H_2PtCl_6 \cdot 6H_2O$ (33 mg, 0.06 mmol) in toluene (5 mL) were refluxed for 1 h. The solvent was then evaporated in vacuo, and the crude cyclic siloxane was directly submitted to Tamao−Kumada oxidation, following the general procedure. The resulting yellow oil was purified by chromatography through silica gel (CH_2Cl_2/ether 3:2), affording the pure racemic diol **42** (64 mg, 43%, three steps). Spectroscopic data were all identical in many respects with those described in the literature.[46]

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Supporting Information Available: Spectroscopic data for compounds (−)-**4**, **10**, **12a**,**b**, **13**, **15**, **18**, **20**, **22a**,**b**, **24**, **26**−**29**, **31a**,**b**, **34**, and **41**. Preparation of (*E*,*E*)-1-bromohepta-1,3-diene. Crystal structure of **29**. This material is available free of charge via the Internet at http://pubs.acs.org.

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