Highly Versatile Stereoselective Synthesis of All Eight Stereoisomers of Branched-Chain Triols Starting from Asymmetrized Bis(hydroxymethyl)acetaldehydes (BHYMA*)

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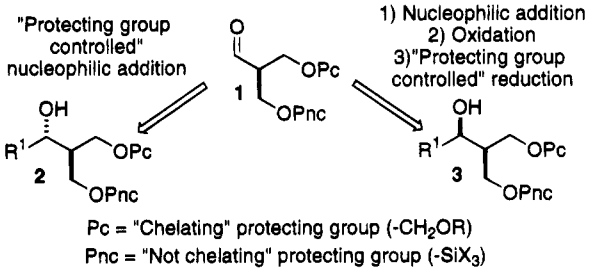
All possible stereoisomers of triols of general formula **5** (R^1 = allyl, R^2 = Me or allyl) have been synthesized stereoselectively starting from asymmetrized bis(hydroxymethyl)acetaldehyde (BHYMA*), a novel chiral building block prepared through a chemoenzymatic methodology. This goal was realized through a sequence of protecting group-controlled nucleophilic additions and/or reductions performed on two side arms of this versatile building block.

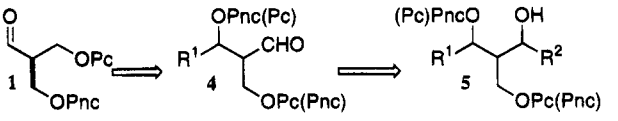
Introduction

We have recently reported the chemoenzymatic preparation of both enantiomers of various diprotected bis(hydroxymethyl)acetaldehydes (BHYMA*) **1**, as new chiral building blocks.[1] We have also demonstrated the possibility to convert diastereoselectively aldehydes **1** into both diastereoisomers of secondary alcohols **2** and **3** (Scheme 1).[2] The stereocontrol was based on the different coordinating capabilities of the two β-oxygens, whose Lewis basicity was modulated by placing on them a "nonchelating" protecting group, like a silyl ether,[3] or a "chelating" protecting group, like an alkoxyalkyl ether ("protecting group-controlled asymmetric synthesis"). This fact allowed good to excellent diastereoselectivities to be achieved in nucleophilic additions to BHYMA* (or to ketones derived from it) proceeding through cyclic chelated transition states.[2] In order to obtain both stereoisomers **2** and **3**, two complementary routes were followed: the first one involves direct chelation controlled addition of organometal compounds to **1**,[2a-g] while in the second one **1** was first converted to the corresponding ketones which then underwent chelation-controlled reduction.[2g,h] A second alternative route for the stereodivergent obtainment of both **2** and **3** exploits the synthetic equivalence of the two protected hydroxymethyl groups in **2** and **3**, which allows easy conversion of **2** into the enantiomer of **3** (and *vice versa*) by a simple protecting group interchange. Since, as already pointed out, both enantiomers of **1** are available, this property, which

Scheme 1



Scheme 2



descends from the latent C_{3v} symmetry of **1**,[2a] allows the synthesis of both **2** or **3**.

We have now proceeded one step further and have examined the possibility of transforming **1** into all eight possible stereoisomers of branched-chain triols of general formula **5**[4] (Scheme 2). These substructures are important since they can be found in many biologically active molecules, like, *e.g.*, in thienamycin[2e] or in the ansa chains of streptovaricin[5] and amphotericin.[6] For this purpose we planned to exploit once again the protocol already employed for the synthesis of **2** and **3**, based on the chelation-controlled (protecting group-controlled) nu-

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(1) Guanti, G.; Banfi, L.; Narisano, E. *J. Org. Chem.* **1992,** *57,* 1540–1554.

(2) (a) Guanti, G.; Banfi, L.; Narisano, E. *Tetrahedron Lett.* **1990,** *31,* 6421–6424. (b) Guanti, G.; Banfi, L.; Ghiron, C.; Narisano, E. *Tetrahedron Lett.* **1991,** *32,* 267–270. (c) Guanti, G.; Banfi, L.; Narisano, E. *Tetrahedron Lett.* **1991,** *32,* 6939–6942. (d) Guanti, G.; Banfi, L.; Narisano, E.; Zannetti, M. T. *J. Org. Chem.* **1993,** *58,* 1508–1514. (e) Guanti, G.; Banfi, L.; Narisano, E. *Tetrahedron* **1993,** *49,* 7385–7392. (f) Guanti, G.; Banfi, L.; Schmid, G. *Tetrahedron Lett.* **1994,** *35,* 4239–4242. (g) Guanti, G.; Banfi, L.; Zannetti, M. T. *Tetrahedron Lett.* **1993,** *34,* 5487–5490. (h) Guanti, G.; Banfi, L.; Riva, R.; Zannetti, M. T. *Tetrahedron Lett.* **1993,** *34,* 5483–5486.

(3) The low tendency of trialkylsilyl ethers to coordinate metal ions is well documented, although it is still debated whether this fact is solely of steric origin or is also due in part to stereoelectronic reasons: (a) Chen, X.; Hortelano, E. R.; Eliel, E. L.; Frye, S. V. *J. Am. Chem. Soc.* **1992,** *114,* 1778–1784. (b) Shambayati, S.; Blake, J. F.; Wierschkae, S. G.; Jorgensen, W. L.; Schreiber, S. L. *J. Am. Chem. Soc.* **1990,** *112,* 697–703. (c) Kahn, S. D.; Keck, G. E.; Hehre, W. *J. Tetrahedron Lett.* **1987,** *28,* 279–280. (d) Keck, G. E.; Castellino, S. *Tetrahedron Lett.* **1987,** *28,* 281–284.

(4) McGarvey, G. J.; Wilson, K. J.; Shanaoltz, C. E. *Tetrahedron Lett.* **1992,** *33,* 2641–2644.

(5) (a) Wang, Z.; Schreiber, S. *Tetrahedron Lett.* **1990,** *31,* 31–34. (b) Mootoo, D. R.; Fraser-Reid, B. *J. Org. Chem.* **1987,** *52,* 4511–4517. (c) Roush, W. R.; Palkowitz, A. D. *J. Org. Chem.* **1989,** *54,* 3009–3011.

(6) (a) Nicolaou, K. C.; Daines, R. A.; Uenishi, J.; Papahatjis, D. P.; Chakraborty, T. K. *J. Am. Chem. Soc.* **1988,** *110,* 4672–4685. (b) Hanessian, S.; Sahoo, S. P.; Botta, M. *Tetrahedron Lett.* **1987,** *28,* 1147–1150. (c) Boschelli, D.; Ellingboe, J. W.; Masamune, S. *Tetrahedron Lett.* **1984,** *25,* 3395–3398.

(7) The synthetic scheme from **1** to **5** presents indeed six binary variables which can be chosen at will: (a) we can start from (*R*)- or (*S*)-**1**; (b) we can introduce R^1 first and R^2 second or *vice versa*; (c) we can create the second stereocenter by organometal additions or by reduction; (d) we can create the third stereocenter by organometal additions or by reduction; (e) After the introduction of the second stereocenter we can chose at will on which of the two remaining hydroxymethyl side arms to perform the second addition; (f) we can carry out, or not, a protecting group interchange (that is replace a "chelating" group with a "not chelating" one or *vice versa*) between the generation of second and third stereocenter. Thus there are 2^6 possibilities, 2^3 for each stereoisomer.

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cleophilic additions or reductions to differently protected β,β'-dihydroxyaldehydes or ketones. It should be noted that in principle by this strategy each of the eight stereoisomers of **5** can be prepared in eight independent ways.[7] However, of course, some of these possibilities may turn out to be practically not viable, because of scarce stereoselectivity or of chemoselectivity problems in the introduction or removal of protecting groups.

Results and Discussion

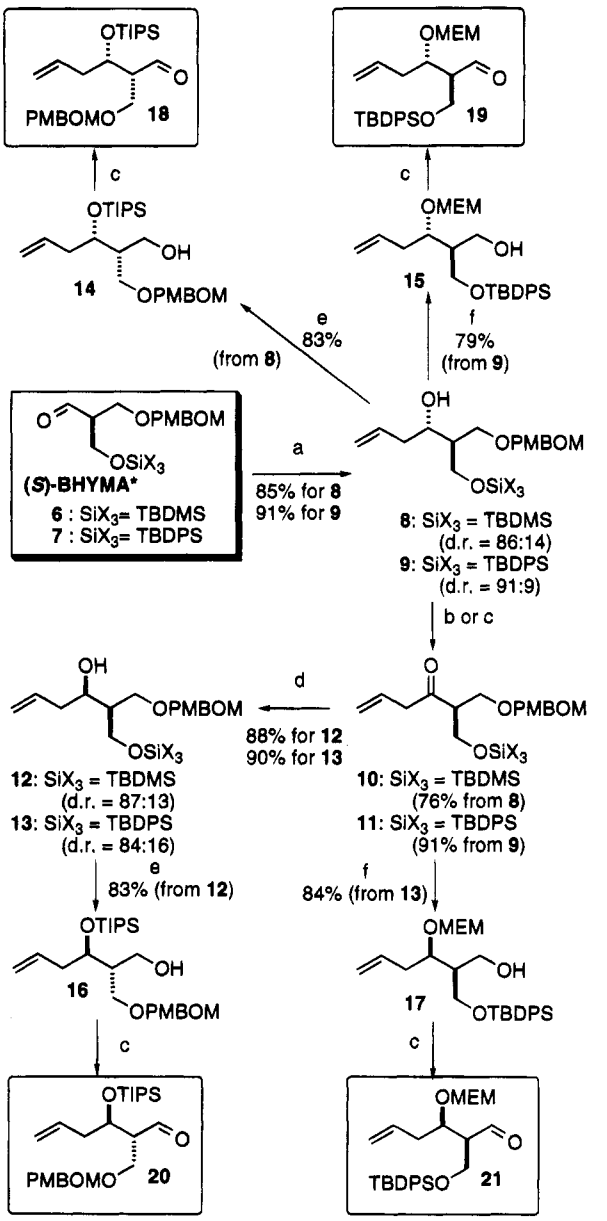
The most important point was to check whether the concept of "protecting group control stereoselection" could still be implemented efficiently in the presence of an additional stereocenter. In order to answer this question, we first prepared a series of four aldehydes of general formula **4**, having the two possible relative configuration and a "chelating" and a "not chelating" protecting groups on the two alcoholic functions (Scheme 3). We chose the allyl group as R^1 and thus synthesized the epimeric pairs **8,12** and **9,13** by previously reported procedures. The adducts **8** and **9** were prepared in excellent chemical yield and high diastereoselectivity by addition of allyl-Sn(nBu)$_3$ in the presence of $MgBr_2 \cdot Et_2O$[2c,d,f] to BHYMA* **6** and **7**, while the adducts **12** and **13** were prepared by oxidation of **8** or **9**, through a modified Swern procedure, followed by diastereoselective reduction with DIBALH and $MgBr_2 \cdot Et_2O$.[2h] The choice of protecting groups was dictated by the need for selective deblocking in the ensuing steps. For this reasons we chose, as "chelating group", the [(p-methoxybenzyl)oxy]methyl (PMBOM)[8] which can be oxidatively removed under conditions compatible with most other acetal-type protections. Aldehydes **18** and **20**, which have the "not chelating" protecting group on the secondary alcohol, required a selective removal of a silyl ether in the presence of another one. For this purpose we started from TBDMS-protected aldehydes **8** and **12** and introduced a TIPS group on the secondary alcohol, taking then advantage of the selective desilylation procedure recently developed by us, which employs p-TSA in anhydrous isopropyl alcohol.[2e] Alcohols **14** and **16** were thus obtained in excellent overall yield and converted, by modified Swern oxidation, into aldehydes **18** and **20** characterized by the presence of a "chelating" protecting group on the primary alcohol and of a "not chelating" protecting group on the secondary alcohol.

On the other hand, aldehydes **19** and **21** were synthesized by protecting the secondary alcohol of adducts **9** and **13** as MEM, another chelating protecting group[9] and by selectively deblocking the primary [(p-methoxybenzyl)-oxy]methyl ether under oxidative conditions.[8,10] The resulting alcohols **15** and **17**, after modified Swern oxidation, furnished aldehydes **19** and **21**, characterized by the presence of a "not chelating" protecting group on the primary alcohol and of a "chelating" protecting group on the secondary alcohol.

We then studied the methylation[2a] and allylation[2c,d,f] of aldehydes **18-21** to give alcohols **22-29** (Scheme 4) under conditions which have been previously demonstrated to favor a cyclic chelated transition state, that is using Me_2CuLi or allyl-Sn(nBu)$_3$ in the presence of $MgBr_2 \cdot Et_2O$ respectively.[11] The results of these reactions are reported in Table 1. In most cases the diastereoselectivity was excellent, even superior to that of the

Scheme 3

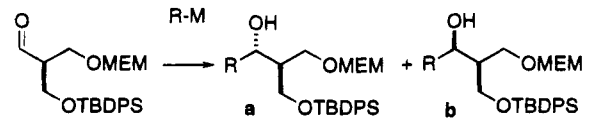
SCHEME 3



a) Allyl-SnBu$_3$, $MgBr_2 \cdot Et_2O$. b) Jones oxidation. c) Modified Swern oxidation. d) DIBALH, $MgBr_2 \cdot Et_2O$. e) 1) (iPr)$_3$Si-OTf, 2,6-lutidine. 2) pTSA, iPrOH, 4Å mol. sieves, 0°C. f) 1) MEM-Cl, Et(iPr)$_2$N. 2) DDQ, tBuOH, pH 7 buffer, CH_2Cl_2.

(8) Kozikowski, A. P.; Wu, J. P. *Tetrahedron Lett.* **1987**, *28*, 5125–5128.

(9) Since in previous studies we have never used the MEM protecting groups, we checked its efficacy as "chelating" protecting group in nucleophilic additions by the following reactions:



The reaction with Me_2CuLi (R = Me) gave an **a/b** ratio 95:5 (yield = 65%), while the reaction with allyl-Sn(nBu)$_3$/$MgBr_2 \cdot Et_2O$ (R = Allyl) afforded an **a/b** ratio of 89:11 (yield = 89%). These results are quite comparable with those achieved with other alkoxyalkyl protecting groups like BOM and PMBOM (refs 2a,c,d).

(10) In this case the *tert*-butyldiphenylsilyl (TBDPS) group gave better yields than the TBDMS in the reaction with MEM–Cl.

(11) For a comparison we also reacted aldehydes **18-21** with MeLi in Et_2O at −78 °C. The results (**22a/22b** 79:21; **24a/24b** 76:24; **26a/26b** 48:52; **28a/28b** 21:79) are in accord with a Felkin model where the allylCH(OR)- plays the role of "large" group.

Scheme 4

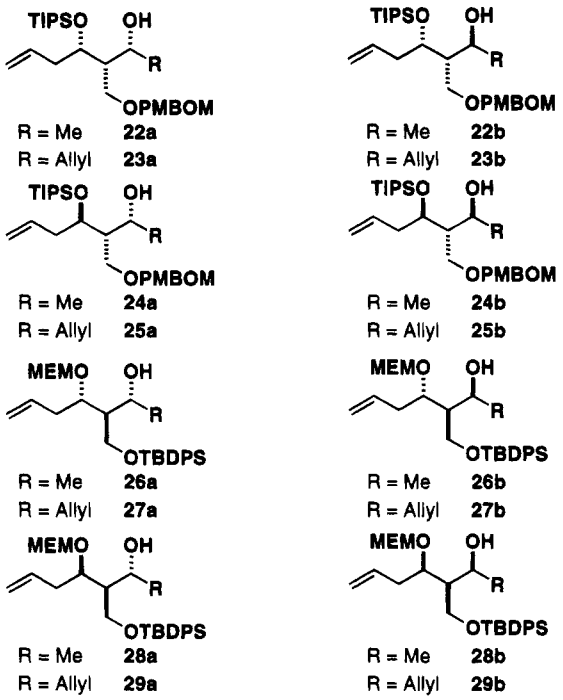


Table 1. Results of Addition of Organometal Reagents R–M to aldehydes 18-21

entry	aldehyde	reagent	products[a]	a/b ratio	% yield[b]
1	18	Me_2CuLi	22a,b	>97:3	79
2	18	allyl-$SnBu_3$/$MgBr_2$	23a,b	95:5	97
3	20	Me_2CuLi	24a,b	>97:3	85
4	20	allyl-$SnBu_3$/$MgBr_2$	25a,b	87:13	86
5	19	Me_2CuLi	26a,b	45:55	85
6	19	allyl-$SnBu_3$/$MgBr_2$	27a,b	92:8	86
7	21	Me_2CuLi	28a,b	>97:3	56
8	21	allyl-$SnBu_3$/$MgBr_2$	29a,b	95:5	91

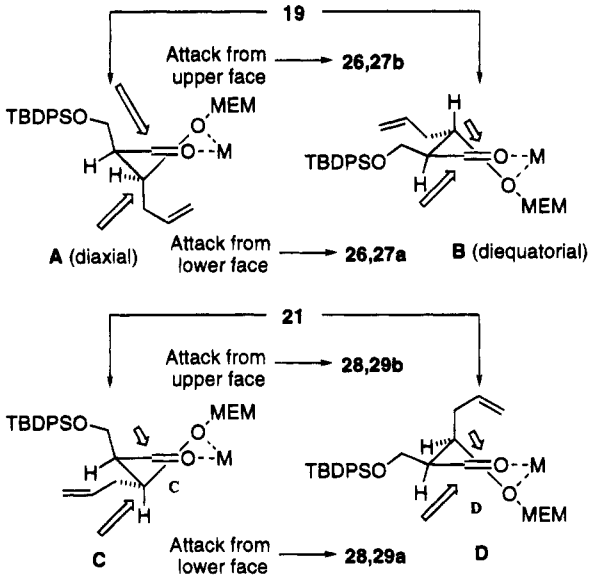
[a] See Scheme 4. [b] Isolated yields of both stereoisomers of two steps (Swern oxidation and nucleophilic addition).

corresponding additions to BHYMA*. The only exception is represented by reaction of Me_2CuLi with aldehyde **19** (entry 5).

When the chelating protecting group is placed on the primary alcohol (entry 1–4), the high stereoselectivity was not surprising: if we suppose, in fact, the intervention of a cyclic chelated transition state, in this case the additional chiral center in β-position to the carbonyl should have little influence on the stereochemical course, because it is positioned outside of the ring. Thus the diastereoselectivity is fully controlled by the α stereocenter. The slight increase in stereoselection may be due to the increased bulkiness of the substituent not involved in chelation.

On the contrary, when the chelating protecting group is placed on the secondary alcohol (entries 5 and 6), the stereocenter in β-position to the carbonyl may influence the selectivity, because it is encompassed in the six-membered ring. From the reported data we can say that in **21** the controls by α and β stereocenters are "matched", leading to excellent induction for both nucleophiles (entries 7 and 8), while in **19** the two controls are "mismatched" (Scheme 5). However the influence of reagent employed is striking. When the nucleophilic reagent was allyl-$Sn(nBu)_3$ in the presence of $MgBr_2$ (entry 6), good selectivity in favor of the expected diastereoisomer **27a** was in fact detected also in the mismatched case, the effect of β stereocenter being nearly negligible (compare entries 6 and 8). On the other hand the induction was almost absent when the nucleophilic reagent was Me_2CuLi (entry 5), and the unexpected stereoisomer **26b** was even slightly favored. This fact is in good agreement with the results of addition of Me_2CuLi to 3-[(benzyloxy)methoxy]-2-methylbutanal, previously reported by Still.[12] It is anyway interesting to note that, in the light of the high diastereoselectivity of entries 6–8, the presence of the chelating protecting group on the secondary alcohol does not seem to decrease in general the capability of the β-oxygen to form a cyclic chelated transition state.[9]

Scheme 5



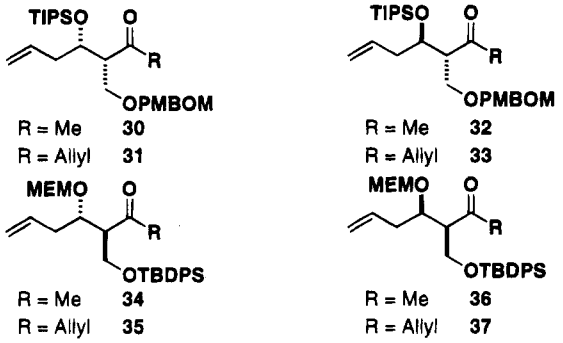
In order to explain the stereochemical behavior of addition to aldehydes **19** and **21** it is important to consider the two possible half-chair conformations of cyclic adducts deriving from chelation of a metal (M) by the carbonyl and the MEM oxygens for each aldehyde.[13]

(12) Still, W. C.; Schneider, J. A. *Tetrahedron Lett.* **1980**, *21*, 1035–1038 [matched case 20:1; mismatched case 2.3:1 (α control predominates as in our case)].

(13) (a) Keck, G. E.; Castellino S. *J. Am. Chem. Soc.* **1986**, *108*, 3847–3849; (b) Keck, G. E.; Castellino, S.; Wiley, M. R. *J. Org. Chem.* **1986**, *51*, 5480–5482. Recent reviews on allylstannane addition to aldehydes: (c) Yamamoto, Y.; Asao, N. *Chem. Rev.* **1993**, *93*, 2207–2293. (d) Nishigaichi, Y.; Takuwa, A.; Naruta, Y.; Maruyama, K. *Tetrahedron* **1993**, *49*, 7395–7426.

(14) This must depend both on the conformational equilibrium between **A** and **B** and on their relative reactivity. With regard to the first point, at first sight one may presume the diequatorial conformation **B** to be more stable. However, the important NMR studies previously reported by Keck on the conformational equilibrium in chelates derived from β-alkoxyaldehydes (refs 13a,b), suggest that this assumption may be wrong. In those papers it was indeed demonstrated that while an α-substituent tends to stay in pseudo-equatorial position, a β-substituent usually prefers to be axial. From those findings, **A** and **B** are expected to have comparable energy. Moreover, other arguments corroborate the hypothesis of a similar energy for **A** and **B**: while in *trans*-3,4-dimethylcyclohexene the diequatorial conformation is favored, although by a small difference, (≈0.71 Kcal/mol) (ref 15), in the present case: (a) in **B** the nonbonding interaction of $CH_2OTBDPS$ with the allyl group, as well as with the aldehydic hydrogen seems more destabilizing than the similar ones involving two methyl groups; (b) the "gauche" interaction which is the main destabilizing factor in 4-axially substituted cyclohexenes is in the case of **A** less important, because both O–M and M–L (metal–ligand) bonds are surely longer than C–C bonds [see Evans D. A.; Nelson J. V., Taber T. R. *Top. Stereochem.* **1982**, *13*, 1–115 (p 38)], thus minimizing 1,3-diaxial interactions with the allyl. For a related discussion on half-chair conformations of β-chelated transition states for mismatched cases, see: Narasaka, K.; Pai, F.-C. *Tetrahedron* **1984**, *40*, 2233–2238.

Scheme 6



It is easy to see that in both conformations **C** and **D**, arising from **21**, the attack from the lower face should be favored. In fact, while in **C** the β stereocenter seems to have little effect, in **D** the axial allyl group and the pseudo-equatorial OTBDPS should cooperate in encumbering the upper face (matched case). On the other hand, in the case of **19**, a different behavior is to be expected depending of which conformation (**A** or **B**) is the reacting one.[14] In **B** the allyl group is expected to have little influence; thus α control should predominate, leading to diastereoisomers **26,27a**, in line with the results obtained in the absence of a β chiral center.[2a-d] On the contrary in **A** the attack from the lower face is disfavored by a 1,3-diaxial interaction between the incoming nucleophile and the axial allyl group; the α and β controls in this case oppose each other (mismatched case) and a low stereoselectivity is expected. This reasoning suggests that allylation may proceed mainly through conformation **B**, leading to **27a** with good stereoselection, while methylation may take place through **A** (or through both **A** and **B**), affording a mixture of **26a** and **26b** with low selectivity.[16]

In order to extend the stereochemical versatility of the synthesis of protected triols **5** from BHYMA*, we investigated also the outcome of the diastereoselective "protecting group-controlled" reduction of α,α'-bis(hydroxymethyl)ketones, employing the novel methodology recently developed by us,[2g,h] based on the reaction of DIBALH with the ketones precomplexed with $MgBr_2 \cdot Et_2O$. For this purpose we prepared **30–37** (Scheme 6) by oxidation of adducts **22–29** with the Jones methodology (yields were in the range 67–94%).

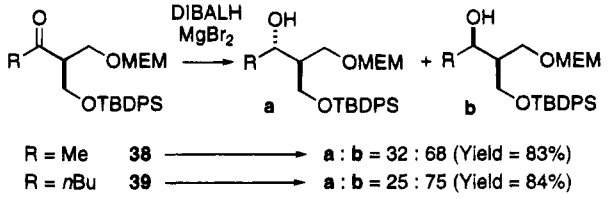
The results of reductions are reported in Table 2. Good selectivity was observed only in the case of reduction of ketones **30–33**, where the chelating protecting group PMBOM is on the primary alcohol; low selectivity was

Table 2. Results of Reduction with DIBALH/$MgBr_2$ of Ketones 30–37

entry	ketone[a]	products[b]	a/b ratio	% yield[c]
1	30	22a,b	**<5:95**	93
2	31	23a,b	**<5:95**	79
3	32	24a,b	**16:84**	87
4	33	25a,b	**20:80**	69
5	34	26a,b	60:40	76
6	35	27a,b	27:73	86
7	36	28a,b	43:57	60
8	37	29a,b	38:62	84

[a] See Scheme 5. [b] See Scheme 4. [c] Isolated yields of both stereoisomers.

Scheme 7



instead invariably detected for ketones **34–37**, where the chelating protecting group MEM is placed on the secondary alcohol. This finding is somewhat surprising, because also the "matched" case, involving ketones **36** and **37** gave unsatisfactory results (however, the expected adducts **28b** and **29b** were still slightly favored). In this case the only reasonable explanation is that chelation is not as efficient as for the PMBOM protected primary alcohols, like **30-33**. In order to check whether the problem was the protecting group or the fact that the alcohol was secondary instead of primary, we prepared ketones **38** and **39** and subjected them to the same reduction conditions (Scheme 7). The diastereoselectivities observed were inferior than the ones achieved with PMBOM instead of MEM as the "chelating" protecting group (9:91 for R = *n*Bu),[2h] suggesting that the MEM group has lower tendency for giving chelated transition states in this reaction. This fact may be due to the presence in MEM of an additional oxygen. Thus a triple metal co-ordination not involving the carbonyl oxygen is in this case possible. Obviously, if reaction goes through this chelated intermediate not involving the carbonyl, the stereoselectivity should be modest. But then, why would this problem be unimportant in the $MgBr_2$-mediated allylation? In our opinion, the difference lies in the fact that while DIBALH reacts well also in the absence of $MgBr_2$, in the case of allylation the reaction takes place only if $MgBr_2$ is coordinated by the carbonyl oxygen.[17] Thus, we think that maybe an increase of selectivity in these reductions could be achieved by the use of a different chelating protecting group for the secondary alcohol.

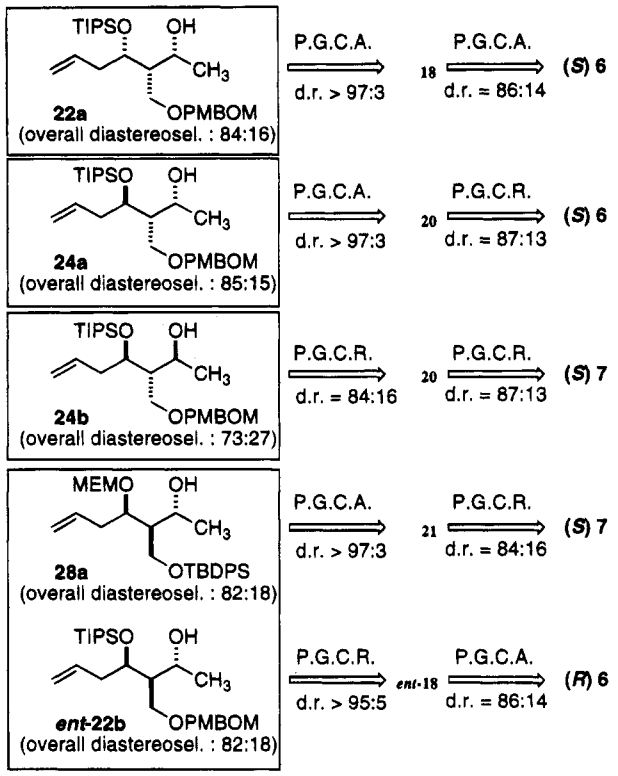
The relative configuration of adducts **22–29** was established through: (a) deblocking of the protecting group on the primary alcoholic function; (b) conversion of the resulting diols into the *O,O*-isopropylidene derivatives by reaction with 2-methoxypropene and *p*TSA.[2d,e] (**c**) ^1H and ^{13}C NMR analysis on them. At ^1H NMR, particularly diagnostic were the coupling constants be-

(15) (a) Anet, F. A. L. Conformational Analysis of Cyclohexenes. In *The Conformational Analysis of Cyclohexenes, Cyclohexadienes, and Related Hydroaromatic Compounds*; Rabideau, P. W. ,Ed.; VCH: Cambridge, U.K., 1989. (b) Allinger, N. L.; Hirsch, J. A.; Miller, M. A.; Tyminski, I. *J. Am. Chem. Soc.* **1968**, *90*, 5773–5788.

(16) This difference in behavior between allyl-$SnBu_3$ and Me_2CuLi is somewhat unexpected. If conformations **A** and **B** are equally stable, and the product composition reflects the conformation stability, one would expect indeed a low selectivity also for the allylation reaction. A possible explanation could be a shift in the conformational equilibrium in the two cases, due to the different Lewis acid involved. On the other hand, an alternative hypothesis is that, in the reaction with allyl-$SnBu_3$, the product ratio depends more on the relative reactivity of the two conformations than on their stability (Curtin–Hammet principle). This may be due to a more product-like transition state in this reaction. Thus the reaction proceeds mainly through conformation **B**, irrespective of the equilibrium position, because attack from the lower face in **B** is the less sterically disfavored among the four possible. On the contrary, if the reaction with Me_2CuLi is more reagent-like, the factors affecting the equilibrium between **A** and **B** should be most important.

(17) Although allyltributyltin is known to react with aldehydes even in the absence of Lewis acids, the reaction is by far slower and takes place only at room temperature or higher. The catalytic effect of $MgBr_2$ is therefore very great. See (a) Yamamoto, Y. *Acc. Chem. Res.* **1987**, *20*, 243–249. (b) Roush, W. R. in *Comprehensive Organic Synthesis*; Heathcock, C. H., Ed.; Pergamon, Oxford, 1992; Vol. 2.

Scheme 8



tween H-4 and H-5 and between H-5 and H-6 (1,3-dioxane numbering). ^{13}C NMR confirmed that all these isopropylidene derivatives were in chair conformation[18] (thus justifying attributions made on the basis of coupling constants). Furthermore the chemical shifts of C-5 carbons were in line with a trend previously observed by us on similar compounds.[2de,19]

Conclusion

In conclusion we want to emphasize that, although not all the protecting group controlled transformation studied turned out to be stereochemically efficient, nevertheless, thanks to the high stereochemical versatility of BHYMA*, and to the complementarity of addition and reduction reactions, we have been able to find at least one efficient route to each of the eight possible stereoisomers of triols **5** (R^1 = allyl, R^2 = allyl or methyl). To better illustrate this point, Scheme 8 summarizes the best protocols (among those explored by now)[20] for the synthesis of protected compounds corresponding to triols **5** (R^1 = allyl, R^2 = Me). Obviously, the availability of both enantiomers of BHYMA* **6** and **7** allows also the preparation of the enantiomers of the compounds shown in the scheme. It is worth noting that **28a** and ***ent*-22b** have the same stereochemistry and are differentiated only by the protecting groups. Thus two different routes, equally efficient, for the preparation of this particular isomer are indeed possible.

Further improvement of this strategy and its application to the synthesis of biologically active products are in progress.

Experimental Section

All NMR spectra were taken in $CDCl_3$ at 200 MHz (^1H) or 50 MHz (^{13}C). Chemical shifts are reported in ppm (δ scale), coupling constants are reported in Hertz. Peak assignment in ^1H NMR spectra, was made with the aid of double resonance experiments: an asterisk (*) means that the value was determined in that way. Peak assignment in ^{13}C spectra was made with the aid of DEPT experiments. Polarimetric values were measured at 20 °C. TLC analyses were carried out on silica gel plates, which were developed by spraying a solution of $(NH_4)_4MoO_4 \cdot 4\ H_2O$ (21g) and $Ce(SO_4)_2 \cdot 4\ H_2O$ (1g) in H_2SO_4 (31 mL) and H_2O (469 mL) and warming. R_f were measured after an elution of 7–9 cm. Chromatographies were carried out on 70–230 mesh silica gel using the "flash" methodology. HPLC analyses were carried out with an Erbasil 10 μm silica column, using an UV dectector at 254 nm and *n*-hexane/diethyl ether as eluant. Petroleum ether (40–60 °C) is abbreviated as PE. In extractive workup aqueous solutions were always reextracted three times with the appropriate organic solvent. Organic extracts were dried over Na_2SO_4 and filtered, before evaporation of the solvent under reduced pressure. All reactions employing dry solvents were carried out under a nitrogen atmosphere. Preparation of (*S*)-BHYMA* **6** is described in ref 2e. Preparation of homoallylic alcohol **9** from **7** is described in ref 2d.

(2*S*,3*S*)-1-[(*tert*-Butyldimethylsilyl)oxy]-2-[[[(*p*-methoxybenzyl)oxy]methoxy]methyl]-5-hexen-3-ol (8).[2f] A solution of crude aldehyde **6**[2e] (4.27 g, 11.6 mmol) in dry CH_2Cl_2 (75 mL) was treated with 4 Å powdered molecular sieves (1 g) and stirred at rt for 15 min. The mixture was cooled to −78 °C and treated with $MgBr_2 \cdot Et_2O$ (6.50 g, 25.5 mmol) and, after 10 min, with allyl-Sn(*n*-Bu)$_3$ (7.1 mL, 22.9 mmol). After 2 h at −78 °C, the temperature was allowed to rise slowly (during 1 h and 30 min) to −40 °C. The reaction was then quenched with saturated aqueous NH_4Cl, filtered through a Celite cake, and extracted with Et_2O to give a crude product. A first chromatography (PE/Et_2O 7:3) gave a mixture of **8** and **12** (86:14, determined by ^1H NMR analysis), slightly contaminated with some tributyltin derivatives. A second chromatography (PE/Et_2O 7:3) afforded either the pure mixture of **8** and **12** (4.05 g, overall yield = 85%), or pure diastereoisomer **8** as an oil. R_f 0.27 (PE/Et_2O 7:3). Anal. Calcd for $C_{22}H_{38}O_5Si$: C, 64.35; H, 9.33. Found: C, 64.6; H, 9.5. $[\alpha]_D$ = −1.2° (*c* 2, $CHCl_3$). ^1H NMR: δ 0.07 (6H, s); 0.89 (9H, s); 1.86 (1H, hexuplet, *J* 4.8); 2.33 (2H, t, *J* 7.0); 3.22 (1H, d, *J* 4.2); 3.81 (3H, s); 3.65–4.00 (5H, m); 4.54 (2H, s); 4.73 (2H, s); 5.00–5.16 (2H, m); 5.87 (1H, ddt, *J*(t) 7.0, *J*(d) 10.2 and 17.1); 6.88 (2H, d, *J* 8.8); 7.26 (2H, d, *J* 8.8).

(*S*)-1-[(*tert*-Butyldimethylsilyl)oxy]-2-[[[(*p*-methoxybenzyl)oxy]methoxy]methyl]-5-hexen-3-one (10). A solution of $(COCl)_2$ (0.218 mL, 2.50 mmol) in dry CH_2Cl_2 (10 mL) was cooled to −78 °C and treated with a 2.8 M solution of DMSO in dry CH_2Cl_2 (1.43 mL, 4.00 mmol). After 10 min, a solution of the diastereomeric mixture of alcohols **8** and **12** obtained as above described (411 mg, 1.00 mmol) in CH_2Cl_2 (5 mL) was added. After 10 min Et_3N (1.11 mL, 8.00 mmol) was introduced, and the mixture was allowed to react at −78 °C until the reaction was complete at TLC (3 h) and then quenched at −78 °C with 5% aqueous $NH_4H_2PO_4$ (15 mL) followed by 1 M HCl (10 mL). After warming to rt, the pH was adjusted to 3 with 1 M HCl, and the aqueous phase was extracted with Et_2O. The organic extracts, washed with saturated NaCl and evaporated to dryness, gave, after chromatography (PE/Et_2O 8:2), 310 mg of ketone **10** as a colorless oil (yield = 76%). R_f 0.50 (PE/Et_2O 7:3). Anal. Calcd for $C_{22}H_{36}O_5Si$: C, 64.67 H, 8.88. Found: C, 64.5; H, 8.95. $[\alpha]_D$ = +13.2° (*c* 2, $CHCl_3$). ^1H NMR: δ 0.03 (3 H, s); 0.04 (3H, s); 0.87 (9H, s); 3.06 (1H, quintuplet, *J* 6.5); 3.32 and 3.34 (2H, AB part of an ABX system, J_{AB} 1.3, J_{AX}, J_{BX} 6.9); 3.68 and 3.79 (2H, AB part of an ABX system, J_{AB} 9.9, J_{AX} 5.5, J_{BX} 10.3);

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(20) For the preparation of compounds **5** (R^2 = allyl) more routes than those shown are available thanks to the more general efficiency of protecting group controlled addition. Moreover, as already stated in note 7, many other routes, either for R^2 = Me or R^2 = allyl are indeed in principle possible: for example we have not here explored the introduction of Me first, or the protecting group interchange.

3.78 (2H, d, *J* 6.0); 3.81 (3H, s); 4.48 (2H, s); 4.67 (2H, s); 5.06–5.23 (2H, m); 5.95 (1H, ddt, *J*(t) 6.8, *J*(d) 10.3, and 17.1); 6.83–6.95 (2H, m); 7.23–7.35 (2H, m).

(*S*)-1-[(*tert*-Butyldiphenylsilyl)oxy]-2-[[[(*p*-methoxybenzyl)oxy]methoxy]methyl]-5-hexen-3-one (11). A solution of a 91:9 diastereomeric mixture of alcohols **9** and **13**[2d] (535 mg, 1.00 mmol) in acetone (5 mL), cooled to 0 °C, was treated slowly with approximately 50 drops of Jones reagent[21] (prepared from 10 g of CrO_3, 8.6 mL of 96% H_2SO_4, 14 mL of H_2O, and brought up to 40 mL). After 20 min the reaction was quenched with 1 M KH_2PO_4, treated with few milliliters of 10% $Na_2S_2O_5$, diluted with Et_2O, and filtered through a Celite cake. Extraction with Et_2O, evaporation under reduced pressure, and chromatography (PE/Et_2O 7:3) gave 485 mg of pure ketone **11** as an oil (yield = 91%). R_f 0.37 (PE/Et_2O 7:3). Anal. Calcd for $C_{32}H_{40}O_5Si$: C, 72.14 H, 7.57. Found: C, 71.8; H, 7.75. $[\alpha]_D = +10.4°$ (*c* 2, $CHCl_3$). ^1H NMR: δ 1.03 (9H, s); 3.10 (1H, quintuplet, *J* 6.5); 3.34 (2H, d, *J* 6.8); 3.68 and 3.88 (2H, AB part of an ABX system, J_{AB} = 0.8, J_{AX} 5.5, J_{BX} 7.0); 3.70–3.90 (2H, m); 3.80 (3H, s); 4.36 (2H, s); 4.63 (2H, s); 5.10 and 5.18 (2H, AB part of an ABX system, J_{AB} 2.0, J_{AX} 17.5, J_{BX} 10.4]; 5.94 (1H, ddt, *J*(t) 6.8, *J*(d) 10.3 and 17.1); 6.83–6.95 (2H, m); 7.23–7.55 (8H, m); 7.60–7.72 (4H, m).

(2*S*,3*R*)-1-[(*tert*-Butyldimethylsilyl)oxy]-2-[[[(*p*-methoxybenzyl)oxy]methoxy]methyl]-5-hexen-3-ol (12). Ketone **10** (409 mg, 1.00 mmol), dissolved in dry Et_2O (3 mL) was treated with 4 Å powdered molecular sieves (activated overnight in oven at 250 °C) (70 mg) and stirred at rt for 30 min. The mixture was cooled to −78 °C and treated with $MgBr_2 \cdot Et_2O$ (1.29 g, 5.00 mmol). After the mixture was stirred at this temperature for 15 min, a 1 M solution of DIBALH in toluene (2.00 mmol, 2.00 mL) was added. After 15 min at −78 °C the reaction was quenched by addition of a saturated solution of NH_4Cl, diluted with a saturated solution of sodium and potassium tartrate, and stirred for 1 h at rt. The phases were separated and the organic layer, after drying, evaporation in vacuo, and chromatography (PE/Et_2O 7:3) gave 361 mg of a diastereoisomeric mixture of **8** and **12** (overall yield = 88%; **8**/**12** 13:87, determined by ^1H NMR analysis). Further chromatography (PE/Et_2O 7:3) gave pure diastereoisomer **12** as an oil. R_f 0.30 (PE/Et_2O 7:3). Anal. Calcd for $C_{22}H_{38}O_5Si$: C, 64.35; H, 9.33. Found: C, 64.6; H, 9.4. $[\alpha]_D = +6.94°$ (*c* 2, $CHCl_3$). ^1H NMR: δ 0.08 (6H, s); 0.90 (9H, s); 1.84 (1H, hexuplet, *J* 5.3); 2.36 (2H, t, *J* 7.0); 3.33 (1H, d, *J* 5.7); 3.70 and 3.76 (2H, AB part of an ABX system, J_{AB} 9.6, J_{AX} 6.45, J_{BX} 5.15); 3.81 (3H, s); 3.80–3.90 (2H, m); 3.86 and 3.94 (2H, AB part of an ABX system, J_{AB} 10.4, J_{AX} 4.95, J_{BX} 4.9); 4.53 (2H, s); 4.73 (2H, s); 5.05–5.20 (2H, m); 5.89 (1H, ddt, *J*(t) 7.0, *J*(d) 10.2 and 17.1); 6.83–6.95 (2H, m); 7.23–7.35 (2H, m).

(2*S*,3*R*)-1-[(*tert*-Butyldiphenylsilyl)oxy]-2-[[[(*p*-methoxybenzyl)oxy]methoxy]methyl]-5-hexen-3-ol (13). It was prepared from **11** (532 mg, 1.00 mmol) following the same procedure employed for **12**. Overall yield = 481 mg (90%); **9**/**13** 16:84, determined by ^1H NMR analysis. R_f 0.37 (PE/Et_2O 7:3). Anal. Calcd for $C_{32}H_{42}O_5Si$: C, 71.87 H, 7.92. Found: C, 71.5; H, 8.2.$[\alpha]_D = -0.3°$ (*c* 2, $CHCl_3$). ^1H NMR: δ 1.06 (9H, s); 1.90 (1H, hexuplet, *J* 5.1); 2.30 (2H, t, *J* 7.1); 3.13 (1H, d, *J* 5.1]; 3.79 (3H, s); 3.72 and 3.83 (2H, AB part of an ABX system, J_{AB} 8.9, J_{AX} 6.3, J_{BX} 3.5); 3.85–4.00 (3H, m); 4.47 (2H, s); 4.67 (2H, s); 5.00–5.15 (2H, m); 5.85 (1H, ddt, *J*(t) 6.6, *J*(d) 9.2 and 17.9); 6.83–6.95 (2H, m); 7.23–7.55 (8H, m); 7.60-7.72 (4H, m).

(2*R*,3*S*)-2-[[[(*p*-Methoxybenzyl)oxy]methoxy]methyl]-3-[(triisopropylsilyl)oxy]-5-hexen-1-ol (14). A solution of **8** (190 mg, 0.463 mmol) in dry CH_2Cl_2 (4 mL) was cooled to 0 °C and treated with 2,6-lutidine (0.129 mL, 1.39 mmol) and with (*i*Pr)$_3$Si-OTf (0.249 mL, 0.926 mmol). After 2 h, the reaction was quenched with saturated aqueous NH_4Cl. Extraction with Et_2O gave, after chromatography (ETP / Et_2O 95:5), 237 mg of pure (5*S*,6*S*)-6-[(*tert*-butyldimethylsilyl)]oxy]-5-[[[(*p*-methoxybenzyl)oxy]methoxy]methyl]-4-[(triisopropylsilyl)oxy]-1-hexene (90%). R_f 0.33 (PE/Et_2O = 95 / 5). $[\alpha]_D$ = −7.37° (*c* 2, $CHCl_3$). ^1H NMR: δ 0.03 (6H, s); 0.88 (9H, s); 1.07 (21H, s); 1.98 (1H, hexuplet, *J* 4.5); 2.20–2.50 (2H, m); 3.54 and 3.78 (2H, AB part of an ABX system, J_{AB} 9.9, J_{AX} 7.3, J_{BX} 5.4); 3.65–3.76 (2H, m); 3.81 (3H, s); 4.20 (1H, ddd, *J* 3.1, 4.6 and 6.6]; 4.52 (2H, s); 4.70 (2H, s); 5.05 and 5.07 (2H, AB part of an ABX system, J_{AB} 2.4, J_{AX} 9.1, J_{BX} 18.7); 5.83 (1H, ddt, *J*(t) 7.1, *J*(d) 10.0 and 16.9); 6.83–6.95 (2H, m); 7.23–7.35 (2H, m). This triprotected adduct (237 mg, 0.418 mmol), dissolved in dry isopropyl alcohol (7 mL) was treated with 4Å powdered molecular sieves (activated overnight in oven at 250 °C) (30 mg) and stirred at rt for 15 min. The mixture was cooled to 0 °C and treated with a 1 M solution of *p*-toluenesulfonic acid monohydrate in *i*PrOH (1.62 mL, 1.62 mmol). The reaction was followed in TLC. After 30 h, it was quenched by addition of saturated solution of $NaHCO_3$, saturated with NaCl, and extracted with Et_2O to give, after chromatography (PE/Et_2O 95:5 → 6:4), 152 mg of pure **14** as an oil (80%) and 31 mg of unreacted starting material (yield = 92%, based on unrecovered substrate). R_f 0.45 (PE/Et_2O 1:1). Anal. Calcd for $C_{25}H_{44}O_5Si$: C, 66.33; H, 9.80. Found: C, 66.2 H, 9.7. ^1H NMR: δ 1.08 (21H, s); 2.05–2.25 (1H, m); 2.38 (2H, t, *J* 6.8); 2.62 (1H, t, *J* 5.5); 3.67 and 3.78 (2H, AB part of an ABX syst, J_{AX} and J_{BX} not determined, J_{AB} 9.5); 3.80–3.90 (2H, m); 3.81 (3H, s); 4.15 (1H, dt, *J*(t) 6.3, *J*(d) 3.7 Hz); 4.53 (2H, s); 4.72 (2H, s); 5.09 and 5.12 (2H, AB part of an ABX system, J_{AB} 2.0, J_{AX} 9.7, J_{BX} 17.4); 5.85 (1H, ddt, *J*(t) 7.0, *J*(d) 10.2 and 17.1); 6.83–6.95 (2H, m); 7.23–7.35 (2H, m).

(2*S*,3*S*)-2-[[(*tert*-Butyldiphenylsilyl)oxy]methyl]-3-[(methoxy)ethoxy]methoxy]-5-hexen-1-ol (15). A solution of *n*Bu_4NI (109 mg, 0.295 mmol) in dry DMF (2 mL), cooled at 0 °C, was treated with Et(*i*Pr)$_2$N (0.256 mL, 1.47 mmol) and with MEMCl (0.135 mL, 1.18 mmol). After being stirred at rt for 1h, a solution of **9**[2d] (315 mg, 0.589 mmol) in DMF (2 mL) was added. After being stirred overnight at 70 °C, the reaction was quenched by addition of a saturated solution of $NaHCO_3$ and extracted with Et_2O to give, after chromatography (PE/Et_2O 7:3) 320 mg of (5*S*,6*S*)-6-[(*tert*-butyldiphenylsilyl)oxy]-5-[[[(*p*-methoxybenzyl)oxy]methoxy]methyl]-4-[[(methoxy)ethoxy]-methoxy]-1-hexene (87%). R_f 0.33 (PE/AcOEt 8:2). ^1H NMR: δ 1.05 (9H, s); 2.06 (1H, hexuplet, *J* 5.7); 2.29 and 2.40 (2H, AB part of an ABXY system, J_{AB}* 14.2, J_{AX}*, J_{BX}* 6.3, 5.6); 3.35 (2H, s); 3.45–3.70 (4H, m); 3.80 (3H, s); 3.91 (1H, quadruplet, *J* 5.8); 4.45 (2H, s); 4.64 and 4.65 (2H, AB syst, J_{AB} 4.5); 4.71 (2H, s); 4.95–5.06 (2H, m); 5.79 (1H, ddt, *J*(t) 6.9, *J*(d) 10.0, 17.5); 6.83–6.95 (2H, m); 7.23–7.55 (8H, m); 7.60–7.72 (4H, m). This triprotected adduct (143 mg, 0.230 mmol) was dissolved in dry CH_2Cl_2 (3 mL) and treated with *t*BuOH (0.250 mL), with a 0.25 M pH 7 buffer solution (KH_2PO_4–K_2HPO_4) (0.250 mL), and with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone DDQ (104 mg, 0.459 mmol). After being stirred for 3 h at rt, the reaction was quenched with saturated aqueous $NaHCO_3$, diluted with Et_2O, and filtered through a Celite cake. The phases were separated, and the organic layer, after drying, evaporation in vacuo, and chromatography (PE/Et_2O 6:4) gave 99 mg of **15** (91%). R_f 0.30 (PE/Et_2O 1:1). Anal. Calcd for $C_{27}H_{40}O_5Si$: C, 68.61; H, 8.53. Found: C, 68.3; H, 8.7. $[\alpha]_D = +9.13°$ (*c* 2, $CHCl_3$). ^1H NMR: δ 1.05 (9H, s); 1.88 (1H, hexuplet, *J* 6.0); 2.29–2.50 (2H, m); 2.83 (1H, dd, *J* 5.1 and 6.7); 3.35 (2H, s); 3.44–3.68 (4H, m); 3.79 (2H, d, *J* 6.3); 3.89–3.95 (3H, m); 4.68 and 4.74 (2H, AB syst, J_{AB} 7.0); 5.01 and 5.05 (2H, AB part of an ABX system, J_{AB} 2.2, J_{AX} 10.4, J_{BX} 17.1); 5.72 (1H, ddt, *J*(t) 7.0, *J*(d) 10.4 and 16.7); 7.30–7.55 (6H, m); 7.60–7.72 (4H, m).

(2*R*,3*R*)-2-[[[(*p*-Methoxybenzyl)oxy]methoxy]methyl]-3-[(triisopropylsilyl)oxy]-5-hexen-1-ol (16). It was prepared from **12** (208 mg, 0.507 mmol) following the same procedure employed for **14**. Yield = 190 mg (83%). R_f 0.30 (PE/Et_2O 6:4). Anal. Calcd for $C_{25}H_{44}O_5Si$: C, 66.33; H, 9.80. Found C, 66.6 H, 10.1. ^1H NMR: δ 1.08 (21H, s); 1.94 (1H, apparent octuplet, *J* 3.4) ; 2.35–2.60 (2H, m); 2.94 (1H, dd, *J* 2.6, 8.5); 3.81 (3H, s); 3.70–3.90 (3H, m); 3.99 (1H, ddd, *J* 2.8, 4.2, 11.3); 4.17 (1H, ddd, *J* 3.1, 5.0, 8.6); 4.52 and 4.55 (2H, AB system, J_{AB} 11.4); 4.74 (2H, s); 5.08 and 5.10 (2H, AB part of an ABX system, J_{AB} 1.9, J_{AX} 9.4, J_{BX} 17.8); 5.74 (1H, ddt, *J*(t) 7.1, *J*(d) 9.9, 17.3); 6.83–6.95 (2H, m); 7.23–7.35 (2H, m).

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(2S,3R)-2-[[(*tert*-Butyldiphenylsilyl)oxy]methyl]-3-[[(methoxy)ethoxy]methoxy]hex-5-en-1-ol (17). It was prepared from **13** (263 mg, 0.49 mmol) following the same procedure employed for **15**. Yield = 195 mg (84%). R_f 0.23 (PE/Et_2O 1:1). Anal. Calcd for $C_{27}H_{40}O_5Si$: C, 68.61; H, 8.53. Found C, 68.5 H, 8.75. $[\alpha]_D = -20.7°$ (*c* 2, $CHCl_3$). ^1H NMR: δ 1.05 (9H, s); 2.10 (1H, hexuplet, *J* 6.0); 2.20–2.40 (2H, m); 2.96 (1H, t, *J* 5.4); 3.37 (2H, s); 3.45–3.70 (4H, m); 3.70–3.95 (5H, m); 4.65 and 4.69 (2H, AB system, J_{AB} 7.4); 5.01 and 5.03 (2H, AB part of an ABX system, J_{AB} 2.0, J_{AX} 14.0, J_{BX} 13.3); 5.73 (1H, ddt, *J*(t) 7.1, *J*(d) 9.6, 17.6); 7.30–7.55 (6H, m); 7.60–7.72 (4H, m).

General Procedure for Modified Swern Oxidation of Alcohols 14–17 to Give Aldehydes 18–21. A solution of $(COCl)_2$ (0.128 mL, 1.47 mmol) in dry CH_2Cl_2 (10 mL) was cooled to −78 °C and treated with a 2.8 M solution of DMSO in dry CH_2Cl_2 (0.84 mL, 2.36 mmol). After 10 min, a solution of alcohols **14–17** (0.590 mmol) in CH_2Cl_2 (3 mL) was added. After 10 min *N*-ethyl diisopropylamine (0.822 mL, 4.72 mmol) was introduced, and the mixture was allowed to react at −78 °C until complete at TLC (usually 6–7 h or overnight). The reaction was quenched at −78 °C with 5% aqueous $NH_4H_2PO_4$ (15 mL) followed by 1 M HCl (10 mL). After warming to rt, the pH was adjusted to 3 with 1 M HCl, and the aqueous phase was extracted with Et_2O. The organic extracts, washed with saturated NaCl, and evaporated to dryness, gave crude **18–21** as a colorless oil, used immediately (or after 1 night at −30 °C) as such for the next reaction. [Aldehyde **18:** R_f 0.62 (PE/Et_2O 7:3). **19:** R_f 0.45 (PE/Et_2O 1:1). **21:** R_f 0.59 (PE/Et_2O 1:1). **20:** R_f 0.58 (PE/Et_2O 7:3)].

General Procedure of Addition of Me_2CuLi to aldehydes 18–21 To Give Compounds 22, 24, 26, and 28. (This reaction was carried out under a helium atmosphere). A suspension of CuI (571 mg, 3.00 mmol) in dry Et_2O (10 mL) was cooled to −50 °C and treated with a 1.6 M solution of MeLi in Et_2O (6.75 mL, 10.4 mmol). The temperature was allowed to rise to −20 °C during 1 h. After being stirred at −20 °C for 10 min, the brown mixture was cooled to −78 °C and treated with a solution of crude aldehyde (0.500 mmol) in Et_2O (8 mL). After 1 h at −78 °C, the temperature was allowed to rise slowly (during 1 h 30 min) to −20 °C. The reaction was then quenched with saturated aqueous NH_4Cl, transferred into a beaker, adjusted to pH 9 with 10% NH_4OH, and stirred in air atmosphere until all the Cu(I) salts passed into solution. The blue aqueous phase was acidified to pH 7 with 2 N HCl, and extracted with Et_2O to give a crude product. Determination of diastereomeric ratios (dr) was carried out at this level by ^1H NMR (for all compounds) or HPLC (for **22** and **26**) Purification by chromatography (PE/Et_2O 6:4 for compounds **22** and **24**, PE/Et_2O 1:1 for compounds **26** and **28**) afforded the pure diastereoisomers. The purity was checked by ^1H NMR, TLC, and HPLC (in all cases the diastereoisomers were separable on silica gel). The analytical data for compounds **22b**, **24b**, and **28b** were determined on the products obtained by ketone reductions (*vide infra*).

General Procedure for the Addition Of Allyl-Sn(*n*Bu)$_3$ to Aldehydes 18–21 in the Presence of $MgBr_2 \cdot Et_2O$ To Give Compounds 23, 25, 27, and 29. A solution of aldehydes **18–21** (0.500 mmol) in dry CH_2Cl_2 (4 mL) was treated with 4 Å powdered molecular sieves (25 mg) and stirred at rt for 15 min. The mixture was cooled to −78 °C and treated with $MgBr_2 \cdot Et_2O$ (284 mg, 1.10 mmol) and, after 10 min, with a solution of allyl-Sn(*n*Bu)$_3$ (0.310 mL, 1.00 mmol) in dry CH_2Cl_2 (4 mL). After 2 h at −78 °C, the temperature was allowed to rise slowly (during 1 h 30 min) to −40 °C. The reaction was then quenched with saturated aqueous NH_4Cl, filtered through a Celite cake and extracted with Et_2O to give a crude product. A first chromatography (PE/Et_2O 8:2 for compounds **23** and **25**, PE/Et_2O 6:4 for compounds **27** and **29**) gave the diastereomeric mixture of alcohols, slightly impure with allyl-Sn(*n*Bu)$_3$ derived impurities. Determination of dr was carried out at this level by ^1H n.m.r (for **23**, **27**, and **29**) or HPLC (for **23** and **25**). A second chromatography afforded the pure diastereoisomers. The purity was checked by ^1H NMR, TLC, and HPLC (in all cases the diastereoisomers were separable on silica gel). The analytical data for compounds **23b**, **25b**, **27b**, and **29b** were determined on the products obtained by ketone reductions (*vide infra*).

(2R,3S,4S)-3-[[[(*p*-methoxybenzyl)oxy]methoxy]methyl]-4-[(triisopropylsilyl)oxy]-6-hepten-2-ol (22a). R_f 0.45 (PE/Et_2O 6:4). $[\alpha]_D = +9.2°$ (*c* 2, $CHCl_3$). ^1H NMR: δ 1.08 (21H, s); 1.27 (3H, d, *J* 6.3); 1.73 (1H, quintuplet, *J* 4.6); 2.30–2.60 (2H, m); 3.24 (1H, broad s); 3.80 (3H, s); 3.89 and 3.78 (2H, AB part of an ABX system, J_{AB} 10.2, J_{AX} 5.6, J_{BX} 4.5); 4.05–4.15 (1H, m); 4.15 (1H, ddd, *J* 3.9, 5.2, 7.8); 4.52 and 4.57 (2H, AB system, J_{AB} = 11.5); 4.70 and 4.74 (2H, AB system, J_{AB} 6.9); 5.05–5.16 (2H, m); 5.81 (1H, ddt, *J*(t) 7.0, *J*(d) 10.3, 16.8); 6.83–6.95 (2H, m); 7.23–7.35 (2H, m). ^{13}C NMR: δ 13.07 (*C*H); 18.22 (*C*H$_3$); 21.87 (*C*H$_3$); 39.70 (*C*H$_2$); 47.96 (*C*H); 65.52 (*C*H$_2$), 69.25 (*C*H$_2$); 69.55 (*C*H); 73.52 (*C*H); 94.45 (*C*H$_2$); 113.80 (*C*H); 117.62 (*C*H$_2$); 129.51 (*C*H); 129.63 (*C*); 134.27 (*C*H), 159.22 (*C*).

(2S,3S,4S)-3-[[[(*p*-Methoxybenzyl)oxy]methoxy]methyl]-4-[(triisopropylsilyl)oxy]-6-hepten-2-ol (22b). R_f 0.50 (PE/Et_2O 6:4). ^1H NMR: δ 1.10 (21H, s); 1.22 (3H, d, *J* 6.3); 2.01 (1H, dq, *J*(d) 2.7, *J*(q) 7.0); 2.48 (2H, dd, *J* 6.3, 11.2); 3.55 (2H, d, *J* 6.1); 3.81 (3H, s); 3.95–4.08 (1H, m); 4.36 (1H, dt, *J*(t) 6.1, *J*(d) 2.7); 4.50 (2H, s); 4.69 (2H, s); 5.09 and 5.14 (2H, AB part of an ABX system, J_{AB} 2.1, J_{AX} 9.7, J_{BX} 17.0); 5.81 (1H, ddt, *J*(t) 7.1, *J*(d) 10.0, 17.1); 6.83–6.95 (2H, m); 7.23–7.35 (2H, m).

(4R,5S,6S)-5-[[[(*p*-Methoxybenzyl)oxy]methoxy]methyl]-6-[(triisopropylsilyl)oxy]nona-1,8-dien-4-ol (23a). R_f 0.20 (PE/Et_2O 8:2). $[\alpha]_D = +5.3°$ (*c* 2, $CHCl_3$). ^1H NMR: δ 1.08 (21H, s); 1.84 (1H, quintuplet, *J* 4.4); 2.37 (2H, t, *J* 6.8); 2.40–2.60 (2H, m); 3.07 (1H, broad s); 3.81 (3H, s); 3.91 (2H, d, *J* 4.7); 3.94 (1H, quintuplet, *J* 5.1); 4.20 (1H, dt, *J*(t) 4.6, *J*(d) 7.5); 4.52 and 4.57 (2H, AB system, J_{AB} 11.4); 4.71 and 4.74 (2H, AB system, J_{AB} 6.8); 5.04–5.18 (4H, m); 5.82 (1H, ddt, *J*(t) 6.9, *J*(d) 10.3 and 17.3); 5.86 (1H, ddt, *J*(t) 7, *J*(d) 10.5, 16.8); 6.83–6.95 (2H, m); 7.23–7.35 (2H, m).

(4S,5S,6S)-5-[[[(*p*-Methoxybenzyl)oxy]methoxy]methyl]-6-[(triisopropylsilyl)oxy]nona-1,8-dien-4-ol 23b. R_f 0.29 (PE/Et_2O 8:2). ^1H NMR: δ 1.09 (21H, s); 2.05 (1H, dq, *J*(d) 2.2, *J*(q) 6.8); 2.10–2.62 (4H, m); 3.60 (2H, d, *J* 6.5); 3.81 (3H, s); 3.92 (1H, quintuplet, *J* 3.7); 4.39 (1H, dt, *J*(d) 2.2, *J*(t) 6.6); 4.52 (2H, s); 4.70 (2H, s); 5.00–5.20 (4H, m); 5.83 (1H, ddt, *J*(t) 7.1 *J*(d) 10.0, 17.0); 5.93 (1H, ddt, *J*(t) 7.0, *J*(d) 10.0, 17.0); 6.83–6.95 (2H, m); 7.23–7.35 (2H, m).

(2R,3S,4R)-3-[[[(*p*-Methoxybenzyl)oxy]methoxy]methyl]-4-[(triisopropylsilyl)oxy]-6-hepten-2-ol (24a). R_f 0.54 (PE/Et_2O 6:4). $[\alpha]_D = +14.4°$ (*c* 2, $CHCl_3$). ^1H NMR: δ 1.08 (21H, s); 1.21 (3H, d, *J* 6.3); 1.71 (1H, apparent octuplet, *J* 2.5); 2.40–2.60 (2H, m); 3.72 (1H, broad s); 3.80 (3H, s); 3.82 and 3.94 (2H, AB part of an ABX system, J_{AB} 9.4, J_{AX} 8.8, J_{BX} 5.0); 4.28–4.35 (1H, m); 4.35 (1H, dt, *J*(t) 6.0, *J*(d) 2.1); 4.52 and 4.55 (2H, AB system, J_{AB} 11.5); 4.71 and 4.76 (2H, AB system, J_{AB} 6.6); 5.03–5.15 (2H, m); 5.69 (1H, ddt, *J*(t) 7.1, *J*(d) 10.3, 16.9); 6.83–6.95 (2H, m); 7.23–7.35 (2H, m).

(2S,3S,4R)-3-[[[(*p*-Methoxybenzyl)oxy]methoxy]methyl]-4-[(triisopropylsilyl)oxy]-6-hepten-2-ol (24b). R_f 0.45 (PE/Et_2O 6:4). ^1H NMR: δ 1.09 (21H, s); 1.29 (3H, d, *J* 6.4); 1.89 (1H, quintuplet, *J* 5.5); 2.25–2.65 (2H, m); 3.23 (1 H, d, *J* 4.4); 3.66 (2H, d, *J* 5.5); 3.81 (3H, s); 4.06 (1H, d of quintuplet, *J* 6.4 (q), 4.4 (d)); 4.24 (1H, dt, *J*(t) 4.6, *J*(d) 7.4); 4.52 (2H, s); 4.69 (2H, s); 5.03–5.17 (2H, m); 5.72–5.96 (1H, m); 6.88 (2 H, d, *J* 8.6); 7.27 (2 H, d, *J* 8.6).

(4R,5S,6R)-5-[[[(*p*-Methoxybenzyl)oxy]methoxy]methyl]-6-[(triisopropylsilyl)oxy]nona-1,8-dien-4-ol (25a). R_f 0.38 (PE/Et_2O 8:2). $[\alpha]_D = +13.0°$ (*c* 2, $CHCl_3$). ^1H NMR: δ 1.09 (21H, s); 1.80 (1H, dt, *J*(t) 5.0, *J*(d) 2.7); 2.52 (2H, t, *J* 8.0); 3.81 and 3.97 (2H, AB part of an ABXY system,* J_{AB} 13.2, J_{AX}, J_{BX} 6.1, 3.8, J_{AY}, J_{BY} not determined); 3.71 (1H, broad s); 3.81 (3H, s); 3.79 and 3.94 (2H, AB part of an ABX system, J_{AB} 10.1, J_{AX} 10.2, J_{BX} 4.6); 4.21 (1H, t, *J* 7.1); 4.37 (1H, ddd, *J* 2.2, 6.2, 8.3); 4.50 and 4.55 (2H, AB system, J_{AB} 11.6); 4.70 and 4.74 (2H, AB system, J_{AB} 6.6); 5.00–5.20 (4H, m); 5.67 (1H, ddt, *J*(t) 7.0, *J*(d) 9.6, 17.7); 5.82 (1H, ddt, *J*(t) 7.0, *J*(d) 10.1, 17.1); 6.83–6.95 (2H, m); 7.23–7.35 (2H, m).

(4S,5S,6R)-5-[[[(*p*-Methoxybenzyl)oxy]methoxy]methyl]-6-[(triisopropylsilyl)oxy]nona-1,8-dien-4-ol (25b). R_f 0.30 (PE/Et_2O 8:2). ^1H NMR: δ 1.09 (21H, s) 1.98 (1H, dq, *J*(q)

5.8, *J*(d) 3.8); 2.15–2.65 (4H, m); 2.94 (1 H, d, *J* 4.0); 3.68 (2H, d, *J* 6.0); 3.81 (3H, s); 3.83–3.96 (1H, m, mc 3.89); 4.22–4.35 (1H, m, mc 4.28); 4.52 (2H, s); 4.70 (2H, s); 5.00–5.20 (4H, m); 5.70–6.05 (2H, m); 6.88 (2H, d, *J* 8.5); 7.26 (2H, d, *J* 8.5).

(2*R*,3*R*,4*S*)-3-[[(*tert*-Butyldiphenylsilyl)oxy]methyl]-4-[(methoxyethoxy)methoxy]-6-hepten-2-ol (26a). R_f 0.15 (PE/Et_2O 1:1). ^1H NMR: δ 1.06 (9H, s); 1.25 (3H, d, *J* 6.4); 1.84 (1H, quintuplet, *J* 5.6); 2.05–2.28 (1H, m); 2.34–2.52 (1 H, m); 3.36 (3H, s); 3.42–3.55 (2H, m); 3.63–3.80 (4 H, m); 3.93 (1H, hexuplet, *J* 5.8); 4.12 (1H, broad q, *J* 5.6); 4.70 and 4.76 (2H, AB system, J_{AB} 7.4); 4.85–5.10 (2H, m); 5.74 (1H, ddt, *J*(t) 6.9, *J*(d) 10.3, 16.8); 7.30–7.55 (6H, m); 7.60–7.72 (4H, m).

(2*S*,3*R*,4*S*)-3-[[(*tert*-Butyldiphenylsilyl)oxy]methyl]-4-[(methoxyethoxy)methoxy]-6-hepten-2-ol (26b). R_f 0.21 (PE/Et_2O 1:1). ^1H NMR: δ 1.05 (9H, s); 1.11 (3H, d, *J* 6.6); 1.65 (1H, broad s); 2.35 (2H, t, *J* 6.6); 3.37 (3H, s); 3.45–3.75 (4H, m); 3.86 and 3.92 (2H, AB part of an ABX system, J_{AB} 10.8, J_{AX} 2.1, J_{BX} 3.6); 4.12 (1H, dt, *J*(t) 6.0, *J*(d) 3.7); 4.22 (1H, dq, *J*(q) 5.7, *J*(d) 3.3); 4.75 (2H, s); 4.90–5.10 (2H, m); 5.72 (1H, ddt, *J*(t) 7.0, *J*(d) 10.4, 16.9); 7.30–7.55 (6H, m); 7.60–7.72 (4H, m).

(4*R*,5*R*,6*S*)-5-[[(*tert*-Butyldiphenylsilyl)oxy]methyl]-6-[(methoxyethoxy)methoxy]nona-1,8-dien-4-ol (27a). R_f 0.28 (PE/Et_2O 6:4). $[\alpha]_D$ = +15.23° (*c* 2.3, $CHCl_3$). ^1H NMR: δ 1.06 (9H, s); 1.91 (1H, quintuplet, *J* 5.5); 2.10–2.60 (4H, m); 3.36 (3H, s, OCH_3); 3.45–3.70 (4H, m); 3.74 (2H, d, *J* 5.4); 3.90–4.50 (2H, m); 4.71 and 4.74 (2H, AB system, J_{AB} 7.2); 4.90–5.15 (4H, m); 5.76 (1H, ddt, *J*(t) 7.0, *J*(d) 10.1, 16.7); 5.90 (1H, ddt, *J*(t) 7.3, *J*(d) 11.3, 16.1); 7.30–7.55 (6H, m); 7.60–7.72 (4H, m).

(4*S*,5*R*,6*S*)-5-[[(*tert*-Butyldiphenylsilyl)oxy]methyl]-6-[(methoxyethoxy)methoxy]nona-1,8-dien-4-ol (27b). R_f 0.33 (PE/Et_2O 6:4). ^1H NMR: δ 1.05 (9H, s); 1.72 (1H, dq, *J*(q) 6.0, *J*(d) 2.5); 2.00–2.40 (2H, m); 2.39 (2H, t, *J* 6.4); 3.36 (3H, s); 3.43 (1 H, d, *J* 3.1); 3.44–3.54 (2H, m); 3.56–3.80 (2H, m); 3.87 and 3.88 (2H, AB part of an ABX system, J_{AB} 10.8; J_{AX} 2.9, J_{BX} 8.8); 4.00–4.15 (1H, m); 4.18 (1H, q, *J* 5.0); 4.77 (2H, s); 4.90–5.10 (4H, m); 5.60–5.85 (2H, m); 7.30–7.55 (6H, m); 7.60–7.72 (4H, m).

(2*R*,3*R*,4*R*)-3-[[(*tert*-Butyldiphenylsilyl)oxy]methyl]-4-[(methoxyethoxy)methoxy]-6-hepten-2-ol (28a). R_f 0.18 (PE/Et_2O 1:1). $[\alpha]_D$ = −18.68° (*c* 2, $CHCl_3$). ^1H NMR: δ 1.05 (9H, s); 1.19 (3H, d, *J* 6.3); 1.91 (1H, dq, *J*(q) 6.4, *J*(d) 3.4); 2.20–2.50 (2H, m); 3.36 (3H, s); 3.45–3.68 (4H, m); 3.71 and 3.76 (2H, AB part of an ABX system, J_{AB} 4.3, J_{AX} 1.7, J_{BX} 1.4); 3.90–4.00 (1H, m); 4.02 (1H, dt, *J*(t) 6.4, *J*(d) 3.3); 4.67 and 4.71 (2H, AB system, J_{AB} 7.1); 5.05 and 5.06 (2H, AB part of an ABX system, J_{AB} 2.2, J_{AX} 10.9, J_{BX} 16.0); 5.77 (1H, ddt, *J*(t) 7.1, *J*(d) 9.6, 17.5); 7.30–7.55 (6H, m); 7.60–7.72 (4H, m).

(2*S*,3*R*,4*R*)-3-[[(*tert*-Butyldiphenylsilyl)oxy]methyl]-4-[(methoxyethoxy)methoxy]-6-hepten-2-ol (28b). R_f 0.26 (PE/Et_2O 1:1). ^1H NMR: δ 1.06 (9 H, s); 1.26 (3 H, d, *J* 6.3); 1.67 (1 H, quintuplet, *J* 5.0); 2.15–2.50 (2 H, m); 3.37 (3 H, s); 3.45–3.55 (2 H, m); 3.57–3.66 (2 H, m); 3.80 (1 H, d, *J* 4.3); 3.86 (mc)(1 H, m, $J_{5\text{-}6}$ * 3.5); 4.02 (2 H, d, *J* = 4.5); 4.12 (1 H, broad hexuplet, *J* 5.2); 4.92–5.08 (2 H, m, * δ 5.01 and 5.04, J_{AB} 2.0; J_{AX}, J_{BX} 16.9, 10.4); 5.70 (1 H, ddt, *J*(d) 10.6, 16.7, *J*(t) 7.1); 7.30–7.55 (6H, m); 7.60–7.72 (4H, m).

(4*R*,5*R*,6*R*)-5-[[(*tert*-Butyldiphenylsilyl)oxy]methyl]-6-[(methoxyethoxy)methoxy]nona-1,8-dien-4-ol (29a). R_f 0.25 (PE/Et_2O 6:4). $[\alpha]_D$ = −9.42° (*c* 2, $CHCl_3$). ^1H NMR: δ 1.05 (9H, s); 1.93 (1H, dq, *J*(q) 6.3, *J*(d) 2.7); 2.10–2.50 (4H, m); 3.36 (3H, s); 3.42–3.70 (4H, m); 3.73 and 3.78 (2H, AB part of an ABX system, J_{AB} 3.9, J_{AX} 2.9, J_{BX} 2.4); 3.80–3.95 (1H, m); 4.09 (1H, dt, *J*(t) 6.7, *J*(d) 2.7) 4.68 and 4.72 (2H, AB system, J_{AB} 7.1); 4.95–5.10 (4H, m); 5.75 (1H, ddt, *J*(t) 7.2, *J*(d) 9.7, 17.1); 5.89 (1H, ddt, *J*(t) 6.8, *J*(d) 10.6, 17.0); 7.30–7.55 (6H, m); 7.60–7.72 (4H, m).

(4*S*,5*R*,6*R*)-5-[[(*tert*-Butyldiphenylsilyl)oxy]methyl]-6-[(methoxyethoxy)methoxy]nona-1,8-dien-4-ol (29b). R_f 0.30 (PE/Et_2O 6:4). ^1H NMR: δ 1.06 (9H, s); 1.77 (1H, quintuplet, *J* 4.8); 2.25–2.48 (4H, m); 3.37 (3H, s); 3.45–3.73 (4H, m); 3.85–4.08 (4H, m); 4.64 (2H, s); 4.95–5.12 (4H, m); 5.62–5.94 (2H, m); 7.30–7.55 (6H, m); 7.60–7.72 (4H, m).

General Procedure for Oxidation Of adducts 22–29 to Ketones 30–37. A solution of alcohol **22–29** (as diastereomeric mixtures) (0.100 mmol) in acetone (5 mL), cooled to 0 °C, was treated slowly with approximately 10 drops of Jones[21] reagent (prepared from 10 g of CrO_3, 8.6 mL of 96% H_2SO_4, 14 mL of H_2O, and brought up to 40 mL). After 20 min the reaction was quenched with 1 M KH_2PO_4, treated with a few milliliters of 10% $Na_2S_2O_5$, diluted with Et_2O, and filtered through a Celite cake. Extraction with Et_2O, evaporation under reduced pressure, and chromatography (PE/Et_2O), gave pure ketones **30–37**.

(3*R*,4*S*)-3-[[[(*p*-Methoxybenzyl)oxy]methoxy]methyl]-4-[(triisopropylsilyl)oxy]-6-hepten-2-one (30). (Yield = 81% from Jones oxidation of **22**.) R_f 0.29 (PE/Et_2O 85:15). Anal. Calcd for $C_{26}H_{44}O_5Si$: C, 67.20; H, 9.54. Found C, 66.85; H, 9.75. $[\alpha]_D$ = −1.96° (*c* 2, $CHCl_3$). ^1H NMR: δ 1.07 (21H, s); 2.25 (3H, s); 2.20–2.50 (2H, m); 3.03 (1H, dt, *J*(d) 8.7, *J*(t) 4.9); 3.81 (3H, s); 3.83 and 3.91 (2H, AB part of an ABX system, J_{AB} 9.5, J_{AX} 4.6, J_{BX} 9.7); 4.25 (1H, q, *J* 4.6); 4.48 (2H, s); 4.68 (2H, s); 5.00–5.18 (2H, m); 5.84 (1H, ddt, *J*(t) 7.0, *J*(d) 10.0, 17.0); 6.83–6.95 (2H, m); 7.23–7.35 (2H, m).

(5*R*,6*S*)-5-[[[(*p*-Methoxybenzyl)oxy]methoxy]methyl]-6-[(triisopropylsilyl)oxy]-1,8-nonadien-4-one (31). (Yield = 93% from Jones oxidation of **23**.) R_f 0.30 (PE/Et_2O 8:2). Anal. Calcd for $C_{28}H_{46}O_5Si$: C, 68.53; H, 9.45. Found C, 68.6; H, 9.6. $[\alpha]_D$ = −5.76° (*c* 2, $CHCl_3$). ^1H NMR: δ 1.07 (21H, s); 2.25 and 2.38 (2H, AB part of an ABXY system,* J_{AB} 14.0, J_{AX}, J_{BX} 3.7, 7.0, J_{AY}, J_{BY} not determined); 3.07 (1H, dt, *J*(d) 8.8, *J*(t) 5.2); 3.36 (2H, apparent t, *J* 6.3); 3.81 (3H, s); 3.82 and 3.90 (2H, AB part of an ABX system, J_{AB} 8.9, J_{AX} 5.1, J_{BX} 9.6); 4.25 (1H, q, *J* 5.5); 4.47 (2H, s); 4.66 (2H, s); 5.00–5.20 (4H, m); 5.86 (1H, ddt, *J*(t) 7.3, *J*(d) 10.9, 16.2); 5.96 (1H, ddt, *J*(t) 6.8, *J*(d) 10.3, 17.2); 6.83–6.95 (2H, m); 7.23–7.35 (2H, m).

(3*R*,4*R*)-3-[[[(*p*-Methoxybenzyl)oxy]methoxy]methyl]-4-[(triisopropylsilyl)oxy]-6-hepten-2-one (32). (Yield = 85% from Jones oxidation of **24**.) R_f 0.42 (PE/Et_2O 8:2). Anal. Calcd for $C_{26}H_{44}O_5Si$: C, 67.20; H, 9.54. Found C, 67.0; H, 9.75. $[\alpha]_D$ = −5.76° (*c* 2, $CHCl_3$). ^1H NMR: δ 1.07 (21H, s); 2.25 (3H, s); 2.20–2.45 (2H, m); 3.05 (1H, apparent quintuplet, *J* 5.0); 3.80 (3H, s); 3.70 and 3.89 (2H, AB part of an ABX system, J_{AB} 9.4, J_{AX} 4.4, J_{BX} 9.6); 4.20 (1H, dd, *J* 5.9, 4.8); 4.48 (2H, s); 4.67 (2H, s); 5.11 and 5.12 (2H, AB part of an ABX system, J_{AB} 2.1, J_{AX} 14.4, J_{BX} 13.0); 5.87 (1H, ddt, *J*(t) 7.7, *J*(d) 9.8, 18.0); 6.83–6.95 (2H, m); 7.23–7.35 (2H, m).

(5*R*,6*R*)-5-[[[(*p*-Methoxybenzyl)oxy]methoxy]methyl]-6-[(triisopropylsilyl)oxy]-1,8-nonadien-4-one (33). (Yield = 93% from Jones oxidation of **25**.) R_f 0.23 (PE/Et_2O 85:15). Anal. calcd for $C_{28}H_{46}O_5Si$: C, 68.53; H, 9.45. Found C, 68.3; H, 9.6. $[\alpha]_D$ = −32.40° (*c* 2, $CHCl_3$). ^1H NMR: δ 1.07 (21H, s); 2.19 and 2.39 (2H, AB part of an ABXY system,* J_{AB} 14.0, J_{AX}, J_{BX} 4.3, 5.6, J_{AY}, J_{BY} not determined); 3.10 (1H, ddd, *J* 4.5, 6.4, 10.3); 3.35 (2H, d, *J* 6.7); 3.81 (3H, s); 3.67 and 3.85 (2H, AB part of an ABX system, J_{AB} 9.2, J_{AX} 4.3, J_{BX} 9.3); 4.21 (1H, q, *J* 5.5); 4.47 (2H, s); 4.65 (2H, s); 5.00–5.20 (4H, m); 5.88 (1H, ddt, *J*(t) 8, *J*(d) 10.7, 16.8); 5.96 (1H, ddt, *J*(t) 6.5, *J*(d) 9.9, 17.2); 6.83–6.95 (2H, m); 7.23–7.35 (2H, m).

(3*S*,4*S*)-3-[[(*tert*-Butyldiphenylsilyl)oxy]methyl]-4-[(methoxyethoxy)methoxy]-6-hepten-2-one (34). (Yield = 94% from Jones oxidation of **26**.) R_f 0.30 (PE/Et_2O 6:4). Anal. Calcd for $C_{28}H_{40}O_5Si$: C, 69.38; H, 8.32. Found C, 68.05; H, 8.5. ^1H NMR: δ 1.01 (9H, s); 2.26 (3H, s); 1.99 and 2.41 (2H, AB part of an ABXY system,* J_{AB} 14.5, J_{AX}, J_{BX} 4.5, 5.1, J_{AY}, J_{BY} not determined); 3.05 (1H, dt, *J*(t) 8.7, *J*(d) 4.8); 3.36 (3H, s); 3.45–3.63 (4H, m); 3.68 and 3.84 (2H, AB part of an ABX system, J_{AB} 9.7, J_{AX} 4.7, J_{BX} 9.7); 3.91 (1H, q, *J* 4.3); 4.62 and 4.68 (2H, AB system, J_{AB} 7.2); 4.85–5.06 (2H, m); 5.74 (1H, dddd, *J* 5.9, 7.9, 10.3, 16.9); 7.30–7.55 (6H, m); 7.60–7.72 (4H, m).

(5*S*,6*S*)-5-[[(*tert*-Butyldiphenylsilyl)oxy]methyl]-6-[(methoxyethoxy)methoxy]-1,8-nonadien-4-one (35). (Yield = 85% from Jones oxidation of **27**.) R_f 0.26 (PE/Et_2O 7:3). Anal. Calcd for $C_{30}H_{42}O_5Si$: C, 70.55; H, 8.29. Found C, 70.35; H, 8.35. $[\alpha]_D$ = +29.43° (*c* 2, $CHCl_3$). ^1H NMR: δ 1.00 (9H, s); 1.96 and 2.43 (2H, AB part of an ABXY system,* J_{AB} 14.8, J_{AX}, J_{BX} 4.2, 4.4 Hz, J_{AY}, J_{BY} not determined); 3.13 (1H, dt,

J(t) 9.9, J(d) 4.7); 3.36 (2H, d, J 6.4); 3.37 (3H, s); 3.43–3.60 (4H, m); 3.66 and 3.84 (2H, AB part of an ABX system, J_{AB} 9.2, J_{AX} 4.4, J_{BX} 10.8); 3.90 (1H, q, J 4.5); 4.59 and 4.67 (2H, AB system, J_{AB} 7.1); 4.80–5.20 (4H, m); 5.74 (1H, dddd, J 5.6, 7.8, 10.3, 17.1); 5.98 (1H, ddt, J(t) 6.8, J(d) 10.3, 17.2); 7.30–7.55 (6H, m); 7.60–7.72 (4H, m).

(3*S*,4*R*)-3-[[(*tert*-butylDiphenylsilyl)oxy]methyl]-4-[(methoxyethoxy)methoxy]-6-hepten-2-one (36). (Yield = 67% from Jones oxidation of **28**.) R_f 0.27 (PE/Et_2O 7:3). Anal. Calcd for $C_{28}H_{40}O_5Si$: C, 69.38; H, 8.32. Found C, 69.6; H, 8.5. $[\alpha]_D$ = −23.06° (*c* 2, $CHCl_3$). ^1H NMR: δ 1.02 (9H, s); 2.24 (3H, s); 2.00–2.40 (2H, m); 3.05 (1H, dt, J(t) 7.8, J(d) 4.9); 3.32 (3H, s); 3.34–3.62 (4H, m); 3.86 and 3.96 (2H, AB part of an ABX system, J_{AB} 9.6, J_{AX} 5.1, J_{BX} 9.2); 3.90–4.00 (1H, m); 4.62 and 4.66 (2H, AB system, J_{AB} 7.2); 4.98–5.10 (2H, m); 5.75 (1H, ddt, J(t) 7, J(d) 10.6, 16.8); 7.30–7.55 (6H, m); 7.60–7.72 (4H, m).

(5*S*,6*R*)-5-[[(*tert*-Butyldiphenylsilyl)oxy]methyl]-6-[(methoxyethoxy)methoxy]-1,8-nonadien-4-one (37). (Yield = 76% from Jones oxidation of **29**.) R_f 0.43 (PE/Et_2O 6:4). Anal. Calcd for $C_{30}H_{42}O_5Si$: C, 70.55; H, 8.29. Found C, 70.25; H, 8.45. $[\alpha]_D$ = −20.46° (*c* 2, $CHCl_3$). ^1H NMR: δ 1.01 (9H, s); 2.05–2.40 (2H, m); 3.11 (1H, dt, J(t) 8.0, J(d) 5.0); 3.31 (3H, s); 3.31–3.36 (6H, m); 3.85 and 3.95 (2H, AB part of an ABX system, J_{AB} 9.6, J_{AX} 5.0, J_{BX} 9.3); 3.95 (1H, q, J 6.6); 4.61 and 4.65 (2H, AB system, J_{AB} 7.2); 4.97–5.22 (4H, m); 5.75 (1H, ddt, J(t) 6.5, J(d) 10.8, 16.4); 5.96 (1H, ddt, J(t) 6.8, J(d) 10.3, 17.1); 7.30–7.55 (6H, m); 7.60–7.72 (4H, m).

General Procedure for Reduction of Ketones 30–37. The substrate (0.100 mmol), dissolved in dry Et_2O (3 mL), was treated with 4Å powdered molecular sieves (activated overnight in oven at 250 °C) (20 mg) and stirred at rt for 30 min. The mixture was cooled to -78 °C and treated with $MgBr_2 \cdot Et_2O$ (129 mg, 0.500 mmol). After the mixture was stirred at this temperature for 15 min, a 1 M solution of DIBALH in toluene (0.200 mmol, 0.200 mL) was added. After 15 min at −78 °C the reaction was quenched by addition of a saturated solution of NH_4Cl, diluted with a saturated solution of sodium and potassium tartrate and stirred for 1 h at rt. The phases were separated and the organic layer, after drying, evaporation in vacuo, and chromatography gave the pure diastereomeric mixtures of products **22–29**. Diastereomeric ratios were determined as above described for the addition reactions. Further chromatography gave the pure diastereoisomers.

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Supporting Information Available: Copies of ^1H NMR of compounds **22a,b-29a,b**, full peak assignment for all NMR and analytical data of isopropylidene derivatives synthesized from **22-29a,b** (26 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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