Tetrahedron Letters, Vol.31, No.52, pp 7567-7570, 1990
Printed in Great Britain

0040-4039/90 $3.00 + .00
Pergamon Press plc

DIISOPROPYL TARTRATE (E)-γ-(DIMETHYLPHENYLSILYL)ALLYLBORONATE, A CHIRAL ALLYLIC ALCOHOL β–CARBANION EQUIVALENT FOR THE ENANTIOSELECTIVE SYNTHESIS OF 2-BUTENE-1,4-DIOLS FROM ALDEHYDES

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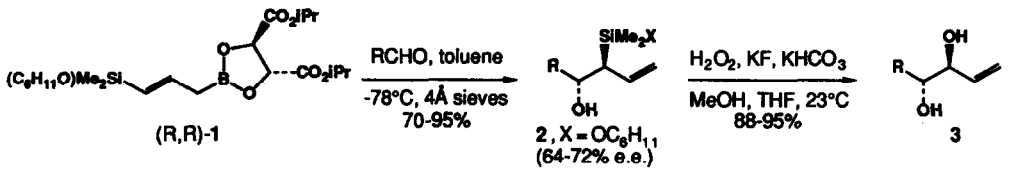
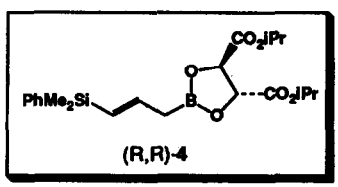
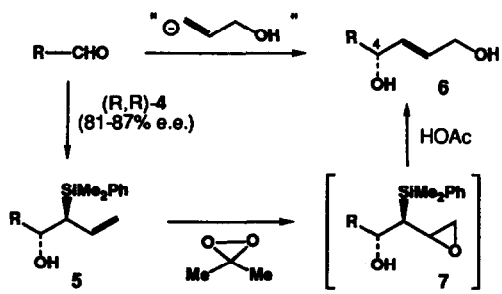
Abstract. An enantioselective synthesis of 4-substituted (E)-2-buten-1,4-diols is described. The method involves the reaction of aldehydes with the chiral $PhMe_2Si$- substituted allylboronate 3 followed by epoxidation (dimethyl dioxirane) and acid catalyzed Petersen rearrangement of the intermediate epoxysilanols.

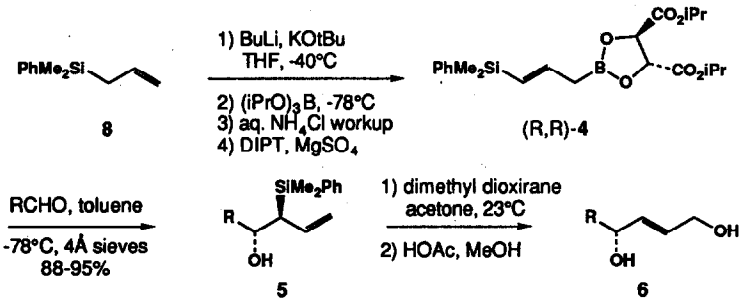
In the preceding communication we described the enantioselective synthesis of anti 1,2-diols **3** via the reactions of aldehydes and the chiral (E)-γ-(alkoxysilyl)allylboronate **1**.[1] Although this method provides anti silanols **2** and the derived anti diols **3** with excellent diastereoselectivity, the enantioselectivity of **1** is only moderate (64-72% e.e.). We report herein the synthesis and aldehyde allylboration reactions of the analogous $PhMe_2Si$- substituted allylboronate **4**. While the enantioselectivity of **4** (81-87% e.e.) is considerably improved compared to **1**, we have been unable to utilize anti silanols **5** in syntheses of anti diols **3** since electrophilic substitution reactions of the allylsilane moiety are faster than protodesilylation or other Ph-Si cleavage reactions required as the first step in the Fleming oxidation procedure.[2] During the course of these investigations, however, we found that silanols **5** are smoothly converted into 4-substituted butene-1,4-diols **6** via oxidation with dimethyl dioxirane[3] followed by the acid catalyzed Petersen elimination of the intermediate epoxysilanes **7**. Allylboronate **4** thus functions as a chiral allylic alcohol β-carbanion equivalent capable of controlling the absolute stereochemistry of the hydroxyl group generated at C(4) of **6**. This method promises to have considerable stereochemical generality especially in reactions with chiral aldehydes, and therefore is likely to find numerous applications in organic synthesis.[4]







(E)-γ-(Dimethylphenylsilyl)allylboronate **4** was prepared from allyl(dimethylphenyl)silane **8** using slight modifications of our standard allylboronate synthesis.[1,5] Thus, a THF solution of **8** was treated with 1.0 equiv. of n-BuLi/KOtBu -40°C for 15 min followed by 1.0 equiv. of $(iPrO)_3B$ at -78°C for 15 min. This mixture was poured into aq. NH_4Cl solution and extracted with ether. The extracts were immediately treated with 1.0 equiv. of DIPT, dried over $MgSO_4$ (2 h), and then concentrated to constant weight in vacuo. The crude product, consisting primarily of **4** and residual **8** and DIPT, is analyzed by ^1H NMR to determine the weight percentage of **4** in the mixture; the yield of **4** is generally 70-80%. Crude **4** was dissolved in toluene (ca. 1 M) and stored over 4Å molecular sieves at -20°C under Ar. Reactions with aldehydes were performed in toluene (0.3-0.5 M) at -78°C in the presence of 4Å molecular sieves ($t_{1/2}$ ~ 4 h at 0.3 M).

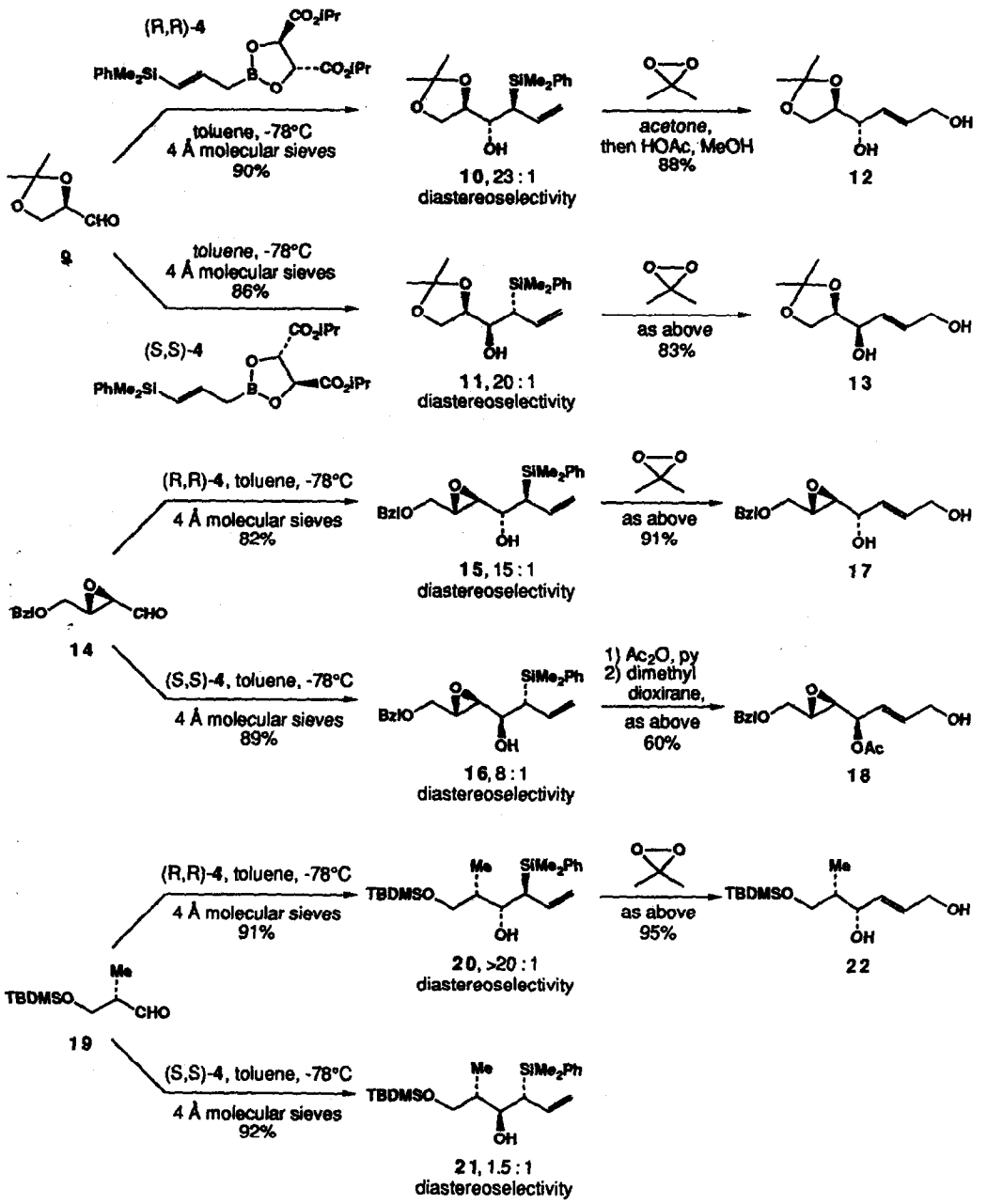


Aldehyde	Yield of 5	%E.e. of 5	Yield of 6
acetaldehyde	95%	84% e.e.	--
hexanal	95%	81% e.e.	89%
cyclohexanecarboxaldehyde	88%	87% e.e.	95%

The enantioselectivity of **4** was assessed via reactions with acetaldehyde, hexanal and cyclohexanecarboxaldehyde. The anti silanols **5** were obtained with excellent diastereoselectivity (the syn diastereomers were not detected) in 88-95% isolated yields and with enantiomeric purities of 81-87% e.e.[6] The enantioselectivity of **3** thus closely parallels that of the tartrate (E)-crotylboronate that we have previously studied.[5,6]

Our main interest in the development of this reagent was for use in double asymmetric reactions with chiral aldehydes.[7,8] As shown in the accompanying Figure, the reactions of (R,R)- and (S,S)-**4** with glyceraldehyde acetonide **9** display outstanding stereoselectivity, providing diastereomers **10** and **11** each with ≥20 : 1 diastereoselectivity. Similarly, the reactions of these reagents and epoxyaldehyde **14** also exhibit excellent stereocontrol. The reaction with (R,R)-**4** provides **15** with 15 : 1 selectivity, while **16** is the major product of an 8 : 1 mixture when (S,S)-**4** is used. It should be noted that the enantiomeric purity of **14** is only 95% e.e., and it can be calculated that the diastereoselectivity of these reactions would be 20 : 1 and 1 : 10, respectively, if enantiomerically pure **14** were used.[9] Finally, the reaction of α-methyl-β-alkoxy aldehyde **19** displays outstanding diastereoselectivity for **20** (>20 : 1) in the matched reaction with (R,R)-**4**, but poor selectivity (ca. 1.5 : 1) in the mismatched case leading leading to the anti, anti diastereomer **21**. Better selectivity for **21** undoubtedly can be obtained by using a more enantioselective chiral auxiliary.

The epoxidation of the anti silanols and the subsequent acid catalyzed Petersen elimination constitutes the second stage of this method. While the epoxidation of allylsilanes has received considerable study,[10] we found that it was not possible to cleanly epoxidize the allylsilanols prepared in this study by using either



MCPBA or $VO(acac)_2$/TBHP. Evidently, the rate of these epoxidations is slow (vinyl groups are poor epoxidation substrates) and Petersen eliminations of the intermediate epoxysilanes are probably competitive. The resulting allylic alcohols undoubtedly undergo a second epoxidation, leading ultimately to a mixture of

products. This problem was solved by using an acetone solution of dimethyl dioxirane as the oxidant.[3,11] This reagent is neutral, the epoxidations are very fast, and competitive Petersen eliminations were not observed. The reaction mixtures were concentrated in vacuo and then treated with methanolic HOAc to effect the rearrangement to the desired allylic alcohols, obtained typically in 88-95% overall yield. This study thus adds to the growing list of applications of dimethyl dioxirane as a mild, selective oxidant in organic synthesis.

In summary, an efficient method for the stereoselective synthesis of (E)-2-buten-1,4-diols by the formal addition of an (E)-prop-2-en-1-ol unit to an aldehyde has been developed. We anticipate that this procedure will find application in the synthesis of carbohydrates and other polyhydroxylated natural products.

Acknowledgement: This research was supported by a grant from the National Institute of General Medical Sciences (GM 38907).

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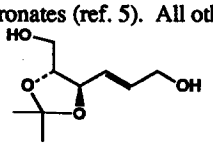
3. Adam, W.; Curci, R.; Edwards, J. O. *Acc. Chem. Res.* **1989**, 22, 205.
4. Alternative methods for the diastereoselective synthesis of **6** from chiral aldehyde precursors: (a) Annunziata, R.; Cinquini, M.; Cozzi, F.; Raimondi, L.; Stefanelli, S. *Tetrahedron* **1986**, 42, 5443 (via allylic sulfoxides). (b) Burgess, K.; Henderson, I. *Tetrahedron Lett.* **1989**, 30, 4325 (conversion of RCH_2CHO to enoates corresponding to **2** via reactions with chiral α-sulfinyl acetates). (c) The stereoselective addition of (E)-3-lithiopropen-1-yl ethers (c.f., Corey, E. J.; Wollenberg, R. H. *J. Org. Chem.* **1975**, 40, 2265) to chiral aldehydes is another possibility.
5. (a) Roush, W. R.; Ando, K.; Powers, D. B.; Halterman, R. L.; Palkowitz, A. D. *J. Am. Chem. Soc.* **1990**, 112, 6339. (b) Roush, W. R.; Hoong, L. K.; Palmer, M. A. J.; Straub, J. A.; Palkowitz, A. D. *J. Org. Chem.* **1990**, 55, 4117.
6. (a) The stereochemistry of anti silanols **5c**, **10**, and **11** was established by Petersen eliminations (NaH, THF) to the corresponding (Z,E)-dienes. (b) The sense of asymmetric induction of **4** was established by the acid catalyzed isomerization of allylic alcohols **12** and **13**. Treatment of **13** with cat. TsOH in acetone provided **i** quantitatively, while similar treatment of **12** provided a 3 : 1 mixture of **12** and **ii**. The absolute stereochemistry of the reactions of **4** is thus the same as for other tartrate ester modified allylboronates (ref. 5). All other stereostructures in text are assigned by analogy.



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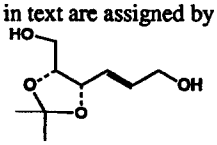

II (cis acetonide)

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8. The intrinsic face selectivities of **9** (58 : 42, favoring **10**) **14** (60 : 40, favoring **16**) and **19** (73 : 27, favoring **20**) were determined via reactions with pinacol (E)-γ-(dimethylphenylsilyl)allylboronate.
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11. For epoxidation of acid labile substrates: Halcomb, R. L.; Danishefsky, S. J. *J. Am. Chem. Soc.* **1989**, 111, 6661.
12. All new compounds reported herein were fully characterized (NMR, IR, mass spectrum, CH analysis).

(Received in USA 17 September 1990)