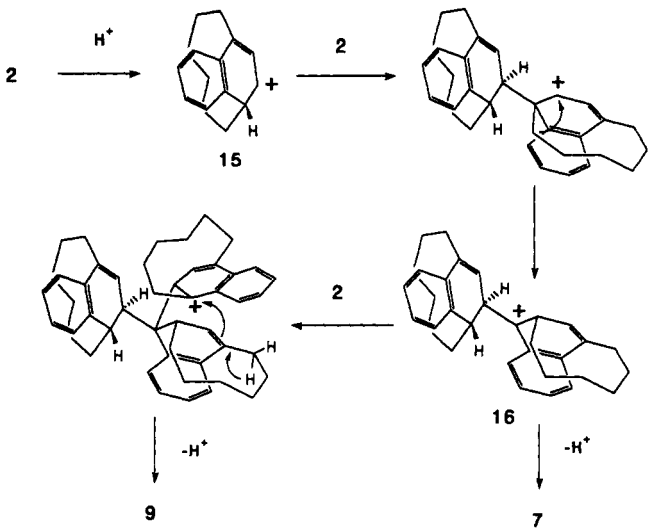
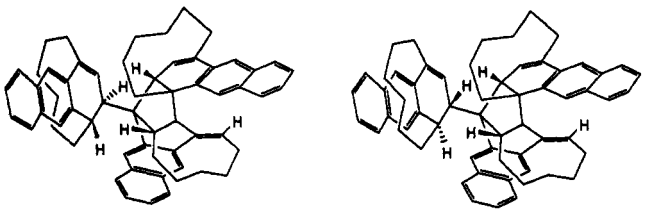
Scheme I



or dimeric products could be detected even after dilute (1.3×10^{-3} M) solutions of 3 were treated with acid.



The formation of dimers 6–8 and trimers 9, 10, 13, and 14 can be readily explained by positing a series of electrophilic attacks by intermediate cations on the respective substrates, as is shown in Scheme I for the naphthalene 2. It should be noted that, in the case of 2, electrophilic attack on the second substrate molecule takes place before the migration of the hexamethylene bridge of the cation 15, and that attack on the third molecule of substrate occurs before loss of proton from the meta-bridged dimeric cation 16. The last attack takes place at a less hindered site (C-2) in the aromatic core. The pronounced tendency of 2 and 3 to telomerize rather than isomerize can be explained in terms of the enhanced reactivity arising from the high HOMO level and the large double-bond character of the C-1–C-2 bond of the acene cores of the molecules.[15] In summary, we have observed, for the first time, an acid-catalyzed telomerization of bridged arenes, the aromatic rings of which are severely deformed into boat conformations by the presence of a 1,4-hexamethylene bridge.

Acknowledgment. We thank to the Crystallographic Research Center of the Institute for Protein Research and the Instrumental Analysis Center of the Faculty of Engineering, Osaka University, for the use of X-ray and NMR and MS facilities, respectively. We are also grateful to the Ministry of Education, Science, and Culture for partial support of this work through a Grant-in-Aid for Scientific Research on Priority Areas (Grant No. 02230217).

Supplementary Material Available: Experimental details of the preparation and isolation of dimers 6–8 and trimers 9, 10, 13, and 14; spectroscopic characteristics and other analytical data; labeled ORTEP drawings and tables of interatomic bond distances and angles, fractional atomic coordinates, and anisotropic thermal parameters for atoms other than hydrogen for 7 and 13·2CH_2Cl_2 (19 pages). Ordering information is given on any current masthead page.

(15) For unusual reactions of 2 and 3, see: Tobe, Y.; Takahashi, T.; Kobiro, K.; Kakiuchi, K. *Tetrahedron Lett.* **1991**, *32*, 359–362; *J. Am. Chem. Soc.*, in press.

B-[3-((Diisopropylamino)dimethylsilyl)allyl]diisopinocampheylborane: An Excellent Reagent for the Stereoselective Synthesis of Anti Vicinal Diols

Anthony G. M. Barrett* and James W. Malecha

Department of Chemistry, Colorado State University, Fort Collins, Colorado 80523

Received June 4, 1991

Summary: Aldehydes reacted stereoselectively with *B*-[3-((diisopropylamino)dimethylsilyl)allyl]diisopinocampheylborane, derived from (+)- and (−)-α-pinene, to provide, on workup with hydrogen peroxide, (3*S*,4*R*)- and (3*R*,4*S*)-dihydroxy-1-alkenes, respectively.

Recently Brown and co-workers have introduced several allyl- and crotylboranes that are spectacularly useful for the conversion of aldehydes into homoallylic alcohols.[1,2] The methods are particularly useful for the preparation of 4-hydroxy- and 4-hydroxy-3-methyl-1-alkenes. In all cases, the products were formed with both excellent relative and absolute stereochemical control. This chemistry is exemplified by the *E* and *Z* isomers of *B*-(crotyl)diisopinocampheylborane (**1a,b**) both of which are available in high enantiomeric purity from the commercial *B*-methoxy compound **1c**.[3] On reaction with aldehydes, the *E* reagent **1a** gave the anti[4] homoallylic alcohol **2**, whereas the *Z* isomer produced the corresponding syn compound **3**. In addition, the antipodal reagents corresponding to **1a** and **1b** are also readily available.[3] Thus, the enantiomers of the anti and syn homoallylic alcohols **2** and **3** are also easily synthesized with outstanding stereochemical control. Since homoallylic alcohols may be oxidized to reveal protected β-hydroxy aldehyde systems, the Brown methodology has found considerable use as a masked aldol strategy in

(1) For example, see: Racherla, U. S.; Brown, H. C. *J. Org. Chem.* **1991**, *56*, 401. Jadhav, P. K.; Bhat, K. S.; Perumal, P. T.; Brown, H. C. *J. Org. Chem.* **1986**, *51*, 432. Brown, H. C.; Bhat, K. S. *J. Am. Chem. Soc.* **1986**, *108*, 5919. Brown, H. C.; Randad, R. S.; Bhat, K. S.; Zaidlewicz, M.; Racherla, U. S. *J. Am. Chem. Soc.* **1990**, *112*, 2389. Srebmik, M.; Ramachandran, P. V. *Aldrichimica Acta* **1987**, *20*, 9 and references therein.

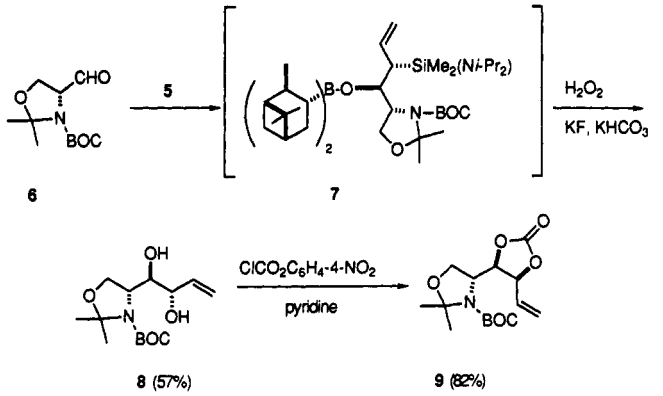
(2) For examples of alternative methods to prepare homoallylic alcohols from allylboranes, see: Mikhailov, B. M.; Pozdnev, V. F. *Izv. Acad. Nauk SSSR, Ser. Khim.* **1967**, 1477. For a review of addition of crotylboronates to aldehydes, see: Hoffmann, R. W. *Angew. Chem., Int. Ed. Engl.* **1982**, *21*, 555. Roush, W. R.; Halterman, R. L. *J. Am. Chem. Soc.* **1986**, *108*, 294 and references therein. Midland, M. M.; Preston, S. B. *J. Am. Chem. Soc.* **1982**, *104*, 2330. Garcia, J.; Kim, B.-M.; Masamune, S. *J. Org. Chem.* **1987**, *52*, 4831.

(3) Either antipode is commercially available from Aldrich. Brown, H. C.; Desai, M. C.; Jadhav, P. K. *J. Org. Chem.* **1982**, *47*, 5065. Brown, H. C.; Jadhav, P. K. *J. Am. Chem. Soc.* **1983**, *105*, 2092.

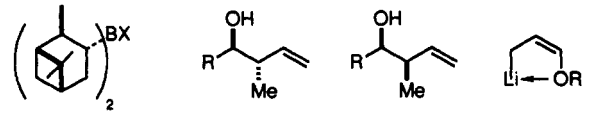
(4) Masamune, S.; Choy, W. *Aldrichimica Acta* **1982**, *15*, 47.

0022-3263/91/1956-5243$02.50/0

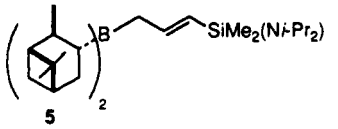
Scheme I



synthesis.[5] Brown has additionally extended these studies to reagents **1d** and **1e** and their antipodes.[6] These reagents are useful for the enantioselective preparation of allylic diols with the syn relative stereochemistry. Herein we report the extension of these methods to the direct synthesis of anti vicinal diols from aldehydes. The method is noteworthy for the excellent relative and absolute stereochemical control and ease of experimental operation.

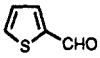
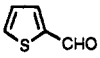
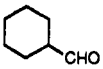


a X = (E)-CH_2CH = CHMe
b X = (Z)-CH_2CH = CHMe
c X = OMe
d X = (Z)-CH_2CH = CH(OMe)
e X = (Z)-CH_2CH = CH(OMEM)
f X = (E)-CH_2CH = CH(OR)



In connection with our studies on the potent marine protein phosphatase inhibitor calyculin A,[7] we needed to devise a method to directly convert the serine derivative **6**[8] into the corresponding vicinal diol **8**. Thus we set out to extend the Brown methodology to prepare such diols with the anti relative stereochemistry. Since the direct metalation of allyl ethers using butyllithium is *Z*-specific and provides the chelate **4**,[9] we sought an indirect method to produce reagents equivalent to the required allylborane **1f**. An allylsilane proved to be an excellent surrogate.[10] Metalation of allyl(diisopropylamino)dimethylsilane[11] using butyllithium in TMEDA at 0 °C and sequential reaction of the resultant *E* lithio derivative with **1c** and boron trifluoride etherate[1] gave the *E* reagent **5**.[12,13] Addition of aldehyde **6** at −78 °C gave an intermediate, which was presumably the corresponding anti β-hydroxy silane boronate ester **7** (Scheme I). This was not isolated but was directly reacted on workup with hydrogen peroxide under basic conditions. This resulted in the oxidative cleavage of the carbon–silicon bond, a process that is known to proceed with retention of stereochemistry,[14] and the hydrolysis of the boronate ester. The resultant diol **8** was obtained in good overall yield as a single diastereoisomer. Inspection of the ^1H NMR spectrum of the crude diol showed only the presence of a single isomer and the stereochemistry of this was unequivocally established by an X-ray crystallographic study of the derived carbonate **9**.[15]

Table I. Synthesis of 3*S*,4*R* Diols and 3*R*,4*S* Diol 13 Using the Borane Reagents 5 and 12

entry	aldehyde	product (%), de	Mosher ester (%), de
1	**6**	**8** (57), >98:<2	
2	**6**	**8** (30), **13** (15)	
3		**10a** (44), >95:<5	**11a** (95), >95:<5
4		**14a** (47), >95:<5	**15a** (82), >95:<5
5	PhCHO	**10b** (50),>95:<5	**11b** (83), >95:<5
6	PhCHO	**14b** (47), >95:<5	**15b** (79), >95:<5
7	n-C_6H_{13}CHO	**10c** (52), >95:<5	*a*
8		**10d** (63), >95:<5	*a*

[a] Not determined.

A series of simple aldehydes was also reacted sequentially with the allylborane derivative **5** and hydrogen peroxide to produce the corresponding anti diols.[10] All these results are summarized in Table I.[16] In each case, the diastereoselectivity of the reaction was estimated by examination of the ^1H NMR spectrum of the diol. Additionally, the enantiomeric purity of each diol was determined from the ^1H NMR spectrum of the derived

(5) For examples, see: Barrett, A. G. M.; Lebold, S. A. *J. Org. Chem.* **1990**, *55*, 5818. Merifield, E.; Steel, P. G.; Thomas, E. J. *J. Chem. Soc., Chem. Commun.* **1987**, 1826. Khandekar, G.; Robinson, G. C.; Stacey, N. A.; Steel, P. G.; Thomas, E. J.; Vather, S. *J. Chem. Soc., Chem. Commun.* **1987**, 877.

(6) Brown, H. C.; Jadhav, P. K.; Bhat, K. S. *J. Am. Chem. Soc.* **1988**, *110*, 1535.

(7) Kato, Y.; Fusetani, N.; Matsunaga, S.; Hashimoto, K.; Fujita, S.; Furuya, T. *J. Am. Chem. Soc.* **1986**, *108*, 2780.

(8) Garner, P.; Park, J. M. *J. Org. Chem.* **1990**, *55*, 3772.

(9) Evans, D. A.; Andrews, G. C.; Buckwalter, B. *J. Am. Chem. Soc.* **1974**, *96*, 5560. Still, W. C.; Macdonald, T. L. *J. Am. Chem. Soc.* **1974**, *96*, 5561.

(10) For a review on allylsilanes, see: Fleming, I. *Org. React.* **1989**, *37*, 2.

(11) Tamao et al. have introduced this reagent for the preparation of racemic anti 3,4-dihydroxy-1-alkenes via metalation, addition to aldehydes, and hydrogen peroxide oxidation. With nonbranched aliphatic aldehydes, the diastereoselectivity of addition of the allylzinc derivative was only modest, see: Tamao, K.; Nakajo, E.; Ito, Y. *J. Org. Chem.* **1987**, *52*, 957.

(12) Both reagents **5** and **12** were prepared and used directly in situ without isolation.

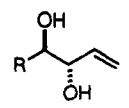
(13) Roush and co-workers have recently demonstrated that diisopropyl tartrate modified borane derivatives of allyl(cyclohexyloxy)dimethylsilane are useful reagents for the synthesis of anti 3,4-dihydroxy-1-alkenes. Again these methods are based upon the initial observations of Tamao et al. Roush, W. R.; Grover, P. T.; Lin, X. *Tetrahedron Lett.* **1990**, *31* 7563. Roush, W. R.; Grover, P. T. *Tetrahedron Lett.* **1990**, *31*, 7567.

(14) For example, see: Tamao, K.; Nakajima, T.; Sumiya, R.; Arai, H.; Higuchi, N.; Ito, Y. *J. Am. Chem. Soc.* **1986**, *108*, 6090.

(15) Details of the crystal structure **9** will be published elsewhere: Miller, M. A.; Anderson, O. P. Submitted for publication.

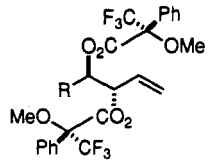
(16) The preparation of diol **8** is representative: to a solution of allyl(diisopropylamino)dimethylsilane (1.28 g, 6.4 mmol) in dry ether (7 mL) at 0 °C were added TMEDA (0.97 mL, 6.4 mmol) and n-BuLi (3.6 mL, 6.4 mmol, 1.6 M in hexane). The solution was kept at 0 °C for 4 h and cooled to −78 °C. The solution was treated with (−)-*B*-methoxydiisopinocampheylborane (2.42 g, 7.6 mmol) in dry ether (1.5 mL) and maintained at −78 °C for 2 h. To this solution were added $BF_3{\cdot}OEt_2$ (1.0 mL, 8.3 mmol) and aldehyde **6** (1.05 g, 4.5 mmol) in dry ether (1 mL). The reaction mixture was kept at −78 °C for 3 h. To this mixture were added THF (6 mL), MeOH (6 mL), potassium fluoride (0.72 g, 12.8 mmol), potassium bicarbonate (1.24 g, 12.8 mmol), and 30% H_2O_2 (14 mL). The mixture was stirred at room temperature for 20 h and cooled to 0 °C, and the excess H_2O_2 was quenched by the addition of sodium thiosulfate. The mixture was diluted with EtOAc (40 mL) and filtered through Celite. The Celite pad was washed with EtOAc (3 × 100 mL), and the filtrate was dried ($MgSO_4$) and concentrated in vacuo. The residue was purified by flash chromatography (silica gel, 3:1 hexanes/EtOAc) to yield 0.74 g (57%) of diol **8**.

(*R*)-Mosher diester 11.[17] The diols 13 and 14 were also



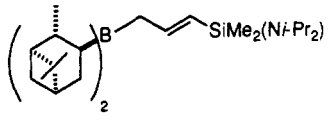
10

a R = 2-thienyl
b R = Ph
c R = *n*-C_6H_{13}
d R = cyclohexyl



11

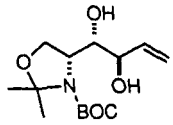
a R = 2-thienyl
b R = Ph



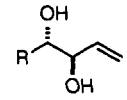
12

prepared from the reaction of the aldehydes with reagent **12**.[12] Again, the diastereoselectivity of the reaction was determined from the ^{1}H NMR spectra and the enantioselectivity from an examination of the derived Mosher diester **15**. All these results are also included in Table I. It is interesting to note that although the reaction of the aldehyde **6** with reagent **5** gave only a single diol **8**, reaction with the antipodal reagent **12** gave both anti diols **8** and **13** (entry 2).[18] Clearly in this second case, the reagent and substrate (Felkin–Ahn control) stereochemical biases are mismatched. The entries 3–8 show that simple aldehydes are converted into the corresponding anti diols **10a–d** and **14a,b**, all with excellent relative stereochemical control.[19]

Additionally, formation of the Mosher diesters **11a,b** and **15a,b** clearly showed that, at least for entries 3–6, the enantioselectivity of reaction[20] was also impressive.

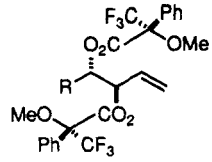


13



14

a R = 2-thienyl
b R = Ph



15

a R = 2-thienyl
b R = Ph

This study further demonstrates the utility of pinene-derived compounds in asymmetric synthesis. The direct conversion of aldehydes into anti diols via an experimentally simple one-pot process should be of very considerable use in synthesis. It is germane to compare the reactivity of the allylboranes **5** and **12** with the analogous tartrate reagents described by Roush.[13] Although the overall yields of diols from the allylsilane precusors were comparable with both methods, reagents **5** and **12** showed superior enantioselectivities in their reactions with aldehydes.

Acknowledgment. We thank the National Institutes of Health for support of this program (AI-20644) and G.D. Searle & Company for unrestricted support and microanalyses.

(17) For the preparation of Mosher esters, see: Dale, J. A.; Dull, D. L.; Mosher, H. S. *J. Org. Chem.* **1969**, *34*, 2543.

(18) The relative stereochemistry of diol **13** was determined from comparison of the chemical shift and *J* values for the C*H*(OH)CH=CH_2 proton in the ^{1}H NMR spectrum with the corresponding data for diol **8**. Corresponding syn diols show larger C*H*(OH)C*H*(OH) coupling constants, see ref 11 and references therein.

(19) The relative stereochemical assignments for the anti diols **10a**, **14a**, **10b**, and **14b** was determined by comparisons of ^{1}H NMR data observed with that reported for the corresponding racemic diols. See: Dana, G.; Chuche, J.; Monot, M.-R. *Bull. Soc. Chim. Fr.* **1967**, 3308. The assignments of relative stereochemistries for the diols **10c** and **10d** followed from the comparisons of the C*H*(OH)CH=CH_2 protons in the ^{1}H NMR spectra with the corresponding resonances for diols **10a** and **10b**.

(20) The absolute stereochemistry of reaction was rigorously established only for the diol **8**. All other absolute stereochemical assignments are based upon comparisons of the ^{1}H NMR spectra of the derived Mosher esters **11a** and **15a** and **11b** with **15b** (see ref 15). The absolute stereochemistries of **10c** and **10d** are based upon analogy with the other examples in Table I and on the basis of the known absolute stereochemical bias of (+)-α-pinene-derived reagents (see ref 1).

Cyclization of Alkoxymethyl Radicals

Viresh H. Rawal,* Surendra P. Singh, Claire Dufour, and Christophe Michoud

Department of Chemistry, The Ohio State University, Columbus, Ohio 43210

Received June 4, 1991

Summary: Alkoxymethyl radicals, generated conveniently from phenylseleno precursors, cyclize to afford substituted tetrahydrofurans and tetrahydropyrans in excellent yield and with good stereoselectivity.

Cyclization of hexenyl radicals to cyclopentylmethyl radicals represents one of the most useful and thoroughly studied reactions in radical chemistry.[1] The analogous cyclization where carbon 3 in the hexenyl chain is replaced by an oxygen (or a nitrogen) is of considerable importance for the synthesis of heterocycles. In this process, illustrated by Stork's classic example (eq 1),[2] an allylic alcohol is extended by a two-carbon unit capable of forming a radical at the terminus. The resulting 2-alkoxyethyl radical undergoes a smooth cyclization to afford 2-alkoxytetrahydrofurans. This process has been studied extensively and nicely incorporated in the synthesis of complex substances.[1,3]

(1) For leading general references, see: (a) Beckwith, A. L. J.; Ingold, K. U. In *Free Radical Rearrangements*; de Mayo, P., Ed.; Academic Press: New York, 1980; Vol. 1, pp 161–310. (b) Hart, D. J. *Science (Washington, D.C.)* **1984**, *223*, 883. (c) Giese, B. *Radicals in Organic Synthesis: Formation of C–C Bonds*; Pergamon Press: New York, 1986. (d) Ramaiah, M. *Tetrahedron* **1987**, *43*, 3541. (e) Curran, D. P. *Synthesis* **1988**, 417 and 489.

(2) Stork, G.; Mook, R., Jr.; Biller, S. A.; Rychnovsky, S. D. *J. Am. Chem. Soc.* **1983**, *105*, 3741. For related studies, see: (a) Tada, M.; Okabe, M. *Chem. Lett.* **1980**, 201 and 831. (b) Okabe, M.; Tada, M. *J. Org. Chem.* **1982**, *47*, 5382. (c) Ueno, Y.; Chino, K.; Watanabe, M.; Moriya, O.; Okawara, M. *J. Am. Chem. Soc.* **1982**, *104*, 5564.

(3) The cyclization of the 2-alkoxyalkyl radical has been utilized extensively. Recent examples include the following: (a) Stork, G.; Sher, P. M.; Chen, H.-L. *J. Am. Chem. Soc.* **1986**, *108*, 6384. (b) Hutchinson, J. H.; Pattenden, G.; Myers, P. L. *Tetrahedron Lett.* **1987**, *28*, 1313. (c) Hart, D. J.; Huang, H.-C.; Krishnamurthy, R.; Schwartz, T. *J. Am. Chem. Soc.* **1989**, *111*, 7507.

0022-3263/91/1956-5245$02.50/0