Facile Synthesis of Terminal 1,2-Diols with High Optical Purity via Oxazaborolidine-Catalyzed Asymmetric Borane Reduction

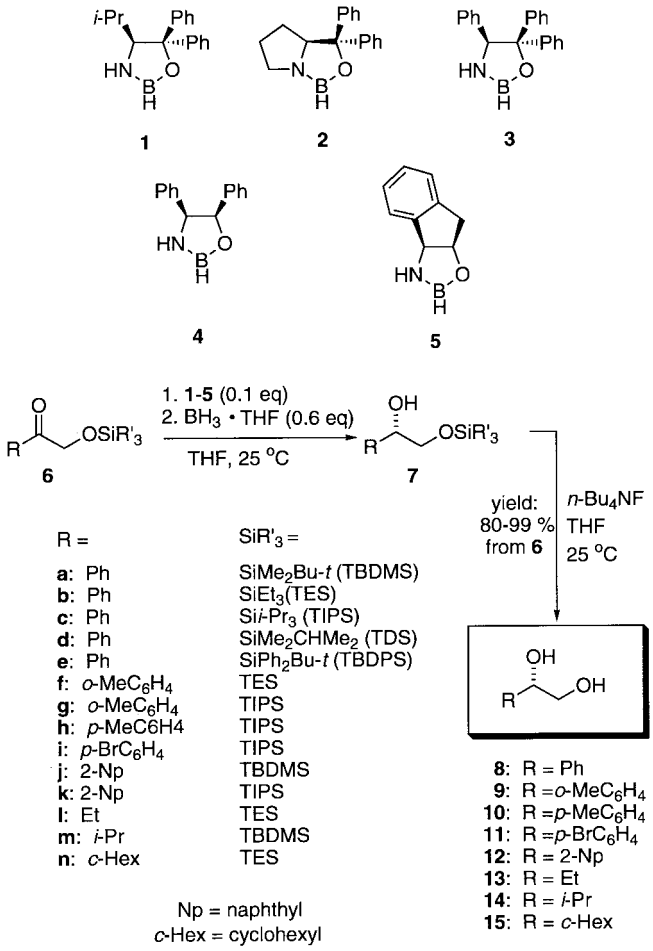
Byung Tae Cho* and Yu Sung Chun

Departmet of Chemistry, Hallym University, Chunchon, Kangwondo 200-702, Republic of Korea

Received March 10, 1998

Optically active terminal 1,2-diols have found widespread use as chiral building blocks[1] and numerous applications as chiral auxiliaries or ligands[2] for asymmetric synthesis. Accordingly, the development of a general methodology for the asymmetric synthesis of these compounds, such as the catalytic asymmetric dihydroxylation of olefins,[3] the catalytic enantioselective addition of dialkylzincs to α-silyloxy aldehyde derivatives,[4] and the enzymatic hydrolysis of diol monoacetates[5] has been extensively investigated. In fact, 1,2-chiral diols have been prepared from the asymmetric reduction of α-hydroxy ketones via chiral boranes[6] and chiral diphosphine-catalyzed hydrosilylations.[7] Recently, a number of asymmetric borane reductions of functionalized prochiral ketones catalyzed by oxazaborolidines has been reported by Corey and others.[8,9] The reductions of α-halo ketones,[9c] 2-acyl-1,3-dithianes,[10] α-ketophosphonates,[11] and other prochiral ketones containing heteroatoms[12] have been reported to give excellent enantioselectivities. We recently have reported asymmetric reduction of functionalized ketones, such as α-amino ketones[13] and α-keto acetals.[14] The extension of this methodology for the asymmetric synthesis of terminal 1,2-diols via asymmetric reduction of α-hydroxy ketone derivatives, however, has not been reported to date.[15] We describe here a simple and convenient procedure for obtaining terminal 1,2-diols with high optical purity by employing the oxazaborolidine-catalyzed asymmetric borane reduction of α-[(triorganosilyl)oxy] ketones.

Scheme 1



The α-[(triorganosilyl)oxy] ketone derivatives (**6a**−**n**) used as substrates were prepared from the silylation of α-hydroxy ketones[16] with 1.2 equiv of triorganosilyl chloride in the presence of 1.5 equiv of imidazole in dichloromethane at room temperature in 62−96% yields, according to the literature procedure.[17]

Initially, five chiral oxazaborolidines (**1**,[18] **2**,[19] **3**,[20] **4**,[21] and **5**[22]) prepared from commercially available materials were chosen as representative catalysts for the reduction of 2-[(*tert*-butyldimethylsilyl)oxy]acetophenone (**6a**). Thus, slow addition of **6a** over 1 h to a solution of 0.6 equiv of borane-THF in the presence of 10 mol % of each oxazaborolidine in THF at 25 °C (Scheme 1) provided

* To whom correspondence should be addressed. Tel.: +82-361-240-1423. Fax: +82-361-242-4572. E-mail: btcho@sun.hallym.ac.kr.

(1) Hanessian, H. *Total Synthesis of Natural Products*: *the "Chiron" Approach*; Pergamon Press: Oxford, 1983.
(2) Seyden-Penn, J. *Chiral Auxiliaries and Ligands in Asymmetric Synthesis*; John Wiley & Sons, Inc.: New York, 1995.
(3) Kolb, H. C.; VanNieuwenhze, M. S.; Sharpless, K. B. *Chem. Rev.* **1994**, *94*, 2483.
(4) Eisenberg, C.; Knochel, P. *J. Org. Chem.* **1994**, *59*, 3760.
(5) Wong, C.-H.; Whitesides, G. M. *Enzymes in Synthetic Organic Chemistry*; Pergamon Press: Oxford, 1994.
(6) Ramachandran, P. V.; Lu, Z.-H.; Brown, H. C. *Tetrahedron Lett.* **1997**, *38*, 761.
(7) Burk, M. J.; Feaster, J. E. *Tetrahedron Lett.* **1992**, *33*, 2099.
(8) For general reviews on the oxazaborolidine-catalyzed reductions, see: (a) Sing, V. K. *Synthesis* **1992**, 605. (b) Wallum, S.; Martens, J. *Tetrahedron*: *Asymmetry* **1992**, *3*, 1475.
(9) (a) Corey, E. J.; Bakshi, R. K.; Shibata, S.; Chen, C.-P.; Singh, V. K. *J. Am. Chem. Soc.* **1987**, *109*, 7925. (b) Corey, E. J.; Bakshi, R. K. *Tetrahedron Lett.* **1990**, *30*, 611. (c) Corey, E. J.; Link, J. O. *J. Org. Chem.* **1991**, *56*, 442.
(10) DeNinno, M. P.; Perner, R. J.; Lijewski, L. *Tetrahedron Lett.* **1990**, *31*, 7415.
(11) Meier, C.; Laux, W. H. G. *Tetrahedron*: *Asymmetry* **1995**, *6*, 1089.
(12) Qallich, G. J.; Woodall, T. M. *Tetrahedron Lett.* **1993**, *34*, 785.
(13) Cho, B. T.; Chun, Y. S. *Tetrahedron*: *Asymmetry* **1992**, *3*, 341.
(14) Cho, B. T.; Chun, Y. S. *Tetrahedron*: *Asymmetry* **1994**, *5*, 1147.
(15) (a) For a catalytic asymmetric borane reduction of benzils, see: Prasad, K. R. K.; Joshi, N. N. *J. Org. Chem.* **1996**, *61*, 3888. (b) For an enzymatic reduction of 1-hydroxy ketones, see: Lee, L. G.; Whitesides, G. M. *J. Org. Chem.* **1986**, *51*, 25.
(16) Levene, P. A.; Walti, A. *Organic Synthesis*; John Wiley & Sons: New York, 1943; Collect. Vol. II, pp 5−6.
(17) Corey, E. J.; Venkateswarlu, A. *J. Am. Chem. Soc.* **1972**, *94*, 6190.
(18) Itsuno, S.; Nakano, M.; Miyazaki, K.; Masuda. H.; Itoh, K.; Hirao, A.; Nakahama, S. *J. Chem. Soc., Perkin Trans. 1* **1985**, 2039.
(19) Corey, E. J.; Bakshi, R. K.; Shibata, S. *J. Am. Chem. Soc.* **1987**, *109*, 5551.
(20) Berenguer, R.; Garcia, J.; Vilarrasa, J. *Tetrahedron*: *Asymmetry* **1994**, *5*, 165.
(21) Qallich, G. J.; Blake, J. F.; Woodall, T. M. *J. Am. Chem. Soc.* **1994**, *116*, 851.
(22) Yaping, H.; Gao, Y.; Nie, X.; Zepp, C. M. *Tetrahedron Lett.* **1994**, *35*, 6631.

S0022-3263(98)00455-1 CCC: $15.00
Published on Web 06/27/1998

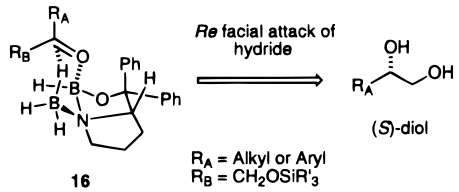
Table 1. Asymmetric Borane Reduction of α-[(Triorganosilyl)oxy] Ketones (6) in the Presence of 10 mol % of Oxazaborolidines in THF at 25 °C[a]

entry	compd	cat.	diol	yield,[b] %	$[\alpha]^{25}_D$ (EtOH)	% ee	config
1	**6a**	**1**	**8**	90	+35.91 (*c* 4.24)	91[c]	*S*[d]
2	**6a**	**2**	**8**	94	+38.90 (*c* 3.61)	99[c](100)[d]	*S*[d]
3	**6a**	**3**	**8**	85	e	52[c]	*S*[d]
4	**6a**	**4**	**8**	84	e	74[c]	*S*[d]
5	**6a**	**5**	**8**	88	e	84[c]	*S*[d]
6	**6b**	**2**	**8**	94	+38.91 (*c* 3.81)	99[c] (100)[d]	*S*[d]
7	**6c**	**2**	**8**	95	+38.91 (*c* 3.59)	99[c] (100)[d]	*S*[d]
8	**6d**	**2**	**8**	92	+34.71 (*c* 3.81)	88[c]	*S*[d]
9	**6e**	**2**	**8**	90	+32.11 (*c* 3.99)	77[c]	*S*[d]
10	**6f**	**2**	**9**	92	+80.59 (*c* 1.01)[g]	87[f] (87)[h]	*S*[h]
11	**6g**	**2**	**9**	99	+53.66 (*c* 1.08)[g]	58[f]	*S*[h]
12	**6h**	**2**	**10**	93	+18.81 (*c* 2.48)	>99[i]	*S*[j]
13	**6i**	**2**	**11**	98	+33.67 (*c* 1.98)[k]	>99[f] (100)[l]	*S*[l]
14	**6j**	**2**	**12**	94	+32.60 (*c* 1.02)	96[f] (100)[m]	*S*[m]
15	**6k**	**2**	**12**	93	+32.52 (*c* 1.04)	96[f] (100)[m]	*S*[m]
16	**6l**	**2**	**13**	82	−9.40 (*c* 2.59)	73[n]	*S*[o]
17	**6m**	**2**	**14**	80	+7.90 (*c* 1.98)[g]	75[n]	*S*[p]
18	**6n**	**2**	**15**	84	+4.94 (*c* 1.05)[g]	96[n] (94)[q]	*S*[q]

[a] [**6**]:[BH_3]:[cat] = 1:0.6:0.1. Cat. = oxazaborolidine. [**6**] = 0.3 M. The reaction was complete within 10 min to give the monosilylated product alcohol (**7**). [b] Isolated and purified yield obtained from reduction of **6**, followed by desilylation with *n*-Bu_4NF (see the Experimental Section). [c] Determined by HPLC analysis using a Daicel Chiralcel OB chiral column; hexane/*i*-PrOH = 9/1. [d] Based on $[\alpha]^{23}_D$ −38.4 (*c* 1.12, EtOH), 99% ee, *R* ref 23. [e] Not measured. [f] Determined by HPLC analysis using a Daicel Chiralcel OD chiral column; hexane/*i*-PrOH = 9/1. [g] Measured in $CHCl_3$. [h] Based on $[\alpha]^{22}_D$ −70.3 (*c* 0.91, $CHCl_3$), 76% ee, *R* ref 24. [i] Determined by HPLC analysis using a Daicel Chiralcel OB chiral column; hexane/*i*-PrOH = 96/4. [j] The absolute configuration is not known, but probably *S*, based on the elution order and the sign of rotation value of the product diol **10**. [k] Measured in acetone. [l] Based on $[\alpha]_D$ −33.5 (*c* 2.0, acetone), *R* ref 25. [m] Based on $[\alpha]^{23}_D$ −31.2 (*c* 0.997, EtOH), 99.5% ee, *R* ref 23. [n] Determined by GC analysis of its bis(trifluoromethyl) acetate using a Chiraldex G-TA column (Astec Inc). [o] Based on $[\alpha]^{25}_D$ −12.87 (*c* 2.5, EtOH), *S* ref 26. [p] Based on $[\alpha]^{20}_D$ +10.3 (*c* 1.15, $CHCl_3$), *S* ref 27. [q] Based on $[\alpha]^{23}_D$ −4.8 (*c* 0.922, $CHCl_3$), 91% ee, *R* ref 23.

1-[(*tert*-butyldimethylsilyl)oxy]-2-phenylethanol (**7a**) within 10 min. This was easily converted to 1-phenyl-1,2-ethanediol (**8**) by the treatment of *n*-Bu_4NF at room temperature in almost quantitative yields. The desilylation could also be accomplished by the addition of methanol to destroy excess hydride, followed by direct treatment of *n*-Bu_4NF to give **8** directly. The enantiomeric excess of the diol **8** was determined by HPLC analysis using a Chiralcel OB column (eluent: hexane/*i*-PrOH = 9:1). Among the catalysts examined, Corey's CBS reagent (**2**) provided the best enantioselectivity approaching 100% ee (Table 1, entries 1−5). Subsequently, the influence of different silyl groups on the selectivity of the asymmetric borane reduction of the silyloxy derivatives (**6a**−**e**) of 2-hydroxyacetophenone was examined. Of the silyloxy ketones tested, compounds **6a**−**c** (*tert*-butyldimethylsilyl (TBDMS), triethylsilyl (TES), and triisopropylsilyl (TIPS) derivatives) produced **8** with optical purities approaching 100% ee (Table 1, entries 2, 6, and 7). In contrast, the more sterically bulky silyl groups, such as thexyldimethylsilyl (TDS) and *tert*-butyldiphenylsilyl (TBDPS) groups, resulted in decreased enantioselectivity, 88% ee and 77% ee, respectively (Table 1, entries 8 and 9). Interestingly, the reduction of 2-[(triisopropylsilyl)oxy]-4′-methylacetophenone (**6h**) provided the corresponding diol in >99% ee in contrast to 58% ee for 2-[(triisopropylsilyl)oxy]-2′-methylacetophenone (**6g**) (Table 1, entries 11 and 12). These results indicate that the asymmetric induction was sensitive to steric effects of the substituent proximal to the carbonyl group. This is a common phenomenon in oxazaborolidine-catalyzed reductions.[28] For other aromatic analogues **6i**−**k** bearing *p*-bromophenyl and 2-naphthyl groups, we also obtained the product diols in 100% ee (Table 1, entries 13−15). In the case of aliphatic analogues, the asymmetric reduction of the silyloxy ketones **6l,m** afforded somewhat lower enantioselectivities compared with those obtained from aromatic analogues (Table 1, entries 16 and 17). However, the silyloxy ketone **6n** having a cyclohexyl group again produced very high enantioselectivity (Table 1, entry 18). Moreover, in all the cases examined, it is noteworthy that the product diols (**8**−**15**) obtained are consistently enriched in the *S*-enantiomers. The stereochemical course of the asymmetric reduction can be explained by the proposed mechanism involving a transition state **16**, where the α-silyloxy ketones are attacked by hydride on their *Re* faces to provide (*S*)-diols (Scheme 2).[19,29]

Scheme 2



In summary, we have established a convenient and simple procedure for the preparation of terminal 1,2-diols with high optical purity via the oxazaborolidine-catalyzed asymmetric borane reduction of α-[(triorganosilyl)oxy] ketone derivatives. Among the oxazaborolidines examined, catalyst **2** provided the best result to give 1,2-diols

(23) Becker, H.; King, S. B.; Taniguchi, M.; Vanhessche, K. P. M.; Sharpless, K. B. *J. Org. Chem*. **1995**, *60*, 3940.
(24) Lohray, B. B.; Bhshan, V. *Tetrahedron Lett*. **1992**, *33*, 5113.
(25) Ferraboshi, P.; Grisenti, P.; Manzocchi, A.; Santaniello, E. *Tetrahedron* **1994**, *50*, 10539.
(26) Mori, K.; Saaki, M.; Tamada, S.; Suguro, T.; Masuda, S. *Tetrahedron* **1979**, *35*, 1601.
(27) Bach, J.; Berenguer, R.; Farras, J.; Garcia, J.; Meseguer, J.; Vilarrasa, J. *Tetrahedron*: *Asymmetry* **1995**, *6*, 2683.
(28) Corey, E. J.; Helal, C. J. *Tetrahedron Lett*. **1996**, *37*, 5675.
(29) Jones, D. K.; Liotta, D. C.; Shinkai, I.; Mathre, D. J. *J. Org. Chem*. **1993**, *58*, 799.

with optical purity approaching 100% ee for most aromatic analogues. This procedure can be used as an excellent alternative to synthesis of optically active terminal 1,2-diols. Further applications using this methodology are now under investigation.

Experimental Section

General Methods. All operations with air-sensitive materials were carried out under a nitrogen atmosphere with oven-dried glassware. Liquid materials were transferred with a double-ended needle. The reactions were monitored by TLC using silica gel plates, and the products were purified by flash column chromatography on silica gel (Merck; 230−400 mesh). NMR spectra were recorded at 200 or 400 MHz for ^{1}H and 100 MHz for ^{13}C using Me_4Si as the internal standard in $CDCl_3$. Optical rotations were measured with a high-resolution digital polarimeter. Melting points were uncorrected. Enantiomeric excesses (% ee's) of the product diols were determined with a GC apparatus equipped with a 20 m Chiraldex G-TA chiral capillary column or with a HPLC apparatus fitted with a 25 cm Chiralcel OB or OD column.

Materials. Most of the organic compounds utilized in this study were commercial products of the highest purity. They were further purified by distillation when necessary. THF was distilled over sodium benzophenone ketyl and stored in ampules under nitrogen atmosphere. BH_3−THF, triethylsilyl chloride, *tert*-butyldimethylsilyl choride, triisopropylsilyl chloride, thexyldimethylsilyl chloride, *tert*-butyldiphenylsilyl chloride, (*S*)-α,α-diphenyl-2-pyrrolidinemethanol, (1*S*,2*R*)-*cis*-1-amino-2-indanol, and (1*R*,2*S*)-2-amino-1,2-diphenylethanol were purchased from the Aldrich Chemical Co. The chiral oxazaborolidines **1**−**5** were prepared from the treatment of the corresponding amino alcohols with BH_3−THF according to the known procedure.[18−22] α-[(Triorganosilyl)oxy] ketone derivatives **6a**−**n** were prepared from the reaction of the corresponding α-hydroxy ketones[16] with triorganosilyl chloride in the presence of imidazole in dichloromethane according to a known procedure[17] (see the Supporting Information).

Preparation of Chiral Terminal 1,2-Diols by Asymmetric Borane Reduction of α-[(Triorganosilyl)oxy] ketones (6) Catalyzed by Oxazaborolidines. The following procedure for reduction of 6 catalyzed by **2** is representative. To a solution of **2** (0.1 mmol; 0.2 M, 0.5 mL) in THF was added a solution of BH_3−THF (0.64 mmol; 0.8 M, 0.8 mL) in THF. To this was added slowly 2 mL of THF solution of **6** (1 mmol) over a period of 1 h using a syringe pump at 25 °C. After the addition, the reaction mixture was stirred for 10 min, quenched cautiously with methanol (0.5 mL), and stirred for additional 30 min. A solution of tetrabutylammonium fluoride (1.5 mmol; 1.0 M, 1.5 mL) in THF was added, and the resulting mixture was stirred for 1 h at room temperature. The solvent was evaporated under reduced pressure, and the residue was directly chromatographed using the appropriate solvents to obtain the chemically pure corresponding diols **8**−**15**.

(*S*)-(+)-1-(*o*-Toluyl)-1,2-ethanediol (9): R_f 0.51 (ethyl acetate/hexane 2:1); mp 98−100 °C; IR (KBr, cm^{-1}) 3274, 3031, 2863, 1485, 1362, 1084, 757; ^{1}H NMR (400 MHz) δ 2.25 (br s, 1H), 2.35 (s, 3H), 2.52 (br s, 1H), 3.59−3.64 (m, 1H), 3.73 (d, 1H, J = 11.1 Hz), 5.07 (dd, 1H, J = 8.0, 3.0 Hz), 7.14−7.26 (m, 3H), 7.50 (d, 1H, J = 7.2 Hz); ^{13}C NMR (100 MHz) δ 138.44, 134.78, 130.46, 127.77, 126.33, 126.65, 71.44, 66.93, 19.03. Anal. Calcd for $C_9H_{12}O_2$: C, 71.03; H, 7.94. Found: C, 70.98; H, 8.03.

(*S*)-(+)-1-(*p*-Bromophenyl)-1,2-ethanediol (11): R_f 0.50 (ethyl acetate/hexane 4:1); mp 100−102 °C; IR (KBr, cm^{-1}) 3406, 3032, 2872, 1487, 1069, 1011, 829; ^{1}H NMR (400 MHz) δ 2.17 (br s, 1H), 2.64 (br s, 1H), 3.60−3.64 (m, 1H), 3.75 (d, 1H, J = 11.3 Hz), 4.80 (dd, 1H, J = 8.0, 3.2 Hz), 7.25 (d, 2H, J = 8.1 Hz), 7.49 (d, 2H, J = 8.2 Hz); ^{13}C NMR (100 MHz) δ 139.45, 131.66, 127.79, 121.88, 74.02, 67.90. Anal. Calcd for $C_8H_9BrO_2$: C, 44.27; H, 4.18; Br, 36.81. Found: C, 44.22; H, 4.30; Br, 36.67.

(*S*)-(+)-1-Cyclohexyl-1,2-ethanediol (15): R_f 0.50 (ethyl acetate/hexane 2:1); mp 50−52 °C; IR (neat, cm^{-1}) 3346, 2874, 1466, 1379, 1072, 1044; ^{1}H NMR (400 MHz) δ 0.94−1.01 (m, 2H), 1.06−1.19 (m, 3H), 1.32−1.34 (m, 1H), 1.55−1.71 (m, 4H), 1.78−1.81 (m, 1H), 2.65 (br s, 2H), 3.34−3.38 (m, 1H), 3.45 (dd, 1H, J = 10.8, 8.2 Hz), 3.62 (dd, 1H, J = 10.9, 2.1 Hz); ^{13}C NMR (100 MHz) δ 63.77, 39.69, 27.94, 27.65, 25.36, 25.06. Anal. Calcd for $C_8H_{16}O_2$: C, 66.63; H, 11.18. Found: C, 66.66; H, 11.03.

Acknowledgment. We are grateful to the Organic Chemistry Research Center sponsored by the Korea Science Engineering Foundation for financial support.

Supporting Information Available: Experimental, spectral, and elemental analysis data for compounds **6**−**8**, **10**, **12**−**14** (11 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.

JO980455V