JOC*Article*

Inter- and Intramolecular Differentiation of Enantiotopic Dioxane Acetals through Oxazaborolidinone-Mediated Enantioselective Ring-Cleavage Reaction: Kinetic Resolution of Racemic 1,3-Alkanediols and Asymmetric Desymmetrization of *Meso*-1,3-polyols

Toshiro Harada,* Takayuki Egusa, Yasuto Igarashi, Motoharu Kinugasa, and Akira Oku

Department of Chemistry, Kyoto Institute of Technology, Matsugasaki, Sakyo-ku, Kyoto 606−8585, Japan

harada@chem.kit.ac.jp

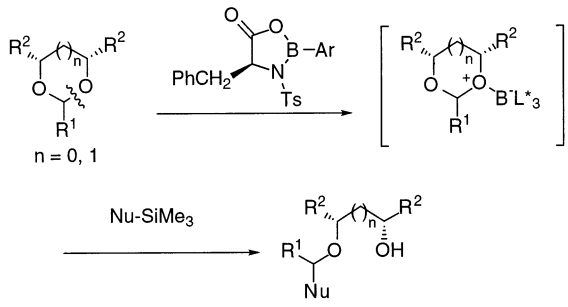
Received May 17, 2002

Acetals derived from racemic 1,3-alkanediols undergo kinetic resolution in chiral oxazaborolidinone-mediated ring-cleavage reaction with nucleophiles such as enol silanes and allylic silanes. Enantioselectivity of the reaction is affected by nucleophiles, the *N*-sulfonyl groups of oxazaborolidinones, and the substituents attached to the acetal carbon. For disubstituted acetals *rac*-**1** and for trisubstituted acetal *rac*-**2**, derived from *syn*-2,4-dimethyl-1,3-pentanediol, satisfactory enantioselectivity is obtained by using methallylsilane **7b**,**c** as a nucleophile in combination with *N*-mesyloxazaborolidinone **4a**. On the other hand, enantioselective reaction of trisubstituted acetal *rac*-**3b**, derived from *anti*-2,4-dimethyl-1,3-pentanediol, is realized by using silyl ketene acetal **5e** in combination with *N*-tosyloxazaborolidinone **4b**. The reaction conditions optimized for the kinetic resolution, or enantiomer differentiating reaction, of the racemic acetals are successfully applied to asymmetric desymmetrization of *meso*-1,3-polyols through intramolecular differentiation of the enantiotopic acetal moieties of the bis-acetal derivatives. The utility of the ring-cleavage reaction as a method for enantioselective terminal differentiation of prochiral polyols is demonstrated in convergent asymmetric synthesis of pentol derivative **35** corresponding to the C(19)−C(27) ansa-chain of rifamycin S.

Introduction

Two-direction chain extension and asymmetric desymmetrization of the resulting *meso* precursors have recently emerged as an efficient strategy for the construction of multiple stereogenic centers.[1] The *meso* precursors can be synthesized in a convergent manner based on the strategy involving the simultaneous, diastereoselective extension of chains in two directions. The final terminus differentiation in an enantioselective manner accomplishes the construction of multiple stereogenic centers. The approach has been successfully employed in asymmetric syntheses of skipped and polypropionate-derived 1,3-polyols of potential σ-symmetry.[1b,2] For the crucial step of terminus differentiation, enantioselective epoxidation,[2a,b] allylation,[2c,e] acetalization,[2d,f] aldol reaction,[2g] Horner−Wardworth−Emmons reaction,[2h] and enzymatic esterification[2i] have been employed.

SCHEME 1



We recently reported an oxazaborolidinone-mediated enantioselective ring-cleavage reaction of cyclic acetals derived from *meso*-1,2- and 1,3-diols (Scheme 1).[3] In this reaction, the chiral Lewis acid selectively activates one of the enantiotopic C−O bonds leading to the ring-cleavage product of high ee. Although there is no prece-

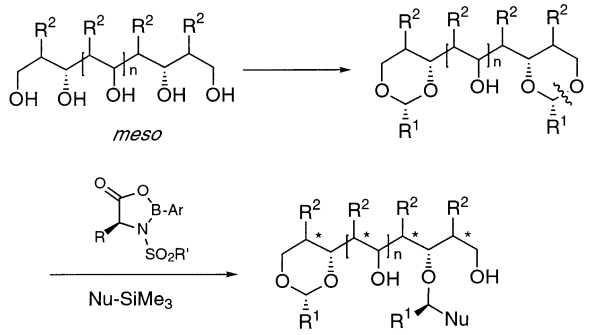
(1) (a) Schreiber, S. L. *Chem. Scr.* **1987**, *27*, 563−566. (b) Poss, C. S.; Schreiber, S. L. *Acc. Chem. Res.* **1994**, *27*, 9−17. (b) Magnuson, S. R.; *Tetrahedron* **1995**, *51*, 2167−2213. (c) Willis, M. C. *J. Chem. Soc., Perkin Trans. 1* **1999**, 1765−1784.

(2) (a) Schreiber, S. L.; Goulet, M. T.; Schulte, G. *J. Am. Chem. Soc.* **1987**, *109*, 4718−4719 (b) Schreiber, S. L.; Goulet, *J. Am. Chem. Soc.* **1987**, *109*, 8120−8121. (c) Wang, Z.; Dechênes, D. *J. Am. Chem. Soc.* **1992**, *114*, 1090−1091. (d) Harada, T.; Kagamihara, T.; Tanaka, S.; Sakamoto, K.; Oku, A. *J. Org. Chem.* **1992**, *57*, 1637−1638. (e) Ward, D. E.; Liu, Y.; Rhee, C. K. *Synlett* **1993**, 561−563. (f) Harada, T.; Oku, A. *Synlett* **1994**, 95−104. (g) Oppolzer, W.; Walther, E.; Balado, C. P.; De Brabander J. *Tetrahedron Lett.* **1997**, *38*, 809−812. (h) Tullis, J. S.; Vares, L.; Kann, N.; Norrby, P.-O. Rein, T. *J. Org. Chem.* **1998**, *63*, 8284−8294. (i) Chênevert, R.; Rose, Y. S. *J. Org. Chem.* **2000**, *65*, 1707−1709.

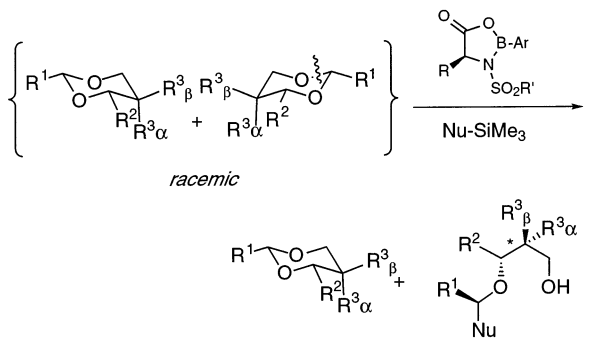
(3) (a) Kinugasa, M. Harada, T.; Oku, A. *J. Am. Chem. Soc.* **1997**, *119*, 9067−9068. (b) Kinugasa, M.; Harada, T.; Oku, A. *Tetrahedron Lett.* **1998**, *39*, 4523−4526. (c) Harada, T.; Nakamura, T.; Kinugasa, M.; Oku, A. *Tetrahedron Lett.* **1999**, *40*, 503−506. (d) Harada, T.; Yamanaka, H.; Oku, A. *Synlett* **2001**, 61−64. (e) Harada, T.; Sekiguchi, K.; Nakamura, T.; Suzuki, J.; Oku, A. *Org. Lett.* **2001**, *3*, 3309−3312.

10.1021/jo025944g CCC: $22.00
Published on Web 09/06/2002

SCHEME 2



SCHEME 3

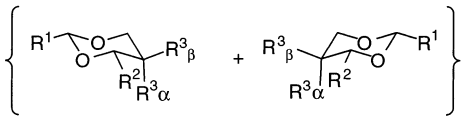


dent, enantiodifferentiating ring-cleavage of prochiral bis-acetal derivatives is expected to provide a straightforward and general method for desymmetrization of *meso*-1,3-polyols (Scheme 2). Lewis acid-mediated ring-cleavage of cyclic acetals derived from 1,3-alkanediols ($RCH(OH)CH_2CH_2OH$) is known to proceed regioselectively at the less hindered C−O bond.[4,5] For a bis-acetal derived from a *meso*-1,3-polyol, selective cleavage of a specific terminal C−O bond is expected to take place through intramolecular differentiation of the enantiotopic acetal moieties by an oxazaborolidinone, leading to the formation of a desymmetrized product.

We wish to report herein a successful application of oxazaborolidinone-mediated enantioselective ring-cleavage to asymmetric desymmetrization of *meso*-1,3-polyols.[6] In the present work, we first investigated intermolecular differentiation, or kinetic resolution, of racemic acetals derived from 1,3-alkanediols (Scheme 3). The optimized conditions established for the kinetic resolution was then applied to intramolecular differentiation of prochiral bis-acetals derived from *meso*-1,3-polyols.

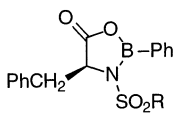
Results and Discussion

Kinetic Resolution of Racemic Acetals Derived from 1,3-Alkanediols. To establish optimum reaction conditions for asymmetric desymmetrization of the bis-acetals, we first investigated kinetic resolution of three types of acetals *rac*-**1**−**3**. Acetals *rac*-**1** (R^3_α, R^3_β = H) were chosen as model compounds for skipped polyol derivatives while *rac*-**2** (R^3_α = Me, R^3_β = H) and -**3** (R^3_α = H, R^3_β = Me) correspond to polypropionate-derived polyol derivatives.

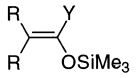


1-3 ***ent*-1-3**

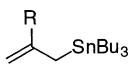
	R^1	R^2	R^3_α	R^3_β
1a	Ph	*i*-Pr	H	H
1b	*p*-ClC_6H_4	*i*-Pr	H	H
1c	*p*-MeC_6H_4	*i*-Pr	H	H
1d	*p*-$MeOC_6H_4$	*i*-Pr	H	H
1e	2-furyl	*i*-Pr	H	H
1f	1-naphthyl	*i*-Pr	H	H
1g	Ph	*t*-Bu	H	H
1h	Ph	$PhCH_2CH_2$	H	H
1i	Ph	Me	H	H
1j	Ph	Ph	H	H
2	Ph	*i*-Pr	Me	H
3a	Ph	*i*-Pr	H	Me
3b	*p*-$MeOC_6H_4$	*i*-Pr	H	Me



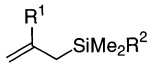
4a; R = Me
4b; R = *p*-MeC_6H_4
4c; R = CF_3



5a; R = H, Y = S*t*Bu
5b; R = H, Y = *t*Bu
5c; R = H, Y = Ph
5d; R = H, Y = *p*-ClC_6H_4
5e; R = Me, Y = OEt
5f; R = H, Y = OEt



6a; R = H
6b; R = Me

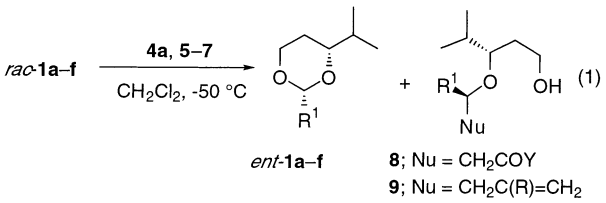


7a; R^1 = H, R^2 = Me
7b; R^1 = Me, R^2 = Me
7c; R^1 = Me, R^2 = Ph

Ring-cleavage reaction of acetal *rac*-**1a** derived from 4-methyl-1,3-pentanediol and benzaldehyde was carried out with a variety of nucleophiles (**5**−**7**) (1.5 equiv) by using *N*-mesyloxazaborolidinone **4a** (0.5 equiv) as a chiral Lewis acid in CH_2Cl_2 at −50 °C (eq 1, Table 1). Because a part of a ring-cleavage product was obtained as a TMS ether derivative except for entry 5, the crude mixture was subsequently hydrolyzed with aqueous acetic acid or with Bu_4NF in THF. Under these conditions, (4*S*)-**1a** reacted selectively, irrespective of the nucleophiles, to give **8a**−**d** or **9a**,**b** with high diastereoselectivity (>90% ds)[8] and enantiomerically enriched acetal (4*R*)-*ent*-**1a** was recovered. The selectivity factor *s* (= k_1/k_{ent-1}) of the reaction was calculated from the percent conversion and ee of the recovered acetal.[10]

(4) Choi, V. M.; Elliott, J. D.; Johnson, W. S. *Tetrahedron Lett.* **1984**, *25*, 591−594.
(5) Kinugasa, M.; Harada, T.; Egusa, T.; Fujita, K.; Oku, A. *Bull. Chem. Soc., Jpn.* **1996**, *69*, 3639−3650.
(6) For a preliminary communication, see: (a) Harada, T.; Egusa, T.; Kinugasa, M.; Oku A. *Tetrahedron Lett.* **1998**, *39*, 5531−5534. (b) Harada, T.; Egusa, T. Oku, A. *Tetrahedron Lett.* **1998**, *39*, 5535−5536.
(7) For the stereoselective formation of the dioxane acetals from the corresponding diols, see: Clode, D. *Chem. Rev.* **1979**, *79*, 491−513.
(8) The stereochemical assignment of major diastereomers is tentative, based on the assumption of the introduction of the nucleophile with inversion of the acetal carbon.[8,3e]

TABLE 1. Kinetic Resolution in Ring-Cleavage Reaction of Acetal *rac*-1a[a]



entry	nucleophile	time (h)	conversion (%)[b]	*ent*-**1a** ee (%)[c]	*s*	product	yield (%)
1	**5a**	24	49	36	3.2	**8a**	42
2	**5b**	24	32	23	3.6	**8b**	28
3	**5c**	24	63	68	4.4	**8c**	61
4	**5d**	9	60	69	5.3	**8d**	52
5	**6a**	24	48	54	6.4	**9a**	39
6	**7b**	3	59	77	7.4	**9b**	40
7	**7c**	4	56	80	10	**9b**	51
8		8	63	92	10	**9b**	nd[d]
9[e]		30	60	88	11	**9b**	58
10[f]		4	44	41	4.7	**9b**	nd[d]

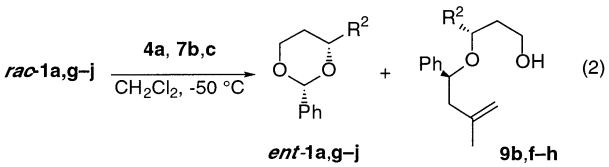
[a] Unless otherwise noted, reactions were carried out by using **4a** (0.5 equiv) and a nucleophile (1.5 equiv) in CH_2Cl_2 (1 M) at −50 °C. [b] Based on the recovery of acetals which was determined by GC analysis using an internal standard. [c] Determined by GC (Chrompack CP−Cyclodextrin-*β*-236-M-19, 25 m). [d] Not determined. [e] 0.3 equiv of **4a** was used. [f] Oxazaborolidinone **4b** (0.5 equiv) was used.

TABLE 2. Kinetic Resolution in Ring-Cleavage Reaction of Acetals 1a−f with Methallylsilane 7c[a]

entry	acetal	time (h)	conversion (%)[b]	*ent*-**1** ee (%)[c]	*s*	product	yield (%)
1	*rac*-**1a**	8	63	92	10	**9b**	nd[d]
2	*rac*-**1b**	10	38	45	10	**9c**	35
3	*rac*-**1c**	1.5	58	81	9.2	**9d**	54
4	*rac*-**1d**	0.7	44	34	3.5	−	nd[d]
5	*rac*-**1e**	1	58	76	7.6	**9e**	49
6	*rac*-**1f**	6	34	34	6.8	−	nd[d]

[a] All reactions were carried out by using **4a** (0.5 equiv) and **7c** (1.5 equiv) in CH_2Cl_2 (1 M) at −50 °C. [b] Based on the recovery of acetals which was determined by GC analysis using an internal standard. [c] Determined by GC (Chrompack CP−Cyclodextrin-*β*-236-M-19, 25 m). For *ent*-**1c**,**d** and *ent*-**1f**, the GC analyses were carried out after conversion to an acetonide derivative and *ent*-**1e**, respectively. [d] Not determined.

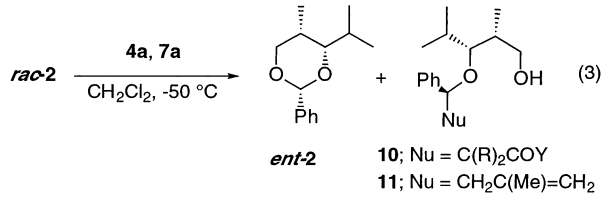
TABLE 3. Kinetic Resolution in Ring-Cleavage Reaction of Acetals 1a,g−j with Methallylsilanes 7b,c[a]



entry	acetals	time (h)	conversion (%)[b]	*ent*-**1** ee (%)[c]	*s*	product	yield (%)
1	*rac*-**1a**	8	63	92	10	**9b**	nd[e]
2[d]	*rac*-**1g**	2.5	41	56	16	**9f**	32
3	*rac*-**1h**	8	58	67	5.6	**9g**	55
4	*rac*-**1i**	2.5	67	79	5.1	**9h**	57
5	*rac*-**1j**	24	69	84	5.4	−	nd[e]

[a] Unless otherwise noted, reactions were carried out by using **4a** (0.5 equiv) and **7c** (1.5 equiv) in CH_2Cl_2 (1 M) at −50 °C. [b] Based on the recovery of acetals which was determined by GC analysis using an internal standard. [c] Determined by GC (Chrompack CP−Cyclodextrin-*β*-236-M-19, 25 m) for *rac*-**1a**,**g**,**i** or HPLC (Chiracel OD) for *rac*-**1h**,**j**. [d] **7b** (1.5 equiv) was used as a nucleophile. [e] Not determined.

TABLE 4. Kinetic Resolution in Ring-Cleavage Reaction of *syn*-2,4-Dimethylpentanediol-Derived Acetal 2



entry	nucleophile	conversion (%)[b]	*ent*-**2** ee (%)[c]	*s*	product	yield (%)
1	**5a**	58	77	8.1	**10a**	42
2	**5e**	43	52	9.3	**10b**	34
3	**7b**	41	55	17	**11**	38

[a] All reactions were carried out by using **4a** (1 equiv) and **7b** (3 equiv) in CH_2Cl_2 (0.4 M) at −50 °C for 24 h. [b] Based on the recovery of acetals which was determined by GC analysis using an internal standard. [c] Determined by GC (Chrompack CP−Cyclodextrin-*β*-236-M-19, 25 m).

The enantioselectivity (*s*) varied significantly depending on the nucleophiles. There is a general trend of higher selectivity for the less reactive nucleophiles.[11] Thus, enol silyl ethers **5b**−**d** exhibited selectivity higher than silyl ketene *S*,*O*-acetal **5a** (entry 1 vs entries 2−4). In comparison with acetophenone enol silyl ether **5c** ($s = 4.4$), **5d** with an electron-withdrawing *p*-chlorophenyl group exhibited improved selectivity ($s = 5.3$). Although the reaction of allyltrimethylsilane (**7a**) was sluggish, methallyltrimethylsilane (**7b**) reacted smoothly with superior selectivity of 7.4 (entry 6). Further improvement ($s = 10$) was obtained when methallyldimethylphenylsilane (**7c**) was used as a nucleophile (entries 7 and 8). Under these conditions, enantiomerically enriched *ent*-**1a** of 92% ee was recovered at 63% conversion. The amount of oxazaborolidinone **4a** could be reduced to 0.3 equiv without lowering the selectivity (entry 9). In the ring-cleavage reaction of acetals derived from *meso*-1,2- and -1,3-diols, *N*-tosyloxazaborolidinone **4b** exhibited higher enantioselectivities than *N*-mesyl derivative **4a**.[3] However, **4b** did not give a better result for *rac*-**1a** (entry 10).

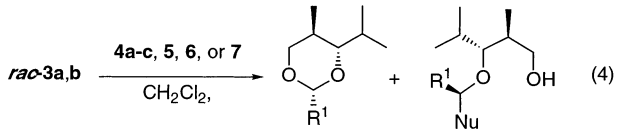
The effect of aryl substituent attached to the acetal carbon was studied in the reaction with methallylsilane **7c** (Table 2). The reaction rate increased significantly in going from electron-withdrawing substituents to electron-donating substituents. Decreased enantioselectivity was observed for electron-donating groups such as *p*-methoxyphenyl (PMP) and 2-furyl (entries 4 and 5) while the electron-withdrawing *p*-chlorophenyl group in *rac*-**1b** did not improve the selectivity (entry 2). The lower selectivity

(9) Harada, T.; Nakamura, T.; Kinugasa, M.; Oku, A. *J. Org. Chem.* **1999**, *64*, 7594−7600.

(10) $s = k_1/k_{ent-1} = \ln[(1 - C)(1 - ee)]/\ln[(1 - C)(1 + ee)]$ where C is the conversion and ee is the enantiomeric excess. Kagan, H. B.; Fiaud, J. C. *Top. Stereochem.* **1988**, *18*, 249−330.

(11) (a) Mayr, H.; Patz, M. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 938−957. (b) Mayr, H.; Kuhn, O.; Gotta, M. F.; Patz, M. *J. Phys. Org. Chem.* **1998**, *11*, 642−654. (c) Burfeindt, J.; Patz, M.; Müller, M.; Mayr, H. *J. Am. Chem. Soc.* **1998**, *120*, 3629−3634.

TABLE 5. Kinetic Resolution in Ring-Cleavage Reaction of *anti*-2,4-Dimethylpentanediol-Derived Acetal 3a,b[a]



ent-**3a**,**b** **12**; Nu = $C(R)_2COY$
13; Nu = $CH_2C(Me)=CH_2$

entry	acetal	oxaza-borolidinone	nucleophile	conversion (%)[b]	*ent*-**3** ee (%)[c]	*s*	product[d]	yield (%)
1[d]	*rac*-**3a**	**4c**	**5a**	46	6.9	1.3	**12a**	36
2	*rac*-**3b**	**4a**	**5a**	78	69	2.7	**12b**	55
3			**5e**	68	74	4.0	**12c**	54
4			**7b**	31	20	3.0	**13**	34
5			**6b**	57	69	6.2	**13**	52
6		**4b**	**5a**	47	53	6.9	**12b**	43
7			**5e**	53	71	9.3	**12c**	49
8			**6b**	65	76	5.1	**13**	58

[a] Unless otherwise noted, reactions were carried out by using an oxazaborolidinone (1 equiv) and a nucleophile (3 equiv) in CH_2Cl_2 (0.4 M) at −60 °C for 16−17 h. [b] Based on the recovery of acetals which was determined by GC analysis using an internal standard. [c] Determined by GC (Chrompack CP−Cyclodextrin-β-236-M-19, 25 m) for *ent*-**3a** or by HPLC (Chirapak AD) for *ent*-**3b**. [d] The reaction was carried out by using 0.5 equiv of **4c** and 1.5 equiv of **5a** at −40 °C.

was observed for sterically more demanding 1-naphthyl derivative *rac*-**1f** (entry 6).

Ring-cleavage reaction of acetals *rac*-**1g**−**j** derived from the other 1,3-alkanediols and benzaldehyde was examined by using oxazaborolidinone **4a** as a chiral Lewis acid and methallylsilanes **7b** or **7c** as a nucleophile (Table 3). The absolute configuration determination of the recovered acetals, by comparison with an authentic sample (for *ent*-**1i**), or by conversion to the known 1,3-diols (for *ent*-**1a**,**g**,**j**) or its diaceate derivative (for *ent*-**1h**), revealed a similar sense of enantioselectivity in all reactions. The degree of enantioselectivity was affected by the structure of the R^2 group. A highly enantioselective reaction ($s = 16$) was observed for 4-*tert*-butyl derivative *rac*-**1g** with **7b** (entry 2). On the other hand, 4-phenylethyl, -methyl, and -phenyl derivatives *rac*-**1h**−**j** exhibited the reduced selectivities in comparison with *rac*-**1a**.

It was shown that the ring-cleavage reaction of disubstituted acetals *rac*-**1** (R^1 = Ph, R^3_α, R^3_β = H) can be carried out in an enantioselective manner by using oxazaborolidinone **4a** as a chiral Lewis acid and methallylsilane **7b** or **7c** as a nucleophile. We then focused our attention to the kinetic resolution of trisubstituted acetals *rac*-**2** and -**3** derived respectively from *syn*- and *anti*-2,4-dimethyl-1,3-pentanediol.

2-Phenyl derivative *rac*-**2** provided significantly high enantioselectivity ($s = 17$) in the reaction with oxazaborolidinone **4a** and methallylsilane **7b** (Table 4, entry 3). The recovered acetal was enriched with (4*S*,5*S*) enantiomer,[12] showing a similar sense of asymmetric induction. The acetal also exhibited relatively high selectivity of 8.1 and 9.3 in the reaction with silyl ketene acetal **5a** and **5e**, respectively (entries 1 and 2).

In sharp contrast to acetals *rac*-**1** and -**2**, trisubstituted acetal *rac*-**3a** derived from the *anti*-1,3-diol and benzaldehyde was found to be quite less reactive, not undergoing ring-cleavage by using *N*-mesyl derivative **4a** either with methallylsilane **7b** or with silyl ketene acetal **5a**. This may probably due to the stability of *rac*-**3a** with the three substituents being equatorial.[3e] The use of more acidic *N*-trifluoromethanesulfonyl-oxazaborolidinone **4c**[5] facilitated the reaction (Table 5, entry 1) but no enantioselectivity was observed.

In accord with the increased reactivity observed for acetals *rac*-**1c**−**e** with electron-donating aryl groups, PMP derivative **3b** exhibited an appropriate reactivity in the reaction using *N*-mesyloxazaborolidinone **4a** at −60 °C (entries 2−5). Examination of several nucleophiles however resulted in unsatisfactory enantioselectivity. Of these, tributylmethallylstannane (**6b**) exhibited the highest selectivity of 6.2.[13] For the reaction of PMP derivative **3b**, *N*-tosyloxazaborolidinone **4b** was found to be a better chiral Lewis acid especially when a silyl ketene acetal was employed as a nucleophile (entries 6−8). Satisfactory enantioselectivity (s = 9.3) was obtained in the reaction with silyl ketene acetal **5e**. Here again, a similar sense of asymmetric induction was observed judging from the recovery of (4*S*,5*R*) enantiomer.[12]

In the kinetic resolution of the racemic acetals, enantiomers **1**−**3** always underwent ring-cleavage in preference to *ent*-**1**−**3**. According to the previous studies on the mechanism of ring-cleavage reaction mediated by achiral[14] and chiral Lewis acids,[9] it is most probable that the enantiomer differentiating reaction of *rac*-**1**−**3** proceeds through an S_N1-type stepwise mechanism involving contact ion pair intermediates **14a**,**b** (Scheme 4). Thus, the dissociation of the acetal-oxazaborolidinone complex **13a** and subsequent attack of a nucleophile to the resulting ion pair **14a** lead to the formation of the major ring-cleavage products.

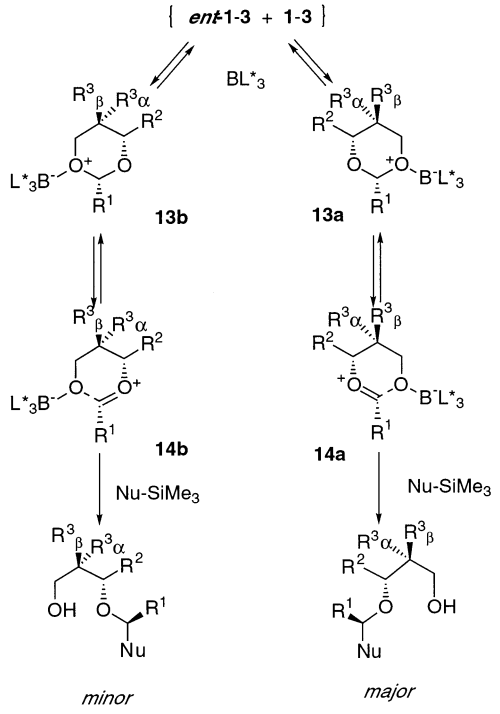
For the reaction of dioxolane acetals derived from *meso*-1,2-diols (Scheme 1; R^2 = PhC≡C, $n = 0$), it was clarified

(12) The absolute structure was determined by conversion to the known 1,3-diol.

(13) The reaction of **6b** with allyltributylstannane **6a** was sluggish.

(14) (a) Denmark, S. E.; Almstead, N. G. *J. Am. Chem. Soc.* **1991**, *113*, 8089−8110. (b) Sammakia, T.; Smith, R. S. *J. Am. Chem. Soc.* **1992**, *114*, 10998−10999. See also references cited in ref 8.

SCHEME 4[a]



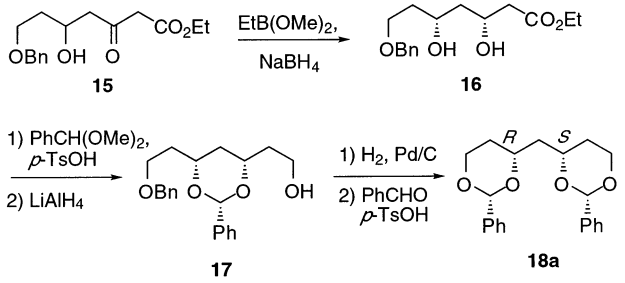
BL* = **4**.

that dissociation to an ion pair is rate-determining step followed by a rapid reaction of nucleophiles.[9] This led us to propose the selective complexation of one of the enantiotopic oxygen atoms to the chiral Lewis acid as a major factor governing the enantioselectivity.[9,3e] If the reaction of *rac*-**1**−**3** also involved a similar mechanistic profile, the observed enantioselectivity would not be affected by nucleophiles. The observed effect of nucleophiles implies that there is a preequilibrium between acetal-oxazaborolidinone complexes **13a**,**b** and ion pairs **14a**,**b** prior to the attack of nucleophiles. In comparison with the corresponding five-membered ring contact ion pair intermediates, six-membered ring ion pairs **14a**,**b** might be more stable, resulting in relatively slow reaction with nucleophiles. The low reactivity observed for *rac*-**3a** of which three substituents are equatorial might be an extreme case of the phenomenon. Owing to such mechanistic complexity, it is difficult to rationalize the selectivity observed in the present enantiomer differentiating ring-cleavage reaction. If we assume that ion pairs **14a** and **14b** possess comparable reactivity toward nucleophiles, the observed selectivity might be again the result of enantiodifferentiating complexation by the oxazaborolidinones to form **13a**. Alternatively, it is conceivable that, in an extreme case, ion pair **14a** produced from less favorable complex **13a** undergoes selective attack by the nucleophiles to give the major ring-cleavage product.

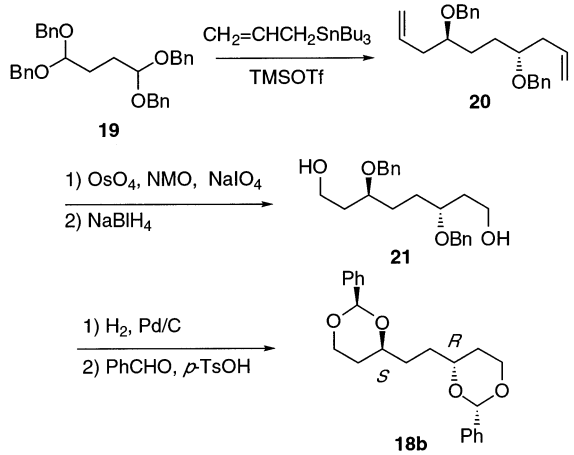
Asymmetric Desymmetrization of Polyols. After establishing the conditions for kinetic resolution, or intermolecular differentiation, of racemic acetals, we then applied them to asymmetric desymmetrization of *meso*-polyols through intramolecular differentiation of the prochiral bis-acetal derivatives.

meso-1,3,5,7-Heptanetetrol bis-acetal **18a** was prepared in five steps from hydroxy ester **15** (Scheme 5).

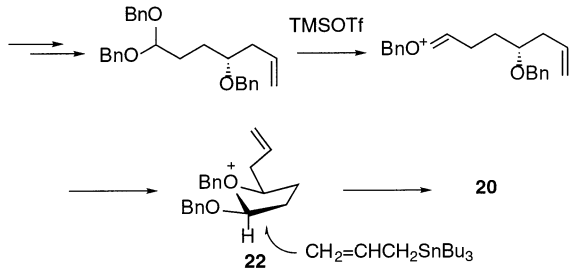
SCHEME 5



SCHEME 6



SCHEME 7

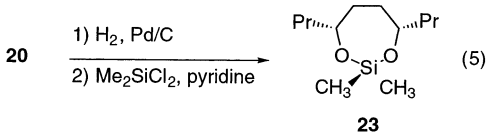


Chelation-controlled reduction[15] of **15** stereoselectively gave *syn* diol **16** in 90% yield. Protection of the diol moiety and subsequent reduction of the resulting ester transformed **16** into acetal **17** in 90% yield. Hydrogenolysis of **17** followed by acetalization of the resulting *meso*-tetrol with benzaldehyde furnished a crystalline bis-acetal **18a** in 63% yield.

Starting from succinaldehyde derivative **19**, homologous *meso*-bis-acetal **18b** was stereoselectively prepared by using 1,4-asymmetric induction, developed by Molander et al.,[16] as a key reaction (Scheme 6). Thus, treatment of **19** with allyltributylstannane in the presence of TMSOTf afforded *meso* diallylation product **20** (75%) stereoselectively (*meso*:*dl* = 9:1). The second allylation presumably proceeded through a cyclic oxonium ion intermediate **22**, leading to the selective formation of *meso* **20** (Scheme 7).[16] The stereochemistry of the diol was

(15) Chen, K.-M.; Gunderson, K. G.; Hardtmann, G. E.; Prasad, K.; Repic, O.; Shapiro, M. J. *Chem. Lett.* **1987**, 1923−1926.
(16) Molander, G. A.; Haar, J. P. *J. Am. Chem. Soc.* **1993**, *113*, 40−49.

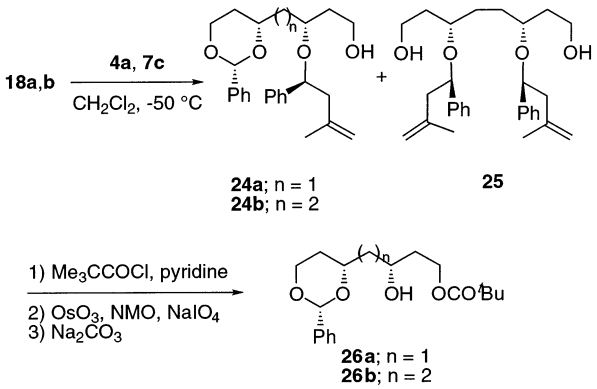
confirmed by converting it into cyclic silyl ether **23** (eq 5), whose methyl groups are inequivalent in NMR



analysis. Oxidative cleavage of the double bond and subsequent reduction of the aldehyde moieties converted **20** into **21** in 69% yield. After deprotection and acetalization of the resulting *meso*-tetrol with benzaldehyde, a crystalline bis-acetal **18b** was isolated in 67% yield.

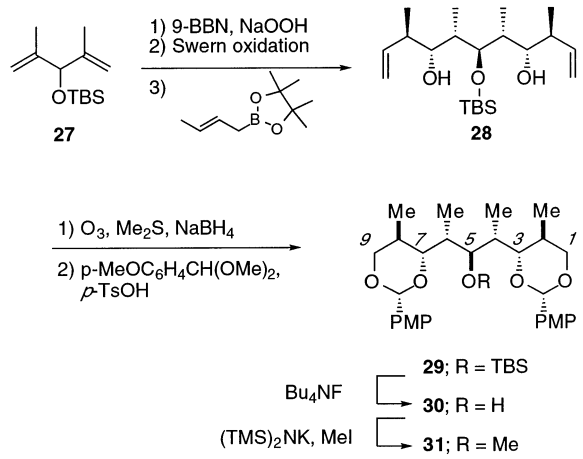
Asymmetric desymmetrization of bis-acetals **18a**,**b** was successfully achieved by carrying out the ring-cleavage reaction under the optimized conditions for kinetic resolution of acetals *rac*-**1**. Thus, treatment of **18a** with methallylsilane **7c** (1.5 equiv) in the presence of *N*-mesyloxazaborolidinone **4a** (1.0 equiv) at −50 °C afforded the mono-cleavage product **24a** in 94% yield (Scheme 8). After protection of the hydroxy group as a pivalate (84%), removal of the 3-methyl-1-phenyl-3-butenyl group by oxidative cleavage of the double bond and subsequent treatment of the resulting β-alkoxy ketone with Na_2CO_3 in ethanol furnished *O*-benzylidene pivalate **26a** of 88% ee[16] in 75% yield.

SCHEME 8



Under similar conditions, ring-cleavage of bis-acetal **18b** afforded the mono-cleavage product **24b** (82%) together with the bis-cleavage product **25** (15%). The minor enantiomer *ent*-**24b** (not shown) with more reactive (*S*)-acetal moiety, if formed, would undergo second ring-cleavage preferentially to give **25**. Therefore, the formation of **25** in relatively large amount suggested a higher ee of **24b** through such sequential kinetic resolution.[18] Indeed, transformation of **24b** through a similar reaction sequence gave *O*-benzylidene pivalate **26b** of high ee (95%)[17] in 63% overall yield. The absolute configurations of **26a** and **26b**, established by the modified Mosher's method,[19] were in accord with the anticipated reaction on the (*S*)-acetal moiety of **18a**,**b**.

SCHEME 9



To further demonstrate the efficiency of the present approach, we then applied it to the stereocontrolled construction of seven contiguous stereogenic centers in the C(19)−C(27) ansa chain of rifamycin S.[20,2d] *Meso*-triol derivative **28** with seven potential stereogenic centers was prepared in a convergent manner according to a method reported previously by us (Scheme 9).[2d,h] Thus, hydroboration of diene **27** followed by Swern oxidation and subsequent crotylboration of the resulting dialdehyde gave **28** stereoselectively. Ozonolysis of **28** and transacetalization of the resulting tetrol with *p*-anisaldehyde dimethyl acetal furnished prochiral bis-acetal **29** in 75% yield.

Ring-cleavage reaction of bis-acetal **29** was carried out first under the conditions optimized for *rac*-**3b**. However, treatment of **29** with silyl ketene acetal **5e** and *N*-tosyloxazaborolidinone **4b** at −60 °C for 22 h resulted in the recovery of the bis-acetal. The outside oxygen atom, O(1) or O(9), might coordinate to the oxazaborolidinone, and the nucleophile needs to attack the acetal carbon from the inside of the molecule. The low reactivity of **29** may have arisen from unfavorable interaction between the nucleophile and the TBS group attached to O(5). We then examined the ring-cleavage reaction of hydroxy derivative **30**, which was obtained by desilylation of **29** in quantitative yield. Under similar conditions, **30** un-

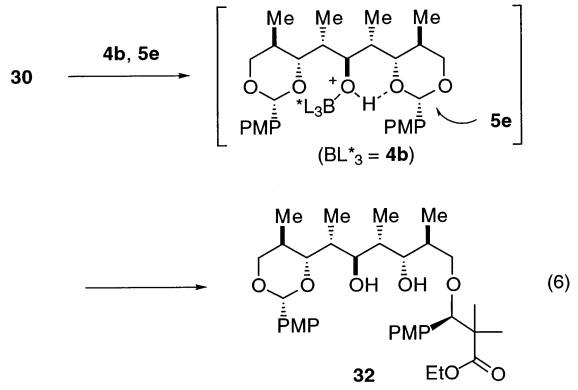
(17) The ee value was determined by ^{1}H NMR analysis of the MTPA ester.

(18) (a) Schreiber, S. L.; Schreiber, T. S.; Smith, D. B. *J. Am. Chem. Soc.* **1987**, *109*, 1525−1529. (b) Ward, D. E.; Liu, Y.; How, D. *J. Am. Chem. Soc.* **1996**, *118*, 3025−3026. (c) Ward, D. E.; How, D.; Yadong, Y. *J. Am. Chem. Soc.* **1997**, *119*, 1884−1894.

(19) Ohtani, I.; Kusumi, T.; Kashman, Y.; Kakisawa, H. *J. Am. Chem. Soc.* **1991**, *113*, 4092−4096.

(20) For the total synthesis of rifamycin S, see; (a) Nagaoka, H.; Rutsh, W.; Schmid, G.; Iio, H.; Johnson, M. R.; Kishi, Y. *J. Am. Chem. Soc.* **1980**, *102*, 7962−7965. (b) Nagaoka, H.; Kishi, Y. *Tetrahedron* **1981**, *37*, 3873. For the synthesis of ansa chain, see: (c) Nakata, M.; Takao, H.; Ikeyama, Y.; Sakai, T.; Tatsuta, K.; Kinoshita, M. *Bull. Chem. Soc. Jpn.* **1981**, *54*, 1749−1756. (d) Masamune, S.; Imperiali, B.; Garvey, D. S. *J. Am. Chem. Soc.* **1982**, *104*, 5528. (e) Hanessian, S.; Pougny, J.-R.; Bossenkool, I. K. *J. Am. Chem. Soc.* **1982**, *104*, 6164−6166. (f) Still, W. C.; Barrish, J. C. *J. Am. Chem. Soc.* **1983**, *105*, 2487−2489. (g) Fraser-Reid, B.; Magdzinski, L.; Molino, B. *J. Am. Chem. Soc.* **1984**, *106*, 731−734. (h) Danishefsky, S. J.; Myles, D. C.; Harvey, D. F. *J. Am. Chem. Soc.* **1987**, *109*, 862−867. (i) Roush, W. R.; Palkowitz, A. D. *J. Am. Chem. Soc.* **1987**, *109*, 953−955. (j) Ziegler, F. E.; Cain, W. T.; Kneisley, A.; Stirchak, E. P.; Wester, R. T. *J. Am. Chem. Soc.* **1988**, *110*, 5442−5452. (k) Katsuki, T.; Hanamota, T.; Yamaguchi, M. *Chem. Lett.* **1989**, 117−120. (l) Paterson, I.; McClure C. K.; Schumann, R. C. *Tetrahedron Lett.* **1989**, *30*, 1293−1296. (m) Roush, W. R.; Palkiwitz, A. D.; Ando, K. *J. Am. Chem. Soc.* **1990**, *112*, 6348−6359. (n) Lautens, M.; Belter, R. K. *Tetrahedron Lett.* **1992**, *33*, 2617−2620. (o) Miyashita, M.; Yoshihara, K.; Kawamine, K.; Hoshino, M.; Irie, H. *Tetrahedron Lett.* **1993**, *34*, 6285−6285. (p) Yadav, J. S.; Srinivas Rao, C.; Chandrasekhar, S.; Rama Rao, A. V. *Tetrahedron Lett.* **1995**, *36*, 7717−7720. (q) Hanessian, S.; Wang, W.; Gai, Y.; Oivier, E. *J. Am. Chem. Soc.* **1997**, *119*, 10034−10041. (r) Hunt, K. W.; Grieco, P. A. *Org. Lett.* **2001**, *3*, 481−484.

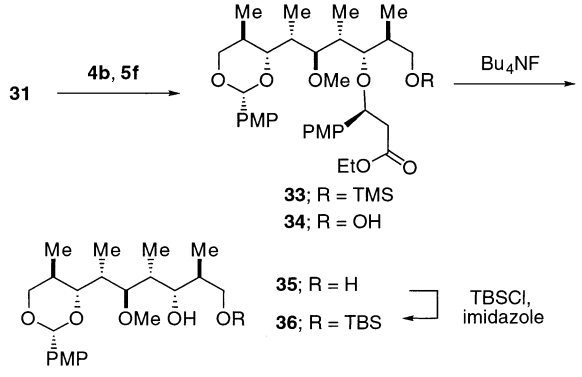
derwent a smooth ring-cleavage reaction to give **32** (86%) as a 7:3 mixture of diastereomers (eq 6).[21] To our surprise,



2D-NMR (H−H, C−H COSEY, and HMBC) analyses revealed the structure of the major isomer to be that produced through the cleavage of the inside C−O bond. Moreover, the major isomer was found to be racemic (3% ee) by a chiral-phase HMPLC analysis. It is probable that a Brønsted acid generated through the coordination of the oxazaborolidinone by the hydroxy group activated the inner oxygen atoms O(3) and O(7) without selectivity.[22]

Protection of the hydroxy group of **30** as a sterically less demanding methyl ether gave *O*-methyl derivative **31** in 93% yield. Although the reaction of **31** with silyl ketene acetal **5e** was sluggish, the bis-acetal underwent smooth ring-cleavage reaction with less bulky ethyl acetate-derived silyl ketene acetal **5f** in the presence of oxazaborolidinone **4b** to give TMS ether **33** (a 9:1 mixture of diastereomers) and free alcohol **34** (a 9:1 mixture of diastereomers) in 58% and 31% yield, respectively (Scheme 10). In the attempted conversion of **33** to **34** by treatment with Bu_4NF, removal of the nucleophile derived moiety leading to diol **35** was also occurred. Taking advantage of the observation, the ring cleavage products as a mixture **33** and **34** was treated with Bu_4NF at room temperature for 18 h to give diol **35** in 73% overall yield from **31**. Selective protection of the terminal hydroxy group as a TBS ether furnished **36** in 96% yield. The enantiomeric purity of **36** was determined to be 87% ee by chiral phase HPLC analysis. The absolute structure determined by the modified Mosher method[18] is the one expected from the study on kinetic resolution of *rac*-**3b**.

SCHEME 10



Conclusion

We have shown that oxazaborolidinone-mediated ring-cleavage reaction can be successfully used in kinetic resolution of racemic acetals derived from 1,3-alkanediols. Enantioselectivity of the reaction was most affected by nucleophiles. For disubstituted acetals *rac*-**1** and for trisubstituted acetal *rac*-**2**, derived from *syn*-2,4-dimethyl-1,3-propanediol, satisfactory enantioselectivity ($s = 5.1-17$) was obtained by using methallylsilane **7a** or **7b** as a nucleophile in combination with *N*-mesyloxazaborolidinone **4a**. On the other hand, enantioselective reaction ($s = 9.3$) of trisubstituted acetal *rac*-**3b** derived from an *anti*-1,3-alkanediol was realized by using silyl ketene acetal **5e** in combination with *N*-tosyloxazaborolidinone **4b**. The reaction conditions optimized in the enantiomer differentiating ring-cleavage reaction were successfully applied to asymmetric desymmetrization of *meso*-1,3-polyols through intramolecular differentiation of the bis-acetal derivatives. Highly convergent asymmetric synthesis of the pentol derivative corresponding to the C(19)−C(27) ansa-chain of rifamycin S demonstrates the utility of the ring-cleavage reaction as a method for terminal differentiation of the prochiral polyols.

Experimental Section

General. Unless otherwise noted, ^1H and ^{13}C NMR spectra were recorded in $CDCl_3$ at 300 and 75.6 MHz, respectively. Unless otherwise noted, mass spectra were measured using the EI (70 eV) ionization. All commercially available reagents were used without further purification. Dichloromethane and DMF were distilled from calcium hydride. THF and benzene were distilled from sodium/benzophenone ketyl. Unless otherwise noted, organic extracts were dried over Na_2SO_4. Flash chromatography was conducted on silica gel (Wakogel C-300). (2*R**,3*R**)-,[23] (2*R**,3*S**)-2,4-Dimethyl-1,3-pentanediol,[24] acetal **1i**,[5] *N*-sulfonyl L-phenylalanines,[25] enol silanes **5a**−**e**,[26] tributylmethallylstannane **6b**,[27] and methallyltrimethylsilane **7b**[28] were prepared according to the literature procedures.

(2*R,4*R**)-4-Isopropyl-2-phenyl-1,3-dioxane (1a).** To a solution of 5-methyl-1,3-pentanediol (0.945 g, 8.0 mmol) and benzaldehyde (0.849 g, 8.00 mmol) in benzene (50 mL) was added and *p*-toluenesulfonic acid monohydrate (15 mg, 0.08 mmol). The reaction flask was equipped with a Dean−Stark trap, and the mixture was heated at reflux for 4 h. The mixture was poured into aq $NaHCO_3$ and extracted twice with hexane. The organic layers were dried and concentrated in vacuo. Distillation of the residue (bp 77−79 °C/0.3 mmHg) gave 2.23 g (74%) of **6a**: ^1H NMR δ 0.95 (3H, d, $J = 6.0$ Hz), 1.02 (3H, d, $J = 6.7$ Hz), 1.53 (1H, m), 1.73−1.88, (2H, m), 3.52 (1H, ddd, $J = 2.4$, 6.8, and 11.2 Hz), 3.94 (1H, dt, $J = 2.7$ and 12 Hz), 4.29 (1H, ddd, $J = 1.4$, 5.0 and 11.3 Hz), 5,0.50 (1H, s),

(21) Attempted esterification (Ac_2O, pyridine, DMAP and MTPACl, *i*-PrNEt_2, DMAP) of **32** as a mixture failed, suggesting that that both isomers possess sterically hindered secondary hydroxy groups.

(22) Ishihara, K.; Kaneeda, M.; Yamamoto, H. *J. Am. Chem. Soc.* **1994**, *116*, 11179−11180.
(23) Harada, T.; Matsuda, Y.; Wada, I.; Uchimura, J.; Oku, A. *J. Chem. Soc., Chem. Commun.* **1989**, 1429−1430.
(24) Montgomery, S. H.; Pirrung, M.; Heathcock, C. H. *Organic Syntheses*; Wiley: New York, 1990; Collect. Vol. VII, pp 190−194.
(25) McChesney, E. W.; Wann, Jr., W. K. *J. Am. Chem. Soc.* **1937**, *58*, 1116.
(26) Kita, Y.; Segawa, J.; Haruta, J.; Yasuda, H.; Tamura, Y. *J. Chem. Soc., Perkin Trans. 1* **1982**, 1099.
(27) Miura, K.; Saito, H.; Fujisawa, H. Hosomi, A. *J. Org. Chem.* **2000**, *65*, 8119−8122.
(28) Ishihara, K.; Mouri, M.; Gao, Q.; Maruyama, T.; Furuta, K.; Yamamoto, H. *J. Am. Chem. Soc.* **1993**, *115*, 11490−111495,

7.31−7.39 (3H, m), 7.48−7.52 (2H, m); ^{13}C NMR δ 17.88, 18.35, 28.24, 32.98, 67.15, 82.22, 100.99, 125.97, 128.12, 128.51, 139.05.

1-Ethoxy-1-(trimethylsilyloxy)ethene (5f).[29] The compound was prepared by the reaction of ethyl acetate with LDA (1.1 equiv) followed by treatment with chlorotrimethylsilane (1.2 equiv) in THF at −78 to −40 °C. The ^{1}H NMR analysis of the crude reaction mixture showed the formation of a 1:1 mixture of **5f** and ethyl trimethylsilyl acetate. Concentration of the crude mixture in vacuo at room temperature and distillation of the residue under reduced pressure (60 °C/10 mmHg) gave **5f** (containing 40% of ethyl trimethylsilyl acetate) in 30% yield.

Dimethyl-(2-methyl-2-propenyl)phenylsilane (7c). The compound was prepared in 88% yield by the reaction of methallyl bromide and chlorodimethylphenylsilane with magnesium. **7c**: bp 47−48 °C/0.5 mmHg; ^{1}H NMR δ 0.31 (6H, s), 1.62 (3H, m), 1.78 (2H, d, J = 0.9 Hz), 4.48 (1H, m), 4.60 (1H, m), 7.37 (3H, m), 7.52 (2H, m).

General Procedure for the Preparation of Oxazaborolidinones 4a−c. To a solution of an *N*-sulfonyl amino acid (0.20 mmol) in CH_2Cl_2 (2 mL) was added dichlorophenylborane (26 μL, 0.20 mmol) at room temperature. After being stirred for 30 min, the mixture was concentrated in vacuo to give **4a−c** as a white solid, which was then dissolved in CH_2Cl_2 (0.27 mL) and used in ring-cleavage reactions.

Ring-Cleavage Product 9b (Representative Procedure for the Ring-Cleavage of Acetals; Table 1, entry 8). To a stirred solution of acetal *rac*-**1a** (62 mg, 0.30 mmol) and **7c** (86 mg, 0.45 mmol) in CH_2Cl_2 (0.1 mL) at −50 °C under argon was added a fleshly prepared CH_2Cl_2 solution of **4a** (0.20 mL, 0.15 mmol). After being stirred for 4 h, the reaction mixture was quenched by the addition of *iso*-Pr_2NEt (0.1 mL). The mixture was diluted with ether, poured into aq $NaHCO_3$, and extracted twice with Et_2O. Tetradecane was added to the dried organic layers as an internal standard. The yield (43.7%) and ee (79.9%) of *ent*-**1a** were determined by GC analyses with an OV101 (30 m) column and with a CP−Cyclodextrin-β-236-M-19 (25 m) column (110 °C, 15 min and then 3 deg/min, (2*R*,4*R*)*t*1 = 28.52 min, (2*S*,4*S*) *t*2 = 28.78 min), respectively. The mixture was then concentrated in vacuo. Because a part of the ring-cleavage product was obtained as a TMS ether derivative, the residue was treated with acetic acid−H_2O−THF (volume ratio; 3:3:4) at room temperature for 1 h. The mixture was poured into water and extracted twice with ether. The organic layers were washed with aq $NaHCO_3$, dried, and concentrated in vacuo. Purification of the residue by flash chromatography (5−10% ethyl acetate in hexane) gave 40.4 mg (51%) of **9b**: ^{1}H NMR δ 0.80 (3H, d, J = 7.0 Hz), 0.91 (3H, d, J = 6.9 Hz), 1.44 (1H, m), 1.59 (1H, m), 1.70 (3H, s), 2.09 (1H, m), 2.36 (1H, dd, J = 6.2 and 13.8 Hz), 2.40 (1H, br), 2.58 (1H, dd, J = 7.8 and 13.8 Hz), 3.26 (1H, m), 3.54 (1H, m), 4.52 (1H, dd, J = 6.2 and 7.8 Hz), 4.67 (1H, m), 4.74 (1H, m), 7.25−7.39 (5H, m);^{13}C NMR δ 15.79, 18.77, 22.90, 28.34, 30.62, 46.43, 61.10, 77.95, 79.35, 113.28, 127.33, 127.93, 128.46, 141.79, 141.96; IR (liquid film) 3400 (br), 1650, 1055, 890, 760, 700 cm^{-1}; MS *m*/*z* (relative intensity) 262 (M^+. 0.1), 207 (100), 107 (100); HRMS calcd for $C_{17}H_{26}O_2$ 262.1933, found; 262.1949. Anal. Calcd for $C_{17}H_{26}O_2$: C, 77.82; H, 9.99. Found: C, 77.58; H, 10.22.

The ring-cleavage reactions of other racemic acetals were carried out according to a procedure similar to that described above. The ee values of the following acetals were determined by capillary GC analyses using a Chrompack CP−Cyclodextrin-β-236-M-19 (25 m) column: *ent*-**1b** (125 °C, 15 min and then 2.5 deg/min, (2*R*,4*R*) *t*1 = 37.17 min, (2*S*,4*S*) *t*2 = 37.38 min), *ent*-**1c** (100 °C, 10 min and then 4 deg/min, (2*R*,4*R*) *t*1 = 19.76 min, (2*S*,4*S*) *t*2 = 20.01 min), *ent*-**1g** (100 °C, 10 min and then 5 deg/min, (2*R*,4*R*) *t*1 = 22.08 min, (2*S*,4*S*) *t*2 = 22.26 min), *ent*-**1j** (100 °C, 10 min and then 5 deg/min, (2*R*,4*S*) *t*1 = 19.31 min, (2*S*,4*R*) *t*2 = 19.44 min), *ent*-**2** (115 °C, 15 min and then 2 deg/min, (2*R*,4*S*,5*S*) *t*1 = 29.91 min, (2*S*,4*R*,5*R*) *t*2 = 30.23 min), *ent*-**3a** (115 °C, (2*R*,4*S*,5*R*) *t*1 = 43.23 min, (2*S*,4*R*,5*S*) *t*2 = 44.57 min). The ee values of *ent*-**1c**,**d** were determined after converting them to an acetonide derivative (50 °C, 10 min and then 3 deg/min, (*R*) *t*1 = 15.47 min, (*S*) *t*2 = 15.92 min). The ee value of *ent*-**1f** was determined after converting it to 2-furyl derivative *ent*-**1e**. The ee values of the following acetals were determined by a chiral phase HPLC: *ent*-**1h** (Daicel Chiracel OD, 1 mL/min,10% 2-PrOH in hexane) (2*R*,4*S*) *t*1 = 4.99 min, (2*S*,4*R*) *t*2 = 8.10 min), *ent*-**1j** (Daicel Chiracel OD, 1 mL/min, 30% 2-PrOH in hexane) (2*R*,4*R*) *t*1 = 4.58 min, (2*S*,4*S*) *t*2 = 7.18 min), *ent*-**3b** (Daicel Chirapak AD, 1 mL/min,10% 2-PrOH in hexane) (2*R*,4*S*,5*R*) *t*1 = 17.64 min, (2*S*,4*R*,5*S*) *t*2 = 19.35 min).

The absolute structures of recovered acetals *ent*-**1a**,**g**,**j**, **2**, and **3b** were determined by hydrolysis (1N HCl, ethanol, reflux) of them to the known 1,3-diols. (2*R*,4*R*)-**1a** (88.2% ee, Table 1, entry 9) gave (*R*)-4-methyl-1,3-pentanediol: $[\alpha]^{23}_D$ 10 (*c* 0.24, $CHCl_3$), lit.[30] 12.0 (*c* 2.43, $CHCl_3$). (2*R*,4*R*)-**1g** (55.6% ee, Table 3, entry 2) gave (*R*)-4,4-dimethyl-1,3-pentanediol: $[\alpha]^{20}_D$ 8.2 (*c* 0.27, $CHCl_3$), lit.[31] 18.0 (*c* 0.4, $CHCl_3$). (2*R*,4*R*)-**1j** (84.0% ee, Table 3, entry 5) gave (*R*)-1-phenyl-1,3-propanediol: $[\alpha]^{23}_D$ 56 (*c* 1,1, $CHCl_3$), lit.[32] ((*S*)-isomer) −63.8 (*c* 1, $CHCl_3$). (2*R*,4*S*,5*S*)-**2** (55.4% ee, Table 4, entry 3) gave (2*S*,3*S*)-2,4-dimethyl-1,3-pentanediol: $[\alpha]^{19}_D$ 5.9 (*c* 0.40, $CHCl_3$), lit.[33] 11.3 (*c* 0.6, $CHCl_3$). (2*R*,4*S*,5*R*)-**3b** (71% ee, Table 5, entry 7**)** gave (2*R*,3*S*)-2,4-dimethyl-1,3-pentanediol: $[\alpha]^{25}_D$ −14.3 (*c* 1,22, $CHCl_3$), lit.[34] ((2*S*,3*R*)-isomer) 19.6 (*c* 0.57, $CHCl_3$). The absolute structure of *ent*-**1h** (67.0% ee, Table 3, entry 3) was determined to be (2*R*,4*S*) by converting it to (*S*)-5-phenyl-1,3-pentanediyl diacetate ((i) H_2, Pd/C, EtOH, (ii) Ac_2O, DMAP, pyridine): $[\alpha]^{23}_D$ 13.8 (*c* 0.68, $CHCl_3$), lit.[29] 18.6 (*c* 0.474, $CHCl_3$). The absolute structure of *ent*-**1i** was determined to be (2*R*,4*S*) by GC analysis of an authentic sample prepared from (*S*)-butane-1,3-diol.

***meso*-Bis-acetal 18a.** A mixture of acetal **17** (3.32 g, 9.55 mmol) and 10% Pd/C (66.4 mg) in ethanol (43 mL) was stirred vigorously under hydrogen atmosphere for 3 days at room temperature. The mixture was filtered through a pad of cellulose powder, and the filtrate was concentrated in vacuo. Acetalization of the crude tetrol with benzaldehyde (2.22 g, 21.0 mmol) was carried out according to a procedure similar to that described above (benzene reflux, 14 h). Purification of the crude product with flash chromatography (15% ethyl acetate in hexane) and recrystallization from benzene and hexane gave 2.05 g (63% yield) of **18a**: mp 91−92 °C; ^{1}H NMR δ 1.61 (2H, m), 1.79 (1H, td, J = 5.8 and 14.1 Hz), 1.84−1.98 (2H, m), 2.15 (1H, td, J = 7.1 and 14.1 Hz), 3.98 (2H, m), 4.12 (2H, m), 4.28 (2H, ddd, J = 1.3, 5.0, and 11.4 Hz), 5.52 (2H, s) 7.32−7.40 (6H, m), 7.47−7.51 (4H, m); ^{13}C NMR δ 31.14, 41.91, 67.05, 73.52, 101.18, 126.02, 128.22, 128.72, 138.70. Anal. Calcd for $C_{21}H_{24}O_4$: C, 74.09; H, 7.11. Found: C, 74.26; H, 7.04.

***meso*-Bis-acetal 18b.** A mixture of diol **21** (0.541 g, 1.51 mmol) and 10% Pd/C (106 mg) in ethanol (7 mL) was stirred vigorously under hydrogen atmosphere for 17 h at room temperature. The mixture was filtered, and the filtrate was concentrated in vacuo. Acetalization of the crude tetrol was carried out by using a mixture of benzaldehyde (384 mg, 3.62 mmol) and benzaldehyde dimethyl acetal (544 mg, 3.62 mmol) according to a procedure similar to that described above.

(29) Mikami, K.; Matsumoto, S.; Ishida, A.; Takemura, S.; Suenobu, T.; Fukuzumi, S. *J. Am. Chem. Soc.* **1995**, *117*, 11134−11141.

(30) Harada, T.; Kurokawa, H.; Kagamihara, Y.; Tanaka, S.; Inoue, A.; Oku, A. *J. Org. Chem.* **1992**, *57*, 1412−1421.

(31) Konoike, T.; Hayashi, T.; Araki, Y. *Tetrahedron Asymm.* **1994**, *5*, 1559−1566.

(32) Chênevert, R, Geneviêre, F.; Rhlid, R. B. *Tetrahedron* **1992**, *48*, 6769−6776.

(33) Helmchen, G.; Leikauf, U.; Taufer-Knopfel, I. *Angew. Chem., Int., Ed. Engl.* **1985,** *24*, 874.

(34) Abiko, A.; Liu, J.-F.; Masamune, S. *J. Am. Chem. Soc.* **1997**, *119*, 2586−2587.

Purification of the crude products with flash chromatography (15% ethyl acetate in hexane) and recrystallization from benzene and hexane gave 0.360 g (67% yield) of **18b**: mp 103−103.5 °C; ^{1}H NMR δ 1.50−1.60 (2H, m), 1.68−1.90 (6H, m), 3.84 (2H, m), 3.94 (2H, dt, J = 2.5 and 11.4 Hz),4.27 (2H, ddd, J = 1.1, 5.0, and 11.4 Hz), 5.51 (2H, s), 7.32−7.40 (6H, m), 7.49−7.52 (4H, m); ^{13}C NMR δ 31.41, 31.81, 67.01, 77.33, 101.09, 125.98, 128.15, 128.62, 138.81. Anal. Calcd for $C_{22}H_{26}O_4$: C, 74.55; H, 7.39. Found: C, 74.31; H, 7.30.

Ring-Cleavage Product 24b. Ring-cleavage reaction of bis-acetal **18b** (70.0 mg, 0.198 mmol) was carried out according to a procedure similar to that described above by using methallylsilane **7c** (113 mg, 0.593 mmol) and oxazaborolidinone **4a** (0.198 mmol) in CH_2Cl_2 (0.38 mL) at −50 °C for 8 h. The reaction mixture was quenched by the addition of *iso*-Pr_2NEt. Tetrabutylammonium fluoride (1 M in THF, 1 mL) was added, and the resulting mixture was stirred at room temperature for 10 min. The mixture was poured into aq $NaHCO_3$ and extracted twice with ether. The organic layers were dried and concentrated in vacuo. Purification of the residue by flash chromatography (10−25% ethyl acetate in hexane) gave 66.4 mg (82% yield) of **24b** and 13.8 mg (15% yield) of bis-cleavage product **25**. Because **25** was contaminated with the decomposition products of **4a**, it was isolated as diacetate (Ac_2O, 4-(*N*,*N*-dimethylamino)pyridine, pyridine). **24b**: ^{1}H NMR δ 1.43−1.90 (11H, m including s (3H) at d 1.69), 2.33 (1H, dd, J = 6.0 and 14 Hz), 2.55 (1H, dd, J = 7.9 and 14 Hz), 2.65 (1H, br), 3.49 (1H, m), 3.59 (1H, m), 3.66 (1H, m), 3.95 (1H, dt, J = 2.5 and 12 Hz), 4.27 (1H, ddd, J = 1.1, 4.9, and 11.4 Hz), 4.55 (1H, dd, J = 6.0 and 7.9 Hz), 4.67 (1H, m), 4.75 (1H, m), 5.51 (1H, s), 7.18−7.55 (10H, m); ^{13}C NMR δ 22.80, 27.22, 30.79, 31.38, 35.81, 46.61, 60.63, 66.97, 74.65, 76.77, 77.74, 101.13, 113.29, 126.00, 127.08, 127.86, 128.16, 128.45, 128.69, 138.78, 141.77, 141.91; MS (CI) *m*/*z* (relative intensity) 411 (M^++1, 3), 243 (100); HRMS calcd for $C_{20}H_{29}O_4$ (M^+ − CH_2=$C(CH_3)CH_2$) 355.1909, found; 355.1927. **25:** ^{1}H NMR δ 1.4−1.8 (16H, m), 2.25−2.60 (4H, m), 3.40−3.80 (6H, m), 4.52 (2H, br t, J = ca. 7 Hz), 4.71 (2H, m), 4.78 (2H, m), 7.20−7.35 (10H, m). **Diacetate of 25:** ^{1}H NMR δ 1.5−1.75 (14 H, m, including br s (6H) at 1.70), 1.85 (6H, s), 2.33 (2H, br dd, J = 6.4 and 13.4 Hz), 2.54 (2H, br dd, J = 7.7 and 13.4 Hz), 3.33 (2H, m), 4.00 (4H, m), 4.44 (2H, dd, J = 6.4 and 7.7 Hz), 4.65 (2H, br s), 4.74 (2H, br s) 7.20−7.35 (10H, m).

Pivalate 26b. To a solution of **24b** (35.0 mg, 0.0865 mmol) and pyridine (0.36 mL) in CH_2Cl_2 (0.1 mL) was added pivaloyl chloride (11.1 μL, 0.130 mmol) and 4-(*N*,*N*-dimethylamino)-pyridine (ca. 2 mg) at room temperature. After being stirred for 11 h, the reaction mixture was poured into water and extracted twice with ether. The organic layers were dried and concentrated in vacuo. Purification of the residue by flash chromatography (5−20% ethyl acetate in hexane) gave 29.8 mg, (70% yield) of the corresponding pivaloyl ester: ^{1}H NMR δ 1.03 (9H, s)1.40−1.90 (11H, m), 2.28 (1H, dd, J = 6.4 and 13.7 Hz), 2.53 (1H, dd, J = 7.5 and 13.7 Hz), 3.35 (1H,m), 3.78 (1H,m), 3.87−4.26 (3H, m), 4.26 (1H, br dd, J = 4.2 and 11.4 Hz), 4.55 (1H, m), 4.63 (1H, m), 4.70 (1H, m), 5.49 (1H, s), 7.20−7.40 (8H, m), 7.48−7.52 (2H, m); IR (neat film) 1725, 890, 755, 700 cm^{-1}. The ester (29.8 mg, 0.0602 mmol) was dissolved in 0.83 mL of acetone and 0.20 mL of water. To this was added a 50 wt % solution of *N*-methylmorpholine oxide in water (30 mL) and a 2.5 wt % solution of OsO_4 in *tert*-butyl alcohol (39 mL, 3.0 mmol), and the reaction mixture was stirred for 12 h. A solution of $NaIO_4$ (39.3 mg, 0.181 mmol) in water (0.25 mL) was added, and the resulting solution was stirred further for 1 h during which time a white precipitate formed. The mixture was diluted with water and extracted twice with ether. The organic layers were washed twice with 0.5 M $Na_2S_2O_3$ and then with brine, dried, and concentrated in vacuo. Purification of the residue by flash chromatography (10% ethyl acetate in hexane) gave 28.5 mg (95%) of the corresponding ketone: ^{1}H NMR δ 1.03 (9H, s)1.40−1.90 (8H, m), 2.21 (3H, s), 2.55 (1H, dd, J = 4.5 and 15.6 Hz), 2.99 (1H, dd, J = 8.7 and 15.6 Hz), 3.35 (1H,m), 3.76−4.13 (4H, m), 4.27 (1H, m), 4.86 (1H, dd, J = 4.5 and 8.7 Hz), 5.50 (1H, s), 7.20−7.55 (10H, m); ^{13}C NMR δ 27.00 27.58, 30.83, 31.21, 33.24, 38.48, 51.80, 61.11, 67.00, 72.57, 75.20, 77.000, 101.14, 126.02, 126.85, 127.93, 128.14, 128.52, 128.62, 138.78, 141.38, 178.25, 206.51; IR (neat film) 1725, 765, 700 cm^{-1}. A solution of the ketone (28.5 mg, 0.0573 mmol) in ethanol (6 mL) was heated under reflux for 3 h in the presence of Na_2CO_3 (56.1 mg). The reaction mixture was poured into brine and extracted twice with ether. The organic layers were dried and concentrated in vacuo. Purification of the residue by flash chromatography (20% ethyl acetate in hexane) gave 19.1 mg, (95% yield) of **26b**: ^{1}H NMR δ 1.18 (9H, s), 1.46−1.93 (8H, m), 2.48 (1H, br), 3.66 (1H,m), 3.83 (1H, m),3.95 (1H, dt, J = 2 and 12 Hz), 4.11 (1H, m), 4.23−4.38 (2H, m), 5.50 (1H, s), 7.26−7.48 (5H, m); ^{13}C NMR δ 27.17, 32.23, 33.19, 33.54, 38.73, 61.60, 67.02, 68.43, 77.46, 101.18, 125.94, 128.22, 128.70, 138.61, 178.94; IR (liquid film), 3450 (br), 1720, 1160, 1105, 750, 700 cm^{-1}; MS (CI) *m*/*z* (relative intensity) 333 (M^+ + 1 − H_2O, 100), 227 (24); HRMS (CI) calcd for $C_{20}H_{29}O_4$ (M^+ + 1 − H_2O) 333.2066, found; 333.2055.

Ring-Cleavage Product 24a. The ring-cleavage product was obtained in 94% yield according to a procedure similar to that described above. **24a**: ^{1}H NMR δ 1.50 (1H, m), 1.64−1.94 (7H, m including s (3H) at d 1.72), 2.05 (1H, ddd, J = 2.8, 9.4 and 14.4 Hz), 2.34 (1H, dd, J = 5.7 and 13.9 Hz), 2.55 (1H, ddd, J = 0.5, 8.2, and 13.9 Hz), 3.48−3.78 (3H, m), 3.85 (1H, m), 3.94 (1H, m), 4.27 (1H, ddd, J = 1.1, 4.9, and 11.4 Hz), 4.53 (1H, dd, J = 5.7 and 8.2 Hz), 4.70 (1H, m), 4.77 (1H, m) 5.43 (1H, s), 7.25−7.43 (10H, m); ^{13}C NMR δ 22.93, 31.84, 36.50, 39.10, 46.24, 60.46, 66.96, 71.83, 73.78, 77.76, 100.82, 113.19, 125.93, 127.25, 127.87, 128.07, 128.40, 128.61, 138.54, 141.70, 142.04; IR (liquid film) 3450 (br), 1650, 915, 760, 745, 700 cm^{-1}; MS *m*/*z* (relative intensity) 396 (M^+, <1), 341 (100), 235 (40), 217 (95); HRMS calcd for $C_{25}H_{32}O_4$ 396.2300, found; 396.2295,

Pivalate of 24a. The compound was prepared in 84% yield according to a procedure similar to that described above. ^{1}H NMR δ 0.98 (9H, s), 1.51 (1H, m), 1.64−2.09 (5H, m including s (3H) at d 1.72), 2.31(1H, dd, J = 5.8 and 14 Hz), 2.54 (1H, dd, J = 7.7 and 14 Hz), 3.58 (1H, m), 3.86−4.31 (5H, m), 4.47 (1H, dd, J = 5.8 and 7.7 Hz), 4.69 (1H, m), 4.75 (1H, m) 5.44 (1H, s), 7.23−7.44 (10H, m).

Pivalate 26a. The compound was prepared in 75% yield according to a procedure similar to that described above. $[\alpha]^{21}_D$ = −33.7 (*c* 1.65, $CHCl_3$); ^{1}H NMR δ 1.18 (9H, s), 1.53 (1H, m), 1.65−1.95 (5H, m), 3.26 (1H, br), 3.94−4.02 (2H, m), 4.08−4.29 (4H, m), 5.54 (1H, s), 7.26−7.46 (5H, m); ^{13}C NMR δ 27.14, 31.34, 36.43, 38.67, 42.70, 61.12, 66.91, 67.67, 77.40, 101.16, 125.89, 128.25, 128.87, 138.12, 178.66; IR (liquid film) 3520 (br), 1725, 755, 700 cm^{-1}; MS *m*/*z* (relative intensity) 336 (M^+, 43), 335 (42), 105 (100); HRMS calcd for $C_{19}H_{28}O_5$ 336.1937, found; 336.1932.

***meso*-Bis-acetal 29.** Ozone was introduced into a stirred solution of diol **28**[2d] (639.4 mg, 1.74 mmol) in 80 mL of methanol at −78°C until the blue color persisted. The excess ozone was removed by allowing nitrogen to bubble through the solution at −78 °C. To this at −78 °C was added dimethyl sulfide (5 mL). The reaction mixture was allowed to warm to room temperature during 0.5 h. To the resulting mixture was added $NaBH_4$ (1.31 g, 34.6 mmol). After being stirred for 1.5 h at 0 °C, the mixture was concentrated in vacuo, poured into brine, and extracted four times with ethyl acetate. The organic layers were dried and concentrated in vacuo. To a solution of the resulting crude tetrol in benzene (64 mL) was added *p*-anisaldehyde dimethyl acetal (1.77 g, 10.4 mmol), *p*-toluenesulfonic acid monohydrate (19 mg, 0.17 mmol), and 4-A molecular sieves (500 mg), and the mixture was stirred at room temperature for 40 h. After removal of the molecular sieves by filtration, the filtrate was poured into aq $NaHCO_3$ and extracted twice with ethyl acetate. The organic layers were dried and concentrated in vacuo. Purification of the residue

by flash chromatography (10−15% ethyl acetate in hexane) gave 789 mg (74% overall yield) of **29**: ^{1}H NMR (500 MHz, benzene−d_6) δ 0.23 (6H, s), 0.59 (6H, d, J = 7.0 Hz), 1.10 (9H, s), 1.31 (6H, J = 7.0 Hz), 2.01 (2H, m), 2.18 (2H, m), 3.37 (6H, s), 3.41 (2H, t, J = 11.0 Hz), 3.79 (2H, d, J = 10.0 Hz), 3.91 (1H, J = 5.5 Hz), 4.08 (2H, dd, J = 4.5 and 11.0 Hz), 5.62 (2H, s), 6.98 (4H, m), 7.76 (4H, m). ^{13}C NMR (125.8 MHz, benzene−d_6) δ −4.02, 9.97, 12.34, 18.28, 26.22, 30.99, 54.40, 73.04, 77.72, 81.86, 101.26, 113.41, 128.02, 132.23, 160.09; MS *m*/*z* (relative intensity) 614 (M^+, 1), 557 (32), 207 (100), 121 (97); HRMS calcd for $C_{35}H_{54}O_7Si$ 614.3639, found; 614.3632,

Bis-acetal 30. Bis-acetal **29** (105 mg, 0.171 mmol) was treated with tetrabutylammonium fluoride (1M in THF) (1.7 mL, 1.7 mmol) at room temperature for 2.5 h. The mixture was poured into water and extracted twice with ethyl acetate. The organic layers were dried and concentrated in vacuo. Purification of the residue by flash chromatography (20−30% ethyl acetate in hexane) gave 74.4 mg (87% yield) of **30**: ^{1}H NMR (500 MHz, benzene-d_6) δ 0.55 (6H, d, J = 6.7 Hz), 1.21 (6H, d, J = 7.0 Hz), 1.45 (1H, br), 1.92−2.18 (4H, m), 3.32−3.40 (8H, m, including s (3H) at 3.36), 3.98 (1H, m), 4.08 (2H, dd, J = 4.7 and 11.1 Hz), 4.15 (2H, dd, J = 1.2 and 11.1 Hz), 5.60 (2H, s), 6.91 (4H, m), 7.69 (4H, m); ^{13}C NMR (125.8 MHz, benzene−d_6) δ 10.99, 11.58, 30.14, 35.74, 54.42, 72.88, 75.72, 82.46, 101.24, 113.58, 125.81, 131.73, 160.15; MS *m*/*z* (relative intensity) 500 (M^+, 16), 265 (30), 207 (86), 137 (100); HRMS calcd for $C_{29}H_{40}O_7$ 500.2774, found; 500.2778.

Bis-acetal 31. To a solution of **30** (488 mg, 0.975 mmol) in THF (8.5 mL) at 0 °C was added KHMDS (0.5 M in toluene) (3.0 mL, 1.5 mmol), and the mixture was stirred at this temperature for 30 min. To the resulting mixture of the alkoxide at 0 °C was added iodomethane (0.28 g, 2.0 mmol). After being stirred for 15 h at room temperature, the mixture was poured into brine and extracted twice with ether. The organic layers were dried ($MgSO_4$) and concentrated in vacuo. Purification of the residue by flash chromatography (10−20% ethyl acetate in hexane) gave 469 mg (93% yield) of **31**: mp 103−104.5 °C (recrystallized from benzene and hexane); ^{1}H NMR (500 MHz, benzene-d_6) δ 0.57 (6H, d, J = 6.7 Hz), 1.22 (6H, d, J = 7.1 Hz), 2.12 (4H, m), 3.37 (6H, s), 3.39 (1H, t, J = 3.5 Hz), 3.40 (2H, t, J = 11.0 Hz), 3.61 (3H, s), 3.89 (2H, dd, J = 1.5 and 10.1 Hz), 4.10 (2H, dd, J = 4.8 and 11.1 Hz), 5.64 (2H, s), 6.95 (4H, m), 7.79 (4H, m); ^{13}C NMR (125.8 MHz, benzene-d_6) δ 11.61, 11.99, 30.68, 37.19, 54.42, 60.93, 73.10, 82.26, 85.68, 101.07, 113.47, 125.81, 132. 31, 160.00; MS *m*/*z* (relative intensity) 514 (M^+, 12), 281 (26), 207 (100); HRMS calcd for $C_{30}H_{42}O_7$ 514.2922, found; 514.2930. Anal. Calcd for $C_{30}H_{42}O_7$: C, 70.01; H, 8.23. Found: C, 70.27; H, 8.19.

Ring-Cleavage Product 32. The ring-cleavage reaction of bis-acetal **30** (40.4 mg, 0.0807 mmol) was carried out according to a procedure similar to that described above by using **5e** (18 mg, 0.097 mmol) and oxazaborolidinone **4b** (0.081 mmol) in CH_2Cl_2 (0.65 mL) at −60 °C for 19 h. Purification of the crude product by flash chromatography (5−20% ethyl acetate in hexane) gave 42.2 mg (86% yield) of **32** (a 7:3 mixture of diastereomers). The major isomer was separated by repeated flash chromatography. **32**: ^{1}H NMR (500 MHz, benzene-d_6) of the major isomer δ 0.47 (3H, C*H*$_3$, d, J = 6.7 Hz), 0.93 (3H, C*H*$_3$, d, J = 7.0 Hz), 1.03 (6H, C*H*$_3$ x 2, br d, J = ca. 7 Hz), 1.20 (3H, t, C*H*$_3$CH$_2$O, J = 7.2 Hz), 1.25 (3H, C*H*$_3$, s), 1.48 (2H, O*H*, br), 1.52 (3H, C*H*$_3$, s), 1.92 (1H, C*H*, m), 2.03−2.13 (3H, C*H* x, 3 m), 3.35 (1H, *H*-9α, t, J = 11.1 Hz), 3.38 (3H, C*H*$_3$O, s), 3.41 (3H, C*H*$_3$O, s), 3.70 (1H, *H*-1, dd, J = 2.3 and 8.6 Hz), 3.95 (1H, *H*-1, dd, J = 5.9 and 8.6 Hz), 4.05 (1H, *H*-9β, dd, J = 4.7 and 11.1 Hz), 4.16−4.30 (5H, CH$_3$C*H*$_2$O-, *H*-3, *H*-5, and *H*-9, m), 4.97 (1H, *H*-1′, s), 5.80 (1H, O−C*H*−O, s), 6.92 (2H, Ar−H, m), 6.97 (2H, Ar−H, m), 7.41 (4H, Ar−H, m) [the minor isomer resonated at δ 0.79 (3H, d, J = 6.8 Hz), 0.94 (3H, d, J = 6.7 Hz), 1.02−1.08 (6H, m), 1.17 (3H, d, J = 6.9 Hz), 1.18 (3H, s), 1.45 (3H, s), 1.75−1.83 (3H, m, including br s (2H) at 1.76), 2.13 (1H, m), 2.22 (1H, m), 2.40 (1H, m), 3.39 (3H, s), 3.46 (3H, s), 3.47 (1H, s, J = 11.1 Hz), 3.65 (3H, dd, J = 2.1 and 8.4 Hz), 3.94 (1H, dd, J = 3.8 and 8.4 Hz), 4.07 (1H, m), 4.14 (1H, dd, J = 4.7 and 10.9 Hz), 4.22 (1H, m), 4.33−4.43 (3H, m), 4.91 (1H, s), 5.86 (1H, s), 6.94 (2H, m), 6.98 (2H, m), 7.35 (2H, m), 7.44 (2H, m)]; ^{13}C NMR (125.8 MHz, benzene-d_6) δ 9.27 (*C*H$_3$CH), 10.94 (*C*H$_3$CH), 11.57 (*C*H$_3$CH), 13.00 (*C*H$_3$CH), 14.13 (*C*H$_3$CH$_2$O), 18.74 (*C*H$_3$C-2′), 22.66 (*C*H$_3$C-2′), 29.89 (CH$_3$*C*H), 30.08 (CH$_3$*C*H), 36.35 (CH$_3$*C*H), 39.25 (CH$_3$*C*H), 48.10 (*C*2′), 54.37 (*C*H$_3$O), 54.45 (*C*H$_3$O), 60.07 (C-3 or C-5), 70.14 (CH$_3$*C*H$_2$O), 70.63 (C-1), 72.79 (C-9), 77.27 (C-3 or C-5), 81.35 (C-7), 85.85 (C-1′), 101.49 (O−*C*H−O), 113.38 (Ar-*C*), 113.47 (Ar-*C*), 125.81 (Ar-*C*), 128.26 (Ar-*C*), 130.82 (Ar-*C*), 132.23 (Ar-*C*), 159.55 (Ar-*C*), 160.10 (Ar-*C*), 175.89 (*C*═O). The ee value was determined by a chiral phase HPLC (Daicel Chirapak AD, 1 mL/min, 2% 2-PrOH in hexane) (minor enantiomer) $t1$ = 22.90 min, (major enantiomer) $t2$ = 35.05 min).

Ring-Cleavage Products 33 and 34. Ring-cleavage reaction of bis-acetal **31** (65.4 mg, 0.127 mmol) was carried out according to a procedure similar to that described above by using **5f** (92 mg, containing 40% of ethyl trimethylsilyl acetate, 0.57 mmol) and oxazaborolidinone **4b** (0.26 mmol) in CH_2Cl_2 (0.51 mL) at −60 °C for 24 h. Purification of the crude product by flash chromatography (5−30% ethyl acetate in hexane) gave, in the order of elution, 49.8 mg (58% yield) of **33** (R = TMS) (a 9:1 mixture of diastereomers) and 23.7 mg (31% yield) of **34** (R = H) (a 9:1 mixture of diastereomers). **33**: ^{1}H NMR (500 MHz, benzene-d_6) δ 0.18 (9H, s), 0.64 (3H, d, J = 7.0 Hz), 0.98−1.03 (9H, m), 1.35 (3H, d, J = 7.5 Hz), 1.95 (1H, m), 2.0−2.2 (3H, m), 2.91 (1H, dd, J = 7.5 and 14.8 Hz), 3.27−3.35 (3H, m), 3.40 (3H, s), 3.44 (3H, s), 3.48 (1H, t, J = 11.0 Hz), 3.77 (2H, m), 3.79 (3H, s), 3.95−4.10 (3H, m), 4.14 (1H, dd, J = 4.5 and 11.0 Hz), 5.54 (1H, t, J = 7.5 Hz), 5.70 (1H, s), 6.92 (2H, m), 6.98 (2H, m), 7.55 (2H, m), 7.79 (2H, m) [a minor diastereomer resonated at 1.22 (3H, d, J = 7.5 Hz), 1.27 (3H, d, J = 7.0 Hz), 2.76 (1H, dd, J = 6.5 and 14.8 Hz), 5.37 (1H, t, J = 6.5 Hz), 5.64 (1H, s), 7.51 (2H, m), 7.75 (2H, m)]. **34**; ^{1}H NMR (500 MHz, benzene-d_6) δ 0.56 (3H, d. J = 7.0 Hz), 0.84 (3H, d, J = 7.0 Hz), 0.92 (3H, d, J = 7.0 Hz), 1.08 (3H, t, J = 7.0 Hz), 1.31 (3H, d, J = 7.0 Hz), 1.66 (1H, m), 1.89 (1H, m), 1.94 (1H, m), 2.05 (1H, m), 2.78 (1H, dd, J = 6.0 and 14.0 Hz), 2.84 (1H, br), 3.13 (1H, dd, J = 8.5 and 14.0 Hz), 3.27 (1H, dd, J = 2.5 and 10.0 Hz), 3.39 (6H, s), 3.46 (1H, t, J = 11.0 Hz), 3.55−3.64 (2H, m), 3.74 (3H, s), 3.94−4.18 (5H, m), 5.62 (1H, br t, J = ca. 6 Hz), 5.68 (1H, s), 6.90 (2H, m), 6.97 (2H, m), 7.55 (2H, m), 7.78 (2H, m) [a minor diastereomer resonated at 0.97 (3H, d, J = 7.0 Hz), 1.13 (3H, d, J = 7.0 Hz), 1.14 (3H, d, J = 7.0 Hz), 1.22 (3H, d, J = 7.0 Hz), 5.33 (1H, br t, J = ca. 6 Hz), and 5.65 (1H, s)]; ^{13}C NMR (125.8 MHz, benzene d_6) δ 10.45, 11.84, 13.82, 13.89, 15.20, 30.19, 36.30, 39.45, 41.48, 42.82, 54.37, 54.47, 60.02, 61.36, 65.50, 73.05, 75.58, 77.30, 81.69, 85.94, 101.17, 113.35, 113.61, 125.82, 128.27, 129.79, 132.38, 159.79, 160.15, 170.40; MS *m*/*z* (relative intensity) 602 (M^+, <1), 556 (<1), 207 (100); HRMS calcd for $C_{34}H_{50}O_9$ 602.3455, found; 602.3448.

Diol 35. TMS ether **33** (36.2 mg, 0.0538 mmol) was treated with a tetrabutylammonium fluoride (1M in THF) (1.0 mL, 1.0 mmol) at room temperature for 18 h. The mixture was poured into water and extracted twice with ethyl acetate. The organic layers were dried and concentrated in vacuo. Purification of the residue by flash chromatography (50% ethyl acetate in hexane) gave 17.2 mg (86% yield) of **34**: ^{1}H NMR (500 MHz, benzene-d_6) δ 0.48 (3H, d, J = 6.7 Hz), 0.65 (3H, d, J = 6.9 Hz), 0.88 (3H, d, J = 7.0 Hz), 1.08 (3H, d, J = 7.1 Hz), 1.76 (1H, br s), 2.00−2.16 (4H, m), 3.29 (3H, s), 3.37 (3H, s), 3.38 (1H, t, J = 11.0 Hz), 3.38 (1H, dd, J = 1.9 and ca. 10 Hz), 3.75 (1H, dd, J = 1.8 and 10.1 Hz), 3.89 (1H, dd, J = 3.6 and 10.7 Hz), 3.94−4.05 (2H, m), 4.08 (1H, dd, J = 4.7 and 11.1 Hz), 4.36 (1H, br), 5.54 (1H, s), 6.97 (2H, m), 7.71 (2H, m); ^{13}C NMR (125.8 MHz, benzene-d_6) δ 9.77, 11.29, 11.35, 13.11, 30.20, 34.53, 36.48, 37.69, 54.48, 61.88, 68.80, 73.00, 76.81, 81.45, 101.25, 113.45, 125.81, 131.97, 160.22; MS *m*/*z* (relative

intensity) 396 (M^+, 18), 281 (32), 207 (100); HRMS calcd for $C_{22}H_{36}O_6$ 396.2511, found; 396.2513.

TBS Ether 36. A mixture of diol **35** (14.6 mg, 0.0369 mmol), TBSCl (7.7 mg, 0.051 mmol), and imidazole (4.0 mg, 0.059 mmol) in DMF (0.4 mL) was stirred at room temperature for 18 h. The mixture was diluted with ether, poured into water, and extracted twice with ether. The organic layers were dried ($MgSO_4$) and concentrated in vacuo. Purification of the residue by flash chromatography (10% ethyl acetate in hexane) gave 18.0 mg (96% yield) of **36**: ^{1}H NMR (500 MHz, benzene−d_6) δ 0.23 (3H, s), 0.27 (3H, s), 0.56 (3H, d, J = 6.7 Hz), 0.98 (3H, d, J = 7.0 Hz), 1.04 (3H, d, J = 7.0 Hz), 1.14 (9H, s), 1.14 (3H, d, J = 6.8 Hz), 1.20 (1H, br), 1.90 (1H, m), 1,98 (1H, m), 2.09 (1H, m), 2.24 (1H, m), 3.33 (3H, s), 3.37 (3H, s), 3.39 (1H, t, J = 11.0 Hz), 3.45 (1H, dd, J = 2.0 and 10.3 Hz), 3.81 (1H, dd, J = 1.7 and 10.1 Hz), 3.97 (1H, br s), 4.06 (2H, m), 5.56 (1H, s), 6.96 (2H, m), 7.71 (2H, m); ^{13}C NMR (125.8 MHz, benzene-d_6) δ −5.50, −5.36, 9.80, 11.06, 11.39, 13.31, 25.97, 29.95, 30.33, 34.16, 36.64, 39.09, 54.51, 61.87, 65.05, 73.08, 81.65, 88.43, 101.29, 113.57, 125.87, 132.11, 160.22; MS m/z (relative intensity) 510 (M^+, <1), 453 (17), 207 (100); HRMS calcd for $C_{28}H_{50}O_6Si$ 510.3376, found; 510.3378; ee determination (HPLC, Daicel Chirapak AD, 1 mL/min, 1−9% 2-PrOH in hexane) (major) $t1$ = 7.16 min, (minor) $t2$ = 14.32 min).

Acknowledgment. This work was supported partially by Grant-in-Aid for Scientific Research from Ministry of Education, Culture, Sports, Science and Technology.

Supporting Information Available: ^{1}H NMR spectra for products, ^{1}H NMR spectra for determination of enantiomeric excess, and detailed experimental procedures and spectral data for products. This material is available free for charge via the Internet at http://pubs.acs.org.

JO025944G