Enantioselective Ring-Cleavage Reaction of 2-Substituted 1,3-Dioxolanes Catalyzed by Arylboron Complexes Derived from *N*-Tosyl-(α*S*,β*R*)-β-methyltryptophan

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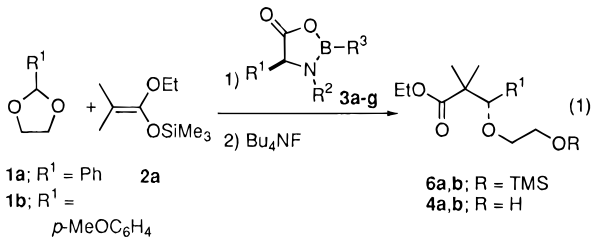
Recently, significant advances have been made in catalytic asymmetric synthesis using chiral Lewis acids.[1] In most instances, substrates are planer carbonyl compounds, whose enantiofaces are differentiated by complexation with chiral Lewis acids. Although Lewis acids also promote a variety of transformations through the activation of carbon−oxygen single bonds, successful application of the chiral catalysts is relatively rare.[2] The auxiliary-based cleavage of chiral cyclic acetals promoted by Lewis acids has been investigated intensively in recent years and proven to be a powerful method for asymmetric carbon−carbon bond formation[3,4] as well as enantiodifferentiating transformation of prochiral diols.[5] We wish to report here the first example of a catalytic, enantioselective ring-cleavage reaction of achiral 1,3-dioxolanes by using amino acid-derived chiral arylboron complexes **3h**,**i** (Scheme 1).

We have recently reported that phenylboron complex **3a** (R^1 = $PhCH_2$, R^2 = Tf, R^3 = Ph) serves as an efficient catalyst for the diastereoselective cleavage of chiral 1,3-dioxanes derived from (*R*)-1,3-butanediol.[6] The application of **3a** (30 mol %) in the reaction of 2-phenyl-1,3-dioxolane **1a** and enol silyl ether **2a** (3 equiv) in CH_2Cl_2 at −20 °C for 1 h followed by treatment of the initial silylated ring-cleavage product **6a** with Bu_4NF led to the clean formation of **4a** but with almost no enantioselection (eq 1) (entry 1 in Table 1). A brief survey of the related



L-amino acid-derived phenylboron complexes revealed that *N*-tosyl derivatives **3b** and **3c** exhibit moderate enantioselection in the reaction of dioxolanes **1a**,**b** (Table 1, entries 2, 3, and 5). The R^3 group attached to the boron atom is also influential. The ring-cleavage reaction was very sluggish when methylboron **3d** was used (Table 1, entry 4). For the reaction of **1b**, both (*p*-chlorophenyl)- and *m*-(chlorophenyl)boron complexes **3e** and **3f** exhibited slightly higher enantioselection than the corresponding phenylboron complex **3b** (Table 1, entry 5 vs entries 6 and 7). A similar trend was also observed for the (*S*)-tryptophan-derived complexes **3c** and **3g** (Table 1, entry 3 vs 8).[7]

Amino acid-derived boron complexes **3** with alkyl or hydrogen as an R^3 group have been utilized as efficient catalysts for asymmetric Diels−Alder reaction[9] and the

Scheme 1

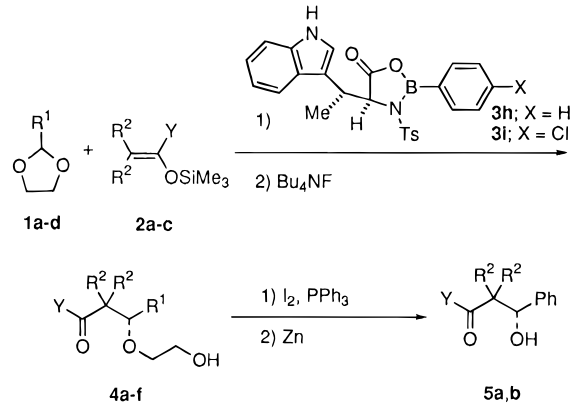


Table 1. Ring Cleavage of 1,3-dioxolanes 1a,b with 2a in the Presence of Boron Complexes 3a−g[a]

entry	dioxolane **1** (R^1)	boron complex **3** (R^1, R^2, R^3)	product	yield (%)	ee[b] (%)
1	**1a** (Ph)	**3a** ($PhCH_2$, Tf, Ph)	**4a**	79	16
2		**3b** ($PhCH_2$, Ts, Ph)		63	57
3		**3c** ($IndCH_2$,[c] Ts, Ph)		90	60
4		**3d** ($IndCH_2$,[c] Ts, Me)		7[d]	55
5	**1b** (*p*-$MeOC_6H_4$)	**3b**	**4b**	88	65
6		**3e** ($PhCH_2$, Ts, *p*-ClC_6H_4)		85	70
7		**3f** ($PhCH_2$, Ts, *m*-ClC_6H_4)		75	69
8		**3g** ($IndCH_2$,[c] Ts, *p*-ClC_6H_4)		84	78

[a] Reactions were carried out in CH_2Cl_2 by using 30 mol % of **3a**−**g** and 3 equiv of **2a** at −20 °C for 1−5 h. [b] The % ee was determined by ^{1}H-NMR (300 MHz) analysis of the (*S*)-MTPA ester derivative. [c] (3-Indolyl)methyl. [d] The starting material **1a** was recovered in 78% yield.

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(7) Organoboron complexes **3d**−**g** were prepared by the reaction of the corresponding dibromoboranes R^3BBr_2[8] and *N*-tosylamino acids.

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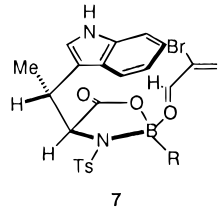
Mukaiyama aldol reaction.[10] For their highly enantioselective tryptophan-derived alkylboron catalysts, Corey et al. have demonstrated the coordination of an aldehyde *cis* to the 3-indolylmethyl group with donor−acceptor interactions (**7**).[9e] According to a molecular model analysis, a similar mode of coordination is quite less likely for the sterically more demanding 1,3-dioxolanes. They would rather coordinate to the opposite face allowing the aryl group (R^3) to orient *cis* to the 3-indolylmethyl groups (**8a**) and/or to the same upper face of the alternative rotational isomer with respect to the $C_\alpha-C_\beta$ bond (**8b**).[11] With the hope of reducing the possible modes of the coordination by fixing the $C_\alpha-C_\beta$ bond rotation, we examined ring-cleavage reactions using ($\alpha S,\beta R$)-β-methyltryptophan-derived arylboron complexes **3h**,**i**.[12]



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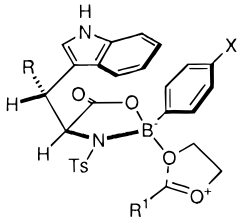
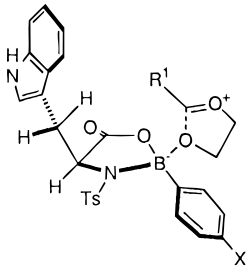


8a; R = H, Me, X = H, Cl



8b; X = H, Cl

Treatment of *N*-tosyl-($\alpha S,\beta R$)-β-methyltryptophan[9e,13] with dichlorophenylborane in CH_2Cl_2 followed by solvent removal *in vacuo* afforded the arylboron complex **3h**, whose structure was established by ^{1}H- and ^{11}B-NMR analysis.[14] The conformation about the $C_\alpha-C_\beta$ bond was ascertained by the observed coupling constant $J_{\alpha,\beta}$ (3.3 Hz). In the presence of 10 mol % catalyst **3h**, treatment of dioxolane **1b** with **2a** at −20 °C for 4 h in CH_2Cl_2 followed by desilylation with Bu_4NF afforded ring-cleavage product (*S*)-**4b** of 87% ee in 91% yield (Scheme 1). When chlorophenylboron complex **3i** was used as a catalyst under similar conditions, the ee of (*S*)-**4b** was improved to 91% (Table 2, entry 2). The reaction can be effected with 5 mol % of the catalyst **3i** without lowering the ee and the chemical yield (Table 2, entry 3). Not only enol silyl ether **2a** but also **2b** and **2c**, derived from a thiol ester and a ketone, respectively, can be employed as nucleophiles leading to the enantioselective formation of the corresponding ring-cleavage products **4c**,**d** (Table 2, entries 4 and 5). Successful results were also obtained in the ring cleavage of other 1,3-dioxolanes with aryl and alkenyl groups at the 2-position (Table 2, entries 1, 6, and 7). The reaction of 2-alkyl derivatives, however, was very sluggish under these conditions.[15]

Table 2. Enantioselective Ring Cleavage of 1,3-Dioxolanes 1 with Enol Silyl Ethers 2 Catalyzed by Boron Complex 3i[a]

entry	dioxolane **1** (R^1)	nucleophile **2** (R^2, Y)	product	yield (%)	% ee[b]
1	**1a** (Ph)	**2a** (Me, OEt)	**4a**	88	86
2	**1b** (*p*-$MeOC_6H_4$)	**2a**	**4b**	86	91
3[c]	**1b**	**2a**	**4b**	82	92
4	**1b**	**2b** (H, S^{t}Bu)	**4c**	80	85
5	**1b**	**2c** (H, Ph)	**4d**	62	89
6	**1c** (2-Furyl)	**2a**	**4e**	73	93
7	**1d** (PhCH=CH)	**2a**	**4f**	89	88

[a] Unless otherwise noted, reactions were carried out in CH_2Cl_2 by using 10 mol % of **3i** and 3 equiv of **2a**−**c** at −20 °C for 2−5 h. [b] The % ee was determined by ^{1}H-NMR (300 MHz) analysis of the (*S*)-MTPA ester derivative. [c] The reaction was carried out in the presence of 5 mol % of **3i** for 10 h.

The 2-hydroxyethyl group in the ring-cleavage products can be removed simply by conversion to the iodides followed by treatment with zinc powder (Scheme 1).[16] Thus, ethyl (*S*)-3-hydroxy-2,2-dimethyl-3-phenylpropanoate (**5a**) of 85% ee and *S*-*tert*-butyl (*R*)-3-hydroxy-3-phenylpropanethioate (**5b**) of 84% ee were obtained in 76% and 76% overall yields starting from **4a** (86% ee) and **4c** (85% ee), respectively. The absolute configurations of **5a**,**b** were determined by converting them into the known (*S*)-MTPA ester derivatives.[6]

In summary, we have shown that arylboron complexes **3h**,**i** derived from *N*-tosyl-($\alpha S,\beta R$)-β-methyltryptophan served as excellent catalysts for enantioselective ring-cleavage reactions of 2-substituted 1,3-dioxanes with enol silyl ethers. Further studies are in progress to expand the scope of the catalytic process to enantiodifferentiating transformation of prochiral acetals derived from *meso*-diols.

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Supporting Information Available: Characterization data for new compounds (4 pages).

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(11) The structures **8a** and **8b** are drawn to show the coordination of 1,3-dioxolanes to the bottom and upper faces of the complex, respectively. Conformation around the B−O(dioxolane) bond is beyond the scope of the present consideration.

(12) Corey et al. have showed that the rotation around the $C_\alpha-C_\beta$ bond can be fixed as depicted in **8a** by the introduction of the (βR)-methyl group.[9e]

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(14) NMR data: ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.74 (3H, d, J = 7.2 Hz), 2.37 (3H, s), 4.31−4.39 (1H, m), 4.41 (1H, d, J = 3.3 Hz), 7.03 (1H, d, J = 2.1 Hz), 7.10−7.29 (7H, m), 7.37−7.55 (3H, m), 7.48 (2H, d, J = 8.4 Hz), 8.00 (1H, br s), 8.06 (1H, d, J = 8.1 Hz); ^{11}B NMR (96.5 MHz, $CDCl_3$, $BF_3\cdot OEt_2$) δ 31.3.

(15) A typical experimental procedure is as follows: To a solution of *N*-tosyl-($\alpha S,\beta R$)-β-methyltryptophan (37.2 mg, 0.10 mmol) in CH_2Cl_2 (1 mL) at rt under argon was added (*p*-chlorophenyl)dibromoborane (11 μL, 0.10 mmol). After being stirred for 30 min, the mixture was concentrated *in vacuo* to give boron complex **3i**, which was dissolved in CH_2Cl_2 (1 mL). The resulting solution of **3i** (0.2 mL, 0.02 mmol) was added to a stirred solution of 1,3-dioxolane **1b** (34.9 mg, 0.19 mmol) and **2a** (113 mg, 0.60 mmol) in CH_2Cl_2 (0.8 mL) at −20 °C, and stirring was continued for 4 h. The reaction was quenched by the addition of the CH_2Cl_2 solution of *i*-Pr_2NEt (1 M, 0.5 mL), and the mixture was treated with Bu_4NF (1 M in THF, 0.5 mL) at rt for 0.5 h. Aqueous workup and purification of the crude product by flash column chromatography (SiO_2, 10% ethyl acetate/hexane) gave 49.3 mg (86% yield) of **5b**, whose ee was determined to be 91% after conversion to a (*S*)-MTPA ester derivative.

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