shita, M.; Matsushita, M.; Sato, H.; Toki, T.; Nakajima, T.; Irie, H. *Chem. Lett.* **1993**, *929*. (f) Melchiorre, C.; Qnaglia, W.; Picchio, M. T.; Giardina, D.; Brasili, L.; Angoli, P. *J. Med. Chem.* **1989**, *32*, 79. (g) Essien, H.; Lai, J. Y.; Hwang, K. *J. Med. Chem.* **1988**, *31*, 898.
2. Stahl, G. L.; Walter, R.; Smith, C. W. *J. Org. Chem.* **1978**, *43*, 2285.
3. Atwell, G. J.; Denny, W. A. *Synthesis* **1984**, 1032.
4. Krapcho, A. P.; Christopher, S. K. *Synth. Commun.* **1990**, *20(16)*, 2559.
5. Hansen, J. B.; Nielsen, M. C.; Ehrbar, U.; Buchardt, O. *Synthesis* **1982**, 404.
6. Houssin, R.; Bernier, J-L.; Henichart, J. P. *Synthesis* **1988**, 259.
7. Our procedure gave only a small amount of the side products (a mixture of the tri- and di-protected amines). Using the procedure described for the preparation of **2a**, pure *N*-Boc-1,7-diamino-4-azaheptane (**5**) was easily obtained by vacuum distillation. ^{1}H NMR ($CDCl_3$) 1.25 (s, 2H), 1.32 (br s, 1H), 1.44 (s, 9H), 1.65 (m, 4H), 2.68 (dt, 4H), 2.77 (t, 2H), 3.25 (q, 2H), 5.62 (br s, 1H) (Lit. reference 4).
8. This bis-substituted *N,N'-tert*-butoxycarbonyl-1,2-ethanediamine was formed (10% yield) and could be easily removed by taking advantage of its water solubility.

Influence of Different Classes of Boranes and Solvents on Asymmetric Induction in Enantioselective Borane Reduction of Prochiral Ketones Catalyzed by a Chiral Oxazaborolidine

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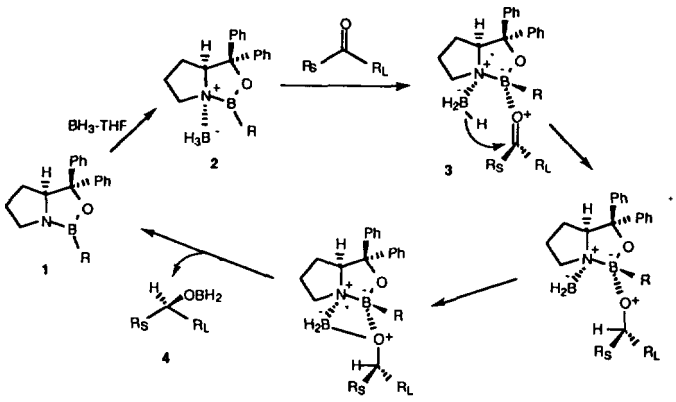
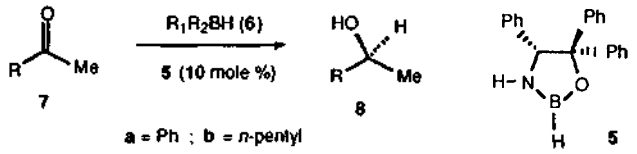
The discovery of chiral oxazaborolidines as catalytic reagents for the enantioselective borane reduction of prochiral ketones has been an important milestone in organic synthesis.[1] As a reasonable reaction mechanism for the catalysts, it has been suggested that Lewis acid-base adducts (**2**) formed by reaction of **1** with BH_3-THF serve as effective reagents for the reduction which occur by coordination of the electrophilic boron of the oxazaborolidine on carbonyl oxygen and then intramolecular hydrogen transfer from the NBH_3 moiety to the activated carbonyl *via* a six-membered ring transition state (**3**), followed by regeneration of **2** by the subsequent ligand exchange with borane to form the alkoxyborane **4** (Scheme 1).[2] Accordingly, it is expected that nature of borane used as a hydride donor plays an important role for the enantioselective reduction. It has been reported that borane-THF, borane dimethylsulfide (BMS), or catecholborane as a source of hydride proves to be successful in achieving high enantioselectivities for the reduction.[1c-d] However, the



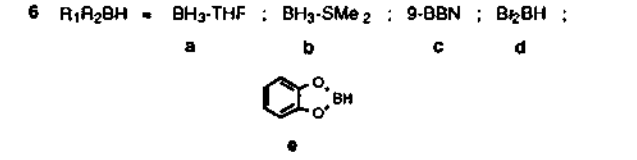
Scheme 1.

direct comparison on the asymmetric inducing effect by different classes of boranes for the reduction has not been accomplished.

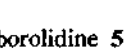
On the other hand, the oxazaborolidine system (R=H in **1**) has been suggested to exist normally as a dimer but to decompose to the corresponding monomer in the presence of a Lewis basic solvent like THF.[2] Recently, Nevalanien reported that solvents played important roles not only in the behavior of a free oxazaborolidine but in the stabilization of reactive intermediates involved in the catalytic cycle on the basis of *ab initio* molecular orbital calculations.[3] However, no data for the influence of solvents in providing the enantioselectivities have been available. Hereby we report the comparison study for the influence of boranes as a source of hydride and solvents on the asymmetric induction in the catalytic enantioselective borane reduction of prochiral ketones.



a = Ph ; **b** = *n*-pentyl



a **b** **c** **d**



e

We first chose oxazaborolidine **5** and different classes of boranes **6**, such as borane-THF (**a**), BMS (**b**), 9-BBN (**c**), dibromoborane (**d**) and catecholborane (**e**),[4] as representatives. And then we examined the influence of boranes **6** as a hydride donor on the asymmetric induction in the reduction of acetophenone **7a** and 2-heptanone **7b** selected as representative aromatic and aliphatic ketones, respectively, with each of **6** catalyzed by **5**. Thus, **5** was prepared from (R)-2-amino-1,1,2-triphenylethanol[5] and BMS in THF at 65 ℃. The reduction was performed by adding a solution of ketone to a solution of each of **6** in the presence of 10 mole% of **5** in THF at room temperature (*ca.* 25 ℃) over 1 h period under a positive nitrogen atmosphere. In this reaction, the stoichiometric ratio of ketone : **5** : hydride was 1 : 0.1 : 2. The

Table 1. Influence of Different Classes of Boranes on Asymmetric Induction in Enantioselective Borane Reduction of Acetophenone and 2-Heptanone Catalyzed by **5** in Tetrahydrofuran[a]

Boranes	Acetophenone				2-heptanone			
6	Time	Yield (%)[b]	% ee[c]	Confg.[d]	Time	Yield (%)[b]	% ee[c]	Confg.[d]
a	10 min	97	88	S	10 min	98	60	S
b	10 min	94	82	S	10 min	98	59	S
c	1 h	84	2 (11)	S	1 h	89	(1)[e]	S
d[f]	12 h	85	22	S	3 h	91	(22)	S
e	30 min	86	64	S	10 min	99	40	S

[a]All the reductions were carried out with ketones : **5** : hydride (1 : 0.1 : 2) in THF at room temperature (*ca.* 25 ℃), unless otherwise noted. [ketones]=0.3 M. [b]Determined by GC analyses using internal standards. [c]Determined by capillary GC analyses through a Chiraldex GTA chiral column. [d]Determined by comparison of the elution orders of capillary GC analyses through a Chiraldex GTA chiral column and the optical rotations of the corresponding optically active authentic alcohols. [e]The figures in parentheses indicated % ee obtained in the presence of 1 equiv of **5**. [f]In THF-CH_2Cl_2 (1 : 1).

Table 2. Influence of Different Classes of Solvents on Asymmetric Induction in Enantioselective Borane Reduction of Acetophenone and 2-Heptanone Catalyzed by **5**[a]

Entry	Solvent	boranes	Acetophenone				2-heptanone			
			Time	Yield (%)[b]	% ee[c]	Confg.[d]	Time	Yield (%)[b]	% ee[c]	Confg.[d]
1	THF	**6b**	10 min	94	82	S	10 min	98	59	S
2		**6e**	30 min	86	64	S	10 min	89	18	S
3	DME	**6b**	10 min	91	83	S	10 min	86	47	S
4		**6e**	30 min	82	31	S	10 min	92	11	S
5	$PhCH_3$	**6b**	10 min	92	79	S	10 min	86	50	S
6		**6e**	10 min	88	71	S	10 min	92	23	S
7	hexane	**6b**	30 min	90	63	S	10 min	85	50	S
8		**6e**	30 min	89	66	S	10 min	89	26	S
9	CH_2Cl_2	**6b**	30 min	89	19	S	10 min	92	50	S
10		**6e**	10 min	86	38	S	10 min	95	5	S

[a]All the reductions were carried out with the stoichiometry of ketones : **5** : hydride on the basis of **6b** or **6e** (1 : 0.1 : 2) at room temperature (*ca.* 25 ℃), unless otherwise noted. [ketone]=0.3 M. [b-d]See the corresponding footnotes in Table 1.

optical purities of alcohol products obtained were determined by capillary GC analysis through a chiral column. As shown in Table 1, the reduction with **6a-b** and **6e** underwent rapidly to give the corresponding alcohols in high yields within 30 min in contrast to much slower reduction with **6d**. In terms of the enantioselectivities, **6a** provided the highest levels of enantioselection, such as 88% ee for **7a** and 60% ee for **7b**. **6b** was also highly effective for the reduction, giving 82% ee and 59% ee for **7a** and **7b**, respectively. The reduction with **6e** showed somewhat lower enantioselectivities such as 64% ee for **7a** and 40% ee for **7b**. In contrast, a dialkylborane 9-BBN **6c** gave very low enantioselectivities even in the presence of a stoichiometric amount of **5**. The reason for this result is unclear, but it seems to be attributable to the steric bulkness of 9-BBN **6c** which may retard the effective coordination on nitrogen of **5** to form the borane adducts (**5**-R_1R_2 BH), leading to a noncatalyzed reduction by **6c** itself. A Lewis acidic borane **6d** provided also low enantioselectvities even in the presence of a stoichiometric amount of **5**.

On the other hand, to examine the effect of solvents on the asymmetric induction, we chose different classes of solvents, such as THF, dimethoxyethane (DME), toluene, hexane, and dichloromethane. The comparison study for such effects was performed by employing the reduction of representative ketones **7** with each of BMS **6b** and catecholborane **6e**, which were utilized as neat forms in each of the selected solvents in the presence of 0.1 equiv of **5**. In the case of the reduction of **7a** with **6b**, the enantioselections obtained in Lewis basic solvents like THF and DME are somewhat higher than those in nonpolar solvents like toluene and hexane, such as 83% ee in DME, 82% ee in THF, 79% ee in toluene, and 63% ee in hexane. For **7b**, however, any significant solvent effects have not been observed in obtaining 47-59% ee. In contrast, using **6e** as a source of hydride in the reduction of **7a**, significant solvent effects were observed in achieving the higher levels of enantioselection in nonpolar solvents than in Lewis basic solvents, such as 71% ee in toluene and 66% ee in hexane in contrast to 64% ee in THF and 31% ee in DMF. The results are summarized in Table 2. In both case, we find that dichloromethane is not a preferable solvent to obtain good enantioselectivities. So far, the reason is unclear.

In summary, of the borane derivatives using as a source of hydride for the enantioselective borane reduction of aceto-

phenone and 2-heptanone catalyzed by **5**, BH_3-THF and BMS provided the best results for the rate of reduction and enantioselection as compared to those by catecholborane, 9-BBN and dibromoborane. To obtain the best enantioselectivities, Lewis basic solvents (*e.g.* THF or DME) for BMS and nonpolar solvents (*e.g.* toluene or hexane) for catecholborane were preferable.

Acknowledgment. This work was generously supported by OCRC/KOSEF.

References

1. For a recent review, see: (a) Singh, V. K. *Synthesis* **1992**, 605. (b) Wallbum, S.; Martens, J. *Tetrahedron: Asymmetry*, **1992**, *3*, 1475. (c) Deloux, A.; Srebnik, M. *Chem. Rev.* **1993**, *93*, 763 and references cited therein. (d) Corey, E. J. *Pure & Appl. Chem.* **1990**, *62*, 1209 and references cited therein.
2. Corey, E. J.; Bakshi, R. K.; Shibata, S. *J. Am. Chem. Soc.* **1987**, *109*, 5551.
3. Nevalainen, V. *Tetrahedron: Asymmetry* **1991**, *2*, 827.
4. Brown, H. C.; Gupta, S. K. *J. Am. Chem. Soc.* **1971**, *93*, 1816.
5. Mckenzie, A.; Wills, G. O. *J. Chem. Soc.* **1925**, *127*, 283.

Stereocontrolled Synthesis of Conjugated *E*-Dienoate Esters *Via* Double Alkylation and then Pyrolysis of Methyl Phenylsulfinylacetate

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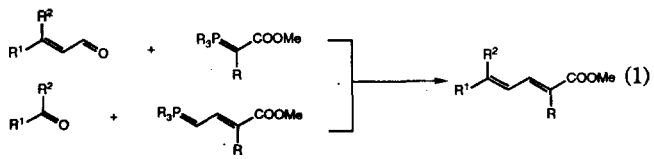
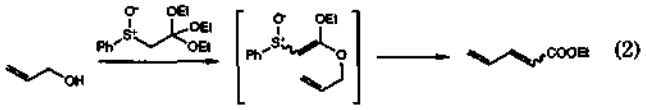
Conjugated dienoate moieties are frequently found in naturally occurring compounds having a wide range of biological activity and in many synthetic intermediates.[1] Sarcopytol A, a 14-membered cyclic terpene cembranoid[2], has a dienoate unit. So far only one synthesis of Sarcopytol A was reported using the Horner-Simmons reaction.[3] Manumycin has been also identified as potent and selective inhibitors of Ras farnesyltransferase, and its aminoacyl side chain having a α-methyldienoate substructure was proposed as pharmocores.[4] A decadienoate has been used in the synthesis of a natural insecticide.[5] The syntheses of these dienoate moieties are generally made by the Wittig or its related reactions[6] as shown in Eq. 1.



(1)

All of these methods involve the addition of a carbanion unit to the carbonyl compounds, followed by some type of elimination. Although these usually proceed with high chemo- and stereo-selectivity in many cases, the application to the dienoate synthesis often encounters some serious problems. In general, allylic ylides do form the conjugated dienes with a moderate degree of stereoselectivity.[7] Furthermore, 2-alkylsubstituted ylides are not only difficult to prepare but diminish the selectivity in many cases.[8] Recently, Posner and his coworkers reported an easy process for dienoate synthesis using Claisen rearrangement of the ketene acetal derived from phenylsulfinyl orthoacetate with various allylic alcohols (Eq. 2).[9] This method has been proven to be a highly efficient process when two-carbon homologated dienoates were desired. They further applied this method to the syntheses of vitamin D analogs. However, their method resulted in the formation of a stereoisomeric mixtures possibly due to the required high temperature in the Claisen rearrangement.

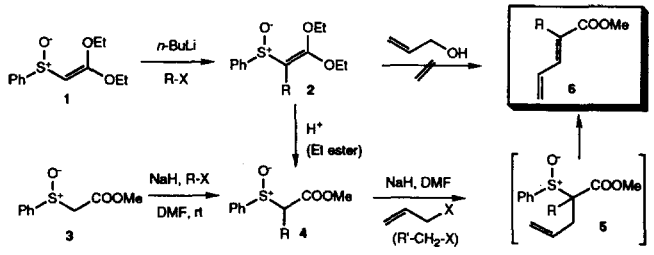


(2)

It was well-known that sulfoxides readily undergo *syn* elimination with a β-hydrogen atom on pyrolysis to form olefins *via* a concerted cyclic pathway.[10] Also pyrolysis of sulfoxides having an α-carbonyl group provides the α,β-unsaturated carbonyl compounds.[11] The *E*-olefins usually predominates in disubstituted ethylenes, but a mixtures of isomers are obtaind in tri- and tetra-substituted compounds. Similar, even better, results could be obtained by using selenoxides.[12] Although these procedures take place under comparatively mild conditions, these have been mostly used in introducing a double bond in a molecule.

We have been interested in synthesizing 2-alkyl substituted dienoates esters and now report a highly stereocontrolled process to the dienoate esters using consecutive alkylations of methyl phenylsulfinylacetate. Scheme 1 shows a general sequence for our new methodology.

Our approach involves consecutive bisalkylation of methyl phenylsulfinylacetate (**3**) with alkyl halides and then allyl halides and followed by spontaneous elimination of phenylsulfenic acid to yield the α-alkyl substituted dienoate esters **6**. Initially, we have tried to alkylate a ketene acetal[13], 2,2-diethoxyvinyl phenylsulfoxide (**1**), to obtain the α-alkyl ketene acetals **2**. The ketene acetal **1** seemed to be smoothly deprotonated by *n*-butyllithium and reacted with electrophiles to form the α-alkyl ketene acetal **2**.[14] The alkylated ketene acetals **2** were too unstable to be isolated and were



Scheme 1.