Arylboron Compounds as Acid Catalysts in Organic Synthetic Transformations

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Keywords: Tris(pentafluorophenyl)borane / Diarylborinic acid / Arylboronic acid / Chiral arylboron catalyst / Lewis acid

Arylboron compounds, $Ar_nB(OH)_{3-n}$ (n = 1–3), bearing electron-withdrawing aromatic groups such as triarylboranes, diarylborinic acids, and arylboronic acids represent a new class of air-stable and water-tolerant Lewis acid or Brønsted acid catalysts in organic synthesis. In particular, while tris(pentafluorophenyl)borane has primarily been used as a co-catalyst in metallocene-mediated olefin polymerization, its potential as a Lewis acid catalyst for organic transformation is now much more extensive. Diarylborinic acids and arylboronic acids have shown themselves to be powerful tools in the design of chiral boron catalysts. This article provides a comprehensive summary of the organic transformations catalyzed by arylboron compounds as acids.

1. Introduction

The classical boron Lewis acids, BX_3, RBX_2, and R_2BX (X = F, Cl, Br, OTf) are now popular tools in organic synthesis. In general, these are used stoichiometrically in organic transformations under anhydrous conditions, since the presence of even a small amount of water causes rapid decomposition or deactivation of the promoters. To obviate some of these inherent problems, the potential of arylboron compounds, $Ar_nB(OH)_{n-3}$ (n = 1−3), bearing electron-withdrawing aromatic groups as a new class of boron catalysts has been recently demonstrated (Figure 1). For example, tris(pentafluorophenyl)borane (**1**) is a convenient, commercially available Lewis acid of comparable strength to BF_3, but without the problems associated with reactive B−F bonds. Although its primary commercial application is as a co-catalyst in metallocene-mediated olefin polymerization, its potential as a Lewis acid catalyst for organic transformations is now recognized as being much more extensive. Diarylborinic acids and arylboronic acids bearing

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Hisashi Yamamoto received his bachelor's degree from Kyoto University in 1967, where his research career commenced in Professor H. Nozaki's laboratory. He then attended Harvard University, earning his Ph. D. under the direction of Professor E. J. Corey. Dr. Yamamoto returned to Japan in 1971 to join Toray Industries, Inc. for one year. His first academic position was as an instructor (Assistant Professor) and then as a lecturer (Associate Professor) at Kyoto University, and in 1977 he was appointed Associate Professor of chemistry at the University of Hawaii. In 1980, he moved to Nagoya University, where he became Professor in 1983. His research focuses on the development of new methodologies for organic synthesis. His laboratory has introduced a number of important methods based on designer Lewis acid catalysts. His laboratory is also well-known for introducing metal reagents that allow highly selective S_N2 cross-coupling with allylic electrophiles.

Kazuaki Ishihara was born in 1963 in Aichi, Japan. He obtained his Ph.D. in 1991 from Nagoya University under the supervision of Professor Hisashi Yamamoto. From 1991 to 1992, he carried out postdoctoral research with Professor E. J. Corey at Harvard University. In 1992, he became Assistant Professor at the Graduate School of Engineering, Nagoya University, and in 1997 he was appointed Associate Professor at the Research Center of Advanced Waste and Emission Management, Nagoya University. His current research is directed towards the development of stereoselective reactions by taking advantage of Brønsted acid/Lewis acid combined asymmetric catalysts (LBA, BLA) and their application to syntheses of biologically important compounds.

MICROREVIEWS: This feature introduces the readers to the authors' research through a concise overview of the selected topic. Reference to important work from others in the field is included.

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electron-withdrawing aromatic groups are also highly effective acid catalysts, and are suitable for the design of chiral acids (Figure 1). As one successful example, we have developed one of the most practical Diels−Alder catalysts, Brønsted acid assisted chiral Lewis acid (BLA) **10**, which is prepared from 3,5-bis(trifluoromethyl)phenylboronic acid (**5**) and the triol derived from optically active binaphthol. This review provides a comprehensive summary of the organic transformations catalyzed by arylboron compounds bearing electron-withdrawing aromatic groups.

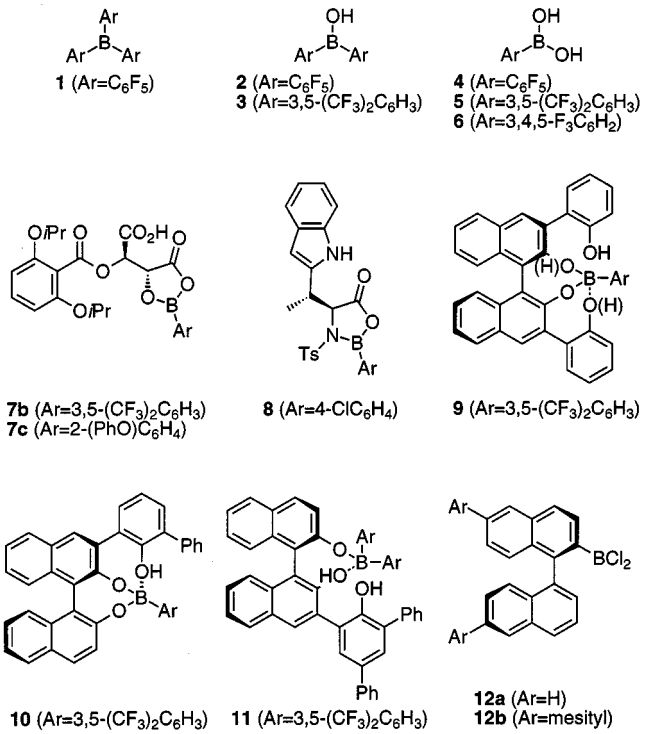
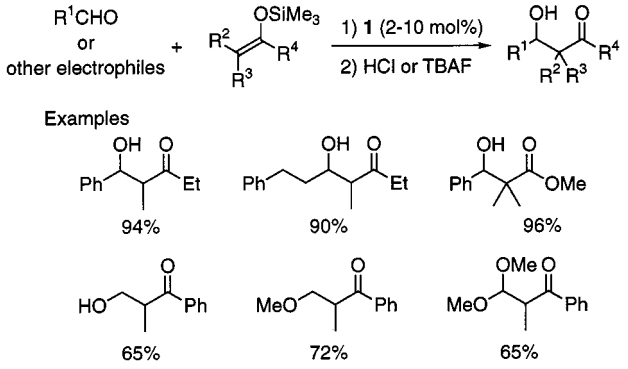


Figure 1. Various arylboron compounds $Ar_nB(OH)_{3-n}$ (n = 1−3) and their chiral complexes

2. Triarylboranes

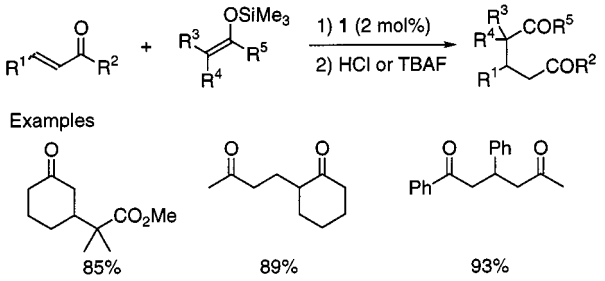
Tris(pentafluorophenyl)borane (**1**) is an air-stable, water-tolerant Lewis acid catalyst, which can be readily prepared as a white solid from boron trichloride by reaction with pentafluorophenyllithium.[1,2] This compound does not react with pure oxygen.[2] It is thermally very stable, even at 270°C, and is soluble in many organic solvents.[2] Although **1** catalyzes reactions most effectively under anhydrous conditions, **1** exposed to air is also available (not anhydrous grade).

Mukaiyama aldol reactions of various silyl enol ethers or ketene silyl acetals with aldehydes or other electrophiles proceed smoothly in the presence of 2 mol-% of **1**.[3a,3c] The following characteristic features can be noted: (1) The products can be isolated as β-trimethylsilyloxy ketones when the crude adducts are worked-up without exposure to acid; (2) this reaction can be carried out in aqueous media, so that the reaction of the silyl enol ether derived from propiophenone with a commercial aqueous solution of formaldehyde does not present any problems; (3) the rate of an aldol reaction is markedly increased when an anhydrous solution of **1** in toluene is used under argon; (4) silyl enol ethers can be brought to reaction with chloromethyl methyl ether or trimethyl orthoformate; hydroxymethyl, methoxymethyl, or dimethoxymethyl C_1 building blocks can be introduced at the position α to the carbonyl group. These aldol-type reactions do not proceed when triphenylborane is used (Scheme 1).



Scheme 1

Conjugate addition of silyl enol ethers to α,β-unsaturated ketones proceeds regioselectively in the presence of 2 mol-% of **1** (not anhydrous grade).[3a,3c] The product can be isolated as a synthetically valuable silyl enol ether when the crude product is worked up without exposure to acid (Scheme 2).



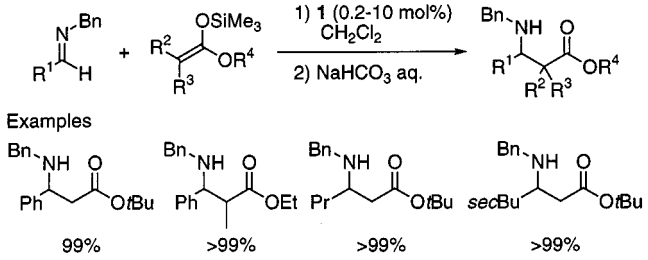
Scheme 2

The Sakurai−Hosomi allylation reaction of benzaldehyde with 2-methallyltrimethylsilane proceeds smoothly in the presence of 5 mol-% of **1** (not anhydrous grade) to afford 3-methyl-1-phenyl-3-buten-1-ol (93%).[3c]

Diels−Alder reaction of cyclopentadiene with 2-methyl-2-propanal also proceeds smoothly in the presence of 5 mol-% of **1** (not anhydrous grade) to give the cyclic adducts (> 99%).[3c]

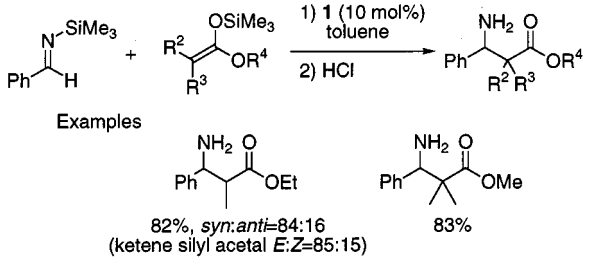
Tris(pentafluorophenyl)borane (**1**) (anhydrous grade) is a highly active catalyst for the aldol-type reaction between ketene silyl acetals and imines because of its stability and comparatively low N−B bond energy and affinity towards nitrogen-containing compounds.[3b,3c] *N*-Benzylimines are useful substrates because the β-benzylamino acid esters produced can be readily debenzylated by hydrogenolysis on palladium/carbon. Catalysis is carried out using a 0.2−10

mol-% catalyst loading in toluene. The following characteristic features can be noted: (1) In most cases, the condensation proceeds smoothly, even with aliphatic enolizable imines derived from primary or secondary aliphatic aldehydes, and (2) the *syn*/*anti* stereoselectivity in these condensations of *N*-benzylidenebenzylamine is dependent on the geometry of the ketene silyl acetal double bond: (*E*)- and (*Z*)-ketene silyl acetals give *anti* and *syn* products, respectively, as the major diastereomers (Scheme 3).



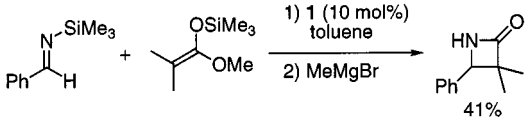
Scheme 3

The use of *N*-trialkylsilylimines can be advantageous, since the protecting *N*-substituent can easily be cleaved from the β-[(trialkylsilyl)amino] acid esters produced in the reaction. The borane Lewis acid **1** is an effective catalyst for the reaction of *N*-trimethylsilylimines.[3c] The reaction of mono- or disubstituted ketene silyl acetals with *N*-(trimethylsilyl)benzylideneamine proceeds smoothly to give the corresponding β-amino acid esters in good yield (Scheme 4).[3c]



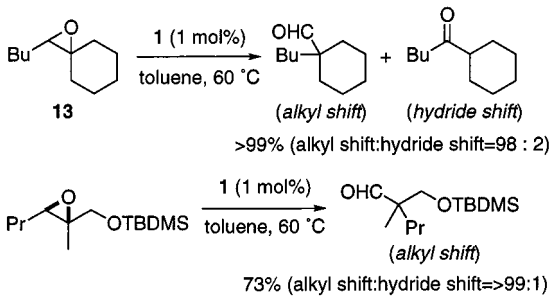
Scheme 4

N-Unsubstituted β-lactams have become very attractive synthetic targets. Most existing methods for their preparation require elaborate procedures to deblock the nitrogen atom. 3,3-Dimethyl-4-phenylazetidin-2-one has been synthesized in moderate yield by in situ treatment of the intermediate β-[bis(trimethylsilyl)amino] acid ester with MeMgBr (Scheme 5).[3c]



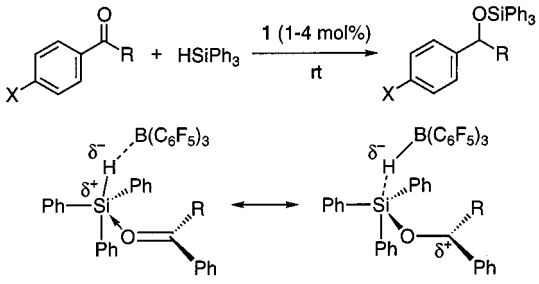
Scheme 5

The protic or Lewis acid promoted rearrangement of epoxides to carbonyl compounds is a well-known synthetic transformation. $BF_3 \cdot OEt_2$ appears to be the most widely used Lewis acid for this purpose.[4] This is often consumed or altered in the course of these reactions, and is thus a reagent rather than a catalyst, although a less than equimolar amount is effective in some instances. We have found **1** to be a highly efficient catalyst in the rearrangement of epoxides.[5] The rearrangement of trisubstituted epoxides readily takes place in the presence of catalytic amounts of **1** (anhydrous grade), resulting in a highly selective alkyl shift to give the corresponding aldehydes. The exceptional bulkiness of **1** may play a role in ensuring the high selectivity of this process. In contrast, treatment of a solution of **13** in benzene with $BF_3 \cdot OEt_2$ affords a diastereomeric mixture in a 33:67 ratio (alkyl shift/hydride shift) (Scheme 6).



Scheme 6

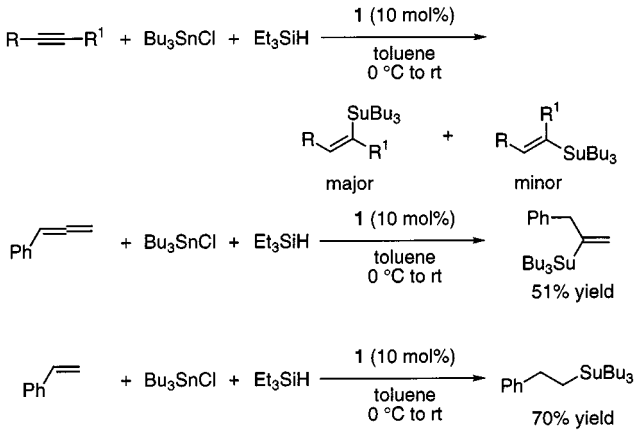
Hydrosilylation of carbon−oxygen bonds is a mild method for the selective reduction of carbonyl functions. Parks and Piers have found that aromatic aldehydes, ketones, and esters are hydrosilylated at room temperature in the presence of 1−4 mol-% of **1** and 1 equiv. of Ph_3SiH.[6] On the basis of the kinetic experiments, the authors have supposed that the reduction takes place by an unusual nucleophilic/electrophilic mechanism: The substrate itself serves to nucleophilically activate the Si−H bond, while hydride transfer is facilitated by the borane Lewis acid (Scheme 7).



Scheme 7

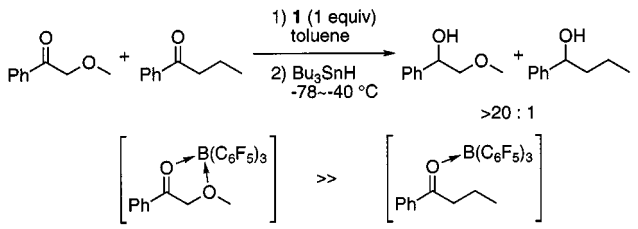
A synthetically useful and convenient method for the **1**-catalyzed hydrostannylation of alkynes with tributyltin hydride, prepared in situ from easily handled and inexpensive chlorostannane and hydrosilane, has been developed by Yamamoto and his colleagues.[7] The hydrostannylation of monosubstituted alkynes proceeds in a regiospecific manner affording exclusively the β-hydrostannylation products. The reaction is *trans*-stereoselective. This method can also be applied to the hydrostannylation of allenes and alkenes (Scheme 8).

Maruoka and his colleagues have reported that **1** is capable of forming a pentacoordinate complex in the re-



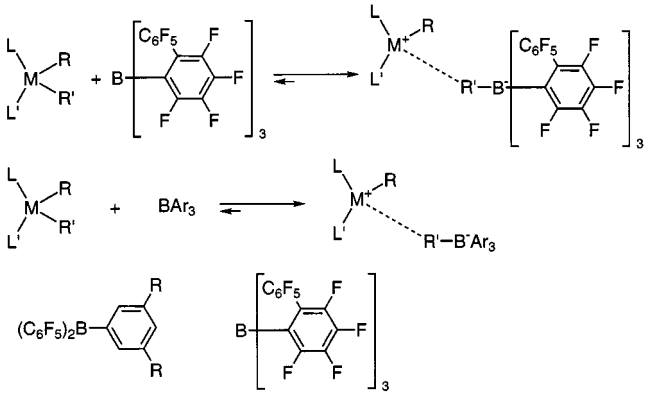
Scheme 8

duction of alkoxy-substituted carbonyl compounds with Bu_3SnH.[8] Reduction of an α-methoxy ketone and its deoxy analogue (1:1 ratio) with **1** (1 equiv.), which was originally believed to be a non-chelating Lewis acid, afforded the α-methoxy alcohol as a major product. Similar results in terms of selectivity were also obtained with Me_3Al in place of **1**. These results imply the preferential formation of a chelating pentacoordinate complex rather than a tetracoordinate complex (Scheme 9).



Scheme 9

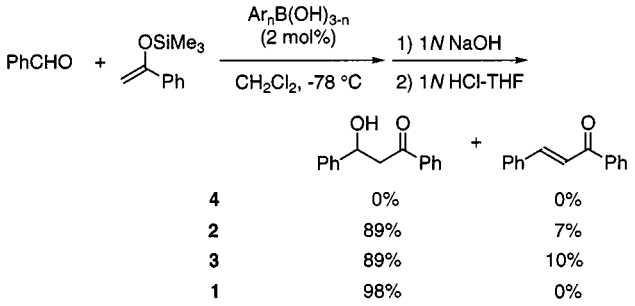
Transformations accompanying alkyl or hydride anion abstraction from Group-4 complexes by strong Brønsted or Lewis acids are currently of great interest since they are central to the activation and function of homogeneous single-site Ziegler−Natta catalysts based on metallocene and quasimetallocene frameworks. Surprisingly few Lewis acids react cleanly with metallocenes to afford soluble complexes with desirable catalytic activities, and still fewer afford rigorously characterized active species. Effective co-catalysts include Ph_3C^+ (with appropriate weakly coordinating counteranions), perfluoroarylboranes,[1] and MAO (methylalumoxane). Marks and his colleagues have reported that sterically encumbered (perfluoroaryl)borane-derived cationic complexes generally exhibit higher catalytic activity than their $MeB(C_6F_5)_3^-$ analogues.[9] Ethylene polymerization activities for eight $(Me_2Cp)2MCH3^+CH3B(C_6F_5)_2Ar^-$ complexes measured in toluene solution (25°C, 1 atm) showed a correlation with the type of metal used (Zr > Hf), as well as a substantial correlation with the triarylborane (Ar = C_6F_5 > 3,5-$F_2C_6H_3$ > Ph ≈ 3,5-$Me_2C_6H_3$) (Scheme 10).



Scheme 10

3. Diarylborinic Acids

Diarylborinic acids bearing electron-withdrawing aromatic groups are effective catalysts for Mukaiyama aldol condensation and the subsequent selective dehydration of β-hydroxy carbonyl compounds.[10] The catalytic activities of diarylborinic acids **2** and **3** in Mukaiyama aldol reactions are much higher than those of the corresponding arylboronic acids. It is noteworthy that small amounts of (*E*)-isomeric dehydrated products have been isolated in reactions catalyzed by diarylborinic acids **2** and **3**. In contrast, no dehydrated products have been isolated in the presence of **1**, despite its extremely high catalytic activity (Scheme 11).

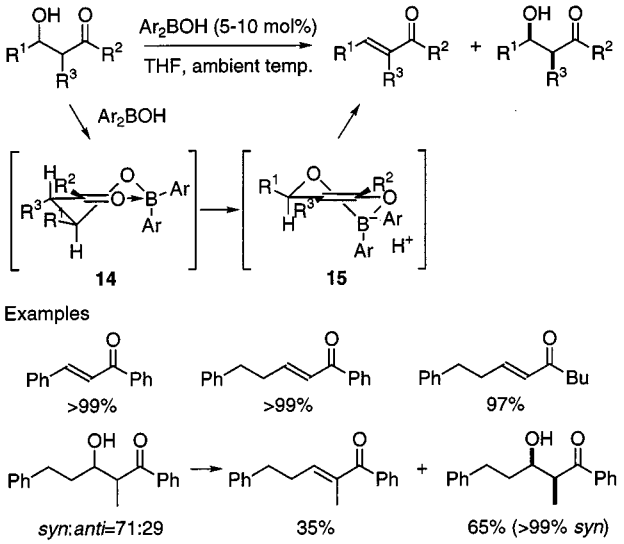


Scheme 11

Significant features of these active borinic acid catalysts are that they are strong Lewis acids and possess a hydroxy group at the boron atom. The dehydration is strongly favoured in THF. In most cases, the reaction proceeds smoothly, and α,β-enones are obtained in high yields as (*E*) isomers. In reactions of α-substituted β-hydroxy carbonyl compounds, α,β-enones are preferentially obtained from *anti*-aldols, while most of the *syn*-aldols are recovered. This dehydration thus represents a useful and convenient method for isolating pure *syn*-aldols from *syn*/*anti*-isomeric mixtures (Scheme 12).

The mechanism that we have proposed to explain borinic acid catalyzed dehydration is also depicted in Scheme 12. Reaction of the β-hydroxy function with the diarylborinic acid leads to a cyclic intermediate **14**, which should be susceptible to dehydration. Subsequent transformation to α,β-enones occurs via an enolate intermediate **15**, resulting from

selective abstraction of a pseudoaxial α-proton perpendicular to the carbonyl face. A cyclic intermediate formed from a *syn*-aldol and a diarylborinic acid would be thermodynamically less stable than **14**, thus dehydration to (*E*)-α,β-enones occurs selectively for *anti*-aldols.



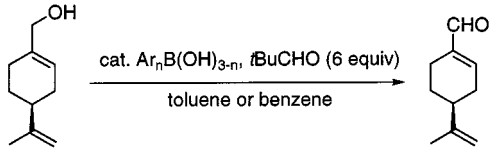
Scheme 12

Oppenauer (OPP) oxidation is one of the most useful methods for transforming secondary alcohols into ketones. Functional groups such as carbon−carbon double and triple bonds, aldehydes, amino groups, halogens, or sulfur-containing groups are not affected by this reaction, which is a great advantage over many oxygen-transferring oxidation processes. For the selective oxidation of allylic alcohols in the presence of saturated alcohols, activated MnO_2 is still one of the most useful reagents, despite the large amount required. We have found bis(pentafluorophenyl)borinic acid (**2**) to be a suitable OPP catalyst for primary and secondary allylic and benzylic alcohols.[11]

Borinic acid **2** is prepared from the known chloroborane $(C_6F_5)_2BCl$ by hydrolysis with 2 N aqueous HCl.[12] It is obtained as a white, microcrystalline solid, which can be readily handled in air, and is soluble in many organic solvents. Furthermore, **2** is a stronger Lewis acid than pentafluorophenylboronic acid (**4**), although it is weaker than **1**.[10]

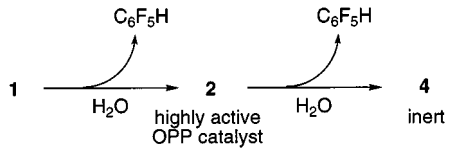
Several arylboron compounds bearing electron-withdrawing aromatic groups have been examined as catalysts for the OPP oxidation of (*S*)-perillyl alcohol (**16**). Catalysis has been carried out using 1−2 mol-% of the catalysts in the presence of 6 equiv. of pivalaldehyde as a hydride acceptor in toluene or benzene solution. Representative results are summarized in Table 1. The catalytic activity of borinic acid **2** is much higher than those of other diarylborinic acids. In contrast, **4** is inert (entry 1). The catalytic activities of these systems correlate with their Lewis acidities. Surprisingly, tris(pentafluorophenyl)borane (**1**) is also active as a catalyst for the present oxidations (entries 4 and 5). The latter result can be explained in terms of the in situ generation of borinic acid **2** from **1**, and that this is the actual active catalyst (Scheme 13). In fact, we have ascertained by ^{19}F-NMR analyses that **1** gradually undergoes conversion to **2** and pentafluorobenzene, and finally to **4**, under these reaction conditions. In general, triarylboranes and diarylborinic acids bearing electron-withdrawing substituents on their aryl groups are relatively stable in acidic aqueous solutions, but are unstable in neutral and basic aqueous solutions, undergoing conversion to arylboronic acids and arenes.

Table 1. The catalytic activities of arylboron compounds in the Oppenauer oxidation of **16**[a]



entry	catalyst (mol%)	conditions (°C, h)	yield (%)
1	**4** (2)	80, 3	0
2	**2** (1)	40, 3[b]	92
3	**2** (2)	80, 3	>99
4	**1** (1)	40, 3[b]	48
5	**1** (2)	80, 3	>99

[a] Unless otherwise noted, the oxidation of **16** (1 equiv., 0.25 M) was carried out in benzene in the presence of pivalaldehyde and a catalyst. − [b] The oxidation of **16** (1 equiv, 0.5 M) was carried out in toluene.



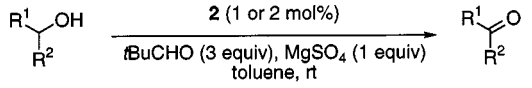
Scheme 13

The addition of magnesium sulfate efficiently prevents the inactivation of **2** and hence promotes the oxidation. Removal of water by the magnesium sulfate may prevent the hydrolysis of **2** and shift the equilibrium between the mixture of **2** and **16** and the mixture of the borinate and water in the direction of the borinate.

The generality and scope of the borinic acid **2** catalyzed OPP oxidation has been explored using various primary and secondary alcohols. The results are summarized in Table 2. All of the allylic alcohols used are seen to be oxidized to α,β-enals and α,β-enones in high yields (entries 1−5). Unfortunately, however, (*E*)/(*Z*) isomerization occurs between geranial and neral (entries 2 and 3). Primary and sterically less hindered secondary benzylic alcohols are oxidized reasonably efficiently in good yields (entries 6 and 7). The oxidation of propiophenone gives 1-phenylpropanol in somewhat lower yield (entry 8). Saturated alcohols are

slowly oxidized to the corresponding carbonyl compounds (entries 9 and 10).

Table 2. The OPP oxidation of various alcohols catalyzed by **2**

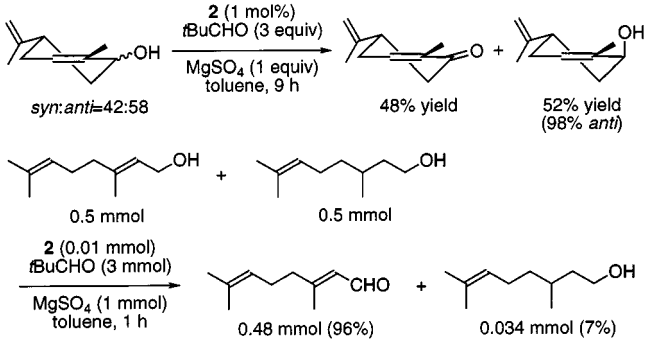


entry	alcohol	**2** (mol%)	time (h)	yield (%)
1[a]	$nC_{10}H_{21}$ OH	2	27	85
2	OH	1	3	95[b]
3	OH	1	3	98[c]
4	OH	1	3	>99
5	OH	1	2	>99
6[a]	OH	2	42	85
7	OH	2	5	90
8[d]	OH	2	5	20
9	$nC_{13}H_{27}OH$	2	6	<26[e]
10	tBu OH [f]	2	8.5	49[g]

[a] 4 equiv. of pivalaldehyde was used. – [b] (*E*)/(*Z*) = 99:1. – [c] (*E*)/(*Z*) = 72:28. – [d] 2 equiv. of $MgSO_4$ was used. – [e] Other products were included. – [f] *cis*/*trans* = 65.5:34.5. – [g] 51% of the recovered alcohols (*cis*/*trans* = 65.5:34.5).

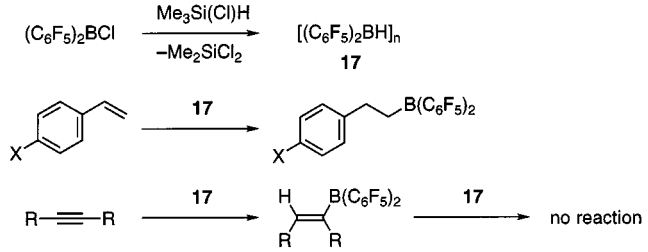
In the oxidation of a diastereomeric mixture of carveol (*syn*/*anti* = 42:58), the *syn*-alcohol is stereoselectively oxidized, while the *anti*-alcohol is recovered in 98% diastereomeric purity. This shows that the catalytic activity of **2** is very sensitive to steric hindrance in the alcohols. In oxidations of equimolar mixtures of geraniol and β-citronellol, geranial is obtained in 96% yield and most of the β-citronellol is recovered unchanged. The selective conversion of allylic alcohols in the presence of saturated alcohols is particularly noteworthy (Scheme 14).

Bis(pentafluorophenyl)borane (**17**) is a highly active hydroboration reagent towards a range of simple alkenes and alkynes. Addition of the olefin or alkyne to a suspension of the borane in benzene leads to rapid dissolution of the solid, and the reaction is complete within two minutes. Even sterically demanding olefins are hydroborated very rapidly, and the rates of hydroboration of methylcyclohexene and methylcyclopentene are identical. These observations are in marked contrast to what is found in reactions



Scheme 14

employing the common hydroboration reagent 9-BBN, which, under identical conditions, require several hours to reach completion with these substrates. The only substrates that do not react rapidly with **17** are those bearing a $B(C_6F_5)_2$ substituent, which apparently deactivates the double bond towards subsequent hydroboration. In addition to the convenience of high rates, **17** offers comparable or better regio- and chemoselectivity compared with other hydroboration reagents (Scheme 15).[13]



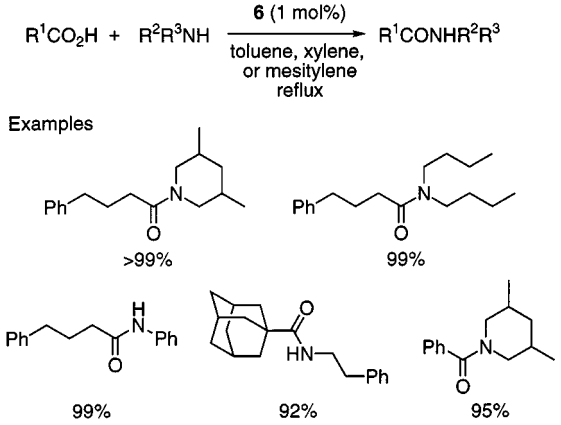
Scheme 15

4. Arylboronic Acids

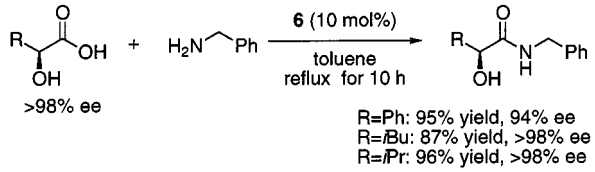
There are several different routes to carboxamides. In most cases, a carboxylic acid is converted to a more reactive intermediate, e.g. an acid chloride, which is then allowed to react with an amine. For practical reasons, it is preferable to form the reactive intermediate in situ. We have found that arylboronic acids bearing electron-withdrawing aromatic groups, e.g. 3,4,5-trifluorophenylboronic acid (**6**) and 3,5-bis(trifluoromethyl)phenylboronic acid (**5**), act as highly efficient catalysts in the amidation of carboxylic acids with amines.[14] The catalysts are useful in the reactions of both primary and secondary amines with various carboxylic acids (Scheme 16).

The catalytic amidation of optically active aliphatic α-hydroxy carboxylic acids with benzylamine proceeds with no measurable loss (< 2%) of enantiomeric purity under reflux conditions in toluene (Scheme 17).

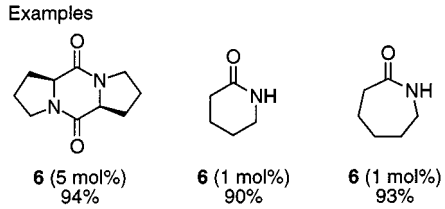
Most amino acids are barely soluble in non-aqueous solvents. Nevertheless, their lactams can be prepared by the present technique under heterogeneous conditions. For example, when 6-aminocaproic acid and 1 mol-% of boron catalyst **6** are suspended in refluxing xylene, the solid slowly



Scheme 16



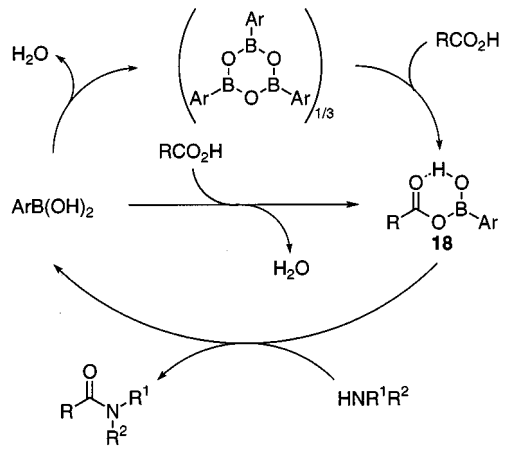
Scheme 17



Scheme 18

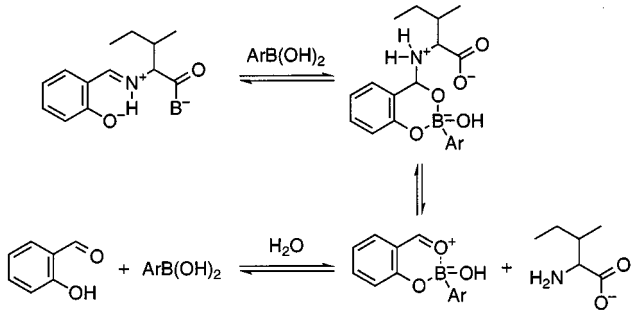
dissolves and caprolactam is formed in 93% yield (Scheme 18).

The mechanism that we have proposed to explain boronic acid catalyzed amidation is depicted in Scheme 19. In general, arylboronic acids contain varying amounts of cyclic trimeric anhydrides (boroxines). The rate-determining step is the generation of **18**.



Scheme 19

The hydrolysis of salicylaldehyde imines is catalyzed by boric acid, substituted arylboronic acids, and diphenylborinic acid. The effect of various substituted phenylboronic acids on the rate of hydrolysis has been studied at pH = 6.0 by Rao and Philipp.[15] The second-order rate constants, k_{cat}/K_m, are higher in the case of phenylboronic acids bearing electron-withdrawing substituents, compared to those measured with phenylboronic acids bearing electron-donating substituents. The highest value obtained was 2.38 $M^{-1}s^{-1}$, using 3,5-bis(trifluoromethyl)phenylboronic acid (**5**), while the lowest value was 0.09 $M^{-1}s^{-1}$, obtained with 4-tolylboronic acid. Phenylboronic acids bearing electron-withdrawing substituents bind the imine more tightly than do boronic acids bearing electron-donating substituents. The effects of boronic acid, phenylboronic acid, and diphenylborinic acid on the hydrolysis of the same imine were also studied at pH = 6.0. Phenylboronic acid and diphenylborinic acid bind the imine more strongly than boronic acid by factors of almost 25 and 4350, respectively (Scheme 20).

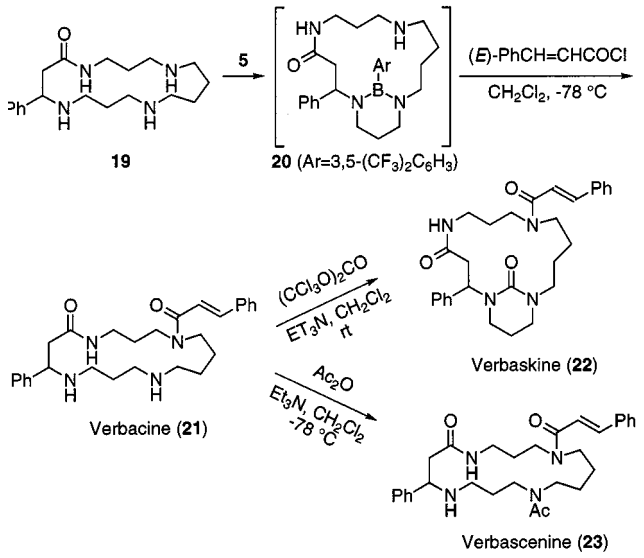


Scheme 20

3,5-Bis(trifluoromethyl)phenylboronic acid (**5**) is amenable to the regioselective protection of amino groups.[16] For example, the synthesis of verbacine (**21**) has been accomplished by addition of cinnamoyl chloride to a 1:1 mixture of **19** and **5** in dichloromethane to give **21** as the major product in 53% yield, together with recovered **19**, the monocinnamamide acylated at N-11 of **19**, and the dicinnamamide acylated at both N-6 and N-11. The acylation of **19** with acyl chloride or acid anhydride in the absence of boronic acid gives only the dicinnamamide. The efficiency of the present regioselective acylation can, therefore, be attributed to the stability of a 1,3-diaza-2-boracyclohexane unit. Thus, the presumed six-membered cyclic intermediate **20**, generated by complexation of **19** with **5** at N-11 and N-15, can reasonably be expected to undergo acylation with the free amino group at N-6. Verbacine (**21**) is readily transformed in good yield to verbaskine (**22**). Moreover, **21** can be converted to verbacenine (**23**) in almost quantitative yield by selective acetylation at N-11.

5. Chiral Arylboron Catalysts

Enantioselective Mukaiyama aldol and Sakurai−Hosomi allylation reactions catalyzed by chiral Lewis acid are

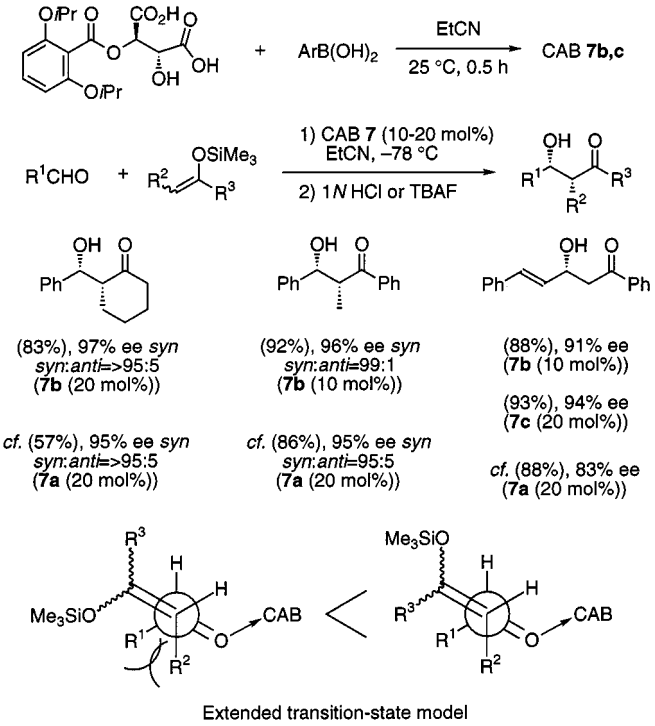


Scheme 21

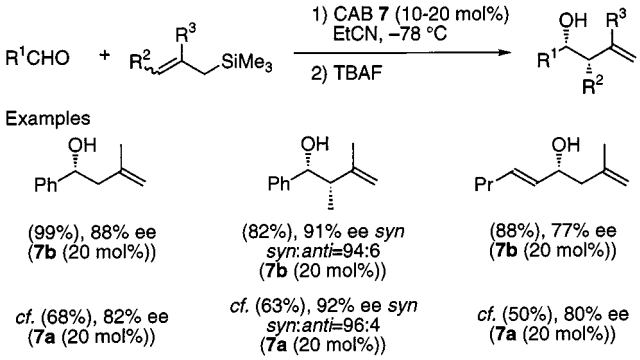
currently of great interest because of their utility for the introduction of asymmetric centers and functional groups.

We have reported chiral(acyloxy)borane (CAB) **7a** (Ar = H) to be an excellent catalyst (20 mol-%) for the enantio- and diastereoselective Mukaiyama condensation of simple enol silyl ethers with various aldehydes.[17a] The rate of the aldol reaction is accelerated without reducing the enantioselectivity by using 10−20 mol-% of **7b** [Ar = 3,5-$(CF_3)_2C_6H_4$].[17c] The enantioselectivity is increased without reducing the chemical yield by using 20 mol-% of **7c** [Ar = 2-$(PhO)C_6H_4$].[17c] A further aldol-type reaction of ketene silyl acetals derived from phenyl esters with achiral aldehydes proceeds smoothly with **7a**, furnishing *syn*-β-hydroxy esters with high optical purity.[17b] Regardless of the stereochemistry of the enol silyl ethers, *syn*-aldols are obtained highly selectively through the acyclic extended transition-state mechanism. Judging from the configurations of the products, CAB **7** (from natural tartaric acid) should effectively cover the *si* face of the carbonyl group upon coordination (Scheme 22).

We have also found CAB **7a** to have a powerful catalytic activity in the Sakurai−Hosomi allylation reaction of aldehydes, leading to homoallylic alcohols with excellent enantiomeric excesses (Scheme 23).[18a] Alkyl substitution at the olefin moiety of the allylsilanes increases the reactivity, permitting a lower reaction temperature and leading to improved asymmetric induction. γ-Alkylated allylsilanes exhibit excellent diastereo- and enantioselectivities, affording *syn*-homoallylic alcohols of even higher optical purity. Regardless of the geometry of the starting allylsilane, the predominant isomer produced in this reaction is of *syn* configuration. The preferred relative and absolute configurations observed for the adducts can be predicted on the basis of an extended transition-state model similar to that for the CAB **7** catalyzed aldol reaction.[17] The boron substituent of **7** has a strong influence on the chemical yield and the enantiomeric excess of the allylation adduct, with the 3,5-bis(trifluoromethyl)phenyl group being most effective.[18b]



Scheme 22

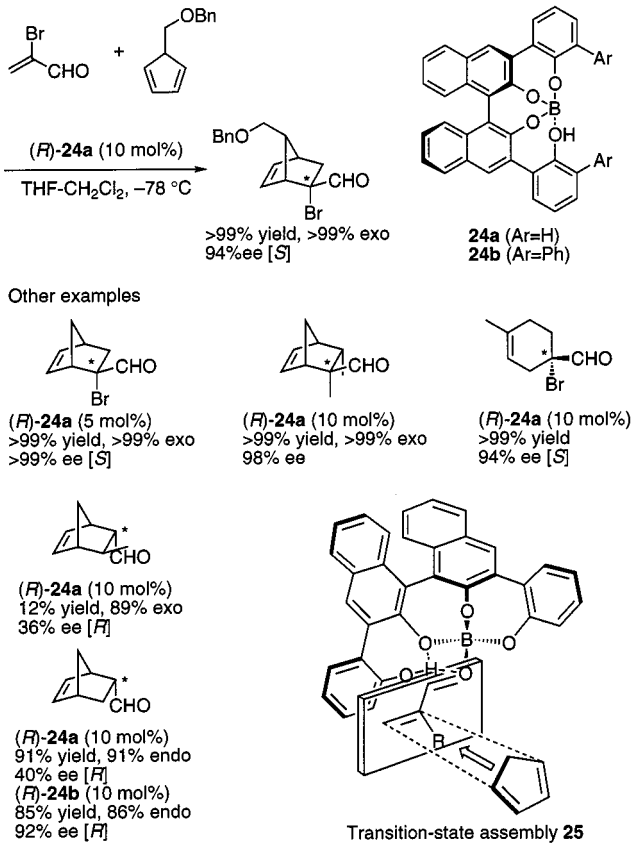


Scheme 23

The asymmetric Diels−Alder reaction is currently of great interest because of its potential to introduce several asymmetric centers simultaneously during carbon−carbon bond formation.

Use of Brønsted acid assisted chiral Lewis acids (BLAs) **24** has led to high selectivity through the double effect of intramolecular hydrogen-bonding interaction and attractive π-π donor-acceptor interaction in the transition state (Scheme 24).[19a,19c,19d] Extremely high enantioselectivity (> 99 to 92% *ee*) and *exo* selectivity (> 99 to 97% *exo*) has been realized for cycloadditions of α-substituted α,β-enals to dienes. The absolute stereopreference of the reaction can be easily understood in terms of the most favorable transition-state assembly **25**. Coordination of the proton of the 2-hydroxyphenyl group to the oxygen atom of the adjacent B−O bond in complex **25** plays an important role in asymmetric induction; this hydrogen-bonding interaction via a

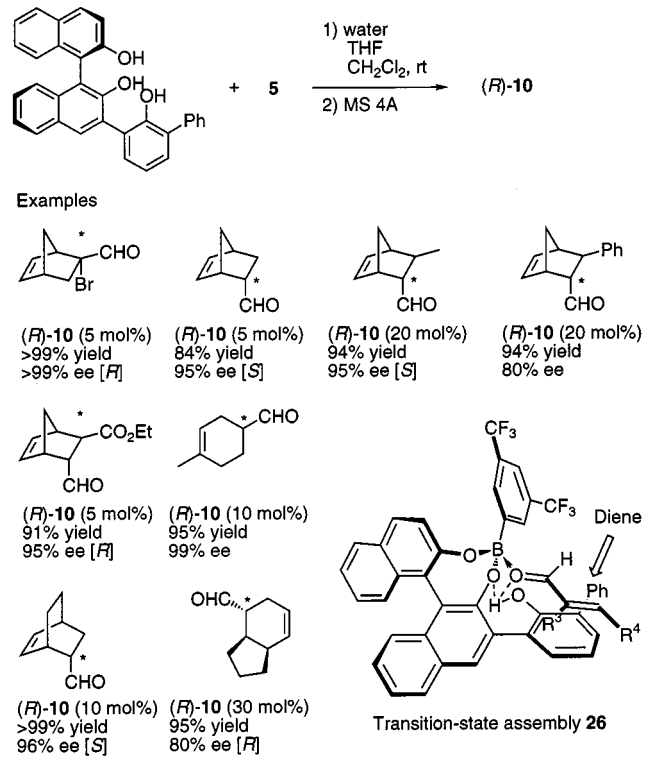
Brønsted acid enhances both the Lewis acidity of the boron atom and the π-basicity of the phenoxy moiety.



Scheme 24

BLA **24a** is one of the best catalysts for the enantio- and *exo*-selective cycloaddition of α-substituted α,β-enals to highly reactive dienes such as cyclopentadiene. However, the corresponding reactions of α-unsubstituted α,β-enals such as acrolein and crotonaldehyde exhibit low enantioselectivity and/or reactivity. The range of dienophiles applicable for less reactive dienes is rather limited. The use of arylboronic acids bearing electron-withdrawing substituents, such as **5**, in the preparation of BLAs greatly enhances their catalytic activity and asymmetry-inducing ability. We have developed a more practical BLA, **10**, which shows greater catalytic activity in the enantioselective cycloaddition of both α-substituted and α-unsubstituted α,β-enals to various dienes (Scheme 25).[19b–19d] It is noteworthy that the presence of a Brønsted acid in BLA catalysts clearly accelerates the cycloaddition. The high enantioselectivity and stereochemical results attained in this reaction can be understood in terms of the transition-state model **26**.

BLA **10** is prepared from a chiral triol and monomeric **5** in the presence of powdered 4-Å molecular sieves in dichloromethane/THF. Although molecular sieves are essential for dehydration, they may also facilitate the aryloxy ligand exchange reaction. Arylboronic acids usually exist as mixtures of the monomer, trimer, and oligomers. To prevent oligomerization of **5** in preparing the catalyst, THF is needed as an additive (Figure 2).[19d]



Scheme 25

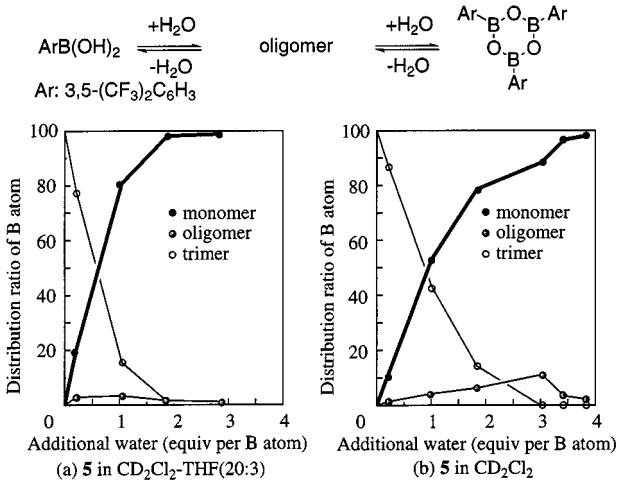
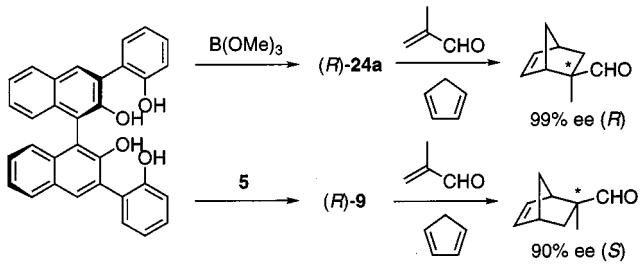


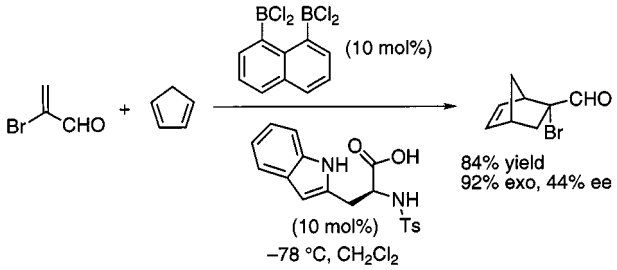
Figure 2. Plot of the distribution ratio of boron atom in a solution of **5** versus additional water

The absolute stereopreference observed in the Diels–Alder reaction catalyzed by (*R*)-**10** is opposite to that found with catalysis by (*R*)-**24a**. This implies that the presence of the 3,5-bis(trifluoromethyl)phenyl group greatly affects the asymmetric induction of BLAs prepared from chiral ligands of the same absolute configuration. In fact, the use of BLAs **24a** and **9**, prepared from the same chiral tetraol, in Diels–Alder reactions leads to the opposite enantiomers with high selectivity (Scheme 26).[19d]

Diarylboronic acids are stronger Lewis acids than the corresponding boronic acids.[20] We have designed BLA **11**, which is prepared from **3** and a chiral triol in dichlorometh-

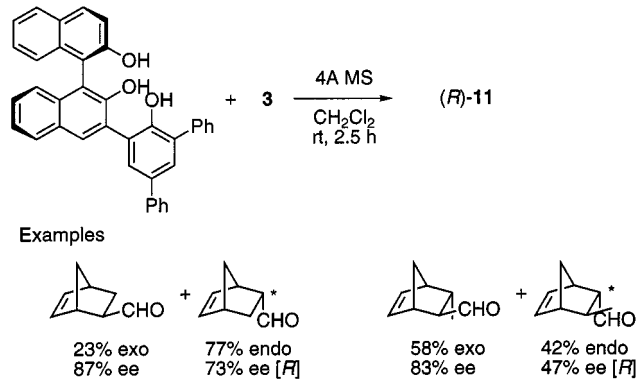


Scheme 26



Scheme 28

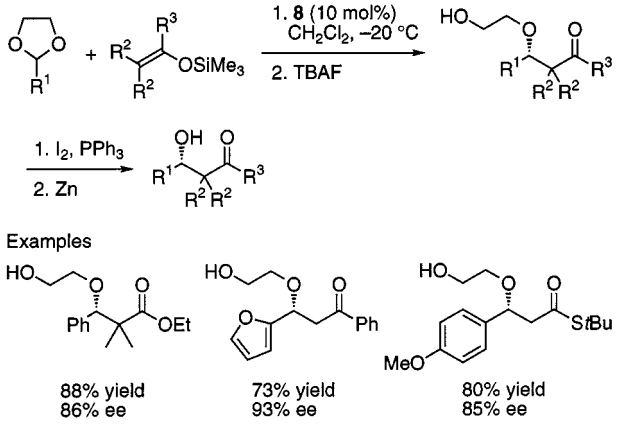
ane in the presence of activated powdered 4-Å molecular sieves at room temperature.[19d] Diels–Alder reaction of cyclopentadiene with various α,β-enals proceeds smoothly in the presence of 5 mol-% of (*R*)-**11**, and good enantioselectivities have been observed for the *exo* adducts. The steric bulk of the aryl groups of the diarylborinic acid is important for a high level of asymmetric induction, because BLAs formed from diarylborinic acids and chiral ligands have a conformationally flexible structure (Scheme 27). Arylboronic acid **5** has the advantage of being strongly Lewis acidic and producing a bidentate complex with a chiral ligand. Diarylborinic acid **3**, on the other hand, is not suited for the construction of a rigid monodentate complex.



Scheme 27

Asymmetric catalysis by bimetallic catalysts is currently a research field of great interest. Investigations into the interactions between bidentate Lewis acids and carbonyl groups are rare.[21a] Only one example of such an asymmetric Diels–Alder reaction, catalyzed by a 1:1 complex of *N*-tosyltryptophan[22] and 1,8-naphthalenediylbis(dichloroborane), where the two Lewis-acidic sites work in a cooperative manner, has been reported by Reilly and Oh (Scheme 28).[21b]

Harada and his colleagues have reported that arylboron complex **8**, derived from *N*-tosyl-(α*S*,β*R*)-β-methyltryptophan[22] and dibromo(*p*-chlorophenyl)borane, serves as an excellent catalyst for enantioselective ring-cleavage reactions of 2-substituted 1,3-dioxolanes with enol silyl ethers.[23c] Interestingly, chiral boron complexes prepared by the reaction of sulfonamide ligands with $BH_3 \cdot THF$ do not exhibit appreciable catalytic activity.[23a,23b] Successful results have been obtained in the ring cleavage of 1,3-dioxolanes with both aryl and alkenyl groups at the 2-position. The reaction of 2-alkyl derivatives, however, is very sluggish under these conditions. 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 29).



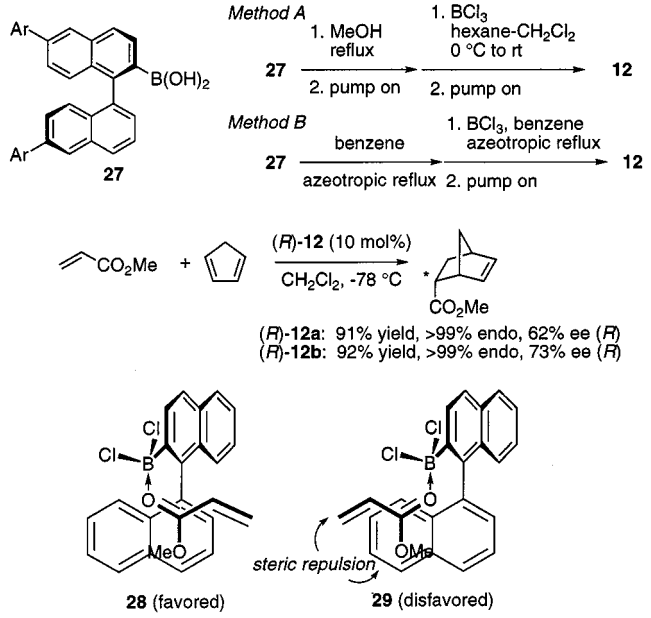
Scheme 29

Chiral alkyldihaloboranes are among the most powerful of chiral Lewis acids. However, since these compounds are often prone to facile decomposition to alkanes or alkenes by protonolysis or β-hydride elimination, it is difficult to recover them quantitatively as alkylboronic acids. Aryldichloroboranes are somewhat more stable and can be reused as the corresponding boronic acids. We have developed chiral aryldichloroboranes **12** bearing binaphthyl skeletons with axial chirality as asymmetric catalysts for the Diels–Alder reaction of dienes with α,β-unsaturated esters (Scheme 30).[24]

(*R*)-2-Dihydroxyboryl-1,1′-binaphthyl (**27**) can be synthesized in several steps from (*R*)-binaphthol.[24] The synthesis of racemic **27a** has also been reported by Kaufmann and co-workers.[25] Conversion of (*R*)-**27** to (*R*)-**12** has been achieved by two different methods: one by exchange of the methanol boronate with trichloroborane (*Method A*), and the other by exchange of the anhydrides of boronic acids with trichloroborane (*Method B*). The latter procedure is simpler and more convenient (Scheme 30).

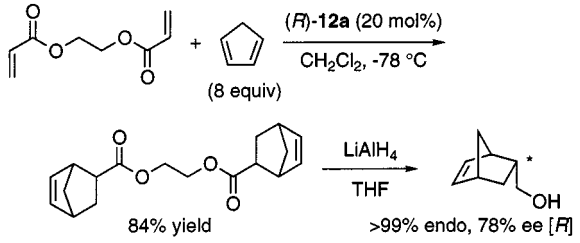
The Diels–Alder reaction of cyclopentadiene with methyl acrylate proceeds smoothly at −78°C in the presence of 10 mol-% of catalyst (*R*)-**12**, to give the *endo* adduct in high yield with > 99% diastereoselectivity. Catalyst **12b** showed the highest asymmetric induction, but even this is insufficient. The absolute configuration of the major *endo* adduct is consistent with the naphthyl moiety shielding the

re face of the coordinated methyl acrylate, leading to attack by cyclopentasidene at the *si* face, as shown in **28**. Coordination of the methyl acrylate with the *re* face exposed, as shown in **29**, is unfavorable due to steric interaction between the alkene and the naphthyl moiety. Increased enantioselectivity obtained using **12b** can be easily understood in terms of steric repulsion between the alkene and mesityl groups (Scheme 30).



Scheme 30

It is noteworthy that the reaction of ethylene diacrylate, which is commercially available, followed by reduction with lithium aluminum hydride, gives *endo*-5-norbornene-2-methanol with 78% *ee*. Although it is not clear as to why the selectivities are increased by the link between the dienophiles, similar effects are expected for other asymmetric reactions (Scheme 31).



Scheme 31

6. Conclusions

Arylboron compounds bearing electron-withdrawing substituents, such as triarylboranes, diarylborinic acids, and arylboronic acids, are useful as air-stable Lewis acid catalysts in performing various organic transformations, and as significant components of chiral acid catalysts such as CAB and BLA. In particular, the potential of tris(pentafluorophenyl)borane (**1**) as a Lewis acid catalyst has increased markedly since our initial study.[3a] Despite these impressive recent advances, many unsolved problems remain. These include limitations with regard to the scope of reactions and frequently encountered practical problems associated with catalyst preparation and use, especially on a large scale. Nonetheless, continued exploratory research on the catalytic applications of arylboron compounds and on the development of chiral arylboron compounds bearing electron-withdrawing aromatic groups as air-stable and reusable asymmetric catalysts can be expected to provide powerful and practical methods for carrying out acid-catalyzed organic transformations.

Acknowledgments

We thank our past and present coworkers, especially Drs. Q. Gao, N. Hanaki, and H. Kurihara, for their help.

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Received September 9, 1998
[O98409]