Enantioselective Diels–Alder Reaction Induced by Chiral Supramolecular Lewis Acid Catalysts Based on CN···B and PO···B Coordination Bonds

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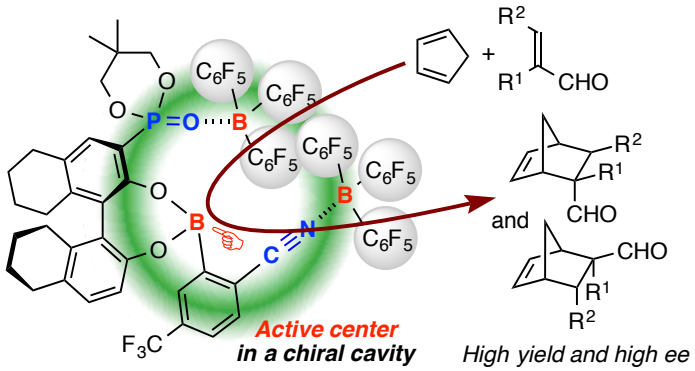

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Abstract Chiral supramolecular boron Lewis acid catalysts were developed with the use of chiral 3-phosphoryl-BINOLs, 2-cyanophenylboronic acids, and tris(pentafluorophenyl)borane based on CN···B and PO···B coordination bonds. In particular, coordinated tris(pentafluorophenyl)boranes can increase the Lewis acidity of the active center based on the Lewis acid-assisted Lewis acid catalyst system. A possible cavity in these catalysts was highly suitable for some probe Diels–Alder reactions of acroleins with cyclic and acyclic dienes, and the corresponding adducts were obtained in good to high yields with high enantioselectivities.

Key words supramolecular catalyst, chiral cavity, Diels–Alder reaction, Lewis acid, phosphoryl moiety, cyano moiety

Making the most of coordinative interactions is the principal approach used to construct conformationally flexible complexes based on supramolecular chemistry, as reflected by early work by Lehn.[1,2] If some small molecules are added based on acid–base chemistry,[3] tailor-made chiral supramolecular catalysts can be fine-tuned *in situ* without producing any corresponding waste. In this regard, we previously developed chiral supramolecular Lewis acid catalysts such as **1** (Figure 1a), which was highly effective for enantioselective Diels–Alder reactions with anomalous *endo*/*exo*-selectivities.[4,5,6] In catalyst **1**, two bulky tris(pentafluorophenyl)boranes ($B(C_6F_5)_3$) are coordinated to phosphoryl (PO) groups[7,8], and provide a deep chiral cavity. Moreover, the coordinated tris(pentafluorophenyl)boranes can increase the Lewis acidity of the active boron center based on a Lewis acid-assisted Lewis acid (LLA)[9] catalyst system. In this context, we envisioned that we might be able to use CN···$B(C_6F_5)_3$[10] as another useful coordination bond to generate a new type of chiral supramolecular catalyst. In particular, the CN moiety is an attractive option at the *ortho*-position of arylboronic acids, which would exert both steric and electron-withdrawing effects on the active boron center (Figure 1b). We report here chiral Lewis acid catalysts **2** based on CN···B and PO···B coordination bonds for the enantioselective Diels–Alder reaction of various acroleins with cyclic and acyclic dienes.

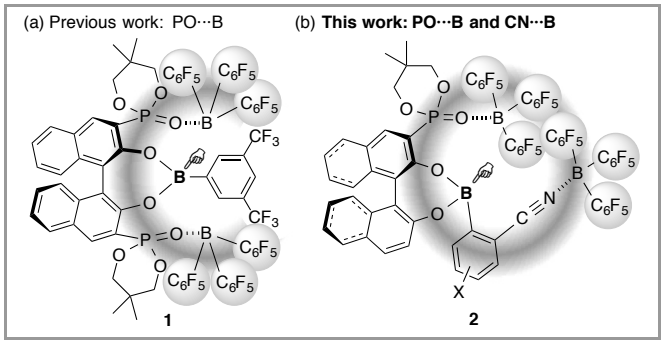
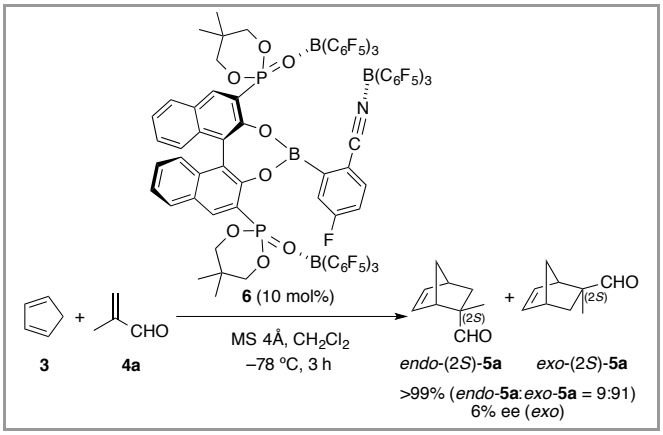


Figure 1 Design of chiral supramolecular catalysts with coordination bonds between PO···$B(C_6F_5)_3$ and CN···$B(C_6F_5)_3$

First, we examined the Diels–Alder reaction of methacrolein **4a** with cyclopentadiene **3** in dichloromethane[11] at –78 °C in the presence of chiral supramolecular catalyst **6** (10 mol%). Catalyst **6** was a simple extension of catalyst **1**, and was prepared *in situ* from (*R*)-3,3'-bis(phosphoryl)-BINOL (BINOL = 1,1'-bi-2-naphthol), 2-cyano-5-fluorophenylboronic acid, and $B(C_6F_5)_3$ (Scheme 1). Unfortunately, however, the enantioselectivity of the corresponding product *exo*-(2*S*)-**5a** was low (6% ee).

To avoid the excessive conflict of three bulky tris(pentafluorophenyl)boranes, we next used (*R*)-3-phosphoryl-BINOL in place of (*R*)-3,3'-bis(phosphoryl)-BINOL (Figure 2). As a result, the enantioselectivity of **5a** was dramatically improved: **5a** was obtained in 93% yield with 89% ee when we used catalyst **2a**. Replacement of the binaphthyl skeleton (**2a**) with an H_8-binaphthyl skeleton (**2b**) slightly improved the enantioselectivity (91% ee) of **5a**. Moreover, replacement of the 5-F moiety in the arylboronic acid part (**2b**) with a 5-CF_3 moiety (**2c**) improved the enantioselectivity (98%

ee) of **5a**.[11] In a control experiment, the use of catalyst **2d** with a 4-CF_3 moiety was slightly less effective than **2c** in terms of the enantioselectivity. Moreover, both catalyst **2e** with no substituents and catalyst **2f** with a 5-CH_3 moiety were much less effective than **2c**.



Scheme 1 Diels–Alder reaction of methacrolein **4a** with cyclopentadiene **3** with the use of chiral supramolecular catalyst **6**

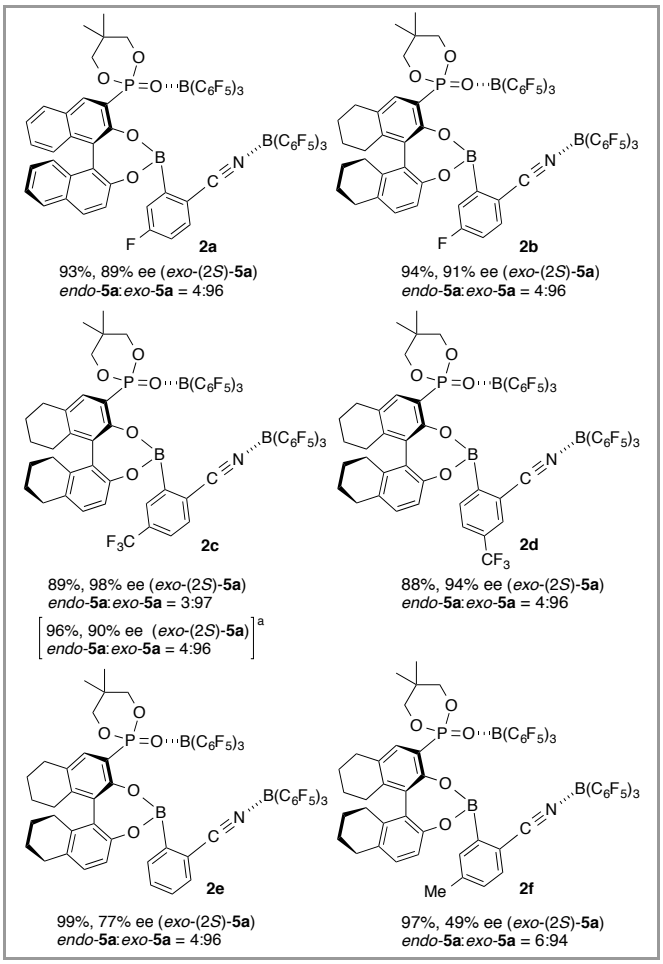


Figure 2 Chiral supramolecular catalysts **2** for the Diels–Alder reaction of **4a** with **3**. The reaction was carried out with the use of **2** (10 mol%) in dichloromethane with MS 4Å at –78 °C for 3 h. [[a] The reaction was carried out with the use of 10 mol% of **2c** and an additional 5 mol% of $B(C_6F_5)_3$.]

We next examined the effect of a bulky 3-substituent in the binaphthyl skeleton of the catalysts. In place of PO···$B(C_6F_5)_3$ in catalyst **2c**, we used a bulky electron-withdrawing aryl moiety, 3,5-(3,5-$(CF_3)_2C_6H_3)_2C_6H_3$, in catalyst **7a** (Figure 3). As a result, catalyst **7a** was also effective in the reaction of **4a** with **3**, and **5a** was obtained in 96% yield with 84% ee. In sharp contrast, catalyst **7b** with a less bulky 3,5-$(CF_3)_2C_6H_3$ moiety was less effective at inducing enantioselectivity, and **5a** was obtained with 50% ee. Overall, when we compared **2c** and **7a**, the enantioselectivity of **5a** with the use of **2c** (98% ee) was higher than that with **7a** (84% ee). Moreover, the catalytic activity of **2c** might be higher than that of **7a**, since the enantioselectivity with the use of **2c** in the presence of an additional 5 mol% of $B(C_6F_5)_3$ was still high (90% ee), unlike with the use of **7a** with an additional 5 mol% of $B(C_6F_5)_3$ (66% ee) (see the brackets a in Figures 2 and 3).

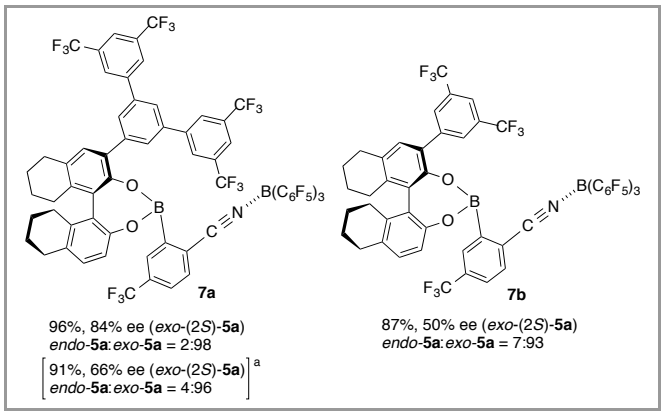
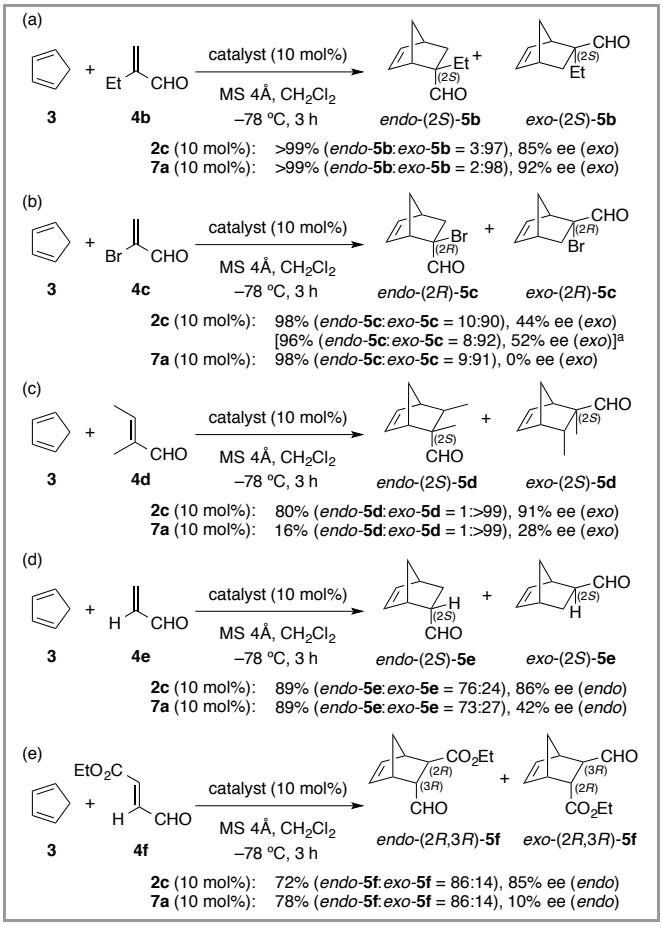


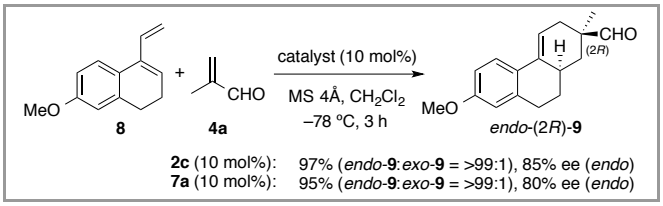
Figure 3 Chiral supramolecular catalysts **7** for the Diels–Alder reaction of **4a** with **3** [[a] The reaction was carried out with the use of 10 mol% of **7a** and an additional 5 mol% of $B(C_6F_5)_3$.]

We next investigated the scope of substrates with the use of catalysts **2c** and **7a** (Scheme 2). α-Substituted acroleins, such as α-ethylacrolein **4b**, α-bromoacrolein **4c**, and tiglic aldehyde **4d**, were examined. As a result, catalyst **7a** was as effective as catalyst **2c** for the reaction of **4b** with **3** (Scheme 2a). However, for the reactions of **4c** and **4d** with **3**, catalyst **7a** was less effective than catalyst **2c** (Schemes 2b and 2c). Compound **4c** was extremely reactive, and enantioselectivity was low (44% ee) at –78 °C. However, the use of catalyst **2c** at –98 °C improved the enantioselectivity up to 52% ee. Catalyst **2c** was also more effective than catalyst **7a** in the reactions of α-non-substituted acroleins, such as acrolein **4e** and ethyl *trans*-4-oxo-2-butenoate **4f** (Schemes 2d and 2e). Moreover, acyclic diene **8** was used in place of cyclopentadiene **3** (Scheme 3). As a result, *endo*-**9** was obtained as a sole product in 97% yield with 85% ee when we used catalyst **2c**, whereas catalyst **7a** gave *endo*-**9** in 95% yield with 80% ee. Overall, in these Diels–Alder reactions of **4a–f** with the use of catalyst **2c**, anomalous *endo*/*exo*-selectivities were not observed, unlike with the use of our previous catalyst **1**.[4] Although catalyst **2c** might have the chiral cavity (see Figure 6), the structure might be too flexible to control anomalous *endo*/*exo*-selectivities. Therefore, moderately rigid conformationally flexible supramolecular catalyst such as **1** might be essential to induce anomalous *endo*/*exo*-selectivities. Instead, more flexible catalyst **2c** showed a relatively wide generality for the substrates to induce

the high enantioselectivities, whereas more rigid catalyst **1** showed the substrate specificity to induce the high enantioselectivities with anomalous *endo*/*exo*-selectivities.



Scheme 2 Generality of acroleins **4** with the use of chiral supramolecular catalysts **2c** and **7a** [a Reaction was carried out at –98 °C for 3 h.]



Scheme 3 Diels–Alder reaction of methacrolein **4a** with acyclic diene **8** with the use of chiral supramolecular catalysts **2c** and **7a**

To confirm the roles of the main parts in the optimized supramolecular catalysts **2c**[12] and **7a**, we performed control experiments with the use of simplified model compounds. First, we investigated the effect of the CN···$B(C_6F_5)_3$ moiety in **2c** and **7a**, and the reaction of **4a** with **3** was conducted with the use of catalysts **10** and **11** (Figure 4). As a result, low and no catalytic reactivities were observed, respectively.[13] Moreover, **5a** was produced as a racemate with the use of catalyst **10**. Therefore, the CN···$B(C_6F_5)_3$ moiety in **2c** and **7a** should be essential for providing the products in high yields with high enantioselectivities in the Diels–Alder reactions.[14]

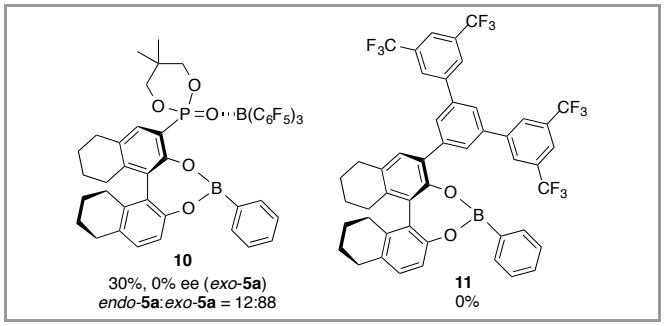
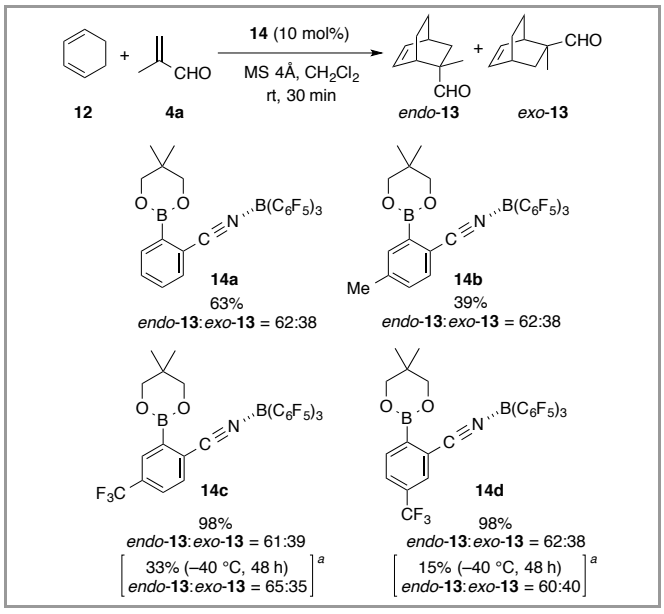


Figure 4 Control experiments to examine the effect of CN···$B(C_6F_5)_3$ on the yield and enantioselectivity in the reaction of **3** with **4a**. The reaction was carried out with the use of **10** or **11** (10 mol%) in dichloromethane with MS 4Å at –78 °C for 3 h.

The next fundamental control experiments were performed with the use of achiral supramolecular catalysts **14a–d** with 4- or 5-substituted arylboronic acids in the reaction of **4a** with poorly reactive cyclohexadiene **12** at room temperature for 30 min (Scheme 4).[15] As a result, electron-withdrawing 5-CF_3- and 4-CF_3-substituted catalysts **14c** and **14d** showed high yields, whereas non-substituted catalyst **14a** and electron-donating 5-Me-substituted catalyst **14b** showed much lower yields. Therefore, an electron-withdrawing group such as CF_3 might be effective for producing high yields in the Diels–Alder reactions. Moreover, the further control experiments at –40 °C for 48 h demonstrated that catalyst **14c** showed higher activity than catalyst **14d** (see the brackets a in Scheme 4).



Scheme 4 Diels–Alder reaction of methacrolein **4a** with cyclohexadiene **12** catalyzed by achiral supramolecular catalysts **14**

Additional control experiments involved ^1H and ^{13}C NMR and analyses (CD_2Cl_2 at –40 °C) with the use of achiral supramolecular catalysts **14a–d** and methacrolein **4a** (Figure 5).[16] We did not observe any shifts (Δ) of the formyl proton (9.50 ppm) or the formyl carbon (195.3 ppm) of **4a** when we used 2-boryl-benzonitrile in the absence of $B(C_6F_5)_3$ (Figure 5b).[17] In contrast, when we used complexes **14a** and **14b**, a slight upfield shift was observed of the formyl proton (Δ –0.02

to –0.04 ppm) and a slight downfield shift was observed of the formyl carbon (Δ +0.3 to +0.5 ppm) (Figures 5c and 5d). Moreover, when we used complex **14c**, which has an electron-withdrawing 5-CF_3 moiety, a large upfield shift was observed of the formyl proton (Δ –0.14 ppm) and a large downfield shift was observed of the formyl carbon (Δ +1.6 ppm) (Figure 5e). Similar shifts (^{1}H: Δ –0.14 ppm; ^{13}C: Δ +0.8 ppm) were observed for **14d**, which has an electron-withdrawing 4-CF_3 moiety (Figure 5f). These results might indicate that methacrolein **4a** coordinates to complex **14c** better than complexes **14a**, **14b**, and **14d**. Overall, **4a** would be more activated with **14c** than with **14a**, **14b**, and **14d**, and this observation agrees well with the reaction yields as shown in Scheme 4. Moreover, the enantioselectivities in the reaction of **4a** with **3** in the presence of catalysts **2c**–**f** in Figure 2 might be rationalized in part, since stronger Lewis acids would activate the substrate in shorter distance with low electronic energies and would help enantio-face discrimination of the substrate better than weaker Lewis acids.[18]

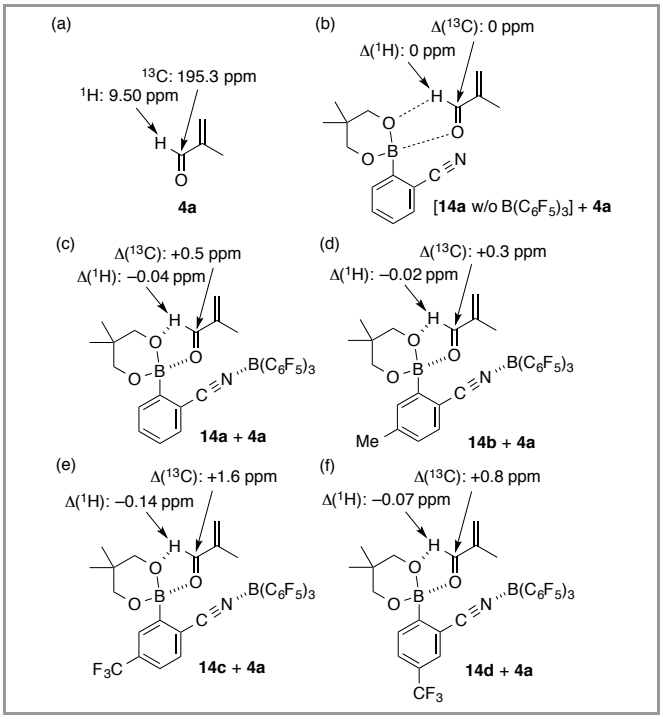


Figure 5 ^{1}H and ^{13}C NMR analysis of achiral complexes **14** with methacrolein **4a** in CD_2Cl_2 at –40 °C.

Finally, we considered possible transition-state (TS) structures of the Diels–Alder reaction of **4a** with **3** by the use of supramolecular catalysts **2c** and **7a** (Figure 6). Based on C_1-symmetric (*R*)-3-R-BINOLs, two major intermediates with **4a** are shown in Figures 6a and 6b. The substituent R of (*R*)-3-R-BINOL is located far from the Ar moiety of arylboronic acid in Figure 6a, while the substituent R is located close to the Ar moiety in Figure 6b. Due to steric reasons, the intermediate shown in Figure 6a might be more favored than that in Figure 6b. Based on this hypothesis, TS-**15** in Figure 6c might be a favored TS for catalyst **2c**. TS-**15** has a *syn*-conformation for two bulky tris(pentafluorophenyl)boranes,[19] which would provide a chiral cavity around the active boron Lewis acid center. On the other hand, much less bulky catalyst **7a** might be much more conformationally flexible than catalyst **2c**, and similar TS-**16** in Figure 6d might be a favored TS. Consequently, a possible chiral cavity in TS-**16** with **7a** might be less effective than TS-**15** with **2c**, which could explain why catalyst **2c** induced generally higher enantioselectivity than catalyst **7a**. Via a *re*-face attack to **4a**, which is activated due to non-covalent inrereactions[17], *exo*-(2*S*)-**5a** might be reasonably provided from TS-**15** and TS-**16**. More information based on experimental and theoretical studies will be needed to discuss further possible structures.[20]

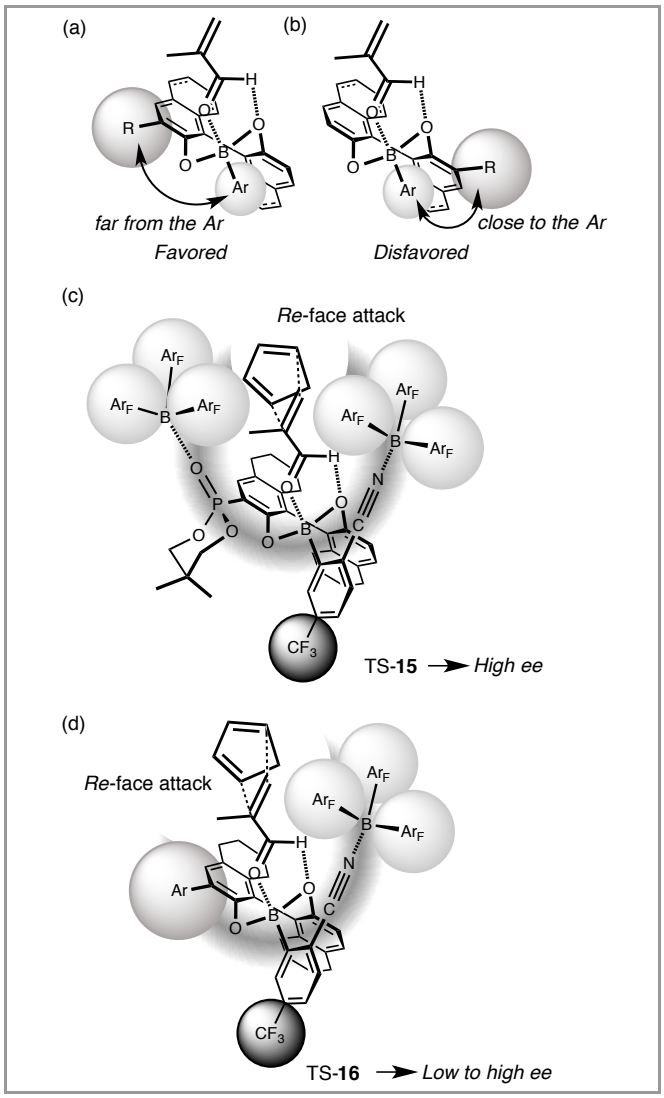


Figure 6 Possible structures and chiral cavities of supramolecular catalysts in transition states (Ar_F = C_6F_5) [(a) Favored intermediate with R far from the Ar moiety. (b) Disfavored intermediate with R close to the Ar moiety. (c) Possible TS-**15** with catalyst **2c**. (d) Possible TS-**16** with catalyst **7a**]

In summary, we have developed conformationally flexible chiral supramolecular Lewis acid catalysts from chiral 3-substituted-BINOLs, 2-cyanophenylboronic acids, and tris(pentafluorophenyl)borane based on a coordination bond between the cyano moiety and tris(pentafluorophenyl)borane. Moreover, a second coordination bond between the phosphoryl moiety at the 3-position of the BINOL and tris(pentafluorophenyl)borane could increase both the catalytic reactivity and enantioselectivity in some Diels–Alder reactions[21]

by providing a chiral cavity. In particular, chiral supramolecular catalyst **2c** was effective for inducing high enantioselectivity for a variety of acroleins and cyclic and acyclic dienes. Further investigations of mechanistic aspects and application to other substrates and/or other catalytic asymmetric reactions are currently underway.

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Supporting Information

Supporting information for this article is available online at http://dx.doi.org/10.1055/s-0034-XXXXXXX.

References and Notes

(1) Lehn, J. M. *Science* **1985**, *227*, 849.

(2) Recent reviews on supramolecular catalysis: (a) Ma, L.; Abney, C.; Lin, W. *Chem. Soc. Rev.* **2009**, *38*, 1248. (b) Corma, A.; García, H.; Llabrés i Xamena, F. X. *Chem. Rev.* **2010**, *110*, 4606. (c) Meeuwissen, J.; Reek, J. N. H. *Nature Chem.* **2010**, *2*, 615. (d) Raynal, M.; Ballester, P.; Vidal-Ferran, A.; van Leeuwena, P. W. N. M. *Chem. Soc. Rev.* **2014**, *43*, 1660. (e) Raynal, M.; Ballester, P.; Vidal-Ferran, A.; van Leeuwena, P. W. N. M. *Chem. Soc. Rev.* **2014**, *43*, 1734. (f) Brown, C. J.; Toste. F. D.; Bergman, R. G.; Raymond, K. N. *Chem. Rev.* **2015**, *115*, 3012.

(3) Reviews on acid–base combination chemistry, see: (a) Kanai, M.; Kato, N.; Ichikawa, E.; Shibasaki, M. *Synlett* **2005**, 1491. (b) Ishihara, K.; Sakakura, A.; Hatano, M. *Synlett* **2007**, 686. (c) Ishihara, K. *Proc. Jpn. Acad. Ser. B* **2009**, *85*, 290. (d) Shibasaki, M.; Kanai, M.; Matsunaga, S.; Kumagai, N. *Acc. Chem. Res.* **2009**, *42*, 1117.

(4) Anomalous *endo*-selective Diels–Alder reactions of α-substituted acroleins: (a) Hatano, M.; Mizuno, T.; Izumiseki, A.; Usami, R.; Asai, T.; Akakura, M.; Ishihara, K. *Angew. Chem. Int. Ed.* **2011**, *50*, 12189. (b) Hatano, M.; Ishihara, K. *Chem. Commun.* **2012**, *48*, 4273.

(5) Anomalous *exo*-selective Diels–Alder reactions of α-nonsubstituted acroleins: (a) Maruoka, K.; Imoto, H.; Yamamoto, H. *J. Am. Chem. Soc.* **1994**, *116*, 12115. (b) Kündig, E. P.; Saudan, C. M.; Alezra, V.; Viton, F.; Bernardinelli, G. *Angew. Chem. Int. Ed.* **2001**, *40*, 4481. (c) Kano, T.; Tanaka Y.; Maruoka, K. *Org. Lett.* **2006**, *8*, 2687. (d) Hayashi, Y.; Samanta, S.; Gotoh H.; Ishikawa, H. *Angew. Chem. Int. Ed.* **2008**, *47*, 6634. (e) Sibi, M. P.; Nie, X.; Shackleford, J. P.; Stanley, L. M.; Bouret, F. *Synlett* **2008**, 2655.

(6) Reviews on the Diels–Alder reaction: (a) Kagan, H. B.; Riant, O. *Chem. Rev.* **1992**, *92*, 1007. (b) Du, H.; Ding, K. In *Handbook of Cyclization Reactions*, Ma, S., Ed.; Wiley-VCH: Stuttgart, **2010**, pp. 1–57. (c) Ishihara, K.; Sakakura, A. In *Science of Synthesis, Stereoselective Synthesis*, Evans, P. A., Ed.; Thieme: Weinheim, **2011**, vol. 3, pp. 67–123.

(7) As a strong Lewis base moiety, a phosphoryl group (P=O) has been highly attractive in asymmetric catalysis. Shibasaki pioneeringly developed a catalytic asymmetric cyanosilylation and Strecker-type reaction, in which Me_3SiCN was effectively activated by coordination of the phosphoryl group. (a) Hamashima, Y.; Sawada, D.; Kanai, M.; Shibasaki, M. *J. Am. Chem. Soc.* **1999**, *121*, 2641. (b) Takamura, M.; Hamashima, Y.; Usuda, H.; Kanai, M.; Shibasaki, M. *Angew. Chem. Int. Ed.* **2000**, *39*, 1650. (c) Takamura, M.; Funabashi, K.; Kanai, M.; Shibasaki, M. *J. Am. Chem. Soc.* **2000**, *122*, 6327. (d) Hamashima, Y.; Kanai, M.; Shibasaki, M. *J. Am. Chem. Soc.* **2000**, *122*, 7412. (e) Funabashi, K.; Ratni, H.; Kanai, M.; Shibasaki, M. *J. Am. Chem. Soc.* **2001**, *123*, 10784.

(8) We used the coordinating P=O moiety in some catalysis. (a) Hatano, M.; Miyamoto T.; Ishihara, K. *Adv. Synth. Catal.* **2005**, *347*, 1561. (b) Hatano, M.; Miyamoto T.; Ishihara, K. *Synlett* **2006**, 1762. (c) Hatano, M.; Miyamoto, T.; Ishihara, K. *J. Org. Chem.* **2006**, *71*, 6474. (d) Hatano, M.; Takagi, E.; Ishihara, K. *Org. Lett.* **2007**, *9*, 4527. (e) Hatano, M.; Miyamoto, T.; Ishihara, K. *Org. Lett.* **2007**, *9*, 4535. (f) Hatano, M.; Ishihara, K. *Chem. Rec.* **2008**, *8*, 143. (g) Hatano, M.; Ikeno, T.; Matsumura, T.; Torii, S.; Ishihara, K. *Adv. Synth. Catal.* **2008**, *350*, 1776. (h) Hatano, M.; Mizuno T.; Ishihara, K. *Chem. Commun.* **2010**, *46*, 5443. (i) Hatano, M.; Mizuno, T.; Ishihara, K. *Synlett* **2010**, 2024. (j) Hatano, M.; Mizuno T.; Ishihara, K. *Tetrahedron* **2011**, *67*, 4417. (k) Hatano, M.; Gouzu, R.; Mizuno, T.; Abe, H.; Yamada, T.; Ishihara, K. *Catal. Sci. Technol.* **2011**, *1*, 1149. (l) Hatano, M.; Goto, Y.; Izumiseki, A.; Akakura, M.; Ishihara, K. *J. Am. Chem. Soc.* **2015**, *137*, 13472. (m) Hatano, M.; Ishihara, H.; Goto, Y.; Ishihara, K. *Synlett* **2015**, ASAP. **DOI:** 10.1055/s-0035-1560369.

(9) Yamamoto developed the pioneering concept of combined acid catalysis. See reviews: (a) Ishibashi, H.; Ishihara, K.; Yamamoto, H. *Chem. Rec.* **2002**, *2*, 177. (b) Yamamoto, H.; Futatsugi, K. *Angew. Chem. Int. Ed.* **2005**, *44*, 1924. (c) Yamamoto, H.; Futatsugi, K. In *Acid Catalysis in Modern Organic Synthesis.* (Eds. Yamamoto, H.; Ishihara, K.) Wiley-VCH, Weinheim, **2008**, vol. 1, pp1–34.

(10) Focante, F.; Mercandelli, P.; Sironi, A.; Resconi, L. *Coord. Chem. Rev.* **2006**, *250*, 170.

(11) Dichloromethane was essential to induce good reactivity and enantioselectivity in this catalytic system. Toluene as another non-polar solvent was also effective to promote the reaction, although the enantioselectivity decreased significantly (ca. 60% ee). In contrast, the use of coordinative polar solvent such as Et_2O and THF showed almost no catalytic activity.

(12) In the ESI-MS (positive mode) analysis of catalyst **2c**, a peak for [**2a**+H_2O+H^+] was observed. See the SI.

(13) Consequently, when we compared the catalytic reactivity of **10** with a phosphoryl moiety to that of **11** with a 3,5-(3,5-$(CF_3)_2C_6H_3)_2C_6H_3$ moiety, **10** showed higher yield. This tendency would be correlated to the reaction with the use of **2c** or **7a** in the presence of competitive 5 mol% of $B(C_6F_5)_3$ (See the brackets a in Figures 2 and 3).

(14) Position of CN group influenced on enantioselectivity. The use of 3-cyanophenylboronic acid and 4-cyanophenylboronic acid in place of 2-cyanophenylboronic acid for catalyst **10** gave *exo*-(2*S*)-**5a** in ca. 80% yields with 9% ee and 11% ee, respectively.

(15) Since cyclopentadiene **3** is too reactive for evaluating meaningful differences in catalytic activity among **14a–d**, we used cyclohexadiene **12**.

(16) ^1H and ^{13}C NMR (CD_2Cl_2) analyses of **14** and **4a** at room temperature did not show clear interactions, since a somewhat broad chart was observed.

(17) The C(=O)H···O hydrogen bonding interaction has been well known. (a) Corey, E. J.; Lee, T. W. *Chem. Commun.* **2001**, 1321. (b) Corey, E. J.; Shibata, T.; Lee, T. W. *J. Am. Chem. Soc.* **2002**, *124*, 3808. (c) Ryu, D. H.; Lee, T. W.; Corey, E. J. *J. Am. Chem. Soc.* **2002**, *124*, 3808.

(18) Energy profiles and bond distances in boron Lewis acid complexes with some coordinating substrates such as aldehydes, ketones, and pyridines have been studied. (a) Reetz, M. T.; Huellmann, M.; Massa, W.; Berger, S.; Rademacher, P.; Heymanns, P. *J. Am. Chem. Soc.* **1986**, *108*, 2405. (b) LePage, T. J.; Wiberg, K. B. *J. Am. Chem. Soc.* **1998**, *110*, 6642. (c) Wu, D.; Jia, D.; Liu, L.; Zhang, L.; Guo, J. *J. Phys. Chem. A* **2010**, *114*, 11738.

(19) The previous supramolecular catalyst **1** was calculated to be in a similar C_1-symmetric *syn*-conformation for two bulky tris(pentafluorophenyl)boranes. See ref. 4.

(20) Other possible TS are discussed in the SI, which also gives the results with other supramolecular catalysts.

(21) **Typical Procedure for the Diels–Alder Reaction**
A solution of (*R*)-3-(5,5-dimethyl-2-oxido-1,3,2-dioxaphosphorinan-2-yl)-5,5',6,6',7,7',8,8'-H_8-BINOL (22.1 mg, 0.050 mmol) and 2-cyano-5-(trifluoromethyl)phenylboronic acid (10.7 mg, 0.050 mmol) in dichloromethane (1 mL), THF (0.3 mL),

and water (9 μL, 0.5 mmol) was stirred at room temperature for 12 h in a Pyrex Schlenk tube under a nitrogen atmosphere. Volatile compounds were removed under reduced pressure, and powdered MS 4Å (250 mg, used as received from a commercial source) was added. The resulting white solid was heated to 100 °C (bath temperature) under <5 Torr for 2 h. After the resulting substance was cooled to room temperature under a nitrogen atmosphere, tris(pentafluorophenyl)borane (51.2 mg, 0.10 mmol) and freshly-distilled dichloromethane (2 mL) were added under an argon atmosphere in a glove box. The pale brown mixture was stirred at room temperature for 1 h and then cooled to –78 °C, and methacrolein **4a** (95% purity, 43.4 μL, 0.50 mmol) was added. Subsequently, freshly-distilled cyclopentadiene **3** (210 μL, 2.5 mmol) was added at –78 °C over 15 min. The resultant mixture was then stirred at –78 °C for 3 h. To quench the reaction, triethylamine (0.5 mL) was poured into the reaction mixture at –78 °C. The product mixture was directly purified by silica gel column chromatography (eluent: *n*-pentane:diethyl ether = 100:1–8:1). Solvents were removed under 200 Torr at 15 °C by a rotary evaporator, and the product **5a** was obtained. ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.76 (d, *J* = 12.0 Hz, 1H), 1.01 (s, 3H), 1.39 (m, 2H), 2.25 (dd, *J* = 12.0, 3.9 Hz, 1H), 2.82 (brs, 1H), 2.90 (brs, 1H), 6.11 (dd, *J* = 6.0, 3.0 Hz, 1H), 6.30 (dd, *J* = 6.0, 3.0 Hz, 1H), 9.69 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.1, 34.6, 43.2, 47.6, 48.5, 53.9, 133.1, 139.6, 205.9. HRMS (EI) calcd for $C_9H_{12}O$ $[M]^+$ 136.0888, found 136.0893. The *endo*/*exo* ratio of **5a** was determined by ^{1}H NMR ($CDCl_3$) analysis; δ 9.40 (s, 1H, CHO (*endo*-**5a**)), 9.69 (s, 1H, CHO (*exo*-**5a**)).[4a] The enantioselectivity and absolute stereochemistry of **5a** were determined by GC analysis according to the literature.[4a]