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Remote Tris(pentafluorophenyl)borane-Assisted Chiral Phosphoric Acid Catalysts for the Enantioselective Diels–Alder Reaction

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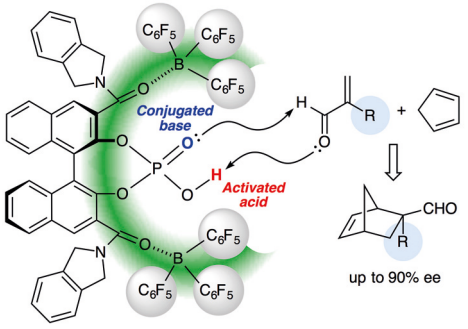

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Abstract Tris(pentafluorophenyl)borane-assisted chiral supramolecular phosphoric acid catalysts were developed for the model Diels–Alder reaction of α-substituted acroleins with cyclopentadiene. Two remotely coordinated tris(pentafluorophenyl)boranes should help to increase the Brønsted acidity of the active center in the supramolecular catalyst and create effective bulkiness for the chiral cavity. The prepared supramolecular catalysts acted as not only conjugated Brønsted acid–Brønsted base catalysts but also bifunctional Lewis acid–Brønsted base catalysts with the addition of a central achiral Lewis acid source such as catecholborane.

Key words Diels–Alder reaction, phosphoric acid, Brønsted acid, Lewis acid, supramolecular catalyst, chiral cavity, molecular recognition

The design of simple artificial enzymes is an ongoing challenge in modern organic chemistry. In particular, tailor-made chiral supramolecular catalysts might be attractive for use as artificial enzymes, since every part of a supramolecular catalyst can be fine-tuned for each substrate to establish higher-ordered substrate-selectivity and/or stereoselectivity.[1,2] In this regard, we previously developed enantioselective Diels–Alder reactions with anomalous *endo*/*exo*-selectivities through the use of conformationally flexible chiral supramolecular Lewis acid catalyst **1** (Figure 1, a).[3,4]

Based on the chiral deep and narrow cavity control of the transition states in the reaction of α-substituted acroleins and cyclopentadiene, anomalous *endo* products were successfully obtained in a highly enantioenriched fashion for the first time.[5] Two coordinated tris(pentafluorophenyl)boranes in catalyst **1** should not only create effective bulkiness for the chiral cavity but also help to increase the Lewis acidity of the active center based on the Lewis acid assisted Lewis acid (LLA)[6] catalyst system. To further develop such a supramolecular methodology, we envisioned that we might be able to use conformationally flexible chiral supramolecular Brønsted acid catalyst **2** based on the Lewis

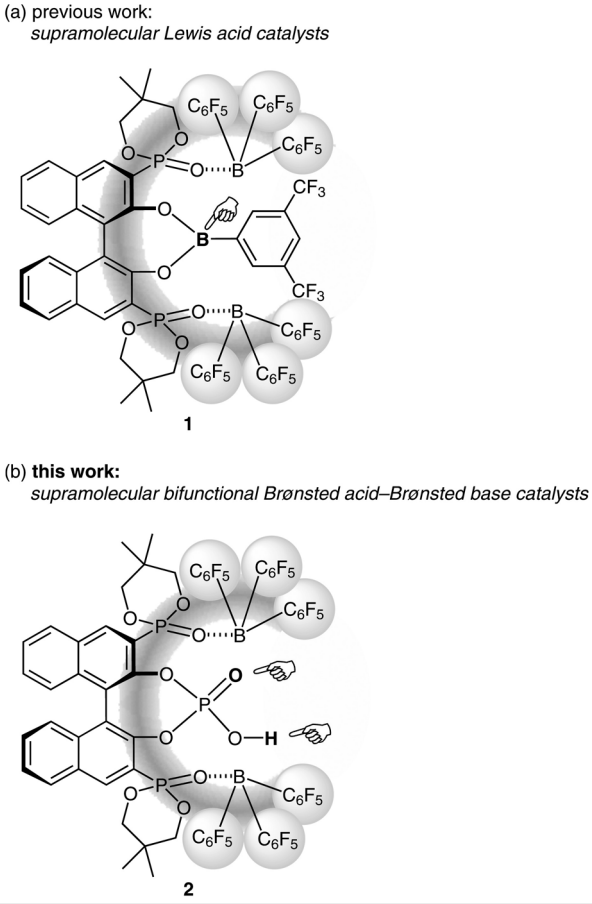


Figure 1 Design of conformationally flexible chiral supramolecular catalysts

acid assisted Brønsted acid (LBA)[6] catalyst system (Figure 1, b). By taking advantage of the conjugated Brønsted acid–Brønsted base bifunction of chiral phosphoric acids **2**,[7,8] aldehydes (i.e., acroleins) should be able to doubly coordinate with the active centers (Figure 2, a). Moreover, the addition of an achiral Lewis acid source (ML_n) should provide bifunctional Lewis acid–Brønsted base catalysts (Figure 2, b). Overall, introduction of the phosphoric acid to the center of supramolecular catalysts might provide additional opportunities for versatile molecular recognition according to the size and/or substitution pattern of acroleins. In this context, we have developed remote tris(pentafluorophenyl)borane-assisted chiral phosphoric acid catalysts for the enantioselective Diels–Alder reaction of α-substituted acroleins with cyclopentadiene as a probe reaction.

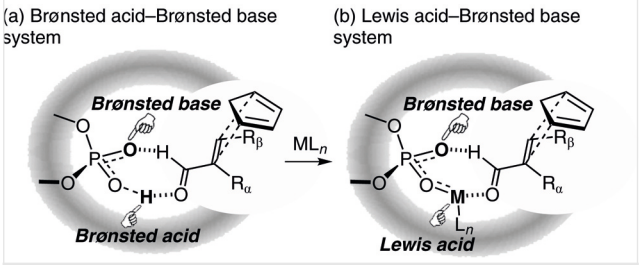


Figure 2 Chiral supramolecular phosphoric acid catalysts as (a) a Brønsted acid–Brønsted base system, and (b) a Lewis acid–Brønsted base system

First, we examined the Diels–Alder reaction of methacrolein **5a** with cyclopentadiene **4** in dichloromethane at –78 °C in the presence of chiral supramolecular catalysts (10 mol%), which were prepared in situ from chiral phosphoric acid (*R*)-**3a** and achiral boron Lewis acids, such as $BF_3{\cdot}Et_2O$, BBr_3, and $B(C_6F_5)_3$ (Table 1). The reaction did not proceed with the use of (*R*)-**3a** alone (Table 1, entry 1). In contrast, the combined use of (*R*)-**3a** and Lewis acids showed strong catalytic activities (Table 1, entries 2–4). In particular, as expected, bulky $B(C_6F_5)_3$ was more effective than $BF_3{\cdot}Et_2O$ and BBr_3, and higher enantioselectivity (53% ee) was observed (Table 1, entry 4). Fortunately, the enantioselectivity was significantly improved when amide-type (*R*)-**3b** and (*R*)-**3c** were used in place of phosphoryl-type (*R*)-**3a**, and *exo*-**6a** was obtained with 90% ee (Table 1, entries 10 and 16). Moreover, for (*R*)-**3b** and (*R*)-**3c** as well as (*R*)-**3a**, $BF_3{\cdot}Et_2O$ and BBr_3 were not effective (Table 1, entries 8, 9, 14, and 15).

In this reaction, preparation of the catalyst at room temperature in advance was critical,[9] and compounds **4** and **5a** were added within five minutes just after the mixture of catalysts was cooled to –78 °C.[10] In this regard, the enantioselectivity significantly decreased when compounds **4** and **5a** were added to the mixture of $2B(C_6F_5)_3$–(*R*)-**3a** or $2B(C_6F_5)_3$–(*R*)-**3b** after cooling at –78 °C for 30 minutes (Table 1, entries 5 and 11). Once $B(C_6F_5)_3$ is adventitiously released from the supramolecular catalysts $2B(C_6F_5)_3$–(*R*)-**3a** and $2B(C_6F_5)_3$–(*R*)-**3b**, the highly basic phosphoryl moiety and pyrrolidine-derived amido moiety would tightly coordinate with the proton of the phosphoric acid at –78 °C. The corresponding species $B(C_6F_5)_3$–(*R*)-**3a** and $B(C_6F_5)_3$–(*R*)-**3b**, which might be inactive (Table 1, entries 6 and 12), would then be formed (Figure 3). Simultaneously, achiral $B(C_6F_5)_3$, which might induce a racemic reaction pathway (Table 1, entries 5 and 11), would be released. In sharp contrast, $2B(C_6F_5)_3$–(*R*)-**3c**, which has a much less basic isoindoline-derived amido moiety, was tolerated under the reaction conditions at –78 °C for 30 minutes before the addition of substrates **4** and **5a**, and *exo*-**6a** was obtained with 85% ee (Table 1, entry 17). The inter-/intramolecular coordination-exchange between the proton center and $B(C_6F_5)_3$ might still occur due to the weak basicity of the isoindoline-derived amido moiety even at –78 °C. As a result, active $2B(C_6F_5)_3$–(*R*)-**3c** would be regenerated from less active $B(C_6F_5)_3$–(*R*)-**3c**. These considerations might be supported by finding that the catalytic activity of $2B(C_6F_5)_3$–(*R*)-**3c** (entry 16) was much higher than those of competitive $B(C_6F_5)_3$–(*R*)-**3c** (Table 1, entry 18) and free $B(C_6F_5)_3$ (Table 1, entry 19).[11]

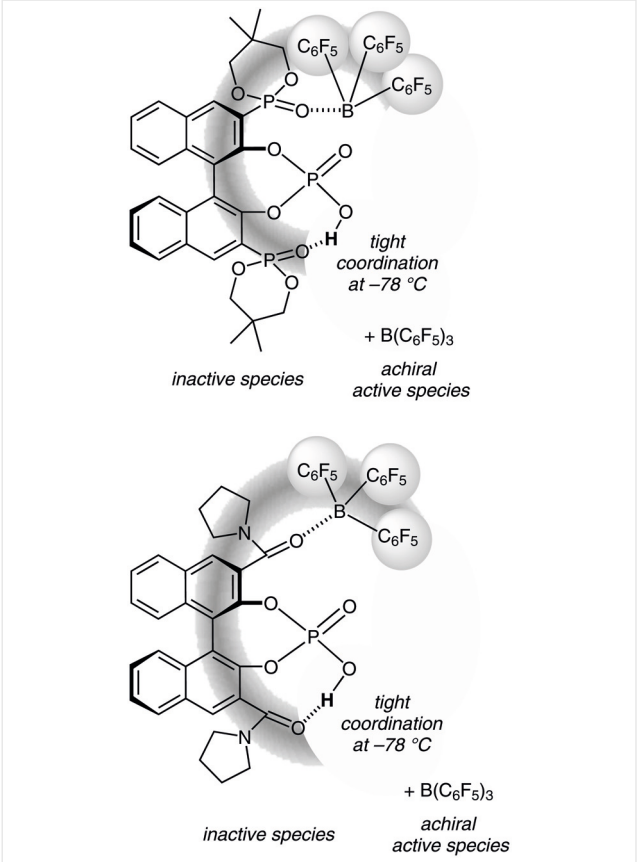
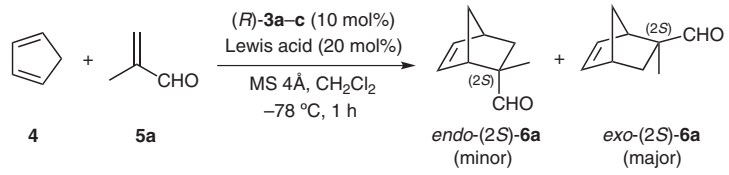


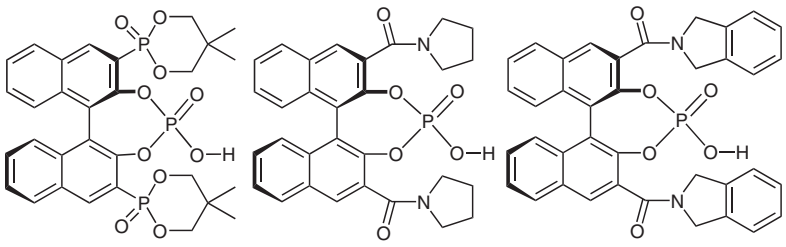
Figure 3 Possible formations of $B(C_6F_5)_3$–(*R*)-**3a** and $B(C_6F_5)_3$–(*R*)-**3b** with intramolecular hydrogen bonding and the release of achiral $B(C_6F_5)_3$

To confirm the complexation of the optimized supramolecular catalyst $2B(C_6F_5)_3$–(*R*)-**3c**, spectroscopic analyses were performed at room temperature (Scheme 1). We found a peak at 1697.146 in ESI–MS analysis (negative mode), which might be unambiguously attributed to $\{[2B(C_6F_5)_3$–(*R*)-**3c**$] + 2H_2O - H\}^-$ (see the Supporting Information). Moreover, peaks at δ = –137.0, –159.5, and –166.3 ppm in ^{19}F NMR (CD_2Cl_2) were slightly shifted from the original peaks of $B(C_6F_5)_3$ at δ = –130.2, –147.1, and –161.4 ppm. However, a peak at δ = 4.6 ppm in ^{31}P NMR (CD_2Cl_2) was scarcely shifted from the original peak at δ = +4.0 ppm. These observations suggest that coordination to $B(C_6F_5)_3$ at the carbonyl groups of the 3,3′-substituents would precede coordination at the central P=O moiety, probably due to ste-

Table 1 Screening of Chiral Supramolecular Catalysts[a]



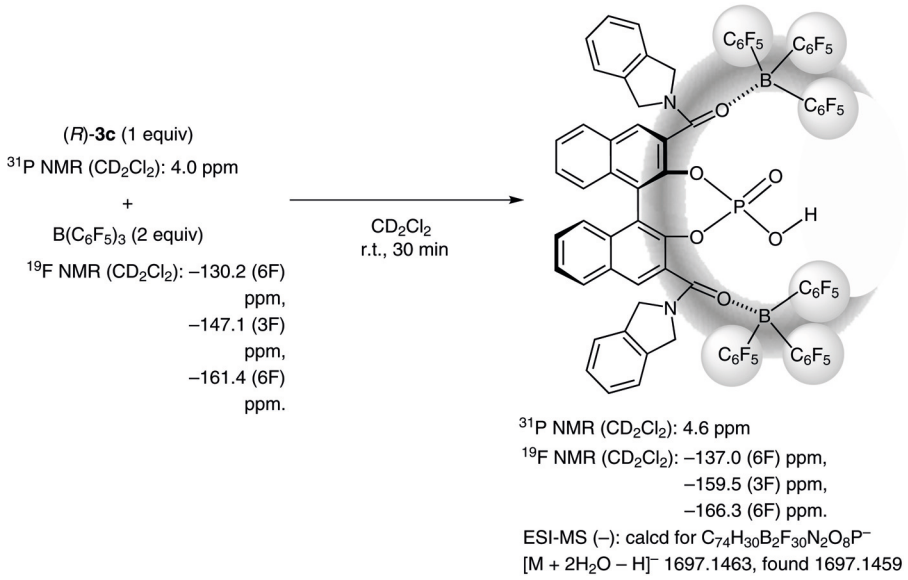
4 **5a** *endo*-(2*S*)-**6a** (minor) *exo*-(2*S*)-**6a** (major)



(*R*)-**3a** (*R*)-**3b** (*R*)-**3c**

Entry	(*R*)-**3**	Lewis acid	Yield (%)	*endo*-**6a**/*exo*-**6a**	ee (%) of *exo*-**6a**
1	(*R*)-**3a**	–	0	–	–
2	(*R*)-**3a**	$BF_3{\cdot}Et_2O$	>99	7:93	2
3	(*R*)-**3a**	BBr_3	98	8:92	14
4	(*R*)-**3a**	$B(C_6F_5)_3$	98	8:92	–53[b]
5[c]	(*R*)-**3a**	$B(C_6F_5)_3$	>99	8:92	–31[b]
6[d]	(*R*)-**3a**	$B(C_6F_5)_3$	20	19:81	–1[b]
7	(*R*)-**3b**	–	0	–	–
8	(*R*)-**3b**	$BF_3{\cdot}Et_2O$	>99	7:93	0
9	(*R*)-**3b**	BBr_3	>99	5:95	0
10	(*R*)-**3b**	$B(C_6F_5)_3$	>99	5:95	90
11[c]	(*R*)-**3b**	$B(C_6F_5)_3$	62	11:89	8
12[d]	(*R*)-**3b**	$B(C_6F_5)_3$	0	–	–
13	(*R*)-**3c**	–	0	–	–
14	(*R*)-**3c**	$BF_3{\cdot}Et_2O$	98	6:94	0
15	(*R*)-**3c**	BBr_3	96	10:90	0
16	(*R*)-**3c**	$B(C_6F_5)_3$	>99	8:92	90
17[c]	(*R*)-**3c**	$B(C_6F_5)_3$	>99	9:91	85
18[d]	(*R*)-**3c**	$B(C_6F_5)_3$	0	–	–
19[e]	–	$B(C_6F_5)_3$	>99	7:93	–

[a] Unless otherwise noted, the reaction of **5a** (0.5 mmol) with **4** (2.5 mmol) was carried out with the use of (*R*)-**3** (10 mol%), Lewis acid (20 mol%), and MS 4Å in CH_2Cl_2 at –78 °C for 1 h. Compounds **4** and **5a** were added to the mixture of catalysts within 5 min just after cooling to –78 °C.
[b] Enantioselectivity of *exo*-(2*R*)-**6a**.
[c] Compounds **4** and **5a** were added to the mixture of catalysts after it was cooled to –78 °C for 30 min.
[d] The reaction was carried out with the use of (*R*)-**3** (10 mol%), $B(C_6F_5)_3$ (10 mol%), and MS 4Å under standard conditions.
[e] The reaction was carried out with the use of $B(C_6F_5)_3$ (20 mol%) alone.



Scheme 1 Spectroscopic analyses of $2B(C_6F_5)_3$–(*R*)-**3c** at room temperature

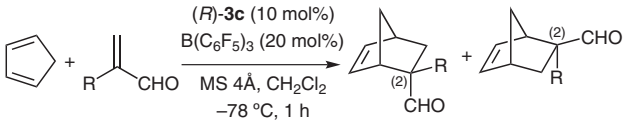
ric constraints at the narrow inner space.[12] Unfortunately, the hydrogen-bonding structures of $B(C_6F_5)_3$–(*R*)-**3a** and $B(C_6F_5)_3$–(*R*)-**3b**, as shown in Figure 3 have not yet been confirmed directly (see the Supporting Information for ^{31}P NMR analysis.). However, in ^{31}P NMR (CD_2Cl_2) analysis at –78 °C, a peak at δ = –4.1 ppm of $2B(C_6F_5)_3$–(*R*)-**3b** gradually decreased, and many other peaks between δ = –5 ppm and δ = –25 ppm were predominantly observed within 30 minutes.[13] In sharp contrast, the decomposition of $2B(C_6F_5)_3$–(*R*)-**3c** to other species at –78 °C was much slower than that of $2B(C_6F_5)_3$–(*R*)-**3b**, and ca. 70% of $2B(C_6F_5)_3$–(*R*)-**3b** was still observed at δ = –0.7 ppm for at least 30 minutes.[13]

Next, we examined the substrate specificity for α-substituted acroleins. In place of methacrolein **5a**, α-ethylacrolein **5b** could be used in the presence of $2B(C_6F_5)_3$–(*R*)-**3c**, and the corresponding normal *exo*-**6b** was obtained with 84% ee (Table 2, entry 3). Partially due to steric mismatch with the chiral cavity, α-isopropylacrolein **5c** and α-bromoacrolein **5d**, which are bulkier than **5a** and **5b**, might be unsuitable for the chiral cavity of $2B(C_6F_5)_3$–(*R*)-**3c**, and low enantioselectivities were observed (Table 2, entries 5 and 7). Moreover, a racemic pathway also might be promoted in the case of highly reactive **5d** (Table 2, entry 7). As compared with thermal conditions (Table 2, entries 2, 4, 6, and 8), a supramolecular catalyst induced a slight *exo* preference for **6a** and **6b** (Table 2, entries 1 and 3).

Moreover, with the use of α-nonsubstituted acrolein **5e**, moderate anomalous *exo*-selectivity was observed (*endo*/*exo* = 49:51) (Scheme 2).[14] Although the enantioselectivities of *endo*-**6e** and *exo*-**6e** were low (30% ee and 25% ee, respectively), an unusual disagreement in stereoselectivity (*R*/*S*) was observed between normal *endo*-(2*S*)-**6e** and anomalous *exo*-(2*R*)-**6e**. These results suggest that $2B(C_6F_5)_3$–(*R*)-**3c** might have an *exo*-inducing chiral cavity as a supramolecular catalyst.

Finally, we used tiglic aldehyde **7** as a much less reactive α,β-disubstituted acrolein, which did not give product **8** under thermal conditions in toluene at 110 °C. Supramolec-

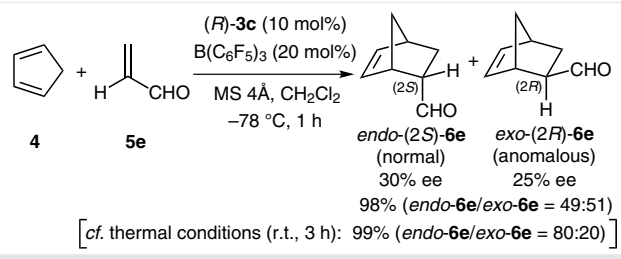
Table 2 Substrate Specificity with the Use of $2B(C_6F_5)_3$–(*R*)-**3c**[a]



4 **5** *endo*-**6** (anomalous, minor) *exo*-**6** (normal, major)

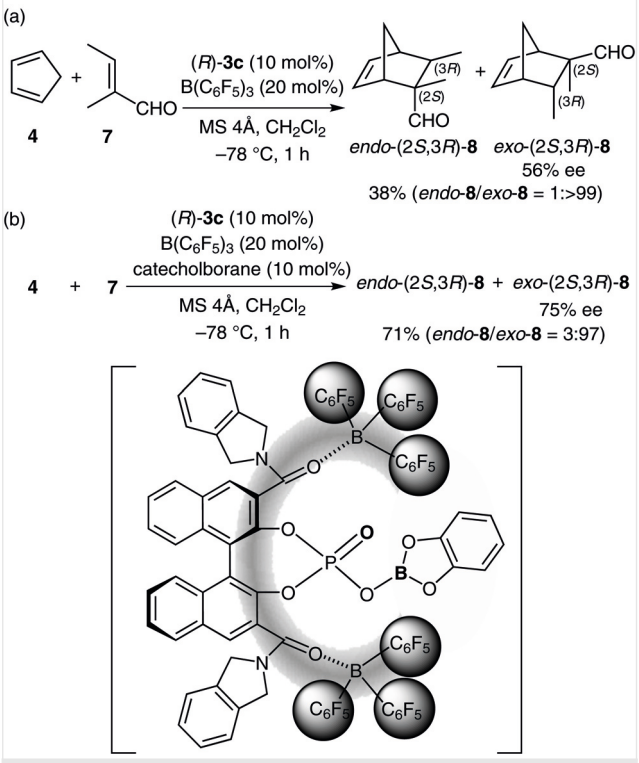
Entry	**5** (R)	Product	Yield (%)	*endo*-**6**/*exo*-**6**	ee (%) of *exo*-**6**
1	**5a** (Me)	**6a**	>99	8:92	90 (2*S*)
2[b]	**5a** (Me)	**6a**	94 (40 °C, 3 h)	16:84	–
3	**5b** (Et)	**6b**	>99	2:98	84 (2*S*)
4[b]	**5b** (Et)	**6b**	73 (110 °C, 24 h)	24:76	–
5	**5c** (*i*-Pr)	**6c**	72	15:85	23 (2*R*)
6[b]	**5c** (*i*-Pr)	**6c**	<5 (110 °C, 3 h)	–	–
7	**5d** (Br)	**6d**	>99	15:85	18 (2*R*)
8[b]	**5d** (Br)	**6d**	>99 (r.t., 3 h)	15:85	–

[a] The reaction of **5** (0.5 mmol) with **4** (2.5 mmol) was carried out with the use of (*R*)-**3c** (10 mol%), $B(C_6F_5)_3$ (20 mol%), and MS 4Å in CH_2Cl_2 at –78 °C for 1 h.
[b] The reactions were carried out under thermal conditions without any catalysts in CH_2Cl_2 at room temperature to 40 °C or in toluene at 110 °C.



Scheme 2 Anomalous *exo*-induced Diels–Alder reaction of acrolein **5e** with cyclopentadiene **4** catalyzed by 2B(C_6F_5)$_3$–(*R*)-**3c**

ular catalyst 2B(C_6F_5)$_3$–(*R*)-**3c** showed low reactivity, and *exo*-**8** was obtained in 38% yield with 56% ee (Scheme 3, a). To improve both the yield and the enantioselectivity, we changed the Brønsted acid–Brønsted base catalyst system (Figure 2, a) to a Lewis acid–Brønsted base catalyst system (Figure 2, b), by using an additional achiral Lewis acid partner. After screening the acid sources,[15] we found that catecholborane was highly effective as a boron Lewis acid center for 2B(C_6F_5)$_3$–(*R*)-**3c**, and *exo*-**8** was obtained in 71% yield with 75% ee (Scheme 3, b).[16] Although the enantioselectivity has still been moderate, these results represent at least a partial demonstration of our conceptual catalytic system in Figure 2.



Scheme 3 Effect of the addition of catecholborane to 2B(C_6F_5)$_3$–(*R*)-**3c** in the Diels–Alder reaction of **7** with **4**

In this preliminary stage, further information based on experimental and theoretical studies will be necessary to discuss possible structures of the supramolecular catalysts in situ. In this regard, the previous supramolecular catalyst **1** has been calculated to be the C_1-symmetric *syn* conformation due to the sp^3 boron Lewis acid center.[3] In contrast, we can speculate that supramolecular catalyst 2B(C_6F_5)$_3$–(*R*)-**3c** would have an *anti* conformation as shown in Figure 4 (b), unlike a sterically hindered *syn* conformation as

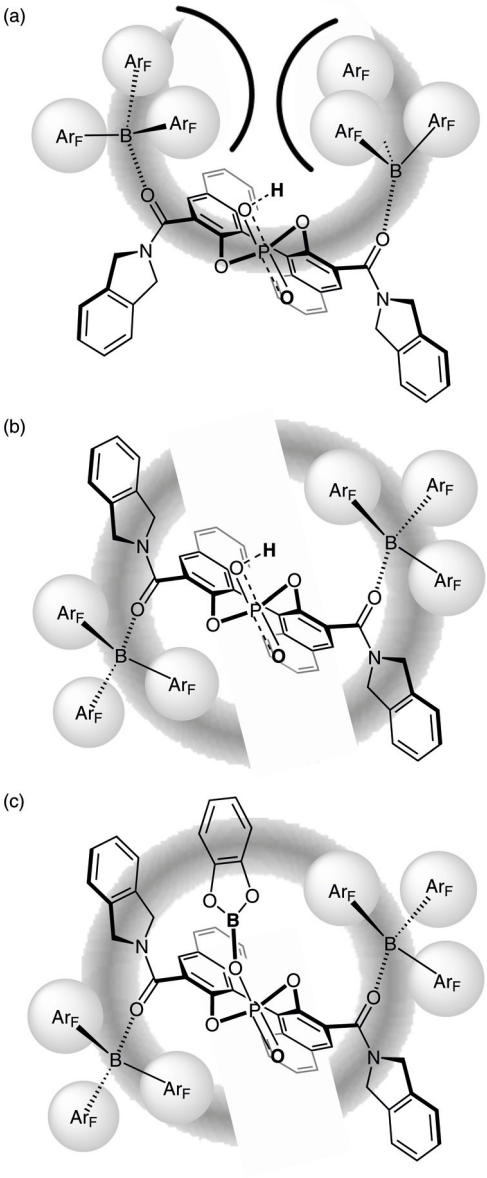


Figure 4 Possible structures and chiral cavities of supramolecular catalysts (Ar_F = C_6F_5). (a) *Syn*-conformation for 2B(C_6F_5)$_3$–(*R*)-**3c**. (b) *Anti*-conformation for 2B(C_6F_5)$_3$–(*R*)-**3c**. (c) *Anti*-conformation for 2B(C_6F_5)$_3$–(*R*)-**3c**–catecholborane.

shown in Figure 4 (a), due to the essentially C_2-symmetric conjugated phosphoric acid moiety. Catecholborane-introduced supramolecular catalyst might have similar structures although the field would then be C_1-symmetric, as shown in Figure 4 (c). In *anti* conformations, as shown in Figure 4 (b and c), a shallow and wide chiral cavity would be formed around the active center which would induce substrate specificity with an *exo*-preference.[3b]

In summary, we have developed bulky and strong Lewis acid $B(C_6F_5)_3$-assisted chiral phosphoric acids, which were designed for the model Diels–Alder reaction of α-substituted acroleins with cyclopentadiene.[17] The corresponding supramolecular catalysts acted not only as highly activated conjugated Brønsted acid–Brønsted base catalysts but also as bifunctional Lewis acid–Brønsted base catalysts with the addition of a central achiral Lewis acid source such as catecholborane. Further investigations with these asymmetric supramolecular methodologies with the use of chiral phosphoric acids, which might contribute to the construction of a conformationally flexible, bulky, and chiral cavity for higher-ordered catalysis, are currently underway.[18]

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Supporting Information

Supporting information for this article is available online at http://dx.doi.org/10.1055/s-0035-1560369.

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(8) 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.
(9) For $2B(C_6F_5)_3$–(*R*)-**3a**/**3b**/**3c**, the aging time (0.5–2 h) at r.t. in advance showed no significant differences in the Diels–Alder reaction.
(10) Lower enantioselectivities (ca. 60% ee) were observed when a solution of the catalyst $2B(C_6F_5)_3$–(*R*)-**3b** or $2B(C_6F_5)_3$–(*R*)-**3c** at r.t. was added to the solution of **4** and **5a** at –78 °C.
(11) Compound **5a** is too reactive to evaluate meaningful differences in the catalytic activity between $2B(C_6F_5)_3$–(*R*)-**3c** and free $B(C_6F_5)_3$. However, the catalytic activity of $2B(C_6F_5)_3$–(*R*)-**3c** was much higher than that of free $B(C_6F_5)_3$. See Scheme 3 and the SI.
(12) To confirm whether or not the coordination of the P=O moiety to $B(C_6F_5)_3$ would occur, we used (*R*)-3,3′-Ph_2BINOL-derived phosphoric acid, which may avoid competitive coordinations. In ^{31}P NMR (CD_2Cl_2) analysis at r.t., a singlet peak at δ = +1.7 ppm changed to δ = –1.0 ppm with a small upfield shift, which suggests the coordination of the P=O moiety to $B(C_6F_5)_3$. Next, as with $2B(C_6F_5)_3$–(*R*)-**3c**, almost the same shifted peaks at δ = –137.0, –158.8, and –165.8 ppm were observed in ^{19}F NMR (CD_2Cl_2) at r.t.
(13) ^{31}P NMR (CD_2Cl_2) analysis of (*R*)-**3b** and (*R*)-**3c** at –78 °C showed a peak at δ = 6.1 ppm and 5.0 ppm, respectively, although solubility of them at –78 °C was low. See the SI.
(14) For anomalous *exo*-selective Diels–Alder reactions of α-nonsubstituted acroleins, see: (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. Also see ref 3.
(15) We examined Me_3Al, Et_3Al, *i*-Bu_2AlH (DIBAL-H), Me_2AlNTf_2, allyltrimethylsilane, pinacolborane, 9-borabicyclo[3.3.1]nonane (9-BBN), etc. However, the combined use of these achiral Lewis acid sources to $2B(C_6F_5)_3$–(*R*)-**3c** showed low reactivities (0–15% yields), and the sole exception was catecholborane. In this regard, the combined use of a stoichiometric amount of catecholborane with chiral phosphoric acid catalyst in the enantioselective reduction of ketones was reported by Antilla. See: Zhang, Z.; Jain, P.; Antilla, J. C. *Angew. Chem. Int. Ed.* **2011**, *50*, 10961.

(16) We examined the reactions of acroleins **5a–e** with cyclopentadiene **4** with the use of a supramolecular catalyst, which was prepared from (*R*)-**3c**, $B(C_6F_5)_3$, and catecholborane, However, better enantioselectivities were not observed compared with $2B(C_6F_5)_3$–(*R*)-**3c** as shown in Table 2 and Scheme 2. The results are summarized in the SI.

(17) **Typical Procedure for the Diels–Alder Reaction**: To a mixture of (*R*)-**3c** (31.9 mg, 0.050 mmol) and powdered MS 4Å (200 mg) in a Schlenk tube under a nitrogen atmosphere, tris(pentafluorophenyl)borane (51.2 mg, 0.10 mmol) and freshly distilled CH_2Cl_2 (2 mL) were added via a cannula, and this suspension was stirred at r.t. for 1 h. Next, the mixture was cooled to –78 °C, and as soon as possible (within 5 min) after cooling to –78 °C, methacrolein **5a** (95% purity, 43.4 µL, 0.50 mmol) and freshly distilled cyclopentadiene **4** (203 µL, 2.5 mmol) were added at –78 °C. After that, the resultant mixture was stirred at –78 °C for 1 h. To quench the reaction, Et_3N (0.2 mL) was poured into the reaction mixture at –78 °C. The product mixture was warmed to r.t. and directly purified by silica gel column chromatography (eluent: pentane–Et_2O, 9:1). Solvents were removed under 200 Torr at 20 °C by a rotary evaporator, and the product **6a** was obtained (68.2 mg, >99% yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.76 (d, *J* = 12.0 Hz, 1 H), 1.01 (s, 3 H), 1.39 (m, 2 H), 2.25 (dd, *J* = 12.0, 3.9 Hz, 1 H), 2.82 (br s, 1 H), 2.90 (br s, 1 H), 6.11 (dd, *J* = 6.0, 3.0 Hz, 1 H), 6.30 (dd, *J* = 6.0, 3.0 Hz, 1 H), 9.69 (s, 1 H). ^{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): *m*/*z* $[M]^+$ calcd for $C_9H_{12}O$: 136.0888; found: 136.0893. The *endo*/*exo* ratio of **6a** was determined by NMR analysis. ^{1}H NMR ($CDCl_3$): δ = 9.40 [s, 1 H, CHO (*endo*-**6a**)], 9.69 [s, 1 H, CHO (*exo*-**6a**)]; see ref 3a. The enantioselectivity and absolute stereochemistry of **6a** were determined by GC analysis according to the literature (see ref. 3a).

(18) We just recently reported boron tribromide assisted chiral phosphoric acid catalyst for a highly enantioselective Diels–Alder reaction of 1,2-dihydropyridines. See: Hatano, M.; Goto, Y.; Izumiseki, A.; Akakura, M.; Ishihara, K. *J. Am. Chem. Soc.* **2015**, *137*, 13472.