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Cage-Shaped Borate Esters with Enhanced Lewis Acidity and Catalytic Activity

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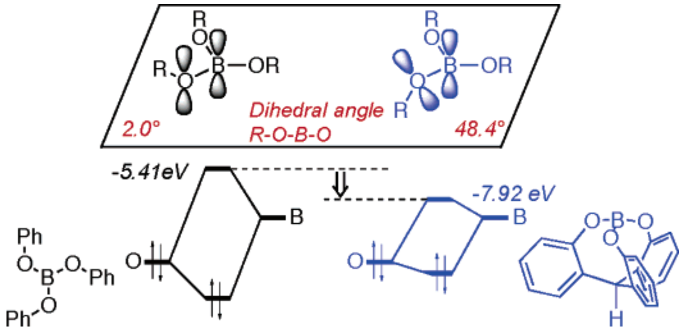
ABSTRACT



A cage shape causes high Lewis acidity and catalytic activity on boron. Borate esters that have cage-shaped ligands have accessible LUMO with lower eigenvalues than normal open-shaped borate esters. A large dihedral angle at C–O–B–O in cage-shaped borate esters induces less overlap between *p*-orbitals on O and B. The hetero-Diels–Alder reaction is effectively catalyzed by the cage-shaped borate, although the open-shaped borate does not act as a catalyst.

Lewis acids greatly contribute to organic synthesis for activation of substrates and control of selectivity.[1] Group 13 metal compounds ML_3 are one of the most important classes of Lewis acids owing to their vacant *p*-orbitals. In view of their high Lewis acidity, M and L have strong affinity to substrates (mainly to a heteroatom in a substrate) and strong ability of delocalizing a negative charge, respectively; for example, metal M (= B or Al) and ligand L (= halogen or OR). However, it means that M is not likely to release the product because of strong affinity of M with a heteroatom, and L readily leaves M with a negative charge. Therefore, a high Lewis acidity and catalytic turnovers are often incompatible. The choice of either L or M is significantly important to design a Lewis acid catalyst. Recently, $B(C_6F_5)_3$ and its related compounds have been used to overcome this problem because C_6F_5 (= L) groups are bound through a strong boron−carbon bond.[2] We have been studying $InCl_3$ or $In(OH)_3$ as Lewis acid catalysts. The moderate affinity of indium as M with a heteroatom realizes catalytic turnovers.[3]

In this context, we planned a Lewis acid having a sterically strained framework, which looks like a cage like **4**B in Scheme 1: The framework changes the metal surroundings

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(1) *Lewis Acids in Organic Synthesis*; Yamamoto, H., Ed.; Wiley-VCH: Weinheim, Germany, 2000; Vols 1 and 2.

(2) (a) Ishihara, K.; Yamamoto, H. *Eur. J. Org. Chem.* **1999**, *527*, 7−538. (b) Piers, W. E. *Adv. Organomet. Chem.* **2005**, *52*, 1−76.

(3) (a) Yasuda, M.; Yamasaki, S.; Onishi, Y.; Baba, A. *J. Am. Chem. Soc.* **2004**, *126*, 7186−7187. (b) Yasuda, M.; Saito, T.; Ueba, M.; Baba, A. *Angew. Chem., Int. Ed.* **2004**, *43*, 1414−1416. (c) Onishi, Y.; Ogawa, D.; Yasuda, M.; Baba, A. *J. Am. Chem. Soc.* **2002**, *124*, 13690−13691. (d) Yasuda, M.; Onishi, Y.; Ueba, M.; Miyai, T.; Baba, A. *J. Org. Chem.* **2001**, *66*, 7741−7744.

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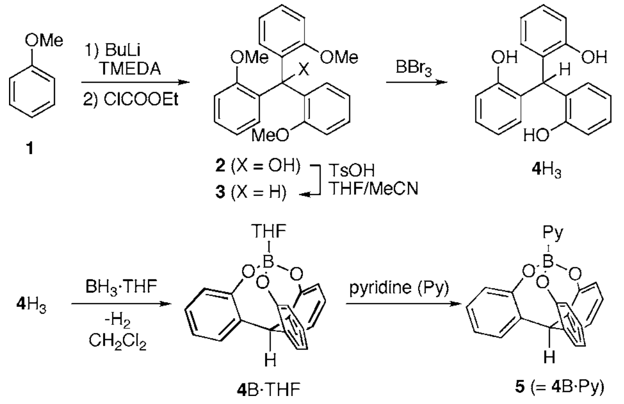
Scheme 1. Triphenolic Methane and Cage-Shaped Borate



which are less sterically hindered and reduces π-electron overlap between boron and its ligand oxygens. Here, we report cage-shaped borates which show high catalytic activity as compared with normal open-shaped ones. Furthermore, the ab initio calculations revealed highly accessible vacant MO and its lowered energy level caused by the cage-shaped framework.

Based on the concept of cage-shaped Lewis acid, we intended to prepare a borate **4**B as a structurally strained Lewis acid, that could be derived from borane and tris(2-hydoxyphenyl)methane **4**H$_3$ (Scheme 1).[4] It has been reported that organic components including preorganized phenoxy moieties nicely act as ligand systems for metal complexes.[5,6] Although some substituted derivatives of **4**H$_3$ are known,[7] its unsubstituted version has not been reported. We were able to synthesize **4**H$_3$ in three steps (Scheme 1). Ortho-lithiation of anisole followed by treatment with ethyl chloroformate gave triarylcarbinol **2**. The treatment of **2** with *p*-toluenesulfonic acid in THF/MeCN directly gave the reduced compound **3**. The in situ-generated carbenium cation stabilized by electron-donating groups[8] can be reduced by THF probably in either an ionic or SET mechanism.[9] The desired compound **4**H$_3$ was obtained after treatment of **3** with BBr$_3$.

The reaction of **4**H$_3$ with BH$_3$·THF generated the cage-shaped borate **4**B·THF. It was easily decomposed in air and thus confirmed by NMR under nitrogen. The ligand-free **4**B was not observed under the conditions. The pyridine complex **5** (= **4**B·Py) was formed by treatment with pyridine and well analyzed by X-ray crystallography. NMR of **5** shows reasonable spectra for the closed cage-shape: The significant upfield shift of the methine proton [Py·B(OC$_6$H$_4$)$_3$C*H*] relative to that of **4**H$_3$ was confirmed (6.07 → 5.19 ppm). This shift is observed in similar cage-shaped compounds.[10] The pyridine signals which appear in lower field relative to those of free pyridine indicate strong coordination of the pyridine to the boron in **5**.[11] The ORTEP drawings of **5** are shown in Figure 1.[12] Boron has a tetrahedral coordination sphere with the average of bond angles (O−B−O, 114.2(9)° and N−B−O, 104.1(9)°). This is the first example of a triphenolic methane-based mononuclear complex which can be a Lewis acid.[13] The top view (pyridine is omitted) clearly shows C_3 symmetry. Interestingly, the aromatic rings deviate from a perpendicular plane to that of three oxygens (ca. 19.2°), and thus, the complex **5** has chirality that is caused by the cage-shape.[14] A similar borate structure whose phenolic rings are connected to nitrogen was reported but its coordination to boron causes almost perpendicular aromatic rings.[15]

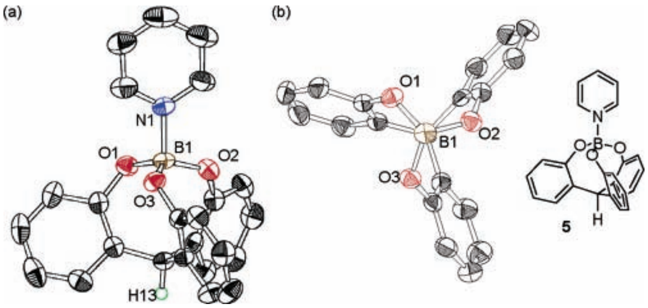


Figure 1. ORTEP drawing of **5** (aryl hydrogens are omitted for clarity): (a) side view and (b) top view (pyridine is omitted for clarity). Selected bond lengths (Å): B−O(1) 1.457(5), B−O(2) 1.432(4), B−O(3) 1.441(4),B−N(1) 1.630(4). Selected bond angles (deg): O(1)−B−O(2) 113.3(3), O(2)−B−O(3) 115.7(3), O(3)−B−O(1) 113.7(3), O(1)−B−N 104.3(3), O(2)−B−N 105.8(3), O(3)−B−N 102.2(3).

Ab initio calculations were performed to investigate the ligand-free borate **4**B comparing with the open-shaped B(OPh)$_3$ **6** (Table 1). We had expected that **4**B had distorted geometry around boron from the planar structure which is typical for open-shaped borate like **6**. However, both species contain planar geometry around boron. The notable difference is the dihedral angles C−O−B−O (2.0° in **6**, 48.4° in **4**B). The diagram of the lowest unoccupied MO[16] of **4**B to which boron p_z orbital contributes (corresponding to next-

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[4] A triphenolic methane-based complex with aluminum does not give a mononuclear cage-shaped complex but a multinuclear one with the methane hydrogen inside. Cottone, A., III; Morales, D.; Lecuivre, J. L.; Scott, M. J. *Organometallics* **2002**, *21*, 418−428.

[5] Recent review; Matsuo T.; Kawaguchi, H. *Chem. Lett.* **2004**, *33*, 640−645.

[6] (a) Verkerk, U.; Fujita, M.; Dzwiniel, T. L.; McDonald, R.; Stryker, J. M. *J. Am. Chem. Soc.* **2002**, *124*, 9988−9989. (b) Fujita, M.; Qi, G.; Verkerk, U. H.; Dzwiniel, T. L.; McDonald, R.; Stryker, J. M. *Org. Lett.* **2004**, *6*, 2653−2656.

[7] Dinger, M. B.; Scott, M. J. *Eur. J. Org. Chem.* **2000**, 2467−2478.

[8] Wada, M.; Kirishima, K.; Oki, Y.; Miyamoto, M.; Asahara, M.; Erabi, T. *Bull. Chem. Soc. Jpn.* **1999**, *72*, 779−785.

[9] Wada, M.; Mishima, H.; Watanabe, T.; Natsume, S.; Konishi, H.; Hayase, S.; Erabi, T. *J. Chem. Soc., Chem. Commun.* **1993**, 1462−1463.

[10] Dinger, M. B.; Scott, M. J. *Inorg. Chem.* **2001**, *40*, 856−864.

[11] See the Supporting Information.

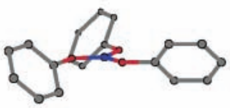
[12] The X-ray crystallographic data of **5** is given in the Supporting Information.

[13] The Lewis basic similar cage-shaped complex has been reported using P or As (ref 10). During the reviewing process of this manuscript, a titanium complex with a similar cage-shape ligand was reported. Akagi, F.; Matsuo, T.; Kawaguchi, H. *J. Am. Chem. Soc.* **2005**, *127*, 11936−11937.

[14] Linear triphenolic compounds shows chirality when complexed with Al. Appiah, W. O.; DeGreeff, A. D.; Razidlo, G. L.; Spessard, S. J.; Pink, M. Young, Jr. V. G.; Hofmeister, G. E. *Inorg. Chem.* **2002**, *41*, 3656−3667.

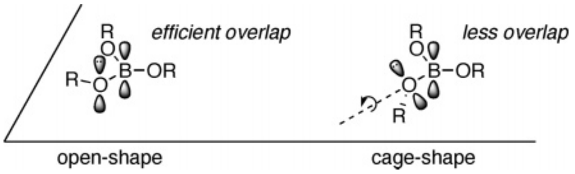
[15] Livant, P. D.; Northcott, J. D.; Shen, Y.; Webb, T. R. *J. Org. Chem.* **2004**, *69*, 6564−6571.

Table 1. Comparison of Open- and Cage-Shaped Borate (**6** and **4**B) by First Principle Calculations (B3PW91/6-31+G(d,p))

	$B(OPh)_3$ **6**	$B(OC_6H_4)_3CH$ **4B**
Optimum structre (Aryl Hs omitted)		
Sum of ∠O-B-O	360.0°	359.7°
Dihedral angle (C-O-B-O)	2.0°	48.4°
MO diagram and Eigen value	 LUMO -12.46 kcal/mol	 next-LUMO -18.25 kcal/mol
Δ*E* in pyridine-complexation	-5 kcal/mol	-19 kcal/mol

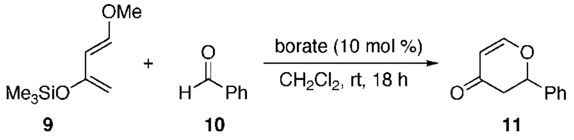
LUMO) shows a large and accessible lobe on boron while the corresponding lobe in **6** (LUMO in this case) is small and buried. The energy level of the MO of **4**B is lower than that of **6**. This energetic stabilization of the MO level comes from the large dihedral angle of **4**B; the lone pair on oxygens is not likely to delocalize with p_z orbital on boron (Scheme 2). Although geometric change on metal often causes change of Lewis acidity,[17] no change on the boron geometry in **4**B is interestingly found in our case. It is noted that geometry change of the ligand affects the Lewis acidity. The borate **4**B has much larger energetic stability $|\Delta E|$ in pyridine complexation than **6**. Those results directly suggest high Lewis acidity of the cage-shaped borate **4**B.

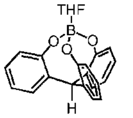
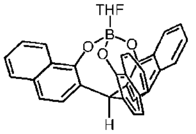
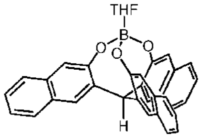
Scheme 2. Nonefficient π-Conjugation in the Cage-Shaped Borate



The ready pyridine-exchange on **4**B was observed by NMR. The equimolar mixture of the complex of **4**B·pyridine-d_5 with unlabeled pyridine gave the scramble (>90%) of ligands in 1 h at rt. This result strongly prompted us to find its catalytic use. We tested the catalytic activity of the borate **4**B for a typical Lewis acid-promoted reaction, hetero Diels−Alder reaction of Danishefsky's diene **9** with benzaldehyde **10** (Table 2).[18] When open-shaped borate **6** generated in situ was used, it showed no catalytic activity (entry 1).[19] We applied the borate **4**B·THF prepared in situ from 0.1 equiv of BH_3·THF and **4**H_3 (Figure 2), to the reaction and obtained the product **11** in 77% yield (entry 2).[20] This result suggests that the Lewis acid **4**B·THF can

Table 2. Borate-Catalyzed Hetero Diels−Alder Reaction[a]



entry	borate[b]		yield/ %
1	$B(OPh)_3$	**6**	7
2		**4**B·THF	77
3		**7**B·THF	75
4		**8**B·THF	41

[a] All reactions were performed using **9** (1.0 mmol), **10** (1.1 mmol), and borate (0.1 mmol) at rt for 24 h. [b] Borates were prepared in situ by mixing of 3PhOH, **4**H_3, **7**H_3, and **8**H_3 with BH_3·THF.

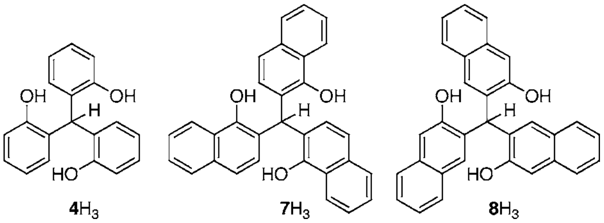


Figure 2. Triphenolic Methane Derivatives

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[16] The next-LUMO of 4**B** is the third lowest unoccupied MO (LUMOs are doubly degenerated) and most important for Lewis acid because the LUMOs are constructed by only π orbitals of phenoxy parts and have no significant contribution to boron p_z orbital.

[17] A structurally induced increase of Lewis acidity on metal has been reported. The distorted geometry on metal is preorganized. (a) Nelson, S. G.; Kim, B.-K.; Peelen, T. J. *J. Am. Chem. Soc.* **2000**, *122*, 9318−9319 and references cited therein. (b) Kobayashi, J.; Kawaguchi, K.; Kawashima, T. *J. Am. Chem. Soc.* **2004**, *126*, 16318−16319.

[18] (a) Danishefsky, S.; Kerwin, J. F.; Kobayashi, S. *J. Am. Chem. Soc.* **1982**, *104*, 358−360. (b) Hattori, K.; Yamamoto, H. *Synlett* **1993**, 129−130.

[19] The formation of $B(OPh)_3$ was confirmed as a ligand- free form by NMR in the reaction of three equivalent of phenol with BH_3·THF after evaporation. Although an interaction of THF could exist, the formula in Table 2 is shown as a ligand-free form. Actually, the reagent $B(OPh)_3$ also showed no catalytic activity under the same conditions with entry 1.

[20] When the pyridine complex **5** was used as a catalyst, a lower yield (32%) of **11** was observed in the reaction of **9** with **10**.

act as a catalyst. Neither **4**H_3 nor BH_3·THF gave the product on its own use. Interestingly, the naphthyl derivatives **7**B·THF and **8**B·THF also gave the product (entries 3 and 4).[21] It is noted that the cage-shaped catalyst can be tunable by varying the tether moieties.

In summary, we have demonstrated the cage-shaped borate with enhanced Lewis acidity and catalytic activity as compared with a normal open-shaped one. Further studies on modification of this simple carbon framework of the cage for other types of catalytic reactions are in progress.

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Supporting Information Available: Experimental procedures, listing of absolute energies and geometries for calculated species, and X-ray data for **5** (CIF). This material is available free of charge via the Internet at http://pubs.acs.org.

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[21] The naphthyl derivatives were generated from **7**H_3 or **8**H_3 (Figure 2) with borane and confirmed by NMR. The triphenolic ligands **7**H_3 or **8**H_3 were synthesized by the similar procedure with that of **4**H_3 except the reduction step using $HSiClMe_2$/cat. $InCl_3$ (see ref 3d and the Supporting Information).