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# Selective Binding of Diamines to a Chiral Lewis Acid with Two Boron Centers

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Recognition of some particular guests from their analogs is a subject of current interest. One of the most challenging targets in this area may be to distinguish guest molecules which have quite similar structures, flexible skeltons, and common functional groups. A host molecule with multifuncional groups may be one of the best candidates for this purpose.[1] Here, we report on two selective bindings of diamines to a chiral bimetallic Lewis acid **1**[2–4] and manifested by (1) a recognition of distance between the two nitrogen atoms in $H_2N(CH_2)_nNH_2$[5] and (2) the different binding manner between (*R,R*)-1,2-diamino-1,2-diphenylethane and its (*S,S*)-isomer.[6]

The Lewis acid **1** has been prepared from phenylboronic acid and L-tartaric acid by azeotropic distillation. Interaction of **1** with the diamines $H_2N(CH_2)_nNH_2$ ($2 \le n \le 6$) was first investigated, and the $^1H$ NMR spectra relevant to the 1:1 complexes are shown in Figure 1.[7] The characteristic features of these spectra are as follows: (1) The four amino $H^b$ and $H^c$ protons exhibit one broad peak when $n \le 3$, while two completely separated peaks are observed when $n \ge 5$. The two separated peaks are mutually coupled, meaning that the protons attached to one nitrogen atom have different chemical shifts. When $n = 4$, two barely separated peaks for $H^b$ and $H^c$ are seen.[8] (2) Only one singlet is obseved for the methine $H^a$ protons when $n \ge 5$. On the other hand, in addition to a similar singlet, a coupled-pair of doublets is shown for $H^a$ at $\delta = 4.7–4.9$ when $n = 1–4$.[9] Thus, there exists a structural difference in the complexes between $n \le 4$ and $n \ge 5$.

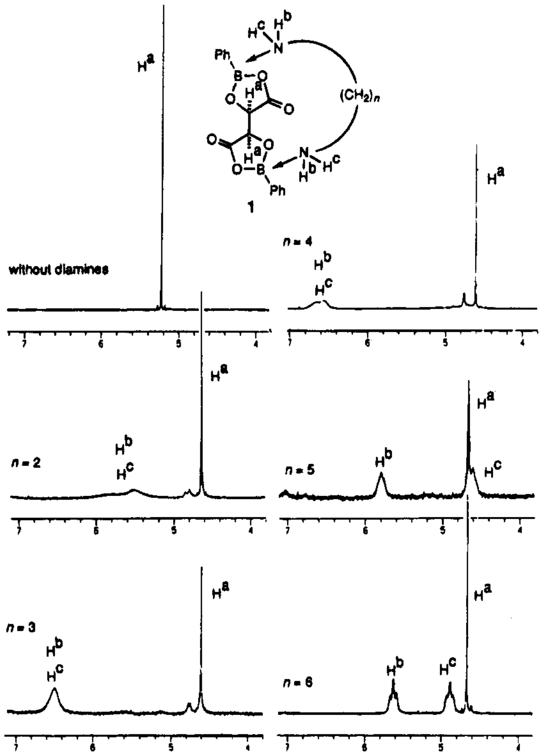

**Figure 1.** $^1H$ NMR spectra of 1:1 complexes of bimetallic Lewis acid **1** and diamines. The amino $H^b$ and $H^c$ protons exhibit different peak shapes for the $n \le 4$ and $n \ge 5$ systems.

As illustrated in Figure 2a, model studies of the 1:1 complex of **1** and 1,6-diaminohexane suggest the existence of two hydrogen bondings in addition to the Lewis acid–Lewis base attractions.[10] The hydrogen bonding binds one amino proton to the carbonyl oxygen of the other dioxaborolanone framework. The complex has an almost $C_2$ symmetric chiral structure, and the two methine $H^a$ protons are equivalent. The result is consistent with the observed singlet $^1H$ NMR peak for $H^a$. However, with 1,2-diaminoethane, the distance between the two amino groups seems to be too short for hydrogen bonding, and thus 1,2-diaminoethane may bind to **1** only with the Lewis acid–Lewis base attractions.[11,12]

A competition experiment has disclosed that 1,6-diaminohexane is favorably bound to the Lewis acid **1** compared to 1,2-diaminoethane. The experiment was carried out by adding **1** to a mixture of the two diamines in the ratio of $1{:}H_2N(CH_2)_6NH_2{:}H_2N(CH_2)_2NH_2 = 1{:}2{:}2$. The relative association constant at 22 °C, $K_{hex}/K_{eth}$ =

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[1] For example: (a) Lehn, J.-M. *Angew. Chem., Int. Ed. Engl.* **1988**, *27*, 89. (b) Diedrich, F. *Angew. Chem., Int. Ed. Engl.* **1988**, *27*, 362. (c) Cram, D. J. *Angew. Chem., Int. Ed. Engl.* **1988**, *27*, 1009. (d) Rebek, J., Jr. *Angew. Chem., Int. Ed. Engl.* **1990**, *29*, 245. (e) Kuroda, Y.; Kato, Y.; Ito, M.; Hasegawa, J.; Ogoshi, H. *J. Am. Chem. Soc.* **1994**, *116*, 10338. (f) Das, G.; Hamilton, A. D. *J. Am. Chem. Soc.* **1994**, *116*, 11139. (g) James, T. D.; Sandanayake, T. R. A. S.; Shinkai, S. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 2207. (h) *Inclusion Phenomena and Molecular Recognition*; Atwood, J. L., Ed.; Plenum Press: New York, 1990. (i) Vögtle, F. *Supramolecular Chemistry*; John Wiley & Sons: Chichester, 1991.

[2] (a) Vance, D. H.; Czarnik, A. W. *J. Am. Chem. Soc.* **1994**, *116*, 9397. (b) Mackay, L. G.; Wylie, R. S.; Sanders, J. K. M. *J. Am. Chem. Soc.* **1994**, *116*, 3141. (c) Simard, M.; Vaugeois, J.; Wuest, J. D. *J. Am. Chem. Soc.* **1993**, *115*, 370. (d) Katz, H. E. In *Inclusion Compounds*; Atwood, J. L., Davis, J. E. D., MacNicol, D. D., Eds.; Oxford University Press: Oxford, 1991; p 391.

[3] Nozaki, K.; Yoshida, M.; Takaya, H. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 2452.

[4] Recognition of primary amines by monometallic phenyl boronates: Reetz, M. T.; Niemer, C. M.; Harmes, M.; Goddard, R. *Angew. Chem., Int. Ed. Engl.* **1992**, *33*, 1017.

[5] (a) Recognition of bis(imidazole) by using two $Hg^{2+}$ centers: Mallik, S.; Johnson, R. D.; Arnold, F. H. *J. Am. Chem. Soc.* **1994**, *116*, 8902. (b) Recognition of bis(ammonium) by using bis-crown ether: Voyer, N.; Deschênes, D.; Bernier, J.; Roby, J. *J. Chem. Soc., Chem. Commun.* **1992**, 134.

[6] General chiral recognition, for example: (a) Corradini, R.; Dossena, A.; Impellizzeri, G.; Maccarrone, G.; Marchelli, R.; Rizzarelli, E.; Sartor, G.; Vecchio, G. *J. Am. Chem. Soc.* **1994**, *116*, 10267. (b) Qian, P.; Matsuda, M.; Miyashita, T. *J. Am. Chem. Soc.* **1993**, *115*, 5624. (c) Pathirana, S.; Neely, W. C.; Myers, L. J.; Vodyanoy, V. *J. Am. Chem. Soc.* **1992**, *114*, 1404. (d) Webb, T. H.; Suh, H.; Wilcox, C. S. *J. Am. Chem. Soc.* **1991**, *113*, 8554. (e) Sanderson, P. E. J.; Kilburn, J. D.; Still, W. C. *J. Am. Chem. Soc.* **1989**, *111*, 8314. (f) Jeong, K. S.; Muehldorf, A. V.; Rebek, J., Jr. *J. Am. Chem. Soc.* **1990**, *112*, 6144.

[7] With the diamines of $n = 2–4$, the 1:1 complex was rather insoluble in $CDCl_3$, and thus excess diamine was added to obtain a clear solution by increasing the solvent polarity. In these cases, nevertheless, only 1:1 complexes are seen by integration of $^1H$ NMR signals. With the diamines of $n = 5–6$, no excess diamine was required, and even if added, the excess did not affect the spectra of the 1:1 complexes.

[8] The two peaks are seen to be coupled to each other by a $^1H–^1H$ COSY study.

[9] The minor complex with a coupled-pair of doublets should have an unsymmetric structure. See ref 11.

[10] We tentatively assign the amino proton at the lower chemical shift, $H^b$, to the one which is involved in a hydrogen bonding.

[11] A structure without $C_2$ symmetry is calculated to be more stable than that shown in Figure 2b by 6.7 kcal/mol. This probably causes the minor complex to exhibit a coupled-pair of doublets for the methine $H^a$ protons. It is not clear why the more stable unsymmetric conformation is observed as a minor complex.

[12] 1,4-Diaminobutane may form a complex with a structure in between those of 1,2-diaminoethane and 1,6-diaminohexane.

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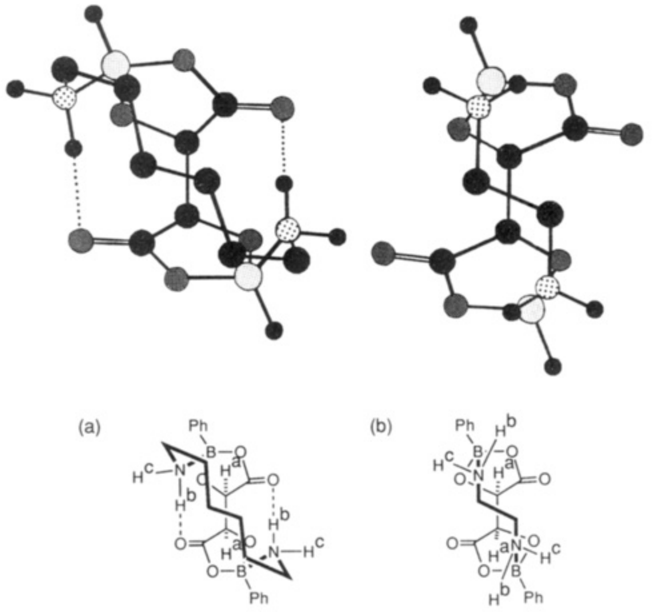


**Figure 2.** Optimized $C_2$ symmetric structures (AM1 of MOPAC ver. 6 in CAChe system) of 1:1 complexes of **1** and diamines with different chain lengths. Hydrogens other than amino protons are omitted. The phenyl group of **1** is replaced by hydrogens. (a) [**1**·1,6-diaminohexane]: two hydrogen bonds are shown in addition to two Lewis acid–Lewis base attractions. (b) [**1**·1,2-diaminoethane]: the two amino groups are too close to form stable hydrogen bonds, and the two molecules are bound by only two Lewis acid–Lewis base attractions.

4.26, has been obtained by $^1H$ NMR, where $K_{hex} = [\mathbf{1}\cdot H_2N(CH_2)_6NH_2]/[\mathbf{1}]\cdot[H_2N(CH_2)_6NH_2]$ and $K_{eth} = [\mathbf{1}\cdot H_2N(CH_2)_2NH_2]/[\mathbf{1}]\cdot[H_2N(CH_2)_2NH_2]$. The same value was obtained regardless of the order of amine addition, showing that the system is under a thermodynamic equilibrium.[13]

The suggested correlation between the $^1H$ NMR peak shapes of the amino protons and the existence of the hydrogen bondings is as follows. A 1:2 complex consisting of Lewis acid **1** and benzylamine exhibits two separated peaks at $\delta$ 5.20 and 5.58 for the four amino protons,[14] while a monometallic counter part **2**, derived from L-lactic acid and phenylboronic acid, gives a broad singlet peak at $\delta$ 5.50 for the amino protons in a 1:1 complex with benzylamine.[15] Formulas **3** and **4** show possible complex structures for **1** and **2** with benzylamine. In the monometallic complex **4**, an amino proton of benzylamine cannot form hydrogen bonding with the carbonyl oxygen because this would require an sp$^2$ carbon placed at the bridgehead position of the bicyclo[3.2.1] skeleton.

The bimetallic Lewis acid **1** recognizes the chirality of (*R,R*)-1,2-diamino-1,2-diphenylethane and the (*S,S*)-isomer. The Lewis acid **1** binds to (*R,R*)-isomer via the two boron–nitrogen interactions, and as shown in Figure 3a, the complex has $C_2$ symmetry as seen with 1,2-diaminoethane (Figure 1, $n = 2$). On the other hand, **1** binds to (*S,S*)-isomer by one boron–nitrogen interaction and one hydrogen bond. The complex is unsymmetrical, and the two methine protons of **1** couple to each other (Figure 3b).

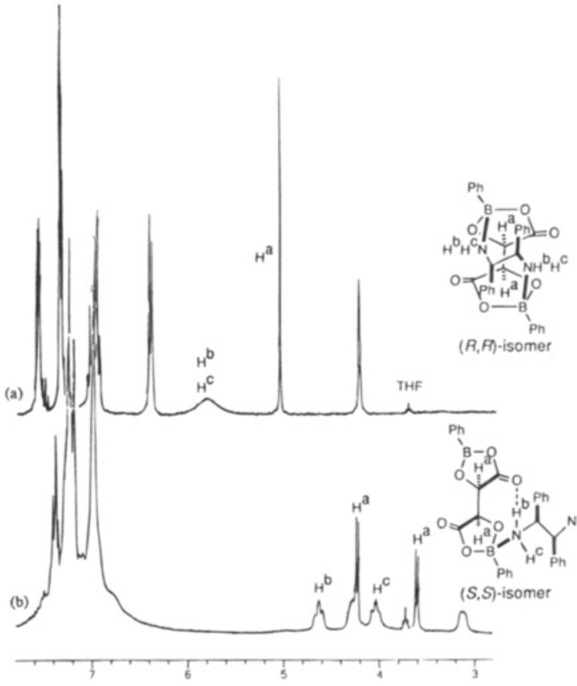
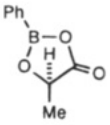
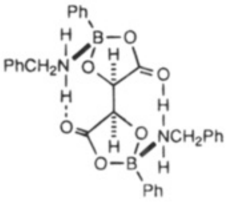


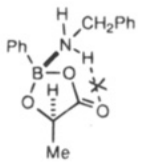
**Figure 3.** $^1H$ NMR spectra of 1:1 complexes of **1** and (*R,R*)- or (*S,S*)-1,2-diamino-1,2-diphenylethane. (a) (*R,R*)-Isomer: the two dioxaborolanone rings are equivalent, and two Lewis acid–Lewis base attractions are suggested. (b) (*S,S*)-Isomer: The two dioxaborolanone rings are nonequivalent, and one Lewis acid–Lewis base attraction and one hydrogen bonding are suggested.



**2**



**3**



**4**

Thus a chiral bimetallic Lewis acid **1** selects 1,6-diaminohexane over 1,2-diaminoethane by using two boron centers and two carbonyl oxygens. In the interaction with 1,2-diamino-1,2-diphenylethane, **1** chooses a different complexation pattern by recognizing the chiralities of the amines. In both cases, the carbonyl groups in **1** play essential roles as Lewis basic sites.

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**Supporting Information Available:** Preparation of Lewis acids **1** and **2** as well as spectral data are available (2 pages).

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[13] Since the entropy loss on forming a 1:1 complex with **1** and free diamine increases with the longer methylene chain between the two amino groups, the shorter diamine would be favorable for complexation if both the diamines bound with the same enthalpy gain. Thus, there should exist an additional enthalpy gain in the case of 1,6-diaminohexane, which we believe involves the hydrogen bonding.

[14] The two peaks are coupled to each other by a $^1H-^1H$ COSY study.

[15] The broad singlet due to the two amino protons of the monometallic complex [**2**·benzylamine] (**4**) has separated into two very broad peaks at −50 °C but the peak shapes are completely different from those seen in the sharp separation in the case of [**1**·benzylamine$_2$] (**3**). This may exclude the possibility of rapid equilibration between the two amino protons at 20 °C.