Effect of Benzylic Methyl Groups on Kinetic Basicity of Amine Ligand in *o*-Boron Substituted *N,N*-Dimethylbenzylamines

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Rates of the dissociation of the intramolecular B–N coordination bond in two series of phenylborane derivatives, the boronate and diethylborane complexes, with $-CHMeNMe_2$ or $-CMe_2NMe_2$ group at the *o*-position were determined by the NMR lineshape analysis or saturation transfer method. The new organoboron compounds were synthesized from the corresponding organolithium compounds with appropriate boron reagents. Comparison of the kinetic data with those of the $-CH_2NMe_2$ compounds reveals that the barrier height to the dissociation, namely the kinetic basicity of the amine ligand, is increased as the molecule possesses more methyl groups at the benzylic position for both of the series of boron compounds. The X-ray structure of one of the boronate complexes and the NMR titration measurements of model amines indicate that the basicity of the amine ligand is not affected much by the methyl substitution in the coordinated form. Therefore, the substituent effect on the kinetic basicity is mainly ascribed to the destabilization of the transition state by the geminal dimethyl groups rather than to any inductive or steric effects at the initial state, especially for the $-CMe_2NMe_2$ compounds.

The kinetic parameters for the dissociation of B–N coordination bonds were determined by the dynamic NMR method for a series of intramolecular borane–amine complexes, **1a**,[1,2] **2a**,[3] and **3**[4] (Chart 1). These data enabled us to discuss various factors influencing the kinetic basicity of amine ligands in the *o*-substituted *N,N*-dimethylbenzylamine system involving the solvent, substituent, and secondary kinetic isotope effects. As for the substituent effect, the influence of the *N*-alkyl groups has been well studied: For example, bulky alkyl groups reduce the Lewis basicity of the amine ligand due to the steric effect in both the boronate (**1a**) and 9-BBN (**3**) compounds.[1,4] However, the substituent effect at the benzylic position has been much less examined for the organoboron complexes.

Besides the wide application of 2-[1-(dimethylamino)-methyl]phenyl group (**4a**) as a *C,N*-bidentate ligand, the ligand carrying a methyl group at the benzylic position (**4b**) is occasionally used as a chiral ligand for organometallic complexes of Cu,[5] Sn,[6] Si,[7] and other metal atoms.[8] The ligand possessing two benzylic methyl groups (**4c**) is much less popular than **4b**. Yoshifuji et al. showed an example of this type of ligand, 4,6-di-*t*-butyl-2-[1-(dimethylamino)-1-methylethyl]phenyl group, for the protection of an unstable $-PS_2$ moiety.[9] They pointed out that the presence of the methyl groups enhanced the stability of the molecule. To see the effect of the benzylic substituents in the ligand system **4a**—**c** in detail, it is necessary to compare the properties of the compounds with the same functionality at the *o*-position. Therefore, we applied the methodology of the dynamic NMR spectroscopy to compounds **1** and **2** with various numbers of methyl groups at the benzylic position. The substituent effect on the kinetic basicity of the intramolecular amine ligand is discussed on the basis of the kinetic data of the dissociation of the B–N bond together with other related experimental data.

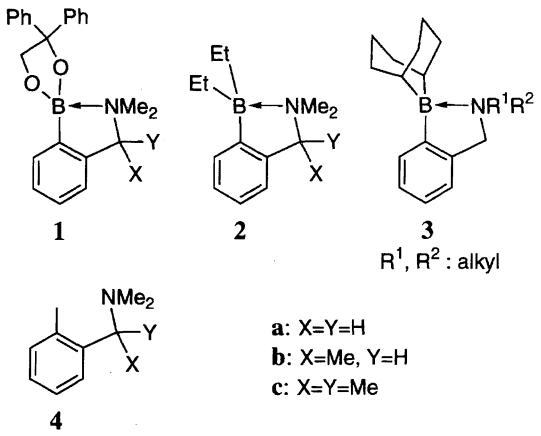
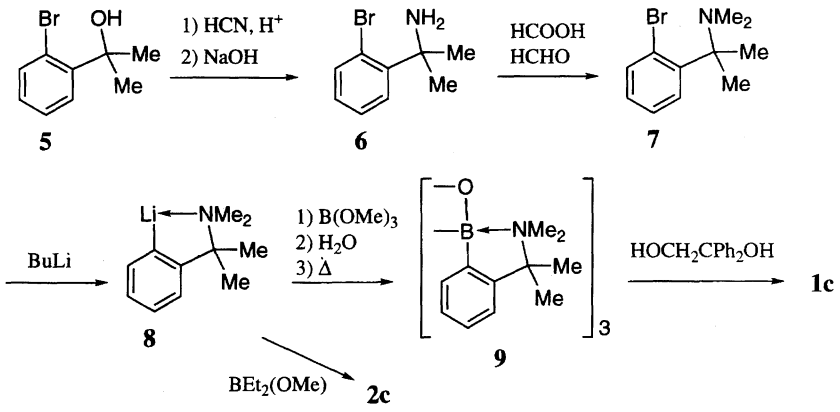


Chart 1.

Results

Synthesis. Compound **1b** was prepared from the corresponding boroxine[10] and 1,1-diphenyl-1,2-ethanediol in an ordinary manner. **2b** was obtained by the reaction of 2-[1-(dimethylamino)ethyl]phenyllithium[10] with $BEt_2(OMe)$.

The bromide **7**, a precursor of **1c** and **2c**, was synthesized according to the route shown in Scheme 1. The tertiary alcohol **5**[11] was converted into the corresponding amine by the Ritter reaction, namely the reaction with HCN in H_2SO_4, followed by the hydrolysis of the formed formamide under basic conditions, in a good yield. The *N*-methylation of **6** with formaldehyde and formic acid gave **7**.



Scheme 1.

The halogen–lithium exchange of **7** with butyllithium gave the organolithium compound **8**, which was then treated with trimethyl borate to form the boroxine **9** after aqueous workup followed by heating. The reaction of **9** with 1,1-diphenyl-1, 2-ethanediol afforded **1c**. **2c** was similarly prepared from **8** and $BEt_2(OMe)$.

X-Ray Structure. The structure of **1c** was analyzed by X-ray crystallography. An ORTEP drawing is shown in Fig. 1 together with important structural parameters in the figure caption. The tetrahedral character of the boron atom,[12] calculated from the bond angles around the boron atom, is 53%.

Dynamic NMR Measurement. The dynamic processes observable in **1b**, **1c**, and **2b** are illustrated in Scheme 2. Each compound carries an appropriate probe for the observation of the site exchange by ^{1}H NMR, which is completed by the dissociation of the B–N coordination bond followed by the rotation around the B–C_{Ph} bond or the nitrogen inversion, and then the recoordination. As discussed in the previous papers, the bond dissociation is the rate-limiting step in the overall dynamic process for **1a** and **2a**, in which the bond rotation and the N inversion takes place rapidly after the dissociation of the coordination bond.[1,3] The MO calculations suggest that this energy relationship holds for the compounds in Scheme 2. The rotational barrier around the B–C bond is low: 4.5 kcal mol^{-1} (1 cal = 4.184 J) in a model compound of **1c**.[13] Therefore, the rates of the dissociation determined by measuring those of the site exchange are those for the B–N dissociation.

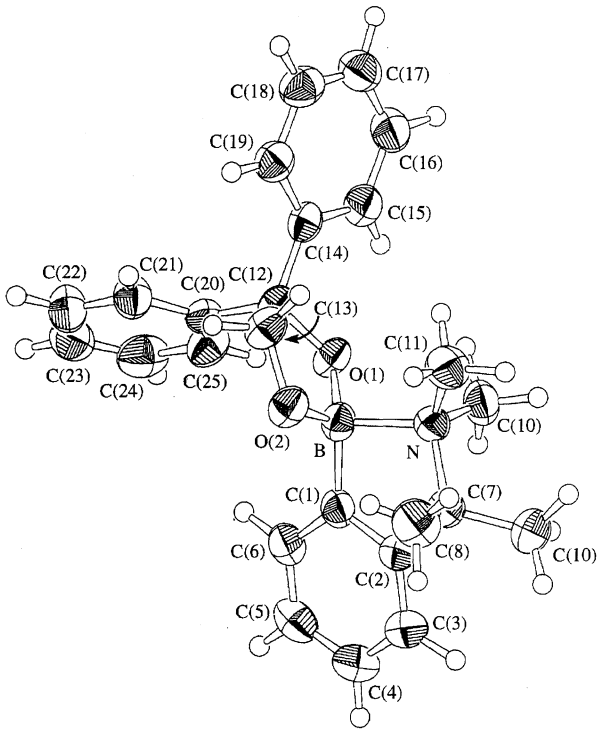
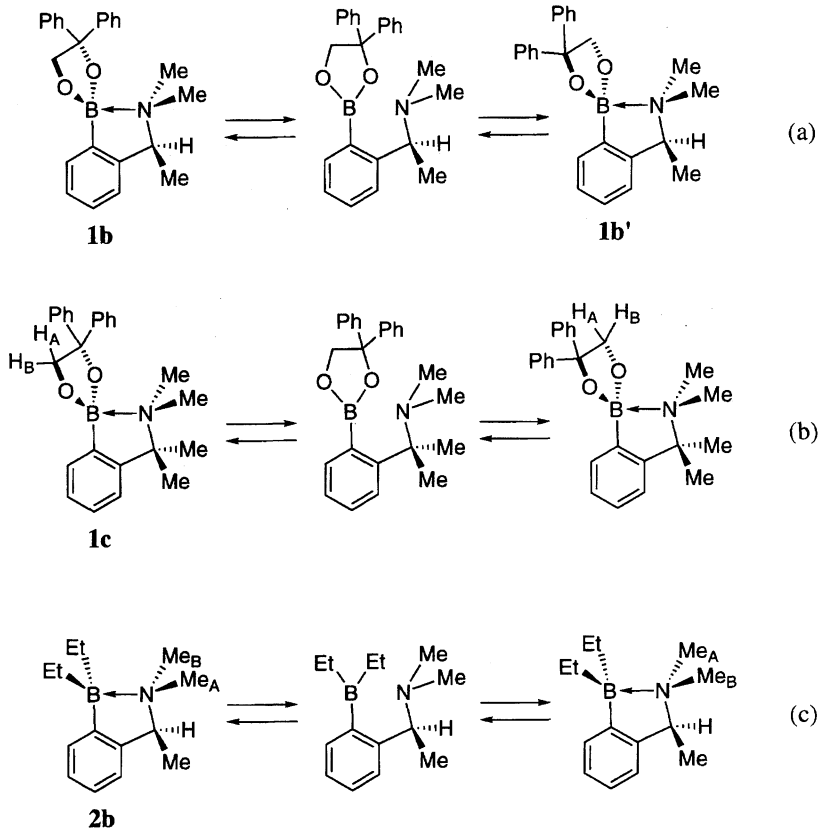


Fig. 1. An ORTEP drawing of **1c** (50% probability ellipsoids). Selected structural parameters: B–N 1.747(2), B–C-(1) 1.596(3), B–O(1) 1.436(2), B–O(2) 1.435(2) Å, N–B–C-(1) 95.4(1), N–B–O(1) 106.9(1), N–B–O(2) 110.3(1)°, tetrahedral character[12] 53%.

All the ^{1}H NMR signals of **1b** were broad at room temperature in toluene-d_8. As the temperature was lowered, these signals decoalesced and finally separated into two sets of signals in 1.21 : 1 ratio, these being attributable to the two diastereomeric coordinated forms, **1b** and **1b′** (Scheme 2(a)). The lineshape changes of the signal due to the benzylic methyl protons (*C*–Me) were analyzed to afford the kinetic parameters for the dissociation of the B–N bond.

The signal due to the methylene protons in the dioxaborolane ring (*O*–CH_2) of **1c** was observed as an AB quartet (H_A and H_B in Scheme 2(b)) at room temperature. This signal broadened and coalesced as the temperature was raised. During the temperature change, similar line shape changes were observed for both the *N*–Me and *C*–Me signals. The lineshape analysis was carried out by use of the *O*–CH_2 probe in various solvents.

Compound **2b** gave two singlets for the *N*–Me protons (Me_A and Me_B in Scheme 2(c)) at room temperature; these showed no lineshape change even though the sample was heated up to 140 °C in 1,1,2,2-tetrachloroethane-d_2 ($C_2D_2Cl_4$). Because the exchange takes place much slower than the time scale of the dynamic NMR method at the temperature, we applied the saturation transfer method.[14,15] The transfer of magnetization was observed at one of the *N*–Me signals on the irradiation of the other one. The rate of the dissociation was determined by the analysis to be 0.46 s^{-1} at



Scheme 2.

128 °C, corresponding to 24.3 kcal mol^{-1} in the free energy of activation.

For **2c**, the signals due to the ethyl–methylene protons were observed as complicated multiplets, an AB part of the ABX_3 system with a further coupling with ^{11}B, at room temperature. This signal pattern remained unchanged during the temperature change up to 140 °C in $C_2D_2Cl_4$. The observation indicates that the coordination bond is still tight at the high temperatures relative to the NMR time scale. The barrier height of the dissociation is estimated to be more than 25.0 kcal mol^{-1}.

These kinetic data were compiled in Table 1 together with those of **1a** and **2a** reported in the literature.[1,3]

NMR Titration. The relative basicity of *N,N*-dimethylbenzylamines **10** was determined by the NMR titration method (Chart 2).[16,17] A 1 : 1 mixture of two amines was titrated with trifluoroacetic acid or BF_3 in $CDCl_3$: The chemical shift of an appropriate signal was monitored as a small amount of the acid was added. The data analysis provided

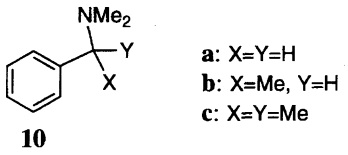


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Chart 2.

Table 1. Kinetic Parameters for Dissociation of B–N Coordination Bond in **1** and **2**[a)]

Compound	Solvent	$\Delta H^{\neq}$ / kcal mol^{-1}	$\Delta S^{\neq}$ / cal mol^{-1}·K^{-1}	$\Delta G^{\neq}_{323}$ / kcal mol^{-1}
1a[b)]	Toluene-d_8	14.4±0.3	14.6±1.0	9.7
1b[c)]	Toluene-d_8	16.9±0.3	14.2±1.2	12.3
1c	Toluene-d_8	17.8±0.6	5.0±1.9	16.2
1c	$C_2D_2Cl_4$[d)]	19.4±0.3	4.9±0.8	17.8
1c	DMSO-d_6	21.0±0.4	8.1±1.1	18.4
2a[e)]	$C_2D_2Cl_4$	14.2±0.4	−16.2±1.1	19.4
2b[f)]	$C_2D_2Cl_4$			24.3 at 401 K
2c	$C_2D_2Cl_4$			>25.0

a) 1 cal = 4.184 J. Unless otherwise mentioned, the data were determined by the NMR lineshape analysis method. b) Ref. 1. c) Kinetic data of isomerization from the major to minor isomers. d) 1,1,2,2-tetrachloroethane-d_2. e) Ref. 3. f) Determined by the saturation transfer method.

Table 2. Difference in pK_a Values of Complexes or Conjugated Acids of Amines **10** against BF_3 and Proton Acid in $CDCl_3$ Determined by the NMR Titration Method[a)]

Amines	$\Delta pK_a(BF_3)$	$\Delta pK_a(CF_3COOH)$
10a	0	0
10b	0.22	0.21
10c	0.24	0.23

a) The pK_a value of the complex or conjugated acid of *N*,*N*-dimethylbenzylamine (**10a**) is the standard for each acid indicated in the parentheses.

the difference in pK_a values (ΔpK_a) between the conjugated acids of two amines (see Experimental). The results are listed in Table 2.

Discussion

In the boronate complexes (**1**), the more methyl groups at the benzylic position in the ligand, the larger the free energy of activation for the dissociation of the B–N bond. In other words, the kinetic basicity of the amine ligand is enhanced as the benzylic hydrogens are replaced by methyl groups. The effect caused by the second methyl group (3.9 kcal mol^{-1}) is larger than that caused by the first one (2.6 kcal mol^{-1}). The diethylboranes (**2**) also showed a similar tendency, although the kinetic information is not quantitative due to experimental limitations.

To interpret the substituent effect, factors at both the initial and transition states should be taken into consideration. In the coordinated form, the inductive and steric effects influence the basicity in the opposite directions. The methyl group at the benzylic position increases the basicity of benzylamines by the inductive effect, as indicated by the pK_a values of their conjugated acids determined by the classical potentiometric measurements in aqueous media: benzylamine (9.37),[18] 1-phenylethylamine (9.47),[19] and 1-methyl-1-phenylethylamine (10.28).[20] On the contrary, the steric effect often works so as to weaken the basicities of sterically crowded amines. This effect, known as the F-strain, is common in Lewis acid-base reactions.[21—23]

Although it is difficult to estimate the contribution of each factor mentioned above from available kinetic data, other experimental results give a few clues for the further discussion. The X-ray data show that the structural parameters around the B–N coordination bond of **1c** are very similar to those of **1a** (B–N 1.754 Å, THC 51%).[12] We proposed that the tetrahedral character (THC) was well correlated with the strength of coordination bonds in variety of organoboron complexes. The THC of **1c** (53%) is almost the same as that of **1a**, indicating that the coordination bonds in the two compounds are of comparable strength.

The data of the NMR titration measurements in Table 2 allow us to compare the base strength of amines in thermodynamic equilibrium in organic solvents. Regardless of the size of the acid, borane or proton, the basicity is increased by ca. 0.2 in the pK_a units by the first substitution of a hydrogen by a methyl group at the benzylic position in *N*,*N*-dimethylbenzylamine, and further substitution has a very small effect. The difference between the pK_a values of **10a** and **10c** is only 0.23 units, corresponding to 0.3 kcal mol^{-1} in the ΔG difference for the acid-base dissociation at 298 K. This small value means that the thermodynamic basicity of *N*,*N*-dimethylbenzylamines is only slightly enhanced by the benzylic methyl groups.

From the above discussion, we consider that the inductive effect to strengthen the basicity is almost, if not completely, canceled by the steric effect at the initial state of **1c**. Hence, the strong coordination bond in **1c** with respect to **1a** can be explained by the fact that the transition state is destabilized more than the initial state. At the transition state, the nitrogen atom moves away from the boron atom enough to facilitate the B–C bond rotation as well as the nitrogen inversion. The steric interaction between the dioxaborolane ring and the substituted dimethylaminomethyl group is still significant in such a structure for **1c**, because the latter group is comparable in size to a *t*-butyl group. The steric effect is expected to be less important for the monomethyl compound **1b**, where the inductive effect at the initial state plays some role in the overall effect. The substituent effect for the diethylborane complexes (**2**) is similarly explained.

We come back to the discussion of the kinetic data in Table 1. There are two points, the solvent effect and the entropy of activation ($\Delta S^{\neq}$), that are worth mentioning in relation to the mechanism of the bond dissociation. The barrier to dissociation is clearly high in polar solvents for **1c**: This tendency is common to other complexes, **1a** and **3**.[1,4] This solvent effect is understood by the fact that the polar-coordinated form is stabilized by solvation in polar solvents better than the transition state, which is less polar. Another feature is the $\Delta S^{\neq}$ value for **1c**, which is still positive but significantly smaller than those for **1a** and **1b**. This is mainly a result of the increase of the entropy at the initial state due to the loose solvation by solvent molecules toward bulky substrates.

In conclusion, the kinetic basicity of the amine ligand toward the *o*-boron atom is strengthened by the methyl substitution at the benzylic position in the 2-[1-(dimethylamino)-methyl]phenyl system. The substituent effect mainly results from the destabilization of the incipient dissociated form at the transition state by the steric effect. In particular, 2-[1-(dimethylamino)-1-methylethyl]phenyl group (**4c**) should be useful as a bulky and strongly coordinating ligand for the syntheses of other metal complexes.

Experimental

^1H NMR spectra were measured on a Varian Gemini-300 and a Bruker ARX-400 spectrometers operating at 300 and 400 MHz, respectively. ^{11}B NMR spectra were measured on the Bruker machine at 128.4 MHz with external reference of $BF_3 : OEt_2$ peak at 0 ppm. Melting points were measured in a glass capillary on a heating block, and are uncorrected. Elemental analyses were performed by a Perkin–Elmer 240C analyzer. High-resolution mass spectra were measured on a JEOL JMS-700 MStation spectrometer. The syntheses and measurements of **1a**[1] and **2a**[3] were reported earlier.

2-{2-[1-(Dimethylamino)ethyl]phenyl}-4,4-diphenyl-1,3,2-

dioxaborolane (1b). A solution of 400 mg (2.07 mmol) of tris{2-[1-(dimethylamino)ethyl]phenyl}boroxine[10] and 443 mg (2.07 mmol) of 1,1-diphenyl-1,2-ethandiol[24] in 30 mL of toluene was refluxed in a flask equipped with a Dean–Stark apparatus for 3 h. The solvent was evaporated, and the residue was recrystallized from hexane-dichloromethane to afford 765 mg (99%) of the product. Mp 127.0—127.5 °C. Found: C, 77.54; H, 7.13; N, 3.91%. Calcd for $C_{24}H_{26}BNO_2$: C, 77.64; H, 7.06; N, 3.77%. ^{1}H NMR (toluene-d_8, 47 °C) δ = 1.17 (3H, d, J = 6.9 Hz), 2.10 (6H, s), 3.85 (1H, q, J = 6.9 Hz), 4.79 and 4.86 (2H, ABq, J = 8.1 Hz), 7.03 (1H, m), 7.19 (1H, m), 7.24—7.28 (2H, m), 7.33—7.41 (5H, m), 7.63 (1H, m), 7.81—7.86 (4H, m). ^{11}B NMR ($CDCl_3$) δ = 14.2 (linewidth $h_{1/2}$ 233 Hz). At a low temperature, the two diastereomers were observed separately in the ratio of 1.21 : 1. The aliphatic signals for each isomer are as follows. ^{1}H NMR (toluene-d_8, −28 °C) δ = 0.99 (3H, d, J = 6.5 Hz), 1.99 (3H, s), 2.01 (3H, s), 3.80 (1H, q, J = 6.4 Hz), 4.58 and 5.13 (2H, ABq, J = 8.9 Hz) for the major isomer, and δ = 1.06 (3H, d, J = 6.5 Hz), 1.86 (3H, s), 2.09 (3H, s), 3.66 (1H, q, J = 6.5 Hz), 4.63 and 5.08 (2H, ABq, J = 8.4 Hz) for the minor. The assignment of the diastereomers by NOE experiment was unsuccessful. The major and minor isomers are tentatively assigned to **1b** and **1b′**, respectively, from a general expectation from the steric interaction between the benzylic methyl group and the phenyl groups in the dioxaborolane ring.

{2-[1-(Dimethylamino)ethyl]phenyl}diethylborane (2b). A solution of 2-[1-(dimethylamino)ethyl]phenyllithium in ether was prepared from 3.00 g (20.1 mmol) of (±)-*N*,*N*-dimethyl-1-phenylethylamine, 15.8 mL (25.5 mmol) of a 1.5 mol L^{-1} solution of butyllithium in hexane, and 3.80 mL (25.4 mmol) of *N*,*N*,*N*′,*N*′-tetramethylethylenediamine by the literature method.[10] To a three-necked flask charged with 5 mL of dry ether were added the organolithium solution and 30.0 mL (30 mmol) of a 1.0 mol L^{-1} solution of diethylmethoxyborane in THF (Aldrich Co.) from respective dropping funnels at room temperature under a nitrogen atmosphere. After the addition was completed, the mixture was refluxed for 20 h. The volatile materials were removed by evaporation, and the residue was extracted with dichloromethane. The crude material was purified by bulb-to-bulb distillation under reduced pressure. The desired compound was obtained as colorless oil in 15% yield. Bp 110 °C (bath temp)/0.4 mmHg (1 mmHg = 133.322 Pa). HRMS (FAB) Found: MH$^+$, m/z 218.2099. Calcd for $C_{14}H_{24}BN$: MH, 218.2080. ^{1}H NMR ($CDCl_3$) δ = 0.28 (1H, m), 0.49 (1H, m), 0.60 (1H, m), 0.70 (3H, t, J = 7.5 Hz), 0.73 (1H, m), 0.95 (3H, t, J = 7.5 Hz), 1.42 (3H, d, J = 6.8 Hz), 2.15 (3H, s), 2.57 (3H, s), 4.31 (1H, q, J = 6.8 Hz), 6.96 (1H, d, J = 7.2 Hz), 7.11 (1H, dt, J = 1.4 and 7.2 Hz), 7.17 (1H, t, J = 7.2 Hz), 7.24 (1H, d, J = 7.2 Hz). ^{11}B NMR ($CDCl_3$) δ = 6.9 (line width $h_{1/2}$ 177 Hz).

2-(2-Bromophenyl)-2-propanol (5). This compound was synthesized from methyl 2-bromobenzoate and methylmagnesium iodide in an ordinary manner. Bp 126—128 °C/17 mmHg (lit, 78 °C/0.3 mmHg).[11] ^{1}H NMR ($CDCl_3$) δ = 1.75 (6H, s), 2.79 (1H, s), 7.09 (1H, dt, J = 1.6 and 7.6 Hz), 7.29 (1H, dt, J = 1.1 and 7.6 Hz), 7.58 (1H, dd, J = 1.3 and 8.0 Hz), 7.66 (1H, dd, J = 1.6 and 8.0 Hz).

1-(1-Amino-1-methylethyl)-2-bromobenzene (6). To 12.9 mL of acetic acid were added 5.70 g (0.12 mol) of sodium cyanide in small portions and then a cooled solution of 13.9 mL (0.25 mol) of sulfuric acid in 12.8 mL of acetic acid in a hood. During the addition, the temperature of the mixture was kept at 20—35 °C. To the solution was slowly added 16.5 g (0.077 mol) of **5** from a dropping funnel. The whole was stirred for 24 h at 35—45 °C. After the passage of nitrogen gas through the mixture for 2 h to remove HCN, the mixture was basified with 30% aqueous NaOH. The reaction mixture was filtered and the white solid was washed with 500 mL of ether. The aqueous filtrate was further extracted with 100 mL of ether. The combined organic solution was dried over $MgSO_4$ and the solvent was evaporated. The residue was recrystallized from hexane–dichloromethane to give 15.6 g (84%) of the formamide as colorless crystals. *N*-[1-(2-Bromophenyl)-1-methylethyl]formamide: Mp 86.5—87.5 °C. Found: C, 49.61; H, 5.00; N, 5.79%. Calcd for $C_{10}H_{12}BrNO$: C, 49.67; H, 5.05; N, 5.65%. The ^{1}H NMR spectrum indicated the presence of the *Z*- and *E*-forms in 1 : 0.64 ratio, which were assignable by the $^3J_{HH}$ value between the N–H and formyl protons. (*Z*)-form: ^{1}H NMR ($CDCl_3$) δ = 1.84 (6H, s), 6.09 (1H, br s), 7.09 (1H, dt, J = 1.7 and 7.6 Hz), 7.30 (1H, dt, J = 1.3 and 7.6 Hz), 7.54 (1H, dd, J = 1.5 and 8.0 Hz), 7.56 (1H, dd, J = 1.3 and 7.8 Hz), 8.06 (1H, d, J = 1.6 Hz). (*E*)-form: ^{1}H NMR ($CDCl_3$) δ = 1.83 (6H, s), 6.53 (1H, br m), 7.15 (1H, dt, J = 1.5 and 7.6 Hz), 7.31 (1H, dt, J = 1.3 and 7.6 Hz), 7.51 (1H, dd, J = 1.5 and 8.0 Hz), 7.64 (1H, dd, J = 1.3 and 7.8 Hz), 8.00 (1H, d, J = 12.3 Hz). The formamide (15.6 g or 64 mmol) was heated in 150 mL of 20% aqueous sodium hydroxide under reflux for 24 h. After cooling, the reaction mixture was extracted with 150 mL of benzene. The organic layer was separated, washed with aqueous NaCl, and dried over $MgSO_4$. The solvent was evaporated and the distillation of the residue gave 13.3 g (97%) of the desired compound as colorless oil. Bp 92—93 °C/0.9 mmHg. HRMS (EI, M$^+$) Found: m/z 213.0138. Calcd for $C_9H_{12}BrN$: M, 213.0153. ^{1}H NMR ($CDCl_3$) δ = 1.65 (6H, s), 2.07 (2H, s), 7.06 (1H, dt, J = 1.6 and 7.5 Hz), 7.26 (1H, dt, J = 1.5 and 7.6 Hz), 7.58 (1H, dd, J = 1.7 and 8.1 Hz), 7.59 (1H, dd, J = 1.4 and 7.8 Hz).

1-Bromo-2-[1-(dimethylamino)-1-methylethyl]benzene (7). A solution of 13.3 g (62 mmol) of **6** in a mixture of 11.7 mL (0.31 mol) of formic acid and 11.3 mL (0.14 mol) of 35% formaldehyde was heated under reflux for 6 h. The reaction mixture was basified with 20% aqueous potassium hydroxide and extracted with 300 mL of ether. The organic layer was separated and dried over $MgSO_4$. The solvent was evaporated and the residue was distilled under a reduced pressure to give 8.7 g (58%) of the desired compound. Bp 69.0—70.5 °C/0.3 mmHg. HRMS (EI, M$^+$) Found: m/z 241.0438. Calcd for $C_{11}H_{16}BrN$: M, 241.0466. ^{1}H NMR ($CDCl_3$) δ = 1.47 (6H, s), 2.16 (6H, s), 7.02 (1H, dt, J = 1.6 and 7.6 Hz), 7.22 (1H, dt, J = 1.3 and 7.6 Hz), 7.51 (1H, dd, J = 1.5 and 7.9 Hz), 7.59 (1H, dd, J = 1.2 and 7.7 Hz).

Tris{2-[1-(dimethylamino)-1-methylethyl]phenyl}boroxine (9). To a solution of 4.00 g (16.4 mmol) of 1-bromo-2-[1-(dimethylamino)-1-methylethyl]benzene in 40 mL of dry ether was added 12.2 mL (19.7 mmol) of a 1.5 mol L^{-1} solution of butyllithium in hexane at −78 °C under a nitrogen atmosphere. The solution was allowed to warm up to room temperature and then stirred for 2 h. To a three-necked flask charged with 5 mL of dry ether were added the organolithium solution and a solution of 3.6 mL (32 mmol) of trimethyl borate in 10 mL of ether from respective dropping funnels at −78 °C under a nitrogen atmosphere. This reaction mixture was slowly warmed up to room temperature, stirred for 24 h at the temperature, and then heated under reflux for 1 h. The volatile materials were evaporated and the residue was treated with 3 mL of dichloromethane and 3 mL of water with stirring for 2 h. This mixture was extracted with dichloromethane, and the organic solution was dried over $MgSO_4$. The evaporation of the solvent gave the crude boronic acid, which was heated in toluene in a flask equipped with a Dean–Stark apparatus for 3 h. The solvent was evaporated, and the residue was recrystallized from hexane–dichloromethane to give 0.90 g (26%) of the boroxine. Mp 231.0—

232.0 °C. HRMS (FAB, MH^+) Found: *m/z* 568.4059. Calcd for $C_{33}H_{48}B_3N_3O_3$: MH, 568.4070. ^{1}H NMR ($CDCl_3$) δ = 1.42 (18H, s), 2.32 (18H, s), 7.05 (3H, d, J = 7.4 Hz), 7.15 (3H, t, J = 7.4 Hz), 7.22 (3H, t, J = 7.0 Hz), 7.68 (3H, d, J = 6.8 Hz).

2-{2-[1-(Dimethylamino)-1-methylethyl]phenyl}-4,4-diphenyl-1,3,2-dioxaborolane (1c). A solution of 200 mg (0.97 mmol) of the boroxine (**9**) and 208 mg (0.97 mmol) of 1,1-diphenyl-1,2-ethandiol in 40 mL of toluene was heated in a flask equipped with a Dean–Stark apparatus for 3 h. The solvent was evaporated, and the residue was recrystallized from hexane-dichloromethane. The yield was 298 mg (89%). Mp 177.0—178.0 °C. Found: C, 77.93; H, 7.32; N, 3.64%. Calcd for $C_{25}H_{28}BNO_2$: C, 78.04; H, 7.44; N, 3.58%. ^{1}H NMR ($CDCl_3$) δ = 1.52 (3H, s), 1.55 (3H, s), 2.28 (3H, s), 2.39 (3H, s), 4.25 and 4.38 (2H, ABq, J = 8.8 Hz), 6.99—7.32 (12H, m), 7.51 (2H, d, J = 7.3 Hz), 7.58 (2H, d, J = 7.3 Hz). ^{11}B NMR ($CDCl_3$) δ = 14.3 (linewidth $h_{1/2}$ 253 Hz).

{2-[1-(Dimethylamino)-1-methylethyl]phenyl}diethylborane (2c). This compound was similarly prepared as **2b** from 1.0 g (4.1 mmol) of 1-bromo-2-[1-(dimethylamino)-1-methylethyl]benzene and 7.40 mmol of diethylmethoxyborane. Recrystallization of the crude material from hexane–dichloromethane gave 136 mg (13%) of the desired compound as colorless crystals. Mp 93.5—94.0 °C. HRMS (EI, M^+) Found: *m/z* 231.2189. Calcd for $C_{15}H_{26}BN$: M, 231.2161. ^{1}H NMR (DMSO-d_6) δ = 0.50 (4H, m), 0.80 (6H, t, J = 7.5 Hz), 1.44 (6H, s), 2.35 (6H, s), 7.02—7.05 (4H, m).

X-Ray Crystallography of 1c.[25] A crystal used for the X-ray measurement was grown from a hexane–dichloromethane solution and its size was 0.35×0.20×0.15 mm^3. X-Ray measurements were performed on a Rigaku AFC7R four circle diffractometer with Cu $K\alpha$ radiation (λ = 1.54178 Å). The scan mode was the ω–2θ method and the scan rate was 16.0° min^{-1}. The scan range was calculated by 1.84° + 0.30° tan θ. The structure was solved by the direct method and refined by the full-matrix least-squares method by using a TEXSAN program. Anisotropic thermal parameters were employed for non-hydrogen atoms and isotropic ones for hydrogens. The reflection data were corrected for the Lorentz and polarization effects and for secondary extinction. Total number of measured unique reflections was 3355 in the range of $2° < 2\theta < 120°$; 2890 reflections within $|F_o| > 2\sigma(F_o)$ were used for the structure determination and refinement. The function minimized was $\sum[w(|F_o| - |F_c|)^2]$, where $w = [\sigma_c^2|F_o|]^{-1}$. Formula $C_{25}H_{28}BNO_2$, F.W. 385.31, Monoclinic, Space group $P2_1/n$, a = 11.954(2), b = 9.788(2), c = 18.300(2) Å, β = 99.534(10)°, V = 2111.7(5) Å^3, Z = 4, D_c = 1.21 g cm^{-3}, μ = 5.86 cm^{-1}, R 0.046, R_w 0.058.

NMR Lineshape Analysis.[25] The ^{1}H NMR spectra at various temperatures were measured by the 400 MHz instrument. Temperatures were read from a thermocouple after it was calibrated for chemical shift differences of the methanol or ethylene glycol signals. The samples were prepared by the dissolution of ca. 2 mg of a compound in 0.6 ml of a solvent. The total lineshape analysis was performed by DNMR3K program.[26] The lineshapes were analyzed as an AB$\rightleftarrows$BA system for the *O*–CH_2 protons in **1c** and as an exchange between two sites of A_3X systems for the benzylic methyl protons in **1b**. Chemical shift differences and coupling constants were measured at several temperatures where the exchange was very slow. The chemical shift differences were assumed to be correlated with the temperature linearly. The coupling constants were independent of the temperature for both the compounds. Because the population of the diastereomers of **1b** was not much affected by the temperature, the value at −28 °C (1.21 : 1) was input for all the simulations. Spin–spin relaxation times (T_2's) were estimated from the lineshapes at the slow exchange limit and from the linewidths of other signals which has no relation with the site exchange. The rate constants are listed in Table 3. Compounds **2b** and **2c** did not show lineshape changes in $C_2D_2Cl_4$ in the temperature range from room temperature to 140 °C.

Saturation Transfer Measurement. About 5 mg of **2b** was dissolved in 0.7 mL of $C_2D_2Cl_4$, and the solution was degassed in a routine manner. The measurement was carried out by the 400 MHz instrument, and the sample temperature was set at 128 °C. The 180° pulse was applied for 34.8 μs for the *N*–Me signals at the temperature. The spin-lattice relaxation time of the *N*–Me signals was measured by the inversion-recovery method, the observed value (T_{1eff}) being 1.9 s. The intensity ratio of the signal due to the *N*–Me signal at the higher magnetic field (δ = 2.2) with and without the saturation of the other *N*–Me signal (δ = 2.6), namely the remaining magnetization (M/M_0), was 0.565. These experimental values were put into the following simultaneous equations: $M/M_0 = (1 + k^*T_1)^{-1}$ and $T_{1eff}^{-1} = T_1^{-1} + k^*$, where k^* is the rate of the exchange between the two *N*–Me signals and T_1 the theoretical spin-lattice relaxation time, to give k^* = 0.23 s^{-1} and T_1 = 3.4 s. The rate of the dissociation of the B–N bond was 0.46 s^{-1}, the double of k^*, because the site exchange should take place at the rate of half of the dissociation.

NMR Titration Experiment.[25] Amines **10a** and **10b** were purchased from Tokyo Kasei Co. and Aldrich Co., respectively, and **10c** was prepared by the known method.[28] A mixture of two amines (150 mmol each) was dissolved in ca. 0.60 mL of $CDCl_3$ containing 0.03% of TMS as an internal standard in an NMR sample tube. The ^{1}H NMR chemical shifts were recorded by the 300 MHz instrument at 22 °C after each addition of ca. 30 mmol of trifluoroacetic acid in a small amount of $CDCl_3$ until the neutralization was completed. The titration with BF_3 was similarly performed with the use of a solution of $BF_3 : OEt_2$, where the presence of ether had little effect on the complexation with amines. The signals due to the *N*–Me, benzylic methyl, or benzylic protons were monitored during the titration. The ratio of acidity constant of the protonated (complexed) species of amine A relative to amine B, K, is expressed

Table 3. Rate Constants of Dissociation of B–N Coordination Bonds in **1b** and **1c**

Compound	Solvent	k/s^{-1} (temp/°C)
1b[a]	Toluene-d_8	24.3(−17.9), 37.6(−14.5), 57.5(−11.1), 90.6(−7.7), 139(−4.2), 210(−0.8), 298(2.6), 464(6.0)
1c	Toluene-d_8	64.0(47.5), 88(52.1), 120(55.6), 192(59.0), 220(62.5), 284(66.0), 380(69.8), 506(72.5), 670(76.3)
1c	$C_2D_2Cl_4$	38.0(70.4), 64(76.9), 110(83.0), 186(89.7), 300(96.1), 470(102.6), 740(109.0), 1160(115.4)
1c	DMSO-d_6	48.0(82.0), 94(89.2), 126(92.9), 160(96.5), 220(100.1), 300(103.8), 400(107.4), 514(111.0), 640(114.6), 870(118.3)

a) Obtained from the rate constants of the isomerization from the major to minor isomers.

by the following equation:

$$(\delta_B - \delta_b)(\delta_{aH} - \delta_A) = K(\delta_A - \delta_a)(\delta_{bH} - \delta_B),$$

where $\delta_{a(or\ b)}$ and $\delta_{aH(or\ bH)}$ are the chemical shifts of unprotonated (uncomplexed) and protonated (complexed) amines, respectively, and $\delta_{A(or\ B)}$ are the observed chemical shifts.[17] The linear-fitting of $(\delta_A - \delta_a)(\delta_{bH} - \delta_B)$ vs. $(\delta_B - \delta_b)(\delta_{aH} - \delta_A)$ afforded the value of K as a slope. The difference between the pK_a's of amines A and B was calculated by the equation of $\Delta pK_a = -\log K$.

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