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ortho-Magnesiation of Boron-Substituted Benzenes by Using (TMP)₂Mg**

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The ortho-metalation (hydrogen-metal exchange) of aromatic compounds assisted by heteroatom-containing functional groups is one of the most efficient methods for the transformation of aromatic compounds.^[1] Among a variety of ortho-directing groups developed so far, good ortho-directing groups have two essential features. The first is the coordinating ability to the metal through the lone pair electrons on the heteroatom, which facilitates the approach of the metal base to the deprotonation site (in other words, the complex-induced proximity effect)^[1c] and contributes to the stabilization of the ortho-metalated species through intramolecular coordination. The second is an electron-withdrawing inductive effect on the aromatic ring, which increases the acidity of the aromatic protons and stabilizes the resulting carbanion. Therefore, the metalation ortho to electropositive elements is considered inefficient and has received little attention.^[2] To our knowledge, there is no example of the ortho-metalation of boron-substituted arenes.

ortho-Metalated borylbenzenes, however, have potential utility for the functionalization of benzenes and recent reports have illustrated alternative pathways to them, such as 1) the iodine–magnesium exchange reaction of *o*-(iodo)borylbenzenes,^[3] 2) the insertion of a transition metal into a carbon–halogen bond of *o*-(halo)borylbenzenes,^[4] 3) the reaction of a metal–benzyne complex with a boron reagent,^[5] and 4) the transition-metal-catalyzed *ortho* C–H activation of borylbenzenes,^[6] However, crystal-structure determination was accomplished only for transition-metal (Ti, Zr, Ni, and Pd) derivatives.^[4,5]

Recently, TMP-based metallic reagents (TMP=2,2,6,6-tetramethylpiperidide) have successfully achieved the direct *ortho*-metalation of functionalized aromatic compounds with excellent regioselectivity and high functional group tolerance.^[7,8] Thus, we anticipated that TMP-based metallic reagents could promote the *ortho*-metalation of borylbenzenes because the advantages of the TMP-based reagents (high

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**]	TMP = 2,2,6,6-tetramethylpiperidide.

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basicity, high steric bulkiness, and low nucleophilicity) could compensate for the disadvantages of the electropositive elements.

We report here the first example of the direct *ortho*-metalation of borylbenzenes by using (TMP)₂Mg.^[8b] Borylbenzenes with an *N*-methyl-1,3-ethylenediamino group on the boron atom undergo *ortho*-magnesiation upon exposure to (TMP)₂Mg, and the resulting *ortho*-magnesiated borylbenzenes can be trapped with electrophiles. The molecular structure of the magnesiated compound is revealed by X-ray crystallographic analysis.

(Diaminoboryl)benzenes **1** were prepared in moderate yields by the condensation of the corresponding phenylboronic acids with *N*-methyl-1,3-diaminopropane, followed by azeotropic distillation.^[9] The reaction of (diaminoboryl)benzene **1a** with (TMP)₂Mg (2.5 molequiv) in refluxing THF and the subsequent treatment with Me₂SO₄, which is a powerful electrophile, at room temperature afforded *ortho*-methylated borylbenzene **2a** together with the *ortho*-protonated product **3a**, as shown in Scheme 1. Since the diaminoboryl moiety is moisture sensitive, compounds **2a** and **3a** were converted into pinacolate derivatives **4a** (20% yield) and **5a** (48% yield), respectively, by treatment of the reaction mixture with MeOH in the presence of NH₄Cl and then with pinacol in THF.

Although the mechanistic details remain unclear, we postulated a two-step mechanism for the *ortho*-magnesiation (Scheme 1). In the initial step, $(TMP)_2Mg$ abstracts the amino proton in **1a**, resulting in the formation of intermediary {borylamide}-Mg-TMP complex **6a**. In the second step, the TMP-Mg moiety in **6a** intramolecularly abstracts an *ortho*-proton on the benzene to form *ortho*-magnesiated borylbenzene **7a**. The magnesium in **7a** is chelated with the nitrogen and the *ortho*-carbon atom. The intramolecular reaction mode^[1c] in the second step may be one of the key factors to promote unfavorable metalation *ortho* to the electropositive atom. When initial intermediate **6a** fails to undergo deprotonation, *ortho*-protonated product **5a** is formed.

The reaction between **1a** and $(TMP)_2Mg$ (1:2.5) was monitored by ¹³C NMR spectroscopy, as shown in Figure 1. After 0.5 h at room temperature, compound **1a** (Figure 1a) was completely consumed and the signals of **6a** and **8a** appeared (Figure 1b): the latter may be formed by the reaction of **1a** with $(TMP)_2Mg$ in the ratio of 2:1. The signals were characterized by comparison with those of authentic samples prepared independently (see the Supporting Information).



Scheme 1. *ortho*-Magnesiation of **1a** and trapping with Me_2SO_4 and its plausible mechanism. THF solvation to the magnesium may be involved throughout the process from **1a** to **2a**. a) (TMP)₂Mg (×2.5)/THF/RT, 0.5 h; reflux, 2 h; b) Me_2SO_4 (×3)/0 °C-RT, 12 h; c) MeOH/NH₄Cl/RT, overnight; d) pinacol/hexane/RT, overnight.



Figure 1. The aromatic regions of the ¹³C NMR spectra of a) **1a** and b) the reaction mixture prepared by the reaction of **1a** with $(TMP)_2Mg$ (1:2.5) in THF at room temperature for 0.5 h; •represents **6a** and • represents **8a**.

After being refluxed for 2 h, the reaction mixture exhibited several new signals that may be attributed to **7a**, in addition to those of remaining **6a** and **8a**. Precise characterization of the signals attributed to **7a**, however, was difficult due to the complexity of the spectra.

The yield of **4a** was improved to 34% when tetrahydropyran (THP) was used as the solvent. It is plausible that the *ortho*-magnesiated compound is so basic that it gradually abstracts the α -proton of THF under the refluxing condition to form **3a**. The α -proton of THP is less acidic than that of THF and thus less prone to abstraction.^[10]

o-(Iodo)borylbenzene **9a** was obtained in 54% yield by using I₂ (6 molequiv) as the trapping agent for **7a**, as shown in Scheme 2. Whereas *p*-fluoro **1b** produced **9b** in only 9% yield under the same reaction conditions, *p*-chloro **1c** afforded **9c** in 41% yield. *p*-Methoxy **1d** provided **9d** in 29% yield together with 3,4-diiodoanisole (15%) and 4-iodoanisole (6%). These two byproducts may arise from the boroniodine exchange reaction^[11] with the remaining I₂ because an electron-donating methoxy group can promote the electrophilic substitution reaction on the benzene. Hence, the



Scheme 2. *ortho*-Magnesiation of 1 and trapping with I_2 . a) (TMP)₂Mg (× 2.5)/THP/RT, 0.5 h; reflux, 2 h; b) I_2 /RT, overnight; c) MeOH/NH₄Cl/RT, overnight; d) pinacol/hexane/RT, overnight.

yield of **9d** was increased to 38% by reducing the amount of I_2 (3 mol equiv). It is also notable that the product expected from the magnesiation *ortho* to the methoxy group was not detected.^[8f] A sequence of the present transformations illustrates a new pathway to multifunctionalized arenes.

The ortho-magnesiated borylbenzene prepared by the reaction of 1a with (TMP)₂Mg (1.7 molequiv) crystallized from THP-hexane as a centrosymmetric dimer coordinated with two molecules of (TMP)₂Mg, which is considered as a co-complex between 7a and (TMP)₂Mg and designated as [7a·Mg(TMP)₂]₂, as shown in Figure 2.^[12] The structural features of $[7a \cdot Mg(TMP)_2]_2$ deserve some comments from the standpoint of not only an ortho-magnesiated benzene, but also a complexed model for a crystal structure of (TMP)₂Mg, which itself is still unknown. First, the ortho magnesiation led to the formation of the distorted fivemembered MgNBC₂ ring. The magnesium (Mg1) is chelated by the anionic ortho-carbon (C2) and the amide nitrogen (N1) with an acute bite angle $(C2-Mg1-N1=90.50(13)^\circ)$. The amide–magnesium bond length (N1–Mg1=2.098(3) Å) and the aryl-magnesium bond length (C2-Mg1= 2.261(4) Å) fall in the ranges observed for magnesium amides (1.90-2.44 Å based on the Cambridge structural database (CSD)) and arylmagnesium compounds (2.09-2.34 Å based on the CSD), respectively.^[13] The N1-B1 bond





Figure 2. Molecular structure of $[7a \cdot Mg(TMP)_2]_2$ with 30% probability ellipsoids. The hydrogen atoms are omitted for clarity.

(1.436(5) Å) is slightly longer than the N2–B1 bond (1.419(5) Å). Therefore, the lone pair of electrons on N1 is shared with Mg2, which is mentioned later, whereas that on N2 participates in the π bonding with B1. The geometry around B1 is trigonal planar (the sum of the bond angles = 359.8°). The plane defined by N1, N2, and B1 is rotated out of the phenyl ring by about 50° (N1-B1-C1-C2=47.6(5)°). Second, the dimerization formed the centrosymmetric fourmembered Mg₂C₂ ring. Each of the two phenyl groups acts as a bridge between the two magnesium atoms (Mg1 and Mg1*) and rotated out of the Mg₂C₂ ring by about 50°. The Mg1...Mg1* atomic distance (2.808(2) Å) is similar to that observed for the Mg₂C₂ rings in arylmagnesium compounds (2.79–2.85 Å),^[14] and there is no bonding interaction between them. Each of the amide ligands is coordinated to Mg1 and Mg1* from above and below the Mg₂C₂ plane, respectively. Third, the two molecules of (TMP)₂Mg are coordinated to the dimer framework through the Mg1-N3 and Mg2–N1 bonds to form the four-membered Mg₂N₂ ring. The four-membered ring is almost planar (the sum of the internal angles=358.7°). The endocyclic Mg-N bond lengths are similar to each other (Mg1-N1=2.098(3), Mg2-N1=2.125(3), Mg2-N3=2.124(3), Mg1-N3=2.134(3) Å), whereas the exocyclic Mg2-N4 bond is shorter (1.971(3) Å). Mg2 adopts a tricoordinate planar geometry (the sum of the bond angles=359.8°). The Mg1···Mg2 atomic distance (2.8768(16) Å) is longer than the Mg1···Mg1* atomic distance. The outer Mg_2N_2 ring is approximately orthogonal to the central Mg₂C₂ ring. Finally, the overall framework consists of the linear tetranuclear arrangement of magnesium atoms^[15] and the heteroanionic bridging of carbon and nitrogen groups (Scheme 3).

Attempted NMR spectroscopic analysis of $[7a\cdot Mg\cdot (TMP)_2]_2$ was unsuccessful because the crystals obtained



Scheme 3. Linear tetranuclear arrangement of Mg with bridging $C^{(-)}$ and $N^{(-)}$ groups in $[{\bf 7a\cdot}Mg(TMP)_2]_2.$

were hardly soluble in common organic solvents. This result may suggest that coordination of the $(TMP)_2Mg$ molecules to **7a** may occur during the crystallization process.

In conclusion, the *ortho*-magnesiation of (diaminoboryl)benzenes 1 with $(TMP)_2Mg$ was achieved for the first time. The *ortho*-magnesiated borylbenzenes were trapped with Me₂SO₄ and I₂, the latter of which led to the formation of multifunctionalized arenes. X-ray crystallographic analysis revealed that the magnesium cation was chelated by the *ortho*-carbon of the benzene and one of the nitrogen atoms of the 1,3-diaminopropane moiety. Although the yields of **9** are low to moderate, this is the important step toward a better system for the *ortho*-metalation of boron–aryl species. Further studies of the structure of **7a** in solution and the mechanistic details of the *ortho*-magnesiation are currently under investigation in our laboratory.

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Göttingen, Germany). R1 $(I > 2\sigma(I)) = 0.0897$, wR2 (all data) = 0.2551, S=1.107 for 346 parameters and 6637 unique reflections. Maximum and minimum electron density $0.419/-0.292 \text{ e}\text{ Å}^{-3}$. CCDC-816159 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/ data_request/cif.

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