Identification of an intermediate in the deboronation of *ortho*-carborane: an adduct of *ortho*-carborane with two nucleophiles on one boron atom†‡

Yoshiyuki Taoda,[a] Takehiko Sawabe,[a] Yasuyuki Endo,*[b] Kentaro Yamaguchi,[c] Shinya Fujii[d] and Hiroyuki Kagechika*[d]

Received (in Cambridge, UK) 17th October 2007, Accepted 29th January 2008
First published as an Advance Article on the web 20th February 2008
DOI: 10.1039/b716079h

The 1 : 2 adduct of 1-bromo-*ortho*-carborane and pyridine has been identified as a significant intermediate in the deboronation of *ortho*-carborane to a *nido*-anion

Icosahedral carboranes (more specifically the *closo*-dicarbadodecaboranes) constitute a class of boron-containing cluster compounds that exhibit a remarkable thermal and chemical stability.[1] An important reaction in icosahedral carborane chemistry is the deboronation of the so-called *ortho* isomer (*closo*-1,2-$C_2B_{10}H_{12}$ (**1**)) by strong Lewis bases, such as alkoxides, amines and fluoride, affording a *nido*-anion ([7,8-$C_2B_9H_{12}]^-$ (**2**), Fig. 1).[2] The *nido*-anionic derivatives can bind strongly to metal ions, and are useful in catalysis or as synthetic intermediates leading to *closo*-carboranes and heteroboranes.[3,4] However, the details of the mechanism of the deboronation of **1** have remained unclear for over 40 years. The generally accepted reaction scheme is shown in Fig. 1.[2d,5,6] Thus, the nucleophile (Nu^-) attacks the most electron-poor boron atom of **1** adjacent to the two carbon atoms to afford the 1 : 1 adduct, **Adduct I**. After the reaction of **Adduct I** with another molecule of nucleophile, the 1 : 2 adduct, **Adduct II**, is deboronated and protonated to afford *nido*-anion **2**. While the first step in the formation of **Adduct I** is supported by theoretical calculations on the electronic properties of carboranes,[7] and by the identification of the 1 : 1 adduct of **1** and $HNP(NMe_2)_3$, **3** (Fig. 2a),[8] there is no experimental evidence for the latter steps.[9] Here, we describe the first identification of **Adduct II**-type derivative **6a** (Fig. 2b) as an intermediate of deboronation in the reaction of *ortho*-carboranes **4** and **5** with pyridines.

In the deboronation of *ortho*-carboranes, the introduction of halogen atoms onto the carbon atoms of the carborane moiety accelerated the reaction; for example, 1,2-dichloro-*ortho*-carborane can be deboronated by treatment with neutral nucleophiles such as alcohol and water.[10] 1-Bromo-*ortho*-carborane (**4**) also reacted with pyridine, and the 1 : 2 adduct was isolated; its structure was assigned as 1-bromo-3,6-dipyrid-1-yl-*ortho*-carborane on the basis of IR spectroscopic analysis (Fig. 3).[11] As we previously reported the significance of the interactions between the most electron-poor 3(6)-boron atom of *ortho*-carboranes and solvents involved in solvolysis occurring adjacent to the carborane moiety,[12] so we examined systematically the reactions of *ortho*-carboranes with several pyridines. The reaction of 1-bromo-*ortho*-carborane (**4**) with pyridine at room temperature for 20 h afforded the 1 : 2 adduct (**6a**; $C_{12}H_{21}B_{10}N_2Br$ from elemental analysis) in 99% yield (Table 1, run 1); this was expected to be the same product as that isolated by Plešek *et al.*[11] However, X-ray crystallography showed that the structure of **6a** was different from their proposed structure, as shown in Fig. 2b and Fig. 4.§ The crystal structure of **6a** is a *nido*-type complex, corresponding to **Adduct II** in Fig. 1.¶ Two pyridines are attached to one boron atom, which was originally at the 3(6)-position of **4**, and has one bond with another boron atom (B–B length = 1.723(4) Å). Other bond lengths and bond angles in the cluster are similar with those of a typical carborane moiety.

Next, the reactions of unsubstituted or *C*-bromo-substituted *ortho*-carboranes with various pyridines were examined (Table 1). The structures of the products were determined by means of ^{1}H- and ^{11}B-NMR spectroscopy, and elemental analysis. 1-Bromo-*ortho*-carborane (**4**) did not react with 3-chloropyridine (91% recovery of **4**), while it afforded similar 1 : 2 adducts in reactions with 3- and 4-methylpyridine, in 86% (**6c**) and 50% (**6d**) yield, respectively. Thus, the formation of 1 : 2 adduct **6** depended on the nucleophilicity of the pyridine

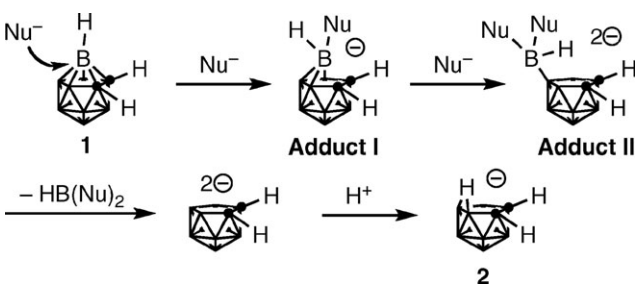


Fig. 1 Possible reaction mechanism of the deboronation of *ortho*-carborane **1** to *nido*-anion **2**.[6]

[a] *Graduate School of Pharmaceutical Sciences, The University of Tokyo, 7-3-1 Hongo, Bunkyo-ku, Tokyo 113-0033, Japan*
[b] *Tohoku Pharmaceutical University, 4-4-1 Komatsushima, Aoba-ku, Sendai 981-8558, Japan. E-mail: yendo@tohoku-pharm.ac.jp; Fax: +81 22-275-2013*
[c] *Faculty of Pharmaceutical Sciences at Kagawa Campus, Tokushima Bunri University, 1314-1 Shido, Sanuki, Kagawa 769-2193, Japan*
[d] *School of Biomedical Science, Institute of Biomaterials and Bioengineering, Tokyo Medical and Dental University, 2-3-10 Kanda-Surugadai, Chiyoda-ku, Tokyo 101-0062, Japan. E-mail: kage.omc@tmd.ac.jp; Fax: +81 3-5280-8032*

† Electronic supplementary information (ESI) available: Experimental procedures and characterization data for **4** and **6–8**. See DOI: 10.1039/b716079h

‡ CCDC 652969. For crystallographic data in CIF or other electronic format see DOI: 10.1039/b716079h

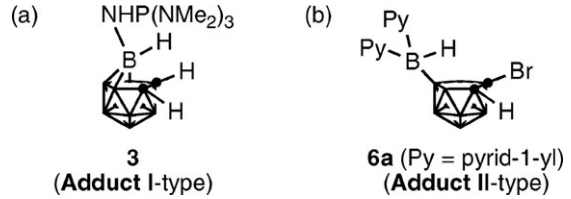


Fig. 2 Isolated intermediates of deboronation.[6]

ring. Unsubstituted *ortho*-carborane **1** did not react with pyridine or with the more reactive 4-methylpyridine, even at 60 °C, while 1,2-dibromo-*ortho*-carborane (**5**) afforded 1 : 2 adduct **7a** in 95% yield under the same conditions, and also reacted with the less reactive 3-chloropyridine. Thus, the introduction of a *C*-bromo atom decreased the electron density at the 3-position and consequently increased its reactivity to nucleophilic attack by pyridines. In each case, the 1 : 1 adduct, corresponding to **Adduct I**, was not detected.‖

The reaction of *ortho*-carboranes and pyridines afforded 1 : 2 adducts, depending on the electron density on the boron atom at the 3-position of the carborane and the nucleophilicity of the pyridine. However, the reaction of **4** with 4-methylpyridine proceeded in lower yield than that of unsubstituted pyridine or 3-methylpyridine, which have lower nucleophilicities, under the same conditions. Extension of the reaction time resulted in lower yield (Table 1, run 4 *vs.* 5), and a mixture of partially decomposed products was observed. Next, the reaction was continued under the same conditions until **6d** disappeared (10 d), which afforded *nido*-anion **8d** in 91% isolated yield (Table 1, run 6). The isolated 1 : 2 adduct **6d** was stirred in 4-methylpyridine under the same conditions to give **8d** in 70% yield (Table 1, run 11). Similarly, the isolated 1 : 2 adduct **6a** afforded **8d** (54%) in the reaction with 4-methylpyridine for 1 month at room temperature. Therefore, the 1 : 2 adducts **6a** and **6d** appear to be intermediates in the deboronation of 1-bromo-*ortho*-carborane (**4**) to form *nido*-anion **8d**, although *ortho*-carborane (**1**) itself is less reactive to pyridines, and requires a more nucleophilic solvent.

Our previous investigations on the solvolysis of α-(*ortho*-carboranyl)benzyl tosylate revealed that the nucleophilic solvent interacts with the most electron-poor 3(6)-boron atom, and it is this that determines the reaction mechanism and stereochemistry of solvolysis.[12] In a solvent of moderate nucleophilicity, such as alcohol, water or aniline, the solvent molecule interacting with the 3(6)-boron atom participates in the solvolysis, while a much more nucleophilic solvent, such as morpholine or piperidine, causes deboronation of the *ortho*-carborane moiety, affording the decomposition products (Fig. 5). Thus, the tendency in solvolysis is similar to that observed in the reaction of *ortho*-carboranes with pyridines. Therefore, the complexation with

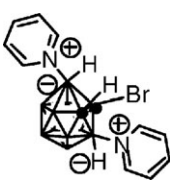
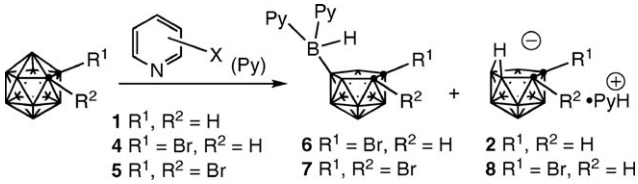


Fig. 3 A proposed structure for the 1 : 2 adduct of **4** and pyridine in ref. 11.

Table 1 The reaction of *ortho*-carboranes with pyridines



Run	Carborane	Pyridine[a] (X)	Temp.	Time/h	Product[a] (Yield (%)) Recovery	1 : 2 adduct	*nido*
1	**4**	H	rt	20	—	**6a** (99%)	—
2	**4**	3-Cl	60 °C	40	**4** (91%)	—	—
3	**4**	3-Me	rt	2	—	**6c** (86%)	—
4	**4**	4-Me	rt	2	—	**6d** (50%)	—
5	**4**	4-Me	rt	20	—	**6d** (35%)	—
6	**4**	4-Me	rt	240	—	—	**8d** (91%)
7	**1**	H	60 °C	20	**1** (96%)	—	—
8	**1**	4-Me	60 °C	20	**1** (66%)	—	—
9	**5**	H	rt	20	—	**7a** (95%)	—
10	**5**	3-Cl	rt	40	—	**7b** (64%)	—
11	**6d**	4-Me	rt	240	—	—	**8d** (70%)

[a] In the illustrated structures of **6–8**, Py represents pyridine (a), 3-chloropyridine (b), 3-methylpyridine (c), or 4-methylpyridine (d).[6]

nucleophiles at the 3(6)-boron atom of *ortho*-carborane is significant, both for the chemical reactivity of the cluster itself and for neighboring group participation.

In conclusion, the key intermediate in the deboronation of *ortho*-carborane at the second reaction step (**Adduct II**) has been identified for the first time. The crystal structure and

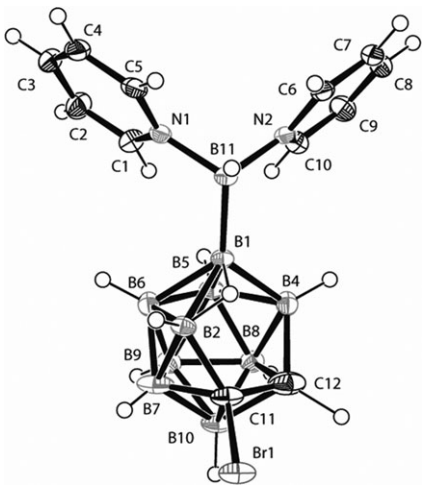


Fig. 4 ORTEP crystal structure of **6a**. The thermal ellipsoids are drawn at the 50% probability level.

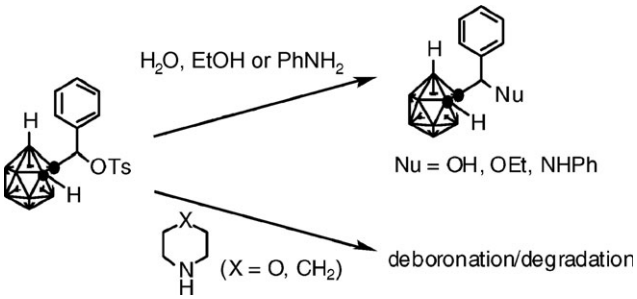


Fig. 5 The solvent-dependent reaction of α-(*ortho*-carboranyl)benzyl tosylate.

reactivity of **6d** clearly suggest that the second nucleophilic attack on the **Adduct I**-type intermediate at the 3(6)-boron atom caused boron–boron bond cleavage, followed by the formation of a *nido*-anion. In a typical deboronation reaction, the rate-limiting step is the formation of **Adduct I**,[2] and the following reactions lead rapidly to the *nido*-anion. The moderate reactivity of both **4** and 4-methylpyridine enabled the isolation of **6d**, and the observation of its deboronation reaction. The results obtained here, together with the results of previous studies on the first step,[7,8] have established the mechanism of the deboronation of *ortho*-carborane.

Notes and references

§ Compound **6a**: Colorless prisms (CH_2Cl_2); mp 148 °C; ^{1}H-NMR (acetone-d_6): δ 8.96 (dd, 2 H, J = 1.5 and 5.1 Hz), 8.92 (dd, 2 H, J = 1.5 and 5.1 Hz), 8.35 (tt, 1 H, J = 1.5 and 7.7 Hz), 8.34 (tt, 1 H, J = 1.5 and 7.7 Hz), 7.92 (dd, 2 H, J = 5.1 and 7.7 Hz), 7.90 (dd, 2 H, J = 5.1 and 7.7 Hz), −3.0 (br s, 1 H), 0–4.0 (br m, 10 H); ^{11}B-NMR (acetone-d_6): δ 8.32 (s, 1 B), −6.28 (d, 1 B), −10.19 (d, 1 B), −10.98 (d, 1 B), −13.08 (d, 1 B), −17.63 (d, 1 B), −19.26 (d, 1 B), −19.60 (d, 1 B), −26.12 (s, 1 B), −34.49 (d, 1 B). Crystal data: formula $C_{12}H_{21}B_{10}BrN_2$, crystal system, monoclinic, space group $P2_1/c$, a = 14.326(2), b = 9.994(1), c = 12.791(1) Å, β = 90.100(2)°, V = 1831.4(4) Å^3, D = 1.383 g cm^{-3}, Z = 4, R = 0.026, Rw = 0.031.‡

¶ The atomic coordinates (B_{iso}/B_{eq}) show there are two boron atoms, each with 0.500 occupancy, which means that there are two molecules (an enantiomeric pair) in the unit cell.

‖ Even after 2 h at 0 °C in the reaction of **4** with pyridine, only **6a** and recovered **4** were isolated, and **Adduct I** was not identified. Furthermore, the reaction of **4** was followed by ^{11}B-NMR in pyridine-d_5, but this did not afford any information about existence of **Adduct I**

1 V. I. Bregadze, *Chem. Rev.*, 1992, **92**, 209–223.
2 (*a*) R. A. Wiesboeck and M. F. Hawthorne, *J. Am. Chem. Soc.*, 1964, **86**, 1642–1643; (*b*) L. I. Zakharkin and V. N. Kalinin, *Tetrahedron Lett.*, 1965, **6**, 407–409; (*c*) M. F. Hawthorne, D. C. Young, P. M. Garrett, D. A. Owen, S. G. Schwerin, F. N. Tebbe and P. A. Wegner, *J. Am. Chem. Soc.*, 1968, **90**, 862–868; (*d*) M. A. Fox, J. A. H. McBride and K. Wade, *Polyhedron*, 1997, **16**, 2499–2507.
3 J. Plešek and S. Heřmánek, *Inorg. Synth.*, 1984, **22**, 231–234.
4 J. Yoo, J.-W. Hwang and Y. Do, *Inorg. Chem.*, 2001, **40**, 568–570 and references cited therein.
5 L. I. Zakharkin and V. S. Kirillova, *Bull. Acad. Sci. USSR Div. Chem. Sci. (Engl. Transl.)*, 1975, 2484–2486.
6 In the icosahedral cage structures throughout this paper, closed circles (●) represent carbon atoms and other vertices represent BH units.
7 (*a*) C.-C. S. Cheung, R. A. Beaudet and G. A. Segal, *J. Am. Chem. Soc.*, 1970, **92**, 4158–4164; (*b*) D. A. Dixon, D. A. Kleier, T. A. Halgren, J. H. Hall and W. N. Lipscomb, *J. Am. Chem. Soc.*, 1977, **99**, 6226–6237; (*c*) M. J. S. Dewar and M. L. McKee, *Inorg. Chem.*, 1980, **19**, 2662–2672.
8 (*a*) M. G. Davidson, M. A. Fox, T. G. Hibbert, J. A. K. Howard, A. Mackinnon, I. S. Neretin and K. Wade, *Chem. Commun.*, 1999, 1649–1650; (*b*) A. S. Batsanov, R. C. B. Copley, M. G. Davidson, M. A. Fox, T. G. Hibbert, J. A. K. Howard and K. Wade, *J. Cluster Sci.*, 2006, **17**, 119–137.
9 The 1 : 2 adduct of 8,9,10,12-tetrafluoro-*ortho*-carborane and diethylamine was concluded to have been formed on the basis of ^{19}F- and ^{11}B-NMR studies at low temperature: V. N. Lebedev, E. V. Balagurova and L. I. Zakharkin, *Russ. Chem. Bull.*, 1995, **44**, 1102–1106.
10 V. I. Stanko, G. A. Anorova and T. P. Klimova, *Zh. Obshch. Khim.*, 1969, **39**, 1045.
11 J. Plešek, T. Hanslík, F. Hanousek and S. Heřmánek, *Collect. Czech. Chem. Commun.*, 1972, **37**, 3403–3409.
12 (*a*) Y. Endo, T. Sawabe and Y. Taoda, *J. Am. Chem. Soc.*, 2000, **122**, 180–181; (*b*) Y. Endo and Y. Taoda, *Tetrahedron Lett.*, 2001, **42**, 6327–6331; (*c*) Y. Taoda and Y. Endo, *Tetrahedron Lett.*, 2003, **44**, 8177–8181.