

Proton-driven conformational change in a 2-aryl-*p*-carborane constrained by an intramolecular C–H···O hydrogen bond

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Abstract—2-(2-Hydroxyphenyl)-*p*-carborane forms an intramolecular hydrogen bonding based on the results of X-ray, IR, and ¹H NMR studies. The hydrogen bonding is released by the addition of acid in solution. Density functional theory (DFT) calculations on the phenol, phenolate and protonated phenol structures indicated two stable conformational state, hydrogen bonding form for phenol and phenolate, and dihydrogen bonding form for protonated phenol.

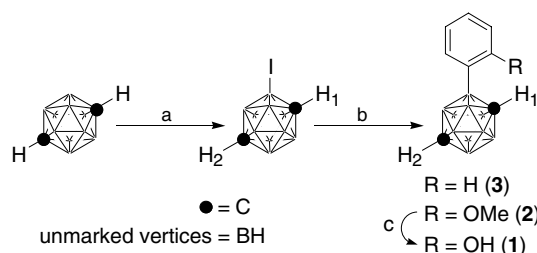
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Control of rotary motion around molecular axis plays an important role in various fields, such as fixation of conformational state of complex molecules and molecular motors. Icosahedral carboranes (dicarbalo-*closo*-docecarboranes) have characteristic molecular geometry with rotational symmetry.¹ The combination of carborane cage and other chemical components provides a useful tool to develop a new control system of molecular rotation. Hawthorne and co-workers have successfully realized a bistable molecular rotor consisting of a metallocarborane complex whose motion can be driven either by electrical or photonic energy.² On the other hand, we are interested in hydrogen bonding character³ of carborane C–H and have designed 1-(2-methoxyphenyl)-*o*-carborane derivative for evaluation of the hydrogen bonding in solution.⁴

Here we present the design and synthesis of the compound with a bistable conformational states consisting of 2-(2-hydroxyphenyl)-*p*-carborane **1**, which has an intramolecular hydrogen bond (H-bond) between one of its C–H moieties and the oxygen atom of the hydroxyl group.⁴ Experimental and computational data indicate that the bistability is associated with protonation/deprotonation of the OH group of **1**.⁵

As shown in Scheme 1, 2-arylated *p*-carborane derivatives can be readily synthesized by iodination at the 2-position, followed by palladium-catalyzed coupling with the corresponding Grignard reagents.⁶ 2-Phenyl-*p*-carborane **3**, which does not have an intramolecular H-bond and was used as a standard compound in this study, was prepared in 71% yield. 2-(2-Methoxyphenyl)-*p*-carborane **2** was also prepared in 94% yield

oxyl group.⁴ Experimental and computational data indicate that the bistability is associated with protonation/deprotonation of the OH group of **1**.⁵



Scheme 1. Synthesis of 2-aryl-*p*-carboranes. Black circles and unmarked vertices indicate carbon atoms and BH, respectively. Reagents: (a) ICl, AlCl₃, CH₂Cl₂; (b) ArMgBr, CuI, Pd(PPh₃)₂Cl₂, THF; (c) BBr₃, CH₂Cl₂.

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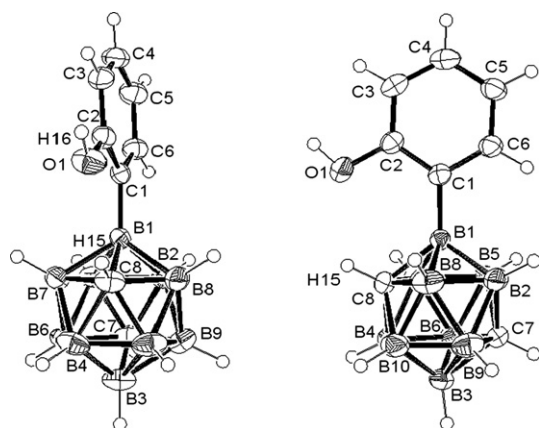


Figure 1. ORTEP representation of **1**. Selected bond lengths (Å) and angles (°): C8–H15, 0.98(2); C1–B1, 1.576(2); C8–B1, 1.710(2); C1–C2, 1.395(2); C2–O1, 1.3697(19); O1–C2–C1, 117.30(13); C2–C1–B1, 124.52(13); C1–B1–C8, 127.04(13); C2–C1–B1–C8, –9.4(2); Hydrogen bonds (Å) and angle (°): O1···H15, 2.343(18); C8···O1, 2.934(2); C8–H15···O1, 118.0(13).

and readily transformed into **1** by demethylation with BBr_3 .

Colorless crystals of **1** were grown from a mixed solution of hexane and CH_2Cl_2 by slow evaporation of the solvent. The structure of **1** in the solid-state was confirmed by single-crystal X-ray diffraction and IR spectroscopic analyses.⁷ An ORTEP view of **1** is shown in Figure 1. The torsion angle of C(2)–C(1)–B(1)–C(8) is close to planar, being $-9.4(2)^\circ$. The H-bond distance between H(15) and O(1) in the crystal structure of **1** is 2.34(18) Å [(H)C(8)···O(1) is 2.93(2) Å], which is considerably shorter than the sum (2.72 Å) of the van der Waals' radii of hydrogen and oxygen.⁸ The solid-state IR spectra (KBr) of **1** exhibited two distinct C–H stretching frequencies at 3086 and 3057 cm^{-1} , respectively. The C–H stretching frequency of **3**, in which the C–H moieties do not participate in any H-bond interaction, is 3056 cm^{-1} suggesting that the stretching mode at higher frequency (3086 cm^{-1}) is that of the C–H₁ bond that is involved in the formation of the intramolecular H-bond. Thus, we found that the C–H···O interaction is a blue-shifted H-bond.⁹ These results strongly support the formation of an intramolecular H-bond between the OH group and carborane C–H in the solid-state.

We examined the strength of the intramolecular H-bond in various solvents and evaluated the change of the chemical shift values of the *p*-carborane C–H hydrogens, H₁ and H₂, of **1** and **3** by means of ¹H NMR spectroscopy at 25 °C (Table 1). We also calculated the difference between the highest and lowest values of H₁ and H₂ ($\Delta \text{ppm} = \delta\text{H}_1 - \delta\text{H}_2$), respectively, in various solvents. Since nuclear Overhauser effect (NOE) was observed between the hydrogen peak at lower field and the hydrogen of the methoxyl group in **2**, we assigned the low-field peak to H₁ and the up-field peak to H₂.¹⁰ The chemical shift values of the C–H were the smallest in benzene-*d*₆ and the largest in DMSO-*d*₆. There was a remarkable solvent effect caused by intermolecular

Table 1. ¹H NMR chemical shift values (ppm) of **1** and **3** in various solvents^a

Solvent	H ₁ of 3 δ (ppm)	H ₂ of 3 δ (ppm)	H ₁ of 1 δ (ppm)	H ₂ of 1 δ (ppm)
Benzene- <i>d</i> ₆	2.36	2.10	3.49	2.08
CDCl_3	3.08	2.91	3.66	2.85
CD_3CN	3.48	3.24	3.96	3.14
CD_3OD	3.58	3.34	4.02	3.19
Pyridine- <i>d</i> ₅	3.84	3.56	4.54	3.47
DMSO- <i>d</i> ₆	4.17	3.84	4.12	3.71
Δ (ppm) ^b	1.81	1.74	0.63	1.63

^a The measurement of ¹H NMR spectra was performed at 270 MHz.

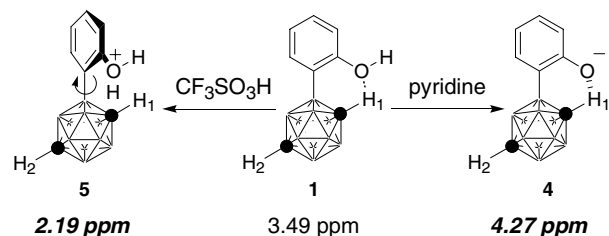
^b The value corresponds to the difference Δ (ppm) of (δ in DMSO-*d*₆)–(δ in benzene-*d*₆).

interactions between the C–H hydrogens and solvents. The solvent effect on H₁ of **1** was small because of the intramolecular C–H···O interaction.

It is noteworthy that H₁ of **1** exhibited the most remarkable downfield shift in pyridine-*d*₅, 4.54 ppm, from the value in DMSO-*d*₆, 4.12 ppm. We suggest that the hydroxyl group of **1** is changed to a phenolate anion by pyridine base to form a stronger H-bond with *p*-carborane C–H hydrogen. We conclude that H₁ of **1** is involved in an intramolecular H-bond at all times.

In order to see if this property might be applicable to the design of functional molecules, we evaluated whether or not **1** could cause conformational changes depending on the solution environment, as shown in Scheme 2. The chemical shift value of **1** in benzene-*d*₆ changed from 3.49 ppm to 4.27 ppm upon the addition of pyridine. When trifluoromethanesulfonic acid (TfSA), a well-known superacid, was added to a solution of **1** in benzene-*d*₆, the chemical shift value of **1** exhibited a remarkable up-field shift from 3.49 to 2.19 ppm. We suggest that the up-field shift caused by shielding effect by the benzene ring of benzene-*d*₆ as a solvent and that the protonated hydroxyl group (OH_2^+) of **1** breaks the H-bond and moves away from the C–H moiety by rotating about the B(1)–C(1) bond (Scheme 2 and Fig. 1).

In order to aid the interpretation of the above observations, we performed a series of density functional theory (DFT) calculations on **1** and its parent species **4** and **5** bearing a deprotonated and protonated OH group, respectively.¹¹ The molecular geometries of **1**, **4**, and **5** were optimized at the PBE1PBE/DGDZVP level of



Scheme 2. Proton-driven conformational change in **1**. The chemical shift values were measured after the addition of pyridine as a base or TfSA as an acid to a solution of **1** in benzene-*d*₆.

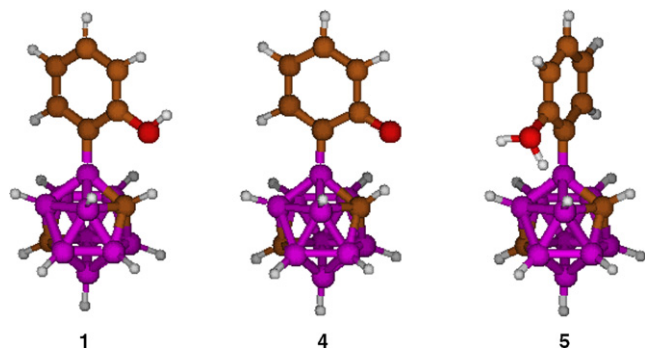


Figure 2. DFT-optimized structures (PBE1PBE/DGDZVP) of **1**, **4**, and **5**.

theory (Fig. 2).¹² The optimized geometry of **1** shows a torsion angle C(2)–C(1)–B(1)–C(8) of -13.32° , in satisfactory agreement with experiment. The computed H-bond distance of **1** is 2.27 Å [(H)C \cdots O is 2.93 Å] which, upon deprotonation to yield **4**, shortens to 2.03 Å [(H)C \cdots O is 2.83 Å]. This result suggests that the H-bond of **4** is stronger than that of **1**. A series of DFT calculations performed on conformers of **1** and **4** with the torsion angle C(2)–C(1)–B(1)–C(8) set at 180° allowed us to estimate the relative strengths of their H-bonds as 3.26 kcal/mol (**1**) and 6.65 kcal/mol (**4**).

In agreement with the above predictions based on analysis of the proton NMR spectra, the optimized structure of **5** exhibited a conformational change mechanism through cleavage of the intramolecular H-bond. To our surprise, the OH₂⁺ group interacts with the neighboring B–H bond at a distance of 1.50 Å (Fig. 2). Thus it appears that the OH₂⁺ group of **5** forms a dihydrogen bond with the B–H moiety (O–H \cdots H–B), a result which has not been previously observed among main group hydrides, including those of boron.¹³ Further confirmation of the experimental results was derived from the computation of the ¹H NMR chemical shifts with the GIAO method¹⁴ at the PBE1PBE/6-311+G(2d,p) level of theory.¹⁵ With respect to TMS, the computed chemical shift of H₁ in **5** corresponds to 3.1 ppm, which is lower than those of 4.2 ppm and 7.8 ppm computed for **1** and **4**, respectively. These gas-phase DFT-based values of the ¹H NMR chemical shift are characterized by the same ordering as that of the measured chemical shift shown in Scheme 2. It is an interesting result that the 2-aryl-*p*-carborane scaffold may be utilized in the design of a controllable, bistable system based on the formation of an H-bond and a dihydrogen bond.

In summary, we found that the C–H hydrogen of **1** forms an intramolecular H-bond of C–H \cdots O type both in crystal and in solution. We also found that the intramolecular H-bond of **1** becomes stronger upon deprotonation (with pyridine) of the hydroxyl group, whereas it is broken upon protonation (with TFSA). Thus, the conformational state of compound **1** is controlled by the protonation/deprotonation process, and the conformational change mechanism of **1** involves a hydrogen bonding. A dihydrogen bonding may participate in the stability of protonated form **5**.

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