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Structures of bis- and tris(2-phenyl-*o*-carboran-1-yl)benzenes. Construction of three-dimensional structures converted from planar arylacetylenic arrays

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Abstract—Compounds (**1**–**3**), which are composed of benzene nuclei linked through 1,2-dicarba-*closo*-dodecaborane (*o*-carborane), were synthesized and their structures were determined by X-ray crystallography. 1,3-Bis(2-phenyl-*o*-carboran-1-yl)benzene and 1,3,5-tris(2-phenyl-*o*-carboran-1-yl)benzene (**3**) have *syn* stereochemistry of all the terminal benzene rings, despite their steric overcrowding.

The icosahedral carboranes (dicarba-*closo*-dodecaboranes) have characteristic properties, such as high boron content, remarkable thermal and chemical stability, spherical geometry and exceptional hydrophobic character. Their unusual properties have been utilized in materials chemistry in the preparation of materials for liquid crystals[1] and non-linear optics,[2] and in medicinal chemistry in the design of boron carriers for boron neutron capture therapy (BNCT)[3] and receptor-ligands as a hydrophobic pharmacophore.[4] Further the potential of *o*-, *m*-, *p*-carboranes (1,2-, 1,7- and 1,12-dicarba-*closo*-dodecaboranes) as components or building blocks in supramolecular systems is beginning to be explored.[5] Recent studies in this area include analyses of the effects of π-bonding interactions between cage CH and calix[5]arene,[6] and hydrogen-bonding interactions between cage CH and diaza-18-crown-6.[7] The construction of linear[8] and macrocyclic[9] molecules, in which carboranes are linked through organic groups or mercury atoms[10] has also progressed. The carboranes have several desirable features in this regard. Their rigid three-dimensional structures hold substituents in well-defined spatial relationships. The two carbon vertices of carboranes bear relatively acidic protons and readily allow substitution with metal and organic groups. Substituents can also be introduced at certain boron vertices. Recently, we have reported aromatic *cis*-ureas bearing the carborane cage as a substituent.[11] The imposition of the *cis*-orientation of urea or amide is achieved by using the *o*-carborane cage, which is prepared by the reaction of decaborane(14) with acetylenic compounds in the presence of a Lewis base. Similarly, it should be possible to construct carborane-containing three-dimensional structures from two-dimensional arylacetylenic arrays,[12] which have been developed in nanoscale architecture. We here describe the structural analysis of aromatic compounds composed of benzene nuclei linked through *o*-carborane (**1**–**3**).

The preparation of the designed compounds is outlined in Scheme 1. The precursors, bis(2-phenylethynyl)-benzenes (**4** and **5**) were prepared by palladium-catalyzed coupling of diethynylbenzene with iodobenzene.[13] 1,3,5-Tris(2-phenylethynyl)benzene (**6**) was prepared by palladium-catalyzed coupling of 1,3,5-tribromobenzene with ethynylbenzene. The reaction of decaborane(14) with acetylenic compounds is general for the preparation of C-substituted *o*-carborane derivatives. The procedure using $B_{10}H_{12}(Et_2S)_2$ seems to be effective for the purpose of 3-dimensional molecular construction employing the *o*-carborane cage as a linker for spatial control. Examples include the synthesis of bis-aryl-substituted *o*-carboranes,[14] aryl derivatives containing more than one carborane substituent[15] and bis(2-phenyl-*o*-carboran-1-yl)benzenes (**1** and **2**).[16] In our

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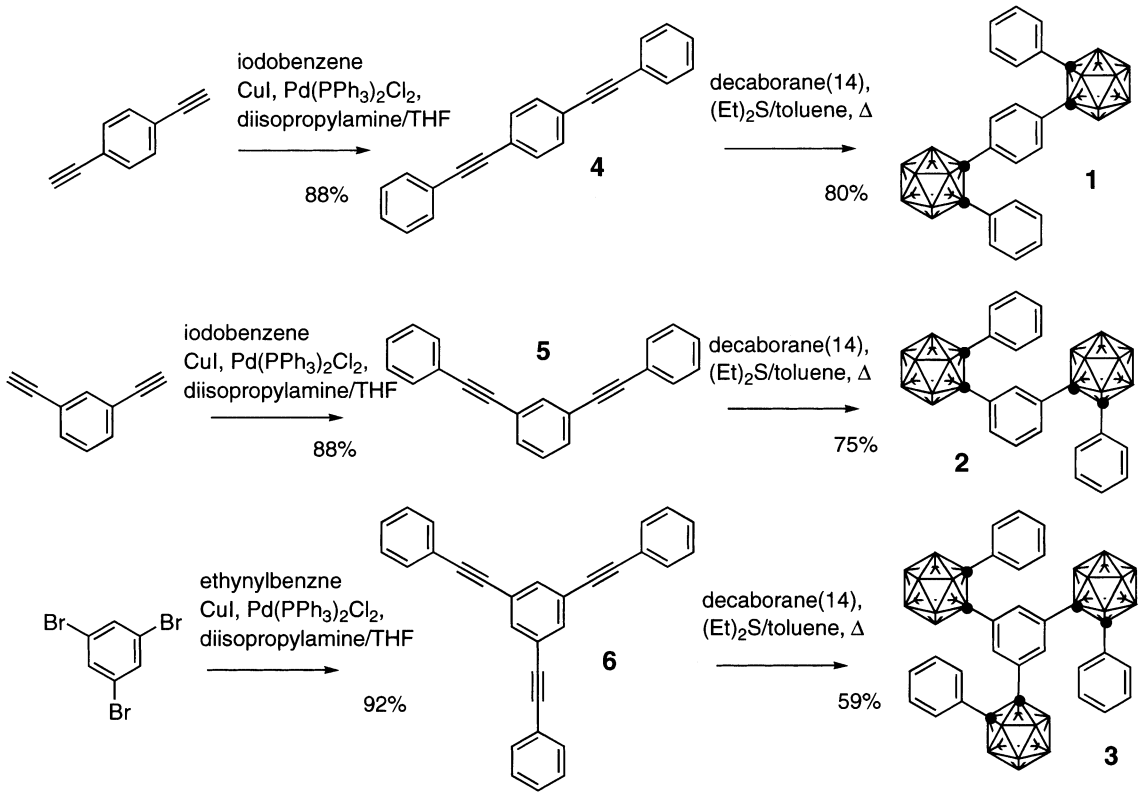

Scheme 1. Synthesis of bis- and tris(2-phenyl-*o*-carboran-1-yl)benzenes (**1**–**3**). In icosahedral cage structures throughout this paper, closed circles (●) represent carbon atoms and other vertexes represent BH units.

experiments, the reaction of compounds **4** and **5** with 3.0 equiv. of decaborane(14) and diethylsulfide (6.1 equiv.) in toluene under reflux for 3 days afforded 1,4- (**1**) and 1,3-bis(2-phenyl-*o*-carboran-1-yl)benzene (**2**) in yields of 80 and 75%, respectively. Compound (**6**) was also converted to **3** by a similar procedure in 59% yield. All of the compounds synthesized were confirmed to have appropriate elemental analysis and NMR spectroscopic data.[17]

The crystal structures of the compounds[18] are shown in Fig. 1. 1,4-Bis(2-phenyl-*o*-carboran-1-yl)benzene (**1**) has the *anti* stereochemistry in which the two terminal benzene rings exist on opposite sides of the central benzene ring, while 1,3-bis(2-phenyl-*o*-carboran-1-yl)benzene (**2**) exists in *syn* conformation, in which they are on the same side. Moreover, all three terminal benzene rings of 1,3,5-tris(2-phenyl-*o*-carboran-1-yl)benzene (**3**) are on the same side (*syn* stereochemistry), despite their steric overcrowding. Dihedral angles between terminal benzene rings are 75.8° for **2** and 97.6° for **3**, and ring center- ring center distances are 5.36 Å for both. We previously reported similar aromatic conformation in the crystal structure of tris(*N*-methyl-*N*-phenyl)-1,3,5-benzenetricarboxamide.[19] The common stabilization of the all-*syn* conformation in the amide and in compound **3** is attributable to T-shaped interaction[20] of the three terminal benzene rings of these compounds.

Their solution structures were examined by ^{1}H NMR using CD_2Cl_2 as a solvent. In the case of **1** and **2**, there was no significant change of ^{1}H NMR spectra even at –80°C. On the other hand, the chemical shifts of the aromatic protons of **3** depend on the temperature. In particular the chemical shifts of the protons of the central benzene rings (7.39 ppm) and *ortho* protons of the terminal benzene rings (7.34 ppm) at 303 K shift to higher field as the temperature is lowered, and the signals appear at 7.24 and 7.17 ppm, respectively at 193 K. Although two possible conformations of **3**, *syn* (similar to the crystal structure) and *anti* (one terminal benzene ring is on the opposite side to the others), could not be distinguished at 193 K, the high field chemical shifts would indicate the increase of *syn* conformation in the population at low temperature, as observed in the ^{1}H NMR spectrum of the triamide.[19] The result suggests that the *syn* conformation of **3** is predominant in solution.

The examples shown here are fundamental compounds that demonstrate the usefulness of the carborane cage in constructing 3-dimensional structures with well-defined spatial relationships. The results described here should provide a basis for synthesizing more complex aromatic molecules containing carborane cages.

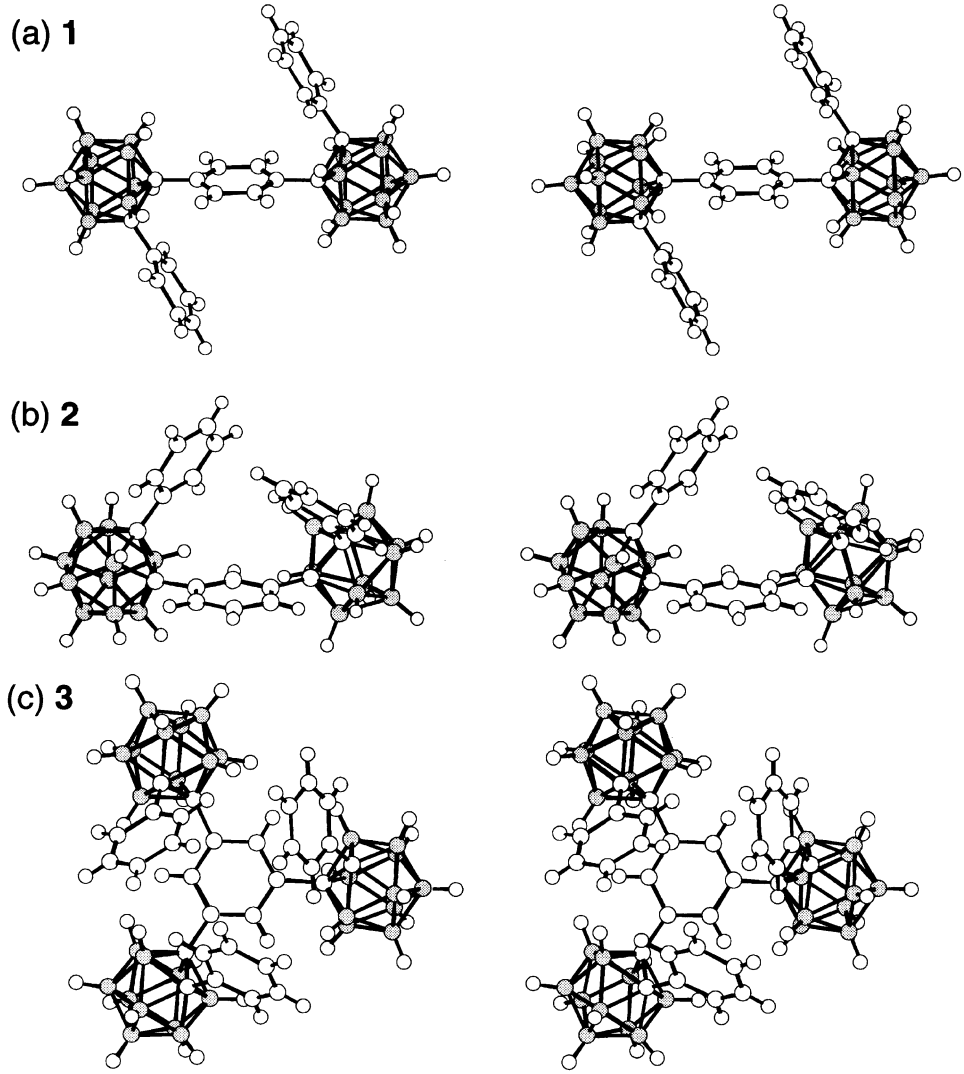

Figure 1. Stereoviews (cross-eyed) of crystal structures of the bis- and tris(2-phenyl-*o*-carboran-1-yl)benzenes.

References

1. Kaszynski, P.; Douglass, A. G. *J. Organomet. Chem.* **1999**, *581*, 28–38.
2. (a) Murphy, D. M.; Mingos, D. M. P.; Haggit, J. L.; Powell, H. R.; Westcott, S. A.; Marder, T. B.; Taylor, N. J.; Kanis, D. R. *J. Mater. Chem.* **1993**, *3*, 139–148; (b) Allis, D. G.; Spencer, J. T. *J. Organomet. Chem.* **2000**, *614–615*, 309–313.
3. For recent reviews see: (a) Hawthorne, M. F. *Angew. Chem., Int. Ed. Engl.* **1993**, *32*, 950–984; (b) Soloway, A. H.; Tjarks, W.; Barnum, B. A.; Rong, F.-G.; Barth, R. F.; Codogni, I. M.; Wilson, J. G. *Chem. Rev.* **1998**, *98*, 1515–1562.
4. (a) Endo, Y.; Iijima, T.; Ohta, K.; Kagechika, H.; Kawachi, E.; Shudo, K. *Chem. Pharm. Bull.* **1999**, *47*, 585–587; (b) Iijima, T.; Endo, Y.; Tsuji, M.; Kawachi, E.; Kagechika, H.; Shudo, K. *Chem. Pharm. Bull.* **1999**, *47*, 398–404; (c) Endo, Y.; Yoshimi, T.; Kimura, K.; Itai, A. *BioMed. Chem. Lett.* **1999**, *9*, 2561–2564; (d) Endo, Y.; Iijima, T.; Yamakoshi, Y.; Yamaguchi, M.; Fukasawa, H.; Shudo, K. *J. Med. Chem.* **1999**, *42*, 1501–1504; (e) Endo, Y.; Iijima, T.; Yamakoshi, Y.; Kubo, A.; Itai, A. *BioMed. Chem. Lett.* **1999**, *9*, 3313–3318; (f) Endo, Y.; Yoshimi, T.; Iijima, T.; Yamakoshi, Y. *BioMed. Chem. Lett.* **1999**, *9*, 3387–3392; (g) Endo, Y.; Yoshimi, T.; Yamakoshi, Y. *Chem. Pharm. Bull.* **2000**, *48*, 312–314; (h) Tsuji, M.; Koiso, Y.; Takahashi, M.; Hashimoto, Y.; Endo, Y. *Biol. Pharm. Bull.* **2000**, *23*, 513–516; (i) Endo, Y.; Yaguchi, K.; Kawachi, E.; Kagechika, H. *BioMed. Chem. Lett.* **2000**, *10*, 1733–1736; (j) Endo, Y.; Iijima, T.; Yamakoshi, Y.; Fukasawa, H.; Miyaura, C.; Inada, M.; Kubo, A.; Itai, A. *Chem. Biol.* **2001**, *8*, 331–345.
5. Andrews, P. C.; Hardie, M. J.; Raston, C. L. *Coordination Chemistry Reviews* **1999**, *189*, 169–198.
6. (a) Hardie, M. J.; Raston, C. L. *Eur. J. Inorg. Chem.* **1999**, 195–200; (b) Hardie, M. T.; Raston, C. L. *Chem. Commun.* **1999**, 1153–1163; (c) Hardie, M. T.; Godfrey, P. D.; Raston, C. L. *Chem. Eur. J.* **1999**, *5*, 1828–1833; (d) Macias, R.; Rath, N. P.; Barton, L. *J. Organomet. Chem.* **1999**, *581*, 39–44.
7. Godfrey, P. D.; Grigsby, W. J.; Nicjols, P. J.; Raston, C. L. *J. Am. Chem. Soc.* **1997**, *119*, 9283–9284.

8. (a) Yang, X.; Jiang, W.; Knobler, C. B.; Hawthorne, M. F. *J. Am. Chem. Soc.* **1992**, *114*, 9719–9720; (b) Muller, J.; Base, K.; Magnera, C. B.; Michl, J. *J. Am. Chem. Soc.* **1992**, *114*, 9721–9722; (c) Jiang, W.; Harwell, D. E.; Mortimer, M. D.; Knobler, C. B.; Hawthorne, M. F. *Inorg. Chem.* **1996**, *35*, 4355–4359.
9. (a) Gill, W. R.; MacBride, J. A. H.; Wade, K. *Angew. Chem., Int. Ed. Engl.* **1993**, *32*, 1328–1329; (b) Coult, R.; Fox, M. A.; Gill, W. R.; Herbertson, P. L.; MacBride, J. A. H.; Wade, K. *J. Organomet. Chem.* **1993**, *462*, 19–29; (c) Jiang, W.; Chizhevsky, I. T.; Mortimer, M. D.; Chen, W.; Knobler, C. B.; Johnson, S. E.; Gomez, F. A.; Hawthorne, M. F. *Inorg. Chem.* **1996**, *35*, 5417–5426; (d) Schoberl, U.; Magnera, T. F.; Harrison, R. M.; Fleischer, F.; Pflug, J. L.; Schwab, P. F. H.; Meng, X.; Lipiak, D.; Noll, B. C.; Allured, V. S.; Rudalevige, T.; Lee, S.; Michl, J. *J. Am. Chem. Soc.* **1997**, *119*, 3907–3917.
10. (a) Zinn, A. A.; Zheng, Z.; Knobler, C. B.; Hawthorne, M. F. *J. Am. Chem. Soc.* **1996**, *118*, 70–74; (b) Zheng, Z.; Knobler, C. B.; Mortimer, M. D.; Kong, G.; Hawthorne, M. F. *Inorg. Chem.* **1996**, *35*, 1235–1243.
11. Songkram, C.; Tanatani, A.; Yamasaki, R.; Yamaguchi, K.; Kagechika, H.; Endo, Y. *Tetrahedron Lett.* **2000**, *41*, 7065–7070.
12. (a) Zhang, J.; Pesak, D. J.; Ludwick, J. J.; Moore, J. S. *J. Am. Chem. Soc.* **1994**, *116*, 4227–4239; (b) Moore, J. S. *Acc. Chem. Res.* **1997**, *30*, 402–413.
13. Takahashi, S.; Kuroyama, Y.; Sonogashira, K.; Hagihara, N. *Synthesis* **1980**, 627–629.
14. Teplyakov, M. M.; Khotina, I. A.; Gelashvili, T. L.; Kovshak, V. V. *Dokl. Akad. Nauk. SSSR* **1983**, *271*, 874–877.
15. Jiang, W.; Knobler, C. B.; Hawthorne, M. F. *Inorg. Chem.* **1996**, *35*, 3056–3058.
16. Tinker, N. D.; Wade, K.; Hibbert, T. G. PCT Int. Appl. WO 98/21216.
17. Compound **1**: mp >290°C (THF) ^{1}H NMR (400 MHz, $CDCl_3$, rt) δ 1.5–3.8 (br, m, 20H), 7.04 (m, 4H), 7.17 (s, 4H), 7.23–7.26 (m, 6H). Anal. calcd for $C_{22}H_{34}B_{20}$: C, 51.34; H, 6.66. Found: C, 51.59; H, 6.65: Compound **2**: mp 230–231°C (diethyl ether). ^{1}H NMR (400 MHz, $CDCl_3$, rt) δ 1.5–3.4 (br, m, 20H), 6.93 (t, $J=8.0$ Hz, 1H), 7.13–7.17 (m, 4H), 7.25–7.31 (m, 6H) 7.28 (t, $J=8.0$ Hz, 2H), 7.38 (t, $J=1.9$ Hz, 1H). Anal. calcd for $C_{22}H_{34}B_{20}$: C, 51.34; H, 6.66. Found: C, 51.29; H, 6.36: Compound **3**: mp >290°C (ethyl acetate). ^{1}H NMR (400 MHz, $CDCl_3$, rt) δ 1.3–3.4 (br, m, 30H), 7.17 (m, 12H), 7.22 (s, 3H), 7.33 (m, 3H). Anal. calcd for $C_{30}H_{48}B_{30}$: C, 49.16; H, 6.60. Found: C, 49.15; H, 6.63.
18. Crystal data of the compounds, **1**: monoclinic; space group, $P2_1/n$ (#14); Z, 2; a, 10.7027(10) Å; b, 13.2247(12) Å; c, 10.8372(9) Å; β, 98.116(2)°; V 1518.5(2) Å^3; D_{calcd}, 1.126 g/cm^3; R, 0.058; **2**: monoclinic; space group, $P2_1/n$ (#14); Z, 4; a, 12.7345(13) Å; b, 12.888(1) Å; c, 18.474(2) Å; β, 100.349(2)°; V 2982.8(5) Å^3; D_{calcd}, 1.146 g/cm^3; R, 0.032; **3**: trigonal; space group, R-3 (#148); Z, 6; a, 20.074(2) Å; b, 18.054(3) Å; β, 100.349(2)°; V 6300.4(13) Å^3; D_{calcd}, 1.159 g/cm^3; R, 0.062.
19. Yamaguchi, K.; Matsumura, G.; Kagechika, H.; Azumaya, I.; Ito, Y.; Shudo, K. *J. Am. Chem. Soc.* **1991**, *113*, 5474–5475.
20. (a) Jorgensen, W. L.; Severance, D. L. *J. Am. Chem. Soc.* **1990**, *112*, 4768–4774; (b) Hobza, P.; Selzle, H. L.; Schlag, E. W. *J. Am. Chem. Soc.* **1994**, *116*, 3500–3506.