Boron-enriched star-shaped molecule via cycloaddition reaction[†]

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Received (in Austin, TX, USA) 12th March 2009, Accepted 5th April 2009 First published as an Advance Article on the web 6th May 2009 DOI: 10.1039/b905076k

The facile synthesis of a thermally stable carborane appended symmetrical star-shaped molecule having six bulky *o*-carborane clusters on the periphery, thereby containing sixty boron atoms was accomplished *via* a cobalt-catalyzed [2 + 2 + 2] cycloaddition reaction.

Carborane clusters are useful synthetic building blocks in the fields of materials science, medicine and organometallic chemistry.¹ Some of the important biomedical applications of carborane clusters include boron neutron capture therapy $(BNCT)^{1a}$ for the treatment of cancer, boron neutron capture synovectomy (BNCS) for the treatment of arthritis,² as contrast agents and as pharmacophores.³ Although a number of boron drug delivery agents have been synthesized so far, delivery of adequate amounts of boron to tissues which would enhance the effectiveness of the treatment is still considered as a challenging task.⁴ To achieve the requisite amount of boron concentration (about 30 $\mu g^{10} B g^{-1}$ tumour for an effective BNCT),⁵ the synthesis of macromolecules containing multiple carborane clusters have attracted significant attention.⁶ Macromolecular and dendritic drug delivery agents are also found to be superior in terms of accumulation and retention in the tumour tissues.6b

However, due to the steric and electronic properties, the syntheses of dendritic and symmetrical star-shaped molecules containing closely placed multiple carborane clusters is a difficult task.⁷ Recently, we have reported the synthesis of symmetrical structures containing three carborane clusters at the periphery of the 1,3,5-phenylene core.⁸ These carborane clusters were attached *via* a boron atom (B-9 position) of the *o*-carborane and therefore can be functionalized to make higher order dendritic molecules. In an attempt to further increase the number of carborane clusters surrounding a symmetrical core, in this paper we report the facile synthesis of a dendritic structure containing six carborane clusters on the periphery of a hexaphenylbenzene core *via* a cobalt-catalyzed [2 + 2 + 2] cycloaddition reactions.

Cobalt-catalyzed cycloaddition reactions of symmetrical alkynes usually generate C_6 -symmetric hexaphenylbenzenes.⁹ Scheme 1 shows a similar cobalt-catalyzed synthetic route for the carborane-appended star-shaped compound **5**. Compound **1**

was synthesized from 1-methyl-*o*-carborane and commercially available 4-iodo benzyl bromide.¹⁰ Then compound **1** underwent Sonogashira coupling reaction with ethynyltrimethylsilane to produce compound **2**. The TMS group of compound **2** was then removed yielding terminal alkyne **3** in excellent yield. Another Sonogashira type coupling reaction between terminal alkyne **3** and compound **1** under copper free conditions worked well for the synthesis of the desired symmetrical alkyne **4**.‡ Compound **4** then underwent facile cobalt catalyzed cycloaddition reaction to produce compound **5** in good yields.§

All compounds were characterized by ¹H, ¹³C and ¹¹B NMR spectra, IR spectra and elemental analysis.† Confirmatory mass spectral analyses of the compounds were also carried out and melting points of all solid compounds were also determined. The dendritic molecule **5** was soluble in relatively non polar organic solvents such as chloroform and dichloromethane. However, compound **5** could be decapitated to



Scheme 1 Synthesis of carborane appended star-shaped molecule.

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[†] Electronic supplementary information (ESI) available: Synthesis and characterization data and NMR spectra of compounds. See DOI: 10.1039/b905076k



Fig. 1 Combined UV-vis and fluorescence spectra of compound 5 recorded at room temperature in dichloromethane at 10^{-4} M and 10^{-6} M, respectively.

convert the neutral *closo*-carboranes to their corresponding $[nido-C_2B_9H_9]^-$ cages that were water soluble. The details of the decapitation reactions and the characterizations of the anion will be given in a later report.

There are few reports on symmetrical compounds having closely placed multiple carborane clusters. We have recently reported the synthesis of a compound that contains *o*-carborane clusters on the periphery of the 1,3,5-phenylene core.⁸ Similar compounds in which *p*-carboranes are attached to a 1,3,5-phenylene core, and trimers of the form $(1,7-C_2B_{10}H_{10}-1,3-C_6H_4)_3$ have been reported.¹¹ In addition, bis-carboranyls of anthraquinones, flourenones and sulfones have been described.¹² Increasing the number of carborane clusters in a molecule increases the boron content of the molecule, which is considered to be very important in making a useful boron drug delivery agent, provided they remain water soluble.^{6a,b} Compound **5** contains six *o*-carborane clusters and thereby possesses about 42% boron by weight.

Not only do carborane appended macromolecular compounds possess a great potential as a boron drug delivery platform, they can also be useful in materials science. Star-shaped hexaphenylbenzenes and their derivatives such as hexabenzocoronenes (HBCs) show remarkable properties such as self assembly and aggregation in solutions, high charge carrier mobilities, and high thermal stability.¹³ Such conjugated systems are also useful in materials science as they can form the core structures for discotic liquid crystals, components in organic field effect transistors, and organic light emitting diodes.^{9a,14} In addition, icosahedral carborane clusters are also considered as versatile building blocks in materials science.^{1b-d} Recent reports reveal that incorporation of icosahedral carborane clusters into different systems have enhanced their thermal stability,15 electrical conductivity16 and also helped in stabilizing different liquid crystalline phases.7b,17 Therefore, carborane containing hexaphenylbenzenes and other such derivatives like HBCs could form the basis for a new class of materials.

Due to the presence of hexaphenylbenzene core, compound **5** shows moderate absorption and emission properties (Fig. 1). The electronic absorption spectrum shows two peaks for compound **5**, one at 230 nm and the other is at 254 nm. The emission spectra of compound **5** showed a major peak at 344 nm. As it is known that carborane clusters do not absorb in the UV-vis region and so any photochemistry is ruled out due to the *o*-carborane clusters,¹⁸ therefore the spectroscopic behaviour of **5** arises from the hexaphenylbenzene core.¹⁹ Compound **5** showed unusual thermal stability which



Fig. 2 TGA curve of compound 5 under nitrogen.

was evidenced from its thermal analysis. To determine the exact melting point of the compound **5**, its DSC analysis was performed and it showed an endothermic peak at 468 °C corresponding to the melting of the compound. In addition, compound **5** shows very little mass loss (less than 10%) up to 491 °C under an inert atmosphere (Fig. 2). This exceptional thermal stability is consistent with its melting point and in accordance with the fact that incorporation of *o*-carborane clusters enhances thermal stability of materials.

In summary, we have developed an expedient synthetic route to the star-shaped molecule 5 containing six bulky o-carborane clusters on the periphery. Due to the presence of hexaphenylbenzene core, compound 5 showed moderate absorbance and emission efficiency and the presence of o-carborane clusters made it highly thermally stable. Deboronation of o-carborane clusters present in compound 5 leads to its water soluble form. Attaching suitable tumour targeting units³ to this boron-rich macromolecular compound in its water soluble form may be useful as a platform for boron drug delivery. Additionally, the deboronated o-carborane clusters may find applications in synthesis of new metallacarboranes.²⁰ The use of *o*-carboranes gives rise to dendrimers where steric crowding is maximized. The synthetic route outlined in Scheme 1 should work just as well with m- and p-carboranes. The use of the latter carborane would decrease steric crowding around the carborane and offer a reactive antipodal C-H for further reactions. Adding more aromatic rings into such structures using similar methodology may form compounds possessing stronger photophysical properties. Such an investigation is currently under way in our laboratory.

This work was supported by grants from National Science Foundation (CHE-0601023), Robert A. Welch Foundation (N-1322), Alexander von Humboldt foundation and NIU Inaugural Board of Trustees Professorship Award. We thank Dr Elizabeth Gaillard and Michael Recchia (Department of Chemistry and Biochemistry, Northern Illinois University) for their assistance during fluorescence studies and TGA/DSC experiments.

Notes and references

[‡] Procedure for synthesis of alkyne **4** via a copper free Sonogashira reaction: to a mixture of compound **1** (55 mg, 0.146 mmol) and terminal alkyne **3** (60 mg, 0.22 mmol) in 2 mL of dry benzene and 5 mL of dry Et₃N was added Pd(PPh₃)₄ (8 mg, 5 mol%) and the reaction mixture was stirred at 70 °C for 20 h. Water was then added to the reaction mixture and it was extracted with dichloromethane and the combined organic fractions were dried over MgSO₄. After evaporation of the solvent, the crude reaction mixture was purified by silica gel column chromatography using 20–25% ethyl acetate in hexane as eluent to obtain pure compound **4** as a white solid. Yield: 30 mg, 40%.

§ Procedure for cobalt-catalyzed trimerization of carborane appended alkyne 4: to the carborane appended alkyne 4 (80 mg, 0.154 mmol) in 10 mL of dioxane, $Co_2(CO)_8$ (15 mg, 30 mol%) was added. The reaction mixture was heated at 110 °C for 20 h. The reaction mixture was then filtered over a silica gel pad. The filtrate was concentrated and purified by silica gel column chromatography using 10–20% ethyl acetate in hexane as eluent to obtain pure compound **5** as a white solid. Yield: 50 mg, 62%.

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