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Icosahedral carboranes as scaffolds for congested regioselective polyaryl compounds: the distinct distance tuning of C–C and its antipodal B–B

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Icosahedral carboranes as scaffolds for congested regioselective polyaryl compounds: the distinct distance tuning of C–C and its antipodal B–B†

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Four-fold aryl substituted o-carborane derivatives with defined patterns of substitution at the antipodal region of the cluster carbon atoms have been achieved. It is proven that this region is congested but lacks steric hindrance. Also, the two antipodal sites Cc–Cc and B9–B12 are affected very distinctly by electron donor substituents.

The closo C2B10H12 icosa-carboranes, o-(1,2), m-(1,7), or p-(1,12), are the most widely studied boron clusters; they can be functionalized by different reactions, in a regioselective manner, with many possible sites of substitution. o-Carborane, 1,2-closo-C2B10H12, acts as a strong electron-withdrawing molecule through the substitution on the carbon, Cc, and as an electron-donating moiety through the boron vertices with a gradation depending on the distance to the carbon atoms. On the other hand, it is well known that the Cc–Cc bond length in o-carborane and metalla-o-carborane strongly depends on the electronic nature of the immediate Cc-substituents; π-donor substituents bonded to the Cc, as well as atoms with lone pairs, donate electron density to the σ+(Cc–Cc) antibonding orbital (negative hyperconjugation) of o-carborane, which lies in the Cc–Cc bond, increasing significantly the Cc–Cc bond distance. In the case of aryl substituents, the orientation of the substituents has a significant impact on the electron donation. The longest Cc–Cc distance ever reported is 2.156(4) Å for the 1,2-(CR2F2)2,1,2-closo-C2B10H10, {R = pentamethylenedene; Fe = (η5-C5H4)Fe(η5-C5H5)} o-carborane cluster derivative. While the plasticity of the Cc–Cc bond has been investigated, the possibility of a similar behaviour at the B–B bonds located antipodal to the cluster carbon atoms remained unexplored.

In addition, if π-aromaticity and tridimensional aromaticity of the icosahedral boranes are two sides of the same coin,
C‐C atoms. In 1, only two adjacent iodo groups are present, again antipodal to the C‐C unit. Four Grignard reagents were used, phenylethynyl magnesium, phenyl magnesium and allyl magnesium chlorides, and 4-benzaldehyde dimethyl acetal magnesium bromide were purified (see ESI†). After refluxing overnight, the corresponding crude compounds were obtained (Scheme 1a), which was confirmed by multinuclear NMR, cis-4-benzaldehyde dimethyl acetal magnesium bromide proceeded to yield (Scheme 1a), which was confirmed by multinuclear NMR, cis-4-benzaldehyde dimethyl acetal magnesium bromide proceeded to yield 9,12-C6H4CHO to produce 9,12-(C6H4CHO)2-closo-C2B10H10, 3, in 71% yield (Scheme 1a), which was confirmed by multinuclear NMR, FTIR, mass spectrometry and elemental analysis.

Deprotection of the carbonyl group was achieved with diethyl ether in aqueous HCl 3 M solution to produce 9,12-(C6H4CHO)2-closo-C2B10H10, 4, in 96% yield (Scheme 1a). Suitable crystals for X-ray diffraction of 3 and 4, which were grown in chloroform (Fig. 1) unambiguously and unequivocally confirmed that 3 and 4 were obtained. Furthermore, tetrasubstitution on 2 to yield 8,9,10,12-Ph4-1,2-closo-C2B10H8 (10) was expected by reaction of 2 with phenyl magnesium chloride but 8,10-Ph2-9,12-I2-1,2-closo-C2B10H8 (5) was obtained with only two substitutions (Scheme 1b). To get more insight into the reason for this atypical or at least unexpected result, we investigated 11B{1H}-NMR chemical shifts (Fig. 2) and performed DFT calculations. The 11B{1H}-NMR chemical shifts of 2 were unambiguously assigned by the aid of a 2D 11B{1H}–11B{1H}-NMR COSY experiment. The B(9,12) resonances of these B–I vertices at 2 appear at –7.1 ppm that are not so different from the B–H resonances of the unreactive B(9,12) vertices in the pristine 1,2-closo-C2B10H12 (–3.1 ppm); on the contrary, the B(8,10) vertex resonances of 2 appear close to –16 ppm being very similar to the B–I reactive B(9,12) vertices in 1 that resonate at –14.9 ppm (Fig. 2). It can be seen in the 11B{1H}-NMR of 1,2-closo-C2B10H12, 9,12-I2-closo-1,2-C2B10H10 (1) and 8,10,9,12-I4-1,2-closo-C2B10H8 (2) that the four iodo groups in the congested area of 2 are not electronically identical. Electronically, the B(8,10) vertices in 2 are strongly affected upon I substitution shifting 12 ppm upfield from B(8,10)–H to B(8,10)–I. These B(8,10)–I vertices are highly reactive and lead readily to disubstitution to obtain B–Ph in 5. The calculated Mulliken charges (Table S1 in ESI†) are in good agreement with the chemical shifts; the charge of the reactive B(8,10)–I vertices in 2 is +0.66, while the charge of the B(8,10)–I vertices in 5 is +0.31.

Clearly, the B(9,12) vertices in 5 are not only less reactive electronically, but less accessible for the reactant (steric hindrance) due to the phenyl substituents at the B(8,10) vertices. Since the four-fold phenylation of 2 was unsuccessful, a new synthetic strategy aiming at 8,9,10,12-Ph4-1,2-closo-C2B10H8 was designed. The positional isomer of 5, 8,10-I2-9,12-Ph2-1,2-closo-C2B10H8 (7) was synthesised starting from 6. In 7 the two iodo substituents would be ready for substitution at less crowded positions than in 5; moreover, DFT calculations suggest a more reactive B–I vertex. This led us to perform the cross coupling reaction of 2 with PhMgCl to obtain 9,12-Ph2-1,2-closo-C2B10H10, 6. This was...
treated with I₂ in a sealed tube at 210 °C for 4 h (73% yield, Scheme 1c).

The ¹¹B NMR spectra of 7 verified the more reactive B–I vertices (they resonate at ~20.1 ppm), in agreement with the DFT calculations. Furthermore, as it was mentioned earlier, the different allocation of the four substituents in 7 with respect to 5 could decrease the steric effect of the two bulky phenyl groups since they are sited at the neighbouring vertices B(9,12), and the two remaining iodo substituents are placed one far from the other and at the lateral position, so the B–I substitutions by the phenyl groups are sterically feasible. However, the cross-coupling reaction of 7 with PhMgCl did not lead to the sought four-fold phenylation, only to unreacted 7 (Scheme 1c).

To check the possibility of further substitution on the 5 congested electron-rich region of the α-carborane cluster, we decided to combine the pre-existing sp² (Ph) in 5, with the sp (PhC≡C) and sp¹ (allyl) units, respectively. The reaction of 5 with phenylethynyl magnesium chloride to produce 8 was unsuccessful as no iodo was exchanged (Scheme 2). Instead, when using a less crowded allylmagnesium chloride, the coupling reaction of 5 with allylmagnesium chloride leads to the four-fold substitution by the formation of 8,10-Ph₂-9,12-(CH₂CH₂)₂-1,2-closo-C₂B₁₀H₈, 9, in 75% yield (Scheme 2). ¹¹B and ¹H NMR spectroscopy, MALDI-TOF-MS and EA data along with its X-ray structure from the crystals grown from a chloroform solution (Fig. 3 and ESI†) confirmed the allylation of B(9,12) vertices on 5. Since the sp and sp² four-fold substitution is possible, the steric hindrance in the proposed tetra-substituted 8,10,9,12-Ph₄-1,2-closo-C₂B₁₀H₈ (10, Scheme 3) compound was investigated by using different hypothetical isodesmic reactions (see more details in ESI†). The DFT calculations indicated that there is not enough steric hindrance in 10 to prevent four-fold phenyl substitution, therefore 10 should be thermodynamically available and so its synthesis should be restricted only by kinetic reasons. To prove this hypothesis, we have modified the reaction conditions by using 1,4-dioxane instead of THF, which increases the reaction temperature up to 101 °C (Scheme 3). After 16 hours of refluxing, the ¹H-NMR spectra of the crude mixture displayed new broad peaks in the region 4.5–5.5 ppm, in which the C–H resonates, indicating the formation of additional compounds.³ By working up (see ESI†), the isolation of four-fold substituted α-carborane derivative 10 as well as the trisubstituted 11 was achieved in 18 and 59% yield, respectively. To further increase the yield of 10, mesitylene (b.p. 165 °C) and diglyme (b.p. 162 °C) were used as solvents however, the yield was lower (12% and 16%, respectively) probably due to other side reactions. Finally, the reaction in toluene, slightly increased the yield of 10 to 21 and 34% after 16 h and 5 days’ reaction time, respectively. The reaction in toluene was carried out under microwave irradiation (see in ESI†) as well, but a similar ratio of 10 and 11 (comparing the reaction in toluene after 16 h reflux) was observed after 2 h irradiation at 120 °C according to the ¹H NMR spectra of the crude product. It is to be emphasized that the by-product of 10 (compound 11) is suitable for recycling, thus the overall yield can be significantly improved. Crystals of 10 and 11 suitable for X-ray diffraction.

Fig. 2 Diagram ¹¹B(¹H)-NMR spectra with the peak assignments for the α-carborane, 1, 2 and 5 derivatives.

Fig. 3 Crystal structures of 9. Thermal ellipsoids have been drawn with 20% probability.

Scheme 2 Kumada cross coupling reactions on 2 by using (i) PhC≡CMgCl, (ii) CH₂=CHCH₂MgCl, in the presence of cis-[PdCl₂(PPh₃)₂] and Cul as catalysts, in refluxing THF overnight.

Scheme 3 Kumada cross coupling reactions on 2 in refluxing dioxane for 16 h.
Fig. 4 Crystal structures of 10 (right) and 11 (left). Thermal ellipsoids have been drawn with 20% probability.

(Fig. 4) were obtained using the vapour diffusion technique (pentane/acetone, see ESI†). The four-fold phenyl groups at the dense antipodal region of the cluster carbon atoms of the closo-o-carborane in 10 parallels the nanohybrid [η₅-C₅₆H₃]₆, which made the extremely hydrophobic C₅₆ fullerene soluble in water.16a

A search at the Cambridge Structural Database17 shows only seven hits for 9,12-(aryl)₄-,1,2-closo-C₅B₁₀H₁₀, whose B₉–B₁₂ distances are in the range 1.781–1.824 Å (Table S1 in ESI†), which are comparable, although a bit longer than that in o-carborane (1.776 Å).18 Although a certain plasticity at the B–B bonds antipodal to the Cc atoms is observed, the effect is considerably smaller than the plasticity found for the adjacent Cc atoms in the o-carborane cluster. This is not surprising as the antibonding orbital is mainly located between the adjacent Cc atoms for these derivatives.5 Compared to the electron-donation to the σ*(Cc–Cc), whose extent in terms of distance has been found experimentally at 2.156(4) Å in 1,2-(Cr₂F₆)₂-,1,2-closo-C₂B₁₀H₁₀7 and computed at 2.64 Å for 1,2-(CH₂)₂-,1,2-C₂B₁₀H₁₀,5 the maximum elongation found in the antipodal region of 10 (1.822 Å) or 11 (1.824) indicates a minor effect, near 0.048 Å. In agreement, the second-order perturbation theory analysis on the NBO basis reveals weak interactions (sum of them ~12 kcal mol⁻¹) between the aryl π-systems and the antibonding orbitals of the boron atoms, which was in good agreement with enlargement of the B–B distances in the cluster. This enforces the concept of the electron back donation to the σ*(Cc–Cc) vs. the very much abused steric hindrance. The proven, although weak, influence of the aryl groups in the plasticity on the B₉–B₁₂ bonds and the possibility of substitution at the Cc–H vertices foresee these o-carborane derivatives as appropriate synths for surface functionalization; research in this direction is underway in our laboratories.

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Conflicts of interest

There are no conflicts to declare.