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Molecular construction based on icosahedral carboranes and aromatic urea groups. A new type of carboracycle

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Abstract—Members of a new family of macrocyclic compounds incorporating icosahedral carboranes are described, together with their precursors. These macrocycles (**1**–**3**) are composed of 1,7-dicarba-*closo*-dodecaborane (*m*-carborane) moieties linked via their carbon vertices through *N*,*N*′-dimethyldiphenylurea groups. The structures of **1**–**3** have been determined by X-ray crystallography.

The icosahedral carboranes (dicarba-*closo*-dodecaboranes)[1] are chemical building blocks of high boron content, remarkable thermal and chemical stability, spherical geometry and exceptional hydrophobic character. Their unusual properties make them uniquely suitable for several specialized applications in the field of materials sciences and biomedical sciences. We have aimed to clarify their electronic properties in the field of physical organic chemistry[2] and to apply their spherical geometry and hydrophobic character in the field of medicinal chemistry.[3] Carboranes have also attracted interest as both guest and host molecules in the field of supramolecular chemistry.[4] Recent studies in this area include the effects of π-bonding interactions between cage CH and aromatics,[5] and the synthesis and inclusion complexes of macrocyclic arrays of carboranes (carboracycles).[6] On the other hand, we have demonstrated that *N*-methyl aromatic amide[7] and urea[8] groups exist in *cis*-orientation to the carbonyl group, both in the crystal and in solution. Recently, we have reported the construction of aromatic molecules by utilizing the *cis*-preference of *N*-methyl aromatic ureas in combination with regulation of the C-substituent on the 1,2-dicarba-*closo*-dodecaborane (*o*-carborane) cage.[9] The results were expected to be useful for construction of cyclic, layered or helical molecules with both hydrophobic and hydrogen-bonding characters. Therefore, we designed and synthesized simple macrocyclic compounds composed of 1,7-dicarba-*closo*-dodecaborane (*m*-carborane) moieties linked via their carbon vertices through *N*,*N*′-dimethyldiphenylurea groups (**1**–**3**) as a new type of carboracycles, aiming

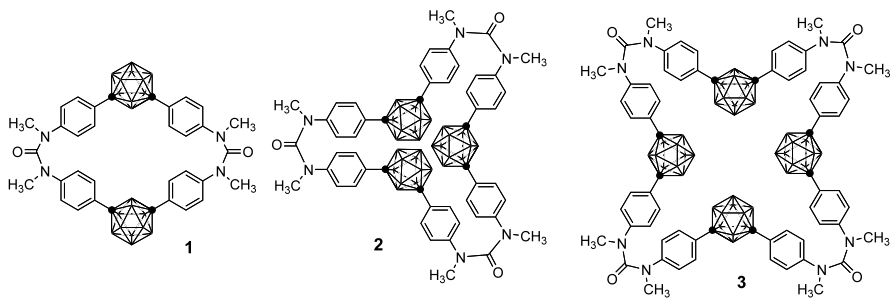

Figure 1. Structures of the designed compounds (**1**–**3**). In icosahedral cage structures throughout this paper, closed circles (●) represent carbon atoms and other vertexes represent BH units.

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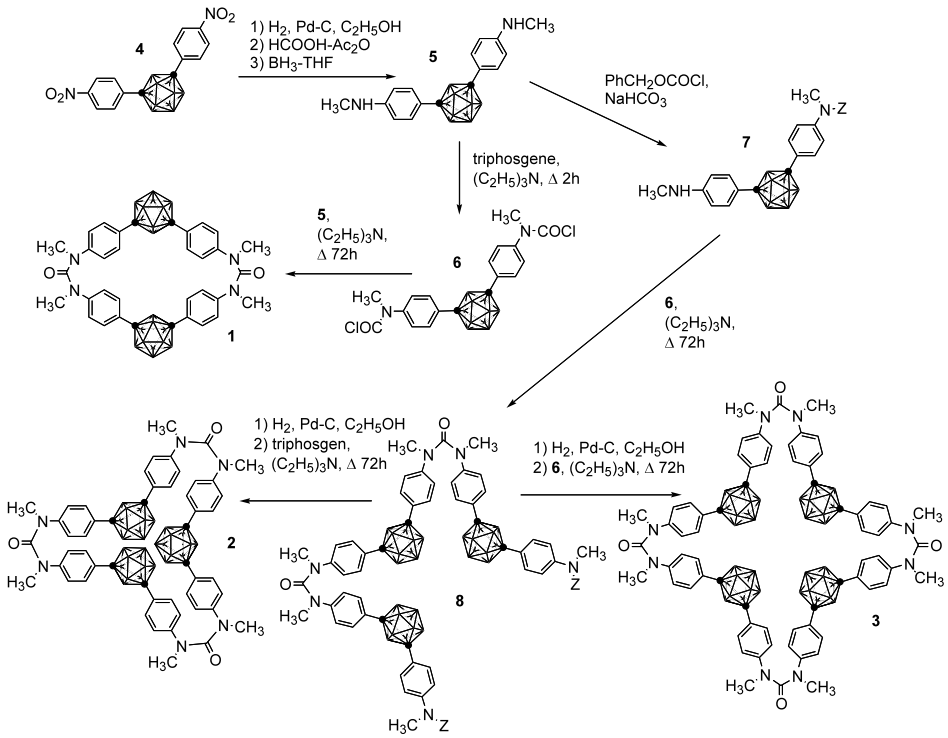
toward carborane-containing functionalized molecules (Fig. 1).

The syntheses of the designed compounds are outlined in Scheme 1. The 1,7-bis(4-nitrophenyl)-*m*-carborane (**4**) was prepared from the *C*-copper derivative of *m*-carborane with 4-nitroiodobenzene in dimethoxyethane in the presence of pyridine in 51% yield.[10] Catalytic hydrogenolysis of the nitro group, formylation of the amine group, and reduction of the formyl group afforded 1,7-bis(4-methylaminophenyl)-*m*-carborane (**5**) in 56% yield. Compound **5** was converted to the carbamoyl chloride (**6**) by treatment with triphosgene and triethylamine in 1,2-dichloroethane under reflux for 2 h in 94% yield. Condensation of the *N*-methylamine (**5**) and the carbamoyl chloride (**6**) with triethylamine gave the cyclic dimer (**1**) in 1,2-dichloroethane under reflux for 72 h in 60% yield. Compound **5** was also converted to the mono-protected *N*-methylamine bearing a carbobenzoxy group (**7**) in 43% yield. Condensation of 2 equivalents of the mono-protected amine (**7**) and the carbamoyl chloride (**6**) with triethylamine in 1,2-dichloroethane under reflux for 72 h gave the protected trimer (**8**) in 66% yield. After deprotection of the carbobenzoxy group of (**8**) (91%), treatment with triphosgene and triethylamine in 1,2-dichloroethane under reflux for 72 h afforded the cyclic trimer (**2**) in 41% yield. Condensation of the protected trimer (**8**) and



Scheme 1.

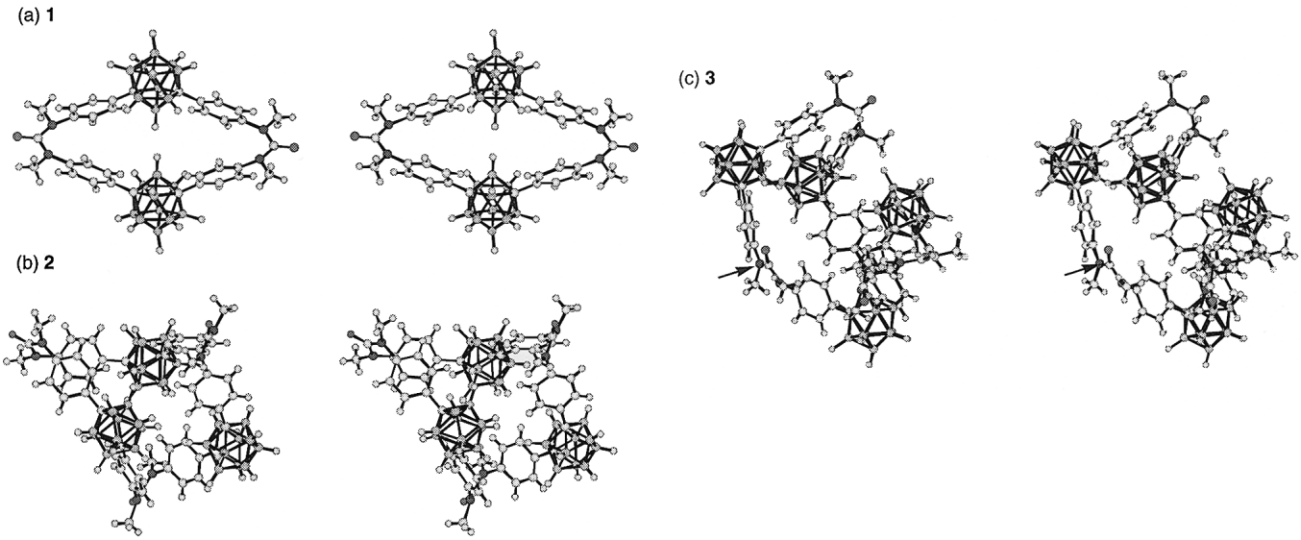
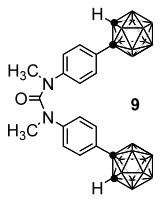


Figure 2. Stereoviews of crystal structures of the cyclic carborane-containing ureas. Solvent molecules (ethyl acetate for **2** and chloroform for **3**)[12] are omitted. The arrow in (c) indicates *trans* conformation.

Table 1. Selected dihedral angles of diarylurea skeletons

	Dihedral angles (°)	
	Ar versus Ar planes	Ar versus urea planes
1[a]	29.0	66.5, 72.0
2	37.1	63.7, 66.2
	36.5	69.3, 69.6
	28.3	65.1, 66.0
3	31.5	66.7, 68.0
	24.8	69.7, 70.3
	28.9	69.7, 70.9
	62.4[b]	23.2,[b] 68.3
9	24.5	68.6, 70.4
10	35.4	65.3, 65.8

[a] Asymmetric center exists in the crystal structure.
[b] The C–N bond, which indicates by an arrow in the Fig. 2(c), is *trans*, with the methyl group *trans* to the carbonyl oxygen atom.



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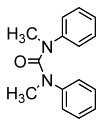

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the carbamoyl chloride (**6**) with triethylamine in 1,2-dichloroethane under reflux for 72 h gave the cyclic tetramer (**3**) in 56% yield. All of the compounds synthesized were confirmed to have appropriate elemental analysis and NMR spectroscopic data.[11]

The structures of the cyclic compounds were examined by ^{1}H NMR. All the cyclic compounds (**1**–**3**) exhibited a single signal of *N*-methyl protons, and two sets of aromatic signals, which indicate that these compounds have symmetrical structures or exist in rapid equilibrium. There was no significant change in the chemical shifts of any compound even at 203 K. Although the detailed conformations in solution were not examined, the comparison of the chemical shifts suggested that the urea bonds in these cyclic molecules are predominantly (*cis*,*cis*). The protons *ortho* to the urea bonds of **1**–**3** are observed at 6.55–6.69 ppm, which is similar to those of *N*,*N*′-bis[4-(*o*-carboran-1-yl)phenyl]-*N*,*N*′-dimethylurea (**9**, 6.74 ppm), having (*cis*,*cis*) conformation, and at significantly higher field than those of *N*,*N*′-bis[4-(*o*-carboran-1-yl)phenyl]urea (7.33 ppm) with (*trans*,*trans*) conformation.

The crystal structures of the cyclic compounds[12] are shown in Fig. 2. As expected, compound **1** with a rather small ring size has a symmetrical structure in which both the urea bonds take (*cis*,*cis*) conformations. Interestingly, the dihedral angle between two face-to-face aromatic rings is 29.0°, which is smaller than that (35.4°) of unsubstituted *N*,*N*′-dimethyl-*N*,*N*′-diphenylurea (**10**, Table 1). This may not be due to ring strain owing to the bulky carborane moieties, since acyclic **9** has a much smaller value (24.5°).[9] Similarly, compound **2** exists in all-(*cis*,*cis*)-urea structure, while compound **3** has one urea bond with (*cis*,*trans*) conformation besides three (*cis*,*cis*) urea bonds. At present, it is unknown whether its crystal structure is essentially more stable than the all-(*cis*,*cis*) conformation. The flexible macrocyclic system in **3** may be subject to some conformational or packing effects in the crystal structure of **3**. The dihedral angles between aromatic rings attached to the same urea bond with (*cis*,*cis*) conformation are 28–37° for **2**, and 25–32° for **3** (Table 1). The dihedral angles between the aromatic and neighboring (*cis*,*cis*) urea planes are similar results (64–71°) among **1**, **2**, **9** and **10**, independently of the substituent or ring system. These results indicate that the macrocyclic structure only slightly affected the folded structure of the (*cis*,*cis*) *N*,*N*′-dimethyl-*N*.*N*′-diphenylurea skeleton.

Among the three compounds, **1** exhibited a unique packing structure in the crystal. As shown in Fig. 3, the crystal structure of **1** is rather planar, viewed from the direction such that the two carborane groups overlap each other. The polar carbonyl groups at the terminals in one molecule exist near the carboranes of other

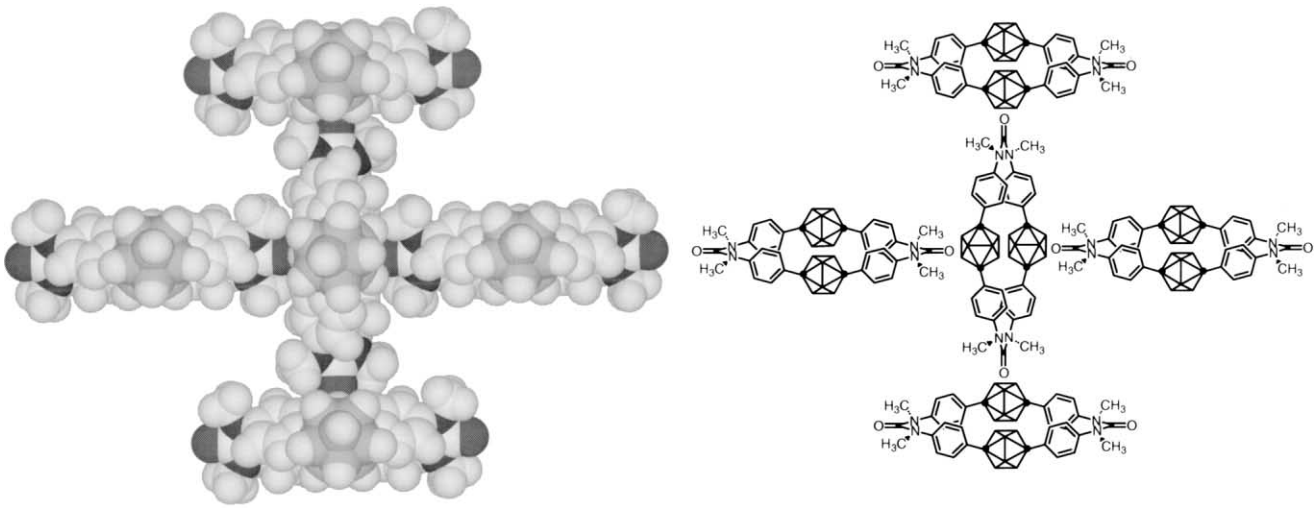

Figure 3. Crystal packing structures of **1**.

molecules close to the cavity, although the cavity of **1** is small. Similarly, the cavity of the molecule is capped by two carbonyl groups of the neighboring molecules from both sides. These molecules are nearly perpendicular each other, and consequently they form a regular lattice structure.

In conclusion, we synthesized several members of a new family of macrocyclic compounds composed of 1,7-dicarba-*closo*-dodecaborane (*m*-carborane) moieties linked via their carbon vertices through *N*,*N*′-dimethyldiphenylurea groups. The results described here should make it possible to develop a range of carborane-containing functionalized molecules.

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11. Compound **1**: mp 270–271°C (*n*-hexane–ethyl acetate) ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.6–3.3 (br, m, 20H), 3.20 (s, 12H), 6.55 (d, $J=8.8$ Hz, 8H), 7.10 (d, $J=8.8$ Hz, 8H). Anal. calcd for $C_{34}H_{48}B_{20}N_4O_2$: C, 53.66; H, 6.36; N, 7.36. Found: C, 53.62; H, 6.36; N, 7.36: Compound **2**: mp 270–271°C (ethyl acetate) ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.6–3.7 (br, m, 30H), 3.16 (s, 18H), 6.69 (d, $J=8.6$ Hz, 12H), 7.15 (d, $J=8.6$ Hz, 12H). Anal. calcd for $C_{51}H_{72}B_{30}N_6O_3$: C, 53.66; H, 6.36; N, 7.36. Found: C, 53.41; H, 6.50; N, 7.22. Compound **3**: mp 270–271°C (ethyl acetate) ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.6–3.5 (br, m, 40H), 3.17 (s, 24H), 6.64 (d, $J=8.6$ Hz, 16H), 7.11 (d, $J=8.8$ Hz, 16H). Anal. calcd for $C_{68}H_{96}B_{40}N_8O_4$: C, 53.66; H, 6.36; N, 7.36. Found: C, 53.62; H, 6.36; N, 7.36.
12. Crystal data of the ureas, **1**: $C_{34}H_{48}B_{20}N_4O_2$; monoclinic; space group, $P2_1/n$ (#14); $Z=2$; $a=10.7789(8)$; $b=16.650(1)$; $c=12.0149(9)$ Å; $\beta=94.879(2)°$; $V=2148.5(2)$ Å^3; $D_{calcd}=1.176$ g/cm^3; $R=0.070$; **2**: $C_{51}H_{72}B_{30}N_6O_3\cdot 2C_4H_8O_2$; triclinic; space group, P-1 (#2); $Z=2$; $a=11.911(2)$; $b=15.619(2)$; $c=20.707(3)$ Å; $\alpha=94.874(2)$; $\beta=99.721(2)$; $\gamma=97.266(2)°$; $V=4744.2(8)$ Å^3; $D_{calcd}=1.012$ g/cm^3; $R=0.095$; **3**: $C_{68}H_{96}B_{40}N_8O_4\cdot 4CHCl_3$; triclinic; space group, P-1 (#2); $Z=2$; $a=16.816(3)$; $b=17.334(4)$; $c=18.634(4)$ Å; $\alpha=67.882(3)$; $\beta=82.890(3)$; $\gamma=81.490(4)°$; $V=4962.5(16)$ Å^3; $D_{calcd}=1.338$ g/cm^3; $R=0.095$.