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Structures of *N*,*N*′-bis(1,2-dicarba-*closo*-dodecaboran-1-yl)-phenylureas: building blocks for carborane-containing macromolecules

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Abstract

We report the preparation and structural analysis of carborane-containing diphenylureas (**1a**–**c** and **2a**–**c**). The secondary ureas (**1**) exist in *trans*-conformation. In spite of the bulkiness of the carborane cage, the *N*-methylated ureas (**2**) exist in *cis*-conformation, both in solution and in the solid-state. The results should make it possible to utilize the construction of more complex molecules. © 2000 Elsevier Science Ltd. All rights reserved.

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Icosahedral carboranes (dicarba-*closo*-dodecaboranes) are a class of carbon-containing boron-cluster compounds having remarkable thermal and chemical stability and exceptional hydrophobic character, compared with other boron-containing compounds. Their unusual properties make them uniquely suitable for several specialized applications in the field of materials sciences and biomedical sciences. The high boron contents and chemical and thermal stability of the carboranes have been utilized in the preparation of thermostable polymers[1] and carrier molecules for boron neutron capture therapy.[2] The delocalization of 26 skeletal electrons in the cage has been utilized in the preparation of materials for liquid crystals[3] and non-linear optics.[4] We have recently reported applications of carboranes for biologically active molecules based on the spherical geometry and hydrophobic surface of the cage.[5] Carboranes have also attracted interest as both guest and host molecules in the field of supramolecular chemistry.[6] Recent studies in this area include the effects of π-bonding interactions between cage CH and aromatics,[7] and the synthesis and inclusion complexes of macrocyclic arrays of carboranes.[8]

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On the other hand, we have described the conformational alteration caused by *N*-methylation of aromatic amides,[9] guanidine[10] and ureas.[11] The *N*-methyl group in these compounds exists in *cis*-orientation to the carbonyl group, both in the crystal and in solution.[12] Combination of the *cis*-preference of *N*-methylamides and regulation of the C-substituent on the carborane cage should be useful for construction of cyclic, layered or helical molecules with both hydrophobic and hydrogen-bonding characters. These considerations led us to design and synthesize compounds having carborane and urea moieties (**1a**–**c** and **2a**–**c**), as shown in Fig. 1, to see whether they might be suitable building blocks for construction of more complex molecules. In icosahedral cage structures throughout this paper, filled circles (●) represent carbon atoms and other vertexes represent BH units.

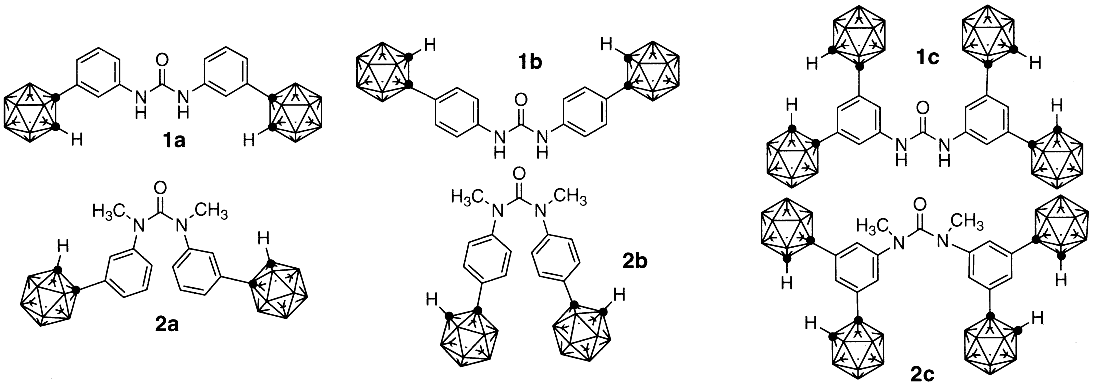
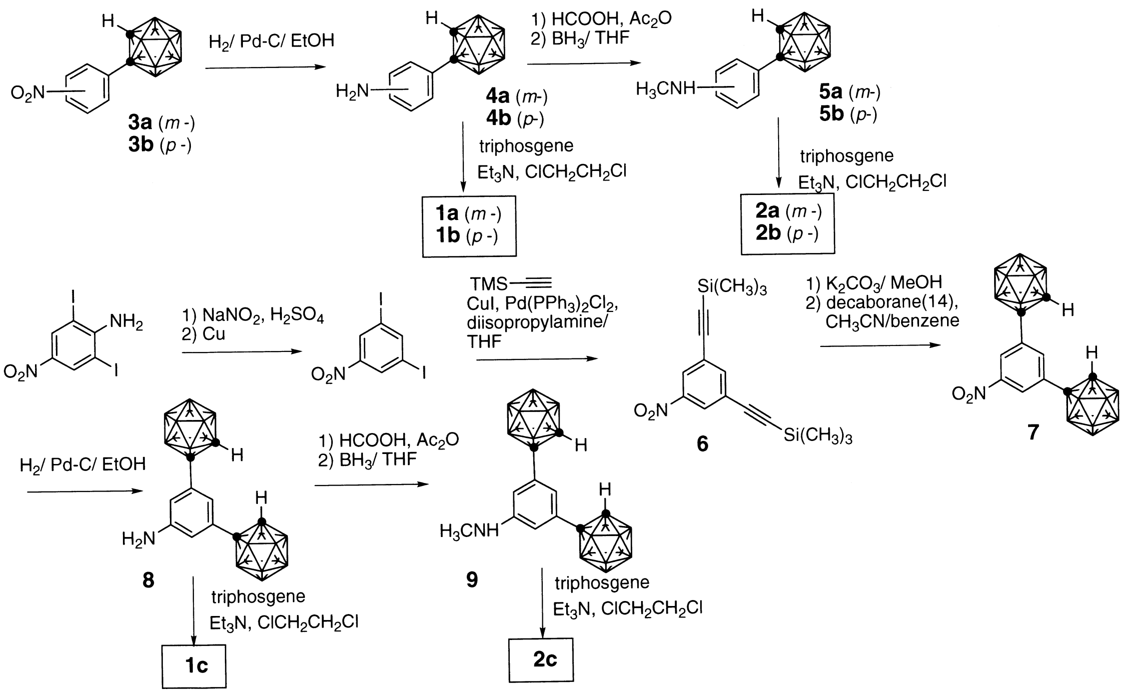


Figure 1. Structures of the designed ureas (**1a**–**c** and **2a**–**c**)

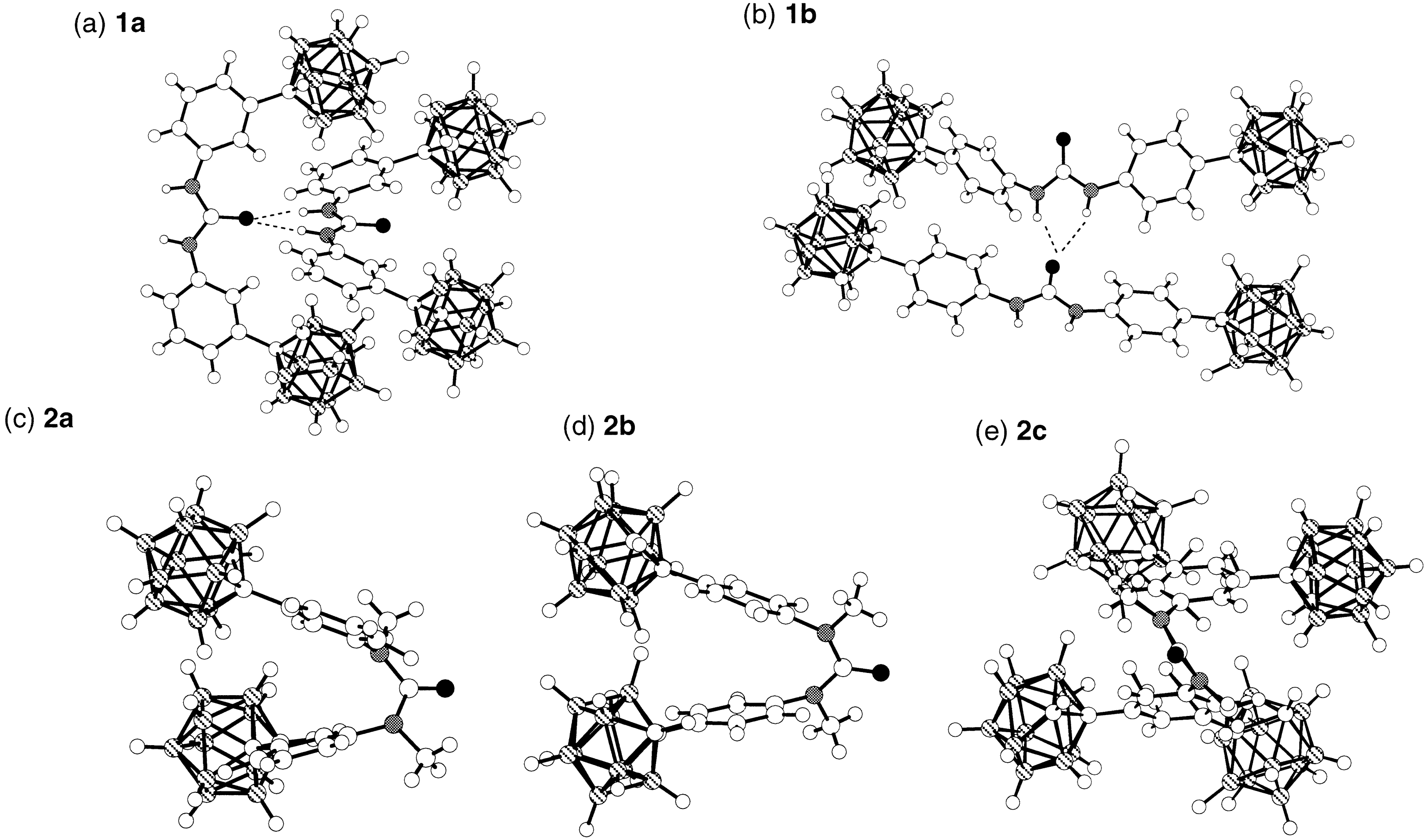
The syntheses of the designed ureas are outlined in Scheme 1. The *N*,*N*′-diphenylureas and the *N*,*N*′-dimethyl-*N*,*N*′-diphenylureas (**1** and **2**) were synthesized in several steps starting from *m*- and *p*-nitrophenylcarborane[13] (**3a** and **3b**). The nitrophenylcarboranes were reduced to the corresponding aniline derivatives (**4a** and **4b**) in 81–82% yields. The anilines were allowed to react with triphosgene in the presence of triethylamine to give the secondary ureas (**1a** and **1b**) in 82–83% yields. Alternatively, formylation of the anilines (**4a** and **4b**) with formic acetic anhydride followed by reduction gave the *N*-methylanilines (**5a** and **5b**) in 80–89% yields. The *N*-methylanilines were then allowed to react with triphosgene under reflux to afford the desired *N*-methylated ureas (**2a** and **2b**) in 68–72% yields. The synthesis of the designed secondary and *N*-methyl ureas with two carboranyl groups on an aromatic nucleus was started from 2,6-diiodo-4-nitroaniline. Deamination of the nitroaniline was performed by diazotization followed by reduction to give 3,5-diiodo-4-nitrobenzene.[14] The nitrobenzene was allowed to react with ethynyltrimethylsilane to afford bis(trimethylsilylethynyl)nitrobenzene (**6**) in a quantitative yield. After removal of the trimethylsilyl groups (84%) of **6**, construction of the *o*-carborane cage with *nido*-decaborane(14) afforded 3,5-dicarboranyl-4-nitrobenzene (**7**) in 12% yield. Compound **7** was reduced to the corresponding aniline derivative (**8**, 86%), which was converted to the secondary urea **1c** in 31% yield. The *N*-methylaniline (**9**) was also converted to the *N*-methylated urea **2c** in 39% yield. All of the compounds synthesized were confirmed to have appropriate elemental analysis and NMR spectroscopic data.[15]



Scheme 1. Synthesis of *N*,*N*′-diphenylureas (**1**) and *N*,*N*′-dimethyl-*N*,*N*′-diphenylureas (**2**)

The crystal structures of five ureas[16] are shown in Fig. 2. Two secondary ureas, **1a** and **1b**, have (*trans*, *trans*) conformation in the crystals, like unsubstituted *N*,*N*′-diphenylurea. As observed in the crystal structures of several ureas,[17] both compounds form intermolecular hydrogen bonds (distance between carbonyl oxygen and nitrogen atoms, 2.86–3.27 Å) that line the molecules in chains. The dihedral angles between the two hydrogen-bonding amide planes are 90.7° for **1a**, and 44.2° and 56.7° for **1b** (two molecules in the asymmetric unit). Thus, each molecule of **1a** exists perpendicular to the neighboring molecules. Interestingly, in the chain structure of **1a**, both carborane moieties in one molecule are located on the amide plane of the neighboring molecule. Consequently, the hydrogen-bonding urea chains are surrounded by hydrophobic groups, phenyls and carboranes.

N-Methylated ureas, **2a**–**c**, have different crystal structures from the secondary ureas, **1a** and **1b**, and exist in (*cis*, *cis*) conformations, as observed in *N*,*N*′-dimethyl-*N*,*N*′-diphenylurea.[11] Thus, the bulky carborane substituents did not affect the *cis* conformational preference of *N*-methylated aromatic ureas. Selected structural parameters are listed in Table 1. The structures of the secondary urea skeletons depend on the substituents (or crystal packings). The diarylurea moiety of **1a** is more planar, compared to unsubstituted *N*,*N*′-diphenylurea, with twisting between the aromatic rings and the urea plane. Similarly, one of the two molecules of **1b** in the asymmetric unit exists in a rather planar conformation, while the other has a twisting conformation at the phenyl–nitrogen bond. This may be caused by intermolecular T-shaped phenyl–phenyl interaction: the dihedral angle between the phenyl rings and the distance between the ring centers are 89.0° and 5.19 Å, respectively.[18] On the other hand, the diarylurea structures of (*cis*, *cis*) conformations of **2a**–**c** are similar to each other, including unsubstituted *N*,*N*′-dimethyl-*N*,*N*′-diphenylurea. The two aromatic rings are twisted with respect to the urea plane at around 60–70°,



(a) **1a**

(b) **1b**

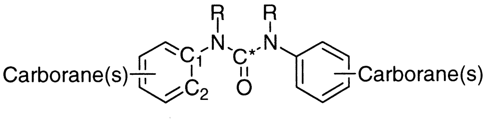
(c) **2a**

(d) **2b**

(e) **2c**

Figure 2. Crystal structures of carborane-containing ureas. Two molecules exist in an asymmetric unit of **1b**. Unrefined solvent molecules in the crystals of **2b** and **2c** are omitted

Table 1
Selected torsion and dihedral angles of diarylurea skeletons



	Torsion Angles (deg)		Dihedral Angles (deg)	
	N–C*–N–C_1	C*–N-C_1-C_2	Ar vs Urea planes	Ar vs Ar planes
N,N'-Diphenylurea	4.4, 0.0	39.1, 43.6	35.8, 42.3	26.4
1a	4.5, 4.5	7.1, 7.0	15.5, 15.5	31.9
1b [a]	10.5, 4.2	6, 1	7.0, 15.7	17.7
	6.8, 22.5	4, 54.3	21.3, 49.5	69.9
N,N'-Dimethyl-*N,N'*-diphenylurea	31.4, 35.3	51.1, 45.0	65.3, 65.8	35.4
2a	42.7, 34.3	44.2, 36.2	66.6, 66.3	39.3
2b	36.6, 29.7	51.4, 46.6	68.6, 70.4	24.5
2c	36.3, 35.5	37.0, 37.9	62.1, 61.5	43.9

[a] Two molecules exists in an asymmetric unit.

and are located face-to-face with 25–40° dihedral angles, independent of the existence of bulky carboranyl substituents.

The structures of the ureas in solution were also examined by ^{1}H NMR. In all cases, the *N*-methylated compounds (**2a**–**c**) exhibited the signals of the aromatic protons at higher field than the corresponding secondary ureas (**1a**–**c**). For example, the protons *ortho* to the urea bonds of **2** are observed at about 0.6 ppm higher than those of **1**, which is similar to the difference between *N*,*N*′-diphenylurea and *N*,*N*′-dimethyl-*N*,*N*′-diphenylurea (0.56 ppm). The detailed conformational features could not be evaluated because of their fast equilibration; there was no significant change of ^{1}H NMR spectra even at 183 K. However, comparison of the chemical shifts indicated that all three *N*-methylated ureas (**2**) exist predominantly in (*cis*, *cis*) conformations, like those in the crystals.

In conclusion, *N*-methylation of aromatic ureas having carborane moieties caused conformational alteration from *trans* to *cis*, regardless of the bulkiness of the substituents. We have shown that the *cis* conformational preference of *N*-methylated ureas is useful to construct aromatic molecules with unique structures and chemical or biological properties.[19] The results described here should make it possible to utilize aromatic molecules with carborane cages.

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15. Compound **1a**: mp 270–271°C (*n*-hexane–ethyl acetate). ^{1}H NMR (400 MHz, DMSO-d_6) δ 1.3–3.2 (br m, 20H), 5.73 (s, 2H), 7.19 (dd, $J=7.7$, 1.8 Hz, 2H), 7.31 (t, $J=7.9$, Hz, 2H), 7.51 (dd, $J=7.7$, 1.8 Hz, 2H), 7.75 (t, $J=1.8$ Hz, 2H), 8.96 (s, 2H). Anal. calcd for $C_{17}H_{32}B_{20}N_2O$: C, 41.11; H, 6.49; N, 5.64. Found: C, 40.94; H, 6.36; N, 5.43. Compound **1b**: mp >298°C (*n*-hexane–dichloromethane). ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.4–3.1 (br m, 20H), 3.88 (br, s, 1H), 6.48 (s, 1H), 7.33 (d, $J=8.8$ Hz, 2H), 7.43 (d, $J=8.9$ Hz, 2H). Anal. calcd for $C_{17}H_{32}B_{20}N_2O$: C, 41.11; H, 6.49; N, 5.64. Found: C, 40.88; H, 6.32; N, 5.52. Compound **2a**: mp 287–288°C (*n*-hexane–dichloromethane). ^{1}H NMR (400 MHz, DMSO-d_6) δ 1.4–3.0 (br m, 20H), 3.11 (s, 6H), 5.67 (br s, 2H), 6.92 (m, 2H), 6.96 (s, 2H), 7.10 (m, 4H). Anal. calcd for $C_{19}H_{36}B_{20}N_2O$: C, 43.49; H, 6.92; N, 5.34. Found: C, 43.25; H, 6.74; N, 5.04. Compound **2b**: mp 268–269°C (*n*-hexane–dichloromethane). ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.6–3.2 (br m, 20H), 3.36 (s, 6H), 3.81 (br s, 2H), 6.74 (d, $J=8.8$ Hz, 4H), 7.16 (d, $J=8.8$ Hz, 4H). Anal. calcd for $C_{19}H_{36}B_{20}N_2O$: C, 43.49; H, 6.92; N, 5.34. Found: C, 43.22; H, 6.80; N, 5.41. Compound **1c**: mp 294–295°C (*n*-hexane–dichloromethane). ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.5–3.4 (br m, 40H), 3.96 (br s, 4H), 6.97 (br s, 2H), 7.31 (t, $J=1.7$ Hz, 2H), 7.60 (d, $J=1.7$ Hz, 4H). Anal. calcd for $C_{21}H_{52}B_{40}N_2O$: C, 32.29; H, 6.71; N, 3.59. Found: C, 32.27; H, 6.61; N, 3.59. Compound **2c**: mp >298°C (*n*-hexane–dichloromethane). ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.6–3.2 (br m, 40H), 3.17 (s, 6H), 3.81 (br s, 4H), 6.99 (d, $J=1.7$ Hz, 4H), 7.22 (d, $J=1.7$ Hz, 2H). Anal. calcd for $C_{23}H_{56}B_{40}N_2O$: C, 34.14; H, 6.98; N, 3.46. Found: C, 34.15; H, 6.93; N, 3.59.
16. Crystal data of the ureas. Compound **1a**: orthorhombic; space group, *P*cca; $Z=4$; $a=22.393(2)$ Å; $b=13.9983(8)$ Å; $c=10.0129(8)$ Å; $V=3138.7(3)$ Å^3; $D_{\text{calc}}=1.051$ g/cm^3; $R=0.100$. Compound **1b**: monoclinic; space group, $P2_1/c$; $Z=8$; $a=15.194(7)$ Å; $b=22.088(7)$ Å; $c=17.80(1)$ Å; $\beta=101.48(4)°$; $V=5927(4)$ Å^3; $D_{\text{calc}}=1.113$ g/cm^3; $R=0.096$. Compound **2a**: triclinic; space group, *P*-1; $Z=2$; $a=11.10(1)$ Å; $b=13.34(2)$ Å; $c=10.98(2)$ Å; $\alpha=112.15(6)°$; $\beta=96.18(9)°$; $\gamma=85.16(7)°$; $V=1495(3)$ Å^3; $D_{\text{calc}}=1.165$ g/cm^3; $R=0.092$. Compound **2b**: triclinic; space group, *P*-1; $Z=2$; $a=11.0843(4)$ Å; $b=12.8759(5)$ Å; $c=13.1756(4)$ Å; $\alpha=83.069(2)°$; $\beta=85.0080(10)°$; $\gamma=64.9700(10)°$; $V=1690.03(10)$ Å^3; $D_{\text{calc}}=1.129$ g/cm^3; $R=0.085$. Compound **2c**: monoclinic; space group, $P2_1/c$; $Z=4$; $a=12.139(1)$ Å; $b=22.920(2)$ Å; $c=22.474(2)$ Å; $\beta=100.756(2)°$; $V=6143.4(8)$ Å^3; $D_{\text{calc}}=1.160$ g/cm^3; $R=0.090$. There are unrefined solvent molecules in the unit cells of **2b** and **2c**. The preliminary crystallographical analysis indicated (*trans*, *trans*) conformation of **1c**, but the presence of several unrefined solvents, which made it impossible to refine the data. No significant changes in the bond lengths and bond angles of the urea bonds were observed by introduction of carborane moieties on *N*,*N′*-diphenylurea or *N*,*N′*-dimethyl-*N*,*N′*-diphenylurea skeletons.
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