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1,2,4-Triazinylcarboranes: a new approach to the synthesis and the crystal structures of 1-(3,6-ditolyl-1,2,4-triazin-5-yl)-2-phenyl-1,2-dicarba-*closo*-dodecaborane and 1,7-bis[6-phenyl-3-(4-chlorophenyl)-1,2,4-triazin-5-yl]-1,7-dicarba-*closo*-dodecaborane

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The S_N^H reactions of the lithio derivatives of 1,2- or 1,7-dicarba-*closo*-dodecaboranes with 1,2,4-triazine 4-oxides represent a versatile synthetic approach to carboranes bearing heteroaromatic substituents.

The development of pharmaceuticals for boron neutron capture therapy (BNCT) and the preparation of biological probes gave a strong impetus to studies of heteroaryl carborane derivatives (HCD).[1–5] Among of possible approaches to their synthesis, the most appropriate methods are (i) a halogen substitution reaction of haloheteroarenes with C-lithium[6] or C-copper[7] derivatives of carboranes; (ii) subsequent reactions of addition of lithiocarboranes to high electrophilic heteroarenes (pyrrilium salts) and dehydrogenation of intermediate σ^H-adducts;[8] and (iii) reactions of ring transformation of carboranylheteroarenes resulting in new heterocycles.[9] At the same time, the reactions of azine *N*-oxides with lithiocarboranes are still absolutely unstudied in spite of their easy functionalization by the direct introduction of various nucleophiles in desoxygenative nucleophilic substitution reactions for hydrogen.[10] Here, we describe a successful application of the latter approach to the introduction of azines into carboranes. 1,2,4-Triazine 4-oxides were chosen as substrates due to their high reactivity.[11]

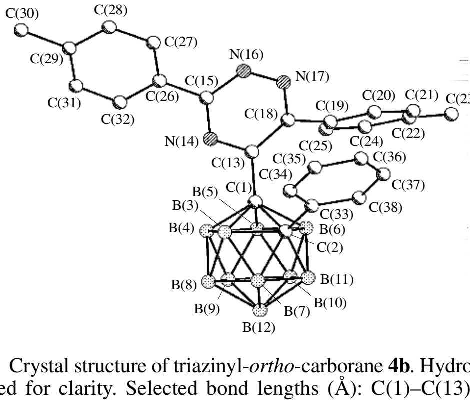

Figure 1 Crystal structure of triazinyl-*ortho*-carborane **4b**. Hydrogen atoms are omitted for clarity. Selected bond lengths (Å): C(1)–C(13) 1.525(2), C(1)–C(2) 1.709(3), C(2)–C(33) 1.502(3).

It was found that 2-lithium-1-phenyl-1,2-dicarba-*closo*-dodecaborane obtained from 1-phenyl-1,2-dicarba-*closo*-dodecaborane **1** and Bu^{t}Li reacts with 1,2,4-triazine 4-oxides **2a**–**e** at a low temperature (–50 °C) in THF to form lithium derivatives **A** of σ^H-adducts 1-(4-hydroxy-4,5-dihydro-1,2,4-triazine-5-yl)-2-phenyl-1,2-dicarba-*closo*-dodecaboranes **3**, which can be isolated from the reaction mixture after diluting with water (Scheme 1). The σ^H-adducts are unstable, and their structures were found from the NMR spectra of compound **3a**. Note that σ-adducts **A** are related to the addition products of lithiocarboranes to pyrrilium or *N*-alkylpyridinium salts.[8] However, adducts **A** easily undergo aromatisation by the action of mild acylating agents. Thus, the treatment of the reaction mixture with *N*,*N*-dimethylcarbamoyl chloride at –50 °C and slow heating to room temperature resulted in 2-phenyl-1-(1,2,4-triazine-5-yl)-1,2-dicarba-*closo*-dodecaboranes **4a**–**e** in 30–70% yields. The reaction proceeded *via* the elimination of a carboxylic acid after acylation at the oxygen atom of σ-adducts **A**. The reaction of 1,2,4-triazine 4-oxide **2a** with *ortho*-carborane **5** proceeded in the same manner giving 1-(1,2,4-triazin-5-yl)-1,2-dicarba-*closo*-dodecaborane **6a** in 41% yield. The reaction was successful in spite of the absence of special efforts for preventing dilithiocarborane formation with the isolation of only a single product. The structures of products **4a**–**e** and **6** were clearly defined by NMR spectroscopy and, for compounds **4a**,**b**, confirmed by X-ray crystallography (Figure 1).†,‡

The reaction of 1,2,4-triazine 4-oxide **2a** with 1-lithium 1,7-dicarba-*closo*-dodecaborane **7**, derived from the *meta*-carborane and Bu^{t}Li (1.1 eq.), followed by the treatment of the reaction mixture with *N*,*N*-dimethylcarbamoyl chloride resulted in 1-(1,2,4-triazin-5-yl)-1,7-dicarba-*closo*-dodecaborane **8a** (Scheme 1). A similar reaction of 1,7-dilithium 1,7-dicarba-*closo*-dodecaborane **9** (2.5 eq. of Bu^{t}Li) with two equivalents of 1,2,4-triazine 4-oxide **2f** allowed us to introduce two residues of the heterocycle into the carborane molecule yielding 1,7-bis-[6-phenyl-3-(4-chlorophenyl)-1,2,4-triazin-5-yl]-1,7-dicarba-*closo*-

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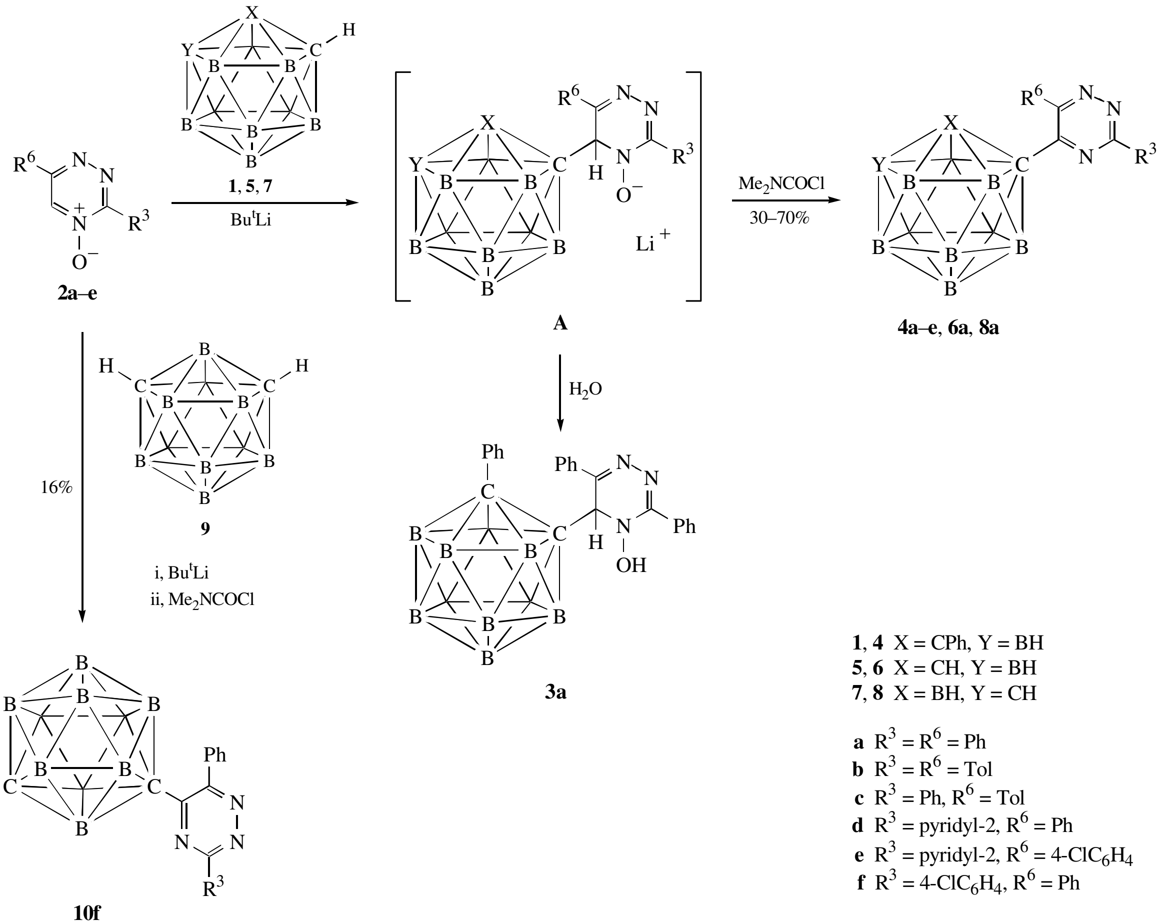
† *General method for the synthesis of triazinylcarboranes* **4**, **6**, **8**. The mixture obtained by the addition of Bu^{t}Li (4.2 mmol) as a 1.6 M solution in pentane to a solution of the corresponding carborane (4.2 mmol) in 10 ml of THF was added to a suspension of 6-aryltriazine-4-oxide **2** (4 mmol) in dry THF under an argon atmosphere at –50 °C with stirring. The mixture was kept at this temperature until the dissolution of the reagent; then *N*,*N*-dimethylcarbamoyl chloride (0.4 ml, 4.2 mmol) was added, and the solution was allowed to warm up to room temperature. After removing the solvent under a reduced pressure, the mixture was extracted with toulene (20 ml). The solvent was evaporated, and the residue was treated with acetonitrile; the resulting crystals of products **4**, **6**, **8** were filtered off.

For **4a**: yield 1.26 g, 70%; mp 205 °C. ^{1}H NMR (250.1 MHz, $CDCl_3$) δ: 1.20–3.20 (m, 10H, B–H), 7.21–7.68 (m, 13H), 8.33 (m, 2H). Found (%): C, 61.03; H, 5.65; N, 9.22. Calc. for $C_{23}H_{25}B_{10}N_3$ (451.55) (%): C, 61.17; H, 5.58; N, 9.31.

For **4b**: yield 1.20 g, 65%; mp 165 °C. ^{1}H NMR (250.1 MHz, $CDCl_3$) δ: 1.20–3.20 (m, 10H, B–H), 2,43 (s, 3H, Me), 2.46 (s, 3H, Me), 7.18–7.46 (m, 11H), 8.21 (m, 2H). Found (%): C, 62.55; H, 6.06; N, 9.00. Calc. for $C_{25}H_{29}B_{10}N_3$ (479.55) (%): C, 62.61; H, 6.09; N, 8.76.

For **4d**: yield 900 mg, 48%; mp 227 °C. ^{1}H NMR (250.1 MHz, $CDCl_3$) δ: 1.20–3.20 (m, 10H, B–H), 7.18–7.70 (m, 11H), 8.11 (m, 1H), 8.33 (m, 1H), 8.87 (m, 1H). ^{13}C NMR (75.5 MHz, $CDCl_3$) δ: 81.6 (carborane, C-2), 86.6 (carborane, C-1), 124.4 (Py), 126.1 (Py), 128.3, 128.5, 129.6, 129.9, 130.4, 130.5, 130.8, 134.7, 137.3 (Py), 145.0 (triazine, C-6), 150.8 (Py), 151.3 (Py), 158.1 (triazine, C-3), 159.00 (triazine, C-5). Found (%): C, 58.33; H, 5.37; N, 12.26. Calc. for $C_{22}H_{24}B_{10}N_4$ (452.57) (%): C, 58.39; H, 5.35; N, 12.38.

For **10f**: yield 450 mg, 16%; mp 227 °C. ^{1}H NMR, δ: 1.20–3.20 (m, 10H, B–H), 2.43 (s, 3H, Me), 2.46 (s, 3H, Me), 7.18–7.46 (m, 11H), 8.21 (m, 2H). Found (%): C, 56.74; H, 4.27; N, 12.29. Calc. for $C_{32}H_{28}B_{10}N_6Cl_2$ (675.64) (%): C, 56.89; H, 4.18; N, 12.44.



1, **4** X = CPh, Y = BH
5, **6** X = CH, Y = BH
7, **8** X = BH, Y = CH

a $R^3 = R^6 = Ph$
b $R^3 = R^6 = Tol$
c $R^3 = Ph, R^6 = Tol$
d R^3 = pyridyl-2, R^6 = Ph
e R^3 = pyridyl-2, $R^6 = 4\text{-}ClC_6H_4$
f $R^3 = 4\text{-}ClC_6H_4$, R^6 = Ph

Scheme 1 The reaction of 1,2,4-triazine 4-oxides **2** with lithium carboranes.

dodecaborane **10f** (Scheme 1). The structure of the latter was proved by X-ray crystallography (Figure 2).

Thus, lithio derivatives of 1,2- and 1,7-dicarba-*closo*-dodecaboranes can be successfully used as nucleophiles in the S_N^H methodology in the series of azine *N*-oxides to give the corresponding C-heteroaryl derivatives of carboranes.

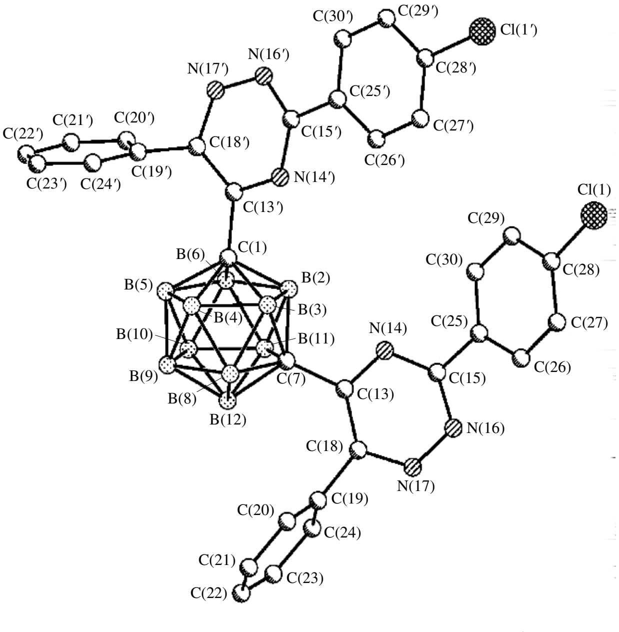


Figure 2 Crystal structure of bistriazinyl-*meta*-carborane **10f**. Hydrogen atoms are omitted for clarity. Selected bond lengths (Å): C(1)–C(13′) 1.520(3), C(1)–B(3) 1.713(3), C(7)–B(3) 1.719(3), C(7)–C(13) 1.520(3).

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‡ *Crystal data for* **4a**: $C_{23}H_{25}B_{10}N_3$, tetragonal, space group $P4_3$, $a = 11.3890(6)$, $c = 18.7520(14)$ Å, $V = 2432.3(3)$ Å^3, $Z = 4$, $M = 451.56$, $d_{calc} = 1.233$ g cm^{-3}, μ(MoKα) = 0.67 cm^{-1}, $F(000) = 936$.

For **4b**: $C_{25}H_{29}B_{10}N_3$, orthorhombic, space group *Pbca*, $a = 11.6446(8)$, $b = 13.2237$, $c = 35.230(3)$ Å, $V = 5424.8(7)$ Å^3, $Z = 8$, $M = 479.61$, $d_{calc} = 1.174$ g cm^{-3}, μ(MoKα) = 0.63 cm^{-1}, $F(000) = 2000$.

For **10f**: $C_{32}H_{28}B_{10}Cl_2N_6$, triclinic, space group *P*1(bar), $a = 8.665(4)$, $b = 12.238(5)$, $c = 16.947(7)$ Å, $\alpha = 79.56(3)°$, $\beta = 77.11(4)°$, $\gamma = 75.39(3)°$, $V = 1680.2(12)$ Å^3, $Z = 2$, $M = 675.60$, $d_{calc} = 1.335$ g cm^{-3}, μ(MoKα) = 2.29 cm^{-1}, $F(000) = 692$.

Intensities of 20366 (**4a**), 34364 (**4b**) and 6570 (**10f**) reflections were measured with a Smart 1000 CCD diffractometer at 110 K (**4a** and **4b**) or Nonius CAD4 at 298 K (**10f**) [λ(MoKα) = 0.71072 Å, ω scans for **4a** and **4b**; $\theta/2\theta$ scans for **10f**, $2\theta < 60°$] and 7043 (**4a**), 5859 (**4b**), 5865 (**10f**) independent reflections were used for a further refinement. The structures were solved by a direct method and refined by the full-matrix least-squares technique against F^2 in the anisotropic–isotropic approximation. Hydrogen atoms were located from the Fourier synthesis and refined in the isotropic approximation. The refinement converged to $wR_2 = 0.1091$ and GOF = 1.003 for all independent reflections [$R_1 = 0.0464$ was calculated against F for 6460 observed reflections with $I > 2\sigma(I)$] for **4a**; $wR_2 = 0.0865$ and GOF = 0.804 ($R_1 = 0.0471$ for 1729 observed reflections) for **4b**; $wR_2 = 0.1162$ and GOF = 0.994 ($R_1 = 0.0477$ for 4341 observed reflections) for **10f**. All calculations were performed using SHELXTL PLUS 5.0.

Atomic coordinates, bond lengths, bond angles and thermal parameters have been deposited at the Cambridge Crystallographic Data Centre (CCDC). These data can be obtained free of charge *via* www.ccdc.cam.uk/conts/retrieving.html (or from the CCDC, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336 033; or deposit@ccdc.cam.ac.uk). Any request to the CCDC for data should quote the full literature citation and CCDC reference numbers 205482–205484. For details, see 'Notice to Authors', *Mendeleev Commun.*, Issue 1, 2003.

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