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Use of carborane carboxylic acids in the synthesis of boronated nitrogen heterocycles

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ABSTRACT

A novel series of 5-substituted carborane tetrazoles was synthesized by acylation of 5-phenyl-1-H-tetrazole with the available *o*- and *m*-carborane carboxylic acid chlorides or *o*- and *m*-carborane acetic acid chlorides in the presence of pyridine. Successive thermolysis of the carborane tetrazoles in toluene followed by the extrusion of nitrogen resulted in a series of previously unknown carborane 1,3,4-oxadiazoles in good yield. Using 2,4-dichloroaniline as an example we showed that carborane-substituted 1,3,4-oxadiazoles can be converted into the corresponding 1,2,4-triazoles.

1. Introduction

Five-membered nitrogen heterocycles are under extensive investigation due to their numerous applications in biomedicine as antimicrobial, antiallergic, anticancer, cardiovascular and CNS agents [1]. Also, these compounds are known to be used as antioxidants, inhibitors of corrosion, luminophores, agents for information recording systems and in agriculture [2]. Among the nitrogen heterocycles, tetrazole derivatives are of special interest because they possess a plethora of biological activities [3]. These compounds can act as metabolically stable analogues of carboxylic or amide groups, ligands in coordination chemistry [4], high energy compounds [5] and are important precursors for preparing other nitrogen-containing heterocycles [6]. The strategy for constructing the tetrazole ring is based on a very efficient azide–nitrile cycloaddition reaction developed by Sharpless and co-workers [7]. This synthetic approach emerged as a common route for the design of new types of molecules, especially conjugates of different subunits that yield a variety of hybrid compounds.

Derivatization of carboranes and other polyhedral boranes especially with heterocycles, is an active area of research in organic and organometallic chemistry [8]. We have recently reported the possibility of using the methodology of 1,3-dipolar cycloaddition (the 'click' reaction) to modify the *closo*-carborane polyhedron, $C_2B_{10}H_{12}$, with 1,2,3-triazole heterocycles starting from 1-azidomethyl-*o*-carborane and terminal alkynes [9]. Our promising results in the synthesis of carborane 1,2,3-triazole derivatives prompted us to prepare novel 5-substituted carborane 1H-tetrazoles via the 1,3-dipolar cycloaddition reaction of 1-azidomethyl-*o*-carborane with organic nitriles. This reaction requires nitriles that possess electron-withdrawing groups and proceeds at high temperature [10]. The carborane derivatives of the tetrazole heterocycles and the methods of their preparation have been unknown until present. Moreover, the conjugation of the carborane polyhedron, a moiety with remarkable thermal and chemical stability, to the tetrazole moiety may result in the formation of new high energy compounds. Surprisingly, despite the fact that several reaction conditions for the generation of tetrazole-containing carboranes have been used [11], including microwave-assisted preparation, no reaction was observed for 1-azidomethyl-*o*-carborane 1 and nitriles.

We obtained tetrazole 2 only from tosyl cyanide, containing the strong electron-withdrawing and easily leaving tosyl group, capable of being substituted by various nucleophiles. However, the reaction of 2 with even a mild nucleophile, for example thiophenol, led to the substitution of the tosyl group and deboronation of the carborane polyhedron to the *nido*-form, $C_2B_9H_{12}^-$ (Scheme 1). These modifications were proven by IR spectra where the bands of the BH groups were downshifted from 2600 to 2560 cm^{-1}.

Failure of the [2+3]cycloaddition approach to prepare the carborane tetrazoles forced us to consider alternative routes, in particular the direct conjugation of the tetrazole fragment to the carborane polyhedra. We took advantage of carborane carboxylic

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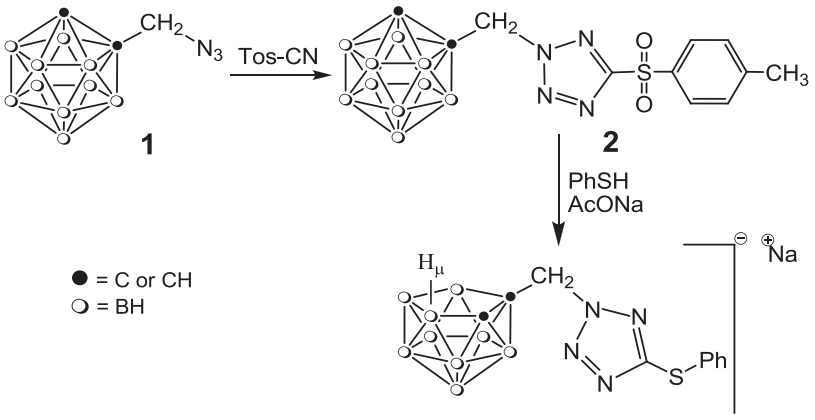


Scheme 1. Synthesis of 2-[(*o*-carboran-1-yl)methyl]-5-tosyltetrazole **2**.

acids as attractive starting materials amongst the functionalized carboranes. These acids are easy to prepare, and a variety of structures is available [12].

2. Experimental

2.1. General information

All solvents were freshly distilled from the appropriate drying agents before use. All other reagents were recrystallized or distilled if necessary. The reactions were performed in an atmosphere of dry argon. The starting compounds **1** [9], **4**, **5** [12a], **8** [12b], **10**, **11** [12c] and **12** [12d] were prepared according to the published procedures. The purity of the newly synthesized compounds was tested by TLC on Sorbfil. Eluents: $CHCl_3$–MeOH (20:1) for compounds **4**, **5**, **11**–**13** and $CHCl_3$ for **14**–**21**. IR spectra were registered on a Brucker FTIR spectrometer Tensor 37 in KBr tablets. UV-irradiation of compounds **6**, **7**, **13**–**15** was carried out with a high-pressure mercury lamp (IMQ-21, 300 W). NMR spectra were recorded on a Bruker Avance-400 spectrometer operating at 400 MHz for ^1H (TMS), 128.28 MHz for ^{11}B ($BF_3{\cdot}OEt_2$). The solvent was $CDCl_3$ except where indicated otherwise.

2.2. X-ray crystallography

X-ray diffraction experiments for compound **16** were carried out on a Bruker KAPPA APEX II autodiffractometer (Mo Kα radiation, $\lambda = 0.71073$ Å, graphite monochromator) at 100(2) K [13]. Data reduction was made using SAINT-Plus program [14]. The structure was resolved by direct method SHELXS97 and refined on F^2 with the full-matrix least-squares procedure (SHELXL97) [15] using all reflections. All non-hydrogen atoms, except a disordered N atom with a lower occupation factor in the structure of **16**, were refined with anisotropic displacement factors. All H-atoms were located from difference Fourier maps and refined isotropically with displacement factors equal to 1.2 U_{eq}^{iso} of their parent B or C atoms and without any constraints or restraints for H atoms of the water molecule.

2.3. 2-[(o-Carboran-1-yl)methyl]-5-tosyltetrazole (*2*)

A mixture of carborane azide **1** (1 g, 5.0 mmol) and *p*-toluenesulfonyl cyanide (1.81 g, 10 mmol) was stirred for 8 h at 100 °C in the absence of solvent under argon. Removal of the excess of *p*-toluenesulfonyl cyanide by sublimation in vacuo (0.5 mbar) afforded tetrazole **2** in 95% yield. White powder. M.p. 163–165 °C (from EtOAc/*n*-heptane). IR (KBr, cm^{-1}) ν_{max}: 3067 (carborane CH), 2605 (BH), 1592, 1355, 1156 (SO_2). ^1H NMR (400 MHz, $CDCl_3$) δ (ppm): 8.00 (d, $J = 8.1$ Hz, 2H, *o*-Ph), 7.49 (d, $J = 8.1$ Hz, 2H, *m*-Ph), 5.47 (s, 2H, CH_2), 4.24 (brs, 1H, carborane CH), 2.52 (s, 3H, CH_3), 3.45–1.39 (m, 10H, BH). ^{11}B NMR (128 MHz, $CDCl_3$) δ (ppm): 0.83 (d, $J = 153$ Hz, 1B), −3.65 (d, $J = 148$ Hz, 1B), −9.04 (d, $J = 154$ Hz, 2B), −11.21 (d, 159 Hz, 2B), −12.46 (d, $J = 170$ Hz, 4B). *Anal.* Calc. for $C_{11}H_{20}B_{10}N_4O_2S$ (380.5): C, 34.72; H, 5.30; B, 28.41; N, 14.73. Found: C, 35.08; H, 5.42; B, 28.35; N, 14.65%.

2.4. General procedure for the preparation of tetrazoles (*6*, *7*, *13*–*15*)

To a solution of corresponding carboranyl acid chloride (5.2 mmol) in dry CH_2Cl_2 (8–10 mL), Py (0.42 mL, 5.3 mmol) was added dropwise at −40 to −50 °C in argon atmosphere. Then tetrazole **3** (0.76 g, 5.2 mmol) was added to the reaction mixture with extensive stirring. The resulting mixture was left at −20 to −30 °C for ~1 h and then stirred at room temperature for 6–8 h until the corresponding carboranyl acid chloride disappeared (monitored by TLC). After the completion of the reaction, water (30 mL) was added to the reaction mixture, and the solution was extracted with EtOAc (2 × 10 mL). The organic phase was washed with water, dried over anhydrous $MgSO_4$ and evaporated in vacuo. The obtained solids were washed with *n*-heptane to give the corresponding carborane tetrazoles **6**, **7**, **13**–**15** in good yields.

2.4.1. (m-Carboran-9-yl)(5-phenyltetrazol-2-yl)ketone (*6*)

Yield: 1.4 g (85%). White powder. M.p. (decomp) 107–110 °C. IR (KBr, cm^{-1}) ν_{max}: 3029 (carborane CH), 2615 (BH), 1721 (C=O). ^1H NMR (400 MHz, CD_3OD) δ (ppm): 8.01 (m, 2H, Ph), 7.58 (m, 3H, Ph), 3.62 (brs, 2H, carborane CH), 3.25–1.20 (m, 9H, BH). ^{11}B NMR (128 MHz, CD_3OD) δ (ppm):–6.80 (d, $J = 163$ Hz, 2B), −7.28 (s, 1B, B^9), −10.21 (d, $J = 151$ Hz, 1B), −13.04 (d, $J = 167$ Hz, 2B), −13.51 (d, $J = 166$ Hz, 2B), −16.89 (d, $J = 182$ Hz, 1B), −17.51 (d, $J = 182$ Hz, 1B). *Anal.* Calc. for $C_{10}H_{16}B_{10}N_4O$ (316.3): C, 37.96; H, 5.10; B, 34.17; N, 17.71. Found: C, 37.58; H, 5.21; B, 33.63; N 17.76%.

2.4.2. (o-Carboran-9-yl)(5-phenyltetrazol-2-yl)ketone (*7*)

Yield: 1.28 g (77%). White powder. M.p. (decomp) 109–111 °C. IR (KBr, cm^{-1}) ν_{max}: 3063 (carborane CH), 2603 (BH), 1723 (C = O). ^1H NMR (400 MHz, CD_3OD) δ (ppm): 8.01 (m, 2H, Ph), 7.58 (m, 3H, Ph), 4.47 (brs, 2H, carborane CH), 3.00–1.20 (m, 9H, BH). ^{11}B NMR (128 MHz, CD_3OD) δ (ppm): −0.87 (s, 1B, B^9), −3.11 (d, $J = 150$ Hz, 1B), −9.47 (d, $J = 151$ Hz, 2B), −13.86 (d, $J = 155$ Hz, 2B), −14.21 (d, $J = 158$ Hz, 2B), −14.99 (d, $J = 164$ Hz, 2B). *Anal.* Calc. for $C_{10}H_{16}B_{10}N_4O$ (316.3): C; 37.96; H, 5.10; B, 34.17; N, 17.71. Found: C, 38.10; H, 4.92; B, 34.29; N, 17.87%.

*2.4.3. [(m-Carboran-9-yl)methyl](5-phenyltetrazol-2-yl)ketone (**13**)*

Yield: 1.49 g (87%). White powder. M.p. 79–81 °C. IR (KBr, cm^{-1}) ν_{max}: 3052 (carborane CH), 2605 (BH), 1767 (C = O). ^1H NMR (400 MHz, $CDCl_3$) δ (ppm): 8.27 (m, 2H, Ph), 7.51 (m, 3H, Ph), 3.19 (brs, 2H, carborane CH), 2.94 (s, 2H, CH_2), 3.00–1.15 (m, 9H, BH). ^{11}B NMR (128 MHz, $CDCl_3$) δ (ppm): −3.35 (s, 1B, B^9), −6.50 (d, J = 163 Hz, 2B), −10.05 (d, J = 150 Hz, 1B), −12.89 (d, J = 162 Hz, 2B), −13.63 (d, J = 164 Hz, 2B), −17.05 (d, J = 182 Hz, 1B), −19.08 (d, J = 184 Hz, 1B). *Anal.* Calc. for $C_{11}H_{18}B_{10}N_4O$ (330.4): C, 39.99; H, 5.49; B, 32.72; N, 16.96. Found: C, 40.18; H, 5.54; B, 32.25; N, 16.64%.

*2.4.4. [(o-Carboran-9-yl)methyl](5-phenyltetrazol-2-yl)ketone (**14**)*

Yield: 1.34 g (80%). White powder. M.p. 83–85 °C. IR (KBr, cm^{-1}) ν_{max}: 3052 (carborane CH), 2602 (BH), 1773 (C = O). ^1H NMR (400 MHz, $CDCl_3$) δ (ppm): 8.26 (m, 2H, Ph), 7.51 (m, 3H, Ph), 3.59 (brs, 1H, carborane CH), 3.53 (brs, 1H, carborane CH), 3.04 (brs, 2H, CH_2), 3.00–1.20 (m, 9H, BH). ^{11}B NMR (128 MHz, $CDCl_3$) δ (ppm): 3.34 (s, 1B, B^9), −2.37 (d, J = 146 Hz, 1B), −9.31 (d, J = 149 Hz, 2B), −13.51 (d, J = 164 Hz, 2B), −14.09 (d, J = 159 Hz, 2B), −14.87 (d, J = 183 Hz, 2B). *Anal.* Calc. for $C_{11}H_{18}B_{10}N_4O$ (330.4): C, 39.99; H, 5.49; B, 32.72; N, 16.96. Found: C, 40.09; H, 5.34; B, 32.69; N, 17.03%.

*2.4.5. [(o-Carboran-1-yl)methyl](5-phenyltetrazol-2-yl)ketone (**15**)*

Yield: 1.34 g (80%). White powder. M.p. 82–83 °C. IR (KBr, cm^{-1}) ν_{max}: 3032 (carborane CH), 2579 (BH), 1724 (C = O). ^1H NMR (400 MHz, Acetone-D_6) δ (ppm): 8.04 (m, 2H, Ph), 7.63 (m, 3H, Ph), 4.97 (brs, 1H, carborane CH), 4.20 (s, 2H, CH_2), 3.00–1.00 (m, 10H, BH). ^{11}B NMR (128 MHz, acetone-D_6) δ (ppm): −2.45 (d, J = 147 Hz, 1B), −5.42 (d, J = 149 Hz, 1B), −9.26 (d, J = 150 Hz, 2B), −11.14 (d, J = 182 Hz, 2B), −11.78 (d, J = 177 Hz, 2B), −12.64 (d, J = 175 Hz, 2B). *Anal.* Calc. for $C_{11}H_{18}B_{10}N_4O$ (330.4): C, 39.99; H, 5.49; B, 32.72; N, 16.96. Found: C, 40.12; H, 5.58; B, 32.59; N, 16.58%.

*2.5. General procedure for the preparation of carborane oxadiazoles **16–20***

A. Rearrangement of tetrazoles under UV irradiation.

A solution of the corresponding tetrazol (**6**, **7**, **13–15**) (3 mmol) in dry MeCN (10 mL) was UV-irradiated for 1–2 h. After the evaporation of the solvent in vacuo the residue was purified by column chromatography on silica gel using $CHCl_3$ as the eluent to give oxadiazoles **16–20** in 69–78% yield.

*B. Thermolysis of tetrazoles **6**, **7**, **13–15** in toluene.*

The tetrazoles **6**, **7** or **13–15** (3 mmol) were boiled in toluene (10 mL) for 3–5 h until the completion of the reaction (monitored by TLC). After the evaporation of the solvent in vacuo the residue was crystallized from *n*-heptane or purified by column chromatography on silica gel (using $CHCl_3$ as the eluent, compound **20**) to give oxadiazoles **16–20** in 60–78% yield.

*C. One pot preparation of carborane 1,3,4-oxadiazoles (**16–20**).*

To a stirred solution of the corresponding carboranyl acid chloride (**4**, **5**, **10–12**) (5.2 mmol) in toluene (10 mL) dry pyridine (0.62 mL, 7.8 mmol) was added at −40 °C under an argon atmosphere. To this mixture tetrazol **3** (0.76 g, 5.2 mmol) was added, and stirring was continued at room temperature for 1 h and then the resulting mixture was boiled for 3–5 h. After the evaporation of the solvent in vacuo the crude product was purified by column chromatography on silica gel using $CHCl_3$ as the eluent to give oxadiazoles **16–20** in 60–78% yield.

*2.5.1. 2-(m-Carboran-9-yl)-5-phenyl-1,3,4-oxadiazole (**16**)*

Yield: A, B – 76%, C – 72%. White powder. M.p. 128–130 °C. IR (KBr, cm^{-1}) ν_{max}: 3038 (carborane CH), 2609 (BH). ^1H NMR (400 MHz, $CDCl_3$) δ (ppm): 8.08 (dd, J_1 = 7.4, J_2 = 1.8 Hz, 2H, Ph), 7.49 (m, 3H, Ph), 3.12 (brs, 2H, carborane CH), 3.23–1.12 (m, 9H, BH). ^{11}B NMR (128 MHz, $CDCl_3$) δ (ppm): −6.2 (d, J = 166 Hz, 2B), −8.12 (s, 1B, B^9), −9.61 (d, J = 154 Hz, 1B), −12.75 (d, J = 169 Hz, 1B), −13.17 (d, J = 167 Hz, 3B), −16.87 (d, J = 183 Hz, 1B), −17.34 (d, J = 181 Hz, 1B). *Anal.* Calc. for $C_{10}H_{16}B_{10}N_2O$ (288.4): C, 41.65; H, 5.59; B, 37.49; N 9.71. Found: C, 41.87; H, 5.55; B, 37.28; N, 9.79%.

*2.5.2. 2-(o-Carboran-9-yl)-5-phenyl-1,3,4-oxadiazole (**17**)*

Yield: A, B – 77%, C – 65%. White powder. M.p. 135–138 °C. IR (KBr, cm^{-1}) ν_{max}: 3054 (carborane CH), 2585 (BH). ^1H NMR (400 MHz, $CDCl_3$) δ (ppm): 8.00 (dd, 2H, J_1 = 7.2, J_2 = 1.8 Hz, Ph), 7.44 (m, 3H, Ph), 4.04 (brs, 1H, carborane CH), 3.74 (brs, 1H, carborane CH), 3.34–1.18 (m, 9H, BH). ^{11}B NMR (128 MHz, $CDCl_3$) δ (ppm): −1.61 (s, 1B, B^9), −2.54 (d, J = 161 Hz, 1B), −8.92 (d, J = 151 Hz, 1B), −9.29 (d, J = 148 Hz, 1B), −14.03 (d, J = 179 Hz, 6B). *Anal.* Calc. for $C_{10}H_{16}B_{10}N_2O$ (288.4): C, 41.65; H, 5.59; B, 37.49; N, 9.71. Found: C, 42.05; H, 5.77; B, 36.99; N, 9.83%.

*2.5.3. 2-[(m-Carboran-9-yl)methyl]-5-phenyl-1,3,4-oxadiazole (**18**)*

Yield: A, B, C – 78%. White powder. M.p. 110–112 °C. IR (KBr, cm^{-1}) ν_{max}: 3044 (carborane CH), 2587 (BH). ^1H NMR (400 MHz, $CDCl_3$) δ (ppm): 8.02 (dd, 2H, J_1 = 7.3, J_2 = 1.9 Hz, Ph), 7.47 (m, 3H, Ph), 2.67 (brs, 2H, carborane CH), 2.46 (brs, 2H, CH_2), 3.08–1.10 (m, 9H, BH). ^{11}B NMR (128 MHz, $CDCl_3$) δ (ppm): −2,21 (s, 1B, B^9), −6.21 (d, J = 163 Hz, 2B), −9.56 (d, J = 151 Hz, 1B), −12.95 (d, J = 164 Hz, 2B), −13.60 (d, J = 166 Hz, 2B), −17.33 (d, J = 181 Hz, 1B), −19.55 (d, J = 182 Hz, 1B). *Anal.* Calc. for $C_{11}H_{18}B_{10}N_2O$, (302.4): C, 43.69; H, 6.00; B, 35.75; N, 9.26. Found: C, 43.81; H 6.15; B, 35.47; N, 9.11%.

*2.5.4. 2-[(o-Carboran-9-yl)methyl]-5-phenyl-1,3,4-oxadiazole (**19**)*

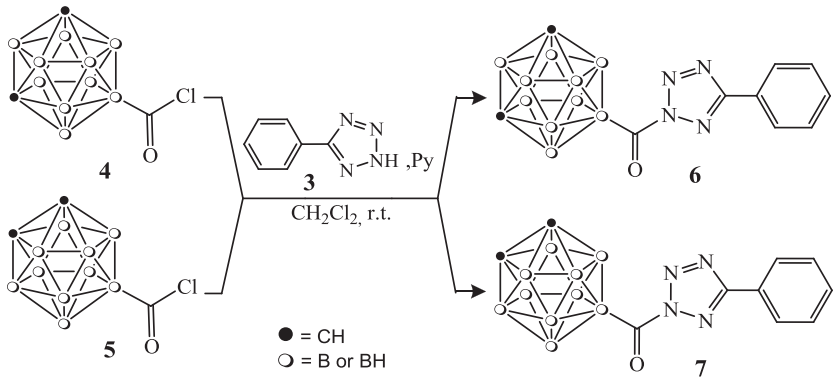
Yield: A, B– 70%, C – 60%. White powder. M.p. 113–114 °C. IR (KBr, cm^{-1}) ν_{max}: 3061 (carborane CH), 2581 (BH). ^1H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.99 (dd, 2H, J_1 = 7.3, J_2 = 1.9 Hz, Ph), 7.46 (m, 3H, Ph), 3.65 (brs, 1H, carborane CH), 3.58 (brs, 1H, carborane CH) 2.49 (brs, 2H, CH_2), 3.14–1.15 (m, 9H, BH). ^{11}B NMR (128 MHz, $CDCl_3$) δ (ppm): 4.98 (s, 1B, B^9), −1.93 (d, J = 149 Hz, 1B), −8.72 (d, J = 162 Hz, 2B), −13.65 (d, J = 166 Hz, 2B), −14.01 (d, J = 159 Hz, 2B), −15.16 (d, J = 178 Hz, 2B). *Anal.* Calc. for $C_{11}H_{18}B_{10}N_2O$, (302.4): C, 43.69; H, 6.00; B, 35.75; N, 9.26. Found: C 43.87; H, 6.18; B, 35.40; N, 9.10%.

*2.5.5. 2-[(o-Carboran-1-yl)methyl]-5-phenyl-1,3,4-oxadiazole (**20**)*

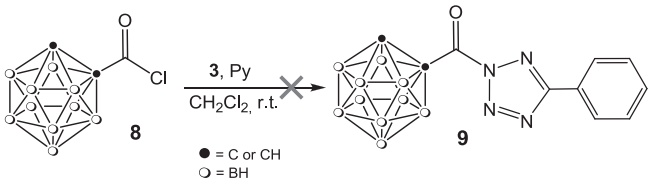
Yield: A, B – 69%, C – 63%. White powder. M.p. 150–152 °C. IR (KBr, cm^{-1}) ν_{max}: 3031 (carborane CH), 2581 (BH). ^1H NMR (400 MHz, $CDCl_3$) δ (ppm): 8.04 (m, 2H, Ph), 7.63 (m, 3H, Ph), 4.02 (brs, 1H, carborane CH), 3.91 (s, 2H, CH_2), 3.00–1.00 (m, 10H, BH). ^{11}B NMR (128 MHz, $CDCl_3$) δ (ppm): −1.43 (d, J = 150 Hz, 1B), −4.89 (d, J = 143 Hz, 1B), −8.96 (d, J = 153 Hz, 3B), −10.95 (d, J = 174 Hz, 2B), −11.97 (d, J = 174 Hz, 1B), −12.49 (d, J = 181 Hz, 2B). *Anal.* Calc. for $C_{11}H_{18}B_{10}N_2O$, (302.4): C, 43.69; H, 6.00; B, 35.75; N, 9.26. Found: C, 43.80; H, 6.08; B, 35.59; N, 9.19%.

*2.6. General procedure for the preparation of carborane 1,2,4-triazoles (**21–23**)*

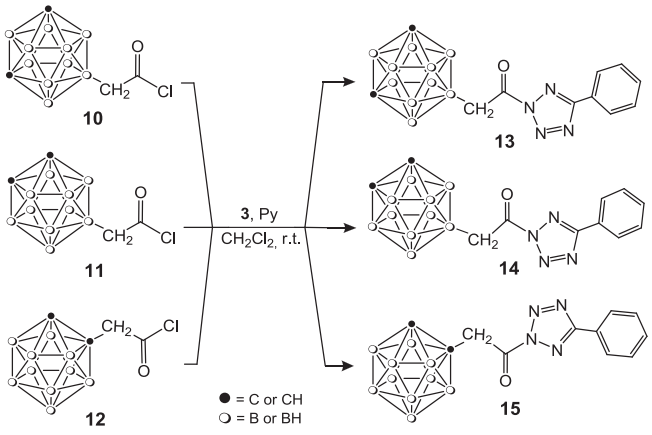
A mixture of corresponding carborane oxadiazole (**18–20**) (3 mmol), 2,4-dichloroaniline (15 mmol) and *p*-toluenesulfonic acid monohydrate (0.3 mmol) was stirred for 5–10 h at 140–170 °C under argon atmosphere. The reaction mixture was cooled to room temperature and the crude product was purified by column chromatography on silica gel using CH_2Cl_2 as the eluent to give the carborane 1,2,4-triazoles in 65–80% yield.



Scheme 2. Synthesis of carborane tetrazoles **6**, **7**.



Scheme 3. Attempts to prepare carborane tetrazole **9**.



Scheme 4. Synthesis of tetrazoles **13**–**15** based on carborane acetic acid chlorides.

*2.6.1. 3-[(o-Carboran-9-yl)methyl]-4-(2,4-dichlorophenyl)-5-phenyl-1,2,4-triazole (**21**)*

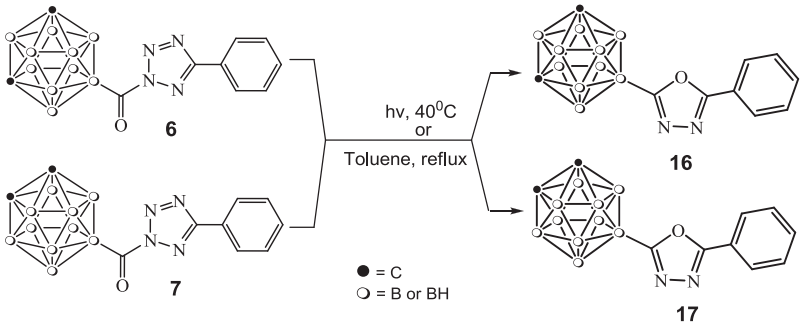
Yield: 0.87 g (65%). White powder. M.p. 168–170 °C. IR (KBr, cm^{-1}) ν_{max}: 3060 (carborane CH), 2587 (BH), 1490 (Ph). ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.54 (d, J = 2.2 Hz, 1H, H^3 in $C_6H_3Cl_2$), 7.36–7.18 (m, 7H, Ph), 3.66 (brs, 1H, carborane CH), 3.56 (brs, 1H, carborane CH), 2.42 (d, J = 15.0 Hz, 1H, C*H*H), 1.94 (d, J = 15.0 Hz, 1H, CH*H*), 3.19–1.58 (m, 9H, BH). ^{11}B NMR (128 MHz, $CDCl_3$) δ (ppm): 5.58 (s, 1B, B^9), −2.21 (d, J = 147 Hz, 1B), −8.88 (d, J = 149 Hz, 2B), −13.58 (d, J = 164 Hz, 2B), −14.29 (d, J = 167 Hz, 2B), −15.14 (d, J = 182 Hz, 2B). *Anal.* Calc. for $C_{17}H_{21}B_{10}Cl_2N_3$, (446.4): C, 45.74; H, 4.74; B, 24.22; N, 9.41. Found: C, 45.48; H, 4.81; B, 23.89; N, 9.39%.

*2.6.2. 3-[(o-Carboran-1-yl)methyl]-4-(2,4-dichlorophenyl)-5-phenyl-1,2,4-triazole (**22**)*

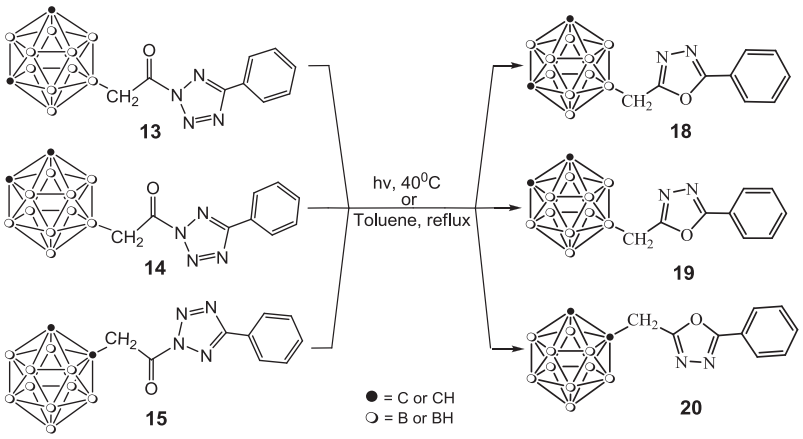
Yield: 0.97 g (73%). White powder. M.p. 163–164 °C. IR (KBr, cm^{-1}) ν_{max}: 3043 (carborane CH), 2587 (BH), 1489 (Ph). ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.64 (d, J = 2.1 Hz, 1H, H^3 in $C_6H_3Cl_2$), 7.45 (m, 1H, Ph), 7.43–7.20 (m, 6H,), 4.68 (brs, 1H, carborane CH), 3.74 (d, J = 16.2 Hz, 1H, C*H*H), 3.42 (d, J = 16.2 Hz, 1H, CH*H*), 3.04–1.50 (m, 10H, BH). ^{11}B NMR (128 MHz, $CDCl_3$) δ (ppm): −1.77 (d, J = 154 Hz, 1B), −5.01 (d, J = 149 Hz, 1B), −9.11 (d, J = 152 Hz, 2B), −9.87 (d, J = 144 Hz, 2B), −11.12 (d, J = 176 Hz, 1B), −12.57 (d, J = 173 Hz, 3B). *Anal.* Calc. for $C_{17}H_{21}B_{10}Cl_2N_3$, (446.4): C, 45.74; H, 4.74; B, 24.22; N, 9.41. Found: C, 45.59; H, 4.65; B, 23.97; N, 9.38%.

*2.6.3. 3-[(o-Carboran-9-yl)methyl]-4-(2,4-dichlorophenyl)-5-phenyl-1,2,4-triazole (**23**)*

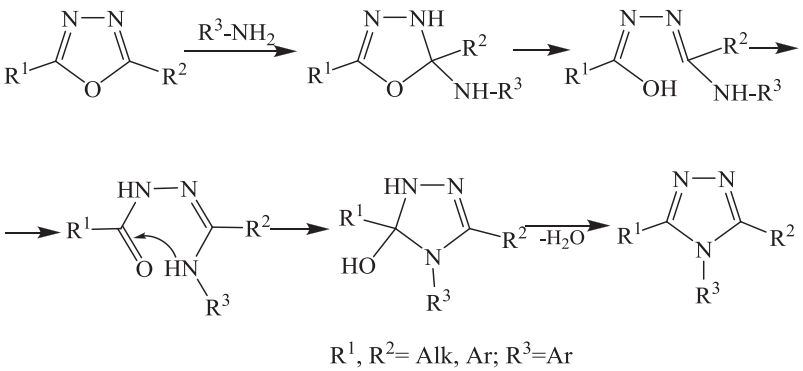
Yield: 1.0 g (80%). White powder. M.p. 158–160 °C. IR (KBr, cm^{-1}) ν_{max}: 3045 (carborane CH), 2600 (BH), 1488 (Ph). ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.59 (d, J = 2.1 Hz, 1H, H^3 in $C_6H_3Cl_2$), 7.40–7.23 (m, 7H, Ph), 2.90 (brs, 2H, carborane CH), 2.58 (d, J = 15.4 Hz, 1H, C*H*H), 2.14 (d, J = 15.4 Hz, 1H, CH*H*), 3.09–1.49 (m, 9H, BH). ^{11}B NMR (128 MHz, $CDCl_3$) δ (ppm): −1.71 (s, 1B, B^9), −6.35 (d, J = 161 Hz, 2B), −9.88 (d, J = 150 Hz, 1B), −12.93 (d, J = 164 Hz, 2B), −13.85 (d, J = 163 Hz, 2B), −17.41 (d, J = 181 Hz, 1B), −19.67 (d, J = 189 Hz, 1B). *Anal.* Calc. for $C_{17}H_{21}B_{10}Cl_2N_3$, (446.4): C, 45.74; H, 4.74; B, 24.22; N, 9.41 Found: C, 45.64; H, 4.79; B, 23.99; N, 9.35%.



Scheme 5. Synthesis of carborane-substituted 1,3,4-oxadiazoles **16**, **17**.



Scheme 6. Synthesis of carborane-substituted 1,3,4-oxadiazoles **18**–**20**.

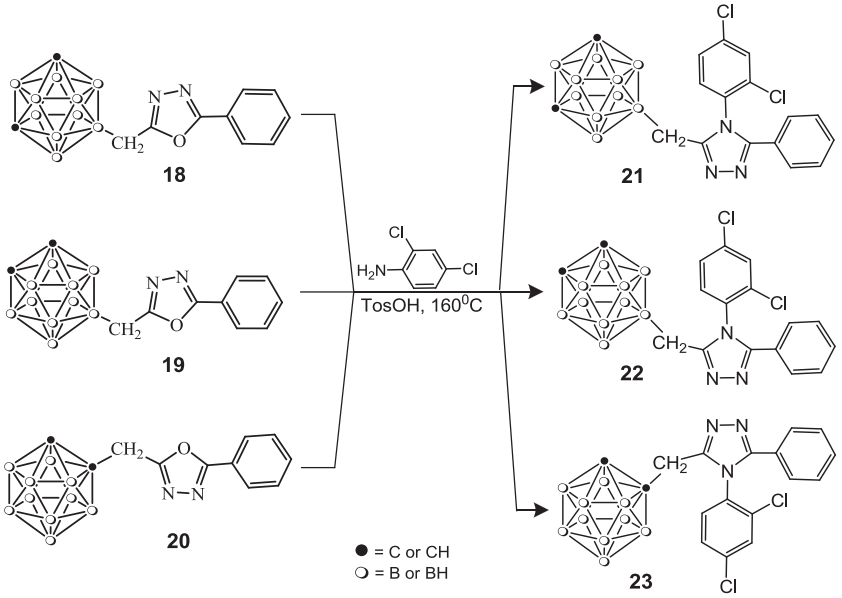


Scheme 7. Transformations of 1,3,4-oxadiazoles into 1,2,4-triazoles under the action of amines.

3. Results and discussion

3.1. Synthesis

Direct acylation of the tetrazole ring in the commercially available 5-phenyl-1H-tetrazole (**3**) with carborane carboxylic acid chlorides (**4**, **5**) (the latter compounds can be readily prepared from the corresponding 9-*o*- and 9-*m*-carborane carboxylic acids and thionyl chloride [12]) afforded carborane tetrazoles (**6**, **7**) in 70–75% yield. The acylation reaction was carried out at room temperature for 1–5 h in dry CH_2Cl_2 in the presence of a base, that is Et_3N or pyridine. The best results were obtained with the latter agent, presumably due to better solubility of tetrazole **3** in pyridine. At room temperature an undesired conversion of the *closo*-carborane polyhedron into the *nido*-form, $C_2B_9H_{12}^-$, is prevented (Scheme 2).



Scheme 8. Synthesis of carborane 1,2,4-triazoles **21**–**23**.

Table 1
Crystal data and structure refinement details of **16**.

Formula	$C_{10}H_{17}B_{10}N_2O_{1.5}$
Mr (g mol^{-1})	297.36
Crystal system	monoclinic
Space group	$P2_1/n$
a (Å)	6.9245(13)
b (Å)	23.626(6)
c (Å)	19.153(4)
α (°)	90.00
β (°)	97.514(8)
γ (°)	90.00
V (Å^3)	3106.49
Z	8
T (K)	100(2)
λ (Mo Kα) (Å)	0.71073
ρ_{calc} (g cm^{-3})	1.272
μ (mm^{-1})	0.072
Crystal size	0.30 × 0.04 × 0.03
θ Range (°)	4.13–25.00
Index range	$-8 \leqslant h \leqslant 5$
	$-28 \leqslant k \leqslant 28$
	$-22 \leqslant l \leqslant 22$
Reflections collected	18330
Independent reflections	5172
Observed reflections	2471
GOOF (S)	0.957
R_1, wR_2 (all)	0.1791, 0.1230
R_1, wR_2 [$I > 2\sigma(I)$]	0.0670, 0.0954

Interestingly, acid chloride **8**, containing a COCl group at the carbon atom of the carborane polyhedron, did not interact with tetrazole **3** (Scheme 3).

Following the same protocol the acid chlorides (**10**–**12**), obtained from corresponding carborane acetic acids [12], were successfully transformed into the corresponding tetrazoles (**13**–**15**) in good yield by the reaction with tetrazole **3** in CH_2Cl_2 (Scheme 4).

The tetrazoles **6**, **7**, **13**–**15** are stable and can be purified on a silica gel column with CH_2Cl_2 as an eluent in high yield. These compounds can be considered as key intermediates for the preparation of 2,5-disubstituted 1,3,4-oxadiazoles, which are important for biomedical purposes [16,17]. Furthermore, 2,5-diaryl-1,3,4-oxadiazoles are excellent electron-transporting units and might be promising as optoelectronic materials [17].

We found that UV irradiation (40 °C) or thermolysis in refluxing toluene of tetrazoles **6**, **7** provided the corresponding 2,5-disubstituted-1,3,4-oxadiazoles in a very clean and efficient manner via the extrusion of nitrogen and formation of 1,5-dipole (nitrileimine) [18]. This agent underwent cyclization to form the desired carborane-substituted oxadiazoles **16**, **17** in which the oxadiazole heterocycle is bound to the boron atom of the polyhedron (Scheme 5).

The same procedure starting from the tetrazoles **13**–**15** yielded the carborane oxadiazoles **18**–**20** with a methylene spacer between the boron atom of the polyhedron and the oxadiazole heterocycle (Scheme 6).

Oxadiazoles **16**–**20** can be prepared by a one-pot synthesis of the carborane acid chlorides **4**, **5**, **10**–**12** with tetrazole **3** in refluxing toluene without isolation of the pre-generated tetrazoles. However, owing to the presence of pyridine in the reaction mixture, the yields decreased for the *o*-carborane derivatives due to partial deboronation of the *closo*-carborane cluster into the *nido*-analogue, $C_2B_9H_{12}^-$. The process of deboronation was not observed with UV irradiation.

The 1,3,4-oxadiazoles are known to react with nucleophiles. For functionalization of the carborane polyhedron, amines seem to be the most interesting because they allow new classes of heterocyclic compounds to be obtained. We studied nucleophilic substitutions at the carbon atom in the oxadiazole ring of compounds **18**–**20** under the action of aromatic amines. In these reactions the formation of 1,2,4-triazole is the most probable, including carborane derivatives (Scheme 7) [19].

Amines that can be used to prepare carborane 1,2,4-triazoles are limited. This reaction can be convenient only for amines with a decreased nucleophilicity of the amino group to avoid deboronation of the carborane polyhedron. Heating of oxadiazoles **18**–**20** (containing the methylene spacer between the carborane polyhedron and the oxadiazole moiety) with 2,4-dichloroaniline at 150–160 °C in the presence of TsOH resulted in carborane 1,2,4-triazoles **21**–**23** in good yield (Scheme 8).

In similar reaction with carborane oxadiazoles **16**, **17**, without the methylene spacer, the expected 1,2,4-triazoles were not obtained; instead, a mixture of side products was detectable. This can be associated with the strong electron donor effect of the 9-*o*-($\sigma_i = -0.23$) and 9-*m*-carboranyl groups ($\sigma_i = -0.12$) [20]. In turn, these groups increased the electron density on the oxadiazole carbon atoms and decreased their reactivity towards the amines.

3.2. Spectroscopic data

The structures of all the newly synthesized compounds were confirmed by IR, ^{1}H and ^{11}B NMR spectra, and elemental analysis. All the compounds showed an intensive absorption band in the infrared spectrum at 2581–2615 cm^{-1} assigned to the stretching vibration of the BH-groups in the *closo*-polyhedron. A band at 3029–3062 cm^{-1} indicated the presence of a carborane CH-group. For the tetrazoles **6**, **7**, **13**–**15**, a band corresponding to the displacement of the C=O group was observed at 1720–1770 cm^{-1}. The ^{1}H NMR spectra of tetrazoles **6**, **7**, **13**–**15** showed the signals

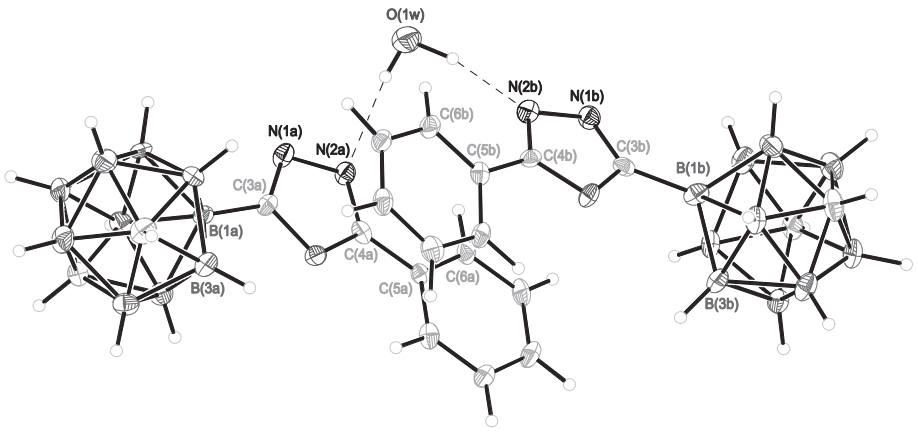


Fig. 1. Displacement ellipsoid plot (50%) of **16**. The hydrogen atoms are included but unlabelled for clarity. The dashed lines indicate hydrogen bonding.

Table 2
Hydrogen bonds observed for 16.

D–H···A	d(D–H) (Å)	d(H···A) (Å)	d(D···A) (Å)	(D–H···A) (°)
O(1w)–H(1wb)···N(2a)	0.86(6)	2.13(6)	2.967(5)	164(5)
O(1w)–H(1wa)···N(2b)	1.07(6)	1.94(6)	2.998(4)	167(4)

Table 3
Values of the torsion angles.

1–2–3–4	Torsion
B(3b)–B(1b)–C(3b)–N(1b)	−147.6(4)
B(3a)–B(1a)–C(3a)–N(1a)	−153.0(4)
C(6a)–C(5a)–C(4a)–N(2a)	−1.3(6)
C(6b)–C(5b)–C(4b)–N(2b)	−16.5(6)

of *o*-protons of the phenyl group in the range δ = 8.00–8.25 ppm, and the signals of *m*- and *p*-protons appeared in the range δ = 7.49–7.61 ppm. The signals of the carborane CH protons in **6**, **7**, **13**–**15** were observed at δ = 3.52–5.01 ppm. In the ^{1}H NMR spectra of compounds **13** and **14**, the protons of the methylene group showed a broadened singlet resonance at δ = 2.78–3.12 ppm that determined a spin-spin interaction of these protons with the boron atom of the polyhedron. In contrast, compound **15**, containing the methylene group at the carbon atom of the polyhedron, demonstrated a narrow singlet. Transformation of tetrazoles **6**, **7**, **13**–**15** into the corresponding oxadiazoles **16**–**20** did not alter the positions of the phenyl protons. However, the proton signals of the carborane CH-groups moved upfield for **16**–**19** (0.5 ppm) and **20** (1.0 ppm). An upfield effect (0.5 ppm) was also observed for the methylene protons (compounds **18** and **19**), while for **20** the upfield shift was only 0.3 ppm. Such a shift can be explained by a lower electron-withdrawal effect of the oxadiazole ring compared to the tetrazole system. The ^{1}H NMR spectra of triazoles **21**–**23** showed the existence of phenyl protons as a multiplet in the range δ = 7.64–7.21 ppm. In addition, the 3-H proton of the 2,4-dichlorophenyl substituent exhibited a doublet signal with a coupling constant of 2.0 Hz. The protons of the carborane CH-groups appeared at δ = 4.62–2.91 ppm. Unlike oxadiazoles **18**–**20**, the protons of the methylene group of **21**–**23** were observed as two doublets, indicating their magnetic non-equivalence.

3.3. X-ray crystallography

The structure of oxadiazole **16** was confirmed by an X-ray structure determination at 100 K and was refined satisfactory. Single crystals of **16** suitable for X-ray diffraction measurements were obtained from toluene by slow evaporation at room temperature as colorless needles. The crystallographic data of compound **16** are shown in Table 1.

In the crystal structure two crystallographically independent molecules of **16** are linked with one molecule of water by hydrogen bonds, via the N(2) atoms of the oxadiazoles (Fig. 1).

Both bonds show D···A distances significantly below the sum of the van der Waals radii (r_w(N) + r_w(O) = 3.07 Å) [21] at 2.967(5) and 2.998(4) Å, therefore representing moderately strong hydrogen bonds (Table 2).

In two molecules of 16 linked by water, the planes of the oxadiazole rings are differently oriented relatively to the phenyl group and the carborane polyhedron. This can be illustrated by different values of the torsion angles (Table 3).

The oxadiazole **16** crystallized in the monoclinic space group $P2_1/n$ with a cell volume of 3106.49 Å^3 and eight molecular moieties in the unit cell (Fig. 2).

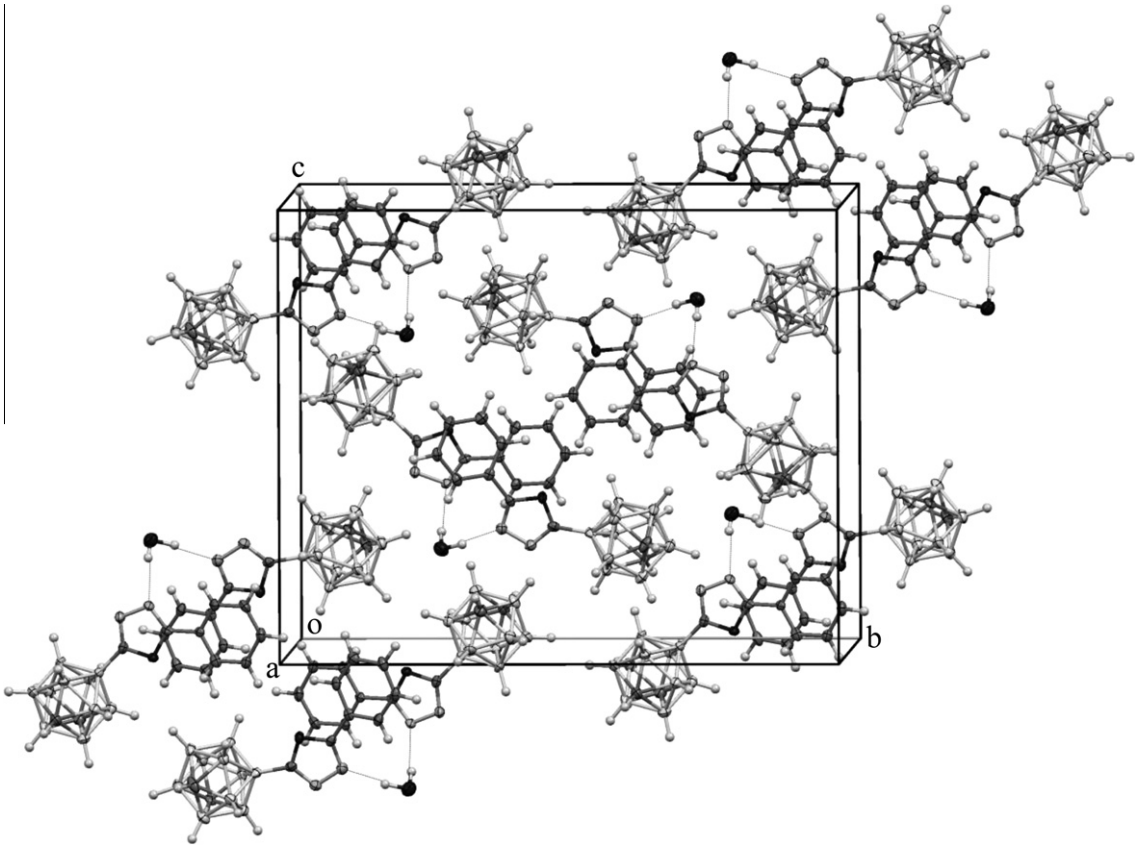


Fig. 2. Presentation of the unit cell and the packing of compound **16** (ellipsoids set at 60% probability). Dashed lines indicate hydrogen bonding.

4. Conclusions

We developed the synthesis of novel nitrogen-containing heterocyclic compounds with *o*- and *m*-carborane clusters starting from the available carborane carboxylic acid chlorides, carboranylacetic acid chlorides and 5-phenyl-1H-tetrazole. The carborane tetrazoles formed in these reactions were subsequently transformed under UV irradiation or thermolysis into the corresponding 1,3,4-oxadiazole derivatives. Under the action of amines, the oxadiazoles with carboranylmethyl substituents were converted to 1,2,4-triazoles in high yield. Importantly, in the new compounds the heterocyclic units are bound directly to the boron atom of the polyhedron or separated from the carborane polyhedron by a methylene spacer group. The suggested synthetic procedures allowed the avoidance of deboronation of the nucleophile-sensitive *closo*-carborane polyhedron.

Appendix A. Supplementary material

CCDC 901027 contains supplementary crystallographic data for **16**. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via http://www.ccdc.cam.ac.uk/conts/retrieving.html, or from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223336033, or e-mail: deposit@ccdc.cam.ac.uk.

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