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Novel bis[(1,2,3-triazolyl)methyl]carborane derivatives via regiospecific copper-catalyzed 1,3-dipolar cycloaddition

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ABSTRACT

1,2-Bis(azidomethyl)-*o*-carborane and 1,7-bis(azidomethyl)-*m*-carborane, prepared from the corresponding carboranylmethyl triflates and sodium azide, were conveniently functionalized by azide–alkyne cycloaddition affording novel bis[(1,2,3-triazolyl)methyl]carborane derivatives. Regiospecificity of this process was achieved by employing copper(II) acetate hydrate. Reaction of bis[(1,2,3-triazolyl)methyl] carborane derivatives with MeI yielded 3-methyl-1,2,3-triazolium carborane salts.

1. Introduction

1,3-Dipolar cycloaddition reactions of organic azides with alkynes in the presence of copper(I) are important for the synthesis of polynitrogen-containing heterocyclic compounds. This regioselective reaction produces 1,4-disubstituted 1,2,3-triazoles in high yields [1]. It employs stable and readily available chemical reagents (azides and alkynes) that react rapidly at ambient temperature, tolerates a wide range of functional groups, including unprotected alcohols, carboxylic acids, and amines, and shows little sensitivity to steric factors [2]. A great number of compounds containing 1,2,3-triazole moieties are reported to show a broad spectrum of biological activities, including fungicidal, antimicrobial, anticonvulsant, analgesic, and antitumor behavior [3]. Furthermore, a number of 1,2,3-triazole derivatives have found wide use as agrochemicals [4], polymers [5], and high-energy materials [6].

We recently reported the possibility of using a 1,3-dipolar cycloaddition (click reaction) to modify the *closo*-carborane polyhedron with 1,2,3-triazole heterocycles [7]. Such a reaction is of particular value, because in the family of icosahedral carboranes the heterocyclic derivatives are the least available. All methods reported are based on direct introduction of heterocyclic fragments into carborane polyhedra. Preparative routes to carborane heterocycles include cross-coupling of iodocarboranes with appropriate derivatives of heterocyclic compounds [8], nucleophilic displacement of a halogen atom in heterocycles with carborane copper derivatives [9], or the addition of carboranyllithium to highly electrophilic heterocycles followed by dehydrogenation of intermediates [10]. These methods have a number of synthetic restrictions imposed by the sensitivity of carborane polyhedra toward bases [11] and the availability of the corresponding heterocyclic component.

2. Experimental

2.1. General information

All solvents used in reactions were freshly distilled from appropriate drying agents before use. All other reagents were recrystallized or distilled as necessary. Reactions were performed under an atmosphere of dry argon. The purity of newly synthesized compounds was checked by TLC on Sorbfil. Eluents: *n*-heptane/ethyl acetate (15:1) for compounds **1**–**4** and dichloromethane for compounds **6a**–**c** and **7a**–**f**. IR spectra were measured on a UR-20 spectrometer in KBr tablets. NMR spectra were recorded on a Bruker Avance-400 spectrometer operating at 400 MHz for ^{1}H (TMS), 128.28 MHz for ^{11}B ($BF_3{\cdot}OEt_2$), and 376.5 MHz for ^{19}F ($BF_3{\cdot}OEt_2$). The solvent was deuterochloroform except where indicated

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otherwise. The synthesis of triflate **3** was carried out according to a known method [12]. Analytically pure samples of the compounds were obtained by recrystallization from ethyl acetate/*n*-heptane (1:5) and further drying in vacuum at room temperature.

2.2. Synthesis of 1,2-bis(azidomethyl)-o-carborane (**1**)

NaN_3 (2.73 g, 42 mmol) was added to a solution of triflate **3** (1 g, 2.14 mmol) in acetone (10 mL) under argon atmosphere with vigorous stirring, and the reaction mixture was heated to reflux for 20 h. Then the reaction mixture was poured into water (50 mL) and extracted with ethyl acetate (3 × 30 mL). The combined organic extracts were washed with water (3 × 10 mL) and dried over anhydrous $MgSO_4$, and the solvent removed in vacuo to give diazide **1**. Yield: 0.29 g (55%). Yellow oil. IR (KBr, cm^{-1}) $\tilde{\nu}_{max}$: 2585 (BH), 2110 (N_3). ^1H NMR (400 MHz, $CDCl_3$): δ 4.04 (s, 4H, CH_2), 3.50–1.50 (m, 10H, BH), ^{11}B NMR (128.3 MHz, $CDCl_3$): δ −3.5 (d, 2B, J = 150 Hz), −10.9 (d, 8B, J = 154 Hz). *Anal.* Calc. for $C_4H_{14}B_{10}N_6$ (254.3): C, 18.89; H, 5.55; B, 42.50; N, 33.05. Found: C, 19.05; H, 5.72; B, 41.85; N, 32.94%.

2.3. Synthesis of 1,7-bis(azidomethyl)-m-carborane (**2**)

NaN_3 (1.37 g, 21.0 mmol) was added to a solution of triflate **4** (1 g, 2.14 mmol) in dry DMSO (10 mL) under argon atmosphere with vigorous stirring. The resulting mixture was stirred for 3 h at room temperature before being poured into water (50 mL) and extracted with AcOEt (3 × 30 mL). The combined organic extracts were washed with water (50 mL) and then dried over anhydrous $MgSO_4$, and the solvent was removed in vacuo to give diazide **2**. Yield: 0.46 g (85%). Yellow oil. IR (KBr, cm^{-1}) $\tilde{\nu}_{max}$: 2606 (BH), 2107 (N_3). ^1H NMR (400 MHz, $CDCl_3$): δ 3.55 (s, 4H, CH_2), 1.4–3.2 (m, 10H, BH). ^{11}B NMR (128.3 MHz, $CDCl_3$): δ −6.6 (d, 2B, J = 163 Hz), −10.5 (d, 2B, J = 150 Hz), −11.4 (d, 4B, J = 158 Hz), −14.5 (d, 2B, J = 180 Hz). *Anal.* Calc. for $C_4H_{14}B_{10}N_6$ (254.3): C, 18.89; H, 5.55; B, 42.50; N, 33.05. Found: C, 19.00; H, 5.61; B, 42.05; N, 32.95%.

2.4. Synthesis of 1,7-bis(trifluormethanesulfonylmethyl)-m-carborane (**4**)

Trifluoromethanesulfonic anhydride (8.5 ml, 13.6 g, 51 mmol) in dry dichloromethane (10 mL) and dry pyridine (4.2 ml, 51 mmol) was added to a solution of 1,7-bis(hydroxymethyl)-*m*-carborane (10 g, 48.8 mmol) in dry dichloromethane (20 mL) under argon atmosphere and the result mixture was stirred for 2 h at r.t. Then the reaction mixture was poured into water (50 mL) and extracted with dichloromethane (3 × 30 mL). The combined organic extracts were washed with water (3 × 10 mL) and dried over anhydrous $MgSO_4$, and the solvent was removed in vacuo to give **4**. Yield: 21.1 g (92%). Colorless oil, IR (KBr, cm^{-1}) $\tilde{\nu}_{max}$: 2590 (BH). ^1H NMR (400 MHz, $CDCl_3$): δ 4.54 (s, 4H, CH_2), 3.50–1.50 (m, 10H, BH), ^{11}B NMR (128.3 MHz, $CDCl_3$): δ −5.6 (d, 2B, J = 165 Hz), −10.1 (d, 2B, J = 159 Hz), −11.4 (d, 4B, J = 175 Hz), −14.8 (d, 2B, J = 182 Hz), ^{19}F NMR (376.5 MHz, $CDCl_3$): −74.38 (s, 6F, CF_3).

2.5. General procedure for the preparation of bis(1,2,3-triazolyl)carborane derivatives (**6a–c, 7a–f**)

Copper acetate hydrate (2 mol%) was added to a solution of the corresponding alkyne **5a–c** (2.06 mmol) and diazide **1** or diazide **2** in toluene (5 mL). Then the reaction mixture was stirred at 40 °C (diazide **1**) or at room temperature (diazide **2**) for 3–20 h until the completion of the reaction (monitored by TLC). After evaporation of the solvent under reduced pressure, the residue was dissolved in ethyl acetate (10 mL) and washed with water (25 mL). The organic layer was dried over $MgSO_4$ and evaporated. The solvent was removed in vacuo and the residue purified by crystallization from ethyl acetate/*n*-heptane.

2.5.1. 1,2-Bis[(4′-acetoxymethyl-1′,2′,3′-triazol-1′-yl)methyl]-o-carborane (**6a**)

Yield: 28%. Colorless oil. IR (KBr, cm^{-1}) $\tilde{\nu}_{max}$: 2587 (BH) 1732 (C=O). ^1H NMR (400 MHz, $CDCl_3$): δ 7.81 (s, 2H, =CH–N), 5.19 (s, 4H, C–CH_2–N), 3.64 (s, 4H, C–CH_2–O), 1.87 (s, 6H, CH_3), 3.00–1.00 (m, 10H, BH). ^{11}B (128.3 MHz, $CDCl_3$): δ −3.6 (d, 2B, J = 162 Hz), −11.0 (d, 6B, J = 175 Hz), −11.7 (d, 2B, J = 174 Hz). *Anal.* Calc. for $C_{14}H_{26}B_{10}N_6O_4$ (450.5): C, 37.32; H, 5.82; B, 24.00; N, 18.65. Found: C, 37.38; H, 6.01; B, 23.99; N, 18.16%.

2.5.2. 1,2-Bis[(4′-phenyl-1′,2′,3′-triazol-1′-yl)methyl]-o-carborane (**6b**)

Yield: 32%. White powder. M.p. 175–176 °C (from AcOEt/*n*-heptane). IR (KBr, cm^{-1}) $\tilde{\nu}_{max}$: 2590 (BH). ^1H NMR (400 MHz, $CDCl_3$): δ 7.82 (m, 4H, *o*-Ph), 7.43 (m, 6H, *m*-Ph, *p*-Ph), 7.37 (s, 2H, =CH–N), 4.21 (s, 4H, CH_2), 3.5–1.5 (m, 10H, BH). ^{11}B NMR (128.3 MHz, $CDCl_3$): δ −3.5 (d, 2B, J = 149 Hz), −11.0 (d, 8B, J = 150 Hz). *Anal.* Calc. for $C_{20}H_{26}B_{10}N_6$ (458.6): C, 52.38; H, 5.71; B, 23.58; N, 18.33. Found: C, 52.44; H, 5.75; B, 23.43; N, 18.10%.

2.5.3. 1,2-Bis[(4′-trimethylsilyl-1′,2′,3′-triazol-1′-yl)methyl]-o-carborane (**6c**)

Yield: 35%. White powder. M.p. 168–171 °C (from AcOEt/*n*-heptane). IR (KBr, cm^{-1}) $\tilde{\nu}_{max}$: 2592 (BH), 842 (Si(CH_3)$_3$). ^1H NMR (400 MHz, $CDCl_3$): δ 7.72 (s, 2H, =CH–N), 4.23 (s, 4H, CH_2), 3.00–1.00 (m, 10H, BH), 0.33 (s, 18H, Si(CH_3)$_3$). ^{11}B NMR (128.3 MHz, $CDCl_3$): δ −3.4 (d, 2B, J = 145 Hz), −10.9 (d, 6B, J = 164 Hz), −11.4 (d, 2B, J = 157 Hz). *Anal.* Calc. for $C_{14}H_{34}B_{10}N_6Si_2$ (450.7): C, 37.31; H, 7.60; B, 23.98; N, 18.64; Si, 12.46. Found: C, 37.37; H, 7.62; B, 24.12; N, 18.74; Si, 12.53%.

2.5.4. 1,7-Bis[(4′-acetoxymethyl-1′,2′,3′-triazol-1′-yl)methyl]-m-carborane (**7a**)

Yield: 87%. Colorless oil. IR (KBr, cm^{-1}) $\tilde{\nu}_{max}$: 2590 (BH) 1733 (C=O). ^1H NMR (400 MHz, $CDCl_3$): δ 7.56 (s, 2H, =CH–N); 5.15 (s, 4H, C–CH_2–N); 4.68 (s, 4H, C–CH_2–O), 2.03 (s, 6H, CH_3). ^{11}B (128.3 MHz, $CDCl_3$): δ −6.4 (d, 2B, J = 154 Hz), −10.1 (d, 2B, J = 147 Hz), −11.2 (d, 4B, J = 156 Hz), −14.3 (d, 2B, J = 172 Hz). *Anal.* Calc. for $C_{14}H_{26}B_{10}N_6O_4$ (450.5): C, 37.32; H, 5.82; B, 24.00; N, 18.65. Found: C, 37.35; H, 5.99; B, 24.05; N, 18.18%.

2.5.5. 1,7-Bis[(4′-phenyl-1′,2′,3′-triazol-1′-yl)methyl]-m-carborane (**7b**)

Yield: 90%. White powder. M.p. 170–172 °C (from AcOEt/*n*-heptane). IR (KBr, cm^{-1}) $\tilde{\nu}_{max}$: 2590 (BH). ^1H NMR (400 MHz, $CDCl_3$): δ 7.79 (m, 4H, *o*-Ph), 7.68 (s, 2H, =CH–N), 7.41 (m, 4H, *m*-Ph), 7.34 (m, 2H, *p*-Ph), 4.72 (s, 4H, C–CH_2–N), 1.5–3.5 (m, 10H, BH). ^{11}B NMR (128.3 MHz, $CDCl_3$): δ −6.4 (d, 2B, J = 108 Hz), −10.1 (d, 2B, J = 149 Hz), −11.2 (d, 4B, J = 146 Hz), −14.3 (d, 2B, J = 172 Hz). *Anal.* Calc. for $C_{20}H_{26}B_{10}N_6$ (458.5): C, 52.38; H, 5.71; B, 23.58; N, 18.33. Found: C, 52.32; H, 5.71; B, 23.55; N, 18.12%.

2.5.6. 1,7-Bis[(4′-trimethylsilyl-1′,2′,3′-triazol-1′-yl)methyl]-m-carborane (**7c**)

Yield: 85%. White powder. M.p. 160–162 °C (from AcOEt/*n*-heptane). IR (KBr, cm^{-1}) $\tilde{\nu}_{max}$: 2592 (BH), 840 (SiMe_3). ^1H NMR (400 MHz, $CDCl_3$): δ 7.41 (s, 2H, =CH–N), 4.71 (s, 4H, C–CH_2–N), 3.5–1.5 (m, 10H, BH), 0.32 (s, 18H, CH_3). ^{11}B NMR (128.3 MHz, $CDCl_3$): δ −6.5 (d, 2B, J = 145 Hz), −10.2 (d, 2B, J = 148 Hz), −11.3 (d, 4B, J = 153 Hz), −14.3 (d, 2B, J = 182 Hz). *Anal.* Calc. for

$C_{14}H_{34}B_{10}N_6Si_2$ (450.7): C, 37.31; H, 7.60; B, 23.98; N, 18.64, Si, 12.46. Found: C, 37.38; H, 7.61; B, 24.11; N, 18.73; Si, 12.55%.

*2.5.7. 1,7-Bis[(4′-carbdimethylhydroxy-1′,2′,3′-triazol-1′-yl)methyl]-m-carborane (**7d**)*

Yield: 78%. White powder. M.p. 185–187 °C (from AcOEt/*n*-heptane). IR (KBr, cm^{-1}) $\tilde{\nu}_{max}$: 2593 (BH). ^1H NMR (400 MHz, THF-D_8): δ 7.62 (s, 2H, =CH–N); 4.80 (s, 4H, C–CH_2–N); 4.54 (br s, 2H, OH), 1.52 (s, 12H, CH_3). ^{11}B NMR (128.3 MHz, THF-D_8): δ −6.7 (d, 2B, J = 155 Hz), −10.8 (d, 2B, J = 147 Hz), −11.1 (d, 4B, J = 150 Hz), −14.4 (d, 2B, J = 184 Hz). *Anal.* Calc. for $C_{14}H_{30}B_{10}N_6O_2$ (422.5): C, 39.80; H, 7.16; B, 25.59; N, 19.89. Found: C, 40.32; H, 7.08; B, 25.10; N, 19.50%.

*2.5.8. 1,7-Bis[(4′-pentyl-1′,2′,3′-triazol-1′-yl)methyl]-m-carborane (**7e**)*

Yield: 79%. Colorless oil. IR (KBr, cm^{-1}) $\tilde{\nu}_{max}$: 2591 (BH). ^1H NMR (400 MHz, $CDCl_3$): δ 7.18 (s, 2H, =CH–N); 4.64 (s, 4H, C–CH_2–N); 2.69 (t, 4H, J = 7.73 Hz, CH_2–$(CH_2)_3CH_3$); 1.69 (m, 4H, –CH_2–CH_2–$(CH_2)_2CH_3$); 1.32–1.42 (m, 8H, –$(CH_2)_2$–CH_2–CH_2–CH_3); 0.88 (t, 6H, J = 6.58 Hz, CH_2–CH_3). ^{11}B (128.3 MHz, $CDCl_3$): δ −6.5 (d, 2B, J = 140 Hz), −10.2 (d, 2B, J = 149 Hz), −11.3 (d, 4B, J = 151 Hz), −14.4 (d, 2B, J = 180 Hz). *Anal.* Calc. for $C_{18}H_{38}B_{10}N_6$ (446.6): C, 48.40; H, 8.58; B, 24.20; N, 18.82. Found: C, 48.76; H, 8.62; B, 23.98; N, 18.63%.

*2.5.9. 1,7-Bis[(4′-adenino-1′,2′,3′-triazol-1′-yl)methyl]-m-carborane (**7f**)*

Yield: 68%. White powder. M.p. > 180 °C (with decomp.). IR (KBr, cm^{-1}) $\tilde{\nu}_{max}$: 2928 (NH), 2597 (BH). ^1H NMR (400 MHz, acetone-D_6): δ 8.21 (s, 2H, 2-H adenine), 8.15 (s, 2H, 8-H adenine), 8.11 (s, 2H, =CH–N), 6.77 (br s, 4H, NH_2), 5.54 (s, 4H, CH_2–adenine), 5.07 (d, 4H, C–CH_2–N), 3.0–1.0 (m, 10H, BH). ^{11}B NMR (128.3 MHz, acetone-D_6): δ −6.8 (d, 2B, J = 162 Hz), −10.9 (d, 2B, J = 146 Hz), −11.5 (d, 4B, J = 166 Hz), −14.1 (d, 2B, J = 181 Hz). *Anal.* Calc. for $C_{14}H_{30}B_{10}N_6O_2$ (600.6): C, 39.99; H, 4.70; B, 18.00; N, 37.31. Found: C, 40.12; H, 4.79; B, 17.88; N, 37.29%.

*2.6. General procedure for the preparation of bis(1,2,3-triazolium)carborane salts (**8b**, **8c**, **8e**)*

Methyl iodide (1.77 mmol) was added to a solution of corresponding compound **7b**, **7c**, or **7e** (0.44 mmol) in nitromethane (7 mL) under argon atmosphere. The resulting mixture was heated to reflux for 5–10 h. Nitromethane was removed in vacuo and the residue washed with *n*-heptane (20 mL) and diethyl ether (10 mL) to give the triazolium carborane derivatives in high yields.

*2.6.1. 1,1′-[(m-Carboran-1,7-yl)bis(methylene)] bis(3-methyl-4-phenyl-1,2,3-triazol-3-ium iodide) (**8b**)*

Yield: 90%. Yellow powder. M.p. 140–143 °C. ^1H NMR (400 MHz, $CDCl_3$): δ 8.83 (s, 2H, =CH–N), 7.91 (m, 4H, *o*-Ph), 7.65 (m, 4H, *m*-Ph), 7.42 (m, 2H, *p*-Ph), 4.42 (s, 6H, N^+–CH_3), 5.61 (c, 4H, C–CH_2–N), 3.0–1.0 (m, 10H, BH). ^{11}B (128.3 MHz, $CDCl_3$): δ −6.6 (d, 2B, J = 149 Hz), −10.7 (d, 4B, J = 140 Hz), −11.1 (d, 2B, J = 148 Hz), −13.9 (d, 2B, J = 177 Hz). *Anal.* Calc. for $C_{22}H_{32}B_{10}I_2N_6$ (742.4): C, 35.59; H, 4.34; B, 14.56; N, 11.32. Found: C, 35.69; H, 4.19; B, 14.20; N, 11.25%.

*2.6.2. 1,1′-[(m-Carboran-1,7-yl)bis(methylene)] bis(3-methyl-1,2,3-triazol-3-ium iodide) (**8c**)*

Yield: 92%. Yellow powder. M.p. > 210 °C (with decomp.). ^1H NMR (400 MHz, $CDCl_3$): δ 8.65 (s, 2H, 4-CH–triazole), 8.61 (s, 2H, 5-CH–triazole), 5.28 (s, 4H, CH_2), 4.37 (s, 6H, N^+–CH_3), 3.00–1.20 (m, 10H, BH). ^{11}B (128.3 MHz, $CDCl_3$): δ −6.4 (d, 1B, J = 165 Hz), −10.2 (d, 3B, J = 148 Hz), −11.3 (d, 4B, J = 150 Hz), −14.2 (d, 2B, J = 177 Hz). *Anal.* Calc. for $C_{10}H_{24}B_{10}I_2N_6$ (509.3): C, 20.35; H, 4.10; B, 18.32; N, 14.24. Found: C, 20.39; H, 4.13; B, 18.27; N, 14.21%.

*2.6.3. 1,1′-[(m-Carboran-1,7-yl)bis(methylene)] bis(3-methyl-4-pentyl-1,2,3-triazol-3-ium iodide) (**8e**)*

Yield: 93%. Yellow powder. M.p. 132–134 °C. ^1H NMR (400 MHz, $CDCl_3$): δ 8.71 (s, 2H, =CH–N), 5.32 (s, 4H, C–CH_2–N), 4.43 (s, 6H, N^+–CH_3), 3.02 (t, 4H, J = 7.56 Hz, CH_2–CH_2–CH_2–CH_2–CH_3), 1.82 (tt, 4H, J = 7.94 Hz, J = 7.48 Hz, CH_2–CH_2–CH_2–CH_2–CH_3), 1.41 (m, 8H, CH_2–CH_2–CH_2–CH_2–CH_3), 3.00–1.00 (m, 10H, BH), 0.89 (t, 6H, J = 6.72 Hz, –$(CH_2)_3$–CH_2–CH_3). ^{11}B (128.3 MHz, $CDCl_3$): δ −6.4 (d, 2B, J = 146 Hz), −10.4 (d, 2B, J = 145 Hz), −11.0 (d, 4B, J = 142 Hz), −14.0 (d, 2B, J = 182 Hz). *Anal.* Calc. for $C_{30}H_{48}B_{10}I_2N_6$ (854.7): C, 42.16; H, 5.66; B, 12.65; N, 9.83. Found: C, 42.51; H, 5.87; B, 12.38; N, 9.79%.

3. Results and discussion

3.1. Synthesis of bis(azidomethyl) carboranes

To explore further the scope of click reactions in carborane chemistry, we prepared new representatives of carborane-substituted azides, namely, 1,2-bis(azidomethyl)-*o*-carborane **1** and 1,7-bis(azidomethyl)-*m*-carborane **2**, and investigated their Cu-catalyzed [3+2] cycloaddition reactions with terminal alkynes. For the preparation of carborane diazides **1** and **2** we exploited the high reactivity of 1,2-bis(trifluoromethanesulfonylmethyl)-*o*-carborane (**3**) [12] and 1,7-bis(trifluoromethanesulfonylmethyl)-*m*-carborane (**4**) toward nucleophilic reagents. When a mixture of triflate **3** and sodium azide was heated to reflux in acetone, diazide **1** was obtained in 55% yield (Scheme 1).

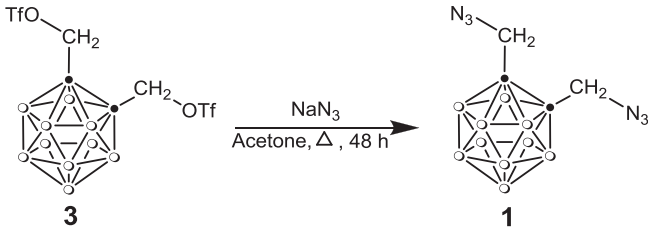
Diazide **2** was easily prepared in good yield and isolated as an oil by nucleophilic substitution of OTf in triflate **4** with sodium azide in DMSO (Scheme 2). Triflate **4** was prepared from 1,7-dihydroxymethyl-*m*-carborane and triflic anhydride according to the previously reported procedure [12].

NaN_3 in DMSO cannot be used for the preparation of diazide **1**, since under these reaction conditions an undesired deboronation reaction of the *closo*-carborane derivative to give the corresponding *nido* cluster occurred. It is noteworthy that diazide **1** is substantially less stable than diazide **2** and must be kept in the refrigerator to prevent fast decomposition. Therefore, it is important to use a freshly prepared sample of diazide **1** for further chemical transformations.

3.2. Synthesis of carborane-substituted 1,2,3-triazoles

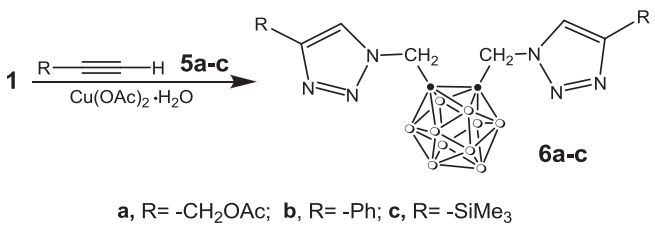
Cycloaddition of diazide **1** with alkynes **5a**–**c** in toluene in the presence of copper(II) acetate hydrate at room temperature under argon atmosphere afforded carborane-substituted 1,2,3-triazoles **6a**–**c** in moderate yields (Scheme 3).

The moderate yields of compounds **6a**–**c** obtained in these reactions are suggested to be due to steric hindrance in the formation of 1,2,3-triazole moieties from diazide **1** and its parallel deboronation reaction. The latter resulted in formation of *nido* clusters,

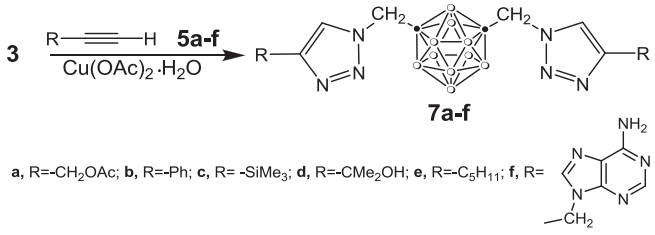


Scheme 1. Synthesis of 1,2-bis(azidomethyl)-*o*-carborane.

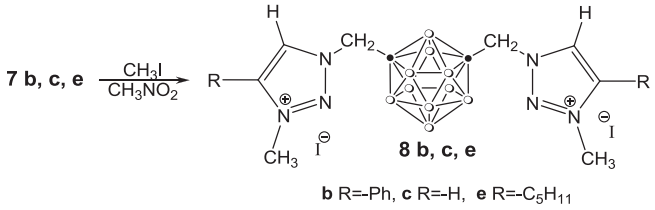
Scheme 2. Synthesis of 1,7-bis(azidomethyl)-*m*-carborane.



Scheme 3. Synthesis of 1,2-bis(triazolylmethyl)-*o*-carboranes.



Scheme 4. Synthesis of 1,7-bis(triazolylmethyl)-*m*-carboranes.



Scheme 5. Synthesis of triazolium salts.

which can be precipitated from the aqueous solution as salts of bulky cations, for example, tetrabutylammonium. Formation of a *nido*-product is presumably due to nucleophilic attack of an azide anion at the boron atom in the 3-position of the carborane polyhedron.

Similarly, cycloaddition reactions of diazide **2** with alkynes **5a–f** under the same reaction conditions (i.e., toluene as solvent and copper(II) acetate as catalyst) gave bis(triazolylmethyl)-*m*-carboranes **7a–f** in high yields as pure 1,4-regioisomers (Scheme 4).

Purification of all cycloadducts was achieved by extraction from the reaction mixture with ethyl acetate after dilution with water, concentrating the extracts, and crystallization from ethyl acetate/*n*-heptane.

High regiospecificity of this cycloaddition reaction was achieved by employing copper(II) acetate hydrate (1–2 mol%) as catalyst under argon atmosphere. Oxygen-free conditions were necessary to avoid oxidative coupling of terminal alkynes [13] during the reaction. Many catalyst systems have been reported in recent years which are efficient for [3+2] cycloaddition of azides with alkynes [1]. Among them copper(I) catalysis is the most promising method for preparation of 1,4-substituted 1,2,3-triazole heterocycles [2]. However, treatment of carborane azides **1** or **2** with alkynes in the presence of a copper(I) salt prepared in situ by reduction of $CuSO_4{\cdot}5H_2O$ with sodium ascorbate led to no reaction. Alternative catalyst systems based on copper(I)/amine ligands, which exhibit enhanced catalytic activity [14] due to stabilization of copper(I), are not suitable for carborane-substituted azides, as deboronation occurs affording *nido* clusters.

The structures of all compounds synthesized were confirmed by IR, ^{1}H and ^{11}B NMR spectroscopy and elemental analysis. The IR spectra of compounds **1**, **2**, **6a–c** and **7a–f** showed intense absorption bands in the range of 2570–2600 cm^{-1} corresponding to carborane BH groups. The azide absorption bands were detected at 2110 cm^{-1} (**1**) and at 2107 cm^{-1} (**2**) and were not observed in triazoles **6a–c** and **7a–f**.

In the ^{1}H NMR spectra the methylene protons of diazide **1** were observed as a singlet at 4.05 ppm, and those in diazide **2** at 3.55 ppm, which is in good agreement with electron-withdrawing effects of 1-*o*- and 1-*m*-carboranyl groups [11].

In products **6a–c** and **7a–f**, the signals of the methylene protons appeared as a singlet between 4.7 and 4.8 ppm, depending on the nature of the substituent in the 4-position of the triazole ring. The presence of the methyne CH group, which indicated the formation of a triazole ring, was confirmed by characteristic narrow singlets between 7.4 and 7.8 ppm (compounds **6a–c** and **7a–f**), supporting formation of only one regioisomer. ^{11}B NMR signals of all products are similar to those of diazides **1** and **2** and are in the range δ −3.6 to −11.7 ppm (**6a–c**) and δ −6.59 to −14.5 ppm (**7a–f**), confirming the *closo* structures of the carborane polyhedra.

3.3. Synthesis of carborane-substituted 1,2,3-triazolium salts

The novel bis(triazolylmethyl) carboranes were used to synthesize trisubstituted 1,2,3-triazolium salts, which have various applications in different fields [15]. *N*-Alkylation of triazoles **7b, c, e** with methyl iodide in nitromethane afforded the expected 1,3,4-trialkyl-1,2,3-triazolium carborane salts **8b, c, e** in quantitative yields (Scheme 5). All compounds were obtained as white powders.

^{1}H NMR and ^{11}B NMR spectra were obtained for salts **8b, c, e**. In the case of triazole **7c**, desilylation of the starting material occurred during alkylation and resulted in the 4-unsubstituted 1,2,3-triazolium salt **8c**. The formation of this compound was confirmed by ^{1}H NMR spectra in which the singlet at 0.32 ppm corresponding to the methyl protons of the trimethylsilyl group of **7c** disappeared in triazolium derivative **8c**. Furthermore, alkylation of the ring nitrogen atom was confirmed by downfield shifts (averaging 1.0 ppm) observed for the signals of the C–H protons of the triazole ring as compared to the corresponding neutral carborane heterocycles. For all compounds, formation of only one regioisomer was observed. The signals of the methyl protons in the 3-position of the triazolium ring were observed at δ 4.37–4.43 ppm [16]. Salts **8b, c, e** are soluble in polar solvents such as water, methanol, ethanol, dimethylformamide, and dimethyl sulfoxide.

4. Conclusion

We have demonstrated the efficiency of 1,3-cycloaddition reactions of bis(azidomethyl)carboranes with alkynes for the preparation of bis[(1,2,3-triazolyl)methyl]-substituted *o*- and *m*-carboranes. Use of copper(II) acetate hydrate led to regiospecific reactions resulting in previously unavailable carborane-substituted heterocycles. *N*-Alkylation of neutral bis(triazolylmethyl)carboranes with methyl iodide resulted in water-soluble 1,2,3-triazolium carborane compounds.

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