Tumour-targetted Boranes. Part 3.[1] Synthesis of Carbamate-linked Nitroimidazolyl Carboranes Designed for Boron Neutron Capture Therapy of Cancer

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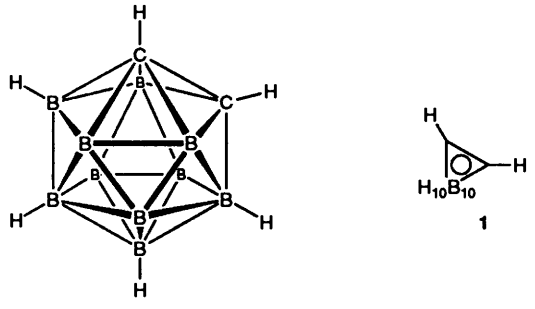
Carboranes targetted to specific tumour tissues are important for boron neutron capture therapy of cancer (BNCT). Carbamoylation of 2-[2-[2-(2-nitroimidazol-1-yl)ethoxy]ethoxy]ethanol **5** and 1-(chloromethyl)-2-(2-nitroimidazol-1-yl)ethanol **6** with carboran-1-yl isocyanate (generated *in situ* by a Curtius rearrangement of carborane-1-carbonyl azide) gave the corresponding carbamate-linked nitroimidazolylcarboranes **16** and **17**. A similar reaction of 4-carboranylphenyl isocyanate with **6** afforded the corresponding carbamate **24**.

Boron neutron capture therapy (BNCT) is of increasing interest for treatment of various cancers, mainly gliomas and melanomas.[2] When the ^{10}B isotope is irradiated with slow ('thermal') neutrons, an [n,α] reaction ensues, giving ^{7}Li and ^{4}He nuclei with kinetic energy (2.31 MeV). With this energy, the α-particle has a range of *ca.* 1 cell diameter in biological tissue and damage is limited to the cell containing the boron. Failures in early studies of BNCT were attributed[3] to inadequate concentrations of ^{10}B in the tumour tissue or to lack of selectivity of disposition of ^{10}B, leading to damage to normal tissue. Carboranes have been linked to nucleosides,[4] to amino acids[5] and to porphyrins[6] in attempts to target boron to tumours. 1-Substituted 2-nitroimidazoles are selectively retained in poorly vascularised hypoxic tumour tissue by reductive metabolism to electrophiles.[7] As part of a programme of synthesis and evaluation of nitroimidazoles in the treatment of cancer,[1,8] we sought compounds containing derivatives of 1,2-dicarba-*closo*-dodecaborane(12) ('carborane', **1**) linked to



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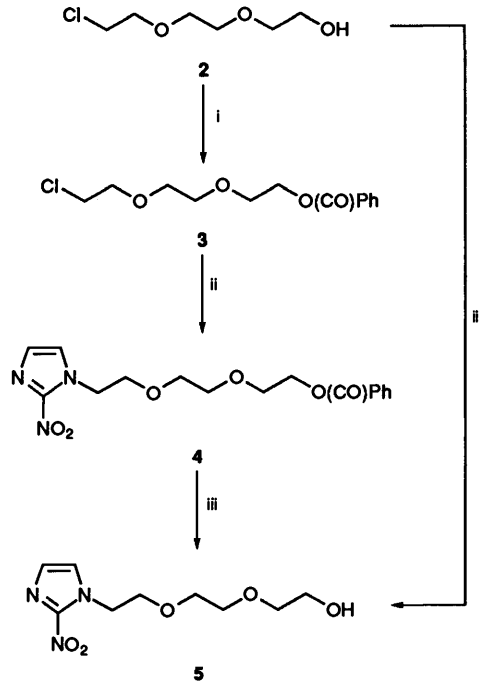
Representations of the structure of 1,2-dicarba-*closo*-dodecaborane(12) (carborane). Each boron atom has one hydrogen attached.

2-nitroimidazole as a strategy to cause selective retention of boron in hypoxic tumour tissue. Prior to our first preliminary communication,[9] no synthesis of a nitroimidazolylcarborane had been published, although reports of preparations of a nitroimidazolyl-*nido*-carborane and a nitroimidazolyl-*meta*-carborane with short links have been made in proceedings of conferences.[10]

Our previous study[1] showed that 'direct' methods of preparation of nitroimidazolylcarboranes, such as formation by treatment of a nitroimidazolylalkyne with decaborane(14) or alkylation of the 2-nitroimidazole anion with carboranyl electrophiles, were not feasible. The 1,3-dipolar cycloaddition of 4-(carboran-1-ylmethoxy)benzonitrile oxide with 1-(ω-alkynyl)-2-nitroimidazoles permitted coupling of the nitroimidazole and the carborane under mild conditions, although the product isoxazoles were insufficiently soluble in water to allow biological evaluation. We therefore sought an alternative mild linking strategy.

The addition of alcohols to isocyanates usually proceeds rapidly under mild conditions to give carbamates which are generally stable under physiological conditions. Addition of a nitroimidazole alcohol to a carborane carrying an isocyanate was therefore selected as a synthetic strategy.

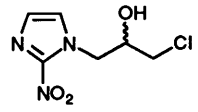
Two nitroimidazole alcohols, **5** and **6**, were prepared. To provide a suitable electrophile for reaction with the 2-nitroimidazole anion, the chloro alcohol **2** was protected as the benzoate ester **3** (Scheme 1). Treatment of this ester with the



Scheme 1 Synthesis of the nitroimidazole alcohol **5**: i, $PhCOCl–Et_3N$; ii, 2-nitroimidazole–$KOBu^t$–DMF; iii, NaOH

potassium salt of 2-nitroimidazole under the usual forcing conditions (DMF, 130 °C) gave the nitroimidazolyl ester **4** which was deprotected under basic conditions to give the required alcohol **5** in <40% overall yield. Other protecting groups for the alcohol, including triphenylsilyl and tetrahydropyranyl, gave lower yields. Alkylation of the nitroimidazole anion with the unprotected chloro alcohol **2** was then

investigated and was found to give the nitroimidazole alcohol **5** in good yield. It was expected that the presence of the oxyethylene ether moiety in carbamoylated derivatives of this alcohol would contribute to the aqueous solubility of the target nitroimidazolylcarborane. The shorter chain substituted nitroimidazol-2-ylethanol **6** was prepared by reaction of 2-nitroimidazole with epichlorohydrin, by the method of Beaman *et al.*[11]



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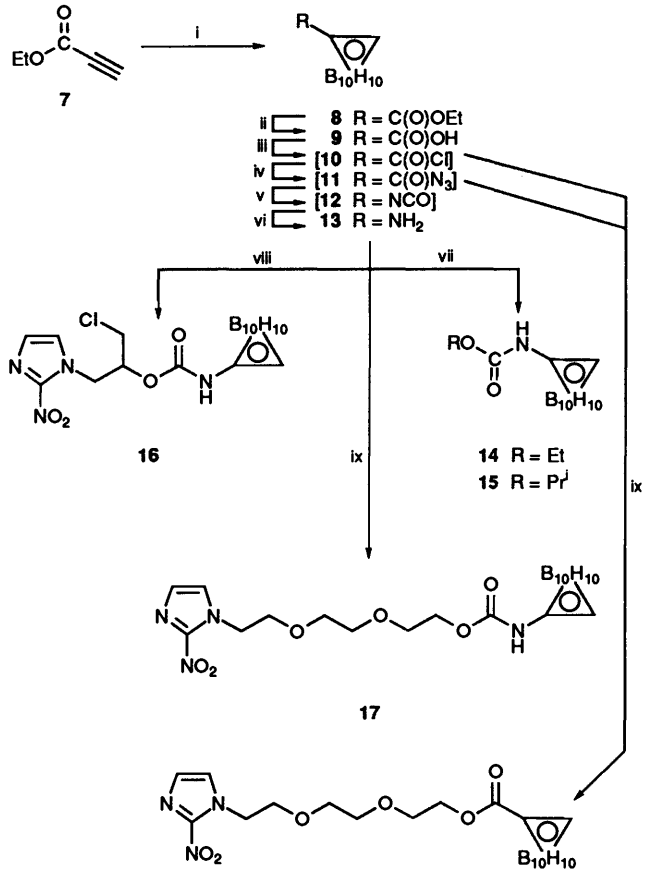
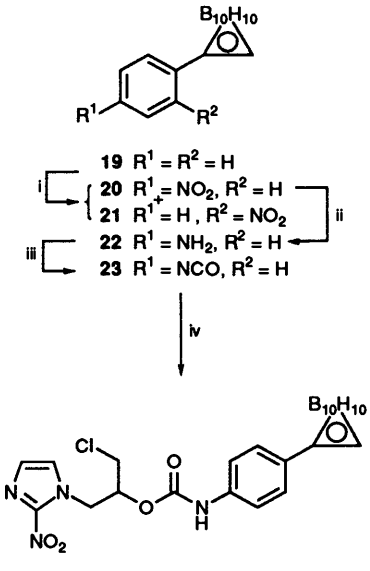
To provide a carborane with isocyanate directly attached to C-1, a strategy based on a Curtius rearrangement was employed. Following the standard method for the synthesis of carboranes from alkynes and decaborane(14) at elevated temperatures in the presence of a Lewis base,[12] the carborane ester **8** was formed from ethyl propynoate **7** and decaborane(14) in good yield. This ester was resistant to acid-catalysed hydrolysis but cleavage under mild basic conditions afforded the carboranecarboxylic acid **9** almost quantitatively. To establish a set of conditions for the Curtius rearrangement of the corresponding acid azide **11**, some preliminary experiments were undertaken. The acid chloride **10** was formed with thionyl chloride. Treatment with azidotrimethylsilane in boiling toluene, followed by hydrolysis of the isocyanate **12** with water in a one-pot process, gave the carboraneamine **13**[13] as a white solid which sublimed at 260–270 °C. In a similar run where ethanol replaced the added water, the major product was the expected ethyl carbamate **14**, formed from the isocyanate **12** generated *in situ*. A minor side-reaction was the trapping of unchanged acid chloride and/or acid azide to give the ethyl ester **8**. The 1-isopropyl carbamate **15** was formed analogously. These simple carbamates were found to be stable to both aqueous acid and aqueous base conditions, in experiments designed to confirm stability of the carborane carbamates under biological conditions. With conditions now established for generation and reaction of the carborane isocyanate with alcohols, the reactions with the nitroimidazole alcohols **5** and **6** were investigated. Treatment of the isocyanate **12** with the sterically hindered secondary alcohol **6** gave the desired carbamate-linked nitroimidazolylcarborane **16** in moderate yield. The yield was improved using the primary alcohol **5**, giving carbamate-linked nitroimidazolylcarborane **17**. A low yield of the corresponding ester **18** was also isolated, presumably arising from the acid chloride or the unrearranged acid azide.

To provide a spacer between carborane and isocyanate units, the carboranylphenyl isocyanate **23** was synthesised. 1-Phenylcarborane **19** was nitrated using the mixed acid system but, in contrast to reports[14–16] that either a mixture of 3- and 4-nitro isomers or a mixture of 2-, 3- and 4-nitro compounds is produced, only the 2- and 4-nitrophenylcarboranes **21** and **20** were isolated in 2 and 85% yield, respectively. The isomers were characterised through their ^{1}H NMR spectra. The 4-nitro compound **20** was reduced with sodium borohydride and palladium, giving the 4-amine **22**. Treatment with phosgene under basic conditions afforded the phenyl isocyanate **23** which reacted smoothly with the secondary nitroimidazole alcohol **6** to furnish the required carbamate-linked nitroimidazolylcarborane **24**. In contrast, the reaction of the isocyanate **23** with the primary nitroimidazole alcohol **5** under the same conditions gave only inseparable mixtures.

The synthesis of the short series of carbamate-linked nitroimidazolylcarboranes **16**, **17** and **24** has demonstrated the



Scheme 2 Syntheses of the carbamate-linked nitroimidazolylcarboranes **16** and **17** and ester-linked nitroimidazolylcarborane **18**: i, $B_{10}H_{14}$–MeCN; ii, NaOH; iii, $SOCl_2$; iv, Me_3SiN_3; v, toluene and heat; vi, water, vii, EtOH or Pr^{i}OH; viii, **6**; ix, **5**



Scheme 3 Synthesis of the carbamate-linked nitroimidazolylcarborane **25**: i, HNO_3–H_2SO_2–CH_2Cl_2; ii, $NaBH_4$–Pd/C; iii, phosgene; iv, **6**

feasibility of this type of coupling for the sensitive nitroimidazole and carborane moieties. The biological evaluation of these stable nitroimidazolylcarboranes will be reported elsewhere. The linkage of the nitroimidazolylalkyl carborane-

carboxylate **18** is relatively labile to hydrolysis under aqueous conditions and would not be capable of ensuring delivery of the boron to tumour tissue.

Experimental

Deuteriochloroform was the solvent for NMR spectroscopy with tetramethylsilane as chemical-shift standard, unless otherwise noted. Solutions in organic solvents were dried with anhydrous magnesium sulphate. Solvents were evaporated under reduced pressure. The chromatographic stationary phase was silica gel. M.p.s are uncorrected. DMF refers to dimethylformamide. *J* Values are recorded in Hz.

2-{2-[2-(2-*Nitroimidazol*-1-*yl*)*ethoxy*]*ethoxy*}*ethanol* **5**.—*Method A*. 2-Nitroimidazole (3.39 g, 30 mmol) was stirred with potassium *tert*-butoxide (3.36 g, 30 mmol) in DMF (50 cm^3) at 130 °C for 1 h after which the mixture was cooled to 80 °C. Sodium iodide (100 mg) and 2-[2-(2-chloroethoxy)ethoxy)]-ethanol **2** (6.74 g, 40 mmol) were added to the mixture which was then stirred at 130 °C for 2 h. The solvent was evaporated and the residue was dissolved in dichloromethane and the solution washed with water and dried. Chromatography (dichloromethane, then dichloromethane–ethyl acetate, 2:1, then ethyl acetate–methanol, 10:1) gave the *title compound* **5** (4.61 g, 63%) as a pale yellow oil; ν_{max}/cm^{-1} 3420br; δ 3.60 (4 H, s), 3.66 (2 H, m), 3.86 (2 H, t, *J* 5.0) and 4.22 (2 H, m) ($CH_2OCH_2CH_2OCH_2CH_2O$), 4.65 (3 H, m, imidazole-CH_2 + OH) and 7.18 (1 H, s) and 7.29 (1 H, s) (imidazole 4,5-H_2); *m*/*z* (CI) 246.1090 (M + H) ($C_9H_{16}N_3O_5$ requires 246.1090).

Method B. 2-[2-(2-Chloroethoxy)ethoxy]ethanol **2** (3.37 g, 20 mmol) was stirred with benzoyl chloride (2.81 g, 20 mmol) and triethylamine (2.02 g, 20 mmol) in dry dichloromethane (50 cm^3) for 24 h after which the mixture was washed with water, aqueous sodium hydroxide (2 mol dm^{-3}) and water and then dried. Chromatography (dichloromethane) gave 2-[2-(2-chloroethoxy)ethoxy]ethyl benzoate **3** (4.71 g, 86%) as a pale yellow oil; ν_{max}/cm^{-1} 1730; δ 3.61 (2 H, t, *J* 5.9), 3.71 (6 H, m) and 3.85 (2 H, m) ($ClCH_2CH_2OCH_2CH_2OCH_2$), 4.49 (2 H, m, CH_2O_2CPh), 7.45 (2 H, t, *J* 7.7, Ar 3,5-H_2), 7.57 (1 H, t, *J* 7.7, Ar 4-H) and 8.06 (2 H, d, *J* 7.7, Ar 2,6-H_2). 2-Nitroimidazole (1.13 g, 10 mmol) was heated at 130 °C with potassium *tert*-butoxide (1.12 g, 10 mmol) in DMF for 30 min after which the benzoate ester **3** (2.72 g, 10 mmol) was added to the mixture and the whole was stirred at 130 °C for 2 h. After this the solvent was evaporated and the residue was dissolved in dichloromethane and the solution washed with water and dried. Chromatography (dichloromethane, then dichloromethane–diethyl ether, 10:1) gave crude 2-{2-[2-(2-nitroimidazol-1-yl)ethoxy]ethoxy}ethyl benzoate **4**: δ 3.62 (4 H, m, $CH_2OCH_2CH_2OCH_2$), 3.82 (4 H, m, $CH_2OCH_2CH_2OCH_2$), 4.48 (2 H, t, *J* 5.0, CH_2O_2CPh), 4.57 (2 H, t, *J* 5.0) (imidazole-CH_2), 7.16 (1 H, s) and 7.21 (1 H, s) (imidazole 4,5-H_2), 7.45 (2 H, t, *J* 7.7, Ar 3,5-H_2), 7.57 (1 H, t, *J* 7.7, Ar 4-H) and 8.05 (2 H, d, *J* 7.7, Ar 2,6-H_2). This ester **4** (350 mg, 1 mmol) in ethanol (7.5 cm^3) was treated with aqueous sodium hydroxide (2 mol dm^{-3}, 2.5 cm^3, 5 mmol) at 50 °C for 1 h after which the ethanol was evaporated and the residue was diluted with water (10 cm^3) and extracted with dichloromethane. The extract was dried and the solvent was evaporated to give the *title compound* **5** (180 mg, 73%) with properties as above.

Ethyl 1,2-*Dicarba*-closo-*dodecaborane*(12)-1-*carboxylate* **8**.—Decaborane(14) (3.66 g, 30 mmol) was stirred with dry acetonitrile (50 cm^3) for 3 h after which ethyl propynoate **7** (2.94 g, 30 mmol) was added to the solution which was then stirred under reflux for 3 d. After this the mixture was evaporated and chromatography (pentane–dichloromethane, 2:1) of the residue gave the carborane ester **8** (3.26 g, 50%) as a white solid, m.p. 55–57 °C (lit.,[17] m.p. 62–62.5 °C); δ_H 1.32 (3 H, t, *J* 7.2, CH_3), 2.3 (10 H, br q, $J_{B,H}$ 150, $B_{10}H_{10}$), 4.08 (1 H, br s, carborane 2-H) and 4.29 (2 H, q, *J* 7.2, CH_2).

1,2-*Dicarba*-closo-*dodecaborane*(12)-1-*carboxylic Acid* **9**.—The ester **8** (2.16 g, 10 mmol) was stirred with sodium hydroxide (1.00 g, 25 mmol) in water (50 cm^3) and methanol (20 cm^3) for 3 d. The methanol was evaporated and the residue was acidified with hydrochloric acid (2 mol dm^{-3}) and extracted with dichloromethane. The extract was dried and the solvent was evaporated to give the carboranecarboxylic acid **9** (1.82 g, 97%) as a white solid, m.p. 148–150 °C (lit.,[18] m.p. 150 °C); δ[$(CD_3)_2SO$] 1.3–3.2 (10 H, br, $B_{10}H_{10}$), 5.20 (1 H, br s, carborane 2-H) and 9.5 (1 H, CO_2H).

Ethyl N-(1,2-*Dicarba*-closo-*dodecaboran*(12)-1-*yl*)*carbamate* **14**.—The carboranecarboxylic acid **9** (380 mg, 2 mmol) was boiled under reflux with thionyl chloride (10 cm^3) and DMF (0.03 cm^3) for 4 h. The excess of reagents was evaporated and the residue, dissolved in toluene (10 cm^3), was treated with azidotrimethylsilane (250 mg, 2.2 mmol) at reflux for 6 h. The mixture was cooled and ethanol (2 cm^3) was added to it; it was then boiled under reflux for 1 h. The solvents were evaporated and the residue was subjected to chromatography (pentane–dichloromethane, 2:1, then pentane–dichloromethane, 1:3). From the first fraction was obtained ethyl 1,2-dicarba-*closo*-dodecaborane(12)-1-carboxylate **8** (70 mg, 16%). From the second fraction was isolated the *title compound* **14** (270 mg, 58%) as a colourless solid. A sample of this material was recrystallised from light petroleum (b.p. 60–80 °C): m.p. 102–104 °C (Found: C, 26.0; H, 7.5; N, 6.3. Calc. for $C_5H_{17}B_{10}NO_2$: C, 25.95; H, 7.36; N, 6.06); ν_{max}/cm^{-1} 3290, 2600 and 1710; δ_H 1.26 (3 H, t, *J* 7.1, CH_3), 2.2 (10 H, br q, $J_{B,H}$ 150, $B_{10}H_{10}$), 4.13 (2 H, q, *J* 7.1, CH_2), 4.59 (1 H, br s, carborane 2-H) and 5.90 (1 H, br s, NH); *m*/*z* (EI) $^{10}B/^{11}B$ isotope cluster centred at 230 (M − H).

Isopropyl N-(1,2-*Dicarba*-closo-*dodecaboran*(12)-1-*yl*)*carbamate* **15**.—A solution of the isocyanate **12** in toluene was treated with propan-2-ol as for the synthesis of the ethyl carbamate **14**, except that chromatography was omitted, to give the title compound **15** (290 mg, 59%) as a white solid, m.p. 148–150 °C (Found: C, 29.6; H, 7.9; N, 5.9. Calc. for $C_6H_{19}B_{10}NO_2$ C, 29.39; H, 7.76; N, 5.71); ν_{max}/cm^{-1} 3330, 2605 and 1710; δ[$(CD_3)_2SO$] 1.18 [6 H, d, *J* 6.2, $(CH_3)_2$], 1.0–3.0 (10 H, br, $B_{10}H_{10}$), 4.78 (1 H, septet, *J* 6.2, $CHMe_2$), 5.35 (1 H, br s, carborane 2-H) and 9.66 (1 H, s, NH); *m*/*z* (EI) $^{10}B/^{11}B$ isotope cluster centred at 244 (M − H).

1-(*Chloromethyl*)-2-(2-*nitroimidazol*-1-*yl*)*ethyl* N-(1,2-*Dicarba*-closo-*dodecaboran*(12)-1-*yl*)*carbamate* **16**.—The carboranecarboxylic acid **9** (380 mg, 2 mmol) was boiled under reflux for 4 h with thionyl chloride (10 cm^3) and dimethylformamide (0.03 cm^3). The excess of reagents was evaporated and the residue, in toluene (10 cm^3), was treated with azidotrimethylsilane (250 mg, 2.2 mmol). The mixture was boiled under reflux for 18 h and then cooled to ambient temperature. 1-(Chloromethyl)-2-(2-nitroimidazol-1-yl)ethanol **6**[11] (410 mg, 2 mmol) was added to the mixture which was then boiled under reflux for 1 h. After evaporation the residue, in chloroform, was cooled to 0 °C. The solid was collected to give the title compound **16** (290 mg, 38%) as a white solid, m.p. 190–193 °C (Found: C, 27.7; H, 4.8. Calc. for $C_9H_{20}B_{10}ClN_4O_4$ C, 27.66; H, 4.87); ν_{max}/cm^{-1} 3160, 2600 and 1740; δ[$(CD_3)_2SO$] 1.5–2.8 (10 H, br, $B_{10}H_{10}$), 3.80 (1 H, dd, *J* 12.2 and 6.4) and 3.94 (1 H, dd, *J* 12.2 and 4.0) (CH_2Cl), 4.46 (1 H, dd, *J* 14.3 and 9.2) and 4.83 (1 H, dd, *J* 14.3 and 3.0) (imidazole-CH_2), 5.12 (1 H, br s, carborane 2-H), 5.30

(1 H, m, C*H*OH), 7.15 (1 H, s, imidazole 4-H), 7.43 (1 H, s, imidazole 5-H) and 9.98 (1 H, s, NH); *m/z* (EI) 344 (M − HCl) and 184 (carborane-N=C=O); *m/z* (FAB +ve ion) $^{10}B/^{11}B$ isotope cluster centred at 391 (M + H), 393.2087 (M + H) ($C_9H_{20}{}^{11}B_{10}{}^{35}ClN_4O_4$ requires 393.2104).

2-{2-[2-(2-*Nitroimidazole*-1-*yl*)*ethoxy*]*ethoxy*}*ethyl* N-(1,2-*Dicarba*-closo-*dodecaboran*(12)-1-*yl*)*carbamate* **17** *and* 2-{2-[2-(2-*Nitroimidazol*-1-*yl*)*ethoxy*]*ethoxy*}*ethyl* 1,2-*Dicarba*-closo-*dodecaborane*(12)-1-*carboxylate* **18**.—The carboranecarboxylic acid **9** (380 mg, 2 mmol) was boiled under reflux for 4 h with dimethylformamide (0.03 cm^3) and thionyl chloride (10 cm^3). The excess of reagent was evaporated and the residue was boiled under reflux with azidotrimethylsilane (250 mg, 2.2 mmol) in toluene (10 cm^3) for 16 h. The alcohol **5** (490 mg, 2 mmol) was added to the mixture and heating was continued for a further 2 h. The residue on evaporation was subjected to chromatography (pentane–dichloromethane, 2:1, then dichloromethane, then dichloromethane–diethyl ether). From the dichloromethane fraction was obtained the *title compound* **18** (141 mg, 17%) as a pale yellow gum; ν_{max}/cm^{-1} 2600, 1750; δ 2.3 (10 H, br q, $J_{B,H}$ 150 Hz, $B_{10}H_{10}$, 3.57 (4 H, s) and 3.65 (2 H, m) and 3.84 (2 H, t, *J* 5.0) ($CH_2OCH_2CH_2OCH_2$), 4.13 (1 H, br s, carborane 2 H), 4.37 (2 H, m, CO_2CH_2), 4.64 (2 H, t, *J* 5.0 Hz, imidazole-CH_2) and 7.14 (1 H, s) and 7.21 (1 H, s) (imidazole 4,5-H_2); *m/z* (FAB + ve ion) 416.2830 (M + H) ($C_{12}H_{26}{}^{10}B_2{}^{11}B_8N_3O_6$ requires 416.2824). From the dichloromethane–diethyl ether fraction was obtained the *title compound* **17** (47%) as a pale yellow gum; ν_{max}/cm^{-1} 3250, 2600 and 1755 cm^{-1}; δ 2.2 (10 H, br q, $J_{B,H}$ 150, $B_{10}H_{10}$), 3.4–3.6 (6 H, m) and 3.81 (2 H, t, *J* 5.0) and 4.10 (2 H, m) ($CO_2CH_2CH_2OCH_2CH_2OCH_2$), 4.62 (1 H, br s, carborane 2-H), 4.66 (2 H, t, *J* 5.0, imidazole-CH_2), 7.12 (1 H, d, *J* 0.8) and 7.16 (1 H, d, *J* 0.8) (imidazole 4,5-H_2) and 8.10 (1 H, br s, NH); *m/z* (FAB +ve ion) 431.2941 (M + H) ($C_{12}H_{27}{}^{10}B_2{}^{11}B_8N_4O_6$ requires 431.2933).

1-(4-*Nitrophenyl*)-1,2-*dicarba*-closo-*dodecaborane*(12) **20** *and* 1-(2-*Nitrophenyl*)-1,2-*dicarba*-closo-*dodecaborane*(12) **21**.—1-Phenyl-1,2-dicarba-*closo*-dodecaborane(12) **19**[12] in dichloromethane (50 cm^3) was stirred vigorously with nitric acid (66%; 6.0 cm^3) and concentrated sulphuric acid (34 cm^3) for 24 h. The organic phase was washed with water and with saturated aqueous sodium hydrogen carbonate and then dried. The residue on evaporation was subjected to chromatography (pentane–dichloromethane, 7:1, then pentane–dichloromethane 1:1). From the first fraction was obtained the title compound **21** (40 mg, 2%) as a white solid, m.p. 159–161 °C (lit.,[16] m.p. 161–161.5 °C); δ 2.3 (10 H, br q, $J_{B,H}$ 150 Hz, $B_{10}H_{10}$), 4.31 (1 H, br s, carborane 2-H), 7.39 (1 H, m, Ar 6-H), 7.55 (2 H, m, Ar 4,5-H_2) and 7.90 (1 H, m, Ar 3 H). From the second fraction was isolated the title compound **20** (2.25 g, 85%) as a white solid, m.p. 165–166 °C (lit.,[19] m.p. 167–168 °C); δ 2.3 (10 H, br q, $J_{B,H}$ 150, $B_{10}H_{10}$), 4.07 (1 H, br s, carborane 2-H), 7.68 (2 H, d, *J* 8.8, Ar 2,6-H_2) and 8.21 (2 H, d, *J* 8.8, Ar 3,5-H_2).

4-(1,2-*Dicarba*-closo-*dodecaboran*(12)-1-*yl*)*aniline* **22**.—Sodium borohydride (3.04 g, 8 mmol) in water (5 cm^3) was added to the 4-nitro compound **20** (2.12 g, 8 mmol) and 10% palladium-on-charcoal (210 mg) in methanol (100 cm^3) and the mixture was stirred for 16 h under nitrogen. The suspension was filtered through Celite®. The residue on evaporation in dichloromethane, was washed with water and dried. The solvent was evaporated to give the amine **22** (1.82 g, 77%) as a white solid: m.p. 101–103 °C (lit.,[15] m.p. 103–105 °C); δ 2.2 (10 H, br q, $J_{B,H}$ 150, $B_{10}H_{10}$), 4.20 (1 H, br s, carborane 2-H), 6.64 (2 H, d, *J* 8.6, Ar 2,6-H_2), 7.36 (2 H, d, *J* 8.6, Ar 3,5-H_2) and 8.5 (2 H, br, NH_2).

4-(1,2-*Dicarba*-closo-*dodecaboran*(12)-1-*yl*)*phenyl Isocyanate* **23**.—The amine **22** (350 mg, 1.5 mmol) in toluene (5 cm^3) was treated with phosgene in toluene (20%; 0.9 cm^3, 1.7 mmol) and triethylamine (303 mg, 3 mmol) under reflux for 2 h. The mixture was cooled and filtered. The solvent was evaporated to afford the isocyanate **23** (400 mg, quant.) as a pale buff solid, m.p. 131–134 °C (reported by Sergeev *et al.*[20] but no m.p. was given); ν_{max}/cm^{-1} 2580 and 2280; δ_H 2.3 (10 H, br q, $J_{B,H}$ 150, $B_{10}H_{10}$), 3.92 (1 H, br s, carborane 2-H), 7.05 (2 H, d, *J* 9.0, Ar 2,6-H_2) and 7.44 (2 H, d, *J* 9.0, Ar 3,5-H_2); *m/z* (EI) $^{10}B/^{11}B$ isotope cluster centred at 261 (M). This material was used directly without further characterisation.

1-(*Chloromethyl*)-2-(2-*nitroimidazol*-1-*yl*)*ethyl* N-(4-(1,2-*Dicarba*-closo-*dodecaboran*(12)-1-*yl*)*phenyl*)*carbamate* **24**.—The isocyanate **23** (130 mg, 500 μmol) was boiled under reflux with 1-(chloromethyl)-2-(2-nitroimidazol-1-yl)ethanol **6**[11] (100 mg, 500 μmol) in toluene (10 cm^3) for 24 h. The solvent was evaporated and the residue was recrystallised from chloroform to give the title compound **24** (190 mg, 81%) as a white solid: m.p. 177–180 °C (decomp.); ν_{max}/cm^{-1} 3270, 2600 and 1740; δ_H[$(CD_3)_2SO$] 1.3–3.0 (10 H, br, $B_{10}H_{10}$), 3.89 (1 H, dd, *J* 12.1 and 5.9) and 4.04 (1 H, dd, *J* 12.1 and 3.9 Hz) (CH_2Cl), 4.63 (1 H, dd, *J* 14.3 and 8.8) and 4.88 (1 H, dd, *J* 14.3 and 2.5 Hz) (imidazole-CH_2), 5.44 (1 H, m, CHO_2C), 5.67 (1 H, br s, carborane 2-H), 7.14 (1 H, s, imidazole 4-H), 7.33 (2 H, d, *J* 8.8) and 7.47 (2 H, d, *J* 8.8) (Ar-H_4), 7.57 (1 H, s, imidazole 5-H) and 10.03 (1 H, br s, NH); *m/z* (FAB +ve ion) 468.2355 (*M* + H) ($C_{15}H_{24}{}^{11}B_{10}{}^{35}ClN_4O_4$ requires 468.2338).

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