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Supplementary Information

Dicarba-*closo*-dodecaborane(12) Derivatives of Phosphonium Salts: Easy Formation of *Nido*-Carborane Phosphonium Zwitterions

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Experimental.

All reactions were performed at under a dry nitrogen atmosphere and manipulations were performed using conventional Schlenk techniques.[1] THF, DME, CH_2Cl_2, MeCN, toluene and DMF were dried prior to use according to Perrin *et. al*.[2,3] THF and DME were dried over sodium wire and freshly distilled from benzophenone ketyl before use. Anhydrous CH_2Cl_2 and MeCN were freshly distilled from CaH_2 before use. Toluene was dried over sodium wire and freshly distilled prior to use. All other solvents were used without purification.

All precursor chemicals used were commercially available. 1,2-, 1,7- and 1,12-carborane were purchased from Katchem (Czech Republic). All other reagents were obtained from Aldrich Chemical Co. Chlorodiphenylphosphine was purified by distillation according to Armarego and Chai.[3] All other chemicals were used without purification.

Column chromatography was carried out on Ajax Finechem 40-63 μm silica gel or Sigma Aldrich standard ~50 Mesh activated neutral aluminium oxide. Column chromatography was performed as described by Still *et. al.*[4] Thin layer chromatography (t.l.c.) was carried out on Merck Kieselgel 60 F_{254} aluminium backed plates or Aldrich aluminium oxide plates. Visualisation was achieved using a 254 nm UV light in addition to iodine vapour staining.

All ^{1}H, $^{13}C\{^{1}H\}$, $^{11}B\{^{1}H\}$ and $^{31}P\{^{1}H\}$ NMR spectra were recorded at 300 K on a Bruker DRX400 spectrometer (^{1}H at 400 MHz, ^{13}C at 101 MHz, ^{11}B at 128 MHz and ^{31}P at 162 MHz). All NMR signals (δ) are reported in ppm. ^{1}H and $^{13}C\{^{1}H\}$ spectra in $CDCl_3$ were referenced to TMS (0 ppm). ^{1}H NMR spectra in all other solvents were referenced according to their residual solvent peaks. $^{11}B\{^{1}H\}$ NMR spectra were referenced to external standard $BF_3{\cdot}OEt_2$ (0 ppm). $^{31}P\{^{1}H\}$ NMR spectra were referenced to external standard $P(OMe)_3$ (140.85 ppm). The solvent used was $CDCl_3$

unless specified otherwise. Commercially-available deuterated solvents of 99.5% isotopic purity or higher were used for all spectra.

Mass spectra were acquired in an appropriate solvent (flow rate 100 μL/min) on a Finnegan LCQ MS Detector (ESI) or Polaris Q MS Detector (EI). An ESI spray voltage of 5 kV was applied with a heated capillary temperature of 200 °C and a nitrogen sheath gas pressure of 60 psi.

Melting points were determined using a Gallenkamp digital melting point apparatus and are uncorrected.

Elemental analyses were performed by Chemical and Microanalytical Services Pty. Ltd., Belmont, Victoria or by the Campbell Microanalytical Laboratory, University of Otago, New Zealand.

Diphenylphosphino-1,2-carborane (1).[5] To a stirred solution of 1,2-carborane (0.71 g, 4.92 mmol) in DME (50 mL) at 0°C was added dropwise *n*-BuLi (1.95 mL, 4.88 mmol) over 10 min. The reaction mixture was stirred for 30 min at this temperature, then for 30 min at room temperature before cooling back to 0°C. To this mixture was added dropwise chlorodiphenylphosphine (0.88 mL, 4.90 mmol) over 30 min. The mixture was stirred for 1 h at 0°C, and then for 1 h at room temperature followed by 12 h at reflux. The solvent was removed *in vacuo* and the crude solids were re-dissolved in toluene (50 mL). Diethyl ether (20 mL) and H_2O (25 mL) were added and the mixture was stirred vigorously for 10 min before separating the layers. The organic layer was dried over anhydrous $MgSO_4$, filtered off and the solvent removed *in vacuo* to afford a pale-yellow solid. The crude solid was recrystallised from 1:1 (*v*/*v*) diethyl ether/petroleum ether and further purified by alumina column chromatography (*n*-hexane). Two products were isolated, **1** (0.50 g, 31%) and bis(diphenylphosphino)-1,2-carborane (0.16 g, 13%) as

colourless solids. R_f = 0.37, m.p. 112.5 – 113.0 °C. ^{1}H NMR δ 7.77 (m, 4H, Ph), 7.47 (m, 6H, Ph), 3.47 (br, 1H, C_{cage}-H). ^{11}B{^{1}H} NMR δ -1.4 (br, 2B), -7.1 (br, 2H), -10.1 (br, 2H), -12.0 (br, 4H). ^{31}P{^{1}H} NMR δ 25.0 (s). ^{13}C{^{1}H} NMR (d_6-acetone) δ 136.22 (d, J_{PC} = 26.97 Hz, Ph), 133.10 (d, J_{PC} = 15.29 Hz, Ph), 132.31 (s, Ph), 129.92 (d, J_{PC} = 9.46 Hz, Ph), 74.87 (d, J_{PC} = 76.33 Hz, C_{cage}P), 65.50 (d, J_{PC} = 65.50 Hz, C_{cage}H). Anal. Calcd for $C_{14}H_{21}B_{10}P$: (%) C 51.20, H 6.45. Found C 51.17, H 6.52.

Diphenylphosphino-1,7- and 1,12-carboranes. A similar procedure to that described for the preparation of **1** was followed, starting with 1,7-carborane (0.65 g, 4.50 mmol) or 1,12-carborane (0.93 g, 6.47 mmol) in THF solution. Chlorodiphenylphosphine (0.28 mL, 1.50 mmol) was added to the lithiated 1,7-carborane and 0.38 mL (2.16 mmol) was added to the lithiated 1,12-carborane. Refluxing was omitted and instead the mixture was stirred overnight at room temperature in both cases. Both products were recrystallised from *n*-hexane. Purification by silica column chromatography (20% (*v/v*) CH_2Cl_2 : *n*-hexane) afforded **2** and **3** as colourless crystals.

Diphenylphosphino-1,7-carborane (2). Yield 110 mg (23%). R_f = 0.43, ^{1}H NMR δ 7.65 (m, 8H, Ph), 7.45 (m, 12H, Ph). ^{11}B{^{1}H} NMR δ -3.3 (br, 1B), -5.8 (br, 1B), -9.2 (br, 2B), -10.0 (br, 2B), -11.9 (br, 2B), -14.4 (br, 2B). ^{31}P{^{1}H} NMR δ 19.3 (s). Anal. Calcd. for $C_{14}H_{21}B_{10}P$: (%) C 51.20, H 6.45. Found C 51.13, H 6.63.

Diphenylphosphino-1,12-carborane (3). Yield 309 mg (47%). R_f = 0.50, ^{1}H NMR δ 7.64 (m, 4H, Ph), 7.40 (m, 6H, Ph), 2.75 (br, 1H, C_{cage}-H). ^{11}B{^{1}H} NMR δ -10.9 (s, 5B), -12.7 (s, 5B). ^{31}P{^{1}H} NMR δ 23.1 (s). ^{13}C{^{1}H} NMR δ 135.23 (d, $J_{P,C}$ = 26.0 Hz, Ph), 133.79 (d, $J_{P,C}$ = 17.3 Hz, Ph), 130.52 (s, Ph), 128.44 (d, $J_{P,C}$ = 9.49 Hz, Ph), 80.58 (d, $J_{P,C}$ = 64.0 Hz, C_{cage}P), 64.1 (s, C_{cage}H). Anal. Calcd. for $C_{14}H_{21}B_{10}P$: (%) C 51.20, H 6.45. Found C 51.21, H 6.52.

1,12-Carboranyldiphenylmethylphosphonium iodide (4). To a concentrated solution of **3** (0.23 g, 0.69 mmol) in THF (2 mL) was added MeI (0.18 mL, 2.9 mmol). The mixture was stirred at room temperature for 12 h and the resulting colourless precipitate was isolated by vacuum filtration. The solid was dried under vacuum over P_2O_5 to afford **4** as a colourless powder (0.16 g, 50%).

1,2-Carboranyldiphenylmethylphosphonium iodide (5). To a concentrated solution of **1** (1.26 g, 3.84 mmol) in THF (3 mL) was added MeI (0.96 mL, 15.39 mmol). The mixture was stirred at reflux for 12 h and the resulting colourless precipitate was isolated by vacuum filtration and washed with diethyl ether. The solid was dried under vacuum over P_2O_5 to afford **5** as a colourless solid (0.93 g, 52%). m.p. 249 – 251 °C.

1,7-Carboranyldiphenylmethylphosphonium iodide (6). To a concentrated solution of **2** (74 mg, 0.23 mmol) in THF (1 mL) was added MeI (0.10 mL, 0.90 mmol). The mixture was stirred at room temperature for 12 h and the resulting colourless precipitate was isolated by vacuum filtration and washed with diethyl ether. The solid was dried under vacuum over P_2O_5 to afford **6** as a colourless solid (13 mg, 12%).

7,8-dicarba-*nido*-undecaboranyldiphenylmethylphosphorane (7). A solution of **5** (0.24 g, 0.50 mmol) and CsF (0.23 g, 1.50 mmol) in ethanol was stirred at reflux for 24 h. The solvent was removed *in vacuo* to afford a colourless residue, which was re-dissolved in acetone (10 mL) and filtered off to remove the insoluble, colourless by-product. Removal of the solvent *in vacuo* yielded **7** as a colourless semi-solid (0.13 g, 80%).

***In vitro* Cytotoxicity Studies**

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All anti-cancer screening was performed in the Andrew Durant Drug Testing Facility, Peter MacCallum Cancer Institute (Melbourne, Australia). SF268 cells were placed into the wells of two culture plates and incubated overnight at 37°C in a humidified 5% CO_2, 95% air atmosphere. One plate was then fixed with TCA (as a measure of cells present at the time of addition of drug). Drugs were dissolved in MeOH to make solutions of concentrations spanning a 4-log range. 100 μL of each drug solution was then added to wells of the second plate. The plate was then incubated for a further 72 h after which viable cells were measured using the sulforhodamine B (SRB) assay.[6,7] Cells were measured by reading the absorbance at 550 nm using an automatic plate reader. The mean absorbance for time zero growth (Tz), control growth (C) and test drug growth (Ti) was determined and the % growth was calculated at each drug concentration as:

[(Ti-Tz)/(C-Tz)] x 100 for concentrations where Ti ≥ Tz

[(Ti-Tz)/Tz] x 100 for concentrations where Ti < Tz

The GI_{50} is defined as the drug concentration that results in a 50 % reduction in the net cellular protein in control cells following drug incubation.

X-ray Diffraction Study.

Data for **7** were collected at 150(2) K to approximately 60° 2θ with φ and ω scans using a Bruker-Nonius APEX2-X8-FR591 diffractometer employing graphite-monochromated Mo-Kα radiation generated from a rotating anode (0.71073 Å). Data integration and reduction were undertaken with SAINT and XPREP[8] and subsequent computations were carried out using the WinGX-32 graphical user interface.[9] The structure was solved by direct methods using SIR97.[10] Multi-scan empirical absorption corrections were applied to data sets using the program SADABS.[11] Data were refined and extended with SHELXL-97.[12] Carbon and boron-bound hydrogen atoms were included in idealised positions and refined using a riding model, except H(12) which was located in the

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difference Fourier map before fixing with bond and angle restraints. Non-hydrogen atoms with occupancies were refined anisotropically.

An ORTEP[13] depiction of the molecular structure of **7** is provided in Fig. 1.

Table 1. Non-Hydrogen Bond Lengths (Å).

atom	atom	Distance	atom	atom	Distance
C(1)	C(2)	1.5680(17)	C(1)	B(1)	1.626(2)
C(1)	B(4)	1.711(2)	C(1)	B(8)	1.7240(19)
C(2)	B(3)	1.6297(18)	C(2)	B(8)	1.7351(19)
C(2)	B(7)	1.7354(19)	C(2)	P(1)	1.7867(14)
C(3)	P(1)	1.7957(14)	C(4)	C(5)	1.3962(18)
C(4)	C(9)	1.4036(18)	C(4)	P(1)	1.7981(13)
C(5)	C(6)	1.3949(19)	C(6)	C(7)	1.383(2)
C(7)	C(8)	1.389(2)	C(8)	C(9)	1.390(2)
C(10)	C(15)	1.3988(18)	C(10)	C(11)	1.4018(18)
C(10)	P(1)	1.7982(13)	C(11)	C(12)	1.3914(19)
C(12)	C(13)	1.393(2)	C(13)	C(14)	1.380(2)
C(14)	C(15)	1.3918(19)	B(1)	B(5)	1.779(2)
B(1)	B(4)	1.803(2)	B(1)	B(2)	1.854(2)
B(2)	B(6)	1.782(2)	B(2)	B(5)	1.784(2)
B(2)	B(3)	1.814(2)	B(3)	B(6)	1.754(2)
B(3)	B(7)	1.796(2)	B(4)	B(9)	1.762(2)
B(4)	B(5)	1.765(2)	B(4)	B(8)	1.766(2)
B(5)	B(9)	1.810(2)	B(5)	B(6)	1.821(2)
B(6)	B(7)	1.760(2)	B(6)	B(9)	1.802(2)
B(7)	B(9)	1.774(2)	B(7)	B(8)	1.789(2)
B(8)	B(9)	1.776(2)			

Table 2. Non Hydrogen Bond Angles (º).

atom	atom	atom	angle
C(2)	C(1)	B(1)	111.37(10)
C(2)	C(1)	B(4)	111.60(10)
B(1)	C(1)	B(4)	65.38(9)
C(2)	C(1)	B(8)	63.41(8)
B(1)	C(1)	B(8)	117.51(11)
B(4)	C(1)	B(8)	61.87(9)
C(1)	C(2)	B(3)	114.74(10)
C(1)	C(2)	B(8)	62.69(8)
B(3)	C(2)	B(8)	117.13(11)
C(1)	C(2)	B(7)	112.79(10)
B(3)	C(2)	B(7)	64.41(8)
B(8)	C(2)	B(7)	62.05(8)
C(1)	C(2)	P(1)	116.46(9)
B(3)	C(2)	P(1)	115.21(9)
B(8)	C(2)	P(1)	120.18(9)
B(7)	C(2)	P(1)	122.78(9)
C(5)	C(4)	C(9)	119.85(12)
C(5)	C(4)	P(1)	120.96(10)
C(9)	C(4)	P(1)	119.20(10)
C(6)	C(5)	C(4)	119.75(13)
C(7)	C(6)	C(5)	120.20(14)
C(6)	C(7)	C(8)	120.34(13)
C(7)	C(8)	C(9)	120.21(13)
C(8)	C(9)	C(4)	119.65(13)
C(15)	C(10)	C(11)	119.56(12)
C(15)	C(10)	P(1)	119.80(10)
C(11)	C(10)	P(1)	120.64(10)
C(12)	C(11)	C(10)	119.90(13)
C(11)	C(12)	C(13)	120.06(13)
C(14)	C(13)	C(12)	120.16(13)
C(13)	C(14)	C(15)	120.44(14)
C(14)	C(15)	C(10)	119.88(13)
C(1)	B(1)	B(5)	104.51(10)
C(1)	B(1)	B(4)	59.57(9)
B(5)	B(1)	B(4)	59.03(9)
C(1)	B(1)	B(2)	106.52(10)
B(5)	B(1)	B(2)	58.77(8)
B(4)	B(1)	B(2)	107.54(10)
B(6)	B(2)	B(5)	61.41(9)
B(6)	B(2)	B(3)	58.38(9)
B(5)	B(2)	B(3)	105.59(10)
B(6)	B(2)	B(1)	105.50(10)
B(5)	B(2)	B(1)	58.49(8)
B(3)	B(2)	B(1)	101.61(10)
C(2)	B(3)	B(6)	104.69(10)
C(2)	B(3)	B(7)	60.65(8)
B(6)	B(3)	B(7)	59.44(9)

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C(2)	B(3)	B(2)	105.59(10)
B(6)	B(3)	B(2)	59.91(9)
B(7)	B(3)	B(2)	109.27(10)
C(1)	B(4)	B(9)	104.34(10)
C(1)	B(4)	B(5)	101.62(10)
B(9)	B(4)	B(5)	61.73(9)
C(1)	B(4)	B(8)	59.44(8)
B(9)	B(4)	B(8)	60.47(9)
B(5)	B(4)	B(8)	109.22(10)
C(1)	B(4)	B(1)	55.04(8)
B(9)	B(4)	B(1)	108.76(10)
B(5)	B(4)	B(1)	59.79(9)
B(8)	B(4)	B(1)	106.75(10)
B(4)	B(5)	B(1)	61.18(9)
B(4)	B(5)	B(2)	112.50(11)
B(1)	B(5)	B(2)	62.73(9)
B(4)	B(5)	B(9)	59.06(9)
B(1)	B(5)	B(9)	107.76(11)
B(2)	B(5)	B(9)	109.47(11)
B(4)	B(5)	B(6)	106.91(11)
B(1)	B(5)	B(6)	107.08(11)
B(2)	B(5)	B(6)	59.25(9)
B(9)	B(5)	B(6)	59.51(8)
B(3)	B(6)	B(7)	61.46(9)
B(3)	B(6)	B(2)	61.71(9)
B(7)	B(6)	B(2)	112.38(11)
B(3)	B(6)	B(9)	108.22(11)
B(7)	B(6)	B(9)	59.73(9)
B(2)	B(6)	B(9)	109.89(10)
B(3)	B(6)	B(5)	106.55(10)
B(7)	B(6)	B(5)	107.73(10)
B(2)	B(6)	B(5)	59.34(9)
B(9)	B(6)	B(5)	59.93(8)
C(2)	B(7)	B(6)	100.12(10)
C(2)	B(7)	B(9)	102.44(10)
B(6)	B(7)	B(9)	61.30(9)
C(2)	B(7)	B(8)	58.97(8)
B(6)	B(7)	B(8)	108.34(10)
B(9)	B(7)	B(8)	59.81(9)
C(2)	B(7)	B(3)	54.94(7)
B(6)	B(7)	B(3)	59.10(8)
B(9)	B(7)	B(3)	107.61(10)
B(8)	B(7)	B(3)	106.47(10)
C(1)	B(8)	C(2)	53.91(7)
C(1)	B(8)	B(4)	58.69(8)
C(2)	B(8)	B(4)	101.59(10)
C(1)	B(8)	B(9)	103.18(10)
C(2)	B(8)	B(9)	102.36(10)
B(4)	B(8)	B(9)	59.67(9)
C(1)	B(8)	B(7)	103.18(9)
C(2)	B(8)	B(7)	58.98(8)

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B(4)	B(8)	B(7)	107.74(11)
B(9)	B(8)	B(7)	59.69(9)
B(4)	B(9)	B(7)	108.53(11)
B(4)	B(9)	B(8)	59.86(9)
B(7)	B(9)	B(8)	60.50(9)
B(4)	B(9)	B(6)	107.87(10)
B(7)	B(9)	B(6)	58.97(8)
B(8)	B(9)	B(6)	107.05(10)
B(4)	B(9)	B(5)	59.20(9)
B(7)	B(9)	B(5)	107.63(10)
B(8)	B(9)	B(5)	106.75(10)
B(6)	B(9)	B(5)	60.56(9)
C(2)	P(1)	C(3)	109.76(6)
C(2)	P(1)	C(4)	112.87(6)
C(3)	P(1)	C(4)	108.23(6)
C(2)	P(1)	C(10)	106.88(6)
C(3)	P(1)	C(10)	109.27(6)
C(4)	P(1)	C(10)	109.79(6)

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