

## Supplementary Information

# One-Pot Synthesis of an Indole-Substituted 7,8-Dicarba-*nido*-dodecahydroundecaborate(-1)

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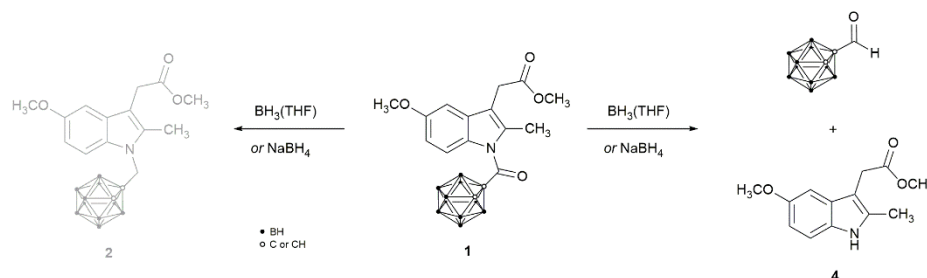
## Experimental details

### General considerations

Reactions were carried out under a nitrogen atmosphere using anhydrous solvents which were purified with an MBRAUN Solvent Purification System MB SPS-800. Chemicals were used as purchased. Thin-layer chromatography (TLC) was performed on pre-coated glass plates (0.25 mm, silica gel 60 F<sub>254</sub>); visualisation of carbaborane compounds on TLC plates was achieved by treatment with a solution of PdCl<sub>2</sub> (1% in MeOH) and gentle heating. Column chromatography was carried out with silica gel (0.035–0.070 mm, 60 Å). <sup>1</sup>H, <sup>11</sup>B and <sup>13</sup>C NMR spectra were recorded on a Bruker AVANCE DRX 400 (400 MHz) with tetramethylsilane as internal standard and referencing to the unified scale.<sup>1</sup> FTIR spectra were recorded on a Perkin-Elmer System 2000 FTIR spectrometer, scanning between 400 and 4000 cm<sup>-1</sup>. Mass spectra (HR-MS) were recorded on an ESI-FT-ICR Bruker-Daltonics spectrometer (APEX II, 7 T). Melting points were measured in sealed tubes.

### Reduction of *N*-acylindole by borane-THF or sodium borohydride

*Indoborin methyl ester (1)*: was synthesised according to the literature.<sup>2</sup>



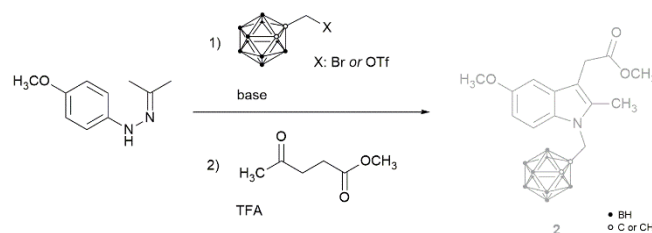
*General procedure for the reduction of 1*: Indoborin methyl ester (1) was dissolved in THF before addition of a reducing agent (BH<sub>3</sub>(THF),<sup>3</sup> NaBH<sub>4</sub>, BH<sub>3</sub>(THF)/BF<sub>3</sub>(OEt<sub>2</sub>) or BH<sub>3</sub>(THF)/NaBH<sub>4</sub>) and the reaction mixture was stirred (at room temperature, refluxing or heating in a microwave reactor). The progress of the reactions was monitored by TLC. The reaction was quenched upon formation of the semi-aminal by addition of methanol, and the product was isolated by extraction. <sup>1</sup>H NMR spectra of the crude product showed a mixture of the free indole 4 and the carbaboranyl aldehyde (1-H(O)C-1,2-C<sub>2</sub>B<sub>10</sub>H<sub>11</sub>).<sup>4</sup>

### Fischer indole synthesis

*Acetone (4-methoxyphenyl)hydrazone*: was synthesised according to a reported procedure<sup>5</sup> by reacting (4-methoxyphenyl)hydrazine hydrochloride with acetone in the presence of NaHCO<sub>3</sub>, yielding the highly air-sensitive product as a colourless solid: <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ = 1.87 (s, 3H, CH<sub>3</sub>), 2.02 (s, 3H, CH<sub>3</sub>), 3.77 (s, 3H, OCH<sub>3</sub>), 6.61 (br s, 1H, NH), 6.82 (m, 2H, CH), 6.99 (m, 2H, CH) ppm.

*1-Bromomethyl-1,2-dicarba-*closo*-dodecaborane (12)*: *n*-BuLi (5.8 mL, 1.32 M in *n*-hexane, 7.6 mmol, 1.1 eq.) was added at -78 °C to a solution of 1,2-dicarba-*closo*-dodecaborane(12) (1.0 g, 6.9 mmol, 1.0 eq.) in Et<sub>2</sub>O (100 mL) and the solution was stirred for 30 min. CH<sub>2</sub>Br<sub>2</sub> (0.63 mL, 9.0 mmol, 1.3 eq.) was added and the reaction mixture was stirred for 1 h at -78 °C and overnight at room temperature. Water (100 mL) was added and the aqueous phase was extracted with Et<sub>2</sub>O. The solvent was removed and the product was purified by column chromatography (hexanes (80–110 °C)/EtOAc 20:1) to yield a colourless oil (0.34 g, 25%): <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ = 1.20–3.20 (br, 10H, B<sub>10</sub>H<sub>10</sub>), 3.69 (s, 2H, CH<sub>2</sub>), 4.00 (br s, 1H, C<sub>cluster</sub>H) ppm; <sup>11</sup>B{<sup>1</sup>H} (128 MHz, CDCl<sub>3</sub>): δ = -12.9 (2B), -12.5 (2B), -10.6 (2B), -8.7 (2B), -5.0 (1B), -2.4 (1B) ppm.

*1-Trifluoromethanesulfonylmethyl-1,2-dicarba-*closo*-dodecaborane (12)*: was synthesised according to the literature.<sup>6</sup>



*General procedure for indole synthesis*: 1-Bromomethyl-1,2-dicarba-*closo*-dodecaborane(12) or 1-trifluoromethanesulfonylmethyl-1,2-dicarba-*closo*-dodecaborane(12) was added to a solution of acetone (4-methoxyphenyl)hydrazone and a base and the reaction mixture was stirred for several

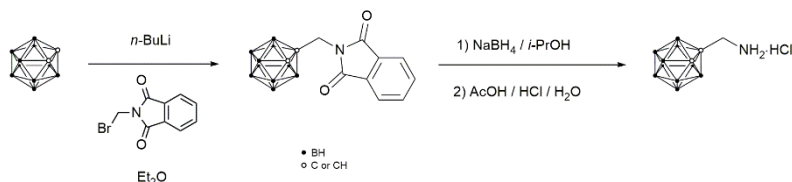
hours. For formation of the heterocycle, trifluoroacetic acid (TFA) and levulinic acid methyl ester were added and the mixture was refluxed.<sup>7</sup> Progress of the reaction was monitored by TLC.

Reaction conditions (base/solvent/reaction temperature) tested for the substitution with 1-bromomethyl-1,2-dicarba-*closo*-dodecaborane(12): NEt<sub>3</sub>/CH<sub>2</sub>Cl<sub>2</sub>/room temperature; NaH/THF/reflux; NaH/CH<sub>3</sub>CN/reflux.

Reaction conditions (base/solvent/reaction temperature) tested for the substitution with 1-trifluoromethanesulfonylmethyl-1,2-dicarba-*closo*-dodecaborane(12): NaOAc/CH<sub>3</sub>CN/reflux;<sup>8</sup> NEt<sub>3</sub>/CH<sub>2</sub>Cl<sub>2</sub>/room temperature; NaH/THF/reflux.

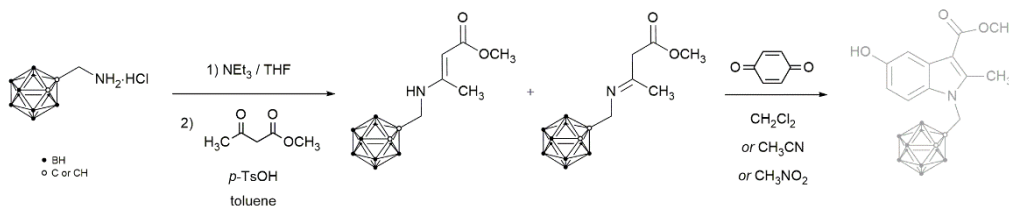
### Nenitzescu indole synthesis

1-Aminomethyl-1,2-dicarba-*closo*-dodecaborane(12) hydrochloride: was synthesised from 1,2-dicarba-*closo*-dodecaborane(12) via 1-(phthalimidomethyl)-1,2-dicarba-*closo*-dodecaborane(12) and deprotection of the latter.



1-(Phthalimidomethyl)-1,2-dicarba-*closo*-dodecaborane(12) (cf.<sup>9</sup>): *n*-BuLi (5.8 mL, 1.32 M in hexane, 7.6 mmol, 1.1 eq.) was added at  $-78\text{ }^{\circ}\text{C}$  to a solution of 1,2-dicarba-*closo*-dodecaborane(12) (1.0 g, 6.9 mmol, 1.0 eq.) in Et<sub>2</sub>O (30 mL) and the solution was stirred for 30 min. A solution of *N*-(bromomethyl)phthalimide (1.8 g, 7.6 mmol, 1.1 eq.) in Et<sub>2</sub>O (70 mL) was added and the reaction mixture was stirred for 1 h at  $-78\text{ }^{\circ}\text{C}$  and overnight at room temperature. Water (50 mL) was added and the aqueous phase was extracted with Et<sub>2</sub>O. The solvent was removed and the product was purified by column chromatography (*n*-hexane/EtOAc 3:1) to yield a white solid (0.38 g, 20%): mp:  $200\text{ }^{\circ}\text{C}$ ; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta = 1.10\text{--}3.10$  (br, 10H, B<sub>10</sub>H<sub>10</sub>), 3.99 (s, 1H, C<sub>cluster</sub>H), 4.38 (s, 2H, CH<sub>2</sub>), 7.81 (dd, <sup>3</sup>J<sub>H,H</sub> = 5.4, <sup>4</sup>J<sub>H,H</sub> = 3.0 Hz, 2H, CH), 7.91 (dd, <sup>3</sup>J<sub>H,H</sub> = 5.4, <sup>4</sup>J<sub>H,H</sub> = 3.0 Hz, 2H, CH) ppm; <sup>11</sup>B{<sup>1</sup>H} (128 MHz, CDCl<sub>3</sub>):  $\delta = -12.6$  (4B),  $-11.3$  (2B),  $-9.7$  (2B),  $-4.8$  (1B),  $-1.0$  (1B) ppm; <sup>13</sup>C{<sup>1</sup>H} (100 MHz, CDCl<sub>3</sub>):  $\delta = 42.5$  (CH<sub>2</sub>), 60.0 (C<sub>cluster</sub>H), 73.1 (C<sub>cluster</sub>), 124.1 (CH), 131.2 (CH), 134.9 (C<sub>q</sub>), 167.1 (CO) ppm.

Deprotection of 1-(phthalimidomethyl)-1,2-dicarba-*closo*-dodecaborane(12): Deprotection was carried out according to reported procedures<sup>10</sup> to yield 1-aminomethyl-1,2-dicarba-*closo*-dodecaborane(12) hydrochloride.

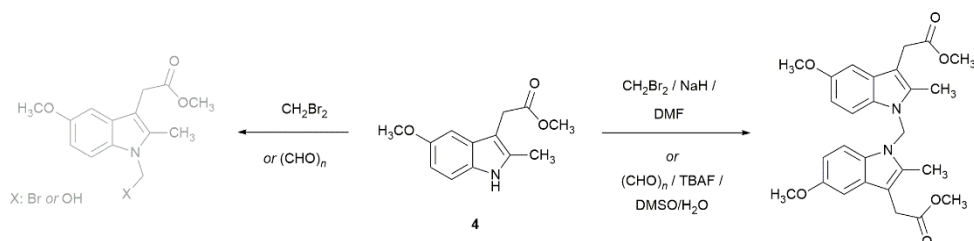


Synthesis of carbaboranyl enamine: 1-Aminomethyl-1,2-dicarba-*closo*-dodecaborane(12) hydrochloride was deprotonated with NEt<sub>3</sub> in THF, filtered and the solvent was removed.<sup>11</sup> The free amine (1 eq.) was then refluxed with methyl acetoacetate (1 eq.) and a catalytic amount of *p*-TsOH in toluene,<sup>12</sup> yielding a mixture of enamine and imine, which could not be completely separated by column chromatography. <sup>11</sup>B{<sup>1</sup>H} (128 MHz, CDCl<sub>3</sub>):  $\delta = -13.1$  (4B),  $-11.7$  (2B),  $-8.9$  (2B),  $-5.1$  (1B), 2.2 (1B); ESI-MS (positive mode, CH<sub>3</sub>OH): *m/z*: 272.3 [M+Na]<sup>+</sup>; the observed isotopic pattern was in agreement with the calculated one.

General procedure for indole synthesis: A solution of carbaboranyl enamine (in CH<sub>2</sub>Cl<sub>2</sub>, CH<sub>3</sub>CN or CH<sub>3</sub>NO<sub>2</sub>) was added dropwise to a solution of *para*-benzoquinone and the reaction mixture was stirred (at room temperature or reflux).<sup>12</sup> The reaction was monitored by TLC.

### Introduction of a methylene group at indole 4

5-Methoxy-2-methyl-1*H*-indole-3-acetic acid methyl ester (4): was synthesised according to the literature.<sup>13</sup>



General procedure for nucleophilic substitution at indole 4 with CH<sub>2</sub>Br<sub>2</sub>: 5-methoxy-2-methyl-1*H*-indole-3-acetic acid methyl ester (4) was dissolved in DMF and deprotonated with NaH at  $0\text{ }^{\circ}\text{C}$ . The deprotonated indole was then added dropwise to a solution of CH<sub>2</sub>Br<sub>2</sub> (excess) and the reaction was stirred for several hours at room temperature. The solvent was removed and purification was carried out by column chromatography, which, however, only yielded the respective methylene-bridged dimer of indole 4.

General procedure for nucleophilic substitution at indole **4** with  $(\text{CHO})_n$  (*cf.*<sup>14</sup>): 5-methoxy-2-methyl-1*H*-indole-3-acetic acid methyl ester (**4**) and paraformaldehyde (excess) were dissolved in DMSO. TBAF (tetrabutylammonium fluoride) and some drops of water were added and the reaction was stirred for 2 h at room temperature. The product was extracted with EtOAc and purification was carried out by column chromatography.

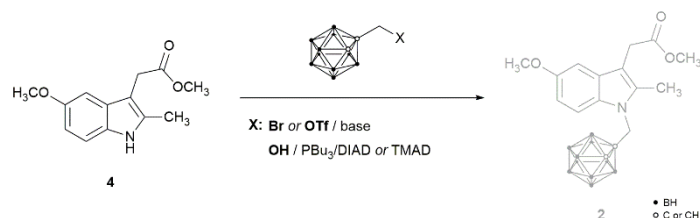
#### Nucleophilic substitution at indole **4**

5-Methoxy-2-methyl-1*H*-indole-3-acetic acid methyl ester (**4**): was synthesised according to the literature.<sup>13</sup>

1-Trifluoromethanesulfonylmethyl-1,2-dicarba-*closo*-dodecaborane(**12**): was synthesised according to the literature.<sup>6</sup>

Bromomethyl-1,2-dicarba-*closo*-dodecaborane(**12**): was synthesised as described above at Fischer indole synthesis.

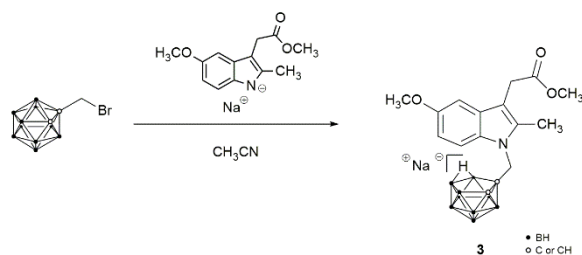
1-Hydroxymethyl-1,2-dicarba-*closo*-dodecaborane(**12**): was synthesised according to the literature.<sup>15</sup>



General procedure for nucleophilic substitution at indole **4**: 5-Methoxy-2-methyl-1*H*-indole-3-acetic acid methyl ester (**4**) was dissolved and deprotonated with a base; then 1-trifluoromethanesulfonylmethyl-1,2-dicarba-*closo*-dodecaborane(**12**) or 1-bromomethyl-1,2-dicarba-*closo*-dodecaborane(**12**) was added and the reaction mixture was either stirred at room temperature or refluxed for several hours.

A variety of bases and solvents was tested:  $\text{K}_2\text{CO}_3$ : THF;<sup>6</sup>  $\text{Cs}_2\text{CO}_3$ : DMF,  $\text{CH}_3\text{CN}$ ; NaOAc:  $\text{CH}_3\text{CN}$ ;<sup>7</sup>  $\text{Na}\{\text{N}(\text{SiMe}_3)_2\}$ : toluene,  $\text{CH}_3\text{CN}$ , THF; NaH: THF, DMF,  $\text{CH}_3\text{CN}$ , 1,4-dioxane; *n*-BuLi: THF.

General procedure for Mitsunobu reaction:<sup>16</sup> The reactions were carried out either using  $\text{PBU}_3/\text{DIAD}$  (diisopropyl azodicarboxylate) in THF or  $\text{PBU}_3/\text{TMAD}$  (tetramethyl azodicarboxamide) in toluene. 1-Hydroxymethyl-1,2-dicarba-*closo*-dodecaborane(**12**) (2 eq.) was added to a solution of 5-methoxy-2-methyl-1*H*-indole-3-acetic acid methyl ester (**4**) (1 eq.) and  $\text{PBU}_3$  (2 eq.). At 0 °C DIAD or TMAD (2 eq.) was added and the reaction mixture was stirred at 40 °C overnight. The reactions were monitored by TLC.



Synthesis of Sodium 7- $\{[5\text{-methoxy-2-methyl-3-(methoxycarbonylmethyl)-1*H*-indolyl] methyl\}$ -7,8-dicarba-*nido*-dodecahydroundecaborate(-1) (**3**): NaH (60% suspension in mineral oil; 0.09 g, 2.2 mmol, 2.6 eq.) was added to a solution of 5-methoxy-2-methyl-1*H*-indole-3-acetic acid methyl ester (**4**) (0.49 g, 2.1 mmol, 2.5 eq.) in  $\text{CH}_3\text{CN}$  (25 mL) at 0 °C. After stirring for 20 min at 0 °C the suspension was added dropwise to a solution of 1-bromomethyl-1,2-dicarba-*closo*-dodecaborane(**12**) (0.20 g, 0.8 mmol, 1.0 eq.) in  $\text{CH}_3\text{CN}$  (15 mL) at 0 °C. After stirring at room temperature overnight the reaction was quenched by addition of water (10 mL). The product was extracted with EtOAc and purified by column chromatography (*n*-hexane/EtOAc 6:1  $\rightarrow$  1:10) yielding an orange oil from which colourless crystals crystallised over several weeks at room temperature. The crystals were washed with  $\text{CH}_2\text{Cl}_2$ , dissolved in  $\text{CH}_3\text{OH}$  and filtered to remove any methyl borates and the product was precipitated with  $\text{CH}_2\text{Cl}_2$  to yield **3** as pale beige solid with moderate water solubility (0.11 g, 34%); mp: 190 °C;  $^1\text{H}$  NMR (400 MHz,  $\text{CD}_3\text{OD}$ ):  $\delta$  = -3.2 to -2.6 (br, 1H, *endo*-H), 0.3–2.5 (br, 9H,  $\text{B}_9\text{H}_9$ ), 1.61 (br s, 1H,  $\text{C}_{\text{cluster}}\text{H}$ ), 2.36 (s, 3H,  $\text{CH}_3$ ), 3.64 (s, 3H,  $\text{COOCH}_3$ ), 3.69 (s, 2H,  $\text{OOC-CH}_2$ ), 3.81 (s, 3H,  $\text{OCH}_3$ ), 4.06 (d,  $^2J_{\text{H,H}} = 16$  Hz, 1H, N- $\text{CH}_2$ ), 4.36 (d,  $^2J_{\text{H,H}} = 16$  Hz, 1H, N- $\text{CH}_2$ ), 6.72 (dd,  $^3J_{\text{H,H}} = 8$  Hz,  $^4J_{\text{H,H}} = 2$  Hz, 1H,  $\text{CH}_{\text{ind}}$ ), 6.92 (d,  $^4J_{\text{H,H}} = 2$  Hz, 1H,  $\text{CH}_{\text{ind}}$ ), 7.22 (d,  $^3J_{\text{H,H}} = 8$  Hz, 1H,  $\text{CH}_{\text{ind}}$ ) ppm;  $^{11}\text{B}$  (128 MHz,  $\text{CD}_3\text{OD}$ ):  $\delta$  = -36.7 (d,  $^1J_{\text{B,H}} = 141$  Hz, 1B), -33.3 (dd,  $^1J_{\text{B,H}} = 129$  Hz, 38 Hz, 1B), -22.8 (d,  $^1J_{\text{B,H}} = 145$  Hz, 1B), -19.2 (d,  $^1J_{\text{B,H}} = 137$  Hz, 1B), -18.7 (d,  $^1J_{\text{B,H}} = 159$  Hz, 1B), -17.6 (d,  $^1J_{\text{B,H}} = 138$  Hz, 1B), -15.0 (d,  $^1J_{\text{B,H}} = 148$  Hz, 1B), -11.1 (d,  $^1J_{\text{B,H}} = 133$  Hz, 1B), -10.5 (d,  $^1J_{\text{B,H}} = 126$  Hz, 1B) ppm;  $^{13}\text{C}\{^1\text{H}\}$  (100 MHz,  $\text{CD}_3\text{OD}$ ):  $\delta$  = 11.0 ( $\text{CH}_3$ ), 31.3 ( $\text{CH}_2$ ), 48.7 ( $\text{C}_{\text{cluster}}\text{H}$ ), 48.9 ( $\text{C}_{\text{cluster}}$ ), 51.8 (N- $\text{CH}_2$ ), 52.3 ( $(\text{CO})\text{OCH}_3$ ), 56.4 ( $\text{OCH}_3$ ), 101.2 ( $\text{CH}_{\text{ind}}$ ), 104.1 ( $\text{C}_{\text{ind}}$ ), 110.9 ( $\text{CH}_{\text{ind}}$ ), 111.6 ( $\text{CH}_{\text{ind}}$ ), 129.1 ( $\text{C}_{\text{ind}}$ ), 133.5 ( $\text{C}_{\text{ind}}$ ), 136.7 ( $\text{C}_{\text{ind}}$ ), 155.1 ( $\text{C}_{\text{ind}}$ ), 174.9 (CO) ppm; IR (KBr):  $\tilde{\nu}$  = 3450 (s), 2963 (m), 2532 (s), 1718 (s), 1620 (m), 1583 (m), 1485 (s), 1460 (m), 1439 (m), 1342 (m), 1262 (m), 1221 (s), 1179 (m), 1156 (m), 1095 (m), 1030 (s), 893 (w), 845 (w), 798 (m), 705 (w), 574 (w), 491 (w), 436 (w)  $\text{cm}^{-1}$ ; HR-ESI-MS (negative mode, DMSO/ $\text{CH}_3\text{OH}$ )  $m/z$  [ $\text{M-Na}$ ]: calcd. for  $\text{C}_{16}\text{H}_{27}\text{B}_9\text{NO}_3$ : 379.2862, found: 379.2870; the observed isotopic pattern was in agreement with the calculated one.

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