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Synthesis and Anti-Cancer Activity of Dinuclear Platinum(II) Complexes Containing Bis(Thioalkyl)dicarba-*closo*-dodecaborane(12) Ligands

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Experimental

General Synthetic and Analytical Methods.

All reactions were performed under an inert atmosphere of dry N_2 utilizing standard Schlenk techniques. All reaction solvents were dried and distilled prior to use. Diethyl ether, dimethoxyethane (DME) and tetrahydrofuran (THF) were dried by distillation from sodium benzophenone ketyl. Toluene and C_6H_6 were pre-dried with anhydrous $CaSO_4$, followed by distillation from sodium. CH_2Cl_2 and *n*-hexane were dried by distillation from CaH_2. *N,N*-dimethylformamide (DMF) was pre-dried with $MgSO_4$ and anhydrous $CuSO_4$, followed by distillation at reduced pressure.

1-D ^{1}H and $^{13}C\{^{1}H\}$ NMR spectra were recorded on a Varian Gemini 2000 NMR Spectrometer or a Bruker DPX300 with Oxford 300 MHz magnet at 298 K, except where otherwise indicated. 200 MHz ^{1}H NMR spectra were recorded on a Varian Gemini 200 instrument. $^{11}B\{^{1}H\}$ and $^{195}Pt\{^{1}H\}$ NMR were recorded on a Bruker DPX400 NMR spectrometer. 2-D NMR spectroscopy experiments were performed on a Varian Unity INOVA 600 MHz NMR instrument. All chemical shifts are reported in ppm, and coupling constants are reported in Hz. ^{1}H and $^{13}C\{^{1}H\}$ NMR chemical shifts are relative to tetramethylsilane (TMS). $^{195}Pt\{^{1}H\}$ and $^{11}B\{^{1}H\}$ NMR chemical shifts were referenced relative to a sealed external standard of 0.1 M $Na_2[PtCl_6]$ in D_2O and $BF_3{\cdot}OEt_2$, respectively (0 ppm).

Melting points (uncorrected) were determined using a Kofler hot-stage apparatus equipped with a Reichert microscope. Elemental Analyses were performed by CMAS (Chemical and Microanalytical Services Pty. Ltd.), Belmont, Victoria (Australia). Electrospray Ionisation

(ESI-MS) mass spectra were obtained by means of a Finnegan LCQ Mass Spectrometer equipped with Finnegan data processing software, using HPLC grade MeOH, or 5% DMF / MeOH.

Thin Layer Chromatography was performed on Merck DC-Alufolien Kieselgel 60 F_{254} sheets. Visualisation of plates was achieved using 254 nm UV light or by staining with either I_2 vapour or a $KMnO_4$ dip solution, followed by heating. Squat and flash Column Chromatography were performed on Merck Kieselgel 60 (230-400 mesh ATSM) silica gel.

Materials and Methods

$[Pt(MeCN)(trpy)](OTf)_2$ was prepared by a modification of the literature procedure.[1] Complex **1**,[2,3] 1,2-bis(bromopropyl)-1,2-carborane,[4] 1,7-bis(bromopropyl)-1,7-carborane,[4] and 1,12-bis(bromopropyl)-1,12-carborane[5] were prepared as described previously. 1,2-, 1,7- and 1,12-carborane were obtained from Katchem (Czech Republic) and used without further purification.

Preparation of Compounds

***μ*-(1,12-Bis(methanethiolato)-1,12-carborane)bis(2,2':6',2"-terpyridine)platinum(II) bis(triflate) (2)**

To a stirred solution of **9** (30 mg, 0.137 mmol) in DMF (5 mL) was added $[Pt(MeCN)(trpy)](OTf)_2$ (155 mg, 0.201 mmol). After stirring for 20 min, triethylamine (0.5 mL, 0.4 mmol) was added, and the solution stirred for 18 h. The precipitate was collected immediately by centrifuging the suspension, yielding orange crystals of **2** (94 mg, 49%), (Found: C, 31.10; H, 2.49; N, 6.05%. $C_{35}H_{36}N_6B_{10}F_6O_6Pt_2S_4$ requires C, 31.15; H, 2.63; N,

6.10); ESI-MS: *m/z* 459.0 ([PtS(trpy)]$^+$); δ_H (300 MHz; d_6-DMSO) 9.00 (dd, 4H, $^4J_{HH}$ = 1.2 Hz, $^3J_{HH}$ = 4.5 Hz, H6, H6"), 8.84 (d, 4H, $^3J_{HH}$ = 8.1 Hz, H3', H5'), 8.67 (d, 4H, $^3J_{HH}$ = 3, H3, H3"), 8.65 (t, 2H, $^3J_{HH}$ = 3, H4'), 8.53 (td, 4H, $^4J_{HH}$ = 1.4 Hz, $^3J_{HH}$ = 7.8 Hz, H4, H4"), 7.99 (td, 4H, $^4J_{HH}$ = 1.5, Hz $^3J_{HH}$ = 5.1 Hz, H5, H5"), 3.17 (s, 4H, $C_{cage}CH_2S$); δ_C (300 MHz; d_6-acetone) 161.1 (C2, C2"), 155.5 (C2', C6'), 154.3 (C6, C6"), 145.3 (C4, C4" + C4'), 129.1 (C5, C5"), 127.2 (C3, C3"), 124.6 (C3', C5'), 57.0 (CH_2SPt), $\mathbf{C}_{cage}$ not observed; δ_B (d_6-DMSO) -13.8 (s, 10B). δ_{Pt} (64.38 MHz; d_6-acetone) –3132.

μ-(1,12-Bis(propanethiolato)-1,12-carborane)-bis(2,2':6',2"-terpyridine)platinum(II) bis(triflate) (3)

To a solution of **7** (15 mg, 51.3 × 10^{-3} mmol) in DMF (2 mL) was added crystalline [Pt(MeCN)(trpy)](OTf)$_2$ (79 mg, 103 × 10^{-3} mmol). The solution immediately turned dark purple and stirring was continued for 12 h. Diethyl ether was then added to precipitate a dark-green solid (45 mg, 61%), (Found: C, 33.17; H, 2.98; N, 5.77%. $C_{40}H_{44}B_{10}F_6N_6O_6Pt_2S_4$ requires C, 33.24; H, 3.07; N, 5.81%); δ_H (600 MHz; d_7-DMF) 9.46 (d, 4H, $^3J_{HH}$ = 5.4 Hz [$^3J_{PtH}$ = 40.0 Hz], H6, H6"), 8.84 (d, 4H, $^3J_{HH}$ = 8.4 Hz, H3', H5'), 8.78 (d, 4H, $^3J_{HH}$ = 7.8 Hz, H3, H3"), 8.73 (t, 2H, $^3J_{HH}$ = 8.4, H4'), 8.61 (td, 4H, $^4J_{HH}$ = 1.2 Hz, $^3J_{HH}$ = 7.8 Hz, H4, H4"), 8.10 (td, 4H, $^4J_{HH}$ = 1.2 Hz, $^3J_{HH}$ = 5.4 Hz, H5, H5"), 2.48 (t, 4H, $^3J_{HH}$ = 6.6 Hz, C$\mathbf{H}_2$S), 1.89 (m, 4H, C$\mathbf{H}_2C_{cage}$), 1.55 (m, 4H, C$\mathbf{H}_2CH_2S$); δ_C (300 MHz; d_7-DMF) 160.1 (C2, C2"), 154.3 (C2', C6'), 153.1 (C6, C6"), 143.0 (C4, C4"), 142.9 (C4'), 129.9 (C5, C5"), 126.6 (C3, C3"), 125.2 (C3', C5'), 80.1 (C_{cage}), 37.2 (CH_2SPt), 35.8 ($CH_2\mathbf{C}H_2CH_2$), 30.2 ($C_{cage}\mathbf{C}H_2$); δ_B (300 MHz; d_7-DMF) -9.3 (s, 10B); δ_{Pt} (64.38 MHz; d_7-DMF) -3206.

μ-(1,7-Bis(propanethiolato)-1,7-carborane)bis(2,2':6',2"-terpyridine)platinum(II) bis(triflate) (4)

To a solution of **11** (9.8 mg, 33.5×10^{-3} mmol) in DMF (2 mL) was added freshly-prepared [Pt(MeCN)(trpy)](OTf)$_2$ (51.4 mg, 67.0×10^{-3} mmol). The solution immediately turned dark purple and stirring was continued for 12 h. Diethyl ether was then added to precipitate **4** as a black solid (44 mg, 87%), (Found: C, 33.26; H, 2.96; N, 5.87%. $C_{40}H_{44}B_{10}F_6N_6O_6Pt_2S_4$ requires C, 33.24; H, 3.07; N, 5.81%); δ_H (600 MHz; d$_7$-DMF) 9.51 (s, 4H, [$^3J_{PtH}$ = 40.6], H6, H6"), 8.84 (s, 4H, H3', H5'), 8.78 (s, 4H, H3, H3"), 8.74 (s, 2H, H4'), 8.62 (t, 4H, $^3J_{HH}$ = 7.2 Hz, H4, H4"), 8.10 (s, 4H, H5, H5"), 2.59 (s, 4H, C**H**$_2$S), 2.20 (s, 4H, C**H**$_2$C$_{cage}$), 1.77 (s, 4H, C**H**$_2$CH$_2$S); δ_C (300 MHz; d$_7$-DMF) 160.0 (C2, C2"), 154.3 (C2', C6'), 153.1 (C6, C6"), 143.2 (C4, C4" + C4'), 129.9 (C5, C5"), 126.7 (C3, C3"), 125.2 (C3', C5'), 77.2 (C$_{cage}$), 36.3 (CH$_2$SPt), 36.0 (CH$_2$**C**H$_2$CH$_2$), 30.9 (C$_{cage}$**C**H$_2$); δ_B (300 MHz; d$_7$-DMF) -7.3 (s, 10B); δ_{Pt} (64.38 MHz; d$_7$-DMF) -3205.

μ-(1,2-Bis(propanethiolato)-1,2-carborane)bis(2,2':6',2"-terpyridine)platinum(II) bis(triflate) (5)

To a solution of **13** (9.6 mg, 32.8×10^{-3} mmol) in DMF (2 mL) was added freshly-prepared [Pt(MeCN)(trpy)](OTf)$_2$ (50.6 mg, 65.9×10^{-3} mmol). The solution immediately turned dark purple and stirring was continued for 12 h. Diethyl ether was then added to precipitate **5** as a purple solid (40 mg, 84%), (Found: C, 33.30; H, 3.10; N, 5.78%. $C_{40}H_{44}B_{10}F_6N_6O_6Pt_2S_4$ requires C, 33.24; H, 3.07; N, 5.81%); δ_H (600 MHz; d$_7$-DMF) 9.34 (dd, 4H, $^3J_{HH}$ = 5.4 Hz,

$^4J_{HH}$ = 1.8 Hz [$^3J_{PtH}$ = 40.6 Hz], H6, H6"), 8.72 (d, 4H, $^3J_{HH}$ = 8.7 Hz, H3', H5'), 8.67 (d, 4H, $^3J_{HH}$ = 8.4 Hz, H3, H3"), 8.58 (t, 2H, $^3J_{HH}$ = 7.5 Hz, H4'), 8.52 (td, 4H, $^4J_{HH}$ = 1.2 Hz, $^3J_{HH}$ = 7.8, H4, H4"), 8.04 (td, 4H , $^4J_{HH}$ = 1.8 Hz, $^3J_{HH}$ = 6.0, H5, H5"), 2.63 (m, 8H, C**H**$_2$S + C**H**$_2$C$_{cage}$), 1.95 (m, 4H, C**H**$_2$CH$_2$S). δ_C NMR (600 MHz; d_7-DMF) 159.8 (C2, C2"), 154.2 (C2', C6'), 152.9 (C6, C6"), 143.0 (C4, C4"), 142.8 (C4'), 129.9 (C5, C5"), 126.6 (C3, C3"), 125.2 (C3', C5'), 81.7 (C$_{cage}$), 34.8 (CH$_2$SPt), the two remaining signals for two carbon atoms of the propyl chain were obscured by DMF peaks; δ_B (300 MHz; d_7-DMF) -1.7 (s, 2B), -6.7 (s, 8B); δ_{Pt} (64.38 MHz; d_7-DMF) -3196.

1,12-Bis[(benzylsulfenyl)propyl]-1,12-carborane (6)

To a solution of NaOEt (3.13 mmol) in dry EtOH (50 mL) was added benzyl mercaptan (481 mg, 3.87 mmol). The solution was stirred at room temperature for 1 h. The solution was then added *via* a canula to a solution of 1,12-bis(bromopropyl)-1,12-carborane (502 mg, 1.30 mmol) in dry EtOH (50 mL). Stirring was continued for 16 h. The reaction mixture was poured onto H_2O (100 mL) and CH_2Cl_2 (100 mL) and the aqueous solution was extracted with another portion of CH_2Cl_2 (100 mL). The combined organic extracts were washed with H_2O (2 × 100 mL), brine (50 mL) and dried over anhydrous $MgSO_4$. The solution was reduced *in vacuo* to afford a crude yellow oil. Purification by flash chromatography on silica (20-33% CH_2Cl_2 in *n*-hexane, R_f = 0.17-0.30) gave **6** as a white solid (590 mg, 96%), mp 65-66 °C; (Found: C, 55.80%; H, 7.71%. $C_{22}H_{36}B_{10}S_2$ requires C, 55.89; H, 7.67%); δ_H (300 MHz; $CDCl_3$) 7.23-7.33 (m, 10H, Ph), 3.63 (s, 4H, SC**H**$_2$Ph), 2.20 (t, 4H, $^3J_{HH}$ = 7.2 Hz, CH$_2$C**H**$_2$S), 1.58-1.67 (m, 4H, C**H**$_2$C$_{cage}$), 1.30-1.41 (m, 4H, C**H**$_2$CH$_2$C$_{cage}$); δ_C (200 MHz;

$CDCl_3$) 138.2 (Ph), 128.8 (Ph), 128.5 (Ph), 127.0 (Ph), 78.7 (C_{cage}), 36.6 (S**C**H_2Ph), 36.2 (**C**H_2C_{cage}), 30.5 (S**C**H_2CH_2), 28.8 (**C**$H_2CH_2C_{cage}$); δ_B (300 MHz; $CDCl_3$) -13.1 (s, 10B).

1,12-Bis(thiopropane)-1,12-carborane (7)

A suspension of freshly sublimed $AlCl_3$ (246 mg, 1.84 mmol) in dry C_6H_6 (50 mL) was stirred at 50 °C for 30 min. **6** (143 mg, 0.302 mmol) was added and stirring was continued at 50 °C for 24 h. The crude reaction mixture was filtered through a pad of silica, followed by a portion of CH_2Cl_2 (100 mL). The filtrate was reduced *in vacuo* to afford a colourless oil. Purification by flash chromatography on silica (2% ethyl acetate in *n*-hexane, R_f = 0.32) gave **7** as a colourless oil (44 mg, 50%), δ_H (200 MHz; $CDCl_3$) 2.34 (dt, 4H, $^3J_{HH}$ = 7.8, 7.0 Hz, C**H**$_2$SH), 1.68-1.74 (m, 4H, C**H**$_2C_{cage}$), 1.42-1.52 (m, 4H, C**H**$_2C_{cage}$), 1.25 (t, 2H, $^3J_{HH}$ = 7.8 Hz, S**H**); δ_C (300MHz; $CDCl_3$) 78.5 (**C**$_{cage}$), 36.3 (C_{cage}**C**H_2), 33.5 (**C**H_2CH_2SH), 23.8 (**C**H_2SH); δ_B ($CDCl_3$) -13.1 (s, 10B); ESI-MS: *m/z* 292 (M^+), 258 ([M-SH_2]$^+$).

1,12-bis(methyldithiolate)-1,12-carborane (8)

To a stirred solution of 1,12-carborane (517 mg, 3.58 mmol) in THF (20 mL) at -10 °C was added ^{n}BuLi (5.32 mL, 1.6 M in hexane, 8.32 mmol) dropwise. The reaction mixture was stirred for 1.5 h before a solution of CuBr (220 mg, 1.53 mmol) and LiBr (275 mg, 3.16 mmol) in THF (20 mL) was slowly added. The yellow solution was stirred for 15 min at -10 °C, and then the temperature reduced to -15 °C and CS_2 (0.5 mL, 8.29 mmol) was added dropwise. The red solution was then allowed to warm to -10 °C. After stirring for 1.5 h, MeI (0.6 mL, 9.63 mmol) was added, the reaction mixture warmed to room temperature and

stirred for a further 1.5 h. After work-up with KCN (639 mg, 9.81 mmol) and water (15 mL), the solution was extracted with diethyl ether (4 × 10 mL). The combined organic layers were washed with brine, dried over Na_2SO_4, and the solvent was removed *in vacuo* to give the crude product as an orange oil. The crude product was purified by flash column chromatography (*n*-hexane, R_f = 0.42) to give **8** as a yellow oil (384 mg, 33%), δ_H (300 MHz; $CDCl_3$) 2.76 (s, 3H, SCH_3); δ_C (300 MHz; $CDCl_3$) 226.4 (C_{cage}**C**SS), 20.1 (S**C**H_3), **C**$_{cage}$ not observed; δ_B (400.2 MHz; $CDCl_3$) -13.7 (s, 10B); ESI-MS: *m/z* 228.7 ($[SCC_2B_{10}H_{10}CS]^+$).

1,12-Bis(thiomethyl)-1,12-carborane (9)

To a stirred solution of **8** (375 mg, 1.56 mmol) in toluene (10 mL) was added a solution of $BH_3{\cdot}SMe_2$ in THF (1.4 mL, 2 M, 2.8 mmol). The resulting solution was refluxed under an inert atmosphere for 4 h, after which time the yellow solution became colourless. When the reaction had cooled to room temperature, an excess of conc. HCl was added (10 mL, 32%) and the solution was stirred at reflux for 20 h. After cooling, the layers were separated and the aqueous layer was extracted with *n*-hexane (3 × 5 mL). The combined organic extracts were washed with brine (3 × 5 mL), and dried over anhydrous Na_2SO_4. The solvent was removed *in vacuo*, and the crude material was purified by flash column chromatography (10% CH_2Cl_2/ *n*-hexane, R_f = 0.43). A colourless solid was obtained (274 mg, 79%), δ_H (300 MHz; $CDCl_3$) 3.12 (d, 4H, $^3J_{HH}$ = 8.0 Hz, C**H**$_2$SH), 1.76 (t, 2H, $^3J_{HH}$ = 7.7 Hz, SH), C_{cage} not observed; δ_C (300 MHz; $CDCl_3$) 33.2 (CH_2), C_{cage} not observed; δ_B (400.2 MHz; $CDCl_3$) -13.8 (s, 10B); ESI-MS: *m/z* 234.9 ($[M-2H]^{2-}$).

1,7-Bis[(benzylsulfenyl)propyl]-1,7-carborane (10)

To a solution of NaOEt (0.74 mmol) in dry EtOH (25 mL) was added benzyl mercaptan (116 mg, 0.93 mmol). The solution was stirred at room temperature for 1 h. The solution was then added *via* a canula to a solution of 1,7-bis(bromopropyl)-1,7-carborane (112 mg, 0.29 mmol) in dry EtOH (10 mL) and stirring was continued for 16 h. The reaction mixture was poured onto H_2O (50 mL) and CH_2Cl_2 (150 mL) and the aqueous solution was extracted with another portion of CH_2Cl_2 (100 mL). The combined organic extracts were washed with H_2O (100 mL), brine (50 mL) and dried over anhydrous $MgSO_4$. The solvent was removed *in vacuo* to afford a crude oil (140 mg). Purification by flash chromatography on silica (20-33% CH_2Cl_2 in *n*-hexane, R_f = 0.17-0.28) gave **10** as a colourless oil (130 mg, 95%), (Found: C, 55.27; H, 6.86%. $C_{22}H_{36}B_{10}S_2$ requires C, 55.89; H, 7.67%); δ_H (300 MHz; $CDCl_3$) 7.24-7.32 (m, 10H, Ph), 3.67 (s, 4H, SC**H**$_2$Ph), 2.31 (t, 4H, $^3J_{HH}$ = 6.9 Hz, $CH_2C\mathbf{H}_2S$), 1.91-1.97 (m, 4H, C**H**$_2C_{cage}$), 1.52-1.60 (m, 4H, C**H**$_2CH_2C_{cage}$); δ_C (200 MHz; $CDCl_3$) 138.2 (Ph), 128.7 (Ph), 128.5 (Ph), 127.0 (Ph), 75.3 (C_{cage}), 36.3 (S**C**H_2Ph), 35.7 ($C_{cage}\mathbf{C}H_2$), 30.5 (**C**H_2S), 29.2 (**C**$H_2CH_2C_{cage}$); δ_B ($CDCl_3$) -7.8 (s, 2B), -11.4 (s, 6B), -14.0 (s, 2B).

1,7-Bis(thiopropane)-1,7-carborane (11)

A suspension of freshly sublimed $AlCl_3$ (368 mg, 2.76 mmol) in dry C_6H_6 (30 mL) was stirred at 50 °C for 30 min. **10** (221 mg, 0.467 mmol) was added to the suspension and stirring was continued for 24 h. The reaction mixture was filtered through a pad of silica, followed by a portion of CH_2Cl_2 (100 mL). The filtrate was reduced *in vacuo* to afford crude

yellow oil. Purification by flash chromatography on silica (0-5% ethyl acetate in *n*-hexane, R_f = 0.14) gave **11** as a yellow oil (50 mg, 37%), δ_H (300 MHz; $CDCl_3$) 2.44 (qu, 4H, $^3J_{HH}$ = 6.9 Hz, C**H**$_2$SH), 2.00-2.06 (m, 4H, C**H**$_2$C$_{cage}$), 1.61-1.71 (m, 4H, C**H**$_2$CH$_2$C$_{cage}$), 1.32 (t, 2H, $^3J_{HH}$ = 8.1 Hz, SH); δ_C (200 MHz; $CDCl_3$) 75.1 (**C**$_{cage}$), 35.5 (C$_{cage}$**C**H$_2$), 33.9 (**C**H$_2$CH$_2$SH), 23.9 (**C**H$_2$SH); δ_B (300 MHz; $CDCl_3$) -7.6 (s, 2B), -11.4 (s, 6B), -13.9 (s, 2B); ESI-MS: *m/z* 292 (M^+), 258 ([M-SH_2]$^+$).

1,2-Bis[(benzylsulfenyl)propyl]-1,2-carborane (12)

To a solution of NaOEt (0.914 mmol) in dry EtOH (40 mL) was added benzyl mercaptan (360 mg, 0.93 mmol). The solution was stirred at room temperature under N_2 atmosphere for 1 h. The solution was then added *via* a canula to a solution of 1,2-bis(bromopropyl)-1,2-carborane (353 mg, 0.29 mmol) in dry EtOH (20 mL). Stirring was continued for 16 h. The reaction mixture was poured onto water (100 mL) and CH_2Cl_2 (100 mL) and the aqueous solution was extracted with another portion of CH_2Cl_2 (100 mL). The combined organic extracts were washed with H_2O (2 × 100 mL), brine (50 mL) and dried over anhydrous $MgSO_4$. The solution was reduced *in vacuo* to afford a crude yellow oil. Purification by flash chromatography on silica (20% CH_2Cl_2 in *n*-hexane, R_f = 0.21) gave **12** as a colourless oil (390 mg, 90%), (Found: C, 55.90; H, 7.71%. $C_{22}H_{36}B_{10}S_2$ requires C, 55.89; H, 7.67%); δ_H (300 MHz; $CDCl_3$) 7.22-7.34 (m, 10H, Ph), 3.68 (s, 4H, SC**H**$_2$Ph), 2.40 (t, 4H, $^3J_{HH}$ = 6.9 Hz, CH$_2$C**H**$_2$S), 2.13-2.19 (m, 4H, C**H**$_2$C$_{cage}$), 1.69-1.77 (m, 4H, C**H**$_2$CH$_2$C$_{cage}$); δ_C (200 MHz; $CDCl_3$) 138.0 (Ph), 128.8 (Ph), 128.6 (Ph), 127.2 (Ph), 79.3 (C$_{cage}$), 36.3 (S**C**H$_2$Ph), 33.7 (**C**H$_2$C$_{cage}$), 30.5 (CH$_2$**C**H$_2$S), 28.8 (**C**H$_2$CH$_2$C$_{cage}$); δ_B (300 MHz; $CDCl_3$) -4.9 (s, 2B), -10.6 (s, 8B).

1,2-Bis(thiopropane)-1,2-carborane (13)

A suspension of freshly sublimed $AlCl_3$ (218 mg, 1.63 mmol) in dry C_6H_6 (30 mL) was stirred at 50 °C for 30 min. **12** (131 mg, 0.277 mmol) was added to the suspension and stirring was continued at 50 °C for 24 h. The reaction mixture was filtered through a pad of silica, followed by a portion of CH_2Cl_2 (100 mL). The filtrate was reduced *in vacuo* to afford a red oil. Purification by flash chromatography on silica (2 mM HCl in 10% ethyl acetate/*n*-hexane, $R_f = 0.15$) gave **13** as a yellow oil (44 mg, 54%), δ_H (300 MHz; $CDCl_3$) 2.56 (dt, 4H, $^3J_{HH}$ = 8.1, 6.6 Hz, C**H**$_2$SH), 2.31-2.36 (m, 4H, C**H**$_2$C$_{cage}$), 1.81-1.91 (m, 4H, C**H**$_2$CH$_2$C$_{cage}$), 1.39 (t, 2H, $^3J_{HH}$ = 7.8 Hz, S**H**); δ_C (200 MHz; $CDCl_3$) 75.1 (**C**$_{cage}$), 33.4 (C$_{cage}$**C**H$_2$), 33.4 (**C**H$_2$CH$_2$SH), 23.9 (**C**H$_2$SH); δ_B (300 MHz; $CDCl_3$) -4.9 (s, 2B), -10.6 (s, 8B). ESI-MS: *m/z* 292 (M^+), 258 ([M-SH_2]$^+$).

***In vitro* Cytotoxicity Studies**

Cytotoxicity studies were conducted at the Peter MacCallum Cancer Institute, Melbourne, Australia. IC_{50} values were determined using a Coulter Counting (CC) assay. Cells were placed into wells of a culture plate. The complexes were dissolved and diluted to a range of concentrations. 5 μL of each drug solution was added to the wells of the plate. Six wells were used as controls: 5 μL vehicle was added to 4 wells (solvent controls) and the remaining two wells represented blank controls. The plate was then incubated at 37 °C in a humidified 5% CO_2, 95% air atmosphere for 48 h after which the cells were diluted and counted using a Sysmex particle counter. The percent cell growth at each drug concentration was determined as the average cell number in the drug treated wells/average cell number of the vehicle control

wells × 100. The results were plotted as percent cell growth against drug concentration. From the dose response curve, the IC_{50} value is defined as the drug concentration that results in a 50% reduction in cell growth.

References

(1) R. Büchner, J. S. Field, R. J. Haines, C. T. Cunningham and D. R. McMillin, *Inorg. Chem*., 1997, **36**, 3952.

(2) J. A. Todd and L. M. Rendina, *Inorg. Chem.,* 2002, **41**, 3331.

(3) J. A. Todd, P. Turner, E. J. Ziolkowski and L. M. Rendina, *Inorg. Chem.*, submitted.

(4) S. L. Woodhouse and L. M. Rendina, *Dalton Trans*., 2004, 3669.

(5) H. Ghaneolhosseini, W. Tjarks and S. Sjöberg, *Tetrahedron*, 1997, **53**, 17519.