[Electronic Supplementary Information]

Synthesis of stable platinum complexes containing carborane in carrier group for potential BNCT agents

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Synthetic methods

3,3’-(3-(1-Methyl-1,2-dicarba-closo-dodecaborane-1-yl)propoxycarbonyl)-2,2’-bipyridine (4)

A solution of dicesium-2,2’-bipyridyl-3,3’-dicarboxylate (2794 mg, 5.50 mmol) and 2 (2594 mg, 11.00 mmol) in 50 ml of dry DMF was heated to 110 °C under an N₂ atmosphere and stirring was continued for 3 days. The white solid precipitate was filtered off by means of a glass frit filter and the reddish yellow solution was reduced completely to dryness under reduced pressure. The residue was extracted with methylene chloride (2 × 30 ml), washed with brine, dried (MgSO₄), and concentrated. The yellow oil was recrystallized from Et₂O to produce the off-white powder 4, which was further washed with Et₂O and hexane, and dried (1653 mg, 47%). ¹H NMR (300 MHz, CDCl₃): δ 8.73 (dd, J = 4.8, 1.5 Hz, 2H), 8.28 (dd, J = 7.9, 1.5 Hz, 2H), 7.46 (dd, J = 7.9, 4.8 Hz, 2H), 4.07 (t, J = 6.2 Hz, 4H), 2.03 (m, 4H), 1.91 (s, 6H), 1.69 (m, 4H). ¹³C{¹H} NMR (75 MHz, CDCl₃): δ 165.6, 158.9, 151.4, 138.0, 125.7, 122.9, 76.8, 74.7, 63.8, 31.6, 28.3, 23.0. ¹¹B{¹H} NMR (96.3 MHz, CHCl₃): δ -4.7 (1B), -6.0 (1B), -10.8 (8B). IR (KBr, cm⁻¹): 2970 w, 2585 vs, 1719 s, 1579 m, 1728 s, 1140 m, 1054 w, 1018 w, 776 w, 731 w.

4,4’-(3-(1-Methyl-1,2-dicarba-closo-dodecaborane-1-yl)propoxycarbonyl)-2,2’-
bipyridine (5)

A solution of dicesium 2,2'-bipyridine-4,4'-dicarboxylate (1746 mg, 3.44 mmol) and 2 (1621 mg, 6.87 mmol) in dry DMF (100 ml) was heated to 110 °C under a nitrogen atmosphere and stirring was continued for 3 days. The white powder that precipitated was filtered off and DMF was removed completely in vacuo. The residue was washed vigorously with water, filtered using a glass frit filter, then washed with EtOH and Et₂O. The crude product was recrystallized from THF/Et₂O to give the pure product 5 (650 mg, 29% yield). \(^1\)H NMR (300 MHz, DMF-d₇, 363 K): \(\delta\) 8.99 (d, \(J = 4.9\) Hz, 2H), 8.95 (d, \(J = 1.5\) Hz, 2H), 8.01 (dd, \(J = 4.9, 1.5\) Hz, 2H), 4.49 (t, \(J = 6.2\) Hz, 4H), 2.67 (m, 4H), 2.23 (s, 6H), 2.13 (m, 4H). \(^{13}\)C\(^{1}\)H NMR (75 MHz, DMF-d₇, 363 K): \(\delta\) 165.3, 156.9, 151.1, 139.5, 123.7, 120.3, 79.7, 77.2, 65.1, 32.1, 29.2, 23.1. \(^{11}\)B\(^{1}\)H NMR (96.3 MHz, DMF, 363K): \(\delta\) -5.4 (1B), -6.5 (1B), -11.1 (8B).

Synthesis of Pt(4)Cl₂ (7)

A solution of Pt(PhCN)₂Cl₂ (472 mg, 1.00 mmol) and the carborane-linked bipyridine 4 (643 mg, 1.00 mmol) in THF (35 ml) was stirred under reflux conditions for 36 h. The reddish brown solution was concentrated to dryness using a rotary evaporator and the remaining solid was re-dissolved in methylene chloride. Slow vapor diffusion of pentane into the yellow solution gave the orange crystals 7, which were filtered off with filter paper and
washed with pentane and Et₂O (640 mg, 70% yield). ¹H NMR (400 MHz, DMF-d7): δ 9.97 (dd, J = 5.7, 1.4 Hz, 2H), 8.87 (dd, J = 7.9, 1.4 Hz, 2H), 8.16 (dd, J = 7.9, 5.7 Hz, 2H), 4.35 (t, J = 6.2 Hz, 4H), 2.45 (m, 4H), 2.10 (s, 6H), 1.97 (m, 4H). ¹³C{¹H} NMR (100 MHz, DMF-d7): δ 164.4, 157.0, 151.4, 141.7, 133.0, 128.7, 79.4, 77.1, 66.5, 31.8, 28.8, 23.0. ¹¹B{¹H} NMR (96.3 MHz, MeNO₂): δ -3.6 (2B), -8.3 (8B). ¹⁹⁵Pt NMR (64.5 MHz, DMF): δ -2199. IR (KBr, cm⁻¹): 3082 w, 2954 w, 2585 vs, 1735 s, 1713 s, 1424 m, 1299 s, 1279 s, 1150 m, 1102 m, 1018 w, 753 m.

**Synthesis of Pt(5)Cl₂ (8)**

A stirred solution of Pt(PhCN)₂Cl₂ (148 mg, 0.31 mmol) and 5 (202 mg, 0.31 mmol) in THF (30 ml) was heated to reflux for 10 h. The color of the reaction mixture changed from yellow to dark yellow. The solvent was removed and the residue was washed vigorously with MeOH, and filtered by means of a glass frit filter. The resulting orange powder was washed further with MeOH and Et₂O (231 mg, 81% yield). Crystals of 8·DMF suitable for X-ray structure determination were obtained by the slow vapor diffusion of Et₂O into the DMF solution of the complex. ¹H NMR (400 MHz, DMF-d7): δ 9.82 (d, J = 6.1 Hz, 2H), 9.15 (d, J = 1.8 Hz, 2H), 8.37 (dd, J = 6.1, 1.8 Hz, 2H), 4.54 (t, J = 6.3 Hz, 4H), 2.69 (m, 4H), 2.24 (s, 6H), 2.15 (m, 4H). ¹³C{¹H} NMR (100 MHz, DMF-d7): δ 163.9, 158.2, 150.3, 141.2, 128.1, 124.8, 79.6, 77.3, 66.0, 31.9, 29.3, 23.2. ¹¹B{¹H} NMR (96.3 MHz, DMF): δ -6.5 (2B), -11.1
Synthesis of Pt(5)(CBDCA) (10)

A solution of Pt(DMSO)$_2$(CBDCA) (171 mg, 0.34 mmol) and 5 (200 mg, 0.31 mmol) in 20 ml of dry THF was stirred under reflux conditions for 12 h. After filtering off the small amount of precipitate by means of a membrane filter, the yellow filtrate was reduced to dryness in vacuo, and then the residue was re-dissolved in MeOH (15 ml). The slow addition of Et$_2$O/hexane (1:1) mixed solvent to the solution of the product afforded the yellow powder 10 (78 mg, 26% yield). $^1$H NMR (300 MHz, DMSO-$d_6$): $\delta$ 9.07 (d, $J$ = 1.6 Hz, 2H), 8.99 (d, $J$ = 5.9 Hz, 2H), 8.27 (dd, $J$ = 5.9, 1.6 Hz, 2H), 4.43 (t, $J$ = 6.2 Hz, 4H), 2.57 (t, $J$ = 7.6 Hz, 4H), 2.53 (m, 4H), 2.13 (s, 6H), 2.03 (m, 4H), 1.67 (quin, $J$ = 7.6 Hz, 2H).

Synthesis of Pt(4)(oxalate) (11)

A reaction mixture consisting of Pt(DMSO)$_2$(oxalate) (71 mg, 0.16 mmol) and 4 (121 mg, 0.19 mmol) in 40 ml of THF was stirred under reflux conditions for 12 h. The resulting yellow solution was reduced to dryness in vacuo and the residue was dissolved in MeOH (15 ml). The slow addition of Et$_2$O/hexane (1:1) to the solution afforded the yellow crystals 11 (84 mg, 58%). $^1$H NMR (300 MHz, DMF-$d_7$): $\delta$ 9.09 (dd, $J$ = 5.5, 1.4 Hz, 2H),
8.92 (dd, $J = 8.0, 1.4$ Hz, 2H), 8.15 (dd, $J = 8.0, 5.5$ Hz, 2H), 4.39 (t, $J = 6.1$ Hz, 4H), 2.50 (m, 4H), 2.11 (s, 6H), 2.01 (m, 4H). $^{11}$B{$^1$H} NMR (96.3 MHz, DMF): $\delta$ -6.7 (2B), -11.3 (8B). $^{195}$Pt NMR (64.5 MHz, DMF): $\delta$ -1950.

Synthesis of Pt(5)Cl4 (13)

To a stirred solution of Na$_2$[PtCl$_6$]·6H$_2$O (105 mg, 0.19 mmol) in MeOH was added *in situ* ligand 5 (100 mg, 0.16 mmol). Stirring was continued under reflux conditions for 1 day. The reaction mixture was reduced to dryness *in vacuo* and the residue was stirred vigorously in MeOH for 1 day. The resulting yellow powder was filtered and washed with MeOH and Et$_2$O. The product 13 was recrystallized from DMF/Et$_2$O (35 mg, 23% yield). $^1$H NMR (300 MHz, DMSO-$d_6$): $\delta$ 9.65 (d, $J = 6.1$ Hz, 2H), 8.98 (d, $J = 1.6$ Hz, 2H), 8.23 (dd, $J = 6.1, 1.6$ Hz, 2H), 4.42 (t, $J = 6.2$ Hz, 4H), 2.54 (m, 4H), 2.13 (s, 6H), 2.01 (m, 4H). $^{13}$C{$^1$H} NMR (75 MHz, DMSO-$d_6$): $\delta$ 163.0, 157.1, 149.5, 140.0, 127.3, 124.1, 78.6, 76.4, 65.1, 30.7, 28.2, 22.5. $^{11}$B{$^1$H} NMR (96.3 MHz, DMSO): $\delta$ -6.5 (2B), -10.9 (8B).

Dicesium 3,3’-(3-(dodecahydro-7-methyl-7,8-dicarba-nido-undecaborate-8-yl)propoxycarbonyl)-2,2’-bipyridine (16)

The same synthesis and work-up procedure as that used for 14 was employed to obtain the off-white powder 16 using 4 and 6 equivalent amounts of CsF. $^1$H NMR (300 MHz,
DMSO-$d_6$: δ 8.67 (dd, $J = 4.9$, 1.7 Hz, 2H), 8.18 (dd, $J = 7.8$, 1.7 Hz, 2H), 7.56 (dd, $J = 7.8$, 4.9 Hz, 2H), 3.87 (m, 4H), 1.37 (m, 4H), 1.19 (m, 4H), 1.17 (s, 6H), -2.83 (v br, 2H). $^{11}$B{$^1$H}

NMR (96.3 MHz, DMSO): δ -9.7 (1B), -10.8 (2B), -18.6 (4B), -34.7 (1B), -37.1 (1B).
NMR characterization

$^1$H NMR spectrum of 3

$^{13}$C NMR spectrum of 3
$^{11}$B NMR spectrum of 3

$^1$H NMR spectrum of 4
$^{13}$C NMR spectrum of 4

$^{11}$B NMR spectrum of 4
$^1$H NMR spectrum of 5

$^{13}$C NMR spectrum of 5
$^{11}$B NMR spectrum of 5 in DMF

$^1$H NMR spectrum of 6
$^{13}$C NMR spectrum of 6

$^{11}$B NMR spectrum of 6
$^{1}H$ NMR spectrum of 7

$^{13}C$ NMR spectrum of 7
$^{11}$B NMR spectrum of 7

$^{195}$Pt NMR spectrum of 7
$^1$H NMR spectrum of 8

$^{13}$C NMR spectrum of 8
Expanded $^{13}$C NMR spectrum of 8

$^{11}$B NMR spectrum of 8
$^{1}H$ NMR spectrum of 9

$^{11}B$ NMR spectrum of 9
$^1$H NMR spectrum of 10

$^1$H NMR spectrum of 11
$^{11}$B NMR spectrum of 11

$^{195}$Pt NMR spectrum of 11
$^{1}H$ NMR spectrum of 12

$^{13}C$ NMR spectrum of 12
$^{11}$B NMR spectrum of 12

$^{195}$Pt NMR spectrum of 12
$^1$H NMR spectrum of 13

$^{11}$B NMR spectrum of 13
$^{13}$C NMR spectrum of 13

$^{1}$H NMR spectrum of 14
$^{13}$C NMR spectrum of 14

Expanded $^{13}$C NMR spectrum of 14
$^{11}$B NMR spectrum of 14

$^{1}$H NMR spectrum of 15
$^{13}$C NMR spectrum of 15

$^{11}$B NMR spectrum of 15
$^1$H NMR spectrum of 16

$^{11}$B NMR spectrum of 16