Electronic Supplementary Information for Dalton Transactions

Electronic Supplementary Information

A template-directed synthetic approach to halogen-bridged mixed-valence platinum complexes on artificial peptides in solution

Kentaro Tanaka,[a,b] Kenji Kaneko,[a] Yusuke Watanabe[a] and Mitsuhiko Shionoya*[a]

[a] *Department of Chemistry, Graduate School of Science, The University of Tokyo, Hongo, Bunkyo-ku, Tokyo 113-0033, Japan.*

Fax: +81 3 5841 8061; Tel: +81 3 5841 8061; E-mail: shionoya@chem.s.u-tokyo.ac.jp

[b] *Department of Chemistry, Graduate School of Science, Nagoya University, Furo-cho, Chikusa-ku, Nagoya 464-8602, Japan.*

Fax: +81 52 789 2940; Tel: +81 52 789 2940; E-mail: kentaro@chem.nagoya-u.ac.jp

Contents

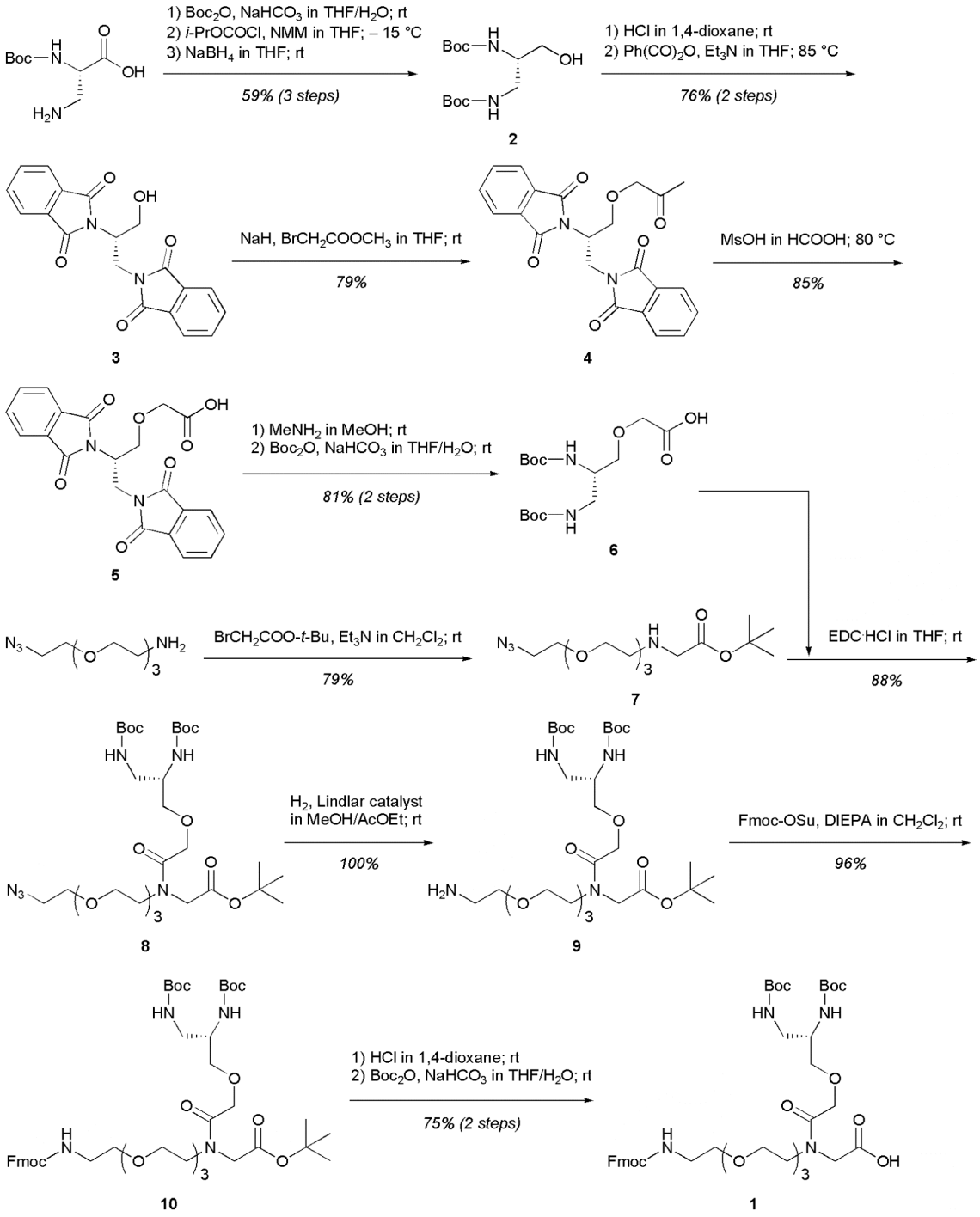
General experimental methods

All reactions were carried out in oven dried glasswares with commercial dehydrated solvents (Wako Pure Chemical Industries). *N*α-*t*-Boc-β-amino-L-alanine,[1] 1-amino-11-azido-3,6,9-trioxaundecane,[2] 1,3-bis-dodecyloxy-propan-2-ol,[3] [Pt(II)Br_2(en)],[4] [Pt(II)$(en)_2$]Br_2[4] and [Pt(IV)$Br_2(en)_2$]Br_2[4] were prepared according to previously published procedures. 0.5 M NH_3/1,4-dioxane was purchased from Sigma-Aldrich. 40% Methylamine/methanol, 4 M HCl/1,4-dioxane, *N*-methyl morpholine and 1-ethyl-3-(3'-dimethylaminopropyl)-carbodiimide·HCl were purchased from Tokyo Chemical Industry. 9-fluorenylmethyloxycarbonyl-*N*-hydroxysuccinimide (Fmoc-OSu), Rink Amide AM-resin and 2-(1H-benzotriazol-1-yl)-1,1,3,3-tetramethylaminium hexafluorophosphate (HBTU) were purchased from Novabiochem. Reverse-phase-high performance liquid chromatography (RP-HPLC) eluents were purchased from Kanto Chemical. All other reagents were purchased from Wako Pure Chemical Industries and were used without further purification. Column chromatography was performed using Wakogel C-300 silica gel (Wako Pure Chemical Industries). Reverse-phase column chromatography was performed using Wakogel 50C18 silica gel (Wako Pure Chemical Industries). Thin-layer chromatography was performed on silica gel 60 F_{254} 1.0554 (Merck). Anion exchange column chromatography was carried out on Amberlite IRA-400 (Organo). ^{1}H, ^{13}C and ^{1}H-^{1}H COSY NMR spectra were recorded on a Bruker DRX 500 (500 MHz ^{1}H; 125.65 MHz ^{13}C) spectrometer. The spectra are referenced to either Me_4Si in acetonitrile-d_3, chloroform-*d*, dichloromethane-d_2 and methanol-d_4 or the signal of the solvent (acetonitrile-d_3; 1.94 ppm). Chemical shifts (δ) are reported in ppm; multiplicities are indicated by: s (singlet), d (doublet), t (triplet), dd (double doublet), dt (double triplet), m (multiplet), br (broad). Coupling constants, *J*, are reported in Hz. Electrospray ionization-time-of-flight (ESI-TOF) mass spectra were recorded on a Micromass LCT spectrometer. RP-HPLC was carried out on a TOSOH instrument equipped with a solvent delivery pump (preparative; CCPP-M, analysis; CCPM-II), an UV-vis absorbance detector (UV-8020) and a temperature controller (CO-8020) with Wakopak Navi C18-5 (preparative; 20 × 250 mm, analysis; 4.6 × 250 mm) columns and eluents specialized in HPLC. Gel permeation chromatography (GPC) was performed on a recycling preparative HPLC (Japan Analytical Industry; LC-928R/U) with an UV-vis absorbance detector (S-3740) with a JAIGEL-2H-40 (40 × 600 mm) column. UV-vis absorption spectra were recorded on a Hitachi U-3500 spectrometer equipped with a Peltier thermoelectric temperature control unit.

Syntheses of the Pt complex-pendant peptides ($[1a\text{-}d(Pt(IV)Br_2(en))_n](RSO_3)_{2n}$ and $[1a\text{-}d(Pt(II)(en))_n](RSO_3)_{2n}$: (n = 2, 3, 9, 10) and mononuclear Pt complexes (R = $(C_{12}H_{25}OCH_2)_2CHO(CH_2)_3$-)

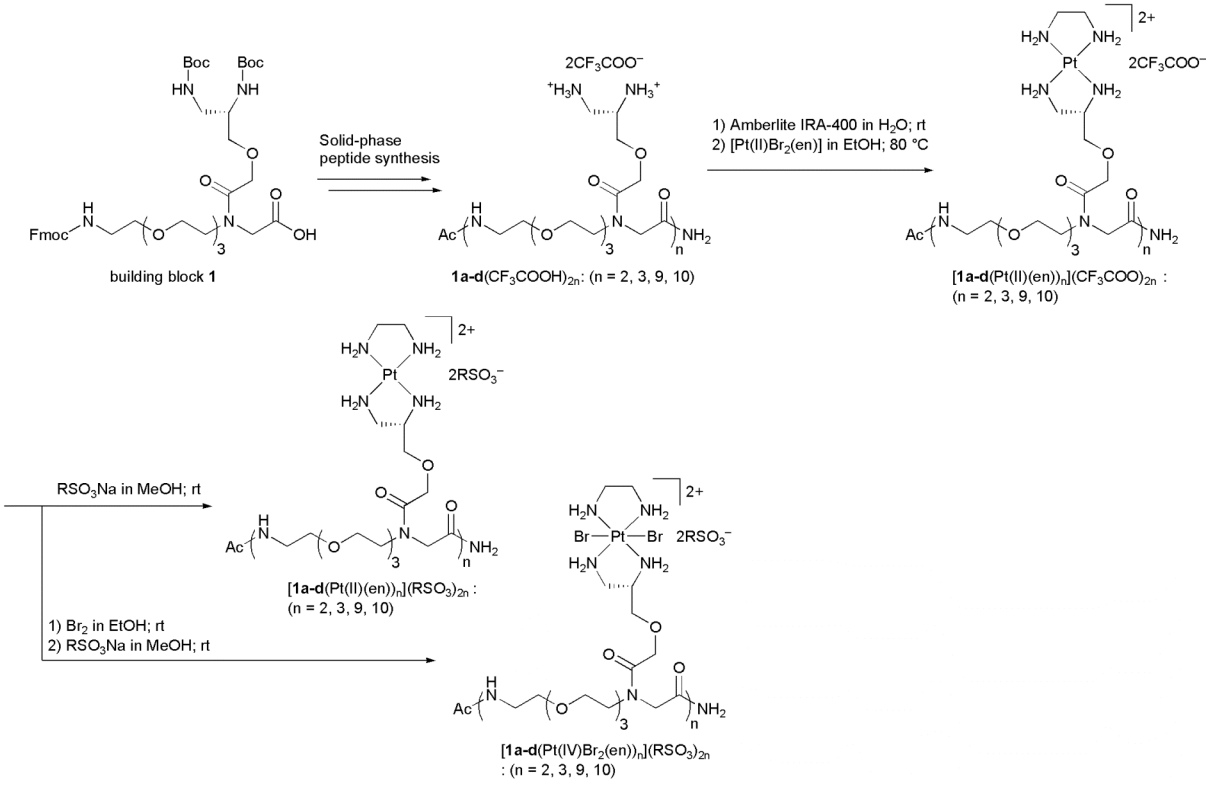
The building block **1** of the template peptides was prepared according to Scheme S1.

Scheme S1 Synthetic route to the building block **1**.



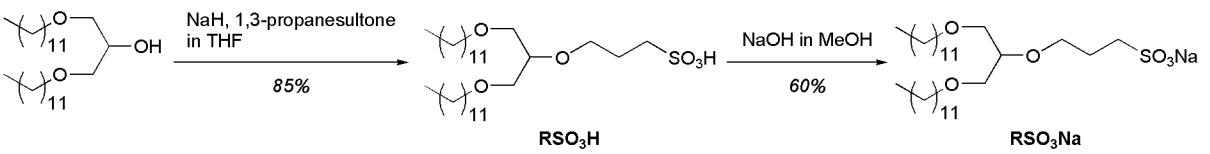
Pt complex-pendant peptides ([**1a-d**(Pt(II)(en))$_n$](RSO$_3$)$_{2n}$ and [**1a-d**(Pt(IV)Br$_2$(en))$_n$](RSO$_3$)$_{2n}$: (n = 2, 3, 9, 10)) were prepared according to Scheme S2.

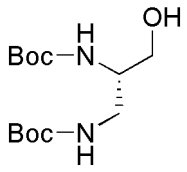
Scheme S2 A synthetic route to Pt complex-pendant peptides ([**1a-d**(Pt(II)(en))$_n$](RSO$_3$)$_{2n}$ and [**1a-d**(Pt(IV)Br$_2$(en))$_n$](RSO$_3$)$_{2n}$).



A sodium dialkylsulfonate, RSO$_3$Na, was synthesized according to Scheme S3.

Scheme S3 Synthesis of RSO$_3$Na.

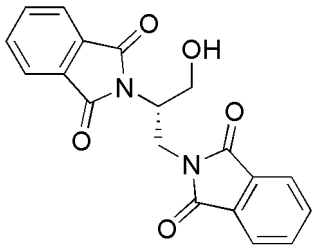




2

Synthesis of (*S*)-*N*,*N*'-di-*t*-Boc-2,3-diaminopropanol 2

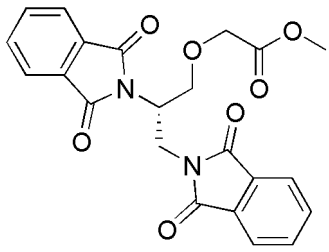
To a solution of *N*α-*t*-Boc-β-amino-L-alanine (6.60 g, 32.3 mmol) and $NaHCO_3$ (2.72 g, 32.3 mmol) in THF/water (1:1, 66 cm^3) was added dropwise a solution of di-*t*-butyl-dicarbonate (Boc_2O, 7.42 cm^3, 32.3 mmol) in THF (50 cm^3) at 0 °C under a nitrogen atmosphere. After stirring for 15 h at room temperature, THF was removed under reduced pressure and dried *in vacuo*. 5% $KHSO_4$ aqueous solution (250 cm^3) was added to the residue, and di-Boc compound was extracted with ethyl acetate (3 × 250 cm^3). The combined organic layer was washed with 5% $KHSO_4$ aqueous solution (100 cm^3) and water (100 cm^3). The organic layer was dried over anhydrous $MgSO_4$ and the solvent was removed under reduced pressure and dried *in vacuo.* To a solution of the residue (10.4 g) in THF (170 cm^3) was added dropwise *N*-methyl morpholine (3.76 cm^3, 34.2 mmol) and isopropyl chloroformate (3.92 cm^3, 34.2 mmol) at -15 °C under a nitrogen atmosphere. After stirring for 15 min at -15 °C, sodium tetrahydroborate (1.94 g, 51.2 mmol) was carefully added to the mixture and stirred for 45 min at room temperature. The reaction was quenched by adding methanol (100 cm^3), and then the solvent was removed under reduced pressure. The residue was dissolved in ethyl acetate (300 cm^3) and washed with 5% $KHSO_4$/brine (3 × 150 cm^3) and water (2 × 100 cm^3). The organic layer was dried over anhydrous $MgSO_4$ and the solvent was removed under reduced pressure and dried *in vacuo*. The crude material was chromatographed on silica gel with CH_2Cl_2/methanol (100:0 - 99:1) to give compound **2** (5.50 g, 59% (3 steps)) as a colorless solid (Found: C, 53.59; H, 9.02; N, 9.50. $C_{13}H_{26}N_2O_5$ requires C, 53.78; H, 9.02; N, 9.65); R_f 0.50 (chloroform/methanol/acetic acid (90:10:1)); δ_H(500 MHz; $CDCl_3$; Me_4Si) 5.14 (d, J = 8.2 Hz, 1H, Boc-N*H*CH-), 5.06 (br, 1H, Boc-N*H*CH_2-), 3.75-3.72 (m, 1H, -OH, D_2O exchangable), 3.69-3.67 (m, 1H, -C*H*HOH), 3.57 (br, 1H, methine), 3.51 (br, 1H, -CH*H*OH), 3.34-3.19 (m, 2H, Boc-NHCH_2-), 1.44 (s, 9H, *t*-Bu), 1.44 (s, 9H, *t*-Bu); δ_C(125 MHz; $CDCl_3$; Me_4Si) 157.9, 155.9, 80.5, 79.8, 61.7, 52.4, 40.3, 28.5, 28.4; *m/z* (ESI-TOF) 313.23 (M + Na^+. $C_{13}H_{26}N_2NaO_5$ requires 313.18).



3

Synthesis of (*S*)-2,3-bis(phthalimido)propanol 3

A solution of compound **2** (5.00 g, 17.2 mmol) in 4 M HCl/1,4-dioxane (25 cm^3, 100 mmol) was stirred for 11 h at room temperature. After the solvent was evaporated, the residue was dissolved in THF (60 cm^3) and then triethylamine (3.48 cm^3, 34.4 mmol) and phthalic anhydride (5.10 g, 34.4 mmol) were added to the solution. The reaction mixture was stirred for 3 h at room temperature, and then heated at reflux for 10 h at 80 °C. The solvent was removed under reduced pressure and 5% $KHSO_4$ aqueous solution (100 cm^3) was added to the residue, which was extracted with ethyl acetate (3 × 100 cm^3) and the combined organic layer was dried over anhydrous $MgSO_4$ and the solvent was removed under reduced pressure. The crude solid was washed with cooled ethanol to afford compound **3** (3.85 g) as a colorless solid. The resulting filtrate was recrystallized with ethanol (30 cm^3) to afford compound **3** (0.74 g) as colorless needles (4.59 g, 76% in total (2 steps)) (Found: C, 64.80; H, 4.31; N, 7.79. $C_{19}H_{14}N_2O_5$ requires C, 65.14; H, 4.03; N, 8.00); R_f 0.80 (*n*-butanol/pyridine/acetic acid/water (4:1:1:2)); δ_H(500 MHz; $CDCl_3$; Me_4Si) 7.82-7.67 (m, 8H, 2 × phthalimide), 4.68-4.63 (m, 1H, methine), 4.34 (dd, J = 14.6, 8.5 Hz, 1H, -NCH*H*CH-), 4.14 (dd, J = 7.0, 5.3 Hz, 2H, -CH_2OH), 4.09 (dd, J = 14.6, 3.5 Hz, 1H, -NC*H*HCH-), 3.44 (t, J = 7.0 Hz, 1H, -OH, D_2O exchangeable); δ_C(125 MHz; $CDCl_3$; Me_4Si) 169.1, 168.5, 134.4, 134.3, 131.9, 131.7, 123.6, 123.6, 61.8, 52.8, 37.3; *m*/*z* (ESI-TOF) 373.10 ($M + Na^+$. $C_{19}H_{14}N_2NaO_5$ requires 373.08).

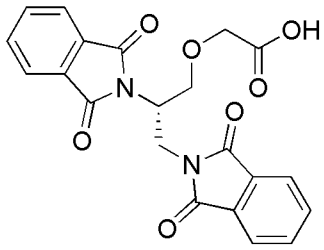


4

Synthesis of methyl (*S*)-5,6-bis(phthalimido)-3-oxahexanoate 4

To a solution of compound **3** (767 mg, 2.19 mmol) in THF (10 cm^3) was added sodium hydride (in oil (60%), 350 mg, 8.75 mmol) at room temperature. After stirring for 5 min at room temperature, methyl

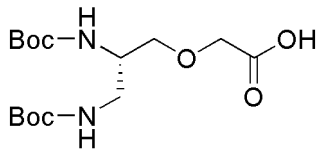
bromoacetate (0.83 cm^3, 8.75 mmol) was added and then stirred for 48 h at room temperature. The mixture was poured into 10 cm^3 of ice water and 5% $KHSO_4$/brine (50 cm^3) was added, which was extracted with ethyl acetate (3 × 50 cm^3). The combined organic layer was dried over anhydrous $MgSO_4$ and the solvent was removed under reduced pressure. The crude material was purified by silica gel column chromatography with *n*-hexane/ethyl acetate (3:1) to obtain compound **4** (735 mg, 79%) as a colorless syrup; R_f 0.74 (chloroform/methanol/acetic acid (90:10:1)); δ_H(500 MHz; $CDCl_3$; Me_4Si) 7.82-7.67 (m, 8H, 2 × phthalimide), 4.80-4.75 (m, 1H, methine), 4.31 (dd, J = 14.3, 8.4 Hz, 1H, -NC*H*HCH-), 4.18 (dd, J = 14.3, 8.4 Hz, 1H, -CHC*H*HO-), , 4.13 (dd, J = 10.2, 6.0 Hz, 1H, -CHCH*H*O-), 4.13 (s, 2H, -OCH_2CO-), 4.12 (dd, J = 14.3, 4.0 Hz, 1H, -NCH*H*CH-), 3.69 (s, 3H, methyl); δ_C(125 MHz; $CDCl_3$; Me_4Si) 173.4, 168.5, 168.3, 134.3, 134.3, 131.8, 131.8, 123.6, 123.6, 69.2, 68.0, 50.5, 37.2, 31.1; *m/z* (ESI-TOF) 445.18 ($M + Na^+$. $C_{22}H_{18}N_2NaO_6$ requires 445.10).



5

Synthesis of (*S*)-5,6-bis(phthalimido)-3-oxahexanoic acid 5

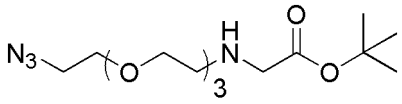
To a solution of compound **4** (1.05 g, 2.49 mmol) in formic acid (25 cm^3) was added methane sulfonic acid (0.16 cm^3, 2.49 mmol) at room temperature. After stirring for 16 h at 80 °C, the mixture was poured into 150 cm^3 of water, and then **5** was extracted with chloroform (3 × 150 cm^3). The combined organic layer was washed with brine (100 cm^3) and dried over anhydrous $MgSO_4$ and the solvent was removed under reduced pressure. The crude material was purified by silica gel column chromatography with chloroform/methanol (99:1) to afford compound **5** (0.86 g, 85%) as a colorless syrup; R_f 0.45 (chloroform/methanol/acetic acid (90:10:1)); δ_H(500 MHz; $CDCl_3$; Me_4Si) 7.82-7.69 (m, 8H, 2 × phthalimide), 4.79-4.74 (m, 1H, methine), 4.33 (dd, J = 14.3, 8.0 Hz, 1H, -NC*H*HCH-), 4.20-4.11 (m, 5H, -NCH*H*CH-, -CHCH_2O-, -OCH_2CO-); δ_C(125 MHz; $CDCl_3$; Me_4Si) 174.1, 168.5, 168.3, 134.3, 134.3, 131.8, 131.8, 123.6, 123.6 69.2, 67.9, 50.5, 37.2; *m/z* (ESI-TOF) 431.16 ($M + Na^+$. $C_{21}H_{16}N_2NaO_7$ requires 431.09).



6

Synthesis of (*S*)-*N,N'*-di-*t*-Boc-5,6-diamino-3-oxahexanoic acid 6

Compound **5** (850 mg, 2.08 mmol) was dissolved in 40% methylamine/methanol (10 cm^3, 253 mmol) and stirred for 8 h at room temperature. After removal of the solvent and dried *in vacuo*, the residue was dissolved in water (100 cm^3) and washed with chloroform/THF (4:1, 8 × 100 cm^3). The solvent of the aqueous layer was removed under reduced pressure and dried *in vacuo*. To a solution of the crude material (362 mg) in THF/water (1:1, 10 cm^3) was added $NaHCO_3$ (350 mg, 4.16 mmol) and Boc_2O (1.00 cm^3, 4.16 mmol). After stirring for 11 h at room temperature, THF was removed under reduced pressure, and then 5% $KHSO_4$ aqueous solution (30 cm^3) was added, which was extracted with ethyl acetate (3 × 40 cm^3). The combined organic layer was dried over anhydrous $MgSO_4$ and the solvent was removed under reduced pressure. The crude material was purified by silica gel column chromatography with chloroform/methanol (100:0 - 99:1) to obtain compound **6** (584 mg, 81% (2 steps)) as a colorless syrup; R_f 0.72 (*n*-butanol/pyridine/acetic acid/water (4:1:1:2)); δ_H(500 MHz; $CDCl_3$; Me_4Si) 5.35-5.20 (m, 2H, Boc-N*H*CH-, Boc-N*H*CH_2-), 4.18-4.05 (m, 2H, -OCH_2CO-), 3.81 (br, 1H, methine), 3.67-3.65 (m, 1H, -CHC*H*HO-), 3.55-3.52 (m, 1H, -CHCH*H*O-), 3.41-3.32 (m, 2H, Boc-NHC*H*$_2$-), 1.44 (m, 18H, 2 × Boc); δ_C(125 MHz; $CDCl_3$; Me_4Si) 172.9, 157.0, 156.1, 80.0, 79.8, 71.4, 68.3, 50.7, 41.6, 28.4; *m/z* (ESI-TOF) 371.19 (M + Na^+. $C_{15}H_{28}N_2NaO_7$ requires 371.18).

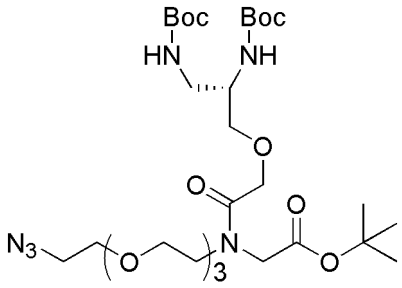


7

Synthesis of *N*-(11-azido-3,6,9-trioxaundecyl)glycine *t*-butyl ester 7

To a solution of 1-amino-11-azido-3,6,9-trioxaundecane (19.5 g, 89.3 mmol) and triethylamine (24.8 cm^3, 179 mmol) in CH_2Cl_2 (200 cm^3) was added dropwise within 1 h a solution of *t*-butyl bromoacetate (13.1 cm^3, 89.3 mmol) in CH_2Cl_2 (300 cm^3) at 0 °C with a dropping funnel under a nitrogen atmosphere. After stirring for 17 h at room temperature, the mixture was washed with brine (3 × 500 cm^3). The organic layer was dried over anhydrous Na_2SO_4 and the solvent was removed under reduced pressure and dried *in vacuo*. The crude material (31.2 g) was purified by silica gel column chromatography with chloroform/methanol (50:1 - 20:1) to obtain compound **7** (23.5 g, 79%) as a yellow-brown solution; R_f 0.61 (*n*-butanol/pyridine/water (4:1:2)); δ_H(500 MHz; $CDCl_3$; Me_4Si)

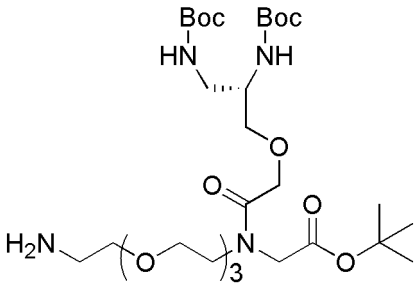
3.70-3.63 (m, 10H, $N_3CH_2CH_2O$-, -$OCH_2CH_2OCH_2CH_2O$-), 3.59 (t, J = 5.6 Hz, 2H, -$NHCH_2CH_2$-), 3.40 (t, J = 5.1 Hz, 2H, N_3CH_2-), 3.33 (m, 2H, -$NHCH_2CO$-), 2.80 (t, J = 5.6 Hz, 2H, -$NHCH_2CH_2$-), 1.47 (s, 9H, *t*-Bu); δ_C(125 MHz; $CDCl_3$; Me_4Si) 171.5, 81.0, 70.7, 70.7, 70.6, 70.6, 70.3, 70.0, 51.7, 51.7, 50.6, 48.7.



8

Synthesis of *N*-[(*S*)-*N*,*N*'-di-*t*-Boc-2,3-diaminopropoxy]acetyl-*N*-(11-azido-3,6,9-trioxaundecyl)glycine *t*-butyl ester 8

To a solution of compound **7** (7.36 g, 22.1 mmol) and compound **6** (7.71 g, 22.1 mmol) in THF (50 cm^3) was added 1-ethyl-3-(3'-dimethylaminopropyl)-carbodiimide·HCl (8.49 g, 44.3 mmol) at 0 °C under a nitrogen atmosphere. After stirring for 12 h at room temperature, THF was removed under reduced pressure and ethyl acetate (600 cm^3) was added. The mixture was washed with 1% $NaHCO_3$ aqueous solution (600 cm^3) and brine (2 × 600 cm^3). The organic layer was dried over anhydrous Na_2SO_4 and the solvent was removed under reduced pressure and dried *in vacuo*. The crude material (15.6 g) was purified by silica gel column chromatography with *n*-hexane/ethyl acetate (1:2) to obtain compound **8** (12.9 g, 88%) as a pale yellow syrup; R_f 0.67 (chloroform/methanol (9:1)); δ_H(500 MHz; CD_3CN) 5.83-5.75 (br, 2H, 2 × Boc-N*H*-), 4.33-3.92 (m, 4H, -OCH_2CO-, -NCH_2CO-), 3.64-3.36 (m, 19H, -C*H*NH-, -OCH_2CH_2N-, -$OCH_2CH_2OCH_2CH_2O$-, $N_3CH_2CH_2O$-, -OCH_2CH-), 3.20-3.16 (m, 2H, Boc-$NHCH_2$-), 1.47-1.41 (m, 27H, *t*-Bu, 2 × Boc); *m/z* (ESI-TOF) 685.30 ($M + Na^+$. $C_{29}H_{54}N_6NaO_{11}$ requires 685.37).

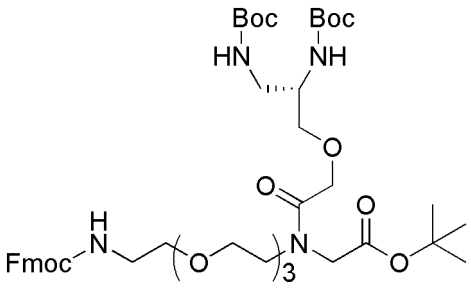


9

Synthesis of

***N*-[(*S*)-*N*,*N*'-di-*t*-Boc-2,3-diaminopropoxy]acetyl-*N*-(11-amino-3,6,9-trioxaundecyl)glycine *t*-butyl ester 9**

To a solution of compound **8** (12.9 g, 19.6 mmol) in methanol/ethyl acetate (1:1, 100 cm^3) was added a suspension of Lindlar catalyst (5% Pd, 1.21 g, 0.57 mmol as Pd) in methanol/ethyl acetate (1:1, 100 cm^3) at room temperature. After stirring for 4 h at room temperature under a hydrogen atmosphere, the catalyst was filtered off. The solvent of the filtrate was removed under reduced pressure and dried *in vacuo*. The crude material was purified by silica gel column chromatography with chloroform/methanol/triethylamine (99.9:0:0.1 - 89.9:10:0.1) to give compound **9** (12.4 g, 100%) as a colorless syrup; R_f 0.15 (chloroform/methanol (9:1)); δ_H(500 MHz; CD_3CN) 5.98-5.80 (m, 2H, 2 × Boc-N*H*-), 4.33-3.96 (m, 4H, -OCH_2CO-, -NCH_2CO-), 3.65 (br, 1H, -C*H*NH-), 3.57-3.40 (m, 16H, -OCH_2CH_2N-, -$OCH_2CH_2OCH_2CH_2O$-, $H_2NCH_2CH_2O$-, -OCH_2CH-), 3.20-3.17 (m, 2H, Boc-NHCH_2-), 2.73-2.71 (m, 2H, H_2NCH_2-), 1.47-1.41 (m, 27H, *t*-Bu, 2 × Boc); *m/z* (ESI-TOF) 659.48 ($M + Na^+$. $C_{29}H_{56}N_4NaO_{11}$ requires 659.38).

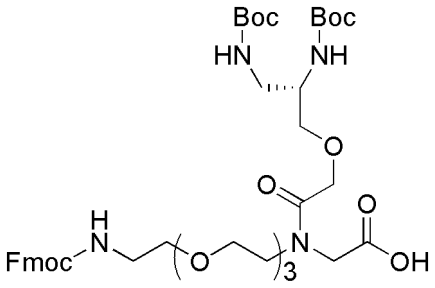


10

Synthesis of

***N*-[(*S*)-*N*,*N*'-di-*t*-Boc-2,3-diaminopropoxy]acetyl-*N*-(*N*-Fmoc-11-amino-3,6,9-trioxaundecyl) glycine *t*-butyl ester 10**

To a solution of compound **9** (162 mg, 0.25 mmol) and *N*,*N*-diisopropylethylamine (DIPEA, 43.4 mm^3, 0.25 mmol) in CH_2Cl_2 (3.0 cm^3) was added Fmoc-OSu (85.6 mg, 0.25 mmol) at 0 °C under a nitrogen atmosphere. After stirring for 50 min at room temperature, ethyl acetate (50 cm^3) was added into the mixture, and then the organic layer was washed with brine (3 × 50 cm^3). The organic layer was dried over anhydrous Na_2SO_4, and the solvent was removed under reduced pressure and dried *in vacuo*. The crude material (217 mg) was purified by silica gel column chromatography with *n*-hexane/ethyl acetate (2:3 - 1:2) to obtain compound **10** (210 mg, 96%) as a colorless syrup; R_f 0.75 (chloroform/methanol/triethylamine (9:1:1)); δ_H(500 MHz; CD_3CN) 7.84 (d, J = 7.5 Hz, 2H, 4,5-fluoren), 7.67 (d, J = 7.4 Hz, 2H, 1,8-fluoren), 7.43 (dd, J = 7.4, 7.4 Hz, 2H, 3,6-fluoren), 7.35 (dd, J = 7.4, 7.4 Hz, 2H, 2,7-fluoren), 5.84-5.74 (br, 3H, Fmoc-N*H*-, 2 × Boc-N*H*-), 4.37-4.35 (m, 2H, fluoren-CH_2), 4.31-3.94 (m, 5H, 9-fluoren, -OCH_2CO-, -NCH_2CO-), 3.65 (1H, br, -C*H*NH-), 3.55-3.37 (m, 16H, -OCH_2CH_2N-, -$OCH_2CH_2OCH_2CH_2O$-, -$NHCH_2CH_2O$-, -OCH_2CH-), 3.25 (dt, J = 5.5, 5.6 Hz, 2H, Fmoc-NHCH_2-), 3.18 (dd, J = 6.2, 6.5 Hz, 2H, Boc-NHCH_2-), 1.45-1.39 (m, 27H, *t*-Bu, 2 × Boc); *m/z* (ESI-TOF) 881.52 ($M + Na^+$. $C_{44}H_{66}N_4NaO_{13}$ requires 881.45).



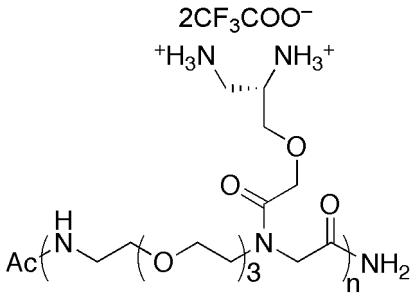
1

Synthesis of

***N*-[(*S*)-*N*,*N*'-di-*t*-Boc-2,3-diaminopropoxy]acetyl-*N*-(*N*-Fmoc-11-amino-3,6,9-trioxaundecyl) glycine 1**

A solution of compound **10** (10.3 g, 12.0 mmol) in 4 M HCl/1,4-dioxane (100 cm^3, 400 mmol) was stirred for 3 h at room temperature. The solvent was removed under reduced pressure and dried *in vacuo*. To a solution of the residue in THF/water (1:1, 200 cm^3) was added $NaHCO_3$ (3.02 g, 35.9 mmol) and Boc_2O (5.23 g, 24.0 mmol) at 0 °C. After stirring for 12 h at room temperature, 5% $KHSO_4$/brine (500 cm^3) was added to the solution and compound **1** was extracted with ethyl acetate (500 cm^3). The organic layer was washed with brine (3 × 500 cm^3) and dried over anhydrous Na_2SO_4, and then the solvent was removed under reduced pressure and dried *in vacuo*. The crude material was purified by silica gel column with chloroform/methanol (100:0 - 50:1), GPC with chloroform and silica gel column chromatography with CH_2Cl_2/methanol (100:1) to obtain compound **1** (7.24 g, 75%) as a colorless syrup (Found: C, 58.59; H, 7.48; N, 6.71. $C_{40}H_{58}N_4O_{13}\cdot H_2O$ requires C, 58.52; H, 7.37;

N, 6.82); R_f 0.59 (chloroform/methanol (3:1)); δ_H(500 MHz; CD_3CN; Me_4Si) 7.84 (d, J = 7.5 Hz, 2H, 4,5-fluoren), 7.67 (d, J = 7.3 Hz, 2H, 1,8-fluoren), 7.43 (dd, J = 7.5, 7.5 Hz, 2H, 3,6-fluoren), 7.35 (dd, J = 7.4, 7.4 Hz, 2H, 2,7-fluoren), 5.90-5.73 (m, 3H, Fmoc-N*H*-, 2 × Boc-N*H*-), 4.36 (m, 2H, fluoren-CH_2), 4.30-4.04 (m, 5H, 9-fluoren, -OCH_2CO-, -NCH_2CO-), 3.64 (br, 1H, -C*H*NH-), 3.57-3.41 (m, 16H, -OCH_2CH_2N-, -$OCH_2CH_2OCH_2CH_2O$-, -$NHCH_2CH_2O$-, -OCH_2CH-), 3.28-3.24 (m, 2H, Fmoc-NHCH_2-), 3.18-3.14 (m, 2H, Boc-NHCH_2-), 1.40 (m, 18H, 2 × Boc); *m/z* (ESI-TOF) 825.46 ($M + Na^+$. $C_{40}H_{58}N_4NaO_{13}$ requires 825.39).



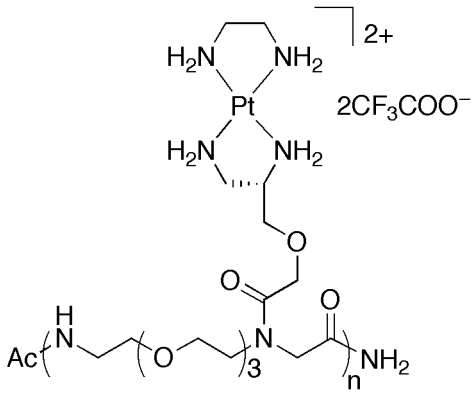
1a-d$(CF_3COOH)_{2n}$: (n = 2, 3, 9, 10)

Synthesis of peptide trifluoroacetate salts 1a-d$(CF_3COOH)_{2n}$: (n = 2, 3, 9, 10)

Peptide trifluoroacetate salts (**1a-d**$(CF_3COOH)_{2n}$: (n = 2, 3, 9, 10)) were manually synthesized using standard solid phase methods in Fmoc chemistry with HBTU/hydroxybenzotriazole (HOBt)/DIPEA activation methods. A polypropylene tube equipped with a polypropylene filter and a luer-lock cap was used as a reaction vessel. Rink Amide AM-resin (0.71 mmol/g) was used to synthesize peptide amides. The resin was swollen in DMF (5 cm^3) for 30 min and Fmoc-deprotected with 20% piperidine in DMF (5 cm^3) twice for 30 min. The resin was filtered and washed with DMF (4 × 5 cm^3), CH_2Cl_2 (3 × 5 cm^3) and DMF (5 × 5 cm^3). The building block **1** (2 equiv) was combined with the resin twice, along with HBTU (2 equiv), HOBt (2 equiv) and DIPEA (4 equiv). The mixture was shaken for 2 h at room temperature, after which the resin was filtered and washed with DMF (3 × 5 cm^3), CH_2Cl_2 (3 × 5 cm^3), methanol (3 × 5 cm^3), CH_2Cl_2 (3 × 5 cm^3) and DMF (3 × 5 cm^3). The deprotection/coupling cycles were repeated in total twice, three, nine and ten times for **1a-d**$(CF_3COOH)_{2n}$, respectively. After removal of the final Fmoc protecting group with 30-min treatment with 20% piperidine in DMF (5 cm^3) twice, the *N*-teminal of the resin-bound peptides were acetylated with Ac_2O (3 equiv) and DIPEA (6 equiv) in DMF (5 cm^3) by shaking for 2 h at room temperature. Then the resin was filtered and washed with DMF (3 × 5 cm^3), CH_2Cl_2 (3 × 5 cm^3), methanol (3 × 5 cm^3) and CH_2Cl_2 (3 × 5 cm^3) and finally dried *in vacuo*. Cleavage from the resin and deprotection of the Boc groups were carried out in standard cleavage cocktail (TFA/triisopropylsilane/water (95:2.5:2.5), 5 cm^3) for 4 h at room temperature. The resin was filtered off and the resulting filtrate was poured into cold diethyl ether (50

cm^3). The formed precipitation was isolated by centrifugation (3000 rpm) for 5 min and decantation and dried *in vacuo*. The crude peptides were purified by preparative RP-HPLC to give **1a-d**$(CF_3COOH)_{2n}$ (**1a**; 81%, **1b**; 65%, **1c**; 61%, **1d**; 40%) as colorless syrup; δ_H(500 MHz; CD_3OD; Me_4Si) for **1a** 4.64-4.10 (m, 8H, 2 × -OCH_2CO-, 2 × -NCH_2CO-), 3.88-3.81 (m, 4H), 3.78-3.76 (m, 2H), 3.69-3.52 (m, 26H), 3.51-3.47 (m, 2H), 3.44-3.34 (m, 8H), 1.95 (m, 3H, Ac), for **1b** 4.64-4.10 (m, 12H, 3 × -OCH_2CO-, 3 × -NCH_2CO-), 3.88-3.84 (m, 6H), 3.78-3.76 (m, 3H), 3.68-3.47 (m, 42H), 3.43-3.34 (m, 12H), 1.95 (m, 3H, Ac), for **1c** 4.63-4.09 (m, 36H, 9 × -OCH_2CO-, 9 × -NCH_2CO-), 3.85 (m, 16H), 3.76 (m, 10H), 3.68-3.53 (m, 114H), 3.51-3.47 (m, 13H), 3.42-3.35 (m, 36H), 1.95 (m, 3H, Ac), for **1d** 4.64-4.09 (m, 40H, 10 × -OCH_2CO-, 10 × -NCH_2CO-), 3.88-3.85 (m, 18H), 3.78 (m, 11H), 3.62-3.53 (m, 124H), 3.49-3.47 (m, 15H), 3.42-3.38 (m, 42H), 1.99-1.93 (m, 3H, Ac); *m/z* (ESI-TOF) for **1a** 806.46 (M + Na^+. $C_{40}H_{69}F_{12}N_9NaO_{21}$ requires 806.46), for **1c** 416.02 (M - $18CF_3COO^-$ - $10H^+$. $C_{137}H_{275}N_{37}O_{55}$ requires 416.01), for **1d** 737.45 (M - $20CF_3COO^-$ - $15H^+$. $C_{152}H_{305}N_{41}O_{61}$ requires 737.45).

Preparative RP-HPLC was performed at room temperature with buffer *A* 0.1vol% TFA in water, buffer *B* 0.1 vol% TFA in acetonitrile, a flow of 10 cm^3/min, wavelength at 210 nm and a linear gradient from 0-80 vol% B (0-150 min). For analysis of **1a-d**$(CF_3COOH)_{2n}$ to check their purity, analytical RP-HPLC was performed under the following condition: 30 °C, a linear gradient from 0-80 vol% B (0-150 min), buffer *A* 0.1 vol% TFA in water, buffer *B* 0.1 vol% TFA in acetonitrile, a flow of 0.7 cm^3/min and UV detection at 210 nm. The retention time (t_R) for **1a-d**$(CF_3COOH)_{2n}$ were 27.5, 30.6, 35.8 and 36.2 min, respectively.

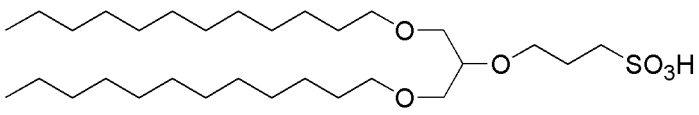


[**1a-d**((Pt(II)(en))$_n$](CF$_3$COO)$_{2n}$

Synthesis of Pt(II) complex-bearing peptides [1a-d(Pt(II)(en))$_n$](CF$_3$COO)$_{2n}$: (n = 2, 3, 9, 10)

1a-d$(CF_3COOH)_{2n}$: (n = 2, 3, 9, 10) were neutralized by anion exchange column chromatography with water to give TFA-free peptides **1a-d** as a colorless syrup. To a solution of **1a-d** in ethanol was added [Pt(II)Br_2(en)] (1.1n equiv) at room temperature. The suspension was heated at reflux for 12 h at

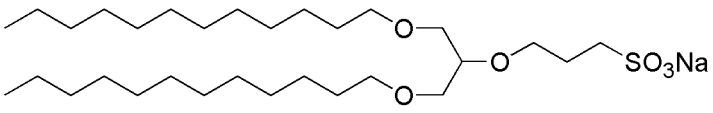
80 °C. The suspension was dissolved in water and filtered off with a membrane filter (hydrophilic, pore size; 0.45 μm). The solvent of the filtrate removed under reduced pressure and purified by RP-HPLC with acetonitrile/water containing 0.1% TFA to obtain [**1a-d**(Pt(II)(en))$_n$](CF$_3$COO)$_{2n}$ (**1a**; 75%, **1b**; 63%, **1c**; 26%, **1d**; 29% (2 steps)) as a colorless syrup (for [**1a**(Pt(II)(en))$_2$](CF$_3$COO)$_4$ Found: C, 29.99; H, 4.80; N, 10.22. $C_{44}H_{81}F_{12}N_{13}O_{21}Pt_2$ requires C, 30.26; H, 4.68; N, 10.43, for [**1b**(Pt(II)(en))$_3$](CF$_3$COO)$_6$ Found: C, 29.31; H, 4.87; N, 10.04. $C_{65}H_{119}F_{18}N_{19}O_{31}Pt_3 \cdot 3H_2O$ requires C, 29.53; H, 4.77; N, 10.07, for [**1c**(Pt(II)(en))$_9$](CF$_3$COO)$_{18}$ Found: C, 28.25; H, 5.09; N, 9.11. $C_{191}H_{347}F_{54}N_{55}O_{91}Pt_9 \cdot 27H_2O$ requires C, 28.19; H, 4.97; N, 9.47, for [**1d**(Pt(II)(en))$_{10}$](CF$_3$COO)$_{20}$ Found: C, 27.82; H, 5.20; N, 9.00. $C_{212}H_{385}F_{60}N_{61}O_{101}Pt_{10} \cdot 30H_2O$ requires C, 28.18; H, 4.96; N, 9.46); δ_H(500 MHz; CD$_3$OD; Me$_4$Si) for [**1a**(Pt(II)(en))$_2$](CF$_3$COO)$_4$ 4.50-4.02 (m, 8H, 2 × -OCH$_2$CO-, 2 × -NCH$_2$CO-), 3.75-3.67 (m, 4H, 2 × NH$_2$CHC*H*$_2$O-), 3.63-3.35 (m, 32H, 2 × -OCH$_2$CH$_2$N-, 2 × -OCH$_2$CH$_2$OCH$_2$CH$_2$O-, 2 × -NHC*H*$_2$C*H*$_2$O-), 3.09 (br, 2H, 2 × NH$_2$C*H*-), 2.78-2.75 (m, 2H, 2 × NH$_2$C*H*HCH-), 2.69-2.62 (m, 10H, 2 × NH$_2$CH*H*CH-, 2 × NH$_2$C*H*$_2$C*H*$_2$NH$_2$), 1.96-1.95 (m, 3H, Ac), for [**1b**(Pt(II)(en))$_3$](CF$_3$COO)$_6$ 4.50-4.03 (m, 12H, 3 × -OCH$_2$CO-, 3 × -NCH$_2$CO-), 3.73-3.67 (m, 6H, 3 × NH$_2$CHC*H*$_2$O-), 3.63-3.35 (m, 48H, 3 × -OCH$_2$CH$_2$N-, 3 × -OCH$_2$CH$_2$OCH$_2$CH$_2$O-, 3 × -NHC*H*$_2$C*H*$_2$O-), 3.09 (br, 3H, 3 × NH$_2$C*H*-), 2.78-2.76 (m, 3H, 3 × NH$_2$C*H*HCH-), 2.69-2.60 (m, 15H, 3 × NH$_2$CH*H*CH-, 3 × NH$_2$C*H*$_2$C*H*$_2$NH$_2$), 1.96-1.94 (m, 3H, Ac), for [**1c**(Pt(II)(en))$_9$](CF$_3$COO)$_{18}$ 4.50-4.03 (m, 36H, 9 × -OCH$_2$CO-, 9 × -NCH$_2$CO-), 3.76-3.73 (m, 18H, 9 × NH$_2$CHC*H*$_2$O-), 3.63-3.35 (m, 144H, 9 × -OCH$_2$CH$_2$N-, 9 × -OCH$_2$CH$_2$OCH$_2$CH$_2$O-, 9 × -NHC*H*$_2$C*H*$_2$O-), 3.08 (br, 9H, 9 × NH$_2$C*H*-), 2.77 (br, 9H, 9 × NH$_2$C*H*HCH-), 2.62 (m, 45H, 9 × NH$_2$CH*H*CH-, 9 × NH$_2$C*H*$_2$C*H*$_2$NH$_2$), 1.96-1.94 (m, 3H, Ac), for [**1d**(Pt(II)(en))$_{10}$](CF$_3$COO)$_{20}$ 4.50-4.03 (m, 40H, 10 × -OCH$_2$CO-, 10 × -NCH$_2$CO-), 3.76-3.69 (m, 20H, 10 × NH$_2$CHC*H*$_2$O-), 3.63-3.34 (m, 160H, 10 × -OCH$_2$CH$_2$N-, 10 × -OCH$_2$CH$_2$OCH$_2$CH$_2$O-, 10 × -NHC*H*$_2$C*H*$_2$O-), 3.10 (br, 10H, 10 × NH$_2$C*H*-), 2.76 (br, 10H, 10 × NH$_2$C*H*HCH-), 2.62 (m, 50H, 10 × NH$_2$CH*H*CH-, 10 × NH$_2$C*H*$_2$C*H*$_2$NH$_2$), 1.99-1.93 (m, 3H, Ac); *m/z* (ESI-TOF) for [**1a**(Pt(II)(en))$_2$](CF$_3$COO)$_4$ 759.71 (M - 2CF$_3$COO$^-$. $C_{40}H_{79}F_6N_{13}O_{17}Pt_2$ requires 759.75), for [**1b**(Pt(II)(en))$_3$](CF$_3$COO)$_6$ 1181.80 (M - 2CF$_3$COO$^-$. $C_{61}H_{117}F_{12}N_{19}O_{27}Pt_3$ requires 1181.86), for [**1c**(Pt(II)(en))$_9$](CF$_3$COO)$_{18}$ 1162.28 (M - 6CF$_3$COO$^-$. $C_{179}H_{341}F_{36}N_{55}O_{79}Pt_9$ requires 1162.19), for [**1d**(Pt(II)(en))$_{10}$](CF$_3$COO)$_{20}$ 1302.89 (M - 6CF$_3$COO$^-$. $C_{200}H_{379}F_{42}N_{61}O_{89}Pt_{10}$ requires 1302.89); t_R for [**1a**(Pt(II)(en))$_2$](CF$_3$COO)$_4$ 29.2, for [**1b**(Pt(II)(en))$_3$](CF$_3$COO)$_6$ 34.3, for [**1c**(Pt(II)(en))$_9$](CF$_3$COO)$_{18}$ 37.7, for [**1d**(Pt(II)(en))$_{10}$](CF$_3$COO)$_{20}$ 38.9 min (the same condition mentioned above).



RSO_3H

Synthesis of 3-[1,3-bis(dodecyoxy)-2-propoxy]propanesulfonic acid RSO_3H

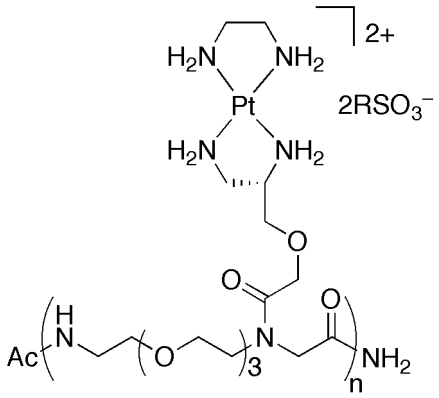
To a suspension of sodium hydride (in oil (60%), 186 mg, 4.66 mmol) in THF (2.3 cm^3) was added slowly dropwise a solution of 1,3-bis-dodecyloxy-propan-2-ol (1.00 g, 2.33 mmol) in THF (2.3 cm^3) at room temperature with a cannula under a nitrogen atmosphere. After stirring for 30 min at 55 °C, 1,3-propanesultone (246 mm^3, 2.80 mmol) was added dropwise within 3 min, and then stirred for 1 h at 55 °C. The reaction was quenched by adding 0.5 cm^3 of methanol, and then the reaction mixture was poured into cooled 1 M HCl/brine (300 cm^3). The target compound was extracted with ethyl acetate (300 cm^3), and then the solvent was removed under reduced pressure and dried *in vacuo*. The crude material (1.56 g) was purified by silica gel column chromatography with *n*-hexane/ethyl acetate (10:1 - 2:1)) to afford RSO_3H (1.08 g, 85%) as a pale yellow syrup; R_f 0.68 (ethyl acetate/methanol (3:1)); δ_H(500 MHz; CD_3OD; Me_4Si) 3.70 (t, J = 6.2 Hz, 2H, -C$H_2$$SO_3H$), 3.58 (m, 1H, methine), 3.53-3.42 (m, 8H, 2 × -CH_2OCH_2-), 2.90 (m, 2H, -C$H_2$$CH_2CH_2SO_3H$), 2.02 (m, 2H, -C$H_2$$CH_2SO_3H$), 1.56 (m, 4H, 2 × -C$H_2$$CH_2OCH_2CH$-), 1.37-1.17 (m, 36H, 2 × CH_3(CH_2)$_9$-), 0.90 (t, J = 6.9 Hz, 6H, 2 × C$H_3$$(CH_2)_9$-); *m/z* (ESI-TOF) 551.49 ($M + H^+$. $C_{30}H_{63}O_6S$ requires 551.43).



RSO_3Na

Synthesis of sodium 3-[1,3-bis(dodecyoxy)-2-propoxy]propanesulfonate RSO_3Na

To a solution of RSO_3H (570 mg, 1.03 mmol) in methanol (1.0 cm^3) was added a solution of NaOH (42.0 mg, 1.05 mmol) in methanol (1.0 cm^3) at room temperature. The resulting precipitate was dissolved in methanol and the remaining insoluble matter was filtered off. The solvent of the filtrate was removed under reduced pressure and dried *in vacuo*. The crude material (611 mg) was purified by recrystallization with methanol/2-propanol (1:1, 5 cm^3) to afford RSO_3Na (357 mg, 60%) as a colorless liquid (Found: C, 62.68; H, 10.93. $C_{30}H_{61}NaO_6S$ requires C, 62.90; H, 10.73); δ_H(500 MHz; CD_3OD; Me_4Si) 3.70 (t, J = 6.2 Hz, 2H, -C$H_2$$SO_3Na$), 3.58 (m, 1H, methine), 3.53-3.42 (m, 8H, 2 × -CH_2OCH_2-), 2.89 (m, 2H, -C$H_2$$CH_2CH_2SO_3Na$), 2.02 (m, 2H, -C$H_2$$CH_2SO_3Na$), 1.56 (m, 4H, 2 × -C$H_2$$CH_2OCH_2CH$-), 1.37-1.29 (m, 36H, 2 × CH_3(CH_2)$_9$-), 0.90 (t, J = 6.9 Hz, 6H, 2 × C$H_3$$(CH_2)_9$-); *m/z* (ESI-TOF) 595.48 ($M + Na^+$. $C_{30}H_{61}Na_2O_6S$ requires 595.40).

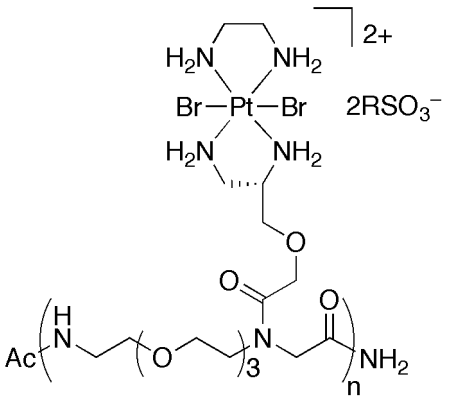


[**1a-d**(Pt(II)(en))$_n$](RSO$_3$)$_{2n}$

Synthesis of Pt(II) complex-bearing peptides [1a-d(Pt(II)(en))$_n$](RSO$_3$)$_{2n}$: (n = 2, 3, 9, 10)

To a solution of [**1a-d**(Pt(II)(en))$_n$](CF$_3$COO)$_{2n}$: (n = 2, 3, 9, 10) in methanol was added RSO$_3$Na (2n equiv) at room temperature. After stirring for 12 h at room temperature, the solvent was removed under reduced pressure and dried *in vacuo*. The residue was washed with water (3 times), reprecipitated with methanol/acetone or dichloromethane/acetone and lyophilized to obtain [**1a-d**(Pt(II)(en))$_n$](RSO$_3$)$_{2n}$ (**1a**; 94%, **1b**; 48%, **1c**; 94%, **1d**; 72%) as a colorless foam (for [**1a**(Pt(II)(en))$_2$](RSO$_3$)$_4$ Found: C, 53.41; H, 9.61; N, 4.92. $C_{156}H_{325}N_{13}O_{37}Pt_2S_4$ requires C, 53.63; H, 9.38; N, 5.21, for [**1b**(Pt(II)(en))$_3$](RSO$_3$)$_6$ Found: C, 53.70; H, 9.38; N, 5.11. $C_{233}H_{485}N_{19}O_{55}Pt_3S_6$ requires C, 53.56; H, 9.67; N, 4.87, for [**1c**(Pt(II)(en))$_9$](RSO$_3$)$_{18}$ Found: C, 52.50; H, 9.35; N, 4.73. $C_{695}H_{1445}N_{55}O_{163}Pt_9S_{18}\cdot 21H_2O$ requires C, 52.52; H, 9.43; N, 4.85, for [**1d**(Pt(II)(en))$_{10}$](RSO$_3$)$_{20}$ Found: C, 53.65; H, 9.65; N, 4.74. $C_{772}H_{1605}N_{61}O_{181}Pt_{10}S_{20}$ requires C, 53.81; H, 9.39; N, 4.96); δ_H(500 MHz; CD$_3$OD; Me$_4$Si) for [**1a**(Pt(II)(en))$_2$](RSO$_3$)$_4$ 4.51-4.02 (m, 8H, 2 × -NCH$_2$CO-, 2 × -OCH$_2$CO-), 3.77-3.69 (m, 12H, 2 × -OC*H*$_2$CHNH$_2$, 4 × -CH$_2$SO$_3$), 3.64-3.41 (m, 68H, 2 × -OCH$_2$CH$_2$N-, 2 × -OCH$_2$CH$_2$OCH$_2$CH$_2$O-, 2 × -NHC*H*$_2$C*H*$_2$O-, 8 × -OC*H*$_2$CHO- (RSO$_3$), 4 × -OCH$_2$C*H*O- (RSO$_3$), 8 × -C*H*$_2$OCH$_2$CHO- (RSO$_3$)), 3.11 (br, 2H, 2 × -OCH$_2$C*H*NH$_2$), 2.93-2.89 (m, 8H, 4 × -C*H*$_2$CH$_2$CH$_2$SO$_3$), 2.79-2.77 (br, 2H, 2 × -CHC*H*HNH$_2$), 2.69-2.63 (m, 10H, 2 × -CHCH*H*NH$_2$, 2 × NH$_2$C*H*$_2$C*H*$_2$NH$_2$), 2.07-2.01 (m, 8H, 4 × -C*H*$_2$CH$_2$SO$_3$), 1.96 (m, 3H, Ac), 1.59-1.54 (m, 16H, 8 × -C*H*$_2$CH$_2$OCH$_2$CHO-), 1.35-1.30 (m, 144H, 8 × CH$_3$(C*H*$_2$)$_9$-), 0.90 (m, 24H, 8 × C*H*$_3$(CH$_2$)$_9$-), for [**1b**(Pt(II)(en))$_3$](RSO$_3$)$_6$ 4.51-4.01 (m, 12H, 3 × -NCH$_2$CO-, 3 × -OCH$_2$CO-), 3.75-3.69 (m, 18H, 3 × -OC*H*$_2$CHNH$_2$, 6 × -CH$_2$SO$_3$), 3.64-3.41 (m, 102H, 3 × -OCH$_2$CH$_2$N-, 3 × -OCH$_2$CH$_2$OCH$_2$CH$_2$O-, 3 × -NHC*H*$_2$C*H*$_2$O-, 12 × -OC*H*$_2$CHO- (RSO$_3$), 6 × -OCH$_2$C*H*O- (RSO$_3$), 12 × -C*H*$_2$OCH$_2$CHO- (RSO$_3$)), 3.10 (br, 3H, 3 × -OCH$_2$C*H*NH$_2$), 2.92-2.89 (m, 12H, 6 × -C*H*$_2$CH$_2$CH$_2$SO$_3$), 2.77 (br, 3H, 3 × -CHC*H*HNH$_2$), 2.69-2.63 (m, 15H, 3 × -CHCH*H*NH$_2$, 3 × NH$_2$C*H*$_2$C*H*$_2$NH$_2$), 2.06-2.01 (m, 12H, 6 × -C*H*$_2$CH$_2$SO$_3$), 1.96-1.95 (m, 3H, Ac), 1.59-1.53 (m, 24H, 12 × -C*H*$_2$CH$_2$OCH$_2$CHO-), 1.35-1.29 (m, 216H, 12 × CH$_3$(C*H*$_2$)$_9$-), 0.90 (m, 36H, 12 × C*H*$_3$(CH$_2$)$_9$-),

for [**1c**(Pt(II)(en))$_9$](RSO$_3$)$_{18}$ 4.53-4.07 (m, 36H, 9 × -NCH$_2$CO-, 9 × -OCH$_2$CO-), 3.75-3.70 (m, 54H, 9 × -OC*H*$_2$CHNH$_2$, 18 × -CH$_2$SO$_3$), 3.64-3.42 (m, 306H, 9 × -OCH$_2$CH$_2$N-, 9 × -OCH$_2$CH$_2$OCH$_2$CH$_2$O-, 9 × -NHC*H*$_2$C*H*$_2$O-, 36 × -OC*H*$_2$CHO- (RSO$_3$), 18 × -OCH$_2$C*H*O- (RSO$_3$), 36 × -C*H*$_2$OCH$_2$CHO- (RSO$_3$)), 3.13 (br, 9H, 9 × -OCH$_2$C*H*NH$_2$), 2.94-2.90 (m, 36H, 18 × -C*H*$_2$CH$_2$CH$_2$SO$_3$), 2.79 (br, 9H, 9 × -CHC*H*HNH$_2$), 2.69-2.64 (m, 45H, 9 × -CHCH*H*NH$_2$, 9 × NH$_2$C*H*$_2$C*H*$_2$NH$_2$), 2.08-2.02 (m, 36H, 18 × -C*H*$_2$CH$_2$SO$_3$), 1.96-1.91 (m, 3H, Ac), 1.59-1.54 (m, 72H, 36 × -C*H*$_2$CH$_2$OCH$_2$CHO-), 1.35-1.29 (m, 648H, 36 × CH$_3$(C*H*$_2$)$_9$-), 0.92-0.89 (m, 108H, 36 × C*H*$_3$(CH$_2$)$_9$-), for [**1d**(Pt(II)(en))$_{10}$](RSO$_3$)$_{20}$ 4.53-4.07 (m, 40H, 10 × -NCH$_2$CO-, 10 × -OCH$_2$CO-), 3.75-3.70 (m, 60H, 10 × -OC*H*$_2$CHNH$_2$, 20 × -CH$_2$SO$_3$), 3.64-3.42 (m, 340H, 10 × -OCH$_2$CH$_2$N-, 10 × -OCH$_2$CH$_2$OCH$_2$CH$_2$O-, 10 × -NHC*H*$_2$C*H*$_2$O-, 40 × -OC*H*$_2$CHO- (RSO$_3$), 20 × -OCH$_2$C*H*O- (RSO$_3$), 40 × -C*H*$_2$OCH$_2$CHO- (RSO$_3$)), 3.14 (br, 10H, 10 × -OCH$_2$C*H*NH$_2$), 2.94-2.91 (m, 40H, 20 × -C*H*$_2$CH$_2$CH$_2$SO$_3$), 2.80 (br, 10H, 10 × -CHC*H*HNH$_2$), 2.64 (m, 50H, 10 × -CHCH*H*NH$_2$, 10 × NH$_2$C*H*$_2$C*H*$_2$NH$_2$), 2.08-2.02 (m, 40H, 20 × -C*H*$_2$CH$_2$SO$_3$), 1.96-1.91 (m, 3H, Ac), 1.59-1.54 (m, 80H, 40 × -C*H*$_2$CH$_2$OCH$_2$CHO-), 1.35-1.30 (m, 720H, 40 × CH$_3$(C*H*$_2$)$_9$-), 0.90 (m, 120H, 40 × C*H*$_3$(CH$_2$)$_9$-); *m/z* (ESI-TOF) for [**1a**(Pt(II)(en))$_2$](RSO$_3$)$_4$ 1196.84 (M - 2RSO$_3^-$. C$_{96}$H$_{201}$N$_{13}$NaO$_{25}$Pt$_2$S$_2$ requires 1196.69), for [**1b**(Pt(II)(en))$_3$](RSO$_3$)$_6$ 1187.02 (M - 3RSO$_3^-$. C$_{143}$H$_{299}$N$_{19}$O$_{37}$Pt$_3$S$_3$ requires 1187.02).



[**1a-d**(Pt(IV)Br$_2$(en))$_n$](RSO$_3$)$_{2n}$

Synthesis of Pt(IV) complex-bearing peptides [1a-d(Pt(IV)Br$_2$(en))$_n$](RSO$_3$)$_{2n}$: (n = 2, 3, 9, 10)

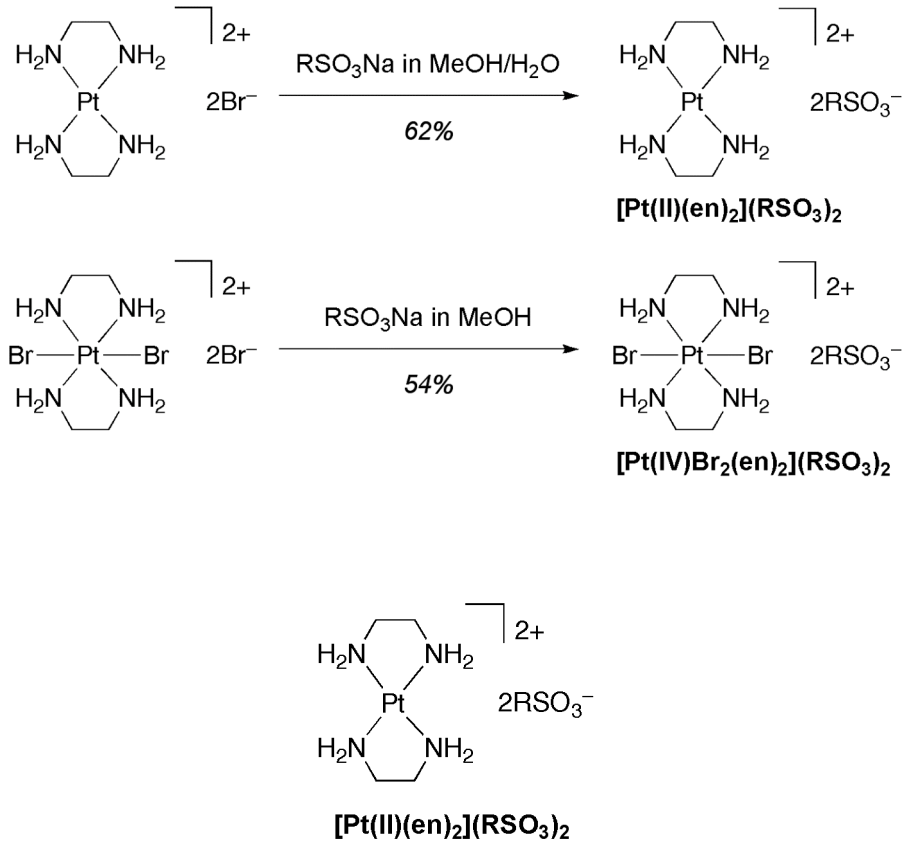
To a solution of [**1a-d**(Pt(II)(en))$_n$](CF$_3$COO)$_{2n}$: (n = 2, 3, 9, 10) in ethanol was added excess bromine at room temperature. After stirring for 15 min at room temperature, the solvent and excess bromine were removed under reduced pressure and dried *in vacuo*. To the residue was added a solution of RSO$_3$Na (2n equiv) in methanol. After stirring for 4 h at room temperature, the solvent was removed under reduced pressure and dried *in vacuo*. The residue was washed with water (8 times) and lyophilized. The crude material was purified by reprecipitaion with acetone/methanol,

methanol/diethyl ether or dichloromethane/diethyl ether to afford [**1a-d**(Pt(IV)Br_2(en))$_n$]$(RSO_3)_{2n}$ (**1a**; 49%, **1b**; 65%, **1c**; 82%, **1d**; 76% (2 steps)) as a yellow foam (for [**1a**(Pt(IV)Br_2(en))$_2$]$(RSO_3)_4$ Found: C, 48.88; H, 8.71; N, 4.54. $C_{156}H_{325}Br_4N_{13}O_{37}Pt_2S_4$ requires C, 49.13; H, 8.59; N, 4.77, for [**1b**(Pt(IV)Br_2(en))$_3$]$(RSO_3)_6$ Found: C, 49.00; H, 8.83; N, 4.47. $C_{233}H_{486}Br_6N_{19}O_{55}Pt_3S_6$ requires C, 49.18; H, 8.59; N, 4.68, for [**1c**(Pt(IV)Br_2(en))$_9$]$(RSO_3)_{18}$ Found: C, 47.94; H, 8.72; N, 4.44. $C_{695}H_{1445}Br_{18}N_{55}O_{163}Pt_9S_{18}\cdot 27H_2O$ requires C, 47.86; H, 8.66; N, 4.42, for [**1d**(Pt(IV)Br_2(en))$_{10}$]$(RSO_3)_{20}$ Found: C, 49.02; H, 8.64; N, 4.37. $C_{772}H_{1605}Br_{20}N_{61}O_{181}Pt_{10}S_{20}$ requires C, 49.24; H, 8.59; N, 4.54); δ_H(500 MHz; CD_3OD; Me_4Si) for [**1a**(Pt(IV)Br_2(en))$_2$]$(RSO_3)_4$ 4.61-4.10 (m, 8H, 2 × -NCH_2CO-, 2 × -OCH_2CO-), 3.94-3.91 (m, 2H, 2 × -OC*H*HCHNH_2), 3.78-3.75 (m, 2H, 2 × -OCH*H*CHNH_2), 3.70 (t, J = 6.2 Hz, 8H, 4 × -CH_2SO_3), 3.63-3.39 (m, 70H, 2 × -OCH_2CHNH$_2$, 2 × -OCH_2CH_2N-, 2 × -$OCH_2CH_2OCH_2CH_2O$-, 2 × -NHCH_2CH_2O-, 8 × -OCH_2CHO- (RSO_3), 4 × -OCH_2CHO- (RSO_3), 8 × -CH_2OCH_2CHO- (RSO_3)), 3.31-3.30 (2H, 2 × -CHC*H*HNH_2), 3.07-2.96 (m, 10H, 2 × -CHCH*H*NH_2, 2 × N$H_2CH_2CH_2$NH_2), 2.91-2.88 (m, 8H, 4 × -C$H_2CH_2CH_2SO_3$), 2.05-1.99 (m, 8H, 4 × -C$H_2CH_2SO_3$), 1.96-1.95 (m, 3H, Ac), 1.59-1.53 (m, 16H, 8 × -C$H_2CH_2OCH_2$CHO-), 1.39-1.29 (m, 144H, 8 × $CH_3(CH_2)_9$-), 0.90 (m, 24H, 8 × $CH_3(CH_2)_9$-), for [**1b**(Pt(IV)Br_2(en))$_3$]$(RSO_3)_6$ 4.63-4.11 (m, 12H, 3 × -NCH_2CO-, 3 × -OCH_2CO-), 3.93 (br, 3H, 3 × -OC*H*HCHNH_2), 3.78-3.76 (m, 3H, 3 × -OCH*H*CHNH_2), 3.70 (t, J = 6.2 Hz, 12H, 6 × -CH_2SO_3), 3.63-3.39 (m, 105H, 3 × -OCH_2CHNH$_2$, 3 × -OCH_2CH_2N-, 3 × -$OCH_2CH_2OCH_2CH_2O$-, 3 × -NHCH_2CH_2O-, 12 × -OCH_2CHO- (RSO_3), 6 × -OCH_2CHO- (RSO_3), 12 × -CH_2OCH_2CHO- (RSO_3)), 3.31-3.30 (3H, 3 × -CHC*H*HNH_2), 3.07-2.98 (m, 15H, 3 × -CHCH*H*NH_2, 3 × N$H_2CH_2CH_2$NH_2), 2.91-2.88 (m, 12H, 6 × -C$H_2CH_2CH_2SO_3$), 2.05-1.99 (m, 12H, 6 × -C$H_2CH_2SO_3$), 1.96-1.95 (m, 3H, Ac), 1.58-1.53 (m, 24H, 12 × -C$H_2CH_2OCH_2$CHO-), 1.35-1.29 (m, 216H, 12 × $CH_3(CH_2)_9$-), 0.91-0.88 (m, 36H, 12 × $CH_3(CH_2)_9$-), for [**1c**(Pt(IV)Br_2(en))$_9$]$(RSO_3)_{18}$ 4.62-4.11 (m, 36H, 9 × -NCH_2CO-, 9 × -OCH_2CO-), 3.93 (br, 9H, 9 × -OC*H*HCHNH_2), 3.79-3.77 (m, 9H, 9 × -OCH*H*CHNH_2), 3.70 (t, J = 6.2 Hz, 36H, 18 × -CH_2SO_3), 3.63-3.39 (m, 315H, 9 × -OCH_2CHNH$_2$, 9 × -OCH_2CH_2N-, 9 × -$OCH_2CH_2OCH_2CH_2O$-, 9 × -NHCH_2CH_2O-, 36 × -OCH_2CHO- (RSO_3), 18 × -OCH_2CHO- (RSO_3), 36 × -CH_2OCH_2CHO- (RSO_3)), 3.31-3.30 (9H, 9 × -CHC*H*HNH_2), 3.07-3.00 (m, 45H, 9 × -CHCH*H*NH_2, 9 × N$H_2CH_2CH_2$NH_2), 2.92-2.89 (m, 36H, 18 × -C$H_2CH_2CH_2SO_3$), 2.05-1.99 (m, 36H, 18 × -C$H_2CH_2SO_3$), 1.96-1.95 (m, 3H, Ac), 1.59-1.53 (m, 72H, 36 × -C$H_2CH_2OCH_2$CHO-), 1.35-1.29 (m, 648H, 36 × $CH_3(CH_2)_9$-), 0.90 (m, 108H, 36 × $CH_3(CH_2)_9$-), for [**1d**(Pt(IV)Br_2(en))$_{10}$]$(RSO_3)_{20}$ 4.62-4.13 (m, 40H, 10 × -NCH_2CO-, 10 × -OCH_2CO-), 3.93 (br, 10H, 10 × -OC*H*HCHNH_2), 3.79 (br, 10H, 10 × -OCH*H*CHNH_2), 3.70 (t, J = 6.2 Hz, 40H, 20 × -CH_2SO_3), 3.63-3.39 (m, 350H, 10 × -OCH_2CHNH$_2$, 10 × -OCH_2CH_2N-, 10 × -$OCH_2CH_2OCH_2CH_2O$-, 10 × -NHCH_2CH_2O-, 40 × -OCH_2CHO- (RSO_3), 20 × -OCH_2CHO- (RSO_3), 40 × -CH_2OCH_2CHO- (RSO_3)), 3.31-3.30 (10H, 10 × -CHC*H*HNH_2), 3.06-2.96 (m, 50H, 10 × -CHCH*H*NH_2, 10 × N$H_2CH_2CH_2$NH_2),

2.91-2.88 (m, 40H, 20 × -C*H*$_2$CH$_2$CH$_2$SO$_3$), 2.05-1.98 (m, 40H, 20 × -C*H*$_2$CH$_2$SO$_3$), 1.96-1.95 (m, 3H, Ac), 1.59-1.53 (m, 80H, 40 × -C*H*$_2$CH$_2$OCH$_2$CHO-), 1.35-1.29 (m, 720H, 40 × CH$_3$(C*H*$_2$)$_9$-), 0.90 (m, 120H, 40 × C*H*$_3$(CH$_2$)$_9$-); *m/z* (ESI-TOF) for [**1a**(Pt(IV)Br$_2$(en))$_2$](RSO$_3$)$_4$ 1356.67 (M - 2RSO$_3^-$. $C_{96}H_{201}Br_4N_{13}NaO_{25}Pt_2S_2$ requires 1356.52), for [**1b**(Pt(IV)Br$_2$(en))$_3$](RSO$_3$)$_6$ 1346.89 (M - 3RSO$_3^-$. $C_{143}H_{299}Br_6N_{19}O_{37}Pt_3S_3$ requires 1346.85).

Lipophilic mononuclear Pt complexes ([Pt(II)(en)$_2$](RSO$_3$)$_2$ and [Pt(IV)Br$_2$(en)$_2$](RSO$_3$)$_2$) were prepared according to Scheme S4.

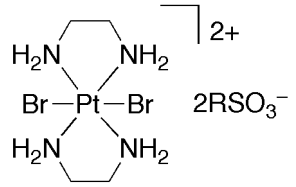
Scheme S4 Preperation of lipophilic mononuclear Pt complexes.



Synthesis of [Pt(II)(en)$_2$](RSO$_3$)$_2$

To a solution of [Pt(II)(en)$_2$]Br$_2$ (30.0 mg, 63.1 μmol) in water (0.5 cm^3) was added RSO$_3$Na (65.1 mg, 114 μmol) at room temperature. After shaking for 4 h at 55 °C with an ultrasonic cleaning machine, the suspension was centrifuged and the precipitate was lyophilized. The residue was dissolved in methanol/water (1:1, 0.4 cm^3) and again shaken for 4 h at 55 °C with an ultrasonic cleaning machine.

The suspension was centrifuged and the precipitate was washed with methanol/water (1:1, 3 × 0.2 cm^3) and lyophilized to obtain $[Pt(II)(en)_2](RSO_3)_2$ (50.1 mg, 62%) as a white solid (Found: C, 54.13; H, 9.96; N, 3.89. $C_{64}H_{138}N_4O_{12}PtS_2$ requires C, 54.32; H, 9.83; N, 3.96); δ_H(500 MHz; $CDCl_3$; Me_4Si) 5.57 (br, 8H, 2 × N*H*$_2$CH$_2$CH$_2$N*H*$_2$), 3.74 (t, *J* = 6.4 Hz, 4H, 2 × -CH$_2$SO$_3$), 3.65-3.61 (m, 2H, 2 × methine), 3.52-3.46 (m, 8H, 4 × -OC*H*$_2$CHO-), 3.45-3.39 (m, 8H, 4 × -C*H*$_2$OCH$_2$CHO-), 3.01-2.98 (m, 4H, 2 × -C*H*$_2$CH$_2$CH$_2$SO$_3$), 2.67 (s, 8H, 2 × NH$_2$C*H*$_2$C*H*$_2$NH$_2$), 2.17-2.11 (m, 4H, 2 × -C*H*$_2$CH$_2$SO$_3$), 1.56-1.52 (m, 8H, 4 × -C*H*$_2$CH$_2$OCH$_2$CHO-), 1.31-1.26 (m, 72H, 4 × CH$_3$(C*H*$_2$)$_9$-), 0.88 (t, *J* = 6.9 Hz, 12H, 4 × C*H*$_3$(CH$_2$)$_9$-); *m/z* (ESI-TOF) 864.61 (M - 2RSO$_3^-$. $C_{34}H_{77}N_4O_6PtS$ requires 864.52).



[Pt(IV)Br$_2$(en)$_2$](RSO$_3$)$_2$

Synthesis of [Pt(IV)Br$_2$(en)$_2$](RSO$_3$)$_2$

To a solution of $[Pt(IV)Br_2(en)_2]Br_2$ (50.0 mg, 78.8 μmol) in methanol (1.0 cm^3) was added RSO_3Na (81.2 mg, 142 μmol) at room temperature. After stirring for 40 h at room temperature, the solvent was removed under reduced pressure and dried *in vacuo*. The residue was washed with water (0.7 cm^3) and acetone/water (1:3, 2 × 0.4 cm^3), and then lyophilized. The crude material (92.3 mg) was recrystallized by methanol/2-propanol (1:10, 5.5 cm^3) to give $[Pt(IV)Br_2(en)_2](RSO_3)_2$ (60.6 mg, 54%) as a yellow solid (Found: C, 48.65; H, 8.75; N, 3.45. $C_{64}H_{138}Br_2N_4O_{12}PtS_2$ requires C, 48.81; H, 8.83; N, 3.56); δ_H(500 MHz; CD_3OD; Me_4Si) 3.70 (t, *J* = 6.2 Hz, 4H, 2 × -CH$_2$SO$_3$), 3.60-3.56 (m, 2H, 2 × methine), 3.53-3.50 (m, 8H, 4 × -OC*H*$_2$CHO-), 3.48-3.42 (m, 8H, 4 × -C*H*$_2$OCH$_2$CHO-), 3.04-2.99 (m, 8H, 2 × NH$_2$C*H*$_2$C*H*$_2$NH$_2$), 2.91-2.88 (m, 4H, 2 × -C*H*$_2$CH$_2$CH$_2$SO$_3$), 2.05-1.99 (m, 4H, 2 × -C*H*$_2$CH$_2$SO$_3$), 1.58-1.53 (m, 8H, 4 × -C*H*$_2$CH$_2$OCH$_2$CHO-), 1.35-1.29 (m, 72H, 4 × CH$_3$(C*H*$_2$)$_9$-), 0.90 (t, *J* = 7.0 Hz, 12H, 4 × C*H*$_3$(CH$_2$)$_9$-); *m/z* (ESI-TOF) 1025.47 (M - 2RSO$_3^-$. $C_{34}H_{77}N_4NaO_6PtS$ requires 1025.36).

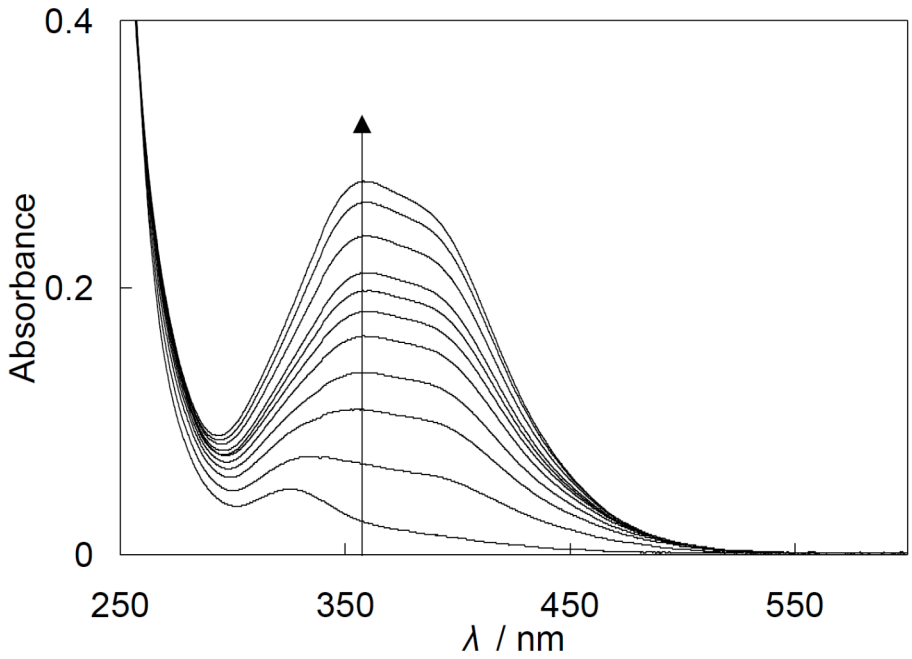


Fig. S1 Photometric titration spectra of [**1b**(Pt(IV)Br_2(en))$_3$]$(RSO_3)_6$ with [**1a**(Pt(II)(en))$_2$]$(RSO_3)_4$ in CH_2Cl_2 at 293 K (l = 1). [[**1b**(Pt(IV)Br_2(en))$_3$]$(RSO_3)_6$] = 12.5 μM. [[**1a**(Pt(II)(en))$_2$]$(RSO_3)_4$] = 0.0, 2.5, 5.0, 7.5, 10, 12.5, 15, 17.5, 20, 25, 37.5 and 50 μM.

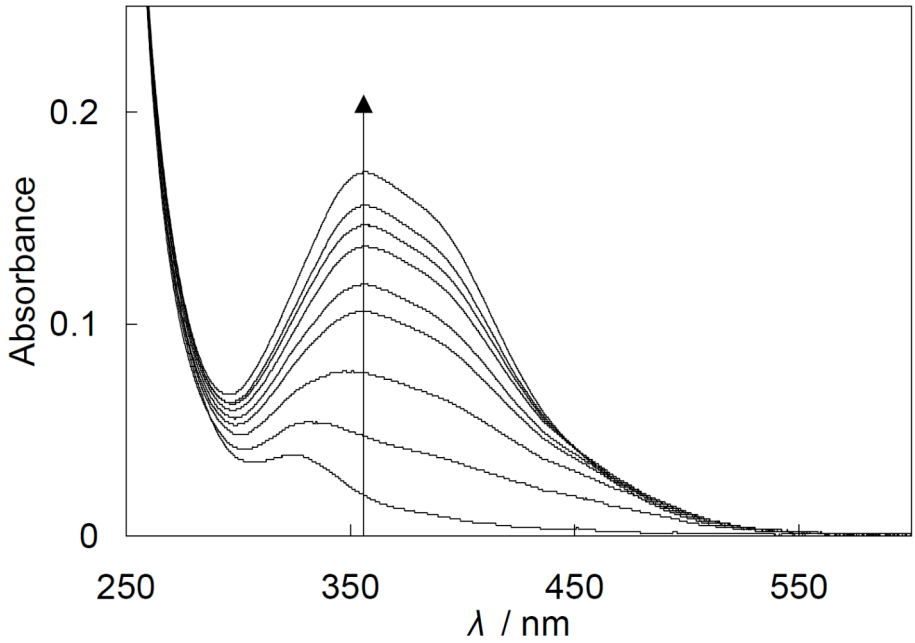


Fig. S2 Photometric titration spectra of [**1d**(Pt(IV)Br_2(en))$_{10}$]$(RSO_3)_{20}$ with [**1c**(Pt(II)(en))$_9$]$(RSO_3)_{18}$ in CH_2Cl_2 at 293 K (l = 1). [[**1d**(Pt(IV)Br_2(en))$_{10}$]$(RSO_3)_{20}$] = 2.5 μM. [[**1c**(Pt(II)(en))$_9$]$(RSO_3)_{18}$] = 0.0, 0.5, 1.0, 1.5, 2.0, 2.5, 3.0, 3.5 and 5.0 μM.

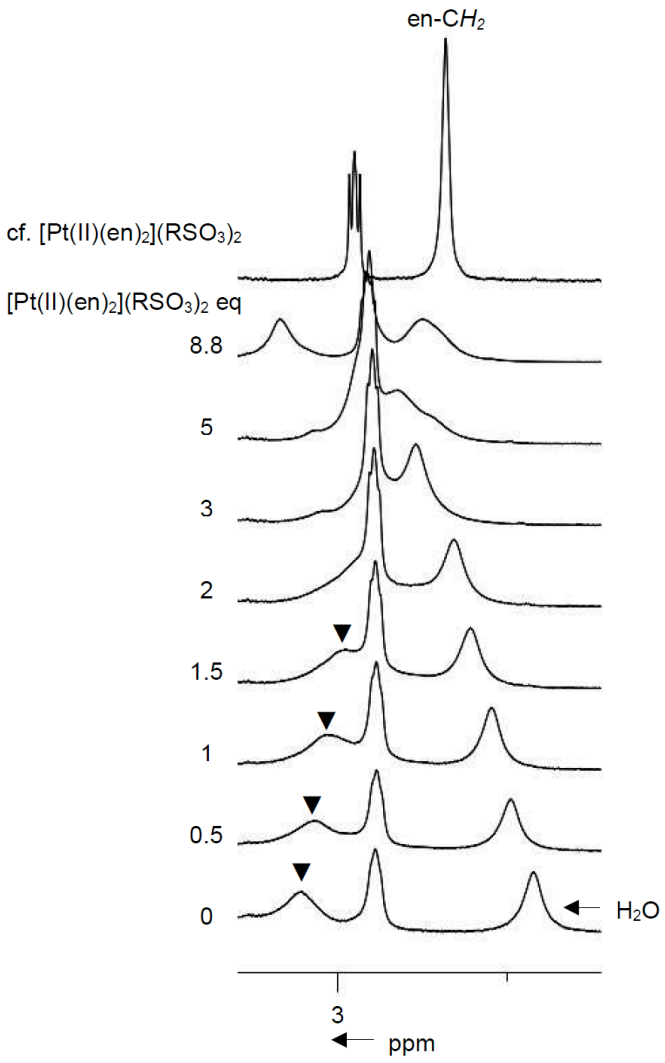


Fig. S3 ^{1}H NMR titration spectra of [**1a**(Pt(IV)Br_2(en))$_2$]$(RSO_3)_4$ (5 mM) with [Pt(II)(en)$_2$]$(RSO_3)_2$ in CD_2Cl_2 at 293 K. ▼ is the peak of methylene groups of ethylenediamine in [**1a**(Pt(IV)Br_2(en))$_2$]$(RSO_3)_4$.

References

1. L. Zhang, G. S. Kauffman, J. A. Pesti, J. Yin, *J. Org. Chem.*, 1997, **62**, 6918-6920.

2. A. W. Schwabacher, J. W. Lane, M. W. Schiesher, K. M. Leigh, C. W. Johnson, *J. Org. Chem.*, 1998, **63**, 1727-1729.

3. F. Basolo, J. C. Bailar, Jr., B. R. Tarr, *J. Am. Chem. Soc.*, 1950, **72**, 2433-2438.

4. G. W. Watt, R. E. McCarley, *J. Am. Chem. Soc.*, 1957, **79**, 3315-3317.