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Designer ligands. Part 12.[1] Synthesis and evaluation of novel palladium(II)–selective ligand systems

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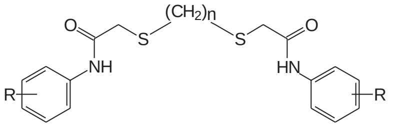
Sulfur-containing, PGM-selective, diamide ligands, developed for solvent extraction applications or use in the construction of molecularly imprinted polymers (MIPs), have been shown to exhibit significant selectivity for palladium(II) over copper(II), nickel(II) and cobalt(II).

Keywords: platinum-selective ligands, sulfur

The discovery of the anti-tumour platinum complexes, cisplatin[2] and carboplatin[3] has highlighted the potential of platinum-selective ligands in medicine – not only as anti-cancer agents, but also as "rescue agents" to remove the nephrotoxic platinum from the body.[4] Apparently, platinum is complexed by sulfur-rich proteins and enzymes in the kidney, and various sulfur-containing amide ligands have been developed to remove platinum from such biomolecules.[4] Separation of the valuable platinum group metals (PGM) from base metals, such as iron, copper, nickel and cobalt,[5] is also typically achieved by solvent extraction, using PGM-selective ligands. Our own research on metal-selective ligands has been concerned with the development of systems capable of selectively chelating nickel,[6] copper,[7] silver,[8] or platinum group metals[9,10] in the presence of specified metal contaminants. In this communication, we discuss: the synthesis of novel ligands; the development of molecularly imprinted polymers (MIPs); and an evaluation of their PGM extraction potential.

Desirable ligand-design criteria for the solvent extraction of metal ions include: solubility in organic solvents; ready synthesis; and cost effectiveness – criteria, which we hoped would be reflected in the ligand systems targeted in this study. The ligands **1** and **2** were also designed to incorporate several important structural features, *viz.*, S- and N-donor atoms for metal chelation; an aromatic ring to increase lipophilicity; an amide function for platinum and palladium selectivity; substituents (R) to fine-tune N-donor capacity; and additional sulfur donors for multidentate coordination with the metal centre.

1 : n=2
2 : n=3



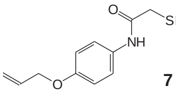
Results and discussion

Ligand synthesis

Synthesis of the known ligands **1**[11] and the novel analogues **2** involved two phases, *viz.*, formation of the monomeric mercaptoacetanilides **5a–f** (Scheme 1) and their subsequent condensation with the 1,2-dibromoethane or 1,3-dibromopropane. The mercaptoacetanilides **5a–f** were obtained in 40–60% yield (following recrystallisation) by heating 1:1 mixtures of mercaptoacetic acid **3** with the corresponding anilines **4a–f** under a gentle stream of dry nitrogen gas.[11,12] While oxidation to the disulfides was normally obviated under these conditions, use of 1-naphthylamine **4g** resulted in the formation of the disulfide **6g** as the sole product.[13] In the second phase, the mercaptoacetanilides **5a–f** were coupled with 1,2-dibromoethane or 1,3-dibromopropane in methanolic potassium hydroxide. Recrystallisation from ethanol or, in some cases, flash chromatography and recrystallisation generally afforded the diamides **1a–f** and **2a–f** in reasonable yields (30–60%).

Molecularly imprinted polymers (MIPs) have found use in separation methodology,[14] and as drug–receptor-binding[15] and antibody-binding[16] mimics. Moreover, as heterogeneous metal-selective extractants,[17] they offer significant potential advantages over the use of classical homogeneous systems, in that separation of the metal may be effected directly from aqueous solution without resorting to the use of organic solvents.

Consequently, attention has also been given to developing co-polymerisable analogues of the monoamide and diamide ligands (**5** and **1**, respectively), with the allylated systems **7** and **8** being investigated as possible "functional monomers".



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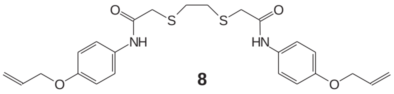
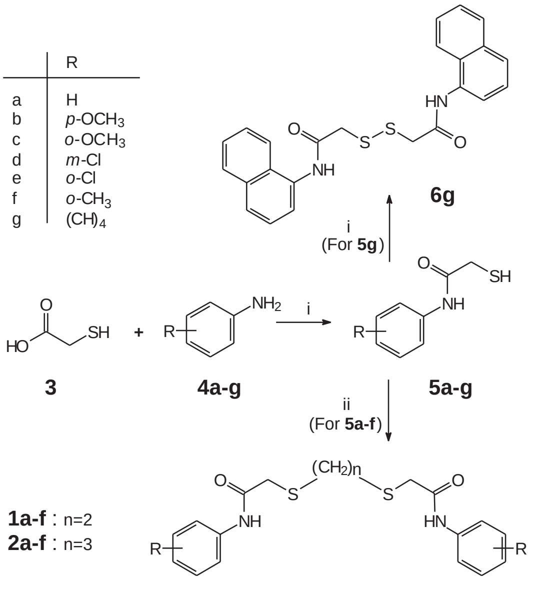


Retrosynthetic analysis of ligands **7** and **8** suggested that they could be accessed from commercially available 4-aminophenol **9** as outlined in Scheme 2. Consequently, 4-aminophenol **9** was reacted with allyl bromide **10** in methanolic potassium hydroxide at room temperature for 24h. Work-up afforded a black oil, subsequently shown to contain the three variously allylated products **11**, **12** and **13**. Vacuum distillation finally afforded, in only 15% yield, 4-(allyloxy)aniline **11** as a yellow oil, which turned black on standing. In an alternative approach,[18] allylation of 4-acetamido-phenol **14** afforded the acetanilide **15** (85%), subsequent hydrolysis of which gave the required 4-(allyloxy)aniline **11** in acceptable yield (49%). Treatment of 4-(allyloxy)aniline **11** with mercaptoacetic acid **3** gave the 4'-(allyloxy)-2-mercaptoacetanilide **7**, which was then coupled with 1,2-dibromoethane to form the allylated diamide **8**.



Scheme 1 *Reagents and conditions:* i, N_2, heat; ii, KOH, MeOH and $Br(CH_2)_2Br$ or $Br(CH_2)_3Br$.

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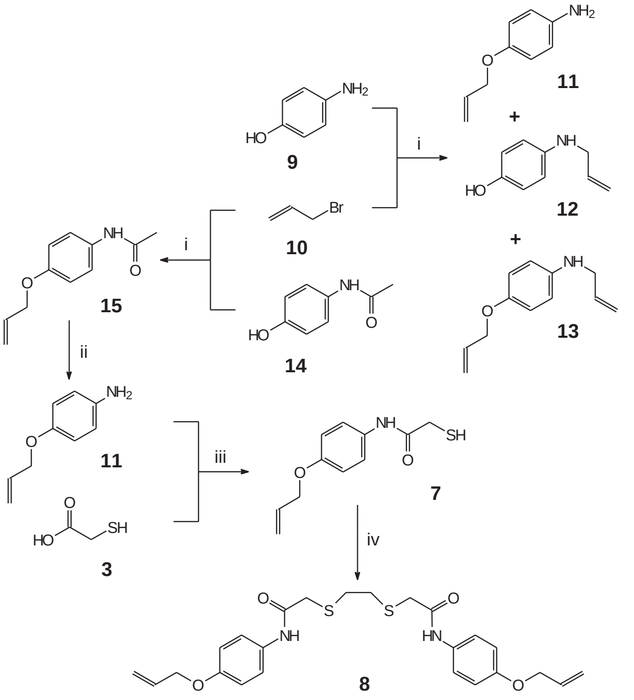
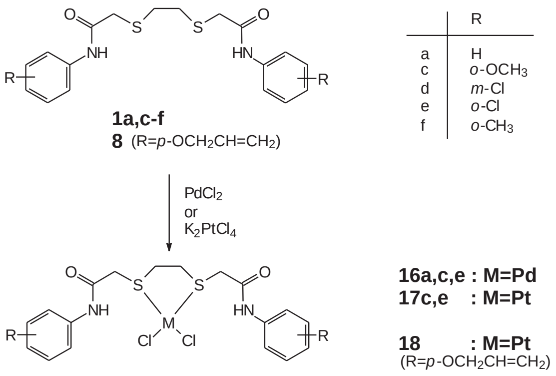


Scheme 2 *Reagents and conditions:* i, KOH, MeOH; ii, H_2SO_4 then NaOH; iii, N_2, heat; iv, KOH, MeOH and $Br(CH_2)_2Br$.

Metal complexation

Pd(II) and Pt(II) complexes were prepared by mixing solutions of selected diamide ligands in either MeOH or MeOH-acetone (1:1) with solutions of $PdCl_2$ or K_2PtCl_4 in hydrochloric acid (Scheme 3). The complexes **16**–**18**, obtained following work-up as yellow powders, failed to afford crystals suitable for single crystal X-Ray analysis and were consequently characterised by elemental (combustion and/or HRMS) and spectroscopic (NMR, IR and MS) analysis. The ^1H and ^{13}C NMR spectra of the complexes typically exhibit doubling of various signals consistent with the presence, in each case, of both *cis*- and *trans*-complexes;[19] these isomeric complexes arise from the configurational stability of the chelating, tetrahedral sulfur atoms. The presence of two amide proton singlets at *ca* 10ppm in the ^1H NMR spectra supports chelation of the metal cation, in each case, by sulfur rather than nitrogen donors. The results clearly indicate the capacity of these ligand systems to chelate both Pd(II) and Pt(II).

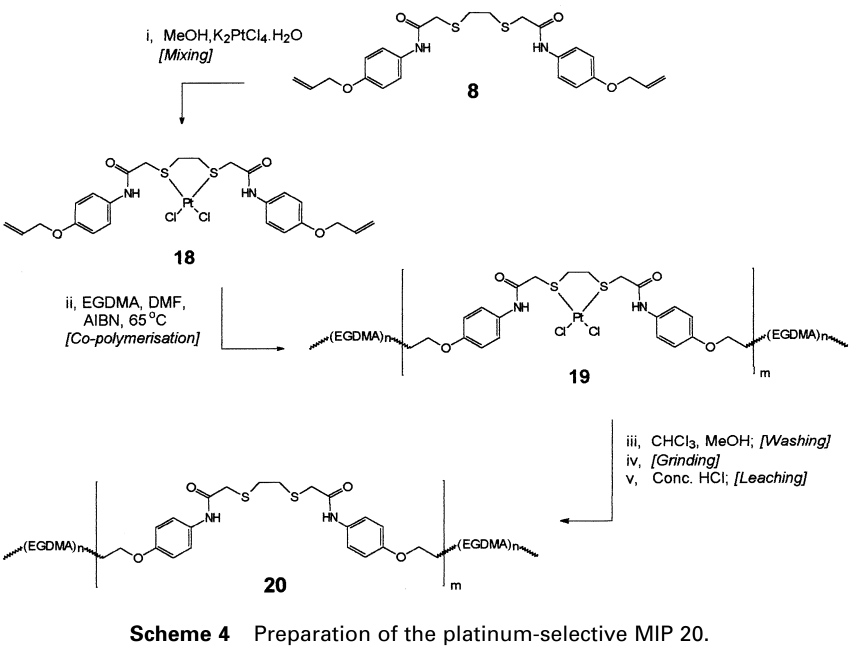


Scheme 3 Preparation of Pd(II) and Pt(II) complexes.

MIP synthesis

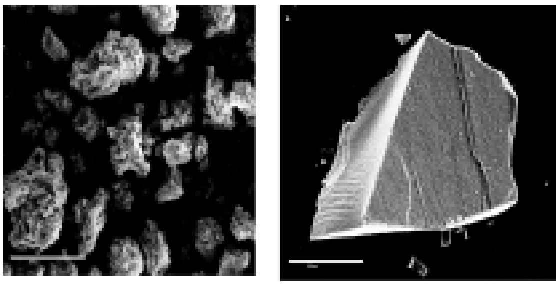
Having prepared the allylated ligands **7** and **8** as “functional monomers”, attention could be given to generating the corresponding MIP`s following the sequence of steps summarised below, and illustrated for the preparation of MIP **20** from the diamide **8** in Scheme 4.

(i) *Mixing* a methanolic solution of the “functional monomer” with an aqueous solution of the “print molecule” (K_2PtCl_4) in a 1:1 molar ratio to afford the corresponding Pt complex.
(ii) *Co-polymerisation* of the Pt complex with a twenty-fold excess of the cross-linking agent, ethylene glycol dimethyl acrylate (EGDMA), in the presence of the initiator, azoisobutyronitrile (AIBN).
(iii) *Washing* the crude co-polymer with chloroform and methanol to remove unreacted “functional monomer.”
(iv) *Grinding* the dried co-polymer to afford granules.
(v) *Leaching* the “print molecule” (K_2PtCl_4) from the co-polymer granules to afford the MIP’s **20** and **21**.



Scheme 4 Preparation of the platinum-selective MIP 20.

"Blank" co-polymers were prepared similarly using the functional monomers but excluding the "print molecule" in each case. Scanning Electron Microscopy (SEM) of the co-polymer particles (Fig. 1) clearly reveals the contrast between the smooth surface of the blank co-polymer granules and the rough, pitted surface of the MIP granules.



(a) (b)

Fig. 1 SEM pictures of the polymer particles: (a) MIP **20** granules; (b) blank co-polymer granules.

Evaluation of ligand extraction efficiency

Disulfides of the type, $RSCH_2SR$ and $RSCH_2CH_2SR$, and dialkyl sulfoxides have been shown to extract selectively palladium and, somewhat less efficiently, platinum,[20] and it is evident that the 3,6-dithiaoctane-(**1**) and 3,7-dithianonanediamides (**2**) prepared in this study exhibit similar selectivity for these PGMs in the presence of the base metals, Cu(II), Ni(II) and Co(II). In view of the kinetic inertness of Pt(II), the solvent extraction studies were conducted using Pd(II) as the representative PGM. The ligands were dissolved in toluene or methyl isobutyl ketone (MIBK), warming when necessary to effect complete dissolution, while the metal salts ($PdCl_2$, $CoCl_2.H_2O$, $NiCl_2.6H_2O$ and $CuCl_2.2H_2O$) were dissolved in 1M-HCl, the concentration of each metal being 1×10^{-3}M. Equal volumes of each phase were stirred vigorously in a jacketed vessel at 30°C; aliquots were removed at 10 minute intervals and the residual aqueous metal concentrations were determined by ICP-MS analysis. The resulting data (illustrated for ligand **1f** in Fig. 2) reveals several interesting features.

(i) The 3,6-dithiaoctanediamide ligands **1a-f** generally show higher selectivity for Pd(II) than the longer chain 3, 7-dithianonanediamides **2a**, **c** and **d**.
(ii) The *ortho*-chloro ligand **1e** in toluene exhibits significantly less selectivity for Pd(II) than the other ligands.
(iii) Equilibration is normally achieved within *ca* 10 minutes for ligands **1** and *ca.* 20 minutes for ligands **2**.

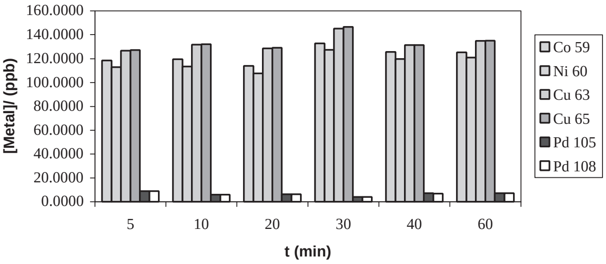


Fig. 2 Results of ICP-MS analysis of residual metal concentrations in the aqueous phase during competitive extraction with the 3,6-dithiaoctanediamide ligand **1f** in toluene.

The Pt(II)-imprinted MIPs **20** and **21** were evaluated *both* by shaking with a concentrated solution containing Co(II), Cu(II), Ni(II), Pd(II) and Pt(II) ions in 2% aq. HCl *and* by using the MIP granules as the stationary phase in "column" separations. In the shaking studies, the supernatant liquid was sampled at various time intervals, and ICP-MS analysis indicated some initial (<4.5h) selectivity for Pd(II) but subsequent displacement by the more kinetically inert Pt(II) ions. Elution of the metal ion solution through granules of MIP **21** in a semi-micro scale "column" resulted in complete removal of Pd(II) and partial removal of Pt(II) (Fig. 3). Not surprisingly, the corresponding blank co-polymer exhibited no selectivity for either Pd(II) or Pt(II). While equilibration was clearly not achieved under these exploratory conditions, the Pt(II) extraction efficiency of MIP **21** should be improved by re-cycling the eluant or increasing the column length. In marked contrast, MIP **20** exhibited significantly less selectivity for either Pd(II) or Pt(II) than MIP **21**.

In conclusion, it is apparent that dithiadiamide ligands of type **1** and **2** and MIP **21** show considerable promise for the selective extraction of PGMs from mixtures containing the base metals, cobalt copper and nickel.

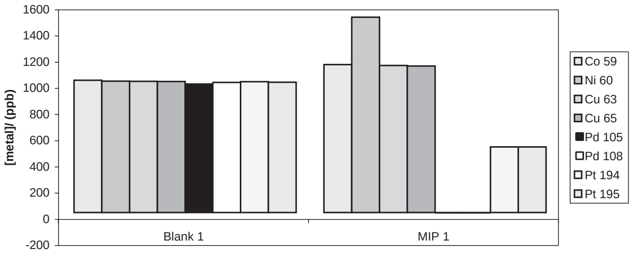


Fig. 3 ICP-MS data showing the metal ions present in the metal ion solution after passage through the reference polymer "blank 1" and MIP **21**. [Note: For MIP **21** the residual Pd(II) concentrations could not be detected!]

Experimental

Reagents were used as supplied by the manufacturers. Where necessary, solvents were dried by literature methods[21] and distilled before use. Silica gel 60 (Merck; particle size 0.040–0.063mm) was used as the stationary phase for flash chromatography. ^1H (400MHz) and ^{13}C (100MHz) NMR spectra were recorded on a Bruker AVANCE 400MHz spectrometer; chemical shifts are reported relative to the solvent signals. Infrared spectra were recorded on a Perkin-Elmer spectrum 2000 FT-IR spectrometer either as KBr discs or as thin films between NaCl windows (mid-infrared) and polyethylene windows (far-infrared). Melting points were determined using a Reichert hot-stage apparatus and are uncorrected. Low-resolution mass spectra were recorded on a Finnigan-MAT GCQ mass spectrometer, while high-resolution mass spectrometric data were obtained by Dr Phillip Boshoff (Cape Technikon Mass Spectrometry Unit or by Dr Louis Fourie (Potchefstroom University). Microanalysis (combustion analysis) data were obtained by Mr P. Benincasa (University of Cape Town). Scanning electron micrographs were obtained on a JEOL JSM 840 SEM instrument, and the ICP-MS data were obtained by Dr Eric Hosten (University of Port Elizabeth).

The preparation and characterisation of compounds **1a–f**, **2a**, **2b** and **5a–f**,[11] **11** and **15**[22] have been reported previously. The synthesis of new compounds in this study is illustrated by the following examples.

N,N'-Bis(2-methoxyphenyl)-3,7-dithianonanediamide **2c**: A solution of 1,3-dibromopropane (0.497g, 2.64mmol) in MeOH (10ml) was added dropwise to a stirred solution of 2-mercapto-*N*-(2-methoxyphenyl)ethanamide **5c** (0.970g, 4.92mmol) and KOH (0.28g, 5.0mmol) in MeOH (60ml). The reaction mixture was stirred at room temperature for 24 h before adding H_2O (30 ml) and evaporating the MeOH *in vacuo*. The residual aqueous phase was extracted with EtOAc (3 × 30ml), and the combined extracts were dried (anhyd. $MgSO_4$). The solvent was evaporated *in vacuo* and the crude oily residue purified by flash chromatography [elution with EtOAc-$CHCl_3$ (1:9)] to afford, as a golden, viscous oil, N,N'-*bis(2-methoxyphenyl)-3,7-dithianonanediamide* **2c** (0.392g, 36.6%) (Found: MH^+, 435.141407. $C_{21}H_{26}N_2O_4S_2$ requires: M+1, 435.141226); ν_{max} (nujol)/cm^{-1} 3326 (NH) and 1661 (C=O); δ_H (400MHz; $CDCl_3$) 1.88 (2H, quintet, 5-CH_2), 2.66 (4H, t, 4- and 6-CH_2), 3.29 (4H, s, 2- and 8-CH_2), 3.80 (6H, s, OCH_3), 6.81 (2H, d, 3'- and 3''-H), 6.89 (2H, t, 5'- and 5''-H), 6.99 (2H, t, 4'- and 4''-H), 8.28 (2H, d, 6'- and 6''-H) and 9.16 (2H, s, NH); δ_C (100MHz; $CDCl_3$) 27.9 (C-5), 31.2 (C-4 and

C-6), 36.9 (C-2 and C-8), 55.4 (2 × OCH$_3$), 109.8, 119.3, 120.6, 123.8, 126.8 and 148.0 (Ar–C) and 166.3 (C=O).

N, N'-Bis(4-allyloxyphenyl)-3,6-dithiaoctanediamide **8**: A solution of 1,2-dibromoethane (0.131g, 0.697mmol) in MeOH (10ml) was added drop-wise to a stirred solution of *N*-(4-allyoxyphenyl)-2-mercaptoethanamide **7** (0.298g, 1.34mmol) and KOH (0.0753g, 1.34mmol) in MeOH (60ml). The reaction mixture was stirred at room temperature for 24 h before adding H$_2$O (30 ml) and evaporating the MeOH *in vacuo*. The residual aqueous phase was extracted with EtOAc (3 × 30ml), and the combined extracts were dried (anhyd. MgSO$_4$). The solvent was evaporated *in vacuo* and the crude diamide recrystallised from EtOH to yield, as yellow crystals, N,N'-*bis(4-allyloxyphenyl)-3,6-dithiaoctanediamide* **8** (0.117g, 37.0%), m.p. 120–124°C (Found: M$^+$, 472.149845. C$_{24}$H$_{28}$N$_2$S$_2$O$_4$ requires: *M*, 472.149051); ν_{max} (KBr)/cm^{-1} 3300 (NH) and 1654 (C=O); δ_H (400MHz, CDCl$_3$) 2.86 (4H, s, SCH$_2$CH$_2$S), 3.33 (4H, s, COCH$_2$), 4.50 (4H, d, CH$_2$O), 5.33 (4H, 2 × d, C*H*$_2$=CH), 6.02 (2H, m, CH$_2$=C*H*), 6.83 (4H, d, 2'-, 2"- 6'- and 6"-H), 7.42 (4H, d, 3'-, 3"-, 5'- and 5"-H) and 8.53 (2H, s, NH); δ_C (100MHz; CDCl$_3$) 31.9 (C-4 and C-5), 36.4 (C-2 and C-7), 69.1 (2 × CH$_2$O), 115.0, 117.7, 121.8, 130.7, 133.2 and 155.7 (CH$_2$=CH and Ar-C) and 167.0 (C=O).

cis-*Dichloro-(N,N'-diphenyl-3,6-dithiaoctanediamide)-S,S'-palladium(II)* **16a**: To a stirred 0.001M solution of PdCl$_2$ in 0.1000M aq.HCl (20ml), a solution of *N,N'*-diphenyl-3,6-dithiaoctanediamide **1a** (7.1mg, 0.020mmol) in MeOH (80ml) was added drop-wise. The mixture was stirred for 48h, and the resulting yellow solution was evaporated *in vacuo*. The residual solid was washed with methanol and dried under high vacuum to yield, as a yellow powder, cis-dichloro-(*N,N'*-diphenyl-3,6-dithiaoctanediamide)-*S,S'*-palladium(II) **16a** (9.6mg, 89%), m.p. 230–236^{o}C (decomp.) (Found: C, 40.6; H, 3.4; N, 5.2%; MH$^+$, 536.945207. C$_{18}$H$_{20}$N$_2$O$_2$S$_2$PdCl$_2$ requires: C, 40.3; H, 3.8; N, 5.2%; *M*+1, 536.945627); ν_{max} KBr/cm^{-1} 3299 (NH) and 1667 (C=O); ν_{max} (polyethylene)/cm^{-1} 336 and 326 (Pd–Cl); δ_H (400MHz; DMSO-d$_6$) 3.56/3.65[†] (4H, m, 4- and 5- CH$_2$), 4.08–4.48 (4H, 4 × d, 2- and 7-CH$_2$), 7.10 (2H, t, 4'- and 4"-H), 7.34 (4H, t, 3', 3"-, 5'- and 5"-H), 7.60 (4H, d, 2'-, 2"-, 6'- and 6"-H) and 10.52/10.58 (2H, 2 × s, NH); δ_C (100MHz; DMSO-d$_6$) 31.5/35.1 (C-4 and C-5), 38.2/41.3 (C-2 and C-7), 119.1/119.4, 123.3/123.9, 128.6/128.7 and 138.2/138.9 (Ar–C) and 163.8 (C=O).

cis-*Dichloro-[N,N'-bis(2-methoxyphenyl)-3,6-dithiaoctanediamide]-S,S'-platinum(II)* **17c**: A stock solution was made by dissolving *N,N'*-bis(2-methoxyphenyl)-3,6-dithiaoctanediamide **1c** (0.068g, 0.162mmol) and *N,N*-dimethylaniline (0.375g, 3.1mmol) in MeOH-acetone (4:1; 40ml). To a stirred 0.001M solution of K$_2$PtCl$_4$ in 0.0974M aq. HCl (2ml), the stock solution (12.8ml) was added dropwise, and the resulting solution was stirred for 24h. The fine precipitate was filtered off, washed with MeOH and dried *in vacuo* to afford, as a fine cream powder, cis-*dichloro*-[N, N'-*bis(2-methoxyphenyl)-3,6-dithiaoctanediamide]*-S,S'-*platinum(II)* **17c** (28.4mg, 25.6%), m.p. 180–184^{o}C (Found: C, 34.5; H, 3.2; N, 3.9%; MH$^+$, 686.029142. C$_{20}$H$_{24}$N$_2$O$_4$S$_2$PtCl$_2$ requires: C, 35.0; H, 3.5; N, 4.1%; *M* +1, 686.028067); ν_{max} (KBr)/cm^{-1} 3410 (NH) and 1685 (C=O); ν_{max} (polyethylene)/cm^{-1} 326 and 316 (Pt–Cl); δ_H (400MHz; DMSO-d$_6$) 3.18/3.47 (4H, 2 × d, *J* 9.5Hz, 4- and 5-CH$_2$), 3.84 (6H, s, OC*H*$_3$), 4.09/4.30/4.46 (4H, 3 × d, 2- and 7-CH$_2$), 6.92, 7.07 (2H, d, 6'- and 6"-H), 7.12 (2H, d, 3'- and 3"-H), 7.87 (2H, t, 5'- and 5"-H), 9.81/9.86 (2H, 2 × s, NH); δ_C (100MHz; CDCl$_3$) 38.0/38.2 (C-4 and C5), 40.0/40.8 (C-2 and C-7), 55.2 (OCH$_3$), 110.9, 119.7, 122.0/122.2, 124.8/124.9, 125.7 and 149.5/149.6 (Ar-C) and 163.9/164.0 (C=O).

Preparation of the MIPs

MIP 20

A solution of *N,N'*-bis(4-allyloxyphenyl)-3,6-dithiaoctanediamide **8** (0.051g, 0.107mmol) in MeOH (3ml) was added drop-wise to a solution of K$_2$PtCl$_4$ (0.044g, 0.106mmol) in water (1ml), and the mixture stirred overnight at room temperature. A fine precipitate formed, and the methanol-water supernatant mixture was removed using a Pasteur pipette. The residual solid was redissolved in DMF (3ml) in a boiling tube and EGDMA (0.420g, 2.47mmol) was added under nitrogen. AIBN (0.0018g) was added, and the mixture was heated at 65˚C for 4h and then left to stand at room temperature overnight. The resulting yellow solid was washed sequentially with CHCl$_3$ and MeOH and then dried *in vacuo* to afford the crude yellow polymer (*ca* 0.8g). After washing with conc. HCl and MeOH, and drying *in vacuo* for 2 days, cream particles of MIP-**20** were obtained.

MIP 21

EGDMA (0.315g, 1.64mmol) was added under nitrogen to a solution of the Pt(II) complex of *N*-(4-allyloxyphenyl)-2-mercaptoethanamide **7** {prepared as described for *cis*-dichloro-[*N,N'*-bis(2-methoxyphenyl)-3,6-dithiaoctanediamide]-*S,S'*-platinum(II) **17c**; 0.040g, 0.082mmol} in DMF (3ml) in a boiling tube. AIBN (1.3mg) was added, and the mixture was heated at 65˚C for 4h and then left to stand at room temperature overnight. The resulting solid was removed from the tube, washed with MeOH and dried *in vacuo* to afford a yellow-green polymer (*ca* 0.7g). The polymer was ground into fine particles and washed several times with conc. HCl and then kept in conc. HCl overnight. Repeated washing with conc. HCl and then with MeOH, followed by drying *in vacuo* for 2 days afforded pale-yellow particles of MIP **21**.

Blank synthesis

The experimental procedure employed for the synthesis of MIP **20** was followed (in the absence of the metal), using the ligands, *N,N'*-(4-allyloxyphenyl)-2,6-dithiaoctanediamide **8** for the preparation of Blank-1 and *N*-(4-allyloxyphenyl)-2-mercaptoethan-amide **7** for Blank-2.

Data for other, new compounds prepared in this study are as follows.

N,N'-Bis(3-chlorophenyl)-3,7-dithianonanediamide **2d**: as cream crystals (0.035g, 3.74%), m.p. 96–98°C (Found: MH$^+$, 443.042896. C$_{19}$H$_{20}$N$_2$O$_2$S$_2$Cl$_2$ requires: *M*+1, 443.042152); ν_{max} (nujol)/cm^{-1} 3338 (NH) and 1647 (C=O); δ_H (400MHz; CDCl$_3$) 1.95 (2H, quintet, 5-CH$_2$), 2.70 (4H, t, 4- and 6-CH$_2$), 3.36 (4H, s, 2- and 8-CH$_2$), 7.10 (2H, d, 4'- and 4"-H), 7.24 (2H, t, 5'- and 5"-H), 7.39 (2H, d, 6'- and 6"-H), 7.66 (2H, s, 2'- and 2"-H) and 8.57 (2H, s, NH); δ_C (100MHz; CDCl$_3$) 27.9 (C-5), 31.4 (C-4 and C-6), 36.8 (C-2 and C-8), 117.7, 119.8, 124.8, 130.1, 134.8 and 138.4 (Ar-C) and 166.9 (C=O).

N,N'-Bis(2-chlorophenyl)-3,7-dithianonanediamide **2e**: as white crystals (0.187g, 17.2%), m.p. 126–128^{o}C (Found: M$^+$, 442.034589. C$_{19}$H$_{20}$N$_2$S$_2$O$_2$Cl$_2$ requires: *M*, 442.034327); ν_{max} (KBr)/cm^{-1} 3296 (NH) and 1662 (C=O); δ_H (400MHz, CDCl$_3$) 1.97 (2H, quintet, 5-CH$_2$), 2.75 (4H, t, 4- and 6-CH$_2$), 3.40 (4H, s, 2- and 8-CH$_2$), 7.05 (2H, t, 4'- and 4"-H), 7.27 (2H, t, 5'- and 5"-H), 7.36 (2H, d, 3'- and 3"-H), 8.35 (2H, d, 6'- and 6"-H) and 9.29 (2H, s, NH); δ_C (100MHz; CDCl$_3$) 28.2 (C-5), 31.7 (C-4 and C-6), 37.4 (C-2 and C-8), 121.3, 123.3, 125.0, 127.7, 129.1 and 134.2 (Ar–C) and 166.7 (C=O).

N,N'-Bis(2-methylphenyl)-3,7-dithianonanediamide **2f**: as white crystals (0.371g, 37.5%), m.p. 116–118^{o}C (Found: M$^+$, 402.143602. C$_{21}$H$_{26}$N$_2$O$_2$S$_2$ requires: *M*, 402.143572); ν_{max} (KBr)/cm^{-1} 3230 (NH) and 1656 (C=O); δ_H (400MHz; CDCl$_3$) 1.98 (2H, quintet, 5- CH$_2$), 2.27 (6H, s, CH$_3$), 2.74 (4H, t, 4- and 6-CH$_2$), 3.38 (4H, s, 2- and 8-CH$_2$), 7.05–7.22 (6H, series of multiplets, 3'-, 3"-, 4'-, 4"-, 5'- and 5"-H), 7.88 (2H, d, 6'- and 6"-H) and 8.59 (2H, s, NH); δ_H (100MHz; CDCl$_3$) 17.6 (CH$_3$), 28.2 (C-5), 31.6 (C-4 and C-6), 36.9 (C-2 and C-8), 122.1, 125.2, 126.8, 128.5, 130.5 and 135.3 (Ar–C) and 166.5 (C=O).

N-(4-Allyloxyphenyl)-2-mercaptoethanamide **7**: as white crystals (0.61g, 40%), m.p. 102–104˚C (Found: M$^+$, 223.0668. C$_{11}$H$_{13}$NO$_2$S requires: *M*, 223.06670); ν_{max} (KBr)/cm^{-1} 3295 (NH), 2569 (SH) and 1657 (C=O); δ_H (400MHz; CDCl$_3$) 2.01 (1H, t, SH), 3.36 (2H, d, CH$_2$S), 4.50 (2H, d, CH$_2$O), 5.33 (2H, 2xd, C*H*$_2$=CH), 6.03 (1H, m, CH$_2$=C*H*), 6.87 (2H, d, 2'- and 6'-H), 7.42 (2H, d, 3'- and 5'-H) and 8.43 (1H, s, NH); δ_C (100MHz; CDCl$_3$) 29.0 (CH$_2$), 69.1 (OCH$_2$), 115.1, 117.7, 121.8, 130.5, 133.2, 155.8 (CH$_2$=CH and Ar–C) and 167.0 (C=O).

cis-*Dichloro-[N,N'-bis(2-methoxyphenyl)-3,6-dithiaoctanediamide]-S,S'-palladium(II)* **16c**: as an orange powder (2.9mg, 26%), m.p. 132–134^{o}C (Found: M$^+$, 595.95876. C$_{20}$H$_{24}$N$_2$O$_4$S$_2$Cl$_2$^{106}Pd requires: *M*, 595.95893); ν_{max} (KBr)/cm^{-1} 3270 NH) and 1661 (C=O); ν_{max} (polyethylene)/cm^{-1} 327 and 302 (Pd–Cl); δ_H (400MHz; DMSO-d$_6$) 3.45/3.63 (4H, 2 × d, 4- and 5-CH$_2$), 3.84 (6H, s, OCH$_3$), 4.23/4.44 (4H, 2 × d, 2- and 7-CH$_2$), 6.92 (2H, t, 4'- and 4"-H), 7.07 (2H, d, 6'- and 6"-H), 7.13 (2H, d, 3'- and 3"-H), 7.88 (2H, t, 5'- and 5"-H) and 9.82/9.86 (2H, 2 × s, NH); δ_C (100MHz; DMSO-d$_6$) 38.2/38.5 (C-4 and C-5), 42.2/42.6 (C-2 and C-7), 55.6 (OCH$_3$), 111.3, 120.1, 122.5/122.7, 125.2/125.3, 126.1/126.2 and 149.9/150.1 (Ar–C) and 163.9/164.0 (C=O).

cis-*Dichloro-[N,N'-bis(2-chlorophenyl)-3,6-dithiaoctanediamide]-S,S'-palladium(II)* **16e**: as an orange powder (10.9mg, 90.0%) (Found: C, 35.50; H, 2.6; N, 4.5%; MH$^+$, 604.868827. C$_{18}$H$_{18}$N$_2$S$_2$O$_2$PdCl$_4$ requires: C, 35.8; H, 3.0; N, 4.6%; *M*+1, 604.867683); ν_{max} (KBr)/cm^1 3264 (NH) and 1662 (C=O); ν_{max} (polyethylene)/cm^{-1} 327 and 305 (Pd–Cl);

[†] Chemical shift data cited in this format, here and elsewhere, indicates signal doubling due to the presence of geometric isomers.

δ_H (400MHz; DMSO-d_6) 3.48/3.65 (4H, series of multiplets, 4- and 5-CH_2), 4.21/4.45 (4H, 2 × overlapping doublets, 2- and 7- CH_2), 7.25 (2H, t, 4'- and 4''-H), 7.36 (2H, t, 5'- and 5''-H), 7.52 (2H, d, 3'- and 3''-H), 7.70 (2H, d, 6'- and 6''-H) and 10.15 and 10.21 (2H, 2 × s, NH); δ_C (100MHz; DMSO-d_6) 38.2/38.6 (C-4 and C-5), 40.5/40.8 (C-2 and C-7), 126.4/126.5, 126.7/126.8, 127.0/127.1, 127.4, 129.5 and 133.9 (Ar–C) and 164.4 (C=O).

cis-*Dichloro-N,N'-bis(2-methylphenyl)-3,6-dithiaoctanediamide palladium(II)* **16f**: as a yellow powder (7.3mg, 66%), m.p. 184–188°C (decomp.) (Found: MH^+, 564.976747. $C_{20}H_{24}N_2O_2S_2PdCl_2$ requires: *M*+1: 564.976927); ν_{max} (KBr)/cm^{-1} 3272 (NH) and 1654 (C=O); ν_{max} (polyethylene)/cm^{-1} 329 and 306 (Pd–Cl); δ_H (400MHz; DMSO-*d_6*) 2.23 (6H, s, CH_3), 3.32–3.64 (4H, series of multiplets, 4- and 5-CH_2), 4.11–4.41 (4H, series of multiplets, 2- and 7-CH_2), 7.10–7.24 (6H, series of multiplets, 3'-, 3''-, 4'-, 4''-, 5'- and 5''-H), 7.41 (2H, t, 6'- and 6''-H) and 9.83/9.90 (2H, 2 × s, NH); δ_C (100MHz; DMSO-d_6) 17.8 (CH_3), 39.0/39.1 (C-3 and C-4), 39.6/40.0 (C-2 and C-7), 125.0/125.2, 125.7/125.8, 125.9, 130.3/130.4, 131.7/132.0 and 135.3/135.4 (Ar-C) and 164.1/164.2 (C=O).

cis-*Dichloro-[N,N'-bis(2-chlorophenyl)-3,6-dithiaoctanediamide]-S,S'-platinum(II)* **17e**: as lemon-yellow powder (49.9mg, 59%), m.p. 250–254°C (Found: C, 31.0; H, 2.2; N, 4.0%; MH^+, 693.929435. $C_{18}H_{18}N_2O_2S_2PtCl_4$ requires: C, 31.1; H, 2.6; N, 4.0%; *M*+1, 693.928993); ν_{max} (KBr)/cm^{-1} 3267 (NH) and 1660 (C=O); ν_{max} (polyethylene)/cm^{-1} 328 and 309 (Pt–Cl); δ_H (400MHz, DMSO-d_6) 3.20/3.52 (2H, d, 4- and 5- CH_2), 4.05–4.58 (4H, 2 × d, 2- and 7- CH_2), 7.23–7.37 (4H, series of multiplets, 3'-, 3''-, 4'- and 4''-H), 7.52 (2H, d, 6'-and 6''-H), 7.70 (2H, t, 5'- and 5''-H) and 10.19/10.28 (2H, 2 × s, NH); δ_C (100MHz; DMSO-*d_6*) 38.5/38.6 (C-4 and C-5), 39.1/39.9 (C-2 and C-7), 126.5/126.5, 126.7/126.8, 127.0/127.1, 127.4/127.4, 129.4/129.5 and 133.9/133.9 (Ar-C) and 164.6/164.7 (C=O).

cis-*Dichloro-[N,N'-bis(4-allyloxyphenyl)-3,6-dithiaoctanediamide]-S,S'-platinum(II)* **18**: as a yellow powder (0.0231g, 59.2%), (Found: MH^+, 738.059844. $C_{24}H_{28}N_2O_4S_2PtCl_2$ requires: *M*+1, 738.059367); ν_{max} (KBr)/cm^{-1} 3301 (NH) and 1658 (C=O); ν_{max} (polyethylene)/cm^1 329 and 310 (Pt–Cl); δ_H (400MHz; DMSO-d_6) 3.23/3.49 (4H, 2 × d, 4- and 5-CH_2), 3.87–4.35 (4H, 2 × d, 2- and 7-CH_2), 4.52 (4H, d, OCH_2), 5.25/5.38 (4H, 2 × d, CH=C*H_2*), 6.03 (2H, m, C*H*=CH_2), 6.93 (4H, d, 2'-, 2''-, 6'- and 6''-H), 7.48 (4H, d, 3'-, 3''-, 5'- and 5''-H) and 10.38/10.34 (2H, 2 × s, NH); δ_C (100MHz; DMSO-d_6) 38.6/39.3 (C-4 and C-5), 40.1/41.2 (C-2 and C-7), 68.2 (OCH_2), 114.6/114.7, 117.3, 120.9/121.0, 131.3/131.4, 133.6/133.7 and 154.6/154.6 (CH=CH_2 and Ar-C) and 163.6/136.6 (C=O).

Solvent extraction using the dithiadiamide ligands

The metal solutions were prepared by dissolving the appropriate quantity of the metal salt ($PdCl_2$, $CoCl_2.H_2O$, $NiCl_2.6H_2O$ or $CuCl_2.2H_2O$) in 1M aq. HCl, such that the concentration of each of the metals was 1×10^{-3}M. The ligand solutions were prepared by dissolving the appropriate amount of each of the 3,6-dithiaoctanediamide ligands **19a–f** or 3,7-dithianonanediamide ligands **20a**, **c** and **d** in either toluene or MIBK, such that the concentration of the ligand was 1.1×10^{-3}M. Equal volumes (50ml for toluene extractions and 20ml for MIBK extractions) of each phase were stirred vigorously in a jacketed beaker (150 ml) maintained at 30°C using a digital thermostat. Aliquots (2ml) of each phase were removed after 5, 10, 20, 30, 40 and 60 minutes. The aqueous aliquots were evaporated to dryness on a steam bath to remove residual organic solvents and then diluted to afford 10ml solutions. The residual metal concentrations were determined by ICP-MS analysis.

Metal extraction using the MIPs

The metal ion solutions were prepared by dissolving the appropriate quantity of the metal salt ($PdCl_2$, $CoCl_2.H_2O$, $NiCl_2.6H_2O$ and $CuCl_2.2H_2O$) in 2% aq. HCl, such that the concentration of each of the metals was 400ppm.

Method A: The finely ground polymer particles (100mg and 50mg for the MIP and blank respectively) were mechanically shaken with the metal solution (5ml and 2.5ml; for the MIP and blank, respectively) for 17.5h. Equilibration was monitored over this period by analysing the solutions after shaking for 5min, 30min, 1.5h, 4.5h and 17.5h; the samples, in each case, were diluted to afford metal concentrations of *ca.*1ppm for ICP-MS analysis.

Method B: The polymer particles (100mg) were loaded into a Pasteur pipette, and the metal ion solution (5ml) was passed through the column. The eluant was then analysed by ICP-MS following dilution as indicated in Method A.

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