DALTON
FULL PAPER

Cycloplatinated ferrocenylamine-carboxylate and dithiocarbamate complexes: synthesis and aqueous properties

Kim McGrouther, Debbrah K. Weston, Delwyn Fenby, Brian H. Robinson * and Jim Simpson

Department of Chemistry, University of Otago, P.O. Box 56, Dunedin, New Zealand.
E-mail: brobinson@alkali.otago.ac.nz

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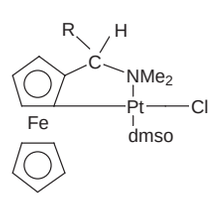
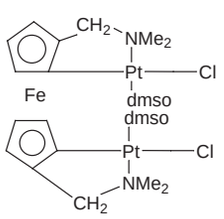
Metathetical reaction of the cyclometallated ferrocenylamine complexes [Pt{FeCp(σ,η^5-$C_5H_3CHRNMe_2$)}(dmso)Cl] (R = H **1** or Me **3**) and [Pt_2{Fe(σ,η^5-$C_5H_3CH_2NMe_2)_2$}$(dmso)_2Cl_2$] **2** with TlX (X = OAc or malonate), or the direct reaction with $P(C_6H_4SO_3$-*m*$)_3^{3-}$ (tppms) and $Et_2NCS_2^-$(dedtc), gave [Pt{FeCp(σ,η^5-$C_5H_3CHRNMe_2$)}(dmso)(OAc)], [{Pt[FeCp(σ,η^5-$C_5H_3CHRNMe_2$)](dmso)}$_2$(mal)] (mal = malonate), Na_5[Pt{FeCp(σ,η^5-$C_5H_3CHRNMe_2$)}$(tppms)_2$], [Pt{FeCp(σ,η^5-$C_5H_3CHRNMe_2$)}(dedtc)] and bis-Pt analogues. These complexes were characterised by analysis, ES-MS and ^{1}H, ^{13}C and ^{195}Pt NMR. Metathetical reaction of **1**–**3** with silver(I) salts generally gave ferrocenium derivatives. Substitution *trans* to the Pt–N or Pt–C bond is determined by the acceptor character of the co-ordinating group and this together with steric constraints limit the range of carboxylato complexes. The acetato complex [Pt{FeCp(σ,η^5-$C_5H_3CH_2NMe_2$)}(dmso)(OAc)] crystallises with one molecule of H_2O and a single crystal structure indicates a hydrogen bond between a solvent H_2O and acetate ligand. Aqueous solutions of the water-soluble OAc, malonate and tppms complexes were studied by electrochemical and spectroscopic techniques. Their chemistry is regulated by pH-dependent equilibria involving aqua and hydroxo complexes and competing oxidation to the ferrocenium compound by molecular oxygen.

Introduction

Ferrocene is a useful building block for the synthesis of derivatives which feature as enzyme inhibitors,[1] therapeutic agents,[2] metabolic competitors,[3] antimicrobial compounds,[4] radiopharmaceutical[5] and histological agents.[6] Their potential as anti-tumour agents is well documented.[7] While their lipophilic character is ideal for crossing cellular membranes, their toxicity is dependent on the metabolism to water soluble derivatives *via* hydroxylation. Detoxification primarily occurs inside the liver microsomes.[8] Conjugates of ferrocenylamines and platinum(II) are of particular interest because they may be selective molecular carriers possessing the antineoplastic properties of ferrocene and the well known cisplatin [$PtCl_2(NH_3)_2$].[9] Ferrocenylamine analogues of cisplatin[10,11] have been made but the facile cycloplatination of ferrocenylamines has provided[12–14] a versatile series of complexes which incorporate the two cytostatic moieties (**1**–**3** are used in the work described herein).



R = H, **1**; R = Me, **2**



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Toxicity, histological, platinum distribution and antitumour studies in mice have shown that these cyclometallated ferrocenylamines exhibit kidney rather than liver dysfunction, that they have reasonable toxicity and are mildly cytotoxic against standard tumours.[15] However, **1**–**3** were active against cisplatin resistant cell lines. One of the difficulties with biological studies on the cyclometallated compounds has been their low solubility in water or saline solution; for example, peanut oil was used as a vehicle for drug injection in the toxicity work and irritation of the kidney may have been a contributing factor in the hepatoxicity.[15] It was also not clear whether, *in vivo*, the complexes remained intact. We therefore set out to increase the aqueous solubility, at the same time extending the range of leaving and biologically active groups in the platinum(II) co-ordination sphere. There are two potential co-ordination sites, *trans* to either the Pt–C (σ site) or the Pt–NMe_2 bond (π site), but each have specific electronic requirements. Hard neutral or anionic monodentate species or a softer donor of a chelate occupy the σ site whereas soft π acceptors can replace dmso.[14] Farrell[16] has shown that Pt^{II}–dmso complexes bind to DNA forming interstrand crosslinks by the displacement of dmso but a ferrocenyl cyclometallated configuration appears to strengthen the Pt–S bond as indicated by the shorter Pt–S bond length[12] and slow reactions with π acceptors.

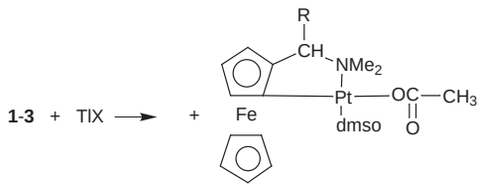
Target ligands for the work described in this paper were those with potential O–O (oxalate, ox; malonate, mal; cyclobutane-1,1-dicarboxylate, cbdc), O–S (*O*-alkyl dithiocarbonate), N–S (cysteine) or S–S (diethyldithiocarbamate, dedtc) functionality as well as OAc and anionic P-donors. Within the O–O group malonate may either bridge, chelate or bind as mal-*O* whereas ox or cbdc must chelate; this sequence would also give an insight on the influence of the bite angle on the leaving group. Malonate is biologically active and platinum(II) complexes in which ferrocene is tethered to mal-*O* were found[17] to be active against P338 murine leukemia cells, with congruent liver and spleen deposition. Diethyldithiocarbamate has also shown clinically therapeutic cytotoxic effects in conjunction with platinum drugs[17,18] and it is capable of S–N, S or S–S binding. Complexes with sulfonated phosphines are a standard method to increase water solublity[19] and ferrocenylphosphines have inherent biological activity.[20] Steric and electronic factors dictated that not all binding modes were achievable and the characterised complexes, solution and redox properties are described herein.

Results and discussion

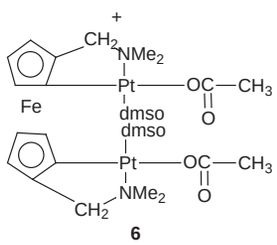
Synthesis and structure

Carboxylates. Metathetical reactions with thallium(I) salts

gave a convenient route to the acetato complexes **4** and **5** (eqn. 1). Although **4** was accessible in good yield from AgOAc,

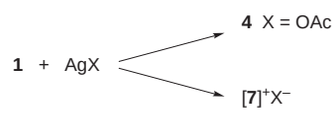


R = H **4**; R = Me **5**



6 (1)

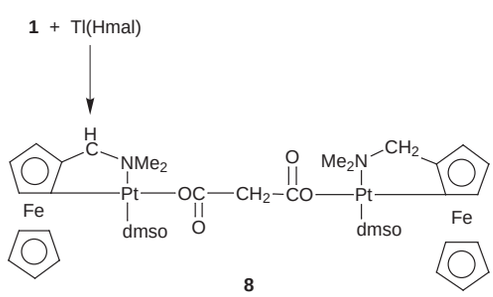
metathetical reactions of **2** and **3** with AgOAc, and **1** with all other silver(I) salts, resulted in oxidation of the ferrocenyl moiety, eqn. (2).



(2)

The hygroscopic ferrocenium salts **7** from $AgNO_3$ oxidation were characterised and provided a set of water-soluble salts for sensitisation studies.[21] Compounds **4–6** were characterised by microanalysis, ES-MS, FAB-MS, ^{1}H, ^{13}C (DEPT and heteronuclear correlation, HETCOR) and ^{195}Pt NMR spectroscopy. Owing to the lability of the acetate group the primary ions of **4–6** in ES-MS are $[(M - OAc) + CH_3CN]^+$; at high cone voltages (40 or 80 V) both the CH_3CN and dmso are lost in the primary ion. Chemical shifts for **4–6** in organic solvents are similar to those for **1–3** with 'up and down' Me of the SMe_2 and NMe_2 groups appearing as four discrete resonances with ^{195}Pt–^{1}H satellites due to the planar chirality. ^{195}Pt NMR is a useful diagnostic tool in this work and the expected[22] upfield shift from δ_{Pt}[**1**] to δ_{Pt}[**4**] is observed. The preparation of racemic **5** is described but both DL and *meso* **5** were also prepared from the appropriate stereoisomer of **2**.

Reaction with thallium malonate gave compound **8**, eqn. (3).



8 (3)

Surprisingly, no reaction was observed between **2** or **3** and malonate, or with TlX, where X is a potential bidentate anion, oxalate, cyclobutanedicarboxylate or acetylacetonate. FAB-MS and ES-MS showed that the malonate **8** was dimeric in the solid. A parent ion was not observed. The primary ion is $[M - 2(dmso)]^+$ followed by the cleavage ion [**1** -Cl]$^+$, an ion which may be expected if the malonato group is *trans* to the (Fc) C–Pt bond. Vapour pressure osmometry also confirmed the dimeric formulation in solution, as did the NMR data. In particular, J(^{195}Pt-^{1}H), the CH_2 (mal) : Cp (Fc) ratio in the ^{1}H NMR and one carboxylato ^{13}C resonance were only compatible with a dimeric, O,O′ structure. Methyl and methylene carbon assignments, established *via* DEPT and HETCOR NMR, were compatible with the proposed structure and the non-equivalence of the prochiral NMe_2 and SMe_2 protons confirmed that the cyclometallated framework was maintained. Finally, the complementarity of δ_{Pt}[**4**] and δ_{Pt}[**8**] shows that only one O-donor is bound per cyclometallated unit. To our knowledge this is the first bridged malonato complex in platinum(II) chemistry. *trans*-Effects normally favour ring closure of an malonato-*O* over the formation of bridged complexes and sequential chelation with the active cisplatin species *cis*-[PtCl-$(NH_3)_2(OH_2)]^+$, and *cis*-$[Pt(NH_3)_2(OH_2)_2]^{2+}$, has been demonstrated.[23] We could find no spectroscopic evidence for either O or O,O′ binding modes during the formation of **8** in buffered or unbuffered solutions, or for bidentate malonato complexes of **2** and **3**. This is difficult to rationalise as, while steric reasons may inhibit the formation of a bis-platinum analogue of **8**, there are no constraints for a staggered structure derived from **2**; for example, complexes of **2** with bulky phosphines are known.[14]

An alternative approach starting with the *cis*-Pt$(dmso)_2$-(carboxylate) did not give cyclometallated products but, instead, resulted in protonation of the amine, a result not unexpected given the strong basicity of the ferrocenylamines.[12] Similarly, metathetical replacement of Cl in the precursors to **1–3**, *trans*-$[PtCl_2$(dmso)(ferrocenylamine)], under the conditions which gave cyclometallated complexes, led to cleavage of the ferrocenylamine L, eqn. (4). The inability to isolate

trans-$[PtCl_2(dmso)L] + TlX \longrightarrow$
trans-$[PtX_2(dmso)L] \longrightarrow$ decomp. (4)

complexes of chelating carboxylates of **1–3** can easily be understood by reference to the structure of **8**. Clearly, these carboxylates cannot bridge two cyclometallated units. Furthermore, the co-ordination of hard bases is restricted to a *trans* C–Pt site and chelation which requires the *trans* Pt–N site is not possible.

Compounds **4–6** and **8** were moderately soluble in water (**5** was the most soluble) but very soluble in 0.1 M NaOH as well as alcohols and CH_2Cl_2. A common feature of **4–6** was the crystallisation with loosely bound water molecules; these could be removed *in vacuo*. Values of δ_{Pt} for **4–6** and **8**, but not for those with other anionic groups *trans* to the Pt–C bond, show a strong solvent dependence (selected data are given in Table 1). For **4** hydrogen-bonding solvents cause a large upfield shift whereas the converse holds for **8**; the explanation for this is not obvious as the intermolecular interactions for individual cyclometallated units should be similar for **4** and **8**. This encouraged us to investigate the inter- and intra-molecular interactions in the crystal structure of **4**.

Crystal structure of compound 4. A perspective view of the molecule is shown in Fig. 1 with selected bond length and angle data in Table 2. Co-ordination about the Pt atom in compound **4** is similar to that observed in the closely related [Pt{CpFe-$(\sigma,\eta^5$-$C_5H_4CH_2NMe_2)$}(dmso)Cl][24] but with the chloro ligand replaced by an acetato group, bound through O(2), *trans* to the metallated C(3) atom of the dimethylaminomethylferrocene moiety. The co-ordination sphere is completed by a dmso ligand bound through S(1) and *trans* to the amine nitrogen N(1). The Pt–C bond distance in the acetato complex, 1.976(8) Å, is not significantly different from that observed in the chloro analogue or from those in other complexes with an equivalent set of donor atoms.[25] The Pt–S and Pt–N distances are also unremarkable. In contrast, the Pt(1)–O(2) distance, 2.115(5) Å, is significantly longer than those reported for platinum(II) acetato complexes.[26] This observation clearly reflects the considerable *trans* influence of the σ-bound C(3) atom noted previously.[12] The cyclopentadiene rings of the ferrocene moiety are planar, and inclined at an angle of 3.8(6)°; they adopt an approximately eclipsed conformation. The platinum bound

Table 1 ^{195}Pt NMR and $E_{1/2}$ data

Compound	Group *trans* to PtC	δ_{Pt}[a]	$E_{1/2}$[b]/V	Compound	Group X *trans* to PtC, L *trans* to PtN	δ_{Pt}[a]
8	mal	−2091	0.06	**9**	L = tppms, X = Cl	*−(2600)*
4	OAc	−2078	0.24	**11**	L = X = tppms	*−(3259)*
4	OAc	*−2122*	*0.23*			
1	Cl	−2143	0.25	**13**	L = X = dedtc	−1974
	Br	−2195	0.27		L = PPh_3, X = Cl	−2553
	I	−2279	0.30		L = CO, X = Cl	−2303
3	Cl	−2136, −2156	0.03	**14**	L = X = dedtc	−1981, −2227
6	OAc	−2075	0.03		L = PPh_3, X = Cl	−2557
	—	—	—	**12**	L = X = tppms	*−(3258)*

[a] δ_{Pt} in $CDCl_3$ except for those in italics which are in D_2O. [b] Recorded in CH_2Cl_2 except for those in italics which are in D_2O; referenced against SCE at 200 mV s^{-1}, platinum electrode at 20 °C.

Table 2 Selected bond lengths (Å) and angles (°) for compound **4**

Pt(1)–O(2)	2.115(5)	C(2)–C(3)	1.468(11)
Pt(1)–S(1)	2.188(2)	C(2)–C(6)	1.404(11)
Pt(1)–N(1)	2.117(6)	C(3)–C(4)	1.416(9)
Pt(1)–C(3)	1.976(8)	C(4)–C(5)	1.448(11)
O(2)–C(17)	1.293(8)	C(5)–C(6)	1.422(9)
O(3)–C(17)	1.218(8)	C(8)–C(9)	1.411(10)
C(17)–C(18)	1.525(10)	C(8)–C(12)	1.428(11)
S(1)–O(1)	1.473(5)	C(9)–C(10)	1.419(11)
S(1)–C(15)	1.785(9)	C(10)–C(11)	1.426(11)
S(1)–C(16)	1.771(7)	C(11)–C(12)	1.398(11)
N(1)–C(13)	1.492(8)	Fe(1)–C(2–6)	2.06(2) (mean)
N(1)–C(14)	1.490(8)	Fe(1)–C(8–12)	2.051(14) (mean)
N(1)–C(1)	1.497(10)	O(3)···O(4)	2.837(7)[a]
C(1)–C(2)	1.477(10)		
O(2)–Pt(1)–S(1)	94.3(1)	N(1)–Pt(1)–C(3)	83.3(3)
O(2)–Pt(1)–N(1)	88.6(2)	C(17)–O(2)–Pt(1)	122.4(5)
O(2)–Pt(1)–C(3)	171.1(2)	O(2)–C(17)–O(3)	124.9(7)
S(1)–Pt(1)–N(1)	175.4(2)	O(2)–C(17)–C(18)	113.1(6)
S(1)–Pt(1)–C(3)	94.1(2)	O(3)–C(17)–C(18)	122.0(7)

[a] Translation $1 + x, \frac{1}{2} - y, \frac{1}{2} - z$.

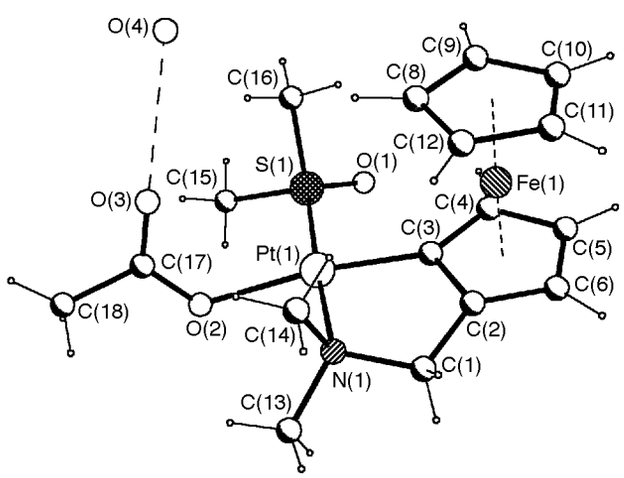
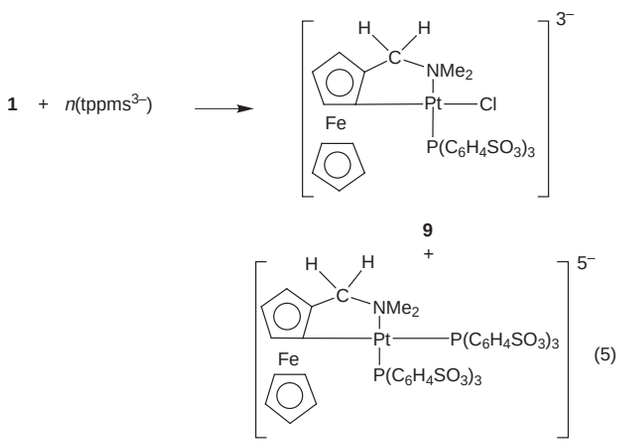


Fig. 1 Perspective view of compound **4** showing the atom numbering scheme. The possible hydrogen-bonding interaction is displayed as a dashed line.

C(2)–C(6) ring is almost coplanar with the adjacent five-membered platinocyclic ring [interplanar angle 0.1(6)°]. The oxygen atom O(4) of the solvent water molecule makes close contact, d[O(3)···O(4)] 2.837(7) Å, with the carbonyl oxygen atom O(3) of the co-ordinated acetate ligand, suggesting a reasonably strong hydrogen bonding interaction in the crystal lattice. Interestingly, similar interactions are observed in two other platinum complexes with monodentate acetate ligands.[26]

Phosphine. A sulfonated phosphine having π-acceptor capability should co-ordinate at a *trans* Pt–N site but unexpectedly the anionic phosphine tppms P($C_6H_4SO_3$-*m*)$_3^{3-}$also bound at the *trans* Pt–C site. Direct addition of an aqueous solution of sodium salt of tris(*m*-sulfonatophenyl)phosphine to a $CHCl_3$ solution of compound **1** at room temperature results in an immediate transfer of the orange colour to the aqueous layer due to the formation of monosubstituted **9** and the dominant bis-substituted **11** tppms complexes, eqn. (5); a similar mono-

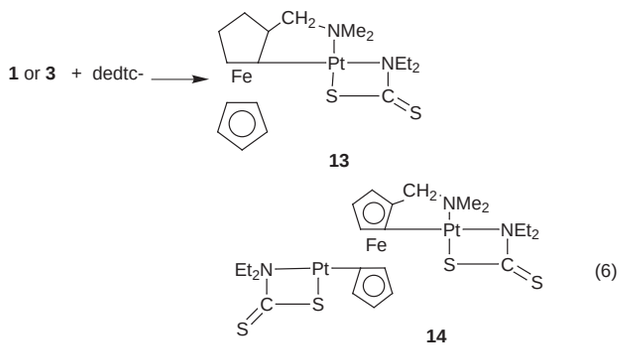


10 and bis-tppms complex **12** were made from **3.** The mono-tppms complexes **9** and **10** were only spectroscopically characterised in solutions of **11** and **12**. This is the opposite of the behaviour found in reactions with PPh_3.[14] Compounds **9–12** rapidly oxidise in water and their syntheses required strictly anaerobic conditions. The formulation of **11** and **12** as bis-substituted adducts is predicated on the ES-MS and NMR spectra. Since they are highly charged species, cations are accumulated in the gas phase to give a net charge of −3. Thus the primary ion in the ES-MS for **11** is [**11** − $4Na^+$ + $7H^+$]; the primary ion for **12** was likewise [**12** − $8Na^+$ + $11H^+$]. The SMe_2 resonances were absent in the ^{1}H NMR of **11** and **12** although, from the NMe_2 profile, planar chirality is maintained. δ_{Pt}[**11**] = −3259 and δ_{Pt}[**12**] = −3258, akin to those for chelated phosphine analogues (*cf.* δ −3970 for the dppm complex).[14] The ^{31}P NMR also supported the *cis* orientation of the ligands. A smaller $^1J_{Pt-P}$ is observed for the phosphorus *trans* to the Pt–C bond (3662/3690 Hz for **11** and **12** respectively) compared to that for phosphorus *trans* to the Pt–N bond (4981/4995 Hz), as expected for a weaker Pt–P bond in the *trans* Pt–C site. Both coupling constants are larger than those for comparable chelates ($^1J_{Pt-P}$ =1510 and 3300 for the dppm analogue), but smaller than for $P(OPh)_3$ ($^1J_{Pt-P}$ = 7153),[14] and presumably reflect the high charge on the complex. For **9** and **10** a single ^{31}P resonance, a typical δ_H for an SMe_2 group in cyclometallated derivatives, and the coupling constants ($^1J_{Pt-P}$ = 3735, 3675 Hz for **9** and **10** respectively) characterised these unstable molecules as having a tppms ligand *trans* to the Pt–N bond.

The anionic phosphine induces water solubility but also functions as both a hard and soft donor. This could be

important for biological activity and we therefore looked at other anions with this capability.

Diethyldithiocarbamate/*O*-alkyl dithiocarbonate. In contrast to sodium carboxylates the direct reaction of sodium diethyldithiocarbamate with compounds **1** and **3** at room temperature gave good yields of the water-insoluble N,S chelates **13** and **14**, eqn. (6). Parent ions were observed in both the FAB- and ES-



(6)

MS (at a cone voltage of 80 V); they are very stable species. Non-equivalence of the NMe and NEt protons and carbons was observed in the ^{1}H and ^{13}C NMR for **13** confirming the N,S chelate structure. The CS_2 resonance δ_C 211 is typical of N,S-chelate complexes. The NMR complexity increases further for **14** as the platinum(II) co-ordination sites are non-equivalent and individual δ_H and δ_C resonances are seen for each CH_3 and CH_2 group. The PtN_2SC co-ordination sphere results in a ^{195}Pt resonance (Table 1) at δ −1974, for **13**, and two at δ −1981 and −2227 for **14**, compared to −2070 *(−2075)*, −2140 *(−2136 and* −2156) and −2550 *(−2557)* for PtNOSC, PtNSClC and PtNPClC respectively (data for di-Pt compounds in italics). The diethylthiocarbamate ligand is a poor π acceptor and the anionic sulfur and tight 'bite' would contribute to the upfield shift but the 240 ppm difference between the two δ_{Pt}, not seen in other bis-Pt cyclometallated complexes (Table 1), suggests that the co-ordination sphere in **14** is distorted.

Given the ready formation of an N,S anionic chelate we anticipated a similar result for an O,S donor ligand but there was no NMR evidence for substitution by *O*-alkyl dithiocarbonate.

Reactivity in aqueous solution

Oxidation of compounds **4**–**6** by Ag^+ in non-aqueous solvents to give green ferrocenium salts **7** has already been mentioned. What was unexpected was the facile oxidation of **4**–**12** in water *by molecular oxygen*, in all solvents, as manifested by the collapse of resonances in the NMR and the onset of ferrocenium absorption bands in the visible spectra. This facile oxidation had a marked influence on reactivity in aqueous solution; in particular, solutions of **4**–**6** and **8** were efficient scavengers of Cl^- ion converting rapidly into **1**–**3**. Electrochemical data were collected for all compounds but detailed spectroscopic studies were only undertaken on **4** and **8** as the oxidation process is extremely fast for **11** and **12**.

Electrochemistry. Cycloplatination shifts $Fc^{+/0}$ approximately 0.2 V cathodic of ferrocene and compounds **4**–**6**, **8** and **13** and **14** displayed typical reversible Nernstian behaviour for the [+/0] couple. There was nothing unusual in the $E_{1/2}$ values except for the dimer **8**, $E_{1/2}$ = 0.06 V, which is ≈ 0.16 V more cathodic than comparable couples[13] (Table 1). Cyclic voltammetric and square wave responses for **11** and **12** were complicated by the lability of the tppms, particularly if traces of water were present, but in non-aqueous solvents E_p[**11**] at ≈ 0.10 V is comparable to $E_{1/2}$ for the $PMePh_2$ and dppm complexes of **2**.[13]

In water $E_{1/2}$[**4**–**6**] and $E_{1/2}$[**8**] are apparently chemically

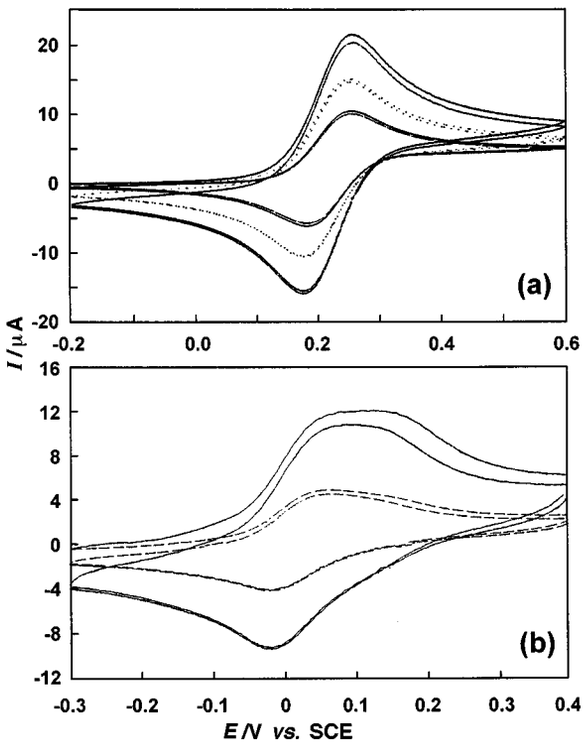
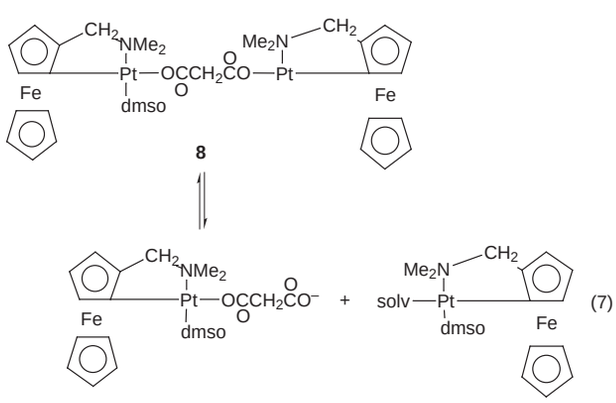


Fig 2 Cyclic voltammograms of compound **8** electrode at a platinum (a) in acetone, NEt_4ClO_4, 20 °C, repeat scans, 50, 100, 800 mV s^{-1}; (b) in water, $NaClO_4$, 20 °C, 2 scans, 100 (dotted) and 800 mV s^{-1}.

reversible but the slow electrode kinetics results in large ΔE_p of ≈ 100 mV. Taking cognisance of junction potentials there is a cathodic shift of ≈ 0.1 V from acetone to water. The electrochemical response for compound **4** was independent of pH, scan rate or solvent mix (*e.g.* methanol–water). However, a second cathodic wave is seen for **8** in water at scan rates > 800 mV s^{-1} (Fig. 2), indicative of an ECE process. We suggest that this is due to dissociation of one end of the bridging malonate ligand on oxidation to give an mal-*O* analogue of **4** (there is evidence for this process in ES-MS, eqn. (7). Compounds **11**



(7)

and **12** oxidised rapidly in water during the electrochemical measurement which, together with the ligand lability and co-ordination of water at the *trans* Pt–C site, led to very complex voltammetric data. When Cl^- was added to an aqueous solution of **4**–**6** or **8** the only redox process seen was that due to the respective **1**–**3**.

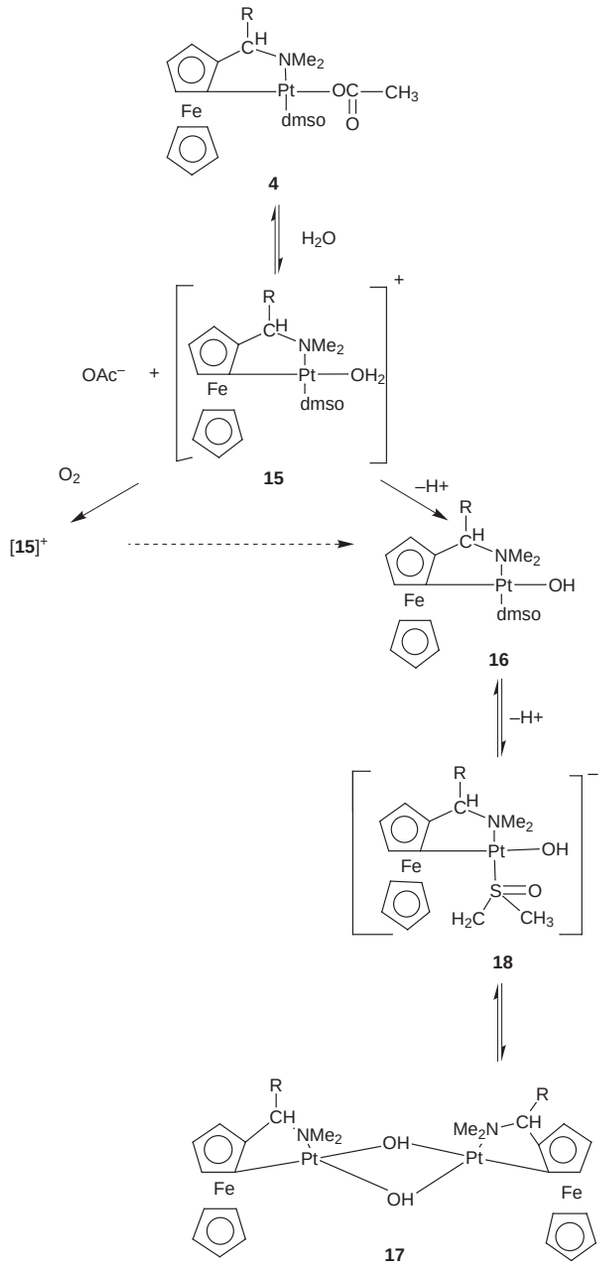
NMR. Provided the sample is sealed under argon, there is no change with time in the profile of the ^{195}Pt resonance for compound **4** in any solvent. δ_{Pt}[**4**] displays a large variation with solvent: −2122 in D_2O, −2078 in $CDCl_3$ −2138 in MeOH and −2038 in acetone. This dependence on solvent is attributed to

hydrogen bonding although the formation of another species could not be ruled out in aqueous solvents. Confirmation that a new species is formed in the presence of water came from the appearance of a new resonance at δ −2073 when D_2O was added to dry MeOH solutions of **4**, the intensity being proportional to the relative amount of D_2O added. A similar downfield shift and new resonances were found in acetone–D_2O and $CDCl_3$–D_2O solvent mixes. Concomitant with this downfield shift in δ_{Pt}, δ_H(OAc) changes to the position of an unco-ordinated OAc but planar chirality is maintained in the co-ordination sphere with only small shifts in the prochiral protons (SMe_2, NMe_2). These data are consistent with the formation of an aqua complex **15**.

However, immediately compound **4** is dissolved in D_2O or 'wet' organic solvents in air the ^{195}Pt resonance broadens and eventually collapses, as do the ferrocene proton resonances, and the solution has a green tinge. These spectral changes are faster at low pH and at pH > 9 spectral collapse due to the oxidation is relatively slow. Similar observations were made for aqueous solutions **5**, **6** and **8**. In acid the resonance attributed to **15** is the major species but at pH 6 **15** and a new species (δ_{Pt} −2257) coexist. At pH > 8 the only remaining species has δ_{Pt} −2027. The addition of ClO_4^- to **4**(aq) in D_2O in air has no immediate effect on δ_{Pt}[**4**] but buffered PO_4^{3-} (pH 7.4), OD^- (pH 9) and glycinate shift δ_{Pt} to −2027, −2024 and −2209 respectively. The ^{1}H NMR spectra show that the cyclometallated skeleton is retained but in the PO_4^{3-} and OD^- solutions (but not glycinate) $\delta_H(SMe_2)$ surprisingly disappeared. Since the dmso cannot be replaced in non-aqueous solutions by other than π acceptors the loss of $\delta_H(SMe_2)$ suggests that another leaving group in the *trans* Pt–N position has been created. In halogenated solvent–water mixtures in air, or with Cl^- present, there is rapid formation of **1**–**3**, clearly seen in the ^{195}Pt NMR, particularly if a trace of acid is present (Scheme 1).

Electronic spectra. The UV/visible spectra were run in conjunction with the NMR as they give an insight into the oxidation step. In dry organic solvents compounds **4**–**6** and **8** have the $^1A_{1g} \longrightarrow {}^1E_{1g}(^1E_{2g})$ transition at ≈450 nm. This oxidation in water gives rise to two new bands at ≈ 570(sh) nm and the major $^2E_{1g} \longrightarrow {}^2E_{1u}$ transition at 750 nm[27] of a ferrocenium species (Fig. 3). There is a red-shift compared to the parent ferrocenylamine and an increase in oscillator strength, features which are common within ferrocene derivatives[28] but not usually seen in complexes with metal ions. Undoubtedly, this is a consequence of cyclometallation causing a mixing of the co-ordinated platinum(II) and ferrocenium orbitals. By monitoring the band at 750 nm it was found that oxidation of **4** to $\mathbf{4}^+$ is a pseudo-first order reaction, $t_{1/2} = 16$ min at pH 2 decreasing with increased pH (pH 6: $t_{1/2} = 68$ h) until, at pH 12, $t_{1/2} = > 120$ h; this substantiates the qualitative NMR results. The λ_{max} of the product and the change in molar absorbance with time differ at pH 2, 6 and 9 (Fig. 3) indicating that different species are present.

Equilibria in aqueous solution. These NMR and spectral data show that two distinct processes influence the aqueous solution chemistry of the water-soluble complexes (Scheme 1). First, there is an equilibrium which leads to a hydrated species **15** which provides a labile group *trans* to the Pt–C bond and subsequent co-ordination of weakly co-ordinating groups like the glycinate anion. Secondly, an oxidation process involving molecular oxygen leading to ferrocenium species. Consequently, the electrochemical investigations in water were with solutions containing both the original complex and **15**. Aside from the oxidation process the equilibria proposed in Scheme 1 are familiar in cisplatin chemistry.[10,29] At pH 2 the aqua species **15** (δ_{Pt} −2122, 580/785 nm) dominates and, as the pH increases, hydroxo species **16** (δ_{Pt} −2257, 575/750 nm) is formed. In strongly basic solutions a hydroxo-bridged species **17** may be



Scheme 1

produced which stabilises the ferrocenyl core of **4**–**6** to oxidation. This explains why δ_{Pt} is the same for solutions buffered by PO_4^{3-} and OD^-. It is postulated that formation of a dimsyl species **18** at this pH provides a good leaving group and the impetus to create the necessary *cis* co-ordination site. Concurrent with the establishment of the equilibria incorporating the neutral species, oxidation gives a parallel series of products incorporating the ferrocenium analogues, the relative concentration being influenced by time and pH. It is well known that ferrocenium species are stabilised in acid solution, and clearly the proportion of oxidised species will decrease with pH, but under physiological conditions for biological testing ferrocenium species will dominate.

Conclusion

Incorporation of carboxylate moieties into the cyclometallated platinum(II) complexes based on ferrocenylamines induces the water solubility necessary for drug use. The *trans* influence and the preference for a π acceptor *trans* to the Pt–N bond dictate the range of ligands which can be co-ordinated, in particular chelating carboxylates. An additional factor is the steric conges-

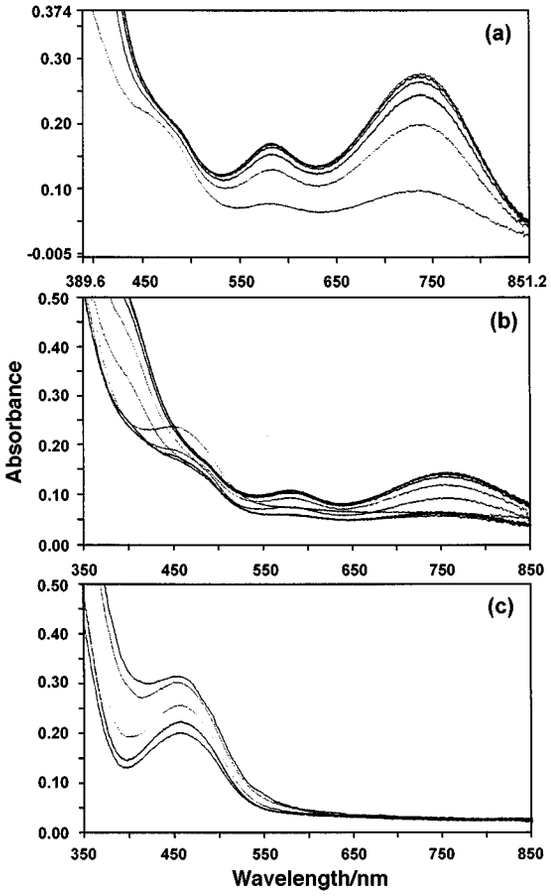


Fig 3 Electronic spectra of compound **4** in water, 20 °C, under argon, at various times after dissolution: (a) pH 2, intervals of 20 min, $t_{1/2}$ = 16 min; (b) pH 6, intervals of ≈ 50 min, $t_{1/2}$ = 68 h; (c) pH 12, over 400 h.

tion around the Pt^{II} but the absence of malonato complexes of **2** and **3** is unexpected. Toxicity and anti-tumour data have been published for **4**.[15] Data now available for **5**, **6** and **8** confirmed that this class of compound shows general hepatotoxicity with lower toxicity than the "free" ligands and there was less intestinal irritation with the water soluble compounds. Most significant, however, is that their cytotoxicities are virtually *identical* to those of the parent chloro complexes **1**–**3**.[21] The reason for this is now clear. In the presence of oxygen, when **4**–**6** or **8** encounter Cl^-(aq) *in vivo*, they are converted into **1**–**3** and consequently *in vivo* biological testing, especially in saline solution, will always be of the chlorocycloplatinated species irrespective of the injected complex.

The evidence strongly supports the formation of an aqua complex **15** at low pH, and hydroxo species at higher pH, in aqueous solutions of the carboxylate derivatives. In principle, **15** should have provided a route to complexes with amino acids and nucleotides (as with cisplatin[30]) but there was no NMR evidence for substitution under strictly anerobic conditions; substitution in aqueous solution is complicated by the facile oxidation to ferrocenium species in air. Although molecular oxygen is definitely involved, there is insufficient evidence to speculate whether oxidation involves a pH-dependent peroxo or radical oxidation mechanism. The oxidation is being thermodynamically driven by the lower $E_{1/2}$ for the cycloplatinated complexes but the system is more subtle than this because the addition of Cl^- to solutions of the ferrocenium species gives neutral **1**–**3**, not $[\mathbf{1}]^+$–$[\mathbf{3}]^+$. From a physiological perspective, the *in vivo* equilibria and biologically active complex will be difficult to unravel.

Experimental

All synthetic work was performed in a fumehood as ferrocenylamines have acrid odours. All reactions were carried out in oven-dried glassware under an atmosphere of argon or oxygen-free nitrogen. The compounds **1**, **2**, **3**,[12] and TlX[31] were prepared by literature methods. The IR and NMR spectra were recorded on Digilab FX60 and Varian VXR300 MHz /Gemini 200 MHz spectrometers respectively, with ^{195}Pt referenced against K_2PtCl_4. Microanalyses were carried out by the Campbell Microanalytical Laboratory, University of Otago. Electrospray mass spectra were recorded on a VG Platform II spectrometer in a 1 : 1 v/v acetonitrile–water or methanol–water mobile phase (0.1 mM in compound) and FAB spectra on a Kratos MS80RFA instrument with an Iontech ZN11NF atom gun. Electrochemical measurements were performed with a three-electrode cell using a computer controlled EG & G PAR 273A potentiostat/galvanostat at scan rates 0.05–10 V s^{-1}. A polished platinum disc electrode was employed; the reference was SCE uncorrected for junction potentials ([ferrocene]$^{+/0}$, $E_{1/2}$ = 0.466 V in acetone), the supporting electrolyte 0.1 M (NEt_4ClO_4) and the substrate ≈ 1×10^{-3} M.

Preparation of compounds 4–6 from thallium(I) acetate

Compound 4. To a solution of compound **1** (52.8 mg, 0.96 mmol) in chloroform (5 ml) was added a solution of thallium(I) acetate (25.3 mg, 0.96 mmol) in ethanol (5 ml). The mixture was left standing at room temperature in the dark for six hours. The thallium(I) chloride which had precipitated and was removed by centrifuge. More precipitated when the supernatant solution was left overnight at room temperature. After all had precipitated and been filtered off, the orange solution was evaporated to dryness and the residue recrystallised from acetone–hexane (1 : 3) to give orange-yellow crystals of **4** (68.3%) (Found: C, 35.63; H, 4.57; N, 2.36. $C_{17}H_{25}FeNO_3PtS$ requires C, 35.55; H, 4.39; N, 2.44%). $\delta_H(CDCl_3)$ 2.04 (s, 3 H, CH_3CO_2); 2.83 (s, 3 H, J_{Pt-H} = 15.5, NCH_3); 3.03 (s, 3 H, J_{Pt-H} = 14.2, NCH_3); 3.37 (s, 3 H, J_{Pt-H} = 12.4, SCH_3); 3.57 (s, 3 H, J_{Pt-H} = 13.5 Hz, SCH_3) and 4.12–4.33 (m, 8 H, C_8H_8). $\delta_{Pt}(CDCl_3)$ −2076. ν(KBr, cm^{-1}) 1614 (C=O), 1319 (C–O) and 1139 (S=O). λ_{max}/nm(ε/M^{-1} cm^{-1}) ($CHCl_3$) 455(332).

Compound 6. This was prepared similarly, from compound **2** (26.2 mg, 0.29 mmol) and thallium(I) acetate (15.2 mg, 0.58 mmol). The orange residue was recrystallised from benzene–hexane (1 : 3) to give pale orange crystals of **6** (Found: C, 30.32; H, 4.12; N, 2.92. $C_{24}H_{40}FeN_2O_6Pt_2S_2$ requires C, 29.94; H, 4.19; N, 2.91%). $\delta_H(CD_2Cl_2)$ 1.93 (s, 6 H, CH_3CO_2); 2.73 (s, 6 H, J_{Pt-H} = 15.0, NCH_3); 2.92 (s, 6 H, J_{Pt-H} = 13.2, NCH_3); 3.33 (s, 6 H, J_{Pt-H} = 11.7, SCH_3); 3.44 (s, 6 H, J_{Pt-H} = 12.3 Hz, SCH_3); and 4.04–4.24 (m, 8 H). $\delta_{Pt}(CD_2Cl_2)$ −2075. ν(KBr, cm^{-1}) 1620 (C=O), 1328 (C–O) and 1140 (S=O).

Compound 5. Compound **3** (43.7 mg, 0.77 mmol) in the minimum volume of chloroform was added to thallium(I) acetate (0.2032 g, 0.77 mmol) dissolved in ethanol (10 ml). The mixture was stirred for 10 mins and then left to stand at room temperature overnight in the dark. The precipitated thallium chloride was centrifuged, the supernatant solution filtered and then left to stand until precipitation had stopped. The orange-yellow residue obtained after the solvent was removed was recrystallised from acetone–methanol to give **5** as an orange solid (62%); mp 182 °C (Found: C, 36.45; H, 4.94; N, 2.41. $C_{18}H_{27}FeNO_3PtS$ requires C, 36.74; H, 4.63; N, 2.38%). ES-MS: *m*/*z* 571, $[M - OAc + CH_3CN]^+$; and 528, $[M - OAc]^+$. $\delta_H(CDCl_3)$ 1.23 (d, 3 H, J = 6.88, $CHCH_3$), 2.03 (s, 3 H, O_2CCH_3), 2.50 (s, 3 H, $^3J_{Pt-H}$ = 36.1, NCH_3), 2.79 (s, 3 H, $^3J_{Pt-H}$ = 32.8, NCH_3), 3.38 (s, 3 H, $^3J_{Pt-H}$ = 22.9, SCH_3), 3.51 (s, 3 H, $^3J_{Pt-H}$ = 30.2 Hz, SCH_3), 4.03 (s, 1 H, one of η^5-C_5H_3), 4.09 (s, 5 H, η^5-C_5H_5), 4.26 (s, 1 H, one of η^5-C_5H_3) and 4.38 (s, 1 H, one of η^5-C_5H_3). δ_C ($CDCl_3$) 11.15 (CCH_3), 25.40 (CH_3CO_2), 29.72 (SCH_3), 43.51 (SCH_3), 46.14 (NCH_3), 47.65 (NCH_3),

63.29 (CH), 65.72 (CH), 69.52 (η^5-C_5H_5), 69.59 (CH), 70.65 (CH), 74.04 (quaternary carbon), 97.73 (quaternary carbon) and 177.58 (CH_3CO_2). $\delta_{Pt}(CDCl_3)$ −2091. ν(KBr, cm^{-1}) 1602(C=O), 1414(CH_3CO_2), 1130(C–O), 1022(S=O) and 688(C–S). λ_{max}/nm(ε/M^{-1} cm^{-1}) 451(339).

Preparation of compound 8

A chloroform solution of compound **1** (0.4591 g, 0.83 mmol, 45 ml) was added to thallium malonate (0.4259 g 0.81mmol), in boiling distilled water–ethanol. Thallium chloride precipitated as the solution was stirred for 48 h in the dark. The liquid was centrifuged, filtered and solvent stripped to give a bright orange oil **8** which eventually solidified on pumping in a high vacuum (83%); mp 150 °C (decomp.) (Found: C, 33.96; H, 4.45; N, 2.31; S, 5.60. $C_{33}H_{48}Fe_2N_2O_6Pt_2S_2{\cdot}2H_2O$ requires C, 33.91; H, 4.31; N, 2.40; S, 5.49%). ES-MS: *m/z* 1055 [M^+-dmso]. $\delta_H(CDCl_3)$ 2.85 (s, 3 H, $^3J_{Pt-H}$ = 15.9, NCH_3), 3.08 (s, 3 H, $^3J_{Pt-H}$ = 14.7, NCH_3), 3.31 (s, 2 H, $C_3H_2O_4$), 3.41 (s, 3 H, $^3J_{Pt-H}$ = 13.8, SCH_3), 3.48 (s, 2 H, CH_2), 3.59 (s, 3 H, $^3J_{Pt-H}$ = 14.2 Hz, SCH_3), 4.15 (s, 5 H, η^5-C_5H_5Fe) and 4.32 (s, 3 H, η^5-C_5H_3Fe). $\delta_C(CDCl_3)$: 45.45 (SCH_3), 46.22 (SCH_3), 49.47 [$(CO_2)_2CH_2$], 51.91 (NCH_3), 52.31 (NCH_3), 61.60 (CH_2), 66.68 (CH_2), 68.84 (C_5H_5Fe), 94.65 (quaternary C) and 174.76 [$(CO_2)_2CH_2$]. $\delta_{Pt}(CDCl_3)$ −2091. ν(KBr, cm^{-1}) 1662(C=O), 1125(C–O) and 1015(S=O). λ_{max}/nm(ε/M^{-1} cm^{-1}) ($CHCl_3$) 455 (72).

A similar reaction with compound **2** gave only starting material; other methods tried unsuccessfully were hot and cold acetone–water and chloroform–hot water solvent mixtures, and ultrasonic reactions.

Reaction of compound 1 with other thallium(I) salts

Thallium cyclobutane-1,1-dicarboxylate, a new salt, was synthesized as follows. Thallium(I) nitrate (0.500 g, 0.19 mmol), dissolved in the minimum amount of hot water, was added to a boiling aqueous solution of cyclobutane-1,1-dicarboxylic acid (0.271 g, 0.19 mmol) and the solution concentrated. White platelets of the salt deposited on cooling (86%); mp 208 °C (Found: C, 12.96; H, 1.01. $C_3H_3O_2Tl$ requires C, 13.08; H, 1.10%). ν(KBr, cm^{-1}) 1703 (C=O). $\delta_H(D_2O)$ 1.95 (2 H, CH_{2B}) and 2.48 (4 H, $CH_{2A,A'}$). $\delta_C(D_2O)$ 180.30. This salt was used in reactions with compounds **1** and **2**, in a variety of solvent mixtures, without success. A similar result was obtained with thallium(I) oxalate and nitrate.

Reaction of compound 1 with silver salts

Silver acetate. Silver acetate (15.2 mg, 0.09 mmol) suspended in acetone (20 cm^3) was added to compound **1** (50 mg, 0.09 mmol) and stirred for at least 5 h at room temperature, in the dark. The mixture was centrifuged, the yellow solution decanted and evaporated to dryness. The orange solid was recrystallised from acetone–hexane; yield 58% of **4** identical to that prepared from the thallium(I) salt.

Silver nitrate. The nitrate (15.42 mg, 0.09 mmol) in water (10 cm^3) was added to compound **1** (50 mg, 0.09 mmol) dropwise, resulting in a green solution. This was centrifuged, then filtered and evaporated to dryness to give green **7**. Recrystallisation was unsatisfactory as **7** is extremely hygroscopic (Found: C, 29.46; H, 3.55; N, 5.43. $C_{15}H_{12}ClFeN_2O_4PtS$ requires C, 29.38; H, 3.63; N, 4.57%). ν(Nujol, cm^{-1}): 1385 (NO_3^-) and 1126 (S=O). $\Lambda_{max}(H_2O)$ 53.5 Ω^{-1} cm^2 mol^{-1}. λ/nm(ε/M^{-1} cm^{-1}) (acetone): 588(364) and 780(515).

Other salts. The salt AgX(aq) [X = ClO_4^-, NO_3^-, SO_4^{2-}, BF_4^-, PF_6^-, ox, or Hmal] was added to compound **1** dissolved in acetone at which point the solutions changed from orange to green giving ferrocenyl derivatives. For non-co-ordinating anions the species produced was $\mathbf{15}^+$.

Reactions of compound 1 with $Pt(dmso)_2X_2$ (X = ox or Hmal)

The compound $[Pt(dmso)_2Cl_2]$ (70.0 mg, 0.17 mmol) was dissolved in warm water (10 ml) and added to a solution of silver malonate (52.7 mg, 1.7 mmol) in HNO_3 (1 mol dm^{-3}, 10 ml). The precipitated AgCl was removed and the solution left overnight during which time further AgCl precipitated. Evaporation of the filtered solution to dryness gave $[Pt(dmso)_2(Omal)]$. ν(Nujol, cm^{-1}): 1736 (C=O) and 1156 (S=O). This was dissolved in acetone–methanol (2:1, 40 ml), **1** (115 mg, 4.7 mmol) added and the solution heated at 50–60 °C in the dark with stirring for three hours. It was then stirred overnight at 20 °C, the resulting pale yellow-orange solution centrifuged and the supernatant liquid evaporated to dryness to give pale yellow crystals of $[FeCp(\eta\text{-}C_5H_4CH_2NHMe_2)]$ (Found: C, 50.09; H, 5.95; N, 9.08. $C_{13}H_{18}FeN_2O_3$ requires C, 51.00; H, 5.93; N, 9.15%). δ_H ($CDCl_3$) 2.73 (6 H, CH_3); 4.11 (2 H, CH_3); 4.20 (5 H, C_5H_3); and 4.31–4.36 (4 H, C_5H_4). Similar results were obtained using silver oxalate and with **1** even if a base (*e.g.* K_2CO_3) was present in the final step.

Preparation of compounds 9–12

Compounds 9 and 11. Compound **1** (0.414 g, 0.75 mmol) was dissolved in 2 ml of rigorously deoxygenated chloroform and added to the sodium salt of tris(*m*-sulfonatophenyl)phosphine (54.6 mg, 1.50 mmol) in 20 ml degassed distilled water. This solution was sealed under nitrogen and left stirring for 2 h. Once the aqueous layer had reached full orange colouration the water was evaporated and the product immediately (due to very rapid oxidation) chromatographed on a octadecyl-functionalised silica gel reversed-phase column with methanol–water (1:2). The solvent was removed and the solid dissolved in hot water, hot methanol added and the solution centrifuged. Removal of solvent and recrystallisation from methanol–acetone gave pure **11** as orange crystals (57%); mp 220 °C (decomp.) (Found: C, 38.21; H, 2.90; Cl, 0.00; N, 0.8; S, 12.13. $C_{49}H_{40}FeNNa_5O_{18}P_2PtS_6$ requires C, 37.94; H, 2.60; Cl, 0.00; N, 0.90; S, 12.40%) ES-MS: *m/z* 488 [$(M - 4Na^+)^- + 7H^+$]. $\delta_H(D_2O)$ 2.72 (s, 3 H, $^3J_{Pt-H}$ = 4.6, NCH_3), 3.35 (s, 3 H, $^3J_{Pt-H}$ = 5.2, NCH_3), 4.11 (s, 1 H, one of η^5-C_5H_3Fe), 4.22 (s, 5 H, η^5-C_5H_5Fe), 4.33 (s, 1 H, one of η^5-C_5H_3Fe), 4.38 (s, 1 H, one of η^5-C_5H_3Fe) and 7.34–8.17 [m, 24 H, $P(C_6H_4SO_3)_3$]. $\delta_C(D_2O)$ 38.72 (NCH_3), 41.35 (NCH_3), 57.34 (CH), 69.11 (η^5-C_5H_5Fe), 70.09 (CH), 71.02 (CH) and 126.96–130.23 [$P(C_6H_4SO_3)_3$]. $\delta_P(D_2O)$ 5.64 (d, $^2J_{P-P}$ = 18.3, $^1J_{Pt-PC}$ = 3128) and 15.91 (d, $^2J_{Pt-P}$ = 19.2, $^1J_{Pt-PN}$ = 3748 Hz). Also characterised spectroscopically in aged solutions, **9**: $\delta_p(D_2O)$ 14.68 (s, $^1J_{Pt-PN}$ = 3735 Hz, N–Pt–P product only); $\delta_{Pt}(D_2O)$ −3259 (d, $^1J_{Pt-PN}$ = 4981, $^1J_{Pt-PC}$ = 3662 Hz); ν(KBr, cm^{-1}) 1466 (P–Ph), 993 (P–Ph) and 622 (C–S); λ_{max}/nm (ε/M^{-1} cm^{-1}) water 480(162), 585(71) and 809(90).

Compounds 10 and 12. A similar procedure to that for compound **11** using **3** gave **12** as orange crystals (54%); mp 264 °C (decomp.) Rapid oxidation and hygroscopic character resulted in poor microanalytical data (Found: C, 37.18; H, 3.44; N, 0.77; S, 12.83. $C_{88}H_{70}FeN_2Na_{10}O_{36}P_4Pt_2S_{12}$ requires C, 36.24; H, 2.40; N, 0.96; S, 13.18%). ES-MS: *m/z* 913 [$(M - 8Na^+)^- + 11H^+$]. ν(KBr, cm^{-1}) 621 (C–S). λ_{max}/nm (ε/M^{-1} cm^{-1}): 407 (534), 504 (257) and 682 (534). $\delta_H(D_2O)$ 2.64 (s, 3 H, $^3J_{Pt-H}$ = 4.3, NCH_3), 2.71 (s, 3 H, $^3J_{Pt-H}$ = 4.6, NCH_3), 2.88 (s, 3 H, $^3J_{Pt-H}$ = 5.3, NCH_3), 3.02 (s, 3 H, $^3J_{Pt-H}$ = 5.6 Hz, NCH_3), 3.92–4.04 (m, 6 H, η^5-C_5H_3Fe) and 7.17–7.97 (m, 48 H, tppms). $\delta_C(D_2O)$ 27.90 (NCH_3), 38.71 (NCH_3), 41.36 (NCH_3), 57.86 (NCH_3), 71.13 (η^5-C_5H_5Fe), 71.74 (η^5-C_5H_5Fe) and 124.84–143.49(tppms). $\delta_P(D_2O)$ 20.29 (d, $^2J_{Pt-P}$ = 18.3, $^1J_{Pt-PN}$ = 4474) and 24.13 (d, $^2J_{Pt-P}$ = 18.3, $^1J_{Pt-PC}$ = 2478 Hz). Characterised spectroscopically in aged solutions, **12**: $\delta_P(D_2O)$ 12.92 (t, $^2J_{P-P}$ = 40.31, $^1J_{Pt-PN}$ = 3675 Hz); δ_{Pt} (D_2O) −3258 (d, $^1J_{Pt-PN}$ = 4995, $^1J_{Pt-PC}$ = 3690).

Table 3 Crystal data and structure refinement for compound **4**

Empirical formula	$C_{17}H_{27}FeNO_4PtS$
Formula weight	592.40
T/K	293(2)
λ/Å	0.71073
Crystal system	Monoclinic
Space group	$P2_1/c$
a/Å	10.066(2)
b/Å	15.265(4)
c/Å	12.997(3)
β/°	103.30(2)
V/Å^3	1943.5(8)
Z	4
D_c/Mg m^{-3}	2.025
μ/mm^{-1}	8.065
F(000)	1152
Crystal size/mm	0.5 × 0.25 × 0.1
Reflections collected	2640
Independent reflections	2060 [R(int) = 0.0435]
Data/parameters	2060/241
Final R,R' [$I > 2\sigma(I)$]	0.0278, 0.0323
Largest difference peak and hole/e Å^{-3}	0.918 and −1.080

Preparation of compounds 13 and 14

Compound 13. Sodium diethyldithiocarbamate (dedtc) (6.4 mg 0.02 mmol) dissolved in 20 ml methanol was added to compound **1** (15.6 mg, 0.02 mmol) dissolved in the minimum volume of degassed chloroform. The solution was stirred for 2 h in the dark and the resulting brown-orange product extracted with hexane. The hexane solution was washed with water to remove the dmso and then solvent removed *in vacuo*. Chromatography on silica in chloroform removed all remaining impurities and recrystallisation of the residue from hot ethyl acetate gave **13** as orange-yellow crystals (67%); mp 95 °C (decomp.) (Found: C, 37.20; H, 5.14; N, 4.31. $C_{18}H_{26}FeN_2PtS_2$·2MeOH requires C, 36.93; H, 4.48; N, 4.79%). ES-MS: m/z 585 (M^+). $\delta_H(CDCl_3)$ 1.30 (t, 3 H, J = 7.3, CH_2CH_3), 1.34 (t, 3 H, J = 7.3, CH_2CH_3), 2.89 (s, 3 H, $^3J_{Pt-H}$ = 18.4, NCH_3), 3.24 (s, 3 H, $^3J_{Pt-H}$ = 16.7, NCH_3), 3.67 (q, 2 H, J = 6.9 Hz, CH_2CH_3), 3.70 (q, 2 H, J = 7.1 Hz, CH_2CH_3), 3.85 (s, 1 H, η^5-C_5H_3Fe), 4.01 (s, 1 H, η^5-C_5H_3Fe), 4.12 (s, 5 H, η^5-C_5H_5Fe) and 4.23 (s, 1 H, η^5-C_5H_3Fe). $\delta_C(CDCl_3)$ 12.48 (CH_2CH_3)$_2$), 43.94 (CH_2CH_3), 45.46 (CH_2-CH_3), 54.00 (CH_3N), 54.93 (CH_3N), 62.09 (CH, η^5-C_5H_3Fe), 68.75 (CH, η-C_5H_3Fe), 69.23 (CH, η^5-C_5H_3Fe) and 69.37 (5CH, η^5-C_5H_5Fe). $\delta_{Pt}(CDCl_3)$ −1974. ν(KBr, cm^{-1}): 1442, 1384 (C–N), 1279(C=S) and 847(C–S). λ_{max}/nm(ε/M^{-1} cm^{-1}) ($CHCl_3$) 455(330) and 362(860).

Compound 14. This was obtained as orange crystals (58%) by a similar route from compound **2**; mp 112 °C (decomp.) (Found: C, 34.25; H, 4.41; N, 5.07. $C_{26}H_{42}FeN_4Pt_2S_4$: C, 34.92; H, 4.30; N, 5.69%). ES-MS: m/z 985 (M^+). $\delta_H(CDCl_3)$ 1.24 (3 H, J = 9.9 Hz, CH_2CH_3), 1.27 (3 H, J = 9.9, CH_2CH_3), 1.28 (3 H, J = 9.4, CH_2CH_3), 1.30 (3 H, J = 9.3, CH_2CH_3), 2.87 (3 H, $^3J_{Pt-H}$ = 13.8, NCH_3), 2.89 (s, 3 H, $^3J_{Pt-H}$ = 13.5, NCH_3), 3.22 (s, 3 H, $^3J_{Pt-H}$ = 16.2, NCH_3), 3.24 (s, 3 H, $^3J_{Pt-H}$ = 18.1, NCH_3), 3.61 (q, 2 H, J = 7.2, CH_2CH_3), 3.65 (q, 2 H, J = 7.5, CH_2CH_3), 3.67 (q, 2 H, J = 7.2 Hz, CH_2CH_3), 3.70 (q, 2 H, J = 7.5 Hz, CH_2CH_3), 3.99 (2 H, η^5-C_5H_3Fe), 4.04 (5 H, η^5-C_5H_5Fe), 4.07 (2 H, η^5-C_5H_3Fe) and 4.10 (2 H, η^5-C_5H_3Fe). $\delta_C(CDCl_3)$ 12.49 (CH_2CH_3), 12.62 (CH_2CH_3), 43.81 (CH_2CH_3), 43.95 (CH_2CH_3), 45.31 (CH_2CH_3), 45.43 (CH_2CH_3), 53.61 (NCH_3), 53.85 (NCH_3), 54.46 (NCH_3), 54.92 (NCH_3), 59.08, 59.46, 62.47, 67.13, 68.68 and 70.66 (CH, η^5-$C_5H_3)_2$Fe). δ_{Pt} ($CDCl_3$) −2227 and −1981. ν(KBr, cm^{-1}): 1272(C=S) and 844(C–S). λ_{max}/nm(ε/M^{-1} cm^{-1}) ($CHCl_3$) 470(75).

Crystal structure determination of compound 4

Crystals of compound **4** were grown as yellow plates from acetone–hexane. Data were collected on a Nicolet, R3M diffractometer using the ω–2θ scan technique. Details of the data collection and structure refinement are summarised in Table 3. The structure was solved by direct methods using SHELXS 86.[32] The E map revealed the location of the Pt, Fe and S atoms with the remaining non-hydrogen atoms located in a series of least-squares refinement on F, Fourier difference cycles. Weighted refinement was performed using SHELX 76,[33] with all non-hydrogen atoms refined anisotropically. A Fourier-difference synthesis following the location of all anticipated non-hydrogen atoms revealed electron density that could be sensibly assigned to a solvent water molecule. Inclusion of this in the refinement led to a significant improvement in R but the associated hydrogen atoms were not located. Other hydrogen atoms were included in the refinements as fixed contributions to F_c.

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