Synthesis and Stereochemistry of Bis(platinum) Complexes of Ferrocenylamines

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Bis(platinum complexes of ferrocenylamines have been prepared from $Pt(DMSO)_2Cl_2$ and $[(\eta^5\text{-}C_5H_4CH(R)NMe_2)_2Fe]$ (R = H, Me). Initial products are *trans*-$\{Pt_2Cl_4(DMSO)_2[(\eta^5\text{-}C_5H_4\text{-}CH(R)NMe_2)_2Fe]\}$ but these rapidly cyclometalate to σ-$\{Pt_2[(\eta^5\text{-}C_5H_3CH(R)NMe_2)_2Fe]Cl_2\text{-}(DMSO)_2\}$; metathetical reactions gave the bromo and iodo analogues while DMSO could be substituted by PPh_3 in the cycloplatinated compounds. Alternative metalation pathways gave stereoisomers of the cycloplatinated derivatives, the stereochemical preference varying with the halide. Cycloplatination is stereospecific for the chiral *C*-methyl ferrocenylamine complex. The compound *trans*-$\{Pt_2Cl_4(DMSO)_2[(\eta^5\text{-}C_5H_4CH_2NMe_2)_2Fe]\}$ crystallizes in the monoclinic system, space group $P2_1/c$ with a = 7.623(2) Å, b = 13.993(4) Å, c = 13.271(3) Å, β = 95.66(2)°, D_c = 2.33 g cm^{-3}, and Z = 2. The yellow, centrosymmetric, *meso* isomer of σ-$\{Pt_2[(\eta^5\text{-}C_5H_3\text{-}CH_2NMe_2)_2Fe]Br_2(DMSO)_2\}$ crystallizes in the monoclinic system, space group $P2_1/c$ with a = 14.277(5) Å, b = 8.974(3) Å, c = 10.951(2) Å, β = 105.77(2)°, D_c = 2.47 g cm^{-3}, and Z = 2; the orange *racemate* crystallizes in the monoclinic system, space group $P2_1/c$ with a = 9.984(3) Å, b = 10.335(3) Å, c = 25.929(7) Å, β = 92.28(2)°, D_c = 2.50 g cm^{-3}, and Z = 4. The stereoisomers are readily distinguished in solution by ^1H and ^{195}Pt NMR; temperature variation of the CH_2 and metalated cyclopentadiene ring proton resonances may be caused by changes in the relative orientation of the CH_2 groups.

In the preceding paper[1] we described the synthesis and structure of a new class of cycloplatinated complexes with ferrocenylamine ligands which may have antitumor activity and radiation sensitization properties. These complexes contained one Pt(II) per ferrocenyl unit but by functionalizing both cyclopentadienyl rings there is the opportunity to prepare complexes containing more than one Pt(II) center. Chemical and biological interest in molecules with more than one Pt(II) center[2,3] has arisen because they can show high *in vitro* activity against cisplatin resistant cell lines.[4] Cytotoxic effects caused by compounds with the single Pt(II) center in cisplatin and analogues are believed to result from a lesion on DNA in the intrastrand link between two adjacent guanine or adenine/guanine bases which block both replication and transcription.[5,6] However, complexes containing more than one Pt(II) coordination center may well take part in different intra- or interstrand interactions with each strand of DNA. An interaction with DNA which is inaccessible to cisplatin is the formation of interstrand cross-links in which two platinum(II) moieties bind to opposite DNA strands. Interstrand linkages will be affected by the stereochemistry, however, and there is evidence that there can be a complicated sequence of intra- and interstrand linkages.[7,8]

Obviously, an even broader spectrum of DNA binding and hence cytotoxic activity might result from a combination of a metallocene[9] and two Pt(II) centers, as a metallocene such as a ferrocenylamine can be involved in radical processes associated with tumor biochemistry.[10] The homoannular ring formed by chelation of a ferrocenylamine ligand to Pt(II) also induces planar chirality.[11] Furthermore the ferrocenylamine ligands themselves may be prochiral substrates. Lithiation of ferrocenylamines is stereoselective[12] due to the chelating effect of the nitrogen lone pair which stabilizes the lithiated *R,R* stereoisomer. This stereoselectivity can be used to synthesize stereoisomers, and the resulting chiral ferrocenylamines have been widely used in asymmetric synthesis.[13,14] A combination of planar chirality and ligand chirality could therefore produce a complex stereochemical situation in a bis(platinum)–ferrocenylamine complex. Since the diastereoisomers or enantiomers of a particular ferrocenylamine–bis(platinum) system may interact differently with DNA, these Pt(II) complexes have the potential to produce a spectrum of toxicity and tumor activity. In this paper we report the synthesis and structure of the stereoisomers of bis(platinum(II)) complexes of the tertiary ferrocenylamine ligands $[(\eta\text{-}C_5H_4CH(R)NMe_2)_2Fe]$ (R =

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H, Me); the structure of one representative has been communicated.[15]

Experimental Section

All reactions were carried out in a dry nitrogen atmosphere as the bis(platinum) complexes are very susceptible to oxidation to ferrocenium compounds, particularly in solution. The ferrocenylamine ligands[16,17] and $Pt(DMSO)_2Cl_2$[18] were prepared by literature procedures. NMR spectra were recorded on a Varian 300-MHz spectrometer at 25 °C unless otherwise specified. ^{195}Pt NMR spectra were obtained typically with a spectrum width of 100 000 Hz, 2000–5000 scans with a relaxation delay of 0.5 s between 16-μs pulses. Spectra were referenced to a Na_2PtCl_6 solution in D_2O as the external reference. IR spectra were recorded on a Digilab FTIR spectrometer. Spectroscopic data were generally collected under a nitrogen (argon) atmosphere in order to minimize complications due to oxidation. Analyses were carried out by the Campbell Microanalytical Laboratory, University of Otago.

***trans*-$Pt_2Cl_4(DMSO)_2[(\eta^5\text{-}C_5H_4CH_2NMe_2)_2Fe]$, 1.** *cis*-$PtCl_2(DMSO)_2$ (1.056 g, 2.5 mmol) was added to a solution of $[(\eta^5\text{-}C_5H_4CH_2NMe_2)_2Fe]$ (0.901 g, 3 mmol) in acetone (200 cm^3). The mixture was heated at 50–55 °C for 1.5 h under nitrogen in the absence of light. Then the mixture was immediately cooled to room temperature and the solvent evaporated *in vacuo*. The yellow oil was dissolved in a minimum amount of the CH_2Cl_2 and layered with ether, and the mixture was cooled. The pale yellow solid was filtered out, washed with ether, and dried *in vacuo*. Recrystallization of the product from CH_2Cl_2/ether gave pure yellow 1; yield 0.86 g (35%). Mp: 172 °C with dec. Anal. Calcd for $C_{20}H_{36}N_2O_2S_2Cl_4FePt_2$: C, 24.30; H, 3.67; N, 2.83. Found: C, 24.29; H, 3.50; N, 2.79. IR (KBr, cm^{-1}): 1146 $\nu_{S=O}$. Far IR (Nujol, cm^{-1}): 340 ν_{Pt-Cl}, 380 ν_{Pt-S}. ^1H NMR ($CDCl_3$): δ 2.68 (t, 12H, $^3J_{Pt-H}$ = 24 Hz, CH_3N), 3.37 (t, 12H, $^3J_{Pt-H}$ = 18 Hz, CH_3S), 4.03 (s, 4H, CH_2N), 4.26–4.56 (m, 6H, *CH* of $(\eta^5\text{-}C_5H_4)_2Fe$). ^{13}C NMR ($CDCl_3$): δ 45.09 (CH_3S, $^2J_{Pt-C}$ = 56.6 Hz), 52.66 (CH_3N), 64.57 (CH_2N), 70.60 and 73.65 (*CH* of $(\eta^5\text{-}C_5H_4)_2Fe$), 80.13 (quaternary C). ^{195}Pt NMR ($CDCl_3$, 25 °C): δ −3044. UV–visible (CH_2Cl_2, λ_{max}, nm): 322 (ϵ = 1076), 450 (ϵ = 224).

σ-$Pt_2[(\eta^5\text{-}C_5H_3CH_2NMe_2)_2Fe]Cl_2(DMSO)_2$, 3. *cis*-$Pt(DMSO)_2Cl_2$ (0.422 g; 1 mmol) was added to a solution of $(\eta^5\text{-}C_5H_4CH_2NMe_2)_2Fe$ (0.300 g; 1 mmol) in dry methanol (40 cm^3). The mixture was heated under reflux at 70–80 °C for 30 min with stirring in the absence of light. The mixture was rapidly cooled to room temperature and the solvent evaporated *in vacuo*, until an orange solid formed. The crude orange product was dissolved in CH_2Cl_2, the solution was filtered through a Celite pad, and the filtrate was reduced *in vacuo* to half of its volume; an orange-yellow crystalline solid was obtained by adding methanol and scratching the glass wall; yield of *dl* and *meso* isomers 0.18 g (20%). Mp: 192 °C with dec. Anal. Calcd for $C_{20}H_{34}N_2O_2S_2Cl_2FePt_2$: C, 26.24; H, 3.74; N, 3.06; S, 7.00; Cl, 7.74. Found: C, 26.20; H, 3.62; N, 3.04; S, 6.75; Cl, 8.09. IR (KBr, cm^{-1}): 1130 $\nu_{S=O}$. Far IR (Nujol, cm^{-1}): 295 ν_{Pt-Cl}, 378 ν_{Pt-S}. ^1H NMR ($CDCl_3$): δ 2.60 (t, 3H, $^3J_{Pt-H}$ = 34 Hz, CH_3N); 2.86 (t, 3H, $^3J_{Pt-H}$ = 32 Hz, CH_3N); 3.06 (t, 3H, $^3J_{Pt-H}$ = 30 Hz, CH_3N); 3.18 (t, 3H, $^3J_{Pt-H}$ = 30 Hz, CH_3N); 3.52, 3.53, 3.60, and 4.10 (t, 12H, CH_3S); 3.98–4.62 (m, 6H, $(\eta^5\text{-}C_5H_3)_2Fe$). ^{13}C NMR ($CDCl_3$): δ 51.30, 51.40, 53.31, and 53.18 (CH_3N); 45.92, 46.96, 42.27, and 47.64 (CH_3S); 67.87 and 68.86 (CH_2N); 61.79, 63.29, 65.61, 70.19, 71.41, and 73.34 (*CH* of $(\eta^5\text{-}C_5H_3)_2Fe$); 81.56, 86.68, 92.18, and 94.19 (quaternary C). ^{195}Pt NMR ($CDCl_3$, 25 °C): δ −3756, −3776. UV–visible (CH_2Cl_2, λ_{max}, nm): 292 (ϵ = 5126), 451 (ϵ = 218).

The DMSO-d_6 analogue was prepared by a similar procedure from *cis*-$PtCl_2(DMSO\text{-}d_6)_2$. ^1H NMR ($CDCl_3$): δ 2.61 (t, 3H, $^3J_{Pt-H}$ = 34 Hz, CH_3N), 2.86 (t, 3H, $^3J_{Pt-H}$ = 32 Hz, CH_3N), 3.06 (t, 3H, $^3J_{Pt-H}$ = 30 Hz, CH_3N), 3.18 (t, 3H, $^3J_{Pt-H}$ = 29 Hz, CH_3N), 3.98–4.62 (m, 6H, $(\eta^5\text{-}C_5H_3)_2Fe$). ^{13}C NMR ($CDCl_3$): δ 51.29, 51.40, 53.18, and 53.32 (CH_3N); 68.87 and 67.88 (CH_2N); 61.75, 63.28, 65.59, 70.19, 71.41, and 73.32 (*CH* of $(\eta^5\text{-}C_5H_3)_2Fe$); 86.68, 81.53, 92.19, and 94.18 (quaternary C) ^{195}Pt NMR (DMSO-d_6): δ −3734, −3744.

***trans*-$Pt_2Cl_4(DMSO)_2[(\eta^5\text{-}Me_2NCH(Me)C_5H_4)_2Fe)]$, 2, and σ-$Pt_2[(\eta^5\text{-}C_5H_3CH(Me)NMe_2)_2Fe)]Cl_2(DMSO)_2$, 4.** *cis*-$PtCl_2(DMSO)_2$ (12 mg; 0.028 mmol) and $(\eta^5\text{-}C_5H_4CH(Me)NMe_2)_2Fe$ (5.2 mg; 0.016 mmol) were dissolved in distilled acetone (5 cm^3), and the mixture was stirred in the dark for 1 h. The solvent was stripped and the residue dissolved in the minimum amount of ethyl acetate. Chromatographic separation on silica gel gave two yellow products. The first product oxidized rapidly to give a green solution, despite workup being carried out at low temperatures and under anaerobic conditions. The solid material obtained always contained 4, and green paramagnetic decomposition materials as well as 2. No crystalline samples of pure 2 were obtained, but NMR data were consistent with the formation of the *trans* product. ^1H NMR ($CDCl_3$): δ 2.65 (3H, CH_3N), 3.37 (3H, CH_3N), 3.4–3.6 (envelope SCH_3), 1.25 (m, $CH(CH_3)$. ^{195}Pt NMR ($CHCl_3$, 25 °C): δ −3006. The second product was shown to be 4. To synthesize 4, *cis*-$PtCl_2(DMSO)_2$ (0.211 g; 0.5 mmol) was added to solution of $(\eta^5\text{-}C_5H_4CH(Me)NMe_2)_2Fe$ (0.16 g; 1.9 mmol) in methanol (20 cm^3) and the mixture heated under reflux for 30 min. The solution was reduced in volume and layered with hexane. Yellow 4 slowly precipitated. Anal. Calcd for $C_{22}H_{38}N_2O_2S_2Cl_2FePt_2$: C, 28.00; H, 4.06; N, 2.97; S, 6.80. Found: C, 28.70; H, 4.22; N, 2.97; S, 6.80. ^1H NMR ($CDCl_3$): the spectrum is very complex because of the large number of diastereoisomers; δ 1.11, 1.19, 1.52, 1.57, 1.62 (J_{H-H} = 4.5 Hz, all $-CHMeNMe_2$); 2.3–2.4, 2.6, 2.99 (all NMe_2); 3.3–3.6 (envelope SMe); 3.9–4.4 (envelope C_5H_3). ^{195}Pt NMR ($CHCl_3$, 25 °C): δ −3756, −3760 (*weak signals at −3778, −3791*).

σ-$Pt_2[(\eta^5\text{-}C_5H_3CH_2NMe_2)_2Fe]Br_2(DMSO)_2$, 5. Lithium bromide (0.854 g; 9.8 mmol) in acetone (30 cm^3) was added to a solution of 3 (0.30 g; 0.33 mmol) in warm acetone (200 cm^3). The reaction mixture was stirred for 2.5 days at room temperature, after which time tlc (acetone/hexane 1:3) indicated that all of 1 had reacted. The solvent was removed in vacuo and the yellow-orange solid recrystallized from CH_2Cl_2/methanol; yield 0.30 g (90%). Mp: 250 °C with dec. Anal. Calcd for $C_{20}H_{34}N_2O_2S_2Br_2FePt_2$: C, 23.92; H, 3.41; N, 2.79; S, 6.38. Found: C, 24.36; H, 3.49; N, 2.82; S, 6.38. ^{195}Pt NMR ($CDCl_3$, 25 °C): δ −3819, −3830. UV–visible (CH_2Cl_2, λ_{max}, nm): 339 (ϵ = 4391), 470 (ϵ = 730). The different crystal forms (orange-red blocks and pale yellow plates), obtained from successive crystallizations from CH_2Cl_2/methanol at room temperature, were separated by microscopic examination.

Yellow Form (Meso), 5a. IR (KBr, cm^{-1}): 1126.4 $\nu_{S=O}$. Far IR (Nujol, cm^{-1}): 204 ν_{Pt-Br}, 380 ν_{Pt-S}. ^1H NMR ($CDCl_3$): δ 2.88 (t, 6H, $^3J_{Pt-H}$ = 32 Hz, CH_3N), 3.26 (t, 6H, $^3J_{Pt-H}$ = 30 Hz, CH_3N), 3.62 (t, 6H, $^3J_{Pt-H}$ = 25 Hz, CH_3S), 3.73 (t, 6H, $^3J_{Pt-H}$ = 23.3 Hz, CH_3S), 3.73 (AX, 4H, J_{AX} = 14.1 Hz, $\Delta\nu$ = 215.7 Hz, CH_2N), 4.47–4.04 (m, 6H, $(\eta^5\text{-}C_5H_3)_2Fe$). ^{13}C NMR ($CDCl_3$): δ 53.54 and 54.52 (CH_3N); 48.04 (CH_3S); 68.90 (CH_2N); 63.49, 69.92, and 71.52 (*CH* of $(\eta^5\text{-}C_5H_3)_2Fe$); 85.27 and 92.43 (quaternary C). ^{195}Pt NMR ($CDCl_3$, 25 °C): δ −3830.

Orange Form (Racemic), 5b. IR (KBr, cm^{-1}): 1130 $\nu_{S=O}$. Far IR (Nujol, cm^{-1}): 204 ν_{Pt-Br}, 380 ν_{Pt-S}. ^1H NMR ($CDCl_3$): δ 2.61 (t, 6H, $^3J_{Pt-H}$ = 33 Hz, CH_3N), 3.16 (t, 6H, $^3J_{Pt-H}$ = 31 Hz, CH_3N), 3.60 (t, 6H, CH_3S), 4.23 (t, 6H, CH_3S), 4.04–4.69 (m, 6H, $(\eta^5\text{-}C_5H_3)_2Fe$). ^{13}C NMR ($CDCl_3$): 51.36 and 52.35 (CH_3N); 48.35 and 48.46 (CH_3S); 67.79 (CH_2N); 61.77, 65.31, and 73.24 (*CH* of $(\eta^5\text{-}C_5H_3)_2Fe$); 90.59 and 94.09 (quaternary C). ^{195}Pt NMR ($CDCl_3$ 25 °C): δ −3819.

σ-$Pt_2[(\eta^5\text{-}C_5H_3CH_2NMe_2)_2Fe]I_2(DMSO)_2$, 6. Lithium iodide (0.88 g; 6.6 mmol) and 3 (0.20 g; 0.22 mmol) in dry acetone (150 cm^3) were stirred at 50 °C for 1.5 h and then 4 days at room

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Table 1. Crystal Data, Data Collection, and Refinement of Compounds 1, 5a, and 5b

	1	5a	5b
empirical formula	$C_{20}H_{36}O_2N_2S_2Cl_4FePt_2$	$C_{20}H_{34}O_2N_2S_2Br_2FePt_2$	$C_{20}H_{34}O_2N_2S_2Br_2FePt_2$
M/g mol^{-1}	988.49	1004.47	1004.47
cryst syst	monoclinic	monoclinic	monoclinic
space group[a]	$P2_1/c$ (No. 14)	$P2_1/c$ (No. 14)	$P2_1/c$ (No. 14)
a/Å	7.623(2)	14.277(5)	9.984(3)
b/Å	13.993(4)	8.974(3)	10.335(3)
c/Å	13.271(3)	10.951(2)	25.929(7)
α/deg	90	90	90
β/deg	95.66(2)	105.77(2)	92.28(2)
γ/deg	90	90	90
V/Å^3	1408.7(6)	1350.1(7)	2673(1)
$D_c(D_m)$/g cm^{-3}	2.33	2.47	2.50
Z	2	2	4
cryst size/mm	0.36 × 0.24 × 0.14	0.32 × 0.14 × 0.08	0.41 × 0.38 × 0.36
μ(Mo Kα)/cm^{-1}	111.88	122.09	148.68
F(000)	936	936	1872
diffractometer	Nicolet R3M	Nicolet R3M	Nicolet R3M
temp/K	163(5)	163(5)	163(5)
radiation	Mo Kα (λ = 0.710 69 Å)	Mo Kα (λ = 0.710 69 Å)	Mo Kα (λ = 0.710 69 Å)
scan type	Wycoff	Wycoff	Wycoff
scan speed/deg min^{-1}	5.86	5.86	5.86
data limits/deg	$4 < 2\theta < 56$	$3 < 2\theta < 50$	$3 < 2\theta < 50$
reflns measd	$h,k,\pm l$	$h,k,\pm l$	$h,k,\pm l$
cryst decay[b]/%	<1	<1	<2.5
abs corr	empirical	empirical	empirical
transm	0.980 (max)	0.972 (max)	0.572 (max)
	0.350 (min)	0.611 (min)	0.294 (min)
total no. of reflns[c]	3395	2369	4670
no. of unique data ($I > 2\sigma_I$)	2472	1534	3897
method of solving	Patterson	Patterson	replacement
no. of variables	163	154	304
treatment of protons	calculated	calculated	calculated
R ($\omega\Delta F/\omega\lvert F_o\rvert$)	0.0453	0.0550	0.0400
R_w [$\omega w^{1/2}(\Delta F)/\omega w^{1/2}F_o$]	0.0371	0.0263	0.0488
weight (w)	$[1.5117/(\sigma^2_F + 0.000159F^2)]$	$[1.3559/(\sigma^2_F + 0.000005F^2)]$	$[1.2570/(\sigma^2_F + 0.00099F^2)]$
residual dens/e Å^{-3}	+1.59, −2.24	+2.78, −1.77	+1.78, −1.75

[a] *International Tables for X-ray Crystallography*; Kynoch Press: Birmingham, England, 1966; Vol. I. [b] Standard reflections: (300), (040), (006) for **1**; (200), (040), (004) for **5a**; (−3,11,1), (−2,10,0), (−1,8,3) for **5b**, measured after every 100 reflections. [c] Lorentz and polarization corrections and empirical absorption corrections were applied using the SHELXTL system.

temperature in the dark. The solvent was evaporated, and the solid was taken up in methanol, filtered out, and dried *in vacuo*; yield of *dl* and *meso* 0.19 g (79%). Mp: 234 °C with dec. Anal. Calcd for $C_{20}H_{34}N_2O_2S_2I_2FePt_2$: C, 21.87; H, 3.12; N, 2.55. Found: C, 22.28; H, 3.12; N, 2.57. IR (KBr cm^{-1}): 1122 ν_{S-O}. Far IR (Nujol mull, cm^{-1}): 133 ν_{Pt-I}, 380 ν_{Pt-S}. ^{1}H NMR ($CDCl_3$): δ 2.61 (t, 3H, $^3J_{Pt-H}$ = 34 Hz, CH_3N); 2.88 (t, 3H, $^3J_{Pt-H}$ = 34 Hz, CH_3N); 3.34 (t, 3H, CH_3N); 3.41 (t, 3H, CH_3N); 3.74, 3.78, 3.92, and 4.42 (t, 3H, CH_3S); 4.01–4.82 (m, 6H, (η^5-C$_5H_3$)$_2$Fe). ^{13}C NMR ($CDCl_3$): δ 51.77, 54.06, 55.75, and 57.00 (*C*H$_3$N); 49.71, 50.64, 50.98, and 51.57 (*C*H$_3$S); 67.58 and 68.81 (*C*H$_2$N); 61.79, 63.73, 64.79, 69.21, 71.64, and 73.06 (*C*H of (η^5-C$_5H_3$)$_2$Fe); 92.25, 92.65, 94.24, and 97.66 (quaternary C). ^{195}Pt NMR ($CDCl_3$, 25 °C): δ −3917. UV-visible (CH_2Cl_2, λ_{max}, nm): 345 (ϵ = 3696), 469 (ϵ = 669).

NMR Investigation of the Conversion of the trans Complex 1 to the Cyclometalated Bromo and Iodo Derivatives, 5 and 6. 1 (0.005 g; 5 × 10^{-3} mmol) and LiX (X = Br, I; 1.3 × 10^{-2} mmol) in methanol were maintained at 35 °C in an NMR tube. The ^{1}H NMR spectrum was monitored until complete conversion to **5** or **6** was obtained, and the resulting *meso*:*dl* ratios were recorded from the relative intensities of the N(CH_3)$_2$ and S(CH_3)$_2$ resonances. The results are summarized in Table 7.

σ-Pt$_2$[(η^5-C$_5$H$_3$CH$_2$NMe$_2$)$_2$Fe]Cl$_2$(PPh$_3$)$_2$, 7. Triphenylphosphine (17 mg; 6.5 × 10^{-2} mmol) was added to a solution of **3** (30 mg; 3.3 × 10^{-2} mmol) in chloroform (2 cm^3). The mixture was stirred at room temperature under nitrogen for 15 min, methanol (2 cm^3) was added, and the volume was reduced by evaporation. The pale orange-yellow solid obtained was recrystallized from CH_2Cl_2/methanol to give pure **7**; yield **34** mg (80%). Mp: 205 °C with dec. Anal. Calcd for $C_{42}H_{52}N_2P_2Cl_2FePt_2$: C, 48.65; H, 4.08; N, 2.18; P, 4.83. Found: C, 48.30; H, 4.13; N, 1.78; P, 4.63. Far IR (Nujol, cm^{-1}): 289 ν_{Pt-Cl}, 259 ν_{Pt-P}. ^{1}H NMR ($CDCl_3$): δ 2.97 (bs, 6H, CH_3N), 3.04 (bs, 6H, CH_3N), 3.20–3.70 (m, 6H, (η^5-C$_5H_3$)$_2$Fe), 7.39–7.77 (m, 30H, P(C$_6H_5$)$_3$). ^{31}P NMR ($CDCl_3$): δ 17.24 ($P(C_6H_5)_3$, $^1J_{Pt-P}$ = 4298 Hz). ^{195}Pt NMR ($CDCl_3$, 25 °C): δ −4117 ($^1J_{Pt-P}$ = 4280 Hz). UV-visible (CH_2Cl_2, λ_{max}, nm): 271 (ϵ = 4502), 449 (ϵ = 507).

X-ray Structure Determinations of 1, 5a, and 5b. Samples of **1**, **5a**, and **5b** were prepared as detailed above. Yellow platelike crystals of **1** were obtained by slow ether diffusion into a solution of the compound in CH_2Cl_2. Recrystallization of **5** from CH_2Cl_2/methanol produced a crystalline solid which contained two distinct crystalline forms. Yellow plates of **5a**, and orange blocks of **5b** were readily separated from the mixture under a microscope. Precession photography (Cu Kα radiation) of all three crystals indicated monoclinic unit cells and the systematic absences $h0l$, $l = 2n + 1$, $0k0$, $k = 2n + 1$, confirmed the space group as $P2_1/c$[19] in each case. Details of the crystals, data collections, and structure refinements are summarized in Table 1.

The structures of **1** and **5a** were solved using the Patterson interpretation procedures of SHELXS-86[20] with the Pt and Fe atoms clearly located in the tangent expansion procedures. In both cases the Fe atoms were located at a center of symmetry (Wycoff position *a* for **1** and *d* for **5a**) and their coordinates were constrained appropriately. The remaining non-hydrogen atoms were found in a series of difference Fourier least-squares refinement cycles. For **5b**, which was found to be isomorphous with the previously determined **3**,[15] coordinates obtained for **3** were used in the initial refinement with appropriate substitution

(19) *International Tables for X-ray Crystallography*; Kynoch Press: Birmingham, England, 1966; Vol. 1.
(20) Sheldrick, G. M. SHELXS-86, A program for the solution of crystal structures from diffraction data. University of Göttingen, 1986.

Table 2. Final Positional and Equivalent Thermal Parameters for 1

atom	x/a	y/b	z/c	U_{eq}, Å^2
Pt(1)	0.18070(5)	0.20920(3)	0.29821(3)	0.013
Cl(1)	0.4241(3)	0.2641(2)	0.2257(2)	0.030
Cl(2)	−0.0565(3)	0.1511(2)	0.3740(2)	0.018
S(1)	0.3561(3)	0.1032(2)	0.3834(2)	0.017
O(1)	0.2773(9)	0.0310(5)	0.4444(5)	0.028
C(15)	0.510(1)	0.1694(8)	0.4651(7)	0.026
C(16)	0.500(1)	0.0435(8)	0.3059(7)	0.024
N(1)	0.0127(9)	0.3166(5)	0.2252(5)	0.015
C(13)	−0.134(1)	0.2710(7)	0.1610(7)	0.020
C(14)	0.100(1)	0.3837(8)	0.1581(7)	0.021
C(1)	−0.068(1)	0.3761(8)	0.3042(6)	0.021
C(2)	0.063(1)	0.4212(7)	0.3794(6)	0.015
C(3)	0.137(1)	0.3790(7)	0.4721(6)	0.020
C(4)	0.253(1)	0.4484(9)	0.5234(7)	0.030
C(5)	0.249(1)	0.5314(9)	0.4630(8)	0.030
C(6)	0.133(1)	0.5144(7)	0.3726(7)	0.020
Fe(1)	0.0000	0.5000	0.5000	0.018

Table 3. Final Positional and Equivalent Thermal Parameters for 5a

atom	x/a	y/b	z/c	U_{eq}, Å^2
Pt(1)	0.2464(1)	0.1164(1)	0.4263(1)	0.016
Br(1)	0.0979(1)	0.2055(2)	0.4879(2)	0.034
S(1)	0.1873(3)	−0.1115(6)	0.3993(4)	0.027
C(15)	0.070(1)	−0.104(3)	0.292(1)	0.040
C(16)	0.167(1)	−0.178(2)	0.543(2)	0.040
O(1)	0.2407(9)	−0.228(1)	0.352(1)	0.038
N(1)	0.3079(9)	0.336(1)	0.438(1)	0.023
C(13)	0.268(1)	0.403(2)	0.307(1)	0.031
C(14)	0.286(2)	0.436(2)	0.534(2)	0.037
C(1)	0.414(1)	0.328(2)	0.467(2)	0.031
C(2)	0.440(1)	0.185(2)	0.406(1)	0.029
C(3)	0.368(1)	0.069(2)	0.382(1)	0.019
C(4)	0.408(1)	−0.051(2)	0.327(1)	0.020
C(5)	0.504(1)	−0.008(2)	0.318(1)	0.026
C(6)	0.521(1)	0.139(2)	0.365(1)	0.036
Fe(1)	0.500	0.000	0.500	0.021

of the scattering factor terms for the Br atoms. Refinement minimizing $\Sigma w(|F_o| - |F_c|)^2$, was performed using SHELX-76.[21] In all cases hydrogen atoms were included in the refinements as fixed contributions to F_c, weighting schemes based on counting statistics were introduced and the non-hydrogen atoms were refined anisotropically. Final positional and equivalent thermal parameters for 1, **5a**, and **5b** are given in Tables 2–4.

Results and Discussion

Initial reaction of $PtCl_2(DMSO)_2$ with the ferrocenylamines $[(\eta^5\text{-}C_5H_4CH(R)NMe_2)_2Fe]$ (R = H, Me) in weak donor solvents gave the bis(platinum) derivatives *trans*-$\{Pt_2Cl_4(DMSO)_2[(\eta\text{-}C_5H_4CH(R)NMe_2)_2Fe]\}$, **1** and **2**. Further reaction in donor solvents leads to the formation of the bis(platinocycles) **3** and **4** (Scheme 1) in high yield. Because of the facile oxidation of all complexes **1-4**, their preparation and subsequent reactions were carried out under an inert atmosphere. This oxidation is a consequence of a marked negative shift in E^0 for the ferrocenyl couple of the bis(platinum) complexes, relative to those of the mono(platinum) analogues.[22] It is interesting that the cycloplatination reaction with these bis(platinum) compounds is much faster than with the mono(platinum) analogues; the reason for this is not obvious as qualitative NMR studies, akin to those carried out for the mono(platinum) compounds,[1] indicate that the cycloplatination mechanism is the same. The *trans* complex **2** decomposed rapidly in solution, partly because of the facile cycloplatination reaction and partly because of oxidation to ferrocenium compounds (this "oxidation" may involve a disproportionation step); as a consequence **2** was only characterized spectroscopically in solution.

Table 4. Final Positional and Equivalent Thermal Parameters for 5b

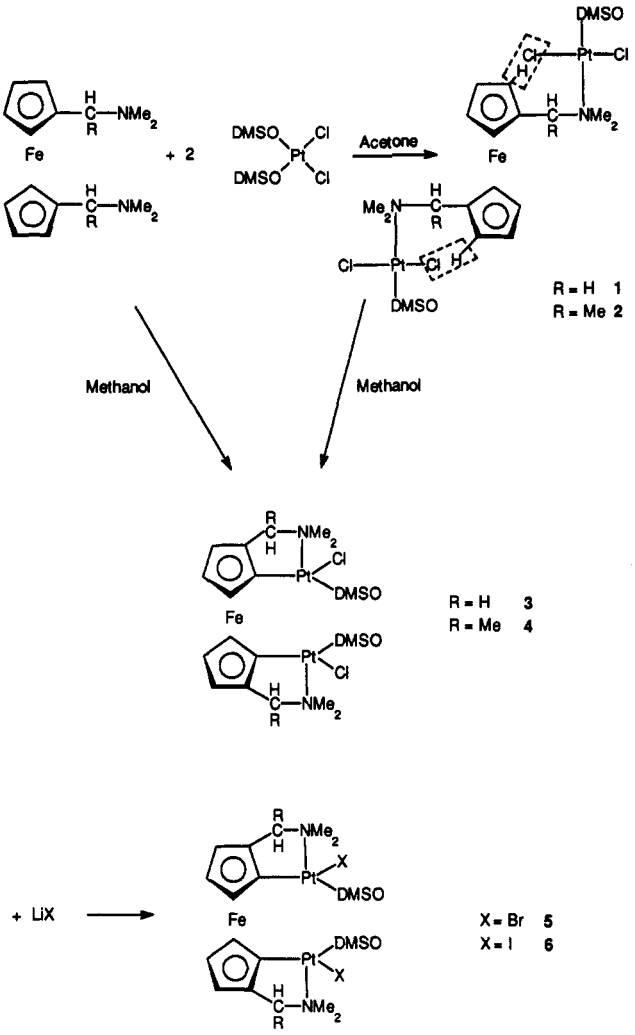
atom	x/a	y/b	z/c	U_{eq}, Å^2
Pt(1)	0.28725(4)	−0.28788(4)	0.44536(1)	0.012
Br(1)	0.5171(1)	−0.2247(1)	0.48227(4)	0.021
S(1)	0.3771(2)	−0.4070(2)	0.3858(1)	0.016
O(1)	0.2915(7)	−0.4725(7)	0.3467(3)	0.022
C(15)	0.478(1)	−0.531(1)	0.4172(5)	0.033
C(16)	0.500(1)	−0.320(1)	0.3533(4)	0.030
N(1)	0.1877(8)	−0.1809(8)	0.5035(3)	0.016
C(13)	0.184(1)	−0.268(1)	0.5492(4)	0.033
C(14)	0.252(1)	−0.055(1)	0.5193(4)	0.023
C(1)	0.045(1)	−0.154(1)	0.4852(4)	0.021
C(2)	0.004(1)	−0.266(1)	0.4526(4)	0.018
C(3)	0.0987(9)	−0.3382(9)	0.4260(4)	0.013
C(4)	0.028(1)	−0.4388(9)	0.3981(4)	0.015
C(5)	−0.109(1)	−0.426(1)	0.4094(4)	0.022
C(6)	−0.128(1)	−0.322(1)	0.4428(4)	0.021
Fe(1)	−0.0485(1)	−0.2625(1)	0.37522(5)	0.015
C(8)	−0.025(1)	−0.247(1)	0.2981(4)	0.019
C(7)	0.064(1)	−0.328(1)	0.2662(4)	0.018
N(2)	0.1639(9)	−0.2391(8)	0.2427(3)	0.019
C(17)	0.277(1)	−0.323(1)	0.2256(5)	0.026
C(18)	0.101(1)	−0.169(1)	0.1982(4)	0.023
C(9)	0.034(1)	−0.135(1)	0.3220(4)	0.017
C(10)	−0.069(1)	−0.0768(9)	0.3508(4)	0.015
C(11)	−0.189(1)	−0.145(1)	0.3426(4)	0.023
C(12)	−0.163(1)	−0.250(1)	0.3084(4)	0.016
Pt(2)	0.21660(4)	−0.09249(4)	0.29922(1)	0.014
Br(2)	0.4347(1)	−0.0440(1)	0.25656(4)	0.027
S(2)	0.2542(3)	0.0622(2)	0.3564(1)	0.018
O(2)	0.1587(8)	0.0847(8)	0.3966(3)	0.030
C(19)	0.415(1)	0.045(1)	0.3871(5)	0.029
C(20)	0.279(1)	0.212(1)	0.3240(4)	0.025

Metathetical reactions of the cycloplatinated chloro complexes gave the bromo and iodo analogues (Scheme 1). Yellow and orange crystalline forms of the bromo derivative **5** were separated and subsequently identified as the *meso* and *dl* stereoisomers, respectively. The formation of stereoisomers of **5** can be explained assuming the intermediacy of **1** which offers two alternatives for the site of concerted intramolecular electrophilic attack on the cyclopentadienyl rings by the two Pt(II) moieties (*vide infra*). With the ligand $[\eta^5\text{-}C_5H_3C^*H(Me)NMe_2]_2Fe$, a combination of planar and central chirality means that the cyclometalation pathway could result in a large number of possible stereoisomers for complex **4**, although the spectroscopic data indicate that two forms dominate (*vide infra*). Attempts to chromatographically separate these isomers failed, as they rapidly decompose on silica or alumina due to their propensity to oxidize. Most of the following discussion will concern complexes with the $-CH_2NMe_2$ functional group [hereafter $(\eta^5\text{-}C_5H_3CH_2NMe_2)_2Fe$ is designated as bis(FMA) and $(\eta^5\text{-}C_5H_3CH(Me)NMe_2)_2Fe$ as bis(FMMA)].

Substitution of the coordinated DMSO in **3** by PPh_3 gave the cycloplatinated phosphine derivative σ-Pt_2(bis(FMA))$(PPh_3)_2Cl_2$, **7**. It was not possible to prepare phosphine derivatives of the intermediate **1** because tertiary phosphines immediately cleave the Pt–N bond and $Pt(PR_3)_2Cl_2$ complexes are produced; this behavior is similar to the mono(platinum) analogues.[1] Ionic com-

(21) Sheldrick, G. M. SHELXS-76, Program for crystal structure determination. University of Cambridge, 1976.
(22) (a) Ranatunge-Bandarage, P. R. R. Thesis, University of Otago, 1989. (b) Duffy, N. W.; Robinson, B. H.; Simpson, J. Unpublished work.

Scheme 1



plexes with chelating phosphines, produced from reactions of **3** and **4**, are described elsewhere.[23]

Characterization and Structure Determination. A general discussion of the IR and NMR spectra expected for a *trans*-Pt(ferrocenylamine)(DMSO)X_2 and Pt(σ-ferrocenylamine)(DMSO)X coordination sphere has been given in the preceding paper[1] and will not be repeated here. In this paper we will concentrate on the stereochemical consequences of the coordination of one ferrocenylamine moiety to two Pt(II) centers and the resulting stereoisomerism for the metalated bis(FMA) complexes. The donor set in the bis(platinum) complexes is identical to those in the mono(platinum) analogues; the ferrocenylamine is N-bound, and the DMSO S-bound. Similarly, the spectroscopic data are consistent with a *trans* configuration in solution for **1** and **2** (confirmed by a solid state structure for **1**; *vide infra*) and a *trans* N-DMSO and *trans* σ-PtC/X ligand configuration about the Pt(II) ion for **3–6**. ^{1}H NMR for **2** were broad due to paramagnetic impurities, but a set of resonances with chemical shifts and relative intensities consistent with the stoichiometry proposed for **2** could be identified. Moreover, the two ^{195}Pt resonances found at −3005 and −3048 ppm were in the region expected for complexes with a *trans*-$PtNCl_2S$ coordination sphere[1,24] and, from the relative intensities

Table 5. Selected Bond Lengths and Angles for 1

	Bond Lengths (Å)		
Pt(1)---Cl(1)	2.304(2)	S(1)---C(15)	1.77(1)
Pt(1)---Cl(2)	2.302(2)	S(1)---C(16)	1.785(9)
Pt(1)---S(1)	2.229(2)	N(1)---C(13)	1.48(1)
Pt(1)---N(1)	2.143(7)	N(1)---C(14)	1.49(1)
S(1)---O(1)	1.460(7)	N(1)---C(1)	1.52(1)
		C(1)---C(2)	1.48(1)
	Bond Angles (deg)		
Cl(1)–Pt(1)–Cl(2)	178.1(1)	O(1)–S(1)–C(16)	107.8(5)
Cl(1)–Pt(1)–S(1)	88.1(1)	C(15)–S(1)–C(16)	101.0(5)
Cl(1)–Pt(1)–N(1)	92.7(2)	Pt(1)–N(1)–C(13)	110.0(6)
Cl(2)–Pt(1)–S(1)	90.1(1)	Pt(1)–N(1)–C(14)	115.5(5)
Cl(2)–Pt(1)–N(1)	89.1(2)	Pt(1)–N(1)–C(1)	109.7(5)
S(1)–Pt(1)–N(1)	176.2(2)	C(13)–N(1)–C(14)	106.4(7)
Pt(1)–S(1)–O(1)	118.9(3)	C(13)–N(1)–C(1)	107.5(7)
Pt(1)–S(1)–C(15)	106.8(4)	C(14)–N(1)–C(1)	107.5(7)
Pt(1)–S(1)–C(16)	113.0(3)	N(1)–C(1)–C(2)	114.2(7)
O(1)–S(1)–C(15)	107.7(5)	C(1)–C(2)–C(3)	125.9(9)
		C(1)–C(2)–C(6)	125.6(9)

of these resonsances, the *R* and *S* antipodes were present in a 1:1 ratio, as expected.

X-ray Crystal Structures of 1, 3, 5a, and 5b. Selected bond lengths and angles for **1** are given in Table 5 with those for **3**, **5a**, and **5b** in Table 6. The structure of the racemic stereoisomer of **3** has been communicated previously.[15] Perspective views of **1**, **5a**, and **5b** are shown in Figures 1–3 respectively, and define the atom numbering schemes.

Structure of 1. Compound **1** consists of well separated molecules with no unusual intermolecular contacts. The Fe atom of the staggered ferrocene moiety is situated on a crystallographically imposed center of symmetry such that, in the solid state, the Pt atoms are located at opposite sides of the ferrocene ring. The coordination sphere of each square-planar Pt atom comprises two mutually trans Cl^- ions, the S atom of a DMSO ligand, and an amine N atom of the bis(FMA) ligand. Bond distances and angles observed in **1** do not differ significantly from those reported for the analogous complex *trans*-{$PtCl_2$(DMSO)[(η^5-C_5H_5)Fe(η^5-$C_5H_4CH_2N(CH_3)_2$]}.[1]

Structures of 3, 5a, and 5b. Crystallization of **5** gave two different crystalline forms, **5a**, and **5b**, which could be separated by crystal picking. The structures of **5a** and **5b** consist of well separated molecules in monoclinic unit cells. General views of the molecules (Figures 2 and 3) show that the compounds each have two Pt(II) coordination spheres bridged by the ferrocenylamine ligand. Each have the Pt(II) ions in distorted square-planar environments with ligand sets consisting of a halide anion (Cl^- for **3** and Br^- for **5a** and **5b**), the S atom of the DMSO ligand, together with an amine N atom and an *ortho* C atom from one of the cyclopentadiene rings of the bis(ferrocenylamine). Corresponding bond distances and angles for **3**, **5a**, and **5b**, and the analogous mono(platinum) complex,[1] σ-Pt[(η^5-C_5H_5)Fe(η^5-$C_5H_3CH_2N(CH_3)_2$)]Cl(DMSO), are similar. The Pt–Br distances in **5a** (2.537(1) Å) and **5b** (2.523(2) Å) are long as a result of the *trans* influence of the σ-PtC bond; these values compare with a Pt–Br distance of 2.388(2) Å in *trans*-$PtBr_2$(cyclohexylamine)$_2$[25] and 2.429(1) and 2.439(2) Å in *cis*-$PtBr_2$(1,2-diaminohexane).[26]

In **5a** the Fe atom of the ferrocenylamine ligand is situated on a crystallographic center of symmetry such

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(26) Lock, C. J. L.; Pilon, P> *Acta Crystallogr., Sect. B* **1981**, *37*, 45.

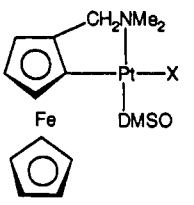
Table 6. Selected Bond Lengths and Angles for 3, 5a, and 5b

	3, X = Cl	5a, X = Br	5b, X = Br
	Bond Lengths (Å)		
Pt(1)---X(1)	2.412(2)	2.537(1)	2.523(2)
Pt(1)---S(1)	2.204(2)	2.194(3)	2.202(5)
Pt(1)---N(1)	2.142(7)	2.145(8)	2.14(1)
Pt(1)---C(3)	2.01(1)	1.998(9)	1.97(2)
S(1)---O(1)	1.473(7)	1.467(7)	1.47(1)
S(1)---C(15)	1.79(1)	1.80(1)	1.77(1)
S(1)---C(16)	1.79(1)	1.76(1)	1.78(2)
N(1)---C(13)	1.51(1)	1.49(1)	1.52(2)
N(1)---C(14)	1.49(1)	1.50(1)	1.48(2)
N(1)---C(1)	1.50(1)	1.51(1)	1.47(2)
C(1)---C(2)	1.48(1)	1.48(1)	1.54(2)
C(7)---C(8)	1.50(1)	1.49(1)	
C(7)---N(2)	1.52(1)	1.50(1)	
N(2)---C(17)	1.48(1)	1.50(1)	
N(2)---C(18)	1.49(1)	1.48(1)	
N(2)---Pt(2)	2.130(8)	2.159(9)	
C(9)---Pt(2)	2.001(9)	1.99(1)	
Pt(2)---X(2)	2.422(2)	2.532(1)	
Pt(2)---S(2)	2.191(2)	2.202(3)	
S(2)---O(2)	1.483(6)	1.460(8)	
S(2)---C(19)	1.790(9)	1.78(1)	
S(2)---C(20)	1.79(1)	1.78(1)	
	Bond Angles (deg)		
X(1)-Pt(1)-S(1)	90.9(1)	91.2(1)	90.6(1)
X(1)-Pt(1)-N(1)	91.8(2)	92.3(2)	93.0(3)
X(1)-Pt(1)-C(3)	172.0(3)	172.4(3)	173.8(4)
S(1)-Pt(1)-N(1)	176.0(2)	175.9(2)	175.2(4)
S(1)-Pt(1)-C(3)	95.8(3)	94.9(3)	95.5(5)
N(1)-Pt(1)-C(3)	81.3(4)	81.5(4)	80.8(6)
Pt(1)-S(1)-O(1)	119.6(3)	120.2(3)	119.5(5)
Pt(1)-S(1)-C(15)	108.9(4)	108.5(4)	108.3(8)
Pt(1)-S(1)-C(16)	110.1(4)	111.1(4)	110.1(6)
Pt(1)-N(1)-C(13)	104.3(6)	105.9(7)	105.2(9)
Pt(1)-N(1)-C(14)	115.9(6)	115.8(6)	116.0(9)
Pt(1)-N(1)-C(1)	108.7(5)	109.4(6)	110(1)
N(1)-C(1)-C(2)	108.0(8)	105.7(8)	107(1)
C(1)-C(2)-C(3)	117.2(8)	121.2(9)	115(1)
C(1)-C(2)-C(6)	134.2(9)	129(1)	134(2)
Pt(1)-C(3)-C(2)	113.8(7)	112.6(7)	115(1)
Pt(1)-C(3)-C(4)	137.5(7)	139.0(8)	138(1)
C(8)-C(7)-N(2)	108.0(7)	107.4(8)	
C(7)-C(8)-C(9)	117.3(8)	117.0(9)	
C(7)-C(8)-C(12)	132.4(9)	133.7(9)	
C(7)-N(2)-Pt(2)	109.4(5)	107.5(6)	
C(17)-N(2)-Pt(2)	116.2(6)	116.1(7)	
C(18)-N(2)-Pt(2)	106.1(6)	105.6(6)	
C(8)-C(9)-Pt(2)	113.9(7)	114.6(8)	
C(10)-C(9)-Pt(2)	139.7(7)	138.8(8)	
N(2)-Pt(2)-C(9)	82.3(3)	81.1(4)	
N(2)-Pt(2)-X(2)	91.7(2)	91.9(2)	
N(2)-Pt(2)-S(2)	176.5(2)	175.6(2)	
C(9)-Pt(2)-X(2)	172.7	171.4(3)	
C(9)-Pt(2)-S(2)	94.9(3)	95.4(3)	
X(2)-Pt(2)-S(2)	90.9(1)	91.4(1)	
Pt(2)-S(2)-O(2)	120.3(3)	119.9(3)	
Pt(2)-S(2)-C(19)	110.9(4)	110.8(4)	
Pt(2)-S(2)-C(20)	108.5(4)	109.7(4)	

that, in the solid state, the Pt atoms are located at opposite sides of the staggered ferrocene ring. This configuration is identified as the *meso* isomer. The Pt atom is displaced only 0.054(1) Å from the mean plane at the cyclopentadiene ring away from the Fe atom, reflecting the absence of significant steric interactions between the ligands in the two Pt(II) coordination spheres in the *meso* conformation, particularly in comparison to the situation observed for **3** and **5b** as described below.

For **3** and **5b**, the complexes crystallize in a centric space group with the *d* and *l* enantiomers present in equivalent proportions. In the solid state structure of these racemates there is an approximately eclipsed configuration for the cyclopentadiene rings of the ferrocene moiety with twist angles of 5(1)° for both **3** and **5b**. The angles between the cyclopentadiene ring planes are not excessive, 4.9(4)° for **3** and 5.9(4)° for **5a**. Interplanar angles >7° have been found in constrained ferrocene molecules,[27-30] suggesting that the configuration adopted here causes little strain for the ferrocenyl moiety. The methylamine and DMSO ligands are roughly staggered, which minimizes nonbonded interactions between the methyl substituents on these ligands. The PtL_4 ring planes are each bent out of the cyclopentadiene ring planes away from the Fe atoms which will further relieve steric interactions. Given the extensive intramolecular repulsions inherent in an eclipsed conformation, one would have anticipated the same staggered conformation for **3** and **5b** as that adopted by **5a**. It is recognized[27-30] that the balance between intramolecular ring interactions and intermolecular packing forces usually results in a preference for an eclipsed conformation of the cyclopentadiene rings, even where there may be the possibility of significant steric interactions between the cyclopentadienyl substituents, for example, in 1,1′,2,2′-tetrachloroferrocene,[30] and there are also several examples where the eclipsed conformations are imposed, or locked, by bridges between the two cyclopentadiene rings.[31] Nevertheless, it is still surprising that the eclipsed configuration is adopted by **3** and **5b** and it may be significant that it results in a head to head arrangement of the Pt coordination planes with Pt···Pt separations of 4.285(5) Å for **3** and 4.327(1) Å for **5b**. A similar head to head arrangement is found[29] in the mercury cation $\{[(\eta^5\text{-}Me_2NCH_2C_5H_4)Fe(\eta^5\text{-}Me_2NCH_2C_5H_4)]Hg\}_2^{2+}$. Does a weak Pt–Pt interaction tip the balance toward an eclipsed conformation? The Pt···Pt distances are considerably greater than those in some of the platinum blues,[32] or in stacked one-dimensional chain systems, where Pt···Pt separations of less than 3 Å are often observed,[33] but a weak interaction cannot be ruled out on the basis of the structural data alone (see ref 34 for a discussion of this point) and there is supportive physical data (*vide infra*).

Spectroscopic Data for the Cycloplatinated Stereoisomers. Spectra of the mono(platinum) analogues **8**[1] provide a useful reference for a discussion of the platinocycles **3–7** and are included in Table 7, which gives the ^1H and ^{195}Pt NMR data for **1–7**. Two discrete NMe



8(a) X = Cl,
8(b) X = Br

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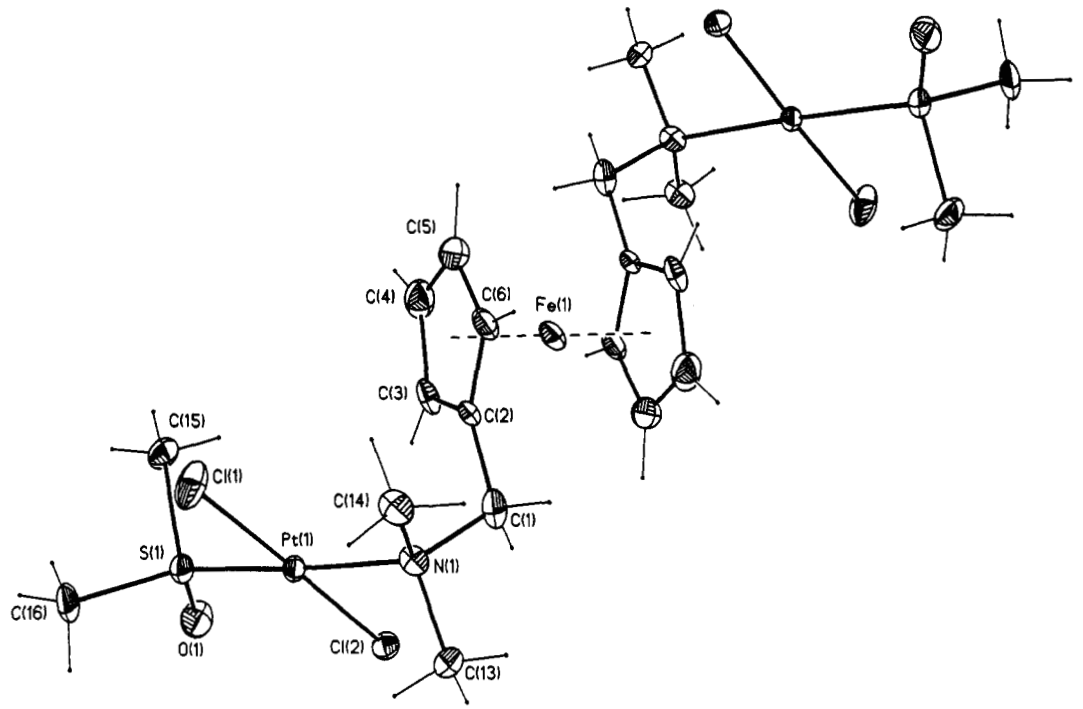

Figure 1. Perspective view of **1**, showing the atom-numbering scheme.

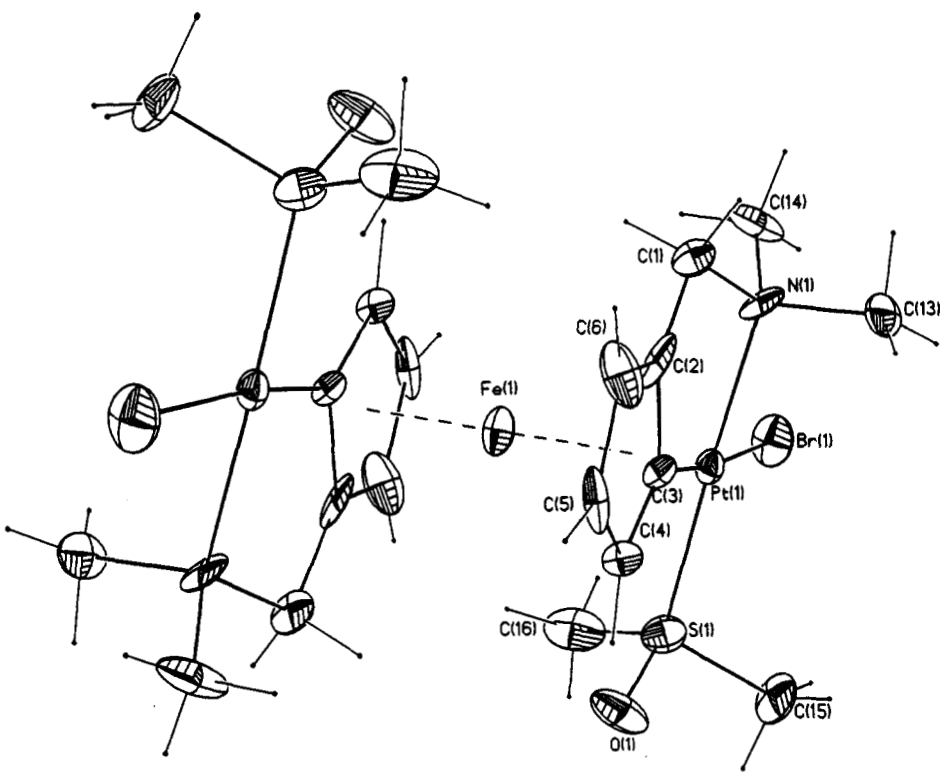

Figure 2. Perspective view of **5a**, showing the atom-numbering scheme.

and two SMe ^{1}H resonances due to the diastereotopic pairs of methyl groups characterize[1] the mono(platinum) complexes. In contrast, ^{1}H NMR spectra for the crude reaction products for **3**, **5**, and **6** displayed a complex profile of NMe and SMe resonances due to the presence of stereoisomers. Fortunately, the isolation of individual stereoisomers of **5** provided the key to an interpretation of the spectra. The pair of NMe resonances for the individual stereoisomers, *meso*-**5a** and *dl*-**5b**, occur at 2.88, 3.26 and 2.61, 3.16 ppm (Figure 4), respectively, compared with 2.93, 3.29 ppm for the mono(platinum) analogue **8b**. In meso-**5a**, with the five-membered rings in a transoid configuration the NMe_2 groups are in an identical conformation to that in the mono(platinum) derivatives **8**; consequently, **5a** (Figure 4a) and **8** have virtually the same ^{1}H NMR and the deshielded resonance at 3.26 ppm can be assigned[1] to the Me group orientated in the interplane region.

By contrast, the NMe groups in *dl*-**5b**, with the cyclopentadiene rings in a cisoid configuration are in a completely different environment, and as a result the NMe resonances are shielded compared to those for **5a** and **8**

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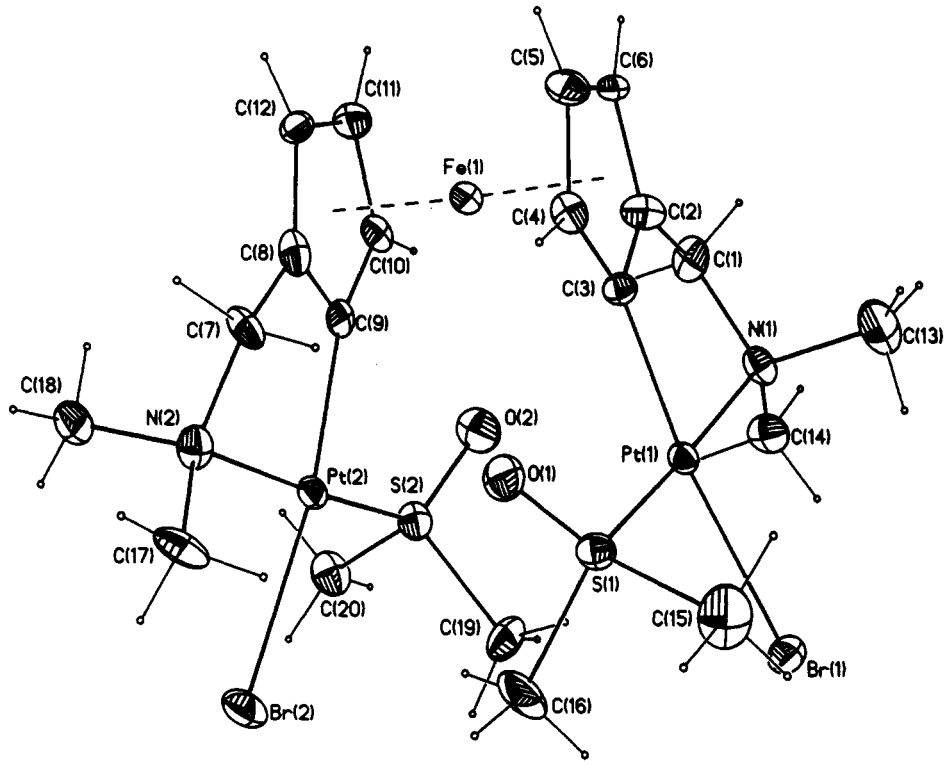

Figure 3. Perspective view of **5b**, showing the atom-numbering scheme.

Table 7. Selected Spectroscopic Data for Bis(platinum) Complexes[a,b]

	^{1}H NMR			
complex	NMe[c]	SMe	^{195}Pt NMR	*meso*/*dl*
3	2.86 (32)	3.52	−3776	0.3[f]
	3.18 (30)	3.60		
	2.60 (34)	*3.53*	*−3756*	
	3.06 (30)	*4.10*		
5a	2.88 (32)	3.62	−3830	0.5[g]
	3.26 (30)	3.73		
5b	*2.61 (33)*	*3.60*	*−3822*	
	3.16 (31)	*4.23*		
6	2.88 (34)	3.74	−3917	0.8[g]
	3.41	3.92		
	2.61 (34)	*3.78*	*−3917*	
	3.34	*4.42*		
7	2.97		−4117	
	3.04			
8a[d]	2.88 (33)	3.49	−3763	
	3.19 (30)	3.55		
8b[e]	2.93 (34)	3.64	−3815	
	3.29 (32)	3.68		

[a] Italics: data for *dl* structure. [b] In $CDCl_3$ at 25 °C. [c] J_{Pt-H} in Parentheses. [d] σ-{PtCl(DMSO)[η-$Me_2NCH_2C_5H_4Fe$(η-C_5H_5)]}. [e] σ-{PtBr(DMSO)[η^5-$Me_2NCH_2C_5H_4Fe$(η-C_5H_5)]}. [f] From the reaction of $PtCl_2(DMSO)_2$ with [(η^5-$Me_2NCH_2C_5H_4)_2$Fe] in methanol. [g] These figures refer to the product ratio for the reaction of **1** with LiBr or LiI in methanol (see Experimental Section).

(Figure 4b). Thus a clear distinction can be made between the ^{1}H spectra of the two stereoisomers using the NMe resonances (there is no significant variation in the J_{Pt-H} coupling constants however). Distinctive SMe resonances can also be assigned by a similar argument, but the significant feature in this case is that two of the SMe resonances in the *dl* isomer are noticeably downfield at 4.23 ppm. This resonance is assigned to the two internal methyl groups of the DMSO ligands. The two sets of stereotopic methylene protons of the CH_2NMe_2 functionality give an AX system of doublets for both isomers at 3.76 ppm for **5a** and 3.79 ppm for **5b** (the slope of the stereotopic pair was more typical of an AB system but the large separation points to AX as the correct designation). Furthermore, the separation between two AX doublets, $\Delta\nu$ = 525 Hz for the *dl* isomer, is larger than that for the *meso* isomer, $\Delta\nu$ = 213 Hz. This must reflect the closer proximity of the NMe groups to each other in the *dl* forms. Finally, there is a significant chemical shift difference between the cyclopentadienyl protons of the stereoisomers, with the multiplet for the *meso* isomer to low field of that for the *dl* isomer.

From these assignments for the stereoisomers of **5** it is possible to recognize the *meso* and *dl* stereoisomers in the ^{1}H NMR spectra of the initial products from the cycloplatination reactions and, from the relative intensities of the stereotopic NMe or SMe pairs, evaluate the *meso*:*dl* ratio (Table 7). The variation in stereochemical composition with coordinated halide anion was also seen in the ^{13}C NMR and, more particularly, the ^{195}Pt NMR (Table 7). Two ^{195}Pt resonances are observed for the reaction products when the coordinated halide is chloride or bromide, in a stereochemical ratio similar to that derived from the ^{1}H NMR (as expected, a single ^{195}Pt resonance is found for **5a** and **5b**). NMR spectra of solutions derived from crystalline **3** always had resonances due to both the *meso* and *dl* stereoisomers; the crystal chosen for the X-ray analysis was of the dominant *dl* isomer. This is not the situation for the iodo analogue **6**. Although the ^{1}H NMR of crude reaction solutions unequivocally show the presence of both the *meso* (in greater amount) and *dl* stereoisomers, only a single ^{195}Pt resonance is observed. An explanation for this observation is provided by noting the difference in ^{195}Pt chemical shift between the stereoisomers as the coordinated halide changes. This difference is 20 and 11 ppm for the chloro and bromo complexes **3** and **5**, respectively, so that it is reasonable to assume that it will be still smaller for the iodo complex; as the line width of the ^{195}Pt resonance for **6** was ~5 ppm, signals for the individual stereoisomers are likely to be unresolved. On the other hand, NMR spectra of solutions derived from

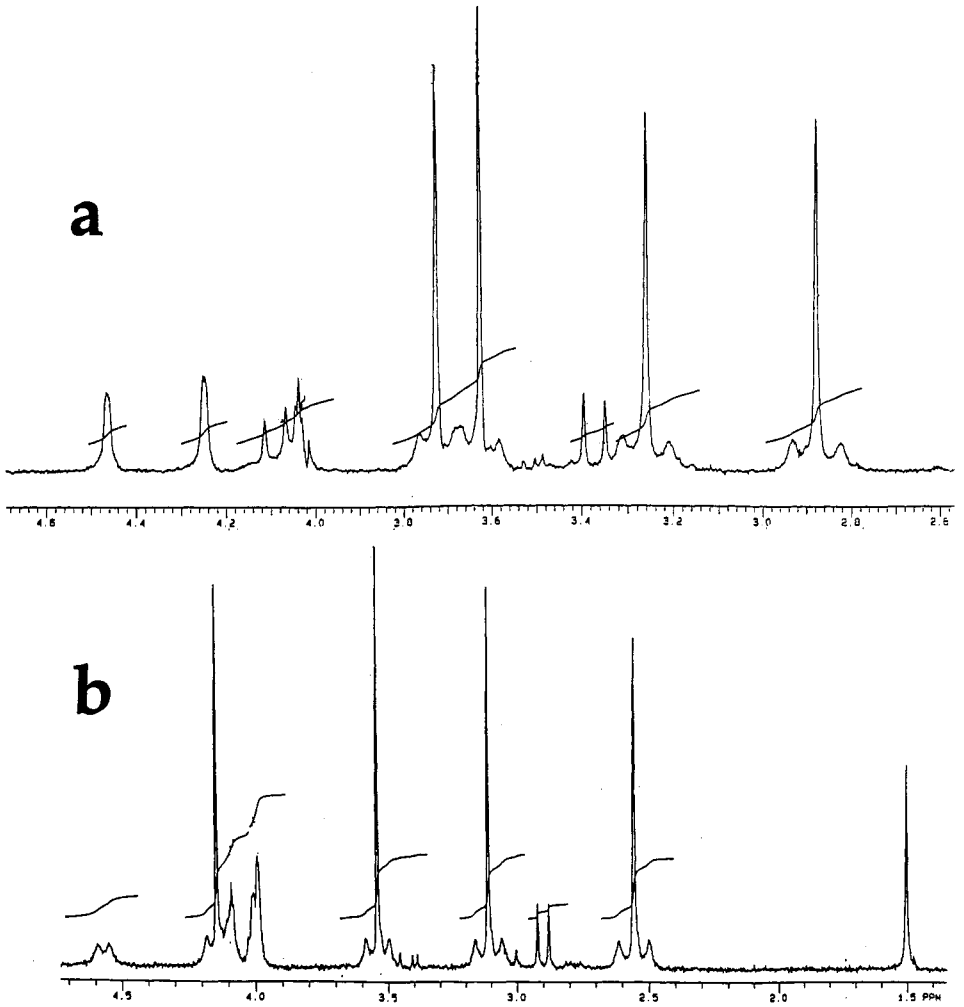

Figure 4. ^{1}H NMR spectra of the stereoisomers of **5**: (a) *meso* **5a**; (b) *dl* **5b**.

crystalline **6** gave one ^{195}Pt resonance but the chemical shift profile for the NMe and CH_2 stereotopic protons in the ^{1}H NMR are consistent with only the *meso* stereoisomer. Therefore, it can be concluded that the solid state structure of crystalline **6** is predominately *meso*. From the NMR spectra it was deduced that the stereochemistry of the PPh_3 derivative **7**, prepared from **3**, was *meso*. Subsequent work[22] has shown that the *dl* stereoisomer can also be synthesized and that the isolation of the *meso* form in this work was a consequence of the preparative procedure.

For bis(FMMA) complex **4** there were only two major ^{195}Pt resonances in the 3500–3700 ppm range typical of cycloplatinated ferrocenylamine complexes (it was estimated that the two resonances at −3756 and −3760 ppm were approximately 85% of the total intensity within this spectral region). Only one ^{195}Pt resonance was found with the mono(platinum) analogue[1] and the two major resonances for **4** can be assigned to the *dl* and *meso* stereoisomers of **4** with the same planar chirality (*S*) adopted by the mono(platinum) analogue.

Variable temperature ^{1}H and ^{195}Pt NMR spectra were recorded for the complexes **3**, **5a**, **5b**, and **6** in order to investigate whether there was any dynamic behavior in or between the stereoisomers. For all complexes the ^{195}Pt NMR spectra and the stereotopic pattern of NMe_2 and SMe resonances in the ^{1}H NMR spectra were temperature invariant confirming that no stereochemical interconversion takes place on the NMR time scale. However, an interesting temperature dependence involving the methylene proton resonances and certain cyclopentadienyl proton resonances was noted. For both **5a** and **5b** the AX pattern was maintained over the temperature range +40 to −40 °C but the separation between the doublets decreased with decreasing temperature; this temperature dependence was more marked for **5b**. In the ^{1}H NMR spectra of only the *dl* isomer there was a concurrent shift to low field and a smaller separation between the cyclopentadienyl protons, α and γ, adjacent to the two ring substituents; the β proton chemical shift does not change. Both of these observations must be stereochemical in origin because they are more marked for the *dl* conformation and not seen in the mono(platinum) analogues. Each CH_2 group of the $-CH_2NMe_2$ substituents has two conformations with respect to the plane defined by the chelated cyclopentadienyl ring and Pt(II) coordination sphere and flipping between these two orientations is likely[35] to be fast on the NMR time scale. However, there will be a continuum of chemical shift profiles associated with the average orientation of the two CH_2 relative to each other at a particular temperature, and this could lead to a temperature-dependent average environment.

Stereochemical Pathway of the Metalation Reaction. In the preceding paper[1] it was established that cycloplatination of mono(platinum) ferrocenylamine complexes proceeds through the intermediacy of a *trans*-PtCl(DMSO)L complex similar to **1**. An explanation for the

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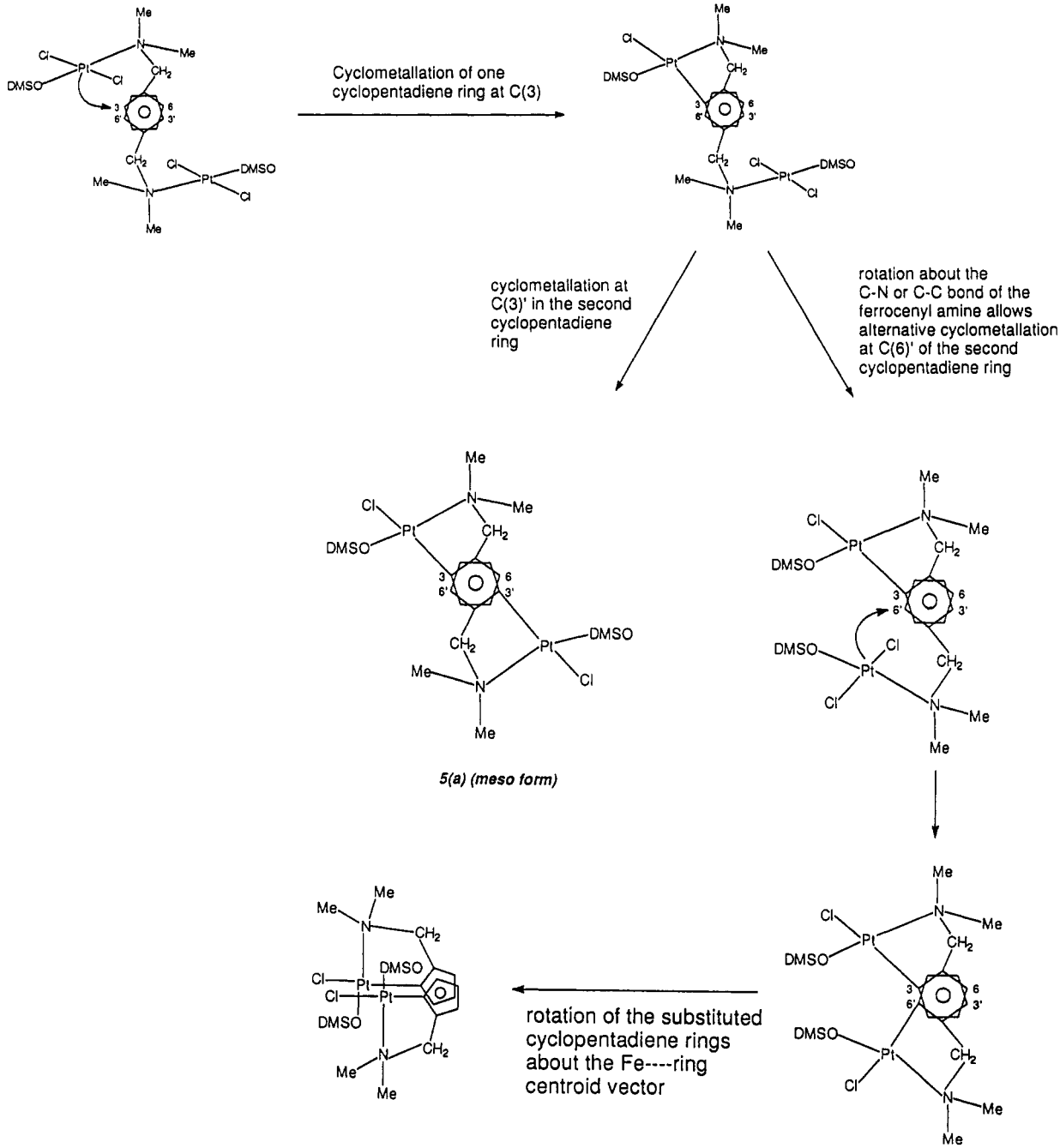
Scheme 2



formation of stereoisomers in cycloplatination reactions of bis(platinum) complexes can be found in the structure of **1**. In **1** the ferrocenylamine substituent and the cyclopentadienyl rings can freely rotate about the Pt(II)–N and Cp–Fe vectors, respectively, so that both the 3′- and 6′-positions on the second cyclopentadienyl ring are available for electrophilic attack by the Pt(II) entity. Scheme 2 shows **1** viewed down the Cp--Fe--Cp vector and corresponding views of the *meso* and *dl* stereoisomers **5a** and **5b**.

Once one chelate ring is formed through the first cyclometalation reaction, the orientation of the other cyclopentadienyl ring during the second metalation step determines the stereochemistry. As viewed in Scheme 2, electrophilic attack and removal of the hydrogen atom in the second cyclopentadienyl ring on the same side of the existing σPt–C bond gives rise to the *dl* isomer, whereas attack on the diametrically opposite side leads to the *meso* form. After the second chelate ring is formed, interconversion of the stereoisomers is not possible without breaking the σPt–C bond of one chelate ring.

Directional preferences for electrophilic attack may therefore be dependent on the ligands in the coordination sphere, as can be seen from the stereoisomer ratios in Table 7. The proportion of *dl* product, with a cisoid ring orientation, decreases as the size of the halide increases, or alternatively as it becomes a better leaving group. It is difficult to see how the electronic factors control the site of electrophilic attack, as the 3′- and 6′-positions are equivalent. Lithiation reactions of ferrocenylamines are highly stereospecific because of an interaction between the electrophilic lithium on the metalated ring and the lone pair of the amine function,[11] but a similar assistance is not available for **1**. Consequently, we need to look for the source of steric control. Given that a transoid ring orientation would be preferred for complexes with large

ligands in the Pt(II) coordination sphere, the increasing *meso* component **3** < **5** < **6** may be the result of steric interference within the Pt(II) coordination sphere during the formation of the transition state.

The bis(FMA) ligand itself has no elements of chirality, and cycloplatination gives both the *R* and *S* diastereoisomers in solution. However, cycloplatination of the *trans* bis(FMMA) complex **2**, in which the ligand has central chirality,[17] incorporates a stereospecific intramolecular homoannular ring fusion by the electrophilic coordinated Pt(II) ion, which is also the case for the mono(platinum) analoque. Cullen and co-workers have shown[36a] that the NMe_2 group lies predominantly above the plane of the ring with the *C*-methyl in the interplane region. In the cycloplatination transition state leading to **4**, steric repulsions between the *C*-methyl group on each ring and the *C*-methyl and the ferrocene moiety in an *endo* conformation would selectively give *R* and *S* planar chirality for the *dl* and *meso* stereoisomers of **4**, respectively. Indeed, the isomer distribution is similar to that found in the lithium-assisted synthesis of a bis(phosphine) derivative of bis(FMMA), where *S* and *R* central chirality leads selectively to *R* and *S* planar chirality.[36b]

Conclusion

Functionalization of both cyclopentadienyl rings provided a template for the formation of unusual bis(platinum), cyclometalated ferrocenylamine complexes displaying stereoisomerism arising from both central and planar chirality. They complement the many chiral complexes which derive their stereoisomerism from the asymmetric ferrocenylamine[13,14,37,38] and which have been used as asymmetric catalysts. Although *in vitro* studies indicated that the ability of ferrocenium derivatives to suppress the proliferation of tumor cells decreased when the metallocene ring was substituted,[9] it is not known whether neutral ferrocenyl compounds follow this trend. Nor is there any work on which to judge whether the biological activity of ferrocenylamines, or their complexes, is affected by the stereochemistry of the ferrocenyl moiety (the influence of ring chirality on antitumor activity has been shown[39] for some ethambutol complexes). The complexes described in this paper will enable both charge and stereochemical effects on the antiproliferative properties to be systematically explored. Their solubility in physiological media is limited, but by modification of the coordination sphere, this class of Pt(II)–ferrocenylamine complex has been extended to include water-soluble derivatives and cytotoxicity testing is underway.

The possibility of a weak interaction between the eclipsed platinum atoms in the *dl* structures needs to be substantiated, as compounds such as the "platinum blues", in which there are fractional or mixed valencies, have significant biological activity. While the Pt–Pt distances in the solid state structures of **3** and **5b** were not strongly supportive of an interaction, other data for the complexes in solution can be interpreted as being supportive. For example, the redox potentials in CH_2Cl_2 for the *dl*-bis(platinum) complexes are appreciably negative of mono(platinum) analogues despite the coordination spheres being the same; in water or other weak nucleophiles, the redox potentials are shifted to even more negative values, to the extent that the bis(platinum) complexes are rapidly oxidized by molecular oxygen.[22] It is also significant that the visible spectra of $\mathbf{3}^+$ are different from those of $\mathbf{8a}^+$. Complexes of ferrocenylamines with a direct Pt–Pt bond currently being studied will provide a useful comparison.

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Supplementary Material Available: Full tables of bond length and angle data, anisotropic thermal parameters, hydrogen positional and thermal parameters, and mean plane data (17 pages). Ordering information is given on any current masthead page.

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