Metallocene-Containing Platinum Complexes as Potential Antitumor Agents. 1. Dichloro(1,6-diferrocenyl-2,5-diazahexane)platinum(II) and *cis*-Dichlorobis(1-ferrocenylethylamine)platinum(II)

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In light of the cytostatic properties of the ferricenium radical cation against certain murine tumors, it has been of interest to combine the biooxidizable ferrocenyl group with the structural framework of the anticancer agent cisplatin (*cis*-diamminedichloroplatinum(II)). Dichloro(1,6-diferrocenyl-2,5-diazahexane)platinum(II) (2), and *cis*-dichlorobis(1-ferrocenylethylamine)platinum(II) (4) are presented as examples of such combination. The synthesis of 2 is brought about by treatment of the 1,2-diamine 1, 1,6-diferrocenyl-2,5-diazahexane, with the $PtCl_4^{2-}$ anion in aqueous EtOH at pH ≥ 7. The analogous reaction of 1-ferrocenylethylamine (3) with $PtCl_4^{2-}$ leads to 4, the cis configuration of the amine ligands in this complex being accepted on a tentative basis. At pH < 7 the formation of (substituted) ammonium tetrachloroplatinate(II) salts (such as 5 and 6) is favored as a consequence of the inductive donor properties of the metallocene substituents, which tend to stabilize the protonated amine sites. Spectroscopic data are presented for 1–6 in support of the assigned structures.

Introduction

Numerous anticancer agents are known to exert their biological activity via free radical metabolites, and indeed free radical processes appear to play a major role in the biochemistry of malignancies.[1] The ferricenium cation, Cp_2Fe^+ (Cp = η^5-cyclopentadienyl), itself an ion radical species of appreciable stability, interacts readily with free-radical precursors and a variety of biologically important electron donor compounds as well as with other nucleophiles.[2] This behavior suggested to us that the ferricenium ion might possess cytostatic properties, and indeed, certain hydrophilic ferricenium salts have since been found[3] to show antineoplastic activity against Ehrlich ascites murine tumor. The encouraging results of that work[3] led us to attempt the preparation of cisplatin-type compounds[4] containing covalently bonded ferrocene as a precursor of the biologically active ferricenium ion. The low formal potential of ferrocene in water (E_f = 0.127 V vs aqueous SCE at 25 °C[5]) should render this metallocene prone to biologically controlled oxidation–reduction processes. Ferrocene is indeed readily oxidized to ferricenium cation by the glucose oxidase–β-D-glucose system in the presence of peroxidase,[6] and the reverse reaction, reduction of the ferricenium ion to the neutral metallocene, is brought about by NADH[2f] or such diverse metalloproteins as cytochrome *c*,[2e] plastocyanin,[2g] or high-potential iron-sulfur protein.[2h] In this paper we report on the incorporation of ferrocenyl groups into two representative *cis*-(diamine)dichloroplatinum(II) derivatives.

Table I. Cl($2p_{3/2}$), N(1s), and Pt($4f_{7/2}$) Core Electron Binding Energies[a]

	binding energy (eV)		
compd	Cl($2p_{3/2}$)	N(1s)	Pt($4f_{7/2}$)
K_2PtCl_4	198.8		72.8
cisplatin[b]	198.5	400.1	72.7
1	198.0	399.0	
1·2HCl	197.8	401.5	
2	198.4	400.2	72.7
4	198.4	400.2	72.7
5	198.4	400.8	72.7_5

[a] From X-ray photoelectron spectra, referenced against binding energy of C(1s) = 284.6 eV; estimated error ± 0.25 eV [b] Lit. 72.8 eV (Barton, J. K.; Best, S. A.; Lippard, S. 284.6 eV Walton, R. A. *J. Am. Chem. Soc.* **1978**, *100*, 3785).

Results and Discussion

Two target structures were chosen in this project, both comrpising the functional *cis*-(diamine)dichloroplatinum(II) framework, with ferrocenyl groups covalently bonded to the amine ligands through methylene- or methinyl-bridging segments. Dichloro(1,6-diferrocenyl-2,5-diazahexane)platinum(II) (2) was obtained by treatment of 1, 1,6-diferrocenyl-2,5-diazahexane (*N,N′*-diferrocylethylenediamine; ferrocyl = ferrocenylmethyl), with potassium tetrachloroplatinate(II) in aqueous ethanol. Complex 4, *cis*-dichlorobis(1-ferrocenylethylamine)platinum(II), was prepared in a similar fashion from the tetrachloroplatinate and 1-ferrocenylethylamine (3). The amine reactant 1 was synthesized from formylferrocene and ethylenediamine and reduction of the azomethine double bonds in the intermediary 1,6-diferrocenyl-2,5-

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(1) See, for example: Halliwell, B.; Gutteridge, J. M. C. *Free Radicals in Biology and Medicine*; Clarendon: Oxford, 1985; notably Chapter 8.

(2) (a) Kornicker, W. A.; Vallee, B. L. *Ann. N.Y. Acad. Sci.* **1968**, *153*, 689. (b) Prins, R.; Korswagen, A. R.; Kortbeek, A. G. T. G. *J. Organomet. Chem.* **1972**, *39*, 335. (c) Bergmann, P. *Acta Biol. Med. Germ.* **1973**, *30*, 441. (d) Nefedov, V. A.; Tarygina, L. K. *Zh. Org. Khim.* **1976**, *12*, 2012; *Russ. j. Org. Chem.* (*Engl.* Transl.) 1976, *12*, 1960. (e) Pladziewicz, J. R.; Carney, M. J. *J. Am. Chem.* Soc. **1982**, *104*, 3544. (f) Carlson, B. W.; Miller, L. L.; Neta, P.; Grodkowski, J. *J. Am. Chem. Soc.* **1984**, *106*, 7233. (g) Pladziewicz, J. R.; Brenner, M. S.; Rodeberg, D. A.; Likar, M. D. *Inorg. Chem.* **1985**, *24*, 1450. (h) Pladziewicz, J. R.; Abrahamson, A. J.; Davis, R. A.; Likar, M. D. *Inorg. Chem.* **1987**, *26*, 2058.

(3) (a) Köpf-Maier, P.; Köpf, H.; Neuse, E. W. *Angew. Chem.* **1984**, *96*, 446; *J. Cancer Res. Clin. Oncol.* **1984**, *108*, 336. (b) Köpf-Maier, P. *Z. Naturforsch., C. Biochem., Biophys., Biol. Virol.* **1985**, *40C*, 843.

(4) *cis*-Diamminedichloroplatinum(II) (cisplatin), one of the most thoroughly investigated antineoplastic compounds, ranks as the first transition-metal complex that has found clinical use as an efficacious, although highly toxic, anticancer drug and represents the prototype of a large family of platinum coordination complexes synthesized for biomedical studies. Among the numerous, more recent reviews available, we mention but three: an outstanding survey article covering structure-activity relationships,[4a] a paper dealing with clinical aspects,[4b] and another one focusing on the mechanism of biological action of platinum drugs.[4c] (a) Cleare, M. J. *Dev. Pharmacol.* **1983**, *3*, 59. (b) Carter, S. K. *Dev. Oncol.* **1984**, *17*, 359. (c) Reedijk, J. *Pure Appl. Chem.* **1987**, *59*, 181.

(5) Sahami, S.; Weaver, M. J. *J. Solution Chem.* **1981**, *10*, 199.

(6) Epton, R.; Hobson, M. E.; Marr, G. *J. Organomet. Chem.* **1978**, *149*, 231.

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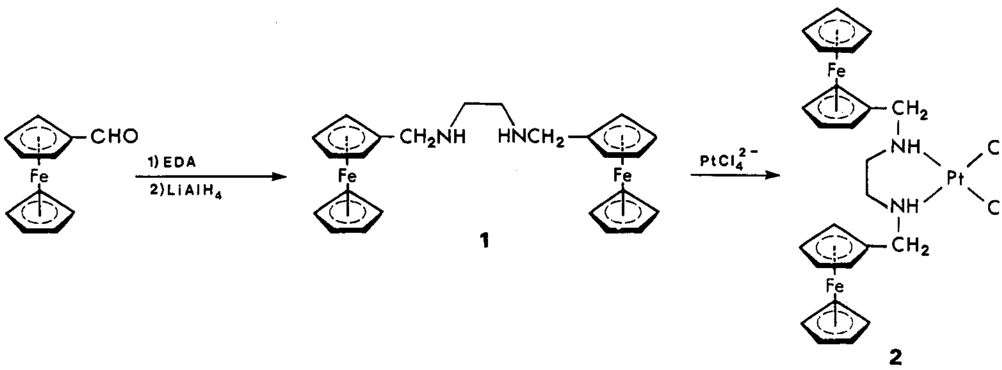
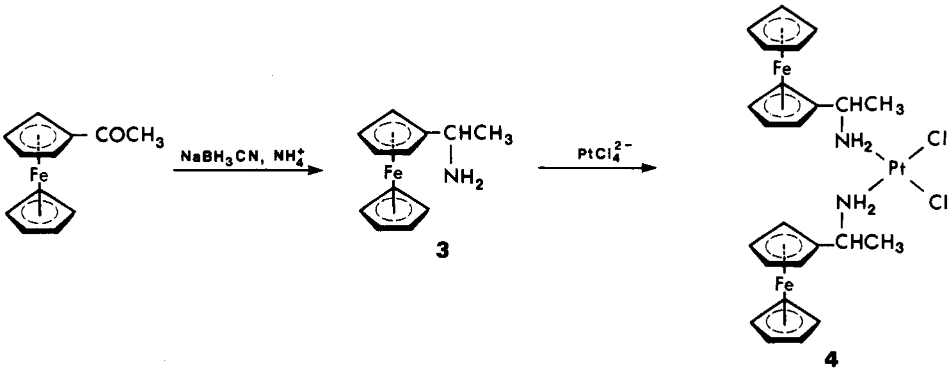
Scheme I



Scheme II



diazahexa-5,5-diene. Reductive amination of acetylferrocene with cyanoborohydride in the presence of NH_4^+ ion gave the amine **3**.[7] The overall synthetic sequences are depicted in Scheme I and II.

Complexes **2** and **4** both are high-melting solids only sparingly soluble in water but readily dissolving in a number of aprotic solvents, from which they can be recrystallized. A minor extent of N - Pt charge transfer, inherent in amine–platinum coordination, manifests itself in the higher N(1s) core electron binding energies (Table I) and, hence, more positive atomic charges on N in **2** and **4** than determined for the free diamine ligand **1**. The N(1s) binding energies in the two complexes are effectively identical with that in the prototype cisplatin (400.1–400.2 eV), indicating comparable atomic charges on N in all three complexes. The same holds for the Cl(2p) binding energies (198.4–198.5 eV) in these compounds. Interestingly, even the tetrachloroplatinate(II) ion possesses a chlorine binding energy closely approaching that of the *cis*-dichloroplatinum complexes, which suggests that, well in accord with bond length data,[8] there is little, if any, difference in the ionicity of the Cl ligand in the L_2PtCl_2 (L = amine ligand) and $PtCl_4^{2-}$ systems. The constancy of the Pt binding energy permits the same conclusion for the ionic character of Pt in these species. The solid-state IR spectra of both **2** and **4** display the characteristic ferrocene absorptions,[9] most prominent being the strong out-of-plane CH deformation band near 810 cm^{-1}, with a shoulder at 840 cm^{-1} (ν_9, ν_{19} in ferrocene[9]), and the equally intense two-component absorption in the vicinity of 500 cm^{-1} due to the skeletal modes ν_{11} and ν_{21} (485 cm^{-1} in **2**; 505, 485 cm^{-1} in **4**), burying any Pt–N stretching absorption anticipated at that position.[10] In the spectrum of **2**, NH stretching and deformation bands emerge at the positions 3155 and 3105 (ν_{NH}) and 1630 cm^{-1} (δ_{NH}), expected for metal-coordinated secondary amines. Complex **4**, comprising primary amine ligands, gives the corresponding stretching bands at 3280, 3205, and 3100 cm^{-1}, and the deformation band appears at 1565 cm^{-1}. Both complexes give a moderately intense band due to ν_{Pt-Cl} in the far-infrared region. The band emerges as an ill-resolved, narrowly split doublet in the vicinity of 320 cm^{-1}. The cis configuration of planar dichloroplatinum(II) (C_{2v} symmetry for identical amine ligands) requires doublet splitting, as the band is associated with two IR-active Pt–Cl stretching modes of very similar energy. The doublet nature of this band in **2** and **4** might thus be taken to confirm the cis configuration of the two chloro ligands in both complexes. However, in view of the reported[10] unreliability of this criterion we are reluctant to evaluate the multiplicity of this band for configurational assignments. In **2** the cis geometry is fixed by structural constraints. This is not so in **4**. While generally favored as a result of the trans effect exerted by the halogen ligands, the cis configuration is not necessarily the sole (or even the major) arrangement in the product of scheme II, in which the bulky amine ligand may well display some steric resistance to cis coordination.[12] Our assignment as

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(7) This synthesis is preferred over the (less efficient) earlier[7a,b] literature methods. (a) Graham, P. J.; Lindsay, R. V.; Parshall, G. W.; Peterson, M. L.; Whitman, G. M. *J. Am. Chem. Soc.* **1957**, *79*, 3416. (b) Schlögl, K.; Fried, M. *Monatsh. Chem.* **1964**, *95*, 558.

(8) The Pt–Cl bond distance is 233 pm in both cisplatin[8a] and K_2PtCl_4.[8b] (a) Milburn, G. H. W.; Truter, M. R. *J. Chem. Soc. A* **1966**, *11*, 1609. (b) *Gmelins Handbuch der Anorganischem Chemie*, 8th ed.; Springer-Verlag: Berlin, 1951; No. 68, Part C, p 172.

(9) Lippincott, E R.; Nelson, R. D. *Spectrochim. Acta* **1958**, *10*, 307.

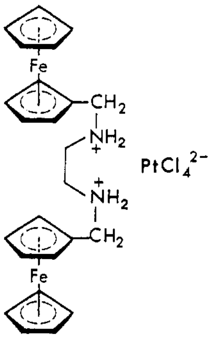
(10) In cisplatin, ν_{Pt-N} emerges at 510 cm^{-1},[10a] and in *cis*-dichlorobis(methylamine)platinum(II) the band is observed at 506 cm^{-1}.[10b] (a) Poulet, H.; Delorme, P.; Mathieu, J. P. *Spectrochim. Acta* **1964**, *20*, 1855. (b) Watt, G. W.; Hutchinson, B. B.; Klett, D. S. *J. Am. Chem. Soc.* **1967**, *89*, 2007.

(11) See, for example: Beaumont, K. P.; McAuliffe, C. A. *Inorg. Chim. Acta.* **1974**, *8*, 105 and references cited therein.

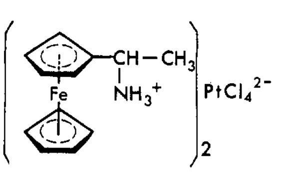
(12) Bulky peptide esters as amine ligands, for example, undergo partial trans coordination with Pt: Beck, W.; Bissinger, H.; Girnth-Weller, M.; Purucker, B.; Thiel, G.; Zippel, H.; Seidenberger, H.; Wappes, B.; Schönenberger, H. *Chem. Ber.* **1982**, *115*, 2256.

a cis-configurated complex (**4**), hence, needs further experimental confirmation.[13]

In the Pt–N coordination steps of Scheme I and II it is important to maintain the pH at or slightly above the neutrality point, preferably in the range of 7–8. Failure to do so will lead, as a consequence of enhanced basicity of the amine nitrogen atom brought about in both **1** and **3** by the (inductive) donor properties of the ferrocene substituent, to the preferential formation of (N-protonated) ammonium cations that are too stable, in equilibrium with free amine, for substantial coordination to Pt. As a result, large proportions of the respective amine hydrochlorides will be recovered. Moreover, ammonium tetrachloroplatinate(II) salt intermediates may be isolated. In the present work (Schemes I and II), for example, reactions of amines **1** and **3** employed as their hydrochloride salts without prior neutralization were found to be halted largely at the stage of formation of salt-like intermediates possessing elemental compositions in agreement with structures **5** and **6**.[14] Treatment of **5** with base completed the coordination process, giving **2**. In a similar fashion, **6** should be convertible to **4**, but this was not attempted. The IR spectra of **5** and **6**, while featuring a strong NH stretching absorption near 3100 cm^{-1} (with shoulders on both flanks in the spectrum of **6**), no longer show the intense, bonded NH stretching component displayed at 3000–2700 cm^{-1} by the hydrochlorides of both **1** and **3**. This is what one would expect for a protonated, yet monomeric amine and suggests that the cationic sites are effectively shielded sterically from intermolecular association in the solid state. In both **5** and **6** the Pt–Cl stretching band due to the asymmetric IR active mode ν_6 of the PtCl$_4$ system emerges as a sharp peak of high intensity at 310 and 320 cm^{-1}, respectively; the literature cites frequencies in the range of 313–320 cm^{-1} for this band in the spectrum of the tetrachloroplatinate(II) anion.[10a,15] The chlorine and nitrogen core electron binding energies determined for **5** (Table I) substantially support the structure proposed for this intermediate. The Cl(2p) energy (198.4 eV), being within the range (198.4–198.8eV) determined for the other listed dichloro- and tetrachloroplatinum(II) compounds, accords with Pt coordination of all four Cl atoms in the molecule. If Cl were partly present as chloride anion, the less positive atomic charge should be reflected in a lower binding energy; for the dihydrochloride of **1** (**1**·2HCl), for example, the observed Cl(2p) energy is 197.8 eV. In accord with the more positive atomic change on N in **5** than in **2**, the N(1s) binding energy in the former is found to be some 0.6 eV higher than in the neutral complexes, although not as high as in **1**·2HCl (401.5 eV), in which thus, for structural reasons still to be elucidated, the cationic (ammonium) character is more in evidence. In future work the scope of the ferrocenyl substitution of *cis*-(diamine)platinum complexes will be widened, and the feasibility of oxidizing the metallocene groups for enhanced hydrophilicity of the product complexes will be investigated.



5



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Experimental Section

Melting points, uncorrected, were obtained in sealed capillaries. Solid-state IR spectra were taken on KBr pellets over the range of 4000–200 cm^{-1}; only significant bands are cited in the text. ^{1}H NMR spectra (60 MHz, internal TMS standard) were recorded on CDCl$_3$ solutions. X-ray photoelectron spectra (AlK$_\alpha$) were recorded for N(1s), Cl(2p$_{3/2}$), and Pt(4f$_{7/2}$) core levels, and core electron binding energies were referenced against that of C(1s) = 284.6 eV. Microanalyses were performed by Robertson Laboratory, Florham Park, NJ, Galbraith Laboratories, Knoxville, TN, and by the Analytical Laboratory, MINTEK, Pretoria, Tvl. Considerable scattering of results was experienced (C, ±0.7%; Cl, ±1.5%; N, ±0.8%; Pt, ±0.5%); therefore, determinations were generally made in duplicate or triplicate and the findings averaged. Fe analyses showed variations too high (±1.8%) for routine evaluation and, hence, were not recorded.

Ferrocene (Strem Chemicals) was recrystallized from hexane. Formylferrocene and acetylferrocene, both prepared by literature procedures,[16] were recrystallized from the same solvent. *N,N*-Dimethylformamide (DMF), 1,2-diaminoethane (EDA), and tetrahydrofuran (THF) were distilled prior to use (the first-named two solvents under N$_2$). K$_2$PtCl$_4$ was obtained from Johnson Matthey. Other chemicals and solvents, including tetramethylene sulfone (sulfolane), dimethyl sulfoxide (DMSO), and tetramethylurea (TMU), all reagent grade (Fluka AG), were used as received. All platinum complexes prepared were routinely dried at 80 ± 5 °C (0.5 Torr); samples submitted for microanalysis were additionally dried for 24 h at 90 ± 5 °C (0.1 Torr).

1,6-Diferrocenyl-2,5-diazahexane (1). The precursor 1,6-diferrocenyl-2,5-diazahexa-1,5-diene was prepared in 87% yield from formylferrocene (60 mmol) and 1,2-diaminoethane (31.5 mmol) in boiling absolute EtOH (60 mL) in the presence of anhydrous K$_2$CO$_3$ (30 mmol) under N$_2$ and with protection from light. After recrystallization from EtOH, The red-orange diazahexadiene showed the following: mp 156–158 °C; IR (cm^{-1}) 1635 (vs, $\nu_{C=N}$); NMR (CDCl$_3$, δ) 8.14 (s, 2 H, –CH=), 4.60 (t, J = 2 Hz, 4 H, α-Cp), 4.30 (t, J = 2 Hz, 4 H, β-Cp), 4.14 (s, 10 H, unsubstituted Cp), 3.75 (s, 4 H, –CH$_2$CH$_2$–). Anal. Calcd for C$_{24}$H$_{24}$Fe$_2$N$_2$ (452.15): C, 63.75; H, 5.35; N, 6.20. Found: C, 63.96, H, 5.44; N, 5.95.

The diazahexadiene so obtained (7.0 mmol) was treated with LiAlH$_4$ (15.3 mmol, added in several portions) in dry Et$_2$O (200 mL) for 20 h at room temperature under N$_2$. The crude reduction product remaining after hydrolysis (ice water, 1 mL) and solvent removal (97% yield) was recrystallized twice from N$_2$-saturated toluene to give yellow-tan **1**: mp 129–132 °C; IR (cm^{-1}) 3400 (vw, br, ν_{NH}), 1640 (w, δ_{NH}); NMR (CDCl$_3$, δ) 4.07 (s, 18 H, Cp), 3.48 (s, 4 H, α-CH$_2$), 2.73 (s, 4 H, –CH$_2$CH$_2$–), 1.60 (s, br, variable, 2 H, NH). Anal. Calcd for C$_{24}$H$_{28}$Fe$_2$N$_2$ (456.2): C, 63.19; H, 6.19; N, 6.14. Found: C, 63.54; 5.86; N, 6.27.

The dihydrochloride (**1**·2HCl), precipitated in 95% yield from dry benzene solution of the free amine **1** by dry, gaseous HCl and twice recrystallized from abs. MeOH, formed yellow microcrystals: mp 228–230 °C (sintering at 211–223 °C); IR (cm^{-1}) 2950 (s,

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(13) (a) The Kurnakov test,[13b] invaluable for the discrimination between the configurational isomers of diamminedichloroplatinum(II) and simple derivatives, in our hands has proved of little diagnostic value in cases involving larger amine ligands, in which we have invariably observed the formation of multicomponent product complexes containing Pt-coordinated amine in addition to thiourea and halogen. (b) Kurnakov, N. *J. Prakt. Chem* **1894**, *50*, 481.

(14) In addition, one experiment per scheme II conducted in the pH range of 6–7 gave rise to the formation of a compound for which analytical results suggested the composition [Fc–CH(CH$_3$)NH$_3$]$^+$[Fc–CH(CH$_3$)-NH$_2$–PtCl$_3$]$^-$ of a partly ionic and partly coordinated complex. Anal. Calcd for C$_{24}$H$_{31}$Cl$_3$Fe$_2$N$_2$Pt (760.6): C, 37.89; H, 4.11; Cl, 13.98; N, 3.68. Found: C, 37.69; H, 3.98; Cl, 13.31; N, 3.50.

(15) (a) Adams, D. M.; Gebbie, H. A. *Spectrochim. Acta* **1963**, *19*, 925. (b) Goggin, P. L.; Mink, J. *J. Chem. Soc., Dalton Trans.* **1974**, *1479*.

(16) Bublitz, D. E.; Rinehart, K. L. *Org. React. (N.Y.)* **1969**, *17*, 1.

($\nu_{NH_2^+}$)$_{asym}$); 2700 (vs, br, ($\nu_{NH_2^+}$)$_{sym}$), 1580 (ms, (d), $\delta_{NH_2^+}$). Anal. Calcd for $C_{24}H_{30}Cl_2Fe_2N_2$ (529.1): Cl, 13.40. Found: Cl, 13.92.

1-Ferrocenylethylamine Hydrochloride (3·HCl). Acetylferrocene (25 mmol) was reduced with $NaBH_4$ (35 mmol, added in several portions) in boiling absolute MeOH (120 mL) containing $AcONH_4$ (250 mmol) for 6 h under a blanket of N_2. To the orange-brown oil left after solvent removal was added water (150 mL) with agitation, and the pH was adjusted to 8–9 (NaOH). The free base, obtained by extraction with Et_2O, drying ($MgSO_4$), and removal of solvent, was treated with dry Et_2O (25 mL) saturated with dry HCl gas, and the precipitated, yellow 3·HCl, after two recrystallization from absolute MeOH (briefly treated with dry HCl gas), showed the following: mp 202–205 °C (highest melting point observed with other samples 208–210 °C (lit.[7a] mp 163–165 °C dec; lit.[7b] mp 165–168 °C dec)); IR (cm^{-1}) 3050–2850 (vs, br, asym, sym $\nu_{NH_3^+}$), 1600 (m, br, $\delta_{NH_3^+}$). Material with a melting point in the range of 198–210 °C was used in the subsequent Pt coordination experiments. Anal. Calcd for $C_{12}H_{16}ClFeN$ (265.6): C, 54.27; H, 6.07; Cl, 13.35; N, 5.27. Found: C, 54.33; H, 6.16; Cl, 13.52; N, 5.09.

Dichloro(1,6-differrocenyl-2,5-diazahexane)platinum(II) (2). EtOH (7.5 mL) was added slowly to K_2PtCl_4 (3.0 mmol) dissolved in warm H_2O (15 mL). The slightly turbid solution was added dropwise, over 90 min, to a stirred solution of 1 (3.09 mmol), in 1:1 H_2O–EtOH (60 mL). A fine, yellow precipitate began to form slowy during this addition. Stirring of the mixture was continued for 20 h at room temperature. The precipitated product complex 2 was filtered off, washed with aqueous EtOH and then H_2O, and dried. Volume reduction of the combined filtrate and washings to 40–45 mL and cooling to 3 °C overnight afforded a small second portion of 2, bringing the total yield to 95%. The crude complex, almost analytically pure at this state (Anal. Found: C, 40.47; H, 4.06; Cl, 10.33; N, 4.10) was recrystallized from TMU (6–7 mL/100 mg), with water added to the hot, filtered solution to beginning turbidity. The product complex, which crystallized overnight at 0 °C, was collected by filtration as a yellow-tan solid, repeatedly digested with boiling 1 M aqueous HCl and then hot aqueous (1:1) MeOH, for complete solvent removal, and dried; IR (cm^{-1}) 3155, 3105 (s (d), ν_{NH}), 1630 (w, br, δ_{NH}), 310, 305 (m d), 322 (sh) (ν_{Pt-Cl}). Anal. Calcd for $C_{24}H_{28}Cl_2Fe_2N_2Pt$ (722.2) (2): C, 39.91; H, 3.91; Cl, 9.82; N, 3.88; Pt, 27.01. Found: C, 39.62 (single values 39.60, 40.27, 38.99); H, 3.96; Cl, 9.94 (single values 9.94, 8.74, 11.15); N, 3.70 (single values 3.22, 4.18); Pt, 26.13.

Complex 2 is infusible up to 300 °C. While but sparingly soluble in H_2O, it dissolves in hot aprotic solvents and can be recovered from these solutions, occasionally in a solvated form (DMSO, DMF, sulfolane), by the addition of H_2O. Rigorous washing, as described in the foregoing, is required for complete solvent removal.

***N,N'*-Diferrocenylethylenediammonium Tetrachloroplatinate(II) (5).** K_2PtCl_4 (0.5 mmol) was dissolved in H_2O (20 mL). To the filtered solution was added 1·2HCl (0.55 mmol). The suspension was stirred for 0.5 h at 80 °C. The pH ranged from about 5 to 4 during this period. The dark yellow solid of crude 5 contaminated with 1·2HCl was collected by filtration, washed with H_2O, and dried; yield 89.5%. The salt was purified by digestion with hot (70–80 °C) aqueous 0.1 M HCl. This removed little admixed dihydrochloride (9 mg recovered), mp 232–234 °C, identified by IR. The dried, yellow 5 had no melting point below 300 °C but underwent gradual darkening on heating; IR (cm^{-1}) 3095 (s, $\nu_{NH_2^+}$), 1545 (w, $\delta_{NH_2^+}$), 310 (s, ν_{Pt-Cl}). Anal. Calcd for $C_{24}H_{30}Cl_4Fe_2N_2Pt$ (795.1) (5): C, 36.25; H, 3.80; Cl, 17.83; N, 3.52; Pt, 24.54. Found: C, 36.74; H, 3.67; Cl, 16.99; N, 3.90; Pt, 24.10. Treatment of the salt in aqueous EtOH with Na_2CO_3 (pH 7.0–7.2), followed by warming of the mixture (60 °C) for 6 h, resulted in conversion to 2 (identified by IR and Cl content), which was isolated by filtration after volume reduction.

***cis*-Dichlorobis(1-ferrocenylethylamine)platinum(II) (4).** Na_2CO_3 (2.2 mmol) was added to the solution of 1-ferrocenylethylamine hydrochloride (3·HCl) (4.2 mmol) in deionized H_2O (30 mL) and EtOH (24 mL). After the base had dissolved, the solution was filtered. To this was added dropwise and with stirring, over a 30-min period, a solution prepared from K_2PtCl_4 (2.0 mmol) in deionized H_2O (20 mL), into which EtOH (15 mL) had slowly been stirred. Stirring of the orange-red solution was continued for 20 h at room temperature, at which point the pH had decreased to 7.0–7.5 and a yellow-tan precipitate of crude 4 had developed. The mixture was heated for 4 h at 60 °C, and the precipitated 4 was filtered off, washed with aqueous EtOH, and dried. The compound melted partially at 168–170 °C, and, at this stage, was almost analytically pure (Anal. Found: C, 39.65; H, 3.92; Cl, 10.60; N, 3.65; Pt, 26.56). Heating of the combined washings and filtrate for another 4 h at 60 °C, followed by volume reduction to 30–40 mL, caused additional 4 to separate from the solution, bringing the total yield to 86%. Evaporation of the combined washing and mother liquor to dryness afforded a light pinkish tan solid, from which 3·HCl (180 mg) could be recovered by extraction with hot EtOH. Recrystallization of combined crude fractions of 4 from TMU–H_2O and thorough washing with hot 1 M aqueous HCl and EtOH–H_2O as described for 2 gave the complex as a fine powdery, yellow-tan solid: mp 190–198 °C (other samples melted partially or completely in the range of 175–200 °C); IR (cm^{-1}) 3280 (m), 3205 (ms), 3100 (m) (ν_{NH}, the last-named band superimposed on ν_{CH} of ferrocene), 1565 (ms, δ_{NH}), 325, 319 (m (d), ν_{Pt-Cl}). Anal. Calcd for $C_{24}H_{30}Cl_2Fe_2N_2Pt$ (774.2) (4): C, 39.80: H, 4.18; Cl, 9.79; N, 3.87; Pt, 26.94. Found: C, 40.23; H, 4.48; Cl, 10.12; N, 3.79; Pt, 27.21. Recrystallization of 4 can also be brought about from THF, in which the complex, contrasting with 2, shows some solubility. The THF-solvated product, which crystallizes on cooling of the filtered solution to −20 °C, needs digestion with hot, diluted aqueous HCl and EtOH–H_2O for solvent removal.

Bis(1-ferrocenylethylammonium) Tetrachloroplatinate(II) (6). To the filtered solution of K_2PtCl_4 (1.0 mmol) in warm H_2O (10 mL) was added, with stirring, 3·HCl (2.24 mmol). The suspension was stirred for 6 h at 40 °C and, upon the addition of more H_2O (70 mL), was briefly (30 min) heated at 80 °C, which caused dissolution of the major part of suspended material. The mixture was filtered while hot, and the filtrate was reduced in volume to 40 mL at 40–45 °C and stored at 0 °C overnight. The crystallized yellow-tan, solid 6 was filtered off, washed with Et_2O, and dried. Further volume reduction of the mother liquor to ca. 20 mL and cooling as before gave a second crop of 6, bringing the total yield to 68%. From the final mother liquor unreacted 3·HCl (150 mg) was recovered (identified by IR).

The salt 6, already analytically pure at this stage (Anal. Found: Cl, 17.62; N, 3.33), was recrystallized from aqueous 1 M HCl (3 mL/100 mg), coming down as a yellow microcrystalline solid infusible up to 350 °C: IR (cm^{-1}) 3115 (vs, br), 3200, 3050, 2990 (sh) ($\nu_{NH_3^+}$), 1585, 1568 (ms (d), $\delta_{NH_3^+}$), 320 (s, ν_{Pt-Cl}). Anal. Calcd for $C_{24}H_{32}Cl_4Fe_2N_2Pt$ (797.1): C, 36.16; H, 4.05; Cl, 17.79; N, 3.51. Found: C, 36.05; H, 3.97; Cl, 17.62; N, 3.70.

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Registry No. 1, 65858-31-3; 1 (diazahexadiene), 63000-26-0; 1·2HCl, 117226-26-3; 2, 117226-22-9; 3, 12215-08-6; 3·HCl, 71159-94-9; 4, 117226-23-0; 5, 117226-24-1; 6, 117226-25-2; K_2PtCl_4, 10025-99-7; formylferrocene, 12093-10-6; 1,2-diaminoethane, 107-15-3; acetylferrocene, 1271-55-2.