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Self-association of new mixed-ligand diimine–*N*-acyl-*N*′,*N*′-dialkyl thioureate complexes of platinum(II) in acetonitrile solution †

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The complexes [Pt(bipy)L]PF_6 and [Pt(phen)L]PF_6 (HL = *N*-acyl-*N*′,*N*′-di-*n*-butylthiourea) showed pronounced self-association in CD_3CN solution at 25 °C according to an equilibrium 2[Pt(diimine)(L-*S*,*O*)]$^+$ ⟾ [{Pt(diimine)(L-*S*,*O*)}$_2$]$^{2+}$ for which association constants, K_D, have been estimated from the concentration dependence of the ^{1}H NMR shifts of these complexes. The values of K_D range from 1.8 to 114 M^{-1} depending on the structure of the diimine as well as the nature of the *N*-acyl group; the values of the 1,10-phenanthroline complexes are generally larger than those for the corresponding 2,2′-bipyridine analogues. In general, *N*-1-naphthoyl-*N*′,*N*′-dibutylthiourea complexes self-associate to a lesser extent than the corresponding *N*-benzoyl analogues. From the temperature dependence of the K_D values, the thermodynamic parameters ΔG, ΔH and ΔS have been estimated. An average $\Delta(\Delta G)$ increment of 2.4 ± 0.4 kJ mol^{-1} per aromatic ring of the diimine moiety co-ordinated to the complexes is consistent with energies generally associated with π–π stacking and cation π interactions observed for other systems.

Non-covalent attractions between planar molecules with delocalised π electrons have long been known, and have recently attracted considerable attention particularly in the context of molecular recognition involving synthetic organic host–guest complexes.[1] Moreover, the importance of cation π interactions in biology and chemistry has recently been reviewed.[2] Porphyrin aggregation was amongst the first known examples of such 'π–π' interactions,[3] and these have been extensively studied,[4,5] while recently a quantitative evaluation of the nature of ligand–porphyrin complex formation has been published.[6] Moreover, such interactions are thought to be responsible for the intercalation of numerous suitably shaped drug molecules between the bases of DNA, there being considerable interest in this area.[7] The intercalation of metal complexes into DNA was first demonstrated by Lippard and co-workers,[8] and continues to attract much recent attention, to mention but a few such studies.[9,10] Porphyrins also strongly interact with DNA, although not always clearly as intercalators however.[11] Not surprisingly, DNA intercalator molecules often show self-aggregation behaviour in solution as exemplified by the porphyrins,[10] as well as the recently described [Pt(terpy)Me]X (X = Cl^-, NO_3^-, PF_6^-, ClO_4^- or BPh_4^-) metallointercalator.[9]

We have become interested in the synthesis of new, cationic mixed-ligand platinum(II) complexes derived from simple diimines (2,2′-bipyridine and 1,10-phenanthroline) and *N*-acyl-*N*′,*N*′-dialkylthioureas (HL), as potentially new 'metallo-intercalators'. *N*-Acyl-*N*,*N*′-dialkylthioureas are easy to synthesize, versatile ligands for the platinum-group metals forming stable *S*,*O*-bonded chelates with Pt^{II} for example,[12] rendering these ligands ideal for the preparation of very soluble monocationic platinum(II) complexes of general structure [Pt(diimine)(L-*S*,*O*)]PF_6. We here report a study of the interesting self-aggregation of these mixed-ligand complexes.

Experimental

Preparation of starting materials

The *N*-benzoyl- (HL[1]) and *N*-1-naphthoyl-*N*′,*N*′-di-*n*-butylthioureas (HL[2]) were prepared and characterised as previously described.[12] Published methods were used to prepare [Pt(bipy)Cl_2] **1**[13] and [Pt(phen)Cl_2] **2**[14] as well as the corresponding 4,4′-dimethyl-2,2′-bipyridine, 4,4′-di-*tert*-butyl-2,2′-bipyridine and 4,7-diphenyl-1,10-phenanthroline complexes from commercially available K_2PtCl_4 and the corresponding diimines, 4,4′-Di-*tert*-butyl-2,2′-bipyridine was prepared from 4-*tert*-butylpyridine according to the method of Hadda and Le Bozec.[15]

Instrumentation and NMR spectroscopy

All ^{1}H and two-dimensional COSY NMR spectra of the [Pt(diimine)L]PF_6 complexes were recorded in 5 mm tubes using a Varian UNITY-400 FT spectrometer operating at 400 MHz at 25 ± 0.1 °C for the concentration-dependence studies, as well as the range (25–55) ± 0.1 °C (at 5 °C intervals) for the variable-temperature studies. Sufficient time between each spectrum recorded was allowed for the system to reach thermal equilibrium. The chemical shifts are recorded in parts per million (ppm) relative to $SiMe_4$ and estimated to be accurate to ±0.05 ppm at 95% confidence. Below the chemical shifts are reported for arbitrary concentrations. The labelling scheme for identification of the H atoms with respect to their NMR assignments used throughout is shown in Scheme 1: those of the two inequivalent *N*-butyl groups are labeled H^a, $H^{a'}$, . . . H^d, $H^{d'}$ of the phenyl/naphthyl moieties $H^{2''}$, $H^{3''}$ . . . $H^{6''}$, $H^{8''}$, of the 2,2′-bipyridine H^3, $H^{3'}$ . . . H^6, $H^{6'}$ and of the 1,10-phenanthroline H^2, H^3 . . . H^9, respectively.

Melting points were measured on a Reichert-Jung Thermovar attached to a DP-4 digital thermometer and are uncorrected. Elemental analyses for C,H,N and S were carried out on a Fissons EA 1108 Elemental Analyser; each analysis was carried out in duplicate. Mass spectra (+FAB) were obtained using a Kratos MS-50 spectrometer equipped with an argon atom FAB gun, using a 3-nitrobenzyl alcohol matrix (courtesy of Inorganic Chemistry Laboratory, University of Cambridge, UK).

Concentration dependence of chemical shift experiments

The concentration dependence of the chemical shifts of all complexes was studied at 25 ± 0.1 °C. A relatively concentrated stock solution (approximately 10^{-2} M) of each complex was prepared by weighing out an accurately known mass and dis-

† *Supplementary data available*: experimental and calculated ^{1}H NMR chemical shifts based on the best association constants. For direct electronic access see http://www.rsc.org/suppdata/dt/1998/689/, otherwise available from BLDSC (No. SUP 57438, 14 pp.) or the RSC Library. See Instructions for Authors, 1998, Issue 1 (http://www.rsc.org/dalton).

solving it in a measured volume of CD_3CN (typically 1.00 cm^3). Aliquots of 50 μl of the stock solution were then transferred using a micropippette to a NMR tube which contained exactly 0.50 cm^3 CD_3CN initially. After each addition the ^1H NMR spectrum was recorded after a 5 min equilibration period, and the complex concentration calculated, assuming additive volumes.

General preparation of mixed-ligand [Pt(diimine)(L^n-*S*,*O*)]PF_6 complexes

A suspension of [Pt(diimine)Cl_2] (0.5 mmol) in dry acetonitrile (40 cm^3) was heated to reflux for 10 min in a round-bottom flask equipped with a dropping funnel and condenser. To this was added the appropriate *N*-acyl-*N*′,*N*′-dialkylthiourea (0.505 mol) dissolved in acetonitrile (10 cm^3) over 5 min, and the mixture heated under reflux for 30–45 min. Sodium acetate (0.75 mmol) and ammonium hexafluorophosphate (2.5 mmol) dissolved in a little acetonitrile were added and the mixture heated to reflux for 30–45 min or until a clear, bright yellow solution was obtained. The precipitated NaCl and NH_4Cl were removed from the cooled solution by filtration through Celite, and the filtrate concentrated to a volume of *ca*. 10 cm^3 by evaporation. Diethyl ether (*ca* 100 cm^3) was added and cooled to −20 °C overnight. The yellow precipitate was collected by centrifugation, resuspended twice with ice-cold diethyl ether, and centrifuged again. The product may be recrystallised by dissolution in the minimum volume of acetonitrile, followed by treatment with diethyl ether and cooling as described. It was dried under vacuum over anhydrous silica gel overnight.

(*N*-Benzoyl-*N*′,*N*′-di-*n*-butylthioureato-*S*,*O*)(2,2′-bipyridyl)-platinum(II) hexafluorophosphate 3a. Yield 78%, m.p. 250–253 °C (Found: C, 39.1; H, 3.9; N, 6.8; S, 3.7. $C_{26}H_{31}F_6N_4OPPtS$ requires C, 39.64; H, 3.97; N, 7.12; S, 4.06%) (+)FAB mass spectrum: *m*/*z* 642.1 (M^+, calc. 642.187), 1284.4 (M_2^+, calc. 1284.4) and 1428.7 ($[M_2 + PF_6]^+$, calc. 1429.3). δ_H(400 MHz, solvent CD_3CN, reference $SiMe_4$) 0.96 (3 H, t, H^d), 1.05 (3 H, t, $H^{d'}$), 1.41 (2 H, m, H^c), 1.49 (2 H, m, $H^{c'}$), 1.70 (2 H, m, H^b), 1.83 (2 H, m, $H^{b'}$), 3.78 (4 H, m, $H^{a'}$, H^a), 7.50 (2 H, t, $H^{3''}$,$H^{5''}$), 7.57 (1 H, t, H^5), 7.65 (1 H, t, $H^{4''}$), 7.91 (1 H, t, $H^{5'}$), 8.11 (2 H, d, $H^{2''}$, $H^{6''}$), 8.17 (1 H, d, H^3), 8.22 (1 H, t, H^4), 8.23 (1 H, d, $H^{3'}$), 8.31 (1 H, t, $H^{4'}$), 8.57 (1 H, d, H^6) and 9.01 (1 H, d, $H^{6'}$).

(*N*-Benzoyl-*N*′,*N*′-di-*n*-butylthioureato-*S*,*O*)(4,4′-dimethyl-2,2′-bipyridyl)platinum(II) hexafluorophosphate 3b. Yield 83.4%, m.p. 272–275 °C (Found: C, 40.8; H, 4.3; N, 6.5; S, 3.7. $C_{28}H_{35}F_6N_4OPPtS$ requires C, 41.22; H, 4.33; N, 6.87; S, 3.92%). δ_H(400 MHz, CD_3CN, $SiMe_4$) 0.95 (3 H, t, H^d), 1.04 (3 H, t, $H^{d'}$), 1.40 (2 H, m, H^c), 1.49 (2 H, m, $H^{c'}$), 1.69 (2 H, m, H^b), 1.80–2.00 (2 H, m, $H^{b'}$), 2.48 (3 H, s, CH_3), 2.53 (3 H, s, CH'_3), 3.78 (4 H, m, $H^{a'}$, H^a), 7.38 (1 H, d, H^5), 7.51 (2 H, t, $H^{3''}$, $H^{5''}$), 7.65 (1 H, t, $H^{4''}$), 7.70 (1 H, d, $H^{5'}$), 8.00 (1 H, s, H^3), 8.07 (1 H, s, $H^{3'}$), 8.10 (2 H, d, $H^{2''}$, $H^{6''}$), 8.37 (1 H, d, H^6) and 8.79 (1 H, d, $H^{6'}$).

(*N*′-Benzoyl-*N*′,*N*′-di-*n*-butylthioureato-*S*,*O*)(4,4′-di-*tert*-butyl-2,2′-bipyridyl)platinum(II) hexafluorophosphate 3c. Yield 71.6%, m.p. 263–265 °C (Found: C, 45.4; H, 5.3; N, 6.1; S, 3.4. $C_{34}H_{48}F_6N_4OPPtS$ requires C, 45.32; H, 5.37; N, 6.22; S, 3.55%). δ_H(400 MHz, CD_3CN, $SiMe_4$) 0.92 (3 H, t, H^d), 1.04 (3 H, t, $H^{d'}$), 1.35 (2 H, m, H^c), 1.48 (2 H, m, $H^{c'}$), 1.42 [9 H, s, $C(CH_3)_3$], 1.46 [9 H, s, $C(CH'_3)_3$], 1.64 (2 H, m, H^b), 1.82 (2 H, m, $H^{b'}$), 3.68–3.78 (4 H, m, $H^{a'}$, H^a), 7.43 (2 H, t, $H^{3''}$, $H^{5''}$), 7.51 (1 H, dd, H^5), 7.60 (1 H, t, $H^{4''}$), 7.86 (1 H, dd, $H^{5'}$), 8.03 (2 H, d, $H^{2''}$, $H^{6''}$), 8.18 (1 H, d, H^3), 8.27 (1 H, d, $H^{3'}$), 8.34 (1 H, d, H^6) and 8.83 (1 H, d, $H^{6'}$).

(*N*-1-Naphthoyl-*N*′,*N*′-di-*n*-butylthioureato-*S*,*O*)(2,2′-bipyridyl)platinum(II) hexafluorophosphate 3d. Yield 73.8%, m.p. 132–135 °C (Found: C, 42.5; H, 3.9; N, 6.7; S, 3.8. $C_{30}H_{33}F_6N_4OPPtS$ requires C, 43.00; H, 3.97; N, 6.69; S, 3.82%). (+)FAB mass spectrum: *m*/*z* 693.5 (M^+, calc. 692.8), 1383.8 (M_2^+, calc. 1384.40) and 1531.1 ($[M_2 + PF_6]^+$, calc. 1529.37). δ_H(400 MHz, CD_3CN, $SiMe_4$) 0.85 (3 H, t, H^d), 1.06 (3 H, t, $H^{d'}$), 1.29 (2 H, m, H^c), 1.53 (2 H, m, $H^{c'}$), 1.69 (2 H, m, H^b), 1.88 (2 H, m, $H^{b'}$), 3.78 (2 H, m, H^a), 3.88 (2 H, m, $H^{a'}$), 7.51–7.61 (3 H, m, $H^{3''}$, $H^{6''}$, $H^{7''}$), 7.64 (1 H, m, H^5), 7.68 (1 H, m, $H^{5'}$), 8.01 (1 H, d, $H^{5''}$), 8.02 (1 H, d, $H^{2''}$), 8.11 (1 H, d, $H^{4''}$), 8.30–8.33 (4 H, m, $H^{3'}$, H^3, $H^{4'}$, H^4), 8.43 (1 H, d, $H^{8''}$), 8.73 (1 H, d, H^6) and 8.78 (1 H, d, $H^{6'}$).

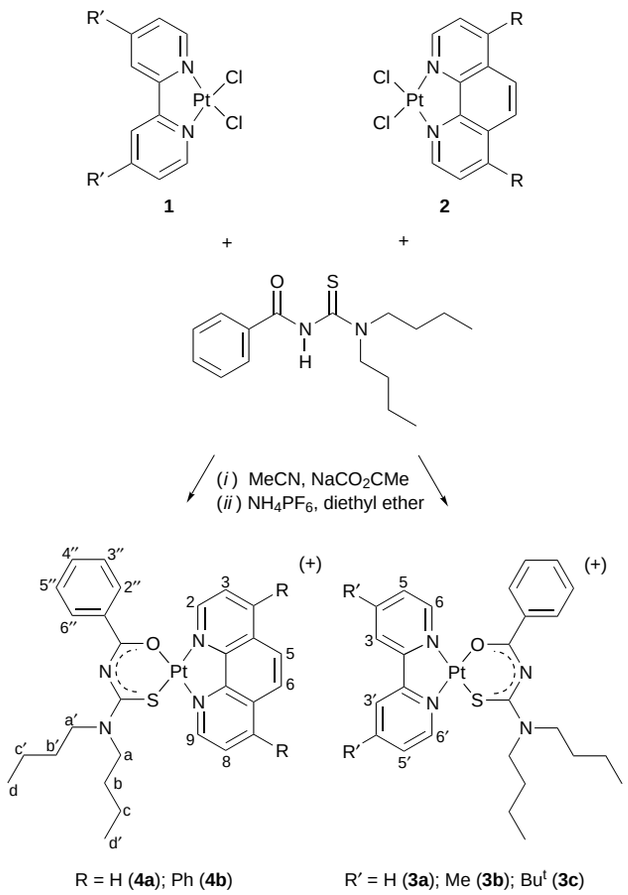
(*N*-1-Naphthoyl-*N*′,*N*′-di-*n*-butylthioureato-*S*,*O*)(4,4′-dimethyl-2,2′-bipyridyl)platinum(II) hexafluorophosphate 3e. Yield 76.7%, m.p. 206–209 °C (Found: C, 44.9; H, 4.2; N, 6.4, S, 3.6. $C_{32}H_{37}F_6N_4OPPtS$ requires C, 44.38; H, 4.31; N, 6.47; S, 3.70%). (+)FAB mass spectrum: *m*/*z* 720.7 (M^+, calc. 720.23), 1438.8 (M_2^+, calc. 1440.46) and 1586.1 ($[M_2 + PF_6]^+$ calc. 1585.43). δ_H(400 MHz, CD_3CN, $SiMe_4$) 0.84 (3 H, t, H^d), 1.04 (3 H, t, $H^{d'}$), 1.27 (2 H, m, H^c), 1.51 (2 H, m, $H^{c'}$), 1.67 (2 H, m, H^b), 1.80–2.00 (2 H, m, $H^{b'}$), 2.49 (3 H, s, CH_3), 2.54 (3 H, s, CH'_3), 3.76 (2 H, t, H^a), 3.86 (2 H, t, $H^{a'}$), 7.43 (1 H, d, H^5), 7.48 (1 H, d, $H^{5'}$), 7.50–7.60 (3 H, m, $H^{3''}$, $H^{6''}$, $H^{7''}$), 7.99 (2 H, d, $H^{2''}$), 8.00 (2 H, d, $H^{5''}$), 8.09 (2 H, d, $H^{4''}$), 8.13 (1 H, d, H^3), 8.16 (1 H, s, $H^{3'}$), 8.40 (1 H, d, $H^{8''}$), 8.51 (1H, d, H^6) and 8.56 (1 H, d, $H^{6'}$).

(*N*-1-Naphthoyl-*N*′,*N*′-di-*n*-butylthioureato-*S*,*O*)(4,4′-di-*tert*-butyl-2,2′-bipyridyl)platinum(II) hexafluorophosphate 3f. Yield 84.1%, m.p. 212–215 °C (Found: C, 47.8; H, 5.2; N, 5.9; S, 3.2. $C_{38}H_{44}F_6N_4OPPtS$ requires C, 48.29; H, 4.70; N, 5.93; S, 3.39%). δ_H(400 MHz, CD_3CN, $SiMe_4$) 0.84 (3 H, t, H^d), 1.06 (3 H, t, $H^{d'}$), 1.27 (2 H, m, H^c), 1.50 (2 H, m, $H^{c'}$), 1.42 [9 H, s, $C(CH_3)_3$], 1.44 [9 H, s, $C(CH'_3)_3$], 1.67 (2 H, m, H^b), 1.87 (2 H, m, $H^{b'}$), 3.74 (2 H, t, H^a), 3.86 (2 H, t, $H^{a'}$), 7.48–7.62 (3 H, m, $H^{3''}$, $H^{6''}$, $H^{7''}$), 7.48–7.62 (2 H, m, $H^{5'}$, H^5), 7.97 (1 H, d, $H^{2''}$), 8.00 (1 H, d, $H^{5''}$), 8.08 (1 H, d, $H^{4''}$), 8.27 (1 H, d, H^3), 8.31 (1 H, d, $H^{3'}$), 8.42 (1 H, d, $H^{8''}$), 8.53 (1 H, d, H^6) and 8.59 (1 H, d, $H^{6'}$).

(*N*-Benzoyl-*N*′,*N*′-di-*n*-butylthioureato-*S*,*O*)(1,10-phenanthroline)platinum(II) hexafluorophosphate 4a. Yield 80.3%, m.p. 270–272 °C (Found: C, 41.1; H, 3.9; N, 6.9. $C_{28}H_{31}F_6N_4OPPtS$ requires C, 41.42; H, 3.85; N, 6.91%). δ_H(400 MHz, CD_3CN, $SiMe_4$) 0.95 (3 H, t, H^d), 1.01 (3 H, t, $H^{d'}$), 1.33 (2 H, m, H^c), 1.38 (2 H, m, $H^{c'}$), 1.48 (2 H, m, H^b), 1.59 (2 H, m, $H^{b'}$), 3.34 (2 H, m, H^a), 3.36 (2 H, m, $H^{a'}$), 7.29 (2 H, t, $H^{3''}$, $H^{5''}$), 7.32 (1 H, dd, H^8), 7.43 (1 H, d, H^6), 7.48 (1 H, d, H^5), 7.45 (2 H, d, $H^{2''}$, $H^{6''}$), 7.54 (1 H, t, $H^{4''}$), 7.68 (1 H, dd, H^3), 7.91 (1 H, dd, H^9), 8.18 (1 H, dd, H^7), 8.22 (1 H, dd, H^4) and 8.24 (1 H, dd, H^2).

(*N*-benzoyl-*N*′,*N*′-di-*n*-butylthioureato-*S*,*O*)(4,7-diphenyl-1,10-phenanthroline)platinum(II) hexafluorophosphate 4b. Yield 50.3%, m.p. 280–283 °C (Found: C, 49.5; H, 3.8; N, 6.0. $C_{40}H_{39}F_6N_4OPPtS$ requires C, 49.83; H, 4.08; N, 5.82%). δ_H(400 MHz, CD_3CN, $SiMe_4$) 0.93 (3 H, t, H^d), 1.03 (3 H, t, $H^{d'}$), 1.38 (2 H, m, H^c), 1.49 (2 H, m, $H^{c'}$), 1.69 (2 H, m, H^b), 1.75–2.00 (2 H, m, $H^{b'}$), 3.79 (4 H, m, $H^{a'}$, H^a), 7.50 (2 H, t, $H^{3''}$, $H^{5''}$), 7.58–7.72 (2 H, m, $H^{4''}$), 7.85 (1 H, d, H^8), 8.04 (1 H, d, H^6), 8.10 (1 H, d, H^5), 8.15 (1 H, m, H^3), 8.15 (2 H, m, $H^{2''}$, $H^{6''}$), 8.89 (1 H, d, H^9) and 9.29 (1 H, d, H^2).

(*N*-1-Naphthoyl-*N*′,*N*′-di-*n*-butylthioureato-*S*,*O*)(1,10-phenanthroline)platinum(II) hexafluorophosphate 4c. Yield 76.3%, m.p. 182–185 °C (Found: C, 43.8; H, 3.7; N, 6.4; S, 3.5. $C_{32}H_{33}F_6N_4OPPtS$ requires C, 44.59; H, 3.86; N, 6.50; S, 3.71%) (+)FAB mass spectrum: *m*/*z* 716.7 (M^+, calc. 716.20), 1431.6 (M_2^+, calc. 1432.40) and 1579.1 ($[M_2 + PF_6]^+$, 1577.37). δ_H(400 MHz, CD_3CN, $SiMe_4$) 0.85 (3 H, t, H^d), 1.07 (3 H, t, $H^{d'}$), 1.29 (2 H, m, H^c), 1.55 (2 H, m, $H^{c'}$), 1.71 (2 H, m, H^b), 1.80–2.00



Scheme 1 Structure, synthesis and numbering scheme for mixed-ligand [Pt(diimine)(L^1-*S*,*O*)]PF_6 complexes. Analogous complexes derived from HL^2 were prepared similarly

(2 H, m, $H^{b'}$), 3.80 (2 H, t, H^a), 3.92 (2 H, t, $H^{a'}$), 7.47 (1 H, t, $H^{7''}$), 7.54 (1 H, t, $H^{6''}$), 7.56 (1 H, t, $H^{3''}$), 7.78–7.86 (2 H, m, H^3, H^8), 7.98 (1 H, d, $H^{5''}$), 8.00 (1 H, d, $H^{4''}$), 8.03 (1 H, d, H^6), 8.08 (1 H, d, H^5), 8.09 (1 H, d, $H^{2''}$), 8.41 (1 H, d, $H^{8''}$), 8.71 (1 H, d, H^9), 8.73 (1 H, d, H^7), 8.76 (1 H, d, H^4) and 8.83 (1 H, d, H^2).

(*N*-1-Naphthoyl-*N*′,*N*′-di-*n*-butylthioureato-*S*,*O*)(4,7-diphenyl-1,10-phenanthroline)platinum(II) hexafluorophosphate 4d. Yield 34.0%, m.p. 236–238 °C (Found: C, 51.6; H, 3.9; N, 5.7. $C_{44}H_{41}F_6N_4OPPtS$ requires C, 52.11; H, 4.08; N, 5.53%). δ_H(400 MHz, CD_3CN, $SiMe_4$) 0.84 (3 H, t, H^d), 1.04 (3 H, t, $H^{d'}$), 1.26 (2 H, m, H^c), 1.51 (2 H, m, $H^{c'}$), 1.65 (2 H, m, H^b), 1.80–2.00 (2 H, m, $H^{b'}$), 3.75 (2 H, t, H^a), 3.83 (2 H, t, $H^{a'}$), 7.80 (1 H, d, H^8), 7.86 (1 H, d, H^3), 7.50–7.68 (3 H, br m, $H^{3''}$, $H^{6''}$, $H^{7''}$), 7.96–8.08 (4 H, m, H^5, H^6, $H^{4''}$, $H^{5''}$), 8.09 (1 H, d, $H^{2''}$), 8.44 (1 H, d, $H^{8''}$), 8.87 (1 H, d, H^9) and 8.90 (1 H, d, H^2).

Results and Discussion

Treatment of the relatively insoluble [Pt(bipy)Cl_2] **1** or [Pt(phen)Cl_2] **2** in boiling acetonitrile with 1 equivalent of *N*-benzoyl-*N*′,*N*′-di-*n*-butylthiourea (HL^1) or *N*,*N*-di-*n*-butyl-*N*′-1-naphthoylthiourea (HL^2) solubilises **1** and **2** to yield bright yellow solutions, from which a series of mixed-ligand [Pt(bipy)(L^n-*S*,*O*)]$^+$ (*n* = 1 **3a**, or 2 **3d**) and [Pt(phen)(L^n-*S*,*O*)]$^+$ (*n* = 1 **4a**, or 2 **4c**) complexes have been isolated as PF_6^- salts. Analogous complexes derived from HL^1 and the 4,4′-dimethyl- (**3b**), 4,4′-di-*tert*-butyl-2,2′-bipyridine (**3c**) and 4,7-diphenyl-1,10-phenanthroline (**4b**), as well as the corresponding HL^2 mixed-ligand complexes **3e**, **3f** and **4d** have also been prepared. The general structure of these compounds as well as the overall method of preparation of the HL^1 complexes **3a**–**3c** and **4a**, **4b** is illustrated in Scheme 1. With the exception of **3b**, the complexes **3a**–**3f** and **4a**–**4d** are all reasonably soluble in acetonitrile as well as slightly soluble in water.

A striking characteristic of these complexes is the marked concentration dependence of their ^{1}H NMR spectra in CD_3CN at 25 °C. This is illustrated for **4a** in Fig. 1, from which it is clear that as the concentration of **4a** decreases from 2.3×10^{-2} to 2.7×10^{-3} M the ^{1}H resonances due to H^2 and H^9 of the phenanthroline moiety undergo substantial downfield shifts (by 0.883 and 0.801 ppm respectively). All other ^{1}H resonances of the phenanthroline group are also shifted downfield, albeit to a lesser extent (between 0.464 and 0.586 ppm) than H^2 and H^9. The resonance due to the phenyl and the butyl groups of the co-ordinated L^1 are shifted downfield to a much smaller extent compared to those of the phenanthroline moiety for the above concentration range. A plot of δ_{obs} of all of the phenanthroline protons of **4a** as a function of concentration in Fig. 2 shows a smooth trend, the upfield shifts levelling off at the maximum practical concentration achievable, before precipitation of the complex occurs. Similar plots may be obtained for all related complexes **3a**–**3f** and **4b**–**4d** in this study, within the limits of their solubility in CD_3CN. It should be noted that, in general, the overall extent of the concentration dependence of the chemical shifts for the L^2 mixed-ligand complexes is smaller compared to that of the L^1 analogues.

The marked concentration dependence of the chemical shifts observed for all the platinum complexes suggests self-association of the [Pt(diimine)(L^n-*S*,*O*)]$^+$ complex cations in acetonitrile solution. Assuming that unassociated complex cations exist in equilibrium with mainly dimeric species according to the equation $2[Pt(diimine)(L^n\text{-}S,O)]^+ \rightleftharpoons [\{Pt(diimine)(L^n\text{-}S,O)\}_2]^{2+}$, we have utilised the method of Horman and Dreux[16] to test this hypothesis and to estimate the relevant association constants, K_D, for each of the complexes **3a**–**3f** and **4a**–**4d**. The procedure involves an iterative estimation of K_D, by fitting of the observed chemical shifts (δ_{obs}) of each proton using the mole fraction of dimer (x_i) present at each concentration, starting from a reasonable guess of the association constant. The optimum K_D value is defined as that which leads to the best linear relationship between δ_i and x_i. We have written a simple computer program to estimate the K_D values, as well as the limiting shift of the monomer (δ_0) and that of the dimer (δ_∞), from the experimental data. Included is a statistical evaluation of the 95% confidence limits for the best-fitting value of K_D. We find, for all cases examined completely linear relationships between δ_i and x_i, from which a consistent set of K_D values may be obtained, supporting the model of dimer formation only. The excellent agreement between the calculated chemical shifts, δ_{calc}, and the δ_{obs} values for all the diimine protons of **4a**, as a function of concentration, is shown in Fig. 2. We have thus estimated a set of K_D values, together with their 95% confidence intervals for each complex, using as many of the diimine ^{1}H resonances as allowed by non-overlapping resonances in the ^{1}H NMR spectrum (Table 1).‡

Additional experimental evidence for the proposed 'dimerisation' equilibrium model is obtained from the temperature dependence of the ^{1}H chemical shifts of these complexes. In general we find that increasing the temperature at fixed complex concentration leads to systematic downfield shifts, consistent with the disaggregation of the dimers in solution. Plots of calculated $\ln K_D$ values against $1/T$ (temperature range 298–328 K) yield reasonably good straight lines, from which the thermodynamic parameters ΔG, ΔH and ΔS have been estimated (Table 1).‡ In those cases for which K_D at 298 K is <2–3 M^{-1}, the temperature dependence of the chemical shift trends show

‡ The ΔH and ΔS values were estimated with estimated relative errors of *ca*. 20% from linear registration analysis of a plot of $\ln K_D$ *vs.* $1/T$; ΔG values were then calculated at 298 K from these data, as shown in Table 1.

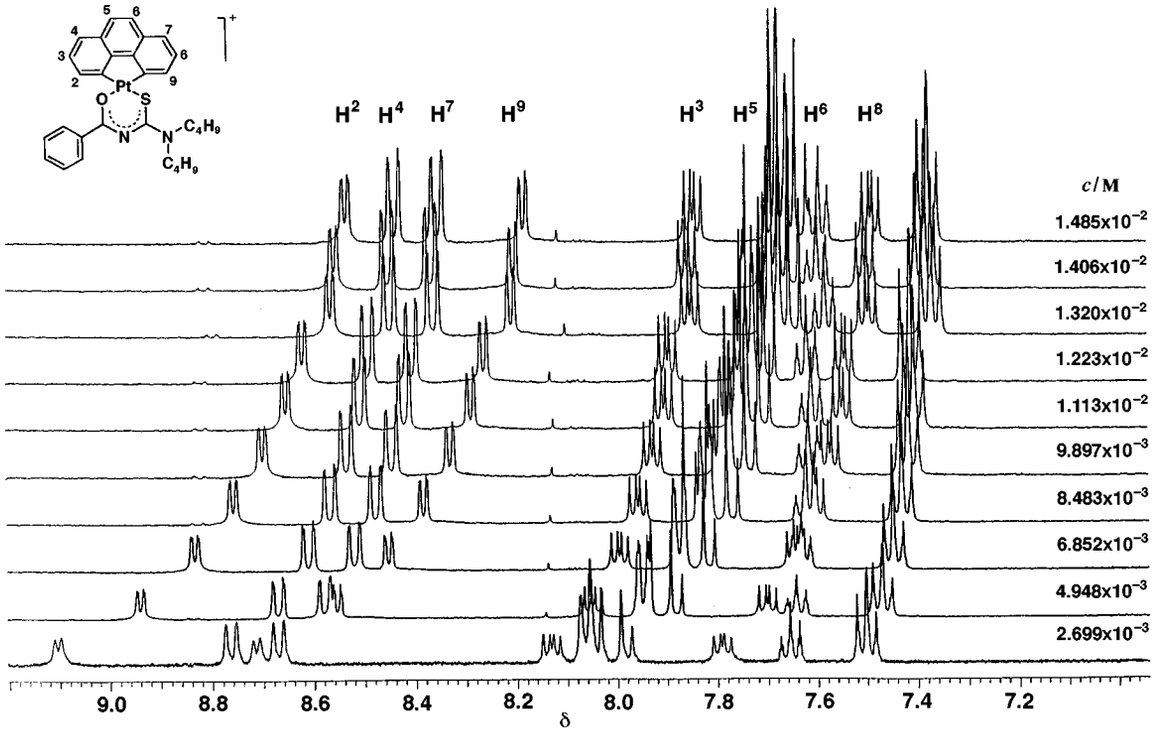


Fig. 1 Low-field portion of ^{1}H NMR spectra of complex **4a** in CD_3CN at 25 °C as a function of concentration

too large an experimental error for the construction of reliable van't Hoff plots.

The existence of dimers derived from the mixed-ligand complex cations is independently confirmed by the (+)FAB mass spectra of these substances, which show, in addition to peaks corresponding to the M^+ cation, significant signals corresponding to species formulated as $[M_2 + PF_6]^+$. Thus for example, the spectrum of **3a** shows substantial peaks at *m*/*z* values of 642.1 and 1428.7, corresponding to $[Pt(bipy)(L^1\text{-}S,O)]^+$ (calc. 642.19) and $[\{Pt(bipy)(L^1\text{-}S,O)\}_2 + PF_6]^+$ (calc. 1429.34), respectively. Similar results pertain to the L^2 complexes **3d** and **3e**, for which peaks at *m*/*z* 693.5, 1531.1 and 720.7, 1586.1 are obtained respectively. Evidently, in the vacuum of the mass spectrometer chamber, self-association of the mixed-ligand complex cations takes place§ in the gas phase forming in addition to M^+ cations, the $[M_2 + PF_6]^+$ species.

Inspection of the data in Table 1 shows that the complex cations derived from 1,10-phenanthroline, **4a**–**4d**, have in general larger K_D values than the corresponding 2,2′-bipyridine analogues **3a**–**3f**. Furthermore the L^1 complexes show substantially larger K_D values than those derived from L^2 (**4a** > **4c**, **4b** > **4d**, **3a** > **3d**, **3c** > **3f**). The relatively large K_D values of the 4,7-diphenyl-1,10-phenanthroline (dpphen) complexes **4b** (114 ± 18) and **4d** (63.5 ± 8 M^{-1}) are presumably consistent with the larger conjugated aromatic π system as compared to those of the corresponding, 1,10-phenanthroline complexes **4a** and **4c** (see below). Considering the bipyridine complexes, of interest is

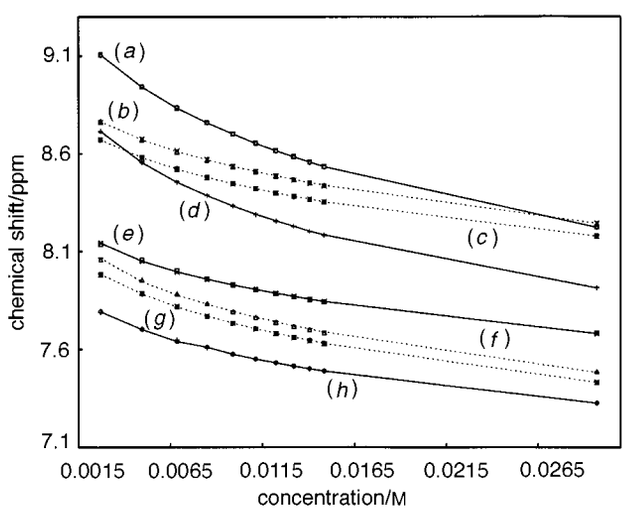


Fig. 2 Plot of δ_{obs} for H^2(*a*), H^9(*d*), H^4(*e*), H^3(*b*), H^6(*f*), H^5(*c*), H^8(*g*) and H^7(*h*) for complex **4a** as a function of concentration (CD_3CN, 25 °C). The excellent agreement between calculated δ_{calc} and δ_{obs} for the protons of **4a** with $K_D = 23.3 \pm 3.1$ M^{-1} is shown by the continuous lines (———) for H^2, H^3, H^8 and H^9 and dashed lines (– – – –) for H^4, H^5, H^6 and H^7 respectively

the relatively large K_D value obtained for the 4,4′-di-*tert*-butyl-2,2′-bipyridine (dmbipy) complex **3c** (28 ± 3) compared to **3a** (3 ± 0.6 M^{-1}). Unfortunately the low solubility of the corresponding 4,4′-dimethyl-2,2′-bipyridine (dmbipy) complex **3b** in CD_3CN prevented us from obtaining a reliable estimate of K_D by means of NMR spectroscopy. On the other hand, for the corresponding L^2 analogues **3d**, **3e** and **3f** one obtains very small values of K_D <2, 6.7 ± 1.4 and 1.8 ± 0.4 M^{-1} respectively. These trends, although incomplete due to the absence of data for **3b**, suggest that 4,4′-dialkyl substituents on the 2,2′-bipyridine moiety result in an increasing tendency for dimer formation roughly in the order H < Me < Bu^t. Significantly, the order of increasing K_D values qualitatively follows the generally observed order of increasing electron-releasing properties of these substituents.[17]

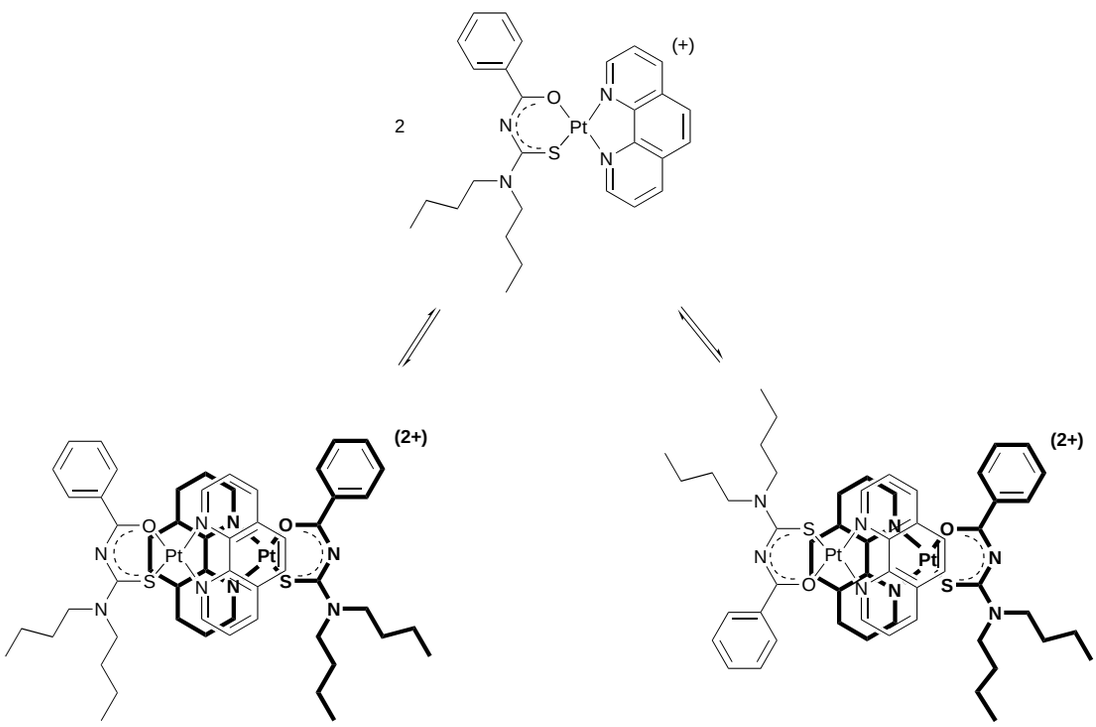
Numerous attempts to obtain suitable crystals from these

§ As pointed out by one referee, the existence of species such as $[M_2 + PF_6]^+$ in the (+)FAB mass spectrum is perhaps somewhat surprising. To the best of our knowledge, there are no other examples in the literature in which such relatively 'weak' binding results in the observation of species such as $[M_2 + PF_6]^+$ under conditions prevailing in (+)FAB experiments. Nevertheless peaks consistent with this assignment are present for all our complexes, with the notable absence of peaks corresponding to any other 'dimer' species such as M_2^+; this clearly attests to the stability of the $[M_2 + PF_6]^+$ in vacuum. The M_2^{2+} species would be difficult to distinguish from M^+ species in any event, since the *m*/*z* ratios for the former would be equal to that of M^+. Such species could be distinguishable only by means of high-resolution mass spectroscopy, taking into account the isotopic distribution of platinum. We thank the referee for drawing our attention to this point.

Table 1 Calculated dimerisation constants, K_D/M^{-1} for complexes **3a**–**3f** and **4a**–**4d** in CD_3CN at 25 °C, and associated thermodynamic data

Complex	K_D/M^{-1}	ΔG/kJ mol^{-1}	ΔG^a/kJ mol^{-1}	ΔH^a/kJ mol^{-1}	ΔS^a/ J K^{-1} mol^{-1}
3a [Pt(bipy)(L^1-*S*,*O*)]$^+$	3.0 ± 0.6	−2.8 ± 0.5	−5.9 ± 1.2	−15.1 ± 2.3	−31.0 ± 4.7
3b [Pt(dmbipy)(L^1-*S*,*O*)]$^+$	—[b]	—	—	—	—
3c [Pt(dtbbipy)(L^1-*S*,*O*)]$^+$	28.0 ± 3.1	−8.3 ± 0.3	−7.6 ± 1.5	−25.6 ± 3.8	−60.4 ± 9.1
3d [Pt(bipy)(L^2-*S*,*O*)]$^+$	<2	—	—	—	—
3e [Pt(dmbipy)(L^2-*S*,*O*)]$^+$	6.7 ± 1.4	−4.7 ± 0.5	−5.5 ± 1.1	−28.8 ± 4.3	−78.3 ± 11.7
3f [Pt(dtbbipy)(L^2-*S*,*O*)]$^+$	1.8 ± 0.4[c]	−1.5 ± 0.6[c]	—	—	—
4a [Pt(phen)(L^1-*S*,*O*)]$^+$	23.3 ± 3.1	−7.8 ± 0.3	−7.9 ± 1.6	−12.6 ± 1.9	−15.4 ± 2.3
4b [Pt(dpphen)(L^1-*S*,*O*)]$^+$	114.1 ± 18.7	−11.7 ± 0.4	−12.5 ± 2.5	−30.8 ± 4.6	−61.3 ± 9.2
4c [Pt(phen)(L^2-*S*,*O*)]$^+$	<2	—	—	—	—
4d [Pt(dpphen)(L^2-*S*,*O*)]$^+$	63.5 ± 8.1	−10.3 ± 0.3	−10.8 ± 2.2	−18.5 ± 2.8	−25.9 ± 3.9

[a] Determined from the temperature dependence of K_D using a van't Hoff plot (see footnote ‡). [b] Poor solubility prevented reliable K_D measurement by NMR spectroscopy. [c] Estimated value; large errors gave inaccurate K_D and thermodynamic parameters.



Scheme 2 Proposed structure of the dimer aggregate of complex **4a** in solution

mixed-ligand complexes have unfortunately not been successful to date. Hence the structure of these dimers in solutions must remain speculative. Nevertheless, from the ^{1}H NMR spectra it is clear that fast exchange between a mononuclear complex and a centrosymmetric dimer takes place in solution at all temperatures studied. It is significant that the diimine protons (notably H^6 and $H^{6'}$ for **3a**–**3f** and H^2 and H^9 for **4a**–**4d**) are generally *most* shielded (upfield shifted) as a function of increasing concentration. Evidently the protons associated with the diimine moiety are most influenced by the ring-current effects of the bipyridine or phenanthroline aromatic rings on the chemical shifts of an adjacent cation in the dimer. This is most likely if a 'stacked', coplanar structure for the dimer is envisaged, similar to those well known for porphyrin aggregation.[3,4] In any event, a 'T-shaped' edge-on geometry for a dimer can clearly be ruled out, given the shielding trends observed. The envisaged coplanar dimers clearly stack *regiospecifically*, since the overall extent of the concentration dependence of the shielding experienced by the diimine resonances is considerably larger than observed for the ^{1}H resonances of the phenyl/naphthyl and *n*-butyl moieties of the L^1 and L^2 ligands, although confirmation of this suggestion must await detailed chemical shift anisotropy and molecular modelling calculations.

We suggest that the structure of the dimers in solution can best be understood by invoking the elegant rules for predicting the nature of 'π-π stacking' interactions developed by Hunter and Sanders.[5] This model predicts that such 'π–π stacking' interactions can qualitatively be explained by net favourable π–σ attractions between the σ and π framework of adjacent aromatic molecules, which overcome the π–π repulsion, leading to overall energetically favourable interactions. Significantly the π–σ attractive forces are dominant only in an *offset* π-stacked geometry between adjacent molecules. The most favourable geometry in the case of porphyrin–porphyrin associations has been predicted to result from a coplanar arrangement (with interplanar separations between 3.4 and 3.6 Å), in which the centres of the porphyrin rings are offset relative to one another by between 3 and 4 Å. Metallation of the porphyrin has been found to enhance the stacking interactions, without affecting the geometry of the stacked aggregate. The predictive power of this model has thus been convincingly substantiated by several crystal structures examined by these authors.[5]

By analogy to porphyrin stacking, we propose an offset coplanar stacking arrangement for our complexes **3a**–**3f** and **4a**–**4d**, in that the diimine end of each cation most strongly interact in such a way that the two complex cations point 180° in opposite directions relative to one another in the dimer. This results in each Pt atom (assumed to have a net point charge of +1) being located over the centre of an adjacent bipyridine or phenanthroline ring. This geometry achieves the favourable off-

Table 2 Estimated interaction energies (ΔG/kJ mol^{-1}) for complexes **3a**, **4a** and **4b**, and dependence on the number of arene rings in the diimine moiety [$\Delta(\Delta G$/kJ mol^{-1} per arene ring]

Complex	n^a	ΔG/kJ mol^{-1}	ΔG^b/kJ mol^{-1}	$\Delta(\Delta G)^c$/kJ mol^{-1}
3a	2	−2.8 ± 0.5	−5.9 ± 1.2	—
4a	3	−7.8 ± 0.4	−7.9 ± 1.6	5.0 (2.0)
4b	5	−11.7 ± 0.4	−12.5 ± 2.5	2.0 (2.3)

[a] Number of aromatic rings. [b] From van't Hoff plot. [c] $\Delta(\Delta G) = |(\Delta G_{4a/4b} - \Delta G_{3a})|$ per aromatic ring; value in parentheses was calculated from ΔG (van't Hoff).

set required by the Sanders and Hunter model as illustrated for **4a** in Scheme 2. It is obviously not possible to differentiate between the at least two possible geometric arrangements shown, in view of the fast exchange within the equilibrium on the NMR time-scale. Our proposed structure for the dimer thus refers to an average structure in solution only. This offset stacking arrangement for the dimer is also likely to minimise the potential electrostatic repulsion between the net (+1) charge of each complex cation, while at the same time ensuring favourable cation π interactions. Dougherty[2] has recently highlighted this type of non-covalent cation π interaction, showing that these can be surprisingly strong, and can even compete with full aqueous solvation of the binding cation.

Inspection of the estimated thermodynamic parameters for the self-association of our platinum complexes in Table 1 shows some interesting trends. Increasing the number of aromatic rings of the diimine moiety of the complex results in increasing ΔG values of the L^1 complexes, for which $\Delta(\Delta G)$ values for **4a** and **4b** relative to **3a** correspond to an increment of between 2 and 5.0 kJ mol^{-1} per aromatic unit respectively (Table 2). The increment $\Delta(\Delta G)$ on going from **3a** to **4a** of between 2 and 5.0 kJ mol^{-1} per aromatic ring (depending on whether ΔG is calculated from the K_D value directly, or obtained from a van't Hoff plot) is probably subject to the largest experimental error in view of the relatively small K_D value of **3a**. Interestingly, the $\Delta(\Delta G)$ increment on going from **4a** to **4b** is between 2.0 and 2.3 kJ mol^{-1}, while that from **3a** to **4b** lies between 2.2 and 3.0 kJ mol^{-1} per aromatic ring, giving an overall average $\Delta(\Delta G)$ value of 2.4 ± 0.4 kJ mol^{-1} per arene ring. These values are of similar magnitude to those estimated by Rebek[18] for stacking associations of the derivatives of his tricarbonic acids and 9-ethyladenine in $CDCl_3$, for which a reasonably constant binding increment of $\Delta G_{\pi/\pi}$ of 1.8 kJ mol^{-1} per aromatic ring was obtained. Moreover, for the electrostatic ion-induced dipole interactions, increments of $\Delta G_{N+/\pi} \approx 2$ kJ mol^{-1} per arene unit have been estimated for the association of cations and arenes in aqueous media.[1,2] Since our complexes carry a +1 charge, a cation π-type electrostatic interaction[2] accounts for the somewhat larger $\Delta(\Delta G)$ values obtained for them. Nevertheless, differences in the nature of the solvents used should be taken into account when making such comparisons, since dispersive and solvophobic effects[1] can play an important role in such cation π interactions. Overall, however, the similarities of the thermodynamic parameters obtained for our dimers to those reported for rather different systems in the literature suggest that, qualitatively at least, the tendency for dimer formation of our platinum complexes may be understood in terms of strong cation π interactions as well as increasing numbers of aromatic rings in the diimine moiety co-ordinated to the Pt^{II}.

The comparatively lower ΔG values for the complexes derived from the L^2 ligand are also interesting, if more difficult to explain. It is tempting to account for the lower tendency of the L^2 complexes to form dimers on steric grounds, with the idea that a freely rotating, larger, naphthyl group of the co-ordinated L^2 increases the average interplanar distance between two adjacent coplanar stacked cations of a dimer, so reducing the magnitude of the attractive electrostatic component of the stacking interactions between the [Pt(diimine)(L^2-*S*,*O*)]$^+$ complexes.¶ Electrostatic interactions of the ion–dipole or ion-induced dipole type generally depend inversely on the cube or fourth power of the intercharge distance,[1] so that small increases in interplanar distances may result in significant effects. This idea is consistent with the experimentally observed lower concentration dependence of the chemical shifts of the naphthyl protons of the L^2 ligands compared to those of the diimine protons for the complexes in this study.

In conclusion, we have found an easy to prepare and synthetically versatile set of mixed-ligand platinum(II) complexes derived from *N*-acyl-*N*′,*N*′-dialkylthioureas which show a pronounced tendency to self-aggregate into dicationic dimers in acetonitrile solution, so providing an interesting non-porphyrin-type model system with which to probe such non-covalent cation π interactions. The extent of self-association is very sensitive to the substituents on the diimine ligand, while the tendency for self-association increases substantially as the number of arene rings of the diimine increases (resulting in an increased π-surface area). Substitution of the phenyl group by a naphthyl moiety in the *N*-acylthiourea ligand results in a considerably lower stability of the dimer, suggesting a steric impediment to self-association in the latter case. Preliminary results show that the addition of water to an acetonitrile solution has a significant effect on the self association of these complexes. Unfortunately the di-*n*-butyl-substituted complexes are not sufficiently soluble in water properly to study their aggregation behaviour in aqueous media, and to examine their potential DNA intercalation properties. Studies with a set of redesigned water-soluble complexes of this type are in progress, with some interesting preliminary results.

¶ We have shown that in the crystal structure[12b] of *trans*-[Pt(L^2-*S*,*O*)$_2$] the naphthyl moieties are approximately coplanar with the plane of co-ordination; the very different ^{1}H chemical shifts for corresponding protons of the naphthyl group between the *cis* and *trans* isomers of the complexes show that the relative orientations of the naphthyl moiety in the *cis*-[Pt(L^2-*S*,*O*)$_2$] complex must be on average approximately perpendicular to the co-ordination plane on steric grounds. Thus, in the case of [Pt(diimine)(L^2-*S*,*O*] complexes, models show that a coplanar orientation of the naphthyl moiety is energetically unfavorable, in contrast to the corresponding *N*-benzoyl-substituted analogues.

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