Reactivity of Heterocyclic Nitrogen Donors in Systems containing the Tetrachloroaurate(III) Anion

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A series of gold(III) complexes of the type $[AuCl_3(L)]$ has been prepared and characterised (L = oxazole, benzoxazole, thiazole, their benzo and methyl-substituted derivatives, or 2-methylbenzoselenazole). The five-membered N,O- N,S- and N,Se-heterocyclic bases are all bound to Au^{III} through nitrogen. The kinetics of the displacement of L by chloride to give $[AuCl_4]^-$ has been studied in methanol–water (95:5, v/v) at 25.0 °C and $I = 0.20$ mol dm^{-3} ($LiClO_4$). The equilibrium constants for the reversible processes have also been determined. The reactions of the corresponding pyridine, 4-chloro-, 4-cyano- and 2,6-bis(chloromethyl)-pyridine complexes have also been re-examined under the same conditions. The equilibrium constants, K_2, depend upon the basicity of the nitrogen in the ligands and points for all ligands, irrespective of ring size and composition, lie roughly on the same $\log K_2$ *versus* pK_a curve. There is no significant systematic steric effect on the equilibrium constants of the sort found for the more basic methyl pyridines. The complexes of the five-membered heterocyclic ligands are approximately ten times less reactive than those of the six-membered N-heterocycles of comparable basicity and exhibit steric retardation from *ortho*-methyl substituents. The nucleophilicities of these ligands have been calculated and five-membered N,O- and N,S-heterocycles are considerably less reactive than six-membered N-heterocycles of similar basicity.

The reactivities of gold(III) systems involving heterocyclic nitrogen-donor bases have been studied with pyridine and substituted pyridines acting either as entering nucleophiles or leaving groups. Substitutions of the type (1) (L = R-py, a

$$[AuCl_4]^- + L \longrightarrow [AuCl_3(L)] + Cl^- \qquad (1)$$

pyridine derivative) take place with anionic and cationic gold(III) complexes,[1–3] and follow the normal two-term rate law, typical[4] of square-planar substrates, *i.e.* $-d[substrate]/dt = (k_1 + k_2[L])[substrate]$, where the first-order rate constant, k_1, and the second-order rate constant, k_2, refer to the nucleophilic attack on the substrate by the solvent and nucleophile respectively. The reactivity, expressed as $\log k_2$, increases linearly with the basicity of L (measured as the pK_a of HL^+) for entering ligands having the same form of steric hindrance, and steric retardation is observed for pyridines containing *ortho* substituents.

The same rate law applies to the reverse reactions (2),[5] *i.e.* to

$$[AuCl_3(L)] + Cl^- \longrightarrow [AuCl_4]^- + L \qquad (2)$$

the displacement of L by a halide ion, In this case, however, the reactivity decreases as the basicity of the leaving group increases, and is not affected by the presence of *ortho* substituents, probably because of a compensation of the steric effects in the ground and transition states.

The corresponding equilibrium constants, K_2, can be estimated from the relationship (3).

$$K_2 = k_2/k_{-2} \qquad (3)$$

In order to compare the behaviour of six- and five-membered heterocyclic nitrogen donors as entering groups and leaving groups, we have investigated a number of bases, such as thiazoles, oxazoles and some pyridines, measuring the equilibrium constants of (1) directly and studying the kinetics of reaction (2). The second-order rate constants for the entry of the weak nucleophiles could then be derived from equation (3).

Experimental

Materials.—All the chemicals involved in this work were reagent-grade materials (Aldrich or Janssen). The compound $HAuCl_4 \cdot 3H_2O$ was prepared from gold foil. The salt $[NEt_4][AuCl_4]$ was precipitated when NEt_4Cl was added to an aqueous solution of $HAuCl_4 \cdot 3H_2O$ and was recrystallised from dichloromethane.

Synthesis of the Complexes.—Two general methods of synthesis have been used.

(*a*) The ligand, dissolved in a small volume of water or methanol, was added to a slight excess of an aqueous solution of $HAuCl_4 \cdot 3H_2O$, and the mixture was neutralised with an equimolar amount of $NaHCO_3$. The yellow precipitate that formed was filtered off, washed with water and a minimum amount of cold methanol and recrystallised from dichloromethane by addition of small amounts of hexane or light petroleum.

(*b*) A stoichiometric amount of ligand was added to a solution of $[NEt_4][AuCl_4]$ in methanol–water (1:1, v/v) and the product precipitated by adding more water. Recrystallisation from dichloromethane as described in (*a*) gave a product identical to that from method (*a*).

The complexes were characterised by elemental analysis, visible, UV and ^1H NMR spectroscopy.

Trichloro(thiazole)gold(III). The compound $HAuCl_4 \cdot 3H_2O$ (472 mg, 1.2 mmol) and thiazole (95 mg, 1.12 mmol) gave 430 mg of complex (yield 99%) (Found: C, 9.20; H, 0.80; Cl, 27.3; N, 3.40. $C_3H_3AuCl_3NS$ requires C, 9.30; H, 0.80; Cl, 27.4; N, 3.60%), m.p. 215–220 °C (decomp.). UV–VIS: 231 ($\varepsilon = 27\,100$) and 310 nm ($\varepsilon = 1670$ cm^2 mmol^{-1}). ^1H NMR: δ 10.02 (dd, J = 2.4 and 1, 1 H), 8.50 (dd, J = 3 and 1, 1 H) and 8.30 (dd, J = 2.4 and 3 Hz, 1 H).

Trichloro(4-*methylthiazole*)*gold*(III). The compound $HAuCl_4 \cdot 3H_2O$ (611 mg, 1.55 mmol) and 4-methylthiazole (150 mg, 1.51 mmol) gave 609 mg of complex (yield 98%) (Found: C, 11.8; H, 1.25; Cl, 26.2; N, 3.25. $C_4H_5AuCl_3NS$ requires C, 11.9; H, 1.25; Cl, 26.4; N, 3.50%), m.p. 200–205 °C (decomp.). UV–VIS: 230 (ε = 19 600) and 309 nm (ε = 2120 cm^2 $mmol^{-1}$). ^1H NMR: δ 10.04 (d, J = 2.4, 1 H), 7.99 (m, 1 H) and 2.77 (d, J = 0.9 Hz, 3 H).

Trichloro(5-*methylthiazole*)*gold*(III). Prepared as for the 4-methylthiazole complex (Found: C, 11.9; H, 1.20; Cl, 26.3; N, 3.40. $C_4H_5AuCl_3NS$ requires C, 11.9; H, 1.25; Cl, 26.4; N, 3.50%), m.p. 175–180 °C. UV–VIS: 229 (ε = 27 100) and 315 nm (ε = 1790 cm^2 $mmol^{-1}$). ^1H NMR: δ 9.85 (s, 1 H), 8.20 (s, 1 H) and 2.78 (s, 3 H).

Trichloro(2,4-*dimethylthiazole*)*gold*(III). The compound $HAuCl_4 \cdot 3H_2O$ (651 mg, 1.65 mmol) and 2,4-dimethylthiazole (184 mg, 1.63 mmol) gave 656 mg of complex (yield 97%) (Found: C, 14.35; H, 1.60; Cl, 25.3; N, 3.20. $C_5H_7AuCl_3NS$ requires C, 14.40; H, 1.70; Cl, 25.5; N, 3,35%), m.p. 191–192 °C (decomp.). UV–VIS: 231 (ε = 26 100) and 312 nm (ε = 2940 cm^2 $mmol^{-1}$). ^1H NMR: δ 7.69 (q, J = 1, 1 H), 3.11 (s, 3 H) and 2.72 (d, J = 1 Hz, 3 H).

Trichloro(4,5-*dimethylthiazole*)*gold*(III). The compound $HAuCl_4 \cdot 3H_2O$ (651 mg, 1.65 mmol) and 4,5-dimethylthiazole (184 mg, 1.63 mmol) gave 649 mg of complex (yield 96%) (Found: C, 14.3; H, 1.65; Cl, 26.0; N, 3.25. $C_5H_7AuCl_3NS$ requires C, 14.40; H, 1.70; Cl, 25.5; N, 3.35%), m.p. 192 °C. UV–VIS: 230 (ε = 22 200) and 312 nm (ε = 3300 cm^2 $mmol^{-1}$).

Trichloro(2,4,5-*trimethylthiazole*)*gold*(III). Prepared as for the complex with thiazole (Found: C, 17.2; H, 2.10; Cl, 25.7; N, 3.10. $C_6H_{12}AuCl_3NS$ requires C, 16.7; H, 2.10; Cl, 24.7; N, 3.25%). ^1H NMR: δ 3.04 (s, 3 H), 2.62 (s, 3 H) and 2.53 (s, 3 H).

Benzothiazoletrichlorogold(III). The compound $HAuCl_4 \cdot 3H_2O$ (429 mg, 1.09 mmol) and benzothiazole (140 mg, 1.04 mmol) gave 385 mg of complex (yield 81%) (Found: C, 18.9; H, 1.10; Cl, 24.1; N, 3.00. $C_7H_5AuCl_3NS$ requires C, 19.2; H, 1.15; Cl, 24.3; N, 3.20%), m.p. 252 °C (decomp.). UV–VIS: 233 (ε = 28 500) and 294 nm (ε = 4510 cm^2 $mmol^{-1}$). ^1H NMR: δ 10.46 (s, 1 H), 8.55 (complex m, 2 H) and 7.89 (complex m, 2 H).

Trichloro(2-*methylbenzothiazole*)*gold*(III). The compound $HAuCl_4 \cdot 3H_2O$ (641 mg, 1.63 mmol) and 2-methylbenzothiazole (235 mg, 1.57 mmol) gave 623 mg of complex (yield 85%) (Found: C, 22.25; H, 1.90; Cl, 23.2; N, 2.85. $C_8H_7AuCl_3NS$ requires C, 21.2; H, 1.55; Cl, 23.5; N, 3.10%), m.p. 180–182 °C (decomp.). UV–VIS: 231 nm (ε = 30 100 cm^2 $mmol^{-1}$). ^1H NMR: δ 8.44 (m, 2 H), 7.84 (m, 2 H) and 3.33 (s, 3 H).

Trichloro(*oxazole*)*gold*(III). The compound $HAuCl_4 \cdot 3H_2O$ (485 mg, 1.23 mmol) and oxazole (80 mg, 1.16 mmol) gave 397 mg of complex (yield 92%) (Found: C, 9.45; H, 0.7; Cl, 28.9; N, 3.55. $C_3H_3AuCl_3NO$ requires C, 9.70; H, 0.80; Cl, 28.6; N, 3.75%), m.p. 178–188 °C (decomp.). UV–VIS: 235 (ε = 18 500), 310 (ε = 1080) and 370 nm (ε = 748 cm^2 $mmol^{-1}$). ^1H NMR: δ 9.59 (br, 1 H), 8.59 (br, 1 H) and 8.05 (br, 1 H).

Trichloro(2,4,5-*trimethyloxazole*)*gold*(III). Prepared as for the complex with oxazole (Found: C, 17.2; H, 2.10; Cl, 26.0; N, 3.25. $C_6H_{12}AuCl_3NO$ requires C, 17.4; H, 2.20; Cl, 25.7; N, 3.40%), m.p. 142–144 °C. UV–VIS: 240 (ε = 19 960) and 311 nm (ε = 1720 cm^2 $mmol^{-1}$).

Benzoxazoletrichlorogold(III). The compound $HAuCl_4 \cdot 3H_2O$ (407 mg, 1.03 mmol) and benzoxazole (20 mg, 1.01 mmol) gave 283 mg of complex (yield 66%) (Found: C, 19.9; H, 1.10; Cl, 25.2; N, 3.30. $C_7H_5AuCl_3NO$ requires C, 19.9; H, 1.20; Cl, 25.2; N, 3.30%), m.p.: 235 °C (decomp.). UV–VIS: 236 (ε = 25 000) and 308 nm (ε = 1730 cm^2 $mmol^{-1}$). ^1H NMR: δ 9.87 (s, 1 H) and 8.03 (m, 4 H).

Trichloro(2-*methylbenzoxazole*)*gold*(III). The compound $HAuCl_4 \cdot 3H_2O$ (496 mg, 1.26 mmol) and 2-methylbenzoxazole (158 mg, 1.19 mmol) gave 409 mg of complex (yield 79%) (Found: C, 21.7; H, 1.50; Cl, 26.5; N, 2.90. $C_8H_7AuCl_3NO$ requires C, 22.0; H, 1.60; Cl, 24.35; N, 3.20%), m.p. 168–174 °C (decomp.). UV–VIS: 237 (ε = 23 400), 269 (ε = 5850), 276 (ε = 4380) and 313 nm (ε = 1720 cm^2 $mmol^{-1}$). ^1H NMR: δ 7.93 (m, 4 H) and 3.24 (s, 3 H).

Trichloro(2-*methylbenzoselenazole*)*gold*(III). The compound $HAuCl_4 \cdot 3H_2O$ (465 mg, 1.18 mmol) and 2-methylbenzoselenazole (223 mg, 1.14 mmol) gave 372 mg of complex (yield 63%) (Found: C, 20.4; H, 1.75; Cl, 19.75; N, 2.90. $C_8H_7AuCl_3NSe$ requires C, 19.2; H, 1.40; Cl, 21.3; N, 2.80%), m.p. 137 °C (decomp.). UV–VIS: 229 (ε = 35 900) and 304 nm (ε = 6010 cm^2 $mmol^{-1}$). ^1H NMR: δ 8.13 (m, 4 H) and 3.34 (s, 3 H).

Trichloro(2,5-*dimethyl*-1,3,4-*thiadiazole*)*gold*(III). The compound $HAuCl_4 \cdot 3H_2O$ (518 mg, 1.31 mmol) and 2,5-dimethyl-1,3,4-thiadiazole (145 mg, 1.27 mmol) gave 324 mg of complex (yield 59%) (Found: C, 10.5; H, 1.45; Cl, 25.6; N, 6.05. $C_5H_7AuCl_3NS$ requires C, 11.5; H, 1.45; Cl, 25.5; N, 6.70%), m.p. 110–115 °C. UV–VIS: 231 (ε = 21 400) and 310 nm (ε = 2190 cm^2 $mmol^{-1}$). ^1H NMR: δ 3.19 (s, 3 H) and 2.92 (s, 3 H).

[2,6-*Bis*(*chloromethyl*)*pyridine*]*trichlorogold*(III). Prepared as for the complex with pyridine[5] (Found: C, 17.8; H, 1.60; Cl, 37.15; N, 2.80. $C_7H_7AuCl_5N$ requires C, 17.5; H, 1.45; Cl, 37.0; N, 2.90%), m.p. 177 °C (decomp.). UV–VIS: 234 (ε = 18 800) and 320 nm (ε = 2190 cm^2 $mmol^{-1}$). ^1H NMR: δ 8.33 (complex m, 3 H) and 5.57 (s, 4 H).

Ultraviolet spectra of dichloromethane solutions were measured, and the kinetic and equilibrium studies were made with a Perkin-Elmer Lambda 5 spectrophotometer. Proton NMR spectra of the ligands and complexes in $[^2H_6]$acetone solution were obtained with a Varian FT 80A spectrometer.

Kinetic Measurements.—All the reactions were carried out at 25.0 °C in the thermostatted cell of a Perkin-Elmer Lambda-5 UV-VIS spectrophotometer. The complex $[AuCl_3(L)]$ was first dissolved in dichloromethane, in which it is stable towards solvolysis, and 80 μl of this solution were added to methanol–water (95:5 v/v, 3 cm^3) solution containing known amounts of LiCl and $HClO_4$ (0.10 mol dm^{-3}) at I = 0.20 mol dm^{-3} ($LiClO_4$).

The concentration of the complex in the reaction mixture was always in the range 6×10^{-5}–9×10^{-5} mol dm^{-3}, and the chloride-ion concentration was at least 10 times greater in order to provide pseudo-first-order conditions.

Results

Equilibrium Studies.—The equilibria were studied spectrophotometrically. Solutions of known amounts of $[AuCl_3(L)]$ and LiCl in methanol–water (95:5, v/v), in the presence of $HClO_4$ (10^{-4} mol dm^{-3}) to prevent deprotonation of the solvento complex, I = 0.20 mol dm^{-3} ($LiClO_4$), were allowed to come to equilibrium in a spectrophotometric cell at 25.0 °C and the absorbance at 320 nm was measured. The method used to treat the data depended upon the basicity of the ligand. For ligands with $pK_a < 3$ the amount of HL^+ at equilibrium could be ignored. When protonation of L is negligible $1/K_2 = [I]^2/(c_0 - [I])([Cl]_0 - [I])$ where $[I] = [AuCl_4^-] = [L]$, c_0 = initial concentration of $[AuCl_3(L)]$, $[Cl]_0$ = initial concentration of Cl^- {$[AuCl_3(L)]$ at equilibrium = $c_0 - [I]$}. For more basic ligands (*e.g.* 4-methylthiazole, 2,4-dimethylthiazole, pyridine) the protonation equilibrium must be taken into account and $(1/K_2)([H^+] + K_a)\{[Cl^-]_0 c_0 - [I](c_0 + [Cl]_0 + [I])\} - K_a[I^2] = 0$ and $[H^+]^2 + [H^+](K_a - c_A - [I]) - K_a c_A = 0$, where c_A = initial concentration of acid. These equations, combined with $A_e = \varepsilon_1[AuCl_3(L)] + \varepsilon_2[AuCl_4^-]$ {ε_1, ε_2 are the molar absorption coefficients of $[AuCl_3(L)]$ and $[AuCl_4^-]$ at 320 nm, L does not absorb significantly at this wavelength}, were used to obtain the best fit of the absorbance at equilibrium (A_e) to total chloride concentration, $[Cl^-]_0$, data, with the known values of ε_1, ε_2, K_a, c_0 and c_A, and with K_2 as the parameter to be optimised. Measured values of A_e at various $[Cl^-]_0$ are collected in Table 1.

Table 1 Absorbance data (A_e) at 320 nm for equilibrated systems containing $[AuCl_4]^-$ (ε = 5030 cm^2 mmol^{-1}), $[AuCl_3(L)]$, L and Cl^- in MeOH–water (95:5, v/v), at 25 °C, $[HClO_4]$ = 0.10 mol dm^{-3}, and I = 0.20 mol dm^{-3} ($LiClO_4$)

L	10^4[complex]/ mol dm^{-3}	ε[$AuCl_3$(L)]/ cm^2 mmol^{-1}	10^4[Cl^-]/ mol dm^{-3}	A_{eq}
Thiazole	1.06	1500	487	0.533
			97.4	0.533
			48.7	0.519
			9.74	0.485
			4.87	0.463
			1.95	0.417
			0.974	0.373
			0.487	0.331
4-Methylthiazole	1.06	1928	974	0.527
			487	0.528
			97.4	0.525
			48.7	0.520
			9.74	0.498
			4.87	0.475
			2.92	0.458
			1.95	0.439
			0.974	0.390
5-Methylthiazole *	0.994	1530	968	0.497
			581	0.495
			194	0.492
			77.4	0.485
			38.7	0.474
			9.68	0.450
			5.81	0.429
			1.94	0.364
2,4-Dimethylthiazole	1.02	2020	97.4	0.498
			9.74	0.470
			4.87	0.431
			2.92	0.393
			1.95	0.374
			0.974	0.328
4,5-Dimethylthiazole *	1.01	2010	968	0.503
			581	0.503
			194	0.501
			77.4	0.497
			38.7	0.490
			9.68	0.465
			5.81	0.441
			1.94	0.380
2,4,5-Trimethylthiazole	1.03	2220	1160	0.496
			581	0.494
			194	0.484
			9.68	0.408
			5.81	0.394
			1.94	0.345
Benzothiazole	1.01	2620	97.4	0.509
			48.7	0.508
			4.87	0.494
			2.92	0.486
			1.95	0.478
			0.974	0.459
			0.487	0.425
			0.195	0.415
2-Methylbenzothiazole	1.03	2555	487	0.518
			97.4	0.516
			4.87	0.505
			1.95	0.498
			0.974	0.462
			0.487	0.409
			0.195	0.393
Oxazole	1.07	1890	97.4	0.539
			9.74	0.538
			4.87	0.534
			2.92	0.524
			0.974	0.478
			0.487	0.423
			0.195	0.379
2,4,5-Trimethyloxazole	1.01	1511	484	0.506
			145	0.506
			67.7	0.499
			38.7	0.490
			19.4	0.478
			7.74	0.456
			3.87	0.432
			1.94	0.389

Table 1 (*continued*)

L	10^4[complex]/ mol dm^{-3}	ε[$AuCl_3$(L)]/ cm^2 mmol^{-1}	10^4[Cl^-]/ mol dm^{-3}	A_{eq}
Benzoxazole	1.05	2440	97.4	0.526
			48.7	0.526
			9.74	0.526
			1.95	0.510
			0.974	0.493
			0.682	0.473
			0.487	0.463
			0.39	0.454
			0.292	0.442
			0.195	0.421
2-Methylbenzoxazole	1.04	1980	97.4	0.533
			48.7	0.533
			2.92	0.525
			1.95	0.520
			0.974	0.480
			0.487	0.452
			0.195	0.424
Pyridine	1.06	1850	974	0.529
			195	0.520
			58.4	0.502
			19.5	0.470
			5.84	0.412
			3.9	0.386
			1.95	0.347
			0.974	0.309
			0.584	0.285
4-Chloropyridine	0.3	3402	57.1	0.151
			2.86	0.139
			0.95	0.134
			0.76	0.131
			0.38	0.116
			0.09	0.105
4-Cyanopyridine	0.317	2857	57.1	0.159
			2.86	0.157
			0.76	0.148
			0.57	0.143
			0.38	0.129
			0.19	0.117
			0.10	0.106
2,6-Bis(chloromethyl)pyridine	0.89	2536	971	0.453
			48.5	0.438
			9.71	0.408
			4.85	0.381
			0.971	0.348
			0.485	0.312

* [$HClO_4$] = 1.94 × 10^{-2} mol dm^{-3}.

Table 2 Absorbance data, A_{eq}, for the solvolytic equilibrium [$AuCl_4$]$^-$ + solv ⇌ [$AuCl_3$(solv)] + Cl^- in MeOH–water (95:5, v/v), 25 °C, [$HClO_4$] = 0.1 mol dm^{-3}, I = 0.20 mol dm^{-3}, 320 nm and [Au] = 2 × 10^{-4} mol dm^{-3}

[Cl^-]$^{-1}$/dm^3 mol^{-1}	A_e
51.5	1.502
172.1	1.487
1146	1.414
5155	1.280

The solvolytic equilibrium (4) was measured in the same

$$[AuCl_4]^- + \text{solv} \overset{K_s}{\rightleftharpoons} [AuCl_3(\text{solv})] + Cl^- \quad (4)$$

solvent mixture and under the same experimental conditions. The optical densities of solutions containing $HAuCl_4 \cdot 3H_2O$ and LiCl with a small amount of $HClO_4$ to prevent deprotonation of the solvento complex and $LiClO_4$ to maintain I = 0.20 mol dm^{-3} were measured as a function of [Cl^-]$_0$. By combining $K_s = \{(c_0 - [I])([Cl^-]_0 - [I])\}/[I]$ with $A_e = \varepsilon_1[I] + \varepsilon_3(c_0 - [I])$ (ε_3 is the molar absorption coefficient of the solvento complex at 320 nm), values of K_s and ε_3 were optimised for the best fit of the A_e *versus* [Cl^-]$_0$ data (Table 2) with ε_2 and c_0 as fixed parameters, using the Marquardt algorithm.[6] This gives $K_s = (3.4 \pm 0.2) \times 10^{-4}$ mol dm^{-3}.

Kinetic Studies.—The kinetics of displacement of L from [$AuCl_3$(L)] by Cl^- [reaction (2)] was followed in the presence of acid (0.1 mol dm^{-3} $HClO_4$) in order to avoid a possible deprotonation of the solvento species [$AuCl_3$(MeOH)] which is an intermediate in the k_{-1}-controlled substitution pathway, and to force the reaction to completion by protonating the displaced base L.

For the weakest bases, oxazole, benzoxazole and 2-methylbenzoxazole, the acid concentration is not sufficient to ensure complete protonation of the released ligand. However, because of their low basicity, these species are also poor ligands towards [$AuCl_4$]$^-$ and it is possible to estimate from the equilibrium constants that even under the most unfavourable kinetic conditions (low [Cl^-] and low pK_a) the amount of starting substrate still present at the end of the reaction is less

Table 3 Pseudo-first-order rate constants, k_{obs}, for the displacement by chloride ion of ligand L from substrates $[AuCl_3(L)]$ in MeOH–water (95:5, v/v), at 25.0 °C, $[HClO_4] = 0.10$ mol dm^{-3} and $I = 0.20$ mol dm^{-3} ($LiClO_4$)

L	$10^3[Cl^-]$/mol dm^{-3}	$10^3\,k_{obs}$/s^{-1}	L	$10^3[Cl^-]$/mol dm^{-3}	$10^3\,k_{obs}$/s^{-1}
Thiazole	0.974	4.78	2,4,5-Trimethyloxazole	48.4	1.17
	1.95	5.74		58.1	1.32
	5.84	10.6		67.7	1.50
	9.74	14.6		77.4	1.73
	19.5	26.3		96.8	2.15
	39.0	47.2		194	4.31
	77.9	91.0	2-Methylbenzoxazole	5.84	10.25
4-Methylthiazole	4.87	2.85		9.7	15.4
	9.74	4.83		19.5	26.7
	19.5	7.21		39.0	48.8
	39.0	13.9		587.3	70.8
	58.4	19.5	2,5-Dimethyl-1,3,4-thiadiazole	1.95	1.94
	77.9	26.1		5.84	2.67
5-Methylthiazole	1.95	2.355		9.74	3.05
	3.9	3.36		19.5	4.31
	7.79	5.26		39.0	6.37
	19.4	11.2		58.4	8.91
	38.7	20.6		77.9	10.9
	58.1	30.7	2-Methylbenzoselenazole	19.4	0.36
2,4-Dimethylthiazole	19.5	0.069		39.0	0.647
	48.7	0.126		58.4	0.99
	77.9	0.185		77.9	1.13
	87.7	0.202		97.4	1.49
	97.4	0.219	Pyridine	5.84	3.31
4,5-Dimethylthiazole	1.94	0.901		9.74	4.67
	3.87	1.447		19.5	7.55
	19.4	4.64		39.0	14.9
	38.7	8.698		58.4	22.8
	77.4	17.2		82.8	30.7
	96.8	21.2		97.4	33.8
Benzothiazole	0.974	14.2	4-Chloropyridine	0.29	4.78
	2.92	21.5		0.581	5.27
	4.87	31.4		0.774	5.83
	7.79	42.0		0.968	6.48
	9.74	52.4		2.90	15.8
2-Methylbenzothiazole	0.984	0.395	4-Cyanopyridine	0.29	57.4
	9.84	0.513		0.581	63.0
	29.3	1.55		0.774	69.0
	59.0	2.80		0.968	75.7
	98.4	4.31		2.90	131
Oxazole	0.974	14.4	2,6-Bis(chloromethyl)pyridine	4.0	0.17
	1.94	17.7		10.0	0.23
	2.92	20.1		20.0	0.28
	5.94	30.9		60.0	0.51
	7.79	36.8			

than 1% of the total complex present. The use of the pK_a values determined in aqueous solution as a measure of the protonation equilibrium constants in the MeOH–water system is acceptable because the protonation constants of weak neutral bases are not very sensitive to the relative permitivity of the solvent.[7] The pK_a of thiazole has been determined spectrophotometrically in water and MeOH–water and the two values are indeed the same.

Repetitive spectrum scanning experiments, in all cases, show the presence of two well defined isosbestic points in the regions 280–305 and 350–370 nm, the actual wavelengths depending on the nature of the substrate $[AuCl_3(L)]$, and indicate that a single-stage reaction is involved, *i.e.* the displacement of the co-ordinated base by chloride ion. The final absorption, in all cases, is that expected for an authentic sample of $[AuCl_4]^-$ plus that of L, measured under the same conditions.

The rate constants were determined from the change, with time, of the absorbance at 320 nm (A_t), a wavelength where the main absorbing species is $[AuCl_4]^-$.

The pseudo-first-order rate constants, k_{obs}, were calculated, according to the expression $A_t = A_\infty + (A_0 - A_\infty)\exp(-k_{obs}t)$, where A_t and A_∞ are the absorbances of the reaction mixture at time t and at the end of the reaction respectively, by using a computer program based on the Marquardt algorithm[6] and optimising k_{obs}, A_0 and A_∞. The values of k_{obs} for any particular kinetic run are presented in Table 3.

Discussion

Although it is known that thiazoles and oxazoles are protonated at nitrogen they are potentially ambidentate ligands (N,S; N,O respectively) and it is necessary to ascertain the site of binding to Au^{III} in its complexes, especially in view of the known 'soft' (class b) character of the metal and its preference for S donors. There is a considerable body of evidence that indicates bonding through nitrogen of which the following is probably the most important: (*i*) thiazoles bind to the analogous 'soft' d^8 Pt^{II} through nitrogen;[8] (*ii*) thiophene does not form a complex with Au^{III} and, while a gold(III) complex of thianthrene is described in the literature,[9] its synthesis requires anhydrous aprotic solvent and it is rapidly solvolysed by methanol;[10] (*iii*) there is a general similarity of the behaviour of these complexes (N,O- and N,S-containing five-membered heterocycles) with corresponding R-py (N-containing six-membered heterocycles) that depends only upon the proton basicity of the nitrogen.

Table 4 Measured equilibrium and kinetic constants for the systems $[AuCl_4]^-$–L in MeOH–water (95:5, v/v) at 25.0 °C, I = 0.20 mol dm^{-3} ($LiClO_4$)

L	pK_a	K_2	k_{-2}/dm^3 mol^{-1} s^{-1}	k_{-1}/s^{-1}
1 Thiazole	2.55	1.20 ± 0.06	1.120 ± 0.005	(3.8 ± 0.2) × 10^{-3}
2 4-Methylthiazole	3.16	0.83 ± 0.07	0.315 ± 0.005	(1.4 ± 0.2) × 10^{-3}
3 5-Methylthiazole	3.12	2.2 ± 0.1	0.504 ± 0.002	(1.36 ± 0.06) × 10^{-3}
4 4,5-Dimethylthiazole	3.73	2.6 ± 0.3	0.214 ± 0.001	(5.2 ± 0.7) × 10^{-4}
5 2,4-Dimethylthiazole	3.98	5.3 ± 0.3	(1.94 ± 0.03) × 10^{-3}	(3.2 ± 0.2) × 10^{-5}
6 2,4,5-Trimethylthiazole	4.55	36 ± 6	*a*	*a*
7 Benzothiazole	1.2	0.27 ± 0.04	4.3 ± 0.1	(9.6 ± 0.9) × 10^{-3}
8 2-Methylbenzothiazole	2.07[b]	0.42 ± 0.09	(4.2 ± 0.2) × 10^{-2}	(2.7 ± 0.8) × 10^{-4}
9 Oxazole	0.8	0.34 ± 0.05	3.31 ± 0.07	(1.10 ± 0.03) × 10^{-2}
10 Benzoxazole	−0.13	0.192 ± 0.007	*c*	*c*
11 2-Methylbenzoxazole	0.6	0.17 ± 0.03	1.147 ± 0.008	(4.03 ± 0.3) × 10^{-3}
12 2,4,5-Trimethyloxazole	3.56	1.7 ± 0.1	(2.06 ± 0.08) × 10^{-2}	(1.4 ± 0.6) × 10^{-4}
13 2-Methylbenzoselenazole	—	*d*	0.117 ± 0.002	(1.89 ± 0.08) × 10^{-3}
14 Pyridine	5.17	89 ± 2	0.35 ± 1	(1.4 ± 0.6) × 10^{-3}
15 4-Cyanopyridine	1.90	0.6 ± 0.1	29.6 ± 0.06	(0.45 ± 0.01) × 10^{-3}
16 4-Chloropyridine	3.84	5 ± 2	4.4 ± 0.3	(2.7 ± 0.4) × 10^{-3}
17 2,6-Bis(chloromethyl)pyridine	2.80	1.8 ± 0.6	(9.8 ± 0.5) × 10^{-2}	(2.6 ± 0.2) × 10^{-3}

[a] Very slow, with some reduction. [b] Evaluated. [c] Fast. [d] Decomposes before equilibrium is reached.

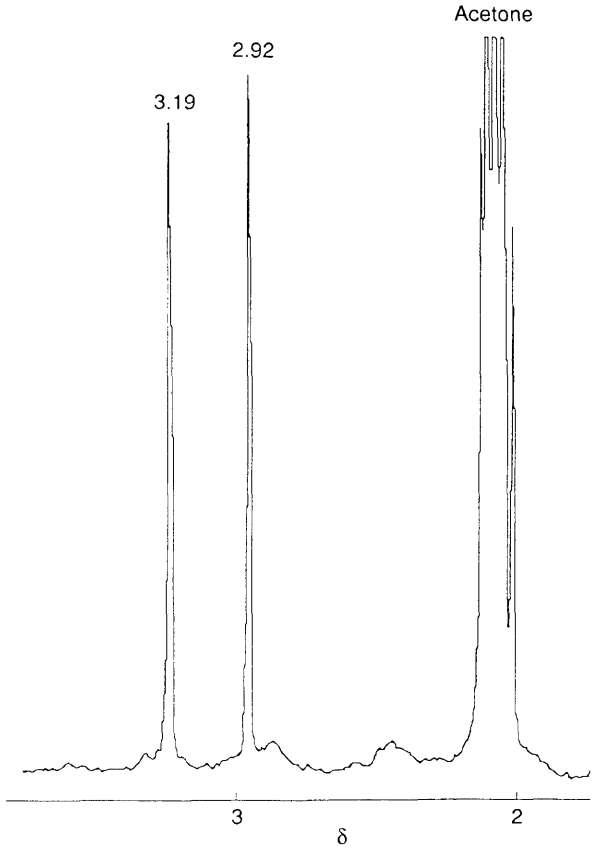
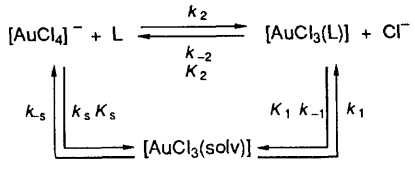


Fig. 1 Proton NMR spectrum of trichloro(2,5-dimethyl-1,3,4-thiadiazole)gold(III)



Scheme 1

A more definitive demonstration comes from the ^{1}H NMR spectrum (Fig. 1) of trichloro(2,5-dimethyl-1,3,4-thiadiazole)-gold(III). The ligand has a plane of symmetry passing through the sulphur atom and the ligand symmetry would be maintained if it were bound to gold through sulphur. As expected, the spectrum of the free ligand has a single peak assigned to the methyl protons but that of the complex has two peaks, consistent with co-ordination through nitrogen.

The reactions occurring in the systems reported in this paper and the labelling of the relevant rate and equilibrium constants can be described by the general Scheme 1 where L is the heterocyclic nitrogen donor and solv the solvent. The system can reach equilibrium both through direct exchange between L and chloride ion and the solvolytic pathway, corresponding to successive solvolyses and solvent substitutions. Since the position of the equilibrium is independent of the reaction pathway, $K_2 = K_sK_1$. Values for the equilibrium constants K_2 and the rate constants for the displacement of the co-ordinated L (k_{-1} and k_{-2}) are collected in Table 4.

In order to compare the behaviour of the five-membered N,O and N,S heterocyclic ligands and their complexes with what is known from the extensive studies of the analogous behaviour of substituted pyridines (six-membered N heterocyclic ligands), the kinetics and equilibria of the displacement of R-py [R = H, 4-Cl, 4-CN or 2,6-$(CH_2Cl)_2$] from $[AuCl_3(R\text{-py})]$ were studied. Three of these ligands cover the same basicity range as the thiazoles and oxazoles, while pyridine itself serves to link this study with that carried out with complexes of the more basic pyridines in dry methanol as solvent. The change in solvent from dry methanol to MeOH–water (95:5, v/v) only has a marginal effect upon the rate constant for the displacement of pyridine by Cl^-, k_{-2} (0.42 [11] and 0.35 dm^3 mol^{-1} s^{-1}). From the relationship $K_2 = k_2/k_{-2} = K_sk_1/k_{-1}$ it is possible to calculate values for k_2 and k_1 and K_1 ($=k_1/k_{-1}$) which are collected in Table 5.

The plot of log K_2 against the pK_a of the conjugate acid of the herocyclic ligand, Fig. 2, is a somewhat scattered but reasonably smooth curve that includes points for the oxazoles, the thiazoles and the pyridines. There are no systematic deviations that can be ascribed to the presence of substituents *ortho* to the nitrogen donor and it must be concluded that there is no significant destabilisation of the $[AuCl_3(L)]$ complex resulting from steric hindrance. This is in marked contrast to the previously reported [1,3] results for the analogous complexes with more basic methylpyridines where, in dry methanol, there is a very marked steric effect amounting to the reduction of the equilibrium constant, K_2, by a factor of approximately 10 for each *ortho*-methyl substituent when comparing ligands of similar basicity. We attempted to see whether this change of behaviour was the result of geometric differences between the five-membered N,O- or N,S-heterocycles on the one hand and the six-membered N-heterocycles on the other (possibly through a change in the cone

Table 5 Derived equilibrium and kinetic constants for the systems $[AuCl_4]^-$–L in MeOH–water (95:5, v/v) at 25.0 °C [$K_S = (3.4 \pm 0.2) \times 10^{-4}$ mol dm^{-3}]

L	$10^{-3} K_1$	k_2/dm^3 mol^{-1} s^{-1}	k_1/s^{-1}
Thiazole	3.5 ± 0.3	1.34 ± 0.07	13 ± 1
4-Methylthiazole	2.4 ± 0.3	0.26 ± 0.02	3.4 ± 0.6
5-Methylthiazole	6.5 ± 0.5	1.11 ± 0.05	8.8 ± 0
4,5-Dimethylthiazole	8 ± 1	0.56 ± 0.06	4.2 ± 0.8
2,4-Dimethylthiazole	16 ± 1	(1.03 ± 0.06) × 10^{-2}	
2,4,5-Trimethylthiazole	110 ± 10	*a*	*a*
Benzothiazole	0.8 ± 0.01	1.2 ± 0.2	8 ± 1
2-Methylbenzothiazole	1.2 ± 0.3	(1.8 ± 0.4) × 10^{-2}	0.3 ± 0.1
Oxazole	1.0 ± 0.2	1.1 ± 0.2	11 ± 2
Benzoxazole	0.56 ± 0.04	*b*	*b*
2-Methylbenzoxazole	0.5 ± 0.09	0.19 ± 0.03	2.0 ± 0.4
2,4,5-Trimethyloxazole	5 ± 0.5	(3.5 ± 0.2) × 10^{-2}	*a*
Pyridine	260 ± 20	31 ± 1	400 ± 200
4-Cyanopyridine	1.7 ± 0.3	17 ± 3	0.8 ± 0.1
4-Chloropyridine	16 ± 5	24 ± 7	43 ± 15
2,6-Bis(chloromethyl)pyridine	3.8	0.18	0.14

[a] Very slow, with some reduction. [b] Fast.

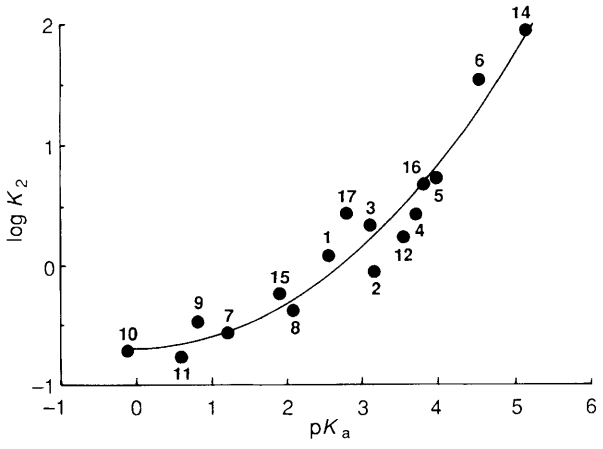


Fig. 2 Dependence of the stability of the $[AuCl_3(L)]$ complexes upon ligand basicity (L is identified by its number in Table 4)

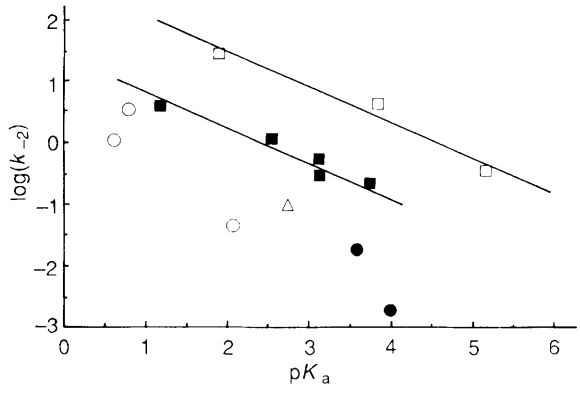


Fig. 3 Plots of log k_{-2} *versus* pK_a for (□) pyridines, (■) unhindered thiazoles and those with a single *ortho*-methyl substituent, (○) oxazole, 2-methylbenzoxazole and 2-methylbenzothiazole, (●) 2,4-dimethylthiazole and 2,4,5-trimethyloxazole and (△) 2,6-bis(chloromethyl)pyridine

angles of the ligands) that affect steric hindrance, or whether it was a property of ligand basicity. For this reason we attempted to make complexes of pyridines with methyl substituents in the 2 and 6 positions and a polar substituent in the 4 position to reduce the basicity of the ligands sufficiently to bring them into the range of the oxazoles and thiazoles. At this stage we have only been able to study the complex of 2,6-bis(chloromethyl)-pyridine (pK_a = 2.8) and the fact that the point for this complex lies on the log K_2 *versus* pK_a curve, Fig. 2, suggests that the extent of steric hindrance in the four-co-ordinate complex depends upon the basicity of the ligand rather than its ring composition. The change in solvent from dry methanol to methanol–water (95:5, v/v) seems a less likely cause (the extent of steric hindrance is not affected by a change in the nature of the alcohol[11]), but until the completion of a systematic study of the ways in which solvent, ligand type and ligand basicity influence the effect of *ortho* substitution on K_2 it would be premature to attempt to explain these observations.

Although the equilibrium constants of the complexes, while dependent upon the proton basicity of the donor nitrogen, are insensitive to the size or composition of the heterocyclic ring, there are marked differences in the labilities of the different systems. Plots of log k_{-2} for the displacement of different types of heterocyclic ligands against their pK_a are approximately linear and parallel to one another (Fig. 3). Points for the unhindered five-membered N,S-heterocycles lie on a common line and the rate constants are approximately 10 times smaller than those for the displacement of the six-membered N-heterocyclic ligands of similar basicity. The presence of a single *ortho*-methyl substituent leads to a small reduction in reactivity, but less than that found on going from thiazole to oxazole. The differences are too small to warrant a discussion of their significance until there is a much larger collection of data. The effect of two *ortho*-methyl substituents is much more substantial with a reduction of approximately two orders of magnitude in k_{-2} for ligands of comparable basicity (*e.g.* 4,5-dimethylthiazole and 2,4-dimethylthiazole). This reduction in reactivity is also observed in the displacement of 2,6-bis(chloromethyl)pyridine, which lies within the same range of basicity as the thiazole ligands. It is to be noted that the rate constants for the displacement of the more strongly basic pyridines (pK_a > 5) are not affected by the presence of either one or two *ortho*-methyl substituents (once the basicity changes have been accounted for) and it has been concluded that the steric congestion in the four-co-ordinate species was not further increased on binding chloride to form the five-co-ordinate rate-determining transition state.[1,3]

Although these systems do not lend themselves to a direct measurement of the rate constants for the reaction between $[AuCl_4]^-$ and the weakly basic heterocycles, values for k_2 can be obtained from the relationship $k_2 = K_2 k_{-2}$. The oxazoles and thiazoles are poorer nucleophiles than pyridines of similar basicity, k_2 being about one order of magnitude smaller, and the

response to steric hindrance is such that, while the influence of a single *ortho* substituent is somewhat less in the five-membered N,O- and N,S-heterocycles than in the six-membered pyridines, the presence of bulky groups on both sides of the donor nitrogen has the same effect in all the heterocycles.

Since the difference in the behaviour of the five- and six-membered heterocycles of similar nitrogen basicity lies in the rates of approach to equilibrium rather than in the position of equilibrium, an explanation must be sought in the differences between the rate-determining transition states. The pyridine derivatives are more able than oxazoles and thiazoles of similar basicity to stabilise these anionic five-co-ordinated transition states with respect to the ground states. It has been suggested elsewhere,[12] in order to account for the fact that, as the basicity of the entering pyridine derivative decreases, k_2 for its reaction with $[PtCl_3(L')]^-$ increases (L′ is a neutral ligand with a moderate to strong *trans* influence), that the heterocycle is biphilic and can function additionally as a π acceptor in the transition state and withdraw some of the excess charge from the metal. While the π basicity of Au^{III}, especially in the absence of strong *trans* influence ligands, is expected to be considerably less than that of Pt^{II}, a similar effect might be invoked to account for the difference between the pyridines and the oxazoles and thiazoles.

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