Novel Luminescent Cyclometalated and Terpyridine Gold(III) Complexes and DNA Binding Studies

Heng-Qian Liu,[a] Tsz-Chun Cheung,[a] Shie-Ming Peng[b] and Chi-Ming Che*[a]

[a] *Department of Chemistry, The University of Hong Kong, Pokfulam Road, Hong Kong*
[b] *Department of Chemistry, National Taiwan University, Taipei, Taiwan*

Two gold complexes, $[Au^{III}\{4\text{-MeOPh-(Phbipy)}\}Cl]\cdot CF_3SO_3$ **1** and $[Au^{III}(4\text{-MeOPh-terpy})Cl]\cdot(ClO_4)_2$ **2** [4-MeOPh-(Phbipy) = 4′-(4-methoxyphenyl)-6′-phenyl-2,2′-bipyridine, 4-MeOPh-terpy = 4′-(4-methoxyphenyl)-2,2′,6′,2″-terpyridine] are prepared, and their interactions with calf-thymus DNA, poly(dG-dC)$_2$ and poly(dA-dT)$_2$, investigated by spectroscopic means; in the reaction with ct DNA, **1** has a higher binding constant than **2**, but the latter has a higher degree of AT specificity.

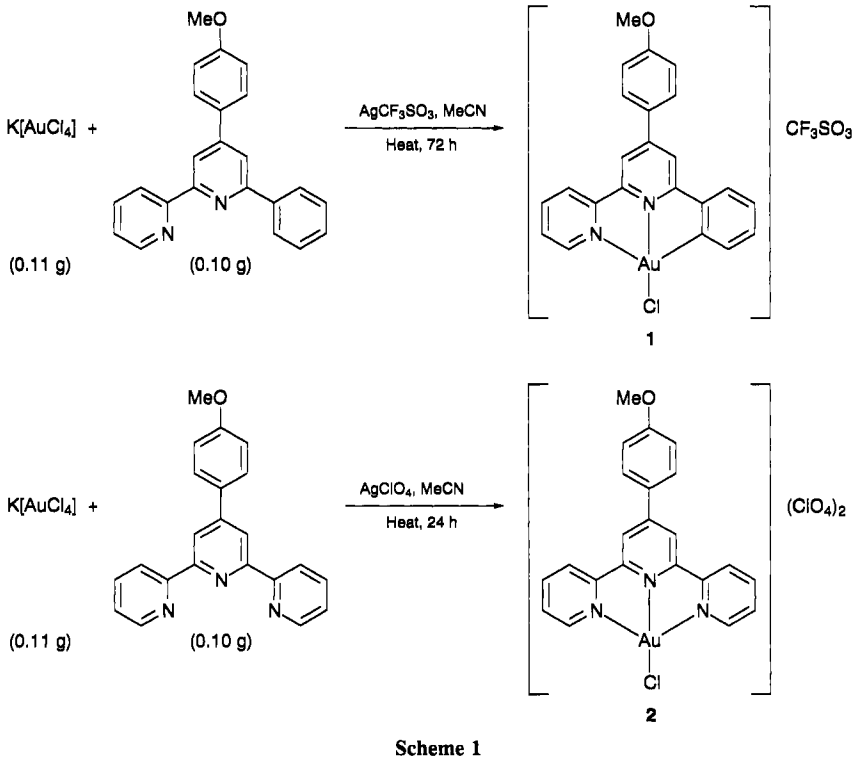
There has been interest in gold(III) complexes because of the prospect of inorganic drug design and their use in studying biochemical reaction mechanisms. Luminescent gold(III) complexes are rare[1] and DNA binding studies are even less known. The high charge of gold(III) should make such compounds potent luminescent metallointercalators *via* binding to nucleic bases[2]. We describe gold(III), in particular cyclometalated gold(III) complexes, that are good luminescent metallointercalators. $[Au^{III}\{4\text{-MeOPh-Phbipy}\}Cl]\cdot CF_3SO_3$ **1** and $[Au^{III}(4\text{-MeOPh-terpy})Cl]\cdot(ClO_4)_2$ **2**, shown in Scheme 1, have been prepared and their interactions with calf-thymus DNA studied. Complexes **1** and **2** are similar structurally, the difference being that one of the coordinated pyridine rings in **2** is a phenyl ring in **1**. Despite this small structural difference, significant changes in photophysical properties and binding reactions with calf-thymus DNA have been found.

The preparation of **1** and **2** are outlined in Scheme 1. Both complexes have been characterized by spectroscopic methods.† The structure of **1** has further been established by an X-ray crystal analysis.‡

Fig. 1 shows a perspective view of the cation of **1**. The coordination geometry of the gold atom is slightly distorted square planar with the N(1)–Au–N(2) angle of 80.1(3)°. The three Au–N distances are comparable with that found in $[Au(terpy)Cl]^{2+}$.[3]

Calf-thymus DNA (ct DNA), type II (Sigma) was purified.[4] Synthetic polynucleotides, poly(dG-dC)$_2$ and poly(dA-dT)$_2$, (Sigma) were used as received. The concentrations of nucleic acids were determined spectrophotometrically by using the following molar extinction coefficients at the given wavelengths: ε^{260nm} = 6600 for ct DNA, ε^{254nm} = 8400 for poly(dG-dC)$_2$ and ε^{260nm} = 6600 dm^3 mol^{-1} cm^{-1} for poly(dA-dT)$_2$.[5] All experiments were carried out in an air saturated mixed MeOH–tris buffer (0.050 NaCl, 0.0050 mol dm^{-3} Tris, pH 7.2) solution.

Absorption titrations of **1** in 7% and **2** in 6% MeOH–tris buffer solutions with addition of ct DNA were performed, and the results are listed in Table 1. Fig. 2 shows the absorption titration data for the reaction of **2** with ct DNA. Circular dichroism measurements revealed that the induced small positive signals at 360 nm for **1** and 359 nm for **2** were formed upon treating the complexes with ct DNA. These positive signals which undoubtedly come from the adduct of **1** and **2** with ct DNA, and the spectroscopic data discussed above, are indicative of a strong DNA binding. The interaction of **1** and **2** with ct DNA should be of an intercalation nature owing to the square planar chelating terpyridine and phenylbipyridine moieties. However, **1** and **2** show different binding properties. The intrinsic binding constants calculated from absorption titration data according to the previous method[4] are 2.8 × 10^5 dm^3 mol^{-1} for **1** and 2.1 × 10^4 dm^3 mol^{-1} for **2**, respectively. Further studies of the interactions with synthetic polynucleotide, poly(dG-dC)$_2$ and poly(dA-dT)$_2$, provide a sequence dependence of the gold complexes. The results are also



Scheme 1

listed in Table 1. For **1** with ct DNA, there appears to be interaction at both GC and AT sites. For **2** with ct DNA, the absorbance maximum and hypochromicity (Table 1) are similar to that obtained with poly(dA-dT)$_2$, suggesting a higher degree of AT specificity. Plots of A_0/A *vs.* [DNA]/[complex] for **1** and **2**, respectively, have been made (see inset in Fig. 2 for **2**) and the absorbance saturations are observed at the ratio of [DNA]/[complex] = 1.9 and 25.0, respectively. For **1**, there could be non-specificity of base pairs, and the complex may bind to ct DNA at both GC and AT sites, hence less amount of ct DNA is required for binding of the complex. For **2**, a greater excess of ct DNA should be used, due to its higher degree of base specificity at AT sites.

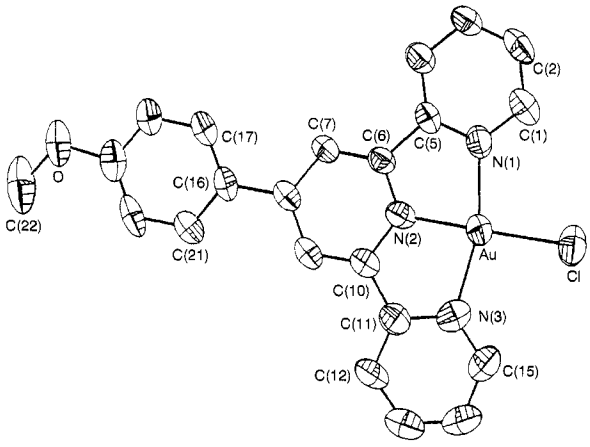


Fig. 1 Perspective drawing of [Au^{III}(4-MeOPh-terpy)Cl]$^{2+}$. Selected bond lengths (Å) and angles (°): Au–N(1) 2.020(7), Au–N(2) 1.924(6), Au–N(3) 2.047(7), Au–Cl 2.2559(24), N(1)–Au–N(2) 80.1(3), N(1)–Au–N(3) 162.6(3), N(2)–Au–N(3) 82.5(3), Au–N(1)–C(1) 126.1(6), Au–N(1)–C(5) 113.6(5), C(1)–N(1)–C(5) 120.3(7), Au–N(2)–C(6) 119.4(5), Au–N(2)–C(10) 117.4(5), Au–N(3)–C(11) 110.8, Au–N(3)–C(15) 127.1(6).

Table 1 Spectroscopic data of **1** and **2** upon interactions with nucleic acids in mixed MeOH–tris Buffer solutions

	λ_{max}/nm				Hypochromicity, H (%)		
Complex	Free complex	ct DNA	GC	AT	ct DNA	GC	AT
1[a]	370	388 (393, 284)[c]	387 (391, 287)	393 (391, 282)	29	18	32
2[b]	371	370 (424, 313)	377 (426, 313)	370 (425, 312)	33	45	31

[a] In 70% MeOH–tris buffer solution. [b] In 6% MeOH–tris buffer solution. [c] In parentheses the wavelengths of isosbestic points indicated.

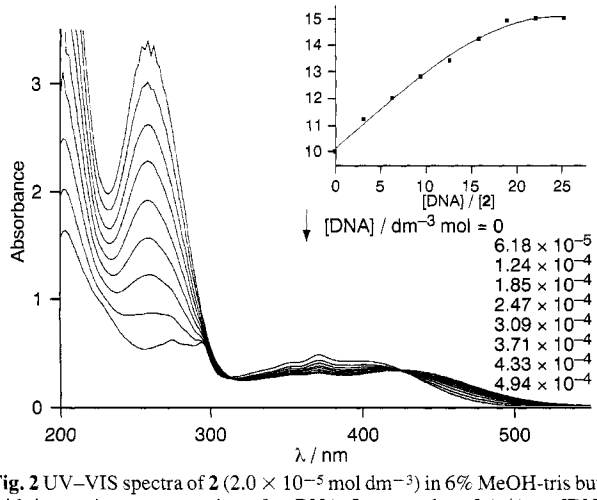


Fig. 2 UV–VIS spectra of **2** (2.0 × 10^{-5} mol dm^{-3}) in 6% MeOH-tris buffer with increasing concentration of ct DNA. Inset: a plot of A_0/A *vs.* [DNA]/[**2**].

In 6–7% MeOH–tris buffer (0.050 mol dm^{-3} NaCl, 0.0050 mol dm^{-3} Tris, pH 7.2) solution, both **1** and **2** display emission at room temp. The emission of **1** at 530 nm (lifetime = 0.46 μs, quantum yield = 2.5 × 10^{-4}) could be assigned to an intraligand excited state with some MLCT character.[1] The emission of **2** at 480 nm (lifetime = 0.25 μs, quantum yield = 2.4 × 10^{-3}) should be intraligand. The emission intensity of **1** decreased with addition of ct DNA, poly(dG-dC)$_2$ and poly(dA-dT)$_2$. Linear Stern–Volmer plots of I_0/I *vs.* [nucleic acid] have been made giving the quenching rate constants 1.5 × 10^4, 4.5 × 10^4 and 1.2 × 10^4 mol dm^{-3}, respectively. The quenching rate constant with ct DNA is between those with poly(dG-dC)$_2$ and poly(dA-dT)$_2$, reflecting the absorption titration results that revealed no specificity at GC and AT sites. Accompanied by the emission quenching, a blue shift of the maximum emission wavelength from 540 to 512 nm was observed. Emission titration data were also treated according to the equation derived by McGhee–von Hippel[6] to give the intrinsic binding constant to be 2.5 × 10^5 dm^3 mol^{-1}. This is in excellent agreement with the value of 2.8 × 10^5 dm^3 mol^{-1} obtained by using the absorption titration data. A value of *n ca.* 2 has been found, indicating that two lattice residue sites are made unavailable by the binding of a single complex **1** to ct DNA. For **2**, there has been no obvious and consistent change of the emission properties upon treating the complex with ct DNA.

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Footnotes

† *Selected data*: satisfactory elemental analyses have been obtained for **1** and **2**. UV–VIS (5% MeOH–H_2O): λ_{max}/nm (ε_{max} dm^3 mol^{-1} cm^{-1}), 370 (1.89 × 10^4), 287 (2.09 × 10^4), 220 (4.64 × 10^4) and 202 (7.15 × 10^4) for **1**, and 404 (2.40 × 10^4), 371 (2.47 × 10^4), 353 (2.01 × 10^4) (sh) 333 (1.59 × 10^4) (sh), 294 (3.21 × 10^4), 283 (3.08 × 10^4) (sh), 274 (3.73 × 10^4) and 200 (1.31 × 10^5) for **2**. FAB–MS for **1**: *m/z* 569 (M$^+$). ^{1}H NMR (CD_3)$_2$SO, 270 MHz) for **1**: δ 2.5 (S, 3H), 7.13–7.17 (m, 2H), 7.50–7.62 (m, 3H), 7.81–7.85 (m, 1H), 8.04–8.76 (m, 2H), 8.38–8.44 (m, 3H), 8.66–8.67 (d, 1H), 8.86–8.89 (m, 2H).

‡ *Crystal data* for **2**: [Au^{III}(4-MeOPh-terpy)Cl](ClO$_4$)$_2$(C_3H_7NO)$_2$, $C_{28}H_{24}N_5Cl_3O_{11}Au$, M = 909.85, triclinic, space group $P\bar{1}$, a = 8.6651(16), b = 12.026(4), c = 17.226(3) Å, α = 106.73(2), β = 102.89(2), γ = 90.22(2)°, V = 1671.2(7) Å^3; D_c = 1.808 g cm^{-3} for Z = 2; μ(Mo-Kα) = 46.78 cm^{-1}, F(000) = 890, crystal dimensions 0.20 × 0.25 × 0.35 mm, No. of variables 421, No. of unique data measured 4359, No. of observed data with $I > 2\sigma(I)$ 3612, R = 0.040, R_w = 0.030, GOF = 2.41, weighting scheme $\omega^{-1} = \sigma^2(F_0)$. The residual extrema in the final difference map were −0.740 and 0.810 e Å^{-3}. Intensity data were collected on an Enraf-Nonius CAD 4 diffractometer with monochromated Mo-Kα radiation (0.7107 Å) at room temp. The structure was solved by Patterson method and refined by least-squares analysis. All computations were performed using the NRCVAX program. Atomic coordinates, thermal parameters, and bond lengths and angles have been deposited at the Cambridge Crystallographic Data Centre. See Information for Authors, Issue No. 1.

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