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Characterisation of bifunctional ruthenium(II) complexes, potential DNA photo-probes. Presence of folded and unfolded conformers †

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Novel bifunctional ruthenium(II) complexes, $[Ru(TAP)_2(POQ\text{-}Nmet)]^{2+}$ and $[Ru(BPY)_2(POQ\text{-}Nmet)]^{2+}$ (**1a**, **2a**), containing a metallic and an organic moiety, have been prepared as photoprobes and photoreagents of DNA (TAP = 1,4,5,8-tetraazaphenanthrene, POQ-Nmet = 5-[6-(7-chloroquinolin-4-yl)-3-thia-6-azaheptanamido]-1,10-phenanthroline). The ES mass spectrometry and ^1H NMR data in organic solvents indicate that the quinoline moiety exists in both the protonated and non-protonated form. Moreover, the comparison of the NMR data with those of the corresponding monofunctional complexes (without quinoline) evidences that $[Ru(TAP)_2(POQ\text{-}Nmet)]^{2+}$ and $[Ru(BPY)_2(POQ\text{-}Nmet)]^{2+}$ are unfolded when the quinoline unit is protonated whereas deprotonation permits folding of the molecule. In the folded state the spatial proximity of the electron donor (the organic moiety) and electron acceptor (the metallic moiety) in $[Ru(TAP)_2(POQ\text{-}Nmet)]^{2+}$ favours intramolecular photo-induced electron transfer, which has been shown in a previous study to be responsible for the very low luminescence of **1a** in non-protonating solutions. The restoration of the luminescence by protonation of the quinoline moiety as observed previously is in agreement with the unfolding of the molecule demonstrated in this work. The existence of such folding–unfolding processes related to protonation is crucial for studies of **1a** with DNA.

Introduction

Ruthenium(II) polypyridyl complexes have extensively been studied as photosensitisers of redox reactions[1,2] and applied in several areas: in solar energy conversion,[3,4] for photoelectrochemical cells[5] and as photosensitising building blocks in supramolecular antenna systems for electron and energy transfers.[6] Owing to their attractive luminescent properties, which are extremely sensitive to the microenvironment, ruthenium(II) complexes have also been used as photoprobes of DNA.[7–9]

In our laboratory a number of complexes have been developed as photoreagents of DNA.[10–12] However, an important drawback of these photoreactive complexes is their low affinity for DNA.[13] One of the strategies which we have adopted to overcome this problem is the design of bifunctional complexes[14–16] composed of two functional units, a metallic complex and an organic DNA binder,[17] connected by a chain ($[Ru(TAP)_2(POQ\text{-}Nmet)]^{2+}$ **1a**, $[Ru(BPY)_2(POQ\text{-}Nmet)]^{2+}$ **2a**, Fig. 1). This concept is based on the observation of an increased affinity for DNA of compounds where two identical units, organic[18] or metallic,[19] are linked by a chain as compared to the affinity of the separate units. An extensive comparative study of the absorption and emission properties of **1a** and **2a** with those of the monofunctional analogues $[Ru(TAP)_2(acPhen)]^{2+}$ **1b** and $[Ru(BPY)_2(acPhen)]^{2+}$ **2b** (Fig. 1) had been performed previously in MeCN and in water in the absence of DNA.[15] From those studies, it was concluded that when the quinoline subunit is protonated the luminescence properties of the metallic unit of **1a** and **2a** are not modified as compared to those of the monofunctional analogues. On the other hand, by deprotonation of the quinoline subunit, 96% of the luminescence of the metallic unit of **1a** was quenched whereas the emission of the BPY complex subunit of **2a** was not affected. It was shown that this difference can be attributed to an intramolecular photo-induced electron transfer present in **1a** and not in **2a**. The TAP complex is indeed much more oxidising in the excited state than the BPY equivalent so that an electron transfer from the quinoline moiety is thermodynamically possible with the TAP but not with the BPY as ligands.[15] In these studies some data were however missing, *i.e.* the capability of the bifunctional complexes to adopt a folded conformation, which is of course crucial for the electron transfer to take place. Moreover it was not demonstrated whether the protonation of the quinoline could induce an unfolding of the complex due for example to an electrostatic repulsion between

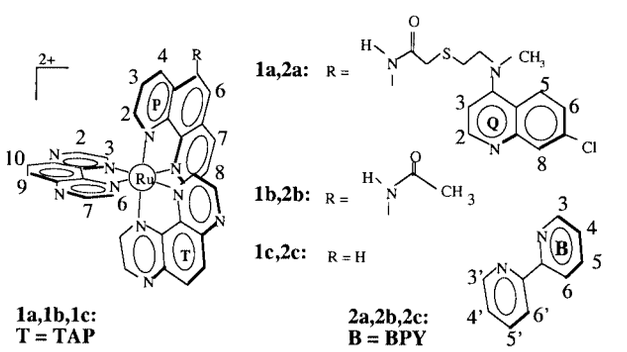

Fig. 1 The complexes studied: $[Ru(TAP)_2(POQ\text{-}Nmet)]^{2+}$ **1a** (TAP = 1,4,5,8-tetraazaphenanthrene, POQ-Nmet = 5-[6-(7-chloroquinolin-4-yl)-3-thia-6-azaheptanamido]-1,10-phenanthroline), $[Ru(TAP)_2(acPhen)]^{2+}$ **1b** (acPhen = 5-acetamido-1,10-phenanthroline), $[Ru(TAP)_2(Phen)]^{2+}$ **1c** (Phen = 1,10-phenanthroline), $[Ru(BPY)_2(POQ\text{-}Nmet)]^{2+}$ **2a** (BPY = 2,2′-bipyridine), $[Ru(BPY)_2(acPhen)]^{2+}$ **2b** and $[Ru(BPY)_2(Phen)]^{2+}$ **2c**.

† Electronic supplementary information (ESI) available: NMR data of the complexes and ligands. See http://www.rsc.org/suppdata/dt/b0/b000197j/

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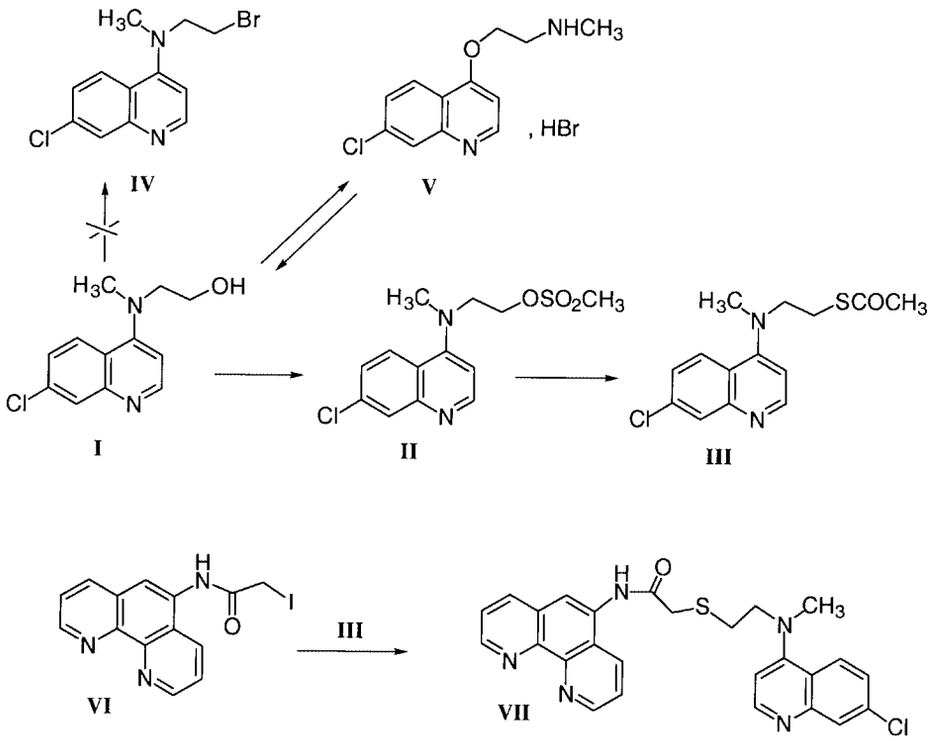

Scheme 1

the two positively charged sub-units. As shown also with other bifunctional rhenium(I) complexes[20,21] for example, the collection of these data constitutes a pre-requisite for the study of the photoprobe in the presence of DNA.[22]

In the present work we report the syntheses of compounds **1a**, **1b**, **2a** and **2b** which were not described before, and their characterisation by NMR and electrospray mass spectrometry. The data for the reference compounds **1c** and **2c** are also presented for comparison purposes. The comparison of the NMR and electrospray mass spectrometry data of **1a** and **2a** with those of the monofunctional analogues **1b** and **2b** provides information on the protonation of the quinoline and its influence on the conformations adopted by the complexes in solution. This study contributes to a better understanding of the luminescence properties of **1a**[15] published previously.

Results

Synthesis of the ligand

The POQ-Nmet ligand **VII** was prepared by reaction of iodoacetamidophenanthroline **VI** with a quinoline functionalised with a thiol precursor **III** (Scheme 1). The compound **III** was prepared in three steps from 4,7-dichloroquinoline. By prolonged heating of 4,7-dichloroquinoline in *N*-methyl-2-aminoethanol, the methylaminoquinoline **I** was formed with a yield of 54%. The hydroxy group of **I** was then esterified by reaction with methanesulfonyl chloride. The mesyl ester **II** was obtained as an oil and presents an NMR spectrum identical to that in the literature.[23] Sodium thioacetate was added to compound **II** and the thioacetate **III** obtained as an oil. It was observed that this compound slowly decomposed on standing, even at 0 °C. The coupling of **III** and **VI** was performed in methanol as previously described,[14] the thiolate anion being generated *in situ* by alkaline hydrolysis of the thioacetate. The ligand **VII** was thus obtained and characterised by mass spectroscopy and NMR.

This synthetic path has been chosen instead of the methodology previously described for the preparation of the heterodimer tosylaminophenanthroline–aminoquinoline (PTsQ).[16] Indeed, in the second step, the addition of 37% hydrobromic acid to **I** led to compound **V**, rather than to the expected **IV**. Compound **V** is isolated by precipitation in acetone and presents a HPLC retention time and a UV/Vis absorption spectrum different from those of aminoquinoline **I**, whereas two peaks are observed by mass spectrometry at *m*/*z* 238 and 236, identical to the mass of the starting material **I** ($M = 236.5$). The NMR spectrum confirmed the presence of a methylaminoethyl residue. ^{1}H–^{1}H Homonuclear irradiations and NOE experiments indicated strong couplings between an exchangeable proton (δ 8.92), the methyl group (δ 2.67) and one methylene (δ 3.57). We therefore can conclude that this compound **V** results from a Smiles rearrangement,[24] which is reversible upon alkaline treatment of **V**.

Syntheses of the corresponding complexes

The complexes $[Ru(TAP)_2(POQ\text{-}Nmet)]^{2+}$ **1a**, $[Ru(BPY)_2(POQ\text{-}Nmet)]^{2+}$ **2a**, $[Ru(TAP)_2(acPhen)]^{2+}$ **1b** and $[Ru(BPY)_2(acPhen)]^{2+}$ **2b** were obtained by substitution of the chlorides in the precursors $Ru(TAP)_2Cl_2$[25] or $Ru(BPY)_2Cl_2$[26] by the ligands POQ-Nmet or acPhen according to the methods previously described.[14] Formation of the complex was approximately 20 times faster for $[Ru(TAP)_2(POQ\text{-}Nmet)]^{2+}$ than for the non-methylated equivalent $[Ru(TAP)_2(POQ)]^{2+}$ previously prepared.[14] The purification of the methylated complexes was also faster and easier. The use of an aqueous solution of $(NH_4)_2CO_3$ as eluent for the cation exchange chromatography of $[Ru(TAP)_2(POQ\text{-}Nmet)]^{2+}$ (see Experimental section) allowed a better control of the pH and facilitated the subsequent desalting. This induced less degradation so that a purity of 98% was achieved.

Characterisations by NMR spectroscopy

The chemical shifts in ^{1}H NMR spectroscopy for the various complexes in DMSO-d_6 and in CD_3CN are presented in Table 1 and in the Experimental section. Fig. 2 shows the ^{1}H NMR spectrum of $[Ru(TAP)_2(POQ\text{-}Nmet)]^{2+}$ (600 MHz; DMSO-d_6 at 30 °C) and the ^{1}H–^{1}H COSY correlation spectrum for the same solution (360 MHz). In both solvents, the amide function on the phenanthroline of the complexes **1b** and **2b** causes a loss of

Table 1 NMR data in CD_3CN. ^1H chemical shifts (±0.05 ppm) of $[Ru(TAP)_2(acPhen)]^{2+}$ **1b** and of the protonated and non-protonated $[Ru(TAP)_2(POQ\text{-}Nmet)]^{2+}$ **1a** and Nmet quinoline **I**

Ligand	Proton	**1a**	**I**	**1b**	**I** + H^+	**1a** + H^+
TAP	T3,3′/T6,6′	8.15/8.23		8.13/8.22		8.16/8.25
	T2,2′/T7,7′	8.95/8.98		8.94/8.94		8.97/8.99
	T9,10	8.60		8.60		8.64
acPhen	P2	8.10		8.13		8.17
	P9	8.04		8.00		8.06
	P3	7.59		7.63		7.69
	P8	7.66		7.72		7.75
	P4	8.49		8.61		8.63
	P7	8.53		8.82		8.78
	P6	8.36		8.62		8.59
	NH	9.03		9.00		9.23
Nmet-Q	Q2	8.20	8.61		8.17	8.21
	Q3	6.82	6.92		6.96	7.00
	Q5	8.10	8.30		8.46	8.29
	Q6	7.36	7.44		7.56	7.55
	Q8	7.34	7.96		7.88	7.84
	$J_{2,3}$/Hz	5.14	5.17		7.47	7.47

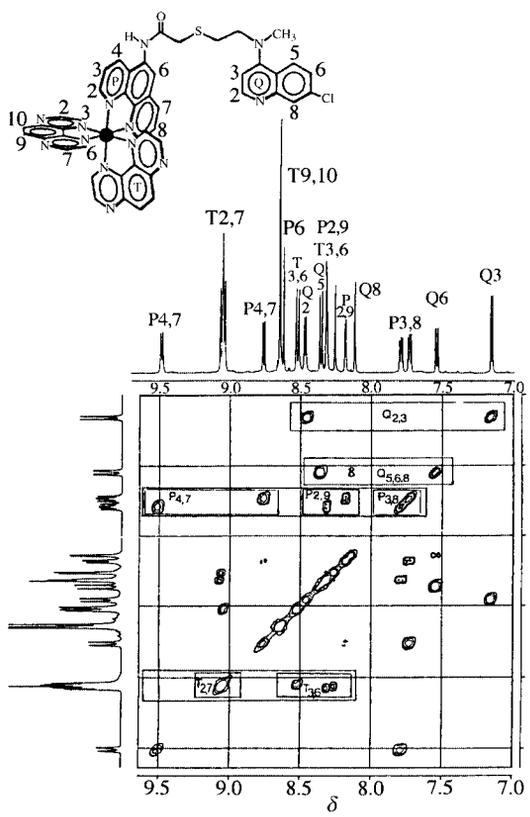

Fig. 2 The ^1H NMR spectrum of $[Ru(TAP)_2(POQ\text{-}Nmet)]^{2+}$ in DMSO-d_6 (600 MHz), and ^1H–^1H correlation spectrum of the same solution (360 MHz). T = TAP; P = Phen; Q = quinoline; T2,7, T3,6 and T9,10 label the protons of *both* TAP ligands.

the C_2 symmetry as compared to the **1c**, **2c** and induces a differentiation of all the protons, the Phen's protons being the most affected.

The bifunctional complex **1a** has the same symmetry as $[Ru(TAP)_2(acPhen)]^{2+}$ and thus all the protons are also diastereotopic. It was observed that by repeating the syntheses or purifications of $[Ru(TAP)_2(POQ\text{-}Nmet)]^{2+}$ the ^1H NMR spectra in CD_3CN were different. These changes can be correlated with the protonation of the sample. Indeed, during the purification process, elution through the cation exchanger may induce a protonation of the complex. On the other hand, it has been shown that the protonation of 4-amino-7-chloroquinolines affects mainly the chemical shifts and coupling constants of the protons Q2 and Q3.[27,28] In the case of the Nmet quinoline **I** (see Scheme 1) in CD_3CN, the coupling constant $J_{2,3}$ varies from 5.14 to 7.47 Hz with increasing concentrations of trifluoroacetic acid, whereas the variation of the other coupling constants remains lower than 0.25 Hz. When an excess of piperidine is added to a neutral solution of **I** the value of the coupling constant $J_{2,3}$ remains 5.14 Hz. For **1a**, $J_{2,3}$ has values varying according to the batch of complex, but remains within the same range (5.14–7.47 Hz). Therefore, we can determine by NMR the degree of protonation of the organic unit in **1a**. In Table 1 the NMR data for **1a** $[Ru(TAP)_2(POQ\text{-}Nmet)]^{2+}$ are presented for two extreme conditions, without protonation and with the maximum of protonation. These data are compared to those of the Nmet quinoline which exhibits the same values of the coupling constant $J_{2,3}$. When the quinoline unit is entirely protonated in the bifunctional complex **1a** the protons chemical shifts of the metallic and organic unit are almost identical to those of the monofunctional complex $[Ru(TAP)_2(acPhen)]^{2+}$ and the protonated Nmet quinoline. In contrast, when the quinoline unit is not protonated, differences are observed between the spectra of **1a** and of the two independent units. Fig. 3 shows schematically the ^1H NMR spectra of **1a**, of each separate unit and of the arithmetic sum. Although the TAP ligands of the bi- and mono-functional complexes exhibit the same proton chemical shifts, the protons of the quinoline and phenanthroline in **1a** are shielded as compared to those of the separate units.

Differential NOE measurements with complex **1a** in CD_3CN (when $J_{2,3}$ = 5.2 Hz) have been performed in order to solve the ambiguity in the attribution of the protons of the phenanthroline ring of the POQ-Nmet ligand and to determine the existence of a possible NOE transfer between the phenanthroline ring and the quinoline unit. Upon irradiation of the singlet at δ_H 8.36, corresponding to the proton P6, the appearance of a doublet signal at δ 8.53 was observed, and thus attributed to P7. The sequential irradiation of all the Phen protons allowed their unambiguous attribution. Moreover, the irradiation of the signal at δ 8.49 (P4) led to a signal at δ 9.04 (NH), and the irradiation of the signal at δ 3.09 (CH_3 of quinoline) induced signals at δ 6.82 (Q3) and 8.12 (Q5). Thus no significant NOE transfer was observed between the Phen ligand and the organic unit. These attributions could be extended to **1a** in DMSO-d_6 and to the other complexes with the help of the ^1H–^1H correlation spectra.

Slow exchange processes do not occur at room temperature, at 250 or 600 MHz, because all the protons peaks are single and well resolved. This contrasts with the non-methylated bifunctional complexes $[Ru(TAP)_2(POQ)]^{2+}$ [14] and $[Ru(TAP)_2(PTsQ)]^{2+}$ (where the linking chain between the phenanthroline

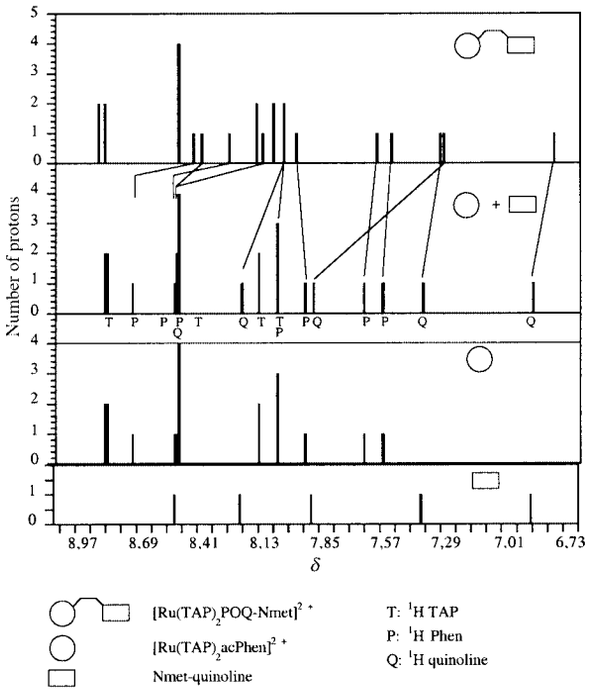

Fig. 3 Schematic representation of the ^{1}H NMR spectra in CD_3CN. From bottom to top: Nmet quinoline (**I**, non-protonated, rectangle), $[Ru(TAP)_2(acPhen)]^{2+}$ **1b** (circle), **I** and **1b** (arithmetic addition), $[Ru(TAP)_2(POQ\text{-}Nmet)]^{2+}$ **1a** (non-protonated, circle-linker-rectangle). The number of protons *versus* the chemical shift ($\delta \pm 0.1$ ppm) is represented in the histograms. The lines between the two spectra relate the Phen and quinoline protons of the bifunctional complex to the corresponding protons of the separate units.

and the aminoquinoline is $N(SO_2C_6H_4Me\text{-}p)(CH_2)_6$).[16] For $[Ru(TAP)_2(POQ)]^{2+}$ the proton peaks of the quinoline are broadened at high field (600 MHz) in DMSO-d_6 at room temperature. For $[Ru(TAP)_2(PTsQ)]^{2+}$ the peaks are doubled and well resolved at 250 and 600 MHz which indicates one or more slow exchange processes.

In the case of $[Ru(BPY)_2(POQ\text{-}Nmet)]^{2+}$ **2a** the comparison of the NMR data to those of the separate units was performed in a situation where the quinoline is only partially protonated. Under such conditions a reciprocal shielding of the protons of the phenanthroline ring and the quinoline unit is also observed, whereas the chemical shifts of the BPY ligands are not affected.

Electrospray mass spectrometry

The complex $[Ru(TAP)_2(POQ\text{-}Nmet)]^{2+}$ $(2Cl^-)$ ($M_w = 1022.81$) exhibits mainly peaks at *m/z* 476.64 ($M - 2Cl^-$, 26%, calculated: 476.43) and 318.24 ($[M + H^+] - 2Cl^-$, 74%, calculated: 317.96), $[Ru(BPY)_2(POQ\text{-}Nmet)]^{2+}$ ($M_w = 970.82$) at 450.81 ($M - 2Cl^-$, 51%, calculated: 450.44) and 301.00 ($[M + H^+] - 2Cl^-$, 49%, calculated: 300.63). For $[Ru(TAP)_2(acPhen)]^{2+}$ ($M_w = 772.63$) a peak is detected at 351.55 ($M - 2Cl^-$, calculated: 351.35). The assignments of the peaks and corresponding charges have been tested by high resolution measurements in order to take into account the isotopic distribution. The correspondence between the calculated and measured distribution for $[Ru(TAP)_2(POQ\text{-}Nmet)]^{2+}$ $(2Cl^-)$ (peak at $m/z = 476.64$) is excellent (Fig. 4). The ESMS data clearly exhibit the expected masses and reveal the presence of protonated and non-protonated species for the two bifunctional complexes when they are dissolved in a MeCN–water (1 : 1).

Discussion

As the irradiation of the proton P6 in $[Ru(TAP)_2(POQ\text{-}Nmet)]^{2+}$ induces a NOE signal at $\delta_H = 8.53$, we attribute this doublet signal to the closest phenanthroline proton, *i.e.* to P7.

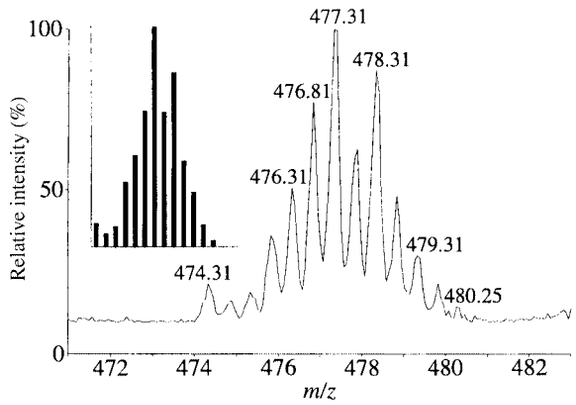

Fig. 4 High resolution ES mass spectrum of the peak at $m/z = 476.64$ of $[Ru(TAP)_2(POQ\text{-}Nmet)]^{2+}$. Correspondence between the calculated (black columns) and measured isotopic distribution.

All the other protons of the POQ-Nmet ligand can then be attributed in **1a**. As proposed by Lewis and Burch,[29] we can also assume that the amide is in the *Z* conformation, usually the most stable for secondary amides.[30] The NOE transfer from the amide's proton to P4 indicates that these two protons are in proximity in most of the conformations adopted by **1a** in solution. This proximity and the absence of transfer to the proton P6 also suggests a coplanarity between the plane of the amide and the plane of the phenanthroline. Nevertheless, for steric reasons, the two planes are probably slightly propeller twisted. The NOE transfer from the methyl group of the quinoline unit to the protons Q3 and Q5 indicates their close proximity in the various conformations of the complex.

The ESMS data of complexes **1a** and **2a** in MeCN–water (1 : 1) clearly indicate the protonation of the complexes in this medium. As a protonation of the metallic unit in the ground state can be excluded because it is clearly not observed in **1b** under the same conditions, the proton must be located on the quinoline unit.

The ^{1}H NMR spectra of the bifunctional complexes depend on the degree of protonation of the quinoline. The percentage of protonation can be estimated from the coupling constant of the protons Q2 and Q3. A comparison between the spectra of the bifunctional complex and those of the separate units with the same degree of protonation reveals the existence of families of conformers with different degrees of folding. In the case of $[Ru(TAP)_2(POQ\text{-}Nmet)]^{2+}$ **1a** when the quinoline is protonated, the signals of the two units are identical to those of the separate units $[Ru(TAP)_2(acPhen)]^{2+}$ and Nmet quinoline$(+H^+)$. This indicates that the complex exists as a family of unfolded conformations where the effects of the ring currents of the quinoline and Phen on each other are negligible. These conformations could be favoured by the electrostatic repulsion between the two units. In contrast, when the quinoline is not protonated, the reciprocal shielding effect of the phenanthroline and organic units indicates their spatial proximity. The existence of a unique folded structure, corresponding for example to a stacking interaction between the quinoline and the phenanthroline, is not confirmed experimentally. Indeed, no significant NOE effect is observed between the protons of the two units. Moreover, according to Corey–Pauling–Koltun (CPK) models, no unique structure can be proposed in which all the protons are shielded by the folding. We conclude therefore that at room temperature the non-protonated bifunctional complex **1a** is present in the form of a family of differently folded conformations, which are in fast equilibrium relative to the timescale of the NMR experiments. This explains that unique, well resolved peaks are observed, with chemical shifts corresponding to an average value for all the conformers. It contrasts with the observations on the bifunctional non-methylated complexes $[Ru(TAP)_2(POQ)]^{2+}$ and $[Ru(TAP)_2$-

$(PTsQ)]^{2+}$. In those cases the slow exchange processes that were observed could be due to different phenomena absent with **1a**: (i) a tautomerism of the non-methylated aminoquinoline[28] in $[Ru(TAP)_2(POQ)]^{2+}$ and in $[Ru(TAP)_2(PTsQ)]^{2+}$, (ii) a rotation with a high activation barrier of the tosyl in $[Ru(TAP)_2(PTsQ)]^{2+}$, and (iii) a conformational equilibrium between families of folded and unfolded conformers occurring within a slower timescale than for **1a**.

The bifunctional BPY complex **2a** presents NMR behaviours similar to those of **1a**, and thus we can also conclude the existence of folded conformers in this bifunctional complex when the quinoline is non-protonated.

In the light of the present work, new conclusions can be drawn on the properties of complex **1a** in solution. (i) The alteration of the acid–base properties observed for the organic moiety in **1a**[15] is probably due to its proximity to the metallic moiety in some conformers of **1a**. Indeed, as determined by absorption spectroscopy at 354 nm, the pK_a of the quinoline has a value of 6.1 in **1a**, which is lower by 1 unit than the pK_a of the non-derivatised Nmet quinoline **I** ($pK_a = 7.1$). (ii) The folding by deprotonation of the quinoline unit of **1a** favours the intramolecular photoelectron transfer demonstrated previously[15] as occurring from the organic part of **1a** to the excited $Ru(TAP)_2^{2+}$ moiety and which is responsible for the luminescence quenching. This inhibition process could not take place in an unfolded conformation because the chain is unfavourable for a long distance electron transfer. Moreover this charge transfer process is thermodynamically unfavorable once the quinoline is protonated (protonated quinoline is not sufficiently reducing).[15,31] As the folding in non-protonating solvents is clearly demonstrated in this work, we can assume presently that the observed luminescence quenching by electron transfer can take place because the electron donor and acceptor are in close contact. For the BPY bifunctional complex **2a** the above considerations are irrelevant. Indeed the excited $Ru(BPY)_2^{2+}$ moiety is not sufficiently oxidising to abstract a proton even from the non-protonated quinoline.[15]

Conclusion

The development of novel synthetic paths for aminomethylated bifunctional ligands allows a much easier preparation of bifunctional ruthenium(II) complexes as compared to the synthesis of bifunctional complexes containing secondary amines.[14,16] The importance of the protonation of the organic sub-unit, shown by ESMS and NMR spectroscopy, is evidenced in this study and has to be considered for future characterisations of these compounds. Moreover, the existence of folded and unfolded conformers for **1a** and the way they are affected by protonation provides a better insight in the parameters affecting the intramolecular luminescence quenching in the TAP bifunctional complexes. The unusually important increase of the luminescence of **1a** in the presence of DNA (a factor of 16), recently observed,[22] suggests that the protonation and/or unfolding on DNA are key factors responsible for this enhancement.

Experimental

Synthesis of the ligands

5-Amino-1,10-phenanthroline **VIII** and 5-iodoacetamidophenanthroline **VI** were prepared as described previously.[14] The NMR spectra were recorded with a Bruker AC200, with the solvent as internal reference. All the starting compounds and solvents (Aldrich) were used as received. Pyridine was kept with potassium hydroxide.

7-Chloro-4-[*N*(2-hydroxyethyl)-*N*-methylamino]quinoline I. 4,7-Dichloroquinoline (2 g, 10 mmol) was added to *N*-methyl-2-aminoethanol (5 ml) and the mixture stirred at 80 °C for 2 days. The solution was diluted with water and extracted twice with dichloromethane. The organic phases were collected, dried on magnesium sulfate and evaporated to dryness. The resulting oil crystallised on standing to give compound **I** (1.28 g, 5.4 mmol) in 54% yield. mp[32] 93–95 °C. NMR (DMSO-d_6): δ 8.57 (d, 1H, $J = 5.1$, H-2), 8.29 (d, 1H, $J = 9.1$, H-5), 7.90 (d, 1H, $J = 2.2$, H-8), 7.46 (dd, 1H, $J = 9.1$ and 2.2 H-6), 6.91 (d, 1H, $J = 5.1$, H-3), 4.87 (m, 1H, OH), 3.73 (m, 2H, CH_2O), 3.34 (t, 2H, $J = 5.7$ Hz, NCH_2) and 2.96 (s, 3H, CH_3). MS (FAB+, 3-nitrobenzyl alcohol): *m*/*z* 239 (M + 1, ^{37}Cl) and 237 (M + 1, ^{35}Cl).

Reaction of compound I in 37% HBr: formation of 7-chloro-4-[2-(*N*-methylamino)ethoxy]quinoline dihydrobromide **V**. Compound **I** (0.3 g, 1.26 mmol) dissolved in 37% hydrobromic acid (20 mL) was stirred at 120 °C for 7 h. The solution was cooled to room temperature and then poured dropwise into a large volume of acetone under vigorous stirring. The white precipitate was filtered off, washed with acetone and diethyl ether. Compound **V** (0.41 g, 1.02 mmol) was obtained with 81% yield. mp 196–198 °C. NMR (DMSO-d_6): δ 9.25 (d, 1H, $J = 6.4$, H-2), 8.92 (broad s, NH), 8.72 (d, 1H, $J = 9.1$, H-5), 8.21 (s, 1H, H-8), 7.95 (d, 1H, $J = 9.1$, H-6), 7.61 (d, 1H, $J = 6.4$ Hz, H-3), 4.79 (m, 2H, OCH_2), 3.57 (m, 2H, NCH_2) and 2.67 (m, 3H, CH_3): MS (EI): *m*/*z* 238 (M^+, ^{37}Cl), 236 (M^+, ^{35}Cl) and 193 ($M^+ - (CH_2NHCH_3)$).

7-Chloro-4-[*N*-(2-methylsulfonyloxyethyl)-*N*-methylamino]-quinoline II. Methanesulfonyl chloride (2 mmol) was added to a solution of compound **I** (0.475 g, 2 mmol) dissolved in pyridine (2 mL) and the mixture stirred overnight at room temperature. Pyridine was then removed under reduced pressure. Diluted aqueous sodium hydroxide was added to the residue and compound **II** extracted with dichloromethane. It was obtained as an oil and rapidly used without purification. NMR ($CDCl_3$): δ 8.67 (d, 1H, $J = 5.1$, H-2), 8.00 (d, 1H, $J = 2.1$, H-8), 7.98 (d, 1H, $J = 9.1$, H-5), 7.42 (dd, 1H, $J = 9.1$ and 2.1, H-6), 6.86 (d, 1H, $J = 5.1$, H-3), 4.43 (t, 2H, $J = 5.5$, CH_2O), 3.64 (t, 2H, $J = 5.5$ Hz, NCH_2), 3.04 (s, 3H, CH_3) and 2.90 (s, 3H, CH_3).[23]

7-Chloro-4-[*N*-2-acetylsulfanyl-*N*-methylamino]quinoline III. The oily residue of compound **II** was diluted with acetonitrile (10 mL) and potassium thioacetate (0.205 g, 1.8 mmol) added. The suspension was stirred overnight at room temperature in the dark. The solution was filtered to remove the salts, and the filtrate evaporated to dryness. The oil thus obtained was purified by flash chromatography on silica gel (elution ethyl acetate). Compound **III** was obtained as an oil (0.19 g, 0.6 mmol) with 32% yield starting from **I**. ^1H NMR ($CDCl_3$): δ 8.64 (d, 1H, $J = 5.4$, H-2), 8.00 (d, 1H, $J = 2.1$, H-8), 7.97 (d, 1H, $J = 9.0$, H-5), 7.41 (dd, 1H, $J = 9.0$ and 2.1, H-6), 6.82 (d, 1H, $J = 5.4$ Hz, H-3), 3.40 (m, 2H, CH_2), 3.16 (m, 2H, CH_2), 3.01 (s, 3H, NCH_3) and 2.30 (s, 3H, $COCH_3$). ^{13}C NMR (50 MHz, $CDCl_3$): δ 194.8 (CO), 156.2, 151.1, 149.9, 134.4, 128.3, 125.5, 125.4, 121.3, 108.4, 54.9, 40.4, 30.4 and 26.2. MS (desorption chemical ionisation, DCI, NH_3 + isobutane): *m*/*z* 297 (M + 1, ^{37}Cl) and 295 (M + 1, ^{35}Cl): IR (neat): 1685 cm^{-1} (CO).

5-[6-(7-Chloroquinolin-4-yl)-3-thia-6-azaheptanamido]-1,10-phenanthroline (POQ-Nmet) VII. A suspension of compound **III** (0.08 g, 0.27 mmol) and 5-iodoacetamidophenanthroline **VI** (0.098 g, 0.27 mmol) was stirred in methanol (20 mL). Addition of 1 mol dm^{-3} NaOH (0.6 mL, 0.6 mmol) to the solution made it transparent. After 30 min of stirring the solution was diluted with water and the methanol evaporated under reduced pressure. The aqueous solution was then extracted twice with dichloromethane. The organic phases were collected, dried on magnesium sulfate and evaporated to dryness. The gummy residue was triturated in ethyl acetate. The solid was filtered off, dissolved in the minimum of methanol and precipitated by

adding ethyl acetate. Compound **VII** was obtained in 50% yield (0.066 g, 0.13 mmol). mp 160 °C. ^{1}H NMR (600 MHz, DMSO-d_6): δ 10.25 (br s, 1H, NH), 9.03–9.13 (m, 2H, P2 and P9), 8.57–8.60 (m, 2H, Q-2 and P4 or P7), 8.42 (dd, 1H, J = 1.5 and 8.1, P7 or P4), 8.13 (s, 1H, P-6), 8.11 (1H, d, J = 9, Q-5), 7.88 (d, 1H, J = 2.1, Q-8), 7.72–7.80 (m, 2H, P3/P8), 7.43 (dd, 1H, J = 2.1 and 9.1, Q-6), 6.97 (d, 1H, J = 5.4 Hz, Q-3), 3.57 (m, 2H, CH_2), 3.55 (s, 2H, CH_2), 3.12 (m, 2H, CH_2) and 3.00 (s, 3H, CH_3). ^{13}C NMR (50 MHz, DMSO-d_6): δ 169.16 (CO), 155.94, 151.44, 149.28, 149.22, 145.65, 143.64, 135.65, 133.16, 131.15, 127.78, 127.70, 126.28, 124.88, 124.24, 123.40, 122.63, 120.94, 119.77, 108.66, 54.92, 40.33, 34.69 and 29.01. MS (FAB+, NBA): m/z 488, $(M + 1)^+$.

5-Acetamido-1,10-phenanthroline IX. A suspension of 5-aminophenanthroline **X** (0.103 g, 0.5 mmol) and acetic anhydride (0.5 mL, 5.2 mmol) in acetonitrile (20 mL) was stirred in the dark. After 2 days at room temperature the solution was cooled and kept overnight at 0 °C. The white precipitate was filtered off and washed with acetonitrile. Compound **IX** was thus obtained with a yield of 62%. mp 230 °C (decomp.). ^{1}H NMR (300 MHz, DMSO-d_6): δ 10.44 (s, 1H, NH), 9.10 (dd, 1H), 9.00 (dd, 1H), 8.67 (dd, 1H), 8.43 (dd, 1H), 8.16 (s, 1H, H-6), 7.81 (m, 1H), 7.73 (m, 1H) and 2.49 (s, 3H, CH_3). ^{13}C NMR (50 MHz, DMSO): δ 169.3 (CO), 149.6, 149.0, 145.6, 143.5, 135.6, 131.6, 131.5, 127.9, 124.4, 123.4, 122.6, 119.6 and 23.4. MS (DCI, NH_3, isobutane): m/z 238, $(M + 1)^+$.

Synthesis of the complexes

The synthesis of $[Ru(TAP)_2(Phen)]^{2+}$ **1c**[33] and $[Ru(BPY)_2(Phen)]^{2+}$ **2c**[34] used as references has been described. The complexes $[Ru(L)_2L']^{2+}$ (L = BPY or TAP, L′ = POQ-Nmet or acPhen) were prepared by refluxing the precursor[26] $Ru(L)_2Cl_2$ and the ligand L′ in MeOH–water (1 : 1) under argon, according to the methods described previously.[14,33,34] The complex $[Ru(TAP)_2(POQ\text{-}Nmet)]^{2+}$ was obtained after 6–9 hours of heating, whereas 6 days were necessary for the non-methylated equivalent $[Ru(TAP)_2(POQ)]^{2+}$.[14] The chelation of $Ru(TAP)_2Cl_2$ by acPhen requires 3–4 hours of heating, as compared to the 1.5–2 hours with the Phen ligand.

The purification of these complexes has been performed on a cation exchange column (Sephadex C25) with an aqueous NaCl gradient as eluent. The NaCl was removed by methanol extraction of the complex which was precipitated afterwards as a PF_6^- salt in water. In the case of $[Ru(TAP)_2(POQ\text{-}Nmet)]^{2+}$ **1a**, an aqueous solution of $(NH_4)_2CO_3$ was used as eluent. This salt plays the role of a buffer at a quasi neutral pH, which guarantees a better stability of the complex, and can be removed by lyophilisation. In order to avoid photodegradation and oxidation, the purification was performed under argon and in the absence of light. We have rejected a purification by HPLC (Waters 991 instrument) because degradation was observed on the columns.

Characterisation. The complexes and the Nmet quinoline have been characterised by ^{1}H NMR. The NMR spectra were recorded in DMSO-d_6 or in CD_3CN at 300 K with a 250 (Bruker), 360 (Bruker) or 600 MHz (Varian) spectrometer. The assignments of the different peaks were made from the corresponding ^{1}H–^{1}H COSY correlation spectra and from comparisons with reference complexes. The reference was TMS (δ_H 0). A list of chemical shifts in DMSO-d_6 and in CD_3CN is also available as supplementary information.

$[Ru(TAP)_2(POQ\text{-}Nmet)]^{2+}$ in CD_3CN, 600 MHz, ^{1}H–^{1}H COSY (360 MHz): δ_H 8.15/8.23 (4H, d, T3,3′,6,6′), 8.60 (4H, s, T9,9′,10,10′), 8.95/8.98 (4H, d, T2,2′,7,7′), 7.59/7.66 (2H, dd, P3,8), 8.04/8.10 (2H, d, P2,9), 8.36 (1H, d, P6), 8.49/8.53 (2H, d, P4,7), 6.82 (1H, d, Q3), 7.34 (1H, d, Q8), 7.36 (1H, dd, Q6), 8.10 (1H, d, Q5), 8.20 (1H, d, Q2) and 9.03 (1H, s, NH). $[Ru(BPY)_2(POQ\text{-}Nmet)]^{2+}$ in CD_3CN, 360 MHz, ^{1}H–^{1}H COSY: δ_H 7.25/7.44 (4H, dd, B5,5′,5″,5‴), 7.57/7.83 (4H, d, B6,6′,6″,6‴), 7.98/8.09 (4H, dd, B4,4′,4″,4‴), 8.48/8.52 (4H, d, B3,3′,3″,3‴), 7.69/7.69 (2H, dd, P3,8), 8.02/8.10 (2H, d, P2,9), 8.38 (1H, d, P6), 8.47/8.51 (4H, d, P4,7), 6.89 (1H, d, Q3), 7.35 (1H, dd, Q6), 7.56 (1H, d, Q8), 8.13 (1H, d, Q5), 8.26 (1H, d, Q2) and 9.05 (1H, s, NH). $[Ru(TAP)_2(acPhen)]^{2+}$ in CD_3CN, 360 MHz: δ_H 8.13/8.22 (4H, d, T3,3′,6,6′), 8.60 (4H, s, T9,9′,10,10′), 8.94 (4H, d, T2,2′,7,7′), 7.63/7.72 (2H, dd, P3,8), 8.00/8.13 (2H, d, P2,9), 8.62 (1H, d, P6), 8.61/8.82 (2H, d, P4,7) and 9.00 (1H, s, NH). $[Ru(BPY)_2(acPhen)]^{2+}$ in CD_3CN, 360 MHz: δ_H 7.23/7.44 (4H, dd, B5,5′,5″,5‴), 7.54/7.83 (4H, d, B6,6′,6″,6‴), 7.99/8.09 (4H, dd, B4,4′,4″,4‴), 8.48/8.52 (4H, d, B3,3′,3″,3‴), 7.68/7.75 (2H, dd, P3,8), 7.98/8.10 (2H, d, P2,9), 8.54/8.74 (4H, d, P4,7), 8.60 (1H, d, P6) and 8.89 (1H, s, NH). Nmet quinoline in CD_3CN, 360 MHz: δ_H 6.92 (1H, d, Q3), 7.44 (1H, dd, Q6), 7.96 (1H, d, Q8), 8.30 (1H, d, Q5) and 8.61 (1H, d, Q2).

Electrospray mass spectrometry and UV-vis spectroscopy

The electrospray mass spectra were obtained on a VG BIO-Q triple-quadrupole mass spectrometer with extraction cone voltages of 65 and 80 V in the laboratory of Professor A. van Dorsselaer, at the University L. Pasteur, Strasbourg, France. The spectra of the different complexes were recorded in MeCN–water (1 : 1). UV-visible absorption and emission spectroscopy, lifetime measurements and flash photolysis were described elsewhere.[15]

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