Unexpected reversible pyrazine based methylation in a Ru(II) complex bearing a pyrazin-2'-yl-1,2,4-triazolato ligand and its effect on acid/base and photophysical properties†‡

Claire Brennan,a Apparao Draksharapu,b Wesley R. Browne,b John J. McGarvey,c Johannes G. Vosa and Mary T. Pryce*ab

The regioselective methylation of a ruthenium polypyridyl complex bearing both a 1,2,4-triazolato and a pyrazine moiety is reported. In contrast to previous studies in which methylation of the 1,2,4-triazolato ring was observed, in the present system methylation takes place exclusively at the non-coordinated nitrogen of the pyrazine ring. The monomethylation is confirmed by 1H NMR spectroscopy and ESI-MS and the electronic properties of the methylated complexes are studied by UV/vis absorption, emission, surface enhanced, resonance and transient resonance Raman spectroscopy. Ligand deuteriation is used to simplify the 1H NMR spectra and to assign definitively the Raman spectra. Acid-base studies show that the triazolato ring of the N-methylated complexes can be protonated at low pH and that at high pH the N-methyl group can be deprotonated reversibly. Furthermore it is shown that under conditions where the methyl group is deprotonated, demethylation occurs to recover the initial complex.

Introduction

Transition metal complexes, many containing polypyridyl ligands, have seen extensive application in the development of molecular devices including solar cells, sensors, and photo-catalysts.1 An essential aspect in controlling the properties of such systems requires the development of synthetic methods that allow for manipulation of their structural and electronic properties. Direct reaction between ligands and metal ions is the conventional method to prepare metal complexes. However, the synthetic modification of ligands post complexation has seen increasing application. Examples of this approach in the synthesis of Ru(II)polypyridyl complexes are the use of coupling reactions to prepare well defined multinuclear assemblies such as those reported by the groups of Tor2, Hanan3 and Vos4 and the modification of coordinated ligands5 for example methylation of complexes as shown by Campagna, Balzani,6 Vos7 and co-workers. In the former case the use of methylation as a protecting group strategy was employed in the synthesis of complex multinuclear assemblies.8 Typically, however, complexes in which only a single site is available for modification by methylation are employed; due to the use of reactive and hence potentially non-selective reagents, such as (CH3)3OBF4.

Pyrazine based ligands have attracted much attention in the last number of years in coordination chemistry, both because of pyrazine’s potential to act as a bridging ligand in multinuclear complexes and its tuneable π-acceptor properties, through the non-coordinated nitrogen atom.9 As such the pyrazine moiety has been used extensively in multinuclear assemblies in particular to manipulate the excited state properties of the compounds and to investigate and promote the intercomponent interaction between different molecular components.10 One of the best known and much studied compounds is the Creutz–Taube ion,11 a species that initiated the investigation of the electronic communication between metal centres via a connecting bridge.12,13 These studies show that in multinuclear systems the pyrazine based π* level is stabilised upon bonding of a second metal centre. In our group, the relatively good π-acceptor ability of pyrazine has been combined with
the strong $\sigma$-donor/weak $\pi$-acceptor 1,2,4-triazole moiety. These ligands, containing both a good $\sigma$-donor and a good $\pi$-acceptor moiety, form Ru(II)polypyridyl complexes in which the photophysical, photochemical and electrochemical properties are strongly dependent on the protonation state of the triazole ring or, albeit less studied, of the pyrazine ring. For example, the complexes are photostable when the triazole ring is deprotonated and photochemically active when protonated. In the case of a pyrazine bridged binuclear complex bearing two 1,2,4-triazole units the reverse was observed with the deprotonated complex being photochemically active.

Here we report an unexpected selectivity for methylation of pyrazine nitrogens of $1a$ ([Ru(bipy)$_2$(phpztr)]PF$_6$ where phpztr$^-$ = 3-pyraz-2-yl-5-phenyl-1,2,4-triazolato) to form $2a$ ([Ru(bipy)$_2$(Mephpztr)]PF$_6$$_2$) over, in principle, more nucleophilic 1,2,4-triazole nitrogens in a heteroleptic Ru(II)polypyridyl complex (Fig. 2). The synthesis, characterisation and the effect of quaternisation of the pyrazine ring nitrogen on the spectroscopic and acid–base properties of ($2a$), together with selectively deuterated analogues ($2b$, $2c$) to facilitate characterisation, are reported. Furthermore we show that subsequent demethylation can proceed under mild conditions making the approach useful in building well defined multinuclear complexes.

**Results and discussion**

**Synthesis and characterisation**

$1a$ was prepared following a literature method previously reported and was isolated as the N2 bound isomer (Fig. 1).

The methylated complex [Ru(bipy)$_2$(Mephpztr)]$^{2+}$ $2a$ and the deuterated analogues [Ru([D$_3$]bipy)$_2$(Mephpztr)]$^{2+}$ $2b$ and [Ru([H$_3$]bipy)$_2$([D$_3$]Mephpztr)]$^{2+}$ $2c$ are dicationic as confirmed by ESI-MS. The $^1$H NMR spectra of the complexes $1b$ and $2a$–$2c$ are shown in Fig. 3. Spectra were assigned using $^1$H COSY NMR spectroscopy and facilitated by the availability of the isotopologues $2b$ and $2c$. Methylation of compound $1a$ led to relatively minor changes in the aromatic region of the spectrum. For $2a$ a full set of the expected aromatic signals and a single resonance at 4.25 ppm, assigned to the N$\text{-CH}_3$ group were observed.

For complex $1a$, there are three possible sites for methylation; the non-coordinated nitrogen atom of the pyrazine ring or the N$_1$ or N$_4$ nitrogen atoms of the 1,2,4-triazolato ring (Fig. 2). $^1$H NMR spectroscopy of related methylated complexes, such as [Ru(bipy)$_2$(pytr)]$^+$ and [Ru(bipy)$_2$(pztr)]$^+$ (where...
Hpytr is 3-(pyridin-2-yl)-1,2,4-triazole, and Hpztr is 3-(pyrazin-2-yl)-1,2,4-triazole, have shown the formation of both the N₁-Me and the N₄-Me isomers in the ratio of 70:30, where the 1,2,4-triazolato ring is methylated. Hence, it was expected that 1a would undergo methylation of the 1,2,4-triazolato ring also. It is apparent from elemental analysis and mass spectrometry that complexes 2a-c are methylated at a single position, which is confirmed by ¹H NMR spectral data.

The methyl group of the N₁-Me isomer [Ru(bipy)₂(1-Mepztr)]⁺ were reported to be at 3.17 ppm, whereas that of the N₄-Me analogue was at 4.26 ppm. For 2a-c the methyl hydrogens was observed at 4.25 ppm indicating that methylation occurs at the N₂-position of the 1,2,4-triazolato ring. However, the purple colour of the complexes (vide infra) suggests that this is not the case as N-methylated 1,2,4-triazole based complexes of this type are typically orange. Furthermore, the chemical shifts for the hydrogens of the pyrazine H₂ (9.13 (H₃), 7.97 (H₅) and 8.32 (H₆) ppm for 1a whereas they were at 9.29 (H₃), 7.60 (H₅) and 8.85 (H₆) ppm for 2a) suggest that this is not the case as N-methylated 1,2,4-triazole based complexes of this type are typically orange. Furthermore, the chemical shifts for the hydrogens of the pyrazine H₂ (9.13 (H₃), 7.97 (H₅) and 8.32 (H₆) ppm for 1a whereas they were at 9.29 (H₃), 7.60 (H₅) and 8.85 (H₆) ppm for 2a) suggest that this is not the case as N-methylated 1,2,4-triazole based complexes of this type are typically orange.

Quantum chemical calculations

Molecular orbital calculations were used to establish the atomic composition of the HOMO of both 1a and the non-phenyl complex, [Ru(bipy)₂(1-Mepztr)]⁺ (where pztr = 3-(pyrazin-2-yl)-1,2,4-triazolato). The calculations (see ESI† for further details) showed that the relative contribution of the pyrazine N atom was approximately three times greater in complex 1a compared to [Ru(bipy)₂(pztr)]⁺. As the HOMO of 1a has a greater contribution of the pyrazine N atom than that of the non-phenylated complex, it is likely that increased nucleophilicity plays a role in the selectivity observed.

Electronic absorption and emission spectroscopy

The UV/Vis absorption spectra of 1a and 2a are shown in Fig. 4 and 5. The absorption spectrum of 1a in its three protonation states, i.e. fully deprotonated (1a, λmax 450 nm), protonated at the 1,2,4-triazolato ring (H₁1a, λmax 430 nm) and protonated at both the 1,2,4-triazolato and pyrazine rings (H₂1a (Ru(bipy)₂[H₂phpztr])⁺, λmax 535 nm) are shown in Fig. 4.

The UV/Vis absorption spectrum of 1a comprises of a broad absorption in the visible region (λmax 450 nm) assigned as an ¹MLCT ← GS manifold. The intense absorption band at ~283 nm is assigned to a (bipy) ligand centred (π-π*) transition. Protonation of the 1,2,4-triazole moiety (H₁1a) results in minor changes to the shape of the ¹MLCT ← GS absorption band with the λmax shifting to 430 nm, due to the changes protonation induces in the σ-donor/π-acceptor properties of the triazole moiety. Under strongly acidic conditions protonation of the non-coordinated nitrogen of the pyrazine moiety occurs, to form H₁1a. Substantial changes are observed in the UV/Vis absorption spectrum with the appearance of an absorption band (λmax 530 nm) assigned earlier to a Ru(ni)-pyrazine H⁺ based ¹MLCT ← GS transitions and at 375 nm assigned to Ru(ni)-bipy based ¹MLCT ← GS transitions.

The spectrum of 2a in acetonitrile is shown in Fig. 5 together with the spectra of H₂2a and H₂1a in acetonitrile for comparison. In all three cases two strong absorption bands at ca. 540 nm and at ca. 375 nm are observed indicating that their electronic properties are similar; i.e. that the pyrazine is cationic, and hence that the pyrazine is N-methylated in the case of 2a/H₂2a. The small blue shift of both ¹MLCT ← GS absorption bands upon protonation of 2a indicates that it
involves the 1,2,4-triazole moiety in this case. The acid base chemistry of 2a is discussed further below.

Room temperature emission spectra and lifetime data for 1a and H1a in acetonitrile were reported earlier and were assigned to arise from MLCT excited states. As observed for the absorption spectra, the emission maximum (655 nm) of H1a is blue shifted compared to 1a (670 nm). By contrast both 2a and H2a were found to be non-emissive, possibly as a result of a decrease in the energy of the MC state due to the reduced σ-donor properties of the (N-methylated)pyrazine-1,2,3-triazole ligands compared with the non-methylated ligand. Lowering of the MC level removes the thermal barrier to deactivation of the emissive MLCT excited states. The lack of emission from 2a further supports the structural assignment made by 1H NMR spectroscopy, as complexes reported earlier in which the 1,2,4-triazolato ring is methylated are emissive.

**Acid base properties**

The acid–base properties of compounds 1a and 2a were investigated in Britton–Robinson buffer, in acetonitrile and in H2SO4 (aq.). A single protonation step, i.e. protonation of the 1,2,4-triazolato moiety, was observed between pH 1 and pH 7 for 1a (pKₐ = 3.1). By contrast the UV/Vis absorption spectrum of 2a is constant over this pH range and protonation of the triazolato takes place only under highly acidic conditions (i.e. <pH 1). Protonation can be achieved in dry organic solvents with strong acids or in conc. H2SO4 (aq.). The increased acidity of a 1,2,4-triazolato moiety in 2a is expected considering the effect, observed previously, of substituents on the triazole ring at the 5 position; for example replacing the phenyl ring in 1a with a bromine results in a decrease in pKₐ to 1.4. By contrast between pH 7 and 12, where 1a does not show acid base chemistry, for 2a dramatic changes in the UV/Vis absorption spectrum are observed. Between pH 9 and 11, with a pKₐ at 9.9, four isosbestic points are maintained (Fig. 6), which is consistent with deprotonation.

As the protonation of the 1,2,4-triazolato ring occurs only under highly acidic conditions the deprotonation at pH 9.9 was tentatively assigned to deprotonation of the N-methyl group of the pyrazine ring. Furthermore after short periods (min) at pH 10.5, the original spectra (i.e. at pH 1) can be recovered fully by addition of acid (Fig. 7).

At high pH deprotonation of the methyl group is followed by irreversible, albeit relatively slow, demethylation to form, 1a. This can be seen in Fig. 8. When held at pH 11.5 for 2 h a decrease in absorbance at 350 nm is observed and upon acidification to pH 2, the spectrum resembles closely that of H1a, with only 20% of the original absorption intensity at ca. 550 nm. 1H NMR spectroscopy of 2b was used to confirm demethylation at high pH. The deuteration of the bipy ligands in 2b simplifies the aromatic region of the spectrum.

Comparison of the 1H NMR spectrum of 2b at pH 9.5 and pH 12 with that of 1b at pH 12, in particular the chemical shift...
of the H3 hydrogen of the pyrazine ring confirms that demethylation results in reversion of 2b to 1b.

Redox properties

The redox processes observed for 2a are assigned by comparison with those of the precursor 1a. The Ru(u)/(iii) redox couple for 1a is observed at 0.93 V, and at 1.09 (vs. SCE) for its protonated (at the 1,2,4-triazolato ring) form H1a. For 2a the Ru(u)/ (iii) based oxidation was observed at 1.12 V and, upon protonation to H2a, at 1.25 V (vs. SCE). The increase in oxidation potential is attributed to the decrease in σ-donor and increase in π-acceptor strength of the methylated pyrazine ring compared to a pyrazine ring. As for 1a, 2a exhibits several reduction waves at negative potentials. The quasi-reversible redox waves at ~1.46 V and ~1.72 V for 2a are equivalent to the bipy based reductions observed for 1a, however an additional reduction wave at ~0.47 V is observed for 2a, but is not present in the cyclic voltammetry of 1a. This reduction process is assigned to reduction of the methylated pyrazine ring. The HOMO–LUMO gap calculated for 2a based on the 1st oxidation and reduction waves is 1.59 eV (780 nm), which is consistent with the lowest energy visible absorption band of 2a.

Surface enhanced and resonance Raman spectroscopy

Although the strong absorption of the complexes in the visible region precluded recording of non-resonant Raman spectra, the surface enhanced Raman spectra (SERS) of 2a–c could be obtained on colloidal gold at 785 nm and allowed for assignment of the bands of the bipy ligands and the pyrazine ring of the methylated phpztr⁻ ligand (Fig. 10). Raman bands in the SERS spectrum of 2a at 1625, 1531, 1214, 1051, 746 and 635 cm⁻¹ are assigned to the pyrazine moiety and at 1602, 1556, 1488, 1315, 1275, 1172, 1107, 1038, 1028, 767, 752 and 660 cm⁻¹ are assigned to the bipy ligands by comparison with the spectra of 2b and 2c. The bands assigned to the bipy ligands are as expected compared to related complexes, however in the case of pyrazine based bands direct comparison with the literature is more difficult due to the sensitivity of the pyrazine modes to protonation/substituents on the non-coordinated pyrazine nitrogen.

Resonance Raman (rR) spectroscopy has proven to be an invaluable tool in the assignment of electronic transitions in ruthenium(u) poly(pyridyl) complexes and is particularly suited to complexes in this study where spectra were obtained in CH₃CN at λexc. 355, 400.8, 449, 473, 532 and 561 nm (Fig. 11). Excitation into an allowed Ru → π* transition in mixed ligand complexes gives rise to enhancement of the symmetrical stretching modes of the ligand involved in the transition. In this section the resonance Raman spectroscopy of 2a–c in all three protonation states is compared with that of 1a, H1a and H₂3a.

The excitation wavelength dependence of the ground and excited state RR spectra of 1a–c were reported previously in all three protonation states (vide supra). RR spectra of 1a at 457.9 nm showed bands attributable to bipy based vibrations at 1610, 1565, 1494, 1429, 1320, 1277 and 1175 cm⁻¹. Only weak bands assigned to modes of the pyrazine ring were observed; at 1334 and 1193 cm⁻¹. The RR spectrum of H1a at 457.9 nm showed only bipy based bands. By contrast, the RR spectra of 1a and H1a at 514.5 nm showed relatively weak bands assigned to the bipy ligands and strong pyrazine based bands at 1600, 1529 and 1337 cm⁻¹ and 1609, 1517 and 1387 cm⁻¹, respectively. For H₂3a, in which the non-coordinated nitrogen
of the pyrazine ring is protonated, the rR spectrum at 514.5 nm is dominated by pyrazine based bands at 1633, 1518 and 1474 cm\(^{-1}\), which are most similar to those observed for the pyrazine modes in the SERS spectrum of 2a–c (vide supra).

The rR spectra of 2a in acetonitrile at various excitation wavelengths is shown in Fig. 11. Notably between 355 nm and 473 nm the Raman spectrum is comprised of bands assignable exclusively to bipy based modes. At 532 and 561 nm the spectrum is dominated by pyrazine based modes, which is confirmed by comparison with the spectra of 1b and 1c. The wavelength dependence of the rR spectrum allows for assignment of the longest wavelength absorption band (at ca. 550 nm) to pyrazine based \(^1\)MLCT ← GS transitions and the absorption band at ca. 430 nm to bipy based \(^1\)MLCT ← GS transitions (Fig. 15).

The absorption spectra for 2a–c show solvatochromic behaviour, with the lowest energy absorption undergoing a red shift, and the second lowest energy band undergoing a slight blue shift, on going from acetonitrile to water. These changes hold consequences for the wavelength dependence of the Raman spectra. In water the excitation wavelength 488 nm lies between the two main visible bands and is centred at the main absorption band of 2a–c at pH > 9 (Fig. 12, vide supra). The Raman spectrum in water has bands assignable to both the bipy ligands and the pyrazine moiety consistent with the overlap of the two visible absorption bands at 488 nm (Fig. 12). In conc. HCl (aq.), both absorption bands undergo a blue shift and hence the lowest energy absorption moves into resonance at 488 nm and the shorter wavelength band moves out of resonance (Fig. 13). Under these conditions the spectra are dominated by the bands arising for pyrazine vibrational modes with negligible contributions from bipy modes. At pH > 9 the Raman spectrum is considerably simplified and shows features of the bipy ligands exclusively (Fig. 14).

Although the wavenumbers of the bipy modes are relatively insensitive to either solvent or pH, the pyrazine modes show
considerable sensitivity. The most prominent band assignable
to the pyrazine ring in the rR spectra of 2a is at around
1625–1632 cm\(^{-1}\), which is comparable with that of H\(_2\)1a
(1633 cm\(^{-1}\)) in which the pyrazine ring is protonated (Fig. 12).
When the triazolato ring of 2a is protonated (i.e. H2a) this
band is blue shifted to 1640 cm\(^{-1}\) (Fig. 13).

**Transient resonance Raman spectroscopy**

Although neither of the complexes 2a–c or their protonated
forms H2a–c are emissive in acetonitrile solution, deprotona-
tion of the complexes at the methyl group results in substi-
tutional changes to the electronic structure of the complexes, not
least by raising the LUMO energy of the pyrazine ring above
that of the bipy ligands, specifically the absorption band at
550 nm undergoes a substantial blue shift to ca. 470 nm
(Fig. 15). If a bipy based \(^{3}\)MLCT state is populated to a signifi-
cant extent then the characteristic features of the bipy anion radical
should be observed using transient resonance Raman
(TR\(^2\)) spectroscopy at \(\lambda_{\text{exc}}\) 355 nm.\(^{36}\) The TR\(^2\) spectra for
complexes 2a–c are shown in Fig. 16. It is clear that the characteristic
[H\(_8\)]-bipy anion radical bands at 1285 and 1212 cm\(^{-1}\) are
observed for 2a and 2c, while for 2b the bands of the [D\(_8\)]-bipy
anion radical are observed at 1332 and 1187 cm\(^{-1}\).\(^{35}\) Addition
of acid to the deprotonated complexes afterwards results in a
complete loss in the bipy radical anion bands and results in a
spectrum similar to that obtained for 2a–c using continuous
wave excitation at 355 nm (vide supra) indicating that demethy-
lolation was not significant on the timescale over which the TR\(^2\)
spectroscopic data was acquired.

**Conclusions**

In the present study the unexpected methylation of the pyra-
zine ring of 1a–c to yield 2a–c is reported. Confirmation of
selective pyrazine methylation of 1a was obtained on the basis
of \(^1\)H NMR, UV/Vis absorption, emission and (resonance)
Raman spectroscopy. This result is in contrast to the related
complex [Ru(bipy)\(_2\)(pztr)]\(^{+}\) in which the phenyl group of 1a is
replaced by a hydrogen. In the case of [Ru(bipy)\(_2\)(pztr)]\(^{+}\) the
1,2,4-triazolato moiety undergoes methylation with a N1/N4
ratio of 70/30 (Fig. 2).\(^{7}\) The difference in behaviour could be
ascribed to the increased steric hindrance provided by the
phenyl ring in 1, which impedes the approach of the (CH\(_3\))\(_3\)O\(^+\)
sufficiently to render pyrazine N-methylation competitive.
However, the increased acidity of the contribution from the pyrazine nitrogen in 1a ($pK_a = 3.1$) compared to the analogous complex without the phenyl group ($pK_a = 3.5$) suggests that the change in selectivity is electronic in origin.

The acid–base chemistry of 2a–c shows that the methyl hydrogens are relatively acidic and undergo deprotonation at pH 9.9. In the deprotonated state the electronic properties of the complexes are similar to those of the non-methylated complexes 1a–c, where the lowest excited state is a bipy based $^3$MLCT state. Although the deprotonated complexes are relatively stable, over time basic conditions lead to loss of the methyl group to recover 1a–c. Hence in addition to methylation being a useful synthetic tool to reversibly modify the electronic properties of the 1a–c, it is also fully reversible and hence useful as a protection method in the synthesis of heterocyclic complexes.

**Experimental**

All solvents employed for synthesis were of HPLC grade and for spectroscopy, UVASOL. All reagents employed were of reagent grade or better and used as received. 2-(5′-phenyl-4′H-[1,2,4]triazol-3′-yl)-pyrazine (Hphpztr), cis-[Ru(bipy)$_2$Cl$_2$]·2H$_2$O, [Ru(bipy)$_2$(phpztr)]PF$_6$ (1a) and [Ru(bipy)$_2$-pyrazine (Hphpztr), cis-[Ru(bipy)$_2$Cl$_2$]·2H$_2$O and [Ru(bipy)$_2$(phpztr)]PF$_6$·2H$_2$O and its isotopologues (1a–c) were available from earlier studies and prepared by literature methods.

**Synthesis**

[Ru(bipy)$_2$(phpztr)]PF$_6$ (2a). An excess of Me$_3$OBF$_4$ was added to 38.7 mg (0.05 mmol) of [Ru(bipy)$_2$(phpztr)]PF$_6$ (1a) and 28 mg (0.21 mmol) of Na$_2$CO$_3$ in 10 cm$^3$ of dry acetonitrile typically 10 s acquisition time. Data were recorded and processed using Solis (Andor Technology) with spectral calibration performed using the Raman spectrum of acetonitrile–toluene 50 : 50 (v : v). Samples were 0.1 mM and held in quartz 10 mm path length cuvettes. Transient Raman scattering was observed in all cases with excitation from the Nd:Yag laser (266 and 355 nm) and Raman scattering collected and collimated in a 180° back-scattering arrangement and focused by a second 5 cm diameter plano-convex lens ($f = 6$ cm) and Raman scattered light detected using a 500 line mm$^{-1}$ grating covering 500 nm, and an Andor Technology. The spectral slit width was set to 10 or 20 μm. Each spectrum was accumulated, typically 10–20 times with 1–5 s acquisition time. Data were recorded and processed using Solis (Andor Technology) with spectral calibration performed using the Raman spectrum of acetonitrile–toluene 50 : 50 (v : v). Samples were 0.1 mM and held in quartz 10 mm path length cuvettes. Transient Raman spectra were recorded using the same system but with excitation from the output of a frequency tripled Innolas Spitlight200 Nd:Yag laser operating at 10 Hz. The leading edge of the pulse excited the sample with the trailing edge probing the excited state formed. The UV/Vis absorption spectra were recorded before and after each Raman measurement to verify that no change had taken place during the measurement. Baseline correction was performed for all spectra.

Elemental analysis was carried out at the Micro-analytical Laboratory at University College Dublin. The pH dependence of the absorption spectra of 1a was monitored in Britton–Robinson buffer. pH adjustments were made by adding 1 M NaOH or 1 M H$_2$SO$_4$ to a 100 mM volume of the dissolved complex.
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Notes and references


