Bis-cyclometallated Ir(III) complexes containing 2-(1H-pyrazol-3-yl)pyridine ligands; influence of substituents and cyclometallating ligands on response to changes in pH†

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Bis-cyclometallated Ir(III) complexes containing 2-(1H-pyrazol-3-yl)pyridine ligands have been synthesised. Their absorption is almost unchanged with changes in pH however the emission intensities vary by a factor of up to three and the complexes have emission $pK_a$s in the range 8.0 to 10.0. Substituents on the pyrazole have only a minor effect on the emission $pK_a$. Surprisingly the complexes with phenylpyrazole cyclometallated ligands $3aL_1$–$3b$ showed an intensity decrease with increasing pH (switch off) whilst the corresponding phenylpyridine ones $3cL_1$–$3d$ showed an increase in emission intensity with increasing pH. Putting electron-withdrawing CF$_3$ substituents on the cyclometallating phenyls reduced the $pK_a$ of the complexes to 6.8–7.8, thereby extending the useful $pK_a$ range; however, in general it tended to reduce the magnitude of the change in emission intensity. Surprisingly the CF$_3$-substituted complexes also showed a complete reversal in the direction of the intensity change when compared to their respective unsubstituted congeners.

Introduction

Luminescent pH sensors have attracted significant interest for measuring pH in biological environments due to their excellent sensitivity, minimal damage to living samples, specificity, the availability of a wide range of indicator dyes, high signal-to-noise ratios and the ability to continuously monitor rapid pH changes. Furthermore, fluorescence microscopic imaging allows mapping of the spatial and temporal distribution of H$^+$ within living cells.¹ To date, pH sensors have primarily focussed on organic molecules; however, transition metal and rare earth metal complexes have also been studied.² Transition metal complexes are attractive as possible pH sensors due to significant Stokes shifts for easy separation of excitation and emission, tuneable emission wavelength, and relatively long emission lifetimes compared to organic molecules allowing for possible luminescent lifetime imaging of pH.³ Several luminescent complexes of the platinum group metal ions have been used as pH sensors, notably Ru(II),⁴ Re(I),⁵ and Pt(II).¹,⁶,⁷

Ir(III) complexes have also been used for pH sensing. An early example by Licini and Williams used Ir bis-terpyridine complexes, (Fig. 1) containing either pyridyl or phenol substituents as the pH responsive groups which exhibit changes in lifetime and intensity with changing pH.⁷ The $pK_a$s of the complexes ranged from 4.1 (cf., pyridinium $pK_a = 5.25$) to 8.1 (cf., phenol $pK_a = 10.0$), in both cases the cationic electron-withdrawing metal terpyridine unit reduces the basicity of the pendant group, pyridine or phenol, respectively.

The coordination of a functionalised ligand to a metal tends to lead to a reduction in electron density due to electron donation to the metal and hence should lead to a lowering of the $pK_a$ for the ligand in the ground state. However, it should

Fig. 1 Early examples of pH sensitive luminescent Ir(III) complexes.⁷

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† Electronic supplementary information (ESI) available: Crystallographic data (CIF), extra molecular structures, absorption and emission spectra and pH titrations, NMR spectra. CCDC 2014697–2014704. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/d0dt02434a
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be noted that it is harder to predict the outcome for an excited state.

In the last 20 years there has been huge interest in the use of cyclometallated Ir(III) complexes of general formula [Ir(C^N)₂(X^Y)]ⁿ⁺ (C^N = a cyclometallated ligand, X^Y = a neutral or anionic bidentate ligand n = 0, 1; Fig. 2 structure A) which have interesting photophysical properties and have found applications particularly in OLEDs, sensors and as labels for biological imaging. A comparatively small number show pH responsive emission, changing wavelength and/or intensity of emission. A number of different pH responsive ligands have been used, and some of these are shown in Fig. 2. The pH responsive group can be on the cyclometallating (C^N) ligands or on the ancillary (X^Y) ligand. For example, tris-cyclometallated complexes with protonatable pyridyl9 or amine10 substituents (B or C Fig. 2) have been reported. Bis-cyclometallated complexes with ligands D were non-emissive at low pH 2–5 but gave red emission at higher pH which was ascribed to deprotonation of the carboxylic acid groups. The pKₐ value was approximately 7.0, suggesting that the probe may be useful for monitoring pH in biological systems.

Several proton responsive N^N ligands have been used as the ancillary X^Y ligand in bis-cyclometallated complexes (Fig. 2 E–H). For example, functionalised bipyridine ligands, with morpholine E12 or carboxylic acid substituents F.13 Several groups have investigated complexes with imidazole or benzimidazole containing ligands e.g. G.14 Similar carboline-containing ligands H gave pH-sensitive iridium(III) complexes used in lysosome targeted photodynamic therapy (PDT).15 The complexes were more emissive at low pH with pKₐ values between 3.6 and 4.4.

Although, imidazole-based ligands have been investigated, pyrazole ligands with an NH moiety have been much less studied. Lam et al. studied a Re-carbonyl complex containing a bidentate pyrazolyl-pyridine.5b Cyclometallated Pt complexes with tridentate pyrazolyl-containing ligands have also been studied which show pH dependent emission some of which have been in used in cell imaging.6b,16 Hence, we have investigated Ir(III) bis-cyclometallated complexes with 2-(1H-pyrazol-3-yl)pyridine ligands. 2-(1H-pyrazol-3-yl)pyridine itself has a pKₐ of 11.6.17 We have investigated the effect of the nature of the cyclometallated ligands, phenylpyrazole and phenylpyridine respectively and ones with an electron-withdrawing CF₃ substituent, and of substituents on the pyrazole.

### Results and discussion

#### Synthesis

The bis-cyclometallated dimers 1a–d (Chart 1) were prepared by a literature method18 and the data are consistent with those published.18,19 The syntheses of cationic complexes 2aHL₁₋₃ are outlined in Scheme 1. The dimer 1a was reacted with the relevant 2-(1H-pyrazol-3-yl)pyridine (HL₁₋₃) in the presence of KPF₆ in methanol at 60 °C under microwave irradiation for 20–40 minutes (see Experimental section). After work up, complexes 2aHL₁₋₃ were formed in good to excellent yields. ¹H and ¹³C NMR spectra for all the complexes were assigned using two-dimensional NMR experiments such as TOCSY, COSY, NOESY, and HMQC. The coordination of the N^N ligand removes the C₂-symmetry of the dimers, causing the two C^N ligands to become inequivalent and therefore doubling the number of peaks for the cyclometallated ligands. The pKₐ value was approximately 7.0, suggesting that the probe may be useful for monitoring pH in biological systems.

#### Chart 1

Iridium dimers used.

Fig. 2 Examples of pH responsive cyclometallating ligands (B to D) or ancillary ligands ligands (E to H) used in bis- or tris-cyclometallated Ir complexes.
lets at δ 6.30 and 6.32, characteristic of cyclometallated phenyl protons which are shifted to high field due to ring current effects. This then allows assignment of the signals for the phenyl and pyrazole rings of the C^N ligands using the TOCSY and NOESY spectra (Fig. S1 and 2). Likewise, the protons of the pyrazole of the N^N ligand are easily identified in the TOCSY spectrum as doublets at δ 7.83 and δ 7.20 slightly shifted downfield compared to the free ligand (by ca. 0.4 and 0.2, respectively) presumably due to the coordination of the (N^N) ligand to the metal. The doublet at δ 7.20 shows an NOE to a triplet at ca. δ 8.20 which is therefore assigned as the closest pyridine proton (H_e see ESI† for NMR labelling) and the other pyridine protons H_{a,b} assigned from the TOCSY and COSY spectra. The protons H_{c-g} are shifted slightly downfield compared to the free ligand (ca. δ 0.2 to 0.4) as might be expected on coordination to the metal, however, the proton next to the N atom (H_h) is observed at δ 8.01 about δ 0.7 upfield compared to the free ligand (δ 8.68) due to ring currents from the neighbouring phenyl ring (A), as noted previously, e.g. for [Ir(R-ppz)_2(bipy)]PF_6. Proton H_h also shows an NOE to a pyrazole proton multiplet at ca. δ 7.07 which is therefore assigned as H_{c-g}. This distinguishes the two cyclometallating ligands and hence allows for assignment of all the other protons. The NH proton was not observed, probably due to exchange with D_2O in the solvent (CD_3CN). The 13C NMR spectrum showed the expected number of signals, and were assigned using the HSQC and HMBC spectra. The high resolution mass spectrum (ASAP) shows a molecular ion with characteristic Ir isotopes pattern for the cation at m/z 624.1497 (624.1488 calculated for C_{28}H_{21}^{193}IrN_7).

The 1H NMR spectra of 2aHL_1 and 2aHL_3 are similar to that of 2aHL_4 except for the substituent on the N^N pyrazole, a singlet due to a Bu at δ 1.26 for 2aHL_2 and extra signals in the aromatic region for 2aHL_3. For 2aHL_4, a downfield singlet at δ 12.01 was assigned to the NH proton. The 13C NMR spectra showed the expected number of signals and both complexes showed an ion corresponding to the cationic complex in their high resolution (ASAP) mass spectra.

The neutral complexes 3aL_1-3 corresponding to loss of a proton from 2aHL_1-3 were synthesised in good yields by reaction of dimer 1a with ligands HL_1-3 and NaOMe in a mixture of DCM/methanol (2:1) (Scheme 2). Additionally, a CF_3 substituted dimer 1b was also used to investigate the effect of an electron withdrawing substituent on the cyclometallating ligand, providing complexes 3bL_1-3.

The 1H and 13C NMR spectra of 3aL_1-3, are similar to those for 2aHL_1-3, respectively, and assignments have been made on this basis. As expected, in the majority of cases the deprotonation of the ancillary ligand causes an upfield shift of the protons of the N^N ligand in the 1H NMR spectra compared to their corresponding cationic complexes. For example, for 3aL_4 the pyrazole protons H_{a,b} are observed as mutually coupled doublets at δ 7.47 and 6.82, respectively, upfield compared to the corresponding signals in the cationic complex 2aHL_4 (δ 7.83 and 7.20 respectively) consistent with deprotonation of the pyrazole. Unusually, for 3aL_4 the most upfield resonance in the aromatic region is a pyrazole proton not a cyclometallated phenyl. The spectra of the CF_3-substituted complexes 3bL_1-3 are similar to those of the unsubstituted complex but with two fewer resonances in the aromatic region. The 19F NMR spectra of 3bL_1-3 exhibit two singlets at about –60 ppm corresponding to two different CF_3 groups. All of the neutral complexes show ions due to [M + H]^+ in their high-resolution mass spectra.

The corresponding complexes containing cyclometallated phenylpyridine ligands in place of phenylpyrazole were prepared by analogous procedures to give cationic complexes 2cHL_1-3 and neutral complexes 3cL_1-3 and CF_3-substituted complex 3dL_3 respectively (see Chart 2). These were fully characterised by 1H and 13C NMR spectroscopy and high-resolution mass spectra.

The 1H NMR spectra of 2cHL_1-3 show the cyclometallated phenyl protons as the most upfield aromatic signals, between δ 6.23, and 6.35. The pyridine proton next to nitrogen for both the cyclometallating ligands and the N^N ligand are all influenced by ring currents from the other ligands and hence are shifted upfield compared to the free ligands, being observed between δ 7.9 and 7.5. The 1H NMR spectra for neutral complexes 3cL_1-3 show the cyclometallated phenyl protons between δ 6.23 and 6.39 within 0.1 ppm of the related cationic

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**Scheme 1** Preparation of cationic bis-cyclometallated phenylpyrazole complexes.

**Scheme 2** Preparation of neutral bis-cyclometallated complexes of phenyl pyrazole.
completes. As for 3aL1,3 deprotonation of the pyrazole NH proton 3cL1,3 leads to an approximately 0.5 ppm upfield shift for pyrazole proton H₂. All the other protons are within 0.2–0.3 ppm of the signals in the corresponding cationic complexes 2cHL1,3. The 13C NMR spectra show the expected number of signals for 2cHL1,3. The 1H and 13C NMR spectra of 3dL2 are similar to 3cL2, except the signals for one proton on each the phenyl rings of the C=N ligands have been replaced by a CF₃ group, as confirmed by 19F NMR spectroscopy. The high-resolution mass spectra (ASAP) each show a molecular ion for the cations 2cHL1,3 and the protonated molecular ions for 3cL1,3 and 3dL2.

X-ray crystallography

The cationic complexes were relatively easy to crystallise as their PF₆ salts, hence complexes 2aHL1,3 and 2cHL1,3 were characterised by X-ray crystallography. In addition, two of the neutral molecules 3aL3 and 3cL3 were also characterised by X-ray crystallography. As examples the structures of two cationic/neutral pairs 2aHL2 and 3aL2, and 2cHL1 and 3cL1 are shown in Fig. 3 and 4 respectively, the remaining structures are in Fig. S3 and S4† with selected bond lengths and angles in Tables S1 and S2.†

All the crystal structures show the expected distorted octahedral coordination geometry with cis metallated carbons and trans nitrogen atoms. The chelate bite angles for the cyclometallated ligands are all about 80°, and about 75° for the N^N

Photophysical properties

The UV-vis absorption spectra of all 16 complexes are shown in Fig. S5–S8† and the data are collated in Table S3.† Cationic complexes 2aHL1,3, and their neutral counterparts 3aL1,3 are shown in Fig. S5† whilst the CF₃-substituted complexes 3bL1,3 are compared with their unsubstituted analogues, 3aL1,3 in Fig. S6.† Similarly, spectra for phenylpyridine complexes 2cHL1,3, and 3cL1,3 are in Fig. S7 and 3dL2, is compared with 3dL2 in Fig. S8.† All the complexes show strong bands between 225 and 300 nm due to π → π* transitions in addition the phenylpyridine complexes 2cHL1,3, 3cL1,3 and 3dL2 show weak bands between 380–405 nm (possibly having contributions from 1MLCT transitions). Adding a CF₃ substituent to the C=N ligand causes only minor changes, and these are in the short wavelength region. The substituent on the N^N ligand also has very little effect on the λₘᵞ. For both the phenylpyrazole and phenylpyridine complexes there are only minor differences in UV-vis spectra between the cationic and neutral species and these are in the UV region, a slight red shift (10 to 30 nm) in λₘᵞ occurring on deprotonation. Since there is no significant change (~20%) in absorbance at any wavelength, these complexes would not be expected to be good pH sensors in their ground states.

Emission spectra of the complexes were run in MeCN in aerated solutions. Each pair of cationic and neutral complexes

Fig. 3 Left, structure of the cation of 2aHL2 and right the structure of 3aL2 showing 50% ellipsoids. All hydrogen atoms (except NH) have been omitted for clarity.
(e.g., 2aHL1 and 3aL1) were irradiated at the same excitation wavelength (see Fig. 5a and Table S4 for excitation spectra). The emission spectra of phenylpyrazole cationic complexes 2aHL1-3 and their neutral analogues 3aL1-3 are shown in Fig. 5a whilst those of 3aL1-3 are compared with their CF3-substituted analogues 3bL1-3 in Fig. 5b and all the associated data are reported in Table S4.†

All three cationic complexes 2aHL1-3 show a broad emission band, each with a similar λmax at 502, 495, and 508 nm, respectively. Hence, the substituent on the pyrazole has only a small effect on the emission wavelength. The corresponding neutral complexes 3aL1-3 show similar spectra with a slight blue shift in λmax of 27 nm (1053 cm⁻¹) for 3aL1, 2 nm (82 cm⁻¹) for 3aL2, and 12 nm (476 cm⁻¹) for 3aL3. The emission intensity for the neutral complexes 3aL1-3 is all reduced by about 50% compared with the cationic complexes 2aHL1-3. Hence, these complexes have potential as luminescent pH sensors. Neutral complexes 3bL1-3 with an electron-withdrawing substituent (CF3) on the phenyl ring each show a broad emission band which is blue-shifted compared to the corresponding unsubstituted complexes 3aL1-3, with 3bL2 showing the largest shift of 35 nm (1550 cm⁻¹) (Fig. 5b and Table S4†), respectively. A blue shift in emission by addition of electron-withdrawing groups to the C=N cyclometallating ligands is a well-known phenomenon that has been ascribed to the electron-withdrawing group stabilising the HOMO.18,22

The emission spectra of the corresponding phenylpyridine complexes 2cHL1-3 and 3cL1-3 are shown in Fig. 6 and their data are reported in Table S4.† Complex 2cHL1 shows a broad emission band (λmax 505 nm); however, complexes 2cHL2-3 both show some structure in the emission band. As for the phenylpyrazole complexes, changing the Rff group on the N^N ligand has only a small effect on the emission wavelength. The neutral complexes 3cL1-3 show similar spectra to the cationic complexes, with a broad emission band with shoulders. Surprisingly there is no significant change in emission intensity between the cationic and neutral complexes, though the neutral complexes are slightly more emissive than the cationic ones which is the opposite case to the phenylpyrazole complexes. Hence, these are not expected to be good pH sensors in their excited states (see pH titrations below for further discussion). The neutral CF3-substituted complex 3cL2 showed a λmax at 502 nm, a small blue shift (ca. 4 nm) compared to the corresponding unsubstituted complex 3cL1, and also shows a distinct shoulder at longer wavelength ca. 533 nm (Fig. S10†).

In conclusion, the UV-vis absorption spectra of all the complexes show strong bands between 200 and 300 nm due to π → π* transitions, with the phenylpyridine complexes also showing weak bands between 380–405 nm. All the complexes are emissive at room temperature in solution in air. There is no significant variation in emission wavelength upon changing the substituent on the ancillary N^N ligands, and there is very

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**Fig. 5** Emission spectra of (a) cationic and neutral complexes 2aHL1-3 (—) and 3aL1-3 (— —), (b) normalised emission spectra of neutral complexes 3aL1-3 (— —) and 3bL1-3 (— —), all in MeCN at 0.02 mM at room temperature in air; excitation at 320–325 nm.

**Fig. 6** Emission spectra of cationic and neutral complexes 2cHL1-3 (—) and 3cL1-3 (— —), in MeCN at 0.02 mM at room temperature in air; excitation at 320–325 nm.

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little change in $\lambda_{\text{max}}$ on deprotonation, except for complex 3aL$_1$ which shows a blue shift of approximately 27 nm. Substituting H with an electron-withdrawing CF$_3$ group on the C$^\text{N}$ ligand causes a blue shift in the emission spectrum, consistent with other bis-cyclometallated Ir complexes.$^{18,22}$ The effect of changing the cyclometallated ligand from phenylpyrazole to phenylpyridine is not uniform, giving a red shift in some cases and a blue shift in others. This is further complicated by the presence of shoulders on some bands.

**pH titrations**

To investigate their potential application as pH sensors, pH titrations of the complexes were carried out in MeCN/H$_2$O (1:9) (see Experimental for details). As expected from the studies of the isolated neutral and cationic complexes there is very little change in the uv-vis spectra with changing pH, hence absorption spectra cannot be used to determine ground state $pK_a$ values. The emission $pK_a$ values$^{23}$ for the complexes were determined by the change in emission intensity with pH over the range ca. 3 to 12.5.

As an example, the emission pH titration data and $pK_a$ values of complex 3aL$_1$ are illustrated in Fig. 7. The emission intensity of 3aL$_4$ at 500 nm was relatively unchanged between pH 7.5 and pH 7.9, but above pH 7.8, there was a gradual decrease in emission intensity by about a factor of two around pH 10, above which the intensity remained essentially constant until pH 12.3. Over the full pH range studied, there was a small blue shift (ca. 6 nm) in $\lambda_{\text{max}}$. The emission $pK_a$ value was determined to be about 9.9 at the equivalent point, which is more acidic than the free 2-(1H-pyrazol-3-yl)pyridine ligand itself ($pK_a$ 11.6).$^{17}$

The emission pH titration spectra of complexes 3aL$_2$-3 (Fig. S12 and S13) were similar to that of 3aL$_4$. In both complexes the emission intensity was relatively constant over the pH range ca. 4.9–7.5 but then decreased at higher pH by a factor of ca. 2 for 3aL$_2$ and ca. 1.3 for 3aL$_3$. The emission $pK_a$ values of complexes 3aL$_2$ and 3aL$_3$ were determined to be ca. 10.0 and 8.9, respectively (Fig. S10 and 11†), which are more acidic than the corresponding free ligands at 12.3 and 11.6, respectively.$^{17}$ Hence, all three complexes 3aL$_{1-3}$ can function as pH sensors. However, even though the $pK_a$ of the complexes is between 1.7 and 2.7 units lower than for the free ligands, none of them are low enough to be of use as biological pH sensors. To lower the $pK_a$ further the complexes need to be made more acidic. Hence, complexes 3bL$_{1-3}$ with electron-withdrawing CF$_3$ groups on the cyclometallating phenyls were examined.

The emission pH titration of complexes 3bL$_{1-3}$ (Fig. S14–16†) did show changes with pH, however, for all three complexes replacing H with the electron-withdrawing CF$_3$ group on the C$^\text{N}$ ligand led to a complete reversal of the shape of the pH titration curve. Thus, at low pH, the complexes show low emission and at high pH the emission intensity is higher, which is the exact opposite of complexes 3aL$_{1-3}$. From the emission intensity changes, a $pK_a$ value of 6.8 was determined for 3bL$_1$ which is much smaller than the $pK_a$ (9.9) for the unsubstituted complex 3aL$_1$. The emission pH titration spectra of 3bL$_2$ and 3bL$_3$ were similar to that of 3bL$_1$. Showing a relatively small (1.2–1.3 fold) increase in intensity with increasing pH. The $pK_a$ values of 3bL$_2$ and 3bL$_3$ were calculated to be 7.8 and 7.5, respectively, both lower than the $pK_a$ of the unsubstituted analogues 3aL$_2$ and 3aL$_3$ of 10.0 and 8.9, respectively. Hence, addition of the CF$_3$ substituents has, as desired, lowered the $pK_a$ of the complexes by between 1.4 and 3.1 units. As noted above, the emission intensity of the CF$_3$-substituted complexes 3bL$_1$ increases with increasing pH whilst the intensity of the unsubstituted analogues 3aL$_1$ decreases with increasing pH. The reason for this difference is not known. In addition, the complexes, particularly 3bL$_2$ and 3bL$_3$, showed only a small change in emission intensity per unit change in pH and hence will clearly not be particularly good sensors. The

Fig. 7 (a) Selected emission spectra of complex 3aL$_4$ (0.02 mM) at various pH values in MeCN/H$_2$O (1:9), in air with excitation at 324 nm. (b) Plot of normalised emission intensity of complex 3aL$_2$ against pH.
1.7 for ca. of stant. The overall increase in intensity at 492 nm is by a factor pH 10.9, above which the intensity remains essentially con-

wavelength (λmax 505 nm. Above pH 8.0, these bands start to shift to longer p

3cL1. Hence, as found for the phenylpyrazole complexes addition of a CF3 substituent to the C=N ligand has the effect of reversing the slope of the pH curve. From the intensity changes a pKa value of 7.8 was determined (Fig. S19†), which is surprisingly similar to that of the unsubstituted complex (pKa 8.0 for 3cL2).

Conclusions

In conclusion, for all the complexes studied changes in pH gave only very minor changes in the associated UV-vis spectra over the full pH range studied. Hence, determining the ground state pKa was not feasible. In contrast, the emission intensity of the complexes was significantly modulated (by a factor of 1.2 to 2.9) by altering the pH. Surprisingly the phenylpyrazole complexes 3aL1-3 showed an intensity decrease with increasing pH (switch off) whilst the phenylpyridine complexes 3cL1-3 showed an increase in emission intensity with increasing pH. Changing the R group on the N=N ligand had an effect of up to 1 pH unit on the subsequent pKa values. However, the trends were not the same for the different series of complexes. More surprisingly, putting CF3 groups on the cyclometallated phenyls, i.e., complexes 3bL1-3 and 3dL2, resulted in a complete reversal in the direction of the intensity change when compared to their respective unsubstituted congeners. The unsubstituted complexes had pKa values ranging from 8.0 to 10.0 and as anticipated, adding the electron-withdrawing group reduced the pKa of the complexes to 6.8–7.8, thereby extending to useful pKa range.

However, whilst adding CF3 substituents had the desired effect on the pKa, in general it tended to reduce the proportional change in emission intensity per unit change in pH. The reason(s) for this difference are not currently known. It is hoped that these studies will provide useful information for the design of other pH sensitive cyclometallated iridium complexes.
**General procedure for the synthesis of neutral complexes**

Samples could be recrystallised from DCM/hexane.

**Synthesis of 2aHL1.** Using the general procedure, 2aHL1 was prepared from 1a (50 mg, 0.049 mmol) and KPF6 (22 mg, 0.12 mmol). After work up, the compound was isolated as a grey yellow solid (58 mg, 78%). 1H NMR (500 MHz, CD2CN, 300 K): \( \delta \) 8.40 (1H, d, \( J = 2.9 \) Hz, \( H_{5b} \)), 8.36 (1H, d, \( J = 2.9 \) Hz, \( H_{5a} \)), 8.20 (1H, dt, \( J = 7.9, 0.9 \) Hz, \( H_c \)), 8.10 (1H, dd, \( J = 5.5, 1.7, 0.8 \) Hz, \( H_h \)), 7.83 (1H, d, \( J = 2.9 \) Hz, \( H_j \)), 7.50 (1H, dd, \( J = 4.7, 1.0 \) Hz, \( H_{5a} \)), 7.47 (1H, dd, \( J = 4.7, 1.0 \) Hz, \( H_{5a} \)), 7.37 (1H, dd, \( J = 7.7, 5.5, 1.3 \) Hz, \( H_g \)), 7.20 (1H, d, \( J = 2.9 \) Hz, \( H_{5a} \)), 7.11–7.03 (3H, m, \( H_{5a,18,7b} \)), 7.01 (1H, d, \( J = 2.2 \) Hz, \( H_{5a} \)), 6.90 (1H, td, \( J = 7.5, 1.2 \) Hz, \( H_{2a} \)), 6.85 (1H, dd, \( J = 7.5, 1.2 \) Hz, \( H_{2a} \)), 6.62 (1H, t, overlapping, \( J = 2.7 \) Hz, \( H_{6b} \)), 6.61 (1H, t, overlapping, \( J = 2.7 \) Hz, \( H_{6a} \)), 6.32 (1H, dd, \( J = 5.0, 1.3 \) Hz, \( H_{5a} \)), 6.30 (1H, dd, \( J = 5.1, 1.3 \) Hz, \( H_{5a} \)). 13C NMR (125 MHz, CD2CN, 300 K): 154.0 (C2), 153.3 (C1), 151.8 (C4), 144.8 (C9a/b), 144.6 (C9a/b), 140.6 (C6), 140.1 (C7a), 139.7 (C7b), 135.0 (C5a), 134.4 (C1a/b), 134.1 (C1a/b), 132.4 (C8a/b), 128.8 (C9a/b), 128.7 (C5a), 128.6 (C8a/b), 127.5 (C2a/b), 127.1 (C2a/b), 127.0 (C2a/b), 124.3 (C3a/b), 124.2 (C3a/b), 123.9 (C4a/b), 113.0 (C4a/b), 112.7 (C4a/b), 109.3 (C6a/b), 106.3 (C6a/b). HRMS (ASAP): m/z 624.1497 (624.1488 calculated for C36H29IrN9).
Synthesis of 3aL1. This was prepared from dimer 1a (50 mg, 0.08 mmol), HL1 (16 mg, 0.11 mmol) and NaOMe (5 mg, 0.11 mmol). After work up, the crude product was purified by column chromatography (aluminium oxide); the product was eluted with CH2Cl2/MeOH (30:1), respectively.

3aL1 was isolated as a grey yellow solid (45 mg, 76%). 1H NMR: (500 MHz, CD3CN, 298 K): δ 8.29 (1H, d, J = 2.7 Hz, H3B), 8.26 (1H, d, J = 2.7 Hz, H7A), 7.90–7.86 (2H, m, H2A), 7.83 (1H, td, J = 7.7, 1.5 Hz, H7), 7.47 (1H, d, J = 7.1 Hz, H3), 7.39 (1H, d, J = 7.6 Hz, H2), 7.35 (1H, d, J = 7.8 Hz, H1B), 7.06 (1H, ddd, J = 7.6, 5.6, 1.2 Hz, H2), 7.00–6.95 (2H, m, H8A/B), 6.91 (1H, td, J = 7.7, 1.1 Hz, H1B), 6.82–6.80 (2H, m, H2A), 6.72–6.79 (2H, m, H2B/3A), 6.53 (1H, t, J = 2.5 Hz, H4B), 6.50 (1H, t, J = 2.5 Hz, H4A), 6.34 (1H, dd, J = 7.3, 1.0 Hz, H6B), 6.22 (1H, dd, J = 7.4, 1.0 Hz, H6A). 13C NMR (125 MHz, MeOD, 298 K): δ 154.4 (C4), 154.1 (C5), 151.7 (C3), 145.2 (CAB), 145.1 (CAB), 140.9 (C11), 140.0 (C7B), 139.5 (C7A/B), 135.2 (C1B), 134.9 (C9a), 134.4 (C12a), 132.7 (CAB), 129.2 (C12b), 128.9 (C18b), 128.8 (C18b), 127.7 (C2A2B), 127.3 (C2A2B), 127.1 (C2A2B), 124.5 (C3A3B), 124.3 (C3A3B), 124.0 (C13a), 112.8 (C4A4B), 109.5 (C6A6B), 109.3 (C6A6B), 106.4 (C10a). HRMS (ASAP): [M + H]+, m/z 700.1812 [700.1801 calculated for C32H25^{193}IrN7].

Synthesis of 3aL2. This was prepared from dimer 1a (71 mg, 0.069 mmol), HL2 (31 mg, 0.15 mmol) and NaOMe (30 mg, 0.15 mmol) in MeOH (3 ml) and DCM (6 ml), and was allowed to stir for 2.5 h. After work up, 3aL2 was isolated as grey yellow solid (73 mg, 76%). 1H NMR (500 MHz, CDCl3, 300 K): δ 7.93 (1H, d, J = 2.9 Hz, H5AB), 7.84 (2H, br, m, H5AB), 7.63 (1H, br, d, J = 7.4 Hz, H2), 7.60 (1H, td, J = 7.7, 1.3 Hz, H1B), 7.15 (1H, td, J = 7.7, 1.1 Hz, HAB), 7.11 (1H, d, J = 7.6 Hz, H3AB), 6.91 (1H, td, J = 7.6, 1.1 Hz, HAB), 6.86 (1H, td, J = 7.6, 0.8 Hz, H3A), 6.82–6.72 (5H, m, H2A,3B,7AB,G), 6.49 (1H, s, H1B), 6.37 (1H, t, J = 2.4 Hz, H6AB), 6.33 (1H, dd, J = 7.3, 1.2 Hz, H1A), 6.30 (1H, dd, J = 7.5, 1.1 Hz, H1B), 6.20 (1H, t, J = 2.4 Hz, H4AB), 12.9 (9H, s, H5Bu). 13C NMR: (125 MHz, CDCl3, 300 K): δ 163.9 (C9a), 157.2 (C9a), 149.5 (C5c), 149.4 (CH3), 144.1 (C4c), 143.3 (C5c), 138.7 (CH3), 137.3 (CH3), 137.1 (C12B), 136.8 (CH), 134.0 (C7A/B), 133.7 (C1B), 126.3 (CH), 126.0 (CH), 125.6 (CH), 125.4 (CH), 122.0 (CH), 121.5 (CH), 120.7 (CH), 119.0 (CH), 111.1 (CH), 110.8 (CH), 107.3 (CH), 107.0 (CH), 98.8 (C10a), 93.2 (C10a), 31.2 (C10a). HRMS (ASAP): [M + H]+, m/z 680.2115 [680.2114 calculated for C32H29^{193}IrN7].
Synthesis of 3bL3. This was prepared from dimer 1b (70 mg, 0.053 mmol), H2A (26.2 mg, 0.12 mmol) and NaOMe (12.7 mg, 0.23 mmol). After work up gave 3bL3 as a pale yellow solid (77 mg, 85%). 1H NMR (400 MHz, DMSO, 298 K): δ 8.99 (1H, d, J = 2.8 Hz, H5B), 8.95 (1H, d, J = 2.5 Hz, H5A), 8.00 (1H, br, d, J = 8.0 Hz, H4), 7.94 (1H, td, J = 7.5, 1.5 Hz, H6), 7.86 (1H, d, J = 8.2 Hz, H3A), 7.82 (1H, d, J = 8.2 Hz, H3B), 7.71 (1H, br, d, J = 5.0 Hz, H1B), 7.66–7.61 (2H, m, H4A), 7.36 (1H, dd, J = 8.5, 1.5 Hz, H5A), 7.31–7.23 (5H, m, H3B,7B,b,1b,m), 7.18 (1H, ddd, J = 6.5, 5.5, 1.5 Hz, H2B), 7.12 (1H, br, J = 7.0 Hz, Hn), 6.84 (1H, d, J = 2.2 Hz, H7A), 6.77 (1H, t, J = 2.5 Hz, H6B), 6.71 (1H, t, J = 2.5 Hz, H6A), 6.47 (1H, br, d, J = 1.6 Hz, H4B), 6.40 (1H, br, d, J = 1.6 Hz, H4A), 1.3C NMR (126 MHz, DMSO, 298 K): δ 155.5 (Ci), 152.0 (Cq), 151.0 (Cq), 149.0 (Cq), 147.0 (Cq), 146.2 (Cq), 139.4 (Cq), 139.0 (2 × C7B,8B), 138.2 (Cq), 135.3 (Cq), 133.8 (Cq), 129.4 (Cq), 129.0 (Cq), 128.8 (Cq), 128.6 (Cq), 128.3 (2 × Ce), 128.7, 128.4 (2 × Cy), 123.4 (2 × Cj), 122.4 (Cq), 120.0 (Ca), 119.6 (Ca), 119.0 (Cq), 111.4 (Cq), 110.9 (Cq), 108.8 (Ca), 108.0 (Cq). The CCF3 carbons were not identified due to low signal-to-noise ratios. 19F NMR (376 MHz, CDCl3, 298 K): δ –61.73 [s], –62.00 (s). HRMS (ESI): [M + H]+ m/z 816.1871 [816.1861 calculated for C158H32F6O28N3].

Synthesis of 2cHL1. This was prepared from dimer 1c (50 mg, 0.046 mmol), H2A (16 mg, 0.10) and KPF6 (21.5 mg, 0.12 mmol) in MeOH (3 ml) were heated in a microwave irradiation for 40 min. After work up, the product was isolated as an yellow solid (53 mg, 84%). 1H NMR (500 MHz, CDCl3, 298 K): δ 8.20 (1H, dt, J = 7.8, 1.1 Hz, H5), 8.11–8.09 (1H, m, H5B), 8.08–8.06 (1H, m, H4), 8.05 (1H, dd, J = 1.2 Hz, H3A), 7.89–7.85 (3H, m, H6A,6B,8A), 7.83 (1H, dd, J = 5, 1.6 Hz, H4A), 7.82–7.78 (2H, m, H5A,4B), 7.72–7.71 (2H, m, H5B), 7.68 (1H, ddd, J = 5.9, 1.4, 0.63 Hz, H6B), 7.52 (1H, s, H7), 7.52–7.46 (3H, m, H1B,m,n), 7.36 (1H, dd, J = 7.6, 5.5 Hz, H7), 7.12–7.01 (1H, m, H3B,7B,b,1b,m), 7.08 (1H, ddd, J = 7.6, 0.9 Hz, H2B), 6.35 (1H, dd, J = 7.6, 0.9 Hz, H1A), 6.27 (1H, dd, J = 7.6, 0.8 Hz, H8B). 11C NMR (125 MHz, CDCl3, 298 K): δ 169.0 (Ca), 168.2 (Ca), 154.3 (Cq), 152.8 (Cq), 151.2 (Ca), 148.6 (Ca), 151.1 (Cq), 150.4 (Cq), 150.3 (Ca), 149.3 (Cq), 147.5 (Ca), 146.0 (Cq), 145.5 (Cq), 140.6 (Ca), 140.4 (Ca), 139.5 (Ca), 139.4 (Ca), 133.5 (Ca), 132.4 (Ca), 131.5 (C2A,B), 131.9 (C1m,n), 130.7 (C1m,n), 130.2 (Cy), 128.6 (Cq), 127.6 (Cm,n), 127.5 (Cq), 125.8 (Ca), 124.6 (Cq), 124.3 (Cq), 124.0 (Cq), 123.6 (C1A/B/7A/B), 123.0 (C1A/B/7A/B), 104.2 (Cq). HRMS (ESI): [M + H]+ m/z 722.1901 [722.1896 calculated for C124H19F6O3N3].

Synthesis of 3cL1. This was prepared from dimer 1c (50 mg, 0.046 mmol), H2A (23.5 mg, 0.10) and KPF6 (20.4 mg, 0.11 mmol) in MeOH (3 ml). After work up, the compound was isolated as a yellow solid (68 mg, 84%). 1H NMR (500 MHz, CDCl3, 298 K): δ 8.23 (1H, dt, J = 7.8, 1.1 Hz, H5), 8.10–8.09 (1H, m, H5B), 8.08–8.06 (1H, m, H4), 8.05 (1H, dd, J = 1.2 Hz, H3A), 7.89–7.85 (3H, m, H6A,6B,8A), 7.83 (1H, dd, J = 5, 1.6 Hz, H4A), 7.82–7.78 (2H, m, H5A,4B), 7.72–7.71 (2H, m, H5B), 7.68 (1H, ddd, J = 5.9, 1.4, 0.63 Hz, H6B), 7.52 (1H, s, H7), 7.52–7.46 (3H, m, H1B,m,n), 7.36 (1H, dd, J = 7.6, 5.5 Hz, H7), 7.12–7.01 (1H, m, H3B,7B,b,1b,m), 7.08 (1H, ddd, J = 7.6, 0.9 Hz, H2B), 6.35 (1H, dd, J = 7.6, 0.9 Hz, H1A), 6.27 (1H, dd, J = 7.6, 0.8 Hz, H8B). 11C NMR (125 MHz, CDCl3, 298 K): δ 169.0 (Ca), 168.2 (Ca), 154.3 (Cq), 152.8 (Cq), 151.2 (Ca), 148.6 (Ca), 151.1 (Cq), 150.4 (Cq), 150.3 (Ca), 149.3 (Cq), 147.5 (Ca), 146.0 (Cq), 145.5 (Cq), 140.6 (Ca), 140.4 (Ca), 139.5 (Ca), 139.4 (Ca), 133.5 (Ca), 132.4 (Ca), 131.5 (C2A,B), 131.9 (C1m,n), 130.7 (C1m,n), 130.2 (Cy), 128.6 (Cq), 127.6 (Cm,n), 127.5 (Cq), 125.8 (Ca), 124.6 (Cq), 124.3 (Cq), 124.0 (Cq), 123.6 (C1A/B/7A/B), 123.0 (C1A/B/7A/B), 104.2 (Cq). HRMS (ESI): [M + H]+ m/z 722.1901 [722.1896 calculated for C124H19F6O3N3].
(CUB), 148.9 (C8A), 145.1 (Cq), 144.2 (Cq), 139.3 (Cq), 138.4 (Cq), 137.5 (C6A/6B), 137.2 (C6A/6B), 132.4 (C1B), 132.3 (C1A), 130.5 (C1B), 130.0 (C1A), 124.8 (C4A/4B), 124.6 (C4A/4B), 123.3 (C3A), 123.2 (C3A), 123.0 (C3A), 122.6 (C2A), 121.2 (C2A), 121.7 (C2A), 120.7 (Cq), 119.5 (Cq), 119.3 (Cq), 104.1 (Cq). 1H NMR (500 MHz, CDCl3, 298 K): δ 7.98 (1H, dd, J = 7.9, 1.9 Hz, H1A), 7.45 (1H, d, J = 7.9 Hz, H1B), 7.40 (1H, d, J = 1.9 Hz, H2A), 7.29 (2H, t, J = 7.4 Hz, H3A), 7.11 (1H, br, t, J = 7.4 Hz, H1A), 7.01 (1H, s, Hq), 6.95 6.78 (6H, m), 6.75 (1H, dd, J = 6.1, 0.9 Hz), 6.39 (1H, dd, J = 7.3 Hz, H1B), 6.33 (1H, br, d, J = 7.2 Hz, H1A).

Due to overlap no assignments are made. 13C NMR (126 MHz, CDCl3, 298 K): δ ppm 168.6 (Cq), 168.1 (Cq), 155.7 (Cq), 155.1 (Cq), 150.5 (Cq), 149.5 (Cq), 148.3 (Cq), 144.5 (Cq), 144.0 (Cq), 138.0 (Cq), 137.0 (Cq), 136.7 (Cq), 132.3 (Cq), 131.9 (Cq), 130.2 (Cq), 129.8 (Cq), 124.4 (Cq), 124.3 (Cq), 123.0 (Cq), 122.9 (Cq), 122.1 (Cq), 121.8 (Cq), 121.6 (Cq), 120.5 (Cq), 119.2 (Cq), 118.7 (Cq), 100.3 (Cq), 30.7 (Cq). The quaternary carbon of the 'Bu was not observed. HRMS (ASAP): [M + H]+, m/z 702.2236 [702.2209 calculated for C36H31N6].

Synthesis of 3CtA. This was prepared from the dimer 1c (75 mg, 0.070 mmol), HCl (31 mg, 0.15 mmol) and NaOMe (30 mg, 0.154 mmol) in MeOH/DCM (3 : 6 ml). After work up, the product was isolated as yellow solid (50 mg, 87%).

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Conflicts of interest

There are no conflicts to declare.

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