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| Complete List of Authors: | Love, Jason; University of Edinburgh, School of Chemistry  
Pankhurst, James; University of Edinburgh, School of Chemistry  
Cadenbach, Thomas; University of Edinburgh, School of Chemistry  
Finn, Colin; University of Edinburgh, School of Chemistry  
Betz, Daniel; University of Edinburgh, School of Chemistry |
Towards dipyrrins: oxidation and metalation of acyclic and macrocyclic Schiff-base dipyrromethanes

James R. Pankhurst, a Thomas Cadenbach, a Daniel Betz, a Colin Finn, a and Jason B. Love a,*

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Oxidation of acyclic Schiff-base dipyrromethanes cleanly results in dipyrrins, whereas the macrocyclic ‘Pacman’ analogues either decompose or form new dinuclear copper(II) complexes that are inert to ligand oxidation; the unhindered hydrogen substituent at the meso-carbon allows new structural motifs to form.

Bimetallic complexes with a well-defined molecular structure and controlled internuclear separation are of significant interest in small molecule activation chemistry. 1 In this context, several polypyrrolic Schiff-base macrocycles reported by us and others act as ligands for s-, d- and f-block metals,2, 3, 4, 5 These complexes have a tendency to fold into cofacial or ‘Pacman’ structures that provide a reactive cleft between the two metals suited to cooperative catalytic reduction chemistry. 6, 7 with the macrocycles disubstituted at each dipyrromethane meso-carbon position providing two dianionic coordination compartments.

A large number of dipyrromethanes that are mono-substituted at the meso-position are readily oxidised to their dipyrrin congeners, most notably by 2,3-dichloro-5,6-dicyanobenzoquinone (DDQ). 8 Significantly, transition metal dipyrrin complexes have interesting photochemical and redox properties,9 carry out unusual chemical transformations, including C-H bond activation,10 and flexible N2-dipyrrin macrocycles have been prepared, although little exploited due to their difficult preparations.11 As such, we are interested in exploring analogous oxidation procedures to form a new set of dipyrrin Pacman macrocycles with two mono-anionic coordination pockets to stabilise metals in lower oxidation states and hence favour small molecule reduction chemistry.

The preparation of acyclic and macrocyclic dipyrromethanes was achieved by exploiting the mono-meso-substituted dialdehyde 1 to form duminodipyrromethane 2 in 74 % yield using standard Schiff-base condensation methods. The solid-state structure of 1 was determined by X-ray crystallography and is shown in the ESL. The 1H NMR spectrum of 2 revealed the appearance of an imine proton resonance at 8.18 ppm accompanied by the loss of the aldehyde resonance of 1 at 9.24 ppm. The absorption band at 1623 cm−1 in the IR spectrum of 2 is assigned to the imine functional group.

Oxidation of 2 was achieved using stoichiometric amounts of DDQ to afford the dipyrrin HL2 in quantitative yield,13 and is supported by the loss of the meso-proton resonance at 5.69 ppm in the 1H-NMR spectrum. Dipyrrin HL2 was synthesised by heating a toluene solution of 1 and 1BuNH2 to 50 °C with Na2SO4, forming directly in air without a separate oxidation step. The 1H NMR spectrum of HL2 includes an imine proton resonance at 7.71 ppm and does not feature a meso-proton resonance. The IR absorption band at 1582 cm−1 is assigned to the imine functional group. The solid-state structure of HL2 was determined by X-ray crystallography (ESI) and displays the expected planar meso-carbon geometry. A C2-symmetric solution-state structure was observed for HL2 by NMR spectroscopy, but in the solid-state, one imine group is rotated away from the N2-pocket, lowering the symmetry to C1. HL2 crystallises as co-planar, π-stacked dimers, arranged head-to-tail.

Reaction between HL1 and LiN(SiMe3)2 cleanly generates the lithium dipyrrolide LiL1 which was then used to form the iron(II) complex FeBr(L1)2 by salt metathesis in THF. While not
characterised by X-ray crystallography and NMR silent, ESI-MS of microcrystalline FeBr(L) supports its formulation. The exclusion of air from these synthetic procedures avoids undesired ligand oxidation reactions which have been shown to occur on oxidation of Group 10 complexes of similar iminodipyromethane ligands.13

Electronic absorption spectra were recorded for 2, HL3 and the iron(II) complex FeBr(L) (Fig. 1), and the spectra for 2 and HL3 were accurately reproduced by TD-DFT calculations using the B3LYP functional and 6-311G(d,p) basis set (ESI). The dominant absorption band for 2 appears at 373 nm and is assigned as a mixture of HOMO (H) to LUMO (L)+1 (59 %) and (H-1)-L (32 %) transitions, with the H-L transition appearing as a shoulder at 413 nm. Upon oxidation to HL3, both the (H-1)-L and H-L transitions are red-shifted to 520 and 540 nm, respectively, while the (H-L+1) transition remains in the UV-region at 290 nm. This change in electronic structure is typical for dipyrromethene compounds14 and reflects a 1.6 eV stabilisation of the LUMO upon oxidation. Although the extinction coefficients of 20,000 M⁻¹ cm⁻¹ for HL3 and FeBr(L) are low compared to BODIPY compounds (80,000 M⁻¹ cm⁻¹) they are similar to pyridomethene-BF2 complexes.15

A small number of crystals were grown from THF/hexane solutions of FeBr(L), and were found to be the oxidised iron(III) oxo dipyrrin (FeBr(L))2(µ-O) (Fig. 2) in which the Fe centres are five-coordinate and adopt a distorted trigonal bipyramidal geometry with pyrrole N1, Br1, and O1 equatorial and pyrrole N3 and imine N2 axial. As with HL3, one imine nitrogen N4 is rotated out of the pocket and is not coordinated. The overall dinuclear structure is reminiscent of a Pacman arrangement, with perfluoraryl groups and 1 Bu-aryl substituted adjacent. The XFe(µ-O)FeX core (X = halide) is common in Fe chemistry, albeit usually as part of a wholly inorganic anion.

The ortho-phenylene bridged macrocycle H4L3 and the 1,8-anthracene bridged macrocycle H4L4 were both prepared by acid-promoted condensation of I with the appropriate diamine. Upon neutralisation with NEt3, the free-base precipitates cleanly from the methanol solution as a dull-yellow solid and is isolated by filtration. For both compounds, characteristic imine proton resonances were observed in the 1H NMR spectra at 8.09 ppm (H4L3) and 8.38 ppm (H4L4) and imine IR absorption bands at 1620 cm⁻¹ (H4L3) and 1614 cm⁻¹ (H4L4) were also recorded. No higher-order cyclisation products were observed by ESI-MS with only the expected molecular ion peaks observed at 937 m/z for H4L3 and 1080 m/z for H4L4.

The solid-state structures for both H4L3 and H4L4 were determined by X-ray crystallography (Fig. 3). Surprisingly, and unlike previous examples, H4L3 crystallises excluding any protic solvent molecules that are usually hydrogen-bonded to the pyrrole nitrogen. Instead, H4L3 crystallises in a bowl geometry in which the anthracene groups are held further apart than they are commonly found in metal complexes; in this case, protic solvent molecules are present within the cleft.

The [2+2] cyclisation between 1 and the diamine could result in either syn- or anti-isomers in which the relative positions of the meso-substituents dictate the identity of the isomer. Importantly, both H4L3 and H4L4 crystallise as the syn-isomer only and, furthermore, there is no evidence to support a mixture of isomers by NMR spectroscopy, which clearly shows a single set of resonances for 1H, 13C and 19F nuclei. Considering the isolated yields of the macrocycles (ca. 40 %), it is likely that some preferential precipitation of the syn-isomer has occurred, with the anti-isomer remaining in solution; we have, as yet, been unable to isolate or characterise material consistent with this latter isomer.

In contrast to the acyclic analogues, attempts to oxidise macrocycles H4L3 and H4L4 to the dipyrrins using DDQ resulted in decomposition to a myriad of unidentified products. Similar decomposition was observed on reaction of H4L3 and H4L4 with chloranil, Ag2O, I2 and Ce(NH4)2(NO3)6. Despite previous reports of dipyrromethane macrocycles being successfully oxidised by MnO2 or by K2MnO4,17 no discernible products have yet been isolated using these oxidants.
To investigate this further, the redox behaviour of $\text{HL}^2$, $\text{H}_2\text{L}^2$ and $\text{H}_3\text{L}^5$ was investigated by cyclic voltammetry. The CV for $\text{HL}^2$ includes a reversible reduction to the radical anion at $E_{pa} = -1.46$ V vs. $\text{Fc}^-/\text{Fc}$ and a second, irreversible reduction at $E_{pa} = -2.28$ V. This second process is assigned tentatively to the two-electron, proton-coupled reduction to the dipyromethane, $\text{H}_2\text{L}^2$. The CVs for macrocycles $\text{H}_2\text{L}^3$ and $\text{H}_3\text{L}^5$ do not feature any oxidation processes, only an irreversible reduction at $E_{pa} = -1.41$ V vs. $\text{Fc}^-/\text{Fc}$ for $\text{H}_2\text{L}^3$ and $E_{pa} = -1.78$ V for $\text{H}_3\text{L}^5$ (ESI).

As an alternative route to dipyrrins, attempts were made to oxidise $\text{H}_2\text{L}^3$ and $\text{H}_3\text{L}^5$ in air in the presence of a metal cation.\textsuperscript{18} As such, bimetallic copper(II) complexes were prepared by stirring THF solutions of $\text{H}_2\text{L}^3$ or $\text{H}_3\text{L}^5$ with Cu(OAc)$_2$$\cdot$H$_2$O in the presence of NEt$_3$ in air. The resulting dipyromethane complexes Cu$_2$($\text{L}^3$) and Cu$_2$($\text{L}^5$) were found to be stable on alumina and were thus purified by column chromatography, eluting the pure products as orange CHCl$_3$ fractions in high yields; ‘accordion’ macrocycles that have dipyromethane head groups but flexible compartmental spacers display similar inertness to oxidation on metatation.\textsuperscript{11} The syntheses of these compounds are supported by ESI-MS, with molecular ion peaks at 1058 m/z for Cu$_2$($\text{L}^3$) and 1203 m/z for Cu$_2$($\text{L}^5$) with the expected isotope pattern for bimetallic complexes, albeit with seemingly oxidised macrocycles. The vibrational frequencies for the imine groups at 1552 cm$^{-1}$ for Cu$_2$($\text{L}^3$) and 1574 cm$^{-1}$ for Cu$_2$($\text{L}^5$) are lower compared to the free ligands and are indicative of metatation. Both compounds are NMR-silent. The copper(II) complex Cu$_2$($\text{L}^5$) that is similar to Cu$_2$($\text{L}^4$), but differs in that the macrocycle is diethyl-substituted at the meso-position, was also made for comparison (ESI).

The solid-state structures for Cu$_2$($\text{L}^3$), Cu$_2$($\text{L}^4$), and Cu$_2$($\text{L}^5$) were determined by X-ray crystallography (Figs 4 and 5, and ESI, respectively) and in all cases show non-oxidised dipyromethane macrocycles, evident from the tetrahedral bond angles around each meso-carbon atom (mean $\alpha = 110.2^\circ$ for Cu$_2$($\text{L}^3$) and 111.0$^\circ$ for Cu$_2$($\text{L}^5$)). This is in disagreement with the mass spectrometry data of these complexes and suggests that the macrocycles may oxidise under MS conditions.

The intermolecular distance in Cu$_2$($\text{L}^4$) is also short compared to related complexes of Co(II), Pd(II) and U(VI) complexes of $\text{L}^5$ (5.377–5.834 Å)\textsuperscript{7,21} and is more similar to that observed for dinuclear Zn(II) complexes of $\text{L}^4$ (3.871–5.532 Å).\textsuperscript{22} The small meso-proton substituent also has the effect of closing the cleft, so that Cu$_2$($\text{L}^4$) has a negative bite angle of $-8.03^\circ$ between the two N$_2$-donor planes, compared to the positive bite angle of 14.83$^\circ$ for Cu$_2$($\text{L}^5$). As with Cu$_2$($\text{L}^4$), Cu$_2$($\text{L}^5$) crystallises as the syn, exo-isomer only, with no evidence for syn, endo- or anti-isomers.

The redox chemistry of Cu$_2$($\text{L}^3$), Cu$_2$($\text{L}^4$) and Cu$_2$($\text{L}^5$) was investigated by cyclic voltammetry. The CVs of Cu$_2$($\text{L}^4$) and Cu$_2$($\text{L}^5$) showed no oxidation features, with only irreversible reductions for both at $E_{pa} = -1.51$ V vs. $\text{Fc}^-/\text{Fc}$ for Cu$_2$($\text{L}^4$) and $E_{pa} = -1.70$ V and $-2.30$ V for Cu$_2$($\text{L}^5$) (ESI). In contrast, the CV of Cu$_2$($\text{L}^3$) shows one quasi-reversible, two-electron oxidation at $E_{pa} = -0.10$ V and two quasi-reversible, one-electron reductions at $E_{pa} = -1.47$ V and $-1.76$ V (Fig. 6). These redox events are assigned tentatively to the formation of Cu$_2$($\text{L}^3$)$_2^+$, Cu$_2$($\text{L}^5$)$_2^+$, and Cu$_2$($\text{L}^5$)$_2^+$, respectively, i.e. oxidation to Cu(III) and sequential reduction to Cu(I). The reversibility of these processes suggest they are metal-based; electrochemical oxidation of the macrocycle to the dipyrrin is anticipated to be irreversible due to the loss of hydrogen atoms and the required change in geometry that would follow.
We have synthesised two new acyclic dipyrrin compounds and two new Schiff-base macrocycles. These macrocycles are not readily oxidised to their dipyrrin congeners, even when metalated, yet due to the sterically unhindered pseudo-reference electrode.

Fig. 6  Cyclic voltammogram of Cu(I), measured as a 3 mM solution in THF. Electrolyte: 0.2 M [Bu4N][BF4]. Pt disc working-electrode, Pt gauze counter-electrode, Ag wire **pseudo**-reference electrode.

Notes and references


