Reactions at the azomethine C=N bonds in the nickel(ii) and copper(ii) complexes of pyridine-containing Schiff-base macrocyclic ligands†

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Template condensation between 2,6-dicarbonylpyridines and a tripodal tetramine tris(3-aminopropyl)amine in the presence of copper(ii) or nickel(ii) yielded macrocyclic complexes that contained a coordinated primary amine as an appended functional group. The derivatives of 2,6-diformylpyrididine contained labile azomethine bonds susceptible to water or alcohol addition, and were isolated in the form of crystallographically characterized hemiaminals or O-ethyl hemiaminals. The nickel(ii) hemiaminal complex produced a macrocyclic product upon reduction with sodium borohydride, and the structures of the two complexes had very similar ligand conformations. The derivatives of 2,6-diacetylpyridine formed stable Schiff-base macrocycles with rigid, nearly planar structures in which azomethine bonds were conjugated with the pyridine ring. The steric strain was relieved upon heating of the complexes in water–alcohol media. The products were determined by the coordination requirements of the metal ions: the copper(ii) underwent a C=N double bond shift, forming a more flexible five-coordinate macroyclic complex, whereas the nickel(ii) compound underwent a partial ring-opening hydrolysis, giving rise to a pseudo-octahedral six-coordinate species. The unusual isomerization of the copper(ii) complex was accompanied by H/D exchange at C-H bonds, and was facilitated by alcohol addition. The mechanism of isomerization is similar to B3-catalyzed transamination reactions (D.E. Metzler, M. Ikawa and E.S. Snell. J. Am. Chem. Soc., 1954, 76, 648). The corresponding four-coordinate copper(ii) complex lacking a pendant arm was more thermally stable than its five-coordinate counterpart, and underwent partial double-bond migration under harsh conditions (prolonged heating at reflux in water–ethanol mixtures at pH > 8.5).

1 Introduction

Template Schiff-base condensations between dicarbonyl compounds and diamines are among the simplest and most popular methods for macrocycle synthesis.1 Pyridine-containing dicarbonyl components give rise to readily accessible and versatile ligands, including mono- and dicompartmental cycles, three-dimensional cages, sterically enforced macrocycles, and ligands with additional functional groups attached to the macrocycle.2–5 The rich chemistry of macrocyclic pyridines prompted successful applications of these platforms as redox catalysts,7–10 potent antibacterial agents,11 selective hosts for heavy metals,12 fluorescence redox switches,13 and building blocks for assembling supramolecular architectures, such as metal-templated catenanes14,15 and macrocycle-decorated dendrimers.16

One of the attractive features of pyridine-containing macrocycles is the presence of inequivalent nitrogen donors that allows for selective functionalization at amino group(s). Interest in macrocycles with pendant arms is growing on account of their unique coordination and structural properties, their utility in enzyme mimicking studies and catalysis, and their rapidly growing applications as radiopharmaceuticals, magnetic resonance imaging reagents, and fluorescent probes.17–22

Unambiguous single-point attachment of the macrocycles to a solid support or to functional biomolecules is best accomplished via reactions with a functional group on the pendant arm.21 The preparation of monofunctionalized macrocycles, however, is usually more elaborate than the synthesis of polyfunctionalized ligands that can be obtained, for example, through extensive alkylation of the secondary amino groups in azamacrocycles.10,22 Wc23,24 and others23–27 have previously reported a one-step synthesis of Schiff-base macrocyclic complexes bearing a primary amino group in the pendant arm via a template condensation between diacetylpyridine and tripodal aliphatic tetriones. The resulting complexes, however, experience significant steric strain due to an imperfect match between the rigid, planar, conjugated bis-iminepyridine fragment and the incorporated 3d-metal ion, demonstrated by X-ray data and molecular mechanics calculations.25 This sometimes resulted in incomplete condensation, producing acyclic products.25,26 On the other hand, “fine tuning” of the macrocyclic ring was also accomplished by an unusual double bond migration that retained the cyclic structure of the copper(ii) complex, and allowed for a greater flexibility of the ligand.23 Azomethine bonds in pyridine macrocycles are rather labile and undergo a variety of reactions, including ring contraction rearrangements23,29–32 and addition of water or alcohol to the C=N bond.33–36 The analogous reduced ligands are more chemically stable and conformationally flexible: they adopt a variety of conformations, producing both tetragonal-pyramidal and...
trigonal-bipyramidal metal complexes. Reduction of azomethine bonds, however, adds an additional step to the preparation of the macrocycles, and alters the chemical properties of the metallolocomplexes (e.g., iron complexes with reduced tridentate iminopyridine ligands show low catalytic activity in olefin polymerization, as opposed to the corresponding Schiff-base compounds that are highly reactive). Therefore, the chemistry of pyridine Schiff-base macrocycles needs to be better understood, in order to rationally synthesize stable functional metallolocomplexes.

We now explore the chemistry of the five-coordinate macrocyclic Schiff-base complexes of copper(ii) and compare it to the chemistry of their four-coordinate counterparts. Coordination of an appended functional metallocomplex.

2 Results and discussion

2.1 Complexes with tetradentate macrocycles derived from diaacetylpyridine

As a prerequisite to detailed investigations of the functionalized pentadentate aminopyridine macrocycles, we studied the structure and reactivity of their tetradentate analogs (Scheme 1). Although the Schiff-base complex [Cu(L1)](ClO₄)₂ was among the first metallomacrocyclic Schiff-base complexes, results of several reactions (water addition, alcohol addition, hydrolytic ring opening, and double bond migration) were isolated and characterized crystallographically. It was found that ethanol addition and double bond migration preserve the macrocycle, while water addition to the C=N bond may have different consequences: reversible formation of carbinolamines allows us to obtain stable macrocyclic products via Schiff-base reduction with BH₄⁻, while hydrolytic ring opening destroys the cycle and, in case of copper(ii) complexes, results in irreversible decomposition of the macrocycle.

![Fig. 1 ORTEP plot of [Cu(L1)](ClO₄)₂. Perchlorate anions are omitted for clarity. Selected bond lengths (Å): Cu(1)–N(1) 1.916(3), Cu(1)–N(2) 2.025(3), Cu(1)–N(3) 1.956(3), Cu(1)–N(4) 2.021(3), Cu(1)–O(1) 2.451, Cu(1)–O(3) 2.592, N(2)–C(6) 1.268(5), N(2)–C(8) 1.461(5), N(4)–C(14) 1.267(5), N(4)–C(13) 1.466(5).](image1)

![Fig. 2 ORTEP plot for the complex [Cu(L2)]²⁺ (which co-crystallized with [Cu(L1)]²⁺). Atom C6 was modeled with disorder. Perchlorate anions are omitted for clarity. Selected bond lengths (Å): Cu(1)–N(1) 1.875(3), Cu(1)–N(2) 1.977(4), Cu(1)–N(3) 1.930(4), Cu(1)–N(4) 2.055(4), Cu(1)–O(3') 2.384(7), Cu(1)–O(1) 2.646(5), C(6)–N(2) 1.246(9), C(6B)–N(2) 1.431(9), N(4)–C(14) 1.217(6).](image2)

Upon refluxing the tetradentate complex [Cu(L1)]²⁺ in H₂O–EtOH mixtures at pH 8.5, the IR band at 1625 cm⁻¹ (C=N stretch) decreased in intensity, a new IR band at 1677 cm⁻¹ appeared, and a broad absorption band in the UV-Vis spectrum (MeOH) shifted from 560 to 552 nm. The mass spectrum of the product showed no signs of hydration, ethanol addition to a C=N bond, or irreversible decomposition, and the composition of the complex did not change (according to C,H,N-microanalysis). These data suggested that a (partial) double bond migration occurred in [Cu(L1)]²⁺ (Scheme 1). X-Ray crystallography confirmed this hypothesis.

The crystals of the reaction product, [Cu(L2)]²⁺, were twinned, and contained a disordered carbon C6 (in addition to disordered perchlorate anions) (Fig. 2). One position of this atom (50% occupancy) corresponded to an sp²-hybridized carbon with a C6A–N2 separation of 1.246 Å. Another position was occupied by a tetrahedral carbon with a C6B–N2 separation of 1.431 Å. The two sides of the macrocycle separated by the N1–N3 axis are not exactly symmetrical: the saturated chelate rings in them have somewhat different conformations, and the copper(ii) ion is shifted towards the isomerized nitrogen (the longest Cu–N bond in the complex is Cu–N4,
2.055 Å. Since the general features of the structures of 
[Cu(L1)]²⁺ and [Cu(L2)]²⁺ are very similar, the two complexes 
co-crystallized, forming a disordered twinned crystal. The 
X-ray data demonstrate that double bond migration occurred 
in the copper complex with tetradentate ligand L1, but this 
process is incomplete.

The isomerization of [Cu(L1)]²⁺ required high temperature, 
alkaline pH (above 8), and the presence of ethanol in the 
mixture. Prolonged heating at 70 °C in H₂O or H₂O–EtOH 
(pH 7.5–8.5) did not lead to any changes in the UV-Vis or IR 
spectra of the products. Refluxing the complex in water also did 
not cause significant decomposition or double bond migration 
as judged by the lack of a new band at 1600–1700 cm⁻¹ in the 
IR spectrum.

Mass spectrometry showed that H/D exchange at methyl 
groups, and possibly additional CH₂ groups of the macrocycle, 
ocurred upon heating in deuterated water or water–ethanol 
mixtures. The conditions of H/D exchange were not as harsh as 
the conditions for a double bond migration: D₂O or D₂O– 
EtOD allowed for incorporation of 6–8 D atoms at 70 °C in 6 h 
(Fig. S1, ESI†), while no new IR band was observed under these 
conditions.

The role of alcohol in isomerization of [Cu(L1)]²⁺ was not 
caused by its axial coordination to the copper(ii) center. Several 
anions (including acetate and azide) were able to coordinate to 
[Cu(L1)]²⁺, as evidenced by changes in the UV-Vis spectra, but 
the addition of these anions had no effect on the double bond 
migration.

A tetradentate nickel(ii) complex [Ni(L1)](ClO₄)₂, when 
heated in water–alcohol media, produced decomposition prod-
ucts that have not been identified. It has been previously shown 
by Busch and co-workers that in strongly alkaline media, 
[Ni(L1)]²⁺ undergoes complete hydrolysis that liberates free 
diacetylpyridine.⁴⁷

The unusual double bond migration in copper complexes 
with pyridine-containing Schiff-base macrocycles deserved 
further investigation. Pentadentate macrocycles were chosen for 
this study, because their reactions were clean. We have reported 
previously the formation and X-ray characterization of the 
isomerized product [Cu(L4)]²⁺ in the template synthesis of a 
related copper(ii) complex with a pentadentate macrocycle 
L3 (Scheme 1).²¹ In order to better understand the role of 
solvents in double bond migration, a series of analogous 
diformyl pyridine hemiaminal derivatives was prepared and 
structurally characterized (Scheme 2). Then, more stable Schiff 
bases were obtained from diacetylpyridine, and isomerization 
of a five-coordinate copper(ii) macrocycle was studied in detail 
(Scheme 3). The behavior of the copper(ii) complexes was 
compared to their nickel(ii) counterparts.

2.2 Complexes with pentadentate ligands derived from 
diformylpyridine

2,6-Diformylpyridine undergoes facile reaction with the tri-
podal tetramine trpn (Scheme 2). The template condensation 
occurs at room temperature in the presence of either copper(ii) 
or nickel(ii) ions, yielding the macrocyclic products [M(L5)]²⁺. 
The disappearance of the C=O absorptions at ~1700 cm⁻¹ in 
the IR spectrum and the appearance of ν(C=N) in the correct 
positions for Schiff-base linkages (~1600–1650 cm⁻¹)²² within 
4 days indicated that the reaction was complete. No further 
changes in the IR spectra were observed upon extended incu-
bation of the reaction mixture at room temperature. The heat-
ing of the reaction mixture resulted in the rapid irreversible 
degradation of the macrocycle through the formation of dark 
decomposition products which were not identified.

The C=N bond(s) in macrocycles derived from 2,6-diformyl-
pyridine were found to be labile, as in both [Ni(L5)](ClO₄)₂ and 
[Cu(L5)](ClO₄)₂ complexes the addition of water to the double 
band was observed and the crystallographically characterized 
monohydrates were the predominant components of the solid 
products. The hydration of the double bond appears to be rapid 
and reversible because it does not interfere in the ability to 
reduce the double bonds with sodium borohydride to form 
complex [Ni(L7)](ClO₄)₂.²⁴

The macrocyclic nature of the hemiaminals [M(L5)]²⁺ was 
also confirmed by their ability to undergo “arm on–arm off” 
reactions upon protonation/deprotonation. The UV-Vis spec-
tral changes for [Ni(L5)]²⁺ upon titration with a strong acid 
(Fig. S2, ESI†) were typical of the macrocyclic complexes with 
pendant arms, where one nitrogen donor in the arm is select-
ively protonated, leaving the macrocyclic fragment of the mole-
cule intact.²³²⁴,⁴⁸⁻⁵⁰ In contrast, full destruction of the com-
plexes due to protonation of multiple donor atoms is usually 
observed for complexes of acrylic polymides.⁴⁴ The pKₐ of the 
aminoazopropyl arm in [Ni(L5)]²⁺ in aqueous solutions was 
determined to be 6.4 ± 0.1, very close to the values for 
[Ni(L3)]²⁺, [Ni(L7)]²⁺ and [Ni(L10)]²⁺.²³²⁴ The copper complex
Scheme 3

[Scheme diagram showing spectral changes upon acid and base addition, and the formation of hemiaminal derivatives.]

**Fig. 3** ORTEP plot of the complex [Ni(L5)](ClO₄)₂·CH₃CN. Perchlorate ions and hydrogen atoms are omitted for clarity.

[Cu(L5)]²⁺ also exhibited spectral changes upon acid and base addition, although this process was not completely reversible and may have been complicated by other reactions at the C=N bonds and/or deprotonation of the water molecule coordinated to the metal.

The lability of a hemiaminal fragment in [Cu(L5)]²⁺ was also illustrated by its reaction with ethanol. The dissolution of [Cu(L5)](ClO₄)₂ in hot ethanol resulted in the shifts of its UV-Vis absorption bands from λ_max = 630 and 925 nm to λ_max = 635 and 940 nm. The isolated crystalline solid compound gave an IR spectrum distinctly different from that of [Cu(L5)]²⁺ (see Experimental section), and was crystallographically characterized as an O-ethoxy hemiaminal [Cu(L6)](ClO₄)₂. These results demonstrated substitution of the water molecule added to the C=N bond for an ethanol molecule. The ethanol adduct [Cu(L6)]²⁺ was substantially more thermally stable than its precursor [Cu(L5)]²⁺, and could be refluxed in ethanol without decomposition.

Although several individual representatives of water- or alcohol-adducts with pyridine macrocycles were described, no direct transformation of a hemiaminal into an O-alkylated hemiaminal was previously reported. Very few of the macrocyclic hemiaminals or O-alkyl hemiaminals were crystallographically characterized, and the limited data did not allow for a direct comparison of the geometries of water adducts and alcohol adducts. X-Ray data for acyclic transition metal complexes with pyridine-containing hemiaminal ligands suggest that the conformations of coordinated RN(H)–C(OH)R’ fragments are similar to the conformations of their O-alkylated analogs RN(H)–C(OR)R’. One can therefore expect similar structures for the macrocyclic hemiaminals and O-alkylated hemiaminals.

We report crystallographic characterization of a series of complexes derived from a water or alcohol addition to a C=N bond in pyridine-containing macrocycles (Figs. 3, 4 and S3, ESI†). Crystallographic data for [Ni(L5)](ClO₄)₂, [Ni(L5)](ClO₄)₂·CH₃CN, [Cu(L5)](ClO₄)₂ and [Cu(L6)](ClO₄)₂ are given in Table 1. The metal atoms within these complexes have five-coordinate, square-pyramidal geometry. The nitrogen donor atoms of the macrocyclic ligands form an approximate plane (N1–N4, occupying the equatorial positions) with the pyramid being completed by the amine nitrogen in the pendant arm.
high-spin Ni($N_4$) nitrogen atoms are sp
reduced complexes with ligands L7 and L10, both the $N_2$ and the nitrogen atom $N_4$ becomes sp
atoms. In the hemiaminal complexes with ligands L5 and L6, placement is smaller in the ethanol adduct [Cu(L6)]
2
and perchlorate anions are omitted for clarity. Selected bond lengths (Å): Ni(1)--N(1) 2.033(5), Ni(1)--N(2) 2.085(4), Ni(1)--N(3) 2.112(4), Ni(1)--N(4) 2.108(5), Ni(1)--O(9) 2.185(4) Å.

The heating of the nickel(II) complex [Ni(L8)]$^{2+}$, unlike its macrocyclic analogs, does not undergo reversible protonation of its pendant arm.

### Table 1

<table>
<thead>
<tr>
<th>Complex</th>
<th>$[	ext{Ni(L5)}]^{2+}$</th>
<th>$[	ext{Ni(L5)}]^{3+}$</th>
<th>$[	ext{Cu(L5)}]^{2+}$</th>
<th>$[	ext{Cu(L6)}]^{2+}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>$M_1-N_1$</td>
<td>1.9758(18)</td>
<td>1.983(3)</td>
<td>1.955(3)</td>
<td>1.951(4)</td>
</tr>
<tr>
<td>$M_2-N_1$</td>
<td>2.080(19)</td>
<td>2.049(3)</td>
<td>2.034(3)</td>
<td>2.041(4)</td>
</tr>
<tr>
<td>$M_1-N_2$</td>
<td>2.0338(18)</td>
<td>2.047(3)</td>
<td>2.030(3)</td>
<td>2.018(4)</td>
</tr>
<tr>
<td>$M_2-N_2$</td>
<td>2.1277(17)</td>
<td>2.127(3)</td>
<td>2.102(3)</td>
<td>2.102(4)</td>
</tr>
<tr>
<td>$M_2-N_3$</td>
<td>2.0157(18)</td>
<td>2.018(3)</td>
<td>2.150(3)</td>
<td>2.129(4)</td>
</tr>
</tbody>
</table>

Metal displacement from $N_2N_3N_4$ mean plane 0.3805 0.4144 0.4388 0.3383

(nitrogen $N_5$, being axial). A similar coordination geometry around the metal center was previously reported for analogous Schiff-base complexes. No coordination of either the solvent molecules or anions to either nickel or copper was observed (the closest M–OClO$_3$ contacts ranged from 3.6 to 3.9 Å). The Ni–N distances in the five-coordinate complexes ranged from 1.98 to 2.13 Å (Table 1) and were typical of high-spin Ni(II).

The structures of two copper(II) complexes, [Cu(L5)]$^{2+}$ and [Cu(L6)]$^{2+}$, are generally similar to their nickel(II) analogs and to each other (Fig. S3, ESI†). The in-plane Cu–N distances (1.95–2.09 Å) are, on average, shorter than the corresponding distances in the high-spin nickel(II) complexes (Table 1), which is consistent with the smaller radius of Cu$^{2+}$. The axial Cu–N5 bond is significantly elongated (to 2.150(3) Å in the complex [Cu(L5)](ClO$_4$)$_2$), and the metal is displaced out of the macrocyclic plane towards the amino group in the pendant arm. The elongation of the axial bond is common for d$^9$ ions and has been previously observed for analogous Schiff-base copper complexes containing pendant arms.$^{12,17}$ The copper–nitrogen bonds are somewhat shorter, and the metal out-of-plane displacement is smaller in the ethanol adduct [Cu(L6)]$^{2+}$ than in the water adduct [Cu(L5)]$^{2+}$.

The conformation of the saturated six-membered chelate rings in the hemiaminal macrocycles [M(L5)]$^{2+}$ is different from that of related Schiff-base macrocycles [M(L3)]$^{2+}$ (Fig. 4), but very similar to the conformations of the reduced complexes [M(L7)]$^{2+}$ (Fig. S4, ESI†). Consequently, addition of water or alcohol to one C=N double bond partially relieved the conformational strain of the five-coordinate Schiff-base macrocycles as they adopted a more “flattened” orientation for the aminopropyl fragments (Fig. 4). The planar geometry of the azomethine fragments conjugated with the pyridine ring in the [M(L3)]$^{2+}$ complexes caused this “flattened” orientation of the saturated six-membered chelate rings attached at sp$^2$ nitrogen atoms. In the hemiaminal complexes with ligands L5 and L6, the nitrogen atom N4 becomes sp$^2$-hybridized, thus changing the orientation of one of the saturated chelate rings. In the reduced complexes with ligands L7 and L10, both the N2 and N4 nitrogen atoms are sp$^2$-hybridized, and the entire macrocycle is even more flexible.

The macrocyclic hemiaminals, such as [M(L5)]$^{2+}$, may exist in equilibrium with an open, acyclic form of the complex that can be considered a product of complete hydrolysis of one C=N bond. Alternatively, these acyclic complexes may arise from incomplete macrocyclization. The open form of a related ligand, bearing an ethyldipyridine pendant arm in place of an aminopropyl group, was reduced into a non-cyclic aminoalcohol [Ni(L8)]$^{2+}$ shown in Scheme 2. This six-coordinate complex has a pseudooctahedral geometry with somewhat elongated axial bonds to N4 and N5 (Fig. 5). The equatorial bond between nickel(II) and an alcohol oxygen atom (2.185(4) Å) is longer than the rest of the equatorial bonds to nitrogen donors (from 2.003 to 2.112 Å). The acyclic compound [Ni(L8)]$^{2+}$, unlike its macrocyclic analogs, does not undergo reversible protonation of its pendant arm.

2.3 Complexes with pentadentate ligands derived from diacetylpyridine

2.6-Diacetylpyridine is less reactive than 2,6-diformylpyridine and undergoes template condensation with the tripod amine trpn only upon heating, yielding the previously described macrocycles [Ni(L3)]$^{2+}$, [Cu(L3)]$^{2+}$, or [Cu(L4)]$^{2+}$ (Scheme 3).

The heating of the nickel(II) complex [Ni(L3)]$^{2+}$ for several hours in slightly alkaline (pH 7.5–9) aqueous media resulted in the growth of a new band at 1662 cm$^{-1}$ in the IR spectrum. Although it was tempting to attribute these spectral changes to an isomerization reaction similar to the reactions of the copper macrocycles (Scheme 1), the mass spectrum of the product contained a very pronounced peak of a hydrate, [Ni(L3)](H$_2$O)$_{2+}$ (Fig. S5, ESI†). Isolation of the single crystals of this material proved that ring-opening hydrolysis of a C=N bond occurred.
Table 2 Initial rates of hydrolysis of [Ni(L3)]²⁺ in the presence of ethanol. (c[NiL] = 3.0 × 10⁻⁴ M, pH 8.0 (0.1 M triethanolamine), 70°C

<table>
<thead>
<tr>
<th>c(ETF)/M</th>
<th>k/min⁻¹</th>
</tr>
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<tbody>
<tr>
<td>0</td>
<td>(3.5 ± 0.8) × 10⁻³</td>
</tr>
<tr>
<td>3 × 10⁻³</td>
<td>(3.0 ± 0.6) × 10⁻³</td>
</tr>
<tr>
<td>6 × 10⁻³</td>
<td>(2.9 ± 0.4) × 10⁻³</td>
</tr>
<tr>
<td>9 × 10⁻³</td>
<td>(3.6 ± 0.4) × 10⁻³</td>
</tr>
<tr>
<td>3.0</td>
<td>(no reaction for 1 h)</td>
</tr>
<tr>
<td>6.0</td>
<td>(no reaction for 2 h)</td>
</tr>
</tbody>
</table>

Table 3 The extent of isomerization of [Cu(L3)]²⁺ into [Cu(L4)]²⁺ under different conditions. The 2 mM solutions of [Cu(L3)]²⁺ were heated for 6 h in sealed ampoules (or refluxed), rotary evaporated to dryness, and relative intensities of IR bands at 1622 cm⁻¹ (C–N conjugated with a pyridine ring) and 1680 cm⁻¹ (non-conjugated C–N) were estimated.

<table>
<thead>
<tr>
<th>Solvent</th>
<th>pH 8.0</th>
<th>pH 9.4</th>
</tr>
</thead>
<tbody>
<tr>
<td>H₂O</td>
<td>70°C</td>
<td>Reflux</td>
</tr>
<tr>
<td>H₂O–EtOH (2 eq.)</td>
<td>0% Decom.</td>
<td>10% Decom.</td>
</tr>
<tr>
<td>H₂O–EtOH (1% v/v)</td>
<td>0% N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>H₂O–EtOH (5% v/v)</td>
<td>25% N/A</td>
<td>70% N/A</td>
</tr>
<tr>
<td>H₂O–EtOH (10% v/v)</td>
<td>40% N/A</td>
<td>70% N/A</td>
</tr>
<tr>
<td>H₂O–EtOH (50% v/v)</td>
<td>80% N/A</td>
<td>90% N/A</td>
</tr>
<tr>
<td>H₂O–MeOH (50% v/v)</td>
<td>50% N/A</td>
<td>80% N/A</td>
</tr>
<tr>
<td>H₂O–TFH (50% v/v)</td>
<td>85% N/A</td>
<td>90% N/A</td>
</tr>
<tr>
<td>None (solid sample)</td>
<td>0% (100°C)</td>
<td>70% N/A</td>
</tr>
</tbody>
</table>

for the [Ni(L3)]²⁺, resulting in the formation of a pseudo-octahedral, six-coordinate species [Ni(L9)]²⁺. The X-ray structure of the hydrolyzed complex [Ni(L9)](ClO₄)₂ is identical to the structure of this high-spin compound described by Keypour et al.⁵⁻²⁶ for the product of incomplete macrocyclization of trpn and diacyetylpyridine. These data, taken together, demonstrate the reversible nature of the cyclization/hydrolysis reaction. The equilibrium shifts toward the hydrolyzed product in alkaline media, and toward the Schiff-base macrocycle in acidic media. Isolation of the pure [Ni(L9)](ClO₄)₂ in bulk quantities proved to be difficult, probably because of the presence of at least one hydrolysis/condensation equilibrium in the system. Nevertheless, the formation of a stable six-coordinate complex [Ni(L9)]²⁺ in a system derived from diacyetylpyridine supports the “open”, acyclic geometry of the precursor to the reduced complex [Ni(L8)]²⁺ derived from more labile diformylypyridine (Fig. 5, Scheme 2).

The initial rate of hydrolysis of [Ni(L3)]²⁺ was determined by UV-Vis spectrophotometry as a function of ethanol concentration (Table 2). The reaction rate is practically independent of the amount of ethanol when small quantities of alcohol were added. Large volume fractions of ethanol, however, suppressed absorbance changes due to ring-opening hydrolysis (no spectral changes were registered for the first 2 h at pH 8.0 at 70°C). It can be concluded that ethanol stabilizes the C–N bond with respect to hydrolysis into carbonyl and amine components. It is likely that an intermediate similar to [M(L6)]²⁺ is formed in the presence of EtOH, that does not undergo facile C–N bond breaking.

In summary, the nickel(ii) complex with ligand L3 undergoes a ring-opening hydrolysis upon heating in water. The steric and electronic effects of the methyl substituents destabilize a macrocyclic water adduct similar to [Ni(L5)]²⁺. The coordination preferences of the high-spin nickel(II) complex dictate the preferential formation of a six-coordinate, pseudo-octahedral hydrolysis product [Ni(L9)]²⁺.

In contrast, the copper(ii) complex [Cu(L3)]²⁺ undergoes isomerization in the process of Schiff-base condensation.²³ In order to investigate the isomerization reaction, substantial quantities of pure [Cu(L3)](ClO₄)₂ were needed. The reaction conditions for Cu(ii)-templated condensation between diacyetylpyridine and trpn were optimized for the preparation of [Cu(L3)]²⁺ free of the isomerized [Cu(L4)]²⁺ macrocycle. The reaction was monitored by IR (aliquots were taken every 30 min and rotary evaporated to dryness). The reaction mixture had a pH of 8.3, which was well suited for the macrocyclization. At higher pH (>8.7), decomposition products dominated. In water–ethanol mixtures at pH 8.3, no carbonyl stretches at ca. 1700 cm⁻¹ were observed after 2 h of reflux. After 2.5–3 h, the IR band at 1680 cm⁻¹ appeared, which corresponded to [Cu(L4)]²⁺. In order to avoid contamination with the isomeric macrocycle, the condensation was stopped after 2 h, yielding ca. 30% of pure [Cu(L3)](ClO₄)₂. Longer reaction times improved the combined yield of [Cu(L3)]²⁺ and [Cu(L4)]²⁺, but more extensive purification of [Cu(L3)](ClO₄)₂ was necessary, and the yield of the symmetric isomer decreased upon prolonged heating.

The pure macrocycle [Cu(L3)]²⁺, when heated in water–alcohol mixtures, undergoes isomerization into [Cu(L4)]²⁺, as evidenced by appearance of an IR band at 1680 cm⁻¹. The IR spectrum of the product isolated after refluxing [Cu(L3)]²⁺ in H₂O–EtOH (1:1) at pH 8.3 is identical to the spectrum obtained previously for crystallographically characterized [Cu(L4)](ClO₄)₂.²³ Both [Cu(L3)]²⁺ and [Cu(L4)]²⁺ gave identical mass spectra, with the molecular ion being a predominant peak, and no hydrate peak observed.

The unusual isomerization of [Cu(L3)]²⁺ was examined further, in order to better understand this process. The reaction was followed by IR, and the extent of isomerization was estimated from the intensity of the band at 1680 cm⁻¹ (relative to the band at 1622 cm⁻¹ in the solid residue obtained by removal of the solvent at room temperature. Unfortunately, the UV-Vis spectral changes in the course of isomerization were small and did not allow for quantitative kinetic studies.

The initial screening identified the relatively narrow “window” of reaction conditions that were suitable for clean isomerization. The [Cu(L3)]²⁺ complex developed a new band at 1680 cm⁻¹ when heated for several hours in water–ethanol mixtures at pH between 7.5 and 9.5. The temperatures were fairly high: from 70 °C to reflux. The isomerization rate increased upon increase in pH, but competitive decomposition into non-macrocyclic products also became significant at high pH values. This irreversible decomposition was partially suppressed by the addition of alcohol to the reaction mixture. The data suggest that alcohol also facilitated the double bond migration (Table 3). Small amounts of ethanol (several equivalents with respect to the copper complex) did not have any effect on the isomerization, while large volume fractions of ethanol or other alcohols were clearly beneficial. Unlike alcohols, THF had no effect on the isomerization even at 50 vol%. The reaction did not depend on the presence of air oxygen, as it also occurred in the sealed ampoules containing degassed solutions. The optimal conditions for preparative isomerization were found to be reflux in 50 vol% aqueous ethanol at pH ca. 8.5.

Several examples of double-bond migration in Schiff-base metal complexes have been reported in the literature.³⁶–⁶³ These isomerization reactions are similar to transaminations catalyzed by vitamin B₆ or other pyridoxal derivatives.⁶³–⁶⁴ The mechanisms of pyridoxal-dependent transaminations involve deprotonation of the C–H bond that yields a resonance-stabilized anion, followed by an addition of a proton to another carbon atom (Scheme 4, pathway A).⁶⁵ Coordination to the metal ion (e.g., copper(ii) in the macrocycle [Cu(L)]³⁺) would increase the acidity of the C–H bond and, consequently, may facilitate the isomerization. Numerous studies demonstrated that metal coordination often (although not always)⁶⁶ catalyzed transamination and related reactions in pyridoxal derivatives.⁶³–⁶⁴ The deprotonation/deprotonation of C–H bonds also
results in rapid H/D exchange at CH₂ groups adjacent to the C=N moiety. The deprotonation of the metal-coordinated picolyl moiety was also recently reported in a study of base-catalyzed hydrolysis of cobalt(III) complexes.

Scheme 4: Reaction scheme showing H/D exchange.

The H/D exchange in [Cu(L₃)]²⁺ was followed under various conditions by MALDI mass spectrometry. The H/D exchange in the copper(II) complex was also compared to the analogous nickel(II) complex [Ni(L₃)]²⁺, which undergoes a C=N bond hydrolysis instead of isomerization. Mass spectrometry clearly shows incorporation of 7–11 deuterium atoms upon heating of [Cu(L₃)]²⁺ or [Ni(L₃)]²⁺ in water or water–ethanol mixtures (Fig. 6). The number of D atoms incorporated into the macrocycle greatly exceeds the number of readily exchangeable NH protons in the pendant arm, indicating H/D exchange at the carbon atoms. The methyl groups adjacent to C=N bonds are the obvious candidates for efficient H/D exchange. These groups, together with the NH₂ group, can account for 8 deuterium atoms in the product. The remaining deuterium atoms are probably incorporated on the other side of the C=N bond, in agreement with the charge delocalization shown in Scheme 4.

Interestingly, the efficiency of H/D exchange is very similar in the copper(II) and nickel(II) complexes. Consequently, the difference in reaction products (double bond shift for Cu vs. ring-opening hydrolysis for Ni) is not caused by substantially different deprotonation rates.

Mass spectrometry also helped clarify the role of ethanol in the isomerization of [Cu(L₃)]²⁺. The H/D exchange was practically independent on the presence of ethanol in the reaction mixture: identical isotopic patterns were observed in the MALDI mass-spectra of the samples incubated in water as compared to the samples incubated in water–ethanol mixtures under otherwise identical conditions. It was found, however, that heating [Cu(L₃)]²⁺ in water at pH 7.5–9.4 gave rise to additional peaks in the MALDI spectra (Fig. 6). The (M + 18) peak was assigned to a hydrate (possibly similar to [Cu(L₅)]²⁺ or [Ni(L₉)]²⁺); the low molecular mass peaks corresponded to unidentified decomposition products. The fractions of both the hydrate and the decomposition products decreased significantly upon addition of ethanol to the reaction mixtures. It can be concluded that ethanol suppressed the hydration of the macrocycle [Cu(L₃)]²⁺ that could lead to ring-opening hydrolysis. The conditions necessary for isomerization are fairly harsh, and ethanol-induced stabilization of the macrocycle under these conditions (extended heating above 70 °C in alkaline media) prevented irreversible decomposition of the complex. The protective effect of ethanol addition to a double bond was also seen in the diformyl-derived complex [Cu(L₆)]²⁺, as described above.

The IR data suggest that the role of alcohol is not limited to preventing the decomposition of the macrocycle: the alcohols also somewhat increase the rates of isomerization (Table 3). One might suggest several possible explanations for the role of ethanol in facilitating [Cu(L₃)]²⁺ isomerization, including the following (Scheme 4): (1) relative stabilization of the macrocycle [Cu(L₃)]²⁺ that could lead to ring-opening hydrolysis; (2) the doublet (m/z 378, 380) corresponds to the molecular ion M⁺; (3) the complex [Cu(L₃)](ClO₄)₂ heated in D₂O–EtOD (5% v/v, pH 8.5) at 70 °C for 24 h; the major multiplet at m/z 380–390 corresponds to variable number of incorporated D atoms, while low intensity multiplets at m/z ca. 330 and ca. 398 correspond to decomposition products and a hydrate, respectively; (iii) complex [Cu(L₃)](ClO₄)₂ heated in D₂O (pH 8.5) at 70 °C for 24 h; the intensity of the peaks of byproducts is higher than that observed in the presence of EtOD.

Fig. 6 MALDI mass spectra of: (i) pure complex [Cu(L₃)](ClO₄)₂; (ii) complex [Cu(L₃)](ClO₄)₂ heated in D₂O–EtOD (5% v/v, pH 8.5) at 70 °C for 24 h; and (iii) complex [Cu(L₃)](ClO₄)₂ heated in D₂O (pH 8.5) at 70 °C for 24 h; the intensity of the peaks of byproducts is higher than that observed in the presence of EtOD.
anion formed upon deprotonation of $\text{[Cu(L3)]}^{2+}$, due to either solvation effects, or stronger basic properties of OEt$^-$ as compared to OH$^-$ (pathway A); (2) an "electronic allosteric effect": addition of EtOH to a C=N double bond changes the electron density at the metal center and facilitates migration of the remaining C=N bond in the other "half" of the macrocyclic ring (pathway B) (the experimental evidence in favor of this hypothesis is provided by different $\lambda_{\text{max}}$ in UV-Vis spectra of $\text{[Cu(L5)]}^{2+}$ vs. $\text{[Cu(L6)]}^{2+}$; (3) a concerted intramolecular rearrangement of the EtOH adduct (pathway C). Pathway A is the most likely mechanism, with precedents in double bond migration in $\text{Bk}_4$ derivatives and in metallocomplexes with Schiff-base ligands.  

3 Summary and conclusions

Pyridine-containing Schiff-base macrocyclic complexes contain a rigid fragment composed of two azomethine C=N bonds conjugated with the aromatic ring. Small 14-membered macrocyclic rings with a coordinating pendant arm attached to a secondary amino group exhibit significant steric strain upon complexation with 3d-metal ions. In order to accommodate copper(ii) or nickel(ii) inside the cavity, the Schiff-base macrocycles undergo several different reactions that yield more flexible ligands. The outcome of these reactions depends on the nature on the ligands, as well as on the coordination preferences of the metal ions.

The copper(ii) and nickel(ii) complexes synthesized from pyridine-containing Schiff-base ligands are substantially more stable than their counterparts lacking the methyl groups. The nickel(ii) complex undergoes ring-opening hydrolysis upon heating in water, producing a six-coordinate, pseudo-octahedral acetylpyridine product. In contrast, the copper(ii) complex retains the cyclic structure, but one of the double bonds shifts, increasing the flexibility of the macrocyclic complex. This double bond migration is similar to the pyridoxal-dependent transamination reactions. Deprotonation/protonation of the C–H bonds in the copper(ii) complex is evidenced by facile H/D exchange proven by MALDI mass spectrometry. The double bond migration occurs in slightly alkaline media and is facilitated by the addition of alcohols. Alcohol addition also prevents full decomposition of the macrocycle.

The difference in reactivity between $\text{[Cu(L3)]}^{2+}$ and $\text{[Ni(L3)]}^{2+}$ appears to be caused by the different coordination requirements of these two metal ions: Ni(ii) adopts a pseudo-octahedral six-coordinate geometry in a non-cyclic hydrolysis product $\text{[Ni(L9)]}^{2+}$, while copper(ii) retains a square-pyramidal, five-coordinated geometry favorable for a d$^9$ metal ion, in the isomerized product $\text{[Cu(L4)]}^{2+}$. In the case of Ni(ii), the steric strain of the conjugated macrocycle is relieved by hydrolysis and ring-opening, whereas in the case of Cu(ii), the steric strain is partially relieved by shifting the C=N double bond further away from the pyridine ring, thus increasing the flexibility of the pyridine-containing fragment of the macrocycle.

The four-coordinate copper(ii) complex without a pendant arm is substantially more stable than its five-coordinate analog with an aminopropyl pendant arm. This complex undergoes a partial double bond migration under harsh conditions (boiling in water-ethanol mixtures above pH 8), as evidenced by IR and UV-Vis spectrometry and by X-ray crystallography.

Experimental

MALDI-TOF MS spectra were obtained on a Bruker Biflex MALDI-TOF spectrometer operating in positive reflection mode. Calibration was performed with externally referenced CsI clusters. Samples were prepared by the dried-droplet method of a 1 : 10 mixture of the analyte in solution and saturated matrix (dithranol) in acetonitrile. Spectra were acquired with XACQ 4.0 and processed with XMASS 5.0. IR spectra were recorded on a Mattson 1000 FTIR Spectrometer in KBr disks. UV-Vis spectra were obtained on a Hitachi U-2000 spectrometer (300–1100 nm). Elemental analyses were performed by Qualitative Technologies Inc (Whitehouse, NJ). Electrospray mass spectra were obtained by HT Laboratory (San Diego, CA).

Synthesis of $\text{[Ni(L1)](ClO}_4\text{)}_2$ and $\text{[Cu(L1)](ClO}_4\text{)}_2$

This was performed according to published procedures, and the corresponding copper(ii) complex $\text{[Cu(L1)](ClO}_4\text{)}_2$ was synthesized as described previously. The copper(ii) complex has a UV-Vis spectrum in methanol ($\lambda_{\text{max}}$ = 560 nm) somewhat different from that described by Lindoy et al. ($\lambda_{\text{max}}$ = 664 nm).

Single crystals of $\text{[Cu(L1)](ClO}_4\text{)}_2$ were obtained by slow diffusion of diethyl ether into an acetonitrile solution. Anal: Found: C, 34.27; H, 4.51; N, 10.63. Calc. for $\text{C}_{34}\text{H}_{34}\text{N}_2\text{CuClO}_4$: C, 34.59; H, 4.26; N, 10.76%.

Isomerization of $\text{[Cu(L1)](ClO}_4\text{)}_2$

The title complex was recrystallized from warm water; pure material contained IR bands at 1585 and 1625 cm$^{-1}$, and did not contain any IR bands between 1630 and 1850 cm$^{-1}$. This complex (0.2 g) was dissolved in 50 ml of water, pH was adjusted to 8.5, and 50 ml of EtOH were added. The solution was refluxed for 7 h, then rotary evaporated yielding a purple microcrystalline residue. The material was dissolved in 5 ml of acetonitrile, and crystallized by slow diffusion of diethyl ether. Dark purple needles of $\text{[Cu(L2)](ClO}_4\text{)}_2$ were filtered off, carefully washed with acetonitrile–diethyl ether, then with diethyl ether, and air-dried. Anal: Found: C, 34.39; H, 4.43; N, 10.92. Calc. for $\text{C}_{36}\text{H}_{34}\text{N}_2\text{CuClO}_4$: C, 34.59; H, 4.26; N, 10.76%. IR: 1585, 1625, 1677 cm$^{-1}$. UV-Vis (MeOH): $\lambda_{\text{max}}$ = 552 nm. MS: m/z: 321, 323 (M$^+$). X-Ray quality crystals were obtained by slow diffusion of diethyl ether into an acetonitrile solution.

The same procedure was also applied to $\text{[Ni(L1)](ClO}_4\text{)}_2$, yielding a yellow oil that contained a new band at 1667 cm$^{-1}$. Attempts to crystallize, purify, and identify this material were unsuccessful.

Synthesis of $\text{[Cu(L3)](ClO}_4\text{)}_2$

The previously described procedure was modified as follows. The triiodopal tetramine trpn (1 mmol) was dissolved in 200 mL of water and mixed with a solution of 1 mmol of $\text{Cu(ClO}_4\text{)}_2$; 6H$_2$O in 50 mL of water. To the resulting mixture, a solution of 1 mmol of 2,6-diacetylpyridine in 300 mL of ethanol was added upon stirring over a period of 10 min. The reaction mixture was stirred at reflux for 2 h, filtered, and rotary evaporated to 70 ml. The blue precipitate formed upon cooling was collected by filtration, washed with small portions of water, ethanol, and diethyl ether, and dried in a desiccator overnight. An additional amount of solid was obtained from the filtrate. The combined crude product was dissolved in a minimum volume of acetonitrile, filtered, and slowly diluted with ethanol. The blue fine precipitate that formed upon standing was collected. Yield
Upon the addition of the copper salt the solution instantly (br, ClO$_4^-$) or electrospray) a brown product was dissolved in 100 mL of water at room temperature. Once cool, the undissolved complex was prepared by heating until boiling and then left to slowly cool to {[Cu(L5)](ClO$_4^-$)} were obtained by slow diffusion of diethyl ether into an acetonitrile solution of the material.

**Synthesis of [Ni(L9)](ClO$_4^-$)**

A solution of [Ni(L3)](ClO$_4^-$) (10 mM) in water (pH 8.3) was heated at 75 °C for 8 h. The solution was rotary evaporated to a small volume, and 5 equiv. of NaClO$_4$·H$_2$O were added. The brick-red precipitate was filtered and recrystallized by slow diffusion of diethyl ether into a concentrated acetonitrile solution. MS (FAB, NBA): m/z 390, 392 (M$^+$). IR: 1585, 1620, 1661 cm$^{-1}$. The crystallographically characterized material is identical to the product of incomplete template condensation described by Keypour et al.~

**X-Ray diffraction studies**

Crystal data are summarized in Table 4. Data for [Cu(L1)]·(ClO$_4^-$), [Cu(L2)]·(ClO$_4^-$), [Ni(L5)]·(ClO$_4^-$), [Ni(L5)]·(ClO$_4^-$)·CH$_3$CN and [Cu(L5)]·(ClO$_4^-$) were collected using a Bruker SMART CCD (charge coupled device) based diffractometer equipped with an LT-3 low-temperature apparatus operating at 213 K. A suitable crystal was chosen and mounted on a glass fiber using paratone oil. Data were measured using $\omega$ scans of 0.3° per frame for 30 s, such that a hemisphere was collected. A total of 1271 frames were collected with a maximum resolution of 0.75 Å. Data for [Cu(L6)]·(ClO$_4^-$) and [Ni(L8)]·(ClO$_4^-$) were collected at 298 K; the crystals were mounted on a glass fiber using glue. A total of 1650 frames were collected with a maximum resolution of 0.75 Å for [Ni(L8)]·(ClO$_4^-$) and for [Cu(L6)]·(ClO$_4^-$). The first 50 frames were recollected at the end of data collection to monitor for decay. None of the crystals showed any decomposition during data collection. Cell parameters were retrieved using SMART~27 software and refined using SAINT on all observed reflections. Data reduction was performed using the SAINT~28 software which corrects for Lp and decay.

Single crystal intensity measurements for [Ni(L9)]·(ClO$_4^-$) were collected at room temperature with a Rigaku AFC5 diffractometer, using Mo-K$_\alpha$ radiation, graphite monochromator and $\omega$-2$\theta$-scans. Lattice parameters were obtained using least squares refinement of the angles of 24 reflections with 22 < 2$\theta$ < 26°. The structure was shown to be identical to previously published by Keypour et al.~

The structures were solved by the direct method using the SHELXS-97~29 program and refined by least squares method on F$^2$. SHELXL-97~30 incorporated in SHELXTL V5.10.~

The absorption corrections were applied using SADABS~31,~32 supplied by Shelldrick. All non-hydrogen atoms are refined anisotropically. Hydrogens were calculated by geometrical methods and refined as a riding model. Illustrations were generated using ORTEP~33 and SHELXTL.~

The crystal of [Cu(L2)]·(ClO$_4^-$) was shown to be twinned, and refined with the twin law, TWIN = -1 0 0 0 -1 0 1 0 1 -4 and refined BAFS 0.21755 0.23530 0.27092. The double bond was through the use of vigorous stirring, yielding a brick-red solution. Once cooled to room temperature the solution was then filtered to remove trace impurities. To this solution 0.874 g of NaBH$_4$ (0.023 mol) was added over a period of 10–15 min. The reaction mixture was seen to become black and precipitation of a gray solid was observed. The solution was left under vigorous stirring overnight. During this time the solid re-dissolved, yielding a violet solution. The pH was then adjusted to between 8.5–9 through the addition of concentrated HClO$_4$, and the solution was rotary evaporated to dryness (water bath temperature ~30–40 °C). The complex was allowed to dry overnight under vacuum. Impurities resulting from the use of NaBH$_4$ were subsequently removed by dissolving the desired product in nitromethane and filtering off insoluble material. Yield 192 mg (32%). MALDI-TOF MS: m/z 415 (M$^+$). X-Ray quality crystals of the material [Ni(L8)]·(ClO$_4^-$) were prepared by slow diffusion of diethyl ether into the acetonitrile solution of the material.

**Synthesis of [Cu(L5)](ClO$_4^-$)**

0.37 g (1 mmol) of Cu(ClO$_4^-$)·6H$_2$O was dissolved in 17 mL of water. This solution was added to a stirred solution of 0.19 g (1 mmol) of tris(3-aminopyrrolidin)e in 67 mL of water. Upon the addition of the copper salt the solution instantly changed from clear to dark blue (pH between 8–9). A solution of 0.132 g (1 mmol) diformylpyridine (synthesized by a previously reported procedure~39) in 100 mL of ethanol was subsequently added to the mixture over a period of 20–25 min (the color changed from the original dark blue to purplish blue) and stirring at room temperature continued for four days. The solution was then rotary evaporated to dryness, using a water bath at ~25 °C and condenser with chilled water (heating the reaction mixture resulted in decomposition of the product), and the dark blue solid containing small amounts of a violet solid (determined by X-ray crystallography to be the same complex with no acetonitrile in the crystal lattice) was allowed to dry overnight under vacuum. Yield: 0.50 g (88%). Crystallization occurred by dissolving the residue in the minimum volume of acetonitrile followed by diethyl ether diffusion into the solution. The complex was allowed to dry overnight under vacuum. Anal. Found: C, 34.37; H, 5.17; N, 11.93; Cu, 10.46. Calc. for C$_{12}$H$_9$N$_3$CuClO$_4$: C, 33.84; H, 4.79; N, 12.33; Cu, 11.19%. IR (KBr): 1637w ($\nu$C=O), 1603m, 1586m, (pyridine and NH), 1100 (br, ClO$_4^-$) cm$^{-1}$. MALDI-TOF Massin 4760 (CuClO$_4^-$), 3391 (ClO$_4^-$) cm$^{-1}$.

**Synthesis of [Cu(L6)](ClO$_4^-$)**

Approximately 10 mL of a saturated ethanolic solution of [Cu(L5)]·(ClO$_4^-$) was prepared in a vial. This solution was prepared by heating until boiling and then left to slowly cool to room temperature. Once cool, the undissolved complex was filtered off via vacuum filtration and the mother-liquid was left in a capped vial. Within 3 days small crystals formed. Anal. Found: C, 36.38; H, 5.33; N, 11.23; Cu, 10.21. Calc. for C$_{12}$H$_9$N$_3$CuClO$_4$: C, 36.28; H, 5.24; N, 11.75; Cu, 10.59%. MALDI-TOF MS: m/z 394 (CuL$^+$), 350 (Cu$^+$· EtOH). UV-Vis (nitromethane), 432 (sym (M$^+$) cm$^{-1}$) and 940 (57). IR (KBr): 1598w ($\nu$C=O), 1490m, 1363m, (pyridine and NH), 1100 (br, ClO$_4^-$) cm$^{-1}$.

**Synthesis of [Ni(L8)](ClO$_4^-$)**

236 mg (1 mmol) of 2,6-bis-(2-aminophenyl)pyridine~35 was dissolved in 50 mL of methanol and mixed with a solution of 366 mg (1 mmol) of Ni(ClO$_4^-$)·6H$_2$O in 50 mL of water. To the resulting light-blue solution was added 135 mg (1 mmol) of 2,6-diformylpyridine~14 dissolved in 50 mL of ethanol over a period of 10 min. The mixture was stirred at room temperature for 24 h. The solvent was removed in vacuo, the resulting solid brown product was dissolved in 100 mL of water at ~50 °C, with the two ligands. 

Upon the addition of the copper salt the solution instantly (br, ClO$_4^-$) or electrospray) a brown product was dissolved in 100 mL of water at room temperature. Once cool, the undissolved complex was prepared by heating until boiling and then left to slowly cool to room temperature. Once cool, the undissolved complex was filtered off via vacuum filtration and the mother-liquid was left in a capped vial. Within 3 days small crystals formed. Anal. Found: C, 36.38; H, 5.33; N, 11.23; Cu, 10.21. Calc. for C$_{12}$H$_9$N$_3$CuClO$_4$: C, 36.28; H, 5.24; N, 11.75; Cu, 10.59%. MALDI-TOF MS: m/z 394 (CuL$^+$), 350 (Cu$^+$· EtOH). UV-Vis (nitromethane), 432 (sym (M$^+$) cm$^{-1}$) and 940 (57). IR (KBr): 1598w ($\nu$C=O), 1490m, 1363m, (pyridine and NH), 1100 (br, ClO$_4^-$) cm$^{-1}$.
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References
