Five coordination modes of 4-aminopyrimidine with N-hydroxy-ethylethlenediamintriacetatoruthenate(II)

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Summary
The complex \([\text{Ru}^0\text{(hedta)}(4\text{NH}_2\text{pym})]^-\), \(\text{hedta}^{3-} = \text{N-hydroxyethylethlenediamintriacetate}, \) \(4\text{NH}_2\text{pym} = \text{4-aminopyrimidine}, \) exists at \(pH\ 7\) as five different coordination isomers, which are most readily distinguished by their electrochemical waves in comparison with the 2-aminopyridine (2NH2py) complex. The 2NH2py complex exhibits \(\eta^1\) (pyridine bound), \(\eta^2\)-NH2 (amine bound) and \(\eta^3\) (NH2-chelated species). The 4NH2pym complex forms \(\eta^1\) (exo-amine and NH2-chelated isomers analogous to the 2NH2py species, but also engages in \(\eta^2\) (olefin bound) coordination of the dearomatized 4NH2pym ring in C(5)-C(6), and another \(\eta^2\) type of complex involving electron density between N(1) and N(3) of the ring \(\eta^2\) form). N(1), \(\eta^2\) and \(\eta^3\) isomers have also been detected for unsubstituted pyrimidine (pym), 4-methylpyrimidine (4CH3pym) and 2-aminopyrimidine (2NH2pym). Electrochemical waves (V versus NHE) for the five isomers are assigned as follows: \([\text{Ru}^0\text{(hedta)}\text{(exo-NH}_2\text{H}_2\text{pym)]]; N(1)(0.29 V), \) \(\eta^2\) (0.49 V); \([\text{Ru}^0\text{(hedta)}\text{(2NH}_2\text{pym)}]; \) \(\eta^3\) (0.76 V); N(3), NH2-chelated (1.09 V).

Introduction
\([\text{Ru}^0\text{(hedta)}\text{]}\), \(\text{hedta}^{3-} = \text{N-hydroxyethylethlenediamintriacetate}, \) readily forms complexes with \(\pi\)-acceptor ligands (CO, pyridines, pyrazines) \(1^{9,10}\) and \(\eta^2\) complexes with olefins, styrenes and acetylenes \(1^{6,9}\). A similar chemistry is known for the closely related \([\text{Ru}^0\text{(hedta)}\text{]}\) \(2^{+}\) species, studied previously by Diamantis and Dubrawski \(4^{4,5}\) and Matsubara and Creutz \(6^{6,7}\). In 1990, Zhang et al. discovered that \([\text{Ru}^0\text{(hedta)}\text{]}\) also form \(\eta^2\) complexes via the C(5)-C(6) bonds of the pyrimidine nucleobases cytidine (C) and uridine (U), and related pyrimidine nucleobase derivatives \(8^{8,9}\). These \(\eta^2\) isomers exist in isomeric competition with coordination of the ruthenium(II) centre at the normal N(3) position and, at high pH, with a chelated form which involves N(3) and, at high pH, with a chelated form that is unavailable for pym and 4CH3pym:

The \(\eta^2\) isomers of \([\text{Ru}^0\text{(hedta)}\text{]}\) and pyrimidines are particularly unusual. There have been over 750 metallo-pyrimidine complexes characterized for a wide range of hard and soft metal centres, and none of these were for \(\eta^2\) complexes \(9^{9,10}\). The affinity of \([\text{Ru}^0\text{(hedta)}\text{]}\) for the \(\eta^2\) pyrimidine structure is increased by the electron withdrawing \(\pi\)-keto functionality of uracils and uridines \(11^{11,12}\) and by fluorine, chlorine, bromine or iodine as a five-substituent of these rings \(12^{12}\), but is decreased by the presence of the exo-amine of cytosine derivatives \(8^{8,11,12}\) and \(\eta^3\) (NH2-chelated) and by methylation at C(5) \(8^{8,11,12}\).

The attachment of \([\text{Ru}^0\text{(hedta)}\text{]}\) to the C(5)-C(6) bond promotes a loss of aromaticity as illustrated by \(^1H\) and \(^13C\) n.m.r. data for the complexes \(9^{8,11,12}\). The decrease in aromaticity occurs when the strength of \(\pi\)-donation from the metal centre plus three isolated double bonds

exceeds the resonance energy of the isolated ring as observed for \([\text{Ru}^0\text{(NH}_3\text{)}\text{]}\) and \([\text{Os}^0\text{(NH}_3\text{)}\text{]}\) \(2^{2} \) \(\eta^2\)-substituted arenes \(13^{13}\), 2,6-lutidine \(14^{14}\), anilines \(15^{15}\) and 3,5-dimethylpyrrole \(16^{16}\).

The coordination of \([\text{Ru}^0\text{(NH}_3\text{)}\text{]}\) \(3^{3}\) and \([\text{Ru}^0\text{(NH}_3\text{)}\text{]}\) to the cytosines has been studied by Clarke \(17^{17}\). The ruthenium(III) form favours coordination on the deprotonated exo-amine at C(4). Reduction of the ruthenium(III) complex to \([\text{Ru}^0\text{(NH}_3\text{)}\text{]}\text{(cytosine)}\) \(2^{2}\) occurs with the facile migration of the metal to the N(3) site, which stabilizes ruthenium(II) by means of greater \(\pi\)-backbonding into the ring structure. \([\text{Ru}^0\text{(hedta)}\text{]}\) coordinates to 5-fluorocytosine at the exo-deprotonated amine \(47^{47}\) as well as N(3) \(24^{24}\) and \(\eta^2\) (27.9\%) \(11^{11,12}\). However, protonation of the deprotonated amine causes the dissociation of \([\text{Ru}^0\text{(hedta)(H}_2\text{O)}\text{]}\) from the 5-fluorocytosine ligand, rather than direct migration to N(3) as seen with the \([\text{Ru}^0\text{(NH}_3\text{)}\text{]}\) \(2^{2}\) unit.

We have recently presented a preliminary disclosure of the first reported \(\eta^2\) complexes of simple \(\pi\)-heterocyclic rings by a ruthenium(II) chromophore \(18^{18}\). The complexes of \([\text{Ru}^0\text{(hedta)}\text{]}\) with the substituted pyrimidine ring (pym), 4-methylpyrimidine (4CH3pym) and 2-aminopyrimidine (2NH2pym) reveal three coordination modes for these ligands. These are the N(1) (pyridine-nitrogen) type of isomer, the \(\eta^2\) complex \(19^{19}\) and an "\(\eta^2\)" form \(19^{19}\) along the arc of electron density between N(1) and N(3).

No evidence for an exo-amine complex was observed for 2NH2pym, probably due to the reduced basicity of the 2-amino moiety which resides between two electron withdrawing nitrogen atoms of the ring.

The \(\eta^2\)-[Ru0(hedta)(2NH2pym)] complex exhibits rapid fluxional behaviour between the C(5)-C(6) and C(4)-C(5) bonds. This is facilitated by an ionic resonance form that is unavailable for pym and 4CH3pym:

Consistent with this explanation, \([\text{Ru}^0\text{(hedta)(pym)}\text{]}\) and \([\text{Ru}^0\text{(hedta)(4CH}_3\text{pym)}\text{]}\) are not fluxional. Studies of the pym, 4CH3pym and 2NH2pym complexes are necessary to interpret the isomeric behaviour when 4-aminopyrimidine (4NH2pym) coordinates \([\text{Ru}^0\text{(hedta)}\text{]}\), wherein two additional interactions with the exo-amine functionality are observed. The isomeric equilibria, together with protonated and deprotonated species which have been found for pym, 4CH3pym and 2NH2pym are shown in Scheme 1.

Forms (1) and (1B) are the N(1) isomers, (2) and (2B) the \(\eta^2\) isomers, and (3) and (3B) the \(\eta^3\) isomers. It will be shown in this paper that 4NH2pym forms analogues of these as well as an exo-amine and N(3), NH2-chelated isomer. The coordination behaviour of 2-aminopyrimidine.

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Scheme 1. R' = H; R = H or Me; R' = NH2; R = H.

pyridine (2NH2py) was also examined as a model system for the latter two interactions with 4NH2pym.

Experimental

Na[Ru4(hedta)(H2O)]·4H2O and K[Ru4(hedta)Cl] were prepared as reported previously. Electrochemical measurements were performed at a glassy carbon working electrode on an IBM EC225 voltammetric analyser as previously. A standard three-electrode assembly using a NaCl saturated calomel reference electrode (s.s.c.e.) was employed. Measurements were performed at room temperature (22°C) with 0.10 N NaCl as the supporting electrolyte. pH adjustments were made by adding 1 M HCl or NaOH via a microsyringe. pH readings were obtained with a Fisher Accument pH meter calibrated with standard commercial buffers. The pH probe was a mini combination glass/s.c.e., mounted in the electrochemical cell via a rubber septum port. Measurements and syntheses were performed under argon. Ruthenium complexes at desired concentrations in aqueous solution (near 5.0 x 10⁻³ M for c.v. or d.p.p., and 0.05 M for 1H and 13C n.m.r. studies) were pretreated with zinc/mercury for 30 min under argon to reduce ruthenium(III) for the ruthenium(II) precursor complex or to remove traces of ruthenium(III) from Na[Ru4(hedta)(H2O)]·4H2O. A slight excess of ligand [1.05:1.0 ruthenium(II)] was added to a 10.0 ml round bottom flask together with a zinc/mercury chip. This flask was sealed with a septum and purged with argon. The reduced [Ru4(hedta)(H2O)]⁻ solution was transferred from the reducing chamber, a similar round-bottom flask, by means of argon pressure with passage of solutions through surgical tygon tubing and stainless steel needles. These systems were either sampled with time for electrochemical analysis to study ligand addition reactions, or were kept sealed for at least 20 h before product characterization using c.v. and d.p.p. Previous experience with [Ru4(hedta)]⁻ olefin and pyridine complexes has shown that 20 h is sufficient to allow formation of most η¹ complexes. In the course of these studies it was determined that equilibrium amounts of N(1) and η¹ complexes required at least 4 days for the linkage isomerism processes to be complete. The additional time was utilized as necessary to achieve equilibrium amounts of species as monitored by d.p.p. and by ¹H n.m.r. methods. Transfers to argon purged n.m.r. tubes were performed by the same syringe or inert atmosphere procedures on the more concentrated solutions, prepared in D₂O. ¹H n.m.r. signals were referenced to the HOD resonance. Spectra were obtained on 300 MHz Bruker and 500 MHz Bruker n.m.r. spectrometers. Assignments of ¹H n.m.r. spectra were assisted by standard decoupling procedures, together with the relative intensity patterns of the different isomers in correlation with the amounts of the same isomers as indicated by the electrochemical procedures. All ligands were obtained from Aldrich and used as supplied.

Results and discussion

The three isomers of [Ru4(hedta)L]⁻ for pym, 4CH₃pym and NH₂pym have been characterized by ¹H n.m.r. as shown in Table 1. The amounts of the three isomers are given in Table 2 as a function of pH. The half-wave (E₁/2) values in volts versus NHE are also given in Table 2 as determined by c.v. and d.p.p. methods. Several features are noteworthy from these tables. The C(4)-H of the pym and 2NH₂pym complexes experience upfield shifts [positive A₅ for (5 free ligand-5 complex)] for the C(4)-H by the influence of these resonance forms:

Species/ligand H(2) H(4)(CH₃) H(5) H(6)

<table>
<thead>
<tr>
<th>Species/ligand</th>
<th>H(2)</th>
<th>H(4)(CH₃)</th>
<th>H(5)</th>
<th>H(6)</th>
</tr>
</thead>
<tbody>
<tr>
<td>pym</td>
<td>9.23(±0.22)d</td>
<td>7.31(+1.37)q</td>
<td>7.43, 7.41(+0.07)q</td>
<td>8.73(±0.03)d</td>
</tr>
<tr>
<td>4CH₃pym</td>
<td>9.02(±0.21)bs</td>
<td>2.52(±0.08)s</td>
<td>7.35, 7.36(±0.03)t</td>
<td>8.68(±0.19)bs</td>
</tr>
<tr>
<td>2NH₂pym</td>
<td>9.17(±0.17)s</td>
<td>7.94(+0.24)d</td>
<td>6.84, 6.82(±0.16)m</td>
<td>8.21(±0.03)m</td>
</tr>
</tbody>
</table>

A positive A₅ is an upfield shift; assignments confirmed by decoupling procedures; ¹H n.m.r. resonance; species (3) is not abundant at pH 7 for 4CH₃pym or 2NH₂pym.