Synthesis and Crystal Structure of 5-(2-Pyridylmethylene)hydantoin (Hpyhy) and Complexes of pyhy with Nickel(II) and Copper(II)

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A new synthesis and the crystal structures of 5-(2-pyridylmethylene)hydantoin (Hpyhy) **1** and its first transition metal complexes **2** and **3** are reported.

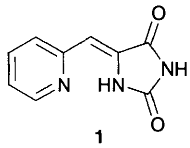
Hydantoins substituted at the C-5 position exhibit a wide range of pharmacological activities including anticonvulsant,[1] antidepressant[2] and platelet aggregation inhibitory activities[3] and they are an important structural feature of several aldose reductase inhibitors.[4] Given this level of biological activity the synthesis of coordination compounds that incorporate the hydantoin fragment could be significant. In this communication, an improved synthesis of the didentate ligand 5-(2-pyridylmethylene)hydantoin **1** is described. It has the appropriate conformation and bite angle enabling it to form stable complexes with transition metals. Furthermore, these complexes retain the ability to form complementary hydrogen bonds with nucleotide bases through the C(O)–NH–C(O) moiety on the hydantoin ring. We have previously suggested[5] that bifunctional coordination compounds of this type may show interesting biological activities and be used for the crystal engineering of coordination compounds.

Previously reported syntheses of Hpyhy have been based either on (i) condensation of hydantoin with 2-pyridylcarboxaldehyde[6] or (ii) bromination of hydantoin at the 5-position followed by a Michaelis–Arbuzov reaction with triethylphosphate and subsequent reaction of the Horner–Wadsworth–Emmons type product with 2-pyridylcarboxaldehyde.[7] The former method is the more selective, giving only the Z-isomer, though the yield would appear to be strongly dependent on the condensation agent used.

The reaction in Scheme 1, which uses piperidine as both base and solvent and high temperatures, has yielded Hpyhy in exclusively the Z-conformation (> 70% yield).

A single crystal structural analysis† on a crystal grown from glacial acetic acid (Fig. 1) has confirmed the Z-conformation. The angle between the mean planes of the hydantoin and pyridyl moieties is only 2.2° as a result of the strong intramolecular hydrogen bond between N(1)–H and N(8) [N(8)–H 1.99 Å]. The C(7)–C(6) [1.461(3) Å] and C(6)–C(5) [1.336(3) Å] bond lengths together with shifts in the ν(C=C) stretching mode suggest the formation of a delocalised system that extends to include the N(1)H atom. This bonding pattern is consistent with that proposed theoretically by Tan.[8]

Despite the obvious relationship between **1** and bipyridyl and phenanthroline, no metal complexes of pyhy have been previously reported. Addition of an aqueous solution of $Ni(ClO_4)_2{\cdot}6H_2O$ to a methanolic solution of Hpyhy gave, on reflux, a green precipitate that analysed correctly for $[Ni(pyhy)(OH_2)_4]ClO_4{\cdot}H_2O$ **2**. A single crystal analysis‡ on crystals obtained from glacial acetic acid, confirmed this formulation and the molecular structure is shown in Fig. 2. The octahedral coordination sphere of the nickel atom is made up from the two chelating nitrogen atoms of the pyhy ligand and four water molecules. The Ni–N(1) and Ni–N(8) bond lengths are 2.009(2) and 2.107(2) Å, respectively, and the N(1)–Ni–N(8) bond angle is 91.7(1)°, a value similar to that observed in complexes of 2-(2-aminoethyl)pyridine.[9] This angle is also, as expected, somewhat larger than that observed for tetra-aqua



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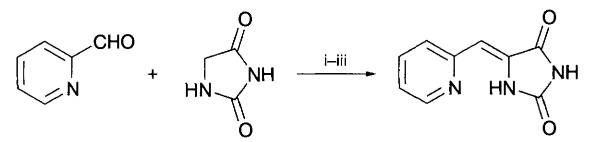


Scheme 1 *Reagents and conditions*: i, piperidine, 130 °C, 1 h; ii, H_2O, 60 °C; iii, HCl, room temp.

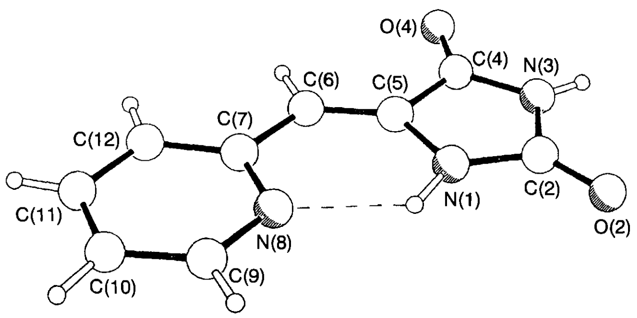
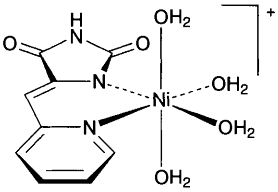


Fig. 1 The molecular structure of 5-(2-pyridylmethylene)hydantoin showing the intramolecular hydrogen bond between N(1)H and N(8)



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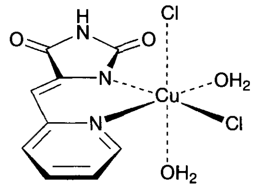

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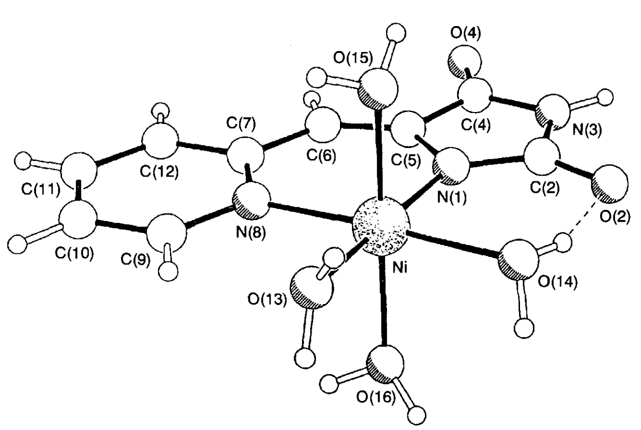

Fig. 2 Molecular structure of the $[Ni(pyhy)(OH_2)_4]^+$ ion showing the octahedral coordination geometry for the nickel atom and the intramolecular hydrogen bond between O(14)H and O(2). Selected bond lengths (Å): Ni–N(1), 2.009(2), Ni–N(8) 2.107(2), Ni–O(13) 2.102(2), Ni-O(14) 2.125(2), Ni-O(15) 2.083(2), Ni–O(16) 2.093(2).

complexes containing bipyridyl[10] and phenanthroline.[11] The Ni–O bond lengths lie between 2.083(2) and 2.125(2) Å, with the Ni–O (axial) distances being significantly shorter than the Ni–O (equatorial). There is an intramolecular hydrogen bond between a hydrogen atom of one of the aqua ligands [O(14)] and hydantoin carbonyl oxygen [O(2)], [H···O(2) 1.76 Å]. The complexes are linked by intermolecular hydrogen bonds that involve the aqua ligands, the hydantoin CO and NH groups, the oxygen atoms of the perchlorate anions and a free water molecule creating a complex three-dimensional network.

Addition of an aqueous solution of $CuCl_2 \cdot 6H_2O$ to a methanolic solution of Hpyhy (2 equiv.) gave a green precipitate that analysed correctly for $[CuCl(pyhy)(OH_2)]$ **3**. Crystals suitable for X-ray diffraction were grown by slow evaporation of an glacial acetic acid solution. The X-ray analysis§ confirmed the above formulation and the molecular structure is shown in Fig. 3. The complex has a polymeric structure based on distorted octahedral coordination centres linked through asymmetric double chloro- and aqua-bridges. The distortions in the copper complex compared to the symmetrical structure observed for the related nickel(II) complex is not surprising given the d^9 configuration of the metal ion. Whereas in **2** accommodation of the nickel ion involves an increase in the interior C-6 angle, in **3** the copper ion coordination is accompanied by a torsional twist about C(6)–C(7), the interior angle remaining unchanged.¶ The Cu–N distances, 2.028(3) and 1.962(2) Å, differ less than those in **2** and the Cu–O lengths within the asymmetric Cu–O–Cu bridges are 2.013(3) and 2.72(1) Å, respectively. The associated Cu–Cl bridge distances are 2.255(1) and 3.25(1) Å.

Each linear polymeric chain of copper complexes is cross-linked *via* intermolecular hydrogen bonds involving the Cu–O–Cu bridging aqua oxygen atoms in one chain and one of the hydantoin carbonyl oxygen atoms in another and *vice versa*. The hydrogen bonded array is further extended by intermolecular hydrogen bonds involving the hydantoin carbonyl and NH groups.

We have established that Hpyhy may be obtained in the appropriate conformation in good yields and that it readily forms octahedral complexes with Ni^{II} and Cu^{II}. We have also established that the complexes form supramolecular aggregates with bases which are able to form complementary hydrogen bonds with the C(O)–NH–C(O) moiety of the hydantoin ring and these results will be reported subsequently.

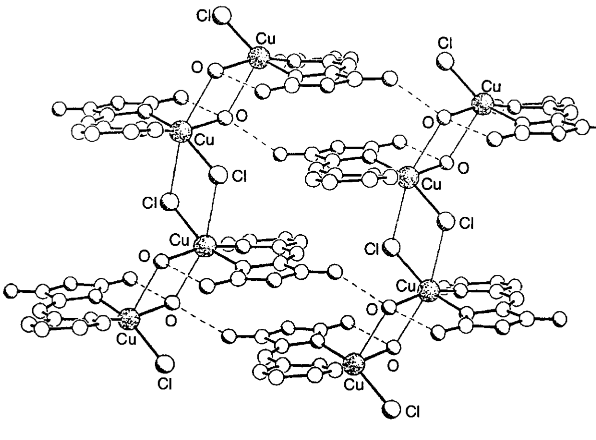

Fig. 3 Crystal packing arrangement for $[CuCl(pyhy)(OH_2)]$ showing the polymeric chain of linked octahedra and the intermolecular interactions between adjacent chains. The longer Cu–O and Cu–Cl linkages are depicted as line bonds.

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Footnotes

† *Crystal data* for $C_9H_7N_3O_2$: M = 189.2, monoclinic, space group $P2_1/n$, a = 3.808(2), b = 14.036(4), c = 15.963(4) Å, β = 92.90(2)°, V = 852.1(3) Å^3, Z = 4, D_c = 1.48 g cm^{-3}, μ(Cu-Kα) = 9.1 cm^{-1}, λ = 1.54178 Å, F(000) = 392. A yellow needle of crystal dimensions 0.07 × 0.10 × 0.40 mm was used. Data were measured on a Siemens P4 rotating anode diffractometer with graphite monochromated Cu-Kα radiation (ω-scans). 1368 independent reflections were measured ($2\theta \leqslant 125°$) of which 1093 had $|F_o| > 4\sigma(|F_o|)$ and were considered to be observed. The structure was solved by direct methods and the non-hydrogen atoms were refined anisotropically by full-matrix least-squares analysis using absorption corrected data to give R = 0.035, R_w = 0.040 [$w^{-1} = \sigma^2(F) + 0.0005F^2$].

‡ *Crystal data* for $C_9H_{16}N_3O_{11}Ni$: M = 436.4, triclinic, space group $P\bar{1}$, a = 6.811(2), b = 10.246(2), c = 12.064(2) Å, α = 95.86(2), β = 92.90(2), γ = 90.85(2)°; V = 814.2(1) Å^3, Z = 2, D_c = 1.78 g cm^{-3}, μ(Cu-Kα) = 38.5 cm^{-1}, λ = 1.54178 Å, F(000) = 448. A green plate-like needle of crystal dimensions 0.24 × 0.07 × 0.14 mm was used. Data were measured on a Siemens P4/PC diffractometer with graphite monochromated Cu-Kα radiation (ω-scans). 2594 independent reflections were measured ($2\theta \leqslant 125°$) of which 2382 had $|F_o| > 4\sigma(|F_o|)$ and were considered to be observed. The structure was solved by direct methods and the non-hydrogen atoms were refined anisotropically by full-matrix least-squares analysis using absorption corrected data to give R = 0.035, R_w = 0.042 [$w^{-1} = \sigma^2(F) + 0.0005F^2$].

§ *Crystal data* for $C_9H_8N_3O_3ClCu$: M = 305.2, triclinic, space group $P\bar{1}$, a = 7.062(2), b = 8.307(2), c = 9.627(2) Å, α = 108.74(2), β = 98.72(2), γ = 93.31(2)°, V = 525.1(2) Å^3, Z = 2, D_c = 1.93 g cm^{-3}, μCu-Kα = 53.16 cm^{-1}, λ = 1.54178 Å, F(000) = 306. A green plate of crystal dimensions 0.19 × 0.09 × 0.02 mm was used. Data were measured on a Siemens P4 rotating anode diffractometer with graphite monochromated Cu-Kα radiation (ω-scans). 1561 independent reflections were measured ($2\theta \leqslant 120°$) of which 1456 and $|F_o| > 4\sigma(|F_o|)$ and were considered to be observed. The structure was solved by direct methods and the non-hydrogen atoms were refined anisotropically by full matrix least squares analysis using absorption corrected data to give R = 0.035, R_w = 0.055 [$w^{-1} = \sigma^2(F) + 0.0005F^2$].

¶ The N(1)···N(8) distances and the associated internal C-6 angles are 2.74, 2.96 and 2.87 Å and 125.6, 128.6 and 126.2° in **1**, **2** and **3**, respectively.

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