DALTON COMMUNICATION

New ring-closure reaction involving co-ordinated amide groups

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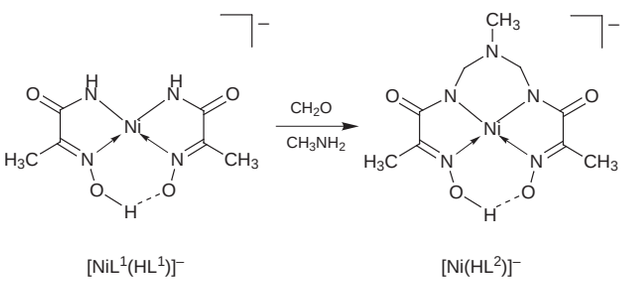
The condensation of $[NiL^1(HL^1)]^-$ [H_2L^1 = 2-(hydroxyimino)propanamide] with formaldehyde and methylamine in methanol solution yields a stable anionic complex based on a tetradentate open-chain ligand and represents the first example of a ring-closure reaction featuring the co-ordinated amide groups.

Template synthesis employing ring-closure reactions between transition metal polyamine complexes, formaldehyde and suitable C–H or N–H acids as locking fragments is widely used for macrocyclic[1] and cage[2] compounds. Among the recent advances in this field is the use of new types of C–H and N–H padlocks, such as diethylmalonate and barbituric acid[3] or primary amides and sulfonamides,[4] respectively. The latter appeared more effective as locking fragments than primary amines due to the higher acidity of their N–H protons which causes them to be significantly more reactive towards formaldehyde. A simple inversion of nitrogen-bearing functions in the template and the padlock in this reaction (*i.e.*, use of co-ordinated secondary amide, formaldehyde and amine) can lead to a very attractive route for amide-containing macrocyclic or acyclic open-chain ligands. Co-ordination compounds with the above-mentioned ligands are under continuous investigation, in particular, due to the remarkable ability of amide macrocyclic donors to stabilise high oxidation states of transition metals[5] and because of the extensive use of mononuclear amidato complexes as "building blocks" for polynuclear assemblies.[6] However, the tetraamide macrocyclic ligands reported to date were obtained by multi-step organic synthesis with relatively small yields.[5] Polydentate amide-containing ligands used in molecular magnetism often undergo hydrolytic destruction in solution on co-ordination, so N-substituted amides should be employed instead.[6] Both of these inconveniences can be avoided by the use of simple ring-closure reactions involving amidato groups. The only example of the metal-directed synthesis of tetraamide macrocyclic or open-chain acyclic complexes is the condensation of non-co-ordinated NH_2 moieties of the hydrazide groups with aliphatic aldehydes.[7] Thus, no ring-closure reactions based on co-ordinated amide groups have been reported to date.

Interaction of primary amides with formaldehyde and amines is known as the Einhorn reaction of amidomethylation.[8] Taking into account the higher acidity of the amide N–H protons as compared to the amine N–H protons, we suggested that *cis*-disposed co-ordinated amidato groups in thermodynamically stable square-planar metal complexes can react readily with formaldehyde and primary amines with ring closure. Here we describe an implementation of this idea and the structure and spectral properties of the obtained products.

We chose the square-planar nickel(II) complex $K[NiL^1(HL^1)]\cdot 2H_2O$ [H_2L^1 = 2-(hydroxyimino)propanamide] (Scheme 1) to begin with since it is stable enough in solution and because of the important stabilisation of its co-ordination sphere by the short intramolecular H-bond between the oximato oxygen atoms which leads to retention of the *cis*-disposition of the ligands in reactions involving co-ordinated amide groups.[7c,9] Secondly, such a template has only one pair of amide groups for ring closing thus making it possible to avoid the problem



Scheme 1

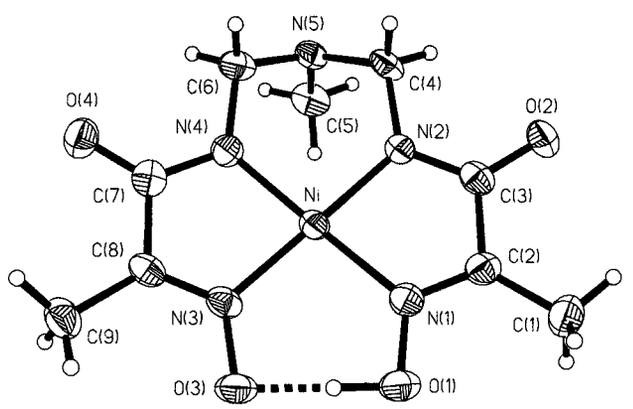


Fig. 1 Structure of the complex anion $[NiL^2]^-$ in **2**. Selected bond lengths (Å) and angles (°) for anion **A** (**B** in parentheses): Ni–N(1) 1.867(5) (1.869(5)), Ni–N(2) 1.866(5) (1.859(5)), Ni–N(3) 1.872(5) (1.863(5)), Ni–N(4) 1.850(5) (1.860(5)), N(1)–C(2) 1.302(8) (1.271(8)), N(2)–C(3) 1.308(8) (1.318(8)), N(2)–C(4) 1.462(8) (1.459(8)), N(3)–C(8) 1.287(8) (1.279(8)), N(4)–C(6) 1.462(8) (1.451(8)), N(4)–C(7) 1.326(8) (1.313(8)), N(5)–C(4) 1.450(8) (1.462(8)), N(5)–C(5) 1.461(8) (1.470(8)), N(5)–C(6) 1.453(8) (1.445(8)); N(1)–Ni–N(2) 82.9(2) (82.8(2)), N(1)–Ni–N(3) 97.6(2) (97.9(2)), N(1)–Ni–N(4) 178.6(2) (178.2(2)), N(2)–Ni–N(3) 179.4(2) (178.1(2)), N(2)–Ni–N(4) 95.9(2) (96.1(2)), N(3)–Ni–N(4) 83.6(2) (83.2(2)).

of the isolation of macrocyclic and open-chain products which normally arises when two pairs of *cis*-disposed reacting groups are present.

Relatively fast and efficient reaction was carried out in methanol solution under mild conditions and in high yield.† As a result of cyclisation with involvement of the co-ordinated amidato groups, two formaldehyde and one methylamine molecules had condensed with $[NiL^1(HL^1)]^-$ giving the product $K[Ni(HL^2)]\cdot 2H_2O$ **1**, in which the six-membered chelate ring which forms is fused with two five-membered chelates (Scheme 1). Thus, the resulting ligand [{[{[2-(hydroxyimino)propanoyl]-amino}methyl](methyl)amino}methyl]-2-(hydroxyimino)-propanamide (H_4L^2) exhibits an open-chain structure.

The structures of the resulting complexes **1** and $Tl[Ni(HL^2)]$ **2**† were established by elemental analysis and NMR spectroscopy and then confirmed by single crystal X-ray analysis of **2** (Fig. 1). The ^{13}C NMR spectrum of **1** in comparison with that of the initial complex showed the presence of two new signals at δ 37.13 and 62.48 characteristic of N-methyl and

methylene groups, respectively. Disappearance of the signals corresponding to labile NH protons in the ^{1}H NMR spectra of **1** and **2**, as well as the sharp bands corresponding to the ν(N–H) stretching mode vibrations of the secondary amide groups in the IR spectrum of **1**, suggests the substitution of these protons with the methylene bridges. At the same time, new resonances for the N-methyl and methylene groups appeared in the ^{1}H NMR spectra of **1** and **2**.

The centrosymmetric unit cell of **2**‡ contains two crystallographically independent complex anions, $[Ni(HL^2)]^-$ (**A** and **B**) which differ insignificantly in their geometrical parameters, and two thallium cations. The central atom in the complex anion is square-planar with four nitrogen donors from the deprotonated amide and oxime groups of the tetradentate open-chain ligand. The latter is triply deprotonated and forms three condensed chelate rings. The central and the donor atoms define the same plane (the deviations do not exceed 0.01 Å), the five-membered chelate rings are in fact planar. The six-membered ring NiN(2)C(4)N(5)C(6)N(4) formed as a result of template condensation indicates clear envelope conformation with the N(5) atoms lying 0.648(7) and 0.678(7) Å above the mean plane defined by the five other atoms, for anions **A** and **B**, respectively. The corresponding dihedral angles along the C(4)–C(6) vector are 54.9(4) (for **A**) and 57.7(4)° (for **B**). The square planar co-ordination of the ligand is additionally stabilised by the short intramolecular H bond between oxime oxygen atoms thus forming a closed pseudo-macrocyclic structure. The O···O separations [2.478(7) and 2.452(7)Å for anions **A** and **B**, respectively] are typical for nickel(II) oximato complexes.[10]

The ring-closure reaction reported here points the way to the elaboration of convenient synthetic methods for amide-containing macrocycles using metal complexes with bidentate amide ligands (*e.g.*, oxamide, biuret, amino acid amides) or tetradentate open-chain amide ligands as starting compounds. Another possibility is the use of suitable C–H acids (*e.g.*, nitroalkanes) as padlocks in this reaction. Such research is in progress and its results are to be reported in a full paper.

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Notes and references

† $K[Ni(HL^2)]\cdot 2H_2O$ (**1**). The compound $K[NiL^1(HL^1)]\cdot 2H_2O$ {0.335 g, 1 mmol, prepared analogously to $Li[NiL^1(HL^1)]\cdot 5H_2O$ as described in ref. 10(*b*) using KOH instead of LiOH} was dissolved in 10 ml of methanol, then paraformaldehyde (0.075 g, 2.5 mmol, depolymerised in 10 ml of methanol), methylamine (33% solution in ethanol, 0.14 ml, 1.1 mmol) and KOH (0.056 g, 1 mmol, dissolved in 5 ml of methanol) were added. The mixture was heated under reflux with continuous stirring for 30 min, then the volume was reduced to 5 ml on a rotary evaporator. In 12 h the product was obtained as a clear yellow crystalline precipitate, which was washed with methanol and dried over $CaCl_2$. Yield 0.285 g (73%) [Calc. for $KNiC_9H_{14}N_5O_4\cdot 2H_2O$ (390.06): C, 27.71; H, 4.65; N, 19.95; Ni, 15.05. Found: C, 27.56; H, 4.81; N, 19.81; Ni, 16.29%]. ^{1}H NMR (DMSO-d_6): δ 1.775 (s; 6H, CH_3), 2.773 (s; 3H, NCH_3), 4.081 (s; 4H, CH_2), 18.613 (s, 1H, NOH). ^{13}C NMR (DMSO-d_6): δ 10.65 (CH_3); 37.13 (NCH_3); 62.48 (CH_2); 149.10 (C=N), 169.29 (C=O). IR (KBr pellet, ν/cm^{-1}): 1126 [ν(N–O)]; 1632 [ν(C=O), Amide I]; 2890, 2925, 2985 [ν(C–H)]; 3455br [ν(O–H)].

$Tl[Ni(HL^2)]$ **2**. Amber-yellow prismatic crystals of **2** [yield 0.089 g (86%)] were grown by evaporation at room temperature of a solution prepared by metathesis of **1** (0.078 g, 0.2 mmol) with Tl_2CO_3 (0.047 g, 0.1 mmol) in water [Calc. for $TlNiC_9H_{14}N_5O_4$ (519.31): C, 20.82; H, 2.72; N, 13.49; Ni, 11.30. Found: C, 20.66; H, 4.79; N, 13.61; Ni, 11.12%]. ^{1}H NMR (DMSO-d_6): δ 1.717 (s; 6H, CH_3), 2.450 (s; 3H, NCH_3), 3.681 (s; 4H, CH_2), 11.154 (s, 1H, NOH).

‡ Crystal data for **2**: $C_9H_{14}N_5NiO_4Tl$, M = 519.33, triclinic, space group $P\bar{1}$, a = 8.586(1), b = 10.256(1), c = 16.422(3) Å, α = 78.40(1), β = 83.36(1), γ = 70.11(1)°, U = 1330.3(3) Å^3, Z = 4, D_c = 2.593 g cm^{-3}, μ(Mo-Kα) = 13.534 mm^{-1}, F(000) = 976, T = 293 K, 4193 measured reflections, 3911 independent reflections, structure solution by direct methods using SHELXL-93.[11] $R1$ = 0.0274, $wR2$ = 0.0658 for 3350 reflections with $I > 2\sigma(I)$ and $R1$ = 0.0367, $wR2$ = 0.0723 for all unique reflections. CCDC reference number 186/1340. See http://www.rsc.org/suppdata/dt/1999/825/ for crystallographic files in .cif format.

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