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Rearrangement of Imidazolidine to Piperazine Rings in the Presence of Dy^{III} †

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Abstract: The formation of imidazolidines from secondary amines and aldehydes is well known. This small cycle can act as nitrogen donor, and it is usually stable when it coordinates to metal ions. Sometimes, the imidazolidines as ligands undergo breaking of the C-N bond when coordinating to the metal centre, yielding related amines. However, the reorganisation of the imidazolidine to a piperazine ring is a quite unusual process. In this work, we describe the transformation of a zinc complex with a ligand containing two imidazolidine moieties into a zinc complex with a piperazine fragment as donor, in the presence of a dysprosium salt.

Keywords: imidazolidine; piperazine; dysprosium(III)

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1. Introduction

Nitrogen heterocycles are undoubtedly the most important structural motifs in medical chemistry and pharmaceuticals [1]. These include imidazolidines and piperazines [2], which are also potential ligands for the formation of metal complexes [3,4]. Stability of imidazolidine based complexes greatly depends on the substituents attached to the nitrogen donors. Thus, there are many complexes with imidazolidine ligands that have shown to be stable in solution, while others undergo hydrolysis very easily [5]. When this hydrolysis takes place, it typically cleaves the imidazolidine ring to transform the ligand into an amine [5]. But in some cases, although very rare, the conversion of the imidazolidine ring into a piperazine heterocycle has also been described. To our knowledge, this transformation has only been described twice in literature, and it took place in the presence of Cu^{II} ions [6,7]. In this work, we describe the conversion of a ligand containing two imidazolidine rings into one with a piperazine cycle, a reaction that occurs in the presence of a dysprosium(III) salt.

2. Materials and Methods

2.1. Materials and General Methods

All chemical reagents and solvents were purchased from commercial sources, and used as received without further purification. ^1H NMR spectra of **1** and **2**$\cdot 1.75H_2O$ were recorded on a Varian Inova 400 spectrometer, using DMSO-d_6 as solvent.

Single X-ray data for **2**$\cdot 1.75H_2O$ were collected at 100 K on a Bruker D8 VENTURE PHOTON III-14 diffractometer, employing graphite monochromated Mo-kα ($\lambda = 0.71073$

Å) radiation. Multi scan absorption corrections were applied using SADABS [8]. The structure was solved by standard direct methods, employing SHELXT [9], and then refined by full matrix least-squares techniques on F^2, using SHELXL [10] from the program package SHELX.

2.2. Syntheses

$[Zn_3(L^1)(OAc)_2]$ (**1**): to a solution of pentaethylenehexamine (0.107 g, 0.461 mmol) in absolute ethanol (12 mL), $Zn(OAc)_2{\cdot}2H_2O$ (0.100 g) and an ethanolic (15 mL) solution of 5-bromo-2-hydroxy-3-methoxybenzaldehyde (0.426 g, 1.844 mmol) were added. The mixture was stirred for 6 h at room temperature, and the solid that precipitated was separated by centrifugation, and dried in air. Yield: 0.125 g (19%). ^1H NMR (400 MHz, DMSO-d_6, δ in ppm): 2.09 (s, 6H, CH_3-COO^-); 2.11–2.24 (m, 2H), 2.64–3.05 (m, 8H), 3.53–3.58 (m, 4H), 3.80-3.90 (m, 2H), 3.75–3.83 (m, 2H), 4.10–4.35 (m, 2H) (4H1+ 4H2 + 4H3 + 4H18 + 4H19); 3.48 (s, 6H, OCH_3); 3.63 (s, 6H, OCH_3); 3.69 (s, 1H), 3.73 (s, 1H) (H17 + H17′); 6.75 (s, 2H), 6.82-6.98 (m, 6H) (2H6 + 2H8 + 2H11 + 2 H13); 8.34 (s, 2H, 2H4).

$[Zn_2L^2(NO_3)_2]{\cdot}1.75H_2O$ (**2**·$1.75H_2O$): To an acetonitrile (8 mL)/methanol (4 mL) solution of **1** (0.022 g, 0.016mmol), $Dy(NO_3)_3{\cdot}xH_2O$ (0.011 g, 0.031 mmol) was added, and the resultant solution was stirred for 4 h at room temperature. Slow evaporation of the obtained solution yields single crystals of $[Zn_2L^2(NO_3)_2]{\cdot}1.75H_2O$, suitable for single X-ray diffraction studies. Yield: 0.010 (66%) ^1H NMR (400 MHz, DMSO-d_6, δ in ppm): aliphatic protons: most of them hidden under the DMSO and water peaks; 3.71 (s, 6H, OCH3); 6.96 (s, 2H), 7.07 (s, 2H) (2H9 + 2H11); 8.51 (s, 2H, H7). Crystal data (at 100(2) K): tetragonal, $I4_1/a$, $C_{28}H_{38}Br_2N_8O_{11.75}Zn_2$, MW = 965.22, with a = 24.077(9) Å, b = 24.077(9) Å, c = 11.8202(6) Å, $\alpha = \beta = \gamma = 90$ °, V = 6864.0(6) Å^3, Z = 8; R_1 = 0.0514 and wR_2 = 0.1241 ($I > 2\sigma I$).

3. Results and Discussion

3.1. Synthesis and Spectroscopic Characterization

The trinuclear zinc complex **1** was obtained by a template method, by mixing pentaethylenehexamine and 5-bromo-2-hydroxy-3-methoxybenzaldehyde in the presence of zinc acetate, as summarized in Figure 1.

Addition of dysprosium(III) nitrate to an acetonitrile/methanol solution of **1** yields the dinuclear zinc complex **2**·$1.75H_2O$ (Figure 1), which contains the new $[L^2]^{2-}$ donor with a piperazine ring. This heterocycle seems to come from the initial imidazolidine rings present in the $[L^1]^{4-}$ ligand in **1**, by a hydrolysis and rearrangement process. This transformation, although uncommon, has been previously described for copper(II) complexes [6,7] but, as far as we now, it has never been reported in the presence of a lanthanoid ion. Both complexes were characterized by ^1H NMR spectroscopy. In addition, **2**·$1.75H_2O$ has been unequivocally identified by single X-ray diffraction studies.

The ^1H NMR spectrum of **1** shows one singlet at 8.4 ppm (2H), assigned to the imine protons, and one singlet (2H) and one multiplet (6H) between 6.75 and 6.98 ppm, in agreement with the existence of four aromatic rings, which are not all equivalent. This confirms the tetracondensation of the amine and the aldehyde. Besides, the presence of two singlets at ca. 3.7 ppm, points to the existence of two inequivalent imidazoline protons (H17 and H17′ in Figure 1), in agreement with previous results [11], and this reinforces the tetracondensation. In addition, it should be noted that only one set of signals is present in the ^1H NMR spectrum of **1**, in agreement with the existence of only one species in solution, and this spectrum does not show any evidence of hydrolysis.

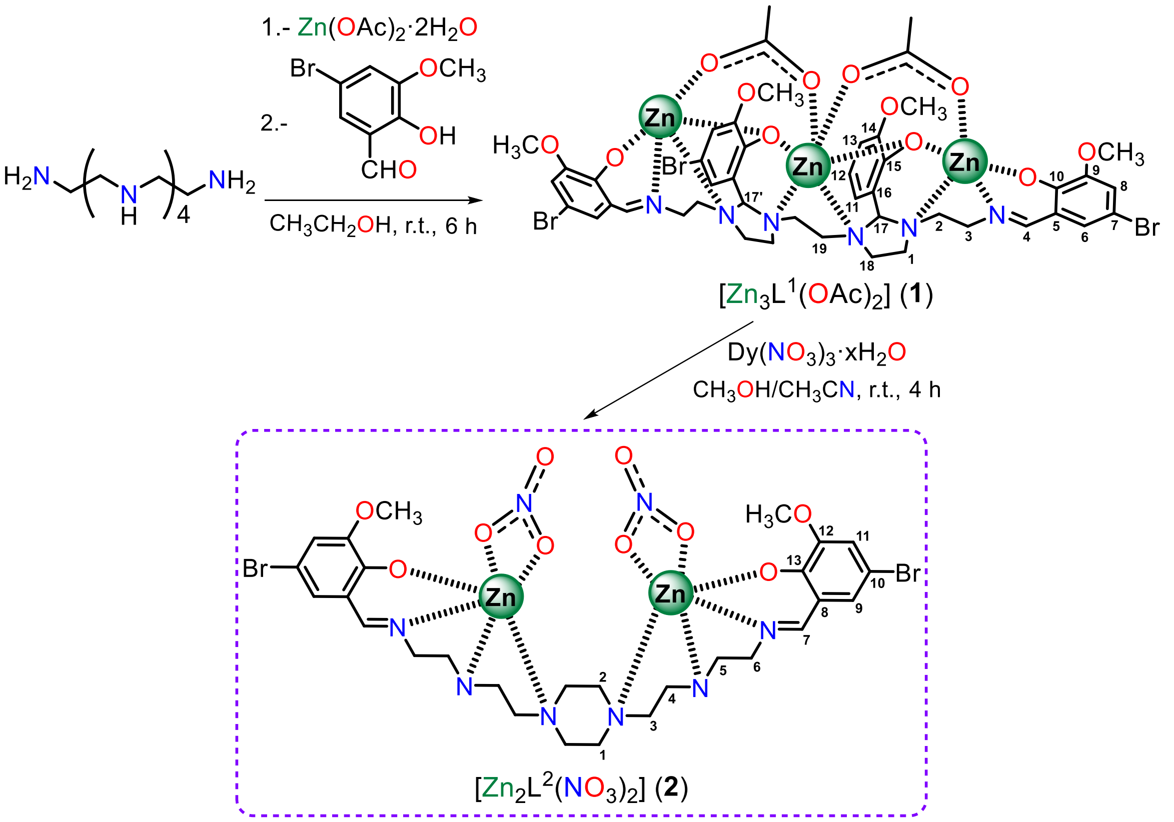

Figure 1. Reaction scheme for isolation of zinc complexes **1** and **2**, with numbering scheme for ^{1}H NMR. Solvate molecules are omitted for clarity.

In the case of **2**·1.75H$_2$O, the ^{1}H NMR spectrum in DMSO-*d*$_6$ (Figure 2) clearly shows the existence of two equivalent imine moieties (singlet at 8.5 ppm), and just two equivalent aromatic rings (two singlets at 6.96 and 7.07 ppm), with any other peak in the aromatic region, indicating the high purity of this specie.

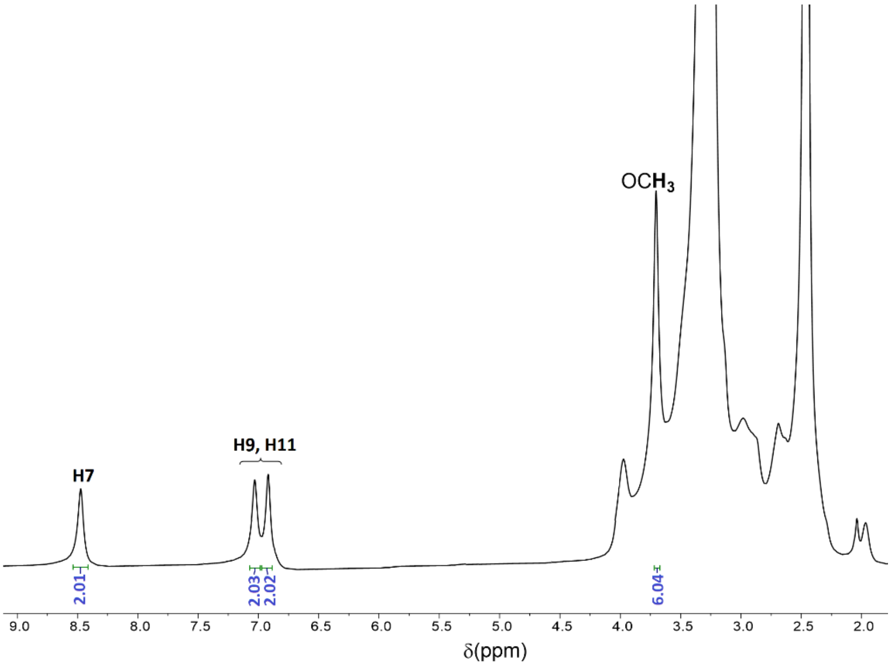

Figure 2. ^{1}H NMR spectrum for **2**·1.75H$_2$O in DMSO-*d*$_6$.

Thus, the comparison of this spectrum with that of **1** shows the disappearance of four aromatic protons, according to the removal of two aromatic rings in **2**·1.75H_2O with respect to **1**. Unfortunately, most of the aliphatic protons of **2**·1.75H_2O are hidden by the DMSO and water peaks, but, despite this, the ^1H NMR spectrum is in complete agreement with the formation of the new piperazine donor.

Accordingly, the ^1H NMR studies suggest that both complexes are stable in solution, and, therefore, that the transformation of complex **1** into **2**·1.75H_2O is mediated by the presence of the dysprosium(III) nitrate.

3.2. Single X ray Diffraction Studies

Single crystals of $[Zn_2L^2(NO_3)_2]\cdot 1.75H_2O$ (**2**·1.75H_2O) were obtained as detailed above. An ellipsoid diagram for **2** is shown in Figure 3, and main distances and angles are recorded in Table 1.

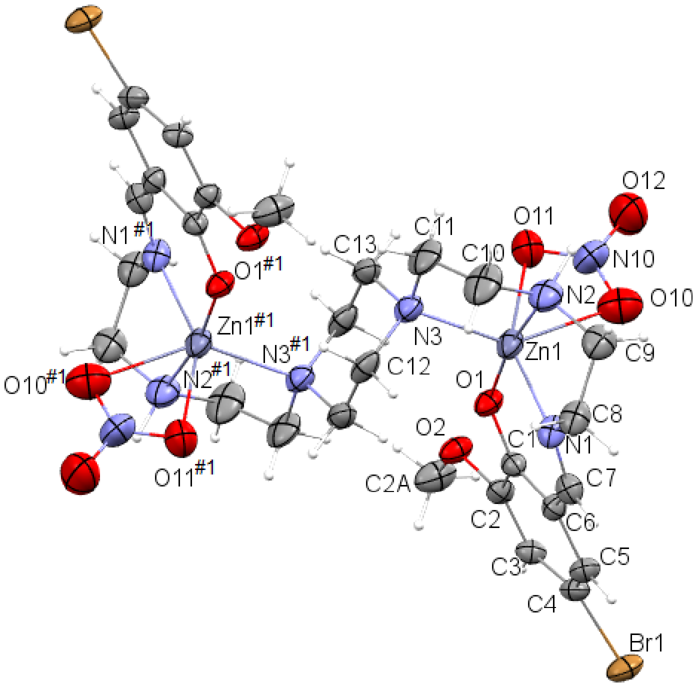

Figure 3. Ellipsoid (50% probability) diagram for $[Zn_2L^2(NO_3)_2]$ in **2**·1.75H_2O.

Table 1. Main bond distances (Å) and angles (°) for **2**·1.75H_2O.

Zn1—O1	1.971 (4)	Zn1—N1	2.072 (5)
Zn1—O10	2.367 (6)	Zn1—N2	2.155 (5)
Zn1—O11	2.233 (5)	Zn1—N3	2.160 (5)
Zn1···Zn1 #1	5.943 (1)		
O1—Zn1—N2	169.64 (18)	N3—Zn1—O10	143.84 (19)
N1—Zn1—O11	148.21 (18)	O11—Zn1—O10	54.68 (18)

#1 $-x + 1, -y, -z - 1$.

The unit cell of **2**·1.75H_2O contains neutral dinuclear $[Zn_2L^2(NO_3)_2]$ molecules and water as solvate. $[Zn_2L^2(NO_3)_2]$ has an inversion centre, which makes both halves of the molecule equivalent. In this complex, the new dianionic ligand $[L^2]^{2-}$ acts as a dinucleating octadentate donor, providing an N_3O (N_{imine}, N_{amine}, $N_{piperazine}$ and $O_{phenolate}$) environment for each Zn^{II} ion, with the methoxy oxygen atoms remaining uncoordinated. The metal centres reach their coordinative saturation with a nitrate group, linked in a bidentate chelate mode. Accordingly, both Zn^{II} ions are hexacoordinated, with distances and bond angles that agree with a distorted octahedral geometry. It should be emphasized that the distortion of the octahedron is considerable, since an angle close to 55° is observed (Table 1), a value much lower than what would be expected, but that is quite typical for bidentate chelate nitrates [12]. Both zinc ions are bridged through the *NCCN* fragment of the piperazine ring, which adopts a chair conformation, leading to a Zn···Zn intramolecular distance of ca. 5.9 Å. The dinuclear $[Zn_2L^2(NO_3)_2]$ units are connected between them through hydrogen bonds, where only the amine nitrogen atoms (N2) and the water solvate are implicated, and the shortest Zn···Zn intermolecular distance in this arrangement is ca. 8.09 Å.

4. Conclusions

This work reports the uncommon conversion of an imidazolidine ligand into a piperazine donor in the presence of a dysprosium(III) salt. Accordingly, herein is described the first piperazine heterocycle isolated from an imidazolidine ligand in the presence of a lanthanoid metal ion.

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Conflicts of Interest: The authors declare no conflict of interest.

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