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Supramolecular interactions in Cobalt(II)–nucleobases complexes: A methyl matter

Khaled Hassanein [a], Félix Zamora [a], Oscar Castillo [b,*], Pilar Amo-Ochoa [a,*]

[a] Departamento de Química Inorgánica y Condensed Matter Physics Center (IFIMAC), Universidad Autónoma de Madrid (UAM), 28049 Madrid, Spain
[b] Departamento de Química Inorgánica, Universidad del País Vasco (UPV/EHU), Apartado 644, e-48080 Bilbao, Spain

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ABSTRACT

Direct reactions between cobalt(II) acetate and the corresponding modified nucleobase lead to the mononuclear complexes $[Co(TAcO)_2(H_2O)_4]$ (**1**) and $[Co(UAcO)_2(H_2O)_4]$ (**2**), (TAcO = thymine-1-acetate, UAcO = uracil-1-acetate). Additionally the reactions between the Co(II) salt with equimolar amount of 2,6-diaminopurine (HDap) and either TAcOH or UAcOH give rise to $\{[Co(HDap)_2(H_2O)_4]\cdot(TAcO)_2\cdot 3H_2O\}$ (**3**) and $\{[Co(HDap)_2(H_2O)_4]\cdot(UAcO)_2\cdot 3H_2O\}$ (**4**), respectively. The X-ray analysis of all of these complexes show a common feature, the presence of four water molecules in the basal plane coordinated to the Co(II) center. In case of complexes **1** and **2** the coordination environment around the Co(II) is a CoO_2O_{w4} with two modified nucleobases coordinated in a monodentate way through one oxygen of the carboxylate group, whereas for **3** and **4** the coordination environment is CoN_2Ow_4 as a consequence of the coordination to the nitrogen atoms of two HDap ligands. The extended inter-H-bond interactions between water molecules and nucleobase moieties, play crucial role in the crystal packing of complexes.

1. Introduction

The last fifty years have completely changed the way how researchers can understand many molecular mechanisms, in part due to access to the information containing in biological molecules, and the ability to manipulate this information controlling structural changes [1].

The supramolecular interactions in biological systems dictate the folding and assembly of these systems [2]. It is well-known that small changes in these supramolecular interactions can drastically affect the structure and properties of the resulting material. Thus, the access to manipulate the supramolecular interactions will allow the control of the structure and function of new soft-materials. Naturally occurring biopolymers based their complex and hierarchical structures in a combination of non-covalent interactions such as London and/or van der Waals forces, and hydrogen bonds, in which the resulting conformations are base in the fine tune of such interactions. Therefore, the precise control of the supramolecular interactions is crucial to develop new materials based on the use of biomolecules. Obviously, an important aspect includes the control of the strength of non-covalent interactions [3]. The strength of these interactions is close related with the functional groups present in the biomolecules and/or solvent competition molecules, as is the case of water in biological medium. As an example, the structure of duplex DNA is governed by a balance of non-covalent forces in aqueous solution. Gaining control over these supramolecular interactions is the key for understanding and targeting (off-regulated) biological processes in diseases.

To study competition between H-bonds forces, the use of metal complexes with nucleobases as ligands is an interesting research subject due to these systems can act as biomimetic models of metal-DNA/RNA interactions and can help to a better understanding their biological effects [4]. Additionally, the presence of nucleobases in the coordination compounds can lead to biologically compatible complexes relevant in the design of novel drugs [5] with potential applications as advanced biocompatible functional materials [4,6,7]. Moreover, from a very basic chemistry view point, nucleobases as ligands provide a power full platform for the construction of functional coordination complexes with different architectures [8–12], which can present also interesting physical–chemical properties [13].

In this work we have selected thymine and uracil carboxylic acid derivatives, named as thymine-1-acetic acid (TAcOH) and uracil-1-acetic acid (UAcOH), in combination with cobalt(II) with the purpose to produce novel complexes with interesting supramolecular architectures [9,14]. These modified nucleobases, containing an acetic group at the N1 position (Fig. 1), increase structural

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* Corresponding authors.

E-mail addresses: oscar.castillo@ehu.es (O. Castillo), pilar.amo@uam.es (P. Amo-Ochoa).

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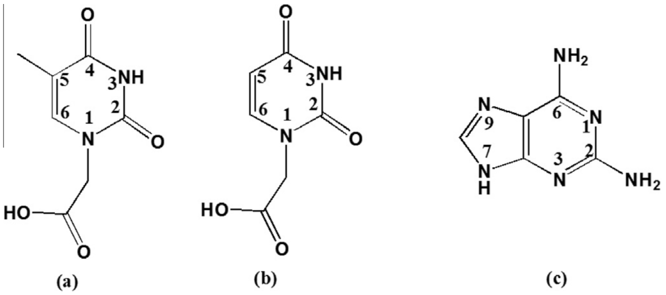

Fig. 1. A schematic representation of thymine-1-acetic acid (a), uracil-1-acetic acid (b) and 2,6-diaminopurine (c) ligands used in this work.

versatility of the ligands since: (*i*) the carboxylic group can adopt a wide range of coordination binding modes, e.g. monodentate, chelating, bidentate or monodentate-bridging, (*ii*) the thymine and uracil moieties retain their specific properties of the pyrimidine ring allowing to establish non-covalent interactions (eg. H-bonding or/and π–π stacking), and (*iii*) the self-assembly through H-bonding involving the carboxylic group can contribute to the supramolecular network.

With the aim to study potential formation of ternary metal–nucleobase complexes which increase the number of possibilities in the supramolecular interactions ways we have selected 2,6-diaminopurine (HDap), closely related analogue of adenine. This is an interesting ligand due to the fact that, in principle, HDap can establish similar binding patterns to that of adenine, because it is structurally related to a pyrimidine ring fused to an imidazole ring. Therefore, HDap could recognize thymine and uracil nucleobases *via* H-bonding. Moreover, the extra exocyclic amino group of HDap, in comparison to adenine, can further serve as functional site for both the coordination and/or intra/intermolecular hydrogen-bonding site, which combined with the polyfunctional purine moiety, can reasonably produce novel complexes with intriguing framework-connectivity and significant HDap-based applications [15].

Thus, the direct reactions between cobalt(II) acetate and thymine-1-acetic acid (TAcOH) or uracil-1-acetic acid (UAcOH); and the equimolar mixture of 2,6-diaminopurine (HDap) and either TAcOH or UAcOH give rise to $[Co(TAcO)_2(H_2O)_4]$ (**1**) and $[Co(UAcO)_2(H_2O)_4]$ (**2**), (TAcO = thymine-1-acetate, UAcO = uracil-1-acetate), or $\{[Co(HDap)_2(H_2O)_4]\cdot(TAcO)_2\cdot 3H_2O\}$ (**3**) and $\{[Co(HDap)_2(H_2O)_4]\cdot(UAcO)_2\cdot 3H_2O\}$ (**4**), respectively. These metal–nucleobase complexes have been characterized by spectroscopic techniques and their structures confirmed by single crystals X-ray diffraction, allowing us to study their supramolecular interactions in solid state.

2. Materials and methods

Uracil-1-acetic acid (UAcOH) was prepared according to the literature [16]. Cobalt(II) acetate tetrahydrate ($Co(AcO)_2\cdot 4H_2O$), thymine-1-acetic acid (TAcOH), 2,6-diamino purine (HDap) and other chemicals were purchased from standard chemical suppliers and used as received. IR spectra were recorded on a PerkinElmer spectrum 100 spectrophotometer using a universal ATR sampling accessory and on a Bruker FT-IR Vector 22 model from 4000 to 400 cm^{-1} in the KBr pellet form. Elemental Analyses were carried out by the microanalytical service of the Autónoma University of Madrid.

Powder X-ray diffraction has been done using a Diffractometer PANalyticalX'Pert PRO theta/2theta primary monochromator and detector with fast X'Celerator. The samples have been analysed with scanning theta/2theta (Figs. S1–S4).

Thermogravimetric analysis (TGA) equipped with a mass spectrometer (MS) was performed on a Netzsch STA 409 CD instrument equipped with a Skimmer QMS 422 mass spectrometer (MS/EI) with the following programmed time-dependent temperature profile: 24–350 °C with 10 °C/min gradient and cooling to room temperature. The initial sample weights were about 5 ± 1 mg, and the whole experiment was executed under air with a gas flow of 80 mL/min (Figs. S5–S8).

The X-ray diffraction data collections and structure determinations were done on a Bruker Kappa Apex II with graphite-monochromated Cu Kα radiation (λ = 1.54178 Å; compounds: **1**, **2** and **3**) and graphite-monochromated Mo Kα radiation (λ = 0.71073 Å; compound **4**). All the structures were solved by direct methods using the SIR92 program [17] and refined by full-matrix least-squares on F^2 including all reflections (SHELXL97) [18]. All calculations were performed using the WINGX crystallographic software package [19]. Compound **1** crystallized as a non-merohedral twin with a twin law of (1 0 0 0 -1 0 -0.376 0 -1). The structure was refined using only reflections from the major component and excluding partially overlapping reflections (HKLF 5). The crystallization water molecules of compound **3** were disordered over two positions related by the inversion symmetry centre. The hydrogen atoms of the disordered water molecules were not located. Information concerning data collection and structure refinement is summarized in Table 1.

3. Experimental

3.1. $[Co(TAcO)_2(H_2O)_4]$ (**1**)

A mixture of $Co(AcO)_2\cdot 4H_2O$ (0.100 g, 0.4 mmol) and of TAcOH (0.150 g, 0.8 mmol) was dissolved in 15 mL of H_2O and fully stirred at 25 °C for 3 h (pH = 3.2). The resulting pink solution was filtered off and left to crystalize by slow evaporation at 25 °C. Pink crystals, were grown by slow evaporation from the pink solutions at 25 °C in three weeks. The pink crystals were filtered off and washed with water, ethanol, diethyl ether and dried in air. Yield: 47.3 % based on the cobalt (0.094 g). *Anal.* Calc. (found) for $C_{14}H_{22}CoN_4O_{12}$: C, 33.81 (33.45); H, 4.46(4.41); N, 11.27(11.26). IR selected data (KBr, cm^{-1}): 3110(m), 3108(w), 3060(w), 1710(s), 1658(s), 1415(m), 1355(m), 1311(m), 1249(m). The purity of the crystals was confirmed by powder X-ray diffraction (Fig. S1).

3.2. $[Co(UAcO)_2(H_2O)_4]$ (**2**)

Complex **2** was prepared using the same procedure as for **1**, but adding UAcOH (0.138 g, 0.8 mmol) instead of TAcOH (pH = 3.7). Pink crystals were grown by slow evaporation from the resulting pink solution at 25 °C in two weeks. The pink crystals were filtered off, washed with water, ethanol, diethyl ether, and dried in air. Yield: 38.4 % based on the cobalt (0.072 g). *Anal.* Calc. (found) for $C_{12}H_{18}CoN_4O_{12}$: C, 30.72(30.2); H, 3.87(3.87); N, 11.94(11.80). IR selected data (KBr, cm^{-1}): 3000(w), 1697(s), 1638(m), 1590(m), 1434(m), 1386(m), 1357(m), 1302(m), 1254(m). The purity of the crystals was confirmed by powder X-ray diffraction (Fig. S2).

3.3. $\{[Co(HDap)_2(H_2O)_4]\cdot(TAcO)_2\cdot 3H_2O\}$ (**3**)

A mixture of $Co(AcO)_2\cdot 4H_2O$(0.100 g, 0.40 mmol), TAcOH (0.073 g, 0.40 mmol) and KOH (0.023 g, 0.40 mmol) in 10 mL of water was added to HDap (0.060 g, 0.40 mmol) dissolved in 10 mL of ethanol (pH = 6.2). Then, the resulting pink solution was refluxed for 2 h at 80 °C. The resulting pink solution was filtered off and allowed to crystallize at 25 °C for one week. The pink crystals obtained were filtered off, washed with water, ethanol, diethyl

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