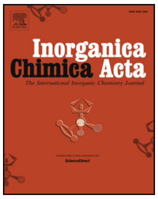
Inorganica Chimica Acta 498 (2019) 119108

Contents lists available at ScienceDirect

Inorganica Chimica Acta

journal homepage: www.elsevier.com/locate/ica



Research paper

Supramolecular association involving antiparallel CO···CO and anion–π contacts in Co(II) and Mn(II) complexes involving 2,5-pyridinedicarboxylate: Anticancer evaluation and theoretical studies

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ARTICLE INFO

Keywords:
Crystal structure
CO···CO contacts
Apoptosis
Docking
Cytotoxicity

ABSTRACT

Two new coordination solids viz. $[Co(2,5\text{-}PDC)(H_2O)_4]\ 2H_2O$ (**1**) and $[Mn(2,5\text{-}PDC)(H_2O)_4]\ 2H_2O$ [2,5-PDC = 2,5-pyridinedicarboxylat] (**2**) have been synthesized and characterized by Single crystal X-ray analysis, FT-IR, electronic spectra and TGA. Single-crystal X-ray diffraction studies reveal that compounds **1** and **2** are isostructural and extensive O—H···O hydrogen bonds along with C—H···O and anion···π interactions stabilize the crystal structures. The lattice water molecules are responsible for the 3D framework of the complexes. The remarkable combination of O—H···O, anion–π and antiparallel CO···CO interactions observed in the solid state structures have been analyzed by means of DFT calculations, molecular electrostatic potential (MEP) surface and non-covalent interaction (NCI plot) index computational tools. The anticancer activity of synthesized complexes has been studied in Dalton's lymphoma (DL) cell line using MTT based cytotoxicity study, fluorescence based apoptosis study, molecular docking and pharmacophore modeling. Both complexes significantly ($P \le 0.05$) induced cytotoxicity through apoptotic cell death in DL cells with negligible cytotoxicity (~5–10%) in normal blood cells. It is worth mentioning that compounds **1** and **2** interact with highly expressed anti-apoptotic cancer target proteins under study with higher binding affinity and the results are comparable with respective reference inhibitors. Moreover, both complexes also bear significant pharmacophore features such as H-bond donor and acceptor, aromatic and hydrophobic sites which are responsible for anticancer activities.

1. Introduction

Current interest in the crystal engineering of coordination complexes is rapidly expanding due not only to their potential applications in catalysis, adsorption, magnetism, molecular recognition, nonlinear optics, and sensors but also to their intriguing structural architectures and topologies [1–3]. The synthesis of carboxylate based coordination compounds have received considerable interest in the fields of supramolecular chemistry and crystal engineering for their rich biochemistry such as antitumor, anti-Candida and anti-microbial etc. [4,5].

Non-covalent interactions form the backbone of supramolecular architectures of coordination solids which include hydrogen bond, stacking, electrostatic and charge-transfer interactions as well as metal ion coordination [6]. Supramolecular interactions involving anionic systems and electron-deficient aromatics, viz., the anion-π [7] and lone pair (lp)-π [8] interactions also contribute towards stability of such structures. It has been accepted that electrostatic forces are the main energetic contributors to such weak interactions involving electron deficient aromatic molecules, while dispersion forces also play role in these interactions [9]. Pyridine 2,5-dicarboxylic acid serves as a suitable H-bonding acceptor [10] and can give rise to the formation of bridging coordination solids and has potential to show variety in self-assembly processes [11]. Recent studies have revealed its rich solid-state coordination modes in inorganic–organic mixed ligand complexes involving transition and rare-earth metals [12–14].

Compounds involving carbonyl moiety are ubiquitous in organic and biological systems and their molecular recognition properties have been studied extensively [15]. It has been observed that the coulombic

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https://doi.org/10.1016/j.ica.2019.119108
Received 25 July 2019; Received in revised form 27 August 2019; Accepted 27 August 2019

Inorganica Chimica Acta 487 (2019) 424–432

Contents lists available at ScienceDirect

Inorganica Chimica Acta

journal homepage: www.elsevier.com/locate/ica

Research paper

Supramolecular association involving nitrile–nitrile interactions in polymeric Mn(II) coordination complexes: A combined experimental and theoretical study

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ARTICLE INFO

Keywords:
Mn(II) polymer
Supramolecular assembly
Layered structure
3D network
Channels

ABSTRACT

Two new Mn(II) coordination polymers viz. $[Mn(p\text{-}NBz)_2(4\text{-}CNpy)_2]_n$ (**1**) and $[Mn(4\text{-}CNpy)_2(H_2BTC)_2]_n$ (**2**) [*p*-NBz = *p*-nitrobenzoate, H_3BTC = 1,3,5-benzenetricarboxylic acid and 4-CNpy = 4-cyanopyridine] have been synthesized at room temperature and characterized by single crystal X-ray diffraction, FT-IR spectroscopy, electronic spectroscopy, elemental analyses and thermogravimetric analysis (TGA). The complexes are stabilized by several non-covalent interactions along with a rather uncommon nitrile(π)–nitrile(π) interactions resulting in layered structures. The supramolecular association in both the polymers results in 3D network structures involving C—H···O interactions in the direction perpendicular to the existing layers. The anti-parallel CN···CN interaction observed in the polymeric chains of the complexes are studied using DFT calculations and characterized using the Bader's theory of "atoms-in-molecules". The interaction energy of the anti-parallel nitrile–nitrile interactions is similar to hydrogen bonds which are enhanced by the coordination of 4-CNpy to the Mn(II) metal centre.

1. Introduction

Crystal engineering of coordination polymers or inorganic–organic hybrid materials has emerged as an important field in chemical research in recent decades due to their potential applications in optical, electrical, magnetic and adsorptive materials [1,2]. The structural diversity and the construction of such promising compounds strongly depend on the chemical nature of the main or ancillary ligands and the coordination geometries of metal ions. Coordination polymers involving carboxylates exhibit various dimensional networks with interesting properties [3–5]. This diversity results from the fact that the carboxylate groups can bind metal centers in different ways and may account for the possible low dimensional materials to higher dimensional supramolecular frameworks.

The structural prediction of coordination polymers in principle is easier than molecular crystals as coordination bonds are stronger and have better directionality than other non covalent interactions. However, self assembly of systems consisting of metal ions, organic ligands, counter anions and solvent molecules with structural uncertainty is an intrinsic characteristic of such systems [6]. Weak non covalent interactions which generally include hydrogen bonding, π–π stacking, C—H···π and cation-π interactions playing a prominent role in sustaining supramolecular assemblies have been widely explored in literature [7]. Besides these weak supramolecular interactions, various emerging non-covalent interactions *viz.* halogen bonding, π(chelate)···π, π(chelate)···π(chelate) etc. interactions also play an important role in stabilization of metallo-supramolecular architectures [8,9]. In addition, non-conventional supramolecular interactions such as C—H···C and nitrile–nitrile interactions also play an important role in stabilizing structures. C—H···C contacts are identified early [10], studied theoretically [11], and established crystallographically [12] and are considered as uncommon type of non-covalent interaction invoked in the description of supramolecular aspects of crystal structures. This weak interaction arises due to the low acidity and basicity of the C—H and C moieties, respectively. The interaction may be enhanced by the use of more acidic proton donor or by increasing the basicity of the acceptor [13]. These contacts are rather scarce in published literature.

Supramolecular interactions involving the nitrile group also play an important role in stabilizing the supramolecular networks and are therefore of particular interest from the viewpoint of crystal engineering [14]. The C≡N group exhibits local dipole moments which are similar to that of the carbonyl group [15], and whose interactions

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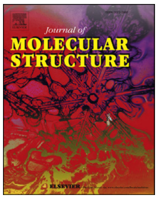
https://doi.org/10.1016/j.ica.2018.12.055
Received 11 October 2018; Received in revised form 30 November 2018; Accepted 31 December 2018

Journal of Molecular Structure 1175 (2019) 130–138

Contents lists available at ScienceDirect

Journal of Molecular Structure

journal homepage: http://www.elsevier.com/locate/molstruc



An unusual werner type clathrate of Mn(II) benzoate involving energetically significant weak C–H⋯C contacts: A combined experimental and theoretical study

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A R T I C L E I N F O

Article history:
Received 30 May 2018
Received in revised form
23 July 2018
Accepted 27 July 2018
Available online 30 July 2018

Keywords:
Enclathration
Supramolecular host
Mn(II) clathrate
Crystal structure
C–H⋯C contact

A B S T R A C T

A new Werner type manganese(II) clatharate $[Mn(Bz)_2(H_2O)_4]\cdot(4{-}CNpy)\cdot 2H_2O$ (**1**), where Bz = benzoate and 4–CNpy = 4–cyanopyridine, has been synthesized at room temperature and characterized by X-ray crystal structure analysis, FT-IR, electronic spectrum and TGA. The crystal structure of cocrystal hydrate of **1** involves a discrete host monomer with enclathrated water and 4-CNpy molecules. Crystallographic studies on the compound **1** reveal that enclathration of guest water molecules in the Mn(II) host units results in a supramolecular tetramer in the crystal structure of **1** involving weak C–H⋯C contacts. The geometry of the supramolecular host tetramer with the guest 4–CNpy molecules has been fully optimized using the crystallographic coordinates and the computational results suggest that the observed C–H⋯C interactions are energetically quite significant. It is observed that both electrostatics as well as dispersion interactions are the most dominant contributors towards the stabilization of the C–H⋯C interaction.

1. Introduction

Clathrate compounds are of interest in crystal engineering because of their inclusion behavior and use as catalysts, antioxidants and stabilizing agents [1]. Studies on inclusion compounds [2,3] are preferred in understanding guest-host interaction [4,5], molecular recognition chemistry [6,7], dynamics of guest molecules in the lattice structures [8] and separation of isomers by selective enclathration [9,10]. Clathrates composed of two-component structures; one of these components is the host structure, whereas the other is the appropriately sized guest molecules that enter into the cavities in the host structure [11]. The guest molecules are stereo selectively trapped in the cavities of host networks leading to the formation of stable inclusion compounds. Although inclusion behavior of organic compounds is well known [12], only a few inorganic compounds viz. Hofmann and Werner complexes exhibit inclusion ability. In various studies, Hofmann-type clathrates [13,14], having general formula $ML_2M'(CN)_4\cdot nG$, were reported, where M is a transition metal atom; M' = Ni, Pd or Pt; L is either a bidentate or two monodentate ligand molecules, G is a guest molecule and n is the number of guest molecules. The Hofmann-type clathrates provide α type cavity for guest molecules which approximates to a rectangular box [15]. The ability of Werner complexes to include a variety of organic guest molecules leads to the other series of inorganic clathrate known as Werner clathrate [16] having the formulae $MX_2A_4\cdot 2G$; where M = Fe, Co, Ni, Cu, Zn, Cd, Mn or Hg; G = benzene, pyrrole, thiophene, dioxane, aniline or biphenyl; X = NCS^-, NCO^-, NO_3^-, NO_2^-, Cl^-, Br^- or I^- and A = pyridine and 4-methylpyridine. Since the discovery of the first clathrate by Hofmann and Küspert in 1897 [17], many studies have been carried out on them in many different fields and are still being carried out [18].

Inclusion of guest molecules in host networks are greatly affected in different ways by the local environment of the atoms involved in complexes and are driven by specific interactions between the guest and host, as well as nonspecific, weak, supramolecular interactions such as coulombic, van der Waals, hydrogen bonding, ion-association forces, and steric interactions [19,20]. Many experimental results have justified the contribution of intra- and intermolecular interactions as well as their cooperation in the synthesis and design of such host-guest supramolecular networks [21,22].

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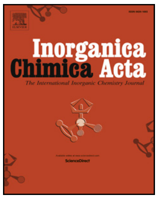
https://doi.org/10.1016/j.molstruc.2018.07.095
0022-2860/

Inorganica Chimica Acta 498 (2019) 119161

Contents lists available at ScienceDirect

Inorganica Chimica Acta

journal homepage: www.elsevier.com/locate/ica



Research paper

Antiproliferative evaluation and supramolecular association involving electrostatically enhanced π-π interaction in isostructural coordination solids of Mn(II), Co(II) and Zn(II) chlorobenzoates: Experimental and theoretical studies

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ARTICLE INFO

Keywords:
Crystal structure
π-π interaction
Cytotoxicity
Apoptosis
Docking
Pharmacophore

ABSTRACT

Three new isostructural coordination solids viz. $[Co(3\text{-}CNpy)_2(2\text{-}ClBz)_2(H_2O)_2]$ (**1**), $[Mn(3\text{-}CNpy)_2(2\text{-}ClBz)_2(H_2O)_2]$ (**2**) and $[Zn(3\text{-}CNpy)_2(2\text{-}ClBz)_2(H_2O)_2]$ (**3**) (3-CNpy = 3-cyanopyridine, 2-ClBz = 2-chlorobenzoate) have been synthesized from purely aqueous media and characterized by X-ray crystal structure analysis, FT-IR, electronic spectra and TGA. Several non-covalent hydrogen bonding interactions of the types O—H···O, C—H···O, C—H···N, C—H···Cl and π-π stacking contacts build up the supramolecular networks in the crystal structures. Electrostatically enhanced π-π interactions are observed in **1**–**3** between the phenyl rings of 2-ClBz and pyridine ring of 3-CNpy of the monomeric units of the complexes. We have used the molecular DFT calculations to evaluate energetically the strength of these contacts and also to analyze the effect of the metal on the interaction energies. The energetic features of the H-bonding and π-stacking interactions for **1**–**3** reveal that the H-bonded assembly is more favorable than the π-stacked contacts. The electrostatically enhanced energy of the π-stacking interactions is stronger than that usually observed for π-stacking interactions involving arenes. The cytostatic potential of all complexes have been studied in Dalton's lymphoma (DL) cell line by MTT assay, apoptosis assay and further corroborated with molecular docking simulation. The complexes exhibit cytotoxicity (~25–30%) through apoptotic cell death with negligible cytotoxicity (~5–10%) in normal PBMC cells. In silico-docking techniques have been performed with apoptosis regulator protein BCL-2 for the identification of critical amino acids and their possible binding affinity with the synthesized complexes. The pharmacophore features based on structure activity relationship (SAR) of the complexes have been identified and the study reveal that the features viz., hydrophobic, aromatic, positive ionizable, negative ionizable, H-bond donor and acceptor and halogen bond donor properties play important role for the biological activities of the complexes.

1. Introduction

The construction of metal-organic networks has emerged as the field of current research interest due to their intriguing variety of structural topologies and various potential applications as functional materials [1]. The rational design and synthesis of the prospective metal-organic networks with the specific properties can be realized by careful selection of the ligands that can explore interesting structures in the solid state [2]. The dynamic character of the metal-ligand bonds, nature and coordinating topologies of the ligands, metal-ligand ratio, different coordination geometries of the metal centers; nature of the counter ions and a variety of experimental conditions (such as the temperature, solvents and methods of crystallization) control the supramolecular assemblies in such networks [3,4].

Carboxylate groups that can display a wide variety of coordination modes are used for designing mixed ligand complexes with interesting structures and topologies [5,6]. The structures of the ancillary ligands and reaction conditions have been shown to have profound effects on

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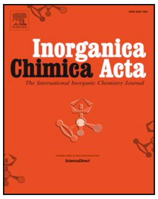
https://doi.org/10.1016/j.ica.2019.119161
Received 17 August 2019; Accepted 17 September 2019

Inorganica Chimica Acta 501 (2020) 119233

Contents lists available at ScienceDirect

Inorganica Chimica Acta

journal homepage: www.elsevier.com/locate/ica



Research paper

Energetically significant antiparallel π-stacking contacts in Co(II), Ni(II) and Cu(II) coordination compounds of pyridine-2,6-dicarboxylates: Antiproliferative evaluation and theoretical studies

Manjit K. Bhattacharyya[a,*], Debajit Dutta[a], Swah Mohd. Nashre-ul-Islam[a], Antonio Frontera[b,*], Pranay Sharma[a], Akalesh K. Verma[c,*], Amal Das[a]

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ARTICLE INFO

Keywords:
Synthesis
Crystal structure
Hydrogen bonding
Antiproliferative
Apoptosis
Docking

ABSTRACT

Three new coordination compounds of types $[Co(py)(2,6\text{-}PDC)(H_2O)_2]\cdot H_2O$ (**1**), $[Ni(py)(2,6\text{-}PDC)(H_2O)_2]\cdot H_2O$ (**2**) and $[Cu(py)(2,6\text{-}PDC)(H_2O)]\cdot 2H_2O$ (**3**) (*py* = pyridine, *2,6-PDC = Pyridine-2,6-dicarboxylate*) have been synthesized from purely aqueous media and characterized using elemental analysis, spectroscopic (IR and electronic) and single crystal X-ray diffraction techniques. Several supramolecular contacts of types O—H···O, C—H···O, C—H···π, C—H···C and π–π stacking stabilize the crystal structures. The layers in the crystal structures stack in perpendicular direction resulting in 1D channel with enclathrated water molecules. The strength of the antiparallel π-stacking interactions involving the pyridine rings in the supramolecular dimer of the compounds have been evaluated using DFT calculations and the influence of the pyridine coordination to the strength of the stacking assembly have been confirmed. The anti-proliferative potential of the compounds has been studied in Dalton's lymphoma (DL) cell line by using MTT cell viability assay and apoptosis assay. All the three complexes exhibit short term (24 h) cytotoxicity (~20–30%) through apoptotic cell death with negligible cytotoxicity (~5–10%) in normal cells. In silico docking simulation has been performed with apoptosis regulator protein BCL-2 for the identification of possible molecular mode of action of the synthesized complexes. The pharmacophore features based on structure activity relationship (SAR) of the complexes have been identified. The SAR results reveal that the molecular features such as, hydrophobic, aromatic, positive ionizable, negative ionizable, H-bond donor and acceptor and halogen bond donor associated with the structures of the compounds play important role in the biological activities. The ADMET features, viz., physicochemical properties, pharmacokinetics, drug-likeness and medicinal chemistry friendliness of the synthesized complexes have been investigated.

1. Introduction

Supramolecular architectures involving organic ligands have gained much importance in the field of crystal engineering because of their potential applications as optical, electrical, magnetic, catalytic and adsorptive materials [1,2]. In recent years, researchers are trying to develop non-covalent supramolecular interactions as a powerful tool for the formation of interesting and fascinating structures of coordination compounds [3–5]. Despite the upsurge in the construction of diverse architectures, the control of dimensionality is still a major challenge in this field [6] due to the fact that the network topologies based on molecular building blocks are usually controlled and modified by the selection of the coordination geometry of the central metal [7,8], the structural chemistry of organic ligands [9,10], the character of solvent used [11,12], and the ratio of metal salt to organic ligands [13].

It is possible to design and construct desired structures of coordination complexes by the proper choice of the organic spacers and the central metals [14,15]. Since long, neutral and rigid N-donor ligands such as pyridine have been widely used to construct supramolecular architectures along with various anionic species that compensate the charge of the resulting metal-organic frameworks [16]. The transition metal supramolecular complexes involving pyridine dicarboxylates provides the possibility of formation of complexes with structural varieties because of the multiple coordination modes as

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https://doi.org/10.1016/j.ica.2019.119233
Received 26 September 2019; Received in revised form 28 October 2019; Accepted 28 October 2019