CRYSTAL GROWTH & DESIGN

ARTICLE

pubs.acs.org/crystal

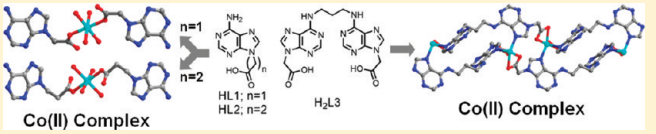
Crystallographic Signatures of Cobalt Coordination with Modified Adenine Nucleobase Containing Carboxyl Group Pendants

Published as part of a virtual special issue on Structural Chemistry in India: Emerging Themes.

Ashutosh Kumar Mishra, Jitendra Kumar, Shruti Khanna, and Sandeep Verma*

Department of Chemistry, Indian Institute of Technology Kanpur Kanpur-208016 (UP), India

ABSTRACT: This paper presents synthesis and crystallographic investigations of certain cobalt complexes of N9-functionalized mono- and bis-adenine analogues, containing a carboxylic group pendant. These observations were meant to expand the coordination space provided by an unmodified adenine moiety, based on known interactions between cobalt and carboxylate functional group, and to examine the structural consequences. A bis-adenine analogue, when compared to the mono-functionalized adenine nucleobase, invokes N7 coordination, in addition to the carboxylate groups, thus supporting formation of complex three-dimensional structures. This study permits entry into novel cobalt-based metallacyclic complexes containing adenine nucleobase as the coordinating N-ligand.



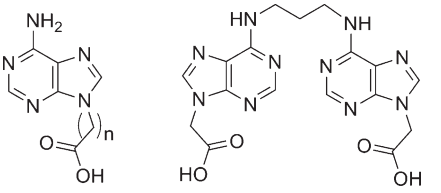
INTRODUCTION

Purine and pyrimidine heterocyclic nucleobases are fundamental constituents required for the composition and functioning of nucleic acids, several vitamins, coenzymes, and antibiotics.[1] Because of the presence of ring and exocyclic nitrogens, sugar hydroxyl, and carbonyl oxygen in nucleosides, a number of stable metal ion interaction sites can be envisaged, which can suitably modulated by the help of modified nucleobases. In particular, N-9 substituted adenine and related analogs exhibit versatile coordination modes toward a number of metal ions as they offer three optimally predisposed ring nitrogens, namely N(1), N(3), and N(7), capable of offering stable coordination with metal ions.[2] Notably, metal-nucleobase interactions not only contribute toward structure, stability, and function of nucleic acids, but they also offer exciting opportunities for the generation of supramolecular architectures that could possibly be exploited for the development of novel functional materials.[3]

While trying to expand the coordination chemistry of modified adenine nucleobase, we have reported synthesis and characterization of adenine-based metalated polymeric matrices with catalytic potential, their ability to form novel supramolecular architecture, and our success in patterning selected coordination geometries on surfaces, followed by their atomic force microscopy studies.[4] In continuation, we wished to study the metal coordination abilities of modified adenine nucleobase toward cobalt ion. Although less frequently encountered in metalloenzymes (e.g., those of zinc and iron), cobalt is an important metal ion cofactor of vitamin B_{12}, where it is held within a corrin macrocycle framework.[5] Furthermore, non-corrin-cobalt-containing enzymes have also been reported.[6]

There are references of numerous studies concerning the understanding of adenine interaction with cobalt(II) ions, by using various techniques covering thermodynamic and kinetic studies.[7] Several X-ray crystallographic findings have also been reported for adenine or N9-methyl adenine Co(II) complexes.[8] In an elegant study, Rosi et al. recently reported structure of an adenine-Co(II) complex, which exhibited excellent selective capture of CO_2 over N_2, with high carbon dioxide capacity and heat of adsorption.[3d] As an extension to our work on metal-adenine interactions, we designed three ligands **HL1**, **HL2**, and **H_2L3** (Scheme 1), bearing carboxylate group at N9-position of adenine to study their coordination properties in water.

Scheme 1. Structure of the Ligands Studied for Metal Coordination



We wished to investigate the complexation behavior of **H_2L3**, as earlier reports have suggested the use of such dinucleotide analogues where bases are connected by a polymethylene chain, as a useful model to probe cross-link formation at adjacent purine bases.[9] In this context, we have explored the possibility of metal ion interaction with N6, N6′-cross-linked modified adenine nucleobase, containing a N9-alkyl substituent, and investigated structural features of its copper and silver complexes.[4h] The ligands used in the present study were synthesized by conventional nucleophilic substitution reactions as reported for adenine nucleobase. The synthetic details and characterization data have been provided in the Experimental Section. This paper strives to discuss the structural consequences and

Received: November 29, 2010
Revised: March 8, 2011
Published: March 11, 2011

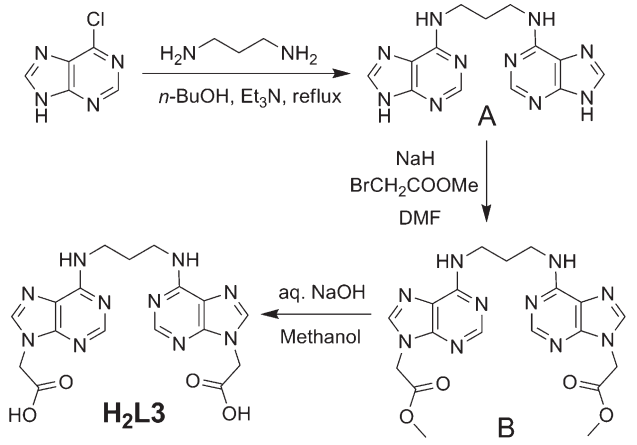
ACS Publications © 2011 American Chemical Society

ramifications in three cobalt complexes of modified adenine derivatives, where N9-substituent offers carboxylic acid functionality for interaction. The beneficial role of carboxylate groups in stabilizing cobalt coordination motifs is well-studied and documented.[10]

EXPERIMENTAL SECTION

1. Synthesis of 2-(N9-adeninyl) Acetic Acid (HL1). The target compound **HL1** was sysnthesized in two steps starting from adenine.

Scheme 2. Synthetic scheme for the Ligand H_2L3



In a typical procedure, adenine (3.0 g, 1.0 equiv) was suspended in dry DMF (50 mL) and the reaction mixture was cooled to 0 °C followed by the addition of NaH (1.06 g, 1.2 equiv). The stirring was continued at 0 °C for 1 h and methyl bromo acetate (2.0 mL, 0.9 equiv) was added slowly. The reaction mixture was brought to room temperature and stirred for another 24 h under nitrogen atmosphere. After this time, the reaction mixture was concentrated under vacuum and the crude reaction mass was purified by column chromatography using $CHCl_3$:CH_3OH (95:5) as an eluent yielding 2.0 g (44%) of 2-(N9-adeninyl) acetic acid methyl ester as white powder. HRMS: $(M+H)^+$ = calculated: 208.0835, found: 208.0835. ^{1}H NMR: (500 MHz, $CDCl_3/CD_3OD$, 25 °C, TMS) δ (ppm) 3.76 (s, 3H, CH_3), 4.94 (s, 2H, CH_2), 7.84 (s, 1H, C2−H), 8.22 (b, 1H, C8−H). ^{13}C NMR (125 MHz, DMSO, 25 °C, TMS); δ (ppm) 44.31, 52.95, 118.74, 141.74, 150.19, 153.19, 156.49, 169.03.

The above methyl ester (2.0 g, 9.6 mmol) was suspended in 44 mL of 5N HCl and refluxed until the completion of reaction as monitored by TLC analysis. The reaction mixture was cooled down to room temperature and neutralized with Na_2CO_3. The compound was precipitated out as white powder which was collected and dried. Yield 1.1 g (60%). HRMS: $(M+H)^+$ = calculated: 194.0678, found: 194.0675. ^{1}H NMR: (500 MHz, DMSO-d_6, 25 °C, TMS) δ (ppm) 4.35 (s, 2H, CH_2), 6.97 (s, 2H, NH_2), 7.93 (s, 1H, C2−H), 8.03 (s, 1H, C8−H). ^{13}C NMR (125 MHz, DMSO-d_6, 25 °C, TMS); δ (ppm) 47.33, 118.68, 142.79, 150.21, 152.36, 156.18, 169.33.

2. Synthesis of 3-(N9-adeninyl) Propanoic Acid (HL2). The synthesis of the target compound 3-(N9-adeninyl) propanoic acid is reported elsewhere.[4i,11]

Table 1. Crystal Structure Refinement Parameters for the Complexes 1−3

identification code	complex **1**	complex **2**	complex **3**
empirical formula	$C_{14}H_{20}CoN_{10}O_8$	$C_{16}H_{28}CoN_{10}O_{10}$	$C_{17}H_{18}CoN_{10}O_5$
M_r	515.33	579.41	501.34
cryst syst	triclinic	monoclinic	triclinic
space group	$P\bar{1}$	$P21/c$	$P\bar{1}$
a (Å)	7.010(5)	7.937(3)	8.451(3)
b (Å)	7.988(4)	12.110(4)	9.032(4)
c (Å)	9.281(5)	12.301(4)	13.264(5)
α (deg)	86.344(5)	90.000	79.914(6)
β (deg)	83.185(5)	99.007(2)	89.183(7)
γ (deg)	69.550(3)	90.000	81.247(7)
V (Å^3)	483.4(5)	1167.8(7)	985.1(7)
Z	1	2	2
Dx (Mg m^{-3})	1.770	1.648	1.690
F(000)	265	602	514
μ (mm^{-1})	0.960	0.811	0. 929
θ range for data collection (deg)	2.21−28.30	2.37−28.37	2.32−26.99
limiting indices	−9 →h →9, −9 →k →10, −12→l →5	−10 →h →10, −15 →k →16, −9 →l →16	−10 →h →10, −5 →k →11, −16 →l →16
reflections collected	3169	7531	5812
unique reflections	2279	2882	4110
R(int)	0. 0224	0.0592	0.0316
completeness to θ	= 28.30, 98.3	= 28.37, 98.5	= 26.99, 97.1
data/restraints/parameters	2279/6/168	2882/0/193	4110/3/306
GOF on F^2	1.180	1.156	1.104
$R1$ and $R2$ [$I > 2\sigma(I)$]	0. 0634, 0. 1495	0.0535, 0.1115	0.0639, 0.1664
$R1$ and $R2$ (all data)	0. 0911, 0. 2147	0.0965, 0.1746	0.0858, 0.2237
largest diff. peak and hole (e Å^{-3})	0. 830 and −1.477	0.754 and −1.156	1.284 and −0.854

dx.doi.org/10.1021/cg101581g |*Cryst. Growth Des.* 2011, 11, 1623–1630

Table 2. Hydrogen Bonding Table for Complexes 1−3[#]

D−H...A	symmetry of A	D−H	H···A	D−A	∠D−H···A
		Complex **1**			
N6−H6A···O1	$1-x, -y, 1-z$	0.88	2.32	3.066(7)	143
N6−H6B···O2	$x, y, 1+z$	0.88	2.12	2.940(6)	155
O1W−H1A···N3	$x, 1+y, z$	0.85(6)	1.95(6)	2.798(6)	173(7)
O1W−H1B···O2	$-x, 1-y, -z$	0.85(7)	1.99(7)	2.795(7)	159(8)
O2W−H2B···N1	$x, 1+y, -1+z$	0.86(5)	1.89(5)	2.744(6)	178(10)
O2W−H2A···O2		0.86(7)	2.04(7)	2.702(6)	133(7)
		Complex **2**			
N6−H6A···O1	$1-x, 1-y, 1-z$	0.86	2.18	3.021(5)	167
N6−H6B···O2W	$1-x, 1/2+y, 1/2-z$	0.86	2.30	3.084(5)	152
O1W−H1A···O2	$1-x, 1-y, -z$	0.76(8)	1.90(8)	2.615(5)	159(9)
O1W−H1B···N7	$1-x, -1/2+y, 1/2-z$	0.90(7)	1.95(7)	2.811(5)	160(7)
O2W−H2A···O3W	$x, 1/2-y, -1/2+z$	0.77(6)	1.93(6)	2.695(5)	173(7)
O2W−H2B···N1	$x, y, -1+z$	0.88(7)	1.92(7)	2.799(5)	178(10)
O3W−H3A···N3		0.90(6)	1.94(6)	2.821(5)	165(5)
O3W−H3B···O2	$-x, -1/2+y, 1/2-z$	0.83(8)	1.91(9)	2.721(5)	163(8)
		Complex **3**			
N6−H6···O1	$-1+x, y, z$	0.86	2.13	2.971(6)	165
N6′−H6′···O1	$2-x, 1-y, 1-z$	0.86	2.22	3.070(5)	168
O1W−H1W1···N1′	$2-x, -y, 1-z$	0.84(3)	1.92(4)	2.733(6)	162(6)
O1W−H1W2···O2		0.84(4)	1.87(6)	2.650(6)	154(7)

[#] Where D is donor and A is acceptor, the bond lengths are in Å and angles are in deg.

3. Synthesis of H_2L3. The synthetic scheme for the ligand H_2L3 is given as Scheme 2.

3.1. Synthesis of Trimethylene-N6, N6′-bis-adenine (A). 6-Chloropurine (2.2 g, 1.0 equiv) was dissolved in *n*-butanol followed by addition of 1,3-diaminopropane (0.57 mL, 0.5 equiv) and triethylamine (2.38 mL, 1.2 equiv). This solution was refluxed for 5 h, after which yellowish precipitate of **A** appeared in the reaction mixture, which was filtered and washed with methanol (2×5 mL) and acetone (2×5 mL). Yield = 1.5 g (68%). HRMS: $(M+H)^+$ calcd, 311.1481; found, 311.1420. ^{1}H NMR: (500 MHz, DMSO-d_6, 25 °C, TMS) δ (ppm) 1.89 (m, 2H, CH_2), 3.94 (bs, 4H, CH_2), 6.68 (bs, 2H, NH), 8.22 (s, 2H, C2−H), 8.30 (s, 2H, C8−H), 12.98 (s, 2H, N9−H). ^{13}C NMR (100 MHz, DMSO-d_6, 25 °C, TMS); δ (ppm) 37.31, 41.25, 119.55, 140.62, 148.23, 153.94, 155.80.

3.2. Synthesis of Trimethylene-N6, N6′-bis-[2-(N9-adeninyl) Acetic Acid Methyl Ester] (B). Compound **A** (1.7 g, 1.0 equiv) was suspended in 20 mL of dry DMF and the solution was cooled to 0 °C followed by the addition of sodium hydride (0.48 g, 2.2 equiv). The stirring was continued at 0 °C for 1 h and methyl bromo acetate (2.08 mL, 4.0 equiv) was added slowly. The reaction mixture was brought to room teperature and stirred for another 8 h, followed by concentration of the reaction mixture under reduced pressure. 30 mL of distilled water was added to the reaction mixture and, after stirring for 15 min, the resulting mixture was kept in refrigerator at 0 °C for overnight. An off-white precipate was setteled which was filtered and washed with water (2×5 mL) to get pure compound. Yield = 1.3 g (52%). HRMS: $(M+H)^+$ calcd, 455.1904; found, 455.1903. ^{1}H NMR: (500 MHz, DMSO-d_6, 25 °C, TMS) δ (ppm) 1.78 (m, 2H, CH_2), 3.51 (bs, 4H, CH_2), 4.36 (s, 6H, CH_3), 4.88 (s, 4H, CH_2), 8.06 (s, 2H, C2−H), 8.20 (s, 2H, C8−H). ^{13}C NMR (100 MHz, DMSO-d_6, 25 °C, TMS); δ (ppm) 33.45, 43.53, 55.27, 59.65, 119.55, 140.62, 148.23, 153.94, 155.80, 169.85.

*3.3. Synthesis of Trimethylene-N6, N6′-bis-[2-(N9-adeninyl) Acetic Acid] (**H_2L1**).* Compound **B** (0.4 g, 1.0 equiv) was dissolved in 5 mL of methanol followed by the addition of 2N NaOH solution (2 mL, 4.5 equiv). The reaction mixture was stirred for 1 h follwed by passing it through Amberlite resin to get the neutral solution, which after evaporation under reduced pressure provided the target compound as white powder. Yield = 245 mg (65%). HRMS: $(M+H)^+$ calcd, 427.1591; found, 427.1598; $(M+Na)^+$ calcd, 449.1410; found, 449.1418. ^{1}H NMR: (500 MHz, DMSO-d_6, 25 °C, TMS) δ (ppm) 1.86 (b, 2H, CH_2), 3.53 (b, 4H, CH_2), 4.76 (s, 4H, CH_2), 7.84 (bs, 2H, NH), 8.04 (s, 2H, C2−H), 8.16 (s, 2H, C8−H). ^{13}C NMR (125 MHz, DMSO-d_6,

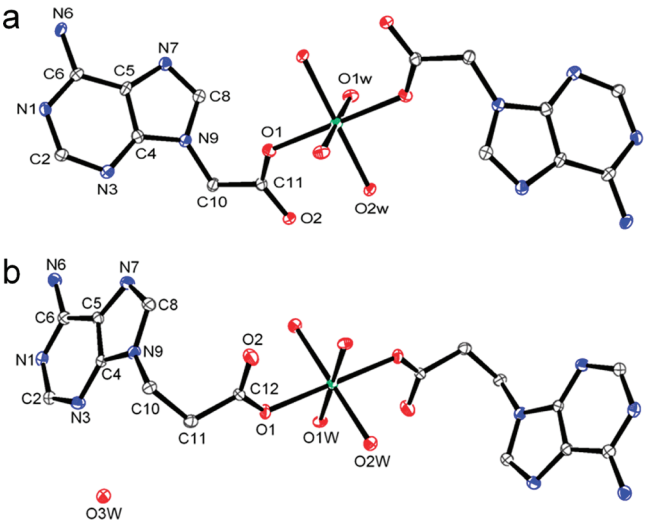


Figure 1. Molecular structure of complexes with the cobalt atom on a crystallographic inversion center. Unique atoms are labeled: (a) for **1**, and (b) for **2**. Bond distances (in Å) for **1**: Co−O1 = 2.086(4), Co−O1*w* = 2.107(4), Co−O2*w* = 2.067(4); and for **2**: Co−O1 = 2.118(3), Co−O1*w* = 2.087(3), Co−O2*w* = 2.108(3).

dx.doi.org/10.1021/cg101581g |*Cryst. Growth Des.* 2011, 11, 1623–1630

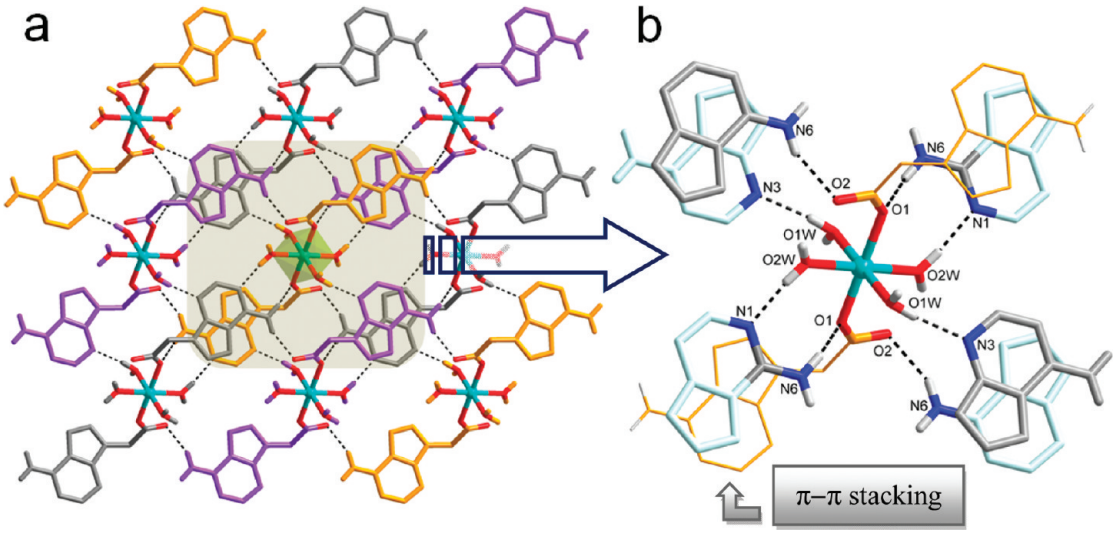


Figure 2. (a) Hydrogen-bonded lattice of **1**; (b) magnified view of the lattice highlighted in part 'a' depicting $\pi-\pi$ stacking interaction; nitrogen atoms involved in hydrogen bonding are shown in blue color.

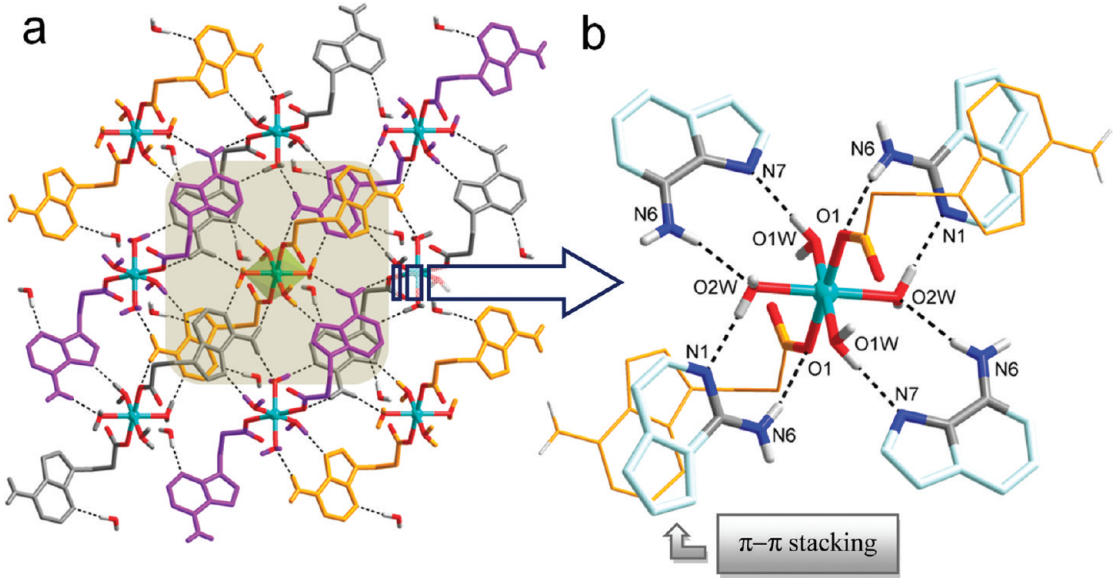


Figure 3. (a) Hydrogen-bonded lattice of complex **2**; (b) Magnified view of the lattice highlighted in part 'a' depicting $\pi-\pi$ stacking interaction; nitrogen atoms involved in hydrogen bonding are shown in blue color.

25 °C, TMS); δ (ppm) 37.62, 45.41, 118.62, 142.02, 149.43, 152.85, 154.95, 170.07.

4. Synthesis of Complex 1 [$C_{14}H_{20}CoN_{10}O_8$] and 2 [$C_{16}H_{28}CoN_{10}O_{10}$]. Block shape pink color crystals of complex **1** [$C_{14}H_{20}CoN_{10}O_8$] and **2** [$C_{16}H_{28}CoN_{10}O_{10}$] have been grown within a week from their aqueous methanolic (1:1) solution by dissolving stoichiometric amounts of $CoCl_2.6H_2O$ and **HL1** or **HL2** ligand in aqueous methanolic solution with the aid of heat. The yield for complex **1** and complex **2** was 74 and 57%, respectively, with respect to the ligand. HRMS: For complex **1** $[2.\mathbf{L1}+Co+H]^+$ calcd, 444.0453; found, 444.0434; for complex **2** $[2.\mathbf{L2}+Co+H]^+$ calcd, 472.0766; found, 472.0788.

5. Synthesis of Complex 3 [CoL3.H_2O]. A mixture of 100 mg of H_2L3 (0.2 mmol) and 55 mg of $Co(II)Cl_2.6H_2O$ (0.2 mmol) was suspended in 5 mL of distilled water and stirred for 10 min in air. The mixture was turned into a 10 mL Teflon-lined stainless steel container and heated at 120 °C for 24 h and cooled down to room temperature at a rate of 10 °C/h. The clear solution thus obtained was filtered and left undisturbed for slow evaporation, which provided block shaped pink color crystals of complex **3** [$CoL3.H_2O$] within the period of two weeks. Yield = 65 mg (55%); HRMS $[H_2L_3+Co+H+CH_3CN]^{+3}$ calcd, 527.1188; found, 527.1151.

CRYSTAL STRUCTURE DETERMINATION AND REFINEMENT

Crystals were coated with light hydrocarbon oil and mounted in the 100 K dinitrogen stream of a Bruker SMART APEX CCD diffractometer equipped with CRYO Industries low-temperature apparatus and intensity data were collected using graphite-monochromated Mo−Kα radiation. The data integration and reduction

were processed with SAINT software.[12] An absorption correction was applied.[13] Structures were solved by the direct method using SHELXS-97 and refined on F^2 by a full-matrix least-squares technique using the SHELXL-97 program package.[14] Non-hydrogen atoms were refined anisotropically. In the refinement, hydrogens were treated as riding atoms using the SHELXL default parameters. In case of **2,** water hydrogen atoms were refined freely, however in case of **1** and **3** constrains were applied to fix the O−H distance and H−O−H angle. Crystal structure refinement parameters and H−bonding parameters are given as Tables 1 and 2, respectively.

RESULTS AND DISCUSSION

Crystal Structure Analysis of 1 and 2. The known beneficial interaction of carboxylate groups with cobalt ions provided us an impetus to introduce a carboxyl pendant in the adenine skeleton. Ligands **HL1** and **HL2**, differing with each other in terms of number of methylene units between adenine and carboxylate group, were synthesized and reacted with $CoCl_2$. Block-shaped pink-colored crystals of **1** $[C_{14}H_{20}CoN_{10}O_8]$ and **2** $[C_{16}H_{28}CoN_{10}O_{10}]$ were grown from their aqueous methanolic (1:1) solution by dissolving stoichiometric amounts of $CoCl_2.6H_2O$ and **HL1** or **HL2** in aqueous methanol, dissolved by gentle heating. X-ray crystallographic analysis revealed that complex **1** crystallized in a triclinic space group $P\bar{1}$, whereas complex **2** crystallized in a monoclinic space group $P2_1/c$. The asymmetric unit in both the cases consisted of a cobalt ion of half-occupancy neutralized by either **L1** or **L2** anion, along with two or three water molecules, respectively (Figure 1).

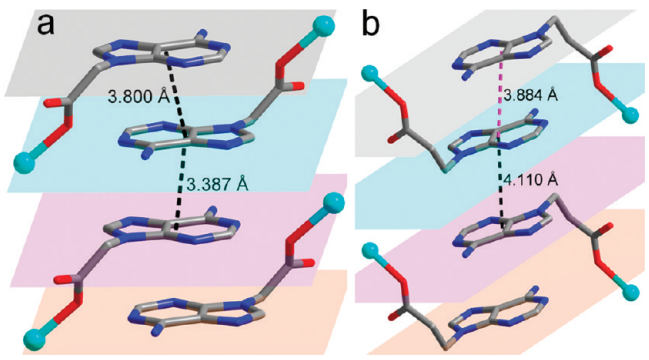


Figure 4. Part of the crystal lattice depicting $\pi-\pi$ stacking interactions between adenine residues: (a) in **1**, and (b) in **2**.

Both of these complexes exhibit formation of coordination complexes with a 1:2 M:L stoichiometry through carboxylate coordination with Co(II) ions in a *trans* manner, with an octahedral geometry around the cobalt center. The primary coordination sphere of Co(II) ion is composed of six oxygen atoms out of which two originate from the carboxylate groups of **L1** or **L2** and rest of them are attributed to the aqua ligands. The structures of the coordination complexes of **1** and **2**, where N9 substituent differs only by the length of one methylene unit, are almost identical with similar coordination bond lengths and bond angles. However, in case of **2**, an extra water molecule is found trapped in the lattice stabilized with the help of hydrogen bonding. The various modes of hydrogen-bonding interactions are worth to be discussed in some detail.

The part of the crystal lattice of **1** built around cobalt octahedron is shown in Figure 2a, where each octahedron unit interacts with six adenine residues belonging to different octahedron units, as denoted with different color code, through N−H···O or O−H···N hydrogen bonding as shown in Figure 2b. Curiously, N7 nitrogen of adenine is not involved in hydrogen bonding interaction. The various H-bonding parameters are given in Table 2.

In the case of **2**, a marked difference in the H-bonding pattern, compared to **1**, arises probably because of the presence of noncoordinated water molecule (O3W) in the crystal lattice although the lattice itself appears to be very similar, as can be compared from Figures 2 and 3. Here, four adenine moieties are found interacting with the cobalt octahedron motif, both through their Watson−Crick and Hoogsteen faces (Figure 3). The adenine N3-nitrogen is found H−bonded to the noncoordinated water molecule in the crystal lattice (Figure 3a) which is utterly different from the complex **1** where N3 nitrogen was interacting with coordinated aqua ligand.

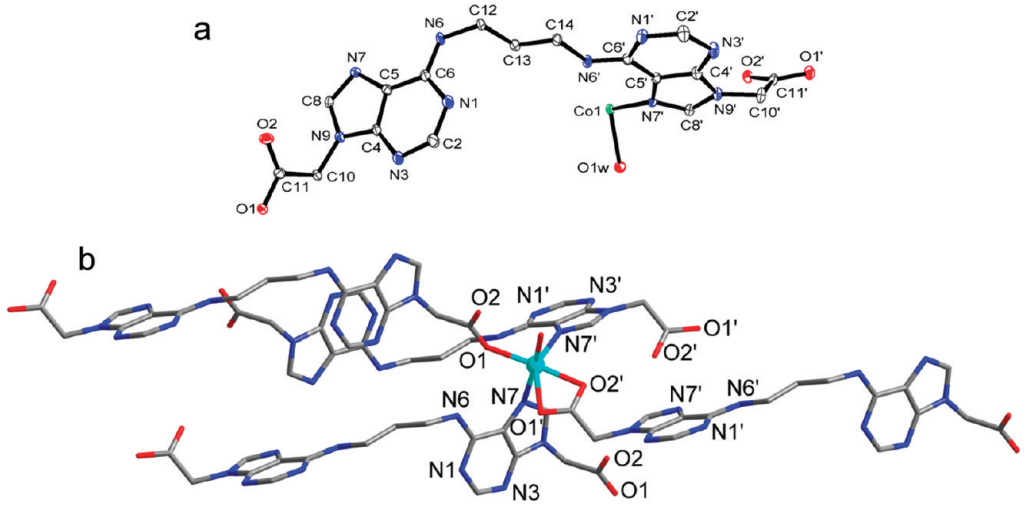


Figure 5. (a) ORTEP diagram of asymmetric unit of **3** (30% ellipsoid probability); (b) part of the coordination framework showing the interaction of **L3** dianions with a single cobalt center. Bond distances Co−N7 = 2.138(4); Co−N7′ = 2.113(4); Co−O1 = 2.080(3); Co−O1′ = 2.296(4), and Co−O2′ = 2.125(3) Å (color code: Co, turquoise; C, gray; N, blue and O, red).

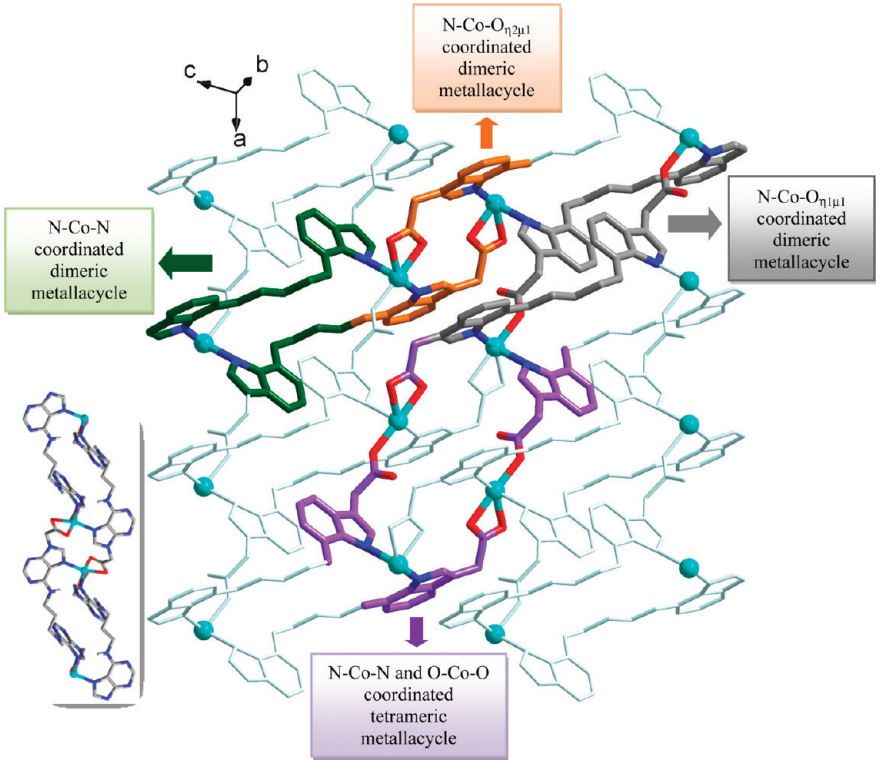


Figure 6. Part of the crystal lattice of **3** with different color codes indicating variably sized embedded and interconnected metallacycles as a result of different coordination modes (Inset: lattice along *a*-axis; turquoise colored spheres represent Co(II) ions; N7 nitrogen and carboxylate oxygens are highlighted with blue and red color, respectively).

Notably, further stabilization of the crystal lattice, in both cases, comes from π-stacking interactions as shown in Figure 4. There are two sets of interactions found between adenine rings for both the complexes. For complex **1**, the interplanar distance between adenine residues is 3.39 Å (gray and turquoise plane) and 3.35 Å (turquoise and purple plane) alternatively, however the distances between the centroids of adenine rings are slightly longer which ranges between 3.38 and 3.80 as shown in Figure 4a. The interplanar distances for complex **2** are found to be 3.58 Å (gray and turquoise plane) and 3.63 Å (turquoise and purple plane) alternatively between adenine residues. However, the distances between the centroids of adenine rings are again slightly longer and ranges between 3.88 and 4.11 Å, as shown in Figure 4b.

Crystal Structure Analysis of 3. Pink-colored crystals of complex **3** [Co**L3**·H_2O] were grown by slow evaporation from an aqueous solution by dissolving $\mathbf{H_2L3}$ and $CoCl_2$ in a ratio of 1:1 under hydrothermal conditions as described in the experimental section. The asymmetric unit consisted of $\mathbf{H_2L3}$ ligand as a dianion, a Co(II) ion and an aqua ligand (Figure 5a). The carboxyl group modified *bis*-adenine entity offers carboxylate oxygens and N7 nitrogens for cobalt coordination, thereby behaving as a tetradentate species; thus leads to the generation of four crystallographically identical cobalt centers. Each cobalt ion is simultaneously coordinated to four different **L3** dianions in the crystal lattice, and the coordination sphere around cobalt ion consist of two N7 ring imino nitrogen, three oxygen atoms from two carboxylate groups and one aqua ligand leading to a distorted octahedral geometry for the Co(II) center as can be seen from the comparison of bond lengths in Figure 5b.

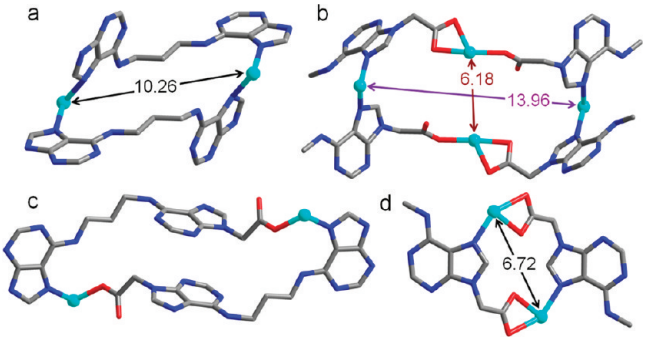


Figure 7. Different metallacycles embedded in the crystal lattice of **3** with Co−Co distances in Å. (a−d) Metallacycles highlighted with green, purple, gray, and golden yellow colors, respectively, in Figure 6.

Detailed crystal structure analysis of complex **3** revealed a complex supramolecular lattice consisting of variably sized metallacycles that arise out of cobalt coordination with modified adenine nucleobase (Figure 6). A closer inspection of the crystal lattice clearly shows that the solid state structure of **3** consists of four different types of interconnected metallacycles, as represented with different color codes, as a result of tetradentate coordination mode offered by **L3**. For instance, four N7 nitrogens of two **L3** dianion get coordinated to cobalt ions (represented by turquoise color) with ∠N−Co−N angle of 94°, resulting in a two Co-four adenine dimeric metallacycle (green colored framework in Figure 6); however, a different type of two Co-four adenine dimeric metallacycle could be identified

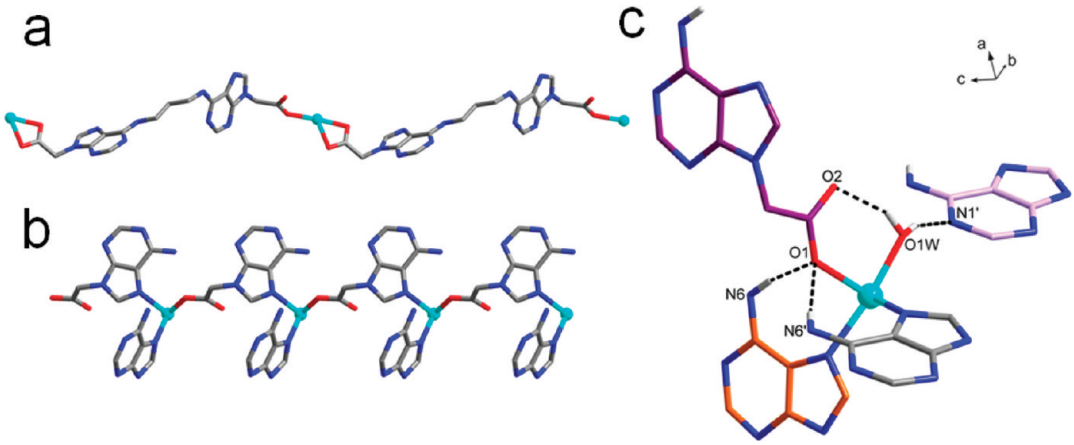


Figure 8. Different types of cobalt tethered coordination polymeric chains: (a) polymeric chain involving extended geometry for ligand via carboxylate-metal coordination; (b) polymeric chain formed via metal coordination with N7 and carboxylate of different adenine moieties. (c) Hydrogen-bonding scheme in complex **3** with different color code representing part of the different **L3** ligands.

where N7 nitrogen and carboxylate oxygen of two **L3** molecules get coordinated to cobalt ion, with $\eta^1\mu^1$ coordination mode, exhibiting a ∠N−Co−O angle of 97.68° (gray colored framework in Figure 6); finally, another dimeric metallacycle could be located as a result of N−Co−O coordination, with $\eta^2\mu^1$ coordination from carboxylate group (golden yellow framework in Figure 6). A singular tetrameric metallacycle was observed where four adenine moieties from four different **L3** ligands coordinated with cobalt in O−Co−O and N−Co−N fashion (purple colored framework in Figure 6). Notably, all these metallacycles were interconnected giving rise to a complex, yet highly unique, formation of supramolecular lattice. A more clear representation of the different types of metallacycles is presented in Figure 7 and the various Co−Co distances.

Two different types of cobalt-tethered 1D coordination polymeric chains are encountered in the crystal lattice of **3**: in one case, oxygen from the carboxylate groups of **L3** coordinate to cobalt ions resulting in the formation of polymeric chain, whereas the other polymeric chain involves cobalt coordination at adenine N7 and carboxylate group from different adenine moieties. The stabilization of crystal lattice also results from the hydrogen bonding schemes offered by coordinated aqua ligand and the exocyclic amino group hydrogens directed toward carboxylate group, which is coordinated in $\eta^1\mu^1$ fashion to cobalt ions. The aqua ligand acts as a hydrogen bond donor toward N1 nitrogen of one adenine residue (N1′) and the noncoordinated oxygen atom (O2) of the carboxylate group, whereas O1 oxygen, coordinated to the cobalt center, simultaneously acts as an acceptor for the two different hydrogens from the exocyclic amino group, as shown in Figure 8c.

CONCLUSION

In conclusion, we have synthesized and investigated the cobalt complexes of N9 functionalized mono- and bis-adenine analogues. This exercise expands the coordination space provided by unmodified adenine moiety and relies on the known interactions between cobalt and carboxylate functional group. It was observed that the bis-adenine analogue, when compared to monofunctionalized adenine, offers N7 adenine nitrogen, in addition to carboxylate groups for metal coordination, resulting in a complex 3D-crystal lattice structures. An interesting interplay of N- and O-coordination results in complex hierarchical design on the crystalline material and affords entry into newer metallacyclic complexes containing adenine nucleobase as coordinating N-ligand.

ASSOCIATED CONTENT

Supporting Information. X-ray crystallographic data in CIF format.This material is available free of charge via the Internet at http://pubs.acs.org. CCDC contains the supplementary crystallographic data for this paper with a deposition number of CCDC **800573** (complex **1**), **800572** (complex **2**), and **787553** (complex **3**). Copies of this information can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB21EZ, UK. [Fax: +44−1223/336−033; E-mail: deposit@ccdc.cam.ac.uk].

AUTHOR INFORMATION

Corresponding Author
*E-mail: sverma@iitk.ac.in.

ACKNOWLEDGMENT

We thank Single Crystal CCD X-ray facility at IIT-Kanpur; CSIR, for SRF (A.K.M.), SPM Fellowship (J.K.), and JRF (S.K.). This work is supported by Bioinorganic Initiative of DST, India (SV).

REFERENCES

(1) (a) Chan, H. S. O.; Lusty, J. R. *J. Therm. Anal.* **1985**, *30*, 25–32. (b) Hueso-Ureña, F.; Illán-Cabeza, N. A.; Moreno-Carretero, M. N.; Martínez-Martos, J. M.; Ramírez-Expósito, M. J *J. Inorg. Biochem.* **2003**, *94*, 326–34. (c) Ibrahim, D. A.; El-Metwally, A. M. *Eur. J. Med. Chem.* **2010**, *45*, 1158–1166.

(2) Schmidt, K. S.; Reedijk, J.; Weisz, K.; Basilio Janke, E. M.; Sponer, J. E.; Sponer, J.; Lippert, B. *Inorg. Chem.* **2002**, *41*, 2855–2863.

(3) (a) Lippert, B. *Coord. Chem. Rev.* **2000**, *200−202*, 487–516 and references therein.. (b) Fish, R. H.; Jaouen, G. *Organometallics* **2003**, *22*, 2166–2177 and references therein.. (c) An, J.; Rosi, N. L. *J. Am. Chem. Soc.* **2010**, *132*, 5578–5579. (d) An, J.; Geib, S. J.; Rosi, N. L. *J. Am. Chem. Soc.* **2010**, *132*, 38–39. (e) An, J.; Geib, S. J.; Rosi, N. L. *J. Am. Chem. Soc.* **2009**, *131*, 8376–8377. (f) An, J.; Fiorella, R. P.; Geib, S. J.; Rosi, N. L. *J. Am. Chem. Soc.* **2009**, *13*, 8401–8403. (g) Fathalla, M.; Lawrence, C. M.; Zhang, N.; Sessler, J. L.; Jayawickramarajah, J. *Chem.*

Soc. Rev. **2009**, *38*, 1608–1620. (h) Rowan, S. J.; Mather, P. T. *Struct. Bonding (Berlin)* **2007**, *128*, 119–149. (i) Araki, K.; Yoshikawa, I. *Top. Curr. Chem.* **2005**, *256*, 133–165.

(4) (a) Srivatsan, S. G.; Verma, S. *Chem. Commun.* **2000**, 515–516. (b) Srivatsan, S. G.; Verma, S. *Chem.—Eur. J.* **2001**, *7*, 828–833. (c) Srivatsan, S. G.; Parvez, M.; Verma, S. *Chem.—Eur. J.* **2002**, *8*, 5184–5191. (d) Mukhopadhyay, R.; Srivatsan, S. G.; Verma, S. *Biochem. Biophys. Res. Commun.* **2003**, *308*, 165–169. (e) Purohit, C. S.; Verma., S. *J. Am. Chem. Soc.* **2006**, *128*, 400–401. (f) Purohit, C. S.; Verma., S. *J. Am. Chem. Soc.* **2007**, *129*, 3488–3489. (g) Purohit, C. S.; Mishra, A. K.; Verma, S. *Inorg. Chem.* **2007**, *46*, 8493–8495. (h) Mishra, A. K.; Purohit, C. S.; Verma, S. *CrystEngComm* **2008**, *10*, 1296–1298. (i) Kumar, J.; Verma., S. *Inorg. Chem.* **2009**, *48*, 6350–6352. (j) Pandey, M. D.; Mishra, A. K.; Chandrasekhar, V.; Verma., S. *Inorg. Chem.* **2010**, *49*, 2020–2022. (k) Verma, S.; Mishra, A. K.; Kumar, J. *Acc. Chem. Res.* **2010**, *43*, 79–91. (l) Mishra, A. K.; Verma, S. *Inorg. Chem.* **2010**, *49*, 3691–3693. (m) Mishra, A. K.; Verma, S. *Inorg. Chem.* **2010**, *49*, 8012–8016. (n) Mishra, A. K.; Prajapati, R. K.; Verma, S. *Dalton Trans.* **2010**, *39*, 10034–10037.

(5) Battersby, A. R. *Acc. Chem. Res.* **1993**, *26*, 15–21.

(6) Kobayashi, M.; Shimizu, S. *Eur. J. Biochem.* **1999**, *261*, 1–9.

(7) (a) Liquier-Milward, J. *Nature* **1951**, *167*, 1068–1069. (b) Pannala, V. A.; Ettaiah, P.; Raju, R. M. *Orient. J. Chem.* **2006**, *22*, 113–118. (c) Ayar, A.; Mercimek, B. *Process Biochem.* **2006**, *41*, 1553–1559. (d) Abd El Wahed, M. G.; Nour, E. M.; Teleb, S.; Fahim, S. *J. Therm. Anal. Calorim.* **2004**, *76*, 343–348. (e) Ayar, A.; Ali Gürten, A. *Colloid. Surface A* **2003**, *229*, 149–155. (f) Özdere, G.; Kurt, G.; Mercimek, B.; Ayar, A. *Colloids Surf., A* **2003**, *223*, 287–293. (g) Cücü, A. K.; Pekin, M.; Demir, H. D.; Aboul-Enein, H. Y. *Toxicol. Environ. Chem.* **2001**, *80*, 165–174. (h) Mishra, L.; Pathak, B. *J. Indian Chem. Soc.* **2001**, *78*, 643–648. (i) Singh, N. P.; Srivastava, M. N.; Kumar, G. *Orient. J. Chem.* **2000**, *16*, 223–227. (j) Demir, H. D.; Pekin, M.; Cücü, A. K.; Dölen, E.; Aboul-Enein, H. Y. *Toxicol. Environ. Chem.* **1999**, *71*, 357–367.

(8) (a) De Meester, P.; Goodgame, D. M. L.; Richman, D. J.; Skapski, A. C. *Nature* **1973**, *242*, 257–258. (b) De Meester, P; Goodgame, D. M. L.; Skapski, A C; Warnke, Z *Biochim. Biophys. Acta* **1973**, *324*, 301–303. (c) García-Terán, J. P.; Castillo, O.; Luque, A.; García-Couceiro, U.; Román, P.; Lloret, F. *Inorg. Chem.* **2004**, *43*, 5761–5770. (d) Zaworotko, M. J.; Hammud, H. H.; Kabbani, A.; McManus, G. J.; Ghannoum, A. M.; Masoud, M. S. *J. Chem. Cryst.* **2009**, *39*, 853–863.

(9) Browne, D. T.; Eisinger, J.; Leonard, N. J. *J. Am. Chem. Soc.* **1968**, *90*, 7302–7323.

(10) (a) Hulvey, Z.; Furman, J. D.; Turner, S. A.; Tang, M.; Cheetham, A. K. *Cryst. Growth Des.* **2010**, *10*, 2041–2043. (b) Su, Z.; Fan, J.; Okamura, T.-A.; Sun, W.-Y.; Ueyama, N. *Cryst. Growth Des.* **2010**, *10*, 3515–3521. (c) Zeng, M.-H.; Zhou, Y.-L.; Wu, M.-C.; Sun, H.-L.; Du, M. *Inorg. Chem.* **2010**, *49*, 6436–6442. (d) Hulvey, Z.; Melot, B. C.; Cheetham, A. K. *Inorg. Chem.* **2010**, *49*, 4594–4598. (e) Li, C.-P.; Yu, Q.; Chen, J.; Du, M. *Cryst. Growth Des.* **2010**, *10*, 2650–2660. (f) Wang, G.-H.; Lei, Y.-Q.; Wang, N.; He, R.-L.; Jia, H.-Q.; Hu, N.-H.; Xu, J.-W. *Cryst. Growth Des.* **2010**, *10*, 534–540. (g) Ma, L.-F.; Wang, L.-Y.; Du, M.; Batten, S. R. *Inorg. Chem.* **2010**, *49*, 365–367. (h) Lama, P.; Aijaz, A.; Sanudo, E. C.; Bharadwaj, P. K. *Cryst. Growth Des.* **2010**, *10*, 283–290. (i) Fabelo, O.; Pasán, J.; Cañadillas-Delgado, L.; Delgado, F. S.; Yuste, C.; Lloret, F.; Julve, M.; Ruiz-Pérez, C. *CrystEngComm* **2009**, *11*, 2169–2179. (j) Kurmoo, M. *Chem. Soc. Rev.* **2009**, *38*, 1353–1379. (k) Ji, J.-W.; Zhang, W.; Zhang, G.-X.; Han, Z.-B. *Inorg. Chem. Commun.* **2009**, *12*, 956–958. (l) Pérez-Yáñez, S.; Castillo, O.; Cepeda, J.; García-Terán, J. P.; Luque, A.; Román, P. *Eur. Jour. Inorg. Chem.* **2009**, *26*, 3889–3899. (m) Yang, J.; Ma, J.-F.; Liu, Y.-Y.; Batten, S. R. *CrystEngComm.* **2009**, *11*, 151–159. (n) Zeng, M.-H.; Zou, H.-H.; Hu, S.; Zhou, Y.-L.; Du, M.; Sun, H.-L. *Cryst. Growth Des.* **2009**, *9*, 4239–4242. (p) Sarma, D.; Ramanujachary, K. V.; Lofland, S. E.; Magdaleno, T.; Natarajan, S. *Inorg. Chem.* **2009**, *48*, 11660–11676. (q) Guillou, N.; Livage, C.; Férey, G. *Eur. J. Inorg. Chem.* **2006**, 4963–4978.

(11) Weisser, M.; Käshammer, J.; Menges, B.; Matsumoto, J.; Nakamura, F.; Ijiro, K.; Shimomura, M.; Mittler, S. *J. Am. Chem. Soc.* **2000**, *122*, 87–95.

(12) *SAINT+*, 6.02 ed.; Bruker AXS, Madison, WI, 1999.

(13) Sheldrick, G. M. *SADABS 2.0*; University of Göttingen: Göttingen, Germany, 2000.

(14) Sheldrick, G. M. *SHELXL-97: Program for Crystal Structure Refinement*; University of Göttingen: Göttingen, Germany, 1997.