

## Reactions of Metal Ions with Vitamins. IV. The Crystal Structure of a Zinc Complex of Pyridoxamine (Vitamin B<sub>6</sub>)

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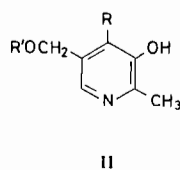
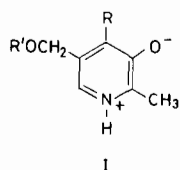
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The structure of  $[\text{Zn}(\text{PM})_2(\text{H}_2\text{O})_2](\text{NO}_3)_2$ ,  $\text{ZnC}_{16}\text{H}_{28}\text{N}_6\text{O}_{12}$ , has been determined from three-dimensional X-ray data collected by counter methods. The compound crystallizes in the monoclinic space group  $P2_1/n$  with  $Z = 2$  and cell dimensions  $a = 15.790(4)$ ,  $b = 4.777(2)$ ,  $c = 15.058(9)$  Å,  $\beta = 95.04(6)^\circ$ . The structure was refined to a final conventional  $R$  factor of 0.060 for 1397 reflections with  $F \geq 3\sigma(F)$ . The zinc atoms lie on centers of symmetry, and are chelated to the 4-aminomethyl and phenolate groups of pyridoxamine (PM) zwitterions. Octahedral coordination is completed by water molecules. The Zn–OH<sub>2</sub>, Zn–O (phenolate), and Zn–N distances are 2.171(5), 2.174(4), and 2.061(5) Å, respectively. The packing is determined by hydrogen bonds involving all of the available N–H and O–H groups in the compound.

### Introduction

We have been examining the structures and spectra of metal complexes of the B<sub>6</sub> vitamers [1–3]. A consistent, chemically reasonable interpretation of the infrared spectra of the complexes was made in the previous paper [3] by assuming that the zwitterionic form *I* of the vitamer was chelated to the metal, rather than the nondipolar form *II*. The X-ray crystal structures of several complexes have been undertaken order to confirm the infrared spectral interpretations and provide detailed bonding information [1, 2]. The present paper reports the crystal structure of a pyridoxamine complex of zinc,  $[\text{Zn}(\text{PM})_2(\text{H}_2\text{O})_2](\text{NO}_3)_2$ , where R is CH<sub>2</sub>NH<sub>2</sub> and R' H in *I* and *II*.



### Experimental

A colorless needle-shaped crystal, 0.05 × 0.05 × 0.85 mm, was chosen from a batch which contained mostly very small crystals and only a few of sufficient size to be useful crystallographically. The crystal was mounted on a glass fiber with epoxy glue. Oscillation and Weissenberg photographs showed systematic absences consistent with space group  $P2_1/n$ . The crystal was transferred to a Picker manual four-circle diffractometer and accurate cell dimensions were obtained. The crystal data are:  $a = 15.790(4)$ ,  $b = 4.777(2)$ ,  $c = 15.058(9)$  Å,  $\beta = 95.04(6)^\circ$ ,  $D_c = 1.65$  g cm<sup>-3</sup> for  $Z = 2$  units of  $\text{ZnC}_{16}\text{H}_{28}\text{N}_6\text{O}_{12}$ ,  $\mu(\text{MoK}\alpha) = 11.99$  cm<sup>-1</sup>.

Data were collected by  $\omega$ - $2\theta$  scans on the Picker diffractometer with Zr-filtered MoK $\alpha$  radiation. Scans were made over a  $2\theta$  range of  $2^\circ$  at a rate of  $1^\circ$  min<sup>-1</sup>. Twenty-second backgrounds were counted at each end of the scan range. A standard was measured after every 25–30 reflections, and did not vary significantly during the data collection. The reflection intensities were corrected for background and converted to structure factors  $F$  by applying Lorentz and polarization corrections. The weighting scheme used in the final stages of least-squares refinement was

$$w = \frac{1.738}{\sigma^2(F) + 0.0016F^2}$$

where  $\sigma(F)$  is the standard deviation based on counting statistics. A total of 1994 reflections with  $2\theta \leq 50^\circ$  were measured. Of these, 1397 had  $F \geq 3\sigma(F)$  and were classified as observed.

The SHELX-76 [4] computer programs were used for structure determination and refinement by full-matrix least-squares methods. Scattering factors for neutral Zn, C, H, N, and O atoms were taken from the International Tables for X-ray Crystallography [5], as were the real and imaginary parts of the anomalous scattering [6].

The Patterson map confirmed the locations of the zinc atoms on centers of symmetry, and also revealed a four-atom fragment of the PM ring.

Subsequent difference maps revealed all of the atoms in the structure, including hydrogen atoms. Positional parameters and anisotropic thermal parameters were refined for all non-hydrogen atoms. All hydrogen atoms were assigned an isotropic temperature factor  $U = 0.05$ . Positional parameters were refined only for those hydrogen atoms whose positions were not geometrically fixed (H(1), H(7), H(8), H(11), H(13), H(14)). The methyl group was treated as a rigid rotor, and the other hydrogens were included as fixed contributions to the structure factor.

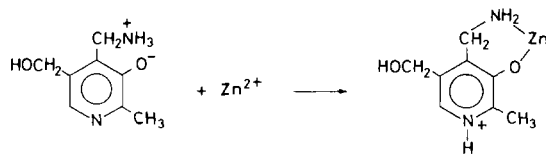
The final conventional  $R$  index for the 1397 observed reflections was 0.060;  $R_w$  was 0.058. The final difference Fourier map revealed no unusual features.

## Results and Discussion

Figure 1 shows the atom numbering scheme and a perspective view of the molecule. Bond distances and angles are given in Fig. 2. The atomic coordinates are listed in Tables I and II, and the equations of important planes in the structure are given in Table III. The molecular packing is shown in Figs. 3 and 4, with hydrogen bonds listed in Table IV.

The atom locations show that pyridoxamine exists as a zwitterion in the zinc complex, as was

also observed in the structure of  $\text{Cu}(\text{PM})_2(\text{NO}_3)_2 \cdot \text{H}_2\text{O}$  [1, 2]. Pyridoxine occurs as a similar zwitterion in its cadmium complex [7]. The reaction between PM and  $\text{Zn}^{2+}$  thus involves a change in the tautomeric form of PM, as proposed previously [3]:



The bond lengths and angles (Fig. 2) in the PM ligands are very close to those observed in other vitamin  $\text{B}_6$  complexes [1, 2, 7], uncomplexed vitamin  $\text{B}_6$  compounds [8–12], and pyridoxylidene Schiff base complexes [13–15]. The  $\text{C}(1)\text{--N}(1)\text{--C}(8)$  angle of  $123.6(6)^\circ$  is normally observed when a pyridine nitrogen is protonated [16]. The  $\text{C}(3)\text{--O}(1)$  distance of  $1.309(6)$  Å is much shorter than a single  $\text{C}\text{--O}$  bond. A number of resonance forms may be drawn which give the  $\text{C}(3)\text{--O}(1)$  bond considerable double-bond character:

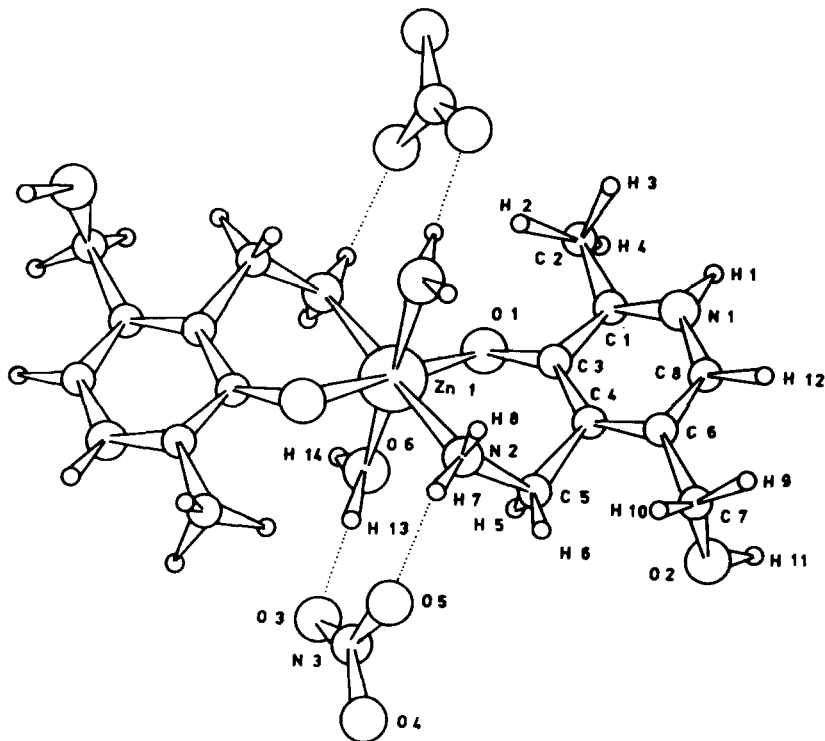
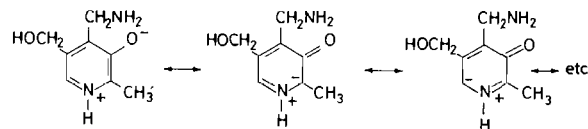


Fig. 1. View of a  $[\text{Zn}(\text{PM})_2(\text{H}_2\text{O})_2](\text{NO}_3)_2$  unit. The dotted lines represent hydrogen bonds which hold the nitrate group in the secondary coordination sphere of zinc.

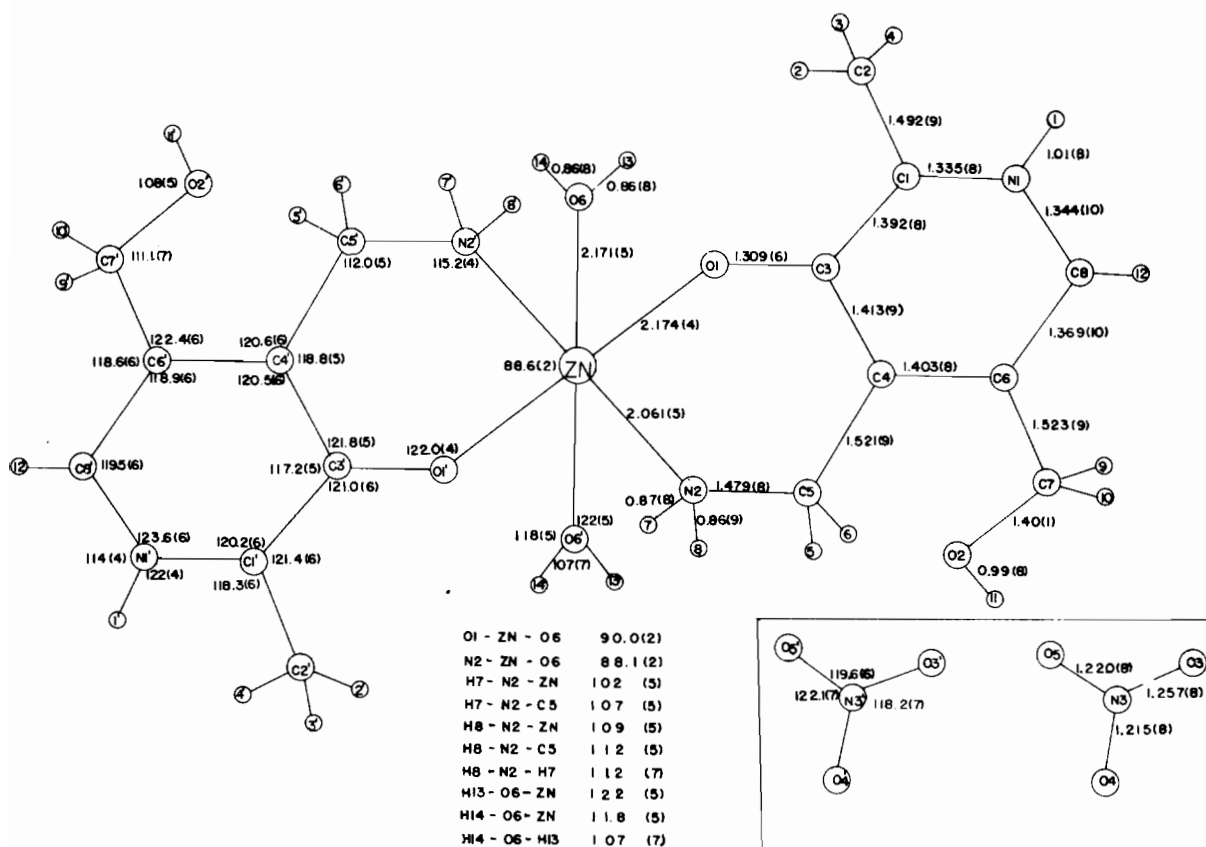


Fig. 2. Bond distances and angles.

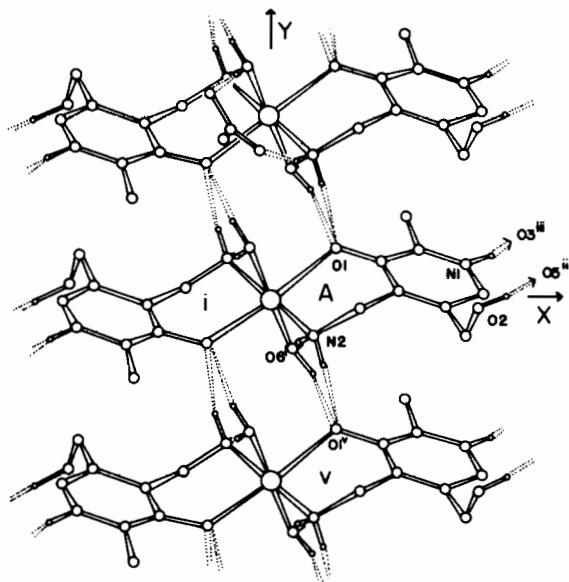


Fig. 3. Linkage of the  $[\text{Zn}(\text{PM})_2(\text{H}_2\text{O})_2](\text{NO}_3)_2$  units to form chains parallel to the  $y$ -axis. Symmetry key: A ( $x, y, z$ ); i ( $-x, -y, -z$ ); ii ( $0.5 - x, 0.5 + y, 0.5 - z$ ); iii ( $0.5 + x, 0.5 - y, -0.5 + z$ ); iv ( $0.5 + x, 0.5 - y, 0.5 + z$ ); v ( $x, -1 + y, z$ ); vi ( $1 - x, 1 - y, -z$ ); vii ( $x, y, 1 + z$ ); viii ( $1 - x, -y, 1 - z$ ). Only one nitrate group is shown in order to avoid obscuring the chain linkages.

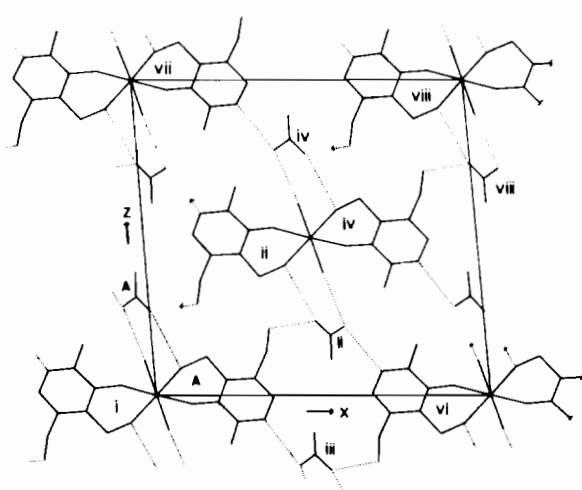


Fig. 4. Packing of  $[\text{Zn}(\text{PM})_2(\text{H}_2\text{O})_2](\text{NO}_3)_2$ . See Fig. 3 for the symmetry key. The symbol  $\cdots$  indicates a hydrogen bond to a nitrate group in a higher or lower unit cell.

The zinc ion is not involved in resonance ( $d\pi \rightarrow \pi^*$  bonding), as there are no significant changes in PM bond lengths when PM is complexed to a metal ion.

The zinc atoms lie on centers of symmetry, and are chelated to two PM ligands through the amino and phenolate groups, N(2) and O(1), respectively.

TABLE I. Positional and Thermal Parameters of the Non-hydrogen Atoms in  $\text{Zn}(\text{C}_8\text{H}_{12}\text{N}_2\text{O}_2)_2(\text{NO}_3)_2 \cdot 2\text{H}_2\text{O}$  (all  $\times 10^4$ ).

Atom	x	y	z	U <sub>11</sub>	U <sub>22</sub>	U <sub>33</sub>	U <sub>23</sub>	U <sub>13</sub>	U <sub>12</sub>
Zn	0	0	0	244(5)	216(5)	284(5)	24(6)	13(3)	24(6)
C(1)	2385(4)	2621(14)	-849(4)	329(34)	301(37)	342(34)	-11(31)	115(27)	-1(30)
C(2)	2107(4)	4476(15)	-1617(5)	443(37)	340(51)	480(40)	6(34)	152(31)	113(33)
C(3)	1832(3)	1892(12)	-216(4)	217(29)	180(32)	325(33)	-37(28)	23(25)	29(26)
C(4)	2163(3)	220(16)	507(4)	298(29)	236(34)	339(31)	-179(37)	3(23)	-5(34)
C(5)	1593(4)	-496(14)	1239(4)	385(33)	287(47)	278(31)	16(29)	-12(25)	-20(29)
C(6)	3014(4)	-662(13)	568(4)	316(33)	324(50)	421(38)	18(30)	-66(28)	39(29)
C(7)	3407(5)	-2393(19)	1348(5)	390(41)	593(55)	529(46)	67(45)	-90(34)	89(40)
C(8)	3518(4)	143(22)	-81(5)	258(29)	633(51)	601(44)	-89(60)	45(29)	78(46)
N(1)	3196(3)	1802(14)	-749(4)	325(30)	491(41)	442(35)	67(33)	143(27)	-38(29)
N(2)	835(3)	-2110(12)	893(4)	250(28)	248(30)	341(32)	20(26)	21(23)	-21(24)
N(3)	-374(4)	-720(14)	3130(4)	366(32)	603(52)	346(33)	68(31)	45(25)	-38(31)
O(1)	1040(2)	2737(9)	-291(3)	232(21)	252(24)	327(23)	37(20)	51(17)	22(19)
O(2)	3562(3)	-744(14)	2116(4)	591(34)	836(54)	493(32)	162(33)	-169(26)	-201(33)
O(3)	-833(3)	1259(14)	2819(4)	552(34)	763(41)	581(35)	142(34)	140(27)	265(33)
O(4)	-337(4)	-1155(20)	3927(4)	973(49)	1428(75)	552(39)	306(44)	257(35)	277(50)
O(5)	51(4)	-2046(16)	2637(4)	778(41)	893(52)	612(38)	-102(38)	159(33)	352(39)
O(6)	-286(3)	2739(10)	1085(3)	392(26)	235(25)	357(25)	14(22)	81(21)	82(21)

TABLE II. Positional Parameters for Hydrogen Atoms in  $\text{Zn}(\text{C}_8\text{H}_{12}\text{N}_2\text{O}_2)_2(\text{NO}_3)_2 \cdot 2\text{H}_2\text{O}$  ( $\times 10^3$ ).<sup>a</sup>

Atom	x	y	z
H(1)	360(4)	217(16)	-121(5)
H(2)*	143	423	-175
H(3)*	242	374	-218
H(4)*	226	666	-150
H(5)*	138	143	153
H(6)*	195	-171	175
H(7)	53(5)	-235(16)	134(5)
H(8)	97(4)	-368(18)	66(5)
H(9)*	400	-329	117
H(10)*	297	-405	149
H(11)	410(5)	30(20)	207(6)
H(12)*	418	-48	-5
H(13)	-44(4)	209(17)	158(5)
H(14)	-60(5)	417(17)	96(5)

<sup>a</sup>Asterisks indicate hydrogen atoms refined as part of a rigid group.

Octahedral coordination is completed by two water molecules as shown in Fig. 1. The Zn–O(1) and Zn–O(6) distances are identical within experimental error, being 2.174(4) and 2.171(5) Å, respectively. The Zn–N(2) distance, 2.061(5) Å, is shorter than the Zn–O distances. These values are quite different from the Zn–O (phenol) and Zn–N (azomethine) distances of 2.02 and 2.10 Å, respectively, found in a zinc complex of a pyridoxylidene Schiff base [13]. However, it seems to be characteristic of zinc to exhibit widely different Zn–ligand bond lengths, even for a given coordination number [17–19].

The valence angles at the zinc atom are all close to 90°, as shown in Fig. 2. The chelate ring 'bite' (O(1) ... N(2)) of 2.958 Å is shorter than the non-bite O(1) ... N(2)<sup>i</sup> distance, 3.033 Å. In the copper

TABLE III. Planes in  $\text{Zn}(\text{C}_8\text{H}_{12}\text{N}_2\text{O}_2)_2(\text{NO}_3)_2 \cdot 2\text{H}_2\text{O}$  and Deviations of the Atoms therefrom.<sup>a, b</sup>

A. Chelate Ring: $0.1692X - 0.7282Y - 0.6642Z = 10.1628$			
Zn*	0.021 Å	O(1)	0.399 Å
N(2)*	-0.026	C(5)	0.684
C(3)*	-0.031		
C(4)*	0.036		
B. Pyridine Ring: $-0.2150X - 0.8208Y - 0.5292Z = 8.8511$			
C(1)*	-0.012 Å	C(2)	0.033 Å
C(3)*	-0.002	C(7)	0.050
C(4)*	0.008	C(5)	0.094
C(6)*	-0.002	O(1)	0.004
C(8)*	-0.011		
N(1)*	0.019		
C. Nitrate Group: $-0.7478X - 0.6441Y - 0.1613Z = 1.2325$			
N(3)*	-0.017		
O(3)*	0.005		
O(4)*	0.006		
O(5)*	0.006		

<sup>a</sup>The atoms used to define the planes are indicated by asterisks. <sup>b</sup>The equations are of the form  $AX + BY + CZ = D$ , where X, Y, and Z are orthogonal coordinates (in Å) of the atoms.

chelates of PM [2], the average bite distance is 2.85 Å, which is longer than the nonbite distance. It has been established [20] that the bite distance increases with increasing metal–ligand bond length, so that the change on going from copper to zinc is not unexpected.

The chelate ring conformation is similar to the boat conformation observed in the copper chelates of PM [2]. The Zn, N(2), C(3) and C(4) atoms define a plane, with the methylene carbon C(5) and the phenolate oxygen O(1) above this plane (Table III). Boat conformations are unusual, but apparently the

TABLE IV. Hydrogen Bonding in Zn(C<sub>8</sub>H<sub>12</sub>N<sub>2</sub>O<sub>2</sub>)<sub>2</sub>(NO<sub>3</sub>)<sub>2</sub> · 2H<sub>2</sub>O.<sup>a</sup>

Atoms a–b...c	ac, Å	bc, Å	Angle, ° abc,
N(2)–H(7)...O(5)	2.999	2.16	162
N(2)–H(8)...O(1) <sup>v</sup>	3.073	2.25	153
N(1)–H(1)...O(3) <sup>iii</sup>	2.906	1.93	164
O(2)–H(11)...O(5) <sup>ii</sup>	2.813	1.87	158
O(6)–H(13)...O(3)	2.906	2.05	170
O(6) <sup>i</sup> –H(14) <sup>i</sup> ...O(1) <sup>v</sup>	2.696	1.88	158

<sup>a</sup>See Fig. 3 for key to symmetry superscripts.

geometric constraints imposed by the trigonal C(3) and C(4) atoms help to stabilize the boat conformation for PM chelates.

The structure is held together by a series of hydrogen bonds whose parameters (Table IV) are normal for N–H...O and O–H...O interactions. The basic packing unit in the structure can be formally described as [Zn(PM)<sub>2</sub>(H<sub>2</sub>O)<sub>2</sub>] complexes attached through hydrogen bonds to the O(3) and O(5) atoms of the nitrate groups, as shown in Fig. 1. These units are then linked into chains parallel to the *y*-axis, as shown in Fig. 3. The hydrogen bonds responsible for the chain linkages involve donation from the N(2)–H(7) and O(6)–H(14) groups to a phenolate oxygen atom O(1) in translationally-related molecules. The H(8)...O(1)<sup>v</sup>...H(14)<sup>i</sup> angle is 73°, thus supporting the participation of both lone pairs of electrons on O(1)<sup>v</sup> in the two hydrogen bonds.

The pyridinium group N(1)–H(1) and the hydroxymethyl group O(2)–H(11) are also hydrogen-bond donors to the O(3) and O(5) atoms of the nitrate groups. It is these interactions which serve to link the chains into a rigid three-dimensional structure. Figure 4, which is a projection of the structure parallel to the chain direction, shows these interactions clearly for nitrate groups N(3)<sup>ii</sup>–O(5)<sup>ii</sup> and N(3)<sup>iii</sup>–O(5)<sup>iii</sup>.

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