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Models of Metal–Nucleoside Polyphosphates: Structures of Unidentate $[CoHP_2O_7(NH_3)_5].H_2O$ [Pentaamminepyrophosphatocobalt(III) Monohydrate] and Bidentate $[CoHP_2O_7(NH_3)_4].2H_2O$ [Tetraamminepyrophosphatocobalt(III) Dihydrate]

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Abstract

The unidentate and bidentate pyrophosphate complexes $[CoHP_2O_7(NH_3)_5].H_2O$ and $[CoHP_2O_7(NH_3)_4].2H_2O$ serve as models for metal–phosphate chelation of MgADP, MgATP and other biological pyrophosphates. Crystals of $[CoHP_2O_7(NH_3)_5].H_2O$ belong to space group *Cc* with $a = 10.095$ (2), $b = 9.436$ (2), $c = 12.423$ (2) Å, $\beta = 98.73$ (2)°, and $Z = 4$. Crystals of $[CoHP_2O_7(NH_3)_4].2H_2O$ belong to space group $P2_1/c$ with $a = 7.358$ (2), $b = 13.881$ (2), $c = 11.216$ (1) Å, $\beta = 92.00$ (1)°, and $Z = 4$. The six-membered chelation ring formed by the bidentate complex is found to be in a distorted boat conformation with the two axial pyrophosphate oxygens forming interligand hydrogen bonds to the two axial ammine nitrogens. In both complexes the pyrophosphate conformation is staggered. The bridging Co—O—P bond angle of 139.3 (2)° and P—O—P bond angle of 131.3 (2)° in the unidentate complex are wider than the equivalent bond angles in the chelation ring of the bidentate complex, where the Co—O—P angles are 126.1 (1) and 127.0 (1)° and the P—O—P angle is 127.1 (1)°. The P—O bonds involving the bridging oxygen are unequal in length. This molecular asymmetry of the two halves of the pyrophosphate group is characteristic of organic pyrophosphates and may prove important to bond-specific cleavage by pyrolytic enzymes. From the chelation geometry of these complexes and a knowledge of nucleotide conformations we have generated models for enzymatically active MgADP and MgATP structures involving bidentate chelation.

Introduction

A large number of the biological reactions involving nucleoside polyphosphates (*e.g.* ADP = adenosine diphosphate, ATP = adenosine triphosphate) require the presence of a metal ion. In nature the nucleotide–metal complex is usually formed with magnesium, although other metal ions may be substituted. Further, some enzymes will accept one stereoisomer of such a complex while rejecting others. It has been shown that isomers of the cobaltammine complexes $Co(NH_3)_nADP$ and $Co(NH_3)_nATP$ will function as substrates for these enzymes, but have the advantage over magnesium complexes of being sufficiently stable for separation and characterization (Cornelius & Cleland, 1978; Li, Mildvan & Switzer, 1978). We are thus studying the X-ray structure of equivalent cobaltammine complexes of pyrophosphate and tripolyphosphate as models for the metal–phosphate chelation of the various stereoisomers of MgADP and MgATP. We report here the structure of two cobaltammine pyrophosphate complexes, one unidentate and one bidentate. We have previously reported the structure and chirality of the bidentate tripolyphosphate complex $[CoH_2P_3O_{10}(NH_3)_4].H_2O$ (Merritt, Sundaralingam, Cornelius & Cleland, 1978). Subsequently we obtained a better set of intensity data for this compound which has allowed a more accurate refinement. The coordinates from this refinement are used in comparisons with the related structures in this paper.

Experimental

Crystals of $[CoHP_2O_7(NH_3)_5].H_2O$, $[CoHP_2O_7(NH_3)_4].2H_2O$, and $[CoH_2P_3O_{10}(NH_3)_4].H_2O$ were supplied by Drs R. D. Cornelius and W. W. Cleland (Cornelius, Hart & Cleland, 1977). Crystals of the former two compounds were purple rods of varying cross-section. Space group and unit-cell parameters were initially determined from Weissenberg photographs and refined before data collection on an Enraf–Nonius CAD-4 κ-geometry diffractometer. Intensity data were collected using Ni-filtered Cu $K\alpha$ radiation. Reflections were measured by a θ–2θ scan in a minimum absorption position (CAD-4 'needle' mode).

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$[CoHP_2O_7(NH_3)_5].H_2O$

Intensity data were collected from a crystal 0·05 × 0·10 × 0·43 mm. Of 1235 unique reflections measured, 1197 were considered observed by the criterion $F_o > 6\sigma(F_o)$. An additional set of 120 Bijvoet pairs of reflections between $\theta = 20°$ and $\theta = 30°$ was collected. Crystal decay was monitored by four standard reflections measured after every 3 h of X-ray exposure. No appreciable drop in the intensity of these standards was detected. Lorentz–polarization correction was applied during data reduction, as was an empirical absorption correction as a function of the Eulerian angle Φ.

$[CoHP_2O_7(NH_3)_4].2H_2O$

Intensity data were collected from a crystal 0·075 × 0·075 × 0·30 mm. Of 2425 unique reflections scanned, 2381 were considered observed by the criterion $F_o > 3\sigma(F_o)$. Crystal decay was monitored using four standard reflections which were measured after every 5 h of exposure time. Corrections for Lorentz–polarization and an overall decay of 4% were applied during data reduction. No correction was made for absorption ($\mu = 14{\cdot}8$ mm^{-1}).

$[CoH_2P_3O_{10}(NH_3)_4].H_2O$

A new set of intensity data were collected from a crystal 0·025 × 0·10 × 0·30 mm. No net decay was observed in the intensity of four standard reflections measured after every 3 h of X-ray exposure. Of 1393 unique reflections scanned, 1379 were considered observed by the criterion $F_o > 3\sigma(F_o)$. Lorentz–polarization correction and an empirical absorption correction based on the Eulerian angle Φ were applied during data reduction.

All computations in this work were performed by a dedicated PDP 11/35 computer in the Crystallography Laboratory using programs developed by members of this laboratory (E. A. Merritt, J. P. McAlister, S. T. Rao). Atomic scattering factors for non-hydrogen atoms were taken from Cromer & Waber (1965); those for H were taken from Stewart, Davidson & Simpson (1965). Anomalous-scattering components for the atoms were taken from Cromer & Liberman (1970).

Structure determination

$[CoHP_2O_7(NH_3)_5].H_2O$

The 16 non-hydrogen atoms were located from a Patterson map and successive Fourier syntheses using coefficients $2F_o - F_c$. These 16 atoms were refined by the full-matrix least-squares technique to an agreement index R of 0·089 ($R = \sum||F_o| - |F_c||/\sum |F_o|$) with isotropic temperature factors for the atoms. No anomalous-scattering terms were included to this point. To preclude parameter errors due to anomalous scattering in this polar space group (Cruickshank & McDonald, 1967), the correct hand of the structure was selected by inclusion of f'' terms. The proper choice of hand yielded $R = 0{\cdot}094$ for $f'' > 0$ and $R = 0{\cdot}125$ for $f'' < 0$. Further refinement with anomalous terms included in F_c and anisotropic thermal parameters brought R to 0·049. Thirteen of the fifteen ammine H atoms appeared in an $F_o - F_c$ Fourier synthesis calculated at this point. The two remaining H atoms were geometrically fixed. All H atoms were given a fixed isotropic thermal parameter of 4·0 Å^2; their positional parameters were refined along with all non-hydrogen atom parameters to final values $R = 0{\cdot}045$, $R_w = 0{\cdot}053\{R_w = [\sum w(|F_o| - |F_c|)^2/\sum w|F_o|^2]^{1/2}$, $w = [\sigma^2_{Fo} + (0{\cdot}07\ F_o)^2]^{-1}\}$. Four reflections were excluded from this refinement due to serious secondary extinction.

The maximum shift/error for non-hydrogen parameters during the final cycle of refinement was 0·052. The water and pyrophosphate H atoms were not located.

$[CoHP_2O_7(NH_3)_4].2H_2O$

The 16 non-hydrogen atoms were located from an origin-removed Patterson map and two subsequent Fourier syntheses. These atoms were refined by the full-matrix least-squares technique with isotropic temperature factors and unit weights to $R = 0{\cdot}075$.

Further refinement using anisotropic temperature factors and terms due to anomalous dispersion brought the R value to 0·047. At this point a Fourier synthesis using coefficients $F_o - F_c$ revealed all 12 ammine H atoms (0·51 e Å^{-3} < ρ < 0·92 e Å^{-3}) and four water H atoms (0·44 e Å^{-3} < ρ < 0·68 e Å^{-3}). A peak near O(222) with $\rho = 67$ e Å^{-3} was interpreted as the pyrophosphate hydroxyl hydrogen. Four final rounds of refinement included positional parameters for all atoms, anisotropic temperature factors for all non-hydrogen atoms, and isotropic temperature factors for the H atoms. Five reflections were excluded from the refinement due to serious secondary extinction. The final R index was 0·035 and the weighted R_w index was 0·052, $w = [\sigma^2_{F_o} + (0{\cdot}03\ F_o)^2]^{-1}$. The maximum shift/error for nonhydrogen parameters during the final cycle of refinement was 0·12. Refined H positions were close to the values generally found in X-ray work (average N–H distance = 0·834 Å; average Co–N–H angle = 111·5°).

$[CoH_2P_3O_{10}(NH_3)_4].H_2O$

The previously reported coordinates (Merritt *et al.*, 1978) for the 19 non-hydrogen atoms were refined using the new data to $R = 0{\cdot}061$ by the block-diagonal least-squares technique. An inadvertent error in the handling of f' terms in the previous work was discovered and corrected. This error had no effect on the correct determination of absolute configuration. Cell parameters for this compound are $a = 8{\cdot}162$ (2), $b = 10{\cdot}229$ (3), $c = 7{\cdot}585$ (2) Å, $\beta = 99{\cdot}44$ (1)° (space group $P2_1$). Nine ammine hydrogens, two water hydrogens, and a hydrogen associated with O(2) were found in a $F_o - F_c$ difference Fourier synthesis. The three remaining ammine hydrogens were fixed geometrically and all H atoms given an isotropic thermal parameter of 4·0 Å^2. All atoms were refined by the full-matrix least-squares technique to a final R of 0·058. Two reflections were excluded from this refinement due to serious secondary extinction. Reflections were weighted by $w = [\sigma^2_{F_o} + (0{\cdot}04F_o)^2]^{-1}$. The second H belonging to the tripolyphosphate ligand was not located. The maximum shift/error for non-hydrogen parameters during the final cycle of refinement was 0·075.*

Results

$[CoHP_2O_7(NH_3)_5].H_2O$

An *ORTEP* (Johnson, 1965) drawing showing bond distances of the unidentate complex is given in Fig. 1. Atomic coordinates and bond angles are given in Tables 1 and 2. There are two interligand close contacts in the complex: O(111)···N(5) 2·884 (6) Å, and O(222)···N(3) 2·933 (5) Å. Both are shown as hydrogen bonds in the crystal-packing diagram in Fig. 2. The shortest intermolecular contact is a hydrogen bond between O(11) and O(22) of 2·444 (6) Å; how-

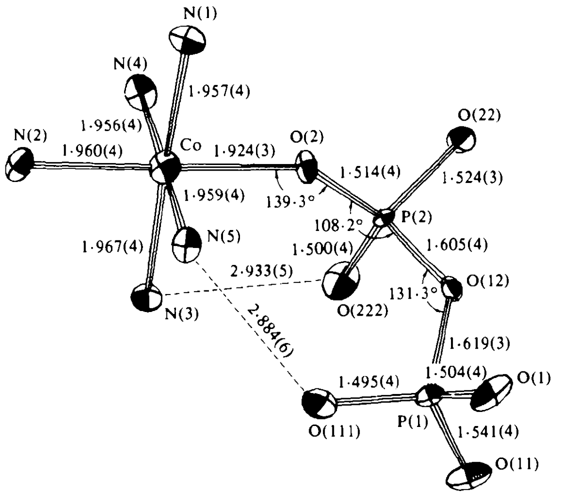

Fig. 1. *ORTEP* drawing of unidentate $[CoHP_2O_7(NH_3)_5]$. Thermal ellipsoids are drawn at the 50% probability level. Bond lengths are given in Å.

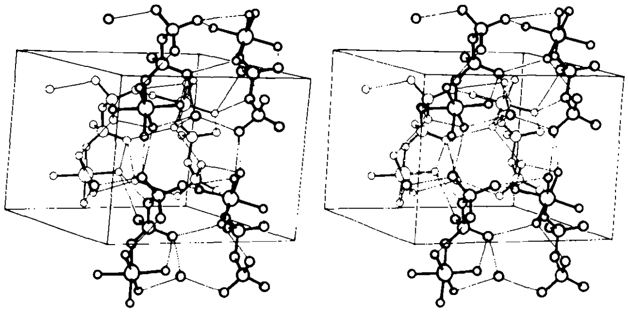

Fig. 2. Stereopair showing the crystal packing of $[CoHP_2O_7(NH_3)_5].H_2O$. The b axis is vertical; the c axis horizontal. Fine lines represent probable hydrogen bonding, including the two interligand close contacts O(111)···N(5) 2·884 (6) Å, O(222)···N(3) 2·933 (5) Å.

Table 1. *Positional* (×10^4, *for* H ×10^3) *and isotropic thermal parameters for unidentate* $[CoHP_2O_7(NH_3)_5].H_2O$

Thermal parameters given for the non-hydrogen atoms are the equivalent B values.

	x	y	z	B (Å^2)
Co	1923 (0)	−2239 (1)	2494 (0)	0·75
P(1)	1605 (1)	2519 (1)	3373 (1)	1·04
P(2)	3440 (1)	166 (1)	4069 (1)	0·79
O(1)	1849 (4)	3640 (4)	2565 (3)	2·06
O(11)	1333 (4)	3199 (4)	4446 (3)	1·89
O(111)	595 (4)	1407 (4)	2971 (3)	2·22
O(12)	3048 (3)	1768 (4)	3722 (3)	1·55
O(2)	3142 (3)	−760 (3)	3066 (3)	1·41
O(22)	4950 (3)	332 (4)	4389 (3)	1·63
O(222)	2715 (4)	−249 (4)	4989 (3)	2·04
N(1)	3195 (4)	−2566 (5)	1478 (3)	1·45
N(2)	722 (4)	−3736 (4)	1831 (4)	1·65
N(3)	685 (4)	−1844 (5)	3536 (3)	1·62
N(4)	2883 (4)	−3606 (5)	3511 (3)	1·48
N(5)	955 (4)	−862 (4)	1487 (3)	1·31
O(*W*)	3170 (5)	2878 (5)	907 (4)	2·67
H(1*A*)	299 (12)	254 (9)	95 (10)	4·0
H(1*B*)	357 (10)	−178 (10)	127 (7)	4·0
H(1*C*)	376 (11)	−285 (9)	205 (7)	4·0
H(2*A*)	85 (10)	−342 (10)	120 (7)	4·0
H(2*B*)	−14 (10)	−394 (10)	210 (8)	4·0
H(2*C*)	110 (10)	−482 (10)	185 (7)	4·0
H(3*A*)	101 (10)	−162 (10)	440 (7)	4·0
H(3*B*)	18 (10)	−143 (10)	328 (7)	4·0
H(3*C*)	−5 (12)	−265 (9)	419 (7)	4·0
H(4*A*)	308 (10)	−352 (10)	434 (7)	4·0
H(4*B*)	393 (11)	−403 (10)	343 (9)	4·0
H(4*C*)	248 (11)	−450 (10)	333 (8)	4·0
H(5*A*)	94 (11)	−67 (10)	64 (8)	4·0
H(5*B*)	0 (11)	−103 (9)	124 (8)	4·0
H(5*C*)	84 (11)	18 (10)	199 (7)	4·0

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* Lists of structure factors, anisotropic thermal parameters and hydrogen-bonding parameters for the three complexes reported here have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 35451 (24 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

ever, the H atom associated with this bond was not located.

$[CoHP_2O_7(NH_3)_4].2H_2O$

The α,β-bidentate complex is shown in Fig. 3(*a*). Bond lengths and ring bond and torsion angles are shown in Fig. 3(*b*). Atomic coordinates and the remaining bond angles are given in Tables 3 and 4.

The six-membered ring formed by bidentate chelation of the pyrophosphate to the metal is in a distorted boat conformation (Fig. 3*a*). This twisted conformation allows the pyrophosphate oxygens protruding axially on each side of the ring to hydrogen bond to an axially ligated ammonia: N(3)···O(22) = 3·116 (3) Å, N(4)···O(111) = 3·067 (3) Å. In the crystal structure molecules of $[CoHP_2O_7(NH_3)_4]$ are linked through hydrogen bonds into sheets roughly normal to the *a* axis (Fig. 4). Neighboring parallel sheets are linked directly through the hydrogen bonds N(1)···O(22) and N(2)···O(22), and indirectly through hydrogen bonding involving O(*W*2), which lies between the sheets. The shortest intermolecular hydrogen bond [2·530 (3) Å] is between O(222) and O(11); the O(222)—H distance is 0·88 (4) Å, the O(11)···H distance is 1·66 (4) Å.

$[CoH_2P_3O_{10}(NH_3)_4].H_2O$

Fig. 5 shows the (*Δ*)β,γ-bidentate complex. Pertinent bond angles and distances are given in Fig. 5(*b*) and Table 6, while atomic coordinates are given in Table 5. The principal improvement of the new refinement is

Table 2. *Bond angles in unidentate* $[CoHP_2O_7(NH_3)_5].H_2O$

The estimated standard deviations in bond angles and torsion angles are about 0·2 and 0·4° respectively.

N(1)—Co—N(2)	92·3°	O(1)—P(1)—O(11)	110·7°
N(1)—Co—N(3)	177·8	O(1)—P(1)—O(111)	116·3
N(1)—Co—N(4)	90·2	O(1)—P(1)—O(12)	104·8
N(1)—Co—N(5)	90·3	O(11)—P(1)—O(111)	112·3
N(1)—Co—O(2)	84·7	O(11)—P(1)—O(12)	102·8
N(2)—Co—N(3)	89·9	O(111)—P(1)—O(12)	108·8
N(2)—Co—N(4)	90·6		
N(2)—Co—N(5)	89·6	O(12)—P(2)—O(2)	108·2
N(2)—Co—O(2)	176·7	O(12)—P(2)—O(22)	99·8
N(3)—Co—N(4)	90·1	O(12)—P(2)—O(222)	108·8
N(3)—Co—N(5)	89·4	O(2)—P(2)—O(22)	109·9
N(3)—Co—O(2)	93·1	O(2)—P(2)—O(222)	114·7
N(4)—Co—N(5)	179·5	O(22)—P(2)—O(222)	114·4
N(4)—Co—O(2)	90·8		
N(5)—Co—O(2)	89·1	Co—O(2)—P(2)	139·3
		P(1)—O(12)—P(2)	131·3

Torsion angles

Co—O(2)—P(2)—O(12)	248·3°
O(2)—P(2)—O(12)—P(1)	71·0
P(2)—O(12)—P(1)—O(111)	337·2

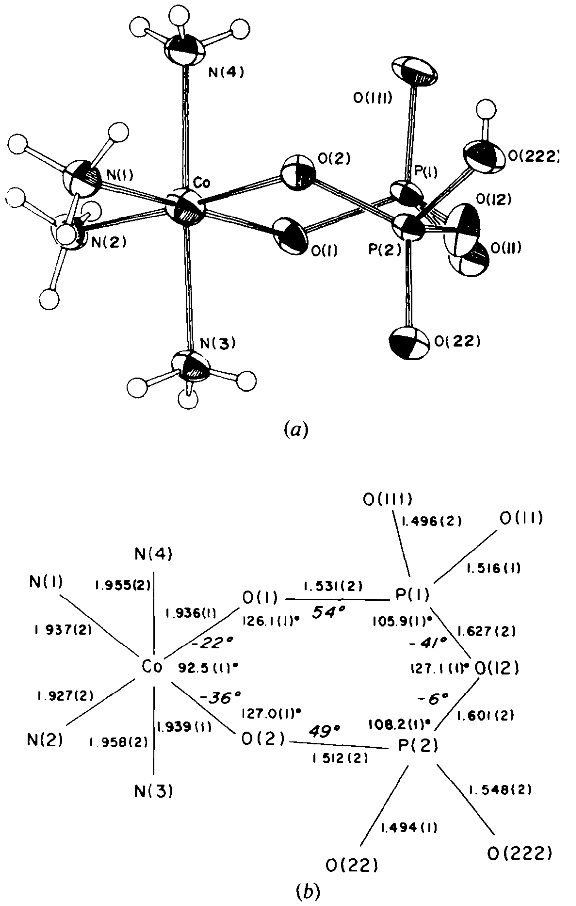


Fig. 3. (*a*) *ORTEP* drawing of bidentate $[CoHP_2O_7(NH_3)_4]$ with thermal ellipsoids at the 50% probability level. (*b*) Bond lengths in Å and bond angles of bidentate $[CoHP_2O_7(NH_3)_4]$. Torsion angles about the six chelation ring bonds are given in italics. The remaining bond angles are listed in Table 4.

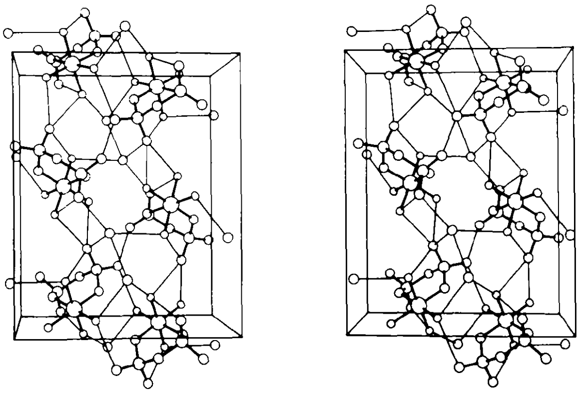


Fig. 4. Stereopair showing the crystal packing of $[CoHP_2O_7(NH_3)_4].2H_2O$. The *b* axis is vertical; the *c* axis is horizontal. Fine lines represent probable hydrogen bonds, including the intramolecular N(4)···O(111) distance of 3·067 (3) Å and N(3)···O(22) distance of 3·116 (3) Å.

seen about the Co atom. The metal–ammine and metal–phosphate coordination distances are more consistent among themselves and with those of the accompanying structures than were the previously reported values.

Discussion

In modelling the biologically important conformations of MgADP, MgATP and other metal-coordinated polyphosphates we draw upon available crystallographic, solution, and enzymatic studies. The crystal structures of the following biological polyphosphates have been reported to date: RbADP (Muller & DeLuke, 1971; Viswamitra, Hosur, Shakked & Kennard, 1976), KADP (Swaminathan & Sundaralingam, 1980), dipotassium uridine 5′-diphosphate (K_2UDP) (Viswamitra, Post & Kennard, 1979), Na_2ATP (Kennard *et al.*, 1972), cytidine 5′-diphosphate (CDP) (Viswamitra, Seshadri, Post & Kennard, 1975), CDP–choline (Nakamachi *et al.*, 1975), NaCDP–choline (Viswamitra *et al.*, 1975), thiamine pyrophosphate (Pletcher & Sax, 1972; Pletcher, Wood, Blank, Shin & Sax, 1977), and lithium nicotinamide adenine dinucleotide ($LiNAD^+$) (Saenger, Reddy, Mühlegger & Weimann, 1977).

Table 3. *Positional* ($\times 10^4$, *for* H $\times 10^3$) *and isotropic thermal parameters for bidentate* $[CoHP_2O_7(NH_3)_4].2H_2O$

Thermal parameters given for the non-hydrogen atoms are the equivalent *B* values.

	x	*y*	*z*	*B* (Å^2)
Co	1067 (0)	4621 (0)	2259 (0)	1·24
P(1)	−1552 (1)	3161 (0)	1013 (0)	1·39
P(2)	−2799 (1)	4157 (0)	3094 (0)	1·39
O(1)	−169 (2)	3980 (1)	929 (1)	1·81
O(11)	−2551 (3)	3044 (1)	−183 (1)	2·05
O(111)	−781 (3)	2252 (1)	1539 (2)	2·44
O(12)	−3106 (2)	3548 (1)	1892 (2)	2·36
O(2)	−776 (2)	4237 (1)	3358 (1)	1·77
O(22)	−3804 (2)	5086 (1)	2936 (2)	2·13
O(222)	−3715 (2)	3563 (1)	4075 (2)	2·19
N(1)	2265 (3)	5272 (1)	3597 (2)	1·99
N(2)	3005 (3)	4963 (1)	1227 (2)	1·91
N(3)	−265 (3)	5781 (1)	1755 (2)	1·77
N(4)	2328 (3)	3428 (2)	2707 (2)	2·15
O(*W*1)	2334 (3)	3485 (2)	5479 (2)	3·76
O(*W*2)	3629 (3)	3323 (2)	−325 (2)	3·78
H(1*A*)	194 (5)	489 (3)	425 (3)	2·5 (7)
H(1*B*)	208 (5)	586 (3)	370 (3)	3·1 (8)
H(1*C*)	359 (6)	523 (3)	354 (4)	3·9 (9)
H(2*A*)	397 (5)	499 (3)	173 (3)	2·9 (7)
H(2*B*)	289 (7)	443 (4)	75 (4)	5·1 (11)
H(2*C*)	288 (6)	548 (3)	76 (4)	3·9 (9)
H(3*A*)	−27 (4)	586 (2)	96 (3)	1·8 (6)
H(3*B*)	24 (4)	629 (2)	200 (2)	1·2 (5)
H(3*C*)	−156 (6)	575 (3)	194 (3)	3·7 (9)
H(4*A*)	240 (7)	334 (3)	339 (4)	5·8 (11)
H(4*B*)	181 (6)	292 (3)	242 (4)	4·0 (9)
H(4*C*)	329 (9)	339 (5)	235 (6)	8·7 (17)
H(*W*1*A*)	302 (6)	393 (3)	599 (4)	5·0 (11)
H(*W*1*B*)	135 (7)	327 (4)	573 (5)	6·2 (12)
H(*W*2*A*)	479 (5)	324 (2)	−32 (3)	2·5 (7)
H(*W*2*B*)	331 (5)	277 (3)	−2 (3)	2·9 (7)
H(222)	−315 (5)	303 (3)	427 (3)	3·2 (8)

Table 4. *Bond angles in bidentate* $[CoHP_2O_7(NH_3)_4].2H_2O$

The estimated standard deviations in bond angles and torsion angles are about 0·1 and 0·2° respectively.

N(1)–Co–N(2)	91·4°	O(1)–P(1)–O(11)	109·2°
N(1)–Co–N(3)	92·9	O(1)–P(1)–O(111)	114·0
N(1)–Co–N(4)	89·8	O(1)–P(1)–O(12)	106·0
N(1)–Co–O(1)	179·0	O(11)–P(1)–O(111)	115·1
N(1)–Co–O(2)	86·9	O(11)–P(1)–O(12)	104·0
N(2)–Co–N(3)	89·9	O(111)–P(1)–O(12)	107·7
N(2)–Co–N(4)	90·5		
N(2)–Co–O(1)	89·3	O(12)–P(2)–O(2)	108·2
N(2)–Co–O(2)	176·6	O(12)–P(2)–O(22)	107·5
N(3)–Co–N(4)	177·3	O(12)–P(2)–O(222)	105·4
N(3)–Co–O(1)	86·5	O(2)–P(2)–O(22)	116·1
N(3)–Co–O(2)	93·2	O(2)–P(2)–O(222)	110·5
N(4)–Co–O(1)	90·8	O(22)–P(2)–O(222)	108·6
N(4)–Co–O(2)	86·6		
O(1)–Co–O(2)	92·5		

Ring torsion angles

Co–O(1)–P(1)–O(12)	53·8°
O(1)–P(1)–O(12)–P(2)	−40·8
P(1)–O(12)–P(2)–O(2)	−5·6
O(12)–P(2)–O(2)–Co	49·1
P(2)–O(2)–Co–O(1)	−36·3
O(2)–Co–O(1)–P(1)	−21·7

From a consideration of ionic radii one might predict that these alkali-metal complexes would be less than satisfactory models for the magnesium–nucleotide coordination. The average phosphate oxygen–metal coordination distances in the Na^+, K^+, Rb^+ complexes are 2·31, 2·86 and 3·03 Å, respectively. The Na^+, K^+, and Rb^+ coordination distances are thus significantly longer than those of Mg^{2+} [average Mg–O distance from α- and β-$Mg_2P_2O_7$ is 2·07 Å (Calvo, 1967)] or transition elements such as Co and Cr, which also form biologically active complexes with the nucleotides (average Co^{3+}–O distance 1·93 Å in the present work). The Li^+–O coordination distance of 1·89 Å in the $LiNAD^+$ complex is much closer to that expected in MgADP, MnADP, *etc.*, and indeed the α,β-bidentate coordination of the pyrophosphate double ester in this compound is an inviting model for the two isomeric species of α,β-bidentate MgADP. The tetrahedral O–Li–O bond angle, however, will probably produce a different ring conformation from that of an equivalent ring containing an octahedrally coordinated metal such as Mg^{II} or Co^{III}. These predictions are borne out by the observed specificity of enzymes such as hexokinase, whose normal substrate is MgATP. The alkali-metal complexes of ATP are not recognized by the enzyme, while the Co^{III} and Cr^{III} complexes are.

Further, as discussed in our previous paper (Merritt *et al.*, 1978), enzymatic studies so far have shown specificity for isomers of CoATP with bidentate coordination. Of the above nucleotide diphosphate–metal complexes only LiNAD$^+$ and K_2UDP exhibit bidentate chelation. The isostructural KADP and RbADP complexes are α,β,β-tridentate; *i.e.* the α-phosphate group is singly coordinated to the metal while the β-phosphate is doubly coordinated (Fig. 6*a*). However, the metal–oxygen coordination distances of the two β-phosphate oxygens are quite disparate [2·953 (9) *vs* 3·238 (9) Å in KADP], and for purposes of comparison, we shall consider the chelation ring involving the shorter distance. The ring conformations of the two bidentate cobalt complexes reported here, though very similar to each other, are quite unlike those of K_2UDP, KADP and RbADP, and unlike either of the rings of the α,β,γ-tridentate Na_2ATP.

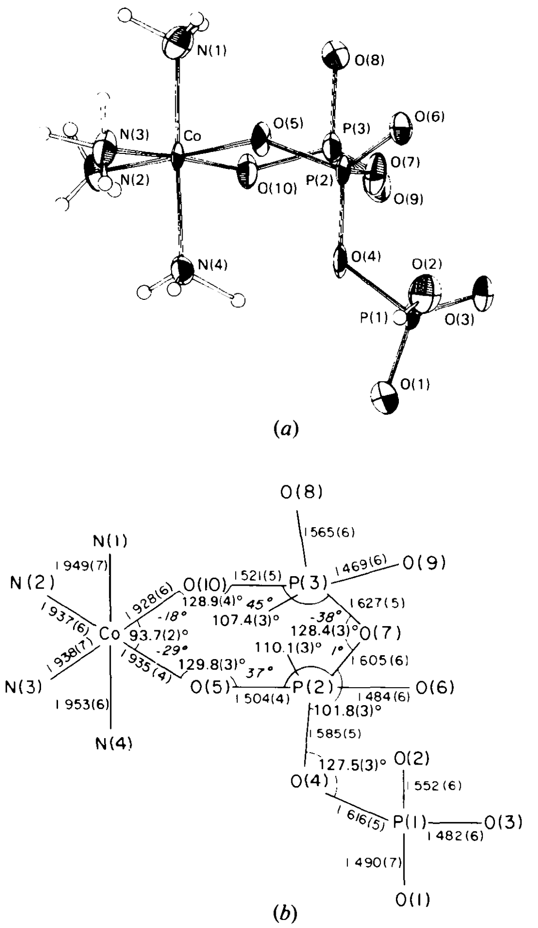


Fig. 5. (*a*) *ORTEP* drawing of $(\Delta)\beta,\gamma$-bidentate $[CoH_2P_3O_{10}(NH_3)_4]$. Thermal ellipsoids are drawn at the 50% probability level. The presumed hydrogen on O(8) was not found in electron density maps. (*b*) Bond lengths in Å and bond angles of $(\Delta)\beta,\gamma$-bidentate $[CoH_2P_3O_{10}(NH_3)_4]$. Torsion angles about the six chelation ring bonds are given in italics. The remaining bond angles are listed in Table 6.

Table 5. *Positional and isotropic thermal parameters for* $(\Delta)\beta,\gamma$*-bidentate* $[CoH_2P_3O_{10}(NH_3)_4].H_2O$

Thermal parameters given for the non-hydrogen atoms are the equivalent *B* values.

	x	*y*	*z*	*B* (Å^2)
Co	−2233 (1)	5000 (0)	3577 (1)	1·46
P(1)	3582 (2)	4892 (2)	7828 (2)	1·70
P(2)	1582 (2)	5510 (2)	4454 (2)	1·68
P(3)	444 (2)	3299 (2)	2165 (2)	1·77
O(1)	3158 (7)	4170 (8)	9398 (8)	3·57
O(2)	4249 (8)	6286 (6)	8336 (8)	2·91
O(3)	4773 (6)	4248 (5)	6829 (7)	2·42
O(4)	1842 (6)	5115 (6)	6502 (6)	2·07
O(5)	−178 (5)	5981 (5)	3945 (6)	2·03
O(6)	2922 (6)	6404 (6)	4099 (7)	2·63
O(7)	1813 (6)	4132 (6)	3514 (7)	2·74
O(8)	320 (7)	4076 (7)	371 (7)	2·91
O(9)	1132 (7)	1976 (6)	2105 (7)	2·70
O(10)	−1211 (6)	3443 (6)	2821 (6)	2·17
N(1)	−2578 (9)	5663 (9)	1135 (9)	3·28
N(2)	−4285 (7)	4012 (6)	3169 (8)	2·11
N(3)	−3320 (8)	6490 (7)	4463 (10)	2·55
N(4)	−1788 (7)	4343 (6)	6026 (7)	1·84
O(*W*)	−3421 (13)	2423 (8)	9029 (9)	5·60
H(1*A*)	−233	529	38	4·0
H(1*B*)	−379	584	55	4·0
H(1*C*)	−208	637	107	4·0
H(2*A*)	−478	407	404	4·0
H(2*B*)	−407	319	300	4·0
H(2*C*)	−492	429	227	4·0
H(3*A*)	−470	646	401	4·0
H(3*B*)	−302	675	557	4·0
H(3*C*)	−337	716	370	4·0
H(4*A*)	−168	481	689	4·0
H(4*B*)	−261	395	628	4·0
H(4*C*)	−74	343	618	4·0
H(O*WA*)	−222	225	938	4·0
H(O*WB*)	−373	330	830	4·0
H(O2)	398	676	928	4·0
H(O8)	189	426	121	4·0

Chelation-ring pucker and interligand hydrogen bonding

The six-membered chelate-ring conformations may be described by the parameters, Q, θ, and φ of Cremer & Pople (1975). These parameters are listed in Table 7. For $[CoHP_2O_7(NH_3)_4]$ and $[CoH_2P_3O_{10}(NH_3)_4]$ we derive the values by starting at the Co atom and proceeding clockwise about the chelation ring as viewed in Figs. 3(*b*) and 5(*b*). The θ value near 90° indicates a boat or twist-boat form depending on the pseudorotation phase angle φ: $\varphi = 0, 60, 120°, \ldots$ for boat; $\varphi = 30, 90, 150°, \ldots$ for twist-boat. The cobalt chelate rings are closer to the boat form. The primary chelation ring of KADP is in a half-chair conformation, as are the rings of the two independent K_2UDP molecules. Note that the cobalt rings are much flatter (low Q value) than any of the potassium or rubidium chelation rings (Fig. 6*a* and *b*).

Table 6. *Additional bond angles in β,γ-bidentate* $[CoH_2P_3O_{10}(NH_3)_4]$

The estimated standard deviations in bond angles and torsion angles are about 0·4 and 0·6° respectively.

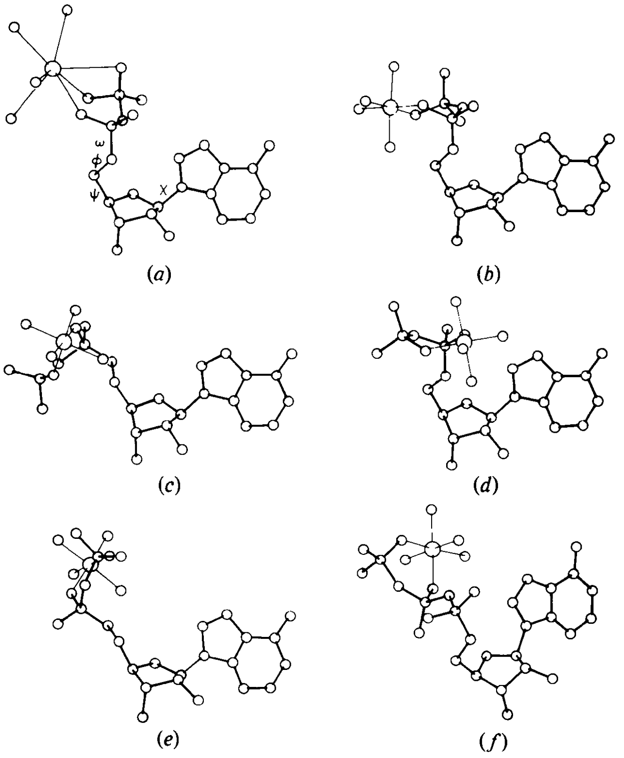
N(1)–Co–N(2)	92·5°	O(1)–P(1)–O(2)	112·0°
N(1)–Co–N(3)	93·0	O(1)–P(1)–O(3)	116·5
N(1)–Co–N(4)	177·6	O(1)–P(1)–O(4)	105·8
N(1)–Co–O(5)	86·8	O(2)–P(1)–O(3)	107·6
N(1)–Co–O(10)	90·4	O(2)–P(1)–O(4)	105·2
N(2)–Co–N(3)	91·9	O(3)–P(1)–O(4)	109·1
N(2)–Co–N(4)	89·6		
N(2)–Co–O(5)	179·1	O(4)–P(2)–O(5)	107·6
N(2)–Co–O(10)	85·8	O(4)–P(2)–O(6)	110·5
N(3)–Co–N(4)	88·0	O(4)–P(2)–O(7)	101·8
N(3)–Co–O(5)	88·7	O(5)–P(2)–O(6)	117·2
N(3)–Co–O(10)	175·9	O(5)–P(2)–O(7)	110·1
N(4)–Co–O(5)	91·1	O(6)–P(2)–O(7)	108·5
N(4)–Co–O(10)	88·7		
O(5)–Co–O(10)	93·7	O(7)–P(3)–O(8)	102·8
		O(7)–P(3)–O(9)	106·0
		O(7)–P(3)–O(10)	107·4
		O(8)–P(3)–O(9)	114·3
		O(8)–P(3)–O(10)	107·5
		O(9)–P(3)–O(10)	117·6

Torsion angles

Co–O(10)–P(3)–O(7)	45·4°
O(10)–P(3)–O(7)–P(2)	−37·8
P(3)–O(7)–P(2)–O(5)	1·0
O(7)–P(2)–O(5)–Co	36·9
P(2)–O(5)–Co–O(10)	−29·0
O(5)–Co–O(10)–P(3)	−18·2
O(7)–P(2)–O(4)–P(1)	80·6
P(2)–O(4)–P(1)–O(2)	77·6

The close similarity of the bidentate cobalt chelation rings may be seen by comparing Figs. 3 and 5. The principal difference between the two is that the ring of the $[CoH_2P_3O_{10}(NH_3)_4]$ complex is flatter. With the addition of the third, unchelated, phosphate residue to the ligand the magnitude of each of the ring torsion angles decreases by 3 to 12°, while the ring bond angles increase by up to 3°. The net effect of this flattening is to decrease the average deviation of the ring atoms from the least-squares plane from 0·233 Å in the pyrophosphate complex to 0·190 Å in the tripolyphosphate complex. Therefore, in modelling the geometries of metal–nucleotides, we may assume a minimal effect on the ring geometry from adding the nucleoside at the unchelated α-phosphate of $[CoH_2P_3O_{10}(NH_3)_4]$ to generate a β,γ-bidentate nucleoside triphosphate. We may similarly assume a small effect from adding the nucleoside to $[CoHP_2O_7(NH_3)_4]$ to generate an α,β-bidentate nucleoside diphosphate (see below).

The ring conformation of both $[CoHP_2O_7(NH_3)_4]$ and $[CoH_2P_3O_{10}(NH_3)_4]$ is stabilized by interligand hydrogen bonding from the axial ammine ligands to the polyphosphate oxygens. The N(4)···O(111) and N(3)···O(22) distances of 3·067 (3) and 3·116 (3) Å in $[CoHP_2O_7(NH_3)_4]$ have corresponding N(1)···O(8) and N(4)···O(4) distances in $[CoH_2P_3O_{10}(NH_3)_4]$ of 3·003 (10) and 3·030 (8) Å. Although the metal coordination in, for example, MgATP would not involve ammine groups, the interligand hydrogen-bonding geometry would remain applicable for other proton-donating groups such as water or an enzyme's active-site residues. Buckingham, Sargeson & Robinson (1980) have observed a similar conformation in the crystal structure of another α,β-bidentate pyrophosphate complex, [Co(ethylenediamine)$_2$HP$_2$O$_7$]. As dis-



(a) (b) (c) (d) (e) (f)

Fig. 6. Models for MgADP, MgATP. These models have been generated by combining the metal–phosphate geometries observed in the present crystal structures $[CoHP_2O_7(NH_3)_4].2H_2O$ and $[CoH_2P_3O_{10}(NH_3)_4].H_2O$ with the adenosine moiety (sugar + base only) from the crystal structure of KADP.2H$_2$O (Swaminathan & Sundaralingam, 1980). Torsion-angle definitions are as follows: ψ = C(3′)–C(4′)–C(5′)–O(5′), φ = C(4′)–C(5′)–O(5′)–P(1), ω = C(5′)–O(5′)–P(1)–O(12), χ = O(4′)–C(1′)–N(9)–C(8). (*a*) The α,β,β-tridentate KADP structure. The sugar pucker is ^2E, while the chain torsion angles are ψ = 58° (*gauche*$^+$), φ = 145° (*trans*) and ω = −64° (*gauche*$^-$). (*b*) Model for α,β-bidentate MgADP. The sugar and base are viewed form the same vantage as in (*a*). Atom O(5′) of the KADP adenosine moiety has been superimposed on atom O(111) of $[CoHP_2O_7(NH_3)_4]$ and the torsion angles φ and ω were set to match those of KADP. The contrast between the potassium and cobalt chelation geometries is clearly visible. (*c*) The model in (*b*) has been varied by changing the torsion angle ψ to *trans*. As mentioned in the text the *trans* conformation is selected in enzyme-bound molecules. (*d*) and (*e*) correspond to the models in (*b*) and (*c*) except that the torsion angle ω has been set to *gauche*$^+$ instead of *gauche*$^-$. (*f*) Model for β,γ-bidentate MgATP. Atom O(5′) of the KADP structure has been superimposed on atom O(2) of $[CoH_2P_3O_{10}(NH_3)_4]$, and chain torsion angles are fixed as in (*b*).

Table 7. *Chelate-ring pucker*

Compound	Q (Å)	θ (°)	φ (°)	$M\cdots$OP (Å)	Reference
$[CoHP_2O_7(NH_3)_4].2H_2O$	0·623	93	72	1·94	This paper
$[CoH_2P_3O_{10}(NH_3)_4].H_2O$	0·503	96	68	1·93	This paper
$K_2UDP.3H_2O$					Viswamitra *et al.* (1979)
Molecule *A*	0·967	68	59	2·92	
Molecule *B*	1·072	66	34	2·89	
$KADP.2H_2O$ (*a*)	0·931	144	127	2·86	Swaminathan & Sundaralingam (1980)
(*b*)	1·120	68	309	3·00	
$RbADP.2H_2O$ (*a*)	0·956	142	131	3·01	Muller & DeLuke (1971)
(*b*)	1·127	65	309	3·17	
$RbADP.H_2O$ (*a*)	0·906	142	126	2·95	Viswamitra *et al.* (1976)
(*b*)	1·083	65	309	3·09	

Notes: The ring parameters Q, θ, φ are as defined by Cremer & Pople (1975). For the α,β,β-tridentate ADP complexes ring (*a*) is taken as containing the shorter metal–β-phosphate coordination distance (lower ring in Fig. 6*a*), while ring (*b*) contains the longer. Column 4 is the average of the two metal–phosphate oxygen distances in each ring.

cussed previously (Merritt *et al.*, 1978), in such bidentate structures one can expect an alternate favorable ring conformation in which the ring torsion angles are of equal magnitude but opposite sign. Pseudorotation of the chelate ring from one form to the other would interchange the axial and equatorial positions of the phosphate oxygens, allowing hydrogen bonding between N(4)–O(11) and N(3)–O(222) instead of N(4)–O(111) and N(3)–O(22), Fig. 3 (Merritt *et al.*, 1978). The two ring conformations are mirror inversions of each other, and both are found in the crystal form of $[CoHP_2O_7(NH_3)_4].2H_2O$. An energetic difference between the two conformations may exist, of course, when the two chelated phosphate residues are part of a larger ligand, as is the case for the tripolyphosphate and ATP itself.

Phosphate-chain conformation

In the chelation rings of the α,β,β-tridentate KADP and RbADP complexes the P—O—P ring bond angle is 131 and 134–135° respectively. This is close to the unconstrained unidentate P—O—P angle of 131·3 (2)° in the unidentate $[CoHP_2O_7(NH_3)_5]$, and is typical of P—O—P bridging angles for metal pyrophosphates (Clark & Morley, 1976). In contrast the six-membered chelation rings of the bidentate cobalt complexes reported here exhibit ring P—O—P angles of 127·1 (1) and 128·4 (3)° which are at the lower end of the range of metal pyrophosphate bridge angles. In the α,β-bidentate K_2UDP complex molecule *A* has a P—O—P bridge angle of 129·6 (5)°, while molecule *B* has 133·7 (5)°. In metal pyrophosphate structures a smaller bridging angle (P—O—P) is correlated with longer P—O bonds to the bridging oxygen (Cruickshank, 1961; Mandel, 1975). This is borne out in the complexes reported here: the P(1)—O(12) and O(12)—P(2) distances are 1·619 (3) and 1·605 (4) Å in the unidentate pyrophosphate, 1·627 (2) and 1·601 (2) Å in the bidentate pyrophosphate, 1·605 (6) and 1·627 (5) Å in the bidentate triphosphate respectively.

It is interesting to note the asymmetry in P—O bond length about the bridging atom in the bidentate rings. Some asymmetry of these bond lengths is a feature common to known organic pyrophosphates, but no general rule for the direction of the inequality has been reported. In the present $[CoH_2P_3O_{10}(NH_3)_4]$ complex it is specifically the O(7)—P(3) bond which is the longer one. In the parent metal–ATP complex, this is the bond cleaved by nucleophilic attack on the γ-phosphate in phosphotransferase reactions (Mildvan, 1979). It is intriguing that these enzymes appear to favor β,γ-bidentate metal coordination of their ATP substrates. The observed conformation of the bidentate ring thus favors the γ-phosphate as a leaving group, which is just what these enzymes require.

Conformational models for bidentate metal–nucleotide polyphosphate complexes

To proceed to models of the full metal—nucleotide complex, we must integrate our determination of metal–polyphosphate chelation geometry with the existing body of knowledge about nucleotide conformation. Theoretical energy calculations and crystal structure determinations have both indicated preferred combinations of sugar pucker, glycosyl-bond geometry, and the sugar–phosphate backbone torsion angles in the absence of metal coordination (Sundaralingam, 1975). A full discussion of these variables is beyond the scope of this paper. We have started with several known favored conformations of the nucleoside (sugar + base) and investigated the consistency of the bidentate metal–phosphate geometry with the predicted favorable torsion angles ψ, φ, ω (Fig. 6*a*) at the sugar–phosphate juncture.

The models shown in Fig. 6 incorporate a 2′-*endo* sugar pucker ($P = 163°$, $\tau_m = 37°$) and a glycosyl torsion angle in the *anti* range ($\chi = 32{\cdot}4°$). These values are taken from the crystal structure of KADP recently determined in this laboratory (Swaminathan & Sundaralingam, 1980), and are representative of one class of favored conformations. Possible structures for CoADP were generated by equating atom O(111) of $[CoHP_2O_7(NH_3)_4]$ to O(5′) of KADP and adjusting the torsion angles φ and ω (Fig. 6). In Fig. 6(*b*), $\varphi = 144{\cdot}6°$ and $\omega = -63{\cdot}6°$, the values found in KADP; Fig. 6(*d*) shows a model where ω has been rotated to +60° instead. Both these conformations might be expected to be energetically favored by analogy with those known for 5′-nucleotides and calculated for polynucleotides (Sundaralingam, 1975). Fig. 6(*c*) and (*e*) shows models in which the torsion angle ψ has been set to *trans*. These models are suggested by the observation that enzyme-bound nucleotides seem to have ψ *trans* or *gauche*$^-$ rather than the *gauche*$^+$ preferred in free nucleotides (Sundaralingam, 1975; Haromy, Raleigh & Sundaralingam, 1980). Fig. 6(*f*) is a model of CoATP constructed by equating atom O(2) of $[CoH_2P_3O_{10}(NH_3)_4]$ to O(5′) of KADP. Again the torsion angles φ and ω have been set to the values found in KADP while the next torsion angle in the chain, ω', is set at 78° by the choice of linkage at O(2). The above represent some plausible conformations for enzyme-bound metal–nucleoside polyphosphates generated from consideration of the phosphate-chain geometry of the cobaltammine compounds reported here. Other conformational models can be generated by considering alternative sugar puckers or χ in the *syn* or *high-anti* ranges.

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