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Crystallographic Evidence of Preferred N(9)-Coordination of Xanthine: Structures of $Cu^{II}(xan)_2(NO_3)_2{\cdot}2H_2O$, $Cu^{II}(xan)_2Cl_2{\cdot}2H_2O$, and $Zn^{II}(xan)_2Cl_2$ (xan = Xanthine)

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The reaction of the oxopurine base xanthine (xan) with the respective metal chlorides has resulted in the formation of compounds of the composition $Cu(xan)_2Cl_2{\cdot}2H_2O$ and $Zn(xan)_2Cl_2$. $Cu(xan)_2(NO_3)_2{\cdot}2H_2O$ has been prepared from aqueous solution using an excess of $Cu(NO_3)_2{\cdot}3H_2O$. Crystal data: $Cu(xan)_2(NO_3)_2{\cdot}2H_2O$, $a = 7.111$ (2) Å, $b = 7.528$ (1) Å, $c = 8.888$ (1) Å, $\alpha = 108.63$ (1)°, $\beta = 98.29$ (2)°, $\gamma = 102.39$ (2)°, $V = 428.6$ (3) Å^3, $Z = 1$, space group $P\bar{1}$; $Cu(xan)_2Cl_2{\cdot}2H_2O$, $a = 3.647$ (5) Å, $b = 9.849$ (2) Å, $c = 12.763$ (4) Å, $\alpha = 72.41$ (2)°, $\beta = 81.07$ (6)°, $\gamma = 82.93$ (6)°, $V = 430.3$ (7) Å^3, $Z = 1$, space group $P\bar{1}$; $Zn(xan)_2Cl_2$, $a = 14.090$ (7) Å, $b = 5.456$ (3) Å, $c = 20.397$ (16) Å, $\beta = 105.82$ (5)°, $V = 1509$ (3) Å^3, $Z = 4$, space group $C2/c$. The structures of all three compounds were refined to final *R*-values of 0.036, 0.051, and 0.056, respectively. In $Cu(xan)_2(NO_3)_2{\cdot}2H_2O$, the copper ion is situated in the center of a 4 + 2 elongated octahedron including two N(9)-coordinating monodentate xanthine ligands, two water molecules in the equatorial plane, and two nitrate groups in the apical positions. The monomeric structure is stabilized by intramolecular bifurcated hydrogen bonding contacts of the type N–H···O forming an indirect chelate complex. The copper complex $Cu(xan)_2Cl_2{\cdot}2H_2O$ exhibits a square planar centrosymmetric coordination of copper by two chloride ions and two xanthines monodentately binding through N(9). The two water molecules are located at disordered positions. In the monomeric zinc complex $Zn(xan)_2Cl_2$, the metal ion is situated in the center of a markedly distorted ZnN_2Cl_2 tetrahedron including two N(9)-coordinating xanthine ligands and two chloride ions. An indirect chelate complex is formed by an intramolecular hydrogen bond of the type N–H···Cl. A review of all structure types of metal xanthine complexes established by X-ray crystallography is given. The crystallographic evidence of preferred N(9)-coordination of neutral xanthine presented here supports those structural models for the oxidation of xanthine catalyzed by xanthine oxidase that suggest intermediate coordination of the molybdenum center of the enzyme through N(9) and not through N(7) of xanthine.

Introduction

Considerable effort has been devoted to the preparation and the structural characterization of metal purine complexes,[1,2] especially in view of their medical and pharmacological significance. Most of the literature on complexation of metals by purines deals with guanine and adenine, their being the major purine bases in DNA and RNA. However, information on the interaction of metal ions with oxopurines, which are also present in biological systems, is limited.

The oxopurines hypoxanthine and xanthine are intermediate products of the biological degradation of nucleic acids. Disturbances in purine metabolism may induce precipitation of oxopurines as pathological biogenic solids, observed in conjunction with diseases like gout and xanthinuria. Xanthinuria is a rare disorder, resulting from a gross deficiency of xanthine oxidase activity. Therefore, patients suffering from this disease excrete hypoxanthine and xanthine instead of uric acid as the end products of purine metabolism.[3] As a consequence of xanthinuria, crystalline xanthine may also be found as a constituent of urinary calculi or even in muscle tissue.[4]

The molybdenum- and iron-containing enzyme xanthine oxidase catalyzes the oxidation of hypoxanthine via xanthine to uric acid, which subsequently is released from the active site of the enzyme.[5] On the basis of structural information from EXAFS data as well as from EPR work on reduced xanthine oxidase bearing a bound substrate molecule, different structures for the enzyme–xanthine complex have been proposed.

The first model for such an association suggests a molybdenum–oxygen coordination (Figure 1, structure I). From EPR measurements with ^{17}O-enriched enzyme a coupling of the molybdenum to a single oxygen atom was deduced, indicating that xanthine is probably bound via a Mo–O–C linkage.[6] Mass spectroscopic analysis with ^{18}O-labeled enzyme revealed that the oxygen atom incorporated into uric acid in the course of oxidation arises from the enzyme.[7] Both results are favoring an oxo transfer mechanism in which the terminal oxygen atom known to be present at the active site of xanthine oxidase is transferred to the substrate in the course of the catalytic reaction.[8]

The second model suggests a molybdenum–carbon coordination (Figure 1, structure II). Experiments using xanthine labeled with ^{13}C in the position C(8) indicated a weak hyperfine coupling to the ^{13}C nucleus, thus indicating that xanthine is covalently associated via C(8) to molybdenum in the signal-giving species.[9,10]

Finally, kinetic considerations are reconcilable with an enzyme substrate complex in which xanthine is coordinating through one of the four ring nitrogen atoms (Figure 1, structure III).[11-13]

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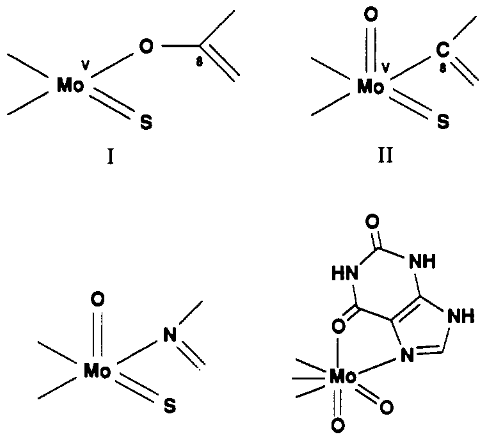

I II

III IV

Figure 1. Schematic presentation of structural models of the enzyme–substrate complex of xanthine oxidase with xanthine proposed in the literature: (I) Mo–O–C linkage with the oxygen atom originating from the enzyme;[6–8] (II) Mo–C coordination;[9,10] (III) Mo–N coordination to one of the four ring nitrogen atoms;[11,13] (IV) N(7)/O(6) chelating xanthine ligand.[14]

With regard to the origin of the coupled nitrogen atom, Stiefel[13] and Bray[11] suggested that the pyrazolo nitrogen atom N(9) of the xanthine molecule is ligated to the molybdenum center, whereas monodentate metal coordination through N(7) has been proposed by Olson.[12]

In addition, an alternative structure of the enzyme substrate complex with a N(7)/O(6) chelating xanthine ligand was proposed by Robins (Figure 1, structure IV).[14] According to X-ray crystallographic data of model complexes presented in this and related papers, however, it seems very unlikely that such a N(7)/O(6) chelated intermediate is realized in the course of the enzymatic oxidation of xanthine.

Structural information on compounds of the oxopurine xanthine is rare. The only structurally characterized xanthine compounds published up to now involve anionic but no neutral xanthine ligands (Table VIII).

In view of the controversy concerning the coordination sites of oxopurines mentioned above, and as part of a study elucidating coordination and protonation properties of purines, the syntheses and structure determinations of three metal complexes containing neutral xanthine ligands have been performed and are presented in this paper.

Experimental Section

Synthesis. Xanthine and the metal salts were obtained from Fluka, Buchs, Switzerland, and used without further purification.

$Cu(xan)_2(NO_3)_2{\cdot}2H_2O$. This complex was synthesized by following a procedure similar to that given by Salas-Peregrin et al.[15] for the preparation of a compound with the formula $Cu(xan^-)_2{\cdot}4H_2O$ (no information on the concentration of the reactants used, however, was given in that paper). A solution of 100 mg (0.66 mmol) of xanthine and 6.0 g (24.8 mmol) of $Cu(NO_3)_2{\cdot}3H_2O$ in 7 mL of water was heated to boiling with continuous stirring. The resulting blue-green solution was filtered to remove any unreacted ligand and then kept for slow evaporation at 40 °C. After 2 weeks intensely green colored crystals with tetragonal prismatic shape could be isolated.

$Cu(xan)_2Cl_2{\cdot}2H_2O$. Single crystals of this complex were obtained using a procedure similar to that reported by Weiss and Venner[16] but applying lower concentrations of the reactants. A solution of 4.0 g (29.8 mmol) of $CuCl_2$ in 20 mL of 2 N HCl was added to 750 mg (4.9 mmol) of xanthine dissolved in 160 mL of 2 N HCl. The reaction mixture was heated to boiling and then kept for crystallization at room temperature. Two weeks later, green needle-shaped crystals were grown from this solution. Most of the crystals appeared to be twinned along the *c*-axis. For the X-ray analysis, however, an untwinned single crystal could be selected.

Table I. Analytical Data (%) for Metal Xanthine Complexes[a]

complex	C	H	N	Cl	H_2O^b
$C_{10}H_{12}N_{10}O_{12}Cu$	22.76	2.29	26.54		6.8
	22.85	2.38	26.48		*c*
$C_{10}H_{12}N_8O_6Cl_2Cu$	25.30	2.55	23.60	14.94	7.6
	25.15	2.42	23.39	15.06	9.2
$C_{10}H_8N_8O_4Cl_2Zn$	27.27	1.83	25.44	16.10	
	27.17	1.98	25.32	16.05	

[a] The first value given is the calculated value, and the second value, the observed value. [b] The water content was derived from thermogravimetric analysis. [c] Calculated according to the assumption that two H_2O and two HNO_3 molecules per formula unit are evolved together in the first step of the thermogravimetric decomposition curve; the total theoretical weight loss is 30.7%, compared to the experimental value of 28.5%.

$Zn(xan)_2Cl_2$. This anhydrous complex was crystallized by following the general method described by Blitz and Beck[17] using a lower concentration of xanthine. A 200-mg sample (1.31 mmol) of xanthine was dissolved in a hot solution of 7.6 g (55.8 mmol) of $ZnCl_2$ in 8 mL of water. The resulting mixture was filtered and stored in a closed vessel at a temperature of 75 °C. Within 5 days, colorless prismatic crystals were formed. Although on a first glance the crystals appeared to be transparent and nicely shaped, higher magnifications show some irregularities. The crystals exhibit some slightly convex faces and small internal fissures.

Analytical data of the compounds are summarized in Table I.

Thermogravimetrical Data. Thermogravimetric data of the xanthine complexes shown in Figure 2 were recorded on a Perkin-Elmer TGS-2 thermobalance in flowing oxygen atmosphere. The final products of these degradations were identified by X-ray powder diffractometry.[18] The thermogravimetric curve of the complex $Cu(xan)_2(NO_3)_2{\cdot}2H_2O$ shows two well-resolved steps. The first weight loss occurring in the temperature range 130–220 °C approximately corresponds to the simultaneous elimination of the two coordinating water molecules as well of the two nitrate groups, probably in the form of HNO_3. The intermediate product is decomposed with a sharp increase in the reaction rate at a temperature of 360 °C to the final residue CuO. The thermal decomposition of $Cu(xan)_2Cl_2{\cdot}2H_2O$ occurs in three steps. The first step observed in the temperature range from 70 to 290 °C could be attributed to the emission of the inserted water molecules. The decrease in weight of the first step of about 9.2% is higher than expected for two water molecules (7.6%). The assumption of a variable water content, averaging from two to three water molecules per formula unit, is supported by the observed density of 1.90 g·cm^{-3}, which corresponds to the composition $Cu(xan)_2Cl_2{\cdot}3H_2O$ (calculated value 1.90 g·cm^{-3}). Since in the structural analysis only two water molecules could be localized and this is in agreement with the analytical data, we report here two water molecules of hydration. The further degradation of the anhydrous complex to CuO occurs in two overlapping dehalogenation and decomposition reactions respectively and is finished at a temperature of about 420 °C.

The thermal analysis of the anhydrous $Zn(xan)_2Cl_2$ shows that the complex is thermally stable under the experimental conditions used up to a temperature of 320 °C. The subsequent degradation occurs in two steps with the formation of an instable intermediate product due to the overlapping of dehalogenation and pyrolysis reactions. The complete decomposition leads to the final residue ZnO at 660 °C.

Crystallographic Studies. Unit cell parameters of all three complexes were determined by least-squares refinement of 25 reflections in the interval $4° < \theta < 22°$, $10° < \theta < 18°$, and $6° < \theta < 19°$, respectively. Intensity data were collected on an Enraf-Nonius CAD-4 diffractometer with graphite-monochromatized Mo Kα radiation (λ = 0.710 73 Å). During the data collections three or four standard reflections were monitored at an interval of every 3 h to check crystal stabilities. For the copper complex $Cu(xan)_2(NO_3)_2{\cdot}2H_2O$, a decrease of intensities of 1.1% was observed, whereas for the two other complexes no loss of intensities

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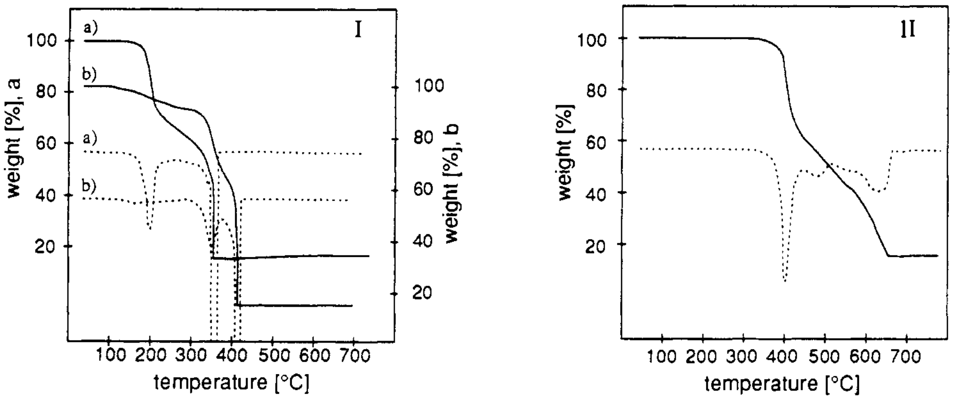

Figure 2. Thermogravimetric degradation of metal xanthine compounds. Dotted lines represent derivative thermogravimetric curves. Key: (I) (a) $Cu(xan)_2(NO_3)_2{\cdot}2H_2O$, (b) $Cu(xan)_2Cl_2{\cdot}2H_2O$; (II) $Zn(xan)_2Cl_2$.

was noted. To control the orientation, three or four standard reflections were collected every 400, 300, and 400 reflections, respectively. The intensities of the three complexes were corrected for Lorentz and polarization effects, and numerical absorption corrections on the basis of eight ($Cu(xan)_2(NO_3)_2{\cdot}2H_2O$), six ($Cu(xan)_2Cl_2{\cdot}2H_2O$), and eight ($Zn(xan)_2Cl_2$) crystal faces were applied. The structure determination of the complex $Cu(xan)_2(NO_3)_2{\cdot}2H_2O$ was started with the atomic coordinates of the non-hydrogen atoms of the analogous alloxanthine complex $Cu(alloxanthin)_2(NO_3)_2{\cdot}2H_2O$,[19] applying the program MOLEN.[20] The two other structures were solved by Patterson syntheses using the program SHELXS86.[21]

Space group assignment ($P\bar{1}$) and structure refinement of $Cu(xan)_2(NO_3)_2{\cdot}2H_2O$ were performed without any problems. The data statistics of $Cu(xan)_2Cl_2{\cdot}2H_2O$ showed a tendency to centrosymmetry ($\langle|E^2 - 1|\rangle = 0.889$, theoretical value 0.968 for centric, 0.736 for noncentrosymmetric data). The averaging of 7524 reflections to 3767 unique data with $R_{int} = 1.96\%$ showed no discrepancies, thus supporting the space group $P\bar{1}$. Rotation and Weissenberg photographs gave no hint for a disordered structure. During refinement of this copper complex, however, the electron density in the difference Fourier map showed two peaks with 3.2 and 1.3 $e{\cdot}Å^{-3}$ at positions 0, 0, $^1/_2$, and $^1/_2$, 0, $^1/_2$, respectively. Test calculations assuming split water molecules at these positions failed. Referring to the paper of Jones,[22] where the refinement of a wrong absolute structure led to a large difference ghost peak at position 0, 0, $^1/_2$, we tried to refine the structure of $Cu(xan)_2Cl_2{\cdot}2H_2O$ in the noncentrosymmetric space group $P1$. This refinement was not successful because of high correlation of symmetry-related parameters and because of several nonpositive definite temperature parameters. In addition, there was no evidence from the difference Fourier maps for a disordered structure. The final refinement therefore was performed in the space group $P\bar{1}$, including two disordered water molecules at general positions with occupancy factors of 0.75 and 0.25. The occupancy factors were deduced from a refinement of the temperature parameters of the two oxygen atoms assuming equal occupancy factors of 0.5.

Owing to the extinction rules for the data of $Zn(xan)_2Cl_2$, the monoclinic space groups $C2/c$, $C2$, or Cc were expected. Data statistics showed a tendency to hypercentricity ($\langle|E^2 - 1|\rangle = 1.013$ for all data), thus preferring the centrosymmetric space group $C2/c$, in which the phase problem could be solved with SHELXS86.[21] The refinement converged with $(\Delta/\sigma)_{max} = 0.001$ and R/R_w values of 0.056 and 0.061. The temperature factors for Zn, Cl, C, O, and N were refined anisotropically, and those of the H atoms, isotropically. The relatively bad agreement factor for the averaged reflections ($R_{int} = 13.1\%$) induces one to examine the intensity data very carefully. It was noticed that the monoclinic symmetry seems to be slightly, but significantly, broken since reflections (h,k,l) and $(h,-k,l)$ were not equivalent as expected for monoclinic symmetry. The data set was transformed to a triclinic cell with lattice parameters $a = 5.456$ Å, $b = 7.553$ Å, $c = 19.868$ Å, $\alpha = 83.16°$, $\beta = 82.11$, $\gamma = 68.87°$, and $V = 754.3$ Å^3. The $P\bar{1}$ refinement converged with $(\Delta/\sigma)_{max} = 0.001$ and R/R_w values of 0.077 and 0.089. Since the resulting standard deviations of corresponding bond distances and angles, however, were greater by a factor of 2 or more compared to the monoclinic refinement, we decided to use the higher symmetric data set with its results as the final structure determination. One reason for the bad agreement of the intensities of equivalent reflections could be a coexistence of small, structurally slightly different domains of the triclinic and monoclinic phases mentioned above.

The structure of $Cu(xan)_2(NO_3)_2{\cdot}2H_2O$ was refined by minimizing $\sum w(|F_o| - |F_c|)^2$, with $w = 1/[\sigma^2(F_o) + 0.0016F_o^2]$. All hydrogen atoms were localized in the subsequent difference Fourier maps and were included in the refinements with fixed positional parameters and thermal parameters assigned to $U = 0.051$ Å^2. Full-matrix least-squares refinements of the structures of $Cu(xan)_2Cl_2{\cdot}2H_2O$ and $Zn(xan)_2Cl_2$ were carried out with SHELX76,[23] minimizing $\sum w(|F_o| - |F_c|)^2$, with $w = 1$. In both structures the positions of the four hydrogen atoms of the coordinating xanthine molecule were deduced from difference Fourier maps and refined with variable positional and isotropic temperature parameters. As a consequence of the disorder of the water oxygen atoms in $Cu(xan)_2Cl_2{\cdot}2H_2O$, no hydrogen atoms of the water molecules could be localized in this complex. The final refinements converged to $R = 0.036$, $R_w = 0.045$ for $Cu(xan)_2(NO_3)_2{\cdot}2H_2O$, $R = 0.051$, $R_w = 0.065$ for $Cu(xan)_2Cl_2{\cdot}2H_2O$, and $R = 0.056$, $R_w = 0.061$ for $Zn(xan)_2Cl_2$. In the complex $Cu(xan)_2(NO_3)_2{\cdot}2H_2O$ maximum and minimum heights of the final difference Fourier map are 0.44 $e{\cdot}Å^{-3}$ located 0.64 Å from O(11) and −0.42 $e{\cdot}Å^{-3}$ located 0.68 Å from Cu. The respective values, beside those at special positions discussed above, are 0.87 $e{\cdot}Å^{-3}$, 0.84 Å from Cu and −0.79 $e{\cdot}Å^{-3}$, 0.56 Å from O(1) in $Cu(xan)_2Cl_2{\cdot}2H_2O$ and 1.26 $e{\cdot}Å^{-3}$ (0.53 Å from Zn) and −1.63 $e{\cdot}Å^{-3}$ (0.81 Å from Zn) in $Zn(xan)_2Cl_2$. All calculations were performed on computers of the type NAS/XL V60 or on a Micro-Vax 3100.

Crystal parameters, details of data collection, and results of the refinements are summarized in Table II. The values of the relevant observed densities of the crystals were derived from flotation in $CHCl_3/CH_2I_2$. Atomic parameters and equivalent isotropic thermal parameters are listed in Tables III–V.

Discussion

Molecular Structures. The molecular structure of the monomeric copper complex $Cu(xan)_2(NO_3)_2{\cdot}2H_2O$ and the usual atom numbering scheme of xanthine is shown in Figure 3. The copper ion is situated at the center of a 4 + 2 elongated coordination octahedron with the equatorial plane defined by two nitrogen atoms of xanthine ligands and by two water molecules, whereas the apical positions are occupied by two nitrate groups. The 1H,3H,7H tautomer of neutral xanthine is monodentately coordinating through the pyrazole nitrogen atom N(9).

Figure 4 represents the molecular structure of the centrosymmetric copper complex $Cu(xan)_2Cl_2{\cdot}2H_2O$. The copper ion exhibits a square planar centrosymmetric CuN_2Cl_2 coordination by two xanthine ligands and two chloride ions arranged in trans positions. Stacking of such molecular complex units along the

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Table II. Crystal Data and Structure Determination Parameters

	$Cu(xan)_2(NO_3)_2\cdot 2H_2O$	$Cu(xan)_2Cl_2\cdot 2H_2O$	$Zn(xan)_2Cl_2$
formula	$C_{10}H_{12}N_{10}O_{12}Cu$	$C_{10}H_{12}N_8O_6Cl_2Cu$	$C_{10}H_8N_8O_4Cl_2Zn$
fw	527.81	474.70	440.51
temp, K	295	295	295
space group, cryst system	$P\bar{1}$, triclinic	$P\bar{1}$, triclinic	$C2/c$, monoclinic
a, Å	7.111 (2)	3.647 (5)	14.090 (7)
b, Å	7.528 (1)	9.849 (2)	5.456 (3)
c, Å	8.888 (1)	12.763 (4)	20.397 (16)
α, deg	108.63 (1)	72.41 (2)	90
β, deg	98.29 (2)	81.07 (6)	105.82 (5)
γ, deg	102.39 (2)	82.93 (6)	90
V, Å^3	428.6 (3)	430.3 (7)	1509 (3)
Z	1	1	4
calcd density, g·cm^{-3}	2.04	1.83	1.94
obsd density, g·cm^{-3}	2.05	1.90	1.94
color, form	green, prism	green, needle	transparent, prism
data cryst, mm	0.24 × 0.10 × 0.11	0.14 × 0.04 × 0.57	0.09 × 0.47 × 0.21
abs coeff (Mo Kα) μ, cm^{-1}	13.70	15.46	20.61
transm coeff	0.816–0.893	0.717–0.947	0.647–0.981
data colln range 2θ, deg	2–80	2–70	2–72
range of h,k,l measd	0,12/±13/±16	±5/±15/±20	–23,0/±9/±33
scan method	ω–2θ	ω–2θ	ω–2θ
scan speed, deg·min^{-1}	1.5–16.5	1.8–8.2	1.5–16.5
max measd time/rfln, s	50	50	50
no. of rflcns measd (including stds)	5672	7705	7440
R_{av}/no. of rflcns averaged	0.019/5291	0.020/7524	0.13/4868
no. of unique rflcns	4982	3767	3216
no. of rflcns with $I \geq 3\sigma(I)$	3356	2824	2379
no. of variables	151	139	132
largest shift/esd (non-hydrogen param)	0.002	0.02	0.001
final max/min $\Delta\rho$, e/Å^3	0.44/–0.42	3.20/–1.30	1.26/–1.63
$R(F_o)$	0.036	0.051	0.056
$R_w(F_o)$	0.045	0.065	0.061

Table III. Positional Parameters and U_{eq}/U_{iso} Values of $Cu(xan)_2(NO_3)_2\cdot 2H_2O$[a]

atom	x	y	z	U_{eq}/U_{iso}, Å^2
Cu	0.000	0.000	1.000	0.0221 (1)
O(1)	0.2536 (2)	–0.0114 (2)	1.1044 (1)	0.0318 (3)
N(11)	0.1475 (2)	0.5289 (2)	1.2565 (1)	0.0281 (3)
O(11)	0.1102 (2)	0.3687 (2)	1.1413 (1)	0.0472 (4)
O(12)	0.2344 (2)	0.6814 (2)	1.2405 (2)	0.0451 (4)
O(13)	0.0960 (3)	0.5360 (2)	1.3823 (1)	0.0574 (4)
N(1)	0.3943 (2)	0.4715 (2)	0.6747 (1)	0.0266 (3)
C(2)	0.3463 (2)	0.5368 (2)	0.8250 (2)	0.0258 (3)
O(2)	0.3874 (2)	0.7119 (2)	0.9031 (1)	0.0395 (3)
N(3)	0.2540 (2)	0.3975 (2)	0.8774 (1)	0.0256 (3)
C(4)	0.2147 (2)	0.2042 (2)	0.7842 (1)	0.0205 (3)
C(5)	0.2681 (2)	0.1460 (2)	0.6379 (1)	0.0228 (3)
C(6)	0.3611 (2)	0.2819 (2)	0.5726 (2)	0.0248 (3)
O(6)	0.4089 (2)	0.2408 (2)	0.4396 (1)	0.0371 (3)
N(7)	0.2070 (2)	–0.0545 (2)	0.5779 (1)	0.0272 (3)
C(8)	0.1222 (2)	–0.1084 (2)	0.6857 (2)	0.0282 (3)
N(9)	0.1220 (2)	0.0444 (2)	0.8151 (1)	0.0244 (3)
H(1)	0.455	0.564	0.638	0.051
H(3)	0.228	0.435	0.972	0.051
H(7)	0.228	–0.138	0.485	0.051
H(8)	0.063	–0.247	0.669	0.051
H(11)	0.281	–0.098	1.052	0.051
H(12)	0.287	0.022	1.192	0.051

[a] $U_{eq} = {}^1/_3\sum_i\sum_j U_{ij}a^*_i a^*_j a_i a_j$.

Table IV. Positional Parameters and U_{eq}/U_{iso} Values of $Cu(xan)_2Cl_2\cdot 2H_2O$[a]

atom	x	y	z	U_{eq}/U_{iso}, Å^2
Cu	0.5000	0.5000	0.5000	0.0239 (1)
Cl	0.0736 (3)	0.6945 (1)	0.4708 (1)	0.0283 (2)
N(1)	0.8069 (10)	0.8191 (3)	0.0521 (2)	0.0299 (7)
C(2)	0.8290 (12)	0.8576 (4)	0.1462 (3)	0.0300 (8)
O(2)	0.9377 (11)	0.9726 (3)	0.1407 (2)	0.0471 (9)
N(3)	0.7340 (10)	0.7593 (3)	0.2450 (2)	0.0278 (7)
C(4)	0.6413 (10)	0.6281 (4)	0.2473 (2)	0.0218 (6)
C(5)	0.6265 (10)	0.5933 (4)	0.1521 (2)	0.0241 (6)
C(6)	0.7082 (11)	0.6905 (4)	0.0453 (3)	0.0277 (7)
O(6)	0.7057 (11)	0.6721 (4)	–0.0452 (2)	0.0440 (9)
N(7)	0.5343 (10)	0.4540 (3)	0.1864 (2)	0.0287 (6)
C(8)	0.5009 (11)	0.4125 (4)	0.2966 (3)	0.0283 (7)
N(9)	0.5630 (9)	0.5162 (3)	0.3380 (2)	0.0233 (5)
O(3)	0.8672 (34)	0.8823 (13)	0.6962 (10)	0.1552 (4)[b]
O(4)	0.4560 (90)	0.9755 (34)	0.5876 (26)	0.1348 (10)[c]
H(1)	0.894 (13)	0.877 (5)	–0.004 (4)	0.027 (11)
H(3)	0.738 (15)	0.789 (6)	0.299 (4)	0.046 (15)
H(7)	0.524 (19)	0.408 (7)	0.143 (6)	0.074 (21)
H(8)	0.435 (13)	0.318 (5)	0.340 (4)	0.036 (13)

[a] $U_{eq} = {}^1/_3\sum_i\sum_j U_{ij}a^*_i a^*_j a_i a_j$. [b] Occupancy factor: 0.75. [c] Occupancy factor: 0.25.

a-axis of the unit cell results in a 4 + 2 elongated copper coordination octahedron with a long intermolecular Cu···Cl distance of 2.915 (3) Å, compared with the intramolecular Cu–Cl distance of 2.289 (2) Å. The nearly perfect octahedral bonding angles (Table VII) support the suggestion of a true bonding interaction between copper and these two distant apical chloride ions. The observed Cu–N bond distance of 2.004 (3) Å is similar to those found in other copper purine complexes,[24-26] where copper is bonded to a nitrogen atom of a five-membered imidazole or a pyrazole ring. The neutral xanthine molecule with the hydrogen atoms covalently bonded to the nitrogen atoms N(1), N(3), and N(7) is monodentately coordinating through the remaining imidazole nitrogen atom N(9). The noncoordinating disordered water molecules are embedded between the columns of stacked complex units, thus leading to sheets of water molecules parallel to the *ac* plane.

The molecular unit of the zinc complex, illustrated in Figure 5, may be characterized by the formula $[Zn(xan)_2Cl_2]$. The zinc

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Table V. Positional Parameters and U_{eq}/U_{iso} Values of $Zn(xan)_2Cl_2$[a]

atom	x	y	z	U_{eq}/U_{iso}, Å^2
Zn	0.0000	0.3417 (1)	0.2500	0.0244 (1)
Cl	0.1488 (1)	0.1654 (2)	0.2702 (1)	0.0356 (2)
N(1)	0.2318 (2)	0.9711 (5)	0.4449 (2)	0.0254 (6)
C(2)	0.2610 (2)	0.7809 (6)	0.4099 (2)	0.0254 (7)
O(2)	0.3482 (2)	0.7430 (5)	0.4154 (1)	0.0358 (6)
N(3)	0.1870 (2)	0.6360 (5)	0.3716 (2)	0.0268 (6)
C(4)	0.0906 (2)	0.6901 (6)	0.3682 (2)	0.0223 (6)
C(5)	0.0649 (2)	0.8762 (6)	0.4047 (2)	0.0239 (6)
C(6)	0.1360 (2)	1.0383 (6)	0.4452 (2)	0.0245 (6)
O(6)	0.1212 (2)	1.2163 (5)	0.4774 (1)	0.0361 (6)
N(7)	−0.0366 (2)	0.8727 (6)	0.3874 (2)	0.0283 (6)
C(8)	−0.0662 (3)	0.6921 (6)	0.3434 (2)	0.0277 (7)
N(9)	0.0091 (2)	0.5722 (5)	0.3295 (1)	0.0250 (6)
H(1)	0.278 (4)	1.050 (9)	0.472 (2)	0.047 (13)
H(3)	0.189 (5)	0.486 (11)	0.347 (3)	0.085 (19)
H(7)	−0.066 (3)	0.976 (8)	0.404 (2)	0.034 (12)
H(8)	−0.127 (3)	0.648 (7)	0.325 (2)	0.033 (11)

[a] $U_{eq} = {}^1/_3\sum_i\sum_j U_{ij}a^*_i a^*_j a_i a_j$.

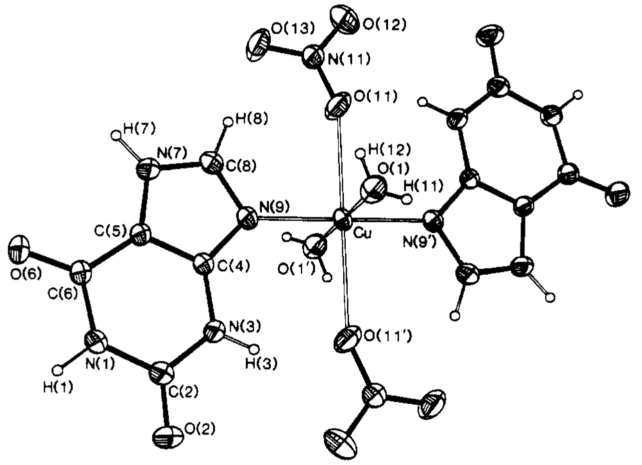

Figure 3. Molecular structure of $Cu(xan)_2(NO_3)_2{\cdot}2H_2O$. The thermal ellipsoids shown are drawn at the 50% probability level.

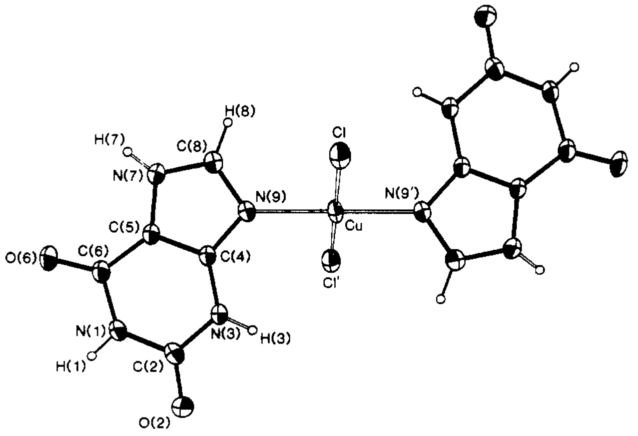

Figure 4. Molecular structure of $Cu(xan)_2Cl_2{\cdot}2H_2O$. The thermal ellipsoids shown are drawn at the 50% probability level.

ion exhibits a tetrahedral ZnN_2Cl_2 coordination including two N(9)-coordinating xanthine ligands and two chloride ions. The zinc ion is lying on a 2-fold symmetry axis parallel to the *b*-axis of the unit cell. The tetrahedral geometry is markedly distorted as evidenced by the polyhedron defining angles in the range 103.4 (1)–129.1 (1)°. The distortion of the ZnN_2Cl_2 polyhedron is also indicated by the interplanar angle of 85.3° between the planes N(9)–Zn–Cl and N(9′)–Zn–Cl′. As in the structure of $Cu(xan)_2Cl_2{\cdot}2H_2O$, in this zinc complex monodentate coordination of the neutral 1H,3H,7H tautomer of xanthine through N(9) is observed. A summary of selected bonding distances and angles is given in Tables VI and VII, respectively.

All metal compounds of unsubstituted xanthine and their coordination and protonation sites deduced from X-ray structural data are summarized in Table VIII. Figure 6 gives the corresponding schematic presentation of the different coordination types observed up to now in metal complexes of neutral or anionic xanthine.

Coordinating Properties of Neutral or Anionic Xanthine. The three xanthine complexes described in this paper represent the first and only examples of coordination compounds involving neutral xanthine. In these monomeric complexes of the type Ia–c, respectively, the 1H,3H,7H tautomer of xanthine is monodentately coordinating through the remaining nitrogen atom N(9). Systematic crystallographic investigations on numerous complexes of different purine derivatives have pointed to the fact that metal cations will preferentially coordinate to that nitrogen atom of the five-membered ring which is not bonded to a hydrogen atom in the neutral free base. Spectroscopic studies[31,32] and CNDO calculations[33] revealed that in neutral xanthine hydrogen atoms are attached at N(1), N(3), and N(7). On the basis of this evidence, monodentate coordination through N(9) of the neutral ligand has to be expected for neutral xanthine and is confirmed by the results presented here.

Protonation of neutral xanthine leads to the xanthinium cation, where all four ring nitrogen atoms are blocked for metal coordination by hydrogen atoms. Therefore, in the saltlike structure of $(xan^+)_2ZnCl_4$[19] the xanthinium cations are linked via hydrogen bonding contacts only to the $ZnCl_4$ tetrahedron.

Deprotonation of xanthine increases the number of possible coordination sites. On the basis of the available spectroscopic data, the ionization sequence of neutral xanthine has not yet been definitely elucidated. The simultaneous deprotonation from more than one site may also result in a mixture of different tautomeric forms. Deprotonation could occur at the nitrogen atom N(3) accompanied by a displacement of the imidazole hydrogen atom from N(9) to N(7).[32] This assumption is supported by the solid-state structure of the sodium salt of xanthine $Na^+(xan^-){\cdot}4H_2O$, lacking a proton at N(3) and bearing a hydrogen atom bonded to N(9) instead of N(7).[27] In contrast, NMR and UV studies led to the assignment that dissociation involves predominantely the nitrogen atom N(7).[31] There is also crystallographic evidence for this suggestion, since in the monomeric complex $Co(xan^-)(dmg^-)_2(Bu_3P){\cdot}H_2O{\cdot}CH_3OH$ (structure type Id, Figure 6) the 1H,3H form of monoanionic xanthine is monodentately coordinating through N(9), leaving N(7) neither protonated nor metalated.[28]

In the 2-fold negatively charged anion of xanthine, the remaining hydrogen atom could be localized at one of the pyrimidine nitrogen atoms N(1) or N(3). Depending on the ionization sequence, coordination of the xanthine dianion involves the three other nitrogen atoms, thus leading to two different structure types, labeled as Ie and If (Figure 6). Type Ie is represented by the structure of $[(CH_3Hg^+)_3(xan^{2-})]NO_3{\cdot}H_2O$, where the xanthine dianion with the remaining hydrogen atom bonded to N(1) acts as tridentate ligand coordinating through N(3), N(7), and N(9) to three different methylmercury cations.[29]

In a trinuclear 3:1 titanocene–xanthine(2–) complex $[(\eta^5\text{-}C_5H_5)_2Ti]_3Cl(xan^{2-})$ exhibiting structure type Ie, monodentate N(9) coordination in combination with N(7)/O(6) and N(1)/O(2) chelation of a dianionic xanthine to three different titanocene units is observed.[30] The remaining hydrogen atom is attached at N(3). This complex provides the only crystallographic evidence for the formation of a five-membered N(7)/O(6) chelate with an unsubstituted oxopurine. In addition, a four-membered chelate

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Table VI. Selected Interatomic Bond Distances (Å)

$Cu(xan)_2(NO_3)_2·2H_2O$		$Cu(xan)_2Cl_2·2H_2O$		$Zn(xan)_2Cl_2$	
		Metal Coordination Polyhedra			
Cu–N(9)	2.050 (1) (2×)	Cu–N(9)	2.004 (3) (2×)	Zn–N(9)	2.029 (3) (2×)
Cu–O(1)	1.938 (1) (2×)	Cu–Cl	2.289 (2) (2×)	Zn–Cl	2.240 (1) (2×)
Cu–O(11)	2.540 (1) (2×)	Cu–Cl″	2.915 (3) (2×)		
		Xanthine			
N(1)–C(2)	1.388 (2)		1.380 (4)		1.384 (4)
C(2)–N(3)	1.360 (2)		1.362 (4)		1.371 (4)
N(3)–C(4)	1.367 (2)		1.367 (4)		1.373 (4)
C(4)–C(5)	1.370 (2)		1.369 (4)		1.365 (4)
C(5)–C(6)	1.421 (2)		1.421 (4)		1.420 (5)
C(6)–N(1)	1.372 (2)		1.389 (5)		1.400 (4)
C(5)–N(7)	1.375 (2)		1.375 (4)		1.377 (4)
N(7)–C(8)	1.325 (2)		1.332 (4)		1.321 (5)
C(8)–N(9)	1.343 (2)		1.339 (4)		1.341 (4)
N(9)–C(4)	1.371 (2)		1.356 (4)		1.364 (4)
C(2)–O(2)	1.223 (2)		1.224 (4)		1.221 (4)
C(6)–O(6)	1.240 (2)		1.224 (4)		1.222 (4)
N(3)–N(9)	2.469 (2)		2.440 (4)		2.443 (4)
		Nitrate			
N(11)–O(11)	1.253 (2)				
N(11)–O(12)	1.243 (2)				
N(11)–O(13)	1.214 (2)				

Table VII. Selected Interatomic Bond Angles (deg)

$Cu(xan)_2(NO_3)_2·2H_2O$		$Cu(xan)_2Cl_2·2H_2O$		$Zn(xan)_2Cl_2$	
		Metal Coordination Polyhedra			
N(9)–Cu–O(1)	89.06 (5) (2×)	N(9)–Cu–N(9′)	180.0	N(9)–Zn–Cl	105.5 (1) (2×)
N(9)–Cu–O(1′)	90.94 (5) (2×)	N(9)–Cu–Cl	89.8 (1)	N(9)–Zn–Cl′	105.4 (1) (2×)
N(9)–Cu–O(11)	86.44 (4) (2×)	N(9)–Cu–Cl′	90.2 (1)	N(9)–Zn–N(9′)	103.4 (1)
N(9)–Cu–O(11′)	93.56 (4) (2×)	N(9)–Cu–Cl″	92.4 (1)	Cl–Zn–Cl′	129.1 (1)
O(1)–Cu–O(11)	89.31 (6) (2×)	N(9)–Cu–Cl‴	87.6 (1)		
O(1)–Cu–O(11′)	90.69 (6) (2×)	N(9′)–Cu–Cl	90.2 (1)		
		N(9′)–Cu–Cl′	89.8 (1)		
		N(9′)–Cu–Cl″	87.6 (1)		
		N(9′)–Cu–Cl‴	92.4 (1)		
		Cl–Cu–Cl′	180.0		
		Cl–Cu–Cl″	88.1 (1)		
		Cl–Cu–Cl‴	91.9 (1)		
		Cl′–Cu–Cl″	91.9 (1)		
		Cl′–Cu–Cl‴	88.1 (1)		
		Cl″–Cu–Cl‴	180.0		
		Xanthine			
C(6)–N(1)–C(2)	127.5 (1)		128.0 (3)		128.4 (3)
N(1)–C(2)–N(3)	116.6 (1)		116.5 (3)		116.1 (3)
C(2)–N(3)–C(4)	120.2 (1)		120.0 (3)		119.5 (3)
N(3)–C(4)–C(5)	121.3 (1)		121.7 (3)		122.6 (3)
C(4)–C(5)–C(6)	122.1 (1)		122.3 (3)		122.0 (3)
C(5)–C(6)–N(1)	112.2 (1)		111.5 (3)		111.3 (3)
C(4)–C(5)–N(7)	106.0 (1)		105.3 (3)		105.2 (3)
C(5)–N(7)–C(8)	107.1 (1)		107.0 (3)		107.3 (3)
N(7)–C(8)–N(9)	112.6 (1)		112.4 (3)		112.7 (3)
C(8)–N(9)–C(4)	104.3 (1)		104.3 (3)		103.7 (3)
N(9)–C(4)–C(5)	110.1 (1)		111.0 (3)		111.1 (3)
N(3)–C(4)–N(9)	128.7 (1)		127.3 (3)		126.3 (3)
C(6)–C(5)–N(7)	131.9 (1)		132.4 (3)		132.6 (3)
N(1)–C(2)–O(2)	119.9 (1)		121.5 (3)		120.9 (3)
N(3)–C(2)–O(2)	123.4 (1)		122.0 (3)		123.0 (3)
N(1)–C(6)–O(6)	121.9 (1)		120.1 (3)		121.2 (3)
C(5)–C(6)–O(6)	125.9 (1)		128.4 (3)		127.6 (3)
		Metal–Xanthine			
Cu–N(9)–C(4)	135.5 (1)	Cu–N(9)–C(4)	131.3 (2)	Zn–N(9)–C(4)	127.9 (2)
Cu–N(9)–C(8)	120.2 (1)	Cu–N(9)–C(8)	124.2 (2)	Zn–N(9)–C(8)	126.2 (2)
		Nitrate			
O(11)–N(11)–O(12)	119.7 (1)				
O(11)–N(11)–O(13)	120.3 (1)				
O(12)–N(11)–O(13)	120.0 (1)				

ring resulting from N(1)/O(2) coordination is suggested to occur in this complex, a binding mode which has not been considered so far. In substituted purines, N(7)/O(6) chelation also is rarely found. There are only two examples, both including structures with anionic theophylline, a xanthine derivative methylated at N(1) and N(3), $[(\eta^5\text{-}C_5H_5)_2Ti](\text{theophylline}^-)$,[34] and $[(CH_3)_3Pt(\text{theophylline}^-)]_6·12CHCl_3$.[35]

The possibility of the formation of metal chelate structures

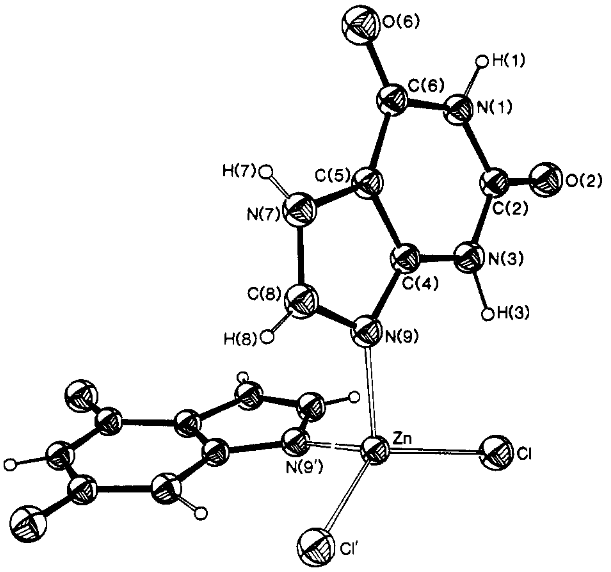
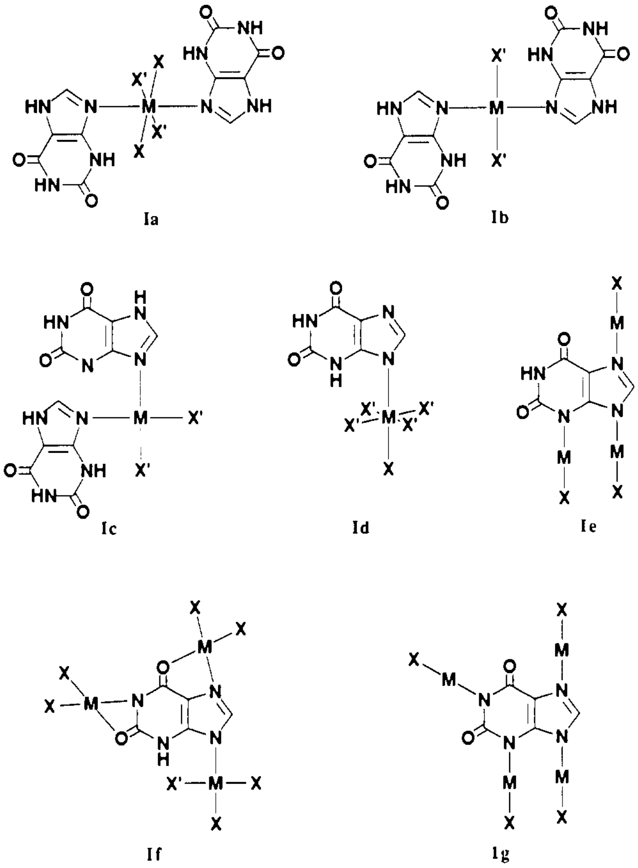


Figure 5. Molecular structure of $Zn(xan)_2Cl_2$. The thermal ellipsoids shown are drawn at the 50% probability level.



Ia Ib Ic Id Ie If Ig

Figure 6. Schematic presentation of the coordinating interactions of xanthine with metal ions (M) established by X-ray crystallography: (Ia) M = Cu, X = H_2O, X' = NO_3^-; (Ib) M = Cu, X' = Cl^-; (Ic) M = Zn, X' = Cl^-; (Id) M = Co, X = Bu_3P, X' = dmg⁻; (Ie) X–M = CH_3Hg^+; (If) M = Ti, X = C_5H_5, X' = Cl^-; (Ig) X–M = CH_3Hg^+.

through N(7) and the exocyclic atom attached to C(6) has been discussed in detail.[2,30,34] In general, this mode of coordination is only observed for complexes where the exocyclic atom is sulfur, as for example in 6-mercaptopurine complexes.[36] The absence of N(7)/O(6) chelation in metal complexes of oxopurines has been explained by Sletten.[37] The construction of a model chelate complex assuming metal–O and metal–N distances of about 2.0 Å results in a C(5)–N(7)–metal bonding angle of approximately 90°. Therefore, the coordinating lone pair orbital on N(7) would be bent roughly 40° from its favored, symmetrical position between C(5) and C(8). If the exocyclic atom is oxygen or nitrogen, these atoms usually take part in hydrogen bonding with neighboring ligands of the metal coordination sphere ("indirecte chelate" formation). If hydrogen bond donors or acceptors are absent, the exocyclic oxygen atom O(6) occasionally has been found to occupy the axial site of a (4 + 1) or a (4 + 1 + 1) distorted metal coordination polyhedron as for example in Cu^{II}(theophylline⁻)(*N*-3,4-benzosalicylidene-*N'*,*N'*-dimethylethylenediamine⁻)·H_2O.[38] In view of the very long metal–O contacts (for example 2.92 Å in the complex mentioned before), such complexes cannot be considered as true N(7)/O(6) chelates. The Ti–xan^{2-} complex,[30] the Ti–theophylline⁻ complex,[34] and the Pt–theophylline⁻ complex[35] described earlier in this paper, however, represent three examples of balanced N(7)/O(6) chelates as evidenced by the corresponding metal–N(7) and metal–O(6) distances of 2.23 Å/2.25 Å, 2.21 Å/2.28 Å, and 2.17 Å/2.34 Å, respectively. Therefore, the Ti–xan^{2-} chelate complex is included in Table VIII and in Figure 6 as an example of a chelate binding mode of xanthine, although this chelate may be a consequence of the very specific steric and electronic properties of the titanocene moiety only. In addition, it has to be kept in mind that 2-fold deprotonated xan^{2-} hardly is a reliable model for the interaction of xanthine with metals in biology, since in physiological media neutral xanthine may be the predominant form.

Abstraction of the third proton of xanthine finally ensures that all four nitrogen atoms of the purine ring are available for coordination. For example, in the structure of $[(CH_3Hg^+)_4(xan^{3-})]NO_3$, four different CH_3Hg^+ cations are bonded to N(1), N(3), N(7), and N(9) of the trianion of xanthine (structure type Ig[29]).

In summation of these structural data, it is evident that the imidazole nitrogen atom N(9) of xanthine in its neutral as well as in its anionic form always is involved in coordination. This observation supports those structural models for oxidation of xanthine catalyzed by the enzyme xanthine oxidase, which suggest coordination to the metal through N(9) and not through N(7).

With regard to the coordination properties of xanthine, contrasting binding modes were observed for the oxopurine hypoxanthine (hyxan), which is also a substrate for the enzyme xanthine oxidase. In monomeric hypoxanthine complexes with the composition $M(hyxan)SO_4{\cdot}5H_2O$ (M = Co, Ni)[24,39] and $Ru(hyxan)(NH_3)_5Cl_3{\cdot}H_2O$,[40] the nitrogen atom N(7) of the imidazole moiety has been established as the primary metal binding site. $Cu(hyxan)SO_4{\cdot}H_2O$ represents a polymeric structure, where hypoxanthine is coordinating through N(3) and N(7) to different metal ions, forming infinite metal hypoxanthine chains.[24] N(9) coordination is observed in conjunction with N(3) binding only in dimeric complexes of the type $[M(\mu\text{-hyxan})_2(SO_4)_2{\cdot}(\mu\text{-}H_2O)_2(H_2O)_2]$, M = Cu, Co, Cd, and Zn,[25,41] and in $Cu(hyxan)_2Cl_2{\cdot}3H_2O$.[42]

Purine Stacking. The packing diagrams of the xanthine complexes are presented in Figures 7–9. The familiar solid-state

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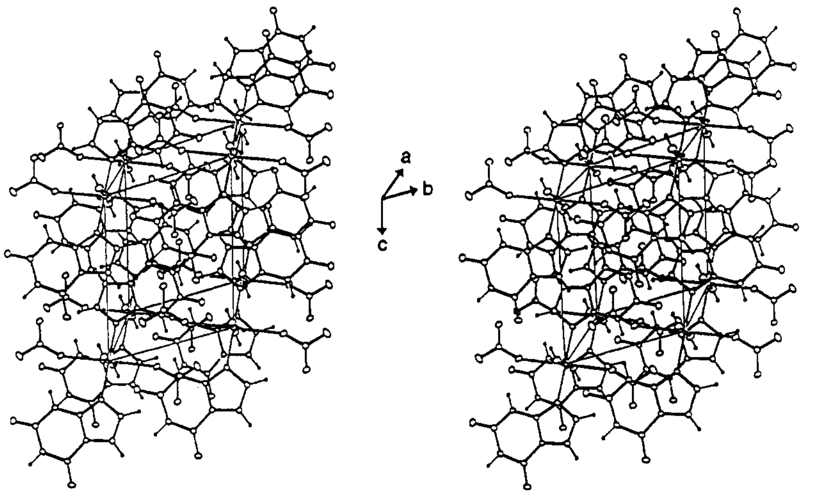

Figure 7. Stereoview of the unit cell of $Cu(xan)_2(NO_3)_2{\cdot}2H_2O$.

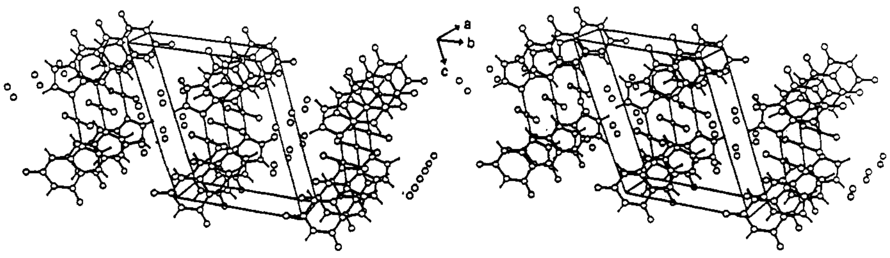

Figure 8. Stereoview of the unit cell of $Cu(xan)_2Cl_2{\cdot}2H_2O$.

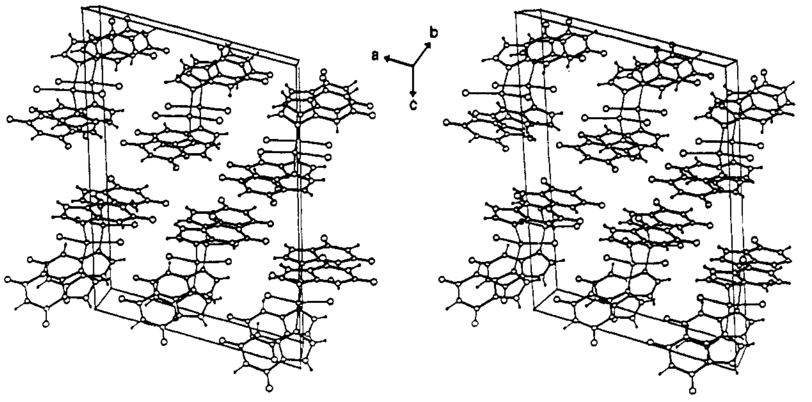

Figure 9. Stereoview of the unit cell of $Zn(xan)_2Cl_2$.

Table VIII. Coordination and Protonation Sites of Xanthine Established by X-ray Crystallography

compd[a]	structure type (Figure 5)	coordination	protonation	ref
$Na^+(xan^-){\cdot}4H_2O$			N(1), N(9)	27
$(xanthinium^+)_2[ZnCl_4]$			N(1), N(3), N(7), N(9)	19
$Cu^{II}(xan)_2(NO_3)_2{\cdot}2H_2O$	Ia	monomeric; N(9)	N(1), N(3), N(7)	this work
$Cu^{II}(xan)_2Cl_2{\cdot}2H_2O$	Ib	monomeric; N(9)	N(1), N(3), N(7)	this work
$Zn^{II}(xan)_2Cl_2$	Ic	monomeric; N(9)	N(1), N(3), N(7)	this work
$Co^{III}(xan^-)(dmg^-)_2(Bu_3P){\cdot}H_2O{\cdot}CH_3OH$	Id	monomeric; N(9)	N(1), N(3)	28
$[(CH_3Hg^+)_3(xan^{2-})]NO_3{\cdot}H_2O$	Ie	N(3), N(7), N(9)	N(1)	29
$[(\eta^5\text{-}C_5H_5)_2Ti^{III}]_3Cl(xan^{2-})$	If	N(9), N(7)/O(6) chelate, N(1)/O(2) chelate	N(3)	30
$[(CH_3Hg^+)(xan^{3-})]NO_3$	Ig	N(1), N(3), N(7), N(9)		29

[a] dmg = dimethylglyoxime; Bu_3P = tributylphosphine.

stacking found in most purine structures is also retained in the complexes described here. According to the classification proposed by Bugg,[43] a solid-state stacking pattern of type II occurs in $Cu(xan)_2(NO_3)_2{\cdot}2H_2O$, where the bases are stacked on top of each other rotated by about 180 °C. The coordinating xanthine ligands are infinitely stacked along the *a*-axis of the unit cell with only minor direct overlap of the purine rings. The shortest stacking distance between purine bases, calculated as the mean distance of all atoms of one molecule from the least-squares plane through the stacking molecule, is 3.35 Å. In addition, the nitrate groups are stacked along the *a*-axis of the cell on top of the pyrimidine

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(43) Bugg, C. E. *The Jerusalem Symposia on Quantum Chemistry and Biochemistry*; Jerusalem Academy of Sciences and Humanities: Jerusalem, 1972; Vol. 4, p 178.

Table IX. Hydrogen Bonding Contacts in the Metal Xanthine Compounds

X–H···Y	X–H, Å	H···Y, Å	X–Y, Å	X–H···Y, deg
	Cu(xan)$_2$(NO$_3$)$_2$·2H$_2$O			
N(1)–H(1)···O(6)	0.91 (1)	1.95 (1)	2.863 (2)	178 (1)
N(3)–H(3)···O(11)	0.86 (1)	1.97 (1)	2.742 (2)	149 (1)
N(3)–H(3)···O(12)	0.86 (1)	2.50 (1)	3.295 (2)	155 (1)
N(7)–H(7)···O(12)	0.92 (1)	2.17 (1)	3.083 (2)	169 (1)
N(7)–H(7)···O(13)	0.92 (1)	2.25 (1)	2.878 (2)	125 (1)
O(1)–H(11)···O(2)	0.75 (1)	1.98 (1)	2.721 (2)	169 (1)
O(1)–H(12)···O(6)	0.72 (1)	1.95 (1)	2.871 (2)	178 (1)
	Cu(xan)$_2$Cl$_2$·2H$_2$O			
N(1)–H(1)···O(2)	0.82 (5)	1.99 (4)	2.799 (4)	175 (4)
N(3)–H(3)···Cl	0.83 (5)	2.54 (6)	3.170 (4)	133 (4)
N(7)–H(7)···O(6)	0.82 (7)	2.00 (8)	2.769 (5)	158 (6)
	Zn(xan)$_2$Cl$_2$			
N(1)–H(1)···O(6)	0.85 (5)	1.98 (5)	2.814 (4)	169 (4)
N(3)–H(3)···Cl	0.97 (6)	2.30 (6)	3.249 (4)	163 (5)
N(7)–H(7)···O(2)	0.82 (4)	1.95 (4)	2.747 (4)	163 (4)

ring of the xanthine ligands with a mean spacing distance of 3.34 Å. In Cu(xan)$_2$Cl$_2$·2H$_2$O, a stacking pattern of type I with the stacking xanthines related by simple crystallographic translation along the *a*-axis of the cell is observed. The shortest stacking distance between xanthine molecules with least-squares planes nearly perpendicular to their translation axis is 3.40 Å. In Zn(xan)$_2$Cl$_2$, finally, no direct stacking interactions between the xanthine ligands are observed.

In all three compounds presented here, the purine rings show a slight nonplanarity in the pseudoaromatic ring system. Maximum deviations of an individual atom from the least-squares plane through the nine ring atoms are –0.015 Å (C(5)), 0.013 Å (N(9)) in Cu(xan)$_2$(NO$_3$)$_2$·2H$_2$O, –0.036 Å (C(5)), 0.032 Å (C(2)) in Cu(xan)$_2$Cl$_2$·2H$_2$O, and –0.041 Å (C(5)) in Zn(xan)$_2$Cl$_2$. The extraannular oxygen atoms O(2) deviate –0.020, 0.125, or 0.003 Å from the corresponding purine planes, whereas deviations of 0.040, –0.004, and 0.057 Å, respectively, are observed for the oxygen atom O(6).

Hydrogen Bonding. A summary of bond distances and angles involving hydrogen bonding contacts is given in Table IX. In Cu(xan)$_2$(NO$_3$)$_2$·2H$_2$O, the hydrogen atoms of the water molecule participate in hydrogen bonding interactions to the exocyclic oxygen atoms O(2) and O(6) of xanthine molecules, thus interconnecting the planes containing the copper atoms, the coordinating xanthine ligands, and the nitrate groups perpendicular to these planes. Two monomeric complex units which are related by a center of inversion in position 0.5, 0.5, 0.5 are connected to dimers via two relatively strong N(1)–H(1)···O(6) hydrogen bonding contacts. In addition, the xanthine molecules are involved in two intermolecular hydrogen bonds of the type N(7)–H(7)···O with the oxygen atoms O(12) and O(13) of a coordinating nitrate group, thus leading to a bifurcated hydrogen bonding system around H(7). An interesting feature of the structure is the existence of indirect chelation via intramolecular hydrogen bonding contacts. Two pseudochelate rings around the copper atom are formed involving the same hydrogen atom H(3): The relatively strong hydrogen bond N(3)–H(3)···O(11) with a donor–acceptor distance of 2.742 (2) Å reveals the formation of a six-membered indirect chelate, whereas the weaker interaction N(3)–H(3)···O(12) with a N···O distance of 3.295 (2) Å results in a eight-membered pseudochelate. In Cu(xan)$_2$Cl$_2$·2H$_2$O, centrosymmetric pairs of hydrogen bonds of the type N(1)–H(1)···O(2) and N(7)–H(7)···O(6) with donor–acceptor distances of 2.799 (4) and 2.769 (5) Å, respectively, interconnect the molecular [Cu(xan)$_2$Cl$_2$] units. The chloride ion participates in an intermolecular hydrogen bonding contact between the complex units stacked along the *a*-axis with a N···Cl distance of 3.170 (4) Å.

In Zn(xan)$_2$Cl$_2$, two xanthine ligands coordinated to two different zinc ions are connected via two N(1)–H(1)···O(6) hydrogen bonding contacts, thus forming hydrogen-bonded dimeric units. Since both of the crystallographically equivalent xanthine molecules of each zinc tetrahedron are involved in hydrogen bonds of this type, infinite zigzag chains of metal ions along the *c*-axis of the unit cell are observed. Xanthine ligands of different zigzag chains are linked to ribbons parallel to the *a*-axis via the relatively strong hydrogen bonding interaction N(7)–H(7)···O(2) with a donor–acceptor distance of 2.747 (4) Å. The intramolecular hydrogen bonding contact N(3)–H(3)···Cl with a N···Cl distance of 3.249 (4) Å again reveals the formation of a six-membered indirect chelate, a binding mode which also is formed in other oxopurines monodentately coordinating through a ring nitrogen atom.[2]

Conclusion. There is strong crystallographic evidence that N(9) is a favored metal binding site of the oxopurine xanthine in its neutral form. This finding supports those structural models for the oxidation of xanthine catalyzed by xanthine oxidase, which suggest intermediate coordination of the molybdenum center of the enzyme through N(9) and not through N(7) of xanthine.

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Supplementary Material Available: Tables of anisotropic thermal parameters and bond distances and angles involving hydrogen atoms (3 pages). Ordering information is given on any current masthead page.