trans-[$Pt(NH_3)_2Cl_2$] is unable to form such adducts, a direct consequence of the stereochemical requirements of the trans square-planar metal center, this lesion uniquely demonstrates the requirement of cis stereochemistry. A deeper understanding of the molecular mechanism of action of *cis*-DDP will require detailed investigations of the dynamic structural changes induced by both *cis*- and *trans*-[$Pt(NH_3)_2Cl_2$] upon binding to duplex oligonucleotides and the ability of cellular repair processes to recognize and eliminate these adducts.

Acknowledgment. This research was supported by U.S. Public Health Service Grant CA 34992 from the National Cancer Institute. We thank M. J. Gait for aid in the synthesis of [d(ApGpGpCpCpT)]$_2$ and C. J. Turner (Department of Chemistry, Columbia University) for helpful discussions with the spin-lattice relaxation measurements and NOESY experiments. The NOESY experiments were performed at the NMR Facility for Biomolecular Research located at the Francis Bitter National Magnet Laboratory at MIT. The NMR facility is supported by Grant No. RR00995 from the Division of Research Resources of the National Institutes of Health and by the National Science Foundation, under Contract No. C-670. We also thank Engelhard Corp. for a loan of K_2PtCl_4, from which *cis*-[$Pt(NH_3)_2Cl_2$] was prepared.

Registry No. *cis*-DDP, 15663-27-1; d(ApGpGpCpCpT), 83026-06-6; *cis*-[$Pt(NH_3)_2${d(ApGpGpCpCpT)-*N7-G(2),N7-G(3)*}] (ammonium salt), 113132-29-9.

---

[90] Fichtinger-Schepman, A. M. J.; van Oosterom, A. T.; Lohman, P. H. M.; Berends, F. *Cancer Res.* **1987**, *47*, 3000-3004.

Contribution from the Institute of Inorganic Chemistry,
University of Zürich, Winterthurerstrasse 190, 8057 Zürich, Switzerland

New Metal Complexes of the Antitumor Drug 6-Mercaptopurine. Syntheses and X-ray Structural Characterizations of Dichloro(6-mercaptopurinium)copper(I), Dichlorotetrakis(6-mercaptopurine)cadmium(II), and Bis(6-mercaptopurinato)cadmium(II) Dihydrate

Erich Dubler* and Ernst Gyr

Received September 17, 1987

Three new metal complexes of the antitumor drug 6-mercaptopurine ($C_5H_4N_4S$, MP) have been crystallized from aqueous solutions. $Cu^I(MP^+)Cl_2$ is triclinic, space group $P\bar{1}$, with a = 7.435 (7) Å, b = 8.848 (5) Å, c = 7.271 (3) Å, α = 109.13 (3)°, β = 99.75 (7)°, γ = 96.83 (7)°, V = 437.5 (12) Å^3, and Z = 2, and is refined to R = 0.028. In contrast to the hydrated complex $Cu^I(MP^+)Cl_2{\cdot}H_2O$, where S-bridged dimers occur, the anhydrate exhibits a new structure with Cl-bridged dimers of the type [$Cu_2(MP^+)_2Cl_4$]. MP$^+$ is protonated at N(1), N(7), and N(9) and binds to copper through its sulfur atom only. The copper(I) coordination is distorted tetrahedral with Cu-S = 2.221 (1) Å and Cu-Cl = 2.465 (1) and 2.493 (1) Å (bridging) and 2.251 (1) Å (terminal). $Cd^{II}(MP)_4Cl_2$ is triclinic, space group $P\bar{1}$, with a = 8.083 (2) Å, b = 11.904 (3) Å, c = 7.374 (2) Å, α = 99.04 (2)°, β = 101.30 (2)°, γ = 91.53 (2)°, V = 685.9 (6) Å^3, and Z = 1, and is refined to R = 0.027. The structure contains one isolated octahedral [$Cd(MP)_2Cl_2$] unit and two noncoordinating MP molecules per cell. The two crystallographically independent MP molecules both are protonated at N(1) and at N(9), but not at N(7). The coordinating molecule acts as a S/N(7) bidentate chelating ligand. Bonding distances are Cd-S = 2.622 (1) Å, Cd-N = 2.366 (1) Å, and Cd-Cl = 2.719 (1) Å. $Cd^{II}(MP^-)_2{\cdot}2H_2O$ is triclinic, space group $P\bar{1}$, with a = 3.918 (3) Å, b = 9.371 (3) Å, c = 11.162 (5) Å, α = 67.89 (3)°, β = 84.40 (4)°, γ = 76.84 (4)°, V = 369.7 (4) Å^3, and Z = 1, and is refined to R = 0.044. This complex exhibits a new polymeric structure type with infinite chains of Cd atoms linked by bridging S atoms. Cd is octahedrally coordinated by four S and two N atoms of the S/N(7)-chelating MP ligand. Bonding distances are Cd-S = 2.689 (1) and 2.868 (1) Å and Cd-N = 2.283 (3) Å. A detailed analysis of bond lengths and angles of MP in its neutral, deprotonated, or protonated form is given. Metal coordination at N(7) induces changes in the geometry of the imidazole moiety of MP similar to, but much smaller than, those induced by protonation at N(7).

Introduction

6-Mercaptopurine ($C_5H_4N_4S$, MP) is a synthetic thio analogue of the natural purine hypoxanthine and is used as an established clinical agent for the therapy of human leukemias. Its antimetabolitic mechanism of action is believed to be due to its being converted intracellularly to the corresponding ribonucleotide, which in turn suppresses purine synthesis and inhibits different purine metabolic processes.[1]

There are different interesting aspects of the formation and reactivity of MP metal complexes. On the basis of the discovery of the anticancer activity of cisplatin (*cis*-dichlorodiammineplatinum(II)) by Rosenberg in 1969,[2] new metal coordination compounds, including those with drugs acting as ligands, have been screened in regard to their anticancer activity. It has been found that some metal complexes of MP, especially those of platinum and palladium, show antitumor activity, which in some cases is even enhanced with respect to the activity of the free ligand.[3] In addition, coordination metal complexes of drugs generally may be of importance in the design of repository, slow-release, or long-acting drugs. According to Hansen et al.,[4] divalent metal ions, e.g. copper(II), may increase the amount of MP binding to yeast RNA. In a study of the interaction between MP, Cu^{2+}, and the enzyme xanthine oxidase, it has been found that Cu^{2+} inhibits the enzyme, whereas MP could protect as well as reverse this enzyme inhibition, and it has been suggested that the formation of a stable Cu-MP complex is an additional mechanism of action of MP with reference to its antiinflammatory properties.[5]

The formation of MP complexes of Mg(II) and Ca(II), of the transition metals Mn(II), Fe(II), Co(II), Co(III), Ni(II), Cu(I), Cu(II), Zn(II), Ru(II), Ru(III), Rh(III), Pd(II), Ag(I), Cd(II),

---

*To whom correspondence should be addressed.

[1] Jewers, K. In *Progress in Drug Research*; Jucker, E., Ed.; Birkhäuser: Basel, Switzerland, 1981; Vol. 25, p 275.

[2] Rosenberg, B.; Van Camp, L.; Trosko, J. E.; Mansour, V. H. *Nature (London)* **1969**, *222*, 385.

[3] (a) Kirschner, S.; Wei, Y. K.; Francis, D.; Bergman, J. G. *J. Med. Chem.* **1969**, *9*, 369. (b) Skinner, S. M.; Swatzell, J. M.; Lewis, R. W. *Res. Commun. Chem. Pathol. Pharmacol.* **1978**, *19*, 165. (c) Das, M.; Livingstone, S. E. *Br. J. Cancer* **1978**, *38*, 325.

[4] Hansen, H. J.; Bennett, S. J.; Nadler, S. B. *Arch. Biochem. Biophys.* **1962**, *98*, 379.

[5] Kela, U.; Vijayvargiya, R. *Biochem. J.* **1981**, *193*, 799.

$\mathrm{W(CO)}_x$, Ir(III), $\mathrm{Ir(CO)}_x$, Pt(II), Pt(IV), Au(I), and Hg(II), and of organotin(IV), Pb(II), and Bi(III) has been described in early[6-12] and recent[13-19] papers. The first crystal structure of a MP metal complex—a Pd(II) compound—was reported by Heitner and Lippard[20] in 1974. Since then, the structures of an additional five complexes involving Cu(I), Cu(II), Ru(II), Cd(II), and Hg(II) have been solved (Table VI). Their coordination scheme can be classified into two types (Figure 1): sulfur-coordinated monomers (type IA) or S/N(7)-chelated monomers (type IB) and S/N(7)-chelated, halogen-bridged dimers (type IIA) or sulfur-coordinated, sulfur-bridged dimers (type IIB). In this context we report here the synthesis and structure of a copper(I) complex with a new dimeric structure (type IIC), of a cadmium(II) complex with a monomeric structure (type IB) including noncoordinating MP molecules, and of a cadmium(II) complex exhibiting a new polymeric structure (type III).

Experimental Section

Preparations and Thermal Analysis. 6-Mercaptopurine hydrate ($\mathrm{MP{\cdot}H_2O}$) was obtained from Fluka and used without further purification. Thermogravimetric data in the temperature range from 25 to 800 °C were recorded in a flowing-air atmosphere, with use of heating rates of 10 °C/min and sample weights of 8–14 mg on a Perkin-Elmer TGA-7 thermobalance. X-ray powder diffraction diagrams were performed on a Guinier type camera with a Johansson monochromator (Cu $K\alpha_1$ radiation).

(a) Synthesis of $\mathrm{Cu^I(MP^+)Cl_2}$. This anhydrous complex was crystallized by using a method similar to that applied by Caira and Nassimbeni[21] to obtain the hydrated complex $\mathrm{Cu^I(MP^+)Cl_2{\cdot}H_2O}$. A 3-mmol amount of $\mathrm{MP{\cdot}H_2O}$ in 300 mL of 20% aqueous HCl was mixed with 3 mmol of $\mathrm{CuCl_2{\cdot}2H_2O}$ (Merck) in 100 mL of 20% aqueous HCl at room temperature. After 3 days, deep red, transparent crystals had grown from the solution. The solid was washed with $\mathrm{H_2O}$ and dried in a desiccator. Crystallization from identical or slightly diluted solutions at lower temperatures (5 °C) yielded microcrystalline samples, which were identified by X-ray powder diffractometry to contain the hydrated complex described by Caira and Nassimbeni.[21] Thermal analysis of the title complex shows that the compound is thermally stable until 270 °C. The subsequent decomposition up to 800 °C finally leads to CuO, identified by X-ray powder diffractometry,[22] in good agreement with the corresponding observed weight loss. Anal. Calcd for $\mathrm{C_5H_5N_4SCl_2Cu}$: C, 20.88; H, 1.76; N, 19.48. Found: C, 21.03; H, 1.71; N, 19.73.

(b) Synthesis of $\mathrm{Cd^{II}(MP)_4Cl_2}$. The complex was synthesized by following the general procedure given by Griffith and Amma[23] for the preparation of $\mathrm{Cd^{II}(MP)Cl_2{\cdot}H_2O}$. A 3-mmol amount of $\mathrm{CdCl_2{\cdot}2.5H_2O}$ (AnalaR) was added to a suspension of 5 mmol of $\mathrm{MP{\cdot}H_2O}$ in 100 mL of 0.2 M HCl, and the mixture was stirred for 3 h at 80 °C. (Using the same preparation method at 70 °C instead of 80 °C, Griffith and Amma[23] were able to crystallize $\mathrm{Cd^{II}(MP)Cl_2{\cdot}H_2O}$, but we could not reproduce these results.) After the solution was cooled to room temperature, yellow, transparent plates of the title complex formed within a few hours. The crystals were washed with water and dried in a desiccator. The complex is thermally stable until 280 °C. The subsequent decomposition up to 800 °C finally leads to CdO, evidenced by the corresponding weight loss and by powder X-ray diffractometry.[24] Anal. Calcd for $\mathrm{C_{20}H_{16}N_{16}S_4Cl_2Cd}$: C, 30.33; H, 2.04; N, 28.30. Found: C, 31.01; H, 1.92; N, 29.62.

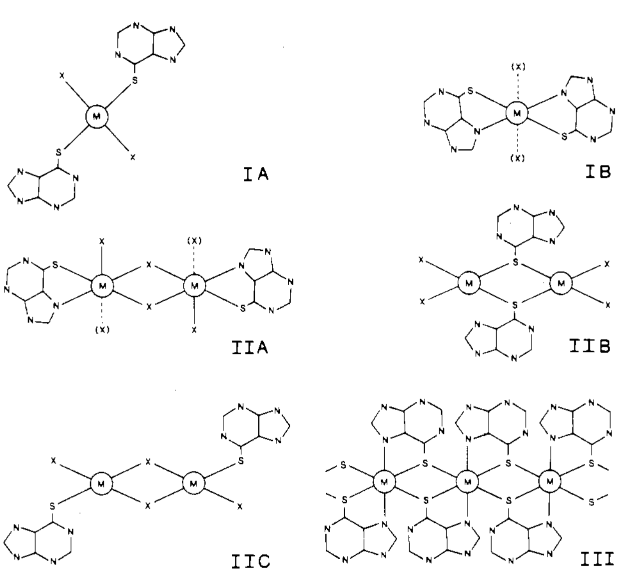

Figure 1. Schematic presentation of different MP–metal coordination types established by X-ray crystallographic investigations.

(c) Synthesis of $\mathrm{Cd^{II}(MP^-)_2{\cdot}2H_2O}$. The complex was synthesized by following the general procedure given by Gosh and Chatterjee[8] for the preparation of $\mathrm{Cd^{II}(MP^-)_2(MP){\cdot}5H_2O}$ (no detailed information on the concentration of the reactants used, however, was given in that paper). A 0.2-mmol amount of $\mathrm{CdClO_4{\cdot}6H_2O}$ (Ventron) was added to a solution of 0.35 mmol of $\mathrm{MP{\cdot}H_2O}$ in 1 L of 0.1 M acetic acid/sodium acetate buffer (pH 4.6) at 95 °C. The solution was stirred for 3 min and then kept at 60 °C. After 2 days, pale yellow, transparent needles of the title complex could be isolated and were washed with $\mathrm{H_2O}$ and dried in a desiccator. The complex exhibits a weight loss between 50 and 120 °C attributable to the elimination of two water molecules per formula unit. The decomposition of the anhydrous compound starts at 350 °C and leads, at 800 °C, to $\mathrm{Cd_3O_2SO_4}$ and minor amounts of β-$\mathrm{CdSO_4}$ and CdO.[24] Anal. Calcd for $\mathrm{C_{10}H_{10}N_8S_2O_2Cd}$: C, 26.65; H, 2.24; N, 24.86; $\mathrm{H_2O}$, 8.0. Found: C, 27.19; H, 2.05; N, 25.36; $\mathrm{H_2O}$ (thermogravimetric analysis), 6.6.

Crystallographic Studies. Symmetry, preliminary unit cell parameters, and space groups of the three complexes were established by precession and Weissenberg photography. Final lattice parameters and crystal orientations were obtained from the least-squares refinement of 25 reflections on an Enraf-Nonius CAD-4 diffractometer.

Intensity data were collected by using graphite-monochromated Mo $K\alpha$ radiation. Six standard reflections chosen to lie in different regions of reciprocal space were monitored periodically and showed no significant changes during data collection for $\mathrm{Cd^{II}(MP)_4Cl_2}$. Intensity data of the other two compounds had to be corrected for a total loss in intensity of −3.6% (Cu complex) and of −4.0% (Cd complex). The intensities were reduced to F_o by applying corrections for Lorentz and polarization effects. A numerical absorption correction based on carefully indexed crystal faces was carried out for the two cadmium complexes. In view of the nearly isotropic morphology of the data crystal and of the excellent agreement of the intensities of equivalent reflections before absorption correction, there was no need for any absorption correction for the copper complex. The function minimized during the least-squares refinement was $\sum w|\Delta|^2$. The weighting scheme used was $w = 1/[\sigma^2(F) + p^2F^2]$. All calculations were performed with the SDP program system[25] on a PDP 11/34 computer.

Crystal parameters, data collection details, and results of the refinements are summarized in Table I.

Results and Discussion

The structures could be solved by a combination of direct methods and Patterson syntheses. All hydrogen atoms, except

---

(6) Cheney, G. E.; Freiser, H.; Fernando, Q. *J. Am. Chem. Soc.* **1959**, *81*, 2611.
(7) Scoran, E. M.; Cefola, M. *Arch. Biochem. Biophys.* **1962**, *97*, 146.
(8) Gosh, A. K.; Chatterjee, S. *J. Inorg. Nucl. Chem.* **1964**, *26*, 1459.
(9) Weiss, R.; Venner, H. *Z. Phys. Chem. (Leipzig)* **1966**, *345*, 122.
(10) Brigando, J.; Colaitis, D. *Bull. Soc. Chim. Fr.* **1969**, *10*, 3440.
(11) Gel'fman, M. I.; Kustova, N. A. *Russ. J. Inorg. Chem. (Engl. Transl.)* **1969**, *14*, 110.
(12) Khan, M. M. T.; Krishnamoorthy, C. R. *J. Inorg. Nucl. Chem.* **1971**, *33*, 1417.
(13) Kottmair, N.; Beck, W. *Inorg. Chim. Acta* **1979**, *34*, 137.
(14) Cinquantini, A.; Cini, R.; Zanello, P. *J. Inorg. Biochem.* **1980**, *12*, 157.
(15) Barbieri, R.; Rivarola, E.; Di Bianca, F.; Huber, F. *Inorg. Chim. Acta* **1982**, *57*, 37.
(16) Perello, L.; Borras, J.; Soto, L.; Gordo, F. J.; Gordo, J. C. *Monatsh. Chem.* **1984**, *115*, 1377.
(17) Grigoratos, A.; Katsaros, N. *Inorg. Chim. Acta* **1985**, *108*, 41.
(18) Katsaros, N.; Grigoratou, A. *J. Inorg. Biochem.* **1985**, *25*, 131.
(19) Wei-Da, Y.; Mei-Qing, L.; Shi-Qi, P. *Inorg. Chim. Acta* **1985**, *106*, 65.
(20) Heitner, H. I.; Lippard, S. J. *Inorg. Chem.* **1974**, *13*, 815.
(21) Caira, M. R.; Nassimbeni, L. R. *Acta Crystallogr., Sect. B: Struct. Crystallogr. Cryst. Chem.* **1975**, *B31*, 1339.
(22) JCPDS, Powder Diffraction File, Swarthmore, PA; Card No. 5-0661.
(23) Griffith, E. A. H.; Amma, E. L. *J. Chem. Soc., Chem. Commun.* **1979**, 1013.
(24) JCPDS, Powder Diffraction File, Swarthmore, PA; Card No. 32-140, 15-86, and 5-0640.
(25) Frenz, B. A. *SDP, Structure Determination Package*; Enraf-Nonius: Delft, Holland, 1985.

Table I. Crystal Data and Structure Determination Parameters

	$Cu^{I}(MP^{+})Cl_2$	$Cd^{II}(MP)_4Cl_2$	$Cd^{II}(MP^{-})_2 \cdot 2H_2O$
fw	287.63	792.02	450.77
cryst syst	triclinic	triclinic	triclinic
space group	$P\bar{1}$	$P\bar{1}$	$P\bar{1}$
a, Å	7.435 (7)	8.083 (2)	3.918 (3)
b, Å	8.848 (5)	11.904 (3)	9.371 (3)
c, Å	7.271 (3)	7.374 (2)	11.162 (5)
α, deg	109.13 (3)	99.04 (2)	67.89 (3)
β, deg	99.75 (7)	101.30 (2)	84.40 (4)
γ, deg	96.83 (7)	91.53 (2)	76.84 (4)
V, Å^3	437.5 (12)	685.9 (6)	369.7 (4)
Z	2	1	1
calcd density, g/cm^3	2.183	1.917	2.025
obsd density, g/cm^3	2.18	1.92	2.00
color	red transparent	yellow transparent	pale yellow transparent
data cryst, mm	0.33 × 0.25 × 0.20	0.36 × 0.26 × 0.08	0.63 × 0.10 × 0.05
radiation	Mo Kα	Mo Kα	Mo Kα
scan method	ω–2θ	ω–2θ	ω–2θ
data collecn range 2θ, deg	1.0–80.0	1.0–70.0	1.0–70.0
data collected	$\pm h,\pm k,\pm l$	$\pm h,\pm k,\pm l$	$\pm h,\pm k,\pm l$
max measd time/rfln, s	30	30	40
no. of rflns measd (excluding stds)	10795	12015	6500
abs coeff μ, cm^{-1}	33.0	13.3	17.6
transmission coeff		0.63–0.89	0.81–0.92
R_{av}/no. of rflns averaged	0.016/6951	0.016/8927	0.018/5225
no. of unique rflns	5398	6012	3256
no. of rflns with $I \geq 3\sigma(I)$	3321	4318	2522
no. of variables	139	221	116
p, fudge factor	0.05	0.03	0.03
g, sec extinction coeff	1.8×10^{-6}	7.0×10^{-7}	6.6×10^{-7}
H atoms; x, y, z values	refined	refined	refined
H atoms; B values	refined	fixed	fixed
final max/min $\Delta\rho$, e/Å^3	+1.08/−0.76	+1.48/−0.58	+1.43/−1.41
R/R_w	0.028/0.041	0.027/0.032	0.044/0.061

Table II. Atomic Parameters for $Cu^{I}(MP^{+})Cl_2$[a]

	x	y	z	B, Å^2
Cu	0.06380 (3)	0.32349 (2)	0.02872 (3)	2.656 (4)
Cl(1)	0.17289 (5)	0.50924 (4)	−0.13530 (5)	1.990 (5)
Cl(2)	0.29655 (7)	0.38733 (5)	0.29902 (5)	3.124 (7)
N(1)	−0.1505 (2)	0.2275 (1)	−0.4403 (2)	2.14 (2)
C(2)	−0.2296 (3)	0.2416 (2)	−0.6153 (2)	2.41 (3)
N(3)	−0.3395 (2)	0.1237 (1)	−0.7669 (2)	2.08 (2)
C(4)	−0.3679 (2)	−0.0168 (2)	−0.7314 (2)	1.55 (2)
C(5)	−0.2939 (2)	−0.0401 (1)	−0.5569 (2)	1.44 (2)
C(6)	−0.1750 (2)	0.0882 (1)	−0.3963 (2)	1.49 (2)
S	−0.07593 (5)	0.07540 (4)	−0.17883 (5)	1.923 (6)
N(7)	−0.3602 (2)	−0.1989 (1)	−0.5823 (2)	1.77 (2)
C(8)	−0.4681 (2)	−0.2700 (2)	−0.7651 (2)	2.03 (2)
N(9)	−0.4756 (2)	−0.1619 (1)	−0.8579 (2)	1.91 (2)
H(1)	−0.101 (4)	0.296 (3)	−0.358 (4)	2.5 (6)*
H(2)	−0.202 (3)	0.350 (3)	−0.611 (3)	1.0 (4)*
H(7)	−0.336 (4)	−0.249 (3)	−0.496 (4)	1.8 (5)*
H(8)	−0.535 (4)	−0.378 (3)	−0.829 (3)	1.4 (5)*
H(9)	−0.548 (4)	−0.186 (3)	−0.966 (4)	2.7 (6)*

[a] B_{equiv} factors in Tables II–IV were calculated as $^4/_3(a^2\beta_{11} + b^2\beta_{22} + c^2\beta_{33} + ab\beta_{12} \cos \gamma + ac\beta_{13} \cos \beta + bc\beta_{23} \cos \alpha)$. B values marked by an asterisk indicate H atoms refined isotropically. Estimated standard deviations in the least significant figure are given in parentheses in this and in subsequent tables.

Table III. Final Atomic Parameters for $Cd^{II}(MP)_4Cl_2$

	x	y	z	B, Å^2
Cd	0.500	0.500	0.500	2.054 (3)
Cl	0.23689 (6)	0.38214 (4)	0.57767 (6)	3.158 (9)
N(1A)	0.1791 (2)	0.5426 (1)	−0.0704 (2)	1.97 (2)
C(2A)	0.0717 (2)	0.6257 (1)	−0.1048 (2)	2.14 (3)
N(3A)	0.0383 (2)	0.7068 (1)	0.0223 (2)	2.12 (2)
C(4A)	0.1280 (2)	0.7021 (1)	0.1962 (2)	1.77 (2)
C(5A)	0.2399 (2)	0.6202 (1)	0.2424 (2)	1.67 (2)
C(6A)	0.2679 (2)	0.5318 (1)	0.1042 (2)	1.66 (2)
S(A)	0.39119 (5)	0.42340 (3)	0.14166 (5)	2.116 (6)
N(7A)	0.3108 (2)	0.6429 (1)	0.4306 (2)	1.96 (2)
C(8A)	0.2425 (2)	0.7359 (1)	0.4947 (2)	2.17 (3)
N(9A)	0.1305 (2)	0.7747 (1)	0.3582 (2)	2.14 (2)
N(1B)	0.1891 (2)	0.1163 (1)	0.0608 (2)	2.06 (2)
C(2B)	0.2606 (2)	0.1404 (1)	0.2447 (2)	2.22 (3)
N(3B)	0.3608 (2)	0.0737 (1)	0.3348 (2)	2.13 (2)
C(4B)	0.3843 (2)	−0.0228 (1)	0.2224 (2)	1.69 (2)
C(5B)	0.3155 (2)	−0.0551 (1)	0.0317 (2)	1.64 (2)
C(6B)	0.2071 (2)	0.0188 (1)	−0.0600 (2)	1.71 (2)
S(B)	0.10812 (6)	−0.00030 (4)	−0.28513 (5)	2.467 (7)
N(7B)	0.3730 (2)	−0.1589 (1)	−0.0345 (2)	2.04 (2)
C(8B)	0.4723 (2)	−0.1861 (1)	0.1138 (2)	2.05 (3)
N(9B)	0.4825 (2)	−0.1078 (1)	0.2728 (2)	1.96 (2)
H(1A)	0.197 (3)	0.493 (2)	−0.169 (4)	2.4*
H(2A)	0.017 (3)	0.619 (2)	−0.233 (4)	2.6*
H(8A)	0.265 (4)	0.772 (2)	0.617 (4)	2.6*
H(9A)	0.078 (3)	0.826 (2)	0.370 (4)	2.6*
H(1B)	0.120 (3)	0.167 (2)	0.020 (4)	2.5*
H(2B)	0.230 (3)	0.202 (2)	0.298 (4)	2.7*
H(8B)	0.530 (3)	−0.250 (2)	0.123 (4)	2.5*
H(9B)	0.546 (3)	−0.110 (2)	0.397 (4)	2.5*

those of the water molecule in $Cd^{II}(MP^{-})_2 \cdot 2H_2O$, which according to its unusually high isotropic thermal parameter of 10.6 (3) Å^2 is affected by some disorder, were located in difference Fourier maps. They were included in the least-squares refinements with variable positional parameters and B values either fixed to be 0.5 Å^2 higher than the B values of the adjacent N and O atoms or also refined (Table I). Positional and isotropic thermal parameters are listed in Tables II–IV, while observed and calculated structure factors and anisotropic thermal parameters are in the supplementary material.

Metal Coordination. In contrast to the case for the monohydrated analogue $Cu^{I}(MP^{+})Cl_2 \cdot H_2O$, where S-bridged dimers occur,[21,26] anhydrous *$Cu^{I}(MP^{+})Cl_2$* exhibits a new structure type with Cl-bridged $[Cu_2(MP^{+})_2Cl_4]$ dimers (structure type IIC, Figure 1). MP binds to Cu through its sulfur atom only. The Cu(I) coordination is distorted tetrahedral by one S and three Cl atoms; the bonding angle at the bridging Cl atom Cl(1) is very close to 90.0° (Figure 2). A stereoscopic view of this structure is given in Figure 3. Copper complexes of MP have been reported with the following stoichiometries: $Cu^{II}(MP)Cl_2$,[9] Cu^{II}(9-

Table IV. Final Atomic Parameters for $Cd^{II}(MP^-)_2\cdot 2H_2O$

	x	y	z	B, Å^2
Cd	0.500	0.500	0.500	2.164 (7)
N(1)	0.7297 (9)	0.9780 (4)	0.4009 (3)	2.33 (6)
C(2)	0.745 (1)	1.0999 (4)	0.2869 (4)	2.59 (8)
N(3)	0.947 (1)	1.0978 (4)	0.1858 (4)	2.84 (7)
C(4)	1.146 (1)	0.9544 (4)	0.2011 (4)	2.19 (7)
C(5)	1.1482 (9)	0.8217 (4)	0.3161 (3)	1.92 (6)
C(6)	0.9300 (9)	0.8324 (4)	0.4183 (4)	1.90 (6)
S	0.9192 (2)	0.6761 (1)	0.56225 (9)	2.12 (2)
N(7)	1.3832 (8)	0.6958 (4)	0.3023 (3)	2.17 (6)
C(8)	1.518 (1)	0.7534 (5)	0.1839 (4)	2.52 (8)
N(9)	1.382 (1)	0.9085 (4)	0.1181 (3)	2.76 (7)
O	0.188 (2)	0.5889 (6)	0.0142 (6)	10.6 (3)
H(2)	0.59 (2)	1.199 (7)	0.309 (6)	2.6*
H(8)	1.73 (2)	0.687 (7)	0.173 (6)	2.3*
H(9)	1.48 (2)	0.941 (7)	0.062 (6)	2.6*

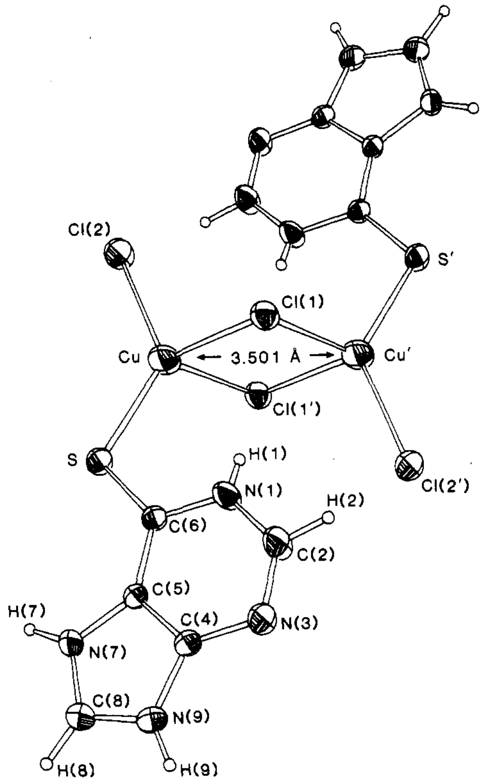

Figure 2. ORTEP plot and atomic numbering scheme of the chloride-bridged dimeric unit in $Cu^I(MP^+)Cl_2$. Thermal ellipsoids are drawn at the 55% probability level.

CH_3-MP)$Cl_2\cdot H_2O$,[27] and $Cu^I(MP^+)Cl_2\cdot H_2O$.[21,26] The complex $Cu^I(MP^+)Cl_2$ described here possibly is identical with the compound synthesized by Weiss and Venner.[9] These authors also obtained red crystals from HCl solutions, but they thought their complex to be the copper(II) compound $Cu^{II}(MP)Cl_2$. Besides the well-known fact that copper(I) complexes may be obtained as the result of a redox reaction of copper(II) with sulfur-containing ligands,[28] further arguments for the occurrence of Cu(I) and protonated MP^+ and not Cu(II) and neutral MP in $Cu^I(MP^+)Cl_2$ are the facts that the protonating hydrogen atom at N(7) as well as the hydrogen atoms at N(1) and N(9) could be localized in difference Fourier maps and that typical shifts in the geometry of the MP ligand due to protonation at N(7) are observed (see Tables VIII and IX).

$Cd^{II}(MP)_4Cl_2$ contains one isolated, distorted-octahedral $[Cd(MP)_2Cl_2]$ unit and two noncoordinating MP molecules per cell. The coordinating MP molecule acts as a S/N(7) bidentate chelating ligand (structure type IB, Figure 1). A representation of this neutral molecular complex $Cd^{II}(MP)_2Cl_2$ is given in Figure 4, while a stereoview of the structure including the noncoordinating MP molecules is shown in Figure 5. It is interesting to note that the formation of metal ion–MP species with the unusual metal to ligand ratio of 1:4 has also been established for the Cd–MP system in ethanolic $NaClO_4$ solutions by polarographic techniques.[14] The hypotheses concerning the corresponding structure given by the authors of that polarographic study, namely a tetrahedral arrangement in which the four MP molecules act monodentately through the sulfur atom or an octahedral arrangement with two S/N(7)-chelating and two sulfur-coordinated ligands, however, could not be confirmed by the solid-state structure of $Cd^{II}(MP)_4Cl_2$ described here.

S/N(7)-chelating MP is also found in *$Cd(MP^-)_2\cdot 2H_2O$*, but, in addition, here the sulfur atoms are bridging two metal atoms. The resulting structure (type III, Figure 1) is a chainlike polymer of sulfur-bridged CdS_4N_2 octahedra and is represented in Figure 6. The bonding distances and angles within the Cd octahedra of the two compounds do not differ significantly from those expected by a comparison with related structures.

The polymeric structure type III (Figure 1) has not been established or postulated for a metal MP complex so far; to our knowledge, it is also unique among purine structures. Coordination through an exocyclic atom attached to C(6) is only observed for metal complexes of 6-mercaptopurine, where the exocyclic atom is sulfur. In addition, the amino groups in purines are generally not involved in the coordination of metal atoms.[29] Therefore, a metal complex with the structure type III of a purine without an exocyclic sulfur atom had to be realized involving a purine ring nitrogen atom bridging two metal atoms. Such a configuration clearly would be disfavored by steric hindrance and a disadvantageous arrangement of the corresponding bonding orbitals. A structure similar to, but not identical with, structure type III has been observed in $[Cu_3(A^+)_2Cl_8]\cdot 4H_2O$ (A = adenine) by de Meester and Skapski.[30] This structure originally has been described as a trinuclear complex, with the purines acting as bridging units by coordinating through N(3) and N(9). If weak interactions between distant chlorine atoms and the terminal copper atoms of the trinuclear units are taken into consideration, however, the structure also can be regarded in terms of a polymeric complex involving bridging purine molecules. In $[Cu_3(A^+)_2Cl_8]\cdot 4H_2O$ as well as in $Cd(MP^-)_2\cdot 2H_2O$, each purine moiety is coordinated to two different metal atoms. A marked difference between the two structures, in contrast, is evidenced by the fact that the metal atoms are attached to one or two purine ligands, respectively, in $[Cu_3(A^+)_2Cl_8]\cdot 4H_2O$, whereas each metal atom in $Cd(MP^-)_2\cdot 2H_2O$ is attached to four different purine ligands.

The literature available on cadmium(II) complexes of MP includes $Cd(MP)Cl_2\cdot H_2O$[23] and $Cd(MP^-)_2(MP)\cdot 5H_2O$.[8] In a recent paper, Perello et al.[16] have described the syntheses of $Cd(MP^{2-})\cdot H_2O$ from dioxane–water solutions and of $Cd(MP^-)_2\cdot 2H_2O$ from methanol–water solutions. On the basis of IR spectra of the last complex, which exhibits the same stoichiometry as the polymeric Cd complex reported here, the authors have concluded that Cd is coordinated to two MP^- molecules through sulfur only. This conclusion is not in agreement with our crystallographic results on $Cd^{II}(MP^-)_2\cdot 2H_2O$, showing that S/N(7) chelation occurs in this complex.

Details of the geometry of metal coordination polyhedra in the three structures determined are reported in Table V. A summary of coordination types, S/N(7) "bite" distances, and protonation sites of all MP structures established by X-ray crystallography up to 1987 is given in Table VI.

---

(26) (a) Shoemaker, A. L.; Singh, P.; Hodgson, D. J. *Acta Crystallogr., Sect. B: Struct. Crystallogr. Cryst. Chem.* **1976**, *B32*, 979. (b) Pope, L.; Laing, M.; Caira, M. R.; Nassimbeni, R. *Acta Crystallogr., Sect. B: Struct. Crystallogr. Cryst. Chem.* **1976**, *B32*, 612.

(27) Sletten, E.; Apeland, A. *Acta Crystallogr., Sect. B: Struct. Crystallogr. Cryst. Chem.* **1975**, *B31*, 2019.

(28) Dubler, E.; Bensch, W. *Inorg. Chim. Acta* **1986**, *125*, 37.

(29) Hodgson, D. J. *Prog. Inorg. Chem.* **1977**, *23*, 211.

(30) De Meester, P.; Skapski, A. C. *J. Chem. Soc., Dalton Trans.* **1972**, 2400.

Table V. Interatomic Bond Distances (Å) and Selected Bond Angles (deg) within the Metal Coordination Polyhedra[a]

$Cu^I(MP^+)Cl_2$		$Cd^{II}(MP)_4Cl_2$		$Cd^{II}(MP^-)_2\cdot 2H_2O$	
Cu-S	2.221 (1)	Cd-S(A)	2.622 (1) (2×)	Cd-S_c	2.689 (1) (2×)
Cu-Cl(1)	2.465 (1)	Cd-N(7A)	2.366 (1) (2×)	Cd-S	2.868 (1) (2×)
Cu-Cl(1′)	2.493 (1)	Cd-Cl	2.719 (1) (2×)	Cd-N(7)	2.283 (3) (2×)
Cu-Cl(2)	2.251 (1)				
Cu-Cu	3.501 (1)	Cd-Cd	7.374 (2)	Cd-Cd	3.918 (3)
Cl(1)-Cu-Cl(1′)	90.17 (1)	S(A)-Cd-Cl	89.61 (1)	S-Cd-S_c	89.62 (3)
Cl(1)-Cu-Cl(2)	102.10 (2)	S(A)-Cd-N(7A)	81.64 (3)	S_c-Cd-N(7)	80.80 (8)
Cl(1)-Cu-S	114.66 (1)	N(7A)-Cd-Cl	87.28 (4)	S-Cd-N(7)	90.2 (1)
Cl(1′)-Cu-Cl(2)	106.68 (2)				
Cl(1′)-Cu-S	109.97 (2)				
Cl(2)-Cu-S	126.91 (2)				
Cu-Cl(1)-Cu′	89.83 (2)			Cd-S-Cd	89.62 (3)
Cu-S-C(6)	108.48 (4)	Cd-S(A)-C(6A)	94.81 (5)	Cd-S-C(6)	102.4 (2)
				Cd-S_c-C(6)	92.6 (1)
		Cd-N(7A)-C(5A)	108.28 (9)	Cd-N(7)-C(5)	109.8 (2)
		Cd-N(7A)-C(8A)	147.0 (2)	Cd-N(7)-C(8)	142.6 (2)

[a] S_c in $Cd^{II}(MP^-)_2\cdot 2H_2O$ indicates the S atom that chelates Cd through S and N(7).

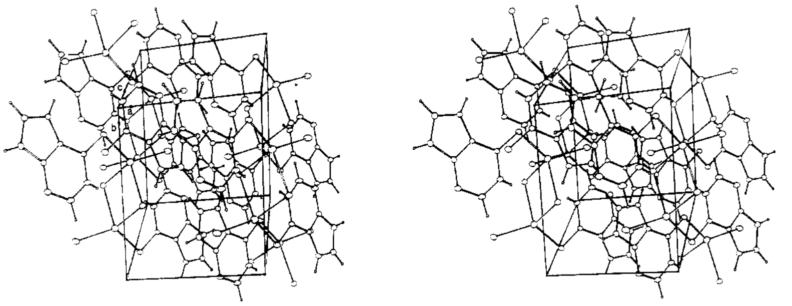

Figure 3. Stereoscopic illustration of the molecular packing in $Cu^I(MP^+)Cl_2$, viewed approximately along [001].

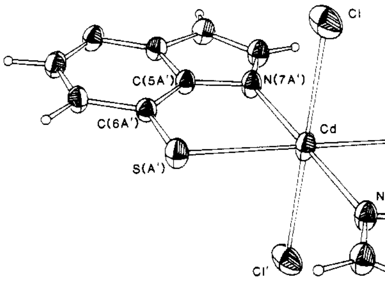

Figure 4. ORTEP plot of the distorted-octahedral $[Cd(MP)_2Cl_2]$ unit in $Cd^{II}(MP)_4Cl_2$. Thermal ellipsoids are drawn at the 50% probability level.

Table VI. Coordination Properties and Protonation Sites of MP[a]

compd	coord type[b]	S/N(7) bite, Å	protonation	C–S, Å	ref
$MP\cdot H_2O$		3.35	N(1), N(7)	1.679 (1)	33
$Hg^{II}(MP)_2Cl_2$	IA	3.21	N(1), N(9)	1.706 (9)	32
$Cd^{II}(MP)_4Cl_2$	IB	3.27	N(1), N(9)	1.676 (2)	*d*
noncoord MP's		3.37	N(1), N(9)	1.673 (1)	
$Ru^{II}(MP)_2(PPh_3)_2Cl_2\cdot$	IB	3.09	N(1), N(9)	1.67 (2)	34
$2EtOH\cdot 2H_2O$	IB	3.10	N(1), N(9)	1.67 (2)	
$Pd^{II}(9\text{-}Bz\text{-}MP^-)_2\cdot DMA$	IB	3.06	none	1.72 (1)	20
	IB	3.03	none	1.72 (1)	
$Cd^{II}(MP)Cl_2\cdot H_2O$	IIA	3.32	N(1), N(9)[e]	1.67 (1)	23
$Cu^{II}(9\text{-}Me\text{-}MP)Cl_2\cdot H_2O$	IIA	3.04	N(1)	1.692 (5)	27
$Cu^I(MP^+)Cl_2\cdot H_2O$	IIB	3.34	N(1), N(7), N(9)	1.686 (6)	26
$Cu^I(MP^+)Cl_2$	IIC	3.32	N(1), N(7), N(9)	1.672 (1)	*d*
$Cd^{II}(MP^-)_2\cdot 2H_2O$	III	3.24	N(9)	1.724 (3)	*d*

[a] All complexes characterized by X-ray structural analysis up to 1987 are included in this table. Abbreviations of ligand and solvent names: MP, 6-mercaptopurine; Bz, benzyl; PPh_3, triphenylphosphine; DMA, dimethylacetamide. [b] See Figure 1. [c] Distances given in the literature or calculated on the basis of published or deposited atomic coordinates. [d] This work. [e] Inferred from the molecular dimensions of MP calculated on the basis of deposited atomic coordinates.

There is a distinct correlation between the intramolecular S/N(7) distance and the nature of the metal coordination. In the free ligand, this distance is 3.35 Å in $MP\cdot H_2O$ and 3.37 Å in the noncoordinating molecule of $Cd^{II}(MP)_4Cl_2$. If S/N(7) chelation occurs, the bite distance is significantly decreased. The extent of this decrease is dependent on the ionic radius of the chelated metal and obviously is more pronounced the smaller the metal atom is: 3.32–3.24 Å for Cd(II) (ionic radius r = 0.95 Å,[31] 3.10–3.09 Å for Ru(II), 3.06–3.03 Å for Pd(II) (r = 0.86 Å), and 3.04 Å for Cu(II) (r = 0.73 Å). If MP is coordinating through its sulfur atom only, no significant decrease is observed in the intramolecular S/N(7) distance, as shown by two Cu(I) complexes listed in Table VI (3.34 and 3.32 Å, respectively). In $Hg^{II}(MP)_2Cl_2$, however, the bite distance, calculated from the published coordinates, is reduced to 3.21 Å, although there is no S/N(7) chelation in this complex. Possibly a certain amount of tension in the MP molecule to improve the hydrogen-bonding efficiency that has been observed in the complex[32] is responsible for this exception from the rule that a decrease of the S/N(7) bite distance in comparison to that in the free molecule only occurs if S/N(7) chelation to a metal ion with an ionic radius of ≲1.0 Å is established.

---

(31) Shannon, R. D. *Acta Crystallogr., Sect. A: Cryst. Phys., Diffr., Theor. Gen. Crystallogr.* **1976**, *A32*, 751.

(32) Laverture, P.; Hubert, J.; Beauchamps, A. L. *Inorg. Chem.* **1976**, *15*, 322.

(33) (a) Sletten, E.; Sletten, J.; Jensen, L. H. *Acta Crystallogr., Sect. B: Struct. Crystallogr. Cryst. Chem.* **1969**, *B25*, 1330. (b) Brown, G. M. *Acta Crystallogr., Sect. B: Struct. Crystallogr. Cryst. Chem.* **1969**, *B25*, 1338.

(34) Cini, R.; Cinquantini, A.; Sabat, M.; Marzilli, L. G. *Inorg. Chem.* **1985**, *24*, 3903.

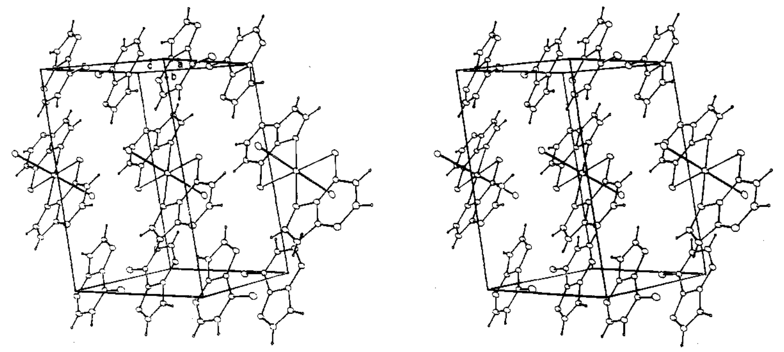

Figure 5. Stereoscopic illustration of the packing of molecular [$Cd(MP)_2Cl_2$] units and noncoordinating MP molecules in $Cd^{II}(MP)_4Cl_2$, viewed approximately along [101].

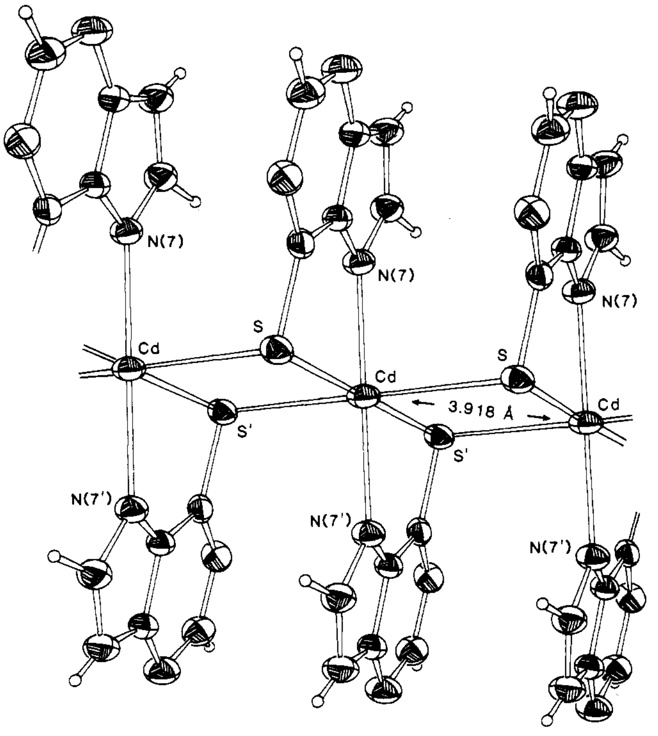

Figure 6. ORTEP plot of the chainlike polymeric structure of Cd(MP^-)$_2$·$2H_2O$ built up from sulfur-bridged CdS_4N_2 octahedra. Thermal ellipsoids are drawn at the 50% probability level.

Mercaptopurine Coordination, Protonation, and Geometry. Reviews on metal binding of nucleic acid bases, nucleosides (base + sugar), nucleotides [base + sugar + phosphate(s)], and polynucleotides have been written by Eichhorn,[35] Sletten,[36] Hodgson,[29] Marzilli et al.,[37,38] Martin et al.,[39] and Barton et al.[40] According to Martin,[41] in solution the N(1) site of 6-oxopurine nucleosides, where N(9) is substituted and is not available for protonation or coordination, possesses intrinsically more than 10^5 times greater basicity than the N(7) site, whereas coordination predominantly occurs at N(7) at low pH and changes to N(1) at higher pH. The crossover pH values determined for Ni^{2+}, Cu^{2+}, and Zn^{2+} are 2.1–2.7 for adenosine, 6.1–7.1 for inosine, and 6.9–7.8 for guanosine.[41]

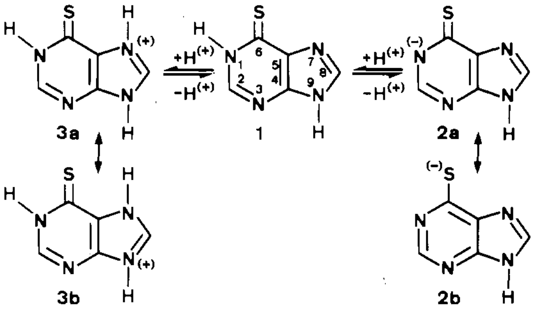

Figure 7. Predominant tautomeric and mesomeric structures of MP in its neutral, deprotonated, or protonated form resulting from an analysis of bond lengths and angles.

In contrast to the case for its oxo analogue hypoxanthine, where N(7) and N(3) and N(9), but not O(6), have been established as metal binding sites in the solid state,[42] MP acts either as a monodentate bridging or nonbridging ligand through its S(6) atom or as a S(6)/N(7)-chelating ligand. No metal coordination at N(3) or N(9) has been observed for MP so far. These findings are confirmed by the structures presented in this paper. In addition, we show here that MP (at least in its anionic monodeprotonated form MP^-) also acts as a S(6) metal-bridging ligand and simultaneously as a S(6)/N(7)-chelating ligand. A summary of all MP metal binding types established by X-ray crystallography is given in Figure 1.

Because of the biological importance of purines, the fine structure of these compounds, including predominant tautomeric and mesomeric forms, has been the subject of several investigations.[43,44] UV and pK_a comparisons suggest that for neutral MP the 1H,9H tautomer is predominant in aqueous solutions.[43] CNDO calculations, in contrast, indicate that the 1H,7H tautomer should be about 15 kJ/mol more stable than the 1H,9H analogue.[45] Despite the misleading common name—6-mercaptopurine instead of the correct purine-6-thione—the thione structure is believed to be the stable form of neutral MP. In solution, however, IR and UV results do not exclude thiol forms existing together with thione forms.[44]

Our crystallographic data show that *neutral MP is protonated at N(1) and N(9)*, but not at N(7) (Figure 7, form **1**), in its noncoordinating molecule as well as in its coordinating molecule of $Cd^{II}(MP)_4Cl_2$. This tautomer has also been found in all other solid-state structures of compounds containing neutral MP with the exception of MP·H_2O, where the 1H,7H tautomer has been observed.[33] It is obvious that the tautomeric forms in crystals are determined not only by electronic factors of the purine bases but also by the different hydrogen-bonding possibilities offered by the arrangement of the molecules in the crystal. The anionic molecule

---

(35) Eichhorn, G. L. In *Inorganic Biochemistry*; Eichhorn, G. L., Ed.; Elsevier: New York, 1973; Vol. 2, p 1191.
(36) Sletten, E. *The Jerusalem Symposium on Quantum Chemistry and Biochemistry*; Reidel: Dordrecht, The Netherlands, **1977**, Vol. 9, p 53.
(37) Marzilli, L. G. *Prog. Inorg. Chem.* **1977**, *23*, 255.
(38) Marzilli, L. G.; Kistenmacher, T. J.; Eichhorn, G. L. In *Nucleic Acid-Metal Interactions*; Spiro, T. G., Ed.; Metal Ions in Biology 1; Wiley: New York, 1980; p 179.
(39) Martin, R. B.; Mariam, Y. H., In *Metal Ions in Biological Systems*; Sigel, H., Ed.; Dekker: New York, 1979; Vol. 8, p 57.
(40) Barton, J. K.; Lippard, S. J. In *Nucleic Acid-Metal Interactions*; Spiro, T. G., Ed.; Metal Ions in Biology 1; Wiley: New York, 1980; p 31.
(41) Martin, R. B. *Acc. Chem. Res.* **1985**, *18*, 32.
(42) Dubler, E.; Hänggi, G.; Bensch, W. *J. Inorg. Biochem.* **1987**, *29*, 269.
(43) Lichtenberg, D.; Bergmann, F.; Neiman, Z. *Isr. J. Chem.* **1972**, *10*, 805.
(44) Elguero, J.; Marzin, C.; Katritzky, A. R.; Linda, P. In *The Tautomerism of Heterocycles*; Advances in Heterocyclic Chemistry Suppl. 1; Academic: New York, 1976; p 502.
(45) Pullman, B.; Pullman, A. *Adv. Heterocycl. Chem.* **1971**, *13*, 77.

Table VII. Interatomic Bond Distances (Å) within the MP Molecule

	$Cu^{I}(MP^{+})Cl_2$	$Cd^{II}(MP)_4Cl_2$[a]		$Cd^{II}(MP^{-})_2\cdot 2H_2O$
N(1)–C(2)	1.360 (3)	1.354 (2)	1.348 (2)	1.361 (5)
C(2)–N(3)	1.307 (2)	1.308 (2)	1.310 (2)	1.318 (6)
N(3)–C(4)	1.350 (2)	1.355 (2)	1.349 (2)	1.349 (5)
C(4)–C(5)	1.385 (2)	1.384 (2)	1.396 (2)	1.411 (4)
C(5)–C(6)	1.406 (1)	1.401 (3)	1.412 (2)	1.378 (5)
C(6)–N(1)	1.372 (2)	1.373 (2)	1.377 (2)	1.363 (4)
C(5)–N(7)	1.374 (2)	1.374 (2)	1.383 (2)	1.371 (5)
N(7)–C(8)	1.333 (2)	1.314 (2)	1.314 (3)	1.332 (5)
C(8)–N(9)	1.340 (2)	1.363 (2)	1.366 (2)	1.363 (5)
N(9)–C(4)	1.366 (1)	1.356 (2)	1.355 (3)	1.360 (5)
C(6)–S	1.672 (1)	1.676 (2)	1.673 (1)	1.724 (3)
N(1)–H(1)	0.70 (2)	0.91 (3)	0.88 (3)	
C(2)–H(2)	0.94 (2)	0.95 (3)	0.85 (3)	1.09 (7)
N(7)–H(7)	0.89 (4)			
C(8)–H(8)	0.95 (2)	0.92 (3)	0.91 (3)	0.95 (6)
N(9)–H(9)	0.82 (3)	0.75 (3)	0.96 (3)	0.69 (6)

[a] First column, coordinating molecule A; second column, noncoordinating molecule B.

Table VIII. Interatomic Bond Angles (deg) of the MP Ligand and Hydrogen-Bonded Contacts (Å, deg)

	$Cu^{I}(MP^{+})Cl_2$	$Cd^{II}(MP)_4Cl_2$[a]		$Cd^{II}(MP^{-})_2\cdot 2H_2O$
C(6)–N(1)–C(2)	125.1 (2)	124.3 (1)	126.0 (1)	120.2 (3)
N(1)–C(2)–N(3)	124.8 (1)	125.1 (1)	124.3 (1)	127.3 (4)
C(2)–N(3)–C(4)	112.5 (1)	112.6 (1)	112.2 (1)	113.4 (4)
N(3)–C(4)–C(5)	126.0 (1)	125.6 (1)	127.5 (1)	123.2 (4)
C(4)–C(5)–C(6)	120.6 (1)	120.3 (1)	118.6 (1)	120.4 (3)
C(5)–C(6)–N(1)	111.0 (1)	111.8 (1)	111.4 (1)	115.6 (3)
C(4)–C(5)–N(7)	107.1 (1)	110.0 (1)	110.0 (1)	109.1 (3)
C(5)–N(7)–C(8)	108.1 (1)	104.8 (1)	103.9 (1)	104.4 (3)
N(7)–C(8)–N(9)	109.7 (1)	112.5 (1)	113.9 (1)	114.2 (4)
C(8)–N(9)–C(4)	108.3 (1)	106.8 (1)	106.3 (1)	105.2 (4)
N(9)–C(4)–C(5)	106.9 (1)	105.9 (1)	106.1 (1)	107.2 (4)
N(3)–C(4)–N(9)	127.1 (1)	128.5 (1)	126.4 (1)	129.6 (3)
C(6)–C(5)–N(7)	132.3 (1)	129.7 (1)	131.4 (1)	130.5 (3)
N(1)–C(6)–S	123.8 (1)	122.6 (1)	120.7 (1)	121.3 (3)
C(5)–C(6)–S	125.2 (2)	125.5 (1)	127.9 (1)	123.2 (2)
C(2)–N(1)–H(1)	121 (2)	119 (2)	115 (2)	...
C(6)–N(1)–H(1)	113 (3)	118 (2)	119 (2)	...
N(1)–C(2)–H(2)	111 (1)	114 (2)	113 (2)	102 (3)
N(3)–C(2)–H(2)	124 (1)	121 (2)	124 (2)	129 (3)
C(5)–N(7)–H(7)	128 (1)	...	...	...
C(8)–N(7)–H(7)	124 (1)	...	...	...
N(7)–C(8)–H(8)	130 (2)	125 (2)	128 (2)	112 (3)
N(9)–C(8)–H(8)	121 (2)	123 (3)	118 (2)	131 (3)
C(4)–N(9)–H(9)	131 (3)	126 (3)	125 (2)	140 (5)
C(8)–N(9)–H(9)	120 (2)	127 (3)	129 (2)	113 (5)
N(1)–H(1)···Cl(1)	3.171 (1)	3.093 (1)		
N(1B)–H(1B)...N-(3A)			2.892 (2)	
N(7)–H(7)...Cl(2)	3.058 (1)			
N(9)–H(9)...N(3′)	2.983 (2)		2.883 (2)	
N(1)–H(1)–Cl(1)	158 (3)	176 (3)		
N(1B)–H(1B)–N(3A)			169 (3)	
N(7)–H(7)–Cl(2)	175 (2)			
N(9)–H(9)–N(3′)	150 (3)		163 (2)	

[a] First column, coordinating molecule A; second column, noncoordinating molecule B.

MP^{-} found in $Cd^{II}(MP^{-})_2\cdot 2H_2O$ is, in accordance with the solution studies mentioned above, deprotonated at N(1) (Figure 7, form **2a**). Protonation of neutral MP finally leads to protonation at N(7) as confirmed by the crystal structure of $Cu^{I}(MP^{+})Cl_2$ (Figure 7, form **3a** or **3b**).

A summary of interatomic bond distances and angles within the MP molecule is given in Tables VII and VIII.

Table IX. Influence of N(7) Coordination and of N(7) Protonation on the Geometry of the Imidazole Moiety of MP[a]

	free ligand[b]	N(7) coordinated[c]	N(7) protonated[d]
C(4)–C(5)–N(7)	110.0 (1) (110.8 (2))	110.0 (1)	107.1 (1) (107.3 (9))
C(5)–N(7)–C(8)	103.9 (1) (104.2 (3))	104.8 (1)	108.1 (1) (108.0 (2))
N(7)–C(8)–N(9)	113.9 (1) (113.5 (4))	112.5 (1)	109.7 (1) (109.4 (2))
C(8)–N(9)–C(4)	106.3 (1) (106.0 (2))	106.8 (1)	108.3 (1) (108.7 (4))
N(7)–C(8)	1.314 (2) (1.304 (3))	1.314 (2)	1.333 (2) (1.328 (14))
C(8)–N(9)	1.366 (2) (1.374 (4))	1.363 (2)	1.340 (2) (1.339 (7))

[a] Average values (Å, deg) given in the literature for neutral ("free ligand") and N(7)-protonated guanine residues are presented in parentheses.[46] [b] Noncoordinating 1H,9H tautomer in $Cd^{II}(MP)_4Cl_2$. [c] S/N(7)-coordinating 1H,9H tautomer in $Cd^{II}(MP)_4Cl_2$. [d] S-coordinating, protonated 1H,7H,9H tautomer in $Cu^{I}(MP^{+})Cl_2$.

Taylor and Kennard[46] have reviewed the influence of protonation on the geometries of nucleic acid constituents, a fact that has already been observed in 1965 by Singh.[47] The major effect of N(7) protonation of guanine derivatives is to widen the C(5)–N(7)–C(8) angle by about 4°, to reduce the adjacent angles at C(5) and C(8) by about 3–4°, and to increase the angle at N(9) by about 2–3°. The only bond lengths significantly affected by N(7) protonation are N(7)–C(8) (increase by about 0.02–0.03 Å) and C(8)–N(9) (decrease by about 0.03–0.04 Å). There is excellent agreement between our geometric data of neutral MP and protonated MP^{+} and the values given by Taylor and Kennard.[46] It is noteworthy that the reverse effect, namely decreasing of a C–N–C bonding angle by about 4° upon deprotonation of the central N atom, is observed in the MP^{-} molecule of $Cd^{II}(MP^{-})_2\cdot 2H_2O$, where deprotonation at N(1) has resulted in a decrease of the C(6)–N(1)–C(2) angle from about 125 to 120.2 (3)°. The same effect has been found in the crystal structure of Mg(hydrogen urate)$_2\cdot 8H_2O$, where uric acid molecules deprotonated at N(3) occur.[48]

Since in this paper we describe highly refined structures of a MP–metal complex simultaneously containing one N(7)/S-coordinating and one noncoordinating ligand ($Cd^{II}(MP)_4Cl_2$) and of a complex with a N(7)-protonated ligand coordinating through its sulfur atom only ($Cu^{I}(MP^{+})Cl_2$), it is interesting to compare the influence of *N(7) protonation* with that of *N(7) coordination*. In Table IX we give a comparison of the geometry of the imidazole moiety of MP in its neutral, noncoordinating form with that of either N(7)-coordinated or N(7)-protonated MP. In contrast to the effect of protonation, the influence of N(7) coordination is very small but still significant. Metal coordination at N(7) seems to induce changes similar to those induced by protonation, but to a much lower extent (0–30%), only detectable if highly refined structures are considered. The same effect recently has been demonstrated for the guanine derivative hypoxanthine and its metal complexes.[49] In view of the limited amount of precisely determined structures available for analysis at that time, it is not surprising that this rather small effect of coordination on the geometry of the MP ligand was overlooked in 1977, when Hodgson,[29] in a detailed review of the stereochemistry of metal complexes of nucleic acid constituents, stated that "metal ion coordination at either N(1), N(3) or N(7) of purines causes virtually no change in the internal angles at these atoms relative to their unsubstituted values".

With respect to the *thione/thiol tautomerism*, our crystallographic data strongly support the thione structure for neutral MP as well as for protonated MP^{+}. In both cases the hydrogen atom has been located at N(1), and the C(6)–S distances of 1.672 (1)–1.676 (2) Å are typical of exocyclic thione structures.[50] They

---

(46) Taylor, R.; Kennard, O. *J. Mol. Struct.* **1982**, *78*, 1.

(47) Singh, C. *Acta Crystallogr.* **1965**, *19*, 861.

(48) Dubler, E.; Jameson, G. B.; Kopajtič, Z. *J. Inorg. Biochem.* **1986**, *26*, 1.

(49) Dubler, E.; Hänggi, G.; Schmalle, H. *Acta Crystallogr., Sect. C: Cryst. Struct. Commun.* **1987**, *C43*, 1872.

Table X. Deviations (Å) of Individual Atoms of MP from the Corresponding Least-Squares Planes[a]

	$Cu^I(MP^+)Cl_2$	$Cd^{II}(MP)_4Cl_2$[b]		$Cd^{II}(MP^-)_2\cdot 2H_2O$
		(a) Mercaptopurine		
N(1)	−0.002 (1)	0.024 (1)	0.014 (1)	−0.008 (3)
C(2)	0.007 (2)	0.024 (2)	0.009 (2)	0.001 (4)
N(3)	0.003 (1)	−0.019 (1)	−0.002 (1)	−0.012 (4)
C(4)	−0.005 (1)	−0.018 (2)	−0.012 (2)	0.014 (4)
C(5)	−0.001 (1)	−0.017 (2)	−0.013 (2)	−0.001 (4)
C(6)	−0.007 (1)	−0.025 (2)	−0.012 (2)	0.012 (4)
N(7)	0.011 (1)	0.009 (1)	0.006 (1)	−0.005 (3)
C(8)	−0.001 (2)	0.022 (2)	0.017 (2)	−0.012 (4)
N(9)	−0.005 (1)	0.000 (1)	−0.006 (1)	0.012 (4)
S*	−0.012 (1)	−0.108 (1)	−0.024 (1)	−0.014 (1)
H(1)*	0.08 (3)	0.10 (3)	−0.03 (3)	
H(2)*	0.08 (3)	0.03 (3)	−0.03 (3)	−0.18 (7)
H(7)*	0.01 (3)			
H(8)*	0.01 (3)	0.04 (3)	0.01 (3)	−0.29 (6)
H(9)*	0.08 (3)	−0.01 (3)	−0.01 (3)	−0.12 (7)
Cu*, Cd*	0.262 (1)	0.007 (1)		−0.577 (1)
		(b) Pyrimidine Ring		
N(1)	−0.002 (1)	0.010 (1)	0.006 (1)	−0.006 (3)
C(2)	0.003 (2)	0.008 (2)	−0.001 (2)	0.007 (4)
N(3)	−0.000 (1)	−0.016 (1)	−0.002 (1)	−0.009 (4)
C(4)	−0.004 (1)	0.006 (2)	0.001 (2)	0.010 (4)
C(5)	0.005 (1)	0.010 (2)	0.003 (2)	−0.009 (4)
C(6)	−0.002 (1)	−0.018 (2)	−0.007 (2)	0.007 (4)
S*	−0.002 (1)	−0.101 (1)	−0.017 (1)	−0.025 (1)
		(c) Imidazole Ring		
C(4)	0.001 (1)	0.002 (2)	0.004 (2)	0.000 (4)
C(5)	−0.003 (1)	−0.001 (2)	−0.002 (2)	−0.003 (4)
N(7)	0.004 (1)	0.000 (1)	−0.001 (1)	0.006 (3)
C(8)	−0.003 (2)	0.002 (2)	0.004 (2)	−0.006 (4)
N(9)	0.001 (1)	−0.002 (1)	−0.005 (1)	0.004 (4)
		(d) Pyrimidine/Imidazole Dihedral Angles (deg)		
	0.6	2.1	1.4	0.9

[a] The atoms used to define the planes were given equal weight in calculating the planes. Atoms designated by an asterisk were given zero weight. [b] First column, coordinating molecule A; second column, noncoordinating molecule B.

indicate a dominant double-bond character of this bond, since significantly longer distances are expected for a single bond. In metal–alkyl mercaptide complexes, where a single-bond character of the C–S bond is assumed, the C–S$^-$ distances are about 1.80–1.85 Å,[20] and in free molecules of alkyl mercaptans in the gas phase, C–SH distances of 1.814 (5) Å for methyl mercaptan and 1.819 (6) Å for ethane-1,2-dithiol have been determined.[51] Similar distances are found in the solid state, for example 1.808 (2) Å in *N*-acetyl-L-cysteine.[52] The C–S separations of 1.672 (1)–1.672 (2) Å found in MP or MP$^+$, however, still do not exclude any single bond character, since the determination of a pure C–S double bond offers some difficulties. Values of 1.61–1.65 Å have been suggested,[53] and 1.611 (2) Å has been measured in thioformaldehyde in the gas phase.[51] In the deprotonated MP$^-$ molecule, the increased C(6)–S distance of 1.724 (3) Å clearly points to a distinct amount of single-bond character of this bond, and hence, a significant contribution of resonance formula **2b** (Figure 7) to the electronic structure of MP$^-$ has to be assumed.

As a summary of the analysis of bond lengths and angles given above, the predominant tautomeric and mesomeric forms for MP in its neutral, deprotonated, or protonated form are presented in Figure 7.

A common feature, finally, of most purine bases is a slight *nonplanarity in the pseudoaromatic ring system.* Small but significant deviations from planarity are also evident from the data presented in Table X for MP, MP$^-$, and MP$^+$. The most pronounced nonplanarity is found in the coordinating MP molecule of $Cd^{II}(MP)_4Cl_2$ with a maximum deviation of a ring atom from the best plane of 0.025 (2) Å, whereas the corresponding maximum deviation in the protonated MP$^+$ molecule of $Cu^I(MP^+)Cl_2$ is only 0.011 (1) Å.

Hydrogen Bonding and Intermolecular Stacking. Bond lengths and angles involving hydrogen-bonded contacts are given in Table VIII. In $Cu^I(MP^+)Cl_2$ there are one intermolecular hydrogen bond of the type N(9)–H(9)···N(3′) and two bonds of the type N–H···Cl. In $Cd^{II}(MP)_4Cl_2$ one N(9)–H(9)···N(3′) bond between noncoordinating MP molecules and one N(1)–H(1)···N(3) bond between a noncoordinating and a coordinating molecule are observed, thus resulting in hydrogen-bonded layers of noncoordinating and coordinating molecules. In addition, a N(1)–H(1)···Cl bond involving the coordinated molecule and a weak interaction of the type N(9)–H(9)···S between coordinating and noncoordinating molecules with a N(9)···S distance of 3.398 (2) Å and an angle of 160 (3)° at H(9) are found. In view of the rather large donor–acceptor distances observed, all of the hydrogen bonds described above have to be considered as medium-strong or weak bonds. In $Cd(MP^-)_2\cdot 2H_2O$ the water molecule does not coordinate to the metal atom, but it is involved in two strong hydrogen bonds to two further water oxygen atoms with O···O distances of 2.58 (1) and 2.69 (1) Å and in one hydrogen bond to N(3) of the mercaptopurine ligand with an O···N(3) distance of 2.911 (6) Å.

An interesting feature of purine compounds is their solid-state stacking pattern involving complete or partial overlap of the polarizable ring systems. The range of interplanar stacking distances generally found is 3.25–3.50 Å.[54] In $Cu^I(MP^+)Cl_2$, there is infinite stacking of partially overlapping MP molecules related by a center of symmetry along the *a* axis. Stacking distances, calculated as the mean distance of individual atoms of the stacking molecules from the least-squares plane through the molecule with the coordinates *x*, *y*, *z*, are 3.47 Å (symmetry operation $-x$, $-y$, $-1 - z$) and 3.36 Å ($-1 - x$, $-y$, $-1 - z$). From the stereodrawing in Figure 5 it is evident that in $Cd^{II}(MP)_4Cl_2$ the main stacking occurs between noncoordinating MP molecules stacked along the *a* axis and related by a center of symmetry. Stacking distances, calculated as above, are 3.44 Å ($-x$, $-y$, $-z$) and 3.31 Å ($1 - x$, $-y$, $-z$). Significantly less stacking interaction is observed between noncoordinating and coordinating MP's. In $Cd^{II}(MP^-)_2\cdot 2H_2O$, finally, infinitely stacked purines are related by simple crystallographic translations along the *a* axis of the cell. In contrast to the case for the two other compounds described here, the stacking purines are positioned with their imidazole moieties pointing in exactly the same direction and are not rotated 180° with respect to each other. Since the planes do not lie perpendicular in relation to the translation axis *a*, the main stacking occurs between pyrimidine and imidazole rings of the bases. The stacking distance, calculated as above, is 3.29 Å.

Acknowledgment. We thank Professor H. R. Oswald for his support of this project. Research grants from the Swiss National Science Foundation (No. 2.023-0.83) are gratefully acknowledged.

Registry No. $Cu^I(MP^+)Cl_2$, 113219-25-3; $Cd^{II}(MP)_4Cl_2$, 113219-27-5; $Cd^{II}(MP^-)_2\cdot 2H_2O$, 94927-85-2.

Supplementary Material Available: Tables of anisotropic thermal parameters for the three structures (3 pages); listings of observed and calculated structure factors (71 pages). Ordering information is given on any current masthead page.

---

(50) Form, G. R.; Raper, E. S.; Downie, T. C. *Acta Crystallogr., Sect. B: Struct. Crystallogr. Cryst. Chem.* **1976**, *B32*, 345.

(51) Landolt-Börnstein, *Numerical Data and Functional Relationships in Science and Technology*, Springer-Verlag: Berlin, 1976; New Series, Vol. 7, p 108.

(52) Takusagawa, F.; Koetzle, T. F.; Kou, W. W. H.; Parthasarathy, R. *Acta Crystallogr., Sect. B: Struct. Crystallogr. Cryst. Chem.* **1981**, *B37*, 1591.

(53) Abrahams, S. C. *Q. Rev., Chem. Soc.* **1956**, *10*, 407.

(54) Bugg, C. E. In *The Jerusalem Symposium on Quantum Chemistry and Biochemistry*; Academic: New York, 1972; Vol. 4, p 178.