Zinc Complexes of Drugs Containing Nitrogen Heterocycles

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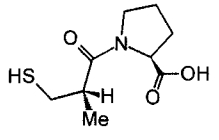
Four drugs whose actions have a relation to the status of zinc-containing species in the human body were used as ligands in zinc complexes. Captopril (H_2Cap) forms the compound [ZnCap] (**1**) presumed to be a coordination polymer with O and S coordination. Isoniazid, in the presence of zinc salts, is converted to 1,2-diisonicotinoyl hydrazide (H_2Nih) which forms polymeric $[Zn(Nih)NH_3]$ (**2**) with trigonal-bipyramidal ZnO_2N_3 coordination. Nalidixic acid (HNal) and zinc perchlorate yield $[Zn(HNal)_2(H_2O)_2](ClO_4)_2 \cdot 2\ H_2O$ (**3**) containing zinc in an octahedral ZnO_6 environment. Mercaptopurine (H_2Mer), in the presence of ammonia, forms $[Zn(Mer)(NH_3)_2] \cdot H_2O$ (**4**) which is a coordination polymer containing tetrahedral ZnN_4 units. The structures of $[Zn(Nih)NH_3]$, $[Zn(HNal)_2(H_2O)_2](ClO_4)_2 \cdot 2\ H_2O$, and $[Zn(Mer)(NH_3)_2] \cdot 2\ H_2O$ were determined diffractometrically.

Most drugs are polyfunctional ligands as they usually contain acidic, amino or thio functions, and/or nitrogen heterocycles. It is therefore quite likely that they all interact with the metal ions in the human body. While prominent medical examples of this exist in the form of the detoxification agents British Anti-Lewisite or D-penicillamine[1], knowlege about drug-metal interactions in terms of structures, stability constants, or distributions in the body is only slowly accumulating and highly dispersed in the literature[2–6]. Some research groups like those of Dubler[7] and Borras[8] focus on certain types of drugs and investigate their ligation behavior towards various metals while others like those of Keppler[6,9], Reedijk[9], and Lippert[10] explore metal complexes of ligands related to the biological action of cytotoxic metal chelates. We focus on the biological coordination chemistry of zinc and try to screen a large variety of substrates which are potential ligands for this metal. One such type of substrates are those drugs of which a medically relevant interaction with zinc in the body has been suspected or proved.

So far we have reported on preparative and structural studies of zinc complexes of sulfonamide-[11–13] or carboxylate[13–15]-containing drugs. This paper deals with our findings of another group. The four drugs whose zinc complexes are described here have in common that they all contain nitrogen heterocycles together with other (N, O, S) donor functions and that they have a relation to zinc species in the body. It was our aim to find out which of their donor functions they use and whether systematic conclusions can be drawn from that.

Captopril

The drug captopril (H_2Cap) is used as a selective inhibitor of the angiotensin-converting enzyme (ACE) in cases of high blood pressure[16]. It is a structural mimic of angiotensin with which it competes for the zinc ion in the enzyme[17]. It is a weaker ligand for zinc than cysteine or penicillamine[18], yet its use as a drug can lead to zinc deficiency symptoms[19]. One zinc complex of captopril, $K_2[ZnCap_2]$, has been mentioned in the literature, and it was concluded from spectroscopic data that its zinc ion is in the highly unusual square planar O_2S_2 environment[20].



Captopril = H_2Cap

$[ZnCap]_x$

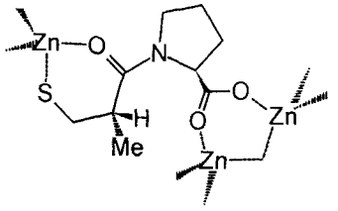
1

We found that captopril reacts with zinc perchlorate or nitrate in neutral or weakly basic aqueous solution to form only the 1:1 compound **1** regardless of the stoichiometric ratio applied. The compound is weakly soluble in water only and has a high decomposition point. This and its 1:1 composition lead to the conclusion that **1** is a coordination polymer. This in turn means that all or most of the five donor atoms of captopril are used for coordination.

As suitable single crystals of **1** could not be obtained we tried to deduce its structure from spectroscopic data. In the IR spectrum (KBr) the ν(SH) band of captopril is missing as expected. The carboxylate bands at 1630 and 1424 cm^{-1} are separated by more than 200 wavenumbers from which it can be concluded[21] that the carboxylate group bridges two zinc ions. The amide I band at 1560 cm^{-1} is shifted by 30 cm^{-1} to lower wavenumbers with respect to that of captopril, i.e. the amide oxygen is also involved in coordination. Structure information by NMR (see Experimental) could only be obtained from solid samples due to the low solubility of **1**. Both captopril[20] and **1** show 9 signals in their ^{13}C-CP-MAS NMR spectra. Of these only those for the carboxylate ($\delta = 182.3$, $\Delta\delta = +9.5$) and the amide ($\delta = 172.7$, $\Delta\delta = -3.7$) carbon atoms are shifted by more than

  0009–2940/95/0808–0779 $ 10.00+.25/0

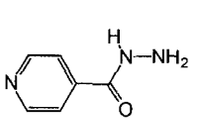
2 ppm in **1**, thereby supporting the coordination assignments from the IR data. The spectroscopic data thus point to an average ZnO_3S coordination. Applied to the molecular shape of captopril this leads to the structural motifs shown below.



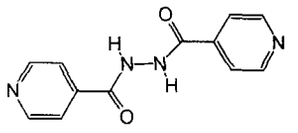
It seems that these motifs cannot be combined to construct a one-dimensional coordination polymer. We therefore conclude that **1** forms a possibly irregular three-dimensional network in the solid state which may explain why single crystals have not yet been obtained. Compared to the binding of captopril to the enzyme (ACE) where the thiolate sulfur and possibly the amide oxygen seem to be the only donor functions that are used[17], the unprotected nature of the zinc ion in **1** seems to result in the "unnatural" use of the other donor capabilities offered by the captopril ligand rather than the more "natural" ligation of more than one captopril unit per metal ion.

Isoniazid

Isoniazid (isonicotinic acid hydrazide) is an important drug for tuberculosis[3]. Its relation to zinc is established by the fact that during treatment with isoniazid the body reacts by a positive balance of zinc in the urine[22]. Isoniazid complexes of divalent metals were used for the spectrophotometric determination of the drug, and 1:1 and 1:2 complexes are described for copper and cadmium halides in ref.[23] Divalent metal ions (Cu, Mn) were also found to catalyze a chemical interconversion of isoniazid occurring in the body, namely its condensation to 1,2-diisonicotinoylhydrazide (H_2Nih) with hydrazine elimination[24].



Isoniazid



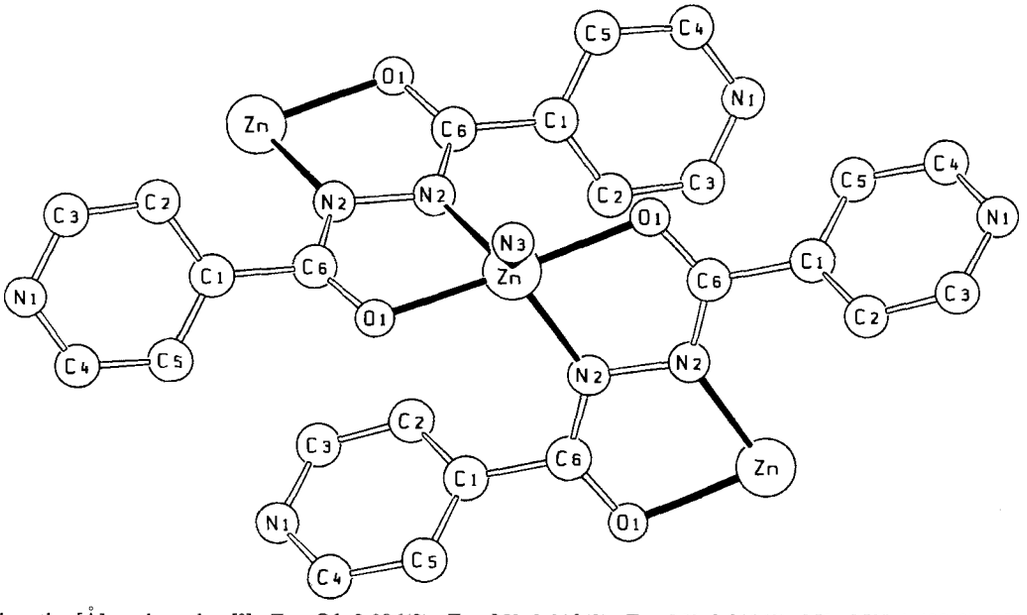
H_2Nih

We found that zinc salts of noncoordinating anions also catalyze this interconversion and that the only isolable compound, e.g. from $Zn(NO_3)_2$, isoniazid, and ammonia in water, is the H_2Nih derivative **2**. Compound **2** is insoluble in all solvents, indicating its polymeric nature, but its slow formation enabled the growth of single crystals. As its IR spectrum is non-informative the constitution of **2** had to be obtained from the crystal structure determination.

$$[Zn(Nih)NH_3]_\infty$$
2

Figure 1 shows a section from the polymeric network of **2** giving the coordination of one zinc ion and indicating the unidimensional linkage of metal ions and ligands by means of anti-oriented N–N–C–O–Zn chelate rings. The asymmetric unit of **2** contains only the zinc ion, the ammonia molecule, and one NC_5H_4CON unit. Thus, there is a good fit of crystal and molecular symmetry as four NC_5H_4CON units are coordinated to each zinc ion. The two dianionic hydrazide (Nih) ligands and the ammonia molecule constitute a fivefold coordination about zinc which is trigonal

Figure 1. Atomic arrangement of **2** in the solid state. Four symmetry-equivalent NC_5H_4CON units, one NH_3 ligand, and three Zn ions are shown



Selected bond lengths [Å] and angles [°]: Zn–O1 2.086(2), Zn–N2 2.018(2), Zn–N3 2.009(3), N2–N2″ 1.428(3), N2–C6″ 1.313(3), C6–O1 1.257(3), C6–C1 1.504(3); O1–Zn–O1′ 167.96(9), O1–Zn–N2 78.19(7), O1–Zn–N3 83.98(5), N2–Zn–N2′ 118.64(11), N2–Zn–N3 120.68(5), N2–Zn–O1′ 108.16(7).

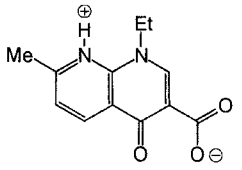
bipyramidal to a good approximation. As expected, the axial Zn–O bonds are the longest while the Zn–NH_3 bond is slightly shorter than the Zn–N(hydrazide) bonds. The zinc–ligand bond lengths are in the normal range as are those of the Nih ligand which can be compared with those of isoniazid[25]. To our knowledge this is the first structure determination of 1,2-diisonicotinoyl hydrazide or a metal complex thereof.

While the structure analysis of **2** clearly identified the diisonicotinoyl hydrazide ligands it could not provide proof for the presence of the NH_3 ligands. It might have been suspected that H_2O ligands are present instead which could not be excluded due to the unsatisfactory elementary analyses. The IR spectrum of **2** in KBr, however, shows no OH valence bands while broad NH bands are observed at 3287 and 3144 cm^{-1}.

As before for captopril, the zinc complex obtained from isoniazid is "unnatural" due to its polymeric nature. It is unnatural in a second sense as it is no longer a complex of isoniazid. Remarkably, also in this case a 1:1 metal-to-ligand stoichiometry is preferred in the isolated complexes which necessitates extensive use of the donor capabilities of the ligand, and like before it could not easily be predicted which donor atoms are involved in complexation (the pyridine N is uncoordinated in **2**!) and how they are bound.

Nalidixic Acid

Nalidixic acid (HNal) is used as a drug against infections of the urinary tract[3]. Its mode of action, the selective inhibition of DNA gyrase, was originally asssumed to be an inhibition of zinc-containing enzymes[26]. While this may not be the case it was shown that complexation with the trace elements copper, cobalt, iron and zinc increases the lipophilicity of nalidixic acid thereby increasing its bioavailability in the cell[27]. Potentiometric determinations showed that the 1:1 metal complexes of HNal are more stable than the 1:2 complexes and that the stability decreases in the order Cu^{2+}, Co^{2+}, Fe^{2+}, Zn^{2+}[28]. Recently, mixed ligand zinc complexes of HNal including [Zn(Nal)(phen)(Hal)] were prepared and investigated by NMR spectroscopy[29].



Nalidixic acid = HNal

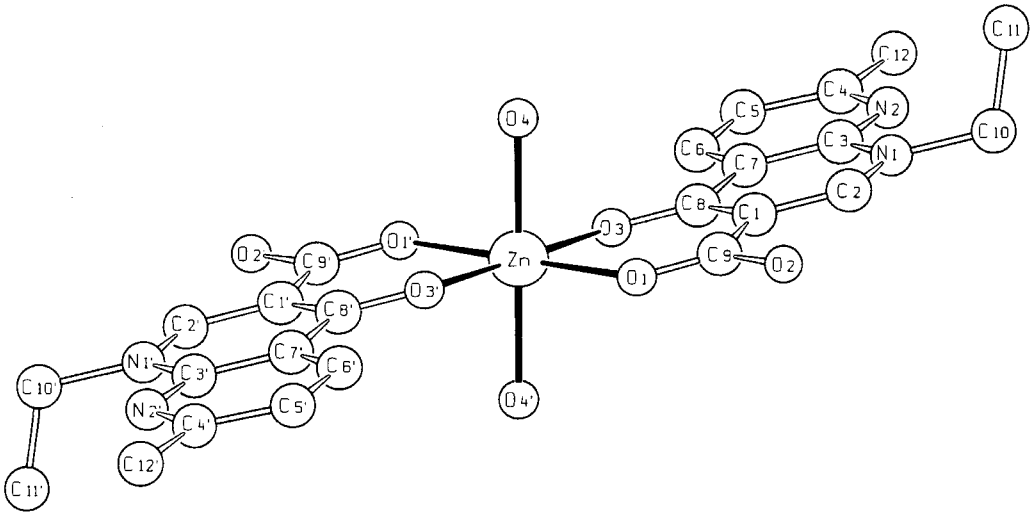
$[Zn(HNal)_2(H_2O)_2]\,(ClO_4)_2(H_2O)_2$

3

We found that the 1:2 complex **3** is the only species that crystallizes from solutions of zinc salts with noncoordinating anions and nalidixic acid in chloroform/acetone. Reactions in water proved impossible due to the low solubility of HNal. The IR spectrum of **3** in KBr is practically identical with that of HNal[28] which means that HNal is zwitterionic in the complex as it is in the free state. This indicated that the β-keto acid function of HNal acts as a chelate ligand towards zinc. NMR spectra of **3** (see Experimental) could only be obtained in the strong donor solvent DMSO. They show only the presence of the free ligand, thus pointing to the low stability of complex **3**.

The structure determination of **3** (see Figure 2) confirmed the conclusion drawn from the IR data by revealing the β-diketonate-like chelation of the HNal ligands which was also deduced from the IR spectra of [Zn(Nal)(phen)(Hal)][29]. Although being on the whole a neutral molecule nalidixic acid can act as an anionic ligand due to ist zwitterionic nature. The octahedral coordination sphere of the dicationic complex is completed by two axial water ligands. As the zinc ion is positioned in a crystallographic inversion center all trans interligand angles are 180°. As all cis angles are also close to 90° the complex geometry is close to ideally octahedral. The Zn–O bond lengths show a spread of 0.06

Figure 2. Molecular structure of the cation in **3**



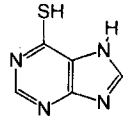
Selected bond lengths [Å] and angles [°]: Zn–O1 2.083(5), Zn–O3 2.048(5), Zn–O4 2.116(5), O1–C9 1.230(8), O3–C8 1.252(8), C9–O2 1.299(9), C9–C1 1.454(10); O1–Zn–O4 89.0(2), O1–Zn–O4′ 91.0(2), O3–Zn–O4 88.4(2), O3–Zn–O4′ 91.6(2), O1–Zn–O3 87.2(2), O1–Zn–O3′ 92.8(2), Zn–O1–C9 128.5(5), Zn–O3–C8 127.4(5).

Å about the average value of 2.08 Å which is normal, cf. **2**. Bond lengths and angles within the HNal ligand show no significant deviation from those in free nalidixic acid[30] or in the complex $[Cu(Nal)(phen)(H_2O)]NO_3$[31]. The two water molecules in the crystal are linked by hydrogen bridges to the carboxylate oxygen atoms O10. To our knowledge other metal complex structures with HNal ligands have not been reported yet.

The structure determination revealed that the drug nalidixic acid forms a "natural" complex with zinc ions, i.e. it does not make extensive use of its remaining donor functions. It can be imagined that the same β-diketonate-like donor set of HNal is used in the more stable 1:1 metal complexes[28] and that HNal binds to metal ions in enzymes in the same way. It is not immediately obvious, though, that this type of dicationic complex should be more lipophilic than free nalidixic acid as was reported[27].

Mercaptopurine

Mercaptopurine (H_2Mer) which is a mimic of the natural purine base hypoxanthine is used clinically for the therapy of leukemia[32]. Its antimetabolic action is enhanced by divalent metal ions[33], and platinum and palladium complexes of H_2Mer display antitumor activity[34]. The stabilities of H_2Mer complexes of various divalent metals were determined[35]. Extensive preparative and structural studies on metal complexes of mercaptopurine were performed by Dubler and Gyr[36]. These include the structure determination of $Zn(H_2Mer)_2Cl_2 \cdot CH_3OH$[36], but only structures of copper and cadmium complexes have been published so far[37].



Mercaptopurine = H_2Mer

$\{[Zn(Mer)(NH_3)_2]\cdot H_2O\}_\infty$

4

Our attempts to obtain a crystalline zinc complex of H_2Mer again led to the use of zinc salts of noncoordinating anions, this time in a 1:3:6 solvent mixture of 25% aqueous ammonia, methanol, and dichloromethane. Under these conditions a 1:1 complex (**4**) was the result again. The low solubility of **4** pointed to the polymeric nature of the complex and prevented NMR measurements. As the IR spectrum in KBr allowed no structural conclusions other than the absence of a SH function the crystalline nature of the compound was essential to establish its constitution.

The structure determination of **4** was hampered by an unusual form of disorder among the bicyclic aromatic ligands which is depicted in Figure 3. The two superimposed mercaptopurine dianions are related to each other by a noncrystallographic twofold axis through the sulfur and C3 atoms. This superposition creates split positions only for C1 and C4 but leads to intramercaptopurine bond lengths which cannot be discussed meaningfully. To illustrate this, the C–S distances C1a–S and C1b–S are listed in Figure 4.

Figure 3. Superposition of the disordered mercaptopurine molecules in **4**

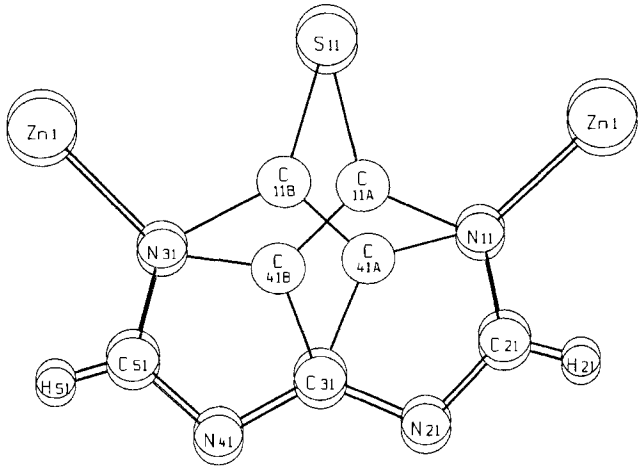
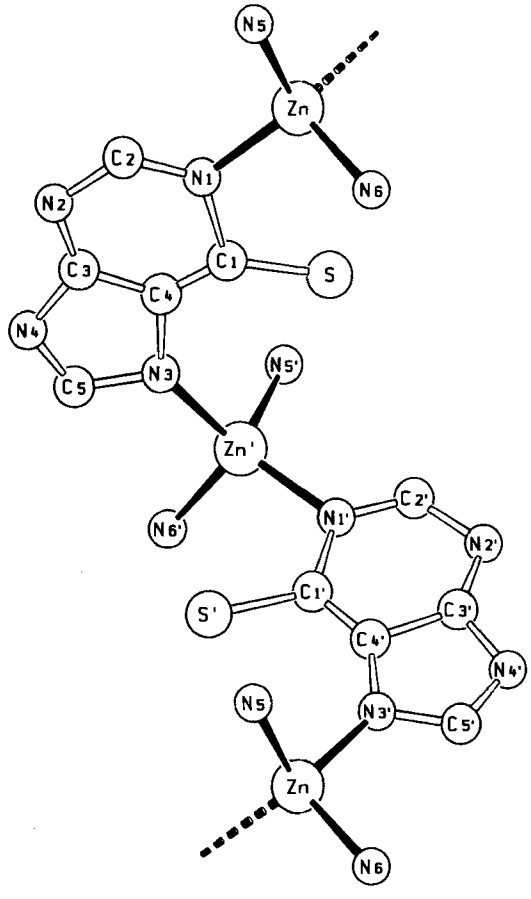


Figure 4. Atomic arrangement of **4** in the solid state. Two symmetry-equivalent mercaptopurine units and three $Zn(NH_3)_2$ units are shown



Selected bond lengths [Å] and angles [°]: Zn–N5 2.062(4), Zn–N6 2.038(4), Zn–N3′ 2.004(4), Zn–N1 1.973(4), C1–S 1.728(7) and 1.798(14) (see text); N3–Zn–N6 106.8(2), N3–Zn–N5 102.5(2), N6–Zn–N5 100.9(2), N3–Zn–N1 128.0(2), N6–Zn–N1 107.7(2), N5–Zn–N1 107.8(2).

The structure determination of **4** (see Figure 3) confirmed the polymeric nature of the compound and yielded the unexpected result that the sulfur atoms are not involved in the complexation, in contrast to the situation in $[(H_3Mer)Cl_2Cu(I)]$, $[(Mer)_2(H_2O)_2Cd(II)]_\infty$, and $[(H_2Mer)Cl_2Cd(II)]$[37]. The bonding of the mercaptopurine dianion to zinc is achieved by the nitrogen atoms in positions 1 and 7 of the purine heterocycle which allow the formation of the chain-like polymer. In free mercaptopurine which crystallizes as the hydrated NH tautomer of H_2Mer[38], it is also N1 and N7 which bear the H atoms. This variant of the thiol/thione tautomerism in **4** is also reflected in the C–S bond length of ca. 1.76 Å which corresponds to some double bond character. Polymeric structures of purine base–metal complexes were also found for $[(Mer)_2(H_2O)_2Cd]$[37] and $[(hypoxanthine)CuSO_4 \cdot H_2O]$[39]. Their comparison with the structure of **4** provides little information as the purine bases use different donor atoms.

The coordination of the zinc ions in **4** is tetrahedrally distorted. The angles formed by the Mer ligands (e.g. N3–Zn–N1) are unusually large and have no correspondence in the structure of the similar sulfonamide–zinc polymer $[(hydrochlorothiazid)(NH_3)_2Zn]$[12]. Correspondingly, the angles between the ammonia ligands are rather small. The Zn–N(Mer) bonds are relatively short (cf. $[(imidazole)_2ZnCl_2]$[40]) reflecting the anionic nature of both heterocyclic nitrogen atoms, while the Zn–N(NH_3) bond lengths are in the normal range for such complexes[11,12]. The water molecules in the lattice establish a two-dimensional network for the polymer, being involved in hydrogen bridges with N2, N6, and the sulfur atom.

With respect to zinc-ligand interactions in biological systems **4** is an "unnatural" example again. It is polymeric, it makes use of untypical donor atoms, and it gives no indication as to how the metal ion affects the hydrogen bonding capabilities which are characteristic of the purine bases. Except for the unexpected absence of a zinc-sulfur interaction it is easy to rationalize the binding of the zinc ion to the nitrogen atoms in the 1- and 7-positions of the heterocycle and not to those in the 3- and 9-positions: the two negative charges of the Mer ligand are located on the sulfur and just these two nitrogen atoms.

Discussion

The four zinc complexes of drugs described here demonstrate vividly the variability and unpredictability in the coordination chemistry of zinc. The donor sets offered are NO_3S (captopril), N_4O_2 (1,2-diisonicotinoyl hydrazide), N_2O_3 (nalidixic acid), and N_4S (mercaptopurine). Of these O_3S, N_2O_2, O_2, and N_2 are used. Efficient nitrogen donors and in one case a sulfur donor remain unused. This means that the zinc ion behaves like a hard Lewis acid in all four cases which in turn may be related to the absence of the soft halide ions in the starting materials. Halide ligands would compete with the four drugs for coordination positions on zinc, thereby "softening" the metal and making it available for the softer donor atoms of the drugs.

For the reactions described here the zinc ions were always employed in the "naked" state, i.e. free from ligating anions and protecting coligands. Thereby the polyfunctionality of the drugs could be exploited leading to the observed results. Under these conditions, however, the simple, i.e. non-polymeric, complexes of the drugs seem to be of rather low stability, and except for nalidixic acid 1:2 or 1:4 (Zn:drug) complexes could not be obtained by combining the reagents in the appropriate ratio. Instead, the low solubility or preferred tendency for crystallization seem to be the decisive factors for the formation of the complexes **1**–**4** under the conditions employed. In order to make such zinc complexes of drugs more "natural" by reducing their aggregation it seems appropriate so start with zinc complexes of encapsulating ligands as we have shown for the case of tris(benzimidazolylmethyl)amine[15] and tris(pyrazolylborate)[13] coligands.

The title of this paper emphasizes the presence of nitrogen heterocycles as the common property of the four drugs employed. However, only in the case of compound **4** are the heterocyclic nitrogen atoms used for complexation. The structural diversity which is reflected here in the donor sets and in the coordination numbers 4–6 may be related to the diversity of the four drugs themselves. On the other hand, when using polyfunctional drugs that contain a sulfonamide[11–13] or a carboxylate function[13–15], we did not observe such a variety of product types. For the four drugs employed here this again suggests that in order to approximate their biological coordination mode one should disable parts of their polyfunctionality by limiting their access to the zinc ions with the help of protecting coligands.

This work was supported by the *Deutsche Forschungsgemeinschaft*. We thank Dr. *W. Deck* for NMR spectra and Mr. *M. Ruf* for help during the structure determinations.

Experimental

For experimental techniques and measuring instruments see ref.[41]. All reactions were performed under inert gas in purified solvents.

Preparation of [ZnCap] (**1**): A solution of 71 mg (0.32 mmol) of H_2Cap in 0.7 ml of water was brought to pH 8.5 by adding of 25% ammonia and then treated with 0.32 ml (0.32 mmol) of a 1 M aqueous solution of $Zn(ClO_4)_2$. After stirring for 1 h the volume was reduced to 0.5 ml in vacuo and the solution cooled to 4 °C. After 1 d the colorless precipitate was filtered off, washed with water, and dried in vacuo. Yield of **1** 35 mg (39%), m.p. 290 °C (dec.). – Starting with $Zn(NO_3)_2$ (0.31 ml, 0.31 mmol) and using the same procedure, we obtained 44 mg (51%) of **1**. – $C_9H_{13}NO_3SZn$ (280.0): calcd. C 38.51, H 4.67, N 4.99, Zn 23.3; found C 38.08, H 4.19, N 4.65, Zn 23.5. – ^{13}C NMR (CP-MAS, δ): 182.3, 172.7, 62.1, 48.8, 39.8, 31.7, 29.6, 26.3, 18.8.

Preparation of [Zn(Nih)NH$_3$] (**2**): A solution of 27.4 mg (0.20 mmol) of isoniazid in 0.4 ml of water was treated with 0.01 ml of 2 M NaOH, 1.0 ml of 25% NH_3, and 0.80 ml (0.40 mmol) of 0.5 M $Zn(NO_3)_2$. The solution was kept under inert gas for 2 months. During this time yellow-brown well-shaped crystals of **2** formed which were filtered off, washed with water, and dried in vacuo. Yield of **2**: 8 mg (24%), m.p. 140 °C. – $C_{12}H_{11}N_5O_2Zn$ (322.7): calcd. C 44.67, H 3.44, N 21.71, Zn 20.3; found C 42.99, H 3.10,

N 19.37, Zn 20.8. – The compound was too insoluble to record an NMR spectrum in solution.

Preparation of [Zn(HNal)$_2$(H$_2$O)$_2$](ClO$_4$)$_2$ · 2 H$_2$O (**3**): 25 mg (0.10 mmol) of HNal was dissolved in 4 ml of chloroform, and 0.34 ml (0.34 mmol) of a 1 M solution of Zn(ClO$_4$)$_2$ · 6 H$_2$O in acetone was added with stirring. The mixture was kept under inert gas for 6 weeks during which time colorless crystals of **3** formed. The mother liquor was removed by means of a syringe, the crystals were washed with cold acetone and dried in air. Yield of **3**: 8 mg (20%), m.p. 110°C. – $C_{24}H_{32}Cl_2N_4O_{18}Zn$ (800.8): calcd. C 35.99, H 4.03, N 7.00, Zn 8.2; found C 35.28, H 3.86, N 6.86, Zn 8.0. – ^{1}H NMR ([D$_6$]DMSO, δ): 9.17 (s, 1H, 2-H), 8.60 (d, J = 8.2, 1H, 5-H), 7.59 (d, J = 8.2, 1H, 6-H), 4.64 (d, J = 7.1, 2H, NCH$_2$), 2.71 (s, 3H, CH$_3$), 1.42 (t, J = 7.1, 3H, CH$_3$). – ^{13}C NMR ([D$_6$]DMSO, δ): 178.0, 165.6, 164.8, 149.3, 148.4, 135.5, 122.4, 118.3, 109.0, 46.6, 24.8, 14.7.

Preparation of [Zn(Mer)(NH$_3$)$_2$] · H$_2$O (**4**): 0.10 g (0.59 mmol) of H$_2$Mer and 0.21 g (0.59 mmol) of Zn(ClO$_4$)$_2$ · 6 H$_2$O were dissolved in 10 ml of a mixture of dichloromethane, methanol, and 25% aqueous ammonia (6:3:1). The solvents were allowed to evaporate slowly through a stopcock while yellow crystals of **4** formed. After 5 d the remaining solvents were removed by means of a syringe, the crystals washed with methanol and dried in vacuo. Yield of **4**: 0.12 g (79%), m.p. ca. 300°C (dec.). – $C_5H_{10}N_6OSZn$ (267.7): calcd. C 22.44, H 3.77, N 31.41, Zn 24.4; found C 22.86, H 3.53, N 30.72, Zn 23.8. – The compound was too insoluble to record an NMR spectrum in solution.

Structure determinations[42]: The crystals of **2**, **3**, and **4** were obtained as described above. Diffraction data were recorded in the ω/2Θ scan mode on a Nonius CAD4 diffractometers fitted with a molybdenum tube (λK_α = 0.71073 Å) and a graphite monochromator at 294 K. Absorption corrections based on psi scans[43] were applied. Sheldrick's[44] and Keller's[45] programs were used for crystallographic computation. The structures were solved by direct methods and refined anisotropically. Hydrogen atoms were included on fixed positions (C–H = N–H = 0.96 Å) and treated with a common isotropic temperature factor. In the structure of **3** the perchlorate ions are disordered. The unusual disorder of the mercaptopurine dianions in the structure of **4** has been discussed in the text. Table 1 lists all crystallographic data.

Table 1. Crystallographic data for compounds **2**–**4**

	2	**3**	**4**
formula	$C_{12}H_{11}N_5O_2Zn$	$C_{24}H_{32}Cl_2N_4O_{18}Zn$	$C_5H_{10}N_6OSZn$
mol. mass	322.7	800.8	267.7
cryst. from	NH_3-water	chloroform/acetone	NH_3-water
cryst. size [mm]	0.6 × 0.6 × 0.6	0.6 × 0.6 × 0.3	0.4 × 0.35 × 0.35
color	yellow-brown	colorless	yellow
space group	$C2/c$	$P2_1/c$	$P2_1/n$
Z	2	2	4
a [Å]	13.188(3)	9.280(1)	8.931(4)
b [Å]	12.542(3)	13.111(3)	10.489(2)
c [Å]	8.796(2)	13.874(2)	10.770(5)
β [°]	113.03(3)	100.14(1)	100.75(4)
V [Å^3]	1338.9(5)	1661.7(5)	991.2(7)
$d_{calcd.}$ [g cm^{-3}]	1.60	1.58	1.79
$d_{obs.}$ [g cm^{-3}]	1.59	1.60	1.78
μ [mm^{-1}]	1.84	0.98	2.67
2Θ range [°]	4 – 52	4 – 52	6 – 50
refl. measured	2745	3394	3447
unique refl. [$I \geq 3\,\sigma(I)$]	1252	1950	1485
variables	92	216	148
R (unweighted)	0.033	0.077	0.038
residual el. density [e/ Å^3]	+0.72 / –0.44	+1.06 / –0.86	+0.63 / –0.48

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