Crystal Structure of Dichlorobis(*N*-{4-[(2-pyrimidinyl- κ N-amino)sulfonyl]phenyl}acetamide)copper(II)

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The X-ray structure of the complex dichlorobis(*N*-{4-[(2-pyrimidinyl- κ N-amino)sulfonyl]phenyl}acetamide)copper(II), containing a metabolite *N*⁴-acetylsulfadiazine (or *N*-{4-[(2-pyrimidinylamino)sulfonyl]phenyl}acetamide) of the antibacterial sulfadiazine as ligand, is reported. The complex crystallizes in the space group $P2_1/n$ with $a = 12.7531(3)\text{\AA}$, $b = 8.0777(2)\text{\AA}$, $c = 14.8548(3)\text{\AA}$, $\beta = 112.237(1)^\circ$, and $Z = 2$, requiring it to be centrosymmetric. Two chloride ions and two *N*⁴-acetylsulfadiazine molecules are coordinated to the metal center, each organic moiety being bonded to Cu(II) through a pyrimidinyl nitrogen atom. The metal coordination sphere includes carbonyl oxygen atoms from symmetry-related complex molecules at the apical sites of the square-planar unit, CuN_2Cl_2 , giving a tetragonally-distorted octahedral geometry around Cu(II). Although *N*⁴-acetylsulfadiazine, itself, has not demonstrated antibacterial activity, the title complex showed moderate growth inhibition of several bacteria in *in vitro* assays.

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The metabolites of the antibacterial sulfadiazine (4-amino-*N*-2-pyrimidinylbenzenesulfonamide) include several hydroxylated species as well as *N*-{4-[(2-pyrimidinylamino)sulfonyl]phenyl}acetamide, better known as *N*⁴-acetylsulfadiazine. While the former metabolites displayed *in vitro* activity against *E. coli*, *N*⁴-acetylsulfadiazine did not.¹ A well-known means of modulating the properties and possible biological activity of a ligand, such as *N*⁴-acetylsulfadiazine is *via* complexation with a metal. In the present study, the complex dichlorobis(*N*-{4-[(2-pyrimidinyl- κ N-amino)sulfonyl]phenyl}acetamide)-copper(II) was prepared and was shown to possess significantly greater *in vitro* growth inhibitory activity against *E. coli*, *S. aureus* and *K. pneumonia* than the control (dimethylsulfoxide) using established assays.^{2,3} A factor that probably contributes to this activity is a higher solubility of the copper complex in the culture media relative to the ligand. Detailed activity data for this and related metal complexes will be reported elsewhere.

An X-ray analysis of the complex was undertaken to confirm its structure, and was considered to be potentially useful for future work aimed at understanding its antimicrobial activity. A survey of the literature on *N*⁴-acetylsulfadiazine indicated that no crystal structures of either this metabolite or any of its metal complexes have been reported to date.

The reaction of $\text{CuCl}_2 \cdot 2\text{H}_2\text{O}$ and *N*⁴-acetylsulfadiazine in 1:1

molar ratio in methanol yielded blue crystals with a melting point of 230°C. Elemental analysis yielded C, 39.8; H, 4.0; N, 15.4; S, 9.2% (Calcd for $\text{C}_{24}\text{H}_{24}\text{N}_8\text{O}_6\text{S}_2\text{CuCl}_2$: C, 40.1; H, 3.4; N, 15.6; S, 8.9%).

Intensity data were collected from a crystal of size $0.09 \times 0.11 \times 0.14$ mm, cooled in a stream of nitrogen vapor at 133 ± 2 K. Laue symmetry $2/m$ indicated the monoclinic crystal system and the space group $P2_1/n$ was deduced from systematic absences. Data were corrected for Lorentz-polarization effects and for absorption. A structure solution by direct methods was followed by full-matrix least-squares refinement against F^2 using SHELXL-97. All hydrogen atoms were located in difference Fourier maps and were added at idealized positions in a riding model with U_{iso} set at 1.2-times those of their parent atoms, the

Table 1 Crystal and experimental data

CCDC deposition number	CCDC 668669
Formula	$\text{C}_{24}\text{H}_{24}\text{N}_8\text{O}_6\text{S}_2\text{CuCl}_2$
Formula weight	719.07
Crystal system	monoclinic
Space group	$P2_1/n$
<i>Z</i>	2
<i>a</i>	12.7531(3) Å
<i>b</i>	8.0777(2) Å
<i>c</i>	14.8548(3) Å
β	112.237(1)°
<i>V</i>	1416.47(6) Å ³
<i>D_x</i>	1.686 g cm ⁻³
No. of reflections used	2589
$2\theta_{\text{max}}$	50.7° with Mo K_α
<i>R</i> (2167 data, $I > 2\sigma(I)$)	0.0324
$(\Delta/\sigma)_{\text{max}}$ final cycle	0.001
$(\Delta\rho)_{\text{max}}$	0.44 e Å ⁻³
$(\Delta\rho)_{\text{min}}$	-0.44 e Å ⁻³
Measurement	Nonius Kappa CCD
Program system	DENZO-SMN
Structure determination	SHELXS-97
Refinement	full-matrix: SHELXL-97

Fig. 1 Chemical structure of I

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Table 2 Atomic coordinates and equivalent thermal parameters ($\text{\AA}^2$)

Atom	x	y	z	U_{eq}
Cu1	0.5000(0)	0.5000(0)	0.5000(0)	0.0236(1)
Cl2	0.47227(5)	0.23876(8)	0.53901(4)	0.0288(2)
N3	0.59998(17)	0.5487(3)	0.64413(15)	0.0243(7)
C4	0.5774(2)	0.5200(3)	0.72453(17)	0.0228(7)
N5	0.65295(18)	0.5147(3)	0.81573(15)	0.0275(7)
C6	0.7600(2)	0.5479(4)	0.82710(19)	0.0307(9)
C7	0.7907(2)	0.5932(4)	0.75165(19)	0.0322(9)
C8	0.7072(2)	0.5913(3)	0.65972(19)	0.0293(8)
N9	0.46513(17)	0.4958(3)	0.70968(15)	0.0249(7)
S10	0.41348(5)	0.44798(8)	0.79239(4)	0.0240(2)
O11	0.29530(14)	0.4246(2)	0.73642(13)	0.0291(6)
O12	0.44713(15)	0.5707(2)	0.86810(13)	0.0290(6)
C13	0.4761(2)	0.2602(3)	0.84383(18)	0.0242(7)
C14	0.5603(2)	0.2586(3)	0.93667(18)	0.0257(8)
C15	0.6123(2)	0.1119(3)	0.97643(18)	0.0273(8)
C16	0.5810(2)	-0.0338(3)	0.92251(18)	0.0254(8)
C17	0.4931(2)	-0.0329(3)	0.83128(19)	0.0293(8)
C18	0.4401(2)	0.1135(3)	0.79150(19)	0.0282(8)
N19	0.63486(17)	-0.1859(3)	0.96126(15)	0.0272(7)
C20	0.7471(2)	-0.2004(3)	1.01643(17)	0.0263(8)
O21	0.81165(15)	-0.0813(2)	1.03017(13)	0.0299(6)
C22	0.7871(2)	-0.3656(4)	1.06128(19)	0.0334(9)

$$U_{eq} = (1/3)\sum_i \sum_j U_{ij}(a_i^* a_j^*)(a_i a_j).$$

Fig. 2 ORTEP drawing of the title complex at the 50% probability level.

latter refining anisotropically. Table 1 lists crystal data and refinement details and Table 2 lists final coordinates and equivalent thermal parameters.

Figure 2 shows the structure of the complex. The metal atom is located on a center of symmetry and is bonded to pyrimidinyl nitrogen atom N3 of each of the two inversion-related N^4 -acetylsulfadiazine molecules, and to two chloride ligands. The Cu-N and Cu-Cl distances (Table 3) are normal for the observed geometry. Coordination of N3 to the metal atom occurs without significantly altering the symmetry of the pyrimidinyl residue; the distances N3-C4 and N5-C4 differ by only $\sim 4\sigma$ and the endocyclic C-N-C angles are identical. The N^4 -acetylsulfadiazine ligand is folded about the $-\text{SO}_2-$ moiety, its conformation being fully defined by the torsion angles listed in Table 3. As discussed below, this conformation is strongly influenced by intermolecular hydrogen bonding involving the amino (N9), amido (N19), sulfonyl (O12) and carbonyl (O21) atoms.

Figure 3 indicates that the coordination geometry of Cu(II) in the complex is tetragonally-distorted octahedral, the apical positions being occupied by carbonyl atoms (O21) of symmetry-related complex molecules, only fragments of which are shown for clarity. The very long Cu...O21^a distance of 2.686(2) $\text{\AA}$ is similar to that found in the complex bis(5-amino-4-carboxamide [1,2,3]triazole- N^3 ,0)-dichloro-copper(II), ~ 2.65 $\text{\AA}$, in which the

Table 3 Selected bond distances ($\text{\AA}$), angles ($^\circ$) and torsion angles ($^\circ$)

Cu1 - Cl2	2.2514(6)	N3 - C4	1.350(3)
Cu1 - N3	2.073(2)	N5 - C4	1.333(3)
Cu1 ... O21 ^a	2.686(2)	C4 - N9	1.378(4)
S10 - O11	1.432(2)	S10 - N9	1.645(2)
S10 - O12	1.438(2)	N19 - C16	1.419(3)
Cl2 - Cu1 - N3	90.41(7)	C4 - N3 - C8	115.8(2)
Cl2 - Cu1 ... O21 ^a	92.94(4)	C4 - N5 - C6	115.6(2)
N3 - Cu1 ... O21 ^a	88.82(7)	S10 - N9 - C4	126.8(2)
Cu1 - N3 - C4	128.8(2)	N9 - S10 - C13	106.5(1)
Cu1 - N3 - C8	114.5(2)	C16 - N19 - C20	123.9(2)
Cl2 - Cu1 - N3 - C4	-50.1(2)	N9 - S10 - C13 - C14	105.7(2)
Cu1 - N3 - C4 - N9	-18.5(3)	C20 - N19 - C16 - C15	-37.9(4)
S10 - N9 - C4 - N3	176.2(2)	C16 - N19 - C20 - O21	-5.7(4)
C13 - S10 - N9 - C4	-59.3(3)		

$$a = -1/2+x, 1/2+y, -1/2+z.$$

Fig. 3 Details of the coordination environment of Cu(II) in the title complex.

ligating O atom occurs in the amide group attached to the triazole ligand.⁴ Deviations from octahedral geometry are small, as indicated by the proximity to 90° of all three unique angles subtended by Cu1 (Table 3). The tilt of $\sim 60^\circ$ of the pyrimidinyl ring out of the CuN_2Cl_2 square plane (Fig. 3) enables the formation of a strong intermolecular hydrogen bond between the amino group and the apical oxygen atom ($\text{N9-H9}\cdots\text{O21}^a$, $\text{N}\cdots\text{O}$ 2.733(3) $\text{\AA}$, $\angle\text{N-H}\cdots\text{O}$ 167°). Further crystal stabilization results from the presence of a second intermolecular hydrogen bond, namely $\text{N19-H10}\cdots\text{O12}^b$ ($\text{N}\cdots\text{O}$ 3.001(3) $\text{\AA}$, $\angle\text{N-H}\cdots\text{O}$ 155° , $b = x, -1+y, z$), between the N-H function of the acetamide residue of one molecule and a sulfonyl oxygen atom.

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