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Binuclear copper(II) complexes of 5-nitrosalicylaldehyde N(3)-substituted thiosemicarbazones

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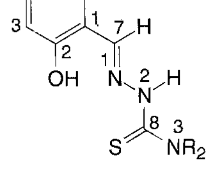
Summary

Binuclear copper(II) complexes with six 5-nitrosalicylaldehyde N(3)-substituted thiosemicarbazones have been prepared and characterized. I.r., electronic and e.s.r. spectra of the complexes, as well as i.r., electronic, and ^{1}H- and ^{13}C-n.m.r. spectra of the thiosemicarbazones, have been obtained. The crystal structure of a monomeric copper(II) complex of 5-nitrosalicylaldehyde piperidylthiosemicarbazone, H_25NO_2Sapip, grown from DMF solution, has been solved. Neither the thiosemicarbazones or their binuclear copper(II) complexes show growth inhibitory activity against *Aspergillus niger*, but the copper(II) complexes show some activity against the fungus *Paecilomyces variotii.*

Introduction

The crystal structures of salicylaldehyde and 5-methoxysalicylaldehyde thiosemicarbazones$^{(1,2)}$ have recently been reported and both were shown to have an *E* conformation with respect to the C=N(1) bond (Figure 1). Because of their potential biological activity$^{(3)}$, there has been considerable interest in metal complexes of heterocyclic thiosemicarbazones$^{(4)}$ as well as salicylaldehyde and 2-hydroxyacetophenone thiosemicarbazones$^{(5)}$.

Either mononuclear complexes of stoichiometry [M(ONS)X] (X = neutral ligand)$^{(6)}$ or binuclear $[M(ONS)]_2$ can be isolated from salicylaldehyde or 2-hydroxyacetophenone thiosemicarbazones on deprotonation of the ring hydroxy group and the N(2) hydrogen of the thiosemicarbazone moiety$^{(7,8)}$. In addition, solution e.s.r. studies$^{(9,10)}$ of binuclear copper(II) complexes of 2-hydroxyacetophenone thiosemicarbazones have been reported which are relevant to this work. We describe here the preparation, spectral characterization and antifungal activity of a series of copper(II) complexes of 5-nitrosalicylaldehyde N(3)-substituted thiosemicarbazones, as well as the crystal structure of a monomeric complex of 5-nitrosalicylaldehyde piperidylthiosemicarbazone, [Cu(5NO_2Sapip)DMF]. Figure 1 shows the various thiosemicarbazones included in this study in their *E* configuration and the symbols used.



N(3)-Substituent	*Symbol*
NHMe	5NO_2Sa3M
NHEt	5NO_2Sa3E
$N(Me)_2$	5NO_2Sa3DM
$N(Et)_2$	5NO_2Sa3DE
$N(CH_2)_5$	5NO_2Sapip
$N(CH_2)_6$	5NO_2Sahexim

Figure 1. Salicylaldehyde N(3)-substituted thiosemicarbazones.

Experimental

The 5-nitrosalicylaldehyde N(3)-substituted thiosemicarbazones were prepared from 0.01 mol of 5-nitrosalicylaldehyde (Aldrich) and the desired substituted thiosemicarbazide (0.01 mol) at room temperature by stirring in 30 cm^3 of EtOH solution with 2–3 drops of concentrated H_2SO_4 added. *N*(3)-methyl- and *N*(3)-ethylthiosemicarbazide were purchased from Aldrich and the remaining thiosemicarbazides were prepared following the procedure developed by Holmberg and Psilanderhielm$^{(11)}$ and modified by Scovill$^{(12)}$. The m.p.s. of the thiosemicarbazones are as follows (°C): H_25NO_2Sa3M, 235–236; H_25NO_2Sa3E, 208–210; H_25NO_2Sa3DM, 231–232; H_25NO_2Sa3DE, 189–191; H_25NO_2Sapip, 201–203; H_25NO_2Sahexim, 196–198.

The binuclear copper(II) complexes were prepared by mixing solutions of 0.002 mol of the desired thiosemicarbazone in 30 cm^3 of EtOH and 0.002 mol of $Cu(OAc)_2 \cdot H_2O$ in 20 cm^3 of EtOH. The mixture was refluxed for *ca.* 2 h, then slowly evaporated at 35 °C until sufficient solid formed. The mixture was filtered and washed with cold *i*-PrOH followed by anhydrous Et_2O. Partial elemental analyses for each of the copper(II) complexes were obtained from MicroAnalytics, Wilmington, Delaware, and are shown in Table 2. The physical and spectral methods of characterization, as well as measurement of the antifungal activity, of both the thiosemicarbazones and their copper(II) complexes were carried out as described previously$^{(13)}$.

The crystal of [Cu(5NO_2Sapip)DMF] was grown by slow evaporation of a DMF solution of $[Cu(5NO_2Sapip)]_2$. Data were collected on a Nicolet P3/F diffractometer$^{(14)}$. Crystal data and data collection parameters are summarized in Table 4. A dark green crystal with dimensions 0.40 × 0.20 × 0.20 mm was mounted in a random orientation on a glass fibre. Lattice parameters were

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Table 1. ^{1}H- and ^{13}C-n.m.r. spectral assignments for 5-nitrosalicylaldehyde N(3)-substituted thiosemicarbazones

Compound	O*H*	N(2)*H*	C(6)*H*	C(7)*H*	C(6)	C(7)	C(8)
$H_2$5NO_2Sa3M	11.544	11.554	8.794	8.358	140.3	161.8	177.8
$H_2$5NO_2Sa3E	11.539	11.482	8.787	8.365	140.3	161.8	176.8
$H_2$5NO_2Sa3DM	12.860	11.526	8.416	8.574	143.7	162.6	179.4
$H_2$5NO_2Sa3DE	12.879	11.407	8.430	8.603	143.5	164.6	177.9
$H_2$5NO_2Sapip	12.799	11.641	8.508	8.533	142.9	162.4	178.7
$H_2$5NO_2Sahexim	12.942	11.489	8.440	8.618	143.7	162.6	178.8

[a] N(3)*H* is at $\delta = 8.663$ and 8.708 for 5NO_2H_2Sa3M and 5NO_2H_2Sa3E, respectively.

obtained from 25 reflections with $7.88 < 2\theta < 25.36°$. Crystal stability was monitored using three standard reflections every 97 reflections; 2255 reflections were collected, 1953 unique reflections (1761 with $F > 3\sigma F$) were used in the structure solution and refinement. Semi-empirical absorption corrections were applied. The structure was solved by Direct Methods(15), and refined by the full-matrix least-squares technique with anisotropic temperature factors for the non-H atoms. The coordinates of the C—H atoms were constrained, the N—H atoms were refined and both assigned a fixed isotropic temperature factor, $U = 0.06\,\text{Å}^2$. The minimized function was $\sum w(F_0 - F_c)^2$, with $w = [\sigma^2(F_0) + 0.0016(F_0)^2]^{-1}$. Residual electron density was within -0.46 and $0.50\,e\text{Å}^{-3}$. Scattering factors were taken from International Tables for X-ray Crystallography (1974, Vol. IV).

Results and discussion

In addition to their m.p.s, these new thiosemicarbazones have been characterized by their ^{1}H- and ^{13}C-n.m.r. spectra. The chemical shifts for both nuclei that are potentially useful for thiosemicarbazone characterization and detection of hydrogen bonding, as well as determining their mode of coordination are compiled in Table 1. The thiosemicarbazones can be separated into two groups [*i.e.* N(3)-alkyl and N(3)-dialkyl/azacyclo] based on whether N(3) is bonded to a hydrogen. For $H_2$5NO_2Sa3M and $H_2$5NO_2Sa3E, the two N(3)-alkyl members of the series with a N(3)H bond, O*H* is found at δ *ca.* 11.5. The other group (*i.e.* $H_2$5NO_2Sa3DM, $H_2$5NO_2Sa3DE, $H_2$5NO_2Sapip and $H_2$5NO_2Sahexim) shows this peak at δ *ca.* 12.85, suggesting greater hydrogen bonding by the hydroxyl hydrogen. These same differences between the N(3)-alkyl and other thiosemicarbazones were observed for 2-hydroxyacetophenone thiosemicarbazones; *i.e.* δ *ca.* 10.8 and 12.5 for the O*H* of N(3)-alkyl and N(3)-dialkyl/azacyclo derivatives, respectively(7). The 2-hydroxyacetophenone *N*(3)-dialkyl/azacyclo thiosemicarbazones showed additional hydrogen-bonded species in their ^{1}H-n.m.r. spectra, but these thiosemicarbazones show the presence of only one isomer. In addition to this difference, the N(3)-dialkyl/azacyclo thiosemicarbazones have C(6)*H* upfield (*i.e. ca.* 0.3 p.p.m.), C(7)*H* downfield (*i.e.* 0.25 p.p.m.) and *C(6)* downfield (*i.e.* 3.3 p.p.m.) compared to the N(3)-alkylthiosemicarbazones, $H_2$5NO_2Sa3M and $H_2$5NO_2Sa3E. These different chemical shifts are all consistent with greater hydrogen bonding by the hydroxyl hydrogen for those thiosemicarbazones having carbons, rather than a hydrogen and carbon, attached to N(3). Thus, it is probable that the N(3)-dialkyl/azacyclo thiosemicarbazones have intramolecular hydrogen bonding by O*H* to N(1) of the thiosemicarbazone moiety, and that the N(3)-alkylthiosemicarbazones have O*H* hydrogen bonding to the DMSO solvent molecules. The position for N(2)*H* is also downfield for all of the thiosemicarbazones of this study, suggesting that this proton is also involved in hydrogen bonding to DMSO. The assigned positions of C(7) and C(8) are consistent with the assignments of Koch(16), as well as our own assignments of thiosemicarbazones prepared from 2-formylpyridine(17) and 2-acetylpyridine(18). In contrast to the copper(II) complexes of 2-hydroxyacetophenone thiosemicarbazones(7), these compounds are insufficiently soluble in chloroform to allow a ^{1}H-n.m.r. spectrum to be recorded. In d_6-DMSO, like the binuclear copper(II) complex of 2-hydroxyacetophenone N(3)-methylthiosemicarbazone, $[Cu(Ap3M)]_2$, no n.m.r. peaks are observed for the present copper(II) complexes due to their dissociation into mononuclear, paramagnetic centres.

All complexes were isolated from boiling EtOH solutions of copper(II) acetates in order to promote formation of the dianion (*i.e.* loss of O*H* and N(2)*H* protons) on complexation and the resulting binuclear complexes(19). Table 2 shows that all of the complexes have been isolated free of acetato ligands, are binuclear and all but $[Cu(5NO_2Sa3E)]_2$ are diamagnetic. The complexes are various shades of brown and are non-electrolytes in DMF.

Table 3 has the i.r. assignments for the thiosemicarbazone moiety and metal–ligand bands. On coordination of the azomethine nitrogen, ν[C(7)=N(1)] shifts to lower wave numbers by 20–40 cm^{-1}(20), but with loss of the proton from N(2), a new band due to ν[N(2)=C(8)] occurs in this same spectral region for these complexes. We have assigned the band at *ca.* 1590 cm^{-1} to ν[N(2)=C(8)] and ν[C(7)=N(1)] to the band shifting from *ca.* 1600 cm^{-1} in the uncomplexed thiosemicarbazones' spectra to *ca.* 1580 cm^{-1} in the complexes' spectra. Coor-

Table 2. Colours, magnetic susceptibilities and partial elemental analyses of copper(II) complexes of 5-nitrosalicylaldehyde N(3)-substituted thiosemicarbazones

Compound	Colour	μ (B.M.)	Found (Calcd.) (%) C	H
$[Cu(5NO_2Sa3M)]_2$	brown	0	34.2(34.2)	2.7(2.6)
$[Cu(5NO_2Sa3E)]_2$	dark brown	1.78	36.9(36.4)	3.3(3.1)
$[Cu(5NO_2Sa3DM)]_2$	brown	0	37.1(36.4)	3.3(3.1)
$[Cu(5NO_2Sa3DE)]_2$	brown	0	40.4(40.3)	3.9(3.9)
$[Cu(5NO_2Sapip)]_2$	brown	0	42.1(42.2)	3.8(3.8)
$[Cu(5NO_2Sahexim)]_2$	brown	0	44.4(43.8)	4.3(4.2)

Table 3. I.r. spectral assignments (cm^{-1}) for the 5-nitrosalicylaldehyde N(3)-substituted thiosemicarbazones and their copper(II) complexes

Compound	ν(OH)	ν(CN)	ν(CO)	ν(CS)	ν(CuN)	ν(CuO)	ν(CuS)
$H_25NO_2Sa3M^a$	3361m	1612s	1278m	836s			
H_25NO_2Sa3E	3330m	1598s	1282m	821s			
H_25NO_2Sa3DM	3271m	1609m	1267m	829s			
H_25NO_2Sa3DE	3308m	1611m	1283m	811m			
H_25NO_2Sapip	3318m	1614m	1292m	831m			
$H_25NO_2Sahexim$	3301m	1613m	1279m	827m			
$[Cu(5NO_2Sa3M)]_2$		1595m 1585s	1229m	740s	429m	407m	340m
$[Cu(5NO_2Sa3E)]_2$		1595s 1591sh	1240s	732m	460m	398m	337m
$[Cu(5NO_2Sa3DM)]_2$		1595m 1586m	1205m	741s	468m	397m	325w
$[Cu(5NO_2Sa3DE)]_2$		1592m 1581s	1211s	742s	463m	391m	331w
$[Cu(5NO_2Sapip)]_2$		1595m 1578sh	1239m	748m	471m	399m	327m
$[Cu(5NO_2Sahexim)]_2$		1594s 1579sh	1235sh	743s	470m	405m	330m

$^a\nu$(N(3)H) = 3358 cm^{-1} for H_25NO_2Sa3M; 3435, 3390 cm^{-1} for $[Cu(5NO_2Sa3M)]_2$; 3280 cm^{-1} for H_25NO_2Sa3E; 3190 cm^{-1} for $[Cu(5NO_2Sa3E)]_2$.

Table 4. Crystallographic data for $[Cu(5NO_2Sapip)DMF]$

Empirical formula	$C_{16}H_{21}N_5O_4SCu$
Crystal system	Orthorhombic
Space group	Pbca (#61)
Unit cell dimensions (Å)	
	$a = 11.391(2)$
	$b = 14.796(3)$
	$c = 22.480(4)$
Volume (Å^3)	3789(2)
Z	8
Formula weight	440.0
Density (calc.) (Mg m^{-3})	1.543
Absorption coefficient (mm^{-1})	2.950
$F(000)$	1808
Radiation	CuK_α($\lambda = 1.54178$ Å)
Temperature (K)	298
Filter	Nickel
2θ range (°)	3.0–50.0
Scan type	2θ:θ
Scan and speed	Variable: 4.00–29.3° min^{-1} in θ
Scan range (2θ)	2.00° + separations $K_{\alpha1} - K_{\alpha2}$
Index ranges	$0 < h < 11$
	$0 < k < 14$
	$0 < l < 22$
Absortion correction	y scan
Min/max transmission	0.2954/0.4292
Final R indices (obs. data)	$R = 5.58\%$, $wR = 8.90\%$
R Indices (all data)	$R = 6.06\%$, $wR = 9.89\%$
Goodness-of-fit	2.00
Largest and mean D/s	0.005, 0.001
Data-to-parameter ratio	7.2:1

dination of the azomethine nitrogen is also consistent with the presence of a band at 450–480 cm^{-1}, assignable to ν(CuN) for these complexes(21). On loss of the N(2)H hydrogen, coordination *via* the thiolate sulfur is indicated by a decrease in the frequency (80–100 cm^{-1}) of the thioamide IV band, which is partially ν(C=S) and found at *ca.* 830 cm^{-1} in the uncomplexed thiosemicarbazones' spectra. Another indication of sulfur coordination is the presence of a band assignable to ν(CuS) in the 320–340 cm^{-1} range(22) in the complexes' spectra. The phenolic oxygen, on loss of the OH proton, occupies the third and fourth (through bridging) coordination sites. This causes ν(CO) to shift to lower wave numbers by 60–80 cm^{-1} from its position at *ca.* 1250 cm^{-1} in the thiosemicarbazones' spectra. A shift of this direction and magnitude has previously been observed for a bridging phenolic oxygen(23). A band in the 390–410 cm^{-1} range in the spectra of the complexes is assignable to ν(CuO) for the bridging phenolato oxygen(24).

In contrast to binuclear copper(II) and nickel(II) complexes of 2-hydroxyacetophenone N(3)-substituted thiosemicarbazones(7), which have some solubility in non-polar solvents such as chloroform and methylene chloride, the analogous salicylaldehyde thiosemicarbazone complexes are soluble only in polar solvents such as DMSO and DMF. Further, we found that dissolution of the 2-hydroxyacetophenone N(3)-substituted thiosemicarbazone complexes in DMF, DMSO or pyridine caused dissociation of the binuclear complexes(7) as is the case for the complexes of this study. Thus, our attempt to grow crystals of the binuclear complexes proved unsuccessful because of their lack of solubility in non-polar solvents and dissociation in polar solvents. Table 4 shows a summary of crystal data and X-ray analysis information for the mononuclear complex, $[Cu(5NO_2Sapip)DMF]$ which crystallized out of a DMF solution of $[Cu(5NO_2Sapip)]_2$. Selected interatomic distances and bond angles are compiled in Table 5, and the Supplementary material contains a complete list of bond distances and angles. A perspective view and the numbering system for $[Cu(5NO_2Sapip)DMF]$ are shown in Figure 2 and the packing of the molecules in Figure 3.

The dianion, $5NO_2Sapip$, bonds as a tridentate ligand and coordinates to the central copper(II) atom *via* the phenoxy oxygen, O(1); the azomethine nitrogen, N(2); and the thiolato sulfur atom with the fourth coordination site occupied by the *N*,*N*-dimethylformamide oxygen, O(4). The copper(II) ion lies in an approximately square-planar coordination environment with all of the atoms tetrahed-

Table 5. Selected bond lengths (Å) and bond angles (°) for [Cu(5NO_2Sapip)DMF]

Bond lengths			
Cu(1)—S(1)	2.225(2)	Cu(1)—O(1)	1.915(4)
Cu(1)—N(1)	1.952(5)	Cu(1)—O(4)	1.986(4)
S(1)—C(8)	1.758(6)	N(3)—C(8)	1.356(8)
N(3)—C(9)	1.465(8)	N(3)—C(13)	1.457(8)
N(2)—C(8)	1.306(7)	N(1)—N(2)	1.395(7)
N(1)—C(7)	1.263(7)	C(1)—C(7)	1.450(8)
O(1)—C(2)	1.293(7)	N(4)—C(5)	1.422(8)
O(2)—N(4)	1.242(8)	O(3)—N(4)	1.219(8)
O(4)—C(1A)	1.199(8)	C(1A)—N(4A)	1.312(8)
N(4A)—C(3A)	1.439(9)	N(4A)—C(4A)	1.376(16)
N(4A)—C(4B)	1.536(17)	C(4A)—C(4B)	0.849(22)
Bond angles			
S(1)—Cu(1)—O(1)	170.8(1)	O(1)—C(2)—C(1)	123.5(5)
S(1)—Cu(1)—N(1)	86.9(2)	O(1)—C(2)—C(3)	119.5(5)
O(1)—Cu(1)—N(1)	94.1(2)	N(4)—C(5)—C(4)	121.3(5)
S(1)—Cu(1)—O(4)	90.6(1)	N(4)—C(5)—C(6)	118.6(5)
O(1)—Cu(1)—O(4)	89.7(2)	N(1)—C(7)—C(1)	126.3(5)
N(1)—Cu(1)—O(4)	171.1(2)	S(1)—C(8)—N(2)	123.8(4)
Cu(1)—S(1)—C(8)	94.8(2)	S(1)—C(8)—N(3)	118.9(4)
Cu(1)—O(1)—C(2)	127.6(3)	N(2)—C(8)—N(3)	117.2(5)
Cu(1)—N(1)—N(2)	119.3(3)	N(3)—C(9)—C(10)	110.9(5)
Cu(1)—N(1)—C(7)	124.7(4)	N(3)—C(13)—C(12)	109.8(5)
N(2)—N(1)—C(7)	115.9(5)	Cu(1)—O(4)—C(1A)	128.5(5)
N(1)—N(2)—C(8)	114.9(5)	O(4)—C(1A)—N(4A)	125.7(6)
C(8)—N(3)—C(9)	122.6(5)	C(1A)—N(4A)—C(3A)	123.2(6)
C(8)—N(3)—C(13)	120.0(5)	C(1A)—N(4A)—C(4A)	120.8(7)
C(9)—N(3)—C(13)	111.6(5)	C(3A)—N(4A)—C(4A)	114.4(7)
O(2)—N(4)—O(3)	121.0(6)	C(1A)—N(4A)—C(4B)	116.3(7)
O(2)—N(4)—C(5)	117.9(5)	C(3A)—N(4A)—C(4B)	116.7(7)
O(3)—N(4)—C(5)	121.1(5)	C(4A)—N(4A)—C(4B)	33.3(9)
C(2)—C(1)—C(7)	123.4(5)	N(4A)—C(4A)—C(4B)	83.7(15)
C(6)—C(1)—C(7)	117.4(5)	N(4A)—C(4B)—C(4A)	62.9(14)

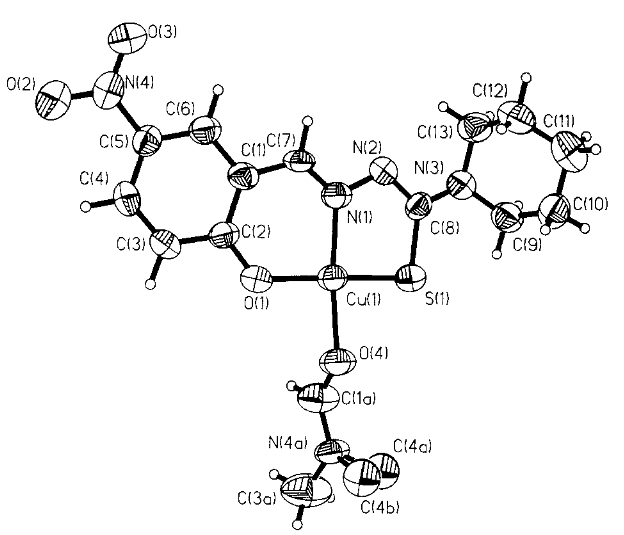

Figure 2. Ortep diagram for [Cu(5NO_2Sapip)DMF].

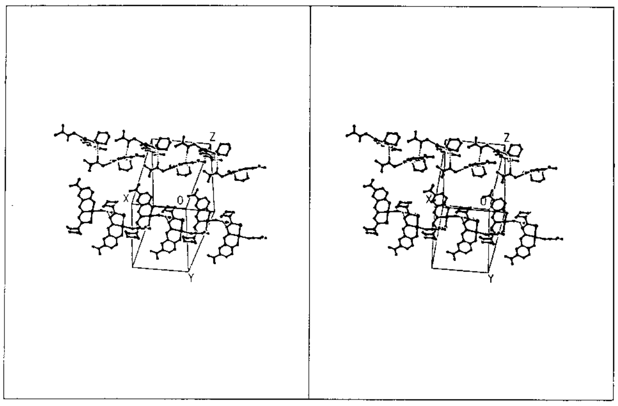

Figure 3. Packing arrangement for [Cu(5NO_2Sapip)DMF].

rally displaced from the mean coordination plane with a maximum deviation of 0.251(4) Å for O(1). The deviation from square-planar geometry is also indicated by the angles involving the *cis* atoms which range from 86.9(2) to 94.1(2)° for S(1)—Cu—N(1) and O(1)—Cu—N(1), respectively, as well as the angles involving the *trans* pairs (Table 5). These same angles were reported to be the smallest and largest for a copper(II) complex of 5-bromosalicylaldehyde *N*(2)-methylthiosemicarbazone, [Cu(5BrSa2M) (NO_3)], and the magnitudes of the two angles are similar for the two complexes(25). The NO_2 group deviates from the plane of the benzene ring, torsion angles C(4)—C(5)—N(4)—O(3) and C(4)—C(5)—N(4)—O(2) are 175(1) and −6(1)°, respectively.

In contrast to the distortion of the thiosemicarbazonato ligands in binuclear copper(II)(7) and nickel(II)(8) complexes, the thiosemicarbazone portion [*i.e.* N(3)—C(8)—S(1)—N(2)—N(1)] of the 5NO_2Sapip ligand in [Cu(5NO_2Sapip)DMF] is essentially planar with a maximum deviation of 0.025(6) for C(8). The angle between the planes formed by the DMF ligand and the mean plane formed by Cu—N(1)—S(1)—O(1)—O(4) atoms is 73.4(4)°. The chelate ring, Cu(1)—S(1)—C(8)—N(2)—N(1), has a mean plane deviation of 0.31 Å, with

Table 6. Comparison of thiosemicarbazone moiety bond lengths (Å) and angles (°) for copper(II) N(3)-substituted thiosemicarbazone complexes

Compound	C(7)—N(1)	N(1)—N(2)	C(8)—N(3)	Cu—N(1)	Cu—S(1)	S—Cu—N(1)	Ref.
[Cu(5NO$_2$Sapip)DMF]	1.263(7)	1.395(7)	1.356(8)	1.952(5)	2.225(2)	86.9(2)	a
[Cu(5BrSa2M)(NO$_3$)][b]	1.297(5)	1.406(4)		1.959(3)	2.220(1)	87.0(1)	25
[Cu(Aphexim)]$_2$[c]	1.306(8)	1.374(7)	1.313(9)	1.938(5)	2.200(2)	88.5(2)	7
[Cu(HBz3P)Cl$_2$][d]	1.293(7)	1.356(5)	1.320(6)	2.001(4)	2.287(2)	84.5(1)	26
[Cu(Bzhexim)Cl][e]	1.295(10)	1.358(9)	1.342(10)	1.968(7)	2.235(3)	84.7(2)	26
[Cu(L3M)Br][f]	1.288(7)	1.363(6)	1.315(7)	1.957(4)	2.243(2)	84.7(1)	27
[Cu(Lpip)Br][g]	1.28(2)	1.39(2)	1.37(2)	2.00(1)	2.230(5)	84.3(5)	28
[Cu(Lhexim)Br][h]	1.275(9)	1.373(7)	1.377(11)	1.963(5)	2.236(3)	85.1(2)	29

[a]This work; [b]5BrSa2M = anion (loss of OH proton) of 5-bromosalicylaldehyde 2-methylthiosemicarbazone; [c]Aphexim = dianion [loss of OH and N(2) protons] of 2-hydroxyacetophenone hexamethyleneiminylthiosemicarbazone; [d]HBZ3P = 2-benzoylpyridine N(3)-propylthiosemicarbazone; [e]Bzhexim = anion [loss of N(2) proton] of 2-benzoylpyridine hexamethyleneiminylthiosemicarbazone; [f]L3M = anion [loss of N(2) proton] of 2-acetylpyridine N(3)-methylthiosemicarbazone; [g]Lpip = anion [loss of N(2) proton] of 2-acetylpyridine piperidinylthiosemicarbazone; [h]Lhexim = anion [loss of N(2) proton] of 2-acetylpyridine hexamethyleneiminylthiosemicarbazone.

Table 7. Electronic spectral assignments (cm^{-1}) for the 5-nitrosalicylaldehyde N(3)-substituted thiosemicarbazones and their copper(II) complexes

Compound	Mode	Intraligand and charge transfer	d→d
H$_2$5NO$_2$Sa3M	Nujol	28820, 23260	
	DMSO	31950, 30120	
H$_2$5NO$_2$Sa3E	Nujol	28820, 25000	
	DMSO	31350sh, 29850, 25770	
H$_2$5NO$_2$Sa3DM	Nujol	28490	
	DMSO	31450sh, 24040	
H$_2$5NO$_2$Sa3DE	Nujol	28010	
	DMSO	31250sh, 26040	
H$_2$5NO$_2$Sapip	Nujol	29410	
	DMSO	31350sh, 23810	
H$_2$5NO$_2$Sahexim	Nujol	29410	
	DMSO	30770sh, 22730	
[Cu(5NO$_2$Sa3M)]$_2$	Nujol	30200, 23260, 20920	13700
	DMSO	30120, 26180, 25320	16750 (2.35)
[Cu(5NO$_2$Sa3E)]$_2$	Nujol	30300, 25910	17700 14200
	DMSO	30120, 26110, 25320	16750 (2.35)
[Cu(5NO$_2$Sa3DM)]$_2$	Nujol	29590, 25640	19120 15500
	DMSO	30030, 25640, 24810	16750 (2.35)
[Cu(5NO$_2$Sa3DE)]$_2$	Nujol	30490, 25510, 20410	16400 13610
	DMSO	29850, 25640, 24880	16920 (2.39)
[Cu(5NO$_2$Sapip)]$_2$	Nujol	30300, 25970	17010 14100
	DMSO	30030, 25640, 24880	16580 (2.41)
[Cu(5NO$_2$Sahexim)]$_2$	Nujol	30120, 26640, 24510, 21980	13850
	DMSO	29940, 25770, 24810	16890 (2.39)

a maximum plane deviation of 0.045(6) Å for C(1), and Cu(1)—O(1)—C(2)—C(1)—C(7)—N(1) has a mean plane deviation of 0.026 Å with a maximum deviation of 0.072(5) for N(1); the angle between these two planes is 8.18(3).

Table 6 contains selected bond distances and angles of other copper(II) N(3)-substituted thiosemicarbazone complexes(26–29) that have been reported recently. Although the differences are small, [Cu(5NO$_2$Sapip)DMF] has a shorter C(7)—N(1) bond and a longer N(1)—N(2) bond distance than copper(II) complexes with heterocyclic thiosemicarbazones. Bulky azacyclo groups involving N(3) cause C(8)—N(3) to be longer than thiosemicarbazones with smaller functional groups (*i.e.* [Cu(L3M)Br]); the lone exception in Table 6 is the dinuclear [Cu(Aphexim)]$_2$, and its short bond may be due to packing effects. The Cu—N(1) and Cu—S(1) bond distances for [Cu(5NO$_2$Sapip)DMF] and the other complexes with phenoxy thiosemicarbazones, [Cu(5BrSa2M)(NO$_3$)] and the binuclear [Cu (Aphexim)]$_2$, are generally shorter than found for the other thiosemicarbazones in Table 6. These same compounds have larger S—Cu—N(1) bond angles than the heterocyclic thiosemicarbazones; this results in a greater distortion from planarity for the tridentate ligand [*e.g.* C(2) is 0.055(6) Å and O(4) 0.618(5) Å above the plane and Cu(1) is 0.182(1) Å below the plane].

Each thiosemicarbazone and copper(II) complex has a ring $\pi \rightarrow \pi^*$ band at *ca.* 40000 cm^{-1} and $n \rightarrow \pi^*$ band at *ca.* 32000 cm^{-1}, both of which have been omitted from Table 7; there is no significant change in the energy of these bands on complexation. A second $n \rightarrow \pi^*$ band, which is found below 30000 cm^{-1} in the uncomplexed thiosemicarbazones' spectra, is found at *ca.* 30000 cm^{-1} in the spectra of the copper(II) complexes. This band, which involves transitions within the thiosemicarbazone

Table 8. Solution (DMF) e.s.r. spectral g and A values of the copper(II) complexes of 5-nitrosalicylaldehyde N(3)-substituted thiosemicarbazones

Compound	Temp.	$g_{\parallel}, g_1$	$A_{\parallel}{}^{a}$	g_2	$g_{\perp}, g_3$	$A_0{}^{a}$	g_{av}, g_0	$A(N)^{a,b}$
$[Cu(5NO_2Sa3M)DMF]$	RT					74.0	2.083	18
	77 K	2.206	174	2.059	2.038		2.101	
$[Cu(5NO_2Sa3E)DMF]$	RT					74.7	2.083	17
	77 K	2.207	175	2.060	2.039		2.102	
$[Cu(5NO_2Sa3DM)DMF]$	RT					73.7	2.079	18
	77 K	2.209	175	2.061	2.051		2.107	
$[Cu(5NO_2Sa3DE)DMF]$	RT					74.7	2.084	16
	77 K	2.191	182	2.052	2.043		2.095	
$[Cu(5NO_2Sapip)DMF]$	RT					75	2.086	19
	77 K	2.203	172	2.048	2.037		2.096	
10:1 py:Cu in DMF	RT					74	2.082	17
	77 K	2.183	184	2.055	2.031		2.090	
in 1:1 (v:v) py:$CHCl_3$	RT					75	2.095	15
	77 K	2.190	179	2.055	2.035		2.093	
$[Cu(5NO_2Sahexim)DMF]$	RT					75.7	2.085	17
	77 K	2.186	182	2.049	2.038		2.091	

[a] A values in G; [b] for one nitrogen.

moiety [mainly C(7)=N(1), C(8)=S groups], is of reduced intensity in the spectra of the complexes. Two ligand-to-metal charge transfer bands are found at *ca.* 26000 and 21000–25000 cm^{-1}. In accordance with studies of previous copper(II) thiosemicarbazone complexes(24), the higher energy band is assigned to $S \rightarrow Cu^{II}$ transitions. Its position is dependent on the steric requirements of the N(3)-substituents such that thiosemicarbazones with bulkier N(3)-substituents show this band at somewhat higher energies. The band in the 21000–25000 cm^{-1} range is assignable to bridging phenoxy $O \rightarrow Cu^{II}$ transitions(30). The solid state spectrum of each complex has two d→d bands (16400–19120 and 13610–15500 cm^{-1}) or a single broad band in the lower energy range. Since these bands appear as shoulders on the intraligand and charge transfer bands, the higher energy bands for $[Cu(5NO_2Sa3M]_2$ and $[Cu(5NO_2Sahexim)]_2$ are presumably obscured by these more intense bands. The lower energy d→d band maximum decreases in energy with increasing size of the N(3)-substituent, which indicates a more distorted copper(II) centre. This distortion generally results from molecular packing effects.

In DMSO solution there is a single broad d→d band, found at essentially the same energy for each of the complexes in DMSO, all have approximately the same molar absorptivity. Furthermore, the difference in the d→d bands in DMSO solution from those in the solid state is indicative of the dissociation of the binuclear complexes to form mononuclear complexes with DMSO completing the coordination sphere in a manner similar to that of DMF in $[Cu(5NO_2Sapip)DMF]$.

As expected, the solid copper(II) complexes are e.s.r. silent at room and liquid nitrogen temperatures. However, as has been found for other ONS dianionic ligands with phenoxy bridging, solutions of these complexes do provide e.s.r. spectra (Table 8) because polar solvent molecules, L, can readily cleave the bridging bonds to give monomeric [Cu(ONS)L] complexes(9,31). A solution e.s.r. study has been reported involving binuclear copper(II) complexes of salicylaldehyde and 2-hydroxynaphthaldehyde thiosemicarbazones and N(3)-phenylthiosemicarbazones(10). There is little variation in the e.s.r. parameters for the four thiosemicarbazone complexes studied by Jezierska(10), who employed DMF, DMSO and pyridine as solvents; the former gave the most highly resolved spectra. We reported a similar study of a series of N(4)-substituted thiosemicarbazone derived from 2-hydroxyacetophenone(7).

The results of our room temperature e.s.r. study are included in Table 8. Similar to the related compounds studied previously(7,9,10), well resolved spectra with four copper hyperfine lines and three superhyperfine lines due to the azomethine nitrogen are observed in DMF. The spectra are centred at g_0 *ca.* 2.085, with A(Cu) *ca.* 75 G and A(N) *ca.* 17.5 G for all six complexes in contrast to g_0 *ca.* 2.090, A(Cu) *ca.* 67 G and A(N) *ca.* 18 G for the previously studied copper(II) complexes of 2-hydroxyacetophenone thiosemicarbazones(7). The small differences in g_0 and A(Cu) suggest bonding to copper(II) to be stronger for the 5-nitrosalicylaldehyde thiosemicarbazones than the 2-hydroxyacetophenone thiosemicarbazones.

Addition of pyridine to the DMF solution of $[Cu(5NO_2Sapip)]_2$ (Table 8) lowers g_0, indicating stronger bonding by a pyridine ligand than a DMF molecule. However, additional superhyperfine coupling is not observed in this solution or a 1:1 by volume $CHCl_3$: pyridine solution consistent with previous studies of these systems(7,10). It is most likely that the species is [Cu(ONS)L] {or $[Cu(ONS)L_2]$}, as suggested previously(9,10), and since superhyperfine coupling by a second nitrogen is not observed in pyridine solution, the suggestion of Jezierska(10) that the solvent molecule(s) are not coplanar with the ONS bichelate rings seems reasonable. A recent crystal structure of [Ni(Sa3Ph)py] shows that the pyridine ligand is not in the plane of the thiosemicarbazonato ligand(32).

E.s.r. parameters for the frozen DMF solutions are included in Table 8. $g_{\parallel}$ is in the 2.185–2.210 range and $A_{\parallel}$ is in the 174–182 G range, with the bulkier substituents having the lower values for $g_{\parallel}$ and higher values for $A_{\parallel}$ suggesting somewhat stronger bonding. It should be noted that $[Cu(5NO_2Sa3M)]_2$ and $[Cu(5NO_2Sa3E)]_2$ produce a green colour in frozen DMF, but the remaining copper(II) complexes of this study yield a brown colour. Addition of pyridine to a DMF solution of

[Cu(5NO_2Sapip)DMF] lowers the g values, particularly $g_{\parallel}$, and increases $A_{\parallel}$, again indicating a stronger coordination by pyridine.

Although none of the 5-nitrosalicylaldehyde N(3)-substituted thiosemicarbazones show growth inhibitory activity against either *Aspergillus niger* or *Paecilomyces variotii*, their copper(II) complexes, except [Cu(5NO_2Sahexim)]$_2$, are active against *Paecilomyces variotii*. At concentrations in DMSO of 1000 µg cm^{-3} [Cu(5NO_2Sa3DM]$_2$ {*i.e.* more likely [Cu(5NO_2 Sa3DM)(DMSO)]}, the most active of the complexes in this study shows growth inhibition zone of 18.3 mm (6 mm, the size of the assay disc, would be zero growth inhibition). This species is active at 600 µg cm^{-3} with an inhibition zone of 14.8 mm; 400 µg cm^{-3}, 13.1 mm; 200 µg cm^{-3}, 12.9 mm and 100 µg cm^{-3}, 10.1 mm. Other inhibition zones at 1000 µg cm^{-3} are [Cu(5NO_2Sa3M]$_2$ = 10.4, [Cu(5NO_2Sa3E]$_2$ = 11.6, [Cu(5NO_2Sa3DE]$_2$ = 13.4 and [Cu(5NO_2Sapip]$_2$ = 10.3. Thus, although the antifungal activity of these copper(II) thiosemicarbazones is not as great as others studied in our laboratory(17), this is another example of the metal complex possessing greater biological activity than the uncomplexed organic molecule.

Supplementary material

The anisotropic displacement coordinates, calculated hydrogen atom coordinates, and calculated and observed structure factors (F_c and F_0) are deposited with the editor.

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References

(1) D. Chattopadhyay, S. K. Mazumdar, T. Banerjee, S. Ghosh and T. C. W. Mak, *Acta Crystallogr.*, **C44**, 1025 (1988).

(2) M. Soriano-Garcia, J. Valdés-Martínez, R. A. Toscano, J. Gomez-Lara and M. Villalobos-Penaloza, *Acta Crystallogr.*, **C42**, 623 (1986).

(3) D. X. West, S. B. Padhye, P. B. Sonawane and R. C. Chikate, *Asian J. Chem. Prev.*, **1**, 125 (1990).

(4) D. X. West, S. B. Padhye and P. B. Sonawane, *Struct. Bonding*, **76**, 1 (1991); D. X. West, A. E. Liberta, S. B. Padhye, R. C. Chikate, P. B. Sonawane, A. S. Kumbhar and R. G. Yerande, *Coord. Chem. Rev.*, **123**, 49 (1993).

(5) E. G. B. Singh and U. Srivastava, *Synth. React. Inorg. Met.-Org. Chem.*, **19**, 279 (1989); S. Laly and G. Parameswaran, *Thermochim. Acta*, **168**, 43 (1990) and refs cited therein.

(6) L. H. Reddy, K. G. Reddy and D. V. Reddy, *Proc. Ind. Sci. Acad.*, **55**, 517 (1989).

(7) D. X. West, Y-H. Yang, T. L. Klein, K. I. Goldberg, A. E. Liberta, J. Valdés-Martınez and R. A. Toscano, *Polyhedron*, **14**, 1681 (1995).

(8) D. X. West, Y-H. Yang, T. L. Klein, K. I. Goldberg, A. E. Liberta, J. Valdés-Martınez and S. Hernández-Ortega, *Polyhedron*, **14**, 3051 (1995).

(9) J. A. De Bolfo, T. D. Smith, J. F. Boas and J. R. Pilbrow, *Aust. J. Chem.*, **29**, 2583 (1976).

(10) J. Jezierska, *Asian J. Chem.*, **4**, 189 (1992).

(11) B. Holmberg and B. Psilanderhielm, *J. Prakt. Chem.*, **82**, 440 (1910).

(12) J. P. Scovill, *Phosphorus, Sulfur and Silicon*, **60**, 15 (1991).

(13) D. X. West, J. S. Saleda and A. E. Liberta, *Transition Met. Chem.*, **17**, 568 (1992) and refs cited therein.

(14) Nicolet XRD Corporation, *Data Collection Operation Manual*, Cupertino, CA, USA, 1980.

(15) Siemens, *SHELEXTL-PC User's Manual*, Madison WI, USA, 1990.

(16) K. R. Koch, *J. Coord. Chem.*, **22**, 289 (1991).

(17) D. X. West, C. E. Ooms, J. S. Saleda, H. Gebremedhin and A. E. Liberta, *Transition Met. Chem.*, **19**, 553 (1994).

(18) D. X. West, B. L. Mokijewski, H. Gebremedhin and T. J. Romack, *Transition Met. Chem.*, **17**, 384 (1992).

(19) K. Dey and D. Bandyopadhyay, *Ind. J. Chem.*, **31A**, 34 (1992).

(20) D. X. West, C. S. Carlson, K. J. Bouck and A. E. Liberta, *Transition Met. Chem.*, **16**, 271 (1991) and refs cited therein.

(21) P. Sousa, J. A. Garcia-Vazquez and J. A. Masaquer, *Transition Met. Chem.*, **9**, 318 (1984); S. K. Agrawal, D. R. Tuflani, R. Gupta and S. K. Hajela, *Inorg. Chim. Acta*, **129**, 257 (1987); N. Saha and S. Sinha, *Indian J. Chem.*, **29A**, 292 (1990).

(22) S. K. Nag and D. S. Joarder, *Can. J. Chem.*, **54**, 2827 (1976); S. K. Sengupta, S. K. Sahni and R. N. Kapoor, *Acta Chim. Acad. Sci. Hungary*, **104**, 89 (1980); R. Roy, M. Chaudhury, S. K. Mondal and K. Nag, *J. Chem. Soc., Dalton Trans.*, 1681 (1984); A. Z. El-Sonbati, E. M. Mabrouk and H. E. Megahed, *Transition Met. Chem.*, **16**, 280 (1991).

(23) J. Jezierska, B. Jęzowska-Trzebiatowska and G. Petrova, *Inorg. Chim. Acta*, **50**, 153 (1981) and refs cited therein.

(24) M. Mikuriya, H. Okawa and S. Kida, *Inorg. Chim. Acta*, **34**, 13 (1979); E. Ainscough, A. M. Brodie and N. G. Larsen, *Inorg. Chim. Acta*, **60**, 25 (1982).

(25) J. Valdés-Martínez, R. A. Toscano, A. Zentella-Dehesa, M. M. Salberg, G. A. Bain and D. X. West, *Polyhedron*, **15**, 427 (1996).

(26) D. X. West, J. S. Ives, J. Krejci, M. M. Salberg, T. L. Zumbahlen, G. A. Bain, A. E. Liberta, J. Valdés-Martínez, S. Hernández-Ortega and R. A. Toscano, *Polyhedron*, **14**, 2189 (1995).

(27) D. X. West, H. Gebremedhin, R. J. Butcher and J. P. Jasinski, *Transition Met. Chem.*, **20**, 84 (1995).

(28) D. X. West, H. Gebremedhin, R. J. Butcher, J. P. Jasinski and A. E. Liberta, *Polyhedron*, **12**, 2489 (1993).

(29) R. J. Butcher and D. X. West, *Transition Met. Chem.*, **18**, 449 (1993).

(30) M. Mikuriya, H. Okawa and S. Kida, *Bull. Chem. Soc. Japan*, **53**, 3717 (1980).

(31) Y. Muto, *Bull. Chem. Soc. Japan*, **33**, 1242 (1960); M. D. Revenko and N. V. Gerbeleu, *Zh. Neorg. Khim.*, **17**, 1018 (1972).

(32) J. Valdés-Martınez and S. Hernández-Ortega, Unpublished work.

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