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Copper(II) Complexes of Thieno[2,3-*d*]pyrimidine Derivatives

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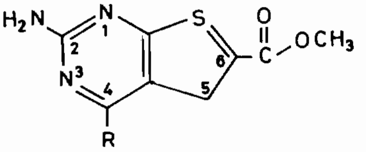
Thieno[2,3-*d*]pyrimidine was first synthesized by Baker *et al.* [1]. Later it was found that 2,4-diaminothieno[2,3-*d*]pyrimidines were potent inhibitors of the enzyme dihydrofolate reductase, showing antimalarial, antibacterial, antihelminthic and antiprotozoal activity [2]. Several of the thieno[2,3-*d*]pyrimidine derivatives found applications as drugs with various activities and uses, as well as virucides, bactericides, fungicides, acaricides and insecticides [2].

Complexation studies of Cu(II) with such thieno[2,3-*d*]pyrimidine derivatives may be useful in the elucidation of their interactions with copper(II) proteins or coenzymes containing Cu(II), or other metal ions.

In this letter we report preliminary results of such studies. To our knowledge similar studies have not as yet been reported.

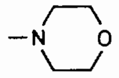
Results and Discussion

The 2,4-diaminothieno[2,3-*d*]pyrimidines used as ligands in this study (I) contain four nitrogen atoms, one sulfur and one oxygen, that could coordinate with Cu(II).



2,4-diaminothieno[2,3-*d*]pyrimidines

L, R = $-NHC_2H_5$
L′, R = $-N(C_2H_5)_2$

L″,R =


I

Two types of complexes corresponding to 1:1 and 1:2 metal-to-ligand ratios were obtained from organic solvents. The complexes of the former series were not obtained in a very pure condition since they were rather contaminated with the 1:2 compounds, as their elemental analyses show.

Table I summarizes the elemental analyses and physical measurements of the 1:2 compounds for the L and L′ ligands and the 1:1 compound of the L″ ligand. The 1:2 and 1:1 compounds of the same ligand have different colors and, during the preparation of the 1:2 compounds, a precipitate with the color of the 1:1 compound first appears which gradually changes to the final precipitate with the color of the 1:2 compound. This seems to be the reason for the difficult isolation of the 1:1 compounds in a very pure condition, since the 1:1 compounds when formed readily convert to 1:2. An exception is the case of L″ which is less soluble. Attempts are made to purify the 1:1 compounds.

The molar conductance values of the compounds in DMF approach the 1:1 electrolyte values for the bromo derivatives, but are less than that for the chloro analogs. This may be due to the rapid

TABLE I. Elemental Analyses and Physical Measurements of the Compounds

Compound	C (%)		H (%)	N (%)	Cu (%)	Λ_M (ohm^{-1} cm^2 mol^{-1})	μ_{eff} (B.M.)
CuL_2Cl_2	Calc.	37.59	3.76	17.54	9.95	21	1.87
	Found	37.69	3.64	17.81	9.80		
CuL_2Br_2	Calc.	33.00	3.30	15.40	8.74	50	2.28
	Found	33.00	3.17	14.97	8.80		
CuL'_2Cl_2	Calc.	41.47	4.60	16.13	9.13	20	
	Found	41.26	4.73	15.52	8.80		
CuL'_2Br_2	Calc.	36.73	4.08	14.28	8.10	44	2.55
	Found	37.03	4.28	13.96	7.80		
$CuL''Cl_2$	Calc.	33.58	3.26	13.06	14.82	24	1.81
	Found	34.10	3.47	12.91	14.60		

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TABLE II. Characteristic IR Frequencies and Electronic Spectra of the Compounds

Compound	IR spectra (cm^{-1})							Electronic spectra (kK)						
	ν(NH) (NH$_2$)	ν(CO)	δ(NH$_2$)	δ(NH)	Skeletal vibration	ν(Cu–M)	ν(Cu–Cl)	Diffuse reflectance		In DMF			In MeOH	
L	3490vs, 3385vs, 3295s	1687vs	1632s	1595s	1572s, 1530s, 1492s (1565s, 1555s)^a							28.7		29.6
CuL$_2$Cl$_2$	3422vs, 3362vs, 3325s	1692vs	1620s	1595s	1560s, 1535s, 1498s (1578s, 1550s)^a	440w	323m	13.7	19.6	11.5		28.6	insoluble	
CuL$_2$Br$_2$	3422vs, 3362vs, 3330s	1697vs	1623s	1595s	1562s, 1538s, 1499s	440w		13.6	18.7	11.5	16.9	28.7	insoluble	
L′	3460(sh), 3330s, 3160s	1705vs	1650s		1550s, 1518s, 1475s							28.6		29.4
CuL$'_2$Cl$_2$	3390s, 3310s, 3210m	1700vs	1630s		1552s, 1520s, 1470s	450w	313m	13.6	20.4	11.5	22.9	28.6	11.8	29.4
CuL$'_2$Br$_2$	3400s, 3315s, 3222m	1700vs	1630s		1552s, 1518s, 1470s	450w		13.5	18.9	11.5	16.8	28.6	11.8	29.3
L″	3460vs, 3295s, 3150s	1724vs	1638s		1540s, 1510s, 1485s							28.6		29.4
CuL″Cl$_2$	3468s, 3340s	1705vs	1632s		1550s, 1520sbr	450w	298m	12.1		13.2		28.8	insoluble	

[a] The numbers in parentheses are the frequencies of the deuterated compounds.

exchange of the more labile bromide ion by a solvent molecule.

The magnetic susceptibilites correspond to the spin-only values for the chloro derivatives and are a little higher for the bromo derivatives, indicating orbital contribution to the magnetic moment.

Characteristic IR bands of the ligands and the complexes are included in Table II and assist in the structural characterization. The –C=O group is not coordinated with Cu(II), since the ν(C=O) frequency is not significantly changed upon complexation. A weak coordination of the –NH$_2$ group is postulated, however, since the δ(NH$_2$) frequencies of the various ligands occur at 1630–1650 cm^{-1} and in the complexes at 1620–1630 cm^{-1}. Analogous shifts are also observed in the ν(NH$_2$) frequencies (see Table II). The band at 1595 cm^{-1} of the ligand L and its complexes is assigned to the δ(NH) motion, coupled with the skeletal vibration at 1560 cm^{-1}, because it disappears upon deuteration, while the skeletal vibration appears at 1578 cm^{-1} in the complex CuL$_2$Cl$_2$. This band is not observed in the other ligands and their complexes. Small shifts are observed to the other skeletal vibrations on passing from the ligands to the complexes. The ν(Cu–N) band is tentatively assigned to bands near 450 cm^{-1} and implies an analogous coordination [3]. The bands at 323 and 313 cm^{-1} for the complexes CuL$_2$Cl$_2$ and CuL$'_2$Cl$_2$ are assigned to ν(Cu–Cl) because they are absent from the spectra of their bromo analogs. The CuL″Cl$_2$ complex, on the other hand, shows ν(Cu–Cl) at 298 cm^{-1}. These values are expected for terminal halogens [3].

The diffuse reflectance spectra are useful in assigning stereochemical configurations of the complexes. Thus, the 1:2 complexes show two bands near 19 000 and 13 500 cm^{-1} assigned to d–d transitions in a rhombic square coplanar environment [4]. The 1:1 complexes, on the other hand, show only one band near 12 000 cm^{-1} assigned to the $^2E \rightarrow {}^2T_2$ transition in a pseudotetrahedral configuration [3, 4]. The positions of these maxima are changed in the electronic spectra of the complexes in DMF solutions, but the stereochemistry is retained. This is not the case in methanolic solutions, where a change in the configuration of the 1:2 complexes to pseudo-octahedral ones occurs, as is shown by the disappearance of the band near 19 000 cm^{-1}. Finally, in the ligands the band near 28 500 cm^{-1} (350 nm) is assigned to an n → π^* transition of the carbonyl group, undergoing a blue shift with increasing solvent polarity [5]. This band is observed at almost the same frequency in all the complexes, thus excluding once more a Cu(II)–O bonding.

The powder ESR spectrum of the complex CuL$_2$Cl$_2$ is shown in Fig. 1, and has $g_\parallel > g_\perp$, thus confirming the possible rhombic geometry assigned to this series of complexes from the electronic spectra.

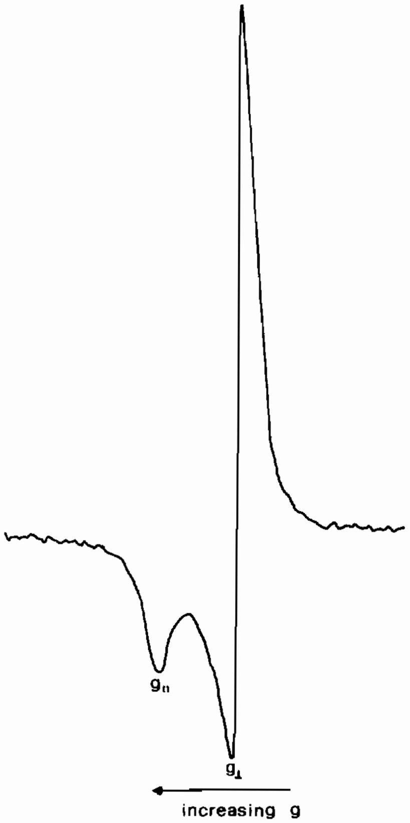

Fig. 1. The ESR spectrum of the CuL_2Cl_2 complex.

Finally, the ^1H NMR spectra give indications for the coordination site of Cu(II) with the ligands, despite the observed paramagnetic broadening. The very small chemical shift (less than 0.2 ppm) of the exocyclic amino ethyl protons at the 4 position, the methyl ester and the aromatic protons at the 6 position may indicate the N1 as the possible coordination site of the ligand with Cu(II). The chemical shifts of these protons are expected to be larger with a sulfur or N3 coordination. A much larger chemical shift is observed for the $-NH_2$ protons (2–3.5 ppm) and this together with the IR data indicate a weak Cu(II) coordination besides the N1, implying a weak chelation. The sulfur coordination is also not observed in thiophene or thiazole metal complexes [6, 7] and this was explained by the participation to the ring resonance of the sulfur lone electron pair. An N3 coordination seems less likely also from the point of view of steric hindrance.

References

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