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Metal Complexes of the Diuretic Drug Furosemide

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New complexes of the formulae $M(fur)_2 \cdot 2\,H_2O$ (M = Mn, Cu, Zn), $M(\mathrm{fur})_2 \cdot 3\,H_2O$ (M = Co, Ni, Cd), $Hg_2(fur)_3Cl_2 \cdot 2\,H_2O$, $Pd(fur)Cl \cdot H_2O$ and $Rh(fur)_3 \cdot 3\,H_2O$, where *fur*H = 4-chloro-N-(2-furfuryl)-5-sulfamoylanthranilic acid, have been prepared and characterized by conductivity measurements, X-ray powder patterns, thermal methods, effective magnetic moments as well as by IR, ligand field, ^{1}H-NMR and ESR spectroscopic studies. The anion fur^- shows a chelated bidentate O(carboxylato), N(imino)-coordinating behaviour.

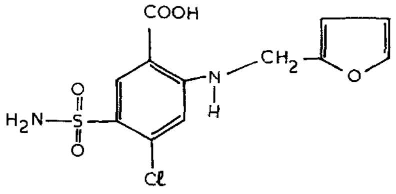
(Keywords: Furosemide; Metal-sulfadrug interactions; Ligand field spectra; IR; ^{1}H-*NMR; Magnetic moments)*

Metallkomplexe der diuretischen Droge Furosemid

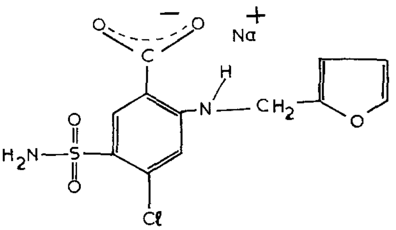
Neue Komplexe der Verbindungen: $M(fur)_2 \cdot 2\,H_2O$ (M = Mn, Cu, Zn), $M(fur)_2 \cdot 3\,H_2O$ (M = Co, Ni, Cd), $Hg_2(fur)_3Cl_2 \cdot 2\,H_2O$, $Pd(fur)Cl \cdot H_2O$ und $Rh(fur)_3 \cdot 3\,H_2O$, wobei *fur*H 4-chlor-N-(2-furfuryl)-5-sulfamoylanthanilsäure ist, wurden dargestellt. Die Komplexe wurden durch Leitfähigkeitsmessungen, Röntgen-Pulver-Aufnahmen, thermogravimetrische Analysen, Messungen des effektiven magnetischen Dipolemomentes sowie durch spektroskopische Untersuchungen (IR, ^{1}H-NMR und ESR) charakterisiert. Das Anion fur^- zeigt das Verhalten einer Chelat-bidentat-O(carboxylato),N(imino)-Koordination.

Introduction

The interactions of metal ions with ligands containing the —SO_2—NH— grouping lead to products with interesting chemical, structural, pharmaceutical or biological properties [1]. We have already performed studies [1–3] on the coordination chemistry of sulfonylamide drugs with transition- and d^{10}-metal ions in an attempt to examine their mode of binding and eventually whether and how drug-metal interactions affect drug delivery to target cells. We report here the preparation and study of the Mn(II), Co(II), Ni(II), Cu(II), Zn(II), Cd(II), Hg(II), Pd(II) and Rh(III) complexes with 4-chloro-N-(2-furfuryl)-5-sulfamoylanthranilic acid (**A**), known as Furosemide or Lasilex and abbreviated as *fur*H. Furosemide is today recognized as one of the most effective diuretics available [4–6] exerting its action on the loop of *Henle*, which is a portion of the nephron, and functioning the regulation of sodium and water balance of the organism; actually furosemide induces a total sodium, chloride and water loss. The molecular and crystal structure of *fur*H has been published [7]. Furosemide has been found [8] to have *pK* values 3.8 and 7.5 in dioxane-water solution; the acidic value is due to the carboxyl group and the basic one to the imino group. The complexation reactions of furosemide with several metal ions in solution have also been studied by using titrimetric and potentiometric methods [8, 9]. The compounds described here are the first characterized examples of solid complexes containing the furosemide ligand system.



A (fur H)



B ($fur^- Na^+$)

Experimental

Elemental analyses, physicochemical measurements and spectroscopic techniques were carried out by published methods [10–13]. Furosemide was obtained from Chinoin, Budapest. In order to obtain a chemically pure sample of the compound, the drug was suspended in acetone. An insoluble minute material was separated by filtration and the resulting solution was evaporated to dryness under reduced pressure. The residue was washed with ether and dried in vacuum over silica gel. Dec. temp.: 220 °C. *Anal.* calc. for $C_{12}H_{11}N_2O_5SCl$: C 43.58, H 3.35, N 8.47%. *Anal.* found: C 44.47, H 3.48, N 8.38%. *Mass spectrum: m/e* of the molecular ion was 330 (43%) [calc. formula weight 330.75]. For the preparation of the sodium salt of furosemide (**B**), to a solution of 1.0 g (3.02 mmol) of *fur*H in 15 ml of ethanol, an ethanolic solution (15 ml) of 0.12 g (3.02 mmol) of NaOH was added dropwise under stirring. A white precipitate was immediately obtained. To the reaction mixture 20 ml of ether were added. The solid was collected by filtration, washed with ethanol (3 × 5 ml) and ether (2 × 10 ml) and dried in vaccum over $CaCl_2$. *Anal.* calc. for $C_{12}H_{10}N_2O_5SClNa$: C 40.86, H 2.86, N 7.94%. *Anal.*

found: C 40.05, H 3.05, N 7.19%. *Yield:* 96%. The metal salts MCl_2 (M = Zn, Hg), $MCl_2 \cdot 2H_2O$ (M = Cu, Cd), $MnCl_2 \cdot 4H_2O$, $MCl_2 \cdot 6H_2O$ (M = Co, Ni), K_2PdCl_4 and $RhCl_3 \cdot 3H_2O$ were employed as starting materials for the preparation of the complexes. The following general preparative method was used: To a suspension of *fur*H in water, an equimolar amount of aqueous standard *N*/9 NaOH solution was added dropwise with stirring. To the clear solution obtained (*pH* = 6.3–6.6), an aqueous solution of the required metal chloride was added until the final metal ion : *fur*H : NaOH molar ratio was 1 : 2 : 2 [1 : 3 : 3 for Rh(III)]. Precipitates were immediately obtained. The reaction mixtures were stirred for 15 min at room temperature, except the Pd(II) system which was stirred overnight. The precipitates were filtered off after cooling to 4 °C, washed with cold water and dried in vacuum over P_4O_{10} for several days. Yields were in the 65–80% range. Pd(*fur*)$_2$ and Hg(*fur*)$_2$ could not be formed. Efforts to prepare 1 : 1 complexes of the types *M*(*fur*)Cl (*M* = Mn, Co, Ni, Cu, Zn, Cd) using 1 : 1 : 1 metal salt : *fur*H : NaOH met with failure. In some cases the same complexes, with lower yields, were again isolated; in other cases products with poor analytical results and spectroscopic evidences were obtained. Numerous attempts were also made to isolate cationic complexes of the formulae $M(furH)_nX_2$ (X = Cl, NCS, NO_3 and n = 1 or 2) from alcoholic media, like other amidic ligands containing a neutral carboxylic group [14]. Using C_2H_5OH or C_2H_5OH—HX as solvents, no solid products could be precipitated in the case of Mn(II), Cd(II), Hg(II), while solids with poor analytical data and of uncertain nature were isolated with Cu(II) and Co(II).

Results and Discussion

Analytical data, colors and molar conductivity values are given in Table 1. The complexes are microcrystalline or powder-like, light-sensitive, insoluble in nonpolar solvents and soluble in alcohols, acetone, *DMF* and *DMSO*; **7** is insoluble in ethanol and acetone. The Λ_M values of the complexes in *DMF* and *DMSO* are in accord with them being formulated as non-electrolytes [15]. The thermogravimetric (TG) and differential thermogravimetric (DTG) curves of **7**, **8** and **9** show a first mass loss between 50–100, 75–135 and 60–110 °C, respectively, which corresponds very well to the release of all the water content. The relatively low temperature of water loss shows that this is lattice held. The thermal behaviour of **2**, **3** and **6** is interesting. The TG-DTG curves show a first mass loss between 65–115 °C. There is a second very distinct inflection in the regions 170–190 °C for **2** and **3** and 195–210 °C for **6**; a clear plateau is not reached above these temperatures, because the decomposition of the complexes starts without formation of stable intermediates. The above experimental observations show clearly the simultaneous presence of crystal and coordinated water; this is also confirmed by IR spectroscopy (see later). Mass loss calculations prove that two water molecules per metal ion are coordinated in **2**, **3** and **6**, while one water molecule is lattice held. The $M(fur)_2 \cdot 2H_2O$ complexes **1**, **4** and **5** are very stable up to 220 (**1**, **5**) and 205 °C (**4**); they begin to decompose over these temperatures with

Table 1. *Colors, analytical results*[a], *and conductivity data for the prepared complexes*

No.	Complex	Color	*M*%	C%	H%	N%	Λ_M^c (S cm^2 mol^{-1})	
							DMF	*DMSO*
1	Mn(*fur*)$_2$ · 2 H_2O	pale yellow	7.38 (7.32)	38.33 (38.41)	3.12 (3.20)	7.24 (7.47)	7	3
2	Co(*fur*)$_2$ · 3 H_2O	brown	7.30 (7.63)	37.38 (37.32)	3.25 (3.37)	7.08 (7.25)	8	10
3	Ni(*fur*)$_2$ · 3 H_2O	greenish	7.92 (7.60)	38.41 (37.33)	3.58 (3.40)	7.10 (7.26)	6	7
4	Cu(*fur*)$_2$ · 2 H_2O	green	8.10 (8.37)	38.94 (37.97)	3.16 (3.19)	7.37 (7.38)	4	7
5	Zn(*fur*)$_2$ · 2 H_2O	pale yellow	8.31 (8.59)	38.76 (37.88)	2.92 (3.15)	7.41 (7.36)	2	3
6	Cd(*fur*)$_2$ · 3 H_2O	pale yellow	13.43 (13.61)	34.74 (34.90)	2.97 (3.16)	6.63 (6.78)	4	1
7	Hg_2(*fur*)$_3$Cl · 2 H_2O	yellowish	27.98 (27.44)	28.61 (29.58)	2.22 (2.35)	5.62 (5.75)	6	4
8	Pd(*fur*)Cl · H_2O[b]	yellow	21.20 (21.73)	30.97 (29.44)	2.45 (2.47)	6.10 (5.72)	4	2
9	Rh(*fur*)$_3$ · 3 H_2O	dark yellow	8.02 (8.98)	37.05 (37.72)	2.91 (3.14)	7.08 (7.33)	4	1

[a] Required values in parentheses

[b] Cl^-%: found 7.13; calc. 7.24

[c] Values of molar conductivity for ca. 10^{-3} *M* solution at 25 °C

rather complex degradation mechanisms. The activation energy values E_a of the reactions:

$$M(fur)_2 \cdot 3\,H_2O \rightarrow M(fur)_2 \cdot 2\,H_2O + H_2O\uparrow,\ M = \text{Co, Ni, Cd, and}$$

$$\text{Pd}(fur)\text{Cl} \cdot H_2O \rightarrow \text{Pd}(fur)\text{Cl} + H_2O\uparrow$$

were determined by the variable heating rate method proposed by *Flynn* and *Wall* [16]; full experimental details of this method were also given in Ref. [13]. The average E_a values are 134.6 (**2**), 139.7 (**3**), 146.1 (**6**) and 178.3 (**8**) kJ mol^{-1}. The first three values are typical for the removal of crystal water [17]. The value for **8** is higher than in the cases of complexes containing crystal water [17], but lower than the expected value for coordinated water [13, 17]. This discrepancy is attributed to the strong hydrogen bonding between the H_2O molecule and the complex. The X-ray powder diffraction data indicate the formation of two pairs of isomorphous compounds; the first pair includes **2** and **3** and the second pair includes the complex **5** and the product Cd(*fur*)$_2 \cdot 2\,H_2O$ obtained from **6** after the removal of crystal water. The small number of diffraction lines observed for **7** may suggest a polynuclear arrangement [1].

The principal IR bands of interest are listed in Table 2. In the $\nu(\text{OH})_{\text{water}}$ region the spectra of **1**–**6** show one sharp band attributed to the presence of coordinated water [18]. In the spectra of **7**–**9**, a medium to weak broad absorption, on top of the characteristic $\nu(\text{NH}_2)$ and $\nu(\text{N—H})$ bands, covering the whole 3 600–3 100 cm^{-1} region indicates the presence of exclusively lattice water [18]; on dehydration of these compounds the broad band is not observed. The spectra of **2**, **3** and **6** show, in addition to the sharp band of coordinated water, a weaker broad continuous absorption; this is apparently due to the simultaneous presence of coordinated and crystal water. Assignments of the characteristic IR bands of *fur*H and *fur*$^-$Na$^+$ were given by studying a) deuterium isotopic substitution shifts, b) the differences between the spectra of *fur*H and its sodium salt, and c) the literature reports [1–3, 19–24]. The N—H stretch at 3 240 cm^{-1} in the spectrum of the parent ligand *fur*$^-$Na$^+$ is shifted to 3 100–3 120 cm^{-1} in the spectra of the complexes **1**–**6** and **9**; thus the secondary amine group is coordinated [25]. The absence of large systematic shifts of the $\nu_{as}(\text{NH}_2)$, $\nu_s(\text{NH}_2)$, $\nu_{as}(\text{SO}_2)$, $\nu_s(\text{SO}_2)$, $\delta(\text{SO}_2)$ and $\delta(\text{COC})_{\text{furane ring}}$ bands in the spectra of the complexes implies that there is no interaction between the —SO$_2$NH$_2$ group and O(ring)-atom and the metal ions. The relatively small shift of the $\nu(\text{NH}_2)$ modes to lower frequencies and the rather broad character of these bands is expected to arise from somewhat stronger hydrogen bonding to the —NH$_2$ protons when compared to the hydrogen bonding in *fur*$^-$Na$^+$, but any reductions in $\nu(\text{NH}_2)$ are not as large as expected if coordination of the primary amino

Table 2. *Diagnostic IR bands* $(cm^{-1})^{a,b}$ *of*

Comp.	$\nu(OH)_{water}$		$\nu_{as}(NH_2)$	$\nu_s(NH_2)$	ν(N—H)
	coordinated	crystal			
fur$^-$Na$^+$			3 380 m	3 327 m	3 240 mb
1	3 500 m		3 372 m	3 295 mb	3 120 m
2	3 430 m	3 580–3 100 mb	3 385 m	3 290 mb	3 100 mb
3	3 430 m	3 580–3 100 mb	3 387 m	3 290 m	3 110 mb
4	3 520 m		3 380 m	3 290 ms	3 110 mb
5	3 510 m		3 375 m	3 300 mb	3 105 mb
6	3 505 m	3 600–3 100 mb	3 385 m	3 280 sb	3 110 mb
7		3 590–3 100 mb	3 350 m	3 290 mb	3 235 mb
8^c		3 600–3 200 wb	3 383 mb	330 mb	n.a.
9		3 580–3 100 wb	3 385 m	3 325 mb	3 100 mb

[a] Assignments of $\nu(NH_2)$, ν(N—H) and ν(OH) bands were assisted by deuterium isotopic substitution

[b] The IR spectrum of *fur*H (not included in the table) exhibits $\nu_{as}(NH_2)$ at 3 380 s, $\nu_s(NH_2)$ at 3 335 s, ν(N—H) at 3 265 s, ν(OH) at 2 850 mb, 2 745 wb, 2 625 wb and 2 540 mb, ν(C=O) at 1 662 vs, δ(OH)[+ν(C—O)] at 1 428 m and 1 239 vs, $\nu_{as}(SO_2)$ at 1 317 s, δ(COC) at 1 252 ms, $\nu_s(SO_2)$ at 1 136 vs and $\delta(SO_2)$ at 572 s cm^{-1}

group had occurred. In the spectra of all the complexes studied, except **7**, $\Delta_{complex} > \Delta_{fur^-Na^+}$, where Δ is the separation between $\nu_{as}(COO^-)$ and $\nu_s(COO^-)$. This indicates that the carboxylate group of *fur*$^-$ is coordinated to the metal ions as a monodentate ligand [26, 27]. The far-IR spectrum of **8** exhibits two characteristic medium bands at 297 and 250 cm^{-1}, which are due to bridging Pd—Cl stretches [28].

The ^{1}H-NMR assignments of *fur*$^-$Na$^+$ in Table 3 were based on comparisons with a number of related ligands and on deuterium assisted experiments. In the spectra of the diamagnetic complexes **5**–**9** the —NH$_2$ signal undergoes only a marginal shift to indicate the non-involvment of the primary amino nitrogen in coordination. The spectra of **5**, **6**, **8** and **9** show a characteristic downfield of the —NH— resonance relative to *fur*$^-$Na$^+$, clearly indicating the coordination of the imino nitrogen to Zn(II), Cd(II), Pd(II) and Rh(III) [1]. The integration ratio of the signals is consistent with the assignments.

Table 4 gives the room temperature magnetic moments and details of the diffuse reflectance electronic spectra of the complexes prepared with transition metal ions. The μ_{eff} value for the Mn(II) complex **1** is as expected *fur*$^-$ *Na*$^+$ *and the metal complexes of fur*$^-$

$\nu_{as}(COO^-)$ [+ ring stretch. vibr.]	$\nu_s(COO^-)$	$\nu_{as}(SO_2)$	δ(COC) of the furane ring	$\nu_s(SO_2)$	$\delta(SO_2)$
1 600 vsb	1 365 m	1 310 ms	1 262 m	1 158 vs	577 s
1 605 vsb	1 298 mb	1 315 m	1 260 m	1 157 vs	580 ms
1 608 vsb	1 295 mb	1 317 m	1 259 m	1 158 vs	579 m
1 612 vsb	1 297 mb	1 316 m	1 261 m	1 162 vs	580 m
1 605 vsb	1 295 m	1 318 m	1 260 m	1 157 vs	583 ms
1 608 vsb	1 297 m	1 321 m	1 261 m	1 159 vs	582 ms
1 604 vsb	1 301 m	1 325 m	1 260 m	1 158 vs	581 s
1 595 vs	1 370 m	1 310 ms	1 262 m	1 160 vs	580 s
1 610 vsb	1 333 m	1 318 ms	1 259 m	1 159 vs	580 ms
1 610 vsb	1 332 m	1 317 m	1 260 m	1 161 vs	589 ms

[c] The far-IR spectrum of **8** shows $\nu(PdCl)_b$ bands at 297 m and 250 m cm^{-1}

ν_{as} antisymmetric stretching; ν_s symmetric stretching; δ deformation mode; *s* strong; *m* medium; *w* weak; *b* broad; *v* very; *n.a.* not assigned

Table 3. *^{1}H-NMR (δ, ppm)*[a,b] *spectral data of fur*$^-$*Na*$^+$ *and the diamagnetic metal complexes of fur*$^-$ *in DMSO-d*$_6$

Comp.	Water[c]	—CH$_2$—	—NH$_2$	Ring Protons	—NH—
fur$^-$Na$^+$		4.56 d	6.34 s	7.00 s, 7.26 s, 7.58 s, 8.38 s	8.58 sb
5	3.40 s	4.46 d	6.30 s	6.86 s, 7.14 s, 7.50 s, 8.46 s	9.18 sb
6	3.42 s	4.55 d	6.38 s	6.96 s, 7.26 s, 7.64 s, 8.56 s	9.34 sb
7	4.26 s	4.56 sb	6.32 s	6.98 s, 7.22 s, 7.56 s, 8.42 s	8.70 sb
8	3.70 s	4.56 s	6.42 s	6.92 s, 7.21 s, 7.64 s, 8.44 s	9.36 sb
9	3.75 s	4.53 d	6.37 s	6.94 s, 7.24 s, 7.62 s, 8.41 s	9.47 sb

[a] *TMS* was used as an internal standard
[b] The spectra were run 20–30 min after dissolution
[c] If the spectra are run immediately after dissolution the water signal is slightly shifted

s singlet; *d* doublet; *b* broad

Table 4. *Solid state magnetic moments and ligand field diffuse reflectance spectral data of the Mn(II), Co(II), Ni(II), Cu(II), Pd(II) and Rh(III) complexes*

Complex	μ_{eff}[a,b] (BM)	Solid state[b] ligand field electronic spectra ($10^3\,cm^{-1}$)			
1	5.90	$^6A_{1g} \rightarrow {}^4T_{2g}(D)$ 27.33	$^4A_{1g}, {}^4E_g(G)$ 24.30	$^4T_{2g}(G)$ 21.83	$^4T_{1g}(G)$ 17.23
2[c]	4.79	$^4T_{1g} \rightarrow {}^4T_{1g}(P)$ 18.69	calc. $^4A_{2g}$ 16.93	$^4T_{2g}$ 7.95	
3[d]	3.24	$^3A_{2g} \rightarrow {}^3T_{1g}(P)$ 23.53	$^3T_{1g}(F)$ 14.08	^1E_g[e] 12.54 sh	$^3T_{2g}$ 9.54, 7.92
4	1.83	d-d 13.51, 9.07 sh	other bands 23.25 sh		
8[f]	dia	$^1A_{1g} \rightarrow {}^1E_g$ 26.81	$^1A_{2g}$ 24.69		
9	dia	$^1A_{1g} \rightarrow {}^1T_{2g}$/CT 34.83	$^1T_{1g}$ 28.01		

[a] Per metal ion

[b] At room temperature

[c] $10\,Dq = 9\,050\,cm^{-1}$; $B = 794\,cm^{-1}$; $\beta = 0.82$

[d] $10\,Dq = 8\,730\,cm^{-1}$; $B = 773\,cm^{-1}$; $\beta = 0.74$

[e] A spin-forbidden band frequently observed in octahedral Ni(II) complexes

[f] The third highest energy spin-allowed transition $^1A_{1g} \rightarrow {}^1B_{1g}$ appears as a shoulder associated with the intense UV maximum above $30\,000\,cm^{-1}$

CT charge-transfer; *sh* shoulder; *dia* diamagnetic

for high-spin $3d^5$ systems; this moment is given by the spin-only term [29]. The symmetry and bonding properties of high-spin Mn(II) complexes cannot be easily considered by ligand field techniques [29, 30]. The spectrum of **1**, however, provides evidence to its octahedral structure and against a tetrahedral stereochemistry in two ways. First, the fact that the characteristic « tetrahedral » reflectance triplet in the 25 000–20 000 cm^{-1} region [31] is not observed indicates octahedrally coordinated Mn(II), and secondly tetrahedral complexes, where the *Laporte* restriction is not so rigid, exhibit spectra with molar extinction coefficients in the range 1–10 $l\,cm^{-1}\,mol^{-1}$ [30]. In the solution spectra of **1** in CH_3NO_2, *DMSO* and ethanol (not included in Table 4) lower values are observed in agreement with an octahedral structure. The μ_{eff} values and the d-d spectra of **2** and **3** are characteristic of an octahedral high-spin stereochemistry [29, 30]. The doublet structure of the $^3A_{2g} \rightarrow {}^3T_{2g}$ transition in the spectrum of the Ni(II) complex is indicative of a *trans* tetragonally distorted octahedral structure [30]; as the symmetry is lowered from O_h to D_{4h} or lower, the $^3A_{2g} \rightarrow {}^3T_{2g}$ transition is split into $^3B_{1g} \rightarrow {}^3B_{2g}$ and $^3B_{1g} \rightarrow {}^3E_g$ transitions. The frequencies of the observed reflectance maxima and the values of the calculated ligand field parameter 10 Dq are in accord with the presence of $[MO_4N_2]$ (M = Co, Ni) chromophores in the solid state [30]. The room temperature μ_{eff} value indicates that **4** is magnetically dilute [29]. Its d-d spectrum is fairly typical of a tetragonally distorted octahedral stereochemistry [30]. The chromophore appears to be CuN_2O_4; several complexes with this chromophore group have a main band near 14000 cm^{-1}, with a shoulder near 9500 cm^{-1} [32]. A square planar structure is assigned for the diamagnetic Pd(II) complex on the basis of its electronic spectrum [30]. The Rh(III) complex **9** is diamagnetic; indeed all the known complexes of Rh(III) are low-spin diamagnetic [30]. The ligand field spectrum of **9** shows two d-d maxima assigned to the two spin-allowed transitions from $^1A_{1g}$ to $^1T_{1g}$ and $^1T_{2g}$, both derived from $(t_{2g})^5(e_g)^1$ [30].

The X-band room temperature ESR spectrum of the polycrystalline complex **4** is typical for a tetragonally elongated structure [33–35] with two g values, $g_{\parallel} = 2.241$ and $g_{\perp} = 2.056$. The average g-value, calculated according to the relation $\langle g \rangle = \frac{1}{3}g_{\parallel} + \frac{2}{3}g_{\perp}$, gives a value of 2.12, which is in agreement with an orbitally non-degenerate ground state [33]. The $g_{\parallel}$ value of **4** is greater than the corresponding $g_{\perp}$ value and, therefore, it has the unpaired electron in the $d_{x^2-y^2}$ orbital [35]. In an axial symmetry the g values are related by the expression $G = (g_{\parallel} - 2)/(g_{\perp} - 2)$, which measures the exchange interaction between Cu(II) centers in the polycrystalline solid. If the value of G is larger than 4 exchange interaction is negligible, while G less than 4 indicates considerable exchange coupling. For **4** the value of G is 4.30 and, thus, polynuclear arrangement can be ruled out [33].

From the overall data presented it is concluded that in all the complexes prepared, except **7**, fur^- acts as a bidentate chelate ligand bonding through one of the carboxylato-O and the imino-N atom. Octahedral structures are proposed for **1**–**6** and **9**. In **1**–**6** the octahedral coordination is completed by two water molecules in *trans* positions to relieve steric hindrance. The presence of three bulky fur^- ligands in **9** appears to have little steric effect; this is not unexpected as the central metal ion has a larger size. The dimeric form $[(fur)PdClClPd(fur)] \cdot 2\,H_2O$ is the most probable for **8**; both chlorides are bridging giving a square planar O(carboxylato), N(imino), Cl^-, Cl^- environment around each Pd(II). Molecular models show that such a dimeric complex could form readily with no large steric strain. The data available for **7** cannot be assigned with certainty to any stereochemistry. The imino N-atom of *fur*$^-$ is not coordinated to Hg(II) as deduced from IR and ^{1}H-NMR data; although it is difficult to decide on a dimeric or polymeric structure, the general insolubility and the X-ray powder pattern of this compound are in agreement with a polymeric unit. A bidentate bridging O(carboxylato), O(carboxylato) coordinating behaviour of each *fur*$^-$ is possibly ascribed; such a behaviour of the carboxylato group has been structurally characterized in several other cases [26]. The work herein seems to indicate that the —SO_2NH_2 group is not coordinated to metal ions, if non-deprotonated, especially in the presence of other powerful donor sites in the ligand system.

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