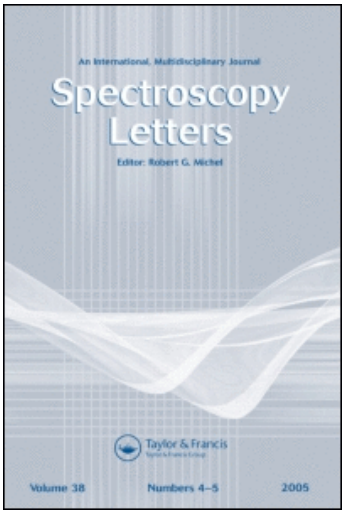

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Synthesis and Spectroscopic Studies on Dirhodium (II) Carboxylate Adducts with Sulfadiazine

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SYNTHESIS AND SPECTROSCOPIC STUDIES ON DIRHODIUM (II) CARBOXYLATE ADDUCTS WITH SULFADIAZINE.

Key words: Rhodium(II) carboxylates, Dirhodium Tetracarboxylates, Tetra-μ-carboxylate-dirhodium(II).

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ABSTRACT

Rhodium carboxylate (acetate, propionate, butyrate, trifluoroacetate, cinnamate and hydrocinnamate) adducts have been obtained with sulfadiazine and characterized by IR, UV-Vis and ^{1}H NMR spectroscopy.

INTRODUCTION

Rhodium formate was the first rhodium (II) carboxylate synthesized. [1] Its structure was determined by X-ray diffraction from the analogous rhodium

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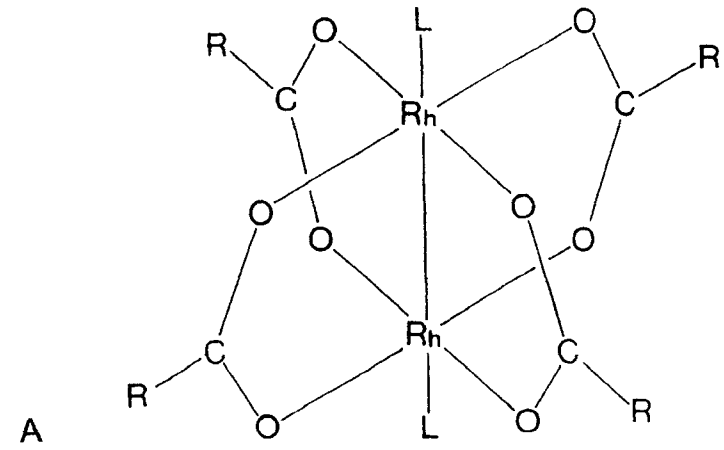

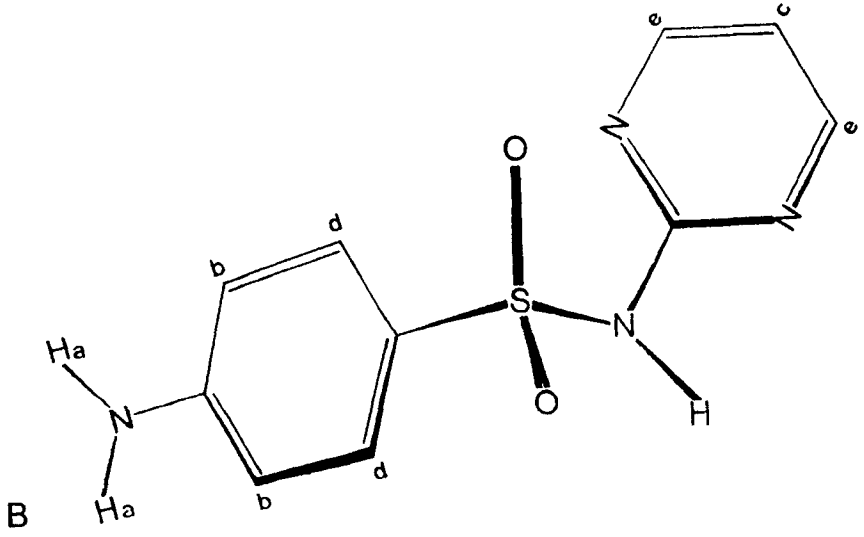

FIG.1. Typical structure of the rhodium (II) carboxylates, where R is an alkylic or arylic radical (A), and sulfadiazine (B).

acetate. It showed a dimeric unity with four carboxylates bridging two rhodium atoms. [2] These compounds exhibit a rhodium-rhodium bond and two axial positions which can be occupied by a wide variety of ligands (L) to form adducts (FIG.1).

The axial positions, unlike the equatorial carboxylates ligands are labile and can be exchanged with relative ease.

Bear *et al.* first reported the antitumor activity of rhodium acetate in 1972. [3] Several articles were published later in an attempt to elucidate the mechanism of action of these compounds. [4-6]

Cotton *et al.* have also contribuited towards the investigation of the electronic configuration and the structure of this class of dimers. [7-10]

We have synthesized some new rhodium carboxylates aiming to get less toxic or more active complexes than those previously studied. [11-13] The best results were obtained with rhodium citrate causing an increase in the survival rate of mice bearing Ehrlich Tumor. [13]

Sulfadiazine (sulfanilamidopyrimidine), SD (FIG.1) has been proposed in the literature as a carrier with a high affinity for tumoral cells. [14] It is thus interesting to coordinate sulfadiazine in the axial positions of rhodium (II) carboxylates to obtain adducts that could present more selective activity on cancerous cells.

In this work, several rhodium carboxylates have been reacted with sulfadiazine to get biadducts which have been characterized by elemental analysis, IR, UV-Vis and ^{1}H NMR spectroscopy.

EXPERIMENTAL

Synthesis of rhodium carboxylates with sulfadiazine

Acetate, propionate, butyrate and hydrocinnamate complexes with sulfadiazine were prepared in the following manner: 50 mg (0.10mmol) of the anhydrous rhodium carboxylate were dissolved in 30 mL of hot methanol and mixed with sulfadiazine (71 mg, 0.30 mmol) under constant stirring to yield a pink solid. After sedimentation, the supernatant was removed with a pipette and the solid was mixed with 30 mL of hot methanol. Then removed after stirring the mixture for some time.

The residue, insoluble in methanol, was washed with anhydrous ether and dried *in vacuo* for 24 hours.

$Rh_2(TFA)_4SD_2$ complex: To 65mg, (0.09 mmol) of rhodium trifluoroacetate dissolved in 25 mL of acetone was added 50 mg (0.19 mmol) of sulfadiazine dissolved in 20 mL of acetone under constant stirring to yield a pink solid. The solvent was evaporated in an air current, the excess of SD was removed by washing with acetone and the product was dried by continuous pumping for 24 hr.

$Rh_2(Cin)_4SD_2$: 50 mg (0.06 mmol) of anhydrous rhodium cinnamate were dissolved in 20 mL of hot acetonitrile and added to 64mg(0.15 mmols) of sulfadiazine in 20 mL of hot acetonitrile under constant stirring giving a pink solid. The solvent was then evaporated and the solid residue washed several times with methanol and maintained in a dessicator over anhydrous $CaCl_2$.

Carbon, hydrogen and nitrogen were determined by the microanalytical laboratory in this Institute on a Perkin-Elmer 2400 CHN. Infrared spectra were recorded on a Perkin-Elmer 180 apparatus using nujol mulls between KBr windows or in KBr discs. Visible absorption spectra were recorded on a Beckman DU-70 spectrometer.

TABLE 1
Analytical data

Compound	Carbon		Hidrogen		Nitrogen	
	Calc.	Found	Calc.	Found	Calc.	Found
$Rh_2(Ac)_4SD_2$	35.6	35.6	3.4	3.5	11.9	12.0
$Rh_2(prop)_4SD_2$	38.4	38.1	4.0	4.2	11.2	11.8
$Rh_2(but)_4SD_2$	40.9	41.0	4.6	4.6	10.6	10.4
$Rh_2(TFA)_4SD_2$	29.0	30.0	1.7	2.3	9.6	9.4
$Rh_2(cin)_4SD_2$	54.6	53.9	3.9	3.8	9.1	8.8
$Rh_2(Hcim)_4SD_2$	51.6	51.0	4.3	4.2	8.6	8.3

AC=Acetate; Pro=propionate; but=butyrate; TFA= trifluorocetate
cin=cinnamate; Hcim= hydrocinnamate.

^1H NMR were recorded on a Bruker AC-200 FT, using deuterated DMF and TMS as an internal reference.

RESULTS AND DISCUSSION

The elemental analysis of the adducts with sulfadiazine suggest the general formula $Rh_2(carboxylate)_4(SD)_2$ for all the compounds (table 1). These compounds are air stable and display low solubility in several common solvents such as water, methanol, ethanol, acetone. They are soluble in acetonitrile, DMSO and DMF.

Infrared Spectra

Figure 2 shows the infrared spectra of sulfadiazine (a), $Rh_2(carboxylate)_4(SD)_2$ (b), and

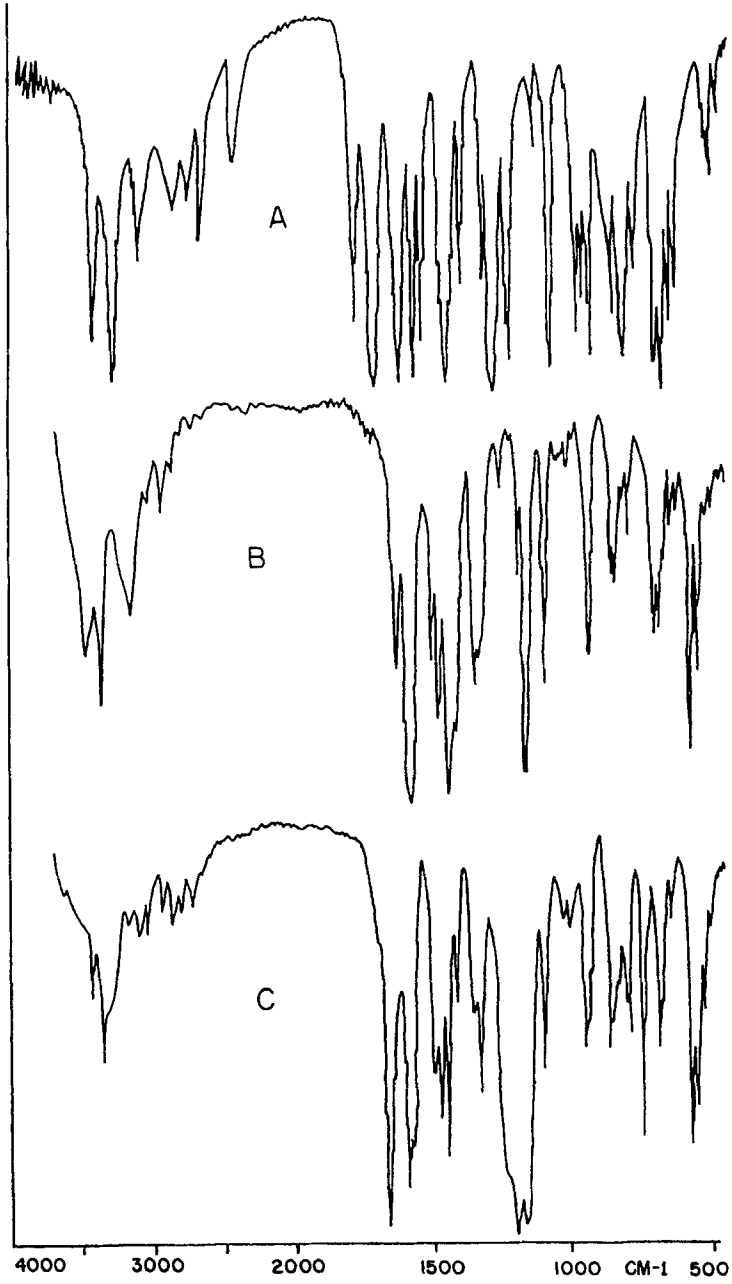

Fig.2. IR spectra of sulfadiazine(a), $Rh_2(carboxylate)_4SD_2$(b), and $Rh_2(TFA)_4SD_2$(c).

TABLE 2
IR data in cm^{-1} for $Rh_2(carboxylate)_4SD_2$

Compound	COO^-		NH_2				SO_2	
	ν_{asym}	ν_{sym}	ν_{asym}	ν_{sym}	ν_{SO_2NH}	δ_{NH_2}	ν_{asym}	ν_{sym}
SD	——	——	3422	3358	3260	1650	1325	1150
$Rh_2(Ac)_4SD_2$	1590	1438	3465	3360	3160	1630	1320	1150
$Rh_2(prop)_4SD_2$	1570	1440	3480	3395	3160	1630	1330	1145
$Rh_2(but)_4SD_2$	1580	1415	3460	3380	3150	1625	1340	1145
$Rh_2(TFA)_4SD_2$	1660	1460	3425	3358	3104	1650	——	1160
$Rh_2(cin)_4SD_2$	1556	1394	3490	3389	3252	1620	1340	1151
$Rh_2(Hcim)_4SD_2$	1580	1410	3470	3370	3160	1620	1335	1150

$Rh_2(TFA)_4SD_2$ (c). The main frequencies of the IR spectral bands are shown in table 2.

By means of IR spectroscopy it has been that the $Rh_2(RCOO)_4$ group preserves its configuration as a dimer after SD coordination since the νasym - νsym (Δ) for the COO group is in the range of 130-170 cm^{-1} except for the trifluoroacetate derivative. These Δ values, lower than 200 cm^{-1}, indicate that a unidentate carboxylate coordination to Rh(II) excluded. The trifluoroacetate adduct with a Δ of 200 cm^{-1} appears to have more ionic character than the others ones.[15]

In most of the compounds, the coordination between SD and Rh appears to take place through a pyrimidine ring nitrogen as infered from the change in the 1580-1200 cm^{-1} region.[16] However, in the case of the trifluoroacetate the coordination should occur through the $-NH_2$ aniline group. This conclusion is based on the fact that in all the adducts, except the rhodium

trifluoroacetate, there is a shift of the N-H stretching of - NH_2 group to higher frequencies when compared with the free ligand. This fact is probably due to hydrogen bonding between the sulfadiazine molecules in the solid state which are broken down after adduct formation. [17-19] A harder acid like rhodium trifluoroacetate, probably prefers to coordinate to the harder base -NH_2 and compensates the shift to higher frequency after the hydrogen bonding breaks down.

Two prominent bands near 1340 and 1160 cm^{-1} are due to the asymmetric and symmetric vibrations of two S=O bonds in the ligand. These vibrations are nevertheless practically unshifted in Rh(II) adducts with sulfadiazine. On the other hand, the low frequency IR reveals the ν asym and ν sym Rh-O at 370 and 450 cm^{-1} respectively for carboxylates and their adducts meanwhile, the ν Rh-N has not beeen observed, presumably because of the existence of a mixing between the Rh-O and Rh-N Stretchings.[20]

This line of reasoning is further reinforced by ^1H NMR spectra (table 3). The spectra (except for the trifluoroacetate) show that the triplet assigned to the *c* proton and the doublet assigned to the *e* proton of SD (7.20 and 8.67 ppm respectively) become complex multiplet in the adducts. This can be explained by the coordination of Rh(II) to one of the two nitrogens of the pyrimidine ring. Which make the *e* protons no longer equivalent. In free SD, the extensive broadening of the δ 6.26 ppm (NH_2) ressonance is probably due to the relaxation of the protons spin by the quadrupole moment of the nitrogen nucleus which is generally taken as characteristic of bonding to the nitrogen protons. [21] In the case of the trifluoroacetate spectrum, this resonance disappears in deuterated DMF solution as

TABLE 3

^1H NMR Chemical Shifts of SD, $Rh_2(prop)_4SD_2$ and $Rh_2(TFA)_4SD_2$ in deuterated DMF.

Protons	SD	$Rh_2(prop)_4SD_2$	$Rh_2(TFA)_4SD_2$
a	6.26 (s)	6.25 (s)	——
b	6.89 (d)	6.89 (d)	6.89 (d)
c	7.20 (t)	—— (m)	7.22 (d)
d	7.90 (d)	7.94 (d)	7.94 (d)
e	8.67 (d)	—— (m)	8.67 (d)

(s)-singlet; (d)-douplet; (t)-triplet; (m)-multiplet

expected for the readily exchangeable acid protons of the $-NH_2$ groups. On the other hand, and since the trifluoroacetate is a good electron withdrawing group, it is likely that the $-NH_2$ proton resonance is shifted to low-field after the amino group coordinates to the rhodium atom.

Electronic Spectra

The colors of the rhodium carboxylates depend on the nature of the donor atom of the axial ligand (L). The O-donors yield green or blue-greenish compounds, the N-donors pink compounds and the S-donors orange complexes.[22]

Our complexes are all pink, which suggest nitrogen coordination to Rh(II). Some exceptions are known to occur as in the cases of the green adducts of 2,2′-bipyridine [23], nitroimidazole [24] and acridine [25] which present coordinated nitrogen.

TABLE 4

Visible spectral absorption data for $Rh_2(carboxylate)_4$ and $Rh_2(carboxylate)_4SD_2$.

COMPOUND	SOLVENT	Absorption (nm)			
		λ_1	ε_1	λ_2	ε_2
$Rh_2(ac)_4$	1	596	——	——	——
	2	582	333	450	188
$Rh_2(Ac)_4SD_2$	1	537	——	——	——
	2	525	250	436	141
$Rh_2(prop)_4$	1	625	——	sh	——
	2	590	296	445	145
$Rh_2(prop)_4SD_2$	1	526	——	——	——
	2	525	248	434	165
$Rh_2(but)_4$	1	635	——	——	——
	2	586	333	sh	——
$Rh_2(But)_4SD_2$	1	534			
	1	525	——	——	——
$Rh_2(TFA)_4$	2	590	233	440	138
$Rh_2(TFA)_4SD_2$	2	525	200	sh	——
$Rh_2(cin)_4$	2	577	233	sh	——
$Rh_2(cin)_4SD_2$	2	525	167	sh	——
$Rh_2(Hcin)_4$	2	586	266	sh	——
$Rh_2(Hcin)_4SD_2$	2	525	333	sh	——

1-Nujol; 2-DMF, dichlorometane.

The visible spectra have two bands, λ_1(635-525 nm) and λ_2 (436-450 nm) (table 4). These compounds show a large dependence of the λ_1 with ligand coordination.

The electronic spectra were recorded in dichlorometane and DMF solutions, behind nujol mulls

and KBr disc. For the complexes $Rh_2(RCOO)_4(SD)_2$, R = acetate, propionate, butyrate, cinnamate, hidrocinnamate and trifluoroacetate, in DMF and dichlorometane solutions, a 100-fold excess of SD was added in order to suppress dissociation of the complexes via the solution equlibrium $Rh_2(RCOO)_4SD_2 \rightleftharpoons Rh_2(RCOO)_4SD + SD$. Under these conditions, the electronic spectra were similar to those obtained for the complexes in the solid state as pressed KBr disks and Nujol mulls.

The band maxima occur in the visible region of the spectrum (635-586 nm) for the carboxylates compounds, while for all the adducts with sulfadiazine this band occurs at 525 nm. These data confirm the SD coordination to Rh(II).

The electronic spectrum of each complex also exhibits a weak shoulder at shorter wavelength at ca 434-450 nm for all the compounds.

The λ_1 band, assigned to the transition π^* (Rh-Rh) $\longrightarrow$ σ^* (Rh-O). [26] Shifts to shorter wavelength upon changing the donor atom from oxygen to nitrogen this is consistent with a d-d transitions following the spectrochemical series. [27] The reason for this possibly lies in the fact that the wavenumbers of the band maxima are sensitive to the extent of admixture of the axial ligand lone-pair orbitals into the molecular orbitals forming the Rh-Rh bond. The energy of the orbital containing the lone-pair eletrons for the SD ligands indeed comes closer to that of the LUMO of the Rh-Rh bond in dirhodium carboxylates resulting in significant mixing of the ligand and the $(Rh)_2$ orbitals. [28]

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