Interaction of Metal Ions with Guanfacine

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In this paper we report the synthesis of a series of transitions metal complexes with guanfacine (GUAF): $[Cu(GUAF)_2](C_6H_5COO)_2$, $[Cd(GUAF)_2](C_6H_5COO)_2$. The given formula was confirmed by elemental analysis. Spectroscopic studies including FT-IR, FT-Raman and EPR spectroscopy were performed in order to establish the conformational and structural changes due to the complexation. Comparison between the FT-IR and FT-Raman spectra of the ligands and the corresponding complexes allowed to predict the coordination geometry. The complexes appear to be tetradentate coordinated and metal to ligand molar ratio is found to be 1:2 for all the compounds.

Keywords: Guanfacine, FT-IR, Raman, metal complexes

Guanfacine hydrochloride (*N*-(aminoiminomethyl)-2,6-dichlorobenzeneacetamide monohydrochloride) is an α 2-adrenergic agonist and has been clinically used as an antihypertensive agent. Guanfacine lowers blood pressure by activation of brain stem receptors with resultant suppression of sympathetic nervous system activity. The crystal structure of the free base form has been reported [7]. Since the guanidine moiety should be protonated under a physiological condition, the conformation of the protonated form of the title compound is more interesting from the pharmacological point of view.

Because of their potential pathological effects, investigation of metal (II) compounds containing aromatic bases [1, 2] or biological ligands as secondary ligands has provoked a pronounced interest recently.

The structure of guanfacine is shown in figure 1.

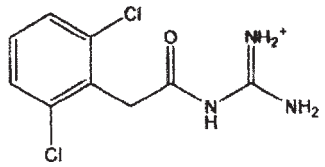

Fig 1. Structure of guanfacine

Guanfacine is able to form colored complexes of distincted spectral characteristic with Cu(II), Cd(II) ions. Such complexes can find important application in the spectrophotometric determination of guanfacine in pharmaceuticals sample.

Experimental part

Materials and methods

Synthesis of the complexes

The Cu(II) and Cd(II) complexes were prepared by adding stoichiometric amounts of hydrated $Cu(C_6H_5COO)_2$, $Cd(C_6H_5COO)_2$ and guanfacine in water. A blue and white powder then preciptated, was filtered and dried over night in the air. The formed complexes are insoluble in water and limited soluble in DMF and dimethilsulphoxide.

The metal to ligand molar ratio is found to be 1:2 for all compounds.

The elemental analyses performed for C, H, N, with respect to the investigated complexes are given in table 1.

The FT-IR spectra of guanfacine, and their complexes with copper(II) and cadmium(II) were recorded in the region 4000-400 cm^{-1} by a Bruker EQUINOX 55 spectrometer, using a diamond ATR unit incorporated into the 'Golden Gate' single reflection diamond ATR accessory. The FT-Raman was performed using BRUKER IFS120HR spectrometer (FRA 106 Raman modul), Nd-Yag laser 1064nm, Ge detector. The EPR spectra of $[Cu(GUAF)_2](C_6H_5COO)_2$ were recorded on an EPR-E-4 spectrometer, operating in the X-band region, with TCNE as reference material, at 300 and 77 K.

Results and discussion

The assignment of some of the most characteristic IR bands of the two complexes and ligand is shown in table 2.

The recorded FT-IR spectra of guanfacine and their complexes combination are shown in figures 2-4 and the Raman spectra of guanfacine, $[Cu(GUAF)_2](C_6H_5COO)_2$ and $[Cd(GUAF)_2](C_6H_5COO)_2$ are shown in figures 5,6.

In order to determine the coordination mode of GUAF in Me-GUAF complexes, the wavenumbers of GUAF in complexes are compared with those free GUAF. When amino nitrogen is involved in coordination, drastic changes occur in amino group vibrational wavenumbers, and when coordination occurs through the oxygen of the carbonyl group, a negative shift of the $\nu_{c=o}$ mode of the coordinated molecule with respect to the free ligand is expected.

Table 1
ELEMENTAL ANALYSIS

Nr.	Formula	M	Colour	Melting point °C	C% Found/ calc.	N% Found/ calc.	H% Found/ calc.
1.	$[Cd(GUAF)_2](C_6H_5COO)_2$	846.78	White	210	52.23/ 52.91	9.71/ 9.92	3.12/ 3.31
2.	$[Cu(GUAF)_2](C_6H_5COO)_2$	797.88	Blue	190	48.04/ 48.12	10.32/ 10.53	3.21/ 3.51

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Tentative Assignment	Guanfacine	$[Cu(GUAF)_2](C_6H_5COO)_2$	$[Cd(GUAF)_2](C_6H_5COO)_2$
		3600w	3620w
ν_{as} NH_2	3350m	3350w	3510m-larg
ν_s NH_2	3210m		3200m
ν_{CH}	3150m	3090w	3100w
ν_{CH}	3000m	3000w	3000m
ν_{CH}	2900m	2870vw	2775m
$\nu_{C=N}$	1700m	1720vw	1730m
$\nu_{C=O}$	1690s	1675m-s	1680m
δ_{NH2}	1570m	1550s	1580m
δ *NH* 2t	1510w	1580w	1600m
ν_{ring}	1450m	1440m	1440m
ν_{ring}	1410m-s	1410m	1385s
ν_{CN}(III)	1350m	1300w	1310m
$\delta_{CH\ ring}$	1170s-m	1180w	1170m
δNH_{2w}	1095m	1065w	1025w
γ_{ring}	935m	930m	915w
δ_{ring}	775m	790w	770w-m
δ_{ring}	740w	700m	740w-m
δ_{ring}	690w	690w	690w
ν_{C-Cl}	650w	670w	675w-m

Table 2
THE ASSIGNMENT OF SOME OF THE MOST CHARACTERISTIC IR BANDS

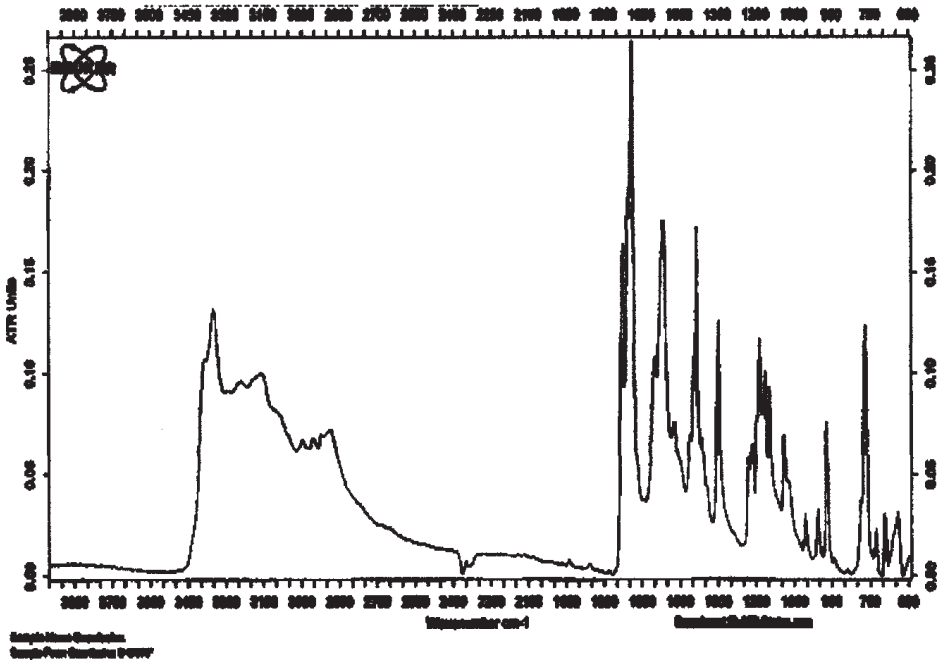

Fig. 2. FT-IR spectra of guanfacine

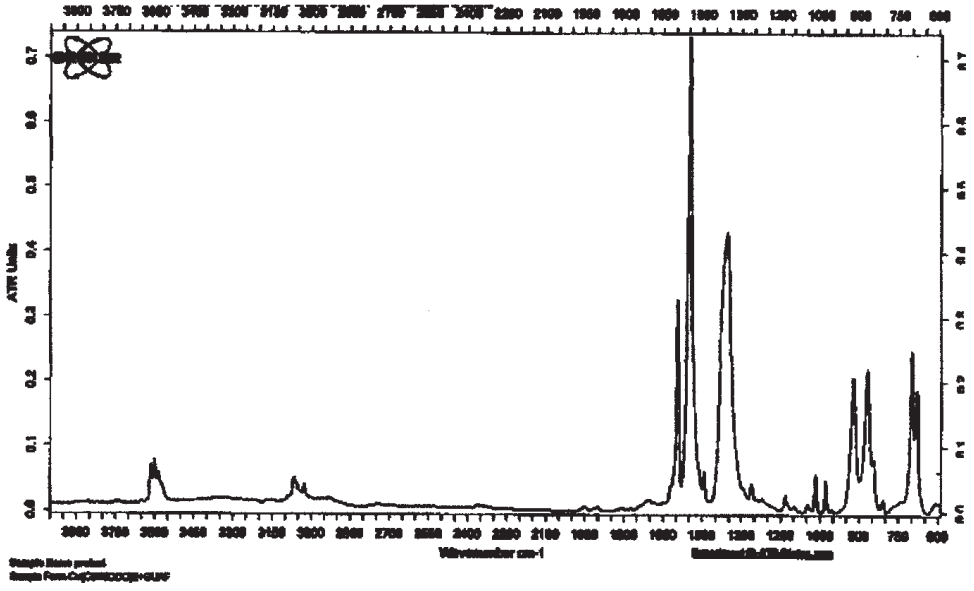

Fig. 3. FT-IR spectra of $[Cu(GUAF)_2](C_6H_5COO)_2$

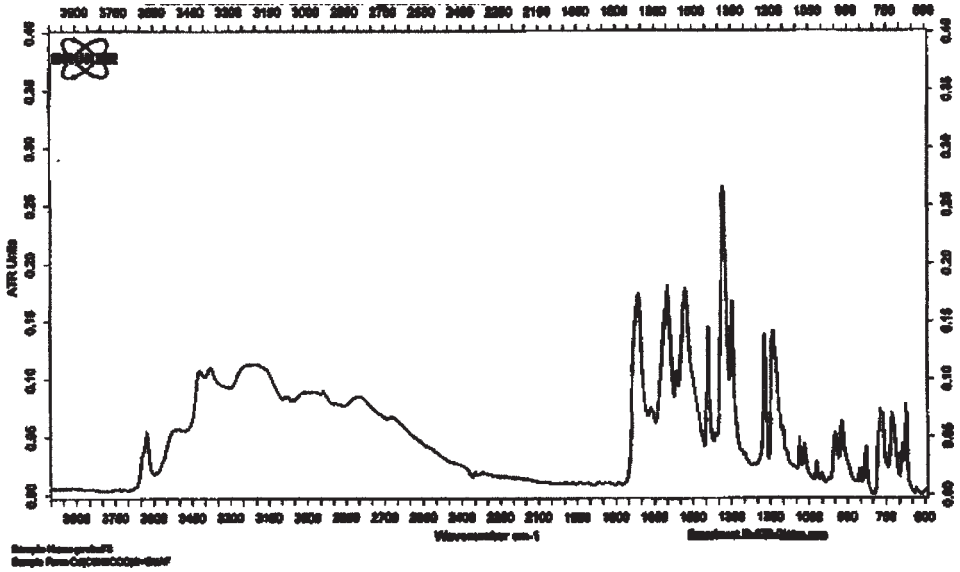

Fig. 4. FT-IR spectra of $[Cd(GUAF)_2](C_6H_5COO)_2$

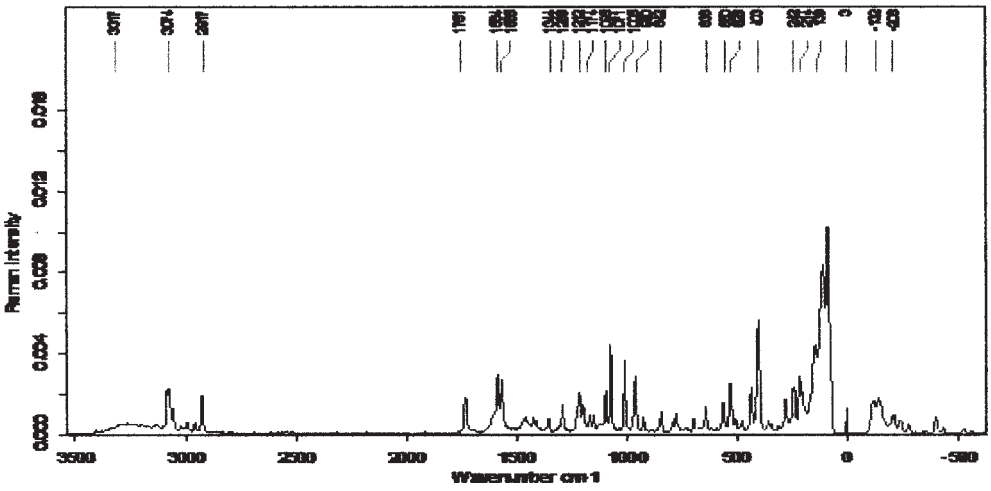

Fig. 5. Raman spectra of guanfacine

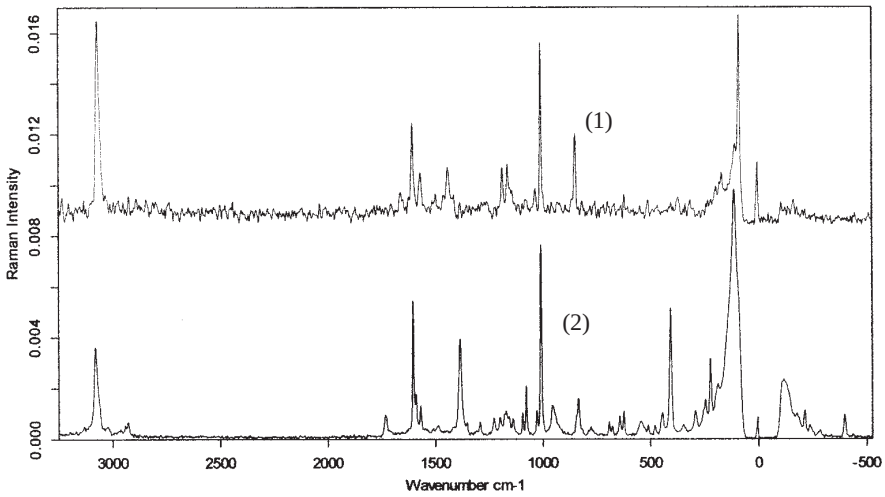

Fig. 6. Raman spectra of $[Cu(GUAF)_2](C_6H_5COO)_2$ (1) and $[Cd(GUAF)_2](C_6H_5COO)_2$ (2)

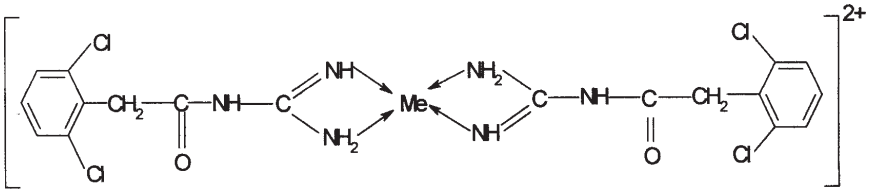

Fig. 7. Structure of the complex combination

In the guanfacine molecule at 3350 cm^{-1} is observed the symmetric valence vibration of the N-H group. At around 3000 cm^{-1} appear the aliphatic and aromatic valence vibrations of C-H group and the vibration of C = N appear at 1700 cm^{-1}.

Comparing this value with the corresponding absorption bands of the complexes of guanfacine shift their stands to higher wavenumbers (Δ = 10-60 cm^{-1}), which means involvement in the formation of the complexes combination of iminic group.

Also the wavenumbers of $\nu_{C=O}$ were not significantly modified , which shows the non-involvement of carbonyl group in complex formation.

The vibrations of δNH_2 and δNH_{2w} (twisting and rocking vibrations from outside the plan) are very different from the ligand. It can be concluded that the NH_2 groups participate in the metal complexation. Then the complexation forms a cycle of four atoms which gives stability for the new combinations.

The low wavenumber region of the Raman spectrum has given information on the strength of the Cu-N and Cd-N bonds in the complex. Analyzing in detail the spectral region of low wavenumbers we observed the apparition of new band characteristics for the metal-ligand bonds. The specific modifications due to the Me- ligand bound are visible around 500 cm^{-1}.

Guanfacine fingerprint:

- $\nu_{(C=O)}$ at 1751 cm^{-1}; -1071 cm^{-1} phenyl trigonal stretching;
- 1055 cm^{-1} phenyl breathing;
- 950 cm^{-1} aliphatic stretching, decrease after the coordination [3,4].

Significant differences between Raman spectra of guanfacine ligand and metallic complexes appear in the range 1100 - 1250 cm^{-1} due to the electronic delocalization of the NH=C-NH_2. After the coordination, two distinct bands are emphasized: at 1212 cm^{-1} from NH=C-NH_2 and 1174 cm^{-1} from NH=C-NH_2. Another major difference appears in the region 200-400 cm^{-1} specific for the bending modes [6,7].

The EPR spectrum recorded from Cu^{2+} ions (electronic configuration [Ar] $3d^9$, fundamental ground state spectral term $^3D_{5/2}$) occurs from resonant centers disposed in an octahedron vicinity, with rhombic symmetry. The values of the spectroscopic splitting factor (g factor) are: g_1 = 2.28, g_2 = 2.12, g_3 = 1.99 [8].

Conclusion

The ligand guanfacine seems to be coordinated with four nitrogen atoms. The complexes appear to be tetradentate coordinated for Cu(II) and Cd(II). The proposed structure is presented in figure 7.

The complexes are crystalline, non-hygroscopic and insoluble in common organic solvents, but to limited extent in DMF and DMSO.

References

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