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NOTES

Synthesis and Characterisation of Divalent Metal Complexes Derived from Phenytoin Sodium

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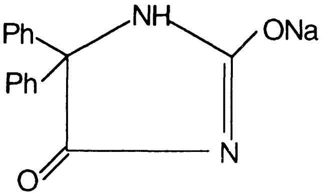
In the present work, we report the synthesis and characterization of the complexes ML_2X_2 [M = Co(II), Ni(II) and Cu(II), L = Phenytoin (5,5-diphenyl-2, 4-imadazolidinedione) and X = H_2O]. Octahedral environment around each metal is proposed by axial coordination of two water molecules.

The study of the stereochemistries and the chemical reactivity of the coordination compounds of the drugs will help to determine the relationship between chemical structure and biological activity of the drugs.[1-5] Phenytoin sodium (5, 5-diphenyl-2,4-imadazolidinedione sodium) (I) is a drug employed in the symptomatic therapy of epilepsy. We have attempted a systematic study of the complexes derived from phenytoin sodium.

All the compounds were prepared by the following general method. To a hot aqueous solution of metal salt, solution of the ligand in the same solvent in ratio 1 : 2 was added. The solution was refluxed for an hour on water-bath. The resulting precipitate was filtered and washed several times with hot distilled water and dried over anhydrous $CaCl_2$ and then at 110°C for an hour.



(I)

Physical and analytical data of the complexes obtained are listed in Table 1. These compounds are microcrystalline, highly soluble in DMF, DMSO and nitrobenzene. The molar conductance values (4.1–7.7 Ω^{-1} in DMF suggest the non-electrolytic nature of these complexes. In electronic spectra of Co(II) complex in DMF three bands are noticed at 9105, 18320 and 21580 cm^{-1} assignable to ${}^4T_{1g}(F) \rightarrow {}^4T_{2g}(F)$, ${}^4T_{1g}(F) \rightarrow {}^4A_{2g}(F)$ and ${}^4T_{1g}(F) \rightarrow {}^4T_{1g}(P)$ transitions respectively which are suggestive of octahedral geometry around the metal ion.[6] Ni(II) complex exhibits bands around 12000, 18000 and 25000 cm^{-1} assigned to $^3A_{2g}(F) \rightarrow {}^3T_{2g}(F)$, $^3A_{2g}(F) \rightarrow {}^3T_{1g}(F)$ and $^3A_{2g}(F) \rightarrow {}^3T_{1g}(P)$ transitions suggesting an octahedral geometry for complexes. Copper complexes show one broad asymmetric ligand field band in the region 3340–15670 cm^{-1} assignable to $^2E_g \rightarrow {}^2T_{2g}$ transition in a distorted octahedral geometry.

TABLE 1
ANALYTICAL AND MAGNETIC DATA OF THE COMPLEXES

Complexes	Decomposition temperature (°C)	Found/(Calcd) % M	C	H	N	μ_{eff} (BM)
$Co(C_{15}H_{11}N_2O_2)_2(H_2O)_2$ (Bluish grey)	161	9.99 (9.86)	60.93 (60.31)	4.78 (4.45)	9.48 (9.37)	4.60
$Ni(C_{15}H_{11}N_2O_2)_2(H_2O)_3$ (Light green)	290	9.71 (9.84)	59.88 (60.33)	4.59 (4.37)	9.29 (9.38)	3.20
$Cu(C_{15}H_{11}N_2O_2)_2(H_2O)$ (Brown)	200	10.45 (10.39)	60.18 (59.98)	4.45 (4.30)	9.48 (9.23)	1.9

The Co(II), Ni(II) and Cu(II) complexes exhibit magnetic moments *ca.* 4.6, 3.20 and 1.9 BM indicating the presence of three, two and one unpaired electrons.

The coordination of ligand is obtained from infrared spectra. The bands in the region 3200–3260 and 1778 cm^{-1} observed due to ν(N–H) and ν(C=O) respectively, in the ligand remained unchanged in all the complexes, thus showing non-involvement of imino or carbonyl groups in chelation. Bands due to ν_{asym}(C=N) and ν_{sym}(C=N) appears near 1575 and 1260 cm^{-1} in the ligand. In the complexes first band shifted to higher wavelength by 40 ± 10 cm^{-1} while the second band due to symmetric vibration of C=N disappeared in the spectra of all complexes. The bands near 2910 and 915 cm^{-1} in ligand assignable to O–Na[7–12] also disappeared in all complexes. Thus it can be inferred that oxygen of position 2 is also involved in chelation by deprotonation of sodium. Two bands appearing near 3400 and 1605 cm^{-1} may be attributed to ν(O–H) and δ(H–O–H) of coordinated water molecules in complexes. In far IR region two bands appearing near 490 and 450 cm^{-1} may be assigned to M–N and M–O stretching vibrations respectively in the spectra of complexes[13–16].

The present study demonstrates that bivalent metal ions are capable of forming stable chelates with phenytoin. Formation of uncharged Co-phenytoin, Ni-phenytoin and Cu-phenytoin species is of particular interest, since it has been shown[17] that such neutral metal drug complexes are essential for effective distribution of the pharmacoactive agents and maintaining the copper balance in plasma.

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