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SYNTHESIS AND CHARACTERIZATION OF COMPLEXES OF MANGANESE (II) WITH 2-(FURAN-2-FORMYLIMINO) BENZIMIDAZOLE AND THEIR PSYCHOPHARMACOLOGICAL DRUG POTENTIAL STUDIES

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ABSTRACT

Complexes of Mn (II) with 2-(furan-2-formylimino) benzimidazole have been synthesized. Characterization has been done on the basis of elemental analysis, conductivity measurements, magnetic studies, IR and electronic spectral studies. Complexes have been found psychopharmacologically more effective in taming, hypnotic activities and possess much higher toxicity as compared to the ligand. Complexes with distorted ºCtahedral geometry with ML_2X_2 stoichiometries have been reported (where $X = Cl^-$, NO_3^-, CH_3COO^- and $C_6H_5COO^-$)

Key words: Synthesis, Characterization, Manganese (II) complexes, 2-(Furan-2-formylimino) benzimidazole, Psychopharmacological activities.

INTRODUCTION

Central nervous system (CNS) depression activity comprising of a muscular hypotonia initially and culminating in complete muscular flaccidity[1] is indicated by benzimidazole. Anticonvulsant properties[2] and paralysing action[3] of some benzimidazoles were reported by Domino and his coworkers. The coordination of the azomethine molecule derived from the condensation of 2-aminobenzimidazole and furan-2-carboxaldehyde (furfural) through the furfural ring oxygen and azomethine nitrogen of the amino group thus hopefully provide a more potent drug for the psychopharmacological disorders.

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EXPERIMENTAL

Material and Methods

2-Aminobenzimidazole was prºCured from Sigma Aldrich Chemical Company (U. S. A) and used as such. Furan-2-carboxaldehyde (furfulal) was purchased from Fluka and was used after redistillation. All other chemicals used were of AnalaR grade or were used after recrystallization.

Ligand preparation

2-Aminobenzimidazole (0.1 mol) and furan-2-carboxaldehyde (0.1 mol) each in 100 mL methanol were mixed together. The mixture was refluxed for 8h on a water bath with anhydrous $CaCl_2$ guard tube at the top of the condenser. The refluxed mass was cooled in a freezing mixture for 2h. The crystals separated were filtered on suction and dried in a hot air oven at 60-70ºC. The yield was approximately 55% (w/w) in the form of brown crystalline powder (m. p. 152-156ºC).

Preparation of complexes

Saturated solution of the ligand in methanol and saturated solution of metal salt in methanol were mixed together and refluxed for 4h on a water bath using anhydrous $CaCl_2$ guard tube at the top of the condenser. The reaction mixture was cooled up to room temperature and then kept in a refrigerator (5-10ºC) for 2h. Separated crystals of the complexes were filtered on suction and dried in a hot air oven at 70-80ºC (yield 40-60% w/w).

Molar conductances of the complexes were measured in solution of the complexes in nitrobenzene on a Sytronics 321 conductivity bridge at room temperature. The IR spectrum of the complexes were recorded on a Perkin-Elmer-577 grating spectrophotometer using KBr pellets in the range 4000-200 cm^{-1}**.** The electronic spectra of all the complexes have been recorded in ethanol at ambient temperature on a CZl Specord UV spectrophotometer in the range 200-1100 nm. The magnetic susceptibility of the complexes was measured at room temperature using Johnson Matthey Alfa products magnetic susceptibility balance. The elemental analysis (CHN) was carried out on a VarioEL CHNO/S elemental analyser. The metal content in the complexes were determined by using atomic absorption spectrophotometer 220 FS

RESULTS AND DISCUSSION

General and elemental analysis

All the synthesized complexes have been found stable in air at room temperature. Fairly soluble in DMSO, DMF and THF but less soluble in methanol and nitrobenzene. Elemental analysis data indicate that in all the complexes the metal-ligand stoichiometric ratio is 1 : 2. Low molar conductivity for all the complexes indicates that the anions have entered into the coordination sphere during the complex formation. The same has been confirmed by the qualitative tests for the anions carried out in aqueous suspensions and ehtanolic solution of the complexes. Elemental analysis data, molar conductance data (10^{-3}M nitrobenzene solution), percentage yield, colour of the complexes and magnetic moment values are shown in Table 1.

Table 1. Elemental and analytical data of complexes of divalent manganese

M. F. (Colour)	Molar conductivity (ohm^{-1} cm^2 mol^{-1})*	Yield (%)	% Analysis, Found (Calc.)				
			C	H	N	Cl	Metal
$C_{12}H_9N_3O$(L) (Dark buff)	3.6	55	68.41 (68.24)	4.3 (4.29)	19.95 (19.89)	-	-
MnL_2Cl_2 (Whitish pink)	6.7	50	52.42 (52.57)	3.30 (3.31)	15.21 (15.33)	12.88 (12.93)	9.88 (10.32)
$MnL_2(NO_3)_2$ (Dirty pink)	6.4	58	47.64 (47.93)	2.98 (3.02)	18.59 (18.63)	-	9.06 (9.93)
$MnL_2(CH_3COO)_2$ (Light buff)	5.8	48	56.32 (56.48)	3.99 (4.06)	14.06 (14.11)	-	9.19 (9.27)
$MnL_2(C_6H_5COO)_2$ (Whitish pink)	6.2	45	63.19 (63.43)	3.89 (3.92)	11.63 (11.68)	-	7.60 (7.63)

L = 2- (Furan formylimino) benzimidazole; *in 10^{-3} M nitrobenzene solution

IR spectral studies

In the IR spectrum of the ligand, the stretching and bending vibrations at 3320, 3150 and 1610 cm^{-1} assigned to $\nu_s(NH_2)$, $\nu_{as}(NH_2)$ and $\delta(NH_2)$ vibrations of the base amino compound 2-aminobenzimidazole were absent[4]. The frequency ν (C = O) corresponding to the aldehydic C = O moeity of the furan-2-carboxaldehyde at 1720 cm^{-1} was also absent in

the spectrum of the ligand. A new sharp band at 1630 cm^{-1} was found in the spectrum of the ligand assignable to ν (C=N) azomethine stretching vibrations[5, 6]. The imino (NH) group stretching frequency at 3210 cm^{-1} of the base compound did not suffer any change except a small change in the band intensity attributable to the polarizing effect of the heterºCyclic aldehydic group due to the condensation.

Comparing the IR spectrum of the ligand with its complexes, the stretching frequencies corresponding to furan ring oxygen and azomethine groups have been shifted to negative side ranging from 30 to 35 cm^{-1} clearly indicating the participation of furyl oxygen[7] and the azomethine nitrogen in coordination[8]. The ν(C=N) and ν(N-H) of imidazole ring at 1580 and 3120 cm^{-1} do not show any appreciable shift indicating that these groups do not participate in the coordination.

In the chloro complexes, medium intensity bands observed in the far IR at 580-520, 440-350 and 330-270 cm^{-1} are assignable to M-O, M-N, M-CI stretching vibrations[9-11] respectively.

In the IR of nitrato complexes, additional sharp bands at ca. 1015-10, ca. 1280-70 and ca. 1435-30 cm^{-1} observed are assignable to ν_2, ν_1 and ν_4 modes of coordinating nitrates ions. The magnitude of separation between ν_4 and ν_1 band is ca. 165-160 cm^{-1}. Hence, coordination of nitrate ion in a unindentate manner is confirmed[12, 13].

In acetato and benzoato complexes, the coordiantaion of X anions with metal has been confirmed by comparing the spectra of metal acetates and benzoate salts with the spectra of respective complexes. Frequencies at ca. 1560-50 and ca. 1425-10 cm^{-1} assignable to ν_{as} and ν_s carboxylic mode[14] of the acetate and benzoate ions (in metal salts) have been found to be shifted to the opposite sides upon complex formation, i. e., ν_{as} shifted to higher side (30-20 cm^{-1}) and ν_s shifted to lower side (30-15 cm^{-1}). This larger difference between the asymmetric and symmetric frequencies in comparison to the uncoordinated acetate and benzoate ion thus confirms the coordination of these ions as unidentate anions through the C-O moiety of their respective carboxylic groups[15].

Magnetic studies and electronic spectra

The magnetic moment values of acetato and benzoato complexes were found to be 5.56 and 5.82 BM. These values suggest the formation of a high spin ºCtahedral complexes with d^5 configuration. In chloro and nitrato complexes, the magnetic moment values were found to be on the lower side (4.87 BM and 5.13 BM)

In the electronic spectra of the complexes, the bands were observed in the region 17430 – 18320, 22460 – 23100 and 25410 – 25600 cm^{-1}, which are tentaivly assignable to $^4T_{1g}(G) \leftarrow {}^6A_{1g}$, $^4T_{2g}(G) \leftarrow {}^6A_{1g}$ and $^4A_{1g}(G) \leftarrow {}^6A_{1g}$ transitions, respectively[16]. The above magnetic moment values[17] and assignments[18] suggest the formation of high spin ºCtahedral complex of Mn (II) with ligand. 10Dq and B values calculated using the Figgis equation indicated considerable metal – ligand overlap resulting in a sufficient covalent character in the metal ligand bonds. ν_2/ν_1 ratio suggests considerable distortion from ideal geometry[19].

Effect of coordination on the drug potential of the ligand

The studies on the central nervous system depressant activity have been done by the prºCedure[20,21], to test the drug potential of the newly synthesized compounds. The study of the complexes in comparison with the ligand and 2-aminobenzimidazole was done on mice by the method of Goodsell et al.[22] and Witkin et al.[23]. The compounds were administered orally and the ED_{50}, PD_{50} and LD_{50} values are shown in Table 2.

Table 2.CNS depressant activity, effect of the treatment of 2-aminobenzimidazole, 2-(furan-2-formylimino) benzimidazole and the complexes on the mice (mucles relaxant activity – oral administration only)

Compound	ED_{50} (Dose mg/kg body weight)	PD_{50} (Dose mg/kg body weight)	LD_{50} (Dose mg/kg body weight)
2-Aminobenzothiazole (4-methyl)	30*	60*	600*
2-Aminobenzimidazole	40	100	900
Azomethine ligand (L)	100	300	1500
MnL_2Cl_2	30	50	300
$MnL_2(C_6H_5COO)_2$	50	80	600

* The values for 2-aminobenzothiazole (4-methyl) were taken from the article of Domino et al[24].

ED_{50} = Effective dose, which induces sleep or unconsciousness in 50% of the mice (The mice recovered to normal state in 4 h after administration)

PD_{50} =Paralysing does, which paralysed 50% of the mice (The mice recovered to normal state after 10-12 h of administration.

LD_{50} = A dose, which is lethal for 50% of the mice (The effected mice were not able to recover to complete normal state even after 12 h).

CONCLUSION

Thus, the evidences obtained from IR, electronic spectra and magnetic measurements suggest a high spin distorted ºCtahedral complexes for manganese (II) complexes with 2-(furan-2-formylimino) benzimidazole as ligand. The four coordination positions are satisfied by two bidentate ligands and the other two positions by two univalent anions. Drug potential studies show that the complexes show higher central nervous system (CNS) depressant activity and they are more toxic as compared to the ligand.

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