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Physico-chemical and Pharmacological Studies of Some Transition Metal Complexes with 2-*cis*-3,7-Dimethyl-2,6-Octadien-1-al

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Acyclic monoterpenoids form complexes with many transition metals. 2-*Cis*-3,7-dimethyl-2,6-octadien-1-al (citral) form complexes with VO(II), Cr(III) and Mn(II). Stereochemistry of the complexes has been studied by physico-chemical methods. Ligand and its metal complexes have been found effective as antiprotozoal, insecticidal and antifungal. The control drugs ampicillin (10 μg/mL) and streptomycin (5 μg/mL) show 22.00 mm and 18.00 mm effective concentration respectively against *E. coli* and 26.00 mm and 24.00 mm against *S. aureus* respectively which is according to NCCLS standard.

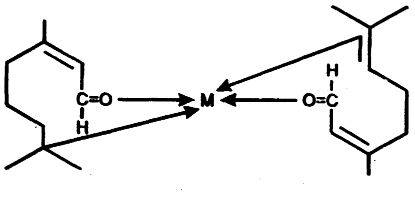
Key words: Transition metal complexes, 2-*cis*-3,7-dimethyl-2,6-octadien-1-al, pharmacology.

INTRODUCTION

2-*Cis*-3,7-dimethyl-2,6-octadien-1-al (citral) is an acyclic monoterpenoid having *n*-allylic bond and an aldehydic group; it shows a great tendency towards complex formation[1–3]. Complexes of metal nitrate and metal chloride with citral have been reported in the present work.

The complexes have been screened for antibacterial and antifungal activities. Citral manganese complex possesses antibacterial activities[4, 5]; at very low concentration the ligand shows positive effects over antifungal activities on Bajra and Jwar seeds.

Biologically active complexes of VO(II), Cr(III) and Mn(II) with citral have been reported. In view of the growing interest in transition metals and their complexes, we report here the synthesis of (transition) metal nitrate and chloride complexes with citral 1 : 2. Stoichiometry of the complexes, stability and thermodynamics of the complexes have been carried out by conductometric, pH-metric, spectrophotometric studies, elemental analysis, infrared spectral measurements and magnetic susceptibility measurements.



EXPERIMENTAL

All the chemicals used were AR grade. Chlorides of chromium and manganese and vanadyl sulphate and citral were used. All these solutions were prepared in absolute alcohol except vanadyl sulphate which was prepared in distilled water.

Conductance studies were carried out on Toshniwal conductivity bridge with a dip type of cell; pH metric studies were carried out on a Phillip pH meter using calomel electrodes.

RESULTS AND DISCUSSION

The complexes are non-hygroscopic and stable at room temperature. They are soluble in DMF and DMSO, slightly soluble in acetonitrile and chloroform and insoluble in water and other common organic solvents. Composition of the complexes formed by the interaction of citral with metal ions was first determined by conductometric titration. The reverse method[6] (citral in cell) was performed. The conductometric titration curves show sharp break at 1 : 2 stoichiometry of the complex, indicating the formation of complex in the solution (Table-1).

TABLE-1
REVERSE CONDUCTOMETRIC AND pH-METRIC TITRATIONS
OF METAL WITH CITRAL

Volume of reagent (in the cell) = 40 mL
Concentration of the reagent = 0.01 M
Concentration of vanadyl sulphate = 0.1 M
Concentration of chromium chloride = 0.1 M
Concentration of manganese chloride = 0.1 M

Complex	Conductance at complexation point	Specific conductance	Molar conductance (mhos)
Vanadyl-citral	0.70×10^{-2}	0.5628×10^{-3}	5.628
Chromium-citral	0.72×10^{-2}	0.5788×10^{-3}	5.788
Manganese-citral	0.51×10^{-2}	0.4100×10^{-3}	4.100

Bjerrum pH-metric tritrations[7] were carried out by the same method as applied before and gave the same results. These titrations were performed by using buffers of pH 4 and pH 9.2 respectively. The lowering in the value of pH was due to complex formation reaction in solution[8, 9].

Elecomagnetic radiations[10] of monochromatic light have been studied in the visible range between 4000 to 7500 Å. The electronic spectrum of citral showed n-π^* and π-π^* transitions. The molar extinction coefficient, *i.e.*, molar absorptivity (Σ) was calculated by Beer's law[11].

Thermal Studies

Stability constants of the complexes were calculated by measuring pH at complexation point. The most convincing correlation regarding the stability of citral complex depends upon pKa value[12]. Citral complexes do not follow the Irving-William's order of stability, *i.e.*, [$Cr^{3+} > VO^{2+} > Mn^{2+}$] (Table-2).

TABLE-2
STABILITY CONSTANT AND THERMODYNAMIC PARAMETERS (FREE ENERGY CHANGE (ΔG°), ENTHALPY (ΔH°) AND ENTROPY (ΔS°)) OF CITRAL COMPLEXES

Metal	Conc.	Temp. T_1...... T_2...... (°C)	pH at Complexation	Stability constant log K_1..... log K_2.....	log β	ΔG°..... ΔG°_1..... ΔG°_2..... in kcal/ mole	ΔH°..... in kcal/ mol	ΔS°..... ΔS°_1..... ΔS°_2..... in kcal/ mole
VO^{2+}	0.001 M	25	1.9	1.800	3.200	–1.486	–16.300	51.38
		35	1.7	1.400		–1.409		49.97
Cr^{3+}	0.01 M	25	5.4	12.800	25.200	–17.455	–16.800	2.19
		35	5.2	12.400		–17.476		2.19
Mn^{2+}	0.01 M	20	2.7	5.400	12.383	–7.240	–64.188	194.36
		30	2.5	6.983		–9.682		176.88

Literature survey[13, 14] reveals greater coordination tendency of ligands having nitrogen, oxygen as well as π-allylic bond. In case of citral, available coordination sites are oxygen and π-allylic bonds.

Thermodyamic parameters, *i.e.*, free energy changes (ΔG°), enthalpy changes (ΔH°) and entropy changes (ΔS°) were calculated by usual relations[15] at 10°C temperature difference and showed that reactions are spontaneous. The negative values of free energy were found in the range of 1.409 kcal/mole to 17.476 kcal/mole and fall in the order $Cr^{3+} > Mn^{2+} > VO^{2+}$ (Table-2).

The enthalpy changes of the reactions show negative values in the range of 16.300 kcal/mole to 64.188 kcal/mole and fall in the decreasing order as $Mn^{2+} > VO^{2+} = Cr^{3+}$ (Table-2).

All the values of entropy were found positive in the range of 2.191 cal/mole to 194.36 cal/mole, *i.e.*, $Mn^{2+} > VO^{2+} > Cr^{3+}$ (Table-2) place at an appreciable speed[16] because the negative value and decrease of free energy are necessary requisites for a spontaneous reaction and the entropy term is favourable for complex formation (Table-2).

Infrared Spectra

The excitation of molecular vibrations and rotations gives rise to absorption bands in the infrared regions[18] of the spectrum. In the IR spectrum of citral about 20 bands appear. In the spectrum of citral we assign sharp band at 1760 cm^{-1} due to aldehyde group[19], weak band at 1655 cm^{-1} due to π-allylic bond[20] and medium sharp peaks at 1460 cm^{-1} may be assigned to methyl group. The shift of 1760 cm^{-1} to lower frequency region or higher frequency region and disappearance or weakening of 1655 cm^{-1} clearly indicates that citral is acting as bidentate ligand (Table-3).

TABLE-3
CHARACTERISTIC FREQUENCIES OF INFRARED SPECTRA (cm^{-1})
OF CITRAL AND ITS METAL COMPLEXES

Compd.	ν(—CHO)	ν(C=C)	δCH_3	ΔCH
Citral	1760 s	1655 wb	1460 s	1415 ms
Vanadyl-citral	disappear	disappear	1450 w	1425 b
Manganese-citral	1780 wb	disappear	1470 b	1420 b

Citral (2-*cis*-3,7-dimethyl-2,6-octadien-1-al) = $C_{10}H_{16}O$
s = sharp, wb = weak band, ms = medium sharp, m = medium,
vs = very sharp, b = broad.

Pharmacological Activity of the Complexes

Complexes of 2-*cis*-3,7-dimethyl-2,6-octa-diene-1-al with vanadyl ion and chromium were found to be hypotensive and active on central nervous system (CNS).

Manganese complexes with this ligand were found active on caradio-vascular system. The compound was hypotensive and studied on mouse and rat.

Chromium complex showed antifungal activity at very small concentration while manganese complex showed antibacterial activity on bacteria and fungi of bread mould, that is, the compound was found to be very effective over ***Rhizobium*** fungi.

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