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Microwave Assisted Synthesis, Spectral and Antibacterial Studies of Complex of 2-Hydroxy-6-methylnicotinic acid with Mn(II)

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ABSTRACT

New transition metal complex of 2-hydroxy-6-methylnicotinic acid ($H_2$6MnicO) $Na_2[Mn(H6MnicO)_2Cl_2]$ has been prepared by microwave irradiation method. 2-Hydroxy-6-methylnicotinate coordinates through O,O-chelation to the transition metal(II) ion to form octahedral complex as shown by FT-IR and UV-Visible spectral analysis. The ligand and its complex have been screened in-vitro for antibacterial studies against Escherichia coli, Staphylococcus aureus and Bascillus subtilis bacteria.

Keywords: 2-Hydroxy-6-methylnicotinic acid, microwave irradiation, antibacterial studies.

I. INTRODUCTION

Last few years there has been intense research on the synthesis of new metal complexes containing pyridine carboxylate derivatives, as many pyridine derivatives possess a diverse array of bioactivities as well as playing crucial roles for physiological functions [1-3]. The studies on the co-ordination complexes of nicotinic acid and its derivatives reveal their antiviral, antifungal, anti-inflammatory, antitumor and antibacterial activity [4-5]. Many nicotinic acid derivatives have known pharmaceutical and physiological properties and are utilized as active principle in antibacterial drugs [6]. 2-Hydroxynicotinic acid can be used for treatment of atherosclerosis and hypoglycaemia, for synthesizing pharmaceuticals and agrochemicals and also for synthesizing new metal complexes having versatile physiological functions [7-8]. 2-Hydroxynicotinic acid undergoes Enol-ketonic tautomerism since the labile H-atom of the OH group at position-2 is in very close proximity to the pyridinic N-atom and can be easily attached to it. The ketonic tautomer is more stable, favoured even in solid state, as it is stabilized by the intramolecular H-bonding between the carboxylic group and ketonic group (at position-2) [9-11]. Dogra studied the effect of solvent and acid or base concentrations on spectral characteristics of 2-Hydroxynicotinic acid under various pH conditions using various spectroscopic methods and quantum chemistry calculations [12]. Nicotinic acid derivatives have versatile coordinating modes and many of these ligands forms 3D metal-organic framework i.e. supramolecular association with metal via hydrogen bonding, π-π interaction and metallophilic interaction. This can be used as a power crystal-engineering tool for constructing and tailoring metal-organic architectures with desirable application [13-14]. 2-Hydroxynicotinic acid can be monodeprotonated to produce 2-hydroxynicotinate anion, depending on the pH, which has multiple coordination sites, namely, monodendate, bridging, N,O-chelation (involving the pyridine nitrogen and the oxygen at position-2, forming a four membered chelate ring), O,O-chelation (involving the COO^- group and the oxygen at position-2, forming a six membered chelate ring [15-17]. Herein, we report the synthesis, spectral

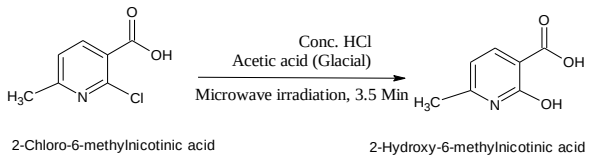
characterization and biological activity of new complex of 2-Hydroxy-6-methylnicotinic acid ($H_26MnicO$) with transition metals Mn(II).

II. MATERIALS AND METHOD

All the chemicals and were of AR grade, purchased from Sigma-Aldrich, and used without further purification. Purity of synthesized ligand and complexes was verified by TLC using different solvent systems. IR spectra are recorded on Bruker Optic Model Alpha (FT-IR) (Zn-Se Optics, ATR) (4000-500 cm^{-1}) using KBr disc. Magnetic susceptibility measurements were carried out on the vibrating sample magnetometer (VSM) model 155 at 5500 Gauss field strength. Microwave assisted synthesis was carried out in domestic microwave oven Model KENSTAR-OM20ACF, 2450MHz, 800W and GMBR (Green Microwave Biochemical Reactor) at GCRC, P.G. Dept. of Chemistry, Govt. Dungar College (NAAC`A` Grade) MGS University, Bikaner, Rajasthan. ECIL Double Beam UV-Visible Spectrophotometer, model UV 5704SS, with quartz cell of 10 mm light path was used for electronic spectra. All biological activities have been carried out with horizontal laminar at BIFR, Bikaner.

Synthesis of $H_26MnicO$ by microwave irradiation method:

Concentrated HCl (3 ml) and glacial acetic acid (3 ml) were added to a 10 ml aqueous suspension of 2-chloro-6-methylnicotinic acid (1.72 g, 10 mmol). This mixture was taken in Erlen-Meyer flask capped with a funnel placed in a microwave oven and irradiated at 200 watt for 3.5 minutes. The reaction was monitored by TLC. After completion of the reaction, the reaction mixture was allowed to attain room temperature and solid separated was filtered. The crude product was recrystalized from redistilled ethanol.



Scheme 1. Synthesis of 2-Hydroxy-6-methylnicotic acid

Synthesis of complex by microwave irradiation method:

To prepare complex, 2.0 mmol (0.08 g) of NaOH were dissolved in 5 ml of distilled water and 2.0 mmol of $H_26MnicO$ were added. The pH value of the solution was maintained to 7-8.5 with saturated aq. solution of NaOH or a suitable acid, respectively. 1 mmol of divalent metal chloride (0.198 g of $MnCl_2.4H_2O$) was added slowly into the basic solution of $H_26MnicO$, with constant stirring. The resulting mixture was irradiated in a microwave oven for 2 to 4 minutes at medium power level (600W) maintaining the occasional shaking. The mixture was cooled to room temperature and poured into ice chilled methanol and dried in vacuum over P_2O_5 [18]. Physico-Chemical Data of prepared ligand and complex are shown in Table 1.

Table 1. Physico-chemical data of ligand and complex

Ligand/ Complex	Colour	M.P. (ºC)	Reaction period (Min.)	R_f value	Yield (%)
$H_26MnicO$	White	253	3.5	(0.74) [b]	65
$Na_2[Mn(H6MnicO)_2Cl_2]$	Brown	255	3.0	(0.80) [c]	68

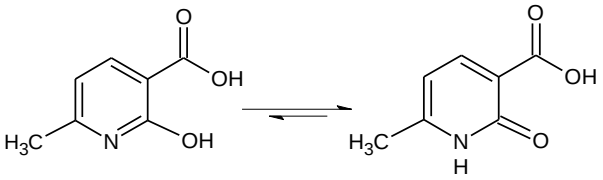
a = Ethanol : Benzene (3:7), b = Ethanol : Benzene (5:5), c = Ethyl acetate : CCl_4 (3:7)

III. RESULTS AND DISCUSSION

IR spectral data:

The significant infrared absorption frequencies for 2-hydroxy-6-methylnicotinic acid and its Mn(II)

complex are reported in the Table-2. The strong band at 1730 cm^{-1}, in ligand, assigned to the ν(C=O) stretch of COOH group, is absent in the spectrum of the complex, which confirms the coordination of respective oxygen atom to the Mn(II) [19]. In complex, the carboxylate form of the monodeprotonated ligand is confirmed by the two bands at 1635 cm^{-1} and 1381 cm^{-1} which are assigned to $\nu_{as}(COO^-)$ and $\nu_s(COO^-)$, asymmetric and symmetric stretch, respectively [20-21]. In case of ligand, another strong band, centred at 1640 cm^{-1}, is assigned to the ν(C=O) stretch of the amide group. The strong and broad band in complex, due to $\nu_{as}(COO^-)$ stretch, can be assumed as a mixed band with ν(C=O) stretch of the amide group [22]. This shifting of the band due to ν(C=O) stretch of the amide group, in form of the mixed band, towards lower frequency in the complex confirms the metal coordination via oxygen atom of the amide group [23-24]. The shift (Δ) between $\nu_{as}(COO^-)$ and $\nu_s(COO^-)$, for the complex, is 254 cm^{-1}, which shows the coordination through COO^- ion in unidentate mode [25-26]. The ν(N-H) stretch, in-plane δ(N-H) bending and out-of-plane γ(N-H) bending (at 3429, 1540 and 581 cm^{-1}, respectively, in the free ligand, are also present in the spectrum of the complex, at almost same range, showing the pyridine nitrogen protonation in ligand as well as in the complexes. It reveals that 2-hydroxyl-6-methylnicotinic acid exists in oxo-form rather than hydroxyl form, as shown in scheme 2. In the IR spectra of the complex absorption of medium intensity, in the region 400-500 cm^{-1}, may be attributed to ν(M-O) stretching [27-28].



2-Hydroxy-6-methylpyridine- 3-carboxylic acid

2-Oxo-1H-6-methylpyridine- 3-carboxylic acid

Scheme 2. Enol-keto tautomers of 2-hydroxyl-6-methylnicotinic acid.

Table 2. Significant IR spectral bands (cm^{-1}) of the ligand and complex

Ligand/ Complex	Carbonyl group		Carboxylate group		Δ	N-H group			ν(M-O)
	ν(C=O)[a]	ν(C=O)[b]	$\nu_{as}(COO^-)$[c]	$\nu_s(COO^-)$		ν(N-H)	δ(N-H)	γ(N-H)	
$H_2$6MnicO	1730 (vs,b)	1640 (vs,b)	-	-	-	3429	1540	581	-
$Na_2[Mn(H6MnicO)_2Cl_2]$	-	-	1635 (vs,br)	1381(s)	254	3430	1556(m)	551	480(m)

a = ν(C=O) stretch of COOH group, b = ν(C=O) stretch of the amide group, c = mixed absorption band of $\nu_{as}(COO^-)$ and ν(C=O) of the amide group, ν_s = symmetric stretch, ν_{as} = asymmetric stretch, $\Delta = \nu_{as}(COO^-) - \nu_s(COO^-)$, vs = very strong, s = strong, m = medium.

Electronic Spectra and Magnetic Moments

The electronic absorption spectra of the complex has been measured in DMSO. Band maxima and corresponding assignments are reported in Table-3. For complex, absorptions bands found in the range characteristic for the octahedral stereochemistry of the complex [29-32]. The observed magnetic moment data of complex also support the expected octahedral geometry [33-35].

Table 3. Magnetic moments and Electronic spectral data of complex

Complex	μ_{eff}(BM)	Electronic Spectral bands $\lambda_{max}(cm^{-1})$	Tentative assignments	Expected
$Na_2[Mn(H6MnicO)_2Cl_2]$	5.85	31496, 27586, 26110, 24680, 18100, 15151	$^6A_{1g} \rightarrow {}^4T_{2g}$,(G) $^6A_{1g} \rightarrow {}^4T_{1g}$,(G) $^6A_{1g} \rightarrow {}^4E_g, {}^4A_{1g}$(G)	Oh

Antimicrobial activities

The antibacterial activity of the compounds against E.coli, S.aureus and B.subtilis were carried out using Muller Hinton Agar media. The activity was carried out using paper disc method is represented in Table 4, which shows that the metal complex has moderate antibacterial activities against S.aureus, E.coli and B.subtilis bacteria, respectively, and showing the maximum clarity of zone.

Table 4. Antimicrobial activity of synthesized compounds

S. No.	Compounds (100 ppm)	Zone of inhibition (in mm)		
		E. coli	S. aureus	B. subtilis
1	$6MH_2nicO$	8.0	5.5	8.0
2	$Na_2[Mn(H6MnicO)_2Cl_2]$	6.5	6.5	8.5

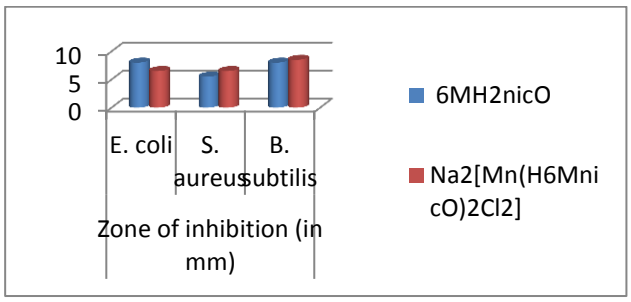


Figure 1. Graphical Representation of Antimicrobial Studies.

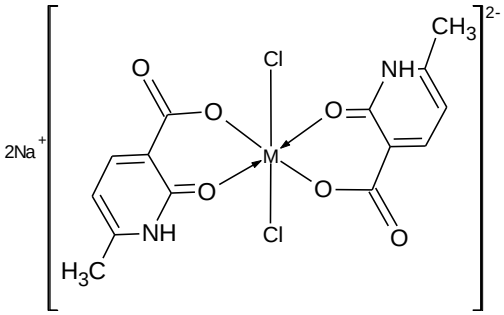


Figure 2. Tentative Structure of the complex, where M= Mn(II).

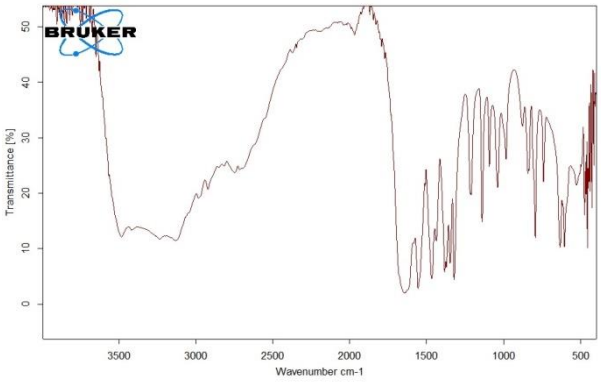


Figure 3. FT-IR Spectrum of Mn(II) complex of 2-hydroxy-6-methylnicotinic acid

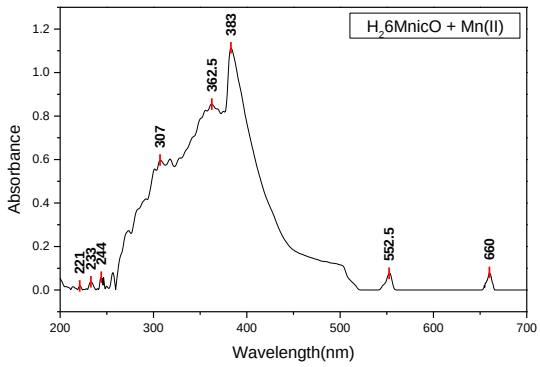


Figure 4. UV-Visible spectrum of Mn(II) complex of 2-hydroxy-6-methylnicotinic acid

IV. CONCLUSION

Synthesis of 2-hydroxy-6-methylnicotinic acid and its complexes with Mn (II) has been carried out by using microwave irradiation successfully with good yield and lesser time. The synthesis of 2-hydroxy-6-methylnicotinic acid by this green method is a first report. A comparative study of IR spectra of free ligand and its metal complex indicates that the ligand

behaves as bidentate, with O,O-chelation mode, via the oxygen atom of carboxyl group and the oxygen atom of the amide group. Infrared spectroscopic analysis also confirms the keto-enolic tautomeric existence of 2-hydroxy-6-methylnicotinic acid. Electronic spectral data, reported herein, suggest that the metal complex probably possess octahedral geometry or nearly octahedral geometry. The antibacterial properties of the ligands and the complex were studied against E.coli, S.aureus and B.subtilis bacteria. The result shows that, the Mn(II) complex has been found to show greater antibacterial activity against S.aureus, E.coli and B.subtilis bacteria, respectively, in comparison to the ligand.

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