International Journal of PharmTech Research
CODEN (USA): IJPRIF ISSN : 0974-4304
Vol.4, No.1, pp 01-04 Jan-Mar 2012

Synthesis and Antimicrobial Activity of Isonitroso 4-methyl-2-pentanone (HIMP) and its dioxime derivative

Dipak J. Garole*[1], V.J. Garole[2] and A.D. Sawant[3]

[1]Department of Organic Chemistry, North Maharashtra University, Jalgoan 425001, Maharashtra, India.

[2]K.E.S. S.P. Jain Jr. College Nagothane, Tal. Roha, Dist. Raigad 402106, Maharashtra India.

[3]Institute of Science, Madam Cama Road Mumbai 400032, India.

Corres.author: drdipakgarole@gmail.com

Abstract: A novel oxime, Isonitroso 4-Methyl-2-pentanone (HIMP) has been synthesized by the reaction of n-pentyl nitrite with 4-Methyl-2-pentanone under acidic conditions. The subsequent treatment of HIMP with $NH_2OH.HCl$ gives 4-Methyl-2,3-pentanedione dioxime (H_2MPDDO). The structures of these compounds have been confirmed by physicochemical and spectral data. A preliminary screening of these compounds for biological activity against various microorganisms has indicated that they are selective growth inhibitors of m-tuberculosis, in particular.

Keywords;- n-amyl nitrite, 4-Methyl-2-pentanone, hydroxylamine hydrochloride, antimicrobial activity**.**

Introduction

The title ligand (HIMP) contains a reactive grouping  , which determines the characteristics reactions of isonitrosoketones (1). Tautomeric oxime compounds are potentially ambient ligands capable of forming metal complexes with different types of structures/ bonding (2). These compounds find several applications as sensitive and selective reagents in the detection and determination of several metal ions. In addition, many of these compounds possess a wide spectrum of biological activity (3). The present paper deals with the preparation and characterization of the title ligand, viz. Isonitroso-4-Methyl-2-pentanone (HIMP), and its derivative, 4-Methyl-2,3-pentanedione dioxime (H_2MPDDO). Various physicochemical techniques such as: element analysis, NMR and IR, have been employed to assign the structures of the two ligands. Their biological activity has been tested to find minimum inhibitory concentrations against various microorganisms.

Experimental:-

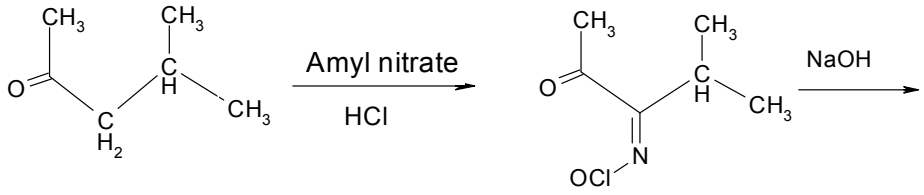
1) Materials and Methods

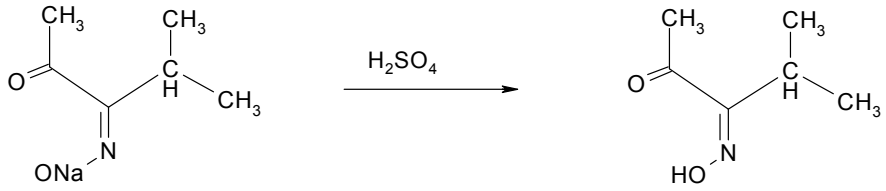
The reactions were carried out with analytical reagent grade chemicals. The ketone (4-Methyl-2-pentanone) and n-amyl alcohol were purchased from M/S Merck Chemicals. The C.P. grade chemicals, whenever used, were purified by standard methods. The organic solvents were redistilled before reuse. A Hoover melting point apparatus was used with open capillary tubes for the determination of melting points, which

were uncorrected. IR spectra were recorded on a Perkin-Elmer 1600 series FTIR spectrophotometer in KBr pellets, ^{1}H NMR spectra were recorded on a Bucker AMX-500 spectrometer in $CDCl_3$. The chemical shifts were reported in □ units relative to tetramethylsilane (TMS) used as an internal standard. The minimum inhibitory concentrations of HIMP and H_2MPDDO were ascertained by using various biological strains, according to the method described elsewhere (4).

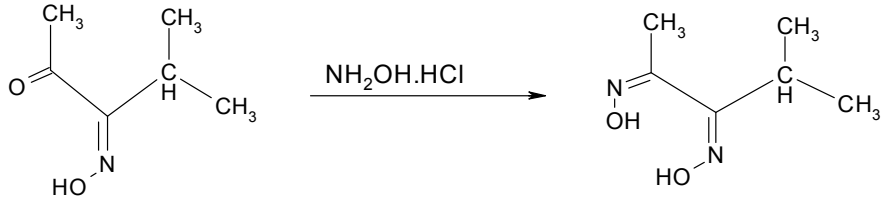
The monooxime HIMP was synthesized by reported method (5) and recrystalized by prior to the synthesis of its dioxime derivative, H_2MPDDO. The latter was synthesized by standard method (6), using an appropriate ratio of $NH_2OH.HCl$ with pure HIMP.

Synthesis of Isonitroso-4-methyl-2-pentanone





Synthesis of 4-Methyl-2,3-pentanonedione dioxime



SCHEME-1.

2) General Method of Synthesis

The freshly prepared n-amyl nitrite (7) was added drop wise to in a methyl isobutyl ketone and small amount of hydrochloric acid with constant stirring and cooling. After complete addition, 33% aq. NaOH solution was added to the mixture and amyl alcohol is formed and was extracted with diethyl ether. The aq. alkaline solution was acidified with dilute sulphuric acid keeping the temperature below 10^0C. The white crystals (HIMP) formed were filtered off and washed with cold water and recrystallised from hot water. A mixture of the purified HIMP and hydroxyl amyl hydrochloride, in 1:1 molar portion was refluxed for 1 h. on water bath. Shiny crystals of 4-Methyl-2,3-pentanedione dioxime (H_2MPDDO) were separated and filtered off, and recrystallized from hot water.

The physical characteristic of HIMP and H2MPDDO is shown in **Table 1.**

Result and Discussion

IR and ^{1}H NMR spectra

Assignments of most important bands (Peaks) are summarized in **Table 2.**

Antimicrobial activity

The two compounds were screened against different strains of gram positive and Gram negative bacteria such as S. aureus, S. typhi, C.albican, A. niger, S. cerevisiae, by using cup-plate method described elsewhere(4). The solvent used was DMF, and the sample concentration was 200-50 □g. The result show good/ moderate activities against the said species. For antituberculosis, the two compounds were screened against m-tuberculosis.

Conclusions

From the physiochemical investigation, the chemical structure proposed as shown in the scheme. Both the compounds revealed good/moderate activities against several microorganisams **Table 3.**

Table 1. Physical characteristics and analytical data of compounds

Compounds	Colour	Yield (%)	Mol. Formula	M.P. (^{0}C)	Elemental analysis (%)found/calc.			
					C	H	N	O
HIMP	white	78	$C_6H_{11}NO_2$	76	58.56 58.32	9.09 9.05	9.75 9.21	22.63 22.60
H_2MPDDO	Yellowish	80	$C_6H_{12}N_2O_2$	114	53.15 53.12	8.86 8.80	17.71 17.75	20.25 20.22

Table 2.Spectral data of compounds

Compound	IR (KBr) Cm^{-1}				^{1}H NMR $CDCl_3$/ TMS (□ ppm)
	V_{NOH}	$V_{C=O}$	$V_{C=N}$	V_{N-O}	
HIMP	3312	1688	1461	962	0.869-0.870 (d-2x CH_3), 2.320 (s-CH_3), 1.948-2.016 (m-CH), 2.450-2.473 10.490 (s=NOH)
H_2MPDDO	3211	--	1450	910	0.856-0.879 (d-2xCH_3), 1.972 (s-CH_3), 1.990-2.060 (m-CH), 2.520-2.530(d-CH_2), 10.540 (s=NOH).

Table 3. Biological activity- MIC (□g/ml) of compounds

Compound	Antibacterial activity		Antifungal activity			Antitubercular activity
	S.typhi	S.aureus	C.albican	A.niger	S.cerevisiac	m.tuberculosis
HIMP	100	100	50	200	200	200
H_2MPDDO	100	10	50	200	200	200

References

1. Haldar B C J, Ind Chem Soc, 1974, 224.
2. Malve S P J, Ind Chem Soc 1997, 74, 316
3. Shetti S N Murty and Tembe G L ,J Ind Chem Soc 1996,73, 91.
4. Hueso-Urena F, Moreno-Carretero M N, Salas-Peregrin J M , Alzarez.de Cienfuegos-Lopez G J, Inorg. Biochem, 1991, 43,17 .
5. More P S & Sawant A D, J Ind Chem Soc,1996, 73,7 .
6. Talwar U B & Haldar B C, Anal Chim Acta, 1967, 39. 264.
7. Vogel A I, A Text Book of Practical Organic Chemistry 3rd ed., Longman's Green and Co. Ltd. 1961.

*****