Acta Poloniae Pharmaceutica – Drug Research, Vol. 59 No. 4 pp. 291–293, 2002

ISSN 0001-6837
Polish Pharmaceutical Society

SYNTHESIS, STRUCTURAL CHARACTERIZATION AND ANTIMICROBIAL STUDIES OF HYDRAZONE DERIVATIVES OF 3–HYDROXYIMINO–5–METHYL–2–HEXANONE

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Abstract: The derivatives of 3–hydroxyimino–5–methyl–2–hexanone oxime have been obtained in good yield by its reactions either with hydrazine hydrate or phenyl hydrazine, respectively. IR and ^{1}H NMR spectral data of these compounds have been discussed. All the newly synthesised compounds have been tested for their biological activity against *S. auerus, S. typhi, C. albicans, A. niger, S. cerevisiae* and *M. tuberculosis* $H_{37}RV$.

Keywords: 3–hydroxyimino–5–methyl–2–hexanone oxime, hydrazine hydrate, phenyl hydrazine, biological activity.

Some α, β–diketone derivatives find applications as drugs regulating the equilibrium of metals in the organisms, and as antidotes in poisoning with heavy metals (1). Hydrazones are, in fact, the azomethines characterised by the presence of a triatomic grouping, >C=N–N<. Many of the physiologically active compounds find applications (2) in the treatment of several diseases, such as tuberculosis, leprosy and mental disorder. Hydrazine hydrate, an anti TB drug, has mainly been responsible for the development of the chemistry of hydrazine (3). Phenylhydrazine has hemolytic and antipyretic action, it is used in manufacturing dyes, and as reagent for sugars, aldehydes and ketones, as well as a stabiliser for explosives (4).

The present paper deals with the synthesis, structural and biological investigations of the derivatives of isonitrosoketones with hydrazine hydrate and phenylhydrazine. The structure of the pure derivatives have been confirmed by elemental analyses, IR and ^{1}H NMR spectra, and by the correlation with standard compounds. The preliminary screening of the ligands obtained for their antibacterial, antifungal and antitubercular activity is reported.

In the present investigation, the synthesis of derivatives of 3–hydroxyimino–5–methyl–2–hexanone (HIMH) is described. These were obtained as a result of the interaction of HIMH either with hydrazine hydrate (5) or phenylhydrazine (6), in 1:1 molar proportions, according to the reported procedures, and were freshly recrystallized.

EXPERIMENTAL

All the reactions were carried out with A.R. grade chemicals. The C.P. grade chemicals, whenever used, were purified by standard methods. The melting points determined were uncorrected. Infrared spectra were recorded on a Perkin–Elmer 1600 series FTIR spectrophotometer, in KBr pellets. The proton magnetic resonance (PMR) spectra were recorded on a Bruker AMX–500 in $CDCl_3$, and chemical shifts were reported in δ units relative to an internal standard, tetramethylsilane (TMS). The elemental microanalyses of C, H, N were carried out with a Thomas and Coleman Analyser–Carlo Erba 1106. Thin–layer chromatographic (TLC) analyses were performed to establish the purity of the compounds on the plates coated with silica gel G (Merck). The minimum inhibitory concentrations (MIC) of the compounds investigated were ascertained by using various biological strains, according to the method described elsewhere (7).

GENERAL PROCEDURE

Synthesis of HMOHOH–

Methanolic solutions of HIMH and hydrazine hydrate, taken in 1:1 molar proportion, were mixed together and left overnight. Then a minimum quantity of cold redistilled water was added to, till pink coloured crystals of 3–hydroxyimino–5–methyl–2–hexanone hydrazone (HMOHOH) were obtai-

Table 1. Physical characteristics and analytical data of the compounds investigated

Compound	Colour	Yield (%)	Mol. formula	M.P. (°C)	Elemental am found			
					C	H	N	O
HMOHOH	yellow	67	$C_7H_{15}N_3O$	84	53.5 (53.50)	9.5 (9.55)	26.7 (26.72)	22.4 (22.48)
HMOHOP	yellowish brown	86	$C_{13}H_{19}N_3O$	141	66.9 (66.95)	8.1 (8.15)	18.0 (18.02)	6.9 (6.88)

Table 2. IR spectral data of the compounds investigated

Compound	$\nu_{=NOH}$	ν_{NH} asymmetric	ν_{NH} symmetric	$\nu_{C=N}$ a	$\nu_{C=N}$ b	ν_{N-O}	$\nu_{C_6H_5}$	$\nu_{C_6H_5\text{-}NH\text{-}N}$
HMOHOH	3120b	3253st	3220s	1465m	1596s	910s	—	—
HMOHOP	3210b	3245s	3225w	1460s	1525s	962s	1615s	750s

s–sharp, st–short, w–weak, m–medium, b–broad; **a**–hydroxyimino group, **b**–hydrazino group

Table 3. NMR spectral data of the compounds investigated

Compound	^{1}H NMR (δ ppm)
HMOHOH	0.896–0.909 (d–2xCH_3), 1.931 (s–1xCH_3), 1.956–2.072 (m–CH), 2.578–2.593 (d–CH_2), 5.479 (NH), 10.29 (NOH)
HMOHOP	0.968–0.981 (d–2xCH_3), 2.056 (s–1xCH_3), 2.141–2.182 (m–CH), 2.656–2.693 (d–CH_2), 7.214–7.354 (C_6H_5), 7.472 (NH), 10.56 (NOH)

Table 4. Biological activity (MIC) in ng/ml of the compounds investigated

Compound	Antibacterial activity		Antifungal activity			Antitubercular activity
	1	2	3	4	5	6
HMQHOH	100	25	50	200	100	200
HMOHOP	100	25	50	200	200	200

1. *S. typhi;* 2. *S. aureus;* 3. *C. albicans;* 4. *A. niger;* 5. *S. cerevisiae;* 6. *M. tuberculosis* $H_{37}RV$.

ned. It was decolourised by using charcoal, which resulted in the yellow coloured crystals.

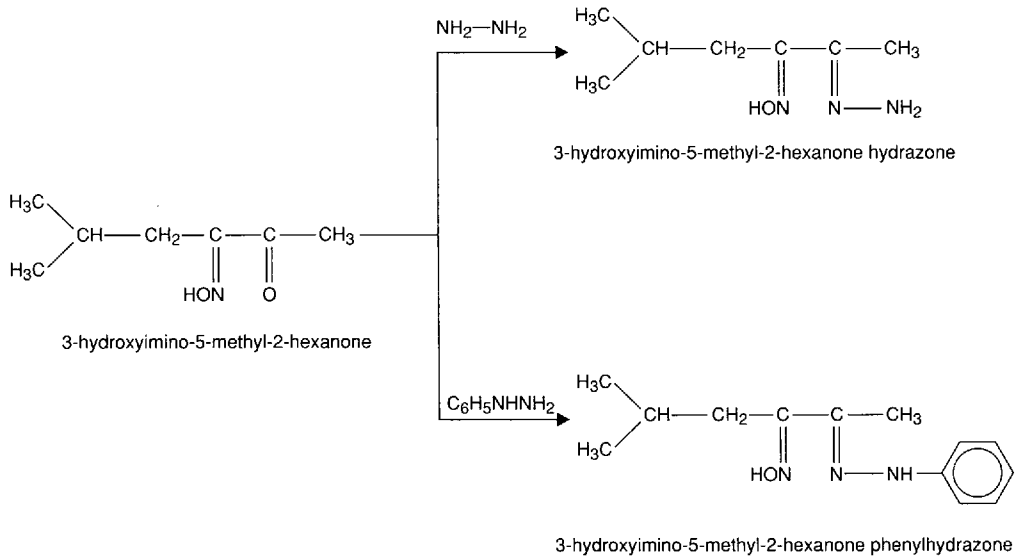
Synthesis of HMOHOP

Methanolic solutions of HIMH and phenylhydrazine, taken in 1:1 molar proportion, were mixed together, and the reaction mixture was refluxed for 1 h. Then, it was poured into cold redistilled water to precipitate out the yellow crystals of 3–hydroxyimino–5–methyl–2–hexanone phenylhydrazone (HMOHOP), which were collected and recrystallized from ethanol.

RESULTS AND DISCUSSION

IR and ^{1}H NMR spectra

The spectral assignments are shown in Table 2 and 3.



Scheme 1.

Antimicrobial studies

Table 4 shows the results of the antimicrobial activity of the compounds investigated. The compounds were assayed for their antimicrobial activity against various microorganisms, such as *S. typhi, S. aureus, C. albicans, A. niger, S. cerevisiae* and *M. tuberculosis* $H_{37}RV$. The solvent used was DMF. It is evident from the preliminary data that the ligands are inhibitory at the screening concentrations, showing either a strong or moderate activity against the aforementioned microorganisms. In the case of antitubercular activity, the both compounds showed the activity at their 200 µg/ml concentration.

CONCLUSION

Based on the physico–chemical, and spectroscopic investigations, the chemical structures for the both compounds have been proposed in Scheme 1.

ACKNOWLEDGEMENT

Authors wish to express their deep gratitude to the Director of the Institute of Science, Mumbai (India) for making research facilities available. Authors wish to thank the Director of the Haffkine Institute of Research, Training and Testing, for providing antimicrobial study.

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Received: 23.01.02