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Synthesis, Characterisation and Antimicrobial Activity of Mannich Bases Derived From Benzhydrazide

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ABSTRACT

The present study deals with the synthesis, structure and antimicrobial properties of Mannich bases derived from Benzyhydrazide. The structures of the synthesized Mannich bases were characterized by spectroscopic methods (IR, H^1-NMR & ^{13}C-NMR) and analytical techniques (elemental analysis, melting point and TLC). The antimicrobial activities of synthesized compounds were also tested against certain organisms (*Staphylococcus aureus, P.aeruginosa, Bacillus spp.* and *Escherichia coli*).

Keywords: Benzhydrazide, Mannich base, Antimicrobial activities.

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INTRODUCTION

Mannich bases have gained importance due to their applications in pharmaceutical chemistry [1,2] and they have several biological activities such as cytotoxic [3], local anaesthetic [4], antimicrobacterial [5], antimalarial [6], antihypertensive [7], antipsychotic, antitubercular [8], and antibacterial [9], activities. Further it has been observed from the literature that there has been a growing interest in the chemistry of aroylhydrazones[10]. Keeping in view of these observations and in continuation of our search for biologically active amino benzylated [11] Mannich bases, we planned to synthesized novel amino benzylated Mannich bases. Several reports are available for the synthesis of Mannich bases using 1^0 and 2^0 amines, aliphatic and aromatic aldehydes and compounds containing active hydrogen atom.

Many compounds such as acetone, substituted acetone, amides like urea, acetamide and semicarbazide were employed as compounds possessing active hydrogen atom but no report is available using benzhydrazide as active hydrogen compound for the synthesis of Mannich base. In the present study, Mannich bases have been prepared by reacting anisaldehyde/ benzaldehyde and benzhydrazide as fixed compounds and varying the amines as diethyl amine, morpholine and N-methyl piperazine.

We thereby report a set of new Mannich bases (I to VI) formed by the three component condensation reaction. The structures of the synthesized compounds have been established on the basis of FTIR, ^{1}H NMR and ^{13}C NMR. The compounds have been screened for the *in vitro* antibacterial activities.

MATERIALS AND METHODS

Experimental

TLC was used to monitor the reactions and purity of the synthesized compounds. The melting points were determined in open capillary tubes and are uncorrected. IR Spectra were recorded in KBr disc on a Shimadzu IR Affinity 1, and ^{1}H NMR & ^{13}C NMR spectra were measured on a Bruker Amx 400 NMR spectrometer using TMS as an internal standard. All Chemical shifts were reported on δ scales. The analytical data of all the compounds are presented in Table -2 and spectral data of all the compounds in

Synthesis of compound I – III

To an ethanolic solution of Benzhydrazide (0.025mol, 3.4 g) and Benzaldehyde (0.025mol, 2.65 ml), the amine (Diethyl amine, Morpholine and N-methyl piperazine) (0.025mol) was added in drops. The reaction mixture was kept on a magnetic stirrer and stirred well at room temperature. The product formed was washed with water and it was recrystallised with ethanol.

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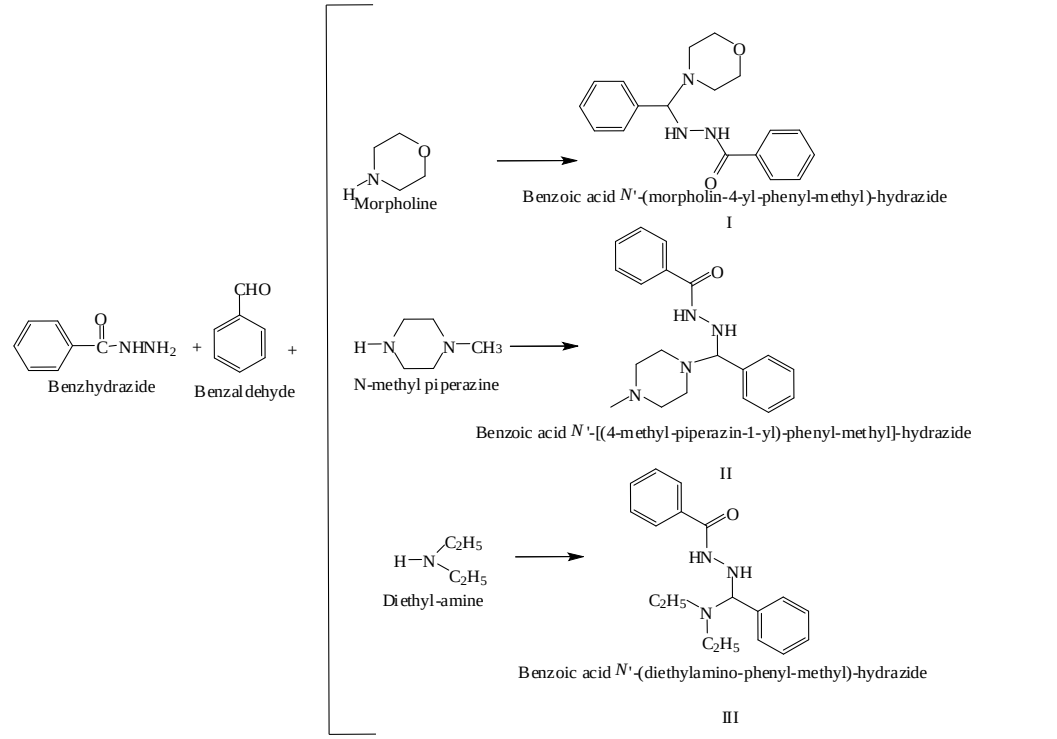

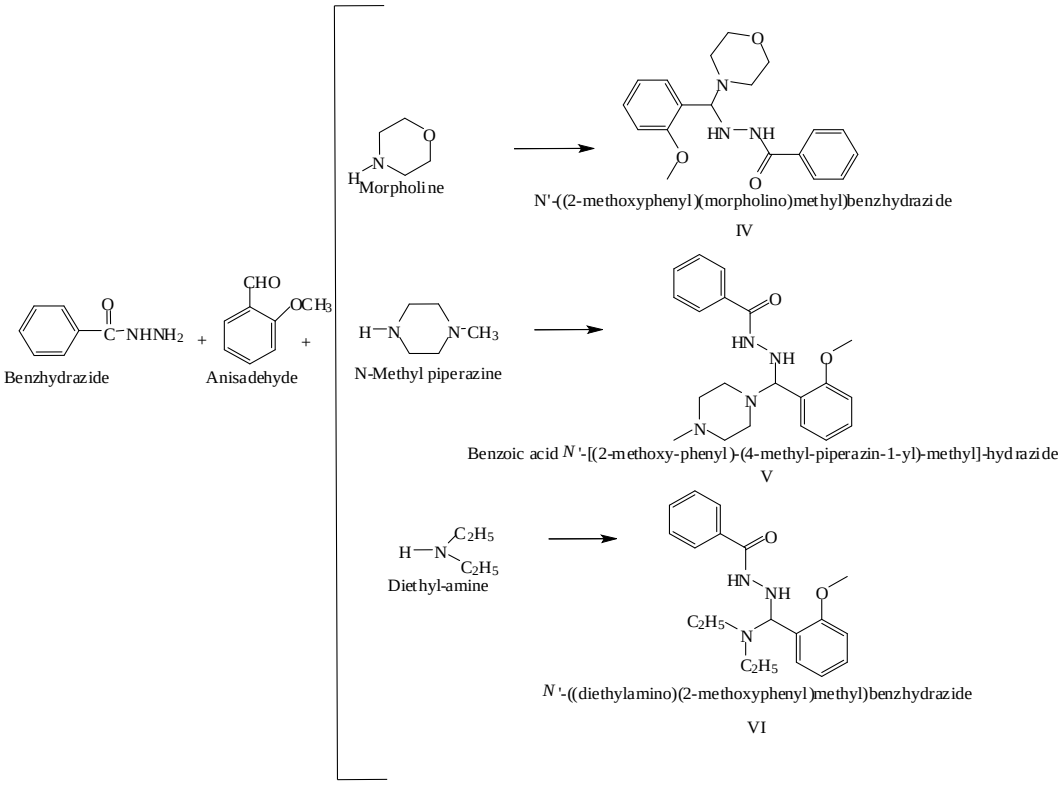

Table -1 Spectral data of compounds I – VI

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Compd	IR (cm^{-1})	^{1}H NMR	^{13}C NMR
I	3123 (N-H) ,2839 (C-H), 1641 (C=O)	δ: 2.37 (m,4H,N-CH_2), 3.67(m,4H,O-CH_2), 5.04 (d,1H,CH), 7.14 (m,5H, Ar), 8.0 (d,2H,NH), 7.95 (m,5H,Ar)	δ: 114.129 (Ar), 51.3 (N-CH_2), 77.8 (N CH – N), 164.9 (C=O)
II	3156 (N-H), 2840(C-H), 1630. (C=O)	δ: 2.27 (s,3H, N-CH_3), 2.46 (m,8H, CH_2), 7.95 (m,5H,Ar), 8.0 (d,2H,NH), 5.04 (d,1H,CH), 7.14 (m,4H,Ar)	δ: 127.5 (Ar), 167.3(C=O), 38.7 (N-CH_3), 50.0 (N-CH_2), 77.5 (N-CH-N)
III	3223 (N-H),2923 (C-H), 1641 (C=O)	δ: 1.02 (t,6H,CH_3), 7.9(m,5H,Ar), 2.0(d,1H,NH), 8.0(d,1H,NH), 5.04(d,1H,CH), 7.14(m,5H,Ar), 2.40 (m,4H, CH_2)	δ: 128.0 (Ar), 167.3 (C=O), 77.6 (CH), 13.7 (CH_3), 41.2 (CH_2)
IV	3128 (N-H),3003 (C-H), 1659 (C=O)	δ: 2.37 (m,4H,CH_2), 3.67 (m, 4H,CH_2), 3.73 (s,3H,CH_3), 5.04 (d,1H,CH), 6.9 (m,4H, Ar), 8.0 (d,2H,NH), 7.44 (m,5H,Ar)	δ: 56.2 (O-CH_3), 114.129 (Ar), 48.66 (N-CH_2), 67.6 (N-CH – N), 164.9 (C=O)
V	3176 (N-H), 3010 (C-H), 1648 (C=O)	δ: 2.27 (s,3H, N-CH_3), 3.73(s,3H,O-CH_3), 2.46 (m,8H, CH_2), 7.95 (m,5H,Ar), 8.0 (d,2H,NH), 5.04 (d,1H,CH), 6.95 (m,4H,Ar)	δ: 127.132 (Ar), 164.9 (C=O), 43.1 (N-CH_3), 56.2 (O-CH_3), 47.55 (N-CH_2), 67 (N-CH-N)
VI	3123 (N-H),2939 (C-H) , 1641 (C=O)	δ: 1.0 (t,6H,CH_3),7.9 (m,5H,Ar), 2.0 (d,1H,NH),5.04 (d,1H,CH),3.73 (s,3H,CH_3),6.94(m,4H,Ar), 2.40 (m,4H, CH_2),7.70(m,5H,Ar)	δ: 128.0 (Ar), 164.9 (C=O), 67.6 (CH), 56.2 (CH_3), 13.4 (CH_3), 44.0 (CH_2)

Table- 2 Analytical Data

Compd	Yield (%)	m.w	m.p	M.F	Elemental analysis. Calculated (found) (%)		
					C	H	N
I	70	311	198	$C_{18}H_{21}N_3O_2$	69.43(69.50)	6.80(6.75)	13.49(13.54)
II	68	324	220	$C_{19}H_{24}N_4O$	70.34(70.30)	7.46(7.50)	17.27(17.18)
III	73	297	210	$C_{18}H_{23}N_3O$	72.70(72.74)	7.80(7.70)	14.13(14.08)
IV	70	341	160	$C_{19}H_{23}N_3O_3$	66.84(66.78)	6.79(6.70)	12.31(12.39)
V	72	354	177	$C_{20}H_{26}N_4O_2$	67.77(67.81)	7.39(7.43)	15.81(15.72)
VI	68	327	182	$C_{19}H_{25}N_3O_2$	69.70(69.65)	7.70(7.60)	12.83(12.73)

Table-3 Antibacterial activity of compounds I-VI.

Test Organisms	Zone of Inhibition (mm)						
	I	II	III	IV	V	VI	Ciprofloxacin
Escherichia coli	20	16	25	27	36	30	27
p.aeruginosa	13	22	15	22	16	19	20
Bacillus spp.	14	14	18	15	15	18	20
Staphylococcus Aureus	8	12	15	26	10	20	22

Synthesis of compound IV – VI

An ethanolic solution of Benzhydrazide, Anisaldehyde and amine (Diethyl amine, Morpholine and N-methyl piperazine) were taken in 1:1:1 mole ratio. Benzhydrazide (3.4 g, 0.025 mol), amine (Diethyl amine, Morpholine and N-methyl piperazine) (0.025 mol) and Anisaldehyde (3.4 ml, 0.025 mol) were mixed under ice-cold condition. The reaction mixture

was kept on a magnetic stirrer and stirred well. The product formed was washed with water and it was recrystallised with ethanol.

Antimicrobial activity

The synthesized compounds (I-VI) were screened for their antimicrobial activities against different strains of gram positive and gram negative bacteria's by disc diffusion method at concentration of 10 µg per ml in DMSO. The zone of inhibition was measured in mm. All the compounds possess appreciable activities against selected organisms. The zone of inhibition values are presented in the Table-3

CONCLUSION

A new series of Mannich base derivatives I-VI were synthesized and screened for antimicrobial activity. Among these, compounds **V** and **VI** have high activity against *Escherichia coli,* compound **II** and **IV** have high activity against *P.aeruginosa* and compound **IV** has high activity against *Staphylococcus aureus* compared with standard Ciprofloxacin, which can be beneficial for further studies. These synthesized compounds could be extended to analyze their various pharmacological activities.

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