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ChemTech

International Journal of ChemTech Research
CODEN (USA): IJCRGG ISSN : 0974-4290
Vol.4, No.1, pp 12-15, Jan-Mar 2012

Synthesis, characterization and antimicrobial activities of salicylaldehyde derivatives

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Abstract: In this work Mannich bases have been prepared by treating morpholine and salicylaldehyde as fixed components and varying a number of compounds possessing active hydrogen atom such as acetanilide, benzoyl hydrazide, semicarbazide and 2-furyl methyl ketone. The structures of the compounds were characterized through analytical (elemental analysis, melting point and TLC) and spectral methods (IR, ^{1}H NMR, ^{13}C NMR and Mass). Further the compounds were screened for the antibacterial and antifungal activities.
Key words: Morpholine derivatives, Mannich bases, Microbial activities.

Introduction

In recent years, Mannich bases have gained importance due to their applications in pharmaceutical industry[1-3] and they have several biological activities such as cytotoxic[4], local anaesthetic[5], antimalerial[7]and antibacterial[8] activities. Literature survey reveals that morpholine derivatives and amide moieties have widely been investigated for various biological activities[9-18] .Many reports are available in the literature for synthesis of Mannich bases using aliphatic and aromatic aldehydes[19-20].Among the aromatic aldehydes, benzaldehyde and substituted benzaldehydes have been extensively used. A few reports are available using heteroaldehyde such as furan and Thiophen-2-aldehydes. Only much lesser attention has been focused on using salicylaldehyde and hence an attempt has been made for the synthesis of Mannich bases using morpholine and salicylaldehyde as fixed components and varying a number of compounds possessing active hydrogen atom such as acetanilide, benzoyl hydrazide, semicarbazide and 2-furyl methyl ketone. All the synthesized compounds are characterized by different physicochemical techniques.Further all the compounds have been screened for biological activities using the organisms such as *B.subtilis, S.aureus,P.aeruginosa, E.coli and C.albicans.*

Experimental

Chemicals

Reagents such as morpholine , salicylaldehyde acetanilide, benzoyl hydrazide, semicarbazide and 2-furyl methyl ketone were of Merck products and were used as such.

The melting point of all compounds was determined in open capillaries and is uncorrected. Purity of the compounds was checked by TLC using Silicagel G coated glass plates with chloroform and ethyl acetate (1:1) as eluent and iodine vapour as visualizing agent and confirmed by retention factor (R_f) values. The IR spectra were recorded in KBr pellets using FT-IR shimadzu IR affinity 1. The ^{1}H NMR and ^{13}C NMR Spectra were recorded on Bruker AMX400 NMR spectrophotometer using TMS as

internal standard and chemical shifts were expressed in ppm. The elemental analysis were performed on Perkin Elmer Series C, H, N & S analyser 2000. Mass Spectra were recorded on a JEOL – 8 x 102.

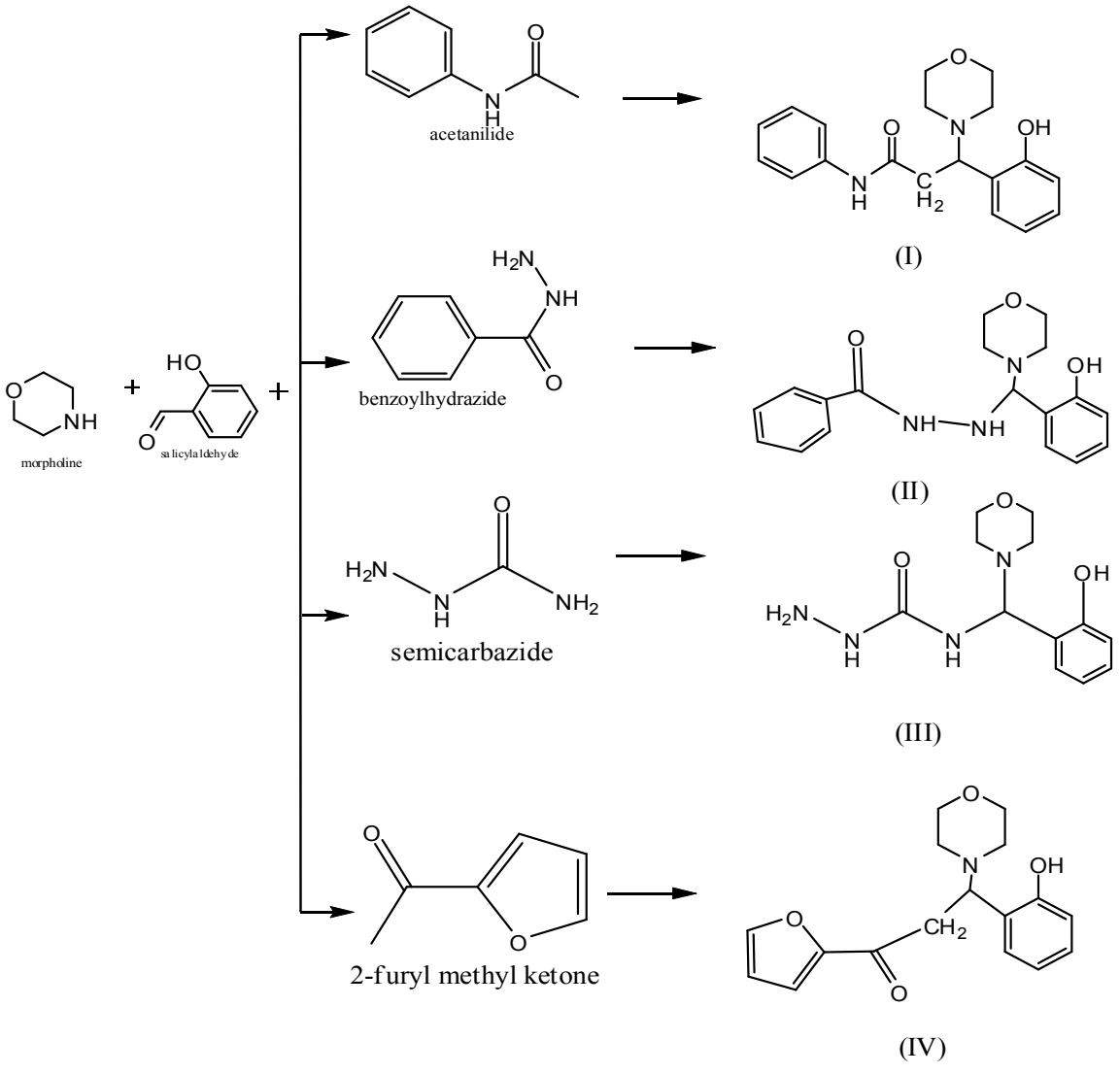
Synthesis of Mannich bases I -IV

In a typical procedure[21], an ethanolic solution of salicyaldehyde, morpholine and acetanilide were taken in 1:1:1 mole ratio. Morpholine 4.4 mL (0.05 mol), acetanilide 6.7 g (0.05 mol) and 6.1 mL of salicylaldehyde (0.05 mol) were mixed and continuously stirred for 3 hours under ice –cold condition. The yellow coloured solid formed was filtered and recrystallised using methanol. The purity of the compound was checked with TLC. The melting point of the recrystallized sample was recorded. A similar technique was employed for the synthesis of all other compounds (**scheme-1).**

Result and Discussion

Morpholine, salicylaldehyde and the compounds such as acetanilide, benzoyl hydrazide, , semicarbazide and 2-furyl methyl ketone in equimolar quantities afford compounds I –IV. All the compounds have been characterized by physical methods (melting point , elemental analysis, molecular weight determination by Rast micro method and TLC) and spectral methods (IR, ^{1}H NMR and ^{13}C NMR and mass). The analytical data of the synthesized compounds are presented in Table-1.

Formation of mannich base



Scheme-1

Table – 1: Analytical Data of the Synthesized Compounds

Compd	Yield (%)	m.f	m.w	m.p(C)	Rf	Elemental analysis (%) : Found (calcd.)			
						C	H	N	S
I	72	$C_{19}H_{22}N_2O_3$	326	127	0.63	6.79 (69.93)	6.55 (6.74)	8.58 (8.28)	-
II	68	$C_{18}H_{21}N_3O_3$	327	187	0.60	66.04 (66.05)	6.24 (6.42)	12.38 (12.84)	-
III	63	$C_{12}H_{18}N_4O_3$	266	212	0.58	56.12 (42.87)	5.96 (6.35)	13.08 (14.04)	-
IV	59	$C_{17}H_{19}N\,O_4$	301	122	0.57	67.76 (67.74)	6.52 (6.47)	20.13 (20.14)	-

3 – (2-hydroxy phenyl)-3-(morpholino)-N-phenyl propanamide (Compound – I):

IR (KBr, ϑmax cm^{-1}): 3467 (Ar-OH, Stretching), 2952 (NH, stretching), 2836 (CH, stretching), 2819 (CH_2, stretching) 1610 (C=O), 1247 (C-N-C). ^{1}H NMR (DMS0)δ:10.2(s,H,OH),8.1 (s,H,NH), 7.62 (m,5H,Ar), 6.7-6.9 (m,Ar),3.5(t,H,CH)3.3 (morpholino OCH_2), 2.6 (morpholino N-CH_2), 2.4 (d,2H,CH_2). ^{13}C NMR (DMSO)δ:156(C=O), 129(Ar CH), 118(Ar), 115(CH), 49(CH_2) , 40,38 (CH_2(O), CH_2(N)). MS : m/z : 326.

N^1 – ((2-hydroxy phenyl) (morpholino) methyl benzohydrazide (compound-II):

IR (KBr, ϑmax cm^{-1}): 3309 (Ar-OH, Stretching), 3056 (NH, stretching), 2855 (CH, stretching), 1612 (C=O), 1205 (C-N-C). ^{1}H NMR (DMS0) δ: 12.1 (s,H,OH) ,7.9 (d,H,NH), 7.6 (m,5H,Ar), 7.3 (q,H,NH), 6.9 (m,Ar), 3.4 (morpholino OCH_2), 2.5 (morpholino N-CH_2),2.2 (d,H,CH). ^{13}C NMR (DMSO) δ: 157 (C=O),126 (Ar-CH), 119(Ar),116(CH),40,38 (CH_2(O), CH_2(N)). MS : m/z : 327.

N–((2-hydroxyphenyl)(morpholino)methyl) hydrazine carboxamide (compound-III):

IR (KBr, ϑmax cm^{-1}): 3501 (Ar-OH, Stretching), 3159 (NH, stretching), 2924 (CH, stretching), 1690 (C=O), 1148 (C-N-C). ^{1}H NMR (DMS0) δ: 11.1(d,2H,NH_2), 10.1 (s,H,OH), 9.9 (t,H,NH), 9.0 (d,H,NH), 8.1 (d,H,CH), 6.9 (m,Ar), 3.4 (morpholino OCH_2), 2.5 (morpholino N-CH_2). ^{13}C NMR (DMSO) :158(C=O), 130 (Ar-CH), 119 (Ar),116 (CH), 40,38 (CH_2(O), CH_2(N)). 165 (C=O) MS : m/z : 266.

1-(furan-2-yl)-3-(2-hydroxyphenyl)-3-morpholino propan-1-one (compound IV):

IR(KBr, ϑmax cm^{-1}): 2297 (Ar-OH, Stretching), 2961 (NH, stretching), 2851(CH, stretching), 2818 (CH_2, stretching), 1610 (C=O), 1247 (C-N-C), 1104 (C-O-C). ^{1}H NMR (DMS0) δ : 10.1 (s,H,OH), 7.0-7.4 (m,Ar), 6.9 (m,Ar), 3.5 (t,H,CH), 3.4 (morpholino OCH_2), 2.3 (morpholino N-CH_2), 2.2 (d,2H,CH_2). ^{13}C NMR (DMSO): 163(C=O, 2-furyl methyl ketone), 156(C=O), 129(Ar-CH), 118(Ar), 115(CH), 49(CH_2), 40,38 (CH_2(O),CH_2(N)). MS : m/z : 301.

Anti microbial activity

The synthesized compounds (I-IV) were screened for antibacterial activity against certain pathogenic bacteria by disc diffusion method at concentration of 10 μg/ ml in DMSO using both gram positive *S.aureus, B.Subtilis*, gram negative *E.Coli*, *P.Aeruginosa* and antifungal activity against *C.albicans*. The zone of inhibition was measured in mm and the activity was compared with Ciprofloxacin 1μg/disc for bacteria, Clotrimazole 10 μg / disc for fungi as standard drugs. The compounds possess appreciable antibacterial activities against selected organisms but lesser when compared with their standards. The zone of inhibition values are presented in Table-2.

Table – 2: Antimicrobial activities of the Synthesized Compounds

Compound	Diameter Zone of Inhibition (mm)				
	Gram Positive		Gram Negative		Fungi
	S.aureus	***B.Subtilis***	***E.Coli***	***P.aeruginosa***	***C.albicans***
I	21	19	17	19	11
II	20	18	16	18	10
III	19	17	18	19	12
IV	23	20	18	20	17
Standard	29	28	30	32	33
DMSO (Solvent)	NI	NI	NI	NI	NI

NI = No Inhibition

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