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Synthesis, characterization and antimicrobial activity of new mannich base

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ABSTRACT

In this report new Mannich bases (2a-2d) were prepared by treating 2,4-dichlorobenzaldehyde, 2-aminopyridine, 2,4-dinitrophenylhydrazine with active hydrogen containing compound such as semicarbazide, thiourea, and acetophenone. The synthesized compounds were characterized by spectral methods (IR, ^{1}H NMR, ^{13}C NMR) and analytical methods like (elemental analysis, melting point and TLC) techniques. Further the synthesized compounds were screened for antimicrobial activities.

Key words: Derivative of 2.4-Dichlorobenzaldehyde, piperazine, Mannich base

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INTRODUCTION

Mannich base is formed by reaction between aldehyde/ketone, primary/secondary amines and compounds containing active hydrogen. Numbers of reports are available for the synthesis of Mannich base using aliphatic, aromatic, substituted aromatic and hetero aldehyde[1-3]. Among the hydrogen containing compounds, phenolic, such as aliphatic ketones, cyclic ketones are extensively exploited. Besides amide moieties are also employed as active hydrogen containing compound. A probe into the literature clearly review that number of reports are available by using urea, substituted urea, semicarbazide, acetophenone as active hydrogen containing compound for the Mannich base synthesis. From the literature it is clearly understood that Mannich base synthesized using amide moieties as hydrogen compound process many biological application[4-9]. It is planned to synthesis Mannich base using 2,4-dichlorobenzaldehyde piperazine 2-amino pyridine and active hydrogen semicarbazide, thiourea.

MATERIALS AND METHODS

(i) Procedure for the synthesis of compounds (2a-2d)

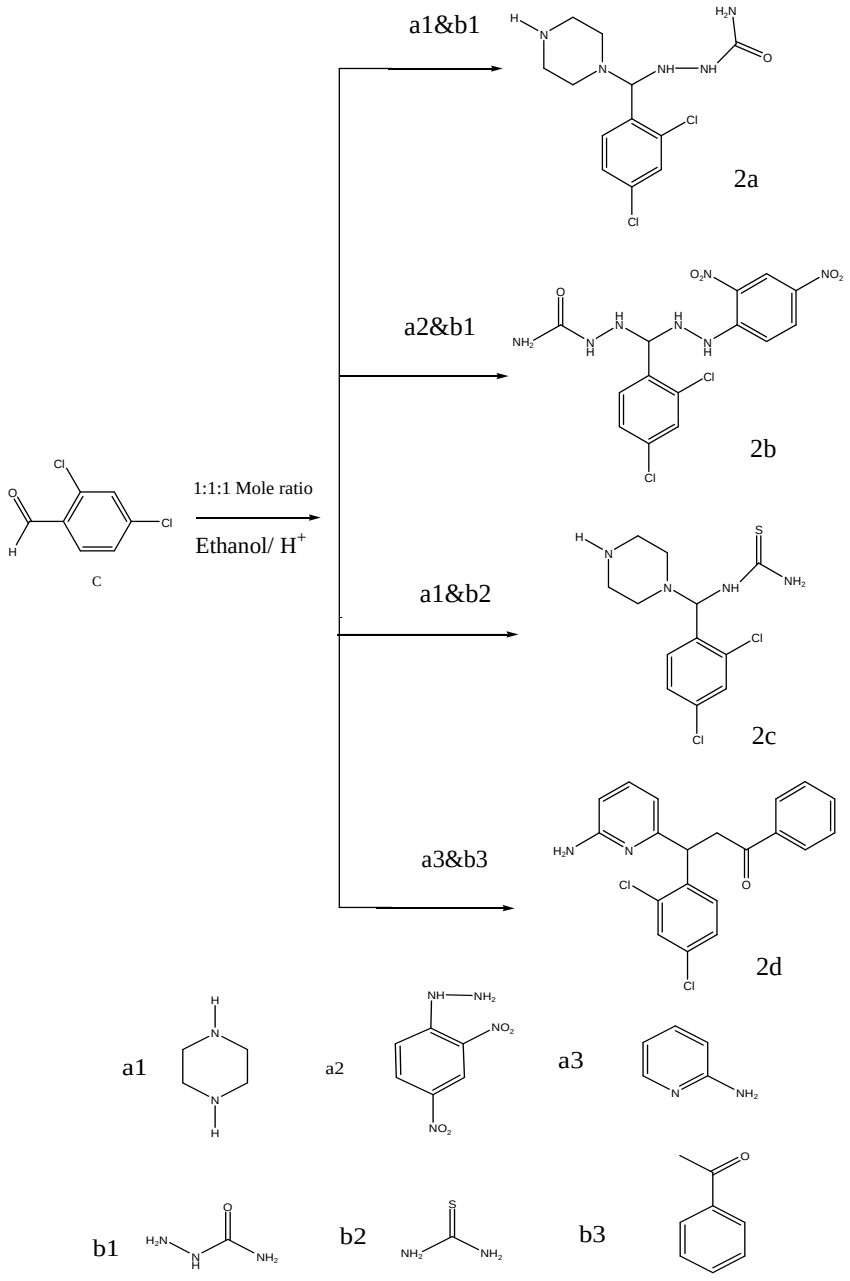
Compound A

An aqueous solution of semicarbazide hydrochloride, few drops of aq NH_3 (0.025 mol, 2.7 g) and Piperazine (0.025 mol, 2.1 g) were added in drops in an ice cold condition. Constants stirrer dissolved in methanol stirred for five minutes. 2.4-dichlorobenzaldehyde (0.025 mol, 4.3g) was added in drops to the above mixture and stirring was continued for two hour. The colorless solution formed was filtered, washed with water and recrystallized from methanol. The above procedure was **(2a-2d)** employed to prepare the remaining compound **(2b-2d)**.

Melting points of the synthesized compounds were determined in one end fused open capillary tube. TLC was used to determine the purity of the compounds. IR spectra were recorded in Ker disc on Shimadzu IR affinity. ^{1}H NMR and ^{13}C NMR spectra were recorded on Bruker AMX 400 NMR spectrometer using TMS as internal standard and DMSO as solvent. Chemical shifts were expressed in ppm. Elemental analysis was performed on Perkin Elmer

Series C, H, N, and analyzed. The antimicrobial activities for the synthesized compounds were carried out by agar-well diffusion method using Ciprofloxacin as standard for bacteria and Nystatin as standard for fungi [10-14]. DMSO was used as solvent and the zone of inhibition was expressed in mm.

Scheme for the synthesis of compounds (2a - 2d)



RESULTS AND DISCUSSION

As outlined in the scheme, 2-((2.4-dichloro-phenyl) piperazine–2-yl)methyl) hydrazinecarboxamide **(2a)**, 2-((2.4-dichloro-phenyl)(2-2.4-dinitrophenyl)hydrazinecarboxamide **(2b)**, ((2.4-dichloro-phenyl)-piperazine-2-yl-methyl)-thiourea **(2c),** and 3-(2.4-dichloro-phenyl)-1-phenyl-3-(pyridine-2-yl amino)-propan-1-one,**(2d)** have been synthesized. The analytical data of the synthesized compounds (**2a-2d)** are given in Table-1. The molecular weight corresponds to the formula of the synthesized compounds. The elemental analysis values are in agreement with the

calculated values. The spectral data of the compounds are (**2a-2d)**. The spectral data confirms the proposed structure. The antimicrobial activities of the compounds (**2a-2d)** are listed in Table-2. It has been observed that compound (**2a)** has high activity against *Streptococcus faecalis* and *Pseudomonas aeruginosa*, compound (**2b)** has high activity against Escherichia *coli* and *Aspergillus Niger* and compound **(2c)** has high activity against *Staphylococcus aureus* and *Candida albicans*as compared with their standards.

Table-I Analytical data of compounds (2a-2d)

Comps	Yield (%)	Molecular weight	Melting point (°C)	Molecular formula	Elemental analysis (%) Found(calculated)		
					C	H	N
I	75	318	160	$C_{12}H_{17}Cl_2N_5O$	70.43(70.50)	6.90(6.8)	14.49(14.59
II	70	430	175	$C_{14}H_{13}Cl_2N_2O_5$	67.77(67.67)	7.49(7.53)	16.81(16.72)
III	65	318	170	$C_2H_{16}Cl_2N_4S$	69.43(69.50)	6.90(6.85)	14.49(14.54)
IV	73	371	180	$C_{20}H_{16}Cl_2N_2O$	68.84(68.70)	6.79(6.70)	13.31(13.39)

2a.2-((2.4-dichloro-phenyl) piperazine –2- y1) methyl) hydrazinecarboxamide
IR (ν cm^{-1}): 3421 (NH_2), 3294 (NH), 2924 (CH), 1653 (CO). ^{1}H-NMR (300 MHz, DMSO-d_6 δ ppm): 7.99 (s, 2H, NH_2), 7.3-7.0 (m, 3H, phenyl ring), 6.1 (s, 1H, NH-CO), 5.2 (d, 1H, CH NH), 2.5-2.3 (m, 8H, Piperazine ring), 2.0 (s, 1H, NHNH), 1.8 (s, 1H, Piperazine NH). ^{13}C –NMR (100 MHz, DMSO-d_6): 165 ($CONH_2$), 136, 135, 134, 131, 130, 127 (Aromatic ring), 85 (-CHNH), 54, 48(Piperazine ring).

2b.2-((2.4-dichloro-phenyl) (2-2.4-dinitrophenyl) hydrazinecarboxamide
IR (ν cm^{-1}): 3469.94 (NH2), 3284.77 (NH), 2924 (CH), 1732.08 (CO). 1H-NMR (300 MHz, DMSO-d_6, δ ppm): 10.8 (s, 1H, NH_2), 8.05-7.4 (m, 3H, phenyl ring), 6.2(s, NHCO), 5.3 (s, 1H, CHNH), 2.1 (s, 1H, NH). ^{13}C-NMR (300MHz, DMSO-d_6, δ ppm): 160.2 (CO), 143, 141, 140, 139.4, 133.4, 133, 130, 129.8, 129.4, 113.8, 70 (CH), (phenyl ring).

2c.((2.4-dichloro-phenyl)-piperazine-2-y1-methyl)-thiourea
IR (ν cm^{-1}): 3244.27 (NH_2), 3094 (NH), 3007.02 (CH). ^{1}H-NMR (300 MHz, DMSO-d_6, δ ppm): 10.5 (s, 2H, CS-NH_2), 7.3-7.02 (m, 3H, Phenyl ring) 5.3 (s, 1H, -CH-Piperazine ring) (-CH_2-O-CH_2-), 2.35 (m, 4H, -CH_2-N-CH_2-), 2.2 (s, 1H, NH). ^{13}C-NMR (300 MHz, DMSO-d_6, δ ppm): 182.4(CO) 135, 134.7, 133.5, 131, 128, 127 (Aromatic ring), 70 (CH), 71.5(-CH_2-O-CH_2-), 52.2 (-CH_2-N-CH_2-), (300 MHz, DMSO-d_6, δ ppm).

2d.3-((2.4-dichloro-phenyl)-1-phenyl-3-(pyridine-2-yl amino)-propan-1-one
IR (ν cm^{-1}): 3431 (NH), Aliphatic CH (2922 Cm^{-1}), 1658 (CO). ^{1}H-NMR: (300 MHz, DMSO-d_6, δ ppm) 8.1-7.8 (m, 4H, Pyridine ring), 7.7-7.4 (m, 5H, Phenyl ring), 7.6-7.0 (m, 3H, 2, 4 dichloro phenyl ring), 4.8 (t, 1H, CH) (d, 1H, NH), 3.2 (d, 2H, CH_2). ^{13}C-NMR: (300 MHz, DMSO-d_6, δ ppm) 190(CO), 152, 142, 134, 132, 126, 120 (2, 4-dicholropheyl ring), 158, 150, 138, 118, 107 (Pyridine ring), 136, 133, 128, 127 (Phenyl ring), 72 (CH_2), 55 (CH).

Table-2 Data of antimicrobial activity of compounds (2a-2d)

Comps	Zone of inhibition(mm)					
	Gram positive bacteria		Gram negative bacteria		Fungi	
	Staphylococcus aureus	*Streptococcus faecalis*	*Escherichia coli*	*Pseudomonas aeruginosa*	*Candida albicans*	*Aspergillus nigar*
I	20	22	20	20	22	23
II	19	23	19	19	20	19
III	21	19	20	18	18	20
IV	19	24	22	20	18	19
Standard	25	30	28	26	22	24
DMSO	NI	NI	NI	NI	NI	NI

Antimicrobial activities
The antimicrobial activities for the compounds **(2a-2d)** were carried out by ager well diffusion technique. The compounds were tested against gram positive bacteria (*S.aureus* and *S.faecalis)*, gram negative bacteria (*E. coli* and *P. aeruginosa*) and fungi (*Candida albicans* & *Aspergillus Niger*). Discs impregnated with known concentration of compounds were placed on agar plate that has been inoculated uniformly over the entire plate with a culture of the micro organism to be tested. The plate was incubated for 24 hours at 37 °C. During the period, the compound diffuses through the agar and prevents the growth of the organism. Effectiveness of the susceptibility is proportional

to the diameter of zone of inhibition. The zone of inhibition was measured in mm and the activities were compared with Ciprofloxacin 5 µg/disc for bacteria and Nystatin100 units/ager well for fungi as reference standard. It has been found that the compounds possess appreciable antimicrobial activities against selected organism.

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