

Novel Synthesis and Characterisation of 7-[Substituted Phenyl Amino] 5-Methyl 1,4 Benzodiazepines

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Abstract: Now a days benzodiazepines compounds have attracted great attention of chemist due to the interesting properties associated with several pharmacological and industrial activities. In present work, a novel series of benzodiazepines were synthesized in good to excellent yield via cyclocondensation 1- N substituted phenyl carboxamido propane-2-one with benzene diamine. This method is easy, rapid and user friendly and without use of any catalyst. Synthesized compounds were eco-friendly. Completion of the reaction was confirmed by thin layer chromatography technique. Elemental analysis, mass spectroscopy and FT- IR spectroscopy were used to characterise the prepared compounds. Antibacterial activities of the synthesized compounds were screened against standard strains of Gram positive and Gram negative bacteria using the Agar plate diffusion technique. Most of the studied compounds showed promising activities against different strains of Gram positive and Gram negative bacteria.

Keywords: 1- N substituted phenyl carboxamido propane-2-one, benzene diamine, benzodiazepines, antibacterial activity, etc.

I. INTRODUCTION

The chemistry of heterocyclic compounds plays an important role in medicinal chemistry. Complex Organic compounds like benzodiazepines 1,2 shows diverse properties, easily accessible path and wide range of biological activities. Benzodiazepines and its derivatives have interesting potential in the field of pharmaceuticals 3-7. Literature survey shows properties of diazepines in biological properties such as anti inflammatory, antibacterial, analgesic, antifungal, antiviral, antibacterial, CNS depressant, potent local anaesthetics etc 8-13. Keeping in view the importance of heterocyclic compounds that synthesized according to Paal- Knorr synthesis. The newly synthesized compounds were screened for the anti microbial activity against gram positive and Gram negative strain.

MATERIALS AND METHODS

All chemicals used for the synthesis are of analytical grade. H NMR spectra were recorded on Bruker Avance II 400 NMR spectrometer. IR spectra were recorded by using Affinity - 1 FT IR spectrophotometer. Melting points were determined by using INDO Melting Point M-AB- 92 apparatus and were uncorrected. All the reactions were monitored by the thin layer chromatography. The crude compounds were purified by recrystallization with ethanol. Mass spectra were also recorded.

EXPERIMENTAL:

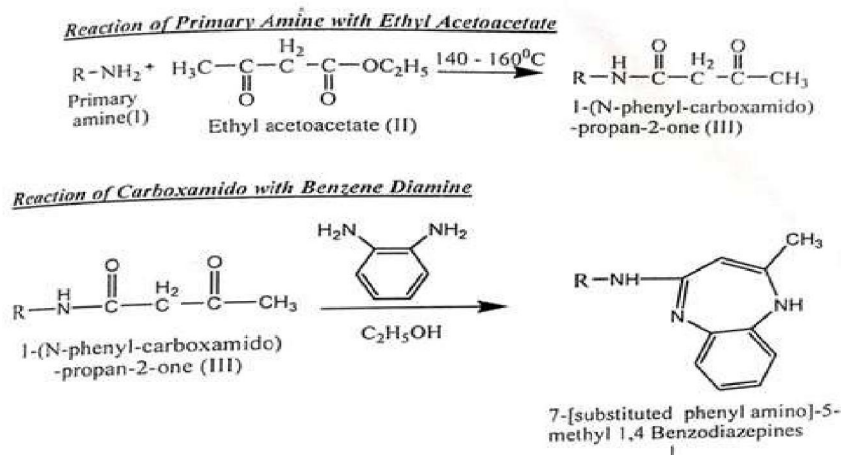
Section A: synthesis of 1- N substituted phenyl carboxamido propane-2-one

An equimolar mixture of substituted primary Amine and ethyl acetoacetate in ethanol was refluxed for 6 to 8 hours. Reaction mixture was cooled and poured on to crushed ice while stirring continuously. Resultant solid was filtered and washed thoroughly with cold water. Dried and purified by recrystallization with ethanol to form 1- N substituted phenyl carboxamido propane-2-one.



Section B: Synthesis of 7-[substituted phenyl amino] 5-methyl 1,4 Benzodiazepines

1- N substituted phenyl carboxamido propane-2-one was refluxed with O- benzene diamine in methanol as a solvent for 2 to 3 hours. After refluxing, the reaction mixture was allowed to cooled and pour it on to crust ice. Crystals of 7-[substituted phenyl amino] 5-methyl 1,4 Benzodiazepines were obtain. These were recrystallised with ethanol. Similarly substituted benzodiazepines also synthesized.



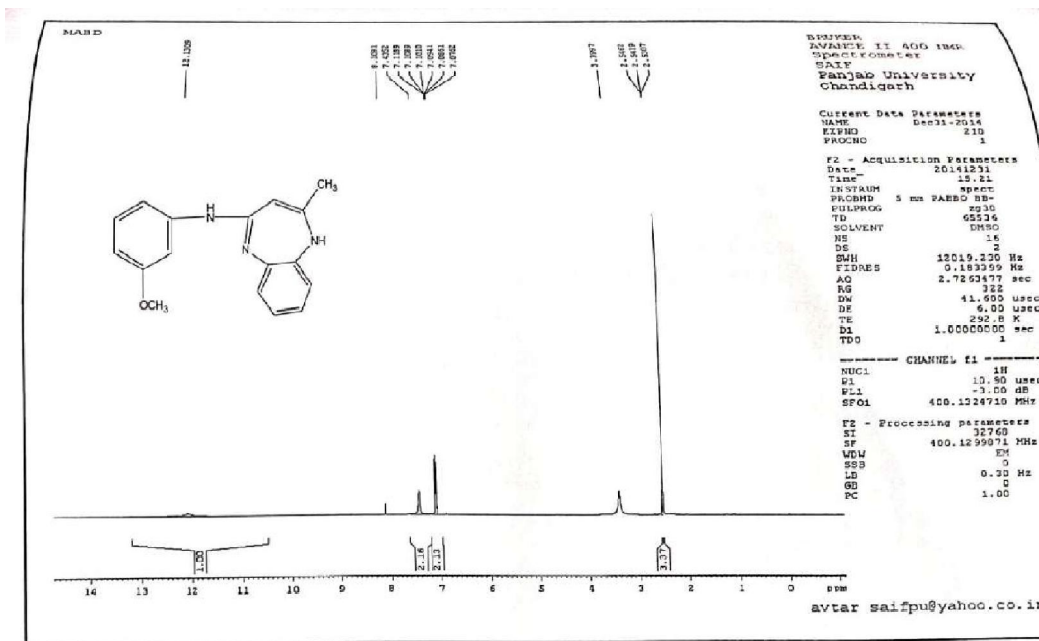
EXPERIMENTAL ANALYSIS:

Substituted benzodiazepines were synthesised and their elemental analysis and H-NMR spectra were as follows.

Reactants: 1-(N-phenyl-carboxamido)-propan-2-one (III) and Phenylene Diamine (IV)

SR. NO	1-(N-phenyl-carboxamido)-propan-2-one (III)	7-[Phenyl amino] 5-Methyl 1,4 Benzodiazepines (VB)	MOL. FORMULA	MP (°C)	YIELD (%)	ELEMENTAL ANALYSIS (%)			
						Found (Cal)			
						C	H	N	O
1	1-[N-(2 methoxy phenyl)-carboxamido]-propan-2-one (IIIa)	7-[2-Methoxy Phenyl amino] 5-Methyl 1,4 Benzodiazepines (VB1)	C ₁₇ H ₁₈ N ₄ O ₂	200	80	70.23 (72.72)	4.15 (5.30)	13.88 (15.90)	7.45 (6.06)
2	1-[N-(3 methoxy phenyl)-carboxamido]-propan-2-one (IIIb)	7-[2-Methoxy Phenyl amino] 5-Methyl 1,4 Benzodiazepines (VB2)	C ₁₇ H ₁₈ N ₄ O ₂	166	68	71.69 (72.72)	5.52 (5.30)	15.34 (15.90)	6.13 (6.06)
3	1-[N-(4 methoxy phenyl)-carboxamido]-propan-2-one (IIIc)	7-[2-Methoxy Phenyl amino] 5-Methyl 1,4 Benzodiazepines (VB3)	C ₁₇ H ₁₈ N ₄ O ₂	88	76	72.36 (72.72)	5.03 (5.30)	14.96 (15.90)	6.84 (6.06)
4	1-[N-(2 hydroxy phenyl)-carboxamido]-propan-2-one (III d)	7-[2-hydroxy Phenyl amino] 5-Methyl 1,4 Benzodiazepines (VB4)	C ₁₆ H ₁₄ N ₄ O ₂	125	54	72.12 (72)	4.54 (4.8)	16.03 (16.8)	6.12 (6.4)
5	1-[N-(3 hydroxy phenyl)-carboxamido]-propan-2-one (III e)	7-[2-hydroxy Phenyl amino] 5-Methyl 1,4 Benzodiazepines (VB5)	C ₁₆ H ₁₄ N ₄ O ₂	>300	82	71.42 (72)	4.09 (4.8)	15.93 (16.8)	6.98 (6.4)
6	1-[N-(4 hydroxy phenyl)-carboxamido]-propan-2-one (III f)	7-[2-hydroxy Phenyl amino] 5-Methyl 1,4 Benzodiazepines (VB6)	C ₁₆ H ₁₄ N ₄ O ₂	147	75	70.33 (72)	3.87 (4.8)	16.02 (16.8)	5.24 (6.4)





Anti microbial activity

Preparation of sample: 0.001g/1mg 7-[substituted phenyl amino] 5-methyl 1,4 Benzodiazepines was taken and dissolved in 1 ml DMSO.

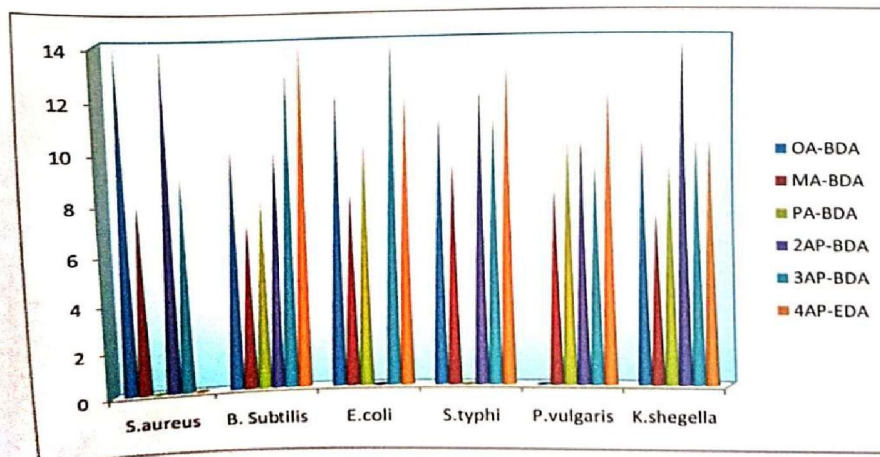
Preparation of inoculums: stock cultures were maintain at 40C on slants of nutrient agar. Active cultures of experiment were prepared by transferring a loopful of cells from the stock culture to test tube of molar heat and growth for bacteria that were incubated for 24 hours at 37 °C.

Screening of bacteria: The disc diffusion method was used for anti-microbial activity. The nutrient agar was poured in Petri plates and allow it to solidify. The above prepared microbial culture was spread uniformly on the surface of the agar. The diffuse discs of each sample are placed on the agar. Plates were then incubated at 37°C for 24 hours.

TABLE 13: Antimicrobial Activity of 5-Methyl 7-Phenyl amino 1,4 Benzodiazepines

Sr. No	7-[Phenyl amino] 5-Methyl 1,4 Benzodiazepines	Zone of Inhibition in mm					
		S. aureus	B. subtilis	E. coli	S. typhi	P. vulgaris	K shegella
01	7-[2-Methoxy Phenyl amino] 5-Methyl 1,4 Benzodiazepines (OA-BDA)	14	08	-	14	09	-
02	7-[2-Methoxy Phenyl amino] 5-Methyl 1,4 Benzodiazepines (MA-BDA)	10	07	08	10	13	14
03	7-[2-Methoxy Phenyl amino] 5-Methyl 1,4 Benzodiazepines (PA-BDA)	12	08	10	-	14	12
04	7-[2-hydroxy Phenyl amino] 5-Methyl 1,4 Benzodiazepines (2AP-BDA)	11	09	-	12	11	13
05	7-[2-hydroxy Phenyl amino] 5-Methyl 1,4 Benzodiazepines (3AP-BDA)	-	08	10	10	09	12
06	7-[2-hydroxy Phenyl amino] 5-Methyl 1,4 Benzodiazepines (4AP-BDA)	10	07	09	14	10	10





II. CONCLUSION

In this study, we synthesized 7-[substituted phenyl amino] 5-methyl 1,4 Benzodiazepines by simple condensation method. All these compounds were eco friendly, non hazardous and biologically active. Antimicrobial results reveals that these substituted benzodiazepines were most important and useful in medicinal chemistry and further studies in pharmaceutical and microbiological studies.

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