International Journal of Pharmacy and Biological Sciences
ISSN: 2321-3272 (Print), ISSN: 2230-7605 (Online)
IJPBS | Volume 9 | Special Issue 2 | 2019 | 51-54
| Research Article | Biological Sciences |Open Access |MCI Approved|
|UGC Approved Journal|

Synthesis, Spectral Characterization and Biological Screening for Some Benzaldehyde Derived Mannich Bases

G. Hema Sindhuja[1], S.R. Bheeter[2] and M. Mohamed Mahroop Raja[3]
Department of Chemistry, Jamal Mohamed College, Trichy.
Department of Chemistry, St. Joseph's College, Trichy
Department of Microbiology, Jamal Mohamed College, Trichy.

Received: 20 Jan 2019 / Accepted: 10 Feb 2019 / Published online: 01 Apr 2019
Corresponding Author Email:

Abstract

The present work focuses to synthesize a novel mannich base using different substituted (OCH_3, $N(CH_3)_2$) aromatic aldehyde via N-linkage Mannich reaction. The newly synthesized mannich bases are characterized using various spectral studies. Infra-red (IR), ^1H and ^{13}C Nuclear Magnetic resonance (NMR) spectroscopy confirmed the structure of the synthesized mannich bases. Antimicrobial studies revealed the activity of mannich base using pathogenic bacteria such as *Klebsiella pneumoniae* and *Staphylococcus epidermidis* and *Bacillus subtilis.* The synthesized Mannich base A, B, C were found to possess a good to moderate high antimicrobial activity.

Keywords
Mannich base, aromatic aldehydes, bacteria, antimicrobial activity

*****

INTRODUCTION

Mannich reaction is a three-component condensation reaction involving aldehyde, amine and an active hydrogen compound. The amino alkylation of aromatic substrates by mannich reaction is of significant status for the synthesis and modification of biologically active compounds[1]. The mannich reaction is a prevailing C-C bond formation process has eclectic applications for the synthesis of various amino derivatives. The designing and studying of complexes derived from Mannich base as ligands is an interesting area of research in both inorganic and organic chemistry [2]. Organic chelating ligands with amide moiety as a functional group have a strong ability to form metal complexes and display a widespread range of biological activities[3]. Mannich bases, in recent years have been used in various applications such as medicine, corrosion inhibitors, coagulation accelerator etc.[4-10] Heterocyclic compounds play an important role in many biological systems, especially N-based ligand, which being a component of several vitamins and drugs.[11-13] Mannich bases are reported as an effective potential agents. It has been used in anti-malarial, anti-cancer, vasorelaxing and analgesic drugs[14-18]. Mannich bases of 1,2,4-triazole moiety have been reported as a good protozocidal and antibacterial agents[19]. The drugs such as Prazosin, Lidoflazine and Urapidil carrying piperazine nucleus are good cardiovascular agents[20]. Some mannich bases are reported to exhibit activity in vitro against murine P388 lymphocytic

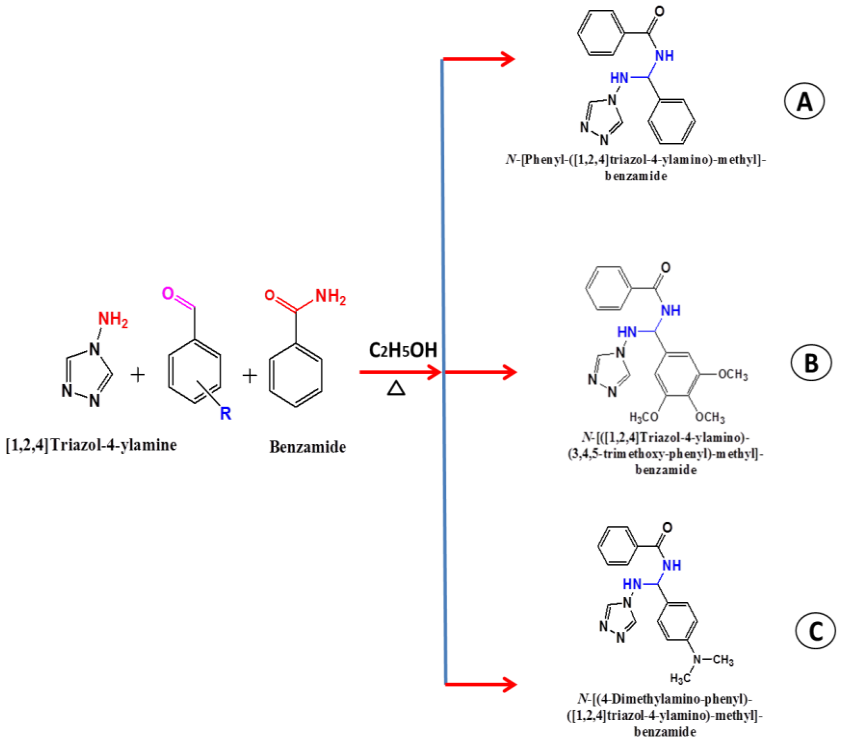
leukemia cells[21]. The 1,2,4 triazole nucleus has been incorporated into a wide variety of therapeutically interesting molecules to transform them into better drugs. Alprazolam, Fluconazole and Itraconazole are the best drugs used in recent days which possess triazole nucleus [22]. In this context we have synthesized three new mannich bases with 1,2,4 triazole nucleus and different aromatic aldehydes with benzamide as an active hydrogen compound. The synthesized mannich bases had shown significant antibacterial activity.

MATERIALS AND METHODS

Analytical grade compounds of 4*H*-1,2,4-triazol-4-amine, benzamide, substituted benzaldehyde from Sigma Aldrich, Methanol, Chloroform: Methanol: Benzene Ethanol from SRL. The compounds and solvents can be used without any purification.

Synthesis

1 mM of 4*H*-1,2,4-triazol-4-amine **1** (0.4004 g), substituted benzaldehyde **2a-c** and benzamide were dissolved in ethanol as a homogeneous mixture. The reactant mixture was refluxed for 5.30 hr in an ice-cold environment. At the end of the reaction light brown coloured precipitate was obtained which was purified using single spot in TLC plate (silica gel). Solvent ratio was about 40:30:20 (Chloroform: Methanol: Benzene). **Scheme-1** shows the synthesis of mannich base using different substituted benzaldehyde derivatives.



Scheme. 1 Synthesis of mannich base (A, B, C) with different substituted aromatic aldehydes

Characterization techniques

The synthesized mannich base compounds were characterized by various techniques. The purity of compounds was determined by TLC techniques using Silica gel G plates and Chloroform: Methanol: Benzene as mobile phase. The spots were visualized in iodine chamber.^{1}H and ^{13}C nuclear magnetic resonance (NMR) spectra were recorded on a Bruker Advance III 500 MHz (AV 500) instrument in a $CDCl_3$ or DMSO-*d*6 solvent using TMS as an internal standard. Infrared spectra were recorded in Shimadzu FTIR spectrophotometer in KBr pellets. Elemental analyses (C, H and N) were performed using a LECO CHNS 932 elemental analyzer. The three newly synthesized compounds were prepared using the reported method and used after recrystallization ethanol.

RESULTS AND DISCUSSION

N-[Phenyl-([1,2,4] triazol-4-ylamino)-methyl]-benzamide

IR (KBr, v/cm -1): 3536 (N-H), 3258(N-N), 2819(Ar C-H), 1670(C=O), 1595(C=N), 1486(Ar- C=C), 1388(C=N), 1181(N-C-N). 1H NMR with solvent: 11.2 (1H, CONH), 8.3(1h Amine NH), 7.2-7.8 (10H- Ar-H), 6.9(2H N=CH),

2.0(1H, Methane-CH): 13C NMR with solvent 175 (C=O), 140 (C=N), 129-132 (Ar-C) and 78(CH methane). The IR spectra stretching frequency values confirmed the mannich base formation. 1181 cm^{-1} stretching frequency indicate that the formation of N-C-N bond in the mannich bases. The NMR shows the proton environment of mannich base, 1H methane CH (2.0) shows the junction of the mannich base

N- [([1,2,4] Triazol-4-ylamino) -(3,4,5-trimethoxy-phenyl)-methyl]-benzamide

IR (KBr, v/cm -1): 3581 (N-H), 3250 (N-N), 2856(Ar C-H), 1686(C=O), 1598(C=N), 1478(Ar- C=C), 1352(C=N), 1102(N-C-N). (C-N-C). 1H NMR with solvent: 10.8 (1H, CONH), 8.5(1H Amine NH), 7.21-7.6 (7H- Ar-H), 6.2(2H N=CH), 1.9 (1H, Methane-CH): 13C NMR with solvent 172 (C=O), 145 (C=N), 125-132 (Ar-C) and 72(CH methane), 57-60 (OCH_3). The similar N-C-N stretching frequency was obtained at 1102 cm^{-1} in mannich base (B), The frequency value was decreased due to presence of $–OCH_3$ in substituted aromatic compound. 1H methane CH (1.9) shows the active center of the mannich base (B), 57-60 ppm range confirmed the substitution of $–OCH_3$ carbon value.

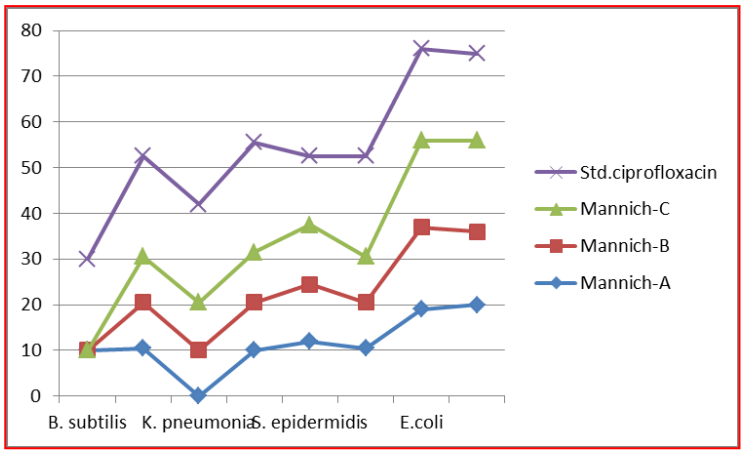
N-[(4-Dimethylamino-phenyl) -([1,2,4] triazol-4-ylamino)-methyl]-benzamide

IR (KBr, v/cm -1): 3449 (N-H), 3218 (N-N), 2847(Ar C-H), 1650(C=O), 1572(C=N), 1430(Ar- C=C), 1393(C=N), 1200 (N-C-N). 1H NMR with solvent: 11.1 (1H, CONH), 8.6(1H Amine NH), 7.4-7.8 (7H- Ar-H), 6.2(2H N=CH), 2.8(6H N-CH_3), 1.8 (1H, Methane-CH): ^{13}C NMR with solvent 178 (C=O), 139 (C=N), 123-128 (Ar-C) and 79(CH methane), 44 (N-CH_3). The similar C-N-C stretching frequency was obtained at 1200 cm^{-1} in mannich base (C), The frequency value was decreased due to presence of $–N(CH_3)_2$ in substituting aromatic compound. 1H methane CH (1.8) shows the active center of the mannich base (C), 44ppm peak was obtained denoted that substitution of N-$(CH_3)_2$ carbon value.

The spectroscopy techniques confirmed the mannich base formation using different substituted aromatic aldehydes.

Antimicrobial activity

The Mannich bases were screened in vitro for their antibacterial activities against three Gram positive (B. Subtilis, K. Pneumonia, S. Epidermidis) and one Gram-negative (Escherichia coli). Activity was determined by measuring the diameter (mm) of zones showing complete inhibition. Mannich base C having high antimicrobial activity compared to Mannich base A and B. Mannich base microbial activity was nearer to the standard used here (commercial medicine of Ciprofloxacin). Figure. 1 show the correlation data between Std. ciprofloxacin and synthesized mannich base of A, B and C



Firgue. 1 Antimicrobial activity for mannich base A, B, C and Std. ciprofloxacin

	B. subtilis		K. pneumonia		S. epidermidis		E. coli	
Con (µg/mL)	50	100	50	100	50	100	50	100
Mannich-A	0	10.5	-	10	12	10.5	19	20
Mannich-B	-	10	10	10.5	12.5	10	18	16
Mannich-C	-	10	10.5	11	13	10	19	20
Std.ciprofloxacin	20	22	21.5	24	15	22	20	19

Table. 1 Zone measurements for Mannich base A B C and Std.ciprofloxacin

CONCLUSION

A series of new mannich bases namely N-[Phenyl-([1,2,4]triazol-4-ylamino)-methyl]-benzamide, N-[([1,2,4]Triazol-4-ylamino)-(3,4,5-trimethoxy-phenyl)-methyl]-benzamide, N-[(4-Dimethylamino-phenyl)-([1,2,4]triazol-4-ylamino)-methyl]-benzamide have been synthesized, characterised and screened for their antibacterial activities against various bacteria such as B. Subtilis, K. pneumonia, S. epidermidis, E.coli. 1,2,4 triazole nucleus is one of the active compounds present in many standard drugs and is known to enhance the pharamacological activity. The synthesized mannich bases were found to possess a good activity against all the tested bacteria where the compound mannich –C possess a good correlation with the standard drug used.

REFERENCES

1. H.G. Dai, J.T. Li, T.S Li, *Syn. Comm*.,36, 2006, 1829.
2. A. Abdul Jameel, M. Syed Ali Padusha, K. Sulthan Syed Ibrahim, *Journal of Applied Chemistry*, 2014,2(3):5-11.
3. Yuting Liu, Hong Xin, Jingyi Yin, Dawei Yin, Zijiang Yang, Jie Li, *Journal of Molecular Structure* (2017),2017.12.089
4. Z. Z. Ji, H. T. Chen, L. Wong. *Chin. J. Med. Chem*. 4(1994) 137-149.
5. D. P. Wei, L. Cao, L. L. Wang. *Lubrication Sci*. 7 (1995) 365-376.
6. W. J. Huang, X. H. Wu. Synth. *Lubrication*. 21, (2004) 231-243.
7. T. H. Ren, Y. Wan, Q. J. Xue, H. Q. Wang. *Lubrication Sci*. 7 (1995) 163-169.
8. T. Singh, R. Singh, V. K. Verma, K. Nakayama. *Tribology Int*. 23 (1990) 41-46.
9. X. Wu, W. S. Li, Z. J. Li. *Chem. Reagents*. 30 (2008) 277-279.
10. R. H. Wang, Z. G. Qi, Y. H. Bu, C. Z. Cao, H.Kong. *Pet. Drilling Tech*. 37 (2009) 13-16.
11. A. Asrar Ahamed, M. Mohamed Sihabudeen. *Asian J. of Pharmacy and Pharmacology* 3(6) (2017) 247-250.
12. Foziah A Al-Saif, *Int J. Chem. Sci*, 11(2), 2013, 1117-1130.
13. Hema Sindhuja. G, *EJBPS*, (2018) Vol 5, Issue 3,
14. M.G. Ferlin, G. Chiarelotto, F. Antonucci, L. Caparrotta, G. Froldi, *Eur. J. Med. Chem*. 37 (2002) 427.
15. B.S. Holla, B. Veerendra, M.K. Shivananda, B. Poojary, *Eur. J. Med. Chem*. 38 (2003) 759.
16. W. Malinka, P. Swiatek, B. Filipek, J. Sapa, A. Jerierska, A. Koll, *Farmaco 60* (2005) 961.
17. V.W. Schoentensack, P. Bischler, E. Dittmann, C. Steinijans, Arzneimittelforschung /*Drug Res*. 27 (1977) 1908.
18. J.R. Dimmock, M. Chamankkah, T.M. Allen, S. Halleran, *Pharmazie* 50 (1995) 221.
19. B.S. Holla, B.S. Rao, B.K. Sarojini, P.M. Akberali, N.S. Kumari, *Eur. J. Med. Chem*. 41 (2006) 657.
20. K. Walczak, A. Gondela, J. Suwinski, *Eur. J. Med. Chem*. 39 (2004)
21. D.H. Jones, R. Slack, S. Squires, K.R.H. Wooldridge, *J. Med. Chem*. 8 (1965) 676.
22. Mithun Ashok, Bantwal Shivarama Holla, Boja Poojary, *E J Me Ch*, 42, 2007, 1095-1101