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Synthesis, characterization, and biological activity of new mannich base N-((2-hydroxyphenyl)(o-tolylamino)methyl)acrylamide

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ABSTRACT

In the present study of a new Mannich base play a major role in biological process in view of this o-toluidine Mannich base was synthesized by using o-toluidine, salicylaldehyde and acrylamide. The newly synthesized compound (TOSA) was characterized by elemental analysis, UV-Vis, FT-IR, FT-RAMAN, ^{1}H NMR, ^{13}C NMR, 2D homo cosy NMR and Mass spectral techniques. In addition to antibacterial and antifungal properties were tested against a panel of five pathogenic bacterial strains namely, (Staphylococcus aureus, Klebsielloa Pneumonia, Bacillus anthracis, Escherichia coli, and, Bacillus cereus) and antifungal activity against a panel of five pathogenic fungal strains namely Aspergillus fumigates, Aspergillus nidulans, Aspergillus terreus, Aspergillus flavus, Aspergillus niger. The Parallel experiments were also carried out with standard drugs (Norfloxacin for bacteria and Fluconazole for fungi).

Keywords: Mannich base, o-toluidine, Antibacterial and Antifungal activities.

INTRODUCTION

Salicylaldehyde Mannich bases are of considerable importance as intermediates in the synthesis of condensed heterocyclic systems.[1] Mannich base type reactions are among the most important carbon-carbon bond forming reactions in organic synthesis.[2] They provide amino methylated, benzylated compounds which are important synthetic intermediates for various pharmaceuticals and natural products.[3] The Microorganisms are closely associated with the health and welfare of human beings. Some microorganisms are beneficial, while others are detrimental.[4] They also help in the production of important products like penicillin, Interferon, and alcohol. On the other hand, certain microorganism can cause disease. The infected with the pathogens may be treated with antibiotics. This can be classified as bactericidal and bacteriostatic.[5] Mannich bases ligand were found to possess potent activities such antibacterial and antifungal.[6] The present study was undertaken in an attempt to synthesis some new Mannich bases of N-((2-hydroxyphenyl)(o-tolylamino)methyl)acrylamide by condensation reaction using Salicylaldehyde, o-toluidine, and acryalamide, carry out their antibacterial and antifungal studies.[7-9]

MATERIALS AND METHODS

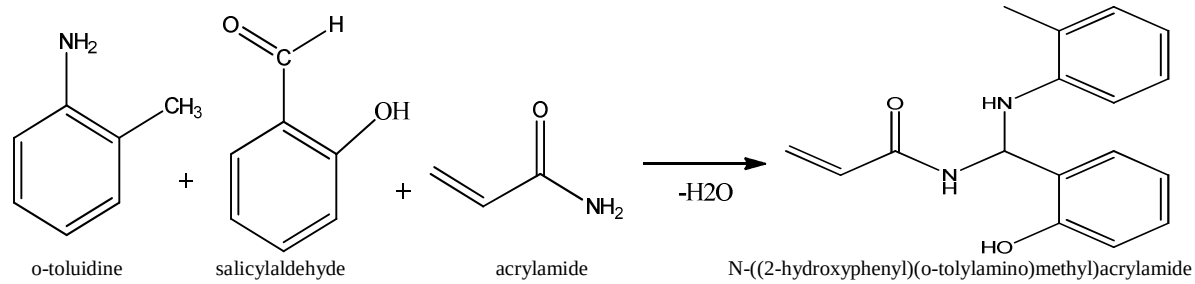
All reagents were commercially available and used without further purification. Solvents were distilled from appropriate drying agents subsequently prior to use. IR spectra were recorded on a shimadzus FT IR affinity 1 spectrophotometer in KBr, melting points were taken in open capillary tubes in oC by using richerkjung Heizbank melting point apparatus, Ultraviolet – visible (UV – Vis) absorption spectra were recorded on a Perkin-Elmer Lambda 35 spectrophotometer at the wavelength of maximum absorption (λ max) in DMSO at room temperature. Raman spectra were Recorded on Bruker RFS 27, ^{1}H NMR, ^{13}C NMR spectra were recorded on a Bruker Advance DPX 300 MHz and 2D homo cosy NMR spectra were recorded on a Bruker Advance DPX 500 MHz ultra-shield FT –NMR spectrophotometer in DMSO-d6 with TMS as internal standard chemical shifts are expressed in (δ units ppm) SAIF IIT Madras-36. The mass spectral studies were recorded on JEOL D - 300 (EI) mass spectrometer. The human pathogenic bacterial and fungal species were purchased from Department of Botany and Microbiology AVVM Sri Pushpam College (Autonomous) Poondi Thanjavur-613503. (*Staphylococcus aureus*, *Klebsielloa Pneumonia*, *Bacillus anthracis*, Escherichia *coli*, and *Bacillus cereus*) and fugal species (*Aspergillus fumigates*, *Aspergillus nidulans*, *Aspergillus terreus*, *Aspergillus flavus*, *Aspergillus niger*) and were used for the antimicrobial studies.

Spectral data

N-((2-hydroxyphenyl)(o-tolylamino)methyl)acrylamide

M.F: $C_{17}H_{18}N_2O_2$, yield: 98%, M.P: 63 ± 2^{o}C, Mol.wt: 282. FT IR KBr ν in cm-1: 3381 (-NH), 2902, 2810 (CH aromatic and aliphatic), 1570 (δ NH), 1567 (C=O stretching), 1400, 1485 (CH symmetrical and Asymmetrical stretching), 1274, 1149, 1109 (C-N-C), 981 (vinyl group CH out of plane bending), 751 (CH opb of disubstituted toluidine aromatic ring) 575 (δ O-C-N), 464 (opb ring C=C). FT Raman Polycrystalline powder ν in cm-1 : 3055.57 (-NH), 2921.89 (CH aromatic), 1614.71 (C=O), 1594.47 ,1571.35 (δ NH), 1459,1482 (CH symmetrical and Asymmetrical stretching), 980 (CH opb of vinyl group), 1361,1241 (C-N stretching), (δ CH), 1155,1112, (C-N-C),1502 (Skeletal vibration of benzene ring),468 (C=O bending), 314 (C=C opb aromatic ring), 158 (skeletal bending vibration), 854 (CH opb of pyridine and benzene ring). ^{1}H NMR (300 MHz, DMSO- d_6) δ 2.32, 2.50 (S, 3H, CH_3), δ 6.96, 6.80 (d, 2H), δ 8.87 (S, NH), δ 7.00 -7.28 (m,4H o- toluidine ring), δ 7.31 -7.67 (m 5H benzene ring). ^{13}C NMR (300 MHz, DMSO- d_6) δ 17.51 (S, methyl carbon), δ116-118 (s,1C), δ119.14 -126.55 (m 4C benzyl ring), δ 126.88- 132.99 (m, 4c,o-toludine aromatic ring), δ 146.67(s 2C), δ 160.21 (s,1C-CH) , δ 162.81 (s 1C, N-amide), δ 170,182 (s2C,C=O). 2D homo cosy NMR (500 MHZ, DMSO d6), The ^{1}H-^{1}H and ^{1}H-^{13}C correlation of TOSA. This shows the better results corresponding to those of ^{1}H NMR and^{13}C NMR spectral data. The 2D homo cosy NMR spectral in the (TOSA) substantiated the ^{1}H NMR and^{13}C NMR spectral Assignment. Mass m/z: 282.14 ($C_{17}H_{18}N_2O_2^{\cdot+}$), m/z: 70 ($C_3H_4NO^{\cdot+}$), m/z: 106 ($C_7H_8N^{\cdot+}$), m/z: 175 ($C_{10}H_{11}N_2O^{+}$), m/z: 177 ($C_{10}H_{13}N_2O^{\cdot+}$). m/z: 212 ($C_{14}H_{14}NO^{\cdot+}$), Elemental analysis: C 72.32 %, H 6.43 %, and N 9.92 %, O 11.33%. Found: C 72.28%, H 6.40%, N 9.89 %, and O 11.31%.

Scheme 1



o-toluidine salicylaldehyde acrylamide N-((2-hydroxyphenyl)(o-tolylamino)methyl)acrylamide

Synthesis of Mannich bases

N-((2-hydroxyphenyl)(o-tolylamino)methyl)acrylamide

o-toluidine (1,06mL, 0.01M), acrylamide (0.71g, 0.01M), were taken in equimolar ratio. A concentrated ethanolic solution of acrylamide and o-toluidine was prepared. To this solution ethanolic solution of salicylaldehyde (1.22mL, 0.01M), was added slowly with constant stirring in an ice bath. A paste like semisolid was observed. After 5 h a pale yellow oily turned into yellow solid mass which was separated by suction filtration and washed with distilled water. The product was dried at 50^{o}C in an air oven and recrystallized from ethanol by slow evaporation method [10, 11]

RESULTS AND DISCUSSION

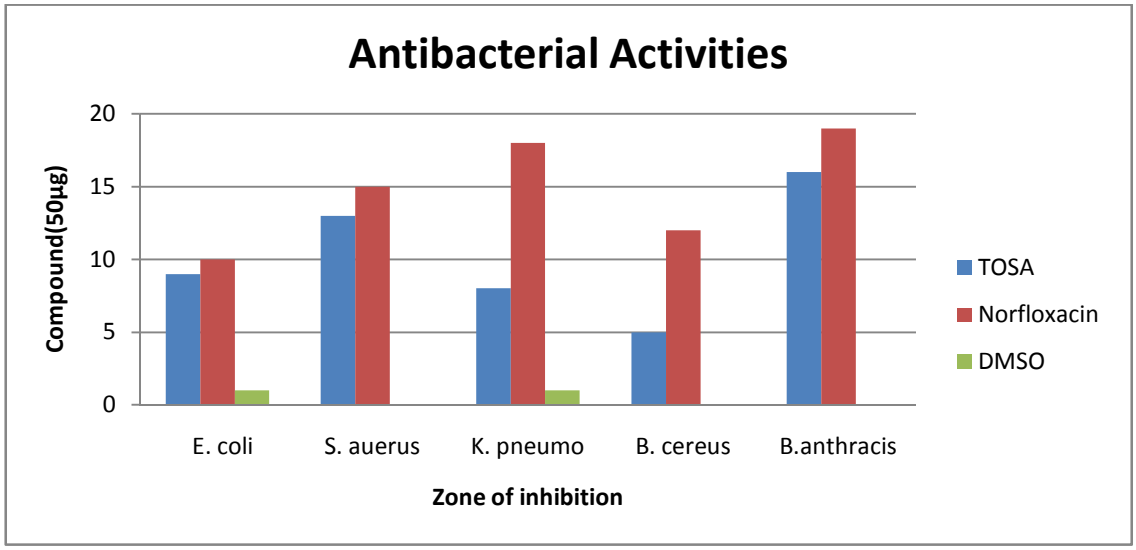
Based on analytical and spectral data, the structure of the ligand confirmed. The fragmentation pattern of the molecular ion also confirms the structure of the Mannich base ligand. These were characterized on the basis of their elemental and spectral analysis. Infrared spectra of each compound showed bands for NH stretching vibrations at about 3381cm–1 and CH stretching vibrations for aromatic and aliphatic were observed in the range of 2902, 2810 cm–1. Amide I band (C=O stretching), for secondary amide was observed near 1567 cm–1 whereas amide II band (NH) was observed near 1570 cm–1. ^{1}H NMR spectra given under the number of hydrogen atoms present in all the synthesized compounds were exact when compared to the number of hydrogen atoms in the expected compounds, The molecular mass of the synthesized compounds were nearer to the molecular mass of the expected compounds.

Antibacterial Activities

The Antibacterial Activities of Mannich bases ligand (TOSA) were carried out against the panel of *Staphylococcus aureus*, *Klebsielloa Pneumonia*, *Bacillus anthracis*, *Escherichia coli*, and *Bacillus cereus* by Agar diffusion plate method.[12-16] The maximum zone of inhibition was observed against *Bacillus anthracis* (16mm) *and Staphylococcus aureus* (13mm) for TOSA. The Mannich base ligands TOSA shows significant inhibition activity with respective bacterium was recorded when compared with standard drug Norfloxacin.

Table: 1 Antibacterial Activities of Mannich Bases ligand

S.NO	Compound(50µg)	Zone of inhibition(in mm) against				
		E. coli	*S. auerus*	*K. pneumo*	*B. cereus*	*B.anthracis*
1	TOSA	9	13	8	5	16
2	Norfloxacin (std)	10	15	18	12	19
3	DMSO (Control)	1	0	1	0	0

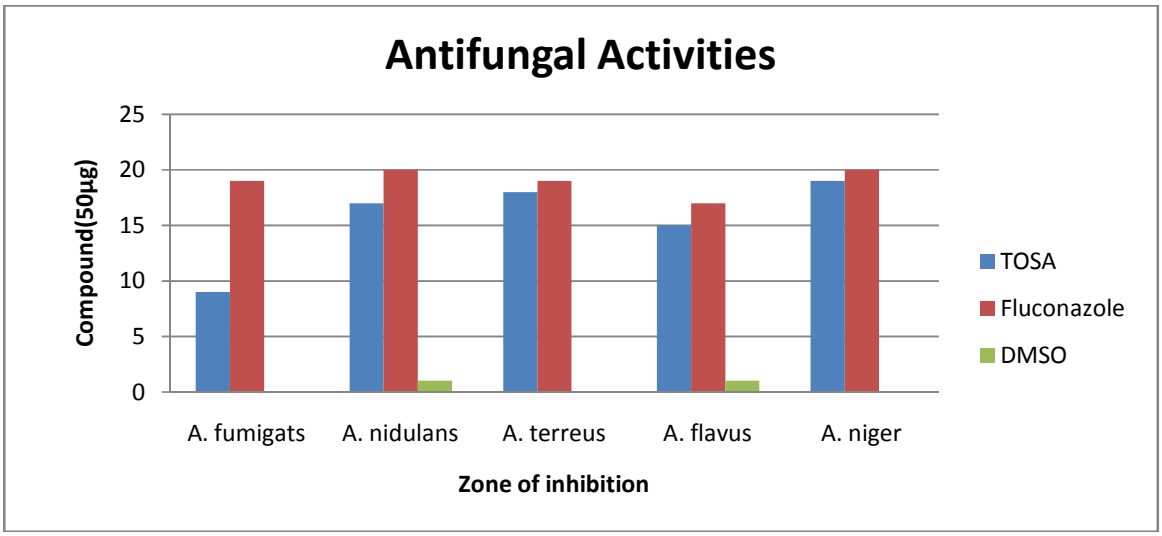


Antifungal activities

The antifungal activities of Mannich bases ligand TOSA were carried out against the panel of *Aspergillus fumigates*, *Aspergillus nidulans*, *Aspergillus terreus*, *Aspergillus flavus* , *Aspergillus niger* by Agar diffusion plate method.[17-20] The maximum zone of inhibition was observed against *Aspergillus niger* (19mm), *Aspergillus terreus* (18mm) and *Aspergillus nidulans* (17mm) for TOSA, The Mannich base ligands TOSA shows significant inhibition activity with respective fungi was recorded when compared with standard drug fluconazole.

Table: 2 Antifungal Activities of Mannich Bases ligand

S.NO	Compound(50µg)	Zone of inhibition(in mm) against				
		A. fumigats	*A. nidulans*	*A. terreus*	*A. flavus*	*A. niger*
1	TOSA	9	17	18	15	19
2	Fluconazole (std)	19	20	19	17	20
3	DMSO(Control)	0	1	0	1	0



CONCLUSION

The Mannich base ligand have been newly synthesized and characterized by elemental analysis, IR, FT Raman, ^{1}H NMR, ^{13}C NMR, 2D homo cosy NMR and mass spectroscopy method and these compounds have been assigned for antibacterial and antifungal studies. The synthesized compounds TOSA have significant activities against the microbes. The antimicrobial activity of the test compounds are comparable to that of the standard drugs used.

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