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Meglumine sulphate catalysed One-Pot Multicomponent Synthesis, Characterization and biological evaluation of 2, 4, 5 triaryl-1*H* Imidazoles.

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Abstract:

A One-pot multicomponent synthesis of 2, 4, 5 triaryl-1H Imidazoles using meglumine sulphate as a catalyst with involves reaction of benzil, substituted aromatic aldehyde and ammonium acetate under reflux in ethanol solvent conditions, synthesised compounds have been categorized through spectroscopic techniques like IR, ^{1}HNMR and Mass spectra, the prepared compounds were nontoxic, excellent yields. The remarkable advantage of this method is a low-cost eco-friendliness catalyst, rapidly completion of reaction and few volumes of using organic solvent, excellent yield and mild condition. Additionally, all synthesized compounds were screened for antimicrobial and antifungal activities.

Keywords: Antifungal, Imidazole, Antibacterial, Heterocyclic.

Introduction

One -pot multicomponent reactions have recently been discovered to a powerful synthetic tool for synthesis of heterocyclic compounds. The very large of manageable imidazole compounds are among the described rewards of multicomponent reactions and the products are synthesised in the one-pot procedure, operational simplicity. (1-2). The 2,4,5 triaryl 1H imidazole compounds exhibit a lot of therapeutic activities such as analgesics, antihypertensive, antifungal, antitumor, antibesity [3], anthelmintic, antitubercular, antiviral [4], antiulcer, antihistaminic [5], antidepressant, anti-inflammatory [6], antidiabetic [7],

anticonvulsant [8], antirheumatic [9], antiallergic [10], alpha-blockers, antiasthematic [11], antiprotozoal [12], antiaging, anticoagulant, antimalarial [13], and ant amoebic activity [14]. Since more application area 2,4,5 Triaryl, 1H imidazole compounds have been focused on new methodology of its synthesis via new catalyst time saving lower wasting material multicomponent one-pot synthesised various substituted triaryl, 1H imidazole. The synthesised compounds were characterised by using FT-IR, 1HNMR spectra in DMSO solvent, LC-MS spectra with screening antibacterial and antifungal activities of various synthesised compounds.

Experimental

All chemicals were used of AR grade purchased from reputed chemical company such as Spectrochem and solvents commercially available were purchased from local provider and used by further purification. The melting point apparatus, Stuart model SMP3, was used for measuring melting points. FT-IR spectra were recorded on a PerkinElmer series II spectrum. ^{1}HNMR spectra were recorded in DMSO-d6 using Bruker Avance Neo 500 MHz NMR Spectrometer and proton chemical shifts were recorded in δ relative to TMS as an internal standard using DMSO as solvent and the LC-MS spectra of synthesised compounds have been carried out with Water Micro mass Q-Tof Micro instrument.

General procedure for the synthesis of 2,4,5-Triaryl Imidazoles

The 2,4,5 Triaryl Imidazoles were synthesised by mixing of Benzyl (1.0 mmol), Substituted aromatic aldehyde (1.0 mmol), ammonium acetate (3.0 mmol), and meglumine sulphate (0.4 mmol), were stirred and refluxed in 5 ml ethanol. TLC monitored the progress of the reaction. After completing the reaction, the mixture was poured on ice (50 ml). The precipitated solid was filtered, washed several times with water, dried then synthesised compounds recrystallized by using ethanol to obtain the corresponding 2,4,5-triaryl-1H-imidazoles.

Characterization of synthesised 2, 4, 5 Triaryl-1-Imidazole compounds

1] 2-(4-Nitrophenyl)-4,5-diphenyl-1H-imidazole[N1a]: Yield: 83%. Colour: Yellow. M.P.: 242-243 ^{O}C. MF. $C_{21}H_{15}N_3O_2$. FT-IR (KBr, cm $^{-1}$): 1667 (C=N), 3194 (N-H), 1586,1499 (Ar. C=C), 1326 (C=C), 1230 (C-N), 847 (N-O), 1100 (N=O). ^{1}HNMR (500Mz, DMSO-d6), δ: (m, 4H, 8.35), (m, 4H, 7.56), (d, 2H, 7.47), (d, 2H, 7.32), (d, 1H, 7.94), (t, 1H, 7.65), (s, 1H, 13.15). LC-MS (m/z): obsv. 342.35.

2] 2-(4-Chlorophenyl)-4,5-diphenyl-1H-imidazole[N1b]: Yield: 73%. Colour: White. M.P.: 205-208 ^{O}C. MF. $C_{21}H_{15}N_2Cl$. FT-IR (KBr, cm^{-1}): 1674 (C=N), 3265 (N-H), 1582, 1486 (Ar. C=C), 1378 (C=C), 1195 (C-N), 665 (C-Cl). ^{1}HNMR (500 MHz, DMSO-d6), δ: (t, 7.4 1H), (t, 7.5 2H), (d, 8.15, 2H), (m, 7.47, 4H), (d, 7.55, 2H), (t, 7.27 2H), (d, 7.6 1H), 12.85 (1H). LC-MS (m/z): obsv 331.17.

3] 2, 4, 5-Triaryl-1 H-Imidazole[N1c]: Yield: 81%. Colour: White. M.P.: 269-272^{O}C. MF. $C_{21}H_{16}N_2$. FT-IR (KBr, cm^{-1}): 1667 (C=N), 3220 (N-H), 1589, 1498 (Ar. C=C), 1362 (C=C), 1222 (C-N).^{1}H NMR (500 MHz, DMSO-d6), δ: (t, 1H, 7.2), (t, 2H, 7.3), (t, 2H, 7.6), 7.4-7.6 (m, 6H), (d, 2H, 7.9), 8.0 (d, 2H), 12.9 (1H). LC-MS (m/z): obsv 296.37.

4] 2-(4-Hydroxyphenyl)-4,5-diphenyl-1H-imidazole[N1g]: Yield: 87%. Colour: White. M.P.: 193-197 ^{O}C. MF. $C_{21}H_{16}N_2O$. FT-IR (KBr, cm^{-1}): 1655 (C=N), 3385 (-O-H), 3162 (N-H), 1575,1467 (Ar. C=C), 1345 (C=C), 1232 (C-N), 1142 (C-O). ^{1}HNMR (500 MHz, DMSO-d6), δ: (s, 1H, 5.5), (t, 2H, 6.9), (d, 2H, 7.9), (m, 4H, 7.5), (d, 2H, 7.3), (d, 2H, 7.4), (t, 2H, 7.6), 12.2 (1H). LC-MS (m/z): obsv 312.47.

Bioassay

Protocol for antibacterial activity

The antibacterial activity of the compounds was performed by enumerating feasible number of cells upon in the nutrient broth containing various concentrations of compounds. The feasible number is represented by colony control method. The test organisms on which the antibacterial activity was performed were *Bacillus subtilis*, *staphylococcus aureus, Pseudomonas aerugenosa, Escherchia coli, & Salmonella typhi.* In this method, the cells of test organisms were grown in nutrient broth till mid log phase and used as an inoculum for performing antimicrobial test. An approximately, $1*10^6$ cells/mL test organisms were each inoculated with 0 to 500 ug/mL concentrations of different compounds, separately, and each incubated for 16 to 18 at 37ºC. During this incubation cells tend to grow and multiply in number. However, if the compounds interfere with growth of the cells, the number of cells of decrease. After, 16 to 18 hrs. available number of cells were recorded by spreading an aliquot, from the broth, inoculated with test organisms and compounds as colony forming units per millilitre.

Protocol for antifungal activity

The Antifungal activity was evaluated against different functional stains such as *Saccharomyces cerevisiae* and *Aspergillus niger.* The medium yeast nitrogen base was

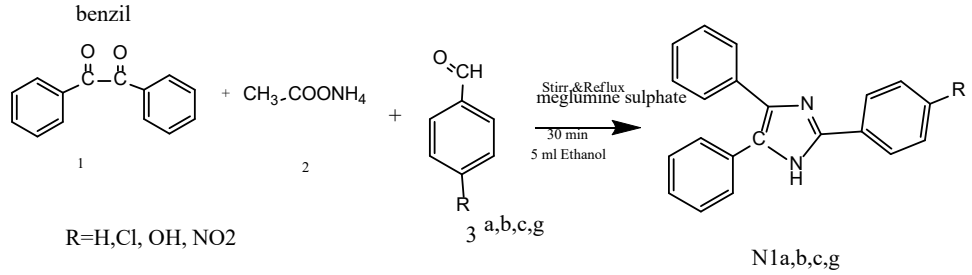
dissolved in phosphate buffer pH 7 and it was autoclaved in 110 ºC for 10 min. The suitable concentration of standard was incorporated in medium. With each set of growth control of without the antifungal agent and solvent control DMSO were included.

The fungal strains were freshly sub cultured on to Sabouraud dextrose agar (SDA) and incubated at 25°C for 72 hrs. The fungal cells were deferred in sterile distilled water and diluted to get 10^5 cells/mL. Ten microlitre of standardized suspension was protected on to the control plates and the media were combined with the antifungal agents. These plates inoculated were incubated at 25^0C for 48 hrs. The readings were taken at the end of 48 hrs and 72 hrs. Minimum inhibitory concentration (MIC) values were determined using standard agar method as per CLSI guidelines.

Result and Discussion

One-pot multicomponent 2,4 and 5 substituted T- aryl 1H imidazole compounds synthesized from Benzil (1mmol), Ammonium acetate (1 mmol), Substituted aromatic aldehyde (1mmol) in presence of catalyst meglumine sulphate (4mmol) with stirred and refluxed in ethanol. The synthesised compounds give various spectral analyses agree well with structure of compounds in figure. 1.

Figure 1. synthesis of substituted 2,4,5-tri phenyl-1H-imidazole using meglumine sulphate catalyst



Spectral Characterization

IR Spectra

In the IR spectra of the Imidazole compounds the band at 3385 cm^{-1} shows for phenolic OH group and its frequency were disappeared in the compounds. 1667cm^{-1} region is assigned C=N band, this band of imidazole experiences small shifts to lower frequencies in the spectra of the Imidazole compounds. 3194 cm-1 spectra show N-H band in the imidazole structure

frequencies. 1230cm-1 spectra show C-N band and 847 cm-1 for N-O bonding spectra. 665 cm^{-1} spectra values indicating C-Cl band with the literature.

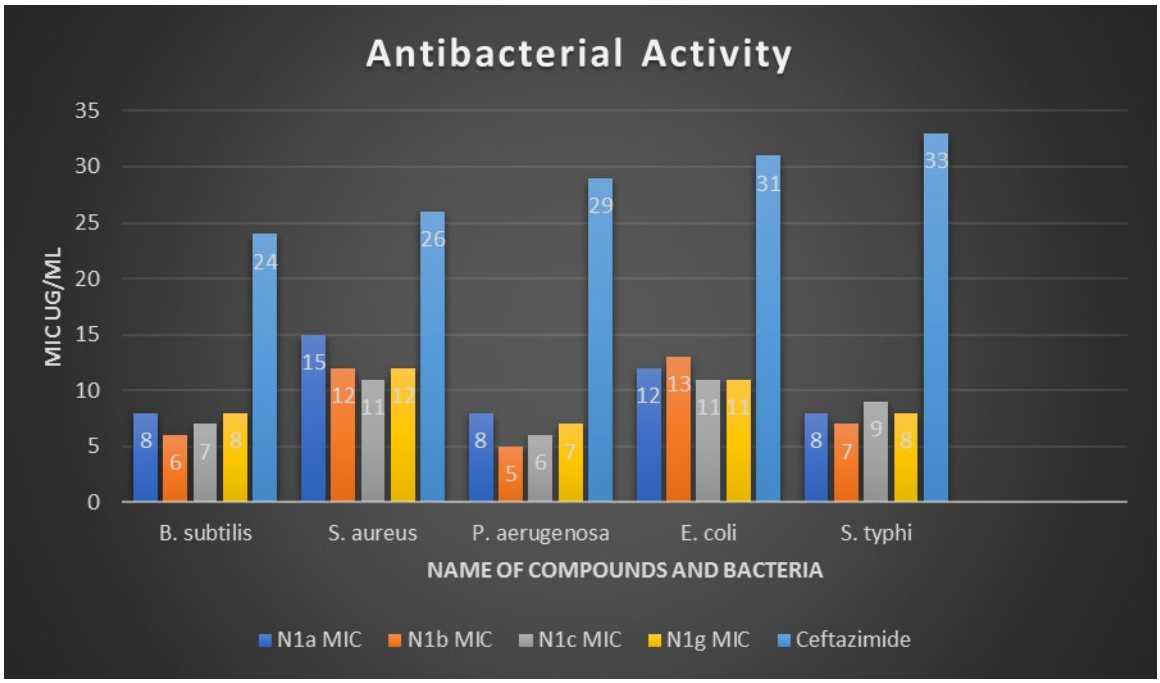
^{1}HNMR Spectra

In the ^{1}HNMR Spectra of the prepared compounds appears δ13.15 s, with 1H indicates presence of N-H bonding & δ 7.32-8.35 indicates Ar-H means presence of phenyl rings in prepared compounds.

LC-MS Spectra

In the present investigation, the mass spectrum of 2,4,5 Triphenyl 1H imidazole shows molecular ion peak at m/z= [296] corresponding to [$C_{21}H_{16}N_2$] ion. The spectrum also exhibits peaks for the spectra of 2 sub. Phenyl,4,5 diphenyl-1 H imidazole compounds show molecular ion peaks at m/z 331[M+1], 312 [M+1], and 341[M+1] respectively that are equivalent to their molecular weight.

Biological activity



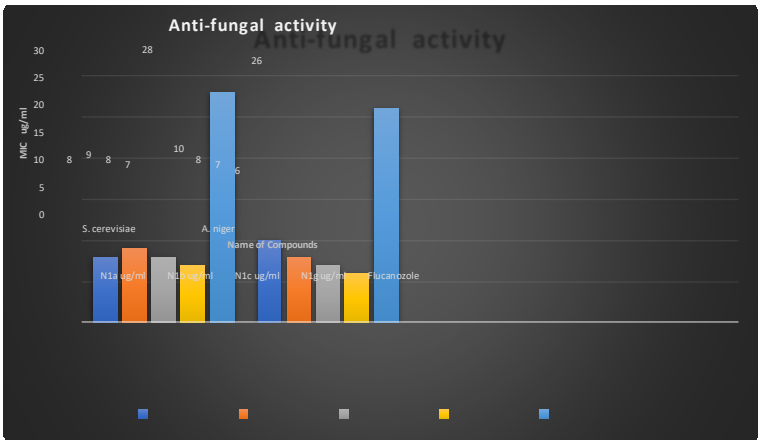
Concentration & ug/ml of various bacteria

The graphically representation of antibacterial activity

Minimum inhibitory concentration (MIC) of 2,4,5 Triaryl 1H Imidazole compounds against bacteria were compared with the MIC values of standard drug Ceftazimide. The MIC values of the prepared 2(4-nitrophenyl)-4,5 diphenyl 1H imidazole compounds(N1a) were observed to be 08ug/ml, 15ug/ml, 08ug/ml, 12ug/ml, 08ug/ml, against *Bacillus subtilis*, *Staphylococcus*

aureus, Pseudomonas aerugenosa, Escherchia coli, & Salmonella typhi respectively the values exhibit similar activities as compared with the standard drug Ceftazimide. The MIC values of 2(4-nitrophenyl)-4,5 diphenyl 1H imidazole compounds(N1a) shows MIC values of *E. coli* 30 ug/ml. exhibits better activities as compared with standard drug Ceftazimide (31ug/ml). The MIC values of 2(4-chlorophenyl)-4,5 diphenyl 1H imidazole compounds(N1b) shows 11ug/ml , 15ug/ml against *Bacillus subtilis* and *Salmonella typhi* as

compared against standard drug Ceftazimide drug. The MIC values of 2,4,5 triphenyl 1H imidazole compounds(N1c) show 8ug/ml, 9ug/ml and 12ug/ml against *Staphylococcus aureus, Pseudomonas aeruginosa* and *Escherchia coli* against to standard drug Ceftazimide compared to shows good activities. The MIC values of 2(4-hydroxyphenyl)-4,5 diphenyl 1H imidazole compounds(N1g) exhibit 9 ug/ml, 9 ug/ml, 8 ug/ml against *Bacillus subtilis*, *Staphylococcus aureus and Pseudomonas aeruginosa* as compared with standard drug Ceftazimide shows moderate activity.



Anti-fungal activity

The graphically representative of antifungal activity.

In the antifungal activity, the MIC values of the 2,4,5 Triaryl 1 H Imidazole compounds of N1a, N1b, N1c and N1g synthesized compounds show moderate activity as compared to standard drug. The results observed by the analysis for Saccharomyces cerevisiae 8 ug/ml, 9 ug/ml, 8 ug/ml and 7 ug/ml and Aspergillus niger 10 ug/ml, 8 ug/ml, 7 ug/ml, 6 ug/ml and 8 ug/ml with standard drug Fluconazole 28 ug/ml and 26 ug/ml only N1a which possesses

better antifungal activity against the fungi *Saccharomyces cerevisiae* and *Aspergillus niger.*

Conclusion

The 2,4,5 Triaryl 1H imidazole compounds have been prepared from a new catalyst meglumine sulphate and characterized through various spectral analysis, from this spectroscopic data, structures of the synthesized multicomponent sub. Triphenyl 1H imidazole compounds have been confirmed. These compounds were characterised by many biological activities shows such as antibacterial and antifungal activities. The *B. subtilus*, *S. aureus, P. aeruginosa, E. coli,* and *S. typhi* bacterial strains for performing antibacterial activity, the result indicated that the activity exhibited above imidazole compounds comparable to Ceftazimide standard drugs. Simultaneously, the fungal strains such as *S. cerevisiae* and *A. niger* for carrying the antifungal activity as compared to Fluconazole standard drugs and all the compound also exhibited moderate activity compared to standard drugs.

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