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SYNTHESIS OF SUBSTITUTED SULFONAMIDE BEARING IMIDAZOLE DERIVATIVES AND ITS CHARACTERIZATION

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Abstract:

The sulfonamide bearing imidazole derivatives have been synthesized via two stages of chemical reactions. In a first stage, various substituted benzaldehyde condensed with benzil and ammonium acetate in presence L-Proline served as green catalyst. In a second stage, the series of substituted imidazole derivatives were reacted with benzene sulfonyl chloride in the presence of triethyl amine base. All synthesized compounds were characterized by various spectral techniques like UV-Visible, FTIR and ^{1}H NMR spectral analysis respectively. UV- Visible and FTIR spectra of each of the synthesized compounds showed characteristic absorption in accordance to their structural functional groups. The ^{1}H NMR spectrum of synthesized compounds were shows chemical shifts is in good agreement with the structure of the synthesized compounds.

Key Words: Substituted Imidazole, ^{1}H –NMR, UV-Visible & Sulfonamides.

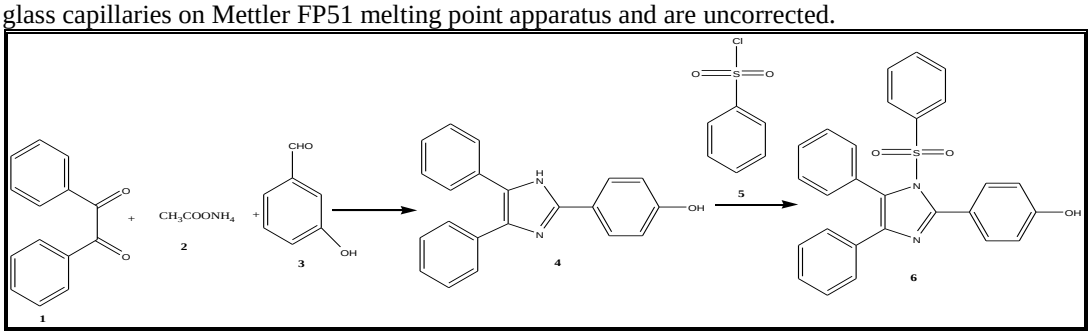
1. Introduction:

Imidazole is planar five-membered ring system with three 3 carbon and two 2 nitrogen atom in 1 and 3 positions. Imidazole was first named as glyoxalin [1]. It is amphotic in nature, susceptible to electrophilic and nucleophilic attack. It also occur in the purine nucleus & amino acid histidine; 4-amino – imidazole-5-carboxamide occurs naturally as a riboside (or ribotide) [1]. The imidazole ring is a constitution of several important natural products, histamine and nucleic acid [2]. Being polar and ionisable aromatic compound, it improves pharmacokinetic characteristics of lead molecules and thus used as a remedy to optimizes solubility and bioavailability parameters of proposed poorly soluble lead molecules [3]. Imidazole derivative have occupied a unique place in the field of medicinal chemistry [4]. Sulfonamides are one of the organosulfur compounds containing the $–SO_2 NH_2$ and/or $-SO_2NH-$ groups [5]. Imidazole derivatives have a wide range of pharmacological activity, literature survey revealed that imidazole and its derivative are reported to have, analgesic and anti-inflammatory activity, cardiovascular activity [6], anti-neoplastic activity[7], anti-fungal activity, enzyme inhibition activity, anti-anthelmintic activity [8], anti-filarial agent, antiviral activity anti-ulcer activity. The sulfonamide or sulfa drugs competitively inhibit folic acid synthesis in micro-organisms and subsequently inhibit multiplication of bacteria but not actively kill them. They have been used against most gram-positive and many gram- negative bacteria, some fungi, and certain protozoa such as medically important sulfonamides [9]. Sulfonamide were the first drugs largely employed and systematically used as preventive and chemotherapeutic agents against various diseases [10]. More recently, sulfonamides are used as an anticancer agent [11], as the antiviral HIV protease inhibitor amprenavir [12] and in Alzheimer's disease [13]. Based on the careful analysis of literature survey, the imiadazole linked sulfonamide derivatives have synthesized.

2. Experimental Section:

Methods and Materials:

The chemicals Benzil (1), Ammonium acetate (2), 3-hydroxybenzaldehyde (3), benzene sulfonylchloride (5), were obtained from Sigma Aldrich, Hyderabad and were used as such without further purification. Silica gel (TLC and Column grade) were purchased from Merck. The solvents were purified as per the standard procedure reported elsewhere. FTIR spectra (KBr pellets) were measured using Alpha Bruker FTIR instrument scanning with the entire region of 4000 - 400 cm^{-1} with typical resolution of 1.0 cm^{-1}. UV-Visible spectra were also recorder using Alpha Bruker UV spectrophotometer. The NMR spectra of the compounds have been recorded on Bruker AV400 spectrometer operating at 400 MHz for recording 1H spectra in DMSO solvent using TMS as internal standard. Melting points of all synthesised compounds have been determined in open glass capillaries on Mettler FP51 melting point apparatus and are uncorrected.



Structure 3-(4, 5 - diphenyl-1H imidazole-2-yl) Sulfonamide:

B) Stage 1: Synthesis of 3-(4, 5 - diphenyl-1H imidazole-2-yl) phenol (4)

An equal molar quantities mixture of compound benzil (1) (3g, 0.014mol),3-hydroxybenzaldehyde (3) (1.742g, 0.014mol), ammonium acetate (2) (5.49g, 0.014mol) andamino acid (0.1g)wererefluxed in ethanol (30mL) for 3 hours at room temperature. After completion of the reaction, the reaction mixture was poured into ice cold water and the off-white solid was obtained recrystallized with ethanol, filtered to get needles like off-white crystals of3-(4, 5 - diphenyl-1H imidazole-2-yl) phenol (4). The purity of the product and progress of reaction was monitored by TLC.

Stage 2: Synthesis of 3-(4, 5 - diphenyl-1H imidazole-2-yl) sulfonamide (6)

An equal molar quantities mixture of compound 3-(4, 5 - diphenyl-1H imidazole-2-yl) phenol(1g, 0.003mol) and benzenesulfonyl chloride (5)(0.42mL, 0.003mol) and dioxane (10mL) contains few drops of triethylamine were refluxed at 8hours. The progress of the reaction maintained by TLC the reaction mixture allowed to cool in to room temperature and poured in to ice cold water. A colorless solid was obtained, recrystallized with ethanol to get a crystals3-(4, 5 - diphenyl-1H imidazole-2-yl) sulfonamide (6).The structure of the compound confirm UV, FT-IR and ^{1}HNMR spectra region.

3. Result and Discussion:

Stage-1 Synthesis of 3-(4, 5 - diphenyl-1H imidazole-2-yl) phenol (4)

Melting Point	:	180^{0}C	
UV –Visible (λ_{max}:nm)	:	204 ($\pi \rightarrow \pi^*$ transition), 330 ($n \rightarrow \pi^*$ transition)	
FTIR (cm^{-1})	:	C-H (3084 cm^{-1}), C=C (1584 cm^{-1}), C=N (1583 cm^{-1}), C-N (1401 cm^{-1}) C-H (871cm^{-1}) N-H (3367cm^{-1})	Figure – 1
^{1}H NMR (ppm)	:	9.8 (1H (OH) 9.8 δ, 1H (N-H) 8.71 δ, 14H (6.8-7.63)	Figure – 2

Stage- 2: Synthesis of 3-(4, 5 - diphenyl-1H imidazole-2-yl) sulfonamide (6)

Melting Point	:	115^{0}C	
UV –Visible (λ_{max}:nm)	:	218 ($\pi \rightarrow \pi^*$ transition), 308 ($n \rightarrow \pi^*$ transition)	
FTIR (cm^{-1})	:	C-H (3040 cm^{-1}), C=C (1640 cm^{-1}) C=S (1358 cm^{-1}), C-N (14025 cm^{-1}), C-H (871 cm^{-1})	Figure – 3
^{1}H NMR (ppm)	:	19 H aromatic proton (6.5-7.2δ), 1H (7.8δ)	Figure – 4

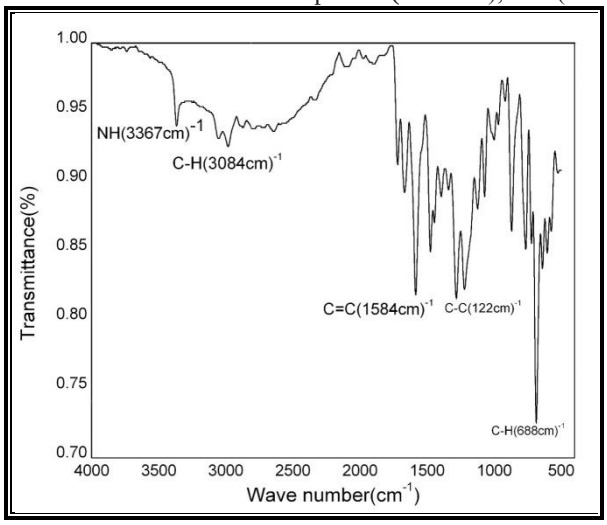


Figure 1: FT-IR Spectrum of Compound (4)

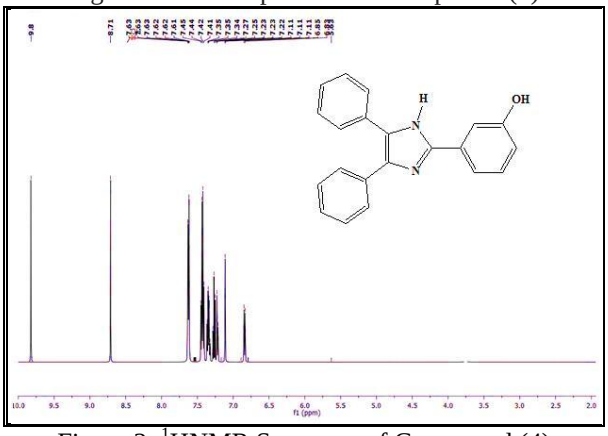


Figure 2: ^{1}HNMR Spectrum of Compound (4)

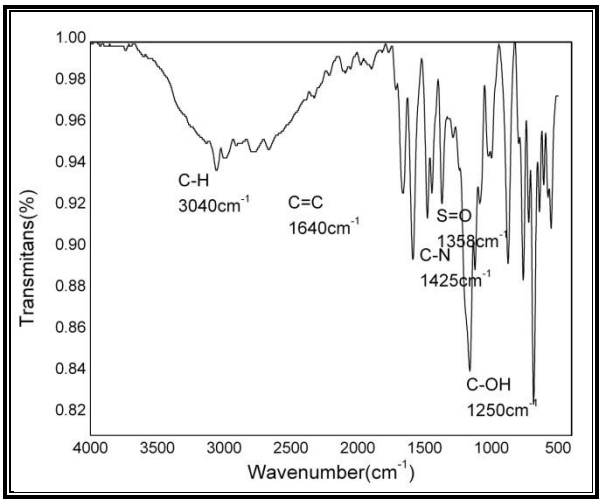


Figure 3: FT-IR spectrum compound (6)

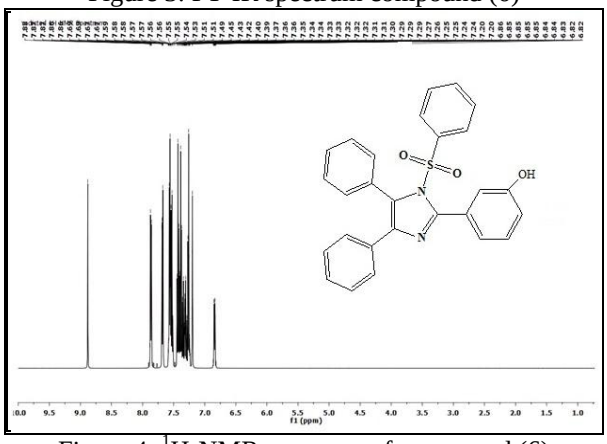


Figure 4: ^{1}H-NMR spectrum of compound (6)

Figure (1-2) revealed the FT-IR, ^{1}HNMR spectra of 3-(4-5-diphenyl-1H imidazole-2-yl) phenol respectively using compound 1 and 2 with compound 3 in the presence L-Proline as catalyst has been shown in the scheme. Figure (4-6) revealed the FT-IR and ^{1}HNMR spectra of 3-(4,5-diphenyl-1H imidazole-2-yl) sulfonamide respectively using compound 4 with compound 6 in the presence of triethylamine as catalyst has shown in the scheme. UV absorption and FT-IR spectra of compound 4 has been provided a preliminary idea in confirmation the formation of product. According to the UV spectrum, presence of peaks at 204 and 330 nm clearly showed that the compound 4 has -CH=CH- group and hetero atom respectively. According to the FT-IR, represented in Figure (1), presence the corresponding peaks at 3084, 1584, 1583, 1401 and 871,3367 cm^{-1} have been related to –OH, C-H aromatic, C-C, C=O stretching and aliphatic C=C stretching respectively in the compound (4). Similarly, proton NMR strongly empowered for the formation of the product by its δ value at 9.8, 8.71, and 6.8-7.63 ppm corresponding to the O-H, Ar-H and N-H protons of compound (4) were mentioned in Figure (2).

UV absorption and FT-IR spectra of compound 6 has provided a preliminary idea in confirmation the formation of product. According to the UV spectrum of compound 6, presence of peaks at 218 and 308nm has been related to aromatic double bond and hetero atom respectively. According to the FT-IR, represented in Figure (3).The corresponding peaks at 3040, 1640, 1358, 14025 and 871 cm^{-1} for –OH, C-H aromatic stretching, C=N, C=C stretching and C=S bending vibrations respectively in the compound 6. All such stretching and bending peaks have also been supported for the formation of the product. Similarly, proton NMR strongly empowered for the formation of the product by its δ value at 9.8, 6.5-7.2 ppm corresponding to the OH, aromatic proton of compound (6) were mentioned in the Figure (4). Similarly, the rest of the compound structures also determined to the above same spectroscopic techniques

4. Conclusions:

Target molecule of sulfonamide bearing imadazole derivatives have been synthesized via two stages of chemical reaction. In a first stage, the substituted imadazole derivatives have been synthesized in the presence of L-Proline as catalyst. L-Proline is an amino acid and easily soluble in water and fulfils the green chemistry protocol. In a second stage, the substituted imadazole derivatives were reacted with benzne sulfonyl chloride in the presence of catalytic amount of triethylamine as catalyst. The substituted imidazole and sulfonamide bearing imadazole derivatives found to have superior antibacterial activity and which served as excellent precursor for

the synthesize of several of medicinal compounds. The chemical structures of compounds 3, 5 and 7 have been confirmed using various spectral techniques viz., FTIR, UV-Visible, and ^{1}H NMR spectra and were found to be in agreement with the chemical structures expected.

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