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Synthesis, Characterization and Antibacterial Activity Of ferrocene Derivatives

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Abstract: *Oxazole derivatives of ferrocene have been synthesized. Acetyl ferrocene was reacted with substituted benzaldehyde to get substituted chalcones of ferrocene. These were further reacted with hydroxylamine hydrochloride to get oxazole derivatives. Synthesized compounds were characterized by FT-IR, and H^1-NMR spectroscopy, these were further evaluated for their Antibacterial activity.*

Keywords- *Acetyl ferrocene, spectral data and anti-bacterial activity.*

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I. Introduction

Metallocene particularly ferrocene derivatives constituent and important group of organometallic compounds [1].Currently ferrocene is considered as widely applicable organometallic scaffold for the synthesis of various functional derivatives useful in medicinal as well as in synthetic fields [2-4].Previous reviews published during the period 1986-2011 were directed at the chemistry of ferrocene covering the area of conducting properties. [5] study of ferrocene and its derivatives [5]. Biological activity[6a-7c]. Bio organometallic chemistry [7]. Metal-catalysed coupling reaction for ferrocene functionalisation [7]. Application in glucose [8]. Cyclometallation [8].Synthesis and electrochemical properties of ferrocene-containing nucleic acid [9]Medical chemistry of ferrocene [10]. Application of ferrocene and its derivatives in cancer research [10].and ferrocene and related compound. [10]Amer et al. reviewed theSynthesis and application of ferrocene derivatives. Ferrocene polymers [11] based on ferrocene have also attracted attention due to several applications such as biosensing, [12]. biomedical engineering [13]. ferrocene derivatives are sensitive to the influence electronic environment and play an important role as catalyst. The electron-donating and electroneffects of a number of group have been established by measurements of the influence of those group on the oxidation potential of ferrocene substituted by such groups [14].

II. Materials and Methods

All the reactionwas carried out in oven dried (120^0c) or flame dried glassware. The purity of all the synthesized compounds was checked by TLC by using appropriate solvents. Column chromatography was carried out using 60-120 mesh silica gel and technical grade solvents. ^{1}H-NMR spectra were recorded on at 600 MHz instruments with tetraMethyl silane as an internal standard. IR spectra were recorded onshimadzu hyper IR instruments.

III. Experimental

3.1 Preparationof Acetyl Ferrocene[15]

Acetylferrocene compound 1 prepared by reported method the mixture of ferrocene(1gm) acetic anhydride (3.3ml) and orthophosphoric acid (0.75ml) was stirring with heated for 1 hours. After cooling down the room temperature ice cold water was added. Then again diluted with sodium bicarbonate was added till precipitate was Formed.it was filtered washed with cold water and dried. The crude product was purified by column chromatography(solvent)

3.2 Preparation ofCompound 3[15]

compound 1g acetyl ferrocene substituted benzaldehyde were taken in ethanol and added with few drops dilute NaOH and heated with water bath for 5hrs. The completion of reaction was checked with TLC. (hexane + ethyl acetate 9:1). The reaction mixture was poured in ice cold water, solid obtained was filtered and washed with sufficient water and recrystallization from methanol.

3.3 Preparation of Compound 4

Compounds (4a-j) were synthesized in a round bottom flask. Compound 3(1mol) and hydroxylamine hydrochloride (1mol) were dissolve in ethanol then few drops of glacial acidwas added. The reaction mixture was refluxed for 8 hrs.Then it was cooled with ice cold water. it was filtered and washed with cold waterand dried, the Crude product was recrystallized from ethanol.

Representative spectral analysis:

IR (KBr) cm^{-1} : 3024(S), 1598,1203, H^1-NMR (DMSO-d^6) δ4.68(4H, S, C_5H_4), 5.082(SH,S, C_5H_4), 7.42-7.83 (SH, M) Ar-H,4-5 H,H (S), 3.8(3H), s, (OCH_3)

Figure1. Schematic Representation of Titled compounds

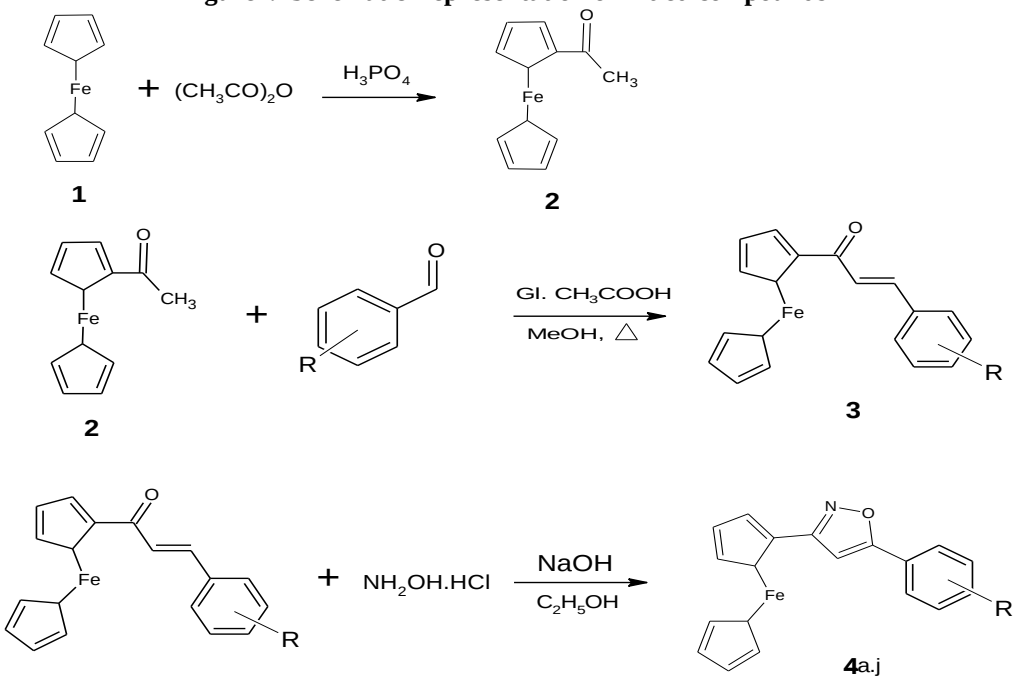
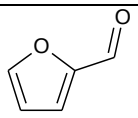
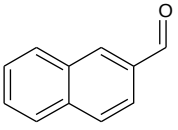


Table 1: Synthesis of substituted oxazoles by conventional heating method:

Entry	R	Conventional Heating		mp.°
		Time in Hours	% Yield	
4a	H	8	71	130°
4b	N,N-DiCH_3	8	65	163°
4c	2-OH,4-OCH3	8	59	126°
4d	4-OH	8	55	143°
4e	2-OH	8	63	151°
4f		8	52	137°
4g	3-NO_2	8	74	118°
4h	4-OCH_3	8	68	155°
4i	4-NO_2	8	66	121°
4j		8	74	118°

Study of antibacterial activity

Synthesized compounds(3a-j) were tested for the antibacterial activity[16] against Gram +ve (*Escherichia coli)* and Gram -ve bacteria (*Staphylococcus aureus*). The nutrient agar medium was prepared by using bactotryptone (4g) broth(3.9g) less than 2% Nacl (2.9g) In 100 ml of water (2.9%) . After 18 hours the exponentially growing culture of the 2 bacteria in nutrient broth at 37°C were diluted culture 1 ml was added to 100ml sterilize and cooled nutrient agar media to give a final bacteria culture. The plates were set at Room

temperature and later dried at 37° for 20 hours paper discs (6mm, punched from Whatmann no 41 paper) were used for the assays. Discs were soaked in DMF and Placed on the inoculated agar media at regular intervals of 6-7 cm, care was taken to Ensure that were taken triplicates. The plates were incubated at 37°C in an inverted fusion. Activity has been determined by zone showing complete inhibition. Growth Inhibition was calculated with reference to positive control. Results of antibacterial activity are given table -2

Table -2: Results of antibacterial activity

	ACTIVITY INDEX	
Compounds	Zone if Inhibition in mm	
	Escherichia Coli gram (-)	Staphylococcus Aureus gram (+)
4a	10	8
4b	11	9
4c	9	10
4d	8	9
4e	7	10
4f	9	11
4g	12	8
4h	10	7
4i	8	10
4j	9	8
Norfloxacin standard	18	20

IV. Result and discussion

Ferrocene chalcones were prepared by acetylation of ferrocene with acetic anhydride and phosphoric acid, acetyl ferrocene was further reacted with aromatic aldehydes substituted with various electron donating and withdrawing groups, both type of substituents gave moderate to good yield of chalcones. Synthesized chalcones were further reacted with hydroxylamine hydrochloride in basic condition. Substituted oxazoles were obtained in good yields. Synthesized compounds were tested for antibacterial activity against gram- positive and gram-negative bacteria.From the result of antibacterial screening given in the table-2 it is evident that most of the compounds are weakly active and few are moderately active against S.Aureusand E. Coli. But compound4g possess very good activity againstE.Coli. It was observed that among all the compound tested. compound 4g shows maximum zone of inhibition while compound and 4e shows minimum zone of inhibition for gram negative E. Coli. Compound 4f shows maximum zone of inhibition and compound 4h shows minimum zone of inhibition for Gram (+) S.Aureusbacteria.All otherCompounds possess moderate activity against bacteria tested.

V. Conclusion

A series of substituted oxazole derivatives of ferrocene were prepared by the reacting chalcones of ferrocene with hydroxylamine hydrochloride. Synthesized compounds were characterized by using ^{1}H-NMR and infrared spectroscopy. Synthesized compounds were tested for their antibacterial activity against one gram positive and one gram negative bacteria. All the compounds shows good to moderate activity against both the bacteria.

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