SYNTHESIS OF NOVEL ISOXAZOLE DERIVATIVES FROM 1,3-DIKETONE DERIVATIVES

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Abstract : Condensation of β-diketone derivative with hydroxylamine hydrochloride ($NH_2OH.HCl$) in pyridine results in the synthesis of isoxazole derivative. By washing with 15% glacial acetic acid and then recrystallization with 95% C_2H_5OH led to crystal formation. Purity of the newly synthesized isoxazole derivative was checked by TLC.The structure of newly synthesized isoxazole derivative were established on the basis of IR, ^1H NMR, ^{13}C NMR and elemental analysis.

Key Words : β-Diketone, hydroxylamine hydrochloride, glacial acetic acid.

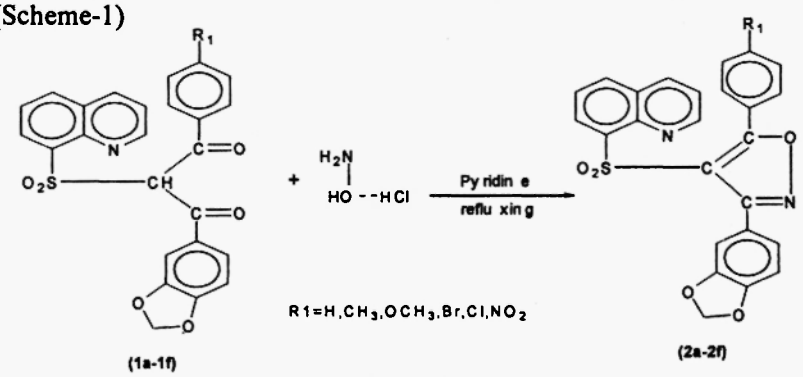
Introduction

Isoxazoles derivative represent a large group of compounds and display a number of medicinal[1] and agricultural properties[2,3]. The isoxazole derivatives are known to exhibit diuretic[4], antifungal[5], antiviral[7], antihelmintic[8], hypolipemic[9], antibacterial[10], cestoidal[11] and antiallergic[12] casting as histamine blocking agent's properties. Pharmacologically useful isoxazole[13] includes semisynthetic penicillin's, semisynthetic lephalosporins, antibacterial sulfonamides, anabolic steroids, monoamine oxidase inhibitor used in psychotherapy etc. Beside these isoxazole derivatives are also employed in the treatment of leprosy[14]. Cycloserine[15], an important isoxazole derivative shows antitubercular and antibacterial activity.

In synthetic organic chemistry isoxazole derivative were prepared by a number of synthetic way viz. Solid phase reaction of polymer bond with RCH_2NO_2, RCHO and RNCS[16], by reaction of chalcone with phenyl cyanate is presence of triethylamin[3], condensation of α,β-dibromochalcones with hydroxyl amine hydrochloridle[17], and by reaction of substituted 1,3-propane dione with hydroxyl amine hydrochloride in ehtanol[18-21]. Various pharmacological activities associated with isoxazole derivative encourages us for synthesis of novel isoxazole.

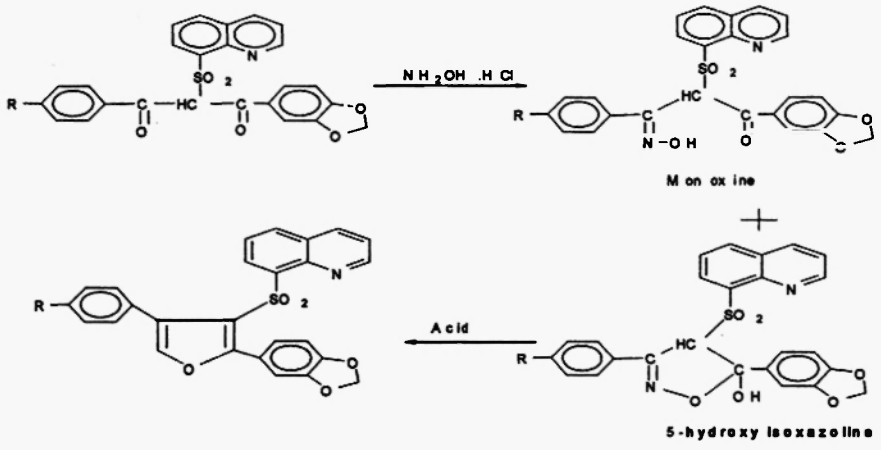
Result and Discussion

In this manuscript we report synthesis of novel isoxazole derivative via synthesis method[18-21]. β-diketone (Ia-If) on condensation with hydroxylamine hydrochloride ($NH_2OH.HCl$) in presence of pyridine and refluxing the mixture for 3 hour on heating mentle led to synthesis of novel isoxazole derivatives. (Scheme-1)



Scheme -1

The reaction of β-diketone with hydroxyl amine first leads to the formation of monoxime of the respective β-diketone and then subsequently cyclise to form 5-hydroxy isoxazoline. Monoxime and 5-hydroxy isoxazoline are the intermediate products of the reaction. These monoxime and 5-hydroxy isoxazaline are readily converted into isoxazole derivatives by treatment with acid. (Scheme-2)



(Scheme-2)

The structure of newly synthesize isoxazoline derivative were established on the basis of IR, ^{1}H NMR and ^{13}C NMR. The elemental analysis of data of titled compounds are given in Table 1.

Table-1: Analytical data of titled compounds

Compounds	M.F	Yields (%)	M.P (^{0}C)	Elemental analysis calc.(founds)				
				C	H	N	S	X
2a	$C_{25}H_{16}O_5N_2S$	53	215	65.78 (65.73)	3.53 (3.51)	6.14 (6.13)	7.02 (7.00)	.....
2b	$C_{26}H_{18}O_5N_2S$	50	235	66.37 (66.33)	3.86 (3.83)	5.95 (5.93)	6.82 (6.81)	.....
2c	$C_{26}H_{18}O_6N_2S$	57	246	64.19 (64.20)	3.73 (3.72)	5.76 (5.74)	6.59 (6.57)	.....
2d	$C_{25}H_{15}O_5N_2SBr$	47	241	56.09 (56.04)	2.82 (2.81)	5.23 (5.23)	5.99 (5.97)	14.93 (14.91)
2e	$C_{25}H_{15}O_5N_2SCl$	50	227	61.16 (61.15)	3.08 (3.06)	5.71 (5.70)	6.53 (6.52)	7.22 (7.20)
2f	$C_{25}H_{15}O_7N_3S$	45	250	59.88 (59.86)	3.01 (3.00)	8.38 (8.36)	6.39 (6.38)	.....

Experimental

All the melting points were uncorrected. IR spectra were recorded on Perkin-Elmer Infrared spectrometer by using KBr pellets. The ^{1}H NMR and ^{13}C NMR spectra were recorded on DRX-300 MHz spectrometer using TMS as an internal standard. Elemental analysis was done using Perkin-Elmer CHNS/O Analyzer 2400. Purity of the compounds was checked by thin layer chromatography using silica gel 'G' as absorbent in suitable solvent system.

General procedure for synthesis of isoxazole derivatives (2a-2f)

The β-diketone derivative (0.005M) and hydroxyl amine hydrochloride (0.005 M) were placed in a round bottom flask and refluxed in pyridine for about 4-6 hours. The resultant mixture are poured onto crushed ice and washed thoroughly several times with 15% acetic acid so as to remove pyridine. The semisolid so obtained was then crystallized with 95% ethanol. Purity of the compound was checked through TLC using petroleum ether : acetone (8:2).

Spectral data:

(2a) I.R. : 1156 & 1367 cm^{-1} (SO_2 vibrations), 1476-1635 cm-1(c=c vibration in Aromatic rings), 1095(C-O linkage).

^{1}H NMR: δ6.02 (2H,S,OCH_2O), 6.83-8.67 (14H, m, aromatic protons).

^{13}C NMR: δ99.97 (OCH_2O), 104 (carbon of isoxazole nucleus attached to -SO_2-) 115-156 (23 lines due to aromatic carbons).

(2b) I.R. : 1152 & 1373 cm^{-1} (SO_2 vibrations), 1457-1625 cm-1(c=c vibration in Aromatic rings), 1074(C-O linkage).

^{1}H NMR: δ6.00 (2H,S,OCH_2O), 6.80-8.56 (13H, m, aromatic protons), 2.14(S,CH_3)

^{13}C NMR: δ100.07 (OCH_2O), 106 (carbon of isoxazole nucleus attached to -SO_2-) 117-157 (23 lines due to aromatic carbons), 23.23(CH_3).

(2c) I.R. : 1134 & 1382 cm^{-1} (SO_2 vibrations), 1476-1627 cm-1(c=c vibration in Aromatic rings), 1064 (C-O linkage).

^{1}H NMR: δ5.99 (2H,S,OCH_2O), 6.77-8.59 (13H, m, aromatic protons), 3.83(OCH_3).

^{13}C NMR: δ99.96 (OCH_2O), 107 (carbon of isoxazole nucleus attached to -SO_2-) 113-155 (23 lines due to aromatic carbons), 57.87(OCH_3).

(2d) I.R. : 1165 & 1370 cm^{-1} (SO_2 vibrations), 1473-1626 cm-1(c=c vibration in Aromatic rings), 1105(C-O linkage).

^{1}H NMR: δ6.00 (2H,S,OCH_2O), 6.90-8.54 (13H, m, aromatic protons).

^{13}C NMR: δ100.23 (OCH_2O), 107 (carbon of isoxazole nucleus attached to -SO_2-) 119-151 (23 lines due to aromatic carbons).

(2e) I.R. : 1150 & 1357 cm^{-1} (SO_2 vibrations), 1450-1625 cm-1(c=c vibration in Aromatic rings), 1079(C-O linkage).

^{1}H NMR: δ5.97(2H,S,OCH_2O), 6.87-8.52 (13H, m, aromatic protons).

^{13}C NMR: δ100 (OCH_2O), 105 (carbon of isoxazole nucleus attached to -SO_2-) 115-157 (23 lines due to aromatic carbons).

(2f) I.R. : 1154 & 1362 cm^{-1} (SO_2 vibrations), 1464-1627 cm-1(c=c vibration in

Aromatic rings), 1098(C-O linkage).

^{1}H NMR: δ6.00 (2H,S,OCH_2O), 7.01-8.79 (13H, m, aromatic protons).

^{13}C NMR: δ100.02 (OCH_2O), 106 (carbon of isoxazole nucleus attached to -SO_2-)

118-154 (23 lines due to aromatic carbons).

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