

Synthesis of 3,5-disubstituted isoxazole

Nagendra Prasad¹ and Manoj Kumar²

¹Research Scholar, Department of Chemistry, J.P. University, Chapra,

²Associate Professor, Department of Chemistry, Raja Singh College Siwan

E-mail : kumarmanoj1921990@gmail.com, prasadnagendra985@gmail.com

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Abstract : In the presence of aqueous NaOH, 2-Acetylthiophene condenses with various aromatic aldehydes in ethanol to produce 1-(2'-thienyl)-3-(substituted phenyl)-2-propen-1-one(Ia-e), which then combines with hydroxylamine hydrochloride and aqueous KOH in the presence of ethanol to produce 3-(2'-thienyl)-5-(sub (IIa-e). Additionally, DMSO was used to dissolve 3-(2'-thienyl)-5-(substituted phenyl)-2-isoxazoline (IIa-e). Iodine was added to this catalytic quantity. cooled and water-diluted. To obtain 3-(2'-thienyl)-5-(substituted phenyl)-isoxazole (II'a-e), the material was thusly separated and then washed with 20% sodium thiosulphate. Analytical, spectroscopic, and melting point studies were used to characterise and clarify the structure of the sample.

(Keywords : Isoxazolines, isoxazoles, synthesis, structural study)

Introduction

Isoxazolines are tautomeric dihydroderivatives of isoxazoles. It was thought that, -unsaturated ketoxime might be an intermediary in the synthesis of isoxazoline. Consider the possibility that isoxazolines aren't created via the simple ring closure of syn-oxime, but rather via disubstituted hydroxylamines or oximino-oxime. A few isoxazolines have anti-inflammatory, antituberculosis, antinociceptive, and anti-inflammatory properties.

When ethanol is present, chalcone interacts with hydroxylamine hydrochloride and aqueous KOH to produce substituted isoxazoline. Isoxazoline synthesis has recently been reported.

Isoxazole is a class of five-membered heterocyclic compounds with neighbouring nitrogen and oxygen heteroatoms. According to

reports, isoxazole derivatives exhibit anti-inflammatory, analgesic, anti-pyretic, antibacterial, antifungal, and antitubercular properties.

In DMSO medium, the previously produced isoxazolines were dissolved. Iodine is added to this after the solid has been refluxed and rinsed with 20% sodium thiosulfate to produce isoxazole.

It has recently been reported on how to make isoxazole. According to a review of the literature, 3-(2'-thienyl)-5- (substituted phenyl) No 1-(2'-thienyl)-isoxazolines have been produced. -3- (substituted phenyl) (substituted phenyl) 3-(2'-thienyl) and 2-propen-1-ones -5-(substituted phenyl) (substituted phenyl) It has not been possible to make isoxazoles from 3-(2'-thienyl)-5-(substituted phenyl)-isoxazolines. In light of this, it was believed intriguing to prepare 1-(2'-thienyl)-3-(2'-thienyl)-5-(substituted phenyl) -isoxazolines. -3-(substituted phenyl) (substituted phenyl) 3-(2'-thienyl) and 2-propen-1-ones -5-(substituted phenyl) (substituted phenyl) 3-(2'-thienyl)-derived isoxazoles -5-(substituted phenyl) (substituted phenyl) -isoxazolines.

Experimental

Chalcone was created using an older method that was known to work for the synthesis of isoxazoline. Chalcone was used to make isoxazoline, which was then used to make isoxazoles using a recognised procedure. Uncorrected melting points were determined in

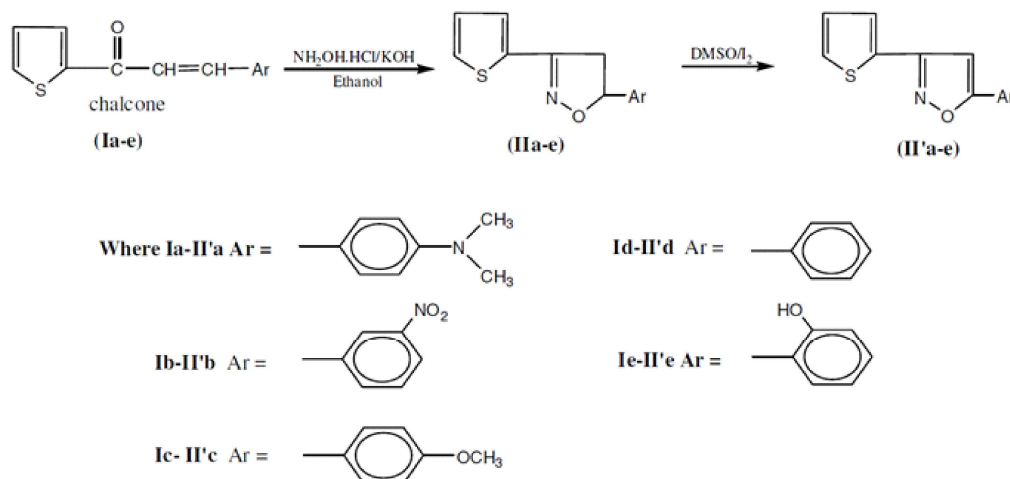
an open capillary tube. Shimadzu spectrophotometer was used to record the IR spectra. Using TMS as an internal reference, PMR spectra were captured in CDCl_3 using a varian mercury YH-300 NMR spectrophotometer (Chemical shifts in a ppm down field from TMS). TLC was used to verify the compounds' purity on silica gel G-coated plates.

Synthesis of 3-(2'-thienyl)-5-(5''-dimethylamino phenyl)- Δ^2 -isoxazoline (IIa)

1-(2'-thienyl) mixture -3-(4 "-dimethylamino phenyl)-2-propen-1-one (Ia) (0.01mol), hydroxyamine hydrochloride (0.02 M), and aqueous KOH (0.3gm in 2ml water) were

refluxed for about six hours in ethanol (20ml). To separate the crude product, the reaction mixture was cooled, acidified with 1:1 HCl, and filtered. From the ethanol, the substance was crystallised to produce solid 3-(2'-thienyl)-5-(4 "-2-isoxazoline)-dimethylamino phenyl) (IIa). Dark orange colour, yield 78% m.p. 1020C.

PMR (CDCl_3): 2.54 (dd, 1H, >CHHA), 2.86 (dd, 1H, >CHBH), 3.2 (s, 6H, -N(CH₃)₂), and 4.5 (dd, 1H, >CHx) IR (KBr) cm^{-1} : 3105.51 (Ar, C-H), 1610.62 (C=N), 1128.38 (C-N-(CH₃)₂), and 654.89 (C 6.3-7.3 (m, 7H, Ar-H and heteroaromatic H) (m, 7H, Ar-H and heteroaromatic H)



Scheme 1: Similar to how the other members of the series have been created, their characterisation information is provided in table 1.

Synthesis of 3-(2'-thienyl)-5-(4"-dimethylamino phenyl)-isoxazole (II'a)

3-(2'-thienyl)-5-(4 "-DMSO was used to dissolve -dimethylamino phenyl)-isoxazoline (IIa) (0.01M) (20ml). Iodine was added in the amount of 0.2 gram to this catalytic amount. Two hours of refluxing the reaction mixture was followed by cooling and water dilution. The isolated substance was then cleaned with a 20%

sodium thiosulfate solution. Using ethanol as a solvent, the product was crystallized to produce solid 3-(2'-thienyl)-5-(4 "-isoxazole (-dimethylamino phenyl) (II'a). Yied 65%, m.p. 2200°C, light brown in color.

IR (KBr) cm^{-1} : 3101.66 (Ar, C-H), 1670.40 (C=C), 1610.60 (C=N), 1055.12 (C-N(CH₃)₂), 673.19(C-S)

PMR (CDCl_3) δ : 2.10 (s, 6H, $-\text{N}(\text{CH}_3)_2$), 6.4-7.3 (m, 8H, Ar-H and heteroaromatic H).

as well as double doublets for CHH_A , CH_BH , and CH_X as well as CH_3 and other peaks.

Results and Discussion

Chalcone (Ia-e), hydroxylamine hydrochloride, and aqueous KOH have been used to create isoxazolines in an ethanol medium. On the basis of analytical evidence, the structures of synthesized isoxazolines (IIa-e) have been established. The IIa's IR spectra revealed bands for ν Ar-CH, C=N, (C-N- $(\text{CH}_3)_2$), and C-S. The PMR data displayed peaks for aromatic protons

In a manner similar to this, the structures of other isoxazolines (IIb-e) were established. On the basis of analytical evidence, the structures of synthetic isoxazoles (ii'a-e) have been established. ν Ar C-H, C=C, C=N, (C-N- $(\text{CH}_3)_2$), and C-S were seen in the IR spectra of ii'a. Peaks for CH_3 , multiplate for Ar-H, and heteroaromatic H were also seen in the PMR data. In a manner similar to this, the structures of other isoxazoles (ii'b-e) were established.

Table 1 : Characterization data of isoxazolines and isoxazoles

S. No.	Code	Molecular Formula	Molecular Weight	Colour $^{\circ}\text{C}$	m.p.	Elemental analysis % Calculated (Found)			
						C	H	N	S
1	IIa	$\text{C}_{15}\text{H}_{16}\text{N}_2\text{OS}$	272	Dark Orange	151 $^{\circ}\text{C}$	66.18 (65.71)	5.89 (5.81)	10.30 (10.15)	11.75 (11.57)
2	IIb	$\text{C}_{13}\text{H}_{10}\text{N}_2\text{O}_3\text{S}$	274	Blackish	125 $^{\circ}\text{C}$	56.94 (65.71)	3.63 (3.61)	10.22 (10.09)	11.68 (11.50)
3	IIc	$\text{C}_{14}\text{H}_{13}\text{NO}_2\text{S}$	259	Brown	82 $^{\circ}\text{C}$	63.87 (64.54)	5.00 (4.96)	5.41 (5.31)	13.34 (12.20)
4	IIId	$\text{C}_{13}\text{H}_{11}\text{NOS}$	229	Brown	84 $^{\circ}\text{C}$	68.11 (67.67)	4.81 (4.74)	7.12 (6.00)	13.98 (13.73)
5	IIe	$\text{C}_{13}\text{H}_{11}\text{NO}_2\text{S}$	245	Light Brown	111 $^{\circ}\text{C}$	63.68 (63.13)	4.49 (4.39)	5.72 (5.60)	13.07 (12.89)
6	II'a	$\text{C}_{15}\text{H}_{14}\text{N}_2\text{OS}$	270	Light Brown	219 $^{\circ}\text{C}$	65.67 (66.19)	6.17 (5.08)	11.38 (10.20)	12.86 (11.70)
7	II'b	$\text{C}_{13}\text{H}_8\text{N}_2\text{O}_3\text{S}$	272	Light Brown	101 $^{\circ}\text{C}$	57.34 (56.96)	2.93 (2.91)	10.30 (10.15)	11.77 (11.61)
8	II'c	$\text{C}_{14}\text{H}_{11}\text{NO}_2\text{S}$	257	Grey	94 $^{\circ}\text{C}$	64.37 (64.86)	4.29 (4.23)	5.43 (5.39)	12.46 (12.30)
9	II'd	$\text{C}_{13}\text{H}_9\text{NOS}$	227	Off White	281 $^{\circ}\text{C}$	68.71 (68.29)	3.97 (3.90)	6.17 (6.00)	14.10 (13.89)
10	II'e	$\text{C}_{13}\text{H}_9\text{NO}_2\text{S}$	243	Brown	136 $^{\circ}\text{C}$	63.20 (63.75)	3.71 (3.63)	5.77 (5.64)	13.17 (12.91)

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