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An Emergent Synthesis of Novel Isoxazolidines *Via* 1,3-Dipolar Cycloaddition of α-Cinnamic Aryl-N-Aryl Nitrone with β-Nitrostyrene and IT'S Antibacterial Activities

M. R. Bhamuni[1], S. R. Jayapradha[2]

[1]Ph.D Research scholar, PG and Research Department of Chemistry, Government Arts College for Women, Nilakottai, Affiliated to Mother Teresa Women's University, Kodaikanal.

[2]Associate Professor, PG And Research Department of Chemistry, Government Arts College for Women, Nilakottai, Affiliated to Mother Teresa Women's University, Kodaikanal
Email: *srjayapradha2023[at]gmail.com*

Abstract: ***A new series of isoxazolidine derivatives are synthesized with good yields by 1,3-dipolar cycloaddition reaction between newly synthesized nitrones and an efficient dipolarophile β-nitrostyrene. The α-Cinnamic aryl-N-aryl nitrone and β-nitrostyrene as a novel class of dipolarophile has been synthesized in shortened reaction time to get an excellent yield. This specific nitrone and dipolarophiles are refluxed in the presence of toluene in a conventional method to give a five membered heterocyclic compound namely isoxazolidine. The structure of all the synthesized isoxazolidines are characterized by FT-IR, Uv-vis spectroscopy, ^{1}H and ^{13}C NMR spectra. The cycloadducts-isoxazolidines formed also exhibit a biological activities.***

Keywords: Isoxazolidine, 1,3-dipolar cycloaddition, Cinnamaldehyde, Nitrone, Dipolarophile

1. Introduction

The 1,3-dipolar cycloaddition reaction is a key intermediate for the preparation of five membered heterocyclic compounds [1]. The good yield of heterocyclic compounds are synthesized with the help of dipolarophiles and novel synthesized nitrones which are derived from aromatic aldehyde and phenyl hydroxyl amine [2]. The nitrones are commonly prepared by the methods of 1) N-substituted hydroxylamine and carbonyl compounds by condensation reaction 2) oxidations of secondary amines, N-substituted hydroxylamines, and imines 3) N-alkylation of oximes 4) N-substituted hydroxylamine by cope-type hydroamination reactions of alkynes and allenes [3]. Most of the research paper describes the nitrone and dipolarophile is an important tool for the preparation of open chain molecules [4]. Usually, dipolarophile are double or triple bonded species and most common dipolarophiles are alkenes, alkynes, carbonyls and nitriles. The multiple bond groups also act as dipolarophiles such as imines, azo and nitroso [5]. Usually, the research paper explains the nitrone is prepared by the readily available aromatic aldehyde with N-phenyl hydroxylamine. It formed with an excellent yield in multigram scale, it requires purification with ethanol. Our research work also follows the same method to synthesize nitrone with one of the aromatic aldehydes and freshly prepared phenyl hydroxylamine [6]. The 1,3-Dipolar cycloaddition reactions of nitrones with dipolarophiles is one of the best routes for the preparation of heterocyclic compounds like isoxazolidine [7]. The kind of multi-substituted isoxazolidines are particularly useful for the large number of natural products and they are biologically active compounds such as antifungal, anti-tuberculosis and antiviral etc., [8] In the present investigation, we have synthesized the β-nitrostyrene from condensation reaction of the benzaldehyde derivative and nitromethane which is used as a dipolarophile to obtain heterocyclic compound in 1, 3-dipolar cycloaddition with nitrone [9]-[12]. Many of the research papers illustrated the use of nitrones in synthetic organic chemistry [13], [14]. The nitrone can act as an efficient starting material to synthesize an isoxazolidine unit, an important heterocyclic unit. So, it makes us interest on cycloaddition reactions [15]-[17]. So far, nitrones and it's cycloaddition reactions are synthesized for the observation of variety of biological active compounds, free radicals with EPR spin trapping technique. It is also used in therapeutic agents i.e., cardiac diseases, anti-cancer, anti-ageing and neuro degenerative diseases [18]-[20].

2. Experimental Section

2.1 Materials and Methods

The chemicals nitrobenzene, toluene, ethanol are purchased from Sigma-Aldrich and Zn powder, cinnamaldehyde, ammonium chloride from nice brand. All the chemicals are used without any further purification. The present dipolarophile β-nitrostyrene is synthesized using commercially available nitromethane, sodium hydroxide and benzaldehyde by the prescribed procedure. The synthesized nitrone and dipolarophile remains stable for a longer time. All the cycloaddition reactions are monitored by TLC using silica gel plates. The conventional method is used to synthesize novel isoxazolidine derivatives and it was confirmed by taking ^{1}H NMR spectra using Bruker 400 MHZ using $CDCl_3$ as a solvent and TMS as internal

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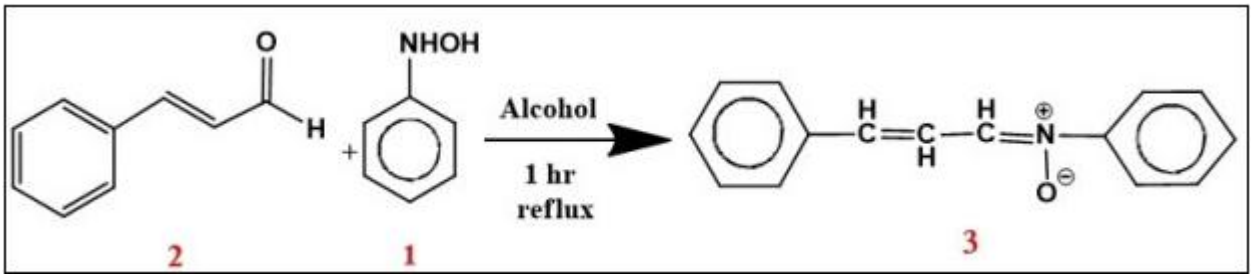
standard. The same instrument is used to record ^{13}C NMR spectra at 100 MHZ. Perkin-Elmer machine was used for recording IR spectra all the molecules and Jasco spectrophotometer used to record Uv-vis spectra.

2.2 Synthesis of phenyl hydroxyl amine

The Ammonium chloride (5g) is dissolved in 160 ml of water was and it is placed in a mechanical stirrer without heating, and 8.3 ml of Nitrobenzene were mixed to it. To this mixture add 11.8 g of Zn powder contains 90% purity about 15 minutes while the temperature increases to 60°-65° C. The reaction continues for further more 15 minutes until the temperature falls down. Then filter the reaction mixture to remove the zinc oxide and wash it with 100 ml of hot water, again the filtered mixture is saturated with common salt (60g) and ice bar. The pale-yellow crystals of phenyl hydroxyl amine **1** are filtered with suction pump. Finally, the phenyl hydroxyl amine is synthesized in a very good yield [21].

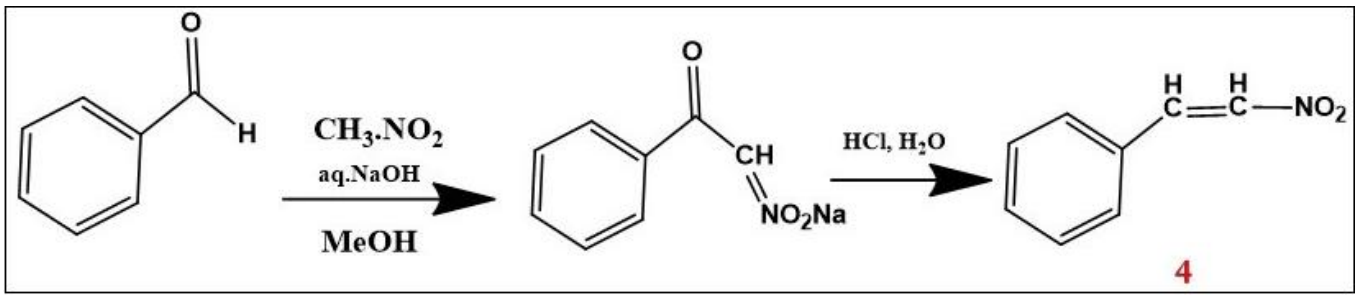
2.3 Synthesis of α-Cinnamic aryl-N-aryl nitrone



Scheme 1: Synthesis of α-Cinnamic aryl-N-aryl nitrone

A mixture of synthesized phenyl hydroxyl amine **1** (0.1 mol, 10.9 g) and cinnamaldehyde **2** (0.1 m, 13.2 g) are added to in ethanol and refluxed for one hour, then the solvent is and the residue (α-Cinnamic aryl-N-aryl nitrone) **3** is crystallized from ethanol [22] as shown in scheme 1. The Chemical structure of the compound **3** are confirmed by ^{1}H NMR, ^{13}C NMR spectrum.

2.4 Synthesis of β-nitrostyrene



Scheme 2: Synthesis of β-nitrostyrene

The β-nitrostyrene **4** is prepared from the mechanical stirrer contains nitromethane (5mol, 305g), benzaldehyde (5mol, 530g) and 1000cc of methyl alcohol. A solution of sodium hydroxide is dissolving (5.25 mol, 210g) with equal amount of water. It is added to the nitromethane mixture with stirring at 10-15°. The bulky white precipitate appears then after fifteen minutes it is converted into clear solution. Then the solution was poured into Hydrochloric acid (1000cc of Conc. HCl in 1500cc of water). The pale-yellow crystals appear then purified with ethanol [23], [24] as shown in Scheme 2.

2.5 Synthesis of 5-nitro-2, 4-diphenyl-3-styrylisoxazolidine

The synthesized α-Cinnamic aryl-N-aryl nitrone **3** [2.23g (0.01m)] and β-nitrostyrene **4** [1.49g (0.01m)] in presence of toluene under reflux for 8-15 hrs to get a compound **5**, in between the reaction condition was noticed by thin layer chromatography. The isoxazolidines compound **5** was purified by column chromatography on silica gel using pet ether-ethyl acetate (4:1) as eluent and recrystallized from acetone-chloroform mixture [25]-[27]. All the obtained heterocyclic compounds **5-5n** from synthesized nitrone and their dipolarophiles were illustrated in Table:1

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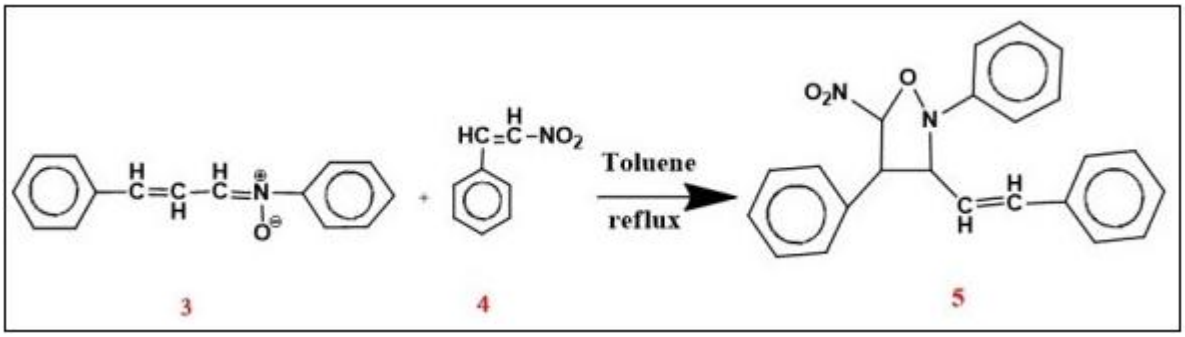

Scheme 3: Synthesis of 5-nitro-2, 4-diphenyl-3-styrylisoxazolidine

3. Results and Discussion

The present study of 1,3-dipolar cycloaddition reaction has been carried out with nitrone **3** and dipolarophiles **4-4n**, all the isoxazolidine compounds **5-5n** are impressive shown in Table: 1.

In the first step, the synthesis of novel nitrone has been achieved phenyl hydroxyl amine and cinnamaldehyde as aldehyde prepared in a simple procedure in excellent yield (scheme 1). The chemical structure of α-Cinnamic aryl-N-aryl nitrone **3** was confirmed by ^{1}H NMR, ^{13}C NMR spectrum. After the good yield of newly synthesized cinnamaldehyde nitrone, we also produced different dipolarophiles such as β-nitrostyrene **4** and substituted β-nitrostyrene **4a-4n**. The β-nitrostyrene is an effective material for the preparation of heterocyclic compounds and also biologically active dipolarophiles such as anti-cancer, anti-fungal etc., β-nitrostyrene is synthesized from the Henry reaction of aldehyde and nitromethane (scheme 2). Due to conjugation of double bond with nitro group, the double bond is stimulating to contribute in organic reactions to synthesize heterocyclic compounds with five or six membered rings such as pyrroles, furans, oxazoles and isoxazolidines derivatives. The isoxazolidines is an important class of heterocyclic compound that existing biological compounds.

In the second step, the synthesis of isoxazolidines derivatives **5** (scheme 3) by β-nitrostyrene and α-Cinnamic aryl-N-aryl nitrone is performed via conventional method by 1,3-dipolar cycloaddition reaction. We have observed that cycloaddition reaction completed after 15 hrs, noticed that the less reaction time leads to low yield which has been increased by increasing reaction time. The cycloaddition reaction also followed under microwave irradiation method and noted that the yields are good. So far there is no report for the synthesis of isoxazolidine **5** using α-Cinnamic aryl-N-aryl nitrone with β-nitrostyrene. The new dipolarophile namely β-nitrostyrene is a fascinating dipolarophile because it has potentially activated double bond along with nitro group and beta position which can lead to the formation of adduct with sufficient quantities of 1,3-dipoles namely α-Cinnamic aryl-N-aryl nitrone. Thus, there is more scope for additional new products in addition to normally expected regio and stereo isomers. For 15-20 hrs an equimolar ration of α-Cinnamic aryl-N-aryl nitrone and β-nitrostyrene are refluxed in toluene after working up it has been found that only one product predominating in the reaction mixture as revealed by TLC and crude NMR sample of the product. The product isolated is identified as 5-nitro-2,4-diphenyl-3-styrylisoxazolidine **5**. Column chromatography is need to purify the product. So, the mixture was separated and purified by column chromatography forms a 5-nitro-2,4-diphenyl-3-styrylisoxazolidine **5** in a reasonable to moderate yield. All the heterocyclic compounds **5-5n** from **4-4n** was illustrated in Table:1. The structure of all the cycloadducts was identified by spectroscopic method ^{1}H and ^{13}C NMR spectrum. ^{1}H NMR spectrum shows the 5.63 (s, 3H), 4.35 (s, 2H), 3.97 (s, 3H), these signals confirm the formation of novel 5-nitro-2,4-diphenyl-3-styrylisoxazolidine **5**. The isoxazolidines product are stable and all the expected results are appeared in ^{1}H and ^{13}C NMR spectrum. On the basis of spectral data of ^{1}H and ^{13}C NMR, structure of all the synthesized isoxazolidine derivatives **5-5n** have been confirmed. The structural characterization of 5-nitro-2,4-diphenyl-3-styrylisoxazolidine **5** was also investigated by FT-IR spectroscopy, the spectra are shown in Figure 1. It can be seen that the peak appears at ~3316 cm^{-1} is attributed to O-H stetching vibration and the peak at ~3056 cm^{-1} corresponds to the NH stretching vibration. The Peaks at ~2165 cm^{-1} and ~1668 cm^{-1} are ascribed to the C≡C and C=O stretching vibration. The peaks appeared at ~1547 cm^{-1} and ~1312 cm^{-1} are due to C=C (olefin) and OH bending vibration. The ~1073 cm^{-1} and ~968 cm^{-1} peaks are C-O stretching and C=C bending vibration of disubstituted alkene. These results confirms the formation of 5-nitro-2,4-diphenyl-3-styrylisoxazolidine **5**. The Uv-vis absorption spectrum of isoxazolidine ring showed absorbance from 200 to 600 nm with three characteristics bands at 239, 266 nm and shoulder at 272 (Figure 2). This suggested that the isoxazolidine derivative formed well.

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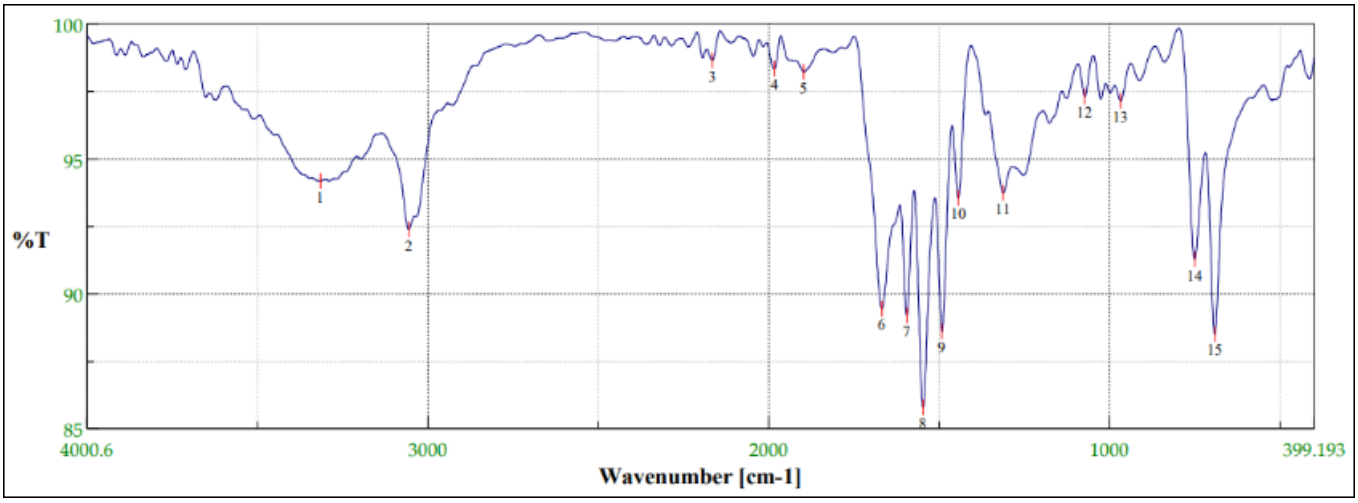

Figure 1: FT-IR spectrum of 5-nitro-2,4-diphenyl-3-styrylisoxazolidine

Antibacterial study of 5-nitro-2,4-diphenyl-3-styrylisoxazolidine

In this study, the synthesized isoxazolidine compound **5** were screened for antimicrobial activities against 3 bacterial strains (Table 2), agar was used and grown for 48 hours at 25°C. The 20 mg compound were dissolved in 20 ml of dimethyl sulfoxide (DMSO) solution is suffiicent for the growth of bacteria in agar plates. The isoxazolidine compound **5** on specific organisms like Bacillus marisflavi [12mm], Exignobacterium indicus [18mm] and there is no zone formation appears in Pseudomonas aeruginosa [28]-[30] as shown in Figure 3.

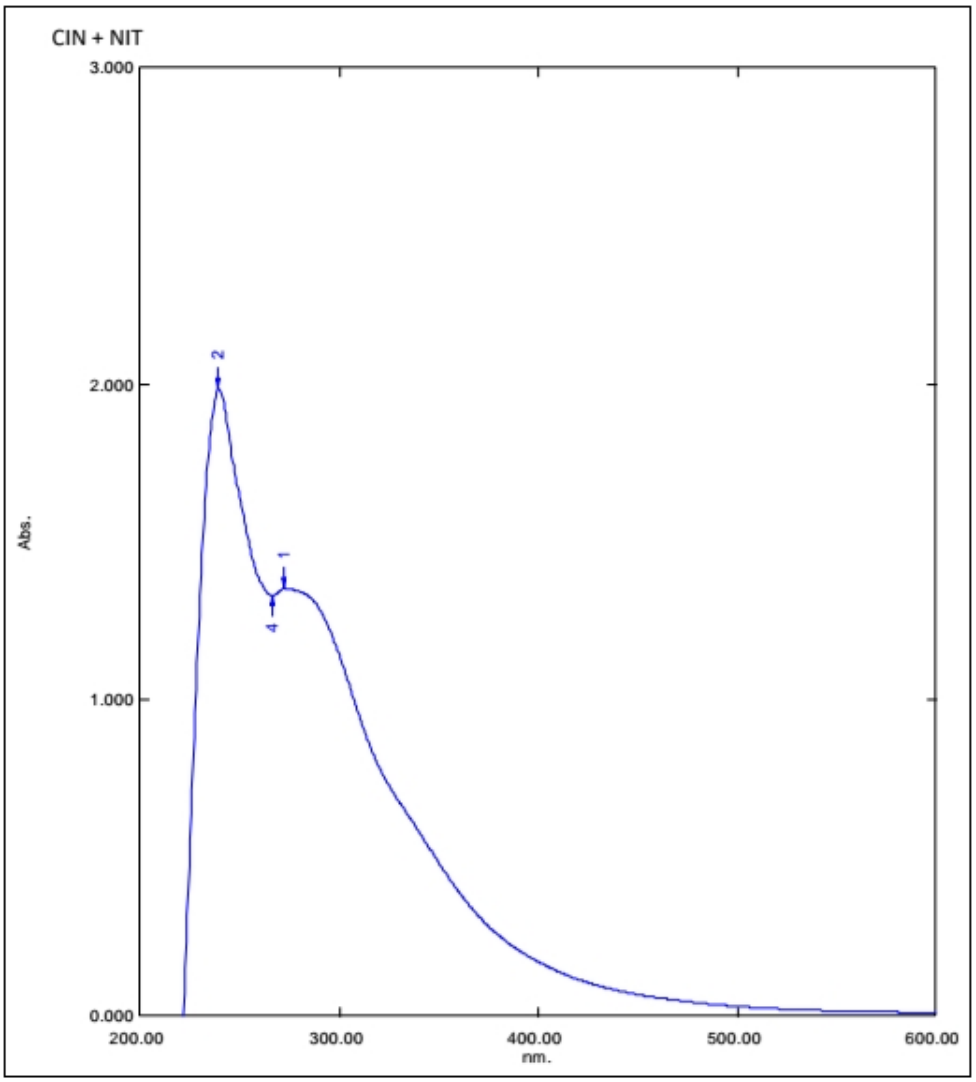

Figure 2: Uv-vis spectrum of 5-nitro-2,4-diphenyl-3-styrylisoxazolidine

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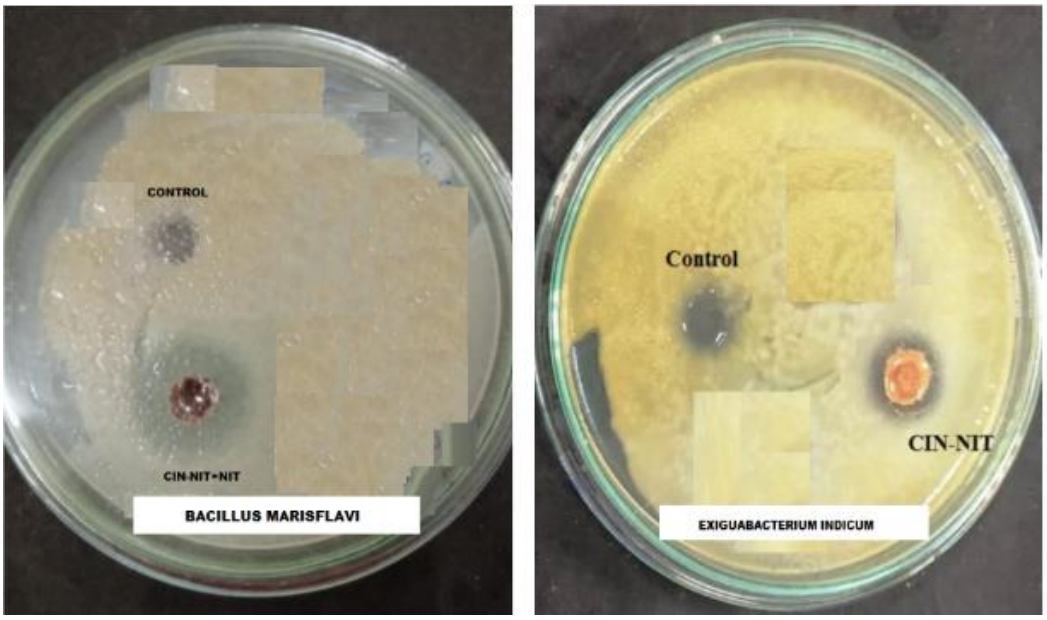

Figure 3: Bacillus marisflavi and Exignobacterium indicus of 5-nitro-2,4-diphenyl-3-styrylisoxazolidine

Table 2: Organisms and values of 5-nitro-2,4-diphenyl-3-styrylisoxazolidine

Concentration: 20mg/ml of DMSO	
Organisms	5-nitro-2,4-diphenyl-3-styrylisoxazolidine
Bacillus marisflavi	12 mm
Exignobacterium indicus	18 mm
Pseudomonas aeruginosa	-

3.1 Spectroscopic data 5-nitro-2,4-diphenyl-3-styrylisoxazolidine (5)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36 – 7.26 (m, 18H), 7.26 – 7.22 (m, 6H), 7.17 (dd, *J* = 14.4, 2.9 Hz, 12H), 6.69 (s, 2H), 6.68 – 6.59 (m, 7H), 6.57 (s, 3H), 6.19 (s, 3H), 5.63 (s, 3H), 5.09 (s, 3H), 3.97 (s, 4H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.03 (s), 136.07 (d, *J* = 8.0 Hz), 134.77 (s), 134.24 (s), 131.13 (s), 129.38 – 128.66 (m), 128.33 – 127.95 (m), 127.85 (s), 127.66 – 127.45 (m), 122.33 (s), 116.39 – 116.00 (m), 67.27 (s), 56.60 (s).

3.2 Spectroscopic data of 4-(2,4-dichlorophenyl)-5-nitro-2-phenyl-3-styrylisoxazolidine (5a)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 – 7.25 (m, 16H), 7.25 – 7.12 (m, 24H), 6.68 (s, 3H), 6.58 (t, *J* = 16.7 Hz, 11H), 6.53 (d, *J* = 0.9 Hz, 2H), 6.19 (s, 4H), 5.63 (s, 4H), 4.35 (s, 2H), 3.97 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.03 (s), 139.47 (s), 136.11 (s), 129.45 – 129.24 (m), 129.22 – 129.01 (m), 128.78 (d, *J* = 5.5 Hz), 128.56 – 128.31 (m), 128.31 – 127.95 (m), 127.85 (s), 127.66 – 127.45 (m), 122.33 (s), 116.39 – 116.00 (m), 67.53 (s), 62.22 (s).

Table 1: Synthesized heterocyclic compounds [5-5n] from nitrone and dipolarophiles

Entry	Nitrone	Dipolarophiles	Product
1	[3]	β-nitrostyrene	5-nitro-2,4-diphenyl-3-styrylisoxazolidine (5)
2	[3]	2,4-dichloro-β-nitrostyrene	4-(2,4-dichlorophenyl)-5-nitro-2-phenyl-3-styrylisoxazolidine (5a)
3	[3]	4-fluoro-β-nitrostyrene	4-(4-fluorophenyl)-5-nitro-2-phenyl-3-styrylisoxazolidine (5b)
4	[3]	2-chloro-β-nitrostyrene	4-(2-chlorophenyl)-5-nitro-2-phenyl-3-styrylisoxazolidine (5c)
5	[3]	2-chloro-6-fluoro-β-nitrostyrene	4-(2-chloro-6-fluorophenyl)-5-nitro-2-phenyl-3-styrylisoxazolidine (5d)
6	[3]	3,4-dimethoxy-β-nitrostyrene	4-(3,4-dimethoxyphenyl)-5-nitro-2-phenyl-3-styrylisoxazolidine (5e)
7	[3]	2,5-dimethoxy-β-nitrostyrene	4-(2,5-dimethoxyphenyl)-5-nitro-2-phenyl-3-styrylisoxazolidine (5f)
8	[3]	5-bromo-2-methoxy-β-nitrostyrene	4-(5-bromo-2-methoxyphenyl)-5-nitro-2-phenyl-3-styrylisoxazolidine (5g)
9	[3]	4-methoxy-β-nitrostyrene	4-(4-methoxyphenyl)-5-nitro-2-phenyl-3-styrylisoxazolidine (5h)
10	[3]	4-bromo- β-nitrostyrene	4-(4-bromophenyl)-5-nitro-2-phenyl-3-styrylisoxazolidine (5i)
11	[3]	2,6-dichloro- β-nitrostyrene	4-(2,6-dichlorophenyl)-5-nitro-2-phenyl-3-styrylisoxazolidine (5j)
12	[3]	4-methoxy- β-nitrostyrene	5-nitro-2-phenyl-3-styryl-4-(p-tolyl)isoxazolidine (5k)
13	[3]	2-hydroxy- β-nitrostyrene	2-(5-nitro-2-phenyl-3-styrylisoxazolidin-4-yl)phenol (5l)
14	[3]	3-chloro- β-nitrostyrene	4-(3-chlorophenyl)-5-nitro-2-phenyl-3-styrylisoxazolidine (5m)
15	[3]	2-fluro-4-chloro- β-nitrostyrene	4-(4-chloro-2-fluorophenyl)-5-nitro-2-phenyl-3-styrylisoxazolidine (5n)

3.3 Spectroscopic data of 4-(4-fluorophenyl)-5-nitro-2-phenyl-3-styrylisoxazolidine (5b)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50 – 7.46 (m, 2H), 7.36 – 7.28 (m, 2H), 7.28 – 7.22 (m, 2H), 7.19 (s, 1H), 7.16 – 7.10 (m, 2H), 7.07 – 7.01 (m, 2H), 6.68 (s, 1H), 6.60 – 6.47 (m, 2H), 6.19 (s, 1H), 4.93 (s, 1H), 4.06 (s, 1H), 3.97 (s, 1H).

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^{13}C NMR (100 MHz, $CDCl_3$) δ 163.51 (s), 147.03 (s), 137.61 (s), 136.11 (s), 129.89 – 129.23 (m), 129.22 – 129.01 (m), 128.78 (d, *J* = 5.5 Hz), 128.33 – 127.95 (m), 127.85 (s), 127.66 – 127.45 (m), 122.33 (s), 116.39 – 116.01 (m), 116.01 – 114.70 (m), 67.53 (s), 62.22 (s).

3.4 Spectroscopic data of 4-(2-chlorophenyl)-5-nitro-2-phenyl-3-styrylisoxazolidine (5c)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35 (s, 1H), 7.33 – 7.17 (m, 5H), 7.17 – 7.08 (m, 5H), 6.70 (s, 1H), 6.63 (s, 1H), 6.61 – 6.48 (m, 2H), 6.19 (s, 1H), 5.59 (s, 1H), 4.15 (s, 1H), 3.97 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.03 (s), 138.22 (s), 136.11 (s), 134.12 (s), 130.51 (s), 129.26 – 129.01 (m), 129.00 – 128.56 (m), 128.33 – 127.95 (m), 127.84 (d, *J* = 2.8 Hz), 127.66 – 127.45 (m), 122.33 (s), 116.39 – 116.00 (m), 67.27 (s), 56.60 (s).

3.5 Spectroscopic data of 4-(2-chloro-6-fluorophenyl)-5-nitro-2-phenyl-3-styrylisoxazolidine (5d)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 – 7.28 (m, 4H), 7.28 – 7.22 (m, 4H), 7.16 (t, *J* = 8.4 Hz, 6H), 7.11 (s, 2H), 7.06 (s, 2H), 6.92 (s, 2H), 6.68 (s, 2H), 6.58 (t, *J* = 16.4 Hz, 5H), 6.53 (d, *J* = 0.9 Hz, 1H), 6.19 (s, 2H), 5.63 (s, 2H), 4.98 (s, 1H), 3.97 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.80 (s), 147.03 (s), 136.11 (s), 134.02 (s), 131.10 (s), 129.22 – 129.01 (m), 128.78 (d, *J* = 5.5 Hz), 128.33 – 127.96 (m), 127.85 (s), 127.66 – 127.45 (m), 126.71 (s), 126.32 (s), 122.33 (s), 118.92 (s), 116.39 – 116.00 (m), 67.72 (s), 56.56 (s).

3.6 Spectroscopic data of 4-(3,4-dimethoxyphenyl)-5-nitro-2-phenyl-3-styrylisoxazolidine (5e)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36 – 7.22 (m, 4H), 7.17 (t, *J* = 5.9 Hz, 3H), 7.09 (d, *J* = 7.1 Hz, 2H), 6.97 (s, 1H), 6.69 (s, 1H), 6.67 – 6.56 (m, 2H), 6.54 (s, 1H), 6.19 (s, 1H), 5.63 (s, 1H), 4.33 (s, 1H), 3.97 (s, 1H), 3.85 – 3.79 (m, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 149.39 (s), 147.75 (s), 147.03 (s), 136.11 (s), 134.35 (s), 129.22 – 129.01 (m), 128.78 (d, *J* = 5.5 Hz), 128.33 – 127.96 (m), 127.85 (s), 127.66 – 127.45 (m), 122.33 (s), 118.66 (s), 116.39 – 116.00 (m), 113.25 (s), 110.43 (s), 67.53 (s), 62.78 (s), 56.89 – 56.58 (m).

3.7 Spectroscopic data of 4-(2,5-dimethoxyphenyl)-5-nitro-2-phenyl-3-styrylisoxazolidine (5f)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35 – 7.21 (m, 12H), 7.17 (t, *J* = 5.2 Hz, 9H), 6.98 (s, 3H), 6.88 (s, 3H), 6.78 (s, 3H), 6.70 – 6.69 (m, 1H), 6.69 – 6.49 (m, 11H), 6.19 (s, 3H), 5.63 (s, 3H), 5.08 (s, 2H), 3.97 (s, 3H), 3.84 – 3.79 (m, 18H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.68 (s), 150.22 (s), 147.03 (s), 136.11 (s), 129.39 (s), 129.22 – 129.01 (m), 128.78 (d, *J* = 5.5 Hz), 128.33 – 127.96 (m), 127.85 (s), 127.66 – 127.45 (m), 122.33 (s), 116.39 – 116.01 (m), 115.99 (s), 114.85 (s), 110.95 (s), 67.27 (s), 56.79 (s), 56.04 (s), 50.03 (s).

3.8 Spectroscopic data of 4-(5-bromo-2-methoxyphenyl)-5-nitro-2-phenyl-3-styrylisoxazolidine (5g)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.54 (s, 4H), 7.35 (d, *J* = 1.4 Hz, 2H), 7.35 – 7.21 (m, 19H), 7.17 (t, *J* = 4.8 Hz, 12H), 6.79 (s, 4H), 6.69 (s, 2H), 6.61 (t, *J* = 9.3 Hz, 14H), 6.19 (s, 4H), 5.63 (s, 4H), 5.06 (s, 3H), 3.97 (s, 4H), 3.82 – 3.78 (m, 12H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.92 (s), 147.03 (s), 136.11 (s), 130.90 (s), 129.22 – 129.01 (m), 129.00 – 128.68 (m), 128.50 (s), 128.33 – 127.95 (m), 127.85 (s), 127.66 – 127.45 (m), 122.33 (s), 117.74 (s), 116.39 – 116.00 (m), 113.92 (s), 67.27 (s), 56.79 (s), 50.03 (s).

3.9 Spectroscopic data of 4-(4-methoxyphenyl)-5-nitro-2-phenyl-3-styrylisoxazolidine (5h)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35 – 7.24 (m, 60H), 7.23 (s, 6H), 7.17 (t, *J* = 5.7 Hz, 33H), 6.97 – 6.83 (m, 22H), 6.69 (s, 7H), 6.68 – 6.59 (m, 26H), 6.57 (s, 11H), 6.19 (s, 11H), 5.63 (s, 11H), 4.27 (s, 8H), 3.97 (s, 10H), 3.84 – 3.80 (m, 32H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.68 (s), 147.03 (s), 136.11 (s), 132.97 (s), 129.22 – 128.88 (m), 128.78 (d, *J* = 5.5 Hz), 128.33 – 127.96 (m), 127.85 (s), 127.66 – 127.45 (m), 122.33 (s), 116.39 – 116.00 (m), 114.75 – 114.53 (m), 67.53 (s), 62.22 (s), 56.04 (s).

3.10 Spectroscopic data of 4-(4-bromophenyl)-5-nitro-2-phenyl-3-styrylisoxazolidine (5i)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.55 – 7.41 (m, 6H), 7.41 – 7.32 (m, 6H), 7.32 – 7.24 (m, 10H), 7.23 (s, 2H), 7.19 (s, 3H), 7.16 – 7.10 (m, 6H), 6.68 (s, 3H), 6.60 – 6.47 (m, 6H), 6.19 (s, 3H), 4.93 (s, 3H), 4.09 (s, 3H), 3.97 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.03 (s), 141.17 (s), 136.11 (s), 131.98 – 131.77 (m), 129.22 – 129.01 (m), 128.78 (d, *J* = 5.5 Hz), 128.33 – 127.93 (m), 127.85 (s), 127.66 – 127.45 (m), 122.33 (s), 118.87 (s), 116.39 – 116.00 (m), 67.53 (s), 62.22 (s).

3.11 Spectroscopic data of 4-(2,6-dichlorophenyl)-5-nitro-2-phenyl-3-styrylisoxazolidine (5j)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37 – 7.27 (m, 2H), 7.27 – 7.22 (m, 2H), 7.19 (dt, *J* = 10.4, 5.2 Hz, 5H), 7.06 (s, 1H), 6.80 – 6.55 (m, 4H), 6.19 (s, 1H), 5.63 (s, 1H), 5.37 (s, 1H), 3.97 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.03 (s), 137.10 (s), 136.11 (s), 135.10 – 134.88 (m), 130.78 (s), 129.38 – 129.01 (m), 128.78 (d, *J* = 5.5 Hz), 128.33 – 127.95 (m), 127.85 (s), 127.66 – 127.45 (m), 122.33 (s), 116.39 – 116.00 (m), 67.72 (s), 56.42 (s).

3.12 Spectroscopic data of 5-nitro-2-phenyl-3-styryl-4-(p-tolyl)isoxazolidine (5k)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33 – 7.23 (m, 11H), 7.22 (s, 1H), 7.21 – 7.12 (m, 10H), 6.76 (s, 2H), 6.72 – 6.61 (m, 6H), 6.19 (s, 2H), 5.62 (s, 2H), 4.56 (s, 2H), 3.97 (s, 2H), 2.37 – 2.33 (m, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.03 (s), 138.56 (d, *J* = 18.2 Hz), 136.11 (s), 130.20 – 129.80 (m), 129.22 – 129.01 (m), 128.78 (d, *J* = 5.5 Hz), 128.66 – 128.30 (m), 128.30 – 127.95 (m), 127.85 (s), 127.66 – 127.45 (m), 122.33 (s), 116.39 – 116.00 (m), 67.53 (s), 62.22 (s), 21.13 (s).

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3.13 Spectroscopic data of 2-(5-nitro-2-phenyl-3-styrylisoxazolidin-4-yl)phenol (5l)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39 – 7.25 (m, 4H), 7.20 (t, *J* = 1.4 Hz, 3H), 7.12 (s, 1H), 7.01 (s, 1H), 6.83 (s, 1H), 6.80 – 6.66 (m, 4H), 6.61 (s, 1H), 6.19 (s, 1H), 5.58 (s, 1H), 4.72 (s, 1H), 3.97 (s, 1H), 3.80 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.76 (s), 147.03 (s), 136.11 (s), 129.34 – 129.01 (m), 128.78 (d, *J* = 5.5 Hz), 128.33 – 127.96 (m), 127.85 (s), 127.72 – 127.45 (m), 126.42 (s), 122.35 (d, *J* = 3.4 Hz), 121.07 (s), 116.39 – 116.00 (m), 67.27 (s), 49.99 (s).

3.14 Spectroscopic data of 4-(3-chlorophenyl)-5-nitro-2-phenyl-3-styrylisoxazolidine (5m)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41 (s, 1H), 7.33 – 7.26 (m, 2H), 7.26 – 7.15 (m, 8H), 6.75 (s, 1H), 6.71 – 6.63 (m, 3H), 6.19 (s, 1H), 5.61 (s, 1H), 4.60 (s, 1H), 3.97 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.03 (s), 141.21 (s), 136.11 (s), 132.95 (s), 129.40 (s), 129.14 (s), 129.14 – 128.66 (m), 128.33 – 127.96 (m), 127.85 (s), 127.66 – 127.45 (m), 126.70 (s), 126.36 (s), 122.33 (s), 116.39 – 116.00 (m), 67.53 (s), 62.78 (s).

3.15 Spectroscopic data of 4-(4-chloro-2-fluorophenyl)-5-nitro-2-phenyl-3-styrylisoxazolidine (5n)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35 – 7.25 (m, 3H), 7.25 – 7.21 (m, 2H), 7.17 (s, 1H), 7.12 – 7.08 (m, 3H), 7.04 (s, 1H), 6.61 (d, *J* = 2.7 Hz, 2H), 6.53 – 6.41 (m, 2H), 6.19 (s, 1H), 5.56 (s, 1H), 4.54 (s, 1H), 3.97 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.50 (s), 147.03 (s), 136.11 (s), 135.37 (s), 129.22 – 129.01 (m), 128.78 (d, *J* = 5.5 Hz), 128.33 – 127.96 (m), 127.85 (s), 127.66 – 127.49 (m), 127.16 (s), 126.01 (s), 124.74 (s), 122.33 (s), 120.75 (s), 116.39 – 116.00 (m), 67.27 (s), 56.92 (s).

4. Conclusion

In this paper, a novel isoxazolidines has been synthesized from nitrone and dipolarophile in a very simple, cost efficient and environmentally friendly. The formation of all the heterocyclic compounds was confirmed by taking ^{1}H NMR, ^{13}C NMR spectra, FT-IR region, Uv-vis region and antimicrobial studies. All the studies is confirmed that the five membered heteroccylic compounds formation formed well.

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