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Transition Metal free One-pot multi-component synthesis of an approach to functionalized Novel ethyl isoxazolidine-3-carboxylate derivatives and their Anti-microbial activity

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Abstract

Here, we report the successful conversion of an efficient Transition metal-free catalysed one-pot three-component approach to the synthesis of different functionalized ethyl 5-(substituted aryl/heteroaryl)-2-(substituted aryl/heteroaryl)isoxazolidine-3-carboxylate derivatives (4a-r). These reactions are silent features of transition metal-free, economically acceptable, cheap, and readily available accessible diazo compounds, nitrosoarenes, and styrene, catalysts and starting materials, good to excellent functional group comparability, a wide range of substrate scope, and exceptional yields. Newly created compounds were characterized by different spectral techniques such as 1H-NMR, 13C-NMR, and HRMS. All the synthesized compounds were evaluated for their anti-bacterial and anti-fungal activities. The antibacterial activity results showed that compounds 4b, 4c, 4e, 4l, 4m, and 4n were more active against S. aureus. In the case of B. subtilis, the compounds 4b, 4c, 4e, 4l, 4m, and 4n were found to be more active. The compounds 4b, 4c, 4e, 4l, 4m, and 4n were more active against E. coli. In the case of P. aeruginosa 4b, 4c, 4e, 4l, 4m and 4n were found to be more active. On the other hand, the anti-fungal activity result shows that the compounds 4b, 4c, 4e, 4l, 4m and 4n were more active against A. niger. The compounds 4b, 4c, 4e, 4l, 4m, and 4n were found to be more active against C. albicans.

Keywords: *Nitroso-benzene, Ethyl diazo acetate, Styrenes, Ethyl isoxazolidine-3-carboxylates, Anti-bacterial and Anti-fungal.*

1. INTRODUCTION

Heterocyclic compounds constitute a significant class of organic molecules due to their widespread occurrence in natural products, pharmaceuticals, agrochemicals, and functional materials. Among these, nitrogen- and oxygen-containing heterocycles have attracted sustained attention because of their diverse biological and pharmacological properties. Isoxazolidine derivatives, in particular, represent an important group of five-membered heterocycles containing adjacent nitrogen and oxygen atoms within the ring structure. These compounds serve as valuable intermediates in organic synthesis and are frequently encountered in biologically active molecules. Consequently, the development of efficient, sustainable, and versatile synthetic methods for functionalized isoxazolidine derivatives remains an important objective in contemporary synthetic chemistry. Isoxazolidines are known for their broad spectrum of biological activities, including antimicrobial, antiviral, anticancer, anti-inflammatory, and enzyme inhibitory properties. Moreover, these heterocycles are versatile precursors for the synthesis of β-amino alcohols, amino acids, and other functionalized compounds via reductive or oxidative ring transformations. Such transformations have been widely exploited in medicinal chemistry for the preparation of pharmacologically relevant

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molecules. Therefore, the efficient construction of functionalized isoxazolidine scaffolds continues to be of high interest to researchers working in heterocyclic and medicinal chemistry.

Traditional methods for synthesizing isoxazolidines often involve stepwise procedures requiring prefunctionalized starting materials, use of transition metal catalysts, or harsh reaction conditions. Although these methods can be effective, they frequently suffer from limitations such as long reaction times, low atom economy, multistep purification processes, and generation of chemical waste. Furthermore, the use of transition metal catalysts, though beneficial in many reactions, introduces concerns related to cost, toxicity, and environmental impact. Residual metal contamination in pharmaceutical intermediates also poses regulatory and safety challenges, prompting increasing interest in metal-free synthetic methodologies.

In recent years, multicomponent reactions have emerged as powerful tools in modern organic synthesis because they allow the construction of complex molecules from simple starting materials in a single operational step. These reactions offer several advantages, including improved atom economy, operational simplicity, reduced reaction time, and minimized waste generation. Multicomponent approaches are particularly attractive for medicinal chemistry and combinatorial synthesis, where rapid generation of molecular diversity is desirable. One-pot multicomponent reactions further enhance synthetic efficiency by avoiding isolation of intermediates and reducing solvent consumption and purification steps.

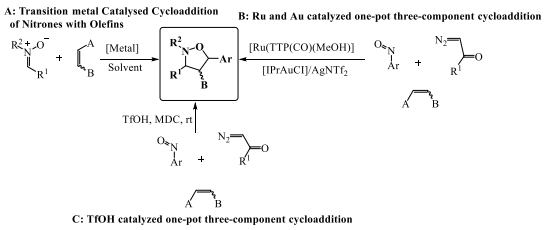
Simultaneously, the principles of green chemistry encourage the development of environmentally benign synthetic protocols that minimize hazardous reagents, energy consumption, and waste production. Transition metal-free reactions align well with these principles, providing safer and more sustainable alternatives to conventional metal-catalyzed processes. Consequently, the exploration of metal-free one-pot multicomponent strategies for constructing biologically relevant heterocycles has become an active area of research.

Ethyl isoxazolidine-3-carboxylate derivatives represent valuable structural motifs due to the presence of ester functionality combined with the heterocyclic framework, offering opportunities for further structural modification and biological evaluation. Functionalization of these scaffolds can lead to compounds with enhanced pharmacological profiles and improved physicochemical properties. Despite their importance, efficient and environmentally friendly synthetic routes to structurally diverse ethyl isoxazolidine derivatives remain relatively underexplored, particularly using transition metal-free methodologies. Another compelling motivation for the synthesis of novel heterocyclic compounds arises from the global challenge posed by microbial resistance. The rapid emergence of drug-resistant bacterial and fungal strains has significantly reduced the effectiveness of many existing antimicrobial agents, creating an urgent demand for new chemotherapeutic candidates. Heterocyclic frameworks, including isoxazolidine derivatives, have demonstrated promising antimicrobial properties, making them attractive targets for further investigation. Exploration of new functionalized derivatives may lead to compounds with improved activity and potential therapeutic applications.

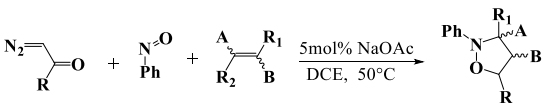
The present study focuses on the development of a transition metal-free one-pot multicomponent synthetic approach for the preparation of novel functionalized ethyl isoxazolidine-3-carboxylate derivatives. The methodology aims to provide a simple, efficient, and environmentally friendly route to structurally diverse heterocycles with potential biological relevance. Additionally, the synthesized compounds were evaluated for their antimicrobial activity against selected microbial strains to investigate their possible application as antimicrobial agents.

The present work thus combines synthetic innovation with biological evaluation, contributing to the ongoing search for sustainable chemical processes and new bioactive molecules. The proposed protocol offers advantages such as operational simplicity, good yields, reduced reaction steps, and avoidance of metal catalysts, making it a promising approach for generating functionalized heterocyclic compounds. Furthermore, biological screening of the synthesized derivatives provides valuable insights into structure–activity relationships and potential pharmaceutical relevance, this study demonstrates an efficient and greener synthetic strategy for accessing functionalized ethyl isoxazolidine derivatives while simultaneously exploring their antimicrobial potential, thereby addressing important challenges in both synthetic chemistry and medicinal research.

Previous works



Present work



SCHEME 1. Different Strategies to Construct Functionalized Isoxazolidines

2. RESULTS AND DISCUSSION

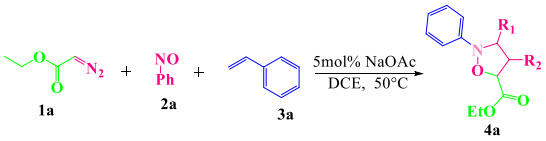
2.1. Chemistry

We started our investigation to synthesize the target compound (4a) as model reaction in one pot by using an equi molar ratio of ethyl diazo acetate (1), nitrosobenzene (2), and styrene (3) was selected as the model reaction to evaluate catalysts.

Gratifyingly, 70% yield could be obtained when 10 mol% KOAc was employed as a catalyst at 50°C temperature in various we screened the effect of different bases such as *t*-BuOK, KOH, K_2CO_3, Na_2PO_4 and DBU. However, no better results were observed. Strong bases (*t*-BuOK, KOH) indicated inferior catalytic activities with trace amount of product 4a (Table 1, entries 2–3), and K_2CO_3, Na_2PO_4 and DBU catalysed the reaction to give slightly lower yields compared to NaOAc (Table 1, entries 4, 5 & 9). Notably, only 8% yield was attained in the absence of a base, which suggested that the existence of a suiTable base was crucial for this transformation (Table 1, entry 7). A series of solvents were then examined and DCE proved to be the best choice (Table 1, entry 1). The use of 1, 4-dioxane, toluene and CH_3CN provided the product 4a in somewhat lower yields (Table 1, entries 11–13).

Other solvents such as CH_3OH, and THF were less effective and gave obviously lower yields (Table 1, entries 8-9). To our delight, reducing the amount of NaOAc to 5 mol% did not affect the yield (Table 1, entry 14). However, the adjustment of reaction temperature resulted in no further improvement in yields (Table 1, entries 14 and 15). Moreover, the reaction proceeded more smoothly and gave the best yield when the 1a/2a/3a molar ratios were 1.2:1.2:1 (99%, Table 1, entry 16).

Table 1: Optimization of Reaction Conditions of (4a)*

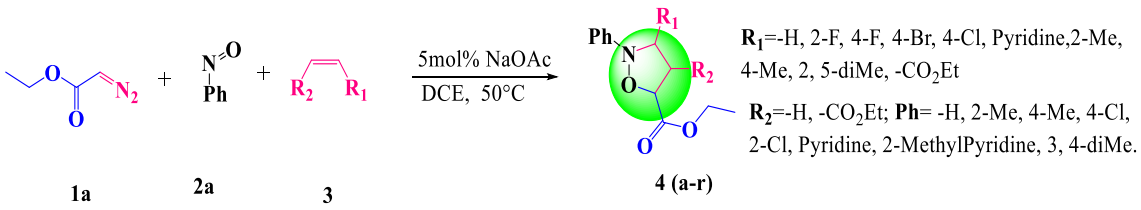


Entry	Catalyst (mol %)	Solvent	Conditions	[d]Yield (%)	Time (hrs)
1.	KOAc	DCE	50°C	70	20
2.	KOH	DCE	50°C	trace	20
3.	^{t}BuOK	DCE	50°C	trace	20
4.	K_2CO_3	DCE	50°C	60	20
5.	DBU	DCE	50°C	62	20
6.	NaOAc	DCE	50°C	75	20
7.	--	DCE	50°C	8	20
8.	NaOAc	THF	50°C	30	20
9.	NaOAc	MeOH	50°C	53	20
10.	Na_2PO_4	DCE	50°C	68	20
11.	NaOAc	Dioxane	50°C	70	20
12.	NaOAc	Toluene	50°C	73	20
13.	NaOAc	CAN	50°C	74	20
[b]14.	NaOAc (5mol %)	DCE	30°C	65	20
[b]15.	NaOAc (5mol %)	DCE	60°C	76	20
[c]16.	NaOAc	DCE	50°C	99	20

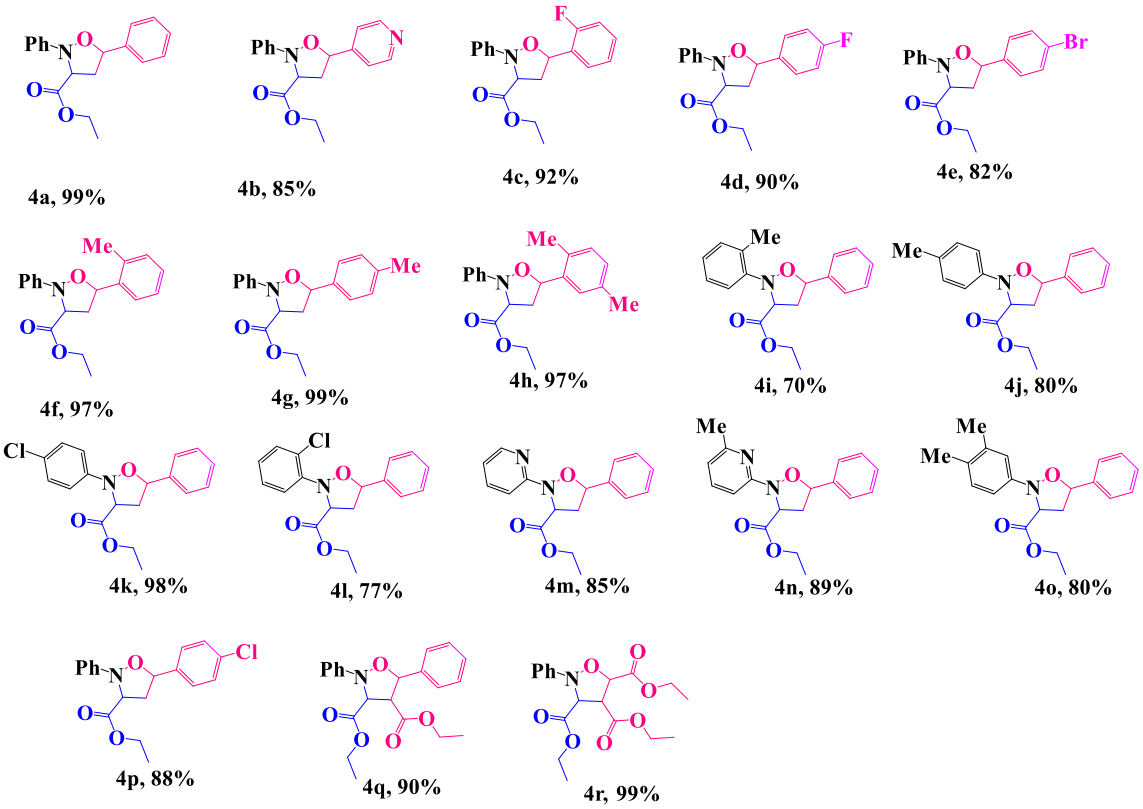
[a]The reaction was carried out by taking compound with 1 (0.1 mmol), 2 (0.1 mmol), 3 (0.1 mmol) and 10 mol% of catalyst in 1.0 mL of solvent for 20hrs. [b]5 mol% of NaOAc was used and 65% yield was obtained; [c]1:2:3: NaOAc = 1.2:1.2:1:0.05. [d]Isolated yields.

With the established optimal reaction conditions using NaOAc as a catalyst in hand, we next evaluated the substrate scope of this transformation using a variety of different olefins 3, and the results are summarized in Scheme 2. Various styrenes bearing electron donating groups such as methyl or electron withdrawing groups such as fluoro, chloro, and bromo at any position, reacted well with 1a and 2a to afford the desired products 4a–4r 70–99% yields with a single isomer which demonstrated that the electronic and steric properties of substituents had little influence on the transformation. It should be noted that dimethyl substituted product 4f was obtained in 98% yield. Moreover, ethylenes substituted with a heteroaryl group such as 4-vinylpyridine also worked well, giving the desired product 4b in 88% yields with excellent diastereoselectivities, respectively. It was respectively. Gratifyingly, 1, 2-disubstituted aryl alkenes such as ethyl cinnamate could be converted successfully into the desired product 4q in 93% with good yields and diastereoselectivities. Affording the corresponding single isomer product 4c in excellent yields. To further demonstrate the utility of this method, more demanding 1, 1-disubstituted olefins were examined as substrates which have never been explored in three-component system. All examined substrates afforded the desired products 4i–4o in 70-98% yields. 77-89% and 80% yields were obtained. Interestingly, these results demonstrated that electronic effect of functional groups played a more important role than steric effect for 1, 1-disubstituted olefins and the stronger the electron-withdrawing ability of substituents was, the higher the yield.

SCHEME 2: Synthesis of Various Isoxazolidene:



Derivatives of isoxazolidine-3-carboxylate (4a-r)



3. PHARMACOLOGICAL STUDIES

3. 1 Test microorganisms

The four bacterial strains used in the present study were collected from Department of Animal biotechnology, University of Hyderabad. The bacteria used are *Bacillus subtilis*, *Escheria coli*, *Pseudomonas euroginosa*, and *Staphylococcus aurous*.

3. 2 Antimicrobial activity

All the newly synthesized compounds (4a-r) were screened for their antibacterial activity against *Bacillus subtilis*, *Escheria coli*, *Pseudomonas euroginosa*, and *Staphylococcus aurous* at 20, 30, 40, 100, and 200 µg/mL concentrations. The Ciprofloxacin is used as standard reference drug. The activity was determined by agar well diffusion method. All these newly synthesized compounds (4a-r) were shown good antibacterial activity. Among all the compounds (4a-r), the compounds 4b, 4c, 4e, 4l, 4m and 4n are active against all the four bacterial strains. The antibacterial activity results are summarized in Table 2.

Table 2: Antibacterial zone of inhibition (mm) of Ethyl isoxazolidine-3-carboxylates (4a-r)

Code of Compounds	Conc.(µg/ml)	Zone of inhibition (mm)			
		S.aureus	*B.subtilis*	*E.coli*	*P.aeruginosa*
4a	100	15	11	23	19
	200	17	19	24	21
4b	**100**	**21.8**	**20.4**	**25**	**31**
	200	**23.1**	**21.2**	**26.1**	**32.2**
4c	**100**	**22**	**20.7**	**25.4**	**31.4**
	200	**23.5**	**21.5**	**26.5**	**32.4**
4d	100	18	17	18	22
	200	20	18	21	29
4e	**100**	**22.5**	**20.9**	**25.9**	**32**
	200	**23.2**	**22**	**27**	**32.7**
4f	100	21	15	18.5	18
	200	21.5	16	20.8	20
4g	100	20	19	20.8	26
	200	21.9	20	21.4	28
4h	100	20.1	18.5	20.4	24
	200	20.8	17.6	22.1	28.7
4i	100	19	16	20	22.9
	200	20	14	21	25.5
4j	100	12	16.5	12.9	12.3
	200	14	17	15	14.5
4k	100	12	16.5	12.5	12.3
	200	14	17	14	14.5

4l	**100**	**22.4**	**20.5**	**25.2**	**31.2**
	200	**23.3**	**21.2**	**26.5**	**32.5**
4m	**100**	**22.6**	**20.7**	**25.8**	**31.6**
	200	**23.9**	**21**	**26.8**	**31.9**
4n	**100**	**22.7**	**21.3**	**25.9**	**32**
	200	**24**	**21.7**	**26.9**	**32.8**
4o	100	12	16.5	12	12.3
	200	14	17	14	14.5
4p	100	19.7	18.1	20.5	30.1
	200	20	17.9	22	31
4q	100	12	16.5	16	12.3
	200	14.9	19.1	14	14.5
4r	100	21	19.5	21	29
	200	20.1	18	22	30
Ciprofloxacin	100	23	21	26	32
	200	24	22	27	33

3.3 Antifungal activity

The antifungal activity of these newly synthesized compounds (4a-r) against *Aspergillus niger* and *Candida albicans* were tested at 100 and 200 µg/mL concentration. Voriconazole is utilized as standard reference drug. The antifungal activity was carried out by using the disk diffusion method. The results of the antifungal activity revealed that the compounds 4b, 4c, 4e, 4l, 4m and 4n exhibiting highest activity, the results are summarized in Table 3.

Table 3: Antifungal zone of inhibition (mm) of Ethyl isoxazolidine-3-carboxylates (4a-r)

Compounds	Conc.(µg/ml)	Zone of inhibition (mm)	
		A. niger	*C. albicans*
4a	100	15	23
	200	16	23
4b	100	27.0	23.0
	200	28.5	25.1
4c	100	27.5	23.9
	200	30	26.0
4d	100	22	19
	200	25	20
4e	100	27	23.3
	200	28.9	25.6
4f	100	20	20
	200	24	21
4g	100	21.2	20.4
	200	22.3	22
4h	100	23	20.7
	200	20.8	21.5
4i	100	27	19.9
	200	23.1	22.9
4j	100	22	20
	200	24.5	21.5
4k	100	22	20
	200	24.5	21.5
4l	100	27.4	23.5
	200	29.1	25
4m	100	27.5	23.7
	200	29.7	25.5
4n	100	27.8	24
	200	30	25.8
4o	100	22	20
	200	24.5	21.5
4p	100	27.4	18
	200	29.4	22
4q	100	22	20
	200	24.5	21.5
4r	100	27.1	19.5
	200	29.7	20.1
Voriconazole	100	28	24
	200	30	26

DOCKING RESULTS

The binding affinity of 6 selected ligands which showed biological activity better than reference molecule towards Staphylococcus aureus. The binding site surrounded by the protein residues were analysed using molecular docking studies. The binding affinities of the molecules are showed strong interaction energies with the Staphylococcus aureus active site and the results are showed in the Table 4.

Table 4: Ligands and their binding energy

S. No.	Ligand name	Binding energy (in kcal/mol)
1	4b	-8.2
2	4c	-8.82
3	4e	-9.38
4	4l	-8.69
5	4m	-8.24
6	4n	-8.91

The molecules bound to the Staphylococcus aureus are stabilized by the aromatic-aromatic and hydrophobic interactions. In these ligands 4e molecule showed highest binding energy such as -9.38 kcal/mol. The 4e molecule stabilised with Pi-alkyl interactions with Leu-141, Val-137 and leu-160 residues. The residues Ala-134, Phe-22, Val-133 and Tyr-248 showed hydrophobic interactions. Remaining molecules stabilised in the active site with pi-alkyl and hydrophobic interactions. All the ligands showed good binding energies between -8.2 kcal/mol to -9.3 kcal/mol.

The binding affinity of 6 selected ligands which showed biological activity better than reference molecule towards Candida albicans. The active site surrounded by the protein residues were analysed using molecular docking studies. The binding affinities of the molecules are showed strong interaction energies with the Staphylococcus aureus active site and those results are showed in the Table 5.

Table 5: Strong interaction energies with the Staphylococcus aureus

S. No.	Ligand name	Binding energy (in kcal/mol)
1	4b	-7.76
2	4c	-7.98
3	4e	-8.48
4	4l	-8.1
5	4m	-7.98
6	4n	-8.19

The molecules bound to the Candida albicans are stabilized with hydrogen bonds, Pi-alkyl and hydrophobic interactions. In these ligands also 4e molecule showed highest binding energy such as -8.48 kcal/mol. The 4e molecule carbonyl group and oxygen molecule showed 2 hydrogen bonding interactions with Tyr-45 and Arg-311 residues. This complex also stabilised with Pi-Pi interactions with Tyr-371 and Trp-436 residues. Further this complex showed hydrophobic interactions with Tyr-259, Trp-196 and Cys-374 residues in the active site. Remaining molecules also stabilised in the active site with hydrogen bonds, Pi-Pi and hydrophobic interactions.

All the ligands showed good binding energies between -7.7 kcal/mol to -8.4 kcal/mol, the selected molecules stabilised with hydrophobic, Pi-Pi, Pi-alkyl and hydrogen bonding interactions with strong binding energies. This study showed good correlation with experimental results.

CONCLUSIONS

In conclusion, we have developed Iodine mediated synthesis of novel Ethyl isoxazolidine-3-carboxylates (4a-r) in good yields. The significant features of this synthesis include shorter reaction time, high yields, and simple workup. All the newly synthesized Compounds (4a-r) were evaluated for their antibacterial and anti-fungal activities. All these synthesized compounds (4a-r) demonstrate good antimicrobial activities, among them, compounds 4b, 4c, 4e, 4l, 4m and 4n displayed highest antibacterial and antifungal activities.

EXPERIMENTAL

MATERIALS AND METHODS:

All reagents and solvents were obtained from commercial sources and used without further purification unless otherwise noted. NaOAc, DCE, THF, Methanol, Dioxane, Toluene, and Acetonitrile, were purchased from Sigma-Aldrich Co. $ClCH_2COOH$, 1, 2-dichloroethane and ethyl acetate were obtained commercially. NMR spectra were recorded on a Bruker AVANCE III 600 MHz NMR spectrometer (400 MHz for ^{1}H and 150 MHz for ^{13}C) in DMSO-d6 with tetramethylsilane (TMS) as an internal standard. TLCs were performed on Merck TLC Silica gel 60 F254 plates eluting with EtOAc and developed with iodine. Melting points were determined in glass capillaries on a Mel-Temp 3.0. Mass spectra were measured on Bruker micrOTOF-Q II or maXis (Bruker, Germany) instruments using electrospray ionization (HRESIMS). All yields were referred to isolated yieldsof Ethyl 2, 5-diphenylisoxazolidine-3-carboxylate.

CHEMISTRY

General Procedure for the synthesis of compounds (4a-r):

To a reaction system of Nitrosoarene **2** (0.12 mmol), α-diazo compound 1 (0.12 mmol) and NaOAc (0.5 mg, 0.005 mmol, 5 mol %) in DCE (1.0 mL) was added alkene 3 (0.1 mmol). Subsequently, the resultant solution was stirred at 50° C and monitored by TLC. Upon completion of consumption of alkene, the reaction mixture was purified by silica-gel column chromatography to give the corresponding cycloaddition product (4a-r).

Ethyl 2, 5-diphenylisoxazolidine-3-carboxylate (4a): Yellow oil; Yield: 99% ^{1}HNMR ($CDCl_3$, 400 MHz); δ 1. 30 (t, *J* = 7. 1 Hz, 3H), 2. 72-2. 79 (m, 1H), 2. 88-2. 95 (m, 1H), 4. 28 (q, *J* = 7.1 Hz, 2H), 4. 50 (dd, *J* = 8.9, 5.8 Hz, 1H), 5. 04 (dd, *J* = 9. 4, 6. 8 Hz, 1H), 7. 0 (t, *J* =7. 3 Hz, 1H), 7. 14(d, *J* =7. 8 Hz, 2H), 7. 29- 7.35 (m, 2H), 7. 367. 41 (m, 3H), 7. 48-7.51 (m, 2H) ppm; ^{13}C NMR ($CDCl_3$, 100MHz); δ 13. 3, 40. 3, 60. 9, 68. 5, 79. 0, 113. 1, 121.1, 126. 0, 127.5, 127. 6, 128. 1, 136. 3, 150. 1, 170. 7 ppm; HRMS (ESI) m/z: [M+ Na] $^+$ Calcd for $C_{18}H_{19}NaNO_3$ 320. 1258; found: 320. 1261; Ele. Anly: C, 72.71; H, 6.44; N, 4.71; O, 16.14; found: C, 72.74; H, 6.45; N, 4.68; O, 16.16.

Ethyl 2-phenyl-5-(pyridin-4-yl) isoxazolidine-3-carboxylate (4b): Yellow oil; Yield: 85% ^{1}HNMR ($CDCl_3$, 400 MHz); δ 1. 30 (t, *J* = 7. 1 Hz, 3H), 2. 66-2. 73 (m, 1H), 2. 91-2. 99 (m, 1H), 4. 25 (q, *J* = 7.1 Hz, 2H), 4. 52 (dd, *J* = 8.9, 5.8 Hz, 1H), 5. 11 (dd, *J* = 9. 4, 6. 8 Hz, 1H), 7. 03 (t, *J* =7. 3 Hz, 1H), 7. 13 (d, *J* =7. 8 Hz, 2H), 7. 29- 7.35 (m, 2H), 7. 33 (t, *J* = 7.8 Hz, 2H), 7. 40 (d, *J* = 4. 9 Hz, 2H), 8. 62 (d, *J* = 4. 8 Hz, 2H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz); δ 14. 1, 40. 4, 61. 9, 68. 3, 78. 3, 114. 3, 121.5, 122. 5, 129.3, 147. 2, 150. 2, 171. 1 ppm; HRMS (ESI) m/z: [M+ H] $^+$ Calcd for $C_{17}H_{19}N_2O_3$ 299. 1391; found: 299. 1398; Ele. Anly: C, 68.43; H, 6.10; N, 9.41; O, 16. 13; found: C, 68.45; H, 6. 08; N, 9. 40; O, 16.12.

Ethyl 5-(2-fluorophenyl)-2-phenylisoxazolidine-3-carboxylate (4c): Yellow oil; Yield: 92% ^{1}HNMR ($CDCl_3$, 400 MHz); δ 1. 32 (t, *J* = 7. 2 Hz, 3H), 2. 67-2. 75 (m, 1H), 2. 93- 3. 01(m, 1H), 4. 26 (q, *J* = 7.2 Hz, 2H), 4. 52 (dd, *J* = 9.9, 5.4 Hz, 1H), 5. 36 (dd, *J* = 8. 8, 7. 4 Hz, 1H), 6. 99-7. 02 (m, 1H), 7. 03- 7.09 (m, 1H), 7. 14 (dd, *J* = 8. 6, 0.9 Hz, 2H), 7. 18 (td, *J* = 7. 7, 1. 1Hz, 1H), 7. 28-7. 35 (m, 3H), 7. 68 (td, *J* = 7. 5, 1. 7Hz, 1H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz); δ 14. 1, 40. 4, 61. 9, 68. 3, 78. 3, 114. 3, 121.5, 122. 5, 129.3, 147. 2, 150. 2, 171. 1 ppm; HRMS (ESI) m/z: [M+ H] $^+$ Calcd for $C_{18}H_{19}FNO_3$ 316. 1344; found: 316. 1348; Ele. Anly: C, 68.56; H, 6.75; F, 6. 02; N, 4.44; O, 15. 22; found: C, 68.51; H, 6. 08; F, 6. 05; N, 4. 40; O, 15.19.

Ethyl 5-(4-fluorophenyl)-2-phenylisoxazolidine-3-carboxylate (4d): Yellow oil; Yield: 90% ^{1}HNMR ($CDCl_3$, 400 MHz); δ 1. 34 (t, *J* = 7. 1 Hz, 3H), 2. 67-2. 75 (m, 1H), 2. 84- 2. 92 (m, 1H), 4. 28 (q, *J* = 7.1 Hz, 2H), 4. 51 (dd, *J* = 8.9, 5.4 Hz, 1H), 5. 03 (dd, *J* = 9. 1, 7. 0 Hz, 1H), 7. 02 (t, *J* = 7. 3 Hz, 1H), 7. 05 (t, J = 8. 7 Hz, 2H), 7. 12 -7. 16 (m, 2H), 7. 29 – 7. 35 (m, 2H), 7. 45-7. 51 (m, 2H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz); δ 14. 2, 41. 0, 61. 9, 79. 5, 114. 3, 115.5 (d, *J* = 21. 6 Hz), 122. 3, 128.9 (d, *J* = 8. 4 Hz), 129. 2, 133. 1 (d, *J* = 3. 2 Hz), 151. 0, 161. 6 (d, *J* = 245. 7 Hz), 171. 5 ppm; HRMS (ESI) m/z: [M+ H] $^+$ Calcd for $C_{18}H_{19}FNO_3$ 316. 1343; found: 316. 1357; Ele. Anly: C, 68.56; H, 6.75; F, 6. 02; N, 4.44; O, 15. 22; found: C, 68.58; H, 6. 08; F, 6. 05; N, 4. 41; O, 15.19.

Ethyl 5-(4-bromophenyl)-2-phenylisoxazolidine-3-carboxylate (4e): Yellow oil; Yield: 84% ^{1}HNMR ($CDCl_3$, 400 MHz); δ 1. 34 (t, *J* = 7. 2 Hz, 3H), 2. 66-2. 74 (m, 1H), 2. 85- 2. 94 (m, 1H), 4. 28 (q, *J* = 7.2 Hz, 2H), 4. 50 (dd, *J* = 8.9, 5. 5 Hz, 1H), 5. 03 (dd, *J* = 9. 0, 7. 2 Hz, 1H), 7. 02 (t, *J* = 7. 4 Hz, 1H), 7. 13 (d, *J* = 8. 7 Hz, 2H), 7. 30 (dd, J = 8. 5, 7. 5 Hz, 2H), 7. 36 (dd, J = 8. 4, 2H), 7. 51 (d, *J* = 8. 4 Hz, 2H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz); δ 14. 2, 41. 2, 61. 5, 78. 5, 80. 0, 116. 5. 3, 120. 5, 126. 3, 127.2, 128. 2, 130. 16, 132. 2, 151. 0, 171. 5 ppm; HRMS (ESI) m/z: [M+ H] $^+$ Calcd for $C_{18}H_{19}BrNO_3$ 375. 2513; found: 375. 2523; Ele. Anly: C, 57.48; H, 4.75; Br, 21. 26; N, 3.74; O, 12. 74; found: C, 57.52; H, 4. 86; Br, 21. 30; N, 3. 70; O, 12.78.

Ethyl 2-phenyl-5-(*o*-tolyl) isoxazolidine-3-carboxylate (4f): Yellow oil; Yield: 97% ^{1}HNMR ($CDCl_3$, 400 MHz); δ 1. 33 (t, *J* = 7. 2 Hz, 3H), 2. 32 (s, 3H), 2. 62 – 2. 69 (m, 1H), 2. 90- 2. 98 (m, 1H), 4. 28 (q, *J* = 7. 2 Hz, 2H), 4. 51 (dd, *J* = 9.0, 5. 8 Hz, 1H), 5. 24 (dd, *J* = 9. 4, 6. 7 Hz, 1H), 7. 01 (t, *J* = 7. 4 Hz, 1H), 7. 13 – 7. 18 (m, 3H), 7. 21 – 7. 27 (m, 2H), 7. 30- 7. 34 (m, 2H), 7. 68 – 7. 70 (m, 1H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz); δ 14. 2, 19. 4, 41. 1, 61. 8, 68. 5, 114. 1, 122. 1, 125. 9, 126.5, 128. 1, 129. 2, 130. 4, 135. 8, 151. 2, 171. 5 ppm; HRMS (ESI) m/z: [M+ H] $^+$ Calcd for $C_{19}H_{22}NO_3$ 312. 1595; found: 312. 1612; Ele. Anly: C, 73.31; H, 6.80; N, 4.51; O, 15. 41; found: C, 73. 35; H, 6. 86; N, 4. 48; O, 15.45.

Ethyl 2-phenyl-5-(*p*-tolyl) isoxazolidine-3-carboxylate (4g): Yellow oil; Yield: 99% ^{1}HNMR ($CDCl_3$, 400 MHz); δ 1. 34 (t, *J* = 7. 2 Hz, 3H), 2. 35 (s, 3H), 2. 70 – 2. 77 (m, 1H), 2. 85- 2. 92 (m, 1H), 4. 28 (q, *J* = 7. 1 Hz, 2H), 4. 49 (dd, *J* = 8.9, 6.0 Hz, 1H), 5. 00 (dd, *J* = 9. 6, 6. 7 Hz, 1H), 7. 01 (t, *J* = 7. 3 Hz, 1H), 7. 14 (d, *J* = 7. 8Hz, 2H), 7. 19 (d, *J* = 8.0Hz, 2H), 7. 29 (dd, *J* = 8.7Hz, 2H), 7. 38 (d, *J* = 8.0 Hz, 2H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz); δ 14. 2, 21. 4, 41. 2, 61. 8, 68. 7, 80. 2, 114. 1, 122. 0, 127. 2, 126.5, 128. 1, 129. 2, 129. 3, 134. 2, 138. 5, 151. 2, 171. 6 ppm; HRMS (ESI) m/z: [M+ H] $^{+}$ Calcd for $C_{19}H_{22}NO_3$ 312. 1595; found: 312. 1605; Ele. Anly: C, 73.30; H, 6.80; N, 4.50; O, 15. 41; found: C, 73. 35; H, 6. 84; N, 4. 48; O, 15.45.

Ethyl 5-(2, 5-dimethylphenyl)-2-phenylisoxazolidine-3-carboxylate (4h): Yellow oil; Yield: 97% ^{1}HNMR ($CDCl_3$, 400 MHz); δ 1. 34 (t, *J* = 7. 2 Hz, 3H), 2. 27 (s, 3H), 2. 34 (s, 3H), 2.60 – 2.69 (m, 1H), 2. 89- 2. 97 (m, 1H), 4. 28 (q, *J* = 7. 1 Hz, 2H), 4. 51 (dd, *J* = 8.9, 6.0 Hz, 1H), 5. 20 (dd, *J* = 9. 6, 6. 6 Hz, 1H), 6.99 (t, *J* = 7. 3 Hz, 1H), 7. 02-7.09 (m, 2H), 7. 14 (dd, *J* = 8.7, 1.0Hz, 2H), 7. 29-7.35 (m, 2H), 7. 51 (s, 1H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz); δ 14. 2, 19. 4, 21. 2, 40. 2, 61. 8, 68. 7, 76. 9, 114. 1, 122. 0, 126. 5, 128. 8, 129. 2, 130. 3, 132. 3, 135. 5, 136.0, 151. 4, 171. 6 ppm; HRMS (ESI) m/z: [M+ H] $^{+}$ Calcd for $C_{20}H_{24}NO_3$ 326. 1750; found: 326. 1754; Ele. Anly: C, 73.82; H, 7.12; N, 4.30; O, 14. 75; found: C, 73. 86; H, 7. 16; N, 4. 33; O, 14.77.

Ethyl 5-phenyl-2-(2-tolyl) isoxazolidine-3-carboxylate (4i): Yellow oil; Yield: 70% ^{1}HNMR ($CDCl_3$, 400 MHz); δ 1. 18 (t, *J* = 7. 1 Hz, 3H), 2. 35 (s, 3H), 2. 64-2. 71 (m, 1H), 3.00 – 3.09 (m, 1H), 4. 12 (q, *J* = 7.1 Hz, 2H), 4. 38 (dd, *J* = 9. 0, 4.3 Hz, 1H), 5. 35 (t, *J* = 7.8 Hz, 1H), 7. 00-7.05(m, 1H), 7. 14-7.19 (m, 2H), 7. 30-7.40 (m, 4H), 7. 52 (d, *J*= 7.2 Hz, 1H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz); δ 14. 1, 18. 4, 40. 2, 61. 4, 67. 3, 79. 4, 119. 1, 125. 2, 126. 3, 126.7, 126.9, 128. 2, 128.5, 128.6, 130. 8, 131. 3, 138.9, 148. 1, 170. 6 ppm; HRMS (ESI) m/z: [M+ H] $^{+}$ Calcd for $C_{19}H_{22}NO_3$ 312. 1597; found: 312. 1604; Ele. Anly: C, 73.30; H, 6.80; N, 4.50; O, 15. 40; found: C, 73. 34; H, 6. 85; N, 4. 55; O, 15.43.

Ethyl 5-phenyl-2-(4-tolyl) isoxazolidine-3-carboxylate (4j): Yellow oil; Yield: 80% ^{1}HNMR ($CDCl_3$, 400 MHz); δ 1. 34 (t, *J* = 7. 1 Hz, 3H), 2. 31 (s, 3H), 2. 70-2. 76 (m, 1H), 2.87 – 2.93 (m, 1H), 4. 29 (qd, *J* = 7. 1, 0.5 Hz, 2H), 4. 48 (dd, *J* = 9. 0, 5.7 Hz, 1H), 5. 05 (dd, *J* = 9.4, 6.9 Hz, 1H), 7. 05 (d, *J*= 8.6 Hz, 2H), 7. 12 d, *J*= 8.3 Hz, 2H), 7. 34 (t, *J* = 7. 3 Hz, 1H), 7.37-7.41 (m, 2H), 7. 48 (d, *J*= 7.1 Hz, 2H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz); δ 17. 1, 23. 4, 44. 1, 64. 7, 71. 7, 83. 0, 117. 2, 130. 1, 131. 3, 131.5, 132.6, 134.5, 140.4, 151. 8, 174. 6 ppm; HRMS (ESI) m/z: [M+ H] $^{+}$ Calcd for $C_{19}H_{22}NO_3$ 312. 1597; found: 312. 1600; Ele. Anly: C, 73.30; H, 6.80; N, 4.50; O, 15. 40; found: C, 73. 34; H, 6. 85; N, 4. 55; O, 15.43.

Ethyl 2-(*o*-chlorophenyl)-5-phenylisoxazolidine-3-carboxylate (4k):
Yellow oil; Yield: 77% ^{1}HNMR ($CDCl_3$, 400 MHz); δ 1. 21 (t, *J* = 7. 1 Hz, 3H), 2. 62-2.68 (m, 1H), 2. 85 (dq, *J*= 6.0, 1.4Hz, 1H), 4. 16 – 4. 24 (m, 2H), 4. 63 (dd, *J* = 8.6, 1.3 Hz, 1H), 5. 44 (dd, *J* = 10. 0, 5.9 Hz, 1H), 7. 01 (dd, *J* = 7.7, 1.6 Hz, 2H), 7. 33-7.37 (m, 2H), 7. 39-7.42 (m, 2H), 7. 47-7.50 (m, 2H), 7.54 (dd, *J*= 8.2, 1.6 Hz, 1H) ppm; ^{13}C NMR ($CDCl_3$, 150 MHz); δ 16. 8, 43. 1, 64. 3, 70. 3, 82. 4, 122. 8, 127. 0, 128.0, 129.8, 130. 2, 131.5, 132.9, 141.5, 149.8, 173. 8 ppm; HRMS (ESI) m/z: [M+ H] $^{+}$ Calcd for $C_{18}H_{19}ClNO_3$ 332. 1051; found: 332. 1054; Ele. Anly: C, 65.15; H, 5.48; Cl, 10.67; N, 4.22; O, 14. 47; found: C, 65. 18; H, 5. 52; Cl, 10.70; N, 4. 25; O, 14.50.

Ethyl 2-(*p*-chlorophenyl)-5-phenylisoxazolidine-3-carboxylate (4l):
Yellow oil; Yield: 98% ^{1}HNMR ($CDCl_3$, 400 MHz); δ 1. 32 (t, *J* = 7. 1 Hz, 3H), 2. 71-2.79 (m, 1H), 2. 87-2.97 (m, 1H), 4. 28 (q, *J*= 7.0Hz, 2H), 4. 43 (dd, *J* = 8.6, 6.1 Hz, 1H), 5. 01 (dd, *J* = 9. 4, 6.9 Hz, 1H), 7. 07 (d, *J* = 8.9 Hz, 2H), 7.25 (d, J=8.7Hz, 2H), 7. 35-7.42 (m, 3H), 7. 47 (d, *J* = 7.4 Hz, 2H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz); δ 14. 2, 41. 3, 62. 0, 68. 6, 80. 4, 115. 5, 127. 0, 128.7, 128.7, 128.7, 129. 2, 137.0, 149.8, 171. 1 ppm; HRMS (ESI) m/z: [M+ Na] $^{+}$ Calcd for $C_{18}H_{19}ClNO_3$ 354. 0867; found: 354. 0871; Ele. Anly: C, 65.15; H, 5.48; Cl, 10.67; N, 4.22; O, 14. 47; found: C, 65. 18; H, 5. 52; Cl, 10.70; N, 4. 25; O, 14.50.

Ethyl 5-phenyl-2-(pyridin-2-yl) isoxazolidine-3-carboxylate (4m):
Yellow oil; Yield: 85% ^{1}HNMR ($CDCl_3$, 400 MHz); δ 1. 32 (t, *J* = 7. 1 Hz, 3H), 2. 64-2.71 (m, 1H), 2. 87-2.96 (m, 1H), 4. 28 (q, *J*= 7.1 Hz, 2H), 4. 86 (dd, *J* = 9.0, 7.4 Hz, 1H), 5. 57 (d, *J* = 5. 2 Hz, 1H), 6. 90 (ddd, *J* = 7.2, 4.9, 0.9 Hz, 1H), 7.30-7.35 (m, 2H), 7. 36-7.42 (m, 2H), 7. 44-7.48 (m, 2H), 7.60-7.64(m, 1H), 8.27 (dq, J 4.9, 0.8 Hz, 1H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz); δ 14. 2, 40. 7, 61. 7, 63. 0, 81. 7, 110.01, 117. 7, 127. 0, 128.7, 128.7, 137.4, 138. 2, 147.6, 161.5, 172. 0 ppm; HRMS (ESI) m/z: [M+ H] $^{+}$ Calcd for $C_{17}H_{19}N_2O_3$ 299. 1390; found: 299. 1394; Ele. Anly: C, 68.44; H, 6.08; N, 9.40; O, 16. 10; found: C, 68. 47; H, 6. 12; N, 9. 43; O, 16.13.

Ethyl 2-(6-methylpyridin-2-yl)-5-phenylisoxazolidine-3-carboxylate (4n):
Yellow oil; Yield: 89% ^{1}HNMR ($CDCl_3$, 400 MHz); δ 1. 33 (t, *J* = 7. 1 Hz, 3H), 2. 45 (s, 3H), 2. 60-2. 67(m, 1H), 2. 85-2.93 (m, 1H), 4. 28 (q, *J*= 7.1 Hz, 2H), 4. 88 (t, *J* = 8.1Hz, 1H), 5. 65 (d, *J* = 5.0 Hz, 1H), 6. 74 (d, *J* = 7.4 Hz, 1H), 7. 12 (d, *J*=8. 2Hz, 1H), 7.30-7. 40 (m, 3H), 7.42-7.48 (m, 2H), 7.50 (t, *J*=7. 7Hz, 1H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz); δ 14. 2, 24. 3, 40. 7, 61. 5, 63. 0, 80. 8, 106.6, 117. 1, 127. 1, 128.5, 128. 6, 137. 7, 138. 3, 156.6, 160.9, 172. 3 ppm; HRMS (ESI) m/z: [M+ H] $^{+}$ Calcd for $C_{18}H_{21}N_2O_3$ 313. 1547; found: 313. 1755; Ele. Anly: C, 69.21; H, 6.45; N, 8.97; O, 15. 37; found: C, 69. 25; H, 6. 47; N, 8. 95; O, 15.40.

Ethyl 2-(*m*, *p*-dimethylphenyl)-5-phenylisoxazolidine-3-carboxylate (4o):
Yellow oil; Yield: 80% ^{1}HNMR ($CDCl_3$, 400 MHz); δ 1. 33 (t, *J* = 7. 2 Hz, 3H), 2. 21 (s, 3H), 2. 25(s, 3H), 2.68-2.76 (m, 1H), 2. 85-2.93 (m, 1H), 4. 28 (q, *J*= 7.1 Hz, 2H), 4. 48 (dd, *J* = 9.0, 5.7 Hz, 1H), 5. 05 (dd, *J* = 9. 2, 7.0 Hz, 1H), 6. 89 (dd, *J* = 8.2, 2.4 Hz, 1H), 6. 95 (d, *J*=2.1Hz, 1H), 7.05 (d, *J*=8.2 Hz, 1H), 7.33-7.41 (m, 3H), 7.48 (d, *J*=6. 9Hz, 2H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz); δ 14. 2, 19. 0, 20. 1, 41. 3, 61. 7, 80. 0, 111.6, 115. 7, 127. 1, 128.5, 128. 6, 130. 2, 130. 3, 137. 4,137.6, 149.3, 171. 6 ppm; HRMS (ESI) m/z: [M+ H] $^{+}$ Calcd for $C_{20}H_{24}NO_3$ 326. 1750; found: 326. 1754; Ele. Anly: C, 73.81; H, 7.12; N, 4.30; O, 14. 73; found: C, 73. 83; H, 7. 16; N, 4. 28; O, 14.71.

Ethyl 5-(4-chlorophenyl)-2-phenylisoxazolidine-3-carboxylate (4p):
Yellow oil; Yield: 88% ^{1}HNMR ($CDCl_3$, 400 MHz); δ 1. 34 (t, *J* = 7. 1 Hz, 3H), 2.68-2.73 (m, 1H), 2. 85-2.93 (m, 1H), 4. 29 (qd, *J*= 7.1, 1.5 Hz, 2H), 4. 50 (dd, *J* = 9.0, 5.5 Hz, 1H), 5. 04 (dd, *J* = 9. 2, 7.0 Hz, 1H), 7. 01 (t, *J* = 7.3 Hz, 1H), 7. 13-7. 15 (m, 2H), 7.31 (dd, *J*=8.7, 7.4 Hz, 2H), 7.34-7.38 (m, 2H), 7.43 (dt, *J*=8. 9, 2.3Hz, 2H) ppm; HRMS (ESI) m/z: [M+ H] $^{+}$ Calcd for $C_{18}H_{19}ClNO_3$ 332. 1810; found: 332. 1815; Ele. Anly: C, 65.16; H, 5.47; Cl, 10. 68; N, 4.22; O, 14. 47; found: C, 65. 20; H, 5. 45; Cl, 10. 71; N, 4. 21; O, 14.50.

Diethyl 2, 5-diphenylisoxazolidine-3, 4-dicarboxylate (4q):
Yellow oil; Yield: 90% ^{1}HNMR ($CDCl_3$, 400 MHz); δ 1. 13(t, *J* = 7. 1 Hz, 3H), 1. 35 (t, *J* = 7. 1 Hz, 3H), 4. 04-4.09 (m, 1H), 4. 33 (t, *J*= 6.8 Hz, 2H), 4. 96 (d, *J* = 4.8 Hz, 1H), 5. 23 (d, *J* = 8.6 Hz, 1H), 7. 01 (t, *J* = 7.3 Hz, 1H), 7. 16 (d, *J* = 8.0 Hz, 2H), 7.32 (t, *J* = 7. 9 Hz, 2H), 7.37-7.43 (m, 3H), 7.52 (d, *J*=6.8Hz, 2H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz); δ 14. 2, 51. 9, 61. 3, 61. 5, 76. 1, 81. 0, 116.6, 126. 1, 126. 5, 127.0, 128. 1, 128. 8, 128. 9, 138. 5, 150.1, 171.5, 173. 1 ppm; HRMS (ESI) m/z: [M+ H] $^{+}$ Calcd for $C_{21}H_{24}NO_5$ 370. 1623; found: 370. 1628; Ele. Anly: C, 68.28; H, 6.28; N, 3.79; O, 21. 65; found: C, 68. 34; H, 6. 39; N, 3. 81; O, 21.70.

Tri ethyl 2-phenylisoxazolidine-3, 4, 5-tri carboxylate (4r): Yellow oil; Yield: 99% ^{1}HNMR ($CDCl_3$, 400 MHz); δ 1. 03(t, *J* = 7. 1 Hz, 3H), 1. 18 (t, *J* = 7. 1 Hz, 3H), 1. 33 (t, *J* = 7. 1 Hz, 3H), 3. 80-3.99 (m, 2H), 4. 11 (dd, *J* = 7.1, 2.5 Hz, 2H), 4. 25-4.37 (m, 3H), 4. 78 (d, *J* = 7.3 Hz, 1H), 4. 97 (d, *J* = 7.3 Hz, 1H), 7.14 (d, *J* = 7. 9 Hz, 2H), 7.24-7.29 (m, 2H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz); δ 14. 2, 45. 0, 61. 3, 61. 6, 67. 1, 76.0, 116. 6, 126. 5, 127.0, 150.1, 168.5, 171.5, 173. 1 ppm; HRMS (ESI) m/z: [M+ H] $^{+}$ Calcd for $C_{18}H_{24}NO_7$ 366. 1576; found: 366. 1582; Ele. Anly: C, 60.19; H, 6.32; N, 3.83; O, 30. 65; found: C, 61. 34; H, 6. 39; N, 3. 81; O, 30.70.

REFERENCES

1. S. Rambabu, A. Kurumanna, B. Sakram, K. Ashok, N. Suryam, P. Shyam, B. Kiran, M. Ariffudin, J Heterocyclic Chem. 2020, 1–9. b) R. Romeo, S. V. Giofré, B. Macchi M. Balestrieri A. Mastino P. Merino C. Carnovale G. Romeo, U. Chiacchio, ChemMedChem. 2012, 7, 565–569.
2. M. Berthet, T. Cheviet, G. Dujardin, I. Parrot, J. Martinez, A, Chem. Rev. 2016, 116, 15235. b) B. D. Ellis, C. D. Vanderwal, A. Hughes and Gleason's Virosaine, Angew. Chem., Int. Ed. 2017, 56, 13940.
3. U. Chiacchio, A. Corsaro, D. Iannazzo, A. Piperno, V. Pistarà, A. Rescifina, R. Romeo, V. Valveri, A. Mastino, G. Romeo, J. Med. Chem. 2003, 46, 3696.
4. G. Vincent, R. Guillot, C. Kouklovsky, Angew. Chem., Int. Ed. 2011, 50, 1350. b) T. Erhard, G. Ehrlich, P. Metz, Angew. Chem., Int. Ed. 2011, 50, 3892. c) S. Diethelm, E. M. Carreira, J. Am. Chem. Soc. 2015, 137, 6084.
5. X. Zhang, P. Cividino, J-F. Poisson, P. Shpak-Kraievskyi, M. Y. Laurent, A. Martel, G. Dujardin, S. Py, Org. Lett.2014, 16, 1936.
6. N. Takeda, E. Futaki, Y. Kobori, M. Ueda, O. Miyata, Angew. Chem., Int. Ed. 2017, 56, 16342.
7. a) J. Salaün, Chem. Rev. 2005, 105, 285. b) L. Klier, F. Tur, P. H. Poulsen, K. A. Jørgensen, Chem. Soc. Rev. 2017, 46, 1080. c) G. Romeo, U. Chiacchio, A. Corsaro, P. Merino, Chem. Rev. 2010, 110, 3337.
8. Y. Kobayashi, Y. Taniguchi, N. Hayama, T. Inokuma, Y. Takemoto, Angew. Chem., Int. Ed. 2013, 52, 11114. b) R. L. LaLonde, Z. J. Wang, M. Mba, A. D. Lackner, F. D.; Toste, Angew. Chem., Int. Ed. 2010, 49, 598. c) F. Pesciaioli, F. D. Vincentiis, P. Galzerano, G. Bencivenni, G. Bartoli, A. Mazzanti, P. Melchiorre, Angew. Chem., Int. Ed. 2008, 47, 8703. d) M. B. Hay, J. P. Wolfe, Angew. Chem., Int. Ed. 2007, 46, 6492. e) C. Gioia, F. Fini, A. Mazzanti, L. Bernardi, A. Ricci, J. Am. Chem. Soc. 2009, 131, 9614.
9. K. M. Partridge, I. A. Guzei, T. P. Yoon, Angew. Chem., Int. Ed. 2010, 49, 930. b) K. M. Partridge, M. E. Anzovino, T. P. Yoon, J. Am. Chem. Soc. 2008, 130, 2920
10. N. Morita, R. Kono, K. Fukui, A. Miyazawa, H. Masu, I. Azumaya, S. Ban, Y. Hashimoto, I. Okamoto, O. Tamura, J. Org. Chem. 2015, 80, 4797. b) O. Tamura, T. Mitsuya, H. Ishibashi, Chem. Commun. 2002, 1128.
11. S. Sugita, N. Takeda, N. Tohnai, M. Miyata, O. Miyata, M. Ueda, Angew. Chem., Int. Ed. 2017, 56, 2469.
12. S. Chakrabarty, I. Chatterjee, B. Wibbeling, C. G. Daniliuc, A. Studer, Angew. Chem., Int. Ed. 2014, 53, 5964.
13. I. Chatterjee, R. Fröhlich, A. Studer, Angew. Chem., Int. Ed. 2011, 50, 11257.
14. S. K. Jackson, A. Karadeolian, A. B. Driega, M. A. Kerr, J. Am. Chem. Soc.2008, 130, 4196.
15. L. M. Stanley, M. P. Sibi, Chem. Rev. 2008, 108, 2887. b) K. V. Gothelf, K. A. Jørgensen, Chem. Rev. 1998, 98, 863. c) P. Appukkuttan, V. P. Mehtaa, E. V. V. der Eycken, Chem. Soc. Rev. 2010, 39, 1467.
16. T. Kano, T. Hashimoto, K. Maruoka, J. Am. Chem. Soc. 2005, 127, 11926. b) D. Carmona, M. P. Lamata, F. Viguri, R. RodrÍguez, L. A. Oro, F. J. Lahoz, A. I. Balana, T. Tejero, P. Merino, J. Am. Chem. Soc. 2005, 127, 13386. c) X. Wang, C. Weigl, M. P. Doyle, J. Am. Chem. Soc. 2011, 133, 9572. d) C. Palomo, M. Oiarbide, E. Arceo, J. M. García, R. López, A. González. A. Linden, Angew. Chem., Int. Ed. 2005, 44, 6187. e) X. Yang, F. Cheng, Y. -D. Kou, S. Pang, Y.-C. Shen, Y.-Y. Huang, N. Shibata, Angew. Chem., Int. Ed. 2017, 56, 1510.
17. W. S. Jen, J. J. M. Wiener, D. W. C. MacMillan, J. Am. Chem. Soc. 2000, 122, 9874. b) R. L. Atienza, H. S. Roth, K. A. Scheidt, Chem. Sci. 2011, 2, 1772. c) L. Zheng, F. Gao, C. Yang, G. -L. Gao, Y. Zhao, Y. Gao, W. Xia, Org. Lett. 2017, 19, 5086. d) J. Hoogenboom, H. Zuilhof, T. Wennekes, Org. Lett. 2015, 17, 5550.
18. aA. Chatterjee, D. K. Maiti, P. K. Bhattacharya, Org. Lett. 2003, 5, 3967. b) R. Rios, I. Ibrahem, J. Vesely, G.-L. Zhao, A. Córdova, Tetrahedron Lett. 2007, 48, 5701. c) J. Vesely, R. Rios, I. Ibrahem, G.-L. Zhao, L. Eriksson, A. Córdova, Chem. - Eur. J. 2008, 14, 2693. d) P. J. Chua, B. Tan, L. Yang, X. Zeng, D. Zhu, G. Zhong, Chem. Commun. 2010, 46, 7611. e) D. Zhu, M. Lu, L. Dai, G. Zhong, Angew. Chem., Int. Ed. 2009, 48, 6089.
19. M.-Y. Wu, W.-W. He, X.-Y. Liu, B. Tan, Angew. Chem., Int. Ed. 2015, 54, 9409. b) G. A. Molander, L. N. Cavalcanti, Org. Lett. 2013, 15, 3166.
20. H. Chen, Z. Wang, Y. Zhang, Y. Huang, J. Org. Chem. 2013, 78, 3503. b) R. K. Kawade, R.-S. Liu, Angew. Chem., Int. Ed. 2017, 56, 2035. c) P. Sharma, P. D. Jadhav, M. Skaria, R.-S. Liu, Org. Biomol. Chem. 2017, 15, 9389.