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KOAc-Catalyzed one-pot three-component 1,3-dipolar cycloaddition of α-diazo compounds, nitrosoarenes, and alkenes: an approach to functionalized isoxazolidines

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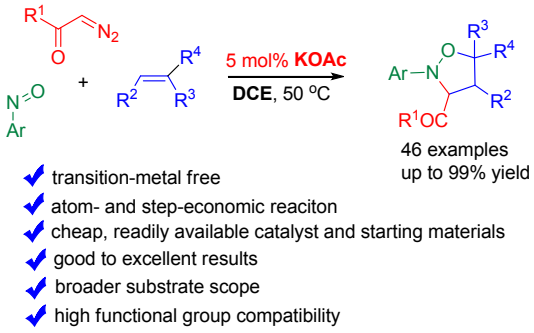
ABSTRACT: A direct, highly efficient KOAc-catalyzed one-pot three-component approach for the preparation of various functionalized isoxazolidines *via* the 1,3-dipolar cycloaddition reactions of readily accessible diazo compounds, nitrosoarenes and alkenes has been reported. The cheap and readily available catalyst and starting materials, excellent functional group compatibility, wide substrate scope, high yields, and excellent chemo-, region- and diastereo-selectivities make this protocol an attractive alternative.

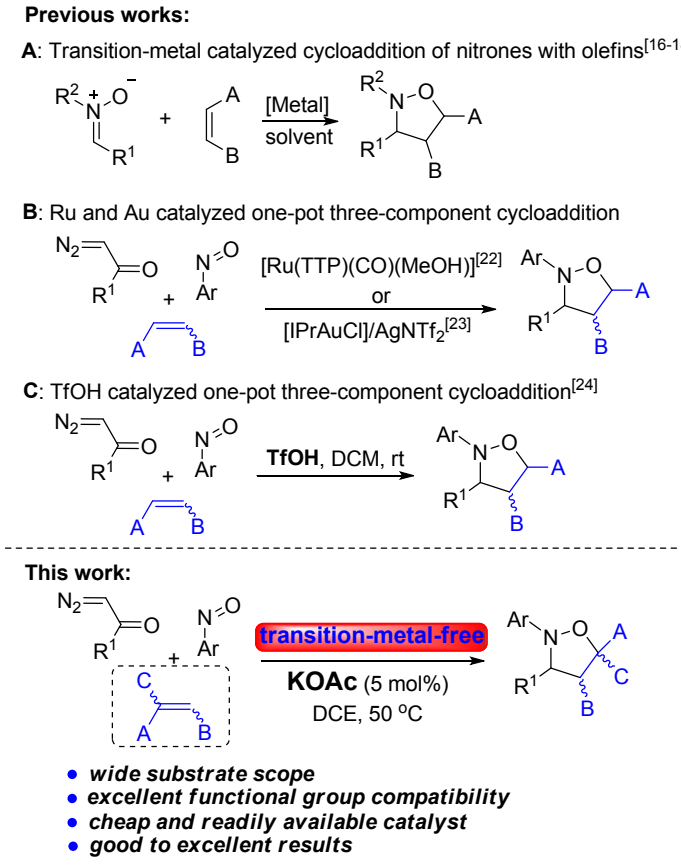


■ INTRODUCTION

Environmentally benign transformations and cost-effective strategies have become the target in modern synthetic organic chemistry. Catalysis plays a crucial role for this purpose, and the development of one-pot multicomponent routes becomes of great interest and importance. Therefore, the developing an efficient transition-metal-free one-pot multicomponent approach that allows for using a cheap and readily available catalyst for the synthesis of target products is highly desirable.

Isoxazolidines represent a class of important and powerful heterocyclic skeletons frequently found in many biologically active natural products and medicinal molecules.[1] In addition, a number of molecules containing isoxazolidine ring have attracted much attention as nucleoside analogues.[2] Isoxazolidines are also vital and versatile intermediates[3] due to the ease of N−O bond cleavage, which could be further converted to β-amino acids,[4] β-lactams[1a] and 3-amino alcohols[5] *via* the reductive cleavage of N−O bonds. Therefore, it is not surprising that great effort has been devoted to the development of novel, efficient and practical methods for the construction of isoxazolidines,[6, 1a] including cycloadditions of hydroxylamines with alkenes,[7] cycloadditions of oxaziridines with olefins or arynes,[8] cycloadditions of *O*-silyloxime with alkenes,[9] cycloaddition of cyclopropanes with nitrosoarenes,[10] annulation of 2-nitrosopyridine with allylstannanes,[11] cascade reaction of *N*-alkoxyazomethine ylides,[12] reaction of oxime ethers and cyclopropane diesters,[13] nitrone cycloadditions of 1,2-cyclohexadiene,[14] and others.[15] Although these approaches have proven to be of importance, the most popular and conventional methods are the [3+2] cycloadditions of nitrones with alkenes (Scheme 1A).[16-18] However, these methods generally involve the use of transition-metals and complex nitrones which require a separate preparation step. In the past decades, more atom-economical one-pot multi-component reactions have been observed for the synthesis of various compounds, which play an increasingly important role in organic synthesis. Bhattacharya, Liu, Zhong and Córdova developed asymmetric three-component methods of aldehydes, aryl hydroxylamine (complex substrates) and olefins to access diverse chiral isoxazolidines, respectively.[19] Additionally, one-pot strategies of diazo compounds, nitrosoarenes and olefins were also well documented to construct this scaffold by Tan and Molander, respectively, and the former is an example of asymmetric catalysis.[20] Liu and Huang independently demonstrated three-component processes of arylenes, functionalized olefins (complicated substrates) and nitrosoarenes for the construction of isoxazolidines, too.[21] Despite the success of these important and valuable multi-component methods, more efficient methods with better results making use of easily accessible and cheap starting materials is still highly appealing. In this context, Che,[22] Liu[23] and their co-workers reported the 1,3-dipolar cycloaddition to synthesize various functionalized isoxazolidines *via* the ruthenium porphyrin and [IPrAuCl]/$AgNTf_2$ catalyzed three-component reactions of diazo compounds, nitrosoarenes and alkenes, respectively (Scheme 1B). Typically, these two strategies also require the utilization of transition-metal catalysts which still suffer from high cost and complicated purifying procedures. It is notable that developing transition-metal-free multicomponent approaches have attracted intense interest and increasing attention. Recently, trifluoromethanesulfonic acid catalyzed three-component

cycloaddition of diazo compounds, nitrosoarenes and alkenes for access to isoxazolidines has been described by Zhong[24] and co-workers (Scheme 1C). Nevertheless, the use of a strong acid greatly lowered the functional group tolerance, reduced the substrate scope and significantly limited its application, and the reaction yields were not high enough for some substrates. On the other hand, to the best of our knowledge, the examples that sterically hindered 1,1-disubstituted olefins are used as substrates in three-component routes are not observed. Therefore, the development of a more efficient transition-metal-free three-component strategy to isoxazolidines which allows for employing readily available, inexpensive and environmentally benign catalysts with broader substrate scope and high functional group compatibility is highly desirable. Potassium acetate (KOAc) is an abundant, cheap and nontoxic reagent. To the best of our knowledge, however, the utilization of KOAc as a catalyst in organic synthesis has received less attention. Herein, we will report a KOAc-catalyzed, atom- and step-economic one-pot three-component cycloaddition of diazo compounds, nitrosoarenes and alkenes for the synthesis of functionalized isoxazolidines without the need of any transition metal as a catalyst, in which broader substrate scope and better results were observed.

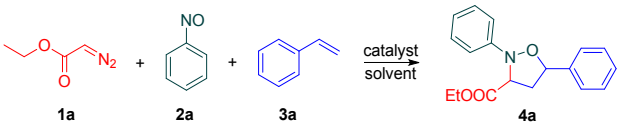


Scheme 1. Different Strategies to Construct Functionalized Isoxazolidines

■ RESULTS AND DISCUSSION

Initially, the cycloaddition of ethyl diazoacetate (EDA, **1a**), nitrosobenzene **2a** and styrene **3a** was selected as the model reaction to evaluate catalysts. Gratifyingly, 75% yield could be obtained when 10 mol% KOAc was employed as a catalyst (Table 1, entry 1). Encouraged by this preliminary result, we screened the effect of different bases such as *t*-BuOK, KOH, K_2CO_3, K_3PO_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, K_3PO_4 and DBU catalyzed the reaction to give slightly lower yields compared to KOAc (Table 1, entries 4−6). 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 CH_3CN, toluene and 1,4-dioxane provided the product **4a** in somewhat lower yields (Table 1, entries 8−10). Other solvents such as CH_3OH, THF and CH_3NO_2 were less effective and gave obviously lower yields (Table 1, entries 11−13). To our delight, reducing the amount of KOAc 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 15 and 16 *vs.* 14). 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 17).

Table 1. Optimization of Reaction Conditions[a]



1a 2a 3a 4a

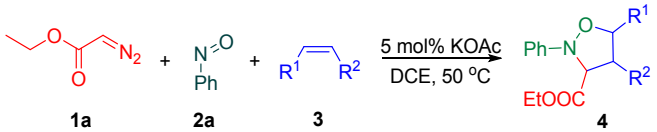
entry	catalyst	solvent	T (°C)	yield of **4a** (%)
1	KOAc	DCE	50	75
2	*t*-BuOK	DCE	50	trace
3	KOH	DCE	50	trace
4	K_2CO_3	DCE	50	61
5	K_3PO_4	DCE	50	68
6	DBU	DCE	50	62
7	---	DCE	50	8
8	KOAc	CH_3CN	50	74
9	KOAc	MePh	50	73
10	KOAc	1,4-dioxane	50	70
11	KOAc	CH_3OH	50	53
12	KOAc	THF	50	30
13	KOAc	CH_3NO_2	50	28
14[b]	KOAc	DCE	50	75

15[b]	KOAc	DCE	30	65
16[b]	KOAc	DCE	60	76
17[c]	KOAc	DCE	50	99

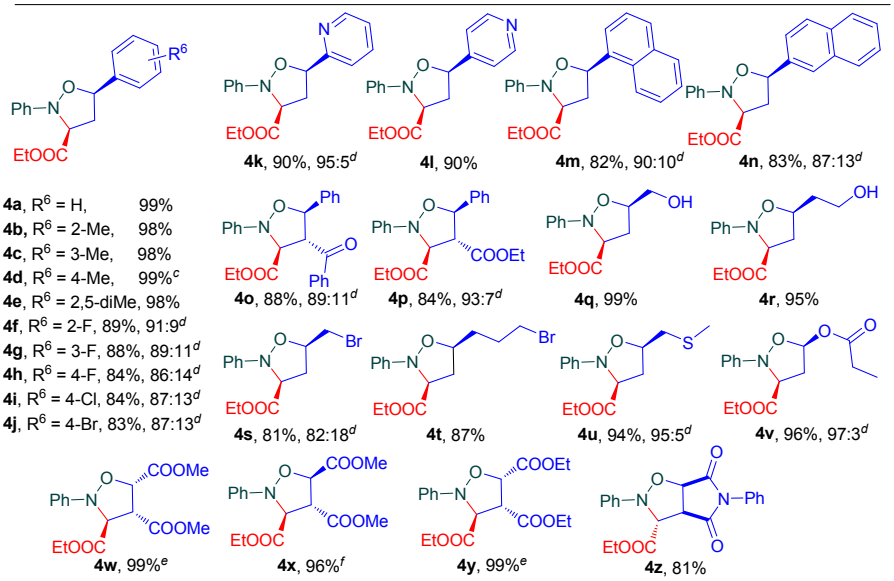
[a] Unless noted, all reactions were performed with **1a** (0.1 mmol), **2a** (0.1 mmol), **3a** (0.1 mmol) and 10 mol% of catalyst in 1.0 mL of solvent for 24 h. [b] 5 mol% of KOAc was used and 48% yield was obtained when 2.5 mol% KOAc was utilized. [c] **1a**:**2a**:**3a**:KOAc = 1.2:1.2:1:0.05.

With the established optimal reaction conditions using KOAc 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**−**4j** in 83−99% yields with a single isomer or high diastereoselectivities, which demonstrated that the electronic and steric properties of substituents had little influence on the transformation. It should be noted that dimethyl substituted product **4e** was obtained in 98% yield. Moreover, ethylenes substituted with a heteroaryl group such as 2-vinylpyridine and 4-vinylpyridine also worked well, giving the desired products **4k** and **4l** in 90% yields with excellent diastereoselectivities, respectively. It was found that the sterically hindered 1-vinylnaphthalene and 2-vinylnaphthalene reacted smoothly to furnish the products **4m** and **4n** in 82% and 83% yields with high diastereoselectivities, respectively. Gratifyingly, 1,2-disubstituted aryl alkenes such as (*E*)-chalcone and ethyl cinnamate could be converted successfully into the desired products **4o** and **4p** with good yields and diastereoselectivities. Then, this process was extended to alkyl alkenes. When a variety of aliphatic terminal alkenes containing various functional groups were subjected to the transformation, high yields and diastereoselectivities were provided (**4q**−**4v**). Notably, the greater the distance between the functional group and C=C double bond of olefin is, the slightly lower the yield (**4q** *vs.* **4r**, and **4s** *vs.* **4t**). For 1,2-disubstituted aliphatic alkenes, not only (*Z*)-isomer but also (*E*)-isomer substrates were suitable for the reaction, affording the corresponding single isomer products **4w**−**4y** in excellent yields. This catalytic method was well applicable to cyclic olefinic bond, too (**4z**).

Scheme 2. Scope of Various Dipolarophiles[a,b]



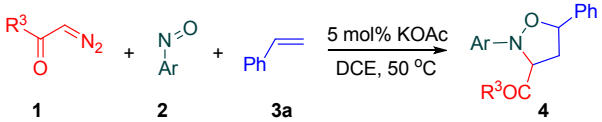
1a **2a** **3** **4**



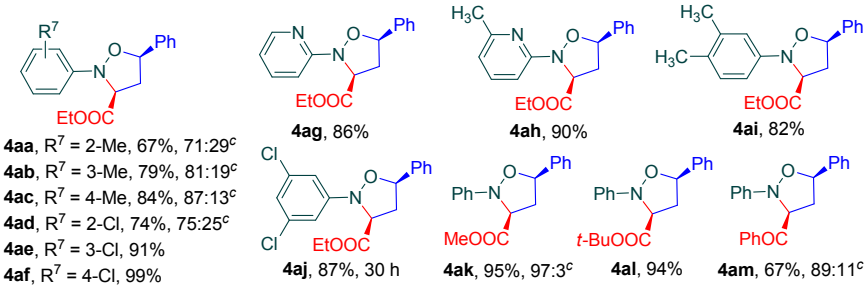
[a] Unless noted, all reactions were carried out with **1a** (0.12 mmol), **2a** (0.12 mmol), **3** (0.1 mmol) and 5 mol% of KOAc as a catalyst in 1.0 mL of DCE at 50 °C for 24 h. [b] Isolated yield. [c] 60 °C was adopted. [d] The dr values were determined by molar mass of isolated diastereomers. [e] *cis*-alkene was used. [f] *trans*-alkene was used.

Subsequently, the scope of various nitrosoarenes **2** was investigated. As shown in Scheme 3, the electronic and steric effects of the substituents on the nitrosobenzene had little influence on the reaction yields. Both electron-rich **(4aa**−**4ac)** and electron-deficient (**4ad**−**4af)** groups on the phenyl ring of the nitrosobenzene were equally well tolerated, giving the corresponding products in good to high yields. With respect to diastereoselectivity, better results were observed for both *meta*- and *para*-substituted substrates compared to *ortho*-substituted substrates, which might be due to the steric hindrance. It was noteworthy that the heteroaryl nitroso compounds, such as 2-nitrosopyridine and 2-methyl-6-nitrosopyridine, were found to be compatible with these conditions, offering the corresponding single isomer products **4ag** and **4ah** in high yields, respectively. To our delight, single isomer products **4ai** and **4aj** could be obtained with good yields when dimethyl and dichloro substituted nitrosobenzenes were employed as substrates. Next, the examination of alkyl diazoacetate **1** revealed that the steric hindrance of ester groups did not obviously affect the transformation. The methyl diazoacetate and bulky *t*-butyl diazoacetate could provide the products **4ak** and **4al** in excellent yields with high diastereoselectivities, respectively. Additionally, the diazoketone was suitable for this reaction with 67% yield and good diastereoselectivity, too (**4am**).

Scheme 3. Scope of Various Nitrosoarenes and *α*-Diazo Compounds[a,b]



1 **2** **3a** **4**

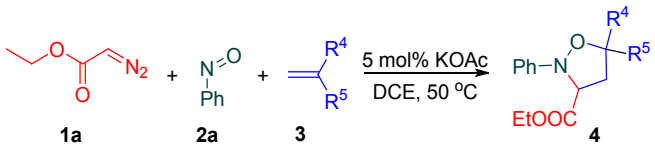


4aa, R^7 = 2-Me, 67%, 71:29[c]
4ab, R^7 = 3-Me, 79%, 81:19[c]
4ac, R^7 = 4-Me, 84%, 87:13[c]
4ad, R^7 = 2-Cl, 74%, 75:25[c]
4ae, R^7 = 3-Cl, 91%
4af, R^7 = 4-Cl, 99%

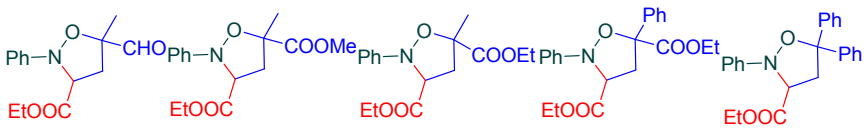
[a] Unless noted, all reactions were performed with **1** (0.12 mmol), **2** (0.12 mmol), **3a** (0.1 mmol) and 5 mol% of KOAc as a catalyst in 1.0 mL of DCE at 50 °C for 24 h. [b] Isolated yield. [c] The d.r. was determined by molar mass of isolated diastereomers.

To further demonstrate the utility of this method, more challenging 1,1-disubstituted olefins were examined as substrates which have never been explored in three-component system. As listed in Scheme 4, all examined substrates afforded the desired products **4an**−**4ar** in 84−90% yields. 87%, 90% and 88% yields were obtained when methacrylaldehyde, methyl methacrylate and ethyl methacrylate were employed as substrates, respectively (**4an**−**4ap**). Interestingly, the presence of a or even two large phenyl groups did not impede this reaction affording the corresponding products **4aq** and **4ar** in 86% and 84% yields, respectively. 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 4. Investigation of Various 1,1-Disubstituted Olefins[a,b]



1a **2a** **3** **4**

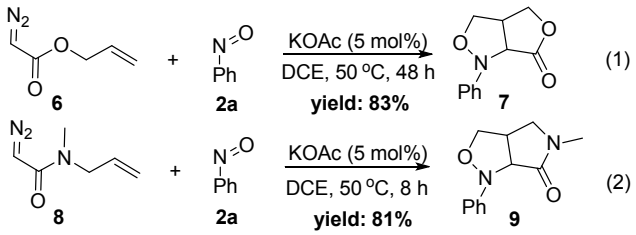


4an, 87%, 30 h **4ao**, 90% **4ap**, 88% **4aq**, 86%, 95:5[c] **4ar**, 84%

[a] all reactions were performed with **1a** (0.12 mmol), **2a** (0.12 mmol), **3** (0.1 mmol) and 5 mol% of KOAc as a catalyst in 1.0 mL of DCE at 50 °C for 24 h. [b] Isolated yield. [c] The d.r. value was determined by molar mass of isolated diastereomers.

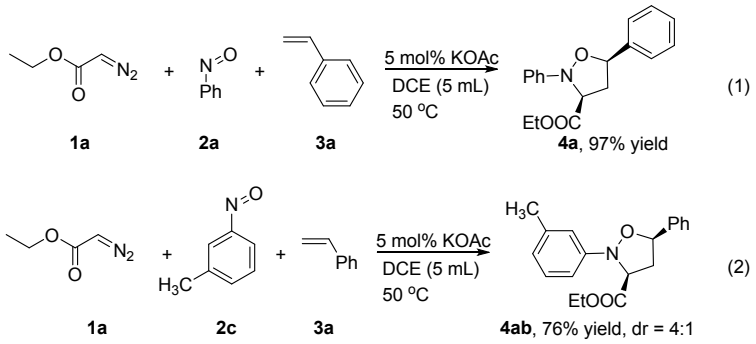
Lactones, lactams and their derivatives have received considerable attention because of their presence in numerous compounds of biological interest and their importance as drugs and biological agents. Bicyclic isoxazolidines containing lactone or lactam belong to this type of useful molecular scaffolds. Subsequently, this newly developed method was investigated and applied in the synthesis of these two kinds of isoxazolo-bicycles. The reaction of allyl α-diazoacetate **6** with **2a** proceeded smoothly under the standard conditions, giving the targeted bicyclic isoxazolidine **7** in 83% yield (Scheme 5, eq 1). Compared with **6**,

allylamine α-diazoacetate **8** was more reactive as a substrate and offered the desired product **9** in 81% yield (Scheme 5, eq 2).



Scheme 5. Synthetic Applications of This Approach

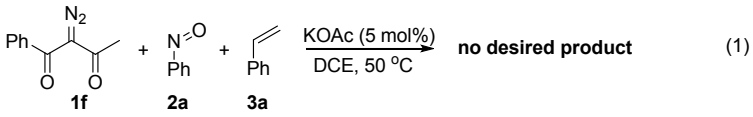
To demonstrate the synthetic potential of this present approach, two selected reactions were performed on a 1.0 mmol scale of starting materials. As shown in Scheme 6, in the presence of 5 mol% KOAc, **4a** was obtained in 97% yield *via* the reaction of 1.0 mmol of styrene **3a** with 1.2 equiv. of **1a** and **2a** (Scheme 6, eq 1). Additionally, the reaction of 1.0 mmol of styrene **3a** with 1.2 equiv. of **1a** and **2c** could provide **4ab** as the major isomer product with 76% yield and 4:1 dr (Scheme 6, eq 2).

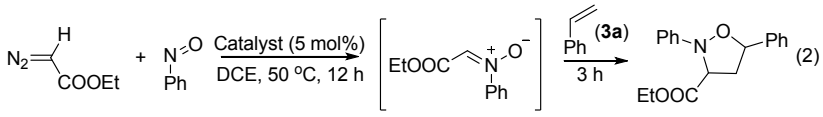


Scheme 6. 1.0 mmol-Scale Version

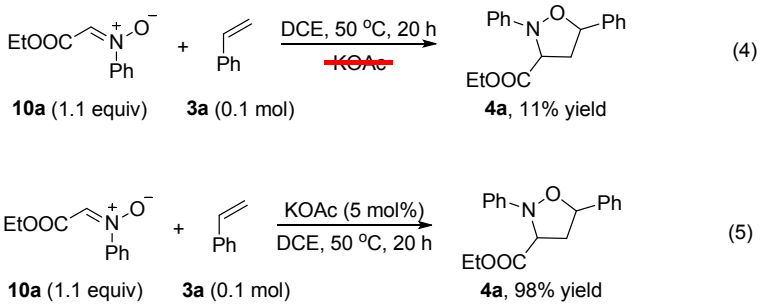
To probe the importance of the hydrogen on the *α*-carbon atom of *α*-diazocarbonyl compounds **1** in this reaction, the three-component cycloaddition of 2-diazo-1-phenyl-1,3-butanedione **1f** which lacks the hydrogen on the *α*-carbon atom, nitrosobenzene **2a** and styrene **3a** was carried out under the standard reaction conditions. The fact that no corresponding isoxazolidine was detected strongly suggested the existence of the hydrogen on the *α*-carbon atom was crucial for this process (Scheme 7, eq 1). In addition, as shown in Table 1, weak bases as catalysts proved to be more efficient, and out of those weak bases examined, KOAc showed better catalytic activity. To gain an insight into the role of KOAc, several control experiments were next carried out. The nitrone intermediate **10a** was successfully obtained when the reaction of EDA **1a** with nitrosobenzene **2a** was performed using KOAc or KOH as a catalyst (Scheme 7, eq 2, entries 1 and 2).[25] However, only 18% yield of **10a** was attained in the absence of any catalyst (Scheme 7, eq 2, entry 3). So the

first role of the base such as KOAc or KOH might promote the deprotonation of EDA **1a** and facilitate the followed generation of intermediate **10a**. Subsequently, when the styrene **3a** was added to these three reaction systems and stirred for another 3 h, the desired product **4a** was obtained in 74% yield for KOAc system (Scheme 7, eq 2, entry 1). However, KOH catalytic system gave trace amount of **4a** and only 5% yield was offered in the absence of any catalyst (Scheme 7, eq 2, entries 2 and 3). These three results indicated the high importance of KOAc during the course of the cyclization. Additionally, only 14% yield of **4a** was obtained if KOAc was removed before styrene **3a** was added (Scheme 7, eq 2, entry 4), and the reaction of the prepared intermediate **10a** with styrene **3a** also offered only 11% yield in the absence of KOAc (Scheme 7, eq 4), which further demonstrated the essential role of KOAc in this step. For justifying the exact role of K^+ and AcO^-, NaOAc, CsOAc and $Ca(OAc)_2$ were utilized as catalysts to realize the reaction, and 72%, 77% and 68% yields were provided (Scheme 7, eq 2, entries 5−7), respectively, which demonstrated that AcO^- really play an important role in this reaction. In contrast, it was observed that the reaction of **1f** and **2a** failed to result in the desired nitrone intermediate in the presence of 5 mol% KOAc (Scheme 7, eq 3), which may be the reason why no final cycloaddition product was detected after the styrene was added. At the same time, the reaction of the intermediate **10a** with styrene **3a** could proceed very smoothly in the presence of KOAc and up to 98% yield of the desired product **4a** was obtained (Scheme 7, eq 5), suggesting that intermediate **10a** is key active intermediate of this multicomponent reaction. All these experiments clearly revealed that AcO^- was indispensable, and the in situ formation of the active nitrone intermediate is crucial.



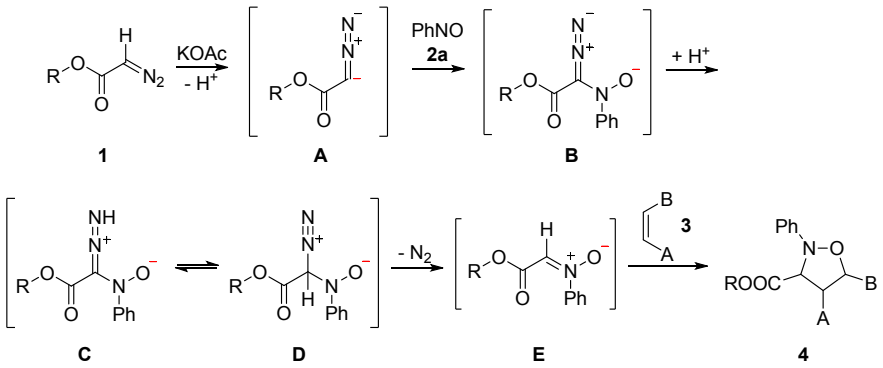


entry	catalyst	yield of **10a**	yield of **4a**
1	KOAc	72%	74%
2	KOH	69%	trace
3	---	18%	5%
4	KOAc	72%	14%
5	NaOAc	69%	72%
6	CsOAc	74%	77%
7	$Ca(OAc)_2$	63%	68%



Scheme 7. Control Experiments

On the basis of the aforementioned experimental results and corresponding literatures[26], a plausible mechanism is proposed in Scheme 8. Initially, the intermediate **A** is provided from the starting material **1** *via* a deprotonation reaction process in the presence of 5 mol% of KOAc. Then, the intermediate **A** reacts with nitrosobenzen **2a** to form the intermediate **B** which further was protonated with H^+ to generate the intermediate **C** that might be transformed to **D**. Subsequently, active nitrone intermediate **E** is smoothly formed through **D** with the releasion of N_2.[25] At last, this *in situ* generated nitrone **E** undergoes 1,3- dipolar cycloaddition reaction with the alkene **3** to afford the final product isoxazolidine **4**. So KOAc first might activate diazo ester to react with nitrosobenzene and promote subsequent cleavage of diazo group to generate the nitrone intermediate. At the same time, it also facilitated the 1,3-dipolar cycloaddition to afford the corresponding isoxazolidines.



Scheme 8. Proposed Mechanism

■ CONCLUSION

In summary, we have developed a low-cost, highly atom-economical KOAc-catalyzed one-pot three-component strategy to synthesize functionalized isoxazolidine derivatives *via* the cycloaddition of readily accessible diazo compounds, nitrosoarenes and alkenes as starting materials. The transformation showed broad substrate scope and good functional group tolerance, and was very suitable for

sterically-hindered 1,1-disubstituted olefines. More importantly, with only 5 mol% KOAc, most products were provided in high yields and excellent diastereoselectivities under mild reaction conditions.

■ EXPERIMENTAL SECTION

General Information. ^{1}H NMR spectra were taken on a Bruker AVANCE III 600 MHz NMR spectrometers. The chemical shifts are reported in ppm downfield to the $CDCl_3$ resonance (δ = 7.27). Spectra are reported as follows: chemical shift (δ ppm), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet), coupling constants (Hz), integration, and assignment. ^{13}C NMR data were collected at 150 MHz with complete proton decoupling. The chemical shifts are reported in ppm downfield to the central $CDCl_3$ resonance (δ = 77.0). High-resolution mass spectra were performed on a micrOTOF-Q II instrument with an ESI source. Melting points were measured with a RD-II melting point apparatus and are uncorrected. Unless otherwise noted, all reagents and solvents obtained from commercial sources were used without further purification. Deuterated solvents were purchased from Sigma–Aldrich. Column chromatography was performed on silica gel (200-300 mesh). All yields were referred to isolated yields (average of two runs) of compounds.

General procedure for KOAc-catalyzed three-component cycloaddition of α-diazo compounds, nitrosoarenes and alkenes. To a reaction system of nitrosoarene **2** (0.12 mmol), α-diazo compound **1** (0.12 mmol) and KOAc (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 (oil bath) 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.

1.0 mmol-Scale preparation of 4a. To a reaction system of nitrosobenzene **2a** (129.0 mg, 1.2 mmol), EDA **1a** (136.8 mg, 1.2 mmol) and KOAc (5.0 mg, 0.05 mmol, 5 mol%) in DCE (3.0 mL) was added styrene **3a** (115.8 μL, 1.0 mmol). The resultant solution was then stirred at 50 °C (oil bath) for 24 h. At last, the reaction mixture was purified by silica gel column chromatography to give the product **4a** (288.3 mg, 97% isolated yield).

1.0 mmol-Scale preparation of 4ab. To a reaction system of 1-methyl-3-nitrosobenzene (145.3 mg, 1.2 mmol), EDA **1a** (136.8 mg, 1.2 mmol) and KOAc (5.0 mg, 0.05 mmol, 5 mol%) in DCE (3.0 mL) was added styrene **3a** (115.8 μL, 1.0 mmol). The resultant solution was then stirred at 50

°C (oil bath) for 24 h. At last, the reaction mixture was purified by silica gel column chromatography to give the product **4ab** (236.5 mg, 76% isolated yield, dr = 4:1).

The KOAc-catalyzed reaction of EDA 1a with nitrosobenzene 2a. To the mixture system of nitrosobenzene **2a** (21.5 mg, 0.2 mmol) and 5 mol% KOAc (1.0 mg, 0.01 mmol) in DCE (1.0 mL) was added EDA **1a** (22.8 mg, 0.2 mmol). Subsequently, the resultant solution was stirred at 50 °C (oil bath) for 24 h and the reaction mixture was purified by silica gel column chromatography to give the corresponding nitrone intermediate **10a**. ^{1}H NMR of the intermediate indicated that the nitrone **10a** had been formed (See Supporting Information).

Characterization Data of All Products.

Ethyl 2,5-diphenylisoxazolidine-3-carboxylate (4a). Yellow oil (99% yield, 29.5 mg), ^{1}H NMR ($CDCl_3$, 400 MHz), δ 1.34 (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), 7.00 (t, J = 7.3 Hz, 1H), 7.14 (d, J = 7.8 Hz, 2H), 7.29-7.35 (m, 2H), 7.36-7.41 (m, 3H), 7.48-7.51 (m, 2H) ppm; ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz), δ 13.2, 40.2, 60.8, 67.6, 79.1, 113.1, 121.1, 126.1, 127.6, 127.6, 128.1, 136.3, 150.2, 170.5 ppm; HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{18}H_{19}NNaO_3$ 320.1257; found 320.1261.

Ethyl 2-phenyl-5-(o-tolyl)isoxazolidine-3-carboxylate (4b). Yellow oil (98% yield, 30.5 mg), ^{1}H NMR ($CDCl_3$, 400 MHz), δ 1.33 (t, J = 7.1 Hz, 3H), 2.32 (s, 3H), 2.62-2.69 (m, 1H), 2.91-2.98 (m, 1H), 4.27 (q, J = 7.2 Hz, 2H), 4.52 (dd, J = 9.0, 5.8 Hz, 1H), 5.24 (dd, J = 9.4, 6.8 Hz, 1H), 7.00 (t, J = 7.3 Hz, 1H), 7.14-7.18 (m, 3H), 7.21-7.27 (m, 2H), 7.30-7.34 (m, 2H), 7.68-7.70 (m, 1H) ppm; ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz), δ 14.2, 19.5, 40.7, 61.9, 68.6, 80.3, 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 $C_{19}H_{22}NO_3$ 312.1594; found 312.1599.

Ethyl 2-phenyl-5-(m-tolyl)isoxazolidine-3-carboxylate (4c). Yellow oil (98% yield, 30.6 mg), ^{1}H NMR ($CDCl_3$, 400 MHz), δ 1.35 (t, J = 6.8 Hz, 3H), 2.38 (s, 3H), 2.71-2.79 (m, 1H), 2.84-2.94 (m, 1H), 4.29 (q, J = 7.0 Hz, 2H), 4.51 (t, J = 7.5 Hz, 1H), 5.03 (t, J = 8.3 Hz, 1H), 7.00 (t, J = 7.3 Hz, 1H), 7.14 (d, J = 8.0 Hz, 3H), 7.25-7.34 (m, 5H) ppm; ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz), δ 14.2, 21.5, 41.3, 61.9, 68.7, 80.3, 114.2, 122.1, 124.2, 127.7, 128.6, 129.2, 137.2, 138.4, 151.3, 171.6 ppm; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{19}H_{22}NO_3$ 312.1594; found 312.1599.

Ethyl 2-phenyl-5-(p-tolyl)isoxazolidine-3-carboxylate (4d). Yellow oil (99% yield, 30.9 mg),

^{1}H NMR ($CDCl_3$, 400 MHz), δ 1.34 (t, J = 7.2 Hz, 3H), 2.36 (s, 3H), 2.70-2.77 (m, 1H), 2.85-2.92 (m, 1H), 4.29 (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), 7.00 (t, J = 7.3 Hz, 1H), 7.14 (d, J = 7.8 Hz, 2H), 7.19 (d, J = 8.0 Hz, 2H), 7.29 (dd, J = 8.7, 7.4 Hz, 2H), 7.38 (d, J = 8.0 Hz, 2H) ppm; ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz), δ 14.2, 21.3, 41.2, 61.9, 68.7, 80.2, 114.2, 122.0, 127.2, 129.2, 129.3, 134.2, 138.5, 151.3, 171.6 ppm; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{19}H_{22}NO_3$ 312.1594; found 312.1598.

Ethyl 5-(2,5-dimethylphenyl)-2-phenylisoxazolidine-3-carboxylate (4e). Yellow oil (98% yield, 32.0 mg), ^{1}H NMR ($CDCl_3$, 400 MHz), δ 1.34 (t, J = 7.1 Hz, 3H), 2.27 (s, 3H), 2.35 (s, 3H), 2.60-2.68 (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), 6.98 (t, J = 7.3 Hz, 1H), 7.02-7.09 (m, 2H), 7.14 (dd, J = 8.7, 1.0 Hz, 2H), 7.29-7.35 (m, 2H), 7.51 (s, 1H) ppm; ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz), δ 14.2, 19.0, 21.2, 40.3, 61.9, 68.7, 76.9, 114.1, 122.0, 126.4, 128.8, 129.2, 130.3, 132.3, 135.4, 136.0, 151.4, 171.6 ppm; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{20}H_{24}NO_3$ 326.1751; found 326.1753.

Ethyl 5-(2-fluorophenyl)-2-phenylisoxazolidine-3-carboxylate (4f). Yellow oil (89% isolated yield, 28.2 mg, dr = 91:9), ^{1}H NMR ($CDCl_3$, 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), 5.37 (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, 1.1 Hz, 1H), 7.28-7.35 (m, 3H) , 7.68 (td, J = 7.5, 1.7 Hz, 1H) ppm; ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz), δ 14.2, 39.8, 61.9, 68.6, 73.3, 73.4, 114.2, 115.2 (d, J = 21.2 Hz), 122.3, 124.4 (d, J = 3.5 Hz), 127.7 (d, J = 3.7 Hz), 129.2, 129.8 (d, J = 8.1 Hz), 150.9, 159.1 (d, J = 245.1 Hz), 171.3 ppm; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{18}H_{19}FNO_3$ 316.1343; found 316.1348.

Ethyl 5-(3-fluorophenyl)-2-phenylisoxazolidine-3-carboxylate (4g). Yellow oil (88% isolated yield, 27.7 mg, dr = 89:11), ^{1}H NMR ($CDCl_3$, 400 MHz), δ 1.33 (t, J = 7.1 Hz, 3H), 2.67-2.75 (m, 1H), 2.88-2.96 (m, 1H), 4.28 (q, J = 7.1 Hz, 2H), 4.50 (dd, J = 8.9, 5.5 Hz, 1H), 5.06 (dd, J = 9.0, 7.1 Hz, 1H), 6.99-7.06 (m, 2H), 7.13 (dd, J = 8.6, 0.9 Hz, 2H), 7.22-7.26 (m, 2H), 7.29-7.38 (m, 3H) ppm; ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz), δ 14.2, 41.0, 61.9, 68.5, 79.3, 79.4, 113.8 (d, J = 22.1 Hz), 114.2, 115.3 (d, J = 21.0 Hz), 122.3, 122.6 (d, J = 2.9 Hz), 129.2, 130.1 (d, J = 8.1 Hz), 140.1 (d, J = 7.3 Hz), 150.9, 161.7 (d, J = 244.8 Hz), 171.3 ppm; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{18}H_{19}FNO_3$ 316.1343; found 316.1348.

Ethyl 5-(4-fluorophenyl)-2-phenylisoxazolidine-3-carboxylate (4h). Yellow oil (84% isolated

yield, 26.5 mg, dr = 86:14), ^{1}H NMR ($CDCl_3$, 400 MHz), δ 1.34 (t, J = 7.1 Hz, 3H), 2.68-2.76 (m, 1H), 2.85-2.93 (m, 1H), 4.28 (qd, J = 7.1, 0.7 Hz, 2H), 4.50 (dd, J = 8.9, 5.6 Hz, 1H), 5.03 (dd, J = 9.2, 7.0 Hz, 1H), 7.0 (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{^{1}H} NMR ($CDCl_3$, 100 MHz), δ 14.2, 41.1, 61.9, 79.6, 114.2, 115.4 (d, J = 21.6 Hz), 122.2, 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 316.1356.

Ethyl 5-(4-chlorophenyl)-2-phenylisoxazolidine-3-carboxylate (4i). Yellow oil (84% isolated yield, 27.9 mg, dr = 87:13), {lit.[22c]: Oil, 77% yield, dr = 80:20}, ^{1}H NMR ($CDCl_3$, 600 MHz), δ 1.34 (t, J = 7.1 Hz, 3H), 2.68-2.73 (m, 1H), 2.87-2.93 (m, 1H), 4.29 (qd, J = 7.1, 1.5 Hz, 2H), 4.51 (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), 7.35-7.38 (m, 2H), 7.43 (dt, J = 8.9, 2.3 Hz, 2H) ppm.

Ethyl 5-(4-bromophenyl)-2-phenylisoxazolidine-3-carboxylate (4j). Yellow oil (83% isolated yield, 31.2 mg, dr = 87:13), {lit.[22c]: Oil, 63% yield, dr = 82:18}, ^{1}H NMR ($CDCl_3$, 400 MHz), δ 1.33 (t, J = 7.2 Hz, 3H), 2.66-2.73 (m, 1H), 2.86-2.94 (m, 1H), 4.28 (q, J = 7.2 Hz, 2H), 4.50 (dd, J = 8.9, 5.5 Hz, 1H), 5.02 (dd, J = 9.0, 7.2 Hz, 1H), 7.01 (t, J = 7.4 Hz, 1H), 7.13 (d, J = 7.8, 2H), 7.30 (dd, J = 8.5, 7.5 Hz, 2H), 7.36 (d, J = 8.4, 2H), 7.51 (d, J = 8.4 Hz, 2H) ppm.

Ethyl 2-phenyl-5-(pyridin-2-yl)isoxazolidine-3-carboxylate (4k). Yellow oil (90% isolated yield, 26.9 mg, dr = 95:5), ^{1}H NMR ($CDCl_3$, 400 MHz), δ 1.27 (t, J = 7.0 Hz, 3H), 2.84-2.92 (m, 1H), 2.93-3.06 (m, 1H), 4.22 (q, J = 7.0 Hz, 2H), 4.49 (dd, J = 8.8, 4.8 Hz, 1H), 5.31 (t, J = 7.1 Hz, 1H), 7.02 (t, J = 7.3 Hz, 1H), 7.16 (d, J = 8.1 Hz, 2H), 7.22-7.28 (m, 1H), 7.32 (t, J = 7.6 Hz, 2H), 7.66-7.77 (m, 2H), 8.55 (d, J = 4.7, 1H) ppm; ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz), δ 14.1, 39.5, 61.7, 80.4, 114.5, 121.0, 122.4, 123.1, 129.1, 136.9, 149.0, 150.8, 158.3, 171.3 ppm; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{17}H_{19}N_2O_3$ 299.1390; found 299.1395.

Ethyl 2-phenyl-5-(pyridin-4-yl)isoxazolidine-3-carboxylate (4l). Yellow oil (90% yield, 26.9 mg), ^{1}H NMR ($CDCl_3$, 400 MHz), δ 1.31 (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 = 8.7, 5.0 Hz, 1H), 5.11 (t, J = 8.0 Hz, 1H), 7.03 (t, J = 7.3 Hz, 1H), 7.13 (d, J = 8.0 Hz, 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{^{1}H} NMR ($CDCl_3$, 100 MHz), δ 14.1, 40.5, 62.0, 68.2, 78.2, 114.3, 121.5, 122.6, 129.3, 147.1, 150.2, 150.6, 171.0 ppm; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{17}H_{19}N_2O_3$

299.1390; found 299.1399.

Ethyl 5-(naphthalen-1-yl)-2-phenylisoxazolidine-3-carboxylate (4m). Yellow oil (82% isolated yield, 28.5 mg, dr = 90:10), ^{1}H NMR ($CDCl_3$, 400 MHz), δ 1.30 (t, J = 7.2 Hz, 3H), 2.77-2.84 (m, 1H), 3.10-3.18 (m, 1H), 4.25 (q, J = 7.1 Hz, 2H), 4.61 (dd, J = 8.9, 5.4 Hz, 1H), 5.79 (dd, J = 8.0, 7.4 Hz, 1H), 7.03 (t, J = 7.2 Hz, 1H), 7.21 (d, J = 7.8 Hz, 2H), 7.32 (dd, J = 8.6, 7.4 Hz, 2H), 7.48-7.54 (m, 3H), 7.82 (d, J = 8.2 Hz, 1H), 7.87-7.91 (m, 2H), 7.95-7.98 (m, 1H) ppm; ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz), δ 14.2, 29.7, 40.6, 61.8, 68.6, 77.0, 114.3, 122.2, 123.0, 123.4, 125.6, 125.7, 126.3, 128.6, 128.8, 129.0, 129.3, 130.6, 133.6, 133.7, 151.2, 171.4 ppm; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{22}H_{22}NO_3$ 348.1594; found 348.1592.

Ethyl 5-(naphthalen-2-yl)-2-phenylisoxazolidine-3-carboxylate (4n). White solid (83% isolated yield, 29.0 mg, dr = 87:13); mp 96-98 ^{o}C; ^{1}H NMR ($CDCl_3$, 400 MHz), δ 1.35 (t, J = 7.1 Hz, 3H), 2.80-2.88 (m, 1H), 2.94-3.02 (m, 1H), 4.30 (q, J = 6.9 Hz, 2H), 4.57 (t, J = 7.2 Hz, 1H), 5.24 (t, J = 8.0 Hz, 1H), 7.02 (t, J = 7.2 Hz, 1H), 7.18 (d, J = 7.9 Hz, 2H), 7.34 (t, J = 7.4 Hz, 2H), 7.50 (t, J = 3.3 Hz, 2H), 7.62 (d, J = 8.5 Hz, 1H), 7.85 (d, J = 3.3 Hz, 2H), 7.87 (d, J = 8.7 Hz, 1H), 7.92 (s, 1H) ppm; ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz), δ 14.2, 41.2, 61.9, 68.7, 80.4, 114.2, 122.2, 124.5, 126.5, 127.8, 128.0, 128.6, 129.2, 133.1, 133.4, 151.2, 171.6 ppm; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{22}H_{22}NO_3$ 348.1594; found 348.1583.

Ethyl 4-benzoyl-2,5-diphenylisoxazolidine-3-carboxylate (4o). Yellow oil (88% isolated yield, 35.3 mg, dr = 89:11), {lit.[24]: 82% yield, dr = 8:1}, ^{1}H NMR ($CDCl_3$, 600 MHz), δ 1.33 (t, J = 7.1 Hz, 3H), 4.31-4.39 (m, 2H), 5.00 (d, J = 5.2 Hz, 1H), 5.04 (dd, J = 8.7, 5.2 Hz, 1H), 5.31 (d, J = 8.8 Hz, 1H), 7.04 (t, J = 7.3 Hz, 1H), 7.18 (dd, J = 8.6, 1.0 Hz, 2H), 7.30-7.35 (m, 4H), 7.35-7.37 (m, 3H), 7.45-7.49 (m, 2H), 7.51 (t, J = 7.4 Hz, 1H), 7.65 (dd, J = 8.5, 1.3 Hz, 2H) ppm.

Diethyl 2,5-diphenylisoxazolidine-3,4-dicarboxylate (4p). Yellow oil (84% isolated yield, 31.0 mg, dr = 93:7), {lit.[24]: 75% yield, dr = 30:1}, ^{1}H NMR ($CDCl_3$, 400 MHz), δ 1.12 (t, J = 7.1 Hz, 3H), 1.35 (t, J = 7.1 Hz, 3H), 4.04-4.09 (m, 3H), 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 = 6.8 Hz, 2H) ppm.

Ethyl-5-(hydroxymethyl)-2-phenylisoxazolidine-3-carboxylat (4q). Yellow oil (99% yield, 24.9 mg), {lit.[22c]: 94% yield, dr = 95:5}, ^{1}H NMR ($CDCl_3$, 400 MHz), δ 1.32 (t, J = 7.0 Hz, 3H), 2.43 (dd, J = 7.4, 5.3 Hz, 1H), 2.48-2.55 (m, 1H), 2.56-2.63 (m, 1H), 3.70-3.77 (m, 1H), 3.95 (d, J

= 12.4 Hz, 1H), 4.25 (q, *J* = 7.1 Hz, 2H), 4.38-4.43 (m, 1H), 4.43 (dd, *J* = 9.3, 4.1 Hz, 1H), 7.00 (t, *J* = 7.2 Hz, 1H), 7.07 (d, *J* = 8.0 Hz, 2H), 7.29 (d, *J* = 7.5 Hz, 2H) ppm.

Ethyl 5-(2-hydroxyethyl)-2-phenylisoxazolidine-3-carboxylate (4r). Yellow oil (95% yield, 25.2 mg), {lit.[22c]: Oil, 88% yield, dr = 95:5}, ^{1}H NMR ($CDCl_3$, 400 MHz), δ 1.33 (t, *J* = 7.1 Hz, 3H), 2.00 (d, *J* = 6.0 Hz, 2H), 2.07 (s, 1H), 2.38-2.46 (m, 1H), 2.60-2.68 (m, 1H), 3.85 (s, 2H), 4.25-4.31 (m, 3H), 4.35 (dd, *J* = 8.7, 7.2 Hz, 1H), 6.97 (t, *J* = 7.3 Hz, 1H), 7.05 (d, *J* = 8.1 Hz, 2H), 7.29 (t, *J* = 7.7 Hz, 2H) ppm.

Ethyl 5-(bromomethyl)-2-phenylisoxazolidine-3-carboxylate (4s). Yellow oil (81% isolated yield, 25.4 mg, dr = 82:18), {lit.[22c]: Oil, 82% yield, dr = 95:5}, ^{1}H NMR ($CDCl_3$, 400 MHz), δ 1.33 (t, *J* = 7.1 Hz, 3H), 2.53-2.69 (m, 2H), 3.53-3.65 (m, 2H), 4.26 (qd, *J* = 7.1, 2.2 Hz, 2H), 4.39 (dd, *J* = 8.8, 4.4 Hz, 1H), 4.45-4.52 (m, 1H), 7.01 (t, *J* = 7.3 Hz, 1H), 7.07 (dd, *J* = 8.6, 0.9 Hz, 2H), 7.27-7.33 (m, 2H) ppm.

Ethyl 5-(3-bromopropyl)-2-phenylisoxazolidine-3-carboxylate (4t). Brown oil (87% yield, 29.8 mg), ^{1}H NMR ($CDCl_3$, 400 MHz), δ 1.33 (t, *J* = 7.1 Hz, 3H), 1.87-1.95 (m, 2H), 1.96-2.05 (m, 1H), 2.10-2.22 (m, 1H), 2.33-2.41 (m, 1H), 2.57-2.65 (m, 1H), 3.43-3.55 (m, 2H), 4.07-4.15 (m, 1H), 4.26 (q, *J* = 7.1 Hz, 2H), 4.35 (dd, *J* = 8.9, 5.7 Hz, 1H), 6.97 (t, *J* = 7.2 Hz, 1H), 7.03 (d, *J* = 8.3 Hz, 2H), 7.29 (t, *J* = 7.8 Hz, 2H) ppm; ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz), δ 14.2, 29.7, 31.3, 33.4, 38.5, 61.8, 68.0, 77.6, 114.1, 121.9, 129.1, 151.1, 171.5 ppm; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{15}H_{21}BrNO_3$ 342.0699; found 342.0698.

Ethyl 5-((methylthio)methyl)-2-phenylisoxazolidine-3-carboxylate (4u). Yellow oil (94% isolated yield, 26.4 mg, dr = 95:5), ^{1}H NMR ($CDCl_3$, 400 MHz), δ 1.33 (t, *J* = 7.1 Hz, 3H), 2.24 (s, 3H), 2.48-2.53 (m, 1H), 2.26-2.68 (m, 1H), 2.78 (dd, *J* = 13.9, 5.9 Hz, 1H), 2.88 (dd, *J* = 13.9, 6.4 Hz, 1H), 4.25-4.32 (m, 2H), 4.34-4.37 (m, 1H), 4.37 (dd, *J* = 9.0, 5.2 Hz, 1H), 6.97 (td, *J* = 8.2, 0.9 Hz, 1H), 7.07 (dd, *J* = 8.6, 1.0 Hz, 2H), 7.27-7.32 (m, 2H) ppm; ^{13}C{^{1}H} NMR ($CDCl_3$, 150 MHz), δ 17.1, 19.6, 39.2, 40.8, 64.7, 70.9, 81.6, 117.2, 125.1, 131.9, 153.8, 174.2 ppm; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{14}H_{20}NO_3S$ 282.1158; found 282.1160.

Ethyl 2-phenyl-5-(propionyloxy)isoxazolidine-3-carboxylate (4v). Yellow oil (96% isolated yield, 28.2 mg, dr = 97:3), ^{1}H NMR ($CDCl_3$, 400 MHz), δ 1.14 (t, *J* = 7.5 Hz, 3H), 1.35 (t, *J* = 7.2 Hz, 3H), 2.33-2.41 (m, 2H), 2.73-2.85 (m, 2H), 4.20 (dd, *J* = 8.9, 3.7 Hz, 1H), 4. 27-4.38 (m, 2H), 6.63 (d, *J* = 5.0 Hz, 1H), 7.04 (t, *J* = 7.0 Hz, 1H), 7.09 (d, *J* = 8.2 Hz, 2H), 7.27-7.32 (m, 2H) ppm;

$^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 100 MHz), δ 8.7, 14.2, 27.6, 38.4, 62.0, 66.7, 94.4, 116.0, 123.4, 128.8, 150.1, 170.3, 173.5 ppm; HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{15}H_{19}NNaO_5$ 316.1155; found 316.1168.

3-ethyl 4,5-dimethyl 2-phenylisoxazolidine-3,4,5-tricarboxylate (4w). Yellow oil (99% isolated yield, 33.4 mg), {lit.[24]: 98% yield}, ^{1}H NMR ($CDCl_3$, 400 MHz), δ 1.31 (t, J = 7.1 Hz, 3H), 3.52 (s, 3H), 3.68 (s, 3H), 4.26-4.33 (m, 2H), 4.33 (d, J = 7.1 Hz, 1H), 4.79 (d, J = 6.9 Hz, 1H), 5.01 (d, J = 7.4 Hz, 1H), 6.98 (t, J = 7.3 Hz, 1H), 7.13 (d, J = 8.2 Hz, 2H), 7.27 (t, J = 7.6 Hz, 2H) ppm.

3-ethyl 4,5-dimethyl 2-phenylisoxazolidine-3,4,5-tricarboxylate (4x). Yellow oil (96% isolated yield, 32.5 mg), {lit.[24]: 90% yield, dr = 20:1}, ^{1}H NMR ($CDCl_3$, 400 MHz), δ 1.32 (t, J = 7.1 Hz, 3H), 3.61 (s, 3H), 3.86 (s, 3H), 4.28 (td, J = 7.2, 2.7 Hz, 2H), 4.34 (dd, J = 5.0, 3.9 Hz, 1H), 4.82 (d, J = 3.4 Hz, 1H), 5.13 (d, J = 5.4 Hz, 1H), 7.04 (t, J = 7.3 Hz, 1H), 7.11 (d, J = 8.2 Hz, 2H), 7.30 (t, J = 7.8 Hz, 2H) ppm.

Triethyl 2-phenylisoxazolidine-3,4,5-tricarboxylate (4y). Yellow oil (99% isolated yield, 36.2 mg), {lit.[24]: 77% yield, dr = 20:1}, ^{1}H NMR ($CDCl_3$, 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), 4.10 (dd, J = 7.1, 2.5 Hz, 2H), 4.26-4.37 (m, 3H), 4.78 (d, J = 7.2 Hz, 1H), 4.97 (d, J = 7.4 Hz, 1H), 6.97 (t, J = 7.3 Hz, 1H), 7.14 (d, J = 7.8 Hz, 2H), 7.24-7.29 (m, 2H) ppm.

Ethyl 4,6-dioxo-2,5-diphenylhexahydro-2H-pyrrolo[3,4-d]isoxazole-3-carboxylate (4z). Colourless oil (81% isolated yield, 29.7 mg), {lit.[22c]: 91% yield, dr = 95:5}, ^{1}H NMR ($CDCl_3$, 400 MHz), δ 1.30 (t, J = 7.1 Hz, 3H), 4.23-4.35 (m, 2H), 4.40 (dd, J = 7.6, 0.6 Hz, 1H), 5.16 (d, J = 7.7 Hz, 1H), 5.25 (s, 1H), 6.52-6.54 (m, 1H), 6.54 (d, J = 2.2 Hz, 1H), 7.03 (t, J = 7.4 Hz, 1H), 7.13 (dd, J = 8.6, 0.8 Hz, 2H), 7.25 (d, J = 2.6 Hz, 1H), 7.27 (d, J =1.3 Hz, 1H), 7.29-7.30 (m, 1H), 7.31 (d, J = 2.2 Hz, 2H) ppm.

Ethyl 5-phenyl-2-(o-tolyl)isoxazolidine-3-carboxylate (4aa). Yellow oil (67% yield, 20.1 mg, dr = 71:29), ^{1}H NMR ($CDCl_3$, 400 MHz), δ 1.18 (t, J = 7.1 Hz, 3H), 2.35 (s, 3H), 2.64-2.71 (m, 1H), 3.01-3.09 (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, 2H) ppm; $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 100 MHz), δ 14.0, 18.4, 40.3, 61.4, 67.3, 79.3, 119.2, 125.2, 126.3, 126.7, 126.97, 128.2, 128.5, 128.6, 130.8, 131.2, 138.9, 148.1, 170.8 ppm; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{19}H_{22}NO_3$ 312.1594; found 312.1607.

Ethyl 5-phenyl-2-(m-tolyl)isoxazolidine-3-carboxylate (4ab). Yellow oil (79% yield, 24.6 mg, dr = 81:19), ^{1}H NMR ($CDCl_3$, 600 MHz), δ 1.34 (t, J = 7.1 Hz, 3H), 2.35 (s, 3H), 2.71-2.76 (m, 1H), 2.88-2.94 (m, 1H), 4.29-4.34 (m, 2H), 4.51 (dd, J = 8.9, 5.8 Hz, 1H), 5.05 (dd, J = 9.5, 6.8 Hz, 1H), 6.81 (d, J = 7.5 Hz, 1H), 6.94-6.98 (m, 2H), 7.20 (t, J = 7.7 Hz, 1H), 7.33-7.37 (m, 1H), 7.38-7.41 (m, 2H), 7.49 (d, J = 7.1 Hz, 2H) ppm; ^{13}C{^{1}H} NMR ($CDCl_3$, 150 MHz), δ 17.1, 24.6, 44.2, 64.7, 71.4, 83.0, 114.2, 117.7, 125.8, 129.9, 131.4, 131.5, 131.9, 140.4, 141.9, 154.1, 174.5 ppm; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{19}H_{22}NO_3$ 312.1594; found 312.1596.

Ethyl 5-phenyl-2-(p-tolyl)isoxazolidine-3-carboxylate (4ac). Yellow oil (84% yield, 26.2 mg, dr = 87:13), ^{1}H NMR ($CDCl_3$, 600 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 = 8.9, 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{^{1}H} NMR ($CDCl_3$, 150 MHz), δ 17.1, 23.5, 44.1, 64.7, 71.7, 82.9, 117.2, 130.0, 131.4, 131.5, 132.6, 134.5, 140.4, 151.8, 174.5 ppm; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{19}H_{22}NO_3$ 312.1594; found 312.1600.

Ethyl 2-(2-chlorophenyl)-5-phenylisoxazolidine-3-carboxylate (4ad). Yellow oil (74% yield, 24.6 mg, dr = 75:25), ^{1}H NMR ($CDCl_3$, 600 MHz), δ 1.21 (t, J = 7.1 Hz, 3H), 2.62-2.68 (m, 1H), 2.85 (qd, J = 6.0, 1.4 Hz, 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 (td, 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{^{1}H} NMR ($CDCl_3$, 150 MHz), δ 16.9, 43.1, 64.3, 70.3, 82.3, 122.8, 127.0, 127.9, 129.7, 130.1, 131.4, 132.9, 141.4, 149.9, 173.7 ppm; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{18}H_{19}ClNO_3$ 332.1048; found 332.1053.

Ethyl 2-(3-chlorophenyl)-5-phenylisoxazolidine-3-carboxylate (4ae). Yellow oil (91% yield, 30.1 mg), ^{1}H NMR ($CDCl_3$, 400 MHz), δ 1.34 (t, J = 7.1 Hz, 3H), 2.72-2.80 (m, 1H), 2.87-2.97 (m, 1H), 4.28 (q, J = 7.1 Hz, 2H), 4.45 (dd, J = 8.7, 6.1 Hz, 1H), 5.02 (dd, J = 9.5, 6.7 Hz, 1H), 6.95-7.01 (m, 2H), 7.14-7.19 (m, 1H), 7.22 (t, J = 8.1 Hz, 1H), 7.34-7.42 (m, 3H), 7.48 (d, J = 7.2 Hz, 2H) ppm; ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz), δ 14.2, 41.2, 62.0, 68.4, 80.5, 112.3, 114.2, 122.0, 127.1, 128.7, 130.3, 135.0, 136.9, 152.5, 171.1 ppm; HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{18}H_{18}ClNNaO_3$ 354.0867; found 354.0865.

Ethyl 2-(4-chlorophenyl)-5-phenylisoxazolidine-3-carboxylate (4af). Yellow oil (99% yield, 32.8 mg), ^{1}H NMR ($CDCl_3$, 400 MHz), δ 1.33 (t, J = 7.1 Hz, 3H), 2.71-2.79 (m, 1H), 2.87-2.97

(m, 1H), 4.28 (q, J = 7.0 Hz, 2H), 4.43 (dd, J = 8.7, 6.1 Hz, 1H), 5.01 (dd, J = 9.4, 6.8 Hz, 1H), 7.07 (d, J = 8.9 Hz, 2H), 7.25 (d, J = 8.7 Hz, 2H), 7.35-7.42 (m, 3H), 7.47 (d, J = 7.4 Hz, 2H) ppm; $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz), δ 14.2, 41.3, 62.0, 68.6, 80.3, 115.5, 127.1, 128.7, 128.7, 128.7, 129.1, 137.0, 149.8, 171.1 ppm; HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{18}H_{18}ClNNaO_3$ 354.0867; found 354.0868.

Ethyl 5-phenyl-2-(pyridin-2-yl)isoxazolidine-3-carboxylate (4ag). Yellow oil (86% yield, 25.7 mg), ^1H NMR ($CDCl_3$, 400 MHz), δ 1.33 (t, J = 7.1 Hz, 3H), 2.64-2.72 (m, 1H), 2.88-2.96 (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), 6.89 (ddd, J = 7.2, 4.9, 0.9 Hz, 1H), 7.31-7.36 (m, 2H), 7.36-7.41 (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; $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz), δ 14.2, 40.6, 61.7, 63.0, 81.8, 109.9, 117.7, 127.1, 128.6, 128.7, 137.4, 138.2, 147.6, 161.4, 172.0 ppm; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{17}H_{19}N_2O_3$ 299.1390; found 299.1390.

Ethyl 2-(6-methylpyridin-2-yl)-5-phenylisoxazolidine-3-carboxylate (4ah). Yellow oil (90% yield, 28.1 mg), ^1H NMR ($CDCl_3$, 400 MHz), δ 1.33 (t, J = 7.1 Hz, 3H), 2.45 (s, 3H), 2.60-2.67 (m, 1H), 2.85-2.94 (m, 1H), 4.28 (q, J = 7.1 Hz, 2H), 4.88 (t, J = 8.1 Hz, 1H), 5.65 (d, J = 5.0 Hz, 1H), 6.74 (d, J = 7.4 Hz, 1H), 7.12 (d, J = 8.2 Hz, 1H), 7.30-7.40 (m, 3H), 7.42-7.48 (m, 2H), 7.50 (t, J = 7.7 Hz, 1H) ppm; $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz), δ 14.2, 24.3, 40.7, 61.5, 62.9, 80.8, 106.7, 117.1, 127.0, 128.5, 128.6, 137.7, 138.3, 156.6, 160.8, 172.3 ppm; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{18}H_{21}N_2O_3$ 313.1547; found 313.1547.

Ethyl 2-(3,4-dimethylphenyl)-5-phenylisoxazolidine-3-carboxylate (4ai). Yellow oil (82% yield, 26.7 mg), ^1H NMR ($CDCl_3$, 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 = 8.9, 5.7 Hz, 1H), 5.05 (dd, J = 9.2, 7.0 Hz, 1H), 6.88 (dd, J = 8.2, 2.4 Hz, 1H), 6.95 (d, J = 2.1 Hz, 1H), 7.05 (d, J = 8.2 Hz, 1H), 7.33-7.41 (m, 3H), 7.48 (d, J = 6.9 Hz, 2H) ppm; $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz), δ 14.2, 18.9, 20.1, 41.2, 61.7, 80.0, 111.7, 115.7, 127.1, 128.5, 128.6, 130.2, 130.3, 137.4, 137.6, 149.2, 171.6 ppm; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{20}H_{24}NO_3$ 326.1751; found 326.1753.

Ethyl 2-(3,5-dichlorophenyl)-5-phenylisoxazolidine-3-carboxylate (4aj). Yellow oil (87% yield, 31.8 mg), ^1H NMR ($CDCl_3$, 400 MHz), δ 1.33 (t, J = 7.1 Hz, 3H), 2.73-2.81 (m, 1H), 2.91-2.99 (m, 1H), 4.28 (q, J = 7.1 Hz, 2H), 4.40 (dd, J = 8.8, 6.2 Hz, 1H), 4.99 (dd, J = 9.7, 6.5 Hz, 1H), 6.95-6.98 (m, 1H), 7.02 (d, J = 1.8 Hz, 2H), 7.36-7.43 (m, 3H), 7.46-7.50 (m, 2H) ppm; $^{13}C\{^1H\}$

NMR ($CDCl_3$, 100 MHz), δ 14.1, 41.2, 62.1, 68.0, 80.7, 112.5, 113.4, 121.7, 127.0, 128.7, 135.6, 136.4, 153.0, 170.5 ppm; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{18}H_{18}Cl_2NO_3$ 366.0658; found 366.0669.

Methyl 2,5-diphenylisoxazolidine-3-carboxylate (4ak). Yellow oil (95% yield, 27.0 mg, dr = 97:3), ^1H NMR ($CDCl_3$, 400 MHz), δ 2.73-2.81 (m, 1H), 2.88-2.96 (m, 1H), 3.86 (s, 3H), 4.53 (dd, J = 8.9, 5.9 Hz, 1H), 5.04 (dd, J = 9.5, 6.8 Hz, 1H), 7.00 (t, J = 7.4 Hz, 1H), 7.1 (d, J = 7.8 Hz, 2H), 7.29-7.36 (m, 3H), 7.36-7.42 (m, 2H), 7.48 (d, J = 6.9 Hz, 2H) ppm; $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz), δ 41.1, 52.9, 68.5, 80.2, 114.1, 122.2, 127.1, 128.7, 129.2, 137.1, 151.1, 172.1 ppm; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{17}H_{18}NO_3$ 284.1281; found 284.1288.

Tert-butyl 2,5-diphenylisoxazolidine-3-carboxylate (4al). Yellow solid (94% yield, 30.6 mg); mp 77-78 ^oC; ^1HNMR ($CDCl_3$, 400 MHz), δ 1.51 (s, 9H), 2.66-2.74 (m, 1H), 2.83-2.91 (m, 1H), 4.40 (t, J = 7.6 Hz, 1H), 5.04 (t, J = 8.2 Hz, 1H), 6.98 (t, J = 7.3 Hz, 1H), 7.14 (d, J = 7.6 Hz, 2H), 7.24-7.33 (m, 2H), 7.34-7.45 (m, 3H), 7.50 (d, J = 7.4 Hz, 2H) ppm; $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz), δ 28.0, 41.3, 69.3, 80.1, 82.1, 114.1, 121.8, 127.1, 128.6, 129.1, 137.6, 151.4, 170.5 ppm; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{20}H_{24}NO_3$ 326.1751; found 326.1744.

(2,5-diphenylisoxazolidin-3-yl)(phenyl)methanone (4am). White solid (67% yield, 22.1 mg, dr = 89:11); mp 178-180 ^oC; ^1H NMR ($CDCl_3$, 400 MHz), δ 2.84-3.99 (m, 2H), 5.11 (t, J = 7.5 Hz, 1H), 5.20 (dd, J = 8.5, 6.0 Hz, 1H), 7.01-7.05 (m, 1H), 7.16 (d, J = 8.6 Hz, 2H), 7.31-7.40 (m, 5H), 7.45-7.50 (m, 4H), 7.55-7.60 (m, 1H), 8.17 (d, J = 8.4 Hz, 2H) ppm; $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz), δ 40.6, 71.8, 80.3, 114.2, 122.2, 127.1, 128.6, 128.6, 129.2, 129.3, 133.4, 134.9, 137.2, 150.8, 196.9 ppm; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{22}H_{20}NO_2$ 330.1489; found 330.1478.

Ethyl 5-formyl-5-methyl-2-phenylisoxazolidine-3-carboxylate (4an). Yellow oil (87% yield, 22.9 mg), ^1H NMR ($CDCl_3$, 400 MHz), δ 1.14 (t, J = 7.1 Hz, 3H), 1.51 (s, 3H), 2.39 (dd, J = 12.8, 4.1 Hz, 1H), 3.05 (dd, J = 12.8, 9.0 Hz, 1H), 4.09 (qd, J = 7.1, 2.9 Hz, 2H), 4.47 (dd, J = 9.0, 4.2 Hz, 1H), 6.98 (t, J = 7.3 Hz, 1H), 7.03 (d, J = 8.1 Hz, 2H), 7.25-7.30 (m, 2H), 9.56 (s, 1H) ppm; $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz), δ 13.9, 18.2, 38.9, 61.4, 64.9, 86.6, 115.0, 122.4, 128.8, 148.1, 170.4, 201.4 ppm; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{14}H_{18}NO_4$ 264.1230; found 264.1233.

3-ethyl 5-methyl 5-methyl-2-phenylisoxazolidine-3,5-dicarboxylate (4ao). Yellow oil (90% yield, 26.4 mg), ^1H NMR ($CDCl_3$, 400 MHz), δ 1.24 (t, J = 7.1 Hz, 3H), 1.67 (s, 3H), 2.52 (dd, J = 12.6, 6.2 Hz, 1H), 3.25 (dd, J = 12.7, 8.6 Hz, 1H), 3.52 (s, 3H), 4.18-4.24 (m, 2H), 4.49 (dd, J =

8.6, 6.2 Hz, 1H), 6.93 (t, *J* = 7.3 Hz, 1H), 7.02 (d, *J* = 7.8 Hz, 2H), 7.22 (dd, *J* = 8.6, 7.4 Hz, 2H) ppm; $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 100 MHz), δ 14.1, 22.0, 42.0, 52.4, 61.7, 66.4, 83.4, 114.3, 122.0, 128.6, 149.8, 171.0, 173.1 ppm; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{15}H_{20}NO_5$ 294.1336; found 294.1334.

Diethyl 5-methyl-2-phenylisoxazolidine-3,5-dicarboxylate (4ap). Yellow oil (88% yield, 27.0 mg), ^{1}H NMR ($CDCl_3$, 400 MHz), δ 1.07 (t, *J* = 7.2 Hz, 3H), 1.26 (t, *J* = 7.1 Hz, 3H), 1.66 (s, 3H), 2.52 (dd, *J* = 12.6, 6.6 Hz, 1H), 3.23 (dd, *J* = 12.7, 8.5 Hz, 1H), 3.91 (q, *J* = 7.2 Hz, 2H), 4.20 (q, *J* = 7.2 Hz, 2H), 4.47 (dd, *J* = 8.3, 6.7 Hz, 1H), 6.92 (t, *J* = 7.3 Hz, 1H), 7.02 (d, *J* = 7.8 Hz, 2H), 7.21 (dd, *J* = 8.4, 7.4 Hz, 2H) ppm; $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 100 MHz), δ 13.6, 14.1, 21.9, 42.1, 61.5, 61.7, 66.5, 83.5, 114.2, 121.7, 128.5, 150.1, 171.0, 172.5 ppm; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{16}H_{22}NO_5$ 308.1492; found 308.1497.

Diethyl 2,5-diphenylisoxazolidine-3,5-dicarboxylate (4aq). Yellow oil (86% yield, 31.8 mg, dr = 95:5), ^{1}H NMR ($CDCl_3$, 400 MHz), δ 1.00 (t, *J* = 7.2 Hz, 3H), 1.06 (t, *J* = 7.1 Hz, 3H), 2.75 (dd, *J* = 12.5, 6.3 Hz, 1H), 3.61 (dd, *J* = 12.5, 8.4 Hz, 1H), 3.88 (q, *J* = 7.1 Hz, 2H), 4.01 (q, *J* = 7.1 Hz, 2H), 4.45 (dd, *J* = 8.4, 6.3 Hz, 1H), 6.89 (t, *J* = 7.3 Hz, 1H), 7.06 (d, *J* = 7.7 Hz, 2H), 7.18-7.22 (m, 2H), 7.25-7.32 (m, 3H), 7.45-7.49 (m, 2H) ppm; $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 100 MHz), δ 13.7, 13.9, 43.4, 61.6, 61.9, 66.2, 87.2, 114.7, 122.1, 125.3, 128.3, 128.4, 128.6, 137.8, 149.6, 170.5, 171.6 ppm; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{21}H_{24}NO_5$ 370.1649; found 370.1645.

Ethyl 2,5,5-triphenylisoxazolidine-3-carboxylate (4ar). Yellow oil (84% yield, 31.4 mg), ^{1}H NMR ($CDCl_3$, 400 MHz):δ 1.07 (t, *J* = 7.2 Hz, 3H), 3.30-3.43 (m, 2H), 3.98 (q, *J* = 7.2 Hz, 2H), 4.35 (dd, *J* = 8.8, 4.8 Hz, 1H), 6.92 (t, *J* = 7.2 Hz, 1H), 7.05 (d, *J* = 8.4 Hz, 2H), 7.19-7.32 (m, 8H), 7.43 (d, *J* = 8.0 Hz, 2H), 7.52 (d, *J* = 7.6 Hz, 2H) ppm; $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 100 MHz): δ 13.9, 45.1, 61.5, 67.1, 87.4, 114.9, 121.7, 126.2, 126.4, 127.4, 127.6, 128.2, 128.3, 128.6, 143.0, 143.2, 150.2, 170.9 ppm; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{24}H_{24}NO_3$ 374.1751; found 374.1742.

1-phenyltetrahydro-3H,6H-furo[3,4-c]isoxazol-6-one (7). White solid (83% yield, 17.1 mg); mp 162-164 ^{o}C; ^{1}H NMR (C_2D_6OS(D-DMSO), 400 MHz), δ 3.46-3.54 (m, 1H), 3.91 (dd, *J* = 8.8, 7.5 Hz, 1H), 4.08 (dd, *J* = 8.9, 2.2 Hz, 1H), 4.33 (dd, *J* = 9.4, 2.9 Hz, 1H), 4.47 (dd, *J* = 9.2, 7.7 Hz, 1H), 5.00 (d, *J* = 8.5 Hz, 1H), 7.00 (t, *J* = 7.3 Hz, 1H), 7.06 (dd, *J* = 8.6, 0.9 Hz, 2H), 7.30 (dd, *J* = 8.7, 7.2 Hz, 1H) ppm; $^{13}C\{^{1}H\}$ NMR (C_2D_6OS(D-DMSO), 100 MHz), δ 42.2, 67.1, 71.6, 72.5, 114.4, 122.4, 129.1, 149.3, 174.6 ppm; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{11}H_{12}NO_3$

206.0812; found 206.0809.

5-methyl-1-phenylhexahydro-6H-pyrrolo[3,4-c]isoxazol-6-one (9). White solid (81% yield, 17.7 mg); mp 114-116 °C; ^{1}H NMR ($CDCl_3$, 400 MHz), δ 2.91 (s, 3H), 3.25-3.31 (m, 1H), 3.31 (dd, J = 10.2, 2.4 Hz, 1H), 3.62 (dd, J = 10.1, 8.3 Hz, 1H), 3.90 (dd, J = 8.6, 1.8 Hz, 1H), 4.05 (dd, J = 8.8, 6.6 Hz, 1H), 4.42 (d, J = 8.5 Hz, 1H), 6.98 (t, J = 7.3 Hz, 1H), 7.16 (dd, J = 8.5, 0.8 Hz, 2H), 7.28-7.30 (m, 2H) ppm; ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz), δ 30.0, 39.4, 53.3, 70.7, 73.0, 114.6, 122.3, 129.0, 150.3, 170.3 ppm; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{12}H_{15}N_2O_2$ 219.1128; found 219.1132.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1039/x0xx00000x

^{1}H NMR spectra of the nitrone intermediate **10a**, and copies of NMR spectra for all compounds

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Notes

The authors declare no competing financial interest.

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