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NBS/DBU-Promoted One-Pot Three-Component Cycloaddition of Malonic Acid Derivatives, Nitrosoarenes, and Alkenes: Synthesis of Isoxazolidines

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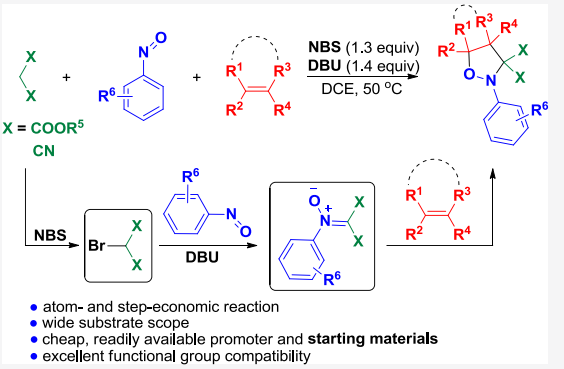
ABSTRACT: A general DBU-mediated one-pot three-component cycloaddition reaction of easily accessible malonic acid derivatives, nitrosoarenes, and alkenes has been successfully established with the aid of NBS to provide direct access to highly functionalized isoxazolidine derivatives with generally good to excellent yields, broad functional group tolerance, and excellent regio- and diastereo-selectivities under mild conditions. The mechanism study shows that the NBS-mediated formation of bromomalonic acid derivatives from malonic acid derivatives and DBU-promoted synthesis of nitrone intermediates *via* the reaction of bromomalonic acid derivatives with nitrosoarenes are key steps.



INTRODUCTION

Multicomponent cycloadditions have proven to be powerful and efficient methods to access diverse polyfunctionalized heterocycles from simple starting materials in a single step.[1] Despite impressive advances in this research area, environmentally benign multicomponent cycloadditions that utilize very cheap and readily available starting materials for the preparation of target products bearing multifunctional groups remain challenging.

Because isoxazolidine motif holds a prominent position in medicinal,[2] synthetic,[3] and pharmaceutical[4] chemistry, various methods have been extensively reported for the synthesis of this skeleton.[5,6] Among these different approaches, the [3+2] cycloaddition of nitrones with alkenes is one of the most classical strategies.[7] However, they usually require the use of expensive reagents and multistep procedures involving the preparation and isolation of nitrones. Therefore, the development of more efficient and practical multicomponent approaches is highly desirable. In this context, the groups of Bhattacharya, Zhong, and Córdova independently demonstrated that aryl hydroxylamines could be used as substrates to participate in metal-free three-component reactions with aldehydes, olefins for access to diverse isoxazolidines (Scheme 1A).[8] Unfortunately, they suffer from the use of expensive, unstable, and poorly accessible aryl hydroxylamines. Recently, three-component processes of functionalized olefins, alkenes, and nitrosoarenes have been well documented to construct this scaffold by Liu, Huang, and their co-workers, respectively (Scheme 1B).[9] However, these reactions are limited to moderate yields. Additionally, Che, Liu, and their co-workers developed ruthenium porphyrin- and [IPrAuCl]/$AgNTf_2$-catalyzed one-pot strategies of diazo compounds, nitrosoarenes, and olefins to synthesize various isoxazolidines, respectively (Scheme 1C1).[10] Nevertheless, these two methods rely on the use of diazo compounds, which are unstable and high cost. Although Zhong, Molander, and Tan groups and our group independently realized the transition-metal-free three-component approaches of these three types of compounds, diazo compounds were still adopted as starting materials (Scheme 1C2).[11] Hence, the development of an environmentally friendly three-component cycloaddition that utilizes cheap and readily available starting materials for the synthesis of highly functionalized isoxazolidines is of high interest. Notably, malonic acid derivatives are very abundant, cheap, stable, and readily accessible reagents, and they have been widely utilized in various bond-forming reactions.[12] To the best of our knowledge, however, reports on their application as one of the key reactants for the preparation of isoxazolidines have never been observed. Herein, we will report a NBS/DBU-promoted one-pot three-component method for the synthesis of various isoxazolidines containing two esters or cyano groups

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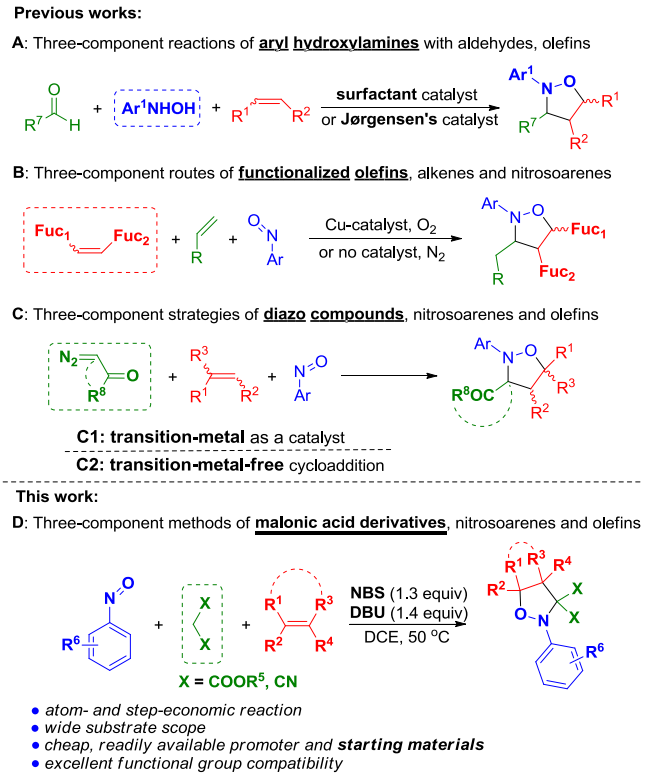
Scheme 1. Three-Component Strategies to Construct Isoxazolidines

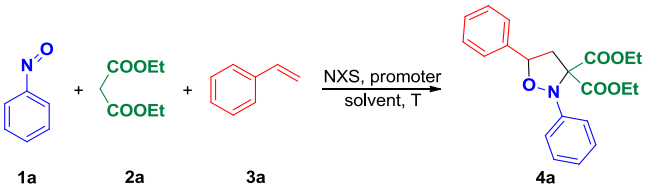


through the reaction of malonic acid derivatives, nitrosoarenes, and olefins (Scheme 1D).

RESULTS AND DISCUSSION

At the outset of our studies, the three-component reaction of nitrosobenzene **1a**, diethyl malonate **2a**, and styrene **3a** was selected as the model reaction to evaluate a range of promoters. When the reaction was performed in the presence of NaH and NBS in DCE under an air atmosphere at 50 °C for 12 h, the isolated yield of the isoxazolidine **4a** was 52% (Table 1, entry 1). Some other bases such as NaOH, Na_2CO_3, NaOAc, KOH, LiOH, and DBU have also been screened as promoters. However, only trace amount of desired product **4a** was observed when NaOH, Na_2CO_3, NaOAc, and KOH were adopted (Table 1, entries 2−5). Gratifyingly, the yields of product **4a** could be increased to 61 and 74% using LiOH and DBU as promoters, respectively (Table 1, entries 6 and 7). DABCO and DIPEA were then employed to further improve the yield (Table 1, entries 8 and 9). Unfortunately, no product **4a** was detected. Subsequently, a number of solvents were examined. CH_3CN, THF, MePh, CH_3NO_2, and dioxane failed to increase the yield (Table 1, entries 10−14 vs 7). Other halogenated alkane solvents such as $CHCl_3$ and CH_2Cl_2 also gave reduced yields (Table 1, entries 15 and 16 vs 7). Additionally, when NCS and NIS were used instead of NBS, inferior results were observed (Table 1, entries 17 and 18 vs 7). The examination of solvent dosage indicated that 0.5 mL of DCE was the most suitable for this transformation (Table 1, entry 19 vs 7, 20, and 21). An 88% yield was achieved when the amount of NBS and DBU was increased to 1.3 and 1.4 equiv, respectively (Table 1, entry 22 vs 19). At last, adjusting substrate ratios (**1a**/**2a**/**3a** = 1.3:1.3:1) further improved the yield to 94%, and up to 99% yield was obtained when the reaction time was 24 h (Table 1, entry 22).

Table 1. Optimization of Reaction Conditions[a]



1a 2a 3a 4a

entry	promoter (equiv)	solvent (mL)	NXS (equiv)	yield[b] (%)
1	NaH (1)	DCE (1)	NBS (1)	52
2	NaOH (1)	DCE (1)	NBS (1)	trace
3	Na_2CO_3 (1)	DCE (1)	NBS (1)	trace
4	NaOAc (1)	DCE (1)	NBS (1)	trace
5	KOH (1)	DCE (1)	NBS (1)	trace
6	LiOH (1)	DCE (1)	NBS (1)	61
7	DBU (1)	DCE (1)	NBS (1)	74
8	DABCO (1)	DCE (1)	NBS (1)	N.D.[c]
9	DIPEA (1)	DCE (1)	NBS (1)	N.D.
10	DBU (1)	CH_3CN (1)	NBS (1)	60
11	DBU (1)	THF (1)	NBS (1)	38
12	DBU (1)	MePh (1)	NBS (1)	N.D.
13	DBU (1)	CH_3NO_2 (1)	NBS (1)	N.D.
14	DBU (1)	dioxane (1)	NBS (1)	47
15	DBU (1)	$CHCl_3$ (1)	NBS (1)	71
16	DBU (1)	CH_2Cl_2 (1)	NBS (1)	54[d]
17	DBU (1)	DCE (1)	NCS (1)	57
18	DBU (1)	DCE (1)	NIS (1)	59
19	DBU (1)	DCE (0.5)	NBS (1)	81
20	DBU (1)	DCE (0.8)	NBS (1)	79
21	DBU (1)	DCE (1.2)	NBS (1)	70
22	DBU (1.4)	DCE (0.5)	NBS (1.3)	88
				94[e]
				99[e,f]

[a]Unless noted, all reactions were performed with nitrosobenzene **1a** (21.6 mg, 0.2 mmol), diethyl malonate **2a** (30.7 uL, 0.2 mmol), and styrene **3a** (23.1 uL, 0.2 mmol) under specified reaction conditions at 50 °C for 12 h. [b]Isolated yield of **4a**. [c]N.D. = not detected. [d]35 °C was used. [e]**1a**/**2a**/**3a** = 1.3:1.3:1. [f]The reaction time was 24 h.

With the optimized reaction conditions in hand, we then explored the substrate scope of different olefins **3** with nitrosobenzene **1a** and diethyl malonate **2a**, and the results are summarized in Scheme 2. First, all screened monosubstituted alkenes including aromatic and aliphatic ones could afford the desired products **4a**−**4v** in good to excellent yields. In terms of monosubstituted aromatic alkenes, when the substituent R^5 on the phenyl ring of styrene was varied, regardless of the positions and electronic nature, good to excellent yields were achieved (**4a**−**4j**), which indicated that the electronic properties of substituents did not affect the reaction yields significantly, and the steric hindrance effect had a little influence on the transformation. Moreover, good to high yields were obtained when styrene was changed to heteroarylenes (**4k** and **4l**) or naphthenes (**4m** and **4n**). It was noteworthy that various aliphatic terminal alkenes bearing different functional groups could be converted successfully into the desired products (**4o**−**4v**) with high yields. Second, diverse sterically hindered 1,1-disubstituted olefins were investigated and the corresponding products **4w**−**4aa** were obtained in excellent yields. Third, a series of 1,2-disubstituted alkenes were examined. Not only symmetrical but also asymmetrical

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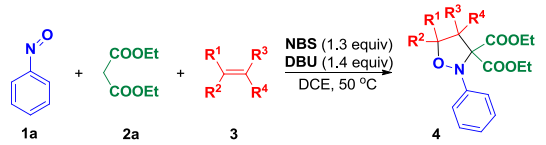
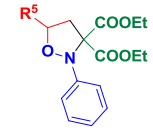
Scheme 2. Scope of Different Types of Olefins[a,b]





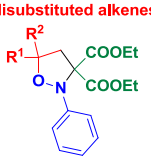
monosubstituted aromatic alkenes

R^5 = Ph	**4a**, 24 h, 99%
R^5 = 2-MeC_6H_4	**4b**, 24 h, 93%
R^5 = 3-MeC_6H_4	**4c**, 24 h, 96%
R^5 = 4-MeC_6H_4	**4d**, 24 h, 98%
R^5 = 2,6-(Me)$_2C_6H_3$	**4e**, 24 h, 90%
R^5 = 2-FC_6H_4	**4f**, 24 h, 91%
R^5 = 3-FC_6H_4	**4g**, 24 h, 94%
R^5 = 4-FC_6H_4	**4h**, 24 h, 97%
R^5 = 2-ClC_6H_4	**4i**, 24 h, 92%
R^5 = 4-ClC_6H_4	**4j**, 24 h, 98%
R^5 = 2-pyridyl	**4k**, 24 h, 89%
R^5 = 4-pyridyl	**4l**, 24 h, 92%
R^5 = 1-naphthyl	**4m**, 24 h, 84%
R^5 = 2-naphthyl	**4n**, 24 h, 92%

monosubstituted aliphatic alkenes

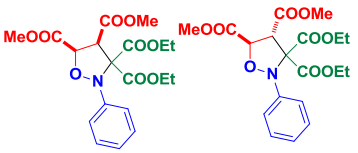
R^5 = $CH_3(CH_2)_{15}$	**4o**, 30 h, 96%
R^5 = $CH_3(CH_2)_3$	**4p**, 27 h, 97%
R^5 = CH_2OH	**4q**, 30 h, 90%
R^5 = $(CH_2)_2OH$	**4r**, 32 h, 95%
R^5 = $(CH_2)_3OH$	**4s**, 32 h, 92%
R^5 = CH_2Br	**4t**, 24 h, 83%
R^5 = CH_2SCH_3	**4u**, 24 h, 91%
R^5 = COOMe	**4v**, 48 h, 96%

1,1-disubstituted alkenes

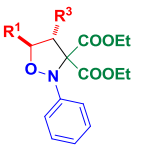


R^1 = Ph, R^2 = Ph	**4w**, 56 h, 93%
R^1 = Me, R^2 = COOMe	**4x**, 48 h, 94%
R^1 = Me, R^2 = Ph	**4y**, 36 h, 96%
R^1 = Me, R^2 = CHO	**4z**, 36 h, 91%
R^1 = Ph, R^2 = COOEt	**4aa**, 48 h, 90%

1,2-disubstituted alkenes



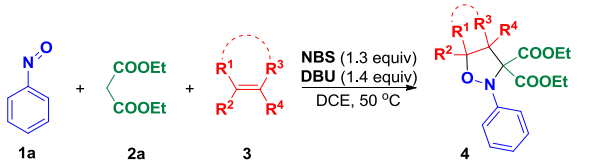
4ab, 36 h, 90% **4ac**, 30 h, 95%

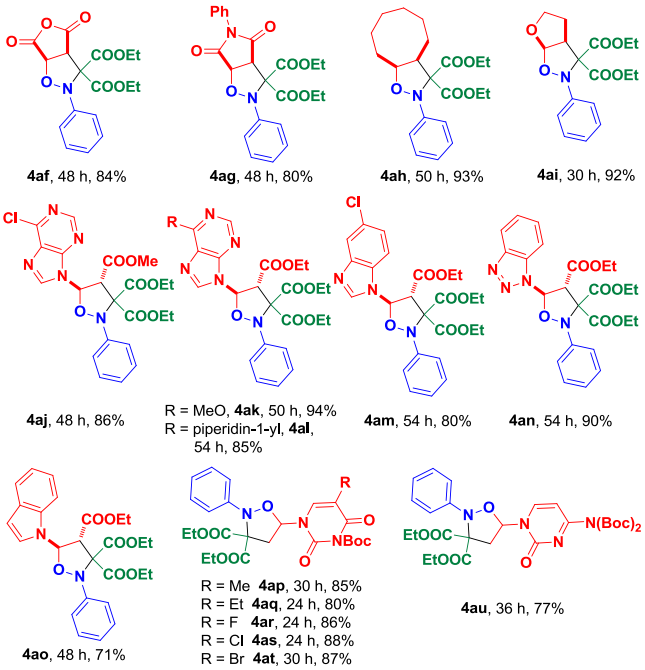


R^1 = Ph, R^3 = C(O)Ph	**4ad**, 48 h, 96%
R^1 = Ph, R^3 = CO_2Et	**4ae**, 48 h, 80%

[a]Unless noted, all reactions were carried out with nitrosobenzene **1a** (0.26 mmol, 1.3 equiv), diethyl malonate **2a** (0.26 mmol, 1.3 equiv), olefin **3** (0.2 mmol), NBS (0.26 mmol, 1.3 equiv), and DBU (0.28 mmol, 1.4 equiv) in 0.5 mL of DCE at 50 °C. [b]Isolated yields of **4**.

Scheme 3. Application of This Methodology[a,b]





[a]Unless noted, all reactions were carried out with nitrosobenzene **1a** (0.26 mmol, 1.3 equiv), diethyl malonate **2a** (0.26 mmol, 1.3 equiv), **3** (0.2 mmol), NBS (0.26 mmol, 1.3 equiv), and DBU (0.28 mmol, 1.4 equiv) in 0.5 mL of DCE at 50 °C. [b]Isolated yields of **4**.

olefins worked very well, affording the single diastereomeric products **4ab**–**4ae** in 80–96% yields. If a *cis*-alkene (dimethyl maleate) was used, the 4,5-*cis* isoxazolidine product **4ab** was provided. The 4,5-*trans* isoxazolidine products were observed (**4ac**–**4ae**) when *trans*-alkenes such as dimethyl fumarate, (*E*)-chalcone, and ethyl cinnamate were utilized, respectively.[11b11c] The stereochemistry was further confirmed by the analysis of NOESY (see the Supporting Information).

Bicyclic isoxazolidines, isoxazolidinyl purines, isoxazolidinyl imidazoles, isoxazolidinyl triazoles, isoxazolidinyl indoles, and isoxazolidinyl pyrimidines represent attractive and privileged structures, which have displayed significant antivirus or anticancer activities. To make this methodology more appealing, the three-component reactions of cyclic olefins, vinyl purines, vinyl imidazole, vinyl triazole, vinyl indole, and vinyl pyrimidine with nitrosobenzene **1a** and diethyl malonate **2a** were also examined, respectively (Scheme 3). To our delight, the corresponding single diastereomeric products **4af**–**4ao** could be smoothly obtained, revealing that the newly developed three-component method was broadly applicable. In the case of various cycloolefins, 80–93% yields were obtained (**4af**–**4ai**). Notably, vinyl purines bearing different functional groups were efficiently applied in this transformation, affording the corresponding products **4aj**–**4al** in 85–94% yields. It was found that vinyl imidazole could be reacted smoothly to furnish the product **4am** in 80% yield. Ethyl 3-(1*H*-benzo[d][1,2,3]triazol-1-yl)acrylate was also compatible with the conditions, delivering the product **4an** in 90% yield. When ethyl 3-(1*H*-indol-1-yl)acrylate was subjected to this transformation, a 71% yield was provided (**4ao**). The above-mentioned *trans*-olefins also gave the 4,5-*trans* isoxazolidine products **4aj**–**4ao**. Among them, the relative configuration of product **4ao** was confirmed by the analysis of NOESY (see the Supporting Information). The ethyl 3-(2,4-dioxo-3,4-dihydropyrimidin-1(2*H*)-yl)acrylates with various substituents were well tolerated, offering the corresponding products **4ap**–**4at** in good yields. Moreover, the vinyl pyrimidine derived from 4-aminopyrimidin-2(1*H*)-one also gave the desired product **4au** in 77% yield.

Subsequently, we investigated the scope of various nitrosoarenes **1** and malonic esters **2**, and the results are listed in Scheme 4. First, all examined nitrosoarenes could afford the corresponding products **4ba**–**4bi** in good to excellent yields. The electronic effect of substituents on the phenyl ring of the nitrosobenzene had some influence on the reaction yields. The nitrosobenzenes with electron-donating substituents on the phenyl ring exhibited higher yields than those with electron-withdrawing substituents (**4ba**–**4bc** vs **4be**–**4bh**), and the stronger electron-withdrawing group (NO_2) showed relatively lower reactivity and yield (**4bh** vs **4bg**). Disubstituted nitrosobenzenes were well tolerated, giving the products **4bd** and **4bi** in good yields. Next, the investigation of malonic ester

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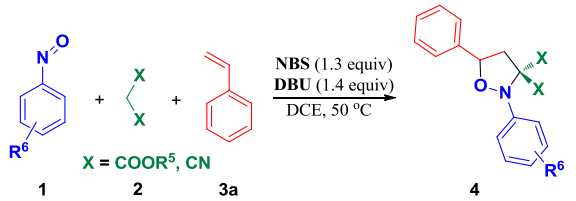
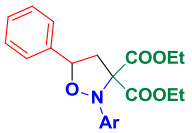
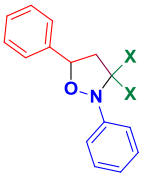
Scheme 4. Scope of Various Nitrosoarenes 1 and Substrates 2[a,b]





Ar = 2-MeC$_6$H$_4$ **4ba**, 30 h, 94%
Ar = 3-MeC$_6$H$_4$ **4bb**, 24 h, 95%
Ar = 4-MeC$_6$H$_4$ **4bc**, 24 h, 96%
Ar = 2,4-(Me)$_2$C$_6$H$_3$ **4bd**, 32 h, 81%
Ar = 2-ClC$_6$H$_4$ **4be**, 32 h, 86%
Ar = 3-ClC$_6$H$_4$ **4bf**, 24 h, 90%
Ar = 4-ClC$_6$H$_4$ **4bg**, 24 h, 91%
Ar = 4-O$_2$NC$_6$H$_4$ **4bh**, 48 h, 70%
Ar = 3,5-(Cl)$_2$C$_6$H$_3$ **4bi**, 30 h, 83%



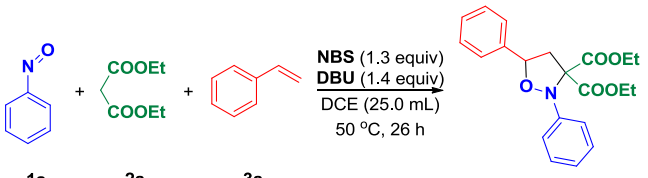
X = COOMe, **4bj**, 24 h, 98%
X = COO-*i*-Pr, **4bk**, 24 h, 96%
X = COO-*t*-Bu, **4bl**, 30 h, 87%
X = CN, **4bm**, 72 h, 80%

[a]Unless noted, all reactions were carried out with **1** (0.26 mmol, 1.3 equiv), **2** (0.26 mmol, 1.3 equiv), **3a** (0.2 mmol), NBS (0.26 mmol, 1.3 equiv), and DBU (0.28 mmol, 1.4 equiv) in 0.5 mL of DCE at 50 °C. [b]Isolated yields of **4**.

2 revealed that the steric hindrance of ester groups did not obviously affect this transformation, and all examined substrates provided excellent yields (**4bj**−**4bl**). When malononitrile was used as a substrate, the reaction produced the product **4bm** with a satisfactory result, too.

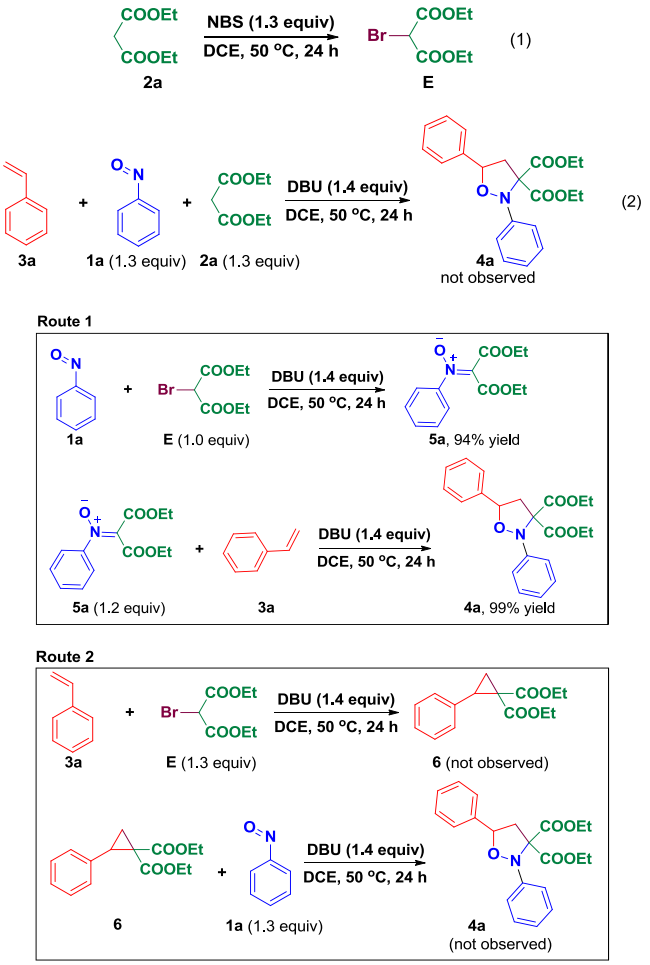
To demonstrate the practicability of this newly developed methodology, the gram-scale (10 mmol scale) reaction was also performed. Treatment of 1.40 g of nitrosobenzene **1a**, 2.00 mL of diethyl malonate **2a** and 1.16 mL of styrene **3a** gave 3.51 g of cycloadduct **4a** with 95% yield (see Scheme 5).

Scheme 5. Gram-Scale Reaction



To explore the function of NBS and mechanism details of this transformation, we first tracked the model reaction using TLC in the reaction process and detected small amount of diethyl bromomalonate that should be formed *via* the reaction of diethyl malonate **2a** with NBS. As imagined, the 86% yield of diethyl bromomalonate **E** was obtained when diethyl malonate **2a** was treated with NBS (Scheme 6, eq 1), which suggested the involvement of diethyl bromomalonate as an intermediate. Furthermore, no final product **4a** was detected when the model reaction was carried out in the absence of NBS (Scheme 6, eq 2), which demonstrated that the existence of NBS is crucial to trigger the reaction. Subsequently, other several control experiments were designed. As listed in Scheme 6, two possible reaction pathways were proposed for this

Scheme 6. Control Experiments



reaction and both began with the formation of diethyl bromomalonate **E**. The first one continued to proceed with subsequent reaction of diethyl bromomalonate **E** with nitrosobenzene **1a** to form intermediate **5a**, which then reacted with styrene **3a** to afford the final product **4a** *via* the [3+2] cycloaddition (Scheme 6, route 1). The second one was followed by the next reaction of diethyl bromomalonate **E** with styrene **3a** to give diethyl 2-phenylcyclopropane-1,1-dicarboxylate **6**, which then reacted with nitrosobenzene **1a** to produce the final product **4a** *via* the [3+2] cycloaddition (Scheme 6, route 2). It was noteworthy that the formation of nitrone intermediate **5a** was indeed observed and determined using ^{1}HNMR and HRMS (see the Supporting Information) when the reaction of nitrosobenzene **1a** with diethyl bromomalonate **E** was performed. Furthermore, nitrone **5a** was found to be able to smoothly react with styrene **3a** to produce the final product **4a** in 99% yield. In sharp contrast, styrene **3a** failed to react with diethyl bromomalonate **E** to provide the imagined cyclopropane intermediate **6** under the same conditions.[13] Moreover, no product **4a** was observed when intermediate **6** was treated with nitrosobenzene **1a**.[6a] These results strongly imply that this reaction should proceed through the proposed reaction pathway route 1.

To gain insights into the exact role of DBU, two other control experiments were next performed (Scheme 7). The reaction of nitrosobenzene **1a** with diethyl bromomalonate **E** failed to proceed to give the desired nitrone intermediate **5a** in

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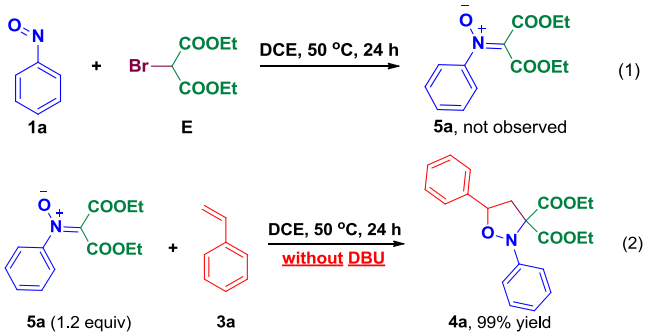
Scheme 7. Control Experiments



the absence of DBU (Scheme 7, eq 1). However, nitrone **5a** could smoothly react with styrene **3a** to produce the final product **4a** in 99% yield without the use of DBU (Scheme 7, eq 2). These two results demonstrated that the role of DBU is to capture the hydrogen proton of diethyl bromomalonate **E** to promote the formation of intermediate **5a**, and it probably did not play any role in the cycloaddition process.

On the basis of above-mentioned results and corresponding literature,[7,11] we proposed the following reaction mechanism (Scheme 8). Initially, NBS could smoothly convert diethyl malonate **2a** into diethyl bromomalonate **E**. Under the action of DBU, subsequently, **E** undergoes the deprotonation to form intermediate **F** that then attacks the nitrosoarene **1** to generate intermediate **G**, which could be transformed to nitrone intermediate **H** *via* the removal of bromine anion. At last, the target product **4** is provided through the [3+2] cycloaddition of olefin **3** with nitrone intermediate **H**.

CONCLUSIONS

In summary, we have established a general metal-free one-pot three-component method for highly diastereoselective construction of highly functionalized isoxazolidine derivatives *via* the cycloaddition of readily accessible malonic acid derivatives, nitrosoarenes, and alkenes as starting materials. In this reaction system, NBS acts as a bromine reagent to prepare bromomalonic acid derivatives from malonic acid derivatives, and DBU serves as a promoter to trigger and accelerate the formation of nitrone intermediates through the reaction of bromomalonic acid derivatives with nitrosoarenes. The operationally simple and practical protocol features good to excellent yields, a broad substrate scope, cheap system, and good functional group tolerance.

EXPERIMENTAL SECTION

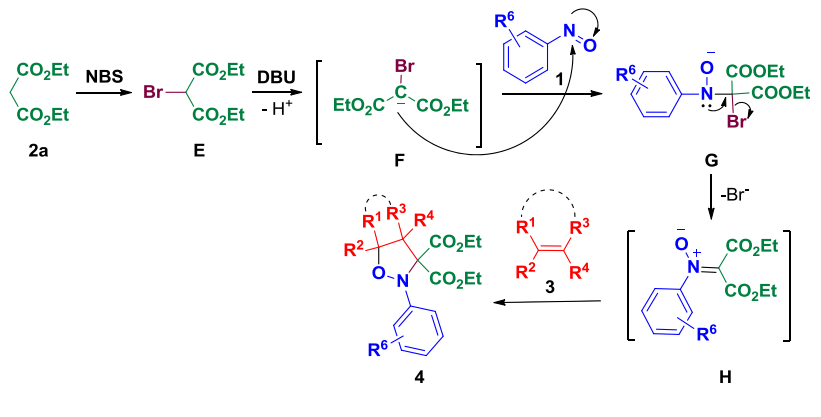
General Information. ^{1}H NMR data were acquired at 300 K on a Bruker Advance 600 or 400 MHz spectrometer. The chemical shifts are reported in ppm downfield to the $CDCl_3$ resonance (δ = 7.27). Spectra are reported as follows: chemical shift (δ ppm), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet), coupling constants (Hz), integration, and assignment. ^{13}C NMR data were acquired at 300 K on a Bruker Advance 150 or 100 MHz spectrometer using $CDCl_3$ as a solvent with complete proton decoupling. The chemical shifts are reported in ppm downfield to the central $CDCl_3$ resonance (δ = 77.0). Structural assignments were also made with additional information from H-H NOESY experiments. High-resolution mass spectra were performed on a micrO-TOF-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. Refinement of the mixed system through column chromatography was performed on silica gel (200−300mesh) with petroleum ether (solvent A)/ethyl acetate (solvent B) gradients as elution. In addition, all yields were referred to isolated yields (average of two runs) of compounds unless otherwise specified. The known compounds were partly characterized by melting points (for solid samples), ^{1}H NMR, and compared to authentic samples or the literature data.

General Procedure for Cycloadditon of Malonic Acid Derivatives, Nitrosoarenes, and Alkenes. To a tube equipped with a magnetic stir bar were added nitrosoarene **1** (0.26 mmol, 1.3 equiv), NBS (47.2 mg, 0.26 mmol, 1.3 equiv), DBU (42.7 μL, 0.28 mmol, 1.4 equiv), alkene **3** (0.2 mmol), malonic acid derivative **2** (0.26 mmol, 1.3 equiv), and DCE (0.5 mL) in turn. The reaction system was then heated to 50 °C (oil bath) and stirred until alkene **3** was completely consumed as determined by TLC. At last, the reaction mixture was purified by silica gel column chromatography to afford the desired pure cycloaddtion product **4**.

10 Mmol Scale Preparation of 4a. To a round-bottom flask equipped with a magnetic stir bar were added nitrosobenzene **1a** (1.433 g, 13 mmol, 1.3 equiv), NBS (2.361 g, 13 mmol, 1.3 equiv), DBU (2.14 mL, 14 mmol, 1.4 equiv), diethyl malonate **2a** (2.00 mL, 13 mmol, 1.3 equiv), styrene **3a** (1.16 mL, 10 mmol), and DCE (25 mL) in turn. The reaction system was then heated to 50 °C (oil bath) and stirred until styrene **3a** was completely consumed as determined by TLC. At last, the reaction mixture was concentrated in vacuum and purified by silica gel column chromatography to afford the desired pure cycloaddtion product **4a** (3.51 g, 95% yield).

Characterization Data for Intermediate 5a. *N-(1,3-Diethoxy-1,3-dioxopropan-2-ylidene)aniline Oxide* ***5a.*** Yellow oil; R_f = 0.3 (PE/EtOAc = 8:1, v/v). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.51−7.40 (m, 5H), 4.42 (q, 2H, J = 14.0, 6.8 Hz), 4.10 (q, 2H, J = 14.4, 7.2 Hz), 1.39 (t, 3H, J = 7.2 Hz), 1.12 (t, 3H, J = 6.8 Hz) ppm; ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ 160.3, 158.7, 147.1, 133.2, 130.9, 129.0,

Scheme 8. Proposed Reaction Mechanism



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123.0, 62.6, 62.3, 13.9, 13.6 ppm. HRMS (ESI) m/z $[M + H]^+$ Calcd for $C_{13}H_{16}NO_5$ 266.1023, found 266.1023.

Characterization Data for Cycloaddition Products 4. *Diethyl 2,5-Diphenylisoxazolidine-3,3-dicarboxylate (**4a**).*[6a] Yellow oil (99% yield, 73.1 mg); TLC, R_f = 0.3 (PE/EtOAc = 20:1, v/v); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.54 (d, 2H, J = 6.8 Hz), 7.42−7.39 (m, 2H), 7.38−7.37 (m, 2H), 7.36−7.32 (m, 1H), 7.25 (t, 2H, J = 8.8 Hz), 7.03 (t, 1H, J = 7.6 Hz), 5.32 (dd, 1H, J = 9.6, 6.4 Hz), 4.17 (q, 2H, J = 7.2 Hz), 4.06−3.98 (m, 1H), 3.87−3.97 (m, 1H), 3.22 (dd, 1H, J = 12.8, 6.0 Hz), 3.12 (dd, 1H, J = 12.8, 9.2 Hz), 1.19 (t, 3H, J = 7.2 Hz), 1.02 (t, 3H, J = 7.2 Hz) ppm.

*Diethyl 2-Phenyl-5-(o-tolyl)isoxazolidine-3,3-dicarboxylate (**4b**).* Yellow oil (93% yield, 71.3 mg); TLC, R_f = 0.3 (PE/EtOAc = 20:1, v/v); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.70 (dd, 1H, J = 7.6, 1.2 Hz), 7.38 (dd, 2H, J = 8.8, 1.2 Hz), 7.26 (d, 2H, J = 7.2 Hz), 7.24 (t, 1H, J = 1.6 Hz), 7.21 (dd, 1H, J = 7.6, 1.6 Hz), 7.16 (t, 1H, J = 7.2 Hz), 7.03 (t, 1H, J = 7.2 Hz), 5.54 (dd, 1H, J = 9.6, 6.0 Hz), 4.17 (qd, 2H, J = 7.2, 1.6 Hz), 4.06−3.98 (m, 1H), 3.89−3.97 (m, 1H), 3.23 (dd, 1H, J = 12.8, 6.0 Hz), 3.01 (dd, 1H, J = 12.8, 9.6 Hz), 2.39 (s, 3H), 1.96 (t, 3H, J = 7.2 Hz), 1.01 (t, 3H, J = 7.2 Hz) ppm; $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz) δ 168.6, 167.9, 147.3, 135.6, 135.5, 130.4, 128.3, 128.1, 126.4, 125.9, 123.8, 118.1, 78.8, 75.8, 62.7, 62.0, 46.8, 19.3, 13.9, 13.7 ppm. HRMS (ESI) m/z $[M + H]^+$ Calcd for $C_{22}H_{26}NO_5$ 384.1805, found 384.1800.

*Diethyl 2-Phenyl-5-(m-tolyl)isoxazolidine-3,3-dicarboxylate (**4c**).* Yellow oil (96% yield, 73.6 mg); TLC, R_f = 0.3 (PE/EtOAc = 20:1, v/v); ^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.38 (t, 3H, J = 9.0 Hz), 7.34 (d, 1H, J = 7.6 Hz), 7.29 (t, 1H, J = 7.6 Hz), 7.26 (t, 2H, J = 9.0 Hz), 7.17 (d, 1H, J = 7.6 Hz), 7.04 (t, 1H, J = 7.2 Hz), 5.31 (dd, 1H, J = 9.6, 6.0 Hz), 4.18 (q, 2H, J = 6.6 Hz), 4.07−4.02 (m, 1H), 3.98−3.93 (m, 1H), 3.21 (dd, 1H, J = 12.6, 6.0 Hz), 3.14 (dd, 1H, J = 13.2, 10.2 Hz), 2.39 (s, 3H), 1.20 (t, 3H, J = 7.2 Hz), 1.04 (t, 3H, J = 7.2 Hz) ppm; $^{13}C\{^1H\}$ NMR ($CDCl_3$, 150 MHz) δ 168.5, 167.9, 147.2, 138.2, 137.0, 129.3, 128.4, 128.1, 127.6, 124.0, 123.6, 117.9, 78.9, 78.7, 62.1, 62.0, 47.9, 21.4, 13.7, 13.6 ppm; HRMS (ESI) m/z $[M + H]^+$ Calcd for $C_{22}H_{26}NO_5$ 384.1805, found 384.1800.

*Diethyl 2-Phenyl-5-(p-tolyl)isoxazolidine-3,3-dicarboxylate (**4d**).* Yellow oil (98% yield, 75.1 mg); TLC, R_f = 0.3 (PE/EtOAc = 20:1, v/v); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.43 (d, 2H, J = 7.2 Hz), 7.36 (d, 2H, J = 8.4 Hz), 7.24 (t, 2H, J = 8.0 Hz), 7.19 (d, 2H, J = 7.6 Hz), 7.02 (t, 1H, J = 7.2 Hz), 5.29 (dd, 1H, J = 9.6, 6.4 Hz), 4.17 (q, 2H, J = 7.2 Hz), 4.06−3.98 (m, 1H), 3.96−3.90 (m, 1H), 3.23−3.12 (m, 2H), 2.36 (s, 3H), 1.19 (t, 3H, J = 7.2 Hz), 1.01 (t, 3H, J = 7.2 Hz) ppm; $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz) δ 168.6, 167.9, 147.3, 138.5, 134.1, 129.3, 128.2, 127.1, 123.7, 118.1, 78.9, 78.8, 62.2, 62.0, 47.9, 21.2, 13.8, 13.6 ppm; HRMS (ESI) m/z $[M + H]^+$ Calcd for $C_{22}H_{26}NO_5$ 384.1805, found 384.1800.

*Diethyl 5-(2,6-Dimethylphenyl)-2-phenylisoxazolidine-3,3-dicarboxylate (**4e**).* Yellow oil (90% yield, 71.5 mg); TLC, R_f = 0.3 (PE/EtOAc = 20:1, v/v); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.51 (s, 1H), 7.38 (d, 2H, J = 8.8 Hz), 7.26 (t, 2H, J = 8.4 Hz), 7.04 (d, 2H, J = 3.6 Hz), 7.01 (d, 1H, J = 7.2 Hz), 5.53 (dd, 1H, J = 10.0, 6.0 Hz), 4.22−4.14 (m, 2H), 4.08−4.02 (m, 1H), 3.98−3.92 (m, 1H), 3.21 (dd, 1H, J = 12.4, 5.6 Hz), 3.00 (dd, 1H, J = 12.4, 10.0 Hz), 2.34 (s, 6H), 1.83 (t, 3H, J = 7.2 Hz), 1.05 (t, 3H, J = 7.2 Hz) ppm; $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz) δ 168.6, 168.0, 147.5, 135.9, 135.2, 135.2, 132.4, 130.4, 128.9, 128.3, 126.3, 123.7, 117.9, 78.9, 76.0, 62.2, 62.0, 46.9, 21.1, 18.8, 13.8, 13.7 ppm. HRMS (ESI) m/z $[M + H]^+$ Calcd for $C_{23}H_{28}NO_5$ 398.1962, found 398.1954.

*Diethyl 5-(2-Fluorophenyl)-2-phenylisoxazolidine-3,3-dicarboxylate (**4f**).* Yellow oil (91% yield, 70.5 mg); TLC, R_f = 0.3 (PE/EtOAc = 20:1, v/v); ^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.71 (td, 1H, J = 7.2, 1.2 Hz), 7.38 (d, 2H, J = 7.6 Hz), 7.30−7.29 (m, 1H), 7.27 (t, 2H, J = 7.6 Hz), 7.19 (t, 1H, J = 7.6 Hz), 7.07−7.04 (m, 2H), 5.65 (dd, 1H, J = 8.4, 6.6 Hz), 4.12 (q, 2H, J = 7.2 Hz), 4.08−4.01 (m, 1H), 3.98−3.93 (m, 1H), 3.33 (dd, 1H, J = 13.2, 6.6 Hz), 3.07 (dd, 1H, J = 13.2, 9.0 Hz), 1.34 (t, 3H, J = 7.2 Hz), 1.03 (t, 3H, J = 7.2 Hz) ppm; $^{13}C\{^1H\}$ NMR ($CDCl_3$, 150 MHz) δ 168.0, 167.8, 147.0, 129.6, 129.6, 128.2, 127.5, 127.5, 124.3, 124.3, 123.9, 118.1, 115.2, 115.1, 78.4, 72.3, 72.3, 62.1, 62.0, 46.7, 13.7, 13.5 ppm. HRMS (ESI) m/z $[M + H]^+$ Calcd for $C_{21}H_{23}FNO_5$ 388.1555, found 388.1550.

*Diethyl 5-(3-Fluorophenyl)-2-phenylisoxazolidine-3,3-dicarboxylate (**4g**).* Yellow solid (94% yield, 72.8 mg); mp 54−55 °C; TLC, R_f = 0.3 (PE/EtOAc = 20:1, v/v); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.52 (dd, 2H, J = 8.8, 5.2 Hz), 7.37 (d, 2H, J = 7.6 Hz), 7.25 (t, 2H, J = 8.4 Hz), 7.08 (t, 2H, J = 8.8 Hz), 7.02 (d, 1H, J = 7.2 Hz), 5.30 (dd, 1H, J = 9.6, 6.4 Hz), 4.17 (q, 2H, J = 7.2 Hz), 4.06−3.98 (m, 1H), 3.96−3.88 (m, 1H), 3.20 (dd, 1H, J = 12.8, 6.4 Hz), 3.09 (dd, 1H, J = 12.8, 9.2 Hz), 1.19 (t, 3H, J = 7.2 Hz), 1.01 (t, 3H, J = 7.2 Hz) ppm; $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz) δ 168.4, 167.8, 164.1, 161.6, 147.1, 133.2, 133.2, 129.0, 128.9, 128.2, 124.0, 118.3, 115.6, 115.4, 78.2, 78.2, 62.2, 62.1, 47.8, 13.8, 13.6 ppm. HRMS (ESI) m/z $[M + H]^+$ Calcd for $C_{21}H_{23}FNO_5$ 388.1555, found 388.1550.

*Diethyl 5-(4-Fluorophenyl)-2-phenylisoxazolidine-3,3-dicarboxylate (**4h**).* White solid (97% yield, 75.1 mg); mp 55−56 °C; TLC, R_f = 0.3 (PE/EtOAc = 20:1, v/v); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.29 (dd, 2H, J = 8.8, 2.0 Hz), 7.25 (dd, 1H, J = 7.6, 2.0 Hz), 7.23−7.15 (m, 4H), 6.96 (t, 2H, J = 7.2 Hz), 5.23 (dd, 1H, J = 9.2, 6.8 Hz), 4.06 (q, 2H, J = 6.8 Hz), 3.98−3.90 (m, 1H), 3.89−3.81 (m, 1H), 3.15 (dd, 1H, J = 12.8, 6.4 Hz), 2.99 (dd, 1H, J = 12.8, 9.2 Hz), 1.08 (t, 3H, J = 7.2 Hz), 0.93 (t, 3H, J = 7.2 Hz) ppm; $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz) δ 167.7, 161.7, 147.0, 130.2, 130.1, 128.3, 124.0, 122.5, 122.5, 118.3, 78.6, 78.0, 62.2, 62.1, 47.7, 13.8, 13.6 ppm. HRMS (ESI) m/z $[M + H]^+$ Calcd for $C_{21}H_{23}FNO_5$ 388.1555, found 388.1550.

*Diethyl 5-(2-Chlorophenyl)-2-phenylisoxazolidine-3,3-dicarboxylate (**4i**).* Yellow oil (92% yield, 74.2 mg); TLC, R_f = 0.3 (PE/EtOAc = 20:1, v/v); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.79 (dd, 1H, J = 8.4, 1.6 Hz), 7.40 (dd, 2H, J = 8.4, 0.8 Hz), 7.35 (dd, 1H, J = 8.0, 1.2 Hz), 7.33−7.22 (m, 4H), 7.06 (d, 1H, J = 7.2 Hz), 5.74 (t, 1H, J = 7.6 Hz), 4.09 (q, 2H, J = 7.2 Hz), 4.07−4.02 (m, 1H), 4.01−3.94 (m, 1H), 3.46 (dd, 1H, J = 12.8, 6.8 Hz), 2.91 (dd, 1H, J = 12.8, 8.0 Hz), 1.12 (t, 3H, J = 7.2 Hz), 1.04 (t, 3H, J = 7.2 Hz) ppm; $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz) δ 167.9, 167.8, 147.1, 136.7, 131.9, 129.3, 129.1, 128.3, 127.2, 127.1, 124.0, 118.3, 78.5, 75.2, 62.1, 62.0, 46.7, 13.7, 13.7 ppm. HRMS (ESI) m/z $[M + H]^+$ Calcd for $C_{21}H_{23}ClNO_5$ 404.1259, found 404.1266.

*Diethyl 5-(4-Chlorophenyl)-2-phenylisoxazolidine-3,3-dicarboxylate (**4j**).* Yellow solid (98% yield, 79.0 mg); mp 70−74 °C; TLC, R_f = 0.3 (PE/EtOAc = 20:1, v/v); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.39 (d, 2H, J = 8.4 Hz), 7.28 (d, 2H, J = 6.4 Hz), 7.26 (d, 2H, J = 6.4 Hz), 7.15 (t, 2H, J = 8.4 Hz), 6.94 (t, 1H, J = 7.2 Hz), 5.21 (dd, 1H, J = 8.8, 6.4 Hz), 4.07 (q, 2H, J = 7.2 Hz), 3.96−3.90 (m, 1H), 3.88−3.80 (m, 1H), 3.13 (dd, 1H, J = 12.8, 6.8 Hz), 2.99 (dd, 1H, J = 12.8, 9.2 Hz), 1.08 (t, 3H, J = 7.2 Hz), 0.92 (t, 3H, J = 7.2 Hz) ppm; $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz) δ 168.3, 167.8, 147.0, 136.1, 134.3, 128.8, 128.4, 124.2, 118.3, 78.6, 78.0, 62.2, 62.1, 47.8, 13.8, 13.6 ppm. HRMS (ESI) m/z $[M + H]^+$ Calcd for $C_{21}H_{23}ClNO_5$ 404.1259, found 404.1266.

*Diethyl 2-Phenyl-5-(pyridin-2-yl)isoxazolidine-3,3-dicarboxylate (**4k**).* Yellow oil (89% yield, 65.9 mg); TLC, R_f = 0.3 (PE/EtOAc = 20:1, v/v); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.55 (d, 1H, J = 4.4 Hz), 7.73−7.67 (m, 2H), 7.39 (d, 2H, J = 7.6 Hz), 7.27 (t, 2H, J = 8.8 Hz), 7.23−7.20 (m, 1H), 7.05 (t, 1H, J = 7.2 Hz), 5.51 (t, 1H, J = 7.2 Hz), 4.13−3.99 (m, 4H), 3.46 (dd, 1H, J = 12.8, 7.2 Hz), 3.28 (dd, 1H, J = 13.2, 7.2 Hz), 1.06 (td, 6H, J = 7.2, 1.6 Hz) ppm; $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz) δ 168.0, 167.8, 158.5, 148.9, 147.0, 136.8, 128.2, 123.9, 122.9, 120.7, 118.2, 78.7, 78.2, 62.1, 62.0, 46.0, 13.7, 13.6 ppm. HRMS (ESI) m/z $[M + H]^+$ Calcd for $C_{20}H_{23}N_2O_5$ 371.1601, found 371.1593.

*Diethyl 2-Phenyl-5-(pyridin-4-yl)isoxazolidine-3,3-dicarboxylate (**4l**).* Yellow oil (92% yield, 68.1 mg); TLC, R_f = 0.3 (PE/EtOAc = 20:1, v/v); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.54 (d, 2H, J = 5.6 Hz), 7.35 (d, 2H, J = 6.0 Hz), 7.30 (t, 2H, J = 8.0 Hz), 7.20 (t, 2H, J = 8.4 Hz), 7.00 (d, 1H, J = 7.2 Hz), 5.27 (t, 1H, J = 7.6 Hz), 4.12−4.02 (m, 2H), 4.00−3.94 (m, 1H), 3.92−3.83 (m, 1H), 3.24 (dd, 1H, J = 12.8, 6.8 Hz), 2.95 (dd, 1H, J = 12.8, 8.4 Hz), 1.05 (t, 3H, J = 7.2 Hz), 0.95 (t, 3H, J = 7.2 Hz) ppm; $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz) δ 167.8, 167.5, 150.1, 147.3, 146.7, 128.3, 124.3, 121.2, 118.5, 78.3, 76.8, 62.2,

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62.1, 47.2, 13.7, 13.6 ppm. HRMS (ESI) m/z $[M + H]^+$ Calcd for $C_{20}H_{23}N_2O_5$ 371.1601, found 371.1593.

*Diethyl 5-(Naphthalen-1-yl)-2-phenylisoxazolidine-3,3-dicarboxylate (**4m**).* Yellow oil (84% yield, 70.4 mg); TLC, R_f = 0.3 (PE/EtOAc = 20:1, v/v); ^{1}H NMR ($CDCl_3$, 600 MHz) δ 8.12 (d, 1H, J = 8.4 Hz), 7.90 (t, 2H, J = 7.2 Hz), 7.85 (d, 1H, J = 7.6 Hz), 7.58−7.51 (m, 3H), 7.46 (dd, 2H, J = 8.4, 0.6 Hz), 7.31 (t, 2H, J = 7.2 Hz), 7.08 (t, 1H, J = 7.6 Hz), 6.11 (dd, 1H, J = 9.0, 6.0 Hz), 4.22 (q, 2H, J = 7.2 Hz), 4.08−4.02 (m, 1H), 4.02−3.96 (m, 1H), 3.52 (dd, 1H, J = 13.2, 6.6 Hz), 3.20 (dd, 1H, J = 12.6, 9.0 Hz), 1.22 (t, 3H, J = 7.2 Hz), 1.05 (t, 3H, J = 7.2 Hz) ppm; $^{13}C\{^1H\}$ NMR ($CDCl_3$, 150 MHz) δ 168.4, 167.9, 147.3, 133.6, 133.3, 130.6, 128.6, 128.3, 126.3, 125.6, 125.5, 123.4, 123.1, 118.0, 78.7, 76.0, 62.2, 62.0, 47.0, 13.8, 13.6 ppm. HRMS (ESI) m/z $[M + H]^+$ Calcd for $C_{25}H_{26}NO_5$ 420.1805, found 420.1803.

*Diethyl 5-(Naphthalen-2-yl)-2-phenylisoxazolidine-3,3-dicarboxylate (**4n**).* Yellow oil (92% yield, 77.1 mg); TLC, R_f = 0.3 (PE/EtOAc = 20:1, v/v); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.85 (s, 1H), 7.77 (d, 1H, J = 8.4 Hz), 7.77−7.72 (m, 2H), 7.59 (dd, 1H, J = 8.4, 1.6 Hz), 7.39−7.37 (m, 2H), 7.32 (d, 2H, J = 7.6 Hz), 7.17 (t, 2H, J = 8.8 Hz), 6.95 (t, 1H, J = 7.2 Hz), 5.41 (dd, 1H, J = 9.6, 6.4 Hz), 4.08 (q, 2H, J = 7.2 Hz), 3.98−3.90 (m, 1H), 3.89−3.81 (m, 1H), 3.25−3.12 (m, 2H), 1.09 (t, 3H, J = 7.2 Hz), 0.92 (t, 3H, J = 7.2 Hz) ppm; $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz) δ 168.5, 168.0, 147.3, 134.8, 134.4, 133.4, 133.2, 128.6, 128.3, 128.1, 127.7, 126.4, 126.3, 124.4, 123.9, 118.2, 79.1, 78.9, 62.3, 62.1, 48.0, 13.9, 13.7 ppm. HRMS (ESI) m/z $[M + H]^+$ Calcd for $C_{25}H_{26}NO_5$ 420.1805, found 420.1803.

*Diethyl 5-Hexadecyl-2-phenylisoxazolidine-3,3-dicarboxylate (**4o**).* White solid (96% yield, 99.3 mg); mp 79−80 °C; TLC, R_f = 0.3 (PE/EtOAc = 20:1, v/v); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.19 (d, 2H, J = 8.4 Hz), 7.12 (t, 2H, J = 8.4 Hz), 6.89 (t, 1H, J = 7.2 Hz), 4.02 (q, 2H, J = 6.8 Hz), 4.00−3.92 (m, 1H), 3.91−3.83 (m, 1H), 2.85 (dd, 1H, J = 12.4, 5.6 Hz), 2.60 (dd, 1H, J = 12.4, 9.2 Hz), 1.77−1.69 (m, 1H), 1.61−1.53 (m, 1H), 1.48−1.39 (m, 1H), 1.25−1.18 (m, 28H), 1.07 (t, 3H, J = 7.2 Hz), 0.96 (t, 3H, J = 7.2 Hz), 0.80 (t, 3H, J = 7.2 Hz) ppm; $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz) δ 168.6, 168.2, 147.5, 128.1, 123.3, 117.7, 78.4, 77.3, 62.0, 61.8, 45.9, 32.5, 31.9, 29.7, 29.5, 29.5, 29.3, 26.2, 22.6, 14.1, 13.7, 13.6 ppm. HRMS (ESI) m/z $[M + H]^+$ Calcd for $C_{31}H_{52}NO_5$ 518.3840, found 518.3836.

*Diethyl 5-Butyl-2-phenylisoxazolidine-3,3-6-dicarboxylate (**4p**).* Yellow oil (97% yield, 67.7 mg); TLC, R_f = 0.3 (PE/EtOAc = 20:1, v/v); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.19 (d, 2H, J = 8.8 Hz), 7.15 (t, 2H, J = 8.8 Hz), 6.92 (t, 1H, J = 7.2 Hz), 4.03 (q, 2H, J = 7.2 Hz), 4.02−3.94 (m, 1H), 3.92−3.84 (m, 1H), 2.86 (dd, 1H, J = 12.4, 5.6 Hz), 2.60 (dd, 1H, J = 12.8, 9.2 Hz), 1.79−1.70 (m, 1H), 1.63−1.55 (m, 1H), 1.42−1.39 (m, 1H), 1.38−1.29 (m, 4H), 1.08 (t, 3H, J = 7.2 Hz), 0.97 (t, 3H, J = 7.2 Hz), 0.86 (t, 3H, J = 7.2 Hz) ppm; $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz) δ 168.7, 168.2, 147.5, 128.1, 123.3, 117.7, 78.4, 77.4, 62.0, 61.9, 45.9, 32.2, 28.3, 22.6, 13.9, 13.7, 13.6 ppm. HRMS (ESI) m/z $[M + H]^+$ Calcd for $C_{19}H_{28}NO_5$ 350.1962, found 350.1967.

*Diethyl 5-(Hydroxymethyl)-2-phenylisoxazolidine-3,3-dicarboxylate (**4q**).* Yellow oil (90% yield, 58.2 mg); TLC, R_f = 0.3 (PE/EtOAc = 5:1, v/v); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.33 (d, 2H, J = 8.0 Hz), 7.25 (t, 2H, J = 8.4 Hz), 7.06 (t, 1H, J = 7.6 Hz), 4.56−4.51 (m, 1H), 4.16−4.06 (m, 2H), 4.06−3.93 (m, 2H), 3.92−3.87 (m, 1H), 3.79−3.73 (m, 1H), 3.03 (dd, 1H, J = 12.8, 7.2 Hz), 2.87 (dd, 1H, J = 12.8, 6.4 Hz), 2.63 (t, 1H, J = 6.0 Hz), 1.12 (t, 3H, J = 7.2 Hz), 1.02 (t, 3H, J = 7.2 Hz) ppm; $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz) δ 168.2, 167.5, 146.7, 128.2, 124.4, 119.0, 78.0, 77.1, 63.1, 62.1, 62.0, 40.8, 13.7, 13.6 ppm. HRMS (ESI) m/z $[M + H]^+$ Calcd for $C_{16}H_{22}NO_6$ 324.1442, found 324.1450.

*Diethyl 5-(2-Hydroxyethyl)-2-phenylisoxazolidine-3,3-dicarboxylate (**4r**).* Yellow oil (95% yield, 64.1 mg); TLC, R_f = 0.3 (PE/EtOAc = 5:1, v/v); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.28 (d, 2H, J = 7.6 Hz), 7.23 (t, 2H, J = 8.8 Hz), 7.02 (t, 1H, J = 7.2 Hz), 4.55−4.48 (m, 1H), 4.14−4.09 (m, 2H), 4.08−4.01 (m, 1H), 4.00−3.92 (m, 1H), 3.82 (s, 2H), 3.00 (dd, 1H, J = 12.8, 6.4 Hz), 2.77 (dd, 1H, J = 12.4, 8.8 Hz), 2.34 (s, 1H), 1.92−2.08 (m, 2H), 1.13 (t, 3H, J = 7.2 Hz), 1.04 (t, 3H, J = 7.2 Hz) ppm; $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz) δ 168.4, 168.1, 147.1, 128.2, 123.8, 118.1, 78.2, 75.2, 62.1, 62.0, 59.8, 45.5, 35.2, 13.7, 13.6 ppm. HRMS (ESI) m/z $[M + H]^+$ Calcd for $C_{17}H_{24}NO_6$ 338.1598, found 338.1594.

*Diethyl 5-(3-Hydroxypropyl)-2-phenylisoxazolidine-3,3-dicarboxylate (**4s**).* Yellow oil (92% yield, 64.6 mg); TLC, R_f = 0.3 (PE/EtOAc = 5:1, v/v); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.26 (t, 3H, J = 8.0 Hz), 7.21 (d, 1H, J = 8.0 Hz), 7.01 (t, 1H, J = 6.8 Hz), 4.39−4.33 (m, 1H), 4.09 (q, 2H, J = 7.2 Hz), 4.07−4.01 (m, 1H), 4.00−3.92 (m, 1H), 3.69 (s, 2H), 2.95 (dd, 1H, J = 12.4, 5.6 Hz), 2.69 (dd, 1H, J = 12.4, 5.2 Hz), 2.02 (s, 1H), 1.90−1.68 (m, 4H), 1.14 (t, 3H, J = 7.2 Hz), 1.04 (t, 3H, J = 7.2 Hz) ppm; $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz) δ 168.5, 168.1, 147.3, 123.2, 117.8, 78.3, 62.3, 62.1, 62.0, 45.8, 29.3, 29.0, 13.7, 13.6 ppm. HRMS (ESI) m/z $[M + H]^+$ Calcd for $C_{18}H_{26}NO_6$ 352.1755, found 352.1749.

*Diethyl 5-(Bromomethyl)-2-phenylisoxazolidine-3,3-dicarboxylate (**4t**).* Yellow oil (83% yield, 64.0 mg); TLC, R_f = 0.3 (PE/EtOAc = 20:1, v/v); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.30 (d, 2H, J = 8.8 Hz), 7.24 (t, 2H, J = 8.4 Hz), 7.05 (t, 1H, J = 7.2 Hz), 4.65−4.55 (m, 1H), 4.17−4.09 (m, 2H), 4.08−4.03 (m, 1H), 4.01−3.94 (m, 1H), 3.70−3.62 (m, 1H), 3.51 (dd, 1H, J = 10.0, 7.2 Hz), 3.21−3.14 (m, 1H), 2.88−2.83 (m, 1H), 1.12 (td, 3H, J = 7.2, 1.2 Hz), 1.03 (td, 3H, J = 7.2, 2.0 Hz) ppm; $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz) δ 168.0, 167.8, 158.5, 148.9, 147.0, 136.8, 128.2, 123.9, 122.9, 120.7, 118.2, 78.7, 75.8, 62.1, 62.0, 44.3, 31.9, 13.7, 13.6 ppm. HRMS (ESI) m/z $[M + H]^+$ Calcd for $C_{16}H_{21}BrNO_5$ 386.0598, found 386.0588.

*Diethyl 5-((Methylthio)methyl)-2-phenylisoxazolidine-3,3-dicarboxylate (**4u**).* Yellow oil (91% yield, 64.3 mg); TLC, R_f = 0.3 (PE/EtOAc = 20:1, v/v); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.28 (d, 2H, J = 8.8 Hz), 7.23 (t, 2H, J = 8.0 Hz), 7.02 (t, 1H, J = 6.8 Hz), 4.59−4.52 (m, 1H), 4.13−3.97 (m, 4H), 3.07 (dd, 1H, J = 12.8, 6.4 Hz), 2.83−2.94 (m, 2H), 2.75 (dd, 1H, J = 14.0, 6.4 Hz), 2.22 (s, 3H), 1.06 (q, 6H, J = 6.4 Hz) ppm; $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz) δ 168.0, 168.0, 147.0, 128.2, 123.8, 118.2, 78.1, 76.9, 62.9, 62.0, 45.0, 36.2, 16.5, 13.7 ppm. HRMS (ESI) m/z $[M + H]^+$ Calcd for $C_{17}H_{24}NO_5S$ 354.1370, found 354.1375.

*3,3-Diethyl 5-Methyl-2-phenylisoxazolidine-3,3,5-tricarboxylate (**4v**).* Yellow oil (96% yield, 67.4 mg); TLC, R_f = 0.3 (PE/EtOAc = 20:1, v/v); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.29 (d, 2H, J = 7.6 Hz), 7.17 (t, 2H, J = 8.4 Hz), 6.99 (t, 1H, J = 7.2 Hz), 4.79 (dd, 1H, J = 8.4, 5.6 Hz), 4.15−4.07 (m, 2H), 3.97−3.87 (m, 1H), 3.84−3.76 (m, 1H), 3.72 (s, 3H), 3.28−3.17 (m, 2H), 1.11 (t, 3H, J = 7.2 Hz), 0.88 (t, 3H, J = 7.2 Hz) ppm; $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz) δ 169.4, 166.5, 166.0, 145.3, 127.1, 123.6, 118.2, 75.8, 73.2, 61.1, 61.0, 51.6, 41.2, 12.8, 12.5 ppm. HRMS (ESI) m/z $[M + H]^+$ Calcd for $C_{17}H_{22}NO_7$ 352.1391, found 352.1395.

*3-Ethyl 4,5-Dimethyl-2-phenylisoxazolidine-3,4,5-tricarboxylate (**4w**).* Yellow oil (93% yield, 82.8 mg); TLC, R_f = 0.3 (PE/EtOAc = 20:1, v/v); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.40 (d, 4H, J = 7.6 Hz), 7.25 (d, 2H, J = 8.0 Hz), 7.22 (t, 4H, J = 7.6 Hz), 7.16 (d, 2H, J = 8.0 Hz), 7.12 (d, 2H, J = 6.8 Hz), 6.90 (t, 1H, J = 7.2 Hz), 3.87−3.77 (m, 4H), 3.71 (s, 2H), 0.86 (t, 6H, J = 7.2 Hz) ppm; $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz) δ 168.3, 147.1, 142.0, 128.3, 127.6, 126.4, 122.8, 116.9, 85.9, 78.9, 62.1, 51.6, 13.7 ppm. HRMS (ESI) m/z $[M + H]^+$ Calcd for $C_{27}H_{28}NO_5$ 446.1962, found 446.1960.

*3,3-Diethyl 5-Methyl-5-methyl-2-phenylisoxazolidine-3,3,5-tricarboxylate (**4x**).* Yellow oil (94% yield, 68.6 mg); TLC, R_f = 0.3 (PE/EtOAc = 20:1, v/v); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.35 (d, 2H, J = 8.0 Hz), 7.23 (t, 2H, J = 7.6 Hz), 7.05 (t, 1H, J = 7.2 Hz), 4.24 (q, 2H, J = 7.2 Hz), 3.94−3.82 (m, 1H), 3.76 (s, 3H), 3.75−3.68 (m, 1H), 3.50 (d, 1H, J = 13.2 Hz), 3.00 (d, 1H, J = 13.2 Hz), 1.68 (s, 3H), 1.27 (t, 3H, J = 7.2 Hz), 0.86 (t, 3H, J = 7.2 Hz) ppm; $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz) δ 173.6, 168.2, 167.0, 146.1, 128.0, 124.4, 119.2, 80.9, 78.0, 61.9, 61.8, 52.8, 47.9, 21.3, 13.9, 13.0 ppm. HRMS (ESI) m/z $[M + H]^+$ Calcd for $C_{18}H_{24}NO_7$ 366.1547, found 366.1557.

*Diethyl 5-Methyl-2,5-diphenylisoxazolidine-3,3-dicarboxylate (**4y**).* Yellow oil (96% yield, 73.6 mg); TLC, R_f = 0.3 (PE/EtOAc = 20:1, v/v); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.46 (d, 2H, J = 8.0 Hz),

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7.30 (q, 4H, J = 8.0 Hz), 7.25 (t, 3H, J = 8.4 Hz), 6.99 (t, 1H, J = 7.2 Hz), 4.08−3.98 (m, 2H), 3.96−3.83 (m, 2H), 3.44 (d, 1H, J = 12.8 Hz), 3.14 (d, 1H, J = 12.4 Hz), 1.73 (s, 3H), 1.03 (t, 3H, J = 7.2 Hz), 0.95 (t, 3H, J = 7.2 Hz) ppm; $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz) δ 168.3, 168.2, 147.0, 144.1, 128.2, 128.1, 127.1, 125.0, 123.0, 117.4, 81.9, 78.7, 62.1, 61.8, 52.3, 27.1, 13.7, 13.6 ppm. HRMS (ESI) m/z $[M + H]^+$ Calcd for $C_{22}H_{26}NO_5$ 384.1805, found 384.1807.

*Diethyl 5-Formyl-5-methyl-2-phenylisoxazolidine-3,3-dicarboxylate (**4z**).* Colorless oil (91% yield, 61.0 mg); TLC, R_f = 0.3 (PE/EtOAc = 20:1, v/v); ^1H NMR ($CDCl_3$, 400 MHz) δ 9.70 (s, 1H), 7.40 (d, 2H, J = 8.0 Hz), 7.29 (t, 2H, J = 6.4 Hz), 7.13 (t, 1H, J = 7.2 Hz), 4.26 (qd, 2H, J = 7.2, 2.8 Hz), 3.94−3.85 (m, 1H), 3.75−3.67 (m, 1H), 3.17 (d, 1H, J = 13.2 Hz), 3.02 (d, 1H, J = 12.8 Hz), 1.51 (s, 3H), 1.29 (t, 3H, J = 7.2 Hz), 0.84 (t, 3H, J = 7.2 Hz) ppm; $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz) δ 203.3, 168.0, 166.6, 145.8, 128.2, 125.0, 119.6, 83.9, 77.8, 62.1, 61.9, 45.8, 17.4, 13.9, 13.4 ppm. HRMS (ESI) m/z $[M + H]^+$ Calcd for $C_{17}H_{22}NO_6$ 336.1442, found 336.1447.

*Triethyl 2,5-Diphenylisoxazolidine-3,3,5-tricarboxylate (**4aa**).* Yellow oil (90% yield, 79.4 mg); TLC, R_f = 0.3 (PE/EtOAc = 20:1, v/v); ^1H NMR ($CDCl_3$, 600 MHz) δ 7.54 (d, 2H, J = 6.6 Hz), 7.45 (dd, 2H, J = 8.4, 1.2 Hz), 7.39 (t, 2H, J = 13.8 Hz), 7.35 (d, 1H, J = 7.2 Hz), 7.27 (t, 2H, J = 8.4 Hz), 7.08 (t, 1H, J = 7.2 Hz), 4.28 (q, 2H, J = 7.2 Hz), 4.27−4.23 (m, 1H), 4.19−4.14 (m, 1H), 3.96 (d, 1H, J = 7.2 Hz), 3.88−3.82 (m, 1H), 3.73−3.67 (m, 1H), 3.32 (d, 1H, J = 12.6 Hz), 1.29 (t, 3H, J = 7.2 Hz), 1.20 (t, 3H, J = 7.2 Hz), 0.84 (t, 3H, J = 7.2 Hz) ppm; $^{13}C\{^1H\}$ NMR ($CDCl_3$, 150 MHz) δ 171.6, 168.1, 166.9, 146.1, 136.7, 128.4, 128.0, 125.3, 124.4, 119.4, 85.0, 77.9, 62.0, 61.9, 48.7, 13.9, 13.8, 13.3 ppm. HRMS (ESI) m/z $[M + H]^+$ Calcd for $C_{24}H_{28}NO_7$ 442.1860, found 442.1864.

*3,3-Diethyl 4,5-Dimethyl-2-phenylisoxazolidine-3,3,4,5-tetracarboxylate (**4ab**).* Yellow oil (90% yield, 73.6 mg), TLC, R_f = 0.3 (PE/EtOAc = 5:1, v/v); ^1H NMR ($CDCl_3$, 400 MHz) δ 7.37 (d, 2H, J = 8.4 Hz), 7.18 (t, 2H, J = 8.0 Hz), 7.01 (t, 1H, J = 7.2 Hz), 5.16 (d, 1H, J = 7.6 Hz), 4.47 (d, 1H, J = 7.6 Hz), 4.10 (q, 2H, J = 7.2 Hz), 3.95−3.87 (m, 1H), 3.78−3.73 (m, 1H), 3.71 (s, 3H), 3.65 (s, 3H), 1.14 (t, 3H, J = 7.2 Hz), 0.86 (t, 3H, J = 7.2 Hz) ppm; $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz) δ 168.1, 168.0, 166.0, 165.7, 146.4, 128.2, 125.0, 119.5, 80.1, 76.7, 62.6, 62.3, 58.5, 52.6, 52.6, 13.7, 13.3 ppm. HRMS (ESI) m/z $[M + H]^+$ Calcd for $C_{19}H_{24}NO_9$ 410.1446, found 410.1434.

*3,3-Diethyl-4,5-dimethyl-2-phenylisoxazolidine-3,3,4,5-tetracarboxylate (**4ac**).* Yellow oil (95% yield, 77.7 mg); TLC, R_f = 0.3 (PE/EtOAc = 5:1, v/v); ^1H NMR ($CDCl_3$, 400 MHz) δ 7.22 (t, 2H, J = 7.6 Hz), 7.18 (t, 2H, J = 7.6 Hz), 7.02 (t, 1H, J = 7.2 Hz), 5.08 (d, 1H, J = 6.4 Hz), 4.51 (d, 1H, J = 6.8 Hz), 4.17−4.09 (m, 1H), 4.06−4.00 (m, 1H), 3.92 (q, 2H, J = 7.2 Hz), 3.76 (s, 3H), 3.69 (s, 3H), 1.07 (t, J = 7.2 Hz, 3H), 0.95 (t, 3H, J = 7.2 Hz) ppm; $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz) δ 168.1, 167.4, 164.2, 144.7, 127.2, 124.0, 118.3, 78.9, 75.2, 61.7, 61.2, 57.6, 51.9, 51.7, 12.6, 12.5 ppm. HRMS (ESI) m/z $[M + H]^+$ Calcd for $C_{19}H_{24}NO_9$ 410.1446, found 410.1434.

*Diethyl 4-Benzoyl-2,5-diphenylisoxazolidine-3,3-dicarboxylate (**4ad**).* White solid (96% yield, 90.9 mg); mp 144−145 °C; TLC, R_f = 0.3 (PE/EtOAc = 20:1, v/v); ^1H NMR ($CDCl_3$, 400 MHz) δ 7.70 (d, 2H, J = 7.6 Hz), 7.49 (d, 2H, J = 7.6 Hz), 7.44 (dd, 2H, J = 7.2, 1.2 Hz), 7.41 (t, 1H, J = 7.6 Hz), 7.27 (t, 2H, J = 7.6 Hz), 7.22 (t, 4H, J = 7.2 Hz), 7.18 (d, 1H, J = 4.0 Hz), 7.05 (t, 1H, J = 7.2 Hz), 5.47 (s, 2H), 4.05−3.96 (m, 1H), 3.86−3.77 (m, 2H), 3.53−3.45 (m, 1H), 0.78 (t, 3H, J = 7.2 Hz), 0.70 (t, 3H, J = 7.2 Hz) ppm; $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz) δ 196.4, 166.6, 166.5, 146.2, 137.1, 135.6, 133.7, 129.1, 128.8, 128.6, 128.6, 128.2, 127.4, 125.7, 121.0, 83.3, 82.5, 62.8, 62.3, 61.8, 13.3, 13.2 ppm. HRMS (ESI) m/z $[M + H]^+$ Calcd for $C_{28}H_{28}NO_6$ 474.1911, found 474.1913.

*Triethyl 2,5-Diphenylisoxazolidine-3,3,4-tricarboxylate (**4ae**).* Yellow oil (80% yield, 70.6 mg), TLC, R_f = 0.3 (PE/EtOAc = 20:1, v/v); ^1H NMR ($CDCl_3$, 400 MHz) δ 7.57 (dd, 2H, J = 7.6, 1.2 Hz), 7.39 (dd, 5H, J = 18.0, 7.6 Hz), 7.27 (t, 2H, J = 8.4 Hz), 7.09 (t, 1H, J = 7.6 Hz), 5.42 (d, 1H, J = 8.8 Hz), 4.38 (d, 1H, J = 9.2 Hz), 4.31−4.23 (m, 1H), 4.17−4.09 (m, 3H), 4.04−3.96 (m, 1H), 3.83−3.75 (m, 1H), 1.19 (td, 6H, J = 7.2, 2.4 Hz), 0.95 (t, 3H, J = 7.2 Hz) ppm; $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz) δ 168.8, 166.4, 146.4, 136.0, 129.1, 128.7, 128.2, 127.4, 124.9, 119.7, 81.8, 81.1, 63.1, 62.4, 62.1, 61.5, 14.0, 13.7, 13.4 ppm. HRMS (ESI) m/z $[M + H]^+$ Calcd for $C_{24}H_{28}NO_7$ 442.1860, found 442.1861.

*Diethyl-4,6-dioxo-2-phenyltetrahydrofuro[3,4-d]isoxazole-3,3(2H)-dicarboxylate (**4af**).* Yellow oil (84% yield, 61.0 mg); TLC, R_f = 0.3 (PE/EtOAc = 10:1, v/v); ^1H NMR ($CDCl_3$, 400 MHz) δ 7.42 (d, 2H, J = 8.4 Hz), 7.28 (t, 2H, J = 8.0 Hz), 7.13 (t, 1H, J = 6.8 Hz), 5.31 (d, 1H, J = 8.0 Hz), 4.61 (d, 1H, J = 7.6 Hz), 4.28−4.17 (m, 1H), 3.98−3.90 (m, 1H), 3.75−3.67 (m, 1H), 3.92−3.84 (m, 1H), 1.20 (t, 3H, J = 7.2 Hz), 0.86 (t, 3H, J = 7.2 Hz) ppm; $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz) δ 171.3, 166.0, 165.4, 145.7, 128.3, 125.9, 120.3, 80.4, 62.9, 62.7, 58.8, 13.5, 13.3 ppm. HRMS (ESI) m/z $[M + H]^+$ Calcd for $C_{17}H_{18}NO_8$ 364.1027, found 364.1030.

*Diethyl-4,6-dioxo-2,5-diphenyltetrahydro-2H-pyrrolo[3,4-d]-isoxazole-3,3(3aH)-dicarboxylate (**4ag**).* Yellow oil (80% yield, 70.1 mg); TLC, R_f = 0.3 (PE/EtOAc = 10:1, v/v); ^1H NMR ($CDCl_3$, 400 MHz) δ 7.50 (t, 2H, J = 7.6 Hz), 7.43 (d, 1H, J = 7.2 Hz), 7.41 (d, 2H, J = 8.0 Hz), 7.33 (d, 2H, J = 8.0 Hz), 7.30 (t, 2H, J = 7.6 Hz), 7.18 (t, 1H, J = 7.2 Hz), 5.19 (d, 1H, J = 7.6 Hz), 4.59 (d, 1H, J = 7.6 Hz), 4.32 (q, 2H, J = 6.8 Hz), 4.10−4.02 (m, 1H), 3.87−3.79 (m, 1H), 1.30 (t, 3H, J = 7.2 Hz), 0.86 (t, 3H, J = 7.2 Hz) ppm; $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz) δ 172.7, 172.0, 164.7, 164.6, 144.7, 131.2, 129.3, 129.1, 128.2, 126.5, 126.0, 120.6, 80.8, 74.5, 63.0, 62.3, 55.0, 13.8, 13.3 ppm. HRMS (ESI) m/z $[M + H]^+$ Calcd for $C_{23}H_{23}N_2O_7$ 439.1500, found 439.1500.

*Diethyl 2-Phenyloctahydrocycloocta[d]isoxazole-3,3(2H)-dicarboxylate (**4ah**).* Yellow oil (93% yield, 69.8 mg); TLC, R_f = 0.3 (PE/EtOAc = 20:1, v/v); ^1H NMR ($CDCl_3$, 400 MHz) δ 7.21 (d, J = 8.4 Hz, 2H), 7.14 (t, J = 8.0 Hz, 2H), 6.95 (d, J = 7.2 Hz, 1H), 4.43 (t, J = 8.8 Hz, 1H), 4.18−4.01 (m, 1H), 4.05−3.99 (m, 1H), 3.96−3.84 (m, 2H), 3.00 (t, J = 9.6 Hz, 1H), 1.90 (q, J = 12.4 Hz, 2H), 1.82 (d, J = 14.4 Hz, 1H), 1.75−1.64 (m, 2H), 1.61−1.49 (m, 3H), 1.37−1.26 (m, 3H), 1.19−1.14 (m, 1H), 1.10 (t, J = 7.2 Hz, 3H), 0.94 (t, J = 7.2 Hz, 3H) ppm; $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz) δ 168.0, 166.1, 146.9, 128.0, 124.0, 119.3, 82.6, 80.9, 61.7, 61.1, 54.8, 29.8, 27.8, 27.4, 25.6, 25.5, 23.3, 13.8, 13.7 ppm. HRMS (ESI) m/z $[M + H]^+$ Calcd for $C_{21}H_{30}NO_5$ 376.2118, found 376.2131.

*Diethyl 2-Phenyltetrahydrofuro[2,3-d]isoxazole-3,3(2H)-dicarboxylate (**4ai**).* Colorless oil (92% yield, 61.7 mg); TLC, R_f = 0.3 (PE/EtOAc = 20:1, v/v); ^1H NMR ($CDCl_3$, 600 MHz) δ 7.42 (d, 2H, J = 7.6 Hz), 7.23 (t, 2H, J = 8.4 Hz), 7.09 (t, 1H, J = 7.2 Hz), 5.96 (d, 1H, J = 5.4 Hz), 4.36−4.31 (m, 1H), 4.29−4.21 (m, 2H), 3.98 (td, 1H, J = 7.6, 2.4 Hz), 3.90−3.86 (m, 2H), 3.67−3.62 (m, 1H), 2.14−2.06 (m, 1H), 1.94−1.90 (m, 1H), 1.28 (t, 3H, J = 7.2 Hz), 0.76 (t, 3H, J = 7.2 Hz) ppm; $^{13}C\{^1H\}$ NMR ($CDCl_3$, 150 MHz) δ 166.6, 165.7, 146.1, 127.9, 125.3, 120.8, 104.2, 82.4, 69.0, 61.8, 61.4, 54.0, 28.9, 13.9, 13.2 ppm. HRMS (ESI) m/z $[M + H]^+$ Calcd for $C_{17}H_{22}NO_6$ 336.1442, found 336.1438.

*Triethyl 5-(6-Chloro-9H-purin-9-yl)-2-phenylisoxazolidine-3,3,4-tricarboxylate (**4aj**).* Yellow oil (86% yield, 86.5 mg); TLC, R_f = 0.3 (PE/EtOAc = 2:1, v/v); ^1H NMR ($CDCl_3$, 600 MHz) δ 8.78 (s, 1H), 8.76 (s, 1H), 7.26 (t, 2H, J = 6.6 Hz), 7.24−7.21 (m, 2H), 7.16 (d, 1H, J = 7.2 Hz), 7.13 (t, 1H, J = 7.2 Hz), 4.80 (d, 1H, J = 4.8 Hz), 4.40−4.32 (m, 2H), 4.00 (dd, 1H, J = 7.2, 3.6 Hz), 3.92 (dd, 1H, J = 7.2, 3.6 Hz), 3.75 (s, 3H), 1.27 (t, 3H, J = 7.2 Hz), 0.94 (t, 3H, J = 7.2 Hz) ppm; $^{13}C\{^1H\}$ NMR ($CDCl_3$, 150 MHz) δ 166.8, 165.7, 164.2, 151.6, 151.1, 144.5, 143.8, 128.4, 125.8, 119.4, 81.4, 80.0, 63.2, 62.3, 62.2, 53.0, 13.8, 13.7, 13.3 ppm. HRMS (ESI) m/z $[M + H]^+$ Calcd for $C_{22}ClH_{23}N_5O_7$ 504.1281, found 504.1288.

*Triethyl 5-(6-Methoxy-9H-purin-9-yl)-2-phenylisoxazolidine-3,3,4-tricarboxylate (**4ak**).* Yellow oil (94% yield, 96.5 mg); TLC, R_f = 0.3 (PE/EtOAc = 2:1, v/v); ^1H NMR ($CDCl_3$, 600 MHz) δ 8.55 (s, 1H), 8.52 (s, 1H), 7.24 (d, 2H, J = 1.2 Hz), 7.23 (s, 2H), 7.09 (d, 2H, J = 4.8 Hz), 4.79 (d, 1H, J = 4.8 Hz), 4.34−4.28 (m, 2H), 4.21−4.16 (m, 2H), 4.15 (s, 3H), 4.04−3.95 (m, 1H), 3.97−3.91 (m, 1H), 1.25 (t, 3H, J = 7.2 Hz), 1.20 (t, 3H, J = 7.2 Hz), 0.95 (t, 3H, J = 7.2 Hz) ppm; $^{13}C\{^1H\}$ NMR ($CDCl_3$, 150 MHz) δ 166.4, 165.9, 164.3, 161.0, 152.5, 151.9, 144.9, 140.6, 128.3, 125.5, 121.1, 119.3, 81.2, 80.0, 63.0, 62.2, 62.1, 54.2, 13.7, 13.7, 13.4 ppm. HRMS (ESI) m/z $[M + H]^+$ Calcd for $C_{24}H_{28}N_5O_8$ 514.1932, found 514.1930.

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*Triethyl 2-Phenyl-5-(6-(piperidin-1-yl)-9H-purin-9-yl)-isoxazolidine-3,3,4-tricar-boxylate (**4al**).* White solid (85% yield, 96.3 mg); mp 93−94 °C; TLC, R_f = 0.3 (PE/EtOAc = 2:1, v/v); ^{1}H NMR ($CDCl_3$, 600 MHz), δ 8.33 (d, 2H, J = 1.8 Hz), 7.24 (s, 2H), 7.23 (d, 2H, J = 2.4 Hz), 7.10−7.07 (m, 1H), 7.06 (d, 1H, J = 4.8 Hz), 4.77 (d, 1H, J = 4.8 Hz), 4.34−4.26 (m, 3H), 4.23−4.14 (m, 5H), 4.04−3.98 (m, 1H), 3.97−3.93 (m, 1H), 1.71−1.64 (m, 6H), 1.25 (t, 3H, J = 7.2 Hz), 1.21 (t, 3H, J = 7.2 Hz), 0.97 (t, 3H, J = 7.2 Hz) ppm; ^{13}C{^{1}H} NMR ($CDCl_3$, 150 MHz) δ 166.5, 166.0, 164.4, 153.7, 152.8, 151.0, 145.1, 136.2, 128.2, 125.3, 119.3, 80.8, 80.0, 62.9, 62.0, 53.3, 46.3, 26.0, 24.7, 13.8, 13.7, 13.4 ppm. HRMS (ESI) m/z [M + H]$^+$ Calcd for $C_{28}H_{35}N_6O_7$ 567.2562, found 567.2565.

*Triethyl 5-(5-Chloro-1H-benzo[d]imidazol-1-yl)-2-phenylisoxazolidine-3,3,4-tricarboxylate (**4am**).* Yellow oil (80% yield, 82.4 mg); TLC, R_f = 0.3 (PE/EtOAc = 2:1, v/v); ^{1}H NMR ($CDCl_3$, 600 MHz) δ 8.30 (s, 1H), 7.97 (d, 1H, J = 8.4 Hz), 7.78 (d, 1H, J = 1.8 Hz), 7.30−7.26 (m, 3H), 7.18 (d, 2H, J = 7.6 Hz), 7.14 (t, 1H, J = 7.2 Hz), 6.72 (d, 1H, J = 6.0 Hz), 4.63 (d, 1H, J = 6.0 Hz), 4.32 (q, 2H, J = 7.2 Hz), 4.21−4.13 (m, 2H), 4.09−4.04 (m, 1H), 4.01−3.96 (m, 1H), 1.29 (t, 3H, J = 7.2 Hz), 1.20 (t, 3H, J = 7.2 Hz), 0.95 (t, 3H, J = 7.2 Hz) ppm; ^{13}C{^{1}H} NMR ($CDCl_3$, 150 MHz) δ 166.5, 165.2, 164.7, 144.9, 144.8, 143.2, 130.4, 128.6, 128.5, 125.4, 124.1, 118.8, 112.4, 120.1, 83.9, 80.5, 63.2, 62.2, 62.1, 60.9, 13.7, 13.7, 13.3 ppm. HRMS (ESI) m/z [M + H]$^+$ Calcd for $C_{25}H_{27}ClN_3O_7$ 516.1532, found 516.1527.

*Triethyl 5-(1H-Benzo[d][1,2,3]triazol-1-yl)-2-phenylisoxazolidine-3,3,4-tricar-Boxylate (**4an**).* Yellow solid (90% yield, 86.8 mg); mp 100−101 °C; TLC, R_f = 0.3 (PE/EtOAc = 2:1, v/v); ^{1}H NMR ($CDCl_3$, 600 MHz) δ 8.06 (dd, 2H, J = 12.0, 8.4 Hz), 7.53 (t, 1H, J = 7.6 Hz), 7.39 (t, 1H, J = 7.2 Hz), 7.26−7.21 (m, 5H), 7.08 (t, 1H, J = 6.6 Hz), 5.47 (d, 1H, J = 5.4 Hz), 4.47−4.38 (m, 2H), 4.26−4.16 (m, 2H), 4.08−4.02 (m, 1H), 3.99−3.94 (m, 1H), 1.36 (t, 3H, J = 7.2 Hz), 1.24 (t, 3H, J = 7.2 Hz), 0.95 (t, 3H, J = 7.2 Hz) ppm; ^{13}C{^{1}H} NMR ($CDCl_3$, 150 MHz) δ 166.5, 165.6, 164.8, 146.8, 145.1, 131.9, 128.3, 128.1, 125.0, 124.4, 120.1, 118.7, 110.8, 85.4, 80.4, 63.1, 62.2, 62.1, 59.6, 13.8, 13.8, 13.4 ppm. HRMS (ESI) m/z [M + H]$^+$ Calcd for $C_{24}H_{27}N_4O_7$ 483.1874, found 483.1869.

*Triethyl 5-(1H-Indol-1-yl)-2-phenylisoxazolidine-3,3,4-tricarboxylate (**4ao**).* Black oil (71% yield, 68.2 mg); TLC, R_f = 0.3 (PE/EtOAc = 2:1, v/v); ^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.76 (d, 1H, J = 7.6 Hz), 7.64 (s, 1H), 7.63 (d, 1H, J = 5.4 Hz), 7.29 (s, 2H), 7.28 (d, 2H, J = 4.2 Hz), 7.26 (d, 1H, J = 8.4 Hz), 7.17 (t, 1H, J = 7.2 Hz), 7.13−7.10 (m, 1H), 6.80 (d, 1H, J = 6.6 Hz), 6.64 (d, 1H, J = 3.6 Hz), 4.75 (d, 1H, J = 6.6 Hz), 4.29−4.23 (m, 1H), 4.21−4.10 (m, 5H), 1.20 (td, 6H, J = 7.2, 3.0 Hz), 1.07 (t, 3H, J = 7.2 Hz) ppm; ^{13}C{^{1}H} NMR ($CDCl_3$, 150 MHz) δ 167.4, 165.9, 165.3, 145.5, 135.8, 129.1, 128.3, 125.4, 124.9, 122.4, 121.0, 120.5, 119.0, 110.2, 104.4, 84.2, 80.5, 62.8, 61.8, 60.7, 13.8, 13.6, 13.5 ppm. HRMS (ESI) m/z [M + H]$^+$ Calcd for $C_{26}H_{29}N_2O_7$ 481.1969, found 481.1965.

*Diethyl 5-(3-(tert-Butoxycarbonyl)-5-methyl-2,4-dioxo-3,4-dihydropyrimidin-1(2H)-yl)-2-phenylisoxazolidine-3,3-dicarboxylate (**4ap**).* Colorless oil (85% yield, 87.9 mg); TLC, R_f = 0.3 (PE/EtOAc = 2:1, v/v); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.66 (d, 1H, J = 1.2 Hz), 7.31 (d, 2H, J = 8.4 Hz), 7.26−7.21 (m, 2H), 7.12−7.05 (m, 1H), 6.39 (d, 1H, J = 7.2 Hz), 4.26−4.16 (m, 2H), 3.91−3.83 (m, 1H), 3.74−3.67 (m, 2H), 2.80 (d, 1H, J = 7.2 Hz), 1.86 (s, 3H), 1.54 (s, 9H), 1.18 (t, 3H, J = 7.2 Hz), 0.79 (t, 3H, J = 7.2 Hz) ppm; ^{13}C{^{1}H} NMR ($CDCl_3$, 150 MHz) δ 166.1, 164.7, 160.2, 147.7, 146.8, 144.1, 133.9, 127.4, 124.9, 119.0, 109.8, 85.8, 80.9, 76.1, 61.6, 61.1, 45.2, 26.4, 12.8, 12.3, 11.7 ppm. HRMS (ESI) m/z [M + H]$^+$ Calcd for $C_{25}H_{32}N_3O_9$ 518.2133, found 518.2138.

*Diethyl 5-(3-(tert-Butoxycarbonyl)-5-ethyl-2,4-dioxo-3,4-dihydropyrimidin-1(2H)-yl)-2-phenylisoxazolidine-3,3-dicarboxylate (**4aq**).* Yellow solid (80% yield, 85.0 mg); mp 100−101 °C; TLC, R_f = 0.3 (PE/EtOAc = 3:1, v/v); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.76 (s, 1H), 7.38 (d, 2H, J = 8.4 Hz), 7.30 (t, 2H, J = 7.6 Hz), 7.17 (t, 1H, J = 6.8 Hz), 6.49 (d, 1H, J = 3.2 Hz, 7.6 Hz), 4.35−4.21 (m, 2H), 3.97−3.89 (m, 1H), 3.83−3.17 (m, 2H), 2.87 (dd, 1H, J = 7.6, 3.2 Hz), 2.34 (q, 2H, J = 7.6 Hz), 1.60 (s, 9H), 1.24 (t, 3H, J = 7.2 Hz), 1.13 (, 3H t, J = 7.2 Hz), 0.85 (t, 3H, J = 7.2 Hz) ppm; ^{13}C{^{1}H} NMR ($CDCl_3$, 150 MHz) δ 167.2, 165.8, 160.9, 148.6, 147.9, 147.0, 145.0, 134.4, 128.4, 126.0, 123.0, 120.1, 116.5, 86.8, 81.8, 77.0, 62.6, 62.2, 46.1, 27.4, 20.2, 13.9, 13.4, 12.4 ppm. HRMS (ESI) m/z [M + H]$^+$ Calcd for $C_{26}H_{34}N_3O_9$ 532.2290, found 532.2297.

*Diethyl 5-(3-(tert-Butoxycarbonyl)-5-fluoro-2,4-dioxo-3,4-dihydropyrimidin-1(2H)-yl)-2-phenylisoxazolidine-3,3-dicarboxylate (**4ar**).* Yellow solid (86% yield, 89.6 mg); mp 90−91 °C; TLC, R_f = 0.3 (PE/EtOAc = 2:1, v/v); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.05 (d, 1H, J = 6.4 Hz), 7.39 (d, 2H, J = 8.0 Hz), 7.33 (t, 2H, J = 8.0 Hz), 7.21 (t, 1H, J = 7.2 Hz), 6.43 (d, 1H, J = 5.2 Hz), 4.38−4.24 (m, 2H), 3.98−3.90 (m, 1H), 3.83 (q, 1H, J = 7.2 Hz), 3.79−3. 71 (m, 1H), 2.88 (dd, 1H, J = 14.8, 2.8 Hz), 1.62 (s, 9H), 1.28 (t, 3H, J = 7.2 Hz), 0.85 (t, 3H, J = 7.2 Hz) ppm; ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ 167.0, 165.6, 154.6, 154.3, 147.2, 146.4, 144.7, 141.2, 138.9, 128.5, 126.3, 124.1, 123.7, 120.2, 87.8, 82.4, 76.9, 62.7, 62.3, 46.3, 27.4, 13.9, 13.3 ppm. HRMS (ESI) m/z [M + H]$^+$ Calcd for $C_{24}H_{29}FN_3O_9$ 522.1882, found 522.1886.

*Diethyl 5-(3-(tert-Butoxycarbonyl)-5-chloro-2,4-dioxo-3,4-dihydropyrimidin-1(2H)-yl)-2-phenylisoxazolidine-3,3-dicarboxylate (**4as**).* Yellow solid (88% yield, 94.5 mg); mp 105−106 °C; TLC, R_f = 0.3 (PE/EtOAc = 2:1, v/v); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.14 (s, 1H), 7.40 (d, 2H, J = 8.0 Hz), 7.34 (t, 2H, J = 8.0 Hz), 7.22 (t, 1H, J = 7.2 Hz), 6.42 (dd, 1H, J = 7.2, 2.4 Hz), 4.39−4.25 (m, 2H), 3.98−3.90 (m, 1H), 3.84 (q, 1H, J = 7.2 Hz), 3.89−3.71 (m, 1H), 2.90 (dd, 1H, J = 14.4, 2.4 Hz), 1.62 (s, 9H), 1.29 (t, 3H, J = 7.2 Hz), 0.86 (t, 3H, J = 7.2 Hz) ppm; ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ 167.0, 165.6, 156.6, 147.7, 146.6, 144.7, 136.3, 128.5, 126.3, 120.3, 109.0, 87.7, 82.8, 76.9, 62.8, 62.3, 46.5, 27.3, 13.9, 13.3 ppm. HRMS (ESI) m/z [M + H]$^+$ Calcd for $C_{24}H_{29}ClN_3O_9$ 538.1587, found 538.1589.

*Diethyl 5-(5-Bromo-3-(tert-butoxycarbonyl)-2,4-dioxo-3,4-dihydropyrimidin-1(2H)-yl)-2-phenylisoxazolidine-3,3-dicarboxylate (**4at**).* Yellow solid (87% yield, 101.1 mg); mp 105−106 °C; TLC, R_f = 0.3 (PE/EtOAc = 2:1, v/v); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.24 (s, 1H), 7.40 (d, 2H, J = 8.0 Hz), 7.34 (t, 2H, J = 8.0 Hz), 7.21 (t, 1H, J = 7.2 Hz), 6.41 (dd, 1H, J = 7.6, 2.8 Hz), 4.38−4.25 (m, 2H), 3.98−3.90 (m, 1H), 3.83 (q, 1H, J = 7.2 Hz), 3.79−3.71 (m, 1H), 2.91 (dd, 1H, J = 14.4, 2.4 Hz), 1.61 (s, 9H), 1.29 (t, 3H, J = 7.2 Hz), 0.85 (t, 3H, J = 7.2 Hz) ppm; ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ 167.0, 165.6, 156.6, 148.0, 146.7, 144.7, 138.9, 128.5, 126.3, 120.3, 96.5, 87.7, 82.8, 76.9, 62.8, 62.3, 46.5, 27.3, 13.9, 13.3 ppm. HRMS (ESI) m/z [M + H]$^+$ Calcd for $C_{24}H_{29}BrN_3O_9$ 582.1082, found 582.1083.

*5-(4-((Di-tert-butoxycarbonyl)amino)-2-oxopyrimidin-1(2H)-yl)-2-phenylisoxazolidine-3,3-carboxylate (**4au**).* White solid (77% yield, 92.7 mg); mp 105−106 °C; TLC, R_f = 0.3 (PE/EtOAc = 2:1, v/v); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.11 (d, 1H, J = 8.0 Hz), 7.41 (d, 2H, J = 8.0 Hz), 7.32 (t, 2H, J = 8.0 Hz), 7.18 (t, 1H, J = 7.2 Hz), 7.07 (d, 1H, J = 8.0 Hz), 6.32 (dd, 1H, J = 6.8, 2.0 Hz), 4.31−4.17 (m, 2H), 3.97−3.86 (m, 2H), 3.76−3.68 (m, 1H), 2.94 (dd, 1H, J = 14.8, 2.4 Hz), 1.56 (s, 18H), 1.23 (t, 3H, J = 7.2 Hz), 0.84 (t, 3H, J = 7.2 Hz) ppm; ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ 167.2, 165.9, 162.6, 154.5, 149.5, 145.1, 143.4, 128.4, 125.9, 120.0, 96.0, 84.9, 84.1, 76.8, 62.4, 62.1, 47.2, 27.6, 13.9, 13.4 ppm. HRMS (ESI) m/z [M + H]$^+$ Calcd for $C_{29}H_{39}N_4O_{10}$ 603.2661, found 603.2656.

*Diethyl 5-Phenyl-2-(o-tolyl)isoxazolidine-3,3-dicarboxylate (**4ba**).* Yellow oil (94% yield, 72.0 mg); TLC, R_f = 0.3 (PE/EtOAc = 20:1, v/v); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.41 (d, 2H, J = 7.6 Hz), 7.37 (d, 1H, J = 8.0 Hz), 7.29 (t, 2H, J = 7.6 Hz), 7.23 (d, 1H, J = 6.8 Hz), 7.05 (t, 2H, J = 6.4 Hz), 7.00 (t, 1H, J = 7.2 Hz), 5.25 (dd, 1H, J = 9.2, 6.4 Hz), 4.12−4.00 (m, 2H), 3.91−3.83 (m, 1H), 3.70−3.62 (m, 1H), 3.21−3.10 (m, 2H), 2.38 (s, 3H), 1.07 (t, 3H, J = 7.2 Hz), 0.90 (t, 3H, J = 7.2 Hz) ppm; ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ 167.2, 166.2, 144.6, 136.4, 134.4, 129.4, 127.5, 125.8, 124.7, 123.0, 78.0, 77.9, 60.9, 60.9, 46.0, 17.6, 12.7, 12.4 ppm. HRMS (ESI) m/z [M + H]$^+$ Calcd for $C_{22}H_{26}NO_5$ 384.1805, found 384.1800.

*Diethyl 5-Phenyl-2-(m-tolyl)isoxazolidine-3,3-dicarboxylate (**4bb**).* Yellow oil (95% yield, 72.8 mg); TLC, R_f = 0.3 (PE/EtOAc = 20:1, v/v); ^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.55 (d, 2H, J = 7.2 Hz), 7.40 (t, 2H, J = 7.6 Hz), 7.35 (t, 1H, J = 7.6 Hz), 7.20 (s, 1H), 7.17 (d, 1H, J = 8.4 Hz), 7.14 (t, 1H, J = 8.4 Hz), 6.85 (d, 1H, J = 7.2 Hz), 5.33 (dd, 1H, J = 9.6, 6.0 Hz), 4.19 (qd, 2H, J = 7.2, 1.8 Hz), 4.07−4.02 (m, 1H), 3.98−3.93 (m, 1H), 3.22 (dd, 1H, J = 12.6, 6.0 Hz),

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3.13 (dd, 1H, J = 12.6, 9.6 Hz), 2.31 (s, 3H), 1.20 (t, 3H, J = 7.2 Hz), 1.04 (t, 3H, J = 7.2 Hz) ppm; $^{13}C\{^1H\}$ NMR ($CDCl_3$, 150 MHz) δ 168.9, 167.9, 147.1, 137.2, 128.5, 128.0, 127.0, 124.5, 118.5, 115.2, 78.8, 78.6, 62.1, 61.9, 47.9, 21.5, 13.7, 13.5 ppm. HRMS (ESI) m/z $[M + H]^+$ Calcd for $C_{22}H_{26}NO_5$ 384.1805, found 384.1800.

*Diethyl 5-Phenyl-2-(p-tolyl)isoxazolidine-3,3-dicarboxylate (**4bc**).*[6a] Yellow oil (96% yield, 73.6 mg); TLC, R_f = 0.3 (PE/EtOAc = 20:1, v/v); ^1H NMR ($CDCl_3$, 400 MHz) δ 7.45 (d, 2H, J = 6.8 Hz), 7.30 (t, 2H, J = 7.2 Hz), 7.25 (d, 1H, J = 7.2 Hz), 7.20 (d, 2H, J = 8.4 Hz), 6.96 (d, 2H, J = 8.4 Hz), 5.22 (dd, 1H, J = 9.2, 6.4 Hz), 4.09 (q, 2H, J = 7.2 Hz), 3.96−3.88 (m, 1H), 3.86−3.78 (m, 1H), 3.15−3.04 (m, 2H), 2.20 (s, 3H), 1.11 (t, 3H, J = 7.2 Hz), 0.93 (t, 3H, J = 7.2 Hz) ppm; $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz) δ 168.6, 167.9, 144.7, 137.6, 133.6, 128.7, 128.6, 128.5, 127.1, 118.8, 78.8, 78.8, 62.1, 61.9, 47.8, 20.8, 13.8, 13.6 ppm. HRMS (ESI) m/z $[M + H]^+$ Calcd for $C_{22}H_{26}NO_5$ 384.1805, found 384.1800.

*Diethyl 2-(2,4-Dimethylphenyl)-5-phenylisoxazolidine-3,3-dicarboxylate (**4bd**).* Yellow oil (81% yield, 64.3 mg); TLC, R_f = 0.3 (PE/EtOAc = 20:1, v/v); ^1H NMR ($CDCl_3$, 400 MHz) δ 7.40 (d, 2H, J = 7.2 Hz), 7.30−7.23 (m, 4H), 6.87 (s, 1H), 6.84 (d, 1H, J = 8.4 Hz), 5.25 (t, 1H, J = 8.0 Hz), 4.16−4.01 (m, 2H), 3.94−3.85 (m, 1H), 3.75−3.67 (m, 1H), 3.14 (d, 2H, J = 8.0 Hz), 2.35 (s, 3H), 2.18 (s, 3H), 1.08 (t, 3H, J = 7.2 Hz), 0.92 (t, 3H, J = 7.2 Hz) ppm; $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz) δ 168.5, 167.4, 143.0, 137.7, 136.6, 135.4, 131.0, 128.5, 128.3, 126.8, 126.5, 124.1, 79.1, 78.8, 62.0, 61.9, 46.9, 20.9, 18.5, 13.8, 13.5 ppm. HRMS (ESI) m/z $[M + H]^+$ Calcd for $C_{23}H_{28}NO_5$ 398.1962, found 398.1954.

*Diethyl 2-(2-Chlorophenyl)-5-phenylisoxazolidine-3,3-dicarboxylate (**4be**).* Yellow oil (86% yield, 69.3 mg); TLC, R_f = 0.3 (PE/EtOAc = 20:1, v/v); ^1H NMR ($CDCl_3$, 400 MHz) δ 7.52 (d, 1H, J = 8.4 Hz), 7.42 (d, 2H, J = 7.2 Hz), 7.30 (t, 2H, J = 7.6 Hz), 7.26 (t, 2H, J = 8.0 Hz), 7.13 (t, 1H, J = 7.6 Hz), 7.01 (t, 1H, J = 7.2 Hz), 5.33 (dd, 1H, J = 9.6, 6.0 Hz), 4.16−4.08 (m, 2H), 3.97−3.89 (m, 1H), 3.79−3.71 (m, 1H), 3.15 (dd, 1H, J = 12.8, 10.0 Hz), 3.08 (dd, 1H, J = 12.8, 6.0 Hz), 1.13 (t, 3H, J = 7.2 Hz), 0.96 (t, 3H, J = 7.2 Hz) ppm; $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz) δ 168.2, 167.0, 144.3, 136.8, 129.7, 128.6, 127.3, 126.9, 126.8, 124.9, 79.3, 78.3, 62.2, 62.1, 47.6, 13.8, 13.5 ppm. HRMS (ESI) m/z $[M + H]^+$ Calcd for $C_{21}H_{23}ClNO_5$ 404.1259, found 404.1266.

*Diethyl 2-(3-Chlorophenyl)-5-phenylisoxazolidine-3,3-dicarboxylate (**4bf**).* Yellow oil (90% yield, 72.6 mg); TLC, R_f = 0.3 (PE/EtOAc = 20:1, v/v); ^1H NMR ($CDCl_3$, 400 MHz) δ 7.42 (d, 2H, J = 6.8 Hz), 7.33−7.24 (m, 4H), 7.13 (d, 1H, J = 8.4 Hz), 7.08 (t, 1H, J = 8.4 Hz), 6.89 (d, 1H, J = 7.6 Hz), 5.23 (dd, 1H, J = 9.6, 6.0 Hz), 4.11 (q, 2H, J = 7.2 Hz), 4.04−3.90 (m, 2H), 3.16 (dd, 1H, J = 12.8, 6.0 Hz), 3.01 (dd, 1H, J = 12.8, 9.6 Hz), 1.13 (t, 3H, J = 7.2 Hz), 0.99 (t, 3H, J = 7.2 Hz) ppm; $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz) δ 168.2, 167.7, 148.5, 136.8, 134.0, 129.3, 128.8, 128.7, 127.0, 123.2, 117.6, 115.6, 115.6, 79.1, 78.5, 62.2, 62.5, 62.3, 48.0, 13.8, 13.7 ppm. HRMS (ESI) m/z $[M + H]^+$ Calcd for $C_{21}H_{23}ClNO_5$ 404.1259, found 404.1266.

*Diethyl 2-(4-Chlorophenyl)-5-phenylisoxazolidine-3,3-dicarboxylate (**4bg**).* Yellow oil (91% yield, 73.4 mg); TLC, R_f = 0.3 (PE/EtOAc = 20:1, v/v); ^1H NMR ($CDCl_3$, 400 MHz) δ 7.51 (d, 2H, J = 6.8 Hz), 7.39 (t, 2H, J = 7.6 Hz), 7.35 (d, 1H, J = 7.2 Hz), 7.31 (d, 2H, J = 8.8 Hz), 7.20 (d, 2H, J = 9.2 Hz), 5.30 (dd, 1H, J = 9.6, 6.4 Hz), 4.19 (q, 2H, J = 7.2 Hz), 4.09−3.93 (m, 2H), 3.22 (dd, 1H, J = 12.8, 6.0 Hz), 3.11 (dd, 1H, J = 12.8, 9.6 Hz), 1.21 (t, 3H, J = 7.2 Hz), 1.05 (t, 3H, J = 7.2 Hz) ppm; $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz) δ 168.3, 167.6, 145.8, 137.0, 128.7, 128.7, 128.2, 127.0, 119.4, 79.0, 78.6, 62.4, 62.2, 47.8, 13.9, 13.7 ppm. HRMS (ESI) m/z $[M + H]^+$ Calcd for $C_{21}H_{23}ClNO_5$ 404.1259, found 404.1266.

*Diethyl 2-(4-Nitrophenyl)-5-phenylisoxazolidine-3,3-dicarboxylate (**4bh**).*[6a] Colorless oil (70% yield, 58.0 mg); TLC, R_f = 0.3 (PE/EtOAc = 20:1, v/v); ^1H NMR ($CDCl_3$, 400 MHz) δ 8.13 (d, 2H, J = 9.6 Hz), 7.48 (dd, 2H, J = 7.8, 1.6 Hz), 7.44−7.39 (m, 3H), 7.23 (d, 2H, J = 9.2 Hz), 5.35 (dd, 1H, J = 9.6, 5.6 Hz), 4.25 (q, 2H, J = 7.2 Hz), 4.16 (q, 2H, J = 7.2 Hz), 3.35 (dd, 1H, J = 12.8, 5.6 Hz), 3.12 (dd, 1H, J = 12.8, 9.6 Hz), 1.25 (t, 3H, J = 7.2 Hz), 1.16 (t, 3H, J = 7.2 Hz) ppm; $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz) δ 167.6, 167.4, 151.7, 141.6, 135.7, 129.1, 128.3, 126.8, 124.7, 114.4, 79.6, 63.0, 62.8, 48.4, 13.9, 13.9 ppm. HRMS (ESI) m/z $[M + H]^+$ Calcd for $C_{21}H_{23}N_2O_7$ 415.1500, found 415.1505.

*Diethyl 2-(3,5-Dichlorophenyl)-5-phenylisoxazolidine-3,3-dicarboxylate (**4bi**).* Yellow oil (83% yield, 72.6 mg); TLC, R_f = 0.3 (PE/EtOAc = 20:1, v/v); ^1H NMR ($CDCl_3$, 400 MHz) δ 7.41 (d, 2H, J = 6.8 Hz), 7.35−7.27 (m, 3H), 7.14 (d, 2H, J = 6.0 Hz), 6.90 (s, 1H), 5.23 (dd, 1H, J = 9.6, 5.6 Hz), 4.25−4.16 (m, 2H), 4.12−4.00 (m, 2H), 3.19 (dd, 1H, J = 12.8, 5.6 Hz), 3.00 (dd, 1H, J = 12.8, 9.6 Hz), 1.18 (t, 3H, J = 7.2 Hz), 1.07 (t, 3H, J = 7.2 Hz) ppm; $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz) δ 167.9, 167.5, 149.0, 136.3, 134.6, 128.9, 128.7, 126.9, 122.6, 115.2, 79.3, 78.3, 62.7, 62.5, 48.1, 13.8, 13.8 ppm. HRMS (ESI) m/z $[M + H]^+$ Calcd for $C_{21}H_{22}Cl_2NO_5$ 438.0870, found 438.0875.

*Dimethyl 2,5-Diphenylisoxazolidine-3,3-dicarboxylate (**4bj**).*[6a] Yellow oil (98% yield, 67.1 mg); R_f = 0.3 (PE/EtOAc = 20:1, v/v); ^1H NMR ($CDCl_3$, 600 MHz) δ 7.54 (d, 2H, J = 7.2 Hz), 7.41 (t, 2H, J = 7.6 Hz), 7.38−7.35 (m, 3H), 7.28 (t, 2H, J = 8.4 Hz), 7.05 (t, 1H, J = 7.2 Hz), 5.34 (dd, 1H, J = 15.6, 6.0 Hz), 3.73 (s, 3H), 3.51 (s, 3H), 3.24 (dd, 1H, J = 12.6, 6.0 Hz), 3.14 (dd, 1H, J = 12.6, 9.6 Hz) ppm.

*Diisopropyl 2,5-Diphenylisoxazolidine-3,3-dicarboxylate (**4bk**).* Yellow oil (96% yield, 76.3 mg); R_f = 0.3 (PE/EtOAc = 20:1, v/v); ^1H NMR ($CDCl_3$, 400 MHz) δ 7.56 (d, 2H, J = 7.2 Hz), 7.41−7.32 (m, 5H), 7.26−7.22 (m, 2H), 7.04−7.00 (m, 1H), 5.35 (dd, 1H, J = 6.4, 2.8 Hz), 5.06 (t, 1H, J = 6.4 Hz), 4.88−4.82 (m, 1H), 3.22−3.11 (m, 2H), 1.19 (dd, 6H, J = 3.6, 2.8 Hz), 1.08 (d, 3H, J = 6.4 Hz), 0.94 (d, 3H, J = 6.4 Hz) ppm; $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz) δ 168.1, 167.5, 147.2, 137.5, 128.6, 128.5, 128.2, 127.1, 123.7, 118.4, 78.7, 78.5, 70.0, 70.0, 48.2, 21.4, 21.4, 21.3, 21.1 ppm. HRMS (ESI) m/z $[M + H]^+$ Calcd for $C_{23}H_{28}NO_5$ 398.1962, found 398.1965.

*Di-tert-butyl 2,5-Diphenylisoxazolidine-3,3-dicarboxylate (**4bl**).* Yellow oil (87% yield, 74.0 mg); R_f = 0.3 (PE/EtOAc = 20:1, v/v); ^1H NMR ($CDCl_3$, 400 MHz) δ 7.46 (d, 2H, J = 6.8 Hz), 7.37−7.24 (m, 5H), 7.19−7.15 (m, 2H), 6.95 (t, 1H, J = 7.6 Hz), 5.22 (dd, 1H, J = 9.2, 6.8 Hz), 3.11−3.00 (m, 2H), 1.32 (s, 9H), 1.17 (s, 9H) ppm; $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz) δ 167.7, 166.9, 147.5, 137.8, 128.5, 128.4, 128.1, 127.1, 123.5, 118.6, 82.9, 82.7, 79.2, 78.2, 48.3, 27.7, 27.5 ppm. HRMS (ESI) m/z $[M + H]^+$ Calcd for $C_{25}H_{32}NO_5$ 426.2275, found 426.2278.

*2,5-Diphenylisoxazolidine-3,3-dicarbonitrile (**4bm**).* Colorless oil (80% yield, 44.0 mg); TLC, R_f = 0.3 (PE/EtOAc = 20:1, v/v); ^1H NMR ($CDCl_3$, 400 MHz) δ 7.52−7.41 (m, 9H), 7.32 (t, 1H, J = 7.2 Hz), 5.41 (t, 1H, J = 8.0 Hz), 3.60 (dd, 1H, J = 13.2, 8.0 Hz), 3.19 (dd, 1H, J = 13.2, 7.2 Hz) ppm; $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz) δ 143.7, 136.0, 129.5, 129.4, 129.1, 127.5, 126.9, 119.8, 112.6, 112.3 ppm. HRMS (ESI) m/z $[M + H]^+$ Calcd for $C_{17}H_{14}N_3O$ 276.1131, found 276.1133.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.joc.0c02567.

H-H NOESY of **4ab**, **4ac**, **4ae**, and **4ao**; ^1H NMR spectra of **4a** and **4bj**; ^1H- and ^{13}C-NMR spectra for nitrone intermediate **5a**; and cycloaddition products **4b−4z**, **4ab−4au**, **4ba−4bi**, and **4bk−4bm** (PDF)

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Notes

The authors declare no competing financial interest.

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