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Metal-free oxysulfonylation and aminosulfonylation of alkenyl oximes: synthesis of sulfonylated isoxazolines and cyclic nitrones†

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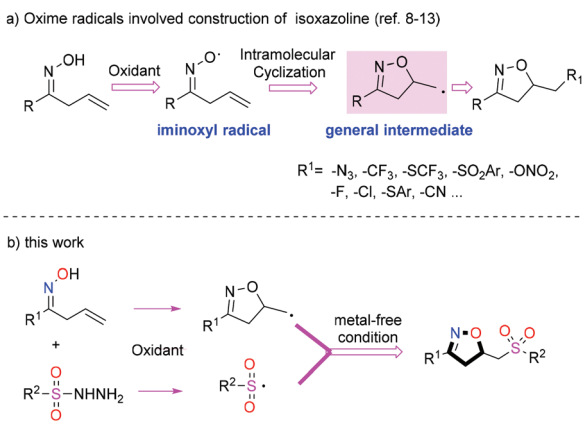
Intramolecular oxysulfonylation of alkenyl oximes was reported. Using iodine as the catalyst, TBHP as the oxidant, and sulfonyl hydrazides as the sulfonyl radical source, a variety of sulfonylated isoxazolines were obtained in moderate to excellent yields. Cyclic nitrones could also be readily obtained under the same conditions.

Introduction

As an important class of nitrogen- and oxygen-containing heterocycles, isoxazolines have been frequently found in natural products,[1] fine chemicals[2] or pharmaceuticals.[3] Such structures can also be utilized as useful building blocks in organic synthesis[4] or coordination groups in chiral ligands.[5] For these reasons, construction of isoxazoline skeletons from readily available starting materials has attracted considerable attention, and 1,2-difunctionalization of unactivated alkenes was proved to be one of the most efficient methods for the preparation of isoxazolines.[6]

Among these studies, generation and subsequent addition of oxime radicals (iminoxyl radical) to C=C double bonds has shown application potential for the construction of isoxazolines due to the easy availability and structural diversity of the starting materials. By changing the substituents in the ketoximes, a variety of functional groups could be introduced into the target molecules. Oxime radicals and their analogous aminoxyl radicals such as TEMPO have been extensively studied since the 1960s,[7] and cyclization of β,γ-unsaturated oximes provided a straightforward approach to a variety of isoxazolines. So far, heterocycles bearing different functional groups such as trifluoromethyl,[8] halogen,[9] cyano,[10] amino group,[11] and azide[12] have been prepared *via* cyclization of β,γ-unsaturated oximes. For example, Han *et al.* reported the cyclization of β,γ-unsaturated oximes to build isoxazolines (Scheme 1a).[13] In this protocol, oxime radicals were generated using commercially available TEMPO or DEAD as the radical initiator, and 4,5-dihydroisoxazoles were obtained in good yields *via* radical cyclization and subsequent capture of the thus formed radical intermediates.

The sulfone functionality has shown important application potential in medicinal chemistry,[14] and cyclization of β,γ-unsaturated oxime radicals and capture of the resulting radicals with sulfonyl radicals would be an ideal route to sulfonyl-containing isoxazolines. Li *et al.* showed that introduction of the sulfonyl group into isoxazolines could be realized *via* radical cyclization of β,γ-unsaturated oximes and subsequent coupling of the thus generated radical intermediates with sulfonyl radicals.[15] In this report, the key sulfonyl radicals were generated using sodium sulfonate as the sulfonyl source in the presence of an excess amount of copper acetate and potassium



Scheme 1 Strategies for the construction of isoxazolines.

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fluoride, and the desired sulfonyl isoxazolines were obtained in up to 88% yields. Two possible reaction pathways were proposed, and the sulfonyl radical pathway seemed to be more likely.

In a previous report, 2 equiv. of $Cu(OAc)_2$ was used to generate sulfonyl radicals. It is always desirable to develop a transition metal-free protocol from medicinal chemistry point of view. Herein we wish to present a new method for the preparation of sulfonylated isoxazolines using sulfonyl hydrazides as the sulfonyl radical source under transition metal-free and mild conditions.

Sulfonyl hydrazides are easily available and shelf-stable reagents and have been widely applied in organic synthesis such as the sulfenylation reaction[16] and arylation reaction.[17] Furthermore, sulfonyl radicals could be readily generated from sulfonyl hydrazides and utilized for *in situ* radical sulfonylation of a variety of unsaturated substrates.[18] For example, Taniguchi *et al.*[18a] reported that sulfonyl radicals were generated from sulfonyl hydrazides using oxygen as the oxidant, and an iron salt as the catalyst. Li *et al.*[18b] showed that sulfonyl radicals could be generated from sulfonyl hydrazides with iodine as the catalyst and TBHP as the oxidant.

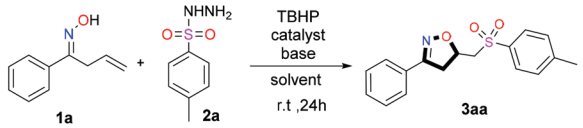
Results and discussion

Inspired by these literature results, we initiated the metal-free oxysulfonylation of alkenyl oximes using sulfonyl hydrazide as the sulfonyl source, and a variety of iodine sources as the catalysts in the presence of an appropriate amount of oxidant. It was assumed that ketoxime substrates and sulfonyl hydrazides would generate the corresponding free radicals in the presence of suitable oxidants provided that C=C double bonds in the substrates remained intact under the oxidation conditions. Intramolecular cyclization produced an isoxazolinomethyl free radical, and subsequent radical coupling yielded the desired sulfonylated isoxazolines.

To test this assumption, oxysulfonylation of β,γ-unsaturated ketoxime **1a** with *p*-toluenesulfonyl hydrazide **2a** was selected as the model reaction (Table 1). Initially, various oxidants such as TBHP, DTBP, and $K_2S_2O_8$ were tested. TBHP was found to be suitable for this protocol, and reactions with DTBP, $K_2S_2O_8$ and other oxidants were not successful.[19] The effect of bases was examined (entries 1–4) and the yield of **3aa** was increased to 30% when $NaHCO_3$ was used (entry 4). A slightly higher yield of the desired **3aa** was obtained when reaction media were changed to 1,4-dioxane (entry 7). Various catalysts containing iodine were screened (entries 8–13), and a pretty good isolated yield (91%) was observed when I_2 was utilized as the catalyst (entry 10). Transition-metal catalyst MnI_2 could also promote this reaction in a satisfactory yield, but FeI_2 and ZnI_2 seemed to be not suitable for this reaction. The product **3aa** was obtained in merely medium yield in the absence of base (entry 14).

Encouraged by these preliminary results, the synthetic viability of the reactions was studied using a series of

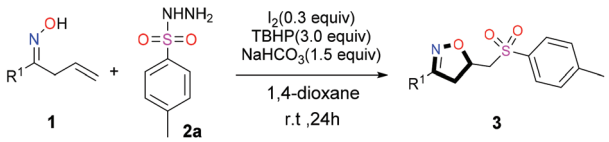
Table 1 Optimization of reaction conditions[a]

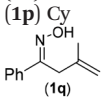
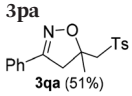


Entry	Base	Solvent	Catalyst	Yield[b] (%)
1	NaOAc	DCE	TBAI	24
2	NaOMe	DCE	TBAI	21
3	KF	DCE	TBAI	24
4	$NaHCO_3$	DCE	TBAI	30
5	$NaHCO_3$	MeCN	TBAI	20
6	$NaHCO_3$	THF	TBAI	28
7	$NaHCO_3$	Diox	TBAI	36
8	$NaHCO_3$	Diox	NaI	74
9	$NaHCO_3$	Diox	NIS	87
10	$NaHCO_3$	Diox	I_2	91
11	$NaHCO_3$	Diox	FeI_2	47
12	$NaHCO_3$	Diox	MnI_2	83
13	$NaHCO_3$	Diox	ZnI_2	Trace
14	None	Diox	I_2	44

[a] Reaction conditions: **1a** (0.25 mmol), **2a** (0.5 mmol, 2.0 equiv.), TBHP (70% aqueous solution, 0.75 mmol, 3.0 equiv.), solvent (2.0 mL), base (1.5 equiv.), catalyst (0.3 equiv.), under argon and stirring at room temperature for 24 h. [b] Isolated yield based on **1a**.

Table 2 Reaction scope of β,γ-unsaturated ketoximes[a]



Entry	R^1	Product	Yield[b] (%)
1	(**1a**) Ph	**3aa**	91
2	(**1b**) 4-FPh	**3ba**	87
3	(**1c**) 4-ClPh	**3ca**	84
4	(**1d**) 4-BrPh	**3da**	85
5	(**1e**) 4-CF_3Ph	**3ea**	80
6	(**1f**) 4-MePh	**3fa**	96
7	(**1g**) 4-OMePh	**3ga**	73
8	(**1h**) 3,4-DiMePh	**3ha**	94
9	(**1i**) 3-MePh	**3ia**	94
10	(**1j**) 2-OMePh	**3ja**	85
11	(**1k**) 4-Biphenyl	**3ka**	61
12	(**1l**) 2-Naphthyl	**3la**	82
13	(**1m**) 2-Thiophene	**3ma**	88
14	(**1n**) *t*-Butyl	**3na**	90
15	(**1o**) *n*-Hexane	**3oa**	79
16	(**1p**) Cy	**3pa**	64
17	 (**1q**)	 **3qa** (51%)	

[a] Reaction conditions: **1** (0.25 mmol), 2**a** (0.5 mmol, 2.0 equiv.), TBHP (0.75 mmol, 3.0 equiv.), I_2 (0.3 equiv.), $NaHCO_3$(1.5 equiv.), 1,4-dioxane (2.0 mL), under argon and stirring at room temperature for 24 h. [b] Isolated yield based on **1a**.

β,γ-unsaturated ketoximes **1** as the substrates and benzenesulfonyl hydrazide **2a** as the sulfonylating agent. The results are summarized in Table 2. As shown in Table 2, this reaction

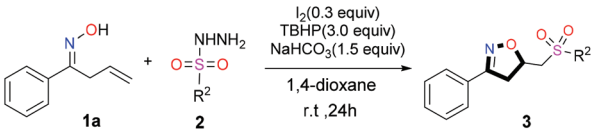
tolerated a wide range of ketoximes. First, various aromatic oximes with a *para*-substituent on the phenyl ring, substrates with both electron-withdrawing groups such as 4-F (**1b**), 4-Cl (**1c**), 4-Br (**1d**) or 4-CF_3 (**1e**) and electron-donating groups such as 4-Me (**1f**) and 4-MeO (**1g**) underwent the oxysulfonylation reactions smoothly, and the desired products (**3aa–3ga**) were obtained in good to excellent yields (entries 1–7). Reactions of ketoxime substrates bearing disubstituted (**1h**) or *m*-/*o*-substituted (**3ia**, **3ja**) benzene rings could also proceed pretty well (entries 8–10). To our delight, thiophene-containing oxime (**1m**) was found adaptable for the reaction and afforded the desired product in 88% yield. In addition, the reaction of aliphatic ketoximes (**1n–1p**) could proceed smoothly, and the target products **3na–3pa** were obtained in high yields. Moreover, product **3qa** containing a quaternary carbon center was obtained in 51% yield.

Then, the scope of sulfonyl hydrazides (**2b–2l**) was studied under the same conditions. The results are summarized in Table 3. The reaction of sulfonyl hydrazides with substituents at the *para*-position, either electron-donating or electron-withdrawing, gave the corresponding products (**3ad–3ah**) in high yields. The reaction of *meta*-substituted substrate **2c** gave product **3ac** in lower yield, and *ortho*-substituted substrate **2j** provided product **3aj** in poor yield, suggesting that the steric effect showed a significant effect on the course of the reaction. Furthermore, *para*-halogen substituted sulfonyl hydrazides (**2f–2h**) were smoothly involved in reactions and provided the target products (**3af–3ah**) in excellent yields. The reaction of alkyl sulfonyl hydrazide **2l** gave the desired product **3al** in low yield, possibly due to the low stability of the aliphatic sulfonyl radical.

To further investigate the applicability of this protocol, the reaction of γ,δ-unsaturated ketoxime **1r** was carried out to see if it could also undergo aminosulfonylation through N atom 5-*exo*-trig cyclization.[10b,11,13d] As shown in Table 4, a series of aryl sulfonyl hydrazides could participate smoothly in the reactions. The electronic properties of sulfonyl hydrazides showed a drastic effect on the course of the reactions when substrate **1r** was subjected to the reaction, probably due to the lower reactivity compared with that of β,γ-unsaturated ketoximes. In these cases, higher yield would be observed when an electron-donating substituent was present in sulfonyl hydrazides (**2a**, **2c**, **2d**). Low yield was observed when sulfonyl hydrazide bearing an electron-withdrawing substituent (**2g**) was subjected to the reaction. The structure of **4ra** was further confirmed by X-ray diffraction analysis.[19]

To demonstrate the application potential of this reaction, oxysulfonylation of substrate **1a** with **2a** was carried out on the gram scale under the optimized conditions, and the desired product **3aa** was obtained in 70% isolated yield (Scheme 2a). In addition, the [3 + 2] cycloaddition of nitrones with dipolarophiles was performed using **4ra** and methyl propiolate as starting materials.[20] As expected, the desired product **5** was obtained in 75% yield as a *cis*-diastereomer with a high diastereoselectivity.[13d,20] The relative configuration of the compound was further confirmed by ^{1}H-NMR and NOE experiments (Scheme 2b).[19]

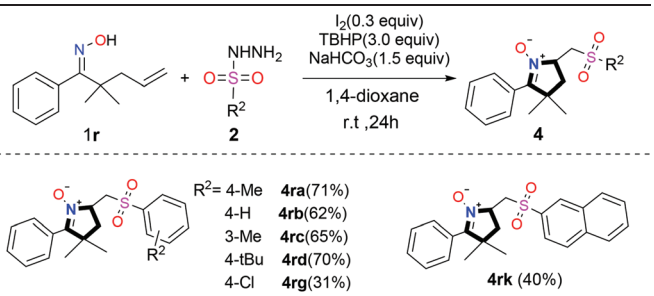
Table 3 Reaction scope of sulfonyl hydrazides[a]



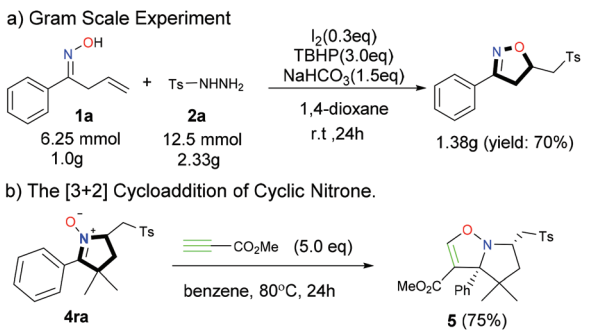
Entry	R^2	Product	Yield[b] (%)
1	(**2b**) Ph	**3ab**	98
2	(**2c**) 3-MePh	**3ac**	82
3	(**2d**) 4-tBuPh	**3ad**	86
4	(**2e**) 4-OMePh	**3ae**	91
5	(**2f**) 4-FPh	**3af**	91
6	(**2g**) 4-ClPh	**3ag**	96
7	(**2h**) 4-BrPh	**3ah**	95
8	(**2i**) 4-CF3Ph	**3ai**	79
9	(**2j**) 2-FPh	**3aj**	35
10	(**2k**) 2-naphthyl	**3ak**	94
11	(**2l**) *n*-Bu	**3al**	38

[a] Reaction conditions: **1a** (0.25 mmol), **2** (0.5 mmol, 2.0 equiv.), TBHP (0.75 mmol, 3.0 equiv.), I_2 (0.3 equiv.), $NaHCO_3$ (1.5 equiv.), 1,4-dioxane (2.0 mL), under argon and stirring at room temperature for 24 h. [b] Isolated yield based on **1a**.

Table 4 Scope of γ,δ-unsaturated ketoximes[a,b]



[a] Reaction conditions: **1r** (0.25 mmol), **2** (0.5 mmol, 2.0 equiv.), TBHP (0.75 mmol, 3.0 equiv.), I_2 (0.3 equiv.), $NaHCO_3$ (1.5 equiv.), 1,4-dioxane (2.0 mL), under argon and stirring at room temperature for 24 h. [b] Isolated yield based on **1r**.

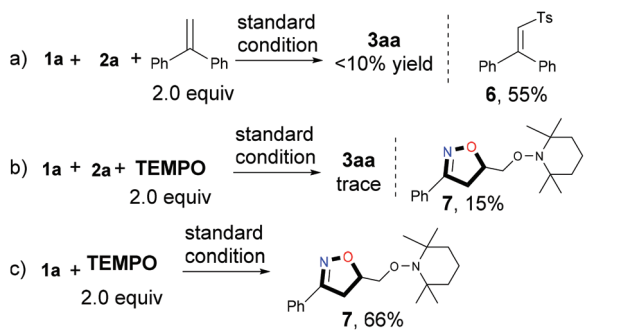


Scheme 2 Extension of the scopes of the reactions.

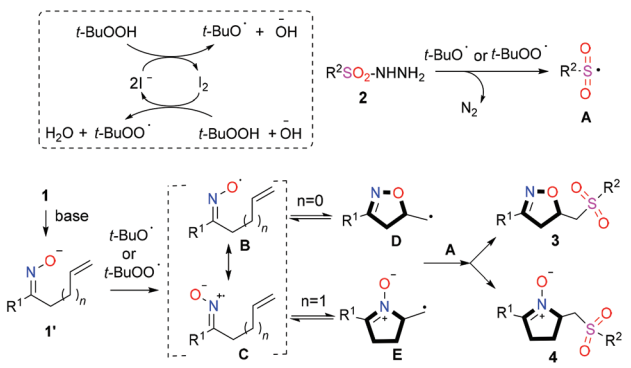
Control reactions were performed to understand the mechanism of the reactions. First, 2.0 equiv. of 1,1-diphenylethylene was added to the reaction mixture of the model reaction, merely less than 10% yield of **3aa** was obtained, but (2-tosylethene-1,1-diyl)dibenzene **6** was isolated in 55% yield, indicating the participation of sulfonyl radicals in the reaction. (Scheme 3a) Then, the radical scavenger TEMPO was added to the reaction system. The oxysulfonylation reaction was almost completely inhibited and the TEMPO-trapped isoxazoline **7** was obtained in 15% yield. In addition, when TEMPO was used as a substrate instead of *p*-tosylhydrazine **2a**, the desired product **7** was obtained up to 66% yield, suggesting the involvement of an iminoxyl radical intermediate in the reaction (Scheme 3b and c).

Based on these observations and the previously reported results, a plausible reaction pathway is proposed in Scheme 4. Initially, TBHP is decomposed to give *tert*-butoxyl and *tert*-butylperoxy radicals with the assistance of iodine. The reaction of sulfonyl hydrazide **2** with these radicals generates sulfonyl radical **A** and releases molecular nitrogen.

The anionic intermediate **1′** was first afforded through the deprotonation of the β,γ-unsaturated oxime **1** with $NaHCO_3$. Single-electron oxidation of **1′** by *t*-BuO˙ or *t*-BuOO˙ gave the O-centered radical **B** or N-centered radical **C**. As reported,[13d] the iminoxyl radical can undergo both O- and N-atom 5-*exo*-trig radical cyclization depending on the structure of the substrates, providing the C-centered radical intermediates **D** and **E**, respectively. Finally, the C-centered radical **D** or **E** reacts with sulfonyl radical **A** to provide the sulfonylated isoxazoline **3** or nitrone **4**, respectively.



Scheme 3 Control reactions.



Scheme 4 Plausible pathway of the reaction.

Conclusions

In summary, we have reported an efficient oxysulfonylation reaction of ketoximes with sulfonyl hydrazides. In the presence of an iodine catalyst and a suitable oxidant, a range of desired sulfonylated isoxazolines were obtained with moderate to excellent yields under mild conditions. Sulfonylated nitrones could be obtained in good yields under the same conditions. Application of this transformation in organic synthesis is underway.

Experimental

Experimental details

Reactions were carried out with commercially available reagents in oven-dried apparatus. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker DRX 400 spectrometer at 298 K using deuterated chloroform as the solvent and TMS as the internal reference. Column chromatography was performed employing 200–300 mesh silica gel unless otherwise noted. Thin layer chromatography (TLC) was performed on silica gel GF_{254}. Melting points were measured on a digital melting-point apparatus without correction of the thermometer. HRMS analyses were carried out with a Varian FTICR-MS 7.0T. IR spectra were recorded on a BRUKER TENSOR 37. Unless otherwise indicated, starting materials and reagents used in the study were purchased and were used as received without further purification.

General procedure for the synthesis of compounds 3

A 35 mL Schlenk-type tube equipped with a magnetic stir bar was charged with β,γ-unsaturated ketoxime **1a** (0.25 mmol, 40 mg) and *p*-toluenesulfonyl hydrazide **2a** (0.5 mmol, 95 mg). Then, I_2 (9.5 mg), $NaHCO_3$ (0.375 mmol, 32 mg), TBHP (0.75 mmol, 97 mg, 70% solution in water), and 1,4-dioxane (2 mL) were added to this system. Hereafter, the reaction tube was purged with argon and the reaction mixture was stirred at room temperature for 24 h. Then, the reaction mixture was filtered and evaporated to give the crude product. The residue was purified by column chromatography (ethyl acetate : petroleum ether = 1 : 10, v/v) to afford the desired product **3aa**.

General procedure for the synthesis of compounds 4

A 35 mL Schlenk-type tube equipped with a magnetic stir bar was charged with γ,δ-unsaturated ketoxime **1r** (0.25 mmol, 51 mg) and *p*-toluenesulfonyl hydrazide **2a** (0.5 mmol, 95 mg). Then, I_2 (9.5 mg), $NaHCO_3$ (0.375 mmol, 32 mg), TBHP (0.75 mmol, 97 mg, 70% solution in water), and 1,4-dioxane

(2 mL) were added to this system. The reaction tube was purged with argon. After stirring at room temperature for 24 h, the reaction mixture was filtered and evaporated to obtain the crude product. The residue was purified by column chromatography (ethyl acetate : petroleum ether = 1 : 2, v/v) to afford the desired product **4ra**.

3-Phenyl-5-tosylmethyl-4,5-dihydroisoxazole (3aa). Compound **3aa** was prepared according to the general procedure and was isolated as a white solid (71.7 mg, 91% yield) after flash chromatography (EtOAc/petroleum ether 10% v/v). M.p. 95–98 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74 (d, J = 8.0 Hz, 2H), 7.59–7.53 (m, 2H), 7.36–7.27 (m, 5H), 5.08–4.93 (m, 1H), 3.58–3.45 (m, 2H), 3.32 (m, 2H), 2.38 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 156.8, 145.3, 136.5, 130.5, 130.1, 128.8, 128.1, 126.8, 74.8, 59.9, 40.4, 21.7. The NMR data were in agreement with reported results.[15]

3-(4-Fluorophenyl)-5-tosylmethyl-4,5-dihydroisoxazole (3ba). Compound **3ba** was prepared according to the general procedure and was isolated as a light-yellow solid (72.5 mg, 87% yield) after flash chromatography (EtOAc/petroleum ether 10% v/v). M.p. 144–147 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75 (d, J = 7.8 Hz, 2H), 7.61–7.52 (m, 2H), 7.32 (d, J = 7.8 Hz, 2H), 7.02 (t, J = 8.3 Hz, 2H), 5.09–4.94 (m, 1H), 3.57–3.47 (m, 2H), 3.38 (dd, J = 17.1, 7.2 Hz, 1H), 3.28 (dd, J = 14.0, 8.8 Hz, 1H), 2.39 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.9 (d, J = 251.4 Hz), 155.9, 145.4, 136.3, 130.2, 128.83 (d, J = 8.5 Hz), 128.0, 125.1 (d, J = 3.3 Hz), 116.0 (d, J = 22.0 Hz), 74.9, 59.8, 40.4, 21.7. ^{19}F NMR (376 MHz, $CDCl_3$) δ −109.1. IR (KBr): ν = 2980.3, 2919.1, 1602.0, 1511.9, 1287.8, 1138.6, 907.4, 836.6 cm^{-1}. HRMS-ESI (m/z): $[M + H]^+$ calcd for: $C_{17}H_{17}FNO_3S^+$, 334.0908; found: 334.0913.

3-(4-Chlorophenyl)-5-tosylmethyl-4,5-dihydroisoxazole (3ca). Compound **3ca** was prepared according to the general procedure and was isolated as a light-yellow solid (73.4 mg, 84% yield) after flash chromatography (EtOAc/petroleum ether 10% v/v). M.p. 148–151 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74 (d, J = 7.6 Hz, 2H), 7.50 (d, J = 7.7 Hz, 2H), 7.36–7.27 (m, 4H), 5.10–4.96 (m, 1H), 3.59–3.45 (m, 2H), 3.42–3.23 (m, 2H), 2.39 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 156.0, 145.4, 136.5, 136.3, 130.2, 129.1, 128.0, 127.3, 75.1, 59.8, 40.2, 21.7. The NMR data were in agreement with reported results.[15]

3-(4-Bromophenyl)-5-tosylmethyl-4,5-dihydroisoxazole (3da). Compound **3da** was prepared according to the general procedure and was isolated as a light-yellow solid (83.8 mg, 85% yield) after flash chromatography (EtOAc/petroleum ether 10% v/v). M.p. 160–162 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74 (d, J = 7.5 Hz, 2H), 7.50–7.41 (m, 4H), 7.32 (d, J = 7.8 Hz, 2H), 5.11–4.95 (m, 1H), 3.58–3.46 (m, 2H), 3.42–3.23 (m, 2H), 2.40 (s, 3H).^{13}C NMR (101 MHz, $CDCl_3$) δ 156.1, 145.4, 136.3, 132.1, 130.2, 128.2, 128.0, 127.7, 124.9, 75.1, 59.7, 40.1, 21.7. The NMR data were in agreement with reported results.[15]

5-Tosylmethyl-3-[4-(trifluoromethyl)phenyl]-4,5-dihydroisoxazole (3ea). Compound **3ea** was prepared according to the general procedure and was isolated as a white solid (76.7 mg, 80% yield) after flash chromatography (EtOAc/petroleum ether 10% v/v). M.p. 204–207 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.73 (dd, J = 22.8, 8.0 Hz, 4H), 7.60 (d, J = 8.1 Hz, 2H), 7.33 (d, J = 7.9 Hz, 2H), 5.14–5.01 (m, 1H), 3.62–3.51 (m, 2H), 3.43 (dd, J = 17.2, 7.4 Hz, 1H), 3.30 (dd, J = 14.0, 8.8 Hz, 1H), 2.40 (s, 3H).^{13}C NMR (101 MHz, $CDCl_3$) δ 155.9, 145.5, 136.3, 132.2, 132.16 (q, J = 32.9 Hz), 130.2, 128.0, 127.1, 125.80 (q, J = 3.8 Hz), 123.71 (q, J = 272.2 Hz), 75.4, 59.7, 40.0, 21.7. ^{19}F NMR (376 MHz, $CDCl_3$) δ −63.0. IR (KBr): ν = 2928.6, 1329.6, 1116.6, 909.4, 847.1, 568.3 cm^{-1}. HRMS-ESI (m/z): $[M + Na]^+$ calcd for: $C_{18}H_{16}F_3NNaO_3S^+$, 406.0695; found: 406.0698.

3-(*p*-Tolyl)-5-tosylmethyl-4,5-dihydroisoxazole (3fa). Compound **3fa** was prepared according to the general procedure and was isolated as a light-yellow solid (79.1 mg, 96% yield) after flash chromatography (EtOAc/petroleum ether 10% v/v). M.p. 125–127 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75 (d, J = 7.4 Hz, 2H), 7.46 (d, J = 7.4 Hz, 2H), 7.32 (d, J = 7.7 Hz, 2H), 7.14 (d, J = 7.6 Hz, 2H), 5.07–4.94 (m, 1H), 3.59–3.46 (m, 2H), 3.36 (dd, J = 17.1, 6.9 Hz, 1H), 3.27 (dd, J = 13.7, 8.8 Hz, 1H), 2.39 (s, 3H), 2.31 (s, 3H).^{13}C NMR (101 MHz, $CDCl_3$) δ 156.8, 145.3, 140.9, 136.4, 130.1, 129.5, 128.1, 126.8, 125.9, 74.6, 59.9, 40.5, 21.7, 21.5. The NMR data were in agreement with reported results.[15]

3-(4-Methoxyphenyl)-5-tosylmethyl-4,5-dihydroisoxazole (3ga). Compound **3ga** was prepared according to the general procedure and was isolated as a white solid (63.0 mg, 73% yield) after flash chromatography (EtOAc/petroleum ether 15% v/v). M.p. 149–152 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75 (d, J = 8.0 Hz, 2H), 7.51 (d, J = 8.6 Hz, 2H), 7.31 (d, J = 7.9 Hz, 2H), 6.84 (d, J = 8.5 Hz, 2H), 5.05–4.93 (m, 1H), 3.76 (s, 3H), 3.56–3.45 (m, 2H), 3.40–3.23 (m, 2H), 2.39 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 161.4, 156.4, 145.3, 136.4, 130.1, 128.4, 128.1, 121.3, 114.2, 74.5, 59.9, 55.4, 40.6, 21.7. The NMR data were in agreement with reported results.[15]

3-(3,4-Dimethylphenyl)-5-tosylmethyl-4,5-dihydroisoxazole (3ha). Compound **3ha** was prepared according to the general procedure and was isolated as a light-yellow solid (80.7 mg, 94% yield,) after flash chromatography (EtOAc/petroleum ether 10% v/v). M.p. 110–113 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75 (d, J = 7.7 Hz, 2H), 7.39–7.25 (m, 4H), 7.08 (d, J = 7.7 Hz, 1H), 5.05–4.92 (m, 1H), 3.57–3.45 (m, 2H), 3.36 (dd, J = 17.1, 7.0 Hz, 1H), 3.27 (dd, J = 13.9, 8.7 Hz, 1H), 2.39 (s, 3H), 2.20 (s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 157.0, 145.3, 139.6, 137.2, 136.4, 130.1, 130.0, 128.1, 127.9, 126.2, 124.4, 74.6, 59.9, 40.5, 21.7, 19.8, 19.7. IR (KBr): ν = 2920.4, 1596.9, 1296.7, 1139.9, 913.5, 814.3, 564.4 cm^{-1}. HRMS-ESI (m/z): $[M + Na]^+$ calcd for: $C_{19}H_{21}NNaO_3S^+$, 366.1134; found: 366.1139.

3-(*m*-Tolyl)-5-tosylmethyl-4,5-dihydroisoxazole (3ia). Compound **3ia** was prepared according to the general procedure and was isolated as a light-yellow solid (77.4 mg, 94% yield) after flash chromatography (EtOAc/petroleum ether 10% v/v). M.p. 113–116 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75 (d, J = 7.6 Hz, 2H), 7.47–7.30 (m, 4H), 7.28–7.13 (m, 2H), 5.17–4.86 (m, 1H), 3.59–3.49 (m, 2H), 3.38 (dd, J = 17.1, 7.1 Hz, 1H), 3.27 (dd, J = 13.9, 8.8 Hz, 1H), 2.39 (s, 3H), 2.30 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 157.0, 145.3, 138.6, 136.4, 131.3, 130.1, 128.7, 128.6, 128.1, 127.4, 124.0, 74.7, 59.9, 40.4, 21.7, 21.3. The NMR data were in agreement with reported results.[15]

3-(2-Mthoxyphenyl)-5-tosylmethyl-4,5-dihydroisoxazole (3ja). Compound **3ja** was prepared according to the general procedure and was isolated as a light-yellow solid (73.4 mg, 85% yield) after flash chromatography (EtOAc/petroleum ether 10% v/v). M.p. 95–98 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75 (d, J = 7.4 Hz, 2H), 7.58 (d, J = 7.6 Hz, 1H), 7.31 (d, J = 7.2 Hz, 3H), 6.94–6.82 (m, 2H), 5.05–4.87 (m, 1H), 3.77 (s, 3H), 3.59 (dd, J = 17.6, 10.3 Hz, 1H), 3.54–3.36 (m, 2H), 3.29 (dd, J = 13.9, 8.2 Hz, 1H), 2.39 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 157.6, 156.5, 145.2, 136.5, 131.7, 130.1, 129.4, 128.1, 120.8, 117.9, 111.4, 74.7, 60.0, 55.5, 43.0, 21.7. The NMR data were in agreement with reported results.[15]

3-[(1,1′-Biphenyl)-4-yl]-5-tosylmethyl-4,5-dihydroisoxazole (3ka). Compound **3ka** was prepared according to the general procedure and was isolated as a white solid (59.7 mg, 61% yield) after flash chromatography (EtOAc/petroleum ether 10% v/v). M.p. 176–179 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76 (d, J = 8.3 Hz, 2H), 7.64 (d, J = 8.4 Hz, 2H), 7.59–7.50 (m, 4H), 7.38 (t, J = 7.5 Hz, 2H), 7.35–7.29 (m, 3H), 5.13–4.95 (m, 1H), 3.63–3.49 (m, 2H), 3.42 (dd, J = 17.1, 7.2 Hz, 1H), 3.30 (dd, J = 14.0, 8.7 Hz, 1H), 2.39 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 156.6, 145.4, 143.2, 140.0, 136.4, 130.2, 128.9, 128.1, 127.9, 127.6, 127.4, 127.3, 127.1, 74.9, 59.9, 40.4, 21.7. IR (KBr): ν = 2919.7, 1595.3, 1316.5, 1150.6, 1085.7, 764.4, 567.5 cm^{-1}. HRMS-ESI (m/z): [M + Na]$^+$ calcd for: $C_{23}H_{21}NNaO_3S^+$, 414.1134; found: 414.1138.

3-(Naphthalen-2-yl)-5-tosylmethyl-4,5-dihydroisoxazole (3la). Compound **3la** was prepared according to the general procedure and was isolated as a light-yellow solid (74.9 mg, 82% yield) after flash chromatography (EtOAc/petroleum ether 10% v/v). M.p. 147–150 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90–7.81 (m, 2H), 7.81–7.72 (m, 5H), 7.54–7.43 (m, 2H), 7.32 (d, J = 7.6 Hz, 2H), 5.13–4.99 (m, 1H), 3.71–3.46 (m, 3H), 3.32 (dd, J = 13.4, 9.2 Hz, 1H), 2.39 (s, 3H).^{13}C NMR (101 MHz, $CDCl_3$) δ 157.0, 145.4, 136.4, 134.2, 132.9, 130.2, 128.7, 128.5, 128.1, 127.9, 127.4, 126.9, 126.3, 123.4, 75.0, 59.9, 40.3, 21.7. The NMR data were in agreement with reported results.[15]

3-(Thiophen-2-yl)-5-tosylmethyl-4,5-dihydroisoxazole (3ma). Compound **3ma** was prepared according to the general procedure and was isolated as a yellow solid (70.7 mg, 88% yield) after flash chromatography (EtOAc/petroleum ether 10% v/v). M.p. 120–122 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74 (d, J = 8.3 Hz, 2H), 7.37–7.28 (m, 3H), 7.17–7.13 (m, 1H), 7.05–6.96 (m, 1H), 5.11–4.91 (m, 1H), 3.63–3.48 (m, 2H), 3.40 (dd, J = 16.9, 7.2 Hz, 1H), 3.29 (dd, J = 14.0, 8.7 Hz, 1H), 2.39 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 152.6, 145.4, 136.3, 131.1, 130.1, 129.1, 128.9, 128.1, 127.5, 75.0, 59.7, 41.1, 21.7. The NMR data were in agreement with reported results.[15]

3-(*tert*-Butyl)-5-tosylmethyl-4,5-dihydroisoxazole (3na). Compound **3na** was prepared according to the general procedure and was isolated as a white solid (66.5 mg, 90% yield) after flash chromatography (EtOAc/petroleum ether 10% v/v). M.p. 93–95 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.73 (d, J = 8.3 Hz, 2H), 7.31 (d, J = 8.1 Hz, 2H), 4.88–4.70 (m, 1H), 3.44 (dd, J = 14.0, 4.4 Hz, 1H), 3.22–3.08 (m, 2H), 2.98 (dd, J = 17.2, 7.2 Hz, 1H), 2.39 (s, 3H), 1.12 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.5, 145.2, 136.4, 130.1, 128.0, 74.0, 59.7, 39.8, 33.1, 28.0, 21.7. The NMR data were in agreement with reported results.[15]

3-Pentyl-5-tosylmethyl-4,5-dihydroisoxazole (3oa). Compound **3oa** was prepared according to the general procedure and was isolated as a white solid (61.1 mg, 79% yield) after flash chromatography (EtOAc/petroleum ether 10% v/v). M.p. 72–75 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.72 (d, J = 8.3 Hz, 2H), 7.31 (d, J = 8.1 Hz, 2H), 4.88–4.73 (m, 1H), 3.44 (dd, J = 14.0, 4.5 Hz, 1H), 3.23–3.06 (m, 2H), 2.93 (dd, J = 17.4, 7.0 Hz, 1H), 2.39 (s, 3H), 2.26 (t, J = 7.7 Hz, 2H), 1.48 (p, J = 7.5 Hz, 2H), 1.32–1.21 (m, 4H), 0.82 (t, J = 6.9 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.5, 145.2, 136.4, 130.1, 128.0, 73.5, 59.8, 42.4, 31.3, 27.5, 25.9, 22.3, 21.7, 13.9. IR (KBr): ν = 2924.9, 2861.2, 1597.9, 1318.8, 1147.8, 1087.8, 814.8, 563.3, 521.6 cm^{-1}. HRMS-ESI (m/z): [M + Na]$^+$ calcd for: $C_{16}H_{23}NNaO_3S^+$, 332.1291; found: 332.1295.

3-Cyclohexyl-5-tosylmethyl-4,5-dihydroisoxazole (3pa). Compound **3pa** was prepared according to the general procedure and was isolated as a white solid (51.4 mg, 64% yield) after flash chromatography (EtOAc/petroleum ether 20% v/v). M.p. 64–67 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.71 (d, J = 8.3 Hz, 2H), 7.30 (d, J = 8.0 Hz, 2H), 4.85–4.69 (m, 1H), 3.42 (dd, J = 14.1, 4.6 Hz, 1H), 3.21–3.02 (m, 2H), 2.92 (dd, J = 17.3, 7.0 Hz, 1H), 2.38 (s, 3H), 2.35–2.25 (m, 1H), 1.85–1.65 (m, 4H), 1.61 (d, J = 11.8 Hz, 1H), 1.30–1.17 (m, 4H), 1.15–1.06 (m, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.1, 145.2, 136.4, 130.1, 128.0, 73.4, 59.8, 40.8, 37.1, 30.3, 30.2, 25.8, 25.7, 21.7. IR (KBr): ν = 2928.5, 2853.3, 1448.6, 1302.5, 1150.7, 819.1, 566.6 cm^{-1}. HRMS-ESI (m/z): [M + Na]$^+$ calcd for: $C_{17}H_{23}NNaO_3S^+$, 344.1291; found: 344.1295.

5-Mehyl-3-phenyl-5-tosylmethyl-4,5-dihydroisoxazole (3qa). Compound **3qa** was prepared according to the general procedure and was isolated as a white solid (42.0 mg, 51% yield) after flash chromatography (EtOAc/petroleum ether 10% v/v). M.p. 110–113 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77–7.69 (m, 2H), 7.61–7.55 (m, 2H), 7.40–7.26 (m, 5H), 3.91 (d, J = 18.9 Hz, 1H), 3.43 (s, 2H), 3.16 (d, J = 17.2 Hz, 1H), 2.38 (s, 3H), 1.65 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 157.3, 145.1, 137.6, 130.3, 130.0, 129.3, 128.8, 127.8, 126.7, 84.1, 63.0, 44.8, 26.2, 21.7. The NMR data were in agreement with reported results.[15]

3-Phenyl-5-[(phenylsulfonyl)methyl]-4,5-dihydroisoxazole (3ab). Compound **3ab** was prepared according to the general procedure and was isolated as a light-yellow solid (73.8 mg, 98% yield) after flash chromatography (EtOAc/petroleum ether 10% v/v). M.p. 140–142 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.88 (d, J = 7.8 Hz, 2H), 7.69–7.49 (m, 5H), 7.44–7.27 (m, 3H), 5.12–4.98 (m, 1H), 3.62–3.47 (m, 2H), 3.43–3.25 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 156.9, 139.3, 134.3, 130.6, 129.5, 128.8, 128.7, 128.1, 126.8, 74.7, 59.8, 40.4. The NMR data were in agreement with reported results.[15]

3-Phenyl-5-[(*m*-tolylsulfonyl)methyl]-4,5-dihydroisoxazole (3ac). Compound **3ac** was prepared according to the general procedure and was isolated as a light-yellow solid (64.6 mg, 82% yield) after flash chromatography (EtOAc/petroleum ether 10% v/v). M.p. 133–136 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.71–7.65 (m, 2H), 7.63–7.53 (m, 2H), 7.47–7.42 (m, 2H), 7.38–7.30 (m,

3H), 5.14–4.87 (m, 1H), 3.67–3.48 (m, 2H), 3.41 (dd, J = 17.1, 7.1 Hz, 1H), 3.29 (dd, J = 14.0, 8.9 Hz, 1H), 2.39 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 156.9, 139.9, 139.1, 135.1, 130.6, 129.4, 128.8, 128.7, 128.3, 126.8, 125.2, 74.7, 59.7, 40.4, 21.4. The NMR data were in agreement with reported results.[15]

5-{[4-(*tert*-Butylphenyl)sulfonyl]methyl}-3-phenyl-4,5-dihydroisoxazole (3ad). Compound **3ad** was prepared according to the general procedure and was isolated as a light-yellow solid (76.8 mg, 86% yield) after flash chromatography (EtOAc/petroleum ether 10% v/v). M.p. 123–125 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79 (d, J = 8.3 Hz, 2H), 7.64–7.48 (m, 4H), 7.44–7.28 (m, 3H), 5.16–4.94 (m, 1H), 3.62–3.48 (m, 2H), 3.40 (dd, J = 17.1, 7.1 Hz, 1H), 3.29 (dd, J = 13.9, 9.2 Hz, 1H), 1.29 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.3, 156.9, 136.3, 130.5, 128.8, 128.8, 127.9, 126.8, 126.6, 74.8, 59.7, 40.3, 35.4, 31.1. IR (KBr): ν = 2966.3, 1595.6, 1311.5, 1159.0, 889.9, 763.7, 572.4 cm^{-1}. HRMS-ESI (m/z): $[M + Na]^+$ calcd for: $C_{20}H_{23}NNaO_3S^+$, 380.1291; found: 380.1295.

5-{[(4-Methoxyphenyl)sulfonyl]methyl}-3-phenyl-4,5-dihydroisoxazole (3ae). Compound **3ae** was prepared according to the general procedure and was isolated as a light-yellow solid (75.5 mg, 91% yield) after flash chromatography (EtOAc/petroleum ether 10% v/v). M.p. 114–117 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80 (d, J = 8.0 Hz, 2H), 7.65–7.52 (m, 2H), 7.44–7.28 (m, 3H), 7.06–6.88 (m, 2H), 5.12–4.92 (m, 1H), 3.82 (s, 3H), 3.62–3.46 (m, 2H), 3.44–3.21 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 164.1, 156.9, 130.8, 130.5, 130.3, 128.8, 128.8, 126.8, 114.7, 74.9, 60.1, 55.8, 40.4. The NMR data were in agreement with reported results.[15]

5-{[(4-Fluorophenyl)sulfonyl]methyl}-3-phenyl-4,5-dihydroisoxazole (3af). Compound **3af** was prepared according to the general procedure and was isolated as a light-yellow solid (72.7 mg, 91% yield) after flash chromatography (EtOAc/petroleum ether 10% v/v). M.p. 128–130 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.96–7.85 (m, 2H), 7.63–7.52 (m, 2H), 7.41–7.29 (m, 3H), 7.26–7.15 (m, 2H), 5.16–5.01 (m, 1H), 3.63–3.48 (m, 2H), 3.41–3.25 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.1 (d, J = 257.2 Hz), 156.8, 135.4 (d, J = 3.0 Hz), 131.1 (d, J = 9.7 Hz), 130.6, 128.9, 128.6, 126.8, 116.8 (d, J = 22.7 Hz), 74.7, 60.1, 40.4. ^{19}F NMR (376 MHz, $CDCl_3$) δ −102.4. The NMR data were in agreement with reported results.[15]

5-{[(4-Chlorophenyl)sulfonyl]methyl}-3-phenyl-4,5-dihydroisoxazole (3ag). Compound **3ag** was prepared according to the general procedure and was isolated as a light-yellow solid (80.6 mg, 96% yield) after flash chromatography (EtOAc/petroleum ether 10% v/v). M.p. 142–145 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.88–7.77 (m, 2H), 7.57 (dd, J = 7.7, 1.8 Hz, 2H), 7.54–7.49 (m, 2H), 7.38–7.30 (m, 3H), 5.14–5.01 (m, 1H), 3.61–3.48 (m, 2H), 3.42–3.24 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 156.8, 141.1, 137.8, 130.6, 129.8, 129.6, 128.9, 128.6, 126.8, 74.7, 60.0, 40.4. The NMR data were in agreement with reported results.[15]

5-{[(4-Bromophenyl)sulfonyl]methyl}-3-phenyl-4,5-dihydroisoxazole (3ah). Compound **3ah** was prepared according to the general procedure and was isolated as a yellow solid (90.3 mg, 95% yield) after flash chromatography (EtOAc/petroleum ether 10% v/v). M.p. 147–150 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.78–7.71 (m, 2H), 7.70–7.65 (m, 2H), 7.57 (dd, J = 7.7, 1.8 Hz, 2H), 7.40–7.30 (m, 3H), 5.15–5.01 (m, 1H), 3.60–3.49 (m, 2H), 3.40–3.26 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 156.8, 138.4, 132.8, 130.6, 129.7, 129.7, 128.9, 128.6, 126.8, 74.6, 60.0, 40.4. IR (KBr): ν = 3082.0, 2932.9, 1571.5, 1302.0, 1141.8, 757.1, 611.4 cm^{-1}. HRMS-ESI (m/z): $[M + H]^+$ calcd for: $C_{16}H_{15}BrNO_3S^+$, 379.9951; found: 379.9955.

3-Phenyl-5-{[(4-trifluoromethylphenyl)sulfonyl]methyl}-4,5-dihydroisoxazole (3ai). Compound **3ai** was prepared according to the general procedure and was isolated as a white solid (72.9 mg, 79% yield) after flash chromatography (EtOAc/petroleum ether 10% v/v). M.p. 153–155 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.04 (d, J = 8.2 Hz, 2H), 7.80 (d, J = 8.3 Hz, 2H), 7.63–7.52 (m, 2H), 7.42–7.27 (m, 3H), 5.22–4.98 (m, 1H), 3.64–3.50 (m, 2H), 3.42–3.28 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 156.8, 142.9, 135.87 (q, J = 33.0 Hz), 130.7, 128.9, 128.9, 128.5, 126.8, 126.62 (q, J = 3.4 Hz), 123.04 (q, J = 273.1 Hz), 74.5, 59.9, 40.4. ^{19}F NMR (376 MHz, $CDCl_3$) δ −63.2. IR (KBr): ν = 2931.5, 1403.1, 1326.0, 1129.6, 842.8, 759.6, 607.3 cm^{-1}. HRMS-ESI (m/z): $[M + Na]^+$ calcd for: $C_{17}H_{14}F_3NNaO_3S^+$, 392.0539; found: 392.0543.

5-{[(2-Fluorophenyl)sulfonyl]methyl}-3-phenyl-4,5-dihydroisoxazole (3aj). Compound **3aj** was prepared according to the general procedure and was isolated as a yellow solid (27.9 mg, 35% yield) after flash chromatography (EtOAc/petroleum ether 10% v/v). M.p. 109–111 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.99–7.82 (m, 1H), 7.69–7.53 (m, 3H), 7.40–7.28 (m, 4H), 7.26–7.14 (m, 1H), 5.28–4.93 (m, 1H), 3.79 (dd, J = 14.0, 4.5 Hz, 1H), 3.65–3.29 (m, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.7 (d, J = 256.1 Hz), 156.8, 136.7 (d, J = 8.6 Hz), 130.6, 130.4, 128.8, 128.7, 127.4, 127.2, 126.8, 124.9 (d, J = 3.7 Hz), 117.4 (d, J = 21.1 Hz), 74.5, 59.4, 40.5. ^{19}F NMR (376 MHz, $CDCl_3$) δ −108.7. IR (KBr): ν = 2925.5, 1597.8, 1475.3, 1312.4, 1140.6, 906.1, 761.0, 689.5 cm^{-1}. HRMS-ESI (m/z): $[M + Na]^+$ calcd for: $C_{16}H_{14}FNNaO_3S^+$, 342.0571; found: 342.0575.

5-[(Naphthalen-2-ylsulfonyl)methyl]-3-phenyl-4,5-dihydroisoxazole (3ak). Compound **3ak** was prepared according to the general procedure and was isolated as a yellow solid (82.6 mg, 94% yield) after flash chromatography (EtOAc/petroleum ether 10% v/v). M.p. 169–171 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.46 (s, 1H), 8.03–7.79 (m, 4H), 7.70–7.50 (m, 4H), 7.41–7.27 (m, 3H), 5.18–4.97 (m, 1H), 3.69–3.52 (m, 2H), 3.51–3.32 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 156.9, 136.1, 135.5, 132.2, 130.6, 130.0, 129.9, 129.6, 129.5, 128.8, 128.7, 128.1, 127.9, 126.8, 122.4, 74.8, 59.8, 40.4. IR (KBr): ν = 3057.3, 1300.8, 1143.4, 1125.2, 910.0, 819.7, 780.5 cm^{-1}. HRMS-ESI (m/z): $[M + Na]^+$ calcd for: $C_{20}H_{17}NNaO_3S^+$, 374.0821; found: 374.0825.

5-[(Butylsulfonyl)methyl]-3-phenyl-4,5-dihydroisoxazole (3al). Compound **3al** was prepared according to the general procedure and was isolated as a yellow solid (26.7 mg, 38% yield) after flash chromatography (EtOAc/petroleum ether 10% v/v). M.p. 89–92 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.66–7.51 (m, 2H), 7.43–7.26 (m, 3H), 5.32–5.06 (m, 1H), 3.57 (dd, J = 17.0, 10.5 Hz, 1H), 3.42 (dd, J = 14.5, 7.5 Hz, 1H), 3.24 (dd, J = 17.0, 7.0 Hz, 1H), 3.14–3.01 (m, 3H), 1.88–1.67 (m, 2H), 1.53–1.33 (m,

2H), 0.91 (t, J = 7.4 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 157.0, 130.7, 128.9, 128.6, 126.9, 75.0, 56.9, 54.5, 40.5, 23.8, 21.7, 13.6. IR (KBr): ν = 2955.3, 2869.9, 1267.7, 1132.1, 912.2, 756.8, 691.5 cm^{-1}. HRMS-ESI (m/z): [M + Na]$^+$ calcd for: $C_{14}H_{19}NNaO_3S^+$, 304.0978; found: 304.0982.

4,4-Dimethyl-5-phenyl-2-tosylmethyl-3,4-dihydro-2*H*-pyrrole 1-oxide (4ra). Compound **4ra** was prepared according to the general procedure and was isolated as a white solid (63.4 mg, 71% yield) after flash chromatography (EtOAc/petroleum ether 50% v/v). M.p. 169–172 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.81–7.72 (m, 4H), 7.38–7.26 (m, 5H), 4.55–4.43 (m, 1H), 4.36 (dd, J = 13.7, 2.6 Hz, 1H), 3.20 (dd, J = 13.7, 11.0 Hz, 1H), 2.47 (dd, J = 13.2, 7.3 Hz, 1H), 2.37 (s, 3H), 2.02 (dd, J = 13.1, 9.8 Hz, 1H), 1.34 (s, 3H), 1.29 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 148.6, 145.3, 136.3, 130.1, 129.9, 128.4, 128.4, 128.2, 127.9, 65.5, 58.7, 43.7, 42.5, 28.0, 26.4, 21.7. IR (KBr): ν = 3026.4, 2966.6, 1578.8, 1303.7, 1142.1, 766.5, 544.4 cm^{-1}. HRMS-ESI (m/z): [M + Na]$^+$ calcd for: $C_{20}H_{23}NNaO_3S^+$, 380.1291; found: 380.1295.

Crystal data for 4ra. $C_{20}H_{23}NO_3S$, M = 357.45, a = 10.1298(3) Å b = 18.7025(5) Å c = 19.0521(5) Å α = 90°, β = 90°, γ = 90°, V = 3609.47(17) Å^3, T = 113.15 K, space group *Pbca*, Z = 8, μ(MoKα) = 0.198 mm^{-1}, 41 041 reflections measured, 4310 independent reflections (R_{int} = 0.0558). The final R_1 values were 0.0400 ($I > 2\sigma(I)$). The final w$R(F^2)$ values were 0.0977 ($I > 2\sigma(I)$). The final R_1 values were 0.0483 (all data). The final w$R(F^2)$ values were 0.1037 (all data). The goodness of fit on F^2 was 1.039. CCDC 1879645.†

4,4-Dimethyl-5-phenyl-2-[(phenylsulfonyl)methyl]-3,4-dihydro-2*H*-pyrrole 1-oxide (4rb). Compound **4rb** was prepared according to the general procedure and was isolated as a light-yellow solid (53.2 mg, 62% yield) after flash chromatography (EtOAc/petroleum ether 50% v/v). M.p. 160–163 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91 (d, J = 7.8 Hz, 2H), 7.79 (d, J = 7.8 Hz, 2H), 7.62 (t, J = 7.4 Hz, 1H), 7.53 (t, J = 7.7 Hz, 2H), 7.39–7.29 (m, 3H), 4.52 (q, J = 10.1 Hz, 1H), 4.39 (dd, J = 13.7, 2.4 Hz, 1H), 3.21 (dd, J = 13.5, 11.2 Hz, 1H), 2.50 (dd, J = 13.2, 7.4 Hz, 1H), 2.05 (dd, J = 13.1, 9.8 Hz, 1H), 1.37 (s, 3H), 1.31 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 148.5, 139.5, 134.2, 129.9, 129.5, 128.4, 128.1, 127.9, 65.5, 58.7, 43.7, 42.6, 28.0, 26.4. IR (KBr): ν = 2929.9, 1553.9, 1449.6, 1306.0, 1151.9, 732.4, 569.3 cm^{-1}. HRMS-ESI (m/z): [M + Na]$^+$ calcd for: $C_{19}H_{21}NNaO_3S^+$, 366.1134; found: 366.1136.

4,4-Dimethyl-5-phenyl-2-[(*m*-tolylsulfonyl)methyl]-3,4-dihydro-2*H*-pyrrole 1-oxide (4rc). Compound **4rc** was prepared according to the general procedure and was isolated as a light-yellow solid (58.1 mg, 65% yield) after flash chromatography (EtOAc/petroleum ether 50% v/v). M.p. 155–158 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.83–7.76 (m, 2H), 7.73–7.65 (m, 2H), 7.47–7.39 (m, 2H), 7.39–7.30 (m, 3H), 4.52 (m, 1H), 4.37 (dd, J = 13.7, 2.6 Hz, 1H), 3.19 (dd, J = 13.6, 11.1 Hz, 1H), 2.51 (dd, J = 13.2, 7.4 Hz, 1H), 2.39 (s, 3H), 2.06 (dd, J = 13.1, 9.7 Hz, 1H), 1.37 (s, 3H), 1.31 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 148.6, 139.9, 139.3, 134.9, 129.9, 129.3, 128.4, 128.1, 125.0, 65.5, 58.7, 43.7, 42.6, 28.0, 26.4, 21.3. IR (KBr): ν = 2959.5, 1553.8, 1297.9, 1142.4, 868.6, 769.1, 719.3 cm^{-1}. HRMS-ESI (m/z): [M + Na]$^+$ calcd for: $C_{20}H_{23}NNaO_3S^+$, 380.1291; found: 380.1294.

2-{[(4-*tert*-Butylphenyl)sulfonyl]methyl}-4,4-dimethyl-5-phenyl-3,4-dihydro-2*H*-pyrrole 1-oxide (4rd). Compound **4rd** was prepared according to the general procedure and was isolated as a light-yellow solid (69.9 mg, 70% yield) after flash chromatography (EtOAc/petroleum ether 50% v/v). M.p. 104–107 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.86–7.75 (m, 4H), 7.57–7.48 (m, 2H), 7.40–7.27 (m, 3H), 4.59–4.43 (m, 1H), 4.42–4.28 (m, 1H), 3.30–3.09 (m, 1H), 2.63–2.39 (m, 1H), 2.18–1.96 (m, 1H), 1.36 (s, 3H), 1.34–1.23 (m, 12H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.2, 148.6, 136.4, 129.9, 128.4, 128.1, 127.8, 126.5, 65.5, 58.8, 43.7, 42.6, 35.3, 31.1, 28.0, 26.4. IR (KBr): ν = 2969.3, 1541.7, 1308.3, 1155.9, 767.3, 694.3, 570.1 cm^{-1}. HRMS-ESI (m/z): [M + Na]$^+$ calcd for: $C_{23}H_{29}NNaO_3S^+$, 422.1760; found: 422.1765.

2-{[(4-Chlorophenyl)sulfonyl]methyl}-4,4-dimethyl-5-phenyl-3,4-dihydro-2*H*-pyrrole 1-oxide (4rg). Compound **4rg** was prepared according to the general procedure and was isolated as a yellow solid (29.3 mg, 31% yield) after flash chromatography (EtOAc/petroleum ether 50% v/v). M.p. 151–154 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85 (d, J = 8.2 Hz, 2H), 7.77 (d, J = 7.5 Hz, 2H), 7.50 (d, J = 8.2 Hz, 2H), 7.40–7.30 (m, 3H), 4.52 (q, J = 9.7, 8.8 Hz, 1H), 4.37 (d, J = 13.8 Hz, 1H), 3.24 (dd, J = 13.5, 11.0 Hz, 1H), 2.50 (dd, J = 13.1, 7.4 Hz, 1H), 2.05 (dd, J = 12.9, 10.0 Hz, 1H), 1.37 (s, 3H), 1.31 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 149.0, 141.0, 137.8, 130.0, 129.9, 129.4, 128.5, 128.2, 128.2, 65.4, 58.6, 43.8, 42.5, 28.0, 26.4. IR (KBr): ν = 2974.3, 1539.0, 1306.4, 1157.3, 1086.1, 865.9, 760.1 cm^{-1}. HRMS-ESI (m/z): [M + Na]$^+$ calcd for: $C_{19}H_{20}ClNNaO_3S^+$, 400.0745; found: 400.0748.

4,4-Dimethyl-2-[(naphthalen-2-ylsulfonyl)methyl]-5-phenyl-3,4-dihydro-2*H*-pyrrole-1-oxide (4rk). Compound **4rk** was prepared according to the general procedure and was isolated as a yellow solid (39.4 mg, 40% yield) after flash chromatography (EtOAc/petroleum ether 50% v/v). M.p. 139–142 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.47 (s, 1H), 8.03–7.91 (m, 1H), 7.90–7.82 (m, 2H), 7.82–7.70 (m, 2H), 7.67–7.51 (m, 2H), 7.40–7.25 (m, 3H), 4.65–4.40 (m, 2H), 3.29 (t, J = 12.3 Hz, 1H), 2.53 (dd, J = 12.8, 7.4 Hz, 1H), 2.15–1.99 (m, 1H), 1.35 (s, 3H), 1.31 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 148.6, 136.2, 135.5, 132.2, 129.9, 129.9, 129.8, 129.5, 129.5, 128.4, 128.4, 128.1, 128.1, 127.9, 122.4, 65.6, 58.7, 43.7, 42.6, 28.0, 26.4. IR (KBr): ν = 2970.4, 2933.8, 1551.4, 1303.3, 1146.2, 1128.2, 768.3, 541.8 cm^{-1}. HRMS-ESI (m/z): [M + Na]$^+$ calcd for: $C_{23}H_{23}NNaO_3S^+$, 416.1291; found: 416.1295.

Methyl 4,4-dimethyl-3a-phenyl-6-tosylmethyl-3a,4,5,6-tetrahydropyrrolo[1,2-*b*]isoxazole-3-carboxylate (5). The compound **3ra** (89.4 mg, 0.25 mmol) was mixed with methyl propiolate (105 mg, 1.25 mmol) using benzene as a solvent in a 50 mL flask. The mixture was heated for 24 h at 80 °C. After removal of the solvent, the residue was purified by silica gel chromatography (ethyl acetate : petroleum ether = 1 : 15, v/v) to give 83 mg of product **5** (75%) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76 (d, J = 7.6 Hz, 2H), 7.61 (d, J = 7.7 Hz, 2H), 7.36–7.27 (m, 3H), 7.23–7.15 (m, 2H), 7.15–7.09 (m, 1H),

3.83–3.63 (m, 5H), 3.31 (dd, J = 13.4, 9.9 Hz, 1H), 2.39 (s, 3H), 1.95 (dd, J = 12.9, 5.0 Hz, 1H), 1.64–1.49 (m, 1H), 1.25 (s, 3H), 0.71 (s, 3H).^{13}C NMR (101 MHz, $CDCl_3$) δ 165.8, 155.5, 145.0, 143.9, 136.9, 130.0, 127.9, 127.8, 126.9, 126.8, 111.9, 83.0, 61.4, 60.0, 51.6, 45.4, 44.1, 27.7, 27.2, 21.7. HRMS-ESI (m/z): $[M + H]^+$ calcd for: $C_{24}H_{28}NO_5S^+$, 442.1683; found: 442.1688. IR (KBr): ν = 2962.9, 1711.2, 1613.5, 1439.9, 1315.5, 1149.9, 768.1, 671.7, 510.9 cm^{-1}.

Conflicts of interest

There are no conflicts to declare.

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