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Trifluoromethyl Vinyl Sulfide: A Building Block for the Synthesis of CF₃S-Containing Isoxazolidines

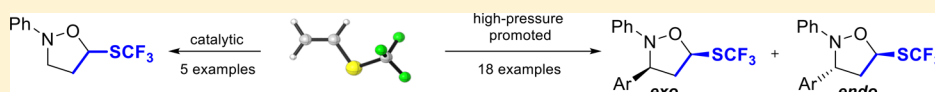
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Supporting Information



ABSTRACT: Trifluoromethyl vinyl sulfide, a potential building block for pharmaceutically and agrochemically relevant products, is prepared and used for the first time in high-pressure-mediated 1,3-dipolar cycloaddition reactions with nitrones to synthesize (trifluoromethyl)sulfanyl isoxazolidines.

INTRODUCTION

The (trifluoromethyl)sulfanyl group (SCF₃) represents a privileged substituent in agrochemicals and pharmaceuticals because of the strong electron-withdrawing effect and the large Hansch lipophilicity parameter ($\pi = 1.44$).¹ Cefazaflur,² a first-generation cephalosporin antibiotic, toltrazuril,³ an antiprotozoal agent, and a losartan analogue,⁴ developed as a potential hypotensive agent, are prominent examples of biologically active compounds bearing the SCF₃ group (Figure 1).

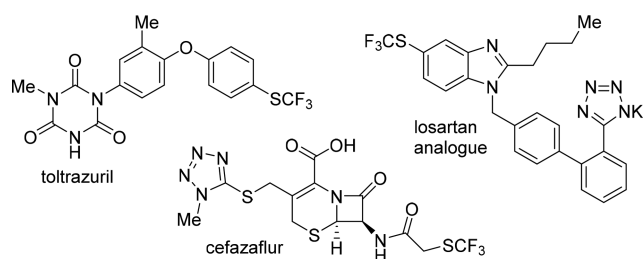


Figure 1. Bioactive heterocycles containing the SCF₃ group.

Hence, CF₃S-containing compounds are considered appealing targets in the agrochemical and pharmaceutical fields, and consequently, modern research has focused on efficient (trifluoromethyl)sulfanylation methods. The main strategies that have been developed to synthesize CF₃S-containing compounds have focused on direct C–S bond formation⁵ and trifluoromethylation of sulfur-containing compounds.⁶ However, incorporation via simple CF₃S-containing building blocks is still unprecedented so that the use of a CF₃S-containing reagent could be an alternative strategy to construct CF₃S-substituted heterocycles. More specifically, trifluoromethyl vinyl sulfide (2) could be an attractive building block to provide straightforward access to a wide variety of hetero- and

carbocycles via cycloaddition reactions. Previously reported examples of cycloaddition reactions of alkene 2 are rather scarce: there is a single example of a Diels–Alder reaction with 2,3-dimethylbutadiene to yield the corresponding CF₃S-cyclohexene,⁷ and two cyclopropanation examples with organomercury reagents to yield CF₃S-substituted cyclopropanes.⁸

The potential of this unexplored chemistry and the inherent biological attractiveness of these molecules motivated us to further study the reactivity of alkene 2 in cycloaddition reactions. Thus, we herewith present the study of the first 1,3-dipolar cycloaddition reactions of 2 with several nitrones⁹ to synthesize a novel group of isoxazolidines (Scheme 1).

Scheme 1. Synthesis of CF₃S-Containing Isoxazolidines



RESULTS AND DISCUSSION

We commenced our investigations by forming alkene 2 in situ. Because of its high volatility,⁹ we first performed the elimination reactions in deuterated solvents in order to instantly measure conversions from commercially available chloroalkane 1 into alkene 2, with no need for further treatment or isolation of the alkene. We tested several bases (Et₃N, DBU, KO^tBu, KOH and KOTMS) in the presence of various deuterated solvents (CD₂Cl₂, THF-*d*₈, CD₃OD and DMF-*d*₇; see the Supporting Information (SI) for experimental details) to eventually choose

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a solution of KO^tBu in THF-*d*₈ at 21 °C for 90 min as the final method for the in situ synthesis of alkene **2** with full conversion.

Initially, we focused on the synthesis of 2,5-disubstituted isoxazolidines **3** using *N*-substituted hydroxylamines **5** and paraformaldehyde as precursors for the in situ synthesis of the dipoles (Table 1). The nitron intermediates were used without

Table 1. Synthesis of Isoxazolidines 3a–e

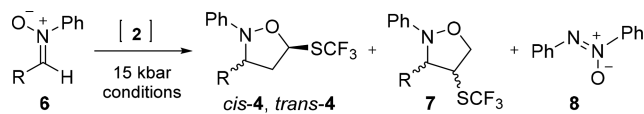
entry	compd	R	yield (%)
1	3a	C ₆ H ₅	38
2	3b	3-CF ₃ C ₆ H ₄	20
3	3c	3,5-Cl ₂ C ₆ H ₃	22
4 ^a	3d	C ₆ H ₅ CH ₂	30
5 ^a	3e	Cy	23

^aEt₃N (1.0 equiv) was used.

isolation in a one-pot process with a preformed solution of alkene **2** (3 equiv) and In(OTf)₃ (0.06 equiv). In this manner, we obtained isoxazolidine **3a** in 22% yield after column chromatography. Increasing the concentration of **2** (6 equiv) resulted in a yield of 38% (entry 1). Isoxazolidines **3b–e** were synthesized in yields between 20 and 30% under the same reaction conditions with different substrates (entries 2–5). However, yields were rather low after column chromatography in all cases (see the SI for experimental details).

With these results in hand and because of the low yields in the synthesis of **3a–e**, we changed our strategy to the synthesis of 2,3,5-trisubstituted isoxazolidines **4**, exhibiting a second (hetero)aromatic group at the 3-position and introducing consequently a second chiral center in the molecule (Scheme 2, Table 2).

Scheme 2. Formation of Compounds 4, 7, and 8



We first performed the reaction with nitron **6a** (R = H), a catalytic amount of In(OTf)₃, and alkene **2** at 21 °C in THF, but no conversion into the product was observed. When the same conditions were applied at 80 °C with nitron **6c** (R = Me), less than 7% conversion into the final product was observed by ¹H NMR, presumably because of the low reactivity of this alkene

and perhaps due to its volatility. Therefore, we decided to perform these reactions under high-pressure conditions (Table 2), which is an established and powerful tool to increase the rate of cycloaddition reactions.¹⁰ Thus, when 1.3 equiv of **2** at 21 °C under a 15 kbar pressure was used (entry 1) we gratifyingly observed an 83% conversion into isoxazolidines **4c** and **7c** (regioisomeric ratio **4c**/**7c** 13:1, diastereomeric ratio [dr] *cis*-**4c**/*trans*-**4c** 7:2). Nitron **6b** gave only 56% conversion under the same reaction conditions (entry 4), with similar regio- and diastereoisomeric ratios. When increasing the concentration of alkene **2**, 93 and 75% conversions into compounds **4c** and **4b** were obtained, respectively (entries 2 and 5). Finally, an increase of the temperature to 50 °C gave nearly full conversion into the desired *cis*- and *trans*-products **4c** and **4b** (entries 3 and 6).

Azoxybenzene¹¹ **8** was formed in all reactions as a side product (Scheme 2) and could not be separated in any case from *trans*-**4** by column chromatography. Thus, we used galvinoxyl to prevent the formation of compound **8**.¹² We were pleased to see that when using 3 equiv of alkene **2** at 50 °C, in the presence of 1–3 mol % of galvinoxyl as radical scavenger (entries 7 and 8), not only full conversion into the desired product **4b** was obtained, but also the formation of the azoxy compound **8** was fully suppressed.

Furthermore, our reactions gave the *exo*-products as the major diastereoisomers (the *cis*-isomers), showing a 3:1 diastereomeric ratio (entries 7 and 8). Having these results in hand, the scope of nitrones in this 1,3-dipolar cycloaddition was examined by employing the conditions shown in entry 7. We first synthesized a total of 18 nitrones (**6a–r**) with phenyl (containing both electron-donating and electron-withdrawing groups at the 2-, 3-, and 4- positions), heterocyclic and carbamoyl substituents in excellent yields (see the SI). We then studied the scope of the 1,3-dipolar cycloaddition reactions between alkene **2** and nitrones **6a–r** (Table 3).

As shown in Table 3, high and excellent yields (total yields) were observed for compounds **4a–c**, **4f–i**, **4l**, and **4n**. In addition, in most of the cases the major product (*cis*-**4**) was separated from the other isomers by column chromatography in good yields (*cis*-**4a–c**, *cis*-**4f–j**, *cis*-**4m**, and *cis*-**4q**). Unfortunately, in a few cases the isomers **4** were obtained as a mixture that could not be separated (**4d,e**, **4k,l**, and **4n**). For compounds **4o** and **4p**, the *trans*-**4** isomer and the corresponding regioisomers **7** were present as a mixture.¹³ The assignment of the *cis*- and *trans*-isomers was performed by 2D NMR studies (NOESY).

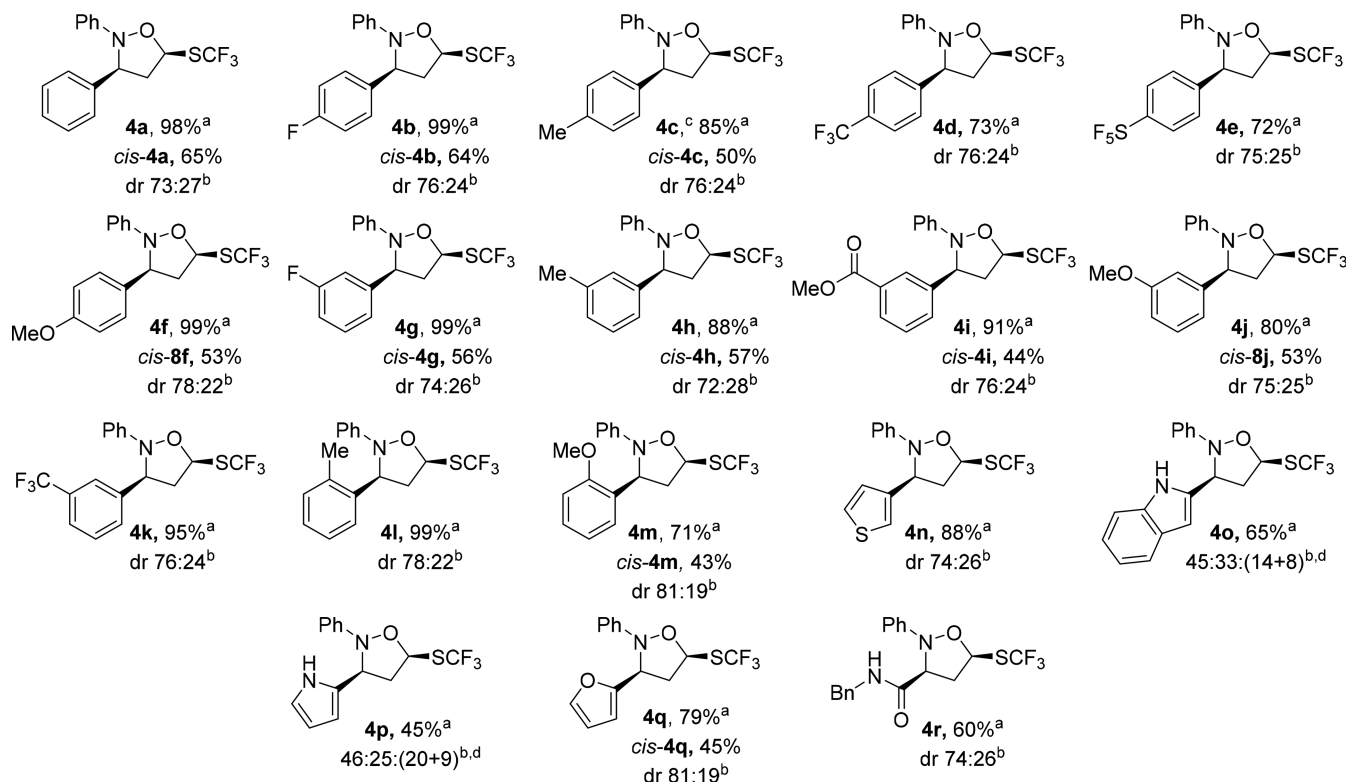
The diastereoselectivity was lower for compounds **4o** and **4p**, which contained an indole and a pyrrole substituent, respectively. In these cases, a mixture of *cis*- and *trans*-diastereoisomers was obtained approximately in a 3:2 ratio. In

Table 2. Optimization Process for the 1,3-Dipolar Cycloaddition Reaction of Nitrones 6 with Alkene 2

entry	nitron	R	2 (equiv)	T (°C)	scavenger	<i>cis</i> - 4 / <i>trans</i> - 4	8 ^a (%)	conv ^a (yield) ^b (%)
1	6c	4-MeC ₆ H ₄	1.3	21		76:22	5	83 (41) ^c
2	6c	4-MeC ₆ H ₄	3	21		79:21	22	93 (–)
3	6c	4-MeC ₆ H ₄	3	50		76:24	6	96 (85) ^c
4	6b	4-FC ₆ H ₄	1.3	21		79:21	7	56 (35) ^c
5	6b	4-FC ₆ H ₄	3	21		79:21	38	75 (–)
6	6b	4-FC ₆ H ₄	3	50		77:23	17	91 (79) ^c
7	6b	4-FC ₆ H ₄	3	50	galvinoxyl (3%)	76:24	0	100 (78)
8	6b	4-FC ₆ H ₄	3	50	galvinoxyl (1%)	76:24	1	100 (–)

^aCalculated by integration of the ¹H NMR signals of the crude mixtures. ^bIsolated after column chromatography. ^c*trans*-Isomer contaminated with **7**.

Table 3. Scope of the High-Pressure-Promoted 1,3-Dipolar Cycloaddition Reaction



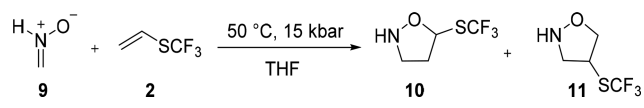
^aCombined yield. ^bCalculated by ¹H NMR of the crude. ^cGalvinoxyl was not used in the reaction. ^d*cis-4o,p/trans-4o,p*/(mixture of isomers 7).

addition, for compounds **4o** and **4p**, a 7:3 ratio of a mixture *cis-7* and *trans-7* from the regioisomer 7 was observed. For these two compounds (**4o** and **4p**), the total yields were significantly lower because of incomplete conversion into the products and purification problems. Finally, when using a nonaromatic nitronium, the final benzyl amide isoxazolidine **4r** was synthesized in 60% yield.

To evaluate the apparent regioselectivity of the cycloaddition, high-level DFT calculations were carried out at the BP86/TZ2P¹⁴ level, using the ADF program.¹⁵ Tetrahydrofuran was simulated using the COSMO solvation model.¹⁶ Thermochemical corrections were computed using the temperature and pressure under which the experiments were performed (see the SI for computational details).

We focused on understanding the regioselectivity of the cycloaddition between a simple model nitronium **9** with alkene **2** (Scheme 3). This reaction proceeds in a concerted and

Scheme 3. Formation of Compounds **10** and **11**



asynchronous manner with a Gibbs free energy barrier of 21.3 and 24.0 kcal mol⁻¹ for **10** and **11**, respectively (Table 4). The $\Delta\Delta G^\ddagger$ of 2.7 kcal mol⁻¹ facilitates a high degree of regioselectivity, resulting in a calculated product ratio of 98:2 for **10/11**. Furthermore, the experimentally observed regioisomer **10** is more stable than **11** ($\Delta\Delta G_{\text{rxn}} = 3.9$ kcal mol⁻¹). The calculated product ratio for the model nitronium cycloaddition is in line with experimentally observed regioselectivity of reactions involving the majority of the nitroniums **6**.

Table 4. Computed Activation Barriers, Reaction Energies (kcal mol⁻¹), and Product Distribution Computed at the COSMO(THF)-BP86/TZ2P Level of Theory

compd	ΔE^\ddagger (ΔG^\ddagger)	ΔE_{rxn} (ΔG_{rxn})	product ratio ^a
10	12.8 (21.3)	-17.6 (-6.1)	98
11	15.0 (24.0)	-14.3 (-2.2)	2

^aCalculated at 50 °C and 15 kbar based on the $\Delta\Delta G^\ddagger$ between **10** and **11** (see the SI for details).

Insight into why regioisomer **10** is favored over the other, **11**, is provided by the activation strain model (ASM)¹⁷ (also known as the distortion-interaction model).¹⁸ In this framework, the potential energy surface $\Delta E(\zeta)$ is decomposed along the reaction coordinate ζ into the strain $\Delta E_{\text{strain}}(\zeta)$ associated with deforming the individual reactants plus the actual interaction $\Delta E_{\text{int}}(\zeta)$ between the deformed reactants.

$$\Delta E^\ddagger(\zeta) = \Delta E_{\text{strain}} + \Delta E_{\text{int}}(\zeta) \quad (1)$$

The $\Delta E_{\text{int}}(\zeta)$ between the reactants is further analyzed by an energy decomposition analysis (EDA) in the conceptual framework provided by the Kohn–Sham molecular orbital (KS-MO) model¹⁹ and is decomposed into three physically meaningful terms:

$$\Delta E_{\text{int}}(\zeta) = \Delta V_{\text{elstat}}(\zeta) + \Delta E_{\text{Pauli}}(\zeta) + \Delta E_{\text{oi}}(\zeta) \quad (2)$$

The $\Delta V_{\text{elstat}}(\zeta)$ term corresponds to the classical electrostatic interaction between unperturbed charge distributions, $\Delta E_{\text{Pauli}}(\zeta)$ is responsible for any steric repulsion, and the $\Delta E_{\text{oi}}(\zeta)$ accounts for charge transfer (HOMO–LUMO interactions) and polarization.

Applying the ASM along the reaction coordinate defined by the bending of the 1,3-dipole, it is revealed that reactivity

differences in the reaction between **9** and **2** leading to **10** (blue curve) and **11** (red curve) are a result of ΔE_{int} (Figure 2a).

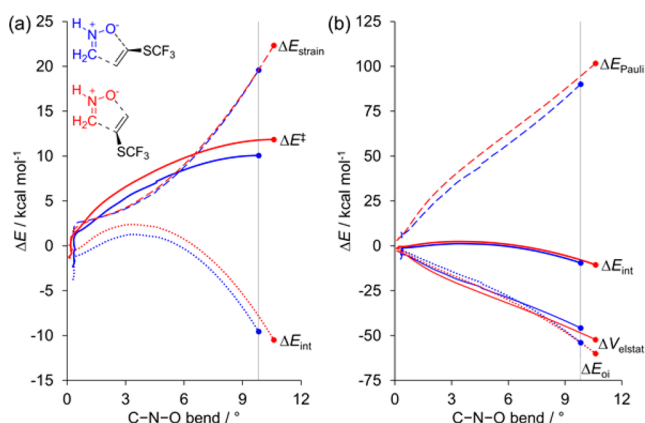


Figure 2. (a) Activation strain and (b) energy decomposition analyses of the cycloaddition reactions of nitrone **9** with alkene **2** up to their respective TS (indicated by the dot) computed at the BP86/TZ2P level.

ΔE_{strain} remains nearly constant for both reactions along the reaction coordinate. Next, the EDA terms were analyzed, and the ΔE_{Pauli} dominates and is chiefly responsible for the difference in the interaction energies (Figure 2b). The more favorable ΔV_{elstat} and ΔE_{or} curves associated with the reaction leading to **11** are unable to overcome for increased steric repulsion associated with this approach. These results highlight the fact that the reaction results from the least hindered approach, leaving the SCF_3 group far away from the CH_2 group. See the SI for an ASA and EDA analysis on **6m** and **6p**.

In summary, we have developed the synthesis of a new class of 5-[(trifluoromethyl)sulfanyl]isoxazolidines. The reactions utilized for their synthesis were high-pressure-promoted 1,3-dipolar cycloaddition reactions between trifluoromethyl vinyl sulfide **2** and various easily synthesized nitrones. The results of our DFT computations are in harmony with experimental results and were leveraged to show that the high regioselectivity of these cycloaddition reactions originates from minimizing steric repulsion.

EXPERIMENTAL SECTION

General Information. Reagents were obtained from commercial suppliers and were used without purification. Standard syringe techniques were applied for the transfer of dry solvents and air- or moisture-sensitive reagents. Tetrahydrofuran was used as a solvent after distillation. Potassium *tert*-butoxide was used as a 1.0 M solution in tetrahydrofuran. The high-pressure experiments were run in a high-pressure apparatus equipped with a one-wall-piston cylinder for pressures up to 15 kbar (1.5 GPa). Reactions were performed in 1–1.5 mL PTFE ampules closed by screwed stainless steel stoppers. These ampules were inserted into the high-pressure vessel filled with 80–100 petroleum ether as transmission medium. Reactions were followed, and R_f values were obtained, using thin layer chromatography (TLC) on silica gel-coated plates (Merck 60 F254) with the indicated solvent mixture. Detection was performed with UV light, and/or by charring at ca. 150 °C after dipping into a solution of KMnO_4 . Infrared spectra were recorded on an IR-ATR Bruker TENSOR 27 spectrometer. High-resolution mass spectra were recorded on a JEOL AccuTOF (ESI) or a MAT900 (EI, CI, and ESI) GC-TOF. NMR spectra were recorded at 298 K on a Varian Inova 400 (400 MHz), Bruker Avance III 400 MHz or Bruker Avance III 500 MHz spectrometer in the solvent indicated. Chemical shifts are given in parts per million (ppm) with respect to

tetramethylsilane (0.00 ppm) as internal standard for ^1H NMR; and CDCl_3 (77.16 ppm) as internal standard for ^{13}C NMR. Coupling constants are reported as J values in hertz (Hz). ^1H NMR data are reported as follows: chemical shift (ppm), multiplicity (s = singlet, d = doublet, dd = doublet of doublets, dt = doublet of triplets, dtdq = doublet of triplet of doublet of quartets, dq = doublet of quartets, ddd = doublet of doublet of doublets, ddt = doublet of doublets of triplets, dddd = doublet of doublets of doublets, ddquint = doublet of doublet of quintets, dddquint = doublet of doublet of doublet of quintets, quint = quintet, t = triplet, td = triplet of doublets, tt = triplet of triplets, m = multiplet, b = broad), coupling constants (Hz), integration and assignment. Compounds were fully characterized by ^1H , ^{13}C , 2D gDQCOSY, gHSQC, gHMBC, NOESY, and HOESY spectra. The characterization and assignment of isoxazolidines **4a–r** were done either from isolated compounds or mixtures of isomers. Column or flash chromatography was carried out using ACROS silica gel (0.035–0.070 mm, and 60 Å pore diameter).

General Procedure for the Synthesis of Trifluoromethyl Vinyl Sulfide 2. 2-Chloroethyl trifluoromethyl sulfide (1.0 equiv) was dissolved in distilled THF (0.40 M) under inert atmosphere and cooled to 0 °C. Then, KO^tBu (1.0 equiv, 1.0 M solution in THF) was added slowly, and the mixture was warmed to 21 °C for 90 min. This solution was used for the cycloaddition reactions of alkene **2**. ^1H NMR [400 MHz, δ (ppm), $\text{THF}-d_8$]: 6.54 (dd, $J = 16.5, 9.4$ Hz, 1 H), 5.75–5.66 (m, 2 H). ^{13}C NMR [101 MHz, δ (ppm), $\text{THF}-d_8$]: 129.8 (q, $J = 306.5$ Hz), 124.4 (q, $J = 1.0$ Hz), 121.3 (q, $J = 3.2$ Hz). ^{19}F NMR [377 MHz, δ (ppm), $\text{THF}-d_8$]: –43.6.⁷

General Procedure for the Synthesis of Hydroxylamines 5b and 5c. The corresponding nitrobenzene (**12b** or **12c**; 1 equiv) was added to a flame-dried Schlenk tube containing a suspension of Pd/C (0.25 equiv) in dry THF (10 mL). The mixture was cooled to 0 °C, and $\text{N}_2\text{H}_4 \cdot \text{H}_2\text{O}$ (2.0 equiv) was added dropwise. The reaction was carefully monitored by TLC until the starting material disappeared. The crude mixture was diluted with THF (10 mL) and filtered over a pad of diatomaceous earth. The solvent was evaporated in vacuo, and the crude mixture was purified by column chromatography using CH_2Cl_2 under a nitrogen atmosphere.

***N*-[3-(Trifluoromethyl)phenyl]hydroxylamine (5b).** According to general procedure, the reaction of 1-nitro-3-(trifluoromethyl)benzene **12b** (1.0 g, 5.23 mmol) afforded hydroxylamine **5b** (885 mg, 5.00 mmol) as a pale yellow oil. ^1H NMR [400 MHz, δ (ppm), CDCl_3]: 7.41–7.34 (m, 1 H), 7.28–7.26 (m, 1 H), 7.23–7.19 (m, 1 H), 7.15–7.10 (m, 1 H), 6.74–4.98 (bs, 2 H). R_f : 0.31 (CH_2Cl_2). Yield: 95%. NMR spectral data are in accordance with previously reported data.²⁰

***N*-[3,5-Dichlorophenyl]hydroxylamine (5c).** According to general procedure, the reaction of 1,3-dichloro-5-nitrobenzene **12c** (1.0 g, 5.22 mmol) afforded hydroxylamine **5c** (827 mg, 4.65 mmol) as a yellow solid. ^1H NMR [400 MHz, δ (ppm), CDCl_3]: 6.93 (t, $J = 1.8$ Hz, 1 H), 6.88 (d, $J = 1.8$ Hz, 2 H), 6.79 (bs, 1 H), 5.31 (bs, 1 H). R_f : 0.33 (CH_2Cl_2). Yield: 89%. NMR spectral data are in accordance with previously reported data.²⁰

General Procedure for the Synthesis of Isoxazolidines 3a–c. A solution of the corresponding hydroxylamine **5** (1 equiv) in THF (0.22 M) was added to a solution of paraformaldehyde (3 equiv) in THF (0.22 M) at 0 °C. Then a cooled solution (0 °C) of alkene **2** (6.0 equiv) was subsequently added to the solution containing paraformaldehyde and the hydroxylamine. Finally, a solution of $\text{In}(\text{OTf})_3$ (0.06 equiv) in dry THF (44 mM) was added to the reaction mixture. The reaction mixture was warmed to 21 °C and stirred for 16 h. Then, the reaction mixture was quenched with a saturated aqueous solution of NaHCO_3 (10 mL), and the aqueous layer was extracted with AcOEt (2 × 10 mL). The combined organic layers were dried over MgSO_4 , filtered off and concentrated in vacuo. The crude mixture was purified by column chromatography using the indicated eluent to afford isoxazolidines **3a–c**.

2-Phenyl-5-[(trifluoromethyl)sulfanyl]isoxazolidine (3a). According to the general procedure, the reaction of *N*-phenylhydroxylamine **5a** (17.8 mg, 0.163 mmol) afforded isoxazolidine **3a** (15.3 mg, 0.163 mmol) as a brown solid after column chromatography (heptane/ AcOEt , 19:1 → 4:1). ^1H NMR [500 MHz, δ (ppm), CDCl_3]: 7.34–

7.27 (m, 2 H), 7.08–7.05 (m, 2 H), 7.03 (tt, $J = 7.3, 1.1$ Hz, 1 H), 5.98 (dd, $J = 8.1, 4.3$ Hz, 1 H), 3.85–3.71 (m, 1 H), 3.24 (ddd, $J = 9.3, 8.2, 7.6$ Hz, 1 H), 2.91 (dtdq, $J = 13.2, 8.2, 4.0, 0.8$ Hz, 1 H), 2.48–2.28 (m, 1 H). ^{13}C NMR [126 MHz, δ (ppm), CDCl_3]: 149.8, 130.1 (q, $J = 307.7$ Hz), 129.0, 123.0, 116.1, 81.1 (q, $J = 2.2$ Hz), 52.0, 36.0 (q, $J = 1.1$ Hz). ^{19}F NMR [471 MHz, δ (ppm), CDCl_3]: –39.8. FTIR [$\bar{\nu}$ (cm^{-1})]: 2860, 1599, 1491, 1295, 1109, 752, 692. HRMS (EI) m/z : [M^+] calcd for $\text{C}_{10}\text{H}_{10}\text{F}_3\text{NOS}$ 249.0435, found 249.0458. R_f : 0.56 (heptane/AcOEt, 4:1). Yield: 38%.

2-[3-(Trifluoromethyl)phenyl]-5-[(trifluoromethyl)sulfanyl]isoxazolidine (3b). According to the general procedure, the reaction of hydroxylamine **5b** (56.2 mg, 0.318 mmol) afforded isoxazolidine **3b** (23.5 mg, 0.071 mmol) as a colorless oil, after column chromatography (heptane/AcOEt/Et₃N, 12.2:1:0.13). ^1H NMR [500 MHz, δ (ppm), CDCl_3]: 7.41 (dd, $J = 8.2, 7.2, 0.8$ Hz, 1 H), 7.29–7.25 (m, 2 H), 7.23–7.19 (m, 1 H), 6.01 (dd, $J = 8.0, 4.2$ Hz, 1 H), 3.83 (ddd, $J = 9.1, 8.2, 4.3$ Hz, 1 H), 3.30 (ddd, $J = 9.1, 8.5, 7.4$ Hz, 1 H), 3.02–2.90 (m, 1 H), 2.48–2.38 (m, 1 H). ^{13}C NMR [126 MHz, δ (ppm), CDCl_3]: 150.1, 131.3 (q, $J = 32.3$ Hz), 129.8 (q, $J = 307.9$ Hz), 129.4, 124.0 (q, $J = 272.4$ Hz), 119.2 (q, $J = 3.8$ Hz), 118.9, 112.3 (q, $J = 4.0$ Hz), 81.1 (q, $J = 2.4$ Hz), 51.7, 35.8 (q, $J = 1.2$ Hz). ^{19}F NMR [471 MHz, δ (ppm), CDCl_3]: –39.9, –62.8. FTIR [$\bar{\nu}$ (cm^{-1})]: 2956, 2925, 2855, 1593, 1328, 1120, 795, 698. HRMS (EI) m/z : [M^+] calcd for $\text{C}_{11}\text{H}_9\text{F}_6\text{NOS}$ 317.0309, found 317.0325. R_f : 0.44 (heptane/AcOEt, 4:1). Yield: 22%.

2-(3,5-Dichlorophenyl)-5-[(trifluoromethyl)sulfanyl]isoxazolidine (3c). According to the general procedure, the reaction of hydroxylamine **5c** (29.3 mg, 0.166 mmol) afforded isoxazolidine **3c** (10.33 mg, 0.033 mmol) as a green oil after column chromatography (heptane/AcOEt/Et₃N, 12.2:1:0.13). ^1H NMR [500 MHz, δ (ppm), CDCl_3]: 6.99 (t, $J = 1.8$ Hz, 1 H), 6.91 (d, $J = 1.8$ Hz, 2 H), 5.98 (dd, $J = 8.0, 4.1$ Hz, 1 H), 3.75 (ddd, $J = 8.9, 8.1, 4.4$ Hz, 1 H), 3.27 (ddd, $J = 9.2, 8.6, 7.1$ Hz, 1 H), 3.01–2.87 (m, 1 H), 2.47–2.36 (m, 1 H). ^{13}C NMR [126 MHz, δ (ppm), CDCl_3]: 151.6, 135.4, 129.7 (q, $J = 307.9$ Hz), 122.5, 114.2, 81.2 (q, $J = 2.6$ Hz), 51.6, 35.8 (q, $J = 1.1$ Hz). FTIR [$\bar{\nu}$ (cm^{-1})]: 2924, 2850, 1587, 1260, 1115, 1051, 796. HRMS (EI) m/z : [M^+] calcd for $\text{C}_{10}\text{H}_8\text{Cl}_2\text{F}_3\text{NOS}$ 316.9656, found 316.9657. R_f : 0.45 (heptane/AcOEt, 4:1). Yield: 20%.

General Procedure for the Synthesis of Isoxazolidines 3d and 3e. A solution of hydroxylamine hydrochloride **5d** or **5e** (1 equiv) in THF (0.22 M) and Et₃N (1 equiv) was added to a solution of paraformaldehyde (3 equiv) in THF (0.22 M) at 0 °C. Then a cooled solution (0 °C) of alkene **2** (6.0 equiv) was subsequently added to the solution containing paraformaldehyde and the hydroxylamine. Finally, a solution of In(OTf)₃ (0.06 equiv) in dry THF (22 mM) was added to the reaction mixture. The reaction mixture was warmed to 21 °C and stirred for 16 h. Then, the reaction mixture was quenched with a saturated aqueous solution of NaHCO₃ (10 mL), and the aqueous layer was extracted with AcOEt (2 × 10 mL). The combined organic layers were dried over MgSO₄, filtered off, and concentrated in vacuo. The crude mixture was purified by column chromatography using the indicated eluent to afford isoxazolidines **3d** and **3e**.

2-Benzyl-5-[(trifluoromethyl)sulfanyl]isoxazolidine (3d). According to the general procedure, the reaction of hydroxylamine hydrochloride **5d** (26.8 mg, 0.169 mmol) afforded isoxazolidine **3d** (13.2 mg, 0.050 mmol) as a colorless oil after column chromatography (heptane/AcOEt/Et₃N, 9:1:0.1). ^1H NMR [500 MHz, δ (ppm), CDCl_3]: 7.40–7.36 (m, 2 H), 7.35–7.30 (m, 2 H), 7.30–7.27 (m, 1 H), 5.86 (dd, $J = 8.3, 4.4$ Hz, 1 H), 4.35–3.82 (m, 2 H), 3.34–3.11 (m, 1 H), 3.11–2.40 (m, 1 H), 2.83 (dtd, $J = 11.9, 8.0, 3.3$ Hz, 1 H), 2.40–2.18 (m, 1 H). ^{13}C NMR [126 MHz, δ (ppm), CDCl_3]: 136.2, 130.3 (q, $J = 307.9$ Hz), 128.9, 128.4, 127.5, 81.3 (q, $J = 2.4$ Hz), 61.7, 53.3, 36.5. ^{19}F NMR [471 MHz, δ (ppm), CDCl_3]: –39.9. FTIR [$\bar{\nu}$ (cm^{-1})]: 2849, 1606, 1497, 1455, 1117, 755, 698. HRMS (EI) m/z : [M^+] calcd for $\text{C}_{11}\text{H}_{12}\text{F}_3\text{NOS}$ 263.0592, found 263.0604. R_f : 0.41 (heptane/AcOEt, 4:1). Yield: 30%.

2-Cyclohexyl-5-[(trifluoromethyl)sulfanyl]isoxazolidine (3e). According to the general procedure, the reaction of hydroxylamine hydrochloride **5e** (23.1 mg, 0.152 mmol) afforded isoxazolidine **3e** (20.4 mg, 0.080 mmol) as a colorless oil, after column chromatography (heptane/AcOEt, 19:1 → 5:1). ^1H NMR [400 MHz, δ (ppm), CDCl_3]:

5.82 (dd, $J = 8.1, 4.2$ Hz, 1 H), 3.43–3.13 (m, 1 H), 2.85–2.73 (m, 1 H), 2.68–2.50 (m, 1 H), 2.68–2.18 (m, 1 H), 2.31–2.18 (m, 1 H), 1.83–1.69 (m, 2 H), 1.66–1.52 (m, 2 H), 1.39–1.13 (m, 6 H). ^{13}C NMR [101 MHz, δ (ppm), CDCl_3]: 130.4 (q, $J = 308.1$ Hz), 80.8 (q, $J = 2.2$ Hz), 65.8, 51.5, 36.6, 26.0, 24.8, 24.4. ^{19}F NMR [377 MHz, δ (ppm), CDCl_3]: –40.0. FTIR [$\bar{\nu}$ (cm^{-1})]: 2924, 2854, 1728, 1455, 1258, 1082, 1009, 788. R_f : 0.44 (heptane/AcOEt, 9:1). Yield: 53%.

General Procedure A for the Syntheses of Nitrones 6d–g, 6i, 6j, 6l–r. The corresponding aldehyde (1.0 equiv, dissolved in 1.5 mL of dry EtOH for solid compounds) was added to a solution of *N*-phenylhydroxylamine (1.05 equiv) in dry EtOH (1.0 mL) at 21 °C under a nitrogen atmosphere. The reaction mixture was stirred for 16–21 h, and then the solvent was removed under vacuo. The crude mixture was purified by column chromatography using the indicated eluent to afford nitrones **6d–g**, **6i**, **6j**, **6l–r**.

General Procedure B for the Syntheses of Nitrones 6a–c, 6h, and 6k. The corresponding aldehyde (1.0 equiv) was added to a solution of *N*-phenylhydroxylamine (1.0 equiv) in dry EtOH (1.0 mL), and the flask was wrapped with aluminum foil. The reaction mixture was stirred at 21 °C for 16–21 h, and then the solvent was removed under vacuo. The crude mixture was purified by column chromatography using the indicated eluent to afford nitrones **6a–c**, **6h**, and **6k**.

(Z)-N,1-Diphenylmethanimine Oxide (6a).²¹ According to general procedure B, the reaction of benzaldehyde (47.0 μL , 0.458 mmol) with *N*-phenylhydroxylamine (50 mg, 0.458 mmol) afforded nitrone **6a** (71 mg, 0.360 mmol) as a white solid, after column chromatography (heptane/AcOEt, 5:1 → 1:1). ^1H NMR [400 MHz, δ (ppm), CDCl_3]: 8.44–8.36 (m, 2 H), 7.92 (s, 1 H), 7.81–7.74 (m, 2 H), 7.53–7.43 (m, 6 H). Yield: 79%.

(Z)-1-(4-Fluorophenyl)-N-phenylmethanimine Oxide (6b).²² According to general procedure B, the reaction of 4-fluorobenzaldehyde (98.0 μL , 0.916 mmol) with *N*-phenylhydroxylamine (100 mg, 0.916 mmol) afforded nitrone **6b** (178.5 mg, 0.829 mmol) as a white solid. ^1H NMR [400 MHz, δ (ppm), CDCl_3]: 8.49–8.42 (m, 2 H), 7.91 (s, 1 H), 7.80–7.75 (m, 2 H), 7.55–7.44 (m, 3 H), 7.23–7.14 (m, 2 H). Yield: 91%.

(Z)-N-Phenyl-1-(4-tolyl)methanimine Oxide (6c).²² According to general procedure B, the reaction of 4-methylbenzaldehyde (163.0 μL , 1.375 mmol) with *N*-phenylhydroxylamine (127 mg, 1.375 mmol) afforded nitrone **6c** (267.2 mg, 1.26 mmol) as yellow crystals, after column chromatography (heptane/AcOEt, 5:1 → 1:1). ^1H NMR [400 MHz, δ (ppm), CDCl_3]: 8.34–8.27 (m, 2 H), 7.89 (s, 1 H), 7.81–7.75 (m, 2 H), 7.51–7.43 (m, 3 H), 7.33–7.28 (m, 2 H), 2.42 (s, 3 H). Yield: 92%.

(Z)-N-Phenyl-1-[4-(trifluoromethyl)phenyl]methanimine oxide (6d).²³ According to general procedure A, the reaction of 4-(trifluoromethyl)benzaldehyde (91 mg, 0.523 mmol) with *N*-phenylhydroxylamine (60 mg, 0.549 mmol) afforded nitrone **6d** (139 mg, 0.523 mmol) as a yellow solid. ^1H NMR [400 MHz, δ (ppm), CDCl_3]: 8.54–8.48 (m, 2 H), 8.00 (s, 1 H), 7.83–7.76 (m, 2 H), 7.76–7.70 (m, 2 H), 7.55–7.47 (m, 3 H). Yield: 99%.

(Z)-1-[4-(Pentafluoro- λ^6 -sulfanyl)phenyl]-N-phenylmethanimine Oxide (6e). According to general procedure A, the reaction of 4-(pentafluoro- λ^6 -sulfanyl)benzaldehyde (120 mg, 0.517 mmol) with *N*-phenylhydroxylamine (59 mg, 0.543 mmol) afforded nitrone **6e** (163.3 mg, 0.505 mmol) as a white-yellow solid. ^1H NMR [400 MHz, δ (ppm), CDCl_3]: 8.52–8.45 (m, 2 H), 8.00 (s, 1 H), 7.89–7.81 (m, 2 H), 7.81–7.74 (m, 2 H), 7.58–7.46 (m, 3 H). ^{13}C NMR [101 MHz, δ (ppm), CDCl_3]: 154.5, 149.1, 133.6, 132.5, 130.7, 129.5, 128.9, 126.5 (quint, $J = 4.4$ Hz), 121.9. FTIR [$\bar{\nu}$ (cm^{-1})]: 3057, 1594, 1573, 1074, 821, 810, 765. HRMS (ESI-TOF) m/z : [$\text{M} + \text{H}$]⁺ calcd for $\text{C}_{13}\text{H}_{11}\text{F}_5\text{NOS}$ 324.0476, found 324.0482. R_f : 0.45 (CH_2Cl_2). Yield: 98%.

(Z)-1-(4-Methoxyphenyl)-N-phenylmethanimine oxide (6f).²⁴ According to general procedure A, the reaction of 4-methoxybenzaldehyde (0.063 mL, 0.514 mmol) with *N*-phenylhydroxylamine (59 mg, 0.540 mmol) afforded nitrone **6f** (110 mg, 0.484 mmol) as a yellow-brown solid, after column chromatography ($\text{CH}_2\text{Cl}_2 \rightarrow \text{CH}_2\text{Cl}_2/\text{MeOH}$, 10:0.2). ^1H NMR [400 MHz, δ (ppm), CDCl_3]: 8.44–8.36

(m, 2 H), 7.84 (s, 1 H), 7.79–7.72 (m, 2 H), 7.50–7.37 (m, 3 H), 7.01–6.93 (m, 2 H), 3.86 (s, 3 H). Yield: 94%.

(Z)-1-(3-Fluorophenyl)-N-phenylmethanimine Oxide (6g).²⁵ According to general procedure A, the reaction of 3-fluorobenzaldehyde (0.060 mL, 0.564 mmol) with *N*-phenylhydroxylamine (62 mg, 0.564 mmol) afforded nitrone **6g** (118 mg, 0.548 mmol) as a light brown solid, after column chromatography (heptane/CH₂Cl₂, 1:4 → CH₂Cl₂/MeOH, 10:1). ¹H NMR [400 MHz, δ (ppm), CDCl₃]: 8.44 (ddd, *J* = 10.6, 2.6, 1.6 Hz, 1 H), 7.94 (s, 1 H), 7.90 (ddt, *J* = 8.1, 1.6, 0.7 Hz, 1 H), 7.80–7.73 (m, 2 H), 7.54–7.47 (m, 3 H), 7.44 (td, *J* = 8.1, 5.9 Hz, 1 H), 7.17 (tdd, *J* = 8.1, 2.6, 1.0 Hz, 1 H). ¹³C NMR [101 MHz, δ (ppm), CDCl₃]: 162.8 (d, *J* = 245.5 Hz), 149.1, 133.5, 132.6 (d, *J* = 9.1 Hz), 130.4, 130.1 (d, *J* = 8.4 Hz), 129.4, 125.1 (d, *J* = 3.0 Hz), 121.8, 118.0 (d, *J* = 21.7 Hz), 115.3 (d, *J* = 24.7 Hz). Yield: 97%.

(Z)-N-Phenyl-1-(3-tolyl)methanimine Oxide (6h).²⁵ According to general procedure B, the reaction of 3-methylbenzaldehyde (42 μL, 0.458 mmol) with *N*-phenylhydroxylamine (50 mg, 0.458 mmol) afforded nitrone **6h** (95.3 mg, 0.451 mmol) as a yellow oil, after column chromatography (heptane/AcOEt, 5:1 → 1:1). ¹H NMR [400 MHz, δ (ppm), CDCl₃]: 8.32 (tq, *J* = 1.8, 0.7 Hz, 1 H), 8.12 (dddquint, *J* = 7.8, 1.8, 1.2, 0.7 Hz, 1 H), 7.89 (s, 1 H), 7.81–7.75 (m, 2 H), 7.53–7.44 (m, 3 H), 7.38 (t, *J* = 7.8 Hz, 1 H), 7.32–7.27 (m, 1 H), 2.43 (s, 3 H). ¹³C NMR [101 MHz, δ (ppm), CDCl₃]: 149.3, 138.5, 134.9, 132.0, 130.8, 130.0, 129.4, 129.3, 128.7, 126.6, 121.9, 21.6. FTIR [$\bar{\nu}$ (cm⁻¹): 3092, 2963, 2920, 1652, 1590, 1459, 1088, 781, 692. HRMS (ESI-TOF) *m/z*: [M + H]⁺ calcd for C₁₄H₁₄NO 212.1070, found 212.1085. Yield: 98%.

(Z)-1-[3-(Methoxycarbonyl)phenyl]-N-phenylmethanimine Oxide (6i). According to general procedure A, the reaction of methyl 3-formylbenzoate (90 mg, 0.548 mmol) with *N*-phenylhydroxylamine (63 mg, 0.576 mmol) afforded nitrone **6i** (112 mg, 0.439 mmol) as a yellow oil, after column chromatography (CH₂Cl₂ → CH₂Cl₂/MeOH, 10:1). ¹H NMR [400 MHz, δ (ppm), CDCl₃]: 8.88 (dddd, *J* = 7.9, 1.7, 1.2, 0.5 Hz, 1 H), 8.80 (tt, *J* = 1.7, 0.5 Hz, 1 H), 8.13 (ddd, *J* = 7.9, 1.7, 1.2 Hz, 1 H), 8.01 (d, *J* = 0.5 Hz, 1 H), 7.83–7.75 (m, 2 H), 7.59 (tt, *J* = 7.9, 0.5 Hz, 1 H), 7.54–7.46 (m, 3 H), 3.95 (s, 3 H). ¹³C NMR [101 MHz, δ (ppm), CDCl₃]: 166.5, 149.0, 133.6, 132.6, 131.6, 131.0, 130.6, 130.4, 130.2, 129.3, 129.0, 121.7, 52.4. FTIR [$\bar{\nu}$ (cm⁻¹): 3064, 2952, 1718, 1434, 1278, 1187, 1072, 912, 729, 684. HRMS (ESI-TOF) *m/z*: [M + H]⁺ calcd for C₁₅H₁₄NO₃ 256.0968, found 256.0984. *R*_f: 0.07 (CH₂Cl₂). Yield: 80%.

(Z)-1-(3-Methoxyphenyl)-N-phenylmethanimine Oxide (6j). According to general procedure A, the reaction of 3-methoxybenzaldehyde (0.063 mL, 0.514 mmol) with *N*-phenylhydroxylamine (59 mg, 0.540 mmol) afforded nitrone **6j** (115 mg, 0.506 mmol) as a yellow oil, after column chromatography (CH₂Cl₂ → CH₂Cl₂/MeOH, 10:0.2). ¹H NMR [400 MHz, δ (ppm), CDCl₃]: 8.38 (dd, *J* = 2.7, 1.5 Hz, 1 H), 7.92 (s, 1 H), 7.81–7.75 (m, 2 H), 7.66 (dddd, *J* = 7.7, 1.5, 1.0, 0.5 Hz, 1 H), 7.52–7.44 (m, 3 H), 7.38 (dd, *J* = 8.3, 7.7 Hz, 1 H), 7.05 (ddd, *J* = 8.3, 2.7, 1.0 Hz, 1 H), 3.89 (s, 3 H). ¹³C NMR [101 MHz, δ (ppm), CDCl₃]: 159.7, 149.1, 134.7, 131.9, 130.0, 129.5, 129.2, 122.3, 121.8, 118.1, 112.7, 55.4. FTIR [$\bar{\nu}$ (cm⁻¹): 3060, 2834, 1553, 1270, 1025, 769, 684. HRMS (ESI-TOF) *m/z*: [M + Na]⁺ calcd for C₁₄H₁₃NO₂Na 250.0839, found 250.0857. *R*_f: 0.06 (CH₂Cl₂). Yield: 98%.

(Z)-N-Phenyl-1-[3-(trifluoromethyl)phenyl]methanimine Oxide (6k).²⁵ According to general procedure B, the reaction of 3-(trifluoromethyl)benzaldehyde (61 μL, 0.458 mmol) with *N*-phenylhydroxylamine (50 mg, 0.458 mmol) afforded nitrone **6k** (116 mg, 0.437 mmol) as a white solid, after column chromatography (heptane/AcOEt, 5:1 → 1:1). ¹H NMR [400 MHz, δ (ppm), CDCl₃]: 8.70 (dq, *J* = 2.3, 1.0 Hz, 1 H), 8.59 (dddd, *J* = 7.9, 1.7, 1.2, 0.6 Hz, 1 H), 8.01 (s, 1 H), 7.84–7.75 (m, 2 H), 7.72 (dq, *J* = 8.5, 1.1 Hz, 1 H), 7.61 (t, *J* = 7.9 Hz, 1 H), 7.55–7.48 (m, 3 H). ¹³C NMR [101 MHz, δ (ppm), CDCl₃]: 149.1, 133.1, 131.8 (q, *J* = 1.0 Hz), 131.5, 131.5, 130.5, 129.5, 129.3, 127.3 (q, *J* = 3.7 Hz), 125.7 (q, *J* = 3.9 Hz), 122.6, 121.9. FTIR [$\bar{\nu}$ (cm⁻¹): 3124, 1604, 1330, 1120, 1068, 770, 692. HRMS (ESI-TOF) *m/z*: [M + H]⁺ calcd for C₁₄H₁₁F₃NO 266.0787, found 266.0799. *R*_f: 0.35 (CH₂Cl₂). Yield: 95%.

(Z)-N-Phenyl-1-(2-tolyl)methanimine Oxide (6l).²⁶ According to general procedure A, the reaction of 2-methylbenzaldehyde (0.061 mL, 0.524 mmol) with *N*-phenylhydroxylamine (60 mg, 0.551 mmol)

afforded nitrone **6l** (107 mg, 0.508 mmol) as a yellow-brown solid, after column chromatography (CH₂Cl₂ → CH₂Cl₂/MeOH, 10:0.2). ¹H NMR [400 MHz, δ (ppm), CDCl₃]: 9.42–9.32 (m, 1 H), 8.07 (s, 1 H), 7.81–7.73 (m, 2 H), 7.53–7.44 (m, 3 H), 7.39–7.33 (m, 2 H), 7.28–7.23 (m, 1 H), 2.46 (s, 3 H). Yield: 97%.

(Z)-1-(2-Methoxyphenyl)-N-phenylmethanimine Oxide (6m).²⁵ According to general procedure A, the reaction of 2-methoxybenzaldehyde (70 mg, 0.514 mmol) with *N*-phenylhydroxylamine (59 mg, 0.540 mmol) afforded nitrone **6m** (106 mg, 0.464 mmol) as an orange-brown solid, after column chromatography (CH₂Cl₂ → CH₂Cl₂/MeOH, 10:0.2). ¹H NMR [400 MHz, δ (ppm), CDCl₃]: 9.48 (dd, *J* = 7.9, 1.7 Hz, 1 H), 8.40 (s, 1 H), 7.85–7.73 (m, 2 H), 7.53–7.39 (m, 4 H), 7.13–7.06 (m, 1 H), 6.93 (dd, *J* = 8.4, 1.1 Hz, 1 H), 3.89 (s, 3 H). ¹³C NMR [101 MHz, δ (ppm), CDCl₃]: 157.6, 149.8, 132.3, 129.8, 129.4, 129.2, 128.9, 122.0, 121.0, 120.1, 110.0, 55.8. FTIR [$\bar{\nu}$ (cm⁻¹): 3058, 1577, 1288, 1046, 746, 691, 611. *R*_f: 0.07 (CH₂Cl₂). Yield: 90%.

(Z)-N-Phenyl-1-(thiophen-3-yl)methanimine Oxide (6n).²⁷ According to general procedure A, the reaction of thiophene-3-carbaldehyde (0.047 mL, 0.535 mmol) with *N*-phenylhydroxylamine (61 mg, 0.562 mmol) afforded nitrone **6n** (109 mg, 0.535 mmol) as a white-yellow solid, after column chromatography (heptane/CH₂Cl₂, 1:1 → heptane/CH₂Cl₂, 0:1). ¹H NMR [400 MHz, δ (ppm), CDCl₃]: 9.16 (ddd, *J* = 3.1, 1.2, 0.7 Hz, 1 H), 8.06 (d, *J* = 0.6 Hz, 1 H), 7.82–7.76 (m, 2 H), 7.52–7.46 (m, 3 H), 7.45 (dd, *J* = 5.2, 1.2 Hz, 1 H), 7.39 (dd, *J* = 5.1, 3.0 Hz, 1 H). Yield: 99%.

(Z)-1-(1*H*-Indol-2-yl)-N-phenylmethanimine Oxide (6o). According to general procedure A, the reaction of 1*H*-indole-2-carbaldehyde (80 mg, 0.551 mmol) with *N*-phenylhydroxylamine (63 mg, 0.579 mmol) afforded nitrone **6o** (130 mg, 0.551 mmol) as a yellow-brown solid. ¹H NMR [500 MHz, δ (ppm), CDCl₃]: 11.69 (s, 1 H), 8.14 (s, 1 H), 7.87–7.80 (m, 2 H), 7.67 (dd, *J* = 8.1, 1.0 Hz, 1 H), 7.55–7.45 (m, 4 H), 7.32 (ddd, *J* = 8.2, 6.9, 1.1 Hz, 1 H), 7.16 (ddd, *J* = 8.0, 6.9, 1.0 Hz, 1 H), 6.94 (s, 1 H). ¹³C NMR [126 MHz, δ (ppm), CDCl₃]: 147.4, 136.0, 130.2, 129.9, 129.4, 127.6, 126.8, 125.2, 121.3, 120.8, 112.3, 108.6. FTIR [$\bar{\nu}$ (cm⁻¹): 3315, 3067, 1593, 1502, 1345, 1234, 818, 733. HRMS (ESI-TOF) *m/z*: [M + Na]⁺ calcd for C₁₅H₁₂N₂O₂Na 259.0842, found 259.0858. *R*_f: 0.13 (CH₂Cl₂). Yield: 99%.

(Z)-N-Phenyl-1-(1*H*-pyrrol-2-yl)methanimine Oxide (6p). According to general procedure A, the reaction of 1*H*-pyrrole-2-carbaldehyde (52 mg, 0.547 mmol) with *N*-phenylhydroxylamine (60 mg, 0.550 mmol) afforded nitrone **6p** (62 mg, 0.333 mmol) as a dark brown solid, after column chromatography (CH₂Cl₂ → CH₂Cl₂/MeOH, 10:0.1). ¹H NMR [500 MHz, δ (ppm), CDCl₃]: 12.21 (s, 1 H), 7.95 (s, 1 H), 7.81–7.73 (m, 2 H), 7.52–7.38 (m, 3 H), 7.07 (td, *J* = 2.7, 1.3 Hz, 1 H), 6.70 (dt, *J* = 3.6, 1.6 Hz, 1 H), 6.40 (dt, *J* = 3.9, 2.5 Hz, 1 H). ¹³C NMR [126 MHz, δ (ppm), CDCl₃]: 147.1, 129.5, 129.3, 126.1, 125.3, 121.3, 121.0, 115.9, 111.3. FTIR [$\bar{\nu}$ (cm⁻¹): 3317, 3062, 1580, 1403, 1294, 1074, 1045, 740, 686. HRMS (ESI-TOF) *m/z*: [M + H]⁺ calcd for C₁₁H₁₁N₂O 187.0866, found 187.0885. *R*_f: 0.45 (heptane/AcOEt, 1:1). Yield: 61%.

(Z)-1-(Furan-2-yl)-N-phenylmethanimine Oxide (6q).²⁸ According to general procedure A, the reaction of furan-2-carbaldehyde (0.043 mL, 0.520 mmol) with *N*-phenylhydroxylamine (60 mg, 0.546 mmol) afforded nitrone **6q** (97 mg, 0.520 mmol) as a light brown solid, after column chromatography (CH₂Cl₂ → CH₂Cl₂/MeOH, 10:0.2). ¹H NMR [400 MHz, δ (ppm), CDCl₃]: 8.16 (s, 1 H), 8.01 (dt, *J* = 3.5, 0.7 Hz, 1 H), 7.83–7.77 (m, 2 H), 7.58 (dd, *J* = 1.8, 0.7 Hz, 1 H), 7.52–7.44 (m, 3 H), 6.65 (dd, *J* = 3.6, 1.8 Hz, 1 H). Yield: 99%.

(Z)-2-(Benzylamino)-2-oxo-*N*-phenylethan-1-imine Oxide (6r). According to general procedure A, the reaction of *N*-benzyl-2-oxoacetamide (56 mg, 0.343 mmol) with *N*-phenylhydroxylamine (26 mg, 0.240 mmol) afforded nitrone **6r** (34.5 mg, 0.135 mmol) as a white solid. ¹H NMR [400 MHz, δ (ppm), CDCl₃]: 10.39 (s, 1 H), 7.72–7.67 (m, 2 H), 7.66 (s, 1 H), 7.58–7.46 (m, 3 H), 7.40–7.27 (m, 5 H), 4.64 (d, *J* = 5.9 Hz, 2 H). ¹³C NMR [101 MHz, δ (ppm), CDCl₃]: 160.8, 147.5, 137.8, 131.7, 130.3, 129.7, 128.9, 128.0, 127.7, 121.6, 43.3. FTIR [$\bar{\nu}$ (cm⁻¹): 3255, 3121, 2945, 1634, 1516, 1059, 768, 751, 683. HRMS (ESI-TOF) *m/z*: [M + Na]⁺ calcd for C₁₅H₁₄N₂O₂Na 277.0948, found 277.0956. *R*_f: 0.68 (CH₂Cl₂/MeOH, 10:0.2). Yield: 39%.

General Procedure for the Synthesis of Isoxazolidines 4a, 4b, 4d–r. The solution containing alkene 2 in distilled THF (3 equiv, 1.48 M) at 0 °C was added to a PTFE tube containing the corresponding nitron 6 (1 equiv) and galvinoxyl (0.03 equiv). The tube was filled up with distilled THF, closed and brought to 15 kbar at 50 °C for 16 h. Then, the reaction mixture was filtered off, and the solvent was removed under vacuo. The crude mixture was purified by column chromatography using the indicated eluent to afford isoxazolidines 4a, 4b, and 4d–r.

2,3-Diphenyl-5-[(trifluoromethyl)sulfanyl]isoxazolidine (4a). According to the general procedure, the reaction of nitron 6a (26 mg, 0.119 mmol) and alkene 2 in a 1 mL PTFE high-pressure tube afforded *cis*-4a (24.9 mg, 0.77 mmol, 65%) as a white solid and a mixture of *cis*- and *trans*-4a and regioisomers 7a (12.6 mg, 0.039 mmol, 33%) as a yellow oil after column chromatography (heptane/CH₂Cl₂, 9:1). Total yield: 98%.

rac-(3R,5R)-2,3-Diphenyl-5-[(trifluoromethyl)sulfanyl]isoxazolidine (cis-4a). ¹H NMR [500 MHz, δ (ppm), CDCl₃]: 7.52–7.47 (m, 2 H), 7.43–7.37 (m, 2 H), 7.35–7.30 (m, 1 H), 7.24–7.18 (m, 2 H), 7.04–6.99 (m, 1 H), 6.99–6.95 (m, 2 H), 6.01 (dd, *J* = 8.1, 4.4 Hz, 1 H), 4.41 (dd, *J* = 9.0, 7.1 Hz, 1 H), 3.41 (dddq, *J* = 13.6, 9.0, 8.1, 0.9 Hz, 1 H), 2.44–2.31 (m, 1 H). ¹³C NMR [126 MHz, δ (ppm), CDCl₃]: 148.8, 139.8, 130.2 (q, *J* = 307.7 Hz), 129.3, 128.8, 128.3, 127.2, 123.8, 117.6, 80.5 (q, *J* = 2.5 Hz), 68.3, 47.2. FTIR [$\bar{\nu}$ (cm⁻¹): 3070, 2963, 1598, 1489, 1258, 1114, 1031, 966, 928, 752, 700. HRMS (EI) *m/z*: [M⁺] calcd for C₁₆H₁₄F₃NOS 325.0748, found 325.0765. *R*_f: 0.20 (heptane/CH₂Cl₂, 9:1).

rac-(3R,5S)-2,3-Diphenyl-5-[(trifluoromethyl)sulfanyl]isoxazolidine (trans-4a). ¹H NMR [500 MHz, δ (ppm), CDCl₃]: 7.50–7.45 (m, 2 H), 7.41–7.36 (m, 2 H), 7.35–7.30 (m, 1 H), 7.25–7.18 (m, 2 H), 7.04–6.98 (m, 2 H), 6.98–6.93 (m, 1 H), 6.07 (dd, *J* = 6.8, 3.8 Hz, 1 H), 4.90 (t, *J* = 7.3 Hz, 1 H), 3.02–2.92 (m, 1 H), 2.88 (ddd, *J* = 13.3, 7.3, 3.8 Hz, 1 H). ¹³C NMR [126 MHz, δ (ppm), CDCl₃]: 151.0, 139.9, 129.9 (q, *J* = 307.8 Hz), 129.2, 128.8, 128.2, 126.7, 122.4, 115.2, 82.3 (q, *J* = 2.0 Hz), 68.1, 46.3. FTIR [$\bar{\nu}$ (cm⁻¹): 3065, 1598, 1489, 1206, 1108, 1049, 842, 796, 665. HRMS (EI) *m/z*: [M⁺] calcd for C₁₆H₁₄F₃NOS 325.0748, found 325.0750. *R*_f: 0.11 (heptane/CH₂Cl₂, 9:1).

3-(4-Fluorophenyl)-2-phenyl-5-[(trifluoromethyl)sulfanyl]isoxazolidine (4b). According to the general procedure, the reaction of nitron 6b (27 mg, 0.125 mmol) and alkene 2 in a 1 mL PTFE high-pressure tube afforded *cis*-4b (27.6 mg, 0.080 mmol, 64%) as a white solid, a mixture of *cis*- and *trans*-4b and regioisomers 7b (13.1 mg, 0.038 mmol, 27%) as a yellow oil and *trans*-4b (3.5 mg, 0.010 mmol, 8%) as a pale yellow oil, after column chromatography (heptane/CH₂Cl₂, 9:1). Total yield: 99%.

rac-(3R,5R)-3-(4-Fluorophenyl)-2-phenyl-5-[(trifluoromethyl)sulfanyl]isoxazolidine (cis-4b). ¹H NMR [500 MHz, δ (ppm), CDCl₃]: 7.49–7.43 (m, 2 H), 7.25–7.19 (m, 2 H), 7.11–7.05 (m, 2 H), 7.05–7.01 (m, 1 H), 6.99–6.93 (m, 2 H), 6.01 (dd, *J* = 8.1, 4.3 Hz, 1 H), 4.40 (dd, *J* = 9.0, 7.0 Hz, 1 H), 3.39 (dddq, *J* = 13.7, 9.0, 8.1, 0.9 Hz, 1 H), 2.39–2.28 (m, 1 H). ¹³C NMR [126 MHz, δ (ppm), CDCl₃]: 162.6 (d, *J* = 247.0 Hz), 148.6, 135.4 (d, *J* = 3.1 Hz), 130.1 (q, *J* = 307.8 Hz), 128.92, 128.91 (d, *J* = 7.2 Hz), 124.0, 117.7, 116.2 (d, *J* = 21.6 Hz), 80.5 (q, *J* = 2.3 Hz), 67.7, 47.1. ¹⁹F NMR [471 MHz, δ (ppm), CDCl₃]: –39.9. FTIR [$\bar{\nu}$ (cm⁻¹): 3071, 1597, 1455, 1256, 1226, 1110, 1029, 905, 804, 754. HRMS (EI) *m/z*: [M⁺] calcd for C₁₆H₁₃F₄NOS 343.0654, found 343.0650. *R*_f: 0.26 (heptane/CH₂Cl₂, 17:3).

rac-(3R,5S)-3-(4-Fluorophenyl)-2-phenyl-5-[(trifluoromethyl)sulfanyl]isoxazolidine (trans-4b). ¹H NMR [500 MHz, δ (ppm), CDCl₃]: 7.44–7.40 (m, 2 H), 7.25–7.20 (m, 2 H), 7.10–7.04 (m, 2 H), 6.99–6.92 (m, 3 H), 6.05 (dd, *J* = 6.8, 3.9 Hz, 1 H), 4.88 (t, *J* = 7.2 Hz, 1 H), 2.98–2.90 (m, 1 H), 2.87 (ddd, *J* = 13.3, 7.3, 3.9 Hz, 1 H). ¹³C NMR [126 MHz, δ (ppm), CDCl₃]: 162.3 (d, *J* = 242.3 Hz), 150.7, 135.6, 128.9, 128.4 (d, *J* = 8.3 Hz), 122.6, 116.2 (d, *J* = 21.7 Hz), 115.3, 81.2, 67.4, 46.2. The carbon signal of SCF₃ was not observed. ¹⁹F NMR [471 MHz, δ (ppm), CDCl₃]: –39.4. FTIR [$\bar{\nu}$ (cm⁻¹): 3071, 1686, 1598, 1154, 1052, 937, 693. HRMS (EI) *m/z*: [M⁺] calcd for C₁₆H₁₃F₄NOS 343.0654, found 343.0676. *R*_f: 0.21 (heptane/CH₂Cl₂, 17:3).

2-Phenyl-3-(4-tolyl)-5-[(trifluoromethyl)sulfanyl]isoxazolidine (4c). The solution containing alkene 2 (3.0 equiv) in distilled THF (500 μL) at 0 °C was added to a PTFE tube containing nitron 6c (1.0 equiv). The tube was filled up with distilled THF, closed and brought to 15 kbar at 50 °C for 16 h. Then, the reaction mixture was filtered off and the solvent was removed under vacuo. The crude mixture was purified by column chromatography (heptane/CH₂Cl₂, 4:1) to afford isoxazolidine *cis*-4c (17.1 mg, 0.050 mmol, 50%) as white solid and *trans*-4c (12.1 mg, 0.36 mmol, 35%) as a brown oil, contaminated with regioisomers 7c and azoxybenzene 8. Total yield: 85%.

rac-(3R,5R)-2-Phenyl-3-(4-tolyl)-5-[(trifluoromethyl)sulfanyl]isoxazolidine (cis-4c). ¹H NMR [500 MHz, δ (ppm), CDCl₃]: 7.40–7.34 (m, 2 H), 7.23–7.16 (m, 4 H), 7.03–6.95 (m, 3 H), 6.00 (dd, *J* = 8.1, 4.3 Hz, 1 H), 4.36 (dd, *J* = 9.0, 7.2 Hz, 1 H), 3.38 (dddq, *J* = 13.7, 9.0, 8.1, 0.9 Hz, 1 H), 2.39–2.32 (m, 1 H), 2.36 (s, 3 H). ¹³C NMR [126 MHz, δ (ppm), CDCl₃]: 148.9, 138.1, 136.6, 130.2 (q, *J* = 307.7 Hz), 130.0, 128.8, 127.1, 123.7, 117.6, 80.5 (q, *J* = 2.2 Hz), 68.1, 47.3, 21.3. ¹⁹F NMR [471 MHz, δ (ppm), CDCl₃]: –39.9. FTIR [$\bar{\nu}$ (cm⁻¹): 3056, 2962, 1597, 1489, 1257, 1107, 752, 691. HRMS (EI) *m/z*: [M⁺] calcd for C₁₇H₁₆F₃NOS 339.0905, found 339.0890. *R*_f: 0.21 (heptane/CH₂Cl₂, 4:1).

rac-(3R,5S)-2-Phenyl-3-(4-tolyl)-5-[(trifluoromethyl)sulfanyl]isoxazolidine (trans-4c). ¹H NMR [500 MHz, δ (ppm), CDCl₃]: 7.36–7.33 (m, 2 H), 7.25–7.16 (m, 4 H), 7.02–6.98 (m, 2 H), 6.97–6.92 (m, 1 H), 6.06 (dd, *J* = 6.8, 3.8 Hz, 1 H), 4.85 (t, *J* = 7.2 Hz, 1 H), 2.95 (dddq, *J* = 13.2, 7.6, 6.8, 0.9 Hz, 1 H), 2.85 (ddd, *J* = 13.2, 7.2, 3.8 Hz, 1 H), 2.36 (s, 3 H). ¹³C NMR [126 MHz, δ (ppm), CDCl₃]: 151.0, 137.9, 136.9, 130.1 (q, *J* = 307.7 Hz), 129.8, 128.8, 126.6, 122.2, 115.2, 82.3 (q, *J* = 2.2 Hz), 67.9, 46.4, 21.3. ¹⁹F NMR [471 MHz, δ (ppm), CDCl₃]: –39.3. FTIR [$\bar{\nu}$ (cm⁻¹): 3063, 2925, 1599, 1487, 1152, 1053, 756, 686. HRMS (EI) *m/z*: [M⁺] calcd for C₁₇H₁₆F₃NOS 339.0905, found 339.0924. *R*_f: 0.13 (heptane/CH₂Cl₂, 4:1).

2-Phenyl-3-[4-(trifluoromethyl)phenyl]-5-[(trifluoromethyl)sulfanyl]isoxazolidine (4d). According to the general procedure, the reaction of nitron 6d (50 mg, 0.190 mmol) and alkene 2 in a 1.5 mL PTFE high-pressure tube, containing approximately 300 μL of glass beads, afforded a mixture of isoxazolidines *cis*- and *trans*-4d and regioisomers 7d (53.1 mg, 0.137 mmol, 73%) as a pale yellow solid oil, after column chromatography (heptane/CH₂Cl₂, 17:3). FTIR [$\bar{\nu}$ (cm⁻¹): 1597, 1490, 1325, 1104, 1051, 850, 754, 692. HRMS (EI) *m/z*: [M⁺] calcd for C₁₇H₁₃F₆NOS 393.0622, found 393.0624. *R*_f: 0.20 (heptane/CH₂Cl₂, 17:3). Total yield: 73%.

rac-(3R,5R)-2-Phenyl-3-[4-(trifluoromethyl)phenyl]-5-[(trifluoromethyl)sulfanyl]isoxazolidine (cis-4d). ¹H NMR [500 MHz, δ (ppm), CDCl₃]: 7.72–7.55 (m, 4 H), 7.25–7.18 (m, 2 H), 7.05–7.00 (m, 1 H), 6.97–6.93 (m, 2 H), 6.00 (dd, *J* = 8.0, 4.3 Hz, 1 H), 4.50 (dd, *J* = 9.1, 6.7, 1 H), 3.43 (dddq, *J* = 13.7, 9.1, 8.0, 0.9, 1 H), 2.33 (ddd, *J* = 13.7, 6.7, 4.3 Hz, 1 H). ¹³C NMR [126 MHz, δ (ppm), CDCl₃]: 148.4, 144.1, 130.6 (q, *J* = 32.6 Hz), 130.0 (q, *J* = 307.8 Hz), 129.0, 127.4, 126.3 (q, *J* = 3.8 Hz), 124.09 (q, *J* = 272.1 Hz), 124.05, 117.4, 80.4 (q, *J* = 2.2 Hz), 67.5, 46.9.

rac-(3R,5S)-2-Phenyl-3-[4-(trifluoromethyl)phenyl]-5-[(trifluoromethyl)sulfanyl]isoxazolidine (trans-4d). ¹H NMR [500 MHz, δ (ppm), CDCl₃]: 7.70–7.56 (m, 4 H), 7.27–7.18 (m, 2 H), 7.00–6.96 (m, 3 H), 6.04 (dd, *J* = 6.3, 4.6 Hz, 1 H), 4.97 (t, *J* = 7.1 Hz, 1 H), 3.01–2.83 (m, 2 H). ¹³C NMR [126 MHz, δ (ppm), CDCl₃]: 150.5, 144.1, 130.5 (q, *J* = 32.5 Hz), 130.0 (q, *J* = 307.8 Hz), 129.0, 127.0, 126.2 (q, *J* = 3.9 Hz), 122.7, 115.1, 82.2 (q, *J* = 2.1 Hz), 67.5, 45.9.

3-[4-(Pentafluoro-λ⁶-sulfanyl)phenyl]-2-phenyl-5-[(trifluoromethyl)sulfanyl]isoxazolidine (4e). According to the general procedure, the reaction of nitron 6e (37.8 mg, 0.143 mmol) and alkene 2 in a 1 mL PTFE high-pressure tube afforded a mixture of isoxazolidines *cis*- and *trans*-4e and regioisomers 7e (41 mg, 0.091 mmol, 72%) as a white solid, after column chromatography (heptane/CH₂Cl₂, 17:3). FTIR [$\bar{\nu}$ (cm⁻¹): 2963, 1670, 1585, 1261, 1120, 1104, 817, 753, 584. HRMS (EI) *m/z*: [M⁺] calcd for C₁₆H₁₃F₈NOS₂ 451.0311, found 451.0318. *R*_f: 0.21 (heptane/CH₂Cl₂, 17:3). Total yield: 72%.

rac-(3R,5R)-3-[4-(Pentafluoro-λ⁶-sulfanyl)phenyl]-2-phenyl-5-[(trifluoromethyl)sulfanyl]isoxazolidine (cis-4e). ¹H NMR [500 MHz, δ (ppm), CDCl₃]: 7.85–7.72 (m, 2 H), 7.64–7.55 (m, 2 H), 7.30–7.21

(m, 2 H), 7.09–7.02 (m, 1 H), 7.02–6.92 (m, 2 H), 6.00 (dd, $J = 8.0$, 4.3 Hz, 1 H), 4.52 (dd, $J = 9.2$, 6.6, 1 H), 3.43 (dt, $J = 13.7$, 8.6, 1 H), 2.32 (ddd, $J = 13.7$, 6.6, 4.3 Hz, 1 H). ^{13}C NMR [126 MHz, δ (ppm), CDCl_3]: 153.7–153.4 (m), 148.3, 144.0, 130.0 (q, $J = 307.9$ Hz), 129.1, 127.3, 127.0, 124.2, 117.3, 80.4 (q, $J = 2.3$ Hz), 67.1, 46.7.

rac-(3*R*,5*S*)-3-[4-(Pentafluoro- λ^6 -sulfanyl)phenyl]-2-phenyl-5-[(trifluoromethyl)sulfanyl]isoxazolidine (*trans*-4*e*). ^1H NMR [500 MHz, δ (ppm), CDCl_3]: 7.80–7.74 (m, 2 H), 7.60–7.56 (m, 2 H), 7.28–7.21 (m, 2 H), 7.01–6.97 (m, 3 H), 6.03 (dd, $J = 5.9$, 5.0, 1 H), 4.97 (t, $J = 7.1$ Hz, 1 H), 3.01–2.80 (m, 2 H). ^{13}C NMR [126 MHz, δ (ppm), CDCl_3]: 153.7–153.4 (m), 150.4, 143.9, 130.0 (q, $J = 307.9$ Hz), 129.0, 127.1, 127.0, 122.8, 115.1, 82.2 (q, $J = 2.2$ Hz), 67.1, 45.8.

3-(4-Methoxyphenyl)-2-phenyl-5-[(trifluoromethyl)sulfanyl]isoxazolidine (*4f*). According to the general procedure, the reaction of nitrene **6f** (54 mg, 0.238 mmol) and alkene **2** in a 1.5 mL PTFE high-pressure tube afforded isoxazolidine *cis*-**4f** (44.3 mg, 0.125 mmol, 53%), a mixture of isoxazolidines *cis*- and *trans*-**4f** (27.3 mg, 0.077 mmol, 32%) and isoxazolidine *trans*-**4f** mixed with *cis*-**4f** and regioisomers **7f** (12.4 mg, 0.035 mmol, 15%) as yellow oils, after column chromatography (heptane/ CH_2Cl_2 , 7:3). Total yield: 99%.

rac-(3*R*,5*R*)-3-(4-Methoxyphenyl)-2-phenyl-5-[(trifluoromethyl)sulfanyl]isoxazolidine (*cis*-**4f**). ^1H NMR [500 MHz, δ (ppm), CDCl_3]: 7.43–7.35 (m, 2 H), 7.23–7.18 (m, 2 H), 7.04–6.99 (m, 1 H), 6.99–6.95 (m, 2 H), 6.94–6.90 (m, 2 H), 6.01 (dd, $J = 8.1$, 4.3 Hz, 1 H), 6.34 (dd, $J = 8.9$, 7.3 Hz, 1 H), 3.82 (s, 3 H), 3.37 (dddq, $J = 13.8$, 8.9, 8.2, 0.9 Hz, 1 H), 2.46–2.25 (m, 1 H). ^{13}C NMR [126 MHz, δ (ppm), CDCl_3]: 159.6, 148.8, 131.4, 130.2 (q, $J = 307.8$ Hz), 128.8, 128.4, 123.8, 117.8, 114.6, 80.5 (q, $J = 2.2$ Hz), 68.0, 55.4, 47.2. ^{19}F NMR [471 MHz, δ (ppm), CDCl_3]: –39.9. FTIR [$\bar{\nu}$ (cm^{-1})]: 3003, 1614, 1515, 1298, 1103, 1031, 816, 773. HRMS (EI) m/z : [$\text{M}^{+\bullet}$] calcd for $\text{C}_{17}\text{H}_{16}\text{F}_3\text{NO}_2\text{S}$ 355.0854, found 355.0861. R_f : 0.15 (heptane/ CH_2Cl_2 , 4:1).

rac-(3*R*,5*S*)-3-(4-Methoxyphenyl)-2-phenyl-5-[(trifluoromethyl)sulfanyl]isoxazolidine (*trans*-**4f**). ^1H NMR [500 MHz, δ (ppm), CDCl_3]: 7.38–7.35 (m, 2 H), 7.22–7.18 (m, 2 H), 7.01–6.98 (m, 2 H), 6.97–6.93 (m, 1 H), 6.92–6.89 (m, 2 H), 6.06 (dd, $J = 6.8$, 3.7 Hz, 1 H), 4.87–4.77 (m, 1 H), 3.81 (s, 3 H), 3.00–2.90 (m, 1 H), 2.84 (ddd, $J = 13.2$, 7.2, 3.7 Hz, 1 H). ^{13}C NMR [126 MHz, δ (ppm), CDCl_3]: 159.5, 151.0, 131.8, 130.0 (q, $J = 307.8$ Hz), 128.8, 127.9, 122.4, 115.4, 114.5, 82.3 (q, $J = 2.3$ Hz), 67.7, 55.5, 46.3. FTIR [$\bar{\nu}$ (cm^{-1})]: 3002, 1512, 1489, 1248, 1109, 1030, 794, 693. HRMS (EI) m/z : [$\text{M}^{+\bullet}$] calcd for $\text{C}_{17}\text{H}_{16}\text{F}_3\text{NO}_2\text{S}$ 355.0854, found 355.0855. R_f : 0.10 (heptane/ CH_2Cl_2 , 4:1).

3-(3-Fluorophenyl)-2-phenyl-5-[(trifluoromethyl)sulfanyl]isoxazolidine (*4g*). According to the general procedure, the reaction of nitrene **6g** (52 mg, 0.242 mmol) and alkene **2** in a 1.5 mL PTFE high-pressure tube afforded isoxazolidine *cis*-**4g** (46.6 mg, 0.136 mmol, 56%) as a white solid, a mixture of *cis*- and *trans*-**4g** (27.8 mg, 0.081, 34%) as a yellow oil, and isoxazolidine *trans*-**4g** mixed with *cis*-**4g** and regioisomers **7g** (8.5 mg, 0.025 mmol, 10%) as a yellow solid, after column chromatography (heptane/ CH_2Cl_2 , 9:1). Total yield: 99%.

rac-(3*R*,5*R*)-3-(3-Fluorophenyl)-2-phenyl-5-[(trifluoromethyl)sulfanyl]isoxazolidine (*cis*-**4g**). ^1H NMR [500 MHz, δ (ppm), CDCl_3]: 7.34 (td, $J = 8.1$, 5.9 Hz, 1 H), 7.28–7.18 (m, 4 H), 7.06–6.98 (m, 2 H), 6.98–6.93 (m, 2 H), 5.98 (dd, $J = 8.1$, 4.3 Hz, 1 H), 4.41 (dd, $J = 9.1$, 6.8 Hz, 1 H), 3.39 (dddq, $J = 13.7$, 9.1, 8.1, 0.9 Hz, 1 H), 2.33 (ddd, $J = 13.7$, 6.8, 4.3 Hz, 1 H). ^{13}C NMR [126 MHz, δ (ppm), CDCl_3]: 163.4 (d, $J = 247.0$ Hz), 148.6, 142.5 (d, $J = 7.2$ Hz), 130.9 (d, $J = 8.3$ Hz), 130.1 (q, $J = 307.9$ Hz), 128.9, 123.9, 122.7 (d, $J = 2.9$ Hz), 117.4, 115.3 (d, $J = 21.3$ Hz), 114.1 (d, $J = 22.6$ Hz), 80.4 (q, $J = 2.4$ Hz), 67.5 (d, $J = 1.9$ Hz), 46.9. ^{19}F NMR [471 MHz, δ (ppm), CDCl_3]: –39.9. FTIR [$\bar{\nu}$ (cm^{-1})]: 3062, 1594, 1489, 1448, 1258, 1111, 1044, 915, 833, 752, 690. HRMS (EI) m/z : [$\text{M}^{+\bullet}$] calcd for $\text{C}_{16}\text{H}_{13}\text{F}_4\text{NOS}$ 343.0654, found 343.0675. R_f : 0.22 (heptane/ CH_2Cl_2 , 17:3).

rac-(3*R*,5*S*)-3-(3-Fluorophenyl)-2-phenyl-5-[(trifluoromethyl)sulfanyl]isoxazolidine (*trans*-**4g**). ^1H NMR [500 MHz, δ (ppm), CDCl_3]: 7.35 (td, $J = 8.1$, 5.9 Hz, 1 H), 7.25–7.20 (m, 4 H), 7.04–6.94 (m, 4 H), 6.05 (dd, $J = 6.8$, 4.0 Hz, 1 H), 4.90 (t, $J = 7.4$ Hz, 1 H), 2.99–2.91 (m, 1 H), 2.33 (ddd, $J = 13.2$, 7.4, 4.0 Hz, 1 H). ^{13}C NMR [126 MHz, δ (ppm), CDCl_3]: 163.4 (d, $J = 247.1$ Hz), 150.6, 142.6 (d, $J =$

7.2 Hz), 130.7 (d, $J = 8.3$ Hz), 128.9, 122.6, 122.2 (d, $J = 2.8$ Hz), 115.2 (d, $J = 21.6$ Hz), 115.1, 113.7 (d, $J = 22.7$ Hz), 80.2 (q, $J = 2.5$ Hz), 67.4 (d, $J = 2.1$ Hz), 46.0. ^{19}F NMR [471 MHz, δ (ppm), CDCl_3]: –39.4. FTIR [$\bar{\nu}$ (cm^{-1})]: 3070, 1593, 1488, 1451, 1256, 1109, 947, 787, 691. HRMS (EI) m/z : [$\text{M}^{+\bullet}$] calcd for $\text{C}_{16}\text{H}_{13}\text{F}_4\text{NOS}$ 343.0654, found 343.0667. R_f : 0.15 (heptane/ CH_2Cl_2 , 17:3).

2-Phenyl-3-(3-tolyl)-5-[(trifluoromethyl)sulfanyl]isoxazolidine (**4h**). According to the general procedure, the reaction of nitrene **6h** (49 mg, 0.234 mmol) and alkene **2** in a 1.5 mL PTFE high-pressure tube afforded isoxazolidine *cis*-**4h** (46 mg, 0.136 mmol, 57%) as an off white solid and isoxazolidine *trans*-**4h** and regioisomers **7h** (26 mg, 0.077 mmol, 31%) as a yellow solid, after column chromatography (heptane/ CH_2Cl_2 , 17:3 \rightarrow 7:3). Total yield: 88%.

rac-(3*R*,5*R*)-2-Phenyl-3-(3-tolyl)-5-[(trifluoromethyl)sulfanyl]isoxazolidine (*cis*-**4h**). ^1H NMR [500 MHz, δ (ppm), CDCl_3]: 7.31–7.28 (m, 1 H), 7.27–7.24 (m, 2 H), 7.22–7.17 (m, 2 H), 7.14–7.10 (m, 1 H), 7.02–6.94 (m, 3 H), 5.98 (dd, $J = 8.1$, 4.4 Hz, 1 H), 4.35 (dd, $J = 9.0$, 7.2 Hz, 1 H), 3.37 (dddq, $J = 13.6$, 9.0, 8.1, 0.9 Hz, 1 H), 2.38–2.32 (m, 1 H), 2.36 (s, 3 H). ^{13}C NMR [126 MHz, δ (ppm), CDCl_3]: 148.9, 139.7, 139.1, 130.2 (q, $J = 307.7$ Hz), 129.1, 129.1, 128.8, 127.6, 124.2, 123.6, 117.5, 80.5 (q, $J = 2.2$ Hz), 68.3, 47.2, 21.6. FTIR [$\bar{\nu}$ (cm^{-1})]: 3028, 1599, 1489, 1040, 1001, 839, 737, 724, 692. HRMS (EI) m/z : [$\text{M}^{+\bullet}$] calcd for $\text{C}_{17}\text{H}_{16}\text{F}_3\text{NOS}$ 339.0905, found 339.0925. R_f : 0.41 (heptane/ CH_2Cl_2 , 4:1).

rac-(3*R*,5*S*)-2-Phenyl-3-(3-tolyl)-5-[(trifluoromethyl)sulfanyl]isoxazolidine (*trans*-**4h**). ^1H NMR [500 MHz, δ (ppm), CDCl_3]: 7.31–7.18 (m, 5 H), 7.14–7.10 (m, 1 H), 7.03–6.98 (m, 2 H), 6.98–6.91 (m, 1 H), 6.06 (dd, $J = 6.8$, 3.7 Hz, 1 H), 4.85 (t, $J = 7.3$ Hz, 1 H), 2.95 (dddq, $J = 13.2$, 7.6, 6.8, 0.9 Hz, 1 H), 2.86 (ddd, $J = 13.2$, 7.3, 3.7 Hz, 1 H), 2.36 (s, 3 H). ^{13}C NMR [126 MHz, δ (ppm), CDCl_3]: 151.2, 139.9, 139.0, 130.0 (q, $J = 307.8$ Hz), 129.0, 128.9, 128.8, 127.1, 123.7, 122.3, 115.1, 82.4 (q, $J = 2.1$ Hz), 68.1, 46.4, 21.6. ^{19}F NMR [471 MHz, δ (ppm), CDCl_3]: –39.3. FTIR [$\bar{\nu}$ (cm^{-1})]: 3029, 1598, 1489, 1150, 1111, 1045, 785, 692. HRMS (EI) m/z : [$\text{M}^{+\bullet}$] calcd for $\text{C}_{17}\text{H}_{16}\text{F}_3\text{NOS}$ 339.0905, found 339.0931. R_f : 0.34 (heptane/ CH_2Cl_2 , 4:1).

Methyl 3-[2-Phenyl-5-[(trifluoromethyl)sulfanyl]isoxazolidin-3-yl]benzoate (**4i**). According to the general procedure, the reaction of nitrene **6i** (26 mg, 0.102 mmol) and alkene **2** in a 1 mL PTFE high-pressure tube, containing approximately 150 μL of glass beads, afforded isoxazolidine *cis*-**4i** (17.3 mg, 0.045 mmol, 44%) as an off-white solid and a mixture of isoxazolidines *cis*- and *trans*-**4i** and regioisomers **7i** (18.2 mg, 0.047 mmol, 47%) as a brown-yellow solid, after column chromatography (heptane/ CH_2Cl_2 , 3:2). Total yield: 91%.

Methyl 3-[*rac*-(3*R*,5*R*)-2-Phenyl-5-[(trifluoromethyl)sulfanyl]isoxazolidin-3-yl]benzoate (*cis*-**4i**). ^1H NMR [500 MHz, δ (ppm), CDCl_3]: 8.11 (t, $J = 1.8$ Hz, 1 H), 8.01 (dt, $J = 7.7$, 1.4 Hz, 1 H), 7.76 (dddd, $J = 7.7$, 1.8, 1.2, 0.5 Hz, 1 H), 7.48 (t, $J = 7.7$ Hz, 1 H), 7.24–7.19 (m, 2 H), 7.07–7.00 (m, 1 H), 6.98–6.94 (m, 2 H), 6.01 (dd, $J = 8.0$, 4.5 Hz, 1 H), 4.50 (dd, $J = 8.9$, 7.0 Hz, 1 H), 3.93 (s, 3 H), 3.43 (dddq, $J = 13.6$, 8.9, 8.0, 0.9 Hz, 1 H), 2.42–2.30 (m, 1 H). ^{13}C NMR [126 MHz, δ (ppm), CDCl_3]: 166.8, 148.6, 140.4, 131.6, 131.1, 130.0 (q, $J = 307.7$ Hz), 129.6, 129.0, 128.3, 124.0, 117.6, 80.4 (q, $J = 2.5$ Hz), 67.9, 52.4, 46.9. ^{19}F NMR [471 MHz, δ (ppm), CDCl_3]: –39.9. FTIR [$\bar{\nu}$ (cm^{-1})]: 3015, 1729, 1598, 1489, 1301, 1247, 1114, 1025, 786, 692, 674. HRMS (EI) m/z : [$\text{M}^{+\bullet}$] calcd for $\text{C}_{18}\text{H}_{16}\text{F}_3\text{NO}_3\text{S}$ 383.0803, found 383.0824. R_f : 0.27 (heptane/ CH_2Cl_2 , 3:2).

Methyl 3-[*rac*-(3*R*,5*S*)-2-Phenyl-5-[(trifluoromethyl)sulfanyl]isoxazolidin-3-yl]benzoate (*trans*-**4i**). ^1H NMR [500 MHz, δ (ppm), CDCl_3]: 8.12 (t, $J = 1.8$ Hz, 1 H), 8.02–7.98 (m, 1 H), 7.69 (dt, $J = 7.8$, 1.6 Hz, 1 H), 7.47 (t, $J = 7.7$, 1 H), 7.26–7.18 (m, 2 H), 7.00–6.98 (m, 2 H), 6.97–6.94 (m, 1 H), 6.06 (dd, $J = 6.7$, 4.0 Hz, 1 H), 4.96 (t, $J = 7.3$ Hz, 1 H), 3.93 (s, 3 H), 3.01–2.94 (m, 1 H), 2.91 (ddd, $J = 13.3$, 7.4, 4.0 Hz, 1 H). ^{13}C NMR [126 MHz, δ (ppm), CDCl_3]: 166.8, 150.7, 140.5, 131.19, 131.14, 130.0 (q, $J = 307.9$ Hz), 129.57, 129.55, 128.9, 127.8, 122.6, 115.2, 82.3 (q, $J = 2.2$ Hz), 67.6, 52.4, 46.1. ^{19}F NMR [471 MHz, δ (ppm), CDCl_3]: –39.4. FTIR [$\bar{\nu}$ (cm^{-1})]: 3064, 1720, 1598, 1489, 1285, 1107, 1020, 799, 751, 692. HRMS (EI) m/z : [$\text{M}^{+\bullet}$] calcd for $\text{C}_{18}\text{H}_{16}\text{F}_3\text{NO}_3\text{S}$ 383.0803, found 383.0810. R_f : 0.22 (heptane/ CH_2Cl_2 , 3:2).

rac-(3*R*,5*R*)-3-(3-Methoxyphenyl)-2-phenyl-5-[(trifluoromethyl)sulfanyl]isoxazolidine (**4j**). According to the general procedure, the reaction of nitron 6j (50 mg, 0.190 mmol) and alkene 2 in a 1.5 mL PTFE high-pressure tube, containing approximately 300 μ L of glass beads, afforded isoxazolidine *cis*-**4j** (33.8 mg, 0.095 mmol, 53%) as a white solid, a mixture of isoxazolidines *cis*- and *trans*-**4j** (3 mg, 0.0084 mmol, 5%) as a yellow oil and isoxazolidines *trans*-**4j** and **7j** (18.2 mg, 0.051 mmol, 22%) as a yellow oil, after column chromatography (heptane/CH₂Cl₂, 7:3). Total yield: 80%.

rac-(3*R*,5*R*)-3-(3-Methoxyphenyl)-2-phenyl-5-[(trifluoromethyl)sulfanyl]isoxazolidine (*cis*-**4j**). ¹H NMR [400 MHz, δ (ppm), CDCl₃]: 7.29 (t, *J* = 7.9 Hz, 1 H), 7.24–7.17 (m, 2 H), 7.09–6.95 (m, 5 H), 6.85 (ddd, *J* = 8.3, 2.7, 1.1 Hz, 1 H), 5.99 (dd, *J* = 8.1, 4.3 Hz, 1 H), 4.37 (dd, *J* = 9.1, 7.0 Hz, 1 H), 3.81 (s, 3 H), 3.43–3.32 (m, 1 H), 2.36 (ddd, *J* = 13.7, 7.0, 4.3 Hz, 1 H). ¹³C NMR [101 MHz, δ (ppm), CDCl₃]: 160.4, 148.9, 141.6, 130.3, 130.2 (q, *J* = 307.7 Hz), 128.8, 123.6, 119.3, 117.3, 113.8, 112.4, 80.5 (q, *J* = 2.5 Hz), 68.0, 55.4, 47.2 (q, *J* = 1.2 Hz). ¹⁹F NMR [377 MHz, δ (ppm), CDCl₃]: –39.9. FTIR [$\bar{\nu}$ (cm⁻¹)]: 3006, 2838, 1599, 1490, 1117, 757, 694. HRMS (EI) *m/z*: [M⁺] calcd for C₁₇H₁₆F₃NO₂S 355.0854, found 355.0868. *R*_f: 0.16 (heptane/CH₂Cl₂, 7:3).

rac-(3*R*,5*S*)-3-(3-Methoxyphenyl)-2-phenyl-5-[(trifluoromethyl)sulfanyl]isoxazolidine (*trans*-**4j**). ¹H NMR [400 MHz, δ (ppm), CDCl₃]: 7.29 (t, *J* = 8.1 Hz, 1 H), 7.25–7.19 (m, 2 H), 7.07–6.92 (m, 5 H), 6.89–6.81 (m, 1 H), 6.06 (dd, *J* = 6.8, 3.8, 1 H), 4.86 (t, *J* = 7.4 Hz, 1 H), 3.81 (s, 3 H), 2.96 (dddq, *J* = 13.3, 7.6, 6.8, 0.9 Hz, 1 H), 2.87 (ddd, *J* = 13.3, 7.3, 3.8 Hz, 1 H). ¹³C NMR [101 MHz, δ (ppm), CDCl₃]: 160.3, 151.0, 141.6, 130.2, 130.0 (q, *J* = 307.8 Hz), 128.8, 122.3, 118.8, 115.1, 113.7, 112.0, 82.3 (q, *J* = 2.3 Hz), 68.0, 55.5, 46.3. ¹⁹F NMR [377 MHz, δ (ppm), CDCl₃]: –39.3. FTIR [$\bar{\nu}$ (cm⁻¹)]: 3064, 1720, 1598, 1489, 1347, 1107, 1020, 799, 750, 692. HRMS (ESI-TOF) *m/z*: [M + H]⁺ calcd for C₁₇H₁₇F₃NO₂S 356.0932, found 356.0939. *R*_f: 0.13 (heptane/CH₂Cl₂, 7:3).

2-Phenyl-3-[3-(trifluoromethyl)phenyl]-5-[(trifluoromethyl)sulfanyl]isoxazolidine (**4k**). According to the general procedure, the reaction of nitron 6k (49 mg, 0.234 mmol) and alkene 2 in a 1.5 mL PTFE high-pressure tube afforded a mixture of isoxazolidines *cis*- and *trans*-**4k** and **7k** (87.4 mg, 0.222 mmol, 95%) as a white-yellow solid, after column chromatography (heptane/CH₂Cl₂, 17:3 \rightarrow 7:3). FTIR [$\bar{\nu}$ (cm⁻¹)]: 2927, 1598, 1490, 1263, 1144, 1045. HRMS (EI) *m/z*: [M⁺] calcd for C₁₇H₁₃F₆NOS 393.0622, found 393.0639. *R*_f: 0.38 (heptane/CH₂Cl₂, 4:1). Total yield: 95%.

rac-(3*R*,5*R*)-2-Phenyl-3-[3-(trifluoromethyl)phenyl]-5-[(trifluoromethyl)sulfanyl]isoxazolidine (*cis*-**4k**). ¹H NMR [500 MHz, δ (ppm), CDCl₃]: 7.73–7.69 (m, 2 H), 7.60–7.56 (m, 1 H), 7.54–7.48 (m, 1 H), 7.26–7.20 (m, 2 H), 7.05–7.00 (m, 1 H), 6.98–6.93 (m, 2 H), 5.99 (dd, *J* = 8.0, 4.5 Hz, 1 H), 4.51 (dd, *J* = 9.0, 6.7 Hz, 1 H), 3.41 (dddq, *J* = 13.6, 9.0, 8.0, 0.8 Hz, 1 H), 2.37–2.28 (m, 1 H). ¹³C NMR [126 MHz, δ (ppm), CDCl₃]: 148.6, 141.1, 131.6 (q, *J* = 32.4 Hz), 130.4 (q, *J* = 1.2 Hz), 129.9 (q, *J* = 308.0 Hz), 129.9, 129.0, 125.2 (q, *J* = 3.8 Hz), 124.0 (q, *J* = 272.4 Hz), 124.1, 123.9 (q, *J* = 3.8 Hz), 117.4, 80.4 (q, *J* = 2.5 Hz), 67.8, 46.8.

rac-(3*R*,5*S*)-2-Phenyl-3-[3-(trifluoromethyl)phenyl]-5-[(trifluoromethyl)sulfanyl]isoxazolidine (*trans*-**4k**). ¹H NMR [500 MHz, δ (ppm), CDCl₃]: 7.73–7.70 (m, 1 H), 7.68–7.64 (m, 1 H), 7.60–7.56 (m, 1 H), 7.53–7.48 (m, 1 H), 7.26–7.20 (m, 2 H), 6.92–6.88 (m, 3 H), 6.06–6.02 (m, 1 H), 4.96 (t, *J* = 7.2 Hz, 1 H), 2.98–2.86 (m, 2 H). ¹³C NMR [126 MHz, δ (ppm), CDCl₃]: 150.6, 141.1, 131.6 (q, *J* = 32.4 Hz), 130.4 (q, *J* = 1.2 Hz), 129.7, 128.9, 125.1 (q, *J* = 4.0 Hz), 123.5 (q, *J* = 3.8 Hz), 122.7, 115.2, 82.3 (q, *J* = 2.4 Hz), 67.5, 46.0.

2-Phenyl-3-(2-tolyl)-5-[(trifluoromethyl)sulfanyl]isoxazolidine (**4l**). According to the general procedure, the reaction of nitron 6l (49 mg, 0.234 mmol) and alkene 2 in a 1.5 mL PTFE high-pressure tube afforded isoxazolidine *cis*-**4l** (1.9 mg, 0.0056 mmol; used for characterization) as a colorless oil and a mixture of isoxazolidines *cis*- and *trans*-**4l** (79.5 mg, 0.234 mmol, 99%) as a yellow solid, after column chromatography (heptane/CH₂Cl₂, 4:1). FTIR [$\bar{\nu}$ (cm⁻¹)]: 3025, 1596, 1489, 1258, 1109, 1041, 972, 754, 695. HRMS (EI) *m/z*: [M⁺] calcd for C₁₇H₁₆F₃NOS 339.0905, found 339.0923. *R*_f: 0.23 (heptane/CH₂Cl₂, 4:1). Total yield: 99%.

rac-(3*R*,5*R*)-2-Phenyl-3-(2-tolyl)-5-[(trifluoromethyl)sulfanyl]isoxazolidine (*cis*-**4l**). ¹H NMR [500 MHz, δ (ppm), CDCl₃]: 7.72 (dd, *J* = 7.2, 1.7 Hz, 1 H), 7.26–7.17 (m, 5 H), 7.00 (tt, *J* = 7.4, 1.2 Hz, 1 H), 6.96–6.88 (m, 2 H), 6.01 (dd, *J* = 8.1, 4.2 Hz, 1 H), 4.61 (dd, *J* = 9.1, 7.1 Hz, 1 H), 3.44 (dddq, *J* = 13.5, 9.1, 8.1, 0.9 Hz, 1 H), 2.35 (s, 3 H), 2.25 (ddd, *J* = 13.5, 7.1, 4.2 Hz, 1 H). ¹³C NMR [126 MHz, δ (ppm), CDCl₃]: 148.9, 138.0, 134.6, 130.8, 130.1 (q, *J* = 307.4 Hz), 128.9, 127.8, 127.3, 126.6, 123.5, 117.2, 80.5 (q, *J* = 2.2 Hz), 64.5, 45.6, 19.7. ¹⁹F NMR [471 MHz, δ (ppm), CDCl₃]: –40.0.

rac-(3*R*,5*S*)-2-Phenyl-3-(2-tolyl)-5-[(trifluoromethyl)sulfanyl]isoxazolidine (*trans*-**4l**). ¹H NMR [500 MHz, δ (ppm), CDCl₃]: 7.65–7.62 (m, 1 H), 7.27–7.15 (m, 5 H), 6.97–6.93 (m, 3 H), 6.06 (dd, *J* = 6.7, 3.9 Hz, 1 H), 5.04 (t, *J* = 7.5 Hz, 1 H), 2.89 (ddd, *J* = 13.1, 7.5, 3.9 Hz, 1 H), 2.80 (dddq, *J* = 13.1, 7.5, 6.7, 0.9 Hz, 1 H), 2.39 (s, 3 H). ¹³C NMR [126 MHz, δ (ppm), CDCl₃]: 151.1, 137.8, 134.3, 130.8, 128.7, 127.8, 127.0, 126.2, 122.1, 114.7, 82.2 (q, *J* = 2.3 Hz), 65.3, 44.6, 19.4.

3-(2-Methoxyphenyl)-2-phenyl-5-[(trifluoromethyl)sulfanyl]isoxazolidine (**4m**). According to the general procedure, the reaction of nitron 6m (53 mg, 0.234 mmol) and alkene 2 in a 1.5 mL PTFE high-pressure tube afforded isoxazolidine *cis*-**4m** (35.6 mg, 0.100 mmol, 43%) as an off white solid and a mixture of isoxazolidines *cis*- and *trans*-**4m** (29.6 mg, 0.083 mmol, 28%) as a yellow solid, after column chromatography (heptane/CH₂Cl₂, 7:3). Total yield: 71%.

rac-(3*R*,5*R*)-3-(2-Methoxyphenyl)-2-phenyl-5-[(trifluoromethyl)sulfanyl]isoxazolidine (*cis*-**4m**). ¹H NMR [500 MHz, δ (ppm), CDCl₃]: 7.65 (dd, *J* = 7.6, 1.7 Hz, 1 H), 7.28 (ddd, *J* = 8.2, 7.5, 1.8 Hz, 1 H), 7.25–7.19 (m, 2 H), 7.01–6.94 (m, 4 H), 6.91 (dd, *J* = 8.3, 1.0 Hz, 1 H), 5.94 (dd, *J* = 8.0, 4.5 Hz, 1 H), 4.87 (dd, *J* = 9.1, 6.1 Hz, 1 H), 3.86 (s, 3 H), 3.40 (dddq, *J* = 13.6, 9.1, 8.0, 0.9 Hz, 1 H), 2.30–2.20 (m, 1 H). ¹³C NMR [126 MHz, δ (ppm), CDCl₃]: 156.3, 149.4, 130.3 (q, *J* = 307.7 Hz), 128.9, 128.4, 127.5, 123.1, 121.3, 116.7, 110.5, 80.6 (q, *J* = 2.4 Hz), 62.1, 55.5, 45.0. FTIR [$\bar{\nu}$ (cm⁻¹)]: 3075, 1599, 1490, 1243, 1106, 1027, 897, 751, 664. HRMS (EI) *m/z*: [M⁺] calcd for C₁₇H₁₆F₃NO₂S 355.0854, found 355.0875. *R*_f: 0.19 (heptane/CH₂Cl₂, 7:3).

rac-(3*R*,5*S*)-3-(2-Methoxyphenyl)-2-phenyl-5-[(trifluoromethyl)sulfanyl]isoxazolidine (*trans*-**4m**). ¹H NMR [500 MHz, δ (ppm), CDCl₃]: 7.59 (dd, *J* = 7.6, 1.5 Hz, 1 H), 7.31–7.26 (m, 2 H), 7.06–7.02 (m, 2 H), 7.00–6.88 (m, 4 H), 5.99–5.96 (m, 1 H), 5.26 (dd, *J* = 7.5, 5.8 Hz, 1 H), 3.88 (s, 3 H), 2.90 (ddd, *J* = 12.7, 7.5, 5.0 Hz, 1 H), 2.84–2.76 (m, 1 H). ¹³C NMR [126 MHz, δ (ppm), CDCl₃]: 156.3, 151.2, 128.9, 128.8, 128.1, 127.2, 122.0, 121.1, 114.9, 110.4, 82.4 (q, *J* = 2.2 Hz), 62.9, 55.5, 43.7. The carbon signal of SCF₃ was not observed. FTIR [$\bar{\nu}$ (cm⁻¹)]: 2839, 1599, 1490, 1256, 1106, 1026, 751, 692. HRMS (EI) *m/z*: [M⁺] calcd for C₁₇H₁₆F₃NO₂S 355.0854, found 355.0862. *R*_f: 0.15 (heptane/CH₂Cl₂, 7:3).

2-Phenyl-3-(thiophen-3-yl)-5-[(trifluoromethyl)sulfanyl]isoxazolidine (**4n**). According to the general procedure, the reaction of nitron 6n (48 mg, 0.234 mmol) and alkene 2 in a 1.5 mL PTFE high-pressure tube afforded a mixture of isoxazolidines *cis*- and *trans*-**4n** (68.4 mg, 0.206 mmol, 88%) as a yellow solid, after column chromatography (heptane/CH₂Cl₂, 3:2). FTIR [$\bar{\nu}$ (cm⁻¹)]: 3095, 1598, 1489, 1257, 1163, 1110, 1031, 837, 792, 754, 692. HRMS (EI) *m/z*: [M⁺] calcd for C₁₄H₁₂F₃NOS₂ 331.0312, found 331.0330. *R*_f: 0.19 (heptane/CH₂Cl₂, 17:3). Total yield: 88%.

rac-(3*R*,5*R*)-2-Phenyl-3-(thiophen-3-yl)-5-[(trifluoromethyl)sulfanyl]isoxazolidine (*cis*-**4n**). ¹H NMR [500 MHz, δ (ppm), CDCl₃]: 7.36 (dd, *J* = 5.0, 3.0 Hz, 1 H), 7.30–7.27 (m, 1 H), 7.25–7.20 (m, 2 H), 7.19 (dd, *J* = 5.0, 1.3 Hz, 1 H), 7.02 (tt, *J* = 7.4, 1.2 Hz, 1 H), 7.00–6.96 (m, 2 H), 6.00 (dd, *J* = 8.2, 4.2 Hz, 1 H), 4.51 (dd, *J* = 8.8, 6.7 Hz, 1 H), 3.36–3.28 (m, 1 H), 2.38 (ddd, *J* = 13.6, 6.7, 4.2 Hz, 1 H). ¹³C NMR [126 MHz, δ (ppm), CDCl₃]: 148.9, 140.4, 130.2 (q, *J* = 307.7 Hz), 128.8, 127.3, 126.1, 123.9, 122.7, 117.5, 80.5 (q, *J* = 2.5 Hz), 64.6, 45.9.

rac-(3*R*,5*S*)-2-Phenyl-3-(thiophen-3-yl)-5-[(trifluoromethyl)sulfanyl]isoxazolidine (*trans*-**4n**). ¹H NMR [500 MHz, δ (ppm), CDCl₃]: 7.32 (dd, *J* = 5.0, 3.0 Hz, 1 H), 7.30–7.27 (m, 1 H), 7.26–7.20 (m, 2 H), 7.09 (dd, *J* = 5.0, 1.4 Hz, 1 H), 7.06–6.95 (m, 3 H), 6.03 (dd, *J* = 7.2, 4.9 Hz, 1 H), 5.01 (t, *J* = 6.5 Hz, 1 H), 2.96 (dt, *J* = 13.0, 6.4 Hz, 1 H), 2.78 (ddd, *J* = 12.7, 7.3, 4.7 Hz, 1 H). ¹³C NMR [126 MHz, δ

(ppm), CDCl₃]: 150.2, 140.6, 130.2 (q, *J* = 307.7 Hz), 128.8, 127.0, 125.8, 122.7, 122.4, 115.7, 81.9 (q, *J* = 2.2 Hz), 64.2, 44.6.

3-(1*H*-Indol-2-yl)-2-phenyl-5-[(trifluoromethyl)sulfanyl]isoxazolidine (4o). According to the general procedure, the reaction of nitron 6o (56 mg, 0.237 mmol) and alkene 2 in a 1.5 mL PTFE high-pressure tube afforded isoxazolidines *cis*- and *trans*-4o (20.3 mg, 0.056 mmol, 24%; contaminated with 8) as a brown-yellow oil and a mixture of isoxazolidine *trans*-4o and regioisomers 7o (35.6 mg, 0.098 mmol, 41%) as a brown oil, after column chromatography (heptane/CH₂Cl₂, 11:9). FTIR [$\bar{\nu}$ (cm⁻¹)] of isoxazolidines *cis*- and *trans*-4o: 3413, 3060, 2962, 1599, 1436, 1258, 1110, 1022, 788, 756, 684, 660. FTIR [$\bar{\nu}$ (cm⁻¹)] of isoxazolidine *trans*-4o and regioisomers 7o: 3406, 3059, 2963, 1597, 1455, 1231, 1107, 1014, 793, 693. Total yield: 65%.

rac-(3*R*,5*R*)-3-(1*H*-Indol-2-yl)-2-phenyl-5-[(trifluoromethyl)sulfanyl]isoxazolidine (*cis*-4o). ¹H NMR [500 MHz, δ (ppm), CDCl₃]: 8.67 (bs, 1 H), 7.61–7.58 (m, 1 H), 7.40–7.37 (m, 1 H), 7.25–7.18 (m, 3 H), 7.15–7.12 (m, 1 H), 7.05–7.02 (m, 3 H), 6.50 (d, *J* = 2.0 Hz, 1 H), 6.07 (dd, *J* = 8.3, 3.5 Hz, 1 H), 4.77 (dd, *J* = 9.4, 5.6 Hz, 1 H), 3.44–3.32 (m, 1 H), 2.50 (ddd, *J* = 13.8, 5.6, 3.5 Hz, 1 H). ¹³C NMR [126 MHz, δ (ppm), CDCl₃]: 148.6, 136.2, 135.6, 130.0 (q, *J* = 306.8 Hz), 129.1, 128.6, 123.9, 122.6, 120.6, 120.4, 116.7, 111.5, 100.9, 80.7 (q, *J* = 2.4 Hz), 62.2, 44.9. *R*_f: 0.51 (heptane/CH₂Cl₂, 1:1).

rac-(3*R*,5*S*)-3-(1*H*-Indol-2-yl)-2-phenyl-5-[(trifluoromethyl)sulfanyl]isoxazolidine (*trans*-4o). ¹H NMR [500 MHz, δ (ppm), CDCl₃]: 8.50 (bs, 1 H), 7.57–7.47 (m, 3 H), 7.32 (dt, *J* = 8.2, 0.9 Hz, 1 H), 7.06–7.03 (m, 1 H), 6.98–6.90 (m, 2 H), 6.86–6.82 (m, 2 H), 6.40 (d, *J* = 2.1 Hz, 1 H), 5.84 (dd, *J* = 8.3, 4.0 Hz, 1 H), 4.28 (dd, *J* = 9.4, 5.7 Hz, 1 H), 2.82 (dt, *J* = 13.7, 8.9 Hz, 1 H), 2.16–2.09 (m, 1 H). ¹³C NMR [126 MHz, δ (ppm), CDCl₃]: 148.5, 134.4, 132.7, 129.0, 128.6, 122.6, 122.5, 120.6, 119.5, 116.2, 111.3, 100.5, 82.1 (q, *J* = 2.4 Hz), 59.8, 44.6. *R*_f: 0.42 (heptane/CH₂Cl₂, 1:1).

3-(1*H*-Indol-2-yl)-2-phenyl-4-[(trifluoromethyl)sulfanyl]isoxazolidine (7o). ¹H NMR [500 MHz, δ (ppm), CDCl₃]: 7.64–7.59 (m, 2 H), 7.38–6.97 (m, 16 H), 6.59–6.55 (m, 2 H), 5.25 (d, *J* = 8.2 Hz, 1 H), 4.94 (d, *J* = 4.4 Hz, 1 H), 4.67–4.61 (m, 1 H), 4.61–4.56 (m, 1 H), 4.31 (q, *J* = 7.6 Hz, 1 H), 4.25–4.18 (m, 2 H), 4.11 (dd, *J* = 9.3, 6.2 Hz, 1 H). ¹³C NMR [126 MHz, δ (ppm), CDCl₃]: 149.3, 148.9, 135.9, 135.7, 135.5, 132.8, 129.2, 129.2, 128.5, 127.9, 123.4, 123.2, 122.7, 122.5, 120.8, 120.6, 120.3, 115.1, 115.0, 111.3, 111.2, 103.1, 100.6, 73.2, 72.7, 70.1, 65.6, 52.4, 48.1.

2-Phenyl-3-(1*H*-pyrrol-2-yl)-5-[(trifluoromethyl)sulfanyl]isoxazolidine (4p). According to the general procedure, the reaction of nitron 6p (44 mg, 0.234 mmol) and alkene 2 in a 1.5 mL PTFE high-pressure tube afforded a mixture of isoxazolidines *cis*- and *trans*-4p and 7p (33 mg, 0.105 mmol, 45%) as a brown oil, after column chromatography (heptane/CH₂Cl₂, 4:1 → CH₂Cl₂/MeOH, 10:1). FTIR [$\bar{\nu}$ (cm⁻¹)]: 3421, 2960, 1597, 1489, 1154, 1109, 1082, 1029, 756, 722. HRMS (EI) *m/z*: [M⁺] calcd for C₁₄H₁₃F₃N₂O₂S 314.0701, found 314.0706. *R*_f (unassigned mixture): 0.46, 0.30, 0.24, 0.20 (heptane/CH₂Cl₂, 1:1). Total yield: 45%.

rac-(3*R*,5*R*)-2-Phenyl-3-(1*H*-pyrrol-2-yl)-5-[(trifluoromethyl)sulfanyl]isoxazolidine (*cis*-4p). ¹H NMR [400 MHz, δ (ppm), CDCl₃]: 8.65 (bs, 1 H), 7.28–7.22 (m, 2 H), 7.08–6.98 (m, 3 H), 6.81–6.77 (m, 1 H), 6.21–6.18 (m, 1 H), 6.15–6.12 (m, 1 H), 6.03 (dd, *J* = 8.3, 3.6 Hz, 1 H), 4.62 (dd, *J* = 8.9, 5.6 Hz, 1 H), 3.34–3.17 (m, 1 H), 2.48–2.36 (m, 1 H). ¹³C NMR [101 MHz, δ (ppm), CDCl₃]: δ 148.9, 130.0 (q, *J* = 307.9 Hz), 129.0, 128.8, 123.8, 116.8, 115.2, 109.1, 106.7, 80.7 (q, *J* = 2.3 Hz), 62.5, 44.6.

rac-(3*R*,5*S*)-2-Phenyl-3-(1*H*-pyrrol-2-yl)-5-[(trifluoromethyl)sulfanyl]isoxazolidine (*trans*-4p). ¹H NMR [500 MHz, δ (ppm), CDCl₃]: 8.57 (bs, 1 H), 7.31–6.66 (m, 7 H), 6.27–6.15 (m, 1 H), 5.97 (t, *J* = 6.4 Hz, 1 H), 5.07 (dd, *J* = 7.0, 4.4 Hz, 1 H), 3.00 (ddd, *J* = 12.2, 7.1, 4.4 Hz, 1 H), 2.68 (dt, *J* = 13.1, 6.4 Hz, 1 H). ¹³C NMR [101 MHz, δ (ppm), CDCl₃]: 150.0, 129.9, 128.9, 123.8, 118.0, 115.8, 107.2, 106.3, 82.1, 62.7, 43.2. The carbon signal of SCF₃ was not observed.

2-Phenyl-3-(1*H*-pyrrol-2-yl)-4-[(trifluoromethyl)sulfanyl]isoxazolidine (7p). ¹H NMR [400 MHz, δ (ppm), CDCl₃]: 8.65 (bs, 1 H), 7.30–7.23 (m, 2 H), 7.06–6.99 (m, 3 H), 6.81–6.77 (m, 1 H), 6.27–6.19 (m, 1 H), 6.19 (m, 1 H), 5.11 (d, *J* = 7.8 Hz, 1 H), 4.66–4.55 (m, 1 H), 4.22 (q, *J* = 7.5 Hz, 1 H), 4.15 (dd, *J* = 8.6, 6.8 Hz, 1 H). ¹³C NMR [101 MHz, δ (ppm), CDCl₃]: 149.2, 129.3, 126.0, 123.4, 118.8,

115.2, 109.0, 108.8, 73.5, 65.3, 48.7 (q, *J* = 1.3 Hz). The carbon signal of SCF₃ was not observed.

2-Phenyl-3-(1*H*-pyrrol-2-yl)-4-[(trifluoromethyl)sulfanyl]isoxazolidine (7p). ¹H NMR [500 MHz, δ (ppm), CDCl₃]: 8.57 (bs, 1 H), 7.31–6.66 (m, 7 H), 6.27–6.15 (m, 1 H), 4.82 (d, *J* = 4.2 Hz, 1 H), 4.65–4.50 (m, 2 H), 4.26–4.10 (m, 1 H). ¹³C NMR [101 MHz, δ (ppm), CDCl₃]: 149.6, 129.4, 126.0, 124.1, 118.1, 115.2, 109.1, 108.7, 70.3, 65.3, 48.7. The carbon signal of SCF₃ was not observed.

3-(Furan-2-yl)-2-phenyl-5-[(trifluoromethyl)sulfanyl]isoxazolidine (4q). According to the general procedure, the reaction of nitron 6q (44 mg, 0.234 mmol) in a 1.5 mL PTFE high-pressure tube afforded isoxazolidine *cis*-4q (33.2 mg, 0.105 mmol, 45%) as an off white solid and isoxazolidines *trans*-4q and 7q (24.7 mg, 0.078 mmol, 34%) as a yellow oil, after column chromatography (heptane/CH₂Cl₂, 23:2 → heptane/CH₂Cl₂, 0:1). Total yield: 79%.

rac-(3*R*,5*R*)-3-(Furan-2-yl)-2-phenyl-5-[(trifluoromethyl)sulfanyl]isoxazolidine (*cis*-4q). ¹H NMR [400 MHz, δ (ppm), CDCl₃]: 7.45 (dd, *J* = 1.8, 0.9 Hz, 1 H), 7.31–7.22 (m, 2 H), 7.10–6.98 (m, 3 H), 6.37 (dd, *J* = 3.2, 1.8 Hz, 1 H), 6.35 (d, *J* = 3.2 Hz, 1 H), 6.00 (dd, *J* = 8.1, 4.5 Hz, 1 H), 4.50 (dd, *J* = 8.8, 6.5 Hz, 1 H), 3.23 (dddq, *J* = 13.5, 8.8, 8.1, 0.9 Hz, 1 H), 2.63 (ddd, *J* = 13.5, 6.5, 4.5 Hz, 1 H). ¹³C NMR [101 MHz, δ (ppm), CDCl₃]: 151.0, 148.7, 143.0, 130.2 (q, *J* = 307.7 Hz), 128.9, 124.2, 117.5, 110.8, 109.0, 80.5 (q, *J* = 2.6 Hz), 63.0, 42.4 (q, *J* = 1.2 Hz). FTIR [$\bar{\nu}$ (cm⁻¹)]: 2922, 1489, 1453, 1254, 1106, 1037, 936, 743, 680. HRMS (EI) *m/z*: [M⁺] calcd for C₁₄H₁₂F₃N₂O₂S 315.0541, found 315.0538. *R*_f: 0.48 (heptane/CH₂Cl₂, 7:3).

rac-(3*R*,5*S*)-3-(Furan-2-yl)-2-phenyl-5-[(trifluoromethyl)sulfanyl]isoxazolidine (*trans*-4q). ¹H NMR [400 MHz, δ (ppm), CDCl₃]: 7.37 (dd, *J* = 1.8, 0.9 Hz, 1 H), 7.27–7.22 (m, 2 H), 7.09–7.05 (m, 2 H), 6.98 (tt, *J* = 7.3, 1.2 Hz, 1 H), 6.30 (dd, *J* = 3.3, 1.8 Hz, 1 H), 6.26 (dt, *J* = 3.3, 0.8, 1 H), 6.11 (dd, *J* = 7.4, 5.2 Hz, 1 H), 5.00 (dd, *J* = 7.7, 4.3, 1 H), 3.17 (dddq, *J* = 13.7, 7.4, 4.3, 0.8, 1 H), 2.77–2.67 (m, 1 H). ¹³C NMR [101 MHz, δ (ppm), CDCl₃]: 151.6, 149.2, 142.8, 130.0 (q, *J* = 307.7 Hz), 128.8, 123.0, 116.2, 110.6, 108.4, 81.8 (q, *J* = 2.5 Hz), 61.6, 41.6 (q, *J* = 1.2 Hz). FTIR [$\bar{\nu}$ (cm⁻¹)]: 2872, 1599, 1490, 1262, 1118, 1046, 757, 694. HRMS (EI) *m/z*: [M⁺] calcd for C₁₄H₁₂F₃N₂O₂S 315.0541, found 315.0545. *R*_f: 0.39 (heptane/CH₂Cl₂, 7:3).

***N*-Benzyl-2-phenyl-5-[(trifluoromethyl)sulfanyl]isoxazolidine-3-carboxamide (4r).** According to the general procedure, the reaction of nitron 6r (25 mg, 0.098 mmol) and alkene 2 in a 1 mL PTFE high-pressure tube afforded isoxazolidine *cis*-4r (3.2 mg, 0.0084 mmol, 9%; used for NMR characterization) as a white solid and a mixture of isoxazolidines *cis*- and *trans*-4r (16.1 mg, 0.042 mmol, 51%) as a yellow-white solid, after column chromatography (heptane/CH₂Cl₂, 17:3 → CH₂Cl₂/MeOH, 24:1). FTIR [$\bar{\nu}$ (cm⁻¹)]: 3385, 3309 2930, 1668, 1597, 1454, 1161, 1029, 697. HRMS (EI) *m/z*: [M⁺] calcd for C₁₈H₁₇F₃N₂O₂S 382.0963, found 382.0964. Total yield: 60%.

rac-(3*R*,5*R*)-*N*-Benzyl-2-phenyl-5-[(trifluoromethyl)sulfanyl]isoxazolidine-3-carboxamide (*cis*-4r). ¹H NMR [400 MHz, δ (ppm), CDCl₃]: 7.59–7.52 (m, 1 H), 7.37–7.27 (m, 7 H), 7.11–7.03 (m, 1 H), 7.02–6.97 (m, 2 H), 5.88 (dd, *J* = 8.1, 4.7 Hz, 1 H), 4.56 (dd, *J* = 14.8, 6.1 Hz, 1 H), 4.49 (dd, *J* = 14.8, 5.9 Hz, 1 H), 4.31 (dd, *J* = 9.6, 3.5 Hz, 1 H), 3.19–3.07 (m, 1 H), 2.75–2.65 (m, 1 H). ¹³C NMR [101 MHz, δ (ppm), CDCl₃]: 169.7, 148.8, 137.6, 129.6 (q, *J* = 308.1 Hz), 129.5, 128.9, 127.9, 127.8, 123.9, 115.1, 80.3 (q, *J* = 2.5 Hz), 67.6, 43.7, 39.4.

rac-(3*R*,5*S*)-*N*-Benzyl-2-phenyl-5-[(trifluoromethyl)sulfanyl]isoxazolidine-3-carboxamide (*trans*-4r). ¹H NMR [500 MHz, δ (ppm), CDCl₃]: 7.52–7.43 (m, 1 H), 7.36–7.23 (m, 7 H), 7.11–7.02 (m, 3 H), 5.91 (t, *J* = 6.8 Hz, 1 H), 4.54–4.49 (m, 2 H), 4.46 (dd, *J* = 15.0, 5.6 Hz, 1 H), 3.29 (ddd, *J* = 13.5, 7.3, 3.9 Hz, 1 H), 2.62 (ddd, *J* = 13.9, 8.1, 6.2 Hz, 1 H). ¹³C NMR [126 MHz, δ (ppm), CDCl₃]: 169.1, 149.4, 137.6, 129.6 (q, *J* = 308.1 Hz), 129.0, 128.8, 127.7, 127.6, 123.6, 115.1, 82.3 (q, *J* = 2.5 Hz), 67.1, 43.5, 39.0.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.7b02639.

Computational details, ASA and EDA of **6m** and **6p**, and Cartesian coordinates (PDF)
Detailed optimization reaction conditions; ¹H and ¹³C NMR spectra (PDF)

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Notes

The authors declare no competing financial interest.

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