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Straightforward Route to γ-Sultams via Novel Tandem S_N/Michael Addition

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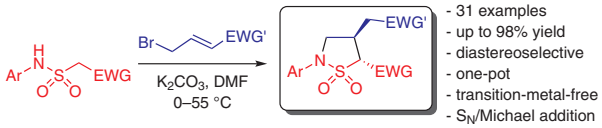

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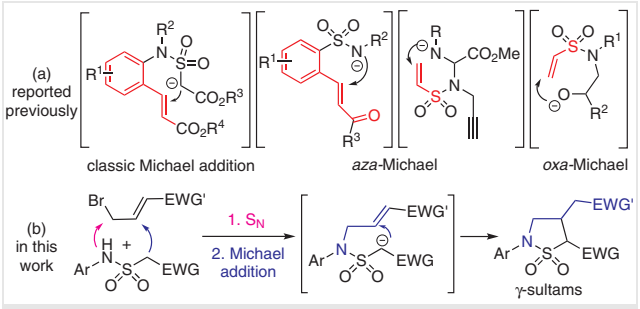
Abstract A novel tandem approach to trisubstituted γ-sultams has been developed involving *N*-alkylation of methanesulfonanilides with EWG-substituted allyl bromides followed by intramolecular Michael addition. A series of various isothiazolidine 1,1-dioxides have been prepared under mild transition-metal-free conditions in high yields and *trans*-diastereoselectivity (confirmed by X-ray crystallography). The dependence of reactivity on electronic properties of substrates has been investigated.

Keywords sultam, isothiazolidine, tandem, nucleophilic substitution, Michael addition, cyclic sulfonamide, allyl bromide, stereoselective



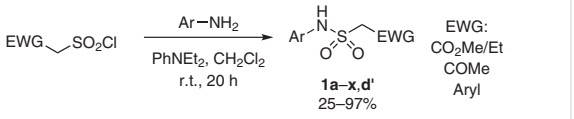
Scheme 1 (a) Key intermediates from previously reported Michael addition-based strategies towards sultams. (b) Novel N-alkylation/Michael tandem addition developed in this work.

The history of fruitful application of sulfonamides in biomedical chemistry goes back almost 100 years and counts more than 100 approved drugs,[1] making them one of the most important pharmacophores. Cyclic sulfonamides – sultams – have gained special attention due to diverse range of bioactivities, such as antiviral,[2] anticancer,[3] antimalarial,[4] antiglaucoma,[5] anticonvulsant,[6] and anticoagulant,[7] combined with increased metabolic stability.[8] Additionally, sultams have found applications in organic synthesis and synthesis of natural products as chiral auxiliaries.[9]

To date, a wide variety of general strategies towards construction of sultams with different ring size and substitution pattern have been reported in the literature, employing following key transformations: cycloaddition,[10] nucleophilic substitution,[11] ring-closing metathesis,[12] CH-activation,[13] Heck reaction,[14] radical cyclizations,[15] Smiles rearrangement,[16] amination,[17] Friedel–Crafts reaction,[18] and Michael addition. The latter approach involved intermediates bearing activated double bond at the sulfonamide sulfur atom[19] or in the aromatic side group[14,20] (Scheme 1a).

In this work, we present the first example of sultam ring formation via intramolecular Michael addition involving Michael acceptor attached to the nitrogen atom of sulfonamide (Scheme 1b). The latter moiety was introduced by reacting allyl bromides with α-EWG-substituted methanesulfonanilides via nucleophilic substitution. These two base-promoted transformations occurred sequentially in a one-pot fashion without changing conditions, thus representing a tandem reaction.

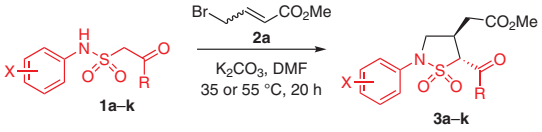
The starting methanesulfonanilides **1** were readily accessed from anilines and α-acyl-/aryl-substituted methanesulfonyl chlorides via standard procedure under mild conditions (Scheme 2).



Scheme 2 Synthesis of methanesulfonanilides **1**

The first dielectrophile studied in tandem reaction with prepared sulfonanilides was commercially available methyl γ-bromocrotonate (**2a**) (Table 1). Employing classical reaction conditions for alkylation of sulfonamides, namely heating with potassium carbonate in DMF, afforded a series of eleven 5-acyl-substituted sultams **3a–k** (Table 1) mostly in high yields and diastereoselectivities after chromatographic purification or crystallization. α-Acetyl-substituted sulfonanilides (**1**, R = Me) were smoothly converted into compounds **3a–c** at slight heating to 35 °C. Switching to carbomethoxy group at α-position (**1**, R = OMe) resulted in decreased reactivity of sulfonanilides; full conversion was achieved only at 55 °C (compounds **3d–k**). Preparation of compound **3k** was performed in a gram-scale (7.3 mmol loading). The substitution pattern in the *N*-aryl moiety was also varied, demonstrating that strong electron-withdrawing groups as well as steric hindrance dropped yields of sultams, most likely due to decreased nucleophilicity of nitrogen atom. Notably, even at room temperature the product of the first step, *N*-alkylation, was not detected (by ^{1}H NMR analysis of crude reaction mixtures).

Table 1 Tandem Sultam Synthesis from Acyl-Substituted Sulfonamides and Bromocrotonate



1/3	R	X	Yield (%) (*dr*)
a[a]	Me	H	96 (16:1)[b]
b[a]	Me	4-F	94 (>20:1)[b]
c[a]	Me	4-MeO	98 (17:1)[b]
d[c]	OMe	H	77 (8:1)[b]/52 (>20:1)[d]
e[c]	OMe	4-MeO	84 (>20:1)[d,e]
f[c]	OMe	4-Me	46 (>20:1)[d]
g[c]	OMe	2,6-Me_2	61 (>20:1)[d]
h[c]	OMe	4-Cl	50 (>20:1)[d]
i[c]	OMe	4-CN	36 (>20:1)[d]
j[c]	OMe	4-CF_3	45 (>20:1)[d]
k[c]	OMe	4-F	83 (>20:1)[f,g]

[a] Reaction temperature: 35 °C.
[b] Isolated yield and diastereomeric ratio after chromatography.
[c] Reaction temperature: 55 °C.
[d] Yield and *dr* after chromatography + crystallization.
[e] Structure confirmed by X-ray crystallography.
[f] Yield after crystallization.
[g] Prepared in gram-scale.

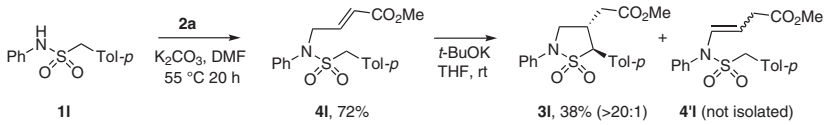
To explore the reaction scope further, we have introduced a series of aryl α-substituents to sulfonanilides **1**. When compound **1l**, bearing *p*-tolyl moiety instead of α-acyl, was reacted with the same dielectrophile **2a**, only intermediate *N*-alkylated sulfonanilide **4l** was isolated (Scheme 3). Most likely this outcome arises from significant decrease in CH-acidity of sulfonanilide, thus making it a poor Michael donor incapable of entering the cyclization step. Treatment of compound **4l** with a stronger base, *t*-BuOK, afforded isolation of the desired sultam **3l** only in 38% yield. Analysis of crude ^{1}H NMR spectrum revealed a side reaction of double bond migration (compound **4'l**, Scheme 3). Notably the isolation of intermediate **4l** supports the reaction pathway proposed on Scheme 1b.

The introduction of strong electron-withdrawing groups such as CN or CO_2Me to α-aryl moiety of sulfonanilide facilitated Michael addition step drastically, which allowed to our delight obtaining a series of fifteen 5-aryl-substituted sultams **3m–aa** under typical conditions in a one-pot fashion (Table 2). The obtained yields and *dr* values were similar to those observed for acyl substituted sulfonanilides.

Another Michael acceptor, namely γ-tosylallyl bromide **2b**, was also introduced into the developed sultam synthesis (Table 3). It was found to be a more potent dielectrophile than **2a**, providing full conversion of α-acetyl-substituted sulfonanilides **1a–c** to sultams within 0.5 hour at 0 °C.

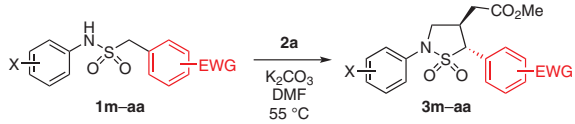
To perform the reaction with the less reactive sulfonamide **1d'** the reaction temperature was elevated to 25 °C. According to the NMR spectra of the reaction mixtures, these reactions proceeded with very high NMR yields (>90%). However, the isolated yields were only moderate since chromatographic isolation of pure compounds failed (due to the presence of a small impurity with similar retention) and crystallization led to significant weight loss. In the case of compound **3ab** (Table 3), we also performed an alternative isolation – HPLC, which afforded 92% yield.

The structure and relative *trans*-configuration of sultams obtained from bromocrotonate were confirmed by X-ray crystallography (Figure 1 and Table S1). Moreover, in all three series of the obtained products (Tables 1–3), the additional criteria for establishing stereochemistry were found: the value of chemical shifts of the proton at C-5 and the value of the coupling constants between the C-4 and C-5 protons (Table S2). These values were well reproduced and



Scheme 3 Reaction of bromocrotonate **2a** with a weak α-CH-acidic sulfonanilide **1l**

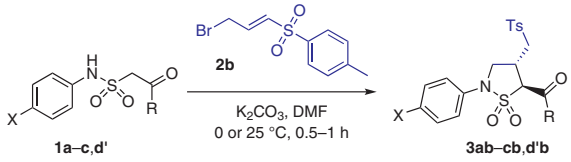
Table 2 Tandem Sultam Synthesis from α-Aryl-Substituted Sulfonamides and Bromocrotonate



1/3	EWG	X	Yield (%)[a] (*dr*)
m	4-CO_2Me	H	82 (>20:1)
n	4-CO_2Me	4-CF_3	65 (>20:1)
o	4-CO_2Me	2,6-Me_2	56 (9:1)
p	4-CO_2Me	4-MeO	62 (>20:1)
q	4-CO_2Me	4-CN	58 (>20:1)
r	4-CN	H	57 (>20:1)[b]
s	4-CN	4-CF_3	67 (>20:1)
t	4-CN	2,6-Me_2	63 (>20:1)
u	4-CN	4-MeO	88 (>20:1)
v	4-CN	4-CN	61 (>20:1)
w	2-CN	H	79 (>20:1)
x	2-CN	4-CF_3	57 (>20:1)
y	2-CN	2,6-Me_2	53 (>20:1)
z	2-CN	4-MeO	79 (>20:1)
aa	2-CN	4-CN	51 (>20:1)

[a] Yield after crystallization.
[b] Structure confirmed by X-ray crystallography.

Table 3 Tandem Sultam Synthesis from Acyl-Substituted Sulfonamides and Allyl Bromide **2b**



1	3	R	X	Yield (%) (*dr*)
a	**ab**[a]	Me	H	92[b]/60[c] (19:1)
b	**bb**[a]	Me	F	66[c] (13:1)
c	**cb**[a]	Me	MeO	62[c] (13:1)
d′	**d′b**[d]	OEt	H	80 (6.4:1)

[a] Reaction temperature: 0 °C.
[b] After HPLC.
[c] After crystallization.
[d] Reaction temperature: 25 °C.

coincided with the data for compounds with crystal structures, therefore, all sultams **3** were assigned the *trans*-configuration.

In conclusion, we have described a new synthesis of trisubstituted γ-sultams involving tandem S_N/Michael addition sequence. A series of α-EWG substituted methanesulfonanilides was *N*-alkylated with allyl bromides followed by cyclization via Michael addition. The CH-acidity of α-position in sulfonamide was found to be crucial for proceeding of the cyclization step. All isolated sultams were assigned *trans*-configuration according to X-ray crystallography and NMR data. The developed approach offers the advantages of cost-effective one-pot protocol, easily accessible substrates, general scope, high yields and stereoselectivity, mild reaction conditions, and lack of metal catalysis. To the best of our knowledge, this is the first example of sultam construction via cyclization of Michael acceptor attached to the nitrogen atom of sulfonamide.

NMR spectra were acquired with a 400 MHz Bruker Avance III spectrometer (400.13 MHz for ^{1}H and 100.61 MHz for ^{13}C) in $CDCl_3$, acetone-d_6 or DMSO-d_6 and were referenced to residual solvent proton signals (δ_H = 7.26, 2.05, or 2.50) and solvent carbon signals (δ_C = 77.2, 29.8, or 39.5, respectively). Melting points were determined with a melting point apparatus Stuart SMP 50 in open capillary tubes. Mass spectra were acquired with a Bruker maXis HRMS-ESI-qTOF spectrometer (electrospray ionization mode, positive ions detection). Column chromatography was carried out on silica gel grade 60 (0.040–0.063 mm) 230–400 mesh. TLC was performed on aluminum-backed precoated plates (0.25 mm) with silica gel 60 F254 and was visualized using UV fluorescence. Preparative HPLC was carried out on Shimadzu

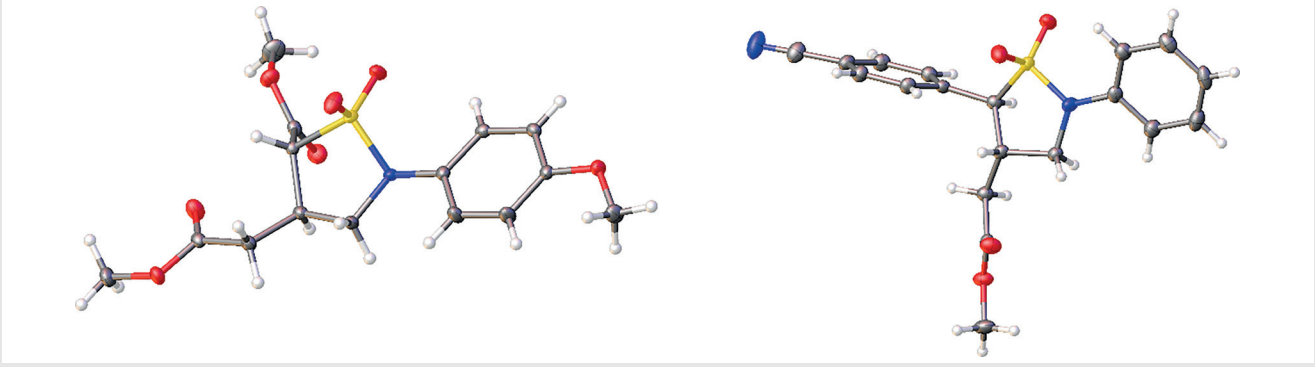


Figure 1 Crystal structure of compounds **3e** and **3r**. Thermal ellipsoid plots shown at 50% probability level.[21]

LC-20AP instrument, equipped with a spectrophotometric detector. Column: Agilent Zorbax prepHT XDB-C18, 5 µm, 21.2 × 150 mm. Mobile phase: MeCN/H_2O + 0.1% TFA, 40 °C, 12 mL/min. Sulfonamides **1d–i**,**l**,**m**,**r**,**d′**[11,22] were prepared according to published procedures. Methyl γ-bromocrotonate (**2a**) was obtained from commercial sources (85:15 *E*/*Z*-mixture).

Sulfonamides 1a–c; General Procedure

To a suspension of finely ground crude sodium 2-oxopropane-1-sulfonate (1.64 g, 7.5 mmol, 1 equiv, containing 27% NaCl by weight) in anhyd MeCN (7 mL) was added DMF (100 µL). The mixture was cooled in an ice-bath and oxalyl chloride (536 µL, 6.25 mmol, 1 equiv) was quickly added under vigorous stirring. The reaction mixture was stirred for 10 min at 0 °C, and then at r.t. until gas evolution (CO_2, CO) had finished. The precipitate was filtered off, washed with anhyd MeCN (3 × 5 mL) and discarded. The resulting solution of sulfonyl chloride in MeCN was directly introduced into the next step (the yield of sulfonyl chloride was estimated as 90% according to NMR of evaporated sample).

A solution of the corresponding aniline (6.75 mmol, 1 equiv), pyridine (616 µL, 7.76 mmol, 1.15 equiv), and DMAP (24 mg, 0.2 mmol, 3 mol%) in anhyd THF (15 mL) was cooled in an ice/salt bath to –10 °C and the solution of sulfonyl chloride from the previous step (6.75 mmol, 1 equiv) was slowly added dropwise with vigorous stirring. The solution was stirred at the same temperature until the amine was completely consumed (about 5 min, TLC: SiO_2, eluent *n*-hexane/acetone, 80:20). The precipitate of $Et_3N{\cdot}HCl$ was filtered off and washed with THF (3 × 7 mL). THF was evaporated in vacuo and the residue was dissolved in EtOAc (70 mL), the organic phase was washed successively with aq 1 M HCl (2 × 30 mL), H_2O (2 × 30 mL) and brine (50 mL), dried (Na_2SO_4), filtered, and concentrated to obtain the desired pure sulfonamide **1a–c**.

2-Oxo-*N*-phenylpropane-1-sulfonamide (1a)

Yield: 1.39 g (97%); brown crystals; mp 96.2–98.1 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.35 (dd, *J* = 8.4, 7.0 Hz, 2 H), 7.29 (d, *J* = 7.3 Hz, 2 H), 7.23 (t, *J* = 7.2 Hz, 1 H), 7.15 (s, 1 H), 4.06 (s, 2 H), 2.33 (s, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 198.2, 136.2, 129.7, 126.4, 122.5, 59.9, 31.6.

HRMS (ESI-TOF): *m*/*z* [M + Na]$^+$ calcd for $C_9H_{11}NO_3SNa$: 236.0352; found: 236.0357.

N-(4-Fluorophenyl)-2-oxopropane-1-sulfonamide (1b)

Yield: 1.48 g (95%); brown crystals; mp 87.8–88.9 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.32–7.26 (m, 2 H), 7.11 (s, 1 H), 7.10–6.96 (m, 2 H), 4.03 (s, 2 H), 2.35 (s, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 198.5, 161.3 (d, $^1J_{C,F}$ = 246.5 Hz), 131.9 (d, $^4J_{C,F}$ = 3.0 Hz), 125.3 (d, $^3J_{C,F}$ = 8.4 Hz), 116.5 (d, $^2J_{C,F}$ = 22.9 Hz), 59.6, 31.7.

^{19}F NMR (376 MHz, $CDCl_3$): δ = –115.2.

HRMS (ESI-TOF): *m*/*z* [M + Na]$^+$ calcd for $C_9H_{10}FNO_3SNa$: 254.0258; found: 254.0257.

N-(4-Methoxyphenyl)-2-oxopropane-1-sulfonamide (1c)

Yield: 1.54 g (94%); brown crystals; mp 71.5–73.0 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.28–7.23 (m, 2 H), 6.91 (s, 1 H), 6.90–6.86 (m, 2 H), 4.03 (s, 2 H), 3.81 (s, 3 H), 2.37 (s, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 198.4, 158.5, 128.4, 125.6, 114.8, 59.4, 55.5, 31.6.

HRMS (ESI-TOF): *m*/*z* [M + Na]$^+$ calcd for $C_{10}H_{13}NO_4SNa$: 266.0457; found: 264.0463.

Methansulfonanilides 1i–k,n–q,s–aa; General Procedure

To a stirred solution of the corresponding aniline (2–27 mmol) and $PhNEt_2$ (1.2 equiv) in anhyd DCM (30–60 mL) was slowly added dropwise a solution of methyl 2-(chlorosulfonyl)acetate (1.2 equiv) at r.t. After 24 h, the reaction mixture was washed with 5% aq HCl (2 × 30 mL), sat. aq $NaHCO_3$ (30 mL), and H_2O (2 × 30 mL). The organic layer was separated, dried (Na_2SO_4), filtered, and concentrated to give crude sulfonamides **1**, which were purified using crystallization.

Methyl 2-[*N*-(4-Cyanophenyl)sulfamoyl]acetate (1i)

Yield: 1.19 g (34%); white solid; mp 134–136 °C ($CHCl_3$).

^{1}H NMR (400 MHz, DMSO-d_6): δ = 10.87 (s, 1 H), 7.79 (d, *J* = 8.7 Hz, 2 H), 7.34 (d, *J* = 8.7 Hz, 2 H), 4.41 (s, 2 H), 3.61 (s, 3 H).

^{13}C NMR (101 MHz, DMSO-d_6): δ = 163.3, 142.4, 133.9, 119.0, 118.9, 105.7, 56.1, 52.9.

HRMS (ESI-TOF): *m*/*z* [M + Na]$^+$ calcd for $C_{10}H_{10}N_2O_4SNa$: 277.0253; found: 277.0252.

Methyl 2-{*N*-[4-(Trifluoromethyl)phenyl]sulfamoyl}acetate (1j)

Yield: 1.33 g (48%); light blue solid; mp 136–138 °C (Et_2O/hexane).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.63 (d, *J* = 8.4 Hz, 2 H), 7.42 (d, *J* = 8.3 Hz, 2 H), 7.33 (s, 1 H), 4.01 (s, 2 H), 3.81 (s, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 164.3, 139.5, 128.2 (q, $^2J_{C,F}$ = 33.1 Hz), 127.1 (q, $^3J_{C,F}$ = 3.7 Hz), 123.9 (q, $^1J_{C,F}$ = 271.9 Hz), 121.5, 53.6, 53.5.

HRMS (ESI-TOF): *m*/*z* [M + Na]$^+$ calcd for $C_{10}H_{10}F_3NO_4SNa$: 320.0175; found: 320.0175.

Methyl 2-[*N*-(4-Fluorophenyl)sulfamoyl]acetate (1k)

Yield: 1.9 g (34%); light blue solid; mp 100–102 °C (Et_2O).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.56–7.22 (m, 1 H), 7.20–6.99 (m, 3 H), 3.96 (s, 2 H), 3.84 (s, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 164.6, 161.3 (d, $^1J_{C,F}$ = 246.6 Hz), 132.0 (d, $^4J_{C,F}$ = 3.1 Hz), 125.4 (d, $^3J_{C,F}$ = 8.4 Hz), 116.6 (d, $^2J_{C,F}$ = 22.8 Hz), 53.5, 52.9.

HRMS (ESI-TOF): *m*/*z* [M + Na]$^+$ calcd for $C_9H_{10}FNO_4SNa$: 270.0207; found: 270.0213.

Methyl 4-({*N*-[4-(Trifluoromethyl)phenyl]sulfamoyl}methyl)benzoate (1n)

Yield: 460 mg (25%); white solid; mp 191–192 °C (Et_2O).

^{1}H NMR (400 MHz, acetone-d_6): δ = 7.95 (d, *J* = 8.4 Hz, 2 H), 7.67 (d, *J* = 8.5 Hz, 2 H), 7.49 (d, *J* = 8.6 Hz, 2 H), 7.46 (d, *J* = 8.3 Hz, 2 H), 4.68 (s, 2 H), 3.89 (s, 3 H).

^{13}C NMR (101 MHz, acetone-d_6): δ = 166.9, 143.1, 135.4, 132.2, 131.3, 130.3, 128.1 (d, $^1J_{C,F}$ = 270.7 Hz), 127.5 (q, $^3J_{C,F}$ = 3.8 Hz), 125.7 (q, $^2J_{C,F}$ = 32.6 Hz), 119.5, 58.3, 52.5.

HRMS (ESI-TOF): *m*/*z* [M + Na]$^+$ calcd for $C_{16}H_{14}F_3NO_4SNa$: 396.0488; found: 396.0505.

Methyl 4-{[*N*-(2,6-Dimethylphenyl)sulfamoyl]methyl}benzoate (1o)

Yield: 415 mg (29%); white solid; mp 171.5–173 °C (Et_2O).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.04 (d, *J* = 8.2 Hz, 2 H), 7.54 (d, *J* = 8.1 Hz, 2 H), 7.17–6.98 (m, 3 H), 5.93 (s, 1 H), 4.47 (s, 2 H), 3.91 (s, 3 H), 2.41 (s, 6 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 166.7, 137.4, 133.9, 133.0, 131.1, 130.7, 130.1, 129.1, 128.2, 60.4, 52.4, 19.5.

HRMS (ESI-TOF): *m*/*z* [M + Na]$^+$ calcd for $C_{17}H_{19}NO_4SNa$: 356.0927; found: 356.0922.

Methyl 4-[(*N*-(4-Methoxyphenyl)sulfamoyl]methyl)benzoate (1p)

Yield: 0.9 g (57%); white solid; mp 121.5–123 °C (Et_2O).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.99 (d, *J* = 8.3 Hz, 2 H), 7.37 (d, *J* = 8.2 Hz, 2 H), 7.12 (d, *J* = 9.0 Hz, 2 H), 6.87 (d, *J* = 9.0 Hz, 2 H), 6.51 (s, 1 H), 4.31 (s, 2 H), 3.90 (s, 3 H), 3.81 (s, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 166.6, 157.9, 133.8, 131.0, 130.7, 130.1, 129.2, 123.8, 115.0, 57.1, 55.7, 52.4.

HRMS (ESI-TOF): *m*/*z* [M + Na]$^+$ calcd for $C_{16}H_{17}NO_5SNa$: 358.0720; found: 358.0712.

Methyl 4-{[*N*-(4-Cyanophenyl)sulfamoyl]methyl}benzoate (1q)

Yield: 430 mg (26%); white solid; mp 180–182 °C (Et_2O).

^{1}H NMR (400 MHz, acetone-d_6): δ = 9.23 (s, 1 H), 7.95 (d, *J* = 8.5 Hz, 2 H), 7.72 (d, *J* = 8.8 Hz, 2 H), 7.46 (dd, *J* = 8.6, 1.8 Hz, 4 H), 4.71 (s, 2 H), 3.89 (s, 3 H).

^{13}C NMR (101 MHz, acetone-d_6): δ = 166.8, 143.7, 135.2, 134.5, 132.2, 131.3, 130.3, 119.4, 119.3, 107.3, 58.5, 52.5.

HRMS (ESI-TOF): *m*/*z* [M + Na]$^+$ calcd for $C_{16}H_{14}N_2O_4SNa$: 353.0566; found: 353.0570.

1-(4-Cyanophenyl)-*N*-[4-(trifluoromethyl)phenyl]methanesulfonamide (1s)

Yield: 420 mg (62%); white solid; mp 146–148 °C (hexane).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.67–7.56 (m, 4 H), 7.41 (d, *J* = 8.3 Hz, 2 H), 7.29 (d, *J* = 8.5 Hz, 2 H), 7.21 (s, 1 H), 4.67–4.35 (m, 2 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 140.1, 133.5, 132.7, 131.7, 127.2 (q, $^3J_{C,F}$ = 3.9 Hz), 127.0, 123.9 (q, $^1J_{C,F}$ = 271.7 Hz), 122.7, 118.9, 118.0, 113.2, 57.9.

HRMS (ESI-TOF): *m*/*z* [M + Na]$^+$ calcd for $C_{15}H_{11}F_3N_2O_2SNa$: 363.0386; found: 363.0371.

1-(4-Cyanophenyl)-*N*-(2,6-dimethylphenyl)methanesulfonamide (1t)

Yield: 0.9 g (62%); light green solid; mp 156–158 °C (Et_2O).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.70–7.62 (m, 2 H), 7.61–7.52 (m, 2 H), 7.19–7.06 (m, 3 H), 5.97 (s, 1 H), 4.45 (s, 2 H), 2.41 (s, 6 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 137.4, 134.2, 132.7, 132.6, 131.8, 129.1, 128.4, 118.4, 112.9, 60.2, 19.5.

HRMS (ESI-TOF): *m*/*z* [M + Na]$^+$ calcd for $C_{16}H_{16}N_2O_2SNa$: 323.0825; found: 323.0811.

1-(4-Cyanophenyl)-*N*-(4-methoxyphenyl)methanesulfonamide (1u)

Yield: 364 mg (60%) after washing with DCM; light purple solid; mp 134–135 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.61 (d, *J* = 8.3 Hz, 2 H), 7.41 (d, *J* = 8.2 Hz, 2 H), 7.12 (d, *J* = 8.9 Hz, 2 H), 6.88 (d, *J* = 9.0 Hz, 1 H), 6.62 (s, 1 H), 4.31 (s, 2 H), 3.81 (s, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 158.3, 134.4, 132.9, 132.0, 129.2, 124.2, 118.6, 115.4, 113.2, 57.3, 56.0.

HRMS (ESI-TOF): *m*/*z* [M + Na]$^+$ calcd for $C_{15}H_{14}N_2O_3SNa$: 325.0617; found: 325.0608.

***N*,1-Bis(4-cyanophenyl)methanesulfonamide (1v)**

Yield: 0.93 g (63%) after washing with DCM; white solid; mp 237–239 °C .

^{1}H NMR (400 MHz, DMSO-d_6): δ = 10.55 (s, 1 H), 7.82 (d, *J* = 8.3 Hz, 2 H), 7.76 (d, *J* = 8.8 Hz, 2 H), 7.46 (d, *J* = 8.3 Hz, 2 H), 7.28 (d, *J* = 8.8 Hz, 2 H), 4.78 (s, 2 H).

^{13}C NMR (101 MHz, DMSO-d_6): δ = 142.8, 134.7, 132.3, 132.0, 118.9, 118.5, 118.0, 111.2, 104.9, 57.2.

HRMS (ESI-TOF): *m*/*z* [M + Na]$^+$ calcd for $C_{15}H_{11}N_3O_2SNa$: 320.0464; found: 320.0449.

1-(2-Cyanophenyl)-*N*-phenylmethanesulfonamide (1w)

Yield: 420 mg (77%); white solid; mp 141–142 °C (Et_2O).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.72–7.60 (m, 1 H), 7.60–7.52 (m, 2 H), 7.44 (td, *J* = 7.4, 1.8 Hz, 1 H), 7.38–7.28 (m, 2 H), 7.23–7.17 (m, 2 H), 7.17–7.12 (m, 1 H), 7.10 (s, 1 H), 4.62 (s, 2 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 136.7, 133.4, 133.2, 132.2, 132.1, 129.8, 129.5, 125.3, 120.2, 117.4, 114.7, 56.4.

HRMS (ESI-TOF): *m*/*z* [M + Na]$^+$ calcd for $C_{14}H_{12}N_2O_2SNa$: 295.0512; found: 295.0498.

1-(2-Cyanophenyl)-*N*-[4-(trifluoromethyl)phenyl]methanesulfonamide (1x)

Yield: 680 mg (67%); white solid; mp 171–172 °C (DCM).

^{1}H NMR (400 MHz, acetone-d_6): δ = 9.37 (s, 1 H), 7.97–7.75 (m, 1 H), 7.74–7.62 (m, 4 H), 7.61–7.55 (m, 1 H), 7.52 (d, *J* = 8.4 Hz, 2 H), 4.81 (s, 2 H).

^{13}C NMR (101 MHz, acetone-d_6): δ = 142.8, 134.0, 133.8, 133.4, 133.3, 130.3, 127.4 (q, $^3J_{C,F}$ = 3.8 Hz), 125.8 (q, $^2J_{C,F}$ = 32.5 Hz), 125.4 (d, $^1J_{C,F}$ = 270.5 Hz), 119.4, 117.8, 115.5, 57.3.

HRMS (ESI-TOF): *m*/*z* [M + Na]$^+$ calcd for $C_{15}H_{12}F_3N_2O_2SNa$: 341.0566; found: 341.0554.

1-(2-Cyanophenyl)-*N*-(2,6-dimethylphenyl)methanesulfonamide (1y)

Yield: 560 mg (47%); light purple solid; mp 168–169 °C (Et_2O).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.36 (dd, *J* = 7.8, 1.4 Hz, 1 H), 7.31 (dd, *J* = 7.9, 1.3 Hz, 1 H), 7.25 (td, *J* = 7.7, 1.4 Hz, 1 H), 7.12 (td, *J* = 7.6, 1.4 Hz, 1 H), 6.82–6.67 (m, 3 H), 5.97 (s, 1 H), 4.37 (s, 2 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 137.6, 133.3, 133.1, 132.8, 132.7, 132.3, 129.4, 129.1, 128.3, 117.6, 114.7, 58.6, 19.4.

HRMS (ESI-TOF): *m*/*z* [M + Na]$^+$ calcd for $C_{16}H_{16}N_2O_2SNa$: 323.0825; found: 323.0812.

1-(2-Cyanophenyl)-*N*-(4-methoxyphenyl)methanesulfonamide (1z)

Yield: 1.0 g (68%); light purple solid; mp 120–121 °C (Et_2O).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.74–7.66 (m, 1 H), 7.65–7.55 (m, 2 H), 7.47 (ddd, *J* = 7.7, 6.5, 2.3 Hz, 1 H), 7.24–7.14 (m, 2 H), 6.94 (s, 1 H), 6.90–6.83 (m, 2 H), 4.60 (s, 2 H), 3.81 (s, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 157.9, 133.4, 133.2, 132.4, 132.2, 129.4, 129.1, 124.0, 117.5, 114.9, 114.6.

HRMS (ESI-TOF): *m*/*z* [M + Na]$^+$ calcd for $C_{15}H_{14}N_2O_3SNa$: 325.0617; found: 325.0618.

1-(2-Cyanophenyl)-*N*-(4-cyanophenyl)methanesulfonamide (1aa)

Yield: 780 mg (52%); white solid; mp 234–235 °C (Et_2O).

^{1}H NMR (400 MHz, acetone-d_6): δ = 9.48 (s, 1 H), 7.79 (dd, *J* = 7.7, 1.4 Hz, 1 H), 7.74–7.67 (m, 3 H), 7.65 (dd, *J* = 7.9, 1.4 Hz, 1 H), 7.59 (td, *J* = 7.6, 1.5 Hz, 1 H), 7.50–7.39 (m, 2 H), 4.83 (s, 2 H).

^{13}C NMR (101 MHz, acetone-d_6): δ = 143.5, 143.4, 134.4, 134.0, 133.9, 133.5, 133.2, 133.1, 130.4, 117.8, 115.5, 107.5, 57.5.

HRMS (ESI-TOF): *m*/*z* [M + Na]$^+$ calcd for $C_{15}H_{11}N_3O_2SNa$: 320.0464; found: 320.0462.

Sultams 3; General Procedure

To a suspension of K_2CO_3 (1.2 equiv) in DMF (5 mL) was added the corresponding sulfonamide **1** (1–1.2 mmol, 1 equiv). The mixture was stirred for 10 min, and then methyl 4-bromocrotonate (**2a**; 1.1 equiv) or (*E*)-1-[(3-bromoallyl)sulfonyl]-4-methylbenzene (**2b**; 1.1 equiv) was added in one portion. The mixture was stirred at 0, 25, 35 or 55 °C until full consumption of sulfonamide (0.5–20 h, TLC: SiO_2, eluent: *n*-hexane/EtOAc 75:25). After full conversion, DMF was evaporated in vacuo and the residue was partitioned between EtOAc and H_2O, and the aqueous phase was extracted with EtOAc (3 × 10 mL). The combined organic phases were washed sequentially with aq 1 M HCl (2 × 15 mL), H_2O (3 × 10 mL) and brine (2 × 20 mL), dried (Na_2SO_4), filtered, concentrated, and purified by column chromatography on silica gel or by crystallization.

Methyl (±)-2-[(4*S*,5*S*)-5-Acetyl-1,1-dioxido-2-phenylisothiazolidin-4-yl]acetate (3a)

Yield: 361 mg (96%), after column chromatography (hexane/EtOAc); brown oil; *dr* = 16:1.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.40–7.34 (m, 2 H), 7.30–7.25 (m, 2 H), 7.22 (t, *J* = 7.3 Hz, 1 H), 4.30 (d, *J* = 7.3 Hz, 1 H), 3.93 (dd, *J* = 9.0, 7.4 Hz, 1 H), 3.70 (s, 3 H), 3.53 (h, *J* = 7.2 Hz, 1 H), 3.48–3.41 (m, 1 H), 2.71 (dd, *J* = 16.5, 7.3 Hz, 1 H), 2.64 (dd, *J* = 16.5, 6.9 Hz, 1 H), 2.52 (s, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 195.7, 171.2, 136.7, 129.6, 126.2, 122.0, 72.0, 52.2, 50.3, 36.4, 30.8, 30.3.

HRMS (ESI-TOF): *m*/*z* [M + Na]$^+$ calcd for $C_{14}H_{17}NO_5SNa$: 334.0725; found: 334.0726.

Methyl (±)-2-[(4*S*,5*S*)-5-Acetyl-2-(4-fluorophenyl)-1,1-dioxidoisothiazolidin-4-yl]acetate (3b)

Yield: 374 mg (94%), after column chromatography (hexane/EtOAc); brown oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.30–7.21 (m, 2 H), 7.09–7.01 (m, 2 H), 4.29 (d, *J* = 7.2 Hz, 1 H), 3.86 (t, *J* = 9.2 Hz, 1 H), 3.68 (s, 3 H), 3.52 (h, *J* = 7.3 Hz, 1 H), 3.39 (t, *J* = 9.2 Hz, 1 H), 2.74–2.58 (m, 2 H), 2.50 (s, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 195.7, 171.2, 161.2 (d, $^1J_{C,F}$ = 246.6 Hz), 132.3 (d, $^4J_{C,F}$ = 3.0 Hz), 125.2 (d, $^3J_{C,F}$ = 8.5 Hz), 116.4 (d, $^2J_{C,F}$ = 22.8 Hz), 71.6, 52.2, 50.9, 36.5, 30.8, 30.3.

HRMS (ESI-TOF): *m*/*z* [M + Na]$^+$ calcd for $C_{14}H_{16}FNO_5SNa$: 352.0631; found: 352.0629.

Methyl (±)-2-[(4*S*,5*S*)-5-Acetyl-2-(4-methoxyphenyl)-1,1-dioxidoisothiazolidin-4-yl]acetate (3c)

Yield: 404 mg (98%), after column chromatography (hexane/EtOAc); brown oil; *dr* = 17:1.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.25–7.17 (m, 2 H), 6.91–6.84 (m, 2 H), 4.25 (d, *J* = 6.9 Hz, 1 H), 3.82 (dd, *J* = 9.3, 7.7 Hz, 1 H), 3.77 (s, 3 H), 3.67 (s, 3 H), 3.51 (h, *J* = 7.4 Hz, 1 H), 3.36 (dd, *J* = 9.3, 7.6 Hz, 1 H), 2.71–2.57 (m, 2 H), 2.49 (s, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 195.9, 171.3, 158.8, 128.7, 125.9, 114.8, 71.6, 55.6, 52.1, 51.4, 36.7, 30.8, 30.3.

HRMS (ESI-TOF): *m*/*z* [M + Na]$^+$ calcd for $C_{15}H_{19}NO_6SNa$: 364.0831; found: 364.0834.

Methyl (±)-(4*S*,5*S*)-4-(2-Methoxy-2-oxoethyl)-2-phenylisothiazolidine-5-carboxylate 1,1-Dioxide (3d)

Yield: 251 mg (77%), after column chromatography (EtOAc/DCM); *dr* = 8:1; yield: 170 mg (52%), after additional crystallization from Et_2O; *dr* = >20:1 white solid; mp 118.5–120 °C (Et_2O).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.39 (t, *J* = 7.7 Hz, 2 H), 7.36–7.27 (m, 2 H), 7.24 (t, *J* = 7.3 Hz, 1 H), 4.20 (d, *J* = 7.4 Hz, 1 H), 4.09–3.98 (m, 1 H), 3.93 (s, 3 H), 3.74 (s, 3 H), 3.64–3.36 (m, 2 H), 2.81 (dd, *J* = 16.6, 6.1 Hz, 1 H), 2.71 (dd, *J* = 16.6, 6.9 Hz, 1 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 171.0, 164.6, 136.8, 129.6, 126.2, 121.9, 66.8, 53.9, 52.3, 50.5, 36.4, 31.9.

HRMS (ESI-TOF): *m*/*z* [M + Na]$^+$ calcd for $C_{14}H_{17}NO_6SNa$: 350.0669; found: 350.0603.

Methyl (±)-(4*S*,5*S*)-4-(2-Methoxy-2-oxoethyl)-2-(4-methoxyphenyl)isothiazolidine-5-carboxylate 1,1-Dioxide (3e)

Yield: 304 mg (84%), after column chromatography (EtOAc/DCM) + crystallization from Et_2O; white solid; mp 93.5–95.5 °C (Et_2O).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.25 (d, *J* = 9.0 Hz, 2 H), 6.89 (d, *J* = 9.0 Hz, 2 H), 4.13 (d, *J* = 7.4 Hz, 1 H), 3.97–3.84 (m, 4 H), 3.79 (s, 3 H), 3.71 (s, 3 H), 3.59–3.45 (m, 1 H), 3.42 (dd, *J* = 9.3, 7.6 Hz, 1 H), 2.76 (dd, *J* = 16.6, 7.0 Hz, 1 H), 2.67 (dd, *J* = 16.6, 7.2 Hz, 1 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 171.1, 164.9, 158.8, 128.9, 125.9, 114.9, 66.5, 55.6, 53.9, 52.2, 51.5, 36.7, 32.0.

HRMS (ESI-TOF): *m*/*z* [M + Na]$^+$ calcd for $C_{15}H_{19}NO_7SNa$: 380.0774; found: 380.0779.

Methyl (±)-(4*S*,5*S*)-4-(2-Methoxy-2-oxoethyl)-2-(*p*-tolyl)isothiazolidine-5-carboxylate 1,1-Dioxide (3f)

Yield: 156 mg (46%), after column chromatography (EtOAc/DCM) + crystallization from Et_2O; white solid; mp 88–90 °C (Et_2O).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.30–6.97 (m, 4 H), 4.15 (d, *J* = 7.6 Hz, 1 H), 4.04–3.83 (m, 4 H), 3.71 (s, 3 H), 3.56–3.36 (m, 2 H), 2.77 (dd, *J* = 16.6, 6.7 Hz, 1 H), 2.67 (dd, *J* = 16.6, 7.1 Hz, 1 H), 2.33 (s, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 171.0, 164.7, 136.5, 134.0, 130.2, 122.7, 66.7, 53.9, 52.3, 50.8, 36.6, 32.0, 21.0.

HRMS (ESI-TOF): *m*/*z* [M + Na]$^+$ calcd for $C_{15}H_{19}NO_6SNa$: 364.0825; found: 364.0818.

Methyl (±)-(4*S*,5*S*)-2-(2,6-Dimethylphenyl)-4-(2-methoxy-2-oxoethyl)isothiazolidine-5-carboxylate 1,1-Dioxide (3g)

Yield: 153 mg (61%) after column chromatography (EtOAc/DCM) + crystallization from Et_2O; white solid; mp 117.5–119 °C (Et_2O).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.20–7.12 (m, 1 H), 7.12–7.02 (m, 2 H), 4.20 (d, *J* = 9.1 Hz, 1 H), 3.91 (s, 3 H), 3.90–3.83 (m, 1 H), 3.71 (s, 3 H), 3.67–3.55 (m, 1 H), 3.49–3.27 (m, 1 H), 2.84 (dd, *J* = 16.6, 6.0 Hz, 1 H), 2.70 (dd, *J* = 16.6, 7.5 Hz, 1 H), 2.40 (s, 3 H), 2.39 (s, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 171.1, 164.9, 140.6, 139.9, 132.4, 129.4, 129.2, 65.3, 53.8, 52.2, 50.6, 36.4, 32.5, 18.9, 18.7.

HRMS (ESI-TOF): *m*/*z* [M + Na]$^+$ calcd for $C_{16}H_{21}NO_6SNa$: 378.0982; found: 378.0971.

Methyl (±)-(4*S*,5*S*)-2-(4-Chlorophenyl)-4-(2-methoxy-2-oxoethyl)-isothiazolidine-5-carboxylate 1,1-Dioxide (3h)

Yield: 180 mg (50%), after column chromatography (EtOAc/DCM) + crystallization from Et_2O; white solid; mp 124–126 °C (Et_2O).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.39–7.31 (m, 2 H), 7.24–7.17 (m, 2 H), 4.17 (d, *J* = 7.7 Hz, 1 H), 3.97 (dd, *J* = 8.8, 6.8 Hz, 1 H), 3.91 (s, 3 H), 3.72 (s, 3 H), 3.58–3.41 (m, 2 H), 2.79 (dd, *J* = 16.6, 6.4 Hz, 1 H), 2.68 (dd, *J* = 16.6, 7.2 Hz, 1 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 170.9, 164.5, 135.4, 131.8, 129.7, 123.2, 66.7, 54.0, 52.3, 50.5, 36.3, 31.9.

HRMS (ESI-TOF): *m*/*z* [M + Na]$^+$ calcd for $C_{14}H_{16}ClNO_6SNa$: 384.0279; found: 384.0272.

Methyl (±)-(4*S*,5*S*)-2-(4-Cyanophenyl)-4-(2-methoxy-2-oxoethyl)-isothiazolidine-5-carboxylate 1,1-Dioxide (3i)

Yield: 125 mg (36%), after column chromatography (EtOAc/DCM) + crystallization from Et_2O; white solid; mp 133–135.5 °C (Et_2O).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.64 (d, *J* = 8.8 Hz, 2 H), 7.30 (d, *J* = 8.9 Hz, 2 H), 4.26 (d, *J* = 8.3 Hz, 1 H), 4.09 (q, *J* = 5.5 Hz, 1 H), 3.92 (s, 3 H), 3.73 (s, 3 H), 3.52 (qd, *J* = 8.3, 6.0 Hz, 2 H), 2.89–2.77 (m, 1 H), 2.69 (dd, *J* = 16.9, 7.1 Hz, 1 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 170.8, 163.8, 141.4, 133.6, 119.0, 118.6, 107.9, 66.7, 54.1, 52.4, 49.5, 35.7, 31.5.

HRMS (ESI-TOF): *m*/*z* [M + Na]$^+$ calcd for $C_{15}H_{16}N_2O_6SNa$: 375.0621; found: 375.0615.

Methyl (±)-(4*S*,5*S*)-4-(2-Methoxy-2-oxoethyl)-2-[4-(trifluoromethyl)phenyl]isothiazolidine-5-carboxylate 1,1-Dioxide (3j)

Yield: 178 mg (45%), after column chromatography (EtOAc/DCM) + crystallization from Et_2O; white solid; mp 100.3–102 °C (hexane/Et_2O).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.62 (d, *J* = 8.5 Hz, 2 H), 7.35 (d, *J* = 8.5 Hz, 2 H), 4.23 (d, *J* = 8.2 Hz, 1 H), 4.14–4.00 (m, 1 H), 3.92 (s, 3 H), 3.73 (s, 3 H), 3.60–3.43 (m, 2 H), 2.82 (dd, *J* = 16.8, 5.6 Hz, 1 H), 2.70 (dd, *J* = 16.7, 6.9 Hz, 1 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 170.9, 164.1, 140.4, 127.2 (q, $^2J_{C,F}$ = 32.9 Hz), 126.8 (q, $^3J_{C,F}$ = 3.7 Hz), 124.0 (q, $^1J_{C,F}$ = 271.7 Hz), 119.7, 66.8, 54.1, 52.4, 49.9, 36.0, 31.7.

HRMS (ESI-TOF): *m*/*z* [M + Na]$^+$ calcd for $C_{15}H_{16}F_3NO_6SNa$: 418.0543; found: 418.0530.

Methyl (±)-(4*S*,5*S*)-2-(4-Fluorophenyl)-4-(2-methoxy-2-oxoethyl)isothiazolidine-5-carboxylate 1,1-Dioxide (3k)

Yield: 2.08 g (83%), 7.3 mmol scale, obtained pure after crystallization from Et_2O; white solid; mp 116–118 °C (Et_2O).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.42–7.20 (m, 2 H), 7.20–6.92 (m, 2 H), 4.18 (d, *J* = 7.6 Hz, 1 H), 3.97 (dd, *J* = 9.1, 7.1 Hz, 1 H), 3.93 (s, 3 H), 3.73 (s, 3 H), 3.64–3.49 (m, 1 H), 3.49–3.42 (m, 1 H), 2.80 (dd, *J* = 16.6, 6.8 Hz, 1 H), 2.70 (dd, *J* = 16.6, 7.3 Hz, 1 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 171.0, 164.7, 161.3 (d, $^1J_{C,F}$ = 246.6 Hz), 132.5 (d, $^4J_{C,F}$ = 3.0 Hz), 125.2 (d, $^3J_{C,F}$ = 8.5 Hz), 116.5 (d, $^2J_{C,F}$ = 22.9 Hz), 66.5, 53.9, 52.3, 51.1, 36.5, 32.0.

HRMS (ESI-TOF): *m*/*z* [M + Na]$^+$ calcd for $C_{14}H_{16}FNO_6SNa$: 368.0575; found: 368.0568.

Methyl (±)-2-[(4*S*,5*S*)-1,1-Dioxido-2-phenyl-5-(*p*-tolyl)isothiazolidin-4-yl]acetate (3l)

Yield: 45 mg (38%), after column chromatography (EtOAc/DCM); brown solid; mp 133–135 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.40–7.33 (m, 4 H), 7.32–7.28 (m, 2 H), 7.28–7.23 (m, 2 H), 7.20–7.11 (m, 1 H), 4.24 (d, *J* = 12.1 Hz, 1 H), 4.05 (dd, *J* = 8.9, 6.9 Hz, 1 H), 3.63 (s, 3 H), 3.59 (t, *J* = 9.2 Hz, 1 H), 3.46–3.32 (m, 1 H), 2.60 (dd, *J* = 16.3, 4.3 Hz, 1 H), 2.46 (dd, *J* = 16.3, 9.3 Hz, 1 H), 2.39 (s, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 170.9, 140.1, 138.0, 130.0, 129.9, 129.5, 125.6, 124.6, 119.5, 68.6, 52.1, 50.5, 35.5, 34.8, 21.4.

HRMS (ESI-TOF): *m*/*z* [M + Na]$^+$ calcd for $C_{19}H_{21}NO_4SNa$: 382.1083; found: 382.1101.

Methyl (±)-4-[(4*S*,5*S*)-4-(2-Methoxy-2-oxoethyl)-1,1-dioxido-2-phenylisothiazolidin-5-yl]benzoate (3m)

Yield: 330 mg (82%), after crystallization from Et_2O; white solid; mp 201–202 °C (Et_2O).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.12 (d, *J* = 8.5 Hz, 2 H), 7.57 (d, *J* = 8.5 Hz, 2 H), 7.48–7.33 (m, 2 H), 7.33–7.27 (m, 2 H), 7.23–7.11 (m, 1 H), 4.35 (d, *J* = 11.8 Hz, 1 H), 4.07 (dd, *J* = 9.0, 6.9 Hz, 1 H), 3.94 (s, 3 H), 3.75–3.53 (m, 4 H), 3.48–3.32 (m, 1 H), 2.58 (dd, *J* = 16.3, 4.7 Hz, 1 H), 2.49 (dd, *J* = 16.3, 8.9 Hz, 1 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 170.7, 166.5, 137.6, 134.0, 131.6, 130.4, 130.1, 129.6, 125.1, 120.0, 68.4, 52.5, 52.2, 50.5, 35.6, 35.2.

HRMS (ESI-TOF): *m*/*z* [M + Na]$^+$ calcd for $C_{20}H_{21}NO_6SNa$: 426.0982; found: 426.0987.

Methyl (±)-4-{(4*S*,5*S*)-4-(2-Methoxy-2-oxoethyl)-1,1-dioxido-2-[4-(trifluoromethyl)phenyl]isothiazolidin-5-yl}benzoate (3n)

Yield: 307 mg (65%), after crystallization from Et_2O; white solid; mp 189–190 °C (Et_2O).

^{1}H NMR (400 MHz, $CDCl_3$: δ = 8.13 (d, *J* = 8.3 Hz, 2 H), 7.62 (d, *J* = 8.5 Hz, 2 H), 7.57 (d, *J* = 8.4 Hz, 2 H), 7.34 (d, *J* = 8.5 Hz, 2 H), 4.40 (d, *J* = 12.4 Hz, 1 H), 4.12 (dd, *J* = 8.9, 6.8 Hz, 1 H), 3.94 (s, 3 H), 3.64 (s, 4 H), 3.54–3.29 (m, 1 H), 2.59 (dd, *J* = 16.5, 4.4 Hz, 1 H), 2.48 (dd, *J* = 16.5, 8.9 Hz, 1 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 170.5, 166.4, 141.0, 132.9, 132.0, 130.5, 130.2, 126.8 (q, $^3J_{C,F}$ = 3.7 Hz), 126.1 (q, $^2J_{C,F}$ = 33.1 Hz), 124.2 (q, $^1J_{C,F}$ = 271.5 Hz), 117.9, 68.4, 52.5, 52.3, 50.0, 35.1, 34.7.

HRMS (ESI-TOF): *m*/*z* [M + Na]$^+$ calcd for $C_{21}H_{20}F_3NO_6SNa$: 494.0856; found: 494.0859.

Methyl (±)-4-[(4*R*,5*R*)-2-(2,6-Dimethylphenyl)-4-(2-methoxy-2-oxoethyl)-1,1-dioxidoisothiazolidin-5-yl]benzoate (3o)

Yield: 240 mg (56%), after crystallization from Et_2O; white solid; *dr* = 8:1.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.11 (d, *J* = 8.4 Hz, 2 H), 7.63 (d, *J* = 8.4 Hz, 2 H), 7.21–7.14 (m, 1 H), 7.13–7.06 (m, 2 H), 4.36 (d, *J* = 12.7 Hz, 1 H), 4.10–3.76 (m, 4 H), 3.64–3.51 (m, 4 H), 3.49–3.37 (m, 1 H), 2.62–2.36 (m, 8 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 170.8, 166.6, 140.6, 139.9, 134.0, 132.8, 131.5, 130.3, 130.2, 129.3, 129.2, 52.4, 52.1, 51.1, 35.5, 35.4, 18.8, 18.8.

HRMS (ESI-TOF): *m*/*z* [M + Na]$^+$ calcd for $C_{22}H_{25}NO_6SNa$: 454.1295; found: 454.1304.

Methyl (±)-4-[(4*S*,5*S*)-4-(2-Methoxy-2-oxoethyl)-2-(4-methoxyphenyl)-1,1-dioxidoisothiazolidin-5-yl]benzoate (3p)

Yield: 260 mg (62%), after crystallization from Et_2O; white solid; mp 133–135 °C (Et_2O).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.11 (d, *J* = 8.4 Hz, 2 H), 7.57 (d, *J* = 8.3 Hz, 2 H), 7.29 (d, *J* = 9.0 Hz, 2 H), 6.92 (d, *J* = 9.0 Hz, 2 H), 4.32 (d, *J* = 11.1 Hz, 1 H), 3.99 (dd, *J* = 9.1, 7.2 Hz, 1 H), 3.93 (s, 3 H), 3.80 (s, 3 H), 3.60 (s, 3 H), 3.56 (t, *J* = 9.0 Hz, 1 H), 3.47–3.27 (m, 1 H), 2.58 (dd, *J* = 16.2, 5.0 Hz, 1 H), 2.51 (dd, *J* = 16.3, 8.7 Hz, 1 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 170.8, 166.5, 158.3, 134.8, 131.5, 130.4, 130.0, 129.8, 124.7, 114.9, 68.0, 55.6, 52.4, 52.2, 51.7, 36.0, 35.7.

HRMS (ESI-TOF): *m*/*z* [M + Na]$^+$ calcd for $C_{21}H_{23}NO_7SNa$: 456.1087; found: 456.1106.

Methyl (±)-4-[(4*S*,5*S*)-2-(4-Cyanophenyl)-4-(2-methoxy-2-oxoethyl)-1,1-dioxidoisothiazolidin-5-yl]benzoate (3q)

Yield: 250 mg (58%), after crystallization from Et_2O; white solid; mp 159–161 °C (Et_2O).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.13 (d, *J* = 8.4 Hz, 2 H), 7.64 (d, *J* = 8.9 Hz, 2 H), 7.56 (d, *J* = 8.5 Hz, 2 H), 7.29 (d, *J* = 8.9 Hz, 2 H), 4.43 (d, *J* = 12.7 Hz, 1 H), 4.13 (dd, *J* = 8.9, 6.7 Hz, 1 H), 3.94 (s, 3 H), 3.69–3.56 (m, 4 H), 3.56–3.27 (m, 1 H), 2.58 (dd, *J* = 16.6, 4.2 Hz, 1 H), 2.46 (dd, *J* = 16.6, 9.0 Hz, 1 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 170.4, 166.3, 141.9, 133.7, 132.3, 132.1, 130.6, 130.2, 118.8, 117.5, 106.8, 68.4, 52.5, 52.4, 49.8, 34.8, 34.3.

HRMS (ESI-TOF): *m*/*z* [M + Na]$^+$ calcd for $C_{21}H_{20}N_2O_6SNa$: 451.0934; found: 451.0917.

Methyl (±)-2-[(4*S*,5*S*)-5-(4-Cyanophenyl)-1,1-dioxido-2-phenylisothiazolidin-4-yl]acetate (3r)

Yield: 210 mg (57%), after crystallization from Et_2O; white solid; mp 159–161 °C (Et_2O).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.74 (d, *J* = 8.4 Hz, 2 H), 7.68–7.57 (m, 2 H), 7.39 (dd, *J* = 8.7, 7.2 Hz, 2 H), 7.34–7.28 (m, 2 H), 7.20 (td, *J* = 7.2, 1.2 Hz, 1 H), 4.37 (d, *J* = 11.6 Hz, 1 H), 4.06 (dd, *J* = 9.1, 7.0 Hz, 1 H), 3.77–3.52 (m, 4 H), 3.52–3.31 (m, 1 H), 2.58 (dd, *J* = 16.4, 5.0 Hz, 1 H), 2.51 (dd, *J* = 16.4, 8.4 Hz, 1 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 170.5, 137.4, 134.7, 132.9, 130.8, 129.7, 125.4, 120.3, 118.2, 113.9, 68.1, 52.3, 50.5, 35.6, 35.3.

HRMS (ESI-TOF): *m*/*z* [M + Na]$^+$ calcd for $C_{19}H_{19}N_2O_4SNa$: 371.1060; found: 371.1057.

Methyl (±)-2-{(4*S*,5*S*)-5-(4-Cyanophenyl)-1,1-dioxido-2-[4-(trifluoromethyl)phenyl]isothiazolidin-4-yl}acetate (3s)

Yield: 295 mg (67%), after crystallization from Et_2O; white solid; mp 188–190 °C (Et_2O).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.76 (d, *J* = 8.4 Hz, 2 H), 7.71–7.48 (m, 4 H), 7.34 (d, *J* = 8.5 Hz, 2 H), 4.42 (d, *J* = 12.2 Hz, 1 H), 4.12 (dd, *J* = 8.9, 6.9 Hz, 1 H), 3.72–3.57 (m, 4 H), 3.50–3.30 (m, 1 H), 2.58 (dd, *J* = 16.5, 4.6 Hz, 1 H), 2.49 (dd, *J* = 16.5, 8.6 Hz, 1 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 170.4, 140.8, 133.6, 133.0, 130.9, 126.9 (q, $J_{C,F}$ = 3.8 Hz), 126.4 (q, $J_{C,F}$ = 33.1 Hz), 124.1 (q, $J_{C,F}$ = 271.7 Hz), 118.2, 118.0, 114.3, 68.2, 52.4, 50.0, 35.0, 34.7.

HRMS (ESI-TOF): *m*/*z* [M + Na]$^+$ calcd for $C_{20}H_{17}F_3N_2O_4SNa$: 461.0753; found: 461.0769.

Methyl (±)-[(4*S*,5*S*)-5-(4-Cyanophenyl)-2-(2,6-dimethylphenyl)-1,1-dioxidoisothiazolidin-4-yl]acetate (3t)

Yield: 250 mg (63%), after crystallization from Et_2O; white solid; mp 194–196 °C (Et_2O).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.74 (d, *J* = 8.5 Hz, 2 H), 7.68 (d, *J* = 8.4 Hz, 2 H), 7.22–7.15 (m, 1 H), 7.14–7.08 (m, 2 H), 4.38 (d, *J* = 12.3 Hz, 1 H), 3.93 (dd, *J* = 8.4, 6.9 Hz, 1 H), 3.60 (s, 3 H), 3.59–3.37 (m, 2 H), 2.55 (dd, *J* = 16.3, 4.4 Hz, 1 H), 2.50–2.30 (m, 7 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 170.6, 140.5, 139.8, 134.6, 132.8, 132.6, 130.9, 129.4, 129.3, 118.2, 113.8, 66.5, 52.2, 51.0, 35.4, 35.3, 18.8, 18.8.

HRMS (ESI-TOF): *m*/*z* [M + Na]$^+$ calcd for $C_{21}H_{22}N_2O_4SNa$: 421.1192; found: 421.1203.

Methyl (±)-2-[(4*S*,5*S*)-5-(4-Cyanophenyl)-2-(4-methoxyphenyl)-1,1-dioxidoisothiazolidin-4-yl]acetate (3u)

Yield: 350 mg (88%), after crystallization from Et_2O; white solid; mp 157–159 °C (Et_2O).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.76 (d, *J* = 8.4 Hz, 2 H), 7.64 (d, *J* = 8.4 Hz, 2 H), 7.31 (d, *J* = 9.0 Hz, 2 H), 6.94 (d, *J* = 9.0 Hz, 2 H), 4.35 (d, *J* = 10.9 Hz, 1 H), 4.01 (dd, *J* = 9.3, 7.3 Hz, 1 H), 3.82 (s, 3 H), 3.64 (s, 3 H), 3.58 (t, *J* = 9.0 Hz, 1 H), 3.44–3.29 (m, 1 H), 2.66–2.36 (m, 2 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 170.5, 158.4, 135.4, 132.7, 130.6, 129.3, 124.8, 118.1, 114.9, 113.6, 67.6, 55.5, 52.1, 51.6, 35.9, 35.7.

HRMS (ESI-TOF): *m*/*z* [M + Na]$^+$ calcd for $C_{20}H_{20}N_2O_5SNa$: 423.0985; found: 423.0973.

Methyl (±)-2-[(4*S*,5*S*)-2,5-Bis(4-cyanophenyl)-1,1-dioxidoisothiazolidin-4-yl]acetate (3v)

Yield: 240 mg (61%), after crystallization from Et_2O; white solid; mp 157–159 °C (Et_2O).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.77 (d, *J* = 8.3 Hz, 2 H), 7.66–7.50 (m, 4 H), 7.29 (d, *J* = 8.9 Hz, 2 H), 4.45 (d, *J* = 12.5 Hz, 1 H), 4.13 (dd, *J* = 8.9, 6.9 Hz, 1 H), 3.66 (s, 4 H), 3.54–3.27 (m, 1 H), 2.58 (dd, *J* = 16.6, 4.4 Hz, 1 H), 2.49 (dd, *J* = 16.6, 8.7 Hz, 1 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 170.3, 141.7, 133.7, 133.1, 133.0, 130.9, 118.7, 118.0, 117.6, 114.4, 107.1, 68.1, 52.4, 49.7, 34.7, 34.4.

HRMS (ESI-TOF): *m*/*z* [M + Na]$^+$ calcd for $C_{20}H_{17}N_3O_4SNa$: 418.0832; found: 418.0837.

Methyl (±)-2-[(4*S*,5*S*)-5-(2-Cyanophenyl)-1,1-dioxido-2-phenylisothiazolidin-4-yl]acetate (3w)

Yield: 380 mg (79%), after crystallization from Et_2O; white solid; mp 168–169 °C (Et_2O).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.85 (dd, *J* = 7.7, 1.0 Hz, 1 H), 7.81–7.67 (m, 2 H), 7.55 (td, *J* = 7.7, 1.2 Hz, 1 H), 7.47–7.36 (m, 2 H), 7.36–7.29 (m, 2 H), 7.23–7.15 (m, 1 H), 4.80 (d, *J* = 11.3 Hz, 1 H), 4.09 (dd, *J* = 9.1, 7.1 Hz, 1 H), 3.67 (t, *J* = 9.2 Hz, 1 H), 3.63 (s, 3 H), 3.44–3.30 (m, 1 H), 2.64–2.57 (m, 2 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 170.4, 137.2, 133.5, 133.4, 133.3, 130.0, 129.9, 129.5, 125.4, 120.7, 116.9, 115.1, 65.8, 52.2, 50.5, 36.3, 35.7.

HRMS (ESI-TOF): *m*/*z* [M + Na]$^+$ calcd for $C_{20}H_{20}N_2O_5SNa$: 423.0985; found: 423.0981.

Methyl (±)-2-{(4*S*,5*S*)-5-(2-Cyanophenyl)-1,1-dioxido-2-[4-(trifluoromethyl)phenyl]isothiazolidin-4-yl}acetate (3x)

Yield: 250 mg (57%, after crystallization from Et_2O; white solid; mp 130–132 °C (Et_2O).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.82 (dd, *J* = 8.2, 1.3 Hz, 1 H), 7.80–7.70 (m, 2 H), 7.63 (d, *J* = 8.5 Hz, 2 H), 7.57 (td, *J* = 7.6, 1.3 Hz, 1 H), 7.37 (d, *J* = 8.5 Hz, 2 H), 4.85 (d, *J* = 12.0 Hz, 1 H), 4.15 (dd, *J* = 9.0, 7.0 Hz, 1 H), 3.72 (t, *J* = 9.2 Hz, 1 H), 3.64 (s, 3 H), 3.51–3.38 (m, 1 H), 2.63–2.52 (m, 2 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 170.4, 140.7, 133.7, 133.7, 132.2, 130.4, 130.1, 126.8 (q, $^3J_{C,F}$ = 3.8 Hz), 126.8 (q, $^1J_{C,F}$ = 271.6 Hz), 126.4 (q, $^2J_{C,F}$ = 33.1 Hz), 118.5, 116.9, 115.4, 66.0, 52.4, 50.1, 35.7, 35.3.

HRMS (ESI-TOF): *m*/*z* [M + Na]$^+$ calcd for $C_{20}H_{17}F_3N_2O_4SNa$: 461.0753; found: 461.0739.

Methyl (±)-2-[(4*S*,5*S*)-5-(2-Cyanophenyl)-2-(2,6-dimethylphenyl)-1,1-dioxidoisothiazolidin-4-yl]acetate (3y)

Yield: 210 mg (53%), after crystallization from Et_2O; white solid; mp 159–161 °C (Et_2O).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.93 (d, *J* = 8.0 Hz, 1 H), 7.84–7.65 (m, 2 H), 7.54 (td, *J* = 7.6, 1.1 Hz, 1 H), 7.23–7.15 (m, 1 H), 7.12 (d, *J* = 7.4 Hz, 2 H), 4.81 (d, *J* = 12.2 Hz, 1 H), 3.98 (dd, *J* = 8.3, 6.8 Hz, 1 H), 3.70–3.42 (m, 5 H), 2.57–2.34 (m, 8 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 170.5, 140.5, 140.0, 133.5, 133.5, 132.9, 132.8, 130.0, 129.9, 129.4, 129.4, 129.1, 117.0, 115.6, 64.3, 52.3, 51.0, 36.4, 35.6, 18.8, 18.8.

HRMS (ESI-TOF): *m*/*z* [M + Na]$^+$ calcd for $C_{21}H_{22}N_2O_4SNa$: 421.1192; found: 421.1209.

Methyl (±)-2-[(4*S*,5*S*)-5-(2-Cyanophenyl)-2-(4-methoxyphenyl)-1,1-dioxidoisothiazolidin-4-yl]acetate (3z)

Yield: 380 mg (79%), after crystallization from Et_2O; white solid; mp 106–108 °C (Et_2O).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.86 (d, *J* = 8.1 Hz, 1 H), 7.78–7.66 (m, 2 H), 7.53 (td, *J* = 7.6, 1.2 Hz, 1 H), 7.37–7.28 (m, 2 H), 7.03–6.81 (m, 2 H), 4.76 (d, *J* = 10.6 Hz, 1 H), 4.02 (dd, *J* = 9.3, 7.4 Hz, 1 H), 3.80 (s, 3 H), 3.61 (d, *J* = 7.3 Hz, 4 H), 3.43–3.30 (m, 1 H), 2.74–2.48 (m, 2 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 170.7, 158.6, 134.3, 133.6, 133.5, 130.0, 130.0, 129.4, 125.4, 117.1, 115.1, 115.0, 65.6, 55.7, 52.3, 51.8, 37.0, 36.3.

HRMS (ESI-TOF): *m*/*z* [M + Na]$^+$ calcd for $C_{20}H_{20}N_2O_5SNa$: 423.0985; found: 423.0981.

Methyl (±)-2-[(4*S*,5*S*)-5-(2-Cyanophenyl)-2-(4-cyanophenyl)-1,1-dioxidoisothiazolidin-4-yl]acetate (3aa)

Yield: 240 mg (51%), after column chromatography; white glassy solid.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.91–7.69 (m, 3 H), 7.65 (d, *J* = 8.9 Hz, 2 H), 7.59 (td, *J* = 7.5, 1.4 Hz, 1 H), 7.32 (d, *J* = 8.9 Hz, 2 H), 4.87 (d, *J* = 12.3 Hz, 1 H), 4.15 (dd, *J* = 8.9, 6.9 Hz, 1 H), 3.71 (t, *J* = 9.4 Hz, 1 H), 3.65 (s, 3 H), 3.54–3.32 (m, 1 H), 2.68–2.41 (m, 2 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 170.3, 141.7, 133.8, 133.7, 133.7, 131.5, 130.6, 130.0, 118.7, 117.9, 116.8, 115.5, 107.2, 65.9, 52.5, 49.9, 35.3, 35.0.

HRMS (ESI-TOF): *m*/*z* [M + Na]$^+$ calcd for $C_{20}H_{17}N_3O_4SNa$: 418.0832; found: 418.0829.

(±)-1-[(4*S*,5*R*)-1,1-Dioxido-2-phenyl-4-(tosylmethyl)isothiazolidin-5-yl]ethan-1-one (3ab)

Yield: 295 mg (60%); white solid; *dr* = ?16:1, crystallization from toluene/Et_2O; yield: 449 mg (92%); white solid; *dr* = ?19:1, HPLC.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.81 (d, *J* = 8.0 Hz, 2 H), 7.51 (d, *J* = 7.9 Hz, 2 H), 7.42 (t, *J* = 7.7 Hz, 2 H), 7.28–7.14 (m, 3 H), 4.91 (d, *J* = 8.7 Hz, 1 H), 3.92 (dd, *J* = 9.6, 7.5 Hz, 1 H), 3.71–3.59 (m, 3 H), 3.36–3.22 (m, 1 H), 2.44 (s, 3 H), 2.36 (s, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 195.2, 144.9, 136.6, 135.6, 130.0, 129.4, 127.8, 125.5, 120.9, 70.7, 56.1, 48.8, 30.7, 28.6, 21.1.

HRMS (ESI-TOF): *m*/*z* [M + Na]$^+$ calcd for $C_{19}H_{21}NO_5S_2Na$: 430.0759; found: 430.0763.

(±)-1-[(4*S*,5*R*)-2-(4-Fluorophenyl)-1,1-dioxido-4-(tosylmethyl)isothiazolidin-5-yl]ethan-1-one (3bb)

Yield: 340 mg (66%); white solid; crystallization from Et_2O; *dr* = 13:1.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.87–7.70 (m, 2 H), 7.51 (d, *J* = 8.0 Hz, 2 H), 7.28 (d, *J* = 6.6 Hz, 4 H), 4.91 (d, *J* = 8.4 Hz, 1 H), 3.90 (dd, *J* = 9.7, 7.5 Hz, 1 H), 3.69–3.58 (m, 3 H), 3.34–3.24 (m, 1 H), 2.44 (s, 3 H), 2.36 (s, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 195.3, 160.1 (d, $^1J_{C,F}$ = 243.3 Hz), 144.9, 135.6, 132.7, 130.0, 127.8, 124.21 (d, $^3J_{C,F}$ = 8.6 Hz), 116.3 (d, $^2J_{C,F}$ = 22.8 Hz), 70.4, 56.2, 49.4, 30.7, 28.7, 21.1.

HRMS (ESI-TOF): *m*/*z* [M + Na]$^+$ calcd for $C_{19}H_{20}FNO_5S_2Na$: 448.0665; found: 448.0670.

(±)-1-[(4*S*,5*R*)-2-(4-Methoxyphenyl)-1,1-dioxido-4-(tosylmethyl)isothiazolidin-5-yl]ethan-1-one (3cb)

Yield: 328 mg (62%); white solid; crystallization from toluene; *dr* = 13:1.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.84–7.79 (m, 2 H), 7.50 (d, *J* = 8.0 Hz, 2 H), 7.25–7.17 (m, 2 H), 7.02–6.95 (m, 2 H), 4.79 (d, *J* = 8.0 Hz, 1 H), 3.83 (dd, *J* = 9.8, 7.6 Hz, 1 H), 3.77 (s, 3 H), 3.66 (dd, *J* = 6.8, 2.6 Hz, 2 H), 3.59 (dd, *J* = 9.8, 8.2 Hz, 1 H), 3.38 (qd, *J* = 7.8, 6.3 Hz, 1 H), 2.44 (s, 3 H), 2.37 (s, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 195.4, 157.9, 144.9, 135.7, 130.0, 128.6, 127.8, 124.9, 114.7, 70.3, 56.3, 55.33, 49.8, 30.7, 28.6, 21.1.

HRMS (ESI-TOF): *m*/*z* [M + Na]$^+$ calcd for $C_{20}H_{23}NO_6S_2Na$: 460.0864; found: 460.0866.

Ethyl (±)-(4*S*,5*R*)-2-Phenyl-4-(tosylmethyl)isothiazolidine-5-carboxylate 1,1-Dioxide (3d'b)

Yield: 419 mg (80%), after column chromatography (hexane/DCM); colorless oil; *dr* = 6.4:1.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.86–7.82 (m, 2 H), 7.54–7.48 (m, 2 H), 7.45–7.39 (m, 2 H), 7.27–7.20 (m, 3 H), 4.72 (d, *J* = 9.4 Hz, 1 H), 4.22 (qd, *J* = 7.1, 1.4 Hz, 2 H), 3.96 (dd, *J* = 9.7, 7.3 Hz, 1 H), 3.83 (dd, *J* = 14.5, 6.2 Hz, 1 H), 3.74–3.61 (m, 2 H), 3.30–3.18 (m, 1 H), 2.44 (s, 3 H), 1.21 (t, *J* = 7.1 Hz, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 163.6, 145.7, 136.5, 135.5, 130.4, 129.6, 128.2, 126.3, 121.9, 66.3, 63.5, 57.9, 50.1, 30.5, 21.8, 14.1.

HRMS (ESI-TOF): *m*/*z* [M + Na]$^+$ calcd for $C_{20}H_{23}NO_6S_2Na$: 460.0864; found: 460.0857.

Methyl (*E*)-4-{[*N*-Phenyl-1-(*p*-tolyl)methyl]sulfonamido}but-2-enoate (4l)

A solution of methyl (*E*)-4-bromobut-2-enoate (188 mg, 1.05 mmol) in DMF (10 mL) was added to a mixture of sulfonamide **1l** (261 mg, 1 mmol) and K_2CO_3 (207 mg, 1.5 mmol) in DMF (15 mL). After stirring for 24 h at r.t., the reaction mixture was poured into 5% aq HCl (50 mL) and extracted with DCM (2 × 25 mL). The combined organic extracts were dried (Na_2SO_4) and concentrated in vacuo to give the crude product, which was crystallized from Et_2O to give the pure title compound; yield: 260 mg (72%); white solid; mp 119–120 °C (Et_2O).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.41–7.33 (m, 2 H), 7.33–7.27 (m, 5 H), 7.21 (d, *J* = 7.8 Hz, 2 H), 6.65 (dt, *J* = 15.7, 5.8 Hz, 1 H), 5.80 (dt, *J* = 15.7, 1.7 Hz, 1 H), 4.25 (s, 2 H), 4.14 (dd, *J* = 5.8, 1.8 Hz, 2 H), 3.68 (s, 3 H), 2.38 (s, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 166.2, 142.8, 139.2, 139.1, 130.8, 129.7, 129.6, 128.1, 127.9, 125.5, 123.5, 57.6, 52.6, 51.7, 21.4.

HRMS (ESI-TOF): *m*/*z* [M + Na]$^+$ calcd for $C_{19}H_{21}NO_4SNa$: 382.1083; found: 382.1081.

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Supporting Information

Supporting information for this article is available online at https://doi.org/10.1055/a-1343-9451. Crystallographic data and copies of NMR spectra are included.

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