Enantioselective Intramolecular Copper-Catalyzed Aziridination of Sulfamates

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Abstract: Intramolecular copper-catalyzed aziridination of sulfamates occurs in very good yields of up to 86% and in up to 84% ee in the presence of (4*S*,4′*S*)-2,2′-(propane-2,2-diyl)bis(4-*tert*-butyl-4,5-dihydro-1,3-oxazole). The resulting aziridines undergo smooth ring opening with different types of nucleophiles in an S_N2-type process.

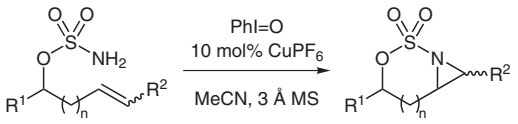
Key words: aziridine, nitrene, copper, asymmetric catalysis, ring opening

Aziridines hold a predominant place in total synthesis of natural and/or biologically active nitrogen-containing products because their ring opening by nucleophiles allows the formation of a large variety of substituted amino derivatives.[1,2] This synthetic interest has led to the development of several methodologies for the preparation of aziridines,[1,3] among which catalytic nitrene addition to alkenes has been extensively studied in the past few years.[4]

A majority of these catalytic aziridinations involves iminoiodanes[5] as nitrene precursors in the presence of transition metal complexes. From a synthetic point of view, copper[6] and rhodium[7] complexes are the catalysts of choice. The capacity of copper to catalyze competitive C–H amination under these conditions is, however, lower than that of rhodium.[4,8] Copper-catalyzed aziridination has also been successfully applied to the total synthesis of natural products or biologically active compounds.[9,10]

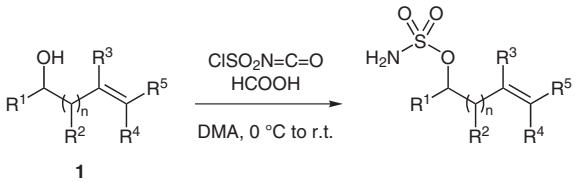
Another key feature of copper is the possibility of using chiral ligands to form aziridines in nearly enantiomerically pure form.[11] In this context, chiral C_2-symmetrical diimines and chiral bis(oxazolines) have been found to be highly efficient, since enantiomeric excesses of up to 99% can be obtained. These asymmetric nitrene transfers are, however, limited to styrene-type derivatives such as cinnamates, chalcones, or chromenes.

We and others have recently demonstrated that iminoiodanes could be generated in situ,[12] a procedure that highly facilitates their troublesome handling and enhances the variety of nitrogen compounds which can be used as nitrene sources. Among the latter, sulfamates have proven to be efficient and versatile reagents which broaden the scope of nitrene transfer.[7b,13,14] In particular, the combination of copper salts and iodosylbenzene has allowed the development of an intramolecular procedure starting from sulfamates that allows the isolation of aziridines from simple aliphatic alkenes in good yields (Scheme 1).[14] It thus appealed to us to test the ability of chiral copper complexes to induce enantioselective intramolecular aziridination of olefins well-known for being poorly reactive under these conditions. In this communication, we describe our results obtained in this context, and which can be considered as the first catalytic asymmetric nitrene transfers to aliphatic alkenes.



Scheme 1 Intramolecular copper-catalyzed aziridination of sulfamates

Unsaturated sulfamates **2a–j** could easily be prepared from the corresponding alcohols **1** by application of a recently published procedure (Scheme 2).[15] This involves the reaction of alcohols **1** in *N*,*N*-dimethylacetamide (DMA) with the sulfamoyl chloride generated in situ from chlorosulfonyl isocyanate and formic acid. Primary and secondary alcohols **1** can be transformed into sulfamates **2a–j** in very good yields (73–95%) (Scheme 2). Sulfamates **2a–j** are stable compounds that can be stored for several months at –20 °C without decomposition.



1

2a: R^1, R^2, R^3, R^4 = H, R^5 = Ph, n = 1, 82%
2b: R^1, R^2, R^3, R^4, R^5 = H, n = 1, 95%
2c: R^1, R^2 = H, R^3 = Me, R^4, R^5 = H, n = 1, 95%
2d: R^1, R^2, R^3, R^4 = H, R^5 = Me, n = 1, 74%
2e: R^1, R^2, R^3, R^4 = H, R^5 = Et, n = 1, 95%
2f: R^1, R^2, R^3 = H, R^4 = Et, R^5 = H, n = 1, 93%
2g: R^1, R^2, R^3, R^4 = H, R^5 = CO_2Me, n = 1, 73%
2h: R^1 = Me, R^2, R^3, R^4, R^5 = H, n = 1, 92%
2i: R^1 = H, R^2 = Me, R^3, R^4, R^5 = H, n = 1, 84%
2j: R^1, R^2, R^3, R^4, R^5 = H, n = 2, 80%

Scheme 2 Preparation of unsaturated sulfamates **2a–j**

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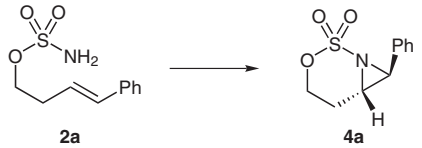
We then turned our attention to the asymmetric intramolecular catalytic aziridination of sulfamates **2**. The optimal reaction conditions were first established with sulfamate **2a** (Table 1). Initial experiments indicated that diiminocyclohexane **3a**[11a] and bis(oxazolines) **3b** and **3c**[11b] (Figure 1) gave the best results (data not shown). It should be mentioned that the asymmetric aziridination of sulfamate **2a** took place stereospecifically, since we obtained only the *trans*-aziridine **4a** (Table 1).

Using these ligands, we then screened different reaction parameters (Table 1). At room temperature, aziridine **4a** was isolated in approximately the same good yields in the 75–80% range both in the absence (Table 1, entry 1) and presence (entries 2, 4, 6) of ligands **3a–c**. However, at a lower temperature of –20 °C, the yields markedly dropped to 48% and 40% respectively, in the cases of diimine **3a** and bis(oxazoline) **3b** (Table 1, entries 3 and 5), while a yield of 75% was maintained with the bis(*tert*-butyloxazoline) **3c** (entry 7). Moreover, as far as the enantioselectivity is concerned, the highest enantiomeric excess, i.e. 76%, was obtained at –20 °C, again in the presence of ligand **3c**, which was therefore used for further optimization.

To further improve the enantioselectivity, the reaction was run at lower temperatures, at –30 °C and –40 °C (Table 1, entries 8 and 9). This did not affect the efficiency in terms of reactivity of the nitrene transfer. However, lower enantiomeric excesses of around 65% were obtained. Interestingly, when the catalytic amount of the chiral copper complex was reduced to 5 mol%, we could isolate aziridine **4a** at –20 °C in a higher yield of 86% and a better enantioselectivity of 84% (Table 1, entry 10). Finally, acetonitrile was found to be the solvent of choice, since reactions conducted in benzene and dichloromethane afforded aziridine **4a** in lower yields and in very modest enantioselectivities of 32% and 25% ee, respectively (Table 1, entries 11 and 12).

Table 1 Determination of the Optimal Aziridination Conditions with Sulfamate **2a**[a]



2a **4a**

Entry	Ligand	Temp (°C)	Solvent	Yield[b] (%)	ee[c] (%)
1	none	25	MeCN	78	–
2	**3a**	25	MeCN	75	56
3	**3a**	–20	MeCN	48	45
4	**3b**	25	MeCN	80	14
5	**3b**	–20	MeCN	40	20
6	**3c**	25	MeCN	80	63
7	**3c**	–20	MeCN	75	76
8	**3c**	–30	MeCN	72	65
9	**3c**	–40	MeCN	72	66
10[d]	**3c**	–20	MeCN	86	84
11	**3c**	25	benzene	56	32
12	**3c**	25	CH_2Cl_2	60	25

[a] Reagents and conditions: $[Cu(NCMe)_4]PF_6$ (10 mol%), ligand **3** (11 mol%), PhIO, 3-Å MS, MeCN.
[b] Isolated yield after column chromatography.
[c] The ee values were determined by HPLC (OD column).
[d] With $[Cu(NCMe)_4]PF_6$ (5 mol%).

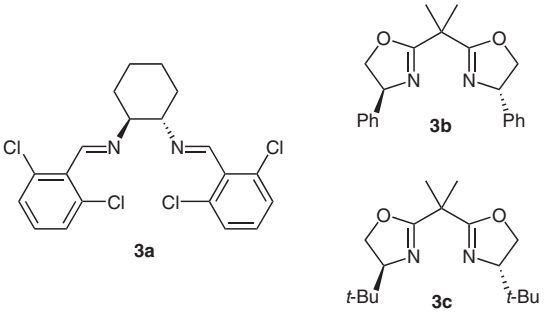


Figure 1

These optimal conditions, that is, 5 mol% $[Cu(NCMe)_4]PF_6$ in the presence of 5.5 mol% ligand **3c** at –20 °C in acetonitrile, were then applied to sulfamates **2b–j** (Table 2).[16] The asymmetric copper-catalyzed aziridination of sulfamate **2b** gave encouraging results, since, in contrast to substrate **2a**, the C=C bond of **2b** is not conjugated to an aromatic system. The corresponding aziridine **4b** was isolated in 81% yield and 52% ee (Table 2, entry 2).

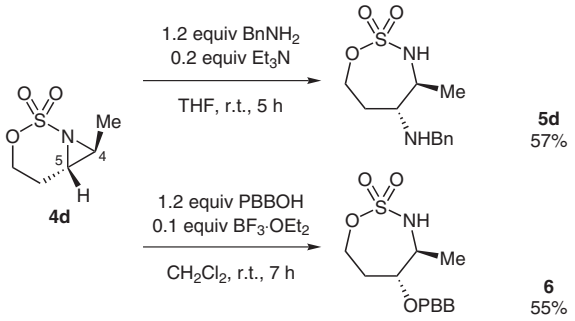
Application of these conditions to disubstituted alkenes then indicated that the substitution pattern of the olefin has an influence on the reactivity. For instance, the reaction with the *gem*-disubstituted alkene **2c** was disappointing (Table 2, entry 3). The aziridine **4c** was obtained in a low yield of 24% and in modest enantioselectivity of 36%. By contrast, disubstituted *trans*- and *cis*-olefins **2d–g** displayed higher reactivity under these conditions, since the corresponding aziridines **4d–g** were isolated in 80%, 83%, 86%, and 79% yields, respectively (Table 2, entries 4–7). Moreover, good enantiomeric excesses of 80% for the *trans*-products **4d** and **4e**, and 72% for the *cis*-isomer **4f** were observed. Surprisingly, while the copper-catalyzed aziridination of the *trans*-alkenes **2a**, **2d**, **2e,** and **2g** was stereospecific, this was not the case for the *cis*-sulfamate **2f**, since traces of the *trans*-aziridine **4e** could be isolated from the reaction mixture. While most copper-catalyzed nitrene transfers are believed to occur by a concerted pathway involving singlet nitrenes,[4b,6a,17] the aforementioned result indicates the intermediacy of triplet nitrene of radical character. It should also be noted that, although slightly lower than that of compounds **4a**, **4d**, and **4e**, the enantiomeric excess of 62% observed with sulfamate **4g** is the first so far described for the aziridination of an α,β-unsaturated ester (with the exception of cin-

namates).[18] This result paves the way for an enantioselective synthesis of amino acids.[1a,2b]

Asymmetric intramolecular nitrene transfer was also attempted with substituted sulfamates. Starting from the secondary derivative **2h**, the corresponding aziridine **4h** was isolated in a very good yield of 82% (Table 2, entry 8). However, the use of the chiral bis(oxazoline) **3c** had an influence on the diastereoselectivity. A 30:70 ratio in favor of the *trans*-**4h** isomer was obtained in this case, while the *cis*-aziridine **4h** was the major compound formed in a diastereomeric ratio of 86:14 under racemic conditions.[19] The same trend was observed with sulfamate **2i**, the aziridine **4i** being isolated in 85% yield and with a reversed *cis*/*trans* diastereomeric ratio of 45:55 (Table 2, entry 9) instead of 2:1 in the absence of ligand **3c**. As far as the enantioselectivity is concerned, the enantiomeric excess was always higher for the minor *cis*-aziridine.

Finally, the homologous sulfamate **2j** was subjected to asymmetric intramolecular aziridination and gave aziridine **4j** in good yield (72%) but moderate enantioselectivity (47% ee) (Table 2, entry 10).

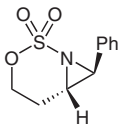
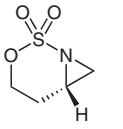
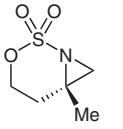
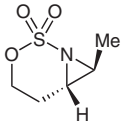
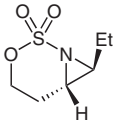
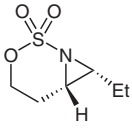
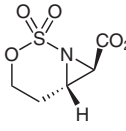
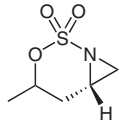
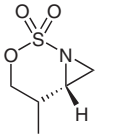
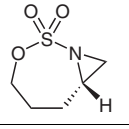
The results in Table 2 show that the reactivities of simple aliphatic alkenes **2b–j** are similar to that of alkene **2a** conjugated to a benzene ring. This intramolecular process therefore broadens the scope of the enantioselective copper-catalyzed aziridination, previously confined to styrene-type derivatives, to other olefins. The asymmetric synthesis of nitrogen-containing compounds can therefore be envisaged starting from the resulting aziridines **4**, since it has been demonstrated previously by Du Bois[13b,f] and our group[14] that they undergo regioselective ring opening with nitrogen, oxygen, and sulfur nucleophiles. This possibility was confirmed with the bicyclic aziridine **4d**, whose reaction with benzylamine or *p*-bromobenzyl alcohol (PBBOH) afforded the seven-membered cyclic sulfamidates **5d** and **6** in 57% and 55% yield, respectively (Scheme 3).



Scheme 3 Regioselective nucleophilic ring opening of aziridine **4d**

As mentioned before,[16] the enantiomeric excesses measured for these ring-opened products **5d** and **6** were identical to that of the aziridine **4d**, i.e. 80%. Compound **6** could be recrystallized and obtained in an optically pure form. X-ray crystallography (Figure 2) allowed the determination of the absolute configuration, namely 4*S*,5*R*, of the asymmetric centers formed during enantioselective

Table 2 Enantioselective Intramolecular Aziridination of Sulfamates **2**[a]

Entry	Product	Yield[b] (%)	ee[c] (%)
1	 **4a**	86	84
2	 **4b**	81	52
3	 **4c**	24	36
4	 **4d**	80	80
5	 **4e**	83	80
6[d]	 **4f**	86	72
7	 **4g**	79	62
8	 **4h**	82 (30:70)[e]	78, 24[f]
9	 **4i**	85 (45:55)[e]	68, 28[f]
10	 **4j**	72	47

[a] Reagents and conditions: **2** (1 equiv), $[Cu(NCMe)_4]PF_6$ (5 mol%), ligand **3c** (5.5 mol%), PhIO (1.5 equiv), 3-Å MS, MeCN, –20 °C.
[b] Isolated yield after column chromatography.
[c] The ee values were determined by HPLC (OD or AD column) after ring opening of aziridines **4** with $BnNH_2$.
[d] Traces of the *trans*-aziridine **4e** were isolated.
[e] The *cis*/*trans* ratio.
[f] The ee values of the *cis*- and *trans*-isomers, respectively.

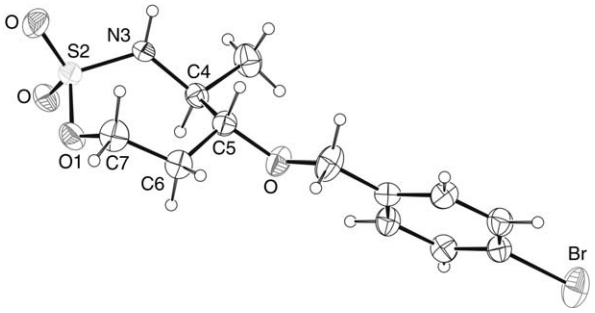


Figure 2 ORTEP view of the crystal structure of **6** at the 30% probability level

aziridination. It was also deduced that the intramolecular nitrene addition occurs preferentially via the *si* face while the nucleophilic ring opening takes place by an S_N2-type process.

The ORTEP view of **6** (Figure 2) also clearly confirmed the regioselectivity of the ring opening, i.e. at the C-5 position of aziridine **4d**. This result was tentatively rationalized by modeling calculations of aziridines of type **4**. It was found that the C5–N bond (1.47 Å) is slightly longer than the C4–N bond (1.45 Å), and therefore more likely to undergo nucleophilic displacement. In a recent paper,[13f] Du Bois and co-workers reported that the same trend was observed when the X-ray structures of the starting bicyclic aziridine and the subsequent ring-opened product were compared. Additional convincing data were also provided by the same authors that are all fully consistent with our experimental findings.

In conclusion, chiral copper complexes efficiently catalyze the intramolecular aziridination of sulfamates in yields of up to 86% and enantiomeric excesses of up to 84%. In particular, this nitrene transfer occurs with equal success for simple aliphatic olefins and electron-poor alkenes, substrates for which no enantioselective aziridination has been reported before. The resulting aziridine undergoes a clean S_N2-type nucleophilic ring opening with excellent regioselectivity. The latter offers the opportunity of introducing a second nucleophile at the C–O position, a reaction that has been demonstrated to occur after carbamoylation of the nitrogen atom.[13a,f,14,20] Stereoselective access to enantiopure substituted amines is therefore conceivable by application of this strategy, an area of investigation that is currently in progress in our laboratory.

Melting points were measured in capillary tubes on a Büchi B-540 apparatus and are uncorrected. IR spectra were recorded with a Perkin Elmer Spectrum BX FT-IR spectrometer. ^{1}H (300 or 250 MHz) and ^{13}C (75 MHz) NMR spectra were measured on a Bruker Aspect 3000 (300 MHz) instrument. EI and CI mass spectra were recorded on an AEI MS-50 and AEI MS-9 spectrometer, respectively. High-resolution mass spectra were obtained on a Kratos MS-80 spectrometer. Optical rotations were determined with a JASCO P-1010 polarimeter. Chiral HPLC was performed on a Waters 2695 spectrometer coupled with a Waters 996 Photodiode Array Detector (PDA) with a ChiralCel™ OD column (10 μm, 250 × 4.6 mm) or a ChiralPack™ AD column (10 μm, 250 × 4.6 mm). All solvents were distilled except DMA (*N*,*N*-dimethylacetamide), which was stored over 3-Å MS. All reagents were purchased from Aldrich Chemical Co. and were used without further purification. Elemental analyses were performed at the ICSN, CNRS, Gif-sur-Yvette, France.

Sulfamates 2a–j; General Procedure

HCO_2H (1.70 mL, 45 mmol, 1.5 equiv) was added dropwise to neat $ClSO_2NCO$ (3.90 mL, 45 mmol, 1.5 equiv) at 0 °C with rapid stirring. Gas evolved during the addition. The resulting viscous suspension was stirred for 18 h at r.t. The mixture was cooled to 0 °C, DMA (8 mL) was added, and the soln was stirred for 5 min. A soln of the appropriate alkenol **1** (1 equiv) in DMA (16 mL) was added dropwise, the resulting soln was allowed to warm to r.t., and stirring was continued until the reaction was complete (3–4 h) as determined by TLC. The reaction was quenched by the successive addition of EtOAc (40 mL) and sat. aq NaCl (20 mL). The mixture was poured into EtOAc (80 mL) and H_2O (30 mL). The organic phase was collected and the aqueous layer was extracted with EtOAc (2 × 30 mL). The organic extracts were combined, washed with sat. aq NaCl (2 × 30 mL), dried ($MgSO_4$), and concentrated under reduced pressure. Purification of the residue by flash chromatography (silica gel, heptane–EtOAc) afforded the desired sulfamic ester.

(*E*)-4-Phenylbut-3-enyl Sulfamate (2a)

Sulfamate **2a** was prepared from 4-phenylbut-3-en-1-ol, and was purified by chromatography (silica gel, heptane–EtOAc, 3:7).

Yield: 82%; white solid; mp 92–93 °C; R_f = 0.24 (heptane–EtOAc, 6:4).

IR (neat): 3402, 3312, 1534, 1345, 1170, 967, 929, 747 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.59 (dq, *J* = 6.5, 1.3 Hz, 2 H), 4.24 (t, *J* = 6.6 Hz, 2 H), 4.72 (br s, 2 H), 6.09 (dt, *J* = 15.9, 7.0 Hz, 1 H), 6.44 (dt, *J* = 15.9 Hz, 1 H), 7.13–7.30 (m, 5 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 32.4, 70.5, 124.0, 126.2, 127.6, 128.6, 133.4, 136.9.

ESI-MS: *m*/*z* (%) = 250.0 (100) [M + Na$^+$], 477.1 (29) [2 × M + Na$^+$].

HRMS [ESI(+)]: *m*/*z* [M + Na$^+$] calcd for $C_{10}H_{13}NO_3S$: 250.0514; found: 250.0509.

But-3-enyl Sulfamate (2b)

Sulfamate **2b** was prepared from but-3-en-1-ol, and was purified by chromatography (silica gel, heptane–EtOAc, 3:7).

Yield: 95%; yellow oil; R_f = 0.44 (heptane–EtOAc, 6:4).

IR (neat): 3384, 3288, 3084, 2985, 2907, 1643, 1556, 1360, 1178, 920, 776 cm^{-1}.

^{1}H NMR (250 MHz, $CDCl_3$): δ = 2.52 (ddt, *J* = 13.2, 6.4, 1.5 Hz, 2 H), 4.27 (t, *J* = 6.6 Hz, 2 H), 4.81 (s, 2 H), 5.16 (m, 1 H), 5.19 (ddd, *J* = 17.1, 3.5, 1.5 Hz, 1 H), 5.81 (ddt, *J* = 17.1, 10.3, 6.6 Hz, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 33.1, 70.4, 118.4, 132.7.

ESI-MS: *m*/*z* (%) = 152 (28) [M + H$^+$], 174 (100) [M + Na$^+$].

Anal. Calcd for $C_4H_9NO_3S$: C, 31.78; H, 6.00; N, 9.26; S, 21.21. Found: C, 31.82; H, 6.06; N, 9.12; S, 20.83.

3-Methylbut-3-enyl Sulfamate (2c)

Sulfamate **2c** was prepared from 3-methylbut-3-en-1-ol, and was purified by chromatography (silica gel, heptane–EtOAc, 3:7).

Yield: 95%; yellow oil; R_f = 0.47 (heptane–EtOAc 6:4).

IR (neat): 3376, 3287, 3081, 2973, 1614, 1557, 1366, 1180, 972, 925, 784 cm^{-1}.

^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.78 (s, 3 H), 2.47 (t, *J* = 6.8 Hz, 2 H), 4.32 (t, *J* = 6.8 Hz, 2 H), 4.80 (s, 1 H), 4.87 (s, 1 H), 4.95 (s, 2 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 22.5, 36.3, 69.3, 113.0, 140.6.

ESI-MS: *m/z* (%) = 188 (100) [M + Na^+].

Anal. Calcd for $C_5H_{11}NO_3S$·l/7 DMA: C, 37.44; H, 7.48; N, 8.95; S, 17.97. Found: C, 37.71; H, 7.10; N, 9.00; S, 17.64.

(*E*)-Pent-3-enyl Sulfamate (2d)
Sulfamate **2d** was prepared from (*E*)-pent-3-en-1-ol, and was purified by chromatography (silica gel, heptane–EtOAc, 6:4).

Yield: 74%; salmon-colored oil; R_f = 0.47 (heptane–EtOAc, 6:4).

IR (neat): 3279, 2919, 2856, 1613, 1556, 1357, 1174, 966, 917 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.65 (dq, *J* = 6.4, 1.2 Hz, 3 H), 2.40 (qq, *J* = 6.7, 1.1 Hz, 2 H), 4.16 (t, *J* = 6.7 Hz, 2 H), 5.01 (br s, 2 H), 5.37 (m, 1 H), 5.56 (m, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 18.0, 32.0, 70.9, 124.9, 129.1.

ESI-MS: *m/z* (%) = 188.0 (30) [M + Na^+], 220.0 (100) [M + MeOH + Na^+].

HRMS [ESI(+)]: *m/z* [M + Na^+] calcd for $C_5H_{11}NO_3S$: 188.0357; found: 188.0366.

(*E*)-Hex-3-enyl Sulfamate (2e)
Sulfamate **2e** was prepared from (*E*)-hex-3-en-1-ol, and was purified by chromatography (silica gel, heptane–EtOAc, 3:7).

Yield: 95%; yellow oil; R_f = 0.5 (heptane–EtOAc, 6:4).

IR (neat): 3383, 3288, 2965, 2935, 1556, 1365, 1182, 970, 932, 814, 775 cm^{-1}.

^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.98 (t, *J* = 7.3 Hz, 3 H), 2.02 (quin, *J* = 7.1 Hz, 2 H), 2.45 (q, *J* = 7.1 Hz, 2 H), 4.21 (t, *J* = 7.1 Hz, 2 H), 4.78 (s, 2 H), 5.38 (dt, *J* = 15.6, 6.7 Hz, 1 H), 5.63 (dt, *J* = 15.6, 6.7 Hz, 1 H).

^{13}C NMR (75MHz, $CDCl_3$): δ = 13.7, 25.7, 32.1, 71.1, 122.7, 136.3.

ESI-MS: *m/z* (%) = 181 (10) [M + H^+], 202 (100) [M + Na^+].

Anal. Calcd for $C_6H_{13}NO_3S$: C, 40.21; H, 7.31; N, 7.81; S, 17.89. Found: C, 40.33; H, 7.56; N, 7.61; S, 17.84.

(*Z*)-Hex-3-enyl Sulfamate (2f)
Sulfamate **2f** was prepared from (*Z*)-hex-3-en-1-ol, and was purified by chromatography (silica gel, heptane–EtOAc, 3:7).

Yield: 93%; yellow oil; R_f = 0.53 (heptane–EtOAc, 6:4).

IR (neat): 3383, 3288, 3014, 2966, 2935, 2876, 1555, 1465, 1364, 1181, 972, 929, 778 cm^{-1}.

^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.99 (t, *J* = 7.4 Hz, 3 H), 2.07 (quin, *J* = 7.4 Hz, 2 H), 2.51 (q, *J* = 6.6 Hz, 2 H), 4.20 (t, *J* = 6.6 Hz, 2 H), 4.86 (s, 2 H), 5.33 (m, 1 H), 5.57 (m, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.1, 20.7, 26.9, 70.8, 122.4, 135.6.

ESI-MS: *m/z* (%) = 233.9 (100) [M + MeOH + Na^+], 201.9 (22) [M + Na^+].

Anal. Calcd for $C_6H_{13}NO_3S$: C, 40.21; H, 7.31; N, 7.81; S, 17.89. Found: C, 40.37; H, 7.59; N, 7.65; S, 17.72.

Methyl (*E*)-5-(Sulfamoyloxy)pent-2-enoate (2g)
Sulfamate **2g** was prepared from methyl (*E*)-5-hydroxypent-2-enoate, and was purified by chromatography (silica gel, heptane–EtOAc, 4:6).

Yield: 73%; white solid; mp 53–54 °C; R_f = 0.56 (heptane–EtOAc 4:6).

IR (neat): 3336, 3255, 1682, 1655, 1553, 1361, 1171, 915 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.63 (qd, *J* = 6.5, 1.6 Hz, 2 H), 3.71 (s, 3 H), 4.29 (t, *J* = 6.3 Hz, 2 H), 5.03 (s, 2 H), 5.93 (dd, *J* = 15.7, 1.5 Hz, 1 H), 6.89 (dt, *J* = 15.6, 6.8 Hz, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 31.4, 51.7, 68.7, 123.9, 143.0, 166.6.

ESI-MS: *m/z* (%) = 232.0 (100) [M + Na^+].

HRMS [ESI(+)]: *m/z* [M + Na^+] calcd for $C_6H_{11}NO_5S$: 232.0256; found: 232.0245.

1-Methylbut-3-enyl Sulfamate (2h)
Sulfamate **2h** was prepared from pent-4-en-2-ol, and was purified by chromatography (silica gel, heptane–EtOAc, 3:7).

Yield: 92%; yellow oil; R_f = 0.44 (heptane–EtOAc, 6:4).

IR (neat): 3381, 3286, 3082, 2983, 2939, 1558, 1358, 1182, 920, 793, 765 cm^{-1}.

^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.43 (d, *J* = 5.9 Hz, 3 H), 2.46 (m, 2 H), 4.75 (sext, *J* = 6.3 Hz, 1 H), 4.86 (s, 2 H), 5.13 (m, 1 H), 5.18 (m, 1 H), 5.81 (m, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 20.1, 40.6, 80.3, 118.9, 132.6.

ESI-MS: *m/z* (%) = 187.8 (100) [M + Na^+].

Anal. Calcd for $C_5H_{11}NO_3S$: C, 36.35; H, 6.71; N, 8.48; S, 19.41. Found: C, 36.47; H, 6.85; N, 8.42; S, 19.12.

2-Methylbut-3-enyl Sulfamate (2i)
Sulfamate **2i** was prepared from 2-methylbut-3-en-1-ol, and was purified by chromatography (silica gel, heptane–EtOAc, 6:4).

Yield: 84%; colorless oil; R_f = 0.67 (heptane–EtOAc 4:6).

IR (neat): 3377, 3280, 1556, 1355, 1175, 969, 916 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.1 (d, *J* = 6.8 Hz, 3 H), 2.62 (m, 1 H), 4.02 (dd, *J* = 9.4, 6.7 Hz, 1 H), 4.11 (dd, *J* = 9.4, 6.7 Hz, 1 H), 4.87 (br s, 2 H), 5.10 (dt, *J* = 10.4, 1.1 Hz, 1 H), 5.14 (dt, *J* = 17.3, 1.1 Hz, 1 H), 5.8 (ddd, *J* = 17.3, 10.4, 7 Hz, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 16.0, 39.9, 74.8, 116.1, 138.6.

ESI-MS: *m/z* (%) = 188.0 (20) [M + Na^+], 421.0 (100).

HRMS [ESI(+)]: *m/z* [M + Na^+] calcd for $C_5H_{11}NO_3S$: 188.0357; found: 188.0349.

Pent-4-enyl Sulfamate (2j)
Sulfamate **2j** was prepared from pent-4-en-1-ol, and was purified by chromatography (silica gel, heptane–EtOAc, 3:7).

Yield: 80%; yellow oil; R_f = 0.5 (heptane–EtOAc 6:4).

IR (neat): 3383, 3288, 3014, 2966, 2935, 2876, 1555, 1465, 1364, 1181, 972, 929, 778 cm^{-1}.

^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.87 (quin, *J* = 6.6 Hz, 2 H), 2.20 (q, *J* = 7.4 Hz, 2 H), 4.24 (t, *J* = 6.3 Hz, 2 H), 4.83 (s, 2 H), 5.01 (m, 1 H), 5.08 (ddd, *J* = 16.9, 3.0, 1.5 Hz, 1 H), 5.80 (ddt, *J* = 16.9, 10.3, 6.6 Hz, 1 H).

^{13}C NMR ($CDCl_3$, 75 MHz): δ = 13.7, 25.7, 32.1, 71.1, 122.7, 136.3.

ESI-MS: *m/z* (%) = 187.8 (100) [M + Na^+].

Anal. Calcd for $C_5H_{11}NO_3S$: C, 36.35; H, 6.71; N, 8.48. Found: C, 36.18; H, 6.95; N, 8.31.

3-Oxa-2-thia-1-azabicyclo[4.1.0]heptane 2,2-Dioxides 4a–i and 3-Oxa-2-thia-1-azabicyclo[5.1.0]octane 2,2-Dioxide 4j by Aziridination of Alkenyl Sulfamates 2a–j; General Procedure
A soln of $[Cu(NCMe)_4]PF_6$ (55.4 mg, 0.15 mmol, 0.05 equiv) and **3c** (48.1 mg, 0.16 mmol, 0.055 equiv) in MeCN (40 mL) containing activated 3-Å MS (8 g) was stirred at –20 °C for 30 min under ar-

gon. A soln of the appropriate sulfamate **2** (2.97 mmol, 1 equiv) in MeCN (40 mL) was introduced by cannula into the homogeneous soln. PhIO (980 mg, 4.46 mmol, 1.5 equiv) was added and the mixture was stirred at –20 °C for 48 h. The MS were removed by filtration over Celite and the filtrate was evaporated to dryness under reduced pressure. The residue was purified by flash chromatography (silica gel); this afforded the corresponding aziridine **4**.

(*E*)-7-Phenyl-3-oxa-2-thia-1-azabicyclo[4.1.0]heptane 2,2-Dioxide (4a)

Compound **4a** was prepared from **2a**, and was purified by chromatography (silica gel, heptane–EtOAc, 8:2).

Yield: 86%; 84% ee; white solid; mp 94–95 °C; R_f = 0.28 (heptane–EtOAc, 6:4); HPLC (OD column, hexane–EtOH, 9:1, flow rate: 1 mL/min, injected volume: 10 μL, detection: UV 225 nm); t_{R1} = 22.6 min, t_{R2} = 28.0 min.

IR (neat): 2985, 1497, 1373, 1357, 1243, 1180, 1054, 955, 905, 693 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 2.39 (m, 2 H), 3.18 (dq, *J* = 4.6, 3.2 Hz, 1 H), 3.80 (d, *J* = 4.4 Hz, 1 H), 4.46 (dt, *J* = 11.5, 6.4 Hz, 1 H), 4.70 (dt, *J* = 11.6, 6.8 Hz, 1 H), 7.19–7.32 (m, 5 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 18.8, 47.8, 50.4, 68.8, 126.3, 128.8, 134.2.

ESI-MS: *m*/*z* (%) = 280.0 (100) [M + MeOH + Na^+], 248.0 (28) [M + Na^+], 226.0 (12) [M + H^+].

HRMS [ESI(+)]: *m*/*z* [M + Na^+] calcd for $C_{10}H_{11}NO_3S$: 248.0357; found: 248.0337.

3-Oxa-2-thia-1-azabicyclo[4.1.0]heptane 2,2-Dioxide (4b)

Compound **4b** was prepared from **2b**, and was purified by chromatography (silica gel, heptane–EtOAc, 1:1).

Yield: 81%; brown oil; R_f = 0.36 (heptane–EtOAc, 1:2).

IR (neat): 3293, 2936, 1723, 1361, 1182, 1035, 982, 952, 932, 786 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 2.26 (ddt, *J* = 15.1, 6.8, 6.4 Hz, 1 H), 2.51 (dq, *J* = 15.1, 6.4 Hz, 1 H), 2.65 (dd, *J* = 5.4, 1.5 Hz, 1 H), 2.73 (dd, *J* = 5.4, 1.5 Hz, 1 H), 3.22 (dd, *J* = 10.3, 5.4 Hz, 1 H), 4.43 (ddd, *J* = 11.7, 6.8, 6.4 Hz, 1 H), 4.69 (dt, *J* = 11.7, 6.4 Hz, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 18.4, 34.3, 41.6, 68.7.

MS (EI): *m*/*z* (%) = 150.0 (22) [M + H^+], 110 (35), 55 (100).

Anal. Calcd for $C_4H_7NO_3S$: C, 32.21; H, 4.73; N, 9.39; S, 21.50. Found: C, 32.21; H, 4.79; N, 9.22; S, 21.31.

6-Methyl-3-oxa-2-thia-1-azabicyclo[4.1.0]heptane 2,2-Dioxide (4c)

Compound **4c** was prepared from **2c**, and was purified by chromatography (silica gel, heptane–EtOAc, 6:4).

Yield: 24%; brown oil; R_f = 0.17 (heptane–EtOAc, 6:4).

IR (neat): 2978, 2933, 1448, 1362, 1264, 1184, 1094, 1023, 961, 934 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 1.49 (s, 3 H), 2.26 (dt, *J* = 15.1, 5.8, 5.4 Hz, 1 H), 2.36 (m, 1 H), 2.45 (dt, *J* = 1.5 Hz, 1 H), 2.85 (dt, *J* = 1.5 Hz, 1 H), 4.37 (ddd, *J* = 11.7, 8.3, 6.4 Hz, 1 H), 4.58 (ddd, *J* = 11.7, 6.4, 5.4 Hz, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 24.4, 25.1, 40.3, 49.4, 67.8.

MS (EI): *m*/*z* (%) = 164.0 (45) [M + H^+], 69 (95), 42 (100).

Anal. Calcd for $C_5H_9NO_3S$: C, 37.01; H, 5.71; S, 8.38; N, 19.41; Found: C, 36.80; H, 5.56; S, 8.58; N, 19.65.

(*E*)-7-Methyl-3-oxa-2-thia-1-azabicyclo[4.1.0]heptane 2,2-Dioxide (4d)

Compound **4d** was prepared from **2d**, and was purified by chromatography (silica gel, heptane–EtOAc, 1:1).

Yield: 80%; peach-colored oil; R_f = 0.23 (heptane–EtOAc, 6:4).

IR (neat): 3474, 3148, 2923, 1449, 1350, 1177, 1042, 887, 768 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 1.34 (d, *J* = 5 Hz, 3 H), 2.20 (m, 1 H), 2.39 (m, 1 H), 2.92 (m, 2 H), 4.35 (ddd, *J* = 11.4, 6.0, 5.7 Hz, 1 H), 4.61 (ddd, *J* = 11.7, 5.8, 5.9 Hz, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 16.9, 18.8, 42.8, 48.8, 68.6.

ESI-MS: *m*/*z* (%) = 218.0 (100) [M + MeOH + Na^+], 186.0 (50) [M + Na^+].

HRMS [ESI(+)]: *m*/*z* [M + Na^+] calcd for $C_5H_9NO_3S$: 186.0201; found: 186.0206.

(*E*)-7-Ethyl-3-oxa-2-thia-1-azabicyclo[4.1.0]heptane 2,2-Dioxide (4e)

Compound **4e** was prepared from **2e**, and was purified by chromatography (silica gel, heptane–EtOAc, 7:3).

Yield: 83%; brown oil; R_f = 0.26 (heptane–EtOAc 6:4).

IR (neat): 2972, 2936, 2879, 1462, 1434, 1364, 1185, 1043, 1022, 965 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 1.06 (t, *J* = 7.4 Hz, 3 H), 1.52 (sext, *J* = 7.4 Hz, 1 H), 1.70 (m, 1 H), 2.22 (m, 1 H), 2.41 (ddd, *J* = 15.1, 6.6, 5.9 Hz, 1 H), 2.84 (dt, *J* = 7.4, 4.4 Hz, 1 H), 3.03 (m, 1 H), 4.39 (dt, *J* = 11.7, 6.6 Hz, 1 H), 4.66 (dt, *J* = 11.7, 5.9 Hz, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 10.3, 19.0, 24.6, 47.9, 48.5, 68.7.

ESI-MS: *m*/*z* (%) = 199.8 (100) [M + Na^+], 177.9 (64) [M + H^+], 231.8 (78) [M + MeOH + Na^+].

Anal. Calcd for $C_6H_{11}NO_3S$: C, 40.66; H, 6.26; N, 7.90; S, 18.09; Found: C, 40.89; H, 6.62; N, 7.50; S, 17.80.

(*Z*)-7-Ethyl-3-oxa-2-thia-1-azabicyclo[4.1.0]heptane 2,2-Dioxide (4f)

Compound **4f** was prepared from **2f**, and was purified by chromatography (silica gel, heptane–EtOAc, 1:1).

Yield: 86% (*Z*/*E*, 10:4); brown oil; R_f = 0.20 (heptane–EtOAc 6:4).

IR (neat): 2973, 2879, 1359, 1281, 1178, 1040, 962, 880, 789, 758 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 1.12 (t, *J* = 7.3 Hz, 3 H), 1.75 (sext, *J* = 7.3 Hz, 1 H), 2.10 (m, 3 H), 2.70 (dt, *J* = 8.4, 5.4 Hz, 1 H), 3.37 (dt, *J* = 8.5, 5.4 Hz, 1 H), 4.45 (ddd, *J* = 11.7, 6.4, 1.5 Hz, 1 H), 4.83 (ddd, *J* = 12.5, 11.7, 4.4 Hz, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 10.9, 16.0, 17.0, 43.2, 47.0, 70.5.

MS (EI): *m*/*z* (%) = 178.0 (27) [M + H^+], 83 (82), 68 (82), 54 (100).

Anal. Calcd for $C_6H_{11}NO_3S$: C, 40.66; H, 6.26; N, 7.90; S, 18.09; Found: C, 40.88; H, 6.43; N, 7.62; S, 17.85.

(*E*)-Methyl 3-Oxa-2-thia-1-azabicyclo[4.1.0]heptane-7-carboxylate 2,2-Dioxide (4g)

Compound **4g** was prepared from **2g**, and was purified by chromatography (silica gel, heptane–EtOAc, 4:6).

Yield: 79%; colorless oil; R_f = 0.12 (heptane–EtOAc, 4:6).

IR (neat): 2960, 1741, 1445, 1368, 1181, 1053, 839, 788 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 2.31 (m, 1 H), 2.46 (m, 1 H), 3.44 (m, 1 H), 3.46 (br s, 1 H), 3.78 (s, 3 H), 4.42 (dt, *J* = 12.0, 6.2 Hz, 1 H), 4.71 (m, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 16.9, 41.6, 45.0, 52.1, 67.8, 165.4.

ESI-MS: *m/z* (%) = 230.0 (100) [M + Na^+].

HRMS [ESI(+)]: *m/z* [M + Na^+] calcd for $C_6H_9NO_5S$: 230.0099; found: 230.0101.

4-Methyl-3-oxa-2-thia-1-azabicyclo[4.1.0]heptane 2,2-Dioxide (4h)

Compound **4h** was prepared from **2h**, and was purified by chromatography (silica gel, heptane–EtOAc, 1:1).

Yield: 82% (dr 30:70); brown oil; R_f = 0.17 (minor) and 0.08 (major diastereomer) (heptane–EtOAc, 6:4).

IR (neat): 2990, 2936, 1371, 1270, 1235, 1187, 971, 909, 865, 800 cm^{-1}.

^1H NMR (250 MHz, $CDCl_3$): δ (minor diastereomer, *cis*) = 1.43 (d, *J* = 6.6 Hz, 3 H), 1.94 (ddd, *J* = 14.7, 3.7, 2.9 Hz, 1 H), 2.31 (ddd, *J* = 14.7, 8.1, 4.4 Hz, 1 H), 2.43 (d, *J* = 5.1 Hz, 1 H), 2.58 (d, *J* = 5.1 Hz, 1 H), 3.20 (m, 1 H), 5.08 (m, 1 H); δ (major diastereomer, *trans*) = 1.47 (d, *J* = 6.3 Hz, 3 H), 2.35 (ddd, *J* = 15.3, 4.5, 1.6 Hz, 1 H), 2.41 (ddd, *J* = 15.3, 11.2, 2.4 Hz, 1 H), 2.63 (dd, *J* = 5.3, 1.9 Hz, 1 H), 2.88 (dd, *J* = 4.9, 1.9 Hz, 1 H), 3.15 (m, 1 H), 4.62 (dq, *J* = 6.2, 4.7 Hz, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ (minor diastereomer) = 21.4, 26.3, 36, 41, 79.9; δ (major diastereomer) = 21.4, 26.1, 29.7, 41, 76.2.

MS (CI): *m/z* (%) = 164.0 (100) [M + H^+].

Anal. Calcd for $C_5H_9NO_3S{\cdot}0.05C_4H_8O$: C, 37.27; H, 5.65; N, 8.36; S, 19.13; Found: C, 37.23; H, 5.46; N, 8.38; S, 18.91.

5-Methyl-3-oxa-2-thia-1-azabicyclo[4.1.0]heptane 2,2-Dioxide (4i)

Compound **4i** was prepared from **2i**, and was purified by chromatography (silica gel, heptane–EtOAc, 8:2).

Yield: 85% (dr 45:55); brown oil; R_f = 0.38 (heptane–EtOAc, 4:6).

IR (neat): 2973, 1462, 1363, 1259, 1181, 975, 788 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ (minor diastereomer) = 1.13 (d, *J* = 6.6 Hz, 3 H), 2.55 (m, 1 H), 2.78 (dd, *J* = 5.3, 1.5 Hz, 1 H), 2.85 (m, 1 H), 3.11 (qd, *J* = 5.2, 1.0 Hz, 1 H), 3.97 (dd, *J* = 11.7, 9.8 Hz, 1 H), 4.44 (qd, *J* = 6.0, 1.0 Hz, 1 H); δ (major diastereomer) = 1.26 (d, *J* = 7.1 Hz, 3 H), 2.45 (m, 1 H), 2.57 (ddd, *J* = 11.6, 5.4, 1.0 Hz, 2 H), 2.9 (td, *J* = 5.1, 2.3 Hz, 1 H), 4.36 (dd, *J* = 15.3, 11.7 Hz, 1 H), 4.36 (dd, *J* = 30.1, 11.9 Hz, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ (minor diastereomer) = 14.7, 23.4, 31.7, 46.4, 72.4; δ (major diastereomer) = 16.8, 25.0, 35.2, 48.1, 74.2.

ESI-MS: *m/z* (%) = 218.0 (100) [M + MeOH + Na^+], 186.0 (50) [M + Na^+].

HRMS [ESI(+)]: *m/z* [M + Na^+] calcd for $C_5H_9NO_3S$: 186.0201; found: 186.0206.

3-Oxa-2-thia-1-azabicyclo[5.1.0]octane 2,2-Dioxide (4j)

Compound **4j** was prepared from **2j**, and was purified by chromatography (silica gel, heptane–EtOAc, 1:1).

Yield: 72%; brown oil; R_f = 0.14 (heptane–EtOAc, 6:4).

IR (neat): 2955, 2854, 1358, 1271, 1175, 1104, 1011, 951, 913, 841 cm^{-1}.

^1H NMR (250 MHz, $CDCl_3$): δ = 1.93 (m, 2 H), 2.50–2.40 (m, 2 H), 2.54 (d, *J* = 5.1 Hz, 1 H), 2.75 (d, *J* = 5.1 Hz, 1 H), 2.85 (m, 1 H), 4.23 (m, 2 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 26.3, 26.6, 32.9 (br), 39.8, 71.5.

MS (EI): *m/z* (%) = 164.0 (11) [M + H^+], 71 (36), 42 (55), 41 (100).

Anal. Calcd for $C_5H_9NO_3S{\cdot}0.04C_7H_{16}$: C, 37.93; H, 5.81; N, 8.38; S, 19.17; Found: C, 37.75; H, 5.69; N, 8.28; S, 18.94.

1,2,3-Oxathiazepane 2,2-Dioxides 5a–j by Ring Opening of 3-Oxa-2-thia-1-azabicyclo[4.1.0]heptane 2,2-Dioxides 4a–i and 3-Oxa-2-thia-1-azabicyclo[5.1.0]octane 2,2-Dioxide 4j; General Procedure

To determine the ee of the aziridine products **4a–j**, they were derivatized to the corresponding 1,2,3-oxathiazepanes **5a–j** as follows: to a soln of the appropriate aziridine **4a–j** (0.78 mmol, 1 equiv) in THF (1.3 mL) were added $BnNH_2$ (102 μL, 0.93 mmol, 1.2 equiv) and Et_3N (22 μL, 0.16 mmol, 0.2 equiv) at 20 °C under argon. The mixture was stirred for 20 h and concentrated under reduced pressure. Purification of the residue by flash chromatography (silica gel, CH_2Cl_2–MeOH–Et_3N, 99:0.5:0.5) afforded the corresponding 1,2,3-oxathiazepane **5a–j**. Chiral-phase HPLC was used for the determination of ee values.

***trans*-*N*-Benzyl-4-phenyl-1,2,3-oxathiazepan-5-amine 2,2-Dioxide (5a)**

From **4a**; yield: 83%; 84% ee; white solid; mp 165–166 °C; R_f = 0.54 (CH_2Cl_2–MeOH–Et_3N, 99:0.5:0.5); HPLC (OD column, hexane–*i*-PrOH–Et_3N, 90:10:0.1, flow rate: 1 mL/min, injected volume: 10 μL, detection: UV 212 nm): t_{R1} = 25.9 min, t_{R2} = 31.3 min.

IR (neat): 3287, 3059, 2849, 1451, 1352, 1172, 1060, 938, 742, 700 cm^{-1}.

^1H NMR (300 MHz, DMSO-d_6): δ = 1.73 (br s, 1 H), 1.91 (m, 1 H), 2.31 (dt, *J* = 15, 3.7 Hz, 1 H), 2.97 (td, *J* = 9.5, 3.8 Hz, 1 H), 3.26 (d, *J* = 13.9 Hz, 1 H), 3.49 (d, *J* = 13.3 Hz, 1 H), 4.09 (d, *J* = 10.6 Hz, 1 H), 4.33 (m, 2 H), 6.86–6.94 (m, 2 H), 7.10–7.20 (m, 3 H), 7.27–7.40 (m, 5 H), 8.41 (br s, 1 H).

^{13}C NMR (75 MHz, DMSO-d_6): δ = 34.7, 49.8, 59.9, 61.2, 67.5, 126.4, 127.3, 127.6, 127.7, 127.9, 128.1, 140.3, 140.5.

ESI-MS: *m/z* (%) 355.1 (100) [M + Na^+], 333.1 (92) [M + H^+].

***N*-Benzyl-1,2,3-oxathiazepan-5-amine 2,2-Dioxide (5b)**

From **4b**; yield: 65%; 52% ee; white solid; mp 78–79 °C; R_f = 0.13 (CH_2Cl_2–MeOH–Et_3N, 99:0.5:0.5); HPLC (OD column, hexane–*i*-PrOH–Et_3N, 90:10:0.1, flow rate: 1 mL/min, injected volume: 50 μL, detection: UV 262 nm): t_{R1} = 47.3 min, t_{R2} = 65.1 min.

IR (neat): 3315, 3056, 2357, 1450, 1336, 1177, 1079, 947, 746, 695 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 1.28 (br s, NH, 1 H), 1.75 (dt, *J* = 15.8, 4.3 Hz, 1 H), 2.14 (ddt, *J* = 14.6, 11.3, 3.2 Hz, 1 H), 2.99 (q, *J* = 3.7 Hz, 1 H), 3.10 (ddd, *J* = 15.0, 4.3, 1.3 Hz, 1 H), 3.26 (d, *J* = 15.5 Hz, 1 H), 3.65 (d, *J* = 13.0 Hz, 1 H), 3.72 (d, *J* = 13.0 Hz, 1 H), 4.06 (ddd, *J* = 13.0, 4.3, 2.5 Hz, 1 H), 4.46 (t, *J* = 12.3 Hz, 1 H), 5.50 (br s, 1 H), 7.15–7.34 (m, 5 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 34.9, 43.6, 51.1, 53.5, 65.2, 127.6, 128.0, 128.8, 139.2.

***N*-Benzyl-5-methyl-1,2,3-oxathiazepan-5-amine 2,2-Dioxide (5c)**

From **4c**; yield: 46%; 36% ee; white solid; mp 98–99 °C; R_f = 0.28 (CH_2Cl_2–MeOH–Et_3N, 99:0.5:0.5); HPLC (OD column, hexane–*i*-PrOH–Et_3N, 80:20:0.1, flow rate: 1 mL/min, injected volume: 50 μL, detection: UV 260 nm): t_{R1} = 16.2 min, t_{R2} = 27.8 min.

IR (neat): 3296, 2961, 1413, 1342, 1181, 1068, 968, 904, 740, 694 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 0.91 (br s, 1 H), 1.16 (s, 3 H), 1.74 (ddd, *J* = 16.1, 3.0, 2.3 Hz, 1 H), 1.92 (ddd, *J* = 16.1, 11.5, 2.8 Hz, 1 H), 2.87 (dd, *J* = 15.2, 3.4 Hz, 1 H), 3.17 (d, *J* = 14.8 Hz, 1 H), 3.54 (d, *J* = 12.0 Hz, 1 H), 3.64 (d, *J* = 12.0 Hz, 1 H), 3.99 (dt, *J* = 13.0, 3.3 Hz, 1 H), 4.48 (td, *J* = 12.3, 1.0 Hz, 1 H), 5.56 (br s, 1 H), 7.17–7.32 (m, 5 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 24.8, 40.4, 46.0, 48.9, 54.3, 65.2, 127.4, 128.1, 128.8, 139.5.

***trans*-*N*-Benzyl-4-methyl-1,2,3-oxathiazepan-5-amine 2,2-Dioxide (5d)**

From **4d**; yield: 57%; 80% ee; white solid; mp 80–81 °C; R_f = 0.39 (CH_2Cl_2–MeOH–Et_3N, 99:0.5:0.5); HPLC (AD column, hexane–*i*-PrOH–Et_3N, 95:5:0.1, flow rate: 1 mL/min, injected volume: 50 μL, detection: UV 259 nm): t_{R1} = 31.3 min, t_{R2} = 35.4 min.

IR (neat): 3318, 3079, 2872, 1339, 1170, 1038, 969, 745, 708 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.4 (d, *J* = 6.9 Hz, 3 H), 1.83 (m, 1 H), 2.27 (m, 1 H), 2.73 (m, 1 H), 3.30 (m, 1 H), 3.75 (d, *J* = 7.3 Hz, 2 H), 4.15 (ddd, *J* = 12.7, 7.4, 1.9 Hz, 1 H), 4.41 (ddd, *J* = 13.0, 8.5, 1.5 Hz, 1 H), 5.44 (br s, 1 H), 7.22–7.36 (m, 5 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 16.6, 32.1, 51.3, 52.3, 60.7, 66.0, 127.5, 126.0, 128.7, 139.5.

ESI-MS: *m*/*z* (%) = 271.1 (100) [M + H$^+$], 293.1 (52) [M + Na$^+$].

HRMS [ESI(+)]: *m*/*z* [M + Na$^+$] calcd for $C_{12}H_{18}N_2O_3S$: 271.1116; found: 271.1121.

***trans*-*N*-Benzyl-4-ethyl-1,2,3-oxathiazepan-5-amine 2,2-Dioxide (5e)**

From **4e**; yield: 82%; 80% ee; white solid; mp 117–118 °C; R_f = 0.33 (heptane–EtOAc, 4:6); HPLC (AD column, hexane–*i*-PrOH–Et_3N, 95:5:0.1, flow rate: 1 mL/min, injected volume: 15 μL, detection: UV 265 nm): t_{R1} = 26.7 min, t_{R2} = 29.7 min.

IR (neat): 3320, 3065, 2864, 1455, 1341, 1169, 1004, 920, 738, 702 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.96 (t, *J* = 7.3 Hz, 3 H), 1.22 (br s, 1 H), 1.62 (m, 1 H), 1.77 (m, 1 H), 1.82 (m, 1 H), 2.19 (ddq, *J* = 16.0, 8.0, 1.6 Hz, 1 H), 2.74 (td, *J* = 6.7, 3.3 Hz, 1 H), 3.00 (m, 1 H), 3.66 (d, *J* = 13.0 Hz, 1 H), 3.74 (d, *J* = 13.0 Hz, 1 H), 4.11 (ddd, *J* = 13.0, 7.9, 1.7 Hz, 1 H), 4.35 (ddd, *J* = 13.0, 8.2, 1.9 Hz, 1 H), 5.09 (br s, 1 H), 7.16–7.30 (m, 5 H).

^{13}C NMR (75 MHz, $CDCl_3$) : δ = 10.8, 24.0, 32.8, 51.4, 59.4, 59.8, 66.5, 127.4, 128.1, 128.6, 139.7.

***cis*-*N*-Benzyl-4-ethyl-1,2,3-oxathiazepan-5-amine 2,2-Dioxide (5f)**

From **4f**; yield: 80%; 72% ee; yellow oil; R_f = 0.39 (CH_2Cl_2–MeOH–Et_3N, 99:0.5:0.5); HPLC (OD column, hexane–*i*-PrOH–Et_3N, 80:20:0.1, flow rate: 1 mL/min, injected volume: 50 μL, detection: UV 265 nm): t_{R1} = 13.1 min, t_{R2} = 15.5 min.

IR (neat): 3290, 2965, 2358, 1422, 1346, 1175, 1004, 929, 748 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.01 (t, *J* = 7.0 Hz, 3 H), 1.46 (m, 1 H), 1.60 (m, 1 H), 2.04 (m, 2 H), 3.03 (t, *J* = 3.2 Hz, 1 H), 3.31 (dd, *J* = 9.2, 5.1 Hz, 1 H), 3.75 (d, *J* = 13.3 Hz, 1 H), 3.87 (d, *J* = 13.3 Hz, 1 H), 4.10 (dt, *J* = 12.7, 3.2 Hz, 1 H), 4.55 (t, *J* = 11.7 Hz, 1 H), 5.70 (br s, 1 H), 7.28–7.39 (m, 5 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 11.0, 26.6, 32.8, 52.0, 55.9, 58.6, 64.6, 127.3, 128.1, 128.7, 139.5.

Methyl 5-(Benzylamino)-1,2,3-oxathiazepane-4-carboxylate 2,2-Dioxide (5g)

From **4g**; yield: 78%; 62% ee; white solid; mp 121–122 °C; R_f = 0.38 (heptane–EtOAc, 4:6); HPLC (OD column, hexane–*i*-PrOH–Et_3N, 80:20:0.1, flow rate: 1 mL/min, injected volume: 50 μL, detection: UV 259 nm); t_{R1} = 16.0 min, t_{R2} = 18.1 min.

IR (neat): 3321, 3040, 2876, 1731, 1433, 1349, 1182, 948, 746, 677 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.96 (dtd, *J* = 15.5, 9.4, 3.0 Hz, 1 H), 2.27 (dtd, *J* = 15.5, 4.3, 1.8 Hz, 1 H), 3.12 (td, *J* = 8.9, 3.2 Hz, 1 H), 3.73 (dtd, *J* = 13.3 Hz, 1 H), 3.77 (s, 3 H), 3.83 (dtd, *J* = 13.3 Hz, 1 H), 3.97 (dtd, *J* = 8.6 Hz, 1 H), 4.28 (q, *J* = 11.1 Hz, 1 H), 4.37 (ddd, *J* = 12.4, 6.0, 2.4 Hz, 1 H), 7.20–7.38 (m, 5 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 33.8, 51.0, 52.9, 59.5, 60.1, 67.4, 127.4, 128.0, 128.5, 139.2, 170.4.

***cis*-*N*-Benzyl-7-methyl-1,2,3-oxathiazepan-5-amine 2,2-Dioxide (*cis*-5h)**

From *cis*-**4h**; yield: 89%; 78% ee; white solid; mp 105–106 °C; R_f = 0.21 (heptane–EtOAc, 4:6); HPLC (OD column, hexane–*i*-PrOH–Et_3N, 80:20:0.1, flow rate: 1 mL/min, injected volume: 50 μL, detection: UV 265 nm): t_{R1} = 13.9 min, t_{R2} = 15.5 min.

IR (neat): 3306, 3056, 1460, 1337, 1175, 1079, 896, 741, 696 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.44 (d, *J* = 6.8 Hz, 3 H), 1.82 (dt, *J* = 14.7, 10.0 Hz, 1 H), 2.14 (dd, *J* = 15.2, 4.2 Hz, 1 H), 2.90 (m, 1 H), 3.13 (dd, *J* = 14.7, 9.5 Hz, 1 H), 3.34 (dd, *J* = 14.2, 2.6 Hz, 1 H), 3.81 (s, 2 H), 4.68 (m, 1 H), 7.26–7.39 (m, 5 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 22.0, 42.6, 46.2, 51.2, 56.9, 77.4, 127.4, 127.9, 128.7, 139.5.

MS (ES+): *m*/*z* (%) = 271.1 (100) [M + H$^+$], 293.1 (25) [M + Na$^+$].

HRMS [ESI(+)]: *m*/*z* [M + H$^+$] calcd for $C_{12}H_{18}N_2O_3S$: 271.1116; found: 271.1116.

***trans*-*N*-Benzyl-7-methyl-1,2,3-oxathiazepan-5-amine 2,2-Dioxide (*trans*-5h)**

From *trans*-**4h**; yield: 90%; 24% ee; colorless oil; mp 105–106 °C; R_f = 0.42 (heptane–EtOAc, 4:6); HPLC (OD column, hexane–*i*-PrOH–Et_3N, 80:20:0.1, flow rate: 1 mL/min, injected volume: 50 μL, detection: UV 254 nm): t_{R1} = 13.5 min, t_{R2} = 28.3 min.

IR (neat): 3287, 2934, 1416, 1344, 1174, 1042, 905, 700 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.36 (d, *J* = 6.5 Hz, 3 H), 1.42 (br s, 1 H), 1.78 (d, *J* = 15.7 Hz, 1 H), 2.08 (ddd, *J* = 15.4, 10.3, 5.1 Hz, 1 H), 3.04 (q, *J* = 3.3 Hz, 1 H), 3.19 (d, *J* = 16.4 Hz, 1 H), 3.35 (d, *J* = 15.7 Hz, 1 H), 3.71 (d, *J* = 12.7 Hz, 1 H), 3.81 (d, *J* = 12.8 Hz, 1 H), 4.92 (ddd, *J* = 11.0, 10.7, 5.7 Hz, 1 H), 5.77 (br s, 1 H), 7.27–7.40 (m, 5 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 21.7, 40.0, 43.1, 51.3, 53.1, 73.6, 127.7, 128.0, 128.8, 139.1.

MS (ES+): *m*/*z* (%) = 271.1 (100) [M + H$^+$], 293.1 (25) [M + Na$^+$].

HRMS [ESI(+)]: *m*/*z* [M + H$^+$] calcd for $C_{12}H_{18}N_2O_3S$: 271.1116; found: 271.1116.

***N*-Benzyl-6-Methyl-1,2,3-oxathiazepan-5-amine 2,2-Dioxide (5i)**

From **4i**; yield: 79%; 68% ee (minor) and 28% ee (major diastereomer); brown oil; R_f = 0.21 (CH_2Cl_2–MeOH–Et_3N, 99:0.5:0.5); HPLC (OD column, hexane–*i*-PrOH–Et_3N, 80:20:0.1, flow rate: 1 mL/min, injected volume: 50 μL, detection: UV 260 nm): t_{R1} (major) = 14.9 min, t_{R2} (major) = 28.7 min; t_{R1} (minor) = 17.6 min, t_{R2} (minor) = 22.4 min.

IR (neat): 3289, 2966, 1413, 1343, 1174, 969, 941, 790, 699 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ (major) = 0.86 (d, *J* = 7.4 Hz, 3 H), 2.24 (m, 1 H), 2.78 (q, *J* = 2.8 Hz, 1 H), 3.16 (d, *J* = 2.8 Hz, 2 H), 3.55 (d, *J* = 13.4 Hz, 1 H), 3.76 (d, *J* = 13.3 Hz, 1 H), 3.79 (dd, *J* = 10.2, 2.7 Hz, 1 H), 4.23 (dd, *J* = 12.4, 9.9 Hz, 1 H), 7.17–7.35 (m, 5 H); δ (minor) = 1.09 (d, *J* = 7.2 Hz, 3 H), 1.73 (m, 1 H), 2.63 (t, *J* = 3.4 Hz, 1 H), 3.01 (ddd, *J* = 15.5, 3.9, 0.9 Hz, 1 H), 3.29 (d, *J* = 15.5 Hz, 1 H), 3.63 (d, *J* = 12.8 Hz, 1 H), 3.73 (d, *J* = 12.8 Hz, 1 H), 3.85 (dd, *J* = 12.5, 3.6 Hz, 1 H), 4.53 (d, *J* = 13.3 Hz, 1 H), 5.62 (br s, 1 H), 7.17–7.35 (m, 5 H).

^{13}C NMR ($CDCl_3$, 75 MHz): δ (major) = 13.3, 37.9, 43.0, 51.2, 58.0, 69.2, 127.7, 128.1, 128.8, 139.1; δ (minor) = 15.1, 38.1, 39.7, 51.2, 59.2, 69.1, 127.6, 128.0, 128.8, 139.2.

4-[(Benzylamino)methyl]-1,2,3-oxathiazepane 2,2-Dioxide (5j)
From **4j**; 67% yield; 47% ee; white solid; mp 103–104 °C; R_f = 0.10 (CH_2Cl_2–MeOH–Et_3N, 99:0.5:0.5); HPLC (OD column, hexane–*i*-PrOH–Et_3N, 80:20:0.1, flow rate: 1 mL/min, injected volume: 50 μL, detection: UV 265 nm): t_{R1} = 10.5 min, t_{R2} = 12.7 min.

IR (neat): 3283, 3024, 2850, 1451, 1342, 1175, 1013, 940, 750, 700 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.67 (q, *J* = 11.2 Hz, 1 H), 1.93 (m, 1 H), 1.96 (m, 1 H), 2.03 (m, 1 H), 2.69 (dd, *J* = 22.5, 12.5 Hz, 1 H), 2.70 (dd, *J* = 20.3, 12.7 Hz, 1 H), 3.27 (br s, 2 H), 3.47 (m, 1 H), 3.76 (d, *J* = 13.1 Hz, 1 H), 3.83 (d, *J* = 13.1 Hz, 1 H), 4.29 (m, 2 H), 7.24–7.38 (m, 5 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 27.7, 32.5, 52.7, 52.8, 53.6, 70.8, 127.5, 128.4, 128.8, 139.7.

(4*S*,5*R*)-5-[(4-Bromobenzyl)oxy]-4-methyl-1,2,3-oxathiazepane 2,2-Dioxide (6)
BF_3·OEt_2 (78 μL, 0.6 mmol, 0.1 equiv) and PBBOH (1.4 g, 7.4 mmol, 1.2 equiv) were added to a soln of **4d** (1 g, 6.1 mmol, 1 equiv) in CH_2Cl_2 (20 mL) at 0 °C under argon. The mixture was stirred at 20 °C for 7 h. The reaction was quenched with 10% aq $NaHCO_3$ (40 mL) and the layers were separated. The aqueous layer was extracted with CH_2Cl_2 (3 × 40 mL) and the combined organic layers were dried ($MgSO_4$). The solvent was removed under reduced pressure; this gave the crude product, which was filtered over silica gel (CH_2Cl_2). The resulting white solid [yield: 55% (by ^{1}H NMR); 80% ee (by chiral HPLC)] was purified by recrystallization (MeOH). A white crystalline solid was obtained (0.47 g), while a second crop (0.34 g) was obtained from the mother liquor.

Total yield: 0.81 g (38%); >99% ee; mp 63–64 °C; $[\alpha]_D^{20}$ –12.25 (*c* 0.52, $CHCl_3$); R_f = 0.42 (heptane–EtOAc, 6:4); HPLC (OD column, hexane–*i*-PrOH–Et_3N, 90:10:0.1, flow rate: 1 mL/min, injected volume: 50 μL, detection: UV 265nm): t_{R1} [(4*R*,5*S*)-**6**] = 22.3 min, t_{R2} [(4*S*,5*R*)-**6**] = 27.4 min.

IR (neat): 3291, 2965, 1434, 1340, 1170, 1125, 1103, 966, 805, 720 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.41 (d, *J* = 6.8 Hz, 3 H), 2.03 (m, 1 H), 2.23 (ddt, *J* = 15.9, 9.0, 2.6 Hz, 1 H), 3.43 (m, 2 H), 4.17 (ddd, *J* = 13.1, 7.1, 2.2 Hz, 1 H), 4.43 (d, *J* = 12.2 Hz, 1 H), 4.46 (m, 1 H), 4.54 (d, *J* = 12.2 Hz, 1 H), 5.09 (d, *J* = 4.7 Hz, 1 H), 7.16 (d, *J* = 8.7 Hz, 2 H), 7.47 (d, *J* = 8.4 Hz, 2 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 16.10, 31.04, 52.79, 65.70, 70.70, 79.76, 122.03, 129.34, 131.76, 136.42.

ESI-MS: *m*/*z* (%) = 371.9 (99.8) [M + Na^+], 373.9 (100) [M + Na^+].

HRMS [ESI(+)]: *m*/*z* [M + Na^+] calcd for $C_{12}H_{16}{}^{79}BrNO_4S$: 371.9881; found: 371.9891; *m*/*z* [M + Na^+] calcd for $C_{12}H_{16}{}^{81}BrNO_4S$: 373.9861; found: 373.9872.

X-ray Crystal Structure Determination of Compound 6
Reflection data were collected on a Nonius-Bruker Kappa CCD diffractometer with graphite-monochromated Mo–K_α radiation (λ = 0.71073 Å). Reflection data were collected according to the Friedel strategy[21] to minimize errors in the Bijvoet differences owing to the bromide atom in the molecule and to optimize the discriminating power between the enantiomeric structures. All of the strongest 118 Friedel related reflections [>4σ (ΔF^2)] (out of a total of 1068) were found[22] to confirm the selected absolute structure, C4(*S*) and C5(*R*).

Crystal Data: $C_{12}H_{16}BrNO_4S$, FW = 350.23, data collection:[21] ω scan frames with 1°/frame and exposure times of 12 s/frame, data reduction:[23] orthorhombic, $P2_12_12_1$, *a* = 5.235(1) Å, *b* = 11.884(1) Å, *c* = 23.666(2) Å, *V* = 1472.36(6) Å^3, *D* = 1.580 Mg/m^3, 12053 collected reflections up to θ_{max} = 25.4°, 2668 unique (R_{int} = 0.0598), structure solution:[24] direct methods, model refinement:[24] on sF^2 by full-matrix least-squares methods with anisotropic thermal parameters for all non-hydrogen atoms, all hydrogen atoms were located on difference Fourier syntheses but were refined with a riding model and with U_{iso} (H) = 1.2 *U*eq (C) (1.5 for a methyl group), R_1 = 0.0655, wR_2 = 0.1029 [R_1 = 0.0405, wR_2 = 0.0913 for $I > 2\sigma$ (*I*)], goodness-of-fit = 1.064, Flack parameter = 0.001(15).

Structural data have been deposited with the Cambridge Crystallographic Data Centre (CIF file) as supplementary publication number CCDC 635135. Copies of the data can be obtained free of charge, on application to CCDC, 12 Union Road, CB2 1EZ, UK [fax:+44(1223)336033, e-mail: deposit@ccdc.cam.ac.uk].

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