Stereoselective preparation of $\gamma$- and $\delta$-sultams by thermal and high-pressure intramolecular Diels–Alder reaction of vinylsulfonamides

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Dedicated to Professor Lutz F. Tietze on the occasion of his 65th birthday

Abstract
A range of novel $\gamma$- and $\delta$-sultams was prepared by intramolecular [4+2] cycloaddition of vinylsulfonamides with purely thermal activation and under high pressure. Using $N$-1-phenylethyl substituted vinylsulfonamides, enantiopure sultams were readily obtained, debenzylation of which provided the corresponding NH sultams in high yields in the case of $\delta$-sultams.

Keywords: Asymmetric synthesis, cycloadditions, debenzylation, high pressure, sulfur heterocycles

Introduction
Sultams$^1$ are useful heterocycles for asymmetric synthesis$^2$ and medicinal chemistry.$^3$ Recently developed powerful methodologies for the generation of these cyclic sulfonamides include the intramolecular Diels–Alder reaction,$^4$ sulfonamide dianion alkylation,$^5$ radical cyclization,$^6$ ring-closing metathesis,$^7$ and intramolecular Heck cyclization.$^8$ In two previous communications,$^{4a,b}$ we reported the efficient preparation of five- and six-membered sultams by thermal- and high-pressure intramolecular [4+2] cycloadditions of vinylsulfonamides possessing an acyclic, furan or carbocyclic 1,3-diene moiety. Here we give a full account on these studies including the concise preparation of enantiomerically pure $\delta$-sultams that can be applied as novel chiral auxiliaries.$^9$
Results and Discussion

The vinylsulfonamides 4–6 incorporating a three-atom tether connecting an acyclic diene and the dienophile were readily available by treatment of \(N\)-benzyldienylamines 1–3\(^{10}\) with vinylsulfonyl chloride\(^{11}\) (Scheme 1). Upon refluxing a solution of 4–6 in toluene, the \(\gamma\)-sultams rac-7, rac-8, and rac-9, respectively, were formed in good yields as single diastereomers. Subjecting a solution of any of 4–6 in dichloromethane to a pressure of 13 kbar at room temperature proved to be even more efficient. The relative configuration of the \(\gamma\)-sultams was elucidated by 2D NOESY experiments and additionally by X-ray diffraction analysis in the case of the sultam rac-9.\(^{4a}\)

\[\text{Scheme 1. Reagents and conditions: (a) CH}_2\text{=CHSO}_2\text{Cl, Et}_3\text{N, CH}_2\text{Cl}_2, 0 \degree \text{C, 1–2 h, 92% 4, 95% 5, 96% 6; (b) toluene, reflux, 1 bar, 70% rac-7 (22 h), 79% rac-8 (8 h), 71% rac-9 (16 h); (c) CH}_2\text{Cl}_2, \text{RT, 13 kbar, 71% rac-7 (29 h), 93% rac-8 (10 h), 90% rac-9 (12 h).}\]

The furan-containing vinylsulfonamide 12 featuring a nitrogen-bound (S)-(−)-1-phenylethyl unit as an external chiral auxiliary and incorporating a three-atom tether connecting the furan diene and the dienophile, was prepared from aldehyde 10 via the known amine 11\(^{12}\) (Scheme 2). While complete conversion was achieved after 14 h for the high-pressure cycloaddition, 13% of 12 was still present after 16 h reflux in toluene. Although the difference is not very pronounced, the 13 kbar cycloaddition was associated with a higher asymmetric induction than the reflux/ambient pressure process.\(^{13,14}\) The \textit{exo} sultams 13 and 14 could be readily separated by
flash chromatography, and their configuration was unequivocally determined by X-ray diffraction analysis of 13.4b Interestingly, the sultam 13 was favored by the (S)-(−)-1-phenylethyl substitution in vinylsulfonamide 12, whereas the corresponding maleic monoamide derivative of 11 led preferentially (65:35) at ambient temperature and pressure to an exo cycloadduct with the opposite diastereofacial selectivity.12 This is probably due to the higher steric demand of a tetrahedral sulfonamide as compared to a trigonal carboxylic amide.15 In contrast to the crystal structures of the furan-derived N-1-phenylethyl δ-sultams obtained in this study, all of which feature an sp² hybridized nitrogen atom, an sp³ hybridization on nitrogen was unveiled by the crystal structure of γ-sultam 13.4b

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\begin{align*}
\text{Scheme 2. Reagents and conditions:} & \quad (a) \ (S)-(−)-1-phenylethylamine, MgSO₄, Et₂O, 0 °C to RT, 15 h, 98%; (b) LiAlH₄, Et₂O, 0 °C to RT, 6 h, 95%; (c) CH₂=CHSO₂Cl, Et₃N, CH₂Cl₂, 0 °C, 2 h, 98%; (d) toluene, reflux, 1 bar, 16 h, 73%; (e) CH₂Cl₂, RT, 13 kbar, 14 h, 94%.
\end{align*}
\]

An earlier investigation revealed a high diastereoselectivity in the cyclization of vinylsulfonamide rac-15 which features a four-atom tether and a furan 1,3-diene, to give the exo δ-sultams rac-16 and rac-17 at ambient pressure (Scheme 3).4f

\[
\begin{align*}
\text{Scheme 3}
\end{align*}
\]

The vinylsulfonamide 21 carrying an (S)-(−)-1-phenylethyl unit on nitrogen was easily available by nucleophilic substitution on the mesylate 19 derived from the alcohol 18,17
followed by treatment of the resultant amine 20 with vinylsulfonyl chloride (Scheme 2). After refluxing a solution of 21 in toluene, or subjecting a solution of 21 in dichloromethane to a pressure of 13 kbar at room temperature, the exo δ-sultams 22 and 23 were isolated in high yield. In this case, the diastereomeric ratio of 22:23 was only 1:1 for the high-pressure reaction, while the (S)-(−)-1-phenylethyl substituent caused a significant, albeit rather low, asymmetric induction under purely thermal activation. Again, the two sultam diastereomers produced were readily separated by flash chromatography, and their configuration was unambiguously established by X-ray diffraction analysis.  

Scheme 4. Reagents and conditions: (a) MsCl, Et$_3$N, CH$_2$Cl$_2$, 0 °C, 45 min, 97%; (b) (S)-(−)-1-phenylethylamine, 80 °C, 12 h, 79%; (c) CH$_2$=CHSO$_2$Cl, Et$_3$N, CH$_2$Cl$_2$, 0 °C, 2 h, 96%; (d) toluene, reflux, 1 bar, 10 h, 80%; (e) CH$_2$Cl$_2$, RT, 13 kbar, 12 h, 98%.

In a further series of experiments, the double stereodifferentiation brought about by the simultaneous presence of a stereogenic center within the tether (see Scheme 3) and a chiral auxiliary on nitrogen (see Scheme 4) was investigated (Scheme 5). To this end, the hydroxyalkylfuran rac-24 was converted by mesylation and nucleophilic substitution to give a 1:1 mixture of the diastereomeric amines 26 and 27, which were separated by flash chromatography. Subsequent treatment of 26 and 27 with vinylsulfonyl chloride delivered the vinylsulfonamides 28 and 29, respectively, as pure stereoisomers. The configuration of 29 was proved by X-ray diffraction analysis. While complete conversion of 28 and 29 was achieved after 14 h for the high-pressure cycloaddition, 5% of the vinylsulfonamides was still present after 16 h reflux in toluene. As depicted in Scheme 5, the diastereoselectivities noted for the high-pressure cycloadditions of 28 and 29 were hardly affected by the (S)-(−)-1-phenylethyl unit (compare Scheme 4), and the equatorial disposition of the methyl substituent on the δ-sultam – and in the corresponding transition state – clearly dominated the stereochemical outcome of these reactions. On the other hand, the diastereoselectivities observed for the thermal process at ambient pressure were critically dependent on the relative configurations of 28 and 29.
Scheme 5. Reagents and conditions: (a) MsCl, Et$_3$N, CH$_2$Cl$_2$, 0 °C, 45 min, 97%; (b) (S)-(−)-1-phenylethylamine, 80 °C, 12 h, 67% 26 + 27; (c) CH$_2$=CHSO$_2$Cl, Et$_3$N, CH$_2$Cl$_2$, 0 °C, 3 h, 84% 28, 82% 29; (d) toluene, reflux, 1 bar, 16 h, 87% 30 + 31, 85% 32 + 33; (e) CH$_2$Cl$_2$, RT, 13 kbar, 14 h, 98% 30 + 31, 98% 32 + 33.

As is apparent from the results listed in Scheme 4, and can be extrapolated from the reaction of N-benzyl vinylsulfonamide rac-15 shown in Scheme 3, formation of sultam 30 should be favored by virtue of both stereogenic elements present in 28. However, for the substrate 29 a mismatched combination arises that causes a decrease in stereocontrol. While this argument provides a consistent rationale in a qualitative sense, any explanation of the very low ratio, 32:33 = 54:46, has to take into account the fact that the two inducing elements are not acting independently of each other. Specifically during formation of 30 and 32, a non-bonded interaction between the methyl group on the sultam and the branched N-1-phenylethyl substituent can hardly be avoided. The sultams 30 and 31 were readily separated by flash
chromatography, but this was not possible for the mixture of sultams 32 and 33. Gratifyingly, pure isomer 32 could instead be obtained by recrystallization from ethanol of the product mixture from the high-pressure reaction. Unambiguous configurational assignment was achieved by X-ray diffraction analysis of the sultams 30, 31 and 32.4b

A consequence of the non-bonded interaction mentioned above is obvious from the crystal structure of sultam 30. In contrast to other furan-derived δ-sultams investigated by X-ray crystallography in this study, all of which have a chair conformation of the sultam ring, a twist-boat conformation avoiding close contacts of the sultam methyl and the exocyclic substituent on nitrogen was revealed for the six-membered heterocycle in 30.4b

Previous studies with carbocyclic 1,3-dienes showed a high diastereoselectivity in the cycloaddition of the vinylsulfonamide rac-34, featuring a 1,3-cyclohexadienyl unit, to give the endo δ-sultams rac-35 and rac-36 under purely thermal activation or high-pressure conditions (Scheme 6).4d Following our studies on furan-containing substrates bearing an external chiral auxiliary attached to the nitrogen atom, we examined a similar approach toward enantiopure δ-sultams derived from a carbocyclic 1,3-diene moiety.

Scheme 6

The primary alcohol 41 was synthesized from the sulfone rac-37 according to a known methodology20,21 (Scheme 7). Nucleophilic substitution of the mesylate 42, derived from 41, with (S)-(−)-1-phenylethylamine and subsequent treatment of the resultant amine 43 with vinylsulfonyl chloride gave rise to the vinylsulfonamide 44 carrying a nitrogen-bound (S)-(−)-1-phenylethyl unit. Both the thermal and the high-pressure cycloaddition led to a roughly 1:1 ratio of endo product diastereomers.22 Nonetheless, the δ-sultams 45 and 46 could be readily isolated in pure form after separation by flash chromatography followed by recrystallization from methanol, and their configuration was unambiguously established by X-ray diffraction analysis of 46.4a
Scheme 7. Reagents and conditions: (a) BuLi, THF, –30 °C, 1 h, then ethylene oxide, –30 °C (1 h) to RT, 98%; (b) 3,4-dihydro-2H-pyrane, PPTS, CH$_2$Cl$_2$, RT, 24 h, 98%; (c) –BuOK, –BuOH, reflux, 2 h, 57%; (d) EtOH, PPTS, 60 °C, 15 h, 63%; (e) MsCl, Et$_3$N, CH$_2$Cl$_2$, 0 °C, 45 min, 93%; (f) (S)-(–)-1-phenylethylamine, 80 °C, 12 h, 79%; (g) CH$_2$=CHSO$_2$Cl, Et$_3$N, CH$_2$Cl$_2$, 0 °C, 1 h, 77%; (h) toluene, reflux, 1 bar, 17 h, 58%; (i) CH$_2$Cl$_2$, RT, 13 kbar, 23 h, 64%.

In an additional series of experiments, the double stereodifferentiation caused by the simultaneous presence of a stereogenic center within the tether (see Scheme 6) and a chiral auxiliary on nitrogen (see Scheme 7) was explored (Scheme 8). Toward this aim, the alcohol rac-47 was converted by mesylation$^{1d}$ and nucleophilic substitution with (S)-(–)-1-phenylethylamine to give a 1:1 mixture of the diastereomeric amines 49 and 50, which were separated by flash chromatography. N-Sulfonation of 49 and 50 with vinylsulfonyl chloride delivered the vinylsulfonamides 51 and 52, respectively, as pure stereoisomers. Due to an extra methyl substituent present in 51 and 52 as compared to 44 or rac-34, a considerably lower reactivity for cycloaddition was noted for these sterically more encumbered substrates. As listed in Scheme 8, the 13 kbar activation was associated with a significantly higher asymmetric induction than the reflux/ambient pressure process for both 51 and 52.$^{22}$ Clearly, a preferential equatorial orientation of the methyl substituent on a chair-like folded tether controlled the stereochemical outcome of these reactions. Interestingly, and in contrast to the situation with the furan substrates discussed above, the diastereoselectivities noted for the thermal reactions of 51 and 52 at ambient pressure were likewise not affected to a great extent by the (S)-(–)-1-phenylethyl unit. Separation of the two resulting sultam mixtures 53/54 and 55/56, respectively,
by flash chromatography was not possible. However, pure isomers 53 and 55 could be obtained by recrystallization from methanol of the product mixtures from the high-pressure reactions instead, and their configuration was unequivocally determined by X-ray diffraction analysis.\textsuperscript{4a}

**Scheme 8.** *Reagents and conditions:* (a) MsCl, Et\textsubscript{3}N, CH\textsubscript{2}Cl\textsubscript{2}, 0 °C, 1 h, 96%; (b) (S)-(−)-1-phenylethylamine, 80 °C, 12 h, 31% 49 + 50; (c) CH\textsubscript{2}=CHSO\textsubscript{2}Cl, Et\textsubscript{3}N, CH\textsubscript{2}Cl\textsubscript{2}, 0 °C, 3 h, 76% 51, 79% 52; (d) toluene, reflux, 1 bar, 24 h, 44% 53 + 54, 36% 55 + 56; (e) CH\textsubscript{2}Cl\textsubscript{2}, RT, 13 kbar, 82 h, 68% 53 + 54, 66% 55 + 56.

Finally, the conditions reported for the debenzylation of N-1-phenylethyl γ-sultams\textsuperscript{23} were optimized to eventually allow a smooth and efficient cleavage of the chiral auxiliary from the δ-sultams prepared in this study (Scheme 9). First attempts with the furan-derived sultams using
formic acid at 70 °C followed by hydrolysis with 10% KOH at room temperature met with failure. However, simply stirring a 0.03 M solution of these δ-sultams in concentrated formic acid at room temperature under argon, removal of the solvent in vacuo at maximum 40 °C, and flash chromatography of the residue, provided the desired debenzylated δ-sultams 57, ent-57, 58, 59, and ent-58 in high yield, whereas no intact γ-sultam was obtained from substrates 13 and 14 using this procedure. Interestingly, X-ray diffraction analysis of sultam 58 (and ent-58) unveiled an \( sp^3 \) hybridized nitrogen with axial orientation of N–H on a chair δ-sultam.\(^{4b} \) The application of the optimized conditions for debenzylation smoothly effected cleavage of the chiral auxiliary from the sultams 45, 46, 53, and 55 in nearly quantitative yield as well.\(^{24} \) As in the furan cases discussed above, X-ray diffraction analysis of the debenzylated sultams 60, 61 [and ent-61] revealed an \( sp^3 \)-hybridized nitrogen atom with axial orientation of N–H on a chair δ-sultam,\(^{4a} \) whereas the crystal structures of the N-1-phenylethyl-δ-sultams 46 and 55 feature an \( sp^2 \) hybridized nitrogen atom, and the N-1-phenylethyl substituent in 53 is oriented nearly equatorially on a chair δ-sultam in the solid state.\(^{4a} \)

![Scheme 9](image)

Scheme 9. Debenzylation of N-1-phenylethyl δ-sultams.

In conclusion, a range of novel γ- and δ-sultams was efficiently prepared by intramolecular Diels–Alder reaction of vinylsulfonamides possessing an acyclic, furan or carbocyclic 1,3-diene
moiety with purely thermal activation and under high pressure. Using N-1-phenylethyl-substituted vinylsulfonamides, enantiopure sultams were readily obtained, debenzylation of which provided the corresponding NH sultams in high yields in the case of δ-sultams. Further synthetic elaboration of these heterocycles will be reported in due course.

**Experimental Section**

**General Procedures.** All reactions requiring exclusion of moisture were run under argon using flame-dried glassware. Solvents were dried by distillation from Na/K and benzophenone (THF), Na (toluene), CaH₂ (Et₂O), or by passing through activated alumina (CH₂Cl₂). All commercially available compounds were used as received unless stated otherwise. Flash chromatography: Merck silica gel 60 (40–63 µm). Thin layer chromatography: Merck silica gel 60 F 254 plates. Melting points: Kleinfeld Labortechnik Electrothermal IA 9100 apparatus. Optical rotation: Perkin–Elmer 341 polarimeter. ¹H- and ¹³C- NMR: Bruker DRX-500 (¹H: 500 MHz, ¹³C: 126 MHz, CDCl₃, calibrated to the residual resonance of the solvent) or Bruker AC-300 (¹H: 300 MHz, ¹³C: 75.4 MHz, CDCl₃, calibrated to the residual resonance of the solvent). FT-IR: Nicolet 205 and Nicolet Avatar 360 spectrometer. Mass spectra: Hewlett Packard 5890 GC coupled with a Hewlett Packard 5972 detector, and Agilent 6890N GC coupled with an Agilent 5973N detector (GC/MS). Elemental analysis: Carlo Erba Instruments EA 1108 and Hekatech EA 3000. High-pressure reactions were run in a Hofer apparatus. RT denotes room temperature.

**Preparation of alcohol 38 from sulfone 37.** A 1.6 M solution of BuLi in hexane (7.75 mL, 12.4 mmol) was added dropwise to a solution of sulfone 37 (2.50 g, 11.25 mmol) in THF (60 mL) under argon at –30 ºC. The resultant deep red solution was stirred for 1 h at –30 ºC, and then ethylene oxide (1.5 g, 34.05 mmol) was added at the same temperature. After an additional 1 h at –30 ºC, the mixture was allowed to warm to RT. Water (100 mL) was added, and the mixture was extracted with Et₂O (4 × 50 mL). The combined organic layers were washed with brine (50 mL), dried over MgSO₄, and the residue obtained after evaporation of the solvent in vacuo was purified by flash chromatography using pentane/EtOAc 1:1 to give 38 (2.95 g, 98%); Rₜ 0.58 (EtOAc); ¹H NMR (300 MHz) δ 1.41–1.55 (m, 1H), 1.61–1.76 (m, 1H), 1.78–1.98 (m, 4H), 2.00–2.12 (m, 4H), 2.22 (dd, J = 7.2, 14.0 Hz, 1H), 2.28–2.33 (m, 1H), 3.80–3.85 (m, 2H), 5.76 (d, J = 10.2 Hz, 1H), 6.12 (ddd, J = 4.0, 7.9, 10.2 Hz, 1H), 7.50–7.57 (m, 2H), 7.62–7.68 (m, 1H), 8.25–8.27 (m, 2H); ¹³C NMR (75.4 MHz) δ 18.49, 24.02, 28.03, 37.94, 58.67, 65.95, 123.23, 128.56, 130.57, 133.61, 135.73; MS (GC/MS, 70 eV) m/z (rel. intensity): 250 (21), 141 (18), 125 (20), 109 (65), 91 (34), 78 (100), 77 (83), 69 (24), 51 (32); IR 3069, 2941, 2863, 2831, 1446, 1323, 1137, 1070, 1044, 1024, 913, 884, 719, 689, 629, 584, 557 cm⁻¹; Anal. Calcd for C₁₄H₁₈O₃S: C 63.13; H, 6.81; S 12.04. Found: C 62.87; H, 7.35; S 11.80.

**Preparation of the THP ether 39 from alcohol 38.** The alcohol 38 (2.900 g, 10.89 mmol) was dissolved in dichloromethane (60 mL), and pyridinium p-toluenesulfonate (0.28 g, 1.10 mmol)
was added followed by 3,4-dihydro-2H-pyran (1.26 g, 15.0 mmol). The resultant mixture was stirred for 20 h at RT and washed with water (50 mL) and brine (20 mL). After drying over MgSO$_4$ and evaporation of the solvent in vacuo, purification of the crude product by flash chromatography using pentane/EtOAc 1:1 afforded the THP ether 39 (3.744 g, 98%) as a colorless oil; $R_f$ 0.62 (EtOAc); $^1$H NMR (300 MHz) $\delta$ 1.49–1.58 (m, 4H), 1.62–1.79 (m, 4H), 1.83–1.92 (m, 3H), 2.08–2.28 (m, 2H), 3.44–3.57 (m, 2H), 3.77–3.89 (m, 2H), 4.52–4.55 (m, 1H), 5.65 (dd, $J = 2.5$, 10.1 Hz, 1H), 6.14 (ddd, $J = 4.0$, 7.9, 10.2 Hz, 1H), 7.50–7.56 (m, 2H), 7.61–7.67 (m, 1H), 7.85–7.88 (m, 2H); $^{13}$C NMR (75.4 MHz) $\delta$ 18.56, 18.61, 19.40, 19.48, 23.92, 25.31, 27.43, 27.51, 30.56, 34.75, 62.22, 62.32, 62.34, 63.43, 63.46, 65.60, 65.65, 98.80, 98.89, 122.99, 123.08, 128.50, 130.50, 133.43, 135.83, 136.10; MS (GC/MS, 70 eV) m/z (rel. intensity) 209 (6), 141 (11), 125 (6), 107 (57), 91 (36), 85 (74), 79 (65), 75 (23), 77 (100), 67 (20), 55 (18), 51 (27); IR 2940, 2872, 1446, 1353, 1288, 1200, 1180, 1137, 1073, 1026, 982, 869, 813, 759, 734, 719, 690, 630, 584, 557 cm$^{-1}$; Anal. Calcd for C$_{19}$H$_{26}$O$_4$S: C, 65.11; H, 7.48; S 9.15. Found: C, 64.97; H, 7.87; S 8.81.

Preparation of diene rac-40 from THP ether 39. Potassium t-butoxide (10.29 g, 91.70 mmol) was added under argon to a solution of the THP ether 39 (3.700 g, 10.56 mmol) in t-butoanol (100 mL). The resultant mixture was vigorously stirred and heated to reflux for 2 h. After cooling to 35–40 ºC, ice (100 g) was added, and the mixture was extracted with Et$_2$O (4 × 50 mL). The combined organic layers were washed with water (4 × 30 mL) and dried over MgSO$_4$. After evaporation of the solvent in vacuo, flash chromatography using pentane/EtOAc 20:1 afforded the diene rac-40 (1.254 g, 57%) as a colorless oil; $R_f$ 0.69 (pentane/EtOAc 1:1); $^1$H NMR (300 MHz) $\delta$ 1.50–1.65 (m, 4H), 1.68–1.75 (m, 1H), 1.76–1.86 (m, 1H), 2.13–2.17 (m, 4H), 2.37 (t, $J = 7.0$ Hz, 2H), 3.51 (m, 2H), 3.82 (m, 2H), 4.58–4.63 (m, 1H), 5.65–5.68 (m, 2H), 5.86–5.90 (m, 1H); $^{13}$C NMR (75.4 MHz) $\delta$ 19.44, 22.75, 25.39, 26.56, 30.60, 37.45, 62.08, 66.05, 98.60, 119.94, 123.74, 124.50, 136.35; MS (GC/MS, 70 eV) m/z (rel. intensity) 208 [M$^+$] (2), 107 (12), 106 (24), 105 (11), 92 (11), 91 (58), 85 (100), 79 (28), 78 (34), 77 (27), 67 (18), 57 (17); IR 3036, 2938, 2869, 1453, 1440, 1352, 1200, 1135, 1118, 1062, 1029, 972, 906, 868, 813, 733, 687 cm$^{-1}$; Anal. Calcd for C$_{13}$H$_{20}$O$_2$: C, 74.96; H, 9.68. Found: C, 74.96; H, 9.68.

Preparation of alcohol 41 from diene rac-40. The diene rac-40 (1.200 g, 5.76 mmol) was dissolved in dry ethanol (80 mL), and pyridinium p-toluenesulfonate (0.165 g, 0.66 mmol) was added. After stirring the resultant solution at 60 ºC for 15 h, the solvent was removed in vacuo. Flash chromatography using pentane/EtOAc 1:1 gave 41 (0.465 g, 63%) as a colorless oil; $R_f$ 0.30 (pentane/EtOAc 5:1); $^1$H NMR (300 MHz) $\delta$ 1.70 (br. s, 1H), 2.07–2.21 (m, 4H), 2.34 (t, $J = 6.3$ Hz, 1H), 2.59–2.69 (m, 1H), 4.32 (t, $J = 6.9$ Hz, 2H), 5.74–5.77 (m, 2H), 5.86–5.90 (m, 1H); $^{13}$C NMR (75.4 MHz) $\delta$ 22.78, 26.05, 40.50, 60.32, 121.25, 124.13, 124.45, 135.45; MS (GC/MS, 70 eV) m/z (rel. intensity) 124 [M$^+$] (24), 105 (6), 93 (24), 91 (100), 79 (28), 78 (61), 77 (54); IR 3358, 3034, 2928, 2872, 2821, 1426, 1395, 1369, 1344, 1240, 1159, 1040, 958, 863, 832, 748, 728, 688, 662, 624, 565 cm$^{-1}$; Anal. Calcd for C$_8$H$_{12}$O: C, 77.38; H, 9.74. Found: C, 77.24; H, 9.86.
General procedure for the preparation of mesylates
A solution of the alcohol (30 mmol) in dry CH₂Cl₂ (150 mL) at 0 °C under Ar was treated slowly with anhydrous triethylamine (6.06 g, 60 mmol) and then with methanesulfonyl chloride (3.60 g, 31.5 mmol) and stirred for 45 min. After this time, cold H₂O (100 mL) was added, and the layers shaken and separated. The organic phase was washed with cold H₂O (3 × 100 mL), dried over MgSO₄, and concentrated in vacuo at max. 35 °C. The residue was purified by flash chromatography (pentane/EtOAc 4:1).

Mesylate 19. Yield 97%; Rₚ 0.47 (pentane/EtOAc 4:1); ¹H NMR (300 MHz) δ 2.89 (s, 3H), 3.07 (t, J = 6.6 Hz, 2H), 6.14 (d, J = 3.2 Hz, 1H), 6.30 (dd, J = 1.9, 3.2 Hz, 1H), 7.32 (d, J = 1.9 Hz, 1H); ¹³C NMR (75.4 MHz) δ 28.20, 37.21, 67.52, 107.28, 110.41, 141.73, 150.13; MS (GC/MS, 70 eV) m/z (rel. intensity) 190 (1) [M⁺], 95 (15), 94 (100), 81 (64), 79 (12), 66 (11), 53 (18), 39 (6); IR 3118, 3027, 2940, 1599, 1507, 1469, 1417, 1346, 1169, 1146, 1083, 1050, 956, 898, 844, 799, 733, 600 cm⁻¹.

Mesylate 25. Yield 97%; Rₚ 0.65 (pentane/EtOAc 4:1); ¹H NMR (300 MHz) δ 1.45 (d, J = 6.3 Hz, 3H), 2.71 (s, 3H), 2.95 (m, 2H), 6.15 (d, J = 3.2 Hz, 1H), 6.30 (dd, J = 1.9, 3.1 Hz, 1H), 7.28–7.38 (m, 1H); ¹³C NMR (75.4 MHz) δ 21.24, 35.27, 37.90, 78.24, 107.99, 110.55, 141.72, 150.49; MS (GC/MS, 70 eV) m/z (rel. intensity) 204 (0.4) [M +], 189 (0.7), 123 (10), 109 (27), 108 (100), 81 (98), 79 (45), 53 (20); IR 3113, 3026, 2984, 2939, 1599, 1506, 1332, 1171, 917, 893, 795, 740, 544 cm⁻¹; Anal. Calcd for C₁₅H₁₉NO: C, 78.56 H, 8.35 N, 6.11. Found: C, 78.89; H, 8.64; N, 6.03.

Mesylate 42. Yield 93%; Rₚ 0.41 (pentane/EtOAc 4:1); ¹H NMR (300 MHz) δ 2.19–2.23 (m, 4H), 2.52 (t, J = 6.8 Hz, 1H), 2.61–2.70 (m, 1H), 3.00 (s, 3H), 3.0 (dd, J = 6.3, 12.5 Hz, 2H), 5.72–5.75 (m, 2H), 5.87–5.91 (m, 1H); ¹³C NMR (75.4 MHz) δ 22.67, 26.11, 36.77, 37.51, 67.92, 121.71, 124.15, 124.91, 133.15; MS (GC/MS, 70 eV) m/z (rel. intensity) 202 [M⁺] (1), 104 (54), 91 (100), 79 (61), 78 (39), 77 (30), 65 (40), 63 (15), 51 (17), 39 (28); IR 3027, 2929, 2859, 1429, 1349, 1333, 1169, 1085, 1044, 951, 844, 820, 796, 729, 701, 664, 582, 570, 557 cm⁻¹; Anal. Calcd for C₉H₁₄O₃S: C, 53.44; H, 6.98; S 15.85. Found: C, 53.03; H, 7.24; S 15.36.

General procedure for the reaction of mesylates with (S)-(–)-1-phenylethylamine
The mesylate (28 mmol) was treated with (S)-(–)-1-phenylethylamine (140 mmol), and the resulting mixture was stirred for 12 h at 80 °C. After cooling to room temperature, 2 N NaOH (80 mL) and Et₂O (50 mL) were added and the layers shaken and separated. The aqueous phase was extracted (2 × 50 mL, Et₂O), and the combined organic extracts were washed with brine (50 mL), dried (MgSO₄), and concentrated in vacuo. Excess (S)-(–)-1-phenylethylamine was removed in vacuo (100 °C bath temperature, 10 mbar), and the residue was purified by flash chromatography (pentane/EtOAc 3:1) to give the product amine as a yellow oil. Diastereomeric amines were separated by flash chromatography (pentane/EtOAc 4:1).

Amine 20. Yield 79%; Rₚ 0.31 (pentane/EtOAc 4:1); [α]D²⁰ = –50.1 (c 1.0, CH₂Cl₂); ¹H NMR (300 MHz) δ 1.34 (d, J = 6.6 Hz, 3H), 1.50 (br. s., 1H), 2.70–2.84 (m, 4H), 3.78 (q, J = 6.6 Hz, 1H), 6.02 (d, J = 3.1 Hz, 1H), 6.28 (dd, J = 1.9, 3.2 Hz, 1H), 7.20–7.35 (m, 6H); ¹³C NMR (75.4 MHz) δ 24.34, 28.73, 45.92, 58.02, 105.68, 110.10, 126.50, 126.84, 128.38, 141.08, 145.55,
154.18; MS (GC/MS, 70 eV) m/z (rel. intensity) 215 (0.3) [M⁺], 200 (1), 134 (50), 105 (100), 95 (5), 77 (24); IR 3025, 2962, 2922, 2837, 1597, 1506, 1450, 1369, 1306, 1207, 1172, 1144, 1130, 1004, 916, 798, 760, 727, 698, 597, 551 cm⁻¹; Anal. Calcd for C₁₄H₁₇NO: C, 78.10; H, 7.96; N, 6.51. Found: C, 78.89; H, 8.64; N, 6.03.

**Amine 26.** Rf 0.26 (pentane/EtOAc 4:1); [α]D²⁰ –33.0 (c 1.0, CH₂Cl₂); ¹H NMR (300 MHz) δ 1.05 (d, J = 6.1 Hz, 3H), 1.31 (d, J = 6.7 Hz, 3H), 1.58 (br. s., 1H), 2.62 (d, J = 6.5 Hz, 2H), 2.74 (m, 1H), 3.90 (q, J = 6.7 Hz, 1H), 6.01 (d, J = 3.2 Hz, 1H), 6.29 (dd, J = 1.9, 3.1 Hz, 1H), 7.07–7.10 (m, 1H), 7.21–7.34 (m, 5H); ¹³C NMR (75.4 MHz) δ 19.91, 24.85, 36.16, 48.95, 54.86, 106.83, 110.13, 126.30, 126.77, 128.38, 141.23, 145.57, 153.52; MS (GC/MS, 70 eV) m/z (rel. intensity) 229 (4) [M⁺], 228 (9), 148 (56), 124 (6), 105 (100), 81 (20), 77 (24); IR 3107, 3062, 3025, 2963, 2924, 2865, 1597, 1505, 1492, 1451, 1372, 1315, 1007, 930, 760, 724, 698, 597, 554 cm⁻¹; Anal. Calcd for C₁₅H₁₉NO: C, 78.56; H, 8.35; N, 6.11. Found: C, 78.89; H, 8.64; N, 6.03.

**Amine 27.** Rf 0.30 (pentane/triethylamine 30:1); [α]D²⁰ –65.3 (c 1.0, CH₂Cl₂); ¹H NMR (300 MHz) δ 0.98 (d, J = 6.3 Hz, 3H), 1.32 (d, J = 6.6 Hz, 3H), 2.41 (br. s., 1H), 2.71–2.76 (m, 2H), 2.79–2.91 (m, 1H), 3.89 (q, J = 6.5 Hz, 1H), 6.02 (d, J = 3.0 Hz, 1H), 6.29 (dd, J = 3.1, 1.9 Hz, 1H, 4-H), 7.24 (m, 1H), 7.27–7.35 (m, 5H); ¹³C NMR (75.4 MHz) δ 106.75, 110.18, 126.62, 126.92, 128.43, 141.19, 145.44, 153.43; MS (GC/MS, 70 eV) m/z (rel. intensity) 229 (4) [M⁺], 228 (5), 148 (40), 105 (100), 81 (20), 77 (24), 53 (6), 44 (35); IR 3112, 3079, 3062, 3025, 2962, 2924, 2866, 1596, 1504, 1493, 1451, 1372, 1146, 1007, 931, 760, 725, 698, 597, 554 cm⁻¹; Anal. Calcd for C₁₅H₁₉NO: C, 78.56; H, 8.35; N, 6.11. Found: C, 78.27; H, 8.81; N, 5.96.

**Amine 43.** Yield 79%; Rf 0.65 (pentane/triethylamine 30:1); [α]D²⁰ –53.5 (c 1.0, CH₂Cl₂); ¹H NMR (300 MHz) δ 1.35 (d, J = 6.7 Hz, 3H), 1.48 (br. s., 1H) 1.97–2.04 (m, 1H), 2.10–2.14 (m, 1H), 2.23 (t, J = 6.8 Hz), 2.53–2.59 (m, 1H), 3.75 (q, J = 6.6 Hz, 1H), 5.65–5.67 (m, 2H), 5.82–5.86 (m, 1H), 7.19–7.35 (m, 5H); ¹³C NMR (75.4 MHz) δ 122.88, 2142, 2620, 37.77, 45.39, 58.23, 120.07, 123.89, 124.54, 126.5, 126.80, 128.35, 137.30, 145.81; MS (GC/MS, 70 eV) m/z (rel. intensity) 227 (2) [M⁺], 226 (2), 134 (36), 105 (100), 91 (14), 79 (12), 77 (17); IR 3033, 2924, 2870, 2822, 1492, 1451, 1368, 1131, 1065, 760, 700 cm⁻¹; Anal. Calcd for C₁₅H₂₁N: C, 84.53; H, 9.31; N, 6.16. Found: C, 84.77; H, 9.55; N, 6.40.

**Amine 49.** Rf 0.25 (pentane/EtOAc 4:1); [α]D²⁰ –94.5 (c 1.0, CH₂Cl₂); ¹H NMR (300 MHz) δ 1.01 (d, J = 6.1 Hz, 3H), 1.34 (d, J = 6.7 Hz, 3H), 1.58 (br. s., 1H) 1.70–1.77 (m, 1H), 1.79–1.87 (m, 1H), 1.98–2.12 (m, 4H), 2.45–2.51 (m, 1H), 3.84 (q, J = 6.7 Hz, 1H), 5.65–5.69 (m, 2H), 5.84–5.87 (m, 1H), 7.17–7.31 (m, 5H); ¹³C NMR (75.4 MHz) δ 20.3, 22.8, 24.7, 25.9, 46.2, 46.8, 54.7, 121.4, 124.1, 124.4, 126.3, 126.7, 136.3, 145.7; MS (GC/MS, 70 eV) m/z (rel. intensity) 241 (20) [M⁺], 240 (5), 148 (36), 136 (5), 121 (6), 105 (100), 79 (17), 77 (20); IR 3035, 2923, 2824, 1466, 1369, 1127, 760, 699 cm⁻¹; Anal. Calcd for C₁₇H₂₃N: C, 84.59; H 9.60; N, 5.80. Found: C, 84.95; H 9.76; N, 5.85.

**Amine 50.** Rf 0.68 (pentane/triethylamine 30:1); [α]D²⁰ –35.4 (c 1.0, CH₂Cl₂); ¹H NMR (300 MHz) δ 0.94 (d, J = 6.4 Hz, 3H), 1.33 (d, J = 6.6 Hz, 3H), 1.43 (br. s., 1H), 1.98–2.05 (m, 3H), 2.11–2.16 (m, 2H), 2.33 (dd, J = 6.0, 13.4 Hz, 1H), 2.72 (dd, J = 6.4, 13.1 Hz, 1H), 3.90 (q, J =
6.6 Hz, 1H), 5.66–5.70 (m, 2H), 5.86–5.90 (m, 1H), 7.21–7.25 (m, 1H), 7.29–7.33 (m, 4H); 13C NMR (75.4 MHz) δ 21.6, 22.8, 24.4, 26.5, 44.9, 48.9, 55.5, 121.1, 123.8, 124.5, 126.4, 126.6, 128.3, 137.1, 146.3; MS (GC/MS, 70 eV) m/z (rel. intensity) 241 (22) [M +], 240 (5), 226 (10), 148 (5), 136 (12), 121 (11), 105 (100), 79 (25), 77 (25); IR 3035, 2959, 2924, 2867, 2824, 1450, 1369, 1127, 760, 699 cm–1; Anal. Calcd for C17H23N: C, 84.59; H, 9.60; N, 5.80. Found: C, 84.43; H, 9.83; N, 5.96.

**General procedure for the preparation of vinylsulfonamides**

To a stirred solution of the amine (2.0 mmol) and anhydrous triethylamine (8.0 mmol) in dry CH2Cl2 (50 mL) under Ar was added vinylsulfonyl chloride (2.2 mmol) slowly at 0 °C. The resulting solution was stirred until TLC showed complete conversion of the amine. After addition of cold water to the mixture, it was extracted with Et2O (60 mL). The organic layer was washed with water, dried over MgSO4, and the solvents were removed under reduced pressure at max. 35 °C. The crude product was purified by flash chromatography (pentane/EtOAc 5:1).

**Vinylsulfonamide 4.** Reaction time 1 h. Yield 92%; Rf 0.43 (pentane/EtOAc 5:1); 1H NMR (300 MHz) δ 1.71 (s, 3H), 3.70 (d, J = 6.9 Hz, 2H), 4.24 (s, 2H), 4.90 (d, J = 10.9 Hz, 2H), 5.41 (dt, J = 6.9, 15.6 Hz, 1H), 5.84 (d, J = 9.8 Hz, 1H), 6.09 (d, J = 15.7 Hz, 1H), 6.15 (d, J = 16.5 Hz, 1H), 6.35 (dd, J = 9.8, 16.5 Hz, 1H), 7.17–7.29 (m, 5H); 13C NMR (75.4 MHz) δ 18.38, 48.49, 49.87, 117.44, 123.26, 126.30, 127.82, 128.49, 128.55, 128.68, 135.83, 135.95, 137.40; MS (GC/MS, 70 eV) m/z (rel. intensity) 277 (5) [M +], 212 (8), 132 (9), 119 (31), 106 (14), 94 (100), 91 (90); IR 3085, 3063, 3031, 2913, 1609, 1455, 1334, 1205, 1144, 1091, 1054, 1028, 966, 923, 896, 849, 774, 742, 697, 648 cm–1; Anal. Calcd for C15H19NO2S: C, 64.95; H, 6.90; N, 5.05; S, 11.56. Found: C, 64.90; H, 6.95; N, 4.87; S, 11.56.

**Vinylsulfonamide 5.** Reaction time 2 h. Yield 95%; Rf 0.85 (pentane/EtOAc 4:1); 1H NMR (300 MHz) δ 0.001 (s, 9H), 1.70 (s, 3H), 3.72 (d, J = 1.6 Hz, 2H), 4.27 (s, 2H), 4.76 (s, 1H), 4.70 (s, 1H), 5.79 (d, J = 9.1 Hz, 1H), 6.13 (d, J = 16.1 Hz, 1H), 6.25 (dd, J = 9.2, 16.5 Hz, 1H), 6.55 (s, 1H), 7.25 (m, 5H); 13C NMR (75.4 MHz) δ 0.16, 22.68, 50.22, 52.20, 114.12, 126.35, 127.91, 128.64, 129.14, 133.83, 135.48, 135.80, 144.18; MS (GC/MS, 70 eV) m/z (rel. intensity) 334 (0.5) [M+ – Me], 212 (11), 166 (38), 151 (9), 120 (23), 106 (12), 92 (32), 91 (100); IR 3085, 3063, 3031, 2913, 1609, 1495, 1455, 1334, 1205, 1144, 1091, 1054, 1028, 966, 923, 896, 849, 774, 742, 697, 648 cm–1; Anal. Calcd for C18H27NO2SSi: C, 61.85; H, 7.79; N, 4.01; S 9.17. Found: C, 61.35; H, 8.12; N, 3.89; S, 8.99.

**Vinylsulfonamide 6.** Reaction time 1 h. Yield 96%; Rf 0.78 (pentane/EtOAc 4:1); 1H NMR (300 MHz) δ 1.69–1.55 (m 4H), 2.06 (br. s, 2H), 2.12 (br. s, 2H), 3.75 (d, J = 7.0 Hz, 2H), 4.31 (s, 2H), 5.41 (m, 1H), 5.75 (br. s, 1H), 5.90 (d, J = 9.7 Hz, 1H), 6.05 (d, J = 15.7 Hz, 1H), 6.23 (d, J = 16.5 Hz, 1H), 6.42 (dd, J = 9.8, 16.5 Hz, 1H), 7.35–7.29 (m, 5H); 13C NMR (75.4 MHz) δ 22.3, 22.4, 24.4, 25.8, 48.6, 49.5, 118.8, 126.2, 127.8, 128.5, 128.6, 130.7, 134.8, 136.0, 136.1, 138.5; MS (GC/MS, 70 eV) m/z (rel. intensity) 317 (4) [M+], 253 (2), 252 (8), 162 (3), 148 (5), 134 (61), 119 (25), 105 (15), 91 (100), 79 (20), 77 (10), 67 (9), 66 (7), 51(6), 41 (5); IR 3041, 2980, 2946, 2825, 1719, 1678, 1494, 1369, 1332, 1142, 1134, 1062, 956, 769, 696, 660, 542
Vinylsulfonamide 12. Reaction time 2 h. Yield 98%; $R_f$ 0.60 (pentane/EtOAc 4:1); $[^{20}\alpha]_D^{20}$ –1.6 (c 1.0, CH$_2$Cl$_2$); $^1$H NMR (300 MHz) $\delta$ 1.55 (d, $J = 7.1$ Hz, 3H), 3.97 (d, $J = 16.4$ Hz, 1H), 4.36 (d, $J = 16.4$ Hz, 1H), 5.17 (q, $J = 7.1$ Hz, 1H), 5.78 (d, $J = 9.5$ Hz, 1H), 6.11 (d, $J = 3.1$ Hz, 1H), 6.14 (d, $J = 16.4$ Hz, 1H), 6.26 (dd, $J = 2.0$, 3.1 Hz, 1H), 6.27 (dd, $J = 9.7$, 16.5 Hz, 1H), 7.25–7.47 (m, 6H); $^{13}$C NMR (75.4 MHz) $\delta$ 17.79, 39.95, 55.80, 109.37, 110.50, 152.17, 127.71, 127.79, 128.46, 136.77, 139.53, 141.93, 150.84; MS (GC/MS, 70 eV) $m/z$ (rel. intensity) 291 (2) [M$^+$], 276 (2), 200 (31), 199 (35), 186 (35), 105 (100), 81 (91), 77 (19), 53 (21); IR (KBr) 3060, 3030, 2980, 2939, 2871, 1603, 1496, 1452, 1331, 1134, 1006, 929, 882, 780, 738, 697, 653, 599, 563, 540 cm$^{-1}$; Anal. Calcd for C$_{15}$H$_{19}$NO$_3$S: C, 61.83; H, 5.88; N, 4.81; S 10.11. Found: C, 62.07; H, 6.35; N, 5.17; S, 10.95.

Vinylsulfonamide 21. Reaction time 2 h. Yield 96%; $R_f$ 0.62 (pentane/EtOAc 4:1); $[^{20}\alpha]_D^{20}$ –2.1 (c 1.0, CH$_2$Cl$_2$); $^1$H NMR (300 MHz) $\delta$ 1.49 (d, $J = 7.1$ Hz, 3H), 2.41 (m, 1H), 2.75 (m, 1H), 3.18 (m, 2H), 5.07 (q, $J = 7.1$ Hz, 1H), 5.81 (d, $J = 9.3$ Hz, 1H), 5.81 (d, $J = 3.0$ Hz, 1H), 6.15 (dd, $J = 1.7$, 3.2 Hz, 1H), 6.15 (d, $J = 16.0$ Hz, 1H), 6.28 (dd, $J = 9.3$, 16.3 Hz, 1H), 7.17 (m, 1H), 7.20–7.36 (m, 5H); $^{13}$C NMR (75.4 MHz) $\delta$ 17.75, 29.78, 42.65, 55.92, 106.15, 110.12, 126.04, 126.71, 128.00, 128.58, 135.91, 139.92, 141.25, 152.51; MS (GC/MS, 70 eV) $m/z$ (rel. intensity) 305 (0.3) [M$^+$], 290 (1), 224 (16), 105 (100), 91 (94), 81 (8), 79 (5), 77 (5); IR (KBr) 3060, 3030, 2978, 2940, 1598, 1496, 1452, 1382, 1333, 1315, 1255, 1199, 1153, 1134, 1082, 1051, 1006, 972, 942, 917, 784, 733, 698, 648, 599, 547 cm$^{-1}$; Anal. Calcd for C$_{16}$H$_{19}$NO$_3$S: C, 62.93; H, 6.27; N, 4.59; S 10.50. Found: C, 63.25; H, 6.18; N, 4.62; S 10.14.

Vinylsulfonamide 28. Reaction time 3 h. Yield 84%; $R_f$ 0.65 (pentane/EtOAc 4:1); $[^{20}\alpha]_D^{20}$ –29.0 (c 1.0, CH$_2$Cl$_2$); $^1$H NMR (300 MHz) $\delta$ 0.97 (d, $J = 6.9$ Hz, 3H), 1.46 (d, $J = 7.0$ Hz, 3H), 3.04 (dd, $J = 8.7$, 14.7 Hz, 1H), 3.21 (dd, $J = 6.1$, 14.8 Hz, 1H), 3.50–3.62 (m, 1H), 6.14 (q, $J = 7.0$ Hz, 1H), 5.89 (d, $J = 9.7$ Hz, 1H), 6.09 (d, $J = 3.1$ Hz, 1H), 6.27 (dd, $J = 3.2$, 1.9 Hz, 1H), 6.28 (d, $J = 16.5$ Hz, 1H), 6.35 (dd, $J = 9.8$, 16.5 Hz, 1H), 7.28–7.38 (m, 4H), 7.44 (d, $J = 7.0$ Hz, 2H); $^{13}$C NMR (75.4 MHz) $\delta$ 17.68, 20.03, 35.87, 52.66, 56.40, 107.32, 110.37, 124.99, 127.87, 127.92, 128.37, 138.53, 139.91, 141.27, 153.05; MS (GC/MS, 70 eV) $m/z$ (rel. intensity) 319 (0.5) [M$^+$], 238 (15), 134 (5), 105 (100), 81 (18), 79 (8), 77 (10), 53 (6); IR (KBr) 3083, 3062, 3028, 2992, 2975, 2940, 2875, 1626, 1494, 1451, 1391, 1374, 1315, 1183, 1152, 1105, 1005, 975, 840, 774, 705, 559, 498 cm$^{-1}$; Anal. Calcd for C$_{17}$H$_{21}$NO$_3$S: C, 63.92; H, 6.63; N, 4.39; S 10.04. Found: C, 63.81; H, 6.84; N, 4.43; S 10.06.

Vinylsulfonamide 29. Reaction time 3 h. Yield 82%; $R_f$ 0.59 (pentane/EtOAc 4:1); mp 49–51 °C; $[^{20}\alpha]_D^{20}$ +38.0 (c 1.0, CH$_2$Cl$_2$); $^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 1.34 (d, $J = 6.9$ Hz, 3H), 1.59 (d, $J = 7.1$ Hz, 3H), 2.48 (dd, $J = 4.1$, 14.6 Hz, 1H), 3.00 (dd, $J = 10.4$, 14.5 Hz, 1H), 3.46–3.56 (m, 1H), 5.01 (q, $J = 7.0$ Hz, 1H), 5.66 (d, $J = 3.1$ Hz, 1H), 5.88 (d, $J = 9.7$ Hz, 1H), 6.14 (dd, $J = 1.9$, 3.1 Hz, 1H), 6.28 (d, $J = 16.5$ Hz, 1H), 6.51 (dd, $J = 9.7$, 16.5 Hz, 1H), 7.12 (dd, $J = 0.7$, 1.8 Hz, 1H), 7.27–7.39 (m, 3H), 7.43–7.48 (m, 2H); $^{13}$C NMR (75.4 MHz) $\delta$ 16.97, 19.54, 36.07, 52.24, 56.09, 106.52, 109.98, 124.94, 127.82, 127.86), 128.38, 138.60, 139.53, 141.09, 153.05;
MS (GC/MS, 70 eV) m/z (rel. intensity) 319 (0.5) [M^+], 238 (18), 134 (7), 105 (100), 81 (18), 79 (8), 77 (10), 53 (6); IR (KBr) 3107, 3061, 3031, 2978, 2938, 2879, 1599, 1497, 1452, 1381, 1329, 1149, 1064, 1008, 961, 773, 731, 699, 684, 651, 543 cm⁻¹; Anal. Calcd for C₁₇H₂₁NO₃S: C, 63.92; H, 6.63; N, 4.39; S 10.04. Found: C, 64.35; H, 6.97; N, 4.46; S 10.18.

**Vinylsulfonamide 44.** Reaction time 1 h. Yield 77%; R_f 0.63 (pentane/EtOAc 4:1); [α]_20^D –14.2 (c 1.0, CH₂Cl₂); ^1^H NMR (300 MHz) δ 1.53 (d, J = 7.1 Hz, 3H), 1.64–1.68 (m, 1H), 1.70–1.86 (m, 2H), 1.94–2.14 (m, 3H), 2.88–3.03 (m, 2H), 5.05 (q, J = 7.0 Hz, 1H), 5.38 (d, J = 5.1 Hz, 1H), 5.57 (m, 1H), 5.70–5.74 (m, 1H), 5.83 (d, J = 9.6 Hz, 1H), 6.22 (d, J = 16.5 Hz, 1H), 6.35 (dd, J = 9.6, 16.5 Hz, 1H), 7.21–7.39 (m, 5H); 13C NMR (75.4 MHz) δ 17.95, 22.75, 26.18, 38.79, 42.92, 55.9, 120.30, 124.32, 125.50, 125.59, 127.74, 127.95, 128.53, 136.53, 138.84, 140.13; MS (GC/MS, 70 eV) m/z (rel. intensity) 317 (6) [M +], 302 (38), 252 (8), 238 (29), 213 (23), 148 (7), 132 (9), 118 (49), 105 (95), 91 (51), 77 (24); Anal. Calcd for C₁₈H₂₃NO₂S: C, 68.10; H, 7.30; N, 4.41; S 10.10. Found: C, 68.03; H, 7.39; N, 4.45; S 10.08.

**Vinylsulfonamide 51.** Reaction time 3 h. Yield 76%; R_f 0.64 (pentane/EtOAc 4:1); [α]_20^D +29.4 (c 1.0, CH₂Cl₂); ^1^H NMR (300 MHz) δ 1.02 (d, J = 6.9 Hz, 3H), 1.68 (d, J = 6.9 Hz, 3H), 2.01–2.18 (m, 3H), 2.58–2.63 (m, 1H), 3.39–3.51 (m, 1H), 4.93 (q, J=7.0 Hz, 1H), 5.40 (d, J = 5.0 Hz, 1H), 5.56–5.60 (m, 1H), 5.68 (m, 1H), 5.83 (d, J = 9.8 Hz, 1H), 6.22 (d, J = 16.5 Hz, 1H), 6.46 (dd, J = 9.8, 16.5 Hz, 1H), 7.29–7.38 (m, 3H), 7.50–7.54 (m, 2H); 13C NMR (75.4 MHz) δ 17.1, 19.4, 22.7, 25.4, 45.7, 51.5, 55.9, 121.6, 124.3, 124.4, 124.6, 127.7, 127.8, 128.3, 135.8, 138.5, 140.0; MS (GC/MS, 70 eV) m/z (rel. intensity) 331 (0.1) [M +– CH₃], 316 (9), 252 (5), 227 (10), 212 (9), 147 (10), 146 (11), 132 (15), 105 (100), 91 (34); IR 3061, 3032, 2976, 2934, 2874, 2818, 1495, 1451, 1329, 1150, 1135, 1065, 962, 739, 699, 649, 560 cm⁻¹; Anal. Calcd for C₁₉H₂₅NO₂S: C, 68.85; H, 7.60; N, 4.23; S 9.67. Found: C, 69.04; H, 7.79; N, 4.07; S 9.23.

**Vinylsulfonamide 52.** Reaction time 3 h. Yield 79%; R_f 0.64 (pentane/EtOAc 4:1); [α]_20^D –10.0 (c 1.0, CH₂Cl₂); mp 96–97 ºC; ^1^H NMR (300 MHz) δ 1.34–1.41 (m, 1H), 1.37 (d, J = 6.9 Hz, 3H), 1.50–1.57 (m, 1H), 1.64 (d, J = 7.0 Hz, 3H), 1.96–2.00 (m, 3H), 2.51 (t, J = 6.0 Hz, 1H), 3.25–3.29 (m, 1H), 5.04 (q, J = 7.0 Hz, 1H), 5.43 (d, J = 5.0 Hz, 1H), 5.60–5.64 (m, 1H), 5.75–5.79 (m, 1H), 5.91 (d, J = 9.8 Hz, 1H), 6.30 (d, J = 16.5 Hz, 1H), 6.55 (dd, J = 9.8, 16.5 Hz, 1H), 7.32 (m, 1H), 7.40 (m, 2H), 7.52 (d, J = 7.5 Hz, 2H); ^1^C NMR (75.4 MHz) δ 17.1, 19.4, 22.7, 25.4, 45.7, 51.5, 55.9, 121.1, 124.1, 124.4, 124.7, 127.8, 128.0, 128.3, 136.1, 138.7, 139.6; MS (GC/MS, 70 eV) m/z (rel. intensity) 316 (4) [M⁺ – CH₃], 252 (3), 227 (4), 212 (7), 147 (10), 146 (11), 132 (8), 105 (100), 91 (34); IR 3065, 3033, 2972, 2932, 2900, 2826, 1450, 1380, 1322, 1150, 1133, 1119, 1062, 968, 783, 742, 686, 648, 554 cm⁻¹; Anal. Calcd for C₁₀H₂₅NO₂S: C, 68.85; H, 7.60; N, 4.23; S, 9.67. Found: C, 69.08; H, 7.73; N, 4.24; S, 9.62.

**General procedure for intramolecular Diels–Alder reactions**

**Thermal.** A solution of the vinylsulfonamide (1 mmol) in toluene (50 mL) was stirred and refluxed under argon for the time indicated in the Schemes.
High pressure. A solution of the vinylsulfonamide (0.5 mmol) in CH$_2$Cl$_2$ (20 mL) was added to a Teflon® vial. The vial was closed, inserted into the high-pressure apparatus, and subjected to a pressure of 13 kbar at room temperature for the time indicated in the Schemes.

Work-up: The reaction mixture was filtered through a pad of silica gel with ethyl acetate (50 mL) and concentrated in vacuo at a temperature not exceeding 40 °C. Diastereomeric ratios were determined by $^1$H NMR integration on a sample of the crude products. Flash chromatography using the solvent systems listed in the individual entries with the $R_f$ values yielded the pure cycloadducts. Pure 32 was obtained after recrystallization of the 32/33 mixture (high-pressure reaction) from ethanol. Pure 53 and 55 were obtained after recrystallization of the 53/54 or 55/56 mixture (high-pressure reaction), respectively, from methanol.

Sultam rac-7. $R_f$ 0.32 (pentane/EtOAc 4:1); $^1$H NMR (300 MHz) $\delta$ 1.68 (s, 3H), 1.71–1.86 (m, 1H), 1.96–2.21 (m, 3H), 2.69 (t, $J$ = 7.6 Hz, 1H), 3.17–3.25 (m, 2H), 3.27–3.33 (m, 1H), 4.14 (d, $J$ = 14.5 Hz, 1H), 4.20 (d, $J$ = 14.5 Hz, 1H), 5.26 (s, 1H), 7.27–7.36 (m, 5H); $^{13}$C NMR (75.4 MHz) $\delta$ 20.46, 23.43, 27.44, 31.65, 47.86, 50.91, 55.03, 118.57, 127.74, 128.36, 128.57, 135.67, 136.37; MS (GC/MS, 70 eV) m/z (rel. intensity) 120 (55), 94 (100), 91 (55), 79 (60); IR 3029, 2912, 1496, 1454, 1359, 1293, 1242, 1206, 1152, 1133, 1086, 1054, 1027, 966, 943, 841, 766, 715, 696, 666, 614 cm$^{-1}$; Anal. Calcd for C$_{15}$H$_{19}$NO$_2$S: C, 64.95; H, 6.90; N, 5.05; S 11.56. Found: C, 65.05; H, 6.89; N, 5.04; S 11.51.

Sultam rac-8. $R_f$ 0.33 (pentane/EtOAc 10:1); $^1$H NMR $\delta$ 0.01 (s, 9H), 1.73 (s, 3H), 1.78–1.92 (m, 2H), 2.33–2.37 (m, 1H), 2.41–2.45 (m, 1H), 2.77 (d, $J$ = 9.7 Hz, 1H), 2.99 (d, $J$ = 9.7 Hz, 1H), 3.42 (m, 1H), 3.87 (d, $J$ = 14.5 Hz, 1H), 4.35 (d, $J$ = 14.5 Hz, 1H), 5.05 (s, 1H), 7.28 (m, 5H); $^{13}$C NMR $\delta$ –3.95, 20.71, 24.00, 24.31, 31.30, 47.53, 53.32, 57.77, 121.21, 127.67, 128.09, 128.51, 134.63, 135.76; MS (GC/MS, 70 eV) m/z (rel. intensity) 334 (0.5) [M + – Me], 285 (0.2), 270 (11), 212 (32), 91 (100); IR 3057, 3031, 2957, 2913, 2851, 1673, 1636, 1606, 1496, 1451, 1299, 1250, 1131, 1061, 835, 730, 696, 602 cm$^{-1}$; Anal. Calcd for C$_{18}$H$_{27}$NO$_2$SSi: C, 61.85; H, 7.79; N, 4.01; S 9.17. Found: C, 61.44; H, 8.21; N, 4.38; S 8.95.

Sultam rac-9. $R_f$ 0.41 (pentane/EtOAc 4:1); mp 94–95 °C; $[^{13}$C NMR (75.4 MHz) $\delta$ 25.4, 26.6, 27.9, 31.7, 34.1, 34.4, 35.3, 48.1, 51.1, 54.9, 116.4, 127.6, 128.2, 128.4, 135.7, 142.4; MS (GC/MS, 70 eV) m/z (rel. intensity) 317 (3) [M$^+$], 252 (5), 148 (4), 134 (58), 119 (25), 105 (9), 91 (100); IR 3085, 3028, 2920, 2879, 2851, 1494, 1439, 1358, 1279, 1205, 1136, 1123, 1061, 838, 761, 715, 697, 608, 580 cm$^{-1}$; Anal. Calcd for C$_{18}$H$_{23}$NO$_2$S: C, 68.10; H, 7.30; N, 4.41; S 9.10. Found: C, 68.16; H, 7.35; N, 4.18; S 9.84.

Sultam 13. $R_f$ 0.19 (pentane/EtOAc 4:1); mp 141–142 °C; $[\alpha]^{20}_D +40.3$ (c 1.0, CH$_2$Cl$_2$); $^1$H NMR $\delta$ 1.70 (d, $J$ = 6.9 Hz, 3H), 1.79 (dd, $J$ = 7.9, 12.4 Hz, 1H), 2.62 (ddd, $J$ = 12.4, 4.3, 3.7 Hz, 1H); 3.17 (dd, $J$ = 4.3, 7.5 Hz, 1H), 3.43 (d, $J$ = 11.0 Hz, 1H), 3.55 (d, $J$ = 11.0 Hz, 1H), 4.96 (q, $J$ = 6.9 Hz, 1H), 5.24 (dd, $J$ = 1.7, 4.5 Hz, 1H), 6.23 (d, $J$ = 5.7 Hz, 1H), 6.50 (dd, $J$ = 1.7, 5.7
Hz, 1H), 7.28–7.45 (m, 5H); $^{13}$C NMR $\delta$ 17.8, 29.1, 44.9, 52.4, 60.8, 79.5, 89.8, 127.4, 127.9, 128.7, 134.0, 139.4, 139.9; MS (GC/MS, 70 eV) m/z (rel. intensity) 291 (2) [M$^+$], 276 (2), 200 (31), 199 (35), 186 (35), 105 (100), 81 (91), 77 (19), 53 (21). IR (KBr) 3129, 3081, 3036, 3001, 2972, 2943, 2864, 1493, 1454, 1298, 1282, 1245, 1138, 1112, 1072, 973, 933, 864, 767, 702, 665, 610, 546 cm$^{-1}$; Anal. Calcd for C$_{15}$H$_{17}$NO$_3$S: C, 61.83; H, 5.88; N, 4.81; S 11.01. Found: C, 62.33; H, 6.05; N, 4.78; S 10.94.

**Sultam 14.** $R_t$ 0.18 (pentane/EtOAc 4:1); mp 120–121 °C; $[\alpha]_{D}^{20}$ –69.0 (c 1.0, CH$_2$Cl$_2$); $^1$H NMR $\delta$ 1.73 (d, $J = 6.9$ Hz, 3H), 1.81 (dd, $J = 7.9$, 12.4 Hz, 1H), 2.65 (dd, $J = 3.7$, 4.3, 12.4 Hz, 1H), 3.23 (dd, $J = 3.5$, 7.9 Hz, 1H), 3.34 (d, $J = 11.0$ Hz, 1H), 3.79 (d, $J = 11.0$ Hz, 1H), 4.95 (q, $J = 6.9$ Hz, 1H), 5.23 (dd, $J = 1.7$, 4.5 Hz, 1H), 6.31 (d, $J = 5.7$ Hz, 1H), 6.51 (dd, $J = 1.7$, 5.7 Hz, 1H), 7.24–7.45 (m, 5H); $^{13}$C NMR $\delta$ 17.8, 29.3, 45.0, 52.4, 60.8, 79.5, 89.7, 127.2, 127.7, 128.6, 133.9, 139.5, 139.9; MS (GC/MS, 70 eV) m/z (rel. intensity) 291 (3) [M$^+$], 276 (2), 200 (39), 199 (37), 186 (34), 105 (100), 81 (95), 77 (19), 53 (18); IR (KBr) 3144, 3093, 2997, 2947, 2889, 1494, 1448, 1350, 1268, 1335, 1258, 1150, 1066, 865, 771, 708, 695, 668, 612, 539 cm$^{-1}$; Anal. Calcd for C$_{15}$H$_{17}$NO$_3$S: C, 61.83; H, 5.88; N, 4.81; S 11.01. Found: C, 62.33; H, 6.06; N, 4.69; S 11.16.

**Sultam 15.** $R_t$ 0.47 (pentane/EtOAc 1:1); mp 137–138 °C (EtOAc); $[\alpha]_{D}^{20}$ –36.2 (c 1.0, CH$_2$Cl$_2$); $^1$H NMR $\delta$ 1.62 (d, $J = 7.0$ Hz, 3H), 1.63 (d, $J = 6.9$ Hz, 3H), 1.76 (dd, $J = 7.8$, 12.3 Hz, 1H), 2.25 (m, 2H), 2.54 (m, 1H), 2.68 (dd, $J = 1.7$, 5.6 Hz, 1H), 7.30 (m, 1H), 7.35 (m, 2H), 7.40 (m, 2H); $^{13}$C NMR $\delta$ 16.48, 27.66, 28.80, 38.54, 52.51, 59.43, 78.21, 89.07, 127.50, 127.78, 128.52, 136.31, 139.71, 140.25; MS (GC/MS, 70 eV) m/z (rel. intensity) 305 (0.3) [M$^+$], 105 (100), 91 (4), 81 (7), 79 (5), 77 (6); IR (KBr) 3068, 3028, 2980, 2950, 2934, 1598, 1495, 1456, 1346, 1309, 1249, 1149, 1125, 1063, 1048, 1030, 975, 900, 877, 829, 778, 697, 627, 562, 547 cm$^{-1}$; Anal. Calcd for C$_{16}$H$_{19}$NO$_3$S: C, 62.93; H, 6.27; N, 4.59; S 10.50. Found: C, 63.43; H, 6.38; N 4.65; S 10.47.

**Sultam 16.** $R_t$ 0.35 (pentane/EtOAc 4:1); mp 164–165 °C; $[\alpha]_{D}^{20}$ +12.5 (c 1.0, CH$_2$Cl$_2$); $^1$H NMR $\delta$ 0.76 (d, $J = 6.3$ Hz, 3H), 1.62 (d, $J = 7.2$ Hz, 3H), 1.89 (dd, $J = 8.4$, 12.7 Hz, 1H), 2.10 (dd, $J = 3.4$, 4.7, 12.7 Hz, 1H), 2.31–2.47 (m, 2H), 3.05 (dd, $J = 4.8$, 8.5 Hz, 1H), 3.69–3.81 (m, 1H), 5.01 (dd, $J = 1.6$, 4.5 Hz, 1H), 5.26 (q, $J = 7.2$ Hz, 1H), 6.22 (d, $J = 5.7$ Hz, 1H), 6.43 (dd, $J =$...
Sultam 31. \( R_f \) 0.31 (pentane/EtOAc 4:1); mp 173–174 °C; \([\alpha]^{20}_D +22.5 \) (c 1.0, CH\(_2\)Cl\(_2\)); \( ^1\)H NMR \( \delta \) 1.08 (d, \( J = 7.5 \) Hz, 3H), 1.63 (d, \( J = 7.1 \) Hz, 3H), 1.80 (dd, \( J = 7.8, 12.3 \) Hz, 1H), 2.21 (d, \( J = 14.9 \) Hz, 1H), 2.38 (dd, \( J = 6.6, 15.2 \) Hz, 1H), 2.64 (ddd, \( J = 3.5, 4.5, 12.2 \) Hz, 1H), 3.01 (dd, \( J = 3.2, 7.6 \) Hz, 1H), 3.61 (m, 1H), 5.17 (dd, \( J = 1.5, 4.7 \) Hz, 1H), 5.57 (q, \( J = 7.0 \) Hz, 1H), 6.02 (d, \( J = 5.6 \) Hz, 1H), 6.52 (dd, \( J = 1.7, 5.6 \) Hz, 1H), 7.33 (m, 3H), 7.49 (d, \( J = 7.5 \) Hz, 2H); \( ^{13}\)C NMR \( \delta \) 17.8, 20.3, 29.5, 33.5, 49.0, 54.6, 58.9, 79.1, 89.7, 127.7, 128.0, 128.4, 137.4, 139.4, 139.8; MS (GC/MS, 70 eV) \( \text{m/z} \) (rel. intensity) 319 (0.5) [M\(^+\)], 238 (18), 134 (7), 105 (100), 81 (18), 79 (8), 77 (10), 53 (6); IR (KBr) 3437, 2977, 1390, 1315, 1151, 979 cm\(^{-1}\); Anal. Calcd for C\(_{17}\)H\(_{21}\)NO\(_3\)S: C, 63.92; H, 6.63; N, 4.39; S 10.40. Found: C, 63.89; H, 6.93; N, 4.44; S 10.18.

Sultam 32. \( R_f \) 0.35 (pentane/EtOAc 4:1); mp 112–113 °C (ethanol); \([\alpha]^{20}_D −9.0 \) (c 1.0, CH\(_2\)Cl\(_2\)); \( ^1\)H NMR \( \delta \) 1.34 (d, \( J = 6.5 \) Hz, 3H), 1.75 (d, \( J = 7.2 \) Hz, 3H), 1.81 (dd, \( J = 8.3, 12.5 \) Hz, 1H), 2.17–2.26 (m, 2H), 2.41 (m, 1H), 2.89 (dd, \( J = 4.5, 8.3 \) Hz, 1H), 3.61 (m, 1H), 4.86 (dd, \( J = 1.7, 4.5 \) Hz, 1H), 5.10 (q, \( J = 7.2 \) Hz, 1H), 6.08 (d, \( J = 5.6 \) Hz, 1H), 6.36 (dd, \( J = 1.5, 5.6 \) Hz, 1H), 7.33 (m, 3H), 7.45 (m, 2H); \( ^{13}\)C NMR \( \delta \) 21.5, 22.4, 30.6, 31.3, 49.7, 56.7, 60.7, 77.5, 87.2, 127.7, 128.1, 128.2, 128.3, 136.8, 138.1; MS (GC/MS, 70 eV) \( \text{m/z} \) (rel. intensity) 319 (0.5) [M\(^+\)], 238 (18), 134 (7), 105 (100), 81 (18), 79 (8), 77 (10), 53 (6); IR (KBr) 3440, 2993, 1450, 1317, 1145, 954 cm\(^{-1}\); Anal. Calcd for C\(_{17}\)H\(_{21}\)NO\(_3\)S: C, 63.92; H, 6.63; N, 4.39; S 10.04. Found: C, 63.90; H, 6.80; N, 4.25; S 10.04.

Sultam 45. \( R_f \) 0.54 (pentane/EtOAc 4:1); \([\alpha]^{20}_D −39.0 \) (c 1.0, CH\(_2\)Cl\(_2\)); mp 139–140 °C (methanol); \( ^1\)H NMR \( \delta \) 1.11–1.17 (m, 1H), 1.22–1.34 (m, 3H), 1.50–1.64 (m, 2H), 1.57 (d, \( J = 7.0 \) Hz, 3H), 1.78–1.83 (dddd, \( J = 2.6, 5.4, 8.2, 11.0 \), 13.2 Hz, 1H), 1.96–2.00 (m, 1H), 2.69–2.73 (m, 1H), 2.88 (dd, \( J = 2.7, 4.4, 7.1, 13.4 \) Hz, 1H), 3.15 (dd, \( J = 5.7, 9.6 \) Hz, 1H), 3.41 (dd, \( J = 2.1, 13.2, 15.3 \) Hz, 1H), 5.36 (q, \( J = 7.0 \) Hz, 1H), 6.04 (d, \( J = 8.3 \) Hz, 1H), 6.38 (t, \( J = 7.5 \) Hz, 1H), 7.25–7.43 (m, 5H); \( ^{13}\)C NMR \( \delta \) 16.0, 24.3, 27.6, 29.5, 34.1, 34.4, 39.1, 39.5, 51.6, 62.1, 127.3, 127.4, 128.3, 131.9, 134.00, 140.5; MS (GC/MS, 70 eV) \( \text{m/z} \) (rel. intensity) 317 (6) [M\(^+\)], 302 (100), 252 (8), 238 (29), 213 (23), 148 (7), 132 (9), 118 (49), 105 (95), 91 (51); IR 3041, 2950, 2871, 1449, 1378, 1304, 1289, 1150, 1136, 1114, 1028, 1010, 931, 899, 843, 786, 768, 706, 624, 603, 554 cm\(^{-1}\); Anal. Calcd for C\(_{18}\)H\(_{23}\)NO\(_2\)S: C, 68.10; H, 6.70; N, 4.41; S 10.10. Found: C, 68.17; H, 7.59; N, 4.38; S 10.46.

Sultam 46. \( R_f \) 0.54 (pentane/EtOAc 4:1); \([\alpha]^{20}_D −29.0 \) (c 1.0, CH\(_2\)Cl\(_2\)); mp 158–159 °C (methanol); \( ^1\)H NMR \( \delta \) 1.19–1.25 (m, 1H), 1.30–1.34 (m, 1H), 1.35–1.43 (m, 1H), 1.52–1.63 (m, 2H), 1.58 (d, \( J = 7.1 \) Hz, 3H), 1.75–1.83 (m, 2H), 2.01 (ddd, \( J = 2.7, 9.6, 12.9 \) Hz, 1H), 2.70–2.74 (m, 1H), 2.95 (dd, \( J = 2.6, 4.5, 7.1, 14.3 \) Hz, 1H), 3.11 (m, 2H), 5.38 (q, \( J = 7.0 \) Hz, 1H), 6.00 (d, \( J = 8.3 \) Hz, 1H), 6.39 (t, \( J = 7.5 \) Hz, 1H), 7.23–7.26 (m, 1H), 7.33 (t, \( J = 7.4 \) Hz, 2H), 7.40 (d, \( J = 7.4 \) Hz, 2H); \( ^{13}\)C NMR \( \delta \) 18.52, 24.46, 28.13, 29.62, 34.38, 35.40, 39.32, 40.67.
53.09, 62.83, 127.37, 127.74, 131.96, 133.93, 139.80; MS (GC/MS, 70 eV) m/z (rel. intensity) 317 (10) [M⁺], 302 (41), 252 (8), 238 (20), 213 (27), 148 (7), 132 (10), 118 (49), 105 (100), 91 (54); IR (KBr) 3086, 3059, 2947, 2865, 1498, 1459, 1309, 1288, 1155, 1123, 1025, 1010, 935, 851, 786, 765, 708, 617, 597, 559 cm⁻¹; Anal. Calcd for C₁₈H₂₃NO₂S: C, 68.10; H, 7.30; N, 4.41; S, 10.10. Found: C, 68.16; H, 7.72; N, 4.43; S, 10.18.

Sultam 53. Rᵣ 0.47 (pentane/EtOAc 4:1); [α]²⁰ D +0.4 (c 1.0, CH₂Cl₂); mp 155–156 °C (methanol); ¹H NMR δ 0.95 (d, J = 6.6 Hz, 3H), 1.15–1.29 (m, 2H), 1.31–1.45 (m, 2H), 1.54–1.64 (m, 2H), 1.77–1.85 (m, 1H), 1.79 (d, J = 7.2 Hz, 3H), 2.00–2.09 (m, 1H), 2.71–2.75 (m, 1H), 3.21 (dd, J = 6.1, 9.8 Hz, 1H), 3.94–4.01 (m, 1H), 5.39 (q, J = 7.0 Hz, 1H), 6.07 (d, J = 8.3 Hz, 1H), 6.39 (t, J = 7.5 Hz, 1H), 7.22–7.38 (m, 3H), 7.42–7.45 (m, 2H); ¹³C NMR δ 17.1, 21.7, 24.2, 28.4, 29.5, 34.4, 37.7, 43.5, 50.6, 50.9, 61.2, 126.6, 126.7, 128.1, 132.4, 134.0, 143.8; MS (GC/MS, 70 eV) m/z (rel. intensity) 331 (0.1) [M⁺], 316 (18), 252 (10), 227 (9), 212 (11), 147 (10), 146 (11), 132 (19), 120 (8), 105 (100), 91 (34); IR (KBr) 3046, 2948, 1447, 1317, 1306, 1288, 1149, 938, 791, 768, 705, 627, 588, 544 cm⁻¹; Anal. Calcd for C₁₉H₂₅NO₂S: C, 68.85; H, 7.60; N, 4.23; S, 9.72. Found: C, 68.98; H, 7.78; N, 4.19; S, 9.72.

General procedure for the debenzylation of sultams
The sultam (1 mmol) was dissolved in formic acid (35 mL) under argon at 25–30 °C, and the resultant solution was stirred at this temperature for the time indicated in Scheme 9. Formic acid was then removed in vacuo at 40 °C, and the crude product was purified by flash chromatography with the gradient solvent system pentane/EtOAc 2:1 → EtOAc.

Sultam 57. Yield 93%; Rᵣ 0.41 (EtOAc; mp 149–150 °C (EtOAc); [α]²⁰ D −10.7 (c 1.0, CH₂Cl₂); ¹H NMR δ 1.77 (dd, J = 7.9, 12.3 Hz, 1H), 2.25 (m, 2H), 2.50 (ddd, J = 3.4, 4.7, 12.3 Hz, 1H), 3.07 (dd, J = 3.4, 7.9 Hz, 1H), 3.38 (m, 1H), 3.61 (m, 1H), 4.68 (br. d, J = 6.9 Hz, 1H), 5.15 (dd, J = 1.7, 4.7 Hz, 1H), 6.02 (d, J = 5.7 Hz, 1H), 6.52 (dd, J = 1.7, 5.7 Hz, 1H); ¹³C NMR δ 27.4, 29.18, 40.56, 58.43, 78.57, 88.60, 136.04, 139.62; MS (GC/MS, 70 eV) m/z (rel. intensity) 201 (17) [M⁺], 120 (100), 94 (86), 91(54), 82 (65), 81 (95), 53 (34); IR (KBr) 3263, 3103, 2997, 2957, 2885, 1446, 1432, 1316, 1292, 1247, 1142, 1097, 1061, 988, 964, 931, 841, 825, 768, 709,
649, 566, 538 cm⁻¹; Anal. Calcld for C₈H₁₁NO₃S: C, 47.75; H, 5.51; N, 6.96; S 15.93. Found: C, 47.48; H, 5.61; N, 6.99; S 15.78.

**Sultam ent-57.** Yield 96%; Rᵣ 0.41 (EtOAc); mp 150–151 °C (EtOAc); [α]D²₀ +10.7 (c 1.0, CH₂Cl₂); ¹H NMR δ 1.77 (dd, J = 7.9, 12.3 Hz, 1H), 2.25 (m, 2H), 2.50 (ddd, J = 3.4, 4.7, 12.3 Hz, 1H), 3.07 (dd, J = 3.4, 7.9 Hz, 1H), 3.38 (m, 1H), 3.61 (m, 1H), 4.71 (br. d, J = 6.8 Hz, 1H), 5.15 (dd, J = 1.7, 4.7 Hz, 1H), 6.02 (d, J = 5.7 Hz, 1H), 6.52 (dd, J = 1.7, 5.7 Hz, 1H); ¹³C NMR δ 27.41, 29.15, 40.56, 58.38, 78.55, 88.59, 136.05, 139.57; MS (GC/MS, 70 eV) m/z (rel. intensity) 201 (17) [M⁺], 120 (100), 94 (86), 91(55), 81 (95), 53 (34); IR (KBr) 3272, 3089, 2996, 2957, 2883, 1445, 1432, 1318, 1292, 1247, 1141, 1096, 1061, 987, 964, 932, 841, 825, 765, 708, 652, 565, 539 cm⁻¹; Anal. Calcld for C₈H₁₁NO₃S: C, 47.75; H, 5.51; N, 6.96; S 15.93. Found: C, 47.58; H, 5.63; N, 7.02; S 15.79.

**Sultam 58.** Yield 95%; Rᵣ 0.55 (EtOAc); mp 175–176 °C; [α]D +3.2 (c 1.0, CH₂Cl₂); ¹H NMR δ 1.32 (d, J = 6.3 Hz, 3H), 1.79 (dd, J = 7.9, 12.2 Hz, 1H), 1.97 (dd, J = 12.0, 15.1 Hz, 1H), 2.34 (dd, J = 2.7, 15.1 Hz, 1H), 2.53 (ddd, J = 3.7, 4.4, 12.3 Hz, 1H), 2.99 (dd, J = 3.3, 7.9 Hz, 1H), 3.82 (m, 1H), 4.33 (br. d, J = 9.6 Hz, 1H), 5.16 (dd, J = 1.5, 4.6 Hz, 1H), 6.04 (d, J = 5.6 Hz, 1H), 6.54 (dd, J = 1.7, 5.6 Hz, 1H); ¹³C NMR δ 21.21, 29.04, 35.60, 47.82, 57.04, 78.66, 89.00, 136.14, 139.67; MS (GC/MS, 70 eV) m/z (rel. intensity) 215 (2) [M⁺], 136 (5), 135 (6), 134 (100), 108 (7), 91 (15), 82 (19), 81 (28), 53 (12); IR 3282, 3244, 2986, 2957, 1448, 1408, 1334, 1302, 1134, 1093, 960, 714 cm⁻¹; Anal. Calcld for C₈H₁₃NO₃S: C, 50.21; H, 6.09; N, 6.51; S 14.90. Found: C, 50.02; H, 6.36; N, 6.88; S 14.58.

**Sultam ent-58.** Yield 96%; Rᵣ 0.55 (EtOAc); mp 175–176 °C; [α]D²₀ –3.2 (c 1.0, CH₂Cl₂); ¹H NMR δ 1.32 (d, J = 6.7 Hz, 3H), 1.79 (dd, J = 7.9, 12.2 Hz, 1H), 1.97 (dd, J = 12.0, 15.1 Hz, 1H), 2.34 (dd, J = 2.7, 15.1 Hz, 1H), 2.53 (ddd, J = 3.7, 4.4, 12.3 Hz, 1H), 2.99 (dd, J = 3.3, 7.9 Hz, 1H), 3.82 (m, 1H); 4.43 (br. d, J = 9.8 Hz, 1H), 5.16 (dd, J = 1.5, 4.6 Hz, 1H), 6.04 (d, J = 5.6 Hz, 1H), 6.54 (dd, J = 1.7, 5.6 Hz, 1H); ¹³C NMR δ 21.15, 29.00, 35.47, 47.85, 56.90, 78.65, 89.02, 136.18, 139.60; MS (GC/MS, 70 eV) m/z (rel. intensity) 215 (0.7) [M⁺], 136 (4), 135 (6), 134 (100), 108 (4), 91 (17), 82 (18), 81 (22), 53 (11); IR 3282, 3244, 2986, 2957, 1409, 1301, 1133, 1092, 984, 959, 873, 829, 712, 625, 573, 541 cm⁻¹; Anal. Calcld for C₈H₁₃NO₃S: C, 50.21; H, 6.09; N, 6.51; S 14.90. Found: C, 49.98; H, 6.28; N, 6.63; S 14.79.

**Sultam 59.** Yield 93%; Rᵣ 0.57 (EtOAc); mp 145–147 °C; [α]D²₀ +17.8 (c 1.0, CH₂Cl₂); ¹H NMR δ 1.30 (d, J = 7.0 Hz, 3H), 1.89 (dd, J = 8.5, 12.8 Hz, 1H), 1.97 (dd, J = 2.5, 15.2 Hz, 1H), 2.35 (dt, J = 4.4, 12.8 Hz, 1H), 2.58 (dd, J = 8.1, 15.2 Hz, 1H), 2.96 (dd, J = 4.1, 8.5 Hz, 1H), 3.82 (m, 1H); 4.1 (br. d, J=7.9 Hz, 1H); 4.97 (dd, J = 1.5, 4.6 Hz, 1H), 6.08 (d, J = 5.7 Hz, 1H), 6.41 (dd, J = 1.7, 5.7 Hz, 1H); ¹³C NMR δ 22.20, 28.89, 32.07, 47.81, 58.83, 77.86, 89.83, 136.49, 138.47; MS (GC/MS, 70 eV) m/z (rel. intensity) 215 (0.6) [M⁺], 136 (5), 135 (6), 134 (100), 108 (8), 91 (16), 82 (18), 81 (27), 53 (12); IR 3272, 3079, 3012, 2993, 2941, 1719, 1416, 1320, 1296, 1257, 1129, 991, 956, 879, 707, 681, 644, 531 cm⁻¹; Anal. Calcld for C₉H₁₃NO₃S: C, 50.21; H, 6.09; N, 6.51; S 14.90. Found: C, 50.18; H, 6.28; N, 6.96; S 14.23.

**Sultam 60.** Yield 98%; Rᵣ 0.47 (EtOAc); mp 137–138 °C (methanol); [α]D²₀ +10.4 (c 1.0, CH₂Cl₂); ¹H NMR δ 1.22–1.50 (m, 3H), 1.54–1.61 (m, 2H), 1.75–1.87 (m, 2H), 1.98–2.07 (m,
1H), 2.73 (m, 1H), 3.09 (dd, J = 5.8, 9.7 Hz, 1H), 3.30–3.39 (m, 1H), 3.59–3.72 (m, 1H), 4.00 (br. s, 1H), 6.06 (d, J = 8.3 Hz, 1H), 6.38 (t, J = 7.5 Hz, 1H); $^{13}$C NMR δ 24.60, 27.85, 29.44, 34.56, 35.34, 38.97, 41.85, 62.11, 131.72, 134.52; MS (GC/MS, 70 eV) m/z (rel. intensity) 213 (39) [M$^+$], 149 (10), 148 (14), 134 (8), 120 (80), 105 (20), 92 (76), 91 (100), 91 (100); IR 3270, 3058, 2954, 2917, 2875, 1697, 1443, 1412, 1329, 1318, 1287, 1257, 1146, 1047, 1030, 914, 765, 727, 694, 591, 558 cm$^{-1}$; Anal. Calcd for C10H15NO2S: C, 56.31; H, 7.09; N, 6.57; S 15.03. Found: C, 56.33; H, 7.29; N, 6.54; S 14.98.

**Sultam ent-60.** Yield 97%; R$^f$ 0.47 (EtOAc); mp 137–138 °C (methanol); $[\alpha]_{D}^{20}$ –10.4 (c 1.0, CH$_2$Cl$_2$); $^1$H NMR δ 1.22–1.50 (m, 3H), 1.54–1.61 (m, 2H), 1.75–1.87 (m, 2H), 1.98–2.07 (m, 1H), 2.73 (m, 1H), 3.09 (dd, J = 5.8, 9.7 Hz, 1H), 3.30–3.39 (m, 1H), 3.59–3.72 (m, 1H), 4.00 (br. s, 1H), 6.06 (d, J = 8.3 Hz, 1H), 6.38 (t, J = 7.5 Hz, 1H); $^{13}$C NMR δ 24.60, 27.85, 29.44, 34.56, 35.34, 38.97, 41.85, 62.11, 131.72, 134.52; MS (GC/MS, 70 eV) m/z (rel. intensity) 213 (20) [M$^+$], 149 (7), 148 (7), 134 (6), 121 (23), 120 (49), 105 (17), 92 (57), 91 (100); IR 3259, 3056, 2950, 2917, 2875, 1697, 1443, 1412, 1329, 1318, 1287, 1257, 1146, 1047, 1030, 914, 765, 727, 694, 591, 558 cm$^{-1}$; Anal. Calcd for C10H15NO2S: C, 56.31; H, 7.09; N, 6.57; S 15.03. Found: C, 56.25; H, 7.43; N, 6.58; S 14.99.

**Sultam 61.** Yield 97%; R$^f$ 0.58 (EtOAc); mp 189–190 °C (methanol); $[\alpha]_{D}^{20}$ +10.1 (c 1.0, CH$_2$Cl$_2$); $^1$H NMR δ 1.27 (d, J = 6.6 Hz, 3H), 1.22–1.44 (m, 4H), 1.53–1.63 (m, 1H), 1.78 (ddddd, J = 2.7, 5.6, 8.5, 11.3, 13.3 Hz, 1H), 1.89 (dd, J = 1.9, 14.1 Hz, 1H), 2.03 (m, 1H), 2.73 (m, 1H), 2.97 (dd, J = 5.7, 9.7 Hz, 1H), 3.65 (br. d, J = 8.9 Hz, 1H), 3.72–3.82 (m, 1H), 6.04 (d, J = 8.3 Hz, 1H), 6.38 (t, J = 7.5 Hz, 1H); $^{13}$C NMR δ 21.52, 24.48, 27.71, 29.48, 34.61, 38.85, 43.38, 48.74, 60.56, 132.15, 134.30; MS (GC/MS, 70 eV) m/z (rel. intensity) 227 (24) [M$^+$], 212 (5), 163 (6), 162 (8), 148 (16), 135 (20), 134 (8), 120 (34), 108 (16), 105 (17), 94 (7), 93 (15), 92 (91), 91 (100); IR 3194, 3042, 2944, 2860, 1449, 1319, 1277, 1162, 1137, 1105, 1059, 971, 891, 768, 749, 699, 576 cm$^{-1}$; Anal. Calcd for C11H17NO2S: C, 58.12; H, 7.54; N, 6.16; S 14.11. Found: C, 57.96; H, 8.02; N, 6.44; S 14.06.

**Sultam ent-61.** Yield 97%; R$^f$ 0.58 (EtOAc); mp 189–190 °C (methanol); $[\alpha]_{D}^{20}$ –10.1 (c 1.0, CH$_2$Cl$_2$); $^1$H NMR δ 1.27 (d, J = 6.6 Hz, 3H), 1.22–1.44 (m, 4H), 1.53–1.63 (m, 1H), 1.78 (ddddd, J = 2.7, 5.6, 8.5, 11.3, 13.3 Hz, 1H), 1.89 (dd, J = 1.9, 14.1 Hz, 1H), 2.03 (m, 1H), 2.73 (m, 1H), 2.97 (dd, J = 5.7, 9.7 Hz, 1H), 3.65 (br. d, J = 8.9 Hz, 1H), 3.72–3.82 (m, 1H), 6.04 (d, J = 8.3 Hz, 1H), 6.38 (t, J = 7.5 Hz, 1H); $^{13}$C NMR δ 21.52, 24.48, 27.71, 29.48, 34.61, 38.85, 43.38, 48.74, 60.56, 132.15, 134.30; MS (GC/MS, 70 eV) m/z (rel. intensity) 227 (24) [M$^+$], 212 (5), 163 (6), 162 (8), 148 (16), 135 (20), 134 (8), 120 (34), 108 (16), 105 (17), 94 (7), 93 (15), 92 (91), 91 (100); IR 3194, 3042, 2944, 2860, 1449, 1319, 1277, 1162, 1137, 1105, 1059, 971, 891, 768, 749, 699, 576 cm$^{-1}$; Anal. Calcd for C11H17NO2S: C, 58.12; H, 7.54; N, 6.16; S 14.11. Found: C, 57.96; H, 8.02; N, 6.44; S 14.06.
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References and Footnotes

13. Diastereomeric ratios were determined by $^1$H- NMR integration of the crude product mixture. Only exo sultams were formed.
15. Compare transition state models depicted in reference 12.
22. Diastereomeric ratios were determined by $^1$H NMR integration of the crude product mixture. Only endo sultams were formed.
24. This reaction proceeds by an $S_N$1 mechanism, since racemic 1-phenylethyl formate was isolated as the byproduct.