Stereoselective preparation of γ- and δ-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 γ- and δ-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 δ-sultams.

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

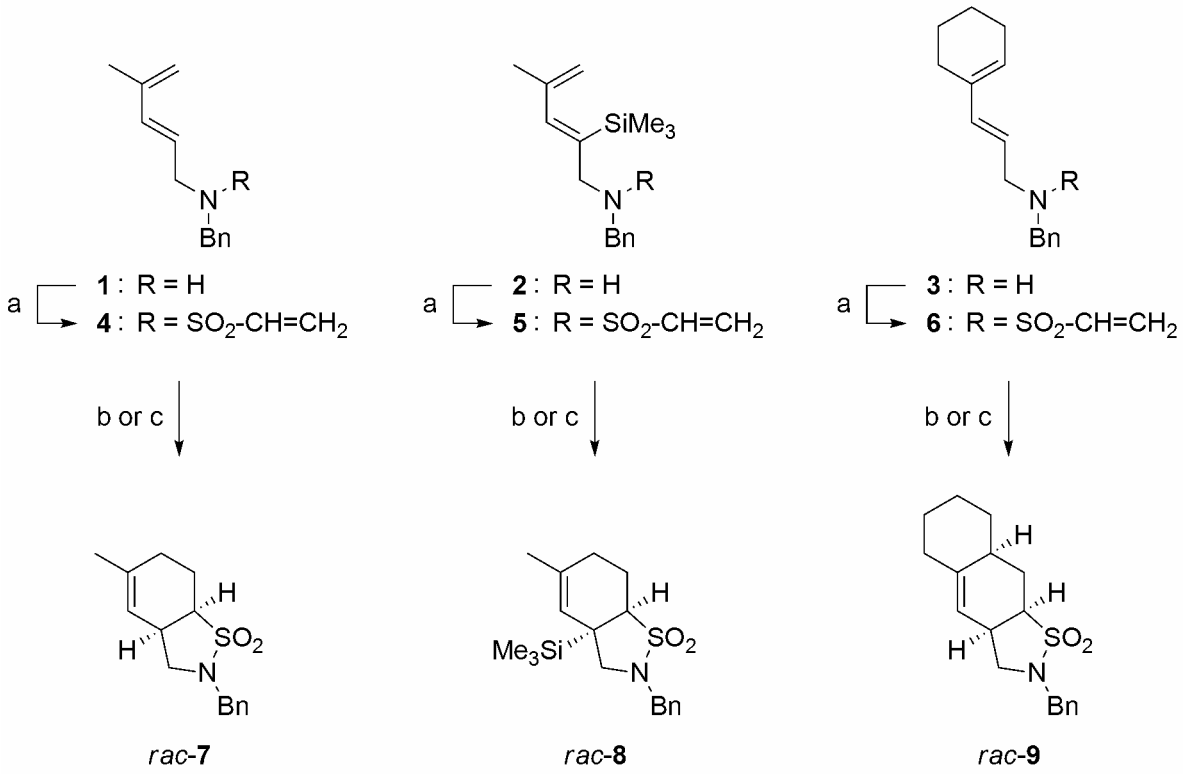
Introduction

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 δ-sultams that can be applied as novel chiral auxiliaries.[9]

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Results and Discussion

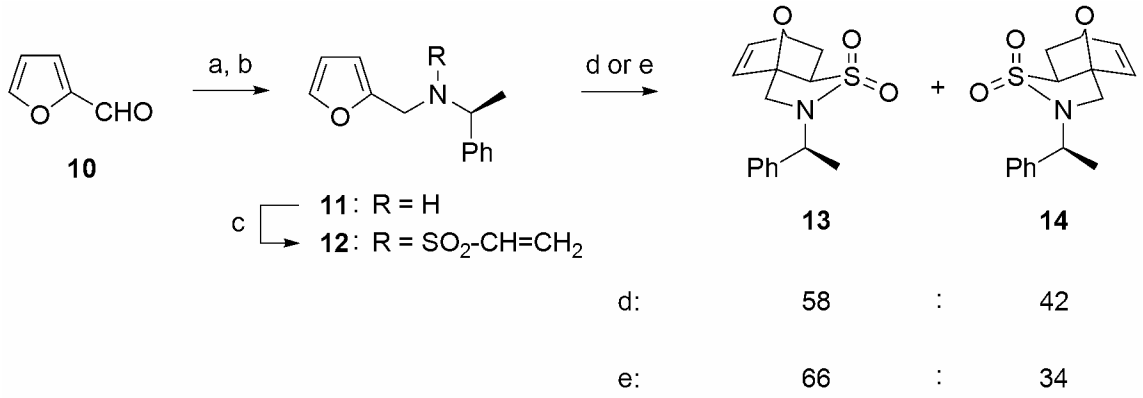
The vinylsulfonamides **4**–**6** incorporating a three-atom tether connecting an acyclic diene and the dienophile were readily available by treatment of *N*-benzyldienylamines **1**–**3**[10] with vinylsulfonyl chloride[11] (Scheme 1). Upon refluxing a solution of **4**–**6** in toluene, the γ-sultams *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 γ-sultams was elucidated by 2D NOESY experiments and additionally by X-ray diffraction analysis in the case of the sultam *rac*-**9**.[4a]



Scheme 1. *Reagents and conditions*: (a) CH_2=$CHSO_2Cl$, Et_3N, CH_2Cl_2, 0 °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_2Cl_2, RT, 13 kbar, 71% *rac*-**7** (29 h), 93% *rac*-**8** (10 h), 90% *rac*-**9** (12 h).

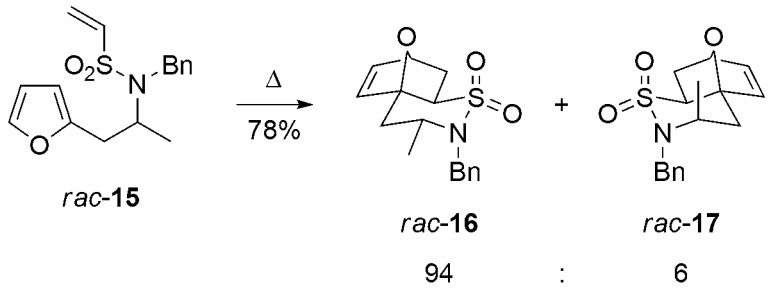
The furan-containing vinylsulfonamide **12** featuring a nitrogen-bound (*S*)-(−)-1-phenylethyl unit as an external chiral auxiliary and incorporating a three-atom tether connecting the furan diene and the dienophile, was prepared from aldehyde **10** *via* the known amine **11**[12] (Scheme 2). While 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 *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 sp^2 hybridized nitrogen atom, an sp^3 hybridization on nitrogen was unveiled by the crystal structure of γ-sultam **13**.[4b]



Scheme 2. *Reagents and conditions*: (a) (*S*)-(−)-1-phenylethylamine, $MgSO_4$, Et_2O, 0 °C to RT, 15 h, 98%; (b) $LiAlH_4$, Et_2O, 0 °C to RT, 6 h, 95%; (c) CH_2=$CHSO_2Cl$, Et_3N, CH_2Cl_2, 0 °C, 2 h, 98%; (d) toluene, reflux, 1 bar, 16 h, 73%; (e) CH_2Cl_2, RT, 13 kbar, 14 h, 94%.

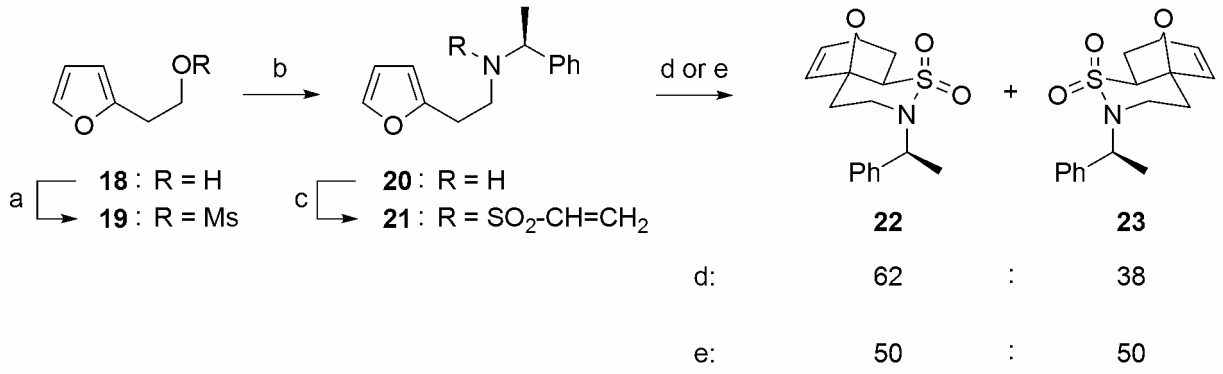
An earlier investigation revealed a high diastereoselectivity in the cyclization of vinylsulfonamide *rac*-**15** which features a four-atom tether and a furan 1,3-diene, to give the *exo* δ-sultams *rac*-**16** and *rac*-**17** at ambient pressure (Scheme 3).[4f]



Scheme 3

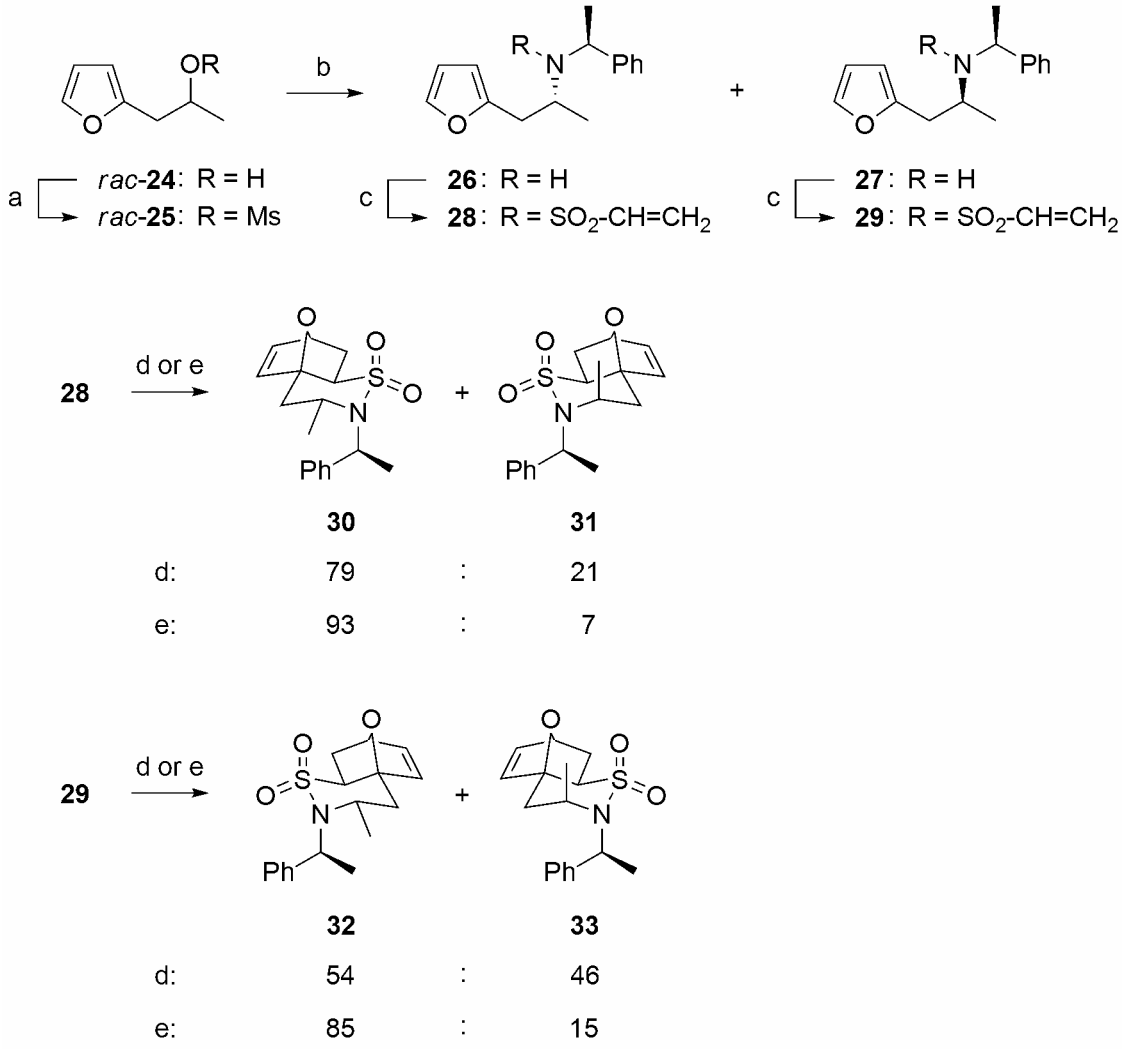
The vinylsulfonamide **21** carrying an (*S*)-(−)-1-phenylethyl unit on nitrogen was easily available by nucleophilic substitution on the mesylate **19**[16] derived from the alcohol **18**,[17]

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[13] **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.[18] Again, the two sultam diastereomers produced were readily separated by flash chromatography, and their configuration was unambiguously established by X-ray diffraction analysis.[4b]



Scheme 4. *Reagents and conditions*: (a) MsCl, Et_3N, CH_2Cl_2, 0 °C, 45 min, 97%; (b) (*S*)-(−)-1-phenylethylamine, 80 °C, 12 h, 79%; (c) CH_2=$CHSO_2Cl$, Et_3N, CH_2Cl_2, 0 °C, 2 h, 96%; (d) toluene, reflux, 1 bar, 10 h, 80%; (e) CH_2Cl_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**[19] 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.[4b] 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[13] 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[13] were critically dependent on the relative configurations of **28** and **29**.



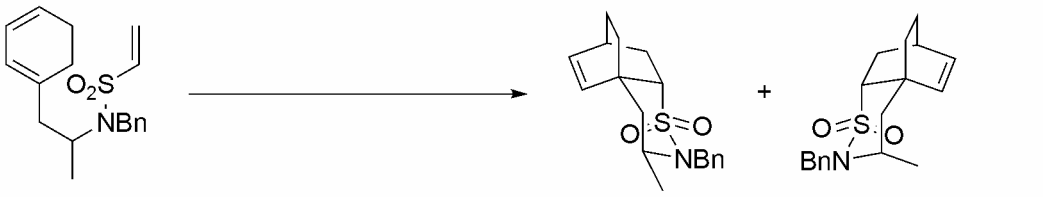
Scheme 5. *Reagents and conditions*: (a) MsCl, Et_3N, CH_2Cl_2, 0 °C, 45 min, 97%; (b) (*S*)-(−)-1-phenylethylamine, 80 °C, 12 h, 67% **26** + **27**; (c) CH_2=$CHSO_2Cl$, Et_3N, CH_2Cl_2, 0 °C, 3 h, 84% **28**, 82% **29**; (d) toluene, reflux, 1 bar, 16 h, 87% **30** + **31**, 85% **32** + **33**; (e) CH_2Cl_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]

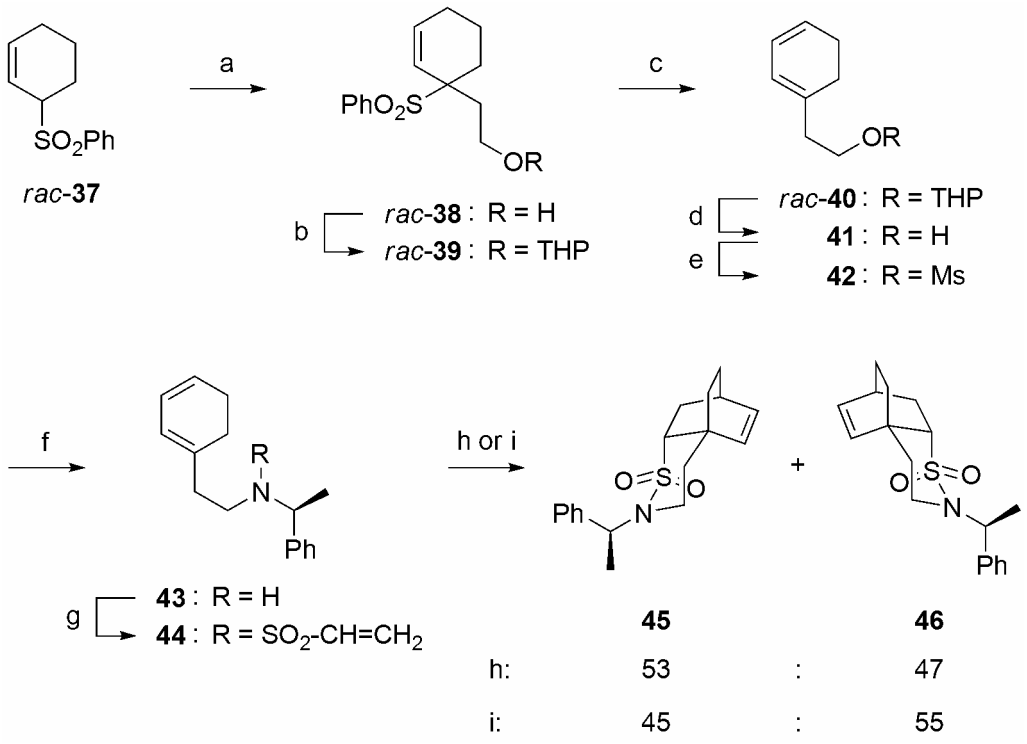
Previous studies with carbocyclic 1,3-dienes showed a high diastereoselectivity in the cycloaddition of the vinylsulfonamide *rac*-**34**, featuring a 1,3-cyclohexadienyl unit, to give the *endo* δ-sultams *rac*-**35** and *rac*-**36** under purely thermal activation or high-pressure conditions (Scheme 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.



toluene, reflux, 1 bar (3 h)	90	:	10	(77%)
CH_2Cl_2, rt, 13 kbar (12 h)	97	:	3	(93%)

Scheme 6

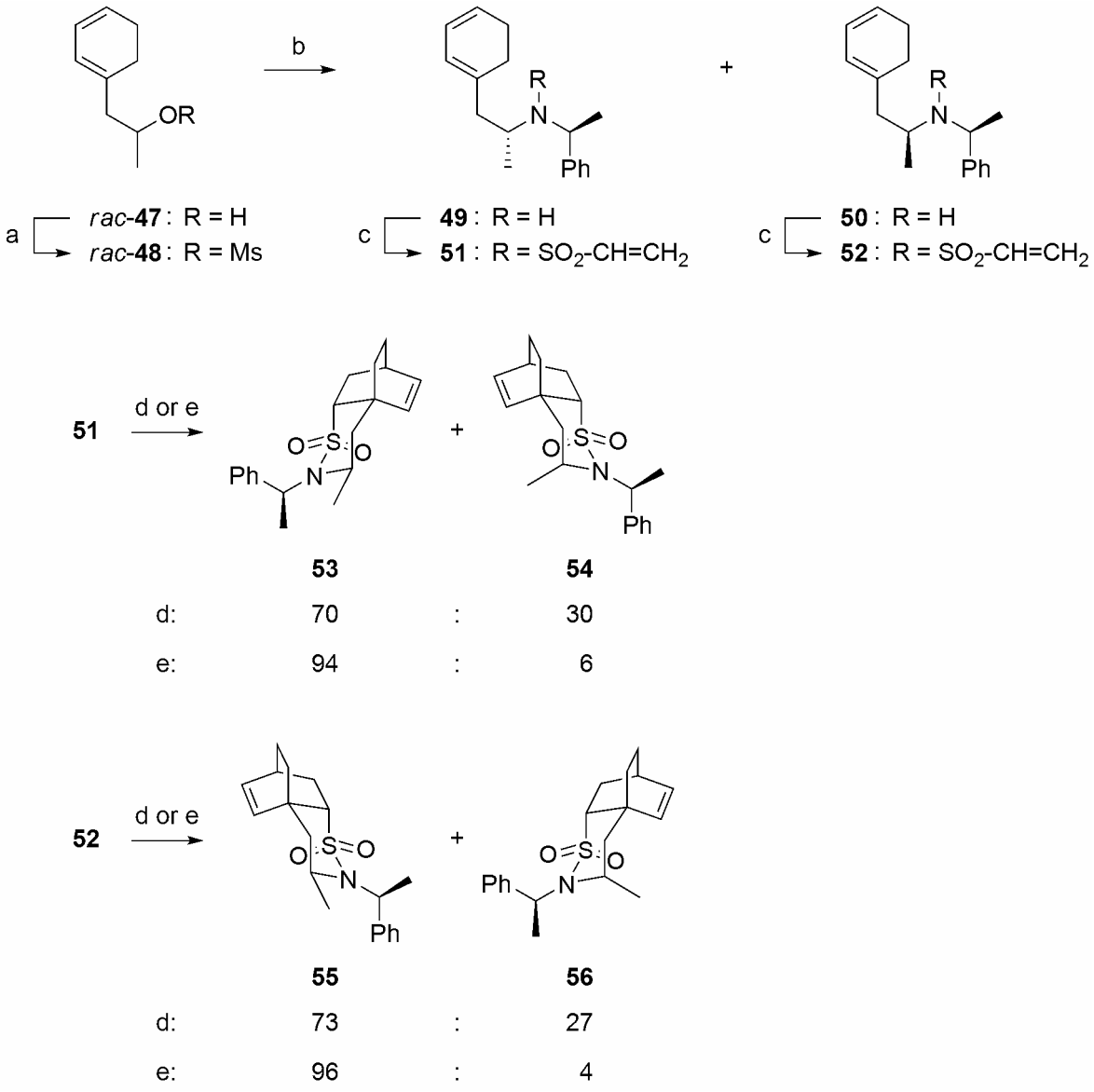
The primary alcohol **41** was synthesized from the sulfone *rac*-**37** according to a known methodology[20,21] (Scheme 7). Nucleophilic substitution of the mesylate **42**, derived from **41**, with (*S*)-(–)-1-phenylethylamine and subsequent treatment of the resultant amine **43** with vinylsulfonyl 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-2*H*-pyrane, PPTS, CH_2Cl_2, RT, 24 h, 98%; (c) *t*-BuOK, *t*-BuOH, reflux, 2 h, 57%; (d) EtOH, PPTS, 60 °C, 15 h, 63%; (e) MsCl, Et_3N, CH_2Cl_2, 0 °C, 45 min, 93%; (f) (*S*)-(–)-1-phenylethylamine, 80 °C, 12 h, 79%; (g) CH_2=$CHSO_2Cl$, Et_3N, CH_2Cl_2, 0 °C, 1 h, 77%; (h) toluene, reflux, 1 bar, 17 h, 58%; (i) CH_2Cl_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**[20] was converted by mesylation[4d] 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,

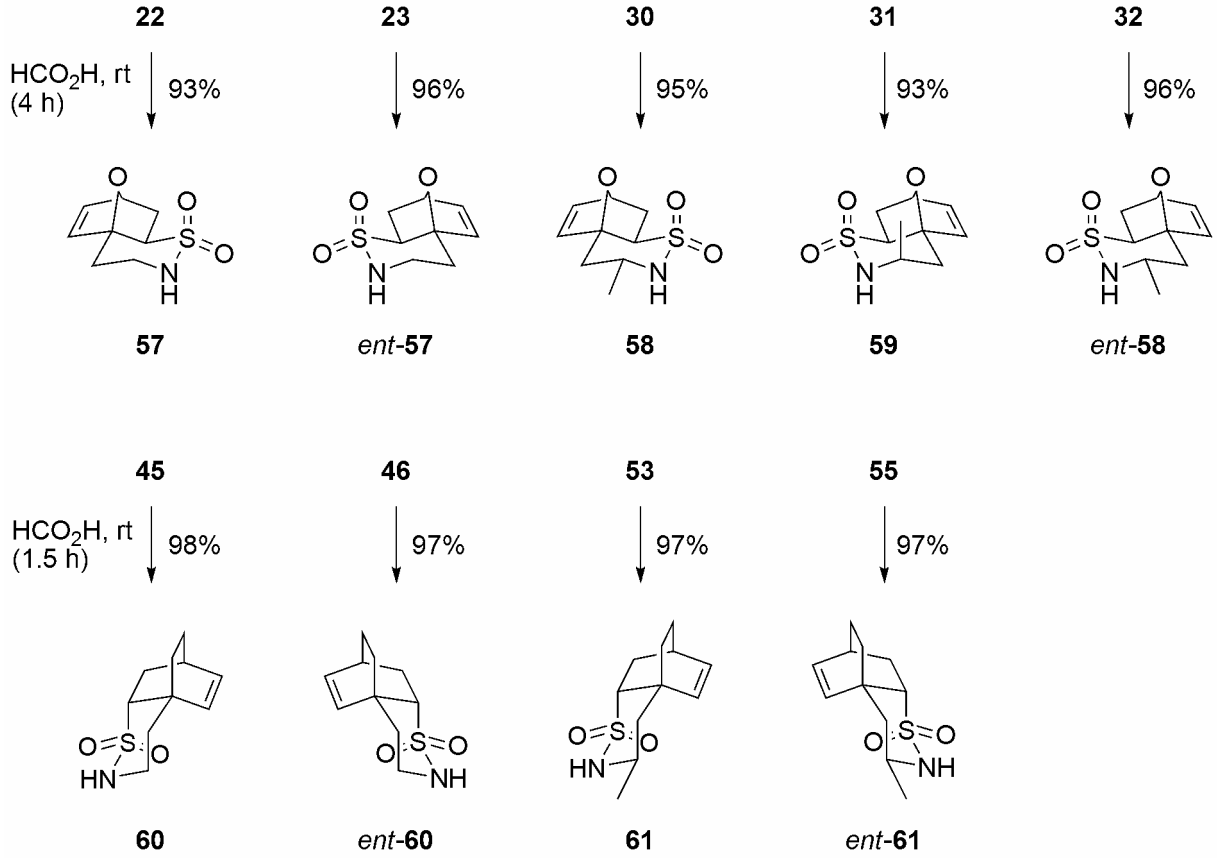
by flash chromatography was not possible. However, pure isomers **53** and **55** could be obtained by recrystallization from methanol of the product mixtures from the high-pressure reactions instead, and their configuration was unequivocally determined by X-ray diffraction analysis.[4a]



Scheme 8. *Reagents and conditions*: (a) MsCl, Et_3N, CH_2Cl_2, 0 °C, 1 h, 96%; (b) (*S*)-(–)-1-phenylethylamine, 80 °C, 12 h, 31% **49** + **50**; (c) CH_2=$CHSO_2Cl$, Et_3N, CH_2Cl_2, 0 °C, 3 h, 76% **51**, 79% **52**; (d) toluene, reflux, 1 bar, 24 h, 44% **53** + **54**, 36% **55** + **56**; (e) CH_2Cl_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[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. 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), CaH_2 (Et_2O), or by passing through activated alumina (CH_2Cl_2). All commercially available compounds were used as received unless stated otherwise. Flash chromatography: Merck silica gel 60 (40–63μm). Thin layer chromatography: Merck silica gel 60 F_{254} plates. Melting points: Kleinfeld Labortechnik Electrothermal IA 9100 apparatus. Optical rotation: Perkin–Elmer 341 polarimeter. ^{1}H- and ^{13}C- NMR: Bruker DRX-500 (^{1}H: 500 MHz, ^{13}C: 126 MHz, $CDCl_3$, calibrated to the residual resonance of the solvent) or Bruker AC-300 (^{1}H: 300 MHz, ^{13}C: 75.4 MHz, $CDCl_3$, 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 Et_2O (4 × 50 mL). The combined organic layers were washed with brine (50 mL), dried over $MgSO_4$, 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%); R_f 0.58 (EtOAc); ^{1}H 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), 7.85–7.89 (m, 2H); ^{13}C 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, 3028, 2941, 2863, 2831, 1446, 1283, 1137, 1070, 1044, 1024, 913, 884, 719, 689, 629, 584, 557 cm^{-1}; Anal. Calcd for $C_{14}H_{18}O_3S$: 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) δ 1.49–1.58 (m, 4H), 1.62–1.79 (m, 4H), 1.83–1.92 (m, 3H), 2.08–2.28 (m, 3H), 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) δ 18.56, 18.61, 19.40, 19.48, 23.92, 25.31, 27.43, 27.51, 30.56, 34.75, 62.22, 62.32, 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), 78 (23), 77 (100), 67 (20), 55 (18), 51 (27); IR 2940, 2872, 1446, 1353, 1288, 1200, 1180, 1137, 1073, 1026, 972, 930, 907, 882, 869, 813, 759, 734, 719, 690, 630, 584, 557 cm^{-1}; Anal. Calcd for $C_{19}H_{26}O_4S$: 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*-butanol (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_2O (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 10:1); ^{1}H NMR (300 MHz) δ 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) δ 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, 74.88; H, 9.80.

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) δ 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) δ 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 $C_8H_{12}O$: 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 CH_2Cl_2 (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 H_2O (100 mL) was added, and the layers shaken and separated. The organic phase was washed with cold H_2O (3 × 100 mL), dried over $MgSO_4$, and concentrated *in vacuo* at max. 35 °C. The residue was purified by flash chromatography (pentane/EtOAc 4:1).

Mesylate 19. Yield 97%; R_f 0.47 (pentane/EtOAc 4:1); ^{1}H NMR (300 MHz) δ 2.89 (s, 3H), 3.07 (t, J = 6.6 Hz, 2H), 4.43 (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); ^{13}C 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%; R_f 0.65 (pentane/EtOAc 4:1); ^{1}H 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); ^{13}C 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 $C_{15}H_{19}NO$: C, 78.56 H, 8.35 N, 6.11. Found: C, 78.89; H, 8.64; N, 6.03.

Mesylate 42. Yield 93%; R_f 0.41 (pentane/EtOAc 4:1); ^{1}H 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); ^{13}C 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 $C_9H_{14}O_3S$: 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 Et_2O (50 mL) were added and the layers shaken and separated. The aqueous phase was extracted (2 × 50 mL, Et_2O), and the combined organic extracts were washed with brine (50 mL), dried ($MgSO_4$), 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%; R_f 0.31 (pentane/EtOAc 4:1); $[\alpha]^{20}_D$ –50.1 (*c* 1.0, CH_2Cl_2); ^{1}H 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); ^{13}C 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 $C_{14}H_{17}NO$: C, 78.10; H, 7.96; N, 6.51. Found: C, 78.89; H, 8.64; N, 6.03.

Amine 26. R_f 0.26 (pentane/EtOAc 4:1); $[\alpha]^{20}_D$ –33.0 (*c* 1.0, CH_2Cl_2); ^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); ^{13}C 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, 1145, 1007, 930, 760, 724, 698, 598, 555 cm^{-1}; Anal. Calcd for $C_{15}H_{19}NO$: C, 78.56; H, 8.35; N, 6.11. Found: C, 78.89; H, 8.64; N, 6.03.

Amine 27. R_f 0.30 (pentane/EtOAc 4:1); $[\alpha]^{20}_D$ –65.3 (*c* 1.0, CH_2Cl_2); ^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); ^{13}C NMR (75.4 MHz) δ 21.20, 24.34, 34.21, 49.74, 55.31, 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 $C_{15}H_{19}NO$: C, 78.56; H, 8.35; N, 6.11. Found: C, 78.27; H, 8.81; N, 5.96.

Amine 43. Yield 79%; R_f 0.65 (pentane/triethylamine 30:1); $[\alpha]^{20}_D$ –53.5 (*c* 1.0, CH_2Cl_2); ^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); ^{13}C NMR (75.4 MHz) δ 22.88, 24.21, 26.20, 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 $C_{16}H_{21}N$: C, 84.53; H, 9.31; N, 6.16. Found: C, 84.77; H, 9.55; N, 6.40.

Amine 49. R_f 0.25 (pentane/EtOAc 4:1); $[\alpha]^{20}_D$ –94.5 (*c* 1.0, CH_2Cl_2); ^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); ^{13}C 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, 128.3, 136.7, 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 $C_{17}H_{23}N$: C, 84.59; H 9.60; N, 5.80. Found: C, 84.95; H 9.76; N, 5.85.

Amine 50. R_f 0.68 (pentane/triethylamine 30:1); $[\alpha]^{20}_D$ –35.4 (*c* 1.0, CH_2Cl_2); ^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); ^{13}C 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 $C_{17}H_{23}N$: 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 CH_2Cl_2 (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 Et_2O (60 mL). The organic layer was washed with water, dried over $MgSO_4$, 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%; R_f 0.43 (pentane/EtOAc 5:1); ^{1}H 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); ^{13}C 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, 1495, 1455, 1334, 1205, 1144, 1091, 1054, 1028, 966, 923, 896, 849, 774, 742, 697, 648 cm^{-1}; Anal. Calcd for $C_{15}H_{19}NO_2S$: C, 64.95; H, 6.90; N, 5.05; S, 11.56. Found: C, 64.90; H, 6.95; N, 4.87; S, 11.48.

Vinylsulfonamide 5. Reaction time 2 h. Yield 95%; R_f 0.85 (pentane/EtOAc 4:1); ^{1}H 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); ^{13}C 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, 144.39, 146.18 ; 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 3063, 3031, 2952, 2898, 2843, 2784, 1633, 1604, 1453, 1337, 1247, 1146, 836, 787, 756, 741, 696, 555 cm^{-1}; Anal. Calcd for $C_{18}H_{27}NO_2SSi$: 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%; R_f 0.78 (pentane/EtOAc 4:1); ^{1}H 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); ^{13}C 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

cm^{-1}; Anal. Calcd for $C_{18}H_{23}NO_2S$: C, 68.14; H, 7.26; N, 4.42; S, 10.09. Found: C, 67.97; H, 7.60; N 4.28; S 9.87.

Vinylsulfonamide 12. Reaction time 2 h. Yield 98%; R_f 0.60 (pentane/EtOAc 4:1); $[\alpha]^{20}_D$ –1.6 (*c* 1.0, CH_2Cl_2); ^{1}H NMR (300 MHz) δ 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) δ 17.79, 39.95, 55.80, 109.37, 110.50, 125.17, 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 3112, 3061, 3030, 2980, 2939, 2871, 1603, 1496, 1452, 1331, 1134, 1006, 929, 882, 780, 738, 697, 653, 599, 563, 540 cm^{-1}; Anal. Calcd for $C_{15}H_{17}NO_3S$: C, 61.83; H, 5.88; N, 4.81; S 11.01. 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); $[\alpha]^{20}_D$ –2.1 (*c* 1.0, CH_2Cl_2); ^{1}H NMR (300 MHz) δ 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) δ 17.75, 29.78, 42.65, 55.92, 106.15, 110.12, 126.04, 127.61, 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 (4), 81 (6), 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 $C_{16}H_{19}NO_3S$: 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); $[\alpha]^{20}_D$ –29.0 (*c* 1.0, CH_2Cl_2); ^{1}H NMR (300 MHz) δ 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), 4.92 (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) δ 17.68, 20.03, 35.87, 52.66, 56.40, 107.32, 110.37, 124.99, 127.87, 127.92, 128.37, 138.53, 139.71, 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 $C_{17}H_{21}NO_3S$: 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; $[\alpha]^{20}_D$ +38.0 (*c* 1.0, CH_2Cl_2); ^{1}H NMR (300 MHz, $CDCl_3$) δ 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) δ 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 $C_{17}H_{21}NO_3S$: 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); $[\alpha]^{20}_D$ –14.2 (*c* 1.0, CH_2Cl_2); ^1H 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); ^{13}C 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 $C_{18}H_{23}NO_2S$: 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); $[\alpha]^{20}_D$ +29.4 (*c* 1.0, CH_2Cl_2); ^1H 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); ^{13}C NMR (75.4 MHz) δ 18.4, 19.5, 22.8, 26.4, 45.3, 51.9, 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^+], 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 $C_{19}H_{25}NO_2S$: 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); $[\alpha]^{20}_D$ –10.0 (*c* 1.0, CH_2Cl_2); mp 96–97 ºC; ^1H 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); ^{13}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) [$M^+ - CH_3$], 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 $C_{19}H_{25}NO_2S$: 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_2Cl_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) δ 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) δ 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 $C_{15}H_{19}NO_2S$: 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 δ 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 = 9.7Hz, 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 δ –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 (0.5), 212 (11), 166 (38), 151 (9), 120 (23), 106 (12), 92 (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 $C_{18}H_{27}NO_2SSi$: 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; ^{1}H NMR (300 MHz) δ 0.89–0.99 (m, 1H), 1.10–1.27 (m, 1H), 1.31–1.44 (m, 2H), 1.72–1.76 (m, 2H), 1.92–2.07 (m, 3H), 2.18–2.26 (m, 2H), 2.71–2.75 (m, 1H), 3.15 (br. s, 1H), 3.24–3.28 (m, 2H), 4.10 (d, J = 14.6 Hz, 1H), 4.30 (d, J = 14.6 Hz, 1H), 6.24 (s, 1H), 7.28 (m, 5H); ^{13}C NMR (75.4 MHz) δ 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 $C_{18}H_{23}NO_2S$: C, 68.10; H, 7.30; N, 4.41; S 10.10. 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_2Cl_2); ^{1}H NMR δ 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 δ 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 $C_{15}H_{17}NO_3S$: 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_f 0.18 (pentane/EtOAc 4:1); mp 120–121 °C; $[\alpha]^{20}_D$ –69.0 (*c* 1.0, CH_2Cl_2); ^{1}H NMR δ 1.73 (d, *J* = 6.9 Hz, 3H), 1.81 (dd, *J* = 7.9, 12.4 Hz, 1H), 2.65 (ddd, *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 δ 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, 1286, 1243, 1168, 1132, 1065, 986, 865, 771, 708, 695, 668, 612, 539 cm^{-1}; Anal. Calcd for $C_{15}H_{17}NO_3S$: 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 22. R_f 0.47 (pentane/EtOAc 1:1); mp 137–138 °C (EtOAc); $[\alpha]^{20}_D$ –36.2 (*c* 1.0, CH_2Cl_2); ^{1}H NMR δ 1.62 (d, *J* = 7.0 Hz, 3H), 1.73 (m, 2H), 2.02 (dt, *J* = 2.3, 14.6 Hz, 1H), 2.55 (m, 1H), 3.00 (dddd, *J* = 2.2, 5.5, 7.5, 13.9 Hz, 1H), 3.08 (dd, *J* = 3.3, 7.8 Hz, 1H), 3.49 (ddd, *J* = 1.7, 4.5, 13.4 Hz, 1H), 5.11 (dd, *J* = 1.6, 4.7 Hz, 1H), 5.45 (q, *J* = 7.0 Hz, 1H), 5.86 (d, *J* = 5.6 Hz, 1H), 6.48 (dd, *J* = 1.7, 5.6 Hz, 1H), 7.30 (m, 1H), 7.35 (m, 2H), 7.40 (m, 2H); ^{13}C NMR δ 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 $C_{16}H_{19}NO_3S$: C, 62.93; H, 6.27; N, 4.59; S 10.50. Found: C, 63.43; H, 6.38; N4.65; S 10.47.

Sultam 23. R_f 0.34 (pentane/EtOAc 1:1); mp 155–156 °C (EtOAc); $[\alpha]^{20}_D$ +10.0 (*c* 1.0, CH_2Cl_2); ^{1}H NMR δ 1.64 (d, *J* = 7.0 Hz, 3H), 1.76 (dd, *J* = 7.8, 12.3 Hz, 1H), 2.25 (m, 2H), 2.54 (m, 1H), 3.03 (m, 1H), 3.04 (dd, *J* = 3.3, 7.8 Hz, 1H), 3.26 (m, 1H), 5.12 (dd, *J* = 1.6, 4.7 Hz, 1H), 5.45 (q, *J* = 7.0 Hz, 1H), 6.02 (d, *J* = 5.6 Hz, 1H), 6.52 (dd, *J* =1.7, 5.6 Hz, 1H), 7.30 (m, 1H), 7.35 (m, 2H), 7.40 (m, 2H); ^{13}C NMR δ 18.88, 28.54, 29.20, 39.48, 53.52, 59.83, 78.28, 89.16, 127.59, 127.64, 128.43, 136.32, 139.59, 139.84; MS (GC/MS, 70 eV) *m/z* (rel. intensity) 305 (2) [M^+], 105 (100), 91 (4), 81 (7), 79 (5), 77 (6); IR (KBr) 3089, 3028, 2968, 2883, 1495, 1451, 1424, 1381, 1363, 1312, 1249, 1233, 1158, 1139, 1080, 1056, 1025, 974, 906, 848, 827, 789, 773, 756, 700, 632, 568, 545 cm^{-1}; Anal. Calcd for $C_{16}H_{19}NO_3S$: C, 62.93; H, 6.27; N, 4.59; S 10.50. Found: C, 63.08; H, 6.35; N, 4.59; S 10.26.

Sultam 30. R_f 0.35 (pentane/EtOAc 4:1); mp 164–165 °C; $[\alpha]^{20}_D$ +12.5 (*c* 1.0, CH_2Cl_2); ^{1}H NMR δ 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 (ddd, *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*

= 1.7, 5.7 Hz, 1H), 7.28–7.36 (m, 3H), 7.46 (d, *J* = 7.25 Hz, 2H); ^{13}C NMR δ 16.9, 22.2, 30.8, 30.9, 48.1, 55.1, 61.2, 77.2, 87.3, 127.4, 127.9, 128.2, 137.2, 137.7, 142.2; 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) 3442, 2993, 1625, 1451, 1391, 1317, 1145, 1005 cm^{-1}; Anal. Calcd for $C_{17}H_{21}NO_3S$: C 63.92; H, 6.63; N, 4.39; S 10.04. Found: C 63.50; H, 6.67; N, 4.20; S 9.83.

Sultam 31. R_f 0.31 (pentane/EtOAc 4:1); mp 173–174 °C; $[\alpha]^{20}_D$ +22.5 (*c* 1.0, CH_2Cl_2); ^{1}H NMR δ 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 δ 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) *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 $C_{17}H_{21}NO_3S$: C, 63.92; H, 6.63; N, 4.39; S 10.04. 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_2Cl_2); ^{1}H NMR δ 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 δ 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) *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 $C_{17}H_{21}NO_3S$: 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_2Cl_2); mp 139–140 °C (methanol); ^{1}H NMR δ 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 (ddddd, *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 (dddd, *J* = 2.7, 4.4, 7.1, 13.4 Hz, 1H), 3.15 (dd, *J* = 5.7, 9.6 Hz, 1H), 3.41 (ddd, *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 δ 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) *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 $C_{18}H_{23}NO_2S$: C, 68.10; H, 7.30; 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_2Cl_2); mp 158–159 °C (methanol); ^{1}H NMR δ 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 (dddd, *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 δ 18.52, 24.46, 28.13, 29.62, 34.38, 35.40, 39.32, 40.67,

53.09, 62.83, 127.37, 127.74, 128.26, 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 $C_{18}H_{23}NO_2S$: 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. R_f 0.47 (pentane/EtOAc 4:1); $[\alpha]^{20}_D$ +0.4 (*c* 1.0, CH_2Cl_2); 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); ^{13}C 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 $C_{19}H_{25}NO_2S$: C, 68.85; H, 7.60; N, 4.23; S 9.67. Found: C, 68.98; H, 7.78; N, 4.19; S 9.72.

Sultam 55. R_f 0.47 (pentane/EtOAc 4:1); $[\alpha]^{20}_D$ –2.3 (*c* 1.0, CH_2Cl_2); mp 149–151 °C (methanol); ^1H NMR δ 1.19 (d, *J* = 7.0 Hz, 3H), 1.21–1.36 (m, 2H), 1.44–1.55 (m, 1H), 1.57–1.70 (m, 3H), 1.79 (d, *J* = 7.2 Hz, 3H), 1.92–2.01 (m, 2H), 2.64–2.68 (m, 1H), 2.84 (dd, *J* = 6.3, 9.7 Hz, 1H), 4.02–4.09 (m, 1H), 5.19 (q, *J* = 7.1 Hz, 1H), 5.92 (d, *J* = 8.3 Hz, 1H), 6.31 (dd, *J* = 8.1, 15.0 Hz, 1H), 7.23–7.39 (m, 3H), 7.42–7.45 (d, *J* = 7.5 Hz, 2H); ^{13}C NMR δ 20.4, 21.7, 24.0, 29.2, 29.6, 34.5, 38.2, 41.9, 51.4, 53.7, 61.8, 127.1, 127.9, 128.1, 132.9, 134.0, 141.8; MS (GC/MS, 70 eV) *m/z* (rel. intensity) 331 (0.1) [M^+], 316 (18), 252 (10), 227 (12), 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, 769, 705, 627, 544 cm^{-1}; Anal. Calcd for $C_{19}H_{25}NO_2S$: C, 68.85; H, 7.60; N, 4.23; S 9.67. Found: C, 68.95; H, 7.94; N, 4.24; S 9.64.

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%; R_f 0.41 (EtOAc); mp 149–150 °C (EtOAc); $[\alpha]^{20}_D$ –10.7 (*c* 1.0, CH_2Cl_2); ^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); ^{13}C 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. Calcd for $C_8H_{11}NO_3S$: 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%; R_f 0.41 (EtOAc); mp 150–151 °C (EtOAc); $[\alpha]^{20}_D$ +10.7 (*c* 1.0, CH_2Cl_2); ^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); ^{13}C 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) 3264, 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. Calcd for $C_8H_{11}NO_3S$: 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%; R_f 0.55 (EtOAc); mp 175–176 °C; $[\alpha]_D$ +3.2 (*c* 1.0, CH_2Cl_2); ^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); ^{13}C 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. Calcd for $C_9H_{13}NO_3S$: 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%; R_f 0.55 (EtOAc); mp 175–176 °C; $[\alpha]^{20}_D$ –3.2 (*c* 1.0, CH_2Cl_2); ^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); ^{13}C 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. Calcd for $C_9H_{13}NO_3S$: C, 50.21; H, 6.09; N, 6.51; O, 22.30; S 14.90. Found: C, 49.98; H, 6.28; N, 6.63; S 14.79.

Sultam 59. Yield 93%; R_f 0.57 (EtOAc); mp 145–147 °C; $[\alpha]^{20}_D$ +17.8 (*c* 1.0, CH_2Cl_2); ^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); ^{13}C 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. Calcd for $C_9H_{13}NO_3S$: 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%; R_f 0.47 (EtOAc); mp 137–138 °C (methanol); $[\alpha]^{20}_D$ +10.4 (*c* 1.0, CH_2Cl_2); ^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_c, 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 $C_{10}H_{15}NO_2S$: 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); $[\alpha]^{20}_D$ –10.4 (*c* 1.0, CH_2Cl_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_c, 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 $C_{10}H_{15}NO_2S$: 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); $[\alpha]^{20}_D$ +10.1 (*c* 1.0, CH_2Cl_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_c, 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 $C_{11}H_{17}NO_2S$: 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); $[\alpha]^{20}_D$ –10.1 (*c* 1.0, CH_2Cl_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_c, 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); IR 3194, 3042, 2944, 2860, 1449, 1319, 1277, 1162, 1137, 1105, 1059, 971, 768, 749, 699, 576 cm^{-1}; Anal. Calcd for $C_{11}H_{17}NO_2S$: 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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