Supporting Information

Ring-Opening Metathesis Phase-Trafficking (ROMpt) Synthesis: Multistep Synthesis on Soluble ROM Supports

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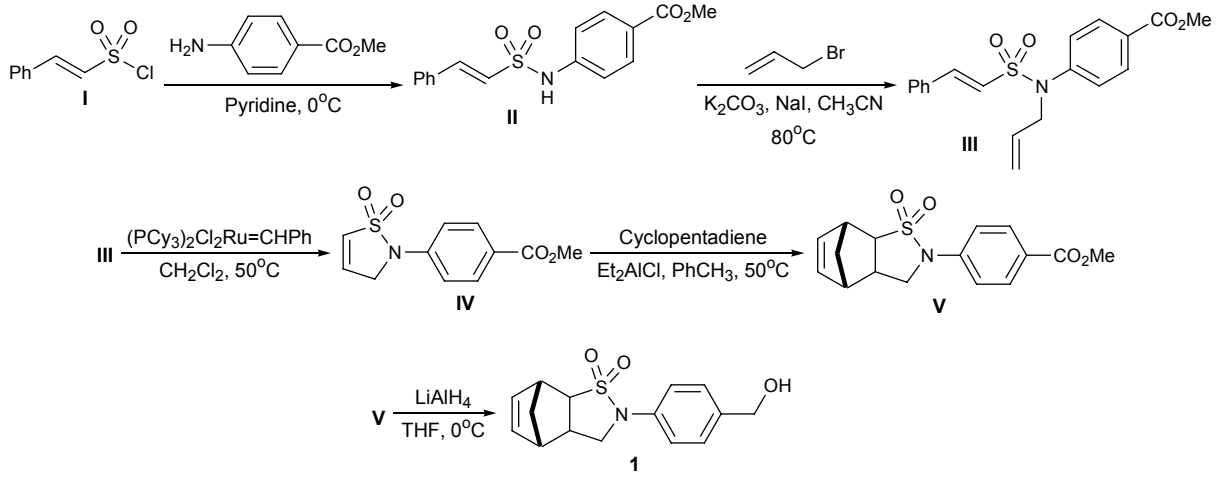
Experimental Section

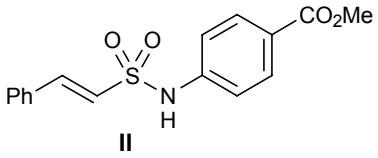
General Methods

All air and moisture sensitive reactions were carried out in flame- or oven-dried glassware under argon using standard gas-tight syringes, cannulaes, and septa. CH_2Cl_2 was purified by distillation over CaH_2 or by passage through a Solv-Tek (www.solvtek.com) purification system employing activated Al_2O_3 (Pangborn, A. B.; Giardello, M. A.; Grubbs, R. H.; Rosen, R. K.; Timmers, F. J. *Organometallics* 1996, *15*, 1518). THF and Et_2O were purified by passage through the Solv-Tek purification system employing activated Al_2O_3. Benzene was purified by distillation over CaH_2. Et_3N was distilled from CaH_2 and stored over KOH. DMAP was purchased from Reilly Chemicals and was not further purified. All amino acid precursors were purchased from Advanced Chem Tech. Thin layer chromatography was performed on silica gel $60F_{254}$ plates (EM-5717, Merck). Visualization of TLC spots was effected using $KMnO_4$ stain. Flash column chromatography was performed with Merck silica gel (EM-9385-9, 230-400 mesh). Deuterochloroform ($CDCl_3$) was purchased from Cambridge Isotope Laboratories and stored over molecular sieves (4 Å) at room temperature. ^1H and ^{13}C NMR spectra were recorded in $CDCl_3$ (unless otherwise mentioned) on either a Bruker DRX-400 MHz spectrometer operating at 400

MHz and 100 MHz, respectively; or a Bruker Avance-500 MHz spectrometer operating at 500 MHz and 126 MHz, respectively. High resolution mass spectrometry (HRMS) and FAB spectra were performed by the Mass Spectrometry Laboratory at the University of Kansas using a VG Instrument ZAB double-focusing mass spectrometer.



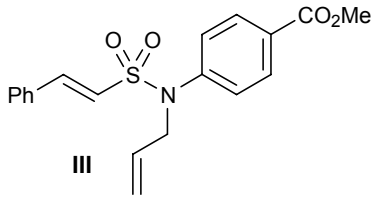
4-(2-Phenyl-ethenesulfonylamino)-benzoic acid methyl ester (II)



An oven-dried flask was charged with methyl 4-aminobenzoate (7.46 g, 49.3 mmol) and 50 mL of dry pyridine was added. The mixture was cooled with an ice bath and styrene sulfonyl chloride (**I**, 9.99 g, 49.3 mmol) was added in portions over 30 min. After complete addition, the reaction was stirred at 0 ^{o}C for 1 hr 45 min. The ice bath was then removed and the reaction was allowed to stir at ambient temperature for 30 min. The reaction mixture was quenched by the addition of 10% aqueous HCl (150 mL). The resulting mixture was extracted with EtOAc (3x 150 mL), and the combined organic extracts were washed with 10% HCl followed by brine, then dried ($MgSO_4$) and concentrated. The crude solid was recrystallized from toluene to yield **II** (14.7 g, 94%) as white needles: mp 142-143 °C; R_f = 0.21 (Heptane/EtOAc: 2/1); FTIR (neat) 3232, 3057, 2950, 1716, 1603, 1342, 1147 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.98 (bd, *J* = 8.7 Hz, 2H), 7.60 (d, *J* = 15.4 Hz, 1H), 7.44-7.35 (m, 5H), 7.28-7.22 (m, 2H), 7.19-7.16 (m, 1H), 6.81 (d, *J* = 15.4 Hz, 1H), 3.88 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.45, 143.91, 140.98,

131.87, 131.32, 131.21, 129.07, 128.45, 125.90, 123.80, 118.33, 52.09; HRMS calcd for $C_{16}H_{16}NO_4S$ $(M+H)^+$ required 318.0800, found 318.0806.

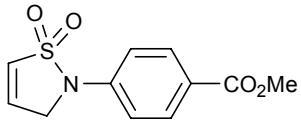
4-[Allyl-(2-phenyl-ethenesulfonyl)-amino]-benzoic acid methyl ester (III)



III

An oven dried flask was charged with compound **II** (14.7 g, 46.3 mmol), K_2CO_3 (13.0 g, 94.1 mmol), and NaI (2.31 g, 15.4 mmol). Acetonitrile (150 mL) was added, followed by allyl bromide (15 mL, 173.3 mmol). The reaction mixture was allowed to stir at reflux for 3 hrs. The reaction was partitioned between water (100 mL) and CH_2Cl_2 (20 mL). The aqueous layer was extracted with CH_2Cl_2 (3x) and the combined organic layer was washed with water, brine and then dried ($MgSO_4$). Evaporation of the organic layer afforded crude compound **III** (9.39 g, 81%) as a pale yellow solid which was used without further purification: mp 109-110 °C; R_f = 0.35 (Heptane/EtOAc: 2/1); FTIR (neat) 3058, 3032, 2950, 1716, 1603, 1347, 1153 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.02 (bd, *J* = 8.6 Hz, 2H), 7.47-7.38 (m, 8H), 6.74 (d, *J* = 15.4 Hz, 1H), 5.81 (ddt, *J* = 16.4, 10.2, 6.2 Hz, 1H), 5.17 (d, *J* = 16.6 Hz, 1 H), 5.14 (d, *J* = 10.2 Hz, 1H), 4.31 (d, *J* = 6.2 Hz, 2H), 3.91 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.10, 143.37, 142.80, 132.42, 132.20, 130.97, 130.36, 129.00, 128.82, 128.19, 127.54, 122.88, 119.16, 53.09, 52.12; HRMS calcd for $C_{19}H_{20}NO_4S$ $(M+H)^+$ required 358.1113, found 358.1123.

4-(1,1-Dioxo-1,3-dihydro-1 λ^6-isothiazol-2-yl)-benzoic acid methyl ester (IV)

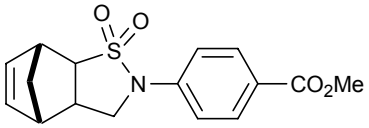


IV

Compound **III** (11.9 g, 33.3 mmol) was dissolved in 420 mL of degassed CH_2Cl_2. Grubbs catalyst ($(PCy_3)_2Cl_2Ru$=CHPh, 1.10 g, 1.33 mmol) was added and the reaction mixture was heated to reflux. After 3 hr 333.2 mg Grubbs catalyst was added and another 146.9 mg was added after 2 more hr. After a further 1.5 hr the reaction was cooled to rt and 2.8 mL DMSO was

added followed by 191 g silica gel.[1] The mixture was stirred open to the air overnight at which time it was poured onto 191 g of fresh silica. The silica was washed repeatedly with CH_2Cl_2 to afford compound **IV** (6.36 g, 75%) as a white solid: mp 210 °C dec; R_f = 0.05 (Heptane/EtOAc: 2/1); FTIR (neat) 3104, 1711, 1619, 1291, 1189, 1132, 845, 768 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.07 (bd, *J* = 9.0 Hz, 2H), 7.33 (bd, *J* = 8.9 Hz, 2H), 7.04 (dt, *J* = 7.22, 2.4 Hz, 1H), 6.83 (dt, *J* = 7.2, 2.3 Hz, 1H), 4.53 (dd, *J* = 2.3, 2.3 Hz, 2H), 3.91 (s, 3H); ^{13}C NMR (125 MHz, $(CD_3)_2CO$) δ 166.72, 142.66, 135.98, 131.71, 128.07, 124.98, 116.38, 52.17, 50.99; HRMS calcd for $C_{11}H_{12}NO_4S$ $(M+H)^+$ required 254.0487, found 254.0485.

4-(3,3-Dioxo-3λ^6-thia-4-aza-tricyclo[5.2.1.0^{2,6}]dec-8-en-4-yl)-benzoic acid methyl ester (V)



V

Et_2AlCl (1.8M in toluene, 26 mL, 46.8 mmol) and cyclopentadiene (2.5 mL, 30 mmol) were added sequentially to a solution of the sulfonamide **IV** (4.86 g, 19.2 mmol) in toluene (40 mL) maintained at –78 ºC. The dry ice bath was removed, and the reaction mixture allowed to stir at rt for 1.5 hr at which time it was heated to 50 ºC overnight. After cooling to rt, the reaction mixture was cooled to 0 ºC and quenched by the slow addition of 10% aqueous HCl. The mixture was then partitioned and that aqueous layer extracted with EtOAc. The combined organic extracts were washed with saturated aq. $NaHCO_3$, dried (Na_2SO_4), and concentrated. Flash chromatography (Hexane/EtOAc: 4:1, then 3:1, then 2:1, then 1:1) afforded 5.54 g (91%) of an 8:1 endo/exo-mixture of **V**. Pure diastereomers were obtained by flash chromatography (Hexane/EtOAc: 2/1).

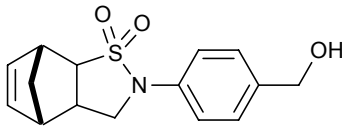
Exo adduct: mp 165-166 °C; R_f = 0.17 (Heptane/EtOAc: 2/1); FTIR (neat) 3078, 2986, 2955, 1711, 1613, 1311, 1132 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.02 (bd, *J* = 8.9 Hz, 2H), 7.38 (bd, *J* = 8.9 Hz, 2H), 6.37 (dd, *J* = 5.7, 3.1 Hz, 1H), 6.25 (dd, *J* = 5.6, 3.1 Hz, 1H), 3.92 (dd, *J* = 10.0, 8.5 Hz, 1H), 3.90 (s, 3H), 3.51 (bs, 1H), 3.47 (dd, *J* = 10.0, 2.5 Hz, 1H), 3.30 (d, *J* = 8.4 Hz, 1H), 2.96 (bs, 1H), 2.74 (dddd, *J* = 8.4, 8.4, 1.6, 1.6 Hz, 1H), 2.18 (bd, *J* = 9.7 Hz, 1H), 1.62 (ddd, *J* = 9.8, 1.4, 1.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.36, 142.10, 140.21, 135.98, 130.80,

[1] For the use of DMSO and silica gel to remove ruthenium byproducts, see: Ahn, Y. M.; Yang, K.; Georg, G. I. *Org. Lett.* **2001**, *3*, 1411-1413.

125.74, 118.68, 62.92, 51.98, 49.07, 48.38, 45.40, 43.45, 38.83; HRMS calcd for $C_{16}H_{18}NO_4S$ $(M+H)^+$ required 320.0957, found 320.0958.

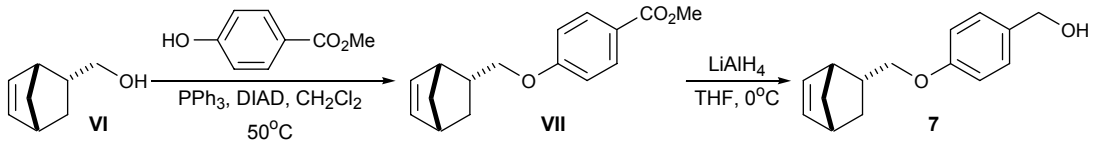
Endo adduct: mp 123-124 °C; R_f = 0.10 (Heptane/EtOAc: 2/1); FTIR (neat) 3078, 2981, 2950, 1716, 1613, 1316, 1132 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.97 (bd, *J* = 8.8 Hz, 2H), 7.26 (bd, *J* = 8.8 Hz, 2H), 6.46 (dd, *J* = 5.6, 2.9 Hz, 1H), 6.27 (dd, *J* = 5.6, 3.1 Hz, 1H), 3.97 (dd, *J* = 9.6, 3.9 Hz, 1H), 3.89 (s, 3H), 3.75 (dd, *J* = 9.7, 9.7 Hz, 1H), 3.52 (bs, 1H), 3.31-3.25 (m, 2H), 3.20 (bs, 1H), 1.69 (bd, *J* = 8.9 Hz, 1H), 1.47 (bd, *J* = 9.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.15, 141.85, 135.74, 133.31, 130.49, 124.92, 117.97, 63.99, 51.73, 50.09, 47.35, 46.63, 46.49, 37.66.

[4-(3,3-Dioxo-3 λ^6-thia-4-aza-tricyclo[5.2.1. 0^{2,6}]dec-8-en-4-yl)-phenyl]-methanol (1)

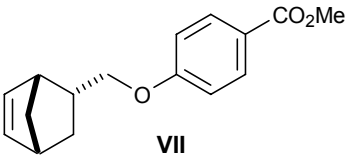


1

Compound **V** (642.7 mg, 2.01 mmol) was dissolved in 5 mL of THF at 0 °C. $LiAlH_4$ (78 mg, 2.06 mmol) was added portionwise and the reaction mixture was allowed to stir cold for 30 min. The reaction was quenched by slow addition of 10% aq. HCl. The mixture was diluted with EtOAc and the organic layer was separated and washed with 10% HCl (2x). The combined aqueous layers were reextracted with EtOAc (2x). The combined organic layers were washed once with saturated aq. $NaHCO_3$, once with brine, dried ($MgSO_4$) and concentrated. Flash chromatography (Heptane/EtOAc: 1/1) afforded **1** (583.3 mg, 99%) as an off-white waxy solid. Major *endo* isomer: R_f = 0.04 (Heptane/EtOAc: 2/1); FTIR (neat) 3498, 3073, 2976, 1609, 1296, 1132 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.31 (bd, *J* = 8.5 Hz, 2H), 7.23 (bd, *J* = 8.6 Hz, 2H), 6.46 (dd, *J* = 5.6, 2.9 Hz, 1H), 6.27 (dd, *J* = 5.6, 3.0 Hz, 1H), 4.63 (s, 2H), 3.90 (dd, *J* = 9.3, 3.9 Hz, 1H), 3.74 (dd, *J* = 9.5, 8.0 Hz, 1H), 3.49 (bs, 1H), 3.24-3.15 (m, 3H), 1.98 (bs, 1H), 1.65 (bd, *J* = 8.9 Hz, 1H), 1.44 (bd, *J* = 8.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 137.90, 136.57, 135.94, 133.31, 127.91, 121.69, 64.74, 63.57, 50.43, 48.27, 46.87, 46.69, 38.12; HRMS calcd for $C_{15}H_{18}NO_3S$ $(M+H)^+$ required 292.1007, found 292.0995.

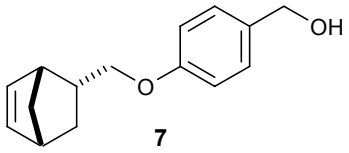


4-(Bicyclo[2.2.1]hept-5-en-2-ylmethoxy)-benzoic acid methyl ester (VII)



DIAD (2.5 mL, 12.6 mmol) was added dropwise slowly to an oven dried flask charged with 5-norbornene-2-methanol (**VI**, 1.05 g, 8.44 mmol), PPh_3 (3.22 g, 12.3 mmol), and methyl 4-hydroxybenzoate (1.42 g, 9.30 mmol) in 10 mL of CH_2Cl_2 at 0 ^oC. The reaction was stirred at rt overnight. The reaction mixture was then concentrated and subjected directly to column chromatography (6:1 heptane:EtOAc) to yield **VII** (1.57 g, 72%) as a white solid: mp 69-70 °C; R_f = 0.55 (Heptane/EtOAc: 2/1); FTIR (neat) 3058, 2945, 1721, 1603, 1285, 1250, 1168 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.97 (bd, *J* = 8.9 Hz, 2H), 6.88 (bd, *J* = 8.9 Hz, 2H), 6.18 (dd, *J* = 5.7, 3.0 Hz, 1H), 5.95 (dd, *J* = 5.7, 2.9 Hz, 1H), 3.88 (s, 3H), 3.76 (dd, *J* = 9.1, 6.5 Hz, 1H), 3.59 (dd, *J* = 9.2, 9.2 Hz, 1H), 3.04 (bs, 1H), 2.86 (bs, 1H), 2.57 (ddddd, *J* = 9.4, 9.4, 9.4, 4.2, 4.2, Hz, 1H), 1.93 (ddd, *J* = 11.9, 9.3, 3.8 Hz, 1H), 1.49 (dd, *J* = 8.2, 2.0 Hz, 1H), 1.31 (bd, *J* = 8.2 Hz, 1H), 0.63 (ddd, *J* = 11.7, 4.4, 2.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.87, 162.93, 137.68, 132.21, 131.50, 122.24, 114.05, 71.60, 51.79, 49.42, 43.84, 42.22, 38.24, 28.99; HRMS calcd for $C_{16}H_{19}O_3$ $(M+H)^+$ required 259.1334, found 259.1323.

[4-(Bicyclo[2.2.1]hept-5-en-2-ylmethoxy)-phenyl]-methanol (7)



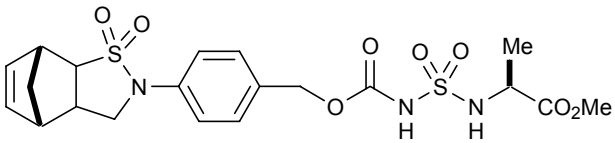
Compound **VII** (774 mg, 3 mmol) was dissolved in 6 mL of THF at 0^oC. $LiAlH_4$ (123 mg, 3.24 mmol) was added portionwise and the reaction mixture was allowed to stir cold for 1.5 hrs. The reaction was quenched by slow addition of 10% aq. HCl. The mixture was diluted with EtOAc and the organic layer was separated. The organic layer was separated and washed with 10% HCl

(2x), saturated aq. $NaHCO_3$, and brine. The combined organic layers were dried (Na_2SO_4) and removed under reduced pressure. The crude product was then eluted through a short column of silica with 1:1 Heptane:EtOAc to afford **7** (689.3 mg, 99%) as an off-white solid: mp 44-45 °C; R_f = 0.26 (Heptane/EtOAc: 2/1); FTIR (neat) 3345, 3053, 2945, 1614, 1245, 1173 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.27 (bd, *J* = 8.3 Hz, 2H), 6.86 (bd, *J* = 8.4 Hz, 2H), 6.17 (dd, *J* = 5.7, 3.0 Hz, 1H), 5.95 (dd, *J* = 5.6, 2.9 Hz, 1H), 4.61 (s, 2H), 3.71 (dd, *J* = 9.1, 6.5 Hz, 1H), 3.54 (dd, *J* = 9.1, 9.1 Hz, 1H), 3.03 (bs, 1H), 2.85 (bs, 1H), 2.56 (ddddd, *J* = 9.4, 9.4, 9.4, 3.9, 3.9, Hz, 1H), 1.91 (ddd, *J* = 13.1, 9.3, 3.8 Hz, 1H), 1.55 (bs, 1H), 1.48 (dd, *J* = 8.2, 1.7 Hz, 1H), 1.30 (bd, *J* = 8.2 Hz, 1H), 0.62 (ddd, *J* = 11.7, 3.7, 2.7 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.78, 137.49, 132.85, 132.32, 128.56, 114.57, 71.52, 65.02, 49.39, 43.86, 42.21, 38.32, 29.02; HRMS calcd for $C_{15}H_{18}O_2$ (M+) required 230.1307, found 230.1291.

General procedure for compounds 2a-d and 8a,b:

To a stirring solution of chlorosulfonyl isocyanate (98 µl, 1.12 mmol) and CH_2Cl_2 (2 mL) at 0 ^0C was added a solution of **1** (328 mg, 1.12 mmol) in CH_2Cl_2 (3 mL) dropwise over a period of 10 min. The resulting solution was transferred via cannula to a mixture of the hydrochloride salt of the respective amino acid methyl ester (1.12 mmol) and Et_3N (312 µL, 2.24 mmol) in CH_2Cl_2 (3 mL) at 0 ^0C. The slurry was allowed to warm to room temperature and stirred for an additional 3h. The organic portion was washed with H_2O (2x), brine (2x), and dried (Na_2SO_4). The mixture was filtered, concentrated and subjected to flash chromatography to afford the desired compound.

Sulfonamide-based alanine-derived sulfamoyl carbamate (2a)

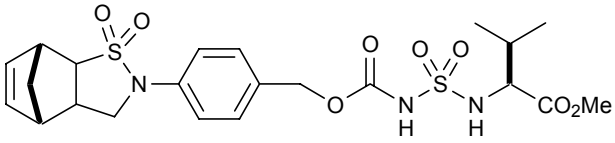


2a

The general procedure above was followed starting with chlorosulfonyl isocyanate (98 µL, 1.12 mmol), **1** (328 mg, 1.12 mmol), H-Ala-OMe·HCl (156 mg, 1.12 mmol) and Et_3N (312 µL, 2.24 mmol). Flash chromatography (CH_2Cl_2/MeOH: 49:1) produced **2a** (460 mg, 82%) as a white solid: R_f = 0.11 (CH_2Cl_2/MeOH: 49/1); FTIR (neat) 3270, 2954, 2875, 1744, 1614, 1515, 1455,

1358, 1297, 1226, 1162, 1130 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.31 (d, *J* = 8.5 Hz, 2H), 7.23 (d, *J* = 8.5 Hz, 2H), 6.41 (dd, *J* = 5.6, 2.9 Hz, 1H), 6.26 (dd, *J* = 5.5, 2.9 Hz, 1H), 6.11 (bs, 1H), 5.10 (d, *J* = 12.2 Hz, 1H), 5.06 (d, *J* = 12.2 Hz, 1H), 4.24 (bd, *J* = 5.7 Hz, 1H), 3.92 (dd, *J* = 9.0, 3.0 Hz, 1H), 3.71 (dd, *J* = 9.5, 8.4 Hz, 1H), 3.66 (s, 3H), 3.47 (bs, 1H), 3.24-3.16 (m, 3H), 1.64 (d, *J* = 8.9 Hz, 1H), 1.45 (d, J = 8.9 Hz, 1H), 1.40 (d, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.71, 151.60, 137.88, 136.00, 133.68, 131.42, 129.63, 121.08, 67.93, 63.95, 52.99, 52.59, 50.57, 48.20, 47.04, 46.88, 38.18, 19.24; HRMS calcd for $C_{20}H_{29}N_4O_8S_2(M+NH_4)^+$ required 517.1427, found 517.1443.

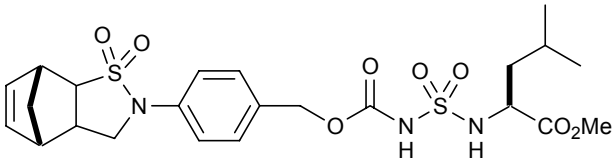
Sulfonamide-based valine-derived sulfamoyl carbamate (2b)



2b

The general procedure above was followed starting with chlorosulfonyl isocyanate (85 μL, 0.98 mmol), **1** (285 mg, 0.98 mmol), H-Val-OMe·HCl (164 mg, 0.98 mmol) and Et_3N (273 μL, 1.96 mmol). Flash chromatography (Hexane/EtOAc: 3:2) afforded **2b** (465 mg, 90%) as a white solid: R_f = 0.52 (Hexane/EtOAc: 1:4); FTIR (neat) 3269, 2967, 1743, 1614, 1515, 1469, 1360, 1303, 1273, 1226, 1163, 1139, 1092 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.31 (d, *J* = 8.5 Hz, 2H), 7.23 (d, *J* = 8.5 Hz, 2H), 6.44 (dd, *J* = 5.6, 2.9 Hz, 1H), 6.26 (dd, *J* = 5.5, 2.9 Hz, 1H), 5.74 (bd, *J* = 8.9 Hz, 1H), 5.13 (d, *J* = 12.1 Hz, 1H), 5.07 (d, *J* = 12.1 Hz, 1H), 4.03 (bs, 1H), 3.93 (dd, *J* = 9.2, 3.8 Hz, 1H), 3.72 (dd, *J* = 9.5, 8.1 Hz, 1H), 3.64 (s, 3H), 3.50 (bs, 1H), 3.26-3.17 (m, 3H), 2.19-2.11 (m, 1H), 1.67 (d, *J* = 8.9Hz, 1H), 1.45 (d, *J* = 8.9 Hz, 1H), 0.98 (d, *J* = 6.8 Hz, 3H), 0.88 (d, J = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.03, 151.29, 138.08, 136.23, 133.66, 131.50, 129.83, 121.30, 68.16, 64..03, 62.47, 52.86, 50.72, 48.32, 47.18, 47.01, 38.35, 31.60, 19.15, 17.54; HRMS calcd for $C_{22}H_{29}N_3O_8S_2$ (M+) required 527.1396 found 527.1390.

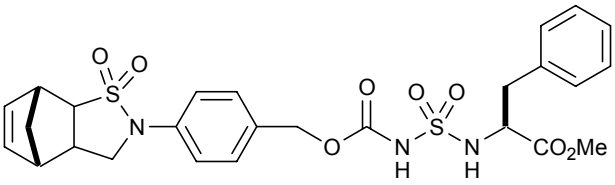
Sulfonamide-based leucine-derived sulfamoyl carbamate (2c)



2c

The general procedure above was followed starting with chlorosulfonyl isocyanate (30 μL, 0.34 mmol), **1** (101 mg, 0.34 mmol), H-Leu-OMe·HCl (63 mg, 0.34 mmol) and Et_3N (96 μL, 0.69 mmol). Flash chromatography (CH_2Cl_2/EtOAc: 9:1) afforded **2c** (159 mg, 85%) as a white solid: R_f = 0.17 (Hexane/EtOAc: 1:1); FTIR (neat) 3261, 2957, 2872, 1744, 1614, 1515, 1470, 1359, 1301, 1235, 1162, 1093 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.28 (d, *J* = 8.3 Hz, 2H), 7.21 (d, *J* = 8.2 Hz, 2H), 6.42 (dd, *J* = 5.5, 2.8 Hz, 1H), 6.25 (dd, *J* = 5.6, 2.9 Hz, 1H), 5.92 (bs,1H), 5.10 (d, *J* = 12.1 Hz, 1H), 5.05 (d, *J* = 12.1 Hz, 1H), 4.18 (bs,1H), 3.91 (dd , *J* = 9.3, 3.9 Hz, 1H), 3.75 (dd, *J* = 9.3, 8.7 Hz, 1H), 3.61 (s, 3H), 3.47 (bs, 1H), 3.24-3.15 (m, 3H), 1.83-1.72 (m, 1H), 1.64 (d, J = 8.9 Hz, 1H), 1.56-1.27 (m, 2H), 1.43 (d, J = 8.8 HZ, 1H), 0.91 (d, J = 2.9 Hz, 3H), 0.89 (d, J = 3.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.91, 152.19, 138.86, 137.00, 134.41, 132.20, 130.56, 121.95, 68.53, 64.36, 55.98, 53.20, 50.96, 48.54, 47.40, 47.23, 42.29, 38.51, 24.67, 23.07, 21.72; HRMS calcd for $C_{23}H_{35}N_4O_8S_2$ $(M+NH_4)^+$ required 559.1896, found 559.1888.

Sulfonamide-based phenylalanine-derived sulfamoyl carbamate (2d)

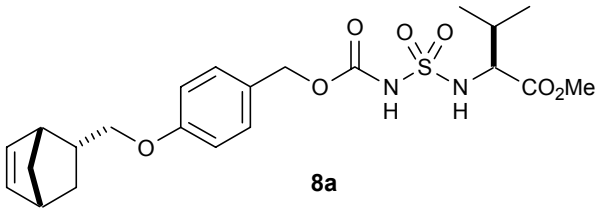


2d

The general procedure above was followed starting with chlorosulfonyl isocyanate (105 μL, 1.20 mmol), **1** (352 mg, 1.20mmol), H-Phe-OMe·HCl (260 mg, 1.20 mmol) and Et_3N (337 μL, 2.41 mmol). Flash chromatography (Hexane/EtOAc: 2:3) afforded **2d** (664 mg, 96%) as a white solid: R_f = 0.50 (Hexane/EtOAc: 1/4); FTIR (neat) 3261, 2953, 1743, 1614, 1515, 1455, 1360, 1298, 1225, 1160, 1128, 1018, 954 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.37-7.13 (m, 9H), 6.45 (dd, *J* = 5.5, 2.9 Hz, 1H), 6.26 (dd, *J* = 5.5, 3.0 Hz, 1H), 5.6 (bd, *J* = 8.0 Hz, 1H), 5.07 (d, *J* = 12.0 Hz, 1H), 5.03 (d, *J* = 12.0 Hz, 1H), 4.49 (t, *J* = 5.9 Hz, 1H), 3.94 (dd, *J* = 9.3, 3.8 Hz, 1H), 3.71 (dd,

J = 9.3, 8.1 Hz, 1H), 3.63 (s, 3H), 3.49 (bs, 1H), 3.27-3.18 (m, 3H), 3.09 (d, *J* = 5.9 Hz, 2H), 1.66 (d, *J* = 8.9 Hz, 1H), 1.45 (d, *J* = 8.9 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.28, 151.24, 138.01, 136.17, 135.04, 133.60, 131.37, 129.77, 129.62, 128.90, 127.60, 121.19, 68.10, 63.97, 57.85, 52.91, 50. 65, 48.23, 47.11, 46.95, 39.14, 38.27; HRMS calcd for $C_{26}H_{33}N_4O_8S_2$ $(M+NH_4)^+$ required 593.1740, found 593.1768.

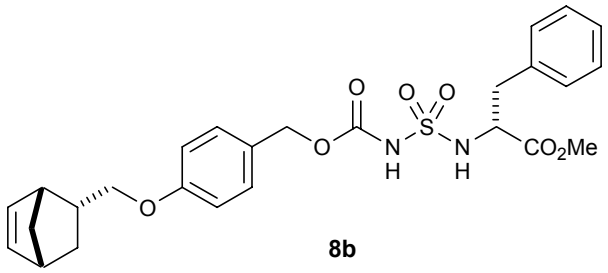
Norbornene-based valine-derived sulfamoyl carbamate (8a)



8a

The general procedure above was followed starting with chlorosulfonyl isocyanate (24 μL, 0.276 mmol), **7** (62.4 mg, 0.271 mmol), H-Val-OMe·HCl (50 mg, 0.298 mmol) and Et_3N (100 μL, 0.718 mmol). Flash chromatography (Heptane/EtOAc: 2:1) afforded **8a** (110.2 mg, 87%) as a white solid: R_f = 0.21 (Heptane/EtOAc: 2/1); FTIR (neat) 3278, 3058, 2965, 2925, 1742, 1614, 1358, 1163 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44 (bs, 1H), 7.27 (bd, *J* = 9.3 Hz, 2H), 6.85 (bd, *J* = 8.7 Hz, 2H), 6.17 (dd, *J* = 5.7, 3.0 Hz, 1H), 5.94 (dd, *J* = 5.7, 2.9 Hz, 1H), 5.66 (bd, *J* = 9.5 Hz, 1H), 5.12 (d, 11.7 Hz, 1H), 5.08 (d, 11.7 Hz, 1H), 4.03 (dd, *J* = 9.5, 5.0 Hz, 1H), 3.70 (dd, *J* = 9.1, 6.5 Hz, 1H), 3.68 (s, 3H), 3.53 (dd, *J* = 9.2, 9.2 Hz, 1H), 3.03 (bs, 1H), 2.85 (bs, 1H), 2.55 (ddddd, *J* = 9.4, 9.4, 9.4, 4.1, 4.1 Hz, 1H), 2.18-2.11 (m, 1H), 1.91 (ddd, *J* = 11.8, 9.3, 3.8 Hz, 1H), 1.48 (dd, *J* = 8.2, 2.0 Hz, 1H), 1.30 (bd, *J* = 8.2 Hz, 1H), 0.99 (d, *J* = 6.8 Hz, 3H), 0.89 (d, *J* = 6.9 Hz, 3H), 0.62 (ddd, *J* = 11.7, 4.4, 2.5 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 171.80, 159.55, 151.17, 137.56, 132.23, 130.29, 126.45, 114.57, 71.50, 68.42, 62.17, 52.44, 49.38, 43.83, 42.19, 38.26, 31.28, 28.99, 18.83, 17.26; HRMS calcd for $C_{22}H_{30}N_2O_7S$ (M+) required 466.1774, found 466.1761.

Norbornene-based D-phenylalanine-derived sulfamoyl carbamate (8b)



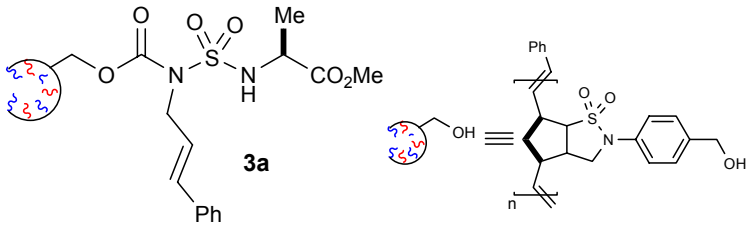
8b

The general procedure above was followed starting with chlorosulfonyl isocyanate (24 μL, 0.276 mmol), **7** (61.9 mg, 0.269 mmol), H-D-Phe-OMe·HCl (64 mg, 0.297 mmol) and Et_3N (100 μL, 0.718 mmol). Flash chromatography (Heptane/EtOAc: 1:1) afforded **8b** (81 mg, 59%) as a white solid: R_f = 0.14 (Heptane/EtOAc: 2/1); FTIR (neat) 3273, 3058, 3032, 2955, 1742, 1614, 1358, 1158 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.46 (bs, 1H), 7.31-7.20 (m, 5H), 7.15-7.12 (m, 2H), 6.84 (bd, *J* = 8.7 Hz, 2H), 6.17 (dd, *J* = 5.7, 3.0 Hz, 1H), 5.94 (dd, *J* = 5.7, 2.9 Hz, 1H), 5.66 (bd, *J* = 8.1 Hz, 1H), 5.07 (d, 11.7 Hz, 1H), 5.04 (d, 11.7 Hz, 1H), 4.50 (dd, *J* = 13.3, 5.9 Hz, 1H), 3.69 (dd, *J* = 9.2, 6.6 Hz, 1H), 3.66 (s, 3H), 3.52 (dd, *J* = 9.1, 9.1 Hz, 1H), 3.09 (d, *J* = 5.9 Hz, 2H), 3.02 (bs, 1H), 2.85 (bs, 1H), 2.54 (ddddd, *J* = 9.4, 9.4, 9.4, 4.1, 4.1 Hz, 1H), 1.91 (ddd, *J* = 11.8, 9.3, 3.8 Hz, 1H), 1.48 (dd, *J* = 8.2, 1.9 Hz, 1H), 1.32 (bd, *J* = 8.1 Hz, 1H), 0.61 (ddd, *J* = 11.7, 4.4, 2.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.20, 159.41, 151.18, 137.49, 134.93, 132.17, 130.21, 129.30, 128.51, 127.17, 126.37, 114.47, 71.39, 68.32, 57.59, 52.49, 49.31, 43.76, 42.12, 38.73, 38.18, 28.91; HRMS calcd for $C_{26}H_{30}N2O_7S$ (M+) required 514.1774, found 514.1747.

General procedure for compounds 3a-d and 9a,b

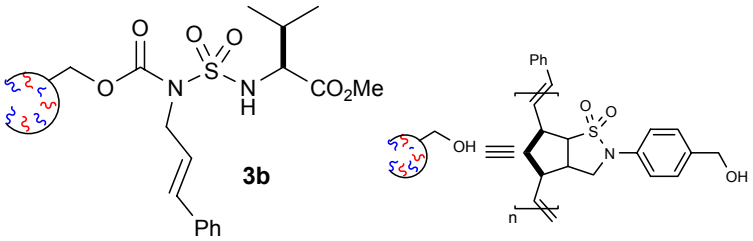
An oven dried flask was charged with the respective sulfamoyl carbamate **2a-d** (0.21 mmol), PPh_3 (67 mg, 0.25 mmol), and cinnamyl alcohol (31.3 mg, 0.23 mmol) in dry THF (3 mL) at room temperature. DIAD (54 μL, 0.27 mmol) was added dropwise at such a rate that the reaction mixture was completely colorless before addition of the next drop. The reaction was stirred overnight at room temperature. After completion of the reaction, the solvent was removed by rotary evaporation. The flask was flushed with argon, and degassed CH_2Cl_2 (1 mL) was added. Grubbs second-generation catalyst (8.9 mg, 0.01 mmol) was added and the reaction mixture was refluxed for 30 min. Ethyl vinyl ether (1 mL) was added and the reaction allowed to stir warm

for 15 min. The reaction mixture was then poured into 100 mL of MeOH. The precipitate was collected by suction filtration and washed with methanol to yield the desired oligomer as a slightly pink solid.



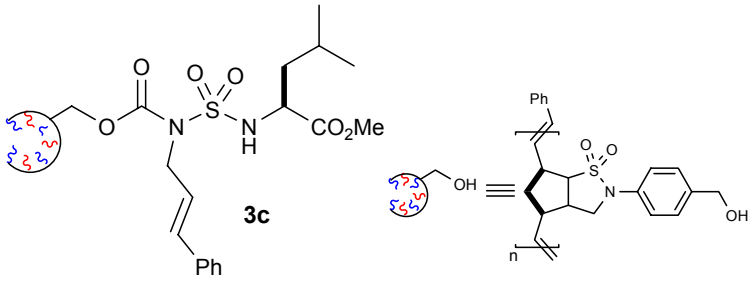
Oligomer 3a

The general procedure above was followed starting with sulfamoyl carbamate **2a** (106 mg, 0.21 mmol), PPh_3 (67 mg, 0.25 mmol), cinnamyl alcohol (31.3 mg, 0.23 mmol) and DIAD (54 µL, 0.27 mmol). Grubbs second-generation catalyst (8.9 mg, 0.01 mmol) was used for polymerization. The desired oligomer **3a** was obtained as a slightly pink solid (101 mg, 78%).



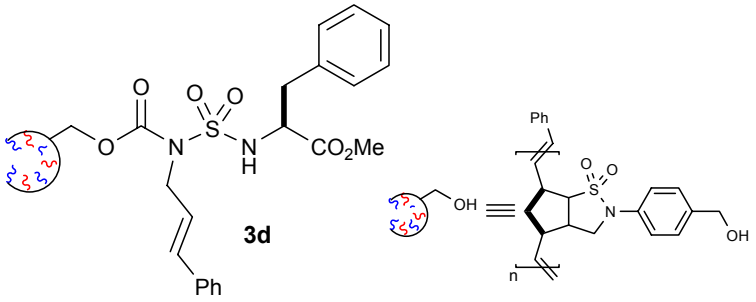
Oligomer 3b

The general procedure above was followed starting with sulfamoyl carbamate **2b** (133 mg, 0.42 mmol), PPh_3 (67 mg, 0.25 mmol), cinnamyl alcohol (31.3 mg, 0.23 mmol) and DIAD (54 µL, 0.27 mmol). Grubbs second-generation catalyst (8.9 mg, 0.01 mmol) was used for polymerization. The desired oligomer **3b** was obtained as a slightly pink solid (101 mg, 83%).



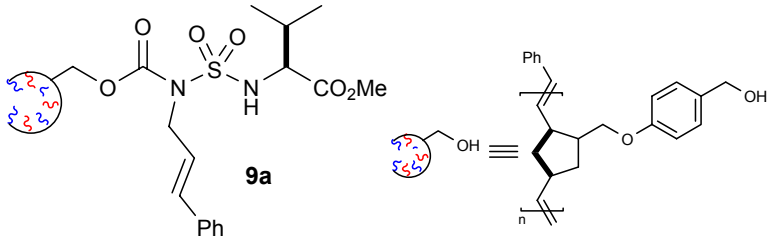
Oligomer 3c

The general procedure above was followed starting with sulfamoyl carbamate **2c** (218 mg, 0.40 mmol), PPh_3 (147 mg, 0.56 mmol), cinnamyl alcohol (75.6 mg, 0.56 mmol) and DIAD (118 µL, 0.60 mmol). Grubbs second-generation catalyst (17 mg, 0.02 mmol) was used for polymerization. The desired oligomer **3c** was obtained as a slightly pink solid (220 mg, 84%).



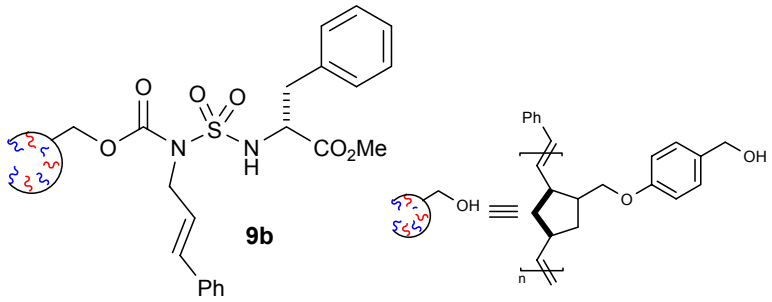
Oligomer 3d

The general procedure above was followed starting with sulfamoyl carbamate **2d** (120 mg, 0.20 mmol), PPh_3 (73 mg, 0.28 mmol), cinnamyl alcohol (29.5 mg, 0.22 mmol) and DIAD (59 µL, 0.30 mmol). Grubbs second-generation catalyst (8.9 mg, 0.01 mmol) was used for the polymerization. The desired oligomer **3d** was obtained as a slightly pink solid (116 mg, 81%).



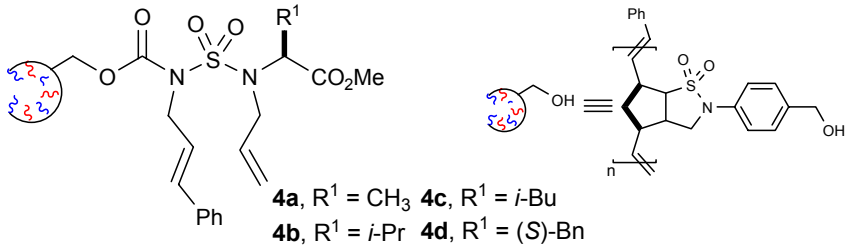
Oligomer 9a

The general procedure above was followed starting with sulfamoyl carbamate **8a** (100 mg, 0.214 mmol), PPh_3 (78.7 mg, 0.300 mmol), cinnamyl alcohol (32.3 mg, 0.22 mmol) and DIAD (63 µL, 0.320 mmol). Grubbs second-generation catalyst (8.7 mg, 0.0102 mmol) was used for polymerization. The desired oligomer **9a** was obtained as a slightly pink solid (126.2 mg, >99%).



Oligomer 9b

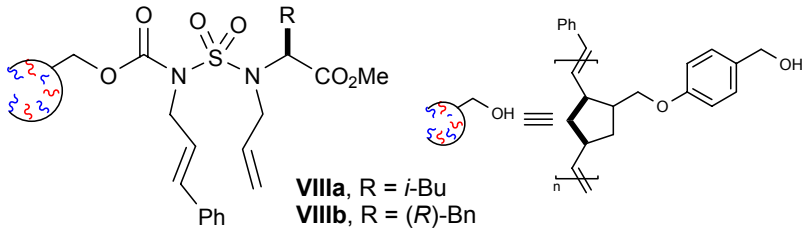
The general procedure above was followed starting with sulfamoyl carbamate **8b** (76.5 mg, 0.149 mmol), PPh_3 (56.7 mg, 0.216 mmol), cinnamyl alcohol (27.1 mg, 0.202 mmol) and DIAD (44 µL, 0.223 mmol). Grubbs second-generation catalyst (6.3 mg, 0.00742 mmol) was used for the polymerization. The desired oligomer **9b** was obtained as a slightly pink solid (87.3 mg, 93%).



4a, R^1 = CH_3 **4c**, R^1 = *i*-Bu
4b, R^1 = *i*-Pr **4d**, R^1 = (*S*)-Bn

General procedure for 4a-d

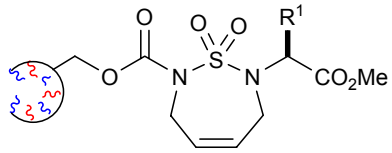
To a stirring solution of **3a** (95 mg, 0.15 mmol) in acetone (4 ml) in a 50 mL round bottom flask was added K_2CO_3 (63.8 mg, 0.46 mmol), allyl bromide (80.1 µL, 0.92 mmol) and NaI (1.1 mg, 0.007 mmol). The flask was fitted with a reflux condenser and the mixture was heated to 60 ^{0}C. After 8 hr the resulting solution was filtered by suction, and the solvent removed under reduced pressure to yield **3a** as a slightly pink solid (100 mg, 99%).

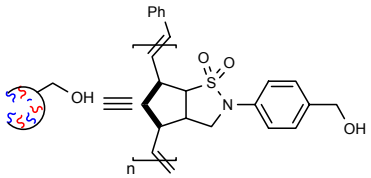


VIIIa, R = *i*-Bu
VIIIb, R = (*R*)-Bn

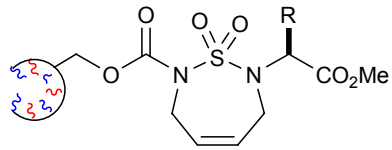
Alternate procedure for VIIIa,b

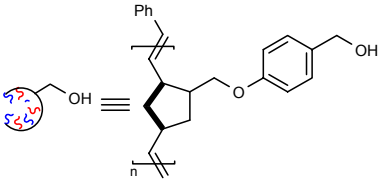
Oligomer **9b** (87.3 mg, 0.138 mmol), Cs_2CO_3 (188.9 mg, 0.580 mmol), and NaI (20.3 mg, 0.135 mmol) were dissolved in 1 mL DMF. Allyl bromide (200 µL, 2.31 mmol) was added and the mixture heated to 80 ^{0}C overnight. The resulting solution was poured into 40 mL H_2O and the mixture stirred for 30 min. The polymer was filtered through a pad of Celite, washed sequentially with fresh H_2O and MeOH. The polymer was recovered by dissolving it in CH_2Cl_2. The solvent was removed under reduced pressure to yield **VIIIb** as a slightly yellow solid (93.7 mg, >99%).





5a, R^1 = CH_3 **5c**, R^1 = *i*-Bu
5b, R^1 = *i*-Pr **5d**, R^1 = (*S*)-Bn





IXa, R = *i*-Bu
IXb, R = (*R*)-Bn

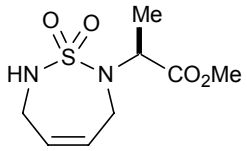
General procedure for 5a-d and IXa,b

The oligomer **4a** (100 mg, 0.15 mmol) was dissolved in degassed CH_2Cl_2 (8 mL). The Grubbs first generation metathesis catalyst (12.3 mg, 0.015 mmol, 10 mol%) was added, the flask was quickly fitted with a condenser. The solution was refluxed for 6h under argon. The reaction mixture was concentrated to ~1/4 the original volume and the reaction mixture was poured into 150 ml of methanol to induce oligomer precipitation (82 mg, 98%). The precipitate was collected by suction filtration and was washed with methanol. It was dried under vacuum before the next reaction.

General procedure for 6a-e

The oligomer **5a** (82 mg, 0.14 mmol) was dissolved in 50% TFA/CH_2Cl_2 (4 ml) and stirred at room temperature. After 5 hr the solvent was removed under reduced pressure, the reaction mixture was redissolved in CH_2Cl_2 (2 ml) and poured into 100 ml of methanol. The polymer was removed by filtration and the filtrate was concentrated under reduced pressure. The filtrate was dissolved in 50% hexane/EtOAC (20 mL) and passed through a silica plug. The solvent was removed under reduced pressure to yield **6a** as a viscous oil (25 mg, 66%).

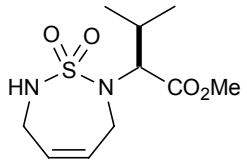
(*S*)-2-(1,1-Dioxo-1,3,6,7-tetrahydro-1λ^6-[1,2,7]thiadiazepin-2-yl)-propionic acid methyl ester (6a)



6a

Sulfamide **6a** was obtained as a viscous oil (25 mg) with an overall yield of 52% starting from **2a** (106 mg, 0.21 mmol): R_f = 0.22 (hexane/EtOAc: 1:1); $[\alpha]^{25}$ = - 32.3 (c = 0.26, $CHCl_3$); FTIR (neat) 3289, 2928, 2835, 2359, 2341, 1738, 1435, 1316, 1173, 1153 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.88 (s, 2H), 5.30 (bs, 1H), 4.68 (q, *J* = 7.2 Hz, 1H), 3.99-3.76 (m, 4H), 3.72 (s, 3H), 1.26 (d, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.37, 130.00, 129.23, 55.76, 52.61, 41.73, 41.32, 16.27; HRMS calcd for $C_8H_{15}N_2O_4S$ $(M+H)^+$ required 235.0753, found 235.0757.

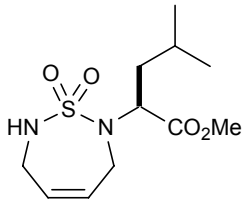
(*S*)-2-(1,1-Dioxo-1,3,6,7-tetrahydro-1λ^6-[1,2,7]thiadiazepin-2-yl)-3-methyl-butyric acid methyl ester (6b)



6b

Sulfamide **6b** was obtained as a viscous oil (35 mg) with an overall yield of 53 % starting from **2b** (133 mg**,** 0.25 mmol): R_f = 0.31 (hexane/EtOAc: 1:1); $[\alpha]^{25}$ = - 50.3 (c = 0.28, $CHCl_3$); FTIR (neat) 3298, 2962, 2929, 1737, 1435, 1319, 1203, 1164 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.76 (s, 2H), 4.84 (bs, 1H), 4.86-4.82 (m, 2H), 3.82-3.75 (m, 2H), 3.70 (s, 3H), 3.67-3.65 (m, 1H), 2.17-2.06 (m, 1H), 1.00 (d, *J* = 6.7 Hz, 3H), 0.93 (d, *J* = 6.5 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.53, 129.39, 129.29, 65.48, 52.15, 41.24, 41.20, 27.90, 19.50, 19.11; HRMS calcd for $C_{10}H_{19}N_2O_4S$ $(M+H)^+$ required 263.1066, found 263.1045.

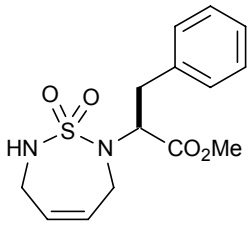
(*S*)-2-(1,1-Dioxo-1,3,6,7-tetrahydro-1λ^6-[1,2,7]thiadiazepin-2-yl)-4-methyl-pentanoic acid methyl ester (6c)



6c

Sulfamide **6c** was obtained as a viscous oil (56 mg) with an overall yield of 50 % starting from **2c** (218 mg, 0.40 mmol): R_f = 0.31 (hexane/EtOAc: 3:2); $[\alpha]^{25}$ = -55.4 (c = 1.00, $CHCl_3$); FTIR (neat) 3294, 2955, 2869, 1737, 1434, 1316,1169, 1130 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.79 (s, 2H), 4.98 (bs, 1H), 4.60 (dd, *J* = 9.5, 5.2 Hz, 1H), 3.93-3.81 (m, 3H), 3.70 (s, 3H), 3.71-3.64 (m, 1H), 1.72-1.58 (m, 3H), 0.97 (d, *J* = 6.2 Hz, 3H), 0.95 (d, *J* = 6.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.36, 129.90, 129.09, 58.00, 52.40, 41.42, 41.39, 38.69, 24.71, 23.27, 21.56; HRMS calcd for $C_{11}H_{21}N_2O_4S$ $(M+H)^+$ required 277.1222, found 277.1229.

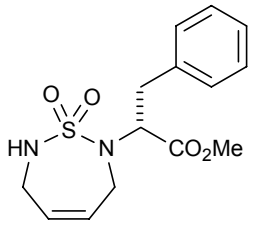
(*S*)-2-(1,1-Dioxo-1,3,6,7-tetrahydro-1λ^6-[1,2,7]thiadiazepin-2-yl)-3-phenyl-propionic acid methyl ester (6d)



6d

Sulfamide **6d** was obtained as a semi-solid (32 mg) with an overall yield of 49 % starting from **2d** (120 mg, 0.20 mmol): R_f = 0.25 (hexane/EtOAc: 1:1); $[\alpha]^{25}$ = -19.7 (c = 0.49, $CHCl_3$); FTIR (neat) 3291, 3028, 2923, 2852, 2359, 2341, 1737, 1496, 1436, 1316, 1221, 1159 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31-7.23 (m, 5H), 5.75-5.70 (m, 1H), 5.67-5.62 (m, 1H), 4.88 (dd, *J* = 8.9, 6.7 Hz, 1H), 4.55 (bs, 1H), 4.03 (bd, *J* = 18.5 Hz, 1H); 3.81 (dd, *J* = 18.5, 4.9 Hz, 1H), 3.71 (s, 3H), 3.53-3.38 (m, 2H), 3.31 (dd, *J* = 14.3, 6.6 Hz, 1H), 2.97 (dd, *J* = 14.3, 9.0 Hz, 1H) ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.41, 136.52, 130.37, 129.61, 128.78, 128.63, 127.17, 61.49, 52.62, 42.44, 41.17, 36.68; HRMS calcd for $C_{14}H_{19}N_2O_4S$ $(M+H)^+$ required 311.1066, found 311.1063.

(*R*)-2-(1,1-Dioxo-1,3,6,7-tetrahydro-1λ^6-[1,2,7]thiadiazepin-2-yl)-3-phenyl-propionic acid methyl ester (6e)



6e

Sulfamide **6e** was obtained as a semi-solid (20.7 mg) with an overall yield of 45 % starting from **8b** (76.5 mg, 0.149 mmol): R_f = 0.20 (Heptane/EtOAc: 1:1); $[\alpha]^{20}$ = +42.8 (c = 0.22, $CHCl_3$); FTIR (neat) 3293, 3032, 2950, 2919, 1737, 1603, 1358, 1157 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.30-7.20 (m, 5H), 5.72 (bd, *J* = 10.9 Hz, 1H), 5.64 (bd, *J* = 9.5 Hz, 1H), 4.86 (dd, *J* = 8.9, 6.7 Hz, 1H), 4.50 (bs, 1H), 4.00 (bd, *J* = 17.0 Hz, 1H), 3.79 (bd, *J* = 11.2 Hz, 1H), 3.70 (s, 3H), 3.51-3.37 (m, 2H), 3.30 (dd, *J* = 14.3, 6.5 Hz, 1H), 2.96 (dd, *J* = 14.3, 9.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.16, 136.26, 130.00, 129.33, 128.40, 128.35, 126.89, 61.18, 52.41, 42.27, 40.88, 36.40; HRMS calcd for $C_{14}H_{19}N_2O_4S$ $(M+H)^+$ required 311.1066, found 311.1083.