Catalytic Asymmetric Synthesis of Allylic Thiol Derivatives

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Materials and Methods.

[(*Rp*,*S*)-COP-Cl]$_2$ (di-μ-chlorobis[(η^5-(*Rp*,*S*)-2-(2'-(4'-methylethyl)oxazolinyl)cyclo-pentadienyl, 1-*C*,3'-*N*)(η^4-tetraphenylcyclo-butadiene)cobalt]dipalladium, **1**) and its enantiomer, [(*Sp*,*R*)-COP-Cl]$_2$, were prepared according to published procedures.[1] Both enantiomers are commercially available from Aldrich Chemical Co. (product # 661791 and 646636). COP-complexes **3**,[2] **4**[1] and **5**[2] were prepared from [(*Rp*,*S*)-COP-OAc]$_2$.[1] Rearrangements with COP complexes were performed in anhydrous solvents (either freshly distilled or passed through activated-alumina columns) in oven-dried 2-dram vials, which were sealed with Thermoset Teflon® PTFE-lined caps. Heating was performed in a multi-bored aluminum block placed on a IKAmag temperature modulator with the probe immersed in a vial well of the aluminum block filled with mineral oil.

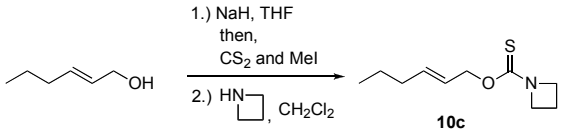
Thin layer chromatography (TLC) was conducted with E. Merck silica gel 60 F254 pre-coated plates, (0.25 mm) and visualized using a combination of UV, anisaldehyde, ceric ammonium molybdate, iodine on silica, and potassium permanganate staining. E. Merck silica gel (particle size 0.040-0.063 mm) was used for flash chromatography. HPLC determination of enantiopurity was carried out on a Mettler Toledo SFC (super critical CO_2 liquid chromatography) using either Chiral OB-H, or AD

[1] (a) Anderson, C. E.; Kirsch, S. F.; Overman, L. E.; Richards, C. J.; Watson, M. P. *Org. Synth.* **2007**, *84*, 148–155. (b) Anderson, C. E.; Overman, L. E.; Richards, C. J.; Watson, M. P; White, N. *Org. Synth.* **2007**, *84*, 139–147.

[2] The preparation and characterization of this COP complex will be described in a forthcoming publication.

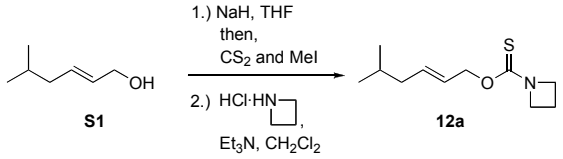
columns. GC determination of enantiopurity was carried out on a Agilent 6850 series II network GC system using a Cyclosil-B capillary 30.0m x 250 μm x 0.25 μm nominal column. ^{1}H NMR spectra were recorded at 500 or 600 MHz and are reported relative to signals of the deuterated solvent. IR spectra were recorded as thin films using an Applied Systems REACT-IR 1000 spectrometer. Optical rotations were measured with a Jasco P-1010 polarimeter. High resolution mass spectra were obtained at the UC Irvine Mass Spectrometry Facility using a Fisions Autospec spectrometer. Concentrations were carried out at reduced pressure using a rotary evaporator.

Experimental Procedures.



(*E*)-*O*-2-Hexenyl 1-azetinylcarbamothioate (10c). Sodium hydride (1.20 g, 30.0 mmol, 3 equiv) was added to a solution of *trans*-hex-2-en-1-ol (1.00 g, 10.0 mmol) and THF (20 mL) at room temperature. After 1.5 h, CS_2 (0.6 mL, 10 mmol, 1 equiv) was added, followed by the dropwise addition of MeI (0.83 mL, 13 mmol, 1.3 equiv). After 3 h, saturated aqueous NH_4Cl (20 mL) was added to the yellow solution, and the aqueous layer was extracted with EtOAc (3 × 20 mL). The combined organic extracts were washed with H_2O, brine, dried ($MgSO_4$), and concentrated to provide 1.89 g of the crude xanthate as a yellow oil, which was used without further purification.

Azetidine (0.1 mL, 1.5 mmol) was added to a solution of a portion (280 mg, 1.47 mmol) of this crude methylxanthate and hexanes (0.5 mL), and the resulting solution was maintained at room temperature for 30 min. Concentration and purification of the residue by silica gel chromatography (100% hexanes, 2% Et_2O-hexanes, 5% Et_2O-hexanes, 10% Et_2O-hexanes) provided *O*-carbamothioate **10c** (285 mg, 97%) as a colorless oil: R_f 0.26 (10% Et_2O-hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.78 (dt, J = 15.3, 6.7 Hz, 1H), 5.62 (dt, J = 15.3, 6.4 Hz, 1H); 4.86 (d, J = 6.4 Hz, 2H), 4.19 (t, J = 7.6 Hz, 2H), 4.10 (t, J = 7.7 Hz, 2H), 2.25 (quintet, J = 7.7 Hz, 2H), 2.04 (m, 2H), 1.41 (m, 2H), 0.90 (t, J = 7.4 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 186.7, 136.4, 124.1, 71.3, 52.4, 50.6, 34.3, 22.0, 14.7, 13.6; IR (thin film) 1507, 1472, 1443 cm^{-1}; HRMS (ES+) m/z calcd for $C_{10}H_{17}NOSNa$ (M+Na) 222.0928, found 222.0929; LRMS (ES+) m/z fragments 200.0, 195.1, 150.0.



(*E*)-*O*-5-Methyl-2-hexenyl 1-azetinylcarbamothioate (12a). Following the procedure described for the preparation of **10c**, alcohol **S1** (0.95 g, 8.3 mmol) was converted to the corresponding methylxanthate (1.38 g, 81% yield). Azetidine hydrochloride (252 mg, 2.69 mmol, 2.5 equiv) was added to a solution of a portion (500 mg, 1.06 mmol) of this crude methylxanthate and CH_2Cl_2 (10 mL). Triethylamine (375 mL, 2.70 mmol, 2.5 equiv) was added and the resulting solution was maintained at room

temperature for 30 min. Concentration and purification of the residue by silica gel chromatography (5% Et_2O:hexanes) provided *O*-carbamothioate **12a** (462 mg, 88%) as a colorless oil: R_f 0.28 (5% Et_2O:hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.76 (dt, J = 16.2, 8.1 Hz, 1H), 5.61 (dt, J = 16.2, 6.4 Hz, 1H), 4.87 (d, J = 6.4 Hz, 2H), 4.19 (t, J = 7.6 Hz, 2 H), 4.10 (t, J = 7.6 Hz, 2H), 2.25 (m, 2H), 1.95 (app. t, J = 7.0 Hz, 2H), 1.64 (m, 1H), 0.89 (d, J = 6.7 Hz, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 186.7, 135.4, 125.1, 71.3, 52.4, 50.6, 41.6, 28.1, 22.3, 14.8; IR (thin film) 1499, 1468, 1443 cm^{-1}; HRMS (ES+) m/z calcd for $C_{11}H_{19}NOSNa$ (M+Na) 236.1085, found 236.1094; LRMS (ES+) m/z fragments 214.2, 150.1, 118.0.

(*E*)-*O*-4-(*tert*-Butyldimethylsilyloxy)but-2-enyl 1-azetinylcarbamothioate (12b). To a solution of (*E*)-4-(*tert*-butyldimethylsilyloxy)but-2-en-1-ol [3] (0.37 g, 1.8 mmol) and CS_2 (158 mL) at 0 °C was added NaH (0.87 g of 60% NaH in mineral oil, 22 mmol, 12 equiv) in one portion. The solution was allowed to warm to rt, and after 4 h CH_3I (5.3 mL, 85 mmol, 47 equiv) was added dropwise. After 30 min, saturated aqueous NH_4Cl (200 mL) was added to the solution, and the mixture was extracted with CH_2Cl_2 (3 × 75 mL). The combined organic extracts were washed with H_2O (100 mL), brine (100 mL), and the combined organic extracts were dried (Na_2SO_4) and concentrated under reduced pressure. Purification by silica chromatography (hexanes, 5:1 hexanes:Et_2O) provided the xanthate (0.359 g, 68% yield) as a yellow oil.

To a solution of the xanthate prepared from the first step (359 mg, 1.23 mmol) and CH_2Cl_2 (7.4 mL) at rt was added azetidine hydrochloride (0.127 g, 1.35 mmol, 1.1 equiv), followed by Et_3N (0.19 mL, 1.4 mmol, 1.1 equiv). After 2 h, the mixture was concentrated under reduced pressure. Purification by silica chromatography (5% Et_2O:hexanes, 10% Et_2O:hexanes) provided *O*-carbamothioate **12b** (383 mg, quant.) as a colorless oil: R_f 0.23 (5% Et_2O:hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.87 (m, 2H), 4.93 (dt, J = 5.9, 1.2 Hz, 2H), 4.20 (d, J = 2.7 Hz, 2H), 4.20 (t, J = 7.6 Hz, 2H), 4.11 (t, J = 7.6 Hz, 2H), 2.26 (quintet, J = 7.6 Hz, 2H), 0.92 (s, 9H), 0.08 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 186.5, 134.0, 123.8, 70.4, 63.0, 52.4, 50.6, 25.9, 18.4, 14.8, -5.3; IR (thin film) 1501, 1472, 1445 cm^{-1}; HRMS (ES+) m/z calcd for $C_{14}H_{27}NO_2SSiNa$ (M+Na) 324.1429, found 324.1422; LRMS (ES+) m/z fragments 269.2, 215.2, 170.1.

(*E*)-*O*-4-(Triisopropylsilyloxy)but-2-enyl 1-azetinylcarbamothioate (12c). Following the procedure described for the preparation of **12b**, (*E*)-4-(triisopropylsilyloxy)but-2-en-1-ol (227 mg, 0.932 mmol) was converted to the *O*-carbamothioate **12c** (196 mg, 61% yield), and was obtained as a colorless oil: R_f 0.37 (10:1 hexanes:EtOAc); ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.89 (m, 2H), 4.93 (m, 2H), 4.28 (m, 2H), 4.20 (t, J = 7.7 Hz, 2H) 4.11 (t, J = 7.7 Hz, 2H), 2.26 (quintet, J = 7.7 Hz, 2H), 1.15-1.07 (m, 21H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 186.7, 134.2, 123.5, 70.5, 63.1, 52.5, 50.7, 18.1, 14.9, 12.1; IR (thin film) 1499, 1445 cm^{-1}; HRMS (ES+) m/z calcd for $C_{17}H_{33}NO_2SSiNa$ (M+Na) 366.1899, found 366.1901; LRMS (ES+) m/z fragments 293.2, 249.2.

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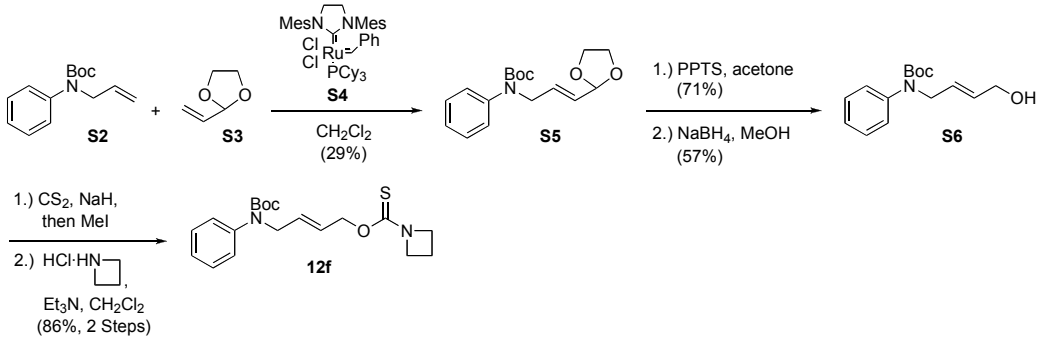
[3] For the various procedures to prepare (*E*)-4-siloxy-2-butene-1-ol's, see: (a) Corlay, H.; Motherwell, W. B.; Pennell, A. M. K.; Shipman, M.; Slawin, A. M. Z.; William, D. J. *Tetrahedron*, **1996**, *52*, 4883–4902. (b) Braddock, D. C.; Bhuva, R.; Millan, D. S.; Pérez-Fuertes, Y.; Roberts, C. A.; Sheppard, R. N.; Solanki, S.; Stokes, E. S. E.; White, A. J. P. *Org. Lett.* **2007**, *9*, 445–448. (c) Vlieghe, P.; Clerc, T.; Pannecouque, C.; Witvrouw, M.; Clercq, E. D.; Salles, J.-P.; Kraus, J.-L. J. Med. Chem. 2001, 44, 3014–3021. (d) Organ, M. G.; Cooper, J. T.; Rogers, L. R.; Soleymanzadeh, F.; Paul, T. *J. Org. Chem.* **2000**, *65*, 7959–7970.

(*E*)-*O*-4-(*tert*-Butyldiphenylsilyloxy)but-2-enyl 1-azetinylcarbamothioate (12d). Following the procedure described for the preparation of **12b**, (*E*)-4-(*tert*-butyldiphenylsilyloxy)but-2-en-1-ol (214 mg, 0.656 mmol) was converted to the *O*-carbamothioate **12d** (151 mg, 54% yield), and was obtained as a colorless oil: R_f 0.50 (5:1 hexanes:EtOAc); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.68 (d, J = 7.1 Hz, 4H), 7.45-7.38 (m, 6H), 5.93 (ddd, J = 15.5, 5.7, 5.7 Hz, 1H), 5.86 (ddd, J = 15.6, 3.8, 3.8 Hz, 1H), 4.93 (d, J = 5.7 Hz, 2H), 4.23-4.19 (m, 4H), 4.11 (t, J = 7.7 Hz, 2H), 2.27 (quintet, J = 7.7 Hz, 2H), 1.07 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 186.8, 135.7, 133.7, 133.7, 129.9, 127.9, 124.0, 70.6, 63.8, 52.6, 50.8, 27.0, 19.5, 15.0; IR (thin film) 1507, 1472, 1443 cm^{-1}; HRMS (ES+) m/z calcd for $C_{24}H_{31}NO_2SSiNa$ (M+Na) 448.1743, found 448.1737; LRMS (ES+) m/z fragments 426.2, 302.2.

(*E*)-*O*-4-Hydroxybut-2-enyl 1-azetinylcarbamothioate (12e). TBAF (0.35 mL, 0.35 mmol, 1M solution in THF, 1.1 equiv) was added to a rt solution of *O*-carbamothioate **12b** (97 mg, 0.32 mmol) in THF (1 mL). The solution was maintained at rt for 50 min, then an additional aliquot of TBAF (0.18 mL, 0.18 mmol, 1M solution in THF, 0.5 equiv) was added. After 25 min, the solution was diluted with H_2O (20 mL) and extracted with Et_2O (3 × 10 mL). The combined organic layers were dried (Na_2SO_4), and concentrated under reduced pressure (CAUTION: Product is Volatile!!). Purification by silica chromatography (100% Et_2O) provided *O*-carbamothioate **12e** (47 mg, 79% yield) as a light yellow oil: R_f 0.45 (100% Et_2O); ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.95 (dt, J = 15.6, 4.8 Hz, 1H), 5.90 (dt, J = 15.6, 5.5 Hz, 1H), 4.96 (d, J = 5.6 Hz, 2H), 4.20 (m, 4H), 4.12 (t, J = 7.8 Hz, 2H), 2.27 (quintet, J = 7.7 Hz, 2H), 1.56 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 186.4, 133.0, 125.3, 70.0, 62.7, 52.4, 50.7, 14.8; IR (thin film) 3421 (br), 1511, 1472, 1445 cm^{-1}; HRMS (ES+) m/z calcd for $C_8H_{13}NO_2SNa$ (M+Na) 210.0565, found 210.0558; LRMS (ES+) m/z fragments 195.2, 186.3, 167.1.



(*E*)-*O*-4-(*tert*-Butoxycarbonyl(phenyl)amino)but-2-enyl 1-azetinylcarbamothioate (12f). A modification of a procedure reported by Grubbs and co-workers was employed.[4,5] To a solution of terminal olefin **S2** (1.0 g, 4.30 mmol) and CH_2Cl_2 (22 mL) at rt, was added vinyl dioxolane **S3** (0.86 mL, 8.6 mmol, 2 equiv) and ruthenium catalyst **S4** (0.092 g, 0.11 mmol, 2.5 mol%) in succession. The solution was heated to reflux for 18 h. The solution was then allowed to cool to rt, and Celite was added. The mixture was concentrated under reduced pressure, and the Celite was loaded directly onto a silica column. Purification by silica chromatography (20:1

[4] O'Leary, D. J.; Blackwell, H. E., Washenfelder, R. A.; Miura, K.; Grubbs, R. H. *Tetrahedron Lett.* **1999**, *40*, 1091–1094.

[5] For the use of an allyl aniline substrate, see: Mennen, S. M. Ph. D. Dissertation, Boston College, 2007.

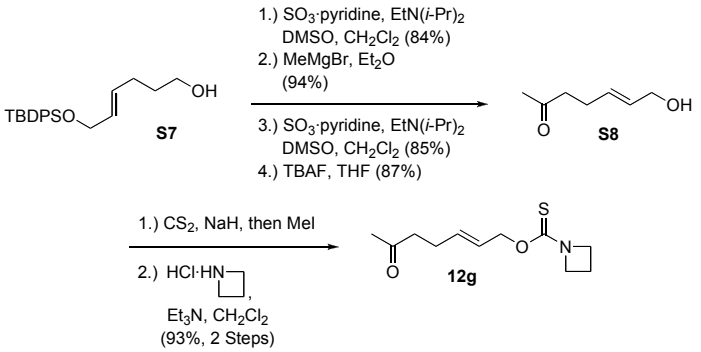
hexanes:EtOAc, 10:1 hexanes:EtOAc, 5:1 hexanes:EtOAc) provided acetal **S5** (380 mg, 29% yield) as a light yellow oil. Diagnostic data: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.32 (app t, *J* = 7.8 Hz, 2H), 7.22-7.16 (m, 3H), 6.02 (ddd, *J* = 15.5, 6.0 6.0 Hz, 1H), 5.60 (dd, *J* = 15.5, 6.0 Hz, 1H), 5.28 (d, *J* = 6.0 Hz, 1H), 4.26 (d, *J* = 5.5 Hz, 2H), 3.99-3.87 (m, 4H), 1.45 (s, 9H).

To a stirred solution of acetal **S5** (0.38 g, 1.3 mmol) and acetone (46 mL) at rt was added pyridinium *p*-toluenesulfonate (31 mg, 0.13 mmol, 0.1 equiv) in one portion. The solution was heated to reflux for 17 h, then allowed to cool to rt and concentrated under reduced pressure. Purification by silica chromatography (10:1 hexanes:EtOAc) provided the aldehyde (233 mg, 71% yield) as a light yellow oil. Diagnostic data: ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.59 (d, *J* = 8.0 Hz, 1H), 7.34 (app t, *J* = 8.0 Hz, 2H), 7.23-7.20 (m, 3H), 6.88 (ddd, *J* = 15.5, 4.5, 4.5 Hz, 1H), 6.24 (dd, *J* = 15.5, 7.5 Hz, 1H), 4.52 (dd, *J* = 5.0, 2.0 Hz, 2H), 1.45 (s, 9H).

A solution of the aldehyde prepared in the previous step (0.055 g, 0.21 mmol) and MeOH (1 mL) was cooled to 0 °C. $NaBH_4$ (0.016 g, 0.42 mmol, 2 equiv) was added in one portion, and the solution was maintained at 0 °C for 2 h. Acetone (2 mL) and saturated aqueous NH_4Cl (10 mL) were added to the solution, and the mixture was extracted with 1:1 hexanes:EtOAc (3 x 10 mL). The combined organic layers were dried (Na_2SO_4), and concentrated under reduced pressure. Purification by silica chromatography (1:1 hexanes:EtOAc) provided alcohol **S6** (32 mg, 57% yield) as a light yellow oil. Diagnostic data: ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.31 (app t, *J* = 7.8 Hz, 2 H), 7.21-7.17 (m, 3H), 5.80 (ddd, *J* = 15.6, 6.0, 6.0 Hz, 1H), 5.74 (ddd, *J* = 15.6, 4.8, 4.8 Hz, 1H), 4.23 (d, *J* = 5.4 Hz, 2H), 4.12 (d, *J* = 4.8Hz, 2H), 1.44 (s, 9H).

To a solution of alcohol **S6** (32 mg, 0.12 mmol) and CS_2 (9.8 mL) at 0 °C was added NaH (59 mg of 60% NaH in mineral oil, 1.4 mmol, 12 equiv) in one portion. The solution was allowed to warm to rt, and after 4 h CH_3I (0.36 mL, 5.6 mmol, 47 equiv) was added dropwise. After 30 min, saturated aqueous NH_4Cl (20 mL) was added to the solution, and the mixture was extracted with CH_2Cl_2 (3 × 10 mL). The combined organic extracts were washed with H_2O, brine, dried (Na_2SO_4), and concentrated under reduced pressure to provide the crude xanthate as a yellow oil, which was used without further purification.

To a solution of the crude xanthate prepared in the previous step (0.12 mmol) and CH_2Cl_2 (0.5 mL) at rt, was added azetidine hydrochloride (12 mg, 0.13 mmol, 1.1 equiv), followed by Et_3N (0.019 mL, 0.13 mmol, 1.1 equiv). The mixture was maintained at rt for 2 h, then concentrated under reduced pressure. Purification by silica chromatography (10:1 hexanes:EtOAc, 5:1 hexanes:EtOAc) provided *O*-carbamothioate **12f** (37 mg, 86% yield) as a light yellow oil: R_f 0.42 (3:1 hexanes:EtOAc); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.31 (t, *J* = 7.8 Hz, 2H), 7.21-7.17 (m, 3H), 5.87 (ddd, *J* = 15.5, 5.8, 5.8 Hz, 1H), 5.73 (ddd, *J* = 15.5, 6.0, 6.0 Hz, 1H), 4.90 (d, *J* = 6.0 Hz, 2H), 4.23 (d, *J* = 5.7 Hz, 2H), 4.18 (t, *J* = 7.7 Hz, 2H), 4.07 (t, *J* = 7.7 Hz, 2H), 2.26 (quintet, *J* = 7.7 Hz, 2H), 1.44 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 186.7 (C), 154.6 (C), 142.8 (CH), 130.9 (CH), 128.8 (CH), 126.7 (CH), 126.1 (CH), 80.6 (C), 70.3 (CH_2), 52.6 (CH_2), 51.9 (CH_2), 50.8 (CH_2), 28.5 (CH_3), 15.0 (CH_2); IR (thin film) 1698, 1598, 1499 cm^{-1}; HRMS (ES+) m/z calcd for $C_{19}H_{26}N_2O_3SNa$ (M+Na) 385.1562, found 385.1550; LRMS (ES+) m/z fragments 360.3, 323.2, 293.2.



(*E*)-*O*-6-Oxohept-2-enyl 1-azetinylcarbamothioate (12g). A solution of alcohol **S7**[6] (279 mg, 0.790 mmol) and CH_2Cl_2 (8 mL) was cooled to 0 °C. EtN(*i*-Pr)$_2$ (0.96 mL, 5.5 mmol, 7 equiv) was added dropwise to the solution. After 10 min, DMSO (0.55 mL, 7.9 mmol, 10 equiv) was added dropwise to the solution. After an additional 10 min, SO_3·pyridine (0.50 g, 3.2 mmol, 4 equiv) was added in one portion, and the solution was maintained at 0 °C for 45 min. Saturated aqueous $NaHCO_3$ (25 mL) was added to the solution, and the mixture was allowed to warm to rt. The mixture was extracted with CH_2Cl_2 (3 x 25 mL), and the combined organic layers were dried (Na_2SO_4), and concentrated under reduced pressure. Purification by silica chromatography (3:1 hexanes:EtOAc) provided the aldehyde (232 mg, 84% yield) as a colorless oil. Diagnostic data: ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.78 (s, 1H), 7.68-7.66 (m, 4H), 7.45-7.37 (m, 6H), 5.70-5.58 (m, 2H), 4.16 (dd, *J* = 6.0, 1.5 Hz, 2H), 2.53-2.50 (m, 2H), 2.40-2.37 (m, 2H), 1.06 (s, 9H).

A solution of the aldehyde prepared in the previous step (214 mg, 0.608 mmol) and Et_2O (3 mL) was cooled to -78 °C. After the dropwise addition of MeMgBr (1.0 mL, 3.0 mmol, 3.0 M in Et_2O, 5 equiv), the Dry Ice/acetone bath was allowed to slowly warm to rt. After 12 h, 0.5 M HCl (10 mL) was slowly added to the solution, and the mixture was extracted with 3:1 hexanes:EtOAc (3 x 25 mL). The combined organic layers were dried (Na_2SO_4), and concentrated under reduced pressure. Purification by silica chromatography (5:1 hexanes:EtOAc) provided the secondary alcohol (210 mg, 94% yield) as a colorless oil. Diagnostic data: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.69 (app d, *J* = 7.0 Hz, 4H), 7.45-7.37 (m, 6H), 5.71-5.58 (m, 2H), 4.17 (d, *J* = 4.5 Hz, 2H), 3.85-3.79 (m, 1H), 2.19-2.06 (m, 2H), 1.59-1.49 (m, 2H), 1.21 (d, *J* = 6.5 Hz, 3H), 1.07 (s, 9H).

A solution of the secondary alcohol prepared in the previous step (397 mg, 1.08 mmol) and CH_2Cl_2 (11 mL) was cooled to 0 °C. EtN(*i*-Pr)$_2$ (1.3 mL, 7.6 mmol, 7 equiv) was added dropwise to the solution. After 10 min, DMSO (0.75 mL, 11 mmol, 10 equiv) was added dropwise to the solution. After and additional 10 min, SO_3·pyridine (0.69 g, 4.3 mmol, 4 equiv) was added in one portion, and the solution was maintained at 0 °C for 45 min. Saturated aqueous $NaHCO_3$ was added to the solution, and the mixture was allowed to warm to rt. The mixture was extracted with CH_2Cl_2 (3 x 25 mL), and the combined organic layers were dried (Na_2SO_4), and concentrated under reduced pressure. Purification by silica chromatography (10:1 hexanes:EtOAc) provided the ketone (335mg, 85% yield) as a colorless oil. Diagnostic data: ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.68-7.67 (m, 4H), 7.44-7.37 (m, 6H), 5.66-5.56 (m, 2H), 4.16-4.15 (m, 2H), 2.49 (app t, *J* = 6.5 Hz, 2H), 2.32-2.29 (m, 2H), 2.15 (s, 3H), 1.06 (s, 9H).

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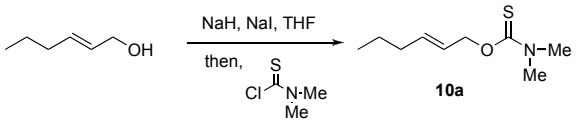
[6] Hayashi, N.; Fujiwara, K.; Murai, A. *Tetrahedron*, **1997**, *53*, 12425-12468.

To a solution of the ketone prepared in the previous step (168 mg, 0.459 mmol) and THF (3 mL) at rt, was added TBAF (0.69 mL, 0.69 mmol, 1 M in THF, 1.5 equiv). After 45 min, dry silica powder was added to the solution and the slurry was concentrated under reduced pressure. The silica powder was loaded onto a silica column and purified by silica chromatography (5:1 hexanes:EtOAc, 1:1 hexanes:EtOAc) to provide alcohol **S8** (52 mg, 87% yield) as a colorless oil. Diagnostic data: ^{1}H NMR (600 MHz, $CDCl_3$) δ 5.68 (m, 2H), 4.09 (d, *J* = 3.5 Hz, 2H), 2.54 (app t, *J* = 6.0 Hz, 2H), 2.34-2.31 (m, 2H), 2.15 (s, 3H).

Following the previously described procedure for *O*-carbamothioate **12f**, alcohol **S8** was converted to the *O*-carbamothioate **12g** (42 mg, 93% yield), and was obtained as a light yellow oil: R_f 0.28 (3:1 hexanes:EtOAc); ^{1}H NMR (500 MHz, CD_2Cl_2) δ 5.77 (ddd, *J* = 15.4, 6.6, 6.6 Hz, 1H), 5.64 (ddd, *J* = 15.4, 6.2, 6.2 Hz, 1H), 4.82 (d, *J* = 6.1 Hz, 2H), 4.12 (t, *J* = 7.7 Hz, 2H), 4.07 (t, *J* = 7.7 Hz, 2H), 2.52 (t, *J* = 7.4 Hz, 2H), 2.30 (q, *J* = 7.0 Hz, 2H), 2.23 (quintet, *J* = 7.7 Hz, 2H), 2.11 (s, 3H); ^{13}C NMR (125 MHz, CD_2Cl_2) δ 208.0 (C), 187.1 (C), 134.7 (CH), 125.6 (CH), 71.2 (CH_2), 53.0 (CH_2), 51.2 (CH_2), 43.0 (CH_2), 30.3 (CH_3), 26.8 (CH_2), 15.3 (CH_2); IR (thin film) 1742, 1717, 1698, cm^{-1}; HRMS (ES+) m/z calcd for $C_{11}H_{17}NO_2SNa$ (M+Na) 250.0878, found 250.0887; LRMS (ES+) m/z fragments 215.1, 213.1, 173.1.



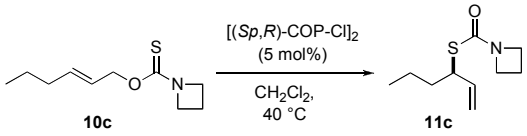
(*E*)-*O*-2-Hexenyl 1-dimethylcarbamothioate (10a). A modified procedure reported by Falck was employed.[7] To a solution of *trans*-2-hexene-1-ol (1.2 mL, 1.0 mmol) and THF (20 mL), was added to a solution of NaH (1.2 g of 60% NaH in mineral oil, 30 mmol, 3 equiv) and THF (40 mL) at 0 °C. The solution was maintained at 0 °C for 30 min, then NaI (150 mg, 0.998 mmol, 0.1 equiv) and *N*,*N*-dimethylthiocarbamoyl chloride (1.48 g, 12.0 mmol, 1.2 equiv) were added successively. The solution was allowed to warm to rt and was maintained at rt for 1 h. Saturated aqueous NH_4Cl was added to the solution, and the mixture was extracted with Et_2O (3 x 20 mL). The combined organic layers were washed with H_2O, brine, dried ($MgSO_4$), and concentrated under reduced pressure. Purification by silica chromatography (5% Et_2O:hexanes) provided *O*-carbamothioate **10a** (1.64 g, 88% yield) as a pale yellow oil: R_f 0.54 (10:1 hexanes:EtOAc); ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.80 (ddd, *J* = 15.4, 6.7, 6.7 Hz, 1H), 5.65 (ddd, *J* = 15.3, 6.4, 6.4 Hz, 1H), 4.91 (d, *J* = 6.3 Hz, 2H), 3.37 (s, 3H), 3.12 (s, 3H), 2.05 (q, *J* = 7.1 Hz, 2H), 1.48 (qn, *J* = 7.4 Hz, 2H), 0.90 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 188.3 (C), 136.4 (CH), 124.4 (CH), 72.5 (CH_2), 42.9 (CH_3), 38.0 (CH_3), 34.6 (CH_2), 22.3 (CH_2), 13.8 (CH_3); IR (thin film) 1522, 1393 cm^{-1}; HRMS (ES+) m/z calcd for $C_9H_{17}NOSNa$ (M+Na) 210.0928, found 210.0933; LRMS (ES+) m/z fragments 188.1, 173.1, 167.1.

(*E*)-*O*-4-(*tert*-Butyldimethylsilyloxy)but-2-enyl 1-dimethylcarbamothioate (13a). Following the procedure described for the preparation of **10a**, 4-(*tert*-butyl-dimethyl-silanyloxy)-but-2-en-1-ol (207 mg, 1.03 mmol) was converted to the *O*-carbamothioate **13a** (234 mg, 78% yield), and was obtained as a pale yellow oil: R_f 0.38 (10:1 hexanes:EtOAc); ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.89-5.88 (m, 2H), 4.97 (s, 2H),

[7] Barma, D. K.; Bandyopadhyay, A.; Capdevila, J. H.; Falk, J. R. *Org. Lett.* **2003**, *5*, 4755-4757.

4.21 (s, 2H), 3.38 (s, 3H), 3.13 (s, 3H), 0.92 (s, 9H), 0.08 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 188.2 (C), 134.0 (CH), 124.2 (CH), 71.6 (CH_2), 63.2 (CH_2), 43.0 (CH_3), 38.0 (CH_3), 26.1 (CH_3), 18.6 (C), -5.0 (CH_3); IR (thin film) 1522, 1463 cm^{-1}; HRMS (ES+) m/z calcd for $C_{13}H_{27}NO_2SSiNa$ (M+Na) 312.1429, found 312.1429; LRMS (ES+) m/z fragment 290.2.

(*E*)-*O*-4-(*tert*-Butoxycarbonyl(phenyl)amino)but-2-enyl 1-dimethylcarbamothioate (13b). To a solution of **S6** (36 mg, 0.14 mmol) and THF (0.6 mL), was added NaH (10 mg of 60% NaH in mineral oil, 0.30 mmol, 2.2 equiv) neat at 0 °C. The solution was maintained at 0 °C for 30 min, then NaI (4 mg, 0.03 mmol, 0.2 equiv) and *N*,*N*-dimethylthiocarbamoyl chloride (41 mg, 0.33 mmol, 2.4 equiv) were added successively. The solution was allowed to warm to rt and was maintained at rt for 1 h. Saturated aqueous NH_4Cl was added to the solution, and the mixture was extracted with Et_2O (3 x 10 mL). The combined organic layers were washed with H_2O, brine, dried ($MgSO_4$), and concentrated under reduced pressure. Purification by silica chromatography (10:1 hexanes:EtOAc, 5:1 hexanes:EtOAc) provided *O*-carbamothioate **13b** (41 mg, 85% yield), and was obtained as a pale yellow oil. R_f 0.38 (3:1 hexanes:EtOAc); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.31 (t, J = 7.8 Hz, 2H),7.21-7.18 (m, 3H), 5.88 (ddd, J = 15.5, 5.7, 5.7 Hz, 1H), 5.76 (ddd, J = 15.4, 5.9, 5.9 Hz, 1H), 4.94 (d, J = 5.9 Hz, 2H), 4.24 (d, J = 5.7 Hz, 2H), 3.36 (s, 3H), 3.10 (s, 3H), 1.44 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 188.0 (C), 154.6 (C), 142.8 (C), 130.8 (CH), 128.8 (CH), 126.7 (CH), 126.7 (CH), 126.1 (CH), 80.6 (C), 71.3 (CH_2), 51.9 (CH_2), 43.0 (CH_3), 38.0 (CH_3), 28.5 (CH_3); IR (thin film) 1698, 1598, 1522 cm^{-1}; HRMS (ES+) m/z calcd for $C_{18}H_{26}N_2O_3SNa$ (M+Na) 373.1562, found 373.1569; LRMS (ES+) m/z fragments 357.2, 351.2, 279.2.



General procedure for rearrangement of *O*-allyl methyl- and 1-azetidinylcarbamothioates using 5 mol% [(*Sp*,*R*)-COP-Cl]$_2$ at 40 °C. Preparation of (*R*)-*S*-1-Hexen-3-yl 1-azetinylcarbamothioate (11c). A solution of *S*-carbamothioate **10c** (53 mg, 0.27 mmol), [(*Sp*,*R*)-COP-Cl]$_2$ (18 mg, 0.013 mmol, 0.05 equiv) and CH_2Cl_2 (0.51 mL) was sealed, protected from light, and maintained at 40 °C. After 13 h, ethylenediamine (0.010 mL, 0.13 mmol, 0.5 equiv) was added to the mixture after allowing it to cool to room temperature. After 15 min, the orange solution was transferred to a round bottom flask with CH_2Cl_2 (10 mL), and dry silica gel (ca. 60 mg) was added to the mixture. The slurry was concentrated, and the yellow powder was loaded onto a short silica gel column. Elution with 10:1 hexanes:EtOAc provided the transposed *S*-1-hexenyl 1-azetinylcarbamothioate (**11c**) (52 mg, 98% yield) as a light yellow oil. SFC analysis indicated an enantiomeric excess of 83% [OB column; flow = 1.5 mL/min; 10% isopropanol/90% CO_2; λ = 230 nm; major enantiomer t_R= 4.24 min; minor enantiomer t_R= 3.88 min]; R_f 0.22 (10% Et_2O:hexanes); ^{1}H NMR (600 MHz, $CDCl_3$) δ 5.79 (ddd, J = 18.2, 10.1, 8.3, 1H), 5.22 (d, J = 17.0 Hz, 1H), 5.05 (d, J = 10.1 Hz, 1H), 4.03-4.00 (m, 5H), 2.29 (quintet, J = 7.7 Hz, 2H), 1.70-1.61 (m, 2H), 1.45-1.35 (m, 2H), 0.91 (t, J = 7.4 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 167.1 (C), 138.7 (CH), 115.4 (CH), 49.7 (CH_2), 46.7 (CH), 36.6 (CH_2), 20.2 (CH_2), 15.9 (CH_2), 13.8 (CH_3); IR (thin film) 1656, 1466,

1360 cm^{-1}; HRMS (ES+) m/z calcd for $C_{10}H_{17}NOSNa$ (M+Na) 222.0928, found 222.0928; LRMS (ES+) m/z fragments 200.0, 195.0; $[\alpha]^{24}_{589}$ +25.0, $[\alpha]^{24}_{577}$ +26.0, $[\alpha]^{24}_{546}$ +29.5, $[\alpha]^{24}_{435}$ +51.1 (*c* = 2.41, CH_2Cl_2).

(*S*)-*S*-5-Methylhex-1-en-3-yl 1-azetinylcarbamothioate (14a). Following the general procedure described for the preparation of **11c** and using [(*Rp*,*S*)-COP-Cl]$_2$, *O*-carbamothioate **12a** (54 mg, 0.25 mmol) was converted to the *S*-5-methylhex-1-en-3-yl 1-azetinylcarbamothioate **14a** (45 mg, 85% yield), a light yellow oil: SFC analysis indicated an enantiomeric excess of 80% [OB column; flow: 1.0 mL/min; 10% isopropanol/ 90% CO_2; λ = 230 nm; major enantiomer t_R= 4.75 min; minor enantiomer t_R= 5.30 min]; R_f 0.33 (20% Et_2O:pentane); ^{1}H NMR (600 MHz, $CDCl_3$) δ 5.77 (ddd, *J* = 17.1, 8.5, 8.5, 1H), 5.24 (d, *J* = 17.0 Hz, 1H), 5.05 (d, *J* = 10.1 Hz, 1H), 4.09-4.04 (m, 5H), 2.29 (quintet, *J* = 7.7 Hz, 2H), 1.74-1.67 (m, 1H), 1.57-1.52 (m, 2H), 0.92 (d, *J* = 4.5 Hz, 3H), 0.91 (d, *J* = 4.3 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 167.3 (C), 139.2 (CH), 115.6 (CH), 50.0 (CH_2), 45.5 (CH), 43.6 (CH_2), 25.9 (CH), 22.9 (CH_3), 22.1 (CH_3), 16.2 (CH_2); IR (thin film) 1656, 1468, 1364 cm^{-1}; HRMS (ES+) m/z calcd for $C_{11}H_{19}NOSNa$ (M+Na) 236.1085, found 236.1076; LRMS (ES+) m/z fragments 214.2, 173.1; $[\alpha]^{24}_{589}$ –21.9, $[\alpha]^{25}_{577}$ –22.6, $[\alpha]^{25}_{546}$ –25.6, $[\alpha]^{24}_{435}$ –44.3, $[\alpha]^{25}_{405}$ –51.5 (*c* = 0.55, CH_2Cl_2).

(*R*)-*S*-1-(*tert*-Butyldimethylsilyloxy)but-3-en-2-yl 1-azetinylcarbamothioate (14b). Following the general procedure described for the preparation of **11c** and using [(*Rp*,*S*)-COP-Cl]$_2$, *O*-carbamothioate **12b** (95 mg, 0.32 mmol) was converted to the *S*-1-(*tert*-butyldimethylsilyloxy)but-3-en-2-yl 1-azetinylcarbamothioate **14b** (81 mg, 85% yield), and was obtained as a light yellow oil: SFC analysis indicated an enantiomeric excess of 88% [OB column; flow: 1.0 mL/min; 10% isopropanol/ 90% CO_2; λ = 230 nm; major enantiomer t_R= 3.48 min; minor enantiomer t_R= 3.79 min]; R_f 0.29 (20% Et_2O:hexanes); ^{1}H NMR (600 MHz, $CDCl_3$) δ 5.93 (ddd, *J* = 18.0, 10.2, 7.9 Hz, 1H), 5.32 (d, *J* = 17.1 Hz, 1H), 5.14 (dd, *J* = 10.3, 0.5 Hz, 1H), 4.15-4.12 (m, 1H), 4.05-4.04 (m, 4H), 3.84 (dd, *J* = 10.1, 4.6 Hz, 1H), 3.73 (dd, *J* = 10.1, 6.7 Hz, 1H), 2.30 (quintet, *J* = 7.7 Hz, 2H), 0.89 (s, 9H), 0.06 (s, 3H), 0.06 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ167.0 (C), 136.1 (CH), 117.3 (CH), 66.1 (CH_2), 50.0 (CH_2), 49.1 (CH), 26.0 (CH_3), 18.5 (C), 16.2 (CH_2), -5.1 (CH_3), -5.1 (CH_3); IR (thin film) 1656, 1472, 1360 cm^{-1}; HRMS (ES+) m/z calcd for $C_{14}H_{27}NO_2SSiNa$ (M+Na) 324.1429, found 324.1429; LRMS (ES+) m/z fragments 302.2, 215.2; $[\alpha]^{24}_{589}$ +31.3, $[\alpha]^{25}_{577}$ +34.0, $[\alpha]^{25}_{546}$ +45.5 (*c* = 2.1, CH_2Cl_2).

(*R*)-*S*-1-(Triisopropylsilyloxy)but-3-en-2-yl 1-azetinylcarbamothioate (14c). Following the general procedure described for the preparation of **11c** and using [(*Rp*,*S*)-COP-Cl]$_2$, *O*-carbamothioate **12c** (59 mg, 0.173 mmol) was converted to the *S*-(triisopropylsilyloxy)but-3-en-2-yl 1-azetinylcarbamothioate **14c** (59 mg, 99% yield), and was obtained as a light yellow oil: R_f 0.42 (5:1 hexanes:EtOAc); ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.99 (ddd, *J* = 18.1, 10.2, 7.9 Hz, 1H), 5.39 (d, *J* = 17.1 Hz, 1H), 5.20 (d, *J* = 10.3 Hz, 1H), 4.24 (app q, *J* = 11.8, 7.0 Hz, 1H), 4.06 (app t, *J* = 7.3 Hz, 4H), 4.00 (dd, *J* = 9.5, 4.5 Hz, 1H), 3.89 (dd, *J* = 9.8, 6.5 Hz, 1H), 2.30 (quintet, *J* = 7.7 Hz, 2H), 1.13-1.06 (m, 21H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 167.2 (C), 136.3 (CH), 117.1 (CH), 66.5 (CH_2), 50.0 (CH_2), 49.4 (CH), 18.2 (CH_3), 16.2 (CH), 12.2 (CH_2); IR (thin film) 1659, 1465, 1362 cm^{-1}; HRMS (ES+) m/z calcd for $C_{17}H_{33}NO_2SSiNa$ (M+Na) 366.1899, found 366.1900; LRMS (ES+) m/z fragments 344.2, 249.2; $[\alpha]^{25}_{589}$ +12.1, $[\alpha]^{25}_{577}$ +13.1, $[\alpha]^{25}_{546}$ +14.6, $[\alpha]^{25}_{435}$ +24.1, $[\alpha]^{25}_{405}$ +29.3 (*c* = 1.0, CH_2Cl_2).

For SFC analysis, the TIPS protecting group was removed. To a solution of **14c** (12 mg, 0.034 mmol) and THF (0.5 mL) at 0 °C, was added pyridine (0.01 mL) and HF·pyridine (0.005 mL). The solution was allowed to warm to rt. After 16 h, saturated aqueous $NaHCO_3$ (15 mL) was slowly added to the solution, and the mixture was extracted with Et_2O (3 x 10 mL). The combined organic layers were washed with saturated aqueous $CuSO_4$ (15 mL), dried (Na_2SO_4), and concentrated under reduced pressure (CAUTION: Product is Volatile!!). Purification by silica chromatography (100% Et_2O) provided alcohol **14e** (4 mg, 67% yield) as a light yellow oil. SFC analysis indicated an enantiomeric excess of 87% [OB column; flow: 1.5 mL/min; 10% isopropanol/ 90% CO_2; λ = 230 nm; major enantiomer t_R= 5.84 min; minor enantiomer t_R= 7.26 min].

(*R*)-*S*-1-(*tert*-Butyldiphenylsilyloxy)but-3-en-2-yl 1-azetinylcarbamothioate (14d). Following the general procedure described for the preparation of **11c** and using [(*Rp*,*S*)-COP-Cl]$_2$, *O*-carbamothioate **12d** (33 mg, 0.078 mmol) was converted to the *S*-1-(*tert*-butyldiphenylsilyloxy)but-3-en-2-yl 1-azetinylcarbamothioate **14d** (29 mg, 86% yield), and was obtained as a light yellow oil: R_f 0.32 (5:1 hexanes:EtOAc); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.69 (app t, *J* = 5.5 Hz, 4H), 7.45-7.37 (m, 6H), 6.00 (ddd, *J* = 17.4, 10.2, 8.1, 1H), 5.35 (d, *J* = 17.1 Hz, 1H), 5.17 (d, *J* = 10.3 Hz, 1H), 4.27 (app q, *J* = 13.1, 5.8 Hz, 1H), 4.05 (app t, *J* = 7.1 Hz, 4H), 3.91 (dd, *J* = 10.2, 4.7 Hz, 1H), 3.83 (dd, *J* = 10.1, 6.1 Hz, 1H), 2.30 (quintet, *J* = 7.6 Hz, 2H), 1.07 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.9 (C), 136.2 (CH), 135.9 (CH), 135.9 (CH), 133.6 (CH), 129.8 (CH), 127.8 (CH), 127.8 (CH), 117.3 (CH), 66.6 (CH_2), 50.0 (CH_2), 49.2 (CH), 27.0 (CH_3), 19.6 (C), 16.2 (CH_2); IR (thin film) 1656, 1428, 1362 cm^{-1}; HRMS (ES+) m/z calcd for $C_{24}H_{31}NO_2SSiNa$ (M+Na) 448.1743, found 448.1734; LRMS (ES+) m/z fragments 426.2, 337.3; $[\alpha]^{25}_{589}$ +4.2, $[\alpha]^{25}_{577}$ +5.6, $[\alpha]^{25}_{546}$ +6.0, $[\alpha]^{25}_{435}$ -5.53 (*c* = 0.6, CH_2Cl_2).

For SFC analysis, the TBDPS protecting group was removed. To a solution of **14d** (13 mg, 0.030 mmol) and THF (0.5 mL) at 0 °C, was added pyridine (0.009 mL) and HF·pyridine (0.005 mL). The solution was allowed to warm to rt. After 16 h, saturated aqueous $NaHCO_3$ (15 mL) was slowly added to the solution, and the mixture was extracted with Et_2O (3 x 10 mL). The combined organic layers were washed with saturated aqueous $CuSO_4$ (15 mL), dried (Na_2SO_4), and concentrated under reduced pressure (CAUTION: Product is Volatile!!). Purification by silica chromatography (100% Et_2O) provided alcohol **14e** (4 mg, 71% yield) as a light yellow oil. SFC analysis indicated an enantiomeric excess of 76% [OB column; flow: 1.5 mL/min; 10% isopropanol/ 90% CO_2; λ = 230 nm; major enantiomer t_R= 5.80 min; minor enantiomer t_R= 7.44 min].

(*R*)-*S*-1-Hydroxybut-3-en-2-yl 1-azetinylcarbamothioate (14e). Following the general procedure described for the preparation of **11c** and using [(*Rp*,*S*)-COP-Cl]$_2$, *O*-carbamothioate **12e** (76 mg, 0.41 mmol) was converted to the *S*-1-hydroxybut-3-en-2-yl 1-azetinylcarbamothioate **14e** (42 mg, 55% yield, CAUTION: Product is Volatile!!!), and was obtained as a light yellow oil: SFC analysis indicated an enantiomeric excess of 61% [OB column; flow: 1.5 mL/min; 10% isopropanol/ 90% CO_2; λ = 230 nm; major enantiomer t_R= 5.81 min; minor enantiomer t_R= 7.15 min]; R_f 0.45 (100% Et_2O); ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.91 (ddd, *J* = 17.4, 10.3, 7.8 Hz, 1H), 5.36 (d, *J* = 17.2 Hz, 1H), 5.24 (d, *J* = 10.4 Hz, 1H), 4.20 (app q, 13.0, 6.8 Hz, 1H), 4.09 (app t, *J* = 7.6 Hz, 4H), 3.88 (dd, *J* = 11.2, 5.4 Hz, 1H), 3.77 (dd, *J* = 11.2, 7.0 Hz, 1H), 2.33 (quintet, *J* = 7.6 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 167.0, 134.2, 118.4, 65.7, 50.0, 49.2, 30.3,

15.9; IR (thin film) 3404 (broad), 1636, 1372 cm^{-1}; HRMS (ES+) m/z calcd for $C_8H_{13}NO_2SNa$ (M+Na) 210.0565, found 210.0562; LRMS (ES+) m/z fragments 188.1, 167.1; $[\alpha]^{23}_{589}$ –0.16, $[\alpha]^{24}_{577}$ –0.30, $[\alpha]^{24}_{546}$ –0.030, $[\alpha]^{24}_{435}$ –3.5 (*c* = 2.2, CH_2Cl_2).

(*R*)-*S*-1-(*tert*-Butoxycarbonyl(phenyl)amino)but-3-en-2-yl 1-azetinylcarbamothioate (14f). Following the general procedure described for the preparation of **11c** and using [(*Rp*,*S*)-COP-Cl]$_2$, *O*-carbamothioate **12f** (23 mg, 0.065 mmol) was converted to the *S*-1-(*tert*-butoxycarbonyl(phenyl)amino)but-3-en-2-yl 1-azetinylcarbamothioate **14f** (16 mg, 68% yield), and was obtained as a light yellow oil: SFC analysis indicated an enantiomeric excess of 71% [AD column; flow: 1.5 mL/min; 10% isopropanol/ 90% CO_2; λ = 230 nm; major enantiomer t_R= 7.92 min; minor enantiomer t_R= 7.39 min]; R_f 0.31 (3:1 hexanes:EtOAc); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.34 (app t, *J* = 7.7 Hz, 2H), 7.22-7.19 (m, 3H), 5.84 (ddd, *J* = 17.7, 9.0, 9.0 Hz, 1H), 5.27 (d, *J* = 17.0 Hz, 1H), 5.15 (d, *J* = 10.2 Hz, 1H), 4.19-4.09 (m, 1H), 4.09-3.93 (m, 5H), 3.89 (dd, *J* = 14.0, 6.9 Hz, 1H), 2.28 (quintet, *J* = 7.6 Hz, 2H), 1.44 (brs, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.4 (C), 154.9 (C), 142.0 (C), 136.2 (C), 128.9 (CH), 127.6 (CH), 126.5 (CH), 118.0 (CH), 80.7 (C), 52.5 (CH_2), 50.0 (CH_2), 46.1 (CH), 28.5 (CH_3), 16.2 (CH_2); IR (thin film) 1698, 1659, 1495, 1364 cm^{-1}; HRMS (ES+) m/z calcd for $C_{19}H_{26}N_2O_3SNa$ (M+Na) 385.1562, found 385.1559; LRMS (ES+) m/z fragments 363.2, 263.1; $[\alpha]^{25}_{589}$ –21.1, $[\alpha]^{25}_{577}$ –22.3, $[\alpha]^{25}_{546}$ –25.2, $[\alpha]^{24}_{435}$ –46.7 (*c* = 0.70, CH_2Cl_2).

(*S*)-*S*-6-Oxohept-1-en-3-yl 1-azetinylcarbamothioate (14g). Following the general procedure described for the preparation of **11c** and using [(*Rp*,*S*)-COP-Cl]$_2$, *O*-carbamothioate **12g** (15 mg, 0.07 mmol) was converted to the *S*-6-oxohept-1-en-3-yl 1-azetinylcarbamothioate **14g** (13 mg, 85% yield), and was obtained as a light yellow oil: SFC analysis indicated an enantiomeric excess of 76% [OB column; flow: 1.5 mL/min; 10% isopropanol/ 90% CO_2; λ = 230 nm; major enantiomer t_R= 7.83 min; minor enantiomer t_R= 9.65 min]; R_f 0.46 (1:1 hexanes:EtOAc); ^{1}H NMR (600 MHz, CD_2Cl_2) δ 5.80 (ddd, *J* = 17.3, 10.2, 7.9 Hz, 1H), 5.20 (d, *J* = 17.1 Hz, 1H), 5.07 (d, *J* = 10.2 Hz, 1H), 4.01 (app t, *J* = 7.6 Hz, 4H), 3.93 (app q, *J* = 15.0, 7.5 Hz, 1H), 2.52 (app t, *J* = 7.5 Hz, 2H), 2.29 (app quintet, *J* = 7.7, 2H), 2.10 (s, 3H), 1.96 (ddd, *J* = 14.5, 14.5, 7.2 Hz, 1H), 1.90 (ddd, *J* = 14.8, 14.8, 7.5 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 208.1 (C), 166.8 (C), 138.9 (CH), 116.1 (CH), 50.4 (CH_2), 46.7 (CH), 41.4 (CH_2), 30.3 (CH_3), 28.9 (CH_2), 16.5 (CH_2); IR (thin film) 1713, 1648, 1362 cm^{-1}; HRMS (ES+) m/z calcd for $C_{11}H_{17}NO_2SNa$ (M+Na) 250.0878, found 250.0870; LRMS (ES+) m/z fragments 228.1, 217.1; $[\alpha]^{24}_{589}$ –16.9, $[\alpha]^{24}_{577}$ –17.4, $[\alpha]^{25}_{546}$ –18.4 (*c* = 0.23, CH_2Cl_2).

(*R*)-*S*-Hex-1-en-3-yl 1-dimethylcarbamothioate (11a). Following the general procedure described for the preparation of **11c** and using [(*Sp*,*R*)-COP-Cl]$_2$, *O*-carbamothioate **10a** (56 mg, 0.30 mmol) was converted to the *S*-hex-1-en-3-yl 1-dimethylcarbamothioate **11a** (41 mg, 72% yield), and was obtained as a light yellow oil: Chiral GC analysis indicated an enantiomeric excess of 82% [Cyclosil-B column; flow: 1.5 mL/min; 120 ºC, ; major enantiomer t_R= 22.6 min; minor enantiomer t_R= 21.8 min]; R_f 0.40 (10:1 hexanes:EtOAc); ^{1}H NMR (600 MHz, $CDCl_3$) δ 5.83 (ddd, *J* = 18.3, 10.2, 8.3 Hz, 1H), 5.25 (d, *J* = 17.0 Hz, 1H), 5.08 (d, *J* = 10.2 Hz, 1H), 4.05 (app q, *J* = 15.1, 7.5 Hz, 1H), 3.00 (s, 6H), 1.74-1.66 (m, 2H), 1.47-1.40 (m, 2H), 0.93 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 167.9 (C), 139.1 (CH), 115.7 (CH), 47.9 (CH), 36.8 (CH_3), 36.8 (CH_2), 20.6 (CH_2), 14.0 (CH_3); IR (thin film) 1652, 1466, 1362 cm^{-1}; HRMS (ES+) m/z calcd for $C_9H_{17}NOSNa$ (M+Na) 210.0928, found 210.0925; LRMS (ES+) m/z

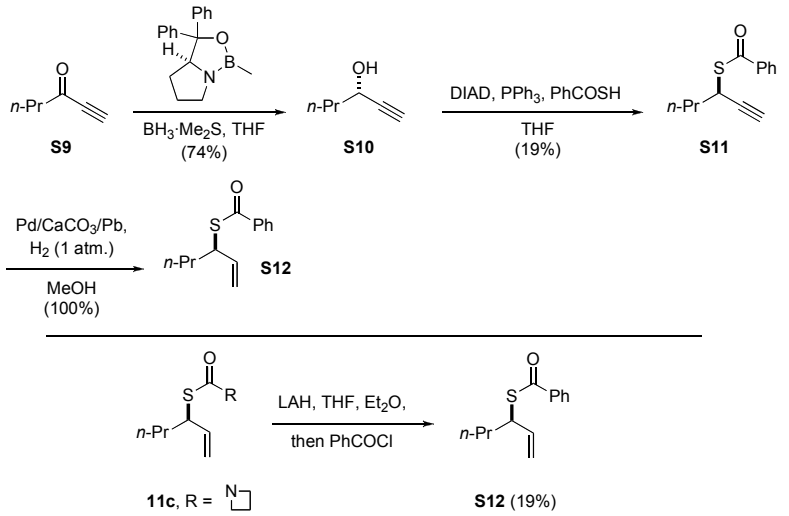
fragments 188.1, 106.0; $[\alpha]^{24}_{589}$ +39.1, $[\alpha]^{24}_{577}$ +40.3, $[\alpha]^{24}_{546}$ +45.6, $[\alpha]^{24}_{435}$ +83.2 (*c* = 1.0, CH_2Cl_2).

(*R*)-*S*-1-(*tert*-Butyldimethylsilyloxy)but-3-en-2-yl 1-dimethylcarbamothioate (15a). Following the general procedure described for the preparation of **11c** and using [(*Rp*,*S*)-COP-Cl]$_2$, *O*-carbamothioate **13a** (45 mg, 0.22 mmol) was converted to the *S*-1-(*tert*-butyldimethylsilyloxy)but-3-en-2-yl 1-dimethylcarbamothioate **15a** (44 mg, 97% yield), and was obtained as a light yellow oil: R_f 0.30 (10:1 hexanes:EtOAc); ^{1}H NMR (600 MHz, $CDCl_3$) δ 5.95 (ddd, *J* = 17.8, 10.3, 8.0 Hz, 1H), 5.34 (d, *J* = 17.1 Hz, 1H), 5.16 (d, *J* = 10.3 Hz, 1H), 4.18 (app q, *J* = 12.2, 6.7 Hz, 1H), 3.86 (dd, *J* = 10.1, 4.7 Hz, 1H), 3.76 (dd, *J* = 10.1, 6.6 Hz, 1H), 3.00 (s, 6H), 0.91 (s, 9H), 0.07 (s, 3H), 0.07 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 167.4 (C), 136.0 (CH), 117.2 (CH), 65.8 (CH_2), 49.9 (CH), 36.7 (CH_3), 25.9 (CH_3), 18.4 (C), -5.22 (CH_3), -5.23 (CH_3); IR (thin film) 1659, 1472, 1362 cm^{-1}; HRMS (ES+) m/z calcd for $C_{13}H_{27}NO_2SSiNa$ (M+Na) 312.1429, found 312.1425; LRMS (ES+) m/z fragments 290.2, 269.1; $[\alpha]^{28}_{589}$ +6.1, $[\alpha]^{28}_{577}$ +6.5, $[\alpha]^{28}_{546}$ +7.3, $[\alpha]^{28}_{435}$ +6.1 (*c* = 0.98, CH_2Cl_2).

For GC analysis, the TBS protecting group was removed. To a solution of **15a** (8 mg, 0.04 mmol) and THF (0.5 mL) at 0 °C, was added pyridine (0.01 mL) and HF·pyridine (0.005 mL). The solution was allowed to warm to rt. After 2 h, saturated aqueous $NaHCO_3$ (15 mL) was slowly added to the solution, and the mixture was extracted with Et_2O (3 x 10 mL). The combined organic layers were washed with saturated aqueous $CuSO_4$ (15 mL), dried (Na_2SO_4), and concentrated under reduced pressure. Purification by silica chromatography (100% Et_2O) provided the alcohol (2 mg, 37% yield) as a light yellow oil. Chiral GC analysis indicated an enantiomeric excess of 88% [Cyclosil-B column; flow: 1.5 mL/min; 110 ºC, ; major enantiomer t_R= 124.2 min; minor enantiomer t_R= 130.0 min]

(*R*)-*S*-1-(*tert*-Butoxycarbonyl(phenyl)amino)but-3-en-2-yl 1-dimethylcarbamothioate (15b). Following the general procedure described for the preparation of **11c** and using [(*Rp*,*S*)-COP-Cl]$_2$, *O*-carbamothioate **13b** (11 mg, 0.031 mmol) was converted to the *S*-1-(*tert*-butoxycarbonyl(phenyl)amino)but-3-en-2-yl 1-dimethylcarbamothioate **15b** (8 mg, 77% yield), and was obtained as a light yellow oil: SFC analysis indicated an enantiomeric excess of 81% [OB column; flow: 1.5 mL/min; 10% of 1:1 hexanes:isopropanol/ 90% CO_2; λ = 230 nm; major enantiomer t_R= 8.83 min; minor enantiomer t_R= 11.41 min]; R_f 0.35 (3:1 hexanes:EtOAc); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.34 (app t, *J* = 7.6 Hz, 2H), 7.22-7.19 (m, 3H), 5.86 (ddd, *J* = 17.6, 9.4, 9.4 Hz, 1H), 5.29 (d, *J* = 17.0 Hz, 1H), 5.16 (d, *J* = 10.2 Hz, 1H), 4.21-4.13 (m, 1H), 4.09-4.00 (m, 1H), 3.91 (dd, *J* = 14.1, 7.0 Hz, 1H), 2.95 (s, 6H), 1.26 (brs, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.7 (C), 154.8 (C), 141.8 (C), 136.2 (CH), 128.8 (CH), 127.5 (CH), 126.3 (CH), 117.8 (CH), 80.5 (C), 52.2 (CH_2), 46.9 (CH), 36.7 (CH_3), 28.3 (CH_3); IR (thin film) 1698, 1659, 1366 cm^{-1}; HRMS (ES+) m/z calcd for $C_{18}H_{26}N_2O_3SNa$ (M+Na) 373.1562, found 373.1556; LRMS (ES+) m/z fragments 337.2, 251.1; $[\alpha]^{29}_{589}$ –28.8, $[\alpha]^{29}_{577}$ –29.6, $[\alpha]^{29}_{546}$ –17.1, $[\alpha]^{29}_{435}$ –71.2 (*c* = 0.24, CH_2Cl_2).

The Absolute Configuration of *S*-1-Hexen-3-yl carbamothioates 11a–e.



Conversion of Alcohol S10 to (*R*)-*S*-Benzothioate S12. A solution of (*S*)-hex-1-yn-3-ol **S10**[8] (22 mg, 0.22 mmol) and THF (1 mL) was dried over activated 4Å molecular sieves for 10 min. This solution was transferred to dry flask, and *S*-phenylthiotic acid (53 μL, 0.45 mmol, 2 equiv), Ph_3P (118 mg, 0.45 mmol, 2 equiv), and diisopropyl azodicarboxylate (64 μL, 0.45 mmol, 2 equiv) were added consecutively at room temperature. After 15 h, the solution was diluted with Et_2O (10 mL), and the organic layer was washed with a saturated solution of $NaHCO_3$ (10 mL), brine (10 mL), dried ($MgSO_4$), and concentrated. Purification of the residue by silica gel chromatography (1% Et_2O-hexanes, 2% Et_2O-hexanes, 3% Et_2O-hexanes, 5% Et_2O-hexanes) provided alkyne **S11** (9 mg, 19% yield) as a colorless oil.

Lindlar catalyst (1 mg) was added at room temperature to a solution of alkyne **S11** (4 mg, 0.002 mmol) and MeOH (1 mL). This mixture was placed under H_2 (1 atm). After 1 h, the mixture was filtered through Celite, the Celite was washed with MeOH (5 mL), and the eluent was concentrated to provide *S*-benzothioate **S12** (4 mg, 100%) as a colorless oil. HPLC analysis indicated a enantiomeric excess of 66% [OB column; flow: 0.8 mL/min; 100% hexanes, major enantiomer t_R= 24.2 min; minor enantiomer t_R = 18.6 min].

Conversion of (*R*)-*S*-1-Hexen-3-yl 1-azetinylcarbamothioate (11c) to (*R*)-*S*-Benzothioate S12. Solid $LiAlH_4$ (29 mg, 0.78 mmol) was added in one portion to a solution of (*R*)-*S*-1-hexen-3-yl 1-azetinylcarbamothioate (**11c**) (77 mg, 0.39 mmol), THF (3 mL) and Et_2O (2 mL) at room temperature. After 2 h, the mixture was cooled to 0 ºC, and benzoyl chloride (0.45 mL, 3.9 mmol) was added dropwise. The resulting mixture was allowed to warm to room temperature. After 30 min, the mixture was filtered through Celite and the eluent was mixed with Et_2O (10 mL) and a saturated solution of K_2CO_3 (10 mL). The aqueous layer was separated, extracted with Et_2O (3 x 3 mL), and the organic extract was dried ($MgSO_4$) and concentrated. Purification of the residue by silica gel chromatography (hexanes, 2% Et_2O-hexanes, 5% Et_2O-hexanes) provided (*R*)-*S*-

[8] For the preparation of **S11**, see the Supporting Information of: Kirsch, S. F.; Overman, L. E.; White, N. S. *Org. Lett.* **2007**, *9*, 911–913.

benzothiate **S12** (16 mg, 19%) as a colorless oil. HPLC analysis [OB column; flow: 0.8 mL/min; 100% hexanes, major enantiomer t_R= 24.1 min; minor enantiomer t_R = 18.9 min].

In an identical fashion, (*R*)-*S*-1-hexen-3-yl carbamothioates **11a,b,d,e** were correlated with (*R*)-*S*-benzothioate **S12**.