A Modular Approach to Polyketide Building Blocks via Nitrile Oxide Cycloadditions with Homoallylic Alcohols and Monoprotected Homoallylic Diols.

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General Methods. All non-aqueous reactions were carried out using oven-dried (135 °C) or flame-dried glassware under a positive pressure of dry argon unless otherwise stated. Tetrahydrofuran, diethyl ether, toluene, acetonitrile, and methylene chloride were purified by distillation and dried by passage over activated alumina under an argon atmosphere (H₂O content <30 ppm, Karl–Fischer titration).¹ Pyridine was distilled from KOH under an atmosphere of dry nitrogen. *n*-Butyl lithium was titrated with *s*BuOH/phenanthroline.² All other commercially available reagents were used without further purification. The reactions were all magnetically stirred and monitored by thin layer chromatography using Merck Silica Gel 60 F₂₅₄ plates and visualized using ceric ammonium molybdate or potassium permanganate stain. Chromatographic purification of products (flash chromatography) was performed on E. Merck Silica Gel 60 (230–400 mesh) using a forced flow of eluant at 0.3–0.5 bar.³ Concentration under reduced pressure was performed by rotary evaporation at 30 °C at the appropriate pressure, unless otherwise stated. Yields refer to chromatographically purified and spectroscopically pure compounds, unless otherwise stated. Melting points were measured on a Büchi 510 apparatus. All melting points were measured in open capillaries and are uncorrected. Optical rotations were measured on a Jasco DIP-1000 polarimeter operating at the sodium D line with a 100 mm path length cell, and are reported as follows: $[\alpha]_D^T$, concentration (g/100 mL), and solvent. NMR spectra were recorded either on a Varian Mercury 300 spectrometer operating at 300 MHz and 75 MHz for ¹H and ¹³C acquisitions, respectively, or on a Bruker DRX500 spectrometer operating at 500 MHz for ¹H acquisitions. Chemical shifts (δ) are reported in ppm with the solvent resonance as the internal standard relative to chloroform (δ 7.26) for ¹H, and (δ 77.0) ¹³C. All ¹³C spectra were measured with complete proton decoupling. Data are reported as follows: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet; coupling constants in Hz. IR spectra were recorded on a

¹ Pangborn, A. B.; Giardello, M. A.; Grubbs, R. H.; Rosen, R. K.; Timmers, F. J. *Organometallics* **1996**, *15*, 1518.

² Watson, S. C.; Eastham, J. F. *J. Organomet. Chem.* **1967**, *9*, 165.

³ Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923.

PerkinElmer Spectrum RXI FT-IR spectrophotometer. Absorptions are given in wavenumbers (cm^{-1}). Mass spectra were recorded by the MS service at ETH Zürich. EI-MS (m/z): VG-TRIBRID spectrometer. MALDI-MS and ESI-MS (m/z): IonSpec Ultima Fourier Transform Mass Spectrometer. Elemental analyses were performed at the Mikrolabor der ETH Zürich.

3-(tert-Butyl-dimethyl-silanyloxy)-propionaldehyde oxime (S1).⁴ To a solution of imidazole (1.36 g, 20.0 mmol, 2.00 equiv) and TBSCl (1.51 g, 10 mmol, 1.00 equiv) in DMF (200 mL) was added 1,3-propanediol (14.4 mL, 200 mmol, 20.0 equiv). The mixture was stirred for 14 h at before Et₂O (300 mL) and H₂O (60 mL) were added. The layers were separated and the organic phase was washed with H₂O (3 x 60 mL) and brine, dried over anhydrous Na₂SO₄, filtered, and concentrated under reduced pressure to give the intermediate monoprotected diol, which was used without further purification.

To the unpurified monoprotected diol in CH₂Cl₂ (100 mL) at 0°C was added TEMPO (31.2 mg, 0.200 mmol, 2.00 mol%) and KBr (119 mg, 1.00 mmol, 10.0 mol%). The mixture was vigorously stirred and NaOCl (approx 1.5 M in H₂O, 14.0 mL, 20.0 mmol, 2.00 equiv) in pH 8.6 buffer (80 mL) was added in portions. Additional NaOCl solution was added in portions until the solution maintained a dark color and TLC analysis indicated the complete consumption of the starting material. The reaction was quenched by addition of MeOH (3 mL). The layers were separated and the aqueous phase extracted with CH₂Cl₂ (3 x 100 mL). The combined organic solutions were washed with brine, dried over anhydrous Na₂SO₄, filtered, and concentrated under reduced pressure to give the intermediate aldehyde. The resulting liquid was used immediately without further purification.

To a solution of the unpurified aldehyde in EtOH (100 mL) at rt was added NH₂OH•HCl (10.4 g, 150 mmol, 1.50 equiv) in pyridine (12 mL). The mixture was stirred at rt for 14 h and subsequently concentrated under reduced pressure. To the resulting residue was added Et₂O (100 mL) and H₂O (30 mL). The layers were separated and the organic layer was washed with H₂O (30 mL), brine (30 mL), dried over anhydrous Na₂SO₄, filtered, and concentrated under reduced

⁴ Bode, J. W.; Fraefel, N.; Muri, D.; Carreira, E. M. *Angew. Chem. Int. Ed.* **2001**, *40*, 2082-2085.

pressure. The pyridine was removed by azeotropic coevaporation with cyclohexane (3 x 30 mL). Purification by flash chromatography (hexane/EtOAc 3:2) afforded oxime **S1** (1.42 g, 70% yield over 3 steps) as a clear, colorless oil. ^1H NMR (300 MHz, CDCl_3 , * denotes signal corresponding to the minor oxime diastereomer) δ 7.48 (t, 1 H, $J = 6.0$ Hz), 6.86* (t, 1 H, $J = 5.2$ Hz), 3.78 (t, 2 H, $J = 6.3$ Hz), 2.59 (q, 2 H, $J = 6.2$ Hz), 2.42* (q, 2 H, $J = 6.2$ Hz), 0.90 (s, 9 H), 0.89* (s, 9 H), 0.07 (s, 6 H), 0.06 (s, 6 H). ^{13}C NMR (75 MHz, CDCl_3 , * denotes signal corresponding to the minor oxime diastereomer) δ 152.8*, 151.9, 60.5*, 59.7, 33.0*, 28.6, 25.9, 18.3, -5.4.

3-(*tert*-Butyl-dimethyl-silanyloxy)-2,2-dimethyl-propionaldehyde oxime (S2). To NaH (4.80 g, 200 mmol, 1.03 equiv) in THF (400 mL) was added at rt 2,2-dimethyl-1,3-propanediol (20.3 g, 195 mmol, 1.00 equiv) in portions over 10 min. The resulting thick slurry was stirred at rt for 1 h before TBSCl (30.1 g, 200 mmol, 1.03 equiv) was added in portions over 5 min. The slurry thinned and was stirred at rt for 14 h. The reaction was diluted with Et_2O (500 mL) and was washed with 10% aqueous K_2CO_3 solution (350 mL, 150 mL) and brine. The organic layer was dried over anhydrous Na_2SO_4 , filtered, and concentrated under reduced pressure to give the intermediate monoprotected diol, which was used without further purification.

To the unpurified monoprotected diol (10.9 g, 50.0 mmol, 1.00 equiv) in CH_2Cl_2 (350 mL) at 0°C was added TEMPO (156 mg, 1.00 mmol, 2.00 mol%) and KBr (595 mg, 5.00 mmol, 10 mol%). The mixture was vigorously stirred and NaOCl (approx. 1.5 M in H_2O , 50.0 mL, 75.0 mmol, 1.50 equiv) in pH 8.6 buffer (300 mL) was added in portions. Additional NaOCl solution was added over the course of 1.5 h until the reaction maintained a dark color and TLC analysis indicated complete consumption of the starting material. The reaction was quenched by addition of MeOH (10 mL). The layers were separated, the aqueous phase was extracted with CH_2Cl_2 (3 x 300 mL). The combined organic solutions were washed with brine, dried over anhydrous

Na₂SO₄, filtered, and concentrated under reduced pressure to give the intermediate aldehyde, which was immediately used without further purification.⁵

To NH₂OH•HCl (5.21 g, 75.0 mmol, 1.50 equiv) in H₂O (75 mL) was added at rt K₂CO₃ (12.1 g, 87.5 mmol, 1.75 equiv) and the mixture was stirred until all solids had dissolved. This solution was added to a solution of the unpurified aldehyde in EtOH (50 mL) and the mixture was stirred at rt for 15 h. H₂O (125 mL) and CH₂Cl₂ (125 mL) were added, the layers separated and the aqueous phase extracted with CH₂Cl₂ (3 x 125 mL). The combined organic solutions were dried over anhydrous Na₂SO₄, filtered, and concentrated under reduced pressure. Purification by flash chromatography (hexane/EtOAc 12:1) afforded oxime **S2** (7.99 g, 69% yield over 3 steps) as a clear, colorless oil. ¹H NMR (300 MHz, CDCl₃) δ 7.41 (s, 1 H), 3.43 (s, 2 H), 1.07 (s, 6 H), 0.89 (s, 9 H), 0.03 (s, 6 H). ¹³C NMR (75 MHz, CDCl₃) 157.1, 70.6, 39.2, 26.0, 22.2, 18.4, -5.4. IR (thin film) ν 3326, 2957, 2930, 2888, 2858, 2741, 2713, 2253, 2178, 1921, 1871, 1752, 1648, 1472, 1391, 1362, 1311, 1255, 1217, 1187, 1104, 1034, 1006, 948, 838, 815, 776, 736, 670. Anal. Calcd for C₁₁H₂₅NO₂Si: C, 57.09; H, 10.89; N, 6.05. Found: C, 57.26; H, 10.84; N, 6.17. HRMS (ESI) calcd for C₁₁H₂₅NO₂SiNa [M+Na]⁺, 254.1547; found, 254.1543.

(R)-2-(tert-Butyl-dimethyl-silanyloxy)-propionaldehyde oxime (S3). To a solution of imidazole (5.67 g, 83.3 mmol, 2.50 equiv) and TBSCl (6.02 g, 40.0 mmol, 1.20 equiv) in dry DMF (10 mL) was added dropwise (R)-(+)-isobutyl lactate (5.00 mL, 33.3 mmol, 1.00 equiv). The mixture was stirred for 16 h at rt before Et₂O (60 mL) and H₂O (30 mL) were added. The layers were separated and the organic phase was washed with water (3 x 30 mL) and brine. The organic layer was dried over anhydrous Na₂SO₄, filtered, and concentrated under reduced pressure to give the intermediate TBS ether which was used without further purification.

Neat DIBAL (5.76 mL, 32.3 mmol, 0.971 equiv) was added dropwise to the unpurified isobutyl ester in CH₂Cl₂ (230 mL) at -78°C. The mixture was stirred 1.5 h before the reaction was quenched with MeOH (1.5 mL) at -78°C and allowed to warm to rt before saturated, aqueous

⁵ This aldehyde has been described: Wender, P.A.; Baryza, J. L.; Bennett, C. E.; Bi, F. C.; Brenner, S. E.; Clarke, M. O.; Horan, J. C.; Kan, C.; Lacôte, E.; Lippa, B.; Nell, P. G.; Turner, T. M. *J. Am. Chem. Soc.* **2002**, *124*, 13648–13649.

sodium potassium tartrate (200 mL) was added. After 5 h the clear layers were separated and the aqueous phase extracted with Et₂O (3 x 100 mL). The combined organic layers were dried over anhydrous Na₂SO₄, filtered, and concentrated carefully under reduced pressure (30°C, 350 torr) to afford the intermediate aldehyde which was used without further purification.

To NH₂OH•HCl (3.47 g, 50.0 mmol, 1.50 equiv) in H₂O (45 mL) was added at rt K₂CO₃ (8.05 g, 58.3 mmol, 1.75 equiv) and the mixture was stirred until all solids had dissolved. This solution was added to a solution of the unpurified aldehyde in EtOH (30 mL) and the mixture was stirred at rt for 14 h. H₂O (100 mL) and CH₂Cl₂ (100 mL) were added, the layers separated and the aqueous phase extracted with CH₂Cl₂ (3 x 100 mL). The combined organic solutions were dried over anhydrous Na₂SO₄, filtered, and concentrated under reduced pressure. Purification by flash chromatography (pentane/EtOAc 10:1) afforded the slightly volatile oxime **S3** (4.34 g, 66% yield over 3 steps) as a clear, colorless oil. Optical Rotation: $[\alpha]_D^{26}$ (*c* = 1.44, CHCl₃) = + 6.2 °. ¹H NMR (300 MHz, CDCl₃, * denotes signal corresponding to the minor oxime diastereomer) δ 7.32 (d, 1 H, *J* = 6.6 Hz), 6.73* (d, 1 H, *J* = 5.5 Hz), 5.02* (quin, 1 H, *J* = 5.5 Hz), 4.41 (quin, 1 H, *J* = 6.6 Hz), 1.30 (d, 3 H, *J* = 6.3 Hz), 1.29* (d, 3 H, *J* = 6.6 Hz), 0.89* (s, 9 H), 0.88 (s, 9 H), 0.10* (s, 3 H), 0.08 (s, 3 H), 0.07* (s, 3 H), 0.06 (s, 3 H). ¹³C NMR (75MHz, CDCl₃, * denotes signal corresponding to the minor oxime diastereomer) δ 156.5*, 154.5, 66.7, 62.7*, 25.9, 22.5, 20.9*, 18.2, -4.3, -4.5, -4.7*, -4.9*. IR (thin film) ν 3272, 3122., 2931, 2889, 2859, 2712, 1926, 1837, 1657, 1472, 1444, 1390, 1371, 1363, 1341, 1258, 1218, 1189, 1158, 1092, 1004, 939, 909, 833, 813, 778, 743, 667. Anal. Calcd for C₉H₂₁NO₂Si: C, 53.16; H, 10.41; N, 6.89. Found: C, 53.38; H, 10.53; N, 6.86. HRMS (ESI) calcd for C₉H₂₁NO₂SiNa [M+Na]⁺, 226.1234; found, 226.1229.

Tributyl-((Z)-4-trityloxy-but-2-enyloxymethyl)-stannane (S4). To a suspension of NaH (0.672 g, 28.0 mmol, 2.00 equiv) in THF (100 mL) at rt was added (Z)-4-trityloxy-but-2-en-1-ol⁶

⁶ This compound has been previously described, see: Kuijpers, J. M. H.; Kardaun, G. A.; Blezer, R.; Pijpers, A. P.; Koole, L. H. J. *J Am. Chem. Soc.* **1995**, *117*, 8691.

(9.25 g, 28.0 mmol, 2.00 equiv) in THF (80 mL) and iodomethyltributyltin⁷ (6.03 g, 14.0 mmol, 1.00 equiv) in THF (80 mL). After HMPA (55 mL) had been added, the mixture was stirred for 16 h at rt. The reaction was quenched by addition of H₂O (150 mL) and brine (50 mL). The layers were separated and the aqueous layer was extracted with Et₂O (3 x 150 mL). The combined organic layers were washed with brine, dried over anhydrous Na₂SO₄, filtered, and concentrated under reduced pressure. Purification by flash chromatography (hexane/EtOAc 20:1 to 4:1) provided **S4** (7.62 g, 86% yield) as a colorless, thick oil. ¹H NMR (300 MHz, CDCl₃) δ 7.48-7.45 (m, 6 H), 7.33-7.21 (m, 9 H), 5.84-5.76 (m, 1 H), 5.66-5.57 (m, 1 H), 3.77-3.74 (m, 2 H), 3.67-3.65 (m, 2 H), 3.60 (t, 2 H, *J* = 7.5 Hz), 1.55-1.42 (m, 6 H), 1.34-1.22 (m, 6 H), 0.91-0.83 (m, 6 H), 0.88 (t, 9 H, *J* = 7.2 Hz).

2-Trityloxymethyl-but-3-en-1-ol (S5). *n*BuLi (1.6 M in hexane, 5.63 mL, 9.00 mmol, 3.00 equiv) was added slowly to a solution of **S4** (1.90 g, 3.00 mmol, 1.00 equiv) in THF (45 mL) at -78 °C. The red mixture was stirred for 45 min at -78 °C before being quenched with H₂O (25 mL). The layers were separated and the aqueous layer was extracted with Et₂O (3 x 25 mL). The combined organic solutions were washed with brine, dried over anhydrous Na₂SO₄, filtered, and concentrated under reduced pressure. Purification by flash chromatography (CH₂Cl₂) provided **S5** (859 mg, 83% yield) as a white solid. ¹H NMR (300 MHz, CDCl₃) δ 7.45-7.41 (m, 6 H), 7.33-7.21 (m, 9 H), 5.77-5.65 (m, 1 H), 5.15-5.06 (m, 2 H), 3.78-3.62 (m, 2 H), 3.28 (dd, 1 H, *J* = 9.1, 4.9 Hz), 3.17 (dd, 1 H, *J* = 9.1, 7.5 Hz), 2.64-2.53 (m, 1 H), 2.02 (t, 1 H, *J* = 6.1 Hz). ¹³C NMR (75 MHz, CDCl₃) δ 143.7, 136.2, 128.5, 127.8, 127.0, 117.5, 86.9, 65.3, 64.8, 46.4. IR (thin film) ν 3414, 3085, 3060, 3033, 2925, 2875, 2246, 1960, 1820, 1640, 1598, 1491, 1448, 1422, 1382, 1318, 1219, 1183, 1154, 1072, 1033, 1002, 911, 775, 764, 734, 706, 646, 633. HRMS (ESI) calcd for C₂₄H₂₄O₂Na [M+Na]⁺, 367.1669; found, 367.1673. mp: 126–128 °C

⁷ For the synthesis of iodomethyltributyltin, see: Åhman, J.; Somfai, P. *Synth. Comm.* **1994**, 24, 1117.

tert-Butyl-diphenyl-((Z)-4-tributylstannanylmethoxy-but-2-enyloxy)-silane (S6). To a suspension of NaH (384 mg, 16.0 mmol, 2.00 equiv) in THF (50 mL) at rt was added primary alcohol (Z)-4-(tert-butyl-diphenyl-silanyloxy)-but-2-en-1-ol⁸ (5.22 g, 16.0 mmol, 2.00 equiv) in THF (30 mL) and iodomethyltributyltin⁷ (3.45 g, 8.00 mmol, 1.00 equiv) in THF (30 mL). After HMPA (30 mL) had been added, the mixture was stirred for 16 h at rt. The reaction was quenched by addition of H₂O (100 mL) and brine (30 mL). The layers were separated and the aqueous layer was extracted with Et₂O (3 x 100 mL). The combined organic layers were washed with brine, dried over anhydrous Na₂SO₄, filtered, and concentrated under reduced pressure. Purification by flash chromatography (pentane/EtOAc 20:1) provided **S6** (4.44 g, 88% yield) as a colorless oil. ¹H NMR (300 MHz, CDCl₃) δ 7.70-7.59 (m, 4 H), 7.45-7.29 (m, 6 H), 5.79-5.70 (m, 1 H), 5.57-5.48 (m, 1 H), 4.27-4.25 (m, 2 H), 3.77-3.75 (m, 2 H), 3.59 (t, 2 H, *J* = 7.5 Hz), 1.56-1.42 (m, 6 H), 1.34-1.22 (m, 6 H), 1.05 (s, 9 H), 0.92-0.84 (m, 6 H), 0.88 (t, 9 H, *J* = 7.2 Hz).

2-(tert-Butyl-diphenyl-silanyloxymethyl)-but-3-en-1-ol (S7).⁹ *n*BuLi (1.6 M in hexane, 12.0 mL, 19.2 mmol, 3.00 equiv) was added slowly to a solution of **S6** (4.00 g, 6.40 mmol, 1.00 equiv) in THF (70 mL) at -78 °C. The orange mixture was stirred for 45 min at -78 °C before being quenched with H₂O (50 mL). The layers were separated and the aqueous layer was extracted with Et₂O (3 x 50 mL). The combined organic solutions were washed with brine, dried over anhydrous Na₂SO₄, filtered, and concentrated under reduced pressure. Purification by flash chromatography (CH₂Cl₂) provided **S7** (1.37 g, 63% yield) as a colorless oil. ¹H NMR (300 MHz, CDCl₃) δ 7.73-7.65 (m, 4 H), 7.48-7.37 (m, 6 H), 5.75-5.63 (m, 1 H), 5.14-5.07 (m, 2 H), 3.87-

⁸ This compound has been previously reported, see: Roush, W. R.; Straub, J. A.; VanNieuwenhze, M. X. *J. Org. Chem.* **1991**, 56, 1636.

⁹ Izzo, I.; Scioscia, M.; Del Gaudio, P.; De Riccardis, F. *Tet. Lett.* **2001**, 42, 5421.

3.69 (m, 4 H), 2.60-2.50 (m, 1 H), 2.24 (t, 1 H, $J = 6.0$ Hz), 1.06 (s, 9 H). ^{13}C NMR (75 MHz, CDCl_3) δ 135.8, 135.5, 133.0, 129.7, 127.7, 117.6, 66.0, 64.8, 47.8, 27.0, 19.3. IR (thin film) ν 3401, 3072, 3050, 2947, 2930, 2858, 2361, 1960, 1893, 1830, 1641, 1590, 1472, 1428, 1390, 1362, 1311, 1254, 1188, 1113, 1030, 998, 918, 823, 794, 740, 702, 614. Anal. Calcd for $\text{C}_{21}\text{H}_{28}\text{O}_2\text{Si}$: C, 74.07; H, 8.29. Found: C, 73.86; H, 8.35. HRMS (ESI) calcd for $\text{C}_{21}\text{H}_{28}\text{O}_2\text{SiNa}$ $[\text{M}+\text{Na}]^+$, 363.1751; found, 363.1755.

Triisopropyl-((Z)-4-tributylstannanylmethoxy-but-2-enyloxy)-silane (S8). To a suspension of NaH (384 mg, 16.0 mmol, 2.00 equiv) in THF (50 mL) at rt was added (Z)-4-triisopropylsilyloxybut-2-en-1-ol¹⁰ (3.91 g, 16.0 mmol, 2.00 equiv) in THF (30 mL) and iodomethyltributyltin⁷ (3.45 g, 8.00 mmol, 1.00 equiv) in THF (30 mL). After HMPA (30 mL) had been added, the mixture was stirred for 35 h at rt. The reaction was quenched by addition of H_2O (100 mL) and brine (30 mL). The layers were separated and the aqueous layer was extracted with Et_2O (3 x 100 mL). The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4 , filtered, and concentrated under reduced pressure. Purification by flash chromatography (pentane/EtOAc 25:1 to 1:1) provided **S8** (4.07 g, 93% yield) as a colorless oil. ^1H NMR (300 MHz, CDCl_3) δ 5.74-5.67 (m, 1 H), 5.58-5.49 (m, 1 H), 4.33-4.30 (m, 2 H), 3.93-3.91 (m, 2 H), 3.69 (t, 2 H, $J = 7.5$ Hz), 1.56-1.45 (m, 6 H), 1.36-1.24 (m, 6 H), 1.10-1.05 (m, 27 H), 0.89 (t, 9 H, $J = 7.2$ Hz). ^{13}C NMR (75 MHz, CDCl_3) δ 132.7, 127.1, 71.3, 61.6, 60.1, 29.4 (t, $J = 10.4$), 27.6 (t, $J = 25.6$), 18.3, 14.0, 12.3, 9.2. IR (thin film) ν 2957, 2929, 2867, 2361, 2329, 1601, 1464, 1407, 1377, 1338, 1289, 1248, 1086, 1068, 1013, 996, 956, 919, 882, 805, 728, 682, 658. HRMS (MALDI) calcd for $\text{C}_{26}\text{H}_{56}\text{O}_2\text{SiSnNa}$ $[\text{M}+\text{Na}]^+$, 571.2964; found, 571.2957.

¹⁰ This compound has been previously reported, see: Hiersemann, M. *Tetrahedron* **1999**, 55, 2625.

2-Triisopropylsilanyloxymethyl-but-3-en-1-ol (S9). *n*BuLi (1.6 M in hexane, 13.7 mL, 21.9 mmol, 3.00 equiv) was added slowly to a solution of **S8** (4.00 g, 7.31 mmol, 1.00 equiv) in THF (100 mL) at -78 °C. The yellow mixture was stirred for 5 h at -78 °C before being quenched with H₂O (50 mL). The layers were separated and the aqueous layer was extracted with Et₂O (3 x 50 mL). The combined organic solutions were washed with brine, dried over anhydrous Na₂SO₄, filtered, and concentrated under reduced pressure. Purification by flash chromatography (CH₂Cl₂) provided **S9** (1.38 g, 73% yield) as a slightly volatile, colorless oil. ¹H NMR (300 MHz, CDCl₃) δ 5.76-5.64 (m, 1 H), 5.18-5.12 (m, 2 H), 3.90 (1 H, dd, *J* = 9.7, 4.4 Hz), 3.93-3.69 (m, 3 H), 2.73 (dd, 1 H, *J* = 6.9, 5.0 Hz), 2.61-2.50 (m, 1 H), 1.12-1.04 (m, 21 H). ¹³C NMR (75 MHz, CDCl₃) δ 135.9, 117.5, 67.0, 66.0, 47.6, 18.1, 11.9. IR (thin film) ν 3838, 3369, 3079, 2943, 2864, 2760, 2726, 2626, 2553, 2362, 2244, 1893, 1836, 1642, 1464, 1422, 1384, 1367, 1291, 1248, 1214, 1113, 1068, 1014, 997, 918, 883, 840, 787, 682, 658. HRMS (ESI) calcd for C₁₄H₃₀O₂SiNa [M+Na]⁺, 281.1907; found, 281.1910.

***tert*-Butyl-dimethyl-((Z)-4-tributylstannanylmethoxy-but-2-enyloxy)-silane (S10).** To a suspension of NaH (672 mg, 28.0 mmol, 2.00 equiv) in THF (100 mL) at rt was added (Z)-4-(*tert*-butyl-dimethyl-silanyloxy)-but-2-en-1-ol¹¹ (5.67 g, 28.0 mmol, 2.00 equiv) in THF (80 mL) and iodomethyltributyltin⁷ (6.03 g, 14.0 mmol, 1.00 equiv) in THF (80 mL). After HMPA (55 mL) had been added, the mixture was stirred for 16 h at rt. The reaction was quenched by addition of H₂O (150 mL) and brine (50 mL). The layers were separated and the aqueous layer was extracted with Et₂O (3 x 150 mL). The combined organic layers were washed with brine, dried over anhydrous Na₂SO₄, filtered, and concentrated under reduced pressure. Purification by flash chromatography (pentane/EtOAc 10:1 to 4:1) provided **S10** (6.30 g, 89% yield) as a colorless oil. ¹H NMR (300 MHz, CDCl₃) δ 5.71-5.62 (m, 1 H), 5.59-5.50 (m, 1 H), 4.25-4.22 (m, 2 H), 3.93-3.91 (m, 2 H), 3.69 (t, 2 H, *J* = 7.5 Hz), 1.59-1.45 (m, 6 H), 1.37-1.24 (m, 6 H), 0.93-0.87 (m, 15 H), 0.90 (s, 9 H), 0.08 (s, 3 H), 0.07 (s, 3 H). ¹³C NMR (75 MHz, CDCl₃) δ 132.5, 127.5, 71.2 (t, *J* = 22.0 Hz), 61.6, 59.8, 29.3 (t, *J* = 10.4 Hz), 27.4 (t, *J* = 26.3 Hz), 26.1, 18.5, 13.9, 9.1, -5.0, -5.1. IR (thin film) ν 3025, 2956, 2929, 2857, 2361, 2342, 1464, 1406, 1389, 1376, 1361, 1339, 1254, 1082, 1006, 961, 939, 838, 815, 776, 728, 668. HRMS (MALDI) calcd for C₂₃H₅₀O₂SiSnNa [M+Na]⁺, 529.2494; found, 529.2486.

2-(*tert*-Butyl-dimethyl-silanyloxymethyl)-but-3-en-1-ol (S11). *n*BuLi (1.6 M in hexane, 22.5 mL, 36.0 mmol, 3.00 equiv) was added slowly to a solution of **S10** (6.07 g, 12.0 mmol, 1.00 equiv) in THF (150 mL) at -78 °C. The yellow mixture was stirred for 1 h at -78 °C before being quenched with H₂O (70 mL). The layers were separated and the aqueous layer was extracted with Et₂O (3 x 70 mL). The combined organic solutions were washed with brine, dried over anhydrous Na₂SO₄, filtered, and concentrated under reduced pressure. Purification by flash chromatography

¹¹ This compound has been previously reported, see: Schmidt, B.; Pohler, M.; Costisella, B. *Tetrahedron* **2002**, 58, 7951.

(CH₂Cl₂) provided **S11** (2.03 g, 78% yield) as a slightly volatile, colorless oil. ¹H NMR (300 MHz, CDCl₃) δ 5.75-5.63 (m, 1 H), 5.18-5.12 (m, 2 H), 3.82-3.65 (m, 4 H), 2.59-2.28 (m, 1 H), 2.58 (t, 1 H, *J* = 6.0 Hz), 0.91 (s, 9 H) 0.10 (s, 3 H), 0.10 (s, 3 H). ¹³C NMR (75 MHz, CDCl₃) δ 135.6, 117.3, 66.2, 65.6, 47.4, 26.0, -5.4, -5.4. IR (thin film) ν 3369, 2958, 2930, 2887, 2858, 1641, 1589, 1472, 1424, 1389, 1362, 1256, 1213, 1098, 1025, 1006, 917, 836, 776, 659. HRMS (ESI) calcd for C₁₁H₂₄O₂SiNa [M+Na]⁺, 239.1438; found, 239.1442.

Triethyl-((Z)-4-tributylstannanylmethoxy-but-2-enyloxy)-silane (S12). To a suspension of NaH (768 mg, 32.0 mmol, 2.00 equiv) in THF (100 mL) at rt was added (Z)-4-triethylsilyloxy-but-2-en-1-ol¹² (6.48 g, 32.0 mmol, 2.00 equiv) in THF (60 mL) and iodomethyltributyltin⁷ (6.90 g, 16.0 mmol, 1.00 equiv) in THF (60 mL). After HMPA (60 mL) had been added, the mixture was stirred for 16 h at rt. The reaction was quenched by addition of H₂O (100 mL) and brine (50 mL). The layers were separated and the aqueous layer was extracted with Et₂O (3 x 150 mL). The combined organic layers were washed with brine, dried over anhydrous Na₂SO₄, filtered, and concentrated under reduced pressure. Purification by flash chromatography (pentane/EtOAc 20:1 to 1:1) provided **S12** (4.27 g, 53% yield) as a colorless oil. ¹H NMR (300 MHz, CDCl₃) δ 5.72-5.64 (m, 1 H), 5.60-5.51 (m, 1 H), 4.25-4.22 (m, 2 H), 3.94-3.91 (m, 2 H), 3.69 (t, 2 H, *J* = 7.5 Hz), 1.56-1.45 (m, 6 H), 1.36-1.24 (m, 6 H), 0.97 (t, 9 H, *J* = 7.9 Hz), 0.93-0.87 (m, 6 H), 0.89 (t, 9 H, *J* = 7.2 Hz), 0.62 (q, 6 H, *J* = 8.1 Hz). ¹³C NMR (75 MHz, CDCl₃) δ 132.3, 127.6, 71.2, 61.7, 59.4, 29.4 (t, *J* = 10.4 Hz), 27.6 (t, *J* = 25.6 Hz), 14.0, 9.2, 7.0, 4.7. IR (thin film) ν 2956, 2925, 2875, 2843, 2362, 1589, 1458, 1415, 1377, 1332, 1239, 1077, 1005, 964, 865, 819, 741, 727. HRMS (MALDI) calcd for C₂₃H₅₀O₂SiSnNa [M+Na]⁺, 529.2497; found, 529.2490.

¹² This compound has been previously reported, see: Stanton, S. A.; Felman, S. W.; Parkhurst, C. S.; Godleski, S. A. *J. Am. Chem. Soc.* **1983**, *105*, 1964.

2-Triethylsilanyloxymethyl-but-3-en-1-ol (S13). *n*BuLi (1.6 M in hexane, 20.3 mL, 32.4 mmol, 3.00 equiv) was added slowly to a solution of **S12** (5.46 g, 10.8 mmol, 1.00 equiv) in THF (150 mL) at -78 °C. The pink mixture was stirred for 3 h at -78 °C before additional *n*BuLi (1.6 M in hexane, 6.75 mL, 10.8 mmol, 1.00 equiv) was added. After total 5 h the reaction was quenched by addition of H₂O (70 mL). The layers were separated and the aqueous layer was extracted with Et₂O (3 x 70 mL). The combined organic solutions were washed with brine, dried over anhydrous Na₂SO₄, and filtered. The THF was removed by distillation (vigreux column, 60 °C, then 80 °C oil bath temperature). Purification by flash chromatography (CH₂Cl₂, removed after purification by distillation with vigreux column) provided **S13** (1.01 g, 43% yield) as a volatile, colorless liquid. ¹H NMR (300 MHz, CDCl₃) δ 5.74-5.62 (m, 1 H), 5.18-5.11 (m, 2 H), 3.83-3.66 (m, 4 H), 2.70 (br t, 1 H, *J* = 5.9 Hz), 2.58-2.47 (m, 1 H), 0.97 (t, 9 H, *J* = 8.0 Hz), 0.62 (q, 6 H, *J* = 7.6 Hz). ¹³C NMR (75 MHz, CDCl₃) δ 135.7, 117.4, 66.2, 66.0, 47.5, 6.9, 4.5. IR (thin film) ν 3339, 3081, 2954, 2912, 2877, 2734, 2361, 2342, 2199, 1642, 1459, 1416, 1380, 1240, 1099, 1017, 974, 917, 839, 794, 740, 677. HRMS (ESI) calcd for C₁₁H₂₄O₂SiNa [M+Na]⁺, 239.1439; found, 239.1444.

(R)-2-[(S)-3-[2-(*tert*-Butyl-dimethyl-silanyloxy)-ethyl]-4,5-dihydro-isoxazol-5-yl]-propan-1-ol (S14). To a solution of oxime **S1** (102 mg, 0.500 mmol, 1.00 equiv) in CH₂Cl₂ (5 mL) at -78 °C was added *t*BuOCl (59.0 μl, 0.500 mmol, 1.00 equiv) dropwise over 15 min. The resulting deep blue solution was stirred 50 min at -78 °C. In a separate flask EtMgBr (3.0 M in Et₂O, 500 μl, 1.50 mmol, 3.00 equiv) was added dropwise to a solution of (*S*)-2-methyl-3-butenol¹³ (56.0 mg, 0.650 mmol, 1.30 equiv) and *i*PrOH (126 μl, 1.65 mmol, 3.30 equiv) in CH₂Cl₂ (10 mL) at 0 °C. The reaction mixture turned momentarily cloudy and became clear and colorless upon stirring at 0 °C for 30 min. At this time, the hydroximinoyl chloride in CH₂Cl₂

¹³ The synthesis of this homoallylic alcohol has been previously reported, see: Batchelor, M. J.; Gillespie, R. J.; Golec, J. M. C.; Hedgecock, C. J. R.; Jones, S. D.; Murdoch, R. *Tetrahedron* **1994**, 50, 809.

was added to the reaction dropwise via cannula over 75 min, followed by 2 rinses (1 mL each). The slightly yellow solution was stirred at 0 °C for 6 h and was slowly allowed to warm to room temperature overnight (large dewar with ice, covered with aluminum foil). After 48 h the reaction was quenched by addition of saturated, aqueous NH₄Cl (15 mL). The mixture was vigorously stirred for 20 min, then the layers were separated and the aqueous phase was extracted with EtOAc (3 x 15 mL). The combined organic solutions were washed with brine, dried over anhydrous Na₂SO₄, filtered, and concentrated under reduced pressure. After filtration over silica gel (hexane/EtOAc 2:1) isoxazoline **S14** (96 mg, 67% yield, d.r. = 8:1 by integration of the signals at 4.37 ppm (major) and 4.60 ppm (minor) in the crude ¹H NMR spectrum) was isolated as a pale, colorless oil. $[\alpha]_D^{28}$ (c 0.75, CHCl₃) = +27.7. ¹H NMR (500 MHz, CDCl₃, * denotes minor diastereomeric peak) δ 4.60* (ddd, 1 H, *J* = 12.9, 8.4, 4.5), 4.37 (ddd, 1 H, *J* = 10.3, 8.3, 8.3 Hz), 3.78 (t, 2 H, *J* = 6.4 Hz), 3.64-3.54 (m, 2 H), 2.98 (dd, 1 H, *J* = 17.1, 10.3 Hz), 2.94* (dd, 1 H, *J* = 17.1, 10.8 Hz), 2.80* (dd, 1 H, *J* = 17.2, 8.4 Hz), 2.75 (dd, 1 H, *J* = 17.1, 8.4 Hz), 2.55-2.45 (m, 2 H), 2.22 (br dd, 1 H, *J* = 4.0 Hz), 1.87-1.78 (m, 1 H), 0.89* (d, 3 H, *J* = 7.0 Hz), 0.85* (s, 9 H), 0.84 (d, 3 H, *J* = 6.9 Hz), 0.83 (s, 9 H), 0.01 (s, 6 H). ¹³C NMR (75 MHz, CDCl₃, * denotes minor diastereomeric peak) δ 157.9, 83.7, 81.5*, 65.9, 64.9*, 60.6, 59.3*, 41.6, 40.2, 39.7*, 31.2, 25.9, 25.7*, 18.2, 13.2, 11.2*, -5.3, -5.4. IR (thin film) ν 3413, 2956, 2930, 2884, 2858, 2362, 1626, 1472, 1434, 1388, 1361, 1313, 1257, 1223, 1103, 1049, 1007, 962, 939, 838, 811, 778, 719, 662. Anal. Calcd for C₁₄H₂₉NO₃Si: C, 58.49; H, 10.17; N, 4.87. Found: C, 58.56; H, 10.27; N, 5.05. HRMS (MALDI) calcd for C₁₄H₂₉NO₃SiNa [M+Na]⁺, 310.1809; found, 310.1812.

(R)-2-[(S)-3-[(R)-2-(*tert*-Butyl-dimethyl-silanyloxy)-1-methyl-ethyl]-4,5-dihydro-isoxazol-5-yl]-propan-1-ol (S15). To a solution of (*S*)-3-(*tert*-butyl-dimethyl-silanyloxy)-2-methyl-propionaldehyde oxime¹⁴ (109 mg, 0.500 mmol, 1.00 equiv) in CH₂Cl₂ (5 mL) at -78 °C was added *t*BuOCl (59.0 μl, 0.500 mmol, 1.00 equiv) dropwise over 10 min. The resulting deep

¹⁴ The synthesis of this oxime has been previously reported, see: Bode, J. W.; Fraefel, N.; Muri, D.; Carreira, E. M. *Angew. Chem., Int. Ed.* **2001**, 40, 2082.

blue solution was stirred 1 h at -78 °C. In a separate flask EtMgBr (3.0 M in Et₂O, 500 µl, 1.50 mmol, 3.00 equiv) was added dropwise to a solution of (*S*)-2-methyl-3-butenol¹³ (56.0 mg, 0.650 mmol, 1.30 equiv) and *i*PrOH (126 µl, 1.65 mmol, 3.30 equiv) in CH₂Cl₂ (10 mL) at 0 °C. The reaction mixture turned momentarily cloudy and became clear and colorless upon stirring at 0 °C for 30 min. At this time, the hydroximinoyl chloride in CH₂Cl₂ was added to the reaction dropwise via cannula over 60 min, followed by 2 rinses (1 mL each). The slightly yellow solution was stirred at 0 °C for 6 h and was slowly allowed to warm to room temperature overnight (large dewar with ice, covered with aluminum foil). After 18 h the reaction was quenched by addition of saturated, aqueous NH₄Cl (15 mL). The mixture was vigorously stirred for 20 min, then the layers were separated and the aqueous phase was extracted with EtOAc (3 x 15 mL). The combined organic solutions were washed with brine, dried over anhydrous Na₂SO₄, filtered, and concentrated under reduced pressure. Purification by flash chromatography (hexane/EtOAc 4:1) provided isoxazoline **S15** (125 mg, 83% yield, d.r. = 7:1 by integration of the signals at 4.40 ppm (major) and 4.65 ppm (minor) in the crude ¹H NMR spectrum) as a clear, colorless oil. Optical Rotation: $[\alpha]_D^{34}$ (c 0.50, CHCl₃) = +37.3. ¹H NMR (300 MHz, CDCl₃, * denotes minor diastereomeric peak) δ 4.65* (ddd, 1 H, *J* = 12.5, 8.1, 4.4 Hz), 4.40 (ddd, 1 H, *J* = 10.3, 8.4, 8.4 Hz), 3.71-3.58 (m, 2 H), 3.68 (d, 2 H, *J* = 6.2 Hz), 3.02 (dd, 1 H, *J* = 17.8, 10.9 Hz), 3.00* (dd, 1 H, *J* = 17.1, 10.6 Hz), 2.85* (dd, 1 H, *J* = 16.8, 8.1 Hz), 2.82-2.71 (m, 1 H), 2.79 (dd, 1 H, *J* = 17.1, 8.7 Hz), 2.33 (br s, 1 H), 1.95-1.82 (m, 1 H), 1.17 (d, 3 H, *J* = 7.2 Hz), 1.14* (d, 3 H, *J* = 7.1 Hz), 0.95* (d, 3 H, *J* = 7.2 Hz), 0.90 (d, 3 H, *J* = 6.8 Hz), 0.90* (s, 9 H), 0.89 (s, 9 H), 0.06* (s, 6 H), 0.05 (s, 6 H). ¹³C NMR (75 MHz, CDCl₃, * denotes minor diastereomeric peak) δ 161.8, 84.0, 81.5*, 66.4, 66.2, 65.0*, 40.4, 40.3, 39.7*, 38.2*, 36.0, 26.1, 18.4, 14.8, 13.5, 11.4*. -5.2. IR (thin film) ν 3428, 2957, 2930, 2884, 2858, 2740, 2710, 2243, 1621, 1472, 1434, 1390, 1362, 1298, 1257, 1213, 1182, 1097, 1046, 1007, 974, 939, 909, 838, 815, 777, 734, 678, 646. Anal. Calcd for C₁₅H₃₁NO₃Si: C, 59.76; H, 10.36; N, 4.65. Found: C, 59.67; H, 10.41; N, 4.82. HRMS (MALDI) calcd for C₁₅H₃₂NO₃Si [M+H]⁺, 302.2146; found, 302.2142.

(R)-2-[(S)-3-[(S)-2-(*tert*-Butyl-dimethyl-silanyloxy)-1-methyl-ethyl]-4,5-dihydroisoxazol-5-yl]-propan-1-ol (S16). To a solution of (*R*)-3-(*tert*-butyl-dimethyl-silanyloxy)-2-methyl-propionaldehyde oxime¹⁴ (109 mg, 0.500 mmol, 1.00 equiv) in CH₂Cl₂ (5 mL) at -78 °C was added *t*BuOCl (59.0 μL, 0.500 mmol, 1.00 equiv) dropwise over 10 min. The resulting deep blue solution was stirred 1 h at -78 °C. In a separate flask EtMgBr (3.0 M in Et₂O, 500 μL, 1.50 mmol, 3.00 equiv) was added dropwise to a solution of (*S*)-2-methyl-3-butenol¹³ (56.0 mg, 0.650 mmol, 1.30 equiv) and *i*PrOH (126 μL, 1.65 mmol, 3.30 equiv) in CH₂Cl₂ (10 mL) at 0 °C. The reaction mixture turned momentarily cloudy and became clear and colorless upon stirring at 0 °C for 30 min. At this time, the hydroximinoyl chloride in CH₂Cl₂ was added to the reaction dropwise via cannula over 60 min, followed by 2 rinses (1 mL each). The slightly yellow solution was stirred at 0 °C for 6 h and was slowly allowed to warm to room temperature overnight (large dewar with ice, covered with aluminum foil). After 20 h the reaction was quenched by addition of saturated, aqueous NH₄Cl (15 mL). The mixture was vigorously stirred for 20 min, then the layers were separated and the aqueous phase was extracted with EtOAc (3 x 15 mL). The combined organic solutions were washed with brine, dried over anhydrous Na₂SO₄, filtered, and concentrated under reduced pressure. Purification by flash chromatography (hexane/EtOAc 4:1) provided isoxazoline **S16** (128 mg, 85% yield, d.r. = 9:1 by integration of the signals at 4.41 ppm (major) and 4.64 ppm (minor) in the crude ¹H NMR spectrum) as a clear, colorless oil. Optical Rotation: [α]_D²⁵ (c 0.98, CHCl₃) = +36.0. ¹H NMR (300 MHz, CDCl₃) δ 4.41 (ddd, 1 H, *J* = 10.3, 8.1, 8.1 Hz), 3.69-3.56 (m, 4 H), 3.03 (dd, 1 H, *J* = 16.8, 10.3 Hz), 2.84-2.72 (m, 1 H), 2.78 (dd, 1 H, *J* = 16.8, 7.8 Hz), 2.41 (br s, 1 H), 1.94-1.81 (m, 1 H), 1.14 (d, 3 H, *J* = 7.2 Hz), 0.88 (d, 3 H, *J* = 6.9 Hz), 0.87 (s, 9 H), 0.05 (s, 6 H). ¹³C NMR (75 MHz, CDCl₃) δ 161.6, 83.7, 66.1, 66.0, 40.2, 39.6, 35.7, 25.9, 18.3, 14.6, 13.4, -5.3, -5.4. IR (thin film) ν 3421, 2957, 2930, 2884, 2858, 2739, 2360, 2341, 1622, 1472, 1463, 1389, 1362, 1297, 1257, 1098, 1045, 1007, 972, 939, 897, 838, 815, 782, 754, 678, 668. Anal. Calcd for C₁₅H₃₁NO₃Si: C, 59.76; H, 10.36; N, 4.65. Found: C, 59.58; H, 10.16; N, 4.85. HRMS (MALDI) calcd for C₁₅H₃₁NO₃SiNa [M+Na]⁺, 324.1965; found, 324.1962.

(R)-2-((S)-3-[2-(*tert*-Butyl-dimethyl-silanyloxy)-1,1-dimethyl-ethyl]-4,5-dihydroisoxazol-5-yl)-propan-1-ol (S17). To a solution of oxime **S2** (118 mg, 0.500 mmol, 1.00 equiv) in toluene (5 mL) at -78 °C was added *t*BuOCl (59.0 μ L, 0.500 mmol, 1.00 equiv) dropwise over 15 min. The solution was stirred at -78 °C for 4 h. After 1 h the solution was still colorless and turned light blue and cloudy over the course of 4 h. In a separate flask EtMgBr (3.0 M in Et₂O, 500 μ L, 1.50 mmol, 3.00 equiv) was added dropwise to a solution of (*S*)-2-methyl-3-butenol¹³ (56.0 mg, 0.650 mmol, 1.30 equiv) and *i*PrOH (126 μ L, 1.65 mmol, 3.30 equiv) in toluene (10 mL) at 0 °C. The reaction mixture was stirred at 0 °C for 30 min. At this time, about 2/3 of the cloudy hydroximinoyl chloride mixture was added to the reaction dropwise via cannula over 60 min. Then the light blue, turbid hydroximinoyl chloride mixture was allowed to warm to rt for 1 min, whereupon it turned deep blue and clear. The solution was cooled again to -78 °C and the addition via cannula was continued over 30 min, followed by 2 rinses (1 mL each). The slightly yellow solution was stirred at 0 °C for 6 h and was slowly allowed to warm to room temperature overnight (large dewar with ice, covered with aluminum foil). After 14 h the reaction was quenched by addition of saturated, aqueous NH₄Cl (15 mL). The mixture was vigorously stirred for 20 min, then the layers were separated and the aqueous phase was extracted with EtOAc (3 x 15 mL). The combined organic solutions were washed with brine, dried over anhydrous Na₂SO₄, filtered, and concentrated under reduced pressure. After filtration over silica gel (hexane/EtOAc 3:1) isoxazoline **S17** (141 mg, 89% yield, d.r. = 4:1 by integration of the signals at 4.39 ppm (major) and 4.64 ppm (minor) in the ¹H NMR spectrum) was isolated as a pale, colorless oil. Optical Rotation: $[\alpha]^{30}_{\text{D}}$ (c 1.08, CHCl₃) = +17.1. ¹H NMR (300 MHz, CDCl₃, * denotes minor diastereomeric peak) δ 4.64* (ddd, 1 H, *J* = 12.8, 8.4, 4.4 Hz), 4.39 (ddd, 1 H, *J* = 10.0, 8.1, 8.1 Hz), 3.74-3.356 (m, 2 H), 3.51* (s, 2 H), 3.50 (s, 2 H), 3.05 (dd, 1 H, *J* = 16.8, 10.3 Hz), 3.02* (dd, 1 H, *J* = 16.8, 10.6 Hz), 2.85* (dd, 1 H, *J* = 16.8, 8.4 Hz), 2.80 (dd, 1 H, *J* = 16.8, 8.4 Hz), 2.37 (dd, 1 H, *J* = 7.5, 4.1 Hz), 1.95-1.81 (m, 1 H), 1.18 (s, 3 H), 1.16 (s, 3 H), 0.93* (d, 3 H, *J* = 7.2 Hz), 0.89 (s, 9 H), 0.88 (d, 3 H, *J* = 7.2 Hz), 0.05 (s, 6 H). ¹³C NMR (75 MHz, CDCl₃, * denotes minor diastereomeric peak) δ 164.6, 164.3*, 83.9, 81.5*, 70.9, 66.0, 65.1*, 40.2, 39.9*, 39.2, 38.6, 38.2*, 26.0, 23.0, 18.4*, 13.3, 11.3*, -5.4. IR (thin film) ν 3414, 2957, 2931, 2886,

2858, 2246, 1611, 1472, 1392, 1363, 1282, 1254, 1217, 1186, 1099, 1046, 1006, 939, 838, 815, 757, 668. Anal. Calcd for C₁₆H₃₃NO₃Si: C, 60.91; H, 10.54; N, 4.44. Found: C, 61.16; H, 10.71; N, 4.36. HRMS (MALDI) calcd for C₁₆H₃₃NO₃SiNa [M+Na]⁺, 338.2122; found, 338.2121.

(R)-2-((S)-3-((S)-1-(tert-Butyl-dimethyl-silanyloxy)-ethyl)-4,5-dihydro-isoxazol-5-yl)-propan-1-ol (S18). To a solution of (*S*)-2-(*tert*-butyl-dimethyl-silanyloxy)-propionaldehyde oxime¹⁵ (102 mg, 0.500 mmol, 1.00 equiv) in toluene (5 mL) at -78 °C was added *t*BuOCl (59.0 µL, 0.500 mmol, 1.00 equiv) dropwise over 10 min. The mixture turned yellow, then green and finally blue over the course of 15 min and was stirred total 105 min at -78 °C. In a separate flask EtMgBr (3.0 M in Et₂O, 500 µL, 1.50 mmol, 3.00 equiv) was added dropwise to a solution of (*S*)-2-methyl-3-butenol¹³ (56.0 mg, 0.650 mmol, 1.30 equiv) and *i*PrOH (126 µL, 1.65 mmol, 3.30 equiv) in toluene (10 mL) at 0 °C. The mixture was stirred at 0 °C for 1 h. At this time, the hydroximinoyl chloride in toluene was added to the reaction dropwise via cannula over 2 h, followed by 2 rinses (1 mL each). The slightly yellow solution was stirred at 0 °C for 6 h and was slowly allowed to warm to room temperature overnight (large dewar with ice, covered with aluminum foil). After 18 h the reaction was quenched by addition of saturated, aqueous NH₄Cl (15 mL). The mixture was vigorously stirred for 20 min, then the layers were separated and the aqueous phase was extracted with EtOAc (3 x 15 mL). The combined organic solutions were washed with brine, dried over anhydrous Na₂SO₄, filtered, and concentrated under reduced pressure. Purification by flash chromatography (hexane/EtOAc 4:1) provided isoxazoline **S18** (114 mg, 82% yield, d.r. = 6:1 by integration of the signals at 83.9 ppm (major) and 81.7 ppm (minor) in the crude ¹³C NMR spectrum (12 h measurement time)) as a clear, colorless oil. Optical Rotation: [α]_D²⁸ (c 0.99, CHCl₃) = -10.9. ¹H NMR (500 MHz, CDCl₃, * denotes minor diastereomeric peak) δ 4.73 (q, 1 H, *J* = 6.4 Hz), 4.67* (ddd, 1 H, *J* = 13.2, 8.6, 4.5 Hz), 4.46 (ddd, 1 H, *J* = 10.4, 8.3, 8.3 Hz), 3.70-3.59 (m, 2 H), 3.07 (dd, 1 H, *J* = 17.1, 10.4 Hz), 3.05* (dd, 1 H, *J* = 17.4, 10.9 Hz), 2.84* (dd, 1 H, *J* = 17.3, 8.6 Hz), 2.81 (dd, 1 H, *J* = 17.2, 8.3 Hz), 2.15

¹⁵ The synthesis of this oxime has been previously described, see: Frederickson, M.; Grigg, R.; Rankovic, Z.; Thronton-Pett, M.; Redpath, J.; Crossley, R. *Tetrahedron* **1995**, *51*, 6835.

(br s, 1 H), 1.94-1.86 (m, 1 H), 1.35 (d, 3 H, $J = 6.451$ Hz), 0.95* (d, 3 H, $J = 6.9$ Hz), 0.92 (d, 3 H, $J = 7.0$ Hz), 0.89 (s, 9 H), 0.88* (s, 9 H), 0.10 (s, 3 H), 0.10* (s, 3 H), 0.07 (s, 3 H), 0.07* (s, 3 H). ^{13}C NMR (75 MHz, CDCl_3 , * denotes minor diastereomeric peak) δ 162.1, 83.9, 81.7*, 65.8, 65.1*, 64.7*, 64.5, 40.3, 40.0*, 36.6, 36.0*, 25.9, 22.4*, 18.2, 13.0, 11.3*, -4.6, -4.7. IR (thin film) ν 3435, 2957, 2931, 2887, 2858, 1627, 1472, 1464, 1408, 1389, 1372, 1362, 1340, 1312, 1294, 1258, 1216, 1116, 1086, 1026, 954, 881, 834, 778, 664. Anal. Calcd for $\text{C}_{14}\text{H}_{29}\text{NO}_3\text{Si}$: C, 58.49; H, 10.17; N, 4.87. Found: C, 58.56; H, 10.41; N, 5.05. HRMS (MALDI) calcd for $\text{C}_{14}\text{H}_{29}\text{NO}_3\text{SiNa}$ $[\text{M}+\text{Na}]^+$, 310.1809; found, 310.1813.

(R)-2-((S)-3-((R)-1-(tert-Butyl-dimethyl-silanyloxy)-ethyl)-4,5-dihydro-isoxazol-5-yl)-propan-1-ol (S19). To a solution of **oxime S3** (102 mg, 0.500 mmol, 1.00 equiv) in toluene (5 mL) at -78 °C was added $t\text{BuOCl}$ (59.0 μL , 0.500 mmol, 1.00 equiv) dropwise over 10 min. The mixture turned yellow, then green and finally blue over the course of 15 min and was stirred total 105 min -78 °C. In a separate flask EtMgBr (3.0 M in Et_2O , 500 μL , 1.50 mmol, 3.00 equiv) was added dropwise to a solution of (*S*)-2-methyl-3-butenol¹³ (56.0 mg, 0.650 mmol, 1.30 equiv) and $i\text{PrOH}$ (126 μL , 1.65 mmol, 3.30 equiv) in toluene (10 mL) at 0 °C. The mixture was stirred at 0 °C for 1 h. At this time, the hydroximinoyl chloride in toluene was added to the reaction dropwise via cannula over 2 h, followed by 2 rinses (1 mL each). The slightly yellow solution was stirred at 0 °C for 6 h and was slowly allowed to warm to room temperature overnight (large dewar with ice, covered with aluminum foil). After 18 h the reaction was quenched by addition of saturated, aqueous NH_4Cl (15 mL). The mixture was vigorously stirred for 20 min, then the layers were separated and the aqueous phase was extracted with EtOAc (3 x 15 mL). The combined organic solutions were washed with brine, dried over anhydrous Na_2SO_4 , filtered, and concentrated under reduced pressure. Purification by flash chromatography (hexane/ EtOAc 4:1) provided isoxazoline **S19** (119 mg, 83% yield, d.r. = 5:1 by integration of the signals at 84.0 ppm (major) and 81.6 ppm (minor) in the crude ^{13}C NMR spectrum (12 h measurement time)) as a clear, colorless oil. Optical Rotation: $[\alpha]_D^{26}$ (c 1.27, CHCl_3) = +59.5. ^1H NMR (500 MHz, CDCl_3 , * denotes minor diastereomeric peak) δ 4.73 (q, 1 H, $J = 6.4$ Hz), 4.70* (ddd, 1 H, $J = 10.9, 8.5,$

4.4 Hz), 4.45 (ddd, 1 H, $J = 10.3, 8.6, 8.6$ Hz), 3.71-3.59 (m, 2 H), 3.07 (dd, 1 H, $J = 17.5, 10.3$ Hz), 3.06* (dd, 1 H, $J = 17.8, 10.5$ Hz), 2.86* (dd, 1 H, $J = 17.3, 8.4$ Hz), 2.79 (dd, 1 H, $J = 17.1, 8.8$ Hz), 2.14 (br s, 1 H), 1.95-1.86 (m, 1 H), 1.36* (d, 3 H, $J = 6.4$), 1.35 (d, 3 H, $J = 6.5$ Hz), 0.95* (d, 3 H, $J = 6.9$ Hz), 0.92 (d, 3 H, $J = 6.4$ Hz), 0.90* (s, 9 H), 0.89 (s, 9 H), 0.10 (s, 3 H), 0.07 (s, 3 H). ^{13}C NMR (75 MHz, CDCl_3 , * denotes minor diastereomeric peak) δ 162.3, 161.8*, 84.0, 81.6*, 65.8, 65.1*, 64.6, 64.5*, 40.3, 40.0*, 36.9, 35.8*, 25.9, 22.4, 18.2, 13.2, 11.1*, -4.6, -4.7. IR (thin film) ν 3414, 2957, 2931, 2887, 2859, 1680, 1627, 1472, 1464, 1409, 1389, 1372, 1362, 1339, 1313, 1294, 1259, 1217, 116, 1094, 1042, 1025, 953, 880, 835, 813, 778, 757, 667. Anal. Calcd for $\text{C}_{14}\text{H}_{29}\text{NO}_3\text{Si}$: C, 58.49; H, 10.17; N, 4.87. Found: C, 58.47; H, 10.24; N, 5.15. HRMS (MALDI) calcd for $\text{C}_{14}\text{H}_{29}\text{NO}_3\text{SiNa}$ $[\text{M}+\text{Na}]^+$, 310.1809; found, 310.1811.

(R)-2-[(S)-3-(tert-Butyl-diphenyl-silanyloxymethyl)-4,5-dihydro-isoxazol-5-yl]-propan-1-ol (3). To a solution of (*tert*-butyl-diphenyl-silanyloxy)-acetaldehyde oxime¹⁶ (314 mg, 1.00 mmol, 1.00 equiv) in toluene (10 mL) at -78 °C was added *t*BuOCl (118 μL , 1.00 mmol, 1.00 equiv) dropwise over 15 min. The mixture turned yellow, then green and finally blue over the course of 2.5 h and was stirred total 2.5 h at -78 °C. In a separate flask EtMgBr (3.0 M in Et_2O , 1.00 mL, 3.00 mmol, 3.00 equiv) was added dropwise to a solution of (*S*)-2-methyl-3-butenol¹³ (112.0 mg, 1.30 mmol, 1.30 equiv) and *i*PrOH (252 μL , 3.30 mmol, 3.30 equiv) in toluene (20 mL) at 0 °C. The mixture was stirred at 0 °C for 1 h. At this time, the hydroximinoyl chloride in toluene was added to the reaction dropwise via cannula over 2 h 15 min, followed by 2 rinses (1 mL each). The slightly yellow solution was stirred at 0 °C for 6 h and was slowly allowed to warm to room temperature overnight (large dewar with ice, covered with aluminum foil). After 16 h the reaction was quenched by addition of saturated, aqueous NH_4Cl (30 mL). The mixture was vigorously stirred for 20 min, then the layers were separated and the aqueous phase was extracted with EtOAc (3 x 30 mL). The combined organic solutions were washed with brine, dried over anhydrous Na_2SO_4 , filtered, and concentrated under reduced pressure. Purification by

¹⁶ The synthesis of this oxime has been previously described, see: Fader, L. D.; Carreira, E. M. *Org. Lett.* **2004**, *14*, 2485.

flash chromatography (hexane/EtOAc 4:1 to 2:1) provided isoxazoline **3** (345 mg, 87% yield, d.r. = 10:1 by integration of the signals at 84.1 ppm (major) and 81.9 ppm (minor) in the crude ^{13}C NMR spectrum (12 h measurement time)) as a clear, slightly yellow oil. Optical Rotation: $[\alpha]^{30}_{\text{D}}$ (c 0.46, CHCl_3) = +22.8. ^1H NMR (500 MHz, CDCl_3 , * denotes minor diastereomeric peak) δ 7.67-7.64 (m, 4 H), 7.49-7.38 (m, 6 H), 4.71* (ddd, 1 H, J = 10.9, 8.5, 4.5 Hz), 4.48 (ddd, 1 H, J = 10.4, 8.4, 8.4 Hz), 4.44 (s, 2 H), 3.70-3.59 (m, 2 H), 3.08 (dd, 1 H, J = 17.1, 10.4 Hz), 3.07* (dd, 1 H, J = 17.2, 10.9 Hz), 2.87* (dd, 1 H, J = 17.3, 8.5 Hz), 2.80 (dd, 1 H, J = 17.2, 8.6 Hz), 2.17 (br s, 1 H), 1.94-1.86 (m, 1 H), 1.11* (s, 9 H), 1.07 (s, 9 H), 0.95* (d, 3 H, J = 6.9 Hz), 0.91 (d, 3 H, J = 7.0 Hz). ^{13}C NMR (75 MHz, CDCl_3 , * denotes minor diastereomeric peak) δ 158.4, 158.2*, 135.5, 132.6, 130.0, 127.8, 84.1, 81.9*, 65.7, 65.0*, 59.3, 40.2, 40.0*, 38.8, 38.1*, 26.9, 19.4, 13.1, 11.2*. IR (thin film) ν 3436, 3071, 3041, 2947, 2932, 2885, 2858, 2363, 1628, 1589, 1472, 1428, 1390, 1363, 1334, 1301, 1259, 1211, 1113, 1083, 1000, 878, 824, 800, 741, 702. Anal. Calcd for $\text{C}_{23}\text{H}_{31}\text{NO}_3\text{Si}$: C, 69.48; H, 7.86; N, 3.52. Found: C, 69.38; H, 7.90; N, 3.43. HRMS (MALDI) calcd for $\text{C}_{23}\text{H}_{31}\text{NO}_3\text{SiNa}$ $[\text{M}+\text{Na}]^+$, 420.1965; found, 420.1960.

(R)-2-((S)-3-Trimethylsilanylethynyl-4,5-dihydro-isoxazol-5-yl)-propan-1-ol

(S20). To a solution of trimethylsilyl-propynal oxime¹⁷ (70.6 mg, 0.500 mmol, 1.00 equiv) in CHCl_3 (0.75 mL) at rt was added pyridine (1 drop), followed by NCS (66.8 mg, 0.500 mmol, 1.00 equiv). The solution was stirred 1.5 h at rt before Et_2O (10 mL) was added. After filtration over Celite the mixture was concentrated, diluted with Et_2O (10 mL), filtered again over Celite and concentrated. In a separate flask EtMgBr (3.0 M in Et_2O , 500 μL , 1.50 mmol, 3.00 equiv) was added dropwise to a solution of (S)-2-methyl-3-butenol¹³ 56.0 mg, 0.650 mmol, 1.30 equiv) and *i*PrOH (126 μL , 1.65 mmol, 3.30 equiv) in toluene (10 mL) at 0 $^\circ\text{C}$. The mixture was stirred at 0 $^\circ\text{C}$ for 1 h. At this time, the previously prepared hydroximinoyl chloride in toluene (5 mL) was added to the reaction dropwise via cannula over 3.5 h, followed by 2 rinses (1 mL each). The slightly yellow solution was stirred at 0 $^\circ\text{C}$ for 6 h and was slowly allowed to warm to room

¹⁷ This oxime has been previously reported: Safronova, L. P.; Medvedeva, A. S.; Vyazankin, N. S. *J. Gen. Chem. USSR (Engl. Transl.)* **1983**, 53, 1177.

temperature overnight (large dewar with ice, covered with aluminum foil). After 2.5 d the reaction was quenched by addition of saturated, aqueous NH_4Cl (15 mL). The mixture was vigorously stirred for 20 min, then the layers were separated and the aqueous phase was extracted with EtOAc (3 x 15 mL). The combined organic solutions were washed with brine, dried over anhydrous Na_2SO_4 , filtered, and concentrated under reduced pressure. The mixture was filtered over a shot pad of silica gel (hexane/EtOAc 1:2). The analysis of the ^1H NMR spectrum (integration of the signals at 4.60 ppm (major) and 4.79 ppm (minor)) revealed a diastereomeric ratio of 5:1. Purification by flash chromatography (hexane/EtOAc 3:1) provided isoxazoline **S20** (63 mg, 66% yield) as a clear, colorless oil. Optical Rotation: $[\alpha]^{26}_{\text{D}}$ (c 0.37, CHCl_3) = +53.4. ^1H NMR (300 MHz, CDCl_3 , * denotes minor diastereomeric peak) δ 4.79* (ddd, 1 H, J = 13.8, 9.0, 4.8 Hz), 4.60 (ddd, 1 H, J = 17.2, 9.1, 8.1 Hz), 3.68 (br s, 2 H), 3.11* (dd, 1 H, J = 17.1, 11.1 Hz), 3.10 (dd, 1 H, J = 17.0, 10.7 Hz), 2.89* (dd, 1 H, J = 17.0, 9.0 Hz), 2.86 (dd, 1 H, J = 17.0, 9.1 Hz), 2.01-1.89 (m, 1 H), 1.85 (br s, 1 H), 0.97* (d, 3 H, J = 6.9 Hz), 0.93 (d, 3 H, J = 7.0 Hz), 0.24 (s, 9 H), 0.23* (s, 9 H). ^{13}C NMR (75 MHz, CDCl_3 , * denotes minor diastereomeric peak) δ 143.3, 143.2*, 104.6, 104.3*, 93.2*, 93.1, 85.3, 83.5*, 65.3, 64.9*, 41.3, 40.9*, 40.0, 39.8*, 12.8, 11.1*, -0.4. IR (thin film) ν 3401, 2963, 2895, 2361, 2160, 1594, 1555, 1462, 1437, 1321, 1252, 1085, 1045, 995, 921, 846, 761. Anal. Calcd for $\text{C}_{11}\text{H}_{19}\text{NO}_2\text{Si}$: C, 58.63; H, 8.50; N, 6.22. Found: C, 58.44; H, 8.47; N, 6.49. HRMS (MALDI) calcd for $\text{C}_{11}\text{H}_{19}\text{NO}_2\text{SiNa}$ $[\text{M}+\text{Na}]^+$, 248.1077; found, 248.1073.

{1-[(S)-5-((R)-2-Hydroxy-1-methyl-ethyl)-4,5-dihydro-isoxazol-3-yl]-ethyl}-phosphonic acid diethyl ester (S21). To (2-hydroxyimino-1-methyl-ethyl)-phosphonic acid diethyl ester¹⁸ (314 mg, 1.50 mmol, 1.00 equiv) in CH_2Cl_2 (15 mL) at -78°C was added $t\text{BuOCl}$ (177 μL , 1.50 mmol, 1.00 equiv) dropwise and the solution turned deep blue within 15 min. The mixture was stirred at -78°C for 1 h, before it was allowed to warm to rt and was stirred at this temperature for 1.5 h whereupon the solution became colorless. Concentration under reduced pressure and purification by flash chromatography (EtOAc) afforded the corresponding

¹⁸ This compound has been previously reported, see: Bode, J. W.; Carreira, E. M. *J. Org. Chem.* **2001**, 66, 6410.

hydroximinoyl chloride¹⁸ (296 mg, 81%) as a clear, colorless oil which was immediately used in the next reaction.

EtMgBr (3.0 M in Et₂O, 500 μ l, 1.50 mmol, 3.00 equiv) was added dropwise to a solution of (*S*)-2-methyl-3-butenol¹³ (56.0 mg, 0.650 mmol, 1.30 equiv) and *i*PrOH (126 μ l, 1.65 mmol, 3.30 equiv) in CH₂Cl₂ (10 mL) at 0 °C. The mixture was stirred at 0 °C for 30 min. At this time, previously prepared and purified hydroximinoyl chloride (vide supra) (122 mg, 0.500 mmol, 1.00 equiv) in CH₂Cl₂ (5 mL) was added to the reaction dropwise via cannula over 2 h, followed by 2 rinses (1 mL each). The slightly yellow solution was stirred at 0 °C for 6 h and was slowly allowed to warm to room temperature overnight (large dewar with ice, covered with aluminum foil). After 24 h the reaction was quenched by addition of saturated, aqueous NH₄Cl (15 mL). The mixture was vigorously stirred for 20 min, then the layers were separated and the aqueous phase was extracted with EtOAc (3 x 15 mL). The combined organic solutions were washed with brine, dried over anhydrous Na₂SO₄, filtered, and concentrated under reduced pressure. ½ of the crude material was used for the determination of the d.r. by derivatization with benzaldehyde to alkene **S22** (vide infra). Analysis of the corresponding crude ¹H NMR spectrum (integration of the signals at 4.60 ppm (major) and 4.81 ppm (minor)) revealed a diastereomeric ratio of 13:1. Purification of ½ of the crude material by flash chromatography (15% acetone in EtOAc) provided isoxazoline **S21** (52 mg, 71% yield) as a clear, colorless oil. ¹H NMR (300 MHz, CDCl₃) δ 4.56-4.45 (m, 1 H), 4.20-4.09 (m, 4 H), 3.72-3.57 (m, 2 H), 3.25-2.87 (m, 3 H), 2.41-2.33 (m, 1 H), 1.96-1.87 (m, 1 H), 1.50-1.40 (m, 3 H), 1.36-1.31 (m, 6 H), 0.93-0.90 (m, 3 H, *J* = 7.2 Hz) (includes both diastereomers). ¹³C NMR (75 MHz, CDCl₃) δ 156.9, 156.8, 85.1, 84.6, 65.7, 62.8, 62.7, 65.7, 62.8, 62.7, 40.2, 33.4, 33.2, 31.5, 31.3, 29.8, 21.6, 21.5, 16.6, 16.5, 13.3, 13.3, 12.4, 12.3 (includes both diastereomers). IR (thin film) ν 3412, 2982, 2927, 1646, 1617, 1458, 1392, 1333, 1250, 1218, 1164, 1093, 1047, 1021, 968, 900, 860, 799, 725. HRMS (MALDI) calcd for C₁₂H₂₄NO₅PNa [M+Na]⁺, 316.1284; found, 316.1282.

(R)-2-[(S)-3-((E)-1-Methyl-2-phenyl-vinyl)-4,5-dihydro-isoxazol-5-yl]-propan-1-ol

(S22). To flame dried LiCl (12.7 mg, 0.300 mmol, 1.20 equiv) was added azeotropically dried unpurified cycloadduct **S21** (0.250 mmol, 1.00 equiv) in MeCN (3 mL) at rt, followed by dropwise addition of DBU (41.1 μ L, 0.275 mmol, 1.10 equiv). The yellow, slightly cloudy mixture was stirred 15 min at rt, before freshly distilled benzaldehyde (37.2 μ L, 0.375 mmol, 1.50 equiv) was added dropwise. After the mixture was stirred at rt for 15 h, H₂O (3 mL) and brine (3 mL) were added and the resulting solution extracted with EtOAc (3 x 10 mL). The combined organic solutions were washed with brine, dried over anhydrous Na₂SO₄, filtered, and concentrated under reduced pressure. Purification by flash chromatography (hexane/EtOAc 1:1) provided isoxazoline **S22** (29 mg, 47% yield over 2 steps, d.r. = 13:1 by integration of the signals at 4.60 ppm (major) and 4.81 ppm (minor) in the crude ¹H NMR spectrum) as a white solid. Optical Rotation: $[\alpha]_D^{28}$ (c 0.28, CHCl₃) = +55.4. ¹H NMR (300 MHz, CDCl₃, * denotes minor diastereomeric peak) δ 7.42-7.27 (m, 5 H), 6.70 (s, 1 H), 4.81* (ddd, 1 H, *J* = 13.7, 9.0, 5.0 Hz), 4.60 (ddd, 1 H, *J* = 10.3, 8.7, 8.7 Hz), 3.78-3.63 (m, 2 H), 3.31 (dd, 1 H, *J* = 15.9, 10.3 Hz), 3.29* (dd, 1 H, *J* = 16.2, 10.6 Hz), 3.06* (dd, 1 H, *J* = 16.5, 9.0 Hz), 3.02 (dd, 1 H, *J* = 16.2, 8.7 Hz), 2.22 (d, 3 H, *J* = 1.3 Hz), 2.17* (d, 3 H, *J* = 1.6 Hz), 2.07-1.94 (m, 1 H), 1.00* (d, 3 H, *J* = 6.9 Hz), 0.98 (d, 3 H, *J* = 6.9 Hz). ¹³C NMR (75 MHz, CDCl₃) δ 160.4, 136.3, 133.4, 129.4, 129.1, 128.4, 127.7, 85.6, 66.3, 40.6, 38.6, 14.9, 13.5. IR (thin film) ν 3402, 2962, 2924, 1560, 1490, 1442, 1372, 1239, 1086, 1028, 918, 864, 814, 758, 698, 618, 581. Anal. Calcd for C₁₅H₁₉NO₂: C, 73.44; H, 7.81; N, 5.71. Found: C, 72.93; H, 7.32; N, 5.21. HRMS (MALDI) calcd for C₁₅H₁₈NO₂ [M-H]⁺, 244.1332; found, 244.1335. mp: 86 °C

(R)-2-[(S)-3-((E)-1-Methyl-2-phenyl-vinyl)-4,5-dihydro-isoxazol-5-yl]-propan-1-ol

(S23). To a solution of *syn*-benzaldehyde oxime¹⁹ (60.6 mg, 0.500 mmol, 1.00 equiv) in CH₂Cl₂

¹⁹ This oxime is commercially available.

(5 mL) at 0 °C was added *t*BuOCl (62.2 μ L, 0.550 mmol, 1.10 equiv) dropwise. After 1.5 h the solution was concentrated under reduced pressure. The resulting off-white solid was dried azeotropically with toluene (3 x 5 mL). Last traces of *t*BuOCl were removed under high vacuum for 10 min. In a separate flask EtMgBr (3.0 M in Et₂O, 500 μ L, 1.50 mmol, 3.00 equiv) was added dropwise to a solution of (*S*)-2-methyl-3-butenol¹³ (56.0 mg, 0.650 mmol, 1.30 equiv) and *i*PrOH (126 μ L, 1.65 mmol, 3.30 equiv) in CH₂Cl₂ (10 mL) at 0 °C. The reaction mixture turned momentarily cloudy and became clear and colorless upon stirring at 0 °C for 30 min. At this time, the hydroximinoyl chloride in CH₂Cl₂ (5 mL) at rt was added to the reaction dropwise via cannula over 1 h 45 min, followed by 2 rinses (1 mL each). The slightly yellow solution was stirred at 0 °C for 6 h and was slowly allowed to warm to room temperature overnight (large dewar with ice, covered with aluminum foil). After 14 h the reaction was quenched by addition of saturated, aqueous NH₄Cl (15 mL). The mixture was vigorously stirred for 20 min, then the layers were separated and the aqueous phase was extracted with EtOAc (3 x 15 mL). The combined organic solutions were washed with brine, dried over anhydrous Na₂SO₄, filtered, and concentrated under reduced pressure. Purification by flash chromatography (hexane/EtOAc 3:1 to 1:1) provided isoxazoline **S23** (89 mg, 87% yield, d.r. = 7:1 by integration of the signals at 4.66 ppm (major) and 4.85 ppm (minor) in the crude ¹H NMR spectrum) as a white solid. Optical Rotation: $[\alpha]_D^{22}$ (*c* 0.89, CHCl₃) = +63.5. ¹H NMR (300 MHz, CDCl₃, * denotes minor diastereomeric peak) δ 7.70-7.63 (m, 2 H), 7.43-7.37 (m, 3 H), 4.85* (ddd, 1H, *J* = 13.4, 8.6, 4.7 Hz), 4.66 (ddd, 1H, *J* = 10.3, 8.4, 8.4 Hz), 3.77-3.66 (m, 2 H), 3.40 (dd, 1 H, *J* = 16.5, 10.3 Hz), 3.39* (dd, 1 H, *J* = 16.8, 10.9 Hz), 3.17* (dd, 1 H, *J* = 16.8, 8.7 Hz), 3.13 (dd, 1 H, *J* = 16.5, 8.7 Hz), 2.26 (br s, 1 H), 2.09-1.85 (m, 1 H), 0.99* (d, 3 H, *J* = 6.8 Hz), 0.98 (d, 3 H, *J* = 6.8 Hz). ¹³C NMR (75 MHz, CDCl₃, * denotes minor diastereomeric peak) δ 156.8, 130.2, 129.5, 128.7, 126.7, 84.9, 82.8*, 65.9, 65.3*, 40.4, 40.0*, 38.9, 38.0*, 13.3, 11.5*. IR (thin film) ν 3401, 3062, 2964, 2931, 2881, 1597, 1570, 1498, 1447, 1357, 1235, 1181, 1077, 1041, 996, 908, 855, 761, 692, 674. Anal. Calcd for C₁₂H₁₅NO₂: C, 70.22; H, 7.37; N, 6.82. Found: C, 70.09; H, 7.45; N, 6.65. HRMS (MALDI) calcd for C₁₂H₁₆NO₂ [M+H]⁺, 206.1176; found, 206.1179. mp: 61 °C

(S)-2-[(S)-3-(*tert*-Butyl-diphenyl-silanyloxymethyl)-4,5-dihydro-isoxazol-5-yl]-3-trityloxy-propan-1-ol (S24). To a solution of (*tert*-butyl-diphenyl-silanyloxy)-acetaldehyde oxime¹⁶ (157 mg, 0.500 mmol, 1.00 equiv) in CH₂Cl₂ (5 mL) at -78 °C was added *t*BuOCl (59 µl, 0.500 mmol, 1.00 equiv) dropwise over 10 min. The resulting deep blue solution was stirred 2.5 h at -78 °C. In a separate flask EtMgBr (3.0 M in Et₂O, 500 µl, 1.50 mmol, 3.00 equiv) was added dropwise to a solution of monoprotected homoallylic diol **S5** (224 mg, 0.650 mmol, 1.30 equiv) and *i*PrOH (126 µl, 1.65 mmol, 3.30 equiv) in CH₂Cl₂ (10 mL) at 0 °C. The reaction mixture turned momentarily cloudy and became clear and colorless upon stirring at 0 °C for 30 min. At this time, the hydroximinoyl chloride in CH₂Cl₂ was added to the reaction dropwise via cannula over 90 min, followed by 2 rinses (1 mL each). The slightly yellow solution was stirred at 0 °C for 6 h and was slowly allowed to warm to room temperature overnight (large dewar with ice, covered with aluminum foil). After 18 h the reaction was quenched by addition of saturated, aqueous NH₄Cl (15 mL). The mixture was vigorously stirred for 20 min, then the layers were separated and the aqueous phase was extracted with EtOAc (3 x 15 mL). The combined organic solutions were washed with brine, dried over anhydrous Na₂SO₄, filtered, and concentrated under reduced pressure. Purification by flash chromatography (hexane/EtOAc 5:1 to 2:1) provided isoxazoline **S24** (269 mg, 82% yield, d.r. = 19:1 by integration of the signals at 4.70 ppm (major) and 4.79 ppm (minor) in the crude ¹H NMR spectrum) as a pale, thick oil. ¹H NMR (300 MHz, CDCl₃) δ 7.67-7.63 (m, 4 H), 7.48-7.22 (m, 21 H), 4.70 (ddd, 1 H, *J* = 10.2, 8.8, 8.8 Hz), 4.41 (dd, 2 H, *J* = 15.7, 12.9 Hz), 3.96-3.83 (m, 2 H), 3.33 (dd, 1 H, *J* = 9.6, 4.9 Hz), 3.19 (dd, 1 H, *J* = 9.6, 5.5 Hz), 3.00 (dd, 1 H, *J* = 17.3, 10.4), 2.71 (dd, 1 H, *J* = 17.3, 8.8 Hz), 2.29 (br s, 1 H), 2.00-1.91 (m, 1 H), 1.07 (s, 9 H). ¹³C NMR (75 MHz, CDCl₃) δ 158.8, 143.7, 135.6, 132.7, 130.1, 128.7, 128.1, 128.0, 127.3, 87.2, 81.0, 62.8, 62.5, 59.3, 46.4, 39.5, 26.9, 19.3. IR (thin film) ν 3436, 3067, 3020, 2947, 2931, 2858, 2361, 1960, 1898, 1825, 1590, 1490, 1472, 1449, 1428, 1391, 1363, 1333, 1254, 1217, 1151, 1113, 1088, 1026, 933, 899, 876, 824, 798, 761, 745, 702, 668. HRMS (MALDI) calcd for C₄₂H₄₅NO₄SiNa [M+Na]⁺, 678.3010; found, 678.3001.

(S)-3-(*tert*-Butyl-diphenyl-silanyloxy)-2-[(S)-3-(*tert*-butyl-diphenyl-silanyloxy-methyl)-4,5-dihydro-isoxazol-5-yl]-propan-1-ol (S25). To a solution of (*tert*-butyl-diphenyl-silanyloxy)-acetaldehyde oxime¹⁶ (157 mg, 0.500 mmol, 1.00 equiv) in CH₂Cl₂ (5 mL) at -78 °C was added *t*BuOCl (59 µl, 0.500 mmol, 1.00 equiv) dropwise over 10 min. The resulting green solution was stirred 2.5 h at -78 °C. In a separate flask EtMgBr (3.0 M in Et₂O, 500 µl, 1.50 mmol, 3.00 equiv) was added dropwise to a solution of monoprotected homoallylic diol **S7** (221 mg, 0.650 mmol, 1.30 equiv) and *i*PrOH (126 µl, 1.65 mmol, 3.30 equiv) in CH₂Cl₂ (10 mL) at 0 °C. The reaction mixture turned momentarily cloudy and became clear and colorless upon stirring at 0 °C for 30 min. At this time, the hydroximinoyl chloride in CH₂Cl₂ was added to the reaction dropwise via cannula over 60 min, followed by 2 rinses (1 mL each). The slightly yellow solution was stirred at 0 °C for 6 h and was slowly allowed to warm to room temperature overnight (large dewar with ice, covered with aluminum foil). After 18 h the reaction was quenched by addition of saturated, aqueous NH₄Cl (15 mL). The mixture was vigorously stirred for 20 min, then the layers were separated and the aqueous phase was extracted with EtOAc (3 x 15 mL). The combined organic solutions were washed with brine, dried over anhydrous Na₂SO₄, filtered, and concentrated under reduced pressure. Purification by flash chromatography (hexane/EtOAc 10:1) provided isoxazoline **S25** (277 mg, 85% yield, d.r. = 21:1 by integration of the signals at 80.6 ppm (major) and 79.4 ppm (minor) in the crude ¹³C NMR spectrum (12 h measurement time)) as a pale, thick oil. ¹H NMR (300 MHz, CDCl₃) δ 7.67-7.61 (m, 8 H), 7.47-7.35 (m, 12 H), 4.67 (ddd, 1 H, *J* = 10.3, 8.7, 8.7 Hz), 4.40 (dd, 2 H, *J* = 15.3, 12.8 Hz), 3.95-3.81 (m, 2 H), 3.81-3.69 (m, 2 H), 3.04 (dd, 1 H, *J* = 17.1, 10.6 Hz), 2.77 (dd, 1 H, *J* = 17.1, 9.0 Hz), 2.30 (dd, 1 H, *J* = 5.6, 6.5 Hz), 1.97-1.87 (m, 1 H), 1.07 (s, 9 H), 1.06 (s, 9 H). ¹³C NMR (75 MHz, CDCl₃) δ 158.7, 135.5, 135.5, 132.9, 132.9, 132.6, 130.0, 129.9, 127.9, 80.6, 63.3, 62.3, 59.4, 47.8, 39.6, 27.1, 27.0, 19.4, 19.4. IR (thin film) ν 3436, 3071, 3050, 3014, 2958, 2931, 2891, 2858, 2361, 1962, 1891, 1825, 1773, 1654, 1628, 1590, 1472, 1428, 1391, 1362, 1334, 1306, 1260, 1216, 1189, 1113, 1000, 998, 938, 880, 824, 803, 741, 702, 668, 613. Anal. Calcd for C₃₉H₄₉NO₄Si₂: C, 71.85; H, 7.57; N, 2.15. Found: C, 71.69; H, 7.71; N, 2.29. HRMS (MALDI) calcd for C₃₉H₄₉NO₄Si₂Na [M+Na]⁺, 674.3092; found, 674.3100.

(S)-2-[(S)-3-(*tert*-Butyl-diphenyl-silanyloxymethyl)-4,5-dihydro-isoxazol-5-yl]-3-triisopropylsilanyloxy-propan-1-ol (S26). To a solution of (*tert*-butyl-diphenyl-silanyloxy)-acetaldehyde oxime¹⁶ (157 mg, 0.500 mmol, 1.00 equiv) in CH₂Cl₂ (5 mL) at -78 °C was added *t*BuOCl (59 μ L, 0.500 mmol, 1.00 equiv) dropwise over 10 min. The resulting green solution was stirred 2.5 h at -78 °C. In a separate flask EtMgBr (3.0 M in Et₂O, 500 μ L, 1.50 mmol, 3.00 equiv) was added dropwise to a solution of monoprotected homoallylic diol **S9** (168 mg, 0.650 mmol, 1.30 equiv) and *i*PrOH (126 μ L, 1.65 mmol, 3.30 equiv) in CH₂Cl₂ (10 mL) at 0 °C. The reaction mixture turned momentarily cloudy and became clear and colorless upon stirring at 0 °C for 30 min. At this time, the hydroximinoyl chloride in CH₂Cl₂ was added to the reaction dropwise via cannula over 90 min, followed by 2 rinses (1 mL each). The slightly yellow solution was stirred at 0 °C for 6 h and was slowly allowed to warm to room temperature overnight (large dewar with ice, covered with aluminum foil). After 18 h the reaction was quenched by addition of saturated, aqueous NH₄Cl (15 mL). The mixture was vigorously stirred for 20 min, then the layers were separated and the aqueous phase was extracted with EtOAc (3 x 15 mL). The combined organic solutions were washed with brine, dried over anhydrous Na₂SO₄, filtered, and concentrated under reduced pressure. Purification by flash chromatography (hexane/EtOAc 10:1) provided isoxazoline **S26** (209 mg, 73% yield, d.r. = 14:1 by integration of the signals at 80.6 ppm (major) and 79.0 ppm (minor) in the crude ¹³C NMR spectrum (12 h measurement time)) as a clear, colorless oil. ¹H NMR (300 MHz, CDCl₃) δ 7.67-7.64 (m, 4 H), 7.48-7.37 (m, 6 H), 4.70 (ddd, 1 H; *J* = 16.5, 9.0, 7.5 Hz), 4.44 (s, 2 H), 3.93-3.80 (m, 4 H), 3.16 (dd, 1 H, *J* = 17.4, 10.6), 2.95 (dd, 1 H, *J* = 17.1, 9.0 Hz), 2.52 (t, 1 H, *J* = 5.9 Hz), 1.99-1.90 (m, 1 H), 1.11-1.04 (m, 30 H). ¹³C NMR (75 MHz, CDCl₃) δ 158.8, 135.6, 132.7, 130.1, 127.9, 80.6, 63.7, 62.9, 59.4, 47.6, 39.5, 27.0, 19.5, 18.2, 12.1. IR (thin film) ν 3436, 3072, 3051, 2942, 2892, 2865, 2717, 2247, 1961, 1891, 1822, 1773, 1656, 1628, 1590, 1464, 1428, 1383, 1363, 1334, 1307, 1257, 1208, 1156, 1113, 1013, 998, 910, 883, 824, 795, 739, 702, 690, 660, 612. HRMS (MALDI) calcd for C₃₂H₅₁NO₄Si₂Na [M+Na]⁺, 592.3249; found, 592.3241.

(S)-3-(*tert*-Butyl-dimethyl-silanyloxy)-2-[(S)-3-(*tert*-butyl-diphenyl-silanyloxy-methyl)-4,5-dihydro-isoxazol-5-yl]-propan-1-ol (S27). To a solution of the (*tert*-butyl-diphenyl-silanyloxy)-acetaldehyde oxime¹⁶ (107 mg, 0.340 mmol, 1.00 equiv) in CH₂Cl₂ (3.5 mL) at -78 °C was added *t*BuOCl (40 μ l, 0.340 mmol, 1.00 equiv) dropwise over 10 min. The resulting green solution was stirred 2.5 h at -78 °C. In a separate flask EtMgBr (3.0 M in Et₂O, 340 μ l, 1.02 mmol, 3.00 equiv) was added dropwise to a solution of monoprotected homoallylic diol **S11** (98.0 mg, 0.450 mmol, 1.30 equiv) and *i*PrOH (86.0 μ l, 1.12 mmol, 3.30 equiv) in CH₂Cl₂ (7 mL) at 0 °C. The reaction mixture turned momentarily cloudy and became clear and colorless upon stirring at 0 °C for 30 min. At this time, the hydroximinoyl chloride in CH₂Cl₂ was added to the reaction dropwise via cannula over 90 min, followed by 2 rinses (1 mL each). The slightly yellow solution was stirred at 0 °C for 6 h and was slowly allowed to warm to room temperature overnight (large dewar with ice, covered with aluminum foil). After 18 h the reaction was quenched by addition of saturated, aqueous NH₄Cl (15 mL). The mixture was vigorously stirred for 20 min, then the layers were separated and the aqueous phase was extracted with EtOAc (3 x 15 mL). The combined organic solutions were washed with brine, dried over anhydrous Na₂SO₄, filtered, and concentrated under reduced pressure. Purification by flash chromatography (hexane/EtOAc 10:1 to 4:1) provided isoxazoline **S27** (141 mg, 78% yield, d.r. = 10:1 by integration of the signals at 80.6 ppm (major) and 79.0 ppm (minor) in the crude ¹³C NMR spectrum (12 h measurement time)) as a clear, colorless oil. ¹H NMR (300 MHz, CDCl₃) δ 7.74-7.65 (4 H), 7.49-7.38 (m, 6 H), 4.66 (ddd, 1 H, *J* = 16.5, 9.1, 7.4 Hz), 4.45 (s, 2 H), 3.83 (br s, 2 H), 3.76 (dd, 2 H, *J* = 5.5, 1.9 Hz), 3.14 (dd, 1 H, *J* = 17.3, 10.7 Hz), 2.93 (dd, 1 H, *J* = 17.3, 9.1 Hz), 2.47 (br s, 1 H), 1.97-1.88 (m, 1 H), 1.07 (s, 9 H), 0.90 (s, 9 H), 0.08 (s, 3 H), 0.07 (s, 3 H). ¹³C NMR (75 MHz, CDCl₃) δ 158.8, 135.5, 132.6, 130.0, 127.9, 80.6, 63.1, 62.6, 59.4, 47.4, 39.4, 27.0, 26.1, 19.5, 18.4, -5.3, -5.3. IR (thin film) ν 3430, 3072, 3050, 2855, 2931, 2889, 2858, 2247, 1958, 1893, 1827, 1712, 1662, 1624, 1585, 1470, 1426, 1390, 1362, 1334, 1255, 1209, 1113, 1007, 938, 910, 838, 779, 739, 702, 611. Anal. Calcd for C₂₉H₄₅NO₄Si₂: C, 65.99; H, 8.59; N, 2.65. Found: C, 66.13; H, 8.50; N, 2.67. HRMS (MALDI) calcd for C₂₉H₄₅NO₄Si₂Na [M+Na]⁺, 550.2779; found, 550.2772.

(S)-2-[(S)-3-(*tert*-Butyl-diphenyl-silanyloxymethyl)-4,5-dihydro-isoxazol-5-yl]-3-triethylsilanyloxy-propan-1-ol (S28). To a solution of (*tert*-butyl-diphenyl-silanyloxy)-acetaldehyde oxime¹⁶ (157 mg, 0.500 mmol, 1.00 equiv) in CH₂Cl₂ (5 mL) at -78 °C was added *i*BuOCl (59 μ L, 0.500 mmol, 1.00 equiv) dropwise over 10 min. The resulting green solution was stirred 2.5 h at -78 °C. In a separate flask EtMgBr (3.0 M in Et₂O, 500 μ L, 1.50 mmol, 3.00 equiv) was added dropwise to a solution of monoprotected homoallylic diol **S13** (141 mg, 0.650 mmol, 1.30 equiv) and *i*PrOH (126 μ L, 1.65 mmol, 3.30 equiv) in CH₂Cl₂ (10 mL) at 0 °C. The reaction mixture turned momentarily cloudy and became clear and colorless upon stirring at 0 °C for 30 min. At this time, the hydroximinoyl chloride in CH₂Cl₂ was added to the reaction dropwise via cannula over 90 min, followed by 2 rinses (1 mL each). The slightly yellow solution was stirred at 0 °C for 6 h and was slowly allowed to warm to room temperature overnight (large dewar with ice, covered with aluminum foil). After 18 h the reaction was quenched by addition of saturated, aqueous NH₄Cl (15 mL). The mixture was vigorously stirred for 20 min, then the layers were separated and the aqueous phase was extracted with EtOAc (3 x 15 mL). The combined organic solutions were washed with brine, dried over anhydrous Na₂SO₄, filtered, and concentrated under reduced pressure. Purification by flash chromatography (hexane/EtOAc 10:1) provided isoxazoline **S28** (139 mg, 53% yield, d.r. = 6:1 by integration of the signals at 79.2 ppm (major) and 78.8 ppm (minor) in the crude ¹³C NMR spectrum (12 h measurement time)) as a clear, colorless oil. ¹H NMR (300 MHz, CDCl₃) δ 7.70-7.64 (m, 4 H), 7.48-7.35 (m, 6 H), 4.70 (ddd, 1 H, *J* = 16.6, 9.2, 7.3 Hz), 4.55 (d, 2 H, *J* = 1.2 Hz), 4.14-4.04 (m, 2 H), 3.74 (dd, 2 H, *J* = 5.4, 0.9 Hz), 3.15-2.97 (m, 2 H), 2.18-2.04 (m, 1 H), 1.07 (s, 9 H), 0.94 (t, 9 H, *J* = 8.0 Hz), 0.58 (q, 6 H, *J* = 8.0 Hz). ¹³C NMR (75 MHz, CDCl₃) δ 158.6, 135.6, 133.0, 130.0, 127.9, 79.2, 60.5, 59.5, 57.4, 45.2, 38.7, 27.0, 19.5, 7.1, 4.5. IR (thin film) ν 3338, 3072, 3050, 2956, 2932, 2876, 2859, 1960, 1889, 1822, 1768, 1657, 1590, 1472, 1428, 1390, 1362, 1308, 1258, 1240, 1209, 1186, 1114, 1006, 939, 909, 881, 823, 802, 740, 702, 612. HRMS (MALDI) calcd for C₂₉H₄₅NO₄Si₂Na [M+Na]⁺, 550.2779; found, 550.2772.

(S)-2-[(S)-3-(*tert*-Butyl-diphenyl-silanyloxymethyl)-4,5-dihydro-isoxazol-5-yl]-propionic acid methyl ester (4**).** To primary alcohol **3** (152 mg, 0.382 mmol, 1.00 equiv) in CH₂Cl₂ (4 mL) at 0 °C was added TEMPO (1.20 mg, 7.60 μmol, 2.00 mol%) and KBr (4.50 mg, 38.2 μmol, 10.0 mol%). The mixture was vigorously stirred and NaOCl (approx 1.5 M in H₂O, 382 μl, 0.573 mmol, 1.50 equiv) in pH 8.6 buffer (3 mL) was added in portions. Additional aq. NaOCl solution (400 μl, 0.600 mmol, 1.57 equiv) was added after 10 min. After total 1.5 h TLC analysis indicated complete consumption of the starting material. The reaction was quenched by addition of MeOH (200 μl). H₂O (10 mL) and CH₂Cl₂ (10 mL) were added, the layers separated, and the aqueous phase extracted with CH₂Cl₂ (3 x 10 mL). The combined organic solutions were washed with brine, dried over anhydrous Na₂SO₄, filtered, and concentrated under reduced pressure to give the intermediate aldehyde which was used without further purification.

A solution of NaClO₂ (207 mg, 2.29 mmol, 6.00 equiv) and 2-methyl-2-butene (404 μl, 3.82 mmol, 10.0 equiv) in pH 3.8 buffer (2.3 mL) and *t*BuOH (11.1 mL) was added at 0 °C to the unpurified aldehyde. The mixture was stirred at 0 °C for 50 min, before pH 3.8 buffer (6 mL) and EtOAc (10 mL) were added. The layers were separated and the aqueous phase was extracted with EtOAc (3 x 10 mL). The combined organic solutions were dried over anhydrous Na₂SO₄, filtered, and concentrated under reduced pressure to give the intermediate carboxylic acid which was used without further purification.

To the unpurified carboxylic acid in 7:1 benzene/MeOH (16 mL) at 0 °C was added dropwise TMSCH₂N₂ (2.0 M in hexane, 1.53 mL, 3.06 mmol, 8.00 equiv). The yellow solution was stirred for 15 min at 0 °C before being quenched with acetic acid (dropwise addition until solution stayed colorless). The volatiles were removed under reduced pressure. Purification by flash chromatography (hexane/EtOAc 8:1) provided methyl ester **4** (113 mg, 70% yield over 3 steps) as a colorless oil. Optical Rotation: $[\alpha]_D^{34}$ (*c* 0.58, CHCl₃) = +29.8. ¹H NMR (300 MHz, CDCl₃, * denotes minor diastereomeric peak) δ 7.67-7.64 (m, 4 H), 7.45-7.37 (m, 6 H), 4.85 (ddd, 1 H, *J* = 10.9, 7.5, 7.5 Hz), 4.72* (ddd, 1 H, *J* = 10.6, 7.5, 7.5 Hz), 4.43 (s, 2 H), 3.72 (s, 3 H), 3.71* (s, 3 H), 3.17* (dd, 1 H, *J* = 17.4, 10.6), 3.10 (dd, 1 H, *J* = 17.7, 10.9), 2.86* (dd, 1 H, *J* = 17.4, 7.5 Hz), 2.85 (dd, 1 H, *J* = 17.4, 7.8 Hz), 2.77 (dq, 1 H, *J* = 7.0, 7.0 Hz), 2.64* (dq, 1 H, *J*

= 7.0, 7.0 Hz), 1.28* (d, 3 H, J = 7.2 Hz), 1.15 (d, 3 H, J = 7.2 Hz), 1.07 (s, 9 H). ^{13}C NMR (75 MHz, CDCl_3 , * denotes minor diastereomeric peak) δ 173.9*, 173.8, 158.2*, 157.9, 135.5, 132.6, 130.0, 127.9, 81.1*, 81.0, 59.2, 52.1, 44.3*, 43.6, 39.1*, 37.5, 29.9, 19.4, 13.6*, 12.1. IR (thin film) ν 3437, 3072, 3049, 2954, 2933, 2892, 2859, 1963, 1893, 1831, 1740, 1629, 1606, 1594, 1502, 1472, 1462, 1429, 1379, 1362, 1338, 1263, 1203, 1166, 1113, 998, 939, 873, 824, 800, 742, 703, 612. Anal. Calcd for $\text{C}_{24}\text{H}_{31}\text{NO}_4\text{Si}$: C, 67.73; H, 7.34; N, 3.29. Found: C, 67.58 H, 7.57; N, 3.54. HRMS (MALDI) calcd for $\text{C}_{24}\text{H}_{31}\text{NO}_4\text{SiNa}$ $[\text{M}+\text{Na}]^+$, 448.1915; found, 448.1914.

(S)-2-((S)-3-Hydroxymethyl-4,5-dihydro-isoxazol-5-yl)-propionic acid methyl ester (5a). To TBDPS ether **4** (111 mg, 0.260 mmol, 1.00 equiv) in THF (2.5 mL) was added at 0 °C TBAF (1.0 M in THF, 0.780 mL, 0.780 mmol, 3.00 equiv). The mixture was stirred at 0 °C for 4 h before additional TBAF (1.0 M in THF, 0.780 mL, 0.780 mmol, 3.00 equiv) was added. The mixture was stirred for 12 h at rt. The reaction was quenched by the addition of saturated, aqueous NaHCO_3 solution (10 mL) and Et_2O (10 mL) was added. The layers were separated and the aqueous phase was extracted with Et_2O (3 x 10 mL). The combined organic solutions were dried over anhydrous Na_2SO_4 , filtered, and concentrated under reduced pressure. Purification by flash chromatography (hexane/ EtOAc 1:1) provided **5a** and **5b** (128 mg, 85% combined yield) as a clear, colorless oil. A second purification by flash chromatography (hexane/ EtOAc 5:1) resulted in separation of the diastereomers. Optical Rotation: $[\alpha]_D^{34}$ (c 0.61, CHCl_3) = +13.5. ^1H NMR (300 MHz, CDCl_3 , * denotes minor diastereomeric peak) δ 4.88 (ddd, 1 H, J = 10.6, 7.5, 7.5 Hz), 4.76* (ddd, 1 H, J = 10.6, 7.5, 7.5 Hz), 4.40 (s, 2 H), 3.71 (s, 3 H), 3.70* (s, 3 H), 3.19* (dd, 1 H, J = 17.4, 10.6 Hz), 3.12 (dd, 1 H, J = 17.4, 10.9 Hz), 2.93* (dd, 1 H, J = 17.4, 7.5 Hz), 2.88 (dd, 1 H, J = 17.4, 7.8 Hz), 2.79 (dq, 1 H, J = 7.2, 7.2 Hz), 2.71* (dq, 1 H, J = 7.2, 7.2 Hz), 2.18 (br s, 1 H), 1.28* (d, 3 H, J = 7.2 Hz), 1.17 (d, 3 H, J = 7.2 Hz). ^{13}C NMR (75 MHz, CDCl_3 , * denotes minor diastereomeric peak) δ 174.0*, 173.8, 158.6*, 158.2, 81.7*, 81.5, 58.3, 52.2, 44.2*, 43.7, 38.8*, 37.6, 13.8*, 12.4. IR (thin film) ν 3419, 2978, 2954, 2885, 2361, 2342, 1734, 1629, 1460, 1437, 1380, 1337, 1266, 1206, 1168, 1051, 991, 922, 867, 668. Anal. Calcd for $\text{C}_8\text{H}_{13}\text{NO}_4$: C,

51.33; H, 7.00; N, 7.48. Found: C, 51.40; H, 7.10; N, 7.62. HRMS (MALDI) calcd for $C_8H_{13}NO_4Na$ $[M+Na]^+$, 210.0737; found, 210.0733.

(S)-2-((R)-3-Benzyloxymethyl-4,5-dihydro-isoxazol-5-yl)-propionic acid methyl ester (6). To a solution of alcohol **5b** (22.0 mg, 0.118 mmol, 1.00 equiv) and benzyl 2,2,2-trichloroacetimidate (44.0 μ L, 0.235 mmol, 2.00 equiv) in cyclohexane (0.5 mL) and CH_2Cl_2 (0.25 mL) at rt was added trifluoromethanesulfonic acid (5.00 μ L, 0.0572 mmol, 0.487 equiv). The mixture was stirred for 15 h at rt. The crystalline trichloroacetamide was removed by filtration (washings with pentane (10 mL), Et_2O dissolves the amide). The filtrate was washed with saturated, aqueous $NaHCO_3$ solution (5 mL) and brine, dried over anhydrous Na_2SO_4 , filtered, and concentrated under reduced pressure. Purification by flash chromatography (hexane/ $EtOAc$ 4:1) provided isoxazoline **6** (20 mg, 62% yield) as a colorless oil. 1H NMR (300 MHz, $CDCl_3$) δ 7.40-7.28 (m, 5 H), 4.74 (ddd, 1 H, J = 10.6, 7.5, 7.5 Hz), 4.53 (s, 2 H), 4.30 (s, 2 H), 3.70 (s, 3 H), 3.17 (dd, 1 H, J = 17.4, 10.6 Hz), 2.89 (dd, 1 H, J = 17.4, 7.5 Hz), 2.73-2.63 (m, 1 H), 1.29 (d, 3 H, J = 7.1 Hz). ^{13}C NMR (75 MHz, $CDCl_3$) δ 173.9, 156.7, 137.3, 128.6, 128.1, 128.0, 81.5, 72.9, 64.7, 52.2, 44.4, 39.4, 13.8. HRMS (MALDI) calcd for $C_{15}H_{19}NO_4Na$ $[M+Na]^+$, 278.1387; found, 278.1393. These spectral characteristics are identical to those previously reported.²⁰

²⁰ Panek, J. S.; Beresis, R. T. *J. Am. Chem. Soc.* **1993**, *115*, 7898.