Supporting Information

Synthesis of Unnatural Amino Acids *via* Suzuki Cross-Coupling of Enantiopure Vinyloxazolidine Derivatives

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General. ^{1}H NMR and ^{13}C NMR spectra were recorded on a Varian Unity 500, a Varian Gemini 300, or a Varian Mercury 400. Chemical shift values (δ) are reported in ppm. High resolution mass spectra were recorded on a Kratos MS80RFA spectrometer. FAB mass spectra were recorded on a Kratos MS50TC spectrometer. Optical rotations were determined with a Perkin-Elmer 241 MC polarimeter. Flash Chromatography was carried out using Merck Kieselgel (230-400 mesh). Thin layer chromatography was performed on silica gel. Melting points were taken on a Hoover UniMelt apparatus and are uncorrected. Solvents were purified according to the standard procedures.

^{1}H NMR and ^{13}C NMR spectra of *N*-Alkoxycarbonyl-2,2-dimethyl-4-substituted oxazolidines frequently displayed complicated spectra with considerable signal doubling and broadening due to interconverting conformers.[5a] The spectra often but not always simplified upon hydrolysis of the acetonide protecting group. When possible every signal has been reported. When line broadening did not allow recording of both frequencies the doubling is designated with a d next to the frequency.

Procedure A: Suzuki Cross-Coupling of *R*-(2) with Aryl Triflate 20[15]. A flame-dried 100-mL round-bottomed flask was charged with 521 mg (1.99 mmol) of *R*-(**2**). To this was added 6-10 mL of dry toluene, followed by 487 mg (3.99 mmol) of 9-BBN dimer, the flask was then fitted with a reflux condenser and placed under an argon atmosphere. The solution was brought to 80-85 ˚C with the aid of a preheated oil bath. The 9-BBN dimer dissolved and the resulting clear solution was stirred at this temperature for

[15] Prepared via standard procedure see: Echavarren, A. M.; Stille, J. K. J. Am. Chem. Soc. 1987, 109, 548.

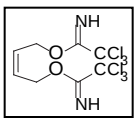
approximately 30-35 min. The heating bath was removed and the reaction was checked by TLC (7:1 petroleum ether /EtOAc) with care being exercised not to introduce oxygen. With complete disappearance of *R*-(**2**), 319 mg (7.98 mmol) of NaOH in approx. 2.5 mL of distilled water was introduced. After a brief time 115 mg of $Pd(PPh_3)_4$ was added followed by 686 mg (2.6 mmol, 1.3 equiv.) of **20**, introduced with the aid of a cannula. Finally 369 mg (1.0 mmol, 0.5 equiv.) of tetrabutylammonium iodide (TBAI) was added and the whole mixture was stirred under argon at 90˚ C overnight. TLC (3:1 petroleum ether/EtOAc) revealed coupled product at R_f 0.56. The reaction mixture was poured into a separatory funnel and extracted (2x) with 25-mL portions of pentane or Et_2O. The organic extracts were combined, dried over $MgSO_4$, and evaporated to give a dark brown oil which was purified by column chromatography on silica gel. Alternatively the crude product was subjected to acid hydrolysis of the acetal group (see procedure B). In certain instances the large difference in polarity between the hydrolyzed product and the coupling by-products made column chromatography simpler.

Procedure B: Hydrolysis of the Acetal Protecting Group in Coupled Products utilizing *R* or *S*-(2). The crude brown oil from procedure A was dissolved in 10 mL of MeOH and 100 µl of conc. HCl was added and the solution was stirred overnight. A small amount of Pd species precipitates from the light orange solution. Approximately 50% of the solvent was removed under vacuum and the remainder was applied to a short silica gel column (3:1 petroleum ether/EtOAc). Collection of appropriate fractions afforded 520 mg (73% for two steps) of **20b** as a brown oil which slowly crystallized (mp 70-72 ˚C).

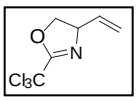
Procedure C: Hydrolysis of the Acetal Protecting Group in Coupled Products Utilizing *R* or *S*-(1). Crude cross-coupling product **20a** 554 mg was dissolved in 13 mL of MeOH and 1.9 g (5 equiv.) of PPTS was added. The mixture was then stirred at rt and monitored by TLC (7:1 and 1:1 petroleum ether/EtOAc). After 72 h only trace quantities of starting material remained and the mixture was concentrated under vacuum. The solids were then partitioned between water/Et_2O. The layers were separated and the aqueous layer was extracted with Et_2O; the combined organic extracts were washed with sat. $NaHCO_3$, water, brine, dried over $MgSO_4$ and evaporated to give a brown oil. The latter was purified by column chromatography on silica gel. Initial elution with (7:1 petroleum ether/EtOAc) removed non-polar impurities and (1:1 petroleum ether/EtOAc) afforded 403 mg (72%) of **20a** as a clear oil which crystallized upon standing mp 76-77 ˚C.

Procedure D: Two-step Dess-Martin/$NaClO_2$ Oxidation of Amino-Alcohols. Compound **12b** (222 mg, 0.675 mmol) was dissolved in 8-10 mL of dry THF. To this solution was added 371 mg (0.877 mmol) of Dess-Martin reagent and the mixture was

stirred under argon for 30-45 min. A 25% sodium thiosulfate solution, and a sat. $NaHCO_3$ solution were added (~4ml each). The biphasic mixture was stirred for an additional 30 min. The phases were separated and the aqueous layer was extracted with Et_2O (2x). The combined organic extracts was dried over $MgSO_4$, and evaporated to give a clear oil. The crude aldehyde was taken up in 10 mL of a (1:1 solution of CH_3CN/*tert*-butyl alcohol) and 3 mL of 2-methyl-2-butene was added. To this solution was added 611 mg of $NaClO_2$ and 745 mg of NaH_2PO_4 in ~5 mL of water; the mixture was vigorously stirred for 10-15 min at rt. This reaction mixture was then extracted 3x with EtOAc. The combined organics were dried over $MgSO_4$ and evaporated to give an oil containing the crude acid. Silica gel column chromatography (10:10:0.1 hexanes/EtOAc/AcOH) or crystallization from Et_2O/hexanes afforded 190 mg (82%) of **39** as white crystals mp 120-122 ˚C.

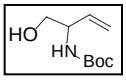


(*Z*)-2-Butene-1,4-diyl-Bis-(2,2,2-trichloroethanimidate) (4).[7] A oven dried 2-L round-bottomed flask equipped with a magnetic stirrer was charged with dry THF (500 mL) under an argon atmosphere. 2-Butene-1,4-diol was added (44.0 g, 0.50 mol) and to the reaction solution was added portionwise KH (5 g 0.043 mol, 35% dispersion in mineral oil). A vigorous reaction ensued and was allowed to subside before additional KH was added. After addition of the final portion, the slurry was stirred for an additional 5 min at rt. The reaction vessel was cooled to -17 °C, and CCl_3CN (105 mL, 1.05 mol) was added in one portion. The reaction mixture was then stirred for 3 h during which time it was allowed to warm to rt. The solvent volume was reduced by ~80% by rotary evaporation. The resulting thick suspension was treated with a solution of 11 mL of MeOH dissolved in 1 L of pentane. The mixture was stirred at rt until a yellow solution containing a brown flocculent resulted (~5-10 min). This mixture was filtered through a pad of Celite® and the filtrate was concentrated to afford **4** (175.4 g, 93%), as a dark yellow oil: ^{1}HNMR ($CDCl_3$) δ 8.35 (bs, 2H), 5.93 (ddt_{app}, 2H, J = 4.4, 4.0, 0.8 Hz), 4.96 (dd_{app}, 4H, J = 4.0, 0.8 Hz); ^{13}CNMR ($CDCl_3$) δ 163.45, 129.03, 92.31, 66.08. These data are in agreement with literature values.[7]

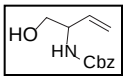


2-Trichloromethyl-4-vinyloxazoline (5). An oven dried 250-mL round-bottomed flask equipped with a magnetic stirrer was charged with dry ether (75 mL) under an argon atmosphere. Compound **4** (17.7g, 47.3 mmol) was added and the reaction mixture was chilled to 4 ˚C with an ice bath. To this solution was added $PdCl_2(CH_3CN)_2$ (602 mg, 2.37 mmol) portionwise to avoid exotherms; the reaction mixture was stirred at rt under argon for 18 h. At which time a yellow precipitate of trichloroacetamide was removed from the reaction mixture by filtration through a Celite® plug. The solids were washed once with a small amount of chilled pentane and the combined organics were concentrated, taking care not to allow evaporation of the somewhat

volatile product **5**. The resulting yellow oil, containing a trace amount of trichloroacetamide, was subsequently treated with 125 mL of pentane and chilled in a -30 ˚C freezer overnight. Additional precipitated trichloroacetamide was filtered off. The pentane filtrate was concentrated to afford essentially pure compound **5** as a yellow oil (8.4 g, 83%). : ^{1}HNMR ($CDCl_3$) δ 5.88 (ddd, 1H, *J* = 25.5, 12.9, 5.1 Hz), 5.32 (m, 2H), 4.87 (m, 1H), 4.76 (dd, 1H, *J* = 8.1, 1.5 Hz) 4.35 (dd_{app}, 1H, *J* = 8.1 Hz); ^{13}CNMR ($CDCl_3$) δ 164.22, 136.66, 119.25, 87.56, 76.87, 69.89. HRMS (EI) calcd. for $C_7H_8O_3$ 212.95149 (M^+), found 212.9515.

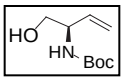


2-(*N*-tert-Butoxycarbonylamino)-3-buten-1-ol (6).[11] A 300-mL round-bottomed flask equipped with a magnetic stirrer was charged with 6N HCl (50 mL). Compound **5** (3.7 g, 17.2 mmol), dissolved in 10-20 mL of MeOH, was then added and the reaction mixture was stirred at rt for 1-2 h. This solution was then refluxed for 48 h. The resulting dark brown solution was cooled and concentrated on a rotary evaporator. The resultant orange crystalline residue was treated with 60 mL of saturated $NaHCO_3$ solution and 120 mL of EtOAc . To this biphasic mixture was added $(Boc)_2O$[10] (4.8 g, 25.8 mmol) and vigorous stirring was continued overnight. The layers were separated and the organic phase was sequentially washed with water and brine, dried over $MgSO_4$ and concentrated in vacuo to give a thick yellow oil. This residue was purified by column chromatography on silica gel (1:1 EtOAc/hexanes). The appropriate fractions were concentrated to afford pure compound **6** as a yellow oil (2.1 g, 65% 2 steps): ^{1}HNMR ($CDCl_3$) δ 5.79 (ddd, 1H, *J* = 17.4, 10.5, 5.4 Hz), 5.25 (ddd, 1H, *J* = 17.4, 1.5, 1.5 Hz), 5.22 (ddd, 1H, *J* = 10.5, 1.5, 1.5 Hz), 4.87 (bs, 1H), 4.22 (bs, 1H), 3.70 (dd, 1H, *J* = 11.1, 4.2 Hz), 3.61 (dd, 1H, *J* = 11.1, 5.7 Hz), 2.18 (bs, 1H), 1.43 (s, 9H); ^{13}CNMR ($CDCl_3$) δ 156.04, 135.59, 116.27, 79.77, 64.91, 54.71, 28.31. These data are in agreement with literature values.[11]

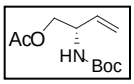


2-(*N*-Benzyloxycarbonylamino)-3-buten-1-ol (7).[12] A 1-L round-bottomed flask equipped with a magnetic stirrer was charged with 6N HCl (150 mL). Compound **5** (12.7 g, 60.1 mmol) in 100 mL of MeOH was added and the reaction mixture was stirred at rt for 1-2 h. This solution was then refluxed for 48 h. The resulting dark solution was cooled and concentrated on a rotary evaporator. The orange crystalline residue was transferred to a 2-L round-bottomed flask with the aid of 400 mL of saturated $NaHCO_3$ solution and 800 mL of EtOAc. To this bi-phasic mixture was added $(Cbz)_2O$[10] (22.0 g, 76.9 mmol) and vigorous stirring was continued overnight. The layers were separated and the organic phase was washed with water followed by brine, dried over $MgSO_4$ and concentrated in vacuo to give a dark viscous oil. This residue was purified by column chromatography on silica (1:1 EtOAc / hex). The appropriate fractions were concentrated to

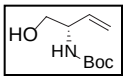
afford pure compound **7** as a yellow oil (8.7 g, 55% 2 steps) which crystallized upon standing, mp 41-42 °C. ^{1}HNMR ($CDCl_3$) δ 7.38 (bs, 5H), 5.79 (ddd, 1H, *J* = 17.1, 10.5, 5.1 Hz), 5.32 (bd, 1H), 5.25 (ddd_{app}, 1H, *J* = 17.7, 1.5 Hz), 5.21 (ddd_{app}, 1H, *J* = 10.5, 1.5 Hz), 5.09 (s, 2H), 4.30 (bs, 1H), 3.70 (dd, 1H, *J* = 10.8, 3.9 Hz), 3.60 (dd, 1H, *J* = 10.8, 5.4 Hz), 2.57 (bs, 1H); ^{13}CNMR ($CDCl_3$) δ 156.42, 136.27, 135.12, 128.52, 128.15, 128.08, 116.74, 66.96, 64.80 , 55.03. HRMS (EI) calcd. for $C_{11}H_{12}NO_2$ 190.0867 (M-CH_2OH), found 190.0867.



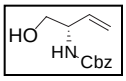
(*S*)-2-(*N*-*tert*-Butoxycarbonylamino)-3-butenyl-Acetate (8) and (*R*)-2-(*N*-*tert*-butoxycarbonylamino)-3-buten-1-ol [*R*-(10)].[11] A 50-mL round-bottomed flask equipped with a magnetic stirrer was charged with 5 mL of CH_2Cl_2 and 5 mL of isopropenylacetate. To this was added **6** (650 mg, 3.4 mmol) and 1.2 g of Amano lipase PS-30. This slurry was agitated vigorously at rt for ~3 h and monitored by TLC (1:1 EtOAc/hexanes). A small aliquot was removed, stripped of solvent in vacuo and assayed *via* ^{1}HNMR ($CDCl_3$). When ~50% conversion to the acetate **8** was confirmed, the reaction mixture was filtered through a Celite® plug and stripped of solvent. Separation by silica gel column chromatography (1:1 EtOAc/ hexanes) afforded **10** (296 mg, 46%) as a clear oil $[\alpha]_D^{20}$-28.5 (*c* 1.0, $CHCl_3$) [Lit.[5i] $[\alpha]_D^{25}$ -30.5 (*c* 1.2, $CHCl_3$)] and another clear oil **8** (406 mg, 48%) $[\alpha]_D^{21}$ +45.6 (*c* 1.5, $CHCl_3$). Compound **8**: ^{1}HNMR ($CDCl_3$) δ 5.79 (ddd, 1H, *J* = 15.6, 10.2, 5.1 Hz), 5.24 (ddd, 1H, *J* = 17.1, 1.5, 1.5 Hz), 5.19 (ddd, 1H, *J* = 10.5, 1.5, 1.5 Hz), 4.72 (bs, 1H), 4.43 (bs, 1H), 4.14 (dd_{app}, 1H, *J* = 11.1, 5.7 Hz), 4.08 (dd_{app}, 1H, *J* = 11.1, 4.8 Hz), 2.05 (s, 3H), 1.44 (s, 9H); ^{13}CNMR ($CDCl_3$) δ 171.87, 155.43, 135.04, 116.77, 79.99, 66.04, 51.89, 28.55, 21.04.



Compound **10**: ^{1}HNMR ($CDCl_3$) δ 5.77 (ddd, 1H, *J* = 15.9, 10.5, 5.4 Hz), 5.22 (ddd, 1H, *J* = 17.1, 1.2, 1.2 Hz), 5.17 (ddd, 1H, *J* = 10.5, 1.5, 1.5 Hz), 5.08 (bs, 1H), 4.17 (bs, 1H), 3.66 (dd_{app}, 1H, *J* = 11.1, 4.2 Hz), 3.55 (dd_{app}, 1H, *J* = 11.1, 5.4 Hz), 2.94 (s, 1H), 1.48 (s, 9H); ^{13}CNMR ($CDCl_3$) δ 156.04, 135.59, 116.27, 79.77, 64.91, 54.71, 28.31.



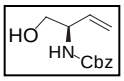
(*S*)-2-*tert*-Butoxycarbonylamino-3-buten-1-ol (*S*-10).[11] To a solution of **8** (406 mg, 2.2 mmol) in MeOH (5 mL) was added a catalytic amount of KCN and the solution was stirred at rt overnight. The solvent was then removed on a rotary evaporator and the residue was partitioned between CH_2Cl_2 and H_2O. The organic phase was washed with an additional aliquot of H_2O and brine. The organic phase was then dried with $MgSO_4$ and concentrated in vacuo to afford *S*-**(10)** as a clear oil (312 mg, 96%) $[\alpha]_D^{21}$ +27.9 (*c* 1.0, $CHCl_3$) [Lit.[5i] $[\alpha]_D^{25}$ -30.5 (*c* 1.2, $CHCl_3$)].



***(S)*-2-Benzyloxycarbonylamino-3-buten-1-ol (*S*-11)**. A 500-mL, round-bottomed flask equipped with a magnetic stirrer was charged with 200 mL of CH_2Cl_2 and 32.5 mL of isopropenyl acetate. To this was added **7** (10.4 g, 0.05 mol) and 10.0 g of Amano lipase PS-30. This slurry was agitated vigorously at rt for ~5 h and monitored with TLC (1:1 EtOAc/hexanes). When ~40% conversion to the acetate **9** was confirmed with HPLC on an Alltech SE-54 silica gel column (1:1 EtOAc/hexanes, retention time 5.55 min for **9**, and 14.60 min for **11**). The reaction mixture was then filtered through a Celite® plug and stripped of solvent. Separation by column chromatography on silica (1:1 EtOAc/hexanes), afforded **9** (5.02 g, 38%) and **11** (6.0 g, 58%). Compound **9** was hydrolyzed to *S*-**11** with KCN in a similar fashion as the corresponding *N*-Boc analogue. *S*-**11**: $[\alpha]_D^{23}$ +32.7 (*c* 7.5, $CHCl_3$) [Lit.[12g] for *R*-**11** $[\alpha]_D^{25}$ -32.1 (*c* 3.1, $CHCl_3$)]; mp 49-50 °C.

Compound **9**: ^{1}HNMR ($CDCl_3$): δ 7.35 (bs, 5H), 5.78 (ddd, 1H, *J* = 16.5, 10.5, 5.0 Hz), 5.24 (d_{app}, 1H, *J* = 10.5 Hz), 5.22 (d_{app}, 1H, *J* = 17.5 Hz), 5.12 (bs, 2H), 5.02 (bs, 1H), 4.51 (bs, 1H), 4.15 (dd, 1H, *J* = 11.5, 5.5 Hz), 4.11 (dd, 1H, *J* = 11.5, 4.5 Hz), 2.03 (s, 3H); ^{13}CNMR ($CDCl_3$) δ 170.87, 155.72, 136.28, 134.42, 128.55, 128.22, 116.93, 66.96, 65.60, 52.28, 20.74.

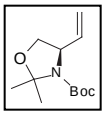
Compound **11**: ^{1}HNMR ($CDCl_3$) δ 7.33 (bs, 5H), 5.79 (ddd, 1H, *J* = 15.9, 10.5, 5.1 Hz), 5.32 (bd, 1H), 5.28-5.20 (m, 2H), 5.09 (s, 2H), 4.30 (bs, 1H), 3.70 (dd, 1H, *J* = 10.8, 3.9 Hz), 3.59 (dd, 1H, *J* = 10.8, 5.4 Hz), 2.57 (s, 1H); ^{13}CNMR ($CDCl_3$) δ 156.42, 136.27, 135.12, 128.52, 128.15, 128.04, 116.74, 66.96, 64.80, 55.03.



***(R)*-2-Benzyloxycarbonylamino-3-buten-1-ol (*R*-11)**.[12] A 500-mL round-bottomed flask equipped with a magnetic stirrer was charged with 100 mL of CH_2Cl_2, and 100 mL of isopropenyl acetate. To this was added **7** (12.3 g, 0.055 mol) and 36 g of Amano lipase PS-30. This slurry was agitated vigorously at rt for ~5 h, and monitored with TLC (1:1 EtOAc / hexanes). When ~58% conversion to the acetate **9** was confirmed with HPLC on an Alltech SE-54 silica gel column (1:1 EtOAc/hexanes, retention time 5.55 min for **9**, and 14.60 min for **11**). The reaction mixture was then filtered through a Celite® plug, and stripped of solvent. Separation by column chromatography on silica (1:1 EtOAc/hexanes) afforded **9** (8.5 g, 58%) and *R*-**11** (5.1 g, 42%) $[\alpha]_D^{25}$ +30.6 (*c* 2.5, $CHCl_3$) [Lit.[12g] $[\alpha]_D^{25}$ +32.1 (*c* 1.0, $CHCl_3$)]. A single recrystallization from Et_2O/petroleum ether afforded white needles of *R*-**11**, mp 50-51 °C. Compound **9**: ^{1}HNMR ($CDCl_3$) δ 7.35 (bs, 5H), 5.78 (ddd, 1H, *J* = 16.5, 10.5, 5.0 Hz), 5.24 (d_{app}, 1H *J* = 10.5 Hz), 5.22 (d_{app}, 1H, *J* = 17.5 Hz), 5.12 (bs, 2H), 5.02 (bs, 1H), 4.51 (bs, 1H), 4.15 (dd, 1H, *J* =

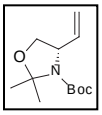
11.5, 5.5 Hz), 4.11 (dd, 1H, *J* = 11.5, 4.5 Hz), 2.03 (s, 3H); ^{13}CNMR ($CDCl_3$) δ 170.87, 155.72, 136.28, 134.42, 128.55, 128.22, 116.93, 66.96, 65.60, 52.28, 20.74.

Compound **11**: ^{1}HNMR ($CDCl_3$) δ 7.33 (bs, 5H), 5.79 (ddd, 1H, *J* = 15.9, 10.5, 5.1 Hz), 5.32 (bd, 1H), 5.28-5.20 (m, 2H), 5.09 (s, 2H), 4.30 (bs, 1H), 3.70 (dd, 1H, *J* = 10.8, 3.9 Hz), 3.59 (dd, 1H, *J* = 10.8, 5.4 Hz), 2.57 (s, 1H); ^{13}CNMR ($CDCl_3$) δ 156.42, 136.27, 135.12, 128.52, 128.15, 128.04, 116.74, 66.96, 64.80, 55.03.



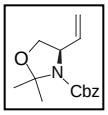
(*R*)-3-(*tert*-Butoxycarbonyl)-2,2-dimethyl-4-vinyloxazolidine (*R*-1).[5]

A similar procedure to (*R*)-**2** was followed. $[\alpha]_D^{20}$ +17.2 (*c* 1.2, $CHCl_3$). [Lit.[5i] for *S*-(**1**) $[\alpha]_D^{20}$ -17.1 (c 1.25, $CHCl_3$)]; ^{1}H-NMR ($CDCl_3$) δ 5.86-5.75 (m, 1H), 5.24-5.07 (m, 2H), 4.38-4.25 (m, 1H), 4.03 (dd, 1H, *J* = 6.6, 9.0 Hz), 3.74 (dd, 1H, *J* = 2.1, 9.0 Hz), 1.59-1.43 (m, 15H); ^{13}CNMR ($CDCl_3$) δ 152.18, 137.58, 137.01, 116.30, 116.02, 94.18d, 79.82d, 68.33, 59.92, 28.63, 27.44, 26.74, 25.02, 23.89. These data are in agreement with literature values.[5]



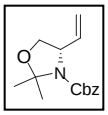
(*S*)-3-(*tert*-Butoxycarbonyl)-2,2-dimethyl-4-vinyloxazolidine (*S*-1).[5]

A similar procedure to (*R*)-**2** was followed. $[\alpha]_D^{20}$ -17.0 (*c* 1.4, $CHCl_3$). [Lit.[5i] $[\alpha]_D^{20}$ -17.1 (*c* 1.25, $CHCl_3$)]; ^{1}HNMR ($CDCl_3$) δ 6.60 (m, 1H), 5.93 (m, 1H), 5.45 (m, 1H), 4.68 (m, 1H), 2.77 (overlapping dt, 1H, *J* = 14.5, 7.5 Hz), 2.46 (broad s, 1H), 2.01 (s, 3H), 1.61 (dt, 1H, *J* = 14.5, 4.0 Hz); ^{13}CNMR ($CDCl_3$) δ 152.18, 137.58, 137.01, 116.30, 116.02, 94.18d, 79.82d, 68.33, 59.92, 28.63, 27.44, 26.74, 25.02, 23.89. These data are in agreement with literature values.[5]

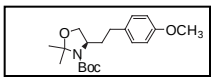


(*R*)-3-(Benzyloxycarbonyl)-2,2-dimethyl-4-vinyloxazolidine (*R*-2).[6]

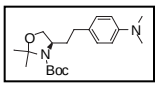
A 100-mL, round-bottomed flask under an argon atmosphere and equipped with a magnetic stirrer was charged with 25 mL of 2,2-dimethoxypropane. To this was added **11** (2.67 g, 12.1 mmol) and the reaction mixture was chilled to -20 °C. BF_3•Et_2O (94 µl) was added *via* syringe and the reaction mixture was allowed to warm to rt overnight. The solution was then poured into a separatory funnel and washed with sat. $NaHCO_3$, H_2O, brine, and dried over Na_2SO_4. Concentration by rotary evaporation afforded (*R*-**2**) (3.2g, 100%) $[\alpha]_D^{21}$ -22.2 (*c* 3.2, $CHCl_3$). ^{1}HNMR ($CDCl_3$) δ 7.34 (bs, 5H), 5.84 (m, 1H), 5.31-5.11 (m, 4H), 4.47-4.39 (m, 1H), 4.09 (dd, 1H, *J* = 6.0, 9.2 Hz), 3.82 (dd, 1H, *J* = 2.0, 8.8 Hz), 1.69-1.51 (m, 6H); ^{13}CNMR ($CDCl_3$) δ 153.85, 153.58, 138.02, 137.67, 129.65, 129.50, 129.23, 129.01, 128.92, 117.85, 117.45, 95.55, 95.03, 69.52, 69.15, 68.29, 68.02, 67.69, 65.99, 61.31, 60.53, 56.17, 28.42, 27.50, 26.03, 24.67. HRMS (EI) calcd. for $C_{14}H_{16}NO_3$ 246.1130 (M^+-CH_3), found 246.1135.



(*S*)-3-(Benzyloxycarbonyl)-2,2-dimethyl-4-vinyloxazolidine (*S*-2).[6] An identical procedure to (*R*)-**2** was followed. $[\alpha]_D^{24}$ +19.6 (*c* 1.6, $CHCl_3$). ^{1}HNMR ($CDCl_3$) δ 7.34 (bs, 5H), 5.84 (m, 1H), 5.31-5.11 (m, 4H), 4.47-4.39 (m, 1H), 4.09 (dd, 1H, *J* = 6.0, 9.2 Hz), 3.82 (dd, 1H, *J* = 2.0, 8.8 Hz) 1.69-1.51 (m, 6H); ^{13}CNMR ($CDCl_3$) δ 153.85, 153.58, 138.02, 137.67, 129.65, 129.50, 129.23, 129.01, 128.92, 117.85, 117.45, 95.55, 95.03, 69.52, 69.15, 68.29, 68.02, 67.69, 65.99, 61.31, 60.53, 56.17, 28.42, 27.50, 26.03, 24.67. HRMS (EI) calcd. for $C_{14}H_{16}NO_3$ 246.1130 (M^+-CH_3), found 246.1135.

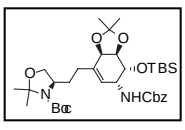


(*R*)-3-(*tert*-Butoxycarbonyl)-4-[2-(*p*-methoxyphenyl)ethyl]-2,2-dimethyloxazolidine (**12a**). Prepared by general procedure A with commercially available **12**. $[\alpha]_D^{24}$ -37.0 (*c* 0.3, $CHCl_3$); clear yellow oil; ^{1}HNMR ($CDCl_3$) δ 7.09 (t_{app}, 2H), 6.82 (d, 2H, *J* = 8.1 Hz), 3.91 (m, 3H), 3.76 (s, 3H), 2.53 (m, 2H), 2.12-1.63 (m, 2H), 1.59-1.43 (m, 15H); ^{13}CNMR ($CDCl_3$) δ 157.80, 152.11d, 133.36, 129.17, 113.84, 93.36d, 79.67d, 66.74, 57.74d, 55.22, 35.15d, 31.82, 28.44, 27.14d, 23.88d. ; HRMS (EI) calcd. for $C_{19}H_{29}NO_4$ 335.2096 (M^+), found 335.2095.



(*R*)-3-(*tert*-Butoxycarbonyl)-2,2-dimethyl-4-[2-(4-*N*,*N*'-dimethylaminophenyl)ethyl]oxazolidine (**13a**). Prepared by general procedure A with commercially available **13**. $[\alpha]_D^{24}$ -34.9 (*c* 0.9, $CHCl_3$);waxy off-white solid, mp 40-41˚C; ^{1}HNMR ($CHCl_3$) δ 7.06 (t_{app}, 2H), 6.68 (d, 2H, *J* = 8.7 Hz), 3.92-3.77 (m, 3H), 2.90 (s, 6H), 2.56-2.42 (m, 2H), 1.88 (m, 2H), 1.59-1.44 (m, 15H); ^{13}CNMR ($CHCl_3$) δ 155.60 157.87, 128.84, 113.09, 66.79, 56.00(2 sets of broad overlapping d), 40.88, 35.49d, 32.04, 31.71, 28.46; HRMS (EI) calcd. for $C_{20}H_{32}N_2O_3$ 348.2412 (M^+), found 348.2411.

(*R*)-4-[2'-(3''*R*,4''*R*,5''*S*,6''*R*)-[3''-[(Benzyloxycarbonyl)amino)]-4''-*O*-[(*tert*-butyldimethylsilyl)oxy]-5'',6''-*O*-(isopropylidenedioxy)-1-cyclohexenylethyl]-2,2-dimethyl-3-(*tert*-Butoxycarbonyl)oxazolidine (**14a**).



Prepared by general procedure A with **14**.[16] $[\alpha]_D^{24}$ -64.3 (*c* 0.7, $CHCl_3$); clear oil; ^{1}HNMR ($CDCl_3$) δ 7.35-7.15 (m, 5H), 5.25 (bd, 1H), 5.14-4.96 (m, 3H), 4.46 (m, 1H), 4.37 (m, 1H), 4.21-4.16 (m, 2H), 3.88 (m, 2H), 3.76-3.72 (m, 2H), 2.35 (s, 1H), 2.16-1.58, 1.58-1.53, 1.46, 1.35-1.31 (m overlapping d, bs, d, 23H), 0.84 (s, 9H), 0.07 (s, 3H), 0.04 (s, 3H); ^{13}CNMR ($CDCl_3$) δ 155.68, 137.81, 137.05,

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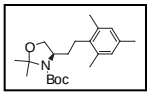
[16] Johns, B. A.; Pan, Y. T.; Elbein, A. D.; Johnson, C. R. *J. Am. Chem. Soc.* **1997**, *119*, 4856.

136.60, 128.99, 128.41, 128.18, 128.00, 125.25, 121.94, 109.54, 93.06d, 79.95d, 75.82, 74.06, 73.51, 69.78, 66.63, 57.48, 48.16, 31.60, 30.45, 29.73, 29.07, 28.42, 27.73, 26.63, 25.63, 24.48, 23.20, 21.41, 17.89, -4.73, -5.06; HRMS (EI) calcd. for $C_{31}H_{47}N_2O_8Si$ 603.3101 (M^+-C_4H_9), found 603.3099.

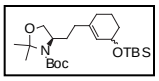
(*R*)-3-(*tert*-Butoxycarbonyl)-4-[2-pyridin-4-ylethyl]-2,2-dimethyl oxazolidine (**16a**).

Prepared by general procedure A with **16**[17] $[\alpha]_D^{24}$ -35.7 (*c* 1.0, $CHCl_3$); yellow solid; mp 49-50 ˚C; ^{1}H-NMR ($CDCl_3$) δ 8.37 (bs, 2H), 7.02 (bs, 2H), 3.85-3.67 (m, 3H), 2.51 (m, 2H), 2.03-1.76 (m, 2H), 1.49-1.32 (overlapping d's, 15H).; ^{13}CNMR ($CDCl_3$) δ 152.12, 150.47, 149.59, 133.13, 132.00, 131.87, 131.81, 128.44, 128.28, 123.66, 93.73, 93.23, 80.01, 79.53, 66.56, 57.13, 56.54, 34.02, 33.33, 31.76, 28.32, 27.49, 26.67, 24.35, 23.02; HRMS (EI) calcd. for $C_{16}H_{23}N_2O_3$ 291.1708 (M^+-CH_3), found 291.1704.



(*R*)-3-(*tert*-Butoxycarbonyl)-4-[2-(2,4,6-trimethylphenyl)ethyl]-2,2-dimethyloxazolidine (**17a**).

Prepared by general procedure A with commercially available **17**. $[\alpha]_D^{24}$ -49.9 (*c* 0.9, $CHCl_3$); white crystalline solid; mp 95-97 ˚C; ^{1}HNMR ($CDCl_3$) δ 6.84 (bs, 2H), 4.04-3.99, 3.89-3.86 (m, bd_{app}, 3H), 2.57 (m, 2H), 2.30 (s, 6H), 2.25 (s, 3H), 1.88-1.47 (m, 17H); ^{13}CNMR ($CDCl_3$) δ 151.86, 135.63, 135.10, 128.91, 93.75d, 79.48d, 66.98, 57.53, 32.98d, 28.44, 27.41d, 25.85, 24.51d, 20.70, 19.60.; HRMS (EI) calcd. for $C_{21}H_{33}NO_3$ 347.2460 (M^+), found 347.2465.

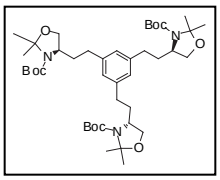


(*R*)-3-(*tert*-Butoxycarbonyl)-4-[2-(3-*tert*-butyldimethylsilyloxy)-1-cyclohexenyl)ethyl]-2,2-dimethyloxazolidine (**18a**).

Prepared by general procedure A with **18**.[18] $[\alpha]_D^{24}$ -18.5 (*c* 0.6, $CHCl_3$); brown oil; ^{1}HNMR ($CDCl_3$) δ 5.34 (bs, 1H), 4.18 (bs, 1H), 3.90-3.86 (m overlapping dd, 2H, *J* = 9.5, 14.0 Hz), 3.71 (d_{app}, 1H), 1.90-1.49, 1.44 (m, overlapping bs, 25H), 0.87 (s, 9H), 0.05 (s, 3H), 0.04 (s, 3H); ^{13}CNMR ($CDCl_3$) δ 150.10, 139.53, 125.66, 99.28, 93.0d, 79.82, 79.39, 67.10, 66.72, 57.14d, 34.29, 32.38, 31.27, 30.63, 28.44, 28.13, 27.49, 26.70, 25.93, 24.51, 23.24, 19.76, 18.26, -4.53, -4.59.; HRMS (EI) calcd. for $C_{20}H_{36}NO_4Si$ 382.2413 (M^+-

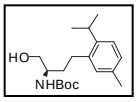
[17] Coudret, C. *Synth. Commun.* **1996**, *26*, 3543.
[18] Paquette, L. A.; Combrink, K. D.; Elmore, S. W.; Rogers, R. D. *J. Am. Chem. Soc.* **1991**, *113*, 1335.

C_4H_9), found 382.2416.



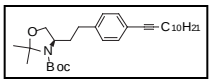
1,3,5-*Tris*-{(*R*)-2-[3-(*tert*-butoxycarbonyl)2,2-dimethyl oxazolidin-4-yl]ethyl}benzene (**19a**).

Prepared by general procedure A with commercially available **19**. $[\alpha]_D^{24}$ +60.3 (*c* 0.9, $CHCl_3$); white solid; mp 98-101 ˚C; ^{1}HNMR ($CDCl_3$) δ 6.82 (bs, 3H), 3.94-3.77 (bs, overlapping m and d, 9H), 2.56-2.50 (m, 6H), 2.08-1.77 (m, 51H); ^{13}CNMR ($CDCl_3$) δ 152.15, 151.76, 141.95, 126.01, 93.69, 93.17, 80.00, 79.41, 66.95, 66.68, 57.67, 57.15, 35.65, 34.86, 32.74, 28.50, 27.60, 26.78, 24.53, 23.23; FABMS calcd. for $C_{42}H_{69}N_3O_9$ 759.5033 $(M+H)^+$, found 760.0 and 782.0 $(M+Na)^+$.



(*R*)-2-[(*tert*-Butoxycarbonyl)amino]-4-(2-isopropyl-5-methylphenyl)-1-butanol (**20a**).

Prepared by general procedure A with **20**.[16] $[\alpha]_D^{24}$ -11.0 (*c* 1.0, $CHCl_3$); white solid; mp 76-77 ˚C; ^{1}HNMR ($CDCl_3$) δ 7.16 (d, 1H, *J* = 7.8 Hz), 7.00 (d, 1H, *J* = 7.8 Hz), 6.94(s, 1H), 4.83 (bd, 1H), 3.71-3.55 (m, 3H), 3.10 (septet, 1H, *J* = 6.6 Hz), 2.77-2.60 (m, 3H), 2.28 (s, 3H), 1.68-185 (m, 2H), 1.47 (s, 9H), 1.22 (d, 6H, *J* = 6.6 Hz); ^{13}CNMR ($CDCl_3$) δ 156.47, 143.41, 138.15, 134.99, 129.94, 127.22, 125.28, 79.66, 65.76, 52.91, 33.64, 29.24, 28.38, 28.30, 24.14, 20.86; HRMS (EI) calcd. for $C_{19}H_{31}NO_3$ 321.2303 (M^+), found 321.2300.

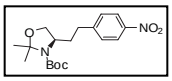


(*R*)-3-(*tert*-Butoxycarbonyl)-4-[2-(4-dodec-1-ynyl phenyl)ethyl] -2,2-dimethyloxazolidine (**21a**).

Prepared by general procedure A with **21** $[\alpha]_D^{24}$ -27.4 (*c* 1.9, $CDCl_3$); yellow oil; ^{1}HNMR ($CDCl_3$) δ 7.31 (d, 2H, *J* = 7.5 Hz), 7.09 (t_{app}, 2H), 3.93-3.74 (m, 3H), 2.59 (m, 2H), 2.39 (t, 2H, *J* = 7.2 Hz), 2.20-1.26 (m, 33H), 0.84 (t, 3H, *J* = 6.0 Hz); ^{13}CNMR ($CDCl_3$) δ 152.90, 141.20, 131.86, 128.44, 80.69, 66.93, 57.77, 57.08, 35.19, 32.83, 32.14, 29.82, 29.78, 29.57, 29.39, 29.15, 29.02, 28.70, 27.81, 27.01, 24.72, 23.44, 22.92, 19.65, 14.36; HRMS (EI) calcd. for $C_{30}H_{47}NO_3$ 469.3555 (M^+), found 469.3554.

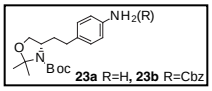
4-(Dodec-1-yne)bromobenzene 21: To a 100-mL round-bottomed flask was added 277 mg (0.98 mmole) of 1-bromo-4-iodobenzene and 3 mL of diethylamine; the flask was briefly sparged with argon. To the reaction mixture was added 14 mg (0.019 mmol) of $(PPh_3)_2PdCl_2$, 8 mg (0.039 mmol) of CuI, and 252 µl (1.18 mmol) of 1-dodecyne. The reaction mixture was stirred at rt for 3.5 h at which time the reaction mixture was stripped of solvent on a rotary evaporator equipped with a trap containing HCl. The crude residue was then taken up in a small volume of CH_2Cl_2, neutral alumina was added and the sample was

stripped of solvent, loaded and flashed through a plug of neutral alumina with petroleum ether to afford **21** (310 mg, 98%): ^{1}HNMR ($CDCl_3$) δ 7.39 (AB 2H, *J* = 8.4 Hz), 7.23 (A'B' 2H, *J* = 8.1 Hz), 2.37 (t, 2H, *J* = 6.9 Hz), 1.59 (m, 2H), 1.45-1.27 (overlapping m, bs, 14H), 0.88 (t, 3H, *J* = 6.6 Hz); ^{13}CNMR ($CDCl_3$) δ 132.97, 131.34, 123.12, 121.47, 91.73, 79.57, 31.89, 29.57, 29.52, 29.30, 29.13, 28.92, 28.63, 28.36, 22.66, 19.40, 19.20, 14.07.



(*R*)-3-(*tert*-Butoxycarbonyl)-4-[2-(4-nitrophenyl)ethyl]-2,2-dimethyloxazolidine (22a).

Prepared by general procedure A with commercially available **22**. $[\alpha]_D^{24}$ -37.9 (*c* 0.5, $CHCl_3$); bright yellow oil; ^{1}HNMR ($CHCl_3$) δ 8.12 (bd, 2H, *J* = 8.1 Hz), 7.33 (bt, 2H, *J* = 8.7 Hz), 3.97-3.76 (m, 3H), 2.74-1.76 (m, 4H), 1.60-1.42 (overlapping d, 15H); ^{13}CNMR ($CHCl_3$) δ 152.53d, 149.75, 146.64, 131.13, 129.38, 128.88, 127.44, 126.84, 126.08, 124.03, 123.93, 98.81, 94.16, 93.62, 80.51, 79.97, 66.81, 57.45, 56.88, 35.03, 32.25, 30.40, 29.92, 28.66, 27.85, 27.35, 27.02, 26.42, 24.63, 23.32, 22.85, 22.20; HRMS (EI) calcd. for $C_{17}H_{23}N_2O_5$ 335.1606 (M^+-CH_3), found 335.1607.



(*S*)-4-[2-(4-Aminophenyl)ethyl]-3-(*tert*-butoxycarbonyl)-2,2-dimethyloxazolidine (23a), and(*S*)-4-[2-(4-benzyloxycarbonyl aminophenyl)ethyl]-3-(*tert*-butoxycarbonyl)-2,2-dimethyl oxazolidine (23b).

Prepared by general procedure A with **23**[19]. Compound (**23a**): $[\alpha]_D^{24}$ +35.9 (*c* 0.7, $CHCl_3$); orange semi-solid at rt; ^{1}HNMR ($CDCl_3$) δ 6.97 (m, 2H), 6.62 (d, 2H, *J* = 6.0 Hz), 3.91-3.64 (m, 5H), 2.50 (m, 2H), 2.08-1.74 (m, 2H), 1.61 (overlapping d, 15H); ^{13}CNMR ($CDCl_3$) δ 153.66, 152.01d, 137.01d, 136.76, 136.32, 136.05, 129.10, 128.84, 128.55, 119.11, 93.94, 93.42, 80.28, 79.76, 76.88, 67.16, 66.96, 57.73, 57.12, 35.46, 34.89, 32.29, 29.94, 28.73, 27.82, 27.63, 27.02, 26.64, 26.43, 24.75, 23.45.; HRMS (EI) calcd. for $C_{18}H_{28}N_2O_3$ 320.2099 (M^+), found 320.2100.

Compound **(23b)**: $[\alpha]_D^{24}$ +28.2 (*c* 0.5, $CHCl_3$); yellow crystalline solid; mp 102-105 ˚C; ^{1}HNMR ($CDCl_3$) δ 7.40-7.25 (m, 7H), 7.11(bs, 2H), 6.76 (bs, 1H), 5.18 (s, 2H), 3.92-3.76 (m, 3H), 2.55 (m, 2H), 2.20-1.43 (m, 17H); ^{13}CNMR ($CDCl_3$) δ 152.02, 144.47, 144.33, 131.95, 131.62, 129.32, 115.62, 113.59, 93.83, 93.34, 79.65d, 67.02, 66.90, 57.83, 57.23, 35.72, 35.17, 32.16, 28.74, 27.82, 27.02, 24.80, 23.49 FABMS (ES+) calcd. for $C_{26}H_{34}N_2O_5$ 477.2365 (M^+ + Na), found 477.03.

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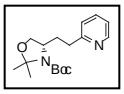
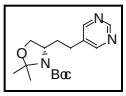
[19] Blaha, K.; Rudinger, J. *Collect. Czech. Chem. Commun.* **1965**, *30*, 585.



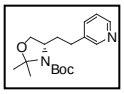
(*S*)-3-(*tert*-Butoxycarbonyl)-2,2-dimethyl-4-[2-(2-pyridinyl)ethyl] oxazolidine (**24a**).

Prepared by general procedure A with commercially available **24**. $[\alpha]_D^{24}$ +40.6 (*c* 1.0, $CHCl_3$); white solid; mp 36-37 ˚C; ^{1}HNMR ($CDCl_3$) δ 8.44 (bs, 1H), 7.58 (bt, 1H), 7.20-7.08 (m, 2H), 3.98-3.78 (m, 3H), 2.81 (m, 2H), 2.20 (m, 1H), 2.08 (m, 1H), 1.62-1.40 (overlapping d's, 15H); ^{13}C NMR ($CDCl_3$) δ 161.17, 149.22, 149.04, 136.38, 138.56, 122.57, 121.05, 66.78, 66.60, 57.36, 56.74, 35.08, 33.51, 32.66, 28.39, 27.50, 26.77, 24.49, 23.15; HRMS (EI) calcd. for $C_{16}H_{23}N_2O_3$ 291.1708 (M^+-CH_3), found 291.1711.



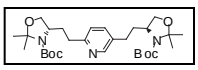
(*S*)-3-(*tert*-Butoxycarbonyl)-2,2-dimethyl-4-[2-(5-pyrimidyl)ethyl] oxazolidine (**25a**).

Prepared by general procedure A with commercially available **25**. $[\alpha]_D^{24}$ +44.7 (*c* 1.4, $CHCl_3$); white solid; mp 93-94 ˚C; ^{1}HNMR ($CDCl_3$) δ 9.06 (bd, 1H), 8.59 (bd, 2H), 3.99-3.77 (m, 3H), 2.67-2.50 (m, 2H), 2.15-1.81 (m, 2H), 1.60-1.41 (overlapping d's, 15H); ^{13}CNMR ($CDCl_3$) δ 156.86, 156.68, 156.59, 135.59, 93.43d, 80.34, 66.63, 57.06, 56.43, 34.60, 34.05, 28.45, 28.37, 27.61, 27.13, 26.73, 24.35, 23.01; HRMS (EI) calcd. for $C_{15}H_{22}N_3O_3$ 292.1661 (M^+-CH_3), found 292.1663.



(*S*)-3-(*tert*-Butoxycarbonyl)-2,2-dimethyl-4-[2-(3-pyridinyl) ethyl]oxazolidine (**26a**).

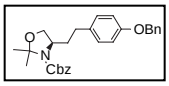
Prepared by general procedure A with commercially available **26**. $[\alpha]_D^{24}$ +39.6 (*c* 1.6, $CHCl_3$); yellow crystals; mp 84-86 ˚C; ^{1}HNMR ($CDCl_3$) δ 8.38 (bs, 2H), 7.44 (bt, 1H), 7.18 (bt, 1H), 3.92-3.72 (m, 3H), 2.54 (m, 2H), 2.17-1.70 (m, 2H), 1.58-1.38 (overlapping d's, 15H); ^{13}CNMR ($CDCl_3$) δ 152.0, 149.74, 147.41, 136.71, 135.60, 132.00, 128.20, 123.27, 93.25d 80.04, 79.54, 66.63, 57.23, 56.63, 34.92, 34.27, 29.66, 28.38, 27.51, 26.70, 24.41, 23.08; HRMS (EI) calcd. for $C_{17}H_{26}N_2O_3$ 306.1943 (M^+), found 306.1940.



(*S,S*)-2,5-Bis{2-[3-(*tert*-butoxycarbonyl-2,2-dimethyl) oxazolidin-4-yl]ethyl}pyridine (**27a**).

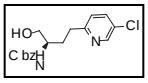
Prepared by general procedure A with commercially available **27**. $[\alpha]_D^{24}$ +48.8 (*c* 1.1, $CHCl_3$); white solid; mp 95-98 ˚C; ^{1}HNMR ($CDCl_3$) δ 8.29 (bs, 1H), 7.44-7.25 (m, 1H) 7.10-7.05 (m, 1H), 3.92-3.75 (m, 6H), 2.76-1.86 (m, 8H), 1.56-1.37 (overlapping d's, 30H); ^{13}CNMR ($CDCl_3$) δ 158.89, 152.15d, 136.22, 134.07, 122.28, 121.06, 93.67, 93.22, 79.56d, 66.66, 57.26, 56.79, 44.79d, 35.07, 34.57, 33.58, 32.71, 29.32, 28.39, 27.51, 26.73,

24.45, 23.16; FABMS calcd. for $C_{29}H_{47}N_3O_6$ 533.3464 $(M+H)^+$, found 534.0 and 556.0 $(M+Na)^+$.



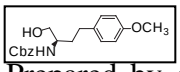
(*R*)-3-(Benzyloxycarbonyl)-4-[2-(4-benzyloxyphenyl)ethyl]-2,2-dimethyloxazolidine (**28a**).

Prepared by general procedure A with **28**.[20] $[\alpha]_D^{20}$ +24.2 (*c* 1.25, $CHCl_3$); light yellow oil; ^{1}HNMR ($CDCl_3$) δ 7.45-7.30,7.12, 6.98-6.81 (m, bd, 3 sets of overlapping bd's 14H), 5.18-5.14, 5.08, 5.02 (m, bs, bs 4H), 4.02-3.80 (m, 3H), 2.58-2.39 (m, 2H), 2.17-1.78 (m, 2H), 1.64-1.45 (overlapping d's, 6H); ^{13}CNMR ($CDCl_3$) δ 157.51, 137.59, 133.74, 129.59, 128.96, 128.98, 128.44, 128.33, 127.87, 115.23, 94.47, 71.34, 70.46, 67.31, 66.97, 58.40, 57.23, 35.43, 34.88, 32.47, 32.03, 27.96, 27.02, 26.65, 25.06, 23.63, 22.43; HRMS (EI) calcd. for $C_{28}H_{31}NO_4$ 445.2253 (M^+), found 445.2256.



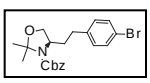
(*R*)-2-(Benzyloxycarbonyl)amino-4-(4-chloropyridin-2-yl)-1-butanol (**29a**).

Prepared by general procedure A with **29**.[21] $[\alpha]_D^{24}$ +18.1 (*c* 1.0, $CHCl_3$); yellow solid; mp 62-63°C; ^{1}HNMR ($CDCl_3$) δ 8.17 (s, 1H), 7.45(d, 1H, *J* = 8.0 Hz), 7.33(m, 5H), 7.20 (d, 1H, *J* = 8.4 Hz), 5.18 (d, 1H, *J* = 8.4 Hz), 5.08 (bs, 2H), 3.71-3.57 (m, 3H), 2.61-2.58 (m, overlapping bs, 3H), 1.84-1.75 (m, 2H); ^{13}CNMR ($CDCl_3$) δ 156.63, 149.49, 149.14, 138.99, 137.00, 136.30, 135.84, 132.24, 128.64, 128.32, 128.19, 124.07, 67.01, 64.94, 52.45, 32.90, 28.79; HRMS (EI) calcd. for $C_{17}H_{19}ClN_2O_3$ 334.1084 (M^+), found 334.1085.



(*R*)-2-(Benzyloxycarbonyl)amino-4-(4-methoxyphenyl)-1-butanol (**12b**).

Prepared by general procedure A with commercially available **12**. $[\alpha]_D^{24}$ +17.8 (*c* 1.0, $CHCl_3$); yellow solid mp 80-82 °C; ^{1}HNMR ($CDCl_3$) δ 7.39-7.31 (m, 5H), 7.09(d, 2H, *J* = 8.0 Hz), 6.82(d, 2H, *J* = 8.4 Hz), 5.12 (s, 2H), 4.90 (bd, 1H), 3.78 (s, 3H), 3.75-3.60 (m, 3H), 2.69-2.58 (m, 2H), 1.93 (bs, 1H), 1.87-1.75 (m, 2H); ^{13}CNMR ($CDCl_3$) δ 158.63, 137.05, 133.98, 129.93, 129.26, 128.90, 128.82, 114.61, 67.62, 66.26, 55.96, 53.55, 34.06, 32.08; HRMS (EI) calcd. for $C_{19}H_{23}NO_4$ 329.1626 (M^+), found 329.1626.



(*R*)-3-(Benzyloxycarbonyl)-4-[2-(4-bromophenyl)ethyl]-2,2-dimethyloxazolidine (**30a**).

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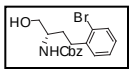
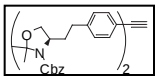
[20] Greenspan, P. D.; Fujimoto, R. A.; Marshall, P. J.; Raychaudhuri, A.; Lipson, K. E.; Zhou, H.; Doti, R. A.; Coppa, D. E.; Zhu, L.; Pelletier, R.; Uziel-Fusi, S.; Jackson, R. H.; Chin, M. H.; Kotyuk, B. L.; Fitt, J. J. *J. Med. Chem.* **1999**, *42*, 164.

[21] Case, F. H. J. Am. Chem. Soc. 1946, 68, 2574.

Prepared by general procedure A with commercially available **30**. $[\alpha]_D^{24}$ +32.3 (*c* 2.0, $CHCl_3$); white solid; mp 34-35 ˚C; ^{1}HNMR ($CDCl_3$) δ 7.40 (m, 7H), 7.11 (d, 1H, *J* = 7.6 Hz), 6.93 (d, 1H, *J* = 8.0 Hz), 5.24-5.07 (m, 2H), 4.05-3.82 (m, 3H), 2.64-2.44 (m, 2H), 2.20-1.84 (m, 2H), 1.69-1.49 (overlapping d, 6H), ^{13}CNMR ($CDCl_3$) δ 153.95, 153.30, 141.44, 141.04, 137.60, 137.44, 132.89, 132.57, 131.25, 131.14, 129.73, 129.56, 129.29, 129.17, 120.81, 95.24, 94.75, 68.25, 67.93, 67.84, 67.77, 58.93, 57.72, 35.74, 35.25, 33.23, 33.04, 32.96, 28.74, 27.79, 27.41, 25.73, 24.30, 23.18; HRMS (EI) calcd.for $C_{21}H_{24}BrNO_3$ 417.0939 (M^+), found 417.0938.



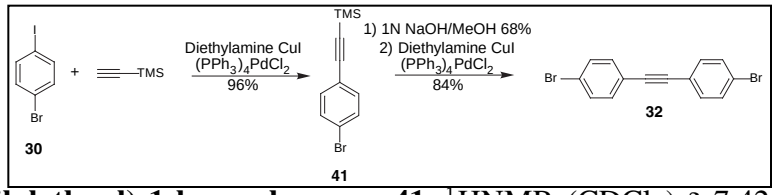
(*S*)-2-[(Benzyloxycarbonyl)amino]-4-(2-bromophenyl)-1-butanol (**31**). Prepared by general procedure A with commercially available **31**. $[\alpha]_D^{24}$ +4.7 (*c* 1.0, $CHCl_3$); white solid mp; 82-85 ˚C; ^{1}HNMR ($CDCl_3$) δ 7.52-7.04 (m, 9H), 5.12 (bs, 2H), 5.03 (bs, 1H), 3.77-3.62 (m, 3H), 2.87-2.73 (m, 2H), 2.18 (bs, 1H), 1.90-1.75 (m, 2H), ^{13}CNMR ($CDCl_3$) δ 157.47, 141.31, 137.04, 133.56, 131.11, 129.28, 128.91, 128.84, 128.57, 128.32, 125.00, 67.64, 66.18, 53.66, 33.48, 32.36; HRMS (EI) calcd. for $C_{18}H_{20}BrNO_3$ 377.0626 (M^+), found 377.0624



Bis-4-{(*R*)-2-[4-(3-benzyloxycarbonyl-2,2-dimethyl) oxazolidinyl}ethyl)phenyl]ethyne (**32a**).

Prepared by general procedure A with **32**[22] or through a three step sequence with 1-bromo-4-iodobenzene and trimethylsilylacetylene. $[\alpha]_D^{24}$ +58.2 (*c* 0.6, $CHCl_3$); off-white solid; mp 68-70 ˚C; ^{1}HNMR ($CDCl_3$) δ 7.49-7.20, 7.06 (m, bd, 18H), 5.22-5.08 (m, 4H), 4.08-3.83 (m, 6H), 2.70-2.51 (m, 4H), 2.21 (m, 2H), 2.04 (m, 2H), 1.68-1.49 (overlapping d, 12H); ^{13}CNMR ($CDCl_3$) δ 153.96, 153.32, 142.82, 142.45, 137.63, 137.45, 132.75, 130.16, 129.70, 129.44, 129.26, 129.21, 122.08, 95.23, 94.73, 90.13, 68.23, 68.00, 67.88, 67.73, 59.04, 57.85, 43.07, 35.78, 35.20, 33.55, 28.71, 28.28, 27.76, 26.79, 25.82, 28.73, 24.30; FABMS calcd. for $C_{44}H_{48}N_2O_6$ 700.3512 $(M+H)^+$, found 701.0.

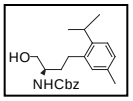
[22] Rudenko, A. P.; Vasil'ev, A. V. *Russ. J. Org. Chem.* **1995**, *31*, 1360.



4-(Trimethylsilylethynl)-1-bromobenzene 41: ^{1}HNMR ($CDCl_3$) δ 7.42 (AB 2H, *J* = 8.7 Hz), 7.31 (A'B' 2H, *J* = 8.7 Hz), 0.24 (s, 9H); ^{13}CNMR ($CDCl_3$) δ 133.34, 131.43, 122.71, 122.07, 103.82, 95.54, -0.151. HRMS (EI) calcd. for $C_{11}H_{13}BrSi$ 251.9970 (M^+), found 251.9973.

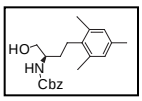
Bis-(4-bromophenyl)ethyne (**32**). 1-Bromo-4-iodobenzene **30** (1 g, 3.53 mmol) was dissolved with the aid of 5 mL of diethylamine in a 25-mL pressure bottle, equipped with a magnetic stirrer. Trimethylsilylacetylene (590 µl, 4.24 mmol), $(PPh_3)_2PdCl_2$ (49 mg), and CuI (27 mg) was added to the reaction mixture. The reaction flask was then briefly purged with argon, capped and stirred at rt for 4 h. At which point the reaction mixture was poured into a sat. NH_4Cl soln. and extracted (2x) with ether. The organic layer was separated and dried over $MgSO_4$, passed through a plug of neutral alumina and concentrated in vacuo to afford **32** (855 mg, 96%) as brown-black crystals; mp 182-183˚C. Compound **32**: ^{1}HNMR ($CDCl_3$) δ 7.48 (AB, 4H, *J* = 8.7 Hz), 7.37 (A'B' 4H, *J* = 8.7 Hz); ^{13}CNMR ($CDCl_3$) δ 132.96, 131.66, 122.75, 121.85, 89.38.

HRMS (EI) calcd. for $C_{14}H_8Br_2$ 333.8993 (M^+), found 333.8990



(*R*)-2-[(Benzyloxycarbonyl)amino]-4-(2-isopropyl-5-methylphenyl)-1-butanol (**20b**).

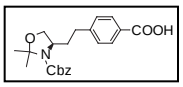
Prepared by general procedure A with **20**.[15] $[\alpha]_D^{23}$ +2.16 (*c* 1.3, $CHCl_3$); off-white solid; mp 70-72 ˚C; ^{1}HNMR ($CDCl_3$) δ 7.35 (m, 5H), 7.12(d, 1H, *J* = 8.0 Hz), 7.05(d, 1H, *J* = 8.4 Hz), 6.97 (s, 1H), 5.17-5.11 (m, 3H), 3.83-3.63 (m, 3H), 3.13-3.08 (m, 1H), 2.77-2.69 (m, 2H), 2.56 (bs, 1H), 2.32 (s, 3H), 1.84-1.72 (m, 2H),1.26(d, 6H, *J* = 6.8 Hz); ^{13}C NMR ($CDCl_3$) δ 157.94, 144.56, 139.14, 137.47, 136.21, 131.11, 129.71, 129.35, 129.25, 128.43, 126.46, 68.05, 66.56, 54.48, 34.65, 30.39, 29.48, 25.32, 22.05; HRMS (EI) calcd. for $C_{22}H_{29}NO_3$ 355.2147 (M^+), found 355.2143.



(*R*)-2-[(Benzyloxycarbonyl)amino]-4-(2,4,6-trimethylphenyl)-1-butanol (**17b**).

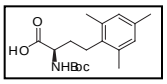
Prepared by general procedure A with commercially available **17**. $[\alpha]_D^{23}$ +15.7 (*c* 2.1, $CDCl_3$); yellow solid; mp 132-133 ˚C; ^{1}HNMR ($CDCl_3$) δ 7.38 (bs, 5H), 6.82 (s, 2H), 5.18-5.12 (m, 3H), 3.80-3.61 (m, 3H), 2.62 (m, 2H), 2.40 (bs, 1H), 2.25 (s, 6H), 2.24 (s,

3H), 1.70 (m, 1H), 1.58 (m, 1H); ^{13}CNMR ($CDCl_3$) δ 157.55, 138.33, 137.06, 136.47, 135.93, 135.85, 129.67, 129.29, 128.94, 128.85 67.63, 65.99, 54.44, 31.61, 26.61, 21.51, 20.37; HRMS (EI) calcd. for $C_{21}H_{27}NO_3$ 341.1990 (M^+), found 341.1992.



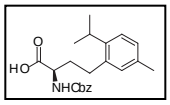
4-[2-(*R*)-3-benzyloxycarbonyl)-2,2-dimethyloxazolidin-4-yl] ethylbenzoic Acid (**33a**).

Prepared by general procedure A with commercially available **33**. $[\alpha]_D^{20}$ +34.7 (*c* 1.0, $CDCl_3$); clear oil; ^{1}HNMR ($CDCl_3$) δ 10.90 (bs 1H), 8.15-8.06 (overlapping d's, 2H), 7.50-7.42, 7.25 (m, d, 7H), 5.31-5.15 (m, 2H), 4.17-3.93 (m, 3H), 2.85-2.79,2.73-2.65 (m, 2H), 2.16-1.96 (m, 2H), 1.77-1.58 (overlapping d's, 6H); ^{13}CNMR ($CDCl_3$) δ 173.01, 148.70, 131.63, 131.38, 129.80, 129.72, 129.61, 129.45, 129.38, 129.26, 128.35, 95.41, 68.43, 67.94, 59.04, 57.84, 35.62, 35.14, 33.75, 28.78, 27.83, 25.77, 24.34; HRMS (EI) calcd. for $C_{22}H_{25}NO_5$ 383.1732 (M^+), found 383.1737.



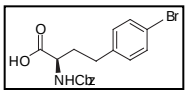
(*R*)-2-*N*-[(*tert*-Butoxy)carbonylamino]-4-[(2,4,6-trimethyl phenyl)]butanoic Acid (**34**)**.**

Prepared by general procedure C and oxidized according to the literature.[14i] $[\alpha]_D^{24}$ -45.6 (c 0.4, $CHCl_3$); white solid; mp 126-128˚C; ^{1}HNMR ($CDCl_3$) δ 6.60 (m, 1H), 5.93 (m, 1H), 5.45 (m, 1H), 4.68 (m, 1H), 2.77 (overlapping dt, 1H, *J* = 14.5, 7.5), 2.46 (broad s, 1H), 2.01 (s, 3H), 1.61 (dt, 1H, *J* = 14.5, 4.0); ^{13}CNMR ($CDCl_3$) δ; HRMS (EI) calcd. for $C_{14}H_{18}NO_4$ 265.1313 (M^+ - C_4H_8), found 265.1311.



(*R*)-2-*N*-(Benzyloxycarbonyl)amino-4-(2-isopropyl-5-methylphenyl)butanoic Acid (**35**)**.**

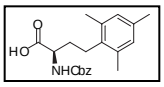
Prepared by general procedure B and oxidized according to the literature.[14b] $[\alpha]_D^{20}$ +26.6 (*c* 1.0, $CHCl_3$); white crystalline solid; mp 88-90 ˚C; ^{1}HNMR ($CDCl_3$) δ 10.95 (bs, 1H), 7.42-7.36 (m, 5H), 7.20 (d, 1H, *J* = 8.0 Hz), 7.05 (d, 1H, *J* = 7.5 Hz), 6.97 (s, 1H), 5.52 (d, 1H, *J* = 8.5 Hz), 5.24-5.15 (m, 2H), 4.58-4.54, 4.42-4.40 (m, 1H), 3.09 (septet, 1H, *J* = 6.0 Hz), 2.76-2.70 (m, 2H), 2.32-2.30 (s with overlapping bs, 3H), 2.24-2.19, 2.04-1.99 (m, 2H), 1.24 (d, 6H, *J* = 6.5 Hz); ^{13}CNMR ($CDCl_3$) δ 177.95, 177.36, 158.05, 156.89, 144.28, 137.81, 136.82, 135.88, 130.82, 129.34, 129.04, 128.90, 128.73, 128.29, 126.16, 68.59, 68.02, 55.04, 54.61, 34.99, 29.19, 29.07, 24.92, 24.88, 21.62; HRMS (EI) calcd. for $C_{22}H_{27}NO_4$ 369.1939 (M^+), found 369.1942



(*R*)-2-*N*-(Benzyloxycarbonyl)amino-4-(4-bromophenyl) butanoic

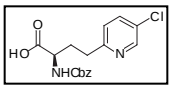
Acid (**36**).

Prepared by direct oxidation of **30a** according to the literature.[14b] $[\alpha]_D^{20}$ +18.3 (*c* 1.1, $CHCl_3$); white crystalline solid mp110-112 ˚C; ^{1}HNMR ($CDCl_3$) δ 9.57 (bs, 1H), 7.39-7.30 (bs, 6H), 7.14-6.73 (m, 3H), 5.34 (bd, 1H), 5.13 (bd, 2H), 4.43-4.27 (m, 1H), 2.67 (m, 2H), 2.21 (m, 1H), 2.01 (m, 1H); ^{13}CNMR ($CDCl_3$) δ 177.55, 156.71, 140.01, 136.67, 132.28, 130.89, 129.32, 129.05, 128.89, 120.78, 68.01, 54.02, 34.52, 31.65; HRMS (EI) calcd. for $C_{18}H_{18}BrNO_4$ 391.0419 (M^+), found 391.0415.



(*R*)-2-*N*-(Benzyloxycarbonyl)amino-4-(2,4,6-trimethyl phenyl)butanoic Acid (**37**).

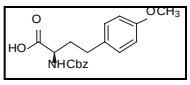
Prepared by direct oxidation of **17b** according to the literature.[14b] $[\alpha]_D^{20}$ +32.7 (*c* 1.1, $CHCl_3$); white crystalline solid; mp152-153 ˚C; ^{1}HNMR ($CDCl_3$) δ 9.69 (bs, 1H), 7.38 (m, 5H), 6.82 (bs, 2H), 5.49 (bd, 1H), 5.21-5.12 (m, 2H), 4.57-4.42 (m, 1H), 2.72-2.58 (m, 2H), 2.25 (bd, 9H), 2.10-1.83 (m, 2H); ^{13}CNMR ($CDCl_3$) δ 177.62, 156.76, 136.81, 136.60, 136.19, 134.86, 129.71, 129.31, 129.02, 128.89, 68.57, 67.96, 54.77, 32.16, 25.52, 21.51, 20.18; HRMS (EI) calcd. for $C_{21}H_{25}NO_4$ 355.1784 (M^+), found 355.1787.



(*R*)-2-*N*-(Benzyloxycarbonyl)amino-4-(5-chloro-2-pyridine)butanoic Acid (**38**)**.**

Prepared by general procedure D on **29a**, *via* general procedure B.

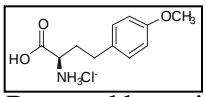
$[\alpha]_D^{24}$ -27.9 (*c* 1.0, $CHCl_3$); white solid; mp 118-119 ˚C; ^{1}HNMR ($CDCl_3$) δ 10.34 (bs, 1H), 8.25 (bs, 1H), 7.52 (bd, 1H, *J* = 8.7), 7.34 (bs, 5H), 7.22 (bd_{app}, overlapping $CHCl_3$, 1H), 5.67 (d, 1H, *J* = 8.1), 5.10 (s, 2H, *J* = 8.1), 4.43-4.29 (m, 1H), 2.68 (m, 2H), 2.23 (m, 1H), 2.03 (m, 1H); ^{13}CNMR ($CDCl_3$) δ 175.10, 169.59, 169.03, 156.26, 149.35, 149.02, 139.87, 128.82, 128.55, 128.40, 124.55, 67.44, 53.33, 33.71, 28.01; HRMS (EI) calcd. for $C_{17}H_{17}N_2O_4Cl$ 348.0876 (M^+), found 348.0871.



(*R*)-*N*-Benzyloxycarbonyl-4'-methoxyhomophenylalanine (39).

Prepared by oxidation of **12b** general procedure B according to the literature.[14i] $[\alpha]_D^{24}$ -15.1 (*c* 0.8, $CDCl_3$); white solid; mp 120-122 ˚C; ^{1}HNMR ($CDCl_3$) δ 9.41 (bs, 1H), 7.33 (bs, 5H), 7.06 (bd, 2H, 8.1 Hz), 6.78 (bd, 2H, 7.8 Hz), 6.54, 5.32 (bd, bd, 1H, 8.4 Hz), 5.11 (bs, 2H), 4.41-4.25 (m, 1H), 3.74 (s, 3H), 2.62 (t, 2H, *J* = 7.8 Hz), 2.16 (m, 1H), 1.97 (m, 1H); ^{13}CNMR ($CDCl_3$) δ 177.51, 158.42, 156.45, 136.45, 132.80, 129.77, 128.97, 128.68, 128.54, 114.32, 67.63, 55.65, 53.82, 34.58, 31.01. Compound **39**

was then converted to **40** and composition and stereochemistry confirmed via. x-ray crystallography.



(*R*)-4'-methoxyhomophenylalanine (40).

Prepared by oxidation with general procedure D of **12b**, obtained via general procedure B. *N*-Cbz protected carboxylic acid **39** (48 mg, 0.140 mmol) was deprotected in 5 mL of MeOH at rt under an atmosphere of hydrogen with a catalytic amount of Degussa catalyst. After 24 h the gray suspension was treated with 3-4 drops of conc. HCl and filtered through a pad of Celite®. Concentration of the filtrate on a rotary evaporator afforded yellow crystals. This material was then taken up in MeOH and triturated with Et_2O to afford pure **40**: $[\alpha]_D^{20}$ -43.4 (c 0.1, 5 M HCl). [Lit.[3a] for (*S*)-**40** $[\alpha]_D^{25}$ +42.2 (c 0.1, 5 M HCl).]; white solid; mp 160 ˚C (decomp.); ^{1}HNMR (CD_3OD) δ 7.14 (d, 2H, *J* = 8.4 Hz), 6.86 (d, 2H, *J* = 8.4 Hz), 3.94 (t, 1H, *J* = 6.4 Hz), 3.76 (s, 3H), 2.78-2.64 (m, 2H), 2.24-2.05 (m, 2H); ^{13}CNMR (CD_3OD) δ 170.99, 159.16, 132.39, 129.65, 114.40, 54.97, 52.71, 33.13, 30.51; x-ray crystallographic data provided for (*R*)-**40**•HCl