Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry.

Homoallylic amines as efficient chiral inducing framework in the conjugated addition of amides to α,β-unsaturated esters. An entry to enantio-enriched diversely substituted amines.

Johann Rogier, Lilia Anani, Aurélien Coelho, Fabien Massicot, Carine Machado-Rodrigues, Jean-Bernard Behr, Jean-Luc Vasse

Institut de Chimie Moléculaire de Reims, CNRS-UMR 7312 and Université de Reims, 51687 Reims Cedex 2, France

Supplementary Information

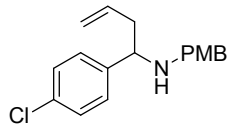
All reactions involving organometallics were conducted under an atmosphere of argon. Prior to use, THF was distilled over sodium-benzophenone ketyl. ^{1}H and ^{13}C NMR spectra were recorded in $CDCl_3$, unless specified, on a Bruker AC-500. Samples were analyzed by Q-TOF HRMS system. The analysis was performed on a Waters SYNAPT G2-Si High Resolution Mass Spectrometry equipped with electrospray ionization (ESI) source (Waters Corp., Manchester, UK). Mass detection was conducted in positive ion mode, with the source temperature at 120◦C, capillary voltage and cone voltage were set at 3 KV and 40 V. The desolvation gas was optimized to 900 L/h, the cone gas flow of 50 L/h and the scan range was from 50 to 2000 m/z. Samples were analyzed in infusion mode and the mass was corrected during acquisition using external reference (Lock-Spray) consisting of a 1 ng/uL solution of leucine encephalin at a flow rate of 5 µL/min, in order to make sure the accuracy and reproducibility during the MS analysis. All data collected were acquired using MassLynxTM (V4.1) software in centroid mode.

General procedure for the synthesis of racemic secondary amines 1.

A solution of benzylic amine (10 mmol) and aldehyde (10 mmol) in CH_2Cl_2 (20 mL) was refluxed for 1h then cooled down to rt. The resulting mixture was dried over Na_2SO_4, filtered and the solvent was removed under reduced pressure to give the corresponding imine which was used in the next step without purification.

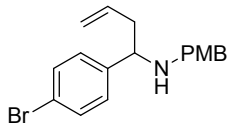
To a solution of imine (10 mmol) in THF (20 mL), was added allylbromide (1.05 mL, 12 mmol) and Zn powder (1.02 g, 15 mmol), and the resulting mixture was stirred at rt for 2 h. Water (10 mL) was added, and the mixture was stirred vigorously for 30 min. Et_2O (20 mL) was added and the stirring was continued for 10 min. The organic layer was discarded and the remaining paste was triturated with Et_2O (2 x 20 mL). The organic phases were combined, dried over Na_2SO_4, filtered and concentrated under reduced pressure to give the secondary amine which was used in the next step without purification.

1-(4-Chlorophenyl)-*N*-(4-methoxybenzyl)but-3-en-1-amine 1c



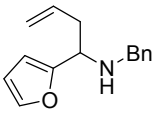
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.36-7.30 (m, 4 H), 7.18 (d, *J* = 8.5 Hz, 2 H), 6.88 (d, *J* = 8.5 Hz, 2 H), 5.69 (dddd, *J* = 16.9, 10.1, 7.6, 6.4 Hz, 1 H), 5.14-5.03 (m, 2 H), 3.82 (s, 3 H), 3.69 (dd, *J* = 7.5, 6.1 Hz, 1 H), 3.61 (d, *J* = 13.1 Hz, 1 H), 3.47 (d, *J* = 13.1 Hz, 1 H), 2.43-2.34 (m, 2 H), 1.72 (br s, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 158.7, 142.6, 135.2, 132.6, 132.6, 129.3, 128.8, 128.6, 118.0, 113.9, 61.0, 55.4, 50.9, 43.2.

1-(4-Bromophenyl)-*N*-(4-methoxybenzyl)but-3-en-1-amine 1d [1]



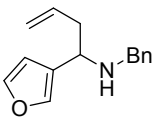
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.49 (d, *J* = 8.3 Hz, 2 H), 7.27 (d, *J* = 8.4 Hz, 2 H), 7.17 (d, *J* = 8.5 Hz, 2 H), 6.87 (d, *J* = 8.6 Hz, 2 H), 5.69 (dddd, *J* = 16.7, 10.3, 7.9, 6.2 Hz, 1 H), 5.15-4.99 (m, 2 H), 3.82 (s, 3 H), 3.67 (dd, *J* = 7.7, 5.9 Hz, 1 H), 3.61 (d, *J* = 13.1 Hz, 1 H), 3.46 (d, *J* = 13.1 Hz, 1 H), 2.46-2.26 (m, 2 H), 1.71 (br s, 1 H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 158.7, 143.1, 135.1, 132.6, 131.6, 129.4, 129.2, 120.8, 118.0, 113.9, 61.0, 55.4, 50.9, 43.1.

***N*-Benzyl-1-(furan-2-yl)but-3-en-1-amine 1f [2]**



^{1}H NMR (500 MHz, $CDCl_3$) δ 7.36-7.03 (m, 6 H), 6.25 (dd, *J* = 3.2, 1.8 Hz, 1 H), 6.11 (d, *J* = 3.1 Hz, 1 H), 5.64 (ddt, *J* = 17.2, 10.2, 7.1 Hz, 1 H), 5.01 (d, *J* = 17.2 Hz, 1 H), 4.96 (d, *J* = 10.2 Hz, 1 H), 3.73-3.65 (m, 2H), 3.52 (d, *J* = 13.2 Hz, 1H), 2.50-2.41 (m, 2 H), 1.80 (br s, 1 H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 156.3, 141.7, 140.4, 135.0, 128.5, 128.3, 127.0, 117.6, 110.0, 55.0, 51.2, 39.4.

***N*-Benzyl-1-(furan-3-yl)but-3-en-1-amine 1g**

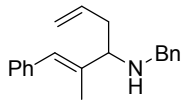


^{1}H NMR (500 MHz, $CDCl_3$) δ 7.44 (d, *J* = 1.7 Hz, 1 H), 7.40-7.23 (m, 6 H), 6.46 (s, 1 H), 5.75 (ddt, *J* = 17.2, 10.2, 7.1 Hz, 1 H), 5.16-5.05 (m, 2 H), 3.81 (d, *J* = 13.3 Hz, 1 H), 3.73 (t, *J* = 6.7 Hz, 1 H), 3.65 (d, *J* = 13.3 Hz, 1 H), 2.48 (t, *J* = 7.0 Hz, 2 H), 2.01 (br s, 1 H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 143.3, 140.6, 139.9, 135.3, 128.5, 128.3, 127.7, 127.0, 117.7, 109.1, 52.8, 51.2, 41.5.

---

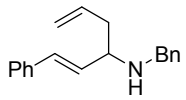
[1] T. J. Cogswell, C. S. Donald, D.-L. Long, R. Marquez, *Org. Biomol. Chem*, **2015**, *13*, 717.
[2] R. A. Fernandes and J. L. Nallasivam, *Org. Biomol. Chem*., 2012, **10**, 7789.

(*E*)-*N*-Benzyl-2-methyl-1-phenylhexa-1,5-dien-3-amine1j [3]



^{1}H NMR (500 MHz, $CDCl_3$) δ 7.44-7.19 (m, 10 H), 6.50 (s, 1 H), 5.80 (ddt, *J* = 17.2, 10.1, 7.1 Hz, 1 H), 5.16 (d, *J* = 17.2 Hz, 1 H), 5.13 (d, *J* = 10.1 Hz, 1 H), 3.86 (d, *J* = 13.3 Hz, 1 H), 3.68 (d, *J* = 13.3 Hz, 1 H), 3.30 (t, *J* = 7.0 Hz, 1 H), 2.43-2.34 (m, 2 H), 1.93 (s, 4 H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 140.9, 139.2, 138.1, 135.8, 129.1, 128.5, 128.3, 128.2, 127.5, 126.9, 126.3, 117.2, 65.6, 51.5, 39.3, 13.2.

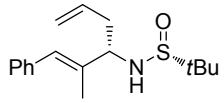
(*E)-N*-Benzyl-1-phenylhexa-1,5-dien-3-amine 1i[2]



^{1}H NMR (500 MHz, $CDCl_3$) δ 7.44 (d, *J* = 7.8 Hz, 2 H), 7.40-7.26 (m, 8 H), 6.55 (d, *J* = 15.9 Hz, 1 H), 6.14 (dd, *J* = 15.9, 8.2 Hz, 1 H), 5.83 (dddd, J = 17.1, 10.1, 7.5, 6.5 Hz, 1 H), 5.21-5.08 (m, 2 H), 3.93 (d, *J* = 13.4 Hz, 1 H), 3.75 (d, *J* = 13.4 Hz, 1 H), 3.35 (q, *J* = 7.0 Hz, 1 H), 2.47-2.35 (hept, *J* = 6.4 Hz, 2 H), 1.81 (br s, 1 H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 140.6, 137.1, 135.1, 132.7, 131.4, 128.7, 128.5, 128.2, 127.51, 127.0, 126.4, 117.8, 59.6, 51.4, 40.8.

Representative procedure for allylmetallation of tert-butylsulfinimines : Procedure A

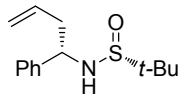
(*R*)-2-Methyl-*N*-[(*S,E*)-2-methyl-1-phenylhexa-1,5-dien-3-yl]propane-2-sulfinamide 5l



To a solution of (*R,E)-2-methyl-N-((E)-2-methyl-3-phenylallylidene)propane-2-sulfinamide* (1.62 g, 6.5 mmol) in CH_2Cl_2 (40 mL) at -50°C, was added a solution of allylmagnesium bromide (1 M in Et_2O, 13 mL, 13 mmol). The resulting mixture was stirred for 1h at -50°C, then 12 h at rt prior to the addition of a saturated aqueous solution of NH_4Cl (20 mL). The organic layer was collected and the aqueous phases was extracted with Et_2O (2 x 20 mL). The organic fractions were combined, dried over Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel eluting with a 70:30→50:50 mixture of PE/AcOEt (70:30→50:50) to give **5l** (1.46 g, 74%) as a white solid. dr 97:3. Mp 80°C. $[\alpha]_D$ -91.4 (*c* 1, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$) δ ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.38-7.29 (m, 4 H), 7.26-7.22 (tt, *J* = 7.2, 1.4 Hz, 6.60 (s, 1 H), 5.81 (dddd, *J* = 16.9, 10.1, 8.2, 6.0 Hz, 1 H), 5.26-5.16 (m, 2 H), 4.04 (t, *J* = 7.0 Hz, 1 H), 3.41 (br s, 1 H), 2.52 (dtt, *J* = 13.4, 5.9, 1.3 Hz, 1 H), 2.39 (dt, *J* = 13.9, 8.2 Hz, 1 H), 1.85 (d, *J* = 1.3 Hz, 3 H), 1.24 (s, 9 H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 137.5, 136.6, 134.4, 129.3, 129.2, 128.2, 126.7, 118.9, 61.0, 55.5, 39.5, 22.79, 13.5; HRMS(ES^+): m/z $[M+Na]^+$ calcd for $C_{17}H_{25}NOSNa$: 314.1555; found : 314.1556.

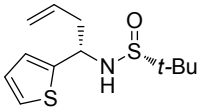
[3] Y. Jiang and S. E. Schaus, *Angew. Chem., Int. Ed*., 2017, **56**, 1544.

(*R*)-2-Methyl-N-[(*S*)-1-phenylbut-3-en-1-yl]propane-2-sulfinamide 5a[4]



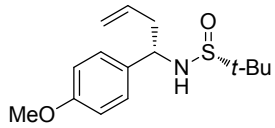
Yield 78%. White solid dr 98:2 after recrystallization from cyclohexane. Mp 68°C; $[\alpha]_D$ -145 (*c* 0.25, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) 7.39-7.29 (m, 5 H), 5.76 (dddd, *J* = 17.0, 10.2, 8.4, 5.8 Hz, 1 H), 5.25-5.16 (m, 2 H), 4.49 (ddd, *J* = 8.0, 5.4, 2.3 Hz, 1 H), 3.69 (br s, 1 H), 2.63 (dtt, *J* = 13.9, 5.7, 1.4 Hz, 1 H), 2.50 (dt, *J* = 14.0, 8.4 Hz, 1 H), 1.22 (s, 9 H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 141.8, 134.3, 128.6, 127.8, 127.6, 119.4, 57.2, 55.8, 43.6, 22.7.

(*R*)-2-Methyl-N-[(*S*)-1-(thiophen-2-yl)but-3-en-1-yl]propane-2-sulfinamide 5e[4c]



Yield 87%. Yellow oil, dr 95:5. $[\alpha]_D$ -117 (*c* 1, CH_2Cl_2); ^1H NMR (500 MHz, $CDCl_3$) δ 7.21 (d, *J* = 5.1 Hz, 1 H), 6.97 (d, *J* = 3.0 Hz, 1 H), 6.93 (m, 1 H), 5.80-5.68 (m, 1 H), 5.21-5.16 (m, 2 H), 4.77 (m, 1 H), 3.78 (br d, *J* = 3.0 Hz, 1 H), 2.67 (dt, *J* = 11.9, 6.0 Hz, 1 H), 2.57 (m, 1 H), 1.19 (s, 9 H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 146.1, 133.5, 126.6, 125.2, 125.0, 119.8, 55.9, 53.6, 43.7, 22.6.

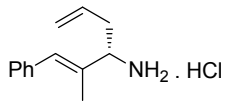
(*R*)-*N*-[(*S*)-1-(4-Methoxyphenyl)but-3-en-1-yl]-2-methylpropane-2-sulfinamide 5k[4b]



Yield 81%. White solid; dr 98:2. Mp 68°C; $[\alpha]_D$ -128 (*c* 1, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) 7.25 (m, 2 H), 6.88(m, 2 H), 5.74 (dddd, *J* = 17.0, 10.2, 8.5, 5.7 Hz, 1 H), 5.22-5.13 (m, 2 H), 4.43 (ddd, *J* = 7.8, 5.5, 1.9 Hz, 1 H), 3.81 (s, 3 H), 3.66 (br s, 1 H), 2.58 (dt, *J* = 12.5, 5.6 Hz, 1 H), 2.47 (dt, *J* = 14.0, 8.4 Hz, 1 H), 1.20 (s, 9 H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 159.2, 134.4, 133.7, 128.7, 119.2, 113.9, 56.6, 55.6, 55.3, 43.6, 22.7.

Representative procedure for the preparation of secondary homoallylilamine: Procedure B

(*S,E*)-2-Methyl-1-phenylhexa-1,5-dien-3-amonium chloride

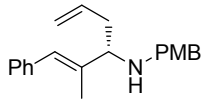


To a solution of the above sulfinamide (1.23 g, 4.06 mmol) in MeOH (7 mL) was added a solution of HCl (2 M in Et_2O, 3 mL) was added at rt. After 1h30 of stirring the solvent was removed under reduced pressure. The white solid was washed with Et_2O (2 x 5 mL), then dried under high vacuum to give the title compound (831 mg, 87%) as a white solid. $[\alpha]_D$ +9.3 (*c* 1, CH_2Cl_2); ^1H NMR (500 MHz, $CDCl_3$) δ 8.76 (br s, 3 H), 7.38-7.16 (m, 5 H), 6.68 (s, 1 H),

[4] (a) M. Medjahadi, J. C. Gonzalez-Gomez, F. Foubelo and M. Yus, *J. Org. Chem*., 2009, **74,** 7859; (b) O. Soares do Rego Barros, J. A. Sirvent, F. Foubelo and M. Yus, *Chem. Commun*., 2014, **50**, 6898 ; (c) X.-W. Sun, M. Liu, M.-H. Xu, G.-Q. Lin, *Org. Lett*., 2008, **10,** 1259.

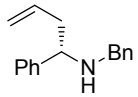
5.75 (ddt, *J* = 17.1, 10.1, 7.0 Hz, 1 H), 5.23 (d, *J* = 16.9 Hz, 1 H), 5.17 (d, *J* = 10.1 Hz, 1 H), 3.88 (m, 1 H), 2.76 (dt, *J* = 13.4, 6.5 Hz, 1 H), 2.66 (dt, *J* = 14.6, 7.6 Hz, 1 H), 1.95 (s, 3 H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 136.4, 132.1, 131.7, 131.6, 129.2, 128.3, 127.2, 120.0, 59.2, 36.3, 14.2.

(*S,E*)-N-(4-Methoxybenzyl)-2-methyl-1-phenylhexa-1,5-dien-3-amine 1l



The above ammonium salt (533 mg, 2.4 mmol) was dissolved in CH_2Cl_2 (25 mL). The resulting solution was washed with an aqueous solution of NaOH (5%, 10 mL), dried over $MgSO_4$, filtered and concentrated to give the free primary amine which was used in the next step without purification. A solution of primary amine (0.45 g, 2.4 mmol) and 4-methoxybenzaldehyde (327 mg, 2.4 mmol) in toluene (5 mL) was refluxed for 1 h. The solvent was distilled off under reduced pressure, then, MeOH (5 mL) was added. The resulting solution was cooled down to 0°C, then by $NaBH_4$ (100 mg, 5.3 mmol) was added in 3 portions. After 1h of stirring, water (5 mL) was added and the mixture was concentrated to half of the volume. The residue was extracted with CH_2Cl_2 (2 x 10 mL) and the organic phases were combined, filtered and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel eluting with a 7.3 mixture of PE/Et_2O to give **1l** (630 mg, 86%) as a pale yellow oil. $[\alpha]_D$ -12.2 (*c* 1, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.42-7.31 (m, 4 H), 7.29-7.22 (m, 3 H), 6.90 (d, *J* = 8.5 Hz, 2 H), 6.48 (s, 1 H), 5.78 (dddd, *J* = 17.1, 10.0, 7.7, 6.7 Hz, 1 H), 5.13 (dd, *J* = 17.1, 1.1 Hz, 1 H), 5.08 (d, *J* = 10.1 Hz, 1 H), 3.83 (s, 3H), 3.75 (d, *J* = 13.1 Hz, 1 H), 3.59 (d, *J* = 13.1 Hz, 1 H), 3.26 (t, *J* = 7.0 Hz, 1 H), 2.34 (m, 2 H), 1.90 (s, 3 H), 1.50 (br s, 1 H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 158.7, 139.3, 138.1, 135.8, 133.0, 129.5, 129.1, 128.2, 127.4, 126.3, 117.1, 113.9, 65.5, 55.4, 50.9, 39.3, 13.2; HRMS(ES^+): m/z $[M+H]^+$ calcd for $C_{21}H_{26}NO$: 308.2014; found : 308.2017.

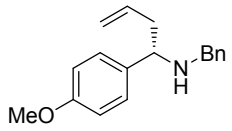
(*S*)-*N*-benzyl-1-phenylbut-3-en-1-amine[5] 1a



Prepared according to procedure **B**. Colorless oil overall yield 48%. $[\alpha]_D$ -52.2 (*c* 1, CH_2Cl_2). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.45-7.17 (m, 10 H), 5.75 (dddd, *J* = 16.6, 10.1, 8.0, 6.2 Hz, 1H), 5.19-4.99 (m, 2 H), 3.73 (dd, *J* = 7.9, 5.8 Hz, 1 H), 3.71 (d, *J* = 13.3 Hz, 1 H), 3.56 (d, *J* = 13.3 Hz, 1 H), 2.52-2.36 (m, 2 H), 1.78 (br s, 1 H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 143.9, 140.8, 135.6, 128.5, 128.5, 128.2, 127.4, 127.2, 126.9, 117.7, 61.7, 51.6, 43.2.

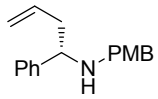
[5] R. A. Fernandes and Y. Yamamoto, *J. Org. Chem*., 2004, **69**, 735

(*S*)-*N*-Benzyl-1-(4-methoxyphenyl)but-3-en-1-amine1k [6]



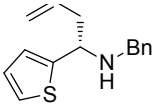
Prepared according to procedure **B,** pale yellow oil, yield 87%. $[\alpha]_D$ -58.5 (*c* 1, CH_2Cl_2). for er > 95:5 ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.41-7.17 (m, 7 H), 6.93 (d, *J* = 8.7 Hz, 2 H), 5.74 (dddd, *J* = 16.8, 10.2, 7.7, 6.4 Hz, 1 H), 5.16-5.01 (m, 2 H), 3.85 (s, 3 H), 3.70 (d, *J* = 13.3 Hz, 1 H), 3.73 (dd, *J* = 7.0, 6.6 Hz, 1 H), 3.55 (d, *J* = 13.3 Hz, 1 H), 2.50-2.35 (m, 2 H), 1.77 (br s, 1 H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 158.8, 140.7, 135.8, 135.7, 128.5, 128.4, 128.3, 126.9, 113.9, 61.0, 55.4, 51.4, 43.2.

***(S)*-*N*-(4-Methoxybenzyl)-1-phenylbut-3-en-1-amine1b [7]**



Prepared according to procedure **B**, pale yellow oil, yield 93%. $[\alpha]_D$ -45.0 (*c* 1, CH_2Cl_2) for er > 95:5; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.39 (d, *J* = 6.1 Hz, 4 H), 7.32-7.29 (m, 1 H), 7.21 (d, *J* = 8.6 Hz, 2 H), 6.89 (d, *J* = 8.6 Hz, 2 H), 5.74 (dddd, *J* = 17.1, 10.2, 8.0, 6.3 Hz, 1 H), 5.13-5.06 (m, 2 H), 3.83 (s, 3 H), 3.72 (dd, *J* = 7.6, 6.0 Hz, 1 H), 3.65 (d, *J* = 13.1 Hz, 1 H), 3.51 (d, *J* = 13.1 Hz, 1 H), 2.49-2.40 (m, 2 H), 1.74 (br s, 1 H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 158.6, 144.0, 135.6, 132.9, 129.4, 128.5, 127.4, 127.1, 117.6, 113.8, 61.6, 55.4, 50.9, 43.2.

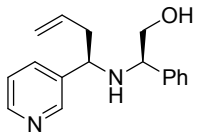
***(S)*-*N*-Benzyl-1-(thiophen-2-yl)but-3-en-1-amine 1e[8]**



Prepared according to procedure **B**, colorless oil, yield 85%. $[\alpha]_D$ -35.1 (*c* 1, CH_2Cl_2) for er = 95:5; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.38-7.25 (m, 6 H), 7.00 (dd, *J* = 5.0, 3.5 Hz, 1 H), 6.96 (m, 1 H), 5.77 (dddd, *J* = 17.3, 10.2, 7.7, 6.6 Hz, 1 H), 5.14 d, *J* = 17.3, Hz, 1 H) 5.11 (d, *J* = 10.2 Hz, 1 H), 4.04 (t, *J* = 6.8 Hz, 1 H), 3.84 (d, *J* = 13.2 Hz, 1 H), 3.65 (d, *J* = 13.2 Hz, 1 H), 2.59-2.48 (m, 2 H), 1.83 (br s, 1 H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 149.2, 140.4, 135.0, 128.5, 128.3, 127.0, 126.5, 124.3, 124.1, 118.1, 57.2, 51.4, 43.6.

[6] A. K. Jha and R. A. Fernandes, *Eur. J. Org. Chem.,* 2019, 2857.
[7] T. J. Cogswell, C. S. Donald, D.-L. Long and R. Marquez, *Org. Biomol. Chem*., 2015, **13**, 717.
[8] K.-H. Shen and C.-F. Yao, *J. Org. Chem*., 2006, **71**, 3980.

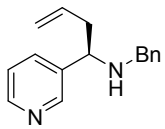
(*R*)-2-Phenyl-2-{[(*R*)-1-(pyridin-3-yl)but-3-en-1-yl]amino}ethanol 5h



A mixture of (*R*)-phenylglycinol (0.93 g, 6.8 mmol) and 3-pyridylcarboxaldehyde (835 g, 6.8 mmol) in CH_2Cl_2 (20 mL) was refluxed for 1 h then cooled down to rt. The resulting mixture was dried over Na_2SO_4, filtered and the solvent was removed under reduced pressure to quantitatively give the corresponding imine which was used in the next step without purification.

To a solution of the above imine in MeOH (20 mL), was added allylbromide (0.78 mL, 8.9 mmol) and In (0.77 g, 6.8 mmol) and the resulting mixture was stirred for 2 h at rt. A saturated aqueous solution of $NaHCO_3$ (30 mL) was added. The precipitate was filtered off and rinsed with MeOH (30 mL). The filtrate was concentrated under reduced pressure and partitioned with AcOEt (60 mL) and water (30 mL). The organic layer was dried over Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel eluting with PE/AcOEt (90:10) to give **5h** (1.41 g, 77%) as a yellow oil. $[\alpha]_D$ -16.9 (*c* 1, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.40 (s, 1 H), 8.38 (m, 1 H), 7.52 (dt, *J* = 7.9, 2.0 Hz, 1 H), 7.27-7.16 (m, 5 H), 7.13 (dd, *J* = 7.8, 4.8 Hz, 1 H), 5.66 (ddt, *J* = 16.4, 10.6, 7.1 Hz, 1 H), 5.13-5.00 (m, 2 H), 3.86 (dd, *J* = 7.6, 4.4 Hz, 1 H), 3.80-3.71 (m, 2 H), 3.60 (dd, *J* = 10.8, 7.7 Hz, 1 H), 3.28 (s, 1 H), 2.55 (dt, *J* = 13.8, 6.9 Hz, 1 H), 2.47 (dt, *J* = 13.9, 6.8 Hz, 1 H), 2.15 (s, 1 H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 149.1, 148.3, 148.3, 140.9, 140.9, 139.4, 134.9, 134.9, 134.1, 128.6, 127.5, 127.4, 123.3, 118.4, 66.3, 62.7, 58.2, 41.3, HRMS(ES$^+$): m/z $[M+H]^+$ calcd for $C_{17}H_{21}N_2O$: 269.1654; found : 269.1649.

(*R*)-*N*-benzyl-1-(pyridin-3-yl)but-3-en-1-amine 1h[5]

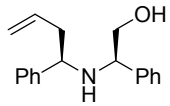


To a solution of the above amino-alcohol (1.4 g, 5.2 mmol) in CH_2Cl_2/MeOH (1:2, 30 mL), was added $Pb(OAc)_4$ (2.78 g, 6.3 mmol) in one portion at 0°C. The resulting mixture was stirred for 20 min at 0°C, and $NH_2OH.HCl$ (6.95 g, 100 mmol) was added. After 45 min of stirring the solvent was removed under reduced pressure. The residue was taken up with CH_2Cl_2 (40 mL), and the solid was filtered off. The filtrate was washed with an aqueous solution of NaOH (10%, 4 x 10 mL), dried with $MgSO_4$, filtered and concentrated under reduced pressure to give the corresponding primary amine (0.41 g, 53%).

A solution of primary amine (0.40 g, 2.7 mmol) and benzaldehyde (286 mg, 2.7 mmol) in toluene (5 mL) was refluxed for 1 h. The solvent was removed under reduced pressure, then MeOH (5 mL) was added. The resulting solution was cooled down to 0°C, then $NaBH_4$ (106 mg, 2.8 mmol) was added in 3 portions. After 1 h of stirring, water (5 mL) was added and the mixture was concentrated to half of the volume. The residue was extracted with

CH_2Cl_2 (2 x 10 mL). The organic phases were combined, dried over Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel eluting with PE/AcOEt (2:1) to give **1h** (0.58 g, 88%) as a colorless oil. $[\alpha]_D$ +50.6 (*c* 1, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.59 (d, *J* = 1.6 Hz, 1 H), 8.54 (dd, *J* = 4.7, 1.4 Hz, 1 H), 7.76 (d, *J* = 7.8 Hz, 1 H), 7.38-7.23 (m, 6 H), 5.71 (dddd, *J* = 17.6, 9.6, 7.9, 6.4 Hz, 1 H), 5.14-5.05 (m, 2 H), 3.76 (dd, *J* = 7.6, 6.0 Hz, 1 H), 3.68 (d, *J* = 13.3 Hz, 1 H), 3.55 (d, *J* = 13.3 Hz, 1 H), 2.51-2.36 (m, 2 H), 1.82 (br s, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 149.6, 148.7, 140.2, 139.1, 134.8, 134.6, 128.5, 128.1, 127.0, 123.6, 118.4, 59.2, 51.5, 42.9; HRMS(ES$^+$): m/z $[M+H]^+$ calcd for $C_{16}H_{19}N_2$: 239.1548; found : 239.1551.

(*R*)-2-Phenyl-2-{[(*R*)-1-phenylbut-3-en-1-yl]amino}ethanol[9]

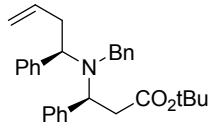


Dr 98 :2, $[\alpha]_D$ -40.4 (*c* 1.1, $CHCl_3$);^{1}H NMR (500 MHz, $CDCl_3$) δ 7.34-7.17 (m, 10 H), 5.68 (ddt, *J* = 17.2, 10.2, 7.1 Hz, 1 H), 5.11-4.98 (m, 2 H), 3.86 (dd, *J* = 6.9, 4.6 Hz, 1 H), 3.80-3.70 (m, 2 H), 3.54 (dd, *J* = 10.8, 7.0 Hz, 1 H), 2.77 (br s, 1 H), 2.55 (dt, *J* = 13.6, 6.7 Hz, 1 H), 2.47 (dt, *J* = 13.9, 6.9 Hz, 1 H), 1.87 (br s, 1 H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 143.7, 141.3, 135.1, 128.6, 128.5, 127.5, 127.2, 127.2, 127.2, 117.5, 65.7, 61.4, 59.8, 41.5.

General procedure for conjugated 1,4-addition of lithium amide onto α,β-unsaturated esters

To a solution of amine **1** (3 mmol) in THF (15 mL) was slowly added a solution of *n*-BuLi (2.5 M in hexanes, 1.2 mL, 3 mmol) at -70°C. The resulting solution was stirred for 10 min at -70°C, then, a solution of ester (2 mmol) in THF (2 mL) was added dropwise. The stirring was continued for 1h30 at -70°C, then a saturated aqueous solution of NH_4Cl (10 mL) was added. The layers were separated and the aqueous phase was extracted with Et_2O (2 x 10 mL). The organic phases were combined, dried over Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel eluting with a PE/Et_2O mixture to give the corresponding aminoester.

(±)-***(S)*-*Tert*-Butyl 3-{benzyl[(*R*)-1-phenylbut-3-en-1-yl]amino}-3-phenylpropanoate 3a**

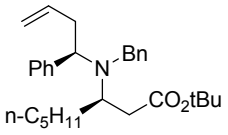


Yield 82%, dr >95:5. Pale yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.44 (d, *J* = 7.5 Hz, 2 H), 7.40-7.33 (m, 6 H), 7.32-7.19 (m, 7 H), 5.54 (ddd, *J* = 17.1, 10.3, 6.7 Hz, 1 H), 5.04-4.81 (m, 2 H), 4.51 (dd, *J* = 10.6, 4.1 Hz, 1 H), 3.86 (dd, *J* = 9.1, 6.0 Hz, 1 H), 3.82 (d, *J* = 14.5 Hz, 1 H), 3.71 (d, *J* = 14.5 Hz, 1 H), 2.65-2.52 (m, 3 H), 2.40 (dd, *J* = 14.9, 4.2 Hz, 1

[9] (a) T. Vilaivan, C. Winotapan, V. Banphavichit, T. Shinada and Y. Ohfune, *J. Org. Chem*., 2005, **70**, 3464, (b) M. Ahari, A. Joosten, J.-L. Vasse and J. Szymoniak, *Synthesis*, 2008, 61.

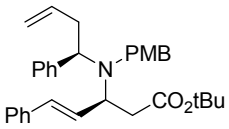
H), 1.27 (s, 9 H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 171.3, 141.9, 141.3, 141.1, 136.4, 128.9, 128.5, 128.4, 128.3, 128.3, 128.2, 127.2, 127.2, 126.8, 116.3, 80.3, 62.3, 58.7, 50.7, 37.3, 36.0, 28.0.

(±)-*(S)*-*Tert*-Butyl 3-{benzyl[(*R*)-1-phenylbut-3-en-1-yl]amino}octanoate 3b



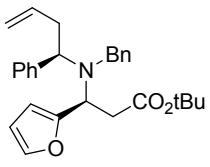
Yield 73%, dr >95:5. Colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.45 (d, *J* = 7.4 Hz, 2 H), 7.41-7.23 (m, 8 H), 5.53 (ddt, *J* = 17.1, 10.0, 6.8 Hz, 1 H), 4.98-4.80 (m, 2 H), 3.84 (d, *J* = 14.7 Hz, 1 H), 3.69 (dd, *J* = 9.0, 6.4 Hz, 1 H), 3.48 (d, *J* = 14.7 Hz, 1 H), 3.38 (m, 1 H), 2.69-2.55 (m, 2 H), 1.82 (dd, *J* = 14.8, 9.3 Hz, 1 H), 1.76 (dd, *J* = 14.8, 3.5 Hz, 1 H), 1.63 (m, 1 H), 1.42 (s, 9 H), 1.40-1.19 (m, 7 H), 0.92 (t, *J* = 7.2 Hz, 3 H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 172.3, 141.4, 140.3, 136.6, 128.9, 128.6, 128.4, 128.2, 127.2, 126.8, 116.2, 80.0, 63.0, 53.8, 50.1, 38.3, 38.2, 34.0, 32.0, 28.2, 26.8, 22.8, 14.2; HRMS(ES$^+$): m/z $[M+H]^+$ calcd for $C_{29}H_{42}NO_2$: 436.3216; found : 436.3219.

(±)-(*S,E*)-*Tert*-Butyl 3-{(4-methoxybenzyl)[(*R*)-1-phenylbut-3-en-1-yl)amino}-5-phenylpent-4-enoate 3c



Yield 60%, dr >95:5. Yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.36-7.22 (m, 12 H), 6.88 (d, *J* = 8.6 Hz, 2 H), 6.48 (dd, *J* = 16.1, 1.3 Hz, 1 H), 6.23 (dd, *J* = 16.1, 6.6 Hz, 1 H), 5.68 (ddt, *J* = 17.1, 10.2, 6.8 Hz, 1 H), 5.01 (dd, *J* = 17.1, 1.6 Hz, 1 H), 4.95 (dd, *J* = 10.1, 1.7 Hz, 1 H), 4.12 (m, 1 H), 3.91 (dd, *J* = 8.9, 6.2 Hz, 1 H), 3.83 (s, 3 H), 3.81 (d, *J* = 14.3 Hz, 1 H) 3.62 (d, *J* = 14.2 Hz, 1 H), 2.78 (m, 1 H), 2.61 (m, 1 H), 2.29 (dd, *J* = 14.5, 9.3 Hz, 1 H), 2.21 (dd, *J* = 14.5, 4.9 Hz, 1 H), 1.39 (s, 9 H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 171.3, 158.6, 141.1, 137.4, 136.7, 133.0, 130.9, 130.7, 129.7, 128.8, 128.7, 128.3, 127.4, 127.2, 126.4, 116.3, 113.7, 80.4, 62.9, 56.6, 55.4, 49.8, 38.8, 36.6, 28.2.

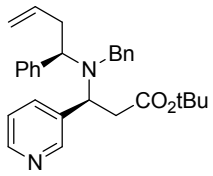
(±)-(*S*)-*Tert*-Butyl 3-{benzyl[(*R*)-1-phenylbut-3-en-1-yl]amino}-3-(furan-2-yl)propanoate 3d



Yield 92%, dr >95:5. Orange oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.43 (dd, *J* = 1.9, 0.8 Hz, 1 H), 7.40-7.21 (m, 10 H), 6.36 (dd, *J* = 3.3, 1.8 Hz, 1 H), 6.22 (d, *J* = 3.3 Hz, 1 H), 5.62 (ddt, *J* = 17.1, 10.2, 6.9 Hz, 1 H), 4.94 (dq, *J* = 17.1, 1.6 Hz, 1 H), 4.89 (m, 1 H), 4.58 (dd, *J* = 9.5, 5.4 Hz, 1 H), 3.89 (dd, *J* = 9.6, 5.3 Hz, 1 H), 3.80 (d, *J* = 14.4 Hz, 1 H), 3.70 (d, *J* = 14.3 Hz, 1 H), 2.65-2.54 (m, 2 H), 2.44-2.39 (m, 2 H), 1.35 (s, 9 H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 170.6, 155.4,

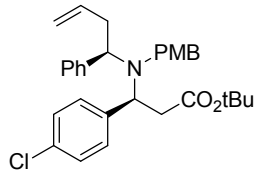
141.6, 141.3, 140.6, 136.6, 128.9, 128.8, 128.2, 128.2, 127.1, 126.9, 116.2, 110.2, 107.3, 80.4, 62.4, 52.3, 50.9, 37.8, 35.3, 28.0; HRMS(ES$^+$): m/z [M+H]$^+$ calcd for $C_{28}H_{34}NO_3$: 432.2539; found : 432.2535.

(±)-**(*S*)-*Tert*-Butyl 3-{benzyl[(*R*)-1-phenylbut-3-en-1-yl]amino}-3-(pyridin-3-yl)propanoate 3e**



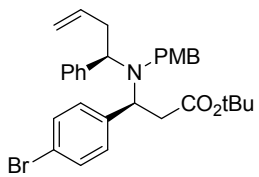
Yield 89%, dr 96:4. Orange oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.68 (d, *J* = 2.3 Hz, 1 H), 8.51 (dd, *J* = 4.8, 1.6 Hz, 1 H), 7.73 (dt, *J* = 8.0, 2.0 Hz, 1 H), 7.41-7.20 (m, 11 H), 5.52 (ddt, *J* = 17.0, 10.2, 6.8 Hz, 1 H), 4.99-4.88 (m, 2 H), 4.57 (dd, *J* = 10.8, 3.7 Hz, 1 H), 3.86-3.77 (m, 2 H), 3.66 (d, *J* = 14.4 Hz, 1 H), 2.67 (dt, *J* = 13.6, 6.8 Hz, 1 H), 2.61-2.49 (m, 2 H), 2.33 (dd, *J* = 15.2, 3.7 Hz, 1 H), 1.28 (s, 9 H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 170.9, 150.2, 148.4, 140.7, 140.3, 137.5, 136.1, 135.5, 128.7, 128.5, 128.4, 128.4, 127.5, 127.1, 123.0, 116.7, 80.8, 62.6, 56.1, 50.7, 36.9, 36.0, 28.0; HRMS(ES$^+$): m/z [M+H]$^+$ calcd for $C_{29}H_{35}N_2O_2$: 443.2699; found : 443.2698.

(±)-**(*S*)-*Tert*-Butyl 3-{[(*R*)-1-(4-chlorophenyl)but-3-en-1-yl](4-methoxybenzyl)amino}-3-phenylpropanoate 3f**



Yield 71%, dr 95:5. Colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.41 (d, *J* = 8.3 Hz, 2 H), 7.39-7.25 (m, 8 H), 7.18 (d, *J* = 8.6 Hz, 2 H), 6.85 (d, *J* = 8.6 Hz, 2 H), 5.49 (ddt, *J* = 17.0, 10.2, 6.7 Hz, 1 H), 5.01-4.82 (m, 2 H), 4.47 (dd, *J* = 10.2, 4.5 Hz, 1 H), 3.84 (dd, *J* = 9.5, 5.3 Hz, 1 H), 3.82 (s, 3 H), 3.73 (d, *J* = 14.2 Hz, 1 H), 3.63 (d, *J* = 14.3 Hz, 1 H), 2.61-2.46 (m, 3 H), 2.43 (dd, *J* = 14.9, 4.5 Hz, 1 H), 1.28 (s, 9 H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 171.2, 158.7, 141.7, 140.1, 136.0, 132.8, 132.7, 130.2, 129.5, 128.4, 128.3, 128.2, 127.3, 116.6, 113.8, 80.4, 61.4, 58.6, 55.4, 50.1, 37.6, 35.7, 28.0; HRMS(ES$^+$): m/z [M+H]$^+$ calcd for $C_{31}H_{38}NO_3Cl$: 506.2462; found : 506.2461.

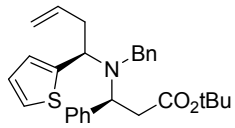
(±)-**(*S*)-*Tert*-Butyl 3-{[(*R*)-1-(4-bromophenyl)but-3-en-1-yl](4-methoxybenzyl)amino}-3-phenylpropanoate 3g**



Yield 74%, dr 95:5. Colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.47 (d, *J* = 8.5 Hz, 2 H), 7.40 (d, *J* = 8.2 Hz, 2 H), 7.35 (t, *J* = 7.6 Hz, 2 H), 7.26 (t, *J* = 7.2 Hz, 1 H), 7.22 (d, *J* = 8.4 Hz, 2 H), 7.16 (d, *J* = 8.6 Hz, 2 H), 6.83 (d, *J* = 8.6 Hz, 2 H), 5.47 (ddt, *J* = 17.0, 10.2, 6.8 Hz, 1 H), 4.93-4.84 (m, 2 H), 4.45 (dd, *J* = 10.2, 4.5 Hz, 1 H), 4.15 (q, *J* = 7.1 Hz, 1 H),

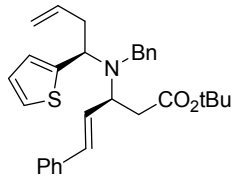
3.81 (m, 4 H), 3.71 (d, *J* = 14.2 Hz, 1 H), 3.61 (d, *J* = 14.3 Hz, 1 H), 2.57-2.44 (m, 3 H), 2.42 (dd, *J* = 14.9, 4.5 Hz, 1 H), 1.27 (s, 9 H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 171.2, 158.7, 141.7, 140.6, 136.0, 132.7, 131.4, 130.6, 129.5, 128.3, 128.3, 127.3, 121.0, 116.7, 113.8, 80.5, 61.5, 58.7, 55.4, 50.1, 37.6, 35.7, 28.0; HRMS(ES$^+$): m/z $[M+H]^+$ calcd for $C_{31}H_{37}NO_3Br$: 550.1957; found : 550.1956.

(±)-***(S)*-*Tert*-Butyl 3-{benzyl[(*R*)-1-(thiophen-2-yl)but-3-en-1-yl]amino}-3-phenylpropanoate 3h**



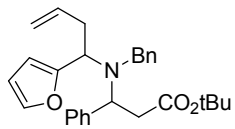
Yield 83%, dr >95:5. Pale yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.34-10 (m, 11 H), 6.87 (m, 2 H), 5.52 (ddt, *J* = 17.0, 10.2, 6.8 Hz, 1H), 4.92-4.74 (m, 2 H), 4.35 (dd, *J* = 10.7, 4.3 Hz, 1 H), 4.02 (dd, *J* = 7.9, 6.4 Hz, 1 H), 3.72 (d, *J* = 14.4 Hz, 1 H), 3.70 (d, *J* = 14.4 Hz, 1 H), 2.52 (dd, *J* = 14.8, 10.7 Hz, 1 H), 2.48-2.41 (m, 2 H), 2.36 (dd, *J* = 14.8, 4.3 Hz, 1 H), 1.13 (s, 9 H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 171.16, 146.43, 141.33, 140.52, 136.21, 128.71, 128.48, 128.35, 128.24, 127.31, 126.99, 126.56, 125.11, 124.47, 116.55, 80.30, 59.01, 57.39, 50.85, 38.08, 37.42, 27.93; HRMS(ES$^+$): m/z $[M+H]^+$ calcd for $C_{28}H_{34}NO_2S$: 448.2310; found : 448.2309.

(±)-**(*S,E*)-*Tert*-Butyl 3-{benzyl[(*R*)-1-(thiophen-2-yl)but-3-en-1-yl]amino}-5-phenylpent-4-enoate 3i**



Yield 92%, dr >95:5. Yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.48 (d, *J* = 7.3 Hz, 2 H), 7.42-7.23 (m, 9 H), 7.09-6.97 (m, 2 H), 6.53 (d, *J* = 16.1 Hz, 1 H), 6.25 (dd, *J* = 16.0, 7.0 Hz, 1 H), 5.83 (ddt, *J* = 17.1, 10.2, 6.8 Hz, 1 H), 5.10 (dq, *J* = 17.1, 1.8 Hz, 1 H), 5.05 (dq, *J* = 10.2, 1.7 Hz, 1H), 4.23 (dd, *J* = 8.5, 5.9 Hz, 1H), 4.11 (dddd, *J* = 8.3, 6.6, 4.7, 1.3 Hz, 1 H), 3.92 (d, *J* = 14.5 Hz, 1 H), 3.82 (d, *J* = 14.4 Hz, 1 H), 2.84 (dt, *J* = 13.0, 6.0 Hz, 1 H), 2.66 (dt, *J* = 14.7, 7.0 Hz, 1 H), 2.45 (dd, *J* = 14.5, 9.5 Hz, 1 H), 2.38 (dd, *J* = 14.5, 4.8 Hz, 1 H), 1.42 (s, 9 H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 171.2, 146.0, 140.5, 137.2, 136.3, 131.2, 130.1, 128.8, 128.6, 128.4, 127.5, 127.0, 126.6, 126.4, 125.2, 124.4, 116.6, 80.4, 58.4, 57.1, 50.4, 39.3, 38.4, 28.2; HRMS(ES$^+$): m/z $[M+H]^+$ calcd for $C_{30}H_{36}NO_2S$: 474.2467; found : 474.2473.

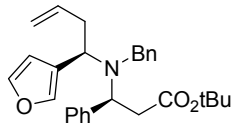
(±)-***Tert*-Butyl 3-{benzyl[-1-(furan-2-yl)but-3-en-1-yl]amino}-3-phenylpropanoate 3j**



Yield 90%, dr 55:45. Orange oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.45-7.25 (m, 11 H), 6.39 (dd, *J* = 3.2, 1.9 Hz, 0.54 H), 6.33 (dd, *J* = 3.2, 1.8 Hz, 0.46 H), 6.22 (d, *J* = 3.2 Hz, 0.54 H), 6.05 (d, *J* = 3.2 Hz, 0.46 H), 5.71 (ddt, *J* = 17.1, 10.2, 6.8 Hz, 0.46 H), 5.58 (ddt, *J* = 17.0, 10.2, 6.8 Hz, 0.54 H), 5.04-4.93 (m, 2 H), 4.52 (dd, *J* = 10.8, 3.8 Hz, 0.54 H), 4.40 (dd, *J* = 10.5, 5.2 Hz, 0.46 H), 4.13 (d, *J* = 15.9 Hz, 0.46 H), 3.96-3.90 (m, 1 H), 3.86 (d, *J* = 14.2 Hz, 0.54 H), 3.71 (d, *J* =

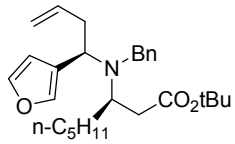
14.1 Hz, 0.54 H), 3.56 (d, *J* = 15.9 Hz, 0.46 H), 2.76 (dd, *J* = 14.1, 5.2 Hz, 0.46 H), 2.69 (dd, *J* = 15.1, 10.8 Hz, 0.54 H), 2.65-2.57 (m, 2 H), 2.49 (dd, *J* = 14.1, 10.5 Hz, 0.46 H), 2.26 (dd, *J* = 15.1, 3.9 Hz, 0.54H), 1.32 (s, 4.9 H), 1.24 (s, 4.1 H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 171.5, 171.0, 115.4, 155.3, 142.3, 141.7, 141.5, 141.5, 141.4, 140.5, 136.1, 135.9, 128.9, 128.4, 128.3, 128.2, 128.10, 128.07, 127.8, 127.3, 127.1, 127.0, 126.6, 116.45, 116.39, 110.3, 109.8, 108.1, 107.7, 80.3, 80.2, 63.1, 58.1, 56.7, 54.8, 51.6, 50.8, 42.2, 36.7, 36.2, 35.9, 28.0, 27.9.

(±)-*(S)*-*Tert*-Butyl 3-{benzyl[(*R*)-1-(furan-3-yl)but-3-en-1-yl]amino}-3-phenylpropanoate 3k



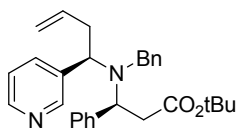
Yield 80%, dr 95:5. Orange oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.44-7.40 (m, 3 H), 7.37-7.23 (m, 9 H), 6.48 (s, 1 H), 5.61 (ddt, *J* = 13.7, 10.2, 6.8 Hz, 1 H), 5.01-4.87 (m, 2 H), 4.47 (dd, *J* = 9.5, 5.3 Hz, 1 H), 3.84 (dd, *J* = 9.0, 5.5 Hz, 1 H), 3.75 (d, *J* = 3.9 Hz, 2 H), 2.65 (dd, *J* = 14.7, 5.4 Hz, 1 H), 2.61 (dd, *J* = 14.7, 10.0 Hz, 1 H), 2.49 (m, 1 H), 2.39 (m, 1 H), 1.28 (s, 9 H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 171.3, 142.9, 141.7, 140.9, 140.4, 136.5, 128.5, 128.4, 128.3, 128.2, 127.3, 126.9, 125.6, 116.3, 111.0, 80.4, 59.1, 53.8, 50.7, 38.3, 36.6, 28.0; HRMS(ES$^+$): m/z $[M+H]^+$ calcd for $C_{28}H_{34}NO_3$: 432.2539; found : 432.2542.

(±)-*(R)*-*Tert*-*Butyl* 3-{benzyl[(*R*)-1-(furan-3-yl)but-3-en-1-yl]amino}octanoate 3l



Yield 78%, dr 94:6. Yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.46-7.22 (m, 7 H), 6.46 (d, *J* = 0.9 Hz, 1 H), 5.62 (ddt, *J* = 17.0, 10.2, 6.8 Hz, 1 H), 4.97 (dd, *J* = 17.1, 1.8 Hz, 1 H), 4.91 (dd, *J* = 10.2, 1.8 Hz, 1 H), 3.83 (d, *J* = 14.3 Hz, 1 H), 3.65 (dd, *J* = 8.9, 6.4 Hz, 1 H), 3.44 (d, *J* = 14.4 Hz, 1 H), 3.34 (m, 1H), 2.59 (dt, *J* = 13.2, 6.6 Hz, 1H), 2.51 (m, 1 H), 2.16 (dd, *J* = 14.8, 2.9 Hz, 1 H), 1.93 (dd, *J* = 14.8, 9.9 Hz, 1 H), 1.62 (m, 1 H), 1.52 (m, 1 H), 1.44 (s, 9 H), 1.40-1.22 (m, 6 H), 0.92 (t, *J* = 7.2 Hz, 3 H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 172.5, 142.9, 141.0, 140.3, 136.5, 128.8, 128.4, 126.9, 123.8, 116.2, 110.6, 80.1, 53.9, 53.5, 50.3, 38.8, 38.5, 34.2, 32.0, 28.2, 26.8, 22.8, 14.2; HRMS(ES$^+$): m/z $[M+H]^+$ calcd for $C_{27}H_{40}NO_3$: 426.3008; found : 426.3008.

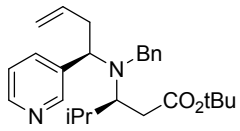
(±)-*(S)*-*Tert*-Butyl 3-{benzyl[(*R*)-1-(pyridin-3-yl)but-3-en-1-yl]amino}-3-phenylpropanoate 3m



Yield 92%, dr >95:5. Orange oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.48 (d, *J* = 2.2 Hz, 1 H), 8.41 (dd, *J* = 4.8, 1.6 Hz, 1 H), 7.60 (d, *J* = 7.9 Hz, 1 H), 7.34-7.23 (m, 4 H), 7.22-7.09 (m, 7 H), 5.38 (ddt, *J* = 17.2, 10.4, 6.8 Hz, 1 H), 4.84-4.78 (m, 2 H), 4.35 (dd, *J* = 9.0, 6.0 Hz, 1 H), 3.83 (dd, *J* = 9.8, 5.1 Hz, 1 H), 3.69 (d, *J* = 14.6 Hz, 1 H), 3.66 (d, *J* = 14.6 Hz, 1 H),

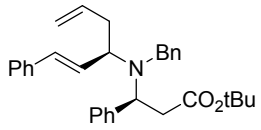
2.52-2.37 (m, 4 H), 1.16 (s, 9 H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 170.9, 150.4, 148.2, 141.1, 140.6, 137.1, 136.3, 135.4, 128.41 (2C), 128.36, 128.30, 127.5, 127.0, 123.3, 117.2, 80.6, 60.1, 59.6, 50.8, 38.5, 34.6; HRMS(ES$^+$): m/z [M+H]$^+$ calcd for $C_{29}H_{35}N_2O_2$: 443.2699; found : 443.2701.

(±)-**(*S*)-*Tert-Butyl* 3-{benzyl[(*R*)-1-(pyridin-3-yl)but-3-en-1-yl]amino}-4-methylpentanoate 3n**



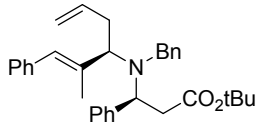
Yield 90%, dr >95:5. Yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.51 (d, *J* = 3.9 Hz, 1 H), 8.43 (s, 1 H), 7.74 (d, *J* = 7.8 Hz, 1 H), 7.47 (d, *J* = 7.5 Hz, 2 H), 7.38 (t, *J* = 7.1 Hz, 2 H), 7.29 (d, *J* = 8.0 Hz, 1 H), 7.23 (dd, *J* = 7.2, 5.2 Hz, 1 H), 5.44 (ddt, *J* = 17.0, 10.1, 6.8 Hz, 1 H), 4.90 (d, *J* = 17.1 Hz, 1 H), 4.84 (d, *J* = 10.2 Hz, 1 H), 3.80 (d, *J* = 14.8 Hz, 1 H), 3.69 (dd, *J* = 8.4, 7.2 Hz, 1 H), 3.45 (d, *J* = 14.9 Hz, 1 H), 3.25 (t, *J* = 8.5 Hz, 1 H), 2.69 (t, *J* = 7.2 Hz, 2 H), 1.98 (dd, *J* = 16.3, 9.5 Hz, 1 H), 1.75 (m, 1 H), 1.69 (d, *J* = 16.3 Hz, 1 H), 1.42 (s, 9 H), 1.14 (d, *J* = 6.6 Hz, 3 H), 0.89 (d, *J* = 6.7 Hz, 3 H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 172.2, 150.6, 148.7, 140.5, 134.8, 128.6, 128.5, 127.0, 123.3, 117.0, 80.3, 60.3, 58.5, 51.3, 37.8, 36.6, 33.2, 28.1, 21.3, 19.6; HRMS(ES$^+$): m/z [M+H]$^+$ calcd for $C_{26}H_{37}N_2O_2$: 409.2855; found : 409.2852.

(±)-**(*S*)-*Tert*-Butyl 3-{benzyl[(*R,E*)-1-phenylhexa-1,5-dien-3-yl]amino}-3-phenylpropanoate 3o**



Yield 83%, dr 80:20. Yellow oil.^{1}H NMR (500 MHz, $CDCl_3$) δ 7.45 (m, 2 H), 7.43-7.25 (m, 13 H), 6.45 (d, *J* = 15.9 Hz, 1 H), 6.28 (dd, *J* = 16.0, 8.2 Hz, 1 H), 5.66 (ddt, *J* = 17.1, 10.2, 6.9 Hz, 1 H), 5.03-4.93 (m, 2 H), 4.57 (dd, *J* = 9.9, 4.5 Hz, 1 H), 3.82 (d, *J* = 14.4 Hz, 1 H), 3.78 (d, *J* = 14.4 Hz, 1 H), 3.46 (m, 1 H), 2.95 (dd, *J* = 14.8, 4.6 Hz, 1 H), 2.80 (dd, *J* = 14.9, 10.0 Hz, 1H), 2.45 (m, 1 H), 2.32 (m, 1 H), 1.35 (s, 9 H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 171.6, 141.7, 140.9, 137.3, 136.4, 131.6, 130.5, 128.7, 128.7, 128.4, 128.3, 128.1, 127.5, 127.2, 126.9, 126.5, 116.2, 80.5, 60.3, 58.8, 50.6, 38.3, 37.7, 28.0; HRMS(ES$^+$): m/z [M+H]$^+$ calcd for $C_{32}H_{38}NO_2$: 468.2903; found : 468.2903.

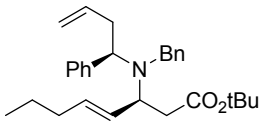
(±)-**(*S*)-*Tert*-Butyl 3-{benzyl[(*R,E*)-2-methyl-1-phenylhexa-1,5-dien-3-yl]amino}-3-phenylpropanoate 3p**



Yield 75%, dr 96:4. Yellow oil.^{1}H NMR (500 MHz, $CDCl_3$) δ 7.46 (d, *J* = 7.8 Hz, 2 H), 7.31 (m, 13 H), 6.49 (s, 1 H), 5.64 (m, 1 H), 4.98-4.94 (m, 2 H), 4.59 (dd, *J* = 9.7, 4.4 Hz, 1 H), 3.88 (d, *J* = 15.0 Hz, 1 H), 3.83 (d, *J* = 15.0 Hz, 1 H), 3.40 (dd, *J* = 9.8, 4.0 Hz, 1 H), 2.95 (dd, *J* = 15.1, 4.3 Hz, 1 H), 2.81 (dd, *J* = 14.0, 11.0 Hz, 1 H), 2.35-2.22 (m, 2 H), 1.98 (s, 3 H), 1.30 (s, 9 H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 171.2, 142.0, 141.2, 138.1, 138.1, 136.5, 129.1, 128.7, 128.2, 128.2,

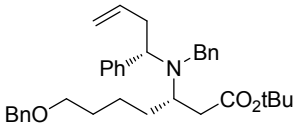
128.2, 128.1, 127.3, 126.6, 126.4, 115.9, 80.4, 67.6, 59.9, 51.2, 37.6, 33.7, 27.9, 16.4; HRMS(ES$^+$): m/z $[M+H]^+$ calcd for $C_{33}H_{40}NO_2$: 482.3059; found : 482.3061.

(*S,E*)-*Tert*-Butyl 3-{benzyl[(*R*)-1-phenylbut-3-en-1-yl]amino}oct-4-enoate 3q



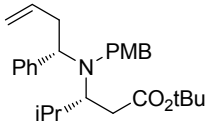
Yield 69%, dr >95:5. Pale yellow oil. $[\alpha]_D$ -22.7 (*c* 0.6, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.40-7.20 (m, 10 H), 5.64 (ddt, *J* = 17.1, 10.2, 6.9 Hz, 1 H), 5.59-5.46 (m, 2 H), 4.98 (dd, *J* = 17.1, 1.8 Hz, 1 H), 4.92 (dd, *J* = 10.2, 1.8 Hz, 1 H), 3.94-3.88 (m, 1H), 3.84 (dd, *J* = 9.1, 6.0 Hz, 1 H), 3.79 (d, *J* = 14.6 Hz, 1 H), 3.61 (d, *J* = 14.6 Hz, 1 H), 2.80-2.70 (m, 1 H), 2.61-2.51 (m, 1 H), 2.20-2.10 (m, 2 H), 2.02 (q, *J* = 6.7 Hz, 2 H), 1.39 (s, 9 H), 0.91 (t, *J* = 7.4 Hz, 3 H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 171.5, 141.5, 141.3, 136.7, 132.0, 130.6, 128.8, 128.6, 128.2, 128.1, 127.1, 126.7, 116.2, 80.1, 63.0, 56.5, 50.3, 38.8, 36.6, 34.8, 28.2, 22.6, 13.8; HRMS(ES$^+$): m/z $[M+H]^+$ calcd for $C_{29}H_{40}NO_2$: 434.3059; found : 434.3061.

(*S*)-*Tert*-Butyl 3-{benzyl[(*S*)-1-phenylbut-3-en-1-yl]amino}-7-(benzyloxy)heptanoate 3r



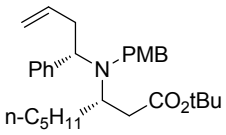
Yield 66%, dr >95:5. Colorless oil. $[\alpha]_D$ -10.2 (*c* 1, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.45 (d, *J* = 7.2 Hz, 2 H), 7.40-7.25 (m, 13 H), 5.53 (ddt, *J* = 17.0, 10.2, 6.8 Hz, 1 H), 4.92 (dd, *J* = 17.1, 1.8 Hz, 1 H), 4.85 (m, 1 H), 4.54 (s, 2 H), 3.84 (d, *J* = 14.7 Hz, 1 H), 3.69 (dd, *J* = 9.0, 6.5 Hz, 1 H), 3.51 (t, *J* = 6.6 Hz, 2 H), 3.48 (d, *J* = 14.8 Hz, 1H), 3.40 (tt, *J* = 9.3, 3.7 Hz, 1 H), 2.69-2.56 (m, 2 H), 1.82 (dd, *J* = 14.9, 9.5 Hz, 1 H), 1.76 (m), 1.68-1.45 (m, 4 H), 1.42 (s, 9 H), 1.32 (m, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 172.2, 141.3, 140.2, 138.9, 136.5, 128.8, 128.6, 128.5, 128.4, 128.2, 127.7, 127.6, 127.2, 126.9, 116.2, 80.1, 73.0, 70.6, 62.9, 53.7, 50.1, 38.2, 38.1, 33.8, 29.9, 28.2, 23.8; HRMS(ES$^+$): m/z $[M+H]^+$ calcd for $C_{35}H_{46}NO_3$: 528.3478; found : 528.3483.

(*R*)-*Tert*-Butyl 3-{(4-methoxybenzyl)[(S)-1-phenylbut-3-en-1-yl]amino]-4-methylpentanoate 3s



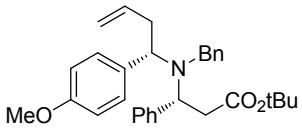
Yield 89%, dr >95:5. Colorless oil. $[\alpha]_D$ -26.7 (*c* 1, CH_2Cl_2); ^1H NMR (500 MHz, $CDCl_3$) δ 7.28 (d, *J* = 8.6 Hz, 2 H), 7.17 (m, 5 H), 6.83 (d, *J* = 8.6 Hz, 2 H), 5.41 (ddt, *J* = 17.0, 10.2, 6.8 Hz, 1 H), 4.82 (dd, *J* = 17.1, 1.9 Hz, 1 H), 4.71 (dm, *J* = 10.2, Hz, 1 H), 3.74 (s, 3 H), 3.61 (d, *J* = 14.5 Hz, 1 H), 3.55 (dd, *J* = 9.6, 5.9 Hz, 1 H), 3.30 (d, *J* = 14.5 Hz, 1 H), 3.18 (m, 1 H), 2.65 (m, 1 H), 2.54 (m, 1 H), 1.80 (dd, *J* = 16.4, 9.8 Hz, 1H), 1.63 (m, 1 H), 1.56 (dd, *J* = 16.3, 1.7 Hz, 1 H), 1.31 (s, 9 H), 1.04 (d, *J* = 6.6 Hz, 3 H), 0.79 (d, *J* = 6.8 Hz, 3 H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 172.5, 158.6, 139.4, 136.6, 132.9, 129.6, 129.1, 128.0, 127.1, 116.2, 113.9, 79.9, 62.0, 58.0, 55.4, 50.4, 38.0, 36.5, 33.1, 28.1, 21.4, 19.7; HRMS(ES^+): m/z $[M+H]^+$ calcd for $C_{28}H_{40}NO_3$: 438.3008; found : 438.3013.

(*S*)-*Tert*-Butyl 3-{(4-methoxybenzyl)[(*S*)-1-phenylbut-3-en-1-yl]amino}octanoate 3t



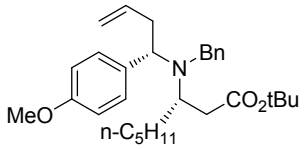
Yield 80%, dr >95:5. Colorless oil. $[\alpha]_D$ -23.8 (*c* 1, CH_2Cl_2); ^1H NMR (600 MHz, $CDCl_3$) δ 7.38-7.24 (m, 7 H), 6.92 (d, *J* = 8.5 Hz, 2 H), 5.54 (ddt, *J* = 17.0, 10.1, 6.8 Hz, 1 H), 4.93 (dd, *J* = 17.2, 1.9 Hz, 1 H), 4.86 (dd, *J* = 10.2, 1.9 Hz, 1 H), 3.85 (s, 3 H), 3.77 (d, *J* = 14.4 Hz, 1 H), 3.68 (dd, *J* = 8.7, 6.7 Hz, 1 H), 3.40 (d, J = 14.4 Hz, 1 H), 3.37 (m, 1 H), 2.66-2.57 (m, 2 H), 1.79 (dd, *J* = 14.8, 9.8 Hz, 1 H), 1.71 (dd, *J* = 14.8, 2.8 Hz, 1 H), 1.61 (m, 1 H), 1.48 (m, 1 H), 1.40-1.18 (m, 6 H), 0.92 (t, *J* = 7.3 Hz, 3 H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 172.4, 158.5, 140.3, 136.7, 133.2, 129.7, 128.8, 128.2, 127.1, 116.1, 113.7, 80.0, 62.4, 55.4, 53.5, 49.3, 38.2, 38.1, 33.9, 32.0, 28.2, 26.8, 22.8, 14.3; HRMS(ESI^+): m/z $[M+H]^+$ calcd for $C_{30}H_{44}NO_3$: 466.3321; found : 466.3325.

(*R*)-*Tert-Butyl* 3-{benzyl[(*S*)-1-(4-methoxyphenyl)but-3-en-1-yl]amino}-3-phenylpropanoate 3u



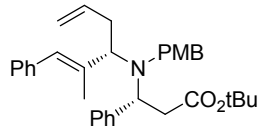
Yield 56%, dr 96:4. Pale yellow oil. $[\alpha]_D$ -0.7 (*c* 1, CH_2Cl_2); ^1H NMR (500 MHz, $CDCl_3$) δ 7.44 (d, *J* = 7.4 Hz, 2 H), 7.36 (t, *J* = 7.6 Hz, 2 H), 7.31-7.21 (m, 8 H), 6.91 (d, *J* = 8.7 Hz, 2 H), 5.54 (ddt, *J* = 17.0, 10.2, 6.8 Hz, 1 H), 4.93 (dd, *J* = 17.2, 1.7 Hz, 1 H), 4.89 (dd, *J* = 10.2, 1.7 Hz, 1 H), 4.51 (dd, *J* = 10.5, 4.2 Hz, 1 H), 3.84 (s, 3 H), 3.82 (dd, *J* = 9.6, 5.9 Hz, 1 H), 3.79 (d, *J* = 14.5 Hz, 1 H), 3.69 (d, *J* = 14.5 Hz, 1 H), 2.65-2.50 (m, 3 H), 2.42 (dd, *J* = 14.9, 4.2 Hz, 1 H), 1.28 (s, 9 H) ; ^{13}C NMR (126 MHz, $CDCl_3$) δ 171.4, 158.7, 142.0, 141.2, 136.5, 133.3, 129.8, 128.4, 128.4, 128.2, 128.1, 127.1, 126.8, 116.2, 113.6, 80.2, 61.5, 58.6, 55.3, 50.6, 37.3, 36.1, 27.9; HRMS(ES^+): m/z $[M+H]^+$ calcd for $C_{31}H_{38}NO_3$: 472.2852; found : 472.2851.

(*S*)-*Tert*-Butyl 3-{benzyl[(*S*)-1-(4-methoxyphenyl)but-3-en-1-yl]amino}octanoate 3v



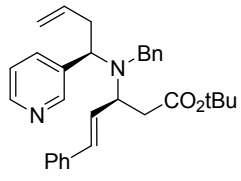
Yield 46%, dr 96:4. Colorless oil. $[\alpha]_D$ -23.8 (*c* 1.4, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.46 (d, *J* = 7.5 Hz, 2 H), 7.38 (t, *J* = 7.6 Hz, 2 H), 7.29 (t, *J* = 7.3 Hz, 1 H), 7.22 (d, *J* = 8.5 Hz, 2 H), 5.55 (ddt, *J* = 17.1, 10.2, 6.8 Hz, 1 H), 4.93 (dt, *J* = 17.2, 1.8 Hz, 1 H), 4.86 (dd, *J* = 10.2, 1.8 Hz, 1 H), 3.84 (d, *J* = 14.7 Hz, 1 H), 3.83 (s, 3 H), 3.66 (dd, *J* = 9.1, 6.4 Hz, 1 H), 3.47 (d, *J* = 14.7 Hz, 1 H), 3.39 (dq, *J* = 10.4, 6.4, 5.2 Hz, 1H), 2.62 (ddt, *J* = 22.6, 14.2, 6.4 Hz, 2H), 1.83 (d, *J* = 6.4 Hz, 2 H), 1.68-1.60 (m, 1 H), 1.55-1.46 (m, 1 H), 1.44 (s, 9 H), 1.41-1.15 (m, 6 H), 0.94 (t, *J* = 7.2 Hz, 3 H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 172.4, 158.7, 141.5, 136.7, 132.3, 129.8, 128.61, 128.3, 126.8, 116.0, 113.5, 78.0, 62.2, 55.3, 53.7, 50.1, 38.4, 38.2, 34.0, 32.0, 28.2, 26.78, 22.8, 14.2 HRMS(ES$^+$): m/z $[M+H]^+$ calcd for $C_{30}H_{44}NO_3$: 466.3321; found : 466.3324.

(*R*)-*Tert*-Butyl 3-{(4-methoxybenzyl)[(*S,E*)-2-methyl-1-phenylhexa-1,5-dien-3-yl]amino}-3-phenylpropano ate 3w



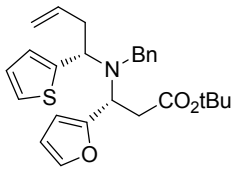
Yield 70%, dr 95:5. Pale yellow oil. $[\alpha]_D$ +45.1 (*c* 1, CH_2Cl_2). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.41 (d, *J* = 7.6 Hz, 2 H), 7.34 (m, 4 H), 7.31-7.18 (m, 7 H), 6.83 (d, *J* = 8.4 Hz, 2 H), 6.44 (s, 1 H), 5.62 (ddt, *J* = 16.6, 9.6, 7.0 Hz, 1 H), 4.97-4.87 (m, 2 H), 4.54 (dd, *J* = 10.3, 5.0 Hz, 1 H), 3.81 (s, 3 H), 3.79 (d, *J* = 14.7 Hz, 1 H), 3.74 (d, *J* = 14.7 Hz, 1 H), 3.34 (dd, *J* = 9.8, 5.1 Hz, 1 H), 2.90 (dd, *J* = 14.7, 5.1 Hz, 1 H), 2.77 (dd, *J* = 14.6, 10.2 Hz, 1 H), 2.29-2.09 (m, 2 H), 1.94 (s, 3 H), 1.26 (s, 9 H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 171.3, 158.4, 141.4, 138.2, 136.6, 133.9, 129.2, 129.2, 128.6, 128.2, 128.1, 128.0, 127.2, 126.3, 115.9, 113.6, 80.4, 67.3, 59.7, 55.4, 50.5, 37.6, 33.7, 28.0, 16.5; HRMS(ES$^+$): m/z $[M+H]^+$ calcd for $C_{34}H_{42}NO_3$: 512.3165; found : 512.3167.

(*S,E*)-*Tert*-Butyl 3-{benzyl[(*R*)-1-(pyridin-3-yl)but-3-en-1-yl]amino}-5-phenylpent-4-enoate 3x



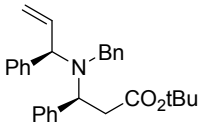
Yield 68%, dr >95:5. Yellow oil. $[\alpha]_D$ -66.5 (*c* 1, CH_2Cl_2); ^1H NMR (500 MHz, $CDCl_3$) δ 8.54 (d, *J* = 2.0 Hz, 1 H), 8.50 (dd, *J* = 4.8, 1.6 Hz, 1 H), 7.65 (dt, *J* = 7.9, 1.8 Hz, 1 H), 7.40-7.19 (m, 11 H), 6.50 (d, *J* = 16.1 Hz, 1 H), 6.25 (dd, *J* = 16.0, 7.1 Hz, 1 H), 5.61 (ddt, *J* = 17.0, 10.2, 6.8 Hz, 1 H), 5.04-4.91 (m, 2 H), 4.06 (q, *J* = 7.1 Hz, 1 H), 3.96 (dd, *J* = 9.5, 5.4 Hz, 1 H), 3.83 (d, *J* = 14.5 Hz, 1 H), 3.74 (d, *J* = 14.5 Hz, 1 H), 2.80 (m, 1 H), 2.62 (m, 1 H), 2.36 (d, *J* = 7.2 Hz, 2 H), 1.37 (s, 9 H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 170.8, 150.7, 148.5, 140.5, 137.0, 136.6, 135.9, 135.6, 131.5, 129.7, 128.7, 128.6, 128.4, 127.7, 127.1, 126.4, 123.2, 117.2, 80.6, 61.0, 57.2, 50.6, 39.5, 35.7, 28.2; HRMS(ES^+): m/z $[M+H]^+$ calcd for $C_{31}H_{37}N_2O_2$: 469.2855; found : 469.2859.

(*R*)-*Tert*-Butyl 3-{Benzyl[(S)-1-(thiophen-2-yl)but-3-en-1-yl]amino}-3-(furan-2-yl)propanoate 3y



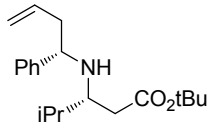
Yield 69%, dr 94:6. Yellow oil. $[\alpha]_D$ +40.1 (*c* 1, CH_2Cl_2); ^1H NMR (500 MHz, $CDCl_3$) δ 7.43-7.41 (m, 1 H), 7.39 (d, *J* = 7.4 Hz, 2 H), 7.33 (t, *J* = 7.5 Hz, 2 H), 7.27-7.23 (m, 2 H), 7.01 (d, *J* = 2.8 Hz, 1 H), 6.98 (dd, *J* = 5.0, 3.6 Hz, 1 H), 6.36 (dd, *J* = 3.2, 1.8 Hz, 1 H), 6.21 (d, *J* = 2.7 Hz, 1 H), 5.72 (ddt, *J* = 16.9, 10.1, 5.0 Hz, 1 H), 4.99 (m, 1 H), 4.96 (d, *J* = 10.3 Hz, 1 H), 4.48 (dd, *J* = 9.6, 4.8 Hz, 1 H), 4.16 (dd, *J* = 8.8, 4.5 Hz, 1 H), 3.82 (d, *J* = 14.5 Hz, 1 H), 3.78 (d, *J* = 14.5 Hz, 1 H), 2.74 (dd, *J* = 15.0, 10.0 Hz, 1 H), 2.55-2.46 (m, 2 H), 2.29 (m, 1 H), 1.33 (s, 9 H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 170.5, 154.8, 147.0, 141.6, 139.9, 136.5, 129.0, 128.3, 127.1, 126.5, 125.0, 124.4, 116.4, 110.3, 107.5, 80.4, 57.5, 52.0, 50.8, 38.12, 36.9, 28.0; HRMS(ES^+): m/z $[M+H]^+$ calcd for $C_{26}H_{32}NO_3S$: 438.2103; found : 438.2104.

(±)-(*S*)-*Tert*-Butyl 3-{benzyl[(*R*)-1-phenylallyl]amino}-3-phenylpropanoate 4



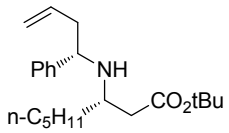
Yield 81%, dr 87:13. Colorless oil. ^1H NMR (500 MHz, $CDCl_3$) δ 7.20 (m, 15 H), 5.90 (dt, *J* = 17.2, 9.6 Hz, 1 H), 5.11 (d, *J* = 10.2 Hz, 1 H), 4.99 (d, *J* = 17.2 Hz, 1 H), 4.36 (dd, *J* = 9.9, 5.5 Hz, 1 H), 4.21 (d, *J* = 8.9 Hz, 1 H), 3.72 (d, *J* = 14.9 Hz, 1 H), 3.54 (d, *J* = 14.9 Hz, 1 H), 2.59 (dd, *J* = 14.3, 5.5 Hz, 1 H), 2.34 (dd, *J* = 14.3, 9.9 Hz, 1 H), 1.14 (s, 10 H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 171.1, 142.8, 141.8, 141.4, 137.5, 128.7, 128.4, 128.3, 128.24, 128.23, 128.19, 128.15, 128.12, 127.3, 127.1, 126.5, 118.2, 80.3, 68.1, 60.9, 51.7, 39.8, 27.9; HRMS(ES^+): m/z $[M+H]^+$ calcd for $C_{29}H_{34}NO_2$: 428.2590; found : 428.2589.

(*R*)-*Tert*-Butyl 4-methyl-3-{[(S)-1-phenylbut-3-en-1-yl]amino}pentanoate 6s



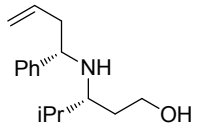
To a solution of **3s** (353 mg, 0.8 mmol) in a 4:1 mixture of CH_3CN/H_2O (7.5 mL) at 0°C was added CAN (1.32 g, 2.42 mmol) in one portion and the resulting solution was stirred for 30 min at 0°C. A solution of NaOH (5%, 5 mL) and the mixture was stirred for 15 min. The heterogeneous media was extracted with CH_2Cl_2 (4 x 10 mL). The organic phases were combined, dried over Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica eluting with PE/Et_2O (95:5) to give **6s** (210 mg, 83%) as a colorless oil. $[\alpha]_D$ -71.4 (*c* 0.4, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.37-7.29 (m, 4 H), 7.24 (m, 1 H), 5.72 (dddd, *J* = 17.1, 10.1, 8.0, 6.1 Hz, 1 H), 5.08 (dq, *J* = 17.1, 1.6 Hz, 1 H), 5.03 (dm, *J* = 10.1 Hz, 1 H), 3.77 (dd, *J* = 7.5, 6.2 Hz, 1 H), 2.56 (q, *J* = 5.7 Hz, 1 H), 2.46-2.28 (m, 4 H), 1.65 (m, 1 H), 1.47 (s, 9 H), 1.44 (br s, 1 H), 0.88 (d, *J* = 6.8 Hz, 3 H), 0.81 (d, *J* = 6.8 Hz, 3 H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 172.4, 144.6, 135.8, 128.2, 127.7, 127.0, 117.4, 80.3, 60.0, 57.6, 43.6, 37.1, 31.7, 28.3, 19.0, 18.7; HRMS(ES$^+$): m/z $[M+H]^+$ calcd for $C_{20}H_{32}NO_2$: 318.2433; found : 318.2435.

(*S*)-*Tert*-Butyl 3-{[(*S*)-1-phenylbut-3-en-1-yl]amino}octanoate 5t



Prepared according to the above procedure in 80% yield as a colorless oil. $[\alpha]_D$ -42.1 (*c* 1, CH_2Cl_2); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.33 (m, 4 H), 7.25 (t, *J* = 6.7 Hz, 1 H), 5.62 (dddd, *J* = 17.1, 10.1, 8.0, 6.0 Hz, 1 H), 5.08 (d, *J* = 17.1 Hz, 1 H), 5.04 (d, *J* = 10.1 Hz, 1 H), 3.79 (dd, *J* = 7.6, 6.1 Hz, 1 H), 2.69 (quint, *J* = 5.8 Hz, 1 H), 2.44-2.34 (m, 2 H), 2.32 (d, *J* = 5.4 Hz, 2 H), 1.55 (br s, 1 H), 1.46 (s, 9 H), 1.40-1.29 (m, 3 H), 1.28-1.19 (m, 3 H), 1.12 (m, 2 H), 0.85 (t, *J* = 7.3 Hz, 3 H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 171.9, 144.4, 135.7, 128.3, 127.5, 127.1, 117.5, 80.4, 59.7, 52.1, 43.6, 39.5, 35.5, 31.8, 28.3, 25.7, 22.7, 14.2; HRMS(ES$^+$): m/z $[M+H]^+$ calcd for $C_{22}H_{36}NO_2$: 346.2746; found : 346.2747.

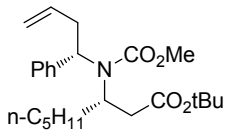
(*R*)-4-Methyl-3-{[(*S*)-1-phenylbut-3-en-1-yl]amino}pentan-1-ol 7



To a solution of **6s** (187 mg, 0.59 mmol) in THF (6 mL) was added a solution of LiAlH4 (2.2 M in THF, 0.7 mmol) at 0°C and the resulting solution was stirred at rt for 16 h. Water was carefully added at 0°C until the gas evolution ceased. A solution of Rochelle salt (3 mL) and Et_2O (10 mL) were added and the stirring was continued for 15 min. The organic phase was isolated and the white paste was triturated with Et_2O (2 x 10 mL). The organic phases were

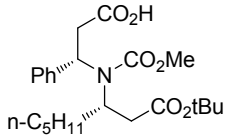
combined, dried over Na_2SO_4, filtered and concentrated under reduced pressure to give **7** (145 mg, 99%) as a colorless oil. $[\alpha]_D$ +13.9 (*c* 1, CH_2Cl_2); ^1H NMR (500 MHz, $CDCl_3$) δ 7.34 (t, *J* = 7.6 Hz, 2 H), 7.30-7.22 (m, 3 H), 5.64 (ddt, *J* = 17.2, 10.2, 7.1 Hz, 1H), 5.07-4.97 (m, 2 H), 3.91 (ddd, *J* = 10.4, 6.7, 3.5 Hz, 1 H), 3.85 (dd, *J* = 7.7, 6.0 Hz, 1 H), 3.81 (ddd, *J* = 11.0, 7.8, 3.3 Hz, 1 H), 2.56 (m, 2 H), 2.47 (m, 1 H), 1.91 (m, 1 H), 1.76 (ddt, *J* = 13.9, 6.7, 3.3 Hz, 1 H), 1.45 (dtd, *J* = 14.7, 7.8, 3.5 Hz, 1 H), 0.89 (d, *J* = 6.8 Hz, 3 H), 0.77 (d, *J* = 6.8 Hz, 3 H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 143.5, 135.0, 128.6, 127.5, 127.3, 117.5, 62.5, 61.3, 60.0, 41.7, 29.5, 29.0, 20.1, 17.2; HRMS(ES^+): m/z $[M+H]^+$ calcd for $C_{16}H_{26}NO$: 248.2014; found : 248.2012.

(*S*)-*Tert*-Butyl 3-{(methoxycarbonyl)[(*S*)-1-phenylbut-3-en-1-yl]amino}octanoate 8



To a solution of **6t** (470 mg, 1.36 mmol) in acetone (5 mL) was added K_2CO_3 (1.13 g, 8.2 mmol) and methylchloroformate (0.41 mL, 5.4 mmol) and the mixture was refluxed for 16 h. CH_2Cl_2 (10 mL) and Et_2O (10 mL) were added, and the solid was filtered off. The filtrate was concentrated under reduced pressure. The residue was dissolved in CH_2Cl_2 (30 mL), and the resulting organic phase was washed with an aquous solution of HCl (1 M, 10 mL), dried over Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica eluting with PE/Et_2O (90:10) to give **7t** (440 mg, 80%) as a colorless oil. $[\alpha]_D$ -9.0 (*c* 1, CH_2Cl_2); ^1H NMR (500 MHz, $CDCl_3$) δ 7.39 (d, *J* = 7.2 Hz, 2 H), 7.32 (t, *J* = 7.5 Hz, 2 H), 7.26 (t, *J* = 7.2 Hz, 1 H), 5.77 (ddt, *J* = 17.0, 10.2, 6.7 Hz, 1 H), 5.22 (br s, 1 H), 5.15 (dd, *J* = 17.1, 1.5 Hz, 1 H), 5.05 (dd, *J* = 10.3, 1.4 Hz, 1 H), 3.74 (s, 3H), 3.67 (br s, 1 H), 2.86 (dt, *J* = 14.5, 7.4 Hz, 1H), 2.76 (dt, *J* = 14.3, 7.0 Hz, 1H), 2.49 (br s, 1H), 1.79 (brs, 1 H), 1.74 (br d, *J* = 16.2 Hz, 1 H), 1.61 (br s, 1 H), 1.40-1.16 (m, 15 H), 0.89 (t, *J* = 6.9 Hz, 3 H);^{13}C NMR (126 MHz, $CDCl_3$) δ 171.0, 139.8, 135.3, 128.5, 127.7, 117.4, 80.3, 59.8, 52.3, 41.1 (br), 36.4 (br), 33.9 (br), 32.1, 28.1, 27.0, 22.7, 14.1, 1 C is missing; HRMS(ES^+): m/z $[M+Na]^+$ calcd for $C_{24}H_{37}NO_4Na$: 426.2620; found : 426.2618.

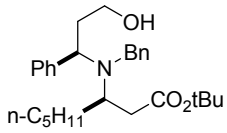
(*S*)-3-{[(*S*)-1-(*Tert*-Butoxy)-1-oxooctan-3-yl](methoxycarbonyl)amino}-3-phenylpropanoic acid 9



To a solution of **8** (156 mg, 0.39 mmol) in a 2/2/3 mixture of $CCl_4/CH_3CN/H_2O$ (8.75 mL) at 0°C was added $NaIO_4$ (334 mg, 1.56 mmol) and $RuCl_3$ (4 mg, 0.02 mmol) and the resulting mixture was stirred for 4 h at rt. Water (10 mL) and CH_2Cl_2 (10 mL) were added. The organic layer was isolated and the aqueous layer was extracted with CH_2Cl_2 (2 x 10 mL). The organic phases were combined, washed with an aqueous solution of HCl (1 M, 10 mL), dried over Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica eluting with a mixture of PE/Et_2O (90:10→50:50) to give **9** (128 mg, 78%) as a colorless oil. $[\alpha]_D$ -4.5 (*c* 1, CH_2Cl_2); ^1H NMR (500 MHz, $CDCl_3$) δ 7.35 (br s, 2 H), 7.29 (t, *J* = 7.4 Hz, 2 H), 7.24 (t, *J* = 7.2 Hz, 1

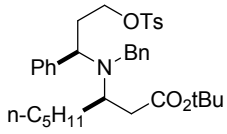
H), 5.43 (br s, 1 H), 3.79 (br s, 1H), 3.70 (s, 3 H), 3.21 (br s, 1 H), 3.04 (br d, *J* = 12.4 Hz, 1 H), 2.44 (br s, 1 H), 1.93 (br d, *J* = 14.7 Hz, 1 H), 1.73 (br s, 1 H), 1.55 (br m, 1 H), 1.32 (s, 9 H), 1.28-1.17 (m, 7 H), 0.85 (t, *J* = 6.8 Hz, 3 H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 176.2, 170.9, 139.5, 128.7, 127.9, 127.6, 80.5, 56.0, 53.8, 52.5, 40.7, 38.4, 33.5, 31.9, 28.1, 26.8, 22.6, 14.1; 1 C is missing; HRMS(ES$^+$): m/z [M+Na]$^+$ calcd for $C_{23}H_{35}NO_6Na$: 444.2362; found : 444.2361.

(±)-(*R*)-*Tert*-Butyl 3-{benzyl[(*R*)-3-hydroxy-1-phenylpropyl]amino}octanoate 10



To a solution of **3b** (515 mg, 1.18 mmol) in a 1:1:1 mixture of tBuOH/THF/H_2O (12 mL) was added NMO (415 mg, 3.55 mmol) and a solution of OsO_4 (2.5% in tBuOH, 0.8 mL) and the resulting mixture was stirred for 1h30 at rt. A saturated solution of Na_2SO_3 (2 mL) and a saturated solution of Na_2CO_3 (2 mL) were added. The mixture was extracted with AcOEt (3 x 10 mL). The residue was diluted in a 2:1 mixture of THF/H_2O (12 mL), then $NaIO_4$ (303 mg, 1.4 mmol) was added at rt. After 1h30 of stirring, MeOH (5 mL) $NaBH_4$ (90 mg, 2.4 mmol) were added at 0°C. After 30 min of stirring, water (5 mL) was added and the mixture was reduced to half of the volume under reduced pressure. The aqueous phase was extracted with CH_2Cl_2 (3 x 10 mL), the organic phases were combined, dried over Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica eluting with a mixture of PE/AcOEt (80:20) to give **10** (365 mg, 70%) as a colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.46 (d, *J* = 7.4 Hz, 2 H), 7.40 (t, *J* = 7.6 Hz, 2 H), 7.35-7.28 (m, 6 H), 3.88-3.79 (m, 2 H), 3.67-3.57 (m, 1 H), 3.53-3.39 (m, 3 H), 2.24 (m, 1 H), 1.92 (br s, 1 H), 1.87-1.79 (m, 2 H), 1.66 (dd, *J* = 15.3, 2.9 Hz, 1 H), 1.60-1.48 (m, 2 H), 1.43 (s, 9 H), 1.37-1.22 (m, 6 H), 0.92 (t, *J* = 7.1 Hz, 3 H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 172.2, 141.0, 140.2, 129.0, 128.7, 128.5, 128.4, 127.4, 127.1, 80.1, 60.8, 60.0, 53.9, 50.0, 38.2, 35.8, 34.2, 32.0, 28.1, 26.7, 22.8, 14.2.

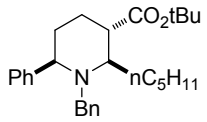
(±)-(*R*)-*Tert*-Butyl 3-{benzyl[(*R*)-1-phenyl-3-(tosyloxy)propyl]amino}octanoate



To a solution of the above alcohol (243 mg, 0.56 mmol), Et_3N (0.09 mL, 0.66 mmol), and DMAP (16 mg, 0.13 mmol) in CH_2Cl_2 (5 mL) was added in one portion TsCl (126 mg, 0.66 mmol), and the resulting mixture was stirred at rt for 5 h. Water (2 mL) was added, and the organic layer was washed with a saturated aqueous solution of Na_2CO_3 (2 mL), dried over Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel eluting with PE/AcOEt (80:20) to give the title compound as a colorless oil (201 mg, 60%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.62 (d, *J* = 8.2 Hz, 2 H), 7.38 (d, *J* = 4.0 Hz, 4 H), 7.29 (m, 7 H), 7.14 (dd, *J* = 7.0, 2.0 Hz, 2 H), 3.89 (dt, *J* = 9.9, 6.0 Hz, 1 H), 3.81 (m, 1 H), 3.77 (d, *J* = 14.5 Hz, 1 H), 3.64 (t, *J* = 7.5 Hz, 1 H), 3.38 (d, *J* = 14.5 Hz, 1 H), 3.38 (m, 1H), 2.46 (s, 3 H), 2.27 (dq, *J* = 14.1, 7.1 Hz, 1 H), 2.00 (dq, *J* = 13.8, 6.2 Hz, 1 H),

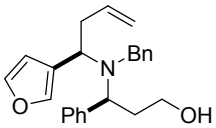
1.78 (dd, *J* = 14.9, 9.9 Hz, 1 H), 1.68 (dd, *J* = 14.9, 2.5 Hz, 1 H), 1.58-1.12 (m, 10 H), 1.40 (s, 9H), 0.91 (t, *J* = 7.1 Hz, 3 H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 172.1, 144.6, 140.9, 139.2, 133.3, 129.8, 128.7, 128.6 (2 C), 128.5, 128.0, 127.6, 127.1, 80.1, 68.7, 59.1, 53.8, 50.1, 34.0, 33.0, 32.0, 28.2, 26.8, 22.8, 21.8, 14.3.

(±)-(2*R*,3*S*,6*R*)-*Tert*-Butyl 1-benzyl-2-pentyl-6-phenylpiperidine-3-carboxylate 11



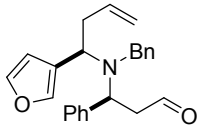
To a solution of the above compound (201 mg, 0.34 mmol) in THF (4 mL) was added at -70°C a solution of LiHMDS (1M in THF, 1.36 mL, 1.36 mmol) and the resulting mixture was stirred at -70°C for 30 min then 4 h at rt. Water (2 mL) and Et_2O (4 mL) were added. The organic layer was collected, and the aqueous layer was extracted with Et_2O (4 mL). The organic phases were combined, dried over Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel eluting with a 9:1 mixture of PE/Et_2O to give **11** as a white solid (103 mg, 72%). Mp 78°C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.44 (d, *J* = 7.6 Hz, 2 H), 7.32 (t, *J* = 7.6 Hz, 2 H), 7.23-7.19 (m, 3 H), 7.18-7.12 (m, 3 H), 3.83 (d, *J* = 15.6 Hz, 1 H), 3.51 (dd, *J* = 10.6, 2.8 Hz, 1 H), 3.46 (d, *J* = 15.6 Hz, 1 H), 2.89 (d, *J* = 10.3 Hz, 1 H), 2.57 (td, *J* = 10.9, 3.5 Hz, 1 H), 1.92 (dt, *J* = 11.7, 5.6 Hz, 1 H), 1.82-1.70 (m, 2 H), 1.68-1.57 (m, 3 H), 1.48 (s, 9 H), 1.40-1.35 (m, 3 H), 1.23-1.15 (m, 2 H), 0.92 (m, 1 H), 0.84 (t, *J* = 7.4 Hz, 4H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 174.8, 145.5, 139.8, 128.9, 128.4, 128.1, 127.8, 127.0, 126.3, 80.2, 66.7, 62.7, 54.0, 47.2, 34.3, 32.2, 31.2, 28.5, 28.2, 23.0, 22.8, 14.3; HRMS(ES$^+$): m/z $[M+H]^+$ calcd for $C_{28}H_{40}NO_2$: 422.3059; found : 422.3062.

(±)-(*S*)-3-{Benzyl[(*R*)-1-(furan-3-yl)but-3-en-1-yl]amino}-3-phenylpropan-1-ol



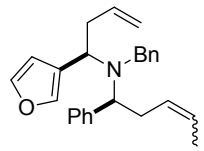
To a solution of **3b** (703 mg, 1.63 mmol) in THF (12 mL) at 0°C was added dropwise a solution of $LiAlH_4$ (2 M in THF, 1 mL, 2 mmol), and the resulting solution was stirred for 14 h at rt. The reaction mixture was cooled to 0°C prior to careful addition of a solution of Rochelle salt (10%, 5 mL). After 15 min of stirring Et_2O (10 mL) was added and the organic layer was collected. The remaining white paste was triturated with AcOEt (2x 5 mL). The organic phases were combined, dried over Na_2SO_4, filtered and concentrated under reduced pressure to give the title compound (480 mg, 81%) which was used in the next step without purification. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.46-7.22 (m, 14 H), 6.47 (s, 1 H), 5.52 (ddt, *J* = 17.1, 10.2, 6.9 Hz, 1 H), 4.87 (d, *J* = 10.2 Hz, 1 H), 4.81 (d, *J* = 17.2 Hz, 1 H), 4.05-3.98 (m, 2H), 3.96 (dd, *J* = 10.5, 3.5 Hz, 1H), 3.69 (d, *J* = 13.9 Hz, 1H), 3.64 (dt, *J* = 10.9, 5.5 Hz, 1H), 3.46 (ddd, *J* = 10.8, 7.7, 4.7 Hz, 1H), 2.32 (dtd, *J* = 14.0, 8.0, 5.1 Hz, 1H), 2.26 (br s, 1 H), 1.93 (m, 1H), 1.77 (dtd, *J* = 14.3, 6.0, 4.7 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 143.1, 141.5, 140.7, 140.6, 136.4, 129.0, 128.7, 128.6 (2 C), 127.5, 127.2, 126.6, 116.3, 111.1, 61.4, 59.9, 53.7, 50.5, 35.1, 34.7.

(±)-(S)-3-{Benzyl[(R)-1-(furan-3-yl)but-3-en-1-yl]amino}-3-phenylpropanal



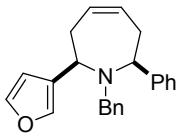
To a solution of oxalylchloride (0.21 mL, 2.39 mmol) in CH_2Cl_2 (15 mL) at -78°C was added dropwise a solution of DMSO (0.42 mL, 5.85 mmol) in CH_2Cl_2 (5 mL). After 15 min of stirring at -78°C, a solution of the above alcohol (480 mg, 1.38 mmol) in CH_2Cl_2 (5 mL) was slowly added. After 30 min of stirring at -78°C, Et_3N (1.15 mL, 8.3 mmol) was added dropwise. The resulting mixture was stirred for 15 min at -78°C, and the reaction mixture was slowly warmed to rt. Water (10 mL) was added and the organic layer was collected. The organic phase was washed with a saturated solution of Na_2CO_3 (5 mL), dried over Na_2SO_4, filtered and concentrated under reduced pressure to give 450 mg of material which contains the aldehyde as the major compound which was used directly in the next step without purification. ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.42 (dd, *J* = 3.4, 1.4 Hz, 1 H), 7.48-7.31 (m, 12 H), 6.44 (s, 1 H), 5.59 (ddt, *J* = 17.0, 10.3, 6.8 Hz, 1 H), 4.96-4.84 (m, 2H), 4.56 (dd, *J* = 8.3, 6.9 Hz, 1 H), 3.90 (m, 1 H), 3.86 (d, *J* = 13.9 Hz, 1 H), 3.70 (d, *J* = 13.9 Hz, 1 H), 2.99 (ddd, *J* = 16.2, 8.3, 3.5 Hz, 1 H), 2.68 (ddd, J =16.2, 7.0, 1.4 Hz, , 1 H), 2.26 (m, 1 H), 2.10 (m, 1 H).

(±)-(*S*)-*N*-Benzyl-*N*-[(*R*)-1-(furan-3-yl)but-3-en-1-yl]-1-phenylpent-3-en-1-amine 12



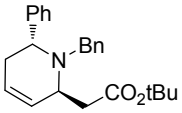
To a suspension of ethyltriphenylphosphonium bromide (1.62 g, 4.3 mmol) in THF (20 mL), was added dropwise a solution of LiHMDS (1 M, in THF, 2.8 mL, 2.8 mmol) at 0°C. After 15 min of stirring, a solution of the above aldehyde (450 mg, 1.25 mmol) in THF (2 mL) was added and the resulting mixture was stirred for 12 h at rt, then filtrated through a plug of celite and rinsed with Et_2O (20 mL). A saturated aqueous solution of NH_4Cl (10 mL) was added to the filtrate. The organic phase was washed with brine (10 mL), dried over $MgSO_4$, filtered and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel eluting with PE/Et_2O (98:2) to give **12** as a colorless oil (260 mg, 58%). Major Z isomer : ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.42-7.22 (m, 12 H), 6.48 (s, 1 H), 5.59 (ddt, *J* = 16.9, 9.0, 6.8 Hz, 1H), 5.36 (tq, *J* = 10.9, 6.6 Hz, 1 H), 5.20-5.09 (m, 1 H), 4.90 (d, *J* = 10.0 Hz, 1 H), 4.89 (d, *J* = 16.9 Hz, 1 H), 3.95-3.87 (m, 2 H), 3.85 (dd, *J* = 9.3, 5.5 Hz, 1 H), 3.74 (d, *J* = 14.4 Hz, 1 H), 2.62 (dt, *J* = 13.6, 6.3 Hz, 1 H), 2.43 (dt, *J* = 15.5, 8.1 Hz, 1 H), 2.22 (t, *J* = 6.8 Hz, 2 H), 1.56 (dd, *J* = 6.3, 1.5 Hz, 1 H), 1.50 (d, *J* = 6.7 Hz, 2 H); HRMS(ES$^+$): m/z $[M+H]^+$ calcd for $C_{26}H_{30}NO$: 372.2327; found : 372.2327.

(±)-(2*R*,7*S*)-1-Benzyl-2-(furan-3-yl)-7-phenyl-2,3,6,7-tetrahydro-1H-azepine 13



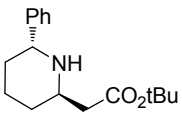
To a solution of **11** (181 mg, 0.5 mmol) in degassed CH_2Cl_2 (12 mL) was added Grubbs II catalyst (37 mg, 0.04 mmol). The resulting mixture was refluxed for 2 h under an atmosphere of Ar. The solvent was removed under reduced pressure and the residue was purified by column chromatography on silica gel eluting with PE/Et_2O (98:2) to give **13** (133 mg, 81%) as a pale yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.60 (d, *J* = 7.2 Hz, 2 H), 7.49 (s, 1 H), 7.40-7.33 (m, 5 H), 7.30-7.24 (m, 3 H), 7.20 (t, *J* = 7.3 Hz, 1 H), 6.54 (s, 1 H), 5.73 (ddt, *J* = 11.2, 5.7, 2.7 Hz, 1 H), 5.66 (ddt, *J* = 11.2, 7.0, 2.4 Hz, 1 H), 4.04 (d, *J* = 9.8 Hz, 1 H), 4.01 (d, *J* = 5.8 Hz, 1 H), 3.74 (d, *J* = 13.8 Hz, 1 H), 3.55 (d, *J* = 13.8 Hz, 1 H), 2.93 (d, *J* = 18.1 Hz, 1 H), 2.57 (m, 1 H), 2.41 (dt, *J* = 18.2, 6.0 Hz, 1 H), 2.18 (dd, *J* = 17.7, 6.8 Hz, 1 H);^{13}C NMR (126 MHz, $CDCl_3$) δ 147.3, 142.0, 140.4, 139.0, 131.2, 130.0, 128.8, 128.5, 128.3, 127.4, 127.1, 127.0, 126.8, 110.6, 68.7, 58.1, 55.3, 34.7, 26.9; HRMS(ES$^+$): m/z $[M+H]^+$ calcd for $C_{23}H_{24}NO$: 330.1858; found : 330.1860.

***Tert*-Butyl 2-[(*2S,6R*)-1-Benzyl-6-phenyl-1,2,5,6-tetrahydropyridin-2-yl]acetate 14**



To a solution of **3q** (91 mg, 0.21 mmol) in degassed CH_2Cl_2 (12 mL) was added Grubbs II catalyst (15 mg, 0.017 mmol). The resulting mixture was refluxed for 2 h under an atmosphere of Ar. The solvent was removed under reduced pressure and the residue was purified by column chromatography on silica gel eluting with PE/Et_2O (9:1) to give **14** (72 mg, 94%) as a pale yellow solid. Mp 60°C; $[\alpha]_D$ +76.2 (*c* 1, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.58 (d, *J* = 7.5 Hz, 2 H), 7.39 (t, *J* = 7.6 Hz, 2 H), 7.24 (tt, *J* = 14.9, 5.4 Hz, 6 H), 6.06 (m, 1 H), 5.82 (m, 1 H), 4.29 (dd, *J* = 11.0, 4.3 Hz, 1 H), 3.62 (m, 1 H), 3.46 (d, *J* = 13.6 Hz, 1 H), 3.40 (d, *J* = 13.6 Hz, 1 H), 2.67 (dd, *J* = 14.3, 7.9 Hz, 1 H), 2.60 (ddq, *J* = 17.4, 11.0, 2.2 Hz, 1 H), 2.48 (dd, *J* = 14.4, 7.0 Hz, 1 H), 2.36 (dt, *J* = 17.5, 4.4 Hz, 1 H), 1.44 (s, 9 H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 171.1, 142.5, 139.9, 128.9, 128.4, 128.2, 128.1, 127.9, 127.0, 126.8 126.2, 80.3, 54.4, 50.5, 41.14, 28.2, 24.2; HRMS(ES$^+$): m/z $[M+H]^+$ calcd for $C_{24}H_{30}NO_2$: 364.2277; found : 364.2277.

***Tert*-Butyl 2-[(2*R*,6*R*)-6-phenylpiperidin-2-yl]acetate**



A solution of **14** (67 mg, 0.18 mmol), HCl (6M, 0.05 mL) and Pd/C (10%, 30 mg) in MeOH (4 mL) and stirred under an atmosphere of H_2 for 14h. The crude mixture was filtered through a pad of celite and the filtrate was

concentrated under reduced pressure. The residue was diluted in CH_2Cl_2 (8 mL) then washed with an aqueous solution of NaOH (5%, 5 mL). The organic phases was dried over $MgSO_4$, filtered and concentrated under reduced pressure to give the title compound (42 mg, 84 %) as a pale yellow oil. $[\alpha]_D$ 0 (*c* 0.7, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.42 (d, *J* = 7.4 Hz, 2 H), 7.35 (t, *J* = 7.6 Hz, 2 H), 7.25 (t, *J* = 7.3 Hz, 1 H), 4.03 (dd, *J* = 8.8, 3.3 Hz, 1 H), 3.58 (dq, *J* = 9.2, 4.6 Hz, 1 H), 2.76 (dd, *J* = 15.1, 9.4 Hz, 1 H), 2.40 (dd, *J* = 15.1, 4.9 Hz, 1 H), 1.90-1.63 (m, 5 H), 1.54-1.49 (m, 1 H), 1.46 (s, 9 H); ^{1}H NMR (126 MHz, $CDCl_3$) δ 172.1, 144.8, 128.5, 126.9, 126.9, 80.7, 54.4, 49.5, 38.8, 33.3, 29.9, 28.3, 20.3.

Literature data for analogous *Cis* methyl ester[10]

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39-7.35 (2 H, m,), 7.34-7.28 (2 H, m), 7.27-7.21 (1 H, m), 3.69 (1 H, dd, *J* = 10.8, 2.5 Hz), 3.66 (3 H, s), 3.17-3.10 (1 H, m), 2.51-2.42 (2 H, m), 1.94-1.85 (1 H, m), 1.81-1.73 (1 H, m), 1.69-1.62 (1 H, m), 1.61-1.41 (2 H, m), 1.32-1.20 (1 H, m); ^{1}H NMR (100 MHz, $CDCl_3$) δ 172.9, 145.1, 128.3,
127.1, 126.8, 61.9, 53.9, 51.6, 41.3, 34.1, 31.8, 25.0;

Literature data for analogous *Trans* methyl ester[10]

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42-7.38 (2 H, m), 7.36-7.30 (2 H, m), 7.27-7.21 (1 H, m), 4.00 (1 H, dd, *J* = 8.7, 3.4 Hz), 3.69 (3 H, s), 3.63-3.56 (1 H, m), 2.86 (1 H, dd, *J* = 15.5, 9.4 Hz), 2.47 (1 H, dd, *J* = 15.5, 4.8 Hz), 1.89-1.61 (5 H, m), 1.55-1.46 (1 H, m); ^{1}H NMR (100 MHz, $CDCl_3$) δ 173.0, 144.2, 128.4, 126.9, 126.7, 54.2, 51.7, 49.1, 37.0, 32.9, 29.7, 20.0;

[10] J. D. Cuthbertson and R. J. K. Taylor, *Angew. Chem., Int. Ed*. 2013, **52**, 1490.