Multi-Component Asymmetric Aziridination of Aldehydes

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Supporting Information

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A. General Information

All reactions were carried out in flame-dried glassware under an atmosphere of nitrogen unless otherwise indicated. Toluene was distilled from sodium under nitrogen. Hexanes and ethyl acetate were ACS grade and used as purchased.

Melting points were recorded on a Thomas Hoover capillary melting point apparatus and are uncorrected. IR spectra were recorded in KBr matrix (for solids) and on NaCl disc (for liquids) on a Nicolet IR/42 spectrometer. ^{1}H NMR and ^{13}C NMR were recorded on a Varian 300 MHz or VXR-500 MHz spectrometer using $CDCl_3$ as solvent (unless otherwise noted) with the residual solvent peak as the internal standard (^{1}H NMR : 7.24 ppm, ^{13}C NMR : 77 ppm). Chemical shifts were reported in parts per million. Low-resolution Mass Spectrometry and High Resolution Mass Spectrometry were performed in the Department of Chemistry at Michigan State University. Analytical thin-layer chromatography (TLC) was performed on Silicycle silica gel plates with F-254 indicator. Visualization was by short wave (254 nm) and long wave (365 nm) ultraviolet light, or by staining with phosphomolybdic acid in ethanol or with potassium permanganate. Column chromatography was performed with silica gel 60 (230 – 450 mesh).

HPLC analyses were peformed using a Varian Prostar 210 Solvent Delivery Module with a Prostar 330 PDA Detector and a Prostar Workstation. Chiral HPLC data for the aziridines were obtained using a CHIRALCEL OD-H column, CHIRALPAK AD column, CHIRALPAK AS column and PIRKLE COVALENT (R, R) WHELK-O 1 column.

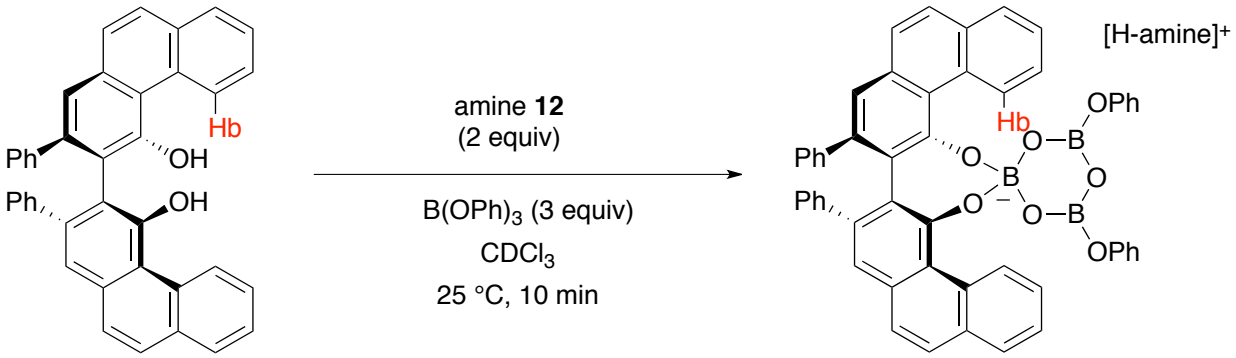
Optical rotations were obtained on a Perkin-Elmer 341 polarimeter at a wavelength of 589 nm (sodium D line) using a 1.0 decimeter cell with a total volume of 1.0 mL. Specific rotations are reported in degrees per decimeter at 20 °C and the concentrations are given in gram per 100 mL in ethyl acetate unless otherwise noted.

All reagents were purified by simple distillation or crystallization with simple solvents unless otherwise indicated. Ethyl diazoacetate **2**, triphenylborate obtained from Aldrich Chemical Co., Inc. and used as received. VAPOL and VANOL were made according to published procedure.[1] These ligands are also commercially available from Aldrich Chemical Co., Inc and Strem Chemicals. bis-(3,5-di-methyl-4-methoxyphenyl)methanamine **12** (MEDAM amine) was made according to the published procedure.[2] Aldehydes **4a**, **4b** and **4g-s** were

obtained from Aldrich Chemical Co., Inc. and and were sublimed or distilled prior to use. Aldehydes **4c**[3], **4d**[4], **4e**[5] and **4f**[6] were made according to published procedure.

B. NMR analysis of a mixture of VAPOL, and $B(OPh)_3$ and amine 12:

As discussed in the manuscript, a mixture of (*S*)-VAPOL and $B(OPh)_3$ gives boroxinate catalyst in 50 % yield when amine **12** was used as the base. The yield was determined by integration against an internal standard (Ph_3CH). It is to be noted that characteristic peaks for a boroxinate catalyst are δ 10.2-10.4 and δ 5.5-5.7 in ^1H NMR and ^{11}B NMR respectively.[7] An additional peak at δ 1.3 in ^{11}B NMR was also observed (Figure 3). This peak is tentatively assigned to be of the tetraphenoxy borate salt of the amine (unpublished results by Gupta, A. K. and Wulff, W. D.).



(*S*)-VAPOL **8**
(1 equiv)
δ = 9.77 ppm
(Hb)

boroxinate
δ = 10.37 ppm
(Hb)

Procedure: To a 10 mL flame-dried single-necked round bottom flask, equipped with a stir bar and a rubber septum and filled with argon was added (*S*)-VAPOL **8** (54 mg, 0.10 mmol, 1.0 equiv), $B(OPh)_3$ (87 mg, 0.30 mmol, 3.0 equiv), amine **12** (59.9 mg, 0.200 mmol), Ph_3CH (12.2 mg, 0.500 mmol) and $CDCl_3$ (1 mL). The resultant mixture was stirred for 10 min at room temperature. The resulting solution was then directly transferred to a quartz NMR tube (freshly flame-dried) and was subjected to NMR analysis. ^1H and ^{11}B NMR spectra for boroxinate catalyst with amine **12** are shown below:

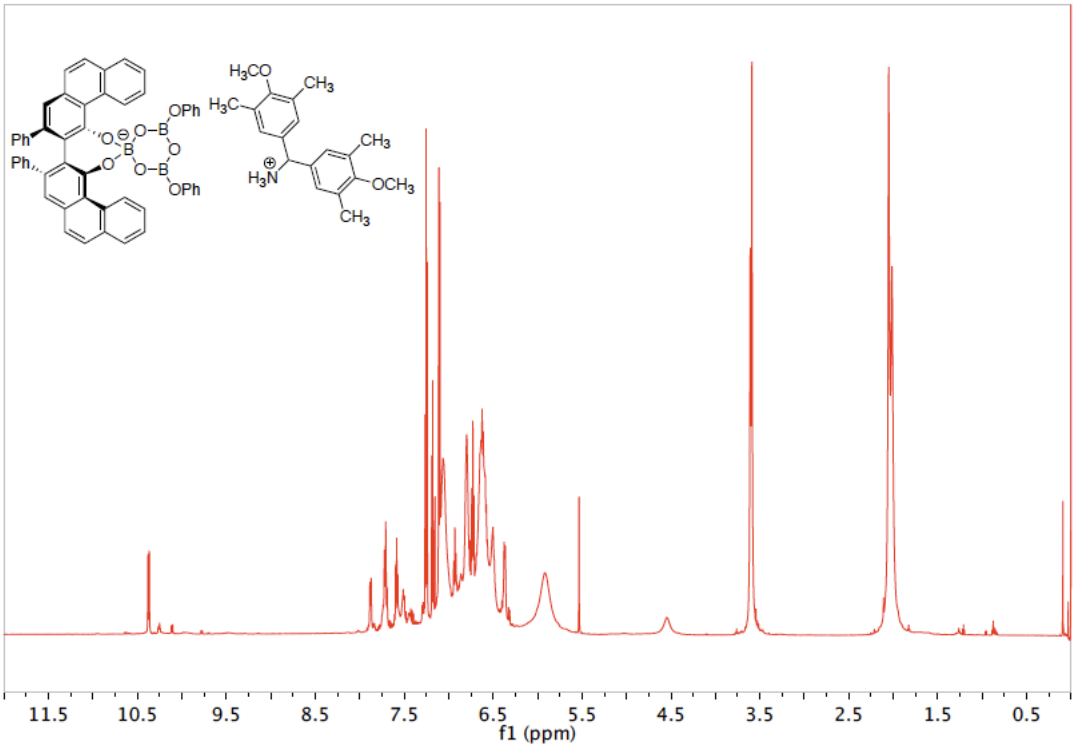


Figure 1: ^{1}H NMR of boroxinate catalyst with amine **12**.

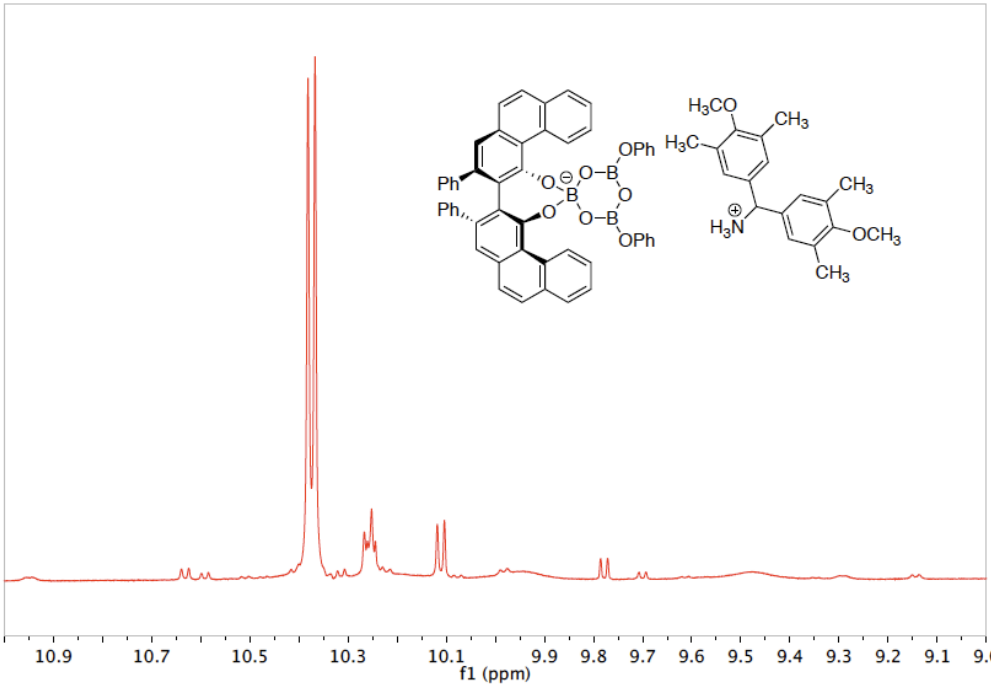


Figure 2: ^{1}H NMR of the bay region of boroxinate catalyst with amine **12**.

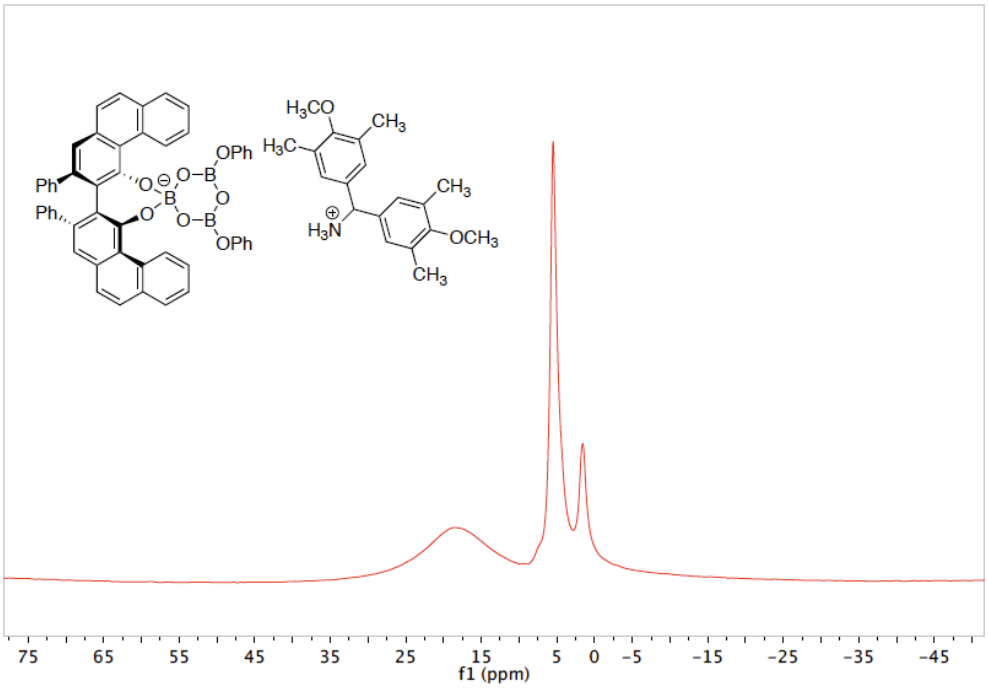
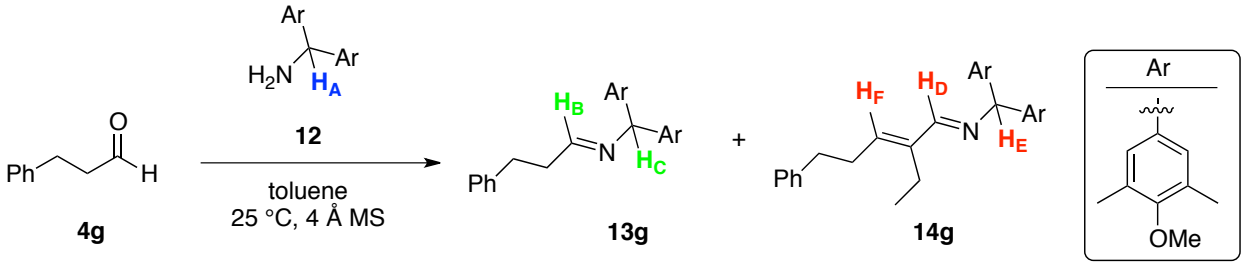


Figure 3: ^{11}B NMR of boroxinate catalyst with amine **12**.

C. Attempt to make imine 13g from aldehyde 4g:

As discussed in the manuscript, when aldehyde **4g** is treated with amine **12**, the imine **13g** does form but long before complete formation of the imine can be realized, self-condensation of the imine begins to occur which gives rise to the conjugated imine **14g** and this imine is very sluggish in the aziridination reaction. The same observations were made for aldehyde **4e** also. The formation of imine was followed by ^{1}H NMR analysis.



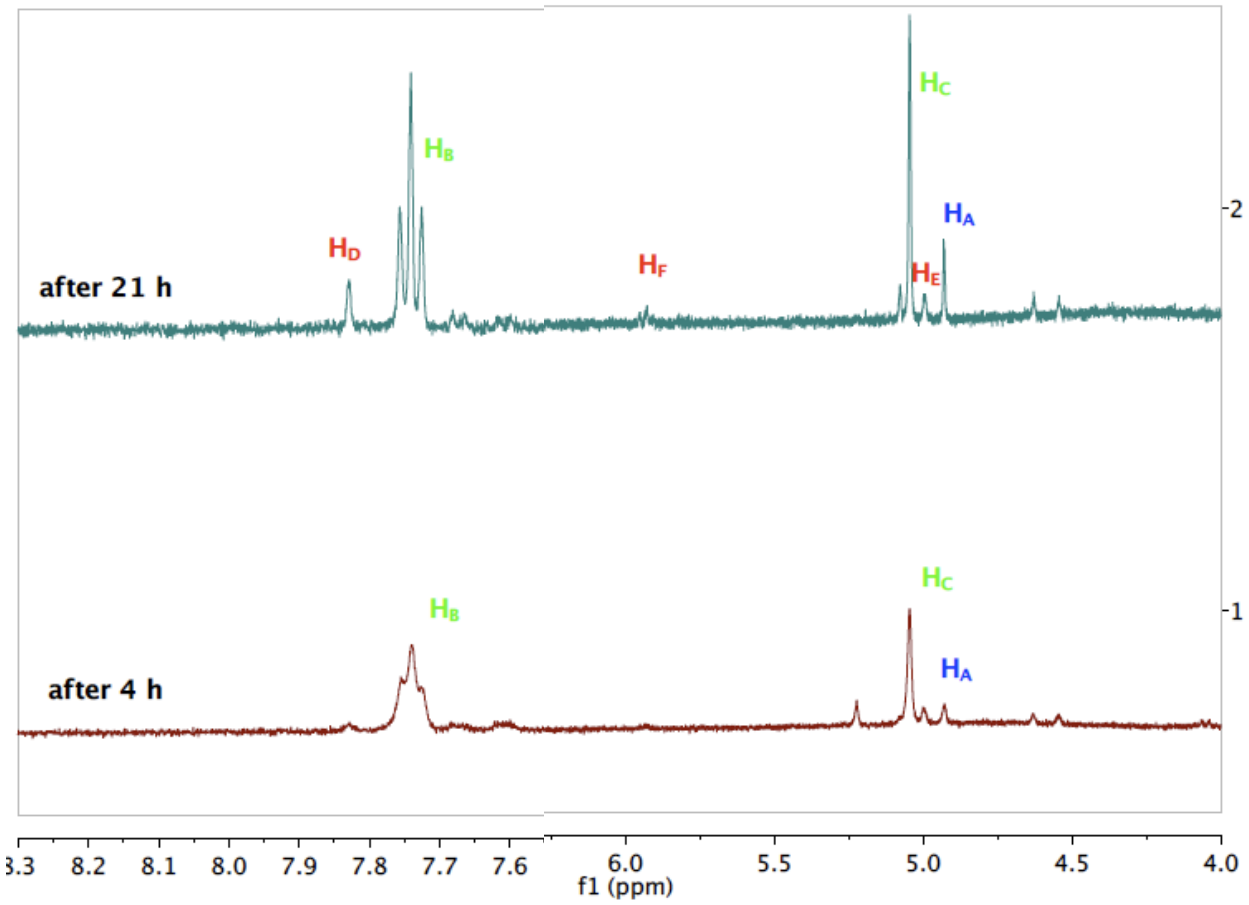


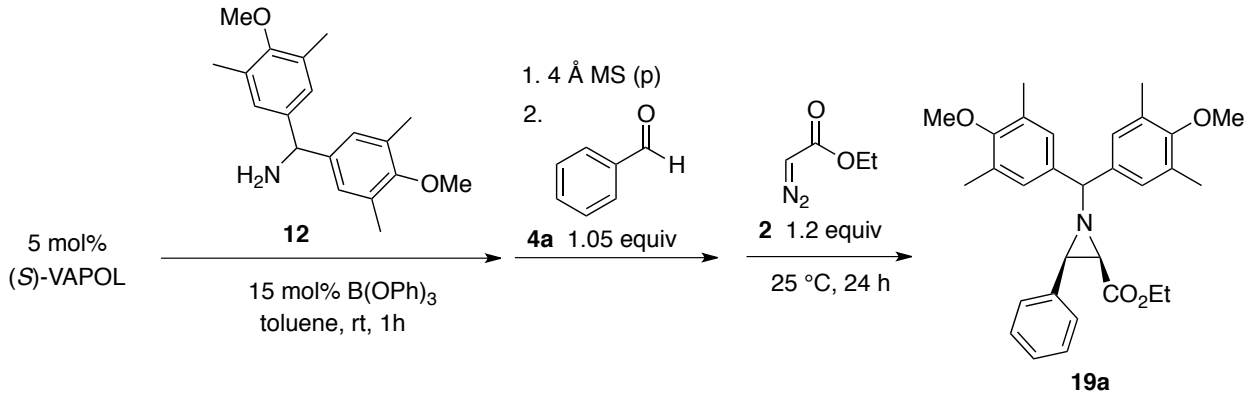
Figure 4: ^{1}H NMR spectra of the reaction mixture (scheme 2 in manuscript) in toluene. Entry 1: ^{1}H NMR taken after 4 h. Entry 2: ^{1}H NMR taken after 21 h.

The above stacked plot depicts the presence of the aldol adduct even before the complete formation of imine.

Procedure: To a 5 mL flame-dried single-necked round bottom flask, equipped with a stir bar, filled with argon was added MEDAM amine **12** (59.9 mg, 0.200 mmol), 4Å MS (50 mg, freshly dried) and dry toluene (1 mL). After stirring for 10 min, aldehyde **4g** (28.2 mg, 0.210 mmol, 1.05 equiv) was added. The reaction mixture was stirred at room temperature. The crude reaction mixture was then monitored at different time intervals by ^{1}H NMR.

D. Different protocols for MCAZ: Procedures A and B

Procedure A: Catalyst @ 25 °C, 1 h and EDA 2 added immediately after the addition of the aldehyde 4a.



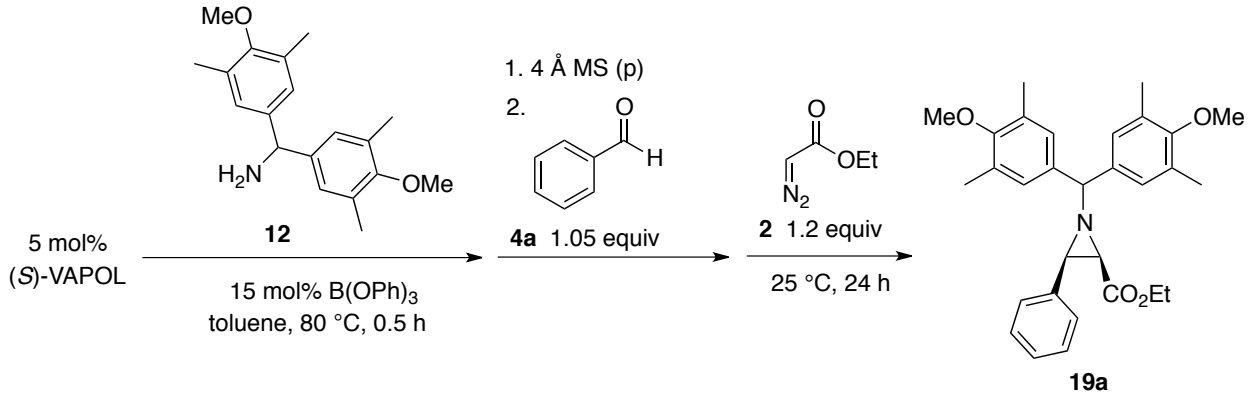
(2*R*,3*R*)-ethyl-1-(bis(4-methoxy-3,5-dimethylphenyl)methyl)-3-phenylaziridine-2-carboxylate 19a: To a 10 mL flame-dried single-necked round bottom flask equipped with a stir bar and filled with argon was added (*S)*-VAPOL (14 mg, 0.025 mmol), $B(OPh)_3$ (22 mg, 0.075 mmol) and amine **12** (149.7 mg, 0.5000 mmol). Dry toluene (1 mL) was added under an argon atmosphere to dissolve the reagents. The flask was fitted with a rubber septum and a nitrogen balloon. The reaction mixture was stirred at room temperature for 1 h. Thereafter, 4Å Molecular Sieves (150 mg, freshly flame-dried) was added followed by the addition of the aldehyde **4a** (52.0 μL, 0.525 mmoL, 1.05 equiv). To this solution was rapidly added ethyl diazoacetate (EDA) **2** (62 μL, 0.60 mmoL, 1.2 equiv). The resulting mixture was stirred for 24 h at room temperature. The reaction was dilluted by addition of hexane (6 mL). The reaction mixture was then filtered through a Celite pad to a 100 mL round bottom flask. The reaction flask was rinsed with EtOAc (3 mL × 3) and the rinse was filtered through the same Celite pad. The resulting solution was then concentrated *in vacuo* followed by exposure to high vacuum (0.05 mm Hg) for 1 h to afford the crude aziridine as an off-white solid.

The *cis/trans* ratio was determined by comparing the ^{1}H NMR integration of the ring methine protons for each aziridine in the crude reaction mixture. The *cis* (J = 7-8 Hz) and the *trans* (J = 2-3 Hz) coupling constants were used to differentiate the two isomers. The yields of the acyclic enamine side products **23a** and **24a** were determined by ^{1}H NMR analysis of the crude reaction mixture by integration of the *N*-H proton relative to the that of the *cis*-aziridine

methine protons with the aid of the isolated yield of the *cis*-aziridine. Purification of the crude aziridine by silica gel chromatography (30 mm × 300 mm column, 9:1 hexanes/EtOAc as eluent, gravity column) afforded pure cis-aziridine **19a** as a white solid (mp 107-108 ºC on 99.8% ee material) in 97 % isolated yield (230 mg, 0.490 mmol); *cis/trans*: >50:1. Enamine side products: <1 % yield of **23a** and <1 % yield of **23a.** The optical purity of **19a** was determined to be 98 % *ee* by HPLC analysis (CHIRALCEL OD-H column, 99:1 hexane/2-propanol at 226nm, flow-rate: 0.7 mL/min): retention times; R_t = 9.26 min (major enantiomer, **19a**) and R_t = 12.52 min (minor enantiomer, *ent*-**19a**).

Spectral data for **19a**: R_f = 0.42 (1:9 EtOAc/hexane); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 0.98 (t, 3H, *J* = 7.1 Hz), 2.18 (s, 6H), 2.24 (s, 6H), 2.55 (d, 1H, *J* = 6.8 Hz), 3.10 (d, 1H, *J* = 6.6 Hz), 3.62 (s, 3H), 3.66 (s, 1H), 3.68 (s, 3H) 3.87-3.97 (m, 2H), 7.09 (s, 2H), 7.18 (s, 2H), 7.21-7.24 (m, 3H), 7.36 (d, 2H, *J* = 7.3 Hz); ^{13}C ($CDCl_3$, 125 MHz) δ 14.01, 16.16, 16.22, 46.26, 48.20, 59.52, 59.58, 60.47, 77.04, 127.21, 127.41, 127.70, 127.80,127.85, 130.59, 130.60, 135.33, 137.79, 137.96, 155.95, 156.10, 168.01; IR (thin film) 2961 vs, 1750 vs, 1414 vs, 1202 vs cm^{-1}; Mass spectrum: *m/z* (% rel intensity) 473 M+ (0.27), 284(78), 283 (100), 268 (34), 253 (20), 237 (11), 210(10), 117 (18), 89 (11); Anal calcd for $C_{30}H_{35}NO_4$: C, 76.08; H, 7.45; N, 2.96. Found: C, 76.31; H, 7.28; N, 2.82; $[\alpha]^{23}_D$ +41.3 (*c* 1.0, EtOAc) on 99% ee material (HPLC). These spectral data match those previously reported for this compound.[2]

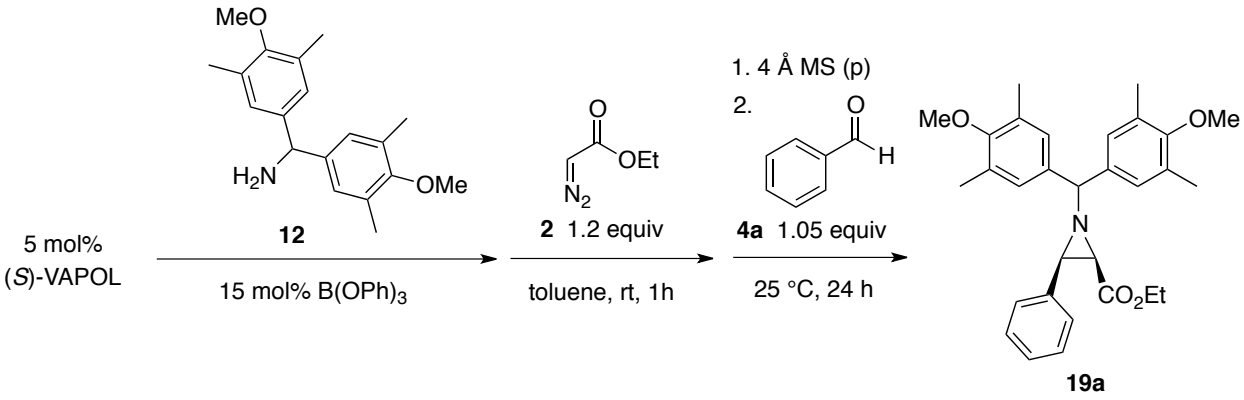
Procedure B: Catalyst @ 80 °C, 0.5 h and EDA 2 added immediately after the addition of the aldehyde 4a.



(2*R*,3*R*)-ethyl-1-(bis(4-methoxy-3,5-dimethylphenyl)methyl)-3-phenylaziridine-2-carboxylate 19a: To a 10 mL flame-dried home-made Schlenk flask, prepared from a single-necked 25 mL pear-shaped flask that had its 14/20 glass joint replaced with a high vacuum threaded Teflon valve, equipped with a stir bar and filled with argon was added (*S)*-VAPOL (14 mg, 0.025 mmol), $B(OPh)_3$ (22 mg, 0.075 mmol) and amine **12** (149.7 mg, 0.5000 mmol). Under an argon flow through the side-arm of the Schlenk flask, dry toluene (2 mL) was added. The flask was sealed by closing the Teflon valve, and then placed in an oil bath (80 ºC) for 0.5 h. The flask was then allowed to cool to room temperature and open to argon through side-arm of the Schlenk flask. To the flask containing the catalyst was added the 4Å Molecular Sieves (150 mg, freshly flame-dried) and aldehyde **4a** (52.0 μL, 0.525 mmoL, 1.05 equiv). To this solution was rapidly added ethyl diazoacetate (EDA) **2** (62 μL, 0.60 mmoL, 1.2 equiv). The resulting mixture was stirred for 24 h at room temperature. The reaction was dilluted by addition of hexane (6 mL). The reaction mixture was then filtered through a Celite pad to a 100 mL round bottom flask. The reaction flask was rinsed with EtOAc (3 mL × 3) and the rinse was filtered through the same Celite pad. The resulting solution was then concentrated *in vacuo* followed by exposure to high vacuum (0.05 mm Hg) for 1 h to afford the crude aziridine as an off-white solid.

The *cis/trans* ratio was determined by comparing the ^{1}H NMR integration of the ring methine protons for each aziridine in the crude reaction mixture. The *cis* (*J* = 7-8 Hz) and the *trans* (*J* = 2-3 Hz) coupling constants were used to differentiate the two isomers. The yields of the acyclic enamine side products **23a** and **24a** were determined by ^{1}H NMR analysis of the crude reaction mixture by integration of the *N*-H proton relative to the that of the *cis*-aziridine methine protons with the aid of the isolated yield of the *cis*-aziridine. Purification of the crude aziridine by silica gel chromatography (30 mm × 300 mm column, 9:1 hexanes/EtOAc as eluent, gravity column) afforded pure cis-aziridine **19a** as a white solid (mp 107-108 ºC on 99.8% ee material) in 97 % isolated yield (230 mg, 0.485 mmol); *cis/trans*: >50:1. Enamine side products: <1 % yield of **23a** and <1% yield of **24a.** The optical purity of **19a** was determined to be 98 % *ee* by HPLC analysis (CHIRALCEL OD-H column, 99:1 hexane/2-propanol at 226nm, flow-rate: 0.7 mL/min): retention times; R_t = 9.26 min (major enantiomer, **19a**) and R_t = 12.52 min (minor enantiomer, *ent*-**19a**).

Procedure A with EDA added prior to aldehyde: Catalyst + EDA 2 @ 25 °C, 1 h and then addition of the aldehyde 4a.

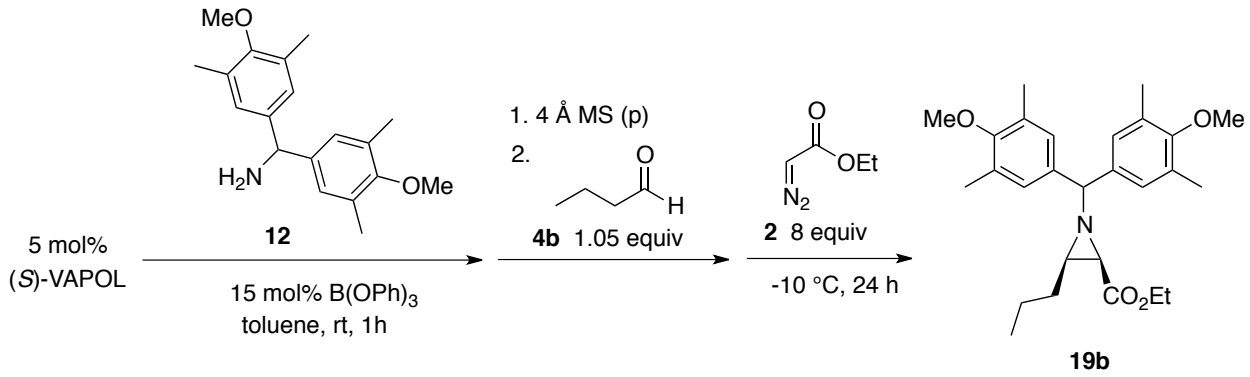


(2*R*,3*R*)-ethyl-1-(bis(4-methoxy-3,5-dimethylphenyl)methyl)-3-phenylaziridine-2-carboxylate 19a: To a 10 mL flame-dried single-necked round bottom flask equipped with a stir bar and filled with argon was added in the following order (*S)*-VAPOL (14 mg, 0.025 mmol), $B(OPh)_3$ (22 mg, 0.075 mmol), amine **12** (149.7 mg, 0.5000 mmol) and ethyl diazoacetate (EDA) **2** (62 μL, 0.60 mmoL, 1.2 equiv). Dry toluene (1 mL) was added under an argon atmosphere to dissolve the reagents. The flask was fitted with a rubber septum and a nitrogen balloon. The reaction mixture was stirred at room temperature for 1 h. Thereafter, 4Å Molecular Sieves (150 mg, freshly flame-dried) was added followed by the addition of the aldehyde **4a** (52.0 μL, 0.525 mmoL, 1.05 equiv). The resulting mixture was stirred for 24 h at room temperature. The reaction was dilluted by addition of hexane (6 mL). The reaction mixture was then filtered through a Celite pad to a 100 mL round bottom flask. The reaction flask was rinsed with EtOAc (3 mL × 3) and the rinse was filtered through the same Celite pad. The resulting solution was then concentrated *in vacuo* followed by exposure to high vacuum (0.05 mm Hg) for 1 h to afford the crude aziridine as an off-white solid.

The *cis/trans* ratio was determined by comparing the ^{1}H NMR integration of the ring methine protons for each aziridine in the crude reaction mixture. The *cis* (J = 7-8 Hz) and the *trans* (J = 2-3 Hz) coupling constants were used to differentiate the two isomers. The yields of the acyclic enamine side products **23a** and **24a** were determined by ^{1}H NMR analysis of the crude reaction mixture by integration of the *N*-H proton relative to the that of the *cis*-aziridine methine protons with the aid of the isolated yield of the *cis*-aziridine. Purification of the crude

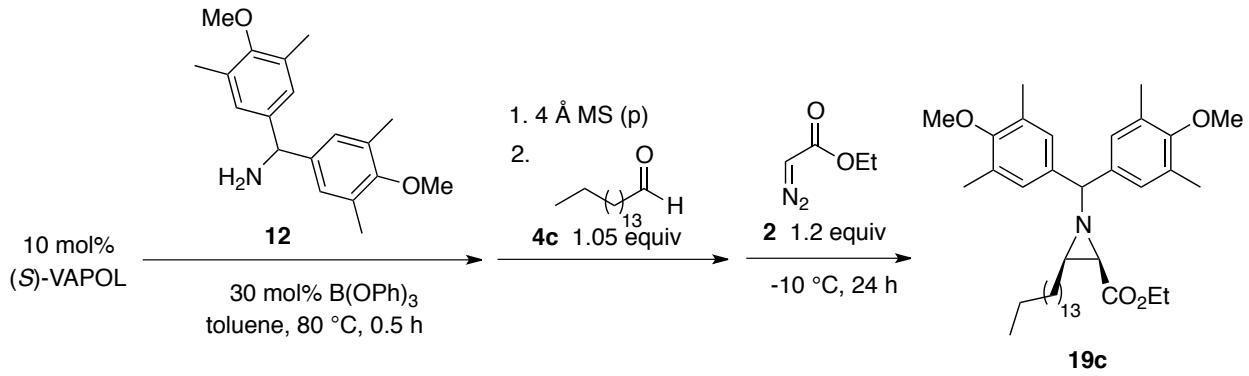
aziridine by silica gel chromatography (30 mm × 300 mm column, 9:1 hexanes/EtOAc as eluent, gravity column) afforded pure cis-aziridine **19a** as a white solid (mp 107-108 ºC on 99.8% ee material) in 94 % isolated yield (223 mg, 0.47 mmol); *cis/trans*: >50:1. Enamine side products: <1 % yield of **23a** and <1 % yield of **24a.** The optical purity of **19a** was determined to be 98 % *ee* by HPLC analysis (CHIRALCEL OD-H column, 99:1 hexane/2-propanol at 226nm, flow-rate: 0.7 mL/min): retention times; R_t = 9.26 min (major enantiomer, **19a**) and R_t = 12.52 min (minor enantiomer, *ent*-**19a**).

F. Synthesis of alkyl MEDAM aziridines 19b-j (*via* Procedure A)



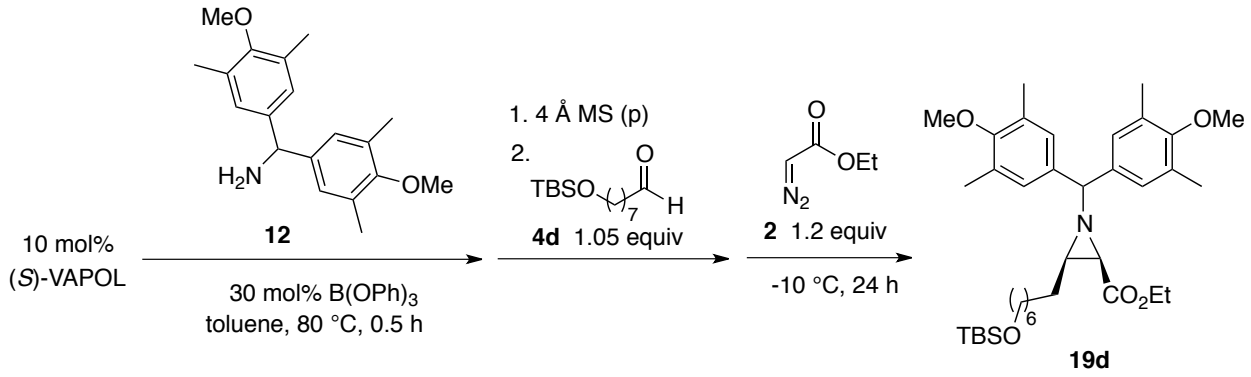
(2*R*,3*R*)-ethyl-1-(bis(4-methoxy-3,5-dimethylphenyl)methyl)-3-propylaziridine-2-carboxylate 19b: Aldehyde **4b** (46.0 μL, 38.0 mg, 0.525 mmol) was reacted according to the general Procedure A described above with (*S*)-VAPOL as ligand except except that the addition of aldehyde **4b** was carried out at –10 °C followed by the addition of EDA **2** (415 μL, 4.00 mmoL, 8.00 equiv) at the same temperature. The reaction was stirred at –10 °C for 24 h. Purification of the crude aziridine by silica gel chromatography (20 mm × 250 mm column, 4:2:0.1 hexanes/CH_2Cl_2/EtOAc, gravity column) afforded pure cis-aziridine **19b** as a yellow oil in 94 % isolated yield (207 mg, 0.490 mmol); *cis/trans*: not determined. Enamine side products: not observed. The optical purity of **19b** was determined to be 96% *ee* by HPLC analysis (CHIRALCEL OD-H column, 99:1 hexane/2-propanol at 226 nm, flow-rate: 0.7 mL/min): retention times; R_t = 4.73 min (major enantiomer, **19b**) and R_t = 5.68 min (minor enantiomer, *ent*-**19b**).

Spectral data for **19b**: R_f= 0.28 (4:2:0.1 hexanes/CH_2Cl_2/EtOAc); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 0.72 (t, 3H, *J* = 7.6 Hz), 0.98-1.08 (m, 1H), 1.11-1.20 (m, 1H), 1.23 (t, 3H, *J* = 7.1 Hz), 1.38-1.45 (m, 1H), 1.49-1.55 (m, 1H), 1.95 (q, 1H, *J* = 6.6 Hz), 2.18 (d, 1H, *J* = 6.8 Hz) 2.22 (s, 12H), 3.39 (s, 1H), 3.65 (s, 3H), 3.67 (s, 3H), 4.12-4.23 (m, 2H), 6.99 (s, 2H), 7.07 (s, 2H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 13.57, 14.33, 16.09, 16.16, 20.33 29.93, 43.53, 46.76, 59.56, 59.60, 60.64, 77.32, 127.41, 128.07, 130.44, 130.47, 137.75, 138.18, 155.81, 156.12, 169.69; IR (thin film) 2957vs, 1744s, 1483s, 1221s, 1182vs cm^{-1}; HRMS (ESI-TOF) *m/z* 440.2817 [(M+H$^+$); calcd. for $C_{27}H_{38}NO_4$: 440.2801]; $[\alpha]^{23}_D$ +95.3 (c 1.0, EtOAc) on 97 % ee material (HPLC). These spectral data match those previously reported for this compound.[2]



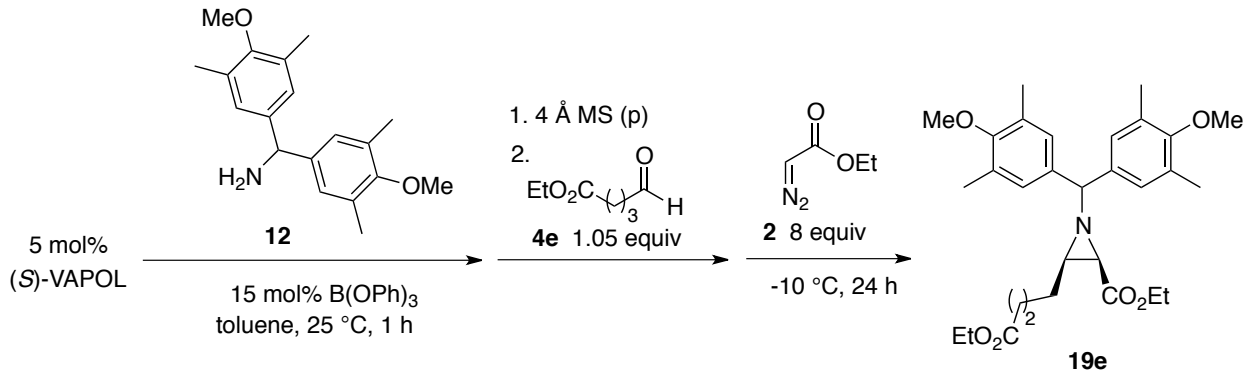
(2*R*,3*R*)-ethyl-1-(bis(4-methoxy-3,5-dimethylphenyl)methyl)-3-pentadecylaziridine-2-carboxylate 19c: Aldehyde **4c** (126 mg, 0.525 mmol) was reacted according to the general Procedure IIA described above with (*S*)-VAPOL as ligand except the following differences : 1) the addition of aldehyde **4c** was carried out at –10 °C followed by the addition of EDA **2** (62 µL, 0.60 mmoL, 1.2 equiv) at the same temperature; 2) the catalyst loading was 10 mol %. The reaction was stirred at –10 °C for 24 h. Purification of the crude aziridine by neutral alumina chromatography (20 mm × 250 mm column, 2:1:0.1 hexanes/CH_2Cl_2/Et_2O, gravity column) afforded pure cis-aziridine **19c** as a white solid (mp 41-42 ºC on 95% ee material) in 80 % isolated yield (243 mg, 0.400 mmol); *cis/trans*: not determined. Enamine side products: 6 % yield of **23c** and 4 % yield of **24c.** The optical purity of **19c** was determined to be 96% *ee* by HPLC analysis (PIRKLE COVALENT (R, R) WHELK-O 1 column, 99.5:0.5 hexane/2-propanol at 226 nm, flow-rate: 0.7 mL/min): retention times; R_t = 18.26 min (major enantiomer, **19c**) and R_t = 33.43 min (minor enantiomer, *ent*-**19c**).

Spectral data for **19c**: R_f= 0.31 (2:1:0.2 hexanes/CH_2Cl_2/Et_2O); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 0.86 (t, 3H, *J* = 7.0 Hz), 1.14-1.28 (m, 1H), 1.43-1.50 (m, 26H), 1.93 (q, 1H, *J* = 6.5 Hz), 2.18 (d, 1H, *J* = 6.5 Hz) 2.22 (s, 12H), 3.38 (s, 1H), 3.65 (s, 3H), 3.67 (s, 3H), 4.12-4.23 (m, 2H), 6.99 (s, 2H), 7.07 (s, 2H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 14.09, 14.34, 16.11, 16.16, 22.68, 27.24, 27.96, 29.18, 29.35, 29.51, 29.61, 29.62, 29.65, 29.68, 31.92, 43.56, 47.01, 59.57, 59.58, 60.64, 77.35, 127.41, 128.10, 130.42, 130.47, 137.78, 138.18, 155.81, 156.15, 169.69 (3 sp^3 carbon not located); IR (thin film) 2925vs, 1746s, 1484s, 1221s, 1183vs cm^{-1}; HRMS (ESI-TOF) *m/z* 608.4683 [(M+H$^+$); calcd. for $C_{39}H_{62}NO_4$: 608.4679]; $[\alpha]^{20}_D$ +57.9 (c 1.0, EtOAc) on 95 % ee material (HPLC).



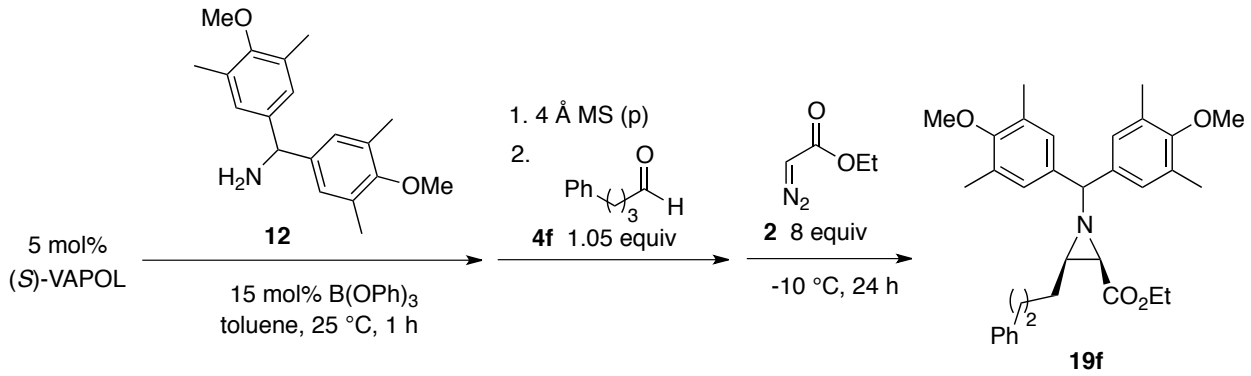
(2*R*,3*R*)-ethyl-1-(bis(4-methoxy-3,5-dimethylphenyl)methyl)-3-(7-((*tert*-butyldimethylsilyl)oxy)heptyl)aziridine-2-carboxylate 19d: Aldehyde **4d** (136 mg, 0.525 mmol) was reacted according to the general Procedure IIA described above with (*S*)-VAPOL as ligand except that the addition of aldehyde **4d** was carried out at –10 °C followed by the addition of EDA **2** (62 μL, 0.60 mmoL, 1.2 equiv) at the same temperature and the catalyst loading was 10 mol %. The reaction was stirred at –10 °C for 24 h. Purification of the crude aziridine by silica gel chromatography (30 mm × 300 mm column, 1:15 EtOAc/hexanes, gravity column) afforded pure cis-aziridine **19d** as a yellow oil in 80 % isolated yield (250 mg, 0.400 mmol); *cis/trans*: not determined. Enamine side products: <1 % yield of **23d** and 2.8 % yield of **24d.** The optical purity of **19d** was determined to be 98% *ee* by HPLC analysis (CHIRALCEL OD-H column, 99.5:0.5 hexane/2-propanol at 226 nm, flow-rate: 0.7 mL/min): retention times; R_t = 5.33 min (major enantiomer, **19d**) and R_t = 7.26 min (minor enantiomer, *ent*-**19d**).

Spectral data for **19d**: R_f = 0.28 (12:1 hexanes/EtOAc); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 0.02 (s, 6H), 0.87 (s, 9H), 1.11-1.21 (m, 8H), 1.24 (t, 3H, *J* = 7.1 Hz), 1.40-1.50 (m, 4H), 1.94 (q, 1H, *J* = 6.6 Hz), 2.19 (d, 1H, *J* = 6.8 Hz) 2.22 (s, 12H), 3.39 (s, 1H), 3.55 (t, 2H, *J* = 6.8 Hz), 3.65 (s, 3H), 3.67 (s, 3H), 4.12-4.22 (m, 2H), 6.99 (s, 2H), 7.08 (s, 2H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ -5.31, 14.31, 16.08, 16.12, 18.32, 25.62, 25.94, 27.17, 27.88, 29.12, 29.38, 32.80, 43.52, 46.92, 59.51, 59.52, 60.59, 63..22, 77.32, 127.37, 128.07, 130.38, 130.43, 137.74, 138.16, 155.79, 156.13, 169.63; IR (thin film) 2930s, 1746s, 1483s, 1221s, 1183vs cm^{-1}; HRMS (ESI-TOF) *m/z* 626.4243 [(M+H$^+$); calcd. for $C_{37}H_{60}NO_5Si$: 626.4241]; $[\alpha]^{20}_D$ +54.5 (c 1.0, EtOAc) on 98 % ee material (HPLC).



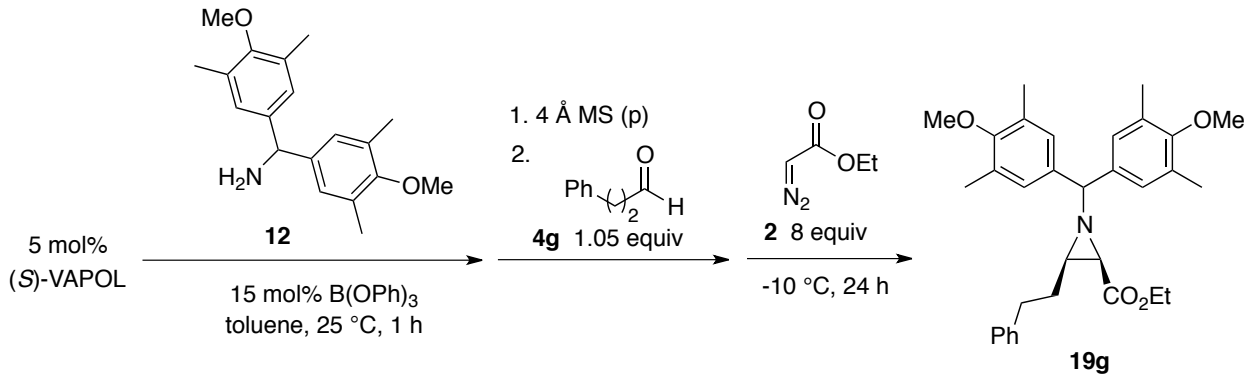
(2*R*,3*R*)-ethyl-1-(bis(4-methoxy-3,5-dimethylphenyl)methyl)-3-(4-ethoxy-4-oxobutyl)aziridine-2-carboxylate 19e: Aldehyde **4e** (72.0 μL, 76.0 mg, 0.525 mmol) was reacted according to the general Procedure A described above with (*S*)-VAPOL as ligand except that the addition of aldehyde **4e** was carried out at –10 °C followed by the addition of EDA **2** (415 μL, 4.0 mmoL, 8 equiv) at the same temperature. The reaction was stirred at –10 °C for 24 h. Purification of the crude aziridine by silica gel chromatography (30 mm × 300 mm column, 1:40 Et_2O/CH_2Cl_2; 1:30 Et_2O/CH_2Cl_2; 1:20 Et_2O/CH_2Cl_2, gravity column) afforded pure cis-aziridine **19e** as a semi solid in 82 % isolated yield (210 mg, 0.410 mmol); *cis/trans*: not determined. Enamine side products: not observed. The optical purity of **19e** was determined to be 97% *ee* by HPLC analysis (CHIRALCEL OD-H column, 99:1 hexane/2-propanol at 226 nm, flow-rate: 0.7 mL/min): retention times; R_t = 11.56 min (major enantiomer, **19e**) and R_t = 12.86 min (minor enantiomer, *ent*-**19e**).

Spectral data for **19e**: R_f = 0.31 (20:1 Et_2O/CH_2Cl_2); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 1.19 (t, 3H, *J* = 7.1 Hz), 1.24 (t, 3H, *J* = 7.1 Hz), 1.31-1.38 (m, 1H), 1.40-1.48 (m, 1H), 1.48-1.56 (m, 2H), 1.95 (q, 1H, *J* = 6.1 Hz), 2.07 (t, 2H, *J* = 7.6 Hz), 2.20 (d, 1H, *J* = 6.8 Hz), 2.22 (s, 12H), 3.39 (s, 1H), 3.65 (s, 3H), 3.66 (s, 3H), 4.04 (q, 2H, *J* = 7.1 Hz), 4.12-4.21 (m, 2H), 6.98 (s, 2H), 7.07 (s, 2H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 14.16, 14.28, 16.08, 16.15, 22.51, 27.28, 33.53, 43.43, 46.22, 59.55, 60.12, 60.73, 77.26, 127.31, 128.02, 130.49, 130.57, 137.61, 138.01, 155.81, 156.21, 169.48, 173.21 (one sp^3 carbon not located) ; IR (thin film) 2940vs, 1738s, 1483s, 1221s, 1183vs cm^{-1}; HRMS (ESI-TOF) *m/z* 512.3015 [$(M+H^+)$; calcd. for $C_{30}H_{42}NO_6$: 512.3012]; $[\alpha]^{20}_D$ –68.5 (c 1.0, EtOAc) on 97 % ee material (HPLC) of *ent*-**19e**.



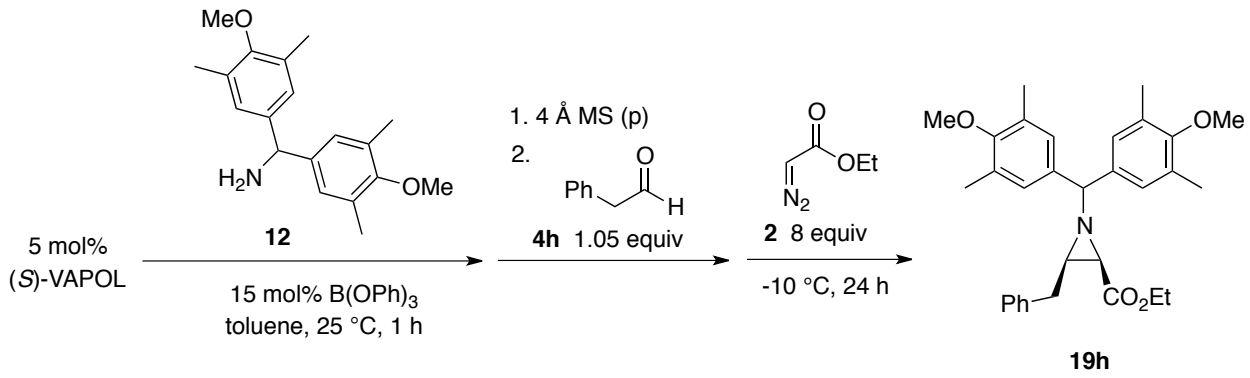
(2*R*,3*R*)-ethyl 1-(bis(4-methoxy-3,5-dimethylphenyl)methyl)-3-(3-phenylpropyl)aziridine-2-carboxylate 19f: Aldehyde **4f** (75.0 μL, 78.0 mg, 0.525 mmol) was reacted according to the general Procedure A described above with (*S*)-VAPOL as ligand except that the addition of aldehyde **4f** was carried out at –10 °C followed by the addition of EDA **2** (415 μL, 4.0 mmoL, 8 equiv) at the same temperature. The reaction was stirred at –10 °C for 24 h. Purification of the crude aziridine by silica gel chromatography (30 mm × 300 mm column, 1:9 EtOAc/hexanes, gravity column) afforded pure cis-aziridine **19f** as a yellow oil in 50 % isolated yield (129 mg, 0.250 mmol); *cis/trans*: not determined. Enamine side products: not observed. The optical purity of **19f** was determined to be 90% *ee* by HPLC analysis (CHIRALCEL OD-H column, 99:1 hexane/2-propanol at 226 nm, flow-rate: 0.7 mL/min): retention times; R_t = 7.47 min (major enantiomer, **19f**) and R_t = 9.52 min (minor enantiomer, *ent*-**19f**).

Spectral data for **19f**: R_f = 0.30 (1:9 hexanes/EtOAc); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 1.23 (t, 3H, *J* = 7.1 Hz), 1.27-1.35 (m, 1H), 1.40-1.48 (m, 1H), 1.50-1.61 (m, 2H), 1.97 (q, 1H, *J* = 7.1 Hz), 2.19 (s, 6H), 2.21 (d, 1H, *J* = 6.8 Hz) 2.23 (s, 6H), 2.42 (t, 2H, *J* = 8.1 Hz), 3.40 (s, 1H), 3.54 (s, 3H), 3.67 (s, 3H), 4.11-4.21 (m, 2H), 6.99-7.00 (m, 4H), 7.09 (s, 2H) 7.10-7.13 (m, 1H), 7.19-7.21 (m, 2H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 14.32, 16.08, 16.15, 27.69, 29.11, 35.38, 43.60, 46.61, 59.49, 59.56, 60.70, 77.36, 125.58, 127.33, 128.11, 128.16, 128.18, 130.49, 130.50, 137.67, 138.08, 142.30, 155.79, 156.24, 169.61; IR (thin film) 2930vs, 1744s, 1483s, 1221s, 1184vs cm^{-1}; HRMS (ESI-TOF) *m/z* 516.3115 [(M+H$^+$); calcd. for $C_{33}H_{42}NO_4$: 516.3114]; $[\alpha]^{20}_D$ +61.7 (c 1.0, EtOAc) on 93 % ee material (HPLC).



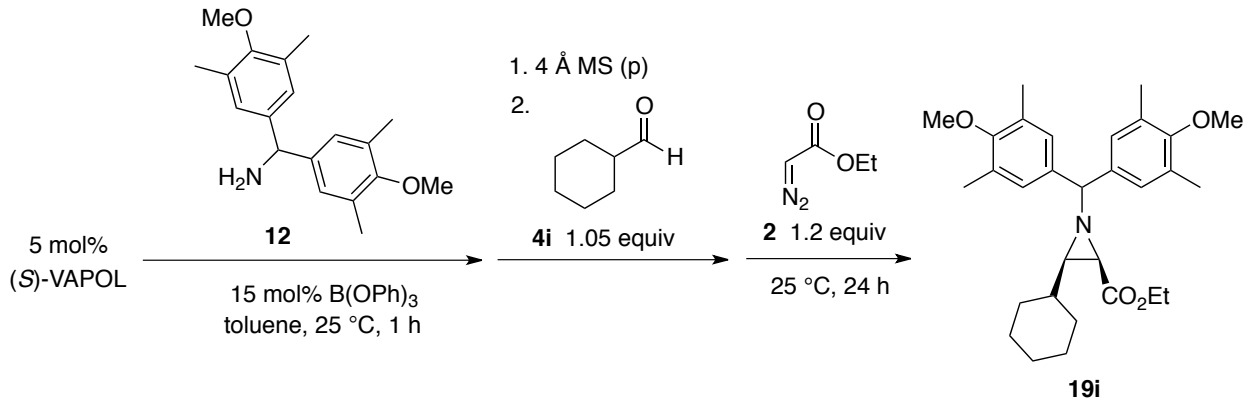
(2*R*,3*R*)-ethyl-1-(bis(4-methoxy-3,5-dimethylphenyl)methyl)-3-phenethylaziridine-2-carboxylate 19g: Aldehyde **4g** (70.0 μL, 70.0 mg, 0.525 mmol) was reacted according to the general Procedure A described above with (*S*)-VAPOL as ligand except that the addition of aldehyde **4g** was carried out at –10 °C followed by the addition of EDA **2** (415 μL, 4.0 mmoL, 8 equiv) at the same temperature. The reaction was stirred at –10 °C for 24 h. Purification of the crude aziridine by silica gel chromatography (30 mm × 300 mm column, 1:12 EtOAc/hexanes, gravity column) afforded pure cis-aziridine **19g** as a semi solid in 91 % isolated yield (228 mg, 0.460 mmol); *cis/trans*: not determined. Enamine side products: <1 % yield of **23g** and 1.8 % yield of **24g**. The optical purity of **19g** was determined to be 96% *ee* by HPLC analysis (CHIRALCEL OD-H column, 99:1 hexane/2-propanol at 226 nm, flow-rate: 0.5 mL/min): retention times; R_t = 11.33 min (major enantiomer, **19g**) and R_t = 12.80 min (minor enantiomer, *ent*-**19g**).

Spectral data for **19g**: R_f = 0.20 (12:1 hexanes/EtOAc); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 1.24 (t, 3H, *J* = 7.1 Hz), 1.80-1.92 (m, 2H), 1.96 (q, 1H, *J* = 7.1 Hz), 2.21 (d, 1H, *J* = 6.8 Hz) 2.24 (s, 6H), 2.27 (s, 6H), 2.29-2.34 (m, 1H), 2.48-2.53 (m, 1H), 3.41 (s, 1H), 3.67 (s, 3H), 3.68 (s, 3H), 4.12-4.20 (m, 2H), 6.91 (d, 2H, *J* = 7.3 Hz), 7.01 (s, 2H), 7.10 (s, 2H), 7.13 (d, 1H, *J* = 7.3 Hz), 7.19 (t, 2H, *J* = 7.3 Hz); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 14.29, 16.12, 16.15, 29.59, 33.25, 43.34, 46.13, 59.54, 59.60, 60.71, 77.22, 125.70, 127.26, 128.06, 128.15, 128.36, 130.50, 130.58, 137.77, 138.30, 141.35, 155.80, 156.22, 169.54; IR (thin film) 2934s, 1744s, 1484s, 1221s, 1182vs cm^{-1}; HRMS (ESI-TOF) *m/z* 502.2962 [($M+H^+$); calcd. for $C_{32}H_{40}NO_4$: 502.2957]; $[\alpha]^{20}_D$ –62.3 (c 1.0, EtOAc) on 96 % ee material (HPLC) of *ent*-**19g**.



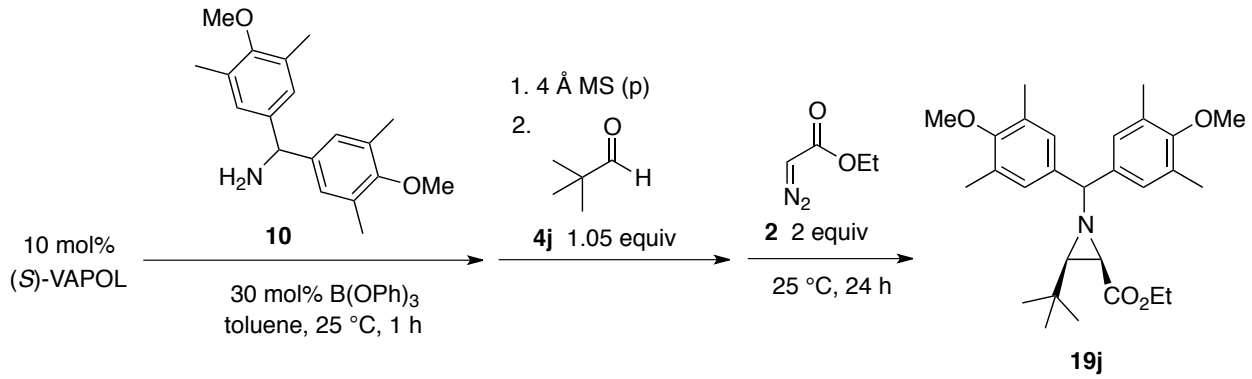
(2*R*,3*R*)-ethyl-3-benzyl-1-(bis(4-methoxy-3,5-dimethylphenyl)methyl)aziridine-2-carboxylate 19h: Aldehyde **4h** (59.0 μL, 63.0 mg, 0.525 mmol) was reacted according to the general Procedure A described above with (*S*)-VAPOL as ligand except that the addition of aldehyde **4h** was carried out at –10 °C followed by the addition of EDA **2** (415 μL, 4.0 mmoL, 8 equiv) at the same temperature. The reaction was stirred at –10 °C for 24 h. Purification of the crude aziridine by silica gel chromatography (30 mm × 300 mm column, 1:12 EtOAc/hexanes, gravity column) afforded pure cis-aziridine **19h** as a semi solid in 86 % isolated yield (209 mg, 0.430 mmol); *cis/trans*: not determined. Enamine side products: not observed. The optical purity of **19h** was determined to be 98% *ee* by HPLC analysis (PIRKLE COVALENT (R, R) WHELK-O 1 column, 95:5 hexane/2-propanol at 226 nm, flow-rate: 0.7 mL/min): retention times; R_t = 11.53 min (major enantiomer, **19h**) and R_t = 16.34 min (minor enantiomer, *ent*-**19h**).

Spectral data for **19h**: R_f = 0.30 (12:1 hexanes/EtOAc); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 1.25 (t, 3H, *J* = 7.2 Hz), 2.20 (s, 6H), 2.24 (s, 6H), 2.25-2.28 (m, 2H), 2.85 (dd, 1H, J = 6.1, 14.7 Hz), 2.94 (dd, 1H, J = 5.6, 14.9 Hz), 3.45 (s, 1H), 3.68 (s, 3H), 3.69 (s, 3H), 4.16-4.25 (m, 2H), 6.96 (s, 2H), 6.98-6.99 (m, 2H), 7.09 (s, 2H), 7.10-7.15 (m, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 14.26, 16.09, 16.13, 34.23, 43.04, 47.79, 59.49, 59.52, 60.78, 77.18, 126.01, 127.33, 127.95, 128.08, 128.53, 130.41, 130.49, 137.65, 137.86, 138.58, 155.80, 155.99, 169.59; IR (thin film) 2937s, 1742vs, 1484s, 1221s, 1182vs cm^{-1}; HRMS (ESI-TOF) *m/z* 440.2808 [(M+H$^+$); calcd. for $C_{31}H_{38}NO_4$: 488.2801]; $[\alpha]^{20}_D$ –54.2 (c 1.0, EtOAc) on 98 % ee material (HPLC) of *ent*-**19h**.



(*2R,3R*)-ethyl-1-(bis(4-methoxy-3,5-dimethylphenyl)methyl)-3-cyclohexylaziridine-2-carboxylate 19i: Aldehyde **4i** (63.0 μL, 59.0 mg, 0.525 mmol) was reacted according to the general Procedure A described above with (*S*)-VAPOL as ligand. Purification of the crude aziridine by silica gel chromatography (30 mm × 300 mm column, 4:2:0.1 hexanes/CH_2Cl_2/Et_2O, gravity column) afforded pure cis-aziridine **19i** as a semi solid in 95 % isolated yield (229 mg, 0.480 mmol); *cis/trans*: > 50:1. Enamine side products: <1 % yield of **23i** and 1.9 % yield of **24i**. The optical purity of **19i** was determined to be 90% *ee* by HPLC analysis (CHIRALCEL OD column, 99:1 hexane/2-propanol at 223 nm, flow-rate: 0.7 mL/min): retention times; R_t = 10.06 min (major enantiomer, **19i**) and R_t = 12.37 min (minor enantiomer, *ent*-**19i**).

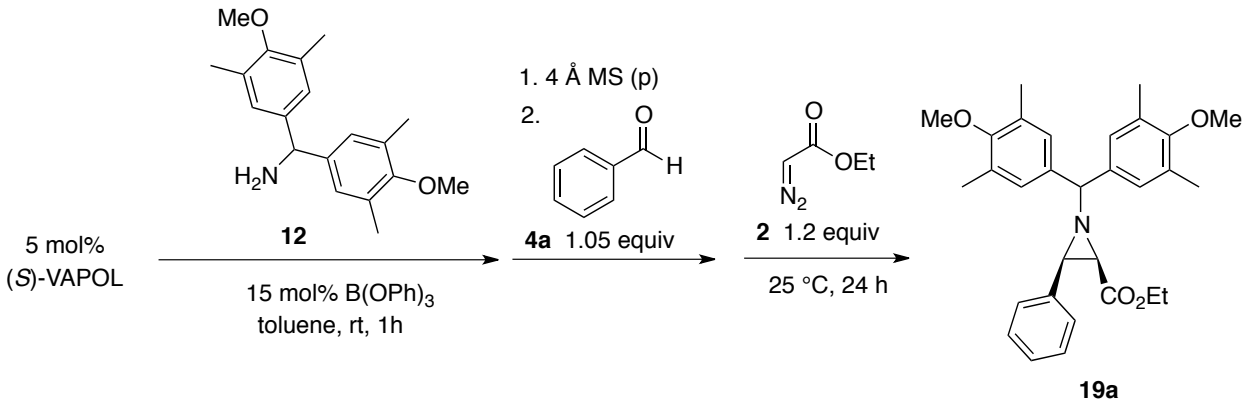
Spectral data for **19i**: R_f = 0.21 (2:1 hexane/CH_2Cl_2); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.46-0.57 (m, 1H), 0.87-1.19 (m, 4H), 1.21 (t, 3H, *J* = 7.1 Hz), 1.22-1.32 (m, 2H), 1.40-1.60 (m, 4H), 1.71-1.76 (m, 1H), 2.16 (m, 1H), 2.19 (s, 6H), 2.20 (s, 6H), 3.35 (s, 1H), 3.60 (s, 3H), 3.63 (s, 3H), 4.10-4.25 (m, 2H), 6.95 (s, 2H), 7.10 (s, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 13.85, 15.56, 15.67, 24.91, 25.09, 25.73, 29.65, 30.38, 35.88, 42.97, 51.76, 59.01, 59.07, 60.12, 77.01, 126.90, 128.10, 129.84, 129.95, 137.16, 137.71, 155.31, 155.83, 169.30; IR (thin film) 2928vs, 1744s, 1483s, 1221s, 1181s, 1017m cm^{-1}; Mass spectrum: *m/z* (% rel intensity) 479 M+ (0.7), 283 (100), 268 (25), 253 (12), 237 (7), 210 (7), 195 (9), 141 (8), 95 (10), 67 (16), 55 (10), 41 (16); $[\alpha]^{23}_D$ +107.9 (c 1.0, CH_2Cl_2) on 90 % ee material (HPLC). These spectral data match those previously reported for this compound.[2]



(2*R*,3*R*)-ethyl-1-(bis(4-methoxy-3,5-dimethylphenyl)methyl)-3-(*tert*-butyl)aziridine-2-carboxylate 19j: Aldehyde **4j** (58.0 μL, 45.0 mg, 0.525 mmol) was reacted according to the general Procedure A described above with (*S*)-VAPOL as ligand except that 2 equiv of EDA **2** was used. Purification of the crude aziridine by silica gel chromatography (30 mm × 300 mm column, 4:2:0.1 hexanes/CH_2Cl_2/Et_2O and then 2:1:0.1 hexanes/CH_2Cl_2/Et_2O, gravity column) afforded pure cis-aziridine **19j** as a semi solid in 95 % isolated yield (216 mg, 0.480 mmol); *cis/trans*: > 50:1. Enamine side products: <1 % yield of **23j** and <1% yield of **24j**. The optical purity of **19j** was determined to be 92% *ee* by HPLC by HPLC analysis (CHIRALCEL OD column, 99:1 hexane/2-propanol at 226 nm, flow-rate: 1.0 mL/min): retention times; R_t = 6.8 min (major enantiomer, **19j**) and R_t = 10.55 min (minor enantiomer, *ent*-**19j**).

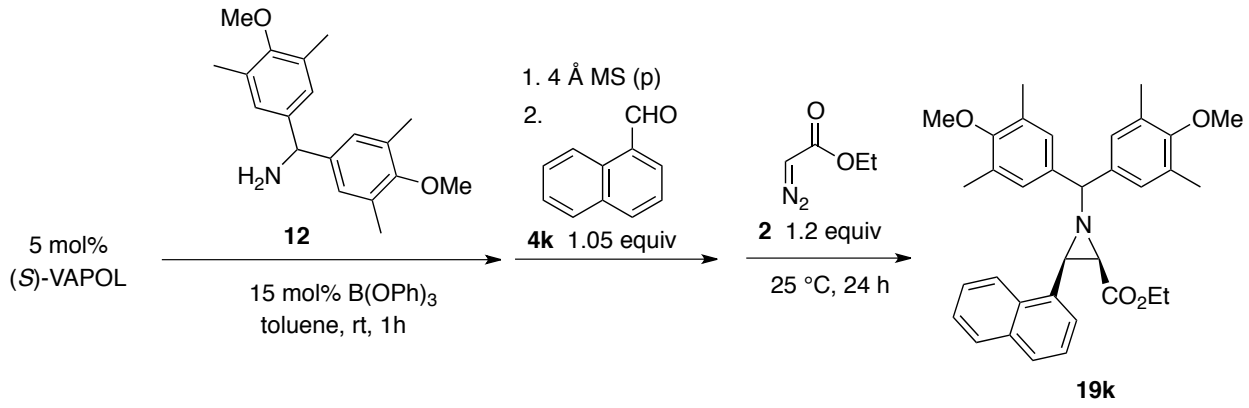
Spectral data for **19j**: R_f = 0.28 (1:2 hexane/CH_2Cl_2); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.72 (s, 9H), 1.29 (t, 3H, *J* = 7.1 Hz), 1.70 (d, 1H, *J* = 7.3 Hz), 2.11 (d, 1H, *J* = 7.2 Hz), 2.24 (s, 6H), 2.26 (s, 6H), 3.38 (s, 1H), 3.63 (s, 3H), 3.66 (s, 3H), 4.05-4.26 (m, 2H), 7.04 (s, 2H), 7.30 (s, 2H); 13C NMR ($CDCl_3$, 75 MHz) δ 13.92, 15.84, 15.96, 27.24, 31.39, 43.16, 55.94, 59.20, 59.27, 60.24, 78.20, 127.30, 128.18, 130.01, 137.77, 138.74, 155.51, 155.98, 169.66 (one *sp2* carbon not located); IR (thin film) 2953vs, 1747s, 1481s, 1221s, 1181s, 1017m cm^{-1}; Mass spectrum: *m/z* (% rel intensity) 453 M+ (1), 283 (100), 268 (45), 253 (26), 237 (17), 225 (11), 210 (13), 195 (17), 164 (9) 141 (26), 132 (11), 127 (12), 91 (11), 69 (18), 55 (37), 41 (55); $[\alpha]^{23}_D$ +110.0 (c 1.0, CH_2Cl_2) on 94 % ee material (HPLC). These spectral data match those previously reported for this compound.[2]

F. Synthesis of aryl and heteroaryl MEDAM aziridines 19a-j (*via* Procedure A)



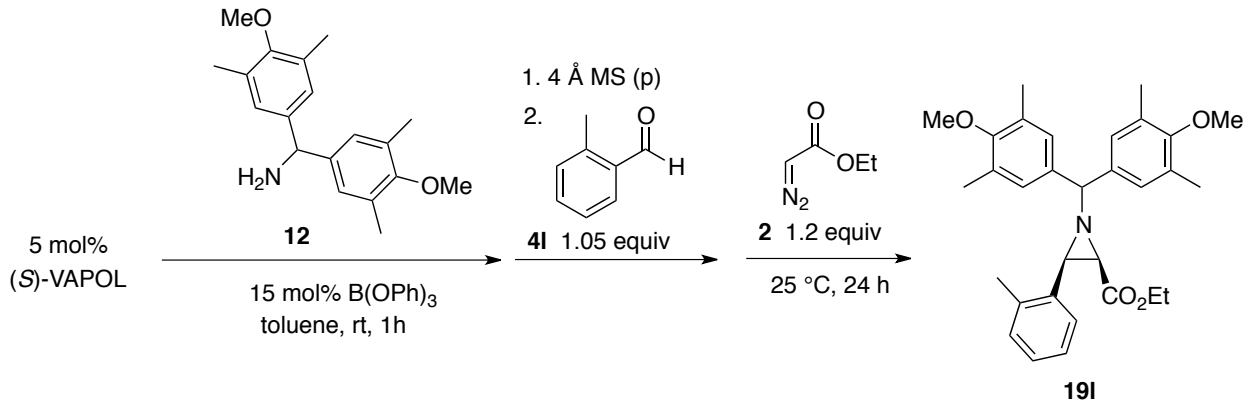
(2*R*,3*R*)-ethyl-1-(bis(4-methoxy-3,5-dimethylphenyl)methyl)-3-phenylaziridine-2-carboxylate 19a: Aldehyde **4a** (52.0 μL, 0.525 mmol) was reacted according to the general Procedure A described above with (*S*)-VAPOL as ligand. Purification of the crude aziridine by silica gel chromatography (30 mm × 300 mm column, 9:1 hexanes/EtOAc as eluent, gravity column) afforded pure cis-aziridine **19a** as a white solid (mp 107-108 ºC on 99.8% ee material) in 98 % isolated yield (232 mg, 0.490 mmol); *cis/trans*: >50:1. Enamine side products: <1 % yield of **23a** and <1 % yield of **24a.** The optical purity of **19a** was determined to be 98 % *ee* by HPLC analysis (CHIRALCEL OD-H column, 99:1 hexane/2-propanol at 226nm, flow-rate: 0.7 mL/min): retention times; R_t = 9.26 min (major enantiomer, **19a**) and R_t = 12.52 min (minor enantiomer, *ent*-**19a**). This reaction was repeated and monitored by ^{1}H NMR Spectroscopy that revealed that the reaction had gone to completion in 1 h. Also, it gave 70 % yield of **19a** and 98 % ee when the same reaction was carried out utilizing 5Å MS instead of 4Å MS.

Spectral data for **19a**: R_f = 0.42 (1:9 EtOAc/hexane); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 0.98 (t, 3H, *J* = 7.1 Hz), 2.18 (s, 6H), 2.24 (s, 6H), 2.55 (d, 1H, *J* = 6.8 Hz), 3.10 (d, 1H, *J* = 6.6 Hz), 3.62 (s, 3H), 3.66 (s, 1H), 3.68 (s, 3H) 3.87-3.97 (m, 2H), 7.09 (s, 2H), 7.18 (s, 2H), 7.21-7.24 (m, 3H), 7.36 (d, 2H, *J* = 7.3 Hz); ^{13}C ($CDCl_3$, 125 MHz) δ 14.01, 16.16, 16.22, 46.26, 48.20, 59.52, 59.58, 60.47, 77.04, 127.21, 127.41, 127.70, 127.80,127.85, 130.59, 130.60, 135.33, 137.79, 137.96, 155.95, 156.10, 168.01; IR (thin film) 2961 vs, 1750 vs, 1414 vs, 1202 vs cm^{-1}; Mass spectrum: *m/z* (% rel intensity) 473 M+ (0.27), 284(78), 283 (100), 268 (34), 253 (20), 237 (11), 210(10), 117 (18), 89 (11); Anal calcd for $C_{30}H_{35}NO_4$: C, 76.08; H, 7.45; N, 2.96. Found: C, 76.31; H, 7.28; N, 2.82; $[\alpha]^{23}_D$ +41.3 (*c* 1.0, EtOAc) on 99% ee material (HPLC). These spectral data match those previously reported for this compound.[2]



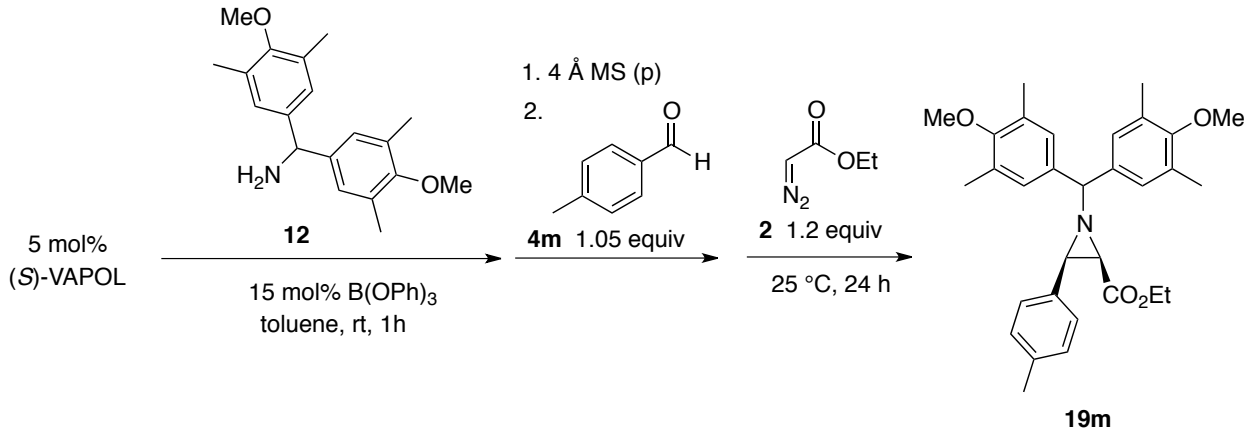
(2*R*,3*R*)-ethyl-1-(bis(4-methoxy-3,5-dimethylphenyl)methyl)-3-(naphthalen-1-yl)aziridine-2-carboxylate 19k: Aldehyde **4k** (71.0 μL, 0.525 mmol) was reacted according to the general Procedure A described above with (*S*)-VAPOL as ligand. Purification of the crude aziridine by silica gel chromatography (30 mm × 300 mm column, 9:1 hexanes/EtOAc) afforded pure cis-aziridine **19k** as a white solid (mp 79-80 ºC on 99% ee material) in 96 % isolated yield (251 mg, 0.480 mmol); *cis/trans*: 50:1. Enamine side products: 2.9 % yield of **23k** and <1 % yield of **24k**. The optical purity of **19k** was determined to be 99.3% *ee* by HPLC analysis (CHIRALCEL OD-H column, 99:1 hexane/2-propanol at 226 nm, flow-rate: 0.7 mL/min): retention times; R_t = 8.15 min (major enantiomer, **19k**) and R_t = 16.15 min (minor enantiomer, *ent*-**19k**).

Spectral data for **19k**: R_f = 0.25 (9:1 hexanes/EtOAc); ^{1}H NMR ($CDCl_3$, 600 MHz) δ 0.65 (t, 3H, *J* = 7.1 Hz), 2.22 (s, 6H), 2.26 (s, 6H), 2.81 (d, 1H, *J* = 6.8 Hz), 3.58 (d, 1H, *J* = 6.8 Hz), 3.63 (s, 3H), 3.69 (s, 3H), 3.69-3.76 (m, 2H), 3.79 (s, 1H), 7.17 (s, 2H), 7.23 (s, 2H), 7.36 (dd, 1H, *J* = 7.8, 7.6 Hz), 7.40-7.46 (m, 2H), 7.67-7.69 (m, 2H), 7.78 (d, 1H, *J* = 7.8 Hz), 8.06 (d, 1H, *J* = 7.6 Hz); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 13.67, 16.18, 16.24, 45.98, 46.63, 59.55, 59.62, 60.33, 77.47, 123.06, 125.31, 125.42, 125.83, 126.61, 127.36, 127.52, 128.12, 128.50, 130.68, 130.71, 130.85, 131.49, 133.08, 137.69, 137.95, 155.95, 156.26, 168.02; IR (thin film) 2942vs, 1748s, 1484s, 1221s, 1186s, 1017m cm^{-1}; HRMS (ESI-TOF) *m/z* 524.2807 [(M+H$^+$); calcd. for $C_{34}H_{38}NO_4$: 524.2801]; $[\alpha]^{20}_D$ –19.3 (c 1.0, EtOAc) on 99 % ee material (HPLC) of *ent*-**19k**.



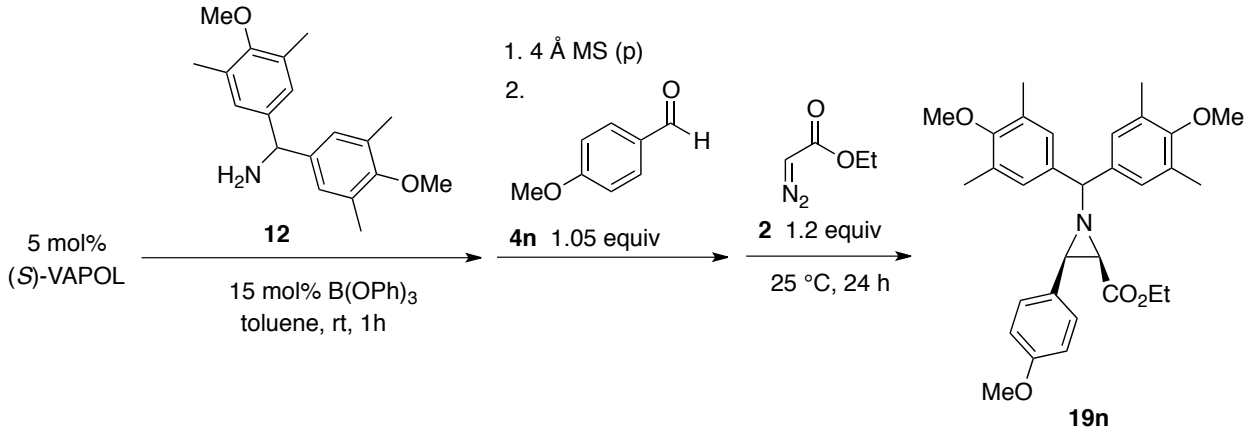
(*2R,3R*)-ethyl-1-(bis(4-methoxy-3,5-dimethylphenyl)methyl)-3-(*o*-tolyl)aziridine-2-carboxylate 19l: Aldehyde **4l** (61.0 μL, 0.525 mmol) was reacted according to the general Procedure A described above with (*S*)-VAPOL as ligand. Purification of the crude aziridine by silica gel chromatography (30 mm × 300 mm column, 9:1 hexanes/EtOAc as eluent, gravity column) afforded pure cis-aziridine **19l** as a white solid (mp 174-175 ºC on 99.7% ee material) in 96 % isolated yield (234 mg, 0.480 mmol); *cis/trans*: 50:1. Enamine side products: 1.9 % yield of **23l** and 1.0 % yield of **24l**. The optical purity of **19l** was determined to be >99% *ee* by HPLC analysis (CHIRALCEL OD-H column, 99:1 hexane/2-propanol at 226 nm, flow-rate: 0.7 mL/min): retention times; R_t = 9.45 min (major enantiomer, **19l**) and R_t = 12.21 min (minor enantiomer, *ent*-**19l**).

Spectral data for **19l**: R_f = 0.38 (1:9 EtOAc/hexane); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 0.89 (t, 3H, *J* = 7.1 Hz), 2.20 (s, 6H), 2.24 (s, 6H), 2.26 (s, 3H), 2.61 (d, 1H, *J* = 6.8 Hz), 3.08 (d, 1H, *J* = 6.6 Hz), 3.62 (s, 3H), 3.66 (s, 1H), 3.68 (s, 3H), 3.88 (q, 2H, *J* = 7.1 Hz), 7.01 (d, 1H, *J* = 6.6 Hz), 7.06-7.09 (m, 2H), 7.13 (s, 2H), 7.18 (s, 2H), 7.53 (d, 1H, *J* = 6.3 Hz); ^{13}C ($CDCl_3$, 125 MHz) δ 13.90, 16.16, 16.22, 18.76, 45.55, 47.15, 59.53, 59.59, 60.36, 77.34, 125.28, 127.05, 127.33, 127.95, 128.62, 129.08, 130.61, 130.63, 133.45, 136.03, 137.85, 138.01, 155.92, 156.18, 168.16; IR (thin film) 2937vs, 1749s, 1485s, 1221s, 1192vs cm^{-1};HRMS (ESI-TOF) *m/z* 488.2801 [(M+H$^+$); calcd. for $C_{31}H_{38}NO_4$: 488.2801]; $[\alpha]^{23}_D$ +46.4 (*c* 1.0, EtOAc) on 97% ee material (HPLC). These spectral data match those previously reported for this compound.[2]



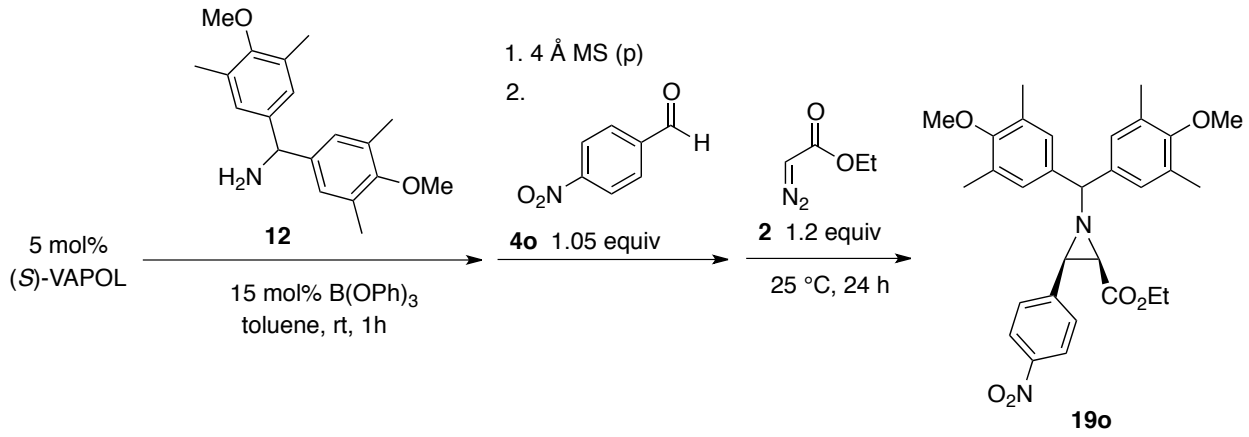
(*2R,3R*)-ethyl-1-(bis(4-methoxy-3,5-dimethylphenyl)methyl)-3-(*p*-tolyl)aziridine-2-carboxylate 19m: Aldehyde **4m** (61.0 μL, 0.525 mmol) was reacted according to the general Procedure A described above with (*S*)-VAPOL as ligand. Purification of the crude aziridine by silica gel chromatography (30 mm × 300 mm column, 9:1 hexanes/EtOAc as eluent, gravity column) afforded pure cis-aziridine **19m** as a white solid (mp 116-117 ºC on 99.5% ee material) in 95 % isolated yield (232 mg, 0.480 mmol); *cis/trans*: 50:1. Enamine side products: 3.8 % yield of **23m** and 1.0 % yield of **24m**. The optical purity of **19m** was determined to be >99% *ee* by HPLC analysis (CHIRALCEL OD-H column, 99:1 hexane/2-propanol at 226 nm, flow-rate: 0.7 mL/min): retention times; R_t = 9.22 min (major enantiomer, **19m**) and R_t = 11.62 min (minor enantiomer, *ent*-**19m**).

Spectral data for **19m**: R_f = 0.30 (1:9 EtOAc/hexanes); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 1.01 (t, 3H, *J* = 7.1 Hz), 2.18 (s, 6H), 2.24 (s, 6H), 2.26 (s, 3H), 2.52 (d, 1H, *J* = 6.6 Hz), 3.07 (d, 1H, *J* = 6.8 Hz), 3.62 (s, 3H), 3.64 (s, 1H), 3.68 (s, 3H) 3.93 (dq, 2H, *J* = 3.2 Hz, 7.1 Hz), 7.02 (d, 2H, *J* = 7.8 Hz), 7.08 (s, 2H), 7.17 (s, 2H), 7.24 (d, 2H, *J* = 8.0 Hz); ^{13}C ($CDCl_3$, 125 MHz) δ 14.05, 16.16, 16.22, 21.11, 46.20, 48.21, 59.52, 59.58, 60.44, 77.11, 127.43, 127.72, 127.81, 128.41, 130.54, 130.57, 132.28, 136.78, 137.86, 138.00, 155.93, 156.08, 168.10; IR (thin film) 2978vs, 1748s, 1483s, 1221s, 1190vs cm^{-1}; HRMS (ESI-TOF) *m/z* 488.2806 [($M+H^+$); calcd. for $C_{31}H_{38}NO_4$: 488.2801]; $[\alpha]^{23}_D$ +29.4 (*c* 1.0, EtOAc) on 99.8 % ee material (HPLC). These spectral data match those previously reported for this compound.[2]



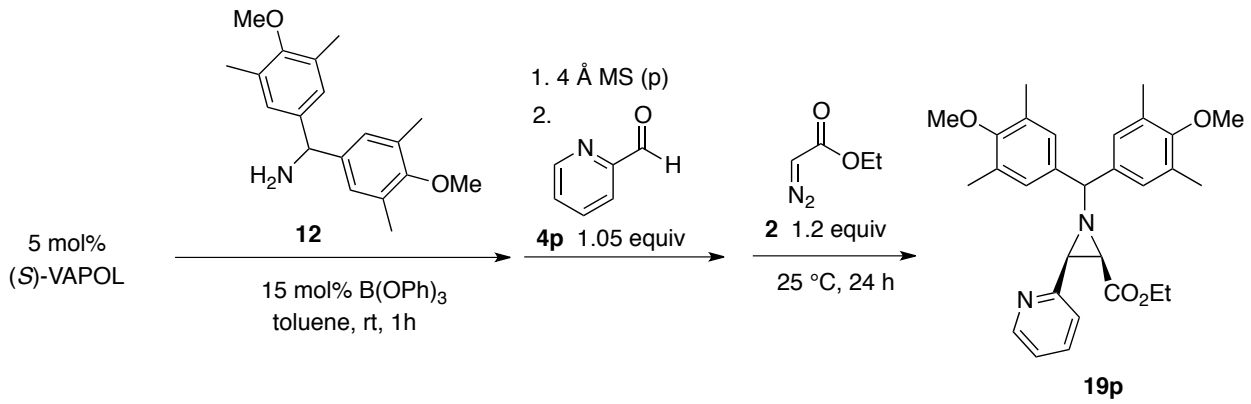
(*2R,3R*)-ethyl-1-(bis(4-methoxy-3,5-dimethylphenyl)methyl)-3-(4-methoxyphenyl)aziridine-2-carboxylate 19n: Aldehyde **4n** (64.0 μL, 0.525 mmol) was reacted according to the general Procedure A described above with (*S*)-VAPOL as ligand. Purification of the crude aziridine by silica gel chromatography (30 mm × 300 mm column, 9:1 hexanes/EtOAc with 1 % Et_3N as eluent, gravity column; the column was set up by making a slurry of silica gel in hexanes with 2 % Et_3N) afforded pure cis-aziridine **19n** as a white solid (mp 56-57 ºC on 98% ee material) in 78 % isolated yield (196 mg, 0.390 mmol); *cis/trans*: 20:1. Enamine side products: <1 % yield of **23n** and 4.7 % yield of **24n**. The optical purity of **19n** was determined to be 98% *ee* by HPLC analysis (CHIRALCEL OD-H column, 99:1 hexane/2-propanol at 226 nm, flow-rate: 0.7 mL/min): retention times; R_t = 12.07 min (major enantiomer, **19n**) and R_t = 19.20 min (minor enantiomer, *ent*-**19n**).

Spectral data for **19n**: R_f = 0.28 (1:9 EtOAc/hexane); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 1.02 (t, 3H, *J* = 7.1 Hz), 2.19 (s, 6H), 2.24 (s, 6H), 2.51 (d, 1H, *J* = 6.8 Hz), 3.06 (d, 1H, *J* = 6.8 Hz), 3.63 (s, 3H), 3.65 (s, 1H), 3.68 (s, 3H), 3.74 (s, 3H), 3.89-3.99 (m, 2H), 6.77 (d, 2H, *J* = 9.5 Hz), 7.09 (s, 2H), 7.18 (s, 2H), 7.29 (d, 2H, *J* = 8.8 Hz); ^{13}C ($CDCl_3$, 125 MHz) δ 14.08, 16.16, 16.21, 46.20, 47.89, 55.19, 59.52, 59.57, 60.45, 77.05, 113.18, 127.43, 127.79, 128.93, 130.55, 130.57, 137.83, 138.01, 155.93, 156.07, 158.86, 168.14 (one sp^2 carbon not located); IR (thin film) 2942vs, 1743s, 1514s, 1250s, 1180vs cm^{-1}; HRMS (ESI-TOF) *m/z* 504.2744 [($M+H^+$); calcd. for $C_{31}H_{38}NO_5$: 504.2750]; $[\alpha]^{23}_D$ +25 (*c* 1.0, EtOAc) on 96 % ee material (HPLC). These spectral data match those previously reported for this compound.[2]



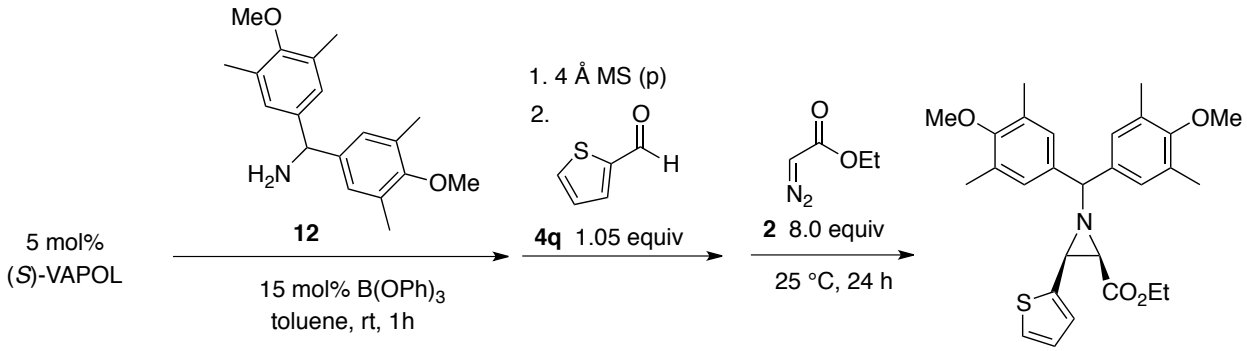
(*2R,3R*)-ethyl-1-(bis(4-methoxy-3,5-dimethylphenyl)methyl)-3-(4-nitrophenyl)aziridine-2-carboxylate 19o: Aldehyde **4o** (79.3 mg, 0.525 mmol) was reacted according to the general Procedure A described above with (*S*)-VAPOL as ligand. Purification of the crude aziridine by silica gel chromatography (30 mm × 300 mm column, 9:1 hexanes/EtOAc) afforded pure cis-aziridine **19o** as a white solid (mp 174-175 ºC on 99.7% ee material) in 92 % isolated yield (239 mg, 0.460 mmol); *cis/trans*: 50:1. Enamine side products: <1 % yield of **23o** and 2.8 % yield of **24o**. The optical purity of **19o** was determined to be 99% *ee* by HPLC analysis (CHIRALCEL OD-H column, 99:1 hexane/2-propanol at 226 nm, flow-rate: 0.7 mL/min): retention times; R_t = 17.12 min (major enantiomer, **19o**) and R_t = 27.13 min (minor enantiomer, *ent*-**19o**).

Spectral data for **19o**: R_f = 0.30 (1:9 EtOAc/hexane); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 1.02 (t, 3H, *J* = 7.1 Hz), 2.18 (s, 6H), 2.25 (s, 6H), 2.68 (d, 1H, *J* = 6.8 Hz), 3.15 (d, 1H, *J* = 6.8 Hz), 3.62 (s, 3H), 3.68 (s, 3H), 3.71 (s, 1H), 3.93 (dq, 2H, *J* = 2.2, 7.1 Hz), 7.06 (s, 2H), 7.16 (s, 2H), 7.57 (d, 2H, *J* = 8.8 Hz), 8.10 (d, 2H, *J* = 8.8 Hz); ^{13}C ($CDCl_3$, 125 MHz) δ 14.08, 16.19, 16.24, 46.81, 47.26, 59.55, 59.59, 60.85, 76.89, 122.98, 127.26, 127.59, 128.81, 130.81, 130.86, 137.25, 137.48, 142.82, 147.28, 156.13, 156.28, 167.20; IR (thin film) 2984 vs, 1745 vs, 1603 s, 1522 vs, 1221 vs cm^{-1}; HRMS (ESI-TOF) *m/z* 519.2505 [($M+H^+$); calcd. for $C_{30}H_{35}N_2O_6$: 519.2495]; $[\alpha]^{23}_D$ -4.8 (*c* 1.0, EtOAc) on 99.8% ee material (HPLC). These spectral data match those previously reported for this compound.[2]



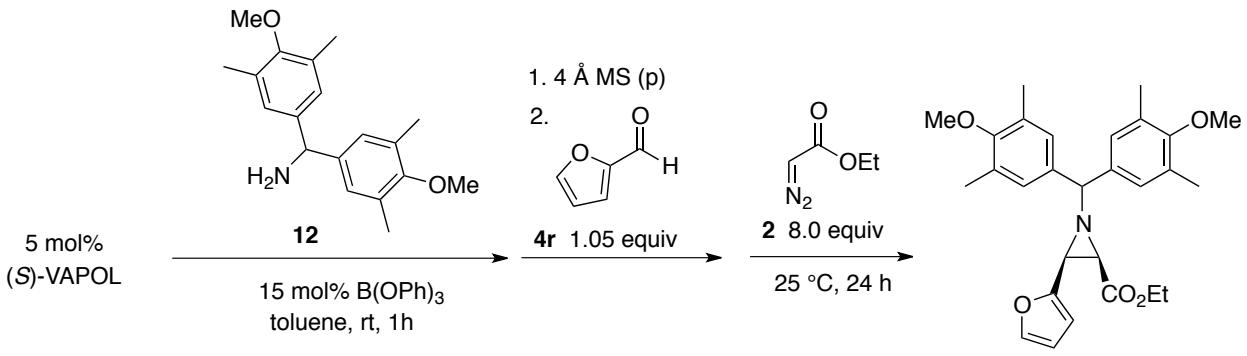
(2*R*,3*S*)-ethyl-1-(bis(4-methoxy-3,5-dimethylphenyl)methyl)-3-(pyridin-2-yl)aziridine-2-carboxylate 19p: Aldehyde **4p** (50.0 μL, 0.525 mmol) was reacted according to the general Procedure A described above with (*S*)-VAPOL as ligand. Purification of the crude aziridine by silica gel chromatography (30 mm × 300 mm column, 4:1 hexanes/EtOAc with 1 % Et_3N followed by 2:1 hexanes/EtOAc with 1 % Et_3N as eluent, gravity column; the column was set up by making a slurry of silica gel in hexanes with 2 % Et_3N) afforded pure cis-aziridine **19p** as a white solid (mp 60-61 ºC on 90.2% ee material) in 96 % isolated yield (456 mg, 0.480 mmol); *cis/trans*: >50:1. Enamine side products: not observed. The optical purity of **19p** was determined to be 90% *ee* by HPLC analysis (CHIRALCEL OD-H column, 99:1 hexane/2-propanol at 226 nm, flow-rate: 0.7 mL/min): retention times; R_t = 16.90 min (major enantiomer, **19p**) and R_t = 31.83 min (minor enantiomer, *ent*-**19p**).

Spectral data for **19p**: R_f = 0.27 (2:1 hexanes/EtOAc); ^{1}H NMR ($CDCl_3$, 600 MHz) δ 1.01 (t, 3H, *J* = 7.1 Hz), 2.18 (s, 6H), 2.24 (s, 6H), 2.66 (d, 1H, *J* = 6.8 Hz), 3.27 (d, 1H, *J* = 6.8 Hz), 3.62 (s, 3H), 3.68 (s, 3H), 3.73 (s, 1H), 3.91-3.96 (m, 2H), 7.08 (s, 2H), 7.09-7.11 (m, 1H), 7.16 (s, 2H), 7.59-7.60 (m, 2H), 8.42 (td, 1H, *J* = 1.4, 4.6 Hz); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 14.00, 16.16, 16.23, 45.91, 49.45, 59.54, 59.60, 60.63, 122.29, 122.83, 127.36, 127.79, 130.65, 130.68, 135.87, 137.56, 137.78, 148.57, 155.48, 155.99, 156.12, 167.75 (one sp^3 carbon not located); IR (thin film) 2984s, 1746s, 1591, 1482s, 1221s, 1184s, 1015m cm^{-1}; HRMS (ESI-TOF) *m/z* 475.2607 [$(M+H^+)$; calcd. for $C_{29}H_{35}N_2O_4$: 475.2597]; $[\alpha]^{20}_D$ +40.2 (c 1.0, EtOAc) on 90% ee material (HPLC).



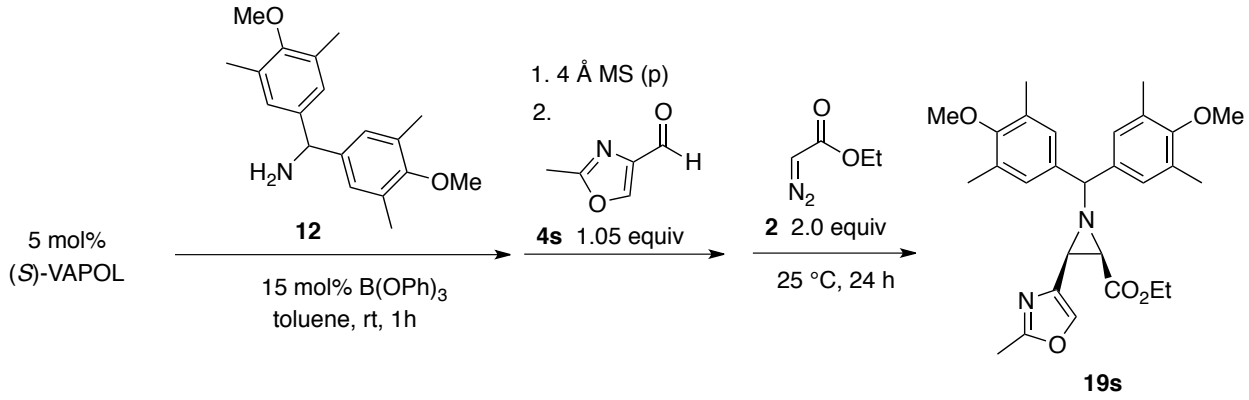
(2*R*,3*S*)-ethyl-1-(bis(4-methoxy-3,5-dimethylphenyl)methyl)-3-(thiophen-2-yl)aziridine-2-carboxylate 19q: Aldehyde **4q** (48.0 μL, 0.525 mmol) was reacted according to the general Procedure A described above with (*S*)-VAPOL as ligand except that an excess of EDA **2** (415 μL, 4.0 mmoL, 8 equiv) was used. Purification of the crude aziridine by silica gel chromatography (30 mm × 300 mm column, 9:1 hexanes/EtOAc with 1 % Et_3N as eluent, gravity column; the column was set up by making a slurry of silica gel in hexanes with 2 % Et_3N) afforded pure cis-aziridine **19q** as a white solid (mp 55-56 ºC on 97% ee material) in 88 % isolated yield (211 mg, 0.440 mmol); *cis/trans*: 25:1. Enamine side products: not observed. The optical purity of **19q** was determined to be 97% *ee* by HPLC analysis (CHIRALCEL OD-H column, 99:1 hexane/2-propanol at 226 nm, flow-rate: 0.7 mL/min): retention times; R_t = 10.54 min (major enantiomer, **19q**) and R_t = 15.27 min (minor enantiomer, *ent*-**19q**).

Spectral data for **19q**: R_f = 0.21 (9:1 hexanes/EtOAc); ^{1}H NMR ($CDCl_3$, 600 MHz) δ 1.08 (t, 3H, *J* = 7.1 Hz), 2.21 (s, 6H), 2.24 (s, 6H), 2.58 (d, 1H, *J* = 6.6 Hz), 3.21 (d, 1H, *J* = 6.6 Hz), 3.64 (s, 3H), 3.66 (s, 1H), 3.67 (s, 3H), 3.96-4.06 (m, 2H), 6.86 (dd, 1H, *J* = 3.4, 4.9 Hz), 6.95-6.96 (m, 1H), 7.11 (dd, 1H, *J* = 1.2, 4.9 Hz), 7.14 (s, 2H), 7.16 (s, 2H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 14.00, 16.12, 16.17, 43.76, 46.65, 59.51, 59.53, 60.70, 76.93, 124.49, 125.74, 126.38, 127.34, 127.71, 130.59, 130.62, 137.50, 137.63, 139.00, 155.94, 156.07, 167.77; IR (thin film) 2942s, 1748s, 1484s, 1221s, 1190s, 1015m cm^{-1}; HRMS (ESI-TOF) *m/z* 480.2216 [$(M+H^+)$; calcd. for $C_{28}H_{34}NO_4S$: 480.2209]; $[\alpha]^{20}_D$ +30.2 (c 1.0, EtOAc) on 97 % ee material (HPLC).



(2*R*,3*S*)-ethyl-1-(bis(4-methoxy-3,5-dimethylphenyl)methyl)-3-(furan-2-yl)aziridine-2-carboxylate 19r: Aldehyde **4r** (44.0 μL, 0.525 mmol) was reacted according to the general Procedure A described above with (*S*)-VAPOL as ligand except that the addition of aldehyde **4r** was carried out at –10 °C followed by the addition of EDA **2** (415 μL, 4.0 mmoL, 8 equiv) at the same temperature. The reaction was stirred for 2 h at –10 °C prior to warming it to room temperature. Purification of the crude aziridine by silica gel chromatography (30 mm × 300 mm column, 15:1 hexanes/EtOAc with 1 % Et_3N as eluent, gravity column; the column was set up by making a slurry of silica gel in hexanes with 2 % Et_3N) afforded pure cis-aziridine **19r** as a white solid (mp 45-46 ºC on 94% ee material) in 65 % isolated yield (151 mg, 0.325 mmol); *cis/trans*: 8.3:1. Enamine side products: not observed. The optical purity of **19r** was determined to be 95% *ee* by HPLC analysis (CHIRALCEL OD-H column, 99.5:0.5 hexane/2-propanol at 226 nm, flow-rate: 0.7 mL/min): retention times; R_t = 23.6 min (major enantiomer, **19r**) and R_t = 39.1 min (minor enantiomer, *ent*-**19r**).

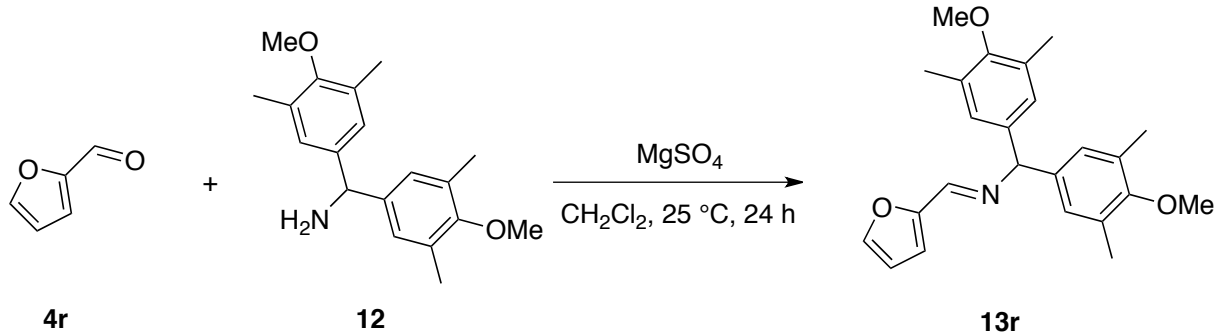
Spectral data for **19r**: R_f = 0.21 (15:1 hexanes/EtOAc); ^{1}H NMR ($CDCl_3$, 600 MHz) δ 1.14 (t, 3H, *J* = 7.1 Hz), 2.21 (s, 6H), 2.24 (s, 6H), 2.60 (d, 1H, *J* = 6.6 Hz), 3.03 (d, 1H, *J* = 6.6 Hz), 3.65 (s, 3H), 3.67 (s, 1H), 3.68 (s, 3H), 4.03-4.13 (m, 2H), 6.28-6.29 (m, 1H), 6.29-6.30 (m, 1H), 7.09 (s, 2H), 7.14 (s, 2H), 7.26-7.27 (m, 1H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 14.05, 16.11, 16.15, 41.73, 45.27, 59.50, 59.52, 60.76, 76.84, 107.97, 110.32, 127.49, 127.64, 130.53, 130.61, 137.34, 137.44, 141.80, 149.77, 156.01, 156.04, 167.70; IR (thin film) 2940s, 1750s, 1485s, 1221s, 1179s, 1013m cm^{-1}; HRMS (ESI-TOF) *m/z* 464.2441 [(M+H$^+$); calcd. for $C_{28}H_{34}NO_5$: 464.2437]; $[\alpha]^{20}_D$ –8.2 (c 1.0, EtOAc) on 94 % ee material (HPLC) of *ent*-**19r**.



(2*R*,3*S*)-ethyl-1-(bis(4-methoxy-3,5-dimethylphenyl)methyl)-3-(2-methyloxazol-4-yl)aziridine-2-carboxylate 19s: Aldehyde **4s** (59.0 mg, 0.525 mmol) was reacted according to the general Procedure A described above with (*S*)-VAPOL as ligand except except that the addition of aldehyde **4s** was carried out at –10 °C followed by the addition of EDA **2** (415 μL, 4.0 mmoL, 8 equiv) at the same temperature. The reaction was stirred for 15 min at –10 °C prior to warming it to room temperature. Purification of the crude aziridine by silica gel chromatography (30 mm × 300 mm column, 3:1 hexanes/EtOAc with 1 % Et_3N as eluent, gravity column; the column was set up by making a slurry of silica gel in hexanes with 2 % Et_3N) afforded pure cis-aziridine **19s** as a white solid (mp 58-59 ºC on 96% ee material) in 98 % isolated yield (235 mg, 0.490 mmol); *cis/trans*: >50:1. Enamine side products: not observed. The optical purity of **19s** was determined to be 97% *ee* by HPLC analysis (CHIRALPAK AS column, 93:7 hexane/2-propanol at 226 nm, flow-rate: 0.7 mL/min): retention times; R_t = 7.7 min (major enantiomer, **19s**) and R_t = 10.55 min (minor enantiomer, *ent*-**19s**).

Spectral data for **19s**: R_f = 0.19 (3:1 hexanes/EtOAc); ^{1}H NMR ($CDCl_3$, 600 MHz) δ 1.13 (t, 3H, *J* = 7.2 Hz), 2.19 (s, 6H), 2.23 (s, 6H), 2.35 (s, 3H), 2.57 (d, 1H, *J* = 6.6 Hz), 2.94 (d, 1H, *J* = 6.0 Hz), 3.64 (s, 4H), 3.67 (s, 3H), 4.05 (q, 2H, *J* = 7.2 Hz), 7.03 (s, 2H), 7.09 (s, 2H), 7.49 (s, 1H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 13.85, 14.12, 16.18, 16.20, 41.75, 45.28, 59.55, 59.58, 60.69, 76.83, 127.40, 127.64, 130.57, 130.64, 135.90, 136.52, 137.44, 137.64, 155.99, 156.08, 160.79, 167.64; IR (thin film) 2936vs, 1746s, 1582s, 1484s, 1223s, 1194s, 1015m cm^{-1}; HRMS (ESI-TOF) *m/z* 479.2547 [(M+H$^+$); calcd. for $C_{28}H_{35}N_2O_5$: 479.2546]; $[\alpha]^{20}_D$ –33.3.0 (c 1.0, EtOAc) on 96 % ee material (HPLC) of *ent*-**19s**.

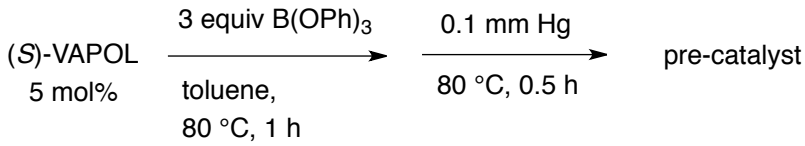
G. Synthesis of MEDAM imine 13r and aziridine 19r (aziridination with preformed imine):

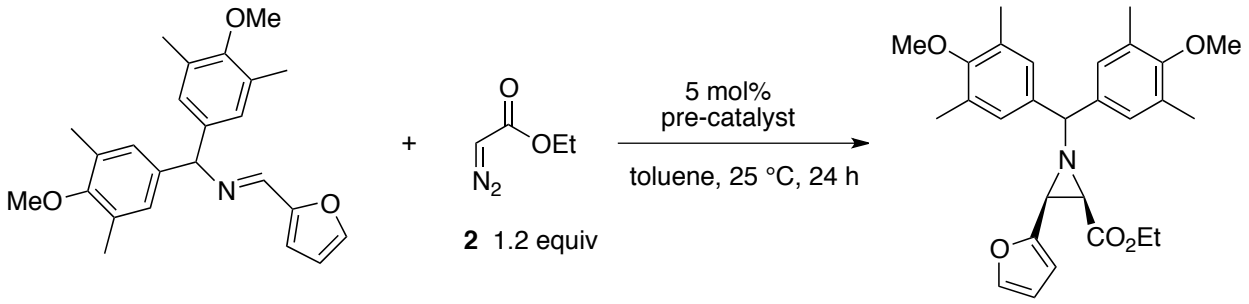


4r **12** **13r**

(*E*)-*N*-(furan-2-ylmethylene)-1,1-bis(4-methoxy-3,5-dimethylphenyl)methanamine 13r: To a 25 mL flame-dried round bottom flask, equipped with a stir bar, filled with argon was added MEDAM amine **12** (598.8 g, 2.000 mmol), $MgSO_4$ (500 mg, freshly flame-dried) and dry CH_2Cl_2 (6 mL). After stirring for 10 min, aldehyde **4r** (174 μL, 2.10 mmol, 1.05 equiv) was added. The reaction mixture was stirred at room temperature for 24 h. The reaction mixture was filtered through Celite and the Celite bed was washed with CH_2Cl_2 (3 mL × 3) and then the filtrate was concentrated by rotary evaporation to give the crude imine as an off-white solid. Crystallization (1:25 CH_2Cl_2 / hexanes) and collection of the first crop afforded **13r** as a white solid (mp 116-117 ºC) in 26% isolated yield (200 mg, 0.520 mmol).

Spectral data for **13r**: ^{1}H NMR ($CDCl_3$, 600 MHz) δ 2.23 (s, 12H), 3.67 (s, 6H), 5.31 (s, 1H), 6.45 (dd, 1H, J = 1.7, 3.4 Hz), 6.77 (d, 1H, J = 3.4 Hz), 6.97 (s, 4H), 7.51 (d, 1H, J = 1.7 Hz), 8.13 (s, 1H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 16.16, 59.60, 77.71, 111.60, 114.46, 127.94, 130.66, 138.74, 144.77, 149.19, 151.73, 155.90; IR (thin film) 2944w, 1646s, 1484s, 1221 cm^{-1}; HRMS (ESI-TOF) *m/z* 378.2075 [(M+H$^+$); calcd. for $C_{24}H_{28}NO_3$: 378.2069]





13r **19r**

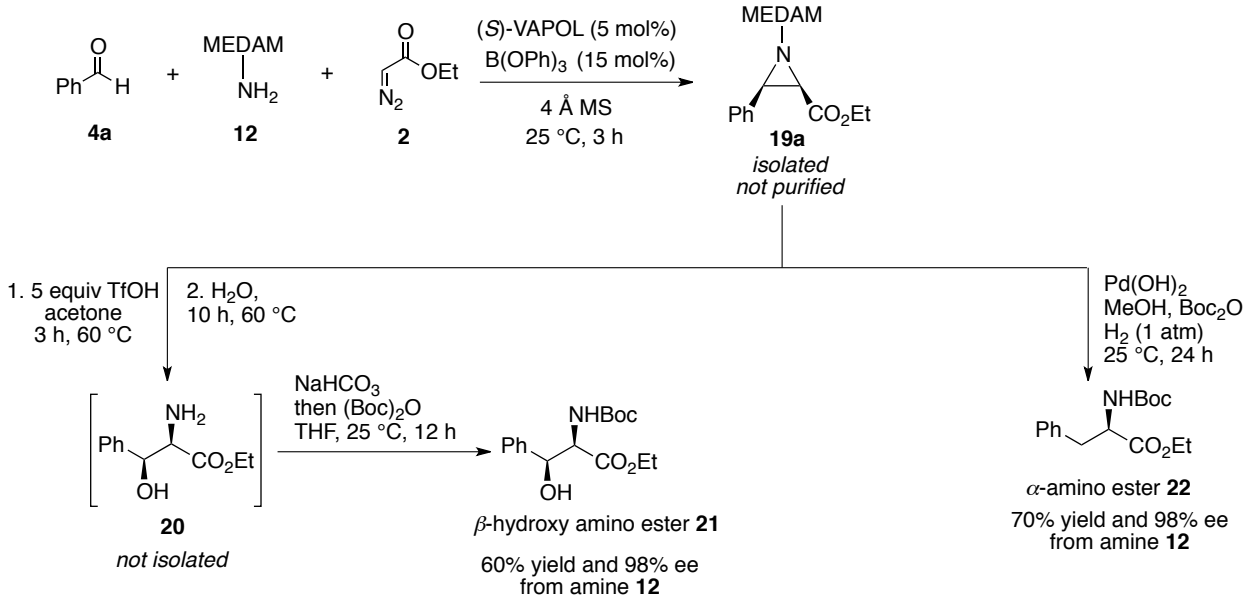
(2*R*,3*S*)-ethyl-1-(bis(4-methoxy-3,5-dimethylphenyl)methyl)-3-(furan-2-yl)aziridine-2-carboxylate 19r: To a 25 mL flame-dried home-made Schlenk flask , prepared from a single-necked 25 mL pear-shaped flask that had its 14/20 glass joint replaced with a high vacuum threaded Teflon valve, equipped with a stir bar and flushed with argon was added (*S)*-VAPOL (7.00 mg, 0.0125 mmol) and $B(OPh)_3$ (11.0 mg, 0.0375 mmol). Under an argon flow through the side-arm of the Schlenk flask, dry toluene (1 mL) was added through the top of the Teflon valve to dissolve the two reagents. The flask was sealed by closing the Teflon valve, and then placed in an 80 ºC oil bath for 1 h. After 1 h, a vacuum (0.5 mm Hg) was carefully applied by slightly opening the Teflon valve to remove the volatiles. After the volatiles were removed completely, a full vacuum was applied and maintained for a period of 30 min at a temperature of 80 ºC (oil bath). The flask was then allowed to cool to room temperature and opened to argon through the side-arm of the Schlenk flask.

To the flask containing the pre-catalyst was first added the aldimine **13r** (94.4 mg, 0.250 mmol) and then dry toluene (0.5 mL) under an argon flow through side-arm of the Schlenk flask. The reaction mixture was stirred for 5 min to give a light orange solution. The flask was then cooled to –10 °C. To this solution was rapidly added ethyl diazoacetate (EDA) **2** (31 μL, 0.30 mmol) followed by closing the Teflon valve. The resulting mixture was stirred for 2 h at –10 °C It was then warmed to room temperature and stirred for 24 h at room temperature. The reaction was dilluted by addition of hexane (6 mL). The reaction mixture was then transferred to a 50 mL round bottom flask. The reaction flask was rinsed with dichloromethane (3 mL × 2) and the rinse was added to the 50 mL round bottom flask. The resulting solution was then concentrated

in vacuo followed by exposure to high vacuum (0.05 mm Hg) for 1 h to afford the crude aziridine as an off-white solid.

The *cis/trans* ratio was determined by comparing the ^{1}H NMR integration of the ring methine protons for each aziridine in the crude reaction mixture. The yields of the acyclic enamine side products **23r** and **24r** were determined by ^{1}H NMR analysis of the crude reaction mixture by integration of the *N*-H proton relative to the that of the *cis*-aziridine methine protons with the aid of the isolated yield of the *cis*-aziridine. Purification of the crude aziridine by silica gel chromatography (30 mm × 300 mm column, 15:1 hexanes/EtOAc with 1 % Et_3N as eluent, gravity column; the column was set up by making a slurry of silica gel in hexanes with 2 % Et_3N) afforded pure cis-aziridine **19r** as a white solid (mp 45-46 ºC on 94% ee material) in 57 % isolated yield (66.0 mg, 0.143 mmol); *cis/trans*: 9.3:1. Enamine side products: 1.3 % yield of **23r** and 1% yield of **24r**. The optical purity of **19r** was determined to be 89% *ee* by HPLC analysis (CHIRALCEL OD-H column, 99.5:0.5 hexane/2-propanol at 226 nm, flow-rate: 0.7 mL/min): retention times; R_t = 23.6 min (major enantiomer, **19r**) and R_t = 39.1 min (minor enantiomer, *ent*-**19r**). The spectral data of **19r** matched to those reported above (see Section F).

H. Synthesis of *β*-hydroxy-*α*-amino ester 21 and *α*-amino ester 22:



(2*R*,3*S*)-ethyl 2-((*tert*-butoxycarbonyl)amino)-3-hydroxy-3-phenylpropanoate 21: Aldehyde **4a** (52.0 μL, 0.525 mmol) was reacted according to the general Procedure A described above with (*S*)-VAPOL as ligand. The reaction time was 3 h. After 3 h, the reaction was dilluted by addition of hexane (6 mL). The reaction mixture was then filtered through a Celite pad to a 100 mL round bottom flask. The reaction flask was rinsed with EtOAc (3 mL × 3) and the rinse was filtered through the same Celite pad. The resulting solution was then concentrated *in vacuo* followed by exposure to high vacuum (0.05 mm Hg) for 1 h to afford the crude aziridine as an off-white solid. The aziridine was used without any further purification. The crude aziridine **19a** was dissolved in acetone (250 mL). To this solution was added trifluoromethanesulfonic acid (2.21 mL, 25 mmol, 5.0 equiv.) at room temperature. The flask was then equipped with an air condenser and a nitrogen balloon at the top of the condenser through a rubber septum. The solution was stirred at 60 ºC for 3 h under nitrogen atmosphere. The reaction was monitored by TLC. To the solution was then added water (50 mL) and the resulting mixture was stirred at 60 ºC for 10 h. The solution was then cooled to room temperature and the volume was reduced to half by rotary evaporation. Water (200 mL) was added to the resulting mixture. The mixture was washed with ether (40 mL × 3). To the water layer was added solid sodium bicarbonate until pH ~ 9. To the resulting mixture was added THF (85 mL) and di t*ert*-butyl dicarbonate (1.75 g, 8.5 mmol, 1.6 equiv). The mixture was stirred at room temperature for 12 h. The mixture was then extracted with ethyl acetate (100 mL × 4).). The combined organic layer was washed with saturated aqueous NaCl solution (40 mL × 2) and dried over anhydrous $MgSO_4$. The ethyl acetate was removed by rotary evaporation. Purification by silica gel chromatography (1:2 ether / hexanes as eluent) afforded **21** as colorless oil in 60% isolated yield (93 mg, 0.30 mmol). The optical purity of **21** was determined to be 98% *ee* by HPLC analysis (CHIRALCEL PAK-AS column, 85:15 hexane/2-propanol at 222 nm, flow-rate: 0.5 mL/min): retention times; R_t = 15.0 min (major enantiomer, **21**) and R_t = 13.9 min (minor enantiomer, *ent*-**21**).

Spectral data for **21**: R_f = 0.49 (2:1 Et_2O/hexanes); ^1H NMR ($CDCl_3$, 300 MHz) δ 1.22 (t, 3H, J = 7.1 Hz), 1.32 (br s, 9H), 3.35 (brs, 1H), 4.17 (q, 2H, J = 7.3 Hz), 4.49 (brd, 1H, J = 7.1 Hz), 5.16-5.19 (m, 1H), 5.42 (brs, 1H), 7.25-7.37 (m, 5H); ^{13}C ($CDCl_3$, 75 MHz) δ 14.05, 28.14, 59.51, 61.67, 74.15, 80.03, 126.06, 128.02, 128.34, 139.80, 155.65, 170.83; $[\alpha]^{20}_D$ +7.0 (*c* 1.1, EtOH). The optical rotation matches to the previously reported for this compound.[8]

(*R*)-ethyl 2-((tert-butoxycarbonyl)amino)-3-phenylpropanoate 22: Aldehyde **4a** (52.0 μL, 0.525 mmol) was reacted according to the general Procedure A described above with (*S*)-VAPOL as ligand. The reaction time was 3 h. After 3 h, the reaction was dilluted by addition of hexane (6 mL). The reaction mixture was then filtered through a Celite pad to a 100 mL round bottom flask. The reaction flask was rinsed with EtOAc (3 mL × 3) and the rinse was filtered through the same Celite pad. The resulting solution was then concentrated *in vacuo* followed by exposure to high vacuum (0.05 mm Hg) for 1 h to afford the crude aziridine as an off-white solid. The aziridine was used without any further purification. The crude aziridine **19a** was dissolved in methanol (10 mL). To this solution was added di t*ert*-butyl dicarbonate (327 mg, 1.50 mmol, 3.00 equiv) and palladium hydroxide (175 mg, 0.150 mmol $Pd(OH)_2$ on carbon powder, 20% Pd, moisture *ca*. 60%) at room temperature. The flask was then equipped with a vacuum transfer adapter connected to vacuum and a balloon filled with hydrogen. The valve to vacuum (5-10 mm Hg) was opened for a few seconds, and then switched to the hydrogen balloon. This process was repeated 5 times. The reaction mixture was stirred at room temperature for 24 h under hydrogen atmosphere. The reaction mixture was filtered through Celite pad and the Celite pad was washed with ether. The solvent was removed by rotary evaporation. Purification by silica gel chromatography (1:2 ether / hexanes as eluent) afforded **22** as colorless oil in 70% isolated yield (103 mg, 0.350 mmol). The optical purity of **22** was determined to be 98% *ee* by HPLC analysis (CHIRALCEL PAK-AS column, 85:15 hexane/2-propanol at 222 nm, flow-rate: 0.2 mL/min): retention times; R_t = 26.1 min (major enantiomer, **22**) and R_t = 31.5 min (minor enantiomer, *ent*-**22**).

Spectral data for **22**: R_f = 0.30 (1:5 EtOAc/hexanes); ^{1}H NMR ($CDCl_3$, 500 MHz) 1.24 (t, 3H, *J* = 7.0 Hz), 1.44 (s, 9H), 3.05-3.15 (m, 2H), 4.17 (q, 2H, *J* = 7.1 Hz), 4.58 (bd, 1H, *J* = 7.4 Hz), 5.00 (bd, 1H, *J* = 6.4 Hz), 7.15 (d, 2H, *J* = 6.9 Hz), 7.24-7.32 (m, 3H); ^{13}C ($CDCl_3$, 125 MHz) δ 14.08, 28.28, 38.39, 54.43 61.23, 79.80, 126.93, 128.45, 129.34, 136.09, 155.07, 171.84; $[\alpha]^{20}_D$ +4.2 (*c* 1.0, EtOH). These spectral data match those previously reported for this compound.[9]

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