Eur. J. Org. Chem. **2007** · © WILEY-VCH Verlag GmbH & Co. KGaA, 69451 Weinheim, 2007 · ISSN 1434–193X

SUPPORTING INFORMATION

Title: Aziridinyl Vinyl Ketones from the Asymmetric Catalytic Aziridination Reaction
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Ref. No.: O200601126

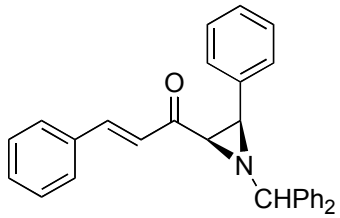
General procedure for the preparation of the vinyl diazomethyl ketones 4.[6]

A flame dried 250 mL three neck round bottom flask equipped with a pressure equalizing liquid addition funnel and a magnetic stir bar was charged with 17.5 mL of dry THF and 3.98 mL (18.75 mmol) of 1,1,1,3,3,3-hexamethyldisilazane and then cooled in an ice-bath. To this solution is added 7.2 mL of a 2.5 M solution (18.0 mmol) of *n*-butyllithium in hexane over a 5 min period. After 10 min, the resulting solution was cooled to -78 °C, and then a solution of the appropriate methyl vinyl ketone **1** (17 mmol) in 17.5 mL of dry THF was added dropwise over 10 min. The dropping funnel was rinsed with two 1-mL portions of THF. The yellow solution was allowed to stir for 30 min at -78 °C, and then 2.53 mL (18.75 mmol) of 2,2,2-trifluoroethyl trifluoroacetate was added rapidly in one portion via syringe. After another 10 min, the reaction mixture was poured into a separatory funnel containing 25 mL diethyl ether and 50 mL 5% aqueous hydrochloric acid. The aqueous layer was separated and extracted with 12 mL diethyl ether. The combined organic layers were washed with 50 mL brine, dried over magnesium sulfate, filtered, and concentrated under reduced pressure to afford a yellow oil. This yellow oil was immediately dissolved in 17.5 mL acetonitrile. Water (0.3 mL), triethylamine (3.6 mL) and a solution of 25.75 mmol of mesylazide in 2.5 mL acetonitrile are then sequentially added via the dropping funnel. The resulting yellow solution was stirred at room temperature for 6 h, and then poured into separatory funnel containing 25 mL diethyl ether and 50 mL 5% aqueous sodium hydroxide. The organic layer was separated and washed with 5% aqueous sodium hydroxide (3 X 50 mL), water, (4 X 50 mL) and 50 mL brine. The organic layer was then dried over magnesium sulfate and concentrated to the give crude product. Further purification by either recrystallization or flash chromatography afforded pure vinyl diazomethyl ketone **4**.

General procedure for catalytic asymmetric aziridination of vinyl diazomethyl ketones 4.

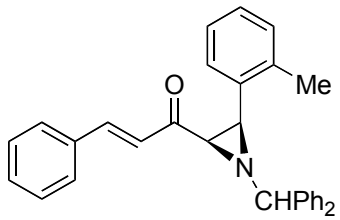
(*S*)-VAPOL (27 mg, 0.05 mmol) and 1 mL of dry dichloromethane were added to a flame-dried 25 mL single-necked round-bottomed flask which had the 14/20 joint replaced with a threaded high-vacuum telfon stopcock. After the addition of 43.5 mg (0.15 mmol) triphenylborate, the stopcock was sealed and the flask was heated to 55 °C for 1 h and then a high vacuum was applied for half an hour with the temperature maintained at 55 °C. The catalyst was then dissolved in 0.5 mL of dichloromethane and transferred by syringe to a 25 mL flame dried flask which had been previously charged with 0.50 mmol of the requisite imine in 0.5 mL of dichloromethane. After stirring for 10 min, 0.6 mmol of the desired vinyl diazomethyl ketone **2** was added. The reaction was monitored by TLC and was found to be complete after 24 h at 25 °C. The reaction mixture was diluted with 5 mL of dichloromethane and then 5 mL of saturated aqueous sodium bicarbonate was added. The organic layer was separated and then washed with brine (3 mL), dried over magnesium sulfate, filtered, and concentrated under vacuum to give the crude product. The *cis/trans* ratio of the aziridine **4** was determined by relative integration of the ^{1}H NMR signals for the methine protons on the three-membered ring in the spectrum of the crude reaction mixture. For most aziridines, these protons appear as doublets between 2 and 4 ppm and have coupling constants of 7 Hz for the *cis*-aziridines and ~2 Hz for the *trans*-aziridines. Purification by flash chromatography on silica gel with hexanes/ethyl acetate as eluent gave the pure *cis*-aziridines as white solids. The asymmetric induction was measured by chiral HPLC on the purified *cis*-aziridines. The amount of the enamine side-product was calculated from the isolated yield of the *cis*-aziridine and the relative integration of the NH signal of the enamine and the 3-membered ring methine proton of the *cis*-aziridine in the crude reaction mixture. The enamine side-product is often formed as a mixture of isomers and the NH absorption for both generally appear between 11.5 and 12.5 ppm. For each different substrate, a sample of the racemic

aziridine was prepared by the reaction of the appropriate imine and vinyl diazomethyl ketone catalyzed by boron trifluoride etherate. The racemic aziridine was utilized in determining the retention time of each enantiomer in the chiral HPLC analysis. The absolute configuration of the *cis*-aziridine product was assumed to result from si-face addition to the imine by the catalyst derived from S-VAPOL as was shown to be the case for the reaction with ethyl diazoacetate.[5] Most of the reactions were run with catalysts generated from both (*R*)-VAPOL and from (*S*)-VAPOL, however, the optical rotations were reported on the product from the reaction with (S)-VAPOL.



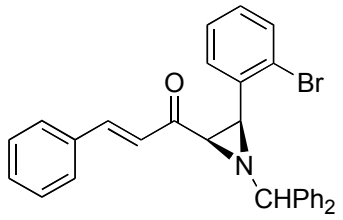
4a

4a: White solid, 79% yield, 95% ee, cis:trans ≥50:1, mp = 150 °C, R_f = 0.33 (hexanes:ethyl acetate, 8:2); ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.91 (d, *J* = 7.1 Hz, 1 H), 3.38 (d, *J* = 7.1 Hz, 1 H), 3.99 (s, 1 H), 6.81 (d, *J* = 16.2 Hz, 1 H), 7.08 - 7.41 (m, 17 H), 7.51 - 7.55 (m, 4 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 49.8, 52.4, 78.3, 123.6, 127.2, 127.3, 127.4, 127.5, 127.60, 127.63, 128.0, 128.3, 128.6, 128.7, 130.3, 134.6, 135.1, 142.2, 142.3, 142.5, 194.8 (1 sp^2 C not located); IR (KBr) 3062, 3029, 1683, 1657, 1610, 1494, 1452, 1206, 1099, 764 cm^{-1}; mass spectrum (EI) *m/z* (% relative intensity): 415 M^+ (1), 248 (77), 167 (100), 131 (40), 115 (42), 103 (34). Anal calcd for $C_{30}H_{25}NO$: C, 86.71; H, 6.06; N, 3.37. Found: C, 86.44; H, 5.97; N, 3.38. $[\alpha]_D^{20}$ + 109.2 (*c* 1, CH_2Cl_2). HPLC (chiralcel OD, hexanes/*i*-PrOH = 90/10, flow rate = 1.0 mL/min): R_t = 8.0 min (major enantiomer), R_t = 11.2 min (minor enantiomer).



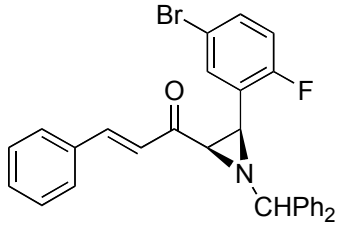
4b

4b: White solid; 45% yield, 91% ee, cis:trans ≥50:1, mp = 149 °C, R_f = 0.15 (hexanes:ethyl acetate, 9:1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.26 (s, 3 H), 2.93 (d, *J* = 7.1 Hz, 1 H), 3.38 (d, *J* = 7.1 Hz, 1 H), 4.04 (s, 1 H), 6.85 (d, *J* = 15.9 Hz, 1 H), 7.01 - 7.10 (m, 3 H), 7.23 - 7.40 (m, 12 H), 7.51 – 7.60 (m, 5 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 18.9, 49.0, 52.2, 78.5, 122.7, 125.3, 127.0, 127.3, 127.4, 127.6, 127.8, 128.0, 128.4, 128.6, 128.6, 128.7, 129.6, 130.3, 133.3, 134.8, 136.3, 142.0, 142.2, 142.5, 195.4; IR (KBr) 3062, 3029, 1683, 1610, 1578, 1489, 1452, 1341, 1192, 1099, 1062, 750 cm^{-1}; mass spectrum (EI) *m/z* (% relative intensity) 429 M^+ (2), 262 (100), 167 (33), 131 (85), 115 (26), 103 (51). Anal calcd for $C_{31}H_{27}NO$: C, 86.68; H, 6.34; N, 3.26. Found: C, 86.71; H, 6.03; N, 3.22. $[\alpha]_D^{20}$ + 57.4 (*c* 1, CH_2Cl_2). HPLC (chiralcel OD, hexanes/*i*-PrOH = 9/1, flow rate = 1.0 mL/min): R_t = 6.0 min (major enantiomer), R_t = 9.1 min (minor enantiomer).



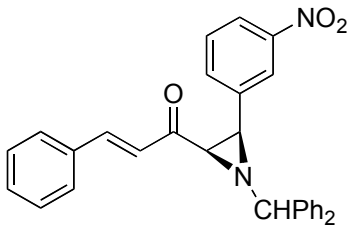
4c

4c: White solid; 55% yield, 93% ee, cis:trans = 12:1, mp = 160-161 °C, R_f = 0.26 (hexanes:ethyl acetate, 9:1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.16 (d, J = 6.9 Hz, 1 H), 3.53 (d, J = 6.9 Hz, 1 H), 4.10 (s, 1 H), 6.74 (d, J = 16.2 Hz, 1 H), 7.02 (t, J = 7.4, 1 H), 7.20 - 7.59 (m, 19 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 50.6, 52.0, 78.0, 123.4, 123.8, 126.8, 127.0, 127.3, 127.6, 127.7, 128.3, 128.56, 128.61, 128.7, 128.9, 130.3, 130.4, 131.9, 134.3, 134.5, 142.0, 142.4, 142.7, 193.3; IR (KBr) 3061, 3029, 1694, 1619, 1578, 1499, 1452, 1364, 1308, 1062, 1029, 983, 764 cm^{-1}; mass spectrum (EI) *m/z* (% relative intensity) 495 M^+ (^{81}Br, 2), 493 M^+ (^{79}Br, 2), 328 (100), 326 (99), 192 (42), 167 (98), 142 (42), 131 (84), 115 (48), 103 (84), 89 (65), 77 (40). Anal calcd for $C_{30}H_{24}BrNO$: C, 72.88; H, 4.89; N, 2.83. Found: C, 72.79; H, 4.66; N, 2.80. $[\alpha]_D^{20}$ + 73.2 (*c* 1, CH_2Cl_2). HPLC (chiralcel OD, hexanes/*i*-PrOH = 90/10, flow rate = 1.0 mL/min): R_t = 7.1 min (major enantiomer), R_t = 10.4 min (minor enantiomer).



4d

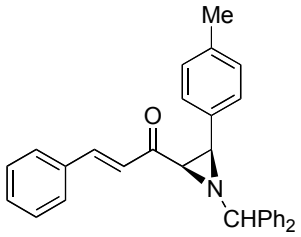
4d: White solid; 64% yield, 95% ee, cis:trans = 14:1, mp = 120-121 °C, R_f = 0.33 (hexanes:ethyl acetate, 8:2); ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.08 (d, J = 7.0 Hz, 1 H), 3.43 (d, J = 7.0 Hz, 1 H), 4.03 (s, 1 H), 6.69 - 6.80 (m, 2 H), 7.16 - 7.65 (m, 18 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 43.7, 51.8, 78.0, 116.3 (d, J = 3 Hz), 116.5 (d, J = 25 Hz), 123.4, 124.6, 124.8, 127.0, 127.5, 127.6 (d, J = 25 Hz), 128.4, 128.6, 128.7, 128.8, 130.6, 131.8 (d, J = 7.5 Hz), 132.6 (d, J = 3 Hz), 134.3, 141.8, 142.1, 143.1, 160.2 (d, J = 248 Hz), 193.1; IR (KBr) 3061, 3029, 1676, 1605, 1495, 1457, 1308, 1253, 1183, 1108, 1071, 816 cm^{-1}; mass spectrum (EI) *m/z* (% relative intensity) 513 M^+ (^{79}Br, 1), 511 M^+ (^{81}Br, 1), 346 (48), 344 (51), 291 (10), 289 (11), 167 (100), 165 (38), 131 (65), 103 (59). Anal calcd for $C_{30}H_{23}BrFNO$: C, 70.32; H, 4.52; N, 2.73. Found: C, 70.40; H, 4.51; N, 2.73. $[\alpha]_D^{20}$ + 199.4 (*c* 1, CH_2Cl_2). HPLC (chiralcel OD, hexanes/*i*-PrOH = 90/10, flow rate = 1.0 mL/min): R_t = 8.8 min (major enantiomer), R_t = 13.6 min (minor enantiomer).



4e

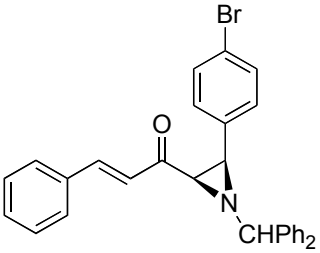
4e: White solid; 78% yield, 94 % ee, cis:trans ≥50:1, mp = 118-119 °C, R_f = 0.15 (hexanes:ethyl acetate, 8:2); ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.07 (d, J = 7.0 Hz, 1 H), 3.40 (d, J = 7.0 Hz, 1 H), 4.04 (s, 1H), 6.81 (d, J = 15.9 Hz, 1 H), 7.19 - 7.57 (m, 17 H), 7.68 (d, J = 7.7 Hz, 1 H), 7.97 (m, 1 H), 8.22 (t, J = 1.6 Hz, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 48.6, 52.5, 78.1,

122.5, 122.8, 123.4, 127.1, 127.4, 127.6, 127.7, 128.4, 128.71, 128.72, 128.9, 129.0, 130.8, 133.8, 134.1, 137.3, 141.8, 142.0, 143.4, 147.9, 193.2; IR (KBr) 3065, 3027, 1651, 1611, 1530, 1494, 1457, 1350, 1201, 1104, 1171, 988, 744 cm^{-1}; mass spectrum (EI) *m/z* (% relative intensity) 460 M^+ (2), 293 (51), 167 (100), 131 (56), 115 (24), 103 (40). Anal calcd for $C_{30}H_{24}N_2O_3$: C, 78.24; H, 5.25; N, 6.08. Found: C, 78.37; H, 5.05; N, 6.01. $[\alpha]_D^{20}$ + 101.6 (*c* 1, CH_2Cl_2). HPLC (chiralcel OD, hexanes/*i*-PrOH = 80/20, flow rate = 1.0 mL/min): R_t = 9.2 min (major enantiomer), R_t = 16.4 min (minor enantiomer).



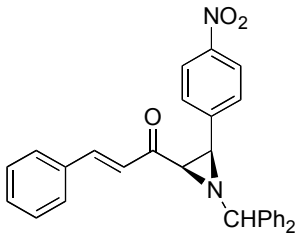
4f

4f: White solid; 71% yield, 99.7% ee, cis:trans ≥50:1, mp = 145 °C, R_f = 0.35 (hexanes:ethyl acetate, 8:2); ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.20 (s, 3 H), 2.90 (d, *J* = 6.9 Hz, 1 H), 3.34 (d, *J* = 6.9 Hz, 1 H), 3.98 (s, 1 H), 6.82 (d, *J* = 16.2 Hz, 1 H), 6.99 (d, *J* = 7.7 Hz, 2 H), 7.18 - 7.56 (m, 18 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 21.1, 49.8, 52.4, 78.4, 123.8, 127.2, 127.3, 127.4, 127.5, 127.6, 128.3, 128.51, 128.54, 128.7, 130.3, 132.0, 134.7, 137.0, 142.2, 142.3, 142.5, 194.8 (1 sp^2 C not located); IR (KBr) 3070, 3031, 1685, 1613, 1576, 1516, 1495, 1450, 1371, 1192, 1185, 1063, 1030, 976, 814, 749 cm^{-1}; mass spectrum (EI) *m/z* (% relative intensity) 429 M^+ (2), 262 (100), 167 (37), 131 (59), 115 (28), 103 (40). Anal calcd for $C_{31}H_{27}NO$: C, 86.68; H, 6.34; N, 3.26. Found: C, 86.77; H, 6.19; N, 3.22. $[\alpha]_D^{20}$ + 121.8 (*c* 1, CH_2Cl_2). HPLC (chiralcel OD, hexanes/*i*-PrOH = 90/10, flow rate = 1.0 mL/min): R*t* = 7.8 min (major enantiomer), R*t* = 10.5 min (minor enantiomer).



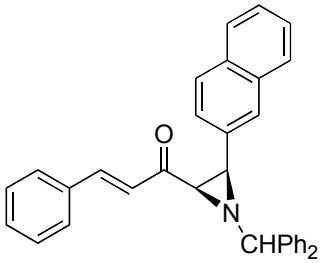
4g

4g: White solid; 51% yield, 96% ee, cis:trans = 14:1, mp = 155-156 °C, R_f = 0.28 (hexanes:ethyl acetate, 8:2); ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.97 (d, *J* = 7.0 Hz, 1 H), 3.28 (d, *J* = 7.0 Hz, 1 H), 3.99 (s, 1 H), 6.77 (d, *J* = 15.9 Hz, 1 H), 7.17 - 7.55 (m, 20 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 49.2, 52.4, 78.2, 121.3, 123.6, 127.2, 127.38, 127.41, 127.51, 128.3, 128.5, 128.8, 129.3, 130.5, 131.1, 134.1, 134.4, 142.0, 142.2, 142.8, 193.8 (1 sp^2 C not located); IR (KBr) 3070, 3038, 1685, 1613, 1576, 1491, 1450, 1342, 1192, 1183, 1068, 976, 817, 744 cm^{-1}; mass spectrum (EI) *m/z* (% relative intensity) 495 M^+ (^{81}Br, 2), 493 M^+ (^{81}Br, 2), 328 (69), 326 (69), 192 (31), 167 (100), 152 (29), 143 (35), 142 (33), 131 (82), 115 (46), 103 (68), 89 (55). Anal calcd for $C_{30}H_{24}BrNO$: C, 72.88; H, 4.89; N, 2.83. Found: C, 72.56; H, 4.64; N, 2.77. $[\alpha]_D^{20}$ + 103.2 (*c* 1, CH_2Cl_2). HPLC (chiralcel OD, hexanes/*i*-PrOH = 90/10, flow rate = 1.0 mL/min): R_t = 8.5 min (major enantiomer), R_t = 14.9 min (minor enantiomer).



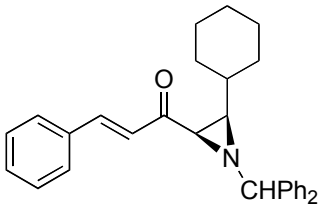
4h

4h: White solid; 80% yield, 95% ee, cis:trans ≥50:1, mp = 153 °C, R_f = 0.17 (hexanes:ethyl acetate, 8:2); ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.12 (d, J = 7.0 Hz, 1 H), 3.39 (d, J = 7.0 Hz, 1 H), 4.05 (s, 1 H), 6.75 (d, J = 16.2 Hz, 1 H), 7.21 - 7.57 (m, 18 H), 8.05 (d, J = 8.8 Hz, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 48.8, 52.8, 78.1, 123.3, 123.5, 127.2, 127.4, 127.6, 127.7, 128.4, 128.5, 128.7, 128.9, 130.8, 134.1, 141.8, 142.0, 142.6, 143.5, 147.1, 192.8 (1 sp^2 C not located); IR (KBr) 3029, 1678, 1605, 1576, 1520, 1495, 1451, 1348, 1192, 1107, 1065, 992, 745 cm^{-1}; mass spectrum (EI) *m/z* (% relative intensity) 460 M^+ (1), 293 (33), 167 (100), 131 (37), 115 (24), 103 (29). Anal calcd for $C_{30}H_{24}N_2O_3$: C, 78.24; H, 5.25; N, 6.08. Found: C, 78.02; H, 5.03; N, 6.09. $[\alpha]_D^{20}$ + 106.1 (*c* 1, CH_2Cl_2). HPLC (chiralcel OD, hexanes/*i*-PrOH = 80/20, flow rate = 1.0 mL/min): R_t = 9.8 min (major enantiomer), R_t = 20.4 min (minor enantiomer).



4i

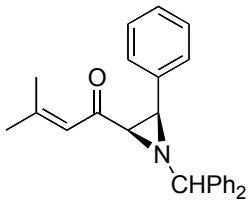
4i: White solid; 84% yield, 98.3% ee, cis:trans ≥50:1, mp = 149-150 °C, R_f = 0.31 (hexanes:ethyl acetate, 8:2); ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.04 (d, J = 6.9 Hz, 1 H), 3.55 (d, J = 6.9 Hz, 1 H), 4.10 (s, 1 H), 6.88 (d, J = 16.2 Hz, 1 H), 7.22 – 7.84 (m, 23 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 50.0, 52.6, 78.2, 123.7, 125.4, 125.6, 125.9, 126.7, 127.26, 127.32, 127.4, 127.5, 127.6, 127.7, 128.2, 128.47, 128.53, 128.6, 130.2, 132.6, 132.9, 134.5, 142.1, 142.3, 142.4, 194.4 (2 sp^2 C not located); IR (KBr) 3061, 3027, 1659, 1609, 1576, 1495, 1451, 1333, 1307, 1192, 1103, 1063, 820, 748 cm^{-1}; mass spectrum (EI) *m/z* (% relative intensity) 465 M^+ (4), 298 (88), 167 (64), 131 (100), 115 (37), 103 (59); HRMS calcd for $C_{34}H_{27}NO$ *m/z* 465.2093, meas 465.2099 (6.5). $[\alpha]_D^{20}$ + 71.7 (*c* 1, CH_2Cl_2). HPLC (chiralcel OD, hexanes/*i*-PrOH = 90/10, flow rate = 1.0 mL/min): R_t = 10.1 min (major enantiomer), R_t = 16.0 min (minor enantiomer).



4j

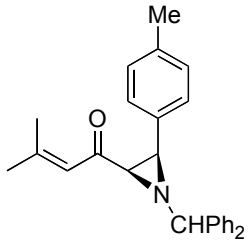
4j: White solid; 90% yield, 93% ee, cis:trans = 5:1, mp = 187-188 °C, R_f = 0.33 (hexanes:ethyl acetate, 85:15); ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.50 (m, 1 H), 0.56-1.63 (m, 10 H), 1.96 (dd, J = 9.4, 6.6 Hz, 1 H), 2.64 (d, J = 6.6 Hz, 1 H), 3.67 (s, 1 H), 7.06 - 7.68 (m, 17 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 25.3, 25.5, 26.0, 30.2, 30.9, 36.4, 50.1, 55.0, 78.7, 124.4, 126.9, 127.0, 127.5, 128.3, 128.36, 128.43, 128.9, 130.5, 134.6, 142.3, 142.5, 142.7, 195.7 (1 sp^2 C not located); IR (KBr) 3063,

3031, 2923, 2847, 1682, 1637, 1609, 1576, 1495, 1449, 1325, 1192, 1030, 980, 765 cm^{-1}; mass spectrum (EI) *m/z* (% relative intensity) 421 M^+ (1), 338 (19), 254 (88), 172 (81), 167 (100), 131 (27), 103 (38). Anal calcd for $C_{30}H_{31}NO$: C, 85.47; H, 7.41; N, 3.32. Found: C, 85.37; H, 7.23; N, 3.28. $[\alpha]_D^{20}$ + 281.6 (*c* 1, CH_2Cl_2). HPLC (chiralcel OD, hexanes/*i*-PrOH = 95/5, flow rate = 1.0 mL/min): R_t = 6.2 min (major enantiomer), R_t = 7.7 min (minor enantiomer).



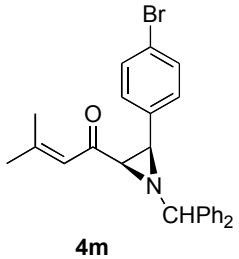
4k

4k: White solid; 76% yield, 98.1% ee, cis:trans = 15:1, mp = 132 °C, R_f = 0.23 (hexanes:ethyl acetate, 9:1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.69 (s, 3 H), 1.81 (s, 3 H), 2.69 (d, *J* = 7.1 Hz, 1 H), 3.24 (d, *J* = 7.1 Hz, 1 H), 3.91 (s, 1 H), 6.15 (m, 1 H), 7.13 - 7.33 (m, 11 H), 7.52 (m, 4 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 20.6, 27.6, 49.5, 53.3, 78.2, 122.5, 122.6, 127.0, 127.2, 127.4, 127.5, 127.7, 128.5, 135.3, 142.4, 142.6, 155.5, 196.6 (2 sp^2 C not located); IR (KBr) 3070, 3033, 2977, 2931, 1685, 1605, 1493, 1450, 1373, 1215, 1119, 890, 748 cm^{-1}; mass spectrum (EI) *m/z* (% relative intensity) 367 M^+ (0.8), 200 (100), 167 (28), 145 (40), 91 (37), 83 (98). Anal calcd for $C_{26}H_{25}NO$: C, 84.98; H, 6.86; N, 3.81. Found: C, 84.62; H, 6.78; N, 3.80. $[\alpha]_D^{20}$ + 64.5 (*c* 1, CH_2Cl_2). HPLC (chiralcel OD, hexanes/*i*-PrOH = 97/3, flow rate = 1.0 mL/min): R_t = 6.6 min (major enantiomer), R_t = 8.4 min (minor enantiomer).



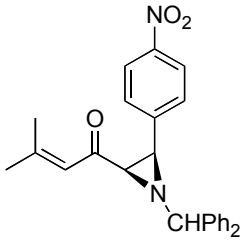
4l

4l: White solid; 83% yield, 96.1% ee, cis:trans ≥50:1, R_f = 0.23 (hexanes:ethyl acetate, 9:1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.70 (s, 3 H), 1.84 (s, 3 H), 2.25 (s, 3 H), 2.66 (d, *J* = 7.1 Hz, 1 H), 3.20 (d, *J* = 7.1 Hz, 1 H), 3.90 (s, 1 H), 6.16 (m, 1 H), 6.99 (d, *J* = 8.0 Hz, 2 H), 7.15 - 7.33 (m, 8 H), 7.51 (m, 4 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 20.6, 21.1, 27.6, 49.4, 53.4, 78.3, 122.6, 127.2, 127.3, 127.5, 127.6, 128.4, 132.3, 136.5, 142.5, 142.7, 155.3, 195.7 (4 sp^2 C not located); IR (KBr) 3029, 2924, 1682, 1607, 1493, 1453, 1375, 1119, 1063, 818, 747 cm^{-1}; mass spectrum (EI) *m/z* (% relative intensity) 381 M^+ (1), 214 (94), 167 (25), 159 (29), 105 (36), 83 (100). Anal calcd for $C_{27}H_{27}NO$: C, 85.00; H, 7.13; N, 3.67. Found: C, 85.00; H, 7.07; N, 3.71. $[\alpha]_D^{20}$ + 140.0 (*c* 1, CH_2Cl_2). HPLC (chiralcel OD, hexanes/*i*-PrOH = 98/2, flow rate = 1.0 mL/min): R_t = 7.3 min (major enantiomer), R_t = 9.6 min (minor enantiomer).



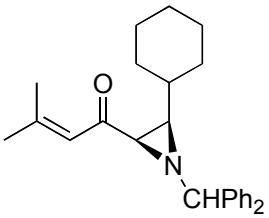
4m

4m: White solid; 76% yield, 98.5% ee, cis:trans = 20:1, mp = 151-152 °C, R_f = 0.17 (hexanes:ethyl acetate, 9:1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.73 (s, 3 H), 1.86 (s, 3 H), 2.72 (d, J = 7.1 Hz, 1 H), 3.15 (d, J = 7.1 Hz, 1 H), 3.90 (s, 1 H), 6.12 (m, 1 H), 7.15 - 7.33 (m, 10 H), 7.45 - 7.53 (m, 4 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 20.7, 27.7, 48.7, 53.4, 78.1, 121.0, 122.3, 122.4, 127.2, 127.3, 127.4, 128.5, 129.4, 130.9, 134.5, 142.2, 142.4, 156.3, 194.8 (1 sp^2 C not located); IR (KBr) 3066, 3029, 2982, 1688, 1624, 1489, 1450, 1373, 1119, 1005, 1015, 816, 742 cm^{-1}; mass spectrum (EI) *m/z* (% relative intensity) 447 M^+ (^{81}Br, 0.3), 445 M^+ (^{79}Br, 0.3), 280 (59), 278 (59), 16 7 (47), 83 (100). Anal calcd for $C_{26}H_{24}BrNO$: C, 69.96; H, 5.42; N, 3.14. Found: C, 69.73; H, 5.35; N, 3.13. $[\alpha]_D^{20}$ + 84.7 (*c* 1, CH_2Cl_2). HPLC (chiralcel OD, hexanes/*i*-PrOH = 98/2, flow rate = 1.0 mL/min): R_t = 8.0 min (major enantiomer), R_t = 12.5 min (minor enantiomer).



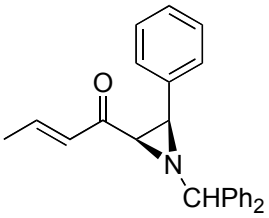
4n

4n: White solid; 67% yield, 95.7% ee, cis:trans = 7:1, mp = 119-120 °C, R_f = 0.22 (hexanes:ethyl acetate, 8:2); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.77 (s, 3 H), 1.89 (s, 3 H), 2.88 (d, J = 7.1 Hz, 1 H), 3.28 (d, J = 7.1 Hz, 1 H), 3.98 (s, 1 H), 6.13 (m, 1 H), 7.23 - 7.39 (m, 6 H), 7.48 – 7.58 (m, 6 H), 8.01 (d, J = 6.9 Hz, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 20.8, 27.7, 48.4, 53.9, 122.1, 123.1, 127.1, 127.3, 127.4, 127.6, 128.6, 141.9, 142.1, 143.0, 147.0, 157.5, 193.5 (3 sp^2 C not located); IR (KBr) 3065, 3031, 2978, 1682, 1605, 1520, 1495, 1452, 1348, 1115, 1067, 911, 735 cm^{-1}; mass spectrum (EI) *m/z* (% relative intensity) 412 M^+ (1.0), 167 (100), 152 (32), 83 (95). Anal calcd for $C_{26}H_{24}N_2O_3$: C, 75.71; H, 5.86; N, 6.79. Found: C, 75.32; H, 5.87; N, 6.78. $[\alpha]_D^{20}$ + 58.5 (*c* 1, CH_2Cl_2). HPLC (chiralcel OD, hexanes/*i*-PrOH = 80/20, flow rate = 1.0 mL/min): R_t = 5.8 min (major enantiomer), R_t = 8.7 min (minor enantiomer).



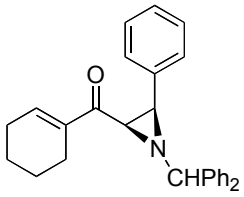
4o

4o: White solid; 75% yield, 94.4% ee, cis:trans = 10:1, mp = 155 °C, R_f = 0.40 (hexanes:ethyl acetate, 9:1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.50 (m, 1 H), 0.80-1.60 (m, 10 H), 1.83 (dd, J = 9.3, 6.9 Hz, 1 H), 1.94 (s, 3 H), 2.16 (s, 3 H), 2.38 (d, J = 6.9 Hz, 1 H), 3.61 (s, 1 H), 6.41 (s, 1 H), 7.18-7.49 (m, 10 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 20.8, 25.3, 25.5, 26.0, 27.7, 30.2, 30.8, 36.2, 51.2, 54.3, 78.6, 100.2, 122.8, 126.8, 127.0, 127.3, 128.16, 128.19, 142.5, 142.9, 155.3, 196.6; IR (KBr) 3066, 3061, 2924, 2851, 1678, 1628, 1495, 1449, 1385, 1334, 1211, 1116, 1064, 1030, 927, 756 cm^{-1}; mass spectrum (EI) *m/z* (% relative intensity) 373 M^+ (0.7), 290 (22), 206 (71), 167 (91), 124 (100), 83 (62). Anal calcd for $C_{26}H_{31}NO$: C, 83.60; H, 8.37; N, 3.75. Found: C, 83.88; H, 8.38; N, 3.74. $[\alpha]_D^{20}$ + 220.2 (*c* 1, CH_2Cl_2). HPLC (chiralcel OD, hexanes/*i*-PrOH = 99/1, flow rate = 1.0 mL/min): R_t = 6.0 min (major enantiomer), R_t = 7.7 min (minor enantiomer).



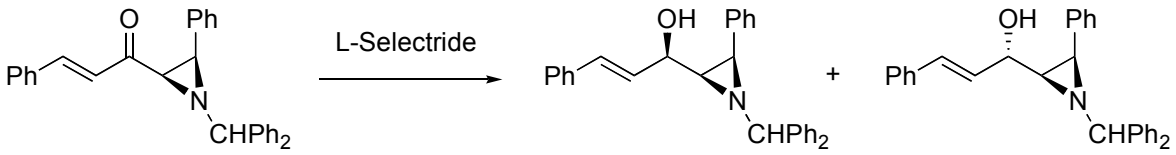
4p

4p: White solid; 85% yield, 95.7% ee, cis:trans = 25:1, mp = 132-133 °C, R_f = 0.17 (hexanes:ethyl acetate, 9:1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.74 (dd, J = 6.9, 1.5 Hz, 3 H), 2.87 (d, J = 7.2 Hz, 1 H), 3.33 (d, J = 7.2 Hz, 1 H), 3.97 (s, 1 H), 6.22 (dd, J = 15.6, 1.5 Hz, 1 H), 6.73 (m, 1 H), 7.15 – 7.36 (m, 11 H), 7.55 (t, J = 7.8 Hz, 4 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 18.2, 49.6, 51.8, 78.2, 127.1, 127.2, 127.4, 127.5, 127.6, 127.8, 128.5, 129.5, 135.0, 142.2, 142.5, 142.8, 194.2 (2 sp^2 C not located); IR (KBr) 3061, 3027, 2921, 1669, 1639, 1495, 1454, 1377, 1304, 1207, 1063, 976, 759 cm^{-1}; mass spectrum (EI) *m/z* (% relative intensity) 353 M^+ (2), 186 (100), 167 (49), 69 (96). $[\alpha]_D^{20}$ + 155.7 (c = 1, CH_2Cl_2). Anal calcd for $C_{25}H_{23}NO$: C, 84.95; H, 6.56; N, 3.96. Found: C, 84.85; H, 6.55; N, 3.89. HPLC (chiralcel OD, hexanes/*i*-PrOH = 90/10, flow rate = 1.0 mL/min): R_t = 6.2 min (major enantiomer), R_t = 7.4 min (minor enantiomer).



4q

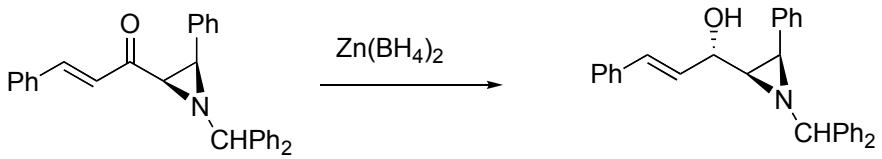
4q: White solid; 40% yield, 82% ee, cis:trans = 6:1, mp = 165 °C, R_f = 0.22 (hexanes:ethyl acetate, 9:1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.44 (m, 4 H), 1.94 (m, 4 H), 3.12 (d, J = 7.0 Hz, 1 H), 3.21 (d, J = 7.0 Hz, 1 H), 3.96 (s, 1 H), 6.82 (m, 1 H), 7.10 - 7.33 (m, 11 H), 7.47 (d, J = 7.1 Hz, 2 H), 7.64 (d, J = 7.4 Hz, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 21.4, 21.6, 22.7, 25.8, 49.2, 50.6, 78.2, 127.0, 127.2, 127.26, 127.32, 127.4, 127.5, 127.8, 128.4, 135.5, 139.4, 140.4, 142.5, 142.7, 193.0 (1 sp^2 C not located); IR (KBr) 3063, 2934, 2857, 1662, 1637, 1495, 1454, 1419, 1204, 1064, 1028, 744 cm^{-1}; mass spectrum (EI) *m/z* (% relative intensity) 393 M^+ (3), 226 (100), 167 (53), 109 (65), 81 (63). Anal calcd for $C_{28}H_{27}NO$: C, 85.46; H, 6.92; N, 3.56. Found: C, 85.26; H, 6.57; N, 3.51. $[\alpha]_D^{20}$ + 125.1 (*c* 1, CH_2Cl_2). HPLC (chiralcel OD, hexanes/*i*-PrOH = 90/10, flow rate = 1.0 mL/min): R_t = 4.7 min (major enantiomer), R_t = 6.2 min (minor enantiomer).



4a **16** 82% **14** 17%

Reduction of 4a with L-Selectride.

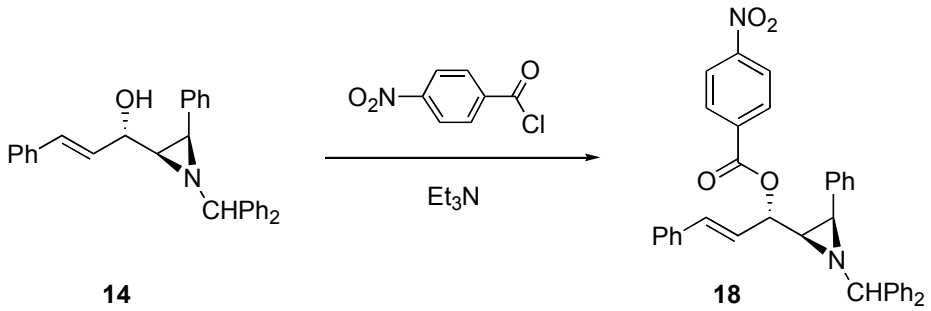
To a solution of ketoaziridine **4a** (0.1 mmol) in 1 mL of THF under argon at -78 °C was added L-Selectride (1M solution in THF, 0.2 mL, 0.2 mmol). The mixture was stirred for 30 min at -78 °C and then warmed to room temperature for a short period. The reaction mixture was treated with 10% aqueous sodium hydroxide and the organic layer was separated. The aqueous layer was extracted with ethyl acetate (3 X 3 mL) and the combined organic extracts were dried over magnesium sulfate, filtered, and concentrated under vacuum. The two isomers **16** and **14** were separated by flash chromatography (hexanes : ethyl acetate = 9 : 1) and were obtained in a total of 99 % yield in a 5: 1 ratio. Spectral data for **16**: colorless oil; R_f = 0.45 (hexanes/ethyl acetate = 8/2); ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.15 (dd, J = 6.9, 7.5 Hz, 1 H), 3.08 (d, J = 6.9 Hz, 1 H), 3.81 (dd, J = 7.5, 6.0 Hz, 1 H), 3.93 (s, 1 H), 5.87 (dd, J = 15.9, 6.0 Hz, 1 H), 6.06 (d, J = 15.9 Hz, 1 H), 7.19 – 7.61 (m, 20 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 47.0, 51.2, 70.7, 78.3, 126.3, 127.0, 127.1, 127.4, 127.5, 127.6, 127.7, 127.8, 128.1, 128.3, 128.4, 129.0, 130.4, 136.2, 136.6, 142.4, 143.6 (1 sp^2 C not located); IR (neat) 1455, 1505, 1605, 3032, 3070, 3439, 3577 cm^{-1}; mass spectrum (EI) *m/z* (% relative intensity) 417 M^+ (2), 250 (63), 117 (82), 91 (100): HRMS calcd for $C_{30}H_{27}NO$ *m/z* 417.2093, meas (EI) 417.2094 (23). Spectral data for **14**: white solid, mp: 145–6 °C; R_f = 0.28 (hexanes/ethyl acetate = 8/2); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.37 (d, J = 3.6 Hz, 1 H), 2.12 (dd, J = 6.3, 8.5 Hz, 1 H), 3.00 (d, J = 6.3 Hz, 1 H), 3.86 (br s, 2 H), 5.71 (dd, J = 5.8, 15.9 Hz, 1 H), 6.38 (d, J = 15.9 Hz, 1 H), 6.99 - 7.50 (m, 20 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 46.4, 50.8, 69.8, 78.7, 126.6, 126.97, 127.02, 127.1, 127.3, 127.6, 128.10, 128.14, 128.3, 128.4, 129.6, 129.8, 136.5, 136.6, 142.8, 142.9 (2 sp^2 C not located); IR (neat) 1449, 1493, 2337, 2362, 3032, 3070, 3414 cm^{-1}; mass spectrum (EI) *m/z* (% relative intensity) 417 M^+ (1), 250 (40), 166 (64), 117 (100), 106 (59), 91 (58); HRMS calcd for $C_{30}H_{28}NO$ (M^+ + 1) *m/z* 418.2171, meas (FAB) 418.2151 (100).



4a **14** 90%

Reduction of 4a with zinc borohydride.

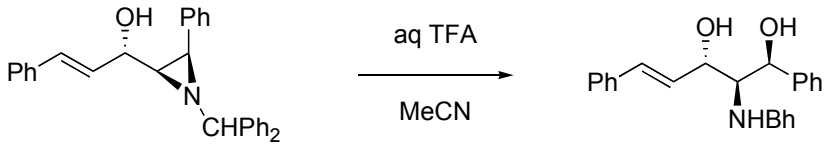
Preparation of zinc borohydride:[7] An ethereal solution of zinc chloride (10 mmol) was added dropwise to a stirred suspension of sodium borohydride (25 mmol) in dry diethyl ether (60 mL). The mixture was stirred at room temperature under argon atmosphere for 12 h. The solid formed (NaCl) was allowed to settle and the liquid was removed and stored in a stoppered bottle under argon atmosphere at -18 °C and was used as a 0.144 M zinc borohydride solution in diethyl ether. To an ice-cold solution of the ketone **4a** in dry diethyl ether was dropwise added a solution of zinc borohydride. After 1 h, the reaction was quenched with water, and then the solution was stirred for another 30 min. The aqueous layer was extracted with diethyl ether and the combined organic layer was washed with brine, dried over magnesium sulfate, filtered, and concentrated under vacuum to afford a light-yellow oil. Purification by flash chromatography on silica gel gave **14** as a white solid in 90 % yield. No trace of the diastereomer **16** could be observed by ^{1}H NMR in the crude reaction mixture (dr ≥50:1).



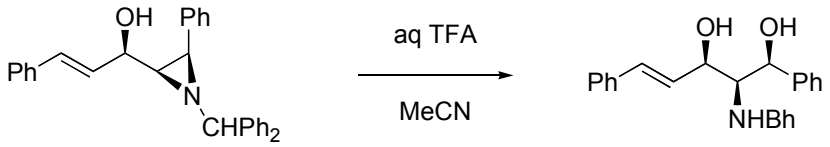
14 **18**

Formation of the *p*-nitrobenzoic acid derivative 18.

To a solution of **14** (40 mg, 0.096 mmol) in dichloromethane (4 mL) was added triethylamine (40 µl, 0.29 mmol) and *p*-nitrobenzoyl chloride (53.4 mg, 0.29 mmol) at 0 °C. The mixture was stirred at room temperature for 24 h and then quenched by the addition of saturated aqueous sodium bicarbonate. The aqueous layer was extracted with dichloromethane (3 X 3 mL). The combined organic layers were washed with brine, dried over magnesium sulfate, filtered, and concentrated under vacuum. Further purification by flash chromatography on silica gel (hexanes : ethyl acetate = 9 : 1) gave 44 mg of **18** as a white solid (78%), mp: 122–4 °C; R_f = 0.40 (hexanes:ethyl acetate, 8:2). The relative stereochemistry of **18** was determined by an X-ray diffraction analysis. The relative stereochemistry in **14** was also determined by its conversion to diol **15** and its corresponding acetonide **19** (see below). Spectal data for **18**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.43 (dd, J = 6.3, 8.4 Hz, 1 H), 3.08 (d, J = 6.3 Hz, 1 H), 3.92 (s, 1 H), 5.11 (dd, J = 8.4, 6.9 Hz, 1 H), 5.76 (dd, J = 6.9, 15.9 Hz, 1 H), 6.37 (d, J = 15.9 Hz, 1 H), 7.01–7.51 (m, 20 H), 7.95 (d, J = 8.7 Hz, 2 H), 8.19 (d, J = 8.7 Hz, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 46.7, 48.0, 74.3, 78.8, 123.3, 125.0, 126.8, 127.1, 127.4, 127.9, 128.0, 128.1, 128.2, 128.4, 128.5, 130.5, 133.1, 135.5, 135.7, 135.8, 142.5, 142.7, 150.3, 162.6 (3 sp^2 C not located); IR (neat) 1104, 1117, 1348, 1455, 1492, 1530, 1605, 1731, 3032, 3070, 3095 cm^{-1}; mass spectrum (EI) *m/z* (% relative intensity) 399 (4), 232 (27), 167 (100); HRMS calcd for $C_{37}H_{31}N_2O_4$ (M^+ + 1) *m/z* 567.2284, meas (FAB) 567.2267 (100).



14 **15** 83%

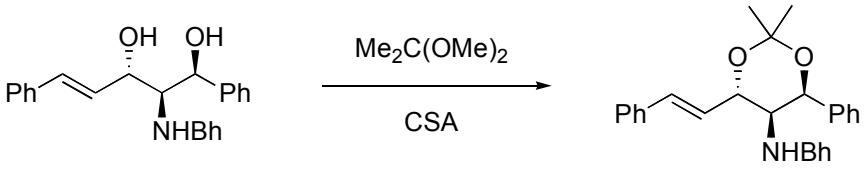


16 **17** 91%

General procedure for ring-opening of aziridine with aqueous trifluoroacetic acid:[8]

To the solution of aziridine **14** or **16** (0.05 mmol) in acetonitrile (2 mL) was treated with 50 % aqueous trifluoroacetic acid (1 mL). The mixture was stirred at room temperature until all the starting material was consumed (~48 h). The reaction was quenched by the addition of saturated aqueous sodium bicarbonate. The aqueous layer was extracted with ethyl acetate (3 X 3 mL). The combined organic layers were washed with brine, dried with magnesium sulfate, filtered, and concentrated under vacuum. Purification by flash chromatography on silica gel (hexanes/ethyl acetate : 85:15) gave the ring-opening products **15** and **17** in 83% and 91% yields, respectively. Spectral data for **15**: colorless oil; R_f = 0.18 (hexanes : ethyl acetate, 8:2); ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.89 (t, J = 3.8 Hz, 1 H), 3.15 (very broad s, 2 H), 4.36 (m, 1 H), 4.50 (s, 1 H), 4.87 (d, J = 4.1 Hz, 1 H), 6.05 (dd, J = 5.8, 15.9 Hz, 1 H), 6.63 (dd, J = 1.4, 15.9 Hz, 1 H), 7.00 – 7.36 (m, 20 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 64.1, 65.1, 72.9, 73.6, 125.9, 126.5, 127.1, 127.2, 127.3, 127.6, 127.7, 128.39, 128.43, 128.5, 128.9, 130.5, 130.9, 136.4, 142.8 (3 sp^2 C not located); IR (neat) 1449, 1499, 2926, 3033, 3063, 3364 cm^{-1}; MS (EI) *m/z* (relative intensity): 167 (100); HRMS (FAB) calcd for $C_{30}H_{30}NO_2$ *m/z* 436.2276, measd 436.2278 (100). Spectral data for **17**: colorless oil; R_f = 0.19 (hexanes:ethyl acetate, 8:2); ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.85 (m, 1 H), 3.20 (very broad s, 2 H), 4.49 (t, J = 4.2 Hz, 1 H), 4.55 (s, 1 H), 5.09 (d, J = 2.5 Hz, 1 H), 6.14 (dd, J = 5.8, 15.9 Hz, 1 H), 6.65 (d, J = 15.9 Hz, 1 H), 6.96 (m, 2 H), 7.13 - 7.33 (m, 18 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 63.8, 65.0, 72.3, 73.6, 125.9, 126.5, 127.0, 127.2, 127.3, 127.5, 127.8, 128.3, 128.4, 128.5, 128.6, 128.8, 131.5, 136.4, 142.4, 142.8, 143.4 (1 sp^2 C not located); IR (neat) 1455, 1486, 1555, 1655, 2331, 2369, 3033, 3345 cm^{-1}; mass spectrum (EI) *m/z* (% relative intensity) 167 (100); HRMS calcd for $C_{30}H_{30}NO_2$ (M^+ + 1) *m/z* 436.2276, measd (FAB) 436.2285 (100).

The keto aziridine **4a** was treated to the same ring-opening conditions and the ring-opened ketone product that was obtained was an unstable colorless oil which could not be properly characterized: R_f = 0.29 (hexanes:ethyl acetate, 8:2); ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.45 (d, 1 H), 4.20 (d, 1 H), 4.30 (s, 1 H), 6.30 (d, 1 H), 7.20 - 7.40 (m, 21 H); mass spectrum (EI) *m/z* (% relative intensity) 166 (100).



15 **19**

Preparation and ^{13}C NMR characterization of the acetonide derivative 19.

A sample of **15** (20 mg, 0.046 mmol) was dissolved in 2 mL CH_2Cl_2 and then 2,2-dimethoxypropane (0.1 mL) and a small amount of camphor sulfonic acid was added and the mixture stirred for 48 h at room temperature. The product was separated from the unreactive starting material. The acetal methyl groups were found at δ = 24.5 and 25.1 ppm and the acetal carbon was found at δ = 101.3 ppm which is consistent with diol **15** having an anti-relationship of the diols according to the analysis of Rychnovsky.[9] Spectral data for **19**: colorless oil; R_f = 0.19 (hexanes:ethyl acetate, 8:2); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.45 (s, 3 H), 1.56 (s, 3 H), 2.02 (br s., 1 H), 2.98 (dd, *J* = 4.1, 6.6 Hz, 1 H), 3.77 (s, 1 H), 4.32 (t, *J* = 6.6, Hz, 1 H), 5.18 (d, *J* = 3.6 Hz, 1 H), 6.24 (dd, *J* = 6.9, 15.9 Hz, 1 H), 6.71 (d, *J* = 15.9 Hz, 1 H), 6.90 (m, 2 H), 7.10 - 7.45 (m, 18 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 24.5, 25.1, 61.0, 64.5, 72.3, 76.1, 101.3, 126.6, 126.7, 126.9, 127.1, 127.6, 127.8, 128.2, 128.4, 128.5, 131.4, 136.8, 138.8, 143.0 (5 sp^2 C not located); IR (neat) 1455, 1492, 2932, 2982, 3032, 3062, 3300 (w) cm^{-1}; mass spectrum (EI) *m/z* (% relative intensity) 475 M^+ (2), 167 (100); HRMS calcd for $C_{33}H_{33}NO_2$ *m/z* 475.2512, measd (EI) 475.2520 (100).

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