Supplementary Information

Preparation of Stable Aziridinium Ions and Their Ring Openings

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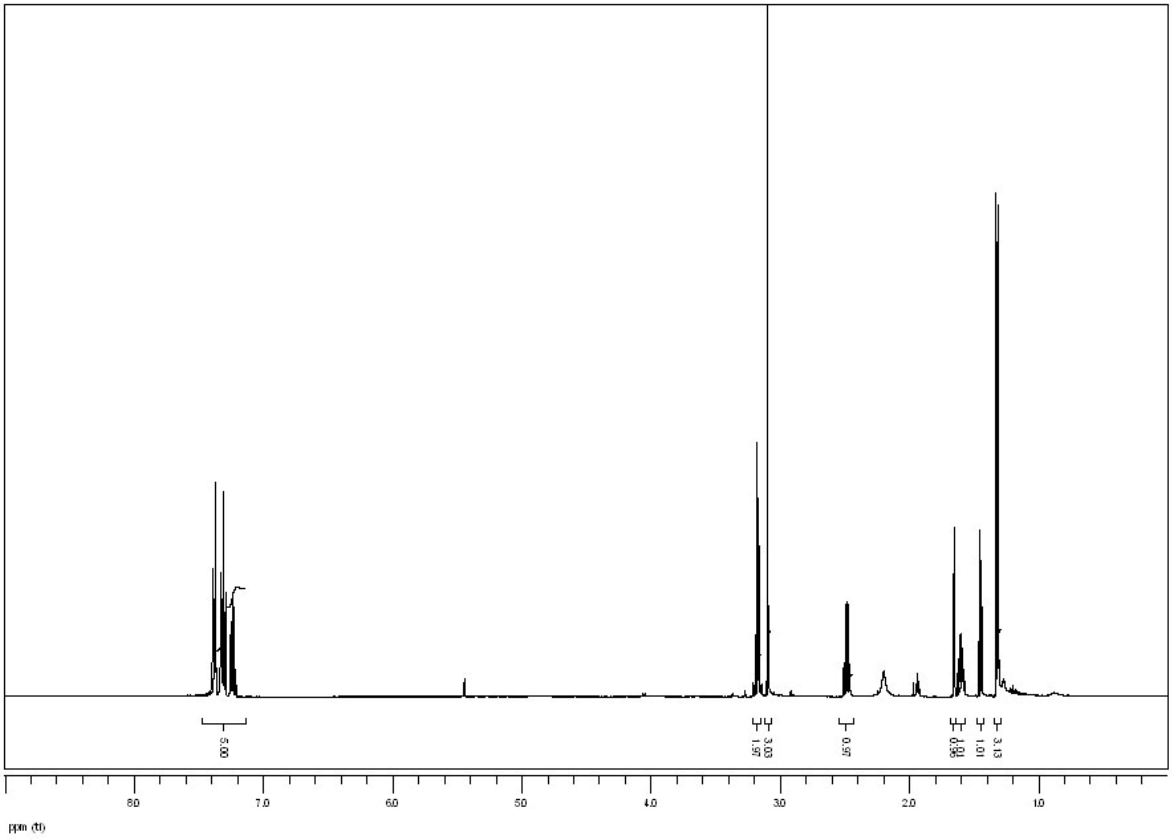
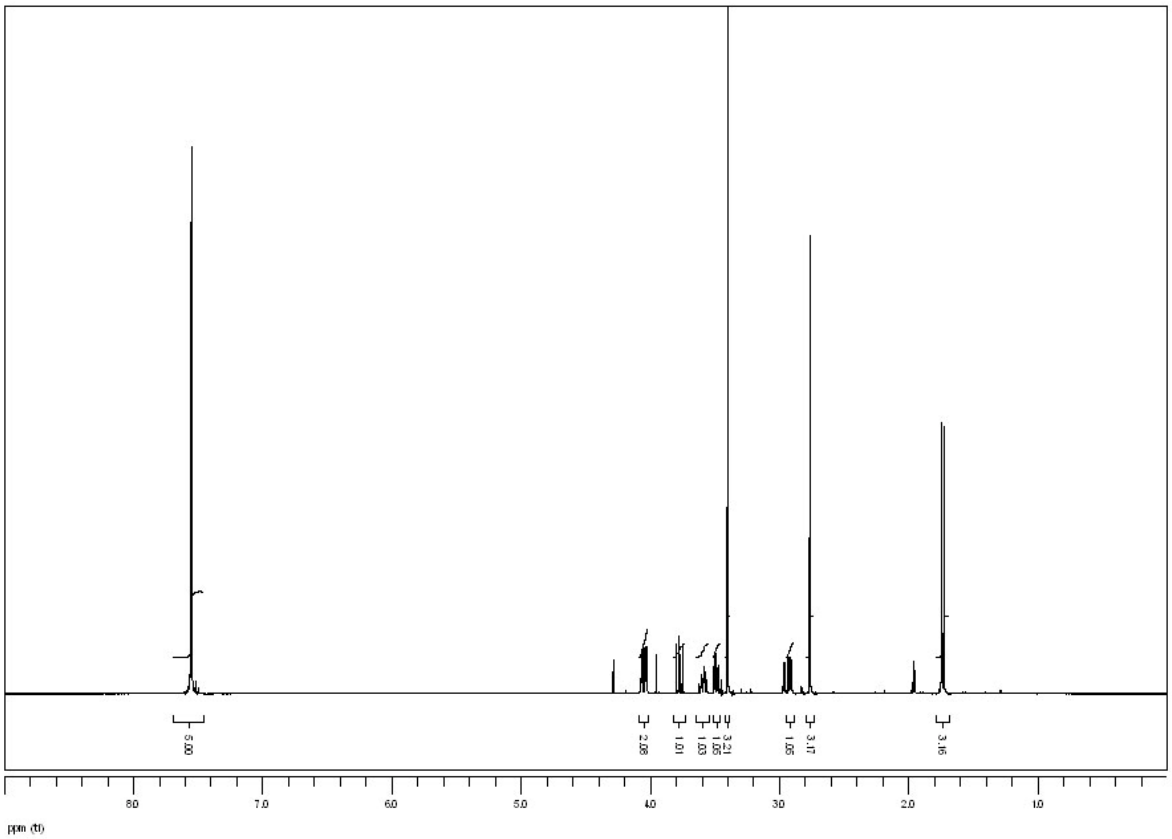
^{1}H NMR Spectra (400 MHz, CD_3CN) of the compounds 1A and 1C before and after adding 1 mole equivalent of MeOTf.

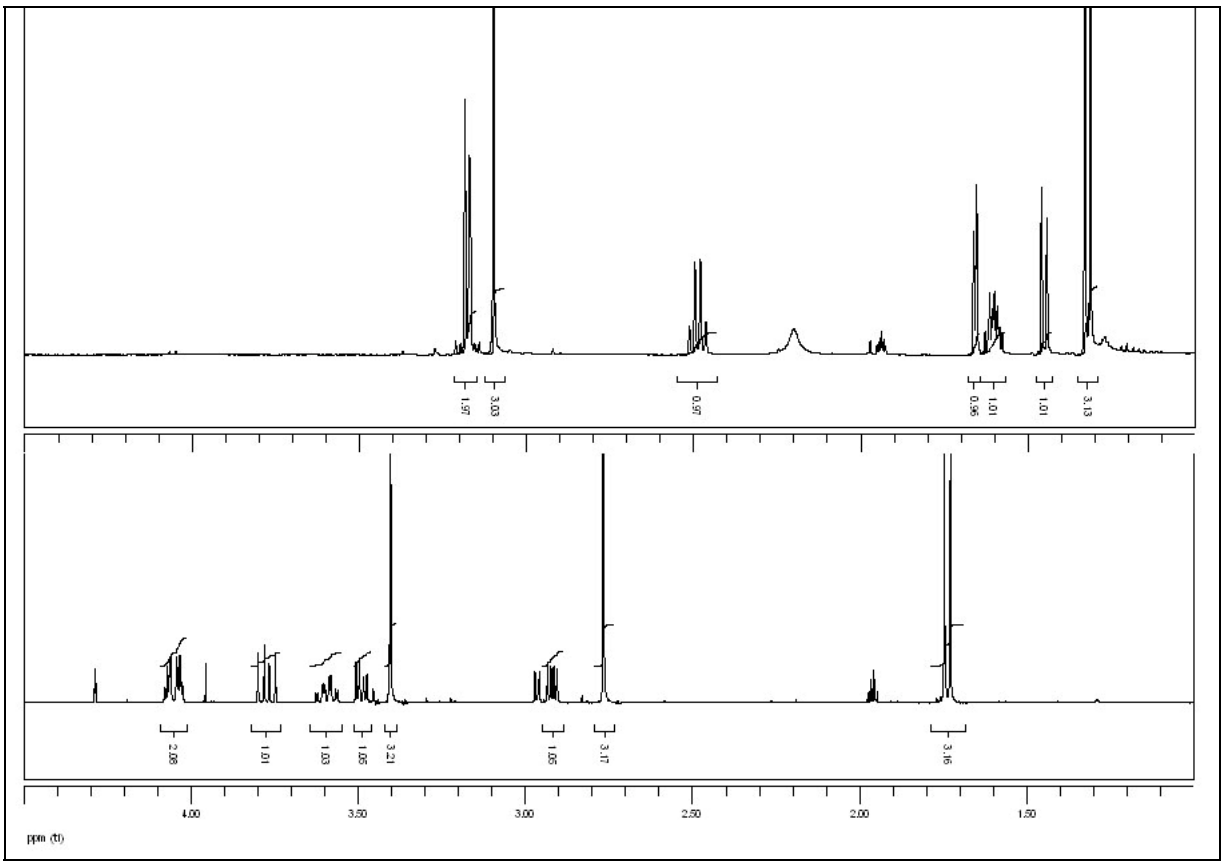
^{1}H NMR Spectrum of the compounds **1A**.



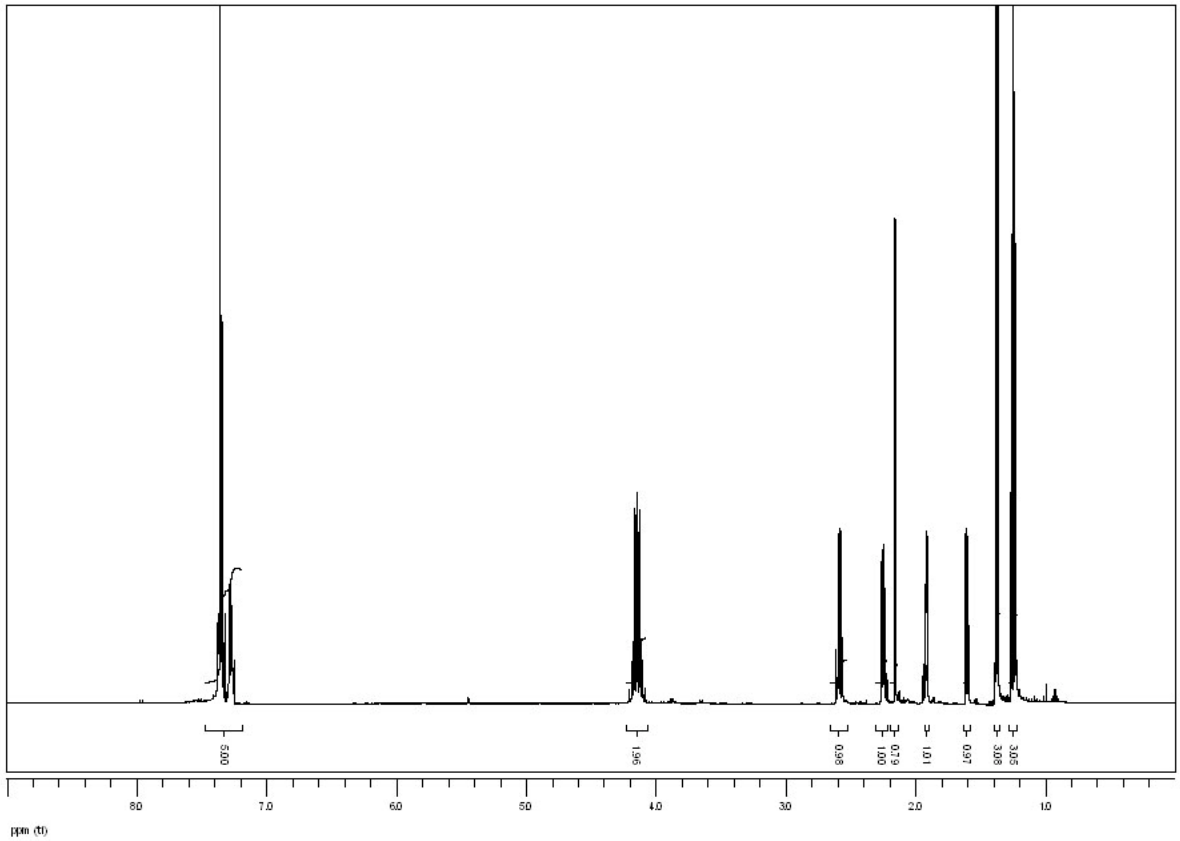
^{1}H NMR Spectrum of the compounds **1A** with MeOTf after 10 min.



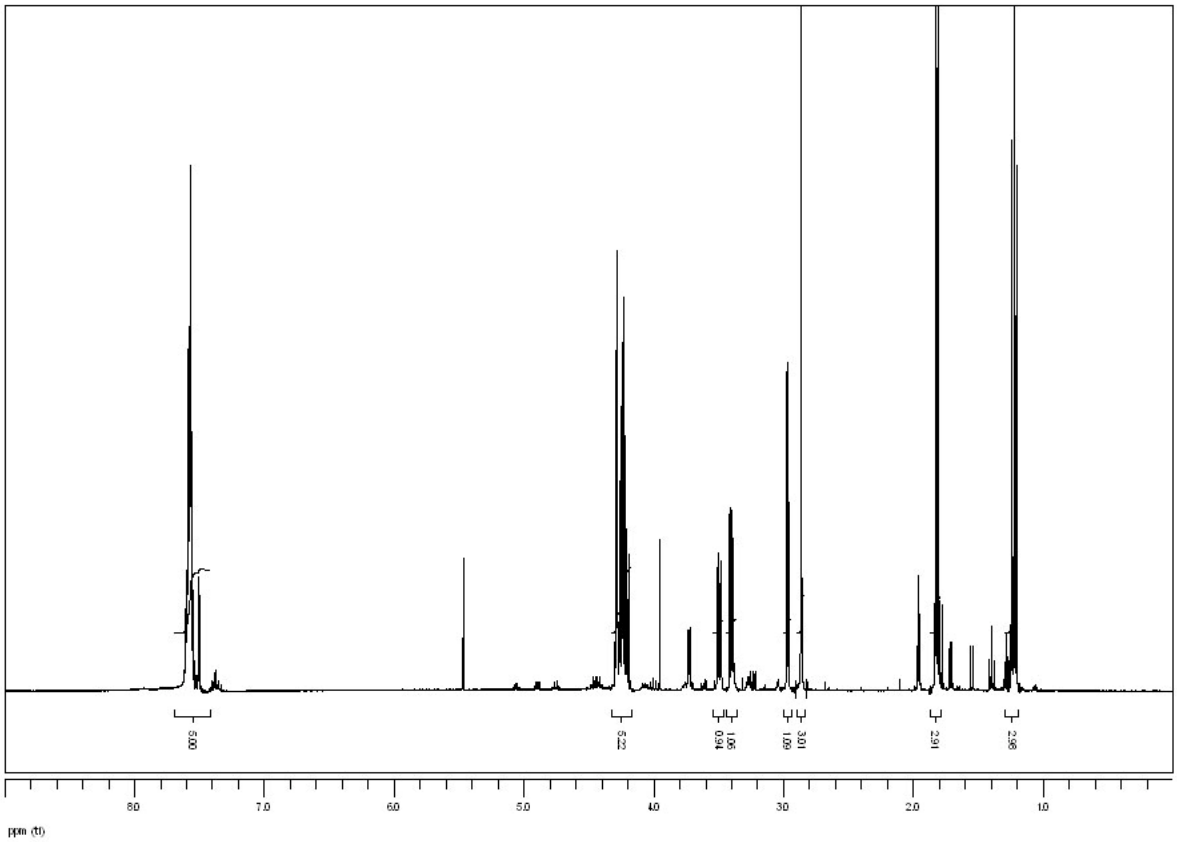
Two spectra at the range δ 1.0 - 4.5



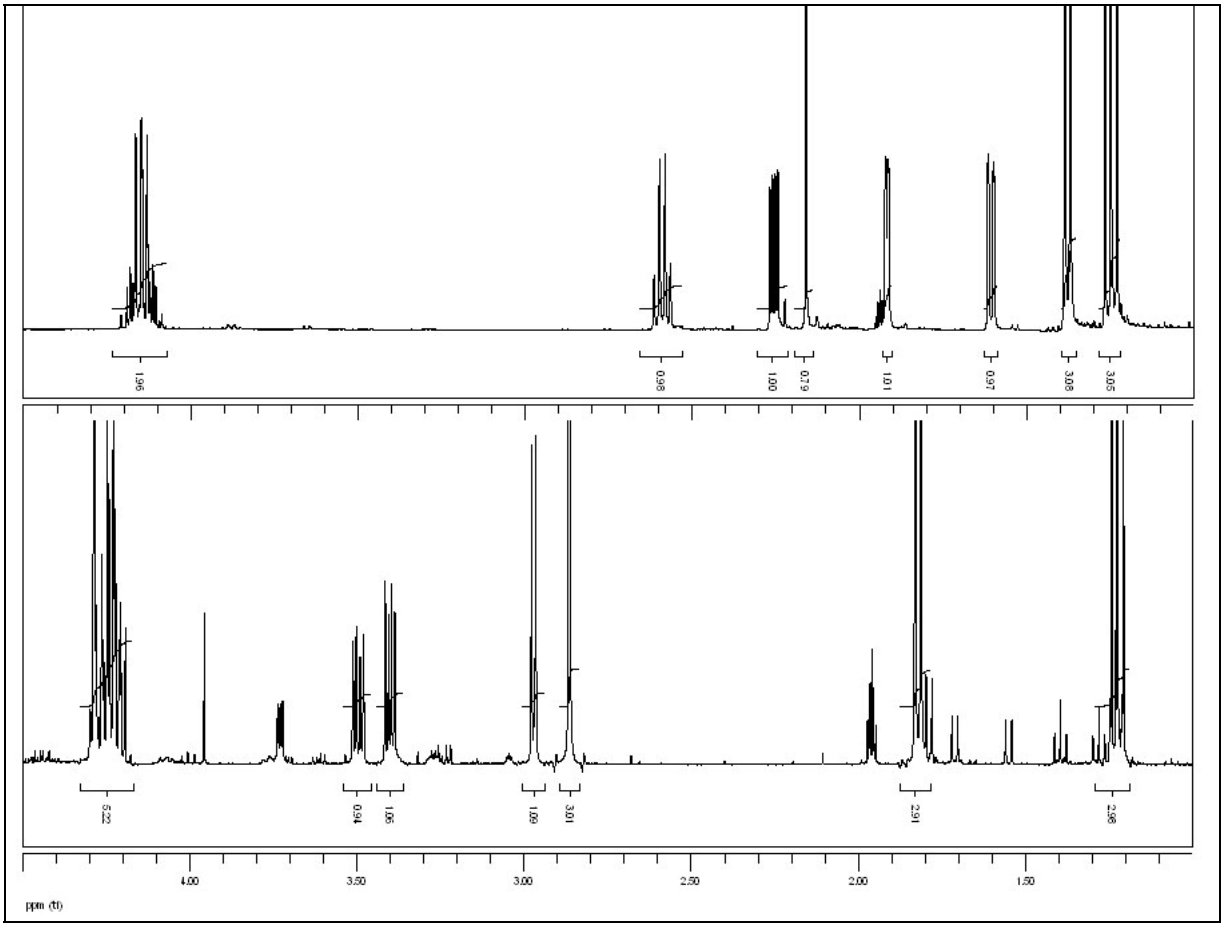
^{1}H NMR Spectrum of the compounds **1C**.



^{1}H NMR Spectrum of the compounds **1C** with MeOTf after 10 min.



Two spectra at the range δ 1.0 - 4.5



Experimental Details

General ; Chiral aziridines are available from Aldrich. All commercially available compounds were used as received unless stated otherwise. All reactions were carried out under an atmosphere of nitrogen in oven-dried glassware with magnetic stirring. Reactions were monitored by thin layer chromatography (TLC) with 0.25 mm E. Merck pre-coated silica gel plates (60 F254). Visualization was accomplished with either UV light, or by immersion in solutions of ninhydrin, *p*-anisaldehyde, or phosphomolybdic acid (PMA) followed by heating on a hot plate for about 10 sec. Purification of reaction products was carried out by flash chromatography using Kieselgel 60 Art 9385 (230-400 mesh). ^{1}H-NMR and ^{13}C-NMR spectra were obtained using a Varian 200 (200 MHz for ^{1}H, and 50.3 MHz for ^{13}C), Varian 400 (400 MHz for ^{1}H, and 100 MHz for ^{13}C) or a Varian Inova-500 (500 MHz for ^{1}H, and 125 MHz for ^{13}C) spectrometer. Chemical shifts are reported relative to chloroform (δ = 7.26) for ^{1}H NMR and chloroform (δ = 77.2) for ^{13}C NMR. Data are reported as (br = broad, s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet.) Coupling constants are given in Hz. Ambiguous assignments were resolved on the basis of standard one dimensional proton decoupling experiments. Optical rotations were obtained using a Rudolph Autopol III digital polarimeter and optical rotation data was reported as follows: $[\alpha]^{25}_{D}$ (concentration c = g/100 mL, solvent). Elemental analyses were performed by the Perkin-Elmer 240 DS elemental analyzer. High resolution mass spectra were recorded on a 4.7 Tesla IonSpec ESI-FTMS or a Micromass LCT ESI-TOF mass spectrometer.

(*S*)-2-Methoxymethyl-1-[(*R*)-1-phenylethyl]aziridine (1A). To a solution of (*S*)-1-[(*R*)-1-phenylethyl)aziridin-2-yl]methanol (5.81 g, 32.78 mmol) in THF (15 mL) was added 1.57 g of NaH

(65.5 mmol) at 0℃. After 30 min at 0℃, iodomethane (7.00 g, 3.07 ml, 49.3 mmol) was added at 0℃. The resulting mixture was stirred for 1h at 0℃ and then quenched with sat. aqueous $NaHCO_3$. The mixture was extracted with EtOAc. The combined organic layer was washed with brine, dried over anhydrous $MgSO_4$, filtered and concentrated under *vacuo*. Purification by column chromatography provided 5.80 g of product in 93% yield. colorless oil; $[\alpha]_D$: +35(c 0.53, in $CHCl_3$) ; ^{1}H NMR (400 MHz, CD_3CN) δ 7.39-7.21(m, 5H), 3.18(d, 2H, -O-$\underline{CH_2}$-, J=5.6Hz), 3.09(s, 3H, -O-$\underline{CH_3}$), 2.51(q, 1H, Ph-$\underline{CH}$-, J=6.4Hz), 1.66(d, 1H, -N-H$\underline{CH}$a-, J=3.2Hz), 1.62-1.57(m, 1H, -N-$\underline{CH}$-CH_2-), 1.45(d, 1H, -N-H$\underline{CH}$b-, J=6.4Hz), 1.32(d, 3H, -CH-$\underline{CH_3}$, J=6.8Hz) ; ^{13}C NMR (100MHz, CD_3CN) δ 146.2, 129.0, 127.8, 127.7, 75.2, 69.9, 58.5, 38.2, 31.9, 23.5. HRMS: m/z calcd for $C_{12}H_{17}NO$ 191.1310, found 191.1305.

(*S*)-2-(Benzyloxymethyl)-1-[(*R*)-1-phenylethyl]aziridine (1B). To a solution of (*S*)-1-[(*R*)-1-phenylethyl)aziridin-2-yl]methanol (3.1 g, 17.49 mmol) in THF (10 mL) was added 0.63 g of NaH (26.2 mmol) at 0℃. After 30 min at 0℃, benzylbromide (2.50 ml, 3.60 g, 21.0 mmol) was added at 0℃. The resulting mixture was stirred for 3h at r.t. and then quenched with sat. aqueous $NaHCO_3$. The mixture was extracted with EtOAc. The combined organic layer was washed with brine, dried over anhydrous $MgSO_4$, filtered and concentrated under *vacuo*. Purification by column chromatography provided 4.44 g of product in 95% yield. colorless oil; $[\alpha]_D$: +15(c 0.23, in $CHCl_3$) ; ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.41-7.15(m, 10H), 4.32(s, 2H, -O-$\underline{CH_2}$-Ph), 3.42(d, 2H, -O-$\underline{CH_2}$-CH-, J=5.8Hz), 2.53(q, 1H, -$\underline{CH}$-CH_3, J=6.6Hz), 1.82(d, 1H, -N-CH$\underline{H_a}$-CH-, J=3.4), 1.78-1.68(m, 1H, -N-$\underline{CH}$-CH_2-), 1.49(d, 1H, -N-CH$\underline{H_b}$-CH-, J=6.4Hz), 1.44(d, 3H, -CH-$\underline{CH_3}$, J=6.6Hz) ; ^{13}C NMR (50MHz, $CDCl_3$) δ 144.5, 138.3, 128.4, 128.2, 127.6, 127.4, 127.1, 126.9, 72.7, 72.3, 69.8, 37.8, 32.0, 23.1. HRMS: m/z calcd for $C_{18}H_{21}NO$ 267.1623, found 267.1625.

Typical Reaction Procedure: To a solution of an aziridine substrate (1.5 mmol) in CH_3CN (5 mL) was treated with methyl trifluoromethanesulfonate (271 mg, 1.65 mmol, 1.1 eq.) at rt. After 10 min at rt., nucleophiles (2.25 mol, 1.5 eq.) were added at 0℃. The resulting reaction mixture was stirred for 1h at rt. before adding H_2O. The mixture was extracted with CH_2Cl_2 and water. The combined organic layer was dried over anhydrous $MgSO_4$, filtered and concentrated under *vacuo*. Purification by column chromatography provided analytically pure product.

3Aa. colorless oil ; $[\alpha]^{24}_D$ +31(c 0.21, in $CHCl_3$) ; ^{1}H NMR (400MHz, $CDCl_3$) δ 7.35-7.19(m, 5H), 3.86(q, 1H, CH_3-$\underline{CH}$-, J=6.4Hz), 3.43-3.18(m, 8H, -O-$\underline{CH_3}$, -O-$\underline{CH_2}$-, -CH_2-$\underline{CH}$-, -$\underline{CH_2}$-N_3), 2.23(s, 3H, -N-$\underline{CH_3}$), 1.38(d, 3H, -CH-$\underline{CH_3}$, J=6.8Hz) ; ^{13}C NMR (100MHz, $CDCl_3$) δ 145.4, 128.6, 127.5, 127.1, 71.5, 62.8, 59.1, 58.0, 49.8, 33.5, 21.1 HRMS: m/z calcd for $C_{13}H_{20}N_4O$ 248.1637, found 248.1641.

3Ab. colorless oil ; $[\alpha]^{24}_D$ +16(c 0.50, in EtOAc) ; ^{1}H NMR (500MHz, $CDCl_3$) δ 7.33-7.20(m, 5H), 4.22-4.08(m, 2H, -$\underline{CH_2}$-O-C-), 3.87(q, 1H, -$\underline{CH}$-CH_3, J=7Hz), 3.47-3.30(m, 2H, -$\underline{CH_2}$-OCH_3), 3.26(s, 3H, -O-$\underline{CH_3}$), 3.21-3.18(m, 1H, -CH_2-$\underline{CH}$-CH_2-), 2.29(s, 3H, -N-$\underline{CH_3}$), 2.05(s, 3H, -C-$\underline{CH_3}$), 1.35(d, 3H, -CH-$\underline{CH_3}$, J=6.5Hz) ; ^{13}C NMR (125MHz, $CDCl_3$) δ 171.1, 145.7, 128.4, 127.5, 126.9, 71.9, 62.7, 62.6, 59.1, 56.6, 33.8, 21.3, 21.2. HRMS: m/z calcd for $C_{15}H_{23}N_3O$: 265.1678, found 265.1673.

3Ac. colorless oil ; $[\alpha]^{24}_D$ +8(c 0.49, in EtOAc) ; ^{1}H NMR (400MHz, $CDCl_3$) δ 7.36-7.19(m, 5H), 3.97(q, 1H, CH_3-$\underline{CH}$-, J=6.4Hz), 3.70-3.62(m, 4H, -$\underline{CH_2}$-O-$\underline{CH_2}$-), 3.48-3.44(m, 2H, -O-$\underline{CH_2}$-), 3.35-3.32(m, 2H, -N-$\underline{CH_2}$-), 3.27(s, 3H, -O-$\underline{CH_3}$), 3.13-3.07(m, 1H, -CH_2-$\underline{CH}$-), 2.50-2.24(m, 7H, -$\underline{CH_2}$-N-$\underline{CH_2}$-, -N-$\underline{CH_3}$), 1.36(d, 3H, -CH-$\underline{CH_3}$, J=6.8Hz) ; ^{13}C NMR (50MHz, $CDCl_3$) δ 146.3, 128.2, 127.3, 126.6, 73.1, 67.1, 62.3, 58.8, 56.8, 54.7, 54.2, 33.4, 21.8. HRMS: m/z calcd for $C_{17}H_{28}N_2O_2$; 292.2151, found 292.2155.

3Ad. $[\alpha]^{24}_D$ +32(c 0.26, in EtOAc) ; ^{1}H NMR (200MHz, $CDCl_3$) δ 7.32-7.19(m, 10H), 3.92(q, 1H, CH_3-$\underline{CH}$-, J=6.6Hz), 3.45(s, 2H, Ph-$\underline{CH_2}$-), 3.21-3.07(m, 5H, -O-$\underline{CH_2}$-, -O-$\underline{CH_3}$), 2.82-2.72(m, 1H, -CH_2-$\underline{CH}$-), 2.53-2.33(m, 2H, -NH-$\underline{CH_2}$-), 2.12(s, 3H, -N-$\underline{CH_3}$), 1.37(d, 3H, -CH-$\underline{CH_3}$, J=6.6Hz) ; ^{13}C NMR

(50MHz, $CDCl_3$) δ 146.4, 139.2, 128.8, 128.2, 128.1, 127.9, 126.8, 126.5, 74.6, 62.8, 59.1, 58.6, 56.7, 53.3, 42.7, 24.8 HRMS: m/z calcd for $C_{20}H_{28}N_2O$: 312.2202, found 312.2205.

3Ae. $[\alpha]^{24}_D$ +54(c 0.42, in CHCl3) ^{1}H NMR (400MHz, $CDCl_3$) δ 7.36-7.21(m, 5H), 3.84(q, 1H, CH_3-CH-, J=6.8Hz), 3.48-3.35(m, 2H, -CH_2-O-), 3.32-3.25(m, 4H, -CH_2-CH-, -O-CH_3), 2.46-2.43(m, 2H, -CH_2-CN), 2.28(s, 3H, -N-CH_3), 1.38(d, 3H, -CH-CH_3, J=6.4Hz) ; ^{13}C NMR (100MHz, $CDCl_3$) δ 144.5, 128.4, 127.2, 127.1, 118.9, 71.5, 62.3, 58.9, 55.0, 32.7, 20.8, 17.8. HRMS: m/z calcd for $C_{14}H_{20}N_2O$: 232.1576, found 232.1582.

3Ba. $[\alpha]^{24}_D$ +29(c 0.044, in CHCl3) ; ^{1}H NMR (200MHz, $CDCl_3$) δ 7.32-7.26(m, 10H), 4.44(s, 2H, -CH_2-Ph), 3.90(q, 1H, -CH-CH_3, J=6.8Hz), 3.55-3.24(m, 5H, -CH_2-CH-CH_2-), 2.23(s, 3H, -N-CH_3), 1.39(d, 3H, -CH-CH_3, J=6.6Hz) ; ^{13}C NMR (50MHz, $CDCl_3$) δ 145.4, 138.2, 128.5, 127.7, 127.6, 127.4, 127.0, 73.3, 68.8, 62.8, 58.0, 49.8, 33.4, 21.1. HRMS: m/z calcd for $C_{19}H_{24}N_4O$: 324.1950, found 324.1946.

3Bb. $[\alpha]^{24}_D$ +12(c 0.16, in MeOH) ; ^{1}H NMR (500MHz, $CDCl_3$) δ 7.33-7.21(m, 10H), 4.43(s, 2H, -CH_2-Ph), 4.25-4.13(m, 2H, -CH_2-O-C-), 3.88(q, 1H, -CH-CH_3, J=6.5Hz), 3.55-3.43(m, 2H, -CH_2-O-CH_2-), 3.28(m, 1H, -CH_2-CH-CH_2-), 2.28(s, 3H, -N-CH_3), 2.02(s, 3H, -C-CH_3), 1.35(d, 3H, -CH-CH_3, J=7.0Hz) ; ^{13}C NMR (125MHz, $CDCl_3$) δ 171.0, 145.8, 138.5, 128.8, 128.6, 128.4, 128.127.6, 127.5, 126.9, 73.3, 69.3, 62.8, 62.6, 56.8, 33.9, 21.2, 21.2. HRMS: m/z calcd for $C_{21}H_{27}NO_3$: 341.1991, found 341.1991.

3Bc. $[\alpha]^{24}_D$ +7(c 0.103, in CHCl3) ; ^{1}H NMR (400MHz, $CDCl_3$) δ 7.33-7.18(m, 10H), 4.43(s, 2H, -CH_2-Ph), 3.82(q, 1H, -CH-CH_3, J=6.8Hz), 3.54-3.34(m, 3H, -CH_2-CH-, -CH-CH_2-O-), 2.51-2.37(m, 2H, -CH_2-CN), 2.26(s, 3H, -N-CH_3), 1.34(d, 3H, -CH-CH_3, J=6.8Hz) ; ^{13}C NMR (50MHz, $CDCl_3$) δ 145.2, 138.1, 128.7, 128.6, 127.8, 127.7, 127.3, 127.2, 119.4, 73.3, 70.1, 62.3, 55.3, 33.4, 21.4, 16.8. HRMS: m/z calcd for $C_{20}H_{24}N_2O$: 308.1889, found 308.1892.

3Bd. $[\alpha]^{24}_D$ +8(c 0.12, in EtOAc) ; ^{1}H NMR (200MHz, $CDCl_3$) δ 7.36-7.20(m, 10H), 4.44(s, 2H, -CH_2-Ph), 3.74(q, 1H, -CH-CH_3, J=6.4Hz), 3.55-3.24(m, 2H, -CH-CH_2-O-), 3.11-3.01(m, 1H, -CH-CH_2-), 3.21(s, 3H, -N-CH_3), 1.35(d, 3H, -CH-CH_3, J=6.8Hz), 0.95(d, 3H, -CH_2-CH-CH_3, J=6.6Hz) ; ^{13}C NMR (50MHz, $CDCl_3$) δ 145.8, 138.6, 128.4, 128.2, 127.7, 127.3, 127.2, 126.6, 73.2, 72.7, 61.8, 53.1, 32.8, 21.4, 11.0. HRMS: m/z calcd for $C_{19}H_{25}NO$: 283.1936, found 283.1933.

4Ca. $[\alpha]^{24}_D$ -2(c 0.043, in CH2Cl2) RR ; ^{1}H NMR (200MHz, $CDCl_3$) δ 7.31-7.27(m, 5H), 4.27(q, 2H, -CH_2-CH_3, J=7.2Hz), 3.94(t, 1H, -CH-N_3, J=6.2Hz), 3.77(q, 1H, -CH-CH_3, J=6.8Hz), 2.88-2.82(m, 2H, -N-CH_2-), 2.24(s, 3H, -N-CH_3), 1.39(d, 3H, -CH-CH_3, J=6.8Hz), 1.32(t, 3H, -CH_2-CH_3, J=7.2Hz) ; ^{13}C NMR (50MHz, $CDCl_3$) δ 169.6, 142.7, 128.2, 127.7, 127.0, 63.4, 61.6, 60.8, 55.6, 38.4, 17.3, 14.1. HRMS: m/z calcd for $C_{14}H_{20}N_4O_2$: 276.1586, found 276.1586.

4Cb. $[\alpha]^{24}_D$ +29(c 0.005, in CHCl3) ; ^{1}H NMR (500MHz, $CDCl_3$) δ 7.31-7.23(m, 5H), 5.15(dd, 1H, -CH-O-, J=7.5Hz, 3.5Hz), 4.20-4.14(m, 2H, -CH_2-CH_3), 3.68(q, 1H, -CH-CH_3, J=7.0Hz), 3.00-2.68(m, 2H, -N-CH_2-), 2.27(s, 3H, -N-CH_3), 2.14(s, 3H, -C-CH_3), 1.36(d, 3H, -CH-CH_3, J=6.5Hz), 1.26(t, 3H, -CH_2-CH_3, J=7.5Hz) ; ^{13}C NMR (125MHz, $CDCl_3$) δ 170.6, 169.6, 143.2, 128.3, 127.8, 127.1, 72.0, 63.5, 61.4, 54.9, 39.2, 20.9, 18.1, 14.2. HRMS: m/z calcd for $C_{16}H_{23}NO_4$: 293.1627, found 293.1624.

4Cc. $[\alpha]^{24}_D$ +16(c 0.24, in CHCl3) ; ^{1}H NMR (400MHz, $CDCl_3$) δ 7.33-7.18(m, 5H), 4.23-4.14(m, 3H, -CH_2-CH_3, -CH-CH_3), 3.71-3.62(m, 5H, -CH_2-O-CH_2-, -CH-C-), 3.33-3.29(m, 2H, -N-CH_2-CH-), 2.61-2.52(m, 4H, -CH_2-N-CH_2-), 2.17(s, 3H, -N-CH_3), 1.34(d, 3H, -CH-CH_3, J=6.8Hz), 1.30-1.26(m, 3H, -CH_2-CH_3) ; ^{13}C NMR (100MHz, $CDCl_3$) δ 171.1, 143.3, 127.9, 127.5, 126.6, 67.1, 62.9, 60.0, 53.6, 50.5, 38.4, 16.9, 14.3. HRMS: m/z calcd for $C_{18}H_{28}N_2O_3$: 320.2100, found 320.2098.

4Cd. $[\alpha]^{24}_D$ +36(c 0.54, in EtOAc) ; ^{1}H NMR (200MHz, $CDCl_3$) δ 7.32-7.19(m, 10H), 4.25-4.05(m, 2H, -O-$\underline{CH_2}$-), 3.77-3.43(m, 4H, CH_3-$\underline{CH}$-, -$\underline{CH_2}$-Ph, -C-$\underline{CH}$-), 3.02-2.56(m, 2H, -N-$\underline{CH_2}$-), 2.24-2.13(m, 3H, -N-$\underline{CH_3}$), 1.35-1.21(m, 6H, -CH-$\underline{CH_3}$, -CH_2-$\underline{CH_3}$) ; ^{13}C NMR (50MHz, $CDCl_3$) δ 171.8, 143.4, 139.3, 128.7, 128.1, 127.9, 127.6, 126.8, 126.6, 64.6, 62.8, 59.9, 58.8, 54.3, 38.5, 17.0, 14.5. HRMS: m/z calcd for $C_{21}H_{28}N_2O_2$: 340.2151, found 340.2157.

4Ce. $[\alpha]^{24}_D$ -42(c 0.22, in EtOAc) ; ^{1}H NMR (200MHz, $CDCl_3$) δ 7.42-7.19(m, 5H), 4.32-4.05(m, 3H, CH_3-$\underline{CH}$-, -O-$\underline{CH_2}$-), 3.88-3.79(m, 1H, -$\underline{CH}$-CN), 2.77-2.73(m, 2H, -N-$\underline{CH_2}$-), 2.12(s, 3H, -N-$\underline{CH_3}$), 1.44(d, 3H, -CH-$\underline{CH_3}$, J=6.6Hz), 1.37(t, 3H, -CH_2-$\underline{CH_3}$, J=7.2Hz) ; ^{13}C NMR (125MHz, $CDCl_3$) δ 170.5, 145.3, 128.7, 127.4, 127.3, 118.1, 63.0, 61.5, 58.0, 34.7, 21.7, 19.1, 14.6. HRMS: m/z calcd for $C_{15}H_{20}N_2O_2$: 260.1525, found 260.1526.

4Da. $[\alpha]^{24}_D$ +5(c 0.09, in CH2Cl2) ; ^{1}H NMR (400MHz, $CDCl_3$) δ 7.32-7.21(m, 5H), 6.75(qd, 1H, -CH-$\underline{CH}$-, J=6Hz, 0.4Hz), 6.02(dt, 1H, -$\underline{CH}$-C-, J=15.6Hz, J=0.4Hz), 4.23(q, 2H, -$\underline{CH_2}$-CH_3, J=7.2Hz), 4.11(q, 1H, -$\underline{CH}$-CH_3, J=6.8Hz), 3.67(q, 1H, -$\underline{CH}$-N_3, J=6.8Hz), 2.64-2.51(m, 2H, -$\underline{CH_2}$-CH-), 2.26(s, 3H, -N-$\underline{CH_3}$), 1.37(d, 3H, -CH-$\underline{CH_3}$, J=6.8Hz), 1.31-1.27(m, 3H, -CH_2-$\underline{CH_3}$) ; ^{13}C NMR (100MHz, $CDCl_3$) δ 165.7, 143.5, 142.9, 128.1, 127.6, 127.0, 123.0, 63.7, 60.6, 60.5, 58.3, 38.9, 17.7, 14.1. HRMS: m/z calcd for $C_{16}H_{22}N_4O_2$: 302.1743, found 302.1746.

4Db. $[\alpha]^{24}_D$ +16(c 0.37, in CHCl3) ; ^{1}H NMR (400MHz, $CDCl_3$) δ 7.31-7.19(m, 5H), 6.94(dd, 1H, -CH-$\underline{CH}$-CH-, J=15.6Hz, 4.8Hz), 5.94(dt, 1H, -C-$\underline{CH}$-, J=16Hz, 0.8Hz), 5.54(qd, 1H, -O-$\underline{CH}$-, J=6.8Hz, 1.6Hz), 4.24-4.17(m, 2H, -$\underline{CH_2}$-CH_3), 3.65(q, 1H, CH_3-$\underline{CH}$-, J=6.8Hz), 2.57-2.55(m, 2H, -N-$\underline{CH_2}$-), 2.27(s, 3H, -N-$\underline{CH_3}$), 2.07(s, 3H, -C-$\underline{CH_3}$), 1.34(d, 3H, -CH-$\underline{CH_3}$, J=6.8Hz), 1.31-1.24(m, 3H, -CH_2-$\underline{CH_3}$) ; ^{13}C NMR (125MHz, $CDCl_3$) δ 169.9, 166.0, 144.7, 128.2, 127.8, 127.0, 121.5, 70.7, 63.6, 60.5, 57.1, 39.4, 21.1, 17.6, 14.3. HRMS: m/z calcd for $C_{18}H_{25}NO_4$: 319.1784, found 319.1778.

4Dc. $[\alpha]^{24}_D$ +94(c 0.29, in CHCl3) ; ^{1}H NMR (400MHz, $CDCl_3$) δ 7.35-7.24(m, 5H), 6.88(dd, 1H, -CH-$\underline{CH}$-CH-, J=16Hz, 8Hz), 5.85(d, 1H, -CH-$\underline{CH}$-C-, J=15.6Hz), 4.24(q, 2H, -$\underline{CH_2}$-CH_3, J=7.2Hz), 3.68-3.63(m, 2H, -$\underline{CH}$-CN, -$\underline{CH}$-CH_3), 2.63-2.39(m, 2H, -N-$\underline{CH_2}$-), 2.29(s, 3H, -N-$\underline{CH_3}$), 1.37(d, 3H, -CH-$\underline{CH_3}$, J=6.4Hz), 1.32(t, 3H, -CH_2-$\underline{CH_3}$, J=7.2Hz) ; ^{13}C NMR (100MHz, $CDCl_3$) δ 165.4, 144.1, 142.9, 128.7, 127.3, 127.2, 124.9, 117.4, 62.1, 60.7, 56.8, 32.3, 21.4, 20.8. HRMS: m/z calcd for $C_{17}H_{22}N_2O_2$: 286.1681, found 286.1685.

***tert*-Butyl (*S*)-1-methoxy-3-[methyl{(*R*)-1-phenylethyl}amino]propan-2-ylcarbamate (5).** To a solution of the substrate (**4Ca**) (370 mg, 1.34 mmol) in THF (5 mL) was added 150 mg of $LiAlH_4$ at 0℃. The resulting mixture was stirred for 30 min at 0℃ and then quenched with sat. aqueous $KHSO_4$. The mixture was filtered with EtOAc and then dried over $MgSO_4$, and concentrated under *vacuo*. The crude product was dissolved in CH_2Cl_2 (5 mL) and $(Boc)_2O$ (292 mg, 1.34 mmol) was added. After stirring 1 h at rt, the reaction mixture was extracted with CH_2Cl_2 (50 mL x 2) and water (50 mL). The organic layer was dried over $MgSO_4$, filtered and concentrated under *vacuo*. And then to a solution of mixture in THF (3 mL) was added NaH (48 mg, 2.0 mmol) at 0℃. After 30 min at 0℃, iodomethane (284 mg, 2.0 mmol) was added at 0℃. The resulting mixture was stirred for 2h at r.t. and then quenched with sat. aqueous $NaHCO_3$. The mixture was extracted with EtOAc. The combined organic layer was washed with brine, dried over anhydrous $MgSO_4$, filtered and concentrated under *vacuo*. Purification by column chromatography provided 250 mg of product in 58% yield. colorless oil; $[\alpha]^{24}_D$ -3 (c 0.13, in $CHCl_3$) ; ^{1}H NMR (500MHz, $CDCl_3$) δ 7.31-7.30(m, 5H), 3.74(br, 1H, -$\underline{CH}$-NH-), 3.66(q, 1H, -$\underline{CH}$-CH_3, J=6.5Hz), 3.47-3.30(m, 2H, -$\underline{CH_2}$-O-), 3.25(s, 3H, -O-$\underline{CH_3}$), 2.50-2.37(m, 2H, -N-$\underline{CH_2}$-), 2.21(s, 3H, -N-$\underline{CH_3}$), 1.44(s, 9H, 3X-C-$\underline{CH_3}$), 1.34(d, 3H, -CH-$\underline{CH_3}$, J=7.0Hz) ; ^{13}C NMR (50MHz, $CDCl_3$) δ 155.7, 143.7, 128.0, 127.6, 126.7, 79.0, 72.3, 63.1, 58.9, 54.4, 48.7, 38.8, 28.3, 16.7. HRMS: m/z calcd for $C_{18}H_{30}N_2O_3$ 322.2256, found 322.2254.

***tert*-Butyl (*R*)-3-methoxy-2-[methyl{(*R*)-1-phenylethyl}amino]propylcarbamate (6).** To a solution of the substrate (**3Aa**) (237mg, 0.95 mmol) in THF (5 mL) was added 54 mg of $LiAlH_4$ at 0℃. The resulting mixture was stirred for 30 min at 0℃ and then quenched with sat. aqueous $KHSO_4$. The mixture was filtered with EtOAc, dried over $MgSO_4$, and concentrated under *vacuo*. The crude product was dissolved in CH_2Cl_2 (5 mL) and then $(Boc)_2O$ (207 mg, 0.95 mmol) was added. After stirring 1 h at rt, the reaction mixture was extracted with CH_2Cl_2 and water. The combined organic layer was dried over anhydrous $MgSO_4$ filtered and concentrated under *vacuo*. Purification by column chromatography provided 204 mg of product in 66% yield ; colorless oil ; $[\alpha]^{24}_D$ -11(c 0.35, in $CHCl_3$) ; ^{1}H NMR (400MHz, $CDCl_3$) δ 7.32-7.19(m, 5H), 3.85(q, 1H, -CH-CH_3, J=6.4Hz), 3.49(dd, 1H, -CH_2-CH-CH_2-, J=9.6Hz, 5.2Hz), 3.31-3.25(m, 5H, -O-CH_3, -O-CH_2-), 3.12-3.04(m, 2H, -NH-CH_2-), 2.13(s, 3H, -N-CH_3), 1.45(s, 9H, 3X-C-CH_3), 1.36(d, 3H, -CH-CH_3, J=6.8Hz) ; ^{13}C NMR (100MHz, $CDCl_3$) δ 155.9, 145.7, 128.2, 127.1, 126.7, 78.8, 71.8, 61.9, 59.0, 56.8, 39.4, 33.0, 28.4, 20.7. HRMS: m/z calcd for $C_{18}H_{30}N_2O_3$ 322.2256, found 322.2257.

(*S*)-2-[(*R*)-Benzyloxy(phenyl)methyl]-1-[(*R*)-1-phenylethyl]aziridine (7). To a solution of (*R*)-phenyl{(*S*)-1-[(*R*)-1-phenylethyl]aziridin-2-yl}methanol[1] (2.48 g, 9.27 mmol) in THF (15 mL) was added 0.35 g of NaH (14.6 mmol) at 0 ℃. After 30 min at 0 ℃, benzylbromide (2.50 g, 1.75 ml, 14.6 mmol) was added at 0 ℃. The resulting mixture was stirred for 3h at r.t. and then quenched with sat. aqueous $NaHCO_3$. The mixture was extracted with EtOAc. The combined organic layer was washed with brine, dried over anhydrous $MgSO_4$, filtered and concentrated under *vacuo*. Purification by column chromatography provided 2.62 g of product in 78% yield. ; colorless oil ; $[\alpha]^{24}_D$ -31(c 0.08, in EtOAc) ; ^{1}H NMR (500MHz, $CDCl_3$) δ 7.33-6.94(m, 15H), 4.45-4.18(d, 2H, -CH_2-Ph, $J_{(Ha)}$=12Hz, $J_{(Hb)}$=12Hz), 3.84(d, 1H, -O-CH-, J=7.0Hz), 2.36(q, 1H, -CH-CH_3, J=6.5Hz), 1.99-1.98(m, 1H, -$CH_{(a)}$-CH-), 1.80(td, 1H, -CH_2-CH-, J=6.5Hz, 3.5Hz), 1.52(d, 1H, -$CH_{(b)}$-CH-, J=6.0Hz), 1.34(d, 3H, -CH-CH_3, J=6.5Hz) ; ^{13}C NMR (125MHz, $CDCl_3$) δ 143.3, 139.8, 138.0, 128.1, 127.9, 127.7, 127.6, 127.4, 127.3, 126.9, 126.4, 126.4, 81.8, 69.8, 69.7, 43.5, 32.8, 22.6. HRMS: m/z calcd for $C_{24}H_{25}NO$ 343.1936, found 343.1943.

(1*R*,2*S*)-1-Benzyloxy-*N*-methyl-1-phenyl-*N*-[(*S*)-1-phenylethyl]propan-2-amine (8). To a solution of the substrate (**7**) (840 mg, 2.34 mmol) in ethylene glycol dimethylether (5 mL) was added methyl trifluoromethanesulfonate (383 mg, 2.34 mmol) at 0℃. After 10 min at 0℃, $NaBH_3CN$ (294 mg, 4.68 mmol) was added at 0℃. The resulting mixture was stirred for 1h at 0℃ and then quenched with deionized water. The mixture was extracted with EtOAc. The combined organic layer was washed with brine, dried over anhydrous $MgSO_4$, filtered and concentrated under *vacuo*. Purification by column chromatography provided 648 mg of the product in 53% yield. ; colorless oil ; $[\alpha]^{24}_D$ -17(c 0. 21, in EtOAc) ; ^{1}H NMR (200MHz, $CDCl_3$) δ 7.31-6.83(m, 15H), 4.43-4.21(m, 3H, Ph-CH_2-, -O-CH-), 3.57(q, 1H, Ph-CH-N-, J=6.4Hz), 2.95-2.85(m, 1H, CH_3-CH-CH-), 2.25(s, 3H, -N-CH_3), 1.18(d, 3H, -CH-CH_3, J=6.6Hz), 1.06(d, 3H, -CH-CH_3, J=6.6Hz) ; ^{13}C NMR (50MHz, $CDCl_3$) δ 145.5, 141.4, 138.6, 128.1, 127.9, 127.7, 127.4, 127.3, 127.2, 126.9, 126.3, 84.6, 70.6, 62.2, 59.8, 32.6, 20.7, 8.8. HRMS: m/z calcd for $C_{25}H_{29}NO$ 359.2249, found 359.2246.

(1*R*,2*S*)-(-)-Ephedrine. To a solution of the substrate (**8**, 145 mg, 0.40 mmol) in EtOH (2.5 mL) was added 10 mg of $Pd(OH)_2$ at rt. under H_2(g) at 50 psi. The reaction mixture was filtered and the filtrate was concentrated in *vacuo*. The residue was dissolved in diethylether (5 mL) and was added dry HCl gas to afford the solid which was filtered and recrystallized from THF. Purification by column chromatography provided (1*R*,2*S*)-(-)-ephedrine in 67% yield.

References

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