Radical Hydroxyalkylation of C-H Bond Adjacent to Nitrogen of Tertiary Amides, Ureas, and Amines

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General procedures. All reagents were used as received from commercial suppliers unless otherwise noted. 4-Methoxybenzaldehyde, benzaldehyde, triethylamine, 3-methyl-2-oxazolidinone, and *N,N*-dimethylacetamide were purified by distillation prior to use. ^1H NMR spectra (400 or 300 MHz) and ^{13}C NMR spectra (100 or 75 MHz) were measured in CDCl_3 . Chemical shifts are reported in ppm relative to the internal solvent signal; CHCl_3 (7.26 ppm) for ^1H NMR and CDCl_3 (77.0 ppm) for ^{13}C NMR. FT-IR spectra were recorded for samples loaded as neat films on NaCl plates. Mass spectra were obtained according to the specified technique. Analytical thin layer chromatography (TLC) was performed using Kieselgel 60 F₂₅₄, and compounds were visualized with UV light, anisaldehyde stain, phosphomolybdic acid in EtOH, iodine, or KMnO_4 stain.

(*R)-5-((*R**)-Hydroxy(4-methoxyphenyl)methyl)-1-methylpyrrolidin-2-one (3a),**
(*R)-5-((*S**)-Hydroxy(4-methoxyphenyl)methyl)-1-methylpyrrolidin-2-one (4a), and**
1-(2-Hydroxy-2-(4-methoxyphenyl)ethyl)pyrrolidin-2-one (5a): To a solution of 4-methoxybenzaldehyde (**2a**) (408 mg, 3.0 mmol) in 1-methyl-2-pyrrolidinone (**1**) (10 mL, 105 mmol) was added Et_3B (2.6 mL, 18 mmol) at room temperature under argon atmosphere. After removal of the argon balloon, the mixture was stirred at the same temperature with continuous bubbling of air through a syringe needle with a balloon [flow rate; ca. $30\text{ mL}\cdot\text{h}^{-1}\cdot\text{mmol aldehyde}^{-1}$] for 14 h. Sat. NH_4Cl solution was added and the mixture was extracted with CH_2Cl_2 . The organic extract was dried over MgSO_4 and concentrated in vacuo. The residue was purified by silica gel column chromatography (EtOAc/Hex 1:4) to give ethyl adduct **6a** (29 mg, 6%) as a colorless oil. Further elution with MeOH/EtOAc (1:40) gave a mixture of alcohols **3a**, **4a**, and **5a** (527 mg, 75%) as a colorless solid. The yields and the ratio of the products were determined by ^1H NMR analysis of the above mixture to be **3a/4a** (480 mg, 68%, dr 68:32) and **5a** (47 mg, 7%). Recrystallization of the mixture from $\text{EtOAc/CH}_2\text{Cl}_2$ gave **3a** and **4a**, both as colorless prisms. A pure sample of alcohol **5a** was obtained as follows: acetylation of the residue obtained by the concentration of the mother liquor that originated from recrystallization (Ac_2O , Et_3N , DMAP, CH_2Cl_2 , r.t.), chromatographic separation (MeOH/EtOAc 1:50), and hydrolysis of the acetates (K_2CO_3 , aq. MeOH , r.t.). Alcohol **6a** was identical to commercially available 1-(4-methoxyphenyl)propan-1-ol. The relative configuration of major product

3a was determined to be *threo* by X-ray crystallographic analysis; details are provided in the CIF file accompanying this Supporting Information. ***threo*-Alcohol 3a**: Mp 157-158 °C (EtOAc/CH₂Cl₂); IR (neat) ν 3371, 1664 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 7.23-7.17 (m, 2H), 6.88-6.83 (m, 2H), 4.68 (d, 1H, *J*=5.9 Hz), 3.78 (s, 3H), 3.75 (m, 1H), 2.94 (s, 3H), 2.77 (br, 1H), 2.06-1.64 (m, 4H); ¹³C NMR (75 MHz, CDCl₃) δ 176.0, 159.4, 132.7, 127.4, 113.9, 75.1, 65.3, 55.2, 30.2, 29.6, 20.9; MS *m/z*: 235 (M⁺), 98 (100%); HRMS (EI) calcd for C₁₃H₁₇O₃N (M⁺): 235.1208, found: 235.1203. ***erythro*-Alcohol 4a**: Mp 143-144 °C (EtOAc/CH₂Cl₂); IR (neat) ν 3371, 1666 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 7.31-7.25 (m, 2H), 6.93-6.87 (m, 2H), 4.97 (d, 1H, *J*=3.0 Hz), 3.81 (s, 3H), 3.70 (dt, 1H, *J*=8.6, 3.0 Hz), 2.90 (s, 3H), 2.37-2.12 (m, 2H), 2.00 (m, 1H), 1.76 (m, 1H); ¹³C NMR (75 MHz, CDCl₃) δ 176.4, 159.2, 132.2, 127.2, 113.9, 71.9, 66.0, 55.3, 30.1, 28.8, 18.3; MS *m/z*: 235 (M⁺), 98 (100%); HRMS (EI) calcd for C₁₃H₁₇O₃N (M⁺): 235.1208, found: 235.1212.

1-(2-Hydroxy-2-(4-methoxyphenyl)ethyl)pyrrolidin-2-one (5a): IR (neat) ν 3383, 1664 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.32-7.29 (m, 2H), 6.91-6.87 (m, 2H), 4.92 (dd, 1H, *J*=7.0, 4.0 Hz), 3.81 (s, 3H), 3.55 (dd, 1H, *J*=14.0, 7.0 Hz), 3.49 (dd, 1H, *J*=14.0, 4.0 Hz), 3.35 (m, 1H), 3.23 (m, 1H), 2.41 (t, 2H, *J*=8.2 Hz), 2.03-1.94 (m, 2H); ¹³C NMR (100 MHz, CDCl₃) δ 177.0, 159.1, 134.0, 126.9, 113.8, 72.9, 55.3, 52.0, 49.6, 30.9, 18.5; MS *m/z*: 235 (M⁺), 99 (100%); HRMS (EI) calcd for C₁₃H₁₇O₃N (M⁺): 235.1208, found: 235.1207.

(*R)-5-((*R**)-Hydroxy(phenyl)methyl)-1-methylpyrrolidin-2-one (3b),**

(*R)-5-((*S**)-Hydroxy(phenyl)methyl)-1-methylpyrrolidin-2-one (4b), and**

1-(2-Hydroxy-2-phenylethyl)pyrrolidin-2-one (5b): The title compounds were obtained according to the above-mentioned procedure from benzaldehyde (**2b**) (318 mg, 3.0 mmol), 1-methyl-2-pyrrolidinone (**1**) (10 mL, 105 mmol) and Et₃B (2.6 mL, 18 mmol). Reaction time: 16 h. Purification by silica gel column chromatography (EtOAc/Hex 1:5) gave benzyl alcohol (**7b**) (13 mg, 4%) as a colorless oil. Further elution with MeOH/EtOAc (1:40) gave a mixture of alcohols **3b**, **4b**, and **5b** (435 mg, 71%) as a colorless solid. The yields and the ratio of the products were determined by ¹H NMR analysis to be **3b/4b** (379 mg, 62%, dr 67:33) and **5b** (56 mg, 9%). Recrystallization of the mixture from EtOAc/CH₂Cl₂ gave **3b** as colorless prisms and **4b** as colorless pillars. The relative

configuration of major product **3b** was determined by its transformation into a known compound; **3b** was reduced with LAH in 1,4-dioxane to provide (*R*^{*})-phenyl((*R*^{*})-1-methylpyrrolidin-2-yl)methanol (93%) whose spectroscopic and analytical data were identical with those reported (See reference 1 in S15). **threo-Alcohol 3b**: Mp 138-139 °C (EtOAc/CH₂Cl₂); IR (neat) ν 3339, 1666 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 7.36-7.25 (m, 5H), 4.72 (d, 1H, *J*=5.7 Hz), 3.76 (m, 1H), 3.08 (br, 1H), 2.91 (s, 3H), 2.24-1.66 (m, 4H); ¹³C NMR (75 MHz, CDCl₃) δ 176.0, 140.7, 128.5, 128.1, 126.3, 75.4, 65.3, 30.2, 29.6, 20.9; MS *m/z*: 205 (M⁺), 98 (100%); HRMS (EI) calcd for C₁₂H₁₅O₂N (M⁺): 205.1103, found: 205.1100. **erythro-Alcohol 4b**: Mp 117-118 °C (EtOAc/CH₂Cl₂); IR (neat) ν 3352, 1668 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.40-7.26 (m, 5H), 5.06 (t, 1H, *J*=3.0 Hz), 3.72 (dt, 1H, *J*=8.8, 3.0 Hz), 3.45 (br, 1H), 2.93 (s, 3H), 2.37 (m, 1H), 2.20 (ddd, 1H, *J*=17.0, 10.4, 4.2 Hz), 2.03 (m, 1H), 1.73 (m, 1H); ¹³C NMR (100 MHz, CDCl₃) δ 176.4, 140.2, 128.4, 127.5, 125.9, 71.5, 66.3, 30.4, 28.6, 17.9; MS *m/z*: 205 (M⁺), 98 (100%); HRMS (EI) calcd for C₁₂H₁₅O₂N (M⁺): 205.1103, found: 205.1098.

1-(2-Hydroxy-2-phenylethyl)pyrrolidin-2-one (5b): Colorless plates of mp 116-117 °C (EtOAc/Hex); IR (neat) ν 3362, 1663 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.41-7.26 (m, 5H), 4.98 (t, 1H, *J*=5.1 Hz), 3.55 (d, 2H, *J*=5.1 Hz), 3.35 (m, 1H), 3.18 (m, 1H), 2.42 (t, 2H, *J*=8.2 Hz), 2.06-1.90 (m, 2H); ¹³C NMR (75 MHz, CDCl₃) δ 177.3, 142.0, 128.4, 127.7, 125.7, 73.3, 52.1, 49.6, 30.8, 18.4; MS *m/z*: 205 (M⁺), 99 (100%); HRMS (EI) calcd for C₁₂H₁₅O₂N (M⁺): 205.1103, found: 205.1098.

(*R*^{*})-5-((*R*^{*})-(3,4-Methylenedioxyphenyl)(hydroxy)methyl)-1-methylpyrrolidin-2-one (3c), (*S*^{*})-5-((*R*^{*})-(3,4-Methylenedioxyphenyl)(hydroxy)methyl)-1-methylpyrrolidin-2-one (4c), and 1-(2-(3,4-Methylenedioxyphenyl)-2-hydroxyethyl)pyrrolidin-2-one (5c): The title compounds were obtained according to the above-mentioned procedure from piperonal (**2c**) (450 mg, 3.0 mmol), 1-methyl-2-pyrrolidinone (**1**) (10 mL, 105 mmol) and Et₃B (2.6 mL, 18 mmol). Reaction time: 14 h. Purification by silica gel column chromatography (EtOAc/Hex 1:4) gave ethyl adduct **6c** (41 mg, 8%) as a colorless oil. Further elution with MeOH/EtOAc (1:40) gave a mixture of alcohols **3c**, **4c**, and **5c** (505 mg, 68%) as a colorless solid. The yields and the ratio of the products were determined by ¹H NMR analysis to be **3c/4c** (465 mg, 62%, dr 77:23) and **5c** (40 mg, 6%). Recrystallization of the mixture from EtOAc/CH₂Cl₂ gave **3c** and **4c**, both as colorless plates. A pure sample of alcohol **5c** was

obtained as follows: acetylation of the residue obtained by concentration of the mother liquor that originated from recrystallization (Ac_2O , Et_3N , DMAP, CH_2Cl_2 , r.t.), chromatographic separation (MeOH/EtOAc 1:50), and hydrolysis of the acetate (K_2CO_3 , aq. MeOH , r.t.). The spectroscopic data of alcohol **6c** were identical to those reported (See reference 2 in S15). The configuration of major compound **3c** was determined to be *threo* by X-ray crystallographic analysis of the 4-bromobenzoate derived from **3c** (For crystallographic data, see CIF file). ***threo*-Alcohol 3c**: Mp 157-158 °C ($\text{EtOAc}/\text{CH}_2\text{Cl}_2$); IR (neat) ν 3350, 1664 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ 6.85-6.71 (m, 3H), 5.95 (s, 2H), 4.64 (d, 1H, $J=6.1$ Hz), 3.72 (ddd, 1H, $J=9.5, 6.1, 3.5$ Hz), 2.96 (s, 3H), 2.44 (br, 1H), 2.14-1.66 (m, 4H); ^{13}C NMR (75 MHz, CDCl_3) δ 175.9, 148.0, 147.5, 134.7, 119.9, 108.3, 106.6, 101.2, 75.9, 65.4, 30.3, 29.7, 21.1; MS m/z : 249 (M^+), 98 (100%); HRMS (EI) calcd for $\text{C}_{13}\text{H}_{15}\text{O}_4\text{N}$ (M^+): 249.1001, found: 249.1004. ***erythro*-Alcohol 4c**: Mp 143-144 °C ($\text{EtOAc}/\text{CH}_2\text{Cl}_2$); IR (neat) ν 3350, 1666 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 6.89-6.76 (m, 3H), 5.95 (s, 2H), 4.96 (d, 1H, $J=3.0$ Hz), 3.65 (dt, 1H, $J=8.8, 3.0$ Hz), 2.89 (s, 3H), 2.36 (m, 1H), 2.20 (ddd, 1H, $J=17.0, 10.5, 4.4$ Hz), 2.00 (m, 1H), 1.74 (m, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ 176.3, 147.7, 146.9, 134.3, 119.2, 108.1, 106.6, 101.0, 71.4, 66.3, 30.3, 28.6, 18.1; MS m/z : 249 (M^+), 98 (100%); HRMS (EI) calcd for $\text{C}_{13}\text{H}_{15}\text{O}_4\text{N}$ (M^+): 249.1001, found: 249.1001.

1-(2-(3,4-Methylenedioxyphenyl)-2-hydroxyethyl)pyrrolidin-2-one (5c): Colorless prisms of mp 170-171 °C ($\text{EtOAc}/\text{CH}_2\text{Cl}_2$); IR (neat) ν 3362, 1663 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ 6.91-6.77 (m, 3H), 5.96 (s, 2H), 4.88 (dd, 1H, $J=6.5, 4.4$ Hz), 3.51-3.48 (m, 2H), 3.37 (ddd, 1H, $J=9.5, 7.7, 6.5$ Hz), 3.25 (ddd, 1H, $J=9.5, 7.7, 6.5$ Hz), 2.42 (t, 2H, $J=7.7$ Hz), 2.00 (m, 2H); ^{13}C NMR (100 MHz, CDCl_3) δ 177.1, 147.8, 147.0, 136.0, 119.0, 108.1, 106.3, 101.0, 73.2, 52.2, 49.6, 30.9, 18.5; MS m/z : 249 (M^+), 99 (100%); HRMS (EI) calcd for $\text{C}_{13}\text{H}_{15}\text{O}_4\text{N}$ (M^+): 249.1001, found: 249.1000.

(*R)-5-((*R**)-(2-Bromophenyl)(hydroxy)methyl)-1-methylpyrrolidin-2-one (3d)**,

(*R)-5-((*S**)-(2-Bromophenyl)(hydroxy)methyl)-1-methylpyrrolidin-2-one (4d)**,

1-(2-(2-Bromophenyl)-2-hydroxyethyl)pyrrolidin-2-one (5d): The title compounds were obtained according to the above-mentioned procedure from 2-bromobenzaldehyde (**2d**) (555 mg, 3.0 mmol), 1-methyl-2-pyrrolidinone (**1**) (20 mL, 210 mmol) and Et_3B (2.6 mL, 18 mmol). Reaction time: 12 h.

Purification by silica gel column chromatography (EtOAc/Hex 1:3) gave ethyl adduct **6d** (84 mg, 13%) as a colorless oil and 2-bromobenzyl alcohol (**7d**) (17 mg, 3%). Further elution with MeOH/EtOAc (1:40) gave a mixture of alcohols **3d**, **4d**, and **5d** (538 mg, 63%) as a colorless solid. The yields and the ratio of the products were determined by ^1H NMR analysis to be **3d/4d** (457 mg, 54%, dr 42:58) and **5d** (81 mg, 9%). Recrystallization of the mixture from EtOAc/ CH_2Cl_2 gave **3d** as colorless pillars and **4d** as colorless plates. Pure compound **5d** was obtained by recrystallization of the mother liquor from EtOAc/ CH_2Cl_2 . Compound **7d** was found to be identical to the commercially available material. Major product **4d** was transformed into compound **4b** via debromination with $\text{Bu}_3\text{SnH/AIBN}$ (83%), thereby confirming its *erythro* configuration. **threo-Alcohol 3d**: Mp 138-139 °C (EtOAc/ CH_2Cl_2); IR (neat) ν 3350, 1666 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 7.57-7.53 (m, 2H), 7.35 (m, 1H), 7.17 (m, 1H), 5.11 (dd, 1H, $J=6.0, 5.0$ Hz), 3.87 (ddd, 1H, $J=9.0, 6.3, 3.1$ Hz), 3.23 (br, 1H), 2.82 (s, 3H), 2.49 (dt, 1H, $J=17.0, 9.0$ Hz), 2.18 (ddd, 1H, $J=17.0, 10.0, 3.7$ Hz), 1.91 (m, 1H), 1.77 (m, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ 176.2, 140.8, 132.8, 129.5, 128.5, 127.9, 122.6, 76.1, 65.2, 31.2, 30.2, 22.5; MS m/z : 283 (M^+), 98 (100%); HRMS (EI) calcd for $\text{C}_{12}\text{H}_{14}\text{O}_2\text{NBr}$ (M^+): 283.0208, found: 283.0201. **erythro-Alcohol 4d**: Mp 218-219 °C (EtOAc/ CH_2Cl_2); IR (neat) ν 3329, 1666 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ 7.68 (dd, 1H, $J=1.0, 8.0$ Hz), 7.53 (dd, 1H, $J=1.0, 8.0$ Hz), 7.38 (dt, 1H, $J=1.0, 8.0$ Hz), 7.17 (dt, 1H, $J=2.0, 8.0$ Hz), 5.42 (d, 1H, $J=1.5$ Hz), 3.90 (ddd, 1H, $J=9.0, 3.0, 1.5$ Hz), 2.54 (m, 1H), 2.25 (ddd, 1H, $J=17.0, 10.6, 4.0$ Hz), 2.10 (m, 1H), 1.63 (m, 1H); ^{13}C NMR (75 MHz, CDCl_3) δ 176.5, 139.3, 132.6, 129.1, 128.5, 127.6, 121.4, 69.9, 63.4, 30.7, 28.0, 16.9; MS m/z : 283 (M^+), 98 (100%); HRMS (EI) calcd for $\text{C}_{12}\text{H}_{14}\text{O}_2\text{NBr}$ (M^+): 283.0208, found: 283.0206. **1-(2-(2-Bromophenyl)-2-hydroxyethyl)pyrrolidin-2-one (5d)**: Colorless prisms of mp 111-112 °C (EtOAc/ CH_2Cl_2); IR (neat) ν 3340, 1666 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ 7.67 (dd, 1H, $J=7.7, 1.7$ Hz), 7.50 (dd, 1H, $J=7.7, 1.0$ Hz), 7.35 (dt, 1H, $J=7.7, 1.0$ Hz), 7.14 (dt, 1H, $J=7.7, 1.7$ Hz), 5.24 (dd, 1H, $J=6.9, 2.4$ Hz), 3.67 (dd, 1H, $J=14.6, 6.9$ Hz), 3.56 (dd, 1H, $J=14.6, 2.4$ Hz), 3.49 (m, 1H), 3.08 (ddd, 1H, $J=9.4, 8.4, 5.7$ Hz), 2.51-2.33 (m, 2H), 2.11-1.86 (m, 2H); ^{13}C NMR (100 MHz, CDCl_3) δ 177.9, 140.5, 132.4, 129.0, 127.9, 127.6, 121.3, 72.9, 50.5, 49.5, 30.8, 18.5; MS m/z : 283 (M^+), 99 (100%); HRMS (EI) calcd for $\text{C}_{12}\text{H}_{14}\text{O}_2\text{NBr}$ (M^+): 283.0208, found: 283.0206.

1-(2-bromophenyl)propan-1-ol (6d): IR (neat) ν 3350 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ 7.56-7.50 (m, 2H), 7.33 (t, 1H, $J=7.5$ Hz), 7.12 (dt, 1H, $J=7.5$, 1.7 Hz), 5.01 (dd, 1H, $J=7.7$, 4.7 Hz), 2.0 (brs, 1H), 1.91-1.64 (m, 2H), 1.05 (t, 1H, $J=7.4$ Hz); ^{13}C NMR (75 MHz, CDCl_3) δ 143.5, 132.6, 128.7, 127.6, 127.4, 122.1, 74.2, 30.5, 10.1; MS m/z : 214 (M^+), 185 (100%); HRMS (EI) calcd for $\text{C}_9\text{H}_{11}\text{BrO}$ (M^+): 213.9993, found: 213.9990.

(*R)-5-((*R**)-1-Hydroxytridecyl)-1-methylpyrrolidin-2-one (3e),**

(*R)-5-((*S**)-1-Hydroxytridecyl)-1-methylpyrrolidin-2-one (4e):** The title compounds were obtained according to the above-mentioned procedure from tridecanal (**2e**) (598 mg, 3.0 mmol), 1-methyl-2-pyrrolidinone (**1**) (20 mL, 210 mmol) and Et_3B (2.6 mL, 18 mmol). Reaction time: 22 h. Purification by silica gel column chromatography (MeOH/EtOAc 1:40) gave an inseparable mixture of alcohols **3e** and **4e** (447 mg, 50%, dr 50:50) as a colorless solid. Product ratio was determined by ^1H NMR analysis. Pure samples of alcohols **3e** and **4e** were obtained as follows: acetylation of the mixture of alcohols **3e** and **4e** (Ac_2O , Et_3N , DMAP, CH_2Cl_2 , r.t.), chromatographic separation (MeOH/ CHCl_3 1:40), and hydrolysis of the acetates (K_2CO_3 , aq. MeOH, r.t.). Alcohol **3e**, the carbinolic proton signal of which is upfield with respect to that of alcohol **4e**, has been tentatively assigned as a *threo* isomer. ***threo*-Alcohol 3e:** Mp 44-46 $^\circ\text{C}$; IR (neat) ν 3393, 1668 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 3.70 (m, 1H), 3.53 (ddd, 1H, $J=8.8$, 5.1, 4.0 Hz), 2.89 (s, 3H), 2.36 (br, 1H), 2.40 (m, 1H), 2.26 (ddd, 1H, $J=16.8$, 10.2, 4.8 Hz), 2.25 (m, 1H), 1.84 (m, 1H), 1.42-1.22 (m, 22H), 0.86 (t, 3H, $J=6.8$ Hz); ^{13}C NMR (100 MHz, CDCl_3) δ 175.8, 73.6, 64.5, 32.4, 31.9, 30.17, 30.12, 29.7, 29.63, 29.62, 29.60, 29.3, 25.9, 22.7, 20.8, 14.1; MS m/z : 296 (M^+-1), 98 (100%); HRMS (FAB) calcd for $\text{C}_{18}\text{H}_{36}\text{O}_2\text{N}$ (MH^+): 298.2746, found: 298.2743. ***erythro*-Alcohol 4e:** Mp 70-71 $^\circ\text{C}$; IR (neat) ν 3391, 1678 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 3.90 (m, 1H), 3.42 (ddd, 1H, $J=8.6$, 4.2, 1.3 Hz), 3.34 (br, 1H), 2.81 (m, 3H), 2.44 (ddd, 1H, $J=17.1$, 10.5, 7.1 Hz), 2.28 (ddd, 1H, $J=16.4$, 10.5, 5.7 Hz), 2.04 (m, 1H), 1.90 (m, 1H), 1.56-1.22 (m, 22H), 0.87 (t, 3H, $J=6.8$ Hz); ^{13}C NMR (100 MHz, CDCl_3) δ 176.0, 69.0, 65.0, 32.8, 31.9, 30.7, 29.7, 29.69, 29.67, 29.62, 29.60, 29.4, 28.0, 26.3, 22.7, 17.5, 14.2; MS m/z : 296 (M^+-1), 98 (100%); HRMS (FAB) calcd for $\text{C}_{18}\text{H}_{36}\text{O}_2\text{N}$ (MH^+): 298.2746, found: 298.2748.

(*R)-4-((*R**)-Hydroxy(4-methoxyphenyl)methyl)-1,3-dimethylimidazolidin-2-one (*threo*-16),**

(*R)-4-((*S**)-Hydroxy(4-methoxyphenyl)methyl)-1,3-dimethylimidazolidin-2-one (*erythro*-16), 1-(2-Hydroxy-2-(4-methoxyphenyl)ethyl)-3-methylimidazolidin-2-one (17):** The title compounds were obtained according to the above-mentioned procedure from 4-methoxybenzaldehyde (**2a**) (408 mg, 3.0 mmol), 1,3-dimethyl-2-imidazolidinone (**8**) (11 mL, 105 mmol) and Et₃B (2.6 mL, 18 mmol). After 10 h, the mixture was partitioned between Et₂O and H₂O. The separated aqueous phase was thoroughly extracted with CH₂Cl₂ and the combined organic extract was dried over MgSO₄. Following solvent evaporation in vacuo, the residue was purified by silica gel column chromatography (EtOAc/Hex 1:4) to give ethyl adduct **6a** (30 mg, 6%) and further elution with MeOH/EtOAc (1:40) gave an inseparable mixture of alcohols *threo*-**16**, *erythro*-**16**, and **17** (623 mg, 83%) as a colorless solid. The yields and the ratio of the products were determined by ¹H NMR analysis to be *threo*-**16**/*erythro*-**16** (561 mg, 75%, dr 62:38) and **17** (62 mg, 8%). Pure samples of alcohols *threo*-**16** and *erythro*-**16** were obtained as follows: acetylation of the mixture of alcohols *threo*-**16**, *erythro*-**16**, and **17** (Ac₂O, Et₃N, DMAP, CH₂Cl₂, r.t.), chromatographic separation (MeOH/EtOAc 1:40), and hydrolysis of the acetates (K₂CO₃, aq. MeOH, r.t.). Recrystallization from EtOAc/CH₂Cl₂ gave *erythro*-**16** as colorless pillars. The configuration of the minor compound *erythro*-**16** was determined by X-ray crystallographic analysis (For crystallographic data, see CIF file). ***threo*-Alcohol 16:** colorless oil; IR (neat) ν 3362, 1678 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 7.29-7.24 (m, 2H), 6.93-6.87 (m, 2H), 4.66 (d, 1H, *J*=6.5 Hz), 3.81 (s, 3H), 3.69 (ddd, 1H, *J*=9.2, 7.5, 6.5 Hz), 3.05 (t, 1H, *J*=9.2 Hz), 2.89 (s, 3H), 2.84 (dd, 1H, *J*=9.2, 7.7 Hz), 2.68 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 161.9, 159.6, 132.7, 127.5, 114.1, 76.5, 61.3, 55.3, 47.9, 32.5, 31.1; MS *m/z*: 250 (M⁺), 113 (100%); HRMS (EI) calcd for C₁₃H₁₈O₃N₂ (M⁺): 250.1317, found: 250.1319. ***erythro*-Alcohol 16:** Mp 135-136 °C (EtOAc/CH₂Cl₂); IR (neat) ν 3368, 1682 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.31-7.26 (m, 2H), 6.91-6.86 (m, 2H), 4.93 (d, 1H, *J*=3.3 Hz), 3.80 (s, 3H), 3.56 (ddd, 1H, *J*=9.0, 8.1, 3.3 Hz), 3.27 (dd, 1H, *J*=9.0, 8.1 Hz), 2.98 (t, 1H, *J*=9.0 Hz), 2.75 (s, 3H), 2.73 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 161.8, 159.0, 131.5, 126.9, 113.8, 69.6, 62.0, 55.3, 45.0, 30.9, 30.3; MS *m/z*: 250 (M⁺), 113 (100%); HRMS (EI) calcd for C₁₃H₁₈O₃N₂ (M⁺): 250.1317, found: 250.1315. **Alcohol 17:** IR (neat) ν 3410, 1670 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 7.22-7.16 (m, 2H), 6.90-6.84 (m, 2H), 4.66 (dd, 1H, *J*=8.9,

4.1 Hz), 4.12 (dd, 1H, $J=11.7, 8.9$ Hz), 3.93 (dd, 1H, $J=11.7, 4.1$ Hz), 3.79 (s, 3H), 3.32-3.19 (m, 3H), 3.05 (m, 1H), 2.81 (s, 3H); ^{13}C NMR (75 MHz, CDCl_3) δ 190.5, 159.2, 129.5, 128.7, 114.1, 63.8, 61.0, 55.3, 45.4, 41.2, 31.4; MS m/z : 232 (M^+-18), 219 (100%); HRMS (FAB) calcd for $\text{C}_{13}\text{H}_{19}\text{O}_3\text{N}_2$ (MH^+): 251.1396, found: 251.1394.

(*R)-Tetrahydro-6-((*R**)-hydroxy(4-methoxyphenyl)methyl)-1,3-dimethylpyrimidin-2(1*H*)-one (*threo*-18),**

(*R)-Tetrahydro-6-((*S**)-hydroxy(4-methoxyphenyl)methyl)-1,3-dimethylpyrimidin-2(1*H*)-one (*erythro*-18), Tetrahydro-3-(2-hydroxy-2-(4-methoxyphenyl)ethyl)-1-methylpyrimidin-2(1*H*)-one (19):**

The title compounds were obtained according to the above-mentioned procedure from 4-methoxybenzaldehyde (**2a**) (408 mg, 3.0 mmol), 1,3-dimethyl-2-pyrimidinone (**9**) (12.6 mL, 105 mmol) and Et_3B (2.6 mL, 18 mmol). After 16 h, the mixture was partitioned between Et_2O and H_2O . The separated aqueous phase was thoroughly extracted with CH_2Cl_2 and the combined organic extract was dried over MgSO_4 . Following solvent evaporation in vacuo, the residue was purified by silica gel column chromatography (EtOAc/Hex 1:4) to give ethyl adduct **6a** (30 mg, 6%) and 4-methoxybenzylalcohol (**7a**) (7 mg, 2%). Further elution with MeOH/EtOAc (1:40) gave a mixture of alcohols *threo*-18, *erythro*-18, and **19** as a colorless oil. The yields and the ratio of the products were determined by ^1H NMR analysis of acetates (761 mg, 83% combined yield) derived from the mixture to be *threo*-18/*erythro*-18 (as acetates, 659 mg, 72%, dr 79:21) and **19** (as acetate, 102 mg, 11%). Pure samples of alcohols *threo*-18, *erythro*-18, and **19** were obtained by chromatographic separation (MeOH/EtOAc 1:50) and hydrolysis of the acetates (K_2CO_3 , aq. MeOH , r.t.). Recrystallization from $\text{EtOAc/CH}_2\text{Cl}_2$ gave *erythro*-18 as colorless plates and alcohol **19** as colorless pillars. The configuration of the minor compound *erythro*-18 was determined by X-ray crystallographic analysis (For crystallographic data, see CIF file). ***threo*-Alcohol 18:** colorless oil; IR (neat) ν 3339, 1612 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ 7.27-7.21 (m, 2H), 6.90-6.85 (m, 2H), 4.72 (d, 1H, $J=8.0$ Hz), 3.79 (s, 3H), 3.41 (m, 1H), 3.13 (s, 3H), 3.10 (m, 1H), 2.91 (m, 1H), 2.87 (s, 3H), 1.84 (m, 1H), 1.50 (m, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ 159.2, 155.9, 133.8, 127.4, 113.7, 74.9, 62.8, 55.1, 44.7, 37.6, 35.4, 22.2; MS m/z : 264 (M^+), 127 (100%); HRMS (EI) calcd for $\text{C}_{14}\text{H}_{20}\text{O}_3\text{N}_2$ (M^+): 264.1474, found:

264.1473. **erythro-Alcohol 18**: Mp 160-161 °C (EtOAc/CH₂Cl₂); IR (neat) ν 3329, 1612 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 7.30-7.25 (m, 2H), 6.92-6.86 (m, 2H), 4.82 (d, 1H, *J*=6.0 Hz), 3.81 (s, 3H), 3.51 (ddd, 1H, *J*=11.5, 11.5, 5.0 Hz), 3.33 (ddd, 1H, *J*=6.0, 6.0, 3.0 Hz), 3.10 (ddd, 1H, *J*=11.5, 6.0, 3.0 Hz), 2.94 (s, 3H), 2.62 (s, 3H), 2.11 (m, 1H), 1.82 (m, 1H); ¹³C NMR (100 MHz, CDCl₃) δ 159.2, 156.5, 133.5, 127.4, 113.9, 72.7, 63.2, 55.3, 45.3, 35.8, 35.6, 21.9; MS *m/z*: 264 (M⁺), 127 (100%); HRMS (EI) calcd for C₁₄H₂₀O₃N₂ (M⁺): 264.1474, found: 264.1473. **Alcohol 19**: Mp 99-100 °C (EtOAc/CH₂Cl₂); IR (neat) ν 3371, 1610 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 7.33-7.28 (m, 2H), 6.90-6.84 (m, 2H), 4.87 (dd, 1H, *J*=7.0, 3.0 Hz), 3.80 (s, 3H), 3.56 (dd, 1H, *J*=15.0, 7.0 Hz), 3.47 (dd, 1H, *J*=15.0, 3.0 Hz), 3.27-3.18 (m, 3H), 2.96 (s, 3H), 2.95-2.88 (m, 1H), 1.91-1.80 (m, 2H); ¹³C NMR (75 MHz, CDCl₃) δ 158.9, 158.5, 135.1, 127.0, 113.6, 73.7, 58.1, 55.3, 48.3, 47.6, 35.8, 22.2; MS *m/z*: 264 (M⁺), 128 (100%); HRMS (EI) calcd for C₁₄H₂₀O₃N₂ (M⁺): 264.1474, found: 264.1474.

(*R)-(4-Methoxyphenyl)((*R**)-1-methylpyrrolidin-2-yl)methanol** (*threo*-**20**),

(*R)-(4-Methoxyphenyl)((*S**)-1-methylpyrrolidin-2-yl)methanol** (*erythro*-**20**),

1-(4-Methoxyphenyl)-2-(pyrrolidin-1-yl)ethanol (21): The title compounds were obtained according to the above-mentioned procedure from 4-methoxybenzaldehyde (**2a**) (408 mg, 3.0 mmol), 1-methylpyrrolidine (**10**) (11 mL, 105 mmol) and Et₃B (2.6 mL, 18 mmol). After 36 h, 28% NH₄OH was added and the mixture was extracted with CH₂Cl₂. The organic extract was dried over Na₂SO₄ and concentrated in vacuo. Purification by silica gel column chromatography (MeOH/EtOAc/28% NH₄OH 1:30:1) gave a mixture of alcohols *threo*-**20**, *erythro*-**20**, and **21** (559 mg, 84%) as a colorless solid. The yields and the ratio of the products were determined by ¹H NMR analysis to be *threo*-**20**/*erythro*-**20** (525 mg, 79%, dr 58:42) and **21** (34 mg, 5%). The configuration of major alcohol *threo*-**20** was determined by chemical correlation with *threo* amine derived from amide **3a** whose configuration was unambiguously determined by X-ray crystallographic analysis (see page S2); the reduction of **3a** with LAH in 1,4-dioxane afforded *threo*-**20** in 86% yield. **threo-Alcohol 20**: Mp 70-74 °C; IR (neat) ν 3383 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 7.31-7.25 (m, 2H), 6.89-6.84 (m, 2H), 4.28 (d, 1H, *J*=5.5 Hz), 3.80 (s, 3H), 3.14-3.06 (m, 1H), 2.71 (m, 1H), 2.37 (m, 1H), 2.28 (s, 3H), 1.93-1.59 (m, 4H); ¹³C NMR (75 MHz, CDCl₃) δ 158.7, 135.8, 127.3, 113.6, 75.3, 71.7, 57.6, 55.2, 44.1, 29.3,

24.4; MS m/z : 220 (M^+-1), 84 (100%); HRMS (FAB) calcd for $C_{13}H_{20}O_2N$ (MH^+): 222.1494, found: 222.1493. **erythro-Alcohol 20**: IR (neat) ν 3425 cm^{-1} ; 1H NMR (400 MHz, $CDCl_3$) δ 7.30-7.26 (m, 2H), 6.89-6.85 (m, 2H), 4.82 (d, 1H, $J=2.9$ Hz), 3.80 (s, 3H), 3.14 (m, 1H), 2.47 (m, 1H), 2.45 (s, 3H), 2.33 (dt, 1H, $J=9.3, 7.6$ Hz), 1.78-1.56 (m, 3H), 1.30 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.4, 133.7, 126.5, 113.5, 71.0, 69.4, 57.6, 55.2, 40.0, 23.9, 22.9; MS m/z : 221 (M^+), 84 (100%); HRMS (FAB) calcd for $C_{13}H_{20}O_2N$ (MH^+): 222.1494, found: 222.1501. **Alcohol 21**: Mp 82-83 $^{\circ}C$; IR (neat) ν 3150 cm^{-1} ; 1H NMR (300 MHz, $CDCl_3$) δ 7.33-7.26 (m, 2H), 6.91-6.85 (m, 2H), 4.65 (dd, 1H, $J=10.5, 3.2$ Hz) 3.80 (s, 3H), 2.80-2.70 (m, 3H), 2.58-2.48 (m, 2H), 2.44 (dd, 1H, $J=12.0, 3.2$ Hz), 1.86-1.71 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.0, 134.5, 127.1, 113.7, 70.3, 64.1, 55.2, 53.8, 23.7; MS m/z : 221 (M^+), 84 (100%); HRMS (EI) calcd for $C_{13}H_{19}O_2N$ (M^+): 221.1416, found: 221.1410.

1-(Diethylamino)-1-(4-methoxyphenyl)propan-1-ol (22): The title compound was obtained according to the above-mentioned procedure from 4-methoxybenzaldehyde (**2a**) (408 mg, 3.0 mmol), triethylamine (**11**) (14.6 mL, 105 mmol) and Et_3B (2.6 mL, 18 mmol). Flow rate of air: 35-40 $mL \cdot h^{-1} \cdot mmol$ aldehyde $^{-1}$. After 16 h, 28% NH_4OH was added and the mixture was extracted with CH_2Cl_2 . The organic extract was dried over Na_2SO_4 and concentrated in vacuo. Purification by silica gel column chromatography (MeOH/EtOAc/28% NH_4OH 2:20:1) gave less polar alcohol major-**22** (390 mg, 55%) and more polar alcohol minor-**22** (283 mg, 40%), both as a yellow oil. The configuration of the products was not determined. **Major-22**: IR (neat) ν 3329 cm^{-1} ; 1H NMR (300 MHz, $CDCl_3$) δ 7.30-7.24 (m, 2H), 6.89-6.83 (m, 2H), 4.15 (d, 1H, $J=9.7$ Hz) 3.80 (s, 3H), 2.75-2.63 (m, 3H), 2.39 (dq, 2H, $J=13.4, 6.9$ Hz), 1.12 (t, 6H, $J=6.9$ Hz), 0.74 (d, 3H, $J=6.6$ Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.1, 134.6, 128.3, 113.6, 74.0, 62.3, 55.2, 43.1, 14.3, 8.4; MS m/z : 236 (M^+-1), 100 (100%); HRMS (FAB) calcd for $C_{14}H_{24}O_2N$ (MH^+): 238.1807, found: 238.1806. **Minor-22**: IR (neat) ν 3404 cm^{-1} ; 1H NMR (300 MHz, $CDCl_3$) δ 7.24-7.20 (m, 2H), 6.88-6.83 (m, 2H), 4.64 (d, 1H, $J=4.8$ Hz) 3.80 (s, 3H), 2.99 (dq, 1H, $J=7.0, 4.8$ Hz), 2.48 (q, 4H, $J=7.0$ Hz), 1.01 (t, 6H, $J=7.0$ Hz), 0.89 (d, 3H, $J=7.0$ Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 158.5, 134.5, 127.2, 113.1, 72.5, 60.1, 55.2, 44.0, 13.1, 10.5; MS m/z : 236 (M^+-1), 100 (100%); HRMS (FAB) calcd for $C_{14}H_{24}O_2N$ (MH^+): 238.1807, found: 238.1801.

2-(*N*-ethyl-*N*-phenylamino)-1-(4-methoxyphenyl)propan-1-ol (23): The title compound was obtained according to the above-mentioned procedure from 4-methoxybenzaldehyde (**2a**) (134 mg, 1.0 mmol), *N,N*-diethylaniline (**12**) (5.6 mL, 35 mmol) and Et₃B (0.87 mL, 6 mmol). Flow rate of air: 35-40 mL·h⁻¹·mmol aldehyde⁻¹. After 21 h, sat. NH₄Cl solution was added and the mixture was extracted with CH₂Cl₂. The organic extract was dried over Na₂SO₄ and concentrated in vacuo. Purification by silica gel column chromatography (EtOAc/Hex 1:4) gave a mixture of alcohols major-**23** and minor-**23** (185 mg, 65%, dr 83:17) as a colorless oil. Ethyl adduct **6a** (11 mg, 7%) and reduction product **7a** (13 mg, 9%) were also obtained as a colorless oil. The data shown below are those of pure alcohols major-**23** and minor-**23**, which were obtained by careful purification via flash silica gel chromatography (EtOAc/CH₂Cl₂ 1:12). The configuration of the products was not determined. **Major-23:** IR (neat) ν 3447 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 7.39-7.26 (m, 4H), 7.07 (d, 2H, *J*=8.2 Hz), 6.95-6.89 (m, 3H), 4.48 (d, 1H, *J*=9.5 Hz), 3.93 (brs, 1H), 3.82 (s, 3H), 3.64 (dq, 1H, *J*=9.5, 6.8 Hz), 3.27 (q, 2H, *J*=7.0 Hz), 1.22 (t, 3H, *J*=7.0 Hz), 0.85 (d, 3H, *J*=6.8 Hz); ¹³C NMR (75 MHz, CDCl₃) δ 159.4, 149.2, 133.4, 129.1, 128.4, 120.3, 118.9, 113.8, 75.1, 65.6, 55.2, 38.5, 14.1, 11.8; MS *m/z*: 285 (M⁺), 148 (100%); HRMS (EI) calcd for C₁₈H₂₃NO₂ (M⁺): 285.1729, found: 285.1722. **Minor-23:** IR (neat) ν 3416 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 7.32-7.20 (m, 4H), 6.90-6.70 (m, 5H), 4.87 (d, 1H, *J*=4.9 Hz) 3.97 (m, 1H), 3.80 (s, 3H), 3.38 (dq, 1H, *J*=21.6, 7.0 Hz), 3.24 (dq, 1H, *J*=21.6, 7.0 Hz), 2.13 (brs, 1H), 1.23 (d, 3H, *J*=6.8 Hz), 1.07 (t, 3H, *J*=7.0 Hz); ¹³C NMR (75 MHz, CDCl₃) δ 158.9, 148.3, 134.8, 129.1, 127.2, 117.3, 115.2, 113.6, 75.2, 60.1, 55.2, 40.1, 13.8, 12.5; MS *m/z*: 285 (M⁺), 148 (100%); HRMS (EI) calcd for C₁₈H₂₃NO₂ (M⁺): 285.1729, found: 285.1728.

(4-Methoxyphenyl)(4-methylmorpholin-3-yl)methanol (24),

1-(4-Methoxyphenyl)-2-morpholinoethanol (25): The title compounds were obtained according to the above-mentioned procedure from 4-methoxybenzaldehyde (**2a**) (408 mg, 3.0 mmol), 4-methylmorpholine (**13**) (11.5 mL, 105 mmol) and Et₃B (2.6 mL, 18 mmol). After 36 h, 28% NH₄OH was added and the mixture was extracted with CH₂Cl₂. The organic extract was dried over Na₂SO₄ and concentrated in vacuo. Purification by silica gel column chromatography (EtOAc/Hex 1:4) gave ethyl

adduct **6a** (30 mg, 6%). Further elution with MeOH/EtOAc/28% NH₄OH (1:30:1) gave a mixture of alcohols major-**24**, minor-**24**, and **25** (481mg, 68%) as a colorless solid. The yields and the ratio of the products were determined by ¹H NMR analysis to be major-**24**/minor-**24** (404 mg, 57%, dr 52:48) and **25** (77 mg, 11%). Recrystallization of the mixture from EtOAc/Hex gave major-**24** as colorless solids and minor-**24** as colorless pillars. The configuration of the products was not determined. **Major-24:** Mp 69-70 °C (EtOAc/Hex); IR (neat) ν 3416 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 7.34-7.28 (m, 2H), 6.90-6.84 (m, 2H), 4.76 (d, 1H, *J*=7.0 Hz), 3.80 (s, 3H), 3.79-3.72 (m, 1H), 3.68 (dd, 1H, *J*=12.0, 3.5 Hz), 3.53 (ddd, 1H, *J*=12.0, 5.0, 3.5 Hz), 3.35 (dd, 1H, *J*=12.0, 4.5 Hz), 3.17 (ddd, 1H, *J*=13.4, 8.6, 3.5 Hz), 2.51 (s, 3H), 2.50-2.44 (m, 1H), 2.39 (dt, 1H, *J*=7.0, 4.0 Hz); ¹³C NMR (100 MHz, CDCl₃) δ 159.0, 134.4, 127.7, 113.7, 69.6, 65.8, 62.9, 62.6, 55.2, 49.8, 42.6; MS *m/z*: 237 (M⁺), 100 (100%); HRMS (EI) calcd for C₁₃H₁₉O₃N (M⁺): 237.1365, found: 237.1367. **Minor-24:** Mp 63-64 °C (EtOAc/Hex); IR (neat) ν 3425 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 7.25-7.21 (m, 2H), 6.90-6.85 (m, 2H), 5.12 (d, 1H, *J*=3.0 Hz), 3.80 (s, 3H), 3.74 (dt, 1H, *J*=11.0, 2.0 Hz), 3.59-3.49 (m, 2H), 3.39 (t, 1H, *J*=11.0 Hz), 3.19 (dd, 1H, *J*=12.0, 4.0 Hz), 2.77 (d, 1H, *J*=11.5 Hz), 2.57-2.46 (m, 1H), 2.50 (s, 3H), 2.38-2.30 (m, 1H); ¹³C NMR (75 MHz, CDCl₃) δ 158.7, 131.5, 126.4, 113.7, 68.6, 66.5, 66.2, 65.5, 55.2, 55.1, 42.6; MS *m/z*: 237 (M⁺), 100 (100%); HRMS (EI) calcd for C₁₃H₁₉O₃N (M⁺): 237.1365, found: 237.1361. **Alcohol 25:** Mp 82-83 °C; IR (neat) ν 3435 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 7.31-7.26 (m, 2H), 6.91-6.85 (m, 2H), 4.71 (dd, 1H, *J*=8.5, 5.0 Hz), 3.80 (s, 3H), 3.77-3.73 (m, 4H), 2.77-2.70 (m, 2H), 2.51-2.42 (m, 4H); ¹³C NMR (75 MHz, CDCl₃) δ 159.1, 133.9, 127.1, 113.8, 68.2, 67.0, 66.7, 55.3, 53.5; MS *m/z*: 237 (M⁺), 100 (100%); HRMS (EI) calcd for C₁₃H₁₉O₃N (M⁺): 237.1365, found: 237.1364.

(R*)-4-((R*)-Hydroxy(4-methoxyphenyl)methyl)-3-methyloxazolidin-2-one (*threo*-**26**),

(R*)-4-((S*)-Hydroxy(4-methoxyphenyl)methyl)-3-methyloxazolidin-2-one (*erythro*-**26**),

3-(2-Hydroxy-2-(4-methoxyphenyl)ethyl)oxazolidin-2-one (27): The title compounds were obtained according to the above-mentioned procedure from 4-methoxybenzaldehyde (**2a**) (408 mg, 3.0 mmol), 3-methyl-2-oxazolidinone (**14**) (9 mL, 105 mmol) and Et₃B (2.6 mL, 18 mmol). After 36 h, the mixture was treated with sat. NH₄Cl and extracted with Et₂O. The separated aqueous phase was

thoroughly extracted with CH₂Cl₂ and the combined organic extract was dried over MgSO₄. After concentration in vacuo, the residue was purified by silica gel column chromatography (EtOAc/Hex 1:4) to give unreacted aldehyde **2a** (35 mg, 9%), ethyl adduct **6a** (56 mg, 11%), and 4-methoxybenzyl alcohol (**7a**) (37 mg, 9%). Further elution with MeOH/CHCl₃ (1:25) afforded a mixture of alcohols *threo*-**26**, *erythro*-**26**, and **27** (306 mg, 43%) as a colorless solid. The yields and the ratio of the products were determined by ¹H NMR analysis to be *threo*-**26**/*erythro*-**26** (272 mg, 38%, dr 56:44) and **27** (34 mg, 5%). Careful purification of the mixture of alcohols *threo*-**26**, *erythro*-**26**, and **27** by flash silica gel chromatography (MeOH/CHCl₃ 1:30) and subsequent recrystallization (EtOAc/CH₂Cl₂) afforded pure major *threo*-**26** as colorless plates, minor *erythro*-**26** as colorless plates, and regioisomeric alcohol **27** as a colorless solid. The relative configuration of major product *threo*-**26** was determined by X-ray crystallographic analysis (See CIF file). ***threo*-Alcohol 26:** Mp 119-120 °C (EtOAc/CH₂Cl₂); IR (neat) ν 3404, 1730 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 7.28-7.23 (m, 2H), 6.94-6.88 (m, 2H), 4.71 (d, 1H, *J*=6.6 Hz), 4.01-3.88 (m, 2H), 3.83 (m, 1H), 3.81 (s, 3H), 3.05 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 159.9, 158.8, 131.4, 127.7, 114.4, 76.4, 63.8, 62.4, 55.3, 31.9; MS *m/z*: 237 (M⁺), 137 (100%); HRMS (EI) calcd for C₁₂H₁₅O₄N (M⁺): 237.1001, found: 237.0999. ***erythro*-Alcohol 26:** Mp 138-139 °C (EtOAc/CH₂Cl₂); IR (neat) ν 3393, 1734 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 7.30-7.26 (m, 2H), 6.94-6.89 (m, 2H), 4.90 (d, 1H, *J*=4.0 Hz), 4.35 (dd, 1H, *J*=8.9, 5.8 Hz), 4.10 (t, 1H, *J*=8.9 Hz), 3.84 (m, 1H), 3.81 (s, 3H), 2.80 (s, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 159.6, 159.2, 131.1, 127.2, 114.3, 70.9, 63.1, 62.9, 55.3, 30.0; MS *m/z*: 237 (M⁺), 137 (100%); HRMS (EI) calcd for C₁₂H₁₅O₄N (M⁺): 237.1001, found: 237.1003. **Alcohol 27:** Mp 113-114 °C; IR (neat) ν 3404, 1728 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.34-7.30 (m, 2H), 6.92-6.88 (m, 2H), 4.93 (dd, 1H, *J*=7.7, 4.2 Hz), 4.30 (t, 2H, *J*=8.2 Hz), 3.81 (s, 3H), 3.63 (dt, 1H, *J*=8.5, 7.7 Hz), 3.55-3.41 (m, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 159.4, 159.2, 133.5, 127.0, 114.0, 72.6, 62.2, 55.3, 52.1, 46.4; MS *m/z*: 237 (M⁺), 137 (100%); HRMS (EI) calcd for C₁₂H₁₅O₄N (M⁺): 237.1001, found: 237.0997.

***N*-(2-Hydroxy-2-(4-methoxyphenyl)ethyl)-*N*-methyleacetamide (28):** The title compound was obtained according to the above-mentioned procedure from 4-methoxybenzaldehyde (**2a**) (408 mg, 3.0 mmol), *N,N*-dimethylacetamide (**15**) (20 mL, 210 mmol) and Et₃B (2.6 mL, 18 mmol). After 41 h, sat.

NH₄Cl was added and the mixture was extracted with CH₂Cl₂. The organic extract was dried over MgSO₄ and concentrated in vacuo. The purification by silica gel column chromatography (EtOAc/Hex 1:4) gave unreacted aldehyde **2a** (76 mg, 19%) as a colorless oil, ethyl adduct **6a** (68 mg, 14%) as a colorless oil, 4-methoxybenzyl alcohol (**7a**) (30 mg, 7%) as a colorless oil. Further elution with MeOH/EtOAc (1:40) gave alcohol **28** (265 mg, 40%) as a colorless solid. **Alcohol 28**: Mp 93-94 °C; IR (neat) ν 3383, 1616 cm⁻¹; ¹H NMR (400 MHz, CDCl₃, *minor rotational isomer) δ 7.30-7.24 (m, 2H), 6.90-6.86 (m, 2H), 4.91 (dt, 0.75H, *J*=8.0, 3.5 Hz), 4.83* (dt, 0.25H, *J*=8.0, 3.5 Hz), 4.33 (d, 1H, *J*=3.4 Hz), 3.79 (s, 3H), 3.65 (dd, 0.75H, *J*=14.0, 8.0 Hz), 3.58* (dd, 0.25H, *J*=14.0, 8.0 Hz), 3.50 (dd, 0.75H, *J*=14.0, 3.5 Hz), 3.31* (dd, 0.25H, *J*=14.0, 3.5 Hz), 2.95* (s, 0.75H), 2.88 (s, 2.25H), 2.09 (s, 2.25H), 1.99* (s, 0.75H); ¹³C NMR (100 MHz, CDCl₃) δ 173.1, 171.4, 159.4, 159.0, 134.4, 133.7, 126.9, 126.8, 114.0, 113.7, 73.2, 71.6, 58.4, 57.4, 55.30, 55.27, 38.4, 34.3, 21.8, 21.5; MS *m/z*: 223 (M⁺), 137 (100%); HRMS (EI) calcd for C₁₂H₁₇O₃N (M⁺): 223.1208, found: 223.1211.

References

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4e

(tentatively assigned as erythro)

threo-16

6.068

0.956

1.056

1.018

3.317

1.000

2.199

2.337

PPM

16 (dr 62:38)

17

major 18

major 23

minor 23

erythro-26

26 (dr 56:44)

27