Supporting Information for the Paper

A Novel Metal-Iodide Promoted Three-Component Synthesis of Substituted Pyrrolidines

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General.

All reactions were carried out in 7 ml vials purchased from Supelco. All the commercial available compounds were used without further purification. Magnesium iodide (MgI_2 >99%) (Fluka) was stored over an argon atmosphere and quickly weighted before use. $\text{Et}_2\text{Al-I}$ (25wt.% solution in toluene) was purchased from Acros. Tetrahydrofuran (THF) (Fluka) was used without further purification and stored over MS (4Å). PS-Isocyanate scavenger resin (Argonaut Tech.) and ionic exchange columns (IEC) (Isolute SCX from IST) were used in the purification of all the reactions carried out in a 0.2 mmol scale.

Purification of compounds was achieved by flash chromatography using a CombiFlash Sq-16x system purchased by ISCO. Diastereoisomeric ratios were determined by GC analysis, using a 6850 GC apparatus from Agilent and employing a 5% phenyl-methyl-polysiloxane (HP5) column 10mX0.25mm (method = 50°C up to 250°C, 10°C/min). All ^1H and ^{13}C -NMR spectra were recorded using a Varian XL 400MHz. NMR spectra were recorded in CDCl_3 solutions; chemical shifts are given in ppm relative to TMS (^1H , 0.0 ppm), or CDCl_3 (^{13}C , 77.2±0.06 ppm). UV-purity was determined using a Waters HPLC-system (600E pump, 2700 autosampler, 996 PDA-detector) (UV scan: 190-450 nm). The pKa values of **4f** and **4l** were determined by an automated titration using a “Sirius pca 200” apparatus.

Representative Procedure for MgI_2 Promoted Synthesis of Pyrrolidines

anti-3-Benzoyl-2-(4-fluorophenyl)-1-(4-methylbenzyl)-pyrrolidine (**4a**)

In a 7ml vial, 4-fluoro-benzaldehyde (**2a**) (124 mg; 108 μL ; 1.0 mmol; 1.0 eq.), MgI_2 (278 mg; 1.0 mmol; 1.0 eq) and cyclopropyl-phenyl-ketone (**1a**) (146 mg; 138 μL ; 1.0 mmol; 1.0 eq.) were added sequentially to a solution of 4-methyl-benzylamine (**3a**) (121 mg; 127 μL ; 1.0 mmol; 1.0 eq.) in THF (4 mL) at room temperature and the resulting mixture was shaken at 80 °C. After 6h, the reaction was cooled to ambient temperature and then quenched with saturated aqueous $\text{Na}_2\text{S}_2\text{O}_3$ solution (2 mL). The mixture was extracted with EtOAc (5 mL) and the organic phase washed with saturated aqueous NaHCO_3 solution (2 mL) and brine (2 mL), dried over Na_2SO_4 , filtered and concentrated. The corresponding crude reaction mixture, consisting of a 82:18 mixture of diastereoisomers **4a/5a**, was purified by flash chromatography on

silica gel (CH₂Cl₂+MeOH 1%) to afford the major diastereoisomer **4a** (241 mg; 64% yield) as an oil.

Anti diastereoisomer (**4a**): *R_f*: 0.7 (silica gel, CH₂Cl₂+MeOH 1%); ¹H NMR (400 MHz, CDCl₃) δ 7.79-7.75 (m, 2H); 7.53-7.48 (m, 3H); 7.40-7.35 (m, 2H); 7.21-7.17 (m, 2H); 7.15-7.11 (m, 2H); 7.04-6.98 (m, 2H); 3.98 (d, 1H, *J*=8.2 Hz); 3.88-3.81 (m, 1H); 3.80 (d, 1H, *J*=13.5 Hz); 3.18-3.13 (m, 1H); 3.11 (d, 1H, *J*=12.9 Hz); 2.45-2.32 (m, 2H); 2.35 (s, 3H); 2.02-1.94 (m, 1H). ¹³C NMR (100 MHz, CDCl₃) δ 200.85; 162.40 (*J*_{C-F}=245.2 Hz); 138.08 (*J*_{C-F}=2.7 Hz); 136.8; 136.7; 136.4; 133.3; 129.6 (2C; *J*_{C-F}=8.1 Hz); 129.1 (2C); 128.8 (2C); 128.7 (2C); 128.7 (2C); 115.6 (2C, *J*_{C-F}=21.1 Hz); 70.7; 57.7; 55.4; 52.7; 28.8; 21.3. HRMS Calcd for C₂₅H₂₄FNO (M)⁺: 373.1842 Found: 373.1834.

***anti*-3-Benzoyl-2-(4-fluorophenyl)-1-pentyl-pyrrolidine (4b)**

The reaction was carried out following the representative procedure for the MgI₂ promoted three-components synthesis of pyrrolidines employing amylamine (**3b**) (87 mg; 116 μL; 1.0 mmol; 1.0 eq.), 4-fluoro-benzaldehyde (**2a**) (124 mg; 108 μL; 1.0 mmol; 1.0 eq.) and cyclopropyl-phenyl-ketone (**1a**) (146 mg; 138 μL; 1.0 mmol; 1.0 eq.) in THF (4 mL). The corresponding crude reaction product, consisting of a 88:12 mixture of diastereoisomers **4b/5b**, was purified by flash chromatography on silica gel (CH₂Cl₂+MeOH 1%) to afford the major diastereoisomer **4b** (238 mg; 70% yield) as an oil.

Anti diastereoisomer (**4b**): *R_f*: 0.49 (silica gel, CH₂Cl₂+MeOH 1%); ¹H NMR (400 MHz, CDCl₃) δ 7.76-7.71 (m, 2H); 7.51-7.45 (m, 1H); 7.38-7.32 (m, 4H); 6.98-6.91 (m, 2H); 3.82-3.74 (m, 2H); 3.42-3.35 (m, 1H); 2.51 (ddd, 1H, *J*=11.9 Hz and 8.2 Hz and 8.2 Hz); 2.42-2.32 (m, 2H); 2.12-1.98 (m, 2H); 1.48-1.41 (m, 2H); 1.29-1.17 (m, 4H); 0.85 (t, 3H, *J*=6.26 Hz). ¹³C NMR (100 MHz, CDCl₃) δ 200.9; 162.3 (*J*_{C-F}=244.8 Hz); 138.4 (*J*_{C-F}=3.1 Hz); 136.8; 133.2; 129.4 (2C, *J*_{C-F}=7.7 Hz); 128.7 (2C); 128.7 (2C); 115.4 (2C, *J*_{C-F}=21.53 Hz); 71.4; 55.3; 54.1; 52.9; 29.8; 28.8; 28.4; 22.7; 14.2. HRMS Calcd for C₂₂H₂₆FNO (M)⁺: 339.1998 Found: 339.2004.

***anti*-3-Benzoyl-2-(4-methoxyphenyl)-1-(4-methylbenzyl)-pyrrolidine (4c)**

The reaction was carried out following the representative procedure for the MgI₂ promoted three-components synthesis of pyrrolidines employing 4-methylbenzylamine (**3a**) (121 mg; 127 μL; 1.0 mmol; 1.0 eq.), 4-methoxy-benzaldehyde (**2b**) (136 mg; 121 μL; 1.0 mmol; 1.0 eq.) and cyclopropyl-phenyl-ketone (**1a**) (146 mg; 138 μL; 1.0 mmol; 1.0 eq.) in THF (4 mL). The corresponding crude reaction product, consisting of a 90:10 mixture of diastereoisomers **4c/5c**, was purified by

flash chromatography on silica gel (CH₂Cl₂+MeOH 1%) to afford the major diastereoisomer **4c** (216 mg; 56% yield) as an oil.

Anti diastereoisomer (**4c**): *R_f*: 0.51 (silica gel, CH₂Cl₂+MeOH 1%); ¹H NMR (400 MHz, CDCl₃) δ 7.79-7.74 (m, 2H); 7.49-7.42 (m, 3H); 7.38-7.33 (m, 2H); 7.22-7.18 (m, 2H); 7.15-7.11 (m, 2H); 6.89-6.85 (m, 2H); 3.94-3.81 (m, 3H); 3.79 (s, 3H); 3.18-3.12 (m, 1H); 3.08 (d, 1H, *J*=12.9 Hz); 2.45-2.28 (m, 2H); 2.34 (s, 3H); 2.02-1.95 (m, 1H). ¹³C NMR (100 MHz, CDCl₃) δ 201.2; 159.23; 136.9; 136.6; 136.5; 134.3; 133.1; 129.2 (2C); 129.1 (2C); 128.9 (2C); 128.7 (2C); 128.6 (2C); 114.2 (2C); 71.1; 57.6; 55.5; 55.2; 52.7; 28.7; 21.3. HRMS Calcd for C₂₆H₂₇NO₂ (M)⁺: 385.2042 Found: 385.2032.

***anti*-3-Benzoyl-2-(4-methoxyphenyl)-1-pentyl-pyrrolidine (4d)**

The reaction was carried out following the representative procedure for the MgI₂ promoted three-components synthesis of pyrrolidines employing amylamine (**3b**) (87 mg; 116 μL; 1.0 mmol; 1.0 eq.), 4-methoxy-benzaldehyde (**2b**) (136 mg; 121 μL; 1.0 mmol; 1.0 eq.) and cyclopropyl-phenyl-ketone (**1a**) (146 mg; 138 μL; 1.0 mmol; 1.0 eq.) in THF (4 mL). The corresponding crude reaction product, consisting of a 95:5 mixture of diastereoisomers **4d/5d**, was purified by flash chromatography on silica gel (CH₂Cl₂+MeOH 1%) to afford the major diastereoisomer **4d** (209 mg; 59% yield) as an oil.

Anti diastereoisomer (**4d**): *R_f*: 0.31 (silica gel, CH₂Cl₂+MeOH 1%); ¹H NMR (400 MHz, CDCl₃) δ 7.76-7.70 (m, 2H); 7.49-7.43 (m, 1H); 7.37-7.26 (m, 4H); 6.84-6.77 (m, 2H); 3.86-3.68 (m, 2H); 3.76 (s, 3H); 3.42-3.34 (m, 1H); 2.58-2.47 (m, 1H); 2.42-2.32 (m, 2H); 2.11-1.96 (m, 2H); 1.48-1.40 (m, 2H); 1.31-1.17 (m, 4H); 0.85 (t, 3H, *J*=6.3 Hz). ¹³C NMR (100 MHz, CDCl₃) δ 201.3; 159.1; 137.0; 134.6; 133.1; 129.0 (2C); 128.7 (2C); 128.6 (2C); 113.9 (2C); 71.8; 55.4; 55.1; 54.1; 53.0; 29.8; 28.8; 28.4; 22.8; 14.2. HRMS Calcd for C₂₃H₂₉NO₂ (M)⁺: 351.2199 Found: 351.2187.

***anti*-3-Benzoyl-2-(2,2-dimethylpropyl)-1-(4-methylbenzyl)-pyrrolidine (4e)**

The reaction was carried out following the representative procedure for the MgI₂ induced three-components synthesis of pyrrolidines employing 4-methyl-benzylamine (**3a**) (121 mg; 127 μL; 1.0 mmol; 1.0 eq.), 3,3-dimethyl-butyraldehyde (**2c**) (100 mg; 125 μL; 1.0 mmol; 1.0 eq.) and cyclopropyl-phenyl-ketone (**1a**) (146 mg; 138 μL; 1.0 mmol; 1.0 eq.) in THF (4 mL). The corresponding crude reaction product, consisting of a >99:1 mixture of diastereoisomers **4e/5e**, was purified by flash chromatography on silica gel (CH₂Cl₂+MeOH 1%) to afford the major diastereoisomer **4e** (254 mg; 73% yield) as an oil.

Anti diastereoisomer (**4e**): *R_f*: 0.24 (silica gel, CH₂Cl₂+MeOH 1%); ¹H NMR (400 MHz, CDCl₃) δ 8.01-7.97 (m, 2H); 7.59-7.54 (m, 1H); 7.50-7.45 (m, 2H); 7.28-7.25

(m, 2H); 7.15-7.11 (m, 2H); 4.08 (d, 1H, $J=12.9$ Hz); 3.77 (ddd, 1H, $J=10.4$ Hz and 4.5 Hz and 3.8 Hz); 3.38 (d, 1H, $J=12.8$ Hz); 3.35 (ddd, 1H, $J=9.8$ Hz and 4.5 Hz and 2.9 Hz); 2.84-2.81 (m, 1H); 2.34 (s, 3H); 2.33-2.18 (m, 2H); 1.78 (dd, 1H, $J=14.5$ Hz and 1.7 Hz); 1.76-1.70 (m, 1H); 1.55 (dd, 1H, $J=14.3$ Hz and 9.4 Hz); 0.86 (s, 9H). ^{13}C NMR (100 MHz, CDCl_3) δ 201.6; 136.9; 136.7; 136.6; 133.2; 129.1 (4C); 128.9 (2C); 128.7 (2C); 62.2; 58.4; 53.9; 51.9; 50.4; 30.5; 30.4; 30.2 (3C); 21.3. HRMS Calcd for $\text{C}_{24}\text{H}_{31}\text{NO}$ (M) $^+$: 349.2405 Found: 349.2408.

***anti*-3-Benzoyl-2-(2,2-dimethylpropyl)-1-pentyl-pyrrolidine (4f)**

The reaction was carried out following the representative procedure for the MgI_2 promoted three-components synthesis of pyrrolidines employing amylamine (**3b**) (87 mg; 116 μL ; 1.0 mmol; 1.0 eq.), 3,3-dimethyl-butyraldehyde (**2c**) (100 mg; 125 μL ; 1.0 mmol; 1.0 eq.) and cyclopropyl-phenyl-ketone (**1a**) (146 mg; 138 μL ; 1.0 mmol; 1.0 eq.) in THF (4 mL). The corresponding crude reaction product, consisting of a >99:1 mixture of diastereoisomers **4f/5f**, was purified by flash chromatography on silica gel (CH_2Cl_2 +MeOH 1%) to afford the major diastereoisomer **4f** (235 mg; 75% yield) as an oil.

Anti diastereoisomer (**4f**): R_f : 0.16 (silica gel, CH_2Cl_2 +MeOH 1%); ^1H NMR (400 MHz, CDCl_3) δ 7.96-7.92 (m, 2H); 7.55-7.50 (m, 1H); 7.47-7.41 (m, 2H); 3.69 (ddd, 1H, $J=10.8$ Hz and 4.3 Hz and 2.1 Hz); 3.16 (m, 1H); 3.06 (dd, 1H, $J=8.9$ Hz and 6.4 Hz); 2.84-2.77 (m, 1H); 2.38-2.27 (m, 2H); 2.17 (ddd, 1H, $J=14.8$ Hz and 8.9 Hz and 5.7 Hz); 1.74-1.70 (m, 2H); 1.63 (dd, 1H, $J=14.3$ Hz and 1.4 Hz); 1.58-1.42 (m, 3H); 1.38-1.26 (m, 4H); 0.89 (t, 3H, $J=6.8$ Hz); 0.80 (s, 9H). ^{13}C NMR (100 MHz, CDCl_3) δ 201.5; 136.5; 133.2; 128.9 (2C); 128.66 (2C); 62.4; 54.5; 53.7; 51.7; 50.2; 30.5; 30.4; 30.1; 30.1 (3C); 28.7; 22.8; 14.2. HRMS Calcd for $\text{C}_{21}\text{H}_{33}\text{NO}$ (M) $^+$: 315.2562 Found: 315.2565.

***anti*-2-(2,2-Dimethylpropyl)-1-(4-methylbenzyl)-3-(2-thenoyl)-pyrrolidine (4g)**

The reaction was carried out following the representative procedure for the MgI_2 promoted three-components synthesis of pyrrolidines employing 4-methylbenzylamine (**3a**) (121 mg; 127 μL ; 1.0 mmol; 1.0 eq.), 3,3-dimethyl-butyraldehyde (**2c**) (100 mg; 125 μL ; 1.0 mmol; 1.0 eq.) and cyclopropyl-2-thienyl-ketone (**1b**) (152 mg; 130 μL ; 1.0 mmol; 1.0 eq.) in THF (4 mL). The corresponding crude reaction product, consisting of a >99:1 mixture of diastereoisomers **4g/5g**, was purified by flash chromatography on silica gel (CH_2Cl_2 +MeOH 1%) to afford the major diastereoisomer **4g** (228 mg; 64% yield) as an oil.

Anti diastereoisomer (**4g**): R_f : 0.25 (silica gel, CH_2Cl_2 +MeOH 1%); ^1H NMR (400 MHz, CDCl_3) δ 7.73-7.71 (m, 1H); 7.64-7.62 (m, 1H); 7.27-7.23 (m, 2H); 7.15-7.11 (m, 3H); 4.04 (d, 1H, $J=12.9$ Hz); 3.59 (ddd, 1H, $J=10.2$ Hz and 4.6 Hz and 2.5 Hz);

3.35 (d, 1H, $J=12.7$ Hz); 3.23 (ddd, 1H, $J=9.2$ Hz and 4.5 Hz and 2.6 Hz); 2.86-2.79 (m, 1H); 2.33 (s, 3H); 2.30-2.23 (m, 2H); 1.83-1.80 (m, 1H); 1.76 (dd, 1H, $J=14.5$ Hz and 1.9 Hz); 1.66 (dd, 1H, $J=14.5$ Hz and 9.0 Hz); 0.87 (s, 9H). ^{13}C NMR (100 MHz, CDCl_3) δ 195.1; 144.4; 137.1; 136.5; 133.9; 131.9; 129.2 (2C); 129.1 (2C); 128.4; 62.6; 58.4; 55.6; 52.1; 50.4; 30.9; 30.5; 30.2 (3C); 21.3. HRMS Calcd for $\text{C}_{22}\text{H}_{29}\text{NOS}$ (M) $^+$: 355.1969 Found: 355.1960.

***anti*-2-(4-Methoxyphenyl)-1-pentyl-3-(2-thenoyl)-pyrrolidine (4h)**

The reaction was carried out following the representative procedure for the MgI_2 promoted three-components synthesis of pyrrolidines employing amylamine (**3b**) (87 mg; 116 μL ; 1.0 mmol; 1.0 eq.), 4-methoxy-benzaldehyde (**2b**) (136 mg; 121 μL ; 1.0 mmol; 1.0 eq.) and cyclopropyl-2-thienyl-ketone (**1b**) (152 mg; 130 μL ; 1.0 mmol; 1.0 eq.) in THF (4 mL). The corresponding crude reaction product, consisting of a >99:1 mixture of diastereoisomers **4h/5h**, was purified by flash chromatography on silica gel (CH_2Cl_2 +MeOH 1%) to afford the major diastereoisomer **4h** (233 mg; 65% yield) as an oil.

Anti diastereoisomer (**4h**): R_f : 0.31 (silica gel, CH_2Cl_2 +MeOH 1%); ^1H NMR (400 MHz, CDCl_3) δ 7.54-7.52 (m, 1H); 7.28-7.24 (m, 3H); 6.96-6.93 (m, 1H); 6.82-6.78 (m, 2H); 3.75 (s, 3H); 3.68-3.62 (m, 1H); 3.59 (d, 1H, $J=8.4$ Hz); 3.41-3.35 (m, 1H); 2.53-2.47 (m, 1H); 2.43-2.26 (m, 2H); 2.18-2.07 (m, 1H); 2.07-2.01 (m, 1H); 1.47-1.38 (m, 2H); 1.29-1.15 (m, 4H); 0.84 (t, 3H, $J=7.1$ Hz). ^{13}C NMR (100 MHz, CDCl_3) δ 194.4; 159.1; 144.8; 134.3; 134.0; 132.4; 129.0 (2C); 128.2; 113.9 (2C); 56.5; 55.4; 55.4; 53.9; 53.1; 29.8; 28.6; 28.4; 22.8; 14.2. HRMS Calcd for $\text{C}_{21}\text{H}_{27}\text{NO}_2\text{S}$ (M) $^+$: 357.1762 Found: 357.1769.

***anti*-3-Acetyl-2-(4-methoxyphenyl)-1-pentyl-pyrrolidine (4i)**

The reaction was carried out following the representative procedure for the MgI_2 promoted three-components synthesis of pyrrolidines employing amylamine (**3b**) (87 mg; 116 μL ; 1.0 mmol; 1.0 eq.), 4-methoxy-benzaldehyde (**2b**) (136 mg; 121 μL ; 1.0 mmol; 1.0 eq.) and acetyl-cyclopropane (**1c**) (84 mg; 94 μL ; 1.0 mmol; 1.0 eq.) in THF (4 mL). The corresponding crude reaction product, consisting of a 93:7 mixture of diastereoisomers **4i/5i**, was purified by flash chromatography on silica gel (CH_2Cl_2 +MeOH 1%) to afford the major diastereoisomer **4i** (47 mg; 16% yield) as an oil.

Anti diastereoisomer (**4i**): R_f : 0.28 (silica gel, CH_2Cl_2 +MeOH 1%); ^1H NMR (400 MHz, CDCl_3) δ 7.31-7.26 (m, 2H); 6.88-6.83 (m, 2H); 3.80 (s, 3H); 3.37-3.28 (m, 2H); 3.10-3.02 (m, 1H); 2.46-2.39 (m, 1H); 2.30-2.21 (m, 1H); 2.20-2.11 (m, 1H); 2.06-1.95 (m, 2H); 1.94 (s, 3H); 1.43-1.1.35 (m, 2H); 1.25-1.12 (m, 4H); 0.82 (t, 3H,

$J=7.1$ Hz). ^{13}C NMR (100 MHz, CDCl_3) δ 209.5; 159.2; 129.1 (2C); 114.1 (2C); 109.9; 72.1; 60.4; 55.5; 53.9; 52.8; 30.6; 29.8; 28.2; 26.4; 22.7; 14.2. HRMS Calcd for $\text{C}_{18}\text{H}_{27}\text{NO}_2$ (M) $^+$: 289.2042 Found: 289.2047.

***anti*-1-Allyl-3-benzoyl-2-(4-fluorophenyl)-pyrrolidine (4j)**

The reaction was carried out following the representative procedure for the MgI_2 promoted three-components synthesis of pyrrolidines employing allylamine (**3c**) (57 mg; 75 μL ; 1.0 mmol; 1.0 eq.), 4-fluoro-benzaldehyde (**2a**) (124 mg; 108 μL ; 1.0 mmol; 1.0 eq.) and cyclopropyl-phenyl-ketone (**1a**) (146 mg; 138 μL ; 1.0 mmol; 1.0 eq.) in THF (4 mL). The corresponding crude reaction product, consisting of a 95:5 mixture of diastereoisomers **4j/5j**, was purified by flash chromatography on silica gel (CH_2Cl_2 +MeOH 1%) to afford the major diastereoisomer **4j** (208 mg; 67% yield) as an oil.

Anti diastereoisomer (**4j**): R_f : 0.51 (silica gel, CH_2Cl_2 +MeOH 1%); ^1H NMR (400 MHz, CDCl_3) δ 7.77-7.73 (m, 2H); 7.51-7.45 (m, 1H); 7.39-7.33 (m, 4H); 6.98-6.92 (m, 2H); 5.89-5.79 (m, 1H); 5.14 (dm, 1H); 5.06 (dm, 1H); 3.89-3.76 (m, 2H); 3.37-3.28 (m, 1H); 3.29-3.22 (m, 1H); 2.79 (dd, 1H, $J=13.5$ Hz and 7.8 Hz); 2.46-2.34 (m, 2H); 2.04-1.96 (m, 1H). ^{13}C NMR (100 MHz, CDCl_3) δ 200.8; 162.4 ($J_{\text{C-F}}=245.2$ Hz); 137.8 ($J_{\text{C-F}}=2.7$ Hz); 136.7; 135.8; 133.3; 129.5 (2C, $J_{\text{C-F}}=8.1$ Hz); 128.7 (2C); 128.7 (2C); 117.1; 115.5 (2C, $J_{\text{C-F}}=21.1$ Hz); 70.5; 56.5; 55.2; 52.9; 28.8. HRMS Calcd for $\text{C}_{20}\text{H}_{20}\text{FNO}$ (M) $^+$: 309.1529 Found: 309.1533.

***anti*-3-Benzoyl-2-(2,2-dimethylpropyl)-1-(4-methoxyphenyl)-pyrrolidine (4l)**

The reaction was carried out following the representative procedure for the MgI_2 promoted three-components synthesis of pyrrolidines employing 4-methoxy-aniline (**3d**) (123 mg; 1.0 mmol; 1.0 eq.), 3,3-dimethyl-butyraldehyde (**2c**) (100 mg; 125 μL ; 1.0 mmol; 1.0 eq.) and cyclopropyl-phenyl-ketone (**1a**) (146 mg; 138 μL ; 1.0 mmol; 1.0 eq.) in THF (4 mL). The corresponding crude reaction product, consisting of a 81:19 mixture of diastereoisomers **4l/5l**, was purified by flash chromatography on silica gel (CH_2Cl_2 +MeOH 1%) to afford the major diastereoisomer **4l** (157 mg; 45% yield) as an oil.

Anti diastereoisomer (**4l**): R_f : 0.75 (silica gel, CH_2Cl_2 +MeOH 1%); ^1H NMR (400 MHz, CDCl_3) δ 7.98-7.95 (m, 2H); 7.61-7.55 (m, 1H); 7.51-7.46 (m, 2H); 6.89-6.84 (m, 2H); 6.72-6.64 (m, 2H); 4.29 (d, 1H, $J=10.76$ Hz); 3.93 (d, 1H, $J=8.4$ Hz); 3.77 (s, 3H); 3.46-3.38 (m, 1H); 3.12-3.04 (m, 1H); 2.62-2.48 (m, 1H); 2.13-2.07 (m, 1H); 1.74 (dd, 1H, $J=14.3$ Hz and 1.2 Hz); 1.48-1.38 (m, 1H); 1.01 (s, 9H). ^{13}C NMR (100 MHz, CDCl_3) δ 200.4; 136.1; 133.3; 128.9 (2C); 128.7 (2C); 128.0; 126.7; 115.2

(2C); 114.2; 56.1; 52.8; 47.4; 46.9; 30.9; 30.5; 30.3; 28.8. HRMS Calcd for $C_{23}H_{29}NO_2$ (M)⁺: 351.2199 Found: 351.2184.

Representative Procedure for Et₂Al-I promoted Synthesis of Pyrrolidines

anti-3-Benzoyl-1-(4-methylbenzyl)-2-pentyl-pyrrolidine (**4k**)

In a 7 ml vial, 1-hexanal (**2d**) (20 mg; 24 μ l; 0.2 mmol; 1.0 eq.), Et₂Al-I (294 μ l; 0.3 mmol; 1.5 eq.) and cyclopropyl phenyl ketone (**1a**) (29 mg; 28 μ l; 0.2 mmol; 1.0 eq.) were added sequentially to a solution of 4-methyl-benzylamine (**3a**) (24 mg; 25 μ l; 0.2 mmol; 1.0 eq.) in THF (0.8 ml) at r.t., and the resulting mixture was shaken at 80 °C. After 6 h, the reaction was cooled to ambient temperature and quenched with a saturated aqueous Na₂S₂O₃ solution (0.5 ml) and extracted with CH₂Cl₂ (5 ml). The phases were separated and PS-Isocyanate scavenger resin (400 mg, 0.6 mmol; 3.0 eq.) was then added to the organic solution. The corresponding mixture was shaken at r.t. for 15 h (to scavenge excess amine). Filtration (to get rid of polymeric resin) and evaporation of the solvent afforded the crude product which consisted of a >99:1 mixture of diastereoisomers **4k/5k**. Further purification by IEC (Isolute SCX) afforded the major diastereoisomer **4k** (40 mg; 57 % yield) as an oil.

Anti diastereoisomer (**4k**): R_f: 0.11 (silica gel, CH₂Cl₂+MeOH 1%); ¹H NMR (400 MHz, CDCl₃) δ 7.97-7.93 (m, 2H); 7.59-7.54 (m, 1H); 7.50-7.45 (m, 2H); 7.27-7.22 (m, 2H); 7.14-7.11 (m, 2H); 4.05 (d, 1H, *J*=12.52 Hz); 3.71 (ddd, 1H, *J*=11.15 Hz and 4.69 Hz); 3.30 (d, 1H, *J*=12.52 Hz); 3.18-3.09 (m, 1H); 2.98-2.91 (m, 1H); 2.33 (s, 3H); 2.32-2.18 (m, 2H); 1.79-1.68 (m, 2H); 1.57-1.48 (m, 1H); 1.29-1.17 (m, 6H); 0.81 (s, 3H, *J*=6.65 Hz). ¹³C NMR (100 MHz, CDCl₃) δ 201.6; 136.8; 133.2; 129.3 (2C); 129.2 (2C); 128.9 (2C); 128.7 (2C); 66.2; 58.4; 53.4; 51.0; 33.4; 32.3; 29.2; 25.8; 22.7; 21.3; 14.2. HRMS Calcd for C₂₄H₃₁NO (M)⁺: 349.2406 Found: 349.2395.

Parallel purification using scavenger resin and IEC

All the reactions described for the MgI₂ promoted synthesis of pyrrolidine derivatives, as well as the same combinations carried out in the presence of Et₂Al-I, were also performed according to a 0.2 mmol scale protocol. In this case, purification was achieved by using PS-Isocyanate scavenger resin (3 eq.) and Isolute SCX columns (eluted with NH₃/MeOH) to afford the isolated compounds with purities stated in Table 1 and Table 2.

Stereochemical assignment *via* NOESY spectroscopy

The relative stereochemistry of the substituents in the 2 and 3 positions was determined by NOESY experiments on both stereoisomers of **4a** (minor and major, see figure below). A NOESY correlation was observed between H-2 and H-3 in the minor isomer. This was not seen with the major isomer. Further, a correlation between the ortho-protons (*p*-fluorophenyl ring) and H-3 in the major isomer was observed. This correlation was not present with the minor isomer.