Highly Enantioselective Friedel-Crafts Alkylations of Indoles with Simple Enones Catalyzed by Zirconium(IV) - Binol Complexes

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SUPPORTING INFORMATION

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General Experimental Methods

General Procedures. Glassware was oven-dried overnight at 120 °C. Reactions were monitored by TLC analysis using Merck Silica Gel 60 F-254 thin layer plates. Flash column chromatography was performed on Merck silica gel 60, 0.040-0.063 mm.

Materials. CH₂Cl₂ was distilled from P₂O₅ and stored on 4 Å molecular sieves. Zirconium *tert*-butoxide was purchased from Fluka. All BINOL-type ligands and all indoles **1** were commercially available and used as purchased without further purification. Enones **2** were prepared according procedures from the literature.¹

Instrumentation. ¹H NMR were run at 300 MHz for ¹H and at 75 MHz for ¹³C NMR in a Bruker Avance 300 spectrometer, and referenced to the solvent as internal standard. Specific optical rotations were measured in a Perkin-Elmer polarimeter using sodium light (D line 589 nm). Chiral GLC analyses were carried out in a Thermo Quest Trace GC 2000 series instrument equipped with a flame ionization detector using nitrogen (1

mL/min) as carrier gas, $T_{\text{injector}} = 220\text{ }^{\circ}\text{C}$, $T_{\text{detector}} = 220\text{ }^{\circ}\text{C}$. Chiral HPLC analyses were performed in an Agilent 1100 series instrument equipped with a refraction index detector using chiral stationary columns from Daicel. Retention times are given in min. Racemic **3** and **5** were prepared using ($\pm$)-BINOL, for comparison.

Typical procedure for the Friedel-Crafts Reaction of Indole derivatives **1 and enones **2**.**

To a solution of ligand **L3** (11.1 mg, 0.025 mmol) in dry CH_2Cl_2 (0.8 mL) at rt under argon was added $\text{Zr}(\text{O}^i\text{Bu})_4$ (10 μL , 0.025 mmol). The mixture was stirred for 1 h and, then, a solution of indole **1** (0.15 mmol) and enone **2** (0.125 mmol) in dry CH_2Cl_2 (0.8 mL) was added via syringe. The reaction mixture was monitorized by TLC until starting material was completely reacted. Water (10 mL) was added and the mixture was extracted with EtOAc ($3 \times 20\text{ mL}$), washed with brine (10 mL) and dried (MgSO_4). Product **3** was obtained pure after column chromatography.

(R)-(+)-3-(1*H*-Indol-3-yl)-1-phenylbutan-1-one (3aa)

Obtained in 87 % yield; enantiomeric excess was determined by HPLC (Chiracel OD-H), hexane:*i*-PrOH 90:10, 1 mL/min, minor enantiomer $t_r = 21.3\text{ min}$, major enantiomer $t_r = 32.1\text{ min}$, to be 97 %; mp 103-105 $^{\circ}\text{C}$ (CH_2Cl_2 -hexane); $[\alpha]_{\text{D}}^{25} = +24.2$ ($c\ 0.4$, CHCl_3); ^1H and ^{13}C NMR data were coincident with those reported in the literature.²

(R)-(-)-3-(1*H*-Indol-3-yl)-1-phenylpentan-1-one (3ab)

Obtained in 87 % yield; enantiomeric excess was determined by HPLC (Chiracel AD-H), hexane:*i*-PrOH 90:10, 1 mL/min, minor enantiomer $t_r = 17.4\text{ min}$, major enantiomer

$t_r = 22.0$ min, to be 94 %; an oil; $[\alpha]_D^{25} = -12.1$ (c 0.5, CHCl_3); MS(EI) 277 (M^+ , 43), 172 (17), 158 (100), 105 (80), 77 (32); HRMS 277.1463, $\text{C}_{19}\text{H}_{19}\text{NO}$ required 277.1467; ^1H NMR (CDCl_3) δ 8.03 (br s, 1H), 7.92 (dd, $J = 7.2, 1.5$ Hz, 2H), 7.70 (d, $J = 7.5$ Hz, 1H), 7.53 (tt, $J = 7.4, 1.5$ Hz, 1H), 7.42 (t, $J = 7.4$ Hz, 2H), 7.34 (d, $J = 7.8$ Hz, 1H), 7.19 (td, $J = 7.5, 1.2$ Hz, 1H), 7.11 (td, $J = 7.5, 1.2$ Hz, 1H), 7.01 (d, $J = 2.1$ Hz, 1H), 3.62 (m, $J = 6.9$ Hz, 1H), 3.43 (dd, $J = 16.2, 5.7$ Hz, 1H), 3.37 (dd, $J = 16.2, 7.5$ Hz, 1H), 1.88 (m, $J = 7.5$ Hz, 2H), 0.89 (t, $J = 7.5$ Hz, 3H); ^{13}C NMR (CDCl_3) δ 199.9 (C), 137.3 (C), 136.5 (C), 132.8 (CH), 128.4 (CH), 128.1 (CH), 126.6 (C), 121.8 (CH), 121.3 (CH), 119.4 (CH), 119.09 (CH), 119.07 (C), 111.2 (CH), 44.8 (CH_2), 34.5 (CH), 28.3 (CH_2), 12.2 (CH_3).

(R)-(-)-3-(1*H*-Indol-3-yl)-1-phenylhexan-1-one (3ac)

Obtained in 82 % yield; enantiomeric excess was determined by HPLC (Chiracel AD-H), hexane:*i*-PrOH 90:10, 1 mL/min, minor enantiomer $t_r = 15.8$ min, major enantiomer $t_r = 19.1$ min, to be 97 %; an oil; $[\alpha]_D^{25} = -15.9$ (c 1.0, CHCl_3); MS(EI) 291 (M^+ , 54), 186 (17), 172 (82.3), 130 (47), 105 (100), 77 (41); HRMS 291.1617, $\text{C}_{20}\text{H}_{21}\text{NO}$ required 291.1623; ^1H NMR (CDCl_3) δ 7.97 (br s, 1H), 7.90 (dd, $J = 7.2, 1.5$ Hz, 2H), 7.69 (d, $J = 7.8$ Hz, 1H), 7.52 (tt, $J = 7.4, 1.5$ Hz, 1H), 7.41 (t, $J = 7.4$ Hz, 2H), 7.34 (d, $J = 7.8$ Hz, 1H), 7.18 (td, $J = 7.5, 1.2$ Hz, 1H), 7.10 (td, $J = 7.5, 1.2$ Hz, 1H), 7.01 (d, $J = 2.7$ Hz, 1H), 3.69 (m, 1H), 3.43 (dd, $J = 16.2, 6.2$ Hz, 1H), 3.34 (dd, $J = 16.2, 7.5$ Hz, 1H), 1.80 (m, 2H), 1.30 (m, $J = 7.5$ Hz, 2H), 0.87 (t, $J = 7.5$ Hz, 3H); ^{13}C NMR (CDCl_3) δ 199.9 (C), 137.3 (C), 136.5 (C), 132.8 (CH), 128.4 (CH), 128.0 (CH), 126.6 (C), 121.8 (CH), 121.2 (CH), 119.5 (C), 119.4 (CH), 119.1 (CH), 111.2 (CH), 42.3 (CH_2), 37.8 (CH_2), 32.6 (CH), 20.8 (CH_2), 14.1 (CH_3).

(S)-(+)-3-(1*H*-Indol-3-yl)-1,3-diphenylpropan-1-one (3ad)

Obtained in 25 % yield; enantiomeric excess was determined by HPLC (Chiracel OD-H), hexane:*i*-PrOH 85:15, 1 mL/min, minor enantiomer $t_r = 18.6$ min, major enantiomer $t_r = 22.4$ min, to be 96 %; mp 148-152 °C (CH₂Cl₂-hexane); $[\alpha]_D^{25} = +25.3$ (*c* 0.3, CHCl₃); MS(EI) 325 (M^+ , 28), 220 (23), 207 (20), 206 (100), 204 (20), 105 (17); HRMS 325.1474, C₂₃H₁₉NO required 325.1467; ¹H NMR (CDCl₃) δ 7.98 (br s, 1H), 7.92 (dd, $J = 7.2, 1.5$ Hz, 2H), 7.53 (tt, $J = 7.2, 1.5$ Hz, 1H), 7.60-7.10 (m, 10H), 7.01 (td, $J = 8.1, 1.0$ Hz, 1H), 6.99 (d, $J = 1.0$ Hz, 1H), 5.07 (t, $J = 7.2$ Hz, 1H), 3.82 (dd, $J = 16.5, 6.9$ Hz, 1H), 3.73 (dd, $J = 16.5, 7.5$ Hz, 1H); ¹³C NMR (CDCl₃) δ 198.5 (C), 144.2 (C), 137.1 (C), 136.6 (C), 133.0 (CH), 128.5 (CH), 128.4 (CH), 128.1 (CH), 127.8 (CH), 126.6 (C), 126.3 (CH), 122.1 (CH), 121.4 (CH), 119.5 (CH), 119.4 (CH), 119.3 (C), 111.1 (CH), 45.2 (CH₂), 38.2 (CH).

(R)-(+)-3-(1*H*-Indol-3-yl)-1-*p*-tolylbutan-1-one (3ae)

Obtained in 91 % yield; enantiomeric excess was determined by HPLC (Chiracel OD-H), hexane:*i*-PrOH 90:10, 1 mL/min, minor enantiomer $t_r = 22.2$ min, major enantiomer $t_r = 43.9$ min, to be 95 %; mp 87-91 °C (CH₂Cl₂-hexane); $[\alpha]_D^{25} = +34.1$ (*c* 1.1, CHCl₃); MS(EI) 277 (M^+ , 61), 158 (32), 144 (100), 119 (18); HRMS 277.1465, C₁₉H₁₉NO required 277.1467; ¹H NMR (CDCl₃) δ 8.01 (br s, 1H), 7.87 (d, $J = 8.4$ Hz, 2H), 7.70 (d, $J = 8.1$ Hz, 1H), 7.36 (d, $J = 7.8$ Hz, 1H), 7.25 (d, $J = 8.1$ Hz, 2H), 7.21 (td, $J = 8.1, 1.2$ Hz, 1H), 7.13 (td, $J = 8.1, 1.2$ Hz, 1H), 7.02 (d, $J = 1.8$ Hz, 1H), 3.83 (m, 1H), 3.46 (dd, $J = 16.2, 4.8$ Hz, 1H), 3.22 (dd, $J = 16.2, 8.9$ Hz, 1H), 2.41 (s, 3H), 1.46 (d, $J = 6.9$

Hz, 3H); ^{13}C NMR (CDCl_3) δ 199.4 (C), 143.7 (C), 136.5 (C), 134.8 (C), 129.2 (CH), 128.2 (CH), 126.3 (C), 122.0 (CH), 121.6 (C), 120.1 (CH), 119.2 (CH), 111.2 (CH), 46.3 (CH_2), 27.2 (CH), 21.6 (CH_3), 20.9 (CH_3).

(R)-(+)-3-(1*H*-Indol-3-yl)-1-*m*-tolylbutan-1-one (3af)

Obtained in 84 % yield; enantiomeric excess was determined by HPLC (Chiracel OD-H), hexane:*i*-PrOH 90:10, 1 mL/min, minor enantiomer t_r = 17.8 min, major enantiomer t_r = 26.6 min, to be 92 %; mp 93-96 °C (CH_2Cl_2 -hexane); $[\alpha]_{\text{D}}^{25}$ = + 25.5 (c 1.0, CHCl_3); MS(EI) 277 (M^+ , 36), 158 (30), 144 (100), 119 (17), 91 (18); HRMS 277.1446, $\text{C}_{19}\text{H}_{19}\text{NO}$ required 277.1467; ^1H NMR (CDCl_3) δ 7.97 (br s, 1H), 7.74 (s, 2H), 7.69 (d, J = 8.1 Hz, 1H), 7.38-7.29 (m, 3H), 7.21 (t, J = 7.2 Hz, 1H), 7.12 (t, J = 7.2 Hz, 1H), 7.03 (s, 1H), 3.81 (m, 1H), 3.47 (dd, J = 16.2, 5.0 Hz, 1H), 3.22 (dd, J = 16.2, 8.8 Hz, 1H), 2.38 (s, 3H), 1.45 (d, J = 6.9 Hz, 3H); ^{13}C NMR (CDCl_3) δ 199.9 (C), 138.3 (C), 137.3 (C), 136.5 (C), 133.6 (CH), 128.7 (CH), 128.4 (CH), 126.3 (C), 125.3 (CH), 122.0 (CH), 121.6 (C), 120.1 (CH), 119.2 (CH), 111.2 (CH), 46.5 (CH_2), 27.1 (CH), 21.3 (CH_3), 20.9 (CH_3).

(R)-(+)-3-(1*H*-Indol-3-yl)-1-*o*-tolylbutan-1-one (3ag)

Obtained in 73 % yield; enantiomeric excess was determined by HPLC (Chiracel OD-H), hexane:*i*-PrOH 90:10, 1 mL/min, minor enantiomer t_r = 17.5 min, major enantiomer t_r = 19.0 min, to be 72 %; an oil; $[\alpha]_{\text{D}}^{25}$ = +12.3 (c 0.8, CHCl_3); MS(EI) 277 (M^+ , 30), 158 (46), 144 (100), 119 (21), 91 (23); HRMS 277.1449, $\text{C}_{19}\text{H}_{19}\text{NO}$ required 277.1467;

^1H NMR (CDCl_3) δ 7.96 (br s, 1H), 7.63 (d, J = 7.8 Hz, 1H), 7.57 (dd, J = 8.4, 1.5 Hz, 1H), 7.36-7.31 (m, 2H), 7.21-7.16 (m, 3H), 7.09 (td, J = 7.5, 1.5 Hz, 1H), 6.98 (d, J = 2.1 Hz, 1H), 3.76 (m, 1H), 3.39 (dd, J = 16.2, 5.1 Hz, 1H), 3.16 (dd, J = 16.2, 8.7 Hz, 1H), 2.40 (s, 3H), 1.43 (d, J = 6.9 Hz, 3H); ^{13}C NMR (CDCl_3) δ 204.2 (C), 138.5 (C), 137.8 (C), 136.5 (C), 131.8 (CH), 131.0 (CH), 128.2 (CH), 126.3 (C), 125.5 (CH), 122.0 (CH), 121.4 (C), 120.2 (CH), 119.22 (CH), 119.18 (CH), 111.2 (CH), 49.6 (CH_2), 27.4 (CH), 21.2 (CH_3), 21.0 (CH_3).

(*R*)-(+)-3-(1*H*-Indol-3-yl)-1-(4-methoxyphenyl)butan-1-one (3ah)

Obtained in 54 % yield; enantiomeric excess was determined by HPLC (Chiracel OD-H), hexane:*i*-PrOH 80:20, 1 mL/min, minor enantiomer t_r = 16.5 min, major enantiomer t_r = 38.0 min, to be 95 %; an oil; $[\alpha]_D^{25}$ = + 36.1 (c 0.4, CHCl_3); MS(EI) 293 (M^+ , 46), 286 (30), 158 (34), 144 (100), 135 (25); HRMS 293.1408, $\text{C}_{19}\text{H}_{19}\text{NO}_2$ required 293.1416; ^1H NMR (CDCl_3) δ 7.96 (br s, 1H), 7.94 (d, J = 9.3 Hz, 2H), 7.69 (d, J = 8.1 Hz, 1H), 7.36 (d, J = 8.1 Hz, 1H), 7.19 (td, J = 7.5, 1.2 Hz, 1H), 7.11 (td, J = 7.5, 0.9 Hz, 1H), 7.03 (d, J = 2.1 Hz, 1H), 6.90 (d, J = 9.3 Hz, 2H), 3.86 (s, 3H), 3.80 (m, 1H), 3.42 (dd, J = 16.2, 4.8 Hz, 1H), 3.18 (dd, J = 16.2, 9.0 Hz, 1H), 1.44 (d, J = 7.2 Hz, 3H); ^{13}C NMR (CDCl_3) δ 198.3 (C), 163.3 (C), 136.5 (C), 130.42 (C), 130.37 (CH), 126.3 (C), 122.0 (CH), 121.7 (C), 120.1 (CH), 119.25 (CH), 119.22 (CH), 113.6 (CH), 111.2 (CH), 55.4 (CH_3), 46.1 (CH_2), 27.3 (CH), 21.0 (CH_3).

(*R*)-(+)-1-(4-Fluorophenyl)-3-(1*H*-indol-3-yl)butan-1-one (3ai)

Obtained in 92 % yield; enantiomeric excess was determined by HPLC (Chiracel OD-H), hexane:*i*-PrOH 80:20, 1 mL/min, minor enantiomer t_r = 11.4 min, major enantiomer

$t_r = 19.0$ min, to be 96 %; mp 86-90 °C (CH₂Cl₂-hexane); $[\alpha]_D^{25} = +24.2$ (c 1.3, CHCl₃); MS(EI) 281 (M^+ , 48), 158 (25), 144 (100), 123 (24); HRMS 281.1212, C₁₈H₁₆FNO required 281.1216; ¹H NMR (CDCl₃) δ 7.99 (br s, 1H), 7.98 (d, $J = 9.0$ Hz, 1H), 7.96 (d, $J = 9.0$ Hz, 1H), 7.68 (d, $J = 8.1$ Hz, 1H), 7.36 (d, $J = 7.8$ Hz, 1H), 7.21 (td, $J = 7.5$, 1.2 Hz, 1H), 7.13 (td, $J = 7.5$, 0.9 Hz, 1H), 7.10 (t, $J = 8.9$ Hz, 1H), 7.02 (s, 1H), 3.82 (m, 1H), 3.45 (dd, $J = 16.2$, 4.8 Hz, 1H), 3.21 (dd, $J = 16.2$, 8.6 Hz, 1H), 1.47 (d, $J = 6.6$ Hz, 3H); ¹³C NMR (CDCl₃) δ 198.1 (C), 165.6 (d, $J_{C-F} = 253$ Hz, C), 136.5 (C), 133.7 (d, $J_{C-F} = 2.9$ Hz, C), 130.7 (d, $J_{C-F} = 9.1$ Hz, CH), 126.2 (C), 122.0 (CH), 121.3 (C), 120.2 (CH), 119.3 (CH), 119.1 (CH), 115.6 (d, $J_{C-F} = 21.7$ Hz, CH), 111.3 (CH), 46.3 (CH₂), 27.2 (CH), 20.9 (CH₃).

(R)-(+)-1-(4-Bromophenyl)-3-(1H-indol-3-yl)butan-1-one (3aj)

Obtained in 95 % yield; enantiomeric excess was determined by HPLC (Chiracel OD-H), hexane:*i*-PrOH 80:20, 1 mL/min, minor enantiomer $t_r = 13.4$ min, major enantiomer $t_r = 24.7$ min, to be 97 %; an oil; $[\alpha]_D^{25} = +35.7$ (c 1.3, CHCl₃); MS(EI) 343 (25), 341 (M^+ , 25), 158 (20), 144 (100); HRMS 341.0388, C₁₈H₁₆BrNO required 341.0415; ¹H NMR (CDCl₃) δ 8.00 (br s, 1H), 7.79 (d, $J = 8.7$ Hz, 2H), 7.67 (d, $J = 7.8$ Hz, 1H), 7.56 (d, $J = 8.7$ Hz, 2H), 7.36 (d, $J = 8.1$ Hz, 1H), 7.23 (td, $J = 7.4$, 1.2 Hz, 1H), 7.13 (td, $J = 7.5$, 1.2 Hz, 1H), 7.0 (d, $J = 2.1$ Hz, 1H), 3.81 (m, 1H), 3.44 (dd, $J = 16.3$, 5.0 Hz, 1H), 3.20 (dd, $J = 16.3$, 8.7 Hz, 1H), 1.46 (d, $J = 6.6$ Hz, 3H); ¹³C NMR (CDCl₃) δ 198.7 (C), 136.5 (C), 135.9 (C), 131.8 (CH), 129.6 (CH), 128.0 (C), 126.2 (C), 122.0 (CH), 121.2 (C), 120.2 (CH), 119.3 (CH), 119.1 (CH), 111.3 (CH), 46.4 (CH₂), 27.2 (CH), 20.9 (CH₃).

(R)-3-(1*H*-Indol-3-yl)-1-(naphthalen-2-yl)butan-1-one (3ak)

Obtained in 89 % yield; enantiomeric excess was determined by HPLC (Chiracel OD-H), hexane:*i*-PrOH 80:20, 1 mL/min, minor enantiomer t_r = 15.0 min, major enantiomer t_r = 19.3 min, to be 98 %; mp 147-149 °C (CH₂Cl₂-hexane); $[\alpha]_D^{25}$ = +71.1 (*c* 0.6, CHCl₃); MS(EI) 313 (M^+ , 38), 158 (31), 144 (100), 127 (20); HRMS 313.1462, C₂₂H₁₉NO required 313.1467; ¹H NMR (CDCl₃) δ 8.43 (s, 1H), 8.05 (dd, *J* = 8.7, 1.8 Hz, 1H), 8.01 (br s, 1H), 7.89-7.86 (m, 3H), 7.75 (d, *J* = 8.1 Hz, 1H), 7.60 (td, *J* = 7.5, 1.2 Hz, 1H), 7.54 (td, *J* = 7.5, 1.5 Hz, 1H), 7.37 (d, *J* = 7.8 Hz, 1H), 7.23 (td, *J* = 7.5, 1.5 Hz, 1H), 7.16 (td, *J* = 7.5, 1.2 Hz, 1H), 7.04 (d, *J* = 1.8 Hz, 1H), 3.91 (m, 1H), 3.64 (dd, *J* = 16.2, 5.1 Hz, 1H), 3.38 (dd, *J* = 16.2, 9.0 Hz, 1H), 1.52 (d, *J* = 6.9 Hz, 3H); ¹³C NMR (CDCl₃) δ 199.8 (C), 136.5 (C), 135.4 (C), 134.6 (C), 132.4 (C), 129.8 (CH), 129.5 (CH), 128.3 (CH), 127.7 (CH), 126.7 (CH), 126.3 (C), 123.9 (CH), 122.0 (CH), 121.4 (C), 120.2 (CH), 119.3 (CH), 119.2 (CH), 111.3 (CH), 46.5 (CH₂), 27.4 (CH), 21.0 (CH₃).

(R)-(+)-3-(1*H*-Indol-3-yl)-1-(thiophen-2-yl)butan-1-one (3al)

Obtained in 87 % yield; enantiomeric excess was determined by HPLC (Chiracel OD-H), hexane:*i*-PrOH 90:10, 1 mL/min, minor enantiomer t_r = 29.8 min, major enantiomer t_r = 54.2 min, to be 96 %; an oil; $[\alpha]_D^{25}$ = +19.5 (*c* 0.9, CHCl₃); MS(EI) 269 (M^+ , 29), 158 (16), 144 (100), 111 (23); HRMS 269.0845, C₁₆H₁₅NOS required 269.0874; ¹H NMR (CDCl₃) δ 8.02 (br s, 1H), 7.70 (d, *J* = 8.1 Hz, 1H), 7.67 (dd, *J* = 3.8, 0.9 Hz, 1H), 7.61 (dd, *J* = 4.9, 0.9 Hz, 1H), 7.36 (d, *J* = 7.8 Hz, 1H), 7.20 (td, *J* = 7.5, 0.9 Hz, 1H), 7.13 (td, *J* = 8.1, 1.2 Hz, 1H), 7.09 (dd, *J* = 4.8, 4.2 Hz, 1H), 7.03 (d, *J* = 2.1 Hz, 1H),

3.84 (m, 1H), 3.41 (dd, $J = 15.6, 5.2$ Hz, 1H), 3.16 (dd, $J = 15.6, 8.7$ Hz, 1H), 1.48 (d, $J = 6.6$ Hz, 3H); ^{13}C NMR (CDCl_3) δ 192.6 (C), 144.8 (C), 136.5 (C), 133.5 (CH), 131.8 (CH), 128.0 (CH), 126.2 (C), 122.0 (CH), 121.2 (C), 120.2 (CH), 119.24 (CH), 119.17 (CH), 111.3 (CH), 47.2 (CH_2), 27.6 (CH), 20.8 (CH_3).

(R)-(+)-3-(5-Methyl-1H-indol-3-yl)-1-phenylbutan-1-one (3ba)

Obtained in 97 % yield; enantiomeric excess was determined by HPLC (Chiracel OD-H), hexane:*i*-PrOH 80:20, 1 mL/min, minor enantiomer $t_r = 8.8$ min, major enantiomer $t_r = 15.7$ min, to be 95 %; mp 99-102 °C (CH_2Cl_2 -hexane); $[\alpha]_{\text{D}}^{25} = +44.8$ (c 1.2, CHCl_3); MS(EI) 277 (M^+ , 36), 172 (22), 158 (100), 105 (16); HRMS 277.1462, $\text{C}_{19}\text{H}_{19}\text{NO}$ required 277.1467; ^1H NMR (CDCl_3) δ 7.97 (dd, $J = 7.2, 1.5$ Hz, 2H), 7.88 (br s, 1H), 7.56 (tt, $J = 7.4, 1.5$ Hz, 1H), 7.48-7.43 (m, 3H), 7.25 (d, $J = 8.4$ Hz, 1H), 7.03 (dd, $J = 8.4, 0.9$ Hz, 1H), 6.99 (d, $J = 2.4$ Hz, 1H), 3.82 (m, 1H), 3.47 (dd, $J = 16.4, 4.7$ Hz, 1H), 3.24 (dd, $J = 16.4, 9.2$ Hz, 1H), 2.47 (s, 3H), 1.45 (d, $J = 6.9$ Hz, 3H); ^{13}C NMR (CDCl_3) δ 199.8 (C), 137.3 (C), 134.8 (C), 132.9 (CH), 128.5 (CH), 128.4 (C), 128.1 (CH), 126.5 (C), 123.6 (CH), 121.0 (C), 120.3 (CH), 118.8 (CH), 110.9 (CH), 46.7 (CH_2), 27.1 (CH), 21.5 (CH_3), 20.9 (CH_3).

(R)-(+)-3-(5-Methoxy-1H-indol-3-yl)-1-phenylbutan-1-one (3ca)

Obtained in 95 % yield; enantiomeric excess was determined by HPLC (Chiracel OD-H), hexane:*i*-PrOH 80:20, 0.5 mL/min, minor enantiomer $t_r = 20.4$ min, major

enantiomer $t_r = 22.1$ min, to be 97 %; an oil; $[\alpha]_D^{25} = +52.1$ (c 1.4, CHCl_3); ^1H and ^{13}C NMR data were coincident with those reported in the literature.²

(R)-(+)-3-(5-Chloro-1H-indol-3-yl)-1-phenylbutan-1-one (3da)

Obtained in 74 % yield; enantiomeric excess was determined by HPLC (Chiracel OD-H), hexane:*i*-PrOH 90:10, 1 mL/min, minor enantiomer $t_r = 16.1$ min, major enantiomer $t_r = 24.4$ min, to be 95 %; mp 134-137 °C (CH_2Cl_2 -hexane); $[\alpha]_D^{25} = +38.6$ (c 0.7, CHCl_3); MS(EI) 297 (M^+ , 17), 192 (22), 180 (31), 178 (100), 143 (30), 105(47), 77 (41); HRMS 297.0913, $\text{C}_{18}\text{H}_{16}\text{ClNO}$ required 297.0920; ^1H NMR (CDCl_3) δ 8.17 (br s, 1H), 7.95 (dd, $J = 7.5, 1.5$ Hz, 2H), 7.63 (d, $J = 1.8$ Hz, 1H), 7.56 (tt, $J = 7.5, 2.1$ Hz, 1H), 7.45 (t, $J = 7.5$ Hz, 2H), 7.23 (d, $J = 9.3$ Hz, 1H), 7.13 (dd, $J = 8.7, 1.8$ Hz, 1H), 7.01 (d, $J = 2.4$ Hz, 1H), 3.78 (m, 1H), 3.43 (dd, $J = 16.4, 5.3$ Hz, 1H), 3.25 (dd, $J = 16.4, 8.4$ Hz, 1H), 1.44 (d, $J = 6.9$ Hz, 3H); ^{13}C NMR (CDCl_3) δ 199.6 (C), 137.0 (C), 134.8 (C), 133.0 (CH), 128.5 (CH), 128.0 (CH), 127.3 (C), 124.8 (C), 122.2 (CH), 121.7 (CH), 121.0 (C), 118.6 (CH), 112.2 (CH), 46.2 (CH_2), 27.0 (CH), 21.1 (CH_3).

Typical procedure for the Friedel-Crafts Reaction of pyrrole 4 and enones 2.

To a solution of ligand **L5** (11.3 mg, 0.025 mmol) in dry CH_2Cl_2 (0.8 mL) at rt under argon was added $\text{Zr}(\text{O}^i\text{Bu})_4$ (10 μL , 0.025 mmol). The mixture was stirred for 1 h and then, a solution of enone **2** (0.125 mmol) in dry CH_2Cl_2 (0.8 mL) followed of pyrrole **4** (87 μL , 1.25 mmol) were added via syringe. The reaction mixture was monitored by TLC until starting material was completely reacted. The usual work up and purification procedure gave product **5**.

(R)-(-)-1-Phenyl-3-(1H-pyrrol-2-yl)butan-1-one (5a)

Obtained in 84 % yield; enantiomeric excess was determined by HPLC (Chiracel AD-H), hexane:*i*-PrOH 90:10, 1 mL/min, minor enantiomer $t_r = 8.3$ min, major enantiomer $t_r = 8.9$ min, to be 83 %; yellow oil; $[\alpha]_D^{25} = -94.4$ (c 0.7, CHCl_3); MS(EI) 213 (M^+ , 36), 108 (89), 105 (30), 94 (100), 77 (37); HRMS 213.1148, $\text{C}_{14}\text{H}_{15}\text{NO}$ required 213.1154; ^1H NMR (CDCl_3) δ 8.70 (br s, 1H), 7.94 (dd, $J = 7.2, 1.2$ Hz, 2H), 7.56 (tt, $J = 7.35, 1.2$ Hz, 1H), 7.45 (t, $J = 7.35$ Hz, 2H), 6.66 (unresolved m, 1H), 6.10 (q, $J = 3.0$ Hz, 1H), 5.96 (unresolved m, 1H), 3.59 (m, 1H), 3.31 (dd, $J = 18.0, 8.0$ Hz, 1H), 3.22 (dd, $J = 18.0, 5.1$ Hz, 1H), 1.42 (d, $J = 7.2$ Hz, 3H); ^{13}C NMR (CDCl_3) δ 200.5 (C), 136.9 (C), 133.3 (CH), 128.6 (CH), 128.0 (CH), 116.4 (CH), 107.6 (CH), 103.1 (CH), 47.4 (CH_2), 27.4 (CH), 20.0 (CH_3).

(R)-(-)-3-(1H-Pyrrol-2-yl)-1-*p*-tolylbutan-1-one (5e)

Obtained in 97 % yield; enantiomeric excess was determined by HPLC (Chiracel AD-H), hexane:*i*-PrOH 90:10, 1 mL/min, minor enantiomer $t_r = 9.8$ min, major enantiomer $t_r = 11.5$ min, to be 96 %; yellow oil; $[\alpha]_D^{25} = -92.2$ (c 1.2, CHCl_3); MS(EI) 227 (M^+ , 66), 119 (29), 108 (100), 94 (85), 91 (25); HRMS 227.1306, $\text{C}_{15}\text{H}_{17}\text{NO}$ required 227.1310; ^1H NMR (CDCl_3) δ 8.73 (br s, 1H), 7.85 (d, $J = 8.1$ Hz, 2H), 7.25 (d, $J = 8.1$ Hz, 2H), 6.66 (unresolved m, 1H), 6.10 (q, $J = 2.7$ Hz, 1H), 5.6 (unresolved m, 1H), 3.57 (m, 1H), 3.28 (dd, $J = 17.7, 7.8$ Hz, 1H), 3.19 (dd, $J = 17.7, 5.1$ Hz, 1H), 2.41 (s, 3H), 1.42 (d, $J = 7.2$ Hz, 3H); ^{13}C NMR (CDCl_3) δ 200.2 (C), 144.1 (C), 137.0 (C), 134.5 (C), 129.2 (CH), 128.1 (CH), 116.4 (CH), 107.5 (CH), 103.0 (CH), 47.2 (CH_2), 27.4 (CH), 21.6 (CH_3), 19.9 (CH_3).

(R)-(-)-1-(4-Methoxyphenyl)-3-(1H-pyrrol-2-yl)butan-1-one (5h)

Obtained in 89 % yield; enantiomeric excess was determined by HPLC (Chiracel AD-H), hexane:*i*-PrOH 90:10, 1 mL/min, minor enantiomer $t_r = 14.5$ min, major enantiomer $t_r = 17.8$ min, to be 99 %; yellow oil; $[\alpha]_D^{25} = -93.9$ (c 1.2, CHCl_3); MS(EI) 243 (M^+ , 42), 135 (32), 108 (100), 94 (82), 77 (13); HRMS 243.1259, $\text{C}_{15}\text{H}_{17}\text{NO}_2$ required 243.1259; ^1H NMR (CDCl_3) δ 8.78 (br s, 1H), 7.93 (d, $J = 9.0$ Hz, 2H), 6.92 (d, $J = 9.0$ Hz, 2H), 6.66 (unresolved m, 1H), 6.10 (q, $J = 2.9$ Hz, 1H), 5.96 (unresolved m, 1H), 3.89 (s, 3H), 3.56 (m, 1H), 3.25 (dd, $J = 18.0, 8.1$ Hz, 1H), 3.17 (dd, $J = 18.0, 5.25$ Hz, 1H), 1.41 (d, $J = 6.9$ Hz, 3H); ^{13}C NMR (CDCl_3) δ 199.1 (C), 163.6 (C), 137.1 (C), 130.3 (CH), 130.0 (C), 116.4 (CH), 113.7 (CH), 107.5 (CH), 103.0 (CH), 55.5 (CH_3), 47.0 (CH_2), 27.4 (CH), 19.9 (CH_3).

(R)-(-)-1-(4-Bromophenyl)-3-(1H-pyrrol-2-yl)butan-1-one (5j)

Obtained in 95 % yield; enantiomeric excess was determined by HPLC (Chiracel AD-H), hexane:*i*-PrOH 90:10, 1 mL/min, minor enantiomer $t_r = 11.1$ min, major enantiomer $t_r = 12.0$ min, to be 65 %; mp 94-98 °C (CH_2Cl_2 -hexane); $[\alpha]_D^{25} = -43.6$ (c 1.4, CHCl_3); MS(EI) 291 (M^+ , 27), 184 (19), 183 (18), 108 (100), 94 (92); HRMS 291.0257, $\text{C}_{14}\text{H}_{14}\text{BrNO}$ required 291.0259; ^1H NMR (CDCl_3) δ 8.63 (br s, 1H), 7.79 (d, $J = 8.4$ Hz, 2H), 7.59 (d, $J = 8.4$ Hz, 2H), 6.66 (unresolved m, 1H), 6.10 (q, $J = 2.8$ Hz, 1H), 5.95 (unresolved m, 1H), 3.57 (m, 1H), 3.27 (dd, $J = 17.7, 8.1$ Hz, 1H), 3.17 (dd, $J = 17.7, 5.1$ Hz, 1H), 1.41 (d, $J = 7.2$ Hz, 3H); ^{13}C NMR (CDCl_3) δ 199.4 (C), 136.6 (C),

135.6 (C), 131.9 (CH), 129.5 (CH), 128.5 (C), 116.5 (CH), 107.7 (CH), 103.2 (CH), 47.3 (CH₂), 27.5 (CH), 20.0 (CH₃).

(R)-(-)-3-(1*H*-Pyrrol-2-yl)-1-(thiophen-2-yl)butan-1-one (5l)

Obtained in 96 % yield; enantiomeric excess was determined by GLC (Supelco β -dex-225), $T_{\text{column}} = 170\text{ }^{\circ}\text{C}$ (70 min) to $200\text{ }^{\circ}\text{C}$ at $3\text{ }^{\circ}\text{C}/\text{min}$), minor enantiomer $t_r = 65.9$ min, major enantiomer $t_r = 67.8$ min, to be 98 %; yellow oil; $[\alpha]_{\text{D}}^{25} = -19.8$ (c 1.0, CHCl₃); MS(EI) 219 (M^+ , 100), 111 (17), 108 (25); HRMS 219.0699, C₁₂H₁₃NOS required 219.0718; ¹H NMR (CDCl₃) δ 8.71 (br s, 1H), 7.69 (dd, $J = 3.9, 0.9$ Hz, 1H), 7.64 (dd, $J = 5.1, 0.9$ Hz, 1H), 7.12 (dd, $J = 5.1, 3.9$ Hz, 1H), 6.67 (unresolved m, 1H), 6.11 (q, $J = 2.8$ Hz, 1H), 5.97 (unresolved m, 1H), 3.56 (m, 1H), 3.22 (dd, $J = 17.4, 7.5$ Hz, 1H), 3.19 (dd, $J = 17.4, 5.5$ Hz, 1H), 1.41 (d, $J = 6.9$ Hz, 3H); ¹³C NMR (CDCl₃) δ 193.3 (C), 144.2 (C), 136.6 (C), 133.9 (CH), 132.1 (CH), 128.2 (CH), 116.5 (CH), 107.6 (CH), 103.2 (CH), 47.8 (CH₂), 27.7 (CH), 19.9 (CH₃).

Assignment of the absolute stereochemistry of compound 5a.

(1) Preparation of (R)-(+)-11 from N-methylpyrrole

The (*R*)-pyrrolyl aldehyde **9** was prepared in 39% yield and 37% ee using **8**-HCl following a modification of the known procedure.³ $[\alpha]_{\text{D}}^{25} = -9.1$ (c 1.0, CHCl₃) for the alcohol resulting after reduction of the aldehyde with NaBH₄. A 2M solution of PhMgBr in THF (0.4 mL, 0.8 mmol) was added dropwise to a solution of compound **9** (78.9 mg, 0.52 mmol) in Et₂O (4 mL) at $0\text{ }^{\circ}\text{C}$. After 3h the reaction was quenched with saturated aqueous NH₄Cl (5 mL) and the mixture extracted with diethyl ether, (3 $\times$ 10 mL) washed with brine (5 mL) and dried over Na₂SO₄. After filtration and removal of the solvent under reduced pressure, column chromatography afforded 92.6 mg of compound **10** as a 56:44 mixture of two diastereomeric alcohols: ¹H NMR (CDCl₃) (major diastereomer, diagnostic signals) δ 4.77 (dd, $J = 5.1, 8.7$ Hz, 1H), 3.50 (s, 3H), 2.91 (m, 1H), 1.86 (dd, $J = 5.1, 8.1$ Hz, 1H); (minor diastereomer, diagnostic signals) δ

4.66 (dd, $J = 5.3, 7.9$ Hz, 1H), 3.50(s, 3H), 3.03 (m, 1H), 1.81 (dd, $J = 5.3, 7.9$ Hz, 1H). The mixture of alcohols **10** (82.6 mg, 0.4 mmol) was dissolved in 8 mL of dry CH_2Cl_2 and activated MnO_2 (139 mg, 1.6 mmol) was added. Two additional portions of MnO_2 (2×140 mg, 2×1.6 mmol) were added after 24 and 30 h, respectively. The mixture was stirred for 24 additional hours. The excess MnO_2 was filtered off through a pad of celite and the solid residue was washed with CH_2Cl_2 . After evaporation of the solvents, chromatography eluting with hexane:EtOAc (9:1) afforded 31.1 mg of (*R*)-**11** (34%) and 54.6 mg of unreacted starting material **10** (59 %).

Compound (*R*)-(+)-**11**: enantiomeric excess was determined by HPLC (Chiracel AD-H), hexane:*i*-PrOH 95:5, 0.3 mL/min, minor enantiomer (*S*) $t_r = 22.6$ min, major enantiomer (*R*) $t_r = 25.1$ min, to be 36%; $[\alpha]_{\text{D}}^{25} = +16.2$ (c 1.1, CHCl_3); MS(EI) 227 (M^+ , 28), 122 (54), 108 (100), 77 (21); HRMS 227.1309, $\text{C}_{15}\text{H}_{17}\text{NO}$ required 227.1310; ^1H NMR (CDCl_3) δ 7.95 (dd, $J = 1.5, 8.7$ Hz, 2H), 7.57 (tt, $J = 1.5, 7.3$ Hz, 1H), 7.46 (t, $J = 7.5$ Hz, 2H), 6.57 (br s, 1H), 6.07 (d, $J = 2.7$ Hz, 1H), 5.95 (d, $J = 3.3$ Hz, 1H), 3.61 (s, 3H), 3.63-3.51 (m, 1H), 3.29 (dd, $J = 5.1, 17.1$ Hz, 1H), 3.18 (dd, $J = 8.7, 17.1$ Hz, 1H), 1.30 (d, $J = 6.9$ Hz, 3H); ^{13}C NMR (CDCl_3) δ 199.0 (C), 137.8 (C), 137.1 (C), 133.1 (CH), 128.6 (CH), 128.0 (CH), 121.2 (CH), 106.6 (CH), 103.6 (CH), 46.0 (CH_2), 35.6 (CH_3), 26.4 (CH), 21.2 (CH_3).

(2) Preparation of (*R*)-(+)-**11** by *N*-Methylation of compound **5a**.

To a solution of compound **5a** (28 mg, 0.13 mmol, 87% ee) and tetrabutylammonium iodide (48 mg, 0.13) in DMF (2 mL) under nitrogen was added NaH (60% suspension in mineral oil, 6.4 mg, 0.16 mmol) followed by MeI (10 μL , 0.16 mmol). After 2h, the reaction mixture was quenched with aqueous NH_4Cl (5 mL) and extracted with diethyl ether (3×10 mL). The usual work up followed by repeated column chromatography (hexane: CH_2Cl_2 , 8:2 to 5:5) afforded 6.2 mg (21 %) of compound (*R*)-(+)-**11** with 87 % ee as determined by chiral HPLC; $[\alpha]_{\text{D}}^{25} = +36.2$ (c 0.4, CHCl_3).

Literature

- (1) Oare, D. A.; Henderson, M. A.; Sanner, M. A.; Heathcock, C. H. *J. Org. Chem.* **1990**, *50*, 132-157.
- (2) Bandini, M.; Fagioli, M.; Garavelli, M.; Melloni, A.; Trigari, V.; Umani-Ronchi, A. *J. Org. Chem.* **2004**, *69*, 7511-7518.
- (3) Paras, N. A.; MacMillan, D. W. C. *J. Am. Chem. Soc.* **2001**, *123*, 4370-4371.

3aa

3aa

3ab

3ab

3ac

S20

3ac

S21

3ad

S23

S24

3ae

3af

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3ag

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3ai

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S34

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S40

3ba

S41

3ca

3ca

3da

S45

5a

S46

5a

S47

5e

5e

5h

S50

5h

S51

5j

S52

5j

5l

S54

5l

11

11

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 Area Percent Report
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Sorted By : Signal
 Multiplier : 1.0000
 Dilution : 1.0000
 Use Multiplier & Dilution Factor with ISTDs

Signal 1: RID1 A, Refractive Index Signal

Peak #	RetTime [min]	Type	Width [min]	Area [nRIU*s]	Height [nRIU]	Area %
1	20.438	MM	0.7279	8.40031e5	1.92330e4	49.2136
2	31.614	MM	1.0657	8.66878e5	1.35578e4	50.7864

Totals : 1.70691e6 3.27908e4

Results obtained with enhanced integrator!

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 *** End of Report ***

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 Area Percent Report
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Sorted By : Signal
 Multiplier : 1.0000
 Dilution : 1.0000
 Use Multiplier & Dilution Factor with ISTDs

Signal 1: RID1 A, Refractive Index Signal

Peak #	RetTime [min]	Type	Width [min]	Area [nRIU*s]	Height [nRIU]	Area %
1	21.358	MM	0.7048	6.54452e4	1547.54358	1.4233
2	32.185	BB	1.2168	4.53268e6	6.03999e4	98.5767

Totals : 4.59812e6 6.19475e4

Results obtained with enhanced integrator!
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 Area Percent Report
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Sorted By : Signal
 Multiplier : 1.0000
 Dilution : 1.0000
 Use Multiplier & Dilution Factor with ISTDs

Signal 1: RID1 A, Refractive Index Signal

Peak #	RetTime [min]	Type	Width [min]	Area [nRIU*s]	Height [nRIU]	Area %
1	16.482	VP	0.4289	1.06882e6	3.68681e4	49.4182
2	21.560	BB	0.5490	1.09398e6	2.98157e4	50.5818

Totals : 2.16280e6 6.66838e4

Results obtained with enhanced integrator!

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 Area Percent Report
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Sorted By : Signal
 Multiplier : 1.0000
 Dilution : 1.0000
 Use Multiplier & Dilution Factor with ISTDs

Signal 1: RID1 A, Refractive Index Signal

Peak #	RetTime [min]	Type	Width [min]	Area [nRIU*s]	Height [nRIU]	Area %
1	17.497	MM	0.3844	7.34853e4	3185.90283	3.0778
2	22.021	BBA	0.6351	2.31413e6	5.25086e4	96.9222

Totals : 2.38761e6 5.56945e4

Results obtained with enhanced integrator!

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 Area Percent Report
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Sorted By : Signal
 Multiplier : 1.0000
 Dilution : 1.0000
 Use Multiplier & Dilution Factor with ISTDs

Signal 1: RID1 A, Refractive Index Signal

Peak #	RetTime [min]	Type	Width [min]	Area [nRIU*s]	Height [nRIU]	Area %
1	15.369	MM	0.4436	1.10768e6	4.16190e4	49.7150
2	19.361	PB	0.4866	1.12039e6	3.53305e4	50.2850

Totals : 2.22807e6 7.69495e4

Results obtained with enhanced integrator!

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 Area Percent Report
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Sorted By : Signal
 Multiplier : 1.0000
 Dilution : 1.0000
 Use Multiplier & Dilution Factor with ISTDs

Signal 1: RID1 A, Refractive Index Signal

Peak #	RetTime [min]	Type	Width [min]	Area [nRIU*s]	Height [nRIU]	Area %
1	15.816	MM	0.3523	5.94896e4	2814.53394	2.3051
2	19.138	MM	0.6284	2.52124e6	6.68737e4	97.6949

Totals : 2.58073e6 6.96883e4

Results obtained with enhanced integrator!

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 *** End of Report ***

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 Area Percent Report
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Sorted By : Signal
 Multiplier : 1.0000
 Dilution : 1.0000
 Use Multiplier & Dilution Factor with ISTDs

Signal 1: RID1 A, Refractive Index Signal

Peak #	RetTime [min]	Type	Width [min]	Area [nRIU*s]	Height [nRIU]	Area %
1	18.531	MM	0.6997	3.03894e5	7238.40137	13.8340
2	22.617	MM	0.9916	1.89283e6	3.18153e4	86.1660

Totals : 2.19672e6 3.90537e4

Results obtained with enhanced integrator!

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 *** End of Report ***

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 Area Percent Report
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Sorted By : Signal
 Multiplier : 1.0000
 Dilution : 1.0000
 Use Multiplier & Dilution Factor with ISTDs

Signal 1: RID1 A, Refractive Index Signal

Peak #	RetTime [min]	Type	Width [min]	Area [nRIU*s]	Height [nRIU]	Area %
1	18.606	MF	0.7657	3.02820e4	659.12073	2.1106
2	22.423	VP	0.8507	1.40446e6	2.61702e4	97.8894

Totals : 1.43474e6 2.68294e4

Results obtained with enhanced integrator!

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 *** End of Report ***

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 Area Percent Report
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Sorted By : Signal
 Multiplier : 1.0000
 Dilution : 1.0000
 Use Multiplier & Dilution Factor with ISTDs

Signal 1: RID1 A, Refractive Index Signal

Peak #	RetTime [min]	Type	Width [min]	Area [nRIU*s]	Height [nRIU]	Area %
1	20.596	MM	0.9025	1.77268e6	3.27352e4	49.5580
2	38.215	MM	1.4775	1.80431e6	2.03534e4	50.4420

Totals : 3.57699e6 5.30885e4

Results obtained with enhanced integrator!

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 Area Percent Report
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Sorted By : Signal
 Multiplier : 1.0000
 Dilution : 1.0000
 Use Multiplier & Dilution Factor with ISTDs

Signal 1: RID1 A, Refractive Index Signal

Peak #	RetTime [min]	Type	Width [min]	Area [nRIU*s]	Height [nRIU]	Area %
1	22.205	MM	0.7227	1.03550e5	2388.16650	2.5835
2	43.873	PB	1.7341	3.90455e6	3.69451e4	97.4165

Totals : 4.00810e6 3.93332e4

Results obtained with enhanced integrator!

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 Area Percent Report
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Sorted By : Signal
 Multiplier : 1.0000
 Dilution : 1.0000
 Use Multiplier & Dilution Factor with ISTDs

Signal 1: RID1 A, Refractive Index Signal

Peak #	RetTime [min]	Type	Width [min]	Area [nRIU*s]	Height [nRIU]	Area %
1	16.124	MM	0.6288	1.41858e6	3.76023e4	49.7706
2	23.939	MM	0.9141	1.43166e6	2.61026e4	50.2294

Totals : 2.85024e6 6.37049e4

Results obtained with enhanced integrator!

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 Area Percent Report
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Sorted By : Signal
 Multiplier : 1.0000
 Dilution : 1.0000
 Use Multiplier & Dilution Factor with ISTDs

Signal 1: RID1 A, Refractive Index Signal

Peak #	RetTime [min]	Type	Width [min]	Area [nRIU*s]	Height [nRIU]	Area %
1	17.775	PP	0.5092	7.63726e4	2347.02905	4.0817
2	26.659	PB	0.9016	1.79473e6	3.07352e4	95.9183

Totals : 1.87110e6 3.30822e4

Results obtained with enhanced integrator!

*** End of Report ***

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                        Area Percent Report
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Sorted By           :      Signal
Multiplier           :      1.0000
Dilution             :      1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: RID1 A, Refractive Index Signal

Peak RetTime Type   Width      Area      Height      Area
#   [min]          [min] [nRIU*s]   [nRIU]         %
----|-----|-----|-----|-----|-----|
  1  17.364 VV      0.5865  4.63106e6  1.24129e5  49.9440
  2  18.970 VB      0.8606  4.64146e6  7.92309e4  50.0560

Totals :                      9.27252e6  2.03360e5

Results obtained with enhanced integrator!
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                        *** End of Report ***

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 Area Percent Report
 =====

Sorted By : Signal
 Multiplier : 1.0000
 Dilution : 1.0000
 Use Multiplier & Dilution Factor with ISTDs

Signal 1: RID1 A, Refractive Index Signal

Peak #	RetTime [min]	Type	Width [min]	Area [nRIU*s]	Height [nRIU]	Area %
1	17.468	BV	0.5142	9.90640e5	2.97168e4	14.2376
2	19.034	VB	0.8718	5.96728e6	9.71970e4	85.7624

Totals : 6.95792e6 1.26914e5

Results obtained with enhanced integrator!

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 *** End of Report ***

S71

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Area Percent Report
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Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: RID1 A, Refractive Index Signal

Peak #	RetTime [min]	Type	Width [min]	Area [nRIU*s]	Height [nRIU]	Area %
1	15.951	VP	0.6381	1.85369e6	4.32655e4	48.4678
2	37.576	PBA	1.5777	1.97089e6	1.99196e4	51.5322

Totals : 3.82458e6 6.31851e4

Results obtained with enhanced integrator!

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 Area Percent Report
 =====

Sorted By : Signal
 Multiplier : 1.0000
 Dilution : 1.0000
 Use Multiplier & Dilution Factor with ISTDs

Signal 1: RID1 A, Refractive Index Signal

Peak #	RetTime [min]	Type	Width [min]	Area [nRIU*s]	Height [nRIU]	Area %
1	16.459	MM	0.5948	1.06269e5	2977.84985	2.3006
2	38.075	BP	1.7236	4.51285e6	3.69327e4	97.6994

Totals : 4.61912e6 3.99105e4

Results obtained with enhanced integrator!

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 Area Percent Report
 =====

Sorted By : Signal
 Multiplier : 1.0000
 Dilution : 1.0000
 Use Multiplier & Dilution Factor with ISTDs

Signal 1: RID1 A, Refractive Index Signal

Peak #	RetTime [min]	Type	Width [min]	Area [nRIU*s]	Height [nRIU]	Area %
1	11.179	MM	0.4520	1.65029e6	6.08454e4	49.9316
2	18.897	PB	0.6711	1.65481e6	3.87447e4	50.0684

Totals : 3.30510e6 9.95901e4

Results obtained with enhanced integrator!

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 *** End of Report ***

=====
 Area Percent Report
 =====

Sorted By : Signal
 Multiplier : 1.0000
 Dilution : 1.0000
 Use Multiplier & Dilution Factor with ISTDs

Signal 1: RID1 A, Refractive Index Signal

Peak #	RetTime [min]	Type	Width [min]	Area [nRIU*s]	Height [nRIU]	Area %
1	11.446	MM	0.3603	7.95492e4	3679.81177	1.7474
2	19.080	PB	0.8084	4.47286e6	9.21211e4	98.2526

Totals : 4.55241e6 9.58009e4

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Area Percent Report
=====

Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: RID1 A, Refractive Index Signal

Peak #	RetTime [min]	Type	Width [min]	Area [nRIU*s]	Height [nRIU]	Area %
1	13.666	MM	0.6322	1.54111e6	4.06264e4	49.8893
2	26.186	MM	1.0705	1.54795e6	2.41001e4	50.1107

Totals : 3.08906e6 6.47265e4

Results obtained with enhanced integrator!

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*** End of Report ***

=====
 Area Percent Report
 =====

Sorted By : Signal
 Multiplier : 1.0000
 Dilution : 1.0000
 Use Multiplier & Dilution Factor with ISTDs

Signal 1: RID1 A, Refractive Index Signal

Peak #	RetTime [min]	Type	Width [min]	Area [nRIU*s]	Height [nRIU]	Area %
1	13.410	MM	0.4264	1.30074e5	5083.88086	1.7166
2	24.746	MM	1.1773	7.44745e6	1.05431e5	98.2834

Totals : 7.57752e6 1.10515e5

Results obtained with enhanced integrator!

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 *** End of Report ***

=====
 Area Percent Report
 =====

Sorted By : Signal
 Multiplier : 1.0000
 Dilution : 1.0000
 Use Multiplier & Dilution Factor with ISTDs

Signal 1: RID1 A, Refractive Index Signal

Peak #	RetTime [min]	Type	Width [min]	Area [nRIU*s]	Height [nRIU]	Area %
1	13.373	PB	0.6550	1.28225e6	2.61108e4	50.6307
2	19.262	PP	0.7605	1.25031e6	2.41125e4	49.3693

Totals : 2.53256e6 5.02233e4

Results obtained with enhanced integrator!

=====
 Area Percent Report
 =====

Sorted By : Signal
 Multiplier : 1.0000
 Dilution : 1.0000
 Use Multiplier & Dilution Factor with ISTDs

Signal 1: RID1 A, Refractive Index Signal

Peak #	RetTime [min]	Type	Width [min]	Area [nRIU*s]	Height [nRIU]	Area %
1	15.026	MM	0.8582	3.04029e4	590.46271	0.9122
2	19.261	MM	0.8792	3.30249e6	6.26071e4	99.0878

Totals : 3.33289e6 6.31976e4

Results obtained with enhanced integrator!

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Area Percent Report
=====

Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: RID1 A, Refractive Index Signal

Peak #	RetTime [min]	Type	Width [min]	Area [nRIU*s]	Height [nRIU]	Area %
1	29.858	MM	1.2449	1.64265e6	2.19916e4	50.5530
2	54.757	MM	2.2239	1.60671e6	1.20412e4	49.4470

Totals : 3.24936e6 3.40328e4

Results obtained with enhanced integrator!
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                        Area Percent Report
=====

Sorted By      :      Signal
Multiplier     :      1.0000
Dilution       :      1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: RID1 A, Refractive Index Signal

Peak RetTime Type Width Area Height Area
# [min] [min] [nRIU*s] [nRIU] %
----|-----|----|-----|-----|-----|
1 29.830 MM 0.8870 7.37518e4 1385.77295 1.7599
2 54.248 MM 2.7588 4.11697e6 2.48717e4 98.2401

Totals : 4.19072e6 2.62575e4

Results obtained with enhanced integrator!
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*** End of Report ***

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=====
Area Percent Report
=====

Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: RID1 A, Refractive Index Signal

Peak #	RetTime [min]	Type	Width [min]	Area [nRIU*s]	Height [nRIU]	Area %
1	8.873	MM	0.3223	4.68880e5	2.42451e4	49.5901
2	14.386	MM	0.5353	4.76632e5	1.48408e4	50.4099

Totals : 9.45512e5 3.90858e4

Results obtained with enhanced integrator!

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=====
 Area Percent Report
 =====

Sorted By : Signal
 Multiplier : 1.0000
 Dilution : 1.0000
 Use Multiplier & Dilution Factor with ISTDs

Signal 1: RID1 A, Refractive Index Signal

Peak #	RetTime [min]	Type	Width [min]	Area [nRIU*s]	Height [nRIU]	Area %
1	8.754	MM	0.2866	1.58513e5	9217.08789	2.5141
2	15.697	MM	0.8469	6.14653e6	1.20964e5	97.4859

Totals : 6.30504e6 1.30181e5

Results obtained with enhanced integrator!

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 *** End of Report ***

=====
 Area Percent Report
 =====

Sorted By : Signal
 Multiplier : 1.0000
 Dilution : 1.0000
 Use Multiplier & Dilution Factor with ISTDs

Signal 1: RID1 A, Refractive Index Signal

Peak #	RetTime [min]	Type	Width [min]	Area [nRIU*s]	Height [nRIU]	Area %
1	20.511	MM	0.6972	3.14088e6	7.50796e4	50.5949
2	23.317	MM	0.8777	3.06701e6	5.82399e4	49.4051

Totals : 6.20789e6 1.33319e5

Results obtained with enhanced integrator!

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 Area Percent Report
 =====

Sorted By : Signal
 Multiplier : 1.0000
 Dilution : 1.0000
 Use Multiplier & Dilution Factor with ISTDs

Signal 1: RID1 A, Refractive Index Signal

Peak #	RetTime [min]	Type	Width [min]	Area [nRIU*s]	Height [nRIU]	Area %
1	20.352	MM	0.5103	1.39841e5	4567.17383	1.5810
2	22.125	MM	1.0113	8.70505e6	1.43468e5	98.4190

Totals : 8.84489e6 1.48036e5

Results obtained with enhanced integrator!

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 Area Percent Report
 =====

Sorted By : Signal
 Multiplier : 1.0000
 Dilution : 1.0000
 Use Multiplier & Dilution Factor with ISTDs

Signal 1: RID1 A, Refractive Index Signal

Peak #	RetTime [min]	Type	Width [min]	Area [nRIU*s]	Height [nRIU]	Area %
1	15.482	MM	0.6113	1.33746e6	3.64630e4	52.0138
2	21.578	MM	0.7926	1.23390e6	2.59466e4	47.9862

Totals : 2.57136e6 6.24096e4

Results obtained with enhanced integrator!

*** End of Report ***

=====
 Area Percent Report
 =====

Sorted By : Signal
 Multiplier : 1.0000
 Dilution : 1.0000
 Use Multiplier & Dilution Factor with ISTDs

Signal 1: RID1 A, Refractive Index Signal

Peak #	RetTime [min]	Type	Width [min]	Area [nRIU*s]	Height [nRIU]	Area %
1	16.106	MM	0.5141	1.28259e5	4158.17383	2.4371
2	24.478	MM	0.9540	5.13450e6	8.96979e4	97.5629

Totals : 5.26276e6 9.38561e4

Results obtained with enhanced integrator!

*** End of Report ***

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 Area Percent Report
 =====

Sorted By : Signal
 Multiplier : 1.0000
 Dilution : 1.0000
 Use Multiplier & Dilution Factor with ISTDs

Signal 1: RID1 A, Refractive Index Signal

Peak #	RetTime [min]	Type	Width [min]	Area [nRIU*s]	Height [nRIU]	Area %
1	8.307	MF	0.1796	5.35177e5	4.96743e4	49.9977
2	8.896	FM	0.1904	5.35227e5	4.68478e4	50.0023

Totals : 1.07040e6 9.65220e4

Results obtained with enhanced integrator!

*** End of Report ***

=====
 Area Percent Report
 =====

Sorted By : Signal
 Multiplier : 1.0000
 Dilution : 1.0000
 Use Multiplier & Dilution Factor with ISTDs

Signal 1: RID1 A, Refractive Index Signal

Peak #	RetTime [min]	Type	Width [min]	Area [nRIU*s]	Height [nRIU]	Area %
1	8.325	MM	0.1724	1.36943e5	1.32399e4	8.8385
2	8.908	MM	0.1927	1.41245e6	1.22178e5	91.1615

Totals : 1.54939e6 1.35418e5

Results obtained with enhanced integrator!

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 *** End of Report ***

=====
 Area Percent Report
 =====

Sorted By : Signal
 Multiplier : 1.0000
 Dilution : 1.0000
 Use Multiplier & Dilution Factor with ISTDs

Signal 1: RID1 A, Refractive Index Signal

Peak #	RetTime [min]	Type	Width [min]	Area [nRIU*s]	Height [nRIU]	Area %
1	9.733	MM	0.2446	1.61811e6	1.10265e5	49.8132
2	11.476	BB	0.2720	1.63025e6	8.99312e4	50.1868

Totals : 3.24836e6 2.00196e5

Results obtained with enhanced integrator!

=====
 Area Percent Report
 =====

Sorted By : Signal
 Multiplier : 1.0000
 Dilution : 1.0000
 Use Multiplier & Dilution Factor with ISTDs

Signal 1: RID1 A, Refractive Index Signal

Peak #	RetTime [min]	Type	Width [min]	Area [nRIU*s]	Height [nRIU]	Area %
1	9.752	BB	0.1897	1.23526e4	1013.49548	1.8334
2	11.520	BB	0.2388	6.61395e5	4.22582e4	98.1666

Totals : 6.73747e5 4.32717e4

Results obtained with enhanced integrator!

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 Area Percent Report
 =====

Sorted By : Signal
 Multiplier : 1.0000
 Dilution : 1.0000
 Use Multiplier & Dilution Factor with ISTDs

Signal 1: RID1 A, Refractive Index Signal

Peak #	RetTime [min]	Type	Width [min]	Area [nRIU*s]	Height [nRIU]	Area %
1	14.324	BB	0.2840	7.83451e5	4.25463e4	51.5096
2	17.670	BB	0.3498	7.37528e5	3.32099e4	48.4904

Totals : 1.52098e6 7.57561e4

Results obtained with enhanced integrator!

=====
 Area Percent Report
 =====

Sorted By : Signal
 Multiplier : 1.0000
 Dilution : 1.0000
 Use Multiplier & Dilution Factor with ISTDs

Signal 1: RID1 A, Refractive Index Signal

Peak #	RetTime [min]	Type	Width [min]	Area [nRIU*s]	Height [nRIU]	Area %
1	14.537	MM	0.2877	7518.21582	435.48892	0.5149
2	17.845	MM	0.3876	1.45259e6	6.24677e4	99.4851

Totals : 1.46010e6 6.29032e4

Results obtained with enhanced integrator!

=====
 Area Percent Report
 =====

Sorted By : Signal
 Multiplier : 1.0000
 Dilution : 1.0000
 Use Multiplier & Dilution Factor with ISTDs

Signal 1: RID1 A, Refractive Index Signal

Peak #	RetTime [min]	Type	Width [min]	Area [nRIU*s]	Height [nRIU]	Area %
1	11.001	MM	0.2482	1.03441e6	6.94518e4	50.0629
2	12.053	MM	0.2819	1.03181e6	6.09973e4	49.9371

Totals : 2.06621e6 1.30449e5

Results obtained with enhanced integrator!

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 *** End of Report ***

=====
 Area Percent Report
 =====

Sorted By : Signal
 Multiplier : 1.0000
 Dilution : 1.0000
 Use Multiplier & Dilution Factor with ISTDs

Signal 1: RID1 A, Refractive Index Signal

Peak #	RetTime [min]	Type	Width [min]	Area [nRIU*s]	Height [nRIU]	Area %
1	11.074	MM	0.2332	3.71369e5	2.65434e4	17.3034
2	12.015	VP	0.2723	1.77485e6	9.77619e4	82.6966

Totals : 2.14621e6 1.24305e5

Results obtained with enhanced integrator!

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 *** End of Report ***

Peak	Time (min)	Area (uV*sec)	Hight (uV)
1	65.948	598838	1744
2	67.855	607530	1739

Peak	Time (min)	Area (uV*sec)	Hight (uV)
1	65.853	16854	61
2	67.840	1893260	5317

Pruebas - Vial 1 Inj 1 CVFCP-58(adh - Best Chrom

Current Data Path: C:\WIN32APP\HSM\Carlos\DATA\CVFCP-58(adh,95,0.3

Data Desc.: DAD Extracted Best Chromatogram

Vial Number: 1 Inj Number: 1 Sample Name: CVFCP-58(adh,95.5,0.3)

No.	RT	Area	Area %
1	22.65	9907270	51.290
2	25.08	9409040	48.710
		19316310	100.000

Peak rejection level: 0

Pruebas - Vial 1 Inj 1 CVFCP-63 PUR - Best Chrom

Current Data Path: C:\WIN32APP\HSM\Carlos\DATA\CVFCP-59(adh, 95,0.3)

Data Desc.: DAD Extracted Best Chromatogram

Vial Number: 1 Inj Number: 1 Sample Name: CVFCP-63 PURIFb(adh,95 5,0.3)

No.	RT	Area	Area %
1	22.63	4296080	31.965
2	25.17	9143910	68.035
		13439990	100.000

Peak rejection level: 0

Pruebas - Vial 1 Inj 1 CVFCP-64A(ad - Best Chrom

Current Data Path: C:\WIN32APP\HSM\Carlos\DATA\CVFCP-64(ADH,95, 0.3
 Data Desc.: DAD Extracted Best Chromatogram
 Vial Number: 1 Inj Number: 1 Sample Name: CVFCP-64A(adh,95 5,0.3)

No.	RT	Area	Area %
1	21.79	1089560	6.539
2	24.47	15574140	93.461
		16663700	100.000

Peak rejection level: 0