Synthesis of Indoles with Amine Side Chains via Tandem Hydroformylation / Fischer Indole Synthesis

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Supporting Information

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Material. Triphenyl phosphite was purchased. Cinnamyl carbonat¹, [Ir(cod)Cl]₂², TPPTS³, 9,9-dimethyl-4,5-bis(diphenylphosphino)-9H-xanthene-2,7-disulfonic acid⁴, *O,O'-(R)-(1,1'-dinaphthyl-2,2'-diyl)-N,N'-di-(R,R)-1-phenylethylphosphoramidite*⁵ and *O,O'-(S)-(1,1'-dinaphthyl-2,2'-diyl)-N,N'-di-(S,S)-1-phenylethylphosphoramidite*⁵ were synthesized according to published procedures. **General Methods.** ¹H-NMR and ¹³C-NMR spectra were measured using CHCl₃ or CH₂Cl₂ as internal standard. All samples were dissolved in CDCl₃. The workup is mentioned, if it varies from the workup in the general procedure.

1-Allyl-piperidine (5b). NaH (8.8 g, 220 mmol) was suspended in dry THF (200 ml). Dry piperidine (17 g, 200 mmol) was added dropwise followed by allylic bromide (26.6 g, 220 mmol). The mixture was stirred over night and was then quenched with water. The product was extracted with EtOAc and the combined organic layer were was dried over

¹ Wuts, P.G.M.; Ashford, S.W.; Anderson, A.M.; Atkins, J.R.; *Org. Lett.*, **2003**, 5, 9, 1483-1485.

² Herde, J.L.; Lambert, J.C.; Senoff, C.V.; *Inorg. Synth.*, **1974**, 15, 18.

³ Herrmann, W.A.; Kulpe, J.A.; Konkol, W.; Bahrmann, H.; *J. Organom. Chem.*; **1990**, 389, 1, 85-101.

⁴ Mul, W.P.; Ramkisoensing, K.; Kramer, P.C.J.; Reek, J.N.H.; Linden, A.J. van der; Marson, A.; Leeuwen, P.W.N.M. van; *Adv. Synth. Catal.*; 344; 3-4; **2002**; 293 - 298.

⁵ Alexakis, A.; Rosset, S.; Allamand, J.; March, S.; Guillen, F.; Benhaim, C.; *Synlett*, **2001**, 1375.

MgSO₄. After evaporation of the solvent the crude product was distilled (bp: 85 °C, 100 mbar) to give 1-allyl-piperidine (23.5 g, 94 %). NMR data fits with literature⁶.

1-Allyl-4-phenyl-piperazine (5c). NaH (4.4 g, 110 mmol) was suspended in dry THF (150 ml). Phenyl-piperidine (16 g, 100 mmol) was added dropwise followed by allylic bromide (13.2 g, 110 mmol). The mixture was stirred over night and was then quenched with water. The product was extracted with EtOAc and the combined organic layer were was dried over MgSO₄. After evaporation of the solvent the crude product was distilled to give 1-allyl-4-phenyl-piperazine (15.2 g, 94 %). NMR data fits with literature⁷.

4-Allyl-piperazine-1-carboxylic acid ethyl ester (5d). NaH (5.5 g, 139 mmol) was suspended in dry THF (200 ml). Piperazine-1-carboxylic acid ethyl ester (20 g, 126 mmol) was added dropwise followed by allylic bromide (16.8 g, 139 mmol). The mixture was stirred over night and was then quenched with water. The product was extracted with EtOAc and the combined organic layer were dried over MgSO₄. After evaporation of solvent the crude product was distilled to give 4-allyl-piperazine-1-carboxylic acid ethyl ester (20.2 g, 81 %). ¹H-NMR: (CDCl₃, 500 MHz) δ = 1.07 (t, 3H, J = 7.2 Hz, CH₃); 2.21 (s, 4H, 2xCH₂); 2.81 (d, 2H, J = 6.7 Hz, CH₂); 3.30 (s, 4H, 2xCH₂); 3.94 (q, 2H, J = 7.2 Hz, CH₂); 4.99 (dd, 2H, J = 10.7 Hz, J = 17.5 Hz, CH₂); 5.65 (ddt, 1H, J = 6.7 Hz, J = 10.7 Hz, J = 17.5 Hz, CH). ¹³C-NMR: (CDCl₃, 125 MHz) δ = 14.3 (CH₃); 43.3 (CH₂); 52.3 (2xCH₂); 60.8 (2xCH₂); 61.4 (CH₂); 117.9 (CH₂); 134.3 (CH); 155.0 (C). IR: $\tilde{\nu}$ [cm⁻¹] = 2979 (vs), 2798 (s), 1705 (vs), 1458 (vs). HRMS found M⁺ 198.1354, C₁₀H₁₈N₂O₂ requires M⁺, 198.1368.

General procedure for the homoallylation of amines. 1-(But-3-enyl)piperidine (5e). In a typical procedure piperidine (2.45 g, 28.7 mmol), 4-bromobut-1-ene (4.67 g, 34.5 mmol), 18-crown[6] (0.38 g, 5 mol%) and K₂CO₃ (5.97 g, 43.1 mmol) were suspended in dry CH₃CN (30 ml). After stirring for 12h under reflux the mixture was filtered through a pad of alumina. The solvent was removed to give 1-(but-3-enyl)piperidine (3.01 g, 76 %) without further purification. NMR data fits with literature⁸.

Ethyl 4-(but-3-enyl)piperazine-1-carboxylate (5f). The general procedure was followed with piperazine-1-carboxylic acid ethyl ester (3.74 g, 23.6 mmol), , 4-bromobut-1-ene (3.82 g, 28.3 mmol), 18-crown[6] (0.31 g, 5 mol%) and K₂CO₃ (4.85 g, 35.3 mmol) to give ethyl 4-(but-3-enyl)piperazine-1-carboxylate (4.0 g, 80 %) without further purification. ¹H-

⁶ Takahashi, K.; *Bull. Chem. Soc. Jpn.*; 45; **1972**; 230-236.

⁷ Bell, L.; Brookings, D.C.; Dawson, G.J.; Whitby, R.J.; *Tetrahedron*; 54; 48; **1998**; 14617-14634.

⁸ Kafka, S.; Ferles, M.; *Collect. Czech. Chem. Commun.*; 49; 1; **1984**; 78-85.

NMR: (CDCl₃, 500 MHz) δ = 1.16 (t, 3H, J = 7.2 Hz, CH₃); 2.14-2.18 (2H, CH₂); 2.32-2.35 (6H, 3xCH₂); 3.39 (bs, 4H, 2xCH₂); 4.04 (q, 2H, J = 7.2 Hz, CH₂); 4.91 (d, 1H, J = 10.2 Hz, CHH); 4.97 (d, 1H, J = 17.2 Hz, CHH); 5.71 (ddt, 1H, J = 6.7 Hz, J = 10.2 Hz, J = 17.2 Hz, CH). ¹³C-NMR: (CDCl₃, 125 MHz) δ = 14.5 (CH₃); 31.1 (CH₂); 43.4 (2xCH₂); 52.6 (2xCH₂); 57.8 (CH₂); 61.1 (CH₂); 115.6 (CH₂); 136.2 (CH); 155.3 (C). IR: $\tilde{\nu}$ [cm⁻¹] = 2937 (s); 2807 (s); 1704 (vs); 1428 (vs); 1378 (s); 1288 (vs); 1241 (vs); 1132 (vs); 997 (vs). HRMS found M⁺ 212.1537, C₁₁H₂₀N₂O₂ requires M⁺, 212.1524.

***N,N*-Diethyl-1-phenylprop-2-en-1-amine (5g).** NaH (431 mg, 10.7 mmol) was suspended in dry Et₂O (60 ml). A solution of cinnamyl alcohol (14.5 g, 107 mmol) in dry Et₂O (20 ml) was added dropwise followed by 2,2,2 trichloroacetonitrile (15.6 g, 107 mmol) at -10°C. The solvent was removed and the residue was taken up in MeOH/pentane (200 ml, 0.25wt% MeOH in pentane). The mixture was filtered through a pad of alumina and the solvent was removed to give cinnamyl 2,2,2-trichloroacetimidate (30.0 g, 100 %), which was used for the next step without purification. Cinnamyl 2,2,2-trichloroacetimidate (30.0 g, 107 mmol) in xylene (500 ml) was stirred over night under reflux. The solvent was removed to give 2,2,2-trichloro-*N*-(1-phenylallyl)acetamide (30.0 g, 100 %) without the need for purification. 2,2,2-Trichloro-*N*-(1-phenylallyl)acetamide (30.0 g, 107 mmol) in EtOH (100 ml) and NaOH solution (6M, 150 ml) was stirred for 40h at ambient temperature. The mixture was extracted with Et₂O. The solvent was removed and the residue was taken up in HCl-saturated Et₂O (100 ml). Filtration gave 1-phenylprop-2-en-1-amine hydrochloride (11.6 g, 64 %), which was not purified for the next step. 1-Phenylprop-2-en-1-amine hydrochloride (1.02 g, 6.0 mmol), bromoethane (6.44 g, 60 mmol), 18-crown[6] (85 mg, 5 mol%) and K₂CO₃ (2.08 g, 15 mmol) in dry CH₃CN (30 ml) were stirred for 12h under reflux. The mixture was filtered through a pad of alumina and the solvent was removed to give *N,N*-diethyl-1-phenylprop-2-en-1-amine (1.0 g, 89 %) without further purification. ¹H-NMR: (CDCl₃, 500 MHz) δ = 1.00 (t, 6H, J = 7.1 Hz, 2xCH₃); 2.54-2.63 (4H, 2xCH₂); 4.15 (d, 1H, J = 8.7 Hz, CH); 5.15 (d, 1H, J = 10.2 Hz, CHH); 5.20 (d, 1H, J = 17.2 Hz, CHH); 5.97 (ddt, 1H, J = 8.0 Hz, J = 10.2 Hz, J = 17.2 Hz, CH); 7.25 (d, 1H, J = 7.2 Hz, CH); 7.32 (dd, 2H, J = 7.2 Hz, J = 7.5 Hz, 2xCH); 7.40 (d, 2H, J = 7.4 Hz, 2xCH). ¹³C-NMR: (CDCl₃, 125 MHz) δ = 11.6 (2xCH₃); 42.9 (2xCH₂); 69.4 (CH); 116.0 (CH₂); 126.7 (CH); 127.8 (2xCH); 128.2 (2xCH); 139.5 (CH); 143.1 (C). IR: $\tilde{\nu}$ [cm⁻¹] = 2969 (s); 2871 (m); 2815 (m); 1450 (s); 1382 (m); 1110 (s); 997 (m); 919 (s); 755 (m); 732 (s); 700 (s).

***rac*-1-(1-Phenylallyl)piperidine (*rac*-5h).** Cinnamyl ethyl carbonate (2.56 g, 12.4 mmol), piperidine (7.68 g, 37.3 mmol), [Ir(cod)Cl]₂ (167 mg, 2 mol%) and triphenyl phosphite (290 mg, 8 mol%) in dry EtOH (25 ml) were stirred for 2h under reflux. The solvent was evaporated and the residue was chromatographed (silica, 2.5 vol% EtOAc in cyclohexane) to give *rac*-1-(1-phenylallyl)piperidine (2.02 g, 81 %). NMR data fits with literature⁹.

(-)-1-(1-Phenylallyl)piperidine ((-)-5h). Cinnamyl ethyl carbonate (2.56 g, 12.4 mmol), piperidine (7.68 g, 37.3 mmol), [Ir(cod)Cl]₂ (167 mg, 2 mol%) and *O,O'*-(*R*)-(1,1'-dinaphthyl-2,2'-diyl)-*N,N'*-di-(*R,R*)-1-phenylethylphosphoramidite (134 mg, 2 mol%) in dry THF (12 ml) were stirred over night at ambient temperature. The solvent was evaporated and the residue was chromatographed (silica, 2.5 vol% EtOAc in cyclohexane) to give (-)-1-(1-phenylallyl)piperidine (2.38 g, 95 %, 96 %*ee*¹⁰). NMR data fits with literature⁹.

(+)-1-(1-Phenylallyl)piperidine ((-)-5h). Cinnamyl ethyl carbonate (2.56 g, 12.4 mmol), piperidine (7.68 g, 37.3 mmol), [Ir(cod)Cl]₂ (167 mg, 2 mol%) and *O,O'*-(*S*)-(1,1'-dinaphthyl-2,2'-diyl)-*N,N'*-di-(*S,S*)-1-phenylethylphosphoramidite (134 mg, 2 mol%) in dry THF (12 ml) were stirred over night at ambient temperature. The solvent was evaporated and the residue was chromatographed (silica, 2.5 vol% EtOAc in cyclohexane) to give (+)-1-(1-phenylallyl)piperidine (2.38 g, 95 %, 96 %*ee*¹⁰). NMR data fits with literature⁹.

1-(3-Phenylbut-3-enyl)piperidine (5i). Acetophenone (27.6 g, 230 mmol), piperidine (19.6 g, 230 mmol) and paraformaldehyde (35.2 g, 391 mmol) in dry ethanol (50 ml) were stirred for 1h under reflux. Hydrochloric acid (0.5 ml) was added and the mixture was filtered. The filtrate was concentrated and the product was collected by filtration. The crude product was recrystallized from EtOH to give 1-phenyl-3-(piperidin-1-yl)propan-1-one (15.9 g, 32 %). Methyl triphenyl phosphonium bromide (28.6 g, 80.2 mmol) was suspended in dry THF (300 ml). At 0°C *n*-butyllithium solution (2.5M in hexane, 32 ml) was added and the mixture was stirred for 1h at ambient temperature. 1-Phenyl-3-(piperidin-1-yl)propan-1-one (15.8 g, 72.9 mmol) was added and the mixture was stirred for an additional hour. The solvent was evaporated and the crude product was distilled (75°C, 2·10⁻² mbar) to give 1-(3-phenylbut-3-enyl)piperidine (8.61 g, 55 %). ¹H-NMR: (CDCl₃, 400 MHz) δ = 1.41 (bs, 2H, CH₂); 1.55-1.60 (4H, 2xCH₂); 2.40-2.44 (6H, 3xCH₂); 2.71 (dd, 2H, *J* = 8.0 Hz, *J* = 8.0 Hz, CH₂); 5.07 (s, 1H, *CHH*); 5.29 (s, 1H, *CHH*); 7.24 (dd, 1H, *J* = 7.2 Hz, *J* = 7.2 Hz, CH); 7.30 (dd, 2H, *J* = 7.2 Hz, *J* = 7.7 Hz, 2xCH); 7.40 (d, 2H, *J* = 7.7 Hz, 2xCH). ¹³C-NMR: (CDCl₃, 100 MHz) δ = 24.4 (CH₂); 26.0 (2xCH₂); 32.9 (CH₂); 54.6 (2xCH₂); 58.7 (CH₂); 112.9 (CH₂); 126.0

⁹ Ohmura, T.; Hartwig, J.F.; *J. Am. Chem. Soc.*; **2002**, *124*, 15164-15165.

¹⁰ Determined by HPLC with a Daicel Chiracel OJ

(2xCH); 127.3 (CH); 128.2 (2xCH); 141.0 (C); 146.8 (C). IR: $\tilde{\nu}$ [cm⁻¹] = 2933 (vs); 2852 (s); 2798 (s); 1442 (s); 1155 (s); 1122 (s); 892 (s); 775 (s); 703 (s); 412 (vs); 404 (vs). HRMS found [M+H]⁺ 216.1776, C₁₅H₂₁N₂ requires [M+H]⁺, 216.1752. Elementary analysis found C 83.13%, H 9.88%, N 6.20%, C₁₅H₂₁N₂ requires C 83.67%, H 9.83%, N 6.50%.

***N,N*-Diethyl-3-methyl-1-phenylbut-3-en-1-amine (5j).** A solution of benzaldehyde (79.7 g, 750 mmol) in Et₂O (250 ml) was added to a solution of EtNH₂ (33.8 g, 750 mmol) in Et₂O (250 ml) at 0°C. MgSO₄ (50 g) was added and the mixture was stirred for 1h at ambient temperature followed by filtration. The solvent was removed and the residue was distilled (86°C, 10 mbar) to give *N*-benzylideneethanamine (78.8 g, 79 %). At 0°C a solution of methallylic chloride (10.8 g, 119 mmol) and *N*-benzylideneethanamine (10.6 g, 79 mmol) in dry THF (50 ml) was added to a suspension of zinc dust (10.4 g, 158 mmol) in dry THF (100 ml). The mixture was stirred for 4h at ambient temperature and was then filtered through a sintered glass filter. Saturated ammonium hydrochloride solution was added to the filtrate and the pH was adjusted to 10 with sodium hydroxide solution. The mixture was extracted with EtOAc and the solvent was removed to give *N*-ethyl-3-methyl-1-phenylbut-3-en-1-amine (15.0 g, 100 %). A suspension of *N*-ethyl-3-methyl-1-phenylbut-3-en-1-amine (4.4 g, 23 mmol), ethylbromide (3.8 g, 35 mmol) and K₂CO₃ (4.8 g, 35 mmol) in dry CH₃CN (25 ml) was stirred for 12h under reflux. The mixture was filtered through a pad of alumina. The solvent was removed and the residue was chromatographed (silica, EtOAc, cyclohexane, NEt₃) to give *N,N*-diethyl-3-methyl-1-phenylbut-3-en-1-amine (3.84 g, 77 %). ¹H-NMR: (CDCl₃, 400 MHz) δ = 1.06 (t, 6H, *J* = 7.1 Hz, 2xCH₃); 1.70 (s, 3H, CH₃); 2.33-2.73 (6H, 3xCH₂); 3.94 (dd, 1H, *J* = 5.8 Hz, *J* = 5.8 Hz, CH); 4.63 (s, 1H, CHH); 4.71 (s, 1H, CHH); 7.24-7.34 (5H, 5xCH). ¹³C-NMR: (CDCl₃, 100 MHz) δ = 13.0 (2xCH₃); 22.5 (CH₃); 40.5 (CH₂); 43.0 (2xCH₂); 62.2 (CH); 112.3 (CH₂); 126.6 (CH); 127.6 (2xCH); 128.5 (2xCH); 140.8 (C); 143.3 (C). IR: $\tilde{\nu}$ [cm⁻¹] = 3025 (m); 2967 (vs); 2813 (s); 1646 (m); 1492 (m); 1373 (s); 1295 (m); 1201 (m); 1029 (m); 887 (s); 700 (vs) Elementary analysis found C 82.20%, H 10.68%, N 6.10%, C₁₅H₂₃N requires C 82.89%, H 10.67%, N 6.44%.

***N,N*-Diethyl-1-phenylbut-3-en-1-amine (5k).** A solution of benzaldehyde (79.7 g, 750 mmol) in Et₂O (250 ml) was added to a solution of ethylamine (33.8 g, 750 mmol) in Et₂O (250 ml) at 0°C. MgSO₄ (50 g) was added and the mixture was stirred for 1h at ambient temperature. The mixture was filtered, the solvent was removed and the residue was distilled (86°C, 10 mbar) to give *N*-Benzylideneethanamine (78.8 g, 79 %). At 0°C a solution of allylic bromide (15.5 g, 128 mmol) and *N*-benzylideneethanamine (11.4 g, 85.6 mmol) in dry THF (50 ml) is added to a suspension of zinc dust (10.4 g, 158 mmol) in dry THF (100 ml). The

mixture was stirred for 4h at ambient temperature and was then filtered through a sintered glass filter. Saturated NH_4Cl solution was added to the filtrate and the pH was adjusted to 10 with NaOH. The mixture was extracted with EtOAc and the solvent was removed to give *N*-ethyl-1-phenylbut-3-en-1-amine (15.0 g, 100 %) without further purification. A suspension of *N*-ethyl-1-phenylbut-3-en-1-amine (5.0 g, 29 mmol), ethylbromide (4.6 g, 43 mmol) and K_2CO_3 (5.9 g, 43 mmol) in dry CH_3CN (25 ml) was stirred for 12h under reflux. The mixture was filtered through a pad of alumina and the solvent was removed to give *N,N*-diethyl-1-phenylbut-3-en-1-amine (4.38 g, 76 %) without further purification. ^1H -NMR: (CDCl_3 , 400 MHz) δ = 1.02 (t, 6H, J = 7.1 Hz, 2x CH_3); 2.37-2.70 (6H, 3x CH_2); 3.72 (dd, 1H, J = 5.7 Hz, J = 5.7 Hz, CH); 4.92 (d, 1H, J = 10.3 Hz, CHH); 4.99 (d, 1H, J = 17.1 Hz, CHH); 5.66 (ddt, 1H, J = 7.0 Hz, J = 10.3 Hz, J = 17.1 Hz, CH); 7.22-7.32 (5H, 5xCH). ^{13}C -NMR: (CDCl_3 , 100 MHz) δ = 12.5 (2x CH_3); 37.0 (CH_2); 42.9 (2x CH_2); 64.3 (CH); 115.9 (CH_2); 126.6 (CH); 127.8 (2xCH); 128.5 (2xCH); 126.4 (CH); 141.2 (C). IR: $\tilde{\nu}$ [cm^{-1}] = 2969 (s); 2813 (m); 1639 (w); 1452 (m); 1382 (m); 1199 (m); 995 (w); 765 (w). Elementary analysis found C 82.53%, H 10.87%, N 6.84%, $\text{C}_{14}\text{H}_{21}\text{N}$ requires C 82.70%, H 10.41%, N 6.89%.

1-Methyl-4-methylene-piperidine (5l). NaH (11.9 g, 297 mmol) is suspended in dry DMSO (100 ml) and is stirred for 45 min at 75 °C. The solution is cooled to 0°C. To this mixture a solution of methyl-triphenyl-phosphonium bromide (106 g, 297 mmol) in dry DMSO (200 ml) is added and is stirred for 10min at ambient temperature. 1-Methyl-piperidin-4-one (30.5 g, 270 mmol) was added and the mixture was stirred for 30 min at ambient temperature. The product was distilled directly from the reaction mixture (bp: 75 °C/100 mbar) to obtain 1-methyl-4-methylene-piperidine (25.3 g, 84%). NMR data fits with literature¹¹.

1-But-3-enyl-4-[2-(3-fluoro-phenyl)-ethyl]-piperazine (5m). (3-Fluoro-phenyl)-acetic acid (10.0 g, 64.9 mmol) in dry THF (150 ml) was dropped to a suspension of LiAlH_4 (4.92 g, 130 mmol) in dry THF (150 ml) at 0°C. The mixture was stirred for 3h under reflux. At 0°C KOH (2.28 g) in water (9 ml) was added dropwise. The resulting suspension was stirred for 15min under reflux. The precipitate was filtered off, washed with THF (50 ml) and dried over MgSO_4 . The solvent was removed to give 2-(3-fluoro-phenyl)-ethanol (8.97 g, 99 %) without further purification. At 0°C Br_2 (13.9 g, 86.9 mmol) was added dropwise to a solution of triphenyl-phosphane (22.8 g, 86.9 mmol) and imidazole (5.91 g, 86.9 mmol) in dry CH_2Cl_2 (60 ml) followed by 2-(3-fluoro-phenyl)-ethanol (8.70 g, 62.0 mmol) in dry CH_2Cl_2 (20 ml). The mixture was stirred for 1h at ambient temperature and was washed consecutively with

¹¹ Della, E.W.; Smith, P.A.; *J.Org.Chem.*; 64; 6; **1999**; 1798 - 1806.

saturated Na₂S₂O₃ solution (10 ml) and saturated NaCl solution (10 ml). The organic layer was dried over MgSO₄ and the solvent was removed. The residue was filtered through a pad of silica (cyclohexane / Et₂O 5:1) and the solvent was removed to give 1-(2-bromo-ethyl)-3-fluoro-benzene (11.3 g, 89 %) without the need for further purification. 1-(2-Bromo-ethyl)-3-fluoro-benzene (4.71 g, 23.2 mmol) was added dropwise to a refluxing suspension of piperazine-1-carboxylic acid ethyl ester (4.41 g, 27.8 mmol) and K₂CO₃ (4.89 g, 35.4 mmol) in dry CH₃CN (10 ml). The mixture was stirred for 12h under reflux and was then filtrated through a pad of alumina. The solvent was removed to give 4-[2-(3-fluoro-phenyl)-ethyl]-piperazine-1-carboxylic acid ethyl ester (5.53 g, 85 %), which was subjected to the next step without purification. 4-[2-(3-Fluoro-phenyl)-ethyl]-piperazine-1-carboxylic acid ethyl ester (5.20 g, 18.5 mmol) in NaOH (20 wt% in warer, 50 ml) and EtOH (50 ml) was stirred for 12h under reflux. The mixture was extracted with EtOAc (3x100 ml). The organic layer was dried over MgSO₄ and the solvent was removed to give 1-[2-(3-fluoro-phenyl)-ethyl]-piperazine (3.80 g, 99 %) without purification. 4-Bromo-but-1-ene (0.9 g, 6.9 mmol) was added dropwise to a refluxing suspension of 1-[2-(3-fluoro-phenyl)-ethyl]-piperazine (1.2 g, 5.7 mmol) and K₂CO₃ (1.2 g, 8.6 mmol) in dry CH₃CN (10 ml). The mixture was stirred for 12h under reflux and was then filtrated through a pad of alumina. The solvent was removed to give 1-but-3-enyl-4-[2-(3-fluoro-phenyl)-ethyl]-piperazine (1.49 g, 99 %). without further purification ¹H-NMR: (CDCl₃, 500 MHz) δ = 2.21-2.25 (2H, CH₂); 2.40 (dd, 2H, *J* = 7.2 Hz, *J* = 8.5 Hz, CH₂); 2.52 (bs, 8H, 4xCH₂); 2.56 (dd, 2H, *J* = 7.6 Hz, *J* = 8.7 Hz, CH₂); 2.76 (dd, 2H, *J* = 7.6 Hz, *J* = 8.7 Hz, CH₂); 4.97 (d, 1H, *J* = 10.2 Hz, *CHH*); 5.03 (d, 1H, *J* = 17.2 Hz, *CHH*); 5.77 (ddt, 1H, *J* = 6.8 Hz, *J* = 10.2 Hz, *J* = 17.2 Hz, CH); 6.83-6.89 (2H, 2xCH); 6.93 (d, 1H, *J* = 7.5 Hz, CH); 7.19 (dd, 1H, *J* = 7.5 Hz, *J* = 7.5 Hz, CH). ¹³C-NMR: (CDCl₃, 125 MHz) δ = 31.3 (CH₂); 33.3 (CH₂); 53.0 (4xCH₂); 57.9 (CH₂); 60.0 (CH₂); 112.8 (d, 1C, *J*_{C-F} = 21 Hz, CH); 115.4 (d, 1C, *J*_{C-F} = 21 Hz, CH); 115.6 (CH₂); 124.3 (d, 1C, *J*_{C-F} = 4 Hz, CH); 129.7 (d, 1C, *J*_{C-F} = 8 Hz, CH); 136.4 (CH); 142.8 (d, 1C, *J*_{C-F} = 8 Hz, C); 162.8 (d, 1C, *J*_{C-F} = 246 Hz, C). IR: $\tilde{\nu}$ [cm⁻¹] = 2938 (s); 2807 (s); 1616 (m); 1589 (s); 1488 (s); 1461 (s); 1251 (s); 1159 (s); 1010 (m); 912 (m); 781 (m).

***N*-[4-(4-Fluoro-benzoylamino)-phenyl]-hydrazinecarboxylic acid tert-butyl ester (6i).** At 0°C 4-fluorobenzoyl chloride (7.0 g, 44 mmol) was added dropwise to solution of 4-iodo-anilin (9.6 g, 44 mmol), DMAP (270 mg, 5 mol%) and NEt₃ (4.9 g, 48 mmol) in dry THF (100 ml). The mixture was stirred for 1h at ambient temperature. The precipitate was filtered off and the solvent was removed to give 4-fluoro-*N*-(4-iodo-phenyl)-benzamide (14.8 g, 99 %), which was subjected to the next step without purification. A suspension of 4-Fluoro-

N-(4-iodo-phenyl)-benzamide (7.4 g, 22 mmol), hydrazinecarboxylic acid tert-butyl ester (3.4 g, 26 mmol), CuI (207 mg, 5 mol%), 1,10-phenantroline (391 mg, 10 mol%) and Cs₂CO₃ (9.9 g, 30 mmol) in dry DMF (21 ml) was stirred for 68h at 80°C. The mixture was poured into EtOAc (100 ml) and the solids were separated by filtration through a pad of silica. The solvent was removed and the residue was purified by chromatography (silica, cyclohexane, CH₂Cl₂, NEt₃) to give *N*-[4-(4-fluoro-benzoylamino)-phenyl]-hydrazinecarboxylic acid tert-butyl ester (5.7 g, 78 %). ¹H-NMR: (CDCl₃, 500 MHz) δ = 1.47 (s, 9H, 3xCH₃); 4.40 (s, 2H, NH₂); 7.04 (dd, 2H, *J* = 8.5 Hz, *J* = 8.5 Hz, 2xCH); 7.38 (d, 2H, *J* = 8.7 Hz, 2xCH); 7.54 (d, 2H, *J* = 8.7 Hz, 2xCH); 7.82 (dd, 2H, *J* = 8.5 Hz, *J* = 8.5 Hz, 2xCH); 8.32 (s, 1H, NH). ¹³C-NMR: (CDCl₃, 125 MHz) δ = 28.3 (3xCH₃); 81.8 (C); 115.5 (d, 2C, *J*_{C-F} = 21 Hz, 2xCH); 120.3 (2xCH); 123.9 (2xCH); 129.5 (d, 2C, *J*_{C-F} = 8 Hz, 2xCH); 131.0 (d, 1C, *J*_{C-F} = 4 Hz, C); 134.5 (C); 139.6 (C); 155.1 (C); 164.7 (d, 1C, *J*_{C-F} = 253 Hz, C); 164.8 (C). IR: $\tilde{\nu}$ [cm⁻¹] = 3367 (s); 2981 (s); 2931 (s); 1691 (s); 1592 (vs); 1525 (vs); 1413 (vs); 1311 (vs); 1232 (vs); 1149 (vs); 1039 (vs); 836 (vs); 759 (vs). HRMS found [M]⁺ 345.1484, C₁₈H₂₀FN₃O₃ requires [M]⁺, 345.1489. Elementary analysis found C 62.16%, H 5.80%, N 12.03 C₁₈H₂₀FN₃O₃ requires C 62.20%, H 5.84%, N 12.17.

***N*-(4-[1,2,4]Triazol-4-yl-phenyl)-hydrazinecarboxylic acid tert-butyl ester (6j).** At 0°C NEt₃ (14.0 g, 139 mmol) followed by TMS-Cl (31.9 g, 294 mmol) were added dropwise to a suspension of 4-iodo-anilin (4.31 g, 19.6 mmol) and *sym*-diformylhydrazine (4.35 g, 49.4 mmol) in dry pyridine (200 ml). The mixture was stirred for 12h under reflux. The solvent was removed and the residue was taken up in water (200 ml). The precipitate was filtered off and dried *in vacuo* to give pure 4-(4-iodo-phenyl)-4H-[1,2,4]triazole (3.70 g, 70 %). A suspension of 4-(4-iodo-phenyl)-4H-[1,2,4]triazole (4.50 g, 16.6 mmol), hydrazinecarboxylic acid tert-butyl ester (2.76 g, 20.9 mmol), CuI (35.0 mg, 1 mol%), 9,10-phenantroline (313 mg, 10 mol%) and Cs₂CO₃ (7.92 g, 24.3 mmol) in dry DMF (18 ml) was stirred for 68h at 80°C. Then the mixture was poured into EtOAc (100 ml) and the solids were separated by filtration through a pad of silica. The solvent was removed and the residue was purified by chromatography (silica, cyclohexane, CH₂Cl₂, NEt₃) to give *N*-(4-[1,2,4]triazol-4-yl-phenyl)-hydrazinecarboxylic acid tert-butyl ester (2.29 g, 48 %). ¹H-NMR: (CDCl₃, 500 MHz) δ = 1.51 (s, 9H, 3xCH₃); 4.43 (s, 2H, NH₂); 7.28 (d, 2H, *J* = 8.8 Hz, 2xCH); 7.71 (d, 2H, *J* = 8.8 Hz, 2xCH); 8.41 (s, 2H, 2xCH). ¹³C-NMR: (CDCl₃, 125 MHz) δ = 28.2 (3xCH₃); 82.7 (C); 122.0 (2xCH); 123.9 (2xCH); 129.4 (C); 130.2 (2xCH); 143.8 (C); 154.5 (C). IR: $\tilde{\nu}$ [cm⁻¹] = 3324 (s); 3108 (s); 2985 (s); 1693 (vs); 1612 (s); 1525 (vs); 1369 (vs); 1288 (vs); 1157 (vs); 836 (vs). HRMS found [M+H]⁺ 276.1470, C₁₃H₁₇N₅O₂ requires

[M+H]⁺, 276.1460. Elementary analysis found C 56.36%, H 6.27%, N 25.31 C₁₃H₁₇N₅O₂ requires C 56.71%, H 6.22%, N 25.44%.

***N*-Phenyl-*N'*-(4-piperidin-1-yl-butyldiene)-hydrazine (7b).** The general procedure for the tandem hydroformylation / hydrazone formation was followed with 1-allyl-piperidine (823 mg, 6.57 mmol), phenylhydrazine (710 mg, 6.57 mmol), Rh(acac)(CO)₂ (5 mg, 0.3 mol%) and XANTPHOS (57 mg, 0.15 mol%) to give *N*-phenyl-*N'*-(4-piperidin-1-yl-butyldiene)-hydrazine (1.57 g, 97 %) without further purification. Analytical data was obtained from the inseparable mixture of *E/Z* isomers. ¹H-NMR: (CDCl₃, 500 MHz) δ = 1.09-1.16 (2H, CH₂); 1.45-1.74 (7H, 3xCH₂, CH); 2.28-2.36 (7H, 3xCH₂, CH); 6.52-7.36 (7H, 6xCH, NH). major isomer: ¹³C-NMR: (CDCl₃, 100 MHz) δ = 22.9 (CH₂); 24.0 (CH₂); 24.2 (CH₂); 25.7 (2xCH₂); 54.3 (2xCH₂); 58.5 (CH₂); 112.2 (2xCH); 119.0 (CH); 128.9 (2xCH); 140.7 (CH); 145.3 (C). minor isomer: ¹³C-NMR: (CDCl₃, 125 MHz) δ = 23.4 (CH₂); 24.2 (CH₂); 24.8 (CH₂); 25.6 (2xCH₂); 54.0 (2xCH₂); 56.7 (CH₂); 112.6 (2xCH); 119.3 (CH); 128.9 (2xCH); 140.6 (CH); 145.4 (C). IR: $\tilde{\nu}$ [cm⁻¹] = 2935 (vs), 2779 (s), 1601 (vs), 1496 (vs), 1257 (vs), 1115 (s), 748 (vs), 694 (vs). HRMS found [M+H]⁺ 246.1987, C₁₅H₂₅N₃ requires [M+H]⁺, 246.1970.

***N*-(4-Methoxy-phenyl)-*N'*-(4-piperidin-1-yl-butyldiene)-hydrazine (7c).** The general procedure for the tandem hydroformylation / hydrazone formation was followed with 1-allyl-piperidine (485 mg, 3.87 mmol), 4-methoxy-phenylhydrazine (538 mg, 3.87 mmol), Rh(acac)(CO)₂ (3 mg, 0.3 mol%) and XANTPHOS (34 mg, 0.15 mol%) to give *N*-(4-Methoxy-phenyl)-*N'*-(4-piperidin-1-yl-butyldiene)-hydrazine (989 mg, 93 %) without further purification. Analytical data was obtained from the inseparable mixture of *E/Z* isomers. major isomer: ¹H-NMR: (CDCl₃, 500 MHz) δ = 1.43 (bs, 2H, CH₂); 1.55-1.60 (4H, 2xCH₂); 1.71-1.76 (2H, CH₂); 2.25-2.38 (8H, 4xCH₂); 3.74 (s, 3H, CH₃); 6.79 (d, 2H, *J* = 9.0 Hz, 2xCH); 6.91 (d, 2H, *J* = 9.0 Hz, 2xCH); 7.04 (t, 1H, *J* = 5.2 Hz, CH); 8.10 (bs, 1H, NH). minor isomer: ¹H-NMR: (CDCl₃, 500 MHz) δ = 1.43 (bs, 2H, CH₂); 1.55-1.60 (4H, 2xCH₂); 1.71-1.76 (2H, CH₂); 2.25-2.38 (8H, 4xCH₂); 3.75 (s, 3H, CH₃); 6.48 (t, 1H, *J* = 6.0 Hz, CH); 6.81 (d, 2H, *J* = 9.0 Hz, 2xCH); 6.99 (d, 2H, *J* = 9.0 Hz, 2xCH); 8.10 (bs, 1H, NH). major isomer: ¹³C-NMR: (CDCl₃, 100 MHz) δ = 23.2 (CH₂); 24.4 (CH₂); 25.9 (2xCH₂); 30.3 (CH₂); 54.6 (2xCH₂); 55.7 (CH₃); 58.8 (CH₂); 114.0 (2xCH); 114.7 (2xCH); 139.6 (C); 140.7 (CH); 153.5 (C). minor isomer: ¹³C-NMR: (CDCl₃, 125 MHz) δ = 23.7 (CH₂); 24.3 (CH₂); 25.8 (2xCH₂); 30.3 (CH₂); 54.3 (2xCH₂); 55.7 (CH₃); 57.2 (CH₂); 114.2 (2xCH); 114.6 (2xCH); 140.0 (C); 140.1 (CH); 153.5 (C). IR: $\tilde{\nu}$ [cm⁻¹] = 3307 (s), 2935 (vs), 2767 (s), 1514 (vs), 1234 (vs), 1115 (s), 823 (vs). HRMS found M⁺ 275.1994 C₁₆H₂₅N₃O requires M⁺, 275.1998.

4-[*N'*-(4-Dimethylamino-butyldiene)-hydrazino]-benzonitrile (7d). The general procedure for the tandem hydroformylation / hydrazone formation was followed with *N,N*-dimethylprop-2-en-1-amine (399 mg, 4.69 mmol), 4-cyano-phenylhydrazine (624 mg, 4.69 mmol), Rh(acac)(CO)₂ (3.6 mg, 0.3 mol%) and XANTPHOS (41 mg, 0.15 mol%) to give 4-[*N'*-(4-dimethylamino-butyldiene)-hydrazino]-benzonitrile (973 mg, 90 %) without further purification. Analytical data was obtained from the inseparable mixture of *E/Z* isomers. major isomer: ¹H-NMR: (CDCl₃, 500 MHz) δ = 1.69-1.78 (2H, CH₂); 2.21-2.39 (10H, CH₃, 2xCH₂); 6.64 (t, 1H, *J* = 6.9 Hz, CH); 6.97 (d, 2H, *J* = 8.7 Hz, 2xCH); 7.45 (d, 2H, *J* = 8.7 Hz, 2xCH); 10.5 (bs, 1H, NH). minor isomer: ¹H-NMR: (CDCl₃, 500 MHz) δ = 1.69-1.78 (2H, CH₂); 2.21-2.39 (10H, CH₃, 2xCH₂); 6.97 (d, 2H, *J* = 8.7 Hz, 2xCH); 7.16 (t, 1H, *J* = 5.2 Hz, CH); 7.45 (d, 2H, *J* = 8.7 Hz, 2xCH); 7.80 (bs, 1H, NH). major isomer: ¹³C-NMR: (CDCl₃, 125 MHz) δ = 23.5 (CH₂); 30.0 (CH₂); 44.8 (2xCH₃); 56.0 (CH₂); 100.4 (C); 112.2 (2xCH); 120.4 (C); 133.6 (2xCH); 143.3 (CH); 149.7 (C). minor isomer: ¹³C-NMR: (CDCl₃, 125 MHz) δ = 24.1 (CH₂); 24.8 (CH₂); 45.4 (2xCH₃); 59.0 (CH₂); 101.1 (C); 112.1 (2xCH); 120.1 (C); 133.5 (2xCH); 143.6 (CH); 148.4 (C). IR: $\tilde{\nu}$ [cm⁻¹] = 3284 (s), 2945 (vs), 2820 (s), 2218 (vs), 1612 (s), 1533 (vs), 1271 (vs), 1167 (s), 833 (vs). HRMS found M⁺ 230.1558 C₁₃H₁₈N₄ requires M⁺, 230.1531.

***N*-(4-Nitro-phenyl)-*N'*-(4-piperidin-1-yl-butyldiene)-hydrazine (7e).** The general procedure for the tandem hydroformylation / hydrazone formation was followed with 1-allyl-piperidine (458 mg, 3.66 mmol), 4-nitro-phenylhydrazine (560 mg, 3.66 mmol), Rh(acac)(CO)₂ (2.8 mg, 0.3 mol%) and XANTPHOS (32 mg, 0.15 mol%) to give *N*-(4-nitro-phenyl)-*N'*-(4-piperidin-1-yl-butyldiene)-hydrazine (845 mg, 80 %) without further purification. Analytical data was obtained from the inseparable mixture of *E/Z* isomers. major isomer: ¹H-NMR: (CDCl₃, 500 MHz) δ = 1.37-1.44 (2H, CH₂); 1.53-1.58 (4H, 2xCH₂); 1.71-1.80 (2H, CH₂); 2.24-2.38 (8H, 4xCH₂); 7.04 (d, 2H, *J* = 9.5 Hz, 2xCH); 7.20 (t, 1H, *J* = 5.2 Hz, CH); 8.09 (d, 2H, *J* = 9.5 Hz, 2xCH); 9.75 (bs, 1H, NH). minor isomer: ¹H-NMR: (CDCl₃, 500 MHz) δ = 1.48-1.52 (2H, CH₂); 1.60-1.64 (4H, 2xCH₂); 1.71-1.80 (2H, CH₂); 2.24-2.38 (8H, 4xCH₂); 6.70 (t, 1H, *J* = 6.7 Hz, CH); 6.95 (d, 2H, *J* = 9.4 Hz, 2xCH); 7.98 (bs, 1H, NH); 8.11 (d, 2H, *J* = 9.4 Hz, 2xCH). major isomer: ¹³C-NMR: (CDCl₃, 100 MHz) δ = 24.0 (CH₂); 24.4 (2xCH₂); 26.0 (2xCH₂); 30.3 (CH₂); 54.0 (CH₂); 58.7 (CH₂); 111.6 (2xCH); 126.2 (2xCH); 136.9 (C); 145.1 (CH); 151.1 (C). minor isomer: ¹³C-NMR: (CDCl₃, 125 MHz) δ = 24.0 (CH₂); 24.3 (2xCH₂); 25.6 (2xCH₂); 30.3 (CH₂); 54.6 (CH₂); 56.1 (CH₂); 111.1 (2xCH); 126.0 (2xCH); 136.9 (C); 145.4 (CH); 150.1 (C). IR: $\tilde{\nu}$ [cm⁻¹] = 3294 (s),

2935 (vs), 2802 (s), 1604 (s), 1504 (vs), 1274 (vs), 1109 (s), 841 (vs). HRMS found $[M+H]^+$ 291.1790 $C_{15}H_{22}N_4O_2$ requires M^+ , 291.1821.

3-(2-Piperidin-1-yl-ethyl)-1H-indole (8b). The first generation protocol was followed with 1-allyl-piperidine (823 mg, 6.57 mmol), phenylhydrazine (710 mg, 6.57 mmol), Rh(acac)(CO)₂ (5 mg, 0.3 mol%) and XANTPHOS (57 mg, 3 mol%) to give 3-(2-piperidin-1-yl-ethyl)-1H-indole (1.45 g, 97 %) without further purification. NMR data fits with literature¹².

3-[2-(4-Phenyl-piperazin-1-yl)-ethyl]-1H-indole hydrochloride (8c). The first generation protocol was followed with 1-allyl-4-phenyl-piperazine (994 mg, 4.91 mmol), phenylhydrazine (531 mg, 4.91 mmol), Rh(acac)(CO)₂ (3.8 mg, 0.3 mol%) and XANTPHOS (42.6 mg, 3 mol%). The crude product was taken up in dry THF (10 ml) and HCl (20 ml, saturated in Et₂O) was added dropwise. The precipitate was collected by filtration giving 3-[2-(4-phenyl-piperazin-1-yl)-ethyl]-1H-indole hydrochloride (1.44 g, 96 %). ¹H-NMR: (DMSO-d₆, 500 MHz) δ = 3.20-3.22 (8H, 4xCH₂); 3.66-3.68 (2H, CH₂); 3.81-3.84 (2H, CH₂); 6.86 (dd, 1H, J = 7.5 Hz, J = 7.5 Hz, CH); 7.00-7.03 (3H, 3xCH); 7.09 (dd, 1H, J = 7.5 Hz, J = 7.5 Hz, CH); 7.23-7.26 (4H, 3xCH, NH); 7.36 (d, 1H, J = 7.5 Hz, CH); 7.66 (d, 1H, J = 7.5 Hz, CH); 11.03 (s, 1H, NH); 11.48 (s, 1H, NH). ¹³C-NMR: (CDCl₃, 125 MHz) δ = 19.5 (CH₂); 45.5 (2xCH₂); 50.5 (2xCH₂); 55.5 (CH₂); 109.2 (C); 111.6 (CH); 114.5 (CH); 116.06 (2xCH); 118.5 (CH); 120.1 (CH); 121.3 (CH); 123.2 (CH); 126.7 (C); 129.2 (2xCH); 136.3 (C); 149.6 (C). IR: $\tilde{\nu}$ [cm⁻¹] = 3415 (s); 3216 (s); 2427 (s); 1596 (s); 1494 (s); 1457 (vs); 1436 (s); 754 (vs); 692 (s). HRMS found $[M]^+$ 305.1868 $C_{20}H_{23}N_3$ requires M^+ , 305.1892.

Ethyl 4-(2-(1H-indol-3-yl)ethyl)piperazine-1-carboxylate (8d). The first generation protocol was followed with 4-allyl-piperazine-1-carboxylic acid ethyl ester (329 mg, 1.66 mmol), Phenylhydrazine (179 mg, 1.66 mmol), Rh(acac)(CO)₂ (1.3 mg, 0.3 mol%) and XANTPHOS (14.4 mg, 3 mol%). The crude product was purified by chromatography (silica, EtOAc, cyclohexane, NEt₃) to give Ethyl 4-(2-(1H-indol-3-yl)ethyl)piperazine-1-carboxylate (468 mg, 94 %). ¹H-NMR: (CDCl₃, 500 MHz) δ = 1.27 (t, 3H, J = 7.0 Hz, CH₃); 2.52 (bs, 4H, 2xCH₂); 2.71 (t, 2H, J = 8.0 Hz, CH₂); 2.97 (t, 2H, J = 8.0 Hz, CH₂); 3.54 (bs, 4H, 2xCH₂); 4.15 (q, 2H, J = 7.0 Hz, CH₂); 7.00 (s, 1H, CH); 7.11 (dd, 1H, J = 7.1 Hz, J = 7.7 Hz, CH); 7.18 (dd, 1H, J = 7.1 Hz, J = 8.0 Hz, CH); 7.33 (d, 1H, J = 8.0 Hz, CH); 7.60 (d, 1H, J = 7.7 Hz, CH); 8.34 (s, 1H, NH). ¹³C-NMR: (CDCl₃, 125 MHz) δ = 14.6 (CH₃); 22.7 (CH₂); 43.6 (2xCH₂); 52.8 (2xCH₂); 59.1 (CH₂); 61.3 (CH₂); 111.1 (CH); 113.9 (C); 118.6 (CH);

¹²; Lounasmaa, M.; Jokela, R.; *Tetrahedron*; **1989**; 45; 12; 3975-3992.

119.1 (CH); 121.5 (CH); 121.8 (CH); 127.4 (C); 136.2 (C); 155.5 (C). IR: $\tilde{\nu}$ [cm⁻¹] = 3268 (w); 2979 (m); 2809 (m); 2485 (w); 1714 (s); 1481 (m); 767 (w). HRMS found [M+H]⁺ 302.1847 C₁₇H₂₃N₃O₂ requires [M+H]⁺, 302.1869.

3-(3-(piperidin-1-yl)propyl)-1H-indole (8e). The first generation protocol was followed with 1-(but-3-enyl)piperidine (574 mg, 4.13 mmol), phenylhydrazine (446 mg, 4.13 mmol), Rh(acac)(CO)₂ (3.2 mg, 0.3 mol%) and XANTPHOS (35.8 mg, 3 mol%) to give 3-(3-(piperidin-1-yl)propyl)-1H-indole (908 mg, 91 %) without further purification. ¹H-NMR: (CDCl₃, 400 MHz) δ = 1.42 (bs, 2H, CH₂); 1.56-16.2 (4H, 2xCH₂); 1.89-1.97 (2H, CH₂); 2.39-2.43 (bs, 6H, 3xCH₂); 2.75 (t, 2H, *J* = 7.6 Hz, CH₂); 6.92 (s, 1H, CH); 7.08 (dd, 1H, *J* = 7.0 Hz, *J* = 7.8 Hz, CH); 7.16 (dd, 1H, *J* = 7.0 Hz, *J* = 8.1 Hz, CH); 7.31 (d, 1H, *J* = 8.1 Hz, CH); 7.59 (d, 1H, *J* = 7.8 Hz, CH); 8.37 (bs, 1H, NH). ¹³C-NMR: (CDCl₃, 125 MHz) δ = 23.1 (CH₂); 24.4 (CH₂); 25.9 (2xCH₂); 27.3 (CH₂); 54.9 (2xCH₂); 59.3 (CH₂); 111.0 (CH); 116.3 (C); 118.9 (CH); 121.1 (CH); 121.7 (CH); 127.5 (C); 136.3 (C). IR: $\tilde{\nu}$ [cm⁻¹] = 3218 (s); 2944 (vs); 2937 (vs); 2805 (s); 1455 (s); 1106 (vs); 781 (s); 732 (vs). HRMS found [M]⁺ 242.1784 C₁₆H₂₂N₂ requires M⁺, 242.1783.

Ethyl 4-(3-(1H-indol-3-yl)propyl)piperazine-1-carboxylate (8f). The first generation protocol was followed with ethyl 4-(but-3-enyl)piperazine-1-carboxylate (337 mg, 1.59 mmol), phenylhydrazine (172 mg, 1.59 mmol), Rh(acac)(CO)₂ (1.2 mg, 0.3 mol%) and XANTPHOS (13.8 mg, 3 mol%) to give ethyl 4-(3-(1H-indol-3-yl)propyl)piperazine-1-carboxylate (455 mg, 91 %) without further purification. ¹H-NMR: (CDCl₃, 500 MHz) δ = 1.27 (t, 3H, *J* = 7.0 Hz, CH₃); 1.88-1.94 (2H, CH₂); 2.40-2.45 (6H, 3xCH₂); 2.78 (t, 2H, *J* = 7.5 Hz, CH₂); 3.51 (bs, 4H, 2xCH₂); 4.16 (q, 2H, *J* = 7.0 Hz, CH₂); 6.93 (s, 1H, CH); 7.10 (dd, 1H, *J* = 7.2 Hz, *J* = 7.5 Hz, CH); 7.17 (dd, 1H, *J* = 7.5 Hz, *J* = 8.0 Hz, CH); 7.31 (d, 1H, *J* = 8.0 Hz, CH); 7.60 (d, 1H, *J* = 7.2 Hz, CH); 8.61 (bs, 1H, NH). ¹³C-NMR: (CDCl₃, 125 MHz) δ = 16.2 (CH₃); 24.4 (CH₂); 28.7 (CH₂); 45.2 (2xCH₂); 54.4 (2xCH₂); 59.8 (CH₂); 62.8 (CH₂); 112.7 (CH); 117.4 (C); 120.4 (2xCH); 122.8 (CH); 123.2 (CH); 129.0 (C); 137.9 (C); 157.1 (C). IR: $\tilde{\nu}$ [cm⁻¹] = 3324 (s); 2935 (s); 2809 (s); 1700 (vs); 1434 (vs); 1243 (vs); 1128 (vs); 740 (vs). HRMS found [M]⁺ 315.1970 C₁₈H₂₅N₃O₂ requires M⁺, 315.1947.

N,N-diethyl-2-(1H-indol-3-yl)-1-phenylethanamine (8g). The first generation protocol was followed with N,N-diethyl-1-phenylprop-2-en-1-amine (250 mg, 1.32 mmol), phenylhydrazine (142 mg, 1.32 mmol), Rh(acac)(CO)₂ (0.34 mg, 1 mol%) and XANTPHOS (38 mg, 5 mol%). The crude product was purified by chromatography (silica, EtOAc, cyclohexane, NEt₃) to give N,N-diethyl-2-(1H-indol-3-yl)-1-phenylethanamine (327 mg, 85 %). ¹H-NMR: (CDCl₃, 500 MHz) δ = 1.06-1.11 (6H, 2xCH₃); 2.50-2.55 (2H, CH₂); 2.78-

2.84 (2H, CH₂); 3.18 (d, 1H, *J* = 9.9 Hz, CHH); 3.46 (d, 1H, *J* = 14.5 Hz, CHH); 4.10 (dd, 1H, *J* = 9.9 Hz, *J* = 14.5 Hz, CH); 6.56 (s, 1H, CH); 7.10-7.28 (8H, 8xCH); 7.61 (d, 1H, *J* = 7.7 Hz, CH); 7.99 (bs, 1H, NH). ¹³C-NMR: (CDCl₃, 125 MHz) δ = 12.8 (2xCH₃); 28.3 (CH₂); 43.4 (2xCH₂); 64.8 (CH); 110.9 (CH); 113.7 (C); 118.6 (CH); 118.9 (CH); 121.5 (CH); 122.5 (CH); 126.5 (CH); 127.6 (2xCH); 127.8 (C); 128.8 (2xCH); 135.9 (C); 141.9 (C). IR: $\tilde{\nu}$ [cm⁻¹] = 3419 (m); 2967 (s); 1492 (m); 1455 (s); 740 (s); 700 (s). HRMS found [M+H]⁺ 293.1986 C₂₀H₂₅N₂ requires [M+H]⁺, 293.1939.

3-(2-Phenyl-2-(piperidin-1-yl)ethyl)-1H-indole ((rac)-8h). The first generation protocol was followed with *rac*-1-(1-phenylallyl)piperidine (661 mg, 3.3 mmol), phenylhydrazine (355 mg, 3.3 mmol), Rh(acac)(CO)₂ (8.5 mg, 1 mol%) and XANTPHOS (95 mg, 5 mol%). The crude product was purified by chromatography (silica, EtOAc, cyclohexane, NEt₃) to give 3-(2-phenyl-2-(piperidin-1-yl)ethyl)-1H-indole (540 mg, 54 %). ¹H-NMR: (CDCl₃, 500 MHz) δ = 1.44 (bs, 2H, CH₂); 1.65 (bs, 4H, 2xCH₂); 2.57 (bs, 4H, 2xCH₂); 3.26 (d, 1H, *J* = 9.7 Hz, CHH); 3.54 (d, 1H, *J* = 4.5 Hz, CHH); 3.80 (dd, 1H, *J* = 4.5 Hz, *J* = 9.7 Hz, CH); 6.59 (s, 1H, CH); 7.13 (dd, 1H, *J* = 7.2 Hz, *J* = 7.7 Hz, CH); 7.18 (dd, 1H, *J* = 7.2 Hz, *J* = 7.7 Hz, CH); 7.24-7.30 (6H, 6xCH); 7.63 (d, 1H, *J* = 7.7 Hz, CH); 8.17 (s, 1H, NH). ¹³C-NMR: (CDCl₃, 125 MHz) δ = 26.2 (CH₂); 27.9 (2xCH₂); 29.8 (CH₂); 53.0 (2xCH₂); 72.4 (CH); 112.5 (CH); 115.0 (C); 120.2 (CH); 120.4 (CH); 123.0 (CH); 124.1 (CH); 128.3 (CH); 129.2 (2xCH); 129.3 (C); 130.5 (2xCH); 137.4 (C); 141.9 (C). IR: $\tilde{\nu}$ [cm⁻¹] = 3426 (s); 2929 (s); 2852 (s); 2798 (s); 1602 (s); 1492 (s); 1469 (s); 1454 (s); 1093 (s); 1068 (m); 1033 (m); 910 (s); 738 (s). HRMS found [M+H]⁺ 305.2037 C₂₁H₂₅N₂ requires [M+H]⁺, 305.2056.

3-(+)-2-Phenyl-2-(piperidin-1-yl)ethyl)-1H-indole ((+)-8h). The title compound was obtained with 95 %*ee*¹³. ¹H-NMR: (CDCl₃, 500 MHz) δ = 1.44 (bs, 2H, CH₂); 1.65 (bs, 4H, 2xCH₂); 2.57 (bs, 4H, 2xCH₂); 3.26 (d, 1H, *J* = 9.7 Hz, CHH); 3.54 (d, 1H, *J* = 4.5 Hz, CHH); 3.80 (dd, 1H, *J* = 4.5 Hz, *J* = 9.7 Hz, CH); 6.59 (s, 1H, CH); 7.13 (dd, 1H, *J* = 7.2 Hz, *J* = 7.7 Hz, CH); 7.18 (dd, 1H, *J* = 7.2 Hz, *J* = 7.7 Hz, CH); 7.24-7.30 (6H, 6xCH); 7.63 (d, 1H, *J* = 7.7 Hz, CH); 8.17 (s, 1H, NH). ¹³C-NMR: (CDCl₃, 125 MHz) δ = 26.2 (CH₂); 27.9 (2xCH₂); 29.8 (CH₂); 53.0 (2xCH₂); 72.4 (CH); 112.5 (CH); 115.0 (C); 120.2 (CH); 120.4 (CH); 123.0 (CH); 124.1 (CH); 128.3 (CH); 129.2 (2xCH); 129.3 (C); 130.5 (2xCH); 137.4 (C); 141.9 (C). [α] = +59.6° (c=1.00, CH₂Cl₂).

3-((-)-2-Phenyl-2-(piperidin-1-yl)ethyl)-1H-indole ((-)-8h). The title compound was obtained with 95 %*ee*¹⁰. ¹H-NMR: (CDCl₃, 500 MHz) δ = 1.44 (bs, 2H, CH₂); 1.65 (bs, 4H,

2xCH₂); 2.57 (bs, 4H, 2xCH₂); 3.26 (d, 1H, *J* = 9.7 Hz, *CHH*); 3.54 (d, 1H, *J* = 4.5 Hz, *CHH*); 3.80 (dd, 1H, *J* = 4.5 Hz, *J* = 9.7 Hz, CH); 6.59 (s, 1H, CH); 7.13 (dd, 1H, *J* = 7.2 Hz, *J* = 7.7 Hz, CH); 7.18 (dd, 1H, *J* = 7.2 Hz, *J* = 7.7 Hz, CH); 7.24-7.30 (6H, 6xCH); 7.63 (d, 1H, *J* = 7.7 Hz, CH); 8.17 (s, 1H, NH). ¹³C-NMR: (CDCl₃, 125 MHz) δ = 26.2 (CH₂); 27.9 (2xCH₂); 29.8 (CH₂); 53.0 (2xCH₂); 72.4 (CH); 112.5 (CH); 115.0 (C); 120.2 (CH); 120.4 (CH); 123.0 (CH); 124.1 (CH); 128.3 (CH); 129.2 (2xCH); 129.3 (C); 130.5 (2xCH); 137.4 (C); 141.9 (C).

3-(1-Phenyl-3-(piperidin-1-yl)propyl)-1H-indole (8i). The first generation protocol was followed with 1-(3-phenylbut-3-enyl)piperidine (676 mg, 3.14 mmol), phenylhydrazine (340 mg, 3.14 mg) and Rh(acac)(CO)₂ (8.1 mg, 1 mol%). The crude product was purified by chromatography (silica, EtOAc, cyclohexane, NEt₃) to give 3-(1-phenyl-3-(piperidin-1-yl)propyl)-1H-indole (414 mg, 41 %). ¹H-NMR: (CDCl₃, 500 MHz) δ = 1.45 (s, 2H, CH₂); 1.60 (s, 4H, 2xCH₂); 2.21-2.45 (8H, 4xCH₂); 4.22 (t, 1H, *J* = 7.1 Hz, CH); 7.01 (dd, 1H, *J* = 7.2 Hz, *J* = 8.0 Hz, CH); 7.03 (s, 1H, CH); 7.13 (d, 1H, *J* = 8.2 Hz, CH); 7.17 (d, 1H, *J* = 8.2 Hz, CH); 7.25 (dd, 2H, *J* = 7.2 Hz, *J* = 7.5 Hz, 2xCH); 7.30-7.32 (3H, 3xCH); 7.46 (d, 1H, *J* = 8.0 Hz, CH); 8.38 (s, 1H, NH). ¹³C-NMR: (CDCl₃, 125 MHz) δ = 24.5 (CH₂); 26.0 (2xCH₂); 33.3 (CH₂); 41.0 (CH); 54.7 (2xCH₂); 57.9 (CH₂); 111.0 (CH); 119.1 (CH); 119.4 (CH); 120.1 (C); 121.0 (CH); 121.8 (CH); 125.9 (CH); 127.0 (C); 127.8 (2xCH); 128.2 (2xCH); 136.5 (C); 145.3 (C). IR: $\tilde{\nu}$ [cm⁻¹] = 3399 (s); 2952 (m); 1666 (s); 1650 (s); 1529 (vs); 1471 (s); 1274 (s); 1095 (s); 835 (m); 804 (s). HRMS found [M+H]⁺ 318.2097 C₂₂H₂₅N₂ requires [M+H]⁺, 318.2098.

***N,N*-Diethyl-3-(1H-indol-3-yl)-1-phenylbutan-1-amine (8j).** The first generation protocol was followed with *N,N*-diethyl-3-methyl-1-phenylbut-3-en-1-amine (678 mg, 3.12 mmol), Phenylhydrazine (337 mg, 3.12 mmol) and Rh(acac)(CO)₂ (8 mg, 1 mol%). The crude product was purified by chromatography (silica, EtOAc, cyclohexane, NEt₃) to give *N,N*-diethyl-3-(1H-indol-3-yl)-1-phenylbutan-1-amine (511 mg, 51 %). Analytical data was obtained from the inseparable mixture of diastereomers: ¹H-NMR: (CDCl₃, 500 MHz) δ = 1.03, 1.10 (t, 6H, *J* = 7.0 Hz, 2xCH₃); 1.41, 1.45 (d, 3H, *J* = 6.8 Hz, CH₃); 2.07-2.25 (1H, CH); 2.33-2.43, 2.69-2.80 (4H, 2xCH₂); 2.54-2.61, 2.96-3.05 (2H, CH₂); 3.77, 3.93 (dd, 1H, *J* = 5.8 Hz, *J* = 9.0 Hz, CH); 6.91 (s, 1H, CH); 7.12-7.64 (9H, 9xCH); 8.36, 8.44 (bs, 1H, NH). ¹³C-NMR: (CDCl₃, 125 MHz) δ = 12.8, 12.9 (2xCH₃); 20.6, 22.5 (CH₃); 27.5, 27.9 (CH); 40.0, 40.7 (CH₂); 43.0, 43.2 (2xCH₂); 61.8, 62.3 (CH); 111.0, 111.1 (CH); 118.6 (CH); 119.2, 119.3 (CH); 119.9, 120.3 (CH); 121.4 (CH); 122.6 (C); 126.5 (C); 126.6, 126.8 (CH); 127.7, 127.8 (2xCH); 128.7, 128.9 (2xCH); 136.3, 136.4 (C); 140.8, 141.0 (C). IR: $\tilde{\nu}$ [cm⁻¹]

= 3419 (s); 2058 (m); 2965 (s); 1670 (m); 1600 (m); 1492 (s); 1455 (s); 1226 (m); 908 (s); 736 (vs). HRMS found $[M]^+$ 320.2277 $C_{22}H_{28}N_2$ requires $[M]^+$, 320.2253.

***N,N*-Diethyl-3-(1H-indol-3-yl)-1-phenylpropan-1-amine (8k).** The first generation protocol was followed with *N,N*-diethyl-1-phenylbut-3-en-1-amine (332 mg, 1.63 mmol), phenylhydrazine (176 mg, 1.63 mmol), Rh(acac)(CO)₂ (1.3 mg, 0.3 mol%) and XANTPHOS (14 mg, 1.5 mol%). The crude product was purified by chromatography (silica, EtOAc, cyclohexane, NEt₃) to give *N,N*-diethyl-3-(1H-indol-3-yl)-1-phenylpropan-1-amine (403 mg, 81 %). ¹H-NMR: (CDCl₃, 500 MHz) δ = 1.06 (t, 6H, *J* = 7.0 Hz, 2xCH₃); 2.15-2.23 (1H, CHH); 2.38-2.45 (3H, CH₂, CHH); 2.59-2.68 (1H, CHH); 2.71-2.77 (3H, CH₂, CHH); 3.81 (dd, 1H, *J* = 8.5 Hz, *J* = 8.7 Hz, CH); 6.92 (s, 1H, CH); 7.12 (dd, 1H, *J* = 7.0 Hz, *J* = 7.7 Hz, CH); 7.21 (dd, 1H, *J* = 7.0 Hz, *J* = 8.0 Hz, CH); 7.31-7.40 (6H, 6xCH); 7.56 (d, 1H, *J* = 7.7 Hz, CH); 8.08 (s, 1H, NH). ¹³C-NMR: (CDCl₃, 125 MHz) δ = 12.8 (2xCH₃); 22.4 (CH₂); 33.2 (CH₂); 43.2 (2xCH₂); 64.3 (CH); 111.0 (CH); 116.6 (C); 118.9 (2xCH); 121.0 (CH); 121.7 (CH); 126.8 (CH); 127.5 (C); 127.9 (2xCH); 128.7 (2xCH); 136.3 (C); 141.4 (C). IR: $\tilde{\nu}$ [cm⁻¹] = 3419 (s); 2967 (vs); 2929 (s); 2869 (s); 1455 (vs); 740 (vs); 701 (s). HRMS found $[M]^+$ 306.2128 $C_{21}H_{26}N_2$ requires $[M]^+$, 306.2098.

3-(1-Methylpiperidin-4-yl)-1H-indole (8l). The first generation protocol was followed with 1-methyl-4-methylene-piperidine (519 mg, 4.67 mmol), phenylhydrazine (505 mg, 4.67 mmol) and Rh(acac)(CO)₂ (3.6 mg, 0.3 mol%) to give 3-(1-methylpiperidin-4-yl)-1H-indole (781 mg, 78 %) without further purification. ¹H-NMR: (CDCl₃, 400 MHz) δ = 1.86 (dt, 2H, *J* = 11.8 Hz, *J* = 12.7 Hz, CH₂); 2.05-2.06 (2H, CH₂); 2.15 (t, 2H, *J* = 11.8 Hz, CH₂); 2.36 (s, 3H, CH₃); 2.82 (t, 1H, *J* = 11.8 Hz, CH); 3.00 (d, 2H, *J* = 11.8 Hz, CH₂); 6.91 (s, 1H, CH); 7.09 (dd, 1H, *J* = 6.8 Hz, *J* = 7.0 Hz, CH); 7.17 (dd, 1H, *J* = 7.0 Hz, *J* = 8.0 Hz, CH); 7.32 (d, 1H, *J* = 8.0 Hz, CH); 7.65 (d, 1H, *J* = 8.0 Hz, CH); 8.72 (s, 1H, NH). ¹³C-NMR: (CDCl₃, 100 MHz) δ = 32.8 (CH); 32.9 (2xCH₂); 46.5 (CH₃); 56.3 (2xCH₂); 111.2 (CH); 118.8 (CH); 119.0 (CH); 119.8 (CH); 120.9 (C); 121.7 (CH); 126.5 (C); 136.4 (C). IR: $\tilde{\nu}$ [cm⁻¹] = 3147 (m); 2935 (s); 2921 (s); 2844 (m); 2782 (s); 1457 (s); 1276 (s); 1222 (m); 1110 (m); 989 (s); 732 (vs). HRMS found $[M]^+$ 214.1490 $C_{14}H_{18}N_2$ requires $[M]^+$, 214.1470.

5-Fluoro-3-(1-methylpiperidin-4-yl)-1H-indole (8m). The first generation protocol was followed with 1-methyl-4-methylene-piperidine (479 mg, 4.3 mmol), 4-fluoro phenylhydrazine (543 mg, 4.3 mmol) and Rh(acac)(CO)₂ (3.3 mg, 0.3 mol%) to give 5-fluoro-3-(1-methylpiperidin-4-yl)-1H-indole (653 mg, 65 %) without further purification. ¹H-NMR: (CDCl₃, 500 MHz) δ = 1.80 (dt, 2H, *J* = 12.3 Hz, *J* = 13.1 Hz, CH₂); 2.02 (d, 2H, *J* = 12.1 Hz, CH₂); 2.13 (t, 2H, *J* = 12.1 Hz, CH₂); 2.34 (s, 3H, CH₃); 2.73 (t, 1H, *J* = 12.1 Hz,

CH); 2.98 (d, 2H, $J = 11.5$ Hz, CH₂); 6.90 (dd, 1H, $J = 9.0$ Hz, $J = 9.0$ Hz, CH); 6.98 (s, 1H, CH); 7.23-7.27 (2H, 2xCH); 8.60 (s, 1H, NH). ¹³C-NMR: (CDCl₃, 125 MHz) $\delta = 32.7$ (CH); 32.8 (2xCH₂); 46.4 (CH₃); 56.2 (2xCH₂); 103.8 (d, 1C, $J_{C-F} = 23$ Hz, CH); 110.1 (d, 1C, $J_{C-F} = 26$ Hz, CH); 111.7 (CH); 121.2 (C); 121.6 (CH); 132.9 (C); 157.4 (d, 1C, $J_{C-F} = 234$ Hz, C). IR: $\tilde{\nu}$ [cm⁻¹] = 3102 (s); 3045 (s); 2942 (vs); 2929 (vs); 2884 (s); 2794 (vs); 1465 (vs); 1274 (s); 1170 (vs); 939 (vs); 790 (s); 757 (s). HRMS found [M]⁺ 232.1405 C₁₄H₁₇FN₂ requires [M]⁺, 232.1375.

5-Chloro-3-(1-methylpiperidin-4-yl)-1H-indole (8n). The first generation protocol was followed with 1-methyl-4-methylene-piperidine (643 mg, 5.78 mmol), 4-chlorophenylhydrazine (825 mg, 5.78 mmol) and Rh(acac)(CO)₂ (4.7 mg, 0.3 mol%) to give 5-chloro-3-(1-methylpiperidin-4-yl)-1H-indole (1.21 g, 85 %) without further purification. ¹H-NMR: (CDCl₃, 500 MHz) $\delta = 1.85$ (dt, 2H, $J = 12.1$ Hz, $J = 12.7$ Hz, CH₂); 2.10 (d, 2H, $J = 12.7$ Hz, CH₂); 2.14 (t, 2H, $J = 11.7$ Hz, CH₂); 2.37 (s, 3H, CH₃); 2.77 (t, 1H, $J = 12.1$ Hz, CH); 3.00 (d, 2H, $J = 11.7$ Hz, CH₂); 7.00 (s, 1H, CH); 7.16 (d, 1H, $J = 8.5$ Hz, CH); 7.28 (d, 1H, $J = 8.5$ Hz, CH); 7.63 (s, 1H, CH); 8.27 (s, 1H, NH). ¹³C-NMR: (CDCl₃, 125 MHz) $\delta = 32.8$ (CH); 33.0 (2xCH₂); 46.5 (CH₃); 56.3 (2xCH₂); 112.1 (C); 112.1 (CH); 118.6 (CH); 121.1 (CH); 122.1 (C); 122.1 (CH); 124.8 (C); 125.5 (C); 127.8 (C). IR: $\tilde{\nu}$ [cm⁻¹] = 3087 (s); 2964 (s); 2917 (vs); 2771 (s); 1494 (s); 1378 (m); 1274 (s); 1122 (s); 1064 (s); 790 (s); 732 (vs). HRMS found [M]⁺ 248.1059 C₁₄H₁₇ClN₂ requires [M]⁺, 248.1080.

5-Bromo-3-(1-methylpiperidin-4-yl)-1H-indole (8o). The first generation protocol was followed with 1-methyl-4-methylene-piperidine (569 mg, 5.12 mmol), 4-bromophenylhydrazine (957 mg, 5.12 mmol) and Rh(acac)(CO)₂ (4 mg, 0.3 mol%) to give 5-bromo-3-(1-methylpiperidin-4-yl)-1H-indole (1.50 g, 100 %) without further purification. ¹H-NMR: (CDCl₃, 400 MHz) $\delta = 1.82$ (dt, 2H, $J = 12.1$ Hz, $J = 12.6$ Hz, CH₂); 1.98-2.02 (2H, 2xCH₂); 2.12 (t, 2H, $J = 12.1$ Hz, CH₂); 2.34 (s, 3H, CH₃); 2.73 (t, 1H, $J = 12.1$ Hz, CH); 2.97 (d, 2H, $J = 11.6$ Hz, CH₂); 6.92 (s, 1H, CH); 7.18-7.21 (2H, 2xCH); 7.74 (s, 1H, CH); 8.64 (s, 1H, NH). ¹³C-NMR: (CDCl₃, 100 MHz) $\delta = 31.7$ (CH); 31.9 (2xCH₂); 45.4 (CH₃); 55.3 (2xCH₂); 111.2 (C); 11.7 (CH); 119.8 (C); 120.1 (CH); 120.6 (CH); 123.5 (CH); 127.4 (C); 134.0 (C). IR: $\tilde{\nu}$ [cm⁻¹] = 2938 (vs); 2786 (vs); 1452 (vs); 1276 (s); 1128 (s); 796 (s); 769 (s). HRMS found [M]⁺ 292.0547 C₁₄H₁₇BrN₂ requires [M]⁺, 292.0575.

5-Methyl-3-(1-methylpiperidin-4-yl)-1H-indole (8p). The first generation protocol was followed with 1-methyl-4-methylene-piperidine (487 mg, 4.38 mmol), 4-methylphenylhydrazine (535 mg, 4.38 mmol) and Rh(acac)(CO)₂ (3.4 mg, 0.3 mol%) to give 5-methyl-3-(1-methylpiperidin-4-yl)-1H-indole (656 mg, 66 %) without further purification. ¹H-

NMR: (CDCl₃, 400 MHz) δ = 1.87 (dt, 2H, J = 11.8 Hz, J = 12.5 Hz, CH₂); 2.03 (d, 2H, J = 12.5 Hz, CH₂); 2.15 (t, 2H, J = 11.8 Hz, CH₂); 2.35 (s, 3H, CH₃); 2.45 (s, 3H, CH₃); 2.78 (t, 1H, J = 11.8 Hz, CH); 3.00 (d, 2H, J = 11.8 Hz, CH₂); 6.89 (s, 1H, CH); 6.99 (d, 1H, J = 8.3 Hz, CH); 7.22 (d, 1H, J = 8.3 Hz, CH); 7.43 (s, 1H, CH); 8.26 (s, 1H, NH). ¹³C-NMR: (CDCl₃, 100 MHz) δ = 21.5 (CH₃); 32.9 (2xCH₂); 37.2 (CH); 46.5 (CH₃); 56.4 (2xCH₂); 110.9 (CH); 118.7 (CH); 119.9 (CH); 120.5 (C); 123.4 (CH); 126.8 (C); 128.1 (C); 134.7 (C). IR: $\tilde{\nu}$ [cm⁻¹] = 2937 (vs); 2690 (s); 1467 (s); 1376 (s); 1274 (s); 1124 (s); 792 (vs); 630 (s). HRMS found [M]⁺ 228.1626 C₁₅H₂₀N₂ requires [M]⁺, 228.1627.

5-Methoxy-3-(1-methylpiperidin-4-yl)-1H-indole (8q). The first generation protocol was followed with 1-methyl-4-methylene-piperidine (455 mg, 4.09 mmol), 4-methoxy-phenylhydrazine (565 mg, 4.09 mmol) and Rh(acac)(CO)₂ (3.2 mg, 0.3 mol%) to give 3-(1-methylpiperidin-4-yl)-1H-indole (845 mg, 85 %) without further purification. ¹H-NMR: (CDCl₃, 400 MHz) δ = 1.84 (dt, 2H, J = 12.1 Hz, J = 12.8 Hz, CH₂); 2.02 (d, 2H, J = 12.1 Hz, CH₂); 2.14 (t, 2H, J = 12.1 Hz, CH₂); 2.34 (s, 3H, CH₃); 2.75 (t, 1H, J = 12.1 Hz, CH); 2.99 (d, 2H, J = 11.5 Hz, CH₂); 3.84 (s, 3H, CH₃); 6.84 (d, 1H, J = 8.8 Hz, CH); 6.91 (s, 1H, CH); 7.05 (s, 1H, CH); 7.21 (d, 1H, J = 8.8 Hz, CH); 8.34 (s, 1H, NH). ¹³C-NMR: (CDCl₃, 100 MHz) δ = 32.8 (2xCH₂); 37.3 (CH); 46.4 (CH₃); 56.0 (CH₃); 56.3 (2xCH₂); 101.0 (CH); 111.9 (2xCH); 120.6 (CH); 120.7 (C); 126.9 (C); 131.6 (C). IR: $\tilde{\nu}$ [cm⁻¹] = 3141 (s); 2935 (vs); 2830 (vs); 1511 (vs); 1448 (vs); 1276 (vs); 1213 (s); 1056 (s); 792 (s). HRMS found [M+H]⁺ 245.1672 C₁₅H₂₁N₂O requires [M+H]⁺, 245.1654.

5-Fluoro-3-(1-methylpiperidin-4-yl)-1H-indole (8m). The second generation protocol was followed with 1-methyl-4-methylene-piperidine (239 mg, 2.15 mmol), 4-fluoro phenylhydrazine hydrochloride (350 mg, 2.15 mmol), Rh(acac)(CO)₂ (1.7 mg, 0.3 mol%) and TPPTS (18 mg, 1.5 mol%) to give 5-fluoro-3-(1-methylpiperidin-4-yl)-1H-indole (477 mg, 95 %) without further purification.

5-Chloro-3-(1-methylpiperidin-4-yl)-1H-indole (8n). The second generation protocol was followed with 1-methyl-4-methylene-piperidine (223 mg, 2.01 mmol), 4-chloro-phenylhydrazine hydrochloride (360 mg, 2.01 mmol), Rh(acac)(CO)₂ (1.6 mg, 0.3 mol%) and TPPTS (17 mg, 1.5 mol%) to give 5-chloro-3-(1-methylpiperidin-4-yl)-1H-indole (500 mg, 100 %) without further purification.

5-Bromo-3-(1-methylpiperidin-4-yl)-1H-indole (8o). The second generation protocol was followed with 1-methyl-4-methylene-piperidine (190 mg, 1.71 mmol), 4-bromo-phenylhydrazine hydrochloride (381 mg, 1.71 mmol), Rh(acac)(CO)₂ (1.3 mg, 0.3 mol%) and

TPPTS (14.5 mg, 1.5 mol%) to give 5-bromo-3-(1-methylpiperidin-4-yl)-1H-indole (479 g, 96 %) without further purification.

7-Chloro-3-(1-methylpiperidin-4-yl)-1H-indole (8r). The second generation protocol was followed with 1-methyl-4-methylene-piperidine (223 mg, 2.01 mmol), 2-chloro-phenylhydrazine hydrochloride (360 mg, 2.01 mmol), Rh(acac)(CO)₂ (1.5 mg, 0.3 mol%) and TPPTS (17 mg, 1.5 mol%) to give 7-chloro-3-(1-methylpiperidin-4-yl)-1H-indole (480 g, 96 %) without further purification. ¹H-NMR: (CDCl₃, 500 MHz) δ = 1.87 (dt, 2H, J = 12.2 Hz, J = 12.7 Hz, CH₂); 2.05 (d, 2H, J = 12.7 Hz, CH₂); 2.14 (t, 2H, J = 11.7 Hz, CH₂); 2.36 (s, 3H, CH₃); 2.79 (t, 1H, J = 11.7 Hz, CH); 3.00 (d, 2H, J = 11.7 Hz, CH₂); 6.99 (s, 1H, CH); 7.02 (dd, 1H, J = 7.7 Hz, J = 8.0 Hz, CH); 7.17 (d, 1H, J = 7.7 Hz, CH); 7.54 (d, 1H, J = 8.0 Hz, CH); 8.68 (s, 1H, NH). ¹³C-NMR: (CDCl₃, 125 MHz) δ = 32.9 (2xCH₂); 33.0 (CH); 46.5 (CH₃); 56.3 (2xCH₂); 116.7 (C); 117.7 (CH); 119.7 (CH); 120.5 (CH); 121.1 (CH); 122.3 (C); 128.2 (C); 133.6 (C). IR: $\tilde{\nu}$ [cm⁻¹] = 3045 (s); 2942 (s); 2848 (s); 2794 (vs); 2742 (s); 1469 (m); 1444 (s); 1199 (s); 1116 (s); 775 (s). HRMS found [M]⁺ 248.1088 C₁₄H₁₇ClN₂O requires [M]⁺, 248.1080.

Ethyl 4-(2-(1H-indol-3-yl)ethyl)piperazine-1-carboxylate (8d). The second generation protocol was followed with 4-allyl-piperazine-1-carboxylic acid ethyl ester (638 mg, 3.2 mmol), phenylhydrazine (174 mg, 1.6 mmol), Rh(acac)(CO)₂ (1.3 mg, 0.3 mol%) and SULFOXANTPHOS (36 mg, 3 mol%). The crude product was purified by chromatography (silica, EtOAc, cyclohexane, NEt₃) to give ethyl 4-(2-(1H-indol-3-yl)ethyl)piperazine-1-carboxylate (485 mg, 100 %).

3-(3-(Piperidin-1-yl)propyl)-1H-indole (8e). The second generation protocol was followed with 1-(but-3-enyl)piperidine (574 mg, 4.13 mmol), phenylhydrazine (223 mg, 2.06 mmol), Rh(acac)(CO)₂ (1.6 mg, 0.3 mol%) and SULFOXANTPHOS (46 mg, 3 mol%). The crude product was purified by chromatography (silica, EtOAc, cyclohexane, NEt₃) to give 3-(3-(piperidin-1-yl)propyl)-1H-indole (249 mg, 50 %).

N,N-Diethyl-3-(1H-indol-3-yl)-1-phenylpropan-1-amine (8k). The second generation protocol was followed with N,N-diethyl-1-phenylbut-3-en-1-amine (664 mg, 3.26 mmol), phenylhydrazine (176 mg, 1.63 mmol), Rh(acac)(CO)₂ (1.3 mg, 0.3 mol%) and SULFOXANTPHOS (36 mg, 3 mol%). The crude product was purified by chromatography (silica, EtOAc, cyclohexane, NEt₃) to give N,N-diethyl-3-(1H-indol-3-yl)-1-phenylpropan-1-amine (500 mg, 100 %).