Supporting Information (5 pages)

Diastereoselective intramolecular Ritter reaction: generation of a *cis*-fused hexahydro-4a*H*-indeno[1,2-*b*]pyridine ring system with 4a,9b diangular substituents.

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Methyl 1-oxo-2-indanecarboxylate (7)

To a stirred suspension of NaH (5 g, 80% in mineral oil, 166.6 mmol) in 20 mL dimethyl carbonate was added dropwise a solution of 1-indanone (10 g, 75.8 mmol) in 70 mL dimethyl carbonate. The mixture was refluxed at 80 °C for 2 h. After cooling to rt, H_2O (200 mL) was added. The aqueous phase was separated and extracted with CH_2Cl_2 (3 x 50 mL). The combined organic extracts were dried ($MgSO_4$) and concentrated under reduced pressure. The crude oil thus obtained was subjected to chromatography (850 g of silica gel, 4:1 hexane/EtOAc), followed by recrystallization (from *i*-Pr_2O) to yield 11.9 g (83%) of **7** as a white crystalline solid: **mp** 59.8 - 60.1 °C; **^{1}H NMR** (400 MHz, $CDCl_3$): keto-enol (42%-58%), δ 7.76 (d, 1H, J = 8 Hz), 7.63 (ddd, 1H, J = 8, 8, 1 Hz), 7.50 (dd, 1H, J = 8, 1 Hz), 7.40 (ddd, 1H, J = 8, 8, 1 Hz), 3.85 (s, 0.58 OH-enol), 3.79 (s, 3H), 3.73 (dd, 1H, J = 8, 4 Hz), 3.55 (dd, 0.42 H, J = 17, 4 Hz), 3.37 (dd, 1H, J = 17, 8 Hz); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 30.2, 32.4, 52.7, 53.1, 120.7, 124.6, 124.7, 126.5, 126.8, 127.8, 129.3, 135.2, 135.4, 153.5, 169.5, 199.3; **EIMS** [m/z (%)]: 190 ($M^{+\bullet}$, 57), 159 ($M^{+\bullet}$-OCH_3, 18), 158 ($M^{+\bullet}$-$HOCH_3$, 21), 130 ($M^{+\bullet}$-HCO_2CH_3, 100), 77 ($C_6H_5^+$, 33); **HRMS** calculated for $C_{11}H_{10}O_3$: 190.0629, found 190.0633

Methyl 2-(2-cyanoethyl)-1-oxo-2-indanecarboxylate (8)

To a solution of the keto ester **7** (2 g, 10.5 mmol) in *t*-BuOH (25 mL) was added solid KOtBu (0.32 g, 2.8 mmol) and acrylonitrile (1.4 mL, 21.3 mmol). The heterogeneous reaction mixture was stirred at rt for 72 h. H_2O (25 mL) was added and the suspension was extracted with CH_2Cl_2 (3 x 10 mL). The combined extracts were dried ($MgSO_4$) and concentrated under reduced pressure. The crude product was subjected to chromatography (250 g of silica gel, 3:1 hexane/EtOAc) and recrystallization (from *i*-Pr_2O) to provide 2.38 g (93%) of the nitrile **8**: **mp** 76.8-77.3°C; **^{1}H NMR** (400 MHz,

$CDCl_3$): δ 7.79 (d, 1H, J = 8 Hz), 7.67 (ddd, 1H, J = 8, 8, 1 Hz), 7.51 (d, 1H, J = 8 Hz), 7.44 (ddd, 1H, J = 8, 8, 1 Hz), 3.72 (d, 1H, J = 18 Hz), 3.70 (s, 3H), 3.15 (d, 1H, J = 18 Hz), 2.58 (m, 2H), 2.37 (m, 1H), 2.26 (m, 1H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 13.1, 30.4, 37.4, 53.0, 58.8, 119.1, 125.1, 126.5, 128.2, 134.5, 135.9, 152.3, 170.6, 201.0; **EIMS** [m/z (%)]: 243 ($M^{+\bullet}$, 27), 228 ($M^{+\bullet}$-CH_3, 45), 212 ($M^{+\bullet}$-OCH_3, 42), 211 ($M^{+\bullet}$-$HOCH_3$, 39), 184 ($M^{+\bullet}$-CO_2CH_3, 100), 183 ($M^{+\bullet}$-HCO_2CH_3, 66), 130 ($M^{+\bullet}$-CO_2CH_3, -CH_2CH_2CN, 100), 77 ($C_6H_5^+$, 26); **HRMS** calculated for $C_{14}H_{13}NO_3$: 243.0895, found 243.0894

Methyl 2-(cyanoethyl)-1-hydroxy-2-indanecarboxylate (5a)

To a stirred solution of the ketone **8** (0.30 g, 1.2 mmol) in MeOH (5 mL) was added $NaBH_4$ (0.02 g, 0.52 mmol) at 0 °C and the mixture was stirred at 0 °C for 1 h. A HCl-solution (10 mL, 0.6 N) was added. The mixture was brought to pH 7 with K_2CO_3 and extracted with CH_2Cl_2 (3 x 10 mL). The combined extracts were dried (Na_2SO_4) and concentrated under reduced pressure. The crude product was subjected to chromatography (40 g silica gel, 9:1 CH_2Cl_2/EtOAc) to give 0.29 g (98 %) of the alcohol **5a** as a yellow oil: **^{1}H NMR** (250 MHz, $CDCl_3$) – an almost 1:1 mixture of diastereomers was obtained (d.e. = 20 %): δ 7.24 (m, 4H), 5.24 (d, 0.6H, J = 4 Hz), 4.93 (d, 0.4H, J = 8 Hz), 3.75 (s, 3H), 3.56 (d, 0.4H, J = 17 Hz), 3.39 (d, 0.6H, J = 17 Hz), 3.26 (d, 0.4H, J = 8 Hz), 2.97 (d, 0.6H, J = 17 Hz), 2.84 (d, 0.4H, J = 17 Hz), 2.32 (m, 4.6H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 13.5-13.7, 28.01-28.02, 32.0-38.3, 52.3-52.4, 57.9-58.7, 78.7-82.0, 119.0-119.5, 124.2-124.4, 124.5-124.8, 127.2-127.3, 128.7-128.9, 138.8-139.4, 141.9-142.0, 174.0-175.2; **EIMS** [m/z (%)]: 245 ($M^{+\bullet}$, 10), 227 ($M^{+\bullet}$ -H_2O, 16), 213 ($M^{+\bullet}$ -CH_3OH, 7), 186 ($M^{+\bullet}$ -CO_2CH_3, 89), 145 ($M^{+\bullet}$ -HCO_2CH_3, -CH_2CN, 100), 91 ($C_7H_7^+$, 53), 77 ($C_6H_5^+$, 28); **HRMS** calculated for $C_{14}H_{15}NO_3$: 245.1052, found 245.1056

Methyl 2-(cyanoethyl)-1-hydroxy-1-methyl-2-indanecarboxylate (5b)

To a stirred suspension of freshly ground Mg turnings (0.16 g, 6.6 mmol) and I_2 (one crystal) in dry THF (10 mL) was added (via a large cannula) a solution of bromomethane (0.20 mL, 6.9 mmol) in dry THF (5 mL) dropwise at room temperature. The Grignard reagent began to form immediately, and the solution of methyl bromide was added at such a rate that reflux was maintained. After the addition was complete, the mixture was stirred at rt for an additional 30 min. The mixture was cooled to -78°C and a solution of the ketone **8** (1.0 g, 4.1 mmol) in dry THF (5 mL) was added dropwise (via a large cannula). The mixture was then warmed to rt overnight and a saturated solution of NH_4Cl (20 mL) was added. The layers were separated and the aqueous phase was extracted with Et_2O (3 x 20 mL). The combined organic extracts were washed (H_2O, 5 x 20 mL), dried ($MgSO_4$), and concentrated under reduced pressure. The residue was subjected to chromatography (100 g of silica gel, 9:1 CH_2Cl_2/EtOAc) and recrystallization (EtOAc/hexane) to yield 1.01 g (95%) of **5b** as a colorless crystalline solid: **mp** 82.4 – 82.6 °C; **^{1}H NMR** (400 MHz, $CDCl_3$) – mixture of diastereomers (d.e. = 98%) : δ 7.24 (m, 4H), 3.77 (s, 3H), 3.48-3.46 (d, 1H, J = 16 Hz), 2.86-2.83 (s, 1H, J = 16 Hz), 2.63 (s, 1H), 2.41 (ddd, 1H, J = 13, 6, 5 Hz), 2.36 (ddd, 1H, J = 17, 10,

6 Hz), 2.16 (ddd, 1H, J = 17, 10, 6 Hz), 1.83 (ddd, 1H, J = 13, 6, 5 Hz), 1.38 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 13.5, 26.3, 28.3, 35.7, 52.0, 62.0, 83.2, 119.2, 122.5, 124.7, 127.3, 128.3, 137.3, 145.6, 174.0; **EIMS** [m/z (%)]: 259 ($M^{+\bullet}$, 33), 244 ($M^{+\bullet}$ -CH_3, 28), 242 ($M^{+\bullet}$ -OH, 55), 199 ($M^{+\bullet}$ -HCO_2CH_3, 54), 145 ($M^{+\bullet}$ -HCO_2CH_3, -CH_2CH_2CN, 100); **HRMS** calculated for $C_{15}H_{17}NO_3$: 259.1208, found 259.1209

Methyl 2-(2-cyanoethyl)-1-hydroxy-1-phenyl-2,3-dihydro-1*H*-indene-2-carboxylate (5c)

Compound **5c** was prepared following the procedure used for **5b** by replacing bromomethane with bromobenzene (0.73 mL, 6.9 mmol). It was obtained as a colorless crystalline solid in 79% yield following chromatographic purification using 100 g of silica gel, 3:1 hexane/EtOAc and recrystallization from *i*-Pr_2O: **mp** 186.4-186.6 °C; **^{1}H NMR** (400 MHz, $CDCl_3$) – mixture of diastereomers (d.e. = 50%) : δ 7.31-7.08 (m, 9H), 3.73-3.64 (s, 1H), 3.53 (d, 1H, J = 16 Hz), 3.18-3.07 (s, 3H), 2.99-2.96 (d, 1H, J = 16 Hz), 2.50 (m, 1H), 2.10-2.05 (m, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 13.6, 13.9, 28.3, 30.6, 37.1, 38.0, 51.6, 52.1, 63.0, 64.3, 88.0, 88.7, 118.9, 119.4, 124.3-145.8, 172.9, 173.7; **EIMS** [m/z (%)]: 321 ($M^{+\bullet}$, 31), 281 ($M^{+\bullet}$-CH_2CN, 76), 261 ($M^{+\bullet}$-HCO_2CH_3, 20), 249 ($M^{+\bullet}$-$HOCH_3$, -CH_2CN, 47), 233 ($M^{+\bullet}$-HCO_2CH_3, -CO, 41), 105 ($C_6H_5CO^+$, 100), 77 ($C_6H_5^+$, 33); **HRMS** calculated for $C_{20}H_{19}NO_3$: 321.1365, found 321.1361

Methyl 2-(cyanoethyl)-1-hydroxy-1-(2-thienyl)-2-indanecarboxylate (5d)

Compound **5d** was prepared following the procedure used for **5b** by replacing bromomethane with 2-bromothiophene (0.67 mL, 6.9 mmol). It was obtained as a colorless crystalline solid in 84% yield: **mp** (decomposition) 170 °C; **^{1}H NMR** (400 MHz, $CDCl_3$) – mixture of diastereomers (d.e. = 98%) : δ 7.30 (m, 4H), 7.22 (dd, 1H, J = 5, 1 Hz), 6.88 (dd, 1H, J = 5, 4 Hz), 6.59 (dd, 1H, J = 4, 1), 3.66 (d, 1H, J = 16 Hz), 3.44 (s, 3H), 2.99-2.96 (d, 1H, J = 16 Hz), 2.85 (s, 1H), 2.61 (ddd, 1H, J = 14, 10, 7 Hz), 2.31 (m, 2H), 2.13 (ddd, 1H, J = 14, 10, 7 Hz); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 14.0, 28.6, 36.9, 52.1, 64.5, 86.6, 119.3, 123.9, 124.7, 125.0, 125.4, 126.7, 127.7, 129.6, 139.8, 144.8, 147.3, 172.9; **EIMS** [m/z (%)]: 327 ($M^{+\bullet}$, 33), 296 ($M^{+\bullet}$ -OCH_3), 255 ($M^{+\bullet}$ -CH_2CH_2CN, -H_2O, 33), 244 ($M^{+\bullet}$ -C_4H_3S, 33), 112 ($M^{+\bullet}$ -HCO_2CH_3, -CH_2CH_2CN, -C_4H_3S, -H_2O, 100); **HRMS** calculated for $C_{18}H_{17}NO_3S$: 327.0927, found 327.0926

Cis- (4aR*,9bR*) methyl 2-oxo-1,2,3,4,5,9b-hexahydro-4a*H*-indeno[1,2-*b*]pyridine-4a-carboxylate (4a)

The alcohol **5a** (0.5 g, 2.0 mmol) was added to 5 mL of chlorobenzene and 5 mL CH_3SO_3H and the mixture was stirred at 70 °C for 4 h, and then added to ice water (50 mL). The layers were separated and the aqueous phase was extracted with CH_2Cl_2 (3 x 50 mL). The combined organic extracts were dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography (50 g of silica gel, EtOAc) of the residue and recrystallization (from CH_2Cl_2/hexane) afforded 0.36 g (71 %) of the lactam **4a** as a white crystalline solid: **mp**: 181.1-181.5 °C; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.82 (s(br), 1H), 7.34 (m, 1H), 7.24 (m, 3H), 5.32 (d, 1H, J = 3 Hz), 3.81 (s, 3H), 3.38 (d, 1H,

J = 16 Hz), 2.96 (d, 1H, J = 16 Hz), 2.30 (m, 3H), 1.90 (m, 1H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 27.2, 28.8, 41.9, 51.2, 52.6, 61.2, 123.9, 124.9, 127.6, 128.2, 137.9, 141.9, 171.9, 174.9; **EIMS** [m/z (%)]: 245 ($M^{+\bullet}$, 12), 217 ($M^{+\bullet}$ -CO, 1), 189 ($M^{+\bullet}$ -CH_2CH_2CO, 100), 158 ($M^{+\bullet}$ -CH_2CH_2CO, -OCH_3, 17), 130 ($M^{+\bullet}$ -CH_2CH_2CO -CO_2CH_3, 67); **HRMS** calculated for $C_{14}H_{15}NO_3$: 245.1052, found 245.1055

Cis- (4aR*,9bR*) methyl 9b-methyl-2-oxo-1,2,3,4,5,9b-hexahydro-4a*H*-indeno[1,2-*b*]pyridine-4a-carboxylate (4b)

Compound **4b** was prepared following the procedure used for **4a**, by changing the reaction conditions from 4h at 70 °C to 23 h at 70 °C. It was obtained as a yellow oil in 67% yield after chromatographic purification (silica gel, EtOAc): **^{1}H NMR** (250 MHz, $CDCl_3$): δ 7.28 (m, 4H), 6.96 (s(br), 1H), 3.82 (s, 3H), 3.67 (d, 1H, J = 16 Hz), 2.89 (d, 1H, J = 16 Hz), 2.70 (m, 1H), 2.27 (m, 1H), 2.13 (m, 2H), 1.42 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 18.2, 25.0, 31.3, 36.5, 43.2, 51.6, 62.9, 120.2, 126.2, 125.0, 126.3, 133.2, 142.7, 173.1, 174.9 **EIMS** [m/z (%)]: 259 ($M^{+\bullet}$, 12), 244 ($M^{+\bullet}$ -CH_3, 31), 227 ($M^{+\bullet}$ -CH_3OH, 23), 212 ($M^{+\bullet}$ -CH_3OH, -CH_3, 22), 203 ($M^{+\bullet}$ -CH_2CH_2CO, 35), 202 ($M^{+\bullet}$ -CH_2CONH, 38); **HRMS** calculated for $C_{15}H_{17}NO_3$: 259.1208, found 259.1210

Cis- (4aR*,9bR*) methyl-2-oxo-9b-phenyl-1,2,3,4,5,9b-hexahydro-4a*H*-indeno[1,2-*b*]pyridine-4a-carboxylate (4c)

The alcohol **5c** (2 g, 6.2 mmol) was added to 20 mL of CH_3SO_3H at 0 °C and the mixture was stirred at rt for 8 h. Ice water (100 mL) was added and the aqueous layer was extracted with CH_2Cl_2 (3 x 50 mL). The combined organic extracts were dried ($MgSO_4$) and concentrated under reduced pressure. Chromatographic purification (100 g of silica gel, 50:1 CH_2Cl_2/MeOH) and recrystallization (from EtOH) afforded 1.84 g (92 %) of the lactam **4c** as white crystalline solid: **mp**: 204.1-204.3 °C; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.73 (s(br), 1H), 7.28-7.36 (m, 3H), 7.20 (m, 4H), 7.00 (m, 2H), 3.90 (d, 1H, J= 15 Hz), 3.28 (s, 3H), 3.10 (ddd, 1H, J = 18, 12, 6 Hz), 2.94 (d, 1H, J = 15 Hz), 2.43 (ddd, 1H, J = 18, 6, 4 Hz), 2.28 (ddd, 1H, J = 16, 6, 4 Hz), 2.05 (ddd, 1H, J = 16, 12, 6 Hz); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 28.1, 28.5, 39.7, 51.5, 56.5, 73.6, 124.3, 124.6, 127.0, 127.8, 127.9, 128.5, 139.6, 140.7, 145.5, 172.0, 172.9; **EIMS** [m/z (%)]: 321 ($M^{+\bullet}$, 2), 293 ($M^{+\bullet}$-CO, 26), 265 ($M^{+\bullet}$ -CH_2CH_2CO, 100), 233 ($M^{+\bullet}$ -CO, -HCO_2CH_3, 17), 205 ($M^{+\bullet}$, -CH_2CH_2CO, -HCO_2CH_3, 29), 77 ($C_6H_5^+$, 11); **HRMS** calculated for $C_{20}H_{19}NO_3$: 321.1365, found 321.1363

Cis- (4aR*,9bR*) methyl-2-oxo-9b-(2-thienyl)-1,2,3,4,5,9b-hexahydro-4a*H*-indeno[1,2-*b*]pyridine-4a-carboxylate (4d)

Compound **4d** was prepared by following the procedure used for **4c**. It was obtained as a colorless crystalline solid in 85% yield (recrystallization from CH_2Cl_2/hexane): **mp** 202.9-203.2 °C; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.33 (m, 3H), 7.20 (m, 2H), 6.88 (m, 1H), 6.75 (s(br), 1H), 6.63 (m, 1H), 3.81 (d, 1H, J = 16 Hz), 3.50 (s, 3H), 2.92 (d, 1H,

J = 16 Hz), 2.30 (m, 3H), 2.04 (ddd, 1H, J = 16, 12, 6 Hz); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 28.3, 28.4, 39.4, 52.0, 56.9, 71.6, 123.9, 125.3, 126.3, 126.5, 126.8, 127.9, 129.2, 139.0, 145.8, 145.9, 171.1, 172.7; **EIMS** [m/z (%)]: 327 ($M^{+\bullet}$, 11), 299 ($M^{+\bullet}$ -CO, 37), 271 ($M^{+\bullet}$ -CH_2CH_2CO, 100), 239 ($M^{+\bullet}$ -CH_2CH_2CO -CH_3OH, 47), 211 ($M^{+\bullet}$ -CH_2CH_2CO -HCO_2CH_3, 51); **HRMS** calculated for $C_{18}H_{17}NO_3S$: 327.0927, found 327.0928