

New Versatile Pd-Catalyzed Alkylation of Indoles via Nucleophilic Allylic Substitution. In Controlling the Regioselectivity

Marco Bandini,* Alfonso Melloni, Achille Umani-Ronchi*

*Dipartimento di Chimica “G. Ciamician”, via Selmi 2 – 40126, Bologna, Italy
marco.bandini@unibo.it; achille.umanironchi@unibo.it*

Supporting Information

General.

CH₂Cl₂, toluene, THF, Et₂O and DMF were supplied by Fluka in Sureseal® bottles and used as received. All starting materials and reagents were obtained from Aldrich and Fluka and used without further purification. All the allylic carbonates were prepared following a procedure reported in the literature.¹ ¹H-NMR spectra were recorded on Varian 200 (200 MHz) or Varian 300 (300 MHz) spectrometers. Chemical shifts are reported in ppm from TMS with the solvent resonance as the internal standard (deuteriochloroform: δ 7.27 ppm). Data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, br = broad, m = multiplet), coupling constants (Hz). ¹³C-NMR spectra were recorded on a Varian 200 (50 MHz) or Varian 300 (75 MHz) spectrometers with complete proton decoupling. Chemical shifts are reported in ppm from TMS with the solvent as the internal standard (deuteriochloroform: δ 77.0 ppm). GC-mass spectra were performed at an ionizing voltage of 70 eV. LC-electrospray ionization mass spectra were obtained with Agilent Technologies MSD1100 single-quadrupole mass spectrometer. Chromatographic purification was done with 70-230 mesh aluminium oxide 90 mesh alumina or with 240-400 mesh silica gel. IR analysis were performed with a FT-IR spectrophotometer. IR spectra are expressed by wavenumber (cm⁻¹). Elemental analyses were carried out by using a EACE 1110 CHNOS analyzer. Melting points are uncorrected.

General procedure for the C-3 alkylation of indoles by 1,3-diphenylprop-2-enyl methyl carbonate (2a).

All the reactions were carried out at reflux under nitrogen atmosphere. A solution of $[\text{PdCl}(\pi\text{-allyl})]_2$ ($7.5 \cdot 10^{-3}$ mmol, 0.05 equiv) and 1,2-bis(diphenylphosphino)-ethane (dppe) ($1.65 \cdot 10^{-2}$ mmol, 0.11 equiv) in the solvent of choice (anhydrous THF or CH_2Cl_2 , 1.0 mL) was stirred for 30 min and then **2a** (0.3 mmol, 2.0 equiv) was added. The yellow solution was stirred for ca 30 min, followed by the addition of the desired indole **1a-h** (0.15 mmol, 1.0 equiv) and Li_2CO_3 (0.3 mmol, 2.0 equiv). The resulting reaction mixture was refluxed for 24h and then quenched with water (4 mL) and extracted with AcOEt. The combined organics were dried over Na_2SO_4 , concentrated under reduced pressure and purified by flash chromatography on alumina.

3-((E)-1,3-Diphenyl-allyl)-1H-indole (3a)

Colorless oil. R_f 0.3 (*n*-Hexane:AcOEt 90:10).

^1H -NMR (300 MHz, CDCl_3): δ 5.05 (d, 1H, $J = 7.5$ Hz), 6.34-6.40 (m, 1H), 6.66 (dd, 1H, $J = 15.9$, 7.2 Hz), 6.80-7.01 (m, 3H), 7.03-7.26 (m, 12H), 7.91 (br s, 1H). ^{13}C -NMR (50 MHz, CDCl_3): δ 46.1, 111.1, 118.5, 119.3, 119.8, 122.0, 122.6, 126.3 (2 C), 126.6, 126.7, 127.2, 127.7, 128.4, 130.5, 132.5, 136.6, 137.4, 143.3. IR (neat): ν 3429, 3067, 2903, 2863, 2727, 1685, 1618, 1499, 1208, 1128, 971, 740 cm^{-1} . Anal. calcd for ($\text{C}_{23}\text{H}_{19}\text{N}$): C, 89.28; H, 6.19; N, 4.53; Found: C, 89.22; H, 6.13; N, 4.51.

3-((E)-1,3-Diphenyl-allyl)-2-methyl-1H-indole (3b)

Pale yellow oil. R_f 0.3 (*n*-Hexane:AcOEt 95:5).

^1H -NMR (200 MHz, CDCl_3): δ 2.39 (s, 3H), 5.14 (d, 1H, $J = 7.0$ Hz), 6.35-6.51 (m, 1H), 6.78-7.05 (m, 2H), 7.06-7.54 (m, 13H), 7.81 (br s, 1H). ^{13}C -NMR (50 MHz, CDCl_3): δ 12.4, 45.0, 110.2, 112.9, 119.2, 119.4, 120.9, 126.0, 126.3, 127.0, 128.3, 128.4, 128.5, 128.6, 130.6, 131.6, 132.1, 135.3, 137.5, 143.4. IR (neat): ν 3409, 3025, 2923, 2854, 1695, 1618, 1459, 1264, 968 cm^{-1} . Anal. calcd for ($\text{C}_{24}\text{H}_{21}\text{N}$): C, 89.12; H, 6.54; N, 4.33; Found: C, 89.10; H, 6.48; N, 4.31.

3-((E)-1,3-Diphenyl-allyl)-2-phenyl-1H-indole (3c)

Pale yellow solid. Mp 64-66°C. R_f 0.3 (*n*-Hexane:AcOEt 95:5).

^1H -NMR (200 MHz, CDCl_3): δ 5.31 (d, 1H, $J = 7.0$ Hz), 6.38-6.47 (m, 1H), 6.85-7.06 (m, 2H), 7.15-7.60 (m, 18H), 8.12 (s, 1H). ^{13}C -NMR (50 MHz, CDCl_3): δ 45.1, 110.9, 113.9, 119.7, 121.2, 122.1, 126.1, 126.3, 127.1, 127.9, 128.0, 128.2, 128.3, 128.4, 128.6, 128.8, 131.1, 132.3, 132.9,

135.6, 136.3, 137.5, 143.5. IR (nujol): ν 3421, 3050, 2923, 2853, 1600, 1490, 1457, 1307, 1023, 966 cm^{-1} . Anal. calcd for ($\text{C}_{29}\text{H}_{23}\text{N}$): C, 90.35; H, 6.01; N, 3.63; Found: C, 90.28; H, 5.97; N, 3.62.

5-Benzoyloxy-3-((E)-1,3-diphenyl-allyl)-1H-indole (3d)

Colorless oil. R_f 0.3 (*n*-Hexane:AcOEt 95:5).

^1H -NMR (200 MHz, CDCl_3): δ 4.94 (s, 2H), 5.04 (d, 1H, $J = 7.2$ Hz), 6.31-6.48 (m, 1H), 6.70 (dd, 1H, $J = 15.6, 6.8$ Hz), 6.78-6.98 (m, 3H), 7.06-7.50 (m, 16H), 7.86 (br s, 1H). ^{13}C -NMR (50 MHz, CDCl_3): δ 46.2, 70.8, 103.4, 111.7, 112.9, 118.3, 123.4, 126.3 (2 C), 126.6, 127.1, 127.6 (2 C), 127.7, 128.4, 128.5, 130.5, 131.5, 132.0, 132.4, 137.5, 137.6, 143.3, 152.9. IR (neat): ν 3427, 3058, 3026, 2925, 2859, 1598, 1487, 1481, 1379, 1264, 1183, 1026, 968 cm^{-1} . Anal. calcd for ($\text{C}_{30}\text{H}_{25}\text{NO}$): C, 86.71; H, 6.06; N, 3.37; Found: C, 86.68; H, 6.02; N, 3.35.

5-Bromo-3-((E)-1,3-diphenyl-allyl)-1H-indole (3e)

Colorless oil. R_f 0.3 (*n*-Hexane:AcOEt 85:15).

^1H -NMR (200 MHz, CDCl_3): δ 5.02 (d, 1H, $J = 7.0$ Hz), 6.28-6.50 (m, 1H), 6.64 (dd, 1H, $J = 15.8, 7.4$ Hz), 6.87 (m, 1H), 7.08-7.55 (m, 13H), 7.98 (br s, 1H). ^{13}C -NMR (50 MHz, CDCl_3): δ 45.8, 112.5, 112.7, 118.5, 122.3, 123.8, 125.0, 126.3 (2 C), 126.5, 127.2, 128.4, 128.5 (2 C), 130.8, 132.0, 135.2, 137.3, 142.9. IR (nujol): ν 3414, 3018, 2859, 1513, 1471, 1268, 1221, 1093, 971 cm^{-1} . Anal. calcd for ($\text{C}_{23}\text{H}_{18}\text{BrN}$): C, 71.14; H, 4.67; N, 3.61; Found: C, 71.10; H, 4.64; N, 3.58.

5-Cyano-3-((E)-1,3-diphenyl-allyl)-1H-indole (3f)

Colorless oil. R_f 0.3 (*n*-Hexane:AcOEt 85:15).

^1H -NMR (200 MHz, CDCl_3): δ 5.05 (d, 1H, $J = 7.0$ Hz), 6.34-6.42 (m, 1H), 6.64 (dd, 1H, $J = 15.8, 7.2$ Hz), 7.02 (m, 1H), 7.16-7.41 (m, 12H), 7.69 (m, 1H), 8.39 (br s, 1H). ^{13}C -NMR (50 MHz, CDCl_3): δ 45.9, 102.5, 112.0, 119.8, 120.7, 124.7, 125.1, 125.5, 126.3, 126.6, 126.8, 127.4, 128.3, 128.5, 128.6, 131.2, 131.5, 137.1, 138.4, 142.5. IR (neat): ν 3408, 3332, 3058, 3026, 2932, 2853, 2220, 1706, 1616, 1470, 1361, 1222, 1094, 909 cm^{-1} . Anal. calcd for ($\text{C}_{24}\text{H}_{18}\text{N}_2$): C, 86.20; H, 5.43; N, 8.38; Found: C, 86.14; H, 5.38; N, 8.37.

3-((E)-1,3-Diphenyl-allyl)-1-methyl-1H-indole (3g)

Pale yellow oil. R_f 0.3 (*n*-Hexane:AcOEt 97:3).

^1H -NMR (300 MHz, CDCl_3): δ 3.77 (s, 3H), 5.15 (d, 1H, $J = 7.2$ Hz), 6.45-6.51 (m, 1H), 6.73-6.81 (m, 2H), 7.03-7.24 (m, 1H), 7.17-7.58 (m, 13H). ^{13}C -NMR (75 MHz, CDCl_3): δ 46.1, 56.4, 109.1, 118.8, 121.6, 126.2, 126.3, 126.5, 126.8, 127.1, 127.2, 127.3, 128.4, 128.5, 130.1, 130.4, 131.4,

132.7, 137.5, 143.5. IR (neat): ν 3418, 3051, 2920, 1741, 1610, 1437, 1351, 1094, 980 cm^{-1} . Anal. calcd for ($\text{C}_{24}\text{H}_{21}\text{N}$): C, 89.12; H, 6.54; N, 4.33; Found: C, 89.05; H, 6.48; N, 4.35.

Preparation of 3-((*E*)-1-methyl-but-2-enyl)-1*H*-indole (**4**)

The reaction was carried out under nitrogen atmosphere. A solution of $[\text{PdCl}(\pi\text{-allyl})]_2$ ($7.5 \cdot 10^{-3}$ mmol, 0.05 equiv) and triphenyl phosphine ($3.30 \cdot 10^{-2}$ mmol, 0.22 equiv) in anhydrous CH_2Cl_2 (0.5 mL) was stirred for 30 min and then **2c** (0.3 mmol, 2.0 equiv) was added. The yellow solution was stirred for ca 30 min, followed by the addition of **1a** (0.15 mmol, 1.0 equiv), Li_2CO_3 (0.3 mmol, 2.0 equiv) and BSA (0.3 mmol, 2.0 equiv). The resulting reaction mixture was stirred for 8h at reflux (complete consumption of the indole as judged by TLC) and then quenched with water. Usual work-up and purification by flash chromatography (silica gel, *n*-Hexane:AcOEt 95:5) afforded **4** as a light brown oil in 80% yield, 22 mg (**4:5** ratio 16:1).

^1H -NMR (200 MHz, CDCl_3): δ 1.34 (d, 3H, $J = 7.0$ Hz), 1.6 (d, 3H, $J = 5.6$ Hz), 3.64 (m, 1H), 5.37-5.69 (m, 2H), 6.85 (m, 1H), 6.98-7.31 (m, 3H), 7.58 (m, 1H), 7.81 (br s, 1H). ^{13}C -NMR (50 MHz, CDCl_3): δ 17.8, 20.9, 33.9, 111.1, 119.0, 119.6, 120.1, 121.2, 121.8, 123.2, 126.8, 136.2, 136.5. IR (neat): ν 3416, 3058, 3018, 2963, 2932, 2872, 1618, 1456, 1414, 1337, 121, 1094, 1009, 966 cm^{-1} . EI-MS (relative intensity): 115 (26), 144 (39), 155 (33), 170 (100), 185 (55, M). Anal. calcd for ($\text{C}_{13}\text{H}_{15}\text{N}$): C, 84.28; H, 8.16; N, 7.56; Found: C, 84.21; H, 8.09; N, 7.55.

Preparation of 1-((*E*)-1-methyl-but-2-enyl)-1*H*-indole (**5**)

The reaction was carried out under nitrogen atmosphere. A solution of $[\text{PdCl}(\pi\text{-allyl})]_2$ ($7.5 \cdot 10^{-3}$ mmol, 0.05 equiv) and dppe ($1.65 \cdot 10^{-2}$ mmol, 0.11 equiv) in anhydrous THF (1.0 mL) was stirred for 30 min and then **2c** (0.3 mmol, 2.0 equiv) was added. The bright yellow solution was stirred for ca 30 min, followed by the addition of **1a** (0.15 mmol, 1.0 equiv) and K_2CO_3 (0.3 mmol, 2.0 equiv). The resulting reaction mixture was stirred for 12h at reflux (complete consumption of the indole as judged by TLC) and then quenched with water. Usual work-up and purification by flash chromatography (silica gel, *n*-Hexane:AcOEt 99:1) afforded **5** as a colorless oil in 90% yield, 25 mg (**4:5** ratio > 1:50).

^1H -NMR (300 MHz, CDCl_3): δ 1.53 (d, 3H, $J = 6.3$ Hz), 1.61 (d, 3H, $J = 6.0$ Hz), 4.96 (m, 1H), 5.40-5.64 (m, 2H), 6.44 (m, 1H), 6.98-7.18 (m, 3H), 7.28-7.31 (m, 1H), 7.54-7.58 (m, 1H). ^{13}C -NMR (50 MHz, CDCl_3): δ 16.7, 20.0, 48.4, 101.5, 109.6, 119.4, 121.0, 121.6, 126.5, 127.7, 128.4, 132.3, 136.2. IR (neat): ν 3063, 3020, 2941, 2830, 1654, 1654, 1601, 1528, 1449, 1404, 1221, 1212,

1048, 893 cm^{-1} EI-MS (relative intensity): 69 (24), 117 (100), 185 (24, M). Anal. calcd for ($\text{C}_{13}\text{H}_{15}\text{N}$): C, 84.28; H, 8.16; N, 7.56; Found: C, 84.25; H, 8.11; N, 7.58.

Preparation of 3-cyclohex-2-enyl-1*H*-indole (6)

Prepared by following the alkylation procedure described above for **4**, with addition of allylic carbonate **2d** instead of **2c**. The reaction was quenched after 24h at reflux (complete consumption of the indole as judged by TLC). Usual work-up and purification by flash chromatography (silica gel, *n*-Hexane:AcOEt 95:5) afforded **6** as a light brown oil in 89% yield, 26 mg (**6**:**7** ratio 8:1).

^1H -NMR (300 MHz, CDCl_3): δ 1.49-1.80 (m, 3H), 1.90-2.06 (m, 3H), 3.61-3.73 (m, 1H), 5.79 (m, 2H), 6.88 (m, 1H), 6.98-7.38 (m, 3H), 7.54-7.86 (m, 1H), 7.85 (br s, 1H). ^{13}C -NMR (50 MHz, CDCl_3): δ 20.8, 25.2, 30.1, 32.6, 111.1, 119.0, 119.2, 120.9, 121.3, 121.8, 126.6, 127.5, 130.3, 136.6. IR (neat): ν 3420, 3038, 3008, 2960, 2922, 2865, 1616, 1444, 1408, 1331, 1208, 1088, 972 cm^{-1} . EI-MS (relative intensity): 63 (8), 83 (17), 117 (48), 168 (100), 197 (100, M). Anal. calcd for ($\text{C}_{14}\text{H}_{15}\text{N}$): C, 85.24; H, 7.66; N, 7.10; Found: C, 85.21; H, 7.61; N, 7.08.

Preparation of 1-cyclohex-2-enyl-1*H*-indole (7)

The reaction was carried out under nitrogen atmosphere. A solution of $[\text{PdCl}(\pi\text{-allyl})]_2$ ($7.5 \cdot 10^{-3}$ mmol, 0.05 equiv) and triphenyl phosphine ($3.30 \cdot 10^{-2}$ mmol, 0.22 equiv) in anhydrous DMF (1.0 mL) was stirred for 30 min and then **2d** (0.3 mmol, 2.0 equiv) was added. The bright yellow solution was stirred for ca 30 min, followed by the addition of **1a** (0.15 mmol, 1.0 equiv) and Cs_2CO_3 (0.3 mmol, 2.0 equiv). The resulting reaction mixture was stirred for 24h at rt (complete consumption of the indole as judged by TLC) and then quenched with water. Usual work-up and purification by flash chromatography (silica gel, *n*-Hexane:AcOEt 99:1) afforded **7** as a colorless oil in 91% yield, 27 mg (**6**:**7** ratio 1:12).

^1H -NMR (300 MHz, CDCl_3): δ 1.62-1.85 (m, 2H), 1.86-2.05 (m, 1H), 2.07-2.32 (m, 3H), 5.08 (m, 1H), 5.82-5.92 (m, 1H), 6.07-6.20 (m, 1H), 6.53 (m, 1H), 7.10-7.30 (m, 3H), 7.40-7.50 (m, 1H), 7.68-7.78 (m, 1H). ^{13}C -NMR (50 MHz, CDCl_3): δ 19.9, 24.9, 29.9, 51.2, 100.6, 109.6, 119.3, 120.9, 121.1, 126.2, 126.6, 129.0, 132.2, 135.4. IR (neat): ν 3051, 3025, 2936, 2866, 2833, 1609, 1508, 1458, 1404, 1309, 1288, 1227, 1211, 882 cm^{-1} EI-MS (relative intensity): 81 (26), 117 (100), 197 (31, M). Anal. calcd for ($\text{C}_{14}\text{H}_{15}\text{N}$): C, 85.24; H, 7.66; N, 7.10; Found: C, 85.18; H, 7.58; N, 7.12.

Preparation of 3-((*E*)-1-Methyl-3-phenyl-allyl)-1*H*-indole (**8**)

Prepared by following the alkylation procedure described above for **4**, with addition of allylic carbonate **2e** instead of **2c**. The reaction was quenched after 14h at reflux (complete consumption of the indole as judged by TLC). Usual work-up and purification by flash chromatography (silica gel, *n*-Hexane:AcOEt 95:5) afforded **8** as a light brown oil in 82% yield, 30 mg (**8:9** ratio >10:1).

Spectral data for **8** were consistent with data reported in the literature.²

Preparation of 1-((*E*)-1-Methyl-3-phenyl-allyl)-1*H*-indole (**9**)

Prepared by following the alkylation procedure described above for **7**, with addition of allylic carbonate **2e** instead of **2d**. The reaction was quenched after 20h at rt (complete consumption of the indole as judged by TLC). Usual work-up and purification by flash chromatography (*n*-Hexane:AcOEt 99:1) afforded **9** as a light yellow oil in 84% yield, 31 mg (**8:9** ratio 1: 50).

¹H-NMR (200 MHz, CDCl₃): δ 1.78 (d, 3H, *J* = 7.0 Hz), 5.28 (dq, 1H, *J* = 7.0, 3.0 Hz), 6.46 (m, 2H), 6.60 (m, 1H), 7.06-7.48 (m, 9H), 7.61-7.73 (m, 1H). ¹³C-NMR (50 MHz, CDCl₃): δ 20.3, 52.8, 101.6, 109.8, 119.4, 120.9, 121.4, 124.6, 126.5, 127.8, 128.6, 128.7, 130.3, 130.5, 135.7, 136.4. IR (neat): ν 3053, 3025, 2975, 2929, 1601, 1508, 1476, 1459, 1309, 1218, 965 cm⁻¹. EI-MS (relative intensity): 91 (43), 131 (100), 247 (21, M). Anal. calcd for (C₁₈H₁₇N): C, 87.41; H, 6.93; N, 5.66; Found: C, 87.38; H, 6.88; N, 6.90.

Preparation of benzyl-(1*H*-indol-2-yl-methyl)-amine (**11**)

To a mixture of **10**³ (6.9 mmol, 1.0 equiv), and MgSO₄ (34.5 mmol, 5.0 equiv) in toluene (40 mL), benzylamine (10.35 mmol, 1.5 equiv) was added. The reaction was kept under reflux for 48h (complete consumption of **10** as judged by GC-MS). The solvent was then evaporated under reduced pressure to give a dark viscous oil (¹H-NMR data of the crude were consistent with data of the benzylimine reported in the literature).⁴ The crude was dissolved in methanol (50 mL) and then NaBH₄ (13.8 mmol, 2.0 equiv) was added at 0°C portionwise. The reaction mixture was stirred at rt for 6h and then quenched with water (10 mL). Methanol was removed under reduced pressure, the aqueous phase was extracted with AcOEt, the combined organics were dried over Na₂SO₄ and then concentrated to give a brown oil which was dissolved in cyclohexane. The insoluble solid was filtered off and evaporation of the solvent gave **11** as a red/brown viscous oil in 89% yield, 1.45 g (starting from **10**).

¹H-NMR (300 MHz, CDCl₃): δ 3.83 (s, 2H), 3.99 (s, 2H), 3.36 (s, 1H), 7.09-7.18 (m, 2H), 7.30-7.39 (m, 6H), 7.58 (d, 1H, *J* = 1.5 Hz), 8.59 (br, 1H). ¹³C-NMR (75 MHz, CDCl₃): δ 46.1, 53.1,

100.4, 110.7, 119.6, 120.1, 121.4, 121.6, 128.2, 128.4, 128.5, 136.0, 137.3, 139.7. IR (nujol): ν 3177, 2930, 1481, 1281, 1088 cm^{-1} . Anal. calcd for ($\text{C}_{16}\text{H}_{16}\text{N}_2$): C, 81.32; H, 6.82; N, 11.85; Found: C, 81.28; H, 6.77; N, 11.81.

Preparation of carbonic acid (*E*)-4-[benzyl-(1*H*-indol-2-yl-methyl)-amino]-but-2-enyl methyl ester (12**)**

To a solution of **11** (2.5 mmol, 1.0 equiv) and Et_3N (3.0 mmol, 1.2 equiv) in dry THF (30 mL), ethyl 4-bromocrotonate (5.0 mmol, 2.0 equiv) was added at 0°C . The ice bath was removed and the reaction mixture was stirred at rt for 4h. Finally, the mixture was filtered and solid residue washed with Et_2O . Evaporation of the volatiles under reduced pressure and subsequent purification by flash-chromatography (silica gel, cyclohexane:AcOEt 85:15) afforded the (*E*)-4-[benzyl-(1*H*-indol-2-yl-methyl)-amino]-but-2-enoic acid ethyl ester as a brown oil in 70% yield, 638 mg. [^1H -NMR, 200 MHz: δ 1.30 (t, J = 6.8 Hz, 3H), 3.26 (d, J = 6.0 Hz, 2H), 3.65 (s, 2H), 3.76 (s, 2H), 4.19 (q, J = 7.0 Hz, 2H), 6.08 (dd, J = 14.8, 2.2 Hz, 1H), 6.40 (s, 1H), 6.97-7.05 (m, 1H), 7.09-7.14 (m, 2H), 7.21-7.35 (m, 6H), 7.56 (d, J = 7.4 Hz, 1H), 8.37 (br, 1H). ^{13}C -NMR, 50 MHz: δ 14.3, 51.3, 54.2, 58.3, 60.4, 101.7, 110.7, 119.7, 120.1, 121.6, 123.3, 127.3, 128.5 (2C), 128.8 (2C), 136.0, 138.2, 145.5, 166.1].

The ethyl ester (1.7 mmol, 1.0 equiv) was dissolved in dry toluene (20 mL) and then DIBAL (1.0 M in hexane, 4.25 mmol, 2.5 equiv) was added dropwise at -78°C . The reaction was stirred at -78°C for 1h (complete consumption of the ester as judged by TLC) and then quenched with 0.5 mL of acetic acid: H_2O (1:1 mixture). The organics were washed with H_2O concentrated under reduced pressure and purified by flash chromatography (silica gel, CH_2Cl_2 :MeOH 9:1) to afford (*E*)-4-[benzyl-(1*H*-indol-2-ylmethyl)-amino]-but-2-en-1-ol as a viscous oil in 82% yield, 426 mg. [^1H -NMR, 300 MHz: δ 3.13 (d, J = 4.8 Hz, 2H), 3.65 (s, 2H), 3.76 (s, 2H), 4.11 (d, J = 5.2 Hz, 2H), 5.77-5.81 (m, 2H), 6.37 (d, J = 1.2 Hz, 1H), 7.08-7.17 (m, 2H), 7.27-7.36 (m, 6H), 7.55 (dd, J = 0.6, 7.8 Hz, 1H), 8.51 (br, 1H). ^{13}C -NMR, 50 MHz: δ 51.1, 55.2, 58.2, 63.1, 101.4, 110.7, 119.6, 120.0, 121.5, 127.2, 128.4 (2C), 128.5, 129.0, 132.6, 136.0, 136.5, 138.5].

To a solution of the alcohol (1.0 mmol, 1.0 equiv) and pyridine (2.0 mmol, 2.0 equiv) in dry Et_2O (10 mL), methyl chloroformate (1.5 mmol, 1.5 equiv) dissolved in dry Et_2O (1.0 mL) was added dropwise at 0°C . The reaction mixture was stirred for 24h at rt then quenched with water (5 mL), extracted with AcOEt, dried over Na_2SO_4 , concentrated under reduced pressure and purified by flash chromatography (silica gel, cyclohexane:AcOEt 9:1) to give **12** as a yellow oil in 65% yield, 237 mg.

¹H-NMR (200 MHz, CDCl₃): δ 3.09 (d, *J* = 5.8 Hz, 2H), 3.59 (s, 2H), 3.70 (s, 2H), 3.75 (s, 3H), 4.58 (d, *J* = 5.6 Hz, 2H), 5.65-5.85 (m, 2H), 6.34 (s, 1H), 7.08-7.22 (m, 2H), 7.28-7.32 (m, 6H), 7.50 (d, *J* = 7.2 Hz, 1H), 8.39 (br, 1H). ¹³C-NMR (75 MHz, CDCl₃): δ 50.8, 54.8, 57.9, 67.8, 101.4, 110.6, 119.5, 120.0, 121.4, 126.7, 127.1, 128.3, 128.4, 128.9, 132.9, 135.9, 136.5, 138.5, 155.6. IR (neat): ν 3407, 3058, 3027, 2952, 2813, 1747, 1455, 1267, 1137, 943 cm⁻¹. Anal. calcd for (C₂₂H₂₄N₂O₃): C, 72.50; H, 6.64; N, 7.69; Found: C, 72.48; H, 6.59; N, 7.63.

Preparation of 2-benzyl-4-vinyl-2,3,4,9-tetrahydro-1*H*-β-carboline (14)

The reaction was carried out at rt under nitrogen atmosphere. A solution of [PdCl(π-allyl)]₂ (5·10⁻³ mmol, 0.05 equiv) and triphenyl phosphine (2.2·10⁻² mmol, 0.22 equiv) in anhydrous CH₂Cl₂ (1.0 mL) was stirred for 30 min and then **12** (0.1 mmol, 1.0 equiv), Li₂CO₃ (0.2 mmol, 2.0 equiv) and BSA (0.2 mmol, 2.0 equiv) were added. The resulting reaction mixture slowly turned from yellow to orange. The reaction was stirred for 4h at rt (complete consumption of **12** as judged by TLC) and then quenched with water (4 mL) and extracted with AcOEt. The combined organics were dried over Na₂SO₄ and concentrated under reduced pressure. The crude was purified by passage through a pad of silica gel (silica gel, *n*-Hexane:AcOEt 90:10) affording **14/15** as a orange oil in 91% yield, 26 mg (**14/15** ratio >50/1, determined by ¹H-NMR on the crude mixture).

¹H-NMR (200 MHz, CDCl₃): δ 2.58 (dd, 1H, *J* = 11.6, 7.0 Hz), 2.89 (dd, 1H, *J* = 11.6, 4.8 Hz), 5.34-5.55 (m, 2H), 3.68 (d, *J* = 3.0 Hz, 3H), 5.03-5.25 (m, 2H), 5.88 (ddd, *J* = 10.0, 8.0, 1.8 Hz, 1H), 6.90-7.12 (m, 2H), 7.15-38 (m, 6H), 7.45 (d, *J* = 8.2 Hz, 1H), 7.60 (br s, 1H). ¹³C-NMR (50 MHz, CDCl₃): δ 38.5, 50.1, 57.3, 61.9, 110.0, 110.7, 115.3, 119.1, 119.3, 121.2, 127.1, 127.2, 128.3, 129.0, 132.1, 136.0, 138.4, 140.4.

IR (neat): ν 3403, 3060, 2932, 2802, 1637, 1453, 1330, 1228, 1012, 915 cm⁻¹. LC-ESI-MS: 289 (M+1). Anal. calcd for (C₂₀H₂₀N₂): C, 83.30; H, 6.99; N, 9.71; Found: C, 83.25; H, 6.94; N, 9.68.

Preparation of 2-benzyl-4-vinyl-1,2,3,4-tetrahydro-pyrazino[1,2-*a*]indole (15)

The reaction was carried out at rt under nitrogen atmosphere. A solution of [PdCl(π-allyl)]₂ (5·10⁻³ mmol, 0.05 equiv) and triphenyl phosphine (2.2·10⁻² mmol, 0.22 equiv) in anhydrous DMF (3.0 mL) was stirred for 30 min and then **12** (0.1 mmol, 1.0 equiv) and Cs₂CO₃ (0.2 mmol, 2.0 equiv) were added. The resulting reaction mixture slowly turned from yellow to orange. The reaction was stirred for 3h at 50°C (complete consumption of **12** as judged by TLC) and then quenched with water (4 mL) and extracted with AcOEt. The combined organics were dried over Na₂SO₄ and

concentrated under reduced pressure. The crude was purified by passage through a pad of silica gel (silica gel, *n*-Hexane:AcOEt 99:1) affording **14/15** as a yellow oil in 85% yield, 24 mg (**14/15** ratio = 1/8, determined by ^1H -NMR on the crude mixture).

^1H -NMR (200 MHz, CDCl_3): δ 2.86 (t, 2H, $J = 3.2$ Hz), 3.54-3.66 (m, 3H), 3.90 (d, 1H, $J = 14.4$ Hz), 4.70-4.77 (m, 1H), 5.10 (d, 1H, $J = 10.6$ Hz), 5.16 (d, 1H, $J = 2.8$ Hz), 5.96 (ddd, 1H, $J = 10.6$, 8.2, 2.8 Hz), 6.11 (s, 1H), 6.95-7.01 (m, 2H), 7.21-7.29 (m, 6H), 7.43-7.48 (m, 1H). ^{13}C -NMR (50 MHz, CDCl_3): δ 51.0, 55.4, 56.0, 61.4, 96.1, 109.9, 116.3, 119.1, 119.3, 119.7, 126.7, 127.8, 127.9, 128.2, 133.7, 135.2, 136.9, 137.0. IR (neat): ν 3078, 3058, 2800, 2746, 1642, 1456, 1331, 1014, 923 cm^{-1} . LC-ESI-MS: 289 (M+1). Anal. calcd for ($\text{C}_{20}\text{H}_{20}\text{N}_2$): C, 83.30; H, 6.99; N, 9.71; Found: C, 83.31; H, 6.98; N, 9.70.

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