General information

All reactions involving air-sensitive compounds were carried out under a N₂ atmosphere in oven-dried glassware with magnetic stirring. Temperatures are reported as bath temperatures. Solvents used in extraction and purification were distilled prior to use. TLC was performed on alumina-backed plates coated with silica gel 60 with F₂₅₄ indicator; the chromatograms were visualized by UV light (254 nm) and/or by staining with a Ce/Mo reagent, anisaldehyde or phosphomolybdic acid solution and subsequent heating. R_f values refer to silica gel. Flash column chromatography was carried out on silica gel 60, 230-400 mesh. Melting points were obtained with open capillary tubes and are uncorrected. ¹H NMR spectra were recorded at 400 or 300 MHz. Chemical shifts are reported in ppm from tetramethylsilane with the residual solvent resonance as the internal standard (CHCl₃: δ 7.26). Data are reported as follows: chemical shift, multiplicity (s: singlet, br s: broad singlet, d: doublet, dd: doublet of doublets, dt: doublet of triplets, ddd: doublet of doublet of doublets, t: triplet, t app: apparent triplet, td: triplet of doublets, tdd: triplet of doublet of doublets, q: quartet, m: multiplet), coupling constants (J in Hz) and integration. ¹³C NMR spectra were recorded at 100.6 or 75.4 MHz using broadband proton decoupling. Chemical shifts are reported in ppm with the solvent resonance as internal standard (CDCl₃: δ 77.16). Carbon multiplicities were assigned by DEPT techniques. GC-MS analysis and low-resolution electron impact mass spectra (EI-LRMS) were obtained at 70 eV on a mass spectrometer and only the molecular ions and/or base peaks as well as significant peaks in MS are given. High-resolution mass spectrometry (HRMS) was carried out on a mass spectrometer. Infrared spectra were recorded with a FT-IR spectrophotometer. Melting points were measured on a Gallenkamp apparatus using open capillary tubes and are uncorrected. All commercially available reagents were used without purification unless otherwise indicated and were purchased from standard chemical suppliers.
Experimental procedures and characterization data for synthesized compounds

**Synthesis of trifluoroacetamides 1:**

1. **2,2,2-Trifluoro-N-(3-fluorophenyl)acetamide (1a):** purification by crystallization from hexane afforded 1a (6.37 g, 77%) as a white solid: 67–69 °C (lit. mp 69–70 °C); 1H NMR (300 MHz, CDCl3) δ = 8.38 (br s, 1H), 7.48 (dt, J = 10.2, 2.1 Hz, 1H), 7.34 (td, J = 8.2, 2.1 Hz, 1H), 7.26 (dd, J = 8.2, 2.1, 1.1 Hz, 1H), 6.95 (td, J = 8.2, 2.5, 1.1 Hz, 1H); 13C NMR (75.4 MHz, CDCl3) δ = 155.5 (q, J = 37.8 Hz, C), 136.5 (d, J = 8.2, 1H), 130.7 (d, J = 9.2 Hz, CH), 116.2 (d, J = 3.2 Hz, CH), 115.7 (q, J = 288.4 Hz, C), 113.5 (d, J = 21.2 Hz, CH), 108.5 (d, J = 26.6 Hz, CH); EI-LRMS m/z 207 (M+, 100), 138 (36), 95 (32), 83 (18).

2. **N-(3-Chlorophenyl)-2,2,2-trifluoroacetamide (1b):** purification by crystallization from hexane afforded 1b (7.15 g, 77%) as a white solid: 68–70 °C (lit. mp 66–68 °C); 1H NMR (300 MHz, CDCl3) δ = 8.24 (br s, 1H), 7.66 (t, J = 2.0 Hz, 1H), 7.42 (ddd, J = 8.0, 2.0, 1.1 Hz, 1H), 7.31 (t, J = 8.0 Hz, 1H), 7.22 (dd, J = 8.0, 2.0, 1.1 Hz, 1H); 13C NMR (75.4 MHz, CDCl3) δ = 155.3 (d, J = 37.8 Hz, 1H), 136.2 (C), 135.2 (C), 130.5 (C), 126.7 (C), 121.0 (CH), 118.8 (CH), 115.7 (d, J = 288.5 Hz, C); EI-LRMS m/z 225 (M+ +2, 33), 223 (M+, 100), 154 (51), 126 (19).

**Synthesis of 2,2,2-trifluoro-N-(3-fluoro-2-iodophenyl)acetamide (2a):**

To a solution of N,N,N′,N′-tetramethylethylenediamine (4.54 cm³, 30.2 mmol) in anhydrous THF (40 cm³) at −80 °C was added slowly tBuLi (20 cm³ of a 1.5M solution in pentane, 30 mmol). After 5 min a solution of 1a (2.48 g, 12 mmol) in THF (10 cm³) was added dropwise avoiding temperature exceed −70 °C. After 40 min at −80 °C, a solution of iodine in THF (10 cm³) was added dropwise to the reaction mixture. The resulting solution was stirred for 40 min at −80 °C. Then, the reaction mixture was allowed to reach room temperature and quenched with an aqueous solution of Na2S2O3 (10%). The aqueous phase was extracted with Et2O (3 × 30 cm³), and the combined organic layers were washed with HCl 1M, dried over anhydrous Na2SO4, and evaporated under reduced pressure. The crude was purified by column chromatography (hexane/EtOAc, 8/1) on silica gel affording 2a (2.31 g, 58%) as a white-pale reddish solid: Rf 0.44 (hexane/AcOEt, 6/1); mp 104–106 °C; 1H NMR (300 MHz, CDCl3) δ = 8.39 (br s, 1H), 8.05 (d, J = 8.3 Hz, 1H), 7.40 (td, J = 8.3, 2.1 Hz, 1H), 7.01–6.94 (m, 1H); 13C NMR (75.4 MHz, CDCl3) δ = 155.0 (q, J = 37.7 Hz, C), 137.4 (d, J = 3.6 Hz, C), 130.9 (d, J = 8.9 Hz, CH), 117.5 (d, J = 3.1 Hz, CH), 115.7 (q, J = 288.5 Hz, C), 113.3 (d, J = 23.8 Hz, CH), 79.0 (d, J = 28.8 Hz, C); EI-LRMS m/z 333 (M+, 53), 206 (100), 186 (26), 137 (13), 109 (22); IR (KBr) 3218, 3061, 1717, 1580, 1548, 1463, 1207, 1165, 788, 733 cm⁻¹; HRMS caleld for C8H4F4INO, 332.9274; found, 332.9283.

**Synthesis of 4-fluoro-2-phenyl-1H-indole (3a) from 2a:**

A mixture of 2a (169 mg, 0.5 mmol), phenylacetylene (77 mg, 0.75 mmol), PdCl2(PPh3)2 (10 mg, 3 mol%), CuI (5 mg, 5 mol%) and Et3NH (54 mg, 0.75 mmol) in anhydrous DMA (4 cm³) was heated for 4 h at 80 °C under a nitrogen atmosphere (cyclization was completed as monitored by GC-MS). CH2Cl2 (20 cm³) and...
water (20 cm³) were added to the cooled reaction mixture. The separated aqueous phase was extracted with CH₂Cl₂ (2 × 20 cm³). The combined organic layers were washed with water (2 × 60 cm³). The organic layer was dried over Na₂SO₄ and concentrated at reduced pressure. The remaining residue was purified by column chromatography (hexane/EtOAc, 8:1) on silica gel affording 3a (92 mg, 87%) as a brown solid: Rf 0.47 (hexane/AcOEt, 4:1); mp 62–64 °C (lit. ² mp 65–67 °C); ¹H NMR (300 MHz, CDCl₃) δ = 8.45 (br s, 1H), 7.70–7.63 (m, 2H), 7.51–7.43 (m, 2H), 7.41–7.33 (m, 1H), 7.21–7.09 (m, 2H), 6.93 (dd, J = 2.2, 0.7 Hz, 1H), 6.84 (ddd, J = 10.3, 7.4 1.2 Hz, 1H); ¹³C NMR (75.4 MHz, CDCl₃) δ = 156.5 (d, J = 246.8 Hz, C), 139.3 (d, J = 11.2 Hz, C), 138.0 (C), 131.9 (C), 129.2 (2 × CH), 128.1 (CH), 125.3 (2 × CH), 122.8 (d, J = 7.6 Hz, CH), 118.6 (d, J = 22.4 Hz, C), 107.1 (d, J = 3.6 Hz, CH), 105.1 (d, J = 18.9 Hz, CH), 95.8 (CH); HRMS calcd for C₁₄H₁₀FN, [M⁺] 211.0797; found, 211.0787.

General procedure for the synthesis of O-2,3-dihalophenyl N,N-diethylcarbamates 4:⁴

nBuLi (8.25 cm³ of a 1.6M solution in hexane, 13.2 mmol) was added to a solution of iPr₂NH (1.85 cm³, 13.2 mmol) in THF (40 cm³) at 0 °C. After 30 min at 0 °C, the LDA solution was cooled to −78 °C, and the corresponding 3-halophenyl N,N-diethylcarbamate (12 mmol) was added. The resulting solution was stirred for 30 min at −78 °C, and then iodine (3.66 g, 14.4 mmol) was added. After 30 min at low temperature, the reaction mixture was allowed to reach room temperature and quenched with saturated aqueous Na₂S₂O₃. The aqueous phase was extracted with Et₂O (3 × 30 cm³), and the combined organic layers were washed with HCl 1M, dried over anhydrous Na₂SO₄, and evaporated under reduced pressure. The crude was purified by column chromatography (hexane/EtOAc, 5:1) on silica gel affording the title compounds 4, whose spectroscopic and characterization data have been previously reported.⁴

Procedure for the synthesis of 2,3-dihalophenyl ethers 5a and 5b:⁵

To a solution of lithium 2,2,6,6-tetramethylpiperidide (20 mmol, generated from nBuLi and 2,2,6,6-tetramethylpiperidine) in dry THF (30 cm³), a solution of tBu₂Zn (22 mmol, generated from tBuLi and ZnCl₂) in dry THF (30 cm³) was added at −78 °C, and the reaction mixture was stirred at 0 °C for 30 min. Then, the corresponding 3-haloanisole (10 mmol) was added at −78 °C, the reaction mixture was allowed to reach −45 °C (for X = Cl) or −30 °C (for X = Br), and it was stirred at this temperature overnight. Iodine (17.78 g, 70 mmol) in THF (30 cm³) was added to the reaction mixture and it was stirred at room temperature for 2 h. The reaction was quenched with saturated Na₂S₂O₃, and the aqueous solution was extracted with EtOAc (3 × 15 cm³). The combined organic layers were washed with water (2 × 30 cm³) and dried over anhydrous Na₂SO₄. The solvent was removed under reduced pressure and the residue was purified by column chromatography (hexane/EtOAc) to afford the 2,3-dihalophenylethers 5a and 5b.

1-Chloro-2-ido-3-methoxybenzene (5a): purification by column chromatography (hexane/EtOAc, 20:1) on silica gel afforded 5a (2.23 g, 86%) as a white solid: Rf 0.28 (hexane/AcOEt, 20:1); mp 52–54 °C (lit. ⁶ mp 53.5 °C); ¹H NMR (300 MHz, CDCl₃) δ = 7.22 (t, J = 8.1 Hz, 1H), 7.08 (ddd, J = 8.1, 1.3, 0.5 Hz, 1H), 6.67 (dd, J = 8.1, 1.3 Hz, 1H), 3.87 (s, 3H); ¹³C NMR (75.4 MHz, CDCl₃) δ = 159.9 (C), 139.8 (C), 129.9 (CH),
121.9 (CH), 108.5 (CH), 91.3 (C), 56.9 (CH₃); EI-LRMS m/z 270 (M⁺+2, 31), 268 (M⁺, 100), 253 (23), 225 (12), 126 (24), 111 (11); HRMS calcd for C₇H₈ClIO, 267.9152; found, 267.9166.

**1-Bromo-2-iodo-3-methoxybenzene (5b):** purification by column chromatography (hexane/EtOAc, 20/1) on silica gel afforded 5b (2.60 g, 83%) as a white solid: Rₜ 0.25 (hexane/AcOEt, 20/1); mp 63–65 ºC (lit. 5b mp 62.5–64 ºC); ¹H NMR (300 MHz, CDCl₃) δ = 7.26 (td, J = 8.0, 1.2 Hz, 1H), 7.18 (dt, J = 8.0, 1.2 Hz, 1H), 6.71 (dd, J = 8.0, 1.2 Hz, 1H), 3.87 (s, 3H); ¹³C NMR (75.4 MHz, CDCl₃) δ = 161.0 (C), 131.2 (C), 130.2 (CH), 125.2 (CH), 108.9 (CH), 94.4 (C), 57.0 (CH₃); EI-LRMS m/z 314 (M⁺+2, 100), 312 (M⁺, 100), 299 (21), 297 (20), 172 (42), 170 (40); HRMS calcd for C₁₀H₇BrIO, 311.8647; found, 311.8635.

**General procedure for the synthesis of N-(2,3-dihalophenyl)-2-hydroxy-2-methylpropanamides 8 from 4:**

To a solution of the corresponding 2,3-dihalophenyl N,N-diethylcarbamate 4 (1 equiv) in EtOH (10 cm³/mmol) NaOH (10 equiv) was added, and the mixture was refluxed for 5–8 h (completion of the hydrolysis was monitored by GC-MS). After the mixture was cooled to room temperature, most of the EtOH was removed under reduced pressure and the residue was diluted with Et₂O and water. The organic phase was rejected and then, the aqueous solution was carefully neutralized with a HCl 1M solution. The aqueous phase was extracted with Et₂O (3 × 30 cm³), and the combined organic layers were washed with brine, dried over anhydrous Na₂SO₄, and evaporated under reduced pressure. Without further purification, the crude phenol 6 was dissolved in anhydrous DMF (2 cm³/mmol) under a nitrogen atmosphere and NaOH (3 equiv) was added to the mixture. After 1 h at room temperature, 2-bromo-2-methylpropanamide (3 equiv) was added and the reaction was stirred for 2 h at room temperature. After complete alkylation of 6 to the corresponding 2-(2,3-dihalophenoxy)-2-methylpropanamide 7 (monitored by GC-MS), NaOH (9 equiv) was added and the mixture was heated at 60 ºC for 2 h. The reaction was quenched with H₂O and the corresponding N-(2,3-dihalophenyl)-2-hydroxy-2-methylpropanamide 8 was recovered as a solid after filtration.

**N-(3-Fluoro-2-iodophenyl)-2-hydroxy-2-methylpropanamide (8a):** Reaction of 3-fluoro-2-iodophenyl N,N-diethylcarbamate 4a (674 mg, 2 mmol) according to the general procedure afforded 8a (536 mg, 83%) as a white solid: mp 95–97 ºC; ¹H NMR (300 MHz, CDCl₃) δ = 9.31 (br s, 1H), 8.13 (d, J = 8.3 Hz, 1H), 7.35–7.26 (m, 1H), 6.83 (t, J = 8.3 Hz, 1H), 2.71 (s, 1H), 1.58 (s, 6H); ¹³C NMR (75.4 MHz, CDCl₃) δ = 175.0 (C), 161.8 (d, J = 243.7 Hz, C), 139.8 (d, J = 3.5 Hz, C), 130.5 (d, J = 9.0 Hz, CH), 116.5 (d, J = 2.9 Hz, CH), 111.2 (d, J = 23.8 Hz, CH), 78.1 (d, J = 27.9 Hz, C), 74.7 (C), 28.1 (2 × CH₃); EI-LRMS m/z 323 (M⁺, 33), 265 (33), 237 (100), 138 (19), 59 (81); IR (KBr) 3420, 3368, 3289, 3289, 1661, 1462, 1416, 776 cm⁻¹; HRMS calcd for C₁₀H₇FONO₂, 322.9819; found, 322.9812.

**N-(3-Chloro-2-iodophenyl)-2-hydroxy-2-methylpropanamide (8b):** Reaction of 3-chloro-2-iodophenyl N,N-diethylcarbamate 4b (3.53 g, 10 mmol) according to the general procedure afforded 8b (2.78 g, 82%) as a white solid: mp 113–115 ºC; ¹H NMR (300 MHz, CDCl₃) δ = 9.33 (br s, 1H), 8.21 (dd, J = 7.8, 1.5 Hz, 1H), 7.31–7.21 (m, 2H), 2.47 (s, 1H), 1.58 (s, 6H); ¹³C NMR (75.4 MHz, CDCl₃) δ = 175.0 (C), 140.4 (C), 139.1 (C), 129.8 (CH), 125.1 (CH), 118.9 (CH), 95.1 (C), 74.7 (C), 28.0 (2 × CH₃); EI-LRMS m/z 341 (M⁺+2, 3),
339 (M⁺, 8), 281 (10), 253 (62), 194 (15), 154 (24), 59 (100); IR (KBr) 3398, 3291, 1662, 1575, 1539, 1444, 1396, 1126, 776 cm⁻¹; HRMS calcd for C₁₀H₁₁ClINO₂, 338.9523; found, 338.9514.

**N-(3-Bromo-2-iodophenyl)-2-hydroxy-2-methylpropanamide (8c):** Reaction of 3-bromo-2-iodophenyl N,N-diethylcarbamate 4c (794 mg, 2 mmol) according to the general procedure afforded 8c (620 mg, 81%) as a white solid: mp 118−120 °C; ¹H NMR (300 MHz, CDCl₃) δ = 9.33 (br s, 1H), 8.23 (dd, J = 8.1, 1.4 Hz, 1H), 7.4 (dd, J = 8.1, 1.4 Hz, 1H), 7.22 (t, J = 8.1 Hz, 1H), 2.55 (s, 1H), 1.57 (s, 6H); ¹³C NMR (75.4 MHz, CDCl₃) δ = 174.9 (C), 140.5 (C), 130.4 (C), 130.1 (CH), 128.5 (CH), 119.4 (CH), 98.2 (C), 74.7 (C), 28.0 (2 × CH₃); EI-LRMS m/z 385 (M⁺+2, 3), 383 (M⁺, 3), 325 (4), 299 (24), 297 (25), 240 (10), 238 (10), 200 (15), 198 (15), 59 (100); IR (KBr) 3387, 3285, 1652, 1525, 1392, 776, 693 cm⁻¹; HRMS calcd for C₁₀H₁₁BrINO₂, 382.9012; found, 382.9012.

**N-(2,3-Diiodophenyl)-2-hydroxy-2-methylpropanamide (8d):** Reaction of 2,3-diiodophenyl N,N-diethylcarbamate 4d (890 mg, 2 mmol) according to the general procedure afforded 8d (680 mg, 79%) as a white solid: mp 144−146 °C; ¹H NMR (300 MHz, CDCl₃) δ = 9.28 (br s, 1H), 8.24 (dd, J = 8.2, 1.4 Hz, 1H), 7.67 (dd, J = 7.8, 1.4 Hz, 1H), 7.09 (t app, J = 8.0 Hz, 1H), 2.53 (br s, 1H), 1.57 (s, 6H); ¹³C NMR (75.4 MHz, CDCl₃): δ = 175.1 (C), 140.0 (C), 135.4 (CH), 130.4 (CH), 120.2 (CH), 108.8 (C), 104.5 (C), 74.5 (C), 28.0 (2 × CH₃); EI-LRMS m/z 431 (M⁺, 21), 372 (8), 345 (85), 286 (62), 246 (44), 218 (14), 91 (15), 59 (100); IR (KBr) 3318, 1651, 1568, 1523, 1386, 773 cm⁻¹; HRMS calcd for C₁₀H₁₁I₂NO₂, 430.8879; found, 430.8873.

**General procedure for the synthesis of N-(2,3-dihalophenyl)-2-hidroxy-2-methylpropanamides 8 from 5:**

BBr₃ (20 cm³ of a 1M solution in CH₂Cl₂, 20 mmol) was added dropwise to a solution of the corresponding anisole 7 (4 mmol) in CH₂Cl₂ (120 cm³) at −78 °C.⁷ The mixture was allowed to reach room temperature overnight, and then NaHCO₃ (1.68 g, 20 mmol) was added. The resulting mixture was cooled to 0 °C, and MeOH (70 cm³) was added dropwise. After 30 min at 0 °C, the mixture was warmed to room temperature and stirred for 1 h. Most of the solvent was removed under reduced pressure and the residue was diluted with water and CH₂Cl₂. The separated aqueous phase was extracted with CH₂Cl₂ (2 × 30 cm³). The combined organic layers were dried over anhydrous Na₂SO₄ and concentrated under reduced pressure. Without further purification, the corresponding crude dihalophenol 6 was dissolved in anhydrous DMF (8 cm³) under a nitrogen atmosphere and NaOH (480 mg, 12 mmol) was added to the mixture. After 1 h at room temperature, 2-bromo-2-methylpropanamide (1.99 g, 12 mmol) was added and the reaction was stirred for 2 h at room temperature. After complete alkylation of 6 to the corresponding 2-(2,3-dihalophenoxy)-2-methylpropanamide 7 (monitored by GC-MS), NaOH (9 equiv) was added and the mixture was heated at 60 °C for 2 h. The reaction was quenched with H₂O and the corresponding N-(2,3-dihalophenyl)-2-hidroxy-2-methylpropanamide 8 was recovered as a solid after filtration.
General procedure for the synthesis of 2-alkynyl-3-haloanilides 9 and 10:

A mixture of the corresponding N-(2,3-dihalophenyl)propanamide 8b or 8c (1 mmol), alkyne (1.5 mmol), PdCl$_2$(PPh$_3$)$_2$ (21 mg, 0.03 mmol), Cul (9.5 mg, 0.05 mmol) and Et$_2$NH (110 mg, 1.5 mmol) in anhydrous DMF (4 cm$^3$) was stirred under a nitrogen atmosphere at 40, 50 or 80 °C for the desired time until complete consumption of starting material as monitored by GC-MS (2–6 h). CH$_2$Cl$_2$ (20 cm$^3$) and aq HCl (20 cm$^3$ of a 0.5M solution) were added to the cooled reaction mixture. The separated aqueous phase was extracted with CH$_2$Cl$_2$ (2 × 20 cm$^3$). The combined organic layers were washed with water (2 × 60 cm$^3$). The organic layer was dried over Na$_2$SO$_4$ and concentrated at reduced pressure. The remaining residue was purified by column chromatography on silica gel (hexane/EtOAc, 5/1) to afford the coupled products.

N-(3-Chloro-2-(2-phenylethynyl)phenyl)-2-hydroxy-2-methylpropanamide (9a): Reaction of 8b (339 mg, 1 mmol) with phenylacetylene (153 mg, 1.5 mmol) for 2 h at 80 °C, according to the general procedure, afforded 9a (268 mg, 86%) as a white solid: R$_f$ 0.36 (hexane/AcOEt, 4/1); mp 139−141 °C; $^1$H NMR (300 MHz, CDCl$_3$) δ = 9.83 (br s, 1H), 8.42 (dd, J = 8.2, 1.1 Hz, 1H), 7.65−7.57 (m, 2H), 7.40−7.34 (m, 3H), 7.24 (t, J = 8.2 Hz, 1H), 7.15 (dd, J = 8.2, 1.1 Hz, 1H), 2.35 (br s, 1H), 1.58 (s, 6H); $^{13}$C NMR (75.4 MHz, CDCl$_3$) δ = 174.7 (C), 140.2 (C), 135.7 (C), 131.8 (2 × CH), 129.9 (CH), 129.2 (CH), 128.7 (2 × CH), 124.2 (CH), 122.4 (C), 116.8 (CH), 112.9 (C), 101.7 (C), 81.6 (C), 74.8 (C), 28.1 (2 × CH$_2$) EI-LRMS m/z 315 (M$^+$+2, 17), 313 (M$^+$, 51), 254 (54), 229 (33), 227 (100), 190 (27), 59 (41); IR (KBr) 3365, 3321, 1665, 1571, 1534, 1452, 759, 692 cm$^{-1}$; HRMS calcd for C$_{18}$H$_{16}$ClNO$_2$, 313.0870; found, 313.0857.

N-(3-Chloro-2-(hex-1-ynyl)phenyl)-2-hydroxy-2-methylpropanamide (9b): Reaction of 8b (339 mg, 1 mmol) with 1(hexyne (123 mg, 1.5 mmol) for 2.5 h at 80 °C, according to the general procedure, afforded 9b (264 mg, 90%) as a pale brown solid: R$_f$ 0.26 (hexane/AcOEt, 5/1); mp 66−68 °C; $^1$H NMR (300 MHz, CDCl$_3$) δ = 9.65 (br s, 1H), 8.37 (d, J = 8.1 Hz, 1H), 7.24−7.07 (m, 2H), 2.55 (t, J = 6.9 Hz, 2H), 2.45 (br s, 1H), 1.70−1.46 (m, 4H), 1.56 (s, 6H), 0.95 (t, J = 7.1 Hz, 3H); $^{13}$C NMR (75.4 MHz, CDCl$_3$) δ = 174.8 (C), 140.2 (C), 135.6 (C), 129.0 (CH), 124.1 (CH), 116.7 (CH), 113.5 (C), 103.7 (C), 74.5 (C), 73.1 (C), 30.7 (CH$_2$), 28.1 (2 × CH$_2$), 22.1 (CH$_2$), 19.6 (CH$_2$), 13.7 (CH$_3$); EI-LRMS m/z 295 (M$^+$+2, 17), 293 (M$^+$; 51), 207 (48), 193 (41), 178 (64), 164 (88), 59 (100); IR (KBr) 3419, 3322, 1670, 1572, 1516, 1450, 981 cm$^{-1}$; HRMS calcd for C$_{16}$H$_{20}$ClNO$_2$, 293.1183; found, 293.1184.

N-(3-Chloro-2-(hept-1-ynyl)phenyl)-2-hydroxy-2-methylpropanamide (9c): Reaction of 8b (339 mg, 1 mmol) with 1(hetptyne (144 mg, 1.5 mmol) for 2.5 h at 80 °C, according to the general procedure, afforded 9c (249 mg, 81%) as a pale brown solid: R$_f$ 0.26 (hexane/AcOEt, 4/1); mp 76–78 °C; $^1$H NMR (300 MHz, CDCl$_3$) δ 9.77 (br s, 1H), 8.32 (dd, J = 7.6, 1.8 Hz, 1H), 7.15−7.05 (m, 2H), 3.49 (s, 1H), 2.49 (t, J = 7.1 Hz, 2H), 1.68−1.56 (m, 2H), 1.53 (s, 6H), 1.47−1.21 (m, 4H), 0.88 (t, J = 7.1 Hz, 3H); $^{13}$C NMR (75.4 MHz, CDCl$_3$) δ = 175.3 (C), 140.0 (C), 135.6 (C), 128.8 (CH), 124.0 (CH), 116.6 (CH), 113.6 (C), 103.8 (C), 74.2 (C), 73.0 (C), 31.1 (CH$_2$), 28.2 (CH$_2$), 27.9 (2 × CH$_3$), 22.2 (CH$_2$), 19.7 (CH$_3$), 14.0 (CH$_2$); EI-LRMS m/z 309 (M$^+$+2, 7), 307 (M$^+$, 21), 206 (20), 180 (35), 164 (44), 59 (100); IR (KBr) 3311, 2953, 1662, 1569, 1520, 1453, 1139, 790, 731 cm$^{-1}$; HRMS calcd for C$_{17}$H$_{22}$ClNO$_2$, 307.1339; found, 307.1342.
N-(3-Chloro-2-(2-cyclohexenylethynyl)phenyl)-2-hydroxy-2-methylpropanamide (9d): Reaction of 8b (339 mg, 1 mmol) with 1-ethynylcyclohexene (159 mg, 1.5 mmol) for 3 h at 80 °C, according to the general procedure, afforded 9d (254 mg, 80%) as a white solid: Rf 0.34 (hexane/AcOEt, 5/1); mp 145–147 °C; 1H NMR (300 MHz, CDCl3) δ = 9.67 (br s, 1H), 8.36 (dd, J = 8.1, 1.3 Hz, 1H), 7.17 (t, J = 8.1 Hz, 1H), 7.10 (dd, J = 8.1, 1.3 Hz, 1H), 6.36–6.30 (m, 1H), 2.80 (s, 1H), 2.30–2.22 (m, 2H), 2.18–2.10 (m, 2H), 1.72–1.57 (m, 4H), 1.55 (s, 6H); 13C NMR (75.4 MHz, CDCl3) δ = 174.9 (C), 139.7 (C), 137.0 (CH), 135.4 (C), 129.2 (CH), 124.1 (CH), 120.3 (C), 116.6 (CH), 113.4 (C), 103.8 (C), 79.0 (C), 74.5 (C), 29.0 (CH2), 28.0 (2 × CH3), 26.0 (CH2), 22.3 (CH3), 21.5 (CH2); EI-MS m/z 319 (M^+ + 2, 23), 317 (M^+, 72), 281 (25), 231 (57), 207 (100), 180 (26), 59 (55); IR (KBr) 3372, 3320, 1652, 1572, 1532, 1450, 1435, 1197, 1184, 778, 725 cm⁻¹; HRMS calecd for C_{19}H_{20}ClNO_2: 317.1183; found, 317.1190.

N-(3-Chloro-2-(2-(trimethylsilyl)ethynyl)phenyl)-2-hydroxy-2-methylpropanamide (9e): Reaction of 8b (339 mg, 1 mmol) with trimethylsilylacetylene (147 mg, 1.5 mmol) for 5.5 h at 40 °C, according to the general procedure, afforded 9e (251 mg, 81%) as a pale brown solid: Rf 0.47 (hexane/AcOEt, 4/1); mp 144–146 °C; 1H NMR (300 MHz, CDCl3) δ = 9.66 (br s, 1H), 8.37 (dd, J = 8.3, 0.9 Hz, 1H), 7.21 (t, J = 8.3 Hz, 1H), 7.09 (dd, J = 8.3, 0.9 Hz, 1H), 2.60 (br s, 1H), 1.55 (s, 6H), 0.29 (d, J = 0.9 Hz, 9H); 13C NMR (75.4 MHz, CDCl3) δ = 175.0 (C), 140.8 (C), 135.8 (C), 130.0 (CH), 124.1 (CH), 116.8 (CH), 112.8 (C), 108.1 (C), 96.6 (C), 74.6 (C), 28.1 (2 × CH3), 0.0 (3 × CH3); EI-MS m/z 311 (M^+ + 2, 10), 309 (M^+, 29), 236 (100), 208 (39); HRMS calecd for C_{19}H_{22}ClNO_2Si: 309.0952; found, 309.0951.

N-(3-Bromo-2-(phenylethynyl)phenyl)-2-hydroxy-2-methylpropanamide (10a): Reaction of 8c (383 mg, 1 mmol) with 1-phenylacetyle (153 mg, 1.5 mmol) for 3.5 h at 50 °C, according to the general procedure, afforded 10a (286 mg, 80%) as a white solid: Rf 0.32 (hexane/AcOEt, 4/1); mp 131–133 °C; 1H NMR (300 MHz, CDCl3) δ = 9.86 (br s, 1H), 8.44 (dd, J = 8.2, 1.0 Hz, 1H), 7.63–7.58 (m, 2H), 7.38–7.29 (m, 4H), 7.13 (t, J = 8.2 Hz, 1H), 2.87 (s, 1H), 1.55 (s, 6H); 13C NMR (75.4 MHz, CDCl3) δ = 175.0 (C), 140.1 (C), 131.7 (2 × CH), 130.1 (CH), 129.2 (CH), 128.6 (2 × CH), 127.3 (CH), 125.0 (C), 122.3 (C), 117.3 (CH), 115.0 (C), 101.1 (C), 83.4 (C), 74.7 (C), 28.0 (2 × CH3); EI-MS m/z 359 (M^+ + 2, 62), 357 (M^+, 62), 300 (60), 298 (58), 273 (100), 271 (100), 191 (60), 165 (53), 59 (83); IR (KBr) 3372, 3312, 1661, 1566, 1532, 1446, 1200, 1131, 752, 726, 689 cm⁻¹; HRMS calecd for C_{18}H_{18}BrNO_2: 357.0364; found, 357.0368.

N-(3-Bromo-2-(hex-1-ynyl)phenyl)-2-hydroxy-2-methylpropanamide (10b): Reaction of 8c (383 mg, 1 mmol) with 1-heptyne (123 mg, 1.5 mmol) for 3.5 h at 50 °C, according to the general procedure, afforded 10b (431 mg, 85%) as a pale brown solid: Rf 0.31 (hexane/AcOEt, 4/1); mp 70–72 °C; 1H NMR (300 MHz, CDCl3) δ = 9.76 (br s, 1H), 8.36 (dd, J = 8.2, 1.0 Hz, 1H), 7.25 (dd, J = 8.2, 1.0 Hz, 1H), 7.05 (t, J = 8.2 Hz, 1H), 3.42 (s, 1H), 2.50 (t, J = 7.0 Hz, 2H), 1.64–1.43 (m, 4H), 1.52 (s, 6H), 0.91 (t, J = 7.2 Hz, 3H); 13C NMR (75.4 MHz, CDCl3) δ = 175.3 (C), 140.1 (C), 129.2 (CH), 127.2 (CH), 125.0 (C), 117.1 (CH), 115.6 (C), 103.1 (C), 74.8 (C), 74.2 (C), 30.5 (CH2), 27.9 (2 × CH3), 22.1 (CH2), 19.5 (CH3), 13.7 (CH3); EI-MS m/z 339 (M^+ + 2, 37), 337 (M^+, 36), 253 (29), 251 (30), 226 (50), 210 (51), 157 (25), 129 (26), 59 (100); IR (KBr) 3419, 3319, 1673, 1567, 1520, 1427, 980, 729 cm⁻¹; HRMS calecd for C_{18}H_{18}BrNO_2: 337.0677; found, 337.0676.

N-(3-Bromo-2-(hept-1-ynyl)phenyl)-2-hydroxy-2-methylpropanamide (10c): Reaction of 8e (383 mg, 1 mmol) with 1-heptyne (144 mg, 1.5 mmol) for 3.5 h at 50 °C, according to the general procedure, afforded...
**10c** (277 mg, 79%) as a white solid: R$_f$ 0.30 (hexane/AcOEt, 4/1); mp 79–81 °C; $^1$H NMR (300 MHz, CDCl$_3$) δ 9.78 (s, 1H), 8.35 (dd, $J = 8.2$, 0.8 Hz, 1H), 7.24 (dd, $J = 8.2$, 0.8 Hz, 1H), 7.03 (t, $J = 8.2$ Hz, 1H), 3.58 (s, 1H), 2.47 (t, $J = 7.2$ Hz, 2H), 1.68–1.57 (m, 2H), 1.52 (s, 6H), 1.49–1.24 (m, 4H), 0.87 (t, $J = 7.2$ Hz, 3H); $^{13}$C NMR (75.4 MHz, CDCl$_3$) δ 175.4 (C), 140.1 (C), 129.1 (CH), 127.1 (CH), 125.0 (C), 117.1 (CH), 115.6 (C), 103.2 (C), 74.8 (C), 74.2 (C), 31.1 (CH$_2$), 28.2 (CH$_2$), 27.8 (2 × CH$_3$), 22.2 (CH$_2$), 19.7 (CH$_3$), 14.0 (CH$_3$); EI-LRMS m/z 353 (M$^+$+2, 15), 351 (M$^+$, 15), 226 (28), 210 (30), 157 (21), 59 (100); IR (KBr) 3295, 2930, 1661, 1564, 1520, 1449, 1130, 981, 788, 730 cm$^{-1}$; HRMS calcd for C$_{17}$H$_{22}$BrNO$_2$, 351.0834; found, 351.0822.

**N-(3-bromo-2-(2-cyclohexenylethynyl)phenyl)-2-hydroxy-2-methylpropanamide (10d)**: Reaction of 8c (383 mg, 1 mmol) with 1-ethynylocyclohexene (159 mg, 1.5 mmol) for 5 h at 50 °C, according to the general procedure, afforded 10d (310 mg, 86%) as a white solid: R$_f$ 0.32 (hexane/AcOEt, 4/1); mp 154–156 °C; $^1$H NMR (300 MHz, CDCl$_3$) δ = 9.65 (br s, 1H), 8.42 (dd, $J = 8.2$, 1.1 Hz, 1H), 7.29 (dd, $J = 8.2$ Hz, 1.1 Hz, 1H), 7.12 (t, $J = 8.2$ Hz, 1H), 6.37–6.32 (m, 1H), 2.48 (br s, 1H), 2.32–2.22 (m, 2H), 2.21–2.12 (m, 2H), 1.77–1.58 (m, 4H), 1.56 (s, 6H); $^{13}$C NMR (75.4 MHz, CDCl$_3$) δ = 174.8 (C), 139.9 (C), 137.1 (CH), 129.6 (CH), 127.2 (CH), 124.9 (C), 120.4 (C), 117.2 (CH), 115.4 (C), 103.2 (C), 80.9 (C), 74.6 (C), 28.9 (CH$_3$), 28.1 (2 × CH$_3$), 26.0 (CH$_2$), 22.3 (CH$_2$), 21.5 (CH$_2$); EI-LRMS m/z 363 (M$^+$+2, 100), 361 (M$^+$, 100), 277 (53), 275 (53), 167 (34), 59 (63); IR (KBr) 3376, 3318, 2929, 1653, 1566, 1530, 1446, 1433, 976, 775, 724 cm$^{-1}$; HRMS calcd for C$_{18}$H$_{26}$BrNO$_2$, 361.0677; found, 361.0677.

**N-(3-bromo-2-(2-(trimethylsilyl)ethynyl)phenyl)-2-hydroxy-2-methylpropanamide (10e)**: Reaction of 8c (383 mg, 1 mmol) with trimethylsilylacetylene (147 mg, 1.5 mmol) for 3 h at 40 °C, according to the general procedure, and afforded 10e (251 mg, 71%) as a pale brown solid: R$_f$ 0.39 (hexane/AcOEt, 4/1); mp 150–152 °C; $^1$H NMR (300 MHz, CDCl$_3$) δ = 9.70 (br s, 1H), 8.40 (dt, $J = 8.2$, 0.9 Hz, 1H), 7.27 (td, $J = 8.2$, 0.9 Hz, 1H), 7.12 (t, $J = 8.2$ Hz, 1H), 2.83 (s, 1H), 1.54 (d, $J = 0.6$ Hz, 6H), 0.28 (d, $J = 0.8$ Hz, 9H); $^{13}$C NMR (75.4 MHz, CDCl$_3$) δ = 175.1 (C), 140.8 (C), 130.3 (CH), 127.2 (CH), 125.0 (C), 117.3 (CH), 114.8 (C), 107.5 (C), 98.3 (C), 74.4 (C), 28.0 (2 × CH$_3$), -0.1 (3 × CH$_3$); EI-LRMS m/z 355 (M$^+$+2, 28), 353 (M$^+$, 27), 282 (100), 280 (100), 254 (37), 252 (37), 238 (19), 236 (18); HRMS calcd for C$_{18}$H$_{26}$BrNO$_2$Si, 353.0447; found, 353.0450.

**N-(3-bromo-2-(2-(thiophen-3-yl)ethynyl)phenyl)-2-hydroxy-2-methylpropanamide (10f)**: Reaction of 8c (383 mg, 1 mmol) with 3-ethynylthiophene (162 mg, 1.5 mmol) for 3.5 h at 50 °C, according to the general procedure, afforded 10f (269 mg, 74%) as a white solid: R$_f$ 0.37 (hexane/AcOEt, 4/1); mp 132–134 °C; $^1$H NMR (400 MHz, CDCl$_3$) δ = 9.82 (br s, 1H), 8.41 (d, $J = 8.3$ Hz, 1H), 7.63 (dd, $J = 2.9$, 1.1 Hz, 1H), 7.31–7.27 (m, 2H), 7.24 (dd, $J = 4.9$, 1.1 Hz, 1H), 7.11 (t, $J = 8.3$ Hz, 1H), 2.90 (s, 1H), 1.53 (s, 6H); $^{13}$C NMR (100.8 MHz, CDCl$_3$) δ = 175.0 (C), 140.1 (C), 130.0 (CH), 129.9 (CH), 129.8 (CH), 127.3 (CH), 125.9 (CH), 124.7 (C), 121.4 (C), 117.3 (CH), 115.1 (C), 96.3 (C), 83.1 (C), 74.7 (C), 28.0 (2 × CH$_3$); EI-LRMS m/z 365 (M$^+$+2, 40), 363 (M$^+$, 44), 305 (19), 279 (61), 277 (59), 226 (14), 198 (29), 196 (32), 171 (23), 59 (100); HRMS calcd for C$_{18}$H$_{16}$BrNO$_2$S, 362.9929; found, 362.9928.
General procedure for the synthesis of 4-halo-1H-indoles 11 and 12 from anilides 9 and 10:

To a solution of the corresponding 2-alkynyl-3-haloanilide 9 or 10 (1 equiv) in anhydrous DMF (4 cm³/mmol) freshly powdered NaOH (3 equiv) was added. The resulting mixture was refluxed under a nitrogen atmosphere at 140 °C until the cyclization was completed (as monitored by GC-MS). CH₂Cl₂ (10 cm³) and aq HCl (10 cm³ of a 0.5M solution) were added to the cooled reaction mixture. The separated aqueous phase was extracted with CH₂Cl₂ (2 × 10 cm³). The combined organic layers were washed with water (2 × 30 cm³), dried over anhydrous Na₂SO₄ and concentrated under reduced pressure. The remaining residue was purified by column chromatography on silica gel (hexane/EtOAc) to afford the corresponding 4-haloindole 11 or 12.

4-Chloro-2-phenyl-1H-indole (11a): From 9a (94 mg, 0.3 mmol) and NaOH (36 mg, 0.9 mmol) according to the general procedure (4 h), and purification by column chromatography (hexane/EtOAc, 7/1) on silica gel afforded 11a (54 mg, 79%) as a white solid: Rₜ 0.32 (hexane/AcOEt, 6/1); mp 73–75 °C (lit. mp 74–77 °C); ¹H NMR (300 MHz, CDCl₃) δ = 8.43 (br s, 1H), 7.70–7.63 (m, 2H), 7.50–7.43 (m, 2H), 7.39–7.33 (m, 1H), 7.31–7.27 (m, 1H), 7.17–7.08 (m, 2H), 6.94 (dd, J = 2.2, 0.8 Hz, 1H); ¹³C NMR (75.4 MHz, CDCl₃) δ = 138.6 (C), 137.4 (C), 131.8 (C), 129.2 (2 × CH), 128.3 (CH), 128.2 (C), 125.9 (C), 125.4 (2 × CH), 122.9 (CH), 120.1 (CH), 98.5 (CH); EI-LRMS m/z 229 (M⁺+2, 33), 227 (M⁺, 100), 191 (10), 165 (16), 113 (10); IR (KBr) 3449, 2961, 2924, 1452, 1261, 1098, 803, 756 cm⁻¹; HRMS calecd for C₁₅H₁₀ClIN, 227.0502; found, 227.0501.

2-Butyl-4-chloro-1H-indole (11b): From 9b (88 mg, 0.3 mmol) and NaOH (36 mg, 0.9 mmol) according to the general procedure (2.5 h), and purification by column chromatography (hexane/EtOAc, 8/1) on silica gel afforded 11b (53 mg, 86%) as a colourless oil: Rₜ 0.46 (hexane/AcOEt, 6/1); ¹H NMR (300 MHz, CDCl₃) δ = 7.90 (br s, 1H), 7.18 (dt, J = 7.7, 1.0 Hz, 1H), 7.12 (dd, J = 7.6, 1.1 Hz, 1H), 7.05 (t, J = 7.7 Hz, 1H), 6.38 (dd, J = 2.2, 0.9 Hz, 1H), 2.74 (t, J = 7.6 Hz, 2H), 1.77–1.66 (m, 2H), 1.51–1.38 (m, 2H), 0.99 (t, J = 7.3, 3H); ¹³C NMR (75.4 MHz, CDCl₃) δ = 141.0 (C), 136.5 (C), 127.6 (C), 125.0 (C), 121.6 (CH), 119.4 (CH), 109.1 (CH), 98.1 (CH), 31.2 (CH₂), 28.0 (CH₂), 22.5 (CH₃), 14.0 (CH₃); EI-LRMS m/z 209 (M⁺+2, 10), 207 (M⁺, 33), 164 (100), 128 (8), 101 (6); IR (KBr) 3417, 2957, 2929, 1575, 1548, 1433, 1330, 1182, 941, 765 cm⁻¹; HRMS calecd for C₁₃H₁₆ClIN, 207.0815; found, 207.0822.

4-Chloro-2-pentyl-1H-indole (11c): From 9c (154 mg, 0.5 mmol) and NaOH (60 mg, 1.5 mmol) according to the general procedure (2.5 h) and purification by column chromatography (hexane/EtOAc, 7/1) on silica gel afforded 11c (93 mg, 84%) as a pale brown solid: Rₜ 0.46 (hexane/AcOEt, 5/1); mp 24–26 °C; ¹H NMR (300 MHz, CDCl₃) δ = 7.96 (br s, 1H), 7.19 (dd, J = 7.6, 0.9 Hz, 1H), 7.11–7.00 (m, 2H), 6.36 (d, J = 0.9 Hz, 1H), 2.75 (t, J = 7.6 Hz, 2H), 1.79–1.68 (m, 2H), 1.43–1.25 (m, 4H), 0.93 (t, J = 6.7 Hz, 3H); ¹³C NMR (75.4 MHz, CDCl₃) δ = 141.0 (C), 136.5 (C), 127.7 (C), 125.0 (C), 121.6 (CH), 119.4 (CH), 109.0 (CH), 98.1 (CH), 31.6 (CH₂), 28.8 (CH₂), 28.3 (CH₃), 22.6 (CH₂), 14.1 (CH₃); EI-LRMS m/z 223 (M⁺+2 11), 221, (M⁺, 34), 178 (24), 164 (100), 128 (9), 101 (6); IR (KBr) 3417, 2956, 2928, 1547, 1433, 1329, 1182, 939, 765 cm⁻¹; HRMS calecd for C₁₃H₁₆ClIN, 221.0971; found, 221.0980.

4-Chloro-2-cyclohexenyl-1H-indole (11d): From 9d (94 mg, 0.3 mmol) and NaOH (36 mg, 0.9 mmol) according to the general procedure (2.5 h), and purification by column chromatography (hexane/EtOAc, 8/1) on silica gel afforded 11d (56 mg, 81%) as a pale brown oil: Rₜ 0.70 (hexane/EtOAc, 6/1); ¹H NMR (300
MHz, CDCl$_3$) $\delta = 8.21$ (br s, 1H), 7.21–7.17 (m, 1H), 7.09–7.02 (m, 2H), 6.54 (d, $J = 2.0$ Hz, 1H), 6.17–6.12 (m, 1H), 2.51–2.44 (m, 2H), 2.29–2.21 (m, 2H), 1.85–1.76 (m, 2H), 1.75–1.65 (m, 2H); $^{13}$C NMR (75.4 MHz, CDCl$_3$) $\delta = 140.1$ (C), 136.8 (C), 128.8 (C), 127.8 (C), 125.6 (C), 123.8 (CH), 122.5 (CH), 119.5 (CH), 109.1 (CH), 97.1 (CH), 26.0 (CH$_2$), 25.6 (CH$_2$), 22.5 (CH$_2$), 22.2 (CH$_2$); EI-LRMS $m/z$ 233 (M$^+$+2, 32), 231 (M$^+$, 100), 203 (35), 164 (34), 151 (29); IR (neat) 3433, 2928, 1569, 1432, 1334, 1184, 947, 764, 731 cm$^{-1}$; HRMS caleld for C$_{14}$H$_{14}$ClN, 231.0815; found, 231.0814.

4-Chloro-1H-indole (11e): From 9e (168 mg, 0.5 mmol) and NaOH (60 mg, 1.5 mmol) according to the general procedure (4 h), and purification by flash column chromatography (hexane/EtOAc, 8/1) on silica gel afforded 11e (55 mg, 73%) as a brown oil: $R_f$ 0.33 (hexane/AcOEt, 5/1); $^1$H NMR (300 MHz, CDCl$_3$) $\delta = 8.25$ (br s, 1H), 7.31–7.21 (m, 2H), 7.16–7.08 (m, 2H), 6.70–6.62 (m, 1H); $^{13}$C NMR (75.4 MHz, CDCl$_3$) $\delta = 136.6$ (C), 126.9 (C), 126.2 (C), 124.9 (CH), 122.7 (CH), 119.7 (CH), 109.8 (CH), 101.4 (CH); EI-LRMS $m/z$ 153 (M$^+$+2, 31), 151 (M$^+$, 100), 116 (18), 89 (27).

4-Bromo-2-phenyl-1H-indole (12a): From 10a (178 mg, 0.5 mmol) and NaOH (60 mg, 1.5 mmol) according to the general procedure (5 h), and purification by flash column chromatography (hexane/EtOAc, 10/1) on silica gel afforded 12a (113 mg, 83%) as a white solid: $R_f$ 0.38 (hexane/AcOEt, 5/1); mp 100–102 ºC; $^1$H NMR (300 MHz, CDCl$_3$) $\delta = 8.42$ (br s, 1H), 7.65 (dd, $J = 8.4$, 1.0 Hz, 2H), 7.49–7.42 (m, 2H), 7.40–7.29 (m, 3H), 7.06 (t, $J = 7.9$ Hz, 1H), 6.91–6.89 (m, 1H); $^{13}$C NMR (75.4 MHz, CDCl$_3$) $\delta = 138.5$ (C), 137.0 (C), 131.7 (C), 130.1 (C), 129.2 (2 $\times$ CH), 128.3 (CH), 125.3 (2 $\times$ CH), 123.2 (CH), 114.6 (C), 110.2 (CH), 100.2 (CH); EI-LRMS $m/z$ 273 (M$^+$+2, 98), 271 (M$^+$, 100), 191 (27), 165 (34), 136 (11); IR (KBr) 3445, 1475, 1452, 1352, 1289, 1181, 916, 758, 691 cm$^{-1}$; HRMS caleld for C$_{14}$H$_{10}$BrN, 270.9997; found, 270.9995.

4-Bromo-2-butyl-1H-indole (12b): From 10b (101 mg, 0.3 mmol) and NaOH (36 mg, 0.9 mmol) according to the general procedure (3 h), and purification by column chromatography (hexane/EtOAc, 7/1) on silica gel afforded 12b (61 mg, 80%) as a white solid: $R_f$ 0.45 (hexane/AcOEt, 5/1); mp 29–31 ºC; $^1$H NMR (300 MHz, CDCl$_3$) $\delta = 7.95$ (br s, 1H), 7.26 (dd, $J = 7.6$, 0.8 Hz, 1H), 7.22 (dt, $J = 8.0$, 0.8 Hz, 1H), 6.99 (t, $J = 7.8$ Hz, 1H), 6.32 (dd, $J = 2.2$, 0.9 Hz, 1H), 2.74 (t, $J = 7.6$ Hz, 2H), 1.77–1.66 (m, 2H), 1.50–1.37 (m, 2H), 0.98 (t, $J = 7.3$ Hz, 3H); $^{13}$C NMR (75.4 MHz, CDCl$_3$) $\delta = 141.0$ (C), 136.0 (C), 129.6 (C), 122.5 (CH), 121.9 (CH), 113.7 (C), 109.6 (CH), 99.8 (CH), 31.2 (CH$_2$), 28.0 (CH$_2$), 22.5 (CH$_2$), 14.0 (CH$_3$); EI-LRMS $m/z$ 253 (M$^+$+2, 37), 251 (M$^+$, 37), 210 (100), 208 (98), 129 (32); IR (KBr) 3407, 2958, 2929, 1539, 1430, 1329, 1178, 917, 763, 729 cm$^{-1}$; HRMS caleld for C$_{14}$H$_{14}$BrN, 251.0310; found, 251.0309.

4-Bromo-2-pentyl-1H-indole (12c): From 10c (123 mg, 0.35 mmol) and NaOH (42 mg, 1.05 mmol) according to the general procedure (2.5 h) and purification by column chromatography (hexane/EtOAc, 7/1) on silica gel afforded 12c (76 mg, 82%) as a pale brown oil: $R_f$ 0.42 (hexane/EtOAc, 6/1); $^1$H NMR (300 MHz, CDCl$_3$) $\delta = 7.97$ (br s, 1H), 7.28–7.20 (m, 2H), 6.98 (t, $J = 8.0$ Hz, 1H), 6.31 (dd, $J = 2.2$, 0.8 Hz, 1H), 2.74 (t, $J = 7.7$, Hz, 2H), 1.79–1.68 (m, 2H), 1.43–1.34 (m, 4H), 0.93 (t, $J = 7.0$ Hz, 3H); $^{13}$C NMR (75.4 MHz, CDCl$_3$) $\delta = 141.0$ (C), 136.1 (C), 129.6 (C), 122.5 (CH), 121.9 (CH), 113.7 (C), 109.6 (CH), 99.9 (CH), 31.6 (CH$_2$), 28.9 (CH$_2$), 28.3 (CH$_2$), 22.6 (CH$_2$), 14.1 (CH$_3$); EI-LRMS $m/z$ 267 (M$^+$+2, 41), 265 (M$^+$, 42), 224
(19), 210 (100), 208 (98), 129 (32); IR (KBr) 3411, 2956, 2928, 1548, 1430, 1327, 1178, 917, 763 cm⁻¹; HRMS calcd for C₁₃H₁₄BrN, 265.0466; found, 265.0467

4-Bromo-2-cyclohexenyl-1H-indole (12d): From 10d (180 mg, 0.5 mmol) and NaOH (60 mg, 1.5 mmol) according to the general procedure (4 h), and purification by flash column chromatography (hexane/EtOAc, 10/1) on silica gel afforded afforded 12d (105 mg, 76%) as a colourless oil: Rf 0.50 (hexane/EtOAc, 6/1); 1H NMR (300 MHz, CDCl₃) δ = 8.27 (br s, 1H), 7.27–7.20 (m, 2H), 6.99 (t, J = 7.8 Hz, 1H), 6.48 (d, J = 1.9 Hz, 1H), 6.17–6.12 (m, 1H), 2.51–2.43 (m, 2H), 2.28–2.20 (m, 2H), 1.84–1.75 (m, 2H), 1.75–1.65 (m, 2H); 13C NMR (75.4 MHz, CDCl₃) δ = 140.2 (C), 136.4 (C), 129.7 (C), 128.9 (C), 123.8 (CH), 122.8 (CH), 122.7 (CH), 114.3 (C), 109.7 (CH), 98.9 (CH), 26.1 (CH₂), 25.6 (CH₂), 22.6 (CH₂), 22.2 (CH₂); EI-LRMS m/z 277 (M⁺+2, 98), 275 (M⁺, 100), 247 (24), 195 (23), 167 (38); IR (KBr) 3427, 2927, 1568, 1524, 1429, 1332, 1179, 917, 762, 730 cm⁻¹; HRMS calcd for C₁₄H₁₄BrN, 265.0466; found, 265.0467.

4-Bromo-1H-indole (12e): From 10e (176 mg, 0.5 mmol) and NaOH (60 mg, 1.5 mmol) according to the general procedure (5 h), and purification by flash column chromatography (hexane/EtOAc, 10/1) on silica gel afforded 12e (73 mg, 75%) as a colourless oil: Rf 0.29 (hexane/EtOAc, 6/1); 1H NMR (300 MHz, CDCl₃) δ = 8.28 (br s, 1H), 7.37–7.23 (m, 3H), 7.06 (t, J = 7.9 Hz, 1H), 6.64–6.60 (m, 1H); 13C NMR (75.4 MHz, CDCl₃) δ = 136.1 (C), 128.8 (C), 124.8 (CH), 123.0 (CH), 122.9 (CH), 114.9 (C), 110.4 (CH), 103.2 (CH); EI-LRMS m/z 197 (M⁺+2, 100), 195 (M⁺, 100), 184 (7), 116 (77), 89 (44); HRMS calcd for C₈H₈BrN, 194.9684; found, 194.9679.

4-Bromo-2-(thiophen-3-yl)-1H-indole (12f): From 10f (181 mg, 0.5 mmol) and NaOH (60 mg, 1.5 mmol) according to the general procedure (3 h), and purification by flash column chromatography (hexane/EtOAc, 10/1) on silica gel afforded 12f (99 mg, 71%) as a pale brown solid: Rf 0.48 (hexane/AcOEt, 4/1); mp 44–46 °C; 1H NMR (300 MHz, CDCl₃) δ = 8.35 (br s, 1H), 7.47–7.38 (m, 2H), 7.29 (d, J = 7.7 Hz, 2H), 7.07–7.00 (m, 1H), 6.75 (d, J = 2.1 Hz, 1H); 13C NMR (75.4 MHz, CDCl₃) δ = 136.6 (C), 134.6 (C), 133.5 (C), 129.9 (C), 127.0 (CH), 125.7 (CH), 123.25 (CH), 123.19 (CH), 119.9 (CH), 114.5 (C), 110.0 (CH), 100.2 (CH); EI-LRMS m/z 281 (M⁺+2, 100), 279 (M⁺, 96), 198 (38), 171 (61), 154 (27), 126 (32); HRMS calcd for C₁₂H₁₂BrNS, 276.9561; found, 276.9576.

General procedure for the synthesis of 4-halo-1H-indoles 3, 11 and 12 from 2,3-dihaloanilides 8 (one pot procedure):

A mixture of the corresponding N-(3-halo-2-iodophenyl)-2-hydroxy-2-methylpropanamide 8 (1 equiv), alkyne (1.5 equiv), PdCl₂(PPh₃)₂ (3 mol%), Cul (5 mol%) and Et₃NH (1.5 equiv) in anhydrous DMA (4 cm³/mol) was stirred under a nitrogen atmosphere at 80 °C (for 8a and 8b), at 50 °C (for 8c), or at 40 °C (when trimethylsilylacetylene is used as alkyne) until complete consumption of starting material 8 as monitored by GC-MS (2–5 h). Then, freshly powdered NaOH (10 equiv) was added to the reaction mixture and it was refluxed under a nitrogen atmosphere at 140 °C until the cyclization was completed (3–4 h, as monitored by GC-MS). After cooling of the reaction mixture, CH₂Cl₂ (20 cm³) and aq HCl (20 cm³ of a 0.5M solution) were added. The separated aqueous phase was extracted with CH₂Cl₂ (2 × 20 cm³) and the combined organic layers were washed with water (2 × 60 cm³). The organic layer was dried over anhydrous Na₂SO₄ and concentrated.
under reduced pressure. The remaining residue was purified by column chromatography on silica gel (hexane/EtOAc) to afford the corresponding 4-halo-1H-indoles 3, 11 and 12.

**4-Fluoro-2-phenyl-1H-indole (3a):** Treatment of 8a (161 mg, 0.5 mmol) with phenylacetylene (77 mg, 0.75 mmol), PdCl₂(PPh₃)₂ (10 mg, 3 mol%), CuI (5 mg, 5 mol%) and Et₂NH (54 mg, 0.75 mmol) in DMA (2 mL) for 3 h and then, with NaOH (200 mg, 5 mmol) for 4 h according to the general procedure, and purification by column chromatography (hexane/EtOAc, 8/1) on silica gel afforded 3a (90 mg, 85%), whose spectroscopic data have been reported above.

**2-Butyl-4-fluoro-1H-indole (3b):** Treatment of 8a (161 mg, 0.5 mmol) with 1-hexyne (62 mg, 0.75 mmol), PdCl₂(PPh₃)₂ (10 mg, 3 mol%), CuI (5 mg, 5 mol%) and Et₂NH (54 mg, 0.75 mmol) in DMA (2 mL) for 3 h and then, with NaOH (200 mg, 5 mmol) for 4 h according to the general procedure, and purification by column chromatography (hexane/EtOAc, 8/1) on silica gel afforded 3b (74 mg, 77%) as a pale brown oil: $R_f$ 0.50 (hexane/EtOAc, 4/1); $^1$H NMR (300 MHz, CDCl₃) δ = 7.92 (br s, 1H), 7.11–7.00 (m, 2H), 6.78 (ddd, $J$ = 10.4, 6.9, 1.7 Hz, 1H), 6.35 (dd, $J$ = 2.2, 0.8 Hz, 1H), 2.75 (t, $J$ = 7.6 Hz, 2H), 1.77–1.66 (m, 2H), 1.51–1.38 (m, 2H), 0.99 (t, $J$ = 7.3 Hz, 3H); $^{13}$C NMR (75.4 MHz, CDCl₃) δ = 155.9 (d, $J$ = 245.2 Hz, C), 140.1 (C), 138.6 (d, $J$ = 11.8 Hz, C), 121.4 (d, $J$ = 7.6 Hz, CH), 117.8 (d, $J$ = 22.4 Hz, C), 106.5 (d, $J$ = 3.4 Hz, CH), 104.5 (d, $J$ = 19.1 Hz, CH), 95.4 (CH), 31.3 (CH₂), 27.9 (CH₂), 22.5 (CH₂), 14.0 (CH₃); HRMS calc'd for C₁₂H₁₂FN, 191.1110; found, 191.1106.

**4-Chloro-2-phenyl-1H-indole (11a):** Treatment of 8b (170 mg, 0.5 mmol) with phenylacetylene (77 mg, 0.75 mmol), PdCl₂(PPh₃)₂ (10 mg, 3 mol%), CuI (5 mg, 5 mol%) and Et₂NH (54 mg, 0.75 mmol) in DMA (2 mL) for 3 h and then, with NaOH (200 mg, 5 mmol) for 4 h according to the general procedure, and purification by column chromatography (hexane/EtOAc, 7/1) on silica gel afforded 11a (92 mg, 81%), whose spectroscopic data have been reported above.

**2-Butyl-4-chloro-1H-indole (11b):** Treatment of 8b (339 mg, 1 mmol) with 1-hexyne (123 mg, 1.5 mmol), PdCl₂(PPh₃)₂ (21 mg, 3 mol%), CuI (9 mg, 5 mol%) and Et₂NH (109 mg, 1.5 mmol) in DMA (4 mL) for 2.5 h and then, with NaOH (400 mg, 10 mmol) for 3 h according to the general procedure, and purification by column chromatography (hexane/EtOAc, 8/1) on silica gel afforded 11b (147 mg, 71%), whose spectroscopic data have been reported above.

**4-Chloro-2-cyclohexenyl-1H-indole (11d):** Treatment of 8b (679 mg, 2 mmol) with 1-ethynylcyclohexene (320 mg, 3 mmol), PdCl₂(PPh₃)₂ (42 mg, 3 mol%), CuI (19 mg, 5 mol%) and Et₂NH (220 mg, 3 mmol) in DMA (6 mL) for 2 h and then, with NaOH (800 mg, 20 mmol) for 3 h according to the general procedure, and purification by column chromatography (hexane/EtOAc, 8/1) on silica gel afforded 11d (379 mg, 82%), whose spectroscopic data have been reported above.

**4-Chloro-1H-indole (11e):** Treatment of 8b (170 mg, 0.5 mmol) with trimethylsilylacetylene (73 mg, 0.75 mmol), PdCl₂(PPh₃)₂ (10 mg, 3 mol%), CuI (5 mg, 5 mol%) and Et₂NH (54 mg, 0.75 mmol) in DMA (2 mL) for 5.5 h and then, with NaOH (200 mg, 5 mmol) for 3 h according to the general procedure, and purification by column chromatography (hexane/EtOAc, 8/1) on silica gel afforded 11e (46 mg, 61%), whose spectroscopic data have been reported above.
4-Chloro-2-(3-chlorophenyl)-1H-indole (11f): Treatment of 8b (170 mg, 0.5 mmol) with 1-chloro-3-ethynylbenzene (102 mg, 0.75 mmol), PdCl$_2$(PPh$_3$)$_2$ (10 mg, 3 mol%), CuI (5 mg, 5 mol%) and Et$_2$NH (54 mg, 0.75 mmol) in DMA (2 mL) for 2 h and then, with NaOH (200 mg, 5 mmol) for 3 h according to the general procedure, and purification by column chromatography (hexane/EtOAc, 7/1) on silica gel afforded 11f (98 mg, 75%) as a brown solid: $R_f$ 0.63 (hexane/AcOEt, 3/1); mp 80–82 °C; $^1$H NMR (300 MHz, CDCl$_3$) $\delta$ = 8.44 (br s, 1H), 7.62 (t, $J$ = 1.7 Hz, 1H), 7.50 (dt, $J$ = 7.5, 1.6 Hz, 1H), 7.36 (t, $J$ = 7.5 Hz, 1H), 7.32–7.24 (m, 2H), 7.17–7.08 (m, 2H), 6.92 (dd, $J$ = 2.2, 0.7 Hz, 1H); $^{13}$C NMR (75.4 MHz, CDCl$_3$) $\delta$ = 137.5 (C), 136.9 (C), 135.1 (C), 133.5 (C), 130.4 (CH), 128.1 (CH), 128.0 (C), 126.1 (CH), 123.39 (CH), 123.38 (CH), 120.3 (CH), 109.7 (CH), 99.4 (CH); EI-LRMS $m/z$ 265 (M$^+$+4, 13), 263 (M$^+$+2, 62), 261 (M$^+$, 100), 226 (13), 199 (30), 190 (35), 164 (30), 89 (49); HRMS calcd for C$_{14}$H$_9$Cl$_2$N, 261.0112; found, 261.0112.

4-Bromo-2-phenyl-1H-indole (12a): Treatment of 8c (192 mg, 0.5 mmol) with phenylacetylene (77 mg, 0.75 mmol), PdCl$_2$(PPh$_3$)$_2$ (10 mg, 3 mol%), CuI (5 mg, 5 mol%) and Et$_2$NH (54 mg, 0.75 mmol) in DMA (2 mL) for 3 h and then, with NaOH (200 mg, 5 mmol) for 4 h according to the general procedure, and purification by column chromatography (hexane/EtOAc, 8/1) on silica gel afforded 12a (66 mg, 49%), whose spectroscopic data have been reported above.

4-Bromo-2-butyl-1H-indole (12b): Treatment of 8c (576 mg, 1.5 mmol) with 1-hexyne (182 mg, 2.25 mmol), PdCl$_2$(PPh$_3$)$_2$ (31 mg, 3 mol%), CuI (14 mg, 5 mol%) and Et$_2$NH (164 mg, 2.25 mmol) in DMA (6 mL) for 2 h and then, with NaOH (600 mg, 15 mmol) for 3 h according to the general procedure, and purification by column chromatography (hexane/EtOAc, 7/1) on silica gel afforded 12b (207 mg, 55%), whose spectroscopic data have been reported above.

4-Bromo-2-(3-chlorophenyl)-1H-indole (12g): Treatment of 8c (192 mg, 0.5 mmol) with 1-chloro-3-ethynylbenzene (102 mg, 0.75 mmol), PdCl$_2$(PPh$_3$)$_2$ (10 mg, 3 mol%), CuI (5 mg, 5 mol%) and Et$_2$NH (54 mg, 0.75 mmol) in DMA (2 mL) for 2 h and then, with NaOH (200 mg, 5 mmol) for 4 h according to the general procedure, and purification by column chromatography (hexane/EtOAc, 8/1) on silica gel afforded 12g (73 mg, 48%) as a brown solid: $R_f$ 0.38 (hexane/AcOEt, 4/1); mp 89–91 °C; $^1$H NMR (300 MHz, CDCl$_3$) $\delta$ = 8.47 (br s, 1H), 7.67–7.64 (m, 1H), 7.55 (ddd, $J$ = 7.6, 2.8, 1.3 Hz, 1H), 7.43–7.27 (m, 4H), 7.06 (td, $J$ = 8.1, 1.2 Hz, 1H), 6.90–6.87 (m, 1H); $^{13}$C NMR (75.4 MHz, CDCl$_3$) $\delta$ = 137.1 (C), 137.0 (C), 135.2 (C), 133.6 (C), 130.5 (CH), 129.9 (C), 128.2 (CH), 125.4 (CH), 123.8 (CH), 123.5 (CH), 123.4 (CH), 114.9 (C), 110.3 (CH), 101.2 (CH); EI-LRMS $m/z$ 309 (M$^+$+4, 23), 307 (M$^+$+2, 100), 305 (M$^+$, 80), 226 (16), 199 (34), 190 (74), 163 (60); HRMS calcd for C$_{14}$H$_9$BrClIN, 304.9620; found, 304.9620.

Synthesis of 2-butyl-4-(furan-2-yl)-1H-indole (13):

Pre-milled Pd(OAc)$_2$ (2 mol%)/XPhos (4 mol%) and CsF (100 mg, 0.66 mmol) were added to a Schlenk tube under a nitrogen atmosphere, and the tube was evacuated and backfilled with nitrogen.$^{10}$ Then, 4-chloroindole derivative 11b (62 mg, 0.3 mmol), tributyl(furan-2-yl)stannane (118 mg, 0.33 mmol) and DME (0.8 cm$^3$) were added to the tube. The reaction was heated to 80 °C with stirring for 3 h (the consumption of the starting material was monitored by GC-MS). After cooling to room temperature of the reaction vessel, the crude was filtered through zelite and washed with EtOAc (20 cm$^3$). The solvent was concentrated under
reduced pressure and the residue was purified by column chromatography on silica gel (hexane/EtOAc, 7/1) to afford 13 (66 mg, 92%) as a white solid: R<sub>f</sub> 0.43 (hexane/AcOEt, 6/1); mp 50–52 ºC; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ = 7.85 (br s, 1H), 7.61 (d, J = 1.8 Hz, 1H), 7.56–7.52 (m, 1H), 7.23–7.20 (m, 2H), 6.85 (d, J = 3.3 Hz, 1H), 6.75 (s, 1H), 6.60 (ddd, J = 3.3 Hz, 1.8, 0.6 Hz, 1H), 2.76 (t, J = 7.6 Hz, 2H), 1.79–1.68 (m, 2H), 1.52–1.39 (m, 2H), 1.01 (t, J = 7.3 Hz, 3H); <sup>13</sup>C NMR (75.4 MHz, CDCl<sub>3</sub>) δ = 154.8 (C), 141.5 (CH), 141.0 (C), 136.6 (C), 124.4 (C), 122.1 (1), 121.0 (CH), 116.4 (CH), 111.6 (CH), 110.0 (CH), 106.2 (CH), 99.6 (CH), 31.4 (CH<sub>2</sub>), 28.1 (CH<sub>2</sub>), 22.5 (CH<sub>2</sub>), 14.0 (CH<sub>3</sub>); EI-LRMS m/z 239 (M<sup>+</sup>, 56), 196 (100), 167 (14), 154 (4); HRMS calcd for C<sub>16</sub>H<sub>15</sub>NNO, 239.1310; found, 239.1319.

**Synthesis of 2,4-Diphenyl-1H-indole (14):**

4-Bromo-1H-indole derivative 12a (81 mg, 0.3 mmol) and [Pd(PPh<sub>3</sub>)<sub>4</sub>] (10 mg, 3 mol%) were introduced in a Schlenk tube under a nitrogen atmosphere. Then, DME (5 cm<sup>3</sup>) was added followed by the addition of Na<sub>2</sub>CO<sub>3</sub> (48 mg, 0.45 mmol) in H<sub>2</sub>O (2 cm<sup>3</sup>). The reaction mixture was vigorously stirred and heated at 80 ºC overnight (the progress of the reaction was monitored by GC-MS).<sup>11,12</sup> Then, CH<sub>2</sub>Cl<sub>2</sub> (10 cm<sup>3</sup>) and H<sub>2</sub>O were added to the cooled reaction mixture. The separated aqueous phase was extracted with CH<sub>2</sub>Cl<sub>2</sub> (3 × 20 cm<sup>3</sup>). The combined organic extracts were dried over anhydrous Na<sub>2</sub>SO<sub>4</sub> and evaporated under reduced pressure. The residue was purified by column chromatography (hexane/EtOAc, 8/1) on silica gel to afford 14 (74 mg, 93%) as a white solid: R<sub>f</sub> 0.48 (hexane/AcOEt, 4/1); mp 205–207 ºC (lit.<sup>13</sup> mp 209 ºC); <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ = 8.42 (br s, 1H), 7.89–7.82 (m, 2H), 7.67 (d, J = 8.1 Hz, 2H), 7.61 (t, J = 7.7 Hz, 2H), 7.53–7.44 (m, 3H), 7.43–7.25 (m, 4H), 7.12 (d, J = 2.2 Hz, 1H); <sup>13</sup>C NMR (75.4 MHz, CDCl<sub>3</sub>) δ = 141.3 (C), 138.3 (C), 137.3 (C), 134.5 (C), 132.2 (C), 129.1 (2 × CH), 128.9 (2 × CH), 128.7 (2 × CH), 127.8 (CH), 127.6 (C), 127.1 (CH), 125.2 (2 × CH), 122.7 (CH), 120.2 (CH), 110.2 (CH), 99.6 (CH); EI-LRMS m/z 269 (M<sup>+</sup>, 100), 190 (10), 165 (53), 133 (11), 77 (28); HRMS calcd for C<sub>20</sub>H<sub>15</sub>N, 269.1204; found, 269.1204.

**Synthesis of 4-(hex-1-ynyl)-2-phenyl-1H-indole (15):**

A mixture of 4-bromo-1H-indole derivative 12a (81 mg, 0.3 mmol), 1-hexyne (37 mg, 0.45 mmol), PdCl<sub>2</sub>(PPh<sub>3</sub>)<sub>2</sub> (12 mg, 6 mol%), Cul (6 mg, 10 mol%) and Et<sub>2</sub>NH (33 mg, 0.45 mmol) in anhydrous DMF (3 cm<sup>3</sup>) was stirred under a nitrogen atmosphere at 80 ºC for 17 h (complete consumption of the starting material was monitored by GC-MS). Then, CH<sub>2</sub>Cl<sub>2</sub> (20 cm<sup>3</sup>) and aq HCl (20 cm<sup>3</sup> of a 0.5M solution) were added to the cooled reaction mixture. The separated aqueous phase was extracted with CH<sub>2</sub>Cl<sub>2</sub> (3 × 15 cm<sup>3</sup>). The combined organic layers were washed with water (2 × 40 cm<sup>3</sup>), dried over anhydrous Na<sub>2</sub>SO<sub>4</sub> and concentrated under reduced pressure. The remaining residue was purified by column chromatography on silica gel (hexane/EtOAc, 8/1) to afford 15 (63 mg, 77%) as a brown solid: R<sub>f</sub> 0.42 (hexane/AcOEt, 5/1); mp 33–35 ºC; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ = 8.39 (br s, 1H), 7.69 (d, J = 7.3 Hz, 2H), 7.45 (t, J = 7.7 Hz, 2H), 7.33 (d, J = 7.3 Hz, 2H), 7.21 (d, J = 7.3 Hz, 1H), 7.11 (t, J = 7.7 Hz, 1H), 6.99–6.97 (m, 1H), 2.55 (t, J = 6.9 Hz, 2H), 1.75–1.63 (m, 2H), 1.62–1.50 (m, 2H), 1.00 (t, J = 7.2 Hz, 3H); <sup>13</sup>C NMR (75.4 MHz, CDCl<sub>3</sub>) δ = 138.2 (C), 136.5 (C), 132.3 (C), 131.1 (C), 129.2 (2 × CH), 128.0 (CH), 125.3 (2 × CH), 123.9 (CH), 122.3 (CH), 115.8 (C), 110.7 (CH), 99.9 (CH), 93.2 (C), 79.3 (C), 31.2 (CH<sub>2</sub>), 22.2 (CH<sub>2</sub>), 19.6 (CH<sub>2</sub>), 13.9 (CH<sub>3</sub>); EI-LRMS m/z
273 (M+, 89), 258 (16), 244 (38), 230 (100), 202 (29), 127 (23); HRMS calcd for C_{20}H_{19}N, 273.1517; found, 273.1511.

**Synthesis of 4-Bromo-3-((Z)-4-methyl-1,3-diphenylpenta-1,3-dienyl)-2-phenyl-1H-indole (16):**

To a solution of 4-bromo-1H-indole derivative 12a (42 mg, 0.155 mmol) and 4-methyl-1,3-diphenylpent-1-yn-3-ol (42 mg, 0.17 mmol) in MeCN (2 cm³) was added p-toluenesulfonic acid monohydrate (13 mg, 10 mol%). ¹⁴ The resulting mixture was heated at 80 °C for 5.5 h and monitored by GC-MS. The solvent was evaporated under reduced pressure. The remaining residue was purified by column chromatography on silica gel (hexane/EtOAc, 10/1) to afford 16 (62 mg, 80%) as a white solid: Rf 0.36 (hexane/AcOEt, 5/1); mp 72–74 °C; ¹H NMR (300 MHz, CDCl₃) δ = 7.98 (br s, 1H), 7.55–7.48 (m, 4H), 7.39–7.23 (m, 7H), 7.05 (d, J = 7.8 Hz, 1H), 6.95 (d, J = 7.8 Hz, 1H), 6.82 (t, J = 7.8 Hz, 1H), 6.77–6.64 (m, 4H), 6.50 (t, J = 7.1 Hz, 1H), 1.43 (s, 6H); ¹³C NMR (75.4 MHz, CDCl₃) δ = 144.2 (C), 141.3 (C), 136.91 (C), 136.86 (C), 134.9 (C), 134.5 (C), 134.1 (C), 133.3 (CH), 132.8 (C), 128.55 (2 × CH), 128.53 (2 × CH), 128.4 (2 × CH), 127.8 (CH), 127.2 (2 × CH), 126.94 (2 × CH), 126.87 (C), 126.8 (CH), 126.2 (2 × CH), 124.3 (CH), 124.0 (CH), 122.7 (CH), 115.1 (C), 113.3 (C), 109.4 (CH), 22.2 (CH₃), 21.0 (CH₃); EI-LRMS m/z 505 (M⁺+2, 37), 503 (M⁺, 36), 424 (41), 409 (72), 207 (100); HRMS calcd for C_{32}H_{26}BrN, 503.1249; found, 503.1255.

**Synthesis of 4-chloro-2-phenyl-3-(phenylthio)-1H-indole (17):**

Freshly powdered NaOH (48 mg, 1.2 mmol) was added to a solution of 9a (125 mg, 0.4 mmol) in anhydrous DMA (3 cm³). The resulting mixture was heated under a nitrogen atmosphere for 5 h at 140 °C (until the cyclization was completed as monitored by GC-MS). Then, Ph₂S₂ (104 mg, 0.48 mmol) was added to the mixture and the reaction was stirred overnight at 140 °C. Then, CH₂Cl₂ (10 cm³) and aq HCl (10 cm³ of a 0.5M solution) were added to the cooled reaction mixture. The separated aqueous phase was extracted with CH₂Cl₂ (3 × 10 cm³). The combined organic layers were washed with water (2 × 30 cm³), dried over anhydrous Na₂SO₄, and concentrated under reduced pressure. The remaining residue was purified by column chromatography on silica gel (hexane/EtOAc, 5/1) to afford 17 (105 mg, 78%) as a white solid: Rf 0.40 (hexane/AcOEt, 5/1); mp 131–133 °C; ¹H NMR (300 MHz, CDCl₃) δ = 8.70 (br s, 1H), 7.66 (dd, J = 6.6, 2.9 Hz, 2H), 7.43–7.38 (m, 3H), 7.36–7.29 (m, 1H), 7.26–7.05 (m, 7H); ¹³C NMR (75.4 MHz, CDCl₃) δ = 144.3 (C), 141.4 (C), 137.3 (C), 131.0 (C), 129.2 (CH), 128.9 (2 × CH), 128.7 (4 × CH), 127.0 (C), 126.8 (C), 125.3 (2 × CH), 124.6 (CH), 123.7 (CH), 122.8 (CH), 110.2 (CH), 98.8 (C); EI-LRMS m/z 337 (M⁺+2, 22), 335 (M⁺, 51), 299 (16), 267 (15), 223 (100), 190 (12), 121 (22), 119 (23), 77 (86), 51 (67); HRMS calcd for C_{20}H_{15}ClIN, 335.0535; found, 335.0534.

**REFERENCES:**


(9) Commercially available.


$^1$H-NMR (300 MHz, CDCl$_3$):

$^{13}$C-NMR (75.4 MHz, CDCl$_3$):
\(^1\)H-NMR (300 MHz, CDCl\(_3\)):

\(^1\)C-NMR (75.4 MHz, CDCl\(_3\)):
$^1$H-NMR (300 MHz, CDCl$_3$):

![$^1$H-NMR spectrum](image)

$^1$C-NMR (75.4 MHz, CDCl$_3$):

![$^1$C-NMR spectrum](image)
$\text{H-NMR (300 MHz, CDCl}_3\text{):}$

![H-NMR spectrum](image)

$\text{C-NMR (75.4 MHz, CDCl}_3\text{):}$

![C-NMR spectrum](image)
$^1$H-NMR (300 MHz, CDCl$_3$):

$^1$C-NMR (75.4 MHz, CDCl$_3$):
\(^1\)H-NMR (300 MHz, CDCl\(_3\)):

\[ \text{5a} \]

\(^{13}\)C-NMR (75.4 MHz, CDCl\(_3\)):
$^1$H-NMR (300 MHz, CDCl$_3$):

$^1$C-NMR (75.4 MHz, CDCl$_3$):
$^1$H-NMR (300 MHz, CDCl$_3$):

$^{13}$C-NMR (75.4 MHz, CDCl$_3$):
$^1$H-NMR (300 MHz, CDCl$_3$):

$^1$C-NMR (75.4 MHz, CDCl$_3$):
$^1$H-NMR (300 MHz, CDCl₃):

![NMR spectrum](image)

$^1$C-NMR (75.4 MHz, CDCl₃):

![NMR spectrum](image)
$^1$H-NMR (300 MHz, CDCl$_3$):

$^{13}$C-NMR (75.4 MHz, CDCl$_3$):
$^1$H-NMR (300 MHz, CDCl$_3$):

![H-NMR Spectrum](image)

$^1$C-NMR (75.4 MHz, CDCl$_3$):

![C-NMR Spectrum](image)
$^1$H-NMR (300 MHz, CDCl$_3$):

$^1$C-NMR (75.4 MHz, CDCl$_3$):
$^1$H-NMR (300 MHz, CDCl₃):

![H-NMR spectrum](image)

$^1$C-NMR (75.4 MHz, CDCl₃):

![C-NMR spectrum](image)
$^1$H-NMR (300 MHz, CDCl$_3$):

![H-NMR spectrum](image)

$^1$C-NMR (75.4 MHz, CDCl$_3$):

![C-NMR spectrum](image)
$^1$H-NMR (300 MHz, CDCl$_3$):

![H-NMR spectrum](image)

$^{13}$C-NMR (75.4 MHz, CDCl$_3$):

![C-NMR spectrum](image)
$^1$H-NMR (300 MHz, CDCl$_3$):

$^{13}$C-NMR (75.4 MHz, CDCl$_3$):
$^1$H-NMR (300 MHz, CDCl$_3$):

$^{13}$C-NMR (75.4 MHz, CDCl$_3$):
$^1$H-NMR (300 MHz, CDCl$_3$):

$^{13}$C-NMR (75.4 MHz, CDCl$_3$):
$^{1}$H-NMR (300 MHz, CDCl$_3$):

![NMR spectrum of 10d](image)

$^{13}$C-NMR (75.4 MHz, CDCl$_3$):

![C-NMR spectrum of 10d](image)
^1H-NMR (300 MHz, CDCl₃):

![NMR spectrum of compound 10e](image)

^13C-NMR (75.4 MHz, CDCl₃):

![NMR spectrum of compound 10e](image)
$^1$H-NMR (400 MHz, CDCl$_3$):

![NMR spectrum of compound 10f]

$^1$C-NMR (100.6 MHz, CDCl$_3$):

![C-NMR spectrum of compound 10f]
$^1$H-NMR (300 MHz, CDCl$_3$):

![1H-NMR Spectrum](image)

$^{13}$C-NMR (75.4 MHz, CDCl$_3$):

![13C-NMR Spectrum](image)
$^1$H-NMR (300 MHz, CDCl$_3$):

$^1$C-NMR (75.4 MHz, CDCl$_3$):
$^1$H-NMR (300 MHz, CDCl$_3$):

$^{13}$C-NMR (75.4 MHz, CDCl$_3$):
\(^1\)H-NMR (300 MHz, CDCl\(_3\)):

\[ \text{Chemical Structure of Compound 11d} \]

\[^{13}\text{C-NMR (75.4 MHz, CDCl}\(_3\)):\]

\[ \text{Chemical Structure of Compound 11d} \]
$^1$H-NMR (300 MHz, CDCl$_3$):

$^{13}$C-NMR (75.4 MHz, CDCl$_3$):
$^1$H-NMR (300 MHz, CDCl$_3$):

$^{13}$C-NMR (75.4 MHz, CDCl$_3$):
$^1$H-NMR (300 MHz, CDCl$_3$):

$^{13}$C-NMR (75.4 MHz, CDCl$_3$):
\[^1\text{H-NMR} (300 \text{ MHz, CDCl}_3)\]:

\[\text{Br}\]

\[\text{12b}\]

\[^13\text{C-NMR} (75.4 \text{ MHz, CDCl}_3)\]:

\[
\begin{align*}
121 & 138.2 & 129.6 & 131.2 & 112.7 & 129.6 & 129.3 & 70.3 & 24.2 & 31.8 & 51.1
\end{align*}
\]
$^1$H-NMR (300 MHz, CDCl$_3$):

![H-NMR spectrum of compound 12c]

$\text{Br}$

$^13$C-NMR (75.4 MHz, CDCl$_3$):

![C-NMR spectrum of compound 12c]
$^1$H-NMR (300 MHz, CDCl$_3$):

\[ \text{12d} \]

$^{13}$C-NMR (75.4 MHz, CDCl$_3$):
\[ \text{H-NMR (300 MHz, CDCl}_3\):} \\
\[ \text{C-NMR (75.4 MHz, CDCl}_3\):}
$^{1}$H-NMR (300 MHz, CDCl$_3$):

![H-NMR spectrum](image)

$^{13}$C-NMR (75.4 MHz, CDCl$_3$):

![C-NMR spectrum](image)
$^1$H-NMR (300 MHz, CDCl$_3$):

![H-NMR spectrum of compound 12g](image)

$^1$C-NMR (75.4 MHz, CDCl$_3$):

![C-NMR spectrum of compound 12g](image)
$^1$H-NMR (300 MHz, CDCl$_3$):

$^{13}$C-NMR (75.4 MHz, CDCl$_3$):
$^1$H-NMR (300 MHz, CDCl$_3$):

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$^{13}$C-NMR (75.4 MHz, CDCl$_3$):
$^1$H-NMR (300 MHz, CDCl$_3$):

$^{13}$C-NMR (75.4 MHz, CDCl$_3$):
$^1$H-NMR (300 MHz, CDCl$_3$):

$^{13}$C-NMR (75.4 MHz, CDCl$_3$):
$^1$H-NMR (300 MHz, CDCl$_3$):

\[
\text{\begin{center}
\includegraphics[width=0.4\textwidth]{hnmr.png}
\end{center}}
\]

$^{13}$C-NMR (75.4 MHz, CDCl$_3$):

\[
\text{\begin{center}
\includegraphics[width=0.4\textwidth]{cnmr.png}
\end{center}}
\]