SUPPORTING INFORMATION

A NOVEL SYNTHESIS OF N-HYDROXY-3-AROYLINDOLES AND 3-AROYLINDOLES

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EXPERIMENTAL DETAILS

All reactions were performed with oven dried laboratory glassware, under nitrogen atmosphere unless otherwise indicated. Anhydrous solvents were purchased in sealed bottles provided with crown cap from Sigma Aldrich, Acros Organics and Alfa Aesar. All reactants used were purchased from Sigma Aldrich, Fluorochem and TCI and used as received without any further purification.

Reactions were monitored with thin-layer chromatography (TLC) using TLCs ALUGRAM[®] Xtra SIL G/UV254 (0.2 mm thin layer depth; Macherey-Nagel). Spots visualization was performed with UV lamp (365 nm and/or 254 nm respectively). Gravimetric chromatography columns were performed using silica gel (particles diameter: 0.63-2.00 mm) as stationary phase.

¹H-NMR spectra were recorded with Bruker AVANCE instrument operating at 400.13 MHz. Chemical shifts are reported in ppm (δ) and to describe spin multiplicity, some abbreviations were used: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad signal, dd = doublet of doublets, td = triplet of doublets, dt = doublet of triplets. Coupling constants are reported in Hz. ¹³C-NMR spectra were recorded with Bruker AVANCE instrument operating at 100.56 MHz, with total proton decoupling. Chemical shifts are reported in ppm (δ). High-resolution mass spectra (HRMS) were recorded using an Electrospray Ionisation (ESI) spectrometer. GC-MS analyses were performed with a Finnigan Trace GC-MS equipped with a quadrupole analyzer and electronic impact source. Other masses were obtained by VG 7070 EQ mass spectrometer with CI (Chemical Ionization). IR spectra were recorded with a FT-IR Thermo Scientific Nicolet iS10 Smart iTR equipped with a Smart OMNI Transmission instrument, interfaced with a Omnic 9.2.98 software; some spectra were recorded with ATR technique, other ones with a KBr disk. Melting points were obtained with a Stuart Melting Point SMP30 instrument.

SYNTHESIS OF NITROSOARENES

4-Nitro-nitrosobenzene (1a). To an aqueous solution of Oxone[®] (32.1 g in 300 mL, 52.13 mmol), 4nitroaniline (7.2 g, 52.13 mmol) was added at 0 °C and the suspension vigorously stirred at r.t. for 48 hours, then filtered. After recrystallization from methanol (twice), 4-nitro-nitrosobenzene was isolated as a yellow solid (5.61 g, yield = 71%). ¹H-NMR (CDCl₃) δ : 8.52 (d, 2H, *J* = 8.9 Hz), 8.06 (d, 2H, *J* = 8.9 Hz) ppm. All the analytical data are in agreement with the ones reported in literature.¹

4-Nitrosobenzoic acid (1b). To a solution of 4-aminobenzoic acid (1.0 g, 7.3 mmol) in dichloromethane (12 mL), an aqueous solution of Oxone[®] (8.97 g in 45 mL, 14.6 mmol), was added and the suspension vigorously stirred at r.t. for 1 hour (TLC CH_2Cl_2 : MeOH = 9:1). 4-nitrosobenzoic acid precipitated as a yellow solid was isolated by filtration, washed with H₂O and dried under vacuum (1.1 g, yield = quant.). ¹H-NMR (DMSO-*d*₆) δ : 13.5 (br, 1H), 8.27 (d, 2H, *J* = 8.8 Hz), 8.08 (d, 2H, *J* = 8.8 Hz) ppm. All the analytical data are in agreement with the ones reported in literature.²

4-Carbethoxy-nitrosobenzene (1d). To a solution of benzocaine (2.48 g, 15 mmol) in a mixture 1:1 of dichloromethane (75 mL) and *n*-pentane (75 mL), sodium tungstate dihydrate (0.50 g, 1.7 mmol), phosphoric acid (0.75 mL of a 85% solution, 12.88 mmol), hydrogen peroxide (15 mL of a 30% solution, 150 mmol) and tetrabutylammonium bromide (0.15 g, 0.5 mmol) were added. After 6 hours at 35–40 °C, the reaction mixture, which became green, was washed with HCl 0.01 M and water. The organic layers were dried over Na₂SO₄, filtered and rotary evaporated to give 4-carbethoxy-nitrosobenzene (1.01 g, yield = 37%). ¹H-NMR (CDCl₃) δ : 8.32 (d, 2H, *J* = 8.4 Hz), 7.95 (d, 2H, *J* = 8.4 Hz), 4.45 (q, 2H, *J* = 7.1 Hz), 1.45 (t, 3H, *J* = 7.1Hz) ppm. All the other analytical data are in agreement with the ones reported in literature.³

4-Nitroso-toluene (1e). *Cis*-Mo(O)₂(acac)₂ (0.326 g, 1 mmol) was suspended in cyclohexane (20 mL) and vigorously stirred for 5 min, then 4-toluidine (1.087 g, 10 mmol) and H_2O_2 (5 mL of a 30% solution, 50 mmol) were added and the biphasic system stirred at r.t. After 1 h, to the mixture, which turned green, additional 20 mL of cyclohexane and about 1 g of Na_2SO_4 were added. After 20 min, the mixture was filtered; the organic layers were dried over Na_2SO_4 and cooled to -4 °C for 2 hours. Precipitation of the product as a yellow solid was observed. Isolation by filtration gave 4-nitroso-toluene (494 mg, yield = 41%). ¹H-NMR (CDCl₃) δ : 7.82 (d, 2H, *J* = 7.8 Hz), 7.40 (d, 2H, *J* = 7.8 Hz), 2.46 (s, 3H) ppm. All the other analytical data are in agreement with the ones reported in literature.⁴

4-Methoxy- nitrosobenzene (1f). Under nitrogen, to a solution of NOBF₄ (3.25 g, 27.8 mmol) in acetonitrile (40 mL), anisole (1 mL, 9.20 mmol) was added and the mixture was stirred at r.t.. After 30 min, water was added and the mixture was extracted with CH_2Cl_2 , dried over Na_2SO_4 , filtered and rotary evaporated. After purification on silica gel (Hexane : $CH_2Cl_2 = 7:3$), 4-methoxynitrosobenzene was isolated as a green–blue oil (884 mg, yield = 70%). ¹H-NMR (CDCl₃, 50 °C) δ : 7.93 (d, 2H, *J* = 7.0 Hz), 7.05 (d, 2H, *J* = 7.0 Hz), 3.97 (s, 3H) ppm. GC-MS (EI): *m/z*: 137. All the other analytical data are in agreement with the ones reported in literature.⁵

2-Carbomethoxy-nitrosobenzene (1g). To a solution of methyl antranilate (1.30 mL, 10 mmol) in ethanol (20 mL), H_3PO_4 (1 mL of a 85% solution), sodium tungstate dihydrate (0.99 g, 3 mmol) and hydrogen peroxide (10 mL of a 30% solution, 100 mmol) were added. The mixture was stirred at 60–65 °C until precipitation of a solid was observed. At reaction completed, the mixture was cooled to r.t., the solid was filtered and washed with water. 2-carbomethoxy-nitrosobenzene was collected as a yellow solid (1.51 g, yield = 92%). ¹H-NMR (DMSO- d_6) δ : 7.93-7.92 (m, 2H), 7.78-7.76 (m, 1H), 7.08-7.06 (m, 1H), 3.96 (s, 3H) ppm. GC-MS (EI): m/z: 166 [*M*H+]. All the other analytical data are in agreement with the ones reported in literature.³

4-Cyano-nitrosobenzene (1h). To a solution of 4-aminobenzonitrile (2.36 g, 20 mmol) in a mixture 1:1 of CH_2CI_2 (50 mL) and *n*-pentane (50 mL), sodium tungstate dihydrate (0.66 g, 1 mmol), phosphoric acid (1 mL of a 85% solution, 14.6 mmol), hydrogen peroxide (20 mL of a 30% solution 195.82 mmol) and tetrabutylammonium bromide (0.2 g, 0.62 mmol) were added. After 2.5 hours at 35–40 °C (TLC CH_2CI_2 : petroleum ether = 8:2) reaction mixture was washed with HCl 0.01 M (50 mL) and water (50 mL), the organic layers dried over Na_2SO_4 , filtered and rotary evaporated. After recrystallization from hexane, 4-cyano-nitrosobenzene was isolated as a yellow solid (1.63 g, yield = 62%). All the other analytical data are in agreement with the ones reported in literature.⁶

SYNTHESIS OF ALKYNOLES AND ALKYNONES

Representative Procedure for the oxidation reaction using Jones Reagent (RP1)

1-Phenylprop-2-yn-1-one (2a). Jones reagent was added dropwise to a solution of 1-phenylprop-2-yn-1-ol (234 mg, 2 mmol) in acetone (30 ml) kept at 0°C, to the point of a persistent orange color. At the end of the reaction, the excess of Jones reagent was removed adding 2-propanol dropwise to the point of a persistent green color. The mixture was filtered through celite and the washings concentrated under reduced pressure to give an oil. The crude residue was dissolved in CH_2CI_2 and washed with saturated Na_2HCO_3 and brine. The organic layers were dried over Na_2SO_4 , filtered and the solvent removed under reduced pressure. 1-phenylprop-2-yn-1-one isolated (quant. yield) as a yellow solid. ¹H-NMR (CDCl₃) δ : 8.19 (d, 2H, *J* = 7.5 Hz); 7.66 (t, 1H, *J* = 7.5 Hz); 7.53 (t, 2H, *J* = 7.5 Hz); 3.45 (s, 1H). Other spectroscopic data for this compound are in agreement with the ones reported in literature.⁷

Representative Procedure for the synthesis of arylalkynoles (RP2)

1-(2-Chlorophenyl)prop-2-yn-1-ol. A solution of ethynylmagnesium bromide 0.5 M in THF (39.6 ml, 17.07 mmol) was added dropwise to a solution of 2-chloro-benzaldehyde (2 g, 14.22 mmol) in THF (35 ml) cooled to 0°C. The mixture was allowed to warm to rt and stirred until the complete conversion of the aldehyde. A saturated aqueous solution of NH₄Cl (40 ml) was added to the reaction solution and the aqueous layer was extracted with EtOAc. The combined organic layers were washed with H₂O and brine, dried over Na₂SO₄ and the solvent removed under reduced pressure. 1-(2-chlorophenyl)prop-2-yn-1-ol was isolated (quant. yield) as a brown oil without any further purification. ¹H-NMR (CDCl₃) δ : 7.80 (dd, 1H, ¹J = 7.5 Hz, ²J = 1.8 Hz), 7.41 (dd, 1H, ¹J = 7.5 Hz, ²J = 1.3 Hz), 7.35 (td, 1H, ¹J = 7.5 Hz, ²J = 1.3 Hz), 7.31 (td, 1H, ¹J = 7.5 Hz, ²J = 1.8 Hz), 5.86 (d, 1H, J = 2.1 Hz), 2.68 (d, 1H, J = 2.1 Hz), 2.49 (br, 1H) ppm. ¹³C-NMR (CDCl₃) δ : 137.4, 132.5, 129.6, 129.5, 128.1, 127.1, 82.4, 74.6, 61.3 ppm. Other spectroscopic data for this compound are in agreement with the ones reported in literature.⁸

1-(2-Chlorophenyl)prop-2-yn-1-one (2b). This compound was prepared according to RP1 starting from 1-(2-chlorophenyl)prop-2-yn-1-ol (2.2 g, 13.22 mmol) to give 1-(2-chlorophenyl)-2-propyn-1-one as a yellow solid (1.99 g, yield = 90%), characterized without further purification. ¹H-NMR (CDCl₃) δ : 8.13 (d, 1H, *J* = 8.0 Hz), 7.54 – 7.49 (m, 2H), 7.44 – 7.40 (m, 1H), 3.49 (s, 1H) ppm. Other spectroscopic data for this compound are in agreement with the ones reported in literature.⁹

1-(2-Bromophenyl)prop-2-yn-1-ol. This compound was prepared according to RP2 starting from 2-bromobenzaldehyde (2.00 g, 10.81 mmol) to give 1-(2-bromophenyl)prop-2-yn-1-ol as a yellow oil (1.78 g, yield = 78%). Spectroscopic data for this compound are in agreement with the ones reported in literature.¹⁰

1-(2-Bromophenyl)prop-2-yn-1-one (2c). This compound was prepared according to RP1 starting from 1-(2-bromophenyl)prop-2-yn-1-ol (1.78 g, 8.44 mmol) to give 1-(2-bromophenyl)-2-propyn-1-one as a yellow-orange solid (1.64 g, yield = 93%), characterized without further purification. Spectroscopic data for this compound are in agreement with the ones reported in literature.¹⁰

1-(3-Nitrophenyl)prop-2-yn-1-ol. This compound was synthesized from 3-nitrobenzaldehyde (2 g, 13.23 mmol) using RP2 and isolated after flash chromatography over silica gel (hexane-EtOAc 8:2, 61 % yield) as a yellow oil. ¹H-NMR (CDCl₃) δ : 8.47 (s, 1H); 8.23 (dd, 1H, *J* = 8.0, 1.4 Hz); 7.92 (d, 1H, *J* = 8.0 Hz); 7.60 (t, 1H, *J* = 8.0 Hz); 5.60 (d, 1H, *J* = 2.2 Hz); 2.77 (d, 1H, *J* = 2.2 Hz). Other spectroscopic data for this compound are in agreement with the ones reported in literature.⁹

1-(3-Nitrophenyl)prop-2-yn-1-one (2d). This compound was synthesized from 1-(3-nitrophenyl)prop-2-yn-1-ol (1.65 g, 9.32 mmol) using RP1 and isolated after flash chromatography over silica gel (petroleum ether - EtOAc 8:2, 64 % yield) as a yellow solid. ¹H-NMR (CDCl₃) δ : 9.00 (s, 1H); 8.51 (dd, 1H, *J* = 7.8, 1.4 Hz); 8.50 (d, 1H, *J* = 7.8 Hz); 7.75 (t, 1H, *J* = 7.8 Hz); 3.62 (s, 1H). Other spectroscopic data for this compound are in agreement with the ones reported in literature.⁹

1-(4-Nitrophenyl)prop-2-yn-1-ol. This compound was synthesized from 4-nitrobenzaldehyde (2 g, 13.23 mmol) using RP2 and isolated after flash chromatography over silica gel (petroleum ether - EtOAc 6:4, 55 % yield) as a yellow oil. Spectroscopic data for this compound were in agreement with the literature. ¹H-NMR (CDCl₃) δ : 8.27 (d, 2H, J = 8.6 Hz), 7.76 (d, 2H, J = 8.6 Hz), 5.60 (d, 1H, J = 2.2Hz), 2.76 (d, 1H, J = 2.2 Hz) ppm.¹¹

1-(4-Nitrophenyl)prop-2-yn-1-one (2e). This compound was synthesized from 1-(4-nitrophenyl)prop-2-yn-1-ol (1.28 g, 7.23 mmol) using RP1 and isolated after flash chromatography over silica gel (petroleum ether - EtOAc 8:2, 64 % yield) as a yellow solid. ¹H-NMR (CDCl₃) δ : 8.37 (d, 2H, *J* = 9.1Hz), 8.34 (d, 2H, *J* = 9.1Hz), 3.63 (s, 1H) ppm. Other spectroscopic data for this compound are in agreement with the ones reported in literature.¹²

1-(4-Methoxyphenyl)prop-2-yn-1-ol. This compound was synthesized from 4-methoxybenzaldehyde (3 g, 22.03 mmol) using RP2 and isolated after flash chromatography over silica gel (hexane -EtOAc 8:2, 59 % yield) as a yellow oil. ¹H-NMR (CDCl₃) δ : 7.42 (d, 2H, *J* = 6.4 Hz); 6.88 (d, 2H, *J* = 6.4 Hz); 5.37 (s, 1H); 3.77 (s, 3H); 2.60 (s, 1H); 2.59 (br s, 1H). Other spectroscopic data for this compound are in agreement with the ones reported in literature.¹³

1-(4-Methoxyphenyl)prop-2-yn-1-one (2f). This compound was synthesized from 1-(4-methoxyphenyl)prop-2-yn-1-ol (1.57 g, 9.69 mmol) using RP1 and isolated as a white solid (77 % yield). ¹H-NMR (CDCl₃) δ : 8.16 (d, 2H, *J* = 8.8 Hz); 6.99 (d, 2H, *J* = 8.8 Hz); 3.92 (s, 3H); 3.39 (s, 1H). Other spectroscopic data for this compound are in agreement with the ones reported in literature.¹⁴

1-(4-Formylphenyl)prop-2-yn-1-ol. This compound was prepared according to the following literature procedure.¹⁵ A solution of (trimethylsilyl)acetylene (1.2 equiv) in THF (50 mL) was stirred in a 100 mL ovendried two-necked round-bottom flask under a nitrogen atmosphere at -70 °C. n-Butyllithium (1.2 equiv, 1.60 M in THF) was introduced over 30 min at -70 °C. After an additional 1 h of stirring, a solution of terephthalaldehyde (1.0 equiv) in THF (5 mL) was added at -70 °C. The resulting mixture was stirred for 1 h and warmed to room temperature slowly, and the stirring was continued for 30 min. The reaction mixture was quenched with saturated NH₄Cl aqueous solution (20 mL) at 0 °C. The organic layer was separated; the aqueous layer was extracted with Et_2O (2 × 20 mL). The combined extracts were washed with water (2 × 20 mL) and brine (25 mL) and dried over Na₂SO₄. The solvent was filtered and evaporated under the reduced pressure. The crude residue was subsequently used for the desilylation reaction. Methanol (15 mL) and K_2CO_3 (2.5 equiv) were introduced to the crude residue obtained in the above reaction, and the heterogeneous mixture was stirred under an argon atmosphere at ambient temperature overnight. The reaction mixture was diluted with ethyl acetate (50 mL) and washed with water (2 × 20 mL) and brine (10 mL). The organic layer was separated, dried over Na₂SO₄, filtered, and concentrated under vacuum to afford 1-(4-Formylphenyl) prop-2-yn-1-ol as a yellow solid. Spectroscopic data for this compound are in agreement with the ones reported in literature.¹⁶

1-(4-Formylphenyl)prop-2-yn-1-one (2g). To a solution of 4-(1-hydroxyprop-2-yn-1-yl)benzaldehyde (400 mg, 2.50 mmol) in DCM (30 mL), MnO₂ (2.8 g, 32.21 mmol) was added. After 4 hours, reaction mixture was filtered through celite. Solvent was then removed by rotary evaporation to obtain 1-(4-Formylphenyl) prop-2-yn-1-one (yield 63%) as an orange solid. ¹H-NMR (CDCl₃) δ : 10.15 (s, 1H), 8.34 (d, 2H, J = 2 Hz), 8.03 (d, 2H, J = 2Hz), 3.55 (s, 1H) ppm.

1-(Benzo[d][1,3]dioxol-5-yl)prop-2-yn-1-ol. This compound was prepared according to the following literature procedure.¹⁸ An oven-dried, round bottom flask equipped with a magnetic stir bar was charged with piperonal (2.5 g, 16.65 mmol) under nitrogen. After adding THF (20 mL) under nitrogen atmosphere, the flask was placed in the ice bath (0 °C). Then ethynylmagnesium bromide solution (3 eq.) was added into the reaction mixture slowly and the ice bath was removed after 30 min. The reaction was allowed to proceed for 5 h and its progress was checked by thin layer chromatography (TLC hexane : EtOAc 4:1). The reaction mixture was then diluted with ethyl acetate and washed with a 1 N HCl solution and brine. The organic layers were dried over MgSO₄, concentrated in vacuo, and purified by flash column chromatography (hexane : EtOAc 4:1) to give 1-(benzo[d][1,3]dioxol-5-yl)prop-2-yn-1-ol as a yellow oil. Spectroscopic data for this compound are in agreement with the ones reported in literature.¹⁷

1-(Benzo[d][1,3]dioxol-5-yl)prop-2-yn-1-one (2h). This compound was prepared according to the following literature procedure.¹⁹ To a solution of 1-(benzo[d][1,3]dioxol-5-yl)prop-2-yn-1-ol (1.2 g, 6.82 mmol), MnO₂ (13 eq.) was added. After 4 hours, reaction mixture was filtered through celite. Solvent was then removed by rotary evaporation to obtain 1-(benzo[d][1,3]dioxol-5-yl)prop-2-yn-1-one **2i** (yield 89%). Spectroscopic data for this compound are in agreement with the ones reported in literature.¹⁸

1-(1*H***-Benzotriazol-1-yl)prop-2-yn-1-one (20a).** Thionyl chloride (3.6 g, 30 mmol) was added to a solution in dichloromethane (150 mL) of 1H-benzotriazole (14.4 g, 120 mmol) at room temperature. After 30 minutes, propiolic acid (2.1g, 30 mmol) was added. When the reaction was finished (TLC hexane – EtOAc 1:1), the mixture is filtered and then washed with dichloromethane. The solution obtained is washed with NaOH 2M, dried with MgSO₄, filtered and then rotary evaporated. The crude product is then purified with gravimetric column cromatography (toluene/DCM 7:3) to afford 2.57 g (12.5%, yield) of a grey solid. Other spectroscopic data for this compound are in agreement with the ones reported in literature.¹⁹

1-(1-Methyl-1H-indol-3-yl)prop-2-yn-1-one (20b). Under nitrogen atmosphere, to a solution of 1-methyl-1*H*-indole-3-carbaldehyde (1.50 g, 9.44 mmol) in THF (30 mL), ethynylmagnesium bromide (38 mL of a 0.5 M solution in THF, 18.87 mmol) was added dropwise at 0 °C. After 16 hours at r.t., THF was removed by rotary evaporation, the oil dissolved in CHCl₃ and washed with saturated NH₄Cl (2 x 75 mL) and brine (2 x 75 mL). The organic layers were dried over Na₂SO₄, filtered and the volume of solvent was reduced to 30 mL by rotary evaporation. To this solution, MnO₂ (1.85 g) was added and the mixture was refluxed for 1 hour. Then, 1.85 g of MnO₂ were added, the mixture was refluxed for one additional hour and, after cooling to r.t., filtered through celite. The solvent was removed by rotary evaporation. After purification of the crude material on silica gel (petroleum ether : ethyl acetate=6:4), 1-(1-methyl-1*H*-indol-3-yl)prop-2-yn-1-one was isolated as a yellow–gold solid (895 mg, yield = 52%). ¹H-NMR (CDCl₃) δ : 8.40 – 8.37 (m, 1H), 7.94 (s, 1H), 7.44 – 7.37 (m, 3H), 3.88 (s, 3H), 3.18 (s, 1H) ppm. Other spectroscopic data for this compound are in agreement with the ones reported in literature.²⁰

1-(1-Methyl-1H-indol-2-yl)prop-2-yn-1-ol. This compound was prepared according to RP2 starting from 1methyl-1H-indole-2-carbaldehyde (1.48 g, 9.30 mmol) to give 1-(1-methyl-1H-indol-2-yl)prop-2-yn-1-ol as a brown oil (1.29 g, yield = 75%). ¹H-NMR (CDCl₃) δ : 7.50 (d, 1H, J = 8 Hz), 7.19 (m, 2H), 7.01 (t, 1H, J = 7.6 Hz), 6.56 (s, 1H), 5.50 (d, 1H, J = 5.2 Hz), 3.68 (s, 3H), 2.58 (d, 1H, J = 2.4 Hz), 2.35 (d, 1H. J = 6.8 Hz) ppm. ¹³C-NMR (CDCl₃) δ : 138.5, 137.4, 126.7, 122.5, 121.2, 119.8, 109.3, 101.6, 81.7, 74.8, 58.2, 31.2 ppm.

1-(1-Methyl-1H-indol-2-yl)prop-2-yn-1-one (20c). To a solution of 1-(1-methyl-1H-indol-2-yl)prop-2-yn-1-ol (1.3 g, 6.9 mmol) in chloroform(60 mL), MnO₂ (3.57 g, 42 mmol) was added and the mixture was refluxed for 60 minutes. Then, reaction mixture was filtered through celite. The solvent was removed by rotary evaporation to afford 1-(1-methyl-1H-indol-2-yl)prop-2-yn-1-one (yield: 78%) as a brown solid. ¹H-NMR (CDCl₃) δ : 7.63 (d, 1H, J = 8 Hz), 7.53 (s 1H), 7.34 (t, 1H), J = 7.2 Hz), 7.28 (d, 1H, J = 8.4 Hz), 7.08 (t, 1H, J = 7.2 Hz), 3.99 (s, 3H), 3.20 (s, 1H) ppm. ¹³C-NMR (CDCl₃) δ : 168.7, 141.2, 135.5, 127.3, 125.9, 123.5, 121.2, 117.5, 110.5, 81.3, 77.4, 32.1 ppm.

(*E*)-1-Phenylpent-1-en-4-yn-3-one (20d). Under nitrogen atmosphere, to a solution of aluminum chloride (267 mg, 2 mmol) in anhydrous dichloromethane (20 mL), kept at -40 °C, a mixture of cinnamoyl chloride (333 mg, 2 mmol, 1 eq.) and trimethylsilylacetylene (340 μ L, 2.4 mmol, 1.2 eq.) in anhydrous dichloromethane (30 mL) were added dropwise (time: 30 min). The reaction mixture was kept at -40 °C for 1 hour, then the temperature was risen to -10 °C in about 3.5 hours. When the reaction was complete, ice was added and the mixture washed with HCl 10% (2 x 50 mL) and sat. NaHCO₃ (2 x 50 mL). The organic layers were dried over Na₂SO₄, filtered and rotary evaporated. After purification on silica gel (petroleum ether : AcOEt=9:1) the product was isolated with 52% yield (162 mg). Spectroscopic data for this compound are in agreement with the ones reported in literature.¹²

1-(1-Methyl-1*H***-pyrrol-2-yl)prop-2-yn-1-ol.** This compound was synthesized from *N*-methyl-2-pyrrolecarboxaldehyde (160 mg, 1.47 mmol) using RP2 and isolated after flash chromatography over silica gel (hexane -EtOAc 7:3, 76 % yield) as a yellow oil.

1-(1-Methyl-1H-pyrrol-2-yl)prop-2-yn-1-one (20e). To a solution of 1-(1-methyl-1*H*-pyrrol-2-yl)prop-2-yn-1ol (135 mg, 1 mmol) in CHCl₃ (10 mL), MnO₂ (255 mg, 2.93 mmol) was added and the mixture was refluxed for 1 hour. Then, 255 mg of MnO₂ were added, the mixture was refluxed for an additional hour and, after cooling to r.t., filtered through celite. The solvent was removed by rotary evaporation. After purification of the crude material on silica gel (petroleum ether : EtOAc = 8:2), 1-(1-methyl-1*H*-pyrrol-2-yl)prop-2-yn-1-one was isolated as a yellow solid (98 mg, yield = 75%). ¹H-NMR (CDCl₃) δ : 7.24 (dd, 1H, J_1 = 4.1 Hz, J_2 = 1.6 Hz), 6.89 (d, 1H, J = 4.1 Hz), 6.19 (dd, 1H, J_1 = 4.1 Hz, J_2 = 2.4 Hz), 3.96 (s, 3H), 3.14 (s, 1H) ppm.

1-(Furan-2-yl)prop-2-yn-1-ol. This compound was synthesized from 2-furancarboxaldehyde using RP2 and isolated after flash chromatography over silica gel (hexane -EtOAc 8:2, 52 % yield) as a yellow oil. ¹H-NMR (CDCl₃) δ : 7.37 (s, 1H), 6.42 (d, 1H, *J* = 2.9 Hz), 6.31 (d, 1H, *J* = 1.8 Hz), 5.40 (d, 1H, *J* = 4.2 Hz), 3.00 (br, 1H), 2.57 (d, 1H, *J* = 1.8 Hz) ppm. Other spectroscopic data for this compound were in agreement with the literature.²¹

1-(Furan-2-yl)prop-2-yn-1-one (20f). To a solution of 1-(furan-2-yl)prop-2-yn-1-ol (350 mg, 2.87 mmol) in CHCl₃ (15 mL). Then, MnO₂ (1.09 g, 12.54 mmol) was added and the mixture was refluxed for 1 h. Other 1.09 g of MnO₂ were added and the mixture was refluxed for an additional hour and, after cooling to r.t., filtered through celite. The solvent was removed by rotary evaporation. After purification of the crude material on silica gel (petroleum ether : ethyl acetate=70:30), 1-(furan-2-yl)prop-2-yn-1- one was isolated as a yellow solid (225 mg, yield = 65%). ¹H-NMR (CDCl₃) δ : 7.68 (s, 1H), 7.40 (d, 1H, J = 3.6 Hz), 6.59 (d, 1H, J = 3.6 Hz), 3.38 (s, 1H) ppm. Other spectroscopic data for this compound were in agreement with the literature.¹⁴

1-(Pyren-1-yl)-3-(trimethylsilyl)prop-2-yn-1-ol. Under nitrogen atmosphere, 7.8 mL of *n*-BuLi (13 mmol) were added to a solution of ethynyltrimethylsilane (1.83 ml, 13 mmol) in Et₂O (30 mL). After 30 minutes, a solution of pyrene-1-carboxaldehyde (2.3 g, 10 mmol) in Et₂O (20 mL) was added dropwise. After that, reaction mixture was allowed to reach r.t. and, after 2 hours, 20 mL of saturated aqueous ammonium chloride were added. Therefore, extraction with DCM was performed and then collected organic phases were dried with MgSO₄, filtered and rotary evaporated to afford final product as a yellow solid (85%). Spectroscopic data for this compound are in agreement with the ones reported in literature.²²

1-(Pyren-1-yl)prop-2-yn-1-ol. In a flask loaded with 1-(pyren-1-yl)-3-(trimethylsilyl)prop-2-yn-1-ol (328mg, 1 mmol) in water (10 mL) at 0°C, a solution of tetrabutyl-ammonium fluoride (340 mg, 1.3 mmol) in THF (10 mL) was added. After 4 hours, reaction was poured into a mixture of 30 mL H₂O and 30 mL Et₂O. Aqueous phase was then extracted with Et₂O (2 x 20 mL). The collected organic phases were then washed with brine, dried with MgSO₄, filtered ad rotary evaporated. The crude product was then purified by gravimetric

chromatography column (DCM/hexane 6:4) to afford a yellow solid (78% yield). Spectroscopic data for this compound are in agreement with the ones reported in literature.²³

1-(Pyren-1-yl)prop-2-yn-1-one (20g). To a solution of 1-(pyren-1-yl)prop-2-yn-1-ol (256 mg, 1 mmol) in DCM (30 mL), MnO_2 (2.61 g, 30 mmol) was added and the mixture was refluxed for 24 h. Then, after cooling to r.t., reaction mixture was filtered through celite. The solvent was removed by rotary evaporation to afford 1-(pyren-1-yl)prop-2-yn-1-one in quantitative yield. Spectroscopic data for this compound are in agreement with the ones reported in literature.²³

N-Phenylpropiolamide (20h). A solution of *n*-BuLi 2.5 M in hexane (1.44 ml, 10.2 mmol) was added dropwise at 0°C to a solution of trimethylsilylacetylene (1.4 ml, 10.2 mmol) in THF (100 ml) under N₂. The reaction mixture was stirred at 0°C for 1 hour, then phenyl isocyanate (1.1 ml, 10.2 mmol) was added dropwise. When the reaction was complete, a saturated aqueous solution of NH₄Cl (50 ml) was added and the water phase extracted with CH₂Cl₂ (3x35 ml). The combined organic layers were dried over Na₂SO₄ and the solvent removed under reduced pressure. The crude material was dissolved in THF (100 ml) at 0°C and tetrabutylammonium fluoride (3%) was added. The reaction mixture was stirred at 0°C for 5 hours, then quenched with H₂O (50 ml). The water phase was extracted with Et₂O (3x35 ml), the combined organic layers were dried over Na₂SO₄ and the solvent removed under reduced pressure. Purification via flash chromatography (Hexane-EtOAc 7:3, 54 % yield) afforded *N*-phenylpropiolamide as a brown oil. ¹H-NMR (CDCl₃) δ : 8.01 (br s, 1H); 7.54 (d, 2H, *J* = 8 Hz); 7.32 (2H, t, *J* = 8 Hz); 7.14 (1H, t, *J* = 8 Hz); 2.92 (s, 1H). Other spectroscopic data for this compound are in agreement with the ones reported in literature.²⁴

1-(Ferrocene)prop-2-yn-1-ol. This compound was synthesized from ferrocene carboxaldehyde (1.00 g, 4.67 mmol) using RP2 and isolated after flash chromatography over silica gel (dichloromethane 8:2, 81% yield) as a yellow solid. ¹H-NMR (CDCl₃) δ : 5.18 – 5.16 (dd, 1H, J₁ = 7.7 Hz, J₂ = 2.1 Hz), 4.40 – 4.37 (m, 2H), 4.25 (s, 5H), 4.22 – 4.25 (m, 2H), 2.62 – 2.61 (d, 1H, J = 2.1 Hz), 2.15 – 2.13 (d, 1H, J = 7.7 Hz) ppm.²⁵

1-(Ferrocene)prop-2-yn-1-one (20i). To a solution of 1-(ferrocene)prop-2-yn-1-ol (480 mg, 2 mmol) in DCM (30 mL), MnO_2 (5.22 g, 60 mmol) was added and the mixture was magnetic stirred for 5 minutes at room temperature. Then, reaction mixture was filtered through celite. The solvent was removed by rotary evaporation to afford 1-(ferrocene)prop-2-yn-1-one in quantitative yield as a dark red solid. ¹H-NMR (CDCl₃) δ : 4.97 (s, 2H), 4.65 (s, 2H), 4.30 (s, 5H), 3.27 (s, 2H) ppm.²⁵

1-(Naphthalen-1-yl)prop-2-yn-1-ol. This compound was synthesized from 1-naphthaldehyde (1.5 g, 9.61 mmol) using RP2 and isolated after flash chromatography over silica gel (hexane -EtOAc 8:2, 83 % yield) as a yellow oil. ¹H-NMR (CDCl₃) δ : 8.30 (d, 1H, *J* = 8.4 Hz), 7.89 - 7.80 (m, 3H), 7.59 - 7.49 (m, 3H), 6.11 (d, 1H, *J* = 2.0 Hz), 3.11 (br, 1H), 2.73 (d, 1H, *J* = 2.0 Hz) ppm. Other spectroscopic data for this compound are in agreement with the ones reported in literature.²⁶

1-(Naphthalen-1-yl)prop-2-yn-1-one (20j). This compound was prepared according to RP1 starting from 1-(naphthalen-1-yl)prop-2-yn-1-ol (1.38 g, 7.58 mmol) to give 1-(naphthalen-1-yl)prop-2-yn-1-one as a yellow solid (1.23 g, yield = 90%) after purification on silica gel (petroleum ether : AcOEt = 9:1). ¹H-NMR (CDCl₃) δ : 9.22 (d, 1H, *J* = 8.7 Hz), 8.63 (dd, 1H, *J*₁ = 7.2 Hz, *J*₂ = 0.8 Hz), 8.11 (d, 1H, *J* = 8.1 Hz), 7.92 (d, 1H, *J* = 8.1 Hz), 7.69 (td, 1H, *J*₁ = 7.8 Hz, *J*₂ = 1.2 Hz), 7.59 (t, 2H, *J* = 7.8 Hz), 3.45 (s, 1H) ppm.²⁷

(*E*)-1-(2-Nitrophenyl)pent-1-en-4-yn-3-ol. This compound was synthesized from *trans*-2nitrocinnamaldehyde using RP2 and the alkynol was isolated as a brown oil (quant. yield) without further purifications. ¹H-NMR (CDCl₃) δ : 7.96 (d, 1H, *J* = 7.9 Hz); 7.63-7.57 (m, 2H); 7.43 (m, 1H); 7.30 (dd, 1H, *J* = 15.6, 1.1 Hz); 6.27 (dd, 1H, *J* = 15.6, 5.6 Hz); 5.11 (m, 1H); 2.66 (d, 1H; *J* = 2.2 Hz); 2.67 (br s, 1H). Other spectroscopic data for this compound are in agreement with the ones reported in literature.²⁸

(*E*)-1-(2-Nitrophenyl)pent-1-en-4-yn-3-one (20k). Dess-Martin periodinane (2.4 g, 5.6 mmol) was added to a solution of (*E*)-1-(2-nitrophenyl)pent-1-en-4-yn-3-ol (1.14 g, 5.6 mmol) in CH_2Cl_2 (60 ml) and the mixture was stirred for 1 hour at rt. At the end of the reaction Et_2O (20 ml) and an aqueous solution of NaOH 1M (40 ml) were added and the mixture was stirred for 5 minutes. The aqueous phase was extracted with Et_2O (3x30 ml) and the combined organic layers were washed with H_2O , dried over Na_2SO_4 and the solvent removed under reduced pressure to afford (*E*)-1-(2-nitrophenyl)pent-1-en-4-yn-3-one as a brown solid (75 % yield).¹H-NMR (DMSO-d₆) δ : 8.25 (d, 1H, *J* = 16 Hz); 8.13 (dd, 1H, *J* = 8.1, 1.2 Hz); 7.98 (dd, 1H, *J* = 7.8, 1.3 Hz); 7.81 (td, 1H, *J* = 7.4, 0.8 Hz); 7.73 (td, 1H, *J* = 7.8, 1.4 Hz); 6.96 (d, 1H, *J* = 16 Hz); 4.99 (s, 1H). ¹³C-NMR (DMSO-d₆) δ : 177.7; 148.8; 144.9; 134.5; 132.2; 131.9; 130.0; 129.3; 125.4; 84.7; 80.3. MS (CI): *m/z* = 202 [M]⁺. IR (KBr disk): v (cm⁻¹) = 3255; 3105; 2099; 1645; 1518; 1347; 1238; 970; 787; 741. m.p.: 102-104 °C.

4-Phenylbut-1-yn-3-ol. This compound was prepared according to general procedure RP2 utilizing ethynylmagnesium bromide (0.5 M in THF, 36.0 mL, 18.0 mmol) and phenylacetaldehyde (1.8 g, 15 mmol). The crude material was purified by silica gel chromatography (hexane/AcOEt = 5:1) to afford the title compound as a yellow oil (1.5 g, 70% yield). Spectroscopic data for this compound are in agreement with the ones reported in literature.²⁹

1-Phenylbut-3-yn-2-one (20l). This compound was prepared according to RP1 starting from 4-phenylbut-1-yn-3-ol (1.8 g, 12.33 mmol) to give 1-phenylbut-3-yn-2-one as a yellow solid (yield = 90%). Spectroscopic data for this compound are in agreement with the ones reported in literature.³⁰

SYNTHESIS OF N-HYDROXY-3-AROYLINDOLES, N-ALKOXY-3-AROYLINDOLES AND 3-AROYLINDOLES

Compound 3. To a solution of 3-benzoyl-1-hydroxy-5-nitro-1*H*-indole (100 mg, 0.35 mmol) in methanol (15 mL), potassium carbonate (294 mg, 2.13 mmol) and dimethylsulphate (270 μ L, 2.85 mmol) were added. The mixture, which turned immediately dark brown after addition of the base, was stirred at r.t. for 24 h, then additional dimethylsulphate (270 μ L, 2.85 mmol, 8 eq.) was added. After additional 24 h the suspension was filtered. The filtrate was rotary evaporated, dissolved in CH₂Cl₂ and washed with water (3x20mL). The organic layers were dried over Na₂SO₄, filtered and rotary evaporated, giving 3-benzoyl-1-methoxy-5-nitro-1*H*-indole **3** as an orange-yellow solid (101 mg, yield = 96%), characterized without further purification. ¹H-NMR (DMSO-*d*₆) δ : 9.17 (d, 1H, J = 2.4 Hz), 8.71 (s, 1H), 8.27 (dd, 1H, J₁ = 8.8 Hz, J₂ = 2.4 Hz), 7.88 (m, 3H), 7.69 (t, 1H, J = 8 Hz), 7.59 (t, 2H, J = 8 Hz), 4.24 (s, 3H) ppm. ¹³C-NMR (DMSO-*d*₆) δ : 189.5, 144.1, 139.4, 136.1, 135.3, 132.5, 129.2, 129.1, 122.6, 119.8, 118.9, 112.3, 110.4, 67.9 ppm. FT-IR (KBr disk): 1631, 1519, 1449, 1382, 1334, 706 cm⁻¹. m.p.: 245°C. MS (CI): *m/z*: 297 [M+1]. HRMS (ESI): calcd. for [C₁₆H₁₂N₂O₄ + H]⁺: 297.0875; found: 297.0869. Elemental Analysis for C₁₆H₁₂N₂O₄: calcd. (%) C 64.86, H 4.08, N 9.46; found (%) C 64.67, H 4.11, N 9.52

Compound 4. A mixture of 4-nitro-nitrosobenzene (500 mg, 3.29 mmol) and 1-phenyl-2-propyn-1-one (428 mg, 3.29 mmol), in toluene (30 mL) was stirred at 80 °C for 5.5 hours under nitrogen. Precipitation of the desired product was observed during the reaction. After cooling to r.t, 3-benzoyl-1-hydroxy-5-nitro-1*H*-indole **4** was isolated by filtration (490 mg of a yellow solid, yield = 54%) and characterized without further purification. ¹H-NMR (DMSO-*d*₆) δ : 12.67 (s, 1H), 9.16 (d, 1H, J = 2.3 Hz), 8.34 (s, 1H), 8.22 (dd, 1H, J₁ = 9 Hz, J₂ = 2.3 Hz), 7.85 (d, 2H, J = 7.5 Hz), 7.75 (d, 1H, J = 9 Hz), 7.67 (t, 1H, J = 8 Hz), 7.58 (t, 2H, J = 8 Hz) ppm. ¹³C-NMR (DMSO-*d*₆) δ : 189.0, 143.3, 139.4, 136.7, 136.5, 131.9, 128.7, 128.6, 122.1, 118.9, 118.3, 111.0, 110.4 ppm. FT-IR (KBr disk): 1619, 1560, 1518, 1336, 850, 817, 740, 700 cm⁻¹. m.p.: 239.5°C. MS (CI): *m/z*: 283 [M+1]. HRMS (ESI): calcd. for [C₁₅H₁₀N₂O₄ + H]⁺: 283.0719; found: 283.0724. Elemental Analysis for C₁₅H₁₀N₂O₄: calcd. (%) C, 63.83, H, 3.57, N, 9.93; found (%) C 63.92, H 3.68, N 9.87

Compound 5. A mixture of 4-nitro nitrosobenzene (100 mg, 0.66 mmol) and 1-(2-chlorophenyl)-2-propyn-1one (108 mg, 0.66 mmol), in toluene (10 mL) was stirred at 80 °C for 4.5 hours under nitrogen. Precipitation of the desired product was observed during the reaction. After cooling to r.t., 3-(2-chlorobenzoyl)-1hydroxy-5-nitro-1*H*-indole **5** was isolated by filtration (146 mg of a pale-yellow solid, yield = 70%) and characterized without further purification. ¹H-NMR (DMSO-*d*₆) δ : 12.75 (s, 1H), 9.03 (d, 1H, J = 1.6 Hz), 8.23 (dd, 1H, J₁ = 9 Hz, J₂ = 1.6 Hz), 8.14 (s, 1H), 7.75 (d, 1H, J = 9 Hz), 7.63 - 7.57 (m, 3H), 7.5 (t, 1H, J = 7.1 Hz) ppm. ¹³C-NMR (DMSO-*d*₆) δ : 187.7, 139.6, 139.2, 137.7, 137.2, 131.4, 130.0, 129.6, 128.9, 127.4, 121.3, 119.1, 117.8, 112.1, 110.6 ppm. FT-IR (KBr disk): 1620, 1581, 1518, 1338, 763, 746 cm⁻¹. m.p.: decomposition from 207°C. MS (CI): *m/z*: 319/317 [M+1 (³⁷Cl/³⁵Cl)]. HRMS (ESI): calcd. for [C₁₅H₉ClN₂O₄ + H]⁺: 317.0329; found: 317.0331. Elemental Analysis for C₁₅H₉ClN₂O₄: calcd. (%) C 56.89, H 2.86, N 8.85; found (%) C 56.95, H 2.91, N 8.97.

Compound 6. A mixture of 4-nitro-nitrosobenzene (100 mg, 0.66 mmol) and 1-(2-bromophenyl)-2-propyn-1-one (138 mg, 0.66 mmol), in toluene (10 mL) was stirred at 80 °C for 4.5 hours under nitrogen. Precipitation of the desired product was observed during the reaction. After cooling to r.t., 3-(2-bromobenzoyl)-1-hydroxy-5-nitro-1*H*-indole **6** was isolated by filtration (124 mg of a yellow solid, yield = 52%) and characterized without further purification. ¹H-NMR (DMSO-*d*₆) δ : 12.73 (s, 1H), 9.02 (d, 1H, J = 2.1 Hz), 8.24 (dd, 1H, J₁ = 9 Hz, J₂ = 2.1 Hz), 8.13 (s, 1H), 7.77 (d, 2H, J = 7.6 Hz), 7.75 (d, 1H, J = 9 Hz), 7.55-7.31 (m, 2H) ppm. ¹³C-NMR (DMSO-*d*₆) δ : 188.5, 143.6, 141.2, 137.7, 136.9, 133.5, 131.5, 128.8, 127.8, 121.3, 119.1, 118.5, 117.8, 111.7, 110.6 ppm. FT-IR (KBr disk): 1602, 1583, 1518, 1338, 761, 744 cm⁻¹. MS (CI): *m/z*: 362 [M+1]. HRMS (ESI): calcd. for [C₁₅H₉BrN₂O₄ + H]⁺: 360.9824; found: 360.9828. Elemental Analysis for C₁₅H₉BrN₂O₄: calcd. (%) C 49.89, H 2.51, N, 7.76; found (%) C 50.01, H 2.63, N 7.84

Compound 7. A mixture of 4-nitro-nitrosobenzene (100 mg, 0.66 mmol) and 1-(3-nitrophenyl)-2-propyn-1one (115 mg, 0.66 mmol), in toluene (10 mL) was stirred at 80 °C for 8 hours under nitrogen. Precipitation of the desired product was observed during the reaction. After cooling to r.t., 1-hydroxy-5-nitro-3-(3nitrobenzoyl)-1*H*-indole **7** was isolated by filtration (149 mg of an orange-brown solid, yield = 69%) and characterized without further purification. ¹H-NMR (DMSO-*d*₆) δ : 12.83 (br, 1H), 9.14 (s, 1H), 8.62 (s, 1H), 8.54 (s, 1H), 8.47 (d, 1H, J = 8.1 Hz), 8.27 -8.25 (m, 2H), 7.87 (t, 1H, J = 7.8 Hz), 7.78 (d, 1H, J = 9 Hz) ppm. ¹³C-NMR (DMSO-*d*₆) δ : 186.9, 147.9, 143.6, 113.3, 137.6, 136.8, 134.8, 130.6, 126.2, 123.4, 122.1, 119.2, 118.2, 110.7, 110.5 ppm. FT-IR (KBr disk): 1620, 1589, 1568, 1533, 1338, 714 cm⁻¹. m.p.: decomposition from 263°C. MS (CI): *m/z*: 328 [M+1]. HRMS (ESI): calcd. for [C₁₅H₉N₃O₆ + H]⁺: 328.0570; found: 328.0578. Elemental Analysis for C₁₅H₉N₃O₆: calcd. (%) C 55.05, H 2.77, N 12.84; found (%) C 55.01, H 2.82, N 12.69

Compound 8. A mixture of 4-nitro-nitrosobenzene (100 mg, 0.66 mmol) and 1-(4-nitrophenyl)-2-propyn-1one (115 mg, 0.66 mmol), in toluene (10 mL) was stirred at 80 °C for 7 hours under nitrogen. Precipitation of the desired product was observed during the reaction. After cooling to r.t, 1-hydroxy-5-nitro-3-(4nitrobenzoyl)-1*H*-indole **8** was isolated by filtration (134 mg of an orange-brown solid, yield = 62%) and characterized without further purification. ¹H-NMR (DMSO-*d*₆) δ : 12.73 (br, 1H), 9.15 (d, 1H, J = 2.2 Hz), 8.46 (s, 1H), 8.37 (dd, 2H, , J₁ = 8.7 Hz, J₂ = 1.9 Hz), 8.23 (dd, 1H, , J₁ = 9 Hz, J₂ = 2.2 Hz), 8.05 (dd, 2H, , J₁ = 8.7 Hz, J₂ = 1.9 Hz), 7.76 (d, 1H, 9 Hz) ppm. ¹³C-NMR (DMSO-*d*₆) δ : 187.5, 149.1, 145.5, 143.5, 137.4, 136.7, 129.8, 123.8, 122.0, 119.2, 118.1, 110.8, 110.5 ppm. FT-IR (KBr disk): 1618, 1597, 1521, 1346, 837 cm⁻¹. m.p.: decomposition from 247°C. MS (CI): *m/z*: 328 [M+1], 301. HRMS (ESI): calcd. for [C₁₅H₉N₃O₆ + H]⁺: 328.0570; found: 328.0574. Elemental Analysis for C₁₅H₉N₃O₆: calcd. (%) C 55.05, H 2.77, N 12.84; found (%) C 55.09, H 2.68, N 12.99

Compound 9. A mixture of 4-nitro-nitrosobenzene (100 mg, 0.66 mmol) and 1-(4-methoxyphenyl)-2-propyn-1-one (106 mg, 0.66 mmol), in toluene (25 mL) was stirred at 80 °C for 2.5 hours under nitrogen. Precipitation of the desired product was observed during the reaction. After cooling to r.t., 1-hydroxy-3-(4-methoxybenzoyl)-5-nitro-1*H*-indole **9** was isolated by filtration (77 mg of a yellow solid, yield = 37%) and characterized without further purification. ¹H-NMR (DMSO-*d*₆) δ : 12.6 (s, 1H), 9.14 (s, 1H), 8.39 (s, 1H), 8.21 (d, 1H, J = 9 Hz), 7.87 (d, 2H, J = 8.4 Hz), 7.73 (d, 1H, J = 9 Hz), 7.11 (d, 2H, J = 8.4 Hz), 3.88 (s, 3H) ppm. ¹³C-NMR (DMSO-*d*₆) δ : 188.5, 163.2, 144.0, 137.2, 136.8, 132.5, 131.8, 123.1, 119.6, 119.2, 114.8, 112.0, 111.0, 56.4 ppm. FT-IR (KBr disk): 1604, 1572, 1521, 1473, 1367, 1331, 1176, 841 cm⁻¹. m.p.: decomposition from 223°C. MS (CI): *m/z*: 313 [M+1]. HRMS (ESI): calcd. for [C₁₆H₁₂N₂O₅ + H]⁺: 313.0824; found: 313.0826. Elemental Analysis for C₁₆H₁₂N₂O₅: calcd. (%) C 61.54, H, 3.87, N 8.97; found (%) C 61.46, H 3.92, N 9.01

Compound 10. A mixture of 4-nitro-nitrosobenzene (100 mg, 0.66 mmol) and 1-(4-formylphenyl)prop-2-yn-1-one (106 mg, 0.66 mmol), in toluene (10 mL) was stirred at 80 °C for 2.5 hours under nitrogen. Precipitation of the desired product was observed during the reaction. After cooling to r.t., 3-(4-formylbenzoyl)-1-Hydroxy-5-nitro-1*H*-indole **10** was isolated by filtration (64.5 mg of a brown solid, yield = 31%) and characterized without further purification. ¹H-NMR (DMSO-*d*₆) δ : 12.73 (s, 1H), 10.15 (s, 1H), 9.15 (d, 1H, J = 1 Hz) 8.34 (s, 1H), 8.23 (td, 1H, J = 9.2 Hz, J₂ = 1 Hz), 8.08 (d, 2H, J = 8 Hz), 8.02 (d, 2H J = 8 Hz), 7.76 (d, 1H, J = 9.2 Hz) ppm. ¹³C-NMR (DMSO-*d*₆) δ : 193.6, 188.8, 144.4, 143.9, 138.4, 137.7, 137.0, 130.2, 129.6, 122.4, 119.5, 118.6, 111.3, 110.9 ppm. FT-IR (ATR): 3118, 1705, 1626, 1582, 1516, 1448, 1365, 1335, 1208, 745 cm⁻¹. m.p.: decomposition from 193°C. MS (CI): *m/z*: 311 [M+1]. HRMS (ESI): calcd. for [C₁₆H₁₀N₂O₅ + H]⁺: 311.0668; found: 311.0672. Elemental Analysis for C₁₆H₁₀N₂O₅: calcd. (%) C 61.94, H 3.25, N 9.03; found (%) C 61.87, H 3.28, N 9.52

Compound 11. A mixture of 4-nitro-nitrosobenzene (100 mg, 0.66 mmol) and 1-(benzo[d][1,3]dioxol-5-yl)prop-2-yn-1-one (115 mg, 0.66 mmol), in toluene (10 mL) was stirred at 80 °C for 2.5 hours under nitrogen. Precipitation of the desired product was observed during the reaction. After cooling to r.t., 3- (benzo[d][1,3]dioxol-5-yl)-1-hydroxy-5-nitro-1*H*-indole **11** was isolated by filtration (131 mg of a brown solid, yield = 61%) and characterized without further purification. ¹H-NMR (DMSO-*d*₆) δ : 12.58 (s, 1H), 9.12

(d, 1H, J = 2 Hz), 8.43 (s, 1H), 8.21 (dd, 1H, J₁ = 9.2 Hz, J₂ = 2 Hz), 7.73 (d, 1H, J = 2.4 Hz), 7.47 (d, 1H, J = 7.2 Hz), 7.38 (s, 1H), 7.08 (d, 1H, J = 8 Hz), 6.17 (s, 2H) ppm. ¹³C-NMR (DMSO- d_6) δ : 187.2, 150.5, 147.6, 143.1, 136.2, 136.0, 133.4, 124.5, 122.1, 118.7, 118.3, 110.9, 110.1, 108.5, 108.0, 101.8 ppm. FT-IR (ATR): 3132, 2553, 1519, 1334, 1254, 1090, 768, 744 cm⁻¹. m.p.: decomposition from 244°C. MS (CI): *m/z*: 327 [M+1]. HRMS (ESI): calcd. for [C₁₆H₁₀N₂O₆ + H]⁺: 327.0617; found: 327.0609. Elemental Analysis for C₁₆H₁₀N₂O₆: calcd. (%) C 58.90, H 3.09, N 8.59; found (%) C 59.01, H 3.05, N 8.61

Compound 12. Under nitrogen atmosphere, 4-nitrosobenzoic acid (100 mg, 0.66 mmol) was suspended in dioxane (10 mL) and heated until the solid was completely dissolved, then 1-(2-chlorophenyl)-2-propyn-1-one (109 mg, 0.66 mmol) was added and the mixture was refluxed for 7.5 hours. During the reaction, precipitation of azoxybenzene-4,4'-dicarboxylic acid was observed. When the reaction was complete, the mixture was cooled to r.t., the solid byproduct (28 mg) removed by filtration and the washings concentrated under reduced pressure. Recrystallization from CH₂Cl₂ gave 3-(2-chlorobenzoyl)-1-hydroxy-1*H*-indole-5-carboxylic acid **12** as a yellow–orange solid (144 mg, yield = 69%). ¹H-NMR (DMSO-*d*₆) δ : 12.78 (br, 1H), 12.59 (br, 1H), 8.82 (d, 1H, J = 1.6 Hz), 7.94 (dd, 1H, J = 8.6 Hz, J = 1.6 Hz), 7.90 (s, 1H), 7.60 (dd, 1H, J = 8.6 Hz, J = 0.6 Hz), 7.57 (dt, 1H, J = 7.2 Hz, J = 1.4 Hz), 7.55 – 7.52 (m, 2H), 7.47 (dt, 1H, J = 7.2 Hz, J = 1.4 Hz) ppm. ¹³C-NMR (DMSO-*d*₆) δ : 187.6, 168.7, 139.6, 136.4, 135.9, 131.1, 129.9, 129.6, 128.8, 127.2, 125.5, 124.8, 123.7, 121.7, 111.3, 109.5 ppm. FT-IR (KBr disk): 1684, 1599, 1520, 1219, 754, 706 cm⁻¹. m.p.: 254°C. MS (CI): *m/z*: 318 / 316 [M+1 (³⁵CI/³⁷CI)]. HRMS (ESI): calcd. for [C₁₆H₁₀CINO₄ + H]⁺: 316.0377; found: 316.0369. Elemental Analysis for C₁₆H₁₀CINO₄: calcd. (%) C 60.87, H 3.19, N 4.44; found (%) C 60.71, H 3.21, N 4.21

Compound 13. A mixture of 4-nitro-nitrosobenzene (100 mg, 0.66 mmol) and 1-(4-nitrophenyl)-2-propyn-1one (115 mg, 0.66 mmol), in toluene (10 mL) was stirred at 80 °C for 7 hours under nitrogen. Precipitation of the desired product was observed during the reaction. After cooling to r.t, 1-hydroxy-5-nitro-3-(4nitrobenzoyl)-1*H*-indole-5-carboxylic acid **13** was isolated by filtration (144 mg of an orange-brown solid, yield = 67%) and characterized without further purification. ¹H-NMR (DMSO-*d*₆) δ : 12.83 (br, 1H), 12.43 (br, 1H), 8.96 (d, 1H, J = 1.6 Hz), 8.36 (d, 2H, J = 8.8 Hz), 8.26 (s, 1H), 8.02 (d, 2H, J = 8.8 Hz), 7.96 (dd, 1H, J₁ = 8.6 Hz, J₂ = 1.6 Hz), 7.63 (d, 1H, J = 8.6 Hz) ppm. ¹³C-NMR (DMSO-*d*₆) δ : 187.5, 167.8, 148.9, 145.2, 136.3, 131.1, 129.8, 125.6, 125.0, 124.1, 123.8, 122.4, 110.1, 109.5 ppm. FT-IR (KBr disk): 1697, 1591, 1517, 1345, 719 cm⁻¹. m.p.: decomposition from 293°C. MS (CI): *m/z*: 327 [M+1]. HRMS (ESI): calcd. for [C₁₆H₁₀N₂O₆ + H]⁺: 327.0617; found: 327.0624. Elemental Analysis for C₁₆H₁₀N₂O₆: calcd. (%) C 58.90, H 3.09, N 8.59; found (%) C 59.03, H 3.02, N 8.62

Compound 14. A mixture of nitrosobenzene (100 mg, 0.93 mmol) and 1-phenylprop-2-yn-1-one (121 mg, 0.93 mmol), in toluene (10 mL) was stirred at 80 °C under nitrogen. After 3 hours, TLC (Hexane:AcOEt = 80:20) displayed total consumption of nitrosobenzene; the solvent was rotary evaporated. After purification of the crude material on silica gel (petroleum ether : AcOEt = 70:30), (1H-indol-3-yl)(phenyl)methanone **14** was isolated as an orange solid (51.4 mg, yield = 25%), together with 320 mg of unreacted alkyne. ¹H-NMR (DMSO-*d*₆) δ : 12.06 (s, 1H), 8.26 (d, 1H, J = 7 Hz), 7.93 (d, 1H, J = 3 Hz), 7.79 (d, 2H, J = 7 Hz), 7.61 – 7.52 (m, 4H), 7.29-7.22 (m, 2H) ppm. Other spectroscopic data for this compound are in agreement with the ones reported in literature.³¹

Compound 15. A mixture of 4-carboethoxy-nitrosobenzene (150 mg, 0.84 mmol) and 1-phenylprop-2-yn-1one (109 mg, 0.84 mmol), in toluene (10 mL) was stirred at 80 °C under nitrogen. After 6 hours, TLC (hexane:AcOEt= 80:20) displayed total consumption of 4-carboethoxy-nitrosobenzene. The solvent was rotary evaporated and the crude material was purified on silica gel (petroleum ether:AcOEt = 55:45). Ethyl 3-benzoyl-1*H*-indole-5-carboxylate **15** was isolated as an orange solid (66 mg, yield = 27%). ¹H-NMR (CDCl₃) δ : 8.96 (br, 1H), 8.73 (s, 1H), 8.40 (d, 1H, *J* = 1.6 Hz), 7.92 (d, 2H, *J* = 7.8 Hz), 7.85 (dd, 1H, *J* = 9.0 Hz, *J* = 1.6 Hz), 7.73 (t, 1H, *J* = 7.8 Hz), 7.67 - 7.61 (m, 3H), 4.39 (q, 2H, *J* = 7.1 Hz), 1.42 (t, 3H, *J* = 7.1 Hz) ppm. Other spectroscopic data for this compound were in agreement with the ones reported in literature.³² **Compound 16.** A mixture of 4-nitrosotoluene (150 mg, 1.24 mmol) and 1-phenylprop-2-yn-1-one (161 mg, 1.24 mmol), in toluene (12 mL) was stirred at 80 °C under nitrogen. After 6 hours,TLC (hexane:AcOEt= 80:20) displayed total consumption of 4- methyl-nitrosobenzene; the solvent was rotary evaporated and the crude material was purified on silica gel (petroleum ether : AcOEt = 55:45). 3-Benzoyl-5-methyl-1*H*-indole **16** (58 mg, yield = 20%) was isolated as a yellow solid. ¹H-NMR (CDCl₃) δ : 12.42 (br, 1H), 8.75 (d, 1H, J = 1.8 Hz), 8.2 (s, 1H), 7.87 (d, 2H, J = 8.6 Hz), 7.79 (d, 1H, J = 9 Hz), 7.75 – 7.72 (m, 2H), 7.67 (t, 2H, J = 8.6 Hz), 2.35 (s, 3H) ppm. Other spectroscopic data for this compound were in agreement with the ones reported in literature.³³

Compound 17. A mixture of 4-methoxy-nitrosobenzene (137 mg, 1 mmol) and 1-phenylprop-2-yn-1-one (130 mg, 1 mmol), in toluene (10 mL) was stirred at 80 °C under nitrogen. After 6 hours the solvent was rotary evaporated and the crude material was purified on silica gel (petroleum ether : AcOEt = 55:45). 3-Benzoyl-5-methoxy-1*H*-indole **17** (75.3 mg, yield = 30%) was isolated as yellow solid. Spectroscopic data for this compound were in agreement with the ones reported in literature.³⁴

Compound 18. A mixture of 2-carbomethoxy-nitrosobenzene (100 mg, 0.61 mmol) and 1-phenylprop-2-yn-1-one (79 mg, 0.61 mmol), in toluene (8 mL) was stirred at 80 °C under nitrogen. After 2.5 hours, TLC (hexane : AcOEt= 80:20) displayed total consumption of 2-carbomethoxy-nitrosobenzene; the solvent was rotary evaporated and the crude material was purified on silica gel (petroleum ether:AcOEt= 80:20). Methyl 3-benzoyl-1-hydroxy-1H-indole-7-carboxylate **18** was isolated as an orange solid (59.5 mg, yield = 33%). ¹H-NMR (CDCl₃) δ : 12.94 (s, 1H), 8.85 (d, 1H, J = 7.8 Hz), 8.07 (d, 1H, J = 7.8 Hz); 7.85 (d, 2H, J = 7 Hz), 7.77 (s, 1H), 7.59 (t, 1H, J = 7 Hz), 7.52 (7, 2H, J = 7 Hz), 7.37 (t, 1H, J = 7.8 Hz), 4.10 (s, 3H) ppm. ¹³C-NMR (CDCl₃) δ : 190.6, 170.7, 140.7, 135.2, 131.9, 131.8, 130.4, 129.1, 128.8, 128.5, 126.3, 122.3, 112.8, 111.2, 54.1 ppm. FT-IR (KBr disk): 1666, 1631, 1601, 1520, 1440, 1385, 750, 700 cm⁻¹. m.p.: 113°C. MS (CI): *m/z*: 296 [M+1], 280. HRMS (ESI): calcd. for [C₁₇H₁₃NO₄ + H]⁺: 296.0923; found: 296.0928. Elemental Analysis for C₁₇H₁₃NO₄: calcd. (%) C 69.15, H 4.44, N 4.74; found (%) C 69.21, H 4.41, N 4.82

Compound 19. Under nitrogen, to a solution of 3-(2-chlorobenzoyl)-1-hydroxy-5-nitro-1*H*-indole (63 mg, 0.20 mmol) in methanol (15 mL), zinc powder (131 mg, 2 mmol) and AcOH (50 µL) were added. After 1 hour at r.t., additional 50 µL of AcOH were added and the mixture was stirred for additional 2 hours. At reaction complete, the mixture was filtered on a pad of cotton and the washings rotary evaporated to obtain 5-amino-3-(2-chlorobenzoyl)-1*H*-indole **19** as a green–yellow solid (38 mg, yield = 70%), characterized without further purification. ¹H-NMR (DMSO-*d*₆) δ : 11.70 (br, 1H), 7.53 (td, 1H, J₁ = 8.0 Hz, J₂ = 0.6 Hz), 7.50 - 7.48 (m, 1H), 7.46 - 7.42 (m, 3H), 7.34 (s, 1H), 7.18 (d, 1H, J = 8.7 Hz), 6.67 (dd, 1H, J₁ = 8.7 Hz, J₂ = 2.1 Hz), 5.20 (br, 2H) ppm. ¹³C-NMR (DMSO-*d*₆) δ : 186.7, 145.6, 140.4, 132.3, 130.5, 129.7, 129.6, 128.6, 127.6, 127.0, 123.9, 113.3, 109.9, 109.0, 104.1. GC-MS (EI): *m/z*: 272 / 270 [*M*+(³⁷Cl/³⁵Cl)], 241, 240, 239. HRMS (ESI): calcd. for [C₁₅H₁₁ClN₂O + H]⁺: 271.0638; found: 271.0645. Elemental Analysis for C₁₅H₁₁ClN₂O: calcd. (%) C 66.55, H 4.10, N 10.35; found (%) C 66.51, H 4.15, N 10.42

Compound 21. A mixture of 4-nitro-nitrosobenzene (100 mg, 0.66 mmol) and 1-(1*H*-benzo[*d*][1,2,3]triazol-1-yl)prop-2-yn-1-one (113 mg, 0.66 mmol), in toluene (10 mL) was stirred at 80 °C for 4 hours under nitrogen. Precipitation of the desired product was observed during the reaction. After cooling to r.t., (1H-benzo[*d*][1,2,3]triazol-1-yl)(1-hydroxy-5-nitro-1H-indol-3-yl)methanone **21** was collected by filtration as a yellow solid (122 mg, yield = 57%) and characterized without further purification. ¹H-NMR (DMSO-*d*₆) δ : 13.02 (br, 1H), 9.24 (d, 1H, J = 2.2 Hz), 9.10 (s, 1H), 8.42 (dt, 1H, J₁ = 8.2 Hz, J₂ = 0.8 Hz), 8.30 (dt, 1H, J₁ = 8.2 Hz, J₂ = 0.8 Hz), 8.28 (dd, 1H, J₁ = 8.9 Hz, J₂ = 2.2 Hz), 7.85 (d, 1H, J = 8.9 Hz), 7.82 (td, 1H, J₁ = 8.2 Hz, J₂ = 0.8 Hz), 7.64 (td, 1H, J₁ = 8.2 Hz, J₂ = 0.8 Hz) ppm. ¹³C-NMR (DMSO-*d*₆) δ : 160.1, 145.1, 143.7, 138.0, 136.0, 131.7, 130.7, 126.4, 123.4, 120.0, 119.2, 117.7, 114.5, 110.9, 102.6 ppm. FT-IR (KBr disk): 1689, 1527, 1450, 1364, 1339, 1288, 1106, 1025, 744 cm⁻¹. MS (CI): *m/z*: 324 [M+1]. HRMS (ESI): calcd. for [C₁₅H₉N₅O₄ + H]⁺: 324.0733; found: 324.0736. Elemental Analysis for C₁₅H₉N₅O₄: calcd. (%) C 55.73, H 2.81, N 21.66; found (%) C 55.82, H 2.91, N 21.57

Compound 22. Under nitrogen atmosphere, 4-nitrosobenzoic acid (181 mg, 1.20 mmol) was suspended in dioxane (15 mL) and heated until the solid was completely dissolved, then 1-(1*H*-benzo[*d*][1,2,3]triazol-1-yl)prop-2-yn-1-one (205 mg, 1.20 mmol) was added and the mixture was refluxed for 5 hours. During the reaction, precipitation of the desired product was observed. When the reaction was complete, the mixture was cooled to r.t. and 3-(1*H*-Benzo[*d*][1,2,3]triazol-1-oyl)-1-hydroxy-1*H*-indole-5-carboxylic acid **22** was isolated by filtration as a yellow solid (261 mg, yield = 68 %). ¹H-NMR (DMSO-*d*₆) δ : 12.79 (s, 1H), 9.03 (d, 1H, J = 1.4 Hz), 8.94 (s, 1H), 8.39 (d, 1H, J = 8.2 Hz), 7.26 (d, 1H, J = 8.2 Hz), 7.98 (dd, 1H, J₁ = 8.6 Hz, J₂ = 1.4 Hz), 7.79 (t, 1H, J = 8.2 Hz), 7.69 (d, 1H, J = 8.6 Hz), 7.61 (t, 1H, J = 8.2 Hz) ppm. ¹³C-NMR (DMSO-*d*₆) δ : 167.9, 160.3, 145.2, 136.4, 135.7, 131.9, 130.6, 126.4, 125.8, 125.1, 123.9, 123.6, 120.1, 114.6, 110.0, 101.7 ppm. FT-IR (KBr disk): 1695, 1608, 1448, 1362, 1292, 1105, 1031, 815, 750 cm⁻¹. MS (CI): *m/z*: 323 [M+1]. HRMS (ESI): calcd. for [C₁₆H₁₀N₄O₄ + H]⁺: 323.0780; found: 323.0786. Elemental Analysis for C₁₆H₁₀N₄O₄: calcd. (%) C 59.63, H 3.13, N 17.38; found (%) C 59.39, H 3.22, N 17.33

Compound 23. A mixture of 4-cyano-nitrosobenzene (158 mg, 1.20) and 1-(1*H*-benzo[*d*][1,2,3]triazol-1-yl)prop-2-yn-1-one (205 mg, 1.20 mmol), in toluene (15 mL) was stirred at 80 °C for 4 hours under nitrogen. Precipitation of the desired product was observed during the reaction. After cooling to r.t., 3-(1H-benzo[*d*][1,2,3]triazole-1-carbonyl)-1-hydroxy-1H-indole-5-carbonitrile **23** was collected by filtration as a pale yellow solid (145 mg, yield = 40%) and characterized without further purification. ¹H-NMR (DMSO-*d*₆) δ : 12.55 (br, 1H), 9.04 (s, 1H), 8.74 (dd, 1H, J1 = 1.4 Hz, J2 = 0.8 Hz), 8.39 (dt, 1H, J₁ = 8.3 Hz, J₂ = 0.9 Hz), 8.28 (dt, 1H, J₁ = 8.3 Hz, J₂ = 0.9 Hz), 7.84 – 7.80 (m, 2H), 7.80 (td, 1H, J₁ = 8.3 Hz, J₂ = 0.9 Hz), 7.63 (td, 1H, J₁ = 8.3 Hz, J₂ = 0.9 Hz) ppm. ¹³C-NMR (DMSO-*d*₆) δ : 160.1, 145.2, 135.1, 132.6, 131.8, 130.7, 126.9, 126.5, 126.3, 123.8, 120.1, 119.8, 114.5, 111.5, 105.6, 101.5 ppm. FT-IR (KBr disk): 2228, 1700, 1448, 1353, 1288, 1102, 1031, 756 cm⁻¹. MS (CI): *m/z*: 304 [M+1]. HRMS (ESI): calcd. for [C₁₆H₉N₅O₂ + H]⁺: 304.0834; found: 304.0835. Elemental Analysis for C₁₆H₉N₅O₂: calcd. (%) C 63.37, H 2.99, N 23.09; found (%) C 63.42, H 2.88, N 23.12

Compound 24. A mixture of nitrosobenzene (128 mg, 1.20 mmol) and 1-(1*H*-benzo[*d*][1,2,3]triazol-1-yl)prop-2-yn-1-one (205 mg, 1.20 mmol), in toluene (15 mL) was stirred at 80 °C for 4 hours under nitrogen. Precipitation of the desired product was observed during the reaction. After cooling to r.t., (1H-benzo[*d*][1,2,3]triazol-1-yl)(1-hydroxy-1H-indol-3-yl)methanone **24** was isolated by filtration as a yellow solid (63 mg). Purification of the crude washings on silica gel (hexane : AcOEt = 8:2) gave additional 70 mg of product (133 mg, yield = 40%). ¹H-NMR (DMSO-*d*₆) δ : 2.49 (s, 1H), 8.86 (s, 1H), 8.38 (dt, 1H, J₁ = 8.3 Hz, J₂ = 1.0 Hz), 8.36 (dd, 1H, J₁ = 8.6 Hz, J₂ = 1.4 Hz), 8.26 (dt, 1H, J₁ = 8.3 Hz, J₂ = 1.0 Hz), 7.78 (tt, 1H, J₁ = 8.3 Hz, J₂ = 1.0 Hz), 7.63 (dd, 1H, J₁ = 8.6 Hz, J₂ = 1.4 Hz), 7.61 (tt, 1H, J₁ = 8.3 Hz, J₂ = 1.0 Hz), 7.40 (dd, 1H, J₁ = 8.6 Hz, J₂ = 1.4 Hz) ppm. ¹³C-NMR (DMSO-*d*₆) δ : 160.2, 145.1, 134.6, 133.5, 131.8, 130.3, 126.1, 124.3, 124.0, 123.4, 121.0, 119.9, 114.4, 109.9, 100.3 ppm. MS (Cl): *m/z*: 279 [*M*+1]. FT-IR (KBr disk): 1690, 1447, 1360, 1288, 1099, 1037, 761, 735 cm⁻¹. HRMS (ESI): calcd. for [C₁₅H₁₀N₄O₂ + H]⁺: 279.0882; found: 279.0878. Elemental Analysis for C₁₅H₁₀N₄O₂: calcd. (%) C 64.74, H 3.62, N 20.13; found (%) C 64.68, H 3.71, N 19.98

Compound 25. A mixture of 4-nitro-nitrosobenzene (100 mg, 0.66 mmol) and 1-(1-methyl-1*H*-indol-3-yl)prop-2-yn-1-one (121 mg, 0.66 mmol), in toluene (8 mL) was stirred at 80 °C for 3 hours under nitrogen. Precipitation of the desired product was observed during the reaction. After cooling to r.t., (1-hydroxy-5-nitro-1H-indol-3-yl)(1-methyl-1H-indol-3-yl)methanone **25** was isolated by filtration (104 mg of a green-yellow solid, yield = 47%) and characterized without further purification. ¹H-NMR (DMSO-*d*₆) δ : 12.50 (s, 1H), 9.23 (d, 1H, J = 2.2 Hz), 8.67 (s, 1H), 8.38 (s, 1H), 8.32 (d, 1H, J = 7.5 Hz), 8.18 (dd, 1H, J₁ = 9 Hz, J₂ = 2.2 Hz), 7.71 (d, 1H, J = 9 Hz), 7.58 (d, 1H, J = 7.5 Hz), 7.32 (t, 1H, J = 7.5 Hz), 7.27 (t, 1H, J = 7.5 Hz), 3.92 (s, 3H) ppm. ¹³C-NMR (DMSO-*d*₆) δ : 183.2, 143.4, 138.0, 137.6, 136.9, 134.3, 127.7, 123.8, 123.0, 122.7, 122.5, 119.5, 119.1, 115.5, 113.7, 111.3, 110.7, 34.0 ppm. FT-IR (KBr disk): 1620, 1562, 1523, 1458, 1381, 1329, 821, 742 cm⁻¹. m.p.: > 300°C. MS (CI): *m/z*: 336 [M+1]. HRMS (ESI): calcd. for [C₁₈H₁₃N₃O₄ + H]⁺: 336.0984;

found: 336.0981. Elemental Analysis for $C_{18}H_{13}N_3O_4$: calcd. (%) C 64.48, H 3.91, N 12.53; found (%) C 64.41, H 3.92, N 12.32

Compound 26. A mixture of 4-nitro-nitrosobenzene (152 mg, 1 mmol) and 1-(1-methyl-1H-indol-2-yl)prop-2-yn-1-one (183 mg, 1 mmol), in toluene (10 mL) was stirred at 80 °C for 3 hours under nitrogen. Precipitation of the desired product was observed during the reaction. After cooling to r.t., (1-hydroxy-5nitro-1H-indol-3-yl)(1-methyl-1H-indol-2-yl)methanone **26** was collected by filtration as an orange-solid (94 mg, yield = 20 %) and characterized without further purification. ¹H-NMR (DMSO-*d*₆) δ : 12.68 (br, 1H), 9.20 (d, 1H, J 0 2 Hz), 8.61 (s, 1H), 8.23 (dd, 1H, J₁ = 1.6 Hz, J₂ = 8.8 Hz), 7.75 (t, 2H, J = 9.2 Hz), 7.63 (d, 1H, J = 8.4 Hz), 7.39 (t, 1H, J = 7.2 Hz), 7.29 (s, 1H), 7.17 (t, 1H, J = 7.2 Hz), 4.02 (s, 3H) ppm. ¹³C-NMR (DMSO-*d*₆) δ : 180.7, 143.1, 139.4, 136.35, 136.1, 135.8, 125.7, 124.9, 122.5, 121.9, 120.4, 118.8, 118.2, 112.4, 110.7, 110.5, 110.2, 31.5 ppm. FT-IR (ATR): 1553, 1518, 1493, 1452, 1424, 1332, 1210, 1154, 1109, 925, 736 cm⁻¹ m.p.: decomposition from 230°C. MS (CI): *m/z*: 336 [M+1]. HRMS (ESI): calcd. for [C₁₈H₁₃N₃O₄ + H]⁺: 336.0984; found: 336.0986. Elemental Analysis for C₁₈H₁₃N₃O₄: calcd. (%) C 64.48, H 3.91, N 12.53; found (%) C 64.59, H 3.88, N 12.64

Compound 27. A mixture of . 2-carbomethoxy-nitrosobenzene (165 mg, 1 mmol) and 1-(1-methyl-1H-indol-2-yl)prop-2-yn-1-one (183 mg, 1 mmol), in toluene (10 mL) was stirred at 80 °C for 4 hours under nitrogen. After complete conversion of nitrosobenzene, the mixture was cooled to r.t. and the solvent removed *in vacuo*. The crude product is purified by gravimetric column cromatography (DCM : toluene 6:4) to afford methyl 3-(1-methyl-1H-indole-2-carbonyl)-1H-indole-7-carboxylate **27** as a brown solid (100 mg, yield 30%). ¹H-NMR (CDCl₃) δ : 12.85 (s, 1H), 8.75 (d, 1H, J 0 8 Hz), 7.99 (d, 1H, J = 7.6 Hz), 7.94 (s, 1H), 7.62 (d, 1H, J = 15.2 Hz), 7.38 (d, 1H, J = 8 Hz), 7.28 (m, 2H), 7.12 (t, 1H, J = 7.2 Hz), 7.03 (s, 1H), 4.02 (s, 3H), 4.00 (s, 3H) ppm.¹³C-NMR (CDCl₃) δ : 181.7, 170.3, 139.8, 136.8, 130.9, 130.7, 129.7, 128.1, 126.2, 124.9, 125.8, 124.9, 122.5, 121.8, 120.57, 112.34, 110.59, 110.2, 53.7, 31.3 ppm. FT-IR (ATR): 2915, 2848, 1590, 1516, 1437, 1424, 1264, 1202, 1143, 1094, 1051, 918, 855, 762, 746 cm¹. m.p.: 176.5°C. GC-MS (EI): *m/z*: 332 [M⁺]. HRMS (ESI): calcd. for [C₂₀H₁₆N₂O₃ + H]⁺: 333.1239; found: 333.1244. Elemental Analysis for C₂₀H₁₆N₂O₃: calcd. (%) C 72.28, H 4.85, N 8.43; found (%) C 72.35, H 4.80, N 8.44

Compound 28. A mixture of 4-nitro-nitrosobenzene (100 mg, 0.66 mmol) and (*E*)-1-phenylpent-1-en-4-yn-3-one (103 mg, 0.66 mmol), in toluene (8 mL) was stirred at 80 °C for 2 hours under nitrogen. Precipitation of the desired product was observed during the reaction. After cooling to r.t., the solid was collected by filtration to give (*E*)-1-(1-hydroxy-5-nitro-1*H*indol-3-yl)-3-phenylprop-2-en-1-one **28** as a yellow solid (132 mg, yield = 65%), characterized without further purification. ¹H-NMR (DMSO-*d*₆) δ : 12.67 (s, 1H), 9.24 (d, 1H, J = 2.2 Hz), 9.23 (s, 1H), 8.21 (dd, 1H, J¹ = 9 Hz, J² = 2.2 Hz), 7.90 (dd, 2H, J¹ = 7.9 Hz, J² = 1.6 Hz), 7.86 (d, 1H, J = 15.7 Hz), 7.75 (d, 1H, 9 Hz), 7.71 (d, 1H, J = 15.7 Hz), 7.51 – 7.45 (m, 3H) ppm. ¹³C-NMR (DMSO-*d*₆) δ : 183.9, 144.1, 142.2, 137.2, 135.2, 134.0, 130.5, 129.2, 128.6, 123.5, 122.4, 120.0, 119.2, 114.5, 109.8 ppm. FT-IR (KBr disk): 1630, 1575, 1525, 1313, 974, 744, 680 cm⁻¹. m.p.: decomposition from 270°C. MS (CI): *m/z*: 309 [M+1], 293. HRMS (ESI): calcd. for [C₁₇H₁₂N₂O₄ + H]⁺: 309.0875; found: 309.0874. Elemental Analysis for C₁₇H₁₂N₂O₄: calcd. (%) C 66.23, H 3.92, N 9.09; found (%) C 66.17, H 3.99, N 9.13

Compound 29. A mixture of 4-nitro-nitrosobenzene (100 mg, 0.66 mmol) and 1-(1-methyl-1*H*-pyrrol-2-yl)prop-2-yn-1-one (88 mg, 0.66 mmol), in toluene (8 mL) was stirred at 80 °C for 7.5 hours under nitrogen. Precipitation of the desired product was observed during the reaction. After cooling to r.t., (1-hydroxy-5-nitro-1H-indol-3-yl)(1-methyl-1H-pyrrol-2-yl)methanone **29** was isolated by filtration (94 mg of a brown solid, yield = 50%) and characterized without further purification. ¹H-NMR (DMSO-*d*₆) δ : 12.51 (s, 1H, 9.11 (d, 1H, J = 2.2 Hz), 8.42 (s, 1H), 8.17 (dd, 1H, J₁ = 9 Hz, J₂ = 2.2 Hz), 7.96 (d, 1H, J = 9 Hz), 7.15 (d, 1H, J 0 4 Hz), 6.97 (dd, 1H, J₁ = 4 Hz, J₂ = 1.7 Hz), 6.18 (dd, 1H, J₁ = 4 Hz, J₂ = 2.5 Hz), 3.92 (s. 3H) ppm. ¹³C-NMR (DMSO-*d*₆) δ : 178.5, 142.8, 136.1, 134.2, 131.1, 130.5, 122.1, 119.1, 118.5, 118.4, 112.3, 110.0, 108.0, 36.5 ppm. FT-IR (KBr disk): 2947, 1617, 1557, 1531, 1455, 1378, 1332, 1215, 743 cm⁻¹ m.p.: decomposition from

254°C. MS (CI): m/z: 286 [M+1]. HRMS (ESI): calcd. for $[C_{14}H_{11}N_3O_4 + H]^+$: 286.0828; found: 286.0826. Elemental Analysis for $C_{14}H_{11}N_3O_4$: calcd. (%) C 58.95, H 3.89, N 14.73; found (%) C 58.82, H 3.96, N 14.88

Compound 30. A mixture of 4-nitro-nitrosobenzene (100 mg, 0.66 mmol) and 1-(furan-2-yl)prop-2-yn-1-one (79 mg, 0.66 mmol), in toluene (8 mL) was stirred at 80 °C for 6.5 hours under nitrogen. Precipitation of the desired product was observed during the reaction. After cooling to r.t., furan-2-yl(1-hydroxy-5-nitro-1H-indol-3-yl)methanone **30** was collected by filtration (92 mg of a yellow-orange solid, yield = 51%) and characterized without further purification. ¹H-NMR (DMSO-*d*₆) δ : 12.70 (br, 1H), 9.20 (d, 1H, J = 2.3 Hz),, 8.83 (s, 1H), 8.20 (dd, 1H, J₁ = 9 Hz, J₂ = 2.3 Hz), 8.03 (dd, 1H, J₁ = 1.7 Hz, J₂ = 0.7 Hz), 7.73 (d, 1H, J = 9 Hz), 7.47 (dd, 1H, J₁ = 3.6 Hz, J₂ = 0.7 Hz), 6.77 (dd, 1H, J₁ = 3.6 Hz, J₂ = 1.7 Hz) ppm. ¹³C-NMR (DMSO-*d*₆) δ : 174.6, 152.4, 147.0, 143.3, 136.1, 135.6, 122.3, 118.9, 118.3, 117.5, 112.6, 110.3, 109.9 ppm. FT-IR (KBr disk): 1633, 1577, 1519, 1453, 1367, 1336, 825, 746 cm⁻¹. m.p.: decomposition from 267°C. MS (CI): *m/z*: 273 [M+1]. HRMS (ESI): calcd. for [C₁₃H₈N₂O₅ + H]⁺: 273.0511; found: 273.0516. Elemental Analysis for C₁₃H₈N₂O₅: calcd. (%) C 57.36, H 2.96, N 10.29; found (%) C 57.09, H 2.86, N 10.37

Compound 31. A mixture of 4-nitro-nitrosobenzene (152 mg, 1 mmol) and 1-(pyren-1-yl)prop-2-yn-1-one (254 mg, 1 mmol), in toluene (10 mL) was stirred at 80 °C for 8 hours under nitrogen. Precipitation of the desired product was observed during the reaction. After cooling to r.t., (1-hydroxy-5-nitro-1H-indol-3-yl)(pyren-1-yl)methanone **31** was collected by filtration (264 mg of a yellow solid, yield = 65%) and characterized without further purification. ¹H-NMR (DMSO-*d*₆) δ : 12.60 (br, 1H), 9.46 (d, 1H, J = 2.2 Hz), 8.45 (d, 1H, J = 9.3 Hz), 8.22–8.41 (m, 7H), 8.31–8.33 (m, 1H), 8.12 – 8. 16 (t, 1H, J = 7.6 Hz), 8.06 (s, 1H), 7.80 – 7.83 (d, 1H, J = 9 Hz) ppm. ¹³C-NMR (DMSO-*d*₆) δ : 191.4, 143.9, 138.4, 137.2, 135.0, 132.5, 131.2, 130.7, 129.1, 128.9, 128.6, 127.8, 127.2, 126.5, 126.4, 126.3, 124.9, 124.8, 124.5, 124.2, 122.2, 119.5, 118.7, 113.9, 110.9 ppm FT-IR (ATR): 3135, 1594, 1526, 1506, 1376, 1333, 1215, 923, 831 cm⁻¹. m.p.: decomposition from 273°C. MS (CI): *m/z*: 407 [M+1]. HRMS (ESI): calcd. for [C₂₅H₁₄N₂O₄ + H]⁺: 407.1032; found: 407.1029. Elemental Analysis for C₂₅H₁₄N₂O₄: calcd. (%) C 73.89, H 3.47, N 6.89; found (%) C 73.96, H 3.45, N 6.78

Compound 32. A mixture of 4-nitro-nitrosobenzene (152 mg, 1 mmol) and *N*-phenylpropiolamide (145 mg, 1 mmol), in toluene (10 mL) was stirred at 80 °C for 8 hours under nitrogen. Precipitation of the desired product was observed during the reaction. After cooling to r.t., 1-hydroxy-5-nitro-*N*-phenyl-1H-indole-3-carboxamide **32** was collected by filtration (107 mg of a yellow solid, yield = 36%) and characterized without further purification. ¹H-NMR (DMSO-*d*₆) δ : 9.87 (br, 1H), 9.16 (dd, 1H, J₁ = 2 Hz, J₂ = 0.4 Hz), 8.67 (s, 1H), 8.13 (dd, 1H, J₁ = 9.2 Hz, J₂ = 2.4 Hz), 7.76 (dd, 2H, J₁ = 8.4 Hz, J₂ = 0.8 Hz), 7.67 (d, 1H, J = 8.8 Hz), 7.35 (t, 2H, J = 8 Hz), 7.08 (t, 1H, J = 7.4 Hz) ppm. ¹³C-NMR (DMSO-*d*₆) δ : 162.0, 142.7, 139.6, 136.2, 131.4, 129.1, 123.7, 122.4, 120.4, 118.7, 118.4, 110.3, 107.7 ppm. FT-IR (KBr disk): 2682, 1635, 1601, 1541, 1513, 1442, 1374, 1323, 1293, 746, 686 cm⁻¹. m.p.: 270-274°C. MS (CI): *m/z*: 298 [M⁺]. HRMS (ESI): calcd. for [C₁₅H₁₁N₃O₄ + H]⁺: 298.0828; found: 298.0826. Elemental Analysis for C₁₅H₁₁N₃O₄: calcd. (%) C 60.61, H 3.73, N 14.14; found (%) C 60.34, H 3.86, N 14.28

Compound 33. A mixture of 4-cyano-nitrosobenzene (132 mg, 1 mmol) and *N*-phenylpropiolamide (145 mg, 1 mmol), in toluene (10 mL) was stirred at 80 °C for 8 hours under nitrogen. Precipitation of the desired product was observed during the reaction. After cooling to r.t., 5-cyano-1-hydroxy-*N*-phenyl-1H-indole-3-carboxamide **33** was collected by filtration (80.3 mg of a yellow solid, yield = 29%) and characterized without further purification. ¹H-NMR (DMSO-*d*₆) δ : 12.36 (br, 1H), 9.83 (s, 1H), 8.63 (s, 2H), 7.75 (d, 2H, J = 7.6 Hz), 7.67 (d, 1H, J = 8.5 Hz), 7.62 (dd, 1H, J₁ = 8.5 Hz, J₂ = 1.4 Hz), 7.35 (t, 2H, J = 7.9 Hz), 7.07 (t, 1H, J = 7.3 Hz) ppm. ¹³C-NMR (DMSO-*d*₆) δ : 162.3, 139.7, 135.1, 130.4, 129.1, 127.1, 125.8, 123.6, 122.9, 120.6, 120.4, 111.0, 106.3, 103.9 ppm. FT-IR (KBr disk): 3340, 2217, 1629, 1538 cm⁻¹. m.p.: 278-280°C. MS (CI): *m/z*: 278 [M⁺]. HRMS (ESI): calcd. for [C₁₆H₁₁N₃O₂ + H]⁺: 278.0930; found: 278.0932. Elemental Analysis for C₁₆H₁₁N₃O₂: calcd. (%) C 69.31, H 4.00, N 15.15; found (%) C 69.46, H 4.09, N 15.11

Compound 34. A mixture of 4-nitro-nitrosobenzene (96 mg, 0.63 mmol) and 1-(ferrocene)prop-2-yn-1-one (150 mg, 0.63 mmol), in toluene (8 mL) was stirred at 80 °C for 24 hours under nitrogen. Solvent is then rotary evaporated and the crude product is purified by gravimetric column cromatography (hexane : AcOEt 6:4) to afford (5-nitro-1H-3-indolyl)(1-ferrocenyl)methanone **34** as a red solid (115.5 mg, yield 49%). ¹H-NMR (DMSO-*d*₆) δ : 12.68(br, 1H), 9.15 (s, 1H), 8.66 (s, 1H), 8.13 (dd, 1H, J₁ = 8Hz, J₂ = 2.3 Hz), 7.70 (d, 1H, J = 8 Hz), 5.05 (s, 2H), 4.64 (s, 2H), 4.24 (s, 5H) ppm. ¹³C-NMR (DMSO-*d*₆) δ : 191.7, 142.9, 139.8, 136.1, 126.3, 118.7, 118.6, 117.5, 113.3, 80.8, 72.0, 70.7, 70.3 ppm. FT-IR (ATR): 3121, 1572, 1528, 1453, 1335, 1107, 1059, 815, 749 cm⁻¹. m.p.: > 300°C. MS (CI): *m/z*: 375 [M+1]. HRMS (ESI): calcd. for [C₁₉H₁₄FeN₂O₃ + H]⁺: 375.0432; found: 375.0436. Elemental Analysis for C₁₉H₁₄FeN₂O₃: calcd. (%) C 60.99, H 3.77, N 7.49; found (%) C 61.05, H 3.88, N 7.41

Compound 35. A mixture of 4-nitro-nitrosobenzene (100 mg, 0.66 mmol) and 1-(naphthalen-1-yl)prop-2yn-1-one (119 mg, 0.66 mmol), in toluene (10 mL) was stirred at 80 °C for 7.5 hours under nitrogen. Precipitation of the desired product was observed during the reaction. After cooling to r.t., (1-hydroxy-5nitro-1H-indol-3-yl)(naphthalen-1-yl)methanone **35** was isolated by filtration as an orange solid (149 mg, yield = 68%) and characterized without further purification. ¹H-NMR (DMSO-*d*₆) δ : 12.60 (br, 1H), 9.19 (d, 1H, J = 2.3 Hz), 8.24 (dd, 1H, J₁ = 9 Hz, J₂ = 2.3 Hz), 8.13 (d, 1H, J = 7 Hz), 8.11 (s, 1H), 8.06 (dd, 1H, J₁ = 7.9 Hz, J₂ = 0.7 Hz), 8.04 (d, 1H, J = 7.9 Hz), 7.77 (dd, 1H, J₁ = 7 Hz, J₂ = 1 Hz), 7.74 (d, 1H, J = 9 Hz), 7.63 (td, 1H, J₁ = 7 Hz, J₂ = 1 Hz), 7.59 (td, 1H, J₁ = 7.9 Hz, J₂ = 1.3 Hz), 7.55 (td, 1H, J₁ = 7.9 Hz, J₂ = 1.3 Hz) ppm. ¹³C-NMR (DMSO-*d*₆) δ : 190.6, 143.6, 137.5, 137.2, 136.8, 133.4, 130.6, 130.0, 128.5, 127.1, 126.6, 126.5, 125.2, 125.0, 121.8, 119.0, 118.2, 113.1, 110.5 ppm. FT-IR (KBr disk): 1602, 1578, 1517, 1334, 775 cm⁻¹. m.p.: decomposition from 261°C. MS (CI): *m/z*: 333 [M+1]. HRMS (ESI): calcd. for [C₁₉H₁₂N₂O₄ + H]⁺: 333.0875; found: 333.0879. Elemental Analysis for C₁₉H₁₂N₂O₄: calcd. (%) C 68.67, H 3.64, N 8.43; found (%) C 68.56, H 3.61, N 8.49

Compound 36. A mixture of 4-cyano-nitrosobenzene (132 mg, 1 mmol) and 1-(naphthalen-1-yl)prop-2-yn-1-one (180 mg, 1 mmol), in toluene (10 mL) was stirred at 80 °C for 16 hours under nitrogen. Precipitation of the desired product was observed during the reaction. After cooling to r.t., 3-(1-naphthoyl)-1-hydroxy-1H-indole-5-carbonitrile **36** was collected by filtration as an orange-solid (95 mg, yield = 30 %) and characterized without further purification. ¹H-NMR (DMSO-*d*₆) δ : 12.54 (br, 1H), 8.66 (d, 1H, J = 1 Hz), 8.12 (d, 1H, J = 8.2 Hz), 8.04 (s, 1H), 8.03 (d, 2H, J = 8 Hz), 7.74 (dd, 1H, J₁ = 8 Hz, J₂ = 1 Hz), 7.73 – 7.72 (m, 2H), 7.63 (dd, 1H, J₁ = 8.2 Hz, J₂ = 1 Hz), 7.58 (td, 1H, J₁ = 8 Hz, J₂ = 1.4 Hz), 7.53 (td, 1H, J₁ = 8 Hz, J₂ = 1.4 Hz) ppm. ¹³C-NMR (DMSO-*d*₆) δ : 190.6, 137.4, 136.5, 135.7, 133.5, 130.5, 130.0, 128.5, 127.1, 126.8, 126.6, 126.5, 125.2, 125.1, 122.3, 120.0, 112.0, 111.2, 105.2 ppm. FT-IR (KBr disk): 2221, 1571, 1509, 1364, 1341, 1225, 775 cm⁻¹. m.p.: 226 – 228°C. MS (CI): *m/z*: 313 [M+1]. HRMS (ESI): calcd. for [C₂₀H₁₂N₂O₂ + H]⁺: 313.0977; found: 313.0969. Elemental Analysis for C₂₀H₁₂N₂O₂: calcd. (%) C 76.91, H 3.87, N 8.97; found (%) C 77.02, H 3.75, N 9.06

Compound 37 and Compound 38. A mixture of nitrosobenzene (214 mg, 2 mmol) and 1-(naphthalen-1-yl)prop-2-yn-1-one (360 mg, 2 mmol), in toluene (16 mL) was stirred at 80 °C for 24 hours under nitrogen. After complete conversion of nitrosobenzene, the mixture was cooled to r.t. and the solvent removed *in vacuo*. After purification on silica gel (Hexane:AcOEt=70:30), (1-hydroxy-1H-indol-3-yl)(naphthalen-1-yl)methanone **37** (154 mg, yield = 38%) and 1-hydroxy-3-(1-naphthoyl)-1*H*-indole **38** (65 mg, yield = 17%) were collected as dark orange solids.

Compound 37 ¹H-NMR (DMSO- d_6) δ : 12.17 (br, 1H), 8.25 (dd, 1H, J1 = 7.3 Hz, J2 = 0.9 Hz), 8.08 (d, 1H, J = 8.1 Hz), 8.00 (td, 2H, J₁ = 7.3 Hz, J₂ = 0.9 Hz), 7.73 (s, 1H), 7.68 (dd, 1H, J₁ = 7 Hz, J₂ = 1.3 Hz), 7.61 (d, 1H, J = 8.1 Hz), 7.60 (t, 1H, J = 8.1 Hz), 7.57 – 7.49 (m, 2H), 7.35 (td, 1H, J₁ = 8 Hz, J₂ = 1.3 Hz), 7.30 (td, 1H, J₁ = 8 Hz, J₂ = 1.3 Hz) ppm. ¹³C-NMR (DMSO- d_6) δ : 190.7, 138.4, 134.3, 134.0, 133.4, 130.1, 130.0, 128.5, 126.9, 126.4, 125.9, 123.3, 125.1, 123.8, 123.1, 122.7, 121.6, 111.6, 109.8 ppm. FT-IR (KBr disk): 1594, 1503, 1364, 1318, 1224, 787, 746 cm⁻¹. m.p.: 102.5°C. MS (CI): *m/z*: 288 [M+1]. HRMS (ESI): calcd. for [C₁₉H₁₃NO₂ + H]⁺:

288.1024; found: 288.1022. Elemental Analysis for C₁₉H₁₃NO₂: calcd. (%) C 79.43, H 4.56, N 4.88; found (%) C 79.36, H 4.68, N 4.96

Compound 38 ¹H-NMR (DMSO- d_6) δ : 12.03 (s, 1H), 8.26 (d, 1H, J = 8.3 Hz), 8.07 (d, 1H, J = 8.1 Hz), 8.01 (d, 1H, J = 8.0 Hz), 7.98 (d, 1H, J = 8.3 Hz), 7.67 (dd, 1H, J₁ = 8.1 Hz, J₂ = 1.3 Hz), 7.65 (d, 1H, J = 3.2 Hz), 7.61 (t, 1H, J = 8.1 Hz), 7.56 (td, 1H, J₁ = 8 Hz, J₂ = 1.3 Hz), 7.50 (td, 1H, J₁ = 8.3 Hz, J₂ = 1.3 Hz), 7.30 – 7.24 (m, 2H) ppm.

¹H-NMR (CDCl₃): δ 11.52 (br, 1H), 8.14 (m, 1H), 7.90-8.02 (m, 3H), 7.79 (m, 1H), 7.49-7.60 (m, 2H), 7.24 (m, 1H), 7.12 (t, 1H, J = 7.7 Hz), 6.99 (m, 1H), 6.89 (m, 1H), 6.64 (t, 1H, J = 7.0 Hz). Other spectroscopic data for this compound were in agreement with the ones reported in literature.³⁵

Compound 39. A mixture of 4-cyano-nitrosobenzene (132 mg, 1 mmol) and (*E*)-1-(2-nitrophenyl)pent-1-en-4-yn-3-one (201 mg, 1 mmol), in toluene (10 mL) was stirred at 80 °C for 8 hours under nitrogen. Precipitation of the desired product was observed during the reaction. After cooling to r.t., (*E*)-1-hydroxy-3-(3-(2-nitrophenyl)acryloyl)-1*H*-indole-5-carbonitrile **39** was collected by filtration as a yellow solid (110 mg, yield = 33 %) and characterized without further purification. ¹H-NMR (acetone- d_6) δ : 11.53 (br, 1H), 8.89 (s, 1H), 8.83 (dd, 1H, J₁ = 1.4 Hz, J₂ = 0.7 Hz), 8.14 – 8.08 (m, 3H), 7.82 (td, 1H, J₁ = 7.6 Hz, J₂ = 0.8 Hz), 7.77 – 7.66 (m, 4H) ppm. ¹³C-NMR (acetone- d_6) δ : 182.5, 149.3, 135.9, 135.7, 134.3, 133.4, 130.5, 130.4, 129.1, 128.1, 127.4, 126.6, 124.6, 122.7, 119.5, 112.8, 110.5, 105.9 ppm. FT-IR (KBr disk): 2924, 2854, 2225, 1643, 1603, 1514, 1452, 1345, 1205, 1069, 973, 740 cm⁻¹. m.p.: degradation from 270°C. MS (CI): *m/z*: 334 [M⁺]. HRMS (ESI): calcd. for [C₁₈H₁₁N₃O₄ + H]⁺: 334.0828; found: 334.0834. Elemental Analysis for C₁₈H₁₁N₃O₄: calcd. (%) C 64.87, H 3.33, N 12.61; found (%) C 65.01, H 3.19, N 12.74

Compound 40. A mixture of 4-nitro-nitrosobenzene (152 mg, 1 mmol) and 1-phenylbut-3-yn-2-one (144 mg, 1 mmol), in toluene (10 mL) was stirred at 80 °C for 8 hours under nitrogen. Precipitation of the desired product was observed during the reaction. After cooling to r.t., 1-(1-hydroxy-5-nitro-1*H*-indol-3-yl)-2-phenylethanone **40** was collected by filtration (35 mg of a yellow solid, yield = 27%) and characterized without further purification. ¹H-NMR (DMSO-*d*₆) δ : 12.62 (br, 1H), 9.04 (s, 1H), 8.98 (s, 1H), 8.15 (d, 1H, 8 Hz), 7.68 (d, 1H, J = 8 Hz), 7.30 (m, 5H), 4.18 (s, 2H) ppm. ¹³C-NMR (DMSO-*d*₆) δ : 192.8, 143.6, 137.0, 136.7, 136.2, 129.9, 128.7, 126.9, 121.8, 119.1, 118.5, 112.4, 110.6, 46.1 ppm. MS (CI): *m/z*: 297 [M⁺]. HRMS (ESI): calcd. for [C₁₆H₁₂N₂O₄ + H]⁺: 297.0875; found: 297.0881. Elemental Analysis for C₁₆H₁₂N₂O₄: calcd. (%) C 64.86, H 4.08, N 9.46; found (%) C 64.72, H 4.11, N 9.56

Compound 41. (*E*)-1-hydroxy-3-(3-(2-nitrophenyl)acryloyl)-1H-indole-5-carbonitrile (333 mg, 1 mmol) and PPh₃ (1.05 g, 4 mmol) were stirred under microwaves irradiation for 5 minutes at 200 W and 100°C. The reaction mixture was then diluted with acetone, filtered and the solvent removed under reduced pressure. The crude residue was purified by flash chromatography elution with Hexane/EtOAc (1:1) afforded 3-(1H-indole-2-carbonyl)-1H-indole-5-carbonitrile **41** (25 % yield) as a brown solid. ¹H-NMR (acetone-d₆) δ : 11.61 (br, 1H), 10.99 (br s, 1H), 8.77 (dd, 1H, *J* = 1.6, 0.7 Hz), 8.68 (s, 1H), 7.77 (dd, 1H, *J* = 8.5, 0.7 Hz), 7.72 (dd, 1H, *J* = 9.0, 0.9 Hz), 7.63-7.60 (m, 2H), 7.43 (dd, 1H, *J* = 2.2, 0.9 Hz), 7.32 (td, 1H, *J* = 7.6, 1.1 Hz), 7.12 (td, 1H, *J* = 7.5, 1.0 Hz) ppm. ¹³C-NMR (acetone-d₆) δ : 180.2, 138.6, 137.6, 135.9, 134.8, 127.9, 127.1, 126.7, 126.0, 125.0, 122.5, 120.3, 119.8, 116.1, 113.4, 112.4, 107.9, 105.0 ppm. FT-IR (KBr disk): 3314; 2922; 2226; 1718; 1602; 1521; 1438; 1343; 1225; 1129; 874; 804 cm⁻¹. m.p.: degradation from 265°C. MS (CI): *m/z* = 286 [M⁺]. HRMS (ESI): calcd. for [C₁₈H₁₁N₃O + H]⁺: 286.0980; found: 286.0969. Elemental Analysis for C₁₈H₁₁N₃O: calcd. (%) C 75.78, H 3.89, N 14.73; found (%) C 75.69, H 3.96, N 14.57

Compound 42. (*E*)-1-hydroxy-3-(3-(2-nitrophenyl)acryloyl)-1H-indole-5-carbonitrile (102 mg, 0.31 mmol) was dissolved in a solution of MeOH (6 ml) and 1,4-dioxane (2 ml) under nitrogen atmosphere. A saturated solution of NH₄Cl (15 ml) and In powder (175 mg, 1.53 mmol) were added to the solution. The mixture was refluxed for 12 hours, cooled to rt and filtered over silica gel (MeOH). The crude residue was purified by flash chromatography (toluene-EtOAc 7:3) and 3-(quinoline2-yl)-1*H*-indole-5-carbonitrile **42** was obtained

as a brown solid. (24 % yield). ¹H-NMR (acetone-d₆) δ : 11.28 (br s, 1H); 9.47 (dd, 1H, *J* = 1.6, 0.7 Hz); 8.45 (d, 1H, *J* = 2.8 Hz); 8.27 (dd, 1H, *J* = 8.7, 0.4 Hz); 8.18 (dd, 1H, *J* = 8.4, 1.0 Hz); 8.04 (d, 1H, *J* = 8.7 Hz); 7.89 (dd, 1H, *J* = 8.1, 1.4 Hz); 7.76 (td, 1H, *J* = 7.7, 1.4 Hz); 7.71 (dd, 1H, *J* = 8.4, 0.7 Hz); 7.56-7.51 (m, 2H).¹³C-NMR (acetone-d₆) δ : 154.7; 148.3; 139.3; 136.0; 129.5; 129.0; 128.9; 128.6; 127.6; 126.5; 126.0; 125.4; 125.1; 120.4; 118.9; 117.1; 112.9; 103.6. MS (CI): *m/z* = 270 [M+1]⁺. IR (KBr disk): v (cm⁻¹) = 3386; 2923; 2854; 2224; 1600; 1524; 1440; 1261; 1093; 803. m.p.: 250°C. HRMS (ESI): calcd. for [C₁₈H₁₁N₃ + H]⁺: 270.1031; found: 270.1028. Elemental Analysis for C₁₈H₁₁N₃: calcd. (%) C 80.28, H 4.12, N 15.60; found (%) C 80.32, H 3.81, N 15.47

Compound 43 (JWH-018). A mixture of 1-hydroxy-3-(1-naphthoyl)-1*H*-indole (211 mg, 0.73 mmol), *n*-pentyl bromide (293 mg, 1.94 mmol), KOH (108.6 mg, 1.94 mmol) is stirred at r.t. for 12 hours. Solvent is removed in vacuo and the crude product is diluted in DCM and washed with acqueous NaOH 5%. Recombined organic phases are dried with MgSO₄, filtered and solvent removed under reducet pressure. Crude product is then purified by gravimetric cromatography (hexane : DCM 4:6) to afford **43** as a brown solid (53 mg, 20% yield). Spectroscopic data for this compound are in agreement with the ones reported in literature.³⁶

REACTIONS CARRIED OUT UNDER UNCONVENTIONAL AND GREEN METHODS

PLANETARY BALL MILL

20 mg (0.187 mmol) of nitrosobenzene **1c** and 24.3 mg (0.187 mmol) of 1-phenyl-2-propyn-1-one **2a** were placed inside a grinding jar with 40 balls (4 mmø). The grinding duration was 2 hours at a speed of 450 rpm; every 5 minutes the direction of rotation was reversed for greater homogeneity of the sample and avoid excessive raising of the temperature. The estimated temperature (around 45-55 °C) was not monitored. At the end of the treatment a sample was taken and by the GC-MS analysis the presence of the two starting reagents, 12% of the product **14** and the related azo derivative **44** in traces as a by-product were observed.

MICROWAVE

20 mg (0.187 mmol) of nitrosobenzene **1c** and 24.3 mg (0.187 mmol) of 1-phenyl-2-propyn-1-one **2a** were placed inside a flask and irradiated in MW with a fixed power of 50W for 2 hours. The program followed was 5 minutes of treatment followed by a minute break until reaching an effective reaction time of 2 hours. Every 40 minutes a withdrawal has been made; after 2 hours (data obtained via GC-MS) 62% of indole product **14**, 7% of azo derivative **44**, 12% of nitrosobenzene and 19% of arylalkynone were afforded.

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