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Supporting Information

Intra- and Intermolecular Reactions of Indoles with Alkynes Catalyzed by Gold

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Contents

General methods

All reactions were carried out under N_2 in solvents dried using a Solvent Purification System (SPS). Extractive workup refers to portioning of the crude reaction between an organic solvent and water, phase separation, drying (Na_2SO_4 or $MgSO_4$), and evaporation under reduced pressure.

Thin layer chromatography was carried out using TLC-aluminium sheets with 0.2 mm of silica gel (Merk GF_{234}). Chromatography purifications were carried out using flash grade silica gel (SDS Chromatogel 60 ACC, 40-60 μm). HPLC chromatography was performed in an Agilent Technologies Series 1100 chromatograph with UV detector.

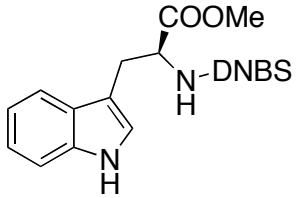
NMR spectra were recorded at 23°C on a Bruker Avance 400 Ultrashield and Bruker Avance 500 Ultrashield apparatous.

Mass spectra were recorded on a Waters LCT Premier (ESI) and Waters GCT (EI, CI) spectrometers. Elemental analyses were performed on a LECO CHNS 932 micro-analyzer at the Universidad Complutense de Madrid. Melting points were determined using a Büchi melting point apparatus. Optical rotations were recorded on a P-1030 polarimeter from Jasco at the sodium D line.

Synthesis of Amino-protected Tryptophane and Tryptamine derivatives

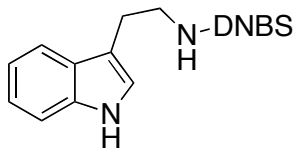
2-(1*H*-indol-3-yl)ethylcarbamate[i]

(*S*)-Methyl 2-(2,4-Dinitrobenzenesulfonylamino)-3-(1*H*-indol-3-yl)propanoate.



To a solution of L-tryptophan methyl ester hydrochloride (3.00 g, 13.72 mmol) in CH_2Cl_2 (40 mL) was added Et_3N (1.91 mL, 13.72 mmol). The mixture was stirred at 0°C and 2,4-dinitrobenzenesulfonyl chloride (3.66 g, 13.72 mmol) dissolved in CH_2Cl_2 (10 mL) was added over a period of 5 min. The reaction was stirred at room temperature for 16 h. After extractive workup (CH_2Cl_2) and chromatography (4:1 hexane-EtOAc), the title compound was obtained as an orange solid (5.34 g, 87%); m.p. 232-234°C; $[\alpha]_D^{23}$ = 54.4 (c = 1.1 in DMSO); ^{1}H NMR (400 MHz, [D_6]DMSO, 23°C): δ = 10.70 (br s, 1H), 9.11 (d, J = 8.1 Hz, 1H), 8.37 (d, J = 2.3 Hz, 1H), 7.92 (dd, J = 8.6, 2.2 Hz, 1H), 7.56 (d, J = 8.6 Hz, 1H), 7.34-7.31 (m, 1H), 7.08 (d, J = 2.4 Hz, 1H), 6.99-6.97 (m, 1H), 6.88-6.86 (m, 2H), 4.25-4.19 (br m, 1H), 3.68 (s, 3H), 3.15 (dd, J = 14.4, 4.2 Hz, 1H), 2.96 (dd, J = 14.6, 10.9 Hz, 1H); ^{13}C NMR (100 MHz, [D_6]DMSO, 23°C, DEPT): δ = 171.41, 148.32, 145.79, 137.03, 135.74, 130.18 (CH), 126.15, 125.86 (CH), 124.97 (CH), 120.71 (CH), 118.95 (CH), 118.37 (CH), 117.84 (CH), 110.98 (CH), 108.16, 56.54 (CH), 52.32 (CH_3), 27.20 (CH_2); HRMS-ESI *m/z* calcd for $C_{18}H_{16}N_4O_8SNa$: 471.0578; found: 471.0564 [M^++Na]; elemental analysis calcd (%) for $C_{18}H_{16}N_4O_8S$: C 48.21, H 3.60, N 12.49, S 7.15; found: C 48.45, H 3.85, N 12.13, S 7.08.

***N*-(2(1*H*-Indol-3-yl)ethyl)-*N*-(2,4-dinitrobenzenesulfonyl)amine.**



To a solution of tryptamine (3.00 g, 18.72 mmol) in CH_2Cl_2 (40 mL) was added Et_3N (2.60 mL, 18.72 mmol). The mixture was stirred at 0°C and 2,4-dinitrobenzenesulfonyl chloride (4.99 g, 18.72 mmol) dissolved in CH_2Cl_2 (10 mL) was added over a period of 5 min. The reaction was stirred at room temperature for 16 h. After extractive workup (CH_2Cl_2) and chromatography (4:1, hexane-EtOAc), the title compound was obtained as an orange solid (6.65 g, 91%); m.p. 208-210°C; ^{1}H NMR (400 MHz, [D_6]DMSO, 23°C): δ = 10.72 (br s, 1H), 8.61 (d, J = 2.4 Hz, 1H), 8.43 (br s, 1H), 8.26 (dd, J = 8.7, 2.3 Hz, 1H), 7.91 (d, J = 8.7 Hz, 1H), 7.38 (d, J = 7.8 Hz, 1H), 7.15 (d, J = 8.0 Hz, 1H), 7.07 (d, J = 2.3 Hz, 1H), 6.96 (td, J = 8.2, 1.2 Hz, 1H), 6.90 (td, J = 7.8, 1.1 Hz, 1H), 3.32 (t, J = 7.1 Hz, 2H), 2.85 (t, J = 7.1 Hz, 2H); ^{13}C NMR (100 MHz, [D_6]DMSO, 23°C, DEPT): δ = 148.81, 146.71, 137.76, 136.00, 130.58 (CH), 126.68 (CH), 126.59, 123.48 (CH), 120.77 (CH), 119.51 (CH), 118.24 (CH), 118.03 (CH), 111.14 (CH), 110.37, 43.67 (CH_2), 25.14 (CH_2); HRMS-CI *m/z* calcd for $C_{16}H_{15}N_4O_6S$: 391.0712; found: 3910.695 [M^++H]; elemental analysis calcd (%) for $C_{16}H_{14}N_4O_6S$: C 49.23, H 3.61, N 14.35, S 8.21; found: C 48.90, H 3.78, N 13.80, S 8.04.

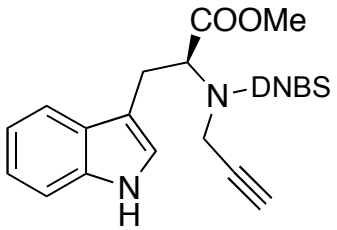
Synthesis of Propargyl Derivatives and Other Alkynyl indoles

General procedure for the preparation of the alkylated indole derivatives: A solution containing 1.2 equiv of NaH (60% in mineral oil) in DMF (volume of DMF necessary to make the concentration of NaH 1.0 M) was cooled at 0°C. A 1.0 equiv solution of the corresponding indole derivative

in DMF (volume of DMF necessary to make the concentration of the indole 1.0 M) was added dropwise. The mixture was warmed up to room temperature and stirred for 20 min and 1.0 equiv of the alkylating agent was added. The reaction was stirred at room temperature for 16 h and after extractive workup it was purified by chromatography.

Indole **12b** has been described previously.[ii]

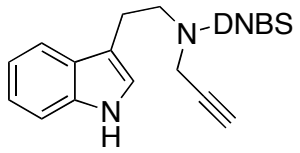
(*S*)-Methyl 2-(*N*-(Prop-2-ynyl)-*N*-(2,4-dinitrobezensulfonylamino))-3-(1*H*-indol-3-yl)propanoate (12a)



(*S*)-methyl 2-(2,4-dinitrobenzenesulfonylamino)-3-(1*H*-indol-3-yl)propanoate (1.70 g, 3.79 mmol) was alkylated following the general procedure using propargyl bromide (0.33 mL, 3.79 mmol). The crude product was purified by chromatography (4:1 hexane-EtOAc) to give **12a** as an orange solid (840 mg, 45%); $[\alpha]_D^{23}$ = 6.4 (c = 1.1, in DMSO); m.p. 178-180°C; ^{1}H NMR (400 MHz, [D_6]DMSO, 23°C): δ = 10.82 (br s, 1H), 8.54 (d, J = 2.3 Hz, 1H), 7.98 (dd, J = 9.3, 2.0 Hz, 1H), 7.70 (d, J = 8.7 Hz, 1H), 7.45-7.43 (m, 1H), 7.18 (d, J = 1.9 Hz, 1H), 7.12-7.10 (m, 1H), 6.96-6.90 (m, 2H), 4.82 (dd, J = 10.2, 5.1 Hz, 1H), 4.50-4.39 (m, 2H), 3.63 (s, 3H), 3.38 (t, J = 3.0 Hz, 1H), 3.37-3.31 (m, 1H), 3.27 (dd, J = 14.9, 10.3 Hz, 1H); ^{13}C NMR (100 MHz, [D_6]DMSO, 23°C, DEPT): δ = 169.87, 148.93, 146.64, 135.85, 135.81, 131.08 (CH), 126.34, 125.57 (CH), 124.77 (CH), 120.98 (CH), 119.03 (CH), 118.51 (CH), 117.98 (CH), 111.16 (CH), 108.06, 78.96 (CH), 75.94, 59.67 (CH), 52.23 (CH_3), 34.43 (CH_2), 27.20 (CH_2); HRMS-ESI *m/z* calcd for $C_{21}H_{18}N_4O_8SNa$: 509.0743; found: 509.0751 [M^++Na]; elemental analysis calcd (%) for

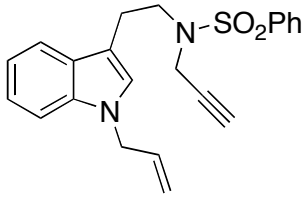
$C_{21}H_{18}N_4O_8S$: C 51.85, H 3.73, N 11.52, S 6.59; found: C 51.85, H 3.80, N 11.42, S, 6.61.

_N_-(2(1_H_-indol-3-yl)ethyl)-_N_-(2,4-dinitrobenzenesulfonyl)prop-2-yn-1-amine (12c)



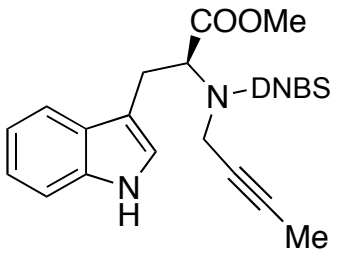
_N_-(2(1H-indol-3-yl)ethyl)-_N_-(2,4-dintrobenzenesulfonyl)amine (2.00 g, 5.12 mmol) was alkylated following the general procedure using propargyl bromide (0.44 mL, 5.12 mmol). The crude product was purified by chromatography (4:1, hexane-EtOAc) to give **12c** as an orange solid (658 mg, 30%); m.p. 138-140°C; ^{1}H NMR (400 MHz, [D_6]DMSO, 23°C): δ = 10.78 (br s, 1H), 8.73 (d, J = 2.5 Hz, 1H), 8.25 (dd, J = 8.7, 2.3 Hz, 1H), 8.06 (d, J = 8.7 Hz, 1H), 7.74 (d, J = 7.7 Hz, 1H), 7.19 (d, J = 7.3 Hz, 1H), 7.15 (d, J = 2.1 Hz, 1H), 6.99 (td, J = 7.1, 1.2 Hz, 1H), 6.94 (td, J = 7.6, 1.2 Hz, 1H), 4.38 (d, J = 2.3 Hz, 2H), 3.64 (t, J = 7.2 Hz, 2H), 3.36 (t, J = 2.3 Hz, 1H), 3.00 (t, J = 7.4 Hz, 2H); ^{13}C NMR (100 MHz, [D_6]DMSO, 23°C, DEPT): δ = 149.42, 146.88, 136.06, 135.91, 131.65 (CH), 126.67, 126.32 (CH), 123.63 (CH), 120.94 (CH), 119.65 (CH), 118.35 (CH), 118.05 (CH), 111.28 (CH), 109.84, 77.45 (CH), 76.60, 47.34 (CH_2), 36.13 (CH_2), 23.10 (CH_2); HRMS-CI _m/z_ calcd for $C_{19}H_{17}N_4O_6S$: 429.0869; found: 429.0863 [M^++H]; elemental analysis calcd (%) for $C_{19}H_{16}N_4O_6S$: C 53.27, H 3.76, N 13.08, S 7.48; found: C 53.24, H 3.93, N 12.98, S 7.02.

_N_-(2-(1-Allyl-1_H_-indol-3-yl)ethyl)-_N_-(prop-2-ynyl)benzenesulfonamide (12d)



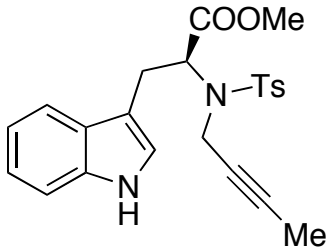
N-(2-(1*H*-Indol-3-yl)ethyl)-*N*-(prop-2-ynyl)benzenesulfonamide (300 mg, 0.88 mmol) was alkylated following the general procedure using allyl bromide (0.08 mL, 0.88 mmol) as the alkylating agent. The crude product was purified by chromatography (10:1 hexane-EtOAc) to give **12d** as a white solid (150 g, 45%); m.p. 93-95°C; ^{1}H NMR (400 MHz, $CDCl_3$, 23°C): δ = 7.85 (d, J = 7.4 Hz, 2H), 7.61 (d, J = 7.8 Hz, 1H), 7.56-7.53 (m, 1H), 7.46 (t, J = 7.8 Hz, 2H), 7.29 (d, J = 8.2 Hz, 1H), 7.21 (t, J = 7.3 Hz, 1H), 7.11 (t, J = 7.2 Hz, 1H), 6.98 (s, 1H), 5.97 (ddt, J = 17.0, 10.6, 5.5 Hz, 1H), 5.19 (dd, J = 10.2, 1.6 Hz, 1H), 5.09 (dd, J = 17.1, 1.2 Hz, 1H), 4.67 (d, J = 5.4 Hz, 2H), 4.19 (d, J = 2.3 Hz, 2H), 3.53 (t, J = 7.6 Hz, 2H), 3.08 (t, J = 8.0 Hz, 2H), 2.04 (t, J = 2.3 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$, 23°C, DEPT): δ = 139.01, 136.41, 133.48 (CH), 132.64 (CH), 128.85 (CH, 2C), 127.90, 127.62 (CH, 2C), 125.91 (CH), 121.74 (CH), 119.14 (CH), 118.85 (CH), 117.31 (CH_2), 111.13, 109.67 (CH), 76.75, 73.74 (CH), 48.71 (CH_2), 47.19 (CH_2), 36.78 (CH_2), 24.37 (CH_2); HRMS-ESI *m/z* calcd for $C_{22}H_{22}N_2O_2SNa$: 401.1300; found: 401.1306 [M^++Na]; elemental analysis calcd (%) for $C_{22}H_{22}N_2O_2S$: C 69.81, H 5.86, N 7.40, S 8.47; found: C 69.99, H 6.15, N 7.95, S 8.04.

(*S*)-Methyl 2-(*N*-(But-2-ynyl)-2,4-dinitrophenylsulfonamido)-3-(1*H*-indol-3-yl)propanoate (12e)



(*S*)-methyl 2-(2,4-dinitrobenzenesulfonylamino)-3-(1*H*-indol-3-yl)propanoate (2.00 g, 3.99 mmol) was alkylated following the general procedure using 1-bromobut-2-yne (0.34 mL, 3.99 mmol). The crude product was purified by chromatography (4:1 hexane-EtOAc) to give **12e** as an orange solid (1.24 g, 62%); $[\alpha]_D^{23}$ = 5.4 (c = 0.6, in acetone); m.p. 166-168°C; ^{1}H NMR (400 MHz, [D_6]DMSO, 23°C): δ = 10.81 (br s, 1H), 8.54 (d, J = 2.2 Hz, 1H), 8.01 (dd, J = 8.7, 2.2 Hz, 1H), 7.69 (d, J = 8.7 Hz, 1H), 7.44 (d, J = 7.0 Hz, 1H), 7.17 (d, J = 2.6 Hz, 1H), 7.14 (d, J = 7.1 Hz, 1H), 6.96 (t, J = 7.0 Hz, 1H), 6.93 (t, J = 7.3 Hz, 1H), 4.83 (dd, J = 10.4, 5.4 Hz, 1H), 4.38 (br s, 2H), 3.64 (s, 3H), 3.38 (dd, J = 14.8, 5.4 Hz, 1H), 3.27 (dd, J = 15.6, 10.4 Hz, 1H), 1.76 (br s, 3H); ^{13}C NMR (100 MHz, [D_6]DMSO, 23°C, DEPT): δ = 170.03, 148.89, 146.74, 136.17, 135.87, 130.95 (CH), 126.40, 125.52 (CH), 124.70 (CH), 120.96 (CH), 118.97 (CH), 118.50 (CH), 117.98 (CH), 111.17 (CH), 108.21, 81.72 (CH), 74.22, 59.72 (CH), 52.34 (CH_3), 35.01 (CH_2), 24.63 (CH_2), 2.99 (CH_3); HRMS-ESI *m/z* for $C_{22}H_{20}N_4O_8SK$: 539.0639; found: 539.0646 [M^++K]; elemental analysis calcd (%) for $C_{22}H_{20}N_4O_8S$: C 52.80, H 4.03, N 11.19, S 6.41, found: C 52.67, H 4.01, N 11.24, S 6.41.

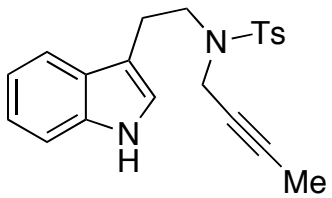
(*S*)-Methyl 2-(*N*-(But-2-ynyl)-*N*-tosylamino)-3-(1*H*-indol-3-yl)propanoate (12f)



To a solution of L-tryptophan methyl ester hydrochloride (3.00 g, 13.72 mmol) in CH_2Cl_2 (40 mL) was added *N*,*N*-dimethylaminopyridine (84 mg, 0.68 mmol) and Et_3N (5.7 mL, 41.23 mmol). The mixture was stirred at 0°C and a solution of 4-methylbenzenesulfonyl chloride (2.62 g, 13.72 mmol)

was added. The reaction was stirred at room temperature for 16 h and after extractive workup (CH_2Cl_2) the crude product was dissolved in DMF and alkylated following the general procedure using 1-bromobut-2-yne (1.2 mL, 13.72 mmol). The crude product was purified by chromatography (3:1, hexane-EtOAc) to give **12f** as a white solid (2.42 g, 43%); m.p. 102-103°C; $[\alpha]_D^{23}$ = -26.4 (c = 1.1, in CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$, 23°C): δ = 8.06 (s, 1H), 7.64 (d, J = 8.0 Hz, 2H), 7.56 (d, J = 8.0 Hz, 1H), 7.33 (d, J = 8.0 Hz, 1H), 7.18 (dd, J = 7.2, 0.8 Hz, 1H), 7.16 (d, J = 8.4 Hz, 2H), 7.12 (d, J = 7.6 Hz, 1H), 7.05 (d, J = 2.4 Hz, 1H), 4.87 (t, J = 7.6 Hz, 1H), 4.23 (t, J = 2.2 Hz, 2H), 3.52 (dd, J = 14.8, 8 Hz, 1H), 3.49 (s, 3H), 3.22 (dd, J = 14.8, 7.2 Hz, 1H), 2.38 (s, 3H), 1.63 (t, J = 2.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, 23°C, DEPT): δ = 171.12, 143.18, 137.13, 136.09, 129.04 (CH, 2C), 127.68, 127.17 (CH, 2C), 123.36 (CH), 122.04 (CH), 119.54 (CH),118.51 (CH), 111.19 (CH), 110.54, 80.80, 74.25, 59.43 (CH), 51.97 (CH_3), 34.68 (CH_2), 26.29 (CH_2), 21.53 (CH_3), 3.47 (CH_3); HRMS-CI *m/z* calcd for $C_{23}H_{24}N_2O_4S$: 424.1457; found: 424.1441 [M^+]; elemental analysis calcd (%) for $C_{23}H_{24}N_2O_4S$: C 65.07, H 5.70, N 6.60, S 7.55; found: C 64.74, H 5.67, N 6.57, S 7.39.

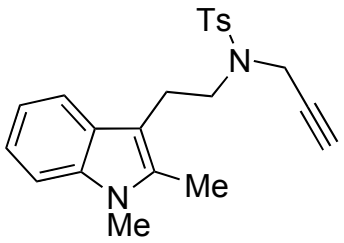
_N_-(2-(1_H_-Indol-3-yl)ethyl)-_N_-(but-2-ynyl)-4-methylbenzenesulfonamide (12g)



To a solution of tryptamine (3.00 g, 18.72 mmol) in CH_2Cl_2 (40 mL) was added *N,N*-dimethylaminopyridine (84 mg, 0.68 mmol) and triethylamine (5.7 mL, 41.23 mmol). The mixture was stirred at 0°C and a solution of 4-methylbenzenesulfonyl chloride (2.62 g, 13.74 mmol) was added. The reaction was stirred at room temperature for 16

h and after extractive workup (CH_2Cl_2) the crude product was dissolved in DMF and alkylated following the general procedure using 1-bromobut-2-yne (1.64 mL, 18.72 mmol). The crude product was purified by chromatography (3:1, hexane:EtOAc) to give **12g** as a white solid (4.32 g, 63%); m.p. 112-115°C; ^{1}H NMR (400 MHz, $CDCl_3$, 23°C): δ = 8.00 (s, 1H), 7.72 (d, J = 8.0 Hz, 2H), 7.62 (d, J = 8.0 Hz, 1H), 7.36 (d, J = 8.4 Hz, 1H), 7.25 (d, J = 7.6 Hz, 2H), 7.19 (dd, J = 7.6, 0.8 Hz, 1H), 7.11 (overlapping td, J = 7.8, .08 Hz, 1H), 7.09 (overlapping d, J = 2.4 Hz, 1H), 4.11 (q, J = 2.4 Hz, 2H), 3.48 (t, J = 7.6 Hz, 2H), 3.06 (t, J = 7.6 Hz, 2H), 2.39 (s, 3H), 1.57 (t, J = 2.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, 23°C, DEPT): δ 143.13, 136.64, 136.26, 129.25 (CH, 2C), 127.79, 127.34 (CH, 2C), 122.17 (CH), 122.09 (CH), 119.44 (CH), 118.70 (CH), 112.57, 111.17 (CH), 81.58, 72.09, 46.93 (CH_2), 37.24 (CH_2), 24.32 (CH_2), 21.48 (CH_3), 3.27 (CH_3); HRMS-CI *m/z* calcd for $C_{21}H_{22}N_2O_2S$: 366.1402; found: 366.1419 [M^+]; elemental analysis calcd (%) for $C_{21}H_{22}N_2O_2S$: C 68.82, H 6.05, N 7.64, S 8.75; found: C 68.53, H 6.06, N 7.64, S 8.74.

_N_-(2-(1,2-Dimethyl-1H-indol-3-yl)ethyl)-4-methyl-_N_-(prop-2-ynyl)benzenesulfonamide (12h)

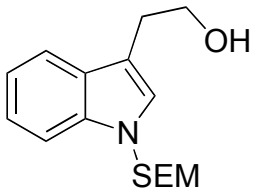


To a solution of 2-(1,2-dimethyl-1*H*-indol-3-yl)ethanamine[iii] (550 mg, 2.92 mmol) in CH_2Cl_2 (10 mL) was added *N,N*-dimethylaminopyridine (18 mg, 0.14 mmol) and triethylamine (0.8 mL, 5.84 mmol). The mixture was stirred at 0°C and a solution of 4-methylbenzenesulfonyl chloride (557 mg, 2.92 mmol) was added. The reaction was stirred at room temperature for 16 h and after extractive workup

(CH_2Cl_2) the crude product was dissolved in DMF and alkylated following the general procedure using propargyl bromide (0.26 mL, 2.92 mmol). The crude product was purified by chromatography (20:1, hexane:EtOAc) to give **12h** as a white solid (520 mg, 56%); m.p. 151-153°C; ^{1}H NMR (400 MHz, $CDCl_3$, 23°C): δ = 7.69 (d, J = 8.1 Hz, 2H), 7.52 (d, J = 7.7 Hz, 1H), 7.52-7.22 (m, 3H), 7.15 (dt, J = 7.0, 1.1 Hz, 1H), 7.07 (td, J = 7.0, 1.0 Hz, 1H), 4.18 (d, J = 2.6 Hz, 2H), 3.03 (s, 3H), 3.37-3.33 (m, 2H), 3.06-3.02 (m, 2H), 2.39 (s, 3H), 2.38 (s, 3H), 2.08 (t, J = 2.5 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$, 23°C, DEPT): δ = 143.36, 136.56, 136.02, 133.79, 129.44 (CH, 2C), 127.62 (CH, 2C), 127.44, 120.72 (CH), 119.00 (CH), 117.73 (CH), 108.62 (CH), 107.05, 77.22, 73.65 (CH), 47.21 (CH_2), 37.06 (CH_2), 29.53 (CH_3), 23.97 (CH_2), 21.51 (CH_3), 10.20 (CH_3); HRMS-IQ *m/z* calcd for $C_{22}H_{25}N_2O_2S$: 381.1637; found: 381.1638 [M^++H]; elemental analysis calcd (%) for $C_{22}H_{24}N_2O_2S$: C 69.44, H 6.36, N 7.36, S 8.43; found: C 69.16, H 6.22, N 7.57, S 8.35.

Synthesis of tryptophol derivatives

2-(1-((2-(Trimethylsilyl)ethoxy)methyl)-1*H*-indol-3-yl)ethanol.

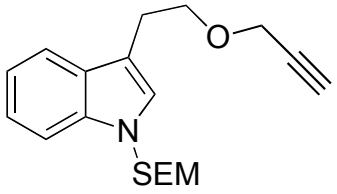


i. To a stirred solution of methyl 2-(1*H*-indol-3-yl)acetate (1.20 g, 6.34 mmol) in DMF (15 mL) was added sodium hydride (228 mg, 9.51 mmol) at 0°C. The mixture was allowed to stir at room temperature for 15 minutes and then (2-(chloromethoxy)ethyl)trimethylsilane (1.12 mL, 6.34 mmol) was added at 0°C. The reaction was stirred at room temperature for 16 h and after extractive workup (EtOAc/10%HCl water solution) the residue was purified by chromatography hexane:EtOAc 20:1 to give methyl 2-(1-((2-

(trimethylsilyl)ethoxy)methyl)-1*H*-indol-3-yl)acetate[iv] as a yellow oil (320 mg, 61%); ^{1}H NMR (400 MHz, $CDCl_3$, 23°C) δ = 7.62 (d, J = 7.9 Hz, 1H), 7.49 (d, J = 8.2 Hz, 1H), 7.27 (t, J = 7.5 Hz, 1H), 7.18 (overlapping t, J = 7.7 Hz, 1H), 7.18 (overlapping s, 1H), 5.47 (s, 2H), 3.79 (s, 2H), 3.72 (s, 2H), 3.50 (t, J = 8.1 Hz, 2H), 0.90 (t, J = 8.1 Hz, 2H), -0.03 (s, 9H).

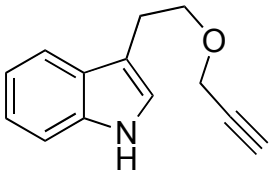
ii. To a suspension of lithium aluminum tetrahydride (292 mg, 7.70 mmol) in THF (15 mL) at 0°C was added a solution of methyl 2-(1-((2-(trimethylsilyl)ethoxy)methyl)-1*H*-indol-3-yl)acetate (1.23 g, 3.85 mmol) in THF (15mL). The reaction was allowed to stir at room temperature for 10 minutes. The mixture was quenched with the equivalents of water needed to neutralize all the lithium aluminum tetrahydride and it was stirred with $MgSO_4$ decahydrate for 1 h. Then it was filtered trough Celite and the solvent evaporated under reduced pressure to give 2-(1-((2-(trimethylsilyl)ethoxy)methyl)-1*H*-indol-3-yl)ethanol (1.10 g, 98%) as a yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$, 23°C): δ = 7.63 (d, J = 7.9 Hz, 1H), 7.49 (d, J = 8.1 Hz, 1H), 7.28 (dt, J = 7.5, 1.1 Hz, 1H), 7.18 (dt, J = 7.0, 0.9 Hz, 1H), 7.09 (s, 1H), 5.47 (s, 2H), 3.93 (q, J = 6.1 Hz, 2H), 3.50 (dd, J = 16.2, 8.1 Hz, 2H), 3.05 (t, J = 6.3 Hz, 2H), 1.55 (t, J = 6.1 Hz, 1H), 0.91 (dd, J = 16.3, 8.2 Hz, 2H), 0.02 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$, 23°C, DEPT): δ = 136.95, 128.59, 126.37 (CH), 122.36 (CH), 119.85 (CH), 119.03 (CH), 112.20, 110.04 (CH), 75.43 (CH_2), 65.86 (CH_2), 62.62 (CH_2), 28.65 (CH_2), 17.73 (CH_2), -1.42 (CH_3, 3C); HRMS-IE *m/z* calcd for $C_{16}H_{25}NO_2Si$: 291.1655; found: 291.1652 [M^+]; elemental analysis (%) calcd for $C_{16}H_{25}NO_2Si$: C 65.93, H 8.65, N 4.81; found: C 66.30, H 8.46, N 4.81.

3-(2-(Prop-2-ynyloxy)ethyl)-1-((2-(trimethylsilyl)ethoxy)methyl)-1*H*-indole.



2-(1-((2-(Trimethylsilyl)ethoxy)methyl)-1*H*-indol-3-yl)ethanol (1.06 g, 3.65 mmol) was alkylated following the general procedure using propargyl bromide (0.39 mL, 4.38 mmol). The crude mixture was purified by chromatography (10:1, hexane:EtOAc) to give 3-(2-(prop-2-ynyloxy)ethyl)-1-((2-(trimethylsilyl)ethoxy)methyl)-1*H*-indole as a colorless oil (700 mg, 58%); ^{1}H NMR (400 MHz, $CDCl_3$, 23°C): δ = 7.62 (d, J = 8.0 Hz, 1H), 7.47 (d, J = 8.1 Hz, 1H), 7.25 (dt, J = 7.7, 1.2 Hz, 1H), 7.16 (dt, J = 7.5, 0.9 Hz, 1H), 7.07 (s, 1H), 5.46 (s, 2H), 4.21 (d, J = 2.3 Hz, 2H), 3.84 (t, J = 7.2 Hz, 2H), 3.84 (dd, J = 16.3, 8.1 Hz, 2H), 3.08 (t, J = 7.2 Hz, 2H), 2.45 (t, J = 2.3 Hz, 1H), 0.90 (dd, J = 16.3, 8.2 Hz, 2H), -0.03 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$, 23°C, DEPT): δ = 136.68, 128.70, 125.94 (CH), 122.11 (CH), 119.66 (CH), 118.94 (CH), 112.60, 109.92 (CH), 79.89, 75.42 (CH_2), 74.30 (CH), 70.17 (CH_2), 65.74 (CH_2), 58.11 (CH_2), 25.46 (CH_2), 17.72 (CH_2), -1.42 (CH_3, 3C); HRMS-IE *m/z* calcd for $C_{19}H_{27}NO_2Si$: 329.1811; found: 329.1815 [M^+]; elemental analysis calcd (%) for $C_{19}H_{27}NO_2Si$: C 69.26, H 8.26, N 4.25; found: C 68.82, H 7.98, N 4.25.

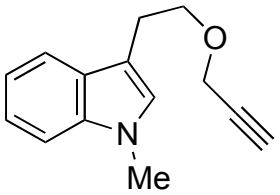
3-(2-(Prop-2-ynyloxy)ethyl)-1*H*-indole (19a).



To a solution of 3-(2-(prop-2-ynyloxy)ethyl)-1-((2-(trimethylsilyl)ethoxy)methyl)-1*H*-indole (580 mg, 1.76 mmol) in DMF (5 mL), was added tetrabutylammonium fluoride trihydrate (1.66 g, 5.28 mmnol) and ethylenediamine (0.53 mL, 7.92 mmol). The reaction was heated at 80°C overnight

and then the it was diluted with water and the product extracted with EtOAc. The residue was purified by chromatography (20:1, hexane:EtOAc) to give **19a** as a colorless oil (230 mg, 65%); ^{1}H NMR (400 MHz, $CDCl_3$, 23°C): δ = 7.98 (br s, 1H), 7.62 (d, J = 7.9 Hz, 1H), 7.35 (d, J = 7.8 Hz, 1H), 7.19 (dt, J = 7.2, 1.1 Hz, 1H), 7.12 (dt, J = 7.4, 1.1 Hz, 1H), 7.07 (d, J = 2.2 Hz, 1H), 4.19 (d, J = 2.3 Hz, 2H), 3.84 (t, J = 7.1 Hz, 2H), 3.08 (td, J = 7.2, 0.8 Hz, 2H), 2.43 (t, J = 2.3 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$, 23°C, DEPT): δ = 136.19, 127.54, 122.00 (CH, 2C), 119.32 (CH), 118.81 (CH), 112.80, 111.10 (CH), 79.94, 74.28 (CH), 70.27 (CH_2), 58.11 (CH_2), 25.60 (CH_2); HRMS-EI *m/z* calcd for $C_{13}H_{13}NO$: 199.0997; found: 199.0997 [M^+]; elemental analysis calcd (%) for $C_{13}H_{13}NO \cdot 1/6H_2O$: C 77.20, H 6.64, N 6.93; found: C 77.54, H 6.67, N 7.10.

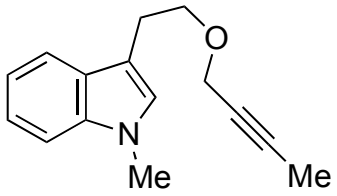
1-Methyl-3-(2-(prop-2-ynyloxy)ethyl)-1*H*-indole (19b)



Tryptophol (500 mg, 3.10 mmol) was alkylated following the general procedure using MeI (0.19 mL, 3.10 mmol). The solution was allowed to react for 3 hours and after extractive workup (Et_2O) the crude product was dissolved in DMF and alkylated following the general procedure using propargyl bromide (0.33 mL, 2.93 mmol). The residue was purified by chromatography over silica (100:3, hexane:EtOAc) to give **19b** as light yellow crystals (319 mg, 51%); m.p. 52 °C; ^{1}H NMR (400 MHz, $CDCl_3$, 23°C): δ = 7.61 (d, J = 7.9 Hz, 1H), 7.29 (d, J = 8.1 Hz, 1H), 7.22 (dt, J = 7.2, 1.1 Hz, 1H), 7.11 (dt, J = 7.3, 1.1 Hz, 1H), 6.93 (s, 1H), 4.20 (d, J = 2.3 Hz, 2H), 3.82 (t, J = 7.2 Hz, 2H), 3.75, (s, 3H) 3.07 (dt, J = 7.2, 0.8 Hz, 2H), 2.43 (t, J = 2.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$, 23°C, DEPT): δ =

137.1 (C), 128.1 (C), 127.0 (CH), 121.7 (CH), 119.1 (CH), 118.9 (CH), 111.3 (C), 109.4 (CH), 74.4 (C), 70.6 (CH_2), 58.3 (CH_2), 32.8 (CH_3), 25.7 (CH_2). HRMS-ESI *m/z* calcd for $C_{14}H_{15}NONa$: 236.1051; found: 236.1045 [M^++Na]; elemental analysis calcd (%) for $C_{14}H_{15}NO$: C 78.84, H 7.09, N 6.57; found: C 78.48, H 7.15, N 6.54.

3-(2-(But-2-ynyloxy)ethyl)-1-methyl-1*H*-indole (19e)

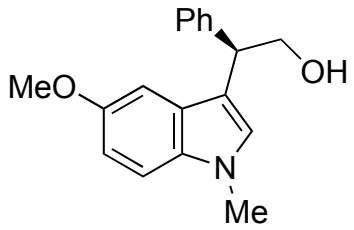


Tryptophol (500 mg, 3.10 mmol) was alkylated following the general procedure using MeI (0.19 mL, 3.10 mmol). The solution was allowed to react for 3 hours and after extractive workup (Et_2O) the crude product was dissolved in DMF and alkylated following the general procedure using 1-bromo-2-butyne (0.28 mL, 3.10 mmol). The residue was purified by chromatography over silica (100:3, hexane:EtOAc) to give **19e** as a yellow oil (472 mg, 67%); ^{1}H NMR (400 MHz, $CDCl_3$, 23°C): δ = 7.61 (d, J = 7.9 Hz, 1H), 7.29 (d, J = 8.2 Hz, 1H), 7.22 (dt, J = 7.9, 1.0 Hz, 1H), 7.11 (dt, J = 7.9, 1.0 Hz, 1H), 6.93 (s, 1H), 4.16 (q, J = 2.3 Hz, 2H), 3.79 (t, J = 7.2 Hz, 2H), 3.75, (s, 3H) 3.07 (t, J = 7.2 Hz, 2H), 1.86 (t, J = 2.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, 23°C, DEPT): δ = 137.1 (C), 128.1 (C), 127.0 (CH), 121.7 (CH), 119.1 (CH), 118.9 (CH), 109.3 (CH), 82.5 (C), 75.5 (C), 70.4 (CH_2), 58.8 (CH_2), 32.8 (CH_3), 25.7 (CH_2) 3.8 (CH_3). HRMS-ESI *m/z* calcd for $C_{15}H_{17}NONa$: 250.1208; found: 250.1209 [M^++Na]; elemental analysis calcd (%) for $C_{15}H_{17}NO \cdot 1/3H_2O$: C 77.22, H 7.63, N 6.00; found: C 77.31, H 7.29, N 6.16.

General procedure for the synthesis of (*R*)-2-indolyl-2-phenylethanol derivatives.

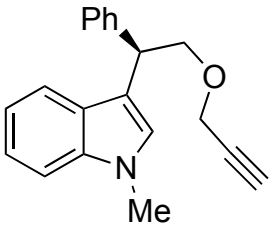
A two-necked flask was charged with CH_2Cl_2 (volume of CH_2Cl_2 necessary to make the concentration of indole 0.75 M), 0.01 equiv of $InBr_3$ and 1 equiv of the indole. The mixture was stirred for few minutes and then 0.65 equiv of (*R*)-styrene epoxide was added. The clear solution was stirred for 16 hours and then the reaction was quenched with a saturated solution of $NaHCO_3$ and extracted with Et_2O. The crude product mixture was purified by flash chromatography.

(*R*)-2-(5-Methoxy-1-methyl-1*H*-indol-3-yl)-2-phenylethanol.



(*R*)-2-(5-Methoxy-1-methyl-1*H*-indol-3-yl)-2-phenylethanol was synthesized following the general procedure using 5-methoxy-1-methyl-1*H*-indole (1.12 g, 6.95 mmol) and (*R*)-styrene oxide (0.53 mL, 4.64 mmol). The crude mixture was purified by chromatography over silica (20:1 hexane:EtOAc) to give (*R*)-2-(5-methoxy-1-methyl-1*H*-indol-3-yl)-2-phenylethanol (906 mg, 69%) as a yellow oil; $[\alpha]_D^{23}$ = 41.3 (c = 1.2 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$, 23°C): δ = 7.38-7.30 (m, 4H), 7.23 (tt, *J* = 7.1, 1.5 Hz, 1H), 7.18 (dd, *J* = 7.9, 1.5 Hz, 1H), 6.92 (s, 1H), 6.88-6.86 (m, 2H), 4.43 (t, *J* = 7.0 Hz, 1H), 4.25-4.13 (m, 2H), 3.77 (s, 3H), 3.74 (s, 3H), 1.55 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$, 23°C, DEPT): δ = 153.9 (C), 141.9 (C), 132.8 (C), 128.8 (CH), 128.4 (CH), 127.9 (C), 127.4 (CH), 126.8 (CH), 114.0 (C), 112.1 (CH), 110.2 (CH), 101.5 (CH), 66.6 (CH_2), 56.0 (CH), 45.7 (CH_3), 33.1 (CH_3); HRMS-ESI *m/z* calcd for $C_{18}H_{19}NO_2Na$: 304.1313; found: 304.1305 [M^++Na]; elemental analysis calcd (%) for $C_{18}H_{19}NO_2 \cdot 1/3H_2O$: C 75.24, H 6.90, N 4.87; found: C 75.23, H 6.70, N 4.95.

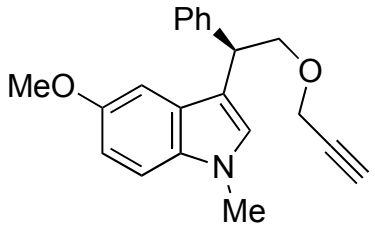
(*R*)-1-Methyl-3-(1-phenyl-2-(prop-2-ynyloxy)ethyl)-1*H*-indole (19c)



i. *N*-Methyl indole (1.63 g, 12.48 mmol) was reacted with styrene oxide (0.95 mL, 8.32 mmol) following the general procedure. The crude mixture was purified by chromatography over silica (10:1, hexane:EtOAc) to give (*R*)-2-(1-methyl-1*H*-indol-3-yl)-2-phenylethanol[v] as a yellow oil (1.13 g, 54%); ^{1}H NMR (400 MHz, $CDCl_3$, 23°C) δ = 7.50 (d, J = 7.6 Hz, 1H), 7.40–7.32 (m, 5H), 7.28–7.22 (m, 2H), 7.08 (t, J = 7.7 Hz, 1H), 6.99 (s, 1H), 4.51 (t, J = 6.6 Hz, 1H), 4.26 (dd, J = 10.5, 6.8 Hz, 1H), 4.19 (dd, J = 10.8, 7.1 Hz, 1H), 3.79 (s, 3H), 1.64 (brs, 1H).

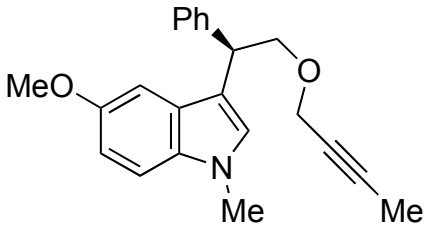
ii. (*R*)-2-(1-methyl-1*H*-indol-3-yl)-2-phenylethanol (2.63 g, 10.46 mmol) was alkylated following the general procedure using propargyl bromide (1.12 mL, 12.55 mmol). The crude mixture was purified by chromatography (30:1, hexane:EtOAc) to give **19c** as a yellow oil (2.51 g, 83%); $[\alpha]_D^{23}$ = -7.7 (c = 1.0 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$, 23°C): δ = 7.44 (d, J = 8.0 Hz, 1H), 7.37–7.35 (m, 2H), 7.32–7.27 (m, 3H), 7.23–7.18 (m, 2H), 7.03 (t, J = 7.5 Hz, 1H), 6.95 (s, 1H), 4.60 (t, J = 6.9 Hz, 1H), 4.25–4.06 (m, 4H), 3.76 (s, 3H), 2.46–2.44 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$, 23°C, DEPT): δ = 142.32, 137.12, 128.37 (CH, 2C), 128.27 (CH, 2C), 127.45, 126.80 (CH), 126.45 (CH), 121.60 (CH), 119.48 (CH), 118.84 (CH), 115.20, 109.17 (CH), 79.85, 74.53 (CH), 73.51 (CH_2), 58.21 (CH_2), 42.88 (CH), 32.74 (CH_3); HRMS-IE *m/z* calcd for $C_{20}H_{19}NO$: 289.1467; found: 289.1469 [M^+]; elemental analysis calcd (%) for $C_{20}H_{19}NO \cdot 1/5H_2O$: C 81.99, H 6.67, N 4.78; found: C 82.27, H 6.59, N 4.94.

(*R*)-5-Methoxy-1-methyl-3-(1-phenyl-2-(prop-2-ynyloxy)ethyl)-1*H*-indole (19d)



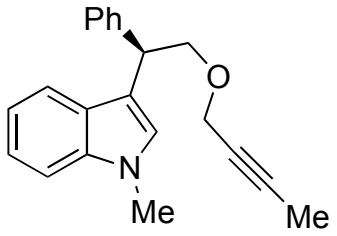
(*R*)-2-(5-Methoxy-1-methyl-1*H*-indol-3-yl)-2-phenylethanol (141 mg, 0.50 mmol) was alkylated following the general procedure using propargyl bromide (0.06 mL, 0.55 mmol). The crude mixture was purified by chromatography over silica (20:1, hexane:EtOAc) to give **19d** (110 mg, 86%) as a yellow solid; $[\alpha]_D^{23}$ = 25.3 (c = 1.0 in $CHCl_3$); m.p. 81 °C; ^{1}H NMR (400 MHz, $CDCl_3$, 23°C): δ = 7.36-7.34 (m, 2H), 7.31-7.28 (m, 2H), 7.21 (tt, J = 7.1, 1.5 Hz, 1H), 7.15 (d, J = 9.3 Hz, 1H), 6.89 (s, 1H), 6.85-6.83 (m, 2H), 4.53 (t, J = 7.0 Hz, 1H), 4.22 (AB doublet, J = 15.9, 2.4 Hz, 1H), 4.17 (AB doublet, J = 15.9, 2.4 Hz, 1H), 4.16 (dd, J = 9.5, 7.4 Hz, 1H), 4.05 (dd, J = 9.5, 7.4 Hz, 1H), 3.76 (s, 3H), 3.72 (s, 3H), 2.44 (t, J = 2.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$, 23°C, DEPT): δ = 153.8 (C), 142.4 (C), 132.7 (C), 128.6 (CH), 128.4 (CH), 127.9 (C), 127.6 (CH), 126.6 (CH), 114.8 (C), 111.8 (CH), 110.1 (CH), 101.7 (CH), 74.7 (C), 73.6 (CH_2), 58.4 (CH), 56.1 (CH_3), 43.1 (CH), 33.1 (CH_3); HRMS-ESI *m/z* calcd for $C_{21}H_{21}NO_2Na$: 342.1470; found: 342.1485 [M^++Na]; elemental analysis calcd (%) for $C_{21}H_{21}NO_2$: C 78.97, H 6.63, N 4.39, found: C 78.47, H 6.58, N 4.39.

(*R*)-3-(2-(But-2-ynyloxy)-1-phenylethyl)-5-methoxy-1-methyl-1*H*-indole (19g)



(*R*)-2-(5-Methoxy-1-methyl-1*H*-indol-3-yl)-2-phenylethanol (184 mg, 0.65 mmol) was alkylated following the general procedure using 1-bromo-2-butyne (0.07 mL, 0.79 mmol). The crude mixture was purified by chromatography over silica (20:1, hexane:EtOAc) to give **19g** (128 mg, 59%) as a colorless oil; $[\alpha]_D^{23}$ = 18.9 (c = 0.9 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$, 23°C): δ = 7.38-7.36 (m, 2H), 7.33-7.29 (m, 2H), 7.22 (tt, *J* = 7.2, 1.2 Hz, 1H), 7.16 (d, *J* = 8.8 Hz, 1H), 6.90 (s, 1H), 6.89-6.85 (m, 2H), 4.54 (t, *J* = 7.1 Hz, 1H), 4.22-4.11 (m, 3H), 4.04 (dd, *J* = 9.4, 7.5 Hz, 1H), 3.77 (s, 3H), 3.72 (s, 3H), 1.87 (t, *J* = 2.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, 23°C, DEPT): δ = 153.7 (C), 142.6 (C), 132.7 (C), 128.5 (CH), 128.4 (CH), 127.9 (C), 127.6 (CH), 126.5 (CH), 115.0 (C), 111.7 (CH), 110.0 (CH), 101.8 (CH), 82.6 (C), 75.4 (C), 73.5 (CH_2), 58.9 (CH_2), 56.0 (CH_3), 43.1 (CH), 33.0 (CH_3), 3.8 (CH_3); HRMS-ESI *m/z* calcd for $C_{22}H_{23}NO_2Na$: 356.1626; found: 356.1616 [M^++Na]; elemental analysis calcd (%) for $C_{22}H_{23}NO_2 \cdot H_2O$: C 75.19, H 7.17, N, 3.99; found: C 75.33, H 6.50, N 4.14.

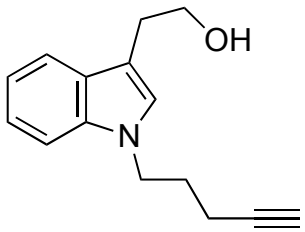
(*R*)-3-(2-(But-2-ynyloxy)-1-phenylethyl)-1-methyl-1*H*-indole (19f)



(*R*)-2-(1-methyl-1*H*-indol-3-yl)-2-phenylethanol (500 mg, 1.98 mmol) was alkylated following the general procedure using 1-bromo-2-butyne (0.21 mL, 2.38 mmol). The crude mixture was purified by chromatography (20:1, hexane:EtOAc) to give **19f** as a yellow oil (410 mg, 68%); $[\alpha]_D^{23}$ = -13.2 (c = 0.9 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$, 23°C): δ = 7.43 (d, *J* = 7.9 Hz, 1H), 7.36-7.34 (m, 2H), 7.30-7.26 (m, 3H), 7.22-7.16 (m, 2H), 7.01 (t, *J* = 7.5 Hz, 1H), 6.93 (s, 1H),

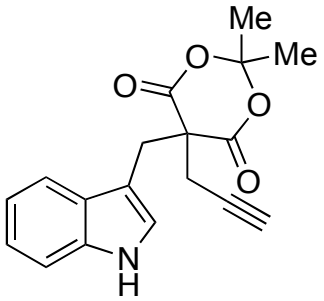
4.58 (t, J = 7.1 Hz, 1H), 4.19-4.10 (m, 3H), 4.03 (dd, J = 9.5, 7.3 Hz, 1H), 3.75 (s, 3H), 1.86 (t, J = 2.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, 23°C, DEPT): δ = 142.49, 137.12, 128.33 (CH, 2C), 128.27 (CH, 2C), 127.48, 126.80 (CH), 126.37 (CH), 121.54 (CH), 119.51 (CH), 118.77 (CH), 115.39, 109.13 (CH), 82.47, 75.27, 73.32 (CH_2), 58.71 (CH_2), 42.89 (CH), 32.74 (CH_3), 3.64 (CH_3); HRMS-IE *m/z* calcd for $C_{21}H_{21}NO$: 303.1623; found: 303.1629 [M^+]; elemental analysis calcd (%) for $C_{21}H_{21}NO \cdot 1/2H_2O$: C 80.74, H 7.10, N 4.48; found: C 80.70, H 6.71, N 4.66.

2-(1-(Pent-4-ynyl)-1*H*-indol-3-yl)ethanol



Tryptophol (700 mg, 4.34 mmol) was alkylated following the general procedure using 5-chloropentyne (0.44 mL, 4.13 mmol). The crude mixture was purified by chromatography (10:1, hexane:EtOAc) to give 2-(1-(pent-4-ynyl)-1*H*-indol-3-yl)ethanol as a yellow oil (822 mg, 88%); ^{1}H NMR (400 MHz, $CDCl_3$, 23°C): δ = 7.61 (d, J = 7.9 Hz, 1H), 7.36 (d, J = 8.3 Hz, 1H), 7.23 (dt, J = 7.0, 1.2 Hz, 1H), 7.12 (dt, J = 7.0, 0.9 Hz, 1H), 7.02 (s, 1H), 4.25 (t, J = 6.7 Hz, 2H), 3.90 (t, J = 5.8 Hz, 2H), 3.03, (dt, J = 6.4, 0.6 Hz, 2H), 2.17 (td, J = 6.7, 2.6 Hz, 2H), 2.07 (t, J = 2.6 Hz, 1H), 2.05-2.00 (m, 2H), 1.51 (bs, 1H); ^{13}C NMR (100 MHz, $CDCl_3$, 23°C, DEPT): δ = 136.6 (C), 128.2 (C), 126.6 (CH), 121.9 (CH), 119.2 (CH), 119.1 (CH), 111.1 (C), 109.6 (CH), 83.2 (CH), 69.8 (C), 62.9 (CH_2), 44.7 (CH_2), 28.9 (CH_2), 28.8 (CH_2), 16.0 (CH_2); HRMS-ESI *m/z* calcd for $C_{15}H_{17}NONa$: 250.1208; found: 250.1213 [M^++Na].

5-((1*H*-Indol-3-yl)methyl)-2,2-dimethyl-5-(prop-2-ynyl)-1,3-dioxane-4,6-dione (23)

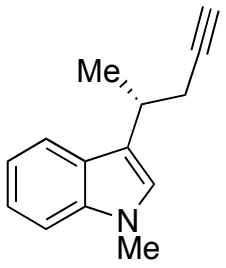


i. To a solution of indole (2.00 g, 17.07 mmol) in acetonitrile (20 mL) was added Meldrum's acid (2.46 g, 17.07 mmol), paraformaldehyde (512 mg, 17.07 mmol) and L-proline (98 mg, 0.85 mmol), and the reaction mixture was stirred at room temperature for 5 h. After removal of the solvent under reduced pressure, the residue was dissolved in warm methanol and crystallized. 5-((1H-Indol-3-yl)methyl)-2,2-dimethyl-1,3-dioxane-4,6-dione[vi] was obtained as a white solid (1.75 mg, 53%); ^{1}H NMR (400 MHz, $CDCl_3$, 23°C): δ = 8.08 (br s, 1H), 7.72 (d, J = 7.6 Hz, 1H), 7.33 (d, J = 8.0 Hz, 1H), 7.21-7.12 (m, 3H), 3.77 (t, J = 4.8 Hz, 1H), 3.66 (d, J = 4.8 Hz, 2H), 1.69 (s, 3H), 1.45 (s, 3H).

ii. 5-((1H-indol-3-yl)methyl)-2,2-dimethyl-1,3-dioxane-4,6-dione (1.00 g, 3.65 mmol) was alkylated following the general procedure using propargyl bromide (0.58 mL, 3.65 mmol). The crude product was purified by chromatography (4:1 hexane-EtOAc) to give **23** as a white solid (382 mg, 37%); m.p. 173-175°C; ^{1}H NMR (400 MHz, $CDCl_3$, 23°C): δ = 8.43 (s, 1H), 7.60 (d, J = 8.0 Hz, 1H), 7.31 (d, J = 8.3 Hz, 1H), 7.18-7.14 (m, 1H), 7.14-7.10 (m, 1H), 7.04 (d, J = 2.68 Hz, 1H), 3.49 (s, 2H), 3.06 (d, J = 2.6 Hz, 2H), 2.14 (t, J = 2.6 Hz, 1H), 1.60 (s, 3H), 0.64 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, 23°C, DEPT): δ = 168.56, 135.77, 126.68, 124.55 (CH), 122.58 (CH), 120.39 (CH), 119.45 (CH), 111.02 (CH), 108.94, 106.37, 78.61 (CH), 72.70, 56.60, 35.31 (CH_2), 30.17 (CH_3), 28.30 (CH_3), 24.17 (CH_2); HRMS-EI *m/z* calcd for $C_{18}H_{17}NO_4$ 311.1158; found: 311.1154 [M^+]; elemental

analysis calcd (%) for $C_{18}H_{17}NO_4$: C 69.44, H 5.50, N 4.50; found: C 69.45, H 5.61, N 4.56.

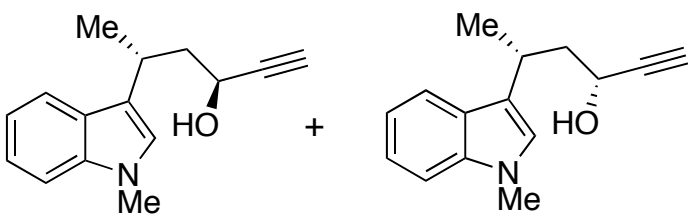
(*R*)-1-Methyl-3-(-pent-4-yn-2-yl)-1*H*-indole (29)



i. A round bottom flask protected from the sun light was charged with (*S*)-5-benzyl-2,2,3-trimethylimidazolidin-4-one (332 mg, 1.52 mmol), *tert*-butanol (2.5 mL), trifluoroacetic acid (0.11 mL, 1.52 mmol) and CH_2Cl_2, and placed at -40°C. The solution was stirred for 5 min before addition of crotonaldehyde (1.90 mL, 22.87 mmol). After stirring for an additional 10 min, 1-methyl-1H-indole (0.97 mL, 7.62 mmol) was added in one portion. The resulting suspension was stirred at constant temperature for 48 h. The reaction mixture was then passed cold through a silica gel plug with Et_2O and then concentrated. The resulting residue was purified by chromatography (toluene) to give (*R*)-3-(1-methyl-1H-indol-3-yl)butanal[vii] as a colorless oil (766 mg, 66% yield, 67% ee); $[\alpha]_D^{23}$ = -3.4 (c = 1.2 in $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$, 23°C): δ = 9.76 (t, J = 2.3 Hz, 1H), 7.64 (d, J = 7.9 Hz, 1H), 7.31 (d, J = 8.2 Hz, 1H), 7.25 (t, J = 7.8 Hz, 1H), 7.13 (t, J = 7.8 Hz, 1H), 6.85 (s, 1H), 3.76 (s, 3H), 3.71-3.67 (m, 1H), 2.88 (ddd, J = 16.2, 6.8, 2.3 Hz, 1H), 2.72 (ddd, J = 16.3, 7.4, 2.2 Hz, 1H), 1.45 (d, J = 6.9 Hz, 3H). The enantiomeric ratio was determined by HPLC analysis of the alcohol, obtained by $NaBH_4$ reduction of the aldehyde, using a Chiralpak AD column (1:99 ethanol/hexanes), flow = 1 ml/min, l = 254 nm. Retention times: 17.77 min, minor isomer; 19.23 min, major isomer.

ii. Tetrabromomethane (2.37 g, 7.15 mmol) was dissolved THF (45 mL) and cooled at -20°C, then a solution of triphenylphosphine (1.87 g, 7.15 mmol) in THF (85 mL) was added and allowed to react for 30 min. After cooling to -60°C, a mixture of (*R*)-3-(1-methyl-1*H*-indol-3-yl)butanal (720 mg, 3.57 mmol) and Et_3N (0.5 mL, 3.57 mmol) in 20 mL of THF, was slowly added and stirred for 30 min at -60°C. The reaction mixture was then heated at room temperature and left for 16 h. Then *n*BuLi (42 mmol) was added at -78°C and it was left to react with stirring for 1 h and then warmed to room temperature. The reaction mixture was left to react for 16 h, cooled again at -78°C, hydrolyzed with 0.01 M NaOH and extracted with ether. The organic phase was washed with brine twice and the solvent evaporated. The mixture was purified by chromatography (10:1 hexane-EtOAc) to give **29** as a yellow oil (479 mg, 68%); $[\alpha]_D^{23}$ = 10.1 (c = 1.2 in CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$, 23°C): δ = 7.61 (d, J = 8.0 Hz, 1H), 7.25 (d, J = 8.4 Hz, 1H), 7.23-7.19 (m, 1H), 7.11-7.07 (m, 1H), 6.88 (s, 1H), 3.72 (s, 3H), 3.35-3.26 (m, 1H), 2.67 (ddd, J = 16.8, 5.2, 2.4 Hz, 1H), 2.44 (ddd, J = 16.4, 8.0, 2.4 Hz, 1H), 1.99 (t, J = 2.4 Hz, 1H), 1.47 (d, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, 23°C, DEPT): δ = 137.06, 126.90, 124.96 (CH), 121.52 (CH), 119.24, 119.07 (CH), 118.63 (CH), 109.25 (CH), 83.60, 69.38 (CH), 32.60 (CH), 30.14 (CH_3), 27.03 (CH_2), 20.22 (CH_3); HRMS-CI *m/z* calcd for $C_{14}H_{16}N$: 198.1283; found: 198.1292 [M^++H]; elemental analysis calcd (%) for $C_{14}H_{15}N$: C 85.24, H 7.66, N 7.10; found: C 85.10, H 8.09, N 6.66.

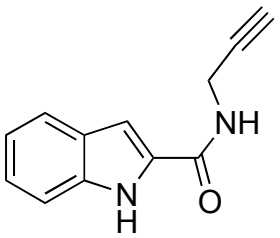
(3*R*,5*R*)-5-Methyl-1*H*-indol-3-yl)hex-1-yn-3-ol + (3*S*,5*R*)-5-Methyl-1*H*-indol-3-yl)hex-1-yn-3-ol (26)



To a stirred solution of trimethylsilylacetylene (0.77 mL, 5.46 mmol) in 20 mL of THF at -78°C was added *n*BuLi (5.46 mmol) and it was left to react for 15 min. Then was added (*R*)-3-(1-methyl-1*H*-indol-3-yl)butanal[vii] (1.00 g, 4.96 mmol) dissolved in THF (40 mL) and it was allowed to react for 2 h at -78°C. The reaction was quenched with aqueous NH_4Cl (10%, pH = 8 with NH_4OH), and after extractive workup (EtOAc) the mixture was dissolved in CH_2Cl_2 (25 mL) and tetrabutylammonium fluoride trihydrate (2.34 g, 7.44 mmol) was added and it was left to react for 10 min. After another extractive workup, the mixture was purified by chromatography (10:1 hexane-EtOAc), to give **26** (2:1 isomer mixture) as a yellow oil (541 mg, 48%); ^{1}H NMR (400 MHz, $CDCl_3$, 23°C): δ = 7.68 (dt, *J* = 8.0, 0.8 Hz, 1H, major), 7.69 (dt, *J* = 7.9, 0.8 Hz, 1H, minor), 7.29 (dd, *J* = 8.2, 0.9 Hz, 1H), 7.22 (td, *J* = 7.1, 1.2 Hz, 1H), 7.10 (td, *J* = 7.9, 1.2 Hz, 1H), 6.86 (s, 1H), 4.32 (dd, *J* = 7.5, 1.9 Hz, 1H, minor), 4.31 (dd, *J* = 6.9, 1.8 Hz, 1H, major), 3.75 (s, 3H, minor), 3.74 (s, 3H, major), 3.42-3.36 (m, 1H, minor), 3.34-3.27 (m, 1H, major), 2.50 (d, *J* = 2.1 Hz, 1H, major), 2.46 (d, *J* = 2.2 Hz, 1H, minor), 2.26 (ddd, *J* = 13.2, 8.6, 6.7 Hz, 1H, major), 2.17 (ddd, *J* = 13.7, 8.8, 5.1 Hz, 1H, minor), 2.09 (ddd, *J* = 13.7, 8.4, 6.0 Hz, 1H, minor), 2.01 (ddd, *J* = 13.4, 7.3, 5.6 Hz, 1H, major), 1.79 (br s, 1H), 1.42 (d, J = 6.9 Hz, 3H, major), 1.41 (d, *J* = 6.5 Hz, 3H, minor); ^{13}C NMR (100 MHz, $CDCl_3$, 23°C, DEPT): δ = 137.23, 126.88, 125.30 (CH, minor), 125.12 (CH, major), 121.60 (CH, minor), 121.56 (CH, major), 119.51 (CH), 118.70 (CH, minor), 118.63 (CH, major), 109.29 (CH, minor), 109.26 (CH, major), 108.51 (minor), 108.43 (major), 85.29 (CH), 73.08 (major), 72.72 (minor), 61.46 (CH, major), 60.86 (CH, minor), 45.84 (CH_2, major), 45.77 (CH_2, minor), 32.61 (CH_3), 27.75 (CH, major), 27.32 (CH, minor), 22.04 (CH_3); HRMS-CI *m/z* calcd for $C_{15}H_{18}NO$: 228.1388; found: 228.1388 [M^++H];

elemental analysis calcd (%) for $C_{15}H_{17}NO \cdot 1/2H_2O$: C 76.24, H 7.68, N 5.93; found: C 76.54, H 7.29, N 6.02.

***N*-(Prop-2-ynyl)-1*H*-indole-2-carboxamide (31)**



To a solution of indole-2-carboxylic acid (1.00 g, 6.21 mmol) in CH_2Cl_2 (30 mL), oxalyl chloride (1.57 mL, 18.61 mmol) and DMF (0.30 mL) were added. The reaction was heated to reflux for 1 h and then the solvent evaporated to dryness in vacuo. The residue was taken up with CH_2Cl_2 (30 mL) and propargylamine (1.28 mL, 18.61 mmol) added at 0°C. After 1 h at room temperature and extractive workup (CH_2Cl_2), the residue was purified by chromatography (4:1 hexane-EtOAc), to give **31** as a white solid (464 mg, 38%); m.p. 198-200°C; ^{1}H NMR (400 MHz, [D_6]DMSO, 23°C): δ = 8.91 (t, J = 5.4 Hz, 1H), 7.61 (d, J = 7.9 Hz, 1H), 7.43 (d, J = 8.2 Hz, 1H), 7.18 (t, J = 7.2 Hz, 1H), 7.13 (d, J = 1.5 Hz, 1H), 7.04 (t, J = 7.3 Hz, 1H), 4.09 (dd, J = 5.6, 2.4 Hz, 2H), 3.14 (t, J = 2.3 Hz, 1H); ^{13}C NMR (100 MHz, [D_6]DMSO, 23°C, DEPT): δ = 160.80, 136.47, 131.06, 126.98, 123.43 (CH), 121.55 (CH), 119.75 (CH), 112.29 (CH), 102.86 (CH), 86.02 (CH), 79.92, 28.02 (CH_2); HRMS-ESI *m/z* calcd for $C_{12}H_9N_2O$ 197.0715; found: 197.0711 [M^++H].

X-Ray Structure of Tetracycle 17

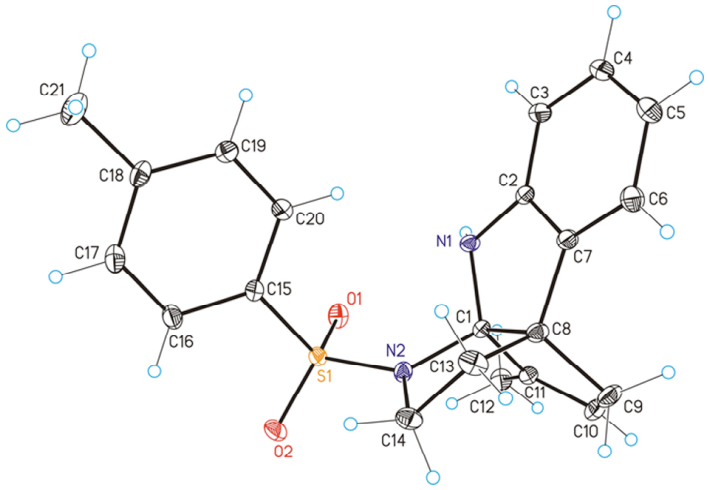


Table S-1. Crystal data and structure refinement for **17**.

Empirical formula	C21 H22 N2 O2 S	
Formula weight	366.47	
Temperature	100(2) K	
Wavelength	0.71073 Å	
Crystal system	Triclinic	
Space group	P-1	
Unit cell dimensions	a = 8.4990(10) Å	α= 110.109(4)°.
	b = 10.7814(13) Å	β= 101.219(4)°.
	c = 11.423(2) Å	γ = 103.200(3)°.
Volume	913.3(2) $Å^3$	
Z	2	
Density (calculated)	1.333 Mg/m^3	
Absorption coefficient	0.195 mm^{-1}	
F(000)	388	
Crystal size	0.10 x 0.10 x 0.10 mm^3	
Theta range for data collection	3.45 to 39.52°.	
Index ranges	-15<=h<=5, -19<=k<=9, -13<=l<=20	
Reflections collected	9455	
Independent reflections	6244 [R(int) = 0.0197]	
Completeness to theta = 39.52°	56.8 %	
Absorption correction	SADABS (Bruker-Nonius)	
Max. and min. transmission	0.9807 and 0.9807	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	6244 / 0 / 241	
Goodness-of-fit on F^2	1.111	

Final R indices [I>2sigma(I)]	R1 = 0.0421, wR2 = 0.1404
R indices (all data)	R1 = 0.0448, wR2 = 0.1433
Largest diff. peak and hole	0.618 and -0.810 e.Å^{-3}

Table S-2. Bond lengths [Å] and angles [°] for **17**.

S(1)-O(2)	1.4372(7)
S(1)-O(1)	1.4421(8)
S(1)-N(2)	1.6068(10)
S(1)-C(15)	1.7665(11)
C(1)-N(1)	1.4560(12)
C(1)-N(2)	1.4927(11)
C(1)-C(11)	1.5145(14)
C(1)-C(8)	1.5664(15)
N(1)-C(2)	1.3968(12)
N(2)-C(14)	1.4670(13)
C(2)-C(7)	1.3884(15)
C(2)-C(3)	1.3959(11)
C(7)-C(6)	1.3858(14)
C(7)-C(8)	1.5115(11)
C(8)-C(9)	1.5419(17)
C(8)-C(13)	1.5450(13)
C(3)-C(4)	1.3962(15)
C(11)-C(10)	1.3345(17)
C(11)-C(12)	1.4896(15)
C(5)-C(4)	1.3839(18)
C(5)-C(6)	1.4035(13)
C(9)-C(10)	1.5024(16)
C(14)-C(13)	1.5261(14)
C(20)-C(19)	1.3854(16)
C(20)-C(15)	1.3984(12)
C(15)-C(16)	1.3959(13)
C(16)-C(17)	1.3883(16)
C(19)-C(18)	1.4016(14)
C(17)-C(18)	1.3969(14)
C(21)-C(18)	1.5014(17)
O(2)-S(1)-O(1)	118.79(5)
O(2)-S(1)-N(2)	108.56(5)
O(1)-S(1)-N(2)	106.14(5)
O(2)-S(1)-C(15)	106.33(4)
O(1)-S(1)-C(15)	108.35(5)
N(2)-S(1)-C(15)	108.33(5)

N(1)-C(1)-N(2)	113.52(9)
N(1)-C(1)-C(11)	115.58(7)
N(2)-C(1)-C(11)	111.24(7)
N(1)-C(1)-C(8)	106.36(7)
N(2)-C(1)-C(8)	103.90(7)
C(11)-C(1)-C(8)	105.03(9)
C(2)-N(1)-C(1)	108.53(8)
C(14)-N(2)-C(1)	110.98(8)
C(14)-N(2)-S(1)	121.28(7)
C(1)-N(2)-S(1)	126.08(6)
C(7)-C(2)-C(3)	121.64(9)
C(7)-C(2)-N(1)	111.86(7)
C(3)-C(2)-N(1)	126.48(10)
C(6)-C(7)-C(2)	120.35(8)
C(6)-C(7)-C(8)	129.98(10)
C(2)-C(7)-C(8)	109.65(8)
C(7)-C(8)-C(9)	114.40(8)
C(7)-C(8)-C(13)	114.75(8)
C(9)-C(8)-C(13)	114.16(8)
C(7)-C(8)-C(1)	101.82(7)
C(9)-C(8)-C(1)	105.36(8)
C(13)-C(8)-C(1)	104.44(8)
C(2)-C(3)-C(4)	117.49(10)
C(10)-C(11)-C(12)	127.29(10)
C(10)-C(11)-C(1)	110.53(9)
C(12)-C(11)-C(1)	122.16(10)
C(4)-C(5)-C(6)	120.37(10)
C(10)-C(9)-C(8)	104.44(10)
C(11)-C(10)-C(9)	113.78(10)
C(7)-C(6)-C(5)	118.73(11)
C(5)-C(4)-C(3)	121.39(8)
N(2)-C(14)-C(13)	102.35(7)
C(14)-C(13)-C(8)	103.90(8)
C(19)-C(20)-C(15)	119.24(8)
C(16)-C(15)-C(20)	120.59(9)
C(16)-C(15)-S(1)	119.34(7)
C(20)-C(15)-S(1)	119.97(7)
C(17)-C(16)-C(15)	119.13(8)

C(20)-C(19)-C(18)	121.31(8)
C(16)-C(17)-C(18)	121.47(9)
C(17)-C(18)-C(19)	118.26(10)
C(17)-C(18)-C(21)	120.30(9)
C(19)-C(18)-C(21)	121.43(9)

Symmetry transformations used to generate equivalent atoms.

Table S-3. Torsion angles [°] for **17**.

N(2)-C(1)-N(1)-C(2)	127.19(8)
C(11)-C(1)-N(1)-C(2)	-102.55(9)
C(8)-C(1)-N(1)-C(2)	13.56(10)
N(1)-C(1)-N(2)-C(14)	-127.20(9)
C(11)-C(1)-N(2)-C(14)	100.40(10)
C(8)-C(1)-N(2)-C(14)	-12.10(10)
N(1)-C(1)-N(2)-S(1)	38.12(11)
C(11)-C(1)-N(2)-S(1)	-94.27(10)
C(8)-C(1)-N(2)-S(1)	153.22(7)
O(2)-S(1)-N(2)-C(14)	-50.26(9)
O(1)-S(1)-N(2)-C(14)	-179.01(7)
C(15)-S(1)-N(2)-C(14)	64.81(8)
O(2)-S(1)-N(2)-C(1)	145.81(8)
O(1)-S(1)-N(2)-C(1)	17.05(9)
C(15)-S(1)-N(2)-C(1)	-99.12(8)
C(1)-N(1)-C(2)-C(7)	-9.84(11)
C(1)-N(1)-C(2)-C(3)	171.72(9)
C(3)-C(2)-C(7)-C(6)	-1.41(16)
N(1)-C(2)-C(7)-C(6)	-179.94(9)
C(3)-C(2)-C(7)-C(8)	-179.88(9)
N(1)-C(2)-C(7)-C(8)	1.59(12)
C(6)-C(7)-C(8)-C(9)	-58.68(14)
C(2)-C(7)-C(8)-C(9)	119.60(10)
C(6)-C(7)-C(8)-C(13)	76.08(15)
C(2)-C(7)-C(8)-C(13)	-105.64(11)
C(6)-C(7)-C(8)-C(1)	-171.77(11)
C(2)-C(7)-C(8)-C(1)	6.51(11)
N(1)-C(1)-C(8)-C(7)	-11.94(10)

N(2)-C(1)-C(8)-C(7)	-132.01(8)
C(11)-C(1)-C(8)-C(7)	111.07(8)
N(1)-C(1)-C(8)-C(9)	-131.62(7)
N(2)-C(1)-C(8)-C(9)	108.31(8)
C(11)-C(1)-C(8)-C(9)	-8.62(8)
N(1)-C(1)-C(8)-C(13)	107.78(8)
N(2)-C(1)-C(8)-C(13)	-12.29(9)
C(11)-C(1)-C(8)-C(13)	-129.22(7)
C(7)-C(2)-C(3)-C(4)	1.46(15)
N(1)-C(2)-C(3)-C(4)	179.77(10)
N(1)-C(1)-C(11)-C(10)	121.86(9)
N(2)-C(1)-C(11)-C(10)	-106.79(9)
C(8)-C(1)-C(11)-C(10)	5.00(8)
N(1)-C(1)-C(11)-C(12)	-59.18(11)
N(2)-C(1)-C(11)-C(12)	72.17(10)
C(8)-C(1)-C(11)-C(12)	-176.04(7)
C(7)-C(8)-C(9)-C(10)	-101.98(9)
C(13)-C(8)-C(9)-C(10)	122.99(9)
C(1)-C(8)-C(9)-C(10)	9.00(8)
C(12)-C(11)-C(10)-C(9)	-177.96(8)
C(1)-C(11)-C(10)-C(9)	0.93(10)
C(8)-C(9)-C(10)-C(11)	-6.53(10)
C(2)-C(7)-C(6)-C(5)	0.75(16)
C(8)-C(7)-C(6)-C(5)	178.87(10)
C(4)-C(5)-C(6)-C(7)	-0.21(17)
C(6)-C(5)-C(4)-C(3)	0.31(18)
C(2)-C(3)-C(4)-C(5)	-0.91(17)
C(1)-N(2)-C(14)-C(13)	31.66(11)
S(1)-N(2)-C(14)-C(13)	-134.48(8)
N(2)-C(14)-C(13)-C(8)	-38.03(11)
C(7)-C(8)-C(13)-C(14)	141.74(10)
C(9)-C(8)-C(13)-C(14)	-83.39(11)
C(1)-C(8)-C(13)-C(14)	31.15(10)
C(19)-C(20)-C(15)-C(16)	-0.85(17)
C(19)-C(20)-C(15)-S(1)	175.44(9)
O(2)-S(1)-C(15)-C(16)	-6.95(11)
O(1)-S(1)-C(15)-C(16)	121.80(9)
N(2)-S(1)-C(15)-C(16)	-123.47(9)

O(2)-S(1)-C(15)-C(20)	176.71(9)
O(1)-S(1)-C(15)-C(20)	-54.55(10)
N(2)-S(1)-C(15)-C(20)	60.19(10)
C(20)-C(15)-C(16)-C(17)	0.61(17)
S(1)-C(15)-C(16)-C(17)	-175.71(9)
C(15)-C(20)-C(19)-C(18)	0.50(17)
C(15)-C(16)-C(17)-C(18)	-0.01(18)
C(16)-C(17)-C(18)-C(19)	-0.33(18)
C(16)-C(17)-C(18)-C(21)	-179.16(12)
C(20)-C(19)-C(18)-C(17)	0.09(17)
C(20)-C(19)-C(18)-C(21)	178.90(12)

Symmetry transformations used to generate equivalent atoms

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