Efficient Synthesis of the Indoloazocine Framework via Intramolecular Alkyne Carbocyclization.

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General Experimental Methods.

^1H and ^{13}C NMR spectra were recorded on Bruker Avance 300 or Bruker 400 instruments at 298 K unless otherwise stated. The ^1H and ^{13}C chemical shifts are reported in parts per million relative to tetramethylsilane using the residual solvent signal as the internal reference. Mass spectra were recorded on Kratos MS50TC and Kratos Mach III system. The ion source temperature was 150-250°C, as required. High-resolution EI-mass spectra were recorded with a resolution of 10000. The low-resolution spectra were obtained with HP5989A MS instrument. For thin-layer chromatography, analytical TLC plates (Alugram SIL G/UV254 and 70-230 mesh silica gel (E. M. Merck) were used. Optical rotations were measured using a PROPOL® Automatic Process Polarimeter.

Microwave Irradiation Experiments.

A monomode CEM Discover™ microwave reactor was used in the standard configuration as delivered, including proprietary software. All experiments were carried out in sealed microwave process vials.

Synthesis of the starting amides 1a-v:

Amides **1a-v** appear as a mixture of two rotamers (with the exception of secondary amide **1d**). ^{13}C spectra of **1a-v** were not registered, since overlapping of multiple peaks of both rotamers (example **1a**) makes the spectra not very characteristic. ^1H NMR spectra of **1a-v** are described for both rotamers considering the ratio. $[\alpha]_D^{20}$ values for enantiomerically pure **1p-v** were not measured. On TLC amides **1a-v** often appear as two interconverting spots. The starting tryptamines **8-10** were prepared according to the references 1-3 respectively.

General procedure for the synthesis of propynoic acid amides 1a-k,p-t,12a,b:

3 substituted 2-propynoic acid **11** (1.15 equiv) and N-hydroxysuccinimide 276 mg (1.2 equiv) were dissolved in dry DCM (6 mL). DCC 475 mg (1.15 equiv) was added and the reaction was stirred at ambient temperature for 3-4 h. Tryptamine (2 mmol, 1 equiv) was added in one portion as solid or as a solution in DCM (4 mL) and the reaction was left with stirring overnight. The subsequently formed precipitate of N,N'-dicyclohexylurea was filtered off and washed

well with Et₂O. The organic layer was washed with successively with HCl (1M), NaHCO₃ (sat), brine, dried (MgSO₄) and concentrated with silica. Pure amides **1a-m,p-t** were isolated by column chromatography on silica gel.

2-Butynoic acid benzyl-[2-(1*H*-indol-3-yl)-ethyl]-amide (1a). Synthesized from tetrolic acid 194 mg and 500 mg of *N*-benzyltryptamine. Eluent DCM / Et₂O (4 / 1) (*R_f* 0.41). Yield: 569 mg (93%). (mixture of rotamers ~ 3 / 2) **¹H NMR** (DMSO-*d*₆, 300 MHz) : δ 10.84 (bs, 1H), 7.18-7.56 (m, 7H), 6.91-7.15 (m, 3H), 4.74 (s, 0.8H), 4.59 (s, 1.2H), 3.64-3.74 (m, 1.2H), 3.41-3.49 (m, 0.8H), 2.91-2.98 (m, 1.2H), 2.78-2.86 (m, 0.8H), 2.02 (s, 1.2H), 1.86 (s, 1.8H); **¹³C NMR** (CDCl₃, 100 MHz) : δ 155.40, 155.06, 136.87, 136.68, 136.56, 136.43, 128.82, 128.73, 128.19, 127.90, 127.67, 127.62, 127.41, 127.34, 122.68, 122.41, 121.94, 121.87, 119.21, 118.66, 118.36, 112.48, 111.85, 111.59, 111.45, 89.34, 89.31, 73.79, 73.35, 53.36, 48.84, 47.67, 45.21, 24.73, 23.11, 4.09, 3.73; **LRMS(EI)** (m/z, relative intensity) : 316 (M⁺, 13), 143 (100), 130 (32), 91 (22), 67 (16)

2-Hexynoic acid benzyl-[2-(1*H*-indol-3-yl)-ethyl]-amide (1b). Synthesized from hex-2-ynoic acid 258 mg and 500 mg of *N*-benzyltryptamine. Eluent DCM / Et₂O (20 / 1) (*R_f* 0.27). Yield: 601 mg (87%). (mixture of rotamers ~ 3 / 2) **¹H NMR** (DMSO-*d*₆, 400 MHz) : δ ; 10.85 (bs, 1H), 7.50 (d, 0.6H, *J* = 7.5 Hz), 7.45 (d, 0.4H, *J* = 7.7 Hz), 7.24-7.41 (m, 6H), 7.03-7.12 (m, 2H), 6.94-7.00 (m, 1H), 4.76 (s, 0.8H), 4.60 (s, 1.2H), 3.66-3.74 (m, 1.2H), 3.43-3.50 (m, 0.8H), 2.91-2.99 (m, 1.2H), 2.80-2.86 (m, 0.8H), 2.37 (t, 0.8H, *J* = 6.9 Hz), 2.22 (t, 1.2H, 6.9 Hz), 1.39-1.53 (m, 2H), 0.90 (t, 3H, *J* = 7.3 Hz); **LRMS(CI)** (m/z, relative intensity) : 345 ([M+H]⁺, 100), 277 (6), 143 (28)

2-Butynoic acid [2-(1*H*-indol-3-yl)-ethyl]-(4-methoxybenzyl)-amide (1c). Synthesized from tetrolic acid 194 mg and 561 mg of *N*-(*p*-methoxybenzyl)tryptamine. Eluent DCM / Et₂O (4 / 1) (*R_f* 0.35). Yield: 637 mg (92%). (mixture of rotamers ~ 3 / 2) **¹H NMR** (DMSO-*d*₆, 300 MHz) : δ 10.84 (bs, 1H), 7.51 (d, 0.6H, *J* = 7.8 Hz), 7.45 (d, 0.4H, *J* = 7.7 Hz), 7.33 (m, 1H), 7.17-7.23 (m, 2H), 7.03-7.11 (m, 3H), 4.67 (s, 0.8H), 4.52 (s, 1.2H), 3.72-3.76 (m, 3H), 3.62-3.69 (m, 1.2H), 3.39-3.45 (m, 0.8H), 2.89-2.95 (m, 0.8H), 2.77-2.85 (m, 1.2H), 2.03 (s, 1.2H), 1.85 (s, 1.8H)

2-Butynoic acid [2-(1*H*-indol-3-yl)-ethyl]-amide (1d). Synthesized from tetrolic acid 194 mg and 320 mg of tryptamine. Eluent DCM / EtOAc (1 / 1) (*R_f* 0.45). Yield: 376 mg (83%). **¹H NMR** (DMSO-*d*₆, 300 MHz) : δ 10.81 (bs, 1H), 8.58 (m, 1H), 7.52 (d, 1H, *J* = 7.6 Hz), 7.35 (d, 1H, *J* = 7.6 Hz), 7.15 (d, 1H, *J* = 1.7 Hz), 7.07 (t, 1H, *J* = 7.6 Hz), 6.99 (t, 1H, *J* = 7.6 Hz), 3.32-3.38 (m, 2H), 2.80-2.88 (m, 2H), 1.95 (s, 3H); **¹³C NMR** (DMSO-*d*₆, 75 MHz) : δ 152.97, 136.69, 127.63, 123.10, 121.40, 118.72, 118.66, 111.98, 111.83, 82.56, 76.29, 40.15, 25.25, 3.46.

2-Butynoic acid [2-(1*H*-indol-3-yl)-ethyl]-methanamide (1e). Synthesized from tetrolic acid 194 mg and 348 mg of *N*-methyltryptamine. Eluent DCM / Et₂O (4 / 1) (*R_f* 0.29 and *R_f* 0.18). Yield: 425 mg (88%). (mixture of rotamers ~ 3 / 2) **¹H NMR** (DMSO-*d*₆, 300 MHz) : δ 10.84 (bs, 1H), 7.53-7.61 (m, 1H), 7.30-7.39 (m, 1H), 7.11-7.17 (m, 1H), 6.95-7.10 (m, 2H), 3.71-3.81 (m, 1.2H), 3.52-3.61 (m, 0.8H), 3.10 (s, 1.2H), 2.83-2.99 (m, 3.8H), 2.01 (s, 1.2H), 1.79 (s, 1.8H); **LRMS(CI)** (m/z, relative intensity) : 241 ([M+H]⁺, 100), 201 (6), 172 (8), 144 (42), 143 (32).

2-Pentynoic acid [2-(1*H*-indol-3-yl)-ethyl]-methanamide (1f). Synthesized from 2-pentynoic acid 225 mg and 348 mg of *N*-methyltryptamine. Eluent DCM / Et₂O (4 / 1) (*R_f* 0.23 and *R_f* 0.32). Yield: 451 mg (89%). (mixture of rotamers ~ 13 / 7) **¹H NMR** (DMSO-*d*₆, 300 MHz) : δ 10.83 (bs, 1H), 7.56 (d, 1H, *J* = 7.8 Hz), 7.34 (d, 1H, *J* = 7.8 Hz), 6.94-7.17 (m, 3H), 3.76 (t, 1.3H, *J* = 7.1 Hz), 3.57 (t, 0.7H, *J* = 7.7 Hz), 3.11 (s, 1.05H), 2.95 (t, 1.3H, *J* = 7.1 Hz),

2.80-2.90 (m, 2.65H), 2.39 (q, 0.7H, $J = 7.4$ Hz), 2.17 (q, 1.3H, $J = 7.4$ Hz), 1.12 (t, 1.05H, $J = 7.4$ Hz), 0.99 (t, 1.95H, $J = 7.4$ Hz); **LRMS(CI)** (m/z, relative intensity) : 255 ($[M+H]^+$, 100), 225 (11), 201 (5), 172 (5), 144 (17), 143 (15).

2-Hexynoic acid [2-(1*H*-indol-3-yl)-ethyl]-methanamide (1g). Synthesized from 2-hexynoic 258 mg and 348 mg of *N*-methyltryptamine. Eluent DCM / Et₂O (4 / 1) (R_f 0.28 and R_f 0.38). Yield: 529 mg (99%). (mixture of rotamers ~ 13 / 7) **¹H NMR** (DMSO-*d*₆, 300 MHz) : δ 10.84 (bs, 1H), 7.56 (d, 1H, $J = 7.8$ Hz), 7.34 (d, 1H, $J = 7.8$ Hz), 6.94-7.17 (m, 3H), 3.76 (t, 1.3H, $J = 7.4$ Hz), 3.57 (t, 0.7H, $J = 7.4$ Hz), 3.11 (s, 1.05H), 2.80-2.99 (m, 3.95H), 2.37 (t, 0.7H, $J = 7.4$ Hz), 2.15 (t, 1.3H, $J = 7.4$ Hz), 1.46-1.60 (m, 0.7H), 1.32-1.45 (m, 1.3H), 0.96 (t, 1.05H, $J = 7.4$ Hz), 0.86 (t, 1.95H, $J = 7.4$ Hz); **LRMS(CI)** (m/z, relative intensity) : 269 ($[M+H]^+$, 100), 201 (7), 172 (6), 144 (21), 143 (25).

4-Methyl-2-pentynoic acid [2-(1*H*-indol-3-yl)-ethyl]-methanamide (1h). Synthesized from 4-methyl-2-pentynoic acid 258 mg and 348 mg of *N*-methyltryptamine. Eluent DCM / Et₂O (4 / 1) (R_f 0.33 and R_f 0.38). Yield: 476 mg (89%). (mixture of rotamers ~ 13 / 7) **¹H NMR** (DMSO-*d*₆, 300 MHz) : δ 10.84 (bs, 1H), 7.52-7.61 (m, 1H), 7.30-7.38 (m, 1H), 6.94-7.17 (m, 3H), 3.75 (t, 1.3H, $J = 7.4$ Hz), 3.56 (t, 0.7H, $J = 7.4$ Hz), 3.11 (s, 1.05H), 2.73-2.99 (m, 4.3H), 2.56 (septet, 0.65H, $J = 6.7$ Hz), 1.17 (d, 2.1H, $J = 6.7$ Hz), 1.04 (d, 3.9H, $J = 6.7$ Hz); **LRMS(CI)** (m/z, relative intensity) : 269 ($[M+H]^+$, 100), 225 (3), 201 (5), 172 (6), 144 (20), 143 (23), 95 (9).

4,4-Dimethyl-2-pentynoic acid [2-(1*H*-indol-3-yl)-ethyl]-methanamide (1i). Synthesized from 4,4-dimethyl-2-pentynoic acid 290 mg and 348 mg of *N*-methyltryptamine. Eluent DCM / Et₂O (4 / 1) (R_f 0.34 and R_f 0.41). Yield: 485 mg (86%). (mixture of rotamers ~ 13 / 7) **¹H NMR** (DMSO-*d*₆, 300 MHz) : δ 10.85 (bs, 1H), 7.52-7.61 (m, 1H), 7.30-7.39 (m, 1H), 6.93-7.19 (m, 3H), 3.75 (t, 1.3H, $J = 7.4$ Hz), 3.56 (t, 0.7H, $J = 7.4$ Hz), 3.11 (s, 1.05H), 2.95 (t, 1.3H, $J = 7.4$ Hz), 2.81-2.90 (m, 2.65H), 1.25 (s, 3.15H), 1.11 (s, 5.85); **LRMS(CI)** (m/z, relative intensity) : 283 ($[M+H]^+$, 100), 201 (4), 172 (6), 144 (16), 143 (29).

3-Phenylpropynoic acid [2-(1*H*-indol-3-yl)-ethyl]-methanamide (1j). Synthesized from 3-phenylpropynoic acid 336 mg and 348 mg of *N*-methyltryptamine. Eluent DCM / Et₂O (4 / 1) (R_f 0.33 and R_f 0.44). Yield: 553 mg (91%). (mixture of rotamers ~ 13 / 7) **¹H NMR** (DMSO-*d*₆, 300 MHz) : δ 3.85 (s, 1H), 7.28-7.66 (m, 7H), 7.13-7.21 (m, 1H), 6.96-7.12 (m, 1.35H), 6.83 (t, 0.65H, $J = 7.4$ Hz), 3.86 (t, 1.3H, $J = 7.4$ Hz), 3.65 (t, 0.7H, $J = 7.4$ Hz), 3.22 (s, 1.05H), 2.89-3.07 (m, 3.95H); **LRMS(CI)** (m/z, relative intensity) : 303 ($[M+H]^+$, 100), 201 (3), 172 (2), 144 (9), 143 (13).

3-(3,4,5-Trimethoxyphenyl)propynoic acid [2-(1*H*-indol-3-yl)-ethyl]-methanamide (1k). Synthesized from 3-(3,4,5-trimethoxyphenyl)propynoic acid 543 mg and 348 mg of *N*-methyltryptamine. Eluent DCM / Et₂O (4 / 1) (R_f 0.17 and R_f 0.24). Yield: 471 mg (60%). (mixture of rotamers ~ 13 / 7) **¹H NMR** (DMSO-*d*₆, 400 MHz) : δ 1.85 (bs, 1H), 7.54-7.61 (m, 1H), 7.29-7.37 (m, 1H), 7.16-7.22 (m, 1H), 6.96-7.11 (m, 1.3H), 6.94 (s, 0.7H), 6.82 (t, 0.7H, $J = 7.5$ Hz), 6.74 (s, 1.3H), 3.84-3.93 (m, 1.3H), 3.81 (s, 2.1H), 3.73 (s, 3.9H), 3.62-3.71 (m, 3.7H), 3.22 (s, 1.05H), 2.89-3.07 (m, 3.95H); **LRMS(EI)** (m/z, relative intensity) : 392 (M^+ , 100), 377 (16), 219 (56), 143 (78), 130 (44).

3-Trimethylsilylpropynoic acid benzyl-[2-(1*H*-indol-3-yl)-ethyl]-amide (12a). Synthesized from 3-trimethylsilylpropynoic acid 327 mg and 500 mg of *N*-benzyltryptamine. Eluent DCM / Et₂O (20 / 1) (R_f 0.44). Yield: 702 mg (94%). (mixture of rotamers ~ 3 / 2) **¹H NMR** (DMSO-*d*₆, 400 MHz) : δ 10.85 (bs, 0.6H), 10.80 (bs, 0.4H), 7.50 (d, 0.6H, $J = 7.9$ Hz), 7.46 (d, 0.4H, $J = 7.9$ Hz), 7.25-7.42 (m, 6H), 7.03-7.13 (m, 2H), 6.94-6.99 (m, 1H), 4.76 (s,

0.8H), 4.63 (s, 1.2H), 3.69-3.76 (m, 1.2H), 3.47-3.53 (m, 0.8H), 2.93-3.00 (m, 1.2H), 2.81-2.86 (m, 0.8H), 0.17-0.20 (m, 9H); **LRMS(CI)** (m/z, relative intensity) : 375 ([M+H]⁺, 100), 359 (21), 143 (32).

3-Trimethylsilylpropynoic acid [2-(1*H*-indol-3-yl)-ethyl]-methanamide (12b). Synthesized from 3-trimethylsilylpropynoic acid 327 mg and 348 mg of *N*-methyltryptamine. Eluent DCM / Et₂O (4 / 1) (*R_f* 0.36 and *R_f* 0.48). Yield: 581 mg (97%). (mixture of rotamers ~ 3 / 2) **¹H NMR** (DMSO-*d*₆, 400 MHz) : δ 10.88 (bs, 0.6H), 10.83 (bs, 0.4H), 7.56 (d, 1H, *J* = 7.8 Hz), 7.32-7.37 (m, 1H), 7.16 (d, 0.4H, *J* = 2.1 Hz), 7.13 (d, 0.6H, *J* = 2.1 Hz), 7.05-7.10 (m, 1H), 6.95-7.01 (m, 1H), 3.75-3.82 (m, 1.2H), 3.55-3.61 (m, 0.8H), 3.14 (s, 1.2H), 2.94-3.00 (m, 1.2H), 2.86-2.92 (m, 2.6H), 0.23 (s, 3.6H), 0.15 (s, 5.4H); **LRMS(CI)** (m/z, relative intensity) : 299 ([M+H]⁺, 100), 283 (21), 172 (6), 144 (13), 143 (21).

1-[(*S*)-2-(1*H*-indol-3-ylmethyl)-pyrrolidin-1-yl]-but-2-yn-1-one (1p). Synthesized from tetrolic acid 194 mg and amine **8** 401 mg. Eluent DCM / Et₂O (4 / 1) (*R_f* 0.15 and *R_f* 0.25). Yield: 383 mg (72%). (mixture of rotamers ~ 1 / 1) **¹H NMR** (DMSO-*d*₆, 300 MHz) : δ 10.90 (bs, 0.5H), 10.84 (bs, 0.5H), 7.55-7.67 (m, 1H), 7.29-7.39 (m, 1H), 6.93-7.20 (m, 3H), 4.25-4.37 (m, 0.5H), 4.13-4.23 (m, 0.5H), 3.45-3.61 (m, 1H), 3.27-3.38 (m, 1H), 3.02-3.17 (m, 1H), 2.74-2.86 (m, 0.5H), 2.58-2.70 (m, 0.5H), 1.95-2.06 (m, 3H), 1.59-1.92 (m, 4H); **LRMS(CI)** (m/z, relative intensity) : 267 ([M+H]⁺, 100), 227 (7), 136 (27).

1-[(*S*)-2-(1*H*-indol-3-ylmethyl)-pyrrolidin-1-yl]-pent-2-yn-1-one (1q). Synthesized from 2-pentynoic acid 226 mg and amine **8** 401 mg. Eluent DCM / Et₂O (4 / 1) (*R_f* 0.23 and *R_f* 0.34). Yield: 480 mg (86%). (mixture of rotamers ~ 1 / 1) **¹H NMR** (DMSO-*d*₆, 400 MHz) : δ 10.89 (bs, 0.5H), 10.83 (bs, 0.5H), 7.64 (d, 0.5H, *J* = 7.8 Hz), 7.59 (d, 0.5H, *J* = 7.8 Hz), 7.31-7.38 (m, 1H), 7.16 (d, 0.5H, *J* = 1.9 Hz), 7.14 (d, 0.5H, *J* = 1.9 Hz), 7.04-7.11 (m, 1H), 6.96-7.02 (m, 1H), 4.30-4.37 (m, 0.5H), 4.16-4.23 (m, 0.5H), 3.47-3.61 (m, 1H), 3.28-3.41 (m, 1H), 3.05-3.17 (m, 1H), 2.82 (dd, 0.5H, *J*₁ = 9.8 Hz, *J*₂ = 13.9 Hz), 2.65 (dd, 0.5H, *J*₁ = 9.8 Hz, *J*₂ = 13.9 Hz), 2.32-2.44 (m, 2H), 1.66-2.00 (m, 4H), 1.09-1.19 (m, 3H); **LRMS(CI)** (m/z, relative intensity) : 281 ([M+H]⁺, 100), 227 (7), 150 (26).

1-[(*S*)-2-(1*H*-indol-3-ylmethyl)-pyrrolidin-1-yl]-3-phenylpropynone (1r). Synthesized from 3-phenylpropynoic acid 336 mg and amine **8** 401 mg. Eluent DCM / Et₂O (4 / 1) (*R_f* 0.25 and *R_f* 0.39). Yield: 604 mg (92%). (mixture of rotamers ~ 1 / 1) **¹H NMR** (DMSO-*d*₆, 300 MHz) : δ 10.87 (bs, 1H), 7.60-7.70 (m, 1.5H), 7.42-7.58 (m, 4.5H), 7.28-7.37 (m, 1H), 7.17 (s, 1H), 6.95-7.11 (m, 1.5H), 6.68-6.77 (m, 0.5H), 4.41-4.53 (m, 0.5H), 4.22-4.33 (m, 0.5H), 3.60-3.76 (m, 1H), 3.37-3.48 (m, 1H), 3.11-3.23 (m, 1H), 2.82-2.95 (m, 0.5H), 2.65-2.77 (m, 0.5H), 1.64-2.08 (m, 4H); **LRMS(CI)** (m/z, relative intensity) : 329 ([M+H]⁺, 100), 227 (15), 198 (25).

Synthesis of propiolic acid amides **1l,m**:

Propiolic acid benzyl-[2-(1*H*-indol-3-yl)-ethyl]-amide (1l). To a solution of amide **12a** 803 mg (2.14 mmol) in THF (10 mL) cooled to 0 °C, a solution of TBAF in THF (1M) 2.14 mL (1 equiv) was added. The reaction was kept with stirring at 0 °C for 30 min followed by dilution with Et₂O. The organic layer was washed with H₂O, brine, dried (MgSO₄), concentrated and applied to a column of silica gel as a solution in DCM. Elution with DCM / Et₂O (20:1) (*R_f* 0.25) afforded pure **1l** 427 mg (66%). (mixture of rotamers ~ 1 / 1) **¹H NMR** (DMSO-*d*₆, 300 MHz) : δ 10.85 (bs, 1H), 7.21-7.55 (m, 7H), 6.92-7.16 (m, 3H), 4.76 (s, 1H), 4.60 (s, 1H), 4.56 (s, 0.5H), 4.54 (s, 0.5H), 3.67-3.75 (m, 1H), 3.42-

3.51 (m, 1H), 2.92-3.01 (m, 1H), 2.79-2.87 (m, 1H); **LRMS(CI)** (m/z, relative intensity) : 303 ([M+H]⁺, 100), 172 (5), 144 (28), 143 (34), 91 (5).

Propynoic acid [2-(1*H*-indol-3-yl)-ethyl]-methanamide (1m). Synthesized analogously to **1l**: from **12b** 640 mg (2.14 mmol). Eluent DCM / Et₂O (4 / 1) (*R_f* 0.30). Yield: 439 mg (92%). (mixture of rotamers ~ 13 / 7) **¹H NMR** (DMSO-*d*₆, 300 MHz) : δ 10.85 (bs, 1H), 7.56 (d, 1H, *J* = 7.9 Hz), 7.34 (d, 1H, *J* = 7.9 Hz), 7.15 (s, 1H), 7.07 (t, 1H, *J* = 7.9 Hz), 6.98 (t, 1H, *J* = 7.9 Hz), 4.51 (s, 0.35H), 4.39 (s, 0.65H), 3.74-3.83 (m, 1.3H), 3.54-3.62 (m, 0.7H), 3.12 (s, 1.05H), 2.93-3.02 (m, 1.3H), 2.84-2.92 (m, 2.65H); **LRMS(CI)** (m/z, relative intensity) : 227 ([M+H]⁺, 100), 172 (12), 144 (81), 143 (34), 130 (12).

Synthesis of tetrolic acid amides **1n,o,s**:

2-Butynoic acid benzyl-{2-[1-(toluene-4-sulfonyl)-1*H*-indol-3-yl]-ethyl}-amide (1n). To a mixture of **1a** 316 mg (1 mmol), Bu₄NHSO₄ 34 mg (10 mol%) and powdered NaOH 200 mg (5 equiv) in DCM (8 mL) a solution of TsCl 478 mg (2.5 equiv) in DCM (5 mL) was added dropwise at rt. After 2 h the reaction mixture was diluted with DCM and washed successively with H₂O and brine, dried (MgSO₄), concentrated and applied to a column of silica gel as a solution in DCM. Elution with DCM / Et₂O (20:1) (*R_f* 0.38) afforded pure **1n** 438 mg (93%). (mixture of rotamers ~ 1 / 1) **¹H NMR** (CDCl₃, 300 MHz) : δ 7.92-8.01 (m, 1H), 7.69-7.78 (m, 1H), 7.37-7.45 (m, 1H), 7.11-7.35 (m, 10H), 4.56-4.62 (m, 2H), 3.69-3.77 (m, 1H), 3.48-3.57 (m, 1H), 2.80-2.92 (m, 2H), 2.27-2.35 (m, 3H), 2.01 (1.5H), 1.55 (s, 1.5H).

2-Butynoic acid [2-(1-acetyl-1*H*-indol-3-yl)-ethyl]-benzylamide (1o). Synthesized analogously to **1n**: from **1a** 949 mg (3 mmol) and AcCl 533 μL (2.5 equiv). Eluent DCM / Et₂O (20 / 1) (*R_f* 0.17). Yield: 879 mg (82%). (mixture of rotamers ~ 1 / 1) **¹H NMR** (DMSO-*d*₆, 300 MHz) : δ 8.26-8.35 (m, 1H), 7.50-7.65 (m, 2H), 7.22-7.42 (m, 7H), 4.81 (s, 1.5H), 4.63 (s, 1H), 3.72-3.80 (m, 1H), 3.47-3.56 (s, 1H), 2.91-3.00 (m, 1H), 2.78-2.87 (m, 1H), 2.59 (s, 3H), 2.02 (s, 1.5H), 1.79 (s, 1.5H); **LRMS(EI)** (m/z, relative intensity) : 392 (M⁺, 13), 185 (100), 143 (51), 130 (32), 120 (26), 91 (45), 67 (27).

(S)-2-[Benzyl-(1-oxo-but-2-ynyl)-amino]-3-(1*H*-indol-3-yl)-propionic acid methyl ester (1s). To a mixture of tryptamine **9** 617 mg (2 mmol), tetrolic acid 193 mg (1.15 equiv) and DMAP 24 mg (10 mol%) in dry DCM (5 mL) DCC 475 mg (1.15 equiv) was added in one portion. The reaction was left with stirring at rt for approximately 12 h. The subsequently formed precipitate of N,N'-dicyclohexylurea was filtered off and washed well with Et₂O. The organic layer was washed successively with HCl (1M), NaHCO₃ (sat), brine, dried (MgSO₄), concentrated with silica and applied to a silica gel column. Elution with DCM / Et₂O (4:1) (*R_f* 0.41 and *R_f* 0.50) afforded pure **1s** 419 mg (56%). (mixture of rotamers ~ 1 / 1) **¹H NMR** (DMSO-*d*₆, 300 MHz) : δ 10.86 (bs, 1H), 7.60 (d, 0.5H, *J* = 7.8 Hz), 6.91-7.40 (m, 9.5H), 5.38 (dd, 0.5H, *J₁* = 6.2 Hz, *J₂* = 9.2 Hz), 4.68 (d, 0.5H, *J* = 16.0 Hz), 4.60 (d, 0.5H, *J* = 16.0 Hz), 4.51 (dd, 0.5H, *J₁* = 6.2 Hz, *J₂* = 9.2 Hz), 4.42 (d, 0.5H, *J* = 16.0 Hz), 4.07 (d, 0.5H, *J* = 16.0 Hz), 3.31-3.45 (m, 4H), 3.09-3.23 (m, 1H), 1.96 (s, 1.5H), 1.72 (s, 1.5H); **LRMS(CI)** (m/z, relative intensity) : 375 ([M+H]⁺, 100), 343 (17), 201 (57), 130 (14).

Synthesis of propynoic acid amides **1u,v**:

A mixture of aminoalcohol **10** 561 mg (2 mmol), imidazole 204 mg (1.5 equiv) and TIPSCI 470 μ L (1.1 equiv) in dry DMF was heated with stirring at 70 °C for approximately 5 h. Then the solvent was removed in vacuo and the residue was partitioned between Et₂O and H₂O. The organic layer was washed excessively with H₂O, then with brine and dried (Na₂SO₄). Concentration afforded ~ 920 mg of crude *O*-TIPS protected aminoalcohol which was dissolved in dry DCM (5 mL). To this solution 3 substituted 2-propynoic acid **11** (1.2 equiv), DMAP 48 mg (20 mol%) was added followed by DCC 495 mg (1.2 equiv). The reaction was left with stirring at rt for approximately 12 h. The subsequently formed precipitate of *N,N'*-dicyclohexylurea was filtered off and washed well with Et₂O. The organic layer was washed with H₂O, brine and dried (MgSO₄). Pure amides **1u,v** were isolated by column chromatography on silica gel.

2-Butynoic acid (S)-benzyl-[2-(1*H*-indol-3-yl)-1-triisopropylsilanyloxymethylethyl]-amide (1u). Synthesized from tetrolic acid 202 mg. Eluent DCM / Et₂O (20 / 1) (*R_f* 0.37 and *R_f* 0.44). Yield: 578 mg (57%). (mixture of rotamers ~ 7 / 3) **¹H NMR** (DMSO-*d*₆, 300 MHz) : δ 10.79 (bs, 1H), 7.55 (d, 0.7H, *J* = 7.5 Hz), 7.15-7.38 (m, 6.3H), 6.87-7.11 (m, 3H), 4.84-5.03 (bs, 0.7H), 4.45-4.74 (m, 2H), 4.21-4.39 (bs, 0.3H), 3.52-3.81 (m, 2H), 2.78-3.06 (m, 2H), 1.92 (s, 0.9H), 1.71 (2.1H), 0.74-1.09 (m, 21H); **LRMS(Cl)** (*m/z*, relative intensity) : 503 ([*M*+*H*]⁺, 15), 459 (20), 357 (8), 329 (100), 286 (11).

2-Octynoic acid (S)-benzyl-[2-(1*H*-indol-3-yl)-1-triisopropylsilanyloxymethylethyl]-amide (1v). Synthesized from 2-octynoic acid 336 mg. Eluent DCM / Et₂O (20 / 1) (*R_f* 0.34 and *R_f* 0.44). Yield: 754 mg (67%). (mixture of rotamers ~ 7 / 3) **¹H NMR** (DMSO-*d*₆, 300 MHz) : δ 7.53 (d, 0.7H, *J* = 7.4 Hz), 7.15-7.37 (m, 6.3H), 6.87-7.10 (m, 3H), 4.80-4.99 (bs, 0.7H), 4.46-4.77 (m, 2H), 4.27-4.44 (bs, 0.3H), 3.53-3.83 (m, 2H), 2.77-3.07 (m, 2H), 2.25-2.33 (m, 0.6H), 2.02-2.13 (m, 1.4H), 1.11-1.39 (m, 6H), 0.74-1.02 (m, 24H); **LRMS(Cl)** (*m/z*, relative intensity) : 559 ([*M*+*H*]⁺, 31), 515 (34), 385 (96), 329 (100), 286 (18).

General procedure for Hg(OTf)₂ catalyzed cyclization:

In ¹H NMR spectra of indoloazocinones **2a-p**, recorded at 298 K, signals of the 8-membered ring protons are often broadened due to the ring flipping.

Hg(OTf)₂ (5-30 mol%) and propynoic acid amide **1a-v** (0.6 mmol) were loaded into the microwave instrument vial followed by dry DCM (2.4 mL). The vial was sealed and irradiated with stirring at a ceiling temperature of 80-120 °C at 60-120 W maximum power level for 15-50 min. Upon completion of the reaction time the vial was cooled with a stream of air. The precipitate of Hg(OTf)₂ was filtered off through a plug of Celite ® and washed well with DCM until TLC analysis indicated absence of product in the flowing filtrate. The DCM layer was washed with NaHCO₃ (sat.), brine, dried (MgSO₄) and concentrated with silica. Pure indoloazocinones **2a-p** were isolated by column chromatography on silica gel.

3-Benzyl-6-methyl-1,2,3,7-tetrahydro-azocino[5,4-*b*]indol-4-one (2a). Synthesized from amide **1a** 190 mg with 15 mg Hg(OTf)₂ (5 mol%). MW irradiation - 60 W, 80 °C, 15 min. Eluent DCM / EtOAc (1 / 1) (*R_f* 0.46). Yield: 162

mg (85%). **¹H NMR** (DMSO-*d*₆, 400 MHz) : δ 10.86 (s, 1H), 7.39 (d, 1H, *J* = 7.7 Hz), 7.31 (d, 1H, *J* = 7.7 Hz), 7.21-7.29 (m, 5H), 7.13 (t, 1H, *J* = 7.5 Hz), 7.00 (t, 1H, *J* = 7.5 Hz), 6.00 (d, 1H, *J* = 1.1 Hz), 4.31-4.80 (bs, 2H), 3.51-4.14 (bs, 2H), 2.89-3.24 (m, 4H), 2.25 (d, 3H, *J* = 1.1 Hz); **¹³C NMR** (DMSO-*d*₆, 100 MHz) : δ 168.50, 138.13, 136.24, 134.25, 132.34, 128.88, 128.83, 128.12, 127.51, 122.78, 122.61, 119.17, 118.90, 111.32, 108.89, 47.18, 44.96, 24.48, 24.22; **HRMS(EI)** calcd. for C₂₁H₂₀N₂O : m/z 316.1576, found m/z 316.1571

3-Benzyl-6-propyl-1,2,3,7-tetrahydro-azocino[5,4-*b*]indol-4-one (2b). Synthesized from amide **1b** 207 mg with 15 mg Hg(OTf)₂ (5 mol%). MW irradiation - 60 W, 80 °C, 15 min. Eluent DCM / Et₂O (4 / 1) (*R*_f 0.29). Yield: 169 mg (82%). **¹H NMR** (DMSO-*d*₆, 400 MHz) : δ 10.84 (s, 1H), 7.39 (d, 1H, *J* = 7.7 Hz), 7.32 (d, 1H, *J* = 7.7 Hz), 7.21-7.29 (m, 5H), 7.13 (t, 1H, *J* = 7.7 Hz), 7.00 (t, 1H, *J* = 7.7 Hz), 6.00 (s, 1H), 4.24-4.97 (bs, 2H), 3.47-4.21 (bs, 2H), 2.85-3.30 (bs, 2H), 2.46-2.83 (bs, 2H), 1.31-1.43 (m, 2H), 0.88 (t, 3H, *J* = 7.3 Hz); **¹³C NMR** (DMSO-*d*₆, 100 MHz) : δ 168.71, 138.60, 138.15, 136.30, 131.42, 128.96, 128.80, 128.11, 127.48, 122.61, 122.34, 119.04, 118.74, 111.30, 109.50, 47.17, 45.16, 39.24, 24.33, 21.23, 13.93; **HRMS(EI)** calcd. for C₂₃H₂₄N₂O : m/z 344.1889, found m/z 316.1885

3-(4-Methoxybenzyl)-6-methyl-1,2,3,7-tetrahydro-azocino[5,4-*b*]indol-4-one (2c). Synthesized from amide **1c** 208 mg with 15 mg Hg(OTf)₂ (5 mol%). MW irradiation - 60 W, 80 °C, 15 min. Eluent DCM / EtOAc (1 / 1) (*R*_f 0.34). Yield: 123 mg (59%). **¹H NMR** (DMSO-*d*₆, 400 MHz) : δ 10.85 (s, 1H), 7.38 (d, 1H, *J* = 7.6 Hz), 7.31 (d, 1H, *J* = 7.6 Hz), 7.19 (d, 2H, *J* = 8.5 Hz), 7.13 (t, 1H, *J* = 7.6 Hz), 6.99 (t, 1H, *J* = 7.6 Hz), 6.82 (d, 2H, *J* = 8.5 Hz), 5.97 (d, 1H, *J* = 1.3 Hz), 4.17-4.85 (bs, 2H), 3.51-3.99 (m, 5H), 2.87-3.25 (bs, 2H), 2.25 (d, 1H, *J* = 1.3 Hz); **¹³C NMR** (DMSO-*d*₆, 100 MHz) : δ 168.35, 158.901, 136.21, 134.12, 132.34, 130.05, 129.65, 128.89, 122.75, 122.70, 119.13, 118.90, 114.25, 111.30, 108.90, 55.49, 46.41, 44.59, 24.40, 24.19; **HRMS(EI)** calcd. for C₂₂H₂₂N₂O₂ : m/z 346.1681, found m/z 316.1687

3,6-Dimethyl-1,2,3,7-tetrahydro-azocino[5,4-*b*]indol-4-one (2d). Synthesized from amide **1e** 144 mg with 15 mg Hg(OTf)₂ (5 mol%). MW irradiation - 60 W, 80 °C, 20 min. Eluent DCM / MeCN (1 / 1) (*R*_f 0.31). Yield: 124 mg (86%). **¹H NMR** (DMSO-*d*₆, 400 MHz) : δ 10.82 (s, 1H), 7.47 (d, 1H, *J* = 7.8 Hz), 7.32 (d, 1H, *J* = 7.8 Hz), 7.13 (t, 1H, *J* = 7.8 Hz), 7.02 (t, 1H, *J* = 7.8 Hz), 5.91 (d, 1H, *J* = 1.1 Hz), 3.66-4.11 (bs, 2H), 3.01-3.22 (bs, 2H), 2.88 (s, 3H), 2.25 (d, 3H, *J* = 1.1 Hz); **¹³C NMR** (DMSO-*d*₆, 100 MHz) : δ 168.14, 136.21, 133.94, 132.31, 128.94, 122.90, 122.76, 119.19, 118.90, 111.30, 108.70, 47.42, 32.07, 24.36, 24.12; **HRMS(EI)** calcd. for C₁₅H₁₆N₂O : m/z 240.1263, found m/z 316.1262

6-Ethyl-3-methyl-1,2,3,7-tetrahydro-azocino[5,4-*b*]indol-4-one (2e). Synthesized from amide **1f** 153 mg with 15 mg Hg(OTf)₂ (5 mol%). MW irradiation - 60 W, 80 °C, 20 min. Eluent DCM / MeCN (1 / 1) (*R*_f 0.30). Yield: 102 mg (67%). **¹H NMR** (DMSO-*d*₆, 400 MHz) : δ 10.81 (s, 1H), 7.46 (d, 1H, *J* = 7.8 Hz), 7.29 (d, 1H, *J* = 7.8 Hz), 7.12 (t, 1H, *J* = 7.8 Hz), 7.00 (t, 1H, *J* = 7.8 Hz), 5.88 (s, 1H), 3.48-4.42 (bs, 2H), 2.94-3.29 (bs, 2H), 2.86 (s, 3H), 2.60 (q, 2H, *J* = 7.5 Hz), 1.01 (t, 3H, *J* = 7.5 Hz); **¹³C NMR** (DMSO-*d*₆, 100 MHz) : δ 168.41, 139.88, 136.22, 131.52, 128.98, 122.62, 121.34, 119.09, 118.76, 111.29, 109.27, 47.48, 32.02, 30.19, 24.18, 13.30; **HRMS(EI)** calcd. for C₁₆H₁₈N₂O : m/z 254.1419, found m/z 254.1431

3-Methyl-6-propyl-1,2,3,7-tetrahydro-azocino[5,4-*b*]indol-4-one (2f). Synthesized from amide **1g** 161 mg with 15 mg Hg(OTf)₂ (5 mol%). MW irradiation - 60 W, 80 °C, 20 min. Eluent DCM / MeCN (1 / 1) (*R*_f 0.36). Yield: 121 mg (75%). **¹H NMR** (DMSO-*d*₆, 400 MHz) : δ 10.81 (s, 1H), 7.45 (d, 1H, *J* = 7.7 Hz), 7.29 (d, 1H, *J* = 7.7 Hz), 7.11 (t,

1H, $J = 7.7$ Hz), 6.99 (t, 1H, $J = 7.7$ Hz), 5.89 (s, 1H), 3.46-4.34 (bs, 2H), 2.91-3.30 (bs, 2H), 2.86 (s, 3H), 2.47-2.72 (bs, 2H), 1.28-1.41 (m, 2H), 0.87 (t, 3H, $J = 7.4$ Hz); ^{13}C NMR (DMSO- d_6 , 100 MHz) : δ 168.33, 138.32, 136.22, 131.34, 128.99, 122.59, 119.08, 118.74, 111.29, 109.27, 47.55, 39.17, 32.01, 24.16, 21.24, 13.93; HRMS(EI) calcd. for $\text{C}_{17}\text{H}_{20}\text{N}_2\text{O}$: m/z 268.1576, found m/z 268.11568

6-Isopropyl-3-methyl-1,2,3,7-tetrahydro-azocino[5,4-*b*]indol-4-one (2g). Synthesized from amide **1h** 161 mg with 45 mg $\text{Hg}(\text{OTf})_2$ (15 mol%). MW irradiation - 90 W, 100 °C, 20 min. Eluent DCM / EtOAc (1 / 1) (R_f 0.51). Yield: 127 mg (79%). ^1H NMR (DMSO- d_6 , 400 MHz, 363 K) : δ 10.44 (s, 1H), 7.46 (d, 1H, $J = 7.7$ Hz), 7.31 (d, 1H, $J = 7.7$ Hz), 7.10 (t, 1H, $J = 7.7$ Hz), 7.00 (t, 1H, $J = 7.7$ Hz), 5.84 (d, 1H, $J = 1.3$ Hz), 3.89 (t, 2H, $J = 6.1$ Hz), 3.12 (t, 2H, $J = 6.1$ Hz), 2.97 (dseptet, 1H, $J_1 = 1.3$ Hz, $J_2 = 6.7$ Hz), 2.86 (s, 3H), 1.14 (d, 6H, $J = 6.7$ Hz); ^{13}C NMR (DMSO- d_6 , 100 MHz, 363K) : δ 168.94, 144.68, 136.63, 132.50, 129.15, 122.29, 120.33, 119.05, 118.38, 111.35, 108.97, 47.78, 33.55, 31.94, 24.01, 21.96; HRMS(EI) calcd. for $\text{C}_{17}\text{H}_{20}\text{N}_2\text{O}$: m/z 268.1576, found m/z 268.11572

3-Methyl-6-phenyl-1,2,3,7-tetrahydro-azocino[5,4-*b*]indol-4-one (2h). Synthesized from amide **1j** 181 mg with 60 mg $\text{Hg}(\text{OTf})_2$ (20 mol%). MW irradiation - 90 W, 100 °C, 20 min. Eluent DCM / MeCN (3 / 1) (R_f 0.37). Yield: 111 mg (61%). ^1H NMR (DMSO- d_6 , 400 MHz, 363 K) : δ 10.02 (s, 1H), 7.54 (d, 1H, $J = 7.9$ Hz), 7.33-7.43 (m, 5H), 7.26 (d, 1H, $J = 7.9$ Hz), 7.11 (t, 1H, $J = 7.9$ Hz), 7.03 (t, 1H, $J = 7.9$ Hz), 6.32 (s, 1H), 3.99 (t, 2H, $J = 6.2$ Hz), 3.27 (t, 2H, $J = 6.2$ Hz), 2.93 (s, 3H); ^{13}C NMR (DMSO- d_6 , 100 MHz, 363K) : δ 168.47, 140.58, 138.20, 136.91, 130.80, 129.05, 128.76, 128.71, 128.22, 124.17, 122.67, 119.18, 118.56, 111.67, 110.93, 47.91, 32.09, 24.15; HRMS(EI) calcd. for $\text{C}_{20}\text{H}_{18}\text{N}_2\text{O}$: m/z 302.1419, found m/z 302.1425

3-Methyl-6-(3,4,5-trimethoxyphenyl)-1,2,3,7-tetrahydro-azocino[5,4-*b*]indol-4-one (2i). Synthesized from amide **1k** 235 mg with 90 mg $\text{Hg}(\text{OTf})_2$ (30 mol%). MW irradiation - 120 W, 120 °C, 50 min. Eluent DCM / MeCN (3 / 1) (R_f 0.23). Yield: 94 mg (40%). ^1H NMR (DMSO- d_6 , 400 MHz, 363 K) : δ 10.08 (s, 1H), 7.54 (d, 1H, $J = 7.7$ Hz), 7.29 (d, 1H, $J = 7.7$ Hz), 7.11 (t, 1H, $J = 7.7$ Hz), 7.03 (t, 1H, $J = 7.7$ Hz), 6.65 (s, 2H), 6.33 (s, 1H), 3.99 (t, 2H, $J = 6.4$ Hz), 3.79 (s, 3H), 3.78 (s, 6H), 3.26 (t, 2H, $J = 6.4$ Hz), 2.92 (s, 3H); ^{13}C NMR (DMSO- d_6 , 100 MHz, 363K) : δ 168.50, 153.58, 140.27, 137.93, 136.83, 135.78, 130.69, 129.04, 123.67, 122.69, 119.13, 118.60, 111.64, 110.88, 107.91, 60.57, 57.22, 47.89, 32.07, 24.16; HRMS(EI) calcd. for $\text{C}_{23}\text{H}_{24}\text{N}_2\text{O}_4$: m/z 392.1736, found m/z 392.1729

3-Benzyl-1,2,3,7-tetrahydro-azocino[5,4-*b*]indol-4-one (2j). Synthesized from amide **1l** 181 mg with 15 mg $\text{Hg}(\text{OTf})_2$ (5 mol%). Conventional heating (oil bath) - 50 °C, 48 h. Eluent DCM / Et₂O (4 / 1) (R_f 0.31). Yield: 45 mg (25%). ^1H NMR (DMSO- d_6 , 300 MHz) : δ 11.04 (s, 1H), 7.23-7.47 (m, 7H), 7.13 (t, 1H, $J = 7.4$ Hz), 6.98 7.13 (t, 1H, $J = 7.4$ Hz), 5.92 (s, 2H), 4.69 (s, 2H), 3.64 (m, 2H), 2.79 (m, 2H); ^{13}C NMR (CDCl₃, 75 MHz) : δ 170.52, 138.27, 137.39, 136.38, 129.05, 128.76, 128.28, 128.18, 127.62, 123.17, 120.62, 119.68, 118.58, 113.11, 111.36, 50.60, 47.01, 24.48; HRMS(EI) calcd. for $\text{C}_{20}\text{H}_{18}\text{N}_2\text{O}$: m/z 302.1419, found m/z 302.1418

3-Methyl-1,2,3,7-tetrahydro-azocino[5,4-*b*]indol-4-one (2k). Synthesized from amide **1m** 136 mg with 15 mg $\text{Hg}(\text{OTf})_2$ (5 mol%). Conventional heating (oil bath) - 50 °C, 48 h. Eluent DCM / MeCN (3 / 1) (R_f 0.14). Yield: 29 mg (21%). ^1H NMR (DMSO- d_6 , 400 MHz) : δ 10.98 (s, 1H), 7.45 (d, 1H, $J = 7.8$ Hz), 7.32 (d, 1H, $J = 7.8$ Hz), 7.13 (t, 1H, $J = 7.8$ Hz), 7.00 (d, 1H, $J = 7.8$ Hz), 5.87 (s, 1H), 5.82 (s, 1H), 3.62-3.69 (m, 2H), 3.04 (s, 3H), 2.88-2.95 (m, 2H); ^{13}C NMR (CDCl₃, 100 MHz) : δ 168.91, 138.60, 136.54, 129.48, 128.27, 123.05, 120.56, 119.37, 118.97, 113.26, 111.53, 49.31, 34.77, 24.21; HRMS(EI) calcd. for $\text{C}_{14}\text{H}_{14}\text{N}_2\text{O}$: m/z 226.1106, found m/z 226.1105

Indoloazocinone 2l. Synthesized from amide **1p** 160 mg with 15 mg $\text{Hg}(\text{OTf})_2$ (5 mol%). MW irradiation - 90 W, 100 °C, 15 min. Eluent DCM / MeCN (1 / 1) (R_f 0.26). Yield: 120 mg (75%). $[\alpha]_D^{20} +605.7$ (0.1, MeOH) **^1H NMR** ($\text{DMSO}-d_6$, 400 MHz) : δ 10.82 (s, 1H), 7.45 (d, 1H, $J = 7.8$ Hz), 7.30 (d, 1H, $J = 7.8$ Hz), 7.12 (t, 1H, $J = 7.8$ Hz), 6.99 (t, 1H, $J = 7.8$ Hz), 5.92 (d, 1H, $J = 1.2$ Hz), 4.54-4.74 (m, 1H), 3.46-3.56 (m, 1H), 3.06-3.23 (m, 2H), 2.83 (dd, 1H, $J_1 = 3.6$ Hz, $J_2 = 16.6$ Hz), 2.24 (d, 3H, $J = 1.2$ Hz), 1.90-2.20 (m, 3H), 1.79 (dd, 1H, $J_1 = 6.9$ Hz, $J_2 = 11.7$ Hz); **^{13}C NMR** ($\text{DMSO}-d_6$, 100 MHz, 363K) : δ 166.42, 136.50, 134.15, 132.57, 129.10, 124.67, 122.61, 119.14, 118.77, 111.30, 109.99, 56.65, 44.30, 32.11, 31.56, 24.04, 21.91; **HRMS(EI)** calcd. for $\text{C}_{17}\text{H}_{18}\text{N}_2\text{O}$: m/z 266.1419, found m/z 266.1420

Indoloazocinone 2m. Synthesized from amide **1q** 168 mg with 15 mg $\text{Hg}(\text{OTf})_2$ (5 mol%). MW irradiation - 90 W, 100 °C, 15 min. Eluent DCM / MeCN (1 / 1) (R_f 0.28). Yield: 119 mg (71%). $[\alpha]_D^{20} +664.5$ (0.1, MeOH) **^1H NMR** ($\text{DMSO}-d_6$, 400 MHz) : δ 10.80 (s, 1H), 7.44 (d, 1H, $J = 7.7$ Hz), 7.28 (d, 1H, $J = 7.7$ Hz), 7.10 (t, 1H, $J = 7.7$ Hz), 6.98 (t, 1H, $J = 7.7$ Hz), 5.89 (s, 1H), 4.64-4.72 (m, 1H), 3.43-3.53 (m, 1H), 3.13-3.20 (m, 1H), 3.08 (dd, 1H, $J_1 = 12.9$ Hz, $J_2 = 16.5$ Hz), 2.82 (dd, 1H, $J_1 = 3.8$ Hz, $J_2 = 16.5$ Hz), 2.60-2.71 (m, 1H), 2.50-2.59 (m, 1H), 1.89-2.23 (m, 3H), 1.78 (dd, 1H, $J_1 = 6.9$ Hz, $J_2 = 11.7$ Hz), 1.00 (t, 3H, $J = 7.4$ Hz); **^{13}C NMR** ($\text{DMSO}-d_6$, 100 MHz) : δ 166.25, 139.81, 135.67, 131.01, 128.38, 122.56, 122.11, 118.55, 118.34, 110.77, 110.04, 56.21, 44.00, 31.12, 30.79, 29.91, 21.25, 12.90; **HRMS(EI)** calcd. for $\text{C}_{18}\text{H}_{20}\text{N}_2\text{O}$: m/z 280.1576, found m/z 266.1575

Indoloazocinone 2n. Synthesized from amide **1r** 197 mg with 75 mg $\text{Hg}(\text{OTf})_2$ (25 mol%). MW irradiation - 90 W, 110 °C, 20 min. Eluent DCM / MeCN (1 / 1) (R_f 0.43). Yield: 114 mg (58%). $[\alpha]_D^{20} +575.7$ (0.1, MeOH) **^1H NMR** ($\text{DMSO}-d_6$, 400 MHz, 363K) : δ 10.18, 7.49 (d, 1H, $J = 7.8$ Hz), 7.29-7.40 (m, 5H), 7.22 (d, 1H, $J = 7.8$ Hz), 7.07 (t, 1H, $J = 7.8$ Hz), 6.98 (t, 1H, $J = 7.8$ Hz), 6.31 (s, 1H), 4.69-4.77 (m, 1H), 3.52-3.61 (m, 1H), 3.11-3.22 (m, 2H), 3.00 (dd, 1H, $J_1 = 4.4$ Hz, $J_2 = 16.4$ Hz), 2.04-2.32 (m, 2H), 1.89-2.00 (m, 1H), 1.77-1.87 (m, 1H); **^{13}C NMR** ($\text{DMSO}-d_6$, 100 MHz, 363 K) : δ 166.59, 140.60, 138.22, 136.73, 130.74, 128.80, 128.77, 128.20, 125.50, 122.64, 119.09, 118.71, 112.29, 111.62, 56.99, 44.48, 31.62, 31.60, 21.88; **HRMS(EI)** calcd. for $\text{C}_{22}\text{H}_{20}\text{N}_2\text{O}$: m/z 328.1576, found m/z 328.1597

(S)-3-Benzyl-6-methyl-2-triisopropylsilanyloxymethyl-1,2,3,7-tetrahydro-azocino[5,4-*b*]indol-4-one (2o).

Synthesized from amide **1u** 302 mg with 30 mg Hg(OTf)₂ (10 mol%). MW irradiation - 90 W, 100 °C, 25 min. Eluent DCM / Et₂O (4 / 1) (*R_f* 0.28). Yield: 236 mg (78%). [α]_D²⁰ -152.7 (1.0, CHCl₃) **¹H NMR** (DMSO-*d*₆, 400 MHz) : δ 10.87 (s, 1H), 7.32 (d, 1H, *J* = 7.8 Hz), 7.25 (d, 1H, *J* = 7.8 Hz), 7.03-7.17 (m, 6H), 6.98 (t, 1H, *J* = 7.8 Hz), 6.06 (d, 1H, *J* = 1.2 Hz), 4.92-5.03 (m, 1H), 4.58 (d, 1H, *J* = 15.7 Hz), 4.52 (d, 1H, *J* = 15.7 Hz), 3.81 (d, 2H, *J* = 6.1 Hz), 3.10 (dd, 1H, *J*₁ = 13.0 Hz, *J*₂ = 16.7 Hz), 2.91 (dd, 1H, *J*₁ = 3.0 Hz, *J*₂ = 16.7 Hz), 2.27 (d, 3H, *J* = 1.2 Hz), 0.90-1.08 (m, 21H); **¹³C NMR** (CDCl₃, 100 MHz) : δ 717.02, 138.30, 136.29, 135.77, 131.96, 128.36, 128.27, 127.18, 126.82, 122.55, 121.70, 118.88, 118.34, 111.34, 108.73, 64.72, 59.11, 44.89, 27.01, 24.13, 18.07, 12.05; **LRMS(Cl)** (*m/z*, relative intensity) : 503 ([M+H]⁺, 100), 459 (23)

(S)-3-Benzyl-6-pentyl-2-triisopropylsilanyloxymethyl-1,2,3,7-tetrahydro-azocino[5,4-*b*]indol-4-one (2p).

Synthesized from amide **1v** 335 mg with 60 mg Hg(OTf)₂ (20 mol%). MW irradiation - 90 W, 100 °C, 45 min. Eluent DCM / Et₂O (20 / 1) (*R_f* 0.12). Yield: 238 mg (71%). [α]_D²⁰ -105.1 (1.0, CHCl₃) **¹H NMR** (DMSO-*d*₆, 400 MHz) : δ 10.87 (s, 1H), 7.31 (d, 1H, *J* = 7.9 Hz), 7.26 (d, 1H, *J* = 7.9 Hz), 7.04-7.15 (m, 6H), 6.98 (t, 1H, *J* = 7.9 Hz), 6.05 (s, 1H), 4.93-5.04 (m, 1H), 4.53 (d, 1H, *J* = 16.3 Hz), 4.49 (d, 1H, *J* = 16.3 Hz), 3.77 (d, 2H, *J* = 6.4 Hz), 3.09 (dd, 1H, *J*₁ = 13.1 Hz, *J*₂ = 16.5 Hz), 2.80-2.94 (m, 2H), 2.40-2.52 (m, 1H), 1.16-1.42 (m, 6H), 0.89-1.04 (m, 21H), 0.79 (t, 3H, *J* = 6.6 Hz); **¹³C NMR** (CDCl₃, 100 MHz) : δ 171.13, 140.28, 138.30, 136.17, 131.00, 128.38, 128.25, 127.16, 127.77, 122.37, 121.33, 118.72, 118.20, 111.24, 109.45, 64.61, 59.33, 44.61, 37.89, 31.39, 27.69, 26.87, 22.42, 18.02, 14.00, 11.97; **LRMS(Cl)** (*m/z*, relative intensity) : 559 ([M+H]⁺, 100), 516 (28), 371 (10).

Indoloazocinones **5a,b** were synthesized from **2o,p** according to the procedure described above for preparation of **1l,m** from **12a,b**:

(S)-3-Benzyl-2-hydroxymethyl-6-methyl-1,2,3,7-tetrahydro-azocino[5,4-*b*]indol-4-one (5a).

Synthesized from **2o** 504 mg (1 mmol). Yield: 297 mg (86%). [α]_D²⁰ -266.4 (1.0, CHCl₃) **¹H NMR** (DMSO-*d*₆, 400 MHz) : δ 10.85 (s, 1H), 7.31 (d, 1H, *J* = 8.0 Hz), 7.17 (d, 1H, *J* = 8.0 Hz), 7.05-7.14 (m, 4H), 6.97-7.03 (m, 2H), 6.95 (t, 1H, *J* = 8.0 Hz), 6.06 (d, 1H, *J* = 1.1 Hz), 4.86-4.96 (m, 2H), 4.69 (d, 1H, *J* = 15.7 Hz), 4.40 (d, 1H, *J* = 15.7 Hz), 3.51-3.63 (m, 2H), 2.81-2.93 (m, 2H), 2.27 (d, 3H, *J* = 1.1 Hz); **¹³C NMR** (DMSO-*d*₆, 100 MHz) : δ 169.60, 139.53, 136.21, 134.07, 132.47, 128.78, 128.25, 127.37, 126.73, 123.20, 122.66, 119.04, 118.77, 111.23, 108.81, 62.57, 58.38, 43.91, 27.08, 23.90; **HRMS(EI)** calcd. for C₂₂H₂₂N₂O₂ : *m/z* 346.1681, found *m/z* 346.1676

(S)-3-Benzyl-2-hydroxymethyl-6-pentyl-1,2,3,7-tetrahydro-azocino[5,4-*b*]indol-4-one (5b).

Synthesized from **2p** 446 mg (0.8 mmol). Yield: 269 mg (84%). [α]_D²⁰ -158.4 (1.0, CHCl₃) **¹H NMR** (CDCl₃, 400 MHz) : δ 9.33 (s, 1H), 7.19-7.30 (m, 5H), 7.10-7.18 (m, 3H), 7.04 (t, 1H, *J* = 7.5 Hz), 6.11 (s, 1H), 5.09-5.23 (m, 1H), 4.81 (d, 1H, *J* = 15.4 Hz), 4.70 (d, 1H, *J* = 15.4 Hz), 3.82-3.91 (m, 1H), 3.69-3.78 (m, 1H), 2.94 (dd, 1H, *J*₁ = 13.1 Hz, *J*₂ = 16.4 Hz), 2.73-2.86 (m, 2H), 2.45-2.54 (m, 1H), 2.36 (t, 1H, *J* = 5.8 Hz), 1.23-1.52 (m, 6H), 0.88 (t, 3H, *J* = 7.0 Hz); **¹³C NMR** (CDCl₃, 100 MHz) : δ 171.81, 140.33, 138.41, 136.18, 131.29, 128.79, 128.46, 127.36, 122.66, 121.26, 119.08, 118.29, 111.21, 108.98, 63.21, 59.33, 44.35, 37.81, 31.61, 27.77, 26.22, 22.43, 14.10; **HRMS(EI)** calcd. for C₂₆H₃₀N₂O₂ : *m/z* 402.2307, found *m/z* 402.2292

General procedure for hydrogenation of 2a,d,j and 5a:

Indoloazocinone **2** (0.2 mmol) was dissolved in an appropriate degassed solvent. 10% Pd/C 32 mg (15 mol%) was added and the resulting suspension was evacuated and flushed back with argon three times. The reaction flask was purged with H₂ from a balloon and maintained with stirring at rt for 24 h. The catalyst was filtered off and the filtrate was evaporated with silica. Pure indoloazocinones **6a-d** were isolated by column chromatography on silica gel.

3-Benzyl-6-methyl-1,2,3,5,6,7-hexahydro-azocino[5,4-*b*]indol-4-one (6a). Synthesized from **2a** 63 mg. Solvent – EtOH / THF 5:2. Eluent DCM / EtOAc (1 / 1) (*R_f* 0.40). Yield: 60 mg (95%). ¹H NMR (DMSO-*d*₆, 400 MHz) : δ 10.73 (s, 1H), 7.32 (d, 1H, *J* = 8.0 Hz), 7.26 (d, 1H, *J* = 8.0 Hz), 7.06-7.14 (m, 3H), 6.97-7.03 (m, 3H), 6.91 (t, 1H, *J* = 7.5 Hz), 4.33 (d, 1H, *J* = 15.3 Hz), 4.16 (d, 1H, *J* = 15.3 Hz), 3.68-3.75 (m, 2H), 3.52-3.61 (m, 1H), 2.98-3.16 (m, 2H), 2.90 (dd, 1H, *J*₁ = 7.1 Hz, *J*₂ = 13.5 Hz), 2.79 (dd, 1H, *J*₁ = 10.5 Hz, *J*₂ = 13.5 Hz), 1.37 (d, 3H, *J* = 7.0 Hz); ¹³C NMR (CDCl₃, 100 MHz) : δ 173.68, 138.14, 137.03, 135.21, 129.35, 128.32, 127.81, 127.11, 121.08, 118.99, 117.18, 110.70, 105.09, 50.13, 46.25, 41.73, 31.96, 22.85, 21.68; HRMS(EI) calcd. for C₂₁H₂₂N₂O : m/z 318.1732, found m/z 318.1726

3,6-Dimethyl-1,2,3,5,6,7-hexahydro-azocino[5,4-*b*]indol-4-one (6b). Synthesized from **2d** 48 mg. Solvent – EtOH / THF 5:2. Eluent DCM / MeCN (1 / 1) (*R_f* 0.31). Yield: 47 mg (98%). ¹H NMR (DMSO-*d*₆, 400 MHz) : δ 10.69 (s, 1H), 7.39 (d, 1H, *J* = 7.7 Hz), 7.24 (d, 1H, *J* = 7.7 Hz), 6.99 (t, 1H, *J* = 7.7 Hz), 6.93 (t, 1H, *J* = 7.7 Hz), 3.87-3.96 (m, 1H), 3.69-3.77 (m, 1H), 3.73 (dt, 1H, *J*₁ = 5.4 Hz, *J*₂ = 15.1 Hz), 2.97-3.14 (m, 2H), 2.92 (dd, 1H, *J*₁ = 7.8 Hz, *J*₂ = 13.8 Hz), 2.54-2.63 (m, 4H), 1.36 (d, 3H, *J* = 6.9 Hz); ¹³C NMR (DMSO-*d*₆, 100 MHz) : δ 172.29, 138.67, 135.40, 129.64, 120.66, 118.66, 117.47, 111.06, 104.95, 48.17, 42.67, 33.65, 30.66, 22.65, 21.32; HRMS(EI) calcd. for C₁₅H₁₈N₂O : m/z 242.1419, found m/z 242.1402

α/β 1:20 Partial assignment for **6c** (β-epimer) is based on COSY and HMQC spectra.

Configuration at C5 is confirmed by NOE effect between H-C2 and H-C5.

Indoloazocinone 6c. Synthesized from **2j** 54 mg. Solvent – EtOH. Eluent DCM / MeCN (1 / 1) (*R_f* 0.17). Yield: 50 mg (94%). (the major β-epimer is described) ¹H NMR (DMSO-*d*₆, 400 MHz) : δ 10.68 (s, 1H), 7.41 (d, 1H, *J* = 7.6 Hz), 7.28 (d, 1H, *J* = 7.6 Hz), 7.00 (t, 1H, *J* = 7.6 Hz), 6.94 (t, 1H, *J* = 7.6 Hz), 4.32-4.40 (m, H-C2), 3.54-3.64 (m, H-C5), 3.27-3.37 (m, H-C4, H-C9), 3.13 (dd, H-C1, *J*₁ = 5.6 Hz, *J*₂ = 15.6 Hz), 2.84-2.96 (m, H-C1, H-C9), 2.24 (dd, H-C4, *J*₁ = 6.5 Hz, *J*₂ = 13.9 Hz), 2.07-2.18 (m, H-C7), 1.64-1.84 (m, H-C7, 2H-C8), 1.43 (d, 3H-C6, *J* = 7.1 Hz); ¹³C NMR (DMSO-*d*₆, 100 MHz) : δ 169.58 (C3), 139.41, 135.33, 129.63, 120.46, 118.79, 117.48, 111.25, 105.84, 57.31 (C2), 46.63 (C9), 43.08 (C4), 34.27 (C7), 29.92 (C5), 29.69 (C1), 21.61 (C8), 19.49 (C6); HRMS(EI) calcd. for C₁₇H₂₀N₂O : m/z 268.1576, found m/z 268.1565

Partial assignment for **6d** is based on COSY and HMQC spectra.

(2S,6R)-3-Benzyl-2-hydroxymethyl-6-methyl-1,2,3,5,6,7-hexahydro-azocino[5,4-b]indol-4-one (6d).

Synthesized from **5a** 70 mg. Solvent – EtOH. Eluent DCM / MeCN (1 / 1) (R_f 0.25). Yield: 67 mg (96%). $[\alpha]_D^{20}$ -136.3 (1.0, MeOH) **$^1\text{H NMR}$** (DMSO- d_6 , 400 MHz, 363 K) : δ 10.46 (s, 1H), 7.25 (d, 1H, J = 7.9 Hz), 7.13 (d, 1H, J = 7.9 Hz), 6.97 (t, 1H, J = 7.9 Hz), 6.80 (t, 1H, J = 7.9 Hz), 6.73 (t, 1H, J = 7.3 Hz), 6.50 (t, 2H, J = 7.3 Hz), 6.35 (d, 2H, J = 7.3 Hz), 4.95 (d, H-C8, J = 15.4 Hz), 4.69 (t, H-O, J = 5.2 Hz), 3.86 (d, H-C8, J = 15.4 Hz), 3.68-3.79 (m, 2H-C7), 3.51-3.61 (m, H-C2), 3.36-3.47 (m, H-C5), 3.19-3.35 (m, H-C4, H-C1), 3.12 (dd, H-C1, J_1 = 7.8 Hz, J_2 = 15.2 Hz), 2.49 (dd, H-C4, J_1 = 5.4 Hz, J_2 = 12.4 Hz), 1.34 (d, 3H-C6, J = 6.7 Hz); **$^{13}\text{C NMR}$** (DMSO- d_6 , 100 MHz, 363 K) : δ 172.96 (C3), 140.22, 138.15, 136.03, 129.63, 127.65, 127.04, 126.08, 120.50, 118.60, 117.26, 110.82, 105.53, 64.42 (C7), 61.11 (C2), 51.19 (C8), 42.52 (C4), 33.00 (C5), 26.29 (C1), 22.68 (C6); **HRMS(EI)** calcd. for $\text{C}_{22}\text{H}_{24}\text{N}_2\text{O}_2$: m/z 348.1838, found m/z 348.1828

General procedure for LAH reduction of 2a,e,g:

Indoloazocinone **2** (0.5 mmol) was dissolved under argon in dry THF (5 mL). To the resulting solution LAH powder 158 mg (5 equiv) was added in one portion. The reaction mixture was kept with stirring at 60 °C for approximately 12 h. After cooling down to rt 15% aqueous NaOH was added dropwise until a solid granular precipitate was formed. The precipitate was excessively washed with EtOAc. The EtOAc layer was washed with brine, dried (Na_2SO_4) and evaporated with silica. Pure indoloazocines **7a-c** were isolated by column chromatography on silica gel.

3-Benzyl-6-methyl-2,3,4,7-tetrahydro-1H-azocino[5,4-b]indole (7a). Synthesized from indoloazocinone **2a** 158 mg. Eluent DCM / MeOH / NH_3 (aq) (100 / 10 / 0.1) (R_f 0.42). Yield: 144 mg (95%). **$^1\text{H NMR}$** (DMSO- d_6 , 400 MHz, 363 K) : δ 10.43 (s, 1H), 7.45 (d, 1H, J = 7.9 Hz), 7.28-7.38 (m, 5H), 7.21-7.26 (m, 1H), 7.09 (t, 1H, J = 7.3 Hz), 6.99 (t, 1H, J = 7.5 Hz), 5.72 (dt, 1H, J_1 = 1.5 Hz, J_2 = 7.8 Hz), 3.71 (s, 2H), 3.17 (d, 2H, J = 8.0 Hz), 2.87-2.96 (m, 4H), 2.20 (d, 3H, J = 1.5 Hz); **$^{13}\text{C NMR}$** (DMSO- d_6 , 100 MHz, 363 K) : δ 140.33, 136.85, 134.44, 132.28, 128.95, 128.61, 128.46, 127.04, 124.58, 121.76, 118.86, 118.40, 112.93, 111.27, 60.07, 51.37, 50.72, 23.25, 22.56; **HRMS(EI)** calcd. for $\text{C}_{21}\text{H}_{22}\text{N}_2$: m/z 302.1783, found m/z 302.1780

6-Ethyl-3-methyl-2,3,4,7-tetrahydro-1H-azocino[5,4-b]indole (7b). Synthesized from indoloazocinone **2e** 127 mg. Eluent DCM / MeOH / NH_3 (aq) (150 / 15 / 1) (R_f 0.14). Yield: 116 mg (97%). **$^1\text{H NMR}$** (DMSO- d_6 , 400 MHz, 363 K) : δ 10.38 (s, 1H), 7.45 (d, 1H, J = 7.8 Hz), 7.33 (d, 1H, J = 7.8 Hz), 7.08 (t, 1H, J = 7.8 Hz), 6.99 (t, 1H, J = 7.8 Hz), 5.77 (t, 1H, J = 7.8 Hz), 3.07 (d, 2H, J = 7.8 Hz), 2.84-2.90 (m, 2H), 2.76-2.82 (m, 2H), 2.56 (q, 2H, J = 7.4 Hz), 2.36 (s, 3H), 1.04 (t, 3H, J = 7.4 Hz); **$^{13}\text{C NMR}$** (DMSO- d_6 , 100 MHz, 363 K) : δ 138.53, 136.94, 133.58, 128.52, 123.04, 121.66, 118.76, 118.27, 113.88, 111.28, 53.25, 52.76, 44.07, 29.10, 22.73, 13.74; **HRMS(EI)** calcd. for $\text{C}_{16}\text{H}_{20}\text{N}_2$: m/z 240.1626, found m/z 240.1622

6-Isopropyl-3-methyl-2,3,4,7-tetrahydro-1H-azocino[5,4-*b*]indole (7c). Synthesized from indoloazocinone **2g** 134 mg. Eluent DCM / MeOH / NH₃ (aq) (150 / 15 / 1) (*R_f* 0.35). Yield: 121 mg (95%). **¹H NMR** (DMSO-*d*₆, 400 MHz, 363 K) : δ 10.37 (s, 1H), 7.45 (d, 1H, *J* = 7.8 Hz), 7.34 (d, 1H, *J* = 7.8 Hz), 7.08 (t, 1H, *J* = 7.8 Hz), 6.99 (t, 1H, *J* = 7.8 Hz), 5.79 (dt, 1H, *J*₁ = 1.2 Hz, *J*₂ = 8.0 Hz), 3.01 (d, 2H, *J* = 8.0 Hz), 2.91 (septet, 1H, *J* = 6.7 Hz), 2.80-2.85 (m, 2H), 2.70-2.75 (m, 2H), 2.36 (s, 3H), 1.11 (d, 6H, *J* = 6.7 Hz); **¹³C NMR** (DMSO-*d*₆, 100 MHz, 363 K) : δ 142.85, 137.01, 134.05, 128.27, 121.78, 121.56, 118.73, 118.20, 114.19, 111.35, 53.42, 53.03, 44.15, 32.85, 22.75, 22.35; **HRMS(EI)** calcd. for C₁₇H₂₂N₂ : *m/z* 254.1783, found *m/z* 254.1778

Crystallographic data for 6d:

Crystals of **6d**, suitable for X-ray diffraction were obtained by slow evaporation from MeCN at rt. A transparent, rod-shaped crystal with approximate dimensions of 0.3 × 0.15 × 0.1 mm, was selected and mounted in a nylon loop for data collection. X-ray intensity data were collected at 100 K on a SMART 6000 diffractometer equipped with CCD detector using CuKα radiation ($\lambda = 1.54178 \text{ \AA}$), using φ and ω scans. The images were interpreted and integrated with the program SAINT from Bruker [4], giving a total of 25331 reflections (3343 independent reflections, $R_{\text{int}} = 0.0695$). The structure was solved by direct methods and refined by full-matrix least-squares on F^2 using the SHELXTL program package [5], converging to a final $R = 0.0507$ for 3059 reflections with $I > 2\sigma(I)$ and $\omega R_2 = 0.1445$ for all data and GOOF = 1.140. Non-hydrogen atoms were anisotropically refined and the hydrogen atoms in the riding mode and isotropic temperature factors fixed at 1.2 times $U(\text{eq})$ of the parent atoms and 1.5 times $U(\text{eq})$ for a methyl and hydroxyl group. The absolute configuration of the structure was established by anomalous-dispersion effects.

Table 1. Summarized crystallographic data for 6d.

formula	C ₂₂ H ₂₄ N ₂ O ₂	ωR_2 (all data)	0.1445
<i>M</i> (g mol ⁻¹)	348.43	GOOF	1.140
crystal dimensions (mm ³)	0.3 × 0.15 × 0.1	μ (mm ⁻¹)	0.661
crystal system	orthorhombic	CCDC-entry	CCDC-735454
space group	<i>P</i> 2 ₁ 2 ₁ 2 ₁		
<i>a</i> (Å)	7.2291(3)		
<i>b</i> (Å)	12.9611(5)		
<i>c</i> (Å)	19.0394(6)		
$\alpha = \beta = \gamma$ (°)	90.00		
<i>V</i> (Å ³)	1783.94(12)		
<i>Z</i>	4		
ρ_{calc} (g cm ⁻³)	1.297		
$2\theta_{\text{max}}$ (°)	141.92		
radiation	CuKα		
λ (Å)	1.54178		
<i>F</i> (000)	744		
<i>T</i> (K)	100(2)		
measured reflections	25331		
unique reflections	3343		
observed reflections ($I_o > 2\sigma(I_o)$)	3059		
parameters refined	237		
<i>R</i> ₁	0.0507		
ωR_2^a	0.1384		
<i>R</i> ₁ (all data)	0.0555		

^a Weighing scheme: $\omega = 1/[\rho^2(F_o^2) + (0.0717P)^2 + 0.9835P]$, $P = [(F_o^2 + 2F_c^2)/3]$

Figure 1. Single crystal X-ray molecular structure of 6d, with atom-labeling scheme. Displacement ellipsoids are drawn at the 50% probability level.

CCDC - 735454 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.cam.ac.uk/contents/retrieving.html (or from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: (+44-1223-336033; or deposit@ccdc.cam.ac.uk).

References.

1. Abatea, C; Kolanosa, R.; Dukat, M.; Setola, V.; Roth, B. L.; Glennon, R. A. *Bioorg. Med. Chem. Lett.* **2005**, *15*, 3510
2. a) Li, J.; Wang, T.; Yu, P.; Peterson, A.; Weber, R.; Grubisha, D.; Bennett, D.; Cook, J. M. *J. Am. Chem. Soc.* **1999**, *121*, 6998 b) Yu, P.; Cook, J. M. *J. Org. Chem.* **1998**, *63*, 9160
3. Franchi, P.; Lucarini, M.; Mezzina, E.; Pedulli, G. F. *J. Am. Chem. Soc.* **2004**, *126*, 4343
4. SAINT, Manual Version 5/6.0, Bruker Analytical X-ray Systems Inc.: Madison, Wisconsin, **1997**
5. SHELXTL-NT, Manual Version 5.1, Bruker Analytical X-ray Systems Inc.: Madison, Wisconsin, **1997**