Synthesis and Biological Evaluation of Triazole-Containing *N*-Acyl Homoserine Lactones as Quorum Sensing Modulators

Danielle M. Stacy,[a] Sebastian T. Le Quement,[b] Casper L. Hansen,[b] Janie W. Clausen,[b] Tim Tolker-Nielsen,[c] Jacob W. Brummond,[a] Michael Givskov,[c,d] Thomas E. Nielsen,[b,d,*] and Helen E. Blackwell[a,*]

[a] *Department of Chemistry, University of Wisconsin–Madison, 1101 University Ave., Madison, WI 53706 USA;* [b] *Department of Chemistry, Technical University of Denmark, DK-2800 Kgs. Lyngby, Denmark;* [c] *Department of International Health, Immunology, and Microbiology, Faculty of Health Sciences, University of Copenhagen, DK-2200 Copenhagen, Denmark;* [d] *Singapore Centre on Environmental Life Sciences Engineering, Nanyang Technological University, Singapore 637551*

Supplementary Information.

- General chemical methods and instrumentation
- Summary – Library syntheses and yields
- *E. coli* (LasR reporter) primary assay data
- *E. coli* (LasR reporter) optical density data
- *A. baumannii* (AbaR reporter) primary data
- *A. baumannii* (AbaR reporter) optical density data
- Dose response curves for LasR antagonists
- Synthetic procedures and full characterization data for all compounds

* To whom correspondence should be addressed. blackwell@chem.wisc.edu; ten@kemi.dtu.dk

General chemical methods and instrumentation.

Unless otherwise stated, all reactions were run under an argon atmosphere. Glassware was dried over a Bunsen flame under vacuum before contact with any of the reactants or solvents. All flasks were equipped with a rubber septum, through which transport of chemicals, from or to the flask, was performed by use of a syringe equipped with a needle. Solvents were typically freshly distilled or dried over molecular sieves. All reactions were monitored by thin-layer chromatography (TLC) and/or reversed-phase high-performance liquid chromatography (RP-HPLC). All solvents were of RP-HPLC quality, and commercially available reagents were used without further purification.

Analytical TLC was conducted on Merck aluminium sheets covered with silica gel (C60). The plates were either visualized under UV-light or stained by dipping in a developing agent followed by heating. Vanillin (15 g in ethanol (250 mL) and conc. H_2SO_4 (2.5 mL)) and/or *p*-anisaldehyde (15 g in ethanol (250 mL) and conc. H_2SO_4 (2.5 mL)) were used as developing agents. Flash column chromatography was performed using a CombiFlash® (Teledyne ISCO) with Matrex 60 Å, 35-70 μ silica gel.

New compounds were characterized by ^{1}H NMR, RP-HPLC, MS (ESI) and IR. For selected compounds TLC (R_f), ^{13}C NMR, HRMS (ESI) and optical rotations data have also been recorded. For some compounds, the ^{13}C signals were determined by ^{1}H-^{13}C gHSQC and ^{1}H-^{13}C gHMBC.

^{1}H NMR and ^{13}C NMR spectra were obtained on a Bruker Aspect-3000 spectrometer (operating at 200 MHz for proton and 50 MHz for carbon), a Varian Mercury-300 spectrometer (operating at 300 MHz for proton and 75 MHz for carbon), or a Varian Unity Inova-500 spectrometer (operating at 500 MHz for ^{1}H NMR) ^{1}H-^{13}C gHSQC and ^{1}H-^{13}C gHMBC were recorded on a Varian Unity Inova-500 spectrometer. The chemical shifts (δ) are reported in parts per million (ppm) and the coupling constants (*J*) in Hz. Usually DMSO-d_6 was used as the solvent, and signal positions were measured relative to the signal for DMSO (δ 2.50 ppm for ^{1}H NMR and δ 39.43 for ^{13}C NMR). For spectra recorded in $CDCl_3$, signal positions were measured relative to the signal for $CHCl_3$ (δ 7.26 for ^{1}H NMR and δ 77.0 for ^{13}C NMR). For spectra recorded in CD_3OD, signal positions were measured relative to the signal for CD_3OD (δ 3.31 ppm for ^{1}H NMR and δ 49.05 for ^{13}C NMR).

IR analysis was performed on a Bruker Alpha FT-IR spectrometer.

Analytical RP-HPLC analysis was performed on a Waters Alliance 2695 RP-HPLC system using a Symmetry 60 Å C18 column (*d* 3.5 μm, 4.6 x 75 mm; column temp: 25 °C; flow: 1 mL/min) with detection at 215 nm and 254 nm. Eluents A (0.1% TFA in H_2O) and B (0.1% TFA in acetonitrile) were used in a linear gradient (100% A to 100% B) in a total run time of 13 min.

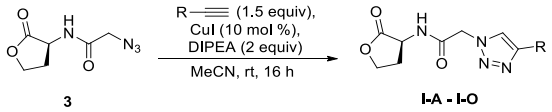
Analytical LC-MS (ESI) analysis was performed on a Waters AQUITY RP-UPLC system equipped with a diode array detector using an AQUITY UPLC BEH C18 column (*d* 1.7 μm, 2.1 × 50 mm; column temp: 65 °C; flow: 0.6 mL/min). Eluents A (0.1% HCO_2H in H_2O) and B (0.1% HCO_2H in acetonitrile) were used in a linear gradient (5% B to 100% B) in a total run time of 2.6 min. The LC system was coupled to a SQD mass spectrometer.

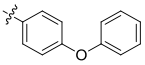
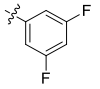
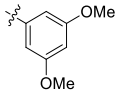
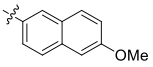
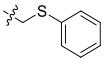
Analytical LC-HRMS (ESI) analysis was performed on an Agilent 1100 RP-LC system equipped with a diode array detector using a Phenomenex Luna C18 column (*d* 3 μm, 2.1 × 50 mm; column temp: 40 °C; flow: 0.4 mL/min). Eluents A (0.1% HCO_2H in H_2O) and B (0.1% HCO_2H in acetonitrile) were used in a linear gradient (20% B to 100% B) in a total run time of 15 min. The LC system was coupled to a Micromass LCT orthogonal time-of-flight mass spectrometer equipped with a Lock Mass probe operating in positive electrospray mode.

Optical rotations were measured using a Perkin-Elmer polarimeter 341. The temperature for all recordings was approximately 20 °C.

Summary – Library syntheses and yields.

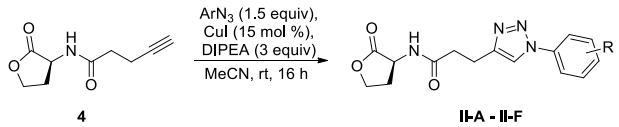
Table S-1. Synthesis of type I triazole HLs **I-A**–**I-O** from azidoacetyl HL building block **3**.



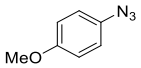
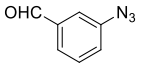
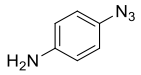
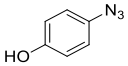
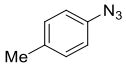
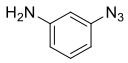
entry	R	product, yield (%)	entry	R	product, yield (%)[a, b]
1		**I-A**, 70	9		**I-I**, 73
2		**I-B**, 58	10		**I-J**, 79
3		**I-C**, 61	11		**I-K**, 84
4		**I-D**, 65	12		**I-L**, 85
5		**I-E**, 77	13		**I-M**, 84
6		**I-F**, 61	14		**I-N**, 69
7		**I-G**, 58	15		**I-O**, 69
8		**I-H**, 63			

[a] Yield after precipitation with diethyl ether. [b] Typical purity >95% (RP-HPLC at 215 nm). Slightly lower purities (~85%) were observed for some aliphatic acetylenes.

Table S-2. Synthesis of type II triazole HLs **II-A**–**II-F** from alkyne-containing HL building block **4**.

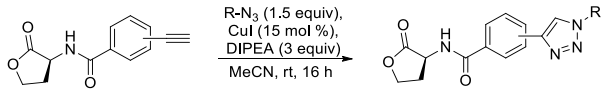


4 **II-A - II-F**

entry	ArN_3	product, yield (%)	entry	ArN_3	product, yield (%)[a, b]
1		**II-A**, 71	4		**II-D**, 61
2		**II-B**, 64	5		**II-E**, 70
3		**II-C**, 72	6		**II-F**, 67

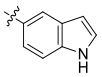
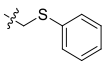
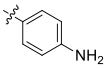
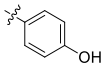
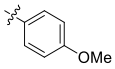
[a] Yields after precipitation with diethyl ether. [b] Typical purity was >95% (RP-HPLC at 215 nm).

Table S-3. Synthesis of type III triazole HLs **III-A**–**III-J** from alkyne-containing HL building blocks **11** and **12**.



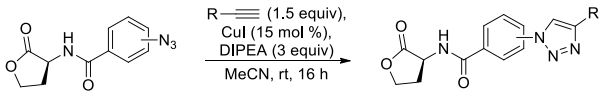
11 (4-CCH)
12 (3-CCH)

III-A - III-G (4-triazole)
III-B - III-H (3-triazole)

entry	R	product, yield (%)[a, b]
1		**III-A**, 88; **III-B**, 64
2		**III-C**, 66; **III-D**, >95
3		**III-E**, 92; **III-F**, >95
4		**III-G**, 63; **III-H**, 56
5		**III-I**, >95; **III-J**, 77

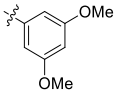
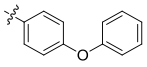
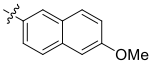
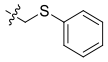
[a] Yield after precipitation with diethyl ether. [b] Typical purity >95% (RP-HPLC at 215 nm).

Table S-4. Synthesis of type IV triazole HLs **IV-A**–**IV-AF** from HL building blocks **13** and **14**.



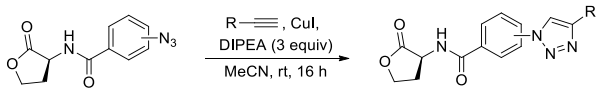
13 (4-N_3)
14 (3-N_3)

IV-A - IV-AE (4-triazole)
IV-B - IV-AF (3-triazole)

entry	R	product, yield (%)	entry	R	product, yield (%)[a, b]
1		**IV-A**, 94; **IV-B**, 56	9		**IV-Q**, 65; **IV-R**, 77
2		**IV-C**, 75; **IV-D**, 55	10		**IV-S**, 93; **IV-T**, 77
3		**IV-E**, 54; **IV-F**, 61	11		**IV-U**, >95; **IV-V**, >95
4		**IV-G**, 87; **IV-H**, 64	12		**IV-W**, >95; **IV-X**, 76
5		**IV-I**, 70; **IV-J**, 93	13		**IV-Y**, 86; **IV-Z**, 89
6		**IV-K**, 70; **IV-L**, 85	14		**IV-AA**, 84; **IV-AB**, 89
7		**IV-M**, 62; **IV-N**, 56	15		**IV-AC**, >95; **IV-AD**, 91
8		**IV-O**, 73; **IV-P**, 81	16		**IV-AE**, 91; **IV-AF**, 83

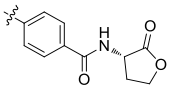
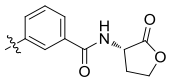
[a] Yield after precipitation with diethyl ether. [b] Typical purity >95% (RP-HPLC at 215 nm).

Table S-5. Synthesis of type V triazole HLs **V-A**–**V-F** and **V-H**–**V-I** from azido-functionalized HL building blocks **13** and **14**.



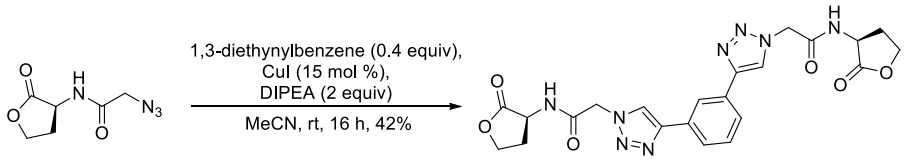
13 (4-N_3)
14 (3-N_3)

V-A - V-H (4-triazole)
V-B - V-I (3-triazole)

entry	R	equiv alkyne	mol % CuI	product, yield (%),[a] purity (%)[b]
1		1	15	**V-A**, 83, >95; **V-B**, 73, >95
2		1	15	**V-C**, 92, >95; **V-D**, 71, >95
3		0.5	15	**V-E**, 84, 81; **V-F**, >95, 94
4		0.34	15 25	**V-H**, >95, >95; **V-I**, >95, >95

[a] Yield after precipitation with diethyl ether. [b] Purity determined by RP-HPLC (215 nm).

Scheme S-1. Synthesis of type V triazole HL **V-G** from azido-functionalized HL building block **3**.



3

V-G (purity: 85 %)

E. coli (LasR reporter) primary assay data.

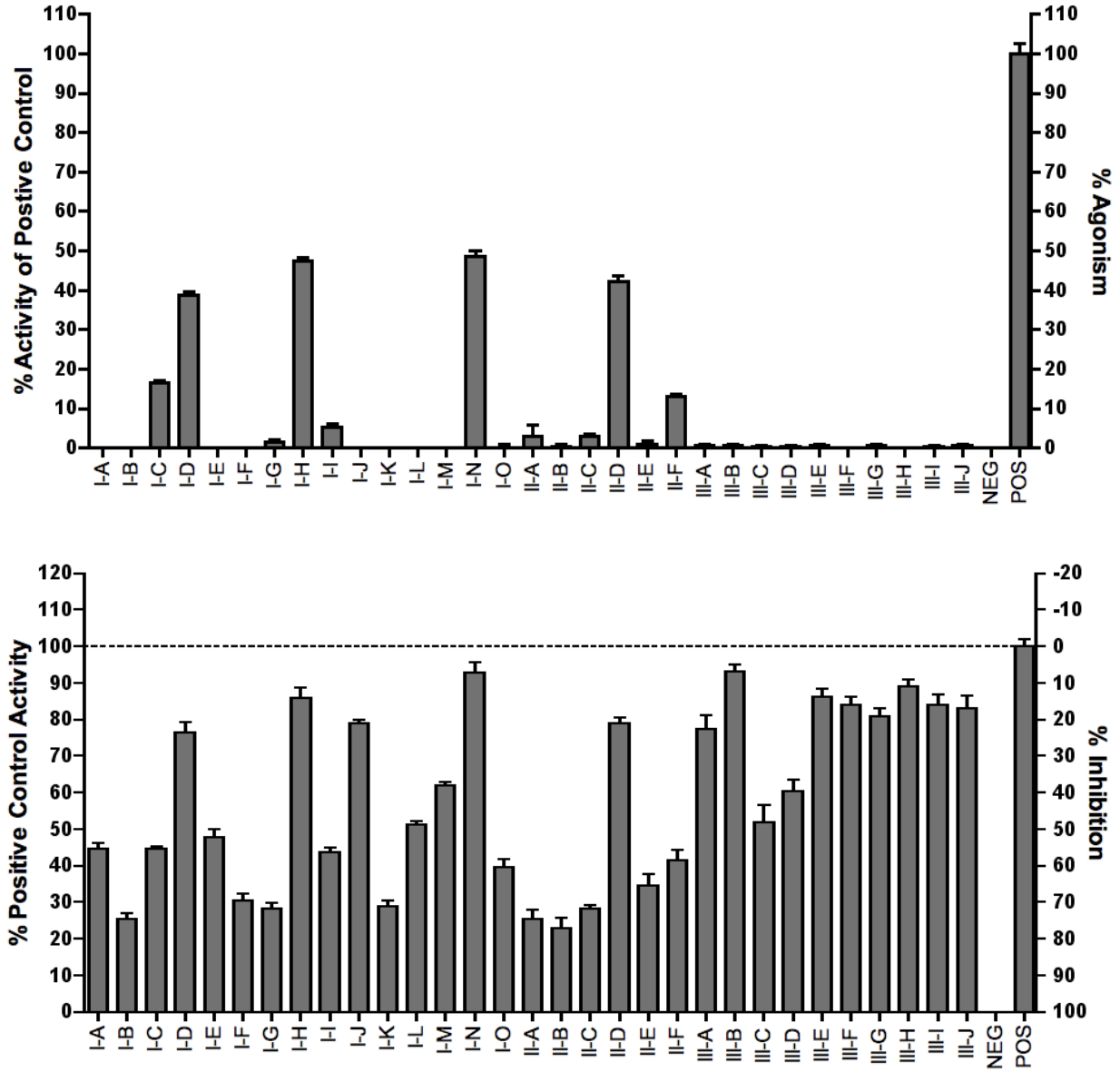


Figure S-1. Primary screening data for the type I, II, and III triazole HL libraries in the *E. coli* β-galactosidase reporter strain (LasR). *Top*: Agonism assay data for 100 μM synthetic ligand. Positive control (POS) = 100 μM OdDHL. Negative control (NEG) = DMSO without compound. *Bottom*: Antagonism assay data for 100 μM synthetic ligand tested against 10 nM OdDHL. Positive control (POS) = 10 nM OdDHL. Negative control (NEG) = DMSO without compound. Error bars in each plot indicate standard error of the mean of nine values.

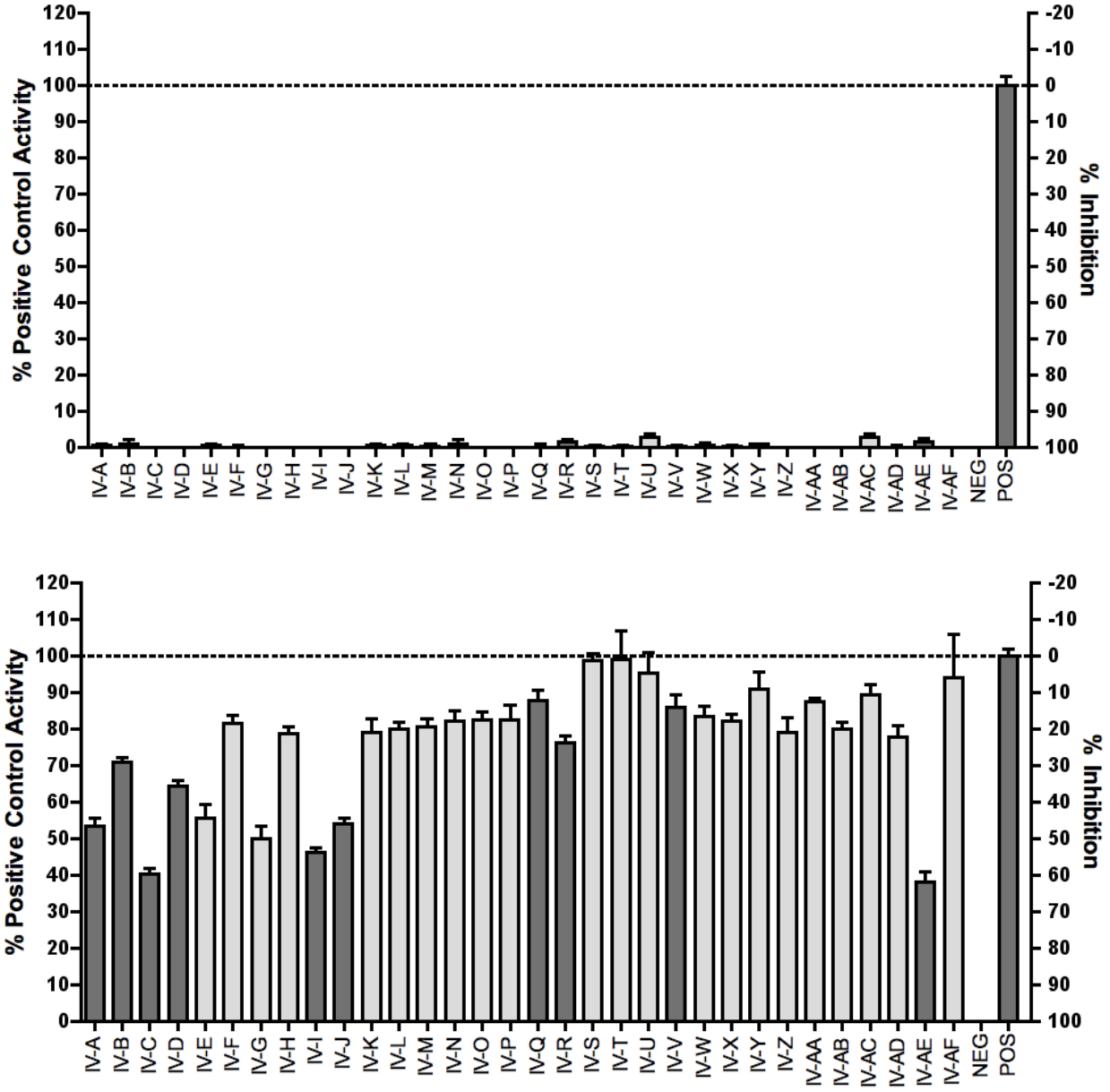


Figure S-2. Primary screening data for the type IV triazole HL library in the *E. coli* β-galactosidase reporter strain (LasR). *Top*: Agonism assay data for 100 μM (dark bar) and 10 μM (light bar) synthetic ligand. Positive control (POS) = 100 μM OdDHL. Negative control (NEG) = DMSO without compound. *Bottom*: Antagonism assay data for 100 μM (dark) and 10 μM (light) synthetic ligand tested against 10 nM OdDHL. Positive control (POS) = 10 nM OdDHL. Negative control (NEG) = DMSO without compound. Error bars in each plot indicate standard error of the mean of nine values.

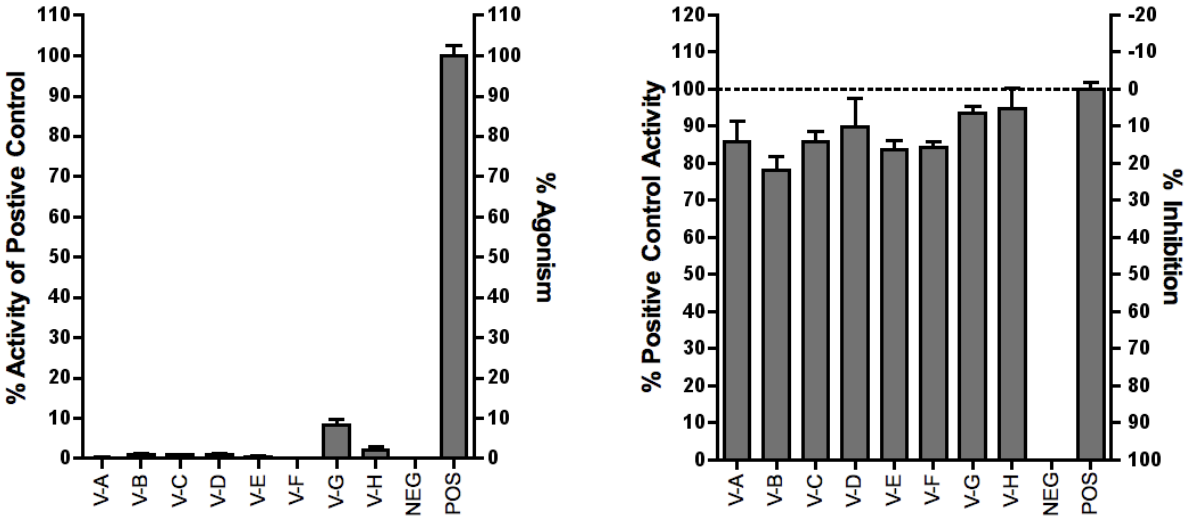


Figure S-3. Primary screening data for the type V triazole HL library in the *E. coli* β-galactosidase reporter strain (LasR). *Left*: Agonism assay data for 100 μM synthetic ligand. Positive control (POS) = 100 μM OdDHL. Negative control (NEG) = DMSO without compound. *Right*: Antagonism assay data for 100 μM synthetic ligand tested against 10 nM OdDHL. Positive control (POS) = 10 nM OdDHL. Negative control (NEG) = DMSO without compound. Error bars in each plot indicate standard error of the mean of nine values.

E. coli **(LasR reporter) optical density data.**

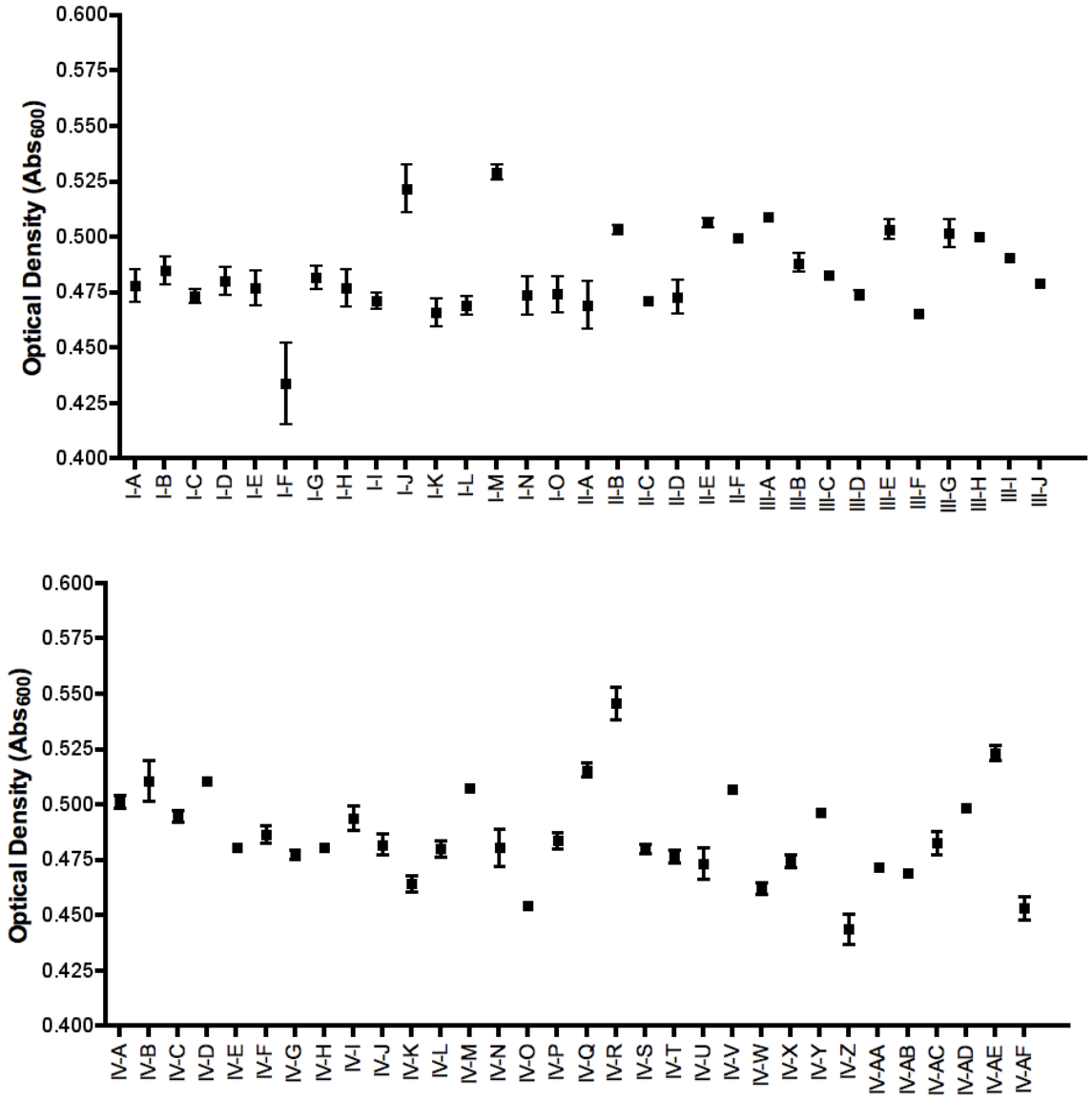


Figure S-4. Optical density (Abs_{600}) of the *E. coli* (LasR) reporter strain as recorded at the initiation of the β-galactosidase assay. *Top:* Average optical density of culture after incubation with the type I–III tirazole HL libraries. *Bottom:* Average optical density of culture after incubation with the type IV triazole HL library. Data indicate the average absorbance of 200 μL culture in 96-well microtiter plates. Error bars in each plot indicate standard error of the mean of nine values.

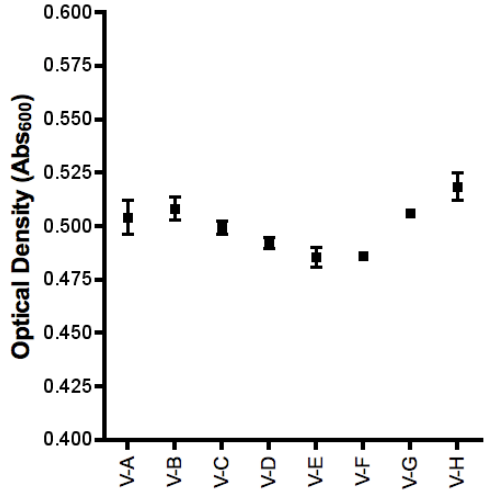


Figure S-5. Optical density (Abs_{600}) of the *E. coli* (LasR) reporter strain as recorded at the initiation of the β-galactosidase assay. Average optical density of culture after incubation with the type V triazole HL library. Data indicate the average absorbance of 200 μL culture in 96-well microtiter plates. Error bars in each plot indicate standard error of the mean of nine values.

A. baumannii (AbaR reporter) primary data.

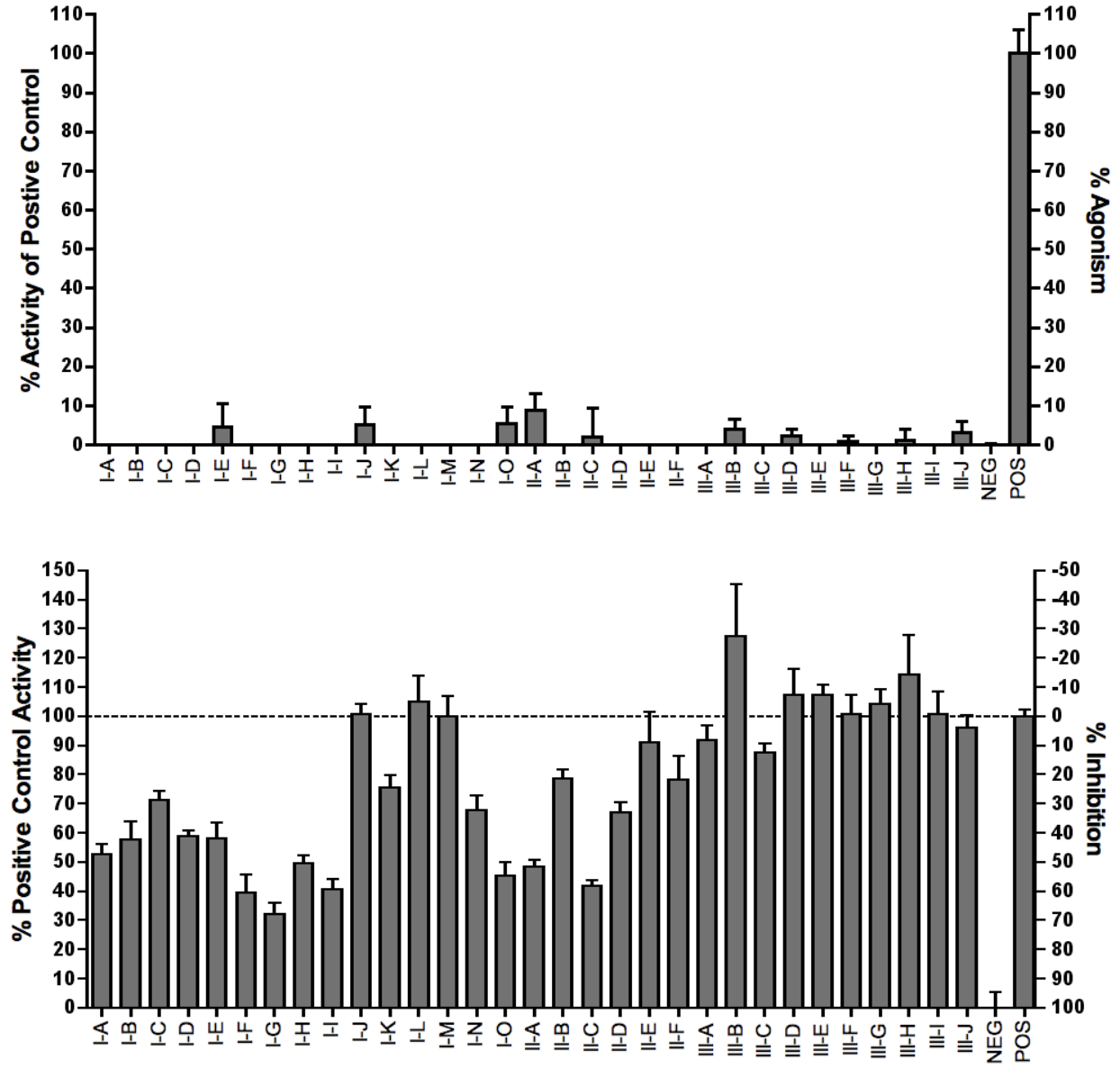


Figure S-6. Primary screening data for the type I–III HL triazole libraries in the *A. baumannii* β-galactosidase reporter strain (AbaR). *Top*: Agonism assay data for 100 μM synthetic ligand. Positive control (POS) = 100 μM OH-dDHL. Negative control (NEG) = DMSO without compound. *Bottom*: Antagonism assay data for 100 μM synthetic ligand tested against 0.70 μM OH-dDHL. Positive control (POS) = 0.70 μM OH-dDHL. Negative control (NEG) = DMSO without compound. Error bars in each plot indicate standard error of the mean of nine values.

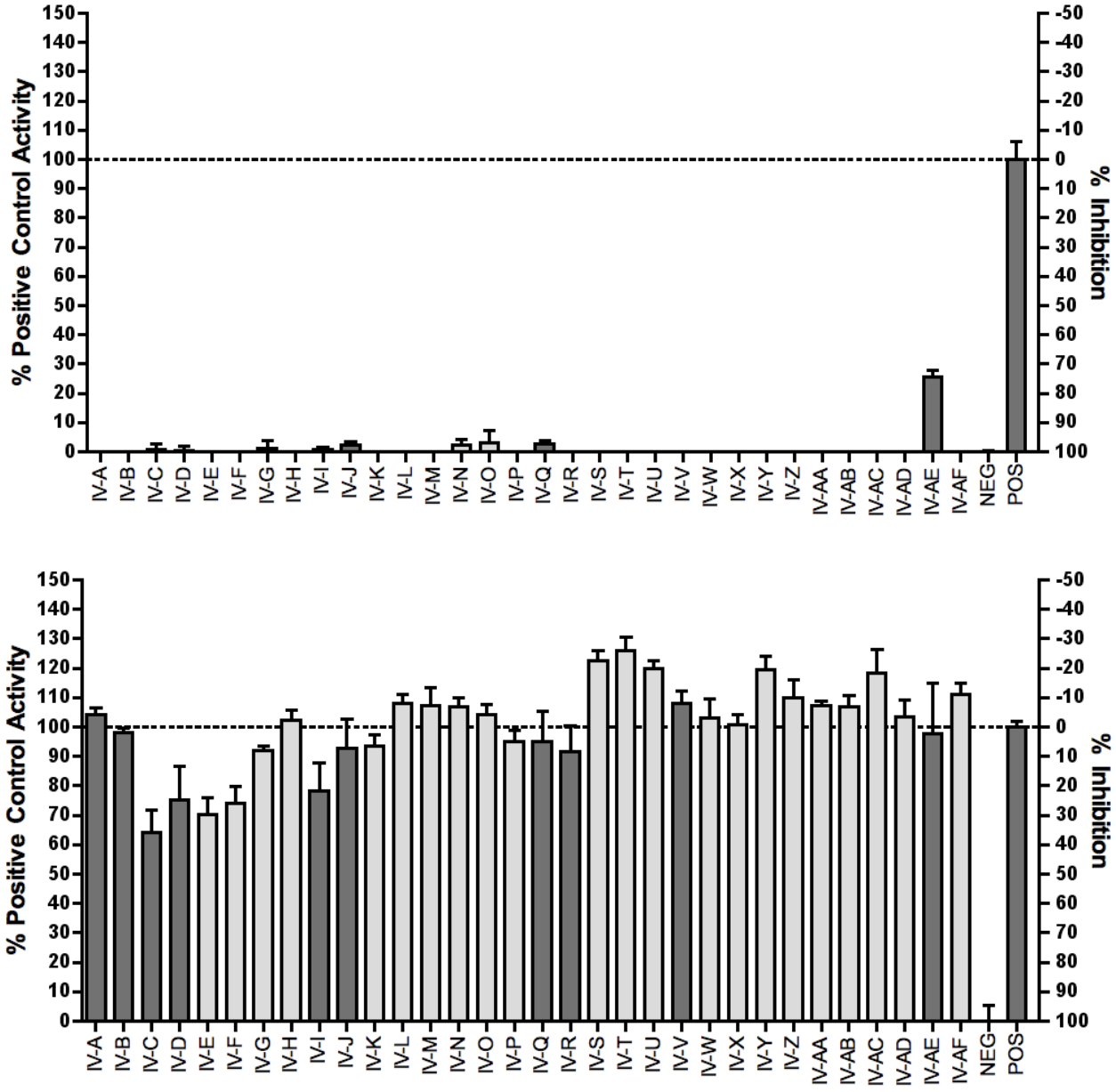


Figure S-7. Primary screening data for the type IV triazole HL library in the *A. baumannii* β-galactosidase reporter strain (AbaR). *Top*: Agonism assay data for 100 μM (dark bar) and 10 μM (light bar) synthetic ligand. Positive control (POS) = 100 μM OH-dDHL. Negative control (NEG) = DMSO without compound. *Bottom*: Antagonism assay data for 100 μM (dark) and 10 μM (light) synthetic ligand tested against 0.70 μM OH-dDHL. Positive control (POS) = 0.70 μM OH-dDHL. Negative control (NEG) = DMSO without compound. Error bars in each plot indicate standard error of the mean of nine values.

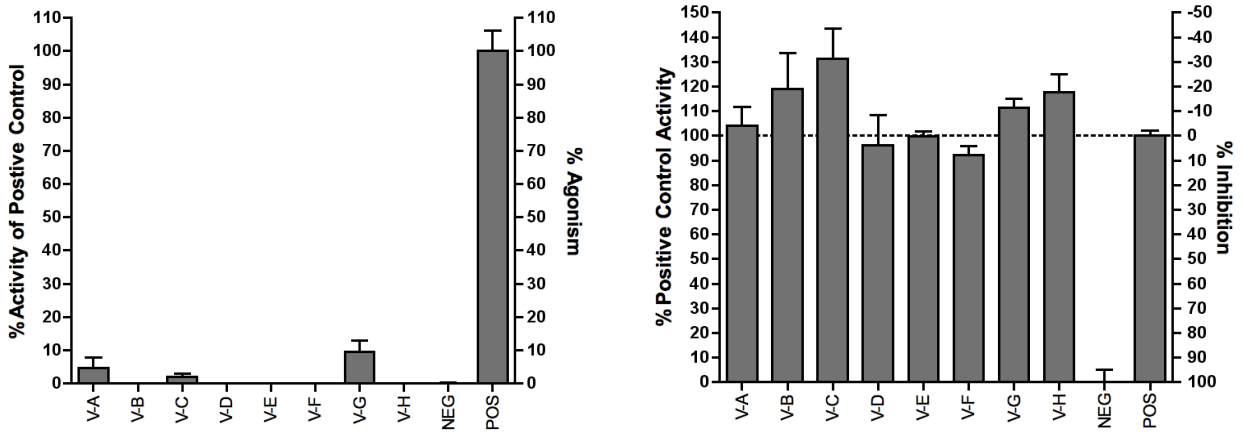


Figure S-8. Primary screening data for the type V triazole HL library in the *A. baumannii* β-galactosidase reporter strain (AbaR). *Left*: Agonism assay data for 100 μM synthetic ligand. Positive control (POS) = 100 μM OH-dDHL. Negative control (NEG) = DMSO without compound. *Right*: Antagonism assay data for 100 μM synthetic ligand tested against 0.70 μM OH-dDHL. Positive control (POS) = 0.70 μM OH-dDHL. Negative control (NEG) = DMSO without compound. Error bars in each plot indicate standard error of the mean of nine values.

A. baumannii (AbaR reporter) optical density data.

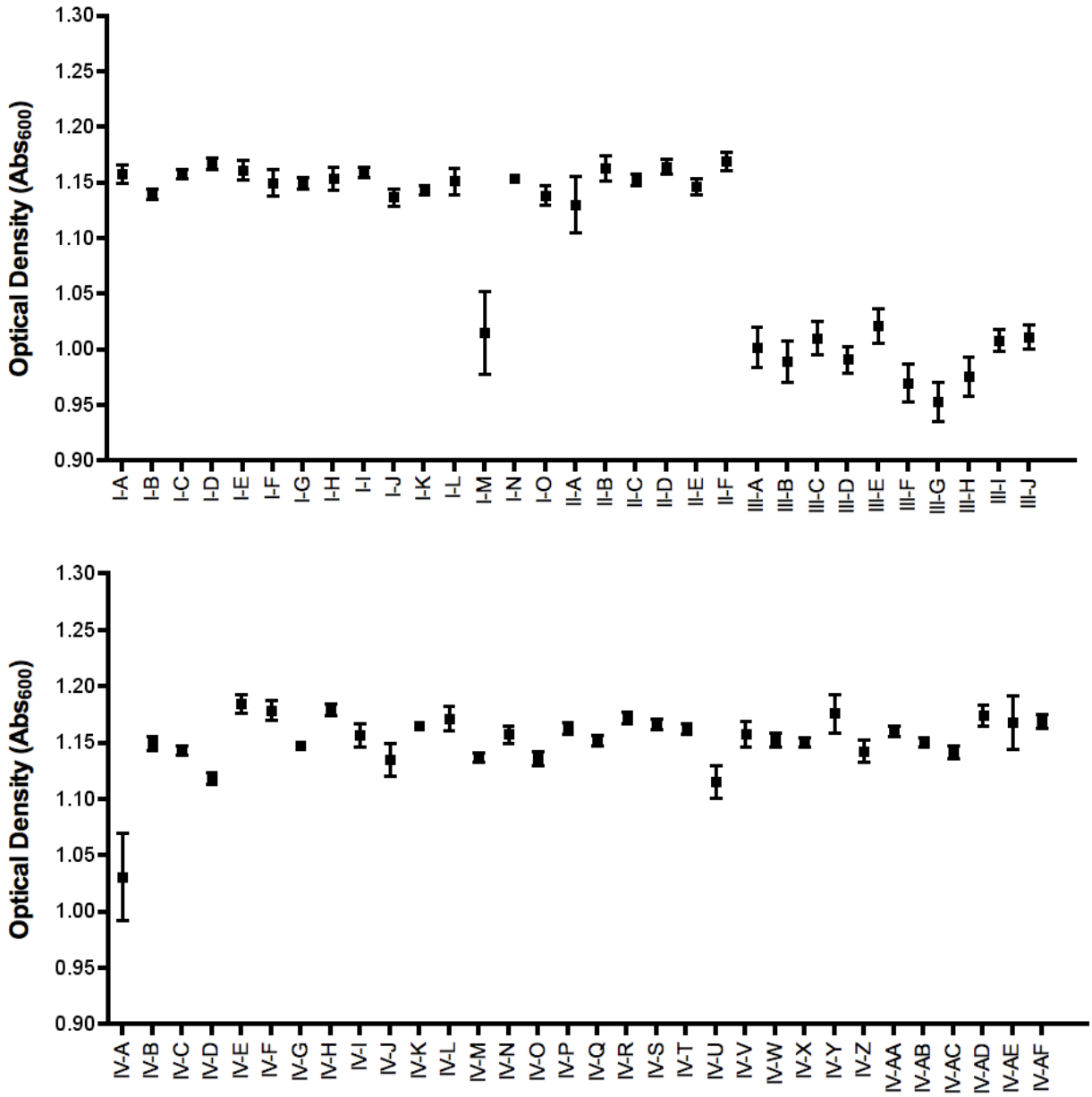


Figure S-9. Optical density (Abs_{600}) of the *A. baumannii* (AbaR) reporter strain as recorded at the initiation of the β-galactosidase assay. *Top:* Average optical density of culture after incubation with the type I–III triazole HL libraries. *Bottom:* Average optical density of culture after incubation with the type IV library. Data indicate the average absorbance of 200 μL culture in 96-well microtiter plates. Error bars in each plot indicate standard error of the mean of nine values.

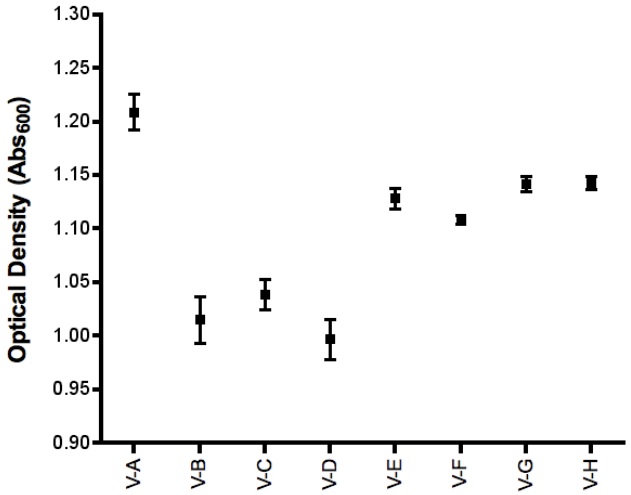
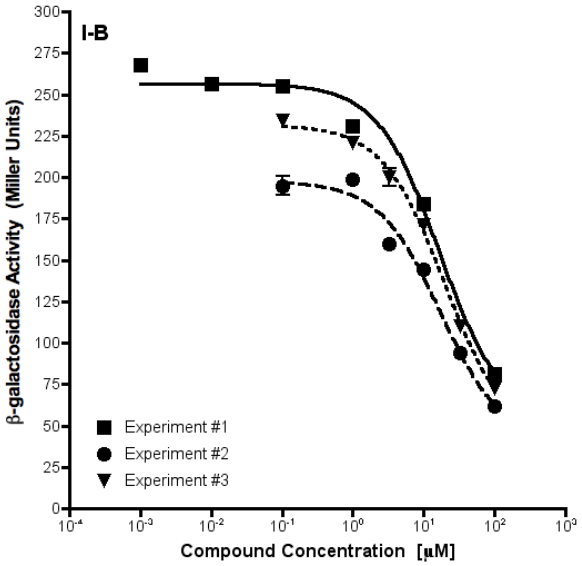
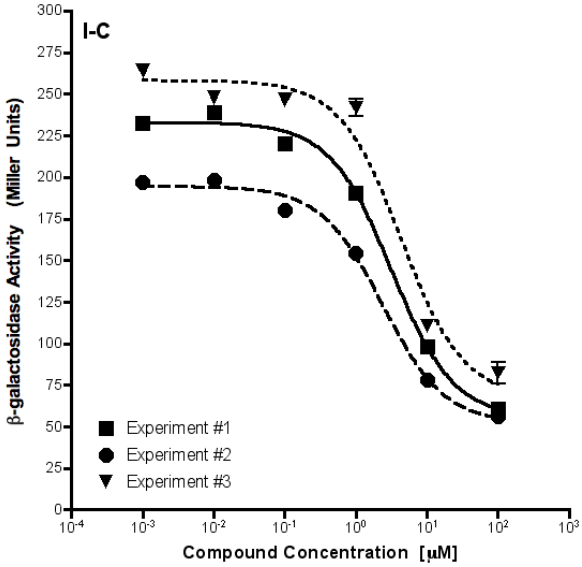


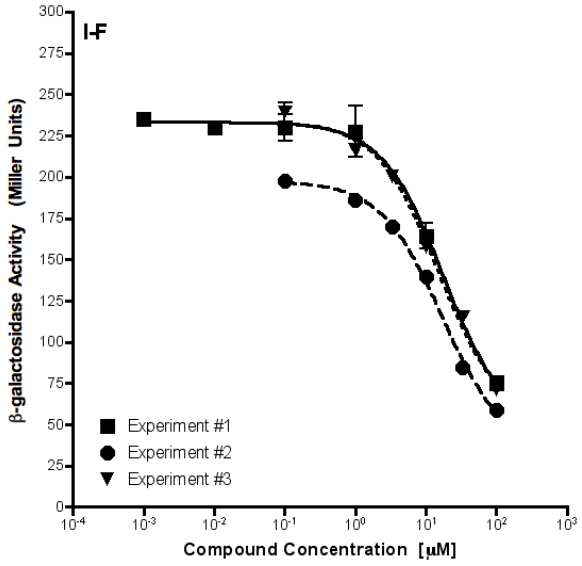
Figure S-10. Optical density (Abs_{600}) of the *A. baumannii* (AbaR) reporter strain as recorded at the initiation of the β-galactosidase assay. Average optical density of culture after incubation with the type V triazole HL library. Data indicate the average absorbance of 200 μL culture in 96-well microtiter plates. Error bars in each plot indicate standard error of the mean of nine values.

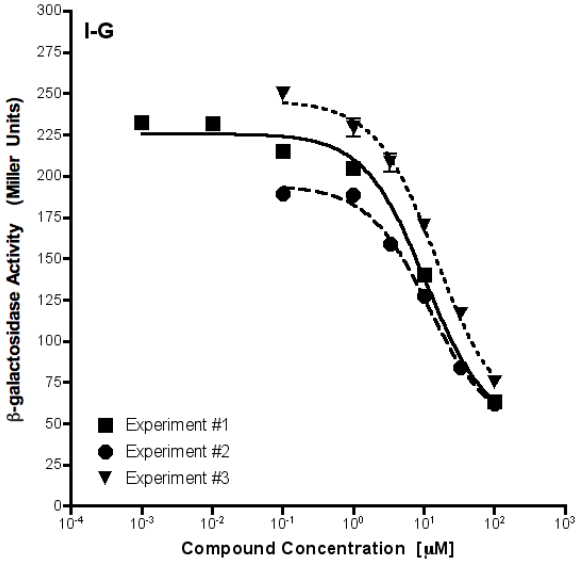
Dose response curves for LasR antagonists.

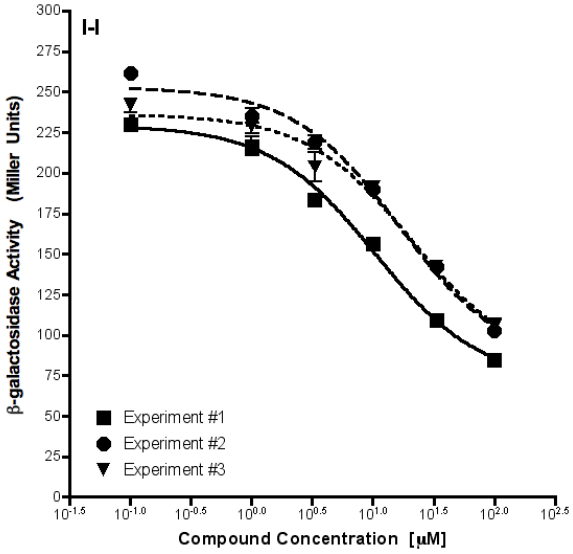
Antagonism dose response curves for triazole HLs **I-B**, **I-C**, **I-F**, **I-G**, **I-I**, **I-K**, **II-A**, **II-C, II-F**, and **IV-AE** in the *E. coli* (LasR reporter) strain are shown below. Synthetic compound was screened against 10 nM OdDHL over varying concentrations. Error bars indicate standard error of the mean of triplicate values.

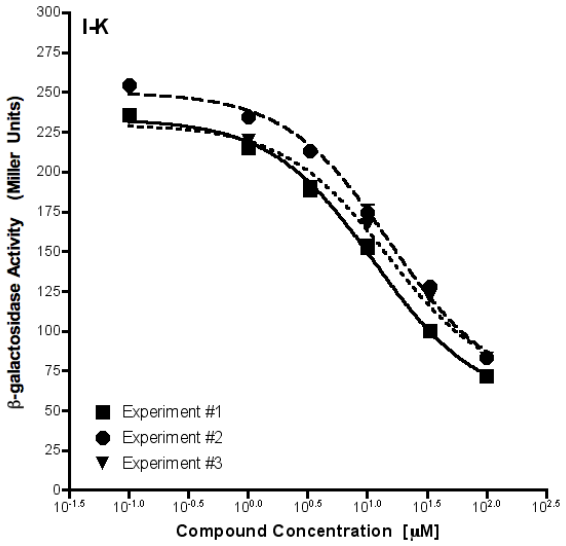


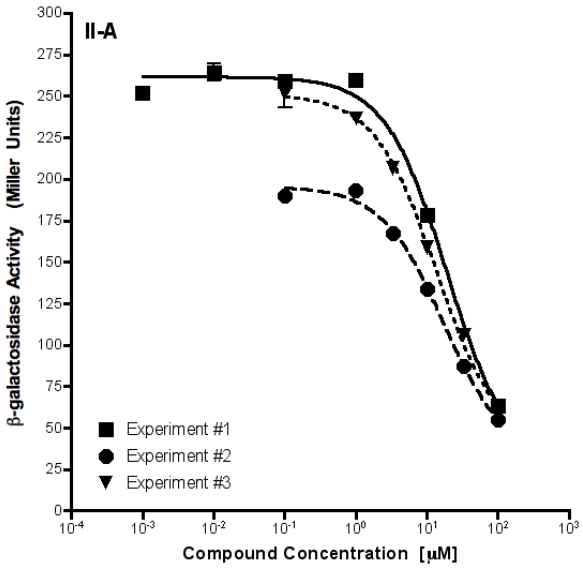


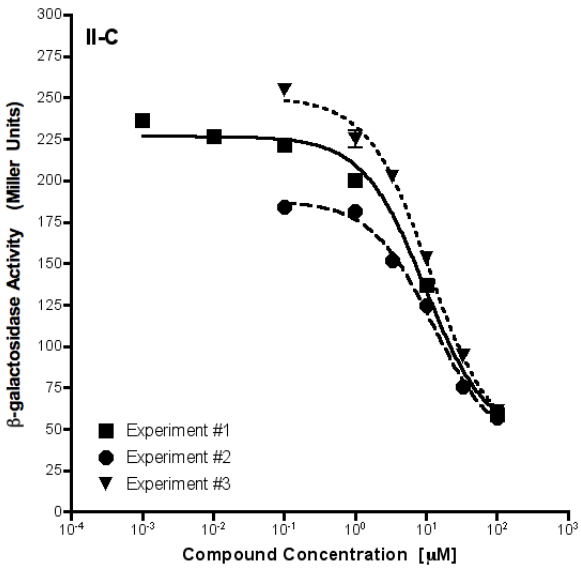


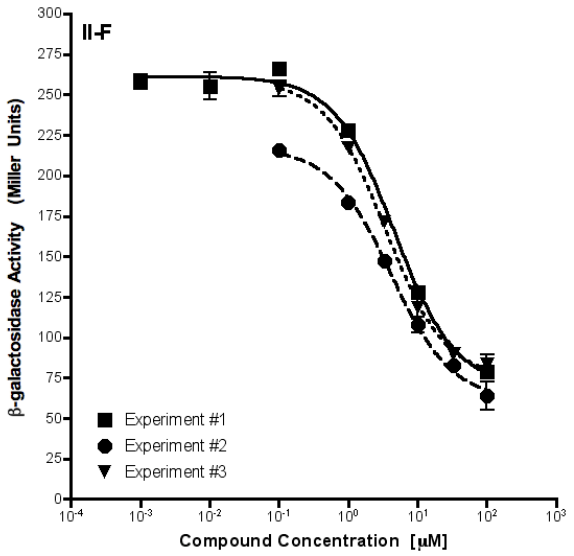


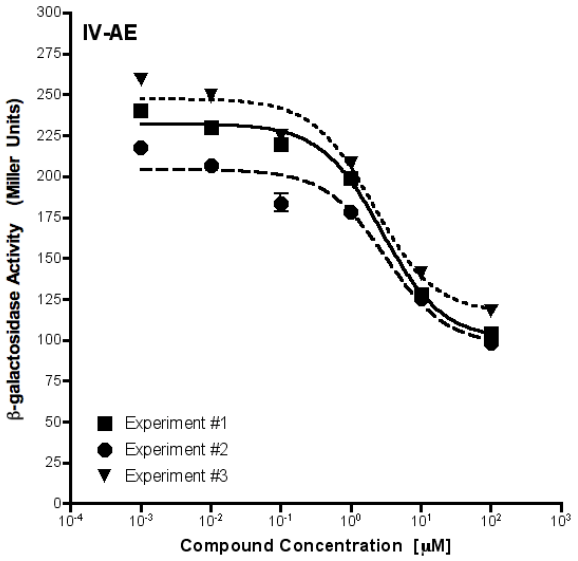

I-I
β-galactosidase Activity (Miller Units)
Compound Concentration [μM]
Experiment #1
Experiment #2
Experiment #3


I-K
β-galactosidase Activity (Miller Units)
Compound Concentration [μM]
Experiment #1
Experiment #2
Experiment #3


II-A
β-galactosidase Activity (Miller Units)
Compound Concentration [μM]
Experiment #1
Experiment #2
Experiment #3

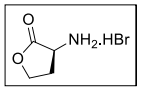

II-C
β-galactosidase Activity (Miller Units)
Compound Concentration [μM]
Experiment #1
Experiment #2
Experiment #3


II-F
β-galactosidase Activity (Miller Units)
Compound Concentration [μM]
Experiment #1
Experiment #2
Experiment #3

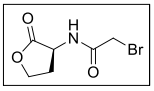

IV-AE
β-galactosidase Activity (Miller Units)
Compound Concentration [μM]
Experiment #1
Experiment #2
Experiment #3

Synthetic procedures and full characterization data for all compounds.

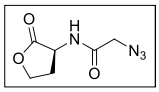
*Synthesis of library building blocks **3–4** and **11–14**.*



L-Homoserine lactone hydrobromide salt (1).[1] L-Methionine (30.4 g, 204 mmol) and bromoacetic acid (30.8 g, 222 mmol) were dissolved in *i*-PrOH:H_2O:AcOH (5:5:2, 300 mL) in a round-bottomed flask fitted with a magnetic stirring bar. The reaction was then placed under stirring and refluxed overnight, whereupon the volatiles were removed *in vacuo*. The resulting brown oil was partly dissolved in a 4:1 mixture of *i*-PrOH:HBr (33% in acetic acid) (200 mL), upon which time a white precipitate formed. This precipitate was collected by filtration and washed with isopropanol. The mother liquor was concentrated *in vacuo* and resubjected to precipitation using a 4:1 mixture of *i*-PrOH:HBr (33% in acetic acid) (200 mL). This procedure was repeated twice. The different crops of precipitate were combined to give the title compound as a white solid (31.9 g, 86 %). Mp: 240-244 °C; ^{1}H NMR (300 MHz, CH_3OD) δ 4.89 (s, 3H), 4.53 (dt, *J* = 9.1, 1.1 Hz, 1H), 4.42-4.33 (m, 2H), 2.74 (dddd, *J* = 12.5, 8.9, 5.9, 1.2 Hz, 1H), 2.33 (dddd, *J* = 12.5, 11.7, 11.0, 9.1 Hz, 1H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 173.2, 66.3, 47.7, 26.9; IR (neat) cm^{-1}: 2986, 2880, 1775, 1496, 1210, 1155, 1009; $[\alpha]_D^{20}$: -25.00° (*c*: 0.020, DMSO).



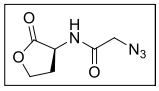
***N*-Bromoacetyl-L-homoserine lactone (2).** L-Homoserine lactone hydrobromide salt (**1**) (4.0 g, 22.0 mmol) and sodium bicarbonate (5.5 g, 66 mmol) were dissolved in CH_2Cl_2:H_2O (1:1, 50 mL) in a round-bottomed flask fitted with a magnetic stirring bar. Bromoacetyl bromide (2.1 mL, 4.69 g, 23.2 mmol) was then added dropwise under stirring. The reaction mixture was left under stirring for 3 h at room temperature, whereupon the dichloromethane was removed *in vacuo*. The remaining aqueous phase was extracted with ethyl acetate (3 × 40 mL). The combined organic layers were dried over sodium sulfate and the solvent was removed *in vacuo* to give the title compound as white crystals (3.2 g, 66 %). ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.83 (d, *J* = 7.7 Hz, 1H), 4.60 (dt, *J* = 10.6, 8.5 Hz, 1H), 4.36 (t, *J* = 8.8 Hz, 1H), 4.21 (ddd, *J* = 9.8, 9.0, 6.4 Hz, 1H), 3.92 (s, 2H), 2.47-2.38 (m, 1H), 2.22-2.08 (m, 1H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 174.7, 166.1, 65.3, 48.3, 28.8, 27.9.



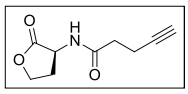
***N*-Azidoacetyl-L-homoserine lactone (3) from *N*-bromoacetyl-L-homoserine lactone.** *N*-Bromoacetyl-L-homoserine lactone (**2**) (1.0 g, 4.50 mmol) and sodium azide (0.59 g, 9.0 mmol) were dissolved in DMSO (25 mL) in a round-bottomed flsak fitted with a magnetic stirring bar. The reaction mixture was left under stirring at room temperature for 16 h, whereupon it was transferred to a separation funnel with brine (90 mL) and ethyl acetate (90 mL). The organic layer was separated and the aqueous phase was extracted with ethyl acetate (3 × 120 mL). The combined organic layers were washed with water (180 mL) and brine (180 mL), and dried over sodium sulfate. The volatiles were then removed *in vacuo* to give the title compound as white crystals (0.5 g, 62 %). Mp: 82-85 °C; ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.66 (d, *J* = 7.8 Hz, 1H) 4.60 (td, *J* = 10.6, 8.5 Hz, 1H), 4.36 (dt, *J* = 8.9, 1.4 Hz, 1H), 4.21 (ddd, *J* = 9.8, 9.0, 6.4 Hz, 1H), 3.92 (s, 2H) 2.46-2.37 (m, 1H) 2.25-2.11 (m, 1H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 175.0, 167.6, 65.4, 50.6 48.1, 28.1; IR (neat) cm-1: 3281, 2111, 1778, 1660,

[1] Persson, T.; Hansen, T. H.; Rasmussen, T. B; Skindersø, M. E.; Givskov, M.; Nielsen, J. *Org. Biomol. Chem.* **2005**, *3*, 253-262

1530, 1384, 1224, 1173, 1026 ; R_f = 0.30 (ethyl acetate, vanillin); $[\alpha]_D^{20}$: -24,4° (*c:* 0.043, DMSO).

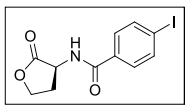


***N*-Azidoacetyl-L-homoserine lactone (3) from L-homoserine lactone hydrobromide salt.** L-Homoserine lactone hydrobromide salt (**7.6**) (15 g, 82.5 mmol) and sodium bicarbonate (13.8 g, 165 mmol) were dissolved in CH_2Cl_2:H_2O (1:1, 600 mL) in a round-bottomed flask fitted with a magnetic stirring bar. Bromoacetyl bromide (7.88 mL, 18.3 g, 90.6 mmol) was then added dropwise under stirring, immediately followed by addition of sodium azide (10.7 g, 165 mmol). The reaction mixture was left under stirring overnight at room temperature, upon which the dichloromethane was removed *in vacuo*. The remaining aqueous phase was extracted with ethyl acetate (7 × 450 mL). The combined organic layers were dried over sodium sulfate and the solvent was removed *in vacuo* to give the title compound as white crystals (13,51 g, 89 %).



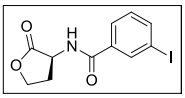
***N*-1-oxo-4-pentyn-L-homoserine lactone (4).** 4-Pentynoic acid (1,0 g, 10.2 mmol), triethylamine (4.25 mL, 3.09 g, 30.6 mmol) and PyBOP (5.30 g, 10.2 mmol,) were dissolved in dry DMF (50 mL) in a round-bottomed flask fitted with a magnetic stirring bar. The reaction mixture was left under stirring for 15 min at room temperature, whereupon L-homoserine lactone hydrobromide salt (**1**) (1.85 g, 10.2 mmol) in dry DMF (20 mL) was added. The reaction was then left under stirring for 2 h. The volatiles were removed *in vacuo*, and water was added (100 mL). The aqueous phase was extracted with ethyl acetate (3 × 300 mL). The combined organic layers were dried over magnesium sulfate and concentrated *in vacuo*. The residue was then purified by flash column chromatography on silica gel (ethyl acetate, vanillin, R_f = 0.51) to give the title compound as a white powder (1.77 g, >95 %). Mp: 117-119 °C; ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.45 (d, *J* = 7.8 Hz, 1H), 4.56 (ddd, *J* = 10.9, 8.9, 8.3 Hz, 1H), 4.34 (dt, *J* = 8.8, 1.8 Hz, 1H), 4.20 (ddd, *J* = 10.5, 8.7, 6.4 Hz, 1H), 2.78 (dd, *J* = 2.6, 2.0 Hz, 1H), 2.45-2.26 (m, 5H), 2.19-2.04 (m, 1H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 175.2, 170.3, 83.4, 71.3, 65.2, 47.8, 33.7, 28.3, 13.9; IR (neat) cm^{-1}: 3339, 3253, 1782, 1648, 1539, 1377, 1224, 1177, 1020; R_f = 0.51 (ethyl acetate, vanillin); $[\alpha]_D^{20}$: -28.7° (*c:* 0.044, DMSO).

- ***General Procedure (I):*** *Coupling of L-HL hydrobromide salt to substituted benzoic acids.*



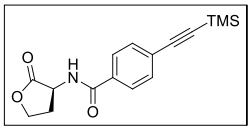
***N*-(4-Iodobenzoyl)-L-homoserine lactone (7).** 4-Iodobenzoic acid (12.40 g, 50.0 mmol) was dissolved in dichloromethane (200 mL) in a round-bottomed flask fitted with a magnetic stirring bar. Oxalyl chloride (10.0 mL, 14.64 g, 115.4 mmol) and dry DMF (192 μL, 0.18 g, 2.5 mmol) were added. The reaction mixture was stirred for 5 h at room temperature, whereupon the volatiles were removed *in vacuo*. he residue was dissolved in dry DMF (130 mL) and triethylamine (16.0 mL, 11.68 g, 115.4 mmol). After 15 min L-homoserine lactone hydrobromide salt (**1**) (7.00 g, 38.5 mmol) dissolved in dry DMF (70 mL) was added. The reaction mixture was stirred for 2 h at room temperature. The volatiles were removed *in vacuo* and the residue was purified by flash column chromatography on silica gel (ethyl acetate followed by dichloromethane) to give a crystalline compound containing the title compound as the major component (as observed by NMR). The material was dissolved in methanol and undissolved residues were filtered off. The filtrate was concentrated *in vacuo* to

give the title compound as an off-white solid (9.67 g, 76 %). Mp: 260-264 °C; RP-HPLC purity: > 95 % (R_t = 6.16 min); ^{1}H NMR (300 MHz, DMSO-d_6) δ 9.05 (d, J = 8.1 Hz, 1H),7.90-7.87 (m, 1H), 7.64-7.61 (m, 1H), 4.76 (td, J = 10.7, 8.7 Hz, 1H), 4.41 (dt, J = 8.8, 1.9 Hz, 1H), 4.27 (ddd, J = 10.3, 8.8, 6.6 Hz, 1H), 2.50-2.40 (m, 1H), 2.38-2.24 (m, 1H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 175.1, 165.3, 137.3, 132.7, 129.1, 99.4, 65.3, 49.2, 48.4, 27.9; IR (neat) cm^{-1}: 3255, 3068, 2992, 2916, 1773, 1643, 1584, 1537, 1478, 1375, 1316, 1216, 1159, 1003, 914, 840, 756, 712, 671, 535, 427; $[\alpha]_D^{20}$: -16.65° (*c*: 0.020, DMSO); MS (ESI) calcd for $C_{11}H_{11}INO_3$ $[M + H]^+$: 332.0, found: 332.1.



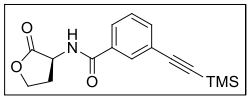
***N*-(3-iodobenzoyl)-L-homoserine lactone (8).** Following *General Procedure (I)*, the reaction of 3-iodobenzoic acid (12.40 g, 50.0 mmol), oxalyl chloride (10.0 mL, 14.64 g, 115.4 mmol), dry DMF (192 μL, 0.18 g, 2.5 mmol), triethylamine (16.0 mL, 11.68 g, 115.4 mmol) and L-homoserine lactone hydrobromide salt (**1**) (7.00 g, 38.5 mmol) gave, after flash column chromatography on silica gel (ethyl acetate followed by dichloromethane), a crystalline compound containing the title compound as the major component. The material was then washed with heptane to give the title compound as an off-white solid (11.48 g, 90 %). Mp: 163-166 °C; RP-HPLC purity: > 95 % (R_t = 6.15 min); ^{1}H NMR (300 MHz, DMSO-d_6) δ 9.08 (d, J = 8.0 Hz, 1H), 8.20 (t, J = 1.6 Hz, 1H), 7.93 (ddd, J = 7.8, 1.7, 1.0 Hz, 1H), 7.86 (ddd, J = 7.8, 1.7, 1.0 Hz, 1H), 7.31 (t, J = 7.8 Hz, 1H), 4.78 (td, J = 10.6, 8.6 Hz, 1H), 4.41 (dt, J = 8.7, 1.7 Hz, 1H), 4.27 (ddd, J = 10.4, 8.8, 6.6 Hz, 1H), 2.51-2.41 (m, 1H), 2.38-2.23 (m, 1H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 175.2, 164.5, 140.1, 135.6, 135.3, 130.6, 126.7, 94.7, 65.3, 49.2, 48.4, 27.9; IR (neat) cm^{-1}: 3263, 1768, 1639, 1537, 1378, 1319, 1221, 1166, 1013, 950, 805, 750, 683; $[\alpha]_D^{20}$: -14.75° (*c*: 0.020, DMSO); MS (ESI) calcd for $C_{11}H_{11}INO_3$ $[M + H]^+$: 332.0, found: 332.1.

- ***General Procedure (II):*** *Sonogashira cross-coupling of TMS-acetylenes to aromatic iodides.*



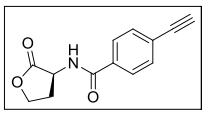
***N*-(4-Trimethylsilylethynylobenzoyl)-L-homoserine lactone (9).** *N*-(4-Iodobenzoyl)-L-homoserine lactone (**7**) (166 mg, 0.5 mmol), tetrakistriphenylphosphine palladium (11.6 mg, 0.01 mmol) and copper(I) iodide (3.8 mg, 0.02 mmol) were charged in a flame-dried Schlenck-flask fitted with a magnetic stirring bar. After three successive vacuum/argon cycles, a mixture of NEM:DMF (1:1, 5 mL) was added, followed by trimethylsilylacetylene (85 μL, 59 mg, 0.6 mmol). A white precipitate formed immediately. The reaction mixture was stirred overnight at room temperature. The volatiles were then removed by *in vacuo*. The black residue was dissolved in dichloromethane (20 mL) and treated with water (20 mL) and aqueous HCl (1 M, 4 mL) for 2 min. The organic layer was separated and the aqueous phase was extracted with dichloromethane (2 × 20 mL). The combined organic layers were dried over magnesium sulfate, filtered and concentrated *in vacuo*. The residue was purified by flash column chromatography on silica gel (gradient 100 % heptane to 100 % ethyl acetate) to give the title compound as a beige solid (137 mg, 91 %). Mp: 165-167 °C; RP-HPLC purity: > 95 % (R_t = 8.19 min); ^{1}H NMR (300 MHz, DMSO-d_6) δ 9.09 (d, J = 7.9 Hz, 1H), 7.86 (d, J = 8.2 Hz, 2H), 7.58 (d, J = 8.1 Hz, 2H), 4.78 (td, J = 10.3, 8.7 Hz, 1H), 4.41 (t, J = 8.6 Hz, 1H), 4.27 (ddd, J = 9.8, 8.7, 6.6 Hz, 1H), 2.46 (m, 1H), 2.34 (m, 1H), 0.24 (d, J = 1.2 Hz, 9H); IR (neat) cm^{-1}: 3288, 2958, 2159, 1774, 1643,

1541, 1497, 1381, 1322, 1248, 1222, 1179, 1013, 839, 758; $[\alpha]_D^{20}$: -17.90° (*c*: 0.020, DMSO); MS (ESI) calcd for $C_{16}H_{20}NO_3Si$ $[M + H]^+$: 302.1, found: 302.2.

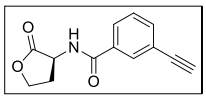


***N*-(3-Trimethylsilylethynylobenzoyl)-L-homoserine lactone (10).** Following *General Procedure (II)*, the reaction of *N*-(3-iodobenzoyl)-L-homoserine lactone (**8**) (166 mg, 0.5 mmol), trimethylsilylacetylene (85 μL, 59 mg, 0.6 mmol), tetrakistriphenylphosphine palladium (11.6 mg, 0.01 mmol) and copper(I) iodide (3.8 mg, 0.02 mmol) gave, after flash column chromatography on silica gel (gradient 100 % heptane to 100 % ethyl acetate), the title compound as a white solid (141 mg, 94 %). Mp: 168 °C; RP-HPLC purity: > 95 % (R_t = 8.19 min); ^{1}H NMR (300 MHz, DMSO-d_6) δ 9.09 (d, *J* = 8.0 Hz, 1H), 7.94 (t, *J* = 1.6 Hz, 1H), 7.89-7.87 (m, 1H), 7.66-7.63 (m, 1H), 7.51 (t, *J* = 7.7 Hz, 1H), 4.80 (td, *J* = 10.8, 8.9 Hz, 1H), 4.42 (dt, *J* = 8.8, 1.8 Hz, 1H), 4.28 (ddd, *J* = 10.2, 8.8, 6.6 Hz, 1H), 2.51-2.42 (m, 1H), 2.39-2.25 (m, 1H), 0.25 (d, *J* = 0.6 Hz, 9H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 175.1, 164.9, 134.4, 133.7, 130.0, 129.0, 128.0, 122.2, 104.2, 95.0, 65.3, 49.2, 48.4, 28.0, -0.3; IR (neat) cm^{-1}: 3375, 2959, 2157, 1758, 1661, 1533, 1301, 1225, 1197, 840, 758, 686; $[\alpha]_D^{20}$: -14.60° (*c*: 0.020, DMSO); MS (ESI) calcd for $C_{16}H_{20}NO_3Si$ $[M + H]^+$: 302.1 found: 302.2.

- ***General Procedure (III):*** *TMS-deprotection.*



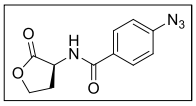
***N*-(4-Ethynylobenzoyl)-L-homoserine lactone (11).** *N*-(4-Trimethylsilylethynylobenzoyl)-L-homoserine lactone (**9**) (1.12 g, 3.72 mmol), TBAF (2.70 mL, 2.43 g, 9.31 mmol) and THF (19 mL) were added to a round-bottomed flask fitted with a magnetic stirring bar. The reaction mixture was stirred overnight at room temperature. The reaction mixture was poured into a separation funnel containing water (130 mL) and dichloromethane (150 mL). The organic layer was separated and the aqueous phase was extracted with dichloromethane (2 × 150 mL). The combined organic layers were dried over magnesium sulfate, filtered and concentrated *in vacuo*. The residue was then filtered through a short silica gel column and the filtrate was concentrated *in vacuo* to give the title compound as a white solid (591 mg, 58 %). Mp: 194-196 °C; RP-HPLC purity: > 95 % (R_t = 5.46 min); ^{1}H NMR (300 MHz, DMSO-d_6) δ 9.08 (d, *J* = 8.0 Hz, 1H), 7.86-7.83 (m, 2H), 7.61-7.58 (m, 2H), 4.81-4.72 (m, 1H), 4.44-4.37 (m, 2H), 4.26 (ddd, *J* = 10.3, 8.7, 6.6 Hz, 1H), 2.50-2.40 (m, 1H), 2.37-2.25 (m, 1H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 175.9, 165.9, 134.1, 132.5, 128.2, 125.6, 83.8, 83.5, 66.1, 49.2, 28.6; IR (neat) cm^{-1}: 3413, 3277, 2913, 1771, 1662, 1534, 1498, 1380, 1316, 1180, 1016, 952, 854, 764, 658; $[\alpha]_D^{20}$: -2.27° (*c*: 0.015, DMSO); MS (ESI) calcd for $C_{13}H_{12}NO_3$ $[M + H]^+$: 230.1, found: 230.2.



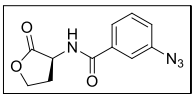
***N*-(3-Ethynylobenzoyl)-L-homoserine lactone (12).** Following *General Procedure (III)*, the reaction of *N*-(3-trimethylsilylethynylobenzoyl)-L-homoserine lactone (**10**) (1.34 g, 4.44 mmol) and TBAF (3.21 mL, 2.90 g, 11.1 mmol) gave, after filtration through a short silica gel column, the title compound as a white solid (553 mg, 65 %). Mp: 158-160 °C; RP-HPLC purity: > 95 % (R_t = 5.47 min); ^{1}H NMR (300 MHz, DMSO-d_6) δ 9.09 (d, *J* = 8.0 Hz, 1H), 7.95 (t, *J* = 1.5 Hz, 1H), 7.89-7.86 (m, 1H), 7.66 (td, *J* = 7.7, 1.2 Hz, 1H), 7.52 (t, *J* = 7.7 Hz, 1H), 4.78 (td, *J* = 10.7, 9.0 Hz, 1H), 4.41 (dt, *J* = 8.7, 1.8 Hz, 1H), 4.31 (s, 1H), 4.29-4.22 (m, 1H), 2.50-2.41 (m, 1H), 2.38-2.24 (m, 1H); ^{13}C

NMR (75 MHz, DMSO-d_6) δ 175.9, 165.7, 135.3, 134.5, 131.0, 129.8, 128.6, 122.6, 83.4, 82.3, 66.1, 49.9, 49.2, 28.7; IR (neat) cm^{-1}: 3269, 3271, 1774, 1644, 1531, 1377, 1223, 1172, 1108, 1016, 950, 819, 692; $[\alpha]_D^{20}$: -3.60° (*c*: 0.015, DMSO); MS (ESI) calcd for $C_{13}H_{12}NO_3$ $[M + H]^+$: 230.1, found: 230.2.

- ***General Procedure (IV):*** *Azidation of aromatic iodides.*[2]



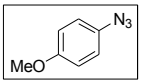
***N*-(4-Azidobenzoyl)-L-homoserine lactone (13).** *N*-(4-Iodobenzoyl)-L-homoserine lactone (**7**) (3.00 g, 9.06 mmol), sodium azide (1.18 g, 18.12 mmol), copper(I) iodide (350 g, 1.81 mmol) and sodium ascorbate (179 mg, 0.91 mmol) were added to a round-bottomed flask fitted with a magnetic stirring bar followed by degassed DMSO:H_2O (5:1, 60 mL) and *N,N'*-dimethylethylenediamine (293 μL, 240 mg, 2.718 mmol). The reaction mixture was stirred overnight at room temperature, whereupon it was poured into a separation funnel containing brine (170 mL) and ethyl acetate (170 mL). The organic layer was separated and the aqueous phase was extracted with ethyl acetate (3 × 170 mL). The combined organic layers were dried over magnesium sulfate, filtered and concentrated *in vacuo*. The residue was then filtered through a short silica gel column, and the filtrate was concentrated *in vacuo* to give the title compound as a light yellow solid (1.61 g, 72 %). Mp: 165 °C; RP-HPLC purity: > 95 % (R_t = 5.49 min); ^{1}H NMR (300 MHz, DMSO-d_6) δ 9.00 (d, *J* = 8.0 Hz, 1H), 7.91 (d, *J* = 8.4 Hz, 2H), 7.23 (d, *J* = 8.4 Hz, 2H), 4.77 (td, *J* = 17.6, 8.9 Hz, 1H), 4.41 (dt, *J* = 8.7, 1.5 Hz, 1H), 4.31-4.23 (m, 1H), 2.54-2.40 (m, 1H), 2.36-2.26 (m, 1H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 175.3, 165.0, 142.7, 129.9, 129.1, 119.0, 65.3, 49.2, 48.4, 27.9; IR (neat) cm^{-1}: 3272, 2408, 2089, 1764, 1638, 1600, 1536, 1596, 1382, 1279, 1220, 1178, 1011, 848, 761, 691; $[\alpha]_D^{20}$: -22.30° (*c*: 0.020, DMSO); MS (ESI) calcd for $C_{11}H_{11}N_4O_3$ $[M + H]^+$: 247.1, found: 247.2.



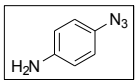
***N*-(3-Azidobenzoyl)-L-homoserine lactone (14).** Following *General Procedure (IV)*, the reaction of *N*-(3-iodobenzoyl)-L-homoserine lactone (**8**) (3.00 g, 9.06 mmol), sodium azide (1.18 g, 18.12 mmol), copper(I) iodide (350 g, 1.81 mmol), sodium ascorbate (179 mg, 0.91 mmol) and *N,N'*-dimethylethylenediamine (293 μL, 240 mg, 2.78 mmol) gave, after filtration through a short silica gel column, the title compound as a light yellow solid (1.74 g, 78 %). Mp: 193-197 °C; RP-HPLC purity: > 95 % (R_t = 5.58 min); ^{1}H NMR (300 MHz, DMSO-d_6) δ 9.11 (d, *J* = 8.0 Hz, 1H), 7.70-7.67 (m, 1H), 7.59-7.58 (m, 1H), 7.53 (t, *J* = 7.9 Hz, 1H), 7.30 (dd, *J* = 8.0, 2.3 Hz, 1H), 4.79 (td, *J* = 10.5, 8.9 Hz, 1H), 4.43 (dt, *J* = 8.8, 1.7 Hz, 1H), 4.29 (ddd, *J* = 9.9, 8.9, 6.8 Hz, 1H), 2.54-2.41 (m, 1H), 2.38-2.27 (m, 1H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 175.1, 164.9, 139.8, 135.0, 130.2, 123.9, 122.3, 117.6, 65.3, 49.1, 48.5, 27.9; IR (neat) cm^{-1}: 3274, 3065, 2925, 2124, 1767, 1642, 1536, 1439, 1372, 1310, 1216, 1168, 1113, 1012, 952, 900, 828, 694, 614, 533; $[\alpha]_D^{20}$: -19.85° (*c*: 0.020, DMSO); MS (ESI) calcd for $C_{11}H_{11}N_4O_3$ $[M + H]^+$: 247.1, found: 247.2.

[2] Andersen, J.; Madsen, U.; Björkling, F.; Liang, X. *Synlett*. **2005**, *14*, 2209-2213.

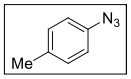
Synthesis of aromatic azide building blocks.



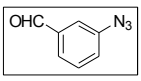
4-Azidoanisole. Following *General Procedure (IV)*, the reaction of 4-iodoanisole (936 mg, 4 mmol), sodium azide (520 mg, 8 mmol), copper(I) iodide (76 mg, 0.40 mmol), sodium ascorbate (40 mg, 0.20 mmol) and *N,N'*-dimethylethylenediamine (64 μL, 53 mg, 0.60 mmol) gave, after filtration through a short silica gel column, the title compound as a brown oil (548 mg, 92 %). ^{1}H NMR (300 MHz, DMSO-d_6) δ 6.97-6.93 (m, 2H), 6.91-6.87 (m, 2H), 3.79 (d, J = 0.4 Hz, 3H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 156.6, 131.3, 120.0, 115.1, 55.2; IR (neat) cm^{-1}: 3225, 2953, 2836, 2097, 1585, 1500, 1463, 1283, 1239, 1179, 1107, 1031, 821, 754, 623, 513; R_f = 0.59 (heptane:ethyl acetate (4:1), *p*-anisaldehyde).



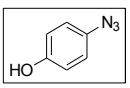
4-Azidoaniline. Following *General Procedure (IV)*, the reaction of 4-iodoaniline (876 mg, 4 mmol), sodium azide (520 mg, 8 mmol), copper(I) iodide (76 mg, 0.40 mmol), sodium ascorbate (40 mg, 0.20 mmol) and *N,N'*-dimethylethylenediamine (64 μL, 53 mg, 0.60 mmol) gave, after filtration through a short silica gel column the, title compound as orange crystals (429 mg, 80 %). ^{1}H NMR (300 MHz, DMSO-d_6) δ 6.78 (d, J = 8.7 Hz, 2H), 6.59 (d, J = 8.6 Hz, 2H), 5.14 (s, 2H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 146.4, 125.9, 119.6, 114.9; IR (neat) cm^{-1}: 3394, 3318, 2101, 1632, 1502, 1257; R_f = 0.17 (heptane:ethyl acetate (4:1), *p*-anisaldehyde).



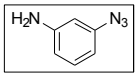
4-Azidotoluene. Following *General Procedure (IV)*, the reaction of 4-iodotoluene (872 mg, 4 mmol), sodium azide (520 mg, 8 mmol), copper(I) iodide (76 mg, 0.40 mmol), sodium ascorbate (40 mg, 0.20 mmol) and *N,N'*-dimethylethylenediamine (64 μL, 53 mg, 0.60 mmol) gave, after filtration through a short silica gel column, the title compound as a yellow oil (520 mg, 88 %). ^{1}H NMR (300 MHz, DMSO-d_6) δ 7.19 (d, J = 8.6 Hz, 2H), 6.98 (d, J = 8.4 Hz, 2H), 2.26 (s, 3H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 136.3, 134.2, 130.2, 118.6, 20.1; IR (neat) cm^{-1}: 2104, 1609, 1521; R_f = 0.62 (heptane, *p*-anisaldehyde).



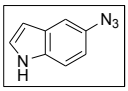
3-Azidobenzaldehyde. Following *General Procedure (IV)*, the reaction of 3-iodobenzaldehyde (928 mg, 4 mmol), sodium azide (520 mg, 8 mmol), copper(I) iodide (76 mg, 0.40 mmol), sodium ascorbate (40 mg, 0.20 mmol) and *N,N'*-dimethylethylenediamine (64 μL, 53 mg, 0.60 mmol) gave, after filtration through a short silica gel column, the title compound as a yellow oil (488 mg, 83 %). ^{1}H NMR (300 MHz, DMSO-d_6) δ 10.01 (s, 1H), 7.72 (td, J = 7.5, 1.3 Hz, 1H), 7.64 (d, J = 7.6 Hz, 1H), 7.60-7.59 (m, 1H), 7.43 (ddd, J = 7.8, 2.4, 1.1 Hz, 1H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 192.3, 140.4, 137.5, 130.6, 125.9, 124.8, 119.2; IR (neat) cm^{-1}: 2838, 2732, 2109, 1694, 1583, 1479, 1283; R_f = 0.39 (heptane:ethyl acetate (4:1), *p*-anisaldehyde).



4-azidophenol. Following *General Procedure (IV)*, the reaction of 4-iodophenol (880 mg, 4 mmol), sodium azide (520 mg, 8 mmol), copper(I) iodide (76 mg, 0.40 mmol), sodium ascorbate (40 mg, 0.20 mmol) and *N,N'*-dimethylethylenediamine (64 μL, 53 mg, 0.60 mmol) gave, after filtration through a short silica gel column, the title compound as a black solid (520 mg, > 95 %). ^{1}H NMR (300 MHz, DMSO-d_6) δ 9.49 (s, 1H), 6.88 (d, J = 8.8 Hz, 2H), 6.76 (d, J = 8.6 Hz, 2H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 155.6, 130.2, 120.7, 117.2; IR (neat) cm^{-1}: 3600-3200, 2105, 1593, 1503, 1210, 822, 631, 507; R_f = 0.31 (heptane:ethyl acetate (4:1), *p*-anisaldehyde).



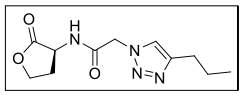
3-Azidoaniline. Following *General Procedure (IV)*, the reaction of 3-iodoaniline (481 μL, 876 mg, 4 mmol), sodium azide (520 mg, 8 mmol), copper(I) iodide (0.40 mmol, 76 mg), sodium ascorbate (40 mg, 0.20 mmol) and *N,N'*-dimethylethylenediamine (64 μL, 53 mg, 0.60 mmol) gave, after filtration through a short silica gel column, the title compound as a brown oil (466 mg, 87 %). ^{1}H NMR (300 MHz, DMSO-d_6) δ 7.02 (t, J = 7.9 Hz, 1H), 6.41-6.37 (m, 1H), 6.30 (dt, J = 2.1, 0.6 Hz, 1H), 6.23-6.19 (m, 1H), 5.34 (s, 2H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 150.2, 139.6, 130.1, 111.0, 106.0, 103.5; IR (neat) cm^{-1}: 3455, 3361, 2104, 1595, 1489, 1299, 1245; R_f = 0.20 (heptane:ethyl acetate (4:1), *p*-anisaldehyde).



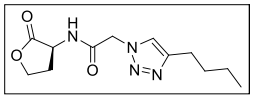
5-Azidoindole. Following *General Procedure (IV)*, the reaction of 5-iodoindole (1.94 g, 8 mmol), sodium azide (1.04 g, 16 mmol), copper(I) iodide (152 mg, 0.8 mmol), sodium ascorbate (79 mg, 0.4 mmol) and *N,N'*-dimethylethylenediamine (129 μL, 106 mg g, 1.2 mmol) gave, after filtration through a short silica gel column, the title compound as a brown solid (1.234 g, > 95 %). Mp: 88-90 °C; ^{1}H NMR (300 MHz, DMSO-d_6) δ 11.24 (s, 1H), 7.45 (tdd, J = 8.6, 1.5, 0.9 Hz, 1H), 7.41 (dt, J = 3.1, 1.1 Hz, 1H), 7.30 (dd, J = 1.4, 0.7 Hz, 1H), 6.87-6.83 (m, 1H), 6.43-6.42 (m, 1H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 133.7, 130.2, 128.4, 127.0, 112.8, 112.7, 109.5, 100.9, 49.2; IR (neat) cm^{-1}: 3395, 3122, 3104, 2099, 1577, 1453, 1419, 1296, 1254, 859, 804, 757, 730, 604, 506.

<u>*Synthesis of triazole HLs.*</u>

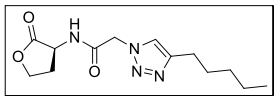
- ***General Procedure (V):*** *Triazole formation using aliphatic acetylenes and azidoacetyl homoserine lactone building block* ***3****.*



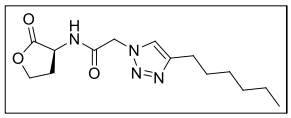
Triazole I-A. 1-Pentyne (241 μL, 166 mg, 2.44 mmol) and azide **3** (300 mg, 1.63 mmol) were dissolved in acetonitrile (6 mL) in a round-bottomed flask fitted with a magnetic stirring bar. Copper(I) iodide (31 mg, 0.16 mmol) and *N,N*-diisopropylethylamine (558 μL, 421 mg, 3.26 mmol) were then added, and the reaction was left under stirring at room temperature. The reaction was monitored by TLC for full conversion of the azide (ethyl acetate, vanillin, R_f = 0.3). Upon full conversion of starting material (16 h), the volatiles were removed *in vacuo*. The residue was dissolved in boiling acetic acid, and then filtered by hot gravity filtration. The acetic acid was removed *in vacuo*. The residue was dissolved in hot methanol. Diethyl ether was added, upon which a precipitate formed. The precipitate was then isolated and washed with diethyl ether, to give the title compound as a green powder (288 mg, 70 %). Mp: 123-126 °C; RP-HPLC purity: 83 % (R_t = 4.27 min); ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.84 (d, J = 7.7 Hz, 1H), 7.81 (s, 1H), 5.11 (s, 2H), 4.64 (td, J = 10.8, 8.8 Hz, 1H), 4.35 (dt, J = 8.8, 1.4 Hz, 1H), 4.22 (ddd, J = 10.1, 8.9, 6.4 Hz, 1H), 2.59 (t, J = 7.5 Hz, 2H), 2.46-2.39 (m, 1H), 2.23-2.09 (m, 1H), 1.67-1.52 (m, 2H,), 0.91 (t, J = 7.3 Hz, 3H); ^{13}C NMR (DMSO-d_6, from ^{1}H-^{13}C gHSQC and ^{1}H-^{13}C gHMBC, 500 MHz) δ 174.8, 165.6, 146.5, 123.1, 65.2, 51.0, 47.8, 28.1, 26.5, 21.9, 13.6; IR (neat) cm^{-1}: 3316, 2925, 2852, 1780, 1674, 1556, 1448, 1387, 1169, 1000, 945; $[\alpha]_D^{20}$: -27.0° (*c:* 0.079, DMSO); MS (ESI) calcd for $C_{11}H_{17}O_3N_4$ $[M + H]^+$: 253.1, found: 253.2.



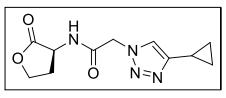
Triazole I-B. Following *General Procedure (V)*, the reaction of azide **3** (200 mg, 1.09 mmol), 1-heptyne (213 μL, 157 mg, 1.63 mmol), copper(I) iodide (21 mg, 0.11 mmol) and *N,N*-diisopropylethylamine (272 μL, 281 mg, 2.18 mmol) in acetonitrile (4 mL) gave, after precipitation with diethyl ether, the title compound as a green powder (168 mg, 58 %). Mp: 119-121 °C; RP-HPLC purity: 84 % (R_t = 5.03 min); ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.83 (d, J = 7.8 Hz, 1H), 7.80 (s, 1H), 5.10 (s, 2H), 4.64 (dt, J = 10.1, 8.2 Hz, 1H), 4.35 (t, J = 8.5 Hz, 1H), 4.26-4.18 (m, 1H), 2.61 (t, J = 7.4 Hz, 2H), 2.46-2.39 (m, 1H), 2.23-2.08 (m, 1H), 1.62-1.52 (m, 2H), 1.39-1.23 (m, 2H), 0.89 (t, J = 7.3 Hz, 3H); ^{13}C NMR (DMSO-d_6, from ^{1}H-^{13}C gHSQC and ^{1}H-^{13}C gHMBC, 500 MHz) δ 174.7, 165.4, 147.0, 123.1, 65.2, 51.0, 47.9, 31.0, 27.9, 24.2, 21.4, 13.3; IR (neat) cm^{-1}: 3296, 2932, 2858, 1776, 1671, 1555, 1372, 1172, 1000, 946; $[\alpha]_D^{20}$: -19.4° (*c:* 0.019, DMSO); MS (ESI) calcd for $C_{12}H_{19}O_3N_4$ $[M + H]^+$: 267.2, found: 267.3.



Triazole I-C. Following *General Procedure (V)*, the reaction of azide **3** (200 mg, 1.09 mmol), 1-hexyne (193 μL, 134 mg, 1.63 mmol), copper(I) iodide (21 mg, 0.11 mmol) and *N,N*-diisopropylethylamine (272 μL, 281 mg, 2.18 mmol) in acetonitrile (4 mL) gave, after precipitation with diethyl ether, the title compound as a green powder (186 mg, 61 %). Mp: 149-151 °C; RP-HPLC purity: 82 % (R_t = 5.74 min); ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.83 (d, J = 7.8Hz, 1H), 7.81 (s, 1H), 5.11 (s, 2H), 4.64 (dt, J = 10.7, 8.6 Hz, 1H), 4.35 (t, J = 8.1 Hz, 1H), 4.22 (ddd, J = 10.0, 8.9, 6.5 Hz, 1H), 2.61 (t, J = 7.4 Hz, 2H), 2.46-2.39 (m, 1H), 2.23-2.08 (m, 1H), 1.61-1.57 (m, 2H), 1.32-1.28 (m, 4H), 0.87 (t, J = 6.6 Hz, 3H); ^{13}C NMR (DMSO-d_6, from ^{1}H-^{13}C gHSQC and ^{1}H-^{13}C gHMBC, 500 MHz) δ 174.4, 165.1, 146.8, 122.8, 64.9, 50.7, 47.6, 30.1, 27.8, 27.6, 24.1, 21.2, 13.0; IR (neat) cm^{-1}: 3295, 2927, 2857, 1777, 1671, 1555, 1372, 1222, 1171, 1001, 946; $[\alpha]_D^{20}$: -11.0 (*c:* 0.014, DMSO); HRMS (ESI) calcd for $C_{13}H_{21}O_3N_4$ $[M + H]^+$: 281.1614, found: 281.1601.

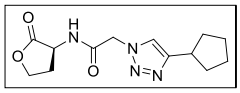


Triazole I-D. Following *General Procedure (V),* the reaction of azide **3** (200 mg, 1.09 mmol), 1-octyne (241 μL, 180 mg, 1.63 mmol), copper(I) iodide (21 mg, 0.11 mmol) and *N,N*-diisopropylethylamine (272 μL, 281 mg, 2.18 mmol) in acetonitrile (4 mL), gave after precipitation with diethyl ether, the title compound as green crystals (207 mg, 65 %). Mp: 142-144 °C; RP-HPLC purity: 86 % (R_t = 6.38 min); ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.83 (d, J = 7.5 Hz, 1H), 7.80 (s, 1H), 5.10 (s, 2H, 4.64 (dt, J = 10.3, 8.6 Hz, 1H), 4.35 (t, J = 8.2 Hz, 1H), 4.22 (ddd, J = 10.2, 8.8, 6.3 Hz, 1H), 2.61 (t, J = 7.4 Hz, 2H), 2.46-2.40 (s, 1H), 2.23-2.08 (m, 1H), 1.60-1.54 (m, 2H), 1.35-1.21 (m, 6H), 0.86 (t, J = 5.8 Hz, 3H); ^{13}C NMR (DMSO-d_6, from ^{1}H-^{13}C gHSQC and ^{1}H-^{13}C gHMBC, 500 MHz) δ 174.5, 165.2, 146.8, 123.0, 65.1, 50.8, 48.2, 30.4, 28.2, 27.8, 27.6, 24.5, 21.6, 13.4; IR (neat) cm^{-1}: 3298, 2923, 2853, 1777, 1671, 1556, 1371, 1172, 1001, 946; $[\alpha]_D^{20}$: -19.0° (*c:* 0.10, DMSO); MS (ESI) calcd for $C_{14}H_{23}O_3N_4$ $[M + H]^+$: 295.2, found: 295.3.

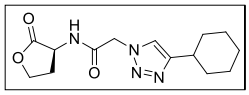


Triazole I-E. Following *General Procedure (V)*, the reaction of azide **3** (200 mg, 1.09 mmol), cyclopropylacetylene (138 μL, 108 mg, 1.63 mmol), copper(I) iodide (21 mg, 0.11 mmol) and *N,N*-diisopropylethylamine (272 μL, 281 mg, 2.18 mmol) in acetonitrile (4 mL) gave, after precipitation with diethyl ether, the title compound as a green powder (211 mg, 77 %). Mp: 104-107 °C; RP-HPLC purity: 69 % (R_t = 3.86 min); ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.81 (d, J = 7.9 Hz, 1H), 7.77 (s, 1H), 5.07 (s, 2H), 4.62 (dt, J = 10.8, 8.6 Hz, 1H), 4.34 (dt, J = 8.4, 1.2 Hz, 1H), 4.21 (ddd, J = 10.1, 8.8, 6.4

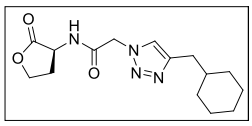
Hz, 1H), 2.46-2.38 (m, 1H), 2.21-2.07 (m, 1H), 1.96-1.89 (m, 1H), 0.92-0.85 (m, 2H), 0.72-0.67 (m, 2H); ^{13}C NMR (DMSO-d_6, from ^{1}H-^{13}C gHSQC and ^{1}H-^{13}C gHMBC, 500 MHz) δ 174.7, 165.5, 148.5, 122.2, 65.2, 51.0, 47.9, 28.1 7.6, 6.5; IR (neat) cm^{-1}: 3297, 1776, 1671, 1553, 1370, 1182, 1015, 1000, 947; $[\alpha]_D^{20}$: -18.6° (*c:* 0.014, DMSO); MS (ESI) calcd for $C_{11}H_{59}O_3N_4$ [M + H]$^+$: 251.1, found: 251.2.



Triazole I-F. Following *General Procedure (V)*, the reaction of azide **3** (300 mg, 1.63 mmol), cyclopentylacetylene (283 μL, 230 mg, 2.44 mmol), copper(I) iodide (31 mg, 0.16 mmol) and *N,N*-diisopropylethylamine (558 μL, 421 mg, 3.36 mmol) in acetonitrile (6 mL) gave, after precipitation with diethyl ether, the title compound as a green powder (271 mg, 61 %). Mp: 137-140 °C; RP-HPLC purity: 79 % (R_t = 5.09 min); ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.84 (d, *J* = 7.7 Hz, 1H), 7.81 (s, 1H), 5.09 (s, 2H), 4.63 (dt, *J* = 10.5, 8.7 Hz, 1H), 4.35 (t, *J* = 8.4 Hz, 1H), 4.22 (ddd, *J* = 10.3, 8.5, 6.6 Hz, 1H), 3.15-3.05 (m, 1H), 2.46-2.38 (m, 1H), 2.23-2.09 (m, 1H), 2.05-1.91 (m, 2H), 1.78-1.51 (m, 6H); ^{13}C NMR (DMSO-d_6, from ^{1}H-^{13}C gHSQC and ^{1}H-^{13}C gHMBC, 500 MHz): δ 174.7, 165.6, 151.0, 122.2 64.9 51.0, 47.7, 35.9, ,32.5, 27.9 24.2; IR (neat) cm^{-1}: 3305, 2949, 2867, 1777, 1671, 1552, 1450, 1171, 1000, 945; $[\alpha]_D^{20}$: -16.0° (*c:* 0.014, DMSO); MS (ESI) calcd for $C_{13}H_{19}O_3N_4$ [M + H]$^+$: 279.2, found: 279.3.

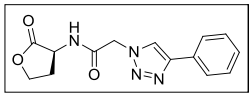


Triazole I-G. Following *General Procedure (V)*, the reaction of azide **3** (300 mg, 1.63 mmol), cyclohexylacetylene (315 μL, 204 mg, 2.44 mmol), copper(I) iodide (31 mg, 0.16 mmol) and *N,N*-diisopropylethylamine (558 μL, 421 mg, 3.26 mmol) in acetonitrile (6 mL) gave, after precipitation with diethyl ether, the title compound as a green powder (277 mg, 58 %). Mp: 136-138 °C; RP-HPLC purity: 92 % (R_t = 5.62min); ^{1}H NMR (300 MHz, DMSO-d_6) δ: 8.85 (d, *J* = 7.8 Hz, 1H), 7.78 (s, 1H), 5.10 (s, 2H), 4.63 (dt, *J* = 10.9, 8.6 Hz, 1H), 4.35 (dt, *J* = 8.8, 1.4 Hz, 1H), 4.22 (ddd, *J* = 10.4, 8.8, 6.3 Hz, 1H), 2.71-2.61 (m, 1H), 2.49-2.38 (m, 1H), 2.26-2.08 (m, 1H), 1.97-1.90 (m, 2H), 1.79-1.62 (m, 3H), 1.43-1.17 (m, 5H); ^{13}C NMR (DMSO-d_6, from ^{1}H-^{13}C gHSQC and ^{1}H-^{13}C gHMBC, 500 MHz) δ 174.6, 165.5, 162.3, 151.8, 65.0, 51.0 47.9, 34.2, 32.2, 32.0, 27.7, 25.3; IR (neat) cm^{-1}: 3316, 2924, 2852, 1780, 1673, 1555, 1387, 1169, 1014, 1000, 944; $[\alpha]_D^{20}$: -20.0° (*c*: 0.0034, DMSO); MS (ESI) calcd for $C_{14}H_{21}O_3N_4$ [M + H]$^+$: 293.2, found: 293.3.

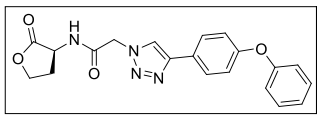


Triazole I-H. Following *General Procedure (V),* the reaction of azide **3** (300 mg, 1.63 mmol), cyclohexylpropargyl (353 μL, 290 mg, 2.44 mmol), copper(I) iodide (31 mg, 0.16 mmol) and *N,N*-diisopropylethylamine (558 μL, 421 mg, 3.26 mmol) in acetonitrile (6 mL) gave, after precipitation with diethyl ether, the title compound as a green powder (315 mg, 63 %). Mp: 114-117 °C; RP-HPLC purity: 92 % (R_t = 6.23 min); ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.82 (d, *J* = 7.7 Hz, 1H), 7.77 (s, 1H), 5.09 (s, 2H), 4.62 (td, *J* = 10.4, 8.5 Hz, 1H), 4.34 (t, *J* = 8.5 Hz, 1H), 4.24-4.16 (m, 1H), 2.45-2.38 (m, 1H), 2.21-2.05 (m, 1H), 1.66-1.42 (m, 7H), 1.23-1.05 (m, 4H), 0.96-0.83 (m, 2H); ^{13}C NMR (DMSO-d_6, from ^{1}H-^{13}C gHSQC and ^{1}H-^{13}C gHMBC, 500 MHz) δ 174.5, 165.4, 145.0, 123.5, 65.0, 50.9, 47.6, 37.5, 32.6, 32.4, 28.2, 25.9, 25.6; IR (neat) cm^{-1}: 3312, 2921, 2850, 1779, 1671, 1550, 1447, 1169, 1014, 1000, 945; $[\alpha]_D^{20}$: -18.5° (*c:* 0.0065, DMSO); MS (ESI) calcd for $C_{15}H_{23}O_3N_4$ [M + H]$^+$: 307.2, found: 307.3.

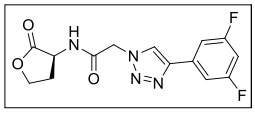
- ***General Procedure (VI):*** *Triazole formation using aromatic acetylenes and azidoacetyl HL building block* ***3****.*



Triazole I-I. Phenylacetylene (268 μL, 250 mg, 2.44 mmol) and azide **3** (300 mg, 1.63 mmol) were dissolved in acetonitrile (16 mL) in a round-bottomed flask fitted with a magnetic stirring bar. Copper(I) iodide (31 mg, 0.16 mmol) and *N*,*N*-diisopropylethylamine (558 μL, 421 mg, 3.76 mmol) were then added, and the reaction was left under stirring at room temperature. The reaction was monitored by TLC for full conversion of the azide (ethyl acetate, vanillin, R_f = 0.3). Upon full conversion of starting material (16 h), the volatiles were removed *in vacuo*. The residue was dissolved in boiling acetic acid, and then filtered by hot gravity filtration. Diethyl ether was added, upon which a precipitate formed. The precipitate was then isolated and washed with diethyl ether, to give the title compound as a white powder (341 mg, 73 %). Mp: 196-199 °C; RP-HPLC purity: > 95 % (R_t = 5.21 min); ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.92 (d, *J* = 7.9 Hz, 1H), 8.55 (s, 1H), 7.87 (dd, *J* = 8.2, 1.2 Hz, 2H), 7.46 (app. t, *J* = 7.5 Hz, 2H), 7.34 (dt, *J* = 7.0, 1.3 Hz, 1H), 5.24 (s, 2H), 4.68 (td, *J* = 11.0, 8.9 Hz, 1H), 4.36 (dt, *J* = 8.7, 1.5 Hz, 1H), 4.23 (ddd, *J* = 10.5, 8.7, 6.4 Hz, 1H), 2.48-2.43 (m, 1H), 2.25-2.11 (m, 1H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 174.8, 165.6, 146.1, 130.6, 128.8, 127.8, 125.0, 122.9, 65.3, 51.4, 48.1, 28.2; IR (neat) cm^{-1}: 3302, 1778, 1555, 1489, 1360, 1227, 1171, 1001; $[\alpha]_D^{20}$: -18.3 (*c:* 0.035, DMSO); MS (ESI) calcd for $C_{14}H_{15}O_3N_4$ [M + H]$^+$: 287.1, found: 287.2.

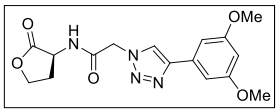


Triazole I-J. Following *General Procedure (VI)*, the reaction of azide **3** (300 mg, 1.63 mmol), 1-ethynyl-4-phenoxybenzene (442 μL, 475 mg, 2.44 mmol), copper(I) iodide (31 mg, 0.16 mmol) and *N*,*N*-diisopropylethylamine (558 μL, 421 mg, 3.76 mmol) gave, after precipitation with diethyl ether, the title compound as an amorphous white solid (487 mg, 79 %). Mp: 190-193 °C; RP-HPLC purity: > 95 % (R_t = 7.13 min); ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.92 (d, *J* = 7.9 Hz, 1H), 8.51 (s, 1H), 7.87 (d, *J* = 8.1 Hz, 2H), 7.42 (dt, *J* = 7.5, 0.8 Hz, 2H), 7.17 (dt, *J* = 7.6, 1.0 Hz, 2H), 7.10-7.05 (m, 4H), 5.23 (s, 2H), 4.68 (td, *J* = 10.5, 8.4 Hz, 1H), 4.36 (t, *J* = 8.4 Hz, 1H), 4.23 (ddd, *J* = 10.8, 9.1, 6.5 Hz, 1H), 2.48-2.42 (m, 1H), 2.25-2.10 (m, 1H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 174.8, 165.6, 156.3, 145.6, 130.0, 126.8, 125.9, 123.5, 122.5, 118.8, 118.7, 65.3, 51.4, 48.1, 28.2; IR (neat) cm^{-1}: 3300, 1779, 1672, 1557, 1489, 1369, 1247, 1168, 1001; $[\alpha]_D^{20}$: -13.4° (*c:* 0.026, DMSO); HRMS (ESI) calcd for $C_{20}H_{19}O_4N_4$ [M + H]$^+$: 379.1406, found: 379. 1393.

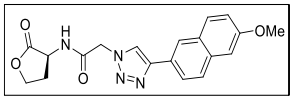


Triazole I-K. Following *General Procedure (VI)*, the reaction of azide **3** (300 mg, 1.63 mmol), 1-ethynyl-3,5-difluorobenzene (290 μL, 337 mg, 2.44 mmol), copper(I) iodide (31 mg, 0.16 mmol) and *N*,*N*-diisopropylethylamine (558 μL, 421 mg, 3.76 mmol) gave, after precipitation with diethyl ether, the title compound as a white powder (442 mg, 84 %). Mp: 240-242 °C; RP-HPLC purity: > 95 % (R_t = 5.99 min); ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.95 (d, *J* = 7.9 Hz, 1H), 8.71 (s, 1H), 7.61 (dd, *J* = 7.4, 1.1 Hz, 2H), 7.23 (dt, *J* = 9.4, 2.0 Hz, 1H), 5.27 (s, 2H), 4.68 (td, *J* = 10.8, 8.6 Hz, 1H), 4.36 (t, *J* = 8.7 Hz, 1H), 4.23 (ddd, *J* = 10.5, 9.4, 6.2 Hz, 1H), 2.47-2.43 (m, 1H), 2.25-2.11 (m, 1H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 174.7, 165.4, 144.2, 134.1, 124.3, 108.1, 107.8, 103.0, 65.3, 51.5, 48.1, 28.2; IR (neat) cm^{-1}: 3276, 1774, 1671, 1633, 1596, 1559, 1283, 1221,

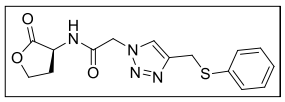
1181, 1122, 850; $[\alpha]_D^{20}$: -21.6° (*c:* 0.031, DMSO); MS (ESI) calcd for $C_{14}H_{13}F_2O_3N_4$ $[M + H]^+$: 323.1, found: 323.2.



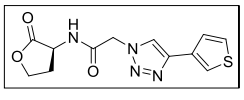
Triazole I-L. Following *General Procedure (VI)*, the reaction of azide **3** (300 mg, 1.63 mmol), 1-ethynyl-3,5,-dimethoxybenzene (336 μL, 362 mg, 2.44 mmol), copper(I) iodide (31 mg, 0.16 mmol) and *N,N*-diisopropylethylamine (558 μL, 421 mg, 3.76 mmol) gave, after precipitation with diethyl ether, the title compound as an off-white powder (481 mg, 85 %). Mp: 157-160 °C; RP-HPLC purity: > 95 % (R_t = 5.64 min); ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.93 (d, *J* = 7.9 Hz, 1H), 8.59 (s, 1H), 7.04 (d, *J* = 2.3 Hz, 2H), 6.47 (t, *J* = 2.2 Hz, 1H), 5.23 (s, 2H), 4.68 (td, *J* = 10.9, 8.6 Hz, 1H), 4.36 (dt, *J* = 8.6, 1.2 Hz, 1H), 4.23 (ddd, *J* = 10.4, 8.8, 6.3 Hz, 1H), 3.79 (s, 6H), 2.49-2.41 (m, 1H), 2.25-2.11 (m, 1H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 174.8, 165.5, 160.7, 146.0, 132.4, 123.4, 102.9, 99.8, 65.3, 55.1, 51.4, 48.1, 28.2; IR (neat) cm^{-1}: 3282, 1756, 1669, 1595, 1534, 1453, 1361, 1151, 1063, 1043, 1002; $[\alpha]_D^{20}$: -17.0° (*c:* 0.029, DMSO); HRMS (ESI) calcd for $C_{16}H_{19}O_5N_4$ $[M + H]^+$: 347.1355, found: 347.1366.



Triazole I-M. Following *General Procedure (VI)*, the reaction of azide **3** (300 mg, 1.63 mmol), 2-ethynyl-6-methoxyl-naphthalene (455 mg, 2.44 mmol), copper(I) iodide (31 mg, 0.16 mmol) and *N,N*-diisopropylethylamine (558 μL, 421 mg, 3.76 mmol) gave, after precipitation with diethyl ether, the title compound as an amorphous off-white solid (510 mg, 84 %). Mp: 219-221 °C; RP-HPLC purity: > 95 % (R_t = 6.38 min); ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.94 (d, *J* = 7.8 Hz, 1H), 8.60 (s, 1H), 8.36 (s, 1H), 7.96 (dd, *J* = 8.5, 1.6 Hz, 1H), 7.89 (d, *J* = 8.7 Hz, 2H), 7.35 (d, *J* = 2.4 Hz, 1H), 7.19 (dd, *J* = 8.9, 2.5 Hz, 1H), 5.27 (s, 2H), 4.69 (td, *J* = 10.9, 8.9 Hz, 1H), 4.37 (dt, *J* = 8.7, 1.4 Hz, 1H), 4.24 (ddd, *J* = 10.3, 8.8, 6.4 Hz, 1H), 3.89 (s, 3H), 2.49-2.42 (m, 1H), 2.27-2.12 (m, 1H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 174.9, 165.6, 157.3, 146.3, 133.8, 129.4, 128.4, 127.3, 125.8, 124.0, 123.3, 122.8, 119.0, 105.9, 65.3, 55.1, 51.5, 48.1, 28.2; IR (neat) cm^{-1}: 3289, 1767, 1672, 1610, 1554, 1882, 1384, 1260, 1219, 1180, 1164, 1016; $[\alpha]_D^{20}$: -16.7° (*c:* 0.0082, DMSO); MS (ESI) calcd for $C_{19}H_{19}O_4N_4$ $[M + H]^+$: 367.1, found: 367.3.

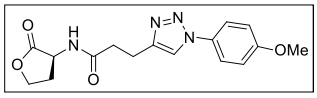


Triazole I-N. Following *General Procedure (VI)*, the reaction of azide **3** (300 mg, 1.63 mmol), phenyl propargyl sulfide (336 μL, 362 mg, 2.44 mmol), copper(I) iodide (31 mg, 0.16 mmol) and *N,N*-diisopropylethylamine (558 μL, 421 mg, 3.76 mmol) gave, after precipitation with diethyl ether, the title compound as a brown powder (389 mg, 72 %). Mp: 80-82 °C; RP-HPLC purity: > 95 % (R_t = 5.78 min); ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.86 (d, *J* = 7.7 Hz, 1H), 7.93 (s, 1H), 7.38-7.27 (m, 4H), 7.17 (t, *J* = 6.8 Hz, 1H), 5.12 (s, 2H), 4.63 (td, *J* = 10.5, 8.6 Hz, 1H), 4.33 (t, *J* = 8.5 Hz, 1H), 4.29 (s, 2H), 4.24-4.16 (m, 1H), 2.45-2.38 (m, 1H), 2.20-2.06 (m, 1H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 175.5, 166.3, 136.5, 129.6, 128.6, 126.5, 125.5, 66.0, 52.0, 48.8, 28.9, 27.7; IR (neat) cm^{-1}: 3242, 1775, 1672, 1551, 1480, 1373, 1222, 1170, 1020; $[\alpha]_D^{20}$: -16.9 (*c:* 0.011, DMSO); MS (ESI) calcd for $C_{15}H_{17}O_3N_4S$ $[M + H]^+$: 333.1, found: 333.0.

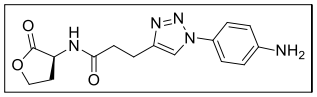


Triazole I-O. Following *General Procedure (VI)*, the reaction of azide **3** (300 mg, 1.63 mmol), 3-ethynylthiophene (241 μL, 264 mg, 2.44 mmol), copper(I) iodide (31 mg, 0.16 mmol) and *N,N*-diisopropylethylamine (558 μL, 421 mg, 3.76 mmol) gave, after precipitation with diethyl ether, the title compound as an off-

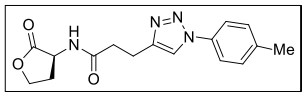
white powder (328 mg, 69 %). Mp: 197-200 °C; RP-HPLC purity: > 95 % (R_t = 4.91 min); ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.91 (d, J = 7.9 Hz, 1H), 8.41 (s, 1H), 7.88 (dd, J = 2.9, 1.2 Hz, 1H), 7.65 (dd, J = 5.0, 3.0 Hz, 1H), 7.54 (dd, J = 5.0, 1.2 Hz, 1H), 5.22 (s, 2H), 4.68 (td, J = 10.9, 8.7 Hz, 1H), 4.36 (dt, J = 8.7, 1.4 Hz, 1H), 4.23 (ddd, J = 10.4, 8.7, 6.4 Hz, 1H), 2.49-2.41 (m, 1H), 2.25-2.10 (m, 1H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 174.8, 165.6, 142.7, 131.9, 127.0, 125.7, 122.6, 120.7, 65.3, 51.4, 48.1, 28.2; IR (neat) cm^{-1}: 3300, 1780, 1556, 1369, 1171, 1001, 779; $[\alpha]_D^{20}$: -20.7° (*c:* 0.010, DMSO); MS (ESI) calcd for $C_{12}H_{13}O_3N_4S$ $[M + H]^+$: 293.1, found: 293.2



Triazole II-A. Following *General Procedure (V)*, the reaction of alkyne **4** (185 mg, 1.02 mmol), 4-azidoanisole (228 mg, 1.53 mmol), copper(I) iodide (29 mg, 0.15 mmol) and *N,N*-diisopropylethylamine (524 μL, 396 mg, 3.06 mmol) in acetonitrile (8 mL) gave, after precipitation with diethyl ether, the title compound as a sand coloured powder (239 mg, 71 %). Mp: 143-144 °C; RP-HPLC purity: > 95 % (R_t = 5.20 min); ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.49 (d, J = 7.8 Hz, 1H), 8.40 (s, 1H), 7.75 (dd, J = 9.0, 1.0 Hz, 2H),7.12 (dd, J = 8.9, 0.8 Hz, 1H), 4.55 (td, J = 10.2, 8.8 Hz, 1H), 4.35 (t, J = 8.7 Hz, 1H), 4.20 (ddd, J = 9.6, 9.0, 6.7 Hz, 1H), 3.82 (s, 3H), 2.94 (t, J = 7.4 Hz, 1H), 2.53 (t, J = 7.1 Hz, 1H), 2.44-2.33 (m, 1H), 2.22-2.08 (m, 1H); ^{13}C NMR (DMSO-d_6, from ^{1}H-^{13}C gHSQC and ^{1}H-^{13}C gHMBC, 500 MHz) δ 176.1, 171.9, 146.6, 130.9, 122.1, 120.9, 119.7, 115.5, 66.0, 56.1, 48.6, 35.1, 28.8, 21.8; IR (neat) cm^{-1}: 3293, 1766, 1650, 1519, 1257, 1221, 1016, 817; $[\alpha]_D^{20}$: -36.0° (*c:* 0.0030, DMSO); MS (ESI) calcd for $C_{16}H_{19}O_4N_4$ $[M + H]^+$: 311.1, found: 331.4.

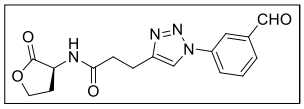


Triazole II-B. Following *General Procedure (V)*, the reaction of alkyne **4** (200 mg, 1.10 mmol), 4-azidoaniline (222 mg, 1.68 mmol), copper(I) iodide (32 mg, 0.15 mmol) and *N,N*-diisopropylethylamine (567 μL, 428 mg, 3.31 mmol) in acetonitrile (10 mL) gave, after precipitation with diethyl ether, the title compound as a black crystals (222 mg, 64 %). Mp: 162-164 °C; RP-HPLC purity: > 95 % (R_t = 3.28 min); ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.47 (d, J = 8.0 Hz, 1H), 8.21 (s, 1H), 7.41 (d, J = 8.3 Hz, 2H), 6.66 (d, J = 8.5 Hz, 2H), 5.45 (s, 2H), 4.54 (td, J = 8.6 Hz, J = 10.4 Hz, 1H), 4.34 (t, J = 8.8 Hz, 1H), 4.19 (dt, J = 9.5, 6.9 Hz, 1H), 2.90 (t, J = 7.5 Hz, 2H), 2.53-2.48 (m, 2H), 2.42-2.32 (m, 1H), 2.20-2.07 (m, 1H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 175.4, 171.2, 159.3, 149.0, 126.1, 121.3, 119.8, 113.7, 65.2, 47.9, 34.4, 28.0, 21.1; IR (neat) cm^{-1}: 3391, 3359, 3141, 1772, 1628, 1520, 1376, 1287, 1156, 1016, 828; $[\alpha]_D^{20}$: -32.0° (*c*: 0.0014, DMSO); MS (ESI) calcd for $C_{15}H_{18}O_3N_5$ $[M + H]^+$: 316.1, found: 316.3.

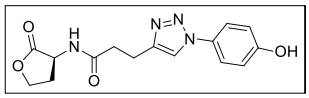


Triazole II-C. Following *General Procedure (V)*, the reaction of alkyne **4** (150 mg, 0.83 mmol), 4-azidotoluene (165 mg, 1.24 mmol), copper(I) iodide (24 mg, 0.12 mmol) and *N,N*-diisopropylethylamine (425 μL, 321 mg, 2.48 mmol) in acetonitrile (8 mL) gave, after precipitation with diethyl ether, the title compound as a off-white powder (186 mg, 72 %). Mp: 149-152 °C; RP-HPLC purity: > 95 % (R_t = 5.62 min); ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.49 (d, J = 8.1 Hz, 1H), 8.46 (s, 1H), 7.73 (d, J = 8.0 Hz, 2H), 7.38 (d, J = 8.1 Hz, 2H), 4.55 (app. q, J = 9.1 Hz, 1H), 4.35 (t, J = 8.3 Hz, 1H), 4.24-4.16 (m, 1H), 2.95 (t, J = 7.2 Hz, 2H), 2.56-2.50 (m, 2H), 2.42-2.33 (m, 1H), 2.37 (s, 3H), 2.22-2.07 (m, 1H); ^{13}C NMR (DMSO-d_6, from ^{1}H-^{13}C gHSQC and ^{1}H-^{13}C gHMBC, 500 MHz) δ 176.1, 171.9, 146.7, 138.6, 135.2, 130.8, 120.3, 119.9, 65.9, 48.6, 35.0, 28.7, 21.8, 21.2;

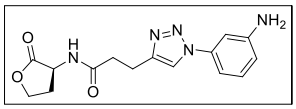
IR (neat) cm^{-1}: 3291, 1767, 1650, 1519, 1376, 1178, 1047, 1014, 816; $[\alpha]_D^{20}$: -11.5° (*c:* 0.0064, DMSO); MS (ESI) calcd for $C_{16}H_{19}O_3N_4$ $[M + H]^+$: 315.2, found: 315.3.



Triazole II-D. Following *General Procedure (V)*, the reaction of alkyne **4** (150 mg, 0.83 mmol), 3-azidobenzaldehyde (183 mg, 1.24 mmol), copper(I) iodide (24 mg, 0.12 mmol) and *N,N*-diisopropylethylamine (425 μL, 321 mg, 2.48 mmol) in acetonitrile (8 mL) gave, after precipitation with diethyl ether, the title compound as a off-white powder (177 mg, 61 %). Mp: 81-83 °C; RP-HPLC purity: > 95 % (R_t = 4.75 min); ^{1}H NMR (300 MHz, DMSO-d_6) δ 10.11 (s, 1H), 8.67 (s, 1H), 8.50 (d, *J* = 7.8 Hz, 1H), 8.39 (s, 1H), 8.21 (d, *J* = 8.2 Hz, 1H), 8.01 (d, *J* = 7.5 Hz, 1H), 7.83 (t, *J* = 7.8 Hz, 1H), 4.56 (app. q, *J* = 9.1 Hz, 1H) ppm 4.35 (t, *J* = 8.4 Hz, 1H), 4.20 (ddd, *J* = 9.2, 8.3, 6.6 Hz, 1H), 2.98 (t, *J* = 7.3 Hz, 2H), 2.56 (t, *J* = 7.4 Hz, 2H), 2.43-2.34 (m, 1H), 2.22-2.08 (m, 1H); ^{13}C NMR (DMSO-*d6*, from ^{1}H-^{13}C gHSQC and ^{1}H-^{13}C gHMBC, 500 MHz) δ 192.3, 175.3, 171.0, 159.3, 137.4, 137.2, 130.8, 129.0, 128.9, 125.0, 119.8, 65.2, 47.9, 34.2, 28.0, 21.0; IR (neat) cm^{-1}: 3300, 2944, 2830, 1774, 1696, 1645, 1543, 1225, 1174, 1010, 843; $[\alpha]_D^{20}$: -22.0° (*c*: 0.0030, DMSO); MS (ESI) calcd for $C_{16}H_{17}O_4N_4$ $[M + H]^+$: 329.1, found: 329.2.

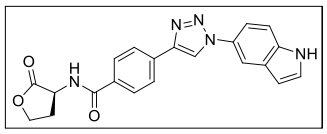


Triazole II-E Following *General Procedure (V)*, the reaction of alkyne **4** (200 mg, 1.10 mmol), 4-azidophenol (224 mg, 1.68 mmol), copper(I) iodide (32 mg, 0.15 mmol) and *N,N*-diisopropylethylamine (567 μL, 428 mg, 3.31 mmol) in acetonitrile (10 mL) gave, after precipitation with diethyl ether, the title compound as a black crystals (244 mg, 70 %). Mp: 84-86 °C; RP-HPLC purity: > 95 % (R_t = 4.19 min); ^{1}H NMR (300 MHz, DMSO-d_6) δ 9.90 (s, 1H), 8.47 (d, *J* = 7.8 Hz, 1H), 8.30 (s, 1H), 7.60 (d, *J* = 8.8 Hz, 2H), 6.90 (d, *J* = 8.8 Hz, 2H), 4.53 (td, *J* = 10.4, 8.8 Hz, 1H), 4.33 (dt, *J* = 8.5, 1.0 Hz, 1H), 4.19 (ddd, *J* = 9.9, 8.7, 6.6 Hz, 1H), 2.91 (t, *J* = 7.4Hz, 2H), 2.53-2.51 (m, 2H), 2.40-2.32 (s, 1H), 2.20-2.06 (s, 1H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 176.1, 171.9, 160.0, 158.2, 129.6, 122.3, 120.8, 116.6, 66.0, 48.6, 35.1, 28.8, 21.8; IR (neat) cm^{-1}: 3600-3200, 3252, 1787, 1651, 1518, 1220, 1016, 836; $[\alpha]_D^{20}$: -7.2° (*c:* 0.00035, DMSO); HRMS (ESI) calcd for $C_{15}H_{17}O_4N_4$ $[M + H]^+$: 317.1250, found: 317.1261.

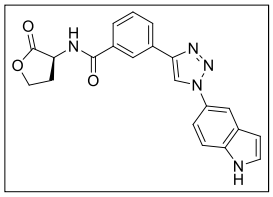


Triazole II-F. Following *General Procedure (V)*, the reaction of alkyne **4** (150 mg, 0.83 mmol), 3-azidoaniline (170 mg, 1.24 mmol), copper(I) iodide (24 mg, 0.12 mmol) and *N,N*-diisopropylethylamine (425 μL, 321 mg, 2.48 mmol) in acetonitrile (8 mL) gave, after precipitation with diethyl ether, the title compound as a brownish powder (175 mg, 67 %). Mp: 92-94 °C; RP-HPLC purity: 89 % (R_t = 3.49 min); ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.48 (d, *J* = 7.8 Hz, 1H), 8.33 (s, 1H), 7.16 (t, *J* = 7.9 Hz, 1H), 7.06-7.03 (m, 1H), 6.87 (dd, *J* = 7.8, 1.7 Hz, 1H), 6.61 (dd, *J* = 8.2, 1.7 Hz, 1H), 5.51 (s, 2H), 4.55 (td, *J* = 11.1, 8.8 Hz, 1H), 4.35 (t, *J* = 8.7 Hz, 1H), 4.24-4.16 (m, 1H), 2.93 (t, *J* = 7.4 Hz, 1H), 2.55-2.50 (m, 1H), 2.42-2.33 (m, 1H), 2.21-2.07 (m, 1H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 175.3, 171.2, 159.3, 150.0, 137.5, 130.0, 120.0, 113.6, 106.6, 104.6, 65.2, 47.9, 34.3, 28.1, 21.1; IR (neat) cm^{-1}: 3468, 3401, 3370, 1766, 1665, 1609, 1492, 1221, 1176, 1020, 840; $[\alpha]_D^{20}$: -14.0° (*c:* 0.0042, DMSO); MS (ESI) calcd for $C_{15}H_{18}O_3N_5$ $[M + H]^+$: 316.1, found: 316.3.

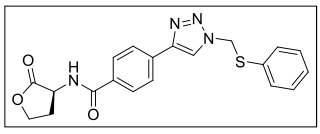
- ***General Procedure (VII):*** *Triazole formation from alkyne-containing HL building blocks* ***11*** *and* ***12****.*



Triazole III-A. 5-Azidoindole (62 mg, 0.39 mmol), alkyne **11** (60 mg, 0.26 mmol), copper(I) iodide (7.5 mg, 0.04 mmol), *N,N*-diisopropylethylamine (134 μL, 101 mg, 0.79 mmol) were dissolved in acetonitrile (2.5 mL) in a round-bottomed flask fitted with a magnetic stirring bar. The reaction was left under stirring at room temperature. The reaction was monitored on RP-HPLC for full conversion of the azide. Upon full conversion of starting material (16 h), the reaction mixture was concentrated *in vacuo*. The residue was dissolved in boiling acetic acid, and filtered by hot gravity filtration. The acetic acid was removed *in vacuo*, and the residue was dissolved in hot methanol. Diethyl ether was added and a precipitate was formed. The precipitate was isolated and dried *in vacuo*, to give the title compound as a black solid (89 mg, 88 %). Mp: 269-271 °C; RP-HPLC purity: > 95 % (R_t = 6.14 min); ^{1}H NMR (300 MHz, DMSO-d_6) δ 11.47 (s, 1H), 9.35 (s, 1H), 9.07 (d, *J* = 8.0 Hz, 1H), 8.09 (d, *J* = 8.2 Hz, 1H), 7.99 (d, *J* = 8.4 Hz, 2H), 7.66-7.59 (m, 2H), 7.54-7.52 (m, 1H), 6.61-6.59 (m, 1H), 4.81 (td, *J* = 10.3, 8.9 Hz, 1H), 4.43 (dt, *J* = 8.6, 1.6 Hz, 1H), 4.33-4.25 (m, 1H), 2.58-2.46 (m, 1H), 2.44-2.29 (m, 1H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 175.0, 165.2, 145.8, 135.2, 133.3, 132.3, 129.0, 127.7, 127.3, 124.8, 120.6, 113.9, 112.0, 111.7, 101.6, 65.0, 48.1, 27.7; IR (neat) cm^{-1}: 3413, 3340, 3112, 1772, 1638, 1516, 1484, 1228, 1183, 809, 765; MS (ESI) calcd for $C_{21}H_{18}N_5O_3$ [M + H]$^+$: 388.1, found: 388.3.

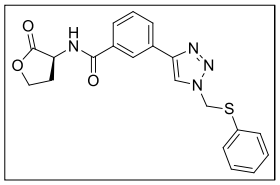


Triazole III-B. Following *General Procedure (VII)*, the reaction of 5-azidoindole (62 mg, 0.39 mmol), alkyne **12** (60 mg, 0.26 mmol), copper(I) iodide (7.5 mg, 0.04 mmol) and *N,N*-diisopropylethylamine (134 μL, 101 mg, 0.79 mmol) gave, after precipitation with diethyl ether the, title compound as an olive solid (65 mg, 64 %). Mp: 211-213 °C; RP-HPLC purity: > 95 % (R_t = 6.28 min); ^{1}H NMR (300 MHz, DMSO-d_6) δ 11.46 (s, 1H), 9.31 (s, 1H), 9.15 (d, *J* = 8.0 Hz, 1H), 8.49 (t, *J* = 1.5 Hz, 1H), 8.13-8.09 (m, 1H), 7.86-7.84 (m, 1H), 7.63 (dq, *J* = 8.6, 3.0 Hz, 3H), 7.54-7.52 (m, 1H), 6.60-6.59 (m, 1H), 4.84 (td, *J* = 10.5, 9.1 Hz, 1H), 4.44 (dt, *J* = 8.6, 1.6 Hz, 1H), 4.30 (ddd, *J* = 10.0, 8.7, 6.5 Hz, 1H), 2.54-2.44 (m, 1H), 2.41-2.30 (m, 1H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 175.3, 165.8, 146.3, 135.5, 134.2, 130.3, 129.3, 129.1, 128.3, 127.7, 127.6, 126.7, 124.0, 120.4, 114.1, 112.3, 111.9, 101.9, 65.3, 48.4; IR (neat) cm^{-1}: 3388, 3246, 3135, 1755, 1656, 1530, 1193, 775, 692; MS (ESI) calcd for $C_{21}H_{18}N_5O_3$ [M + H]$^+$: 388.1, found: 388.3.

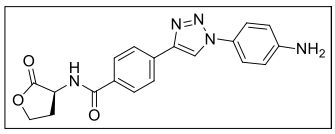


Triazole III-C. Following *General Procedure (VII)*, the reaction of azidomethyl phenyl sulfide (55 μL, 65 mg, 0.39 mmol), alkyne **11** (60 mg, 0.26 mmol), copper(I) iodide (7.5 mg, 0.04 mmol) and *N,N*-diisopropylethylamine (134 μL, 101 mg, 0.79 mmol) gave, after precipitation with diethyl ether, the title compound as a light green solid (63 mg, 66 %). Mp: 175-177 °C; RP-HPLC purity: > 95 % (R_t = 6.63 min); ^{1}H NMR (300 MHz, DMSO-d_6) δ 9.03 (d, *J* = 8.1 Hz, 1H), 8.71 (s, 1H), 7.94 (d, *J* = 3.8 Hz, 4H), 7.46-7.42 (m, 2H), 7.38-7.27 (m, 3H), 6.01 (s, 2H), 4.78 (td, *J* = 10.5, 9.1 Hz, 1H), 4.42 (dt, *J* = 8.7, 1.7 Hz, 1H), 4.28 (ddd, *J* = 10.3, 8.9, 6.7 Hz, 1H), 2.51-2.44 (m, 1H), 2.42-2.30 (m, 1H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 175.3,.165.4, 145.8, 133.3, 132.6, 132.2, 130.5, 129.3, 127.9, 127.7, 125.0, 121.9, 65.3, 51.9,

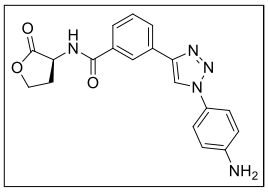
48.4, 27.9; IR (neat) cm^{-1}: 3343, 3102, 1762, 1655, 1535, 1171, 739, 687; MS (ESI) calcd for $C_{20}H_{19}N_4O_3S$ $[M + H]^+$: 395.1, found: 395.3.



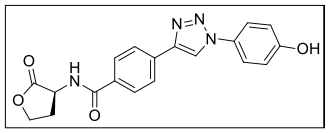
Triazole III-D. Following *General Procedure (VII)*, the reaction of azidomethyl phenyl sulfide (55 μL, 65 mg, 0.39 mmol), alkyne **12** (60 mg, 0.26 mmol), copper(I) iodide (7.5 mg, 0.04 mmol) and *N,N*-diisopropylethylamine (134 μL, 101 mg, 0.79 mmol) gave, after precipitation with diethyl ether, the title compound as a light green solid (91 mg, > 95 %). Mp: 140-142 °C; RP-HPLC purity: > 95 % (R_t = 6.74 min); ^{1}H NMR (300 MHz, DMSO-d_6) δ 9.11 (d, J = 8.1 Hz, 1H), 8.65 (s, 1H), 8.34 (t, J = 1.5 Hz, 1H), 7.99 (dd, J = 6.5, 1.2 Hz, 1H), 7.82-7.80 (m, 1H), 7.56 (t, J = 7.8 Hz, 1H), 7.45-7.41 (m, 2H), 7.37-7.27 (m, 3H), 6.01 (s, 2H), 4.82 (td, J = 10.6, 9.1 Hz, 1H), 4.42 (dt, J = 8.7, 1.7 Hz, 1H), 4.28 (ddd, J = 10.1, 8.7, 6.6 Hz, 1H), 2.53-2.43 (m, 1H), 2.41-2.30 (m, 1H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 175.0, 165.4, 145.7, 133.7, 131.9, 130.3, 130.2, 128.9, 128.8, 127.9, 127.4, 126.5, 123.5, 121.1, 65.0, 51.7, 48.1, 27.7; IR (neat) cm^{-1}: 3223, 3059, 1774, 1639, 1535, 1184, 731, 687; MS (ESI) calcd for $C_{20}H_{19}N_4O_3S$ $[M + H]^+$: 395.1, found: 395.3.



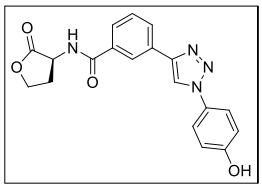
Triazole III-E. Following *General Procedure (VII)*, the reaction of 4-azidoaniline (53 mg, 0.39 mmol), alkyne **11** (60 mg, 0.26 mmol), copper(I) iodide (7.5 mg, 0.04 mmol) and *N,N*-diisopropylethylamine (134 μL, 101 mg, 0.79 mmol) gave, after precipitation with diethyl ether, the title compound as a grey solid (87 mg, 92 %). Mp: decompose at 238 °C; RP-HPLC purity: 92 % (R_t = 6.72 min); ^{1}H NMR (300 MHz, DMSO-d_6) δ 9.15 (s, 1H), 9.05 (d, J = 8.0 Hz, 1H), 8.04 (d, J = 8.4 Hz, 2H), 7.97 (d, J = 8.5 Hz, 2H), 7.53 (d, J = 8.7 Hz, 2H), 6.71 (d, J = 8.7 Hz, 2H), 5.55 (s, 1H), 4.80 (td, J = 10.6, 9.1 Hz, 1H), 4.43 (dt, J = 8.5, 1.4 Hz, 1H), 4.29 (ddd, J = 15.3, 8.7, 6.6 Hz, 1H), 2.51-2.48 (m, 1H), 2.44-2.32 (m, 1H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 176.0, 166.3, 146.6, 134.3, 133.2, 128.7, 126.5, 125.7, 122.3, 120.8, 114.5, 66.1, 49.2, 28.7; IR (neat) cm^{-1}: 3415, 3347, 3118, 1761, 1633, 1520, 1276, 1188, 825, 772; MS (ESI) calcd for $C_{19}H_{18}N_5O_3$ $[M + H]^+$: 364.1, found: 364.3.



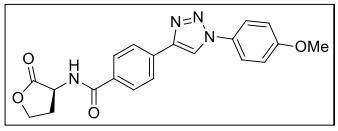
Triazole III-F. Following *General Procedure (VII)*, the reaction of 4-azidoaniline (53 mg, 0.39 mmol), alkyne **12** (60 mg, 0.26 mmol), copper(I) iodide (7.5 mg, 0.04 mmol) and *N,N*-diisopropylethylamine (134 μL, 101 mg, 0.79 mmol) gave, after precipitation with diethyl ether, the title compound as a brown solid (92 mg, > 95 %). Mp: 254-256 °C; RP-HPLC purity: 91 % (R_t = 6.84 min); ^{1}H NMR (300 MHz, DMSO-d_6) δ 9.14 (d, J = 8.2 Hz, 1H), 9.11 (s, 1H), 8.44 (s, 1H), 8.07 (d, J = 7.8 Hz, 1H), 7.83 (d, J = 7.7 Hz, 1H), 7.60 (t, J = 7.8 Hz, 1H), 7.55 (d, J = 8.7 Hz, 2H), 6.71 (d, J = 8.7 Hz, 2H), 5.53 (s, 1H), 4.88-4.78 (m, 1H), 4.43 (dt, J = 8.7, 1.5 Hz, 1H), 4.29 (ddd, J = 15.3, 8.7, 6.6 Hz, 1H), 2.50-2.49 (m, 1H), 2.40-2.33 (m, 1H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 175.0, 165.5, 145.8, 133.9, 130.6, 128.8, 128.0, 126.4, 125.5, 123.7, 121.2, 119.3, 113.5, 65.1, 48.2, 27.7; IR (neat) cm^{-1}: 3469, 3363, 3212, 2114, 1758, 1627, 1517, 1163, 801; MS (ESI) calcd for $C_{19}H_{18}N_5O_3$ $[M + H]^+$: 364.1, found: 364.3.



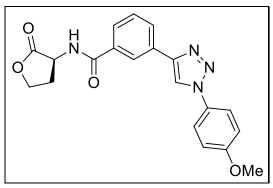
Triazole III-G. Following *General Procedure (VII)*, the reaction of 4-azidophenol (53 mg, 0.39 mmol), alkyne **11** (60 mg, 0.26 mmol), copper(I) iodide (7.5 mg, 0.04 mmol) and *N,N*-diisopropylethylamine (134 μL, 101 mg, 0.79 mmol) gave, after precipitation with diethyl ether, the title compound as a black solid (60 mg, 63 %). Mp: 274-276 °C; RP-HPLC purity: > 95 % (R_t = 5.40 min); ^{1}H NMR (300 MHz, DMSO-d_6) δ 10.01 (s, 1H), 9.25 (s, 1H), 9.06 (d, *J* = 8.0 Hz, 1H), 8.05 (d, *J* = 8.4 Hz, 2H), 7.98 (d, *J* = 8.4 Hz, 2H), 7.72 (d, *J* = 8.8 Hz, 1H), 6.97 (d, *J* = 8.8 Hz, 2H), 4.80 (dd, *J* = 18.4, 9.4 Hz, 1H), 4.43 (dt, *J* = 8.3, 0.9 Hz, 1H), 4.29 (td, *J* = 8.6, 6.9 Hz, 1H), 2.50-2.43 (m, 1H), 2.39-2.28 (m, 1H); IR (neat) cm^{-1}: 3400-3200, 3135, 1758, 1635, 1523, 1189, 1025, 832, 771; MS (ESI) calcd for $C_{19}H_{17}N_4O_4$ $[M + H]^+$: 365.1, found: 365.3.



Triazole III-H. Following *General Procedure (VII)*, the reaction of 4-azidophenol (53 mg, 0.39 mmol), alkyne **12** (60 mg, 0.26 mmol), copper(I) iodide (7.5 mg, 0.04 mmol) and *N,N*-diisopropylethylamine (134 μL, 101 mg, 0.79 mmol) gave, after precipitation with diethyl ether, the title compound as a black solid (53 mg, 56 %). Mp: 262-264 °C; RP-HPLC purity: > 95 % (R_t = 5.56 min); ^{1}H NMR (300 MHz, DMSO-d_6) δ 10.01 (s, 1H), 9.22 (s, 1H), 9.15 (d, *J* = 7.8 Hz, 1H), 8.46 (s, 1H), 8.09 (d, *J* = 7.6 Hz, 1H), 7.85 (d, *J* = 7.4 Hz, 1H), 7.74 (d, *J* = 8.6 Hz, 2H), 7.62 (t, *J* = 7.7 Hz, 1H), 6.97 (d, *J* = 8.6 Hz, 2H), 4.84 (dd, *J* = 18.6, 9.0 Hz, 1H), 4.44 (t, *J* = 8.6 Hz, 1H), 4.30 (td, *J* = 8.9, 7.0 Hz, 1H), 2.56-2.44 (m, 1H), 2.42-2.33 (m, 1H); IR (neat) cm^{-1}: 3600-3000, 1744, 1514, 1220, 1035, 800; MS (ESI) calcd for $C_{19}H_{17}N_4O_4$ $[M + H]^+$: 365.1, found: 365.3.



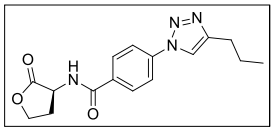
Triazole III-I. Following *General Procedure (VII)*, the reaction of 4-azidoanisole (59 mg, 0.39 mmol), alkyne **11** (60 mg, 0.26 mmol), copper(I) iodide (7.5 mg, 0.04 mmol) and *N,N*-diisopropylethylamine (134 μL, 101 mg, 0.79 mmol) gave, after precipitation with diethyl ether, the title compound as a grey solid (94 mg, > 95 %). Mp: 258-260 °C; RP-HPLC purity: > 95 % (R_t = 6.49 min); ^{1}H NMR (300 MHz, DMSO-d_6):δ 9.34 (s, 1H), 9.08 (d, *J* = 8.0 Hz, 1H), 8.07 (d, *J* = 8.4 Hz, 2H), 7.99 (d, *J* = 8.5 Hz, 2H), 7.87 (d, *J* = 9.0 Hz, 2H), 7.19 (d, *J* = 9.0 Hz, 2H), 4.86-4.77 (m, 1H), 4.44 (td, *J* = 4.2 Hz, *J* = 8.3 Hz, 1H), 4.30 (ddd, *J* = 10.1, 8.7, 6.6 Hz, 1H), 3.85 (s, 3H), 2.54-2.47 (m, 1H), 2.45-2.33 (m, 1H); ^{13}C NMR (75 MHz, DMSO-d_6):δ 174.9, 165.0, 158.9, 145.7, 132.9, 132.2, 129.4, 127.5, 124.6, 121.2, 120.0, 114.4, 64.9, 55.1, 48.0, 27.5; IR (neat) cm^{-1}: 3363, 3134, 2917, 1780, 1639, 1519, 1162, 1013, 827, 768, 608; MS (ESI) calcd for $C_{20}H_{19}N_4O_4$ $[M + H]^+$: 396.3, found: 396.6.



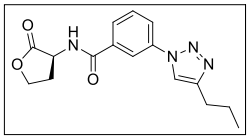
Triazole III-J. Following *General Procedure (VII)*, the reaction of 4-azidoanisole (59 mg, 0.39 mmol), alkyne **12** (60 mg, 0.26 mmol), copper(I) iodide (7.5 mg, 0.04 mmol) and *N,N*-diisopropylethylamine (134 μL, 101 mg, 0.79 mmol) gave, after precipitation with diethyl ether, the title compound as a beige solid (76 mg, 77 %). Mp: 242-244 °C; RP-HPLC purity: > 95 % (R_t = 6.60 min); ^{1}H NMR (300 MHz, DMSO-d_6) δ 9.29 (s, 1H), 9.14 (d, *J* = 8.0 Hz, 1H), 8.45 (s, 1H), 8.09 (d, *J* = 7.8 Hz, 1H), 7.86 (dd, *J* = 12.1, 5.0 Hz, 3H), 7.62 (t, *J* = 7.7 Hz, 1H), 7.19-7.14 (m, 2H), 4.83 (td, *J* = 10.4, 9.0 Hz, 1H), 4.43 (dt, *J* = 8.6, 1.6 Hz, 1H), 4.33-4.25 (m, 1H), 3.83 (s, 3H), 2.50-2.48 (m, 1H), 2.44-2.32 (m, 1H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 175.2, 165.7, 159.2, 146.3, 134.1, 130.5, 129.8, 129.0, 128.2, 126,7, 124.0, 121.5,

119.9, 114.8, 65.2, 55.4, 48.3, 27.9; IR (neat) cm^{-1}: 3240, 3121, 2913, 1762, 1641, 1517, 1163, 1002, 808, 690; MS (ESI) calcd for $C_{20}H_{19}N_4O_4$ $[M + H]^+$: 396.3, found: 396.7.

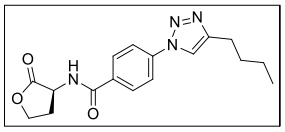
- ***General Procedure (VIII):*** *Triazole formation from HL building blocks* ***13*** *and* ***14****.*



Triazole IV-A. 1-Pentyne (90 μL, 62 mg, 0.91 mmol), azide **13** (150 mg, 0.61 mmol), copper(I) iodide (17 mg, 0.09 mmol), *N,N*-diisopropylethylamine (313 μL, 236 mg, 1.83 mmol) and acetonitrile (8 mL) were added to a round-bottomed flask fitted with a magnetic stirring bar and the reaction was left under stirring at room temperature. The reaction was monitored on RP-HPLC for full conversion of the azide. Full conversion of starting material was observed after 16 h upon which a first crop of product had precipitated from the reaction mixture. This crop was collected by filtration. The filtrate was concentrated *in vacuo*. The residue was dissolved in boiling acetic acid, and filtered by hot gravity filtration. The acetic acid was removed *in vacuo*, and the residue was dissolved in hot methanol. Diethyl ether was added and the formed precipitate was isolated. The different crops of precipitate were combined and dried *in vacuo,* to give the title compound as a beige solid (179 mg, 94 %). Mp: 226-228 °C; RP-HPLC purity: >95 % (R_t = 5.75 min); ^{1}H NMR (300 MHz, DMSO-d_6) δ 9.15 (d, J = 8.0 Hz, 1H), 8.70 (s, 1H), 8.05 (s, 4H), 4.82 (m, 1H), 4.43 (td, J = 8.5, 4.3 Hz, 1H), 4.29 (m, 1H), 2.69 (t, J = 7.5 Hz, 2H), 2.49 (m, 1H), 2.35 (m, 1H), 1.69 (m, 2H), 0.96 (t, J = 7.3 Hz, 3H); IR (neat) cm^{-1}: 3271, 2958, 1768, 1635, 1542, 1513, 1174, 1012, 851, 767; MS (ESI) calcd for $C_{16}H_{19}N_4O_3$ $[M + H]^+$: 315.1, found: 315.3.

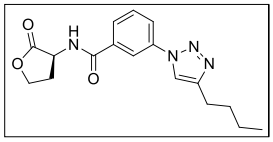


Triazole IV-B. Following *General Procedure (VIII)*, the reaction of 1-pentyne (90 μL, 62 mg, 0.91 mmol), azide **14** (150 mg, 0.61 mmol), copper(I) iodide (17 mg, 0.09 mmol) and *N,N*-diisopropylethylamine (313 μL, 236 mg, 1.83 mmol) gave, after filtration and precipitation with diethyl ether, the title compound as a beige solid (107 mg, 56 %). Mp: 167-169 °C; RP-HPLC purity: > 95 % (R_t = 5.84 min); ^{1}H NMR (300 MHz, DMSO-d_6) δ 9.22 (d, J = 8.0Hz, 1H), 8.66 (s, 1H), 8.37 (t, J = 1.7 Hz, 1H), 8.07 (dd, J = 7.8, 1.6 Hz, 1H), 7.94 (d, J = 7.9 Hz, 1H), 7.72 (t, J = 7.9 Hz, 1H), 4.84 (td, J = 10.8, 9.1 Hz, 1H), 4.44 (dt, J = 8.6, 1.5 Hz, 1H), 4.30 (ddd, J = 10.2, 8,8, 6.6 Hz, 1H), 2.70 (t, J = 7.5 Hz, 2H), 2.50 (m, 1H), 2.34 (m, 1H), 1.70 (m, 2H), 0.96 (t, J = 7.3 Hz, 3H); IR (neat) cm^{-1}: 3271, 2959, 1769, 1645, 1545, 1381, 1180, 1012, 812, 683; MS (ESI) calcd for $C_{16}H_{19}N_4O_3$ $[M + H]^+$: 315.1, found: 315.3.

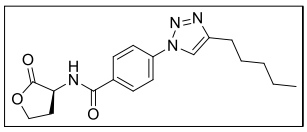


Triazole IV-C. Following *General Procedure (VIII)*, the reaction of 1-hexyne (140 μL, 100 mg, 1.22 mmol), azide **13** (200 mg, 0.81 mmol), copper(I) iodide (23 mg, 0.12 mmol) and *N,N*-diisopropylethylamine (417 μL, 315 mg, 2.44 mmol) gave, after filtration and precipitation with diethyl ether, the title compound as a light yellow solid (209 mg, 75 %). Mp: 217-220 °C; RP-HPLC purity: >95 % (R_t = 6.40 min); ^{1}H NMR (300 MHz, DMSO-d_6) δ 9.14 (d, J = 8.0 Hz, 1H), 8.70 (s, 1H), 8.03 (s, 4H), 4.81 (td, J = 10.7, 9.1 Hz, 1H), 4.44 (dt, J = 8.8, 1.8 Hz, 1H), 4.29 (ddd, J = 10.1, 8.8, 6.6 Hz, 1H), 2.72 (t, J = 7.5 Hz, 2H), 2.54-2.44 (m, 1H), 2.42-2.28 (m, 1H), 1.71-1.61 (m, 2H), 1.44-1.31 (m, 2H), 0.92 (t, J = 7.3 Hz, 3H); IR (neat) cm^{-1}: 3272, 2931, 1770,

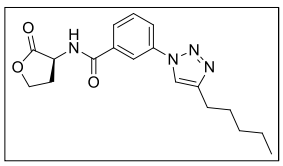
1609, 1541, 1513, 1171, 1045, 1012, 850, 767; MS (ESI) calcd for $C_{17}H_{21}N_4O_3$ $[M + H]^+$: 329.2, found: 329.3.



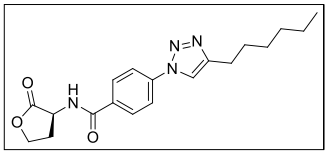
Triazole IV-D. Following *General Procedure (VIII)*, the reaction of 1-hexyne (140 μL, 100 mg, 1.22 mmol), azide **14** (200 mg, 0.81 mmol), copper(I) iodide (23 mg, 0.12 mmol) and *N,N*-diisopropylethylamine (417 μL, 315 mg, 2.44 mmol) gave, after filtration and precipitation with diethyl ether, the title compound as a grey solid (154 mg, 55 %). Mp: 165-167 °C; RP-HPLC purity: > 95 % (R_t = 6.47 min); ^{1}H NMR (300 MHz, DMSO-d_6) δ 9.22 (d, J = 8.0 Hz, 1H), 8.66 (s, 1H), 8.37 (t, J = 1.8 Hz, 1H), 8.09-8.06 (m, 1H), 7.94 (td, J = 8.0, 1.3 Hz, 1H), 7.72 (t, J = 7.9 Hz, 1H), 4.84 (td, J = 10.7, 9.1 Hz, 1H), 4.44 (dt, J = 8.7, 1.6 Hz, 1H), 4.30 (ddd, J = 10.1, 8.8, 6.6 Hz, 1H), 2.72 (t, J = 7.6 Hz, 2H), 2.51-2.49 (m, 1H), 2.35 (ddd, J = 20.2, 15.3, 9.9 Hz, 1H), 1.66 (td, J = 15.2, 7.5 Hz, 2H), 1.37 (qd, J = 14.4, 7.3 Hz, 2H), 0.92 (t, J = 7.3 Hz, 3H); ^{13}C NMR (50 MHz, DMSO-d_6) δ 175.1, 164.9, 148.3, 136.9, 135.0, 130.1, 127.0, 122.7, 120.2, 118.5, 65.3, 48.5, 30.8, 28.0, 24.6, 21.6, 13.6, 6.5; IR (neat) cm^{-1}: 3272, 2931, 1771, 1645, 1574, 1488, 1382, 1223, 1181, 1046, 1012, 684; MS (ESI) calcd for $C_{17}H_{21}N_4O_3$ $[M + H]^+$: 329.2, found: 329.3.



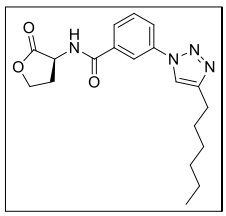
Triazole IV-E. Following *General Procedure (VIII)*, the reaction of 1-heptyne (120 μL, 88 mg, 0.91 mmol), azide **13** (150 mg, 0.61 mmol), copper(I) iodide (17 mg, 0.09 mmol) and *N,N*-diisopropylethylamine (313 μL, 236 mg, 1.83 mmol) gave, after filtration and precipitation with diethyl ether, the title compound as a light yellow solid (113 mg, 54 %). Mp: 207-209 °C; RP-HPLC purity: > 95 % (R_t = 7.03 min); ^{1}H NMR (300 MHz, DMSO-d_6) δ 9.14 (d, J = 8.1 Hz, 1H), 8.70 (s, 1H), 8.05 (s, 4H), 4.81 (td, J = 10.0, 8.6 Hz, 1H), 4.43 (t, J = 8.5 Hz, 1H), 4.33-4.25 (m, 1H), 2.70 (t, J = 7.5 Hz, 2H), 2.53-2.44 (m, 1H), 2.42-2.28 (m, 1H), 1.72-1.62 (m, 2H), 1.34 (dt, J = 6.4, 3.3 Hz, 4H), 0.90-0.86 (m, 3H); ^{13}C NMR (50 MHz, DMSO-d_6) δ 175.2, 164.9, 138.8, 132.7, 129.0, 120.1, 119.3, 65.4, 48.5, 30.7, 28.4, 28.0, 24.9, 21.8, 13.8; IR (neat) cm^{-1}: 3280, 2929, 1778, 1644, 1541, 1514, 1174, 1015, 850, 768; MS (ESI) calcd for $C_{18}H_{23}N_4O_3$ $[M + H]^+$: 343.2, found: 343.3.



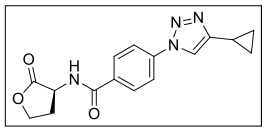
Triazole IV-F. Following *General Procedure (VIII)*, the reaction of 1-heptyne (120 μL, 88 mg, 0.91 mmol), azide **14** (150 mg, 0.61 mmol), copper(I) iodide (17 mg, 0.09 mmol) and *N,N*-diisopropylethylamine (313 μL, 236 mg, 1.83 mmol) gave, after filtration and precipitation with diethyl ether, the title compound as a light yellow solid (127 mg, 61 %). Mp: 178-180 °C; RP-HPLC purity: > 95 % (R_t = 7.08 min); ^{1}H NMR (300 MHz, DMSO-d_6) δ 9.22 (d, J = 7.9 Hz, 1H), 8.66 (s, 1H), 8.37 (s, 1H), 8.09-8.05 (m, 1H), 7.95-7-92 (m, 1H), 7.71 (t, J = 8.0 Hz, 1H), 4.83 (td, J = 10.1, 8.6 Hz, 1H), 4.43 (dt, J = 8.6, 1.3 Hz, 1H), 4.33-4.25 (m, 1H), 2.70 (t, J = 7.6 Hz, 2H), 2.54-2.45 (m, 1H), 2.42-2.31 (m, 1H), 1.67 (q, J = 7.6 Hz, 2H), 1.42-1.31 (m, 4H), 0.88 (q, J = 6.5 Hz, 3H); IR (neat) cm^{-1}: 3274, 2929, 1771, 1645, 1550, 1382, 1182, 1013, 684; MS (ESI) calcd for $C_{18}H_{23}N_4O_3$ $[M + H]^+$: 343.2, found: 343.3.



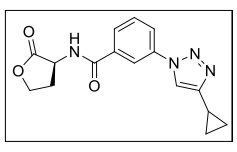
Triazole IV-G. Following *General Procedure (VIII)*, the reaction of 1-octyne (135 μL, 101 mg, 0.91 mmol), azide **13** (150 mg, 0.61 mmol), copper(I) iodide (17 mg, 0.09 mmol) and *N,N*-diisopropylethylamine (313 μL, 236 mg, 1.83 mmol) gave, after filtration and precipitation with diethyl ether, the title compound as a light yellow solid (188 mg, 87 %). Mp: 204-206 °C; RP-HPLC purity: > 95 % (R_t = 7.61 min); ^{1}H NMR (300 MHz, DMSO-d_6) δ 9.15 (d, J = 7.9 Hz, 1H), 8.70 (s, 1H), 8.05 (s, 4H), 4.81 (dd, J = 17.9, 9.7 Hz, 1H), 4.44 (t, J = 8.0 Hz, 1H), 4.29 (dt, J = 9.3, 6.6 Hz, 1H), 2.71 (t, J = 7.5 Hz, 2H), 2.54-2.45 (m, 1H), 2.43-2.29 (m, 1H), 1.71-1.62 (m, 2H), 1.38-1.29 (m, 6H), 0.89-0.85 (t, J = 6.6 Hz, 3H); IR (neat) cm^{-1}: 3271, 2958, 2932, 1774, 1641, 1541, 1514, 1173, 1044, 851, 767; MS (ESI) calcd for $C_{19}H_{24}N_4O_3$ [M + H]$^+$: 357.2, found: 357.3.



Triazole IV-H. Following *General Procedure (VIII)*, the reaction of 1-octyne (135 μL, 101 mg, 0.91 mmol), azide **14** (150 mg, 0.61 mmol), copper(I) iodide (17 mg, 0.09 mmol) and *N,N*-diisopropylethylamine (313 μL, 236 mg, 1.83 mmol) gave, after filtration and precipitation with diethyl ether, the title compound as a light yellow solid (138 mg, 64 %). Mp: 162-164 °C; RP-HPLC purity: > 95 % (R_t = 7.66 min); ^{1}H NMR (300 MHz, DMSO-d_6) δ 9.22 (d, J = 8.4 Hz, 1H), 8.66 (s, 1H), 8.37 (s, 1H), 8.07 (dd, J = 8.1, 0.7 Hz, 1H), 7.94 (d, J = 6.9 Hz, 1H), 7.72 (dt, J = 8.1, 0.8 Hz, 1H), 4.84 (td, J = 9.7, 8.5 Hz, 1H), 4.44 (t, J = 8.8 Hz, 1H), 4.30 (td, J = 9.4, 7.7 Hz, 1H), 2.71 (t, J = 7.4 Hz, 2H), 2.55-2.46 (m, 1H), 2.42-2.28 (m, 1H), 1.72-1.62 (m, 2H), 1.38-1.29 (m, 6H), 0.87 (q, J = 5.9 Hz, 3H); ^{13}C NMR (50 MHz, DMSO-d_6) δ 175.2, 164.9, 148.4, 136.9, 135.0, 130.2, 127.0, 122.7, 120.2, 118.5, 65.4, 48.5, 31.0, 28.7, 28.2, 28.0, 25.0, 22.0, 13.9; IR (neat) cm^{-1}: 3272, 2928, 2855, 1770, 1664, 1549, 1382, 1182, 1012, 813, 684; MS (ESI) calcd for $C_{19}H_{24}N_4O_3$ [M + H]$^+$: 357.2, found: 357.3.

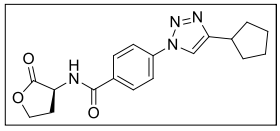


Triazole IV-I. Following *General Procedure (VIII)*, the reaction of cyclopropylacetylene (103 μL, 80 mg, 1.22 mmol), azide **13** (200 mg, 0.81 mmol), copper(I) iodide (23 mg, 0.12 mmol) and *N,N*-diisopropylethylamine (417 μL, 315 mg, 2.44 mmol) gave, after filtration and precipitation with diethyl ether, the title compound as a light yellow solid (178 mg, 70 %). Mp: 210-212 °C; RP-HPLC purity: > 95 % (R_t = 5.46 min); ^{1}H NMR (300 MHz, DMSO-d_6) δ 9.14 (d, J = 8.0 Hz, 1H), 8.66 (s, 1H), 8.06 (d, J = 8.9 Hz, 2H), 8.01 (d, J = 9.0 Hz, 2H), 4.81 (td, J = 10.6, 9.1 Hz, 1H), 4.44 (dt, J = 8.7, 1.7 Hz, 1H), 4.30 (ddd, J = 10.1, 8.7, 6.6 Hz, 1H), 2.90-2.44 (m, 1H), 2.43-2.29 (m, 1H), 2.09-2.00 (m, 1H), 1.02-0.96 (m, 2H), 0.84-0.79 (m, 2H); ^{13}C NMR (50 MHz, DMSO-d_6) δ 175.1 ,164.8, 150.5, 138.7, 128.9, 119.1, 118.8, 65.3, 48.4, 27.9, 7.7, 6.4; IR (neat) cm^{-1}: 3340, 3153, 1779, 1751, 1654, 1638, 1605, 1530, 1507, 1227, 1182, 1154, 1039, 1015, 851, 765; MS (ESI) calcd for $C_{16}H_{17}N_4O_3$ [M + H]$^+$: 313.1, found: 313.2.

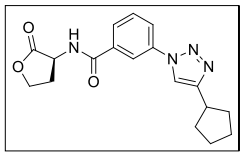


Triazole IV-J. Following *General Procedure (VIII)*, the reaction of cyclopropylacetylene (103 μL, 80 mg, 1.22 mmol), azide **14** (200 mg, 0.81 mmol), copper(I) iodide (23 mg, 0.12 mmol) and *N,N*-diisopropylethylamine (417 μL, 315 mg, 2.44 mmol) gave, after filtration and precipitation with diethyl ether, the title compound as a grey solid (235 mg, 93 %). Mp: 156-158 °C; RP-HPLC purity: > 95 % (R_t = 5.49 min); ^{1}H NMR (300 MHz, DMSO-d_6) δ, 9.22 (d, J = 7.9 Hz, 1H), 8.62 (s, 1H), 8.34 (s, 1H), 8.04 (m, 1H), 7.93 (d, J = 7.8 Hz, 1H), 7.71 (t, J = 7.9 Hz, 1H), 4.83 (dd, J

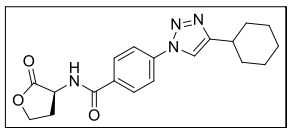
= 18.9, 9.1 Hz, 1H), 4.44 (dt, *J* = 8.8, 1.2 Hz, 1H), 4.29 (m, 1H), 2.50 (m, 1H), 2.34 (m, 1H), 2.04 (m, 1H), 0.98 (m, 2H), 0.82 (m, 2H); IR (neat) cm^{-1}: 3269, 1772, 1646, 1539, 1382, 1223, 1182, 1013, 810, 683; MS (ESI) calcd for $C_{16}H_{17}N_4O_3$ $[M + H]^+$: 313.1, found: 313.2.



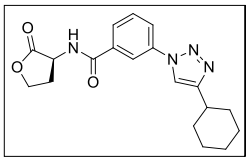
Triazole IV-K. Following *General Procedure (VIII)*, the reaction of cyclopentylacetylene (106 μL, 86 mg, 0.91 mmol), azide **13** (150 mg, 0.61 mmol), copper(I) iodide (17 mg, 0.09 mmol) and *N,N*-diisopropylethylamine (313 μL, 236 mg, 1.83 mmol) gave, after filtration and precipitation with diethyl ether, the title compound as an off-white solid (145 mg, 70 %). Mp: 214-216 °C; RP-HPLC purity: > 95 % (R_t = 6.45 min); ^{1}H NMR (300 MHz, DMSO-d_6) δ 9.13 (d, *J* = 8.0 Hz, 1H), 8.70 (s, 1H), 8.04 (s, 4H), 4.80 (td, *J* = 10.7, 9.1 Hz, 1H), 4.42 (dt, *J* = 8.7, 1.8 Hz, 1H), 4.28 (ddd, *J* = 10.2, 8.7, 6.5 Hz, 1H), 3.21 (dd, *J* = 15.5, 7.9 Hz, 1H), 2.53-2.43 (m, 1H), 2.41-2.26 (m, 1H), 2.07-2.01 (m, 2H), 1.68 (m, 6H); ^{13}C NMR (50 MHz, DMSO-d_6) δ 175.2, 165.0, 152.8, 138.9, 132.7, 129.0, 119.3, 65.4, 48.5, 36.1, 32.7, 28.0, 24.7; IR (neat) cm^{-1}: 3292, 2952, 1777, 1633, 1541, 1513, 1174, 1013, 851; MS (ESI) calcd for $C_{18}H_{21}N_4O_3$ $[M + H]^+$: 341.2, found: 341.3.



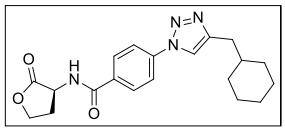
Triazole IV-L. Following *General Procedure (VIII)*, the reaction of cyclopentylacetylene (106 μL, 86 mg, 0.91 mmol), azide **14** (150 mg, 0.61 mmol), copper(I) iodide (17 mg, 0.09 mmol) and *N,N*-diisopropylethylamine (313 μL, 236 mg, 1.83 mmol) gave, after filtration and precipitation with diethyl ether the title, compound as a white solid (176 mg, 85 %). Mp: 190-192 °C; RP-HPLC purity: > 95 % (R_t = 6.52 min ^{1}H NMR (300 MHz, DMSO-d_6) δ 9.21 (d, *J* = 8.0 Hz, 1H), 8.67 (s, 1H), 8.37 (t, *J* = 1.8 Hz, 1H), 8.08 (dd, *J* = 7.7, 1.7 Hz, 1H), 7.93 (d, *J* = 7.8 Hz, 1H), 7.72 (t, *J* = 7.9 Hz, 1H), 4.83 (td, *J* = 10.7, 9.1 Hz, 1H), 4.44 (dt, *J* = 8.8, 1.9 Hz, 1H), 4.30 (ddd, *J* = 10.3, 8.7, 6.6 Hz, 1H), 3.25-3.16 (m, 1H), 2.55-2.45 (m, 1H), 2.43-2.28 (m, 1H), 2.09-2.03 (m, 1H), 1.75-1.64 (m, 1H); ^{13}C NMR (50 MHz, DMSO-d_6) δ 175.2, 165.0, 152.7, 136.9, 135.0, 130.1, 127.0, 122.8, 119.4, 118.6, 65.4, 48.5, 36.1, 32.7, 28.0, 24.7;); IR (neat) cm^{-1}: 3269, 2954, 2867, 1773, 1644, 1550, 1383, 1223, 1046, 812, 685; MS (ESI) calcd for $C_{18}H_{21}N_4O_3$ $[M + H]^+$: 341.2, found: 341.3.



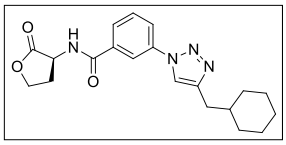
Triazole IV-M. Following *General Procedure (VIII)*, the reaction of cyclohexylacetylene (118 μL, 99 mg, 0.91 mmol), azide **13** (150 mg, 0.61 mmol), copper(I) iodide (17 mg, 0.09 mmol) and *N,N*-diisopropylethylamine (313 μL, 236 mg, 1.83 mmol) gave, after filtration and precipitation with diethyl ether, the title compound as a light yellow solid (133 mg, 62 %). Mp: 230-232 °C; RP-HPLC purity: > 95 % (R_t = 6.98 min); ^{1}H NMR (300 MHz, DMSO-d_6) δ 9.14 (d, *J* = 8.0 Hz, 1H), 8.68 (d, *J* = 1.0 Hz, 1H), 8.04 (d, *J* = 1.5 Hz, 4H), 4.80 (ddd, *J* = 18.6, 9.3, 0.9 Hz, 1H), 4.43 (t, *J* = 8.8 Hz, 1H), 4.33-4.24 (m, 1H), 2.75 (dd, *J* = 11.5, 9.3 Hz, 1H), 2.58-2.43 (m, 1H), 2.41-2.27 (m, 1H), 2.05 (dd, *J* = 15.6, 5.8 Hz, 2H), 1.78-1.67 (m, 3H), 1.51-1.32 (m, 4H), 1.30-1.19 (m, 1H); IR (neat) cm^{-1}: 3295, 2926, 2850, 1771, 1643, 1543, 1512, 1181, 1012, 848, 666; MS (ESI) calcd for $C_{19}H_{23}N_4O_3$ $[M + H]^+$: 355.2, found: 355.3.



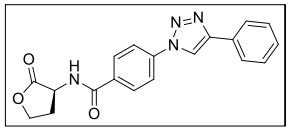
Triazole IV-N. Following *General Procedure (VIII)*, the reaction of cyclohexylacetylene (118 μL, 99 mg, 0.91 mmol), azide **14** (150 mg, 0.61 mmol), copper(I) iodide (17 mg, 0.09 mmol) and *N*,*N*-diisopropylethylamine (313 μL, 236 mg, 1.83 mmol) gave, after filtration and precipitation with diethyl ether, the title compound as a white solid (120 mg, 56 %). Mp: 193-194 °C; RP-HPLC purity: > 95 % (R_t = 7.05 min); ^{1}H NMR (300 MHz, DMSO-d_6) δ 9.21 (d, *J* = 8.0 Hz, 1H), 8.64 (s, 1H), 8.36 (s, 1H), 8.09-8.05 (m, 1H), 7.93 (dd, *J* = 7.7, 0.8 Hz, 1H), 7.71 (t, *J* = 7.9 Hz, 1H), 4.83 (td, *J* = 10.5, 9.1 Hz, 1H), 4.43 (dt, *J* = 8.6, 1.2 Hz, 1H), 4.34-4.25 (m, 1H), 2.75 (dt, *J* = 10.7, 3.5 Hz, 1H), 2.54-2.45 (m, 1H), 2.42-2.28 (m, 1H), 2.03 (d, *J* = 10.2 Hz, 2H), 1.79-1.67 (m, 3H), 1.42 (qd, *J* = 23.7, 12.0 Hz, 4H), 1.30-1.19 (m, 1H); IR (neat) cm^{-1}: 3270, 2923, 2851, 1772, 1645, 1548, 1182, 1012, 811, 683; MS (ESI) calcd for $C_{19}H_{23}N_4O_3$ [M + H]$^+$: 355.2, found: 355.3.



Triazole IV-O. Following *General Procedure (VIII)*, the reaction of cyclohexylpropargyl (132 μL, 112 mg, 0.91 mmol), azide **13** (150 mg, 0.61 mmol), copper(I) iodide (17 mg, 0.09 mmol) and *N*,*N*-diisopropylethylamine (313 μL, 236 mg, 1.83 mmol) gave, after filtration and precipitation with diethyl ether, the title compound as a light yellow solid (165 mg, 73 %). Mp: 204-205 °C; RP-HPLC purity: > 95 % (R_t = 7.49 min); ^{1}H NMR (300 MHz, DMSO-d_6) δ 9.14 (d, *J* = 8.0 Hz, 1H), 8.68 (s, 1H), 8.05 (d, *J* = 1.2 Hz, 4H), 4.81 (td, *J* = 9.6, 8.7 Hz, 1H), 4.43 (t, *J* = 8.7 Hz, 1H), 4.29 (td, *J* = 9.1, 6.9 Hz, 1H), 2.59 (d, *J* = 6.7 Hz, 1H), 2.53-2.44 (m, 1H), 2.42-2.28 (m, 1H), 1.72-1.59 (m, 6H), 1.26-1.10 (m, 3H), 1.06-0.91 (m, 2H); IR (neat) cm^{-1}: 3370, 3141, 2919, 2850, 1751, 1656, 1640, 1507, 1183, 1154, 1016, 852, 766, 589; MS (ESI) calcd for $C_{20}H_{24}N_4O_3$ [M + H]$^+$: 369.2, found: 369.3.

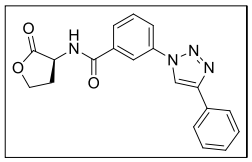


Triazole IV-P. Following *General Procedure (VIII)*, the reaction of cyclohexylpropargyl (132 μL, 112 mg, 0.91 mmol), azide **14** (150 mg, 0.61 mmol), copper(I) iodide (17 mg, 0.09 mmol) and *N*,*N*-diisopropylethylamine (313 μL, 236 mg, 1.83 mmol) gave, after filtration and precipitation with diethyl ether, the title compound as an off-white solid (183 mg, 81 %). Mp: 220-222 °C; RP-HPLC purity: > 95 % (R_t = 7.54 min); ^{1}H NMR (300 MHz, DMSO-d_6) δ 9.22 (d, *J* = 7.9 Hz, 1H), 8.64 (s, 1H), 8.37 (s, 1H), 8.09-8.06 (m, 1H), 7.93 (dd, *J* = 7.8, 0.9 Hz, 1H), 7.71 (t, *J* = 7.9 Hz, 1H), 4.83 (td, *J* = 10.4, 8.9 Hz, 1H), 4.43 (dt, *J* = 8.6, 1.2 Hz, 1H), 4.29 (ddd, *J* = 9.7, 9.1, 6.8 Hz, 1H), 2.60 (d, *J* = 6.7 Hz, 2H), 2.54-2.45 (m, 1H), 2.42-2.28 (m, 1H), 1.73-1.58 (m, 6H), 1.28-1.10 (m, 3H), 1.03-0.90 (m, 2H); IR (neat) cm^{-1}: 3291, 2922, 2850, 1770, 1647, 1530, 1182, 1014, 685; MS (ESI) calcd for $C_{20}H_{24}N_4O_3$ [M + H]$^+$: 369.2, found: 369.3.

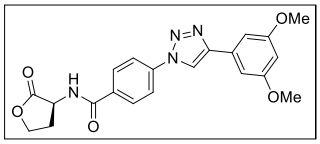


Triazole IV-Q. Following *General Procedure (VIII)*, the reaction of phenylacetylene (134 μL, 124 mg, 1.22 mmol), azide **13** (200 mg, 0.81 mmol), copper(I) iodide (23 mg, 0.12 mmol), *N*,*N*-diisopropylethylamine (417 μL, 315 mg, 2.44 mmol) gave, after filtration and precipitation with diethyl ether, the title compound as an off-white solid (184 mg, 65 %). Mp: 285-287 °C; RP-HPLC purity: > 95 % (R_t = 6.59 min); ^{1}H NMR (300 MHz, DMSO-d_6) δ 9.42 (s, 1H), 9.17 (d, *J* = 8.0 Hz, 1H), 8.11 (s, 4H), 7.95 (dd, *J* = 8.4, 1.2 Hz, 2H), 7.50 (t, *J* = 7.5 Hz, 2H), 7.39 (t, *J* = 7.3 Hz, 1H), 4.82 (td, *J* = 10.3, 9.2 Hz, 1H), 4.43 (dt, *J* = 8.7, 1.7 Hz,

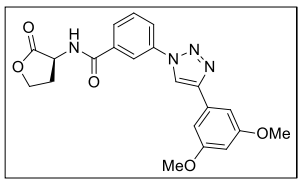
1H), 4.29 (ddd, *J* = 9.9, 8.9, 6.6 Hz, 1H), 2.57-2.45 (m, 1H), 2.43-2.28 (m, 1H); ^{13}C NMR (50 MHz, DMSO-d_6) δ 175.1, 164.9, 147.5, 138.6, 133.1, 129.9, 129.0, 128.3, 125.3, 119.5, 65.3, 48.5, 27.9; IR (neat) cm^{-1}: 3428, 3124, 1767, 1666, 1608, 1530, 1503, 1271, 1229, 1179, 995, 858, 764, 700; $[\alpha]_D^{20}$: -14.95° (*c*: 0.020, DMSO); MS (ESI) calcd for $C_{19}H_{17}N_4O_3$ $[M + H]^+$: 349.1, found: 349.2.



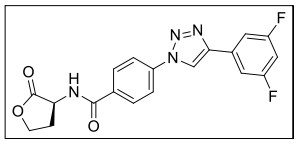
Triazole IV-R. Following *General Procedure (VIII)*, the reaction of phenylacetylene (134 μL, 124 mg, 1.22 mmol), azide **14** (200 mg, 0.81 mmol), copper(I) iodide (23 mg, 0.12 mmol) and *N,N*-diisopropylethylamine (417 μL, 315 mg, 2.44 mmol) gave, after filtration and precipitation with diethyl ether, the title compound as an off-white solid (219 mg, 77 %). Mp: 251-254 °C; RP-HPLC purity: > 95 % (R_t = 6.66 min); ^{1}H NMR (300 MHz, DMSO-d_6) δ 9.42 (s, 1H), 9.27 (d, *J* = 8.0 Hz, 1H), 8.46 (t, *J* = 1.8 Hz, 1H), 8.16 (dd, *J* = 7.8, 1.7 Hz, 1H), 8.00-7.96 (m, 3H), 7.78 (t, *J* = 7.9 Hz, 1H), 7.52 (dd, *J* = 10.4, 4.7, 2H), 7.40 (ddd, *J* = 7.4, 3.7, 1.1 Hz, 1H), 4.85 (td, *J* = 10.8, 9.0 Hz, 1H), 4.45 (dt, *J* = 8.8, 1.8 Hz, 1H), 4.31 (ddd, *J* = 10.1, 8.7, 6.6 Hz, 1H), 2.51-2.49 (m, 1H), 2.37 (ddt, *J* = 12.3, 9.9, 4.4 Hz, 1H); IR (neat) cm^{-1}: 3282, 1772, 1648, 1528, 1384, 1231, 1184, 1015, 762, 687; $[\alpha]_D^{20}$: -14.25° (*c*: 0.015, DMSO); MS (ESI) calcd for $C_{19}H_{17}N_4O_3$ $[M + H]^+$: 349.1, found: 349.3.



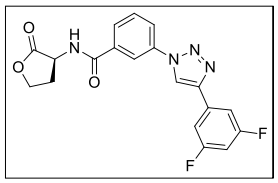
Triazole IV-S. Following *General Procedure (VIII)*, the reaction of 1-ethynyl-3,5-dimethoxybenzene (148 mg, 0.91 mmol), the azide **13** (150 mg, 0.61 mmol), copper(I) iodide (17 mg, 0.09 mmol) and *N,N*-diisopropylethylamine (313 μL, 236 mg, 1.83 mmol) gave, after filtration and precipitation with diethyl ether, the title compound as a yellow solid (249 mg, 93 %). Mp: 204-206 °C; RP-HPLC purity: > 95 % (R_t = 6.82 min); ^{1}H NMR (300 MHz, DMSO-d_6) δ 9.46 (s, 1H), 9.18 (d, *J* = 8.0 Hz, 1H), 8.11 (s, 1H), 7.14 (d, *J* = 2.3 Hz, 2H), 6.53 (t, *J* = 2.3 Hz, 1H), 4.83 (td, *J* = 10.8, 9.2 Hz, 1H), 4.45 (dt, *J* = 8.7, 1.8 Hz, 1H), 4.30 (ddd, *J* = 10.3, 8.8, 6.7 Hz, 1H), 3.83 (s, 6H), 2.55-2.45 (m, 1H), 2.44-2.30 (m, 1H); IR (neat) cm^{-1}: 3381, 1760, 1647, 1604, 1510, 1207, 1159, 1030, 837, 789, 682; $[\alpha]_D^{20}$: -13.73° (*c*: 0.015, DMSO); MS (ESI) calcd for $C_{21}H_{21}N_4O_5$ $[M + H]^+$: 409.1, found: 409.3.



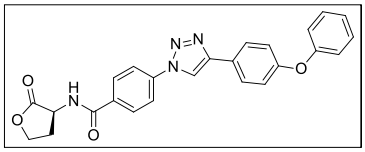
Triazole IV-T. Following *General Procedure (VIII)*, the reaction of 1-ethynyl-3,5-dimethoxybenzene (148 mg, 0.91 mmol), azide **14** (150 mg, 0.61 mmol), copper(I) iodide (17 mg, 0.09 mmol) and *N,N*-diisopropylethylamine (313 μL, 236 mg, 1.83 mmol) gave, after filtration and precipitation with diethyl ether, the title compound as a yellow solid (207 mg, 77 %). Mp: 216-218 °C; RP-HPLC purity: > 95 % (R_t = 6.91 min); ^{1}H NMR (300 MHz, DMSO-d_6) δ 9.43 (s, 1H), 9.25 (d, *J* = 8.0 Hz, 1H), 8.42 (t, *J* = 1.8 Hz, 1H), 8.13 (dd, *J* = 7.6, 1.8 Hz, 1H), 7.97 (d, *J* = 7.9 Hz, 1H), 7.76 (t, *J* = 8.0 Hz, 1H), 7.14 (d, *J* = 2.3 Hz, 2H), 6.51 (t, *J* = 2.3 Hz, 1H), 4.83 (td, *J* = 10.6, 9.1 Hz, 1H), 4.43 (dt, *J* = 8.7, 1.8 Hz, 1H), 4.29 (ddd, *J* = 10.2, 8.8, 6.6 Hz, 1H), 3.81 (s, 6H); IR (neat) cm^{-1}: 3279, 1766, 1644, 1592, 1531, 1205, 1182, 1036, 825, 792, 684; $[\alpha]_D^{20}$: -10.80° (*c*: 0.005, DMSO); MS (ESI) calcd for $C_{21}H_{21}N_4O_5$ $[M + H]^+$: 409.1, found: 409.3.



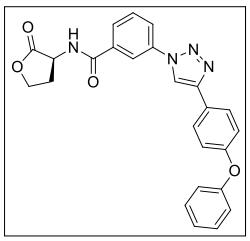
Triazole IV-U. Following *General Procedure (VIII)*, the reaction of 1-ethynyl-3,5-difluorobenzene (108 μL, 126 mg, 0.91 mmol), azide **13** (150 mg, 0.61 mmol), copper(I) iodide (17 mg, 0.09 mmol) and *N*,*N*-diisopropylethylamine (313 μL, 236 mg, 1.83 mmol) gave, after filtration and precipitation with diethyl ether, the title compound as a yellow solid (225 mg, > 95 %). Mp: 255-257 °C; RP-HPLC purity: > 95 % (R_t = 7.33 min); ^{1}H NMR (300 MHz, DMSO-d_6) δ 9.55 (s, 1H), 9.18 (d, *J* = 8.3 Hz, 1H), 8.12 (d, *J* = 9.3 Hz, 2H), 8.07 (d, *J* = 9.3 Hz, 2H), 7.65 (dd, *J* = 8.9, 2.2 Hz, 2H), 7.29 (tt, *J* = 9.3, 2.4 Hz, 1H), 4.83 (dd, *J* = 19.1, 8.9 Hz, 1H), 4.44 (dt, *J* = 8.8, 1.3 Hz, 1H), 4.30 (ddd, *J* = 10.3, 9.0, 6.7 Hz, 1H), 2.54-2.45 (m, 1H), 2.43-2.29 (m, 1H); IR (neat) cm^{-1}: 3337, 3154, 1779, 1752, 1503, 1118, 982, 850; MS (ESI) calcd for $C_{19}H_{15}F_2N_4O_3$ [M + H]$^+$: 385.1, found: 385.2.



Triazole IV-V. Following *General Procedure (VIII)*, the reaction of 1-ethynyl-3,5-difluorobenzene (108 μL, 126 mg, 0.91 mmol), azide **14** (150 mg, 0.61 mmol), copper(I) iodide (17 mg, 0.09 mmol) and *N*,*N*-diisopropylethylamine (313 μL, 236 mg, 1.83 mmol) gave, after filtration and precipitation with diethyl ether, the title compound as a light yellow solid (227 mg, > 95 %). Mp: 251-253 °C; RP-HPLC purity: > 95 % (R_t = 7.40 min); ^{1}H NMR (300 MHz, DMSO-d_6) δ 9.55 (s, 1H), 9.27 (d, *J* = 8.0 Hz, 1H), 8.43 (t, *J* = 1.8 Hz, 1H), 8.12 (dd, *J* = 8.0, 1.4 Hz, 1H), 8.00 (d, *J* = 7.9 Hz, 1H), 7.79 (t, *J* = 8.0 Hz, 1H), 7.67 (dd, *J* = 8.7, 2.2 Hz, 2H), 7.29 (tt, *J* = 9.4, 2.4 Hz, 1H), 4.85 (td, *J* = 10.7, 9.1 Hz, 1H), 4.44 (dt, *J* = 8.8, 1.8 Hz, 1H), 4.30 (ddd, *J* = 10.1, 8.7, 6.6 Hz, 1H), 2.56-2.46 (m, 1H), 2.43-2.29 (m, 1H); IR (neat) cm^{-1}: 3280, 1772, 1646, 1593, 1526, 1183, 1120, 856, 673; MS (ESI) calcd for $C_{19}H_{15}F_2N_4O_3$ [M + H]$^+$: 385.1, found: 385.3.

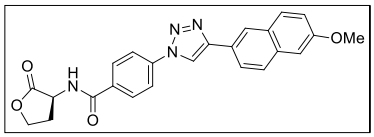


Triazole IV-W. Following *General Procedure (VIII)*, the reaction of 1-ethynyl-4-phenoxybenzene (165 μL, 177 mg, 0.91 mmol), azide **13** (150 mg, 0.61 mmol), copper(I) iodide (17 mg, 0.09 mmol) and *N*,*N*-diisopropylethylamine (313 μL, 236 mg, 1.83 mmol) gave, after filtration and precipitation with diethyl ether, the title compound as a yellow solid (257 mg, > 95 %). Mp: 244-246 °C; RP-HPLC purity: 92 % (R_t = 8.11 min); ^{1}H NMR (300 MHz, DMSO-d_6) δ 9.39 (s, 1H), 9.19 (d, *J* = 8.0 Hz, 1H), 8.12 (s, 1H), 7.97 (d, *J* = 8.5 Hz, 2H), 7.43 (t, *J* = 7.7 Hz, 2H), 7.21-7.08 (m, 5H), 4.83 (td, *J* = 10.0, 9.0 Hz, 1H), 4.45 (dd, *J* = 8.8, 7.5 Hz, 1H), 4.35-4.26 (m, 1H), 2.55-2.44 (m, 1H), 2.41-2.30 (m, 1H); IR (neat) cm^{-1}: 3297, 1755, 1639, 1537, 1486, 1226, 1189, 1038, 849, 751, 690; MS (ESI) calcd for $C_{25}H_{21}N_4O_4$ [M + H]$^+$: 441.2, found: 441.3.

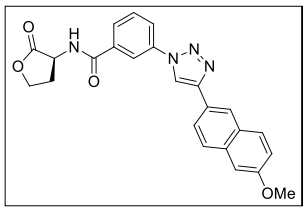


Triazole IV-X. Following *General Procedure (VIII)*, the reaction of 1-ethynyl-4-phenoxybenzene (165 μL, 177 mg, 0.91 mmol), azide **14** (150 mg, 0.61 mmol), copper(I) iodide (17 mg, 0.09 mmol) and *N*,*N*-diisopropylethylamine (313 μL, 236 mg, 1.83 mmol) gave, after filtration and precipitation with diethyl ether, the title compound as a white solid (203 mg, 76 %). Mp: 225-227 °C; RP-HPLC purity: > 95 % (R_t = 8.17 min); ^{1}H NMR (300 MHz, DMSO-d_6) δ 9.38 (s, 1H), 9.27 (d, *J* = 8.0 Hz, 1H), 8.46 (s, 1H), 8.16 (dd, *J* = 8.1, 1.8 Hz, 1H), 7.98 (dd, *J* = 8.6, 2.6 Hz, 3H), 7.78 (t, *J* = 7.8 Hz, 1H), 7.43 (t, *J* = 7.8 Hz, 2H), 7.21-7.08 (m, 5H), 4.85 (dd, *J* = 18.8, 9.3 Hz, 1H), 4.45 (dd, *J*

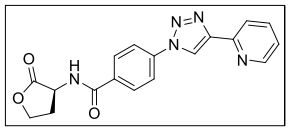
= 9.1, 8.0 Hz, 1H), 4.35-4.26 (m, 1H), 2.56-47 (m, 1H), 2.44-2.30 (m, 1H); IR (neat) cm^{-1}: 3278, 1773, 1644, 1546, 1484, 1247, 1183, 1012, 871, 752, 692; MS (ESI) calcd for $C_{25}H_{21}N_4O_4$ $[M + H]^+$: 441.3, found: 441.3.



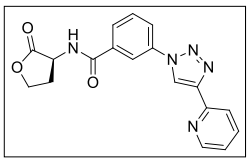
Triazole IV-Y. Following *General Procedure (VIII)*, the reaction of 2-ethynyl-6-methoxynaphthalene (167 mg, 0.91 mmol), azide **13** (150 mg, 0.61 mmol), copper(I) iodide (17 mg, 0.09 mmol) and *N,N*-diisopropylethylamine (313 μL, 236 mg, 1.83 mmol) gave, after filtration and precipitation with diethyl ether, the title compound as a dark yellow solid (225 mg, 86 %). Mp: 259-261 °C; RP-HPLC purity: > 95 % (R_t = 7.52 min); ^{1}H NMR (300 MHz, DMSO-d_6) δ 9.49 (d, J = 1.4 Hz, 1H), 9.19 (d, J = 7.9 Hz, 1H), 8.44 (s, 1H), 8.14 (s, 4H), 8.05-8.02 (m, 1H), 7.96-7.91 (m, 2H), 7.38 (d, J = 1.6 Hz, 1H), 7.22 (ddd, J = 9.2, 2.5, 1.2 Hz, 1H), 4.84 (td, J = 9.7, 8.5 Hz, 1H), 4.45 (t, J = 8.6 Hz, 1H), 4.30 (td, J = 9.6, 7.3 Hz, 1H), 3.90 (d, J = 1.1 Hz, 3H), 2.58-2.46 (m, 1H), 2.37 (qd, J = 10.4, 9.5 Hz, 1H); IR (neat) cm^{-1}: 3298, 1786, 1770, 1640, 1607, 1508, 1223, 1166, 1031, 856, 817, 767; MS (ESI) calcd for $C_{24}H_{21}N_4O_4$ $[M + H]^+$: 429.2, found: 429.3.



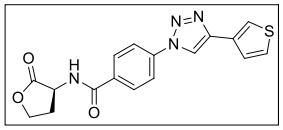
Triazole IV-Z. Following *General Procedure (VIII)*, the reaction of 2-ethynyl-6-methoxynaphthalene (167 mg, 0.91 mmol), azide **14** (150 mg, 0.61 mmol), copper(I) iodide (17 mg, 0.09 mmol) and *N,N*-diisopropylethylamine (313 μL, 236 mg, 1.83 mmol) gave, after filtration and precipitation with diethyl ether, the title compound as a yellow solid (232 mg, 89 %). Mp: 262-263 °C; RP-HPLC purity: > 95 % (R_t = 7.60 min); ^{1}H NMR (300 MHz, DMSO-d_6) δ 9.48 (s, 1H), 9.28 (d, J = 8.0 Hz, 1H), 8.47 (d, J = 9.6 Hz, 2H), 8.19 (d, J = 8.2 Hz, 1H), 8.06-7.91 (m, 4H), 7.79 (t, J = 8.0 Hz, 1H), 7.38 (d, J = 1.9 Hz, 1H), 7.22 (dd, J = 9.2, 2.0 Hz, 1H), 4.86 (dd, J =18.1, 9.3 Hz, 1H), 4.49-4.43 (m, 1H), 4.31 (td, J = 9.4, 7.7 Hz, 1H), 3.90 (s, 3H), 2.57-2.50 (m, 1H), 2.45-2.31 (m, 1H); ^{13}C NMR (50 MHz, DMSO-d_6) δ 175.2, 164.9, 157.6, 147.7, 136.8, 135.1, 134.1, 130.3, 129.6, 128.5, 127.5, 127.3, 125.3, 124.1, 123.8, 122.9, 119.6, 119.3, 118.7, 105.1, 65.4, 55.2, 48.6, 28.0; IR (neat) cm^{-1}: 3217, 1779, 1632, 1543, 1489, 1180, 1029, 854, 819, 665, 477; MS (ESI) calcd for $C_{24}H_{21}N_4O_4$ $[M + H]^+$: 429.2, found: 429.3.



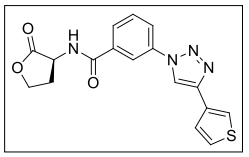
Triazole IV-AA. Following *General Procedure (VIII)*, the reaction of 2-ethynylpyridine (92 μL, 94 mg, 0.91 mmol), azide **13** (150 mg, 0.61 mmol), copper(I) iodide (17 mg, 0.09 mmol) and *N,N*-diisopropylethylamine (313 μL, 236 mg, 1.83 mmol) gave, after filtration and precipitation with diethyl ether, the title compound as a beige solid (179 mg, 84 %). Mp: 229-231 °C; RP-HPLC purity: > 95 % (R_t = 4.26 min); ^{1}H NMR (300 MHz, DMSO-d_6) δ 9.48 (s, 1H), 9.18 (d, J = 7.9 Hz, 1H), 8.68 (s, 1H), 8.21 (d, J = 8.5 Hz, 2H), 8.09 (d, J = 8.5 Hz, 2H), 8.02-7.91 (m, 1H), 7.44 (d, J = 7.2 Hz, 1H), 4.83 (dd, J = 18.7, 9.4 Hz, 1H), 4.43 (td, J = 8.6, 4.4 Hz, 1H), 4.34-4.25 (m, 1H), 2.54-2.45 (m, 1H), 2.43-2.29 (m, 1H); IR (neat) cm^{-1}: 3337, 1784, 1634, 1603, 1539, 1513, 1234, 1023, 848, 781, 621; MS (ESI) calcd for $C_{18}H_{16}N_5O_3$ $[M + H]^+$: 350.1, found: 350.2.



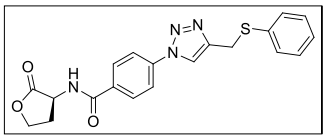
Triazole IV-AB. Following *General Procedure (VIII)*, the reaction of 2-ethynylpyridine (92 μL, 94 mg, 0.91 mmol), azide **14** (150 mg, 0.61 mmol), copper(I) iodide (17 mg, 0.09 mmol) and *N,N*-diisopropylethylamine (313 μL, 236 mg, 1.83 mmol) gave, after filtration and precipitation with diethyl ether, the title compound as an orange solid (189 mg, 89 %). Mp: 189-191 °C; RP-HPLC purity: > 95 % (R_t = 4.32 min); ^{1}H NMR (300 MHz, DMSO-d_6) δ 9.42 (s, 1H), 9.25 (d, *J* = 7.9 Hz, 1H), 8.69 (s, 1H), 8.52 (s, 1H), 8.24 (d, *J* = 7.9 Hz, 1H), 8.00 (d, *J* = 7.7 Hz, 1H), 7.76 (t, *J* = 7.9 Hz, 1H), 7.43 (s, 1H), 4.86 (dd, *J* = 18.6, 9.1 Hz, 1H), 4.45 (t, *J* = 8.4 Hz, 1H), 4.35-4.27 (m, 1H), 2.57-2.50 (m, 1H), 2.44-2.30 (m, 1H); IR (neat) cm^{-1}: 3269, 1769, 1643, 1533, 1377, 1176, 1014, 817, 686; MS (ESI) calcd for $C_{18}H_{16}N_5O_3$ [M + H]$^+$: 350.1, found: 350.3.



Triazole IV-AC. Following *General Procedure (VIII)*, the reaction of 3-ethynylthiophene (90 μL, 99 mg, 0.91 mmol), azide **13** (150 mg, 0.61 mmol), copper(I) iodide (17 mg, 0.09 mmol) and *N,N*-diisopropylethylamine (313 μL, 236 mg, 1.83 mmol) gave, after filtration and precipitation with diethyl ether, the title compound as a light yellow solid (210 mg, > 95 %). Mp: 274-276 °C; RP-HPLC purity: > 95 % (R_t = 6.30 min); ^{1}H NMR (300 MHz, DMSO-d_6) δ 9.29 (d, *J* = 0.8 Hz, 1H), 9.18 (d, *J* = 8.0 Hz, 1H), 8.10 (s, 4H), 7.97 (td, *J* = 2.9, 1.1 Hz, 1H), 7.72 (ddd, *J* = 5.0, 2.9, 1.1 Hz, 1H), 7.59 (td, *J* = 5.0, 1.1 Hz, 1H), 4.87-4.77 (m, 1H), 4.44 (dt, *J* = 8.6, 1.0 Hz, 1H), 4.29 (ddd, *J* = 9.6, 8.7, 6.6 Hz, 1H), 2.55-2.45 (m, 1H), 2.43-2.29 (m, 1H); ^{13}C NMR (50 MHz, DMSO-d_6) δ 175.2, 164.9, 144.1, 138.7, 133.2, 131.3, 129.1, 127.5, 125.8, 121.7, 119.6, 119.4, 65.4, 48.5, 28.0; IR (neat) cm^{-1}: 3425, 3371, 3128, 1768, 1664, 1504, 1230, 857, 791, 618; MS (ESI) calcd for $C_{17}H_{15}N_4O_3S$ [M + H]$^+$: 355.1, found: 355.2.

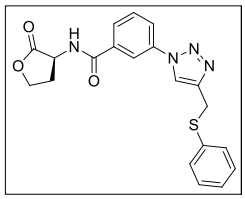


Triazole IV-AD. Following *General Procedure (VIII)*, the reaction of 3-ethynylthiophene (90 μL, 99 mg, 0.91 mmol), azide **14** (150 mg, 0.61 mmol), copper(I) iodide (17 mg, 0.09 mmol) and *N,N*-diisopropylethylamine (313 μL, 236 mg, 1.83 mmol) gave, after filtration and precipitation with diethyl ether, the title compound as a yellow solid (197 mg, 91 %). Mp: 218-219 °C; RP-HPLC purity: > 95 % (R_t = 6.39 min); ^{1}H NMR (300 MHz, DMSO-d_6) δ 9.26 (t, *J* = 3.0 Hz, 2H), 8.42 (s, 1H), 8.15-8.12 (m, 1H), 7.99-7.96 (m, 2H), 7.78 (d, *J* = 7.9 Hz, 1H), 7.74-7.70 (m, 1H), 7.60 (td, *J* = 5.0, 1.0 Hz, 1H), 4.85 (dtd, *J* = 9.3, 8.9, 0.4 Hz, 1H), 4.44 (dt, *J* = 8.5, 1.7 Hz, 1H), 4.34-4.26 (m, 1H), 2.58-5.46 (m, 1H), 2.43-2.29 (m, 1H); IR (neat) cm^{-1}: 3279, 1772, 1646, 1530, 1182, 1014, 782, 665; MS (ESI) calcd for $C_{17}H_{15}N_4O_3S$ [M + H]$^+$: 355.1, found: 355.2.

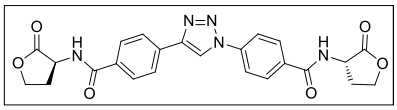


Triazole IV-AE. Following *General Procedure (VIII)*, the reaction of phenyl propargyl sulfide (126 μL, 135 mg, 0.91 mmol), azide **13** (150 mg, 0.61 mmol), copper(I) iodide (17 mg, 0.09 mmol) and *N,N*-diisopropylethylamine (313 μL, 236 mg, 1.83 mmol) gave, after filtration and precipitation with diethyl ether, the title compound as a yellow solid (218 mg, 91 %). Mp: 221-225 °C; RP-HPLC purity: > 95 % (R_t = 6.81 min); ^{1}H NMR (300 MHz, DMSO-d_6) δ 9.14 (d, *J* = 8.0 Hz, 1H), 8.80 (s, 1H), 8.03 (s, 4H), 7.40 (td, *J* = 3.0, 1.9 Hz, 2H), 7.34-7.28 (m, 2H), 7.21-7.16 (m, 1H), 4.80 (td, *J* = 10.6, 9.1 Hz, 1H), 4.42 (dt, *J* = 8.9, 2.0 Hz, 1H), 4.38 (s,

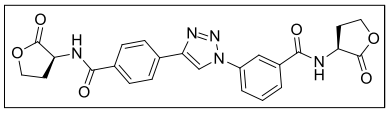
2H), 2.53-2.43 (m, 1H), 2.41-2.27 (m, 1H); IR (neat) cm^{-1}: 3268, 1771, 1633, 1606, 1543, 1512, 1179, 1013, 853, 688; MS (ESI) calcd for $C_{20}H_{19}N_4O_3S$ $[M + H]^+$: 395.1, found: 395.3.



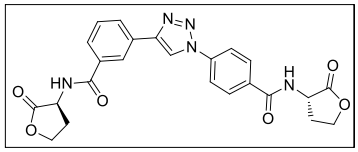
Triazole IV-AF. Following *General Procedure (VIII)*, the reaction of phenyl propargyl sulfide (126 μL, 135 mg, 0.92 mmol), azide **14** (150 mg, 0.61 mmol), copper(I) iodide (17 mg, 0.09 mmol) and *N,N*-diisopropylethylamine (313 μL, 236 mg, 1.83 mmol) gave, after filtration and precipitation with diethyl ether, the title compound as a yellow solid (198 mg, 83 %). Mp: 165-167 °C; RP-HPLC purity: 84 % (R_t = 6.89 min); ^{1}H NMR (300 MHz, DMSO-d_6) δ 9.21 (d, J = 8.0 Hz, 1H), 8.76 (s, 1H), 8.33 (t, J = 1.9 Hz, 1H), 8.04 (dd, J = 8.0, 2.2 Hz, 1H), 7.94 (d, J = 7.9 Hz, 1H), 7.71 (t, J = 8.0 Hz, 1H), 7.40 (ddd, J = 2.3, 1.3, 0.5 Hz, 2H), 7.34-7.29 (m, 2H), 7.22-7.16 (m, 1H), 4.82 (td, J = 10.7, 9.0 Hz, 1H), 4.43 (dt, J = 9.0, 2.0 Hz, 1H), 4.38 (s, 2H), 4.28 (ddd, J = 10.3, 8.7, 6.7 Hz, 1H), 2.53-2.43 (m, 1H), 2.41-2.25 (m, 1H); ^{13}C NMR (50 MHz, DMSO-d_6) δ 175.1, 164.8, 145.0, 136.6, 135.5, 135.0, 130.2 129.0, 128.3, 127.3, 126.0, 123.0, 121.6, 118.7, 65.3, 48.5, 28.0, 27.2; IR (neat) cm^{-1}: 3269, 1755,1644, 1586, 1534, 1478, 1437, 1382, 1327, 1182, 1016, 806, 734, 679; MS (ESI) calcd for $C_{20}H_{19}N_4O_3S$ $[M + H]^+$: 395.1, found: 395.2.



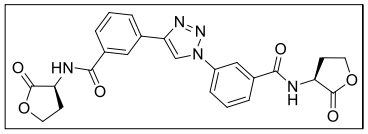
Bis-homoserine lactone V-A. Following *General Procedure (VII)*, the reaction of azide **13** (64 mg, 0.26 mmol), *N*-(4-ethynylobenzoyl)-L-homoserine lactone (**11**) (60 mg, 0.26 mmol), copper(I) iodide (7.5 mg, 0.04 mmol) and *N,N*-diisopropylethylamine (134 μL, 101 mg, 0.79 mmol) gave, after precipitation with diethyl ether, the title compound as a sand colored solid (103 mg, 83 %). Mp: 325-327 °C; RP-HPLC purity: > 95 % (R_t = 5.27 min); ^{1}H NMR (300 MHz, DMSO-d_6) δ 9.57 (s, 1H), 9.20 (d, J = 8.0 Hz, 1H), 9.09 (d, J = 8.0 Hz, 1H), 8.13 (s, 4H), 8.09 (d, J = 8.4 Hz, 2H), 8.02 (d, J = 8.4 Hz, 2H), 4.89-4.78 (m, 2H), 4.45 (t, J = 8.7 Hz, 2H), 4.30 (dd, J = 16.5, 9.7 Hz, 2H), 2.59-2.44 (m, 2H), 2.41-2.30 (m, 2H) ; ^{13}C NMR (75 MHz, DMSO-d_6) δ 175.0, 165.2, 164.6, 149.4, 146.4, 142.9, 138.3, 132.7, 128.8, 127.8, 124.9, 120.4, 119.4, 65.1, 48.2, 27.7; IR (neat) cm^{-1}: 3324, 1780, 1751, 1644, 1524, 1156, 1017, 854, 766; MS (ESI) calcd for $C_{24}H_{22}N_5O_6$ $[M + H]^+$: 476.2, found: 476.3.



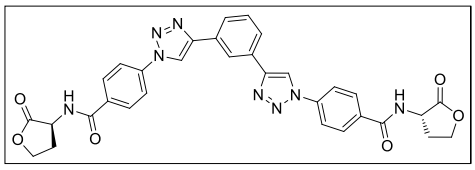
Bis-homoserine lactone V-B. Following *General Procedure (VII)*, the reaction of azide **14** (64 mg, 0.26 mmol), *N*-(4-ethynylobenzoyl)-L-homoserine lactone (**11**) (60 mg, 0.26 mmol), copper(I) iodide (7.5 mg, 0.04 mmol) and *N,N*-diisopropylethylamine (134 μL, 101 mg, 0.79 mmol) gave, after precipitation with diethyl ether, the title compound as a sand colored solid (90 mg, 73 %). Mp: 281-283 °C; RP-HPLC purity: > 95 % (R_t = 5.39 min); ^{1}H NMR (300 MHz, DMSO-d_6) δ 9.55 (s, 1H), 9.29 (d, J = 7.9 Hz, 1H), 9.09 (d, J = 8.0 Hz, 1H), 8.48 (s, 1H), 8.17 (dd, J = 8.0, 1.7 Hz, 1H), 8.10 (d, J = 8.3 Hz, 2H), 8.01 (d, J = 8.5 Hz, 3H), 7.80 (t, J = 7.9 Hz, 1H), 4.84 (ddd, J = 18.0, 11.5, 9.5 Hz, 2H), 4.48-4.42 (m, 2H), 4.36-4.26 (m, 2H), 2.54-2.48 (m, 2H), 2.45-2.31 (m, 2H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 175.1, 175.0, 165.3, 164.7, 146.4, 136.4, 134.9, 132.9, 132.7, 130.1, 127.9, 127.2, 125.0, 122.8, 120.6, 118.7, 65.2, 65.2, 48.4, 48.3, 27.8; IR (neat) cm^{-1}: 3292, 1771, 1643, 1528, 1182, 1015, 806; MS (ESI) calcd for $C_{24}H_{22}N_5O_6$ $[M + H]^+$: 476.2, found: 476.3.



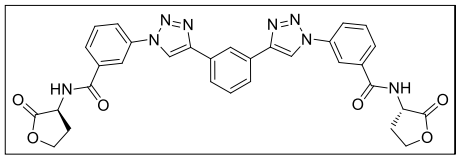
Bis-homoserine lactone V-C. Following *General Procedure (VII)*, the reaction of azide **13** (64 mg, 0.26 mmol), *N*-(3-ethynylobenzoyl)-L-homoserine lactone (**12**) (60 mg, 0.26 mmol), copper(I) iodide (7.5 mg, 0.04 mmol) and *N*,*N*-diisopropylethylamine (134 μL, 101 mg, 0.79 mmol) gave, after precipitation with diethyl ether, the title compound as a sand colored solid (114 mg, 92 %). Mp: 253-255 °C; RP-HPLC purity: > 95 % (R_t = 5.41 min); ^{1}H NMR (300 MHz, DMSO-d_6) δ 9.54 (s, 1H), 9.19 (t, *J* = 7.2 Hz, 2H), 8.50 (s, 1H), 8.18-8.11 (m, 6H), 7.88 (d, *J* = 7.7 Hz, 1H), 7.66 (t, *J* = 7.7 Hz, 1H), 4.84 (dt, *J* = 10.6, 2.5 Hz, 4H), 4.45 (t, *J* = 8.2 Hz, 2H), 4.31 (td, *J* = 8.4, 6.6 Hz, 2H), 2.55-2.45 (m, 2H), 2.41-2.31 (m, 2H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 174.8, 174.7, 165.3, 164.4, 146.4, 138.1, 133.8, 132.7, 129.8, 128.8, 128.6, 127.9, 126.5, 123.7, 119.7, 119.1, 64.9, 48.7, 48.0, 48.0, 27.5, 27.5; IR (neat) cm^{-1}: 3270, 1768, 1641, 1536, 1162, 1014, 848, 760; MS (ESI) calcd for $C_{24}H_{22}N_5O_6$ [M + H]$^+$: 476.2, found: 476.3.



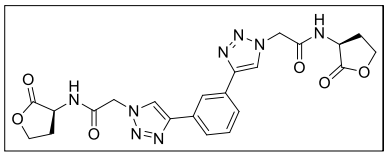
Bis-homoserine lactone V-D. Following *General Procedure (VII)*, the reaction of azide **14** (64 mg, 0.26 mmol), *N*-(3-ethynylobenzoyl)-L-homoserine lactone (**12**) (60 mg, 0.26 mmol), copper(I) iodide (7.5 mg, 0.04 mmol) and *N*,*N*-diisopropylethylamine (134 μL, 101 mg, 0.79 mmol) gave, after precipitation with diethyl ether, the title compound as a sand colored solid (88 mg, 71 %). Mp: 280-282 °C; RP-HPLC purity: > 95 % (R_t = 5.53 min); ^{1}H NMR (300 MHz, DMSO-d_6) δ 9.49 (s, 1H), 9.26 (d, *J* = 8.0 Hz, 1H), 9.15 (d, *J* = 7.9 Hz, 1H), 8.47 (d, *J* = 5.5 Hz, 2H), 8.18-8.11 (m, 2H), 7.98 (d, *J* = 7.8 Hz, 1H), 7.85 (d, *J* = 7.7 Hz, 1H), 7.77 (t, *J* = 7.9 Hz, 1H), 7.63 (t, *J* = 7.7 Hz, 1H), 4.88-4.78 (m, 2H), 4.43 (t, *J* = 8.6 Hz, 2H), 4.33-4.24 (m, 2H), 2.56-2.44 (m, 2H), 2.42-2.28 (m, 2H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 175.2, 175.1, 165.7, 164.8, 146.7, 146.7, 136.5, 135.0, 134.2, 130.2, 130.2, 129.1, 128.3, 127.2, 126.9, 126.9, 124.1, 122.8, 120.1, 118.7, 65.3, 48.4, 48.4, 27.9; IR (neat) cm^{-1}: 3231, 1775, 1638, 1535, 1181, 1010, 811, 684; MS (ESI) calcd for $C_{24}H_{22}N_5O_6$ [M + H]$^+$: 476.2, found: 476.4.



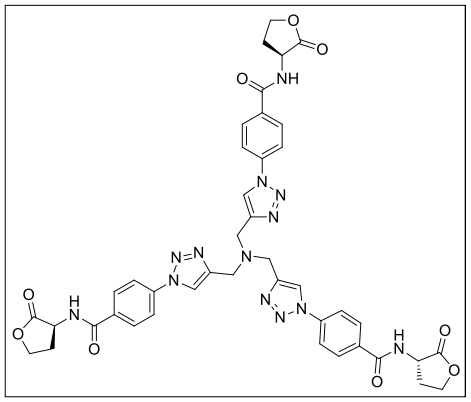
Bis-homoserine lactone V-E. Following *General Procedure (VIII)*, the reaction of 1,3-diethynylbenzene (38 mg, 0.31 mmol), azide **13** (150 mg, 0.61 mmol), copper(I) iodide (16 mg, 0.09 mmol) and *N*,*N*-diisopropylethylamine (418 μL, 314 mg, 2.44 mmol) gave, after filtration and precipitation with diethyl ether, the title compound as a dark brown solid (157 mg, 84 %). Mp: > 350 °C; RP-HPLC purity: 81 % (R_t = 6.39 min); ^{1}H NMR (300 MHz, DMSO-d_6) δ 9.56 (s, 2H), 9.20 (d, *J* = 7.8 Hz, 2H), 8.63 (s, 1H), 8.15 (q, *J* = 8.8 Hz, 8H), 7.98 (d, *J* = 7.7 Hz, 1H), 7.67 (t, *J* = 7.7 Hz, 1H), 4.84 (dd, *J* = 18.3, 9.3 Hz, 2H), 4.45 (t, *J* = 8.5 Hz, 2H), 4.35-4.26 (m, 2H), 2.55-2.47 (m, 2H), 2.45-2.30 (m, 2H); ^{13}C NMR (50 MHz, DMSO-d_6) δ 175.2, 164.9, 147.2, 138.6, 133.2, 130.8, 129.8, 129.1, 125.3, 122.1, 120.0, 119.6, 65.4, 48.5, 28.0; IR (neat) cm^{-1}: 3291, 1765, 1636, 1605, 1537, 1505, 1161, 1013, 847, 763; MS (ESI) calcd for $C_{32}H_{26}N_8O_4$ [M + H]$^+$: 619.2, found: 619.5.



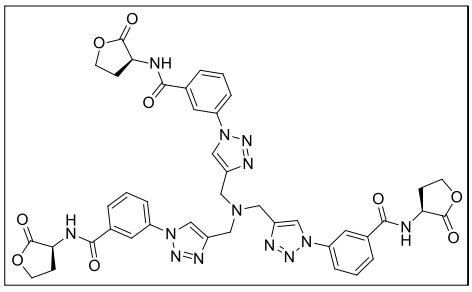
Bis-homoserine lactone V-F. Following General Procedure (VIII), the reaction of 1,3-diethynylbenzene (38 mg, 0.31 mmol), azide **14** (150 mg, 0.61 mmol), copper(I) iodide (16 mg, 0.09 mmol) and *N,N*-diisopropylethylamine (418 μL, 314 mg, 2.44 mmol) gave, after filtration and precipitation with diethyl ether, the title compound as a yellow solid (180 mg, > 95 %). Mp: 260-262 °C; RP-HPLC purity: 94 % (R_t = 6.59 min); ^{1}H NMR (300 MHz, DMSO-d_6) δ 9.53 (s, 2H), 9.28 (d, *J* = 8.0 Hz, 2H), 8.64 (s, 1H), 8.50 (s, 2H), 8.20 (dd, *J* = 8.4, 1.5 Hz, 2H), 8.01-7.97 (m, 4H), 7.79 (t, *J* = 7.9 Hz, 2H), 7.66 (t, *J* = 7.7 Hz, 1H), 4.86 (td, *J* = 10.2, 9.0 Hz, 1H), 4.45 (dt, *J* = 8.6, 1.1 Hz, 2H), 4.31 (ddd, *J* = 15.5, 8.9, 6.8 Hz, 2H), 2.57-2.49 (m, 2H), 2.45-2.31 (m, 2H); ^{13}C NMR (50 MHz, DMSO-d_6) δ 175.2, 164.9, 147.2, 136.7, 135.2, 130.9, 130.3, 129.8, 127.3, 125.3, 123.0, 122.2, 120.2, 118.8, 65.4, 48.6, 28.0; IR (neat) cm^{-1}: 3281, 1770, 1647, 1534, 1380, 1223, 1177, 1013, 793, 683; MS (ESI) calcd for $C_{32}H_{26}N_8O_4$ [M + H]$^+$: 619.2, found: 619.5.



Bis-homoserine lactone V-G. Following *General Procedure (VI)*, the reaction of azide **3** (200 mg, 1.09 mmol), 1,3-diethynylbenzene (60 μL, 57 mg, 0.45 mmol), copper(I) iodide (34 mg, 0.18 mmol) and *N,N*-diisopropylethylamine (310 μL, 234 mg, 1.81 mmol) gave, after precipitation with diethyl ether, the title compound as a brownish solid (95 mg, 42 %). Mp: 212-214 °C; RP-HPLC purity: 85 % (R_t = 4.50 min); ^{1}H NMR (300 MHz, DMSO-d_6): δ 8.93 (d, *J* = 7.8 Hz, 2H), 8.65 (s, 2H), 8.40 (s, 1H), 7.84 (dd, *J* = 7.8, 1.3 Hz, 2H), 7.54 (t, *J* = 7.8 Hz, 1H) , 5.26 (s, 4H), 4.68 (td, *J* = 10.8, 8.6 Hz, 2H), 4.36 (dt, *J* = 8.8, 0.8 Hz, 2H), 4.23 (ddd, *J* = 10.4, 9.0, 6.5 Hz, 2H), 2.49-2.42 (m, 2H), 2.26-2.12 (m, 2H); ^{13}C NMR (DMSO-d_6, from ^{1}H-^{13}C gHSQC and ^{1}H-^{13}C gHMBC, 500 MHz): δ 174.4, 165.3, 145.4, 131.1, 129.0, 124.0, 122.6, 121.2, 65.1, 51.3, 47.8, 28.0; IR (neat) cm^{-1}: 3280, 1769, 1672, 1553, 1382, 1180, 1018, 796; $[\alpha]_D^{20}$: -16.9° (*c*: 0.0022, DMSO); MS (ESI) calcd for $C_{22}H_{23}N_8O_4$ [M + H]$^+$: 495.2, found: 495.3.



Tris-homoserine lactone V-H. Following *General Procedure (VIII)*, the reaction of tripropargylamine (29 μL, 27 mg, 0.03 mmol), azide **13** (150 mg, 0.61 mmol), copper(I) iodide (17 mg, 0.09 mmol) and *N,N*-diisopropylethylamine (417 μL, 315 mg, 2.44 mmol) gave, after filtration and precipitation with diethyl ether, the title compound as a brown solid (170 mg, > 95 %). Mp: 297-298 °C; RP-HPLC purity: > 95 % (R_t = 4.96 min); ^{1}H NMR (300 MHz, DMSO-d_6) δ 9.16 (d, *J* = 8.0 Hz, 3H), 8.95 (s, 2H), 8.08 (s, 12H), 4.81 (dd, *J* = 18.8, 9.2 Hz, 1H), 4.43 (dt, *J* = 8.6, 1.5 Hz, 3H), 4.29 (td, *J* = 8.7, 6.6 Hz, 3H), 3.96 (s, 3H), 3.34 (s, 3H), 2.53-2.45 (m, 3H), 2.43-2.28 (m, 3H); IR (neat) cm^{-1}: 3290, 1771, 1640, 1608, 1538, 1508, 1174, 1016, 849; MS (ESI) calcd for $C_{42}H_{40}N_{13}O_9$ [M + H]$^+$: 870.3, found: 870.5



Tris-homoserine lactone V-I. Following *General Procedure (VIII)*, the reaction of tripropargylamine (29 μL, 27 mg, 0.03 mmol), azide **14** (150 mg, 0.61 mmol), copper(I) iodide (30 mg, 0.152 mmol) and *N*,*N*-diisopropylethylamine (695 μL, 525 mg, 4.06 mmol) gave, after filtration and precipitation with diethyl ether, the title compound as a brown solid (172 mg, > 95 %). Mp: 303-304 °C; RP-HPLC purity: > 95 % (R_t = 5.16 min); ^{1}H NMR (300 MHz, DMSO-d_6) δ 9.24 (d, J = 8.0 Hz, 3H), 8.90 (s, 1H), 8.41 (s, 1H), 8.12 (d, J = 8.1 Hz, 1H), 7.96 (d, J = 7.8 Hz, 1H), 7.74 (t, J = 7.9 Hz, 1H), 4.88-4.79 (m, 3H), 4.43 (dt, J = 8.6, 1.3 Hz, 1H), 4.29 (ddd, J = 15.4, 8.8, 6.6 Hz, 3H), 3.95 (s, 1H), 2.54-2.45 (m, 3H), 2.42-2.28 (m, 3H), 2.07 (s, 1H); ^{13}C NMR (50 MHz, DMSO-d_6) δ 175.1, 164.9, 135.0, 130.2, 127.2, 123.1, 118.9, 65.4, 48.5, 28.0; IR (neat) cm^{-1}: 3267, 1772, 1639, 1588, 1536, 1155, 1018, 681; MS (ESI) calcd for $C_{42}H_{40}N_{13}O_9$ $[M + H]^+$: 870.3, found: 870.7.

******Note***: ^{1}H NMR spectra and RP-HPLC chromatograms for all compounds are included in the next section.