Supporting Information

**Indole/triazole conjugates are selective inhibitors and inducers of bacterial biofilms.**

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**Synthesis**: All reagents used for chemical synthesis were purchased from commercially available sources and used without further purification. Chromatography was performed using 60 mesh standard silica gel from Sorbtech. NMR solvents were obtained from Cambridge Isotope Labs and were used as is. $^1$HNMR (300 MHz or 400 MHz) and $^{13}$C NMR (75 MHz or 100 MHz) spectra were recorded at 25 °C on Varian Mercury spectrometers. Chemical shifts ($\delta$) are given in ppm relative to the respective NMR solvents; coupling constants ($J$) are in hertz (Hz). Abbreviations used are s = singlet, bs = broad singlet, d = doublet, dd= doublet of doublets, t = triplet, td = triplet of doublets, dt = doublet of triplets, m = multiplet, d$_{ab}$ = ab doublet, dd$_{ab}$ = ab doublet of doublet. Mass spectra were obtained at the NCSU Department of Chemistry Mass Spectrometry Facility. Infrared spectra were obtained on a FT/IR-4100 spectrophotometer ($\nu_{\text{max}}$ in cm$^{-1}$). UV absorbance was recorded on a Genesys 10 scanning UV/visible spectrophotometer ($\lambda_{\text{max}}$ in nm).

![Indole/triazole conjugate](image)

3-(prop-2-ynyl)-1H-indole (2) was prepared following the synthetic procedure of Yu, R. T.; Friedman, R. K. and Rovis, T. *JACS*, 2009, 131, 13250.

**General procedure for the Cu (I) - catalyzed alkyne/azide cycloadditions**: The appropriate alkyne compound was added to a round bottom flask and dissolved in a mixture of water, tert-butanol and dichloromethane (2:2:1). To this mixture the corresponding azide (1.1 equivalents) was added, followed by sodium ascorbate (0.45 equivalent) and copper sulfate (0.15 equivalent). The reaction mixture was allowed to stir overnight at room temperature. The crude product was then extracted with dichloromethane. The organic phase was washed with brine, dried over magnesium sulfate and concentrated under vacuum.
N-(2-(4-((1H-indol-3-yl)methyl)-1H-1,2,3-triazol-1-yl)ethyl)benzamide (3a)

3-(prop-2-ynyl)-1H-indole (2) was subjected to the general procedure for the Cu (I) - catalyzed alkyne/azide cycloadditions. The crude residue was purified by flash chromatography (1-15% EtOAc:Hexanes) to afford the product 3a as a light yellow oil (0.35 mmol, 131 mg, 82% yield).

$^1$H NMR (400 MHz, DMSO-$d_6$) $\delta$ 10.94 (s, 1H), 8.60 (t, 1H, $J = 5.2$ Hz), 7.76-7.75 (m, 3H), 7.53-7.42 (m, 4H), 7.33 (d, 1H, $J = 8.4$ Hz), 7.12 (s, 1H), 7.05 (t, 1H, $J = 7.6$ Hz), 6.91 (t, 1H, $J = 7.2$ Hz), 4.49 (t, 2H, $J = 5.6$ Hz), 4.06 (s, 2H), 3.66 (q, 2H, $J = 5.6$ Hz); $^{13}$C NMR (100 MHz, DMSO-$d_6$) $\delta$ 167.3, 147.2, 134.9, 131.9, 128.9, 127.9, 127.6, 123.7, 123.3, 121.7, 119.2, 118.9, 112.9, 112.0, 49.2, 22.3; HRMS (ESI) calcd for C$_{20}$H$_{20}$N$_5$O (M$^+$H)+ 346.1662, found 346.1659; IR $\nu_{\text{max}}$/cm$^{-1}$ 3417, 2252, 1648, 1024; $\lambda_{\text{max}}$: 244 nm.

N-(2-(4-((1H-indol-3-yl)methyl)-1H-1,2,3-triazol-1-yl)ethyl)-4-pentylbenzamide (3b)

3-(prop-2-ynyl)-1H-indole (2) was subjected to the general procedure for the Cu (I) - catalyzed alkyne/azide cycloadditions. The crude residue was purified by flash chromatography (1-15% EtOAc:Hexanes) to afford the product 3b as a yellow oil (0.27 mmol, 112 mg, 40% yield).

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.35 (s, 1H), 7.65 (d, 2H, $J = 8.0$ Hz), 7.44 (d, 1H, $J = 7.6$ Hz), 7.32 (d, 1H, $J = 8.0$ Hz), 7.27 (d, 1H, $J = 2.4$ Hz), 7.22 (s, 1H), 7.16 (d, 2H, $J = 7.6$ Hz), 7.15-7.13 (m, 1H), 7.01 (t, 1H, $J = 7.2$ Hz), 6.96 (s, 1H), 4.43 (t, 2H, $J = 4.8$ Hz), 4.14 (s, 2H), 3.85 (d, 2H, $J = 2.4$ Hz), 3.61 (t, 2H, $J = 7.2$ Hz), 1.60 (quintet, 2H, $J = 6.4$ Hz), 1.34-1.31 (m, 4H), 0.89 (t, 3H, $J = 6.8$ Hz); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 168.2, 147.9, 147.5, 136.6, 131.3, 128.9, 127.3, 127.1, 123.0, 122.8, 122.4, 119.7, 118.9, 113.0, 111.6, 49.8, 40.0, 36.0, 31.6, 31.1, 22.7, 22.1, 14.3; HRMS (ESI) calcd for C$_{25}$H$_{29}$N$_5$O (M$^+$H)+ 416.2445, found 416.2439; IR $\nu_{\text{max}}$/cm$^{-1}$ 3313, 2333, 1642, 1537; $\lambda_{\text{max}}$: 240 nm.
N-(2-(4-((1H-indol-3-yl)methyl)-1H-1,2,3-triazol-1-yl)ethyl)-4-hexylbenzamide (3c)

3-(prop-2-ynyl)-1H-indole (2) was subjected to the general procedure for the Cu (I) - catalyzed alkyne/azide cycloadditions. The crude residue was purified by flash chromatography (1-15% EtOAc:Hexanes) to afford the product 3c as a white oil (0.07 mmol, 31 mg, 23% yield). $^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 8.42 (s, 1H), 7.71 (d, 2H, $J = 7.6$ Hz), 7.52 (s, 1H), 7.40 (d, 1H, $J = 7.6$ Hz), 7.31 (d, 1H, $J = 7.6$ Hz), 7.26 (s, 1H), 7.17 (d, 2H, $J = 7.6$ Hz), 7.13 (t, 1H, $J = 7.6$ Hz), 7.00 (s, 1H), 6.98 (t, 1H, $J = 7.6$ Hz), 4.51-4.50 (m, 2H), 4.13 (s, 2H), 3.86-3.85 (m, 2H), 2.60 (t, 2H, $J = 7.6$ Hz), 1.57 (quintet, 2H, $J = 7.2$ Hz), 1.28-1.24 (m, 6H), 0.88 (t, 3H, $J = 6.8$ Hz); $^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$ 168.3, 147.6, 146.7, 136.5, 131.0, 128.9, 127.5, 126.8, 123.3, 122.4, 119.8, 118.7, 111.7, 111.4, 50.7, 39.8, 36.0, 31.9, 31.4, 29.1, 22.8, 21.4, 14.3; HRMS (ESI) calcd for C$_{26}$H$_{31}$N$_5$O (M$^+$H)$^+$ 430.2601, found 430.2605; IR $\nu_{max}$/cm$^{-1}$ 3382, 2349, 1642, 1079; $\lambda_{max}$: 240 nm.

N-(2-(4-((1H-indol-3-yl)methyl)-1H-1,2,3-triazol-1-yl)ethyl)-4-heptylbenzamide (3d)

3-(prop-2-ynyl)-1H-indole (2) was subjected to the general procedure for the Cu (I) - catalyzed alkyne/azide cycloadditions. The crude residue was purified by flash chromatography (1-15% EtOAc:Hexanes) to afford the product 3d as a yellow oil (0.12 mmol, 53 mg, 37% yield). $^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 8.09 (s, 1H), 7.59 (d, 2H, $J = 7.8$ Hz), 7.48 (d, 1H, $J = 7.8$ Hz), 7.34 (dd, 1H, $J = 8.1$ Hz, $J = 0.9$ Hz), 7.25 (s, 1H), 7.19-7.17 (m, 2H), 7.16-7.14 (m, 1H), 7.05 (d, 1H, $J = 0.9$ Hz), 7.03-7.00 (m, 1H), 6.81 (t, 1H, $J = 7.2$ Hz), 4.45 (t, 2H, $J = 4.8$ Hz), 4.19 (s, 2H), 3.89 (q, 2H, $J = 4.8$ Hz), 2.62 (t, 2H, $J = 7.8$ Hz), 1.57 (quintet, 2H, $J = 6.6$ Hz), 1.29-1.25 (m, 8H), 0.88 (t, 3H, $J = 6.0$ Hz); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 168.0, 148.3, 147.5, 136.6, 131.2, 128.8, 127.2, 127.1, 122.8, 122.5, 122.4, 119.7, 119.0, 113.4, 111.4, 49.6, 39.9, 36.0, 32.0, 31.4, 29.4, 29.3, 22.8, 22.3, 14.3; HRMS (ESI) calcd for C$_{27}$H$_{33}$N$_5$O (M$^+$H)$^+$ 444.2758, found 444.2761; IR $\nu_{max}$/cm$^{-1}$ 3382, 2348, 1642, 1392; $\lambda_{max}$: 240 nm.
N-(2-(4-((1H-indol-3-yl)methyl)-1H-1,2,3-triazol-1-yl)ethyl)-2-fluorobenzamide (3e)

3-(prop-2-ynyl)-1H-indole (2) was subjected to the general procedure for the Cu (I) - catalyzed alkyne/azide cycloadditions. The crude residue was purified by flash chromatography (1-15% EtOAc:Hexanes) to afford the product 3e as an orange oil (0.23 mmol, 83 mg, 75% yield).

$^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 8.21 (s, 1H), 7.99 (t, 1H, $J = 7.8$ Hz), 7.50-7.47 (m, 2H), 7.34 (d, 1H, $J = 8.1$ Hz), 7.23-7.18 (m, 2H), 7.16 (s, 1H), 7.12 (d, 1H, $J = 6.0$ Hz), 7.08 (d, 1H, $J = 2.7$ Hz), 7.04-7.00 (m, 2H), 4.49 (t, 2H, $J = 5.7$ Hz), 4.21 (s, 2H), 3.92 (q, 2H, $J = 5.1$ Hz);

$^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 164.0, 162.0, 159.6, 148.4, 133.9, 133.8, 131.9, 127.2, 125.0, 122.6, 122.5, 122.3, 119.6, 119.0, 116.5, 116.3, 113.2, 111.5, 49.5, 40.0, 22.3; HRMS (ESI) calcd for C$_{20}$H$_{18}$FN$_5$O (M$^+$H)+ 364.1568, found 364.1559; IR $\nu_{max}$/cm$^{-1}$ 3285, 1655, 1454, 1280; $\lambda_{max}$: 238 nm.

2-(4-((1H-indol-3-yl)methyl)-1H-1,2,3-triazol-1-yl)-N-phenylacetamide (3f)

3-(prop-2-ynyl)-1H-indole (2) was subjected to the general procedure for the Cu (I) - catalyzed alkyne/azide cycloadditions. The crude residue was purified by flash chromatography (1-15% EtOAc:Hexanes) to afford the product 3f as a yellow oil (0.08 mmol, 27 mg, 26% yield).

$^1$H NMR (300 MHz, DMSO-$d_6$) $\delta$ 10.83 (br s, 1H), 10.38 (s, 1H), 7.75 (s, 1H), 7.53 (d, 2H, $J = 8.1$ Hz), 7.49 (d, 1H, $J = 9.0$ Hz), 7.33-7.27 (m, 3H), 7.14 (d, 1H, $J = 2.1$ Hz), 7.05 (t, 2H, $J = 8.1$ Hz), 6.94 (t, 1H, $J = 6.6$ Hz), 5.21 (s, 2H), 4.08 (s, 2H);

$^{13}$C NMR (100 MHz, DMSO-$d_6$) $\delta$ 165.0, 147.3, 139.1, 129.6, 127.5, 124.5, 124.4, 123.7, 121.7, 119.9, 119.2, 118.9, 112.9, 112.0, 52.75, 22.2, 18.7; HRMS (ESI) calcd for C$_{10}$H$_{17}$N$_5$O (M$^+$H)+ 332.1506, found 332.1499; IR $\nu_{max}$/cm$^{-1}$ 3354, 2127, 1642, 989; $\lambda_{max}$: 244 nm.
2-(4-((1H-indol-3-yl)methyl)-1H-1,2,3-triazol-1-yl)-N-hexylacetamide (3g)

3-(prop-2-ynyl)-1H-indole (2) was subjected to the general procedure for the Cu (I) - catalyzed alkyne/azide cycloadditions. The crude residue was purified by flash chromatography (1-15% EtOAc:Hexanes) to afford the product 3g as a white oil (0.11 mmol, 39 mg, 35% yield). $^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 8.06 (br s, 1H), 7.50 (d, 1H, $J = 7.2$ Hz), 7.38 (d, 1H, $J = 8.4$ Hz), 7.28 (s, 1H), 7.20 (td, 1H, $J = 8.1$ Hz, $J = 1.2$ Hz), 7.11 (m, 1H), 7.11-7.09 (m, 1H), 7.06 (d, 1H, $J = 0.6$ Hz), 5.94 (s, 1H), 4.91 (s, 2H), 4.26 (s, 2H), 3.19 (q, 2H, $J = 7.5$ Hz), 1.40 (quintet, 2H, $J = 7.2$ Hz), 1.26-1.21 (m, 6H), 0.86 (t, 3H, $J = 6.9$ Hz); $^{13}$C NMR (100 MHz, CD$_3$OD) $\delta$ 177.3, 172.4, 165.0, 160.4, 146.6, 122.5, 121.1, 119.7, 116.9, 116.6, 109.5, 50.4, 37.9, 29.9, 27.5, 24.9, 20.9, 19.9, 11.6; HRMS (ESI) calcd for C$_{19}$H$_{25}$N$_5$O (M$^+$H)$^+$ 340.2132, found 340.2129; IR $\nu_{\text{max}}$/cm$^{-1}$ 3423, 1655, 1447, 747; $\lambda_{\text{max}}$: 240 nm.

2-(4-((1H-indol-3-yl)methyl)-1H-1,2,3-triazol-1-yl)-N-(4-methoxybenzyl)acetamide (3h)

3-(prop-2-ynyl)-1H-indole (2) was subjected to the general procedure for the Cu (I) - catalyzed alkyne/azide cycloadditions. Purification by flash chromatography (1-10% EtOAc:Hexanes) afforded the product 3h as a white oil (0.45 mmol, 168 mg, 67% yield). $^1$H NMR (400 MHz, DMSO-$d_6$) $\delta$ 10.84 (s, 1H), 8.66 (t, 1H, $J = 5.6$ Hz), 7.68 (s, 1H), 7.48 (d, 1H, $J = 8.0$ Hz), 7.32 (dd, 1H, $J = 8.0$ Hz, $J = 1.2$ Hz), 7.15 (d, 2H, $J = 8.4$ Hz), 7.13 (d, 1H, $J = 1.6$ Hz), 7.03 (t, 1H, $J = 6.8$ Hz), 6.94 (t, 1H, $J = 7.6$ Hz), 6.86 (d, 2H, $J = 8.0$ Hz), 5.02 (s, 2H), 4.20 (d, 2H, $J = 6.0$ Hz), 4.06 (s, 2H), 3.70 (s, 3H); $^{13}$C NMR (100 MHz, DMSO-$d_6$) $\delta$ 166.1, 159.0, 147.2, 137.0, 131.3, 129.5, 127.5, 124.4, 123.7, 121.7, 119.2, 118.9, 114.4, 114.4, 112.8, 112.0, 55.8, 52.2, 42.5, 22.2; HRMS (ESI) calcd for C$_{21}$H$_{25}$N$_5$O$_2$ (M$^+$H)$^+$ 376.1768, found 376.1750; IR $\nu_{\text{max}}$/cm$^{-1}$ 3410, 2127, 1648, 823; $\lambda_{\text{max}}$: 238 nm.
2-bromo-3-(prop-2-ynyl)-1H-indole (4)

3-(prop-2-ynyl)-1H-indole (2) was added to a round bottom flask and dissolved in a mixture of formic acid and acetic acid (1:3). To this mixture was added a solution of N-bromosuccinimide (1.0 equivalent) in formic acid and acetic acid (1:3) dropwise at room temperature. The mixture was allowed to stir at room temperature under nitrogen during 45 minutes. The mixture was then added to ice in a separatory funnel and was subjected to extraction with ethyl acetate. The organic layer was washed with a solution of sodium hydroxide (1 M), water and brine. The organic phase was dried over magnesium sulfate and concentrated under vacuum. The crude residue was purified by flash chromatography (1-10% EtOAc:Hexanes) to afford the product 4 as a brown oil (0.44 mmol, 102 mg, 31% yield).

1H NMR (300 MHz, CD3OD) δ 7.61 (dt, 1H, J = 7.8 Hz, J = 1.2 Hz), 7.27 (dt, 1H, J = 8.1 Hz, J = 1.5 Hz), 7.10 (td, 1H, J = 6.9 Hz, J = 1.5 Hz), 7.02 (td, 1H, J = 8.1 Hz, J = 1.5 Hz), 3.58 (d, 2H, J = 2.7 Hz), 2.27 (t, 1H, J = 2.7 Hz); 13C NMR (100 MHz, CD3OD) δ 136.7, 127.0, 121.7, 119.3, 117.9, 110.4, 109.1, 107.9, 81.2, 68.2, 14.2; HRMS (ESI) calcd for C11H8NBr (M+H)+ 234.1383, found 234.1383; IR νmax/cm⁻¹ 3430, 3250, 1642, 593; λmax: 240 nm.

N-(2-(4-((2-bromo-1H-indol-3-yl)methyl)-1H-1,2,3-triazol-1-yl)ethyl)-4-hexylbenzamide (5c)

2-bromo-3-(prop-2-ynyl)-1H-indole (4) was subjected to the general procedure for the Cu (I) - catalyzed alkyne/azole cycloadditions. The crude residue was purified by flash chromatography (30-100% EtOAc:Hexanes) to afford the product 5c as a yellow oil (0.23 mmol, 117 mg, 61% yield).

1H NMR (300 MHz, CDCl3) δ 8.08(br s, 1H), 7.57 (d, 2H, J = 8.4 Hz), 7.49 (d, 1H, J = 1.5 Hz), 7.33 (d, 1H, J = 7.2 Hz), 7.25 (s, 1H), 7.19 (d, 2H, J = 8.4 Hz), 7.11 (dd, 1H, J = 8.1 Hz, J = 1.5 Hz), 7.02 (s, 1H), 6.64 (t, 1H, J = 1.2 Hz), 4.50 (t, 2H, J = 5.4 Hz), 4.17 (s, 2H), 3.93 (q, 2H, J = 5.1 Hz), 2.64 (t, 2H, J = 7.2 Hz), 1.29-1.34 (m, 6H), 0.88 (t, 3H, J = 7.2 Hz); 13C NMR (100 MHz, DMSO-d6) δ 167.2, 146.6, 137.9, 132.3, 128.8, 127.8, 126.6, 124.9, 123.3, 121.3, 121.0, 114.5, 114.4, 111.3, 49.2, 39.8, 35.6, 31.8, 28.9, 22.7, 22.1, 14.6; HRMS (ESI) calcd for C26H30BrN5O (M+Na)+ 331.1417, found 331.1416; IR νmax/cm⁻¹ 3403, 3250, 1642, 593; λmax: 248 nm.
N-(2-(4-((2-bromo-1H-indol-3-yl)methyl)-1H-1,2,3-triazol-1-yl)ethyl)-4-heptylbenzamide (5d)

2-bromo-3-(prop-2-ynyl)-1H-indole (4) was subjected to the general procedure for the Cu (I) -catalyzed alkyne/azide cycloadditions. The crude residue was purified by flash chromatography (30-100% sat EtOAc:Hexanes) to afford the product 5d as a pink oil (0.07 mmol, 34 mg, 27% yield). 1H NMR (300 MHz, CDCl3) δ 8.28 (s, 1H), 7.58 (d, 2H, J = 8.4 Hz), 7.43 (d, 1H, J = 7.5 Hz), 7.29-7.27 (m, 2H), 7.14 (d, 2H, J = 8.4 Hz), 7.15 (s, 1H), 7.02 (td, 1H, J = 7.2 Hz, J = 0.9 Hz), 6.73 (t, 1H, J = 1.2 Hz), 4.45 (t, 2H, J = 5.1 Hz), 4.17 (s, 2H), 3.90 (q, 2H, J = 5.7 Hz), 2.63 (t, 2H, J = 7.2 Hz), 1.69 (m, 2H), 1.60 (t, 2H, J = 1.5 Hz), 1.3-1.27 (m, 8H), 0.88 (t, 3H, J = 6.9 Hz); 13C NMR (100 MHz, CDCl3) δ 168.1, 147.5, 147.2, 136.4, 131.2, 128.9, 127.4, 127.2, 122.9, 122.8, 120.5, 118.6, 112.8, 110.8, 108.8, 49.8, 39.9, 36.1, 29.4, 29.3, 22.9, 21.9, 14.4; HRMS (ESI) calcd for C27H32BrN5O (M+H)+ 522.1863, found 522.1856; IR νmax/cm−1 3445, 2328, 1655; λmax: 240 nm.

N-(2-(4-((2-bromo-1H-indol-3-yl)methyl)-1H-1,2,3-triazol-1-yl)ethyl)-2-fluorobenzamide (5e)

2-bromo-3-(prop-2-ynyl)-1H-indole (4) was subjected to the general procedure for the Cu (I) -catalyzed alkyne/azide cycloadditions. The crude residue was purified by flash chromatography (50-60% EtOAc:Hexanes) to afford the product 5e as an orange oil (0.08 mmol, 36 mg, 35% yield). 1H NMR (400 MHz, CD3OD) δ 5.52 (td, 1H, J = 7.6 Hz, J = 1.6 Hz), 7.50-7.49 (m, 1H), 7.49-7.46 (m, 1H), 7.36 (dt, 1H, J = 8.0 Hz, J = 0.8 Hz), 7.26 (dt, 1H, J = 8.4 Hz, J = 1.2 Hz), 7.19 (td, 1H, J = 7.6 Hz, J = 1.2 Hz), 7.15-7.10 (m, 1H), 7.06 (td, 1H, J = 8.4 Hz, J = 1.2 Hz), 6.92 (td, 1H, J = 7.6 Hz, J = 0.8 Hz), 4.53 (t, 2H, J = 5.2 Hz), 4.11 (s, 2H), 3.75 (t, 2H, J = 5.6 Hz); 13C NMR (100 MHz, CD3OD) δ 167.3, 162.6, 160.2, 148.4, 138.2, 134.4, 134.3, 131.5, 128.6, 125.7, 124.3, 123.1, 120.7, 119.1, 117.4, 117.2, 112.4, 111.8, 109.9, 50.2, 41.2, 22.4; HRMS (ESI) calcd for C20H17BrFN5O (M+H)+ 442.0673, found 442.0662; IR νmax/cm−1 3341, 2924, 1655; λmax: 240 nm.
2-(4-((2-bromo-1H-indol-3-yl)methyl)-1H-1,2,3-triazol-1-yl)-N-phenylacetamide (5f)

2-bromo-3-(prop-2-ynyl)-1H-indole (4) was subjected to the general procedure for the Cu (I) -catalyzed alkyne/azide cycloadditions. The crude residue was purified by flash chromatography (30-100% EtOAc:Hexanes) to afford the product 5f as an orange oil (0.04 mmol, 18 mg, 19% yield). ¹H NMR (300 MHz, CDCl₃) δ 8.50 (br s, 1H), 8.44 (s, 1H), 7.45-7.39 (m, 3H), 7.36 (s, 1H), 7.30-7.24 (m, 3H), 7.16-7.08 (m, 2H), 7.03 (td, 1H, J = 7.8 Hz, J = 1.2 Hz), 5.05 (s, 2H), 4.15 (s, 2H); ¹³C NMR (100 MHz, CDCl₃) δ 163.3, 136.9, 136.4, 129.3, 127.3, 125.4, 123.9, 122.9, 120.6, 120.5, 118.4, 110.9, 60.7, 54.0, 21.7, 21.3, 14.4; HRMS (ESI) calcd for C₁₉H₁₇BrN₅O (M⁺H)+ 410.0611, found 410.0606; IR v max/cm⁻¹ 3445, 2355, 2072, 1634, 580, ; λ max: 238 nm.

2-(4-((2-bromo-1H-indol-3-yl)methyl)-1H-1,2,3-triazol-1-yl)-N-hexylacetamide (5g)

2-bromo-3-(prop-2-ynyl)-1H-indole (4) was subjected to the general procedure for the Cu (I) -catalyzed alkyne/azide cycloadditions. The crude residue was purified by flash chromatography (30-100% EtOAc:Hexanes) to afford the product 5g as a white oil (0.04 mmol, 16 mg, 22% yield). ¹H NMR (400 MHz, CD₃OD) δ 7.52 (s, 1H), 7.39 (dd, 1H, J = 8.4 Hz, J = 1.2 Hz), 7.07 (td, 1H, J = 6.8 Hz, J = 1.2 Hz), 6.97 (td, 1H, J = 7.2 Hz, J = 0.8 Hz), 4.98 (s, 2H), 4.14 (s, 2H), 3.15 (t, 2H, J = 7.2 Hz), 1.46 (quintet, 2H, J = 6.8 Hz), 1.32-1.28 (m, 6H), 0.88 (t, 3H, J = 7.2 Hz); ¹³C NMR (100 MHz, CD₃OD) δ 166.5, 147.2, 136.8, 127.3, 123.9, 121.7, 119.4, 117.8, 111.1, 110.5, 108.7, 51.9, 39.5, 31.4, 26.4, 22.4, 21.2, 13.2; HRMS (ESI) calcd for C₁₃H₁₆N₂O₂Br (M⁺H)+ 418.1237, found 418.1222; IR v max/cm⁻¹ 3389, 2924, 1665, 1065, 747. λ max: 270 nm.

3-(prop-2-ynyl)-1H-benzothiophene (8) was prepared following the synthetic procedure of Gonzales Bello, C.; Sanchez Sixto, C.; Sedes Diaz, A.; Blanco Rodriguez, B. Ester Derivatives as Competitive Inhibitors of type II Dehydroquinate Enzyme, WO2010146125, December 23, 2010.

N-(2-(4-(benzo[b]thiophen-3-ylmethyl)-1H-1,2,3-triazol-1-yl)ethyl)benzamide (9a)

3-(prop-2-ynyl)-1H-benzothiophene (8) was subjected to the general procedure for the Cu (I) - catalyzed alkyne/azide cycloadditions. The crude residue was purified by flash chromatography (5-40% EtOAc:Hexanes) to afford the product 9a as a white oil (0.22 mmol, 79 mg, 47% yield), as a white oil. \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 7.84 (dd, 1H, \(J = 7.2\) Hz, \(J = 1.2\) Hz), 7.71-7.68 (m, 3H), 7.51-7.47 (m, 1H), 7.38 (td, 2H, \(J = 8.0\) Hz, \(J = 1.2\) Hz), 7.31 (td, 2H, \(J = 7.6\) Hz, \(J = 1.6\) Hz), 7.26 (d, 1H, \(J = 2.8\) Hz), 7.15 (s, 1H), 7.00 (s, 1H), 4.52 (t, 2H, \(J = 4.0\) Hz), 4.29 (s, 2H), 3.93 (q, 2H, \(J = 5.2\) Hz); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 168.1, 146.1, 140.8, 138.4, 133.8, 132.9, 132.1, 130.3, 128.9, 128.6, 127.3, 124.7, 124.4, 123.7, 123.4, 123.2, 121.9, 49.9, 39.9, 25.5; HRMS (ESI) calcd for C\(_{20}\)H\(_{18}\)N\(_4\)O\(_4\) (M\(^+\)) + 363.1274, found 363.1272; IR \(\nu_{\text{max}}/\text{cm}^{-1}\) 3232, 2043, 1630, 698; \(\lambda_{\text{max}}\): 248 nm.

Electronic Supplementary Material (ESI) for Medicinal Chemistry Communications
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N-(2-(4-(benzo[b]thiophen-3-ylmethyl)-1H-1,2,3-triazol-1-yl)ethyl)-4-pentylbenzamide (9b)

3-(prop-2-ynyl)-1H-benzo[thiophene (8) was subjected to the general procedure for the Cu (I) -catalyzed alkyne/azide cycloadditions. The crude residue was purified by flash chromatography (5-40% EtOAc:Hexanes) to afford the product as a white oil (0.3 mmol, 129 mg, 65% yield). 1H NMR (400 MHz, CDCl3) δ 7.84 (dt, 1H, J = 8.4 Hz, J = 1.2 Hz), 7.69 (dd, 1H, J = 7.6 Hz, J = 1.2 Hz), 7.62 (dd, 2H, J = 6.4 Hz, J = 1.6 Hz), 7.31 (td, 2H, J = 7.6 Hz, J = 1.2 Hz), 7.27 (s, 1H), 7.17 (d, 2H, J = 8.0 Hz), 7.13 (s, 1H), 7.02 (t, 1H, J = 5.6 Hz), 4.51 (t, 2H, J = 6.0 Hz), 4.28 (s, 2H), 3.90 (q, 2H, J = 5.6 Hz), 2.61 (t, 2H, J = 7.6 Hz), 1.60 (quintet, 2H, J = 7.2 Hz), 1.36-1.27 (m, 4H), 0.89 (t, 3H, J = 7.2 Hz); 13C NMR (100 MHz, CDCl3) δ 168.1, 145.5, 146.0, 140.8, 138.5, 133.0, 131.2, 128.9, 127.3, 124.7, 124.4, 123.7, 123.4, 123.2, 121.9, 49.9, 39.9, 36.0, 31.6, 31.1, 25.5, 22.7, 14.3; HRMS (ESI) calcd for C25H29N4OS (M+H)+ 433.2057, found 433.2054; IR νmax/cm⁻1 3306, 2924, 1642, 1301; λmax: 248 nm.

N-(2-(4-(benzo[b]thiophen-3-ylmethyl)-1H-1,2,3-triazol-1-yl)ethyl)-4-hexylbenzamide (9c)

3-(prop-2-ynyl)-1H-benzo[thiophene (8) was subjected to the general procedure for the Cu (I) -catalyzed alkyne/azide cycloadditions. The crude residue was purified by flash chromatography (5-40% EtOAc:Hexanes) to afford the product 9c as a yellow oil (0.34 mmol, 150 mg, 73% yield). 1H NMR (400 MHz, CDCl3) δ 7.82 (d, 1H, J = 8.0 Hz), 7.66 (d, 1H, J = 7.6 Hz), 7.63 (d, 2H, J = 8.4 Hz), 7.33-7.27 (m, 3H), 7.25 (s, 1H), 7.12 (d, 2H, J = 8.0 Hz), 7.06 (s, 1H), 4.87 (t, 2H, J = 6.0 Hz), 4.21 (s, 2H), 3.87 (q, 2H, J = 5.6 Hz), 2.58 (t, 2H, J = 7.6 Hz), 1.57 (quintet, 2H, J = 7.6 Hz), 1.28-1.27 (m, 6H), 0.88 (t, 3H, J = 6.8 Hz); 13C NMR (100 MHz, CDCl3) δ 168.2, 147.4, 146.0, 140.8, 138.5, 133.3, 131.3, 128.8, 127.3, 124.7, 123.5, 123.3, 123.1, 121.9, 49.7, 40.0, 36.0, 31.9, 31.4, 29.2, 25.6, 22.8, 14.3; HRMS (ESI) calcd for C26H31N4OS (M+H)+ 447.2213, found 447.2215; IR νmax/cm⁻1 3313, 2855, 1642, 1537, 1427, 1301; λmax: 244 nm.
**N-(2-(4-(benzo[b]thiophen-3-ylmethyl)-1H-1,2,3-triazol-1-yl)ethyl)-4-heptylbenzamide (9d)**

3-(prop-2-ynyl)-1H-benzo[b]thiophene (8) was subjected to the general procedure for the Cu (I) -catalyzed alkyne/azide cycloadditions. The crude residue was purified by flash chromatography (5-40% EtOAc:Hexanes) to afford the product 9d as a white oil (0.10 mmol, 44 mg, 15% yield). 

$^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 7.84 (dd, 1H, $J = 7.2$ Hz, $J = 2.4$ Hz), 7.69 (dd, 1H, $J = 7.2$ Hz, $J = 2.1$ Hz), 7.61 (d, 2H, $J = 8.1$ Hz), 7.33-7.29 (m, 2H), 7.24 (s, 1H), 7.16 (d, 2H, $J = 8.1$ Hz), 7.12 (s, 1H), 6.97 (t, 1H, $J = 5.6$ Hz), 5.51 (t, 2H, $J = 5.7$ Hz), 4.27 (s, 2H), 3.91 (q, 2H, $J = 5.4$ Hz); 13C NMR (100 MHz, CDCl$_3$) $\delta$ 168.1, 147.5, 146.2, 140.8, 138.5, 133.2, 131.2, 128.9, 128.7, 127.2, 124.7, 124.3, 123.6, 123.2, 123.1, 121.9, 49.8, 39.9, 36.1, 32.0, 31.4, 29.4, 29.3, 25.6, 22.9, 14.3; HRMS (ESI) calcd for C$_{27}$H$_{33}$N$_4$OS (M$^+$H)$^+$ 461.2370, found 461.2369; IR $\nu$$_{max}$/cm$^{-1}$ 3345, 2249, 1640, 1011; $\lambda$$_{max}$: 248 nm.

**N-(2-(4-(benzo[b]thiophen-3-ylmethyl)-1H-1,2,3-triazol-1-yl)ethyl)-2-fluorobenzamide (9e)**

3-(prop-2-ynyl)-1H-benzo[b]thiophene (8) was subjected to the general procedure for the Cu (I) -catalyzed alkyne/azide cycloadditions. The crude residue was purified by flash chromatography (5-40% EtOAc:Hexanes) to afford the product 9e as a yellow oil (0.10 mmol, 37 mg, 32% yield). 

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.96 (td, 1H, $J = 8.0$ Hz, $J = 1.6$ Hz), 7.84-7.81 (m, 1H), 7.71-7.69 (m, 1H), 7.48-7.41 (m, 1H), 7.31 (d, 1H, $J = 5.2$ Hz), 7.30-7.28 (m, 1H), 7.24-7.20 (m, 2H), 7.13-7.12 (m, 2H), 7.08-7.02 (m, 1H), 4.51 (t, 2H, $J = 6.0$ Hz), 4.27 (s, 2H), 3.92 (q, 2H, $J = 5.6$ Hz); 13C NMR (100 MHz, CDCl$_3$) $\delta$ 164.1, 161.9, 159.5, 146.4, 140.8, 138.6, 133.9, 133.8, 133.4, 131.9, 125.0, 124.6, 124.5, 124.3, 123.5, 123.1, 122.9, 122.0, 116.5, 116.2, 49.5, 40.1, 25.7; HRMS (ESI) calcd for C$_{20}$H$_{18}$FN$_4$OS (M$^+$H)$^+$ 381.118, found 381.118; IR $\nu$$_{max}$/cm$^{-1}$ 3345, 2249, 1640, 1011; $\lambda$$_{max}$: 238 nm.
2-(4-(benzo[b]thiophen-3-ylmethyl)-1H,1,2,3-triazol-1-yl)-N-phenylacetamide (9f)

3-(prop-2-ynyl)-1H-benzo thiophene (8) was subjected to the general procedure for the Cu (I) -
catalyzed alkyne/azide cycloadditions. The crude residue was purified by flash chromatography
(5-40% EtOAc:Hexanes) to afford the product 9f as a yellow oil (0.03 mmol, 12 mg, 11% yield).
$^1$H NMR (300 MHz, CD$_3$OD) $\delta$ 10.20 (br s, 1H), 7.86 (dd, 1H, $J = 8.4$ Hz, $J = 1.8$ Hz), 7.82-7.79
(m, 2H), 7.53 (d, 2H, $J = 7.5$ Hz), 7.38-7.33 (m, 2H), 7.31-7.28 (m, 3H), 7.11 (t, 1H, $J = 7.5$ Hz),
5.27 (s, 2H), 4.86 (s, 2H), 4.32 (s, 2H); $^{13}$C NMR (100 MHz, DMSO-d$_6$) $\delta$ 164.9, 145.3, 140.5,
139.1, 139.0, 134.6, 129.6, 125.0, 124.7, 124.1, 123.6, 122.8, 119.9, 119.8, 52.8, 25.3;
HRMS (ESI) calcd for C$_{23}$H$_{21}$N$_3$NaO$_4$S (M+H)$^+$ 349.1118, found 349.1118. IR $\nu_{max}$/cm$^{-1}$ 3367,
2129, 1644, 997; $\lambda_{max}$: 240 nm.

2-(4-(benzo[b]thiophen-3-ylmethyl)-1H,1,2,3-triazol-1-yl)-N-hexylacetamide (9g)

3-(prop-2-ynyl)-1H-benzo thiophene (8) was subjected to the general procedure for the Cu (I) -
catalyzed alkyne/azide cycloadditions. The crude residue was purified by flash chromatography
(5-40% EtOAc:Hexanes) to afford the product 9g as a white oil (0.10 mmol, 35 mg, 25% yield).
$^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 7.84-7.82 (m, 1H), 7.72-7.69 (m, 1H), 7.39 (s, 1H), 7.34-7.31 (m,
2H), 7.17 (s, 1H), 6.50 (t, 1H, $J = 6.0$ Hz), 4.92 (s, 2H), 4.29 (s, 2H), 3.16 (q, 2H, $J = 6.8$ Hz),
1.39 (quintet, 2H, $J = 7.2$ Hz), 1.25-1.21 (m, 6H), 0.84 (t, 3H, $J = 6.4$ Hz); $^{13}$C NMR (100 MHz,
CDCl$_3$) $\delta$ 165.3, 146.8, 140.8, 138.5, 133.1, 124.7, 124.4, 123.7, 123.2, 121.9, 53.2, 40.1, 31.6,
29.4, 26.6, 25.7, 22.7, 14.2; HRMS (ESI) calcd for C$_{19}$H$_{24}$N$_4$OS (M+H)$^+$ 357.1744, found
357.1738; IR $\nu_{max}$/cm$^{-1}$ 3306, 2924, 2355, 1718, 1655, 1447; $\lambda_{max}$: 238 nm.

2-(4-(benzo[b]thiophen-3-ylmethyl)-1H,1,2,3-triazol-1-yl)-N-(4-methoxybenzyl)acetamide (9h)
3-(prop-2-ynyl)-1H-benzothiophene (8) was subjected to the general procedure for the Cu(I) -
catalyzed alkyne/azide cycloadditions. The crude residue was purified by flash chromatography
(5-40% EtOAc:Hexanes) to afford the product 9h as a white oil (0.12 mmol, 48 mg, 29% yield).
$^1$H NMR (300 MHz, DMSO-$d_6$) δ 8.69 (t, 1H, $J = 7.5$ Hz), 7.99-7.95 (m, 1H), 7.89-7.85 (m, 1H),
7.83 (s, 1H), 7.43 (s, 1H), 7.37 (t, 2H, $J = 3.3$ Hz), 7.17 (d, 2H, $J = 6.9$ Hz), 6.88 (d, 2H, $J = 6.9$
Hz), 5.06 (s, 2H), 4.24 (s, 2H), 4.21-4.20 (m, 2H), 3.72 (s, 3H). $^{13}$C NMR (75 MHz, DMSO-$d_6$) δ
196.89, 166.0, 159.0, 145.2, 140.5, 139.0, 134.6, 131.3, 129.5, 125.0, 124.8, 124.2, 123.6, 122.8,
114.4, 55.8, 52.2, 42.5, 25.3; HRMS (ESI) calcd for C$_{21}$H$_{21}$N$_4$O$_2$S (M$^+$H)$^+$ 393.138, found
393.1371; IR $\nu_{max}$/cm$^{-1}$ 3445, 2355, 2072, 1634, 1024, 820; $\lambda_{max}$: 238 nm.
Inhibition and Promotion of *A. baumannii*, *E. coli*, *S. aureus* and MRSA Biofilms with Indole/triazole and Benzothiophene/triazole Analouges

Biofilm Inhibition/Promotion Procedure (Dose Reponse Curve): to determine the inhibitory effects of test compounds against *A. baumannii* (19606), *E. coli* (K12 ER2718), *S. aureus* (29213) and MRSA (BAA 44) biofilm formation. Inhibition assays were performed by taking an overnight culture and sub-culturing it with an OD600 of 0.01 into the necessary media; Luria-Bertani (LB) for *A. baumannii* and *E. coli*, and Tryptic Soy Broth with 5% Glucose (TSBG) for *S. aureus* and MRSA. Stock solutions of predetermined concentrations of the test compounds were then made with DMSO (biology grade). These stock solutions were aliquoted (100 µL) into the wells of a 96-well PVC microtiter plate. Sample plates were wrapped in GLAD Press n’ Seal followed by incubation under stationary conditions for 24 h at 37 °C. After incubation the media was discarded and the plates were washed with water. The sample plates were then stained with 110 µL of 0.1% solution of crystal violet (CV) and then incubated at ambient temperature for 30 min. The CV stain was then discarded and the plates were washed with water. The remaining stain was solubilized with 200 µL of 95% ethanol. After the biofilms was dissolved (10 minutes) a sample of 125 µL of solubilized CV stained ethanol was transferred from each well into the corresponding wells of a polystyrene microtiter dish. Biofilm inhibition or promotion was quantified by measuring the OD540 of each well in which a negative control lane wherein no biofilm was formed served as a background and was subtracted out. The percent inhibition and the percent formation were calculated by the comparison of the OD540 for established biofilm (control) versus treated established biofilm (compound treated) under identical conditions.

All dose-response curves for IC$_{50}$, PC$_{25}$, PC$_{50}$ and PC$_{75}$ value determinations were run in triplicate or more.
**Growth Curve Analysis**: We determined the toxicity of the test compound at its corresponding IC$_{50}$, PC$_{25}$, PC$_{50}$ and PC$_{75}$ values. In the growth curve assay, bacterial cell density was evaluated in the appropriate media by taking its optical density (OD$_{540}$). In three test tubes the control was prepared in one tube with the appropriate media and bacteria and in the other two test tubes the IC$_{50}$ concentration of compound dissolved in DMSO (biological grade), media and bacteria were combined. The three test tubes were placed at 37 °C and the OD$_{600}$ was determined at time (t) = 2, 4, 6, 8, 24 hours. A compound was determined to be non-toxic if comparable ODs were observed at the same time points. Toxicity can also be determined qualitatively by determining the degree of cloudiness of each test tube at each time point, clear indicates that the compounds are killing the bacteria. All growth curves were performed in duplicates.
Colony counts (Time kill curve): We determined the toxicity of the test compound at its corresponding IC_{50}, PC_{25}, PC_{50} and PC_{75} values. Appropriate fresh media is inoculated with an overnight bacterial culture. In three test tubes the control was prepared in one tube with the appropriate media and bacteria and in the other two test tubes the IC_{50} concentration (or PC_{25}, PC_{50} and PC_{75}) of compound dissolved in DMSO (biological grade), media and bacteria were combined. The three test tubes were placed at 37 °C with shaking and colony counts was determined at time (t) = 2, 4, 6, 8, 24 hours. At required time points, 100 μL were taken from each tube and 900 μL of fresh media were added in an autoclaved eppendorf tube. Each sample was ten-fold serially diluted and 10 μL were spread on agar plates and incubated at 37°C overnight. A compound was determined to be non-toxic if calculated CFU/mL were comparable to the control at the same time points. All time kill curves were performed in duplicates.
**Inhibitor/Inducer Competition Assay:** We determined the combined effect of compounds 3c and 1 against *E. coli* (K12 ER2718) biofilm formation. Inhibition assays were performed by taking an overnight culture and sub-culturing it with an OD$_{600}$ of 0.01 into Luria-Bertani (LB). Three stock solutions were prepared by dissolving the compounds of interest in DMSO (biology grade): one solution resulting in the mixture of compound 1 at its IC$_{50}$ concentration with compound 3c at its PC$_{25}$ concentration, a solution resulting in the mixture of compound 1 at its IC$_{50}$ concentration with compound 3c at its PC$_{50}$ concentration and finally a third solution resulting in the mixture of compound 1 at its IC$_{50}$ with compound 3c at its PC$_{75}$. The dose-response curves were obtained in triplicate using the procedure previously described.