Supporting Information

Direct 1,3-bis(tert-butoxycarbonyl)guanidine cyclization towards 2-amino substituted imidazole-based biofilm modulators capable of increasing MRSA susceptibility to β-lactams

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Representative Dose-Response Curves

Biofilm inhibition (IC50 values) Dose-Response Curves were performed in a minimum of triplicate experiments.
Biofilm Inhibition
Dose Response (MRSA BAA-1685)

IC50 = 5.27

Biofilm Inhibition
Dose Response (MRSA BAA-1685)

IC50 = 3.60
Biofilm Inhibition
Dose Response (MRSA BAA-1770)

IC50 = 4.95

Biofilm Inhibition
Dose Response (MRSA BAA-1770)

IC50 = 5.20
Representative Planktonic Growth Curves

All growth curves were performed in a minimum of duplicate experiments.

Growth Curve in TSBG at 5.90 μM

Growth Curve in TSBG at 7.35 μM
Growth Curve in TSBG at 4.40 μM

- BAA-1770 no compound
- BAA-1770 w/ 13l

Growth Curve in TSBG at 5.32 μM

- BAA-1770 no compound
- BAA-1770 w/ 13g
Experimental procedures and characteristic data for all compounds 9, 12, and 13.

All reagents used for chemical synthesis were purchased from commercially available sources and used without further purification. Chromatography was performed using 60 Å mesh standard grade silica gel from Sorbtech. Deuterated NMR solvents were obtained from Cambridge Isotope Labs and used as is. All $^1$H NMR (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 solvent; coupling constants ($J$) are in hertz (Hz). Abbreviations used are s = singlet, bs = broad singlet, d = doublet, dd = doublet of doublets, t = triplet, dt = doublet of triplets, bt = broad triplet, qt = quartet, m = multiplet, bm = broad multiplet, p = pentet, sep = septet, and br = broad. Mass spectra were obtained at the NCSU Department of Chemistry Mass Spectrometry Facility. Funding was obtained from the North Carolina Biotechnology Center and the NCSU Department of Chemistry. 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).

MRSA (ATCC # BAA-44, ATCC # 1685, and ATCC # BAA 1770) were obtained from the ATCC. Oxacillin sodium salt was purchased from TCI (# O0353). Mueller-Hinton broth was made based on the following procedure. To 1 L deionized water was added 2 g BBL TM beef extract (# 212303) and 1.5 g Difco TM soluble starch (# 217820) which were obtained from BD. Casein hydrolysate (17.5 g) purchased from MP Biomedicals (# 101290) was then added and the pH was adjusted to 7.4 at ambient temperature. The resulting solution was autoclaved at 120 °C for 15 min.

General procedures for alkylation of tert-butyl 2-((tert-butoxycarbonyl)amino)-4-(hept-6-yn-1-yl)-1H-imidazole-1-carboxylate 8.

From alkyl halides: To a 0 °C solution of tert-butyl 2-((tert-butoxycarbonyl)amino)-4-(hept-6-yn-1-yl)-1H-imidazole-1-carboxylate 8 (~ 0.3 or ~0.6 mmol) in DMF (4 mL) was added 60% sodium hydride dispersion in mineral oil (1 eq) and stirred until complete dissolution. To this solution was then added the alkyl halide (1.1 eq) dropwise. The reactions were then heated to 70 °C for four hours. Note that longer heating lead to increased decomposition or loss of the protected 2-amino imidazole material. The reactions were then diluted with EtOAc and washed with water and brine. The organic layer was then dried (MgSO$_4$), filtered, and concentrated in vacuo. The crude material was then purified by flash chromatography (typically 5 -10% EtOAc in Hexanes).

From alkyl alcohols: To a 0 °C solution of tert-butyl 2-((tert-butoxycarbonyl)amino)-4-(hept-6-yn-1-yl)-1H-imidazole-1-carboxylate 8 (~0.3 mmol), triphenylphosphine (2 eq), and alcohol (3 eq) in THF (2.5 mL) was added DIAD or DEAD (1.5 eq) dropwise and allowed cold bath to warm to room temperature. DEAD or DIAD were used interchangeably depending on the retention factor of the final product and thus aiding in final purification. After 16 hrs the reaction was concentrated in vacuo and purified by flash chromatography (typically 5 -10% EtOAc in Hexanes).

Note: Many alkylated di-Boc 2-aminoimidazoles exhibited rotomers in both the $^1$H and $^{13}$C NMR. An attempt has been made to single out the minor rotamer peaks if and when possible. The observed minor rotamer frequencies have been denoted by “rotamer” following the observed frequencies for the $^1$H NMR. For clarity the proton count for these frequencies corresponds to the expected proton count for the
molecule rather than the fraction or ratio of the two rotamers. For $^{13}$C NMR, when possible the carbon peak pairs corresponding to the different rotamers have been singled out but no 2D experiments were performed to distinguish their identities.

tert-butyl 2-(N-(tert-butoxycarbonyl)(methyl)amino)-4-(hept-6-yn-1-yl)-1H-imidazole-1-carboxylate (9a). Following the general procedure for alkylation with alkyl halides tert-butyl 2-((tert-butoxycarbonyl)amino)-4-(hept-6-yn-1-yl)-1H-imidazole-1-carboxylate was reacted with iodomethane to provide tert-butyl 2-((tert-butoxycarbonyl)(methyl)amino)-4-(hept-6-yn-1-yl)-1H-imidazole-1-carboxylate (50 mg, 47%) as an impure oil. This mixture was carried through the next step to allow for better separation after the following step.

**<Chemical Structure>**

tert-butyl 2-(N-(tert-butoxycarbonyl)methylsulfonamido)-4-(hept-6-yn-1-yl)-1H-imidazole-1-carboxylate (9b). Following the general procedure for alkylation with alkyl halides tert-butyl 2-((tert-butoxycarbonyl)amino)-4-(hept-6-yn-1-yl)-1H-imidazole-1-carboxylate was reacted with mesyl chloride to provide tert-butyl 2-(N-(tert-butoxycarbonyl)methylsulfonamido)-4-(hept-6-yn-1-yl)-1H-imidazole-1-carboxylate (65 mg, 24%) as a clear oil. $R_f = 0.36$ (30% EtOAc/Hexanes); $^1$H NMR (CDCl$_3$, 400MHz) $\delta$ 7.12 (s, 1H), 3.42 (s, 3H), 3.10 (s, 3H, rotamer), 2.51 (t, $J = 7.6$ Hz, 2H), 2.33 (dt, $J = 6.8$, 2.6 Hz, 2H), 1.91 (t, $J = 2.6$ Hz, 1H), 1.66-1.4 (m, 6H), 1.58 (s, 9H), 1.48 (s, 9H), 1.43 (s, 9H); $^{13}$C NMR (CDCl$_3$, 100MHz) $\delta$ 149.7, 147.5 and 146.5 (rotamers), 141.0, 134.3, 115.6, 86.5, 85.5, 84.7, 68.4, 43.2 and 41.7 (rotamers), 28.3, 28.3, 28.1, 28.1, 28.0, 27.9, 18.4; IR (CDCl$_3$) 3286, 2980, 2937, 2862, 1748, 1643, 1513, 1459, 1396, 1371, 1293, 1255, 1146, 1075, 968, 770; UV ($\lambda_{\max}$ nm) 251; HRMS (ESI+) m/z 478.1969 [(M+H)$^+$]; calculated mass for C$_{21}$H$_{21}$N$_3$O$_5$S$^+$: 478.1982 amu].

**<Chemical Structure>**

tert-butyl 2-(N-(tert-butoxycarbonyl)(isopropyl)amino)-4-(hept-6-yn-1-yl)-1H-imidazole-1-carboxylate (9c). Following the general procedure for alkylation with alcohols tert-butyl 2-((tert-butoxycarbonyl)amino)-4-(hept-6-yn-1-yl)-1H-imidazole-1-carboxylate was reacted with isopropanol to provide tert-butyl 2-((tert-butoxycarbonyl)(isopropyl)amino)-4-(hept-6-yn-1-yl)-1H-imidazole-1-carboxylate (38 mg, 36%) as a clear oil. $R_f = 0.55$ (20% EtOAc/Hexanes); $^1$H NMR (CDCl$_3$, 400MHz) $\delta$ 7.01 (s, 1H), 4.42 (sep, $J = 6.6$, 1H), 4.23 (m, 1H, rotamer)2.48 (dt, $J = 7.1$, 3.0 Hz, 2H), 2.16 (dt, $J = 7.1$, 2.6 Hz, 2H), 1.89 (t, $J = 2.6$ Hz, 1H), 1.75-1.18 (m, 6H), 1.55 (s, 9H), 1.31 (s, 9H), 1.34 (d, $J = 6.58$ Hz, 6H, rotamer), 0.89 (d, $J = 6.88$ Hz, 6H). $^{13}$C NMR (CDCl$_3$, 100MHz) $\delta$ 153.3, 146.6, 139.6 and 139.6
(rotamers), 113.6, 113.4, 84.6, 84.5, 80.4, 68.1, 50.3 and 49.0 (rotamers), 28.2, 28.1, 28.99, 28.95, 27.9, 22.3, 19.0, 18.3; IR (CDCl₃) 3311, 2976, 2933, 2859, 2338, 1762, 1717, 1538, 1457, 1369, 1301, 1154, 1109; UV (λ_max nm) 250, HRMS (ESI+) m/z 420.2838 [(M+H)+; calculated mass for C₂₅H₃₁N₅O₄⁺: 420.2857 amu].

**tert-butyl 2-(N-(tert-butoxycarbonyl)(hexyl)amino)-4-(hept-6-yn-1-yl)-1H-imidazole-1-carboxylate (9e).** Following the general procedure for alkylation with alkyl halides tert-butyl 2-((tert-butoxycarbonyl)amino)-4-(hept-6-yn-1-yl)-1H-imidazole-1-carboxylate was reacted with iodoheptane to provide tert-butyl 2-((tert-butoxycarbonyl)(hexyl)amino)-4-(hept-6-yn-1-yl)-1H-imidazole-1-carboxylate (62 mg, 27%) as a clear oil. Rᵣ = 0.74 (30% EtOAc/Hexanes); ¹H NMR (CDCl₃, 400MHz) δ 6.96 (s, 1H), 6.94 (s, 1H, rotamer), 3.66 (ddd, J = 13.6, 9.5, 6.3 Hz, 1H), 3.53 (m, 2H, rotamer), 3.37 (ddd, J = 13.7, 9.6, 5.8 Hz, 1H), 2.47 (t, J = 7.5 Hz, 2H), 2.16 (dt, J = 7.1, 2.6 Hz, 2H), 1.90 (t, J = 2.6 Hz, 1H), 1.66-1.18 (m, 14H), 1.56 (s, 9H), 1.32 (s, 9H), 0.82 (t, J = 6.8, 3H); ¹³C NMR (CDCl₃, 100MHz) δ 153.2 and 153.7 (rotamers), 146.7 and 146.6 (rotamers), 142.0 and 141.8 (rotamers), 139.6 and 139.4 (rotamers), 131.2 and 131.2 (rotamers), 84.8, 84.5, 81.1 and 80.6 (rotamers), 68.1, 49.8 and 48.8 (rotamers), 31.4 and 31.3 (rotamers), 28.2, 28.1, 28.0, 27.9, 27.7, 26.4, 22.5, 18.3, 14.0; IR (CDCl₃) 3311, 2933, 2860, 1762, 1719, 1540, 1457, 1392, 1368, 1300, 1152, 1110, 851, 768; UV (λ_max nm) 250, HRMS (ESI+) m/z 462.3333 [(M+H)+; calculated mass for C₂₆H₃₅N₅O₄⁺: 462.3326 amu].

**tert-butyl 2-((N-(tert-butoxycarbonyl)(heptan-2-yl)amino)-4-(hept-6-yn-1-yl)-1H-imidazole-1-carboxylate (9f).** Following the general procedure for alkylation with alkyl halides tert-butyl 2-((tert-butoxycarbonyl)amino)-4-(hept-6-yn-1-yl)-1H-imidazole-1-carboxylate (22 mg, 9%) as a clear oil. Rᵣ = 0.22 (20% EtOAc/Hexanes); ¹H NMR (CDCl₃, 400MHz) δ 7.0 (s, 1H), 4.45 (m, 1H), 4.25 (m, 1H, rotamer), 2.51 (dt, J = 7.2, 3.1 Hz, 2H), 2.18 (dt, J = 7.1, 2.6 Hz, 2H), 1.92 (t, J = 2.6 Hz, 1H), 1.57 (s, 9H), 1.72-1.24 (m, 14H), 1.36 (d, J = 6.6 Hz, 3H, rotamer), 1.33 (s, 9H), 0.92 (d, J = 6.9 Hz, 3H); ¹³C NMR (CDCl₃, 100MHz) δ 153.8, 147.0, 139.9 and 139.7 (rotamers), 113.6, 113.4, 84.8, 80.7 and 80.6 (rotamers), 68.4, 54.1 and 53.5 (rotamers), 36.7, 33.4, 32.1 and 32.0 (rotamers), 28.5, 28.4, 28.2, 28.2, 26.5 and 26.4 (rotamers), 22.9, 22.7, 19.9, 18.6, 16.9, 14.2; IR (CDCl₃) 3311, 2978, 2860, 1762, 1719, 1540, 1457, 1392, 1368, 1300, 1152, 1110, 851, 768; UV (λ_max nm) 250, HRMS (ESI+) m/z 476.3483 [(M+H)+; calculated mass for C₂₇H₄₀N₅O₄⁺: 476.3483 amu].
tert-butyl 2-(N-(tert-butoxycarbonyl)(octyl)amino)-4-(hept-6-yn-1-yl)-1H-imidazole-1-carboxylate (9g). Following the general procedure for alkylation with alkyl halides tert-butyl 2-((tert-butoxycarbonyl)amino)-4-(hept-6-yn-1-yl)-1H-imidazole-1-carboxylate was reacted with iodoctane to provide tert-butyl 2-((tert-butoxycarbonyl)(octyl)amino)-4-(hept-6-yn-1-yl)-1H-imidazole-1-carboxylate (40 mg, 28%) as a clear oil. Rf = 0.7 (30% EtOAc/Hexanes); 1H NMR (CDCl3, 400MHz) δ 7.0 (s, 1H), 6.9 (s, 1H, rotamer), 3.67 (ddd, J = 13.7, 9.6, 6.3 Hz, 1H), 3.54 (m, 2H, rotamer), 3.38 (ddd, J = 13.6, 9.7, 5.8 Hz, 1H), 2.48 (t, J = 7.6, 2H), 2.17 (dt, J = 2.6, 7.1, 2H), 1.91 (t, J = 2.6, 1H), 1.72-1.40 (m, 8H) 1.57 (s, 9H), 1.33 (s, 9H); 13C NMR (CDCl3, 100MHz) δ 154.0, 146.9, 142.0, 139.9, 113.5 and 113.4 (rotamers), 85.1, 84.8, 81.4 and 80.9 (rotamers), 68.4, 50.1 and 49.1 (rotamers), 32.0, 29.5, 29.4, 29.0, 28.5, 28.4, 28.2, 28.0, 27.0, 22.8, 18.6, 14.3; IR (CDCl3) 3312, 2929, 2857, 1762, 1719, 1537, 1456, 1393, 1368, 1334, 1299, 1258, 1150, 1044, 1017, 977, 850, 768; UV (λmax nm) 251, HRMS (ESI+) m/z 490.3636 [(M+H)+]; calculated mass for C28H37N3O4+: 490.3639 amu.

tert-butyl 2-(N-(tert-butoxycarbonyl)decanamido)-4-(hept-6-yn-1-yl)-1H-imidazole-1-carboxylate (9i). Following the general procedure for alkylation with alkyl halides tert-butyl 2-((tert-butoxycarbonyl)amino)-4-(hept-6-yn-1-yl)-1H-imidazole-1-carboxylate was reacted with nonanoyl chloride to provide tert-butyl 2-(N-(tert-butoxycarbonyl)decanamido)-4-(hept-6-yn-1-yl)-1H-imidazole-1-carboxylate as an impure oil. Product contained nonanoic acid but was carried through the next step and purified thereafter.

tert-butyl 2-(N-(tert-butoxycarbonyl)(cyclopentyl)amino)-4-(hept-6-yn-1-yl)-1H-imidazole-1-carboxylate (9j). Following the general procedure for alkylation with alkyl halides tert-butyl 2-((tert-butoxycarbonyl)amino)-4-(hept-6-yn-1-yl)-1H-imidazole-1-carboxylate was reacted with bromocyclopentane to provide tert-butyl 2-((tert-butoxycarbonyl)(cyclopentane)amino)-4-(hept-6-yn-1-yl)-1H-imidazole-1-carboxylate (19 mg, 14%) as a clear yellow oil. Rf = 0.68 (30% EtOAc/Hexanes); 1H NMR (CDCl3, 400MHz) δ 7.0 (s, 1H), 4.46 (s, 1H), 4.25 (m, 1H, rotamer), 2.50 (t, J = 7.5 Hz, 1H), 2.17 (dt, J = 7.1, 2.6 Hz, 1H), 2.08 (m, 1H), 1.92 (t, J = 2.6 Hz, 1H), 1.85 (m, 1H), 1.74 (m, 2H), 1.70-1.28 (m, 10H), 1.57 (s, 9H), 1.33 (s, 9H); 13C NMR (CDCl3, 100MHz) δ 154.0, 146.9, 140.2, 139.8, 113.7, 85.1, 84.8, 80.7, 68.4, 60.1 and 58.9 (rotamers), 31.6, 29.9, 28.8, 28.5, 28.4, 28.3, 28.2, 28.1, 23.5, 23.2, 18.6; IR (CDCl3) 3311, 2975, 2935, 2866, 2360, 2339, 1761, 1716, 1537, 1456, 1393, 1370, 1334, 1299, 1258, 1150, 1044, 1017, 977, 850, 768; UV (λmax nm) 241, HRMS (ESI+) m/z 446.3021 [(M+H)+]; calculated mass for C25H31N3O4+: 446.3013 amu.
**tert-butyl 2-N-(benzyl(tert-butoxycarbonyl)amino)-4-(hept-6-yn-1-yl)-1H-imidazole-1-carboxylate (9k).** Following the general procedure for alkylation with alkyl halides tert-butyl 2-(tert-butoxycarbonyl)amino)-4-(hept-6-yn-1-yl)-1H-imidazole-1-carboxylate was reacted with benzyl bromide to provide tert-butyl 2-(benzyl(tert-butoxycarbonyl)amino)-4-(hept-6-yn-1-yl)-1H-imidazole-1-carboxylate (50 mg, 37%) as a clear oil. R_t = 0.6 (30% EtOAc/Hexanes); ^1H NMR (CDCl_3, 400MHz) δ 7.4-7.15 (m, 5H), 6.93 (s, 1H, rotamer), 6.88 (s, 1H), 4.86-4.71 (m, 2H, both rotamers), 2.45 (t, J = 7.7 Hz, 1H), 2.17 (dt, J = 7.1, 2.6 Hz, 2H), 1.92 (t, J = 2.6 Hz, 1H), 1.65-1.49 (m, 6H), 1.48 (s, 9H), 1.41 (s, 9H, rotamer), 1.38 (s, 9H); ^13C NMR (CDCl_3, 100MHz) δ 154.0, 146.5, 139.8, 137.0, 129.8, 129.2, 128.6 and 128.4 (rotamers), 127.5 and 127.4 (rotamers), 113.6 and 113.4 (rotamers), 84.9, 84.9, 81.3, 68.4, 54.1 and 52.9 (rotamers), 28.5, 28.4, 28.2, 28.0, 18.6; IR (CDCl_3) 3310, 2979, 2935, 2860, 1761, 1719, 1538, 1456, 1393, 1369, 1301, 1249, 1150, 1030, 854, 768, 699; UV (λ_max nm) 251; HRMS (ESI+) m/z 468.2860 [(M+H)^+] calculated mass for C_{27}H_{38}N_{3}O_{4}: 468.2857 amu.

**tert-butyl 2-N-(tert-butoxycarbonyl)4-butylbenzyl)amino)-4-(hept-6-yn-1-yl)-1H-imidazole-1-carboxylate (9l).** Following the general procedure for alkylation with alkyl halides tert-butyl 2-(tert-butoxycarbonyl)amino)-4-(hept-6-yn-1-yl)-1H-imidazole-1-carboxylate was reacted with 4-butylbenzyl bromide to provide tert-butyl 2-(tert-butoxycarbonyl)(3-(trifluoromethyl)benzyl)amino)-4-(hept-6-yn-1-yl)-1H-imidazole-1-carboxylate (158 mg, 70%) as a clear oil. R_t = 0.4 (20% EtOAc/Hexanes); ^1H NMR (CDCl_3, 400MHz) δ 7.22 (d, J = 8.2 Hz, 2H, rotamer), 7.15 (d, J = 8.0 Hz, 2H), 7.05 (d, J = 8.0 Hz, 2H, rotamer), 7.01 (d, J = 7.9 Hz, 2H), 6.92 (s, 1H, rotamer), 6.87 (s, 1H), 4.83-4.59 (m, 2H, both rotamers), 2.53 (m, 2H), 2.45 (m, 2H), 2.15 (dt, J = 7.1, 2.6 Hz, 2H), 1.90 (t, J = 2.6 Hz, 1H), 1.62-1.20 (m, 10H), 1.45 (s, 9H), 1.45 (s, 9H), 0.87 (t, J = 7.4, 3H); ^13C NMR (CDCl_3, 100MHz) δ 154.2 and 153.9 (rotamers), 146.8 and 146.5 (rotamers), 142.4 and 142.1 (rotamers), 142.0 and 141.9 (rotamers), 139.7, 135.0 and 134.1 (rotamers), 129.2, 128.6 and 128.4 (rotamers), 113.6 and 113.4 (rotamers), 84.8, 84.7, 81.8 and 81.2 (rotamers), 68.4, 53.8 and 52.6 (rotamers), 35.5, 33.8, 28.5, 28.4, 28.2, 28.0, 22.5, 18.6, 14.1; IR (CDCl_3) 3310, 2933, 2859, 1763, 1717, 1539, 1456, 1370, 1302, 1249, 1151, 1043, 1028, 851, 768, 630; UV (λ_max nm) 253; HRMS (ESI+) m/z 524.3482 [(M+H)^+]; calculated mass for C_{31}H_{48}N_{3}O_{4}: 524.3483 amu.
** tert-butyl 2-(N-(tert-butoxycarbonyl)(3-(trifluoromethyl)benzyl)amino)-4-(hept-6-yn-1-yl)-1H-imidazole-1-carboxylate (9m).** Following the general procedure for alkylation with alkyl halides tert-butyl 2-((tert-butoxycarbonyl)amino)-4-(hept-6-yn-1-yl)-1H-imidazole-1-carboxylate was reacted with 3-(trifluoromethyl)benzyl bromide to provide tert-butyl 2-((tert-butoxycarbonyl)(3-(trifluoromethyl)benzyl)amino)-4-(hept-6-yn-1-yl)-1H-imidazole-1-carboxylate (177 mg, 54%) as a clear oil. Rf = 0.37 (20% EtOAc/Hexanes); 1H NMR (CDCl3, 400MHz) δ 7.70-7.30 (m, 4H), 6.91 (s, 1H, rotamer), 6.85 (s, 1H), 4.9-4.77 (m, 2H, both rotamers), 2.42 (t, J = 7.6 Hz, 2H), 1.34 (s, 9H, rotamer), 1.37 (s, 9H, rotamer), 1.48 (s, 9H, rotamer), 1.55 (s, 9H, rotamer), 1.59 (s, 9H, rotamer); 13C NMR (CDCl3, 100MHz) δ 153.9 and 153.9 (rotamers), 146.7 and 146.44 (rotamers), 142.3 and 141.8 (rotamers), 139.8, 139.1 and 138.2 (rotamers), 132.4, 131.9, 130.6 (q, J = 32 Hz), 128.8, 125.7 and 125.4 (rotamers), 124.3, 113.6 and 113.4 (rotamers), 85.0 and 84.9 (rotamers), 84.7, 82.3 and 81.7 (rotamers), 68.4, 53.5 and 52.4 (rotamers), 28.3, 28.0, 27.9, 18.5; IR (CDCl3) 3311, 2980, 2936, 2862, 2360, 2333, 1760, 1722, 1538, 1454, 1394, 1370, 1328, 1301, 1238, 1201, 1156, 1121, 1075, 1030, 936, 868, 659; UV (λmax nm) 256, HRMS (ESI+) m/z 535.256 [(M+Na)+; calculated mass for C29H30N3NaO4+: 535.255 amu].

** tert-butyl 2-N-((tert-butoxycarbonyl)(cinnamyl)amino)-4-(hept-6-yn-1-yl)-1H-imidazole-1-carboxylate (9o).** Following the general procedure for alkylation with alcohols tert-butyl 2-((tert-butoxycarbonyl)amino)-4-(hept-6-yn-1-yl)-1H-imidazole-1-carboxylate was reacted with cinnamyl alcohol to provide tert-butyl 2-((tert-butoxycarbonyl)(cinnamyl)amino)-4-(hept-6-yn-1-yl)-1H-imidazole-1-carboxylate (48 mg, 39%) as a clear oil. Rf = 0.6 (30% EtOAc/Hexanes); 1H NMR (CDCl3, 400MHz) δ 7.30-7.17 (m, 5H), 6.94 (s, 1H), 6.42 (d, J = 16.8 Hz, 1H), 6.30 (m, 1H), 4.47-4.32 (m, 2H, both rotamers), 2.48 (t, J = 7.8 Hz, 1H), 2.14 (m, 2H), 1.92 (t, J = 2.8 Hz, 1H), 1.65-1.49 (m, 6H), 1.55 (s, 9H, rotamer), 1.50 (s, 9H, rotamer), 1.37 (s, 9H); 13C NMR (CDCl3, 100MHz) δ 153.8, 146.8, 141.7, 139.9, 137.0, 133.3 and 132.9 (rotamers), 128.68, 127.7 125.3 and 124.9 (rotamers), 113.6, 85.1, 84.9, 81.3, 68.4, 52.4 and 51.1 (rotamers), 28.5, 28.4, 28.2, 28.1, 28.1, 18.5; IR (CDCl3) 3306, 2979, 2935, 2858, 1759, 1719, 1539, 1455, 1392, 1369, 1303, 1248, 1149, 966, 851, 767, 693; UV (λmax nm) 250, HRMS (ESI+) m/z 516.2809 [(M+H)+; calculated mass for C29H29N3O4+: 516.2833 amu].

** tert-butyl 4-(hept-6-yn-1-yl)-2-(pyrrolidin-1-yl)-1H-imidazole-1-carboxylate (17).** To a 0 ºC solution of N,N'-Di-Boc-1H-pyrrolidine-1-carboxamidine (100 mg, 0.32 mmol) in DMF (5 mL) was added a 60% dispersion of sodium hydride (11 mg, 0.28 mmol). After complete dissolution 1-bromonon-8-yl-one (73 mg, 0.34 mmol) was added as a solution in DMF. After two hours TLC showed completion and the reaction was quenched with water then diluted with EtOAc. The organic layer was then washed with
water and brine, dried with magnesium sulfate, filtered, and concentrated in vacuo. The crude material was then dissolved in 30% TFA in CH₂Cl₂ and stirred at room temperature for 16 hours. Concentration provided the unprotected heterocycle, which is dissolved in DMF (5 mL), Et₃N (0.23 mL, 1.7 mmol), DMAP (1 crystal), and di-tert-butyl dicarbonate (136 mg, 0.62 mmol) then stirred for 20 hours. The reaction was then diluted in EtOAc and washed with water and brine. The organic layer was then dried with magnesium sulfate, filtered and concentrated in vacuo. The crude material was then purified by flash chromatography (10-20% EtOAc/Hexanes gradient) to afford a yellow oil (64 mg, 58% yield).

\(^1\)H NMR (CDCl₃, 400MHz) \(\delta\) 6.63 (s, 1H), 3.44 (t, \(J = 6.8\) Hz, 4H), 2.42 (t, \(J = 7.6\) Hz, 2H), 2.18 (dt, \(J = 7.0, 2.8\) Hz, 2H), 1.92-1.86 (m, 5H), 1.69-1.21 (m, 6H), 1.56 (s, 9H). \(^1\)C NMR (CDCl₃, 100MHz) \(\delta\) 152.2, 147.8, 139.2, 109.9, 84.9, 83.9, 68.3, 51.2, 28.7, 28.5, 28.5, 28.3, 28.1, 25.6, 18.6; IR (CDCl₃) 3301, 2974, 1555, 1459, 1392, 1370, 1323, 1254, 1156, 1114, 1060, 962, 852, 772, 630; UV (\(\lambda_{\text{max}}\) nm) 275, HRMS (ESI+) m/z 332.2324 [(M+H)+]; calculated mass for \(\text{C}_{19}\text{H}_{30}\text{N}_{3}\text{O}_{2}\): 332.2333 amu.

**General procedure for the azide-alkyne Huisgen cycloaddition between 9 and \(N\)-(2-azidoethyl)-4-pentylbenzamide.**

To a solution of alkyne # in BuOH (2 mL), water (2 mL), and CH₂Cl₂ (1 mL) was added \(N\)-(2-azidoethyl)-4-pentylbenzamide (1.1 eq), CuSO₄ (0.2 eq), and sodium ascorbate (0.4 eq). The above mixture was stirred vigorously until TLC indicated complete conversion of the alkyne starting material (1-5 hrs). The reaction was then diluted with water and extracted with CH₂Cl₂. The combined organic layers were then dried (MgSO₄), filtered, and concentrated in vacuo to afford the crude material. The crude material was then purified by flash chromatography (typically 70 -100% EtOAc in Hexanes or 0-5% MeOH in CH₂Cl₂). In cases were copper color was still present in final material (typical of MeOH/CH₂Cl₂ purification) the final product was dissolved in CH₂Cl₂ and washed with a 0.01 M EDTA solution until organic layer was free of blue-green color.

**tert-butyl 2-((tert-butoxycarbonyl)(methyl)amino)-4-(5-(1-(2-(4-pentylbenzamido)ethyl)-1H-1,2,3-triazol-4-yl)pentyl)-1H-imidazole-1-carboxylate (12a).** Following the general procedure for the cycloaddition tert-butyl 2-((tert-butoxycarbonyl)(methyl)amino)-4-(hept-6-yn-1-yl)-1H-imidazole-1-carboxylate was reacted with \(N\)-(2-azidoethyl)-4-pentylbenzamide to provide tert-butyl 2-((tert-butoxycarbonyl)(methyl)amino)-4-(5-(1-(2-(4-pentylbenzamido)ethyl)-1H-1,2,3-triazol-4-yl)pentyl)-1H-imidazole-1-carboxylate (76 mg, 97%) as a clear oil. \(^1\)H NMR (CDCl₃, 400MHz) 7.67 (d, \(J = 8.4\) Hz, 2H), 7.30 (s, 1H), 7.23 (m, 1H), 7.18 (d, \(J = 8.0\) Hz, 2H), 6.94 (s, 1H), 6.92 (s, 1H rotamer), 4.54 (t, \(J = 5.8\) Hz, 2H), 3.91 (m, 2H), 3.16 (s, 3H, rotomer), 3.14 (s, 3H), 2.65 (t, \(J = 7.8\) Hz, 2H), 2.60 (t, \(J = 7.8\) Hz, 2H), 1.70-1.40 (m, 6H), 1.56 (s, 9H), 1.47 (s, 9H, rotamer), 1.40-1.21 (m, 6H), 1.32 (s, 9H), 0.85 (t, \(J = 6.8\) Hz, 3H); \(^1\)C NMR (CDCl₃, 100MHz) \(\delta\) 168.2, 154.1, 145.1, 147.4, 146.8, 142.6, 139.9, 131.3, 128.8, 127.3, 122.1, 113.6 and 113.4 (rotamers), 85.4, 81.7 and 81.2 (rotamers), 49.5, 40.1, 36.0, 35.6, 31.6, 31.1, 29.3, 28.9, 28.5, 28.3, 28.2, 28.0, 25.7, 22.7, 14.2; IR (CDCl₃) 3333, 2931, 2858, 1759,
tert-butyl 2-((tert-butoxycarbonyl)decanamido)-4-(5-(1-(2-(4-pentylbenzamido)ethyl)-1H-1,2,3-triazol-4-yl)pentyl)-1H-imidazole-1-carboxylate (12b). Following the general procedure for the cycloaddition tert-butyl 2-((tert-butoxycarbonyl)methylsulfonamido)-4-(hept-6-yn-1-yl)-1H-imidazole-1-carboxylate was reacted with N-(2-azidoethyl)-4-pentylbenzamide to provide tert-butyl 2-((tert-butoxycarbonyl)methylsulfonamido)-4-(5-(1-(2-(4-pentylbenzamido)ethyl)-1H-1,2,3-triazol-4-yl)pentyl)-1H-imidazole-1-carboxylate (95 mg, 95%) as a clear oil. $^1$H NMR (CDCl$_3$, 400MHz) 7.65 (d, $J = 8.0$ Hz, 2H), 7.30 (s, 1H), 7.25 (m, 1H), 7.19 (d, $J = 8.4$ Hz, 2H), 7.08 (s, 1H), 4.52 (t, $J = 6.2$ Hz, 2H), 3.91 (dt, $J = 5.2$, 6.0 Hz, 2H), 3.42 (s, 3H), 2.63 (t, $J = 7.4$ Hz, 2H), 2.58 (t, $J = 7.8$ Hz, 2H), 2.47 (t, $J = 7.4$ Hz, 2H), 1.70-1.52 (m, 6H), 1.56 (s, 9H), 1.36 (s, 9H), 1.35-1.20 (m, 6H), 0.84 (m, 3H); $^{13}$C NMR (CDCl$_3$, 100MHz) $\delta$ 168.1, 149.8, 148.3, 147.4, 146.6, 141.1, 134.4, 128.8, 127.3, 122.1, 115.7, 86.6, 85.7, 49.5, 41.9, 40.1, 36.0, 31.5, 31.1, 29.3, 28.7, 28.4, 28.1, 28.0, 25.0, 22.7, 14.2; IR (CDCl$_3$) 3316, 2858, 2858, 1749, 1651, 1539, 1505, 1460, 1396, 1371, 1295, 1255, 1146, 1074, 968, 834, 769; UV ($\lambda_{\text{max}}$ nm) 239; HRMS (ESI+) m/z 716.3802 [(M+H)$^+$]; calculated mass for C$_{44}$H$_{50}$N$_5$O$_5$: 716.3800 amu.

tert-butyl 2-((tert-butoxycarbonyl)(isopropyl)amino)-4-(5-(1-(2-(4-pentylbenzamido)ethyl)-1H-1,2,3-triazol-4-yl)pentyl)-1H-imidazole-1-carboxylate (12c). Following the general procedure for the cycloaddition tert-butyl 2-((tert-butoxycarbonyl)(isopropyl)amino)-4-(hept-6-yn-1-yl)-1H-imidazole-1-carboxylate was reacted with N-(2-azidoethyl)-4-pentylbenzamide to provide tert-butyl 2-((tert-butoxycarbonyl)(isopropyl)amino)-4-(5-(1-(2-(4-pentylbenzamido)ethyl)-1H-1,2,3-triazol-4-yl)pentyl)-1H-imidazole-1-carboxylate (28 mg, 86%) as a clear oil. $^1$H NMR (CDCl$_3$, 400MHz) 7.66 (d, $J = 8.4$ Hz, 2H), 7.30 (s, 1H), 7.20 (d, $J = 8.0$ Hz, 2H), 6.99 (s, 1H), 6.94 (s, 1H), 4.55 (t, $J = 5.8$ Hz, 2H), 4.41 (m, 1H), 3.92 (m, 2H), 2.68 (t, $J = 7.8$ Hz, 2H), 2.62 (t, $J = 7.6$ Hz, 2H), 2.44 (t, $J = 7.4$ Hz, 2H), 1.57 (s, 9H), 1.75-1.45 (m, 6H), 1.45-1.2 (m, 8H), 1.33 (s, 9H), 0.90 (m, 2H), 0.87 (t, $J = 6.8$ Hz, 3H); $^{13}$C NMR (CDCl$_3$, 100MHz) $\delta$ 168.1, 153.5, 148.6, 147.5, 146.9, 139.9, 139.8, 131.4, 128.9, 127.3, 122.0, 113.6, 85.1, 80.8, 49.6 and 49.3 (rotamers), 40.0, 36.0, 31.6, 31.1, 29.9, 29.4, 28.9, 28.6, 28.4, 28.1, 25.7, 22.7, 22.5, 19.3, 14.2; IR (CDCl$_3$) 2978, 2931, 2858, 2360, 2337, 1760, 1715, 1650, 1539, 1503, 1457, 1368, 1300, 1155, 1089, 1052, 972, 850, 768; UV ($\lambda_{\text{max}}$ nm) 241; HRMS (ESI+) m/z 680.4487 [(M+H)$^+$]; calculated mass for C$_{37}$H$_{50}$N$_5$O$_5$: 680.4494 amu.

tert-butyl 2-((tert-butoxycarbonyl)(isopropyl)amino)-4-(5-(1-(2-(4-pentylbenzamido)ethyl)-1H-1,2,3-triazol-4-yl)pentyl)-1H-imidazole-1-carboxylate (12d). Following the general procedure for the
cycloaddition tert-butyl 2-(allyl(tert-butoxycarbonyl)amino)-4-(hept-6-yn-1-yl)-1H-imidazole-1-carboxylate was reacted with N-(2-azidoethyl)-4-pentylenzamide to provide tert-butyl 2-(allyl(tert-butoxycarbonyl)amino)-4-(5-(1-(2-(4-pentylenzamido)ethyl)-1H-1,2,3-triazol-4-yl)pentyl)-1H-imidazole-1-carboxylate (69 mg, 51% over two steps) as a clear oil. $^1$H NMR (CDCl$_3$, 400MHz) 7.67 (d, J = 8.0 Hz, 2H), 7.27 (s, 1H), 7.17 (d, J = 8.0 Hz, 2H), 6.92 (s, 1H), 6.94 (s, 1H), 5.88 (m, 1H), 5.11 (d, J = 17 Hz, 1H), 5.02 (d, J = 9.6 Hz, 1H), 4.53 (m, 2H), 4.17 (m, 2H), 3.90 (m, 2H), 2.63 (m, 2H), 2.59 (t, J = 7.8 Hz, 2H), 2.41 (t, J = 7.2 Hz, 2H), 1.56 (s, 9H), 1.75-1.45 (m, 6H), 1.45-1.2 (m, 6H), 1.45 (s, 9H, rotamer), 1.32 (s, 9H), 0.84 (t, J = 6.8 Hz, 3H); $^{13}$C NMR (CDCl$_3$, 100MHz) $\delta$ 168.1, 153.9, 148.5, 147.4, 146.8, 146.8, 141.6, 139.9, 133.3, 131.4, 128.8, 127.3, 122.1, 118.2, 117.6, 113.5, 85.2, 81.9 and 81.3 (rotamers), 52.8 and 51.6 (rotamers), 49.5, 40.1, 36.0, 31.6, 31.1, 29.3, 28.9, 28.5, 28.3, 28.2, 28.0, 25.7, 22.7, 14.2; IR (CDCl$_3$) 3316, 2979, 2931, 2857, 1760, 1719, 1655, 1539, 1503, 1456, 1370, 1301, 1253, 1152, 1043, 923, 853, 767; UV ($\lambda_{max}$ nm) 241; HRMS (ESI+) m/z 678.4317 [(M+H)$^+$; calculated mass for C$_{37}$H$_{56}$N$_7$O$_5$: 678.4337 amu].

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tert-butyl 2-((tert-butoxycarbonyl)(hexyl)amino)-4-(5-(1-(2-(4-penylenzamido)ethyl)-1H-1,2,3-triazol-4-yl)pentyl)-1H-imidazole-1-carboxylate (12e). Following the general procedure for the cycloaddiction tert-butyl 2-((tert-butoxycarbonyl)(hexyl)amino)-4-(hept-6-yn-1-yl)-1H-imidazole-1-carboxylate was reacted with N-(2-azidoethyl)-4-pentylenzamide to provide tert-butyl 2-((tert-butoxycarbonyl)(hexyl)amino)-4-(5-(1-(2-(4-penylenzamido)ethyl)-1H-1,2,3-triazol-4-yl)pentyl)-1H-imidazole-1-carboxylate (70 mg, 75%) as a clear oil. $^1$H NMR (CDCl$_3$, 400MHz) 7.67 (d, J = 8.4 Hz, 2H), 7.28 (s, 1H), 7.19 (s, 1H), 7.18 (d, J = 8.0 Hz, 2H), 6.94 (s, 1H), 4.53 (t, J = 5.2 Hz, 2H), 3.92 (m, 2H), 3.71-3.61 (m, 1H, both rotamers), 3.53 (m, 1H, rotamer), 3.40-3.35 (m, 1H), 2.65 (t, J = 7.2 Hz, 2H), 2.62 (t, J = 7.6 Hz, 2H), 2.59 (t, J = 7.4 Hz, 2H), 2.43 (t, J = 7.4 Hz, 2H), 1.70-1.52 (m, 8H), 1.56 (s, 9H), 1.46 (s, 9H, rotamer), 1.40-1.20 (m, 12H), 1.31 (s, 9H), 0.90 (m, 6H); $^{13}$C NMR (CDCl$_3$, 100MHz) $\delta$ 168.1, 153.9, 148.5, 147.4, 146.8, 146.8, 142.0, 139.8, 131.4, 128.8, 127.3, 122.0, 113.6 and 113.4 (rotamers), 85.1, 80.9, 50.2 and 49.5 (rotamers), 49.1, 40.1, 36.0, 31.7, 31.6, 31.1, 29.4, 29.0, 28.5, 28.4, 28.2, 28.0, 26.7, 25.7, 22.8, 22.7, 14.2; IR (CDCl$_3$) 3329, 2930, 2857, 2360, 1761, 1718, 1651, 1539, 1504, 1457, 1393, 1368, 1300, 1151, 1110, 852, 767; UV ($\lambda_{max}$ nm) 239; HRMS (ESI+) m/z 722.4964 [(M+H)$^+$; calculated mass for C$_{40}$H$_{64}$N$_7$O$_5$: 722.4963 amu].

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tert-butyl 2-((tert-butoxycarbonyl)(heptan-2-yl)amino)-4-(5-(1-(2-(4-pentylenzamido)ethyl)-1H-1,2,3-triazol-4-yl)pentyl)-1H-imidazole-1-carboxylate (12f). Following the general procedure for the cycloaddiction tert-butyl 2-((tert-butoxycarbonyl)(heptan-2-yl)amino)-4-(hept-6-yn-1-yl)-1H-imidazole-1-carboxylate was reacted with N-(2-azidoethyl)-4-petylenzamide to provide tert-butyl 2-((tert-
butoxycarbonyl)(heptan-2-yl)amino)-4-(5-(1-(2-(4-pentylbenzamido)ethyl)-1H-1,2,3-triazol-4-yl)pentyl)-1H-imidazole-1-carboxylate (46 mg, 87%) as a clear yellow oil. $^1$H NMR (CDCl$_3$, 400MHz) 7.66 (d, $J = 7.6$ Hz, 2H), 7.20 (d, $J = 7.6$ Hz, 2H), 7.15 (m, 1H, both rotamers), 7.02 (m, 1H, both rotamers), 6.95 (s, 1H, rotamer), 6.88 (s, 1H), 4.74 (m, 2H), 4.56 (m, 2H), 3.95 (m, 2H) 2.69 (brs, 2H), 2.62 (t, $J = 7.6$ Hz, 2H), 2.51 (t, $J = 7.8$ Hz, 2H), 2.43 (brs, 2H), 1.8-1.5 (m, 8H), 1.47 (s, 9H), 1.43 (s, 9H, rotamer), 1.40-1.26 (m, 15H), 1.35 (s, 9H), 0.88 (m, 6H); $^{13}$C NMR (CDCl$_3$, 100MHz) δ 168.2, 154.1, 148.5, 147.4, 146.8, 142.6, 139.9, 131.3, 128.8, 127.3, 122.1, 113.6 and 113.4 (rotamers), 85.4, 81.7 and 81.2 (rotamers), 49.5, 40.1, 36.0, 35.6, 31.6, 31.1, 29.3, 28.9, 28.5, 28.3, 28.2, 28.0, 25.7, 22.7, 14.2; IR (CDCl$_3$) 3336, 2931, 2858, 1761, 1719, 1650, 1538, 1504, 1458, 1393, 1298, 1150, 1111, 850, 767; UV ($\lambda_{	ext{max}}$ nm) 239; HRMS (ESI+) m/z 750.5269 [(M+H)$^+$]; calculated mass for C$_{42}$H$_{60}$O$_5$N$_5$: 750.5276 amu.

**tert-butyl** 2-((tert-butoxycarbonyl)(octyl)amino)-4-(5-(1-(2-(4-pentylbenzamido)ethyl)-1H-1,2,3-triazol-4-yl)pentyl)-1H-imidazole-1-carboxylate (12g). Following the general procedure for the cycloaddition tert-butyl 2-((tert-butoxycarbonyl)(octyl)amino)-4-(hept-6-yn-1-yl)-1H-imidazole-1-carboxylate was reacted with N-(2-azidoethyl)-4-pentylbenzamide to provide tert-butyl 2-((tert-butoxycarbonyl)(octyl)amino)-4-(5-(1-(2-(4-pentylbenzamido)ethyl)-1H-1,2,3-triazol-4-yl)pentyl)-1H-imidazole-1-carboxylate (69 mg, 100%) as a clear oil. $^1$H NMR (CDCl$_3$, 400MHz) 7.70 (s, 1H), 7.18 (s, 1H), 7.18 (d, $J = 8.4$ Hz, 2H), 6.95 (s, 1H), 6.93 (s, 1H, rotamer), 4.54 (t, $J = 5.6$ Hz, 2H), 3.91 (m, 2H), 3.66-3.61 (m, 1H), 3.52 (m, 2H, rotamer), 3.42-3.38 (m, 1H), 2.65 (t, $J = 7.8$ Hz, 2H), 2.60 (t, $J = 7.8$ Hz, 2H), 2.43 (t, $J = 7.4$ Hz, 2H), 1.70-1.52 (m, 8H), 1.56 (s, 9H), 1.46 (s, 9H, rotamer), 1.40-1.20 (m, 16H), 1.31 (s, 9H), 0.87 (m, 6H); $^{13}$C NMR (CDCl$_3$, 100MHz) δ 168.2, 153.9, 148.5, 147.5, 146.8, 142.0, 139.8, 131.3, 128.8, 127.3, 122.1, 113.6 and 113.4 (rotamers), 85.2, 81.0, 50.2 and 49.5 (rotamers), 49.1, 40.1, 36.0, 32.0, 31.6, 31.1, 29.4, 29.0, 28.5, 28.4, 28.2, 28.0, 27.0, 25.7, 22.8, 22.7, 21.5, 17.7, 14.2; IR (CDCl$_3$) 3333, 2929, 2856, 2360, 1761, 1719, 1650, 1538, 1504, 1458, 1393, 1298, 1150, 1111, 850, 767; UV ($\lambda_{	ext{max}}$ nm) 239; HRMS (ESI+) m/z 750.5269 [(M+H)$^+$]; calculated mass for C$_{42}$H$_{60}$N$_5$O$_5$: 750.5276 amu.

**tert-butyl** 2-((tert-butoxycarbonyl)(2-(2-methoxyethoxy)ethyl)amino)-4-(5-(1-(2-(4-pentylbenzamido)ethyl)-1H-1,2,3-triazol-4-yl)pentyl)-1H-imidazole-1-carboxylate (12h). Following the general procedure for the cycloaddition tert-butyl 2-((tert-butoxycarbonyl)(2-(2-methoxyethoxy)ethyl)amino)-4-(hept-6-yn-1-yl)-1H-imidazole-1-carboxylate was reacted with N-(2-azidoethyl)-4-pentylbenzamide to provide tert-butyl 2-((tert-butoxycarbonyl)(2-(2-methoxyethoxy)ethyl)amino)-4-(5-(1-(2-(4-pentylbenzamido)ethyl)-1H-1,2,3-triazol-4-yl)pentyl)-1H-imidazole-1-carboxylate (48 mg, 23% over two steps) as a clear oil. $^1$H NMR (CDCl$_3$, 400MHz) 7.66 (d,
Following the general procedure for the cycloaddition tert-butyl 2-((tert-butoxycarbonyl)decanamido)-4-(5-(1-(2-(4-pentylbenzamido)ethyl)-1H-1,2,3-triazol-4-yl)pentyl)-1H-imidazole-1-carboxylate (12i). Following the general procedure for the cycloaddition tert-butyl 2-((tert-butoxycarbonyl)decanamido)-4(hept-6-yn-1-yl)-1H-imidazole-1-carboxylate was reacted with N-(2-azidoethyl)-4-pentylbenzamide to provide tert-butyl 2-((tert-butoxycarbonyl)decanamido)-4-(5-(1-(2-(4-pentylbenzamido)ethyl)-1H-1,2,3-triazol-4-yl)pentyl)-1H-imidazole-1-carboxylate (44 mg, 25%) as a clear oil. 1H NMR (CDCl3, 400MHz) 7.67 (d, J = 8.0 Hz, 2H), 7.30 (s, 1H), 7.19 (d, J = 8.0 Hz, 2H), 7.01 (s, 1H, rotamer), 7.00 (s, 1H), 4.54 (t, J = 5.6 Hz, 2H), 3.91 (dt, J = 5.6, 6.0 Hz, 2H), 2.95-2.89 (m, 2H), 2.66 (t, J = 7.6 Hz, 2H), 2.61 (t, J = 7.8 Hz, 2H), 2.47 (t, J = 7.2 Hz, 2H), 1.70-1.52 (m, 8H), 1.53 (s, 9H), 1.40 (s, 9H), 1.38-1.20 (m, 16H), 0.86 (m, 6H); 13C NMR (CDCl3, 100MHz) δ 168.2, 153.9, 148.5, 147.5, 146.8, 142.0, 139.8, 131.3, 128.8, 127.3, 122.1, 113.6 and 113.4 (rotamers), 85.2, 81.0, 50.2 and 49.5 (rotamers), 49.1, 40.1, 36.0, 32.0, 31.6, 31.1, 29.4, 29.0, 28.5, 28.5, 28.4, 28.2, 28.0, 27.0, 25.7, 22.8, 22.7, 21.5, 17.7, 14.2; IR (CDCl3) 3333, 2928, 2856, 1754, 1659, 1538, 1504, 1458, 1392, 1371, 1293, 1151, 1086, 852, 769; UV (λmax nm) 239; HRMS (ESI+) m/z 792.5309 [(M+H)+]; calculated mass for C44H70N3O4+: 792.5382 amu.

Following the general procedure for the cycloaddition tert-butyl 2-((tert-butoxycarbonyl)(cyclopentyl)amino)-4-(5-(1-(2-(4-pentylbenzamido)ethyl)-1H-1,2,3-triazol-4-yl)pentyl)-1H-imidazole-1-carboxylate (12j). Following the general procedure for the cycloaddition tert-butyl 2-((tert-butoxycarbonyl)(cyclopentyl)amino)-4(hept-6-yn-1-yl)-1H-imidazole-1-carboxylate was reacted with N-(2-azidoethyl)-4-pentylbenzamide to provide tert-butyl 2-((tert-butoxycarbonyl)(cyclopentyl)amino)-4-(5-(1-(2-(4-pentylbenzamido)ethyl)-1H-1,2,3-triazol-4-yl)pentyl)-1H-imidazole-1-carboxylate (26 mg, 99%) as a clear oil. 1H NMR (CDCl3, 400MHz) 7.67 (m, 2H, both rotamers), 7.30 (m, 1H), 7.20 (m, 2H, both rotamers), 7.04 (brs, 1H, rotamer), 6.95 (s, 1H), 6.63 (s, 1H), 4.46 (m, 2H), 4.44 (t, J = 8.0 Hz, 1H), 3.92 (m, 2H), 3.61 (m, 2H), 3.53 (m, 2H), 2.60 (m, 4H), 2.45 (t, J = 7.0 Hz, 2H), 2.07 (m, 1H), 1.90-1.40 (m, 8H), 1.57 (s, 9H), 1.43 (s, 9H, rotamer), 1.40-1.20 (m, 6H).
1.30 (s, 9H), 0.85 (m, 5H); 13C NMR (CDCl3, 100MHz) δ 168.1 and 168.0 (both rotamers), 154.0, 147.5, 146.9, 140.3, 139.9, 131.6, 131.4, 128.9, 127.3, 122.3, 113.7, 85.2, 80.8, 58.9, 51.2 and 49.6 (rotamers), 40.0, 39.6, 36.0, 32.0, 31.6, 31.4, 31.1, 29.9, 29.4, 28.9, 28.8, 28.6, 28.4, 28.2, 28.1, 25.7, 23.4, 23.2, 22.7, 14.2; IR (CDCl3) 3300, 2931, 2858, 1760, 1719, 1650, 1540, 1501, 1457, 1369, 1299, 1153, 1097, 850, 767; UV (λ<sub>max</sub> nm) 241; HRMS (ESI+) m/z 706.4653 [(M+H)<sup>+</sup>; calculated mass for C<sub>30</sub>H<sub>39</sub>N<sub>5</sub>O<sub>5</sub>: 706.4650 amu].

**tert-butyl 2-(benzyl((tert-butoxycarbonyl)amino)-4-(5-(1-(2-(4-pentylbenzamido)ethyl)-1H-1,2,3-triazol-4-yl)pentyl)-1H-imidazole-1-carboxylate (12k).** Following the general procedure for the cycloaddition tert-butyl 2-(benzyl((tert-butoxycarbonyl)amino)-4-(hept-6-yn-1-yl)-1H-imidazole-1-carboxylate was reacted with N-(2-azidoethyl)-4-pentylbenzamide to provide tert-butyl 2-(benzyl((tert-butoxycarbonyl)amino)-4-(5-(1-(2-(4-pentylbenzamido)ethyl)-1H-1,2,3-triazol-4-yl)pentyl)-1H-imidazole-1-carboxylate (62 mg, 85%) as a clear oil. 1H NMR (CDCl3, 400MHz) 7.66 (d, J = 8.4 Hz, 2H), 7.30 (m, 1H), 7.24 (s, 1H), 7.18 (d, J = 8.8 Hz, 2H), 6.95 (s, 1H, rotamer), 6.85 (s, 1H), 4.80-4.71 (m, 2H, both rotamers), 4.52 (t, J = 5.6 Hz, 2H), 3.90 (m, 2H), 2.65 (t, J = 7.2 Hz, 2H), 2.60 (t, J = 7.6 Hz, 2H), 2.40 (t, J = 7.2 Hz, 2H), 1.70-1.52 (m, 6H), 1.47 (s, 9H), 1.40 (s, 9H, rotamer), 1.40-1.20 (m, 6H), 1.34 (s, 9H), 0.86 (t, J = 7.0 Hz, 3H); 13C NMR (CDCl3, 100MHz) δ 168.2, 154.0, 148.5, 147.5, 146.4, 142.4, 139.7, 136.9, 131.3, 129.2, 128.8, 128.5, 128.4, 127.6, 127.3, 122.0, 113.7 and 113.4 (rotamers), 85.0, 82.0 and 81.4 (rotamers), 54.1 and 52.9 (rotamers), 49.5, 40.1, 36.0, 31.6, 31.1, 29.4, 28.9, 28.5, 28.4, 28.2, 28.0, 25.7, 22.7, 14.2; IR (CDCl3) 3328, 2930, 2858, 1759, 1719, 1656, 1537, 1500, 1455, 1369, 1300, 1249, 1149, 1044, 854; UV (λ<sub>max</sub> nm) 239; HRMS (ESI+) m/z 728.4486 [(M+H)<sup>+</sup>; calculated mass for C<sub>41</sub>H<sub>37</sub>N<sub>5</sub>O<sub>5</sub>: 728.4494 amu].

**tert-butyl 2-((tert-butoxycarbonyl)(4-butylbenzyl)amino)-4-(5-(1-(2-(4-pentylbenzamido)ethyl)-1H-1,2,3-triazol-4-yl)pentyl)-1H-imidazole-1-carboxylate (12l).** Following the general procedure for the cycloaddition tert-butyl 2-((tert-butoxycarbonyl)(4-butylbenzyl)amino)-4-(hept-6-yn-1-yl)-1H-imidazole-1-carboxylate was reacted with N-(2-azidoethyl)-4-pentylbenzamide to provide tert-butyl 2-((tert-butoxycarbonyl)(4-butylbenzyl)amino)-4-(5-(1-(2-(4-pentylbenzamido)ethyl)-1H-1,2,3-triazol-4-yl)pentyl)-1H-imidazole-1-carboxylate (163 mg, 78%) as a clear oil. 1H NMR (CDCl3, 400MHz) 7.67 (d, J = 8.4 Hz, 2H), 7.40 (m, 1H), 7.14 (d, J = 8.0 Hz, 2H), 7.12 (d, J = 8.0 Hz, 2H), 7.10 (m, 1H), 7.14 (d, J = 7.6 Hz, 2H), 6.85 (s, 1H, both rotamers), 4.80-4.69 (m, 2H, both rotamers), 4.51 (m, 2H), 3.88 (m, 2H), 2.63 (m, 2H), 2.58 (t, J = 7.8 Hz, 2H), 2.48 (t, J = 7.6 Hz, 2H), 2.39 (m, 2H), 1.70-1.52 (m, 8H),
Following the general procedure for the cycloaddition tert-butyl 2-((tert-butoxycarbonyl)(3-(trifluoromethyl)benzyl)amino)-4-(5-(1-(2-(4-pentylbenzamido)ethyl)-1H,1,2,3-triazol-4-yl)pentyl)-1H-imidazole-1-carboxylate (12m). tert-butyl 2-((tert-butoxycarbonyl)(1-phenylethyl)amino)-4-(5-(1-(2-(4-pentylbenzamido)ethyl)-1H,1,2,3-triazol-4-yl)pentyl)-1H-imidazole-1-carboxylate (12n).
NMR (CDCl₃, 300MHz) 7.67 (d, J = 7.8 Hz, 2H), 7.61 (m, 1H), 7.30-7.10 (m, 6H), 6.70 (s, 1H), 5.52 (m, 1H), 5.23 (m, 1H, rotamer), 4.53 (m, 2H), 3.92 (m, 2H), 2.67 (m, 2H), 2.60 (t, J = 8.1 Hz, 2H), 2.48 (m, 2H), 1.70-1.52 (m, 12H), 1.50-1.20 (m, 22H), 0.86 (t, J = 6.9 Hz, 3H); ¹³C NMR (CDCl₃, 75MHz) δ 168.1, 153.6, 147.4, 145.9, 144.3, 140.1, 139.2, 131.3, 128.8, 128.8, 128.5, 127.9, 127.3, 127.1, 127.0, 113.8 and 113.5 (rotamers), 85.2 and 84.3 (rotamers), 81.4 and 81.0 (rotamers), 58.5 and 56.8 (rotamers), 49.7, 40.0, 36.0, 31.6, 31.1, 29.4, 28.9, 28.4, 28.2, 28.1, 28.0, 25.7, 22.7, 20.1, 14.2; IR (CDCl₃) 2929, 2857, 1756, 1715, 1656, 1538, 1500, 1456, 1369, 1301, 1150, 1058; UV (λ max nm) 241; HRMS (ESI+) m/z 742.4661 [(M+H)+; calculated mass for C₄₂H₅₉N₇O₅+: 742.465 amu].

tert-butyl 2-(benzyl(tert-butoxycarbonyl)amino)-4-(5-(1-(2-(4-pentylbenzamido)ethyl)-1H-1,2,3-triazol-4-yl)pentyl)-1H-imidazole-1-carboxylate (12o). Following the general procedure for the cycloaddition tert-butyl 2-(benzyl(tert-butoxycarbonyl)amino)-4-(hept-6-yn-1-yl)-1H-imidazole-1-carboxylate was reacted with N-(2-azidoethyl)-4-pentylbenzamide to provide tert-butyl 2-(benzyl(tert-butoxycarbonyl)amino)-4-(5-(1-(2-(4-pentylbenzamido)ethyl)-1H-1,2,3-triazol-4-yl)pentyl)-1H-imidazole-1-carboxylate (62 mg, 85%) as a clear oil. Rf = 0.52 (100% EtOAc); ¹H NMR (CDCl₃, 400MHz) 7.66 (d, J = 8.0 Hz, 2H), 7.27-6.95 (m, 9H), 6.91 (s, 1H), 6.40 (d, J = 15.6 Hz, 1H), 6.30 (m, 1H), 4.54 (t, J = 5.6 Hz, 2H), 4.33 (m, 2H), 3.92 (m, 2H), 2.61 (m, 4H), 2.43 (t, J = 7.6 Hz, 2H), 1.70-1.52 (m, 6H), 1.54 (s, 9H), 1.45-1.15 (m, 6H), 1.35 (s, 9H), 0.87 (t, J = 6.8 Hz, 3H); ¹³C NMR (CDCl₃, 100MHz) δ 168.5, 153.8, 148.5, 147.4, 146.7, 141.7, 139.9, 137.0, 133.3, 131.4, 128.8, 128.6, 127.7, 127.3, 126.7, 124.8, 122.0, 113.6, 85.1, 81.3, 51.2, 49.5, 40.0, 36.0, 31.6, 31.1, 29.3, 28.9, 28.5, 28.2, 28.1, 27.9, 25.7, 22.7, 14.2; IR (CDCl₃) 3330, 2931, 2857, 1759, 1718, 1654, 1539, 1502, 1456, 1369, 1301, 1252, 1150, 1047, 967, 913, 853, 767, 733; UV (λ max nm) 244; HRMS (ESI+) m/z 754.4658 [(M+H)+; calculated mass for C₄₁H₅₇N₇O₅+: 754.465 amu].

tert-butyl 4-(5-(1-(2-(4-pentylbenzamido)ethyl)-1H-1,2,3-triazol-4-yl)pentyl)-2-(pyrrolidin-1-yl)-1H-imidazole-1-carboxylate (12p). Following the general procedure for the cycloaddition tert-butyl 4-(hept-6-yn-1-yl)-2-(pyrrolin-1-yl)-1H-imidazole-1-carboxylate was reacted with N-(2-azidoethyl)-4-pentylbenzamide to provide tert-butyl 4-(5-(1-(2-(4-pentylbenzamido)ethyl)-1H-1,2,3-triazol-4-yl)pentyl)-2-(pyrrolidin-1-yl)-1H-imidazole-1-carboxylate (18 mg, 43%) as a yellow oil. ¹H NMR (CDCl₃, 400MHz) 7.67 (d, J = 8.0 Hz, 2H), 7.30 (s, 1H), 7.20 (d, J = 8.4 Hz, 2H), 6.94 (m, 1H), 6.61 (s, 1H), 4.55 (t, J = 5.6 Hz, 2H), 3.94 (dt, J = 5.2, 5.8 Hz, 2H), 3.44 (t, J = 6.6 Hz, 4H), 2.69 (t, J = 7.6 Hz, 2H), 2.62 (t, J = 7.6 Hz, 2H), 2.39 (t, J = 7.4 Hz, 2H), 1.89 (m, 4H), 1.70-1.50 (m, 6H), 1.57 (s, 9H),
1.40-1.20 (m, 6H), 0.87 (t, J = 7.2 Hz, 3H); \( ^{13} \)C NMR (CDCl\(_3\), 100MHz) δ 168.0, 148.7, 147.7, 147.5, 139.0, 131.3, 128.9, 127.3, 122.0, 109.9, 84.1, 51.3, 49.6, 40.0, 36.0, 36.0, 31.6, 31.1, 29.4, 28.4, 28.2, 28.1, 25.7, 25.7, 22.7, 14.2; IR (CDCl\(_3\)) 2929, 2857, 1752, 1650, 1611, 1552, 1503, 1459, 1392, 1370, 1321, 1254, 1155, 1116, 1051, 962, 853, 771, 732; UV (\( \lambda_{\text{max}} \) nm) 238; HRMS (ESI+) m/z 592.3976 [(M+H)\(^+\); calculated mass for C\(_{33}\)H\(_{50}\)N\(_7\)O\(_3\): 592.3970 amu.

**General procedure for the azide-alkyne Huisgen cycloaddition between 11 and N-(2-azidoethyl)-4-pentylbenzamide.**

Di-tert-butoxycarbonyl # is dissolved in 30% TFA/CH\(_2\)Cl\(_2\) (2 mL) or 10% for branched derivatives (such as #) prone to loss of the substitution as a stable cation. This solution was then monitored by TLC for completion (approximately 3 three hours for 30% TFA/CH\(_2\)Cl\(_2\) and overnight for 10%). The reaction is then concentrated in vacuo to afford the TFA salt then dissolved in MeOH (2 mL) with 1-2 drops of concentrated HCl. Any solid particulates are filtered through a cotton plug and the solution is then concentrated in vacuo to afford the HCl salt. The majority of samples are pure by \(^1\)H NMR. Impure products were purified by flash chromatography (1-10% concentrated ammonia in MeOH/CH\(_2\)Cl\(_2\)). The ammonia free dried samples are then dissolved in MeOH with concentrated HCl as above and concentrated to afford the HCl salt.

2-(methylamino)-4-(5-(1-(2-(4-pentylbenzamido)ethyl)-1H-1,2,3-triazol-4-yl)pentyl)-1H-imidazol-3-ium chloride (13a). Reacted in 30% TFA to provide the 2-(methylamino)-4-(5-(1-(2-(4-pentylbenzamido)ethyl)-1H-1,2,3-triazol-4-yl)pentyl)-1H-imidazol-3-ium chloride (58 mg, quantitative yield) as a clear oil. \(^1\)H NMR (CD\(_3\)OD, 400MHz) 8.52 (s, 1H), 7.69 (d, J = 8.0 Hz, 2H), 7.25 (d, J = 8.0 Hz, 2H), 6.55 (s, 1H), 4.82 (t, J = 5.2 Hz, 2H), 3.92 (t, J = 5.6 Hz, 2H), 2.94 (s, 3H), 2.86 (t, J = 7.6 Hz, 2H), 2.63 (t, J = 7.6 Hz, 2H), 2.47 (t, J = 7.4 Hz, 2H), 1.73 (m, 2H), 1.58 (m, 4H), 1.40 (m, 2H), 1.28 (m, 4H), 0.88 (t, J = 7.0 Hz, 3H); \( ^{13} \)C NMR (CD\(_3\)OD, 100MHz) δ 170.4, 149.3, 148.7, 146.1, 132.2, 129.7, 129.1, 128.4, 128.2, 109.9, 53.8, 49.1, 40.5, 36.7, 32.6, 32.2, 29.7, 29.1, 29.0, 28.8, 25.3, 24.2, 23.6, 14.4; IR (CD\(_3\)OD) 3415, 2929, 2858, 2376, 2348, 2310, 1678, 1640, 1544, 1507, 1434, 1307, 1181; UV (\( \lambda_{\text{max}} \) nm) 238; HRMS (ESI+) m/z 452.3116 [(M+H)\(^+\); calculated mass for C\(_{25}\)H\(_{38}\)N\(_7\)O\(_3\): 452.3132 amu.

2-(methylsulfonamido)-4-(5-(1-(2-(4-pentylbenzamido)ethyl)-1H-1,2,3-triazol-4-yl)pentyl)-1H-imidazol-3-ium chloride (13b). Reacted in 30% TFA to provide the 2-(methylsulfonamido)-4-(5-(1-(2-(4-pentylbenzamido)ethyl)-1H-1,2,3-triazol-4-yl)pentyl)-1H-imidazol-3-ium chloride (58 mg, quantitative yield). \(^1\)H NMR (CD\(_3\)OD, 400MHz) 8.49 (s, 1H), 7.69 (d, J = 8.0 Hz, 2H), 7.26 (d, J = 8.4 Hz,
2-(isopropylamino)-4-(5-(1-(2-(4-pentylbenzamido)ethyl)-1H-1,2,3-triazol-4-yl)penty1)-1H-imidazol-3-ium chloride (13c). Reacted in 30% TFA to provide the 2-(isopropylamino)-4-(5-(1-(2-(4-pentylbenzamido)ethyl)-1H-1,2,3-triazol-4-yl)penty1)-1H-imidazol-3-ium chloride (17 mg, 85%) as a clear oil. \(^1H\) NMR (CD\(_2\)OD, 400MHz) 8.14 (s, 1H), 7.67 (d, \(J = 8.4\) Hz, 2H), 7.25 (d, \(J = 8.0\) Hz, 2H), 6.52 (s, 1H), 4.72 (t, \(J = 5.8\) Hz, 2H), 3.88 (t, \(J = 5.6\) Hz, 2H), 3.69 (m, 1H), 2.78 (t, \(J = 7.4\) Hz, 2H), 2.64 (t, \(J = 7.8\) Hz, 2H), 2.46 (t, \(J = 7.6\) Hz, 2H), 1.71 (m, 2H), 1.62 (m, 4H), 0.89 (t, \(J = 7.0\) Hz, 3H); \(^{13}C\) NMR (CD\(_2\)OD, 100MHz) \(\delta\) 170.3, 148.4, 147.1, 134.1, 132.3, 129.5, 129.1, 128.2, 116.9, 109.8, 52.0, 46.6, 40.5, 36.5, 32.3, 30.9, 29.3, 28.7, 25.2, 24.8, 23.4, 22.6, 14.2; IR (CD\(_2\)OD) 2926, 2852, 1666, 1635, 1542, 1503, 1456, 1370, 1303, 1195, 1173, 1062, 978; UV (\(\lambda_{max}\) nm) 238; HRMS (ESI+) m/z 516.2743 [(M+H)+; calculated mass for C\(_{25}\)H\(_{37}\)N\(_7\)O\(_3\)S\(^+\): 516.2751 amu].

2-(allylamino)-4-(5-(1-(2-(4-pentylbenzamido)ethyl)-1H-1,2,3-triazol-4-yl)penty1)-1H-imidazol-3-ium chloride (13d). Reacted in 30% TFA to provide the 2-(allylamino)-4-(5-(1-(2-(4-pentylbenzamido)ethyl)-1H-1,2,3-triazol-4-yl)penty1)-1H-imidazol-3-ium chloride (18 mg, 96%) as a clear oil. \(^1H\) NMR (CD\(_2\)OD, 400MHz) 8.18 (s, 1H), 7.67 (d, \(J = 8.0\) Hz, 2H), 7.25 (d, \(J = 8.4\) Hz, 2H), 6.53 (s, 1H), 5.92 (m, 1H), 5.28 (d, \(J = 17.2\) Hz, 1H), 5.21 (d, \(J = 10.6\) Hz, 1H), 4.73 (t, \(J = 5.6\) Hz, 2H), 3.89 (m, 4H), 2.77 (m, 2H), 2.63 (t, \(J = 7.6\) Hz, 2H), 2.46 (t, \(J = 7.6\) Hz, 2H), 1.69 (m, 2H), 1.59 (m, 4H), 1.45-1.23 (m, 6H), 0.89 (t, \(J = 7.8\) Hz, 3H); \(^{13}C\) NMR (CD\(_2\)OD, 100MHz) \(\delta\) 170.3, 148.4, 147.1, 134.1, 132.3, 129.5, 129.1, 128.2, 116.9, 109.8, 52.2, 45.7, 40.5, 36.5, 32.3, 31.9, 29.2, 29.0, 28.6, 27.9, 25.1, 24.9, 23.4, 14.2; IR (CD\(_2\)OD) 3363, 2926, 2857, 1666, 1635, 1542, 1503, 1456, 1370, 1303, 1140, 1058; UV (\(\lambda_{max}\) nm) 238; HRMS (ESI+) m/z 480.3444 [(M+H)+; calculated mass for C\(_{27}\)H\(_{42}\)N\(_7\)O\(_2\)S\(^+\): 480.3445 amu].
2-(hexylamino)-4-(5-(1-(2-(4-pentylbenzamido)ethyl)-1H-1,2,3-triazol-4-yl)pentyl)-1H-imidazol-3-ium chloride (13e). Reacted in 30% TFA to provide the 2-(hexylamino)-4-(5-(1-(2-(4-pentylbenzamido)ethyl)-1H-1,2,3-triazol-4-yl)pentyl)-1H-imidazol-3-ium chloride (55 mg, 99%) as a clear oil. $^1$H NMR (CD$_3$OD, 400MHz) 8.63 (s, 1H), 7.71 (d, $J = 8.4$ Hz, 2H), 7.25 (d, $J = 8.0$ Hz, 2H), 6.54 (s, 1H), 4.86 (t, $J = 5.4$ Hz, 2H), 3.95 (t, $J = 5.2$ Hz, 2H), 3.26 (t, $J = 7.2$ Hz, 2H), 2.89 (t, $J = 7.6$ Hz, 2H), 2.63 (t, $J = 7.6$ Hz, 2H), 2.48 (t, $J = 7.4$ Hz, 2H), 1.75 (m, 2H), 1.62 (m, 6H), 1.45-1.27 (m, 12H), 0.89 (m, 6H); $^{13}$C NMR (CD$_3$OD, 100MHz) δ 170.4, 148.7, 148.4, 145.5, 132.2, 129.7, 129.0, 128.7, 128.5, 109.8, 54.3, 49.9, 44.3, 40.4, 36.7, 32.6, 32.5, 32.2, 30.2, 29.1, 28.8, 28.7, 27.5, 25.3, 23.9, 23.7, 23.6, 14.4; IR (CD$_3$OD) 3241, 2929, 2857, 2360, 2323, 1668, 1635, 1544, 1508, 1456, 1379, 1335, 1306; UV ($\lambda_{max}$ nm) 238; HRMS (ESI+) m/z 522.3905 [(M+H)$^+$]; calculated mass for C$_{30}$H$_{48}$N$_7$O$: 522.3915$ amu.

2-(heptan-2-ylamino)-4-(5-(1-(2-(4-pentylbenzamido)ethyl)-1H-1,2,3-triazol-4-yl)pentyl)-1H-imidazol-3-ium chloride (13f). Reacted in 30% TFA to provide the 2-(heptanes-2-ylamino)-4-(5-(1-(2-(4-pentylbenzamido)ethyl)-1H-1,2,3-triazol-4-yl)pentyl)-1H-imidazol-3-ium chloride (28 mg, 97%) as a clear oil. $^1$H NMR (CD$_3$OD, 400MHz) 8.57 (s, 1H), 7.69 (d, $J = 8.4$ Hz, 2H), 7.26 (d, $J = 8.4$ Hz, 2H), 6.53 (s, 1H), 4.84 (t, $J = 5.2$ Hz, 2H), 3.94 (t, $J = 5.2$ Hz, 2H), 3.56 (m, 1H), 2.89 (t, $J = 7.6$ Hz, 2H), 2.64 (t, $J = 7.6$ Hz, 2H), 2.48 (t, $J = 7.2$ Hz, 2H), 1.75 (m, 2H), 1.64 (m, 6H), 1.45-1.27 (m, 15H), 0.89 (m, 6H); $^{13}$C NMR (CD$_3$OD, 100MHz) δ 170.4, 148.6, 147.8, 143.4, 132.1, 129.5, 128.8, 128.2, 109.5, 54.1, 51.0, 40.2, 37.5, 36.5, 32.6, 32.3, 31.9, 28.9, 28.6, 28.6, 26.6, 25.1, 23.8, 23.5, 23.4, 21.0, 14.2; IR (CD$_3$OD) 3254, 2956, 2930, 2858, 1662, 1541, 1503, 1455, 1380, 1303, 1123, 1020, 977, 856, 763; UV ($\lambda_{max}$ nm) 238; HRMS (ESI+) m/z 536.4085 [(M+H)$^+$]; calculated mass for C$_{31}$H$_{50}$N$_7$O$: 536.4071$ amu.

2-(octylamino)-4-(5-(1-(2-(4-pentylbenzamido)ethyl)-1H-1,2,3-triazol-4-yl)pentyl)-1H-imidazol-3-ium chloride (13g). Reacted in 30% TFA to provide the 2-(octylamino)-4-(5-(1-(2-(4-pentylbenzamido)ethyl)-1H-1,2,3-triazol-4-yl)pentyl)-1H-imidazol-3-ium chloride (56 mg, 98%) as a clear oil. $^1$H NMR (CD$_3$OD, 400MHz) 8.57 (s, 1H), 7.70 (d, $J = 8.0$ Hz, 2H), 7.26 (d, $J = 8.0$ Hz, 2H), 6.54 (s, 1H), 4.84 (t, $J = 5.4$ Hz, 2H), 3.95 (t, $J = 5.4$ Hz, 2H), 3.26 (t, $J = 7.2$ Hz, 2H), 2.88 (t, $J = 7.6$ Hz, 2H), 2.64 (t, $J = 7.8$ Hz, 2H), 2.48 (t, $J = 7.6$ Hz, 2H), 1.74 (m, 2H), 1.61 (m, 6H), 1.44-1.31 (m, 16H), 0.89 (m, 6H); $^{13}$C NMR (CD$_3$OD, 100MHz) δ 170.4, 148.7, 148.5, 145.7, 132.2, 129.7, 129.0, 128.7, 128.5, 108.6, 54.1, 49.9, 44.3, 40.4, 36.7, 33.0, 32.6, 32.5, 32.2, 30.4, 30.3, 29.1, 28.9, 28.8, 27.8, 25.3, 23.8, 23.6, 14.5, 14.4; IR (CD$_3$OD) 3265, 2928, 2857, 2375, 2310, 1671, 1635, 1544, 1506, 1457, 1376, 1308; UV ($\lambda_{max}$ nm) 238; HRMS (ESI+) m/z 550.4222 [(M+H)$^+$]; calculated mass for C$_{33}$H$_{52}$N$_7$O$: 550.4228$ amu.
2-((2-(2-methoxyethoxy)ethyl)amino)-4-(5-(1-(2-(4-pentylbenzamido)ethyl)-1H-1,2,3-triazol-4-yl)pentyl)-1H-imidazol-3-ium chloride (13h). Reacted in 30% TFA to provide the 2-((2-(2-methoxyethoxy)ethyl)amino)-4-(5-(1-(2-(4-pentylbenzamido)ethyl)-1H-1,2,3-triazol-4-yl)pentyl)-1H-imidazol-3-ium chloride (33 mg, 96%) as a clear oil. $^1$H NMR (CD$_3$OD, 400MHz) 8.33 (s, 1H), 7.67 (d, $J = 8.0$ Hz, 2H), 7.26 (d, $J = 8.0$ Hz, 2H), 6.52 (s, 1H), 4.77 (t, $J = 5.4$ Hz, 2H), 3.90 (t, $J = 5.6$ Hz, 2H), 3.63 (m, 4H), 3.53 (m, 2H), 3.45 (t, $J = 5.0$ Hz, 2H), 2.82 (t, $J = 7.4$ Hz, 2H), 2.64 (t, $J = 7.6$ Hz, 2H), 2.47 (t, $J = 7.6$ Hz, 2H), 1.80-1.70 (m, 2H), 1.70-1.56 (m, 4H), 1.44-1.20 (m, 6H), 0.89 (t, $J = 7.0$ Hz, 3H); $^{13}$C NMR (CD$_3$OD, 100MHz) δ 170.3, 148.5, 146.2, 132.2, 130.8, 129.5, 128.9, 128.2, 126.9, 109.6, 72.7, 71.1, 70.8, 59.0, 52.9, 44.2, 40.4, 36.5, 32.4, 32.0, 29.0, 28.6, 25.1, 24.4, 23.4, 14.2; IR (CD$_3$OD) 3181, 2930, 2861, 1734, 1670, 1583, 1541, 1503, 1457, 1407, 1302, 1246; UV ($\lambda_{max}$ nm) 238; HRMS (ESI+) m/z 540.3662 [(M+H)$^+$]; calculated mass for C$_{29}$H$_{45}$N$_7$O$_4$$^+$: 540.3657 amu.

2-decanamido-4-(5-(1-(2-(4-pentylbenzamido)ethyl)-1H-1,2,3-triazol-4-yl)pentyl)-1H-imidazol-3-ium chloride (13i). Reacted in 30% TFA to provide the 2-(decanamido)-4-(5-(1-(2-(4-pentylbenzamido)ethyl)-1H-1,2,3-triazol-4-yl)pentyl)-1H-imidazol-3-ium chloride (33 mg, 96%) as a clear oil. $^1$H NMR (CD$_3$OD, 400MHz) 8.38 (s, 1H), 7.68 (d, $J = 8.0$ Hz, 2H), 7.75 (d, $J = 8.4$ Hz, 2H), 6.89 (s, 1H), 4.78 (t, $J = 5.6$ Hz, 2H), 3.91 (t, $J = 5.4$ Hz, 2H), 2.83 (t, $J = 7.2$ Hz, 2H), 2.63 (t, $J = 7.6$ Hz, 2H), 2.60 (t, $J = 7.6$ Hz, 2H), 2.51 (t, $J = 7.4$ Hz, 2H), 1.80-1.52 (m, 8H), 1.44-1.20 (m, 18H), 0.89 (m, 6H); $^{13}$C NMR (CD$_3$OD, 100MHz) δ 173.7, 170.3, 148.5, 146.2, 139.2, 132.1, 130.8, 129.5, 128.2, 127.2, 111.7, 53.1, 40.4, 36.7, 36.5, 32.9, 32.4, 32.0, 30.4, 30.3, 30.2, 30.0, 29.1, 28.9, 28.9, 28.7, 25.7, 24.9, 24.3, 23.6, 23.4, 14.3, 14.2; IR (CD$_3$OD) 3266, 2930, 2861, 1734, 1670, 1583, 1541, 1503, 1457, 1407, 1302, 1246; UV ($\lambda_{max}$ nm) 241; HRMS (ESI+) m/z 592.4333 [(M+H)$^+$]; calculated mass for C$_{34}$H$_{55}$N$_7$O$_4$$^+$: 592.4334 amu.

2-(cyclopentylamino)-4-(5-(1-(2-(4-pentylbenzamido)ethyl)-1H-1,2,3-triazol-4-yl)pentyl)-1H-imidazol-3-ium chloride (13j). Reacted in 30% TFA to provide the 2-(cyclopentylamino)-4-(5-(1-(2-(4-pentylbenzamido)ethyl)-1H-1,2,3-triazol-4-yl)pentyl)-1H-imidazol-3-ium chloride (33 mg, 96%) as a clear oil. $^1$H NMR (CD$_3$OD, 400MHz) 8.22 (s, 1H), 7.67 (d, $J = 8.0$ Hz, 2H), 7.25 (d, $J = 8.4$ Hz, 2H),
6.51 (s, 1H), 4.73 (t, J = 5.6 Hz, 2H), 3.89 (t, J = 5.6 Hz, 2H), 3.85 (m, 1H), 2.79 (t, J = 7.6 Hz, 2H), 2.64 (t, J = 7.6 Hz, 2H), 2.46 (t, J = 7.2 Hz, 2H), 2.03 (m, 2H), 1.85-1.50 (m, 12H), 1.44-1.21 (m, 6H), 0.89 (t, J = 7.0 Hz, 3H); \(^1^3\)C NMR (CD\(_2\)OD, 100MHz) \(\delta\) 170.3, 148.5, 147.8, 132.3, 129.5, 129.0, 128.2, 126.3, 109.6, 95.6, 55.9, 52.4, 40.4, 36.5, 33.5, 32.4, 31.9, 29.2, 29.0, 28.6, 25.1, 24.6, 24.3, 23.4, 14.2; IR (CD\(_2\)OD) 3258, 2928, 2855, 1665, 1541, 1502, 1440, 1303, 1189, 1056, 974; UV (\(\lambda_{\text{max}}\) nm) 204, 232; HRMS (ESI+) m/z 540.3662 [(M+H)]\(^+\); calculated mass for C\(_{29}\)H\(_{48}\)N\(_7\)O\(_3\): 540.3657 amu.

2-(benzylamino)-4-(5-(1-(2-(4-pentylbenzamido)ethyl)-1H-1,2,3-triazol-4-yl)pentyl)-1H-imidazol-3-ium chloride (13k). Reacted in 30% TFA to provide the 2-(benzylamino)-4-(5-(1-(2-(4-pentylbenzamido)ethyl)-1H-1,2,3-triazol-4-yl)pentyl)-1H-imidazol-3-ium chloride (45 mg, 99%) as a clear oil. \(^1\)H NMR (CD\(_2\)OD, 400MHz) 8.62 (s, 1H), 7.70 (d, J = 8.4 Hz, 2H), 7.4-7.26 (m, 5H), 7.25 (d, J = 8.4 Hz, 2H), 6.56 (s, 1H), 4.84 (t, J = 5.2 Hz, 2H), 4.50 (s, 2H), 3.94 (t, J = 5.2 Hz, 2H), 2.86 (t, J = 7.4 Hz, 2H), 2.62 (t, J = 7.6 Hz, 2H), 2.48 (t, J = 7.2 Hz, 2H), 1.72 (m, 2H), 1.58 (m, 4H), 1.44-1.31 (m, 6H), 0.88 (t, J = 7.2 Hz, 3H); \(^1^3\)C NMR (CD\(_2\)OD, 100MHz) \(\delta\) 170.3, 148.6, 148.1, 144.3, 137.0, 131.0, 129.7, 129.5, 129.0, 128.8, 128.6, 128.3, 128.2, 109.9, 54.2, 47.3, 40.2, 36.5, 32.4, 32.0, 28.9, 28.5, 25.1, 23.7, 23.4, 14.2; IR (CD\(_2\)OD) 3258, 2929, 2856, 2376, 2312, 1665, 1542, 1502, 1454, 1374, 1308, 750, 700; UV (\(\lambda_{\text{max}}\) nm) 239; HRMS (ESI+) m/z 528.3451 [(M+H)]\(^+\); calculated mass for C\(_{31}\)H\(_{42}\)N\(_7\)O\(_3\): 528.3445 amu.

2-((4-butylbenzyl)amino)-4-(5-(1-(2-(4-pentylbenzamido)ethyl)-1H-1,2,3-triazol-4-yl)pentyl)-1H-imidazol-3-ium chloride (13l). Reacted in 30% TFA to provide the 2-((4-butylbenzyl)amino)-4-(5-(1-(2-(4-pentylbenzamido)ethyl)-1H-1,2,3-triazol-4-yl)pentyl)-1H-imidazol-3-ium chloride (105 mg, 89%) as a clear oil. \(^1\)H NMR (CD\(_2\)OD, 400MHz) 9.01 (brs, 1H), 7.67 (d, J = 7.0 Hz, 2H), 7.26 (d, J = 7.6 Hz, 2H), 7.21 (d, J = 7.6 Hz, 2H), 7.15 (d, J = 7.6 Hz, 2H), 6.53 (s, 1H), 4.84 (brs, 2H), 4.43 (s, 2H), 3.93 (brs, 2H), 2.85 (brs, 2H), 2.58 (m, 4H), 2.46 (brs, 2H), 1.78 (brs, 2H), 1.52 (m, 6H), 1.40 (m, 2H), 1.38-1.20 (m, 6H), 0.88 (m, 6H); \(^1^3\)C NMR (CD\(_2\)OD, 100MHz) \(\delta\) 170.2, 148.4, 148.1, 143.7, 135.2, 132.1, 129.9, 129.7, 129.5, 129.1, 128.3, 128.2, 109.9, 53.7, 47.3, 40.2, 36.5, 36.1, 34.7, 32.4, 31.9, 28.6, 28.0, 25.2, 24.6, 23.4, 23.1, 14.2, 14.1; IR (CD\(_2\)OD) 3117, 2929, 2857, 2360, 2339, 1665, 1540, 1505, 1404, 1301, 669; UV (\(\lambda_{\text{max}}\) nm) 232; HRMS (ESI+) m/z 584.4061 [(M+H)]\(^+\); calculated mass for C\(_{35}\)H\(_{49}\)N\(_7\)O\(_3\): 584.4071 amu.
4-(5-(1-(2-(4-pentylbenzamido)ethyl)-1H-1,2,3-triazol-4-yl)pentyl)-2-((3-trifluoromethyl)benzyl)amino)-1H-imidazol-3-ium chloride (13m). Reacted in 30% TFA to provide the 4-(5-(1-(2-(4-pentylbenzamido)ethyl)-1H-1,2,3-triazol-4-yl)pentyl)-1H-imidazol-3-ium chloride (57 mg, 100%) as a clear oil. \(^1\)H NMR (CD\(_3\)OD, 400MHz) 8.32 (s, 1H), 7.67 (d, \(J = 8.0\) Hz, 2H), 7.69-7.46 (m, 4H), 7.24 (d, \(J = 8.0\) Hz, 2H), 6.57 (s, 1H), 4.77 (t, \(J = 4.8\) Hz, 2H), 4.60 (s, 2H), 3.90 (t, \(J = 5.2\) Hz, 2H), 2.81 (t, \(J = 7.6\) Hz, 2H), 2.62 (t, \(J = 7.6\) Hz, 2H), 2.47 (t, \(J = 7.6\) Hz, 2H), 1.73 (m, 2H), 1.60 (m, 4H), 1.42-1.24 (m, 6H), 0.88 (t, \(J = 7.0\) Hz, 3H); \(^13\)C NMR (CD\(_3\)OD, 100MHz) \(\delta\) 170.5, 148.7, 148.1, 146.9, 139.8, 132.4, 132.1, 131.9 (q, \(J = 31.8\)), 129.7, 129.5, 128.4, 127.2, 126.9 (m), 125.7 (q, \(J = 3.8\)), 125.0 (q, \(J = 4.5\)), 124.2, 110.2, 52.9, 47.0, 40.6, 36.7, 32.5, 31.2, 29.2, 28.8, 25.3, 24.7, 23.6, 14.4; IR (CD\(_3\)OD) 2931, 2861, 1665, 1542, 1500, 1451, 1328, 1122, 1071, 978, 802; UV (\(\lambda_{\text{max}}\) nm) 226; HRMS (ESI+) m/z 596.3319 [(M+H)+]; calculated mass for C\(_{32}\)H\(_{41}\)F\(_3\)N\(_7\)O+: 596.3325 amu.

4-(5-(1-(2-(4-pentylbenzamido)ethyl)-1H-1,2,3-triazol-4-yl)pentyl)-1H-2-((1-phenylethyl)amino)imidazol-3-ium chloride (13n). Reacted in 30% TFA to provide the 4-(5-(1-(2-(4-pentylbenzamido)ethyl)-1H-1,2,3-triazol-4-yl)pentyl)-1H-2-((1-phenylethyl)amino)imidazol-3-ium chloride after flash chromatography (1-10% MeOH(sat. w/ NH\(_3\))/CH\(_2\)Cl\(_2\)) as a clear oil (9 mg, 89%). \(^1\)H NMR (CD\(_3\)OD, 400MHz) 8.57 (s, 1H), 7.68 (d, \(J = 8.0\) Hz, 2H), 7.50-7.20 (m, 7H), 6.49 (s, 1H), 4.84 (t, \(J = 5.6\) Hz, 2H), 4.74 (q, \(J = 6.8\) Hz, 1H), 3.93 (t, \(J = 5.6\) Hz, 2H), 2.85 (t, \(J = 7.6\) Hz, 2H), 2.62 (t, \(J = 7.8\) Hz, 2H), 2.43 (t, \(J = 7.4\) Hz, 2H), 1.69 (m, 2H), 1.52 (m, 7H), 1.48-1.20 (m, 6H), 0.88 (t, \(J = 7.6\) Hz, 3H); \(^13\)C NMR (CD\(_3\)OD, 100MHz) \(\delta\) 170.3, 148.6, 147.3, 145.3, 143.7, 132.0, 129.7, 129.5, 129.1, 128.7, 128.5, 128.2, 126.7, 109.8, 53.2, 40.2, 36.5, 32.3, 31.9, 28.9, 28.6, 28.5, 25.0, 23.7, 23.7, 23.4, 14.2; IR (CD\(_3\)OD) 3257, 2929, 2856, 2372, 2316, 1665, 1541, 1503, 1404, 1306, 669; UV (\(\lambda_{\text{max}}\) nm) 239; HRMS (ESI+) m/z 528.3598 [(M+H)+]; calculated mass for C\(_{32}\)H\(_{44}\)N\(_2\)O+: 542.3602 amu.
2-(cinnamylamino)-4-(5-(1-(2-(4-pentylbenzamido)ethyl)-1H-1,2,3-triazol-4-yl)pentyl)-1H-imidazol-3-ium chloride (13o). Reacted in 10% TFA and purification by flash chromatography (1-10% MeOH/CH₂Cl₂ gradient) provided 2-(cinnamylamino)-4-(5-(1-(2-(4-pentylbenzamido)ethyl)-1H-1,2,3-triazol-4-yl)pentyl)-1H-imidazol-3-ium chloride (16 mg, 38%) as a clear oil. ¹H NMR (CD₃OD, 400MHz) 8.08 (s, 1H), 7.65 (d, J = 8.0 Hz, 2H), 7.56-7.50 (m, 5H), 7.25 (d, J = 8.4 Hz, 2H), 7.02 (s, 1H), 5.48 (m, 1H), 4.69 (t, J = 6.0 Hz, 2H), 4.37 (m, 1H), 4.00-3.80 (m, 4H), 2.77 (t, J = 7.6 Hz, 2H), 2.66 (m, 4H), 1.80-1.55 (m, 6H), 1.45-1.20 (m, 6H), 0.89 (t, J = 7.6 Hz, 3H); ¹³C NMR (CD₃OD, 100MHz) δ 170.3, 150.3, 148.3, 147.9, 146.9, 132.4, 129.5, 129.4, 128.2, 124.5, 110.0, 50.9, 40.7, 36.6, 32.4, 32.0, 30.6, 30.0, 29.7, 29.1, 28.7, 26.4, 25.5, 25.3, 23.4, 14.3; IR (CD₃OD) 3271, 2930, 2857, 1724, 1639, 1589, 1545, 1502, 1455, 1405, 1245, 1171, 1055, 745, 700; UV (λmax nm) 201, 233; HRMS (ESI+) m/z 554.3608 [(M+H)+]; calculated mass for C₃₃H₄₄N₇O+: 554.3602 amu.

4-(5-(1-(2-(4-pentylbenzamido)ethyl)-1H-1,2,3-triazol-4-yl)pentyl)-2-(pyrrolidin-1-yl)-1H-imidazol-3-ium chloride (13p). Reacted in 30% TFA to provide the 2-(octylamino)-4-(5-(1-(2-(4-pentylbenzamido)ethyl)-1H-1,2,3-triazol-4-yl)pentyl)-1H-imidazol-3-ium chloride (15 mg, quantitative yield) as a yellow oil. ¹H NMR (CD₃OD, 400MHz) 7.95 (s, 1H), 7.65 (d, J = 8.4 Hz, 2H), 7.25 (d, J = 8.4 Hz, 2H), 6.55 (s, 1H), 4.66 (t, J = 5.8 Hz, 2H), 3.85 (t, J = 6.0 Hz, 2H), 3.45 (t, J = 6.6 Hz, 4H), 2.73 (t, J = 7.4 Hz, 2H), 2.64 (t, J = 7.4 Hz, 2H), 2.47 (t, J = 7.4 Hz, 2H), 2.08 (m, 4H), 1.75-1.55 (m, 6H), 1.44-1.20 (m, 6H), 0.89 (t, J = 7.2 Hz, 3H); ¹³C NMR (CD₃OD, 100MHz) δ 170.3, 148.3, 147.9, 146.9, 132.4, 129.5, 129.4, 128.2, 124.5, 110.0, 50.9, 40.7, 36.6, 32.4, 32.0, 30.6, 30.0, 29.7, 29.1, 28.7, 26.4, 25.5, 25.3, 23.4, 14.3; IR (CD₃OD) 3135, 2930, 2858, 2791, 1668, 1589, 1545, 1455, 1405, 1245, 1171, 1055, 745, 700; UV (λmax nm) 204; HRMS (ESI+) m/z 492.3445 [(M+H)+]; calculated mass for C₂₈H₄₂N₇O+: 492.3445 amu.
$^1$H NMR for 8

$^{13}$C NMR for 8
$^1$H NMR for 9b

$^{13}$C NMR for 9b
$^1$H NMR for 9e

$^{13}$C NMR for 9e
$^1$H NMR for 9f

$^{13}$C NMR for 9f
$^1$H NMR for 9g

$^{13}$C NMR for 9g
$^1$H NMR for 9j

$^{13}$C NMR for 9j
$^{1} \text{H NMR for 12c}$

$^{13} \text{C NMR for 12c}$
\( ^1H \text{ NMR for 12d} \)

\( ^13C \text{ NMR for 12d} \)
$^{1}H$ NMR for 12e

$^{13}C$ NMR for 12e
**1H NMR for 12g**

![1H NMR spectrum for 12g](image1)

**13C NMR for 12g**

![13C NMR spectrum for 12g](image2)
$^1$H NMR for 12i

$^{13}$C NMR for 12i
$^1$H NMR for 12j

$^{13}$C NMR for 12j
$^1$H NMR for 12k

$^{13}$C NMR for 12k
$^1$H NMR for 13a

$^{13}$C NMR for 13a
$^1$H NMR for 13b

$^{13}$C NMR for 13b
**1H NMR for 13c**

![1H NMR spectrum for 13c](image1)

**13C NMR for 13c**

![13C NMR spectrum for 13c](image2)
**$^1$H NMR for 13d**

**$^{13}$C NMR for 13d**
$^1$H NMR for 13e

$^{13}$C NMR for 13e
$^1$H NMR for 13g

$^{13}$C NMR for 13g
$^1$H NMR for 13h

$^{13}$C NMR for 13h
$^1$H NMR for 13i

$^{13}$C NMR for 13i
$^1$H NMR for 13j

$^{13}$C NMR for 13j
$^1$H NMR for 13n

$^{13}$C NMR for 13n
$^1$H NMR for 13p

$^{13}$C NMR for 13p