Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry

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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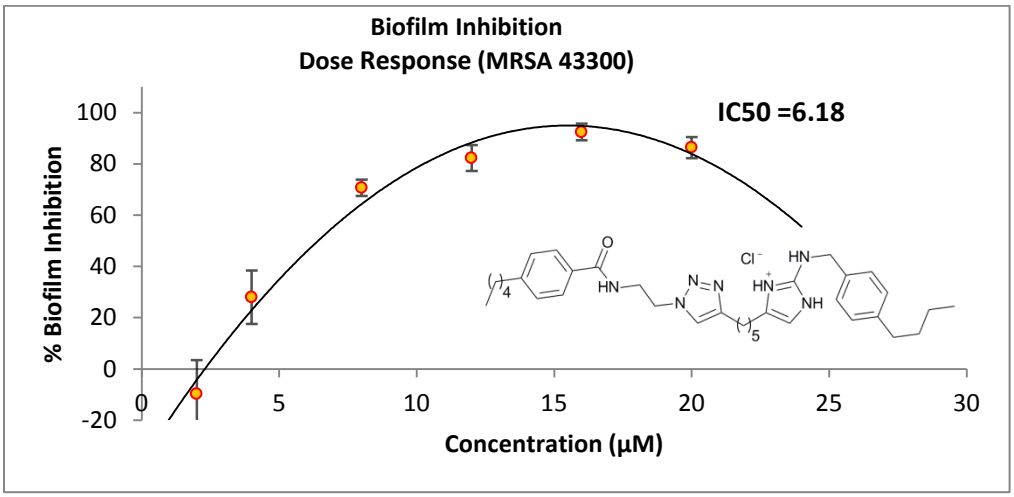
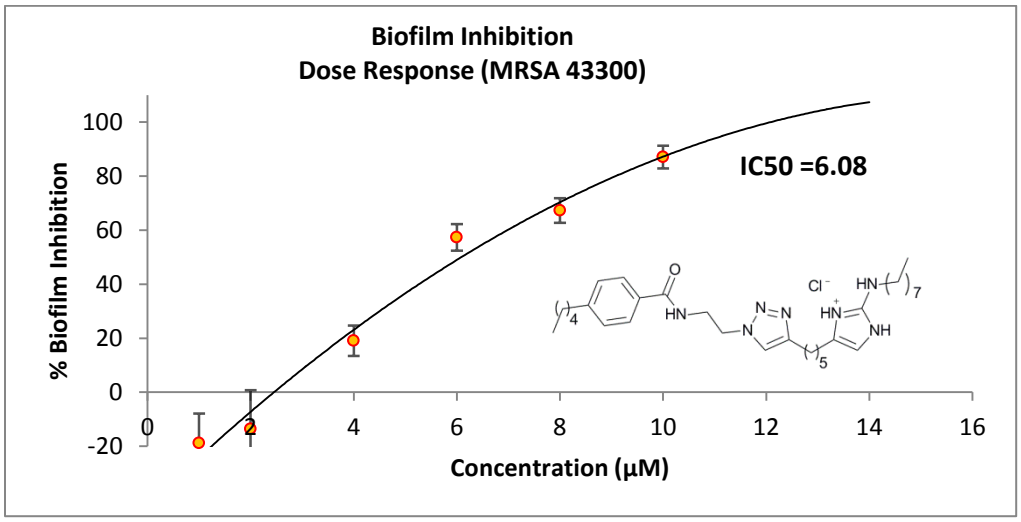
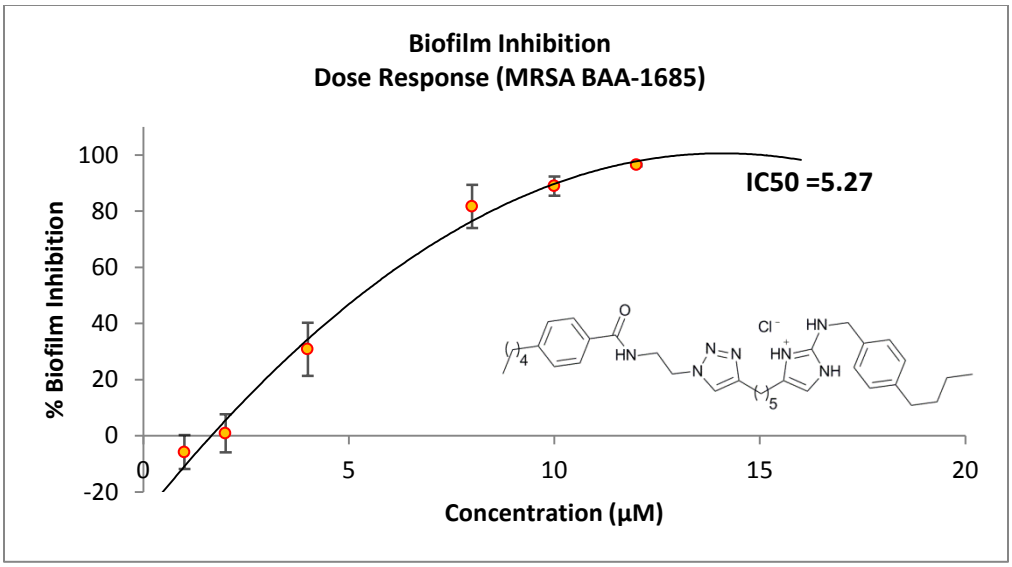
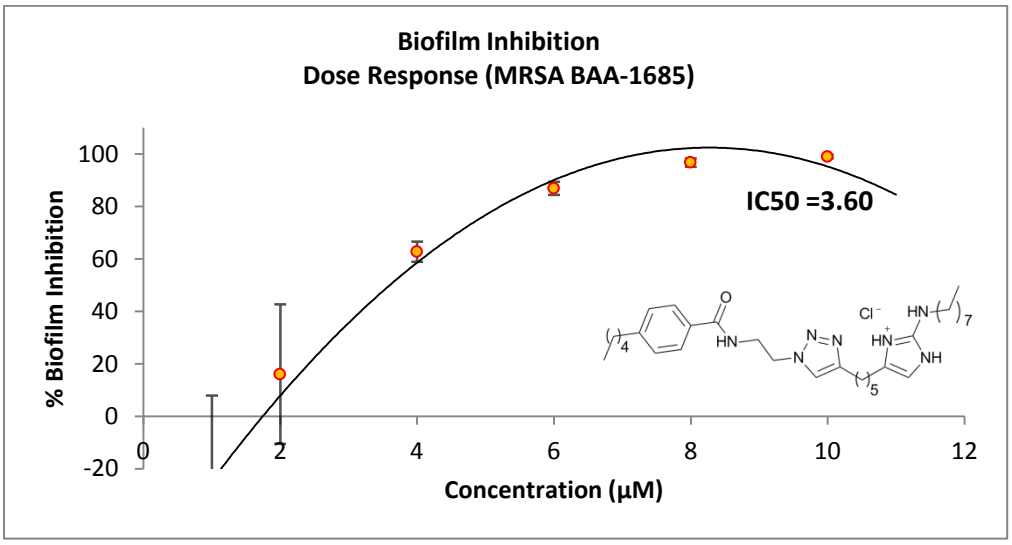
Representative Dose-Response Curves

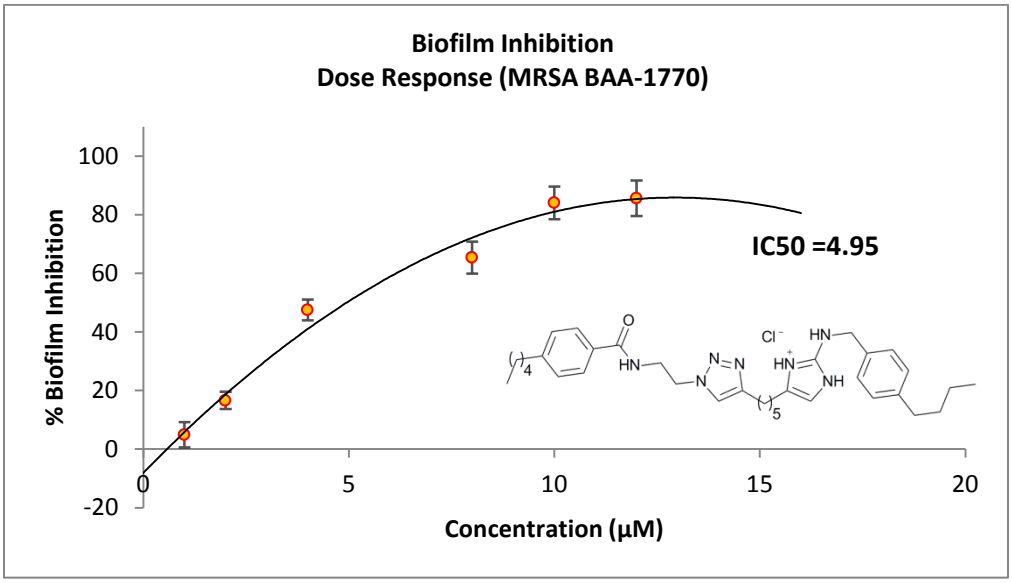
Biofilm inhibition (IC_{50} values) Dose-Response Curves were performed in a minimum of triplicate experiments.

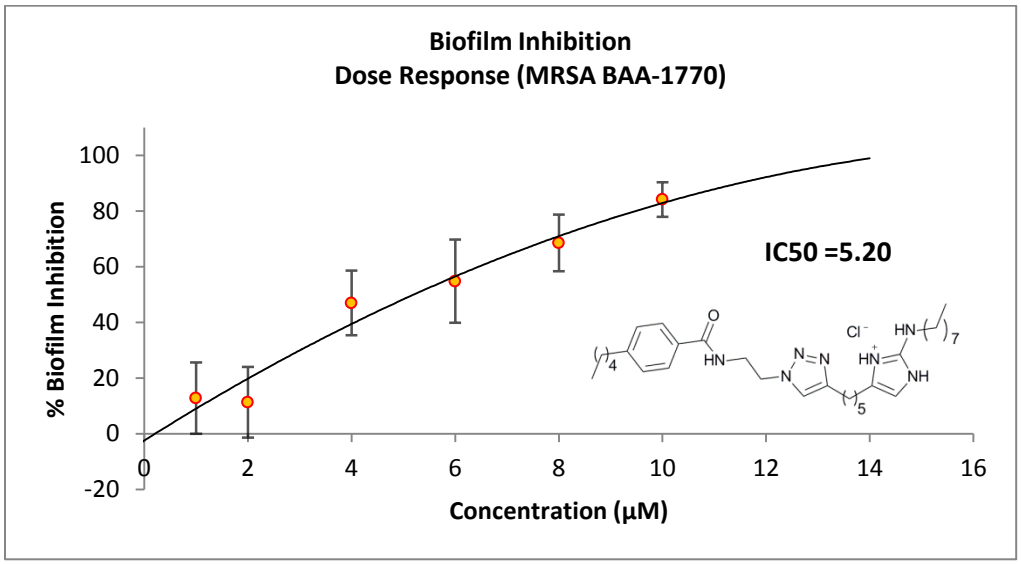






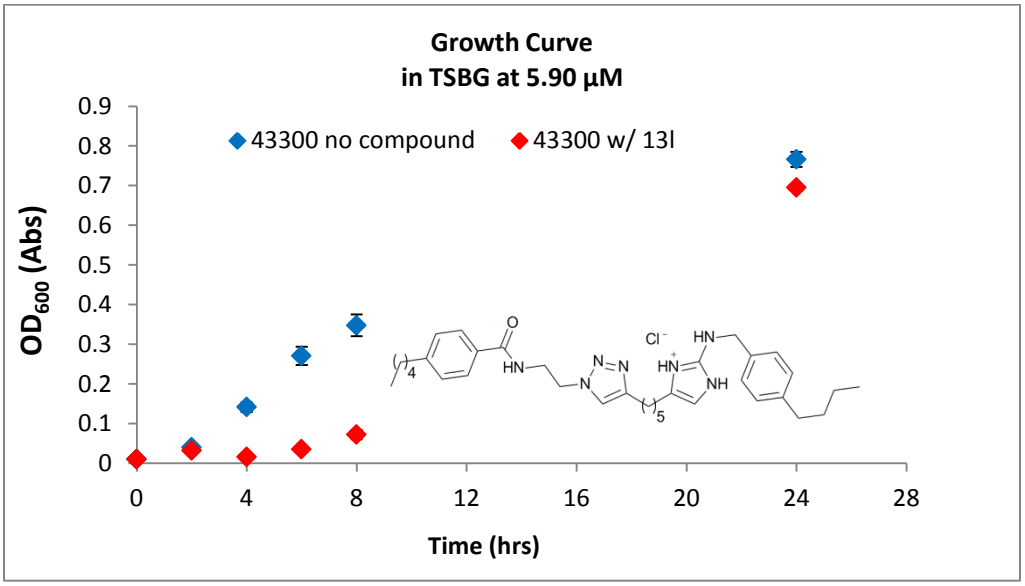


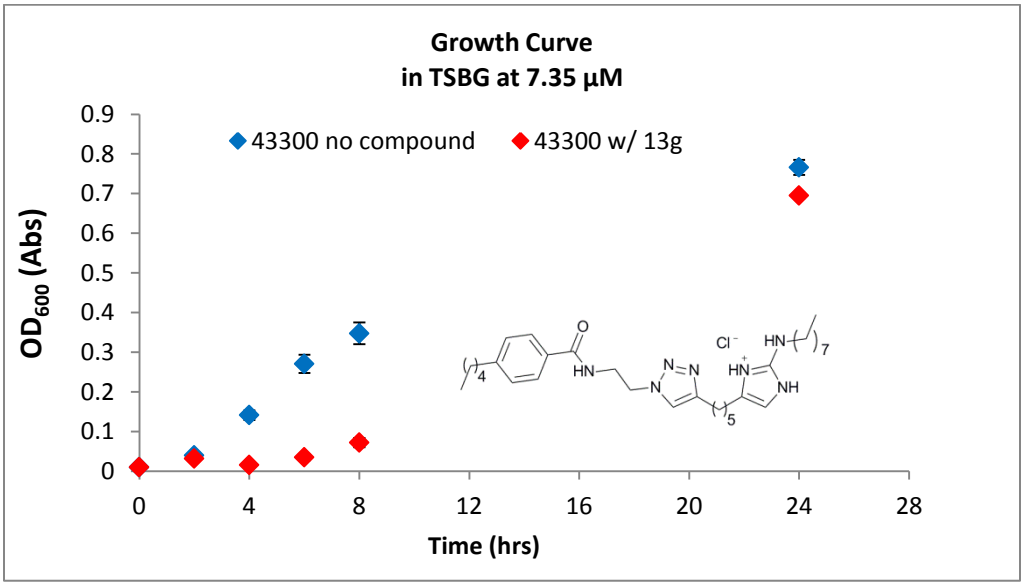


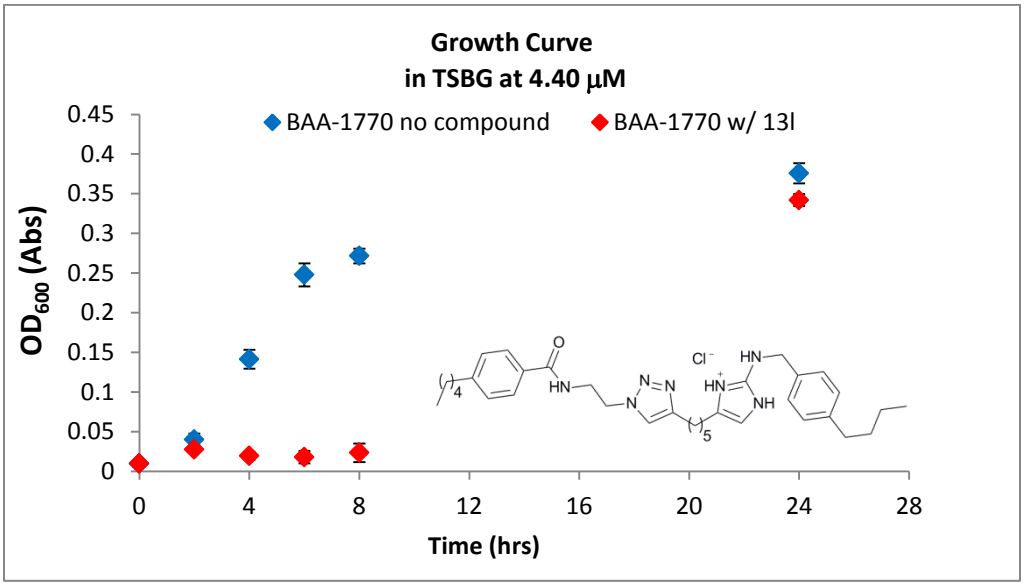


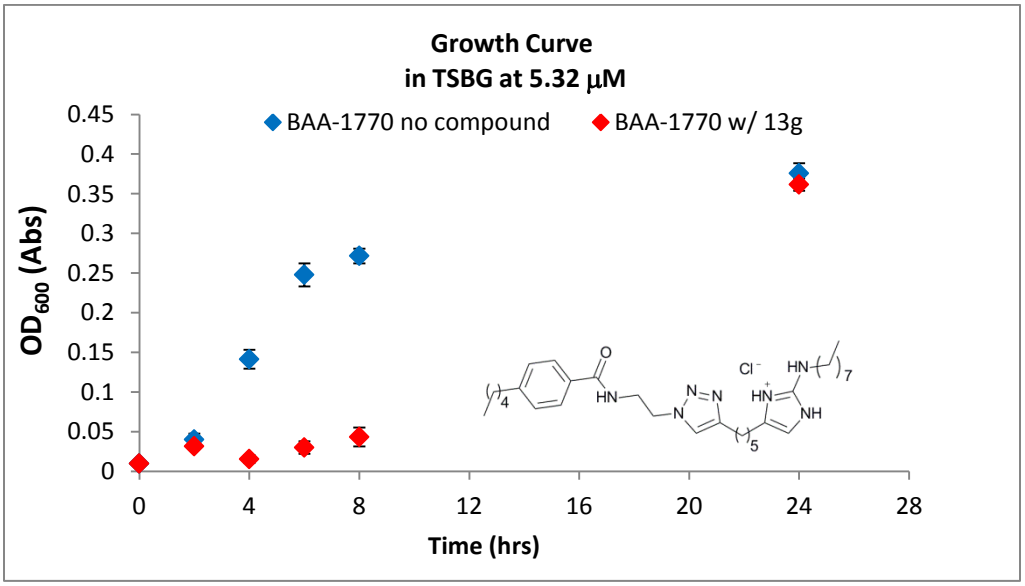
Representative Planktonic Growth Curves

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









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 (δ) 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 (ν_{max} in cm^{-1}). UV absorbance was recorded on a Genesys 10 scanning UV/visible spectrophotometer (λ_{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™ beef extract (# 212303) and 1.5 g Difco™ 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.

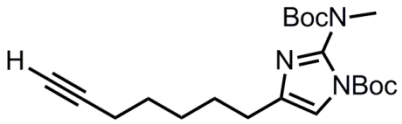
General procedures for alkylation of *tert*-butyl 2-((*tert*-butoxycarbonyl)amino)-4-(hept-6-yn-1-yl)-1*H*-imidazole-1-carboxylate 8.

From alkyl halides: To a 0 °C solution of *tert*-butyl 2-((*tert*-butoxycarbonyl)amino)-4-(hept-6-yn-1-yl)-1*H*-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).

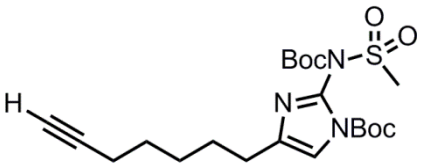
From alkyl alcohols: To a 0 °C solution of *tert*-butyl 2-((*tert*-butoxycarbonyl)amino)-4-(hept-6-yn-1-yl)-1*H*-imidazole-1-carboxylate **8** (~0.3 mmol), triphenylphosphine (2 eq), and alcohol (3 eq) in THF (2.5 mL) was added DIAD or DEAD (1.5 eq) dropwise and allowed cold bath to warm to room temperature. 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

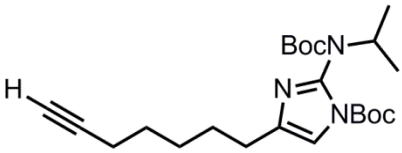
molecule rather than the fraction or ratio of the two rotamers. For ^{13}C NMR, when possible the carbon peak pairs corresponding to the different rotamers have been singled out but no 2D experiments were performed to distinguish their identities.



***tert*-butyl 2-(*N*-(*tert*-butoxycarbonyl)(methyl)amino)-4-(hept-6-yn-1-yl)-1*H*-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)-1*H*-imidazole-1-carboxylate was reacted with iodomethane to provide *tert*-butyl 2-((*tert*-butoxycarbonyl)(methyl)amino)-4-(hept-6-yn-1-yl)-1*H*-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.

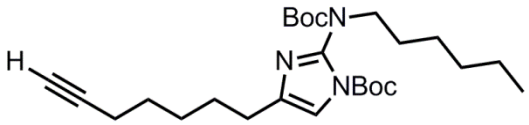


***tert*-butyl 2-(*N*-(*tert*-butoxycarbonyl)methylsulfonamido)-4-(hept-6-yn-1-yl)-1*H*-imidazole-1-carboxylate (9b).** Following the general procedure for alkylation with alkyl halides *tert*-butyl 2-((*tert*-butoxycarbonyl)amino)-4-(hept-6-yn-1-yl)-1*H*-imidazole-1-carboxylate was reacted with mesyl chloride to provide *tert*-butyl 2-(*N*-(*tert*-butoxycarbonyl)methylsulfonamido)-4-(hept-6-yn-1-yl)-1*H*-imidazole-1-carboxylate (65 mg, 24%) as a clear oil. R_f = 0.36 (30% EtOAc/Hexanes); ^1H NMR ($CDCl_3$, 400MHz) δ 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) δ 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 (λ_{max} nm) 251; HRMS (ESI+) m/z 478.1969 [$(M+H)^+$; calculated mass for $C_{21}H_{33}N_3O_6S^+$: 478.1982 amu].

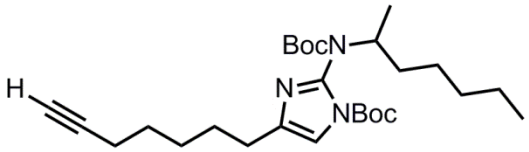


***tert*-butyl 2-(*N*-(*tert*-butoxycarbonyl)(isopropyl)amino)-4-(hept-6-yn-1-yl)-1*H*-imidazole-1-carboxylate (9c).** Following the general procedure for alkylation with alcohols *tert*-butyl 2-((*tert*-butoxycarbonyl)amino)-4-(hept6-yn-1-yl)-1*H*-imidazole-1-carboxylate was reacted with isopropanol to provide *tert*-butyl 2-((*tert*-butoxycarbonyl)(isopropyl)amino)-4-(hept-6-yn-1-yl)-1*H*-imidazole-1-carboxylate (38 mg, 36%) as a clear oil. R_f = 0.55 (20% EtOAc/Hexanes); ^1H NMR ($CDCl_3$, 400MHz) δ 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) δ 153.3, 146.6, 139.6 and 139.6

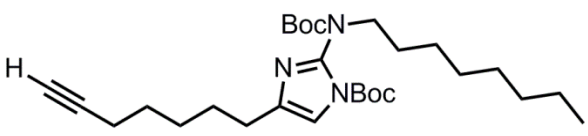
(rotamers), 113.6, 113.4, 84.6, 84.5, 80.4, 68.1, 50.3 and 49.0 (rotamers), 28.2, 28.1, 28.99, 28.95, 27.9, 22.3, 19.0, 18.3; IR ($CDCl_3$) 3311, 2976, 2933, 2859, 2338, 1762, 1717, 1538, 1457, 1369, 1301, 1154, 1109; UV (λ_{max} nm) 250, HRMS (ESI+) m/z 420.2838 [$(M+H)^+$; calculated mass for $C_{23}H_{38}N_3O_4^+$: 420.2857 amu].



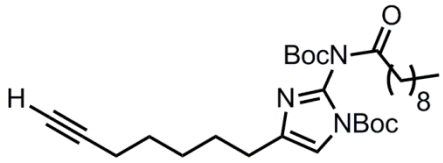
***tert*-butyl 2-(*N*-(*tert*-butoxycarbonyl)(hexyl)amino)-4-(hept-6-yn-1-yl)-1*H*-imidazole-1-carboxylate (9e).** Following the general procedure for alkylation with alkyl halides *tert*-butyl 2-((*tert*-butoxycarbonyl)amino)-4-(hept-6-yn-1-yl)-1*H*-imidazole-1-carboxylate was reacted with iodohexane to provide *tert*-butyl 2-((*tert*-butoxycarbonyl)(hexyl)amino)-4-(hept-6-yn-1-yl)-1*H*-imidazole-1-carboxylate (62 mg, 27%) as a clear oil. R_f = 0.74 (30% EtOAc/Hexanes); ^{1}H NMR ($CDCl_3$, 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); ^{13}C NMR ($CDCl_3$, 100MHz) δ 154.2 and 153.7 (rotamers), 146.7 and 146.6 (rotamers), 142.0 and 141.8 (rotamers), 139.6 and 139.4 (rotamers), 113.2 and 113.2 (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 ($CDCl_3$) 3311, 2933, 2860, 1762, 1719, 1540, 1457, 1392, 1368, 1300, 1152, 1110, 851, 768; UV (λ_{max} nm) 250, HRMS (ESI+) m/z 462.333 [$(M+H)^+$; calculated mass for $C_{26}H_{43}N_3O_4^+$: 462.3326 amu].



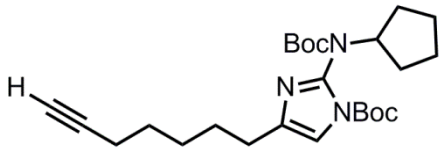
***tert*-butyl 2-(*N*-(*tert*-butoxycarbonyl)(heptan-2-yl)amino)-4-(hept-6-yn-1-yl)-1*H*-imidazole-1-carboxylate (9f).** Following the general procedure for alkylation with alkyl halides *tert*-butyl 2-((*tert*-butoxycarbonyl)amino)-4-(hept-6-yn-1-yl)-1*H*-imidazole-1-carboxylate was reacted with 2-iodoheptane to provide *tert*-butyl 2-((*tert*-butoxycarbonyl)(heptan-2-yl)amino)-4-(hept-6-yn-1-yl)-1*H*-imidazole-1-carboxylate (22 mg, 9%) as a clear oil. R_f = 0.22 (20% EtOAc/Hexanes); ^{1}H NMR ($CDCl_3$, 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); ^{13}C NMR ($CDCl_3$, 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 ($CDCl_3$) 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 $C_{27}H_{46}N_3O_4^+$: 476.3483 amu].



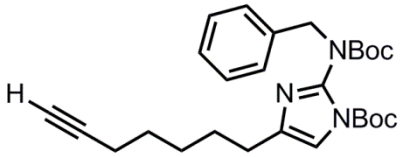
***tert*-butyl 2-(*N*-(*tert*-butoxycarbonyl)(octyl)amino)-4-(hept-6-yn-1-yl)-1*H*-imidazole-1-carboxylate (9g).** Following the general procedure for alkylation with alkyl halides *tert*-butyl 2-((*tert*-butoxycarbonyl)amino)-4-(hept-6-yn-1-yl)-1*H*-imidazole-1-carboxylate was reacted with iodooctane to provide *tert*-butyl 2-((*tert*-butoxycarbonyl)(octyl)amino)-4-(hept-6-yn-1-yl)-1*H*-imidazole-1-carboxylate (40 mg, 28%) as a clear oil. R_f = 0.7 (30% EtOAc/Hexanes); ^{1}H NMR ($CDCl_3$, 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), 1.30-1.14 (m, 10H), 0.8 (t, *J* = 6.3, 3H); ^{13}C NMR ($CDCl_3$, 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, 28.2, 28.0, 27.0, 22.8, 18.6, 14.3; IR ($CDCl_3$) 3312, 2929, 2857, 1762, 1719, 1540, 1457, 1393, 1368, 1300, 1254, 1150, 1111, 850, 768; UV (λ_{max} nm) 251, HRMS (ESI+) m/z 490.3636 [$(M+H)^+$; calculated mass for $C_{28}H_{48}N_3O_4^+$: 490.3639 amu].



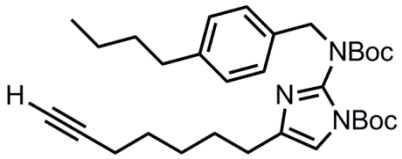
***tert*-butyl 2-(*N*-(*tert*-butoxycarbonyl)decanamido)-4-(hept-6-yn-1-yl)-1*H*-imidazole-1-carboxylate (9i).** Following the general procedure for alkylation with alkyl halides *tert*-butyl 2-((*tert*-butoxycarbonyl)amino)-4-(hept-6-yn-1-yl)-1*H*-imidazole-1-carboxylate was reacted with nonanoyl chloride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



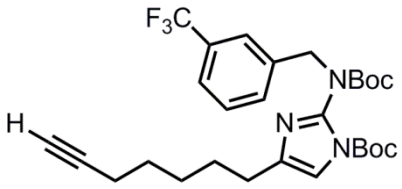
***tert*-butyl 2-(*N*-(*tert*-butoxycarbonyl)(cyclopentyl)amino)-4-(hept-6-yn-1-yl)-1*H*-imidazole-1-carboxylate (9j).** Following the general procedure for alkylation with alkyl halides *tert*-butyl 2-((*tert*-butoxycarbonyl)amino)-4-(hept-6-yn-1-yl)-1*H*-imidazole-1-carboxylate was reacted with bromocyclopentane to provide *tert*-butyl 2-((*tert*-butoxycarbonyl)(cyclopentane)amino)-4-(hept-6-yn-1-yl)-1*H*-imidazole-1-carboxylate (19 mg, 14%) as a clear yellow oil. R_f = 0.68 (30% EtOAc/Hexanes); ^{1}H NMR ($CDCl_3$, 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); ^{13}C NMR ($CDCl_3$, 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 ($CDCl_3$) 3311, 2975, 2935, 2866, 2360, 2339, 1761, 1716, 1537, 1456, 1393, 1370, 1334, 1299, 1258, 1150, 1044, 1017, 977, 850, 768; UV (λ_{max} nm) 241, HRMS (ESI+) m/z 446.3021 [$(M+H)^+$; calculated mass for $C_{25}H_{40}N_3O_4^+$: 446.3013 amu].



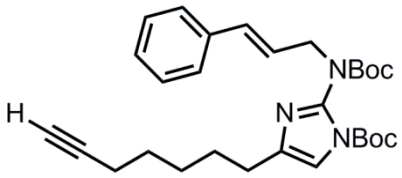
***tert*-butyl 2-*N*-(benzyl(*tert*-butoxycarbonyl)amino)-4-(hept-6-yn-1-yl)-1*H*-imidazole-1-carboxylate (9k).** Following the general procedure for alkylation with alkyl halides *tert*-butyl 2-((*tert*-butoxycarbonyl)amino)-4-(hept-6-yn-1-yl)-1*H*-imidazole-1-carboxylate was reacted with benzyl bromide to provide *tert*-butyl 2-(benzyl(*tert*-butoxycarbonyl)amino)-4-(hept-6-yn-1-yl)-1*H*-imidazole-1-carboxylate (50 mg, 37%) as a clear oil. R_f = 0.6 (30% EtOAc/Hexanes); ^{1}H 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); ^{13}C 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, 28.2, 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 $C_{27}H_{38}N_3O_4^+$: 468.2857 amu].



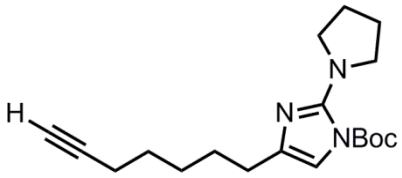
***tert*-butyl 2-(*N*-(*tert*-butoxycarbonyl)(4-butylbenzyl)amino)-4-(hept-6-yn-1-yl)-1*H*-imidazole-1-carboxylate (9l).** Following the general procedure for alkylation with alkyl halides *tert*-butyl 2-((*tert*-butoxycarbonyl)amino)-4-(hept-6-yn-1-yl)-1*H*-imidazole-1-carboxylate was reacted with 4-butylbenzyl bromide to provide *tert*-butyl 2-((*tert*-butoxycarbonyl)(3-(trifluoromethyl)benzyl)amino)-4-(hept-6-yn-1-yl)-1*H*-imidazole-1-carboxylate (158 mg, 70%) as a clear oil. R_f = 0.4 (20% EtOAc/Hexanes); ^{1}H 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); ^{13}C 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, 28.2, 28.0, 22.5, 18.6, 14.1; IR ($CDCl_3$) 3310, 2933, 2859, 1763, 1717, 1586, 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 $C_{31}H_{45}N_3O_4^+$: 524.3483 amu].



***tert*-butyl 2-(*N*-(*tert*-butoxycarbonyl)(3-(trifluoromethyl)benzyl)amino)-4-(hept-6-yn-1-yl)-1*H*-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)-1*H*-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)-1*H*-imidazole-1-carboxylate (177 mg, 54%) as a clear oil. R_f = 0.37 (20% EtOAc/Hexanes); ^{1}H NMR ($CDCl_3$, 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), 2.13 (dt, *J* = 6.9, 1.9 Hz, 2H), 1.88 (t, *J* = 2.2 Hz, 1H), 1.65-1.50 (m, 6H), 1.48 (s, 9H), 1.37 (s, 9H, rotamer), 1.34 (s, 9H); ^{13}C NMR ($CDCl_3$, 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), 28.4, 28.3, 28.2, 28.1, 28.0, 27.9, 18.5; IR ($CDCl_3$) 3311, 2980, 2936, 2862, 2360, 2333, 1760, 1722, 1538, 1454, 1394, 1370, 1328, 1301, 1251, 1165, 1127, 1075, 1030, 853, 768, 659; UV (λ_{max} nm) 256; HRMS (ESI+) m/z 535.256 [$(M+Na)^+$; calculated mass for $C_{28}H_{36}N_3NaO_4^+$: 535.255 amu].



***tert*-butyl 2-*N*-((*tert*-butoxycarbonyl)(cinnamyl)amino)-4-(hept-6-yn-1-yl)-1*H*-imidazole-1-carboxylate (9o).** Following the general procedure for alkylation with alcohols *tert*-butyl 2-((*tert*-butoxycarbonyl)amino)-4-(hept-6-yn-1-yl)-1*H*-imidazole-1-carboxylate was reacted with cinnamyl alcohol to provide *tert*-butyl 2-((*tert*-butoxycarbonyl)(cinnamyl)amino)-4-(hept-6-yn-1-yl)-1*H*-imidazole-1-carboxylate (48 mg, 39%) as a clear oil. R_f = 0.6 (30% EtOAc/Hexanes); ^{1}H NMR ($CDCl_3$, 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), 1.50 (s, 9H, rotamer), 1.37 (s, 9H); ^{13}C NMR ($CDCl_3$, 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 ($CDCl_3$) 3306, 2979, 2935, 2858, 1759, 1719, 1539, 1455, 1392, 1369, 1303, 1248, 1149, 966, 851, 767, 693; UV (λ_{max} nm) 250, HRMS (ESI+) m/z 516.2809 [$(M+H)^+$; calculated mass for $C_{29}H_{39}N_3O_4^+$: 516.2833 amu].

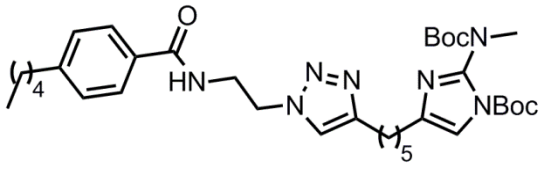


***tert*-butyl 4-(hept-6-yn-1-yl)-2-(pyrrolidin-1-yl)-1*H*-imidazole-1-carboxylate (17).** To a 0 °C solution of N,N'-Di-Boc-1*H*-pyrolidine-1-carboxamidine (100 mg, 0.32 mmol) in DMF (5 mL) was added a 60% dispersion of sodium hydride (11 mg, 0.28 mmol). After complete dissolution 1-bromonon-8-yl-one (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 oil was then dissolved in 30% TFA in CH_2Cl_2 and stirred at room temperature for 16 hours. Concentration provided the unprotected heterocycle, which is dissolved in DMF (5 mL), Et_3N (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 ($CDCl_3$, 400MHz) δ 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). ^{13}C NMR ($CDCl_3$, 100MHz) δ 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 ($CDCl_3$) 3301, 2974, 2934, 2860, 1752, 1555, 1459, 1392, 1370, 1323, 1254, 1156, 1114, 1060, 962, 852, 772, 630; UV (λ_{max} nm) 275, HRMS (ESI+) m/*z* 332.2324 [$(M+H)^+$; calculated mass for $C_{19}H_{30}N_3O_2^+$: 332.2333 amu].

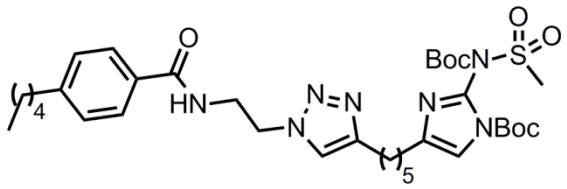
General procedure for the azide-alkyne Huisgen cycloaddition between 9 and *N*-(2-azidoethyl)-4-pentylbenzamide.

To a solution of alkyne # in ^{t}BuOH (2 mL), water (2 mL), and CH_2Cl_2 (1 mL) was added *N*-(2-azidoethyl)-4-pentylbenzamide (1.1 eq), $CuSO_4$ (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 CH_2Cl_2. The combined organic layers were then dried ($MgSO_4$), 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 CH_2Cl_2). In cases were copper color was still present in final material (typical of MeOH/CH_2Cl_2 purification) the final product was dissolved in CH_2Cl_2 and washed with a 0.01 M EDTA solution until organic layer was free of blue-green color.



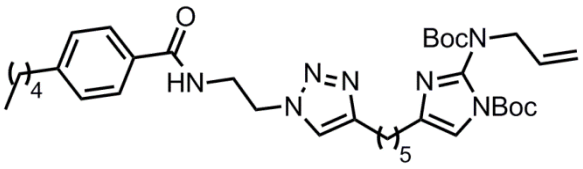
tert-butyl 2-((tert-butoxycarbonyl)(methyl)amino)-4-(5-(1-(2-(4-pentylbenzamido)ethyl)-1H-1,2,3-triazol-4-yl)pentyl)-1H-imidazole-1-carboxylate (12a). Following the general procedure for the cycloaddition *tert*-butyl 2-((*tert*-butoxycarbonyl)(methyl)amino)-4-(hept-6-yn-1-yl)-1*H*-imidazole-1-carboxylate 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 ($CDCl_3$, 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); ^{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, 81.7and 81.2 (rotamers), 49.5, 40.1, 36.0, 35.6, 31.6, 31.1, 29.3, 28.9, 28.5, 28.5, 28.3, 28.2, 28.0, 25.7, 22.7, 14.2; IR ($CDCl_3$) 3333, 2931, 2858, 1759,

1720, 1650, 1542, 1504, 1432, 1369, 1301, 1155, 1092, 853, 768; UV (λ_{max} nm) 239; HRMS (ESI+) m/z 652.4172 [$(M+H)^+$; calculated mass for $C_{35}H_{54}N_7O_5^+$: 652.4181 amu].



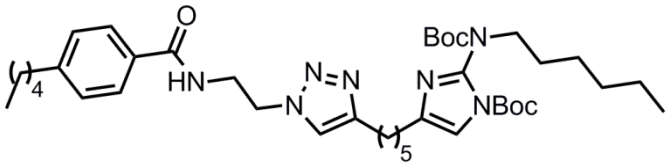
tert-butyl 2-((tert-butoxycarbonyl)decanamido)-4-(5-(1-(2-(4-pentylbenzamido)ethyl)-1H-1,2,3-triazol-4-yl)pentyl)-1H-imidazole-1-carboxylate (12b). Following the general procedure for the cycloaddition *tert*-butyl 2-((*tert*-butoxycarbonyl)methylsulfonamido)-4-(hept-6-yn-1-yl)-1*H*-imidazole-1-carboxylate 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) δ 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, 28.1, 28.0, 25.6, 22.7, 14.2; IR ($CDCl_3$) 3316, 2932, 2858, 1749, 1651, 1539, 1505, 1460, 1396, 1371, 1295, 1255, 1146, 1074, 968, 834, 769; UV (λ_{max} nm) 239; HRMS (ESI+) m/z 716.3802 [$(M+H)^+$; calculated mass for $C_{44}H_{70}N_7O_5^+$: 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)-1*H*-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) δ 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 (λ_{max} nm) 241; HRMS (ESI+) m/z 680.4487 [$(M+H)^+$; calculated mass for $C_{37}H_{58}N_7O_5^+$: 680.4494 amu].

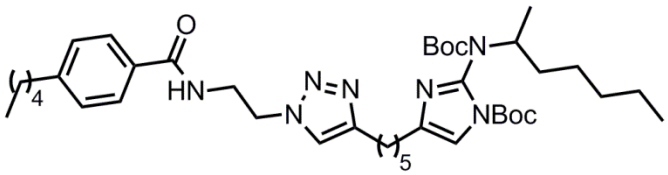


tert-butyl 2-((tert-butoxycarbonyl)(isopropyl)amino)-4-(5-(1-(2-(4-pentylbenzamido)ethyl)-1H-1,2,3-triazol-4-yl)pentyl)-1H-imidazole-1-carboxylate (12d). Following the general procedure for the

cycloaddition *tert*-butyl 2-(allyl(*tert*-butoxycarbonyl)amino)-4-(hept-6-yn-1-yl)-1*H*-imidazole-1-carboxylate was reacted with *N*-(2-azidoethyl)-4-pentylbenzamide to provide tert-butyl 2-(allyl(tert-butoxycarbonyl)amino)-4-(5-(1-(2-(4-pentylbenzamido)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) δ 168.1, 153.7, 147.4, 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, 28.1, 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 (λ_{max} nm) 241; HRMS (ESI+) m/z 678.4317 [$(M+H)^+$; calculated mass for $C_{37}H_{56}N_7O_5^+$: 678.4337 amu].

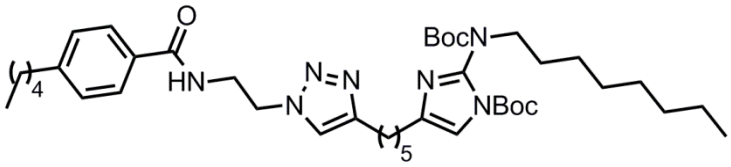


tert-butyl 2-((tert-butoxycarbonyl)(hexyl)amino)-4-(5-(1-(2-(4-pentylbenzamido)ethyl)-1H-1,2,3-triazol-4-yl)pentyl)-1H-imidazole-1-carboxylate (12e). Following the general procedure for the cycloaddition *tert*-butyl 2-((*tert*-butoxycarbonyl)(hexyl)amino)-4-(hept-6-yn-1-yl)-1*H*-imidazole-1-carboxylate was reacted with *N*-(2-azidoethyl)-4-pentylbenzamide to provide tert-butyl 2-((tert-butoxycarbonyl)(hexyl)amino)-4-(5-(1-(2-(4-pentylbenzamido)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) δ 168.1, 153.9, 148.5, 147.4, 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, 28.5, 28.4, 28.2, 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 (λ_{max} nm) 239; HRMS (ESI+) m/z 722.4964 [$(M+H)^+$; calculated mass for $C_{40}H_{64}N_7O_5^+$: 722.4963 amu].

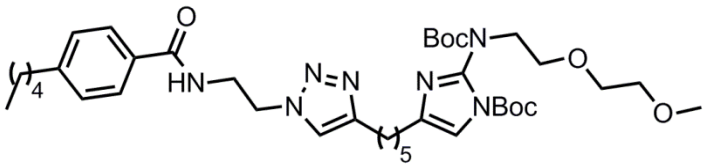


tert-butyl 2-((tert-butoxycarbonyl)(heptan-2-yl)amino)-4-(5-(1-(2-(4-pentylbenzamido)ethyl)-1H-1,2,3-triazol-4-yl)pentyl)-1H-imidazole-1-carboxylate (12f). Following the general procedure for the cycloaddition *tert*-butyl 2-((*tert*-butoxycarbonyl)(heptan-2-yl)amino)-4-(hept-6-yn-1-yl)-1*H*-imidazole-1-carboxylate was reacted with *N*-(2-azidoethyl)-4-pentylbenzamide 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, 81.7and 81.2 (rotamers), 49.5, 40.1, 36.0, 35.6, 31.6, 31.1, 29.3, 28.9, 28.5, 28.5, 28.3, 28.2, 28.0, 25.7, 22.7, 14.2; IR ($CDCl_3$) 3336, 2931, 2858, 1761, 1716, 1655, 1539, 1503, 1457, 1369, 1301, 1154, 1110, 851, 768; UV (λ_{max} nm) 239; HRMS (ESI+) m/*z* 736.5120 [$(M+H)^+$; calculated mass for $C_{41}H_{66}N_7O_5^+$: 736.5120 amu].

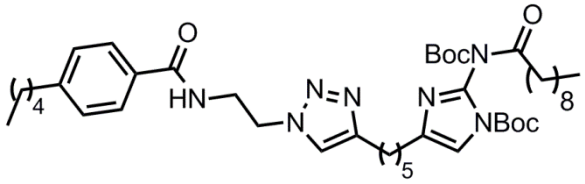


tert-butyl 2-((tert-butoxycarbonyl)(octyl)amino)-4-(5-(1-(2-(4-pentylbenzamido)ethyl)-1H-1,2,3-triazol-4-yl)pentyl)-1H-imidazole-1-carboxylate (12g). Following the general procedure for the cycloaddition *tert*-butyl 2-((*tert*-butoxycarbonyl)(octyl)amino)-4-(hept-6-yn-1-yl)-1*H*-imidazole-1-carboxylate 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) 7.67 (d, *J* = 8.4 Hz, 2H), 7.30 (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, 28.5, 28.4, 28.2, 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, 1368, 1298, 1150, 1111, 850, 767; UV (λ_{max} nm) 239; HRMS (ESI+) m/*z* 750.5269 [$(M+H)^+$; calculated mass for $C_{42}H_{67}N_7O_5^+$: 750.5276 amu].

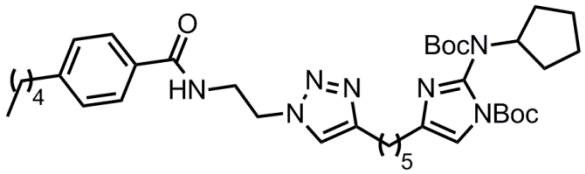


tert-butyl 2-((tert-butoxycarbonyl)(2-(2-methoxyethoxy)ethyl)amino)-4-(5-(1-(2-(4-pentylbenzamido)ethyl)-1H-1,2,3-triazol-4-yl)pentyl)-1H-imidazole-1-carboxylate (12h). Following the general procedure for the cycloaddition *tert*-butyl 2-((*tert*-butoxycarbonyl)(2-(2-methoxyethoxy)ethyl)amino)-4-(hept-6-yn-1-yl)-1*H*-imidazole-1-carboxylate 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,

J = 8.4 Hz, 2H), 7.31 (s, 1H), 7.19 (d, *J* = 8.4 Hz, 2H), 7.00 (s, 1H), 6.94 (s, 1H), 4.55 (t, *J* = 5.2 Hz, 2H), 3.93 (m, 2H), 3.60-3.90 (m, 4H), 3.50-3.40 (m, 2H), 3.30-3.39 (m, 2H), 3.28 (s, 3H), 2.68 (t, *J* = 7.4 Hz, 2H), 2.61 (t, *J* = 7.6 Hz, 2H), 2.44 (t, *J* = 7.6 Hz, 2H), 1.70-1.52 (m, 6H), 1.57 (s, 9H), 1.45 (s, 9H, rotamer), 1.40-1.20 (m, 6H), 1.33 (s, 9H), 0.87 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100MHz) δ 168.2, 168.1, 153.9, 148.5, 148.3, 147.4, 146.8, 142.2, 139.7, 131.4, 128.8, 127.3, 122.1, 122.0, 113.7 and 113.4 (rotamers), 84.9, 81.7, 81.2, 71.9, 70.4, 69.2, 49.5 and 49.0 (rotamers), 48.2, 40.0, 36.0, 31.6, 31.1, 29.4, 29.3, 29.0, 28.9, 28.8, 28.7, 28.6, 28.5, 28.4, 28.2, 28.1, 25.7, 14.2; IR ($CDCl_3$) 3330, 2930, 2858, 1759, 1719, 1654, 1540, 1503, 1456, 1393, 1369, 1300, 1254, 1152, 1099, 852, 765; UV (λ_{max} nm) 238; HRMS (ESI+) m/z 740.4703 [$(M+H)^+$; calculated mass for $C_{39}H_{62}N_7O_7^+$: 740.4705 amu].

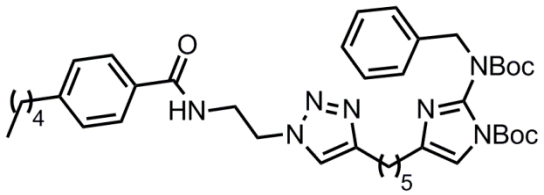


tert-butyl 2-((tert-butoxycarbonyl)decanamido)-4-(5-(1-(2-(4-pentylbenzamido)ethyl)-1H-1,2,3-triazol-4-yl)pentyl)-1H-imidazole-1-carboxylate (12i). Following the general procedure for the cycloaddition *tert*-butyl 2-((*tert*-butoxycarbonyl)decanamido)-4-(hept-6-yn-1-yl)-1*H*-imidazole-1-carboxylate 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. ^{1}H NMR ($CDCl_3$, 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); ^{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, 28.5, 28.4, 28.2, 28.2, 28.0, 27.0, 25.7, 22.8, 22.7, 21.5, 17.7, 14.2; IR ($CDCl_3$) 3333, 2928, 2856, 1754, 1659, 1538, 1504, 1458, 1392, 1371, 1293, 1151, 1086, 852, 769; UV (λ_{max} nm) 239; HRMS (ESI+) m/z 792.5309 [$(M+H)^+$; calculated mass for $C_{44}H_{70}N_7O_5^+$: 792.5382 amu].

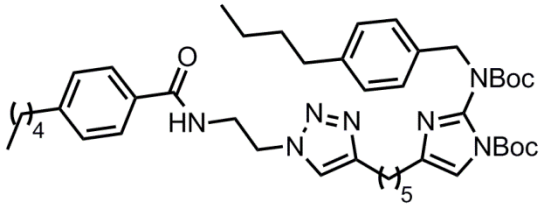


tert-butyl 2-((tert-butoxycarbonyl)(cyclopentyl)amino)-4-(5-(1-(2-(4-pentylbenzamido)ethyl)-1H-1,2,3-triazol-4-yl)pentyl)-1H-imidazole-1-carboxylate (12j). Following the general procedure for the cycloaddition *tert*-butyl 2-((*tert*-butoxycarbonyl)(cyclopentyl)amino)-4-(hept-6-yn-1-yl)-1*H*-imidazole-1-carboxylate 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. ^{1}H NMR ($CDCl_3$, 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); ^{13}C NMR ($CDCl_3$, 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 ($CDCl_3$) 3330, 2931, 2858, 1760, 1719, 1650, 1540, 1501, 1457, 1369, 1299, 1153, 1097, 850, 767; UV (λ_{max} nm) 241; HRMS (ESI+) m/z 706.4653 [$(M+H)^+$; calculated mass for $C_{39}H_{59}N_7O_5^+$: 706.4650 amu].

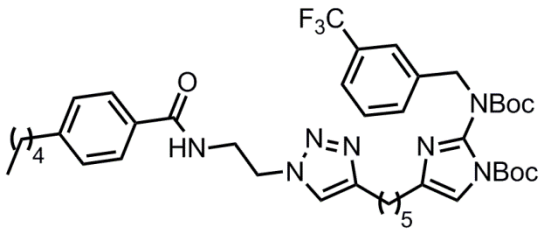


tert-butyl 2-(benzyl(tert-butoxycarbonyl)amino)-4-(5-(1-(2-(4-pentylbenzamido)ethyl)-1H-1,2,3-triazol-4-yl)pentyl)-1H-imidazole-1-carboxylate (12k). Following the general procedure for the cycloaddition *tert*-butyl 2-(benzyl(*tert*-butoxycarbonyl)amino)-4-(hept-6-yn-1-yl)-1*H*-imidazole-1-carboxylate 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. ^{1}H NMR ($CDCl_3$, 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); ^{13}C NMR ($CDCl_3$, 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 ($CDCl_3$) 3328, 2930, 2858, 1759, 1719, 1656, 1537, 1500, 1455, 1369, 1300, 1249, 1149, 1044, 854; UV (λ_{max} nm) 239; HRMS (ESI+) m/z 728.4486 [$(M+H)^+$; calculated mass for $C_{41}H_{57}N_7O_5^+$: 728.4494 amu].

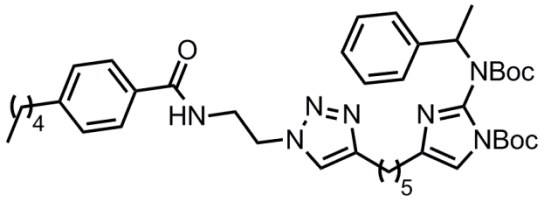


tert-butyl 2-((tert-butoxycarbonyl)(4-butylbenzyl)amino)-4-(5-(1-(2-(4-pentylbenzamido)ethyl)-1H-1,2,3-triazol-4-yl)pentyl)-1H-imidazole-1-carboxylate (12l). Following the general procedure for the cycloaddition *tert*-butyl 2-((*tert*-butoxycarbonyl)(4-butylbenzyl)amino)-4-(hept-6-yn-1-yl)-1*H*-imidazole-1-carboxylate 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. ^{1}H NMR ($CDCl_3$, 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),

1.44 (s, 9H), 1.40 (s, 9H, rotamer), 1.40-1.20 (m, 10H), 1.32 (s, 9H), 0.84 (m, 6H); ^{13}C NMR ($CDCl_3$, 100MHz) δ 168.1, 154.3 and 153.9 (rotamers), 147.3, 146.4, 142.2, 142.0, 139.7, 134.8 and 131.4 (rotamers), 129.1, 128.8, 128.6, 128.4, 127.4, 122.1, 113.4, 85.0, 82.0 and 81.3 (rotamers), 53.8 and 52.7 (rotamers), 49.6, 40.1, 36.0, 35.5, 33.8, 31.6, 31.1, 29.9, 29.3, 28.9, 28.4, 28.2, 28.0, 25.7, 22.7, 22.5, 14.2, 14.2; IR ($CDCl_3$) 2930, 2857, 1760, 1718, 1655, 1539, 1504, 1456, 1369, 1301, 1252, 1150, 1045, 853, 767; UV (λ_{max} nm) 239; HRMS (ESI+) m/z 784.5117 [$(M+H)^+$; calculated mass for $C_{45}H_{65}N_7O_5^+$: 784.5120 amu].

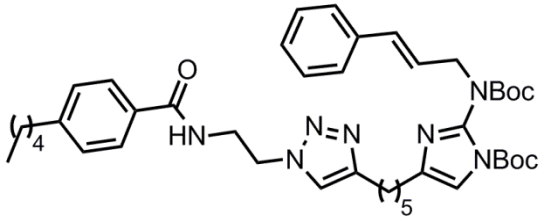


tert-butyl 2-((*tert*-butoxycarbonyl)(3-(trifluoromethyl)benzyl)amino)-4-(5-(1-(2-(4-pentylbenzamido)ethyl)-1H-1,2,3-triazol-4-yl)pentyl)-1H-imidazole-1-carboxylate (12m). Following the general procedure for the cycloaddition *tert*-butyl 2-((*tert*-butoxycarbonyl)(3-(trifluoromethyl)benzyl)amino)-4-(hept-6-yn-1-yl)-1*H*-imidazole-1-carboxylate was reacted with *N*-(2-azidoethyl)-4-pentylbenzamide to provide 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 (90 mg, 86%) as a clear oil. R_f = 0.2 (80% EtOAc/Hexanes); ^{1}H NMR ($CDCl_3$, 400MHz) 7.66 (d, *J* = 8.4 Hz, 2H), 7.60-7.31 (m, 4H), 7.29 (s, 1H), 7.20 (d, *J* = 8.0 Hz, 2H), 6.92 (brs, 1H), 6.86 (s, 1H), 4.95-4.79 (m, 2H, both rotamers), 4.54 (t, *J* = 5.4 Hz, 2H), 3.94 (m, 2H), 2.68 (t, *J* = 7.8 Hz, 2H), 2.61 (t, *J* = 7.6 Hz, 2H), 2.41 (t, *J* = 7.4 Hz, 2H), 1.70-1.52 (m, 6H), 1.50 (s, 9H), 1.40 (s, 9H, rotamer), 1.43-1.20 (m, 6H), 1.36 (s, 9H), 0.87 (t, *J* = 6.6 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100MHz) δ 168.1, 153.9, 148.5, 147.5, 146.4, 141.8, 139.9, 138.2, 132.5, 131.9, 131.4, 130.7 (q, *J* = 32 Hz), 128.8, 127.3, 125.7 and 125.5 (rotamers), 124.4, 122.0, 113.7 and 113.4 (rotamers), 83.0, 82.8 and 82.5 (rotamers), 53.6 and 52.4 (rotamers), 49.6, 40.1, 36.0, 32.1, 31.6, 31.1, 30.1, 29.8, 29.4, 29.0, 28.5, 28.3, 28.1, 28.0, 25.7, 22.7, 14.2; IR ($CDCl_3$) 3330, 2932, 2858, 1760, 1720, 1650, 1539, 1503, 1454, 1328, 1299, 1164, 1074, 1045, 853, 768, 703; UV (λ_{max} nm) 241; HRMS (ESI+) m/z 796.4368 [$(M+H)^+$; calculated mass for $C_{42}H_{57}F_3N_7O_5^+$: 796.4368 amu].

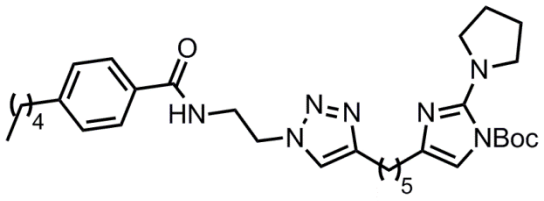


tert-butyl 2-((tert-butoxycarbonyl)(1-phenylethyl)amino)-4-(5-(1-(2-(4-pentylbenzamido)ethyl)-1H-1,2,3-triazol-4-yl)pentyl)-1H-imidazole-1-carboxylate (12n). Following the general procedure for the cycloaddition *tert*-butyl 2-((*tert*-butoxycarbonyl)(1-phenylethyl)amino)-4-(hept-6-yn-1-yl)-1*H*-imidazole-1-carboxylate was reacted with *N*-(2-azidoethyl)-4-pentylbenzamide to provide 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 (60 mg, 78%) as a clear oil. R_f = 0.7 (80% EtOAc/Hexanes); ^{1}H

NMR ($CDCl_3$, 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); ^{13}C NMR ($CDCl_3$, 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, 28.4, 28.2, 28.1, 28.0, 25.7, 22.7, 20.1, 14.2; IR ($CDCl_3$) 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 $C_{42}H_{59}N_7O_5^+$: 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)-1*H*-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. R_f = 0.52 (100% EtOAc); ^{1}H NMR ($CDCl_3$, 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); ^{13}C NMR ($CDCl_3$, 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, 28.4, 28.2, 28.1, 27.9, 25.7, 22.7, 14.2; IR ($CDCl_3$) 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 $C_{41}H_{57}N_7O_5^+$: 754.4650 amu].

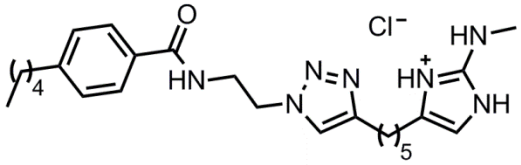


tert-butyl 4-(5-(1-(2-(4-pentylbenzamido)ethyl)-1*H*-1,2,3-triazol-4-yl)pentyl)-2-(pyrrolidin-1-yl)-1*H*-imidazole-1-carboxylate (12p). Following the general procedure for the cycloaddition *tert*-butyl 4-(hept-6-yn-1-yl)-2-(pyrrolin-1-yl)-1*H*-imidazole-1-carboxylate was reacted with *N*-(2-azidoethyl)-4-pentylbenzamide to provide tert-butyl 4-(5-(1-(2-(4-pentylbenzamido)ethyl)-1*H*-1,2,3-triazol-4-yl)pentyl)-2-(pyrrolidin-1-yl)-1*H*-imidazole-1-carboxylate (18 mg, 43%) as a yellow oil. ^{1}H NMR ($CDCl_3$, 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),

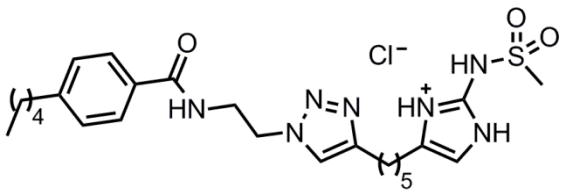
1.40-1.20 (m, 6H), 0.87 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100MHz) δ 168.0, 148.7, 147.7, 147.5, 139.0, 131.3, 128.9, 127.3, 122.0, 109.9, 84.1, 51.3, 49.6, 40.0, 36.0, 36.0, 31.6, 31.1, 29.4, 28.4, 28.2, 28.1, 25.7, 25.7, 22.7, 14.2; IR ($CDCl_3$) 2929, 2857, 1752, 1650, 1611, 1552, 1503, 1459, 1392, 1370, 1321, 1254, 1155, 1116, 1051, 962, 853, 771, 732; UV (λ_{max} nm) 238; HRMS (ESI+) m/z 592.3976 [$(M+H)^+$; calculated mass for $C_{33}H_{50}N_7O_3^+$: 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_2Cl_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_2Cl_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_2Cl_2). The ammonia free dried samples are then dissolved in MeOH with concentrated HCL as above and concentrated to afford the HCl salt.

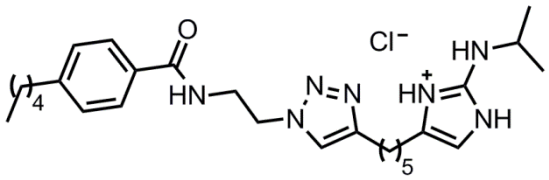


2-(methylamino)-4-(5-(1-(2-(4-pentylbenzamido)ethyl)-1H-1,2,3-triazol-4-yl)pentyl)-1H-imidazol-3-ium chloride (13a). Reacted in 30% TFA to provide the 2-(methylamino)-4-(5-(1-(2-(4-pentylbenzamido)ethyl)-1H-1,2,3-triazol-4-yl)pentyl)-1H-imidazol-3-ium chloride (58 mg, quantitative yield) as a clear oil. ^{1}H NMR (CD_3OD, 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_3OD, 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_3OD) 3415, 2929, 2858, 2376, 2348, 2310, 1678, 1640, 1544, 1507, 1434, 1307, 1181; UV (λ_{max} nm) 238; HRMS (ESI+) m/z 452.3116 [$(M+H)^+$; calculated mass for $C_{25}H_{38}N_7O^+$: 452.3132 amu].

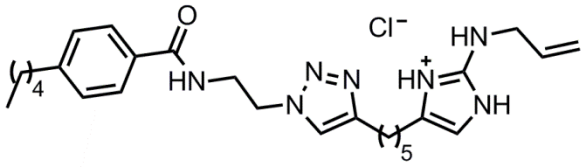


2-(methylsulfonamido)-4-(5-(1-(2-(4-pentylbenzamido)ethyl)-1*H*-1,2,3-triazol-4-yl)pentyl)-1*H*-imidazol-3-ium chloride (13b). Reacted in 30% TFA to provide the 2-(methylsulfonamido)-4-(5-(1-(2-(4-pentylbenzamido)ethyl)-1H-1,2,3-triazol-4-yl)pentyl)-1H-imidazol-3-ium chloride (58 mg, quantitative yield). ^{1}H NMR (CD_3OD, 400MHz) 8.49 (s, 1H), 7.69 (d, *J* = 8.4, 2H), 7.26 (d, *J* = 8.4 Hz,

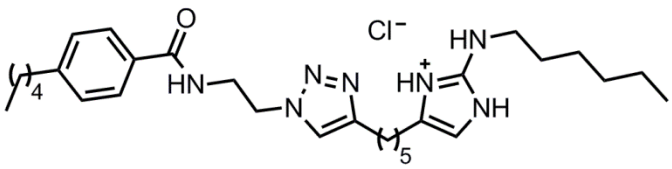
2H), 7.03 (s, 1H), 4.82 (t, *J* = 5.4 Hz, 2H), 3.93 (t, *J* = 5.4 Hz, 2H), 3.29 (s, 3H), 2.86 (t, *J* = 7.6 Hz, 2H), 2.63 (t, *J* = 8.0 Hz, 2H), 2.61 (m, 2H), 1.73 (m, 2H), 1.68 (m, 2H), 1.60 (m, 2H), 1.41 (m, 2H), 1.35-1.28 (m, 4H), 0.88 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (CD_3OD, 100MHz) δ 170.5, 148.7, 146.0, 138.1, 133.0, 132.3 129.7, 128.4, 128.0, 114.0, 53.8, 42.3, 40.5, 36.7, 32.6, 32.2, 29.0, 28.926, 28.9, 25.3, 24.2, 23.6, 14.4; IR (CD_3OD) 3329, 2928, 2857, 2375, 2348, 2310, 1641, 1556, 1507, 1339, 1164, 1129, 771; UV (λ_{max} nm) 238; HRMS (ESI+) m/*z* 516.2743 [$(M+H)^+$; calculated mass for $C_{25}H_{37}N_7O_3S^+$: 516.2751 amu].



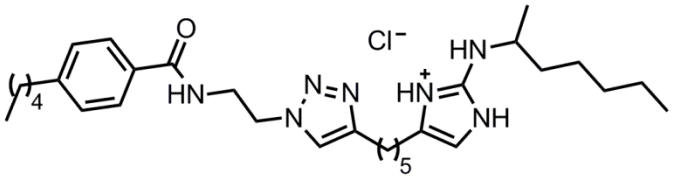
2-(isopropylamino)-4-(5-(1-(2-(4-pentylbenzamido)ethyl)-1H-1,2,3-triazol-4-yl)pentyl)-1H-imidazol-3-ium chloride (13c). Reacted in 30% TFA to provide the 2-(isopropylamino)-4-(5-(1-(2-(4-pentylbenzamido)ethyl)-1H-1,2,3-triazol-4-yl)pentyl)-1H-imidazol-3-ium chloride (17 mg, 85%) as a clear oil. ^{1}H NMR (CD_3OD, 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), 1.45-1.25 (m, 6H), 1.27 (d, *J* = 7.4, 6H), 0.89 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (CD_3OD, 100MHz) δ 170.3, 148.4, 147.5, 146.9, 132.3, 129.5, 128.9, 128.2, 125.9, 109.6, 52.0, 46.6, 40.5, 36.5, 32.3, 32.0, 29.3, 28.7, 25.2, 24.8, 23.4, 22.6, 14.2; IR (CD_3OD) 2926, 2852, 1663, 1543, 1505, 1459, 1370, 1302, 1195, 1173, 1062, 978; UV (λ_{max} nm) 238; HRMS (ESI+) m/*z* 480.3444 [$(M+H)^+$; calculated mass for $C_{27}H_{42}N_7O^+$: 480.3445 amu].



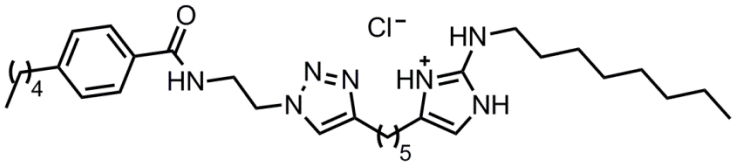
2-(allylamino)-4-(5-(1-(2-(4-pentylbenzamido)ethyl)-1H-1,2,3-triazol-4-yl)pentyl)-1H-imidazol-3-ium chloride (13d). Reacted in 30% TFA to provide the 2-(allylamino)-4-(5-(1-(2-(4-pentylbenzamido)ethyl)-1H-1,2,3-triazol-4-yl)pentyl)-1H-imidazol-3-ium chloride (18 mg, 96%) as a clear oil. ^{1}H NMR (CD_3OD, 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_3OD, 100MHz) δ 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_3OD) 3363, 2929, 2857, 1666, 1635, 1542, 1503, 1456, 1370, 1303, 1140, 1058; UV (λ_{max} nm) 238; HRMS (ESI+) m/*z* 478.3284 [$(M+H)^+$; calculated mass for $C_{27}H_{40}N_7O^+$: 478.3289 amu].



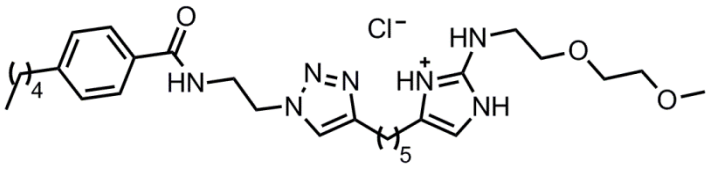
2-(hexylamino)-4-(5-(1-(2-(4-pentylbenzamido)ethyl)-1H-1,2,3-triazol-4-yl)pentyl)-1H-imidazol-3-ium chloride (13e). Reacted in 30% TFA to provide the 2-(hexylamino)-4-(5-(1-(2-(4-pentylbenzamido)ethyl)-1H-1,2,3-triazol-4-yl)pentyl)-1H-imidazol-3-ium chloride (55 mg, 99%) as a clear oil. ^{1}H NMR (CD_3OD, 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_3OD, 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_3OD) 3241, 2929, 2857, 2360, 2323, 1668, 1635, 1544, 1508, 1456, 1379, 1335, 1306; UV (λ_{max} nm) 238; HRMS (ESI+) m/*z* 522.3905 [$(M+H)^+$; calculated mass for $C_{30}H_{48}N_7O^+$: 522.3915 amu].



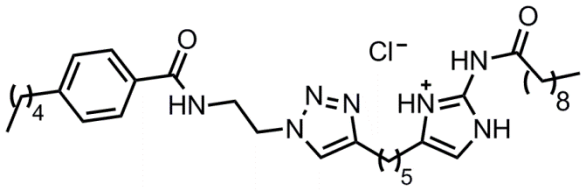
2-(heptan-2-ylamino)-4-(5-(1-(2-(4-pentylbenzamido)ethyl)-1H-1,2,3-triazol-4-yl)pentyl)-1H-imidazol-3-ium chloride (13f). Reacted in 30% TFA to provide the 2-(heptanes-2-ylamino)-4-(5-(1-(2-(4-pentylbenzamido)ethyl)-1H-1,2,3-triazol-4-yl)pentyl)-1H-imidazol-3-ium chloride (28 mg, 97%) as a clear oil. ^{1}H NMR (CD_3OD, 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_3OD, 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_3OD) 3254, 2956, 2930, 2858, 1662, 1541, 1503, 1455, 1380, 1303, 1123, 1020, 977, 856, 763; UV (λ_{max} nm) 238; HRMS (ESI+) m/*z* 536.4085 [$(M+H)^+$; calculated mass for $C_{31}H_{50}N_7O^+$: 536.4071 amu].



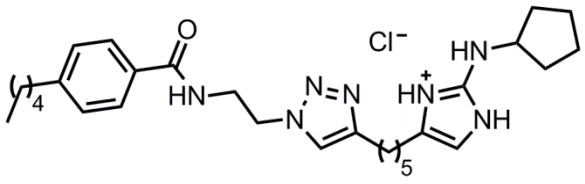
2-(octylamino)-4-(5-(1-(2-(4-pentylbenzamido)ethyl)-1H-1,2,3-triazol-4-yl)pentyl)-1H-imidazol-3-ium chloride (13g). Reacted in 30% TFA to provide the 2-(octylamino)-4-(5-(1-(2-(4-pentylbenzamido)ethyl)-1H-1,2,3-triazol-4-yl)pentyl)-1H-imidazol-3-ium chloride (56 mg, 98%) as a clear oil. ^{1}H NMR (CD_3OD, 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_3OD, 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_3OD) 3265, 2928, 2857, 2375, 2310, 1671, 1635, 1544, 1506, 1457, 1376, 1308; UV (λ_{max} nm) 238; HRMS (ESI+) m/*z* 550.422 [$(M+H)^+$; calculated mass for $C_{33}H_{52}N_7O^+$: 550.4228 amu].



2-((2-(2-methoxyethoxy)ethyl)amino)-4-(5-(1-(2-(4-pentylbenzamido)ethyl)-1*H*-1,2,3-triazol-4-yl)pentyl)-1*H*-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_3OD, 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_3OD, 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, 29.0, 28.6, 25.1, 24.4, 23.4, 14.2; IR (CD_3OD) 3181, 2930, 2861, 1734, 1670, 1583, 1541, 1503, 1457, 1407, 1302, 1246; UV (λ_{max} nm) 238; HRMS (ESI+) m/*z* 540.3662 [$(M+H)^+$; calculated mass for $C_{29}H_{45}N_7O_3^+$: 540.3657 amu].

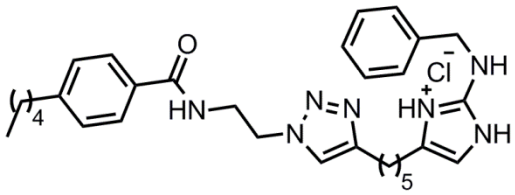


2-decanamido-4-(5-(1-(2-(4-pentylbenzamido)ethyl)-1*H*-1,2,3-triazol-4-yl)pentyl)-1*H*-imidazol-3-ium chloride (13i). Reacted in 30% TFA to provide the 2-(decanamino)-4-(5-(1-(2-(4-pentylbenzamido)ethyl)-1H-1,2,3-triazol-4-yl)pentyl)-1H-imidazol-3-ium chloride (33 mg, 96%) as a clear oil. ^{1}H NMR (CD_3OD, 400MHz) 8.38 (s, 1H), 7.68 (d, *J* = 8.0 Hz, 2H), 7.25 (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_3OD, 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_3OD) 3266, 2927, 2856, 2363, 2310, 1713, 1642, 1610, 1543, 1507, 1458, 1304, 1200; UV (λ_{max} nm) 241; HRMS (ESI+) m/*z* 592.4333 [$(M+H)^+$; calculated mass for $C_{34}H_{53}N_7O_2^+$: 592.4334 amu].

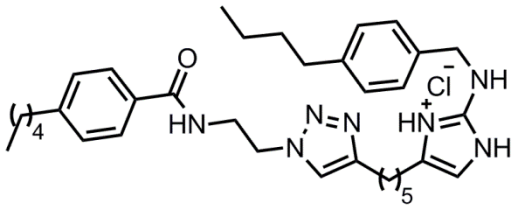


2-(cyclopentylamino)-4-(5-(1-(2-(4-pentylbenzamido)ethyl)-1*H*-1,2,3-triazol-4-yl)pentyl)-1*H*-imidazol-3-ium chloride (13j). Reacted in 30% TFA to provide the 2-(cyclopentylamino)-4-(5-(1-(2-(4-pentylbenzamido)ethyl)-1H-1,2,3-triazol-4-yl)pentyl)-1H-imidazol-3-ium chloride (33 mg, 96%) as a clear oil. ^{1}H NMR (CD_3OD, 400MHz) 8.22 (s, 1H), 7.67 (d, *J* = 8.0 Hz, 2H), 7.25 (d, *J* = 8.4 Hz, 2H),

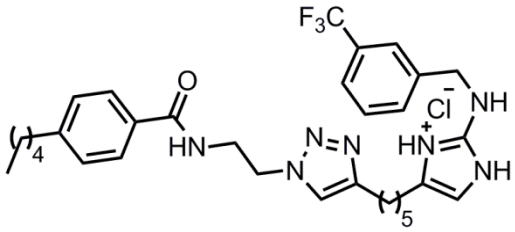
6.51 (s, 1H), 4.73 (t, *J* = 5.6 Hz, 2H), 3.89 (t, *J* = 5.6 Hz, 2H), 3.85 (m, 1H), 2.79 (t, *J* = 7.6 Hz, 2H), 2.64 (t, *J* = 7.6 Hz, 2H), 2.46 (t, *J* = 7.2 Hz, 2H), 2.03 (m, 2H), 1.85-1.50 (m, 12H), 1.44-1.21 (m, 6H), 0.89 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (CD_3OD, 100MHz) δ 170.3, 148.5, 147.8, 132.3, 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_3OD) 3258, 2928, 2855, 1665, 1541, 1502, 1440, 1303, 1189, 1056, 974; UV (λ_{max} nm) 204, 232; HRMS (ESI+) m/*z* 540.3662 [$(M+H)^+$; calculated mass for $C_{29}H_{45}N_7O_3^+$: 540.3657 amu].



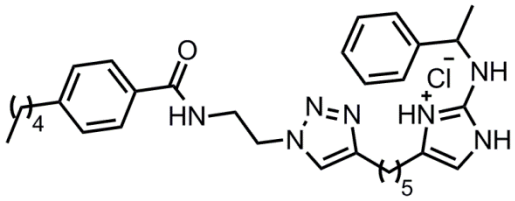
2-(benzylamino)-4-(5-(1-(2-(4-pentylbenzamido)ethyl)-1*H*-1,2,3-triazol-4-yl)pentyl)-1*H*-imidazol-3-ium chloride (13k). Reacted in 30% TFA to provide the 2-(benzylamino)-4-(5-(1-(2-(4-pentylbenzamido)ethyl)-1H-1,2,3-triazol-4-yl)pentyl)-1H-imidazol-3-ium chloride (45 mg, 99%) as a clear oil. ^{1}H NMR (CD_3OD, 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); ^{13}C NMR (CD_3OD, 100MHz) δ 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_3OD) 3258, 2929, 2856, 2376, 2312, 1665, 1542, 1502, 1454, 1374, 1308, 750, 700; UV (λ_{max} nm) 239; HRMS (ESI+) m/*z* 528.3451 [$(M+H)^+$; calculated mass for $C_{31}H_{42}N_7O^+$: 528.3445 amu].



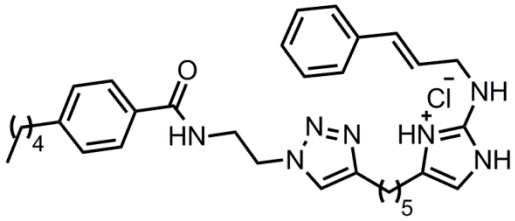
2-((4-butylbenzyl)amino)-4-(5-(1-(2-(4-pentylbenzamido)ethyl)-1*H*-1,2,3-triazol-4-yl)pentyl)-1*H*-imidazol-3-ium chloride (13l). Reacted in 30% TFA to provide the 2-((4-butylbenzyl)amino)-4-(5-(1-(2-(4-pentylbenzamido)ethyl)-1H-1,2,3-triazol-4-yl)pentyl)-1H-imidazol-3-ium chloride (105 mg, 89%) as a clear oil. ^{1}H NMR (CD_3OD, 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); ^{13}C NMR (CD_3OD, 100MHz) δ 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_3OD) 3117, 2929, 2857, 2360, 2339, 1665, 1540, 1505, 1404, 1301, 669; UV (λ_{max} nm) 232; HRMS (ESI+) m/*z* 584.4061 [$(M+H)^+$; calculated mass for $C_{35}H_{50}N_7O^+$: 584.4071 amu].



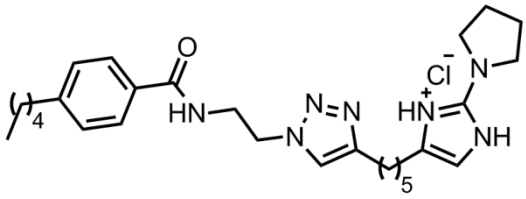
4-(5-(1-(2-(4-pentylbenzamido)ethyl)-1*H*-1,2,3-triazol-4-yl)pentyl)-2-((3-trifluoromethyl)benzyl)amino)-1*H*-imidazol-3-ium chloride (13m). Reacted in 30% TFA to provide the 4-(5-(1-(2-(4-pentylbenzamido)ethyl)-2-((3-trifluoromethyl)benzyl)amino)-1H-1,2,3-triazol-4-yl)pentyl)-1H-imidazol-3-ium chloride (57 mg, 100%) as a clear oil. ^{1}H NMR (CD_3OD, 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_3OD, 100MHz) δ 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_3OD) 2931, 2861, 1665, 1542, 1500, 1451, 1328, 1122, 1071, 978, 802; UV (λ_{max} nm) 226; HRMS (ESI+) m/*z* 596.3319 [$(M+H)^+$; calculated mass for $C_{32}H_{41}F_3N_7O^+$: 596.3325 amu].



4-(5-(1-(2-(4-pentylbenzamido)ethyl)-1*H*-1,2,3-triazol-4-yl)pentyl)-1*H*-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_2Cl_2) as a clear oil (9 mg, 89%) . ^{1}H NMR (CD_3OD, 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_3OD, 100MHz) δ 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_3OD) 3257, 2929, 2856, 2372, 2316, 1665, 1541, 1503, 1404, 1306, 669; UV (λ_{max} nm) 239; HRMS (ESI+) m/z 528.3598 [$(M+H)^+$; calculated mass for $C_{32}H_{44}N_7O^+$: 542.3602 amu].

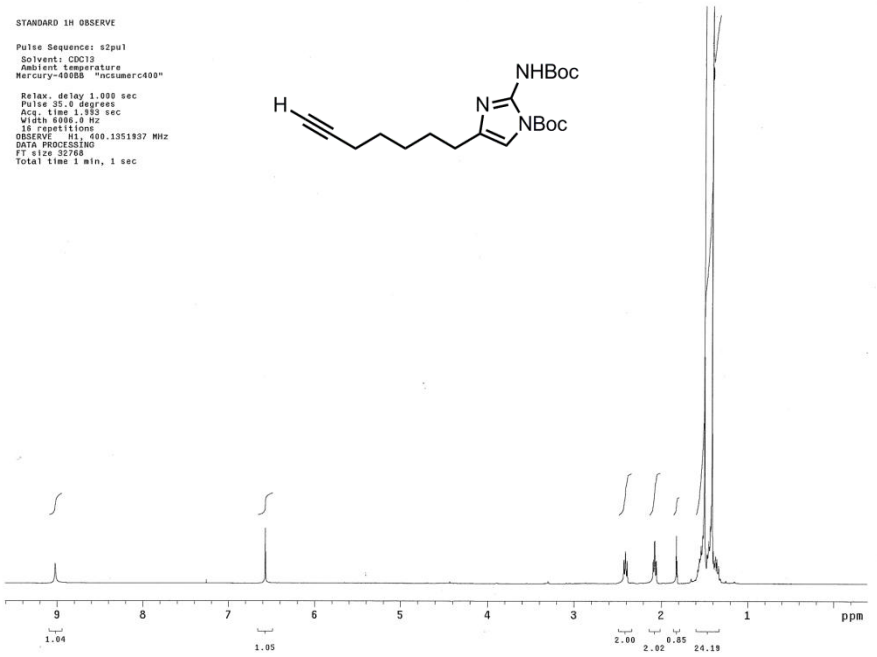


2-(cinnamylamino)-4-(5-(1-(2-(4-pentylbenzamido)ethyl)-1*H*-1,2,3-triazol-4-yl)pentyl)-1*H*-imidazol-3-ium chloride (13o). Reacted in 10% TFA and purification by flash chromatography (1-10% MeOH/CH_2Cl_2 gradient) provided 2-(cinnamylamino)-4-(5-(1-(2-(4-pentylbenzamido)ethyl)-1H-1,2,3-triazol-4-yl)pentyl)-1H-imidazol-3-ium chloride (16 mg, 38%) as a clear oil. ^{1}H NMR (CD_3OD, 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); ^{13}C NMR (CD_3OD, 100MHz) δ 170.3, 150.3, 148.4, 141.1, 136.9, 132.3, 132.1, 130.0, 129.8, 129.5, 128.2, 127.2, 125.5, 113.0, 85.4, 65.1, 51.8, 51.1, 40.5, 36.5, 32.3, 32.0, 29.3, 28.8, 28.8, 25.0, 24.9, 23.3, 14.2; IR (CD_3OD) 3271, 2930, 2857, 1724, 1639, 1589, 1545, 1502, 1455, 1405, 1245, 1171, 1055, 745, 700; UV (λ_{max} nm) 201, 233; HRMS (ESI+) m/*z* 554.3608 [$(M+H)^+$; calculated mass for $C_{33}H_{44}N_7O^+$: 554.3602 amu].

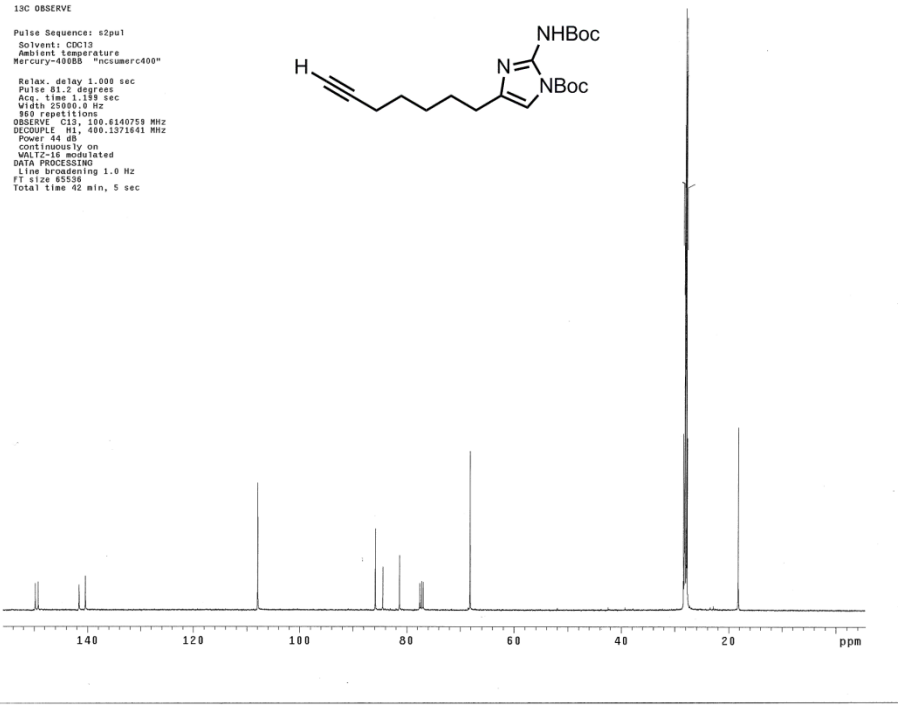


4-(5-(1-(2-(4-pentylbenzamido)ethyl)-1*H*-1,2,3-triazol-4-yl)pentyl)-2-(pyrrolidin-1-yl)-1*H*-imidazol-3-ium chloride (13p). Reacted in 30% TFA to provide the 2-(octylamino)-4-(5-(1-(2-(4-pentylbenzamido)ethyl)-1H-1,2,3-triazol-4-yl)pentyl)-1H-imidazol-3-ium chloride (15 mg, quantitative yield) as a yellow oil. ^{1}H NMR (CD_3OD, 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); ^{13}C NMR (CD_3OD, 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 (CD_3OD) 3135, 2930, 2858, 2791, 1668, 1542, 1503, 1459, 1363, 1302, 1200, 1154, 922; UV (λ_{max} nm) 204; HRMS (ESI+) m/*z* 492.3445 [$(M+H)^+$; calculated mass for $C_{28}H_{42}N_7O^+$: 492.3445 amu].

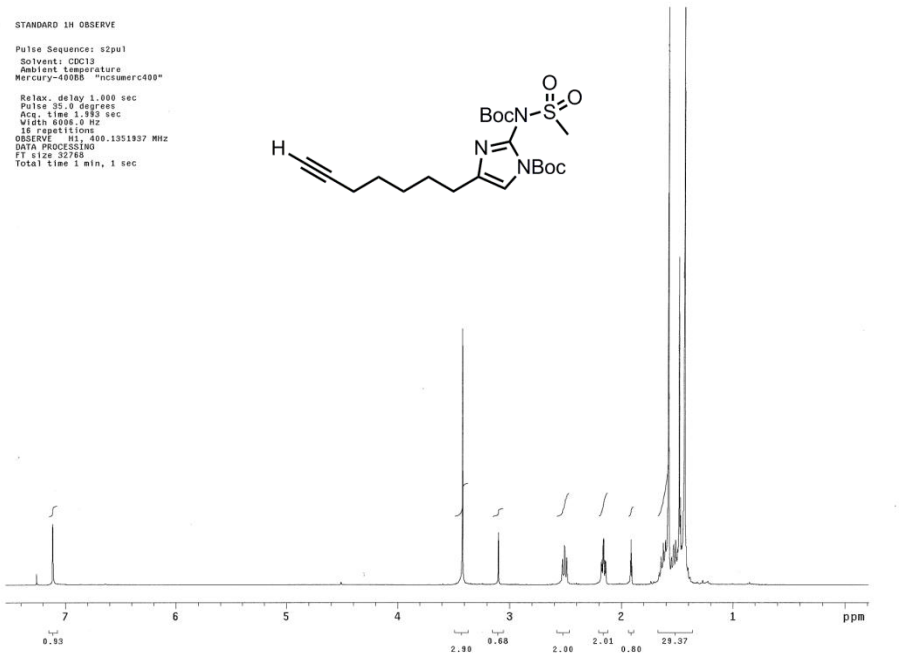
^{1}H NMR for **8**



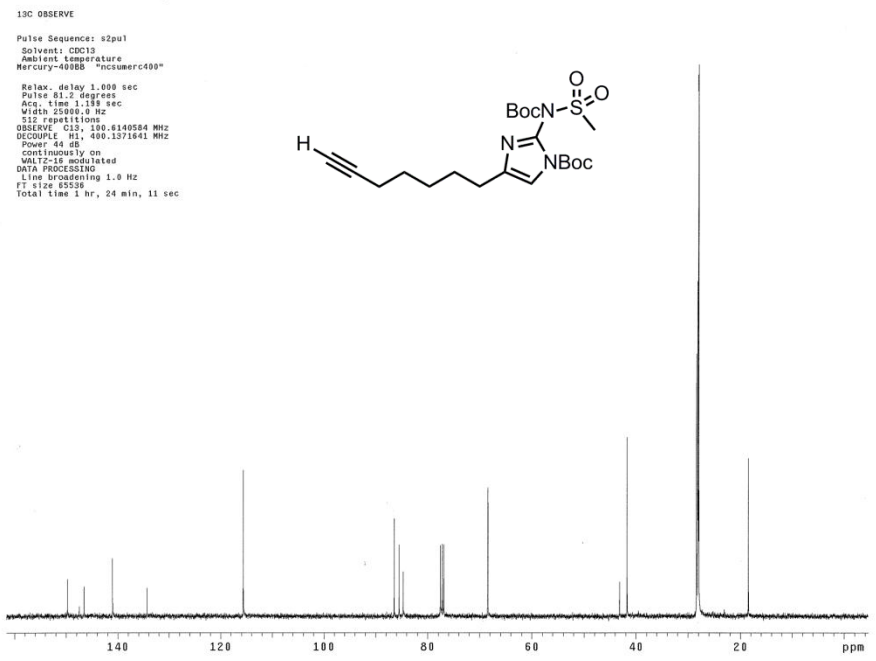
^{13}C NMR for **8**



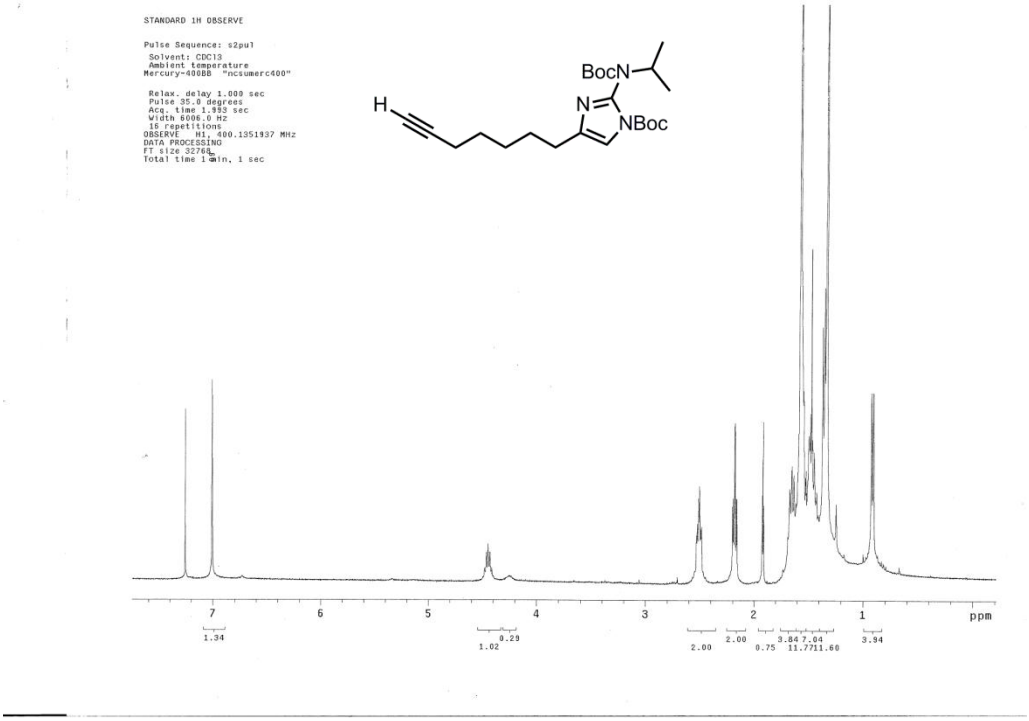
^{1}H NMR for **9b**



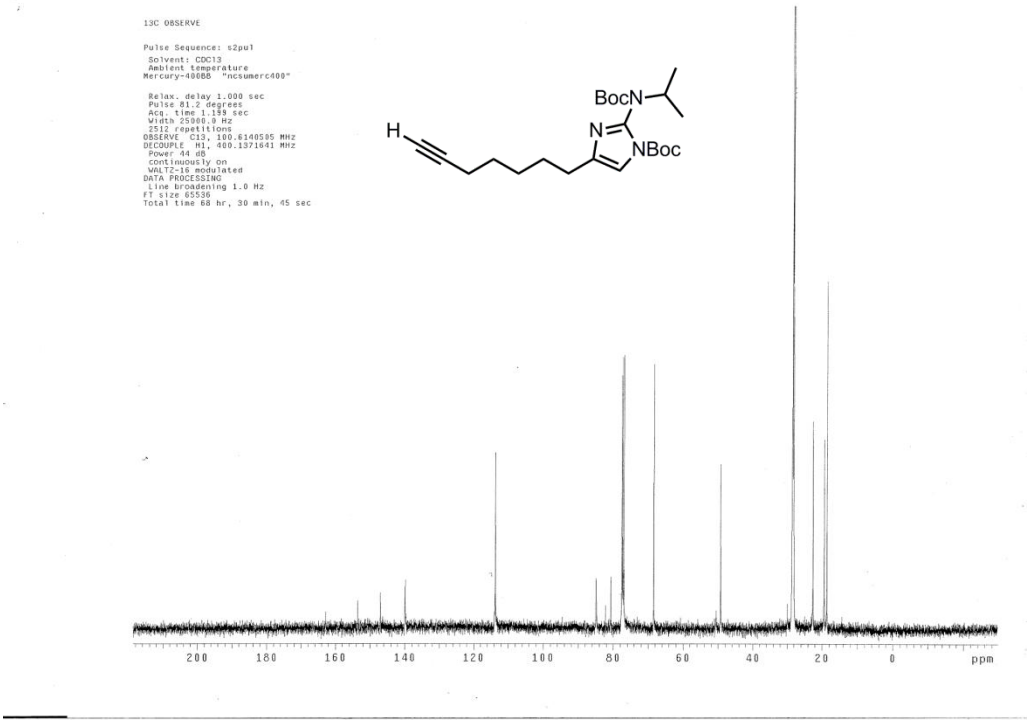
^{13}C NMR for **9b**



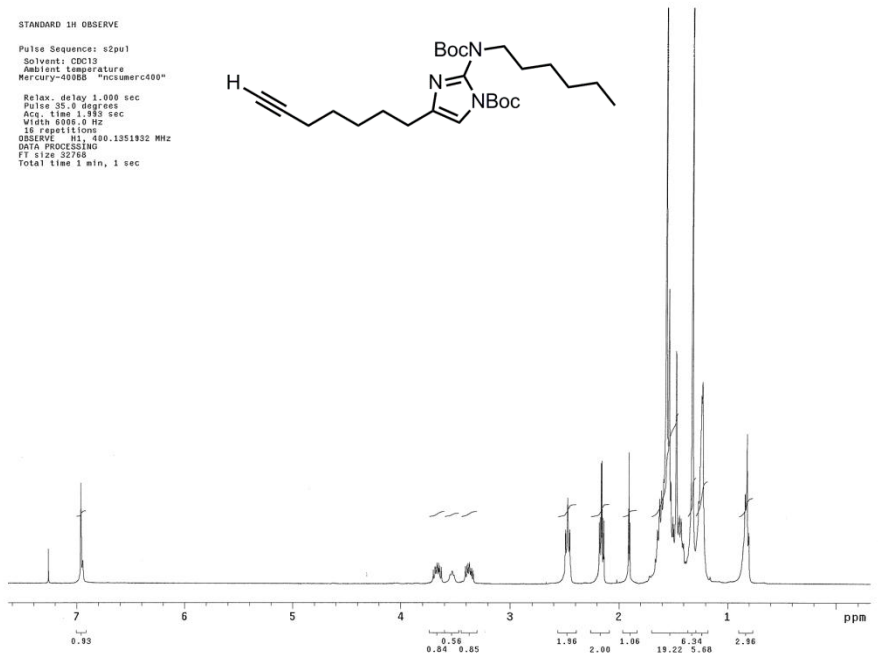
^{1}H NMR for **9c**



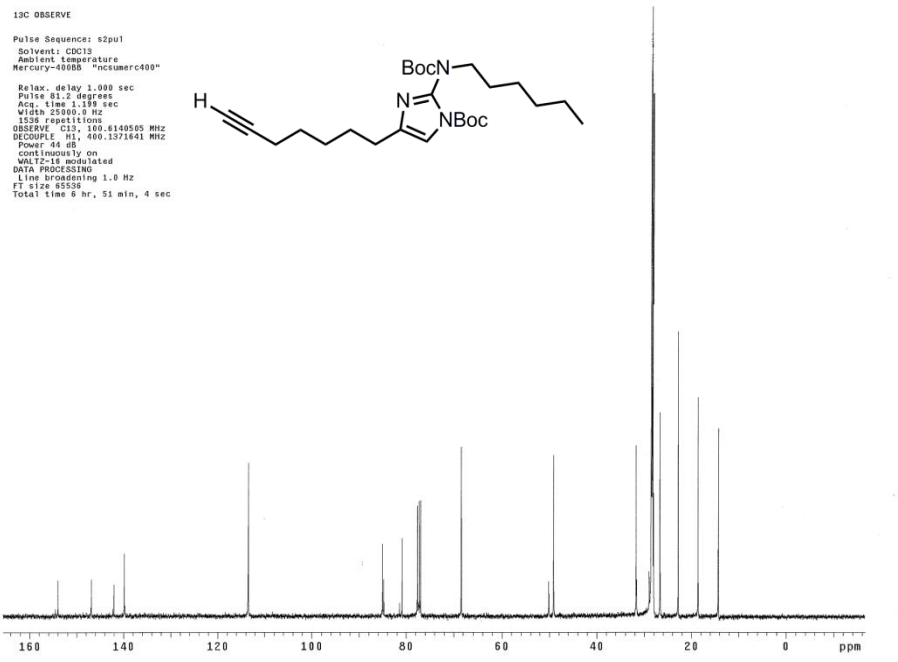
^{13}C NMR for **9c**



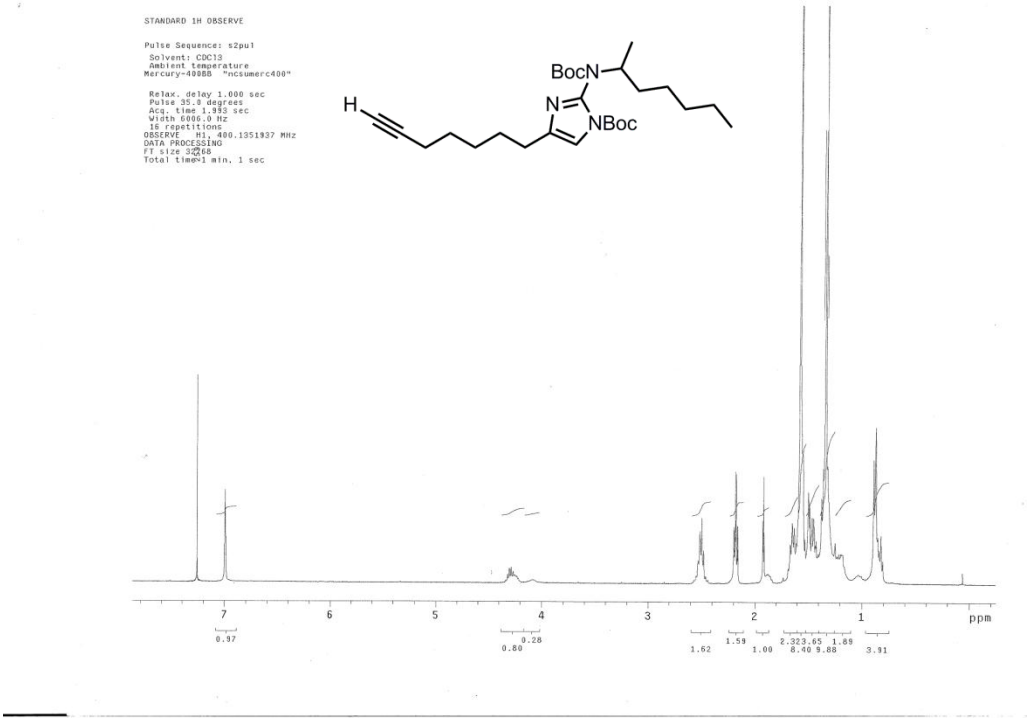
^{1}H NMR for **9e**



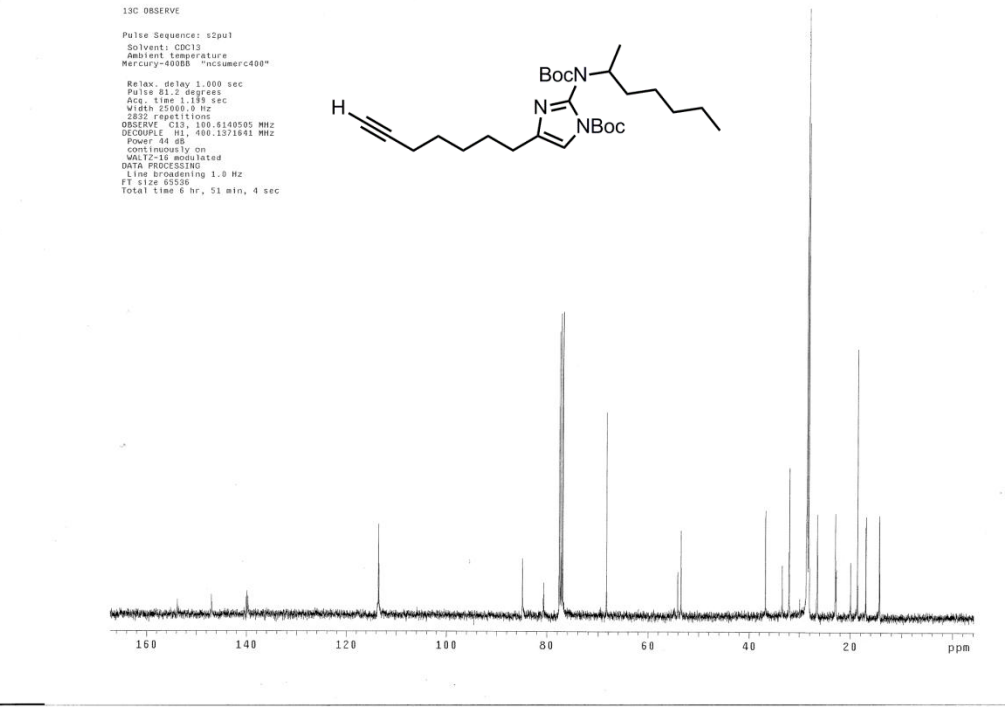
^{13}C NMR for **9e**



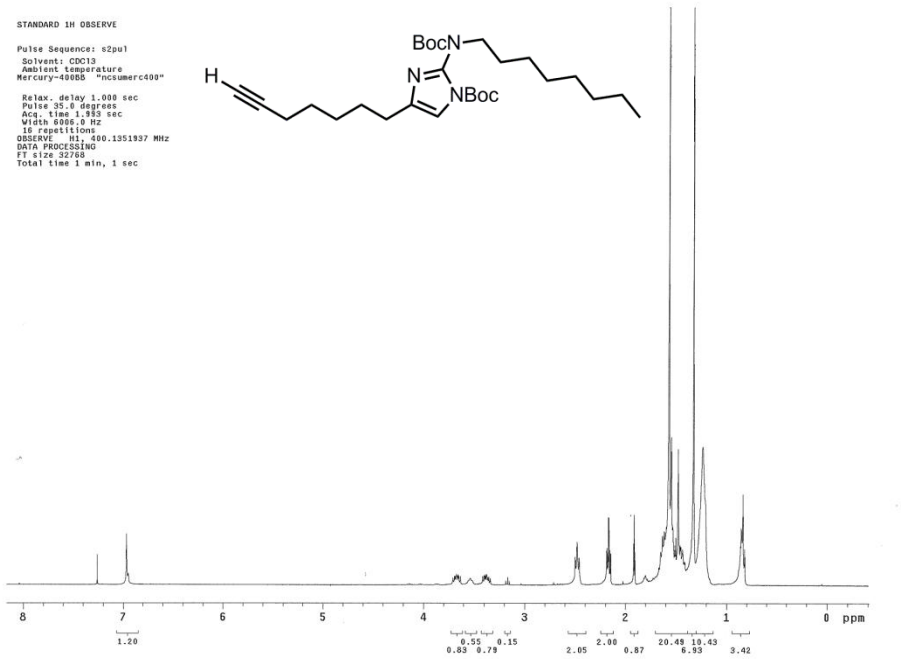
^{1}H NMR for **9f**



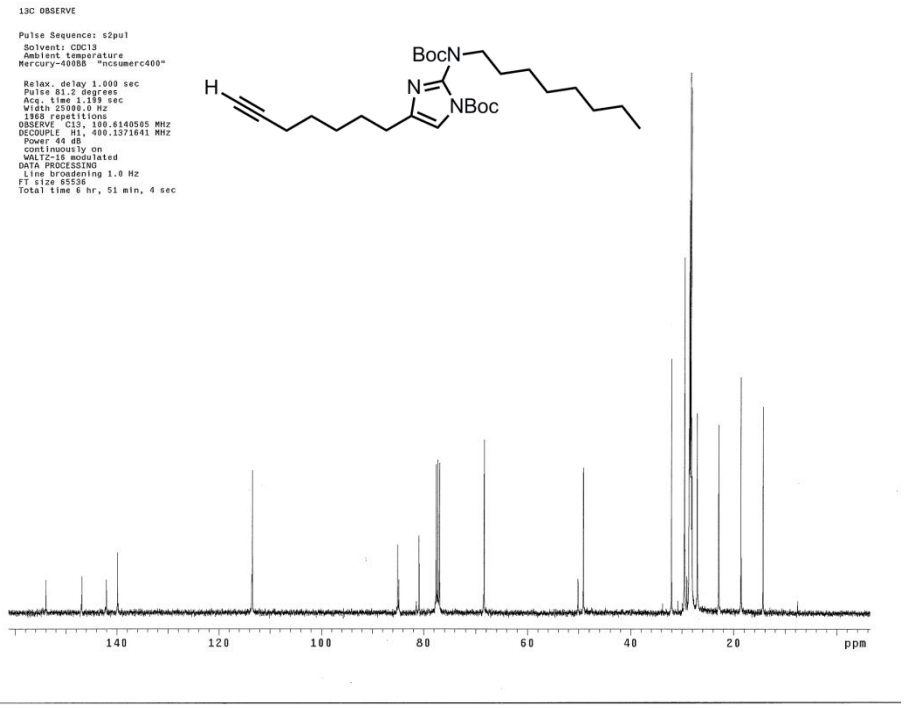
^{13}C NMR for **9f**



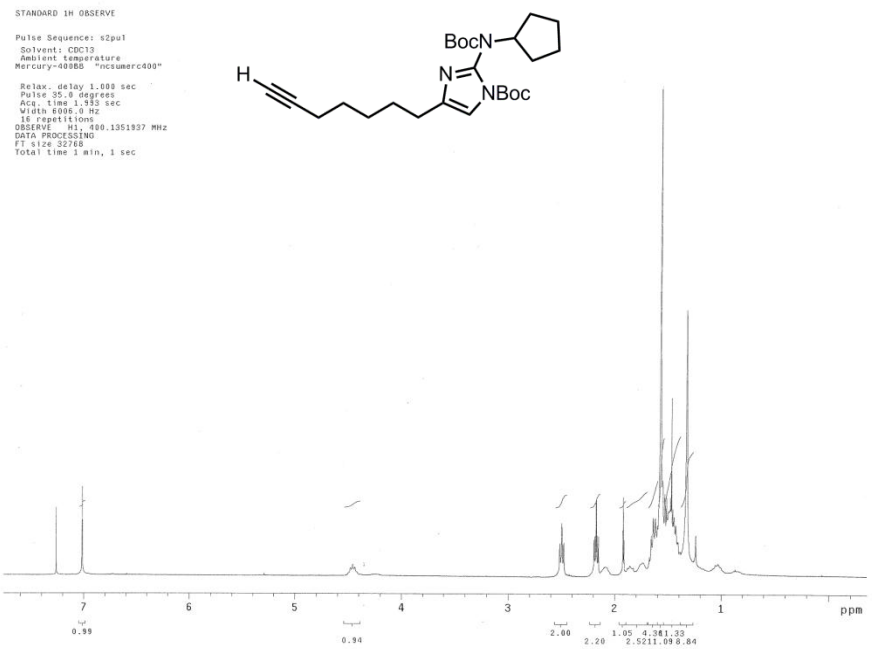
^{1}H NMR for **9g**



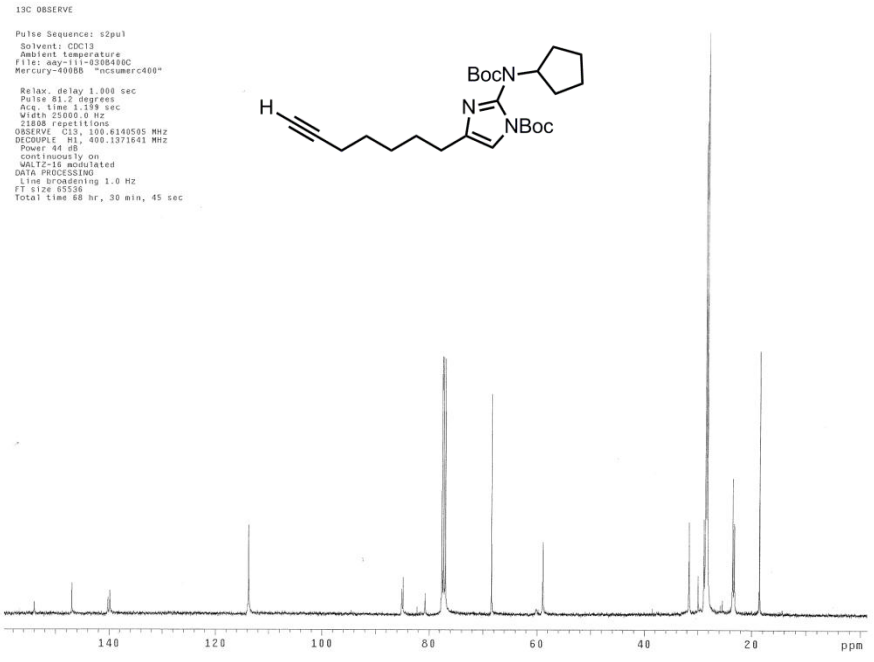
^{13}C NMR for **9g**



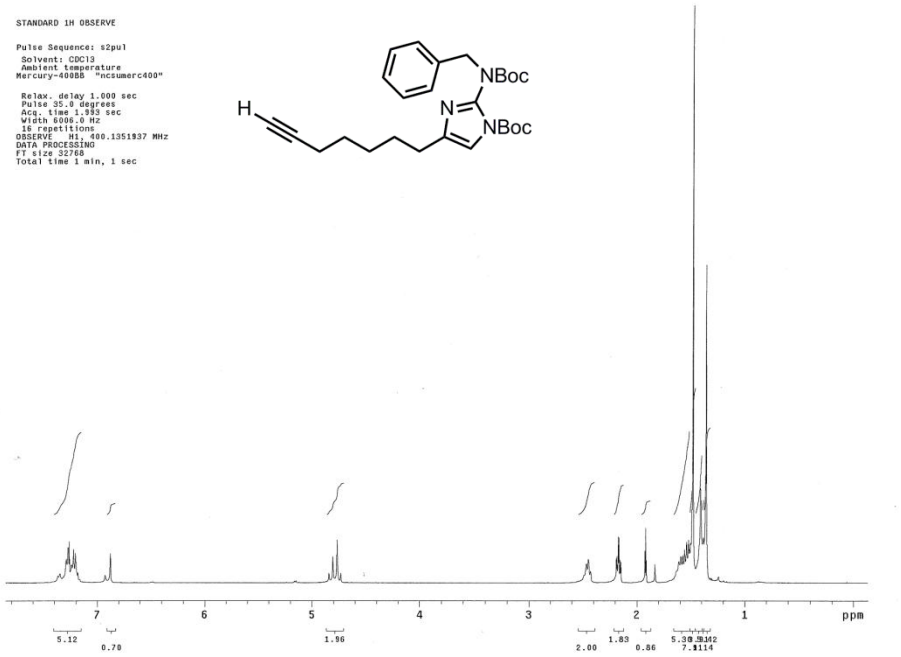
^{1}H NMR for **9j**



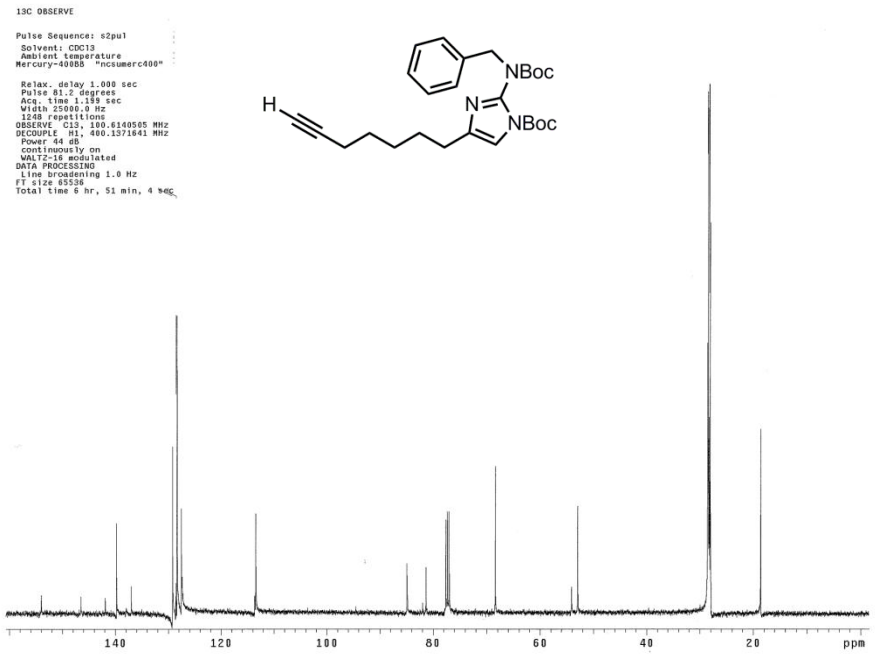
^{13}C NMR for **9j**



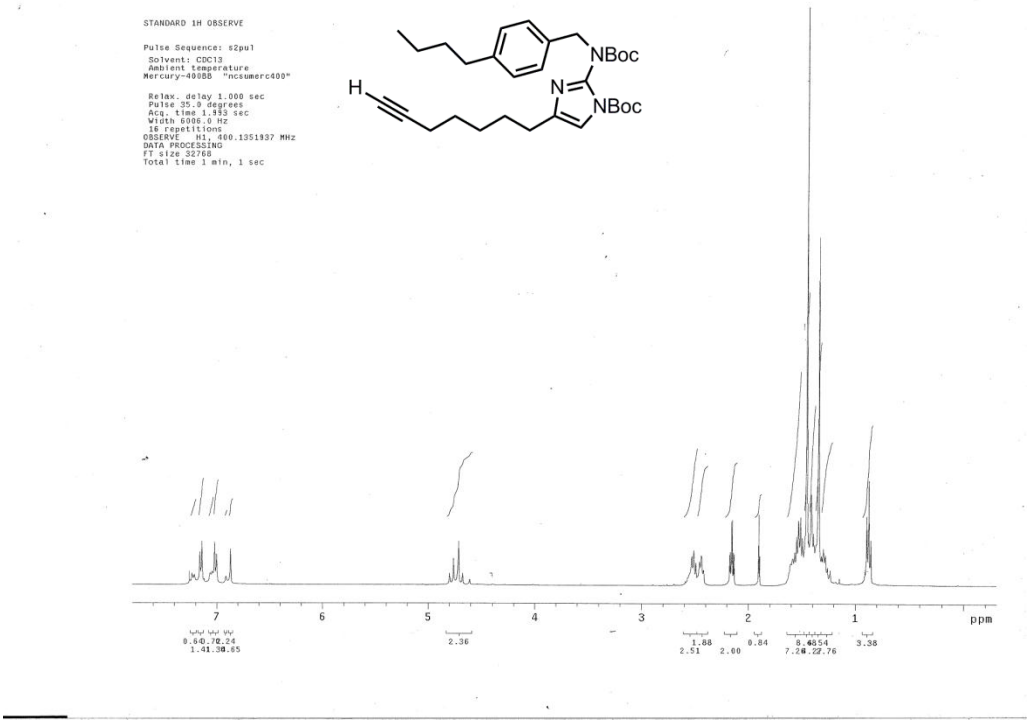
^{1}H NMR for **9k**



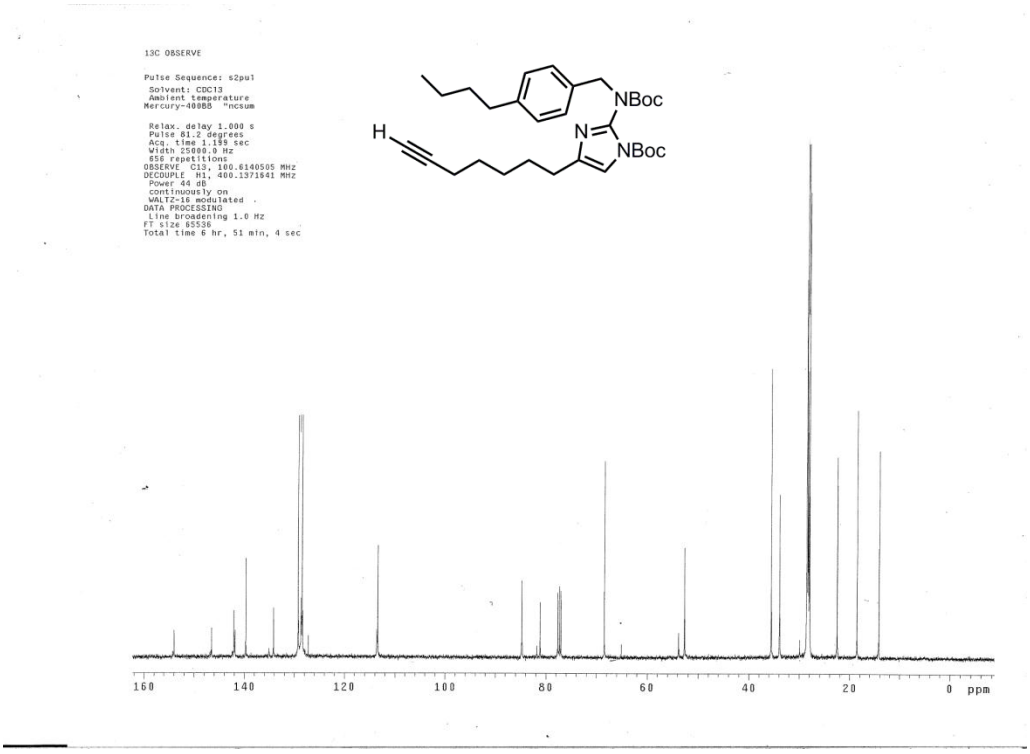
^{13}C NMR for **9k**



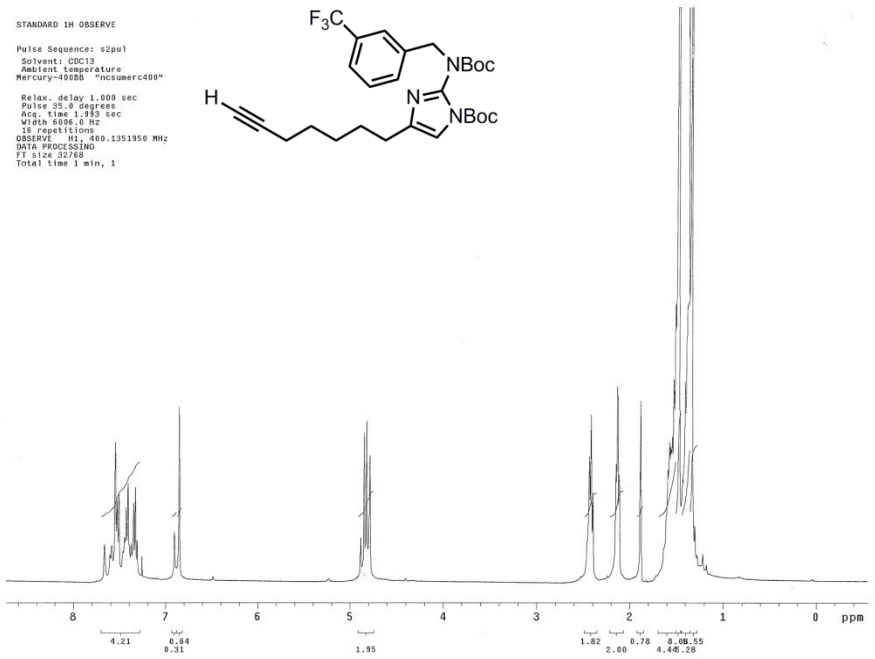
^{1}H NMR for **9l**



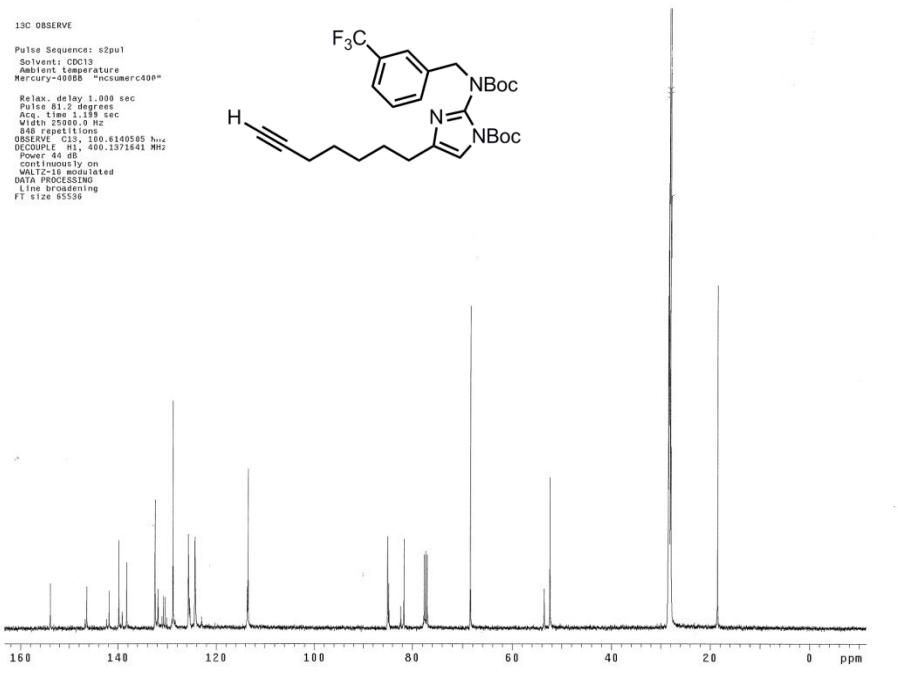
^{13}C NMR for **9l**



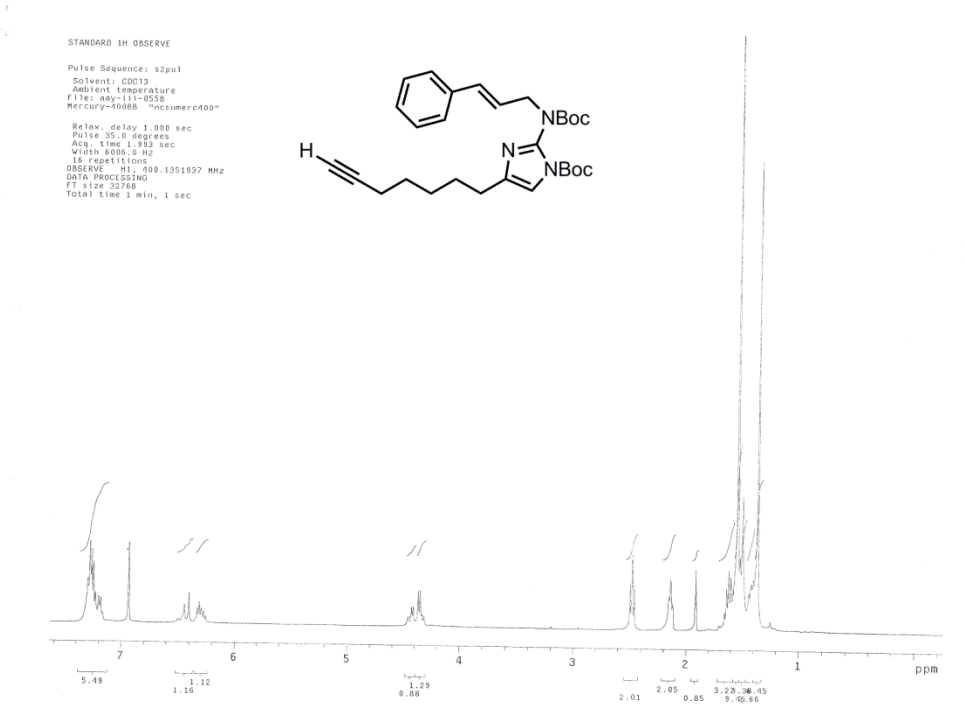
^{1}H NMR for **9m**



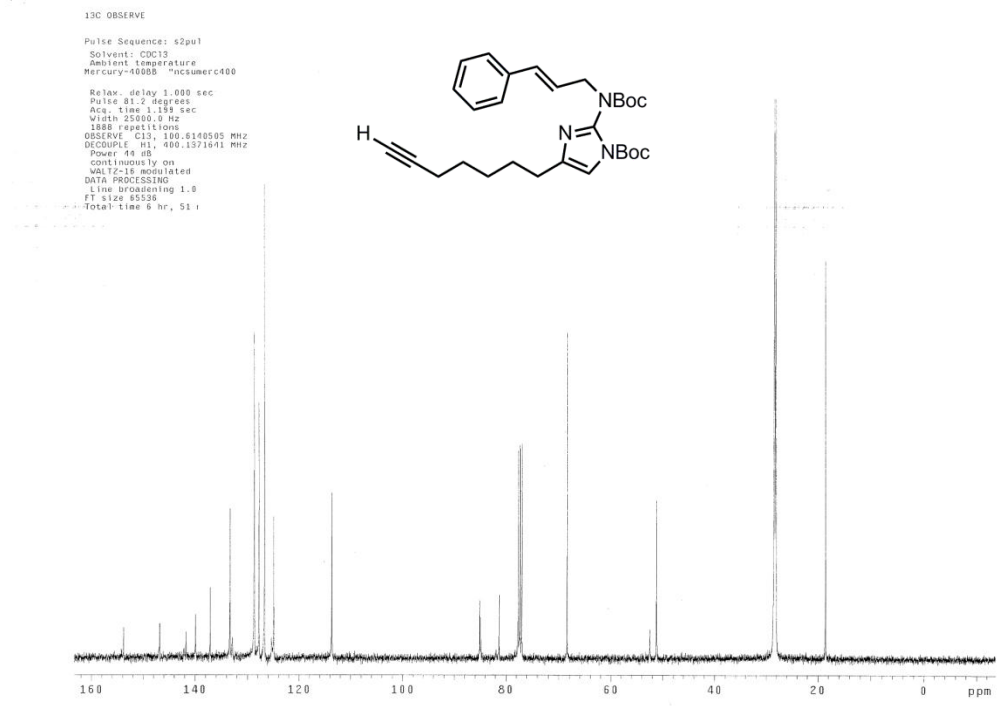
^{13}C NMR for **9m**



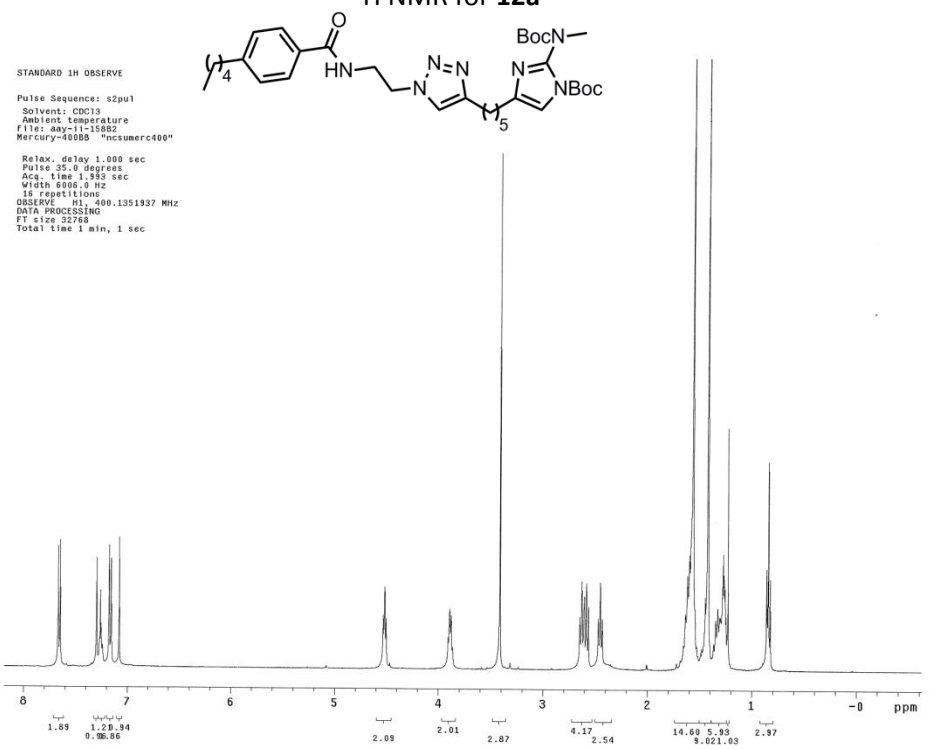
^{1}H NMR for **9o**



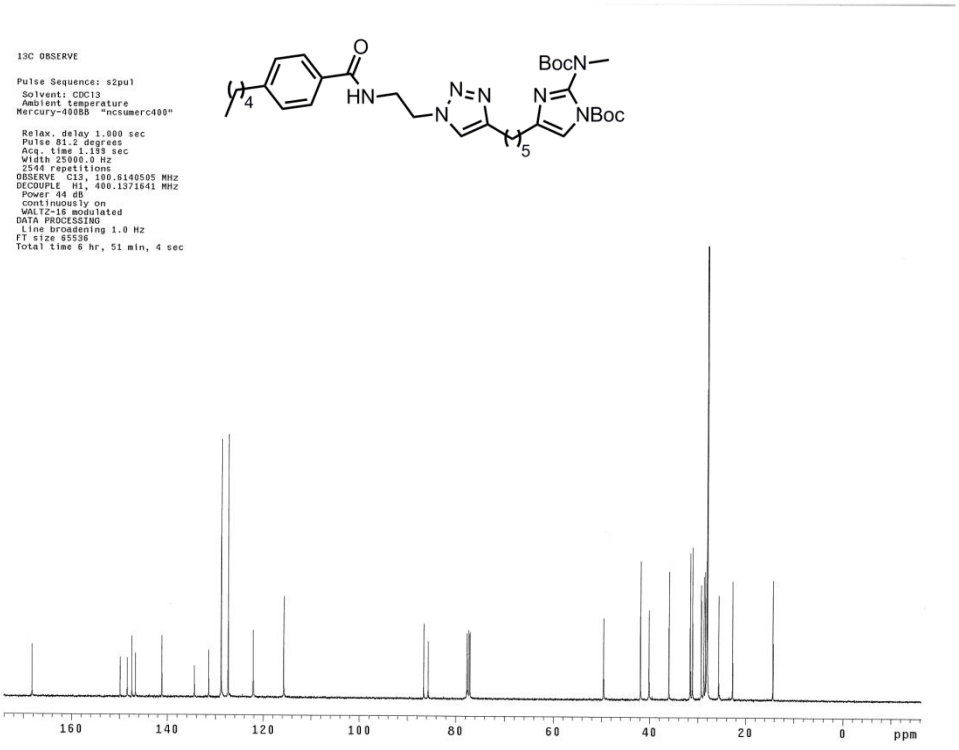
^{13}C NMR for **9o**



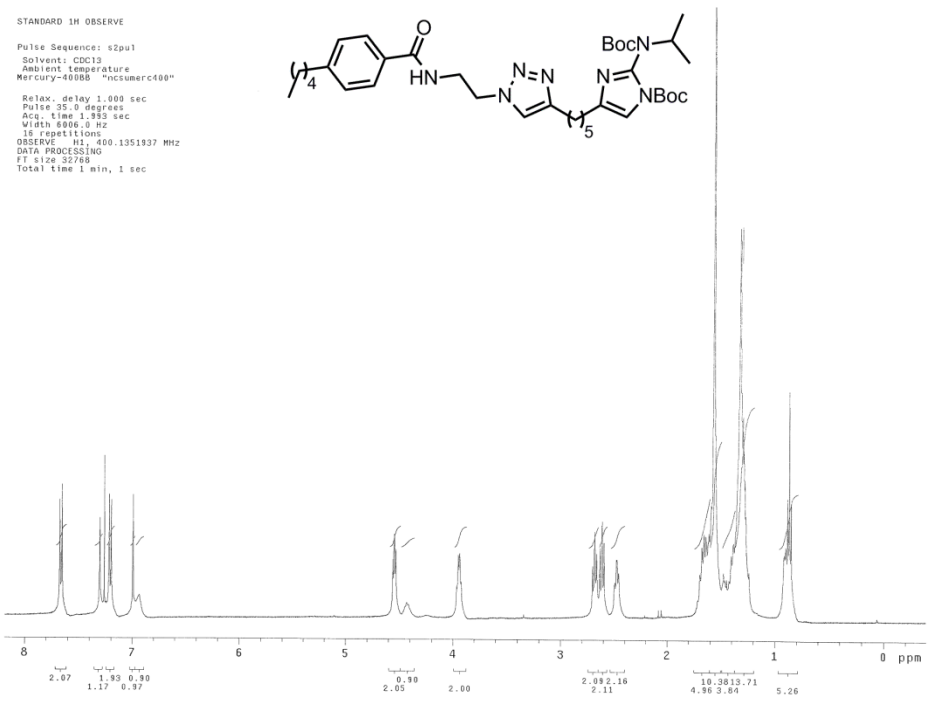
^{1}H NMR for **12a**



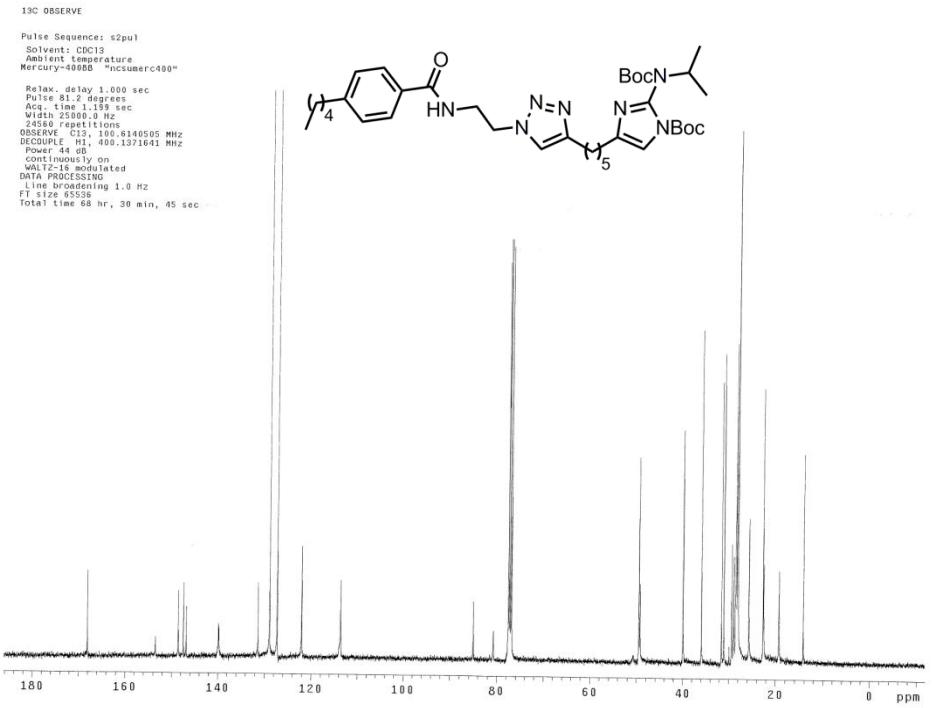
^{13}C NMR for **12a**



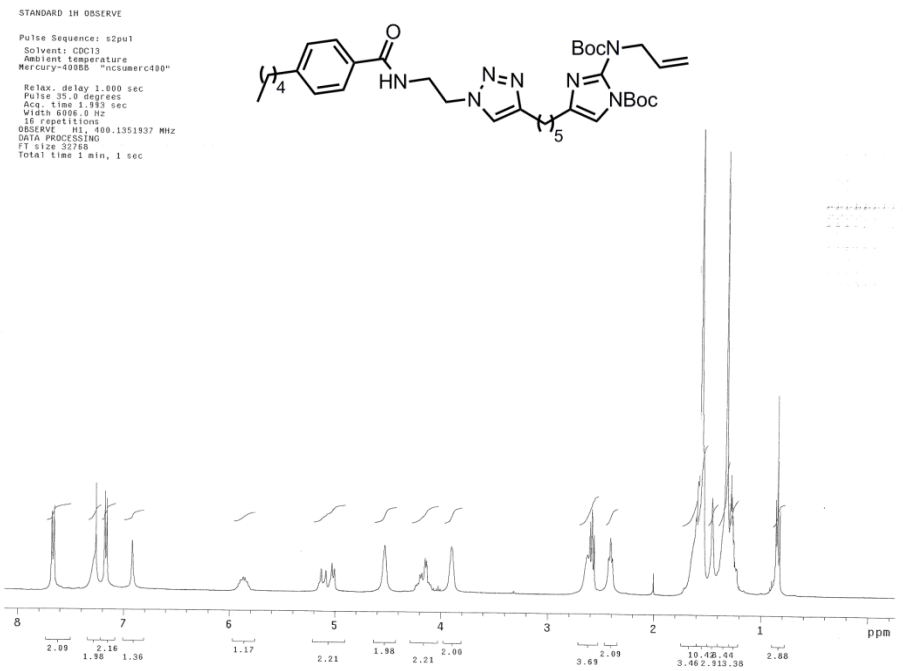
^{1}H NMR for **12c**



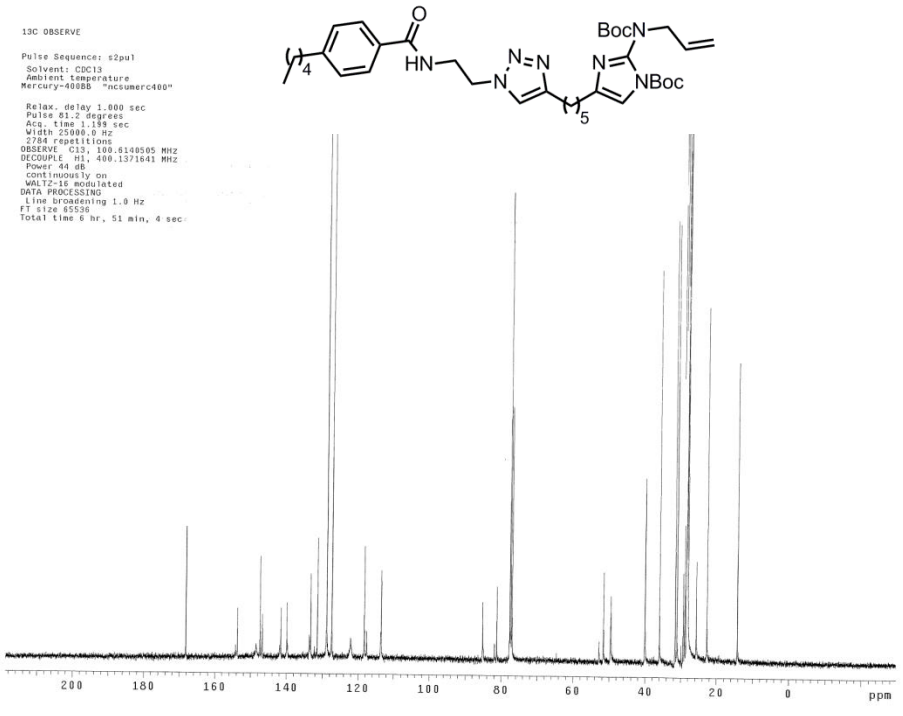
^{13}C NMR for **12c**



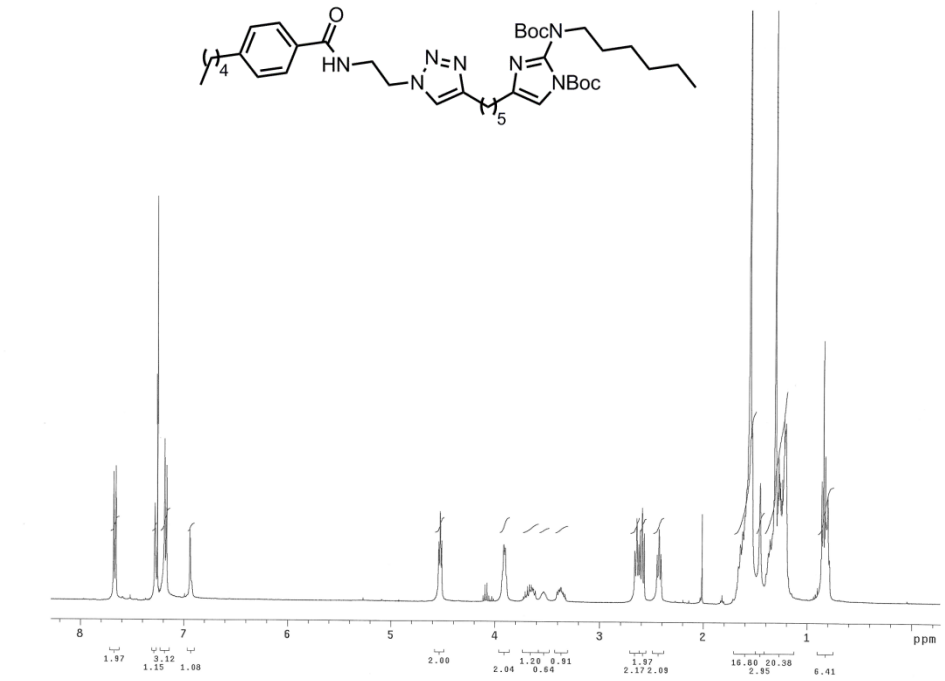
^{1}H NMR for **12d**



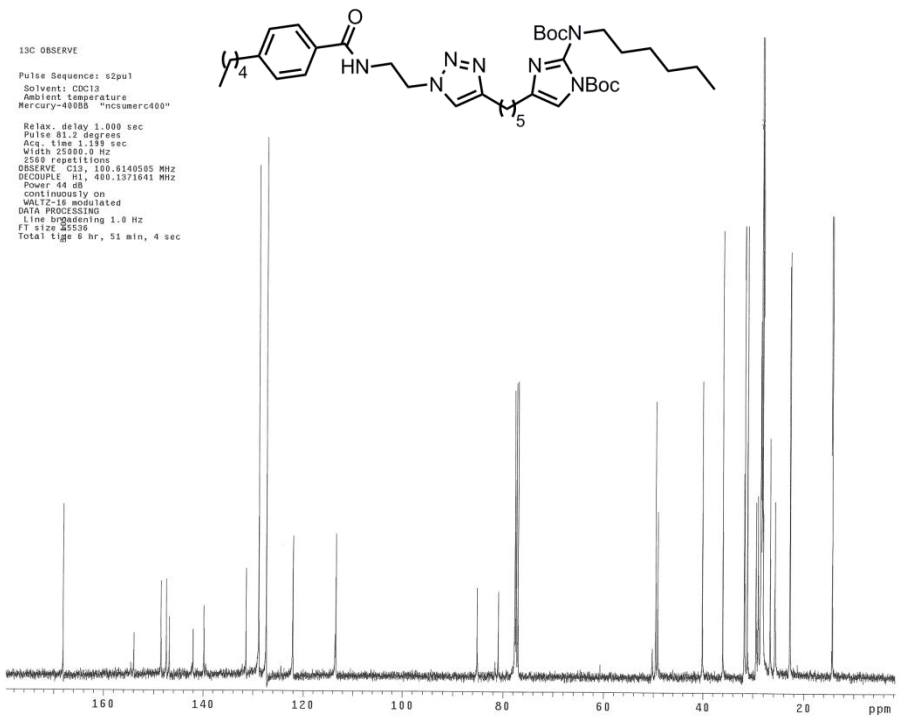
^{13}C NMR for **12d**



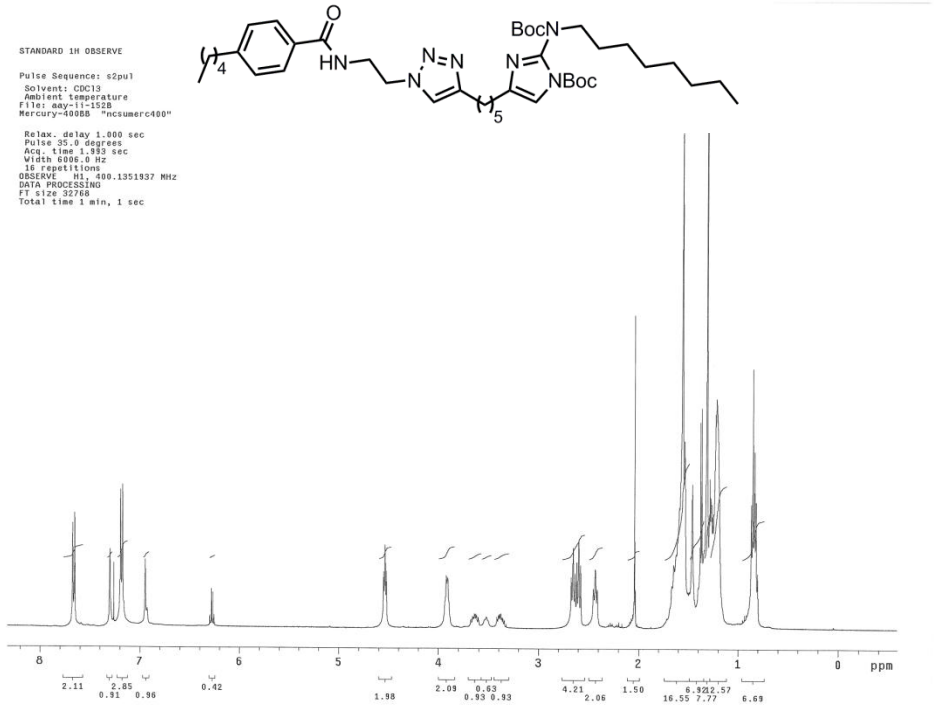
^{1}H NMR for **12e**



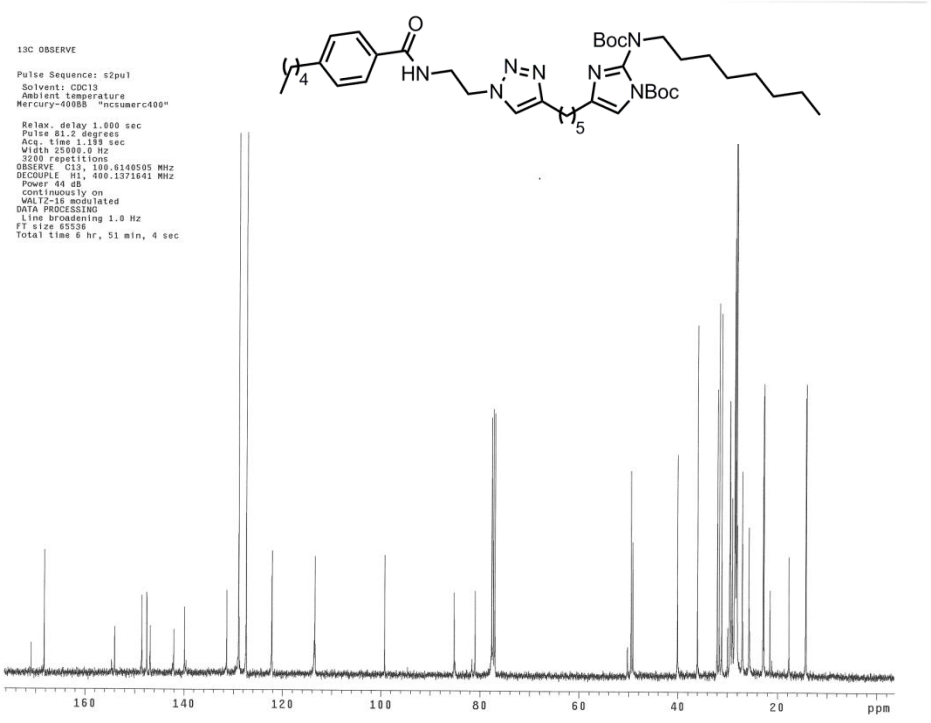
^{13}C NMR for **12e**



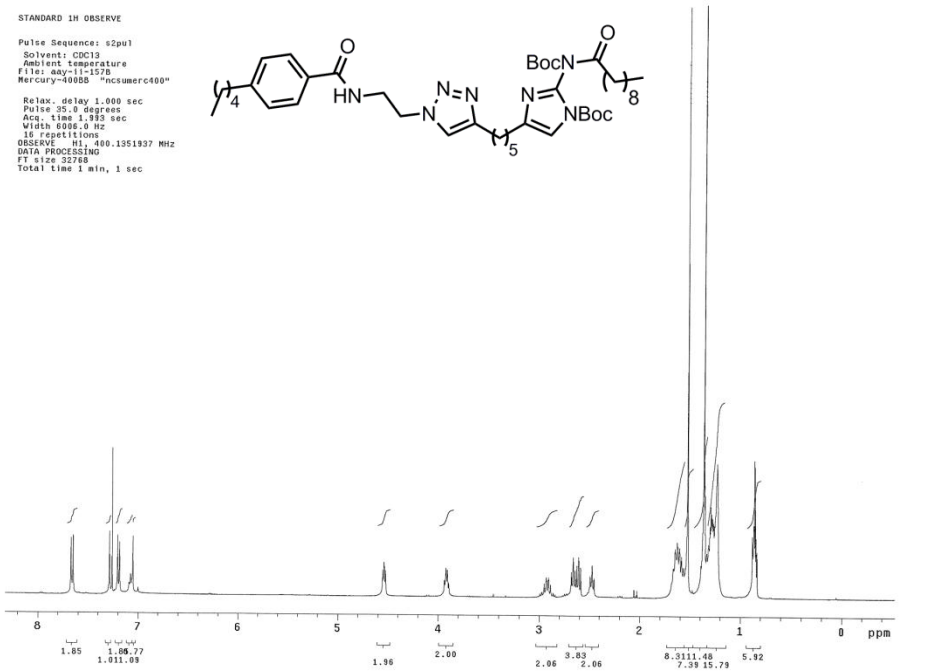
^{1}H NMR for **12g**



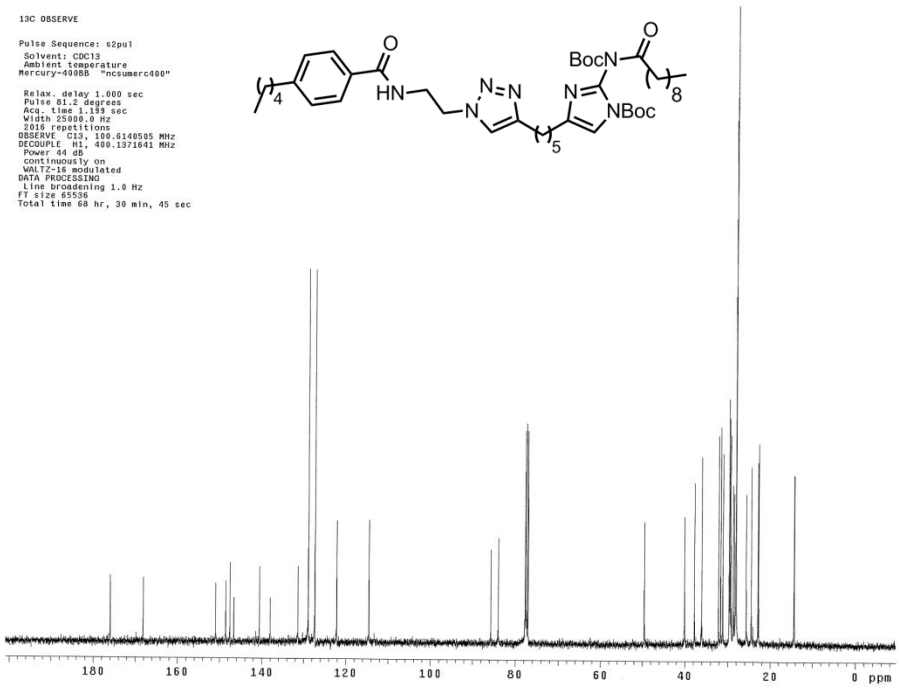
^{13}C NMR for **12g**



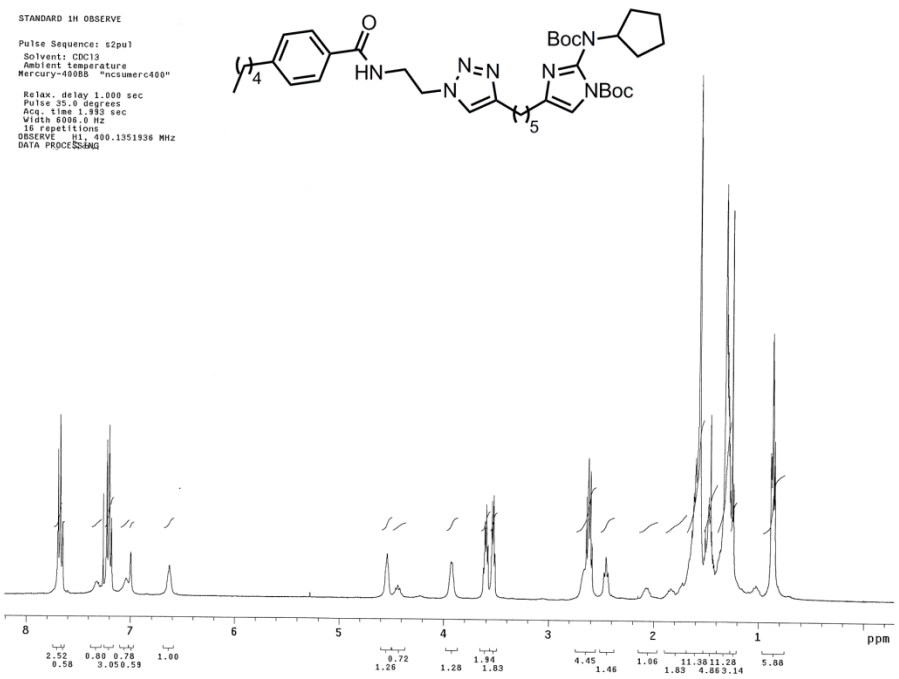
^{1}H NMR for **12i**



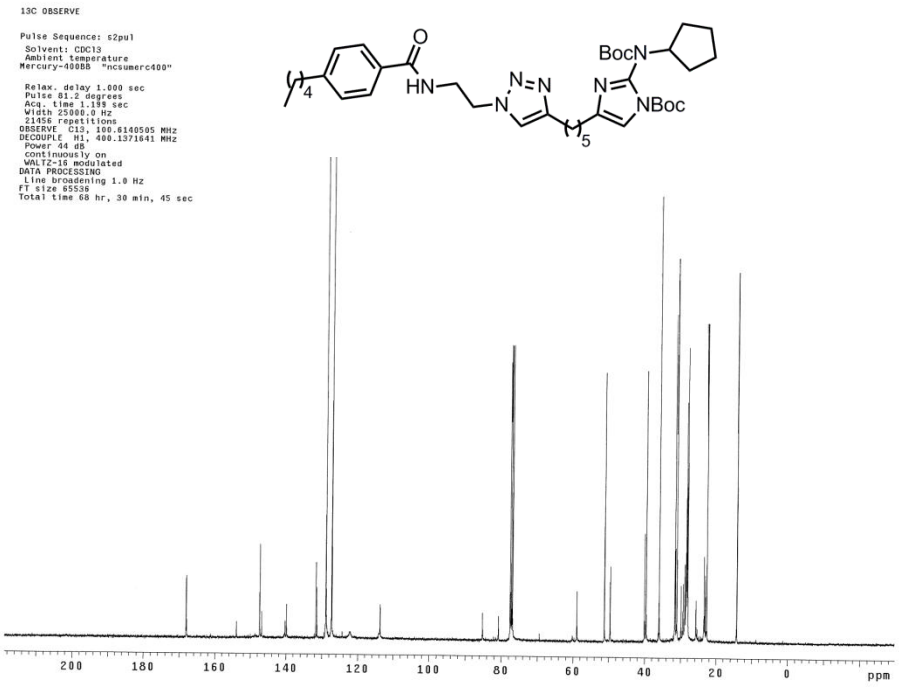
^{13}C NMR for **12i**



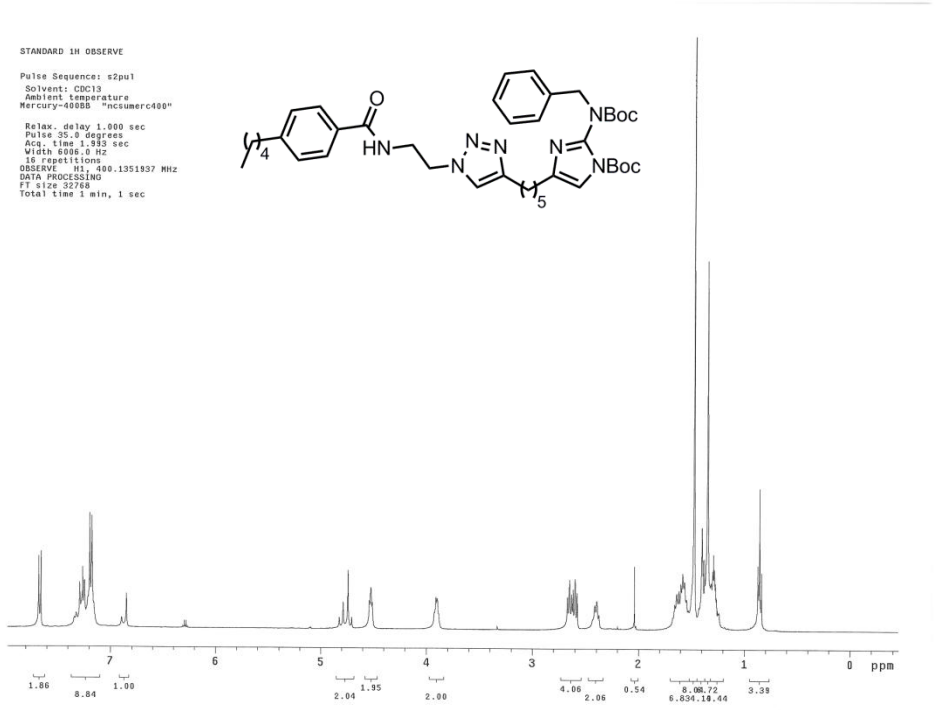
^{1}H NMR for **12j**



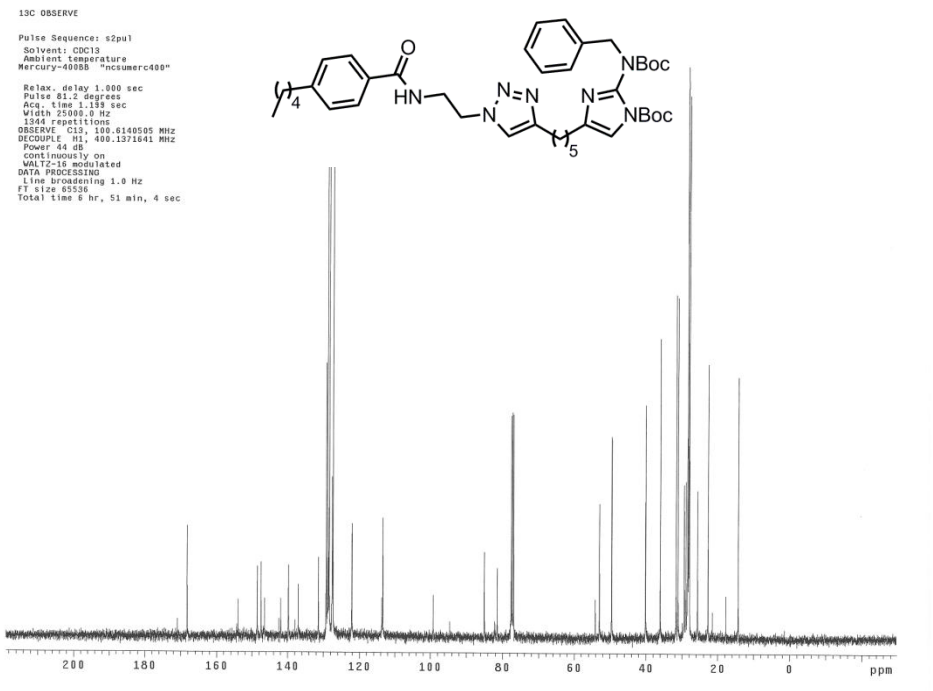
^{13}C NMR for **12j**



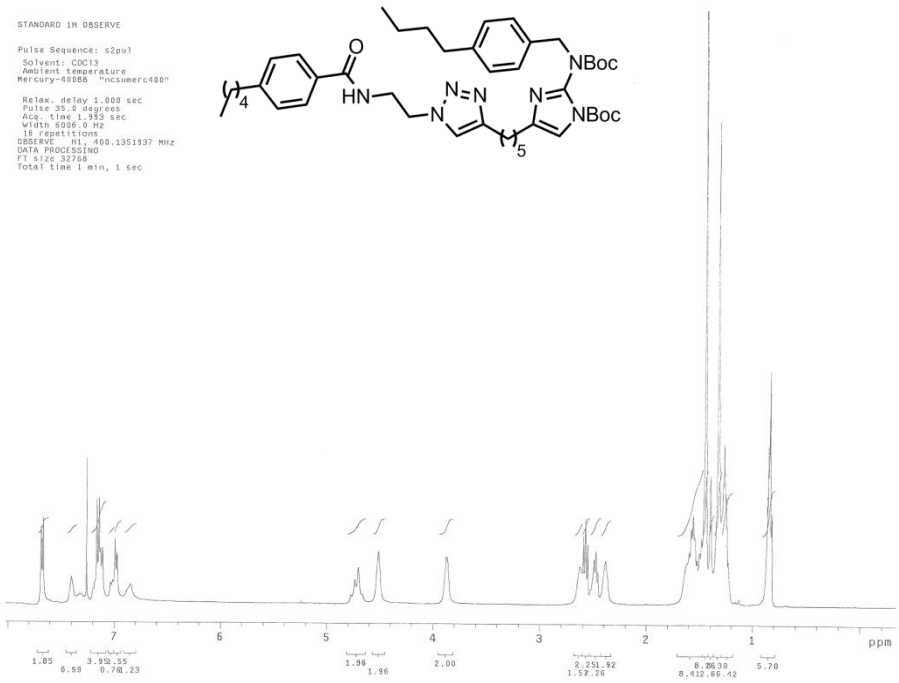
^{1}H NMR for **12k**



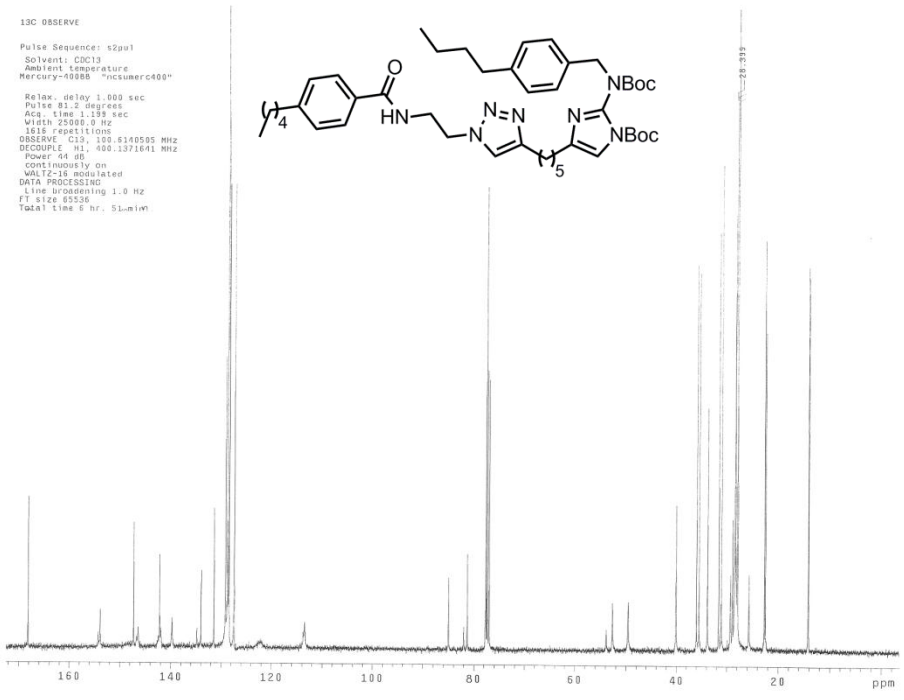
^{13}C NMR for **12k**



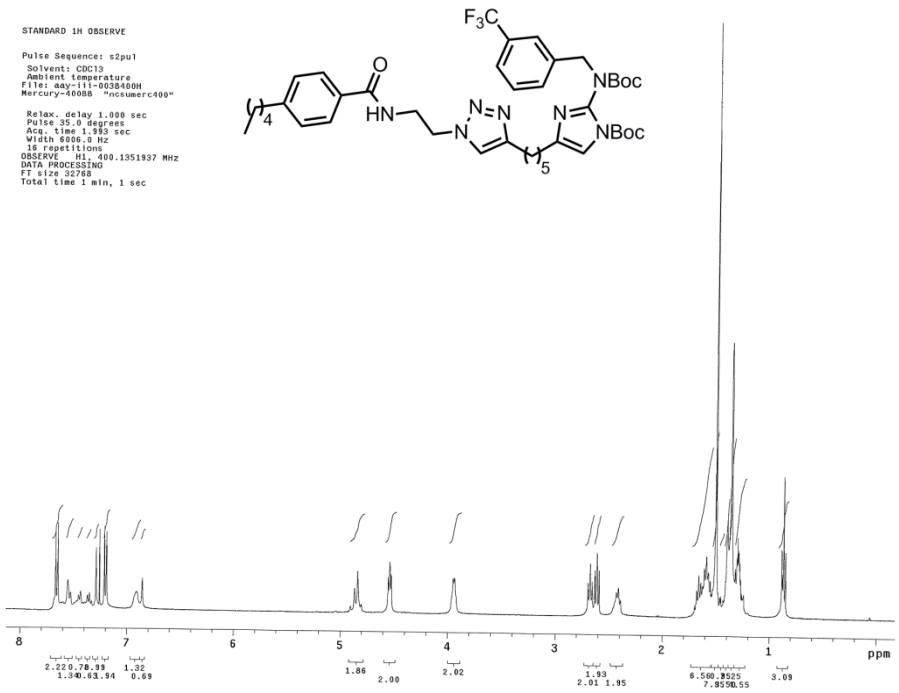
^{1}H NMR for **12l**



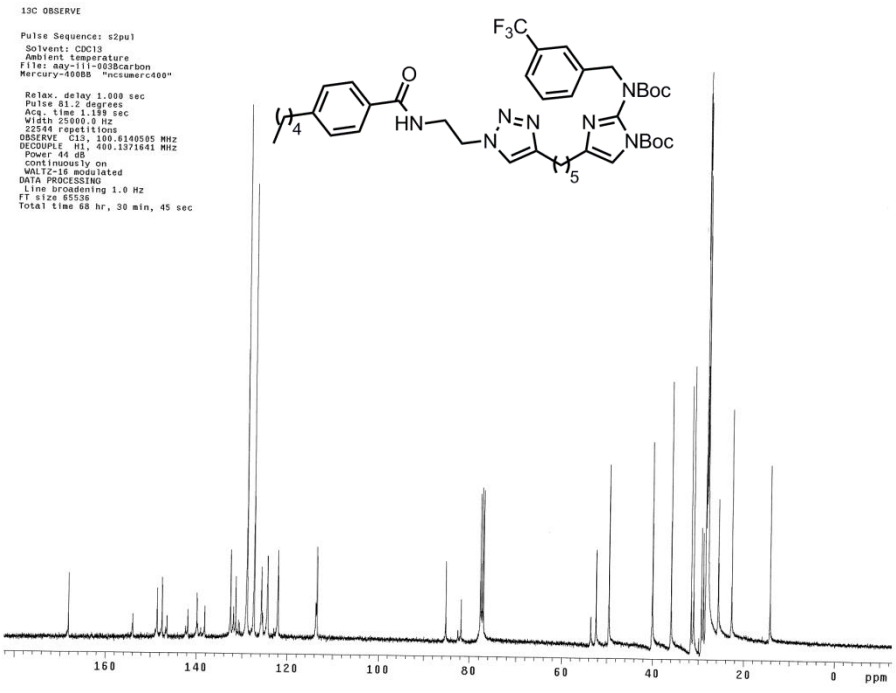
^{13}C NMR for **12l**



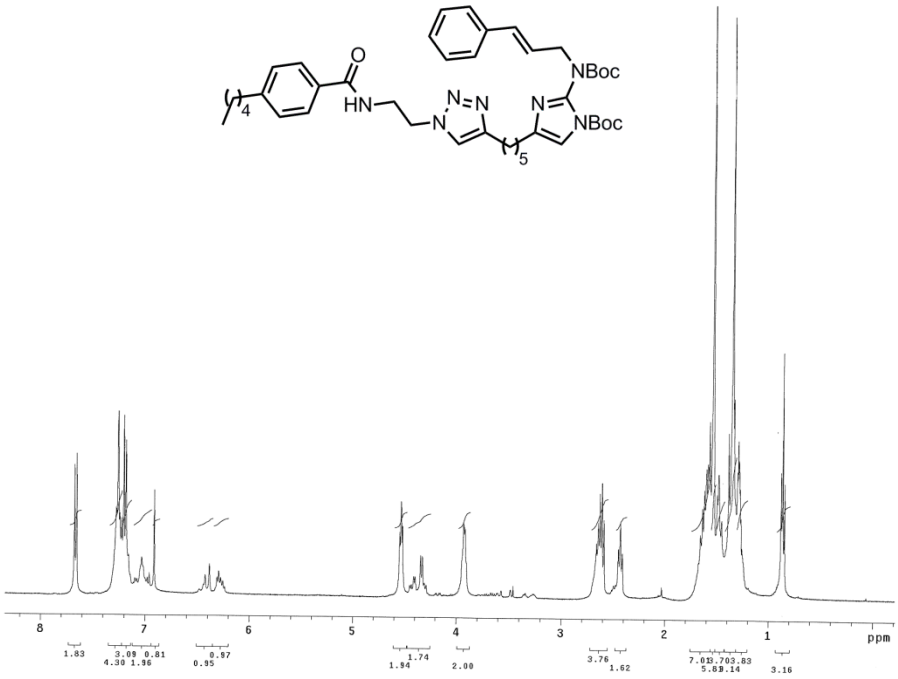
^{1}H NMR for **12m**



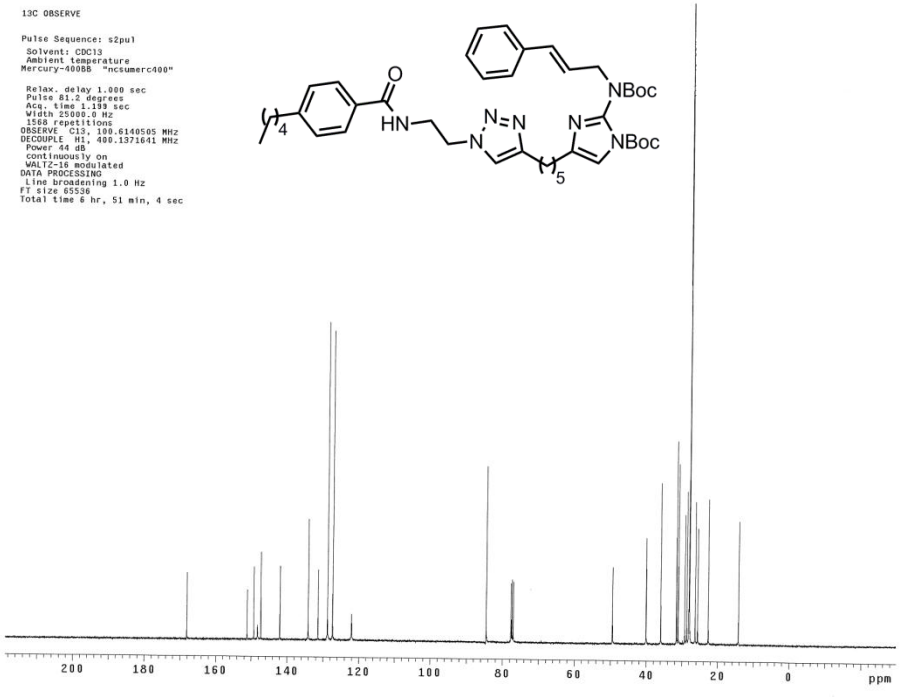
^{13}C NMR for **12m**



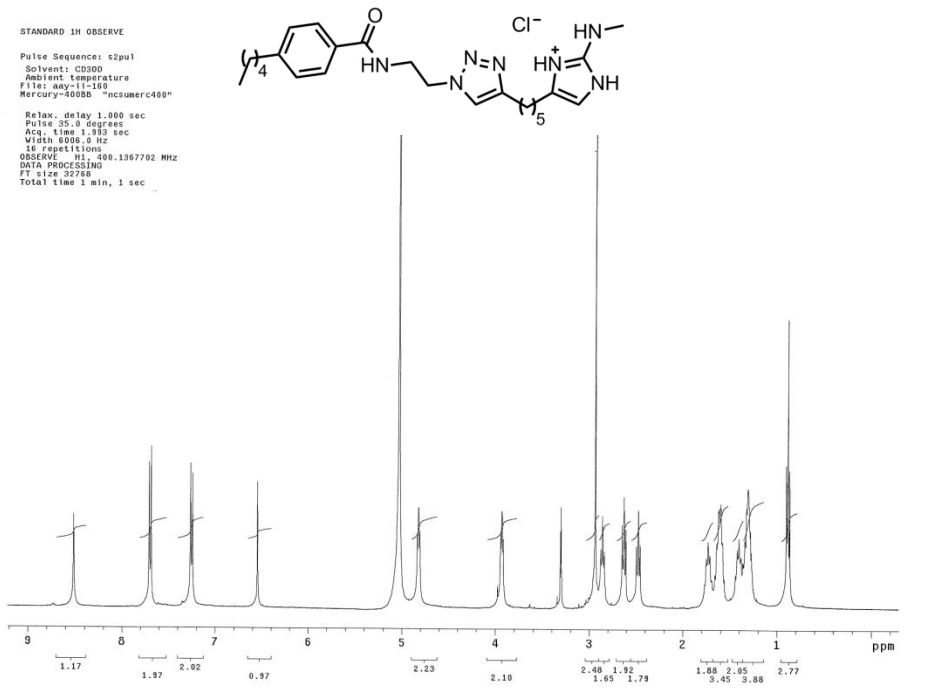
^{1}H NMR for **12o**



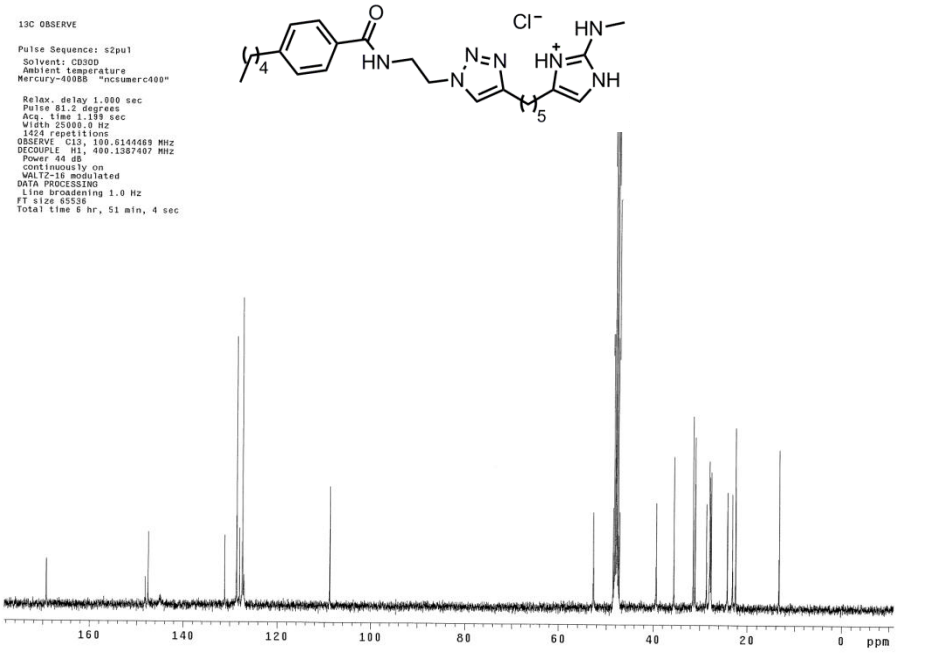
^{13}C NMR for **12o**



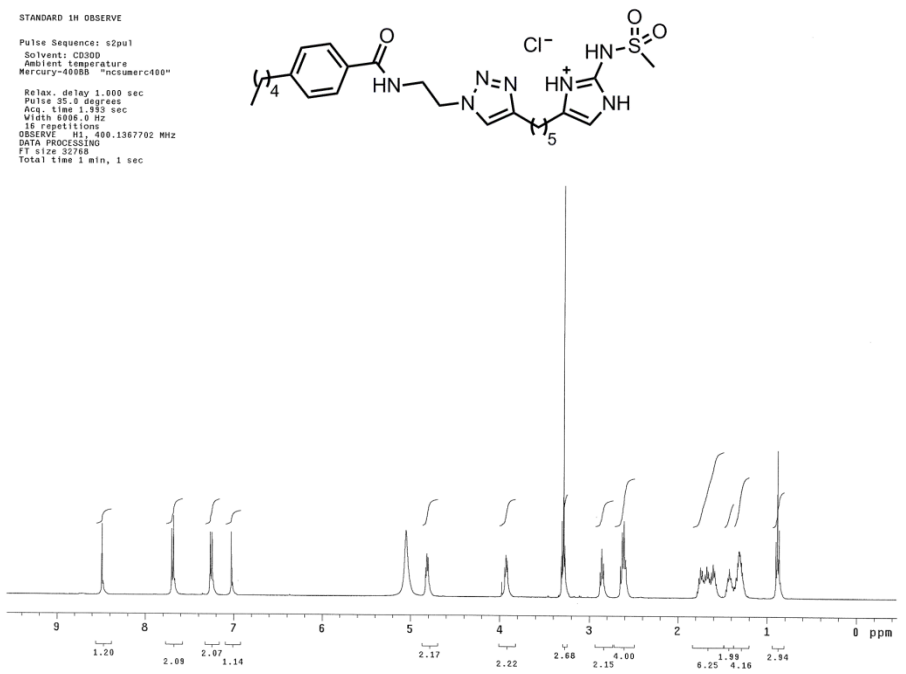
^{1}H NMR for **13a**



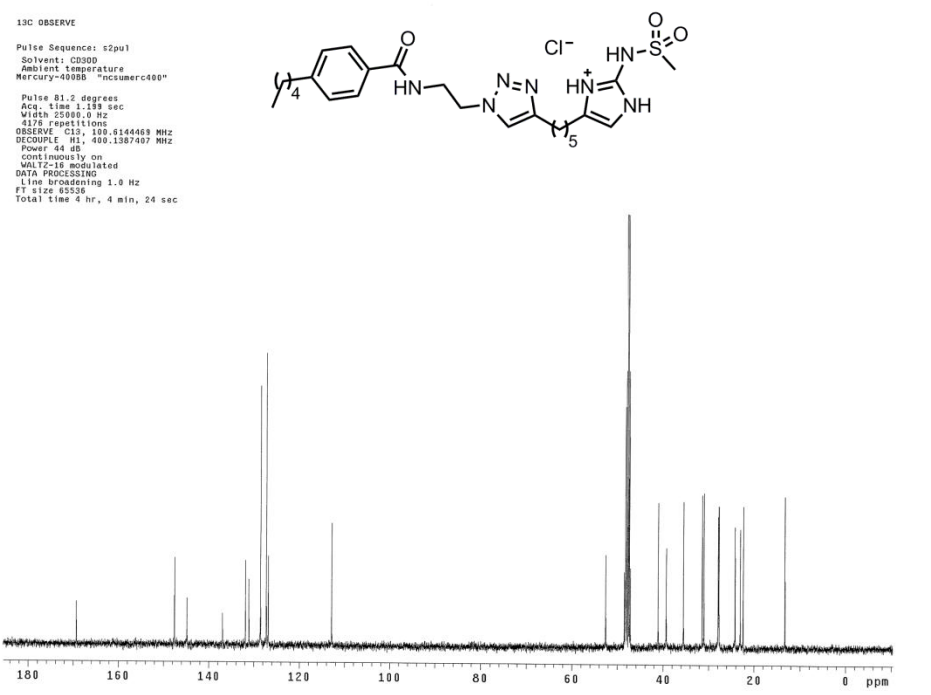
^{13}C NMR for **13a**



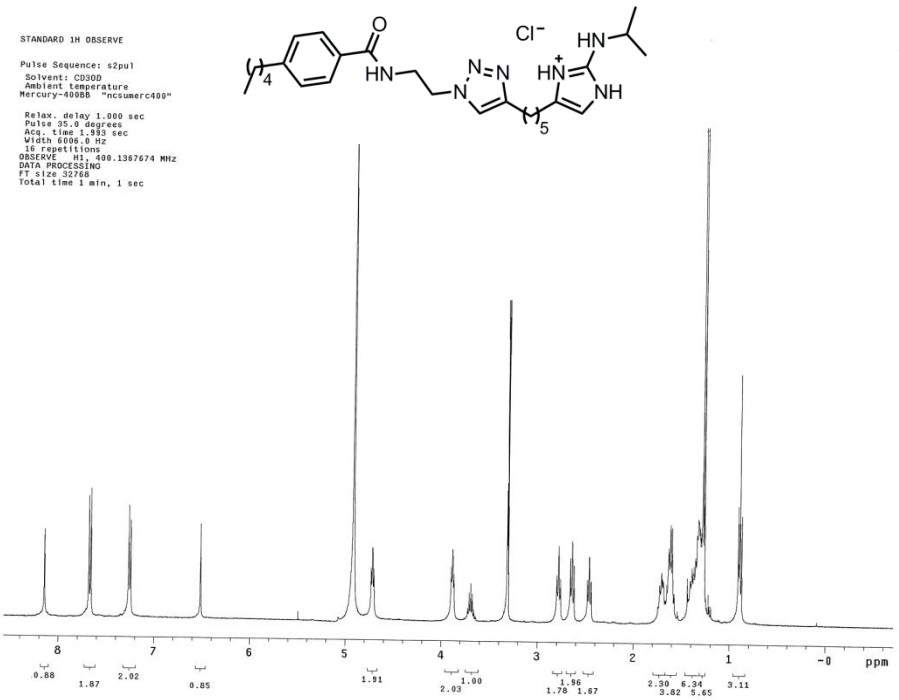
^{1}H NMR for **13b**



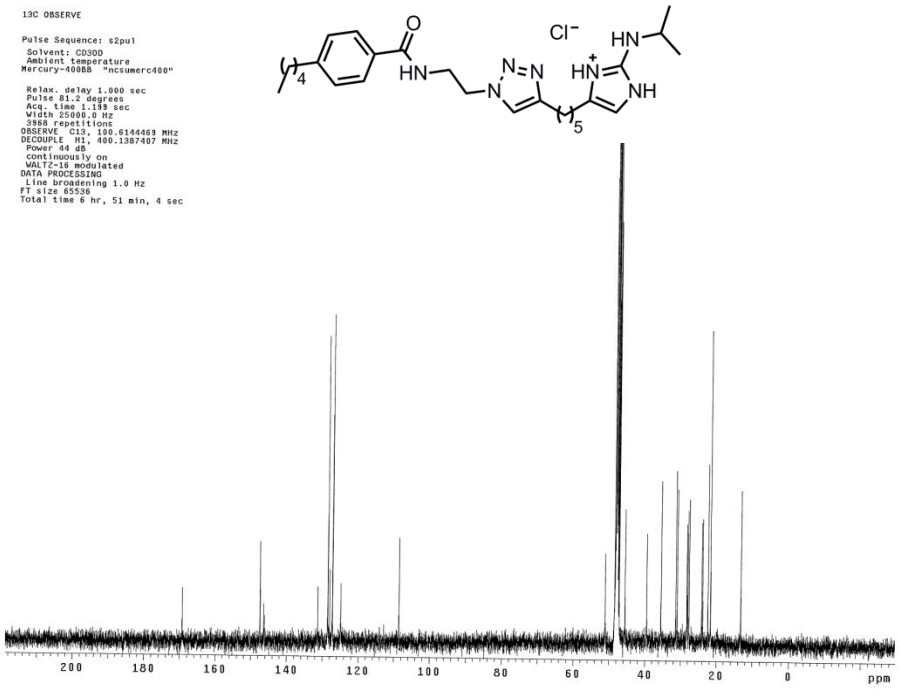
^{13}C NMR for **13b**



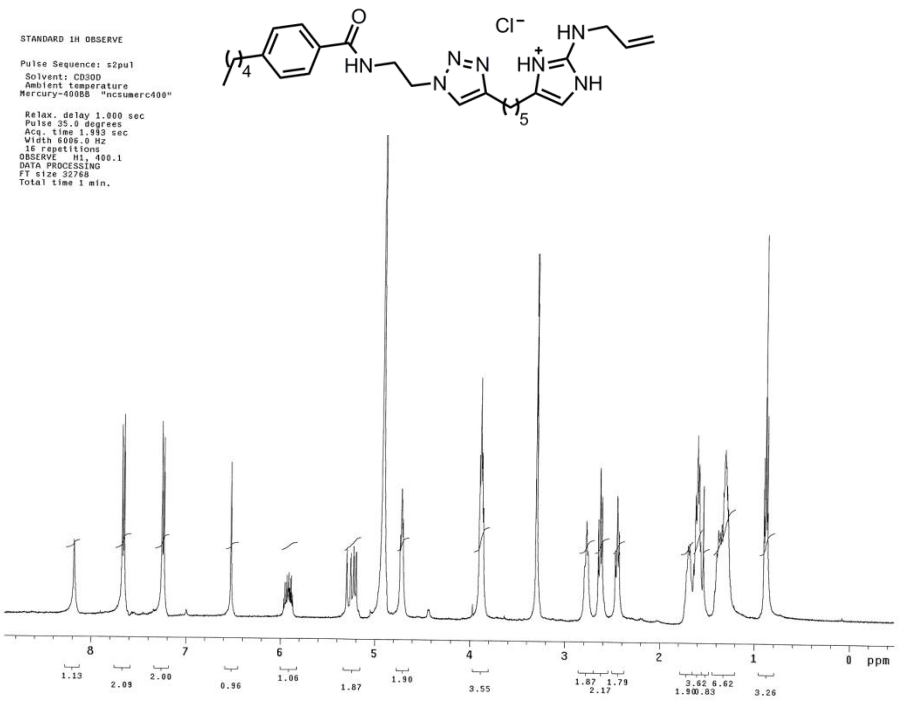
^{1}H NMR for **13c**



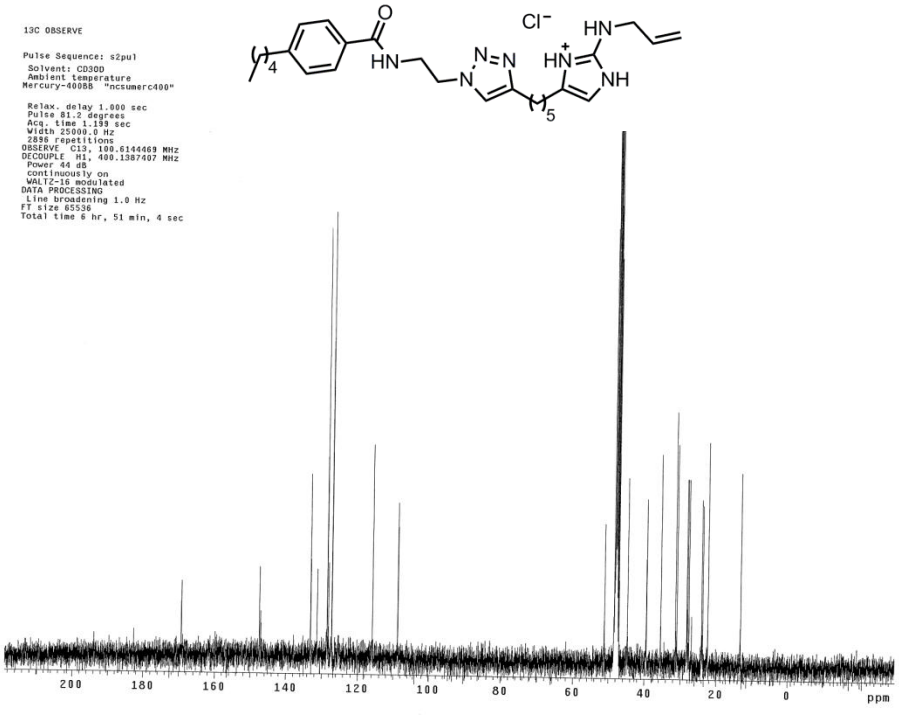
^{13}C NMR for **13c**



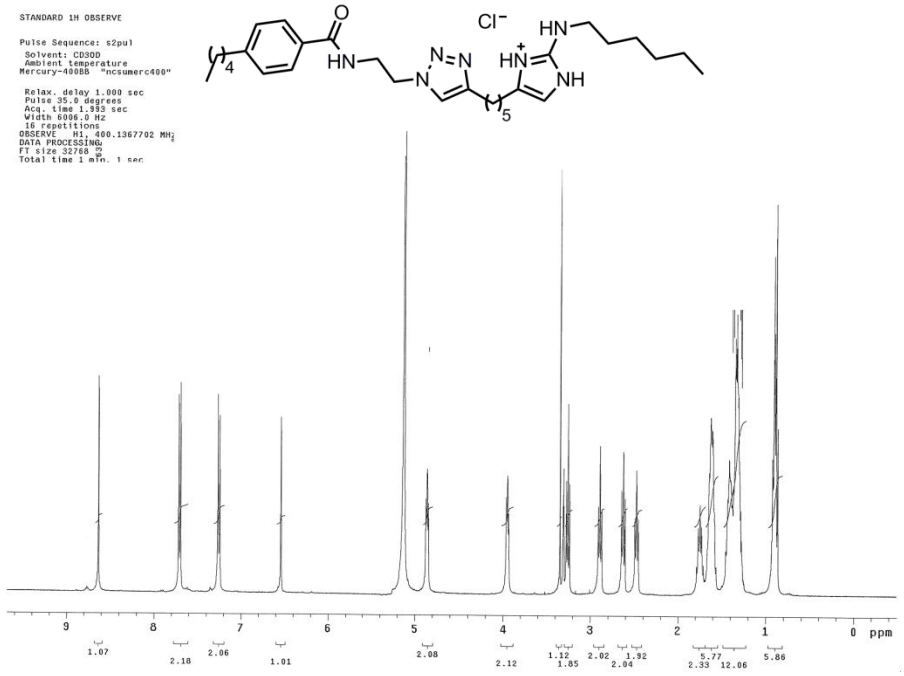
^{1}H NMR for **13d**



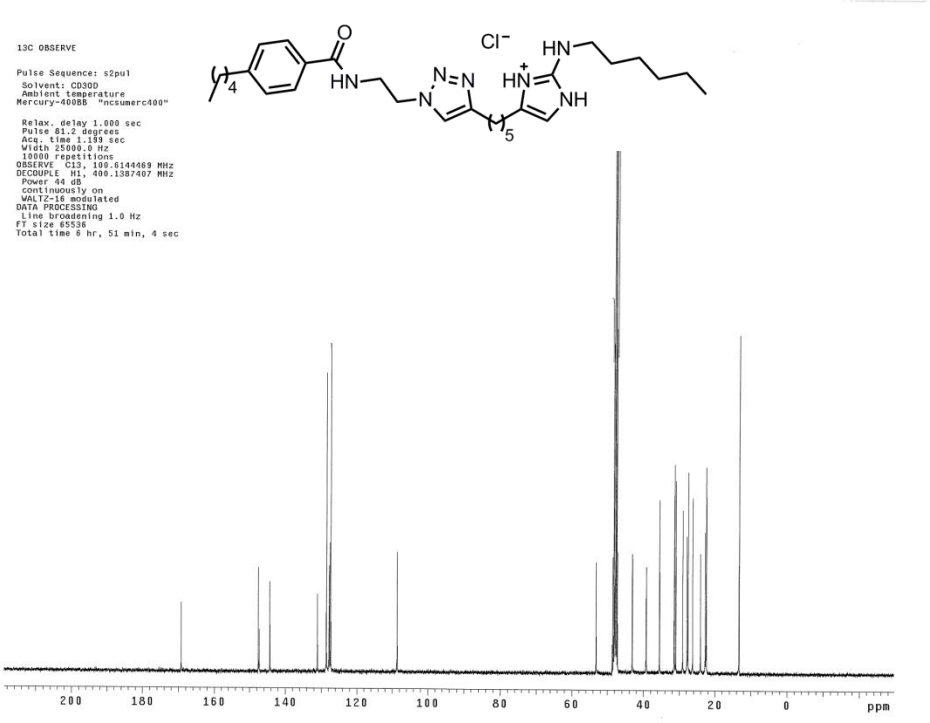
^{13}C NMR for **13d**



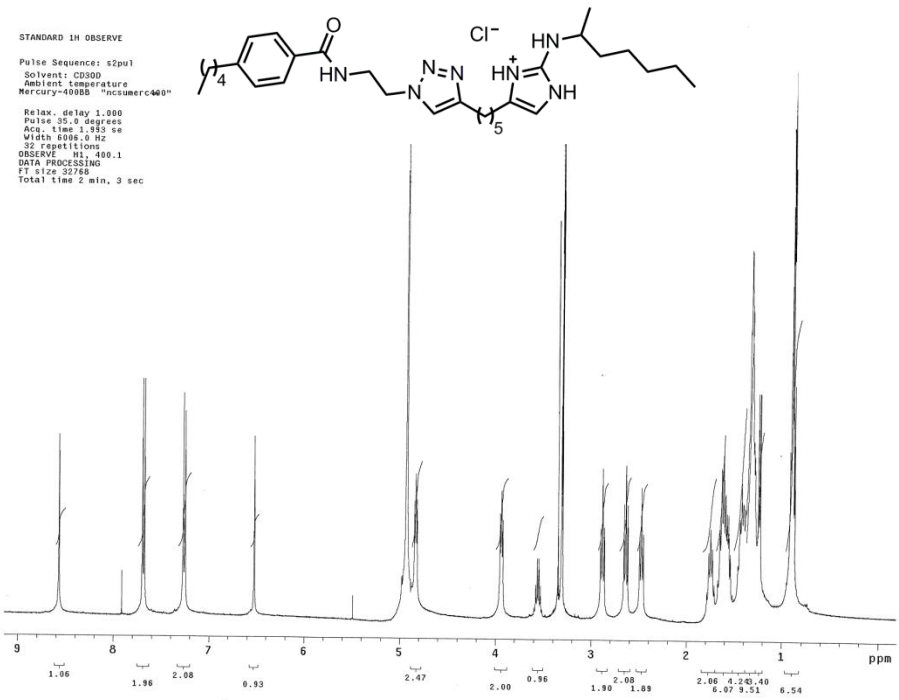
^{1}H NMR for **13e**



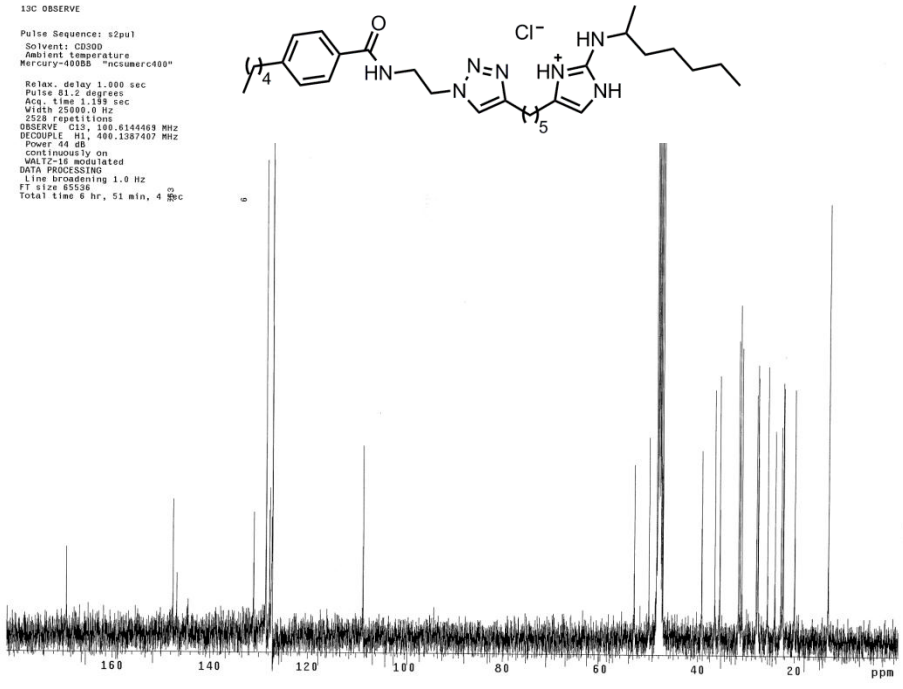
^{13}C NMR for **13e**



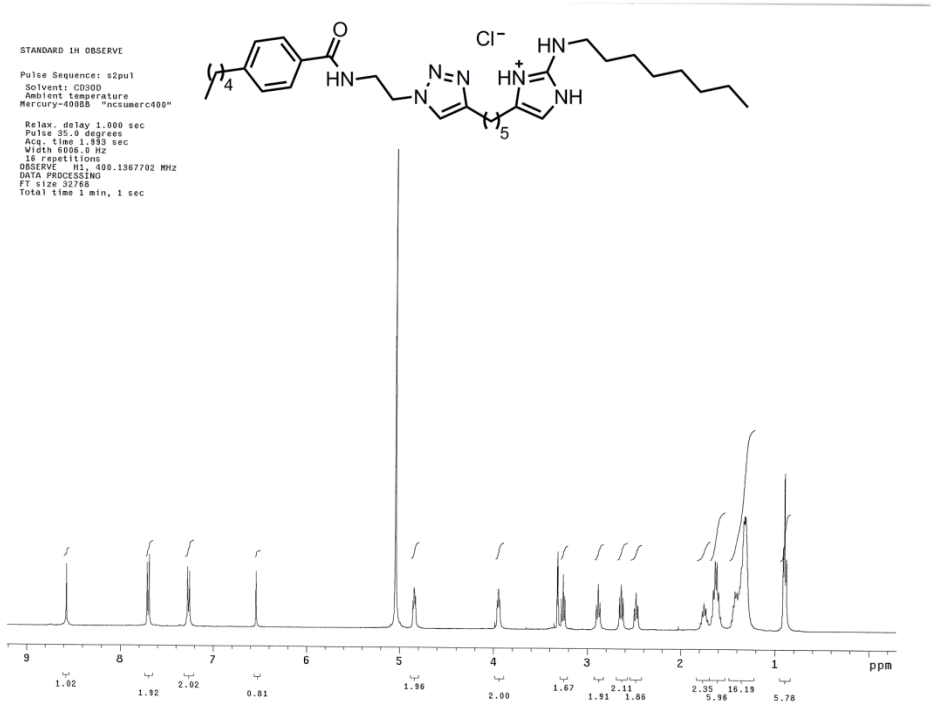
^{1}H NMR for **13f**



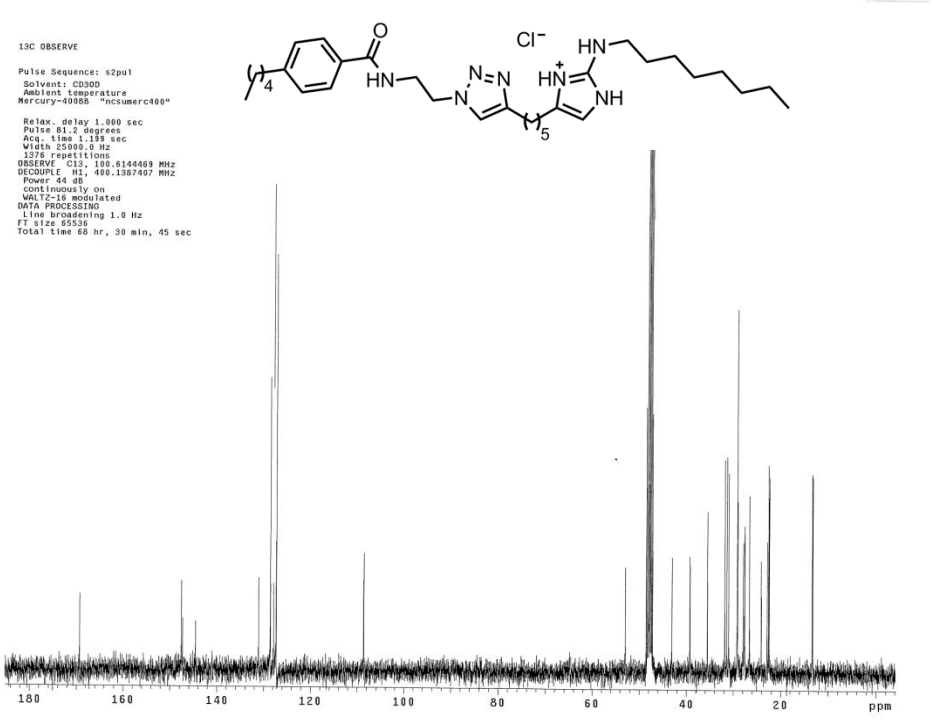
^{13}C NMR for **13f**



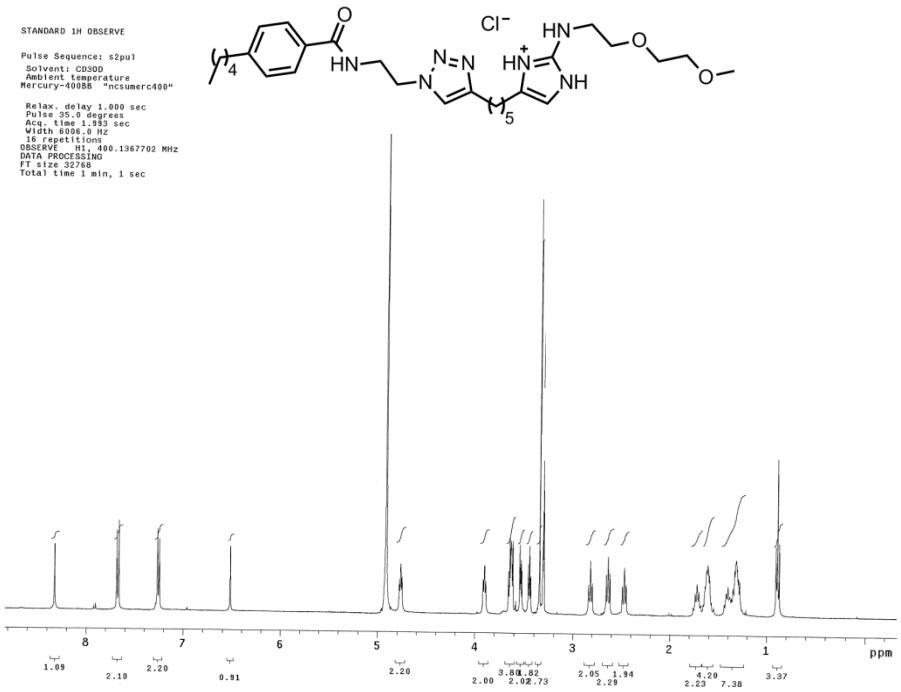
^{1}H NMR for **13g**



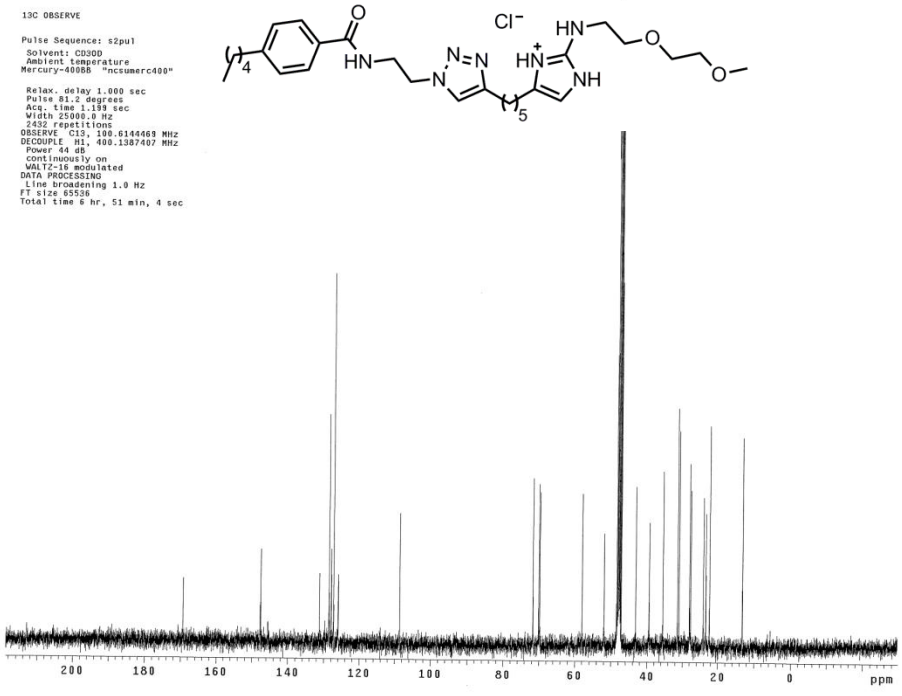
^{13}C NMR for **13g**



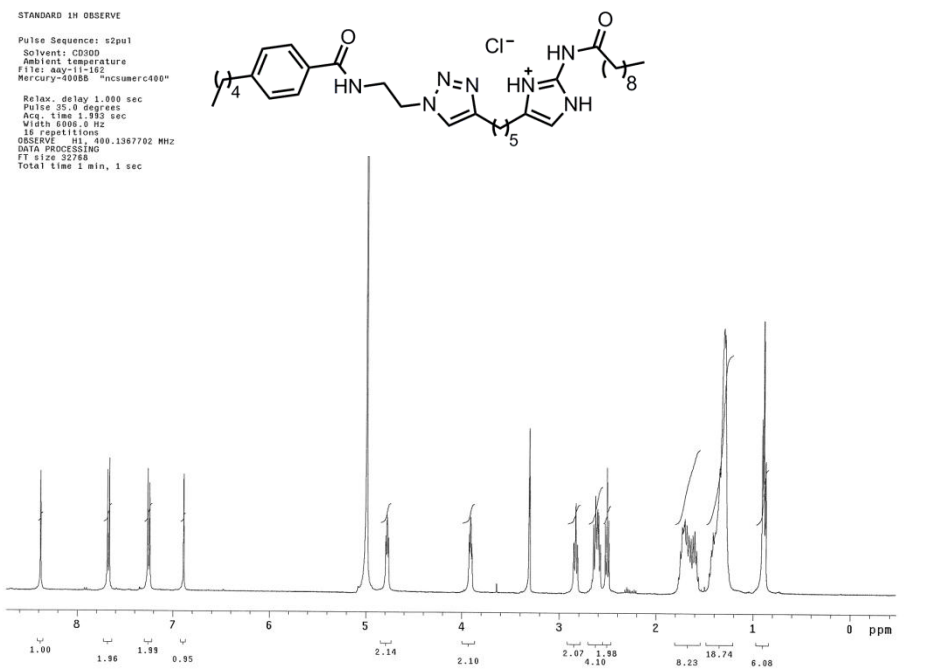
^{1}H NMR for **13h**



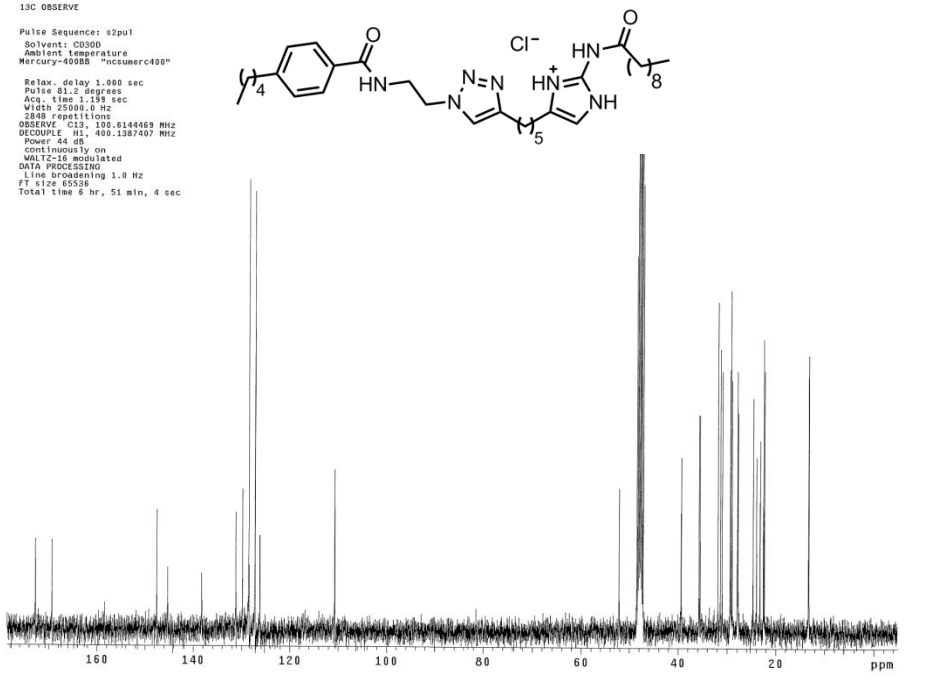
^{13}C NMR for **13h**



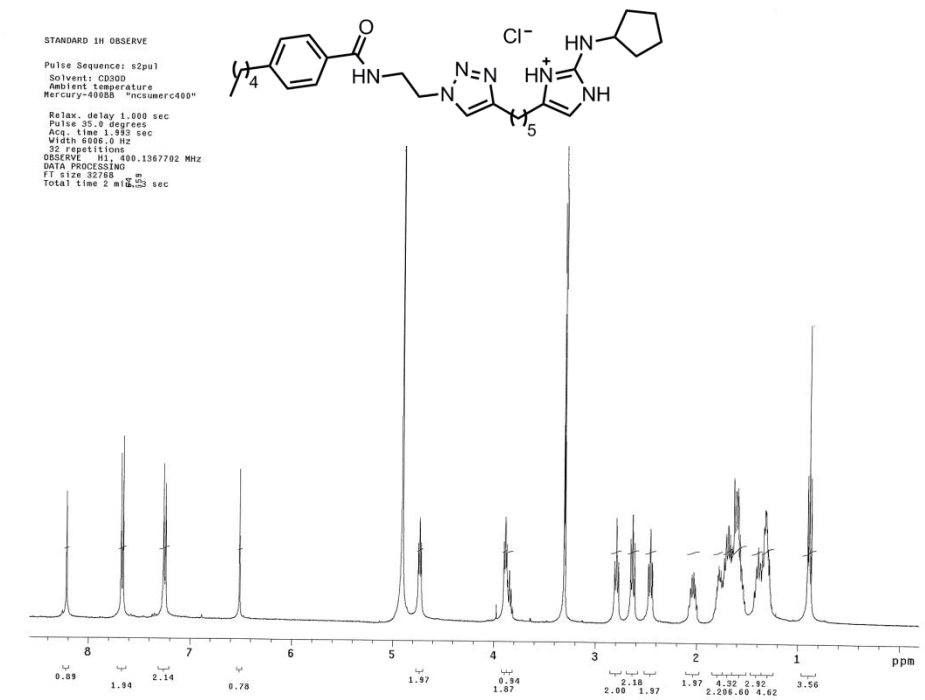
^{1}H NMR for **13i**



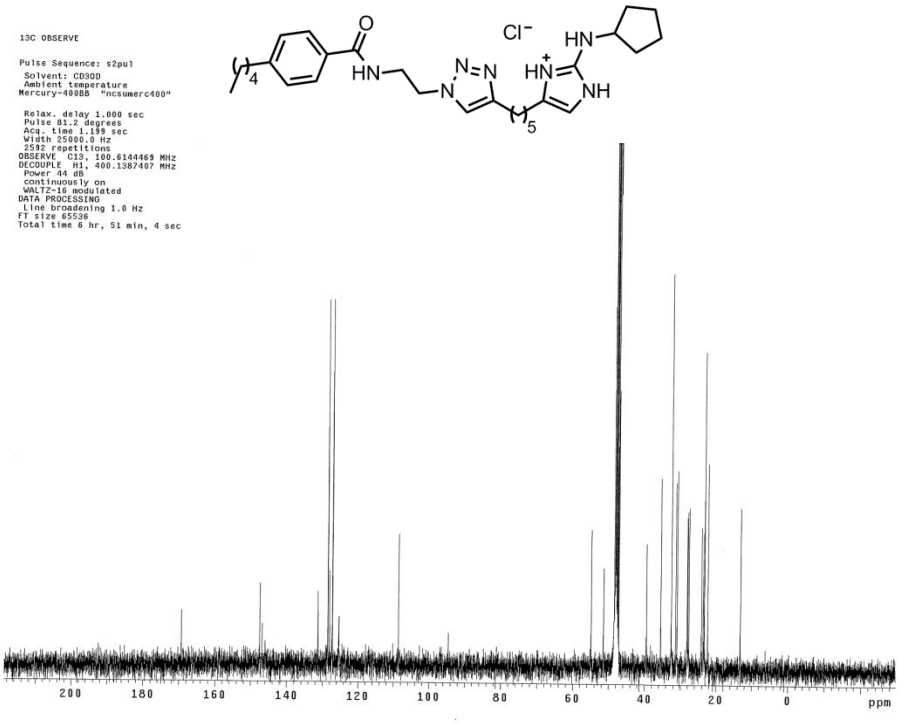
^{13}C NMR for **13i**



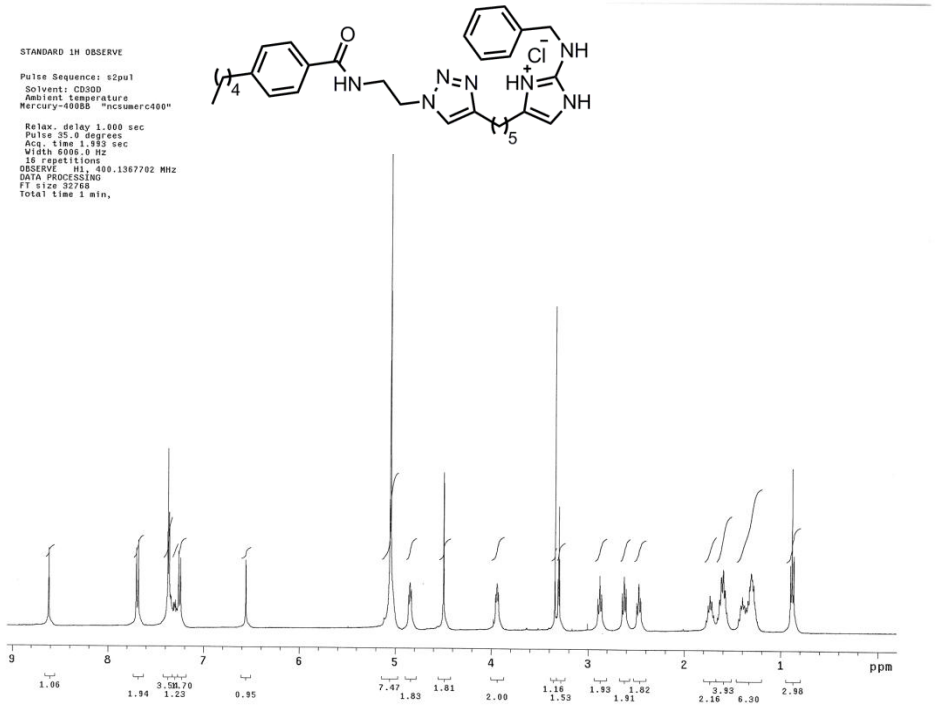
^{1}H NMR for **13j**



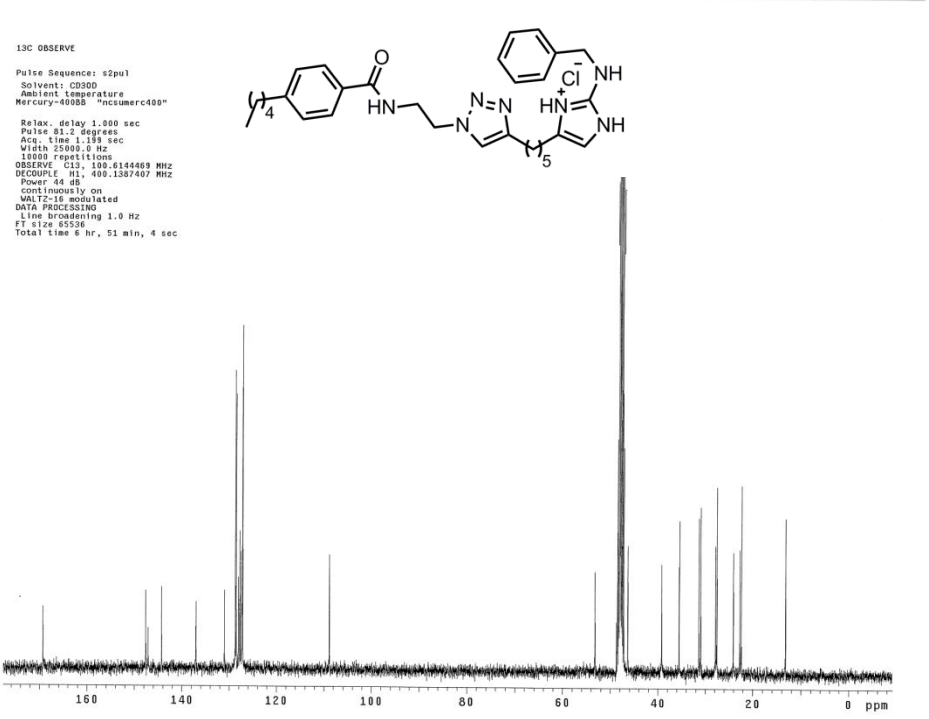
^{13}C NMR for **13j**



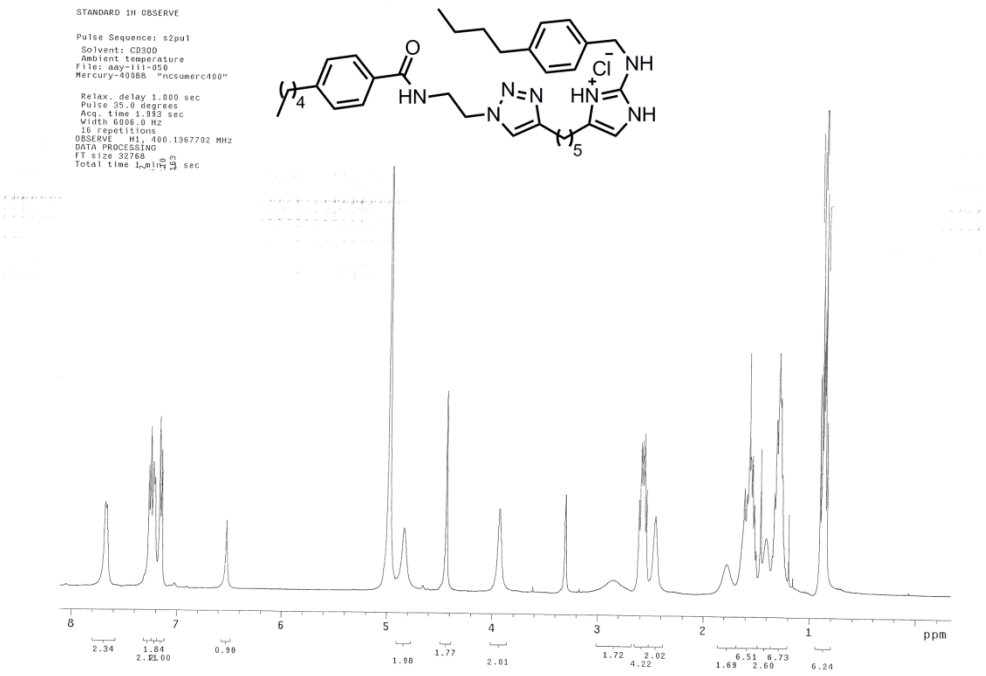
^{1}H NMR for **13k**



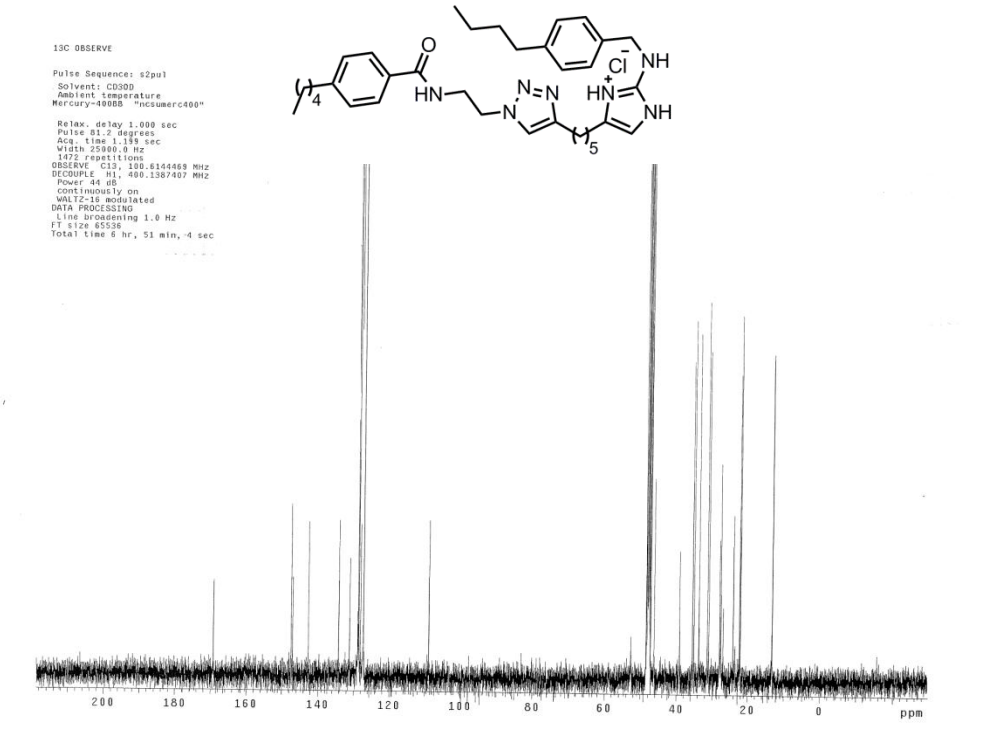
^{13}C NMR for **13k**



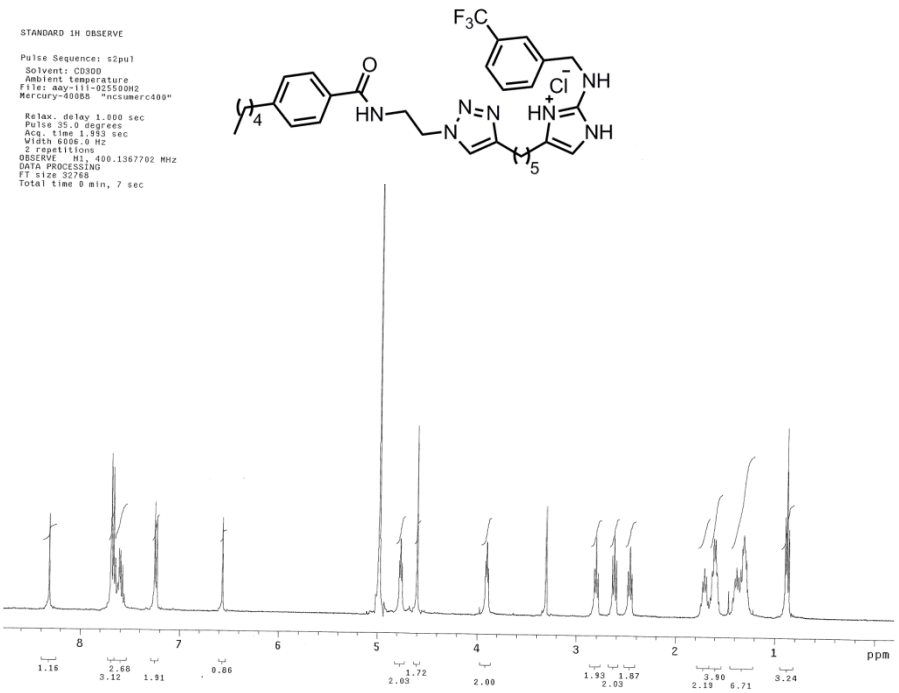
^{1}H NMR for **13l**



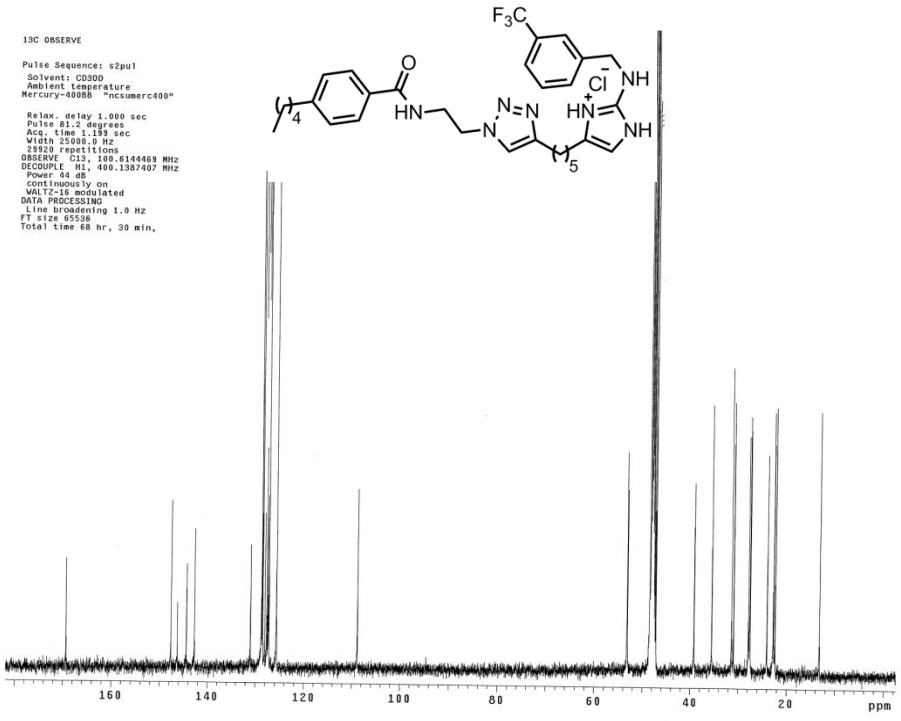
^{13}C NMR for **13l**



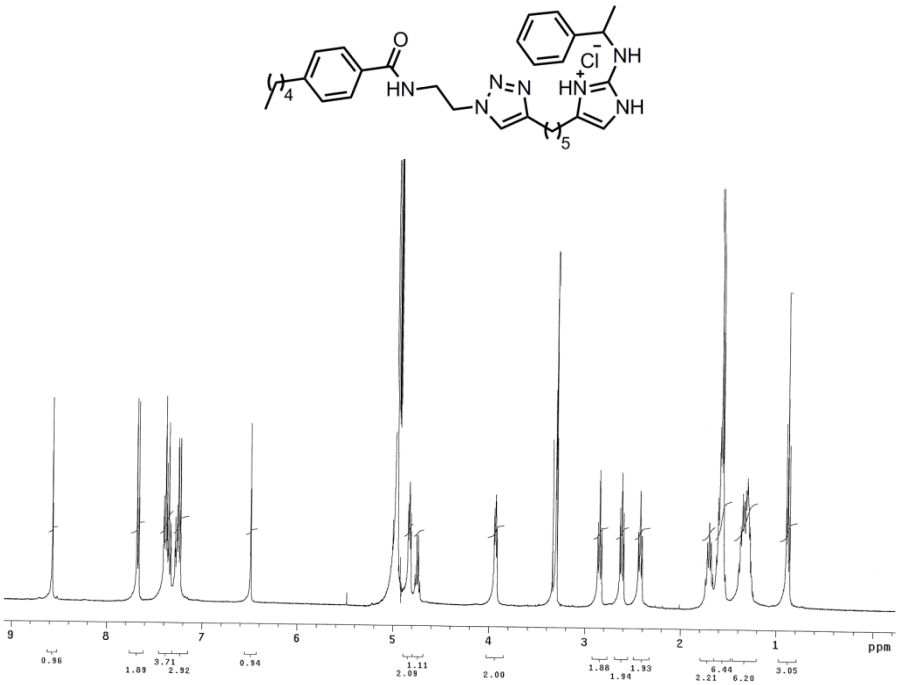
^{1}H NMR for **13m**



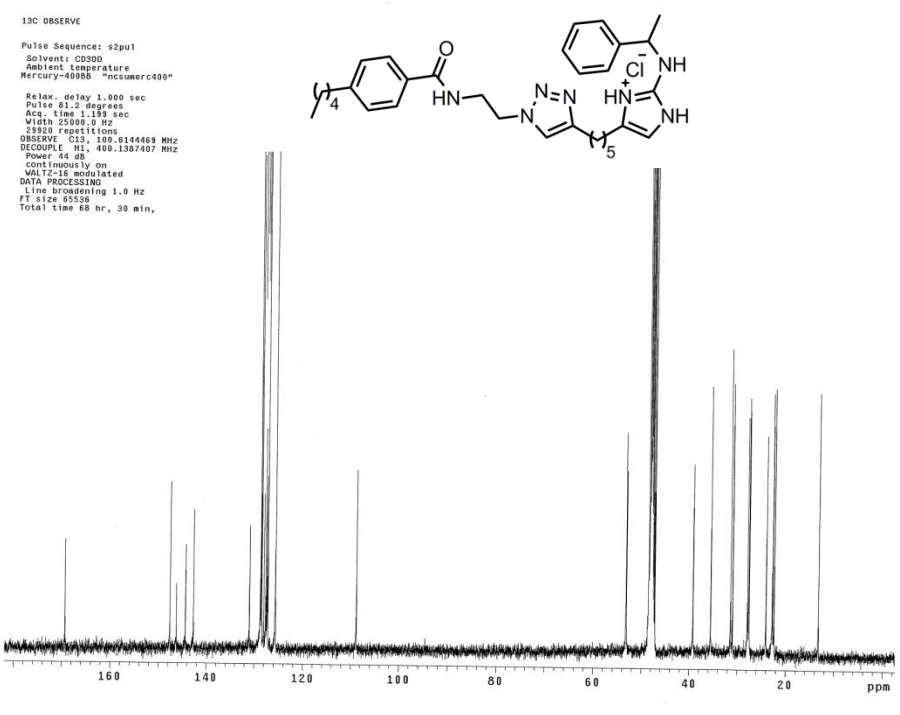
^{13}C NMR for **13m**



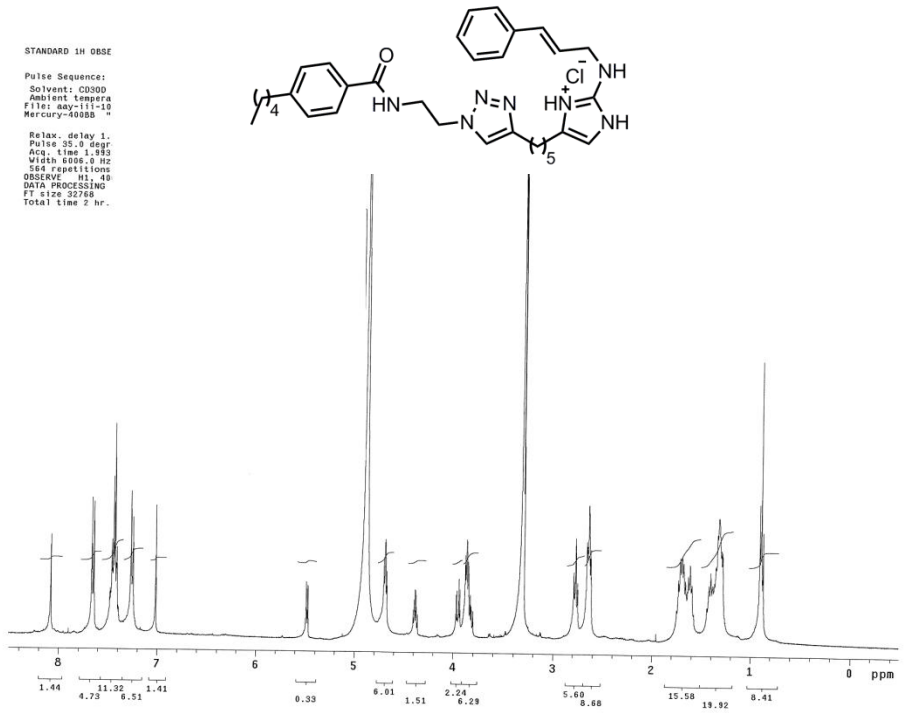
^{1}H NMR for **13n**



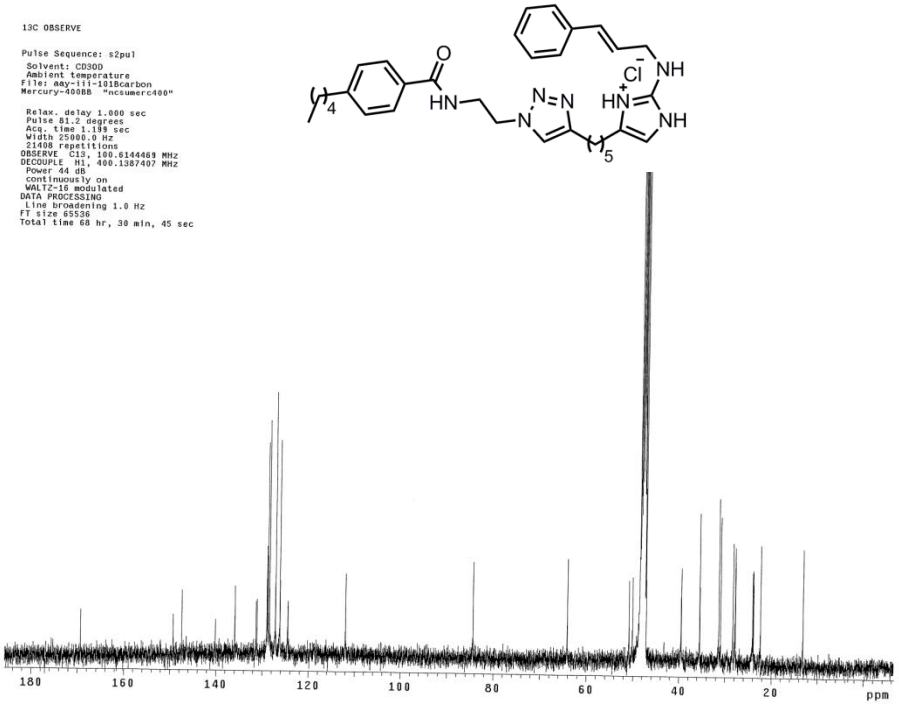
^{13}C NMR for **13n**



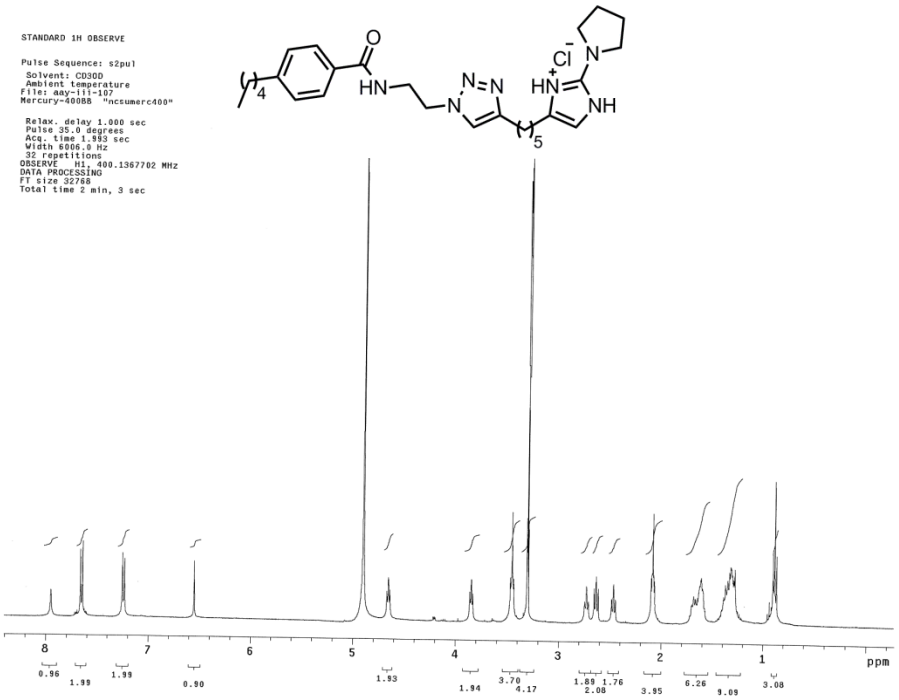
^{1}H NMR for **13o**



^{13}C NMR for **13o**



^{1}H NMR for **13p**



^{13}C NMR for **13p**