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Chemical Synthesis and Biological Screening of 2-Aminoimidazole-Based Bacterial and Fungal Antibiofilm Agents

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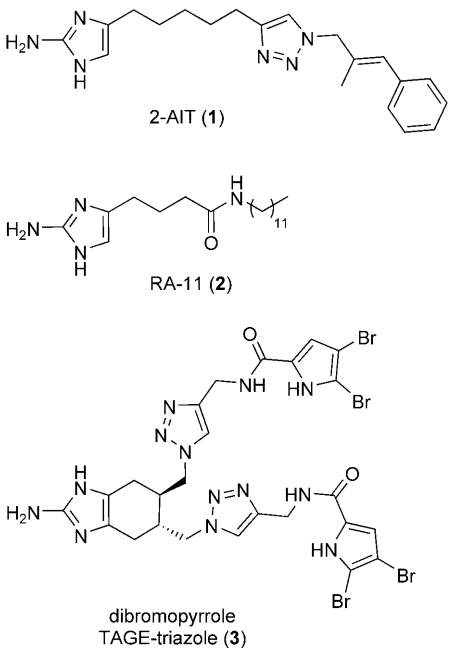
A collection of 2-aminoimidazole/triazole amides has been synthesized and screened for antibiofilm activity. This class of small molecules was found to modulate the biofilm activity of *Pseudomonas aeruginosa*, a multidrug-resistant strain of *Acinetobacter baumannii* (MDRAB), a methicillin-resistant *Staphylococcus aureus* strain (MRSA), *Escherichia coli*, *Rhodospirillum salexigens*, *Staphylococcus epidermidis*, *Vibrio vulnificus*, and vancomycin-resistant *Enterococcus faecium* as well as the yeast *Candida albicans* and *Cryptococcus neoformans*. Furthermore, lead compounds were found to not lyse red blood cells at active concentrations.

Introduction

A biofilm is defined as a surface-accreted microcolony that is surrounded by a self-produced extracellular polymeric matrix (EPS).[1] This EPS is a biosynthetic polymer composed of nucleic acids, polysaccharides, phospholipids, and proteins that acts dually as a cement and protective barrier against antibiotics and other generic microbicidal agents. It has been estimated that bacteria within a biofilm can display up to 1000-fold increased resistance to antibiotic treatment in comparison to their planktonic counterparts.[2] Since biofilms drive 80% of all bacterial infections,[3] this increased tolerance to antimicrobial therapy is detrimental to human health; causing many biofilm-related infections to become chronic.[4] Prolonged disease states can increase mortality rates as well as place significant financial burden on our health-care system.

Due to the ubiquitous nature of biofilm-driven disease, much attention has been focused on the development of small-molecule modulators of biofilm development.[5] We have previously shown that 2-aminoimidazole analogues (Scheme 1) are highly successful in inhibiting and dispersing bacterial biofilms through nonmicrobicidal mechanisms.[6–18] Within this class of molecules, 2-aminoimidazole triazole (2-AIT) conjugates[13] were the first small molecules reported to inhibit and disperse biofilms across bacterial order, class, and phylum. Further analogue development has yielded the dibromopyrrole TAGE-triazole conjugate **3**[11] as a potent inhibitor of *Staphylococcus aureus* biofilm formation and RA-11[17] as a highly potent inhibitor of *Pseudomonas aeruginosa* biofilm formation.

Recent advances in our understanding of pathogen behavior suggest that fungal and bacterial species can coordinate their behavior using small-molecule signals.[19] Therefore, molecules that control bacterial behavior might be able to control fungal behavior. Furthermore, given that fungal strains also form biofilms and represent an important pathogen target for biomedical science,[20] we became interested in determining whether we could identify 2-AI derivatives that were capable of inhibiting and dispersing fungal biofilms.



Scheme 1. Previously studied 2-AI antibiofilm agents.

Results and Discussion

Our first attempt focused on evaluating the ability of 2-AIT **1** to inhibit the formation of *Candida albicans* biofilms. Triazole **1** was deemed the most likely 2-AI derivative to inhibit the formation of fungal biofilms because of its broad-spectrum activity.[13]

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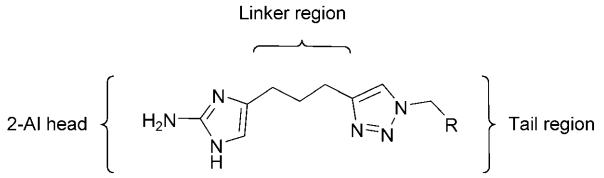
Compound **1** was screened at 100 μM for its ability to inhibit to the formation of *C. albicans* biofilms by using a crystal violet (CV) reporter assay.[21] Briefly, biofilms were allowed to form for 24 h in a 96-well microtiter plate in the absence or presence of 100 μM of **1**. The wells were subsequently washed thoroughly with water to remove free-floating and loosely adherent fungus and then treated with crystal violet. Crystal violet stains the remaining surface-attached fungus (i.e., the biofilm), which following solubilization, can be quantified by spectrophotometry (A_{540}).

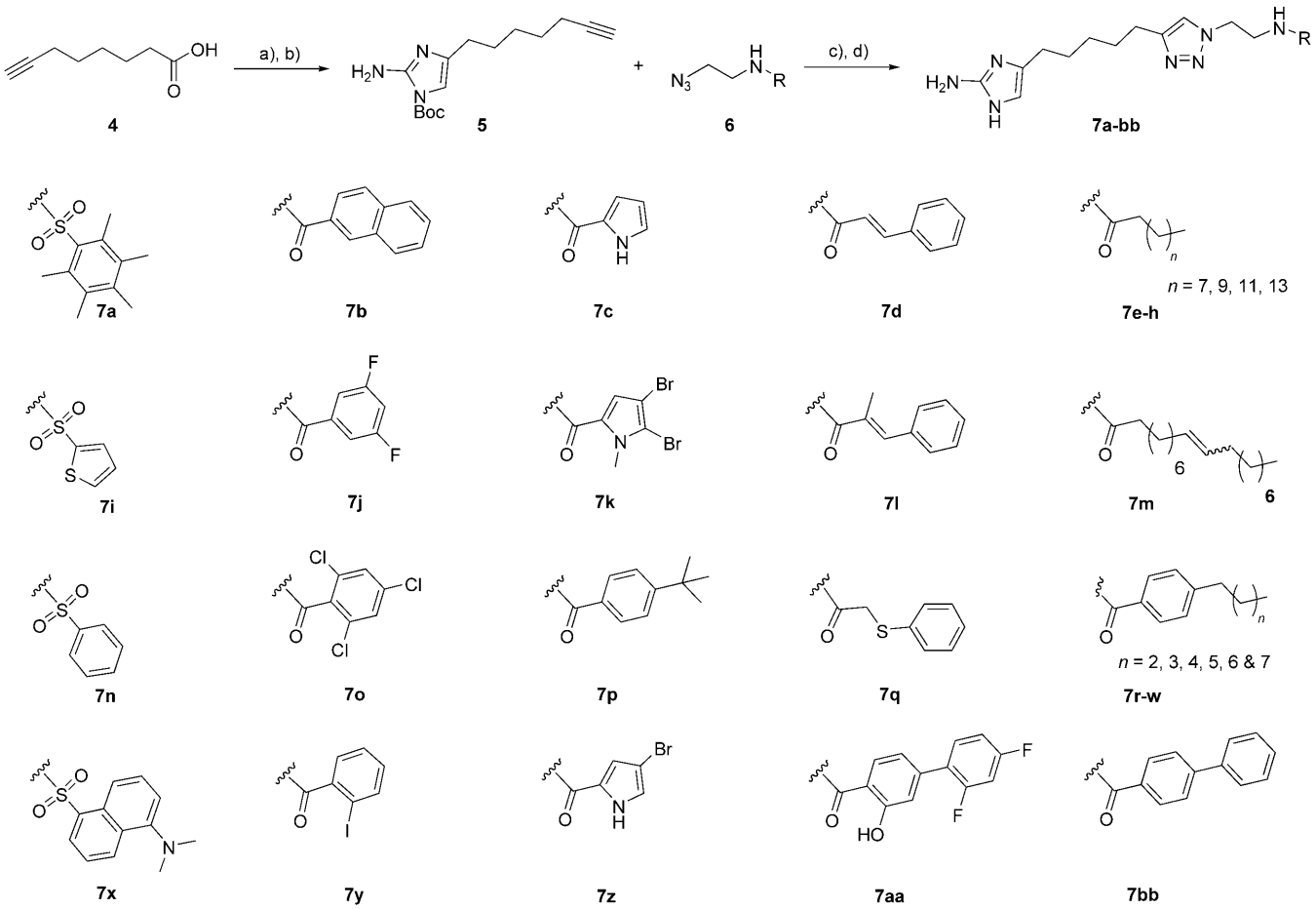
Compound **1** was able to inhibit *C. albicans* formation by 12% at 100 μM. Follow-up growth curves at 100 μM demonstrated that this antibiofilm activity was nonfungicidal.



Scheme 2. 2-AI structure analysis.

With this initial success, we asked the question whether analogue synthesis could deliver alternative 2-AIT derivatives with enhanced anti-fungal-biofilm activity. Previous work in our laboratory had demonstrated that 2-AI-based inhibitors of biofilms can be subdivided into three separate sections:[18] 1) the 2-AI head, 2) the linker region, and 3) the tail region (Scheme 2). Structure–activity relationship (SAR) data indicate that selectivity and activity can be tuned/enhanced by modification of the tail region.[6–18] Based upon these data, we elected to synthesize a new pilot collection of 2-AI derivatives for antibiofilm testing in which diversity could be rapidly achieved by substituents on the triazole ring through commercially available carboxylic acids.

The synthetic approach to this 2-AIT derivatization is outlined in Scheme 3. In our previous synthesis of 2-AIT conjugates,[13] we employed the alkyne-derived 2-AI as a precursor for the Cu^{I}-mediated[3+2] alkyne/azide cycloaddition (click reaction).[22] Although this reaction worked well, purification of the resulting product was cumbersome, due to the need for copious amounts of ammonia saturated methanol for column chromatography. Therefore, we decided to revise the route by employing a Boc-protected 2-AI alkyne that would allow more traditional means of purification (i.e., methanol/dichloromethane



Scheme 3. Synthesis of triazole-substituted 2-AI derivatives. a) i: $(COCl)_2$, CH_2Cl_2, DMF (cat.), ii: CH_2N_2, Et_2O/CH_2Cl_2, iii: HBr (82%); b) Boc-guanidine, DMF, RT (59%); c) azide, $CuSO_4$, Na ascorbate, EtOH, CH_2Cl_2, H_2O; d) trifluoroacetic acid, CH_2Cl_2 (58–94% over two steps).

columns). The Boc-protected scaffold was synthesized from oct-7-ynoic acid by treatment with oxayl chloride followed by diazomethane and quenching of the resulting α-diazo ketone with HBr to generate the intermediate α-bromo ketone. Cyclization with Boc-guanidine then delivered the target 2-AI alkyne **5**.[23]

Once **5** had been synthesized, we assembled a diverse array of azido amides to employ in the click reaction to create our pilot collection of 2-AIT conjugates. Briefly, 2-bromo-ethylamine was treated with sodium azide to deliver 2-azido-ethylamine, which following acylation (via the respective acid chloride) generated the azido amides for elaboration into the 2-AIT collection. Each azido amide was then subjected to the click reaction with **5**. Boc-deprotection (TFA/CH_2Cl_2) followed by counterion exchange (trifluoroacetate for chloride) delivered the target 2-AIT compounds for antibiofilm screening.

Each 2-AIT conjugate was assayed at 100 μM for its ability to inhibit the formation of *C. albicans* biofilms by using the CV reporter assay. From this assay, derivatives **7f** and **7m** were determined to be the most potent. Subsequent dose–response studies revealed that **7f** had an IC_{50} of 2.9 μM while **7m** had an IC_{50} of 3.3 μM (Table 1). Growth-curve and colony-count analysis of **7f** and **7m** at respective IC_{50} values demonstrated their antibiofilm activity to be nonfungicidal.

Table 1. Fungal biofilm data.

Compound	IC_{50} [μM]	EC_{50} [μM]	Compound	IC_{50} [μM]	EC_{50} [μM]
C. albicans			*S. cerevisiae*		
7f	2.9 ± 0.7	37.2 ± 5.7	**7g**	2.7 ± 0.1	207.4 ± 7.3
7m	3.3 ± 1.6	24.7 ± 4.5	**7h**	50.4 ± 2.2	353.7 ± 7.3
C. neoformans			**7j**	130.6 ± 16.9	> 400
7e	1.3 ± 0.3	–			
7m	8.0 ± 3.4	–			

Next, we addressed whether **7f** and **7m** could disperse preformed *C. albicans* biofilms. *C. albicans* was allowed to establish biofilms in a 96-well microtiter plate for 24 h. The plate was then washed to remove any free floating or loosely adherent fungus. 2-AIT **7f** or **7m** was then added to each well at 75 μM, and the plate was incubated at 37 °C for 24 h. The wells were then washed with water and stained with CV to quantify any remaining biofilms. In comparison to biofilms treated with medium only, compound **7f** dispersed 56%, while **7m** dispersed 62% of the biofilm. Once we had established that both compounds could disperse preformed biofilms, the effect was quantified by determining **7f** and **7m**'s EC_{50} values against preformed *C. albicans* biofilms. Here, EC_{50} is defined as the concentration at which the compound will disperse 50% of a preformed biofilm. Dose–response studies revealed EC_{50} values of 37.2 μM and 24.7 μM for **7f** and **7m**, respectively (Table 1). From a medical perspective, molecules that simply inhibit the formation of a biofilm could be used in a prophylactic sense; however, given that a majority of patients already have an established biofilm infection when they seek medical intervention, molecules that are effective against a preformed biofilms are more clinically significant.

Once we had established that these next-generation 2-AIT conjugates had the ability to inhibit and disperse *C. albicans* biofilms, we addressed whether these compounds would also inhibit and disperse biofilms from *Cryptococcus neoformans*, an opportunistic fungal strain known to infect immunosuppressed patients, especially those with HIV infections.[24] Initial screening of our 2-AIT derivatives showed that **7e** and **7m** had potent antibiofilm activity against *C. neoformans*. Follow up dose–response studies revealed IC_{50} values of 1.3 μM and 8.0 μM (Table 1). Comparison of fungal growth in the presence or absence of either compound indicated that they were not fungicidal. Unfortunately, neither compound was able to disperse preformed *C. neoformans* biofilms. We are currently trying to identify analogues of these two compounds that would.

After demonstrating that the 2-AIT conjugates had activity against opportunistic fungal strains, we wanted to investigate this library's activity against Gram-negative and -positive bacterial biofilms. (It has been shown that a select number of small molecules are employed in cross-kingdom communication.[19]) As representative Gram-negative pathogens, we chose multidrug-resistant *Acinetobacter baumannii* (MDRAB), *E. coli*, and *Pseudomonas aeruginosa* (strains PAO1 and PA14). Two representative marine-based bacteria were chosen: *Vibrio vulnificus and Rhodospirillum salexigens*. As representative Gram-positive pathogens, MRSA, vancomycin-resistant enterococci (VRE) and *Staphylococcus epidermidis* were chosen.

Each 2AIT was screened at 100 μM against each bacterial strain for the ability to inhibit biofilm formation as assessed by the CV reporter assay.[25] As with the fungal studies delineated above, the strongest compounds with the highest percentage inhibition were screened at various concentrations so that IC_{50} values could be calculated from the dose–response curves. Active compounds were then screened for their ability to disperse preformed biofilms. The dispersal capability of each active compound was quantified by determining their EC_{50} values. Finally, toxicity studies were performed for all compounds reported, and they were found to be nonmicrobicidal at their IC_{50} values.

Against the Gram-negative bacterial strains, 2-AIT conjugates with *para*-alkyl phenyl substituents displayed the strongest antibiofilm activity, which could be tuned by methylene chain length (Table 2). For example, compound **7u**, which has seven methylene units *para* to the amide, displayed the strongest biofilm-development modulation against MDRAB and *E. coli*, giving IC_{50}/EC_{50} values of 1.9 μM/7.9 μM and 11.2 μM/23.4 μM, respectively. Compound **7w**, with nine methylene units, demonstrated nanomolar IC_{50} values against PA14 and PAO1 giving IC_{50}/EC_{50} values of 0.8 μM/2.5 μM against PA14 and 0.5 μM/15.4 μM against PAO1. Compound **7w** shows an increase of PAO1-biofilm inhibition in comparison to **1**, which gave a 5.6 μM IC_{50}, as well as an increase of PA14 biofilm dispersal activity, in which **1** has a reported 22 μM EC_{50}. Finally, **7t**, with six methylene units, gave an IC_{50}/EC_{50} of 21.4 μM/36.2 μM against *V. vulnificus* and an IC_{50} of 8.9 μM against *R. salexigens*. Interest-

Table 2. Gram-negative bacterial biofilm data.

Compound	IC_{50} [μM]	EC_{50} [μM]	Compound	IC_{50} [μM]	EC_{50} [μM]
MDRAB			*E. coli*		
7s	15.1±2.4	17.2±0.4	**7e**	43.8±4.2	114.1±18.79
7t	4.5±0.2	5.4±0.7	**7s**	40.1±0.3	93.1±3.6
7u	1.9±0.6	7.9±1.4	**7u**	11.2±0.4	23.4±7.9
7v	5.5±2.4	–	**7v**	53.1±3.0	–
7w	11.2±3.6	–	**7w**	13.5±0.7	–
PA14			PAO1		
7s	34.4±0.8	39.3±4.8	**7t**	1.1±0.5	7.2±1.8
7t	38.2±0.7	42.7±2.3	**7u**	1.2±0.3	45.9±1.2
7u	2.2±0.4	4.3±1.4	**7v**	62.5±2.2	67.9±2.4
7v	5.8±1.9	13.8±3.2	**7w**	0.5±0.1	15.4±5.3
7w	0.8±0.1	2.5±1.6	**7bb**	64.5±2.3	119.7±9.9
V. vulnificus			*R. salexigens*		
7t	21.4±1.8	36.2±5.5	**7t**	8.9±0.4	–
7u	56.9±3.7	94.7±5.2	**7u**	27.1±3.1	–

ingly, the marine-sponge-derived alkaloids bromoageliferin and oroidin, which served as structural inspiration for the 2-AI antibiofilm agents, have reported IC_{50} values for *R. salexigens* of 1.2 μM (1.7 μg mL^{-1}) and 24.5 μM (63 μg mL^{-1}), respectively. Compound **7u** shows better inhibitory activity than oroidin and similar activity to bromoageliferin.

As we have seen with other 2-AIT-based antibiofilm agents, these 2-AIT derivatives also displayed substantial antibiofilm activity against Gram-positive bacteria. This information is summarized in Table 3. Compound **7u** displayed the highest bio-

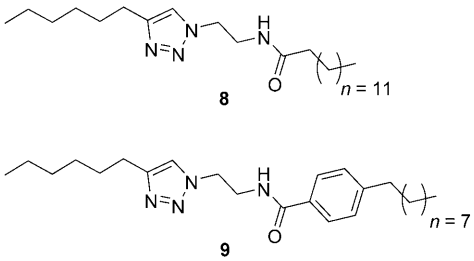
Table 3. Gram-positive bacterial biofilm data.

Compound	IC_{50} [μM]	EC_{50} [μM]	Compound	IC_{50} [μM]	EC_{50} [μM]
VRE			MRSA		
7s	14.4±2.8	15.9±0.9	**7s**	4.3±1.9	80.6±9.5
7t	19.5±5.3	21.2±1.5	**7t**	0.7±0.4	0.9±0.3
7u	0.5±0.1	0.7±0.3	**7u**	1.9±0.1	5.5±0.5
S. epidermidis			**7v**	4.7±0.1	–
7f	5.2±0.4	–			
7m	2.8±0.9	–			
7u	0.6±0.3	28.1±7.5			
7w	0.9±0.2	–			

film regulatory activity of any reported 2-AI against VRE, giving an IC_{50}/EC_{50} of 0.5 μM/0.7 μM. Compound **7t** gave a nanomolar IC_{50}/EC_{50} of 0.7 μM/0.9 μM against MRSA, and **7u** an IC_{50}/EC_{50} of 0.6 μM/28.1 μM against *S. epidermidis*.

We then studied the ability of lead compounds to inhibit the formation of mixed-species biofilms. *S. epidermidis* and *C. albicans* are common sources of medical-implant-based infections, and studies show that these species coexist well in the biofilm form.[26,27] These mixed-species biofilm infections represent a major hurdle for health care, as treatment with an antibiotic or antifungal alone would be less likely to be successful. Given the success of compounds **7f** and **7m** against both *S. epidermidis* and *C. albicans*, we investigated the ability of these compounds as mixed-species antibiofilm agents. We used tryptic soy broth (TSB) as a growth medium since it was previously shown that these strains develop equally well in TSB in both the planktonic and biofilm forms.[27] Compounds **7f** and **7m** gave IC_{50} values of 40 μM and 62 μM, respectively, this indicates that 2-AI-based antibiofilm agents are active against multispecies biofilms.

Once we had established the cross-kingdom activity of 2-AIT-based antibiofilm agents, we wanted to examine if the 2-AI scaffold was necessary for the antibiofilm activity. Analogues of compounds **7g** and **7w** were synthesized that did not have the 2-aminoimidazole scaffold (Scheme 4). Both compounds **8** and **9** were tested and found not to have antibiofilm activity at 100 μM against any of the bacterial and yeast strains.



Scheme 4. Analogues of **4g** and **4w** without 2-aminoimidazole scaffolds.

Finally, red-blood-cell hemolysis analysis of **7u** and **7f** was performed with defibrinated sheep's blood.[29] These compounds were chosen because **7u** was the lead compound against most bacterial strains and **7f** was a leading fungal antibiofilm agent. The HD_{50} (hemolytic dose that lyses 50% of the red blood cells) was found to be 194 μM for **7u** and 210 μM for **7f**. Even more promising is that neither compound showed more than 5% lysis until after 50 μM, a concentration well above their respective IC_{50} values.

Conclusions

We have shown that 2-aminoimidazole/triazole conjugates can be designed to have cross-kingdom activity in that they can regulate prokaryotic and eukaryotic biofilm development in a nonmicrobicidal manner. Furthermore, we have also successfully explored and executed a more efficient synthesis to these 2-aminoimidazoles that avoids undesirable purification techniques. Finally, we have demonstrated that these compounds do not lyse red blood cells until concentrations well past their IC_{50} and EC_{50} values. This information, coupled with previous results from our group that established that 2-AI-based antibiofilm agents are nontoxic to both mammalian cell culture[6] and model organisms,[9] makes these molecules candidates for exploring in vivo remediation efforts for biofilm infections.

Experimental Section

General: MRSA (ATCC BAA-44), *S. aureus* (ATCC 29213), *E. coli* (ATCC 35695), vancomycin resistant *Enterococcus faecium* (VRE; ATCC 51559), MDRAB (ATCC BAA-1605), *R. salexigens* (ATCC 35888), *S. cerevisiae* (ATCC 204508), *C. albicans* (ATCC 76615), *C. neoformans*

(ATCC MYA-422), and *Staphylococcus epidermidis* (ATCC 29886) were obtained from the ATCC. *P. aeruginosa* strain PAO1 was provided by Dr. Wozniak (Wake Forest School of Medicine). All other reagents were purchased from commercially available sources.

Synthesis: All reagents used for chemical synthesis were purchased from commercial sources and used without further purification. Chromatography was performed by using 60 Å mesh standard-grade silica gel from Sorbtech (Atlanta, MA, USA). NMR solvents were obtained from Cambridge Isotope Labs and used as supplied. ^{1}H NMR (300 or 400 MHz) and ^{13}C NMR (75 or 100 MHz) spectra were recorded at 25 °C on Varian Mercury spectrometers. Chemical shifts (δ) are given in ppm relative to tetramethylsilane or the respective NMR solvent. Mass spectra were obtained at the NCSU Department of Chemistry Mass Spectrometry Facility.

***N*-(2-Azidoethyl)tetradecanamide:** 2-Azidoethanamine (0.102 g, 1.18 mmol), DCM (5 mL), and then triethylamine (0.239 g, 2.37 mmol) were added to a 25 mL round-bottomed flask equipped with a magnetic stirrer. To this reaction mixture, tetradecanoyl chloride (0.292 g, 1.18 mmol) was added dropwise, and the mixture was allowed to stir at room temperature for 24 h. The reaction mixture was concentrated in vacuo and then purified by silica gel column chromatography (dichloromethane→methanol/dichloromethane 1:40) to give *N*-(2-azidoethyl)tetradecanamide (0.245 g, 79% yield). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 5.86 (s, 1H), 3.42 (s, 4H), 2.18 (t, J = 7.8 Hz, 2H), 1.62 (m, 2H), 1.24 (m, 20H), 0.87 ppm (t, J = 3.9 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 173.7, 51.2, 39.1, 36.9, 32.1, 29.9, 29.8, 29.7, 29.6, 29.5, 25.9, 22.9, 14.4 ppm; HRMS (ESI) calcd for $C_{16}H_{32}N_4O$: 296.2576 $[M]^+$, found 296.2566.

***N*-(2-Azidoethyl)octadec-9-enamide:** As in the synthesis of *N*-(2-azidoethyl)tetradecanamide, octadec-9-enoyl chloride (0.374 g, 1.24 mmol) was treated with 2-azidoethanamine (0.107 g, 1.24 mmol) and triethylamine (0.252 g, 2.49 mmol) in dichloromethane (5 mL) to give *N*-(2-azidoethyl)octadec-9-enamide (0.309 g, 71% yield). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.30 (s, 1H), 5.29 (m, 2H), 3.39 (d, J = 2.1 Hz, 2H), 3.38 (d, J = 2.4 Hz, 2H), 2.19 (t, J = 7.2 Hz, 2H), 1.97 (m, 4H), 1.59 (t, J = 7.5 Hz, 2H), 1.26 (m, 20H), 0.84 ppm (t, J = 6.6 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 173.9, 130.2, 129.9, 51.1, 39.1, 36.8, 32.1, 30.0, 29.9, 29.7, 29.5, 29.4, 29.3, 27.4, 27.3, 25.9, 22.9, 14.3 ppm; HRMS (ESI) calcd for $C_{20}H_{38}N_4O$: 350.3046 $[M]^+$, found 350.3039.

***N*-(2-Azidoethyl)thiophene-2-sulfonamide:** As in the synthesis of *N*-(2-azidoethyl)tetradecanamide, thiophene-2-sulfonyl chloride (0.218 g, 1.19 mmol) was treated with 2-azidoethanamine (0.103 g, 1.19 mmol) and triethylamine (0.241 g, 2.39 mmol) in dichloromethane (5 mL) to give *N*-(2-azidoethyl)thiophene-2-sulfonamide (0.221 g, 80% yield). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.62 (d, J = 1.2 Hz, 1H), 7.59 (d, J = 1.2 Hz, 1H), 7.08 (t, J = 3.9 Hz, 1H), 5.52 (s, 1H), 3.41 (t, J = 5.4 Hz, 2H), 3.17 ppm (q, J = 5.4, 3.8 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 140.6, 132.7, 132.6, 127.9, 50.9, 42.9 ppm; HRMS (ESI) calcd for $C_6H_8N_4O_2S_2$: 232.0089 $[M]^+$, found 232.0084.

***N*-(2-Azidoethyl)-5-(dimethylamino)naphthalene-1-sulfonamide:** As in the synthesis of *N*-(2-azidoethyl)tetradecanamide, 5-(dimethylamino)naphthalene-1-sulfonyl chloride (0.321 g, 1.19 mmol) was treated with 2-azidoethanamine (0.103 g, 1.19 mmol) and triethylamine (0.241 g, 2.38 mmol) in dichloromethane (5 mL) to give *N*-(2-azidoethyl)-5-(dimethylamino)naphthalene-1-sulfonamide (0.328 g, 86% yield). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.52 (d, J = 8.4 Hz, 1H), 8.28 (d, J = 8.4 Hz, 1H), 8.22 (d, J = 0.9 Hz, 1H), 7.53 (t, J = 8.1 Hz, 1H), 7.50 (t, J = 7.5 Hz, 1H), 7.17 (d, J = 7.8 Hz, 1H), 5.58 (t, J = 1.8 Hz, 1H), 3.28 (t, J = 5.7 Hz, 2H), 3.03 (q, J = 6.3, 5.7 Hz, 2H), 2.85 ppm (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 152.3, 134.8, 130.9, 130.1, 129.7, 128.9, 123.4, 118.9, 115.6, 51.0, 45.6, 42.6 ppm; HRMS (ESI) calcd for $C_{14}H_{17}N_5O_2S$: 319.1103 $[M]^+$, found 319.1104.

***N*-(2-Azidoethyl)-2,3,4,5,6-pentamethylbenzenesulfonamide:** As in the synthesis of *N*-(2-azidoethyl)tetradecanamide, 2,3,4,5,6-pentamethylbenzene-1-sulfonyl chloride (0.304 g, 1.23 mmol) was treated with 2-azidoethanamine (0.106 g, 1.23 mmol) and triethylamine (0.249 g, 2.46 mmol) in dichloromethane (5 mL) to give *N*-(2-azidoethyl)-2,3,4,5,6-pentamethylbenzenesulfonamide (0.296 g, 81% yield). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 5.12 (t, J = 3.9 Hz, 1H), 3.35 (t, J = 5.4 Hz, 2H), 3.05 (q, J = 6.0, 5.1 Hz, 2H), 2.59 (s, 6H), 2.28 (s, 3H), 2.24 ppm (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 139.9, 136.1, 135.2, 134.2, 51.1, 42.3, 19.2, 17.9, 17.3 ppm; HRMS (ESI) calcd for $C_{13}H_{20}N_4O_2S$: 296.1307 $[M]^+$, found 296.1304.

***N*-(2-Azidoethyl)benzenesulfonamide:** As in the synthesis of *N*-(2-azidoethyl)tetradecanamide, benzenesulfonyl chloride (0.201 g, 1.16 mmol) was treated with 2-azidoethanamine (0.100 g, 1.16 mmol) and triethylamine (0.235 g, 2.32 mmol) in dichloromethane (5 mL) to give *N*-(2-azidoethyl)benzenesulfonamide (0.289 g, 84% yield). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.90 (d, J = 1.8 Hz, 2H), 7.55 (m, 3H), 5.47 (s, 1H), 3.39 (t, J = 5.1 Hz, 2H), 3.12 ppm (t, J = 5.4 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 139.8, 133.2, 129.5, 127.2, 50.9, 42.6 ppm; HRMS (ESI) calcd for $C_6H_8N_4O_2S$: 226.0524 $[M]^+$, found 226.0523.

***(E)*-*N*-(2-Azidoethyl)-4-phenylbut-3-enamide:** As in the synthesis of *N*-(2-azidoethyl)tetradecanamide, (*E*)-4-phenylbut-3-enoyl chloride (0.198 g, 1.19 mmol) was treated with 2-azidoethanamine (0.114 g, 1.19 mmol) and triethylamine (0.239 g, 2.37 mmol) in dichloromethane (5 mL) to give (*E*)-*N*-(2-azidoethyl)-4-phenylbut-3-enamide (0.168 g, 55% yield). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.68 (d, J = 15.6 Hz, 1H), 7.45 (d, J = 3.3 Hz, 2H), 7.29 (m, 3H), 7.04 (t, J = 4.1 Hz, 1H), 6.59 (d, J = 15.9 Hz, 1H), 3.55 (q, J = 6.0, 5.1 Hz, 2H), 3.47 ppm (t, J = 1.5 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 166.9, 141.6, 134.9, 130.1, 129.1, 128.1, 120.8, 51.1, 39.4 ppm; HRMS (ESI) calcd for $C_{11}H_{12}N_4O$: 216.1011 $[M]^+$, found 216.1005.

***N*-(2-Azidoethyl)-2-(phenylthio)acetamide:** As in the synthesis of *N*-(2-azidoethyl)tetradecanamide, 2-(phenylthio)acetyl chloride (0.222 g, 1.19 mmol) was treated with 2-azidoethanamine (0.102 g, 1.19 mmol) and triethylamine (0.240 g, 2.37 mmol) in dichloromethane (5 mL) to give *N*-(2-azidoethyl)-2-(phenylthio)acetamide (0.179 g, 64% yield). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.29 (m, 4H), 7.18 (m, 2H), 3.60 (s, 2H), 3.34 ppm (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 168.6, 134.8, 129.5, 128.6, 127.1, 50.8, 39.3, 37.7 ppm; HRMS (ESI) calcd for $C_{10}H_{12}N_4OS$: 236.0732 $[M]^+$, found 236.0729.

***N*-(2-Azidoethyl)palmitamide:** As in the synthesis of *N*-(2-azidoethyl)tetradecanamide, palmitoyl chloride (0.338 g, 1.23 mmol) was treated with 2-azidoethanamine (0.106 g, 1.23 mmol) and triethylamine (0.249 g, 2.46 mmol) in dichloromethane (5 mL) to give *N*-(2-azidoethyl)palmitamide (0.336 g, 84% yield). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.11 (s, 1H), 3.41 (s, 4H), 2.17 (t, J = 7.5 Hz, 2H), 1.60 (m, 2H), 1.23 (m, 24H), 0.85 ppm (t, 6.3 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 173.9, 51.1, 39.1, 36.9, 32.1, 29.9, 29.8, 29.8, 29.7, 29.6, 29.5, 25.9, 22.9, 14.3 ppm; HRMS (ESI) calcd for $C_{18}H_{36}N_4O$: 324.2889 $[M]^+$, found 324.2879.

***N*-(2-Azidoethyl)decanamide:** As in the synthesis of *N*-(2-azidoethyl)tetradecanamide, decanoyl chloride (0.251 g, 1.32 mmol) was treated with 2-azidoethanamine (0.114 g, 1.32 mmol) and triethylamine (0.267 g, 2.64 mmol) in dichloromethane (5 mL) to give *N*-(2-azidoethyl)decanamide (0.262 g, 83% yield). ^{1}H NMR (300 MHz,

$CDCl_3$): $\delta = 6.49$ (s, 1H), 3.36 (s, 2H), 3.35 (s, 2H), 2.14 (t, $J = 7.2$ Hz, 2H), 1.46 (m, 2H), 1.21 (m, 12H), 0.81 ppm (t, $J = 6.0$ Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 174.1$, 50.9, 39.1, 36.8, 32.0, 29.7, 29.6, 29.5, 29.4, 25.9, 22.8, 14.3 ppm; HRMS (ESI) calcd for $C_{12}H_{24}N_4O$: 240.1950 $[M]^+$, found 240.1947.

***N*-(2-Azidoethyl)-2-iodobenzamide:** As in the synthesis of *N*-(2-azidoethyl)tetradecanamide, 2-iodobenzoyl chloride (0.312 g, 1.17 mmol) was treated with 2-azidoethanamine (0.101 g, 1.17 mmol) and triethylamine (0.237 g, 2.34 mmol) in dichloromethane (5 mL) to give *N*-(2-azidoethyl)-2-iodobenzamide (0.272 g, 74% yield). ^1H NMR (300 MHz, $CDCl_3$): $\delta = 7.84$ (d, $J = 7.2$ Hz, 1H), 7.33 (m, 2H), 7.08 (t, $J = 3.3$ Hz, 1H), 6.51 (s, 1H), 3.54 (s, 2H), 3.53 ppm (s, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 169.9$, 141.9, 140.0, 131.5, 128.4, 128.4, 92.7, 50.8, 39.6 ppm; HRMS (ESI) calcd for $C_9H_9IN_4O$: 315.9821 $[M]^+$, found 315.9820.

***N*-(2-Azidoethyl)-4-*tert*-butylbenzamide:** As in the synthesis of *N*-(2-azidoethyl)tetradecanamide, 4-*tert*-butylbenzoyl chloride (0.244 g, 1.23 mmol) was treated with 2-azidoethanamine (0.106 g, 1.23 mmol) and triethylamine (0.249 g, 2.47 mmol) in dichloromethane (5 mL) to give *N*-(2-azidoethyl)-4-*tert*-butylbenzamide (0.221 g, 73% yield). ^1H NMR (300 MHz, $CDCl_3$): $\delta = 7.73$ (d, $J = 6.6$ Hz, 2H), 7.43 (d, $J = 9.0$ Hz, 2H), 6.95 (t, $J = 3.9$ Hz, 1H), 3.59 (q, $J = 5.4$, 5.7 Hz, 2H), 3.50 (t, $J = 5.1$ Hz, 2H), 1.31 ppm (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 168.2$, 155.4, 131.4, 127.2, 125.8, 51.1, 39.7, 35.2, 31.4 ppm; HRMS (ESI) calcd for $C_{13}H_{18}N_4O$: 246.1480 $[M]^+$, found 246.1479.

***N*-(2-Azidoethyl)-3,5-difluorobenzamide:** As in the synthesis of *N*-(2-azidoethyl)tetradecanamide, 3,5-difluorobenzoyl chloride (0.219 g, 1.24 mmol) was treated with 2-azidoethanamine (0.107 g, 1.24 mmol) and triethylamine (0.251 g, 2.48 mmol) in dichloromethane (5 mL) to give *N*-(2-azidoethyl)-3,5-difluorobenzamide (0.280 g, 59% yield). ^1H NMR (300 MHz, $CDCl_3$): $\delta = 7.32$ (s, 2H), 7.29 (s, 1H), 6.91 (t, $J = 2.4$ Hz, 1H), 3.58 (q, $J = 5.7$, 5.1 Hz, 2H), 3.51 ppm (t, $J = 4.8$ Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 165.9$, 164.7, 161.5, 161.4, 137.6, 110.7, 106.9, 50.7, 39.9 ppm; HRMS (ESI) calcd for $C_9H_8F_2N_4O_2S$: 226.0666 $[M]^+$, found 226.0662.

***N*-(2-Azidoethyl)-2,4,6-trichlorobenzamide:** As in the synthesis of *N*-(2-azidoethyl)tetradecanamide, 2,4,6-trichlorobenzoyl chloride (0.301 g, 1.23 mmol) was treated with 2-azidoethanamine (0.106 g, 1.23 mmol) and triethylamine (0.249 g, 2.47 mmol) in dichloromethane (5 mL) to give *N*-(2-azidoethyl)-2,4,6-trichlorobenzamide (0.317 g, 88% yield). ^1H NMR (300 MHz, $CDCl_3$): $\delta = 7.27$ (2H, s), 6.88 (s, 1H), 3.54 (s, 2H), 3.53 ppm (s, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 164.4$, 135.9, 134.3, 132.9, 128.2, 50.7, 39.4 ppm; HRMS (ESI) calcd for $C_9H_7N_4O$: 291.9685 $[M]^+$, found 291.9681.

***N*-(2-Azidoethyl)-2-naphthamide:** As in the synthesis of *N*-(2-azidoethyl)tetradecanamide, 2-naphthoyl chloride (0.237 g, 1.24 mmol) was treated with 2-azidoethanamine (0.107 g, 1.24 mmol) and triethylamine (0.252 g, 2.49 mmol) in dichloromethane (5 mL) to give *N*-(2-azidoethyl)-2-naphthamide (0.234 g, 77% yield). ^1H NMR (300 MHz, $CDCl_3$): $\delta = 8.69$ (s, 1H), 7.84 (m, 4H), 7.50 (m, 2H), 6.97 (t, $J = 4.2$ Hz, 1H), 3.68 (q, $J = 4.8$, 1.2 Hz, 2H), 3.56 ppm (t, $J = 3.0$ Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 168.3$, 135.1, 132.8, 131.5, 129.2, 128.8, 128.0, 127.9, 127.1, 123.8, 51.2, 39.8 ppm; HRMS (ESI) calcd for $C_{13}H_{12}N_4O$: 240.1011 $[M]^+$, found 240.1007.

***N*-(2-Azidoethyl)-4-heptylbenzamide:** As in the synthesis of *N*-(2-azidoethyl)tetradecanamide, 4-heptylbenzoyl chloride (0.289 g, 1.21 mmol) was treated with 2-azidoethanamine (0.104 g, 1.21 mmol) and triethylamine (0.245 g, 2.42 mmol) in dichloromethane (5 mL) to give *N*-(2-azidoethyl)-4-heptylbenzamide (0.260 g, 75% yield). ^1H NMR (300 MHz, $CDCl_3$): $\delta = 7.73$ (d, $J = 7.8$ Hz, 2H), 7.19 (d, $J = 7.8$ Hz, 3H), 3.57 (q, $J = 5.7$, 5.4 Hz, 2H), 3.47 (t, $J = 5.7$ Hz, 2H), 2.61 (t, $J = 7.5$ Hz, 2H), 1.61 (m, 2H), 1.26 (m, 8H), 0.87 ppm (t, $J = 6.0$ Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 168.3$, 147.3, 131.7, 128.8, 127.4, 50.9, 39.7, 36.1, 32.0, 31.4, 29.4, 29.3, 22.9, 14.3 ppm; HRMS (ESI) calcd for $C_{16}H_{24}N_4O$: 288.1950 $[M]^+$, found 288.1943.

***N*-(2-Azidoethyl)-4-butylbenzamide:** As in the synthesis of *N*-(2-azidoethyl)tetradecanamide, 4-butylbenzoyl chloride (0.242 g, 1.22 mmol) was treated with 2-azidoethanamine (0.105 g, 1.22 mmol) and triethylamine (0.246 g, 2.43 mmol) in dichloromethane (5 mL) to give *N*-(2-azidoethyl)-4-butylbenzamide (0.224 g, 75% yield). ^1H NMR (300 MHz, $CDCl_3$): $\delta = 7.73$ (d, $J = 8.4$ Hz, 2H), 7.39 (t, $J = 1.8$ Hz, 1H), 7.17 (d, $J = 8.1$ Hz, 2H), 3.55 (q, $J = 8.7$, 5.7 Hz, 2H), 3.45 (t, $J = 5.7$ Hz, 2H), 2.60 (t, $J = 7.8$ Hz, 2H), 1.56 (m, 2H), 1.30 (m, 2H), 0.90 ppm (t, $J = 4.2$ Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 168.5$, 147.2, 131.7, 128.8, 127.4, 50.9, 39.7, 35.7, 33.5, 22.5, 14.1 ppm; HRMS (ESI) calcd for $C_{13}H_{18}N_4O$: 246.1481 $[M]^+$, found 246.1476.

***N*-(2-Azidoethyl)-4-hexylbenzamide:** As in the synthesis of *N*-(2-azidoethyl)tetradecanamide, 4-hexylbenzoyl chloride (0.293 g, 1.30 mmol) was treated with 2-azidoethanamine (0.112 g, 1.30 mmol) and triethylamine (0.264 g, 2.61 mmol) in dichloromethane (5 mL) to give *N*-(2-azidoethyl)-4-hexylbenzamide (0.299 g, 84% yield). ^1H NMR (300 MHz, $CDCl_3$): $\delta = 7.75$ (d, $J = 8.1$ Hz, 2H), 7.43 (t, $J = 3.9$ Hz, 1H), 7.17 (d, $J = 7.8$ Hz, 2H), 3.55 (q, $J = 6.3$, 5.7 Hz, 2H), 3.46 (t, $J = 5.7$ Hz, 2H), 2.59 (t, $J = 7.5$ Hz, 2H), 1.58 (m, 2H), 1.29 (m, 4H), 0.87 ppm (t, $J = 6.9$ Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 168.6$, 147.3, 131.7, 130.3, 128.8, 127.5, 50.9, 39.7, 35.9, 31.6, 31.1, 22.7, 14.2 ppm; HRMS (ESI) calcd for $C_{15}H_{22}N_4O$: 274.1794 $[M]^+$, found 274.1789.

***N*-(2-Azidoethyl)-4-pentylbenzamide:** As in the synthesis of *N*-(2-azidoethyl)tetradecanamide, 4-pentylbenzoyl chloride (0.283 g, 1.35 mmol) was treated with 2-azidoethanamine (0.116 g, 1.35 mmol) and triethylamine (0.273 g, 2.69 mmol) in dichloromethane (5 mL) to give *N*-(2-azidoethyl)-4-pentylbenzamide (0.267 g, 76% yield). ^1H NMR (300 MHz, $CDCl_3$): $\delta = 7.74$ (d, $J = 8.1$ Hz, 2H), 7.61 (t, $J = 5.1$ Hz, 1H), 7.15 (d, $J = 8.4$ Hz, 2H), 3.54 (q, $J = 5.7$, 5.1 Hz, 2H), 3.44 (t, $J = 5.7$ Hz, 2H), 2.58 (t, $J = 7.5$ Hz, 2H), 1.57 (m, 2H), 1.26 (m, 4H), 0.86 ppm (t, $J = 6.6$ Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 168.6$, 147.2, 131.7, 128.7, 127.5, 50.8, 39.7, 35.9, 31.6, 31.1, 22.7, 14.2 ppm; HRMS (ESI) calcd for $C_{14}H_{20}N_4O$: 260.1637 $[M]^+$, found 260.1632.

***N*-(2-Azidoethyl)biphenyl-4-carboxamide:** As in the synthesis of *N*-(2-azidoethyl)tetradecanamide, biphenyl-4-carboxylic acid chloride (0.283 g, 1.31 mmol) was treated with 2-azidoethanamine (0.113 g, 1.31 mmol) and triethylamine (0.264 g, 2.61 mmol) in dichloromethane (5 mL) to give *N*-(2-azidoethyl)biphenyl-4-carboxamide (0.297 g, 85% yield). ^1H NMR (300 MHz, $CDCl_3$): $\delta = 7.88$ (d, 2H), 7.67 (m, 4H), 7.44 (m, 3H), 6.63 (s, 1H), 3.67 (q, $J = 6.0$, 1.8 Hz, 2H), 3.58 ppm (t, $J = 6.0$ Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 167.8$, 144.8, 140.1, 132.9, 129.2, 128.3, 127.8, 127.5, 127.4, 51.2, 39.7 ppm; HRMS (ESI) calcd for $C_{15}H_{14}N_4O$: 266.1168 $[M]^+$, found 266.1162.

***N*-(2-Azidoethyl)-4,5-dibromo-1-methyl-1*H*-pyrrole-2-carboxamide:** As in the synthesis of *N*-(2-azidoethyl)tetradecanamide, 4,5-dibromo-1-methyl-1*H*-pyrrole-2-carboxylic acid chloride (0.529 g, 1.38 mmol) was treated with 2-azidoethanamine (0.119 g, 1.38 mmol) and triethylamine (0.279 g, 2.75 mmol) in dichloromethane (5 mL) to give *N*-(2-azidoethyl)-4,5-dibromo-1-methyl-1*H*-pyr-

role-2-carboxamide (0.331 g, 69% yield). ^{1}H NMR (300 MHz, CD_3OD): $\delta = 6.84$ (s, 1H), 3.91 (s, 3H), 3.50 (t, $J = 3.6$ Hz, 2H), 3.25 ppm (t, $J = 1.5$ Hz, 2H); ^{13}C NMR (75 MHz, CD_3OD): $\delta = 161.7$, 127.7, 114.7, 111.4, 97.8, 50.4, 38.9, 35.1 ppm; HRMS (ESI) calcd for $C_8H_9N_5O$: 348.9174 $[M]^+$, found 348.9183.

***N*-(2-Azidoethyl)-1*H*-pyrrole-2-carboxamide:** As in the synthesis of *N*-(2-azidoethyl)tetradecanamide, 1*H*-pyrrole-2-carboxylic acid chloride (0.249 g, 1.17 mmol) was treated with 2-azidoethanamine (0.101 g, 1.17 mmol) and triethylamine (0.237 g, 2.34 mmol) in dichloromethane (5 mL) to give *N*-(2-azidoethyl)-1*H*-pyrrole-2-carboxamide (0.137 g, 66% yield). ^{1}H NMR (300 MHz, CD_3OD): $\delta = 6.88$ (d, $J = 1.5$ Hz, 1H), 6.77 (d, $J = 2.4$ Hz, 1H), 6.14 (t, $J = 2.4$ Hz, 1H), 3.46 (t, $J = 5.7$ Hz, 2H), 3.37 ppm (q, $J = 5.7$, 14.7 Hz, 2H); ^{13}C NMR (75 MHz, CD_3OD): $\delta = 162.9$, 125.6, 122.2, 121.9, 110.9, 109.2, 50.6, 38.9 ppm; HRMS (ESI) calcd for $C_7H_9N_5O$: 179.0807 $[M]^+$, found 179.0803.

***N*-(2-Azidoethyl)-4-bromo-1*H*-pyrrole-2-carboxamide:** As in the synthesis of *N*-(2-azidoethyl)tetradecanamide, 4-bromo-1*H*-pyrrole-2-carboxylic acid chloride (0.408 g, 1.34 mmol) was treated with 2-azidoethanamine (0.115 g, 1.34 mmol) and triethylamine (0.270 g, 2.67 mmol) in dichloromethane (5 mL) to give *N*-(2-azidoethyl)-4-bromo-1*H*-pyrrole-2-carboxamide (0.299 g, 82% yield). ^{1}H NMR (300 MHz, CD_3OD): $\delta = 6.93$ (s, 1H), 6.80 (s, 1H), 3.49 (t, $J = 0.6$ Hz, 2H), 3.41 ppm (t, $J = 0.9$ Hz, 2H); ^{13}C NMR (75 MHz, CD_3OD): $\delta =$ 161.7, 126.1, 122.0, 112.4, 96.4, 50.5, 38.9 ppm; HRMS (ESI) calcd for $C_7H_8BrN_5O$: 256.9912 $[M]^+$, found 256.9908.

***N*-(2-Azidoethyl)-4-nonylbenzamide:** As in the synthesis of *N*-(2-azidoethyl)tetradecanamide, the acid chloride (0.354 g, 1.40 mmol) was treated with 2-azidoethanamine (0.121 g, 1.40 mmol) and triethylamine (0.284 g, 2.80 mmol) in dichloromethane (5 mL) to give *N*-(2-azidoethyl)-4-nonylbenzamide (0.339 g, 80% yield). ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 6.21$ (s, 1H), 3.40 (s, 4H), 2.19 (t, $J = 7.2$ Hz, 2H), 1.62 (t, $J = 6.0$ Hz, 2H), 1.22 (br s, 14H), 0.842 ppm (t, $J =$ 6.3 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 173.8$, 51.1, 30.1, 36.8, 32.1, 29.8, 29.7, 29.6, 29.5, 29.2, 25.9, 22.9, 14.3 ppm; HRMS (ESI) calcd for $C_{14}H_{28}N_4O$: 268.2263 $[M]^+$, found 268.2259.

***N*-(2-Azidoethyl)-4-nonylbenzamide:** As in the synthesis of *N*-(2-azidoethyl)tetradecanamide, the acid chloride (0.383 g, 1.43 mmol) was treated with 2-azidoethanamine (0.124 g, 1.43 mmol) and triethylamine (0.290 g, 2.87 mmol) in dichloromethane (5 mL) to give *N*-(2-azidoethyl)-4-nonylbenzamide (0.441 g, 97% yield). ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 7.72$ (d, 2H), 7.26 (t, 1H), 7.18 (d, 2H), 3.57 (q, 2H), 3.45 (t, 2H), 2.60 (t, 2H), 1.58 (m, 2H), 1.27 (m, 12H), 0.86 ppm (t, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 168.5$, 147.3, 131.7, 128.8, 127.4, 50.9, 39.7, 36.1, 32.1, 31.5, 29.8, 29.7, 29.6, 29.5, 22.9, 14.4 ppm; HRMS (ESI) calcd for $C_{18}H_{28}N_4O$: 316.2263 $[M]^+$, found 316.2268.

***N*-(2-Azidoethyl)-4-octylbenzamide:** As in the synthesis of *N*-(2-azidoethyl)tetradecanamide, the acid chloride (0.262 g, 1.19 mmol) was treated with 2-azidoethanamine (0.103 g, 1.19 mmol) and triethylamine (0.242 g, 2.39 mmol) in dichloromethane (5 mL) to give *N*-(2-azidoethyl)-4-octylbenzamide (0.220 g, 69% yield). ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 7.73$ (d, 2H), 7.37 (t, 1H), 7.17 (d, 2H), 3.56 (q, 2H), 3.44 (t, 2H), 2.59 (t, 2H), 1.58 (m, 2H), 1.27 (m, 10H), 0.86 ppm (t, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 168.4$, 147.3, 131.7, 128.8, 127.4, 50.9, 39.7, 36.1, 32.1, 31.5, 29.7, 29.5, 29.5, 22.9, 14.3 ppm; HRMS (ESI) calcd for $C_{17}H_{28}N_4O$: 302.2107 $[M]^+$, found 302.2104.

(*E*)-*N*-(2-Azidoethyl)-2-methyl-3-phenylacrylamide: (*E*)-2-Methyl-3-phenylacrylic acid (0.0.512 g, 3.15 mmol) and dichloromethane (10 mL) were added to a 25 mL round-bottomed flask equipped with a magnetic stir bar. Oxalyl chloride (0.400 g, 3.15 mmol) was added dropwise, and the reaction mixture was allowed to stir for 1 h, then concentrated in vacuo. Dichloromethane (10 mL), 2-azidoethanamine (0.299 g, 3.47 mmol), and then triethylamine (0.351 g, 3.47 mmol) was added to the crude mixture, and it was allowed to stir for 2 h. The reaction mixture was then concentrated in vacuo and purified by silica gel column chromatography (dichloromethane→methanol/dichloromethane 1:40) to give (*E*)-*N*-(2-azidoethyl)-2-methyl-3-phenylacrylamide (0.698 g, 96% yield). ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 7.39$ (m, 6H), 7.01 (s, 1H), 3.51 (t, $J =$ 4.5 Hz, 2H), 3.45 (t, $J = 4.8$ Hz, 2H), 2.13 ppm (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 170.5$, 136.2, 134.5, 132.0, 130.3, 129.6, 128.9, 128.6, 128.3, 50.9, 39.8, 14.5 ppm; HRMS (ESI) calcd for $C_{12}H_{14}N_4O$: 230.1168 $[M]^+$, found 230.1165.

***N*-(2-Azidoethyl)-2′,4′-difluoro-3-hydroxybiphenyl-4-carboxamide:** 2′,4′-Difluoro-3-hydroxybiphenyl-4-carboxylic acid (0.301, 1.20 mmol), *N*,*N*-dimethylformamide (5 mL), *N*,*N*′-dicyclohexylcarbodiimide (0.248 g, 1.20 mmol), and *n*-methylmorpholine (0.25 mL) were added to a 25 mL round-bottomed flask equipped with a magnetic stirrer. The reaction mixture was cooled to 0 °C and allowed to stir. Then, 2-azidoethanamine (0.1037 g, 1.20 mmol) was added dropwise, and the mixture was allowed to warm slowly to room temperature with stirring over 24 h. The reaction mixture was diluted with water, extracted with dichloromethane, washed with 1 N HCl, saturated sodium bicarbonate, and brine, and then concentrated in vacuo. The resulting residue was then purified by silica gel column chromatography (methanol/dichloromethane 1:40→1:10) to give *N*-(2-azidoethyl)-2′,4′-difluoro-3-hydroxybiphenyl-4-carboxamide (0.232 g, 61% yield). ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 7.60$ (s, 1H), 7.47 (d, $J = 6.0$ Hz, 1H), 7.29 (m, 2H), 7.02 (d, $J =$ 6.6 Hz, 1H), 6.88 ppm (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 170.3$, 160.8, 135.1, 131.3, 131.2, 131.3, 131.2, 126.8, 118.8, 114.6, 112.0, 111.8, 104.8, 104.6, 104.3, 50.7, 39.3 ppm; HRMS (ESI) calcd for $C_{15}H_{12}F_2N_4O_3$: 318.0928 $[M]^+$, found 318.0933.

General procedure for click reactions and subsequent Boc deprotection: The terminal alkyne (1.0 equiv) was dissolved in ethanol/water/dichloromethane (1:1:1; ca. 9 mL per 0.300 g of terminal alkyne). The appropriate azide (1.0 equiv) was added to this solution at room temperature, with vigorous stirring. Copper(II) sulfate (15 mol%) and sodium ascorbate (45 mol%) were then added to the solution sequentially. Mixtures were allowed to stir until completion of the reaction by TLC analysis (12–24 h). The solvents were then removed in vacuo, and the resulting residue was dissolved in dichloromethane and purified by silica gel column chromatography (methanol/dichloromethane 1:40→1:10). To remove the Boc protecting group, the resulting product was dissolved in trifluoroacetic acid/dichloromethane (1:4), and the solution was allowed to stir for 5 h. Upon completion, the reaction mixture was concentrated in vacuo and then left under a high vacuum, overnight. Then, methanol supplemented with HCl was added to the product to form the HCl salt of the deprotected product, and this was then concentrated in vacuo. The resulting residue was washed with diethyl ether and then placed under a high vacuum overnight.

***N*-(2-(4-(5-(2-Amino-1*H*-imidazol-4-yl)pentyl)-1*H*-1,2,3-triazol-1-yl)ethyl)-2-(phenylthio)acetamide hydrochloride (7q):** *tert*-Butyl 2-amino-4-(hept-6-ynyl)-1*H*-imidazole-1-carboxylate (0.112 g, 0.405 mmol) was treated with *N*-(2-azidoethyl)-2-(phenylthio)acetamide (0.096 g, 0.405 mmol) according to the general click procedure to give *tert*-butyl 2-amino-4-(5-(1-(2-(2-(phenylthio)acetamido)ethyl)-1*H*-1,2,3-triazol-4-yl)pentyl)-1*H*-imidazole-1-carboxylate. ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 7.45$ (s, 1H), 7.19 (m, 5H), 7.13 (s,

1H), 6.43 (s, 1H), 6.13 (br s, 2H), 4.29 (s, 2H), 3.68 (s, 2H), 3.57 (s, 2H), 2.56 (s, 2H), 2.35 (s, 2H), 1.52 ppm (m, 15H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 187.8, 172.0, 169.1, 162.4, 156.9, 135.0, 129.5, 128.3, 126.8, 121.8, 85.00, 49.4, 39.9, 37.4, 29.4, 28.9, 28.4, 28.2, 27.6, 25.6 ppm; HRMS (ESI) calcd for $C_{25}H_{35}N_7O_3S$: 513.2522 $[M]^+$, found 513.2522. The carboxylate was subsequently deprotected to give **7q** (0.133 g, 73% yield). ^{1}H NMR (300 MHz, CD_3OD): δ = 8.47 (s, 1H), 7.30 (s, 4H), 7.19 (s, 1H), 6.58 (s, 1H), 4.66 (s, 2H), 3.76 (s, 2H), 3.64 (s, 2H), 2.84 (s, 2H), 2.34 (s, 2H), 1.73 (s, 2H), 1.64 (s, 2H), 1.26 ppm (s, 2H); ^{13}C NMR (75 MHz, CD_3OD): δ = 170.9, 159.3, 158.9, 147.2, 135.6, 128.1, 128.9, 127.6, 126.6, 108.7, 108.6, 52.0, 39.1, 37.5, 37.2, 36.6, 36.1, 30.8, 28.1, 27.9, 27.7, 24.2, 23.7, 23.6 ppm; HRMS (ESI) calcd for $C_{20}H_{27}N_7OS$: 413.1998 $[M]^+$, found 413.1991.

***N*-(2-(4-(5-(2-Amino-1*H*-imidazol-4-yl)pentyl)-1*H*-1,2,3-triazol-1-yl)ethyl)thiophene-2-sulfonamide hydrochloride (7i):** *tert*-Butyl 2-amino-4-(hept-6-ynyl)-1*H*-imidazole-1-carboxylate (0.105 g, 0.379 mmol) was treated with *N*-(2-azidoethyl)thiophene-2-sulfonamide (0.099 g, 0.379 mmol) according to the general click procedure to give *tert*-butyl 2-amino-4-(5-(1-(2-(thiophene-2-sulfonamido)ethyl)-1*H*-1,2,3-triazol-4-yl)pentyl)-1*H*-imidazole-1-carboxylate. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.49 (s, 3H), 7.39 (s, 1H), 6.99 (s, 1H), 6.41 (br m, 3H), 4.43 (s, 2H), 3.42 (s, 2H), 2.54 (s, 2H), 2.09 (s, 2H), 1.51 (m, 13H), 1.19 ppm (s, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 150.8, 149.4, 148.1, 141.1, 138.3, 132.2, 132.1, 127.7, 122.6, 85.2, 53.8, 50.2, 43.2, 31.2, 29.9, 29.2, 28.8, 28.1, 25.5 ppm; HRMS (ESI) calcd for $C_{21}H_{31}N_7O_4S_2$: 509.1879 $[M]^+$, found 509.1879. The carboxylate was subsequently deprotected to give **7i** (0.098 g, 58% yield). ^{1}H NMR (400 MHz, CD_3OD): δ = 8.37 (s, 1H), 7.76 (s, 1H), 7.57 (s, 1H), 7.11 (s, 1H), 6.46 (s, 1H), 4.79 (s, 2H), 3.55 (s, 2H), 2.50 (s, 2H), 1.66–1.18 ppm (br m, 8H); ^{13}C NMR (100 MHz, CD_3OD): δ = 175.6, 155.6, 147.2, 140.9, 132.7, 132.3, 127.8, 127.7, 108.8, 53.1, 42.2, 36.8, 28.1, 27.8, 27.5, 24.9, 24.3, 23.8 ppm; HRMS (ESI) calcd for $C_{16}H_{23}N_7O_2S_2$: 409.1355 $[M]^+$, found 409.1354.

***N*-(2-(4-(5-(2-Amino-1*H*-imidazol-4-yl)pentyl)-1*H*-1,2,3-triazol-1-yl)ethyl)-5-(dimethylamino)naphthalene-1-sulfonamide hydrochloride (7x):** *tert*-Butyl 2-amino-4-(hept-6-ynyl)-1*H*-imidazole-1-carboxylate (0.112 g, 0.403 mmol) was treated with *N*-(2-azidoethyl)-5-(dimethylamino)naphthalene-1-sulfonamide (0.140 g, 0.403 mmol) according to the general click procedure to give *tert*-butyl 2-amino-4-(5-(1-(2-(5-(dimethylamino)naphthalene-1-sulfonamido)ethyl)-1*H*-1,2,3-triazol-4-yl)pentyl)-1*H*-imidazole-1-carboxylate. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.48 (d, J = 8.4 Hz, 1H), 8.24 (d, J = 8.4 Hz, 1H), 8.17 (d, J = 7.2 Hz, 1H), 7.44 (m, 3H), 7.09 (s, 1H), 7.07 (d, J = 7.5 Hz, 1H), 6.44 (s, 1H), 6.09 (br s, 2H), 4.32 (s, 2H), 3.36 (s, 2H), 2.52 (s, 2H), 2.22 (s, 2H), 1.43 (m, 13H), 1.22 ppm (s, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 176.9, 152.1, 149.6, 148.0, 138.6, 135.1, 130.7, 130.1, 129.7, 129.4, 128.5, 123.3, 122.4, 119.1, 115.5, 84.9, 67.5, 50.3, 50.2, 45.6, 42.9, 37.9, 29.1, 28.9, 28.2, 28.0, 25.5 ppm; HRMS (ESI) calcd for $C_{29}H_{40}N_8O_4S$: 596.2893 $[M]^+$, found 596.2881. The carboxylate was subsequently deprotected to give **7x** (0.139 g, 65% yield). ^{1}H NMR (400 MHz, CD_3OD): δ = 8.70 (t, J = 4.8 Hz, 2H), 8.31 (s, 1H), 8.08 (s, 2H), 7.82 (s, 2H), 6.43 (s, 1H), 4.55 (s, 2H), 3.32 (s, 8H), 2.63 (s, 2H), 2.48 (s, 2H), 1.66 (s, 4H), 1.40 ppm (s, 2H); ^{13}C NMR (100 MHz, CD_3OD): δ = 159.9, 147.3, 140.7, 136.8, 129.9, 129.3, 127.8, 127.7, 126.5, 119.3, 108.6, 108.4, 76.7, 67.3, 51.5, 42.3, 37.4, 36.5, 28.3, 27.9, 27.6, 24.1, 24.0, 23.7 ppm; HRMS (ESI) calcd for $C_{24}H_{32}N_8O_2S$: 496.2369 $[M]^+$, found 496.2359.

***tert*-Butyl 2-amino-4-(5-(1-(2-(phenylsulfonamido)ethyl)-1*H*-1,2,3-triazol-4-yl)pentyl)-1*H*-imidazole-1-carboxylate hydrochloride (7n):** *tert*-Butyl 2-amino-4-(hept-6-ynyl)-1*H*-imidazole-1-carboxylate (0.114 g, 0.410 mmol) was treated with *N*-(2-azidoethyl)benzenesulfonamide (0.104 g, 0.410 mmol) according to the general click procedure to give *tert*-butyl 2-amino-4-(5-(1-(2-(phenylsulfonamido)ethyl)-1*H*-1,2,3-triazol-4-yl)pentyl)-1*H*-imidazole-1-carboxylate. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.81 (d, J = 6.9 Hz, 2H), 7.44 (m, 5H), 6.44 (s, 1H), 6.07 (s, 2H), 4.42 (t, J = 5.7 Hz, 2H), 3.36 (t, J = 5.4 Hz, 2H), 2.57 (t, J = 7.2 Hz, 2H), 2.20 (s, 2H), 1.47 (m, 13H), 1.29 ppm (s, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 202.9, 149.5, 148.2, 140.2, 132.8, 129.4, 127.1, 122.5, 106.5, 85.0, 53.7, 50.3, 42.9, 32.7, 31.2, 29.9, 29.2, 28.9, 28.2, 26.3, 25.5 ppm; HRMS (ESI) calcd for $C_{23}H_{33}N_7O_4S$: 503.2315 $[M]^+$, found 503.2310. The carboxylate was subsequently deprotected to give **7n** (0.142 g, 64% yield). ^{1}H NMR (300 MHz, CD_3OD): δ = 7.81 (d, J = 6.6 Hz, 2H), 7.56 (m, 4H), 6.47 (s, 1H), 4.62 (s, 2H), 3.41 (s, 2H), 2.78 (s, 2H), 2.48 (s, 2H), 1.72 (s, 2H), 1.63 (s, 2H), 1.42 ppm (s, 2H); ^{13}C NMR (75 MHz, CD_3OD): δ = 176.2, 165.6, 159.9, 147.3, 140.2, 132.8, 129.3, 127.7, 126.8, 108.5, 108.4, 515.8, 42.3, 28.1, 27.9, 27.6, 24.1 ppm; HRMS (ESI) calcd for $C_{18}H_{25}N_7O_2S$: 403.1790 $[M]^+$, found 403.1781.

***N*-(2-(4-(5-(2-Amino-1*H*-imidazol-4-yl)pentyl)-1*H*-1,2,3-triazol-1-yl)ethyl)-2,3,4,5,6-pentamethylbenzenesulfonamide hydrochloride (7a):** *tert*-Butyl 2-amino-4-(hept-6-ynyl)-1*H*-imidazole-1-carboxylate (0.120 g, 0.434 mmol) was treated with *N*-(2-azidoethyl)-2,3,4,5,6-pentamethylbenzenesulfonamide (0.141 g, 0.434 mmol) according to the general click procedure to give *tert*-butyl 2-amino-4-(5-(1-(2-(2,3,4,5,6-pentamethylphenylsulfonamido)ethyl)-1*H*-1,2,3-triazol-4-yl)pentyl)-1*H*-imidazole-1-carboxylate. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.30 (s, 1H), 7.01 (s, 1H), 6.44 (s, 1H), 6.17 (s, 2H), 4.35 (s, 2H), 3.34 (s, 2H), 2.47 (s, 2H), 2.48 (s, 6H), 2.20 (m, 11H), 1.43 ppm (m, 15H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 149.6, 148.1, 139.7, 136.2, 134.9, 134.3, 122.4, 84.9, 53.7, 50.2, 42.5, 31.1, 29.3, 28.9, 28.4, 28.2, 25.6, 19.1, 17.9, 17.2 ppm; HRMS (ESI) calcd for $C_{28}H_{43}N_7O_4S$: 573.3097 $[M]^+$, found 573.3086. The carboxylate was subsequently deprotected to give **7a** (0.143 g, 76% yield). ^{1}H NMR (400 MHz, CD_3OD): δ = 8.11 (s, 1H), 6.42 (s, 1H), 4.48 (s, 2H), 3.34 (s, 2H), 2.65 (s, 2H), 2.40 (s, 8H), 2.12 (s, 9H), 1.58 (s, 4H), 1.19 ppm (s, 2H); ^{13}C NMR (100 MHz, CD_3OD): δ = 159.9, 147.3, 139.6, 136.1, 134.8, 134.0, 127.8, 127.6, 108.6, 108.4, 54.1, 51.5, 41.8, 36.5, 28.2, 28.1, 27.7, 24.1, 23.7, 18.2, 16.8, 16.1 ppm; HRMS (ESI) calcd for $C_{23}H_{35}N_7O_2S$: 473.2573 $[M]^+$, found 473.2565.

(*E*)-*N*-(2-(4-(5-(2-Amino-1*H*-imidazol-4-yl)pentyl)-1*H*-1,2,3-triazol-1-yl)ethyl)-2-methyl-3-phenylacrylamide hydrochloride (7l): *tert*-Butyl 2-amino-4-(hept-6-ynyl)-1*H*-imidazole-1-carboxylate (0.1103 g, 0.397 mmol) was treated with (*E*)-*N*-(2-azidoethyl)-2-methyl-3-phenylacrylamide (0.092 g, 0.397 mmol) according to the general click procedure to give (*E*)-*tert*-butyl 2-amino-4-(5-(1-(2-(2-methyl-3-phenylacrylamido)ethyl)-1*H*-1,2,3-triazol-4-yl)pentyl)-1*H*-imidazole-1-carboxylate. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.28 (m, 7H), 6.94 (s, 2H), 6.06 (s, 2H), 4.46 (s, 2H), 3.79 (s, 2H), 2.61 (s, 2H), 2.27 (s, 2H), 1.99 (s, 3H), 1.49 (br s, 11H), 1.18 ppm (s, 4H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 192.4, 191.3, 170.4, 150.9, 140.2, 136.2, 134.8, 131.6, 129.6, 128.6, 128.1, 122.1, 95.8, 85.2, 74.3, 53.7, 52.6, 50.7, 49.4, 40.1, 29.9, 29.3, 28.9, 28.2, 25.6, 14.4 ppm; HRMS (ESI) calcd for $C_{27}H_{37}N_7O_3$: 507.2958 $[M]^+$, found 507.2942. The carboxylate was subsequently deprotected to give **7l** (0.148 g, 84% yield). ^{1}H NMR (400 MHz, CD_3OD): δ = 8.78 (s, 1H), 7.33 (s, 4H), 7.26 (s, 1H), 7.19 (s, 1H), 6.42 (s, 1H), 4.78 (s, 2H), 3.84 (s, 2H), 2.87 (s, 2H), 2.44 (s, 2H), 1.99 (s, 3H), 1.76 (s, 2H), 1.59 (s, 2H), 1.42 ppm (s, 2H); ^{13}C NMR (100 MHz, CD_3OD): δ = 174.7, 136.0, 134.4, 131.5, 129.3, 128.7, 128.3, 128.0, 127.6, 108.6, 94.6, 53.1, 39.2, 27.6, 27.9, 27.7, 27.6, 24.1, 23.8, 23.1, 14.3, 13.4 ppm; HRMS (ESI) calcd for $C_{22}H_{29}N_7O$: 407.2434 $[M]^+$, found 407.2429.

***N*-(2-(4-(5-(2-Amino-1*H*-imidazol-4-yl)pentyl)-1*H*-1,2,3-triazol-1-yl)ethyl)cinnamamide hydrochloride (7d):** *tert*-Butyl 2-amino-4-(hept-6-ynyl)-1*H*-imidazole-1-carboxylate (0.106 g, 0.384 mmol) was

treated with *N*-(2-azidoethyl)cinnamamide (0.083 g, 0.384 mmol) according to the general click procedure to give (*E*)-*tert*-butyl 2-amino-4-(5-(1-(2-cinnamamidoethyl)-1*H*-1,2,3-triazol-4-yl)pentyl)-1*H*-imidazole-1-carboxylate. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.67 (s, 1H), 7.51 (d, J = 11.1 Hz, 1H), 7.28 (m, 6H), 6.45 (t, J = 14.1 Hz, 2H), 6.08 (s, 2H), 4.47 (s, 2H), 3.79 (s, 2H), 2.57 (s, 2H), 2.23 (s, 2H), 1.50 (br s, 13H), 1.28 ppm (s, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 166.9, 150.4, 149.5, 148.3, 141.2, 138.9, 134.9, 129.9, 128.9, 128.0, 122.1, 120.8, 106.5, 84.8, 53.7, 49.5, 39.9, 31.1, 29.3, 28.9, 28.3, 28.2, 25.6 ppm; HRMS (ESI) calcd for $C_{26}H_{35}N_7O_3$: 493.2801 $[M]^+$, found 493.2800. The carboxylate was subsequently deprotected to give **7d** (0.097 g, 59% yield). ^{1}H NMR (400 MHz, CD_3OD): δ = 8.10 (s, 1H), 7.49 (s, 3H), 7.32 (s, 3H), 6.30 (d, J = 10.8 Hz, 1H), 6.39 (s, 1H), 4.66 (s, 2H), 3.83 (s, 2H), 2.73 (s, 2H), 2.40 (s, 2H), 1.57 (s, 2H), 1.55 (s, 2H), 1.36 ppm (s, 2H); ^{13}C NMR (100 MHz, CD_3OD): δ = 167.8, 160.5, 150.2, 147.3, 141.1, 134.8, 130.7, 129.9, 128.8, 127.8, 127.6, 124.9, 123.9, 120.2, 108.5, 108.3, 53.1, 39.3, 36.5, 30.6, 28.4, 28.1, 27.6, 26.5, 24.2, 24.1, 23.7 ppm; HRMS (ESI) calcd for $C_{21}H_{27}N_7O$: 393.2277 $[M]^+$, found 393.2273.

***N*-(2-(4-(5-(2-Amino-1*H*-imidazol-4-yl)pentyl)-1*H*-1,2,3-triazol-1-yl)ethyl)heptadec-8-enamide hydrochloride (7m):** *tert*-Butyl 2-amino-4-(hept-6-ynyl)-1*H*-imidazole-1-carboxylate (0.098 g, 0.353 mmol) was treated with *N*-(2-azidoethyl)octadec-9-heptadec-8-enamide (0.124 g, 0.353 mmol) according to the general click procedure to give *tert*-butyl 2-amino-4-(5-(1-(2-heptadec-8-enamidoethyl)-1*H*-1,2,3-triazol-4-yl)pentyl)-1*H*-imidazole-1-carboxylate. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.26 (s, 1H), 6.81 (s, 1H), 6.42 (s, 2H), 5.88 (s, 1H), 5.27 (s, 2H), 4.38 (s, 2H), 3.65 (s, 2H), 2.60 (s, 2H), 2.09 (s, 2H), 1.53–1.01 (m, 35H), 0.79 ppm (t, J = 6.3 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 174.2, 173.8, 148.3, 130.3, 130.1, 129.9, 129.8, 121.9, 85.1, 67.1, 49.5, 39.5, 39.1, 38.0, 37.7, 36.7, 36.6, 32.8, 32.3, 32.1, 31.7, 29.9, 29.8, 29.7, 29.5, 29.3, 29.2, 28.9, 28.7, 28.1, 28.0, 27.9, 27.4, 27.3, 27.3, 26.9, 25.9, 25.6, 25.3, 22.9, 22.8, 22.6, 14.3, 14.2 ppm; HRMS (ESI) calcd for $C_{35}H_{61}N_7O_3$: 627.4836 $[M]^+$, found 627.4823. The carboxylate was subsequently deprotected to give **7m** (0.128 g, 66% yield). ^{1}H NMR (400 MHz, CD_3OD): δ = 8.36 (s, 1H), 6.96 (s, 1H), 6.45 (s, 1H), 6.09 (s, 1H), 4.58 (s, 2H), 3.58 (s, 2H), 2.75 (s, 2H), 2.10 (s, 2H), 1.96 (s, 4H), 1.69 (s, 2H), 1.41 (m, 4H), 1.23 (s, 24H), 0.84 ppm (s, 3H); ^{13}C NMR (100 MHz, CD_3OD): δ = 175.5, 158.8, 155.7, 147.3, 129.7, 129.6, 127.6, 108.5, 94.6, 76.7, 51.3, 50.4, 48.6, 48.4, 48.2, 47.9, 47.8, 47.5, 47.3, 38.9, 37.5, 36.6, 45.9, 45.8, 33.9, 32.6, 31.9, 31.5, 29.8, 29.5, 29.4, 29.3, 29.2, 29.1, 28.2, 27.8, 27.0, 25.8, 24.9, 24.2, 23.8, 22.5, 13.5, 13.3 ppm; HRMS (ESI) calcd for $C_{30}H_{53}N_7O$: 527.4312 $[M]^+$, found 527.4298.

***N*-(2-(4-(5-(2-Amino-1*H*-imidazol-4-yl)pentyl)-1*H*-1,2,3-triazol-1-yl)ethyl)decanamide hydrochloride (7e):** *tert*-Butyl 2-amino-4-(hept-6-ynyl)-1*H*-imidazole-1-carboxylate (0.114 g, 0.412 mmol) was treated with *N*-(2-azidoethyl)decanamide (0.099 g, 0.412 mmol) according to the general click procedure to give *tert*-butyl 2-amino-4-(5-(1-(2-decanamidoethyl)-1*H*-1,2,3-triazol-4-yl)pentyl)-1*H*-imidazole-1-carboxylate. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.23 (s, 1H), 6.57 (s, 1H), 6.43 (s, 1H), 6.09 (s, 2H), 4.38 (s, 2H), 3.67 (s, 2H), 2.61 (t, J = 5.4 Hz, 2H), 2.08 (s, 2H), 2.08 (t, J = 5.7 Hz, 2H), 1.42 (m, 15H), 1.17 (m, 14H), 0.79 ppm (t, J = 4.5 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 174.2, 149.7, 148.4, 138.8, 121.9, 106.6, 84.9, 49.5, 39.5, 36.7, 32.1, 31.3, 30.6, 29.9, 29.7, 29.6, 29.5, 29.5, 29.3, 29.0, 28.3, 28.2, 25.9, 25.6, 25.5, 22.9, 14.3 ppm; HRMS (ESI) calcd for $C_{27}H_{47}N_7O_3$: 517.3740 $[M]^+$, found 517.3736. The carboxylate was subsequently deprotected to give **7e** (0.137 g, 73% yield). ^{1}H NMR (300 MHz, CD_3OD): δ = 8.55 (s, 1H), 6.53 (s, 1H), 4.72 (s, 2H), 3.75 (s, 2H), 2.89 (s, 2H), 2.54 (t, J = 6.8 Hz, 2H), 2.16 (t, J = 7.2 Hz, 2H), 1.81 (s, 2H), 1.69 (s, 2H), 1.49 (m, 4H), 1.28 (s, 12H), 0.89 ppm (t, 3H); ^{13}C NMR (75 MHz, CD_3OD): δ = 175.7, 147.3, 128.5, 127.6, 125.1, 120.8, 108.6, 108.4, 105.6, 63.1, 59.3, 52.5, 48.6, 48.3, 48.1, 47.9, 47.7, 47.5, 57.3, 38.7, 336.6, 35.8, 36.6, 35.8, 31.8, 30.6, 29.4, 29.3, 29.3, 29.2, 28.0, 27.8, 27.7, 25.8, 24.1, 23.9, 23.3, 22.6 ppm; HRMS (ESI) calcd for $C_{22}H_{39}N_7O$: 417.3216 $[M]^+$, found 417.3209.

***N*-(2-(4-(5-(2-Amino-1*H*-imidazol-4-yl)pentyl)-1*H*-1,2,3-triazol-1-yl)ethyl)dodecanamide hydrochloride (7f):** *tert*-Butyl 2-amino-4-(hept-6-ynyl)-1*H*-imidazole-1-carboxylate (0.107 g, 0.387 mmol) was treated with *N*-(2-azidoethyl)dodecanamide (0.104 g, 0.387 mmol) according to the general click procedure to give *tert*-butyl 2-amino-4-(5-(1-(2-dodecanamidoethyl)-1*H*-1,2,3-triazol-4-yl)pentyl)-1*H*-imidazole-1-carboxylate. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.36 (s, 1H), 6.94 (s, 1H), 6.49 (s, 1H), 6.23 (s, 2H), 4.46 (t, J = 5.1 Hz, 2H), 3.74 (q, J = 5.1, 5.7 Hz, 2H), 2.68 (t, J = 7.5 Hz, 2H), 2.34 (t, J = 6.9 Hz, 2H), 2.16 (t, J = 7.5 Hz, 2H), 1.54 (m, 13H), 1.47 (m, 2H), 1.24 (m, 18H), 0.87 ppm (t, J = 6.6 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 174.3, 150.4, 149.5, 148.3, 138.5, 121.9, 106.5, 84.9, 49.5, 39.5, 36.6, 34.1, 32.1, 29.8, 29.8, 29.7, 29.6, 29.5, 29.3, 28.9, 28.2, 28.1, 29.0, 26.9. 25.6, 22.9, 14.3 ppm; HRMS (ESI) calcd for $C_{29}H_{51}N_7O_3$: 545.4053 $[M]^+$, found 545.4053. The carboxylate was subsequently deprotected to give **7f** (0.155 g, 83% yield). ^{1}H NMR (400 MHz, CD_3OD): δ = 8.31 (s, 1H), 6.49 (s, 1H), 4.63 (s, 2H), 3.97 (s, 2H), 2.81 (s, 2H), 2.51 (t, J = 7.2 Hz, 2H), 2.14 (t, J = 7.2 Hz, 2H), 1.76 (s, 2H), 1.67 (s, 2H), 1.51 (s, 2H), 1.44 (s, 2H), 1.26 (br s, 16H), 0.71 ppm (s, 3H); ^{13}C NMR (100 MHz, CD_3OD): δ = 175.6, 159.4, 147.3, 127.6, 108.5, 51.3, 48.6, 38.8, 35.8, 31.9, 29.6, 29.5, 29.4, 29.3, 29.2, 28.2, 28.1, 27.7, 24.8, 24.2, 23.9, 22.6, 22.5, 13.4, 13.3 ppm; HRMS (ESI) calcd for $C_{24}H_{43}N_7O$: 445.3429 $[M]^+$, found 445.3524.

***N*-(2-(4-(5-(2-Amino-1*H*-imidazol-4-yl)pentyl)-1*H*-1,2,3-triazol-1-yl)ethyl)tetradecanamide hydrochloride (7g):** *tert*-Butyl 2-amino-4-(hept-6-ynyl)-1*H*-imidazole-1-carboxylate (0.111 g, 0.401 mmol) was treated with *N*-(2-azidoethyl)tetradecanamide (0.130 g, 0.401 mmol) according to the general click procedure to give *tert*-butyl 2-amino-4-(5-(1-(2-tetradecanamidoethyl)-1*H*-1,2,3-triazol-4-yl)pentyl)-1*H*-imidazole-1-carboxylate. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.26 (s, 1H), 6.85 (s, 1H), 6.42 (s, 1H), 6.05 (s, 1H), 4.38 (s, 2H), 3.66 (s, 2H), 2.60 (s, 2H), 2.11 (s, 2H), 2.08 (t, J = 3.6 Hz, 2H), 1.41 (m, 13H), 1.32 (s, 2H), 1.17 (s, 18H), 0.77 ppm (t, J = 6.6 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 202.9, 174.3, 149.6, 148.3, 121.9, 100.1, 84.8, 49.5, 42.3, 39.5, 36.7, 32.1, 29.9, 29.8, 29.7, 29.6, 29.5, 29.5, 29.3, 28.9, 28.1, 25.9, 25.6, 22.9, 14.3 ppm; HRMS (ESI) calcd for $C_{31}H_{55}N_7O_3$: 573.4366 $[M]^+$, found 573.4365. The carboxylate was subsequently deprotected to give **7g** (0.118 g, 87% yield). ^{1}H NMR (400 MHz, CD_3OD): δ = 8.51 (s, 1H), 6.53 (s, 1H), 4.71 (s, 2H), 3.75 (s, 2H), 2.89 (s, 2H), 2.54 (t, J = 6.8 Hz, 2H), 2.17 (t, J = 6.8 Hz, 2H), 1.80 (s, 2H), 1.69 (s, 2H), 1.54 (s, 2H), 1.48 (s, 2H), 1.28 (s, 20H), 0.88 ppm (t, J = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, CD_3OD): δ = 175.6, 161.8, 147.2, 127.6, 127.4, 108.5, 52.3, 38.8, 36.6, 35.8, 31.9, 30.6, 29.7, 29.6, 29.5, 29.4, 29.2, 28.0, 27.9, 27.7, 25.8, 24.1, 23.6, 23.4, 22.6, 13.4 ppm; HRMS (ESI) calcd for $C_{26}H_{47}N_7O$: 473.3842 $[M]^+$, found 473.3834.

***N*-(2-(4-(5-(2-Amino-1*H*-imidazol-4-yl)pentyl)-1*H*-1,2,3-triazol-1-yl)ethyl)palmitamide hydrochloride (7h):** *tert*-Butyl 2-amino-4-(hept-6-ynyl)-1*H*-imidazole-1-carboxylate (0.087 g, 0.313 mmol) was treated with *N*-(2-azidoethyl)palmitamide (0.102 g, 0.313 mmol) according to the general click procedure to give *tert*-butyl 2-amino-4-(5-(1-(2-palmitamidoethyl)-1*H*-1,2,3-triazol-4-yl)pentyl)-1*H*-imidazole-1-carboxylate. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.29 (s, 1H), 6.78 (t, J = 4.5 Hz, 1H), 6.41 (s, 1H), 6.19 (s, 2H), 4.39 (t, J = 5.4 Hz, 2H), 3.67 (q, J = 5.5, 4.8 Hz, 2H), 2.61 (t, J = 6.9 Hz, 2H), 2.12 (t, J = 6.5 Hz, 2H), 2.07 (t, J = 7.5 Hz, 2H), 1.42 (m, 13H), 1.42 (m, 2H), 1.32 (m, 22H), 0.81 ppm (t, J = 5.4 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ =

176.8, 174.3, 173.9, 149.5, 148.3, 121.9, 106.4, 85.0, 67.2, 51.1, 49.5, 39.5, 39.1, 38.1, 36.8, 36.7, 32.1, 29.9, 29.8, 29.7, 29.6, 29.5, 29.3, 28.9, 28.3, 28.2, 27.9, 25.9, 25.6, 22.9, 14.3 ppm; HRMS (ESI) calcd for $C_{33}H_{59}N_7O_3$: 601.4679 $[M]^+$, found 601.4671. The carboxylate was subsequently deprotected to give **7h** (0.155 g, 92% yield). ^{1}H NMR (300 MHz, CD_3OD): δ = 8.59 (s, 1H), 6.53 (s, 1H), 4.72 (s, 2H), 3.75 (s, 2H), 2.90 (s, 2H), 2.54 (s, 2H), 2.16 (t, J = 7.2 Hz, 2H), 1.80 (s, 2H), 1.69 (s, 2H), 1.51 (s, 4H), 1.28 (br s, 24H), 0.71 ppm (t, J = 6.3 Hz, 3H); ^{13}C NMR (75 MHz, CD_3OD): δ = 175.7, 147.2, 145.6, 128.4, 127.6, 108.6, 67.2, 52.7, 37.4, 36.5, 35.8, 31.9, 29.7, 29.5, 29.4, 29.2, 28.0, 27.9, 27.8, 27.7, 25.8, 24.1, 23.6, 23.2, 22.6 ppm; HRMS (ESI) calcd for $C_{28}H_{51}N_7O$: 501.4155 $[M]^+$, found 501.4143.

***N*-(2-(4-(5-(2-Amino-1*H*-imidazol-4-yl)pentyl)-1*H*-1,2,3-triazol-1-yl)ethyl)-4,5-dibromo-1-methyl-1*H*-pyrrole-2-carboxamide hydrochloride (7k):** *tert*-Butyl 2-amino-4-(hept-6-ynyl)-1*H*-imidazole-1-carboxylate (0.116 g, 0.417 mmol) was treated with *N*-(2-azidoethyl)-4,5-dibromo-1-methyl-1*H*-pyrrole-2-carboxamide (0.145 g, 0.417 mmol) according to the general click procedure to give *tert*-butyl 2-amino-4-(5-(1-(2-(4,5-dibromo-1-methyl-1*H*-pyrrole-2-carboxamido)ethyl)-1*H*-1,2,3-triazol-4-yl)pentyl)-1*H*-imidazole-1-carboxylate. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.76 (s, 1H), 7.32 (s, 1H), 6.81 (s, 1H), 6.49 (s, 1H), 6.17 (s, 2H), 4.52 (s, 2H), 3.94 (s, 3H), 3.84 (s, 2H), 2.65 (t, J = 7.2 Hz, 2H), 2.30 (m, 2H), 1.58 (m, 13H), 1.35 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 161.2, 149.6, 148.2, 138.8, 127.4, 122.2, 114.9, 111.9, 106.5, 98.2, 84.5, 49.5, 39.7, 35.9, 29.3, 28.9, 28.2, 28.0, 27.7, 25.6 ppm; HRMS (ESI) calcd for $C_{23}H_{32}N_8O_3$: 626.0964 $[M]^+$, found 626.0960. The carboxylate was subsequently deprotected to give **7k** (0.151 g, 64% yield). ^{1}H NMR (400 MHz, CD_3OD): δ = 8.24 (s, 1H), 6.86 (s, 1H), 6.56 (s, 1H), 4.71 (s, 2H), 3.81 (s, 5H), 2.78 (s, 2H), 2.44 (t, J = 7.2 Hz, 2H), 1.69 (s, 2H), 1.59 (s, 2H), 1.37 ppm (s, 2H); ^{13}C NMR (100 MHz, CD_3OD): δ = 161.4, 150.2, 159.8, 159.4, 147.3, 127.6, 127.3, 114.9, 111.6, 108.4, 97.9, 51.3, 39.0, 35.2, 28.3, 28.0, 27.6, 24.2, 23.8 ppm; HRMS (ESI) calcd for $C_{18}H_{24}Br_2N_8O$: 526.0439 $[M]^+$, found 526.0425.

***N*-(2-(4-(5-(2-Amino-1*H*-imidazol-4-yl)pentyl)-1*H*-1,2,3-triazol-1-yl)ethyl)-4-bromo-1*H*-pyrrole-2-carboxamide hydrochloride (7z):** *tert*-Butyl 2-amino-4-(hept-6-ynyl)-1*H*-imidazole-1-carboxylate (0.104 g, 0.375 mmol) was treated with *N*-(2-azidoethyl)-4-bromo-1*H*-pyrrole-2-carboxamide (0.131 g, 0.375 mmol) according to the general click procedure to give *tert*-butyl 2-amino-4-(5-(1-(2-(4-bromo-1*H*-pyrrole-2-carboxamido)ethyl)-1*H*-1,2,3-triazol-4-yl)pentyl)-1*H*-imidazole-1-carboxylate. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 11.44 (s, 1H), 7.84 (s, 1H), 7.28 (s, 1H), 6.84 (s, 1H), 6.74 (s, 1H), 6.46 (s, 1H), 4.89 (s, 2H), 3.82 (s, 2H), 2.57 (s, 2H), 2.28 (s, 2H), 1.55 (m, 13H), 1.29 ppm (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 186.8, 161.4, 150.7, 149.3, 148.2, 137.6, 126.3, 122.5, 122.1, 113.1, 100.4, 96.9, 85.4, 49.6, 29.1, 28.7, 28.2, 27.7, 25.5 ppm; HRMS (ESI) calcd for $C_{22}H_{31}BrN_8O_3$: 534.1703 $[M]^+$, found 534.1705. The carboxylate was subsequently deprotected to give **7z** (0.129 g, 73% yield). ^{1}H NMR (400 MHz, CD_3OD): δ = 8.42 (s, 1H), 6.93 (s, 1H), 6.82 (s, 1H), 6.47 (s, 1H), 4.76 (s, 2H), 3.87 (s, 2H), 2.79 (s, 2H), 2.45 (s, 2H), 1.69 (s, 2H), 1.60 (s, 2H), 1.37 ppm (s, 2H); ^{13}C NMR (100 MHz, CD_3OD): δ = 161.4, 159.5, 159.1, 147.3, 147.2, 127.6, 125.8, 122.3, 122.1, 112.8, 108.6, 108.5, 96.4, 51.9, 38.9, 28.0, 27.9, 27.6, 24.1, 23.6 ppm; HRMS (ESI) calcd for $C_{17}H_{23}BrN_8O$: 434.1178 $[M]^+$, found 434.1171.

***N*-(2-(4-(5-(2-Amino-1*H*-imidazol-4-yl)pentyl)-1*H*-1,2,3-triazol-1-yl)ethyl)-1*H*-pyrrole-2-carboxamide hydrochloride (7c):** *tert*-Butyl 2-amino-4-(hept-6-ynyl)-1*H*-imidazole-1-carboxylate (0.097 g, 0.349 mmol) was treated with *N*-(2-azidoethyl)-1*H*-pyrrole-2-carboxamide (0.063 g, .349 mmol) according to the general click procedure to give *tert*-butyl 4-(5-(1-(2-(1*H*-pyrrole-2-carboxamido)ethyl)-1*H*-1,2,3-triazol-4-yl)pentyl)-2-amino-1*H*-imidazole-1-carboxylate. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.18 (s, 1H), 7.36 (d, J = 5.7 Hz, 2H), 7.24 (s, 1H), 6.84 (t, J = 8.1 Hz, 1H), 6.43 (s, 1H), 6.04 (s, 2H), 4.49 (s, 2H), 3.89 (s, 2H), 2.53 (s, 2H), 2.09 (s, 2H), 1.44 (m, 13H), 1.24 ppm (s, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 165.9, 164.8, 164.6, 161.5, 137.5, 122.3, 111.0, 110.7, 107.5, 107.1, 106.8, 85.1, 49.4, 40.5, 29.3, 28.9, 28.2, 25.5 ppm; HRMS (ESI) calcd for $C_{22}H_{32}N_8O_3$: 456.2597 $[M]^+$, found 456.2590. The carboxylate was subsequently deprotected to give **7c** (0.129 g, 94% yield). ^{1}H NMR (400 MHz, CD_3OD): δ = 8.65 (s, 1H), 7.41 (s, 2H), 7.17 (s, 1H), 6.50 (s, 1H), 4.74 (s, 2H), 3.98 (s, 2H), 2.88 (s, 2H), 2.49 (s, 2H), 1.78 (m, 4H), 1.44 ppm (s, 2H); ^{13}C NMR (100 MHz, CD_3OD): δ = 166.3, 164.5, 162.0, 161.9, 137.4, 110.6, 110.3, 110.2, 108.5, 107.1, 106.8, 59.3, 52.4, 39.5, 36.5, 27.9, 27.8, 27.6, 24.1, 23.5, 23.3 ppm; HRMS (ESI) calcd for $C_{17}H_{24}N_8O$: 356.2073 $[M]^+$, found 356.2080.

***N*-(2-(4-(5-(2-Amino-1*H*-imidazol-4-yl)pentyl)-1*H*-1,2,3-triazol-1-yl)ethyl)-4-*tert*-butylbenzamide hydrochloride (7p):** *tert*-Butyl 2-amino-4-(hept-6-ynyl)-1*H*-imidazole-1-carboxylate (0.070 g, 0.253 mmol) was treated with *N*-(2-azidoethyl)-4-*tert*-butylbenzamide (0.062 g, 0.253 mmol) according to the general click procedure to give *tert*-butyl 2-amino-4-(5-(1-(2-(4-*tert*-butylbenzamido)ethyl)-1*H*-1,2,3-triazol-4-yl)pentyl)-1*H*-imidazole-1-carboxylate. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.71 (d, J = 7.5 Hz, 2H), 7.64 (t, J = 5.7 Hz, 1H), 7.36 (d, J = 7.5 Hz, 2H), 7.27 (s, 1H), 6.42 (s, 1H), 5.99 (s, 2H), 4.51 (t, J = 5.7 Hz, 2H), 3.88 (q, J = 5.1, 5.3 Hz, 2H), 2.58 (t, J = 7.5 Hz, 2H), 2.22 (t, J = 7.5 Hz, 2H), 1.52 (m, 13H), 1.21 ppm (m, 11H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 168.2, 155.3, 150.4, 149.6, 148.3, 138.9, 131.2, 127.3, 125.6, 122.2, 106.5, 84.8, 49.4, 40.2, 35.1, 31.3, 31.1, 29.3, 28.9, 28.3, 28.2, 28.1, 25.6 ppm; HRMS (ESI) calcd for $C_{28}H_{41}N_7O_3$: 523.3271 $[M]^+$, found 523.3270. The carboxylate was subsequently deprotected to give **7p** (0.105 g, 90% yield). ^{1}H NMR (400 MHz, CD_3OD): δ = 8.48 (s, 1H), 7.76 (d, J = 6.3 Hz, 2H), 7.48 (d, J = 6.3 Hz, 2H), 6.50 (s, 1H), 4.84 (s, 2H), 3.95 (s, 2H), 2.85 (s, 2H), 2.46 (t, J = 5.4 Hz, 2H), 1.73 (s, 2H), 1.57 (m, 2H), 1.39 (s, 2H), 1.31 ppm (s, 9H); ^{13}C NMR (100 MHz, CD_3OD): δ = 169.2, 155.6, 147.3, 130.8, 129.9, 127.6, 127.2, 127.1, 126.7, 125.4, 125.3, 119.5, 108.6, 108.5, 52.3, 39.4, 34.6, 30.4, 27.9, 27.8, 27.6, 24.1, 23.2, 22.2 ppm; HRMS (ESI) calcd for $C_{23}H_{33}N_7O$: 423.2747 $[M]^+$, found 423.2741.

***N*-(2-(4-(5-(2-Amino-1*H*-imidazol-4-yl)pentyl)-1*H*-1,2,3-triazol-1-yl)ethyl)-2-naphthamide hydrochloride (7b):** *tert*-Butyl 2-amino-4-(hept-6-ynyl)-1*H*-imidazole-1-carboxylate (0.095 g, 0.344 mmol) was treated with *N*-(2-azidoethyl)-2-naphthamide (0.083 g, 0.344 mmol) according to the general click procedure to give *tert*-butyl 4-(5-(1-(2-(2-naphthamido)ethyl)-1*H*-1,2,3-triazol-4-yl)pentyl)-2-amino-1*H*-imidazole-1-carboxylate. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.24 (s, 1H), 8.01 (s, 1H), 7.72 (m, 4H), 7.39 (m, 2H), 7.26 (s, 1H), 6.33 (s, 1H), 6.04 (s, 2H), 4.51 (s, 2H), 3.88 (s, 2H), 2.48 (t, 2H), 2.12 (s, 2H), 1.47 (m, 13H), 1.17 ppm (s, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 168.5, 150.4, 149.5, 148.3, 138.6, 134.9, 132.7, 131.4, 129.2, 128.5, 128.1, 127.9, 126.8, 124.0, 122.3, 106.5, 84.9, 49.4, 40.4, 29.9, 29.2, 28.9, 28.6, 28.2, 27.9, 28.6, 27.9, 27.8, 25.6 ppm; HRMS (ESI) calcd for $C_{28}H_{35}N_7O_3$: 517.2801 $[M]^+$, found 517.2792. The carboxylate was subsequently deprotected to give **7b** (0.140 g, 90% yield). ^{1}H NMR (400 MHz, CD_3OD): δ = 8.38 (s, 1H), 7.96 (m, 3H), 7.83 (t, J = 7.2 Hz, 2H), 7.58 (t, J = 6.4 Hz, 2H), 7.33 (s, 1H), 6.22 (s, 1H), 5.89 (s, 2H), 4.54 (t, J = 5.6 Hz, 2H), 3.72 (q, J = 5.2, 3.3 Hz, 2H), 2.56 (q, J = 7.6, 7.2 Hz, 2H), 2.24 (t, J = 7.6 Hz, 2H), 1.54 (t, J = 6.8 Hz, 2H), 1.47 (t, J = 7.2 Hz, 2H), 1.23 (m, 4H) ppm; ^{13}C NMR (100 MHz, CD_3OD): δ = 167.8, 161.1, 148.7, 147.4, 134.8, 132.8, 132.2, 129.5, 128.9, 128.6, 128.3, 128.2, 127.5, 126.4, 124.5, 122.9, 110.4, 65.8, 49.1, 32.3, 29.4, 28.7, 26.3, 25.7 ppm; HRMS (ESI) calcd for $C_{23}H_{27}N_7O$: 417.2277 $[M]^+$, found 417.2274.

***N*-(2-(4-(5-(2-Amino-1*H*-imidazol-4-yl)pentyl)-1*H*-1,2,3-triazol-1-yl)ethyl)-2-iodobenzamide hydrochloride (7y):** *tert*-Butyl 2-amino-4-(hept-6-ynyl)-1*H*-imidazole-1-carboxylate (0.083 g, 0.299 mmol) was treated with *N*-(2-azidoethyl)-2-iodobenzamide (0.095 g, 0.299 mmol) according to the general click procedure to give *tert*-butyl 2-amino-4-(5-(1-(2-(2-iodobenzamido)ethyl)-1*H*-1,2,3-triazol-4-yl)pentyl)-1*H*-imidazole-1-carboxylate. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.74 (d, J = 7.5 Hz, 2H), 7.57 (t, J = 4.5 Hz, 1H), 7.36 (s, 1H), 7.22 (s, 2H), 6.97 (m, 1H), 6.39 (s, 1H), 5.97 (s, 2H), 4.48 (t, J = 5.1 Hz, 2H), 3.85 (m, 2H), 2.44 (t, J = 7.5 Hz, 2H), 2.18 (t, J = 6.6 Hz, 2H), 1.45 (m, 13H), 1.18 ppm (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 170.3, 150.4, 149.5, 148.2, 141.8, 139.9, 138.7, 131.3, 128.4, 128.3, 122.3, 106.5, 92.8, 84.9, 49.2, 40.5, 29.2, 28.9, 28.3, 28.2, 28.0, 25.5 ppm; HRMS (ESI) calcd for $C_{24}H_{32}IN_7O_3$: 593.1611 $[M]^+$, found 593.1603. The carboxylate was subsequently deprotected to give **7y** (0.125 g, 79% yield). ^{1}H NMR (400 MHz, CD_3OD): δ = 8.35 (s, 1H), 7.88 (d, J = 7.8 Hz, 1H), 7.45 (t, J = 6.9 Hz, 1H), 7.34 (d, J = 6.9 Hz, 1H), 7.15 (t, J = 7.5 Hz, 1H), 6.47 (s, 1H), 4.78 (s, 2H), 3.99 (s, 2H), 2.83 (s, 2H), 2.44 (t, J = 6.9 Hz, 2H), 1.76 (s, 2H), 1.64 (s, 2H), 1.29 ppm (s, 2H); ^{13}C NMR (75 MHz, CD_3OD): δ = 171.6, 159.2, 147.3, 142.1, 139.8, 131.2, 128.2, 127.7, 124.4, 92.1, 52.2, 40.8, 39.4, 31.2, 28.3, 28.1, 27.7, 24.1, 20.9, 15.9, 10.7 ppm; HRMS (ESI) calcd for $C_{19}H_{24}IN_7O$: 493.1087 $[M]^+$, found 493.1085.

***N*-(2-(4-(5-(2-Amino-1*H*-imidazol-4-yl)pentyl)-1*H*-1,2,3-triazol-1-yl)ethyl)-4-heptylbenzamide hydrochloride (7u):** *tert*-Butyl 2-amino-4-(hept-6-ynyl)-1*H*-imidazole-1-carboxylate (0.125 g, 0.449 mmol) was treated with *N*-(2-azidoethyl)-4-heptylbenzamide (0.129 g, 0.449 mmol) according to the general click procedure to give *tert*-butyl 2-amino-4-(5-(1-(2-(4-heptylbenzamido)ethyl)-1*H*-1,2,3-triazol-4-yl)pentyl)-1*H*-imidazole-1-carboxylate. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.78 (s, 1H), 7.65 (d, 2H), 7.27 (s, 1H), 7.09 (d, 2H), 6.39 (s, 1H), 6.22 (s, 2H), 4.47 (s, 2H), 3.81 (s, 2H), 3.96 (s, 4H), 2.20 (s, 2H), 2.05 (s, 2H), 1.48 (m, 12H), 1.17 (m, 8H), 0.77 (t, J = 6.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 168.3, 149.6, 148.2, 147.1, 138.6, 131.5, 128.6, 127.4, 122.1, 106.4, 84.8, 67.1, 49.4, 40.2, 37.9, 36.9, 31.9, 31.3, 31.1, 29.8, 28.4, 29.3, 28.9, 28.3, 28.1, 28.0, 25.5, 22.8, 14.3 ppm; HRMS (ESI) calcd for $C_{31}H_{47}N_7O_3$: 565.3704 $[M]^+$, found 656.3737. The carboxylate was subsequently deprotected to give **7u** (0.194 g, 86% yield). ^{1}H NMR (300 MHz, CD_3OD): δ = 8.25 (s, 1H), 7.71 (d, J = 5.4 Hz, 2H), 7.24 (d, J = 5.7 Hz, 2H), 6.45 (s, 1H), 4.74 (s, 2H), 3.90 (s, 2H), 2.63 (s, 2H), 2.61 (t, 2H), 2.41 (s, 2H), 1.58 (m, 6H), 1.26 (m, 10H), 0.85 ppm (t, J = 4.8 Hz, 3H); ^{13}C NMR (100 MHz, CD_3OD): δ = 169.2, 150.2, 147.4, 131.2, 128.5, 127.6, 127.3, 108.4, 51.4, 39.6, 36.5, 35.6, 31.8, 331.3, 29.1, 29.1, 28.3, 28.0, 27.7, 24.1, 22.6, 13.4, 13.3 ppm; HRMS (ESI) calcd for $C_{26}H_{39}N_7O$: 465.3216 $[M]^+$, found 465.3207.

***N*-(2-(4-(5-(2-Amino-1*H*-imidazol-4-yl)pentyl)-1*H*-1,2,3-triazol-1-yl)ethyl)-4-hexylbenzamide hydrochloride (7t):** *tert*-Butyl 2-amino-4-(hept-6-ynyl)-1*H*-imidazole-1-carboxylate (0.097 g, 0.349 mmol) was treated with *N*-(2-azidoethyl)-4-hexylbenzamide (0.096 g, 0.349 mmol) according to the general click procedure to give *tert*-butyl 2-amino-4-(5-(1-(2-(4-hexylbenzamido)ethyl)-1*H*-1,2,3-triazol-4-yl)pentyl)-1*H*-imidazole-1-carboxylate. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.65 (d, J = 8.1 Hz, 2H), 7.55 (t, J = 6.7 Hz, 1H), 7.26 (s, 1H), 7.09 (d, J = 7.8 Hz, 2H), 6.39 (s, 1H), 6.04 (s, 2H), 4.48 (t, J = 4.8 Hz, 2H), 3.83 (q, J = 5.6, 4.8 Hz, 2H), 2.56 (q, J = 7.5, 8.1 Hz, 4H), 2.24 (t, J = 6.9 Hz, 2H), 1.50 (m, 13H), 1.21 (m, 1H), 0.77 ppm (t, J = 5.7 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 168.3, 148.3, 147.3, 138.7, 131.4, 128.7, 127.4, 122.2, 106.4, 84.9, 73.9, 49.5, 40.2, 36.0, 31.8, 31.3, 29.9, 29.3, 29.1, 28.9, 28.2, 28.1, 28.0, 25.6, 22.8, 14.3 ppm; HRMS (ESI) calcd for $C_{30}H_{45}N_7O_3$: 551.3584 $[M]^+$, found 551.3581. The carboxylate was subsequently deprotected to give **7t** (0.164 g, 96% yield). ^{1}H NMR (400 MHz, CD_3OD): δ = 8.28 (s, 1H), 7.67 (d, J = 7.6 Hz, 2H), 7.21 (d, J = 7.6 Hz, 2H), 6.43 (s, 1H), 4.72 (s, 2H), 3.87 (s, 2H), 2.74 (s, 2H), 2.58 (t, J = 7.6 Hz, 2H), 2.31 (t, J = 6.8 Hz, 2H), 1.66 (s, 2H), 1.55 (s, 4H), 1.35 (s, 2H), 1.25 (s, 6H), 0.66 ppm (t, J = 8.8 Hz, 3H); ^{13}C NMR (100 MHz, CD_3OD): δ = 169.2, 159.5, 147.4, 147.3, 131.2, 108.4, 51.2, 48.5, 48.3, 48.1, 47.9, 47.7, 47.5, 47.3, 39.5, 36.5, 35.6, 31.6, 31.7, 31.2, 28.8, 28.2, 27.9, 27.7, 24.1, 23.9, 22.6, 13.3, 9.9 ppm; HRMS (ESI) calcd for $C_{25}H_{37}N_7O$: 451.3059 $[M]^+$, found 451.3058.

***N*-(2-(4-(5-(2-Amino-1*H*-imidazol-4-yl)pentyl)-1*H*-1,2,3-triazol-1-yl)ethyl)-4-butylbenzamide hydrochloride (7r):** *tert*-Butyl 2-amino-4-(hept-6-ynyl)-1*H*-imidazole-1-carboxylate (0.123 g, 0.443 mmol) was treated with *N*-(2-azidoethyl)-4-butylbenzamide (0.109 g, 0.443 mmol) according to the general click procedure to give *tert*-butyl 2-amino-4-(5-(1-(2-(4-butylbenzamido)ethyl)-1*H*-1,2,3-triazol-4-yl)pentyl)-1*H*-imidazole-1-carboxylate. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.67 (s, 1H), 7.67 (d, J = 7.5 Hz, 2H), 7.29 (s, 1H), 7.11 (d, J = 7.5 Hz, 2H), 6.42 (s, 1H), 6.25 (s, 2H), 4.48 (s, 2H), 3.83 (s, 2H), 2.56 (t, J = 7.2 Hz, 4H), 2.21 (s, 2H), 1.47 (m, 13H), 1.21 (m, 4H), 0.83 ppm (t, J = 7.2 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 168.3, 140.6, 149.5, 148.2, 147.1, 138.4, 131.5, 128.7, 127.4, 122.2, 106.4, 84.9, 49.4, 40.2, 35.7, 33.5, 29.2, 28.9, 28.3, 28.1, 27.9, 25.5, 22.4, 14.1 ppm; HRMS (ESI) calcd for $C_{28}H_{41}N_7O_3$: 523.3271 $[M]^+$, found 523.3261. The carboxylate was subsequently deprotected to give **7r** (0.191 g, 94% yield). ^{1}H NMR (300 MHz, CD_3OD): δ = 8.43 (s, 1H), 7.69 (s, 2H), 7.22 (s, 2H), 6.44 (s, 1H), 4.73 (s, 2H), 3.89 (s, 2H), 3.34 (s, 2H), 2.59 (s, 4H), 2.41 (s, 2H), 1.54 (s, 4H), 1.29 (s, 4H), 0.88 ppm (t, J = 6.9 Hz, 3H); ^{13}C NMR (75 MHz, CD_3OD): δ = 169.2, 165.1, 160.3, 158.1, 147.4, 141.4, 131.2, 128.5, 127.7, 127.3, 126.9, 92.9, 39.6, 36.3, 33.4, 30.9, 28.0, 27.7, 24.1, 22.2, 13.2, 12.1, 10.9, 8.9, 6.2, 2.5 ppm; HRMS (ESI) calcd for $C_{23}H_{33}N_7O$: 423.2747 $[M]^+$, found 423.2738.

***N*-(2-(4-(5-(2-Amino-1*H*-imidazol-4-yl)pentyl)-1*H*-1,2,3-triazol-1-yl)ethyl)-4-pentylbenzamide hydrochloride (7s):** *tert*-Butyl 2-amino-4-(hept-6-ynyl)-1*H*-imidazole-1-carboxylate (0.113 g, 0.408 mmol) was treated with *N*-(2-(4-(5-(2-amino-1*H*-imidazol-4-yl)-pentyl)-1*H*-1,2,3-triazol-1-yl)ethyl)biphenyl-4-carboxamide hydrochloride (0.106 g, 0.408 mmol) according to the general click procedure to give *tert*-butyl 2-amino-4-(5-(1-(2-(4-pentylbenzamido)ethyl)-1*H*-1,2,3-triazol-4-yl)pentyl)-1*H*-imidazole-1-carboxylate. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.75 (s, 1H), 7.67 (d, J = 7.5 Hz, 2H), 7.27 (s, 1H), 7.12 (d, J = 7.8 Hz, 2H), 4.48 (s, 2H), 3.84 (s, 2H), 2.55 (m, 4H), 2.22 (s, 2H), 1.50 (s, 13H), 1.23 (s, 8H), 0.80 ppm (t, J = 5.7 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 168.3, 150.5, 149.5, 148.2, 147.2, 138.6, 131.5, 128.7, 127.4, 106.4, 84.8, 49.4, 40.2, 35.9, 31.6, 31.0, 29.3, 28.9, 28.1, 27.9, 25.6, 22.6, 14.2 ppm; HRMS (ESI) calcd for $C_{29}H_{43}N_7O_3$: 537.3427 $[M]^+$, found 537.3420. The carboxylate was subsequently deprotected to give **7s** (0.178 g, 92% yield). ^{1}H NMR (300 MHz, CD_3OD): δ = 8.41 (s, 1H), 7.69 (d, J = 7.5 Hz, 2H), 7.21 (d, J = 7.2 Hz, 2H), 6.46 (s, 1H), 4.84 (s, 2H), 3.90 (s, 2H), 2.79 (s, 2H), 2.58 (t, J = 7.8 Hz, 2H), 2.39 (t, J = 7.2 Hz, 2H), 1.68 (s, 2H), 1.55 (s, 4H), 1.26 (s, 6H), 0.84 ppm (t, J = 6.6 Hz, 3H); ^{13}C NMR (75 MHz, CD_3OD): δ = 169.2, 159.5, 158.9, 147.5, 147.3, 131.1, 128.5, 127.6, 127.4, 108.5, 54.2, 51.9, 39.5, 35.6, 31.4, 30.9, 30.6, 28.4, 27.9, 27.6, 26.9, 24.1, 23.5, 22.9, 22.4, 13.3 ppm; HRMS (ESI) calcd for $C_{24}H_{35}N_7O$: 437.2903 $[M]^+$, found 437.2892.

***N*-(2-(4-(5-(2-Amino-1*H*-imidazol-4-yl)pentyl)-1*H*-1,2,3-triazol-1-yl)ethyl)-2,4,6-trichlorobenzamide hydrochloride (7o):** *tert*-Butyl 2-amino-4-(hept-6-ynyl)-1*H*-imidazole-1-carboxylate (0.088 g, 0.318 mmol) was treated with *N*-(2-azidoethyl)-2,4,6-trichlorobenzamide (0.093 g, 0.318 mmol) according to the general click procedure to give *tert*-butyl 2-amino-4-(5-(1-(2-(2,4,6-trichlorobenzami-

do)ethyl)-1*H*-1,2,3-triazol-4-yl)pentyl)-1*H*-imidazole-1-carboxylate. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.22 (s, 1H), 7.34 (s, 1H), 7.26 (s, 2H), 6.42 (s, 1H), 5.97 (s, 2H), 4.51 (s, 2H), 3.94 (s, 2H), 2.45 (t, 2H), 2.20 (s, 2H), 1.47 (m 13H), 1.21 ppm (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 164.7, 148.0, 135.7, 134.6, 132.9, 128.7, 128.1, 127.3, 122.3, 84.9, 53.7, 49.3, 39.9, 31.8, 29.2, 28.9, 28.2, 25.5, 22.8, 14.3 ppm; HRMS (ESI) calcd for $C_{24}H_{30}Cl_3N_7O_3$: 569.1476 $[M]^+$, found 569.1477. The carboxylate was subsequently deprotected to give **7o** (0.116 g, 72% yield). ^{1}H NMR (300 MHz, CD_3OD): δ = 8.36 (s, 1H), 7.45 (s, 2H), 6.46 (s, 1H), 4.77 (s, 2H), 3.97 (s, 2H), 2.80 (s, 2H), 2.48 (t, J = 6.9 Hz, 2H), 1.73 (s, 2H), 1.62 (s, 2H), 1.41 ppm (s, 2H); ^{13}C NMR (75 MHz, CD_3OD): δ = 165.5, 147.3, 136.9, 134.5, 132.7, 128.2, 128.0, 127.6, 108.6, 51.2, 39.0, 28.1, 27.7, 24.1, 23.8 ppm; HRMS (ESI) calcd for $C_{19}H_{22}Cl_3N_7O$: 469.0951 $[M]^+$, found 469.0941.

***N*-(2-(4-(5-(2-Amino-1*H*-imidazol-4-yl)pentyl)-1*H*-1,2,3-triazol-1-yl)ethyl)-3,5-difluorobenzamide hydrochloride (7aa):** *tert*-Butyl 2-amino-4-(hept-6-ynyl)-1*H*-imidazole-1-carboxylate (0.123 g, 0.442 mmol) was treated with *N*-(2-azidoethyl)-3,5-difluorobenzamide (0.100 g, 0.442 mmol) according to the general click procedure to give *tert*-butyl 2-amino-4-(5-(1-(2-(3,5-difluorobenzamido)ethyl)-1*H*-1,2,3-triazol-4-yl)pentyl)-1*H*-imidazole-1-carboxylate. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.25 (s, 1H), 7.39 (m, 3H), 6.88 (t, J = 4.8 Hz, 1H), 6.43 (s, 1H), 6.38 (br s, 2H), 4.55 (s, 2H), 3.93 (s, 2H), 2.56 (t, J = 5.1 Hz, 2H), 2.24 (s, 2H), 1.55 (m, 14H), 1.23 ppm (s, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 165.9, 164.3, 164.2, 161.9, 150.3, 149.3, 148.2, 137.6, 122.4, 111.0, 110.8, 107.3, 107.1, 106.8, 106.6, 85.5, 49.3, 40.4, 29.9, 29.5, 29.1, 28.7, 28.2, 27.9, 27.5, 25.4 ppm; HRMS (ESI) calcd for $C_{24}H_{31}F_2N_7O_3$: 503.2456 $[M]^+$, found 503.2458. The carboxylate was subsequently deprotected to give **7aa** (0.115 g, 59% yield). ^{1}H NMR (400 MHz, CD_3OD): δ = 8.55 (s, 1H), 7.42 (d, J = 2.0 Hz, 2H), 7.29 (t, J = 2.40 Hz, 1H), 6.51 (s, 1H), 4.84 (t, J = 4.8 Hz, 2H), 3.96 (q, J = 13.2, 4.8 Hz, 2H), 2.89 (t, J = 7.2 Hz, 2H), 2.49 (t, J = 7.2 Hz, 2H), 1.79 (m, 2H), 1.75 (m, 2H), 1.44 ppm (m, 2H); ^{13}C NMR (100 MHz, CD_3OD): δ = 164.5, 164.4, 127.6, 126.9, 110.6, 110.6, 110.3, 108.5, 107.1, 106.8, 106.6, 52.5, 39.5, 30.4, 27.9, 27.8, 27.6, 24.0, 23.8, 23.1 ppm; HRMS (ESI) calcd for $C_{19}H_{23}F_2N_7O$: 403.1932 $[M]^+$, found 403.1926.

***N*-(2-(4-(5-(2-Amino-1*H*-imidazol-4-yl)pentyl)-1*H*-1,2,3-triazol-1-yl)ethyl)biphenyl-4-carboxamide hydrochloride (7bb):** *tert*-Butyl 2-amino-4-(hept-6-ynyl)-1*H*-imidazole-1-carboxylate (0.093 g, 0.334 mmol) was treated with *N*-(2-azidoethyl)biphenyl-4-carboxamide (0.089 g, 0.334 mmol) according to the general click procedure to give *tert*-butyl 2-amino-4-(5-(1-(2-biphenyl-4-carboxamidoethyl)-1*H*-1,2,3-triazol-4-yl)pentyl)-1*H*-imidazole-1-carboxylate. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.91 (d, J = 5.1 Hz, 3H), 7.57 (t, J = 8.4 Hz, 4H), 7.44 (t, J = 6.9 Hz, 3H), 7.34 (1H), 4.60 (t, J = 5.1 Hz, 2H), 3.96 (q, J = 5.1, 5.4 Hz, 2H), 2.63 (t, J = 7.2 Hz, 2H), 2.27 (t, J = 7.5 Hz, 2H), 1.62 (m, 13H), 1.33 ppm (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 168.0, 149.6, 148.3, 144.6, 140.1, 138.8, 132.8, 129.1, 128.2, 128.0, 127.4, 127.3, 122.2, 84.9, 49.4, 40.3, 29.3, 28.9, 28.3, 28.2, 28.1, 25.6 ppm; HRMS (ESI) calcd for $C_{30}H_{37}N_7O_3$ $[M]^+$ 543.2958, found 543.2949. The carboxylate was subsequently deprotected to give **7bb** (0.093 g, 58% yield). ^{1}H NMR (300 MHz, CD_3OD): δ = 8.35 (s, 1H), 7.88 (d, J = 8.1 Hz, 2H), 7.65 (d, J = 8.4 Hz, 2H), 7.57 (d, J = 7.5 Hz, 2H), 7.39 (t, J = 7.5 Hz, 2H), 7.34 (t, J = 7.2 Hz, 1H), 6.39 (s, 1H), 4.81 (s, 2H), 3.96 (s, 2H), 2.78 (s, 2H), 2.37 (t, J = 7.5 Hz, 2H), 1.67 (s, 2H), 1.56 (t, 2H), 1.33 ppm (s, 2H); ^{13}C NMR (75 MHz, CD_3OD): δ = 203.6, 158.9, 160.1, 159.5, 159.1, 159.0, 158.5, 149.8, 147.2, 144.6, 132.4, 128.9, 127.9, 127.6, 126.9, 126.4, 108.4, 51.7, 39.5, 27.9, 27.6, 24.0, 23.5, 7.2 ppm; HRMS (ESI) calcd for $C_{25}H_{29}N_7O$: 443.2434 $[M]^+$, found 443.2423.

***N*-(2-(4-(5-(2-Amino-1*H*-imidazol-4-yl)pentyl)-1*H*-1,2,3-triazol-1-yl)ethyl)-4-octylbenzamide hydrochloride (7v):** *tert*-Butyl 2-amino-4-(hept-6-ynyl)-1*H*-imidazole-1-carboxylate (0.078 g, 0.282 mmol) was treated with *N*-(2-azidoethyl)-4-octylbenzamide (0.085 g, 0.282 mmol) according to the general click procedure to give *tert*-butyl 2-amino-4-(5-(1-(2-(4-octylbenzamido)ethyl)-1*H*-1,2,3-triazol-4-yl)pentyl)-1*H*-imidazole-1-carboxylate. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.64 (s, 2H), 7.47 (s, 1H), 7.21 (s, 1H), 7.09 (s, 2H), 6.47 (br s, 3H), 4.48 (s, 2H), 3.84 (s, 2H), 2.53 (s, 4H), 2.28 (t, J = 15.9 Hz, 2H), 1.51 (br s, 6H), 1.18 (br s, 10H), 0.77 ppm (t, J = 6.6 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 180.7, 180.2, 168.3, 147.4, 142.4, 139.2, 131.4, 128.8, 127.4, 107.4, 49.6, 40.2, 36.1, 32.1, 31.4, 29.9, 29.6, 29.5, 28.8, 28.2, 28.1, 25.4, 22.9, 14.3 ppm; HRMS (ESI) calcd for $C_{32}H_{49}N_7O_3$: 579.3896 $[M]^+$, found 579.3890. The carboxylate was subsequently deprotected to give **7v** (0.097 g, 67% yield). ^{1}H NMR (400 MHz, CD_3OD): δ = 7.65 (s, 2H), 7.23 (s, 3H), 6.45 (s, 1H), 3.97 (s, 4H), 2.60 (s, 4H), 2.47 (s, 2H), 1.57 (m, 6H), 1.27 (br m, 12H), 0.83 ppm (t, J = 6.4 Hz, 3H); ^{13}C NMR (100 MHz, CD_3OD): δ = 183.5, 172.0, 169.3, 161.8, 153.9, 147.4, 131.2, 128.5, 127.7, 127.3, 119.1, 108.8, 104.7, 94.6, 63.4, 38.7, 35.6, 31.8, 31.3, 29.3, 29.2, 29.1, 28.1, 27.7, 27.1, 24.2, 22.5, 13.3, 12.6 ppm; HRMS (ESI) calcd for $C_{27}H_{41}N_7O$: 479.3372 $[M]^+$, found 479.3378.

***N*-(2-(4-(5-(2-Amino-1*H*-imidazol-4-yl)pentyl)-1*H*-1,2,3-triazol-1-yl)ethyl)-4-nonylbenzamide hydrochloride (7w):** *tert*-Butyl 2-amino-4-(hept-6-ynyl)-1*H*-imidazole-1-carboxylate (0.636 g, 2.29 mmol) was treated with *N*-(2-azidoethyl)-4-nonylbenzamide (0.726 g, 2.29 mmol) according to the general click procedure to give *tert*-butyl 2-amino-4-(5-(1-(2-(4-nonylbenzamido)ethyl)-1*H*-1,2,3-triazol-4-yl)pentyl)-1*H*-imidazole-1-carboxylate. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.70 (d, J = 7.2 Hz, 2H), 7.29 (s, 1H), 7.27 (t, J = 8.7 Hz, 1H), 7.16 (d, J = 7.2 Hz, 2H), 4.53 (s, 2H), 3.91 (s, 2H), 2.61 (m, 4H), 2.41 (m, 1H), 2.14 (s, 1H), 1.56 (br s, 15H), 1.23 (br s, 14H), 0.83 ppm (t, J = 6.6 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 188.1, 169.7, 168.3, 164.4, 148.0, 147.4, 131.4, 128.8, 127.4, 122.2, 51.6, 49.5, 40.2, 36.0, 32.1, 31.4, 29.7, 29.6, 29.5, 29.4, 29.3, 28.2, 25.6, 22.9, 14.3 ppm; HRMS (ESI) calcd for $C_{33}H_{51}N_7O_3$: 593.4053 $[M]^+$, found 593.4049. The carboxylate was subsequently deprotected to give **7w** (0.183 g, 74% yield). ^{1}H NMR (400 MHz, CD_3OD): δ = 8.66 (s, 1H), 7.69 (s, 2H), 7.25 (s, 2H), 6.54 (s, 1H), 4.81 (s, 2H), 3.62 (s, 2H), 2.85 (s, 2H), 2.63 (s, 2H), 2.46 (s, 2H), 1.75 (s, 2H), 1.39 (s, 4H), 1.29 (m, 14H), 0.88 ppm (s, 3H); ^{13}C NMR (100 MHz, CD_3OD): δ = 205.0, 169.2, 147.5, 147.3, 131.2, 128.5, 127.3, 108.9, 108.6, 96.0, 52.4, 51.6, 39.3, 38.9, 35.6, 31.9, 31.3, 30.6, 29.5, 29.4, 29.3, 29.2, 28.1, 27.9, 27.7, 24.1, 23.6, 22.6, 13.4 ppm; HRMS (ESI) calcd for $C_{28}H_{43}N_7O$: 493.3529 $[M]^+$, found 493.3522.

***N*-(2-(4-(5-(2-Amino-1*H*-imidazol-4-yl)pentyl)-1*H*-1,2,3-triazol-1-yl)ethyl)-2′,4′-difluoro-3-hydroxybiphenyl-4-carboxamide hydrochloride (7j):** *tert*-Butyl 2-amino-4-(hept-6-ynyl)-1*H*-imidazole-1-carboxylate (0.085 g, 0.306 mmol) was treated with *N*-(2-azidoethyl)-2′,4′-difluoro-3-hydroxybiphenyl-4-carboxamide (0.097 g, 0.306 mmol) according to the general click procedure to give *tert*-butyl 2-amino-4-(5-(1-(2-(2′,4′-difluoro-3-hydroxybiphenyl-4-ylcarboxamido)ethyl)-1*H*-1,2,3-triazol-4-yl)pentyl)-1*H*-imidazole-1-carboxylate. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.54 (s, 1H), 7.83 (s, 1H), 7.37 (d, J = 7.2 Hz, 1H), 7.28 (s, 1H), 7.18 (s, 1H), 6.89 (d, J = 7.8 Hz, 1H), 6.72 (s, 2H), 6.39 (s, 1H), 4.57 (s, 2H), 3.81 (s, 2H), 3.34 (s, 1H), 2.47 (s, 2H), 2.07 (s, 2H), 1.49 (m, 13H), 1.17 ppm (s, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 169.5, 163.7, 161.3, 160.5, 159.9, 150.5, 149.2, 148.2, 137.1, 136.3, 134.5, 131.4, 12.8, 126.8, 124.4, 122.3, 117.9, 116.1, 111.9, 111.6, 106.7, 104.8, 104.4, 104.1, 85.8, 50.5, 49.4, 46.6, 50.0, 37.9, 29.9, 28.9, 28.5, 28.3, 28.1, 27.4, 25.3, 25.0 ppm; HRMS (ESI) calcd for $C_{30}H_{35}F_2N_4O_4$: 595.2729 $[M]^+$, found 595.2717. The

carboxylate was subsequently deprotected to give **7j** (0.137 g, 84% yield). ^{1}H NMR (400 MHz, CD_3OD): $\delta = 8.60$ (s, 1H), 7.89 (s, 1H), 7.52 (s, 2H), 6.97 (t, $J = 6.3$ Hz, 3H), 6.45 (s, 1H), 4.81 (s, 2H), 2.78 (s, 2H), 2.42 (s, 2H), 1.72 (s, 2H), 1.61 (d, $J = 7.8$ Hz, 2H), 1.38 ppm (s, 2H); ^{13}C NMR (100 MHz, CD_3OD): $\delta = 172.9$, 169.8, 161.6, 159.5, 147.2, 134.4, 131.7, 128.4, 127.6, 126.0, 117.5, 115.6, 111.7, 111.5, 108.5, 104.2, 104.0, 103.7, 94.6, 51.9, 39.0, 27.9, 27.6, 26.8, 24.1, 23.8 ppm; HRMS (ESI) calcd for $C_{25}H_{27}F_2N_7O_2$: 459.2194 $[M]^+$, found 459.2190.

Procedure to determine the inhibitory effect of test compounds on *E. faecium*, MRSA, *S. epidermidis*, PAO1, PA14, *E. coli*, and MDRAB biofilm formation: Inhibition assays were performed by taking an overnight culture of bacterial strain and subculturing it at an OD_{600} of 0.01 into the necessary medium (brain heart infusion for *E. faecium*, tryptic soy broth with a 0.5% glucose supplement (TSBG) for MRSA, LB medium for MDRAB, LB medium without NaCl (LBNS) for PAO1 and PA14, LB medium for *E. coli* and tryptic soy broth with a 0.5% glucose supplement and a 3.0% NaCl supplement (TGN) for *S. epidermidis*). Stock solutions of predetermined concentrations of the test compound were then made in the necessary medium. These stock solutions were aliquoted (100 μL) into the wells of the 96-well PVC microtiter plate. Sample plates were then wrapped in GLAD Press n′ Seal and incubated under stationary conditions for 24 h at 37 °C. After incubation, the medium was discarded from the wells, and the plates were washed thoroughly with water. Plates were then stained with a 0.1% solution of CV (100 μL) and incubated at ambient temperature for 30 min. The plates were washed with water again, and the remaining stain was solubilized with 95% ethanol (200 μL). A sample of solubilized CV stain from each well (125 μL) was transferred to the corresponding wells of a polystyrene microtiter dish. Biofilm inhibition was quantitated by measuring the OD_{540} of each well. A negative control wherein no biofilm was formed served as a background and was subtracted out.

Procedure to determine the dispersal effect of test compounds on *E. faecium*, MRSA, *S. epidermidis*, PAO1, PA14, *E. coli*, and MDRAB preformed biofilms: Dispersion assays were performed by taking an overnight culture of bacterial strain and subculturing it at an OD_{600} of 0.01 into the necessary medium (as above). The resulting bacterial suspension was aliquoted (100 μL) into the wells of a 96-well PVC microtiter plate. Plates were then wrapped in GLAD Press n′ Seal and incubated under stationary conditions at ambient temperature to establish the biofilms. After 24 h, the medium was discarded from the wells, and the plates were washed thoroughly with water. Stock solutions of predetermined concentrations of the test compound were then made in the necessary medium. These stock solutions were aliquoted (100 μL) into the wells of the 96-well PVC microtiter plate with the established biofilms. Medium alone was added to a subset of the wells to serve as a control. Sample plates were then incubated for 24 h at 37 °C. After incubation, the medium was discarded from the wells, and the plates were washed thoroughly with water. Plates were then stained with a 0.1% solution of CV (100 μL) and incubated at ambient temperature for 30 min. The plates were washed with water again, and the remaining stain was solubilized with 95% ethanol (200 μL). A sample of solubilized CV stain (125 μL) from each well was transferred to the corresponding wells of a polystyrene microtiter dish. Biofilm dispersion was quantitated by measuring the OD_{540} of each well. A negative-control wherein no biofilm was formed served as a background and was subtracted out.

Procedure to determine the inhibitory effect of test compounds on *C. albicans, C. neoformans*, and a mixed *S. epidermidis/C. albicans* biofilm formation: Inhibition assays were performed by taking an overnight culture of yeast or yeast/bacteria strain and subculturing it at an OD_{600} of 0.05 into YPD (yeast extract, peptone and dextrose (BD 242820)) medium for the yeast alone or tryptic soy broth for the *S. epidermidis/C. albicans*. Stock solutions of predetermined concentrations of the test compound were then made in the necessary medium. These stock solutions were aliquoted (100 μL) into the wells of the 96-well PVC microtiter plate. Sample plates were then wrapped in GLAD Press n′ Seal followed by an incubation under stationary conditions for 24 h at 37 °C. After incubation, the medium was discarded from the wells, and the plates were washed thoroughly with water. Plates were then stained with a 0.1% solution of CV (100 μL) and incubated at ambient temperature for 30 min. Plates were washed with water again, and the remaining stain was solubilized with 95% ethanol (200 μL). A sample of solubilized CV stain from each well (125 μL) was transferred to the corresponding wells of a polystyrene microtiter dish. Biofilm inhibition was quantitated by measuring the OD_{540} of each well. A negative control wherein no biofilm was formed served as a background and was subtracted out.

MRSA, *S. epidermidis*, PAO1, PA14, *E. coli*, and MDRAB preformed biofilms: Dispersion assays were performed by taking an overnight culture of bacterial strain and subculturing it at an OD_{600} of 0.01 into the necessary medium (as above for dispersal effects). The resulting bacterial suspension was aliquoted (100 μL) into the wells of a 96-well PVC microtiter plate. Plates were then wrapped in GLAD Press n′ Seal and incubated under stationary conditions at ambient temperature to establish the biofilms. After 24 h, the medium was discarded from the wells, and the plates were washed thoroughly with water. Stock solutions of predetermined concentrations of the test compound were then made in the necessary medium. These stock solutions were aliquoted (100 μL) into the wells of the 96-well PVC microtiter plate with the established biofilms. Medium alone was added to a subset of the wells to serve as a control. Sample plates were then incubated for 24 h at 37 °C. After incubation, the medium was discarded from the wells, and the plates were washed thoroughly with water. The plates were then stained with a 0.1% solution of CV (100 μL) and incubated at ambient temperature for 30 min. The plates were washed with water again, and the remaining stain was solubilized with 95% ethanol (200 μL). A sample (125 μL) of solubilized CV stain from each well was transferred to the corresponding wells of a polystyrene microtiter dish. Biofilm dispersion was quantitated by measuring the OD_{540} of each well. A negative control lane wherein no biofilm was formed served as a background and was subtracted out.

Procedure to determine the dispersal effect of test compounds on *C. albicans* and *C. neoformans* preformed biofilms: Dispersion assays were performed by taking an overnight culture of bacterial strain and subculturing it at an OD_{600} of 0.01 into yeast extract, peptone, and dextrose (BD 242820) medium. The resulting bacterial suspension was aliquoted (100 μL) into the wells of a 96-well PVC microtiter plate. The plates were then wrapped in GLAD Press n′ Seal and incubated under stationary conditions at ambient temperature to establish the biofilms. After 24 h, the medium was discarded from the wells, and the plates were washed thoroughly with water. Stock solutions of predetermined concentrations of the test compound were then made in the necessary medium. These stock solutions were aliquoted (100 μL) into the wells of the 96-well PVC microtiter plate with the established biofilms. Medium alone was added to a subset of the wells to serve as a control. Sample plates were then incubated for 24 h at 37 °C. After incuba-

tion, the medium was discarded from the wells, and the plates were washed thoroughly with water. The plates were then stained with a 0.1% solution of CV (100 μL) and then incubated at ambient temperature for 30 min. The plates were washed with water again, and the remaining stain was solubilized with 95% ethanol (200 μL). A sample (125 μL) of solubilized CV stain from each well was transferred to the corresponding wells of a polystyrene microtiter dish. Biofilm dispersion was quantitated by measuring the OD_{540} of each well. A negative control lane wherein no biofilm was formed served as a background and was subtracted out.

Procedure to determine the effect of leading test compounds on *E. faecium*, MRSA, *S. epidermidis*, PAO1, PA14, *E. coli*, and MDRAB planktonic viability by growth curve analysis: Growth curves were generated by taking an overnight culture of bacterial strain and subculturing it at an OD_{600} of 0.01 into the necessary medium (as above for dispersal effects, save nutrient broth for *S. epidermidis*). The resulting bacterial suspension was then aliquoted (3.0 mL) into culture tubes. The test compound was then added at a predetermined concentration to the medium of the test samples. Controls were employed in which no test compound was added to the bacterial suspension. Samples were then placed in an incubator at 37 °C and shaken at 200 rpm. The OD_{600} of the samples was measured at time intervals starting at 2 h and ending at 24 h.

Procedure to determine the effect of leading test compounds on *C. albicans* and *C. neoformans* planktonic viability by growth curve analysis: Growth curves were generated by taking an overnight culture of yeast strain and subculturing it at an OD_{600} of 0.01 into YPD medium. The resulting bacterial suspension was then aliquoted (3.0 mL) into culture tubes. The test compound was added at a predetermined concentration to the medium of the test samples. Controls were employed in which no test compound was added to the bacterial suspension. Samples were then incubated at 37 °C and shaken at 200 rpm. The OD_{600} of the samples was measured at time intervals starting at 2 h and ending at 24 h.

Colony-count procedure to determine the effect of leading test compounds on *E. faecium*, MRSA, *S. epidermidis*, PAO1, PA14, *E. coli*, and MDRAB planktonic viability: Colonies were counted by taking an overnight culture of bacterial strain and subculturing it at an OD_{600} of 0.01 into the necessary medium (as above for effect of leading test compounds). The resulting bacterial suspension was then aliquoted (3.0 mL) into culture tubes. A test compound was added to the medium of the test samples at a predetermined concentration. Controls were employed in which no test compound was added to the bacterial suspension. Samples were then incubated at 37 °C and shaken at 200 rpm until the OD_{600} of the control samples reached approximately 1.2. At this point, 100 μL was taken from each culture tube and then diluted serially into LB medium. Then, 10 μL were removed from each serial dilution and plated out on a square gridded Petri dish. The dishes were incubated for 16 h at 37 °C to grow viable colonies, which were quantified by using the track-dilution method.

Colony count procedure to determine the effect of leading test compounds on *C. albicans* and *C. neoformans* planktonic viability: Colonies were counted by taking an overnight culture of bacterial strain and subculturing it at an OD_{600} of 0.01 into YPD medium. The resulting bacterial suspension was then aliquoted (3.0 mL) into culture tubes. A test compound was added to the medium of the test samples at a predetermined concentration. Controls were employed in which no test compound was added to the bacterial suspension. Samples were then incubated at 37 °C and shaken at 200 rpm until the OD_{600} of the control samples reached approximately 1.2. At this point, 100 μL was taken from each culture tube and then diluted serially into LB medium. Then, 10 μL was removed from each serial dilution and plated out on a square gridded Petri dish. The dishes were incubated for 16 h at 37 °C to grow viable colonies, which were quantified by using the track-dilution method.

Red blood cell hemolysis assay: Hemolysis assays were performed on mechanically defibrinated sheep's blood (DSB100, Hemostat Labs, Dixon, USA). A sample (1.5 mL) of blood was placed into a microcentrifuge tube and separated at 10000 rpm for 10 min. The supernatant was removed, and the cells were resuspended in phosphate-buffered saline (PBS; 1 mL). The suspension was centrifuged, the supernatant was removed, and the cells were resuspended two more times. The final cell suspension was then diluted tenfold. Test compound solutions were made in PBS in small culture tubes and then added to aliquots of the tenfold-diluted suspension. PBS alone was used as a negative control and as a zero hemolysis marker, while a 1% Triton X sample was used as a positive control and the 100% lysis marker. Samples were then placed in an incubator at 37 °C while being shaken at 200 rpm. After 1 h, the samples were transferred to microcentrifuge tubes and then separated at 10000 rpm for 10 min. The resulting supernatant was diluted by a factor of 40 in distilled water. The absorbance of the supernatant was measured on a UV spectrometer at a 540 nm wavelength.

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