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A facile synthesis of N–C linked 1,2,3-triazole-oligomers

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ABSTRACT

The synthesis of the title oligomers was performed by means of an iterative sequence of 1,3-dipolar cycloaddition reactions of appropriate azides, starting from commercial 4-bromo-1-butyne as a key intermediate.

1. Introduction

Huisgen's thermal 1,3-dipolar cycloaddition between azides and alkynes is one of the most widely used methods for the synthesis of 1,2,3-triazoles.[1] However, the harsh conditions of this uncatalyzed cycloaddition lead to a mixture of 1,4-and 1,5-regioisomers. Subsequently, Cu(I)-catalyzed azide–alkyne cycloadditions (CuAACs)[2,3] have been reported for the synthesis of 1,4-disubstituted-1,2,3-triazoles from a wide range of substrates with excellent selectivity.[4] After this discovery, in the past decade CuAAC has gained considerable attention as 'click chemistry', which proceeds in a variety of solvents, including aqueous media, and in the presence of numerous functional groups.[5,6] The simplicity of these 'click' reactions offers several advantages from a synthetic point of view for the functionalization or ligation of biological systems,[7] in material science[8] and in combinatorial chemistry for drug discovery.[9] In particular, recently, many groups have extended the potential of CuAAC by developing methods for multiple successive cycloadditions, which led to 1,2,3-triazole-oligomers.[10–12] A common tactic for the synthesis of higher order triazole cycloadducts involves the repetition of a two-stage process consisting of the introduction of an azido group in an appropriate substrate, followed by a CuAAC with the suitable alkyne to obtain triazole-based biomimetic oligomers[10] or triazole linked oligonucleotides analogues.[11] Another approach is based upon the successive CuAAC on a single scaffold, containing both the azide and the alkyne moieties.[12]

In connection with our previous studies dealing with the synthesis of heterocyclic compounds,[13] we have recently reported a general approach to novel unsymmetrically substituted 4,4′-bi-1,2,3-triazoles[14a] and an easy synthesis of 1,2,3-triazole-fused heterocycles.[14b] On the basis of these results, we decided to evaluate the possibility of devising an easy synthetic approach to new triazole-based oligomers containing only triazole rings linked by an alkyl chain in the 1,4-positions. Herein we wish to report on these studies, which enabled the synthesis of the N–C type 1,2,3-triazoles-linked oligomers. This strategy is based on the use of commercially available 4-bromo-1-butyne **1**, a difunctional compound bearing both an alkyne moiety and a bromoalkyl group as the site for azide substitution, which led to an iterative formation of triazole rings.

2. Results and discussion

Our methodology is depicted in Scheme 1. We started with the cycloaddition reaction between alkyl azides and compound **1**. The reactions were performed in H_2O at room temperature in the presence of $Cu(OAc)_2 \cdot H_2O$, leading regioselectively to 4-(2-bromoethyl)-1,2,3-triazoles **2** in high yields. Subsequently, the bromides were displaced by azide groups by treatment with sodium azide in DMF and compounds **2** were transformed in the corresponding azides **3**. A new cycloaddition reaction on the same alkyne **1** led to the bis-triazoles **4** in good yields. The same iterative sequence performed on triazoles **4** provided the azides **5** and **7** in excellent yields (Table 1).

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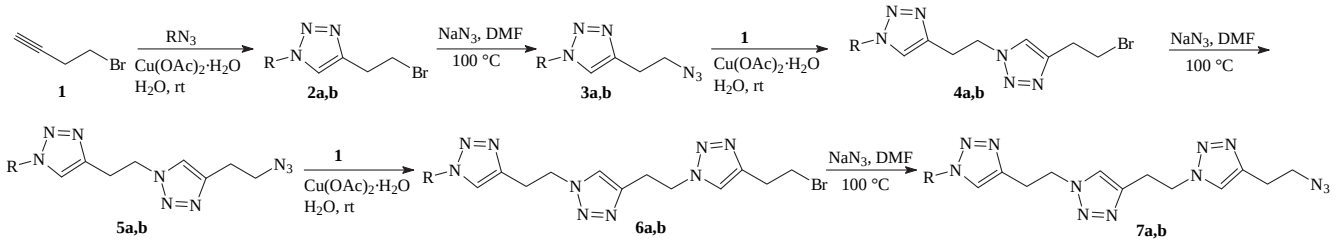
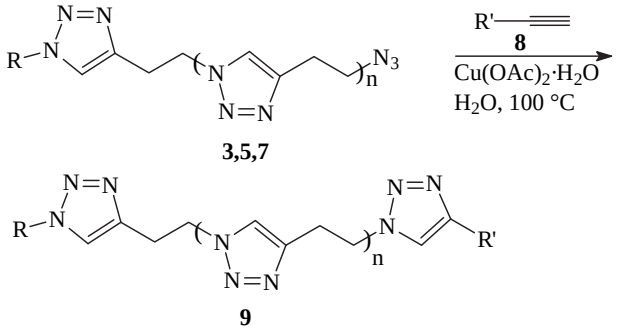


Scheme 1.

Table 1
Yields (%) of compounds **2**–**7**

R	2a	2b	3a	3b	4a	4b	5a	5b	6a	6b	7a	7b
$PhCH_2$	89		95		82		85		75		88	
n-C_8H_{17}		96		96		92		97		95		86

Thus, in order to complete the formation of oligomeric chains containing two, three and four triazole rings, these compounds were reacted with different alkynes in the presence of $Cu(OAc)_2 \cdot H_2O$ in H_2O at 100 °C (Scheme 2).



Scheme 2.

We were pleased to find that the cycloaddition reactions proceeded successfully with a variety of terminal alkynes. Indeed, as reported in the Table 2, good to excellent yields of desired 1,2,3-triazole derivatives **9** were obtained employing terminal alkynes with different groups, including alkyl (entries 1, 4 and 11), aryl (entries 2, 3, 5, 6, 8, 10, 12 and 13) and heteroaryl (entries 7 and 9) alkynes. Thus, a variety of N–C type 1,2,3-bis-triazoles **9a**–**g**, bearing benzyl or alkyl groups on nitrogen and aryl or alkyl groups on C-4′ were obtained regioselectively from 4-(2-azidoethyl)-1,2,3-triazoles **3**. Moreover, trimeric cycloadducts **9h**–**k** and tetrameric cycloadducts **9l**,**m** containing a series of alkyl and aryl groups at the end of the triazole oligomeric chain, were easily generated from functionalized azides **5** and **7**.

3. Conclusion

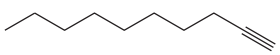
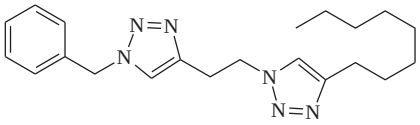
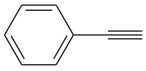
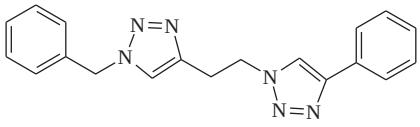
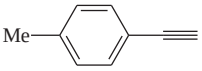
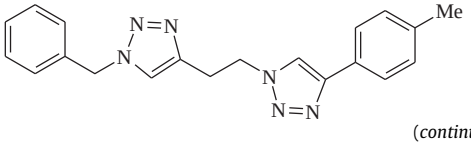
In conclusion, starting from the easily available commercial 4-bromo-1-butyne **1**, we have developed a direct route to N–C linked 1,2,3-triazole-oligomers, using alternatively cycloaddition and azidation reactions. Our procedure requires simple reaction conditions for all steps, allows the efficient preparation of a series of N–C type dimeric, trimeric and tetrameric cycloadducts and, in principle, the methodology could be applied to the synthesis of other similar oligomeric chains containing a higher number of triazole rings.

4. Experimental section

4.1. General

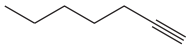
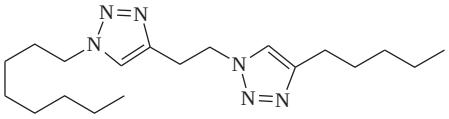
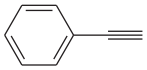
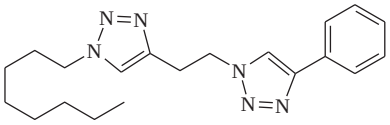
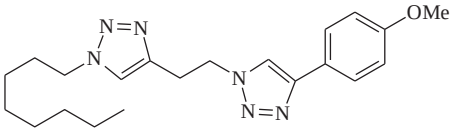
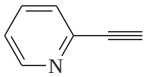
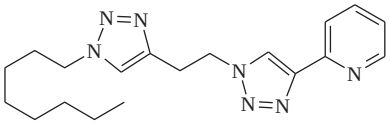
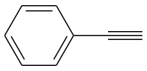
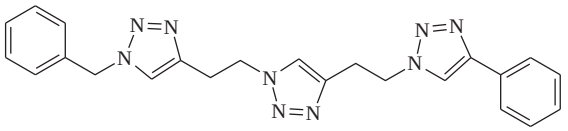
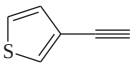
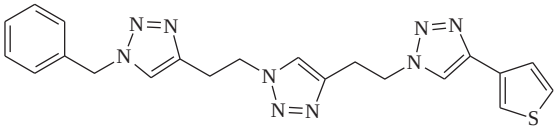
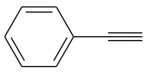
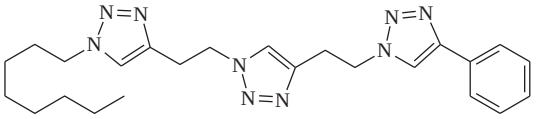
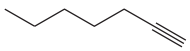
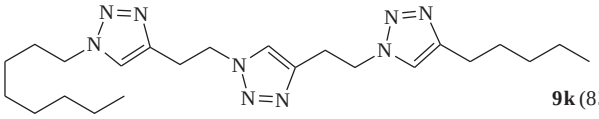
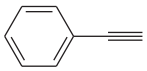
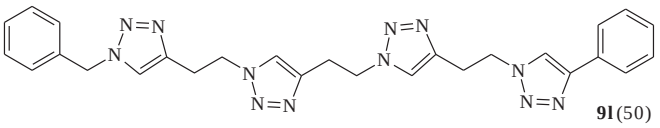
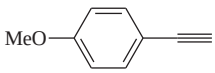
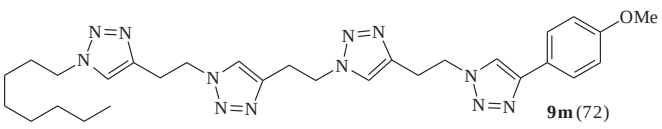
Macherey–Nagel silica gel (60, particle size 0.040–0.063 mm) for column chromatography and Macherey–Nagel aluminium sheets with silica gel 60 F_{254} for TLC were used. GC analysis was performed on a Varian 3900 gas chromatograph equipped with a Supelco SLB™-5 ms capillary column (30 m×0.25 mm id). GC/mass-spectrometry analysis was performed on a Shimadzu GCMS-QP5000 gas chromatograph-mass spectrometer equipped with a Supelco SLB™-5 ms capillary column (30 m×0.25 mm id). ^1H NMR spectra were recorded in deuterochloroform, or DMSO-d_6 on

Table 2
Synthesis of N–C type 1,2,3-triazole derivatives **9a**–**m**

Entry	Azides	Alkynes 8	Products **9**, Yields[a] (%)
1	**3a**		 **9a** (78)
2	**3a**		 **9b** (62)
3	**3a**		 **9c** (64)

(*continued on next page*)

Table 2 (*continued*)

Entry	Azides	Alkynes 8	Products **9**, Yields[a] (%)
4	**3b**		 **9d** (71)
5	**3b**		 **9e** (93)
6	**3b**		 **9f** (92)
7	**3b**		 **9g** (88)
8	**5a**		 **9h** (87)
9	**5a**		 **9i** (90)
10	**5b**		 **9j** (67)
11	**5b**		 **9k** (83)
12	**7a**		 **9l** (50)
13	**7b**		 **9m** (72)

[a] Yields of purified isolated products.

a Varian Inova at 400 MHz ^{13}C NMR spectra were recorded in deuterochloroform, or DMSO-d_6 on a Varian Inova at 100.6 MHz ^{1}H and ^{13}C NMR chemical shifts are reported in parts per million relative to the residual solvent peak in $CDCl_3$ or in DMSO-d_6. IR spectra were recorded on a Perkin–Elmer FTIR Spectrum Bx. Elemental analyses were recorded on a Carlo Erba EA 1108 elemental analyzer, at the Centre CNR ICCOM, University of Bari. Melting points (uncorrected) were determined on a Reichert Microscope.

4.2. General procedure for the synthesis of azides 3,5,7

4-Bromo-1-butyne **1** (1.2 equiv) and alkyl azide (1 equiv) were added at room temperature to a solution (0.05–0.10 M) of $Cu(OAc)_2{\cdot}H_2O$ (0.2 equiv) in H_2O in a capped flask. The reaction mixture was stirred at room temperature and, after completion (1–6 h), was quenched with a saturated aqueous solution of NH_4Cl (30 mL) and extracted with ethyl acetate or CH_2Cl_2 (3×40 mL). The

organic extracts were washed with an aqueous solution of brine (3×30 mL), dried over Na_2SO_4 and concentrated under vacuum. The bromides **2**,**4**,**6** were purified by column chromatography on silica gel and/or by crystallization. Sodium azide (1.2 equiv) was added to a solution (0.4 M) of bromide (1 equiv) in DMF. The mixture was warmed at 100 °C and, after completion (3–4 h), was quenched with a saturated aqueous solution of NH_4Cl (30 mL) and extracted with ethyl acetate or CH_2Cl_2 (3×40 mL). The organic extracts were washed with an aqueous solution of NaCl (3×30 mL) and dried over Na_2SO_4. After evaporation of the solvent at reduced pressure, pure azides were isolated.

*4.2.1. 1-Benzyl-4-(2-bromoethyl)-1H-1,2,3-triazole (**2a**).* Compound **2a** was prepared from benzylazide (0.261 g, 1.96 mmol) and 4-bromo-1-butyne **1** (0.313 g, 2.35 mmol) and the reaction was performed at room temperature in accordance with general procedure. Purification by column chromatography, R_f (silica gel, 30% ethyl acetate/petroleum ether) 0.34, afforded 0.465 g of compound **2a** (89% yield). After crystallization from ethyl acetate/petroleum ether, compound **2a** was obtained as a white solid, mp 78–79 °C. [Found: C, 49.70; H, 4.48; N, 15.70. $C_{11}H_{12}BrN_3$ requires C, 49.64; H, 4.54; N, 15.79%.] ν_{max} (KBr) 3130, 3067, 3032, 2952, 2921, 1455, 1449, 1438, 1262, 1215, 1205, 1127, 1051, 815, 723, 696; δ_H (400 MHz, $CDCl_3$) 7.38–7.31 (m, 4H), 7.26–7.21 (m, 2H), 5.49 (s, 2H), 3.61 (t, *J*=6.8 Hz, 2H), 3.24 (t, *J*=6.8 Hz, 2H); δ_C (100.6 MHz, $CDCl_3$) 145.2, 134.6, 129.0, 128.6, 127.9, 121.6, 54.0, 31.4, 29.4; MS *m*/*z* 158 (1), 156 (1), 148 (1), 146 (1), 144 (1), 130(4), 104 (2), 91 (100), 65 (12), 51 (6).

*4.2.2. 4-(2-Bromoethyl)-1-octyl-1H-1,2,3-triazole (**2b**).* Compound **2b** was prepared from *n*-octylazide (0.300 g, 1.93 mmol) and 4-bromo-1-butyne **1** (0.309 g, 2.32 mmol) and the reaction was performed at room temperature in accordance with general procedure. Purification by crystallization from petroleum ether afforded 0.536 g of compound **2b** (96% yield) as a white solid, mp 37–38 °C. [Found: C, 49.95; H, 7.58; N, 14.60. $C_{12}H_{22}BrN_3$ requires C, 50.01; H, 7.69; N, 14.58%.] ν_{max} (KBr) 3151, 2952, 2921, 2847, 1463, 1256, 1215, 1144, 1052, 916, 817; δ_H (400 MHz, $CDCl_3$) 7.40 (s, 1H), 4.29 (t, *J*=7.2 Hz, 2H), 3.61 (t, *J*=6.8 Hz, 2H), 3.25 (t, *J*=6.8 Hz, 2H), 1.90–1.80 (m, 2H), 1.35–1.15 (m, 10H), 0.83 (t, *J*=6.8 Hz, 3H); δ_C (100.6 MHz, $CDCl_3$) 144.7, 121.4, 50.3, 31.6, 31.6, 30.2, 29.4, 29.0, 28.9, 26.4, 22.5, 14.0; MS *m*/*z* 273 (1), 271 (1), 232 (1), 230 (1), 204 (4), 202 (4), 140 (4), 96 (4), 82 (9), 80 (10), 71 (21), 57 (61), 55 (25), 54 (33), 43 (100), 41 (80).

*4.2.3. 4-(2-Azidoethyl)-1-benzyl-1H-1,2,3-triazole (**3a**).* Compound **3a** was prepared from **2a** (0.460 g, 1.73 mmol) and sodium azide (0.135 g, 2.08 mmol). The reaction was performed at 100 °C in accordance with general procedure leading to 0.375 g (95% yield) of azide **3a** as a pale yellow oil. [Found: C, 57.91; H, 5.38; N, 36.95. $C_{11}H_{12}N_6$ requires C, 57.88; H, 5.30; N, 36.82%.] ν_{max} (neat) 3135, 3060, 3032, 2935, 2873, 2099, 1668, 1451, 1296, 1260, 1219, 1128, 1053, 729; δ_H (400 MHz, $CDCl_3$) 7.36–7.31 (m, 3H), 7.30 (s, 1H), 7.25–7.21 (m, 2H), 5.47 (s, 2H), 3.56 (t, *J*=6.8 Hz, 2H), 2.94 (t, *J*=6.8 Hz, 2H); δ_C (100.6 MHz, $CDCl_3$) 144.6, 134.6, 129.0, 128.6, 127.9, 121.6, 54.0, 50.5, 25.7; MS *m*/*z* 200 (1), 173 (8), 144 (4), 143 (3), 104 (4), 91 (100), 65 (23), 39 (21).

*4.2.4. 4-(2-Azidoethyl)-1-octyl-1H-1,2,3-triazole (**3b**).* Compound **3b** was prepared from **2b** (0.525 g, 1.83 mmol) and sodium azide (0.143 g, 2.20 mmol). The reaction was performed at 100 °C in accordance with general procedure leading to 0.436 g (96% yield) of azide **3b** as a pale yellow oil. [Found: C, 57.61; H, 8.75; N, 33.50. $C_{12}H_{22}N_6$ requires C, 57.57; H, 8.86; N, 33.57%.] ν_{max} (neat) 3136, 2927, 2856, 2099, 1458, 1374, 1290, 1258, 1217, 1054; δ_H (400 MHz, $CDCl_3$) 7.36 (s, 1H), 4.28 (t, *J*=7.4 Hz, 2H), 3.57 (t, *J*=6.8 Hz, 2H), 2.96 (t, *J*=6.8 Hz, 2H), 1.89–1.80 (m 2H), 1.33–1.15 (m, 10H), 0.83 (t, *J*=6.8 Hz, 3H); δ_C (100.6 MHz, $CDCl_3$) 144.0, 121.4, 50.6, 50.2, 31.6, 30.2, 28.9, 28.9, 26.4, 25.7, 22.5, 14.0; MS *m*/*z* 195 (2), 166 (3), 110 (3), 95 (4), 83 (7), 82 (6), 71 (16), 68 (14), 57 (51), 55 (28), 54 (31), 43 (89), 41 (100), 39 (29).

*4.2.5. 1-[2-(1-Benzyl-1H-1,2,3-triazol-4-yl)ethyl]-4-(2-bromoethyl)-1H-1,2,3-triazole (**4a**).* Compound **4a** was prepared from **3a** (0.320 g, 1.40 mmol) and 4-bromo-1-butyne **1** (0.223 g, 1.68 mmol) and the reaction was performed at room temperature in accordance with general procedure. Purification by crystallization from CH_2Cl_2/petroleum ether afforded 0.414 g of compound **4a** (82% yield) as a white solid, mp 160–161 °C. [Found: C, 49.90; H, 4.78; N, 23.35. $C_{15}H_{17}BrN_6$ requires C, 49.87; H, 4.74; N, 23.26%.] ν_{max} (KBr) 3133, 3074, 2952, 1459, 1448, 1433, 1419, 1270, 1207, 1126, 1054, 1028, 821, 733, 710, 700; δ_H (400 MHz, $CDCl_3$) 7.34–7.29 (m, 3H), 7.23 (s, 1H), 7.19–7.14 (m, 2H), 7.03 (s, 1H), 5.40 (s, 2H), 4.65 (t, *J*=6.8 Hz, 2H), 3.53 (t, *J*=6.8 Hz, 2H), 3.27 (t, *J*=6.8 Hz, 2H), 3.15 (t, *J*=6.8 Hz, 2H); δ_C (100.6 MHz, $CDCl_3$) 144.4, 143.4, 134.5, 129.0, 128.7, 127.9, 122.3, 121.9, 54.0, 49.3, 31.7, 29.2, 26.7.

*4.2.6. 4-(2-Bromoethyl)-1-[2-(1-octyl-1H-1,2,3-triazol-4-yl)ethyl]-1H-1,2,3-triazole (**4b**).* Compound **4b** was prepared from **3b** (0.250 g, 1.00 mmol) and 4-bromo-1-butyne (0.160 g, 1.20 mmol) and the reaction was performed at room temperature in accordance with general procedure. Purification by crystallization from ethyl acetate/petroleum ether afforded 0.351 g of compound **4b** (92% yield) as a white solid, mp 104–105 °C. [Found: C, 50.00; H, 7.08; N, 21.80. $C_{16}H_{27}BrN_6$ requires C, 50.13; H, 7.10; N, 21.92%.] ν_{max} (KBr) 3149, 3134, 3078, 2952, 2919, 2847, 1554, 1462, 1258, 1222, 1052, 1026, 827, 808; δ_H (400 MHz, $CDCl_3$) 7.30 (s, 1H), 7.10 (s, 1H), 4.68 (t, *J*=6.4 Hz, 2H), 4.22 (t, *J*=7.2 Hz, 2H), 3.59 (t, *J*=6.6 Hz, 2H), 3.32 (t, *J*=6.4 Hz, 2H), 3.21 (t, *J*=6.6 Hz, 2H), 1.85–1.73 (m, 2H), 1.35–1.15 (m, 10H), 0.83 (t, *J*=6.8 Hz, 3H); δ_C (100.6 MHz, $CDCl_3$) 144.5, 143.1, 122.5, 121.9, 50.3, 49.4, 31.8, 31.6, 30.2, 29.2, 29.0, 28.9, 26.7, 26.4, 22.5, 14.0; MS *m*/*z* 273 (3), 245 (3), 161 (7), 147 (4), 133 (13), 106 (11), 96 (6), 82 (17), 80 (17), 71 (11), 68 (17), 57 (39), 55 (27), 54 (20), 53 (31), 43 (87), 41 (100).

*4.2.7. 4-(2-Azidoethyl)-1-[2-(1-benzyl-1H-1,2,3-triazol-4-yl)ethyl]-1H-1,2,3-triazole (**5a**).* Compound **5a** was prepared from **4a** (0.400 g, 1.11 mmol) and sodium azide (0.087 g, 1.33 mmol). The reaction was performed at 100 °C accordance with general procedure leading to 0.305 g (85% yield) of azide **5a**. After crystallization from ethyl acetate/petroleum ether, a white solid was obtained, mp 103–104 °C. [Found: C, 55.66; H, 5.40; N, 38.90. $C_{15}H_{17}N_9$ requires C, 55.72; H, 5.30; N, 38.99%.] ν_{max} (KBr) 3132, 3069, 2960, 2108, 1458, 1449, 1439, 1261, 1209, 1124, 1096, 1054, 1030, 811, 734; δ_H (400 MHz, $CDCl_3$) 7.34–7.30 (m, 3H), 7.22 (s, 1H), 7.19–7.15 (m, 2H), 7.06 (s, 1H), 5.41 (s, 2H), 4.65 (t, *J*=6.8 Hz, 2H), 3.49 (t, *J*=6.8 Hz, 2H), 3.27 (t, *J*=6.8 Hz, 2H), 2.86 (t, *J*=6.8 Hz, 2H); δ_C (100.6 MHz, $CDCl_3$) 143.7, 143.4, 134.5, 129.0, 128.7, 127.9, 122.3, 121.9, 54.0, 50.4, 49.2, 26.7, 25.5.

*4.2.8. 4-(2-Azidoethyl)-1-[2-(1-octyl-1H-1,2,3-triazol-4-yl)ethyl]-1H-1,2,3-triazole (**5b**).* Product **5b** was prepared from compound **4b** (0.340 g, 0.89 mmol) and sodium azide (0.070 g, 1.07 mmol). The reaction was performed at 100 °C in accordance with general procedure leading to 0.298 g (97% yield) of azide **5b**. After crystallization from ethyl acetate/petroleum ether, a white solid was obtained, mp 80–81 °C. [Found: C, 55.66; H, 7.79; N, 36.55. $C_{16}H_{27}N_9$ requires C, 55.63; H, 7.88; N, 36.49%.] ν_{max} (KBr) 3146, 3120, 3069, 2954, 2914, 2847, 2131, 1461, 1279, 1222, 1053, 1027, 810; δ_H (400 MHz, $CDCl_3$) 7.26 (s, 1H), 7.11 (s, 1H), 4.63 (t, *J*=6.8 Hz, 2H), 4.19 (t, *J*=7.2 Hz, 2H), 3.50 (t, *J*=6.8 Hz, 2H), 3.26 (t, *J*=6.8 Hz, 2H), 2.86 (t, *J*=6.8 Hz, 2H), 1.80–1.70 (m, 2H), 1.28–1.10 (m, 10H), 0.79 (t, *J*=6.8 Hz, 3H); δ_C (100.6 MHz, $CDCl_3$) 143.7, 142.9, 122.3,

121.6, 50.4, 50.1, 49.2, 31.5, 30.1, 28.8, 28.7, 26.6, 26.2, 25.5, 22.4, 13.9.

*4.2.9. 1-[2-(1-Benzyl-1H-1,2,3-triazol-4-yl)ethyl]-4-{2-[4-(2-bromoethyl)-1H-1,2,3-triazol-1-yl]ethyl}-1H-1,2,3-triazole (**6a**).* Compound **6a** was prepared from **5a** (0.295 g, 0.91 mmol) and 4-bromo-1-butyne **1** (0.195 g, 1.09 mmol) and the reaction was performed at room temperature in accordance with general procedure. Purification by crystallization from CH_2Cl_2/petroleum ether afforded 0.312 g of compound **6a** (75% yield) as a white solid, mp 183–184 °C (CH_2Cl_2/ethyl acetate). [Found: C, 49.95; H, 4.78; N, 27.70. $C_{19}H_{22}BrN_9$ requires C, 50.01; H, 4.86; N, 27.62%.] ν_{max} (KBr) 3126, 3074, 2951, 2922, 1458, 1448, 1435, 1261, 1211, 1226, 1055, 1026, 837, 820, 805, 739, 716, 698; δ_H (400 MHz, DMSO-d_6) 7.91 (s, 1H), 7.80 (s, 1H), 7.74 (s, 1H), 7.40–7.28 (m, 3H), 7.27–7.21 (m, 2H), 5.55 (s, 2H), 4.66–4.55 (m, 4H), 3.71 (t, J=6.8 Hz, 2H), 3.21–3.12 (m, 6H); δ_C (100.6 MHz, DMSO-d_6) 143.8, 143.0, 142.5, 136.0, 128.6, 127.9, 127.6, 122.7, 122.6, 122.5, 52.6, 48.7, 48.6, 32.6, 28.8, 26.2, 26.1.

*4.2.10. 4-{2-[4-(2-Bromoethyl)-1H-1,2,3-triazol-1-yl]ethyl}-1-[2-(1-octyl-1H-1,2,3-triazol-4-yl)ethyl]-1H-1,2,3-triazole (**6b**).* Compound **6b** was prepared from **5b** (0.299 g, 0.87 mmol) and 4-bromo-1-butyne **1** (0.138 g, 1.04 mmol) and the reaction was performed at room temperature in accordance with general procedure. Purification by crystallization from ethyl acetate afforded 0.394 g of compound **6b** (95% yield) as a white solid, mp 174–175 °C. [Found: C, 50.11; H, 6.78; N, 26.40. $C_{20}H_{32}BrN_9$ requires C, 50.21; H, 6.74; N, 26.35%.] ν_{max} (KBr) 3145, 3116, 3071, 2954, 2919, 2849, 1462, 1453, 1259, 1216, 1055, 1034, 814, 805; δ_H (400 MHz, $CDCl_3$) 7.32 (s, 1H), 7.14 (s, 1H), 7.07 (s, 1H), 4.68–4.54 (m, 4H), 4.23 (t, J=7.2 Hz, 2H), 3.56 (t, J=6.8 Hz, 2H), 3.28–3.12 (m, 6H), 1.84–1.70 (m, 2H), 1.30–1.10 (m, 10H), 0.79 (t, J=6.8 Hz, 3H); δ_C (100.6 MHz, $CDCl_3$) 144.5, 142.8, 122.4, 122.2, 121.6, 50.2, 49.3, 49.2, 31.7, 31.5, 30.1, 29.2, 28.9, 28.8, 26.6, 26.6, 26.3, 22.4, 13.9 (one coincident peak not observed).

*4.2.11. 4-{2-[4-(2-Azidoethyl)-1H-1,2,3-triazol-1-yl]ethyl}-1-[2-(1-benzyl-1H-1,2,3-triazol-4-yl)ethyl]-1H-1,2,3-triazole (**7a**).* Compound **7a** was prepared from **6a** (0.310 g, 0.68 mmol) and sodium azide (0.053 g, 0.82 mmol). The reaction was performed at 100 °C in accordance with general procedure leading to 0.250 g (88% yield) of azide **7a**. After crystallization from ethyl acetate/petroleum ether, a white solid was obtained, mp 176–177 °C. [Found: C, 54.49; H, 5.37; N, 40.25. $C_{19}H_{22}N_{12}$ requires C, 54.53; H, 5.30; N, 40.17%.] ν_{max} (KBr) 3129, 3073, 2923, 2850, 2103, 1547, 1449, 1435, 1261, 1210, 1125, 1056, 1029, 836, 810, 739, 718, 697; δ_H (400 MHz, DMSO-d_6) 7.89 (s, 1H), 7.79 (s, 1H), 7.76 (s, 1H), 7.40–7.28 (m, 3H), 7.27–7.21 (m, 2H), 5.55 (s, 2H), 4.62–4.54 (m, 4H), 3.58 (t, J=6.8 Hz, 2H), 3.22–3.12 (m, 4H), 2.88 (t, J=6.8 Hz, 2H); δ_C (100.6 MHz, DMSO-d_6) 143.3, 143.0, 142.5, 136.0, 128.6, 127.9, 127.6, 122.7, 122.6, 122.5, 52.6, 49.8, 48.6, 48.6, 26.2, 26.1, 24.9.

*4.2.12. 4-{2-[4-(2-Azidoethyl)-1H-1,2,3-triazol-1-yl]ethyl}-1-[2-(1-octyl-1H-1,2,3-triazol-4-yl)ethyl]-1H-1,2,3-triazole (**7b**).* Product **7b** was prepared from compound **6b** (0.218 g, 0.46 mmol) and sodium azide (0.036 g, 0.55 mmol). The reaction was performed at 100 °C in accordance with general procedure leading to 0.175 g (86% yield) of azide **7b**. After crystallization from ethyl acetate a white solid was obtained, mp 158–159 °C. [Found: C, 54.49; H, 7.37; N, 38.20. $C_{20}H_{32}N_{12}$ requires C, 54.53; H, 7.32; N, 38.15%.] ν_{max} (KBr) 3145, 3120, 3069, 2954, 2923, 2848, 2110, 1458, 1450, 1261, 1217, 1055, 1031, 806; δ_H (400 MHz, $CDCl_3$) 7.30 (s, 1H), 7.14 (s, 1H), 7.09 (s, 1H), 4.65–4.55 (m, 4H), 4.22 (t, J=7.2 Hz, 2H), 3.50 (t, J=6.8 Hz, 2H), 3.21 (t, J=6.8 Hz, 4H), 2.88 (t, J=6.8 Hz, 2H), 1.80–1.72 (m, 2H), 1.28–1.10 (m, 10H), 0.78 (t, J=6.8 Hz, 3H); δ_C (100.6 MHz, $CDCl_3$) 143.8, 142.7, 122.3, 122.2, 121.6, 50.4, 50.1, 49.2, 49.1, 31.5, 30.1, 28.8, 28.7, 26.5, 26.5, 26.2, 25.5, 22.4, 13.9 (one coincident peak not observed).

4.3. General procedure for the synthesis of compounds 9

Alkyne (1.2 equiv) and azide (1 equiv) were added at room temperature to a solution (0.02–0.04 M) of $Cu(OAc)_2 \cdot H_2O$ (0.2 equiv) in H_2O in a capped flask. The mixture was warmed at 100 °C and, after completion (1–2 h), was quenched with a saturated aqueous solution of NH_4Cl (30 mL) and extracted with ethyl acetate or CH_2Cl_2 or $CHCl_3$ (3×40 mL). The organic extracts were washed with an aqueous solution of NaCl (3×30 mL), dried over Na_2SO_4 and concentrated under vacuum. The residue was purified by column chromatography on silica gel and/or by crystallization.

*4.3.1. 1-[2-(1-Benzyl-1H-1,2,3-triazol-4-yl)ethyl]-4-octyl-1H-1,2,3-triazole (**9a**).* Compound **9a** was prepared from **3a** (0.200 g, 0.88 mmol) and 1-decyne (0.146 g, 1.06 mmol) and the reaction was performed at 100 °C in accordance with general procedure. Purification by crystallization from ethyl acetate afforded 0.251 g of compound **9a** (78% yield) as a white solid, mp 126–127 °C. [Found: C, 68.91; H, 8.30; N, 23.00. $C_{21}H_{30}N_6$ requires C, 68.82; H, 8.25; N, 22.93%.] ν_{max} (KBr) 3111, 3063, 2950, 2917, 2849, 1466, 1457, 1436, 1221, 1214, 1051, 1028, 720, 694; δ_H (400 MHz, DMSO-d_6) 7.83 (s, 1H), 7.74 (s, 1H), 7.39–7.29 (m, 3H), 7.26–7.20 (m, 2H), 5.54 (s, 2H), 4.58 (t, J=7.2 Hz, 2H), 3.20 (t, J=7.2 Hz, 2H), 2.54 (t, J=7.6 Hz, 2H), 1.58–1.48 (m, 2H), 1.32–1.18 (m, 10H), 0.85 (t, J=6.8 Hz, 3H); δ_C (100.6 MHz, DMSO-d_6) 146.6, 143.1, 136.0, 128.5, 127.8, 127.5, 122.7, 121.6, 52.5, 48.4, 31.1, 28.8, 28.6, 28.5, 28.4, 26.1, 24.9, 21.9, 13.8; MS m/z 268 (3), 187 (8), 173 (9), 110 (5), 97 (9), 96 (11), 91 (100), 65 (9), 55 (7), 41 (27), 39 (10).

*4.3.2. 1-[2-(1-Benzyl-1H-1,2,3-triazol-4-yl)ethyl]-4-phenyl-1H-1,2,3-triazole (**9b**).* Compound **9b** was prepared from **3a** (0.100 g, 0.44 mmol) and phenylacetylene (0.053 g, 0.53 mmol) and the reaction was performed at 100 °C and extracted with ethyl acetate in accordance with general procedure. Purification by column chromatography, R_f (silica gel, 10% petroleum ether/ethyl acetate) 0.36, afforded 0.090 g of compound **9b** (62% yield). After crystallization from ethyl acetate/petroleum ether, compound **9b** was obtained as a white solid, mp 186–187 °C. [Found: C, 68.98; H, 5.44; N, 25.40. $C_{19}H_{18}N_6$ requires C, 69.07; H, 5.49; N, 25.44%.] ν_{max} (KBr) 3130, 3109, 3080, 3028, 2965, 2933, 1458, 1437, 1218, 1210, 1199, 1128, 1089, 1052, 863, 811, 761, 725, 697, 688; δ_H (400 MHz, DMSO-d_6) 8.50 (s, 1H), 7.89 (s, 1H), 7.79 (d, J=7.2 Hz, 2H), 7.48–7.40 (m, 2H), 7.37–7.25 (m, 4H), 7.24–7.16 (m, 2H), 5.54 (s, 2H), 4.70 (t, J=7.2 Hz, 2H), 3.29 (t, J=7.2 Hz, 2H); δ_C (100.6 MHz, DMSO-d_6) 146.0, 142.9, 136.0, 130.7, 128.7, 128.5, 127.8, 127.6, 127.5, 125.0, 122.9, 121.3, 52.5, 48.8, 26.0; MS m/z 246 (6), 183 (6), 173 (5), 156 (5), 130 (8), 116 (6), 103 (11), 91 (100), 77 (11), 65 (13), 39 (16).

*4.3.3. 1-[2-(1-Benzyl-1H-1,2,3-triazol-4-yl)ethyl]-4-p-tolyl-1H-1,2,3-triazole (**9c**).* Compound **9c** was prepared from **3a** (0.200 g, 0.88 mmol) and *p*-tolylacetylene (0.123 g, 1.06 mmol) and the reaction was performed at 100 °C in accordance with general procedure. Purification by column chromatography, R_f (silica gel, 10% petroleum ether/ethyl acetate) 0.44, afforded 0.194 g of compound **9c** (64% yield). After crystallization from ethyl acetate/petroleum ether, compound **9c** was obtained as a white solid, mp 170–171 °C. [Found: C, 69.88; H, 5.84; N, 24.45. $C_{20}H_{20}N_6$ requires C, 69.75; H, 5.85; N, 24.40%.] ν_{max} (KBr) 3129, 3087, 3060, 3046, 3032, 2972, 2933, 1458, 1437, 1216, 1197, 1129, 1088, 1052, 817, 724, 697; δ_H (400 MHz, $CDCl_3$) 7.60 (d, J=8.4 Hz, 2H), 7.52 (s, 1H), 7.26–7.15 (m, 5H), 7.13–7.08 (m, 2H), 7.06 (s, 1H), 5.39 (s, 2H), 4.71 (t, J=6.8 Hz, 2H), 3.31 (t, J=6.8 Hz, 2H), 2.34 (s, 3H); δ_C (100.6 MHz, $CDCl_3$) 147.4, 143.4, 137.9, 134.4, 129.4, 129.0, 128.6, 127.7, 127.6, 125.5, 122.0,

119.9, 54.0, 49.3, 26.7, 21.2; MS *m/z* 260 (6), 197 (6), 144 (6), 130 (7), 115 (12), 103 (4), 91 (100), 77 (5), 65 (11), 39 (10).

*4.3.4. 1-[2-(1-Octyl-1H-1,2,3-triazol-4-yl)ethyl]-4-pentyl-1H-1,2,3-triazole (**9d**).* Compound **9d** was prepared from **3b** (0.200 g, 0.80 mmol) and 1-heptyne (0.092 g, 0.96 mmol) and the reaction was performed at 100 °C in accordance with general procedure. Purification by crystallization from ethyl acetate/petroleum ether afforded 0.197 g of compound **9d** (71% yield) as a white solid, mp 97–98 °C. [Found: C, 65.88; H, 9.84; N, 24.35. $C_{19}H_{34}N_6$ requires C, 65.86; H, 9.89; N, 24.25%.] ν_{max} (KBr) 3146, 3114, 3065, 2954, 2925, 2848, 1459, 1220, 1217, 1052, 1029; δ_H (400 MHz, DMSO-d_6) 7.75 (s, 1H), 7.74 (s, 1H), 4.58 (t, *J*=7.2 Hz, 2H), 4.26 (t, *J*=7.2 Hz, 2H), 3.19 (t, *J*=7.2 Hz, 2H), 2.55 (t, *J*=7.6 Hz, 2H), 1.79–1.68 (m, 2H), 1.59–1.50 (m, 2H), 1.35–1.10 (m, 14H), 0.90–0.81 (m, 6H); δ_C (100.6 MHz, DMSO-d_6) 146.5, 142.6, 122.3, 121.6, 49.1, 48.5, 31.1, 30.7, 29.6, 28.5, 28.4, 28.2, 26.1, 25.6, 24.8, 21.9, 21.7, 13.8, 13.7; MS *m/z* 261 (3), 208 (3), 180 (4), 177 (3), 149 (4), 124 (43), 110 (14), 97 (10), 96 (10), 95 (10), 82 (17), 68 (19), 57 (29), 55 (31), 43 (72), 41 (100), 39 (19).

*4.3.5. 1-[2-(1-Octyl-1H-1,2,3-triazol-4-yl)ethyl]-4-phenyl-1H-1,2,3-triazole (**9e**).* Compound **9e** was prepared from **3b** (0.200 g, 0.80 mmol) and phenylacetylene (0.098 g, 0.96 mmol) and the reaction was performed at 100 °C in accordance with general procedure. Purification by column chromatography, R_f (silica gel, 2% CH_3OH/CH_2Cl_2) 0.29, afforded 0.262 g of compound **9e** (93% yield). After crystallization from ethyl acetate, compound **9e** was obtained as a white solid, mp 135–136 °C. [Found: C, 68.28; H, 7.94; N, 23.80. $C_{20}H_{28}N_6$ requires C, 68.15; H, 8.01; N, 23.84%.] ν_{max} (KBr) 3140, 3107, 3082, 2953, 2921, 2846, 1464, 1449, 1222, 1196, 1081, 1048, 1026, 837, 762, 694; δ_H (400 MHz, $CDCl_3$) 7.74–7.69 (m, 2H), 7.61 (s, 1H), 7.36–7.31 (m, 2H), 7.28–7.22 (m, 1H), 7.11 (s, 1H), 4.72 (t, *J*=6.8 Hz, 2H), 4.18 (t, *J*=7.4 Hz, 2H), 3.33 (t, *J*=6.8 Hz, 2H), 1.78–1.66 (m, 2H), 1.25–1.10 (m, 10H), 0.80 (t, *J*=6.8 Hz, 3H); δ_C (100.6 MHz, $CDCl_3$) 147.2, 142.8, 130.4, 128.7, 128.0, 125.4, 121.8, 120.3, 50.1, 49.3, 31.5, 30.1, 28.8, 28.7, 26.6, 26.2, 22.4, 13.9; MS *m/z* 295 (4), 268 (5), 197 (8), 180 (6), 156 (7), 130 (8), 116 (7), 103 (13), 102 (11), 82 (18), 68 (17), 57 (41), 55 (29), 43 (91), 41 (100), 39 (20).

*4.3.6. 4-(4-Methoxyphenyl)-1-[2-(1-octyl-1H-1,2,3-triazol-4-yl) ethyl]-1H-1,2,3-triazole (**9f**).* Compound **9f** was prepared from **3b** (0.200 g, 0.80 mmol) and *p*-methoxyphenylacetylene (0.127 g, 0.96 mmol) and the reaction was performed at 100 °C in accordance with general procedure. Purification by column chromatography, R_f (silica gel, 2% CH_3OH/CH_2Cl_2) 0.34, afforded 0.281 g of compound **9f** (92% yield). After crystallization from ethyl acetate, compound **9f** was obtained as a white solid, mp 157–158 °C. [Found: C, 66.00; H, 7.94; N, 21.88. $C_{21}H_{30}N_6O$ requires C, 65.94; H, 7.91; N, 21.97%.] ν_{max} (KBr) 3140, 3088, 2953, 2919, 2846, 1620, 1561, 1502, 1462, 1442, 1253, 1221, 1030, 823; δ_H (400 MHz, $CDCl_3$) 7.64 (d, *J*=8.6 Hz, 2H), 7.51 (s, 1H), 7.12 (s, 1H), 6.87 (d, *J*=8.6 Hz, 2H), 4.70 (t, *J*=6.8 Hz, 2H), 4.19 (t, *J*=7.2 Hz, 2H), 3.77 (s, 3H), 3.32 (t, *J*=6.8 Hz, 2H), 1.79–1.68 (m, 2H), 1.16–1.10 (m, 10H), 0.81 (t, *J*=6.8 Hz, 3H); δ_C (100.6 MHz, $CDCl_3$) 159.5, 147.2, 143.0, 126.8, 123.2, 121.9, 119.5, 114.1, 55.2, 50.2, 49.3, 31.6, 30.1, 28.9, 28.7, 26.6, 26.3, 22.4, 13.9.

*4.3.7. 2-{1-[2-(1-Octyl-1H-1,2,3-triazol-4-yl)ethyl]-1H-1,2,3-triazol-4-yl}pyridine (**9g**).* Compound **9g** was prepared from **3b** (0.200 g, 0.80 mmol) and 2-ethynylpyridine (0.099 g, 0.96 mmol) and the reaction was performed at 100 °C in accordance with general procedure. Purification by column chromatography, R_f (silica gel, 3% CH_3OH/CH_2Cl_2) 0.21, afforded 0.248 g of compound **9g** (88% yield). After crystallization from ethyl acetate/petroleum ether, compound **9g** was obtained as a pale brown solid, mp 115–116 °C. [Found: C, 64.60; H, 7.74; N, 27.83. $C_{19}H_{27}N_7$ requires C, 64.56; H, 7.70; N, 27.74%.] ν_{max} (KBr) 3121, 3104, 3082, 2953, 2919, 2850, 1604, 1595, 1469, 1420, 1216, 1202, 1055, 1048, 788; δ_H (400 MHz, $CDCl_3$) 8.48 (d, *J*=3.6 Hz, 1H), 8.05 (d, *J*=7.8 Hz, 1H), 7.96 (s, 1H), 7.69 (t, *J*=7.8 Hz, 1H), 7.19–7.10 (m, 2H), 4.72 (t, *J*=6.8 Hz, 2H), 4.18 (t, *J*=7.2 Hz, 2H), 3.34 (t, *J*=6.8 Hz, 2H), 1.79–1.68 (m, 2H), 1.25–1.08 (m, 10H), 0.79 (t, *J*=6.8 Hz, 3H); δ_C (100.6 MHz, $CDCl_3$) 150.0, 149.2, 148.0, 142.7, 136.6, 122.6, 122.4, 121.6, 119.9, 50.1, 49.5, 31.5, 30.0, 28.8, 28.7, 26.6, 26.2, 22.4, 13.9; MS *m/z* 209 (7), 198 (6), 184 (11), 171 (17), 169 (9), 158 (7), 157 (7), 131 (57), 118 (9), 104 (20), 82 (17), 78 (27), 68 (16), 57 (35), 55 (30), 43 (82), 41 (100), 39 (23).

*4.3.8. 1-[2-(1-Benzyl-1H-1,2,3-triazol-4-yl)ethyl]-4-[2-(4-phenyl-1H-1,2,3-triazol-1-yl)ethyl]-1H-1,2,3-triazole (**9h**).* Compound **9h** was prepared from **5a** (0.150 g, 0.46 mmol) and phenylacetylene (0.056 g, 0.55 mmol) and the reaction was performed at 100 °C in accordance with general procedure. Purification by column chromatography, R_f (silica gel, 2% CH_3OH/CH_2Cl_2) 0.24, afforded 0.170 g of compound **9h** (87% yield). After crystallization from CH_2Cl_2/petroleum ether, compound **9h** was obtained as a white solid, mp 193–195 °C. [Found: C, 64.85; H, 5.50; N, 29.73. $C_{23}H_{23}N_9$ requires C, 64.92; H, 5.45; N, 29.63%.] ν_{max} (KBr) 3144, 3118, 3082, 3069, 2956, 2927, 1457, 1449, 1438, 1222, 1207, 1054, 1048, 1028, 763, 735, 694; δ_H (400 MHz, DMSO-d_6) 8.56 (s, 1H), 7.85–7.80 (m, 3H), 7.77 (s, 1H), 7.47–7.41 (m, 2H), 7.39–7.29 (m, 4H), 7.26–7.22 (m, 2H), 5.54 (s, 2H), 4.66 (t, *J*=7.2 Hz, 2H), 4.59 (t, *J*=7.2 Hz, 2H), 3.25 (t, *J*=7.2 Hz, 2H), 3.17 (t, *J*=7.2 Hz, 2H); δ_C (100.6 MHz, DMSO-d_6) 146.1, 143.0, 142.5, 136.0, 130.7, 128.8, 128.6, 127.9, 127.7, 127.6, 125.0, 122.7, 122.6, 121.3, 52.5, 49.0, 48.6, 26.1, 26.0.

*4.3.9. 1-[2-(1-Benzyl-1H-1,2,3-triazol-4-yl)ethyl]-4-{2-[4-(thiophen-3-yl)-1H-1,2,3-triazol-1-yl]ethyl}-1H-1,2,3-triazole (**9i**).* Compound **9i** was prepared from **5a** (0.145 g, 0.45 mmol) and 3-ethynylthiophene (0.058 g, 0.54 mmol) and the reaction was performed at 100 °C in accordance with general procedure. Purification by crystallization from $CHCl_3$/petroleum ether afforded 0.175 g of compound **9i** (90% yield) as a white solid, mp 186–187 °C. [Found: C, 58.60; H, 4.98; N, 29.33; S, 7.38. $C_{21}H_{21}N_9S$ requires C, 58.45; H, 4.91; N, 29.21; S, 7.43%.] ν_{max} (KBr) 3129, 3087, 3062, 2922, 2850, 1458, 1447, 1220, 1056, 1028, 830, 785, 732; δ_H (400 MHz, DMSO-d_6) 8.40 (s, 1H), 7.84–7.80 (m, 2H), 7.77 (s, 1H), 7.63 (dd, *J*=4.8, 2.8 Hz, 1H), 7.49 (d, *J*=4.8 Hz, 1H), 7.39–7.28 (m, 3H), 7.26–7.21 (m, 2H), 5.54 (s, 2H), 4.65 (t, *J*=7.0 Hz, 2H), 4.59 (t, *J*=7.0 Hz, 2H), 3.23 (t, *J*=7.0 Hz, 2H), 3.18 (t, *J*=7.0 Hz, 2H); δ_C (100.6 MHz, DMSO-d_6) 143.0, 142.6, 142.5, 136.0, 132.0, 128.6, 127.9, 127.6, 126.9, 125.6, 122.7, 122.6, 121.0, 120.6, 52.5, 48.9, 48.6, 26.1, 26.1.

*4.3.10. 1-[2-(1-Octyl-1H-1,2,3-triazol-4-yl)ethyl]-4-[2-(4-phenyl-1H-1,2,3-triazol-1-yl)ethyl]-1H-1,2,3-triazole (**9j**).* Compound **9j** was prepared from **5b** (0.150 g, 0.435 mmol) and phenylacetylene (0.053 g, 0.52 mmol) and the reaction was performed at 100 °C in accordance with general procedure. Purification by column chromatography, R_f (silica gel, 4% CH_3OH/CH_2Cl_2) 0.31, afforded 0.130 g of compound **9j** (67% yield). After crystallization from ethyl acetate, compound **9j** was obtained as a white solid, mp 180–181 °C. [Found: C, 64.50; H, 7.50; N, 28.28. $C_{24}H_{33}N_9$ requires C, 64.40; H, 7.43; N, 28.16%.] ν_{max} (KBr) 3138, 3132, 3081, 2954, 2919, 2847, 1462, 1445, 1224, 1048, 1026, 762, 694; δ_H (400 MHz, $CDCl_3$) 7.76–7.71 (m, 2H), 7.67 (s, 1H), 7.40–7.32 (m, 2H), 7.30–7.24 (m, 1H), 7.08 (s, 1H), 7.00 (s, 1H), 4.72 (t, *J*=6.8 Hz, 2H), 4.60 (t, *J*=6.8 Hz, 2H), 4.18 (t, *J*=7.2 Hz, 2H), 3.28 (t, *J*=6.8 Hz, 2H), 3.19 (t, *J*=6.8 Hz, 2H), 1.80–1.68 (m, 2H), 1.30–1.12 (m, 10H), 0.82 (t, *J*=6.8 Hz, 3H); δ_C (100.6 MHz, $CDCl_3$) 147.3, 142.8, 130.5, 128.8, 128.1, 125.5, 122.5, 121.7, 120.2, 50.2, 49.4, 49.2, 31.6, 30.2, 28.9, 28.8, 26.7, 26.6, 26.3, 22.5, 14.0 (one coincident peak not observed).

*4.3.11. 1-[2-(1-Octyl-1H-1,2,3-triazol-4-yl)ethyl]-4-[2-(4-pentyl-1H-1,2,3-triazol-1-yl)ethyl]-1H-1,2,3-triazole (**9k**).* Compound **9k** was

prepared from **5b** (0.150 g, 0.435 mmol) and 1-heptyne (0.050 g, 0.52 mmol) and the reaction was performed at 100 °C and extracted with CH_2Cl_2 in accordance with general procedure. Purification by crystallization from ethyl acetate afforded 0.159 g of compound **9k** (83% yield) as a white solid, mp 165–166 °C. [Found: C, 62.50; H, 8.80; N, 28.48. $C_{23}H_{39}N_9$ requires C, 62.55; H, 8.90; N, 28.55%.] ν_{max} (KBr) 3141, 3074, 2955, 2923, 2852, 1549, 1463, 1450, 1212, 1056, 1028, 838, 812; δ_H (400 MHz, $CDCl_3$) 7.15 (s, 1H), 7.11 (s, 1H), 7.08 (s, 1H), 4.60–4.51 (m, 4H), 4.21 (t, *J*=6.8 Hz, 2H), 3.25–3.15 (m, 4H), 2.55 (t, *J*=7.4 Hz, 2H), 1.85–1.70 (m, 2H), 1.60–1.45 (m, 2H), 1.30–1.05 (m, 14H), 0.85–0.70 (m, 6H); δ_C (100.6 MHz, $CDCl_3$) 148.1, 142.9, 142.8, 122.2, 121.6, 120.9, 50.1, 49.2, 48.9, 31.5, 31.2, 30.0, 28.9, 28.8, 28.7, 26.5, 26.5, 26.2, 25.4, 22.3, 22.3, 13.8, 13.7.

*4.3.12. 1-(2-(1-Benzyl-1H-1,2,3-triazol-4-yl)ethyl)-4-(2-(4-(2-(4-phenyl-1H-1,2,3-triazol-1-yl)ethyl)-1H-1,2,3-triazol-1-yl)ethyl)-1H-1,2,3-triazole (**9l**).* Compound **9l** was prepared from **7a** (0.150 g, 0.36 mmol) and phenylacetylene (0.044 g, 0.43 mmol) and the reaction was performed at 100 °C in accordance with general procedure. Purification by column chromatography, R_f (silica gel, 2% CH_3OH/CH_2Cl_2) 0.14, afforded 0.094 g of compound **9l** (50% yield). After crystallization from CH_2Cl_2/petroleum ether, compound **9l** was obtained as a white solid, mp 227–228 °C.; [Found: C, 62.35; H, 5.40; N, 32.35. $C_{27}H_{28}N_{12}$ requires C, 62.29; H, 5.42; N, 32.29%.] ν_{max} (KBr) 3119, 3085, 3066, 2950, 1449, 1438, 1211, 1125, 1054, 1028, 848, 838, 762, 738, 694; δ_H (400 MHz, DMSO-d_6) 8.55 (s, 1H), 7.84–7.78 (m, 4H), 7.70 (s, 1H), 7.46–7.40 (m, 2H), 7.37–7.27 (m, 4H), 7.26–7.21 (m, 2H), 5.55 (s, 2H), 4.68 (t, *J*=7.2 Hz, 2H), 4.57 (t, *J*=7.2 Hz, 2H), 4.54 (t, *J*=7.2 Hz, 2H), 3.26 (t, *J*=7.2 Hz, 2H), 3.17 (t, *J*=7.2 Hz, 2H), 3.12 (t, *J*=7.2 Hz, 2H); δ_C (100.6 MHz, DMSO-d_6) 146.1, 143.0, 142.6, 142.5, 136.0, 130.7, 128.7, 128.6, 127.9, 127.7, 127.6, 125.0, 122.7, 122.6, 122.5, 121.3, 52.5, 49.0, 48.7, 48.6, 26.2, 26.1, 26.0.

*4.3.13. 4-(2-(4-(2-(4-(4-Methoxyphenyl)-1H-1,2,3-triazol-1-yl)ethyl)-1H-1,2,3-triazol-1-yl)ethyl)-1-(2-(1-octyl-1H-1,2,3-triazol-4-yl)ethyl)-1H-1,2,3-triazole (**9m**).* Compound **9m** was prepared from **7b** (0.175 g, 0.40 mmol) and *p*-methoxyphenylacetylene (0.063 g, 0.48 mmol) and the reaction was performed at 100 °C and extracted with CH_2Cl_2 in accordance with general procedure. Purification by column chromatography, R_f (silica gel, 5% CH_3OH/CH_2Cl_2) 0.31, afforded 0.165 g of compound **9m** (72% yield). After crystallization from CH_2Cl_2/petroleum ether, compound **9m** was obtained as a white solid, mp 239–240 °C. [Found: C, 60.90; H, 7.15; N, 29.45. $C_{29}H_{40}N_{12}O$ requires C, 60.82; H, 7.04; N, 29.35%.] ν_{max} (KBr) 3144, 3119, 3089, 3064, 2953, 2923, 2849, 1459, 1448, 1251, 1220, 1207, 1053, 1033, 826; δ_H (400 MHz, DMSO-d_6, 70 °C) 8.34 (s, 1H), 7.78 (s, 1H), 7.73 (d, *J*=8.4 Hz, 2H), 7.69 (s, 1H), 7.67 (s, 1H), 7.00 (d, *J*=8.4 Hz, 2H), 4.67 (t, *J*=7.0 Hz, 2H), 4.63–4.51 (m, 4H), 4.28 (t, *J*=7.0 Hz, 2H), 3.80 (s, 3H), 3.28 (t, *J*=7.0 Hz, 2H), 3.23–3.07 (m, 4H), 1.73–1.61 (m, 2H), 1.35–1.15 (m, 10H), 0.85 (t, *J*=6.8 Hz, 3H); δ_C (100.6 MHz, DMSO-d_6, 70 °C) 158.7, 145.8, 142.4, 142.3, 126.1, 123.2, 122.2, 122.1, 121.9, 119.9, 114.0, 54.8, 48.9, 48.6, 48.4, 48.4, 30.7, 29.2, 28.0, 27.9, 25.9, 25.4, 21.5, 13.3 (three coincident peaks not observed).

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