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An easy access to unsymmetrically substituted 4,4′-bi-1,2,3-triazoles

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ABSTRACT

A convenient synthesis of 4-alkynyl-1,2,3-triazoles and novel unsymmetrically substituted 4,4′-bi-1,2,3-triazole derivatives has been devised starting from easily available 1-trimethylsilyl-1,3-butadiyne. The starting compound was reacted with several azides, leading to 4-(silylalkynyl)-1,2,3-triazoles, which were easily transformed into 4-arylalkynyl-1,2,3-triazoles by a Pd catalyzed coupling reaction with aryl halides, or into novel 4,4′-bi-1,2,3-triazole derivatives by a subsequent cyclization reaction with azides.

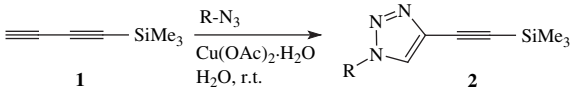
1. Introduction

Nitrogen heterocycles, such as 1,2,3-triazoles, have found a wide range of important applications in the agrochemical, pharmaceutical, polymer, and materials field.[1] In addition, several compounds of the 1,2,3-triazole family have shown a broad spectrum of biological properties such as antibacterial,[2] antiallergic,[3] and anti-HIV activity.[4] An important methodology for the synthesis of 1,2,3-triazoles is based upon the Huisgen cycloaddition using azides and alkynes.[5] However, the high reaction temperatures and the low regioselectivity are major limitations of the original reactions. These limitations have been overcome by the introduction of the copper catalyzed 1,3-dipolar cycloaddition of azides and terminal alkynes, the so-called 'click chemistry', which was pioneered by Sharpless[6] and Meldal.[7] It was found that cycloadditions of terminal alkynes with azides catalyzed by Cu(I) can be conducted at room temperature and are highly regioselective leading exclusively to 4-substituted-1,2,3-triazoles. In addition, many new catalyst systems have been reported in recent years and the number of publications dealing with click chemistry has grown exponentially over the last few years.[8]

Owing to our continuing interest in the synthesis of novel structures of biological significance, we recently reported the successful applications of our methodology[9] to the synthesis of a variety of naturally occurring diacetylenic and polyacetylenic compounds.[10,11] Moreover, more recently, a further application of our method led to a straightforward synthesis of a variety of heterocyclic compounds, with an indole and benzofuran skeleton, starting from easily available silylated diynes.[12,13] On the basis of these results, we decided to evaluate the possibility of devising an easy and general approach to more complex 4-substituted-1,2,3-triazoles, based upon the use of 1-trimethylsilyl-1,3-butadiyne[9] as starting material, via click chemistry. Indeed, up to date, only one report described the synthesis of a 4-substituted-1,2,3-triazole obtained by reaction of the above compound with a complex azide.[14] Moreover, a few and scattered examples of the synthesis of 1,2,3-triazoles were reported, by reaction of a mono-silylated 1,3-butadiyne[8i] or of aryl 1,3-butadiynes with benzyl azide.[15]

2. Results and discussion

We investigated the catalytic activity of various copper salts and found that compound **1** was easily cyclized with several azides in the presence of $Cu(OAc)_2$ as a catalyst,[8l] according to Scheme 1.



1 **2**

Scheme 1.

All reactions were performed in H_2O in the presence of $Cu(OAc)_2 \cdot H_2O$ as a catalyst (20 mol %) at room temperature and the overall results are reported in Table 1. The reactions of several azides with compound **1** provided reasonable to good yields (51–92%) of the 1,4-triazole adducts, regardless of the substituted azide. Indeed, we employed arylalkyl azides (entries 1–4) also with the aryl group *ortho*- or *para*-iodosubstituted (entries 2 and 3), or arylazides (entries 5 and 6) and finally alkyl azides (entries 7 and 8).

These results encouraged us to extend the methodology to the synthesis of more triazole derivatives, starting from compounds **2**. Then, we subjected some mono-silylated compounds **2** to a direct cross-coupling reaction[9] with different aryl iodides, in the presence of catalytic amounts of $Pd(PPh_3)_4$ and AgCl, obtaining various substituted 4-(arylalkynyl)-1,2,3-triazoles **3** (Scheme 2).

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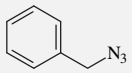
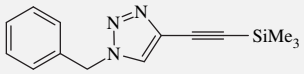
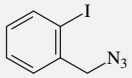
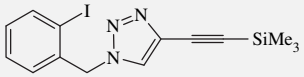
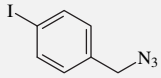
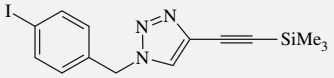
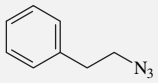
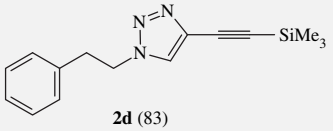
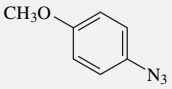
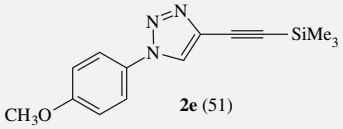
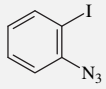
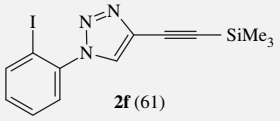
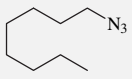
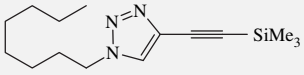
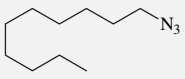
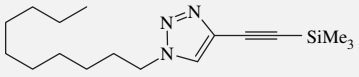
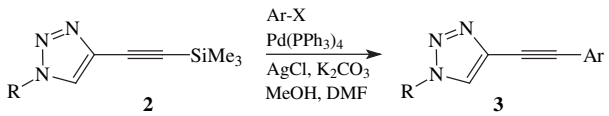
Table 1
Synthesis of 4-trimethylsilylalkynyl-1,2,3-triazoles **2**

Entry	R–N_3	Products **2**[a], yield[b] (%)
1		 **2a** (77)
2		 **2b** (81)
3		 **2c** (92)
4		 **2d** (83)
5		 **2e** (51)
6		 **2f** (61)
7		 **2g** (80)
8		 **2h** (87)

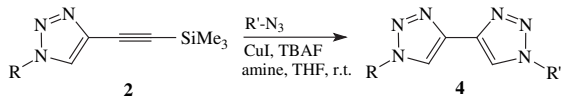
[a] All reactions were carried out in H_2O at room temperature for 1–6 h, according to a general procedure.
[b] Yields of purified isolated products.



Scheme 2.

Several aryl and *p*-substituted aryl iodides were employed (Table 2, entries 2 and 5–8) and also heteroaryl iodides, such as 3-iodopyridine (entry 1), 2-iodobenzofuran (entry 3), and 2-iodothiophene (entry 4) and functionalized 4-alkynyl-1,2,3-triazoles **3** were obtained in good to high yields (67–86%).

Moreover, in order to demonstrate the high versatility of compound **2**, we started to investigate the possibility of performing a new cyclization reaction, with the aim of obtaining novel unsymmetrically substituted 4,4′-bi-triazole derivatives, compounds, to the best of our knowledge, never synthesized. Indeed, more recently, only some symmetrically substituted 4,4′-bi-triazole derivatives have been prepared, by copper catalyzed reactions of 1,4-bis(trimethylsilyl)-1,3-butadiyne[16] or 1,3-butadiyne[17] with some azides and these symmetrical adducts have been evaluated as multidentate ligands of transition metals.[16,17] We found that, by employing an in situ deprotection and clicking reaction,[8a] compounds **2** reacted with several azides leading to 4,4′-bi-triazole derivatives **4** (Scheme 3).



Scheme 3.

The reactions were performed in THF, at room temperature, by employing a Cu(I) copper source and TBAF as in situ desilylating agent, in the presence of an amine, 1,1,4,7,7-pentamethyldiethylenetriamine. The overall results are reported in Table 3. In particular, as representative examples, we subjected compounds **2a** and **2g** to the cyclization reaction. Compound **2a** was reacted with arylalkyl azides (entries 1 and 2) and with alkyl azides (entries 3 and 4), whereas compound **2g** was reacted with alkyl and arylalkyl azides (entries 5–7) and an arylazide (entry 8), obtaining the unsymmetrically substituted 4,4′-bi-triazole derivatives in good yields (52–86%). It is noteworthy that the same product **4d** can be obtained starting from compound **2a** (entry 4) or from compound **2g** (entry 5) and that the ready availability of compounds **2** can provide a wide range of unsymmetrically substituted 4,4′-bi-triazole adducts.

In summary, we have shown that a variety of 4-alkynyl-1,2,3-triazoles (products **2** and **3**) can be easily synthesized via 'click' chemistry starting from the easily available compound **1** and, especially, we have devised a general approach to novel unsymmetrically substituted 4,4′-bi-triazole adducts **4** by simple sequential cyclization reactions.

3. Experimental

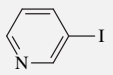
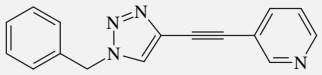
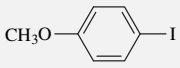
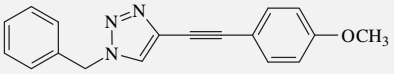
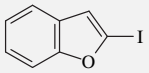
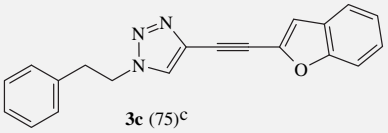
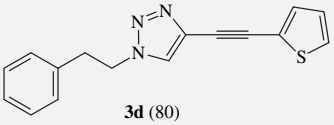
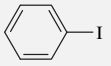
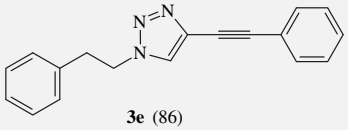
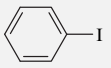
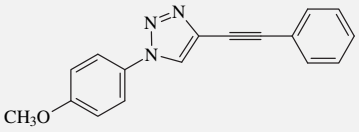
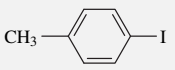
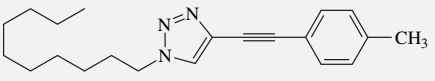
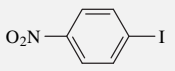
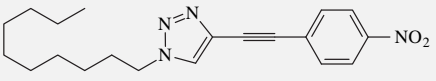
3.1. General

Macherey–Nagel silica gel (60, particle size 0.040–0.063 mm) for column chromatography and Macherey–Nagel aluminum 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™-5ms 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™-5ms capillary column (30 m×0.25 mm id). ^{1}H NMR spectra were recorded in deuterochloroform or DMSO-d_6 on 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. IR spectra were recorded on a Perkin–Elmer FT-IR Spectrum Bx. Elemental analyses were recorded on a Carlo Erba EA 1108 elemental analyzer. Melting points were determined on a Reichert Microscope or on a Stuart Scientific Melting point apparatus SMP3. Tetrahydrofuran was distilled from sodium and *N*,*N*-dimethylformamide was used as supplied.

3.2. General procedure for the synthesis of compounds 2

1-Trimethylsilyl-1,3-butadiyne (1.2 equiv) and azide (1 equiv) were added at room temperature to a solution (0.10 M) of $Cu(OAc)_2\cdot H_2O$ (0.2 equiv) in H_2O in a capped flask. The mixture was stirred at room temperature and, after reaction completion (1–6 h), was quenched with a saturated aqueous solution of NH_4Cl (20 mL) and extracted with ethyl acetate (3×30 mL). The organic extracts were washed with water (3×20 mL), dried over Na_2SO_4, and concentrated under vacuum. The residue was purified by column chromatography on silica gel and by crystallization.

Table 2
Synthesis of substituted 4-arylalkynyl-1,2,3-triazoles **3**

Entry	Compound **2**	Ar–I	Products **3**[a], yield[b] (%)
1	**2a**		 **3a** (71)
2	**2a**		 **3b** (68)[c]
3	**2d**		 **3c** (75)[c]
4	**2d**		 **3d** (80)
5	**2d**		 **3e** (86)
6	**2e**		 **3f** (70)
7	**2h**		 **3g** (67)[c]
8	**2h**		 **3h** (83)[c]

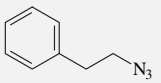
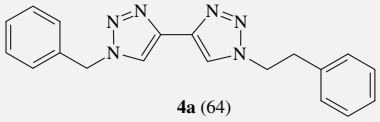
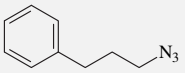
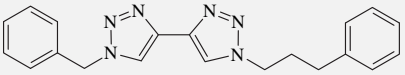
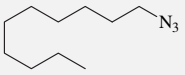
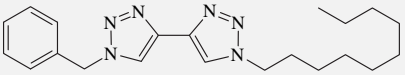
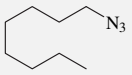
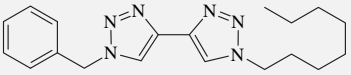
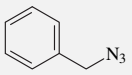
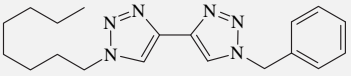
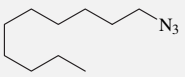
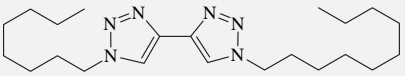
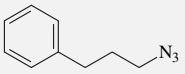
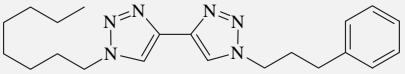
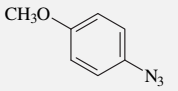
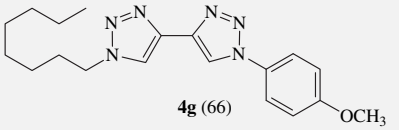
[a] Unless otherwise indicated, all reactions were performed in DMF at room temperature for 4–18 h.
[b] Yields of purified isolated products.
[c] Reactions performed at 40 °C for 2–6 h.

*3.2.1. 4-(Trimethylsilylethynyl)-1-benzyl-1H-1,2,3-triazole (**2a**).* Compound **2a** was prepared from 1-trimethylsilyl-1,3-butadiyne (0.220 g, 1.80 mmol) and benzyl azide (0.200 g, 1.50 mmol) in accordance with general procedure. Purification by column chromatography (silica gel, 20% ethyl acetate/petroleum ether) afforded 0.295 g of compound **2a** (77% yield). After crystallization from petroleum ether, compound **2a** was obtained as a white solid, mp=90–91 °C. [Found: C, 65.90; H, 6.68; N, 16.50. $C_{14}H_{17}N_3Si$ requires C, 65.84; H, 6.71; N, 16.45%.] ν_{max} (KBr) 3130, 2959, 2170, 1456, 1333, 1251, 1223, 1052, 854, 836, 756, 718, 704; δ_H (400 MHz, $CDCl_3$) 7.52 (s, 1H), 7.37–7.32 (m, 3H), 7.25–7.20 (m, 2H), 5.49 (s, 2H), 0.19 (s, 9H); δ_C (100.6 MHz, $CDCl_3$) 134.0, 131.3, 129.1, 128.9, 128.1, 126.2, 98.8, 93.4, 54.2, −0.4; MS *m*/*z* 227 (3), 226 (4), 212 (5), 185 (4), 182 (3), 150 (3), 108 (7), 91 (100), 84 (4), 83 (6), 73 (17), 65 (20), 59 (8), 55 (4), 53 (7), 43 (20%).

*3.2.2. 4-(Trimethylsilylethynyl)-1-(2-iodobenzyl)-1H-1,2,3-triazole (**2b**).* Compound **2b** was prepared from 1-trimethylsilyl-1,3-butadiyne (0.113 g, 0.93 mmol) and 2-iodobenzylazide (0.202 g, 0.78 mmol) in accordance with general procedure. Purification by column chromatography (silica gel, 20% ethyl acetate/petroleum ether) afforded 0.241 g of compound **2b** (81% yield). After crystallization from ethyl acetate/petroleum ether, compound **2b** was obtained as a light brown solid, mp=116–117 °C. [Found: C, 44.15; H, 4.28; N, 11.08. $C_{14}H_{16}IN_3Si$ requires C, 44.10; H, 4.23; N, 11.02%.] ν_{max} (KBr) 3147, 2960, 2172, 1457, 1450, 1437, 1424, 1339, 1249, 1222, 1051, 1012, 860, 844, 746; δ_H (400 MHz, $CDCl_3$) 7.87 (dd, *J*=7.9, 0.9 Hz, 1H), 7.64 (s, 1H), 7.37–7.30 (m, 1H), 7.12 (dd, *J*=7.7, 1.4 Hz, 1H), 7.09–7.02 (m, 1H), 5.60 (s, 2H), 0.22 (s, 9H); δ_C (100.6 MHz, $CDCl_3$) 139.9, 136.7, 131.2, 130.6, 129.9, 129.1, 126.4, 98.9, 98.8, 93.4, 58.4, −0.4; MS *m*/*z* 353 (2), 338 (2), 226 (13), 217 (100), 210 (4), 196 (12), 185 (5), 150 (5), 108 (12), 91 (22), 90 (47), 89 (24), 73 (38), 63 (10), 59 (14), 53 (11), 43 (31%).

*3.2.3. 4-(Trimethylsilylethynyl)-1-(4-iodobenzyl)-1H-1,2,3-triazole (**2c**).* Compound **2c** was prepared from 1-trimethylsilyl-1,3-butadiyne (0.113 g, 0.93 mmol) and 4-iodobenzylazide (0.202 g,

Table 3
Synthesis of unsymmetrically substituted 4,4′-bi-1,2,3-triazole derivatives **4**

Entry	Compound **2**	R′–N_3	Products **4**[a] yield,[b] (%)
1	**2a**		 **4a** (64)
2	**2a**		 **4b** (65)
3	**2a**		 **4c** (75)
4	**2a**		 **4d** (62)
5	**2g**		 **4d** (86)
6	**2g**		 **4e** (52)
7	**2g**		 **4f** (78)
8	**2g**		 **4g** (66)

[a] All reactions were carried out in THF at room temperature for 2–4 h.
[b] Yields of isolated purified products.

0.78 mmol) in accordance with general procedure. Purification by column chromatography (silica gel, 20% ethyl acetate/petroleum ether) afforded 0.273 g of compound **2b** (92% yield). After crystallization from ethyl acetate/petroleum ether, compound **2c** was obtained as a light brown solid, mp=138–140 °C. [Found: C, 44.17; H, 4.25; N, 11.00. $C_{14}H_{16}IN_3Si$ requires C, 44.10; H, 4.23; N, 11.02%.] ν_{max} (KBr) 3133, 2956, 2165, 1484, 1455, 1423, 1404, 1337, 1275, 1249, 1227, 1051, 1022, 1007, 860, 846, 799, 787, 763, 731; δ_H (400 MHz, $CDCl_3$) 7.69 (d, *J*=8.2 Hz, 2H), 7.55 (s, 1H), 6.98 (d, *J*=8.2 Hz, 2H), 5.44 (s, 2H), 0.21 (s, 9H); δ_C (100.6 MHz, $CDCl_3$) 138.3, 133.7, 131.5, 129.8, 126.1, 99.0, 94.7, 93.2, 53.6, −0.4; MS *m*/*z* 353 (8), 338 (3), 226 (3), 217 (100), 196 (12), 150 (5), 136 (2), 108 (16), 90 (45), 89 (25), 83 (9), 73 (28), 63 (8), 59 (13), 53 (9), 43 (28%).

*3.2.4. 4-(Trimethylsilylethynyl)-1-(2-phenylethyl)-1H-1,2,3-triazole (**2d**).* Compound **2d** was prepared from 1-trimethylsilyl-1,3-butadiyne (0.299 g, 2.45 mmol) and 2-phenylethylazide (0.300 g, 2.04 mmol) in accordance with general procedure. Purification by column chromatography (silica gel, 20% ethyl acetate/petroleum ether) afforded 0.455 g of compound **2d** (83% yield). After crystallization from ethyl acetate/petroleum ether, compound **2d** was obtained as a white solid, mp=101–103 °C. [Found: C, 66.90; H, 7.17; N, 15.55. $C_{15}H_{19}N_3Si$ requires C, 66.87; H, 7.11; N, 15.60%.] ν_{max} (KBr) 3132, 3027, 2957, 2170, 1454, 1437, 1333, 1249, 1224, 1053, 1027, 863, 846, 763, 752, 717, 704, 696; δ_H (400 MHz, $CDCl_3$) 7.35 (s, 1H), 7.30–7.20 (m, 3H), 7.08–7.04 (m, 2H), 4.55 (t, *J*=7.2 Hz, 2H), 3.17 (t, *J*=7.2 Hz, 2H), 0.21 (s, 9H); δ_C (100.6 MHz, $CDCl_3$) 136.5, 130.6, 128.8, 128.6, 127.1, 126.4, 98.5, 93.5, 51.7, 36.5, −0.4; MS *m*/*z* 241 (1), 240 (3), 226(3), 168 (2), 150 (13), 122 (4), 105 (100), 91 (19), 86 (13), 79 (20), 77 (18), 73 (22), 59 (26), 43 (21%).

*3.2.5. 4-(Trimethylsilylethynyl)-1-(4-methoxyphenyl)-1H-1,2,3-triazole (**2e**).* Compound **2e** was prepared from 1-trimethylsilyl-1,3-butadiyne (0.196 g, 1.61 mmol) and 4-methoxyphenylazide (0.200 g, 1.34 mmol) in accordance with general procedure. Purification by column chromatography (silica gel, 20% ethyl acetate/petroleum ether) afforded 0.185 g of compound **2e** (51% yield). After crystallization from ethyl acetate/petroleum ether, compound **2e** was obtained as a bronze solid, mp=126–128 °C. [Found: C, 61.90; H, 6.27; N, 15.42. $C_{14}H_{17}N_3OSi$ requires C, 61.96; H, 6.31; N, 15.48%.] ν_{max} (KBr) 3137, 2959, 2166, 1516, 1308, 1255, 1236, 1049, 1035, 863, 842, 832, 760; δ_H (400 MHz, $CDCl_3$) 7.96 (s, 1H), 7.57 (d, *J*=8.8 Hz, 2H), 6.99 (d, *J*=8.8 Hz, 2H), 3.83 (s, 3H), 0.24 (s, 9H); δ_C (100.6 MHz, $CDCl_3$) 160.0, 131.4, 129.8, 124.4, 122.2, 114.8, 99.4, 93.2, 55.6, −0.4; MS *m*/*z* 243 (14),

228 (100), 213 (12), 200 (7), 198 (6), 185 (5), 170 (5), 164 (5), 154 (5), 121 (4), 107 (13), 93 (18), 79 (15), 77 (13), 69 (9), 67 (14), 64 (13), 63 (11), 59 (9), 55 (11), 53 (16), 43 (45%).

*3.2.6. 4-(Trimethylsilylethynyl)-1-(2-iodophenyl)-1H-1,2,3-triazole (**2f**).* Compound **2f** was prepared from 1-trimethylsilyl-1,3-butadiyne (0.300 g, 2.46 mmol) and 2-iodophenylazide (0.502 g, 2.05 mmol) in accordance with general procedure. Purification by column chromatography (silica gel, 20% ethyl acetate/petroleum ether) afforded 0.459 g of compound **2f** (61% yield). After crystallization from ethyl acetate/petroleum ether, compound **2f** was obtained as a light brown solid, mp=93–95 °C. [Found: C, 42.48; H, 3.75; N, 11.48. $C_{13}H_{14}IN_3Si$ requires C, 42.51; H, 3.84; N, 11.44%.] ν_{max} (KBr) 3138, 2957, 2899, 2175, 1485, 1247, 1230, 1040, 860, 840, 764; δ_H (400 MHz, $CDCl_3$) 7.99 (dd, *J*=8.0, 1.2 Hz, 1H), 7.94 (s, 1H), 7.53–7.47 (m, 1H), 7.40 (dd, *J*=8.0, 1.6 Hz, 1H), 7.27–7.21 (m, 1H), 0.26 (s, 9H); δ_C (100.6 MHz, $CDCl_3$) 140.3, 139.4, 131.7, 130.9, 129.3, 128.1, 127.8, 99.5, 93.7, 93.0, −0.3; MS *m*/*z* 339 (58), 324 (100), 197 (24), 182 (29), 162 (27), 154 (17), 140 (8), 127 (10), 106 (13), 85 (10), 77 (13), 53 (23), 43 (42%).

*3.2.7. 4-(Trimethylsilylethynyl)-1-octyl-1H-1,2,3-triazole (**2g**).* Compound **2g** was prepared from 1-trimethylsilyl-1,3-butadiyne (0.284 g, 2.33 mmol) and *n*-octylazide (0.300 g, 1.94 mmol) in accordance with general procedure. Purification by column chromatography (silica gel, 20% ethyl acetate/petroleum ether) afforded 0.430 g of compound **2g** (80% yield) as a pale yellow oil. [Found: C, 64.90; H, 9.78; N, 15.08. $C_{15}H_{27}N_3Si$ requires C, 64.93; H, 9.81; N, 15.14%.] ν_{max} (neat) 3134, 2956, 2927, 2856, 2172, 1458, 1250, 1048, 863, 844, 760; δ_H (400 MHz, $CDCl_3$) 7.60 (s, 1H), 4.30 (t, *J*=7.2 Hz, 2H), 1.89–1.80 (m, 2H), 1.30–1.16 (m, 10H), 0.83 (t, *J*=6.8 Hz, 3H), 0.21 (s, 9H); δ_C (100.6 MHz, $CDCl_3$) 130.8, 126.0, 98.5, 93.6, 50.5, 31.6, 30.1, 29.0, 28.9, 26.3, 22.5, 14.0, −0.4; MS *m*/*z* 277 (M^+, <1), 262 (2), 234 (2), 207 (4), 192 (3), 178 (4), 176 (4), 165 (13), 164 (12), 150 (73), 137 (20), 122 (36), 109 (11), 107 (14), 86 (23), 73 (48), 59 (43), 57 (27), 55 (26), 43 (100), 41 (81%).

*3.2.8. 4-(Trimethylsilylethynyl)-1-decyl-1H-1,2,3-triazole (**2h**).* Compound **2h** was prepared from 1-trimethylsilyl-1,3-butadiyne (0.300 g, 2.46 mmol) and *n*-decylazide (0.375 g, 2.05 mmol) in accordance with general procedure. Purification by column chromatography (silica gel, 20% ethyl acetate/petroleum ether) afforded 0.544 g of compound **2h** (87% yield) as a pale yellow oil. [Found: C, 66.80; H, 10.28; N, 13.78. $C_{17}H_{31}N_3Si$ requires C, 66.83; H, 10.23; N, 13.75%.] ν_{max} (neat) 3134, 2955, 2929, 2854, 2172, 1457, 1436, 1250, 1223, 1047, 861, 843, 760; δ_H (400 MHz, $CDCl_3$) 7.58 (s, 1H), 4.27 (t, *J*=7.2 Hz, 2H), 1.85–1.73 (m, 2H), 1.27–1.10 (m, 14H), 0.80 (t, *J*=6.6 Hz, 3H), 0.17 (s, 9H); δ_C (100.6 MHz, $CDCl_3$) 130.7, 126.0, 98.3, 93.6, 50.3, 31.7, 30.0, 29.3, 29.2, 29.1, 28.8, 26.2, 22.5, 13.9, −0.5; MS *m*/*z* 290 (2), 262 (2), 235 (2), 234 (2), 220 (2), 204 (3), 192 (3), 178 (3), 166 (11), 165 (13), 164 (10), 150 (56), 137 (14), 124 (10), 122 (22), 109 (9), 107 (11), 86 (15), 73 (43), 59 (36), 57 (28), 55 (28), 43 (100), 41 (80%).

3.3. General procedure for the synthesis of compounds 3

To a solution (0.5–0.8 N) of aryl iodide (1 equiv) in DMF at room temperature under nitrogen were successively added $Pd(PPh_3)_4$ (0.05 equiv), AgCl (0.2 equiv), and K_2CO_3 (8 equiv). The resulting mixture was stirred for 5 min and then MeOH (8 equiv) was added followed by a solution (0.2–0.3 N) of compound **2** (1 equiv) in DMF. The mixture was stirred at room temperature (Table 2, entries 1 and 4–6) or at 40 °C (Table 2, entries 2, 3, 7, and 8) and, after reaction completion (2–18 h), was quenched with aqueous NH_4Cl (20 mL) and extracted with ethyl acetate (3×30 mL). The organic extracts were washed with an aqueous solution of NaCl (3×20 mL), dried over anhydrous Na_2SO_4, and concentrated under vacuum. The residue was purified by column chromatography on silica gel and by crystallization.

*3.3.1. 3-[(1-Benzyl-1H-1,2,3-triazol-4-yl)ethynyl]pyridine (**3a**).* Compound **3a** was prepared from **2a** (0.200 g, 0.78 mmol) and 3-iodopyridine (0.160 g, 0.78 mmol) and the reaction was performed at room temperature in accordance with general procedure. Purification by column chromatography (silica gel, 40% petroleum ether/ethyl acetate) afforded 0.144 g of compound **3a** (71% yield). After crystallization from ethyl acetate/petroleum ether, compound **3a** was obtained as a pale yellow solid, mp=111–113 °C. [Found: C, 73.85; H, 4.60; N, 21.49. $C_{16}H_{12}N_4$ requires C, 73.83; H, 4.65; N, 21.52%.] ν_{max} (KBr) 3081, 3032, 2949, 2230, 1474, 1457, 1407, 1339, 1241, 1213, 1054, 1022, 814, 715, 702; δ_H (400 MHz, $CDCl_3$) 8.70 (br s, 1H), 8.51 (br s, 1H), 7.74 (dt, *J*=7.9, 1.8 Hz, 1H), 7.62 (s, 1H), 7.37–7.31 (m, 3H), 7.27–7.21 (m, 3H), 5.52 (s, 2H); δ_C (100.6 MHz, $CDCl_3$) 152.1, 149.0, 138.4, 133.9, 130.8, 129.2, 129.0, 128.1, 126.1, 123.1, 119.5, 89.2, 81.8, 54.4; MS *m*/*z* 260 (M^+, 2), 231 (14), 204 (18), 154 (3), 141 (5), 114 (5), 102 (5), 91 (100), 74 (6), 65 (22), 51 (8%).

*3.3.2. 4-[(4-Methoxyphenyl)ethynyl]-1-benzyl-1H-1,2,3-triazole (**3b**)*[8i,15]. Compound **3b** was prepared from **2a** (0.142 g, 0.56 mmol) and 4-methoxyiodobenzene (0.131 g, 0.56 mmol) and the reaction was performed at 40 °C. Purification by column chromatography (silica gel, 30% ethyl acetate/petroleum ether) afforded 0.110 g of compound **3b** (68% yield). After crystallization from ethyl acetate/petroleum ether, compound **3b** was obtained as a yellow solid, mp=163–166 °C. [Found: C, 74.80; H, 5.28; N, 14.59. $C_{18}H_{15}N_3O$ requires C, 74.72; H, 5.23; N, 14.52%.] ν_{max} (KBr) 3128, 2959, 2929, 2834, 2219, 1605, 1541, 1501, 1456, 1292, 1250, 1227, 1172, 1052, 1027, 834, 817, 709, 700; δ_H (400 MHz, $CDCl_3$) 7.56 (s, 1H), 7.42 (d, *J*=9.0 Hz, 2H), 7.38–7.32 (m, 3H), 7.28–7.23 (m, 2H), 6.83 (d, *J*=9.0 Hz, 2H), 5.51 (s, 2H), 3.78 (s, 3H); δ_C (100.6 MHz, $CDCl_3$) 159.9, 134.1, 133.0, 131.7, 129.1, 128.9, 128.1, 125.5, 114.2, 114.0, 92.6, 77.1, 55.2, 54.2; MS *m*/*z* 289 (M^+, 9), 260 (23), 246 (13), 234 (26), 219 (23), 217 (25), 203 (16), 191 (20), 170 (11), 143 (21), 127 (10), 113 (13), 100 (15), 91 (100), 74 (14), 65 (44), 63 (21) 51 (18%).

*3.3.3. 4-(1-Benzofuran-2-ylethynyl)-1-(2-phenylethyl)-1H-1,2,3-triazole (**3c**).* Compound **3c** was prepared from **2d** (0.200 g, 0.74 mmol) and 2-iodobenzofuran (0.181 g, 0.74 mmol) and the reaction was performed at 40 °C in accordance with general procedure. Purification by column chromatography (silica gel, 20% ethyl acetate/petroleum ether) afforded 0.173 g of compound **3c** (75% yield). After crystallization from ethyl acetate/petroleum ether, compound **3c** was obtained as a pale yellow solid, mp=118–120 °C. [Found: C, 76.70; H, 4.79; N, 13.38. $C_{20}H_{15}N_3O$ requires C, 76.66; H, 4.82; N, 13.41%.] ν_{max} (KBr): 3116, 2959, 2924, 2227, 1447, 1259, 1100, 1050, 1022, 798, 744, 697; δ_H (400 MHz, $CDCl_3$): 7.58–7.54 (m, 1H), 7.47–7.42 (m, 2H), 7.36–7.21 (m, 5H), 7.10–7.06 (m, 2H), 7.03 (d, *J*=0.8 Hz, 1H), 4.62 (t, *J*=7.2 Hz, 2H), 3.22 (t, *J*=7.2 Hz, 2H); δ_C (100.6 MHz, $CDCl_3$) 154.9, 137.9, 136.5, 129.6, 128.9, 128.6, 127.4, 127.3, 126.9, 125.9, 123.4, 121.4, 112.6, 111.3, 84.3, 82.8, 51.9, 36.5; MS *m*/*z* 313 (M^+, 40), 284 (72), 257 (58), 167 (89), 166 (86), 139 (95), 138 (51), 126 (34), 105 (98), 103 (37), 91 (100), 79 (67), 77 (93), 65 (55), 63 (46), 51 (69%).

*3.3.4. 4-[(Thiophen-2-yl)ethynyl]-1-(2-phenylethyl)-1H-1,2,3-triazole (**3d**).* Compound **3d** was prepared from **2d** (0.200 g, 0.74 mmol) and 2-iodothiophene (0.155 g, 0.74 mmol) and the reaction was performed at room temperature. Purification by column chromatography (silica gel, 30% ethyl acetate/petroleum ether) afforded 0.165 g of compound **3d** (80% yield). After crystallization from ethyl acetate/petroleum ether, compound **3d** was obtained as a yellow-orange solid, mp=156–158 °C. [Found: C, 68.85; H, 4.63; N, 15.08; S, 11.55. $C_{16}H_{13}N_3S$ requires C, 68.79; H, 4.69; N, 15.04; S, 11.48%.] ν_{max} (KBr) 3131, 3099, 2953, 2928, 2863, 1456, 1436, 1329,

1230, 1217, 1184, 1108, 1052, 850, 830, 749, 717, 711, 701, 695; δ_H (400 MHz, $CDCl_3$) 7.38 (s, 1H), 7.32–7.20 (m, 5H), 7.12–7.05 (m, 2H), 6.98 (dd, J=5.0, 3.8 Hz, 1H), 4.59 (t, J=7.2 Hz, 2H), 3.20 (t, J=7.2 Hz, 2H); δ_C (100.6 MHz, $CDCl_3$) 136.5, 132.5, 130.3, 128.8, 128.5, 127.8, 127.1, 127.0, 126.1, 122.0, 85.6, 82.1, 51.7, 36.4; MS m/z 279 (M^+, 24), 250 (72), 223 (53), 217 (25), 191 (27), 160 (26), 133 (100), 116 (25), 105 (90), 91 (75), 89 (76), 79 (62), 77 (83), 65 (56), 51 (52), 45 (70%).

*3.3.5. 4-(Phenylethynyl)-1-(2-phenylethyl)-1H-1,2,3-triazole (**3e**).* Compound **3e** was prepared from **2d** (0.200 g, 0.74 mmol) and iodobenzene (0.151 g, 0.74 mmol) and the reaction was performed at room temperature in accordance with general procedure. Purification by column chromatography (silica gel, 30% ethyl acetate/petroleum ether) afforded 0.174 g of compound **3e** (86% yield). After crystallization from ethyl acetate/petroleum ether, compound **3c** was obtained as a light brown solid, mp=140–143 °C. [Found: C, 79.13; H, 5.58; N, 15.42. $C_{18}H_{15}N_3$ requires C, 79.10; H, 5.53; N, 15.37%.] ν_{max} (KBr) 3125, 3070, 2953, 2929, 2864, 1484, 1457, 1437, 1348, 1229, 1210, 1053, 1026, 836, 757, 729, 697, 689; δ_H (400 MHz, $CDCl_3$) 7.53–7.47 (m, 2H), 7.40 (s, 1H), 7.36–7.20 (m, 6H), 7.09 (br d, J=7.2 Hz, 2H), 4.59 (t, J=7.2 Hz, 2H), 3.21 (t, J=7.2 Hz, 2H); δ_C (100.6 MHz, $CDCl_3$) 136.6, 131.5, 130.7, 128.9, 128.7, 128.6, 128.3, 127.2, 126.1, 122.3, 92.3, 78.5, 51.8, 36.5; MS m/z 273 (M^+, 3), 244 (16), 230 (2), 217 (10), 203 (7), 202 (8), 168 (4), 154 (6), 141 (3), 127 (37), 113 (6), 105 (100), 91 (20), 79 (21), 77 (30), 65 (11), 63 (10), 51 (15%).

*3.3.6. 4-(Phenylethynyl)-1-(4-methoxyphenyl)-1H-1,2,3-triazole (**3f**).* Compound **3f** was prepared from **2e** (0.150 g, 0.55 mmol) and iodobenzene (0.112 g, 0.55 mmol) and the reaction was performed at room temperature. Purification by column chromatography (silica gel, 40% ethyl acetate/petroleum ether) afforded 0.106 g of compound **3f** (70% yield). After crystallization from ethyl acetate/petroleum ether, compound **3f** was obtained as a bronze solid, mp=168–170 °C. [Found: C, 74.20; H, 4.72; N, 15.20. $C_{17}H_{13}N_3O$ requires C, 74.17; H, 4.76; N, 15.26%.] ν_{max} (KBr) 3113, 3072, 1516, 1439, 1248, 1227, 1050, 1033, 1024, 832, 761, 692, 641; δ_H (400 MHz, DMSO) 9.13 (s, 1H), 7.83 (d, J=9.0 Hz, 2H), 7.65–7.55 (m, 2H), 7.50–7.42 (m, 3H), 7.15 (d, J=9.0 Hz, 2H), 3.83 (s, 3H); δ_C (100.6 MHz, DMSO) 159.4, 131.2, 129.9, 129.4, 129.2, 128.8, 125.8, 121.8, 121.3, 114.8, 92.1, 79.0, 55.5; MS m/z 247 (100), 232 (31), 204 (48), 176 (20), 152 (11), 151 (11), 124 (27), 116 (12), 102 (35), 88 (36), 75 (16), 63 (10), 51 (12%).

*3.3.7. 4-[(4-Methylphenyl)ethynyl]-1-decyl-1H-1,2,3-triazole (**3g**).* Compound **3g** was prepared from **2h** (0.150 g, 0.49 mmol) and 4-methyliodobenzene (0.107 g, 0.49 mmol) and the reaction was performed at 40 °C, in accordance with general procedure. Purification by column chromatography (silica gel, 20% ethyl acetate/petroleum ether) afforded 0.106 g of compound **3g** (67% yield). After crystallization from ethyl acetate/petroleum ether, compound **3g** was obtained as a light brown solid, mp=95–96 °C. [Found: C, 77.93; H, 9.00; N, 13.02. $C_{21}H_{29}N_3$ requires C, 77.97; H, 9.04; N, 12.99%.] ν_{max} (KBr) 3123, 2954, 2914, 2847, 1503, 1465, 1458, 1234, 1050, 812; δ_H (400 MHz, $CDCl_3$) 7.65 (s, 1H), 7.40 (d, J=8.2 Hz, 2H), 7.12 (d, J=8.2 Hz, 2H), 4.33 (t, J=7.2 Hz, 2H), 2.33 (s, 3H), 1.93–1.82 (m, 2H), 1.33–1.15 (m, 14H), 0.84 (t, J=6.8 Hz, 3H); δ_C (100.6 MHz, $CDCl_3$) 138.9, 131.4, 131.0, 129.1, 125.5, 119.2, 92.5, 77.9, 50.5, 31.8, 30.1, 29.4, 29.3, 29.2, 28.9, 26.3, 22.6, 21.5, 14.1; MS m/z 323 (M^+, 4), 295 (4), 294 (3), 266 (3), 252 (3), 238 (4), 224 (5), 210 (6), 196 (9), 183 (23), 182 (29), 168 (26), 155 (38), 142 (25), 139 (19), 128 (23), 115 (16), 105 (10), 70 (8), 69 (7), 57 (20), 55 (35), 43 (86), 41 (100%).

*3.3.8. 4-[(4-Nitrophenyl)ethynyl]-1-decyl-1H-1,2,3-triazole (**3h**).* Compound **3h** was prepared from **2h** (0.150 g, 0.49 mmol) and 4-nitroiodobenzene (0.122 g, 0.49 mmol) and the reaction was performed at 40 °C. Purification by column chromatography (silica gel, 30% ethyl acetate/petroleum ether) afforded 0.144 g of compound **3h** (83% yield). After crystallization from ethyl acetate/petroleum ether, compound **3h** was obtained as a pale orange solid, mp=84–85 °C. [Found: C, 67.80; H, 7.36; N, 15.79. $C_{20}H_{26}N_4O_2$ requires C, 67.77; H, 7.39; N, 15.81%.] ν_{max} (KBr) 3154, 2954, 2915, 2848, 2227, 1596, 1511, 1467, 1343, 1049, 859, 811, 749; δ_H (400 MHz, $CDCl_3$) 8.17 (d, J=7.9 Hz, 2H), 7.76 (s, 1H), 7.63 (d, J=7.9 Hz, 2H), 4.36 (t, J=7.2 Hz, 2H), 1.94–1.84 (m, 2H), 1.33–1.14 (m, 14H), 0.82 (t, J=6.8 Hz, 3H); δ_C (100.6 MHz, $CDCl_3$) 147.1, 132.2, 129.9, 129.2, 126.4, 123.6, 90.4, 83.8, 50.6, 31.7, 30.1, 29.3, 29.2, 29.1, 28.8, 26.3, 22.6, 14.0; MS m/z 214 (16), 201 (6), 186 (12), 173 (16), 167 (16), 155 (6), 154 (6), 153 (5), 143 (5), 141 (7), 127 (7), 126 (9), 113 (8), 83 (6), 70 (8), 69 (8), 67 (7), 63 (7), 57 (32), 55 (37), 43 (100), 41 (95%).

3.4. General procedure for the synthesis of compounds 4

A THF solution (0.2–0.3 M) of silylated derivative **3** (1 equiv) was added at room temperature, under nitrogen, to a stirred suspension (0.2–0.3 M) of azide (1.2 equiv) and CuI (1 equiv) in THF, then 1,1,4,7,7-pentamethyldiethylenetriamine (1.2 equiv) and soon afterward TBAF (1 M in THF, 1.2 equiv) were added. The mixture was stirred at room temperature until reaction completion (2–4 h), then was quenched with a saturated aqueous solution of NH_4Cl (20 mL) and extracted with ethyl acetate (3×50 mL). The organic extracts were washed with H_2O (3×30 mL), dried over Na_2SO_4, and concentrated under vacuum. The residue was purified by column chromatography on silica gel and by crystallization.

*3.4.1. 1-Benzyl-1′-(2-phenylethyl)-1H,1′H-4,4′-bi-1,2,3-triazole (**4a**).* Compound **4a** was prepared from **2a** (0.100 g, 0.39 mmol) and 2-phenylethylazide (0.069 g, 0.47 mmol) in accordance with general procedure. Purification by column chromatography (silica gel, from 60% to 80% ethyl acetate/petroleum ether) afforded 0.082 g of compound **4a** (64% yield). After washing with ethyl acetate, compound **4a** was obtained as a white solid, mp=204–206 °C. [Found: C, 69.00; H, 5.43; N, 25.48. $C_{19}H_{18}N_6$ requires C, 69.07; H, 5.49; N, 25.44%.] ν_{max} (KBr) 3129, 3094, 3062, 3028, 2950, 2913, 2851, 1496, 1454, 1438, 1424, 1229, 1220, 1087, 1056, 958, 833, 709, 695; δ_H (400 MHz, DMSO) 8.54 (s, 1H), 8.43 (s, 1H), 7.42–7.32 (m, 5H), 7.31–7.24 (m, 2H), 7.23–7.17 (m, 3H), 5.64 (s, 2H), 4.67 (t, J=7.2 Hz, 2H), 3.21 (t, J=7.2 Hz, 2H); δ_C (100.6 MHz, DMSO) 139.3, 138.7, 137.5, 135.9, 128.7, 128.6, 128.3, 128.1, 127.9, 126.5, 121.6, 121.5, 52.8, 50.5, 35.4; MS m/z 273 (15), 183 (18), 156 (28), 154 (22), 129 (19), 128 (16), 105 (18), 91 (100), 77 (17), 65 (37), 51 (19), 44 (12%).

*3.4.2. 1-Benzyl-1′-(3-phenylpropyl)-1H,1′H-4,4′-bi-1,2,3-triazole (**4b**).* Compound **4b** was prepared from **2a** (0.092 g, 0.36 mmol) and 3-phenylpropylazide (0.069 g, 0.43 mmol) in accordance with general procedure. Purification by column chromatography (silica gel, from 60% to 80% ethyl acetate/petroleum ether) afforded 0.081 g of compound **4b** (65% yield). After washing with ethyl acetate, compound **4b** was obtained as a white solid, mp=188–190 °C. [Found: C, 69.80; H, 5.88; N, 24.50. $C_{20}H_{20}N_6$ requires C, 69.75; H, 5.85; N, 24.40%.] ν_{max} (KBr) 3136, 3091, 3031, 2940, 2863, 1496, 1456, 1430, 1305, 1223, 1087, 1057, 964, 847, 749, 722, 693; δ_H (400 MHz, DMSO) 8.57 (s, 1H), 8.56 (s, 1H), 7.45–7.13 (m, 10H), 5.67 (s, 2H), 4.42 (t, J=6.8 Hz, 2H), 2.57 (t, J=7.6 Hz, 2H), 2.24–2.12 (m, 2H); δ_C (100.6 MHz, DMSO) 140.6, 139.4, 139.0, 135.9, 128.7, 128.3, 128.2, 128.1, 127.9, 125.9, 121.7, 121.5, 52.9, 49.0, 31.8, 31.2; MS m/z 344 (M^+, 6), 287 (10), 259 (3), 258 (4), 197 (5), 183 (9), 170 (6), 156 (11), 154 (11), 143 (6), 128 (9), 117 (6), 115 (6), 91 (100), 77 (8), 65 (31), 52 (9), 51 (11), 41 (16%).

*3.4.3. 1-Benzyl-1′-decyl-1H,1′H-4,4′-bi-1,2,3-triazole (**4c**).* Compound **4c** was prepared from **2a** (0.100 g, 0.39 mmol) and *n*-decylazide (0.086 g, 0.47 mmol) in accordance with general procedure.

Purification by column chromatography (silica gel, from 60% to 80% ethyl acetate/petroleum ether) afforded 0.107 g of compound **4c** (75% yield). After washing with ethyl acetate, compound **4c** was obtained as a white solid, mp=175–176 °C. [Found: C, 68.80; H, 8.28; N, 22.88. $C_{21}H_{30}N_6$ requires C, 68.82; H, 8.25; N, 22.93%.] ν_{max} (KBr) 3136, 3075, 2954, 2918, 2846, 1457, 1438, 1220, 1085, 1055, 719, 695; δ_H (400 MHz, $CDCl_3$) 8.02 (s, 1H), 7.95 (s, 1H), 7.39–7.24 (m, 5H), 5.54 (s, 2H), 4.36 (t, *J*=7.0 Hz, 2H), 1.95–1.82 (m, 2H), 1.35–1.10 (m, 14H), 0.83 (t, *J*=6.6 Hz, 3H); δ_C (100.6 MHz, $CDCl_3$) 140.5, 140.0, 134.2, 129.1, 128.8, 128.2, 120.5, 120.4, 54.3, 50.4, 31.8, 30.2, 29.4, 29.3, 29.2, 28.9, 26.3, 22.6, 14.0; MS *m*/*z* 219 (12), 197 (8), 183 (8), 169 (9), 156 (15), 154 (12), 144 (9), 128 (10), 91 (100), 80 (10), 70 (14), 65 (21), 55 (25), 43 (43), 41 (59%).

*3.4.4. 1-Benzyl-1′-octyl-1H,1′H-4,4′-bi-1,2,3-triazole (**4d**).* Compound **4d** was prepared from **2a** (0.200 g, 0.78 mmol) and *n*-octylazide (0.146 g, 0.94 mmol) in accordance with general procedure. Purification by column chromatography (silica gel, from 60% to 80% ethyl acetate/petroleum ether) afforded 0.164 g of compound **4d** (62% yield). After crystallization from ethyl acetate/petroleum ether, compound **4d** was obtained as a white solid, mp=177–178 °C. [Found: C, 67.40; H, 7.80; N, 24.88. $C_{19}H_{26}N_6$ requires C, 67.43; H, 7.74; N, 24.83%.] ν_{max} (KBr) 3136, 3096, 3076, 2954, 2916, 2870, 2847, 1494, 1455, 1441, 1429, 1300, 1224, 1084, 1055, 960, 842, 833, 719, 709, 695; δ_H (400 MHz, $CDCl_3$) 8.01 (s, 1H), 7.95 (s, 1H), 7.38–7.26 (m, 5H), 5.54 (s, 2H), 4.36 (t, *J*=7.0 Hz, 2H), 1.94–1.83 (m, 2H), 1.35–1.14 (m, 10H), 0.83 (t, *J*=6.8 Hz, 3H); δ_C (100.6 MHz, $CDCl_3$) 140.5, 139.9, 134.2, 129.1, 128.8, 128.2, 120.5, 120.3, 54.3, 50.4, 31.6, 30.2, 29.0, 28.9, 26.4, 22.5, 14.0; MS *m*/*z* 338 (M^+, 6), 281 (5), 225 (5), 197 (7), 191 (14), 183 (7), 169 (8), 156 (13), 154 (11), 144 (8), 128 (11), 91 (100), 80 (10), 70 (14), 65 (27), 55 (17), 43 (37), 41 (68%).

Compound **4d** was prepared from **2g** (0.400 g, 1.44 mmol) and benzyl azide (0.230 g, 1.73 mmol) in accordance with general procedure. Purification by column chromatography (silica gel, from 60% to 80% ethyl acetate/petroleum ether) afforded 0.419 g of compound **4d** (86% yield).

*3.4.5. 1-Octyl-1′-decyl-1H,1′H-4,4′-bi-1,2,3-triazole (**4e**).* Compound **4e** was prepared from **2g** (0.199 g, 0.72 mmol) and *n*-decylazide (0.157 g, 0.86 mmol) in accordance with general procedure. Purification by column chromatography (silica gel, from 60% to 80% ethyl acetate/petroleum ether) afforded 0.145 g of compound **4e** (52% yield). After crystallization from ethyl acetate/petroleum ether, compound **4e** was obtained as a white solid, mp=165–166 °C. [Found: C, 68.05; H, 10.32; N, 21.68. $C_{22}H_{40}N_6$ requires C, 68.00; H, 10.38; N, 21.63%.] ν_{max} (KBr) 3141, 3106, 2957, 2929, 2847, 1465, 1261, 1222, 1103, 1084, 1057, 1022, 801; δ_H (400 MHz, $CDCl_3$) 8.03 (s, 2H), 4.37 (t, *J*=7.2 Hz, 4H), 1.96–1.84 (m, 4H), 1.36–1.13 (m, 24H), 0.83 (t, *J*=6.8 Hz, 6H); δ_C (100.6 MHz, $CDCl_3$) 140.2, 120.4, 50.5, 31.8, 31.6, 30.2, 29.4, 29.3, 29.2, 29.0, 28.9, 28.9, 26.4, 22.6, 22.5, 14.0, 14.0; MS *m*/*z* 275 (7), 247 (9), 166 (6), 162 (5), 148 (7), 135 (8), 121 (11), 120 (12), 108 (14), 94 (15), 93 (16), 80 (23), 70 (15), 68 (13), 67 (13), 57 (21), 55 (38), 43 (87), 41 (100%).

*3.4.6. 1-Octyl-1′-(3-phenylpropyl)-1H,1′H-4,4′-bi-1,2,3-triazole (**4f**).* Compound **4f** was prepared from **2g** (0.379 g, 1.37 mmol) and 3-phenylpropylazide (0.264 g, 1.64 mmol) in accordance with general procedure. Purification by column chromatography (silica gel, from 60% to 80% ethyl acetate/petroleum ether) afforded 0.391 g of compound **4f** (78% yield). After crystallization from ethyl acetate/petroleum ether, compound **4f** was obtained as a white solid, mp=152–153 °C. [Found: C, 68.80; H, 8.28; N, 22.88. $C_{21}H_{30}N_6$ requires C, 68.82; H, 8.25; N, 22.93%.] ν_{max} (KBr) 3136, 3102, 2953, 2916, 2849, 1458, 1438, 1425, 1304, 1234, 1221, 1086, 1055, 959, 952, 839, 744, 697; δ_H (400 MHz, $CDCl_3$) 8.03 (s, 2H), 7.30–7.13 (m, 5H), 4.39 (t, *J*=7.2 Hz, 2H), 4.38 (t, *J*=7.2 Hz, 2H), 2.65 (t, *J*=7.2 Hz, 2H), 2.27 (quintet, *J*=7.2 Hz, 2H), 1.97–1.87 (m, 2H), 1.36–1.16 (m, 10H), 0.84 (t, *J*=6.8 Hz, 3H); δ_C (100.6 MHz, $CDCl_3$) 140.2, 140.0, 140.0, 128.6, 128.4, 126.3, 120.5, 120.4, 50.5, 49.6, 32.4, 31.6, 31.6, 30.2, 29.0, 28.9, 26.4, 22.5, 14.0; MS *m*/*z* 211 (19), 182 (20), 170 (19), 121 (20), 107 (16), 94 (25), 93 (23), 91 (66), 80 (34), 67 (18), 65 (24), 55 (24), 53 (22), 43 (51), 41 (100%).

*3.4.7. 1-Octyl-1′-(4-methoxyphenyl)-1H,1′H-4,4′-bi-1,2,3-triazole (**4g**).* Compound **4g** was prepared from **2g** (0.150 g, 0.54 mmol) and 4-methoxyphenylazide (0.097 g, 0.65 mmol) in accordance with general procedure. Purification by column chromatography (silica gel, from 60% to 80% ethyl acetate/petroleum ether) afforded 0.126 g of compound **4g** (66% yield). After crystallization from ethyl acetate/petroleum ether, compound **4g** was obtained as a light brown solid, mp=166–168 °C. [Found: C, 64.41; H, 7.33; N, 23.78. $C_{19}H_{26}N_6O$ requires C, 64.38; H, 7.39; N, 23.71%.] ν_{max} (KBr) 3114, 2954, 2919, 2850, 1522, 1464, 1438, 1306, 1254, 1237, 1111, 1087, 1044, 1028, 835, 819; δ_H (400 MHz, $CDCl_3$) 8.40 (s, 1H), 8.08 (s, 1H), 7.66 (d, *J*=8.8 Hz, 2H), 7.02 (d, *J*=8.8 Hz, 2H), 4.41 (t, *J*=7.2 Hz, 2H), 3.85 (s, 3H), 1.99–1.87 (m, 2H), 1.40–1.15 (m, 10H), 0.84 (t, *J*=6.8 Hz, 3H); δ_C (100.6 MHz, $CDCl_3$) 159.9, 140.7, 139.8, 130.3, 122.1, 120.6, 118.7, 114.8, 55.6, 50.6, 31.7, 30.2, 29.0, 28.9, 26.4, 22.6, 14.0; MS *m*/*z* 298 (23), 199 (22), 171 (17), 156 (24), 134 (26), 107 (14), 92 (19), 80 (20), 77 (23), 66 (17), 64 (17), 55 (28), 43 (50), 41 (100%).

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