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PAPER

A general procedure for the synthesis of alkyl- and arylethynyl-1,2,3-triazole-fused dihydroisoquinolines

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A general procedure for the synthesis of the title compounds has been devised starting from the available 2-halophenylethyl azides, by means of click reactions with trimethylsilylacetylene or 1-trimethylsilyl-1,3-butadiyne followed by a transition metal-catalyzed functionalization of C–H bond. A further extension of this procedure led us to devise the synthesis of more complex 4,4′-bitriazole-fused dihydroisoquinolines.

Introduction

An extensively studied reaction for the synthesis of 1,2,3-triazoles is the Huisgen 1,3-dipolar cycloaddition reaction of azides with alkynes.[1] The limitations of the original reactions, due to the high reaction temperature and to the low regioselectivity, have been overcome by the copper(I)-catalyzed 1,3-dipolar cycloaddition (CuAAC) reaction, which is the most prominent example of 'click chemistry', developed by the groups of Sharpless[2] and Meldal.[3] The cycloaddition reactions 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. Since its extraordinary success under different reaction conditions,[4,5] the click reaction has been applied widely in drug discovery,[6] bioconjugation,[7] and materials science.[8] In particular, this methodology has been extensively used by many research groups for the synthesis of several bicyclic, as well as polycyclic fused triazole heterocycles,[9] compounds of great interest for their biological and pharmaceutical activities.[9,10] Generally, fused triazoles are prepared by an intramolecular [3 + 2] cycloadditon between azides and alkynes[9e,m] and a one pot palladium-[9g,h,n] or copper-catalyzed[9f] coupling reaction followed by 1,3-dipolar cycloaddition. An alternative approach involves an intramolecular direct transition metal-catalyzed arylation of 1,2,3-triazoles with aryl halides,[9k,l] by functionalization of a C–H bond, a recent methodology widely used for functionalization of heterocycles.[11]

Our previous studies have regarded the synthesis of several heterocyclic compounds,[12] and recently we have developed a general approach for preparing a variety of novel unsymmetrically substituted 4,4′-bi-1,2,3-triazoles,[13a] several 1,2,3-triazole-fused heterocycles[13b] and various N–C linked 1,2,3-triazole oligomers.[13c] We now report some extensions of our initial discovery regarding 1,2,3-triazole fused heterocycles, that have led to the facile synthesis of a number of novel members of this intriguing class of compounds, including more complex analogs possessing substituted ethynyl chains easily transformed in additional 1,2,3-triazole rings.

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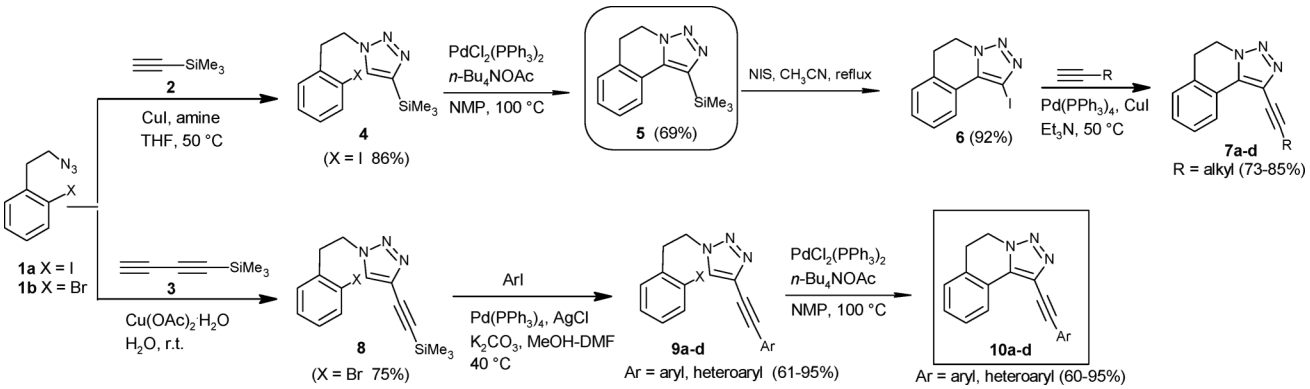
Results and discussion

In accord with the plan outlined in Scheme 1 we started with the cycloaddition reaction between (2-haloaryl)alkyl azides, 1-(2-azidoethyl)-2-iodobenzene **1a** with trimethylsilylacetylene **2** or 1-(2-azidoethyl)-2-bromobenzene **1b** with 1-trimethylsilyl-1,3-butadiyne **3** affording in good yields the triazole derivatives **4** (86%) and **8** (75%). In the case of compound **4** the intramolecular direct C–H arylation of the triazole ring led easily to the silyl-substituted-1,2,3-triazole-fused dihydroisoquinoline **5** (69% yield). A further substitution of the silyl group with an iodine atom afforded in 92% yield the compound **6** that, when subjected to cross-coupling reactions with different aliphatic alkynes, led to a variety of alkylethynyl-1,2,3-triazole-fused dihydroisoquinolines **7a–d** in high yields (Table 1). Whereas aryl- and heteroarylethynyl-1,2,3-triazole-fused dihydroisoquinolines **10a–d** were obtained from compound **8**, which was first subjected to cross-coupling reactions with aryliodides, leading to compounds **9a–d** and then to an intramolecular direct C–H arylation that afforded in good yields the arylethynyl-1,2,3-triazole-fused dihydroisoquinolines **10a–d** (Table 2). We wish to underline that we start from the bromo azide **1b**, instead of the iodo azide **1a**, towards the compounds **10**, to avoid—in the cross-coupling reactions between the haloalkynyl silane derivative and the aryl iodides, which lead to compounds **9**—undesired coupling reactions.

Moreover, we were able to devise an alternative strategy leading to the same compounds **7** and **10**, as outlined in Scheme 2. Indeed, compound **5**, the intermediate for the synthesis of compounds **7**, was also obtained in high yield (91%) by a preliminary coupling of trimethylsilylacetylene **2** with 1-(2-azidoethyl)-2-iodobenzene **1a** followed by a thermal intramolecular cycloaddition reaction[14] in toluene at 130 °C, without a catalyst, of the resulting coupled product **11**. It is noteworthy that this reaction represents an



Scheme 1 Procedure for the synthesis of the title compounds **7** and **10**.

Table 1 Synthesis of alkylethynyl-1,2,3-triazole-fused dihydroisoquinolines **7**

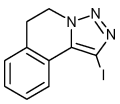
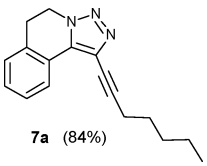
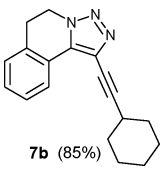
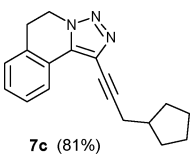
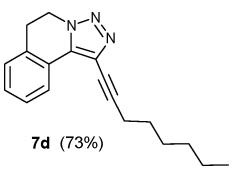
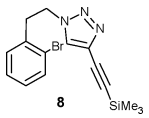
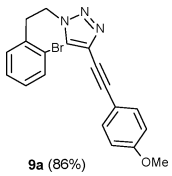
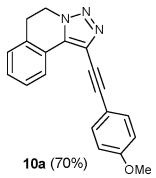
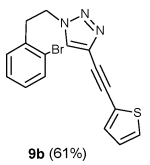
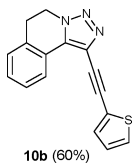
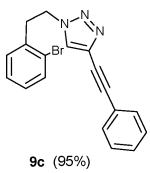
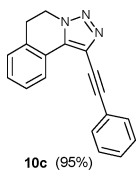
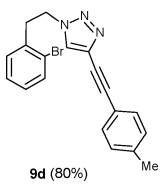
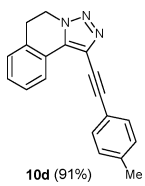
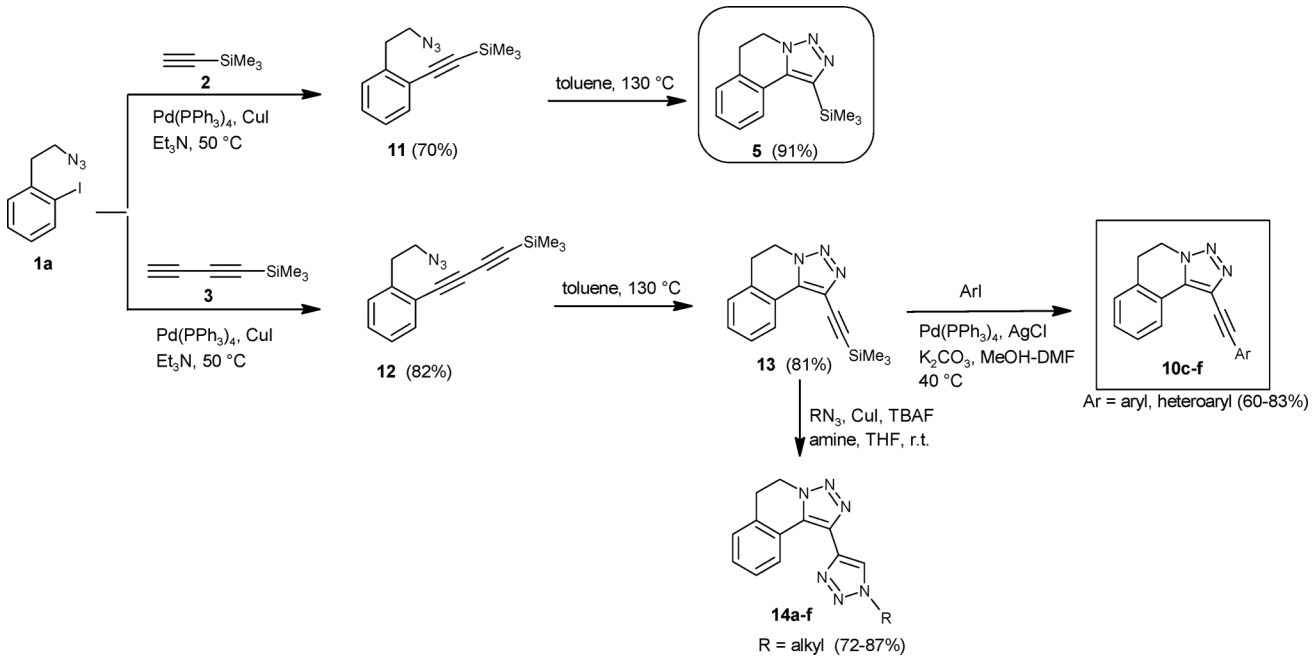
Halide **6**	Alkyne	Products **7** (yields %)
 **6**	1-Heptyne	 **7a** (84%)
6	Ethynylcyclohexane	 **7b** (85%)
6	Prop-2-yn-1-ylcyclopentane	 **7c** (81%)
6	1-Octyne	 **7d** (73%)

Table 2 Synthesis of arylethynyl-1,2,3-triazole-fused dihydroisoquinilines **10**

Compound **8**	Aryliodide	Products **9** (yields %)	Products **10** (yields %)
 **8**	*p*-Iodoanisole	 **9a** (86%)	 **10a** (70%)
8	2-Iodothiophene	 **9b** (61%)	 **10b** (60%)
8	Iodobenzene	 **9c** (95%)	 **10c** (95%)
8	*p*-Iodotoluene	 **9d** (80%)	 **10d** (91%)

additional example of an intramolecular [3 + 2]cycloaddition of azides on disubstituted alkynes[9e,f] without a catalyst.[9e,15] The same approach was followed for the synthesis of compounds **10c–f**. Indeed, a preliminary coupling reaction of the silyldiyne **3** with the iodo azide **1a**, followed by the thermal cycloaddition reaction in toluene at 130 °C of the resulting coupling product **12**, led to the silylethynyl-1,2,3-triazole-fused dihydroisoquinoline **13** in high yield (81%). The compound **13** was further elaborated to give, by cross-coupling reactions with aryl- and heteroaryl iodides, the series of arylethynyl-1,2,3-triazole-fused dihydroisoquinolines **10c–f** (Table 3).

Moreover, owing to our experience on the synthesis of unsymmetrically substituted 4,4′-bi-triazole derivatives,[13a] we decided to explore the possibility of obtaining a new complex class of bi-triazole derivatives by further cycloaddition reactions of compound **13** with alkyl azides. We were pleased to find that these cycloaddition reactions proceeded smoothly in our conditions leading to the desired compounds **14a–f** in high yields (Table 4). Furthermore, we wish to emphasize that, as reported in Table 4, the azides **1a** and **1b** were intentionally used to prepare the compounds **14d** and **14e**, with the aim of evaluating the possibility of obtaining a new class of 4,4′-bitriazole-fused dihydroisoquinoline derivatives by a subsequent intramolecular C–H arylation of the compound **14d** or of the compound **14e**. We were delighted to find that the desired compound **15** was obtained in good yield starting from the compound **14e** (eqn (1)).



Scheme 2 Alternative procedure for the synthesis of compounds **5** and **10**.

Conclusions

In summary, we have described an efficient method for the synthesis of ethynyl substituted 1,2,3-triazole-fused dihydroisoquinolines **7** and **10** starting from readily available silyl alkynes and 2-halophenylethyl azides and employing simple cycloaddition reactions, cross-coupling reactions and finally intramolecular cyclization by direct arylation of the C–H bond of the triazole ring. Moreover, the versatility of this procedure is further demonstrated by the possibility of an easy synthesis of more complex bitriazole-fused dihydroisoquinoline derivatives.

Experimental

General

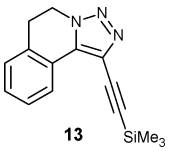
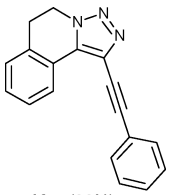
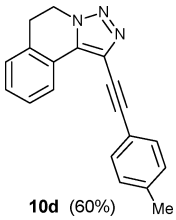
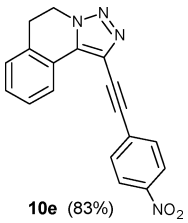
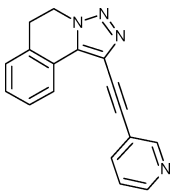
Macherey-Nagel silica gel (60, particle size 0.040–0.063 mm) for column chromatography and Macherey-Nagel aluminum sheets with silica gel 60 F_{254} for TLC were used. GC analysis was performed on a Varian 3900 gas chromatograph equipped with a Supelco SLB™-5 ms capillary column (30 m × 0.25 mm id). 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). ^{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 Stuart Scientific Melting point apparatus SMP3. Tetrahydrofuran was distilled from sodium, *N*,*N*-dimethylformamide, 1-methyl-2-pyrrolidinone, acetonitrile, toluene and triethylamine were used as supplied.

Synthesis of products 7 according to the Scheme 1

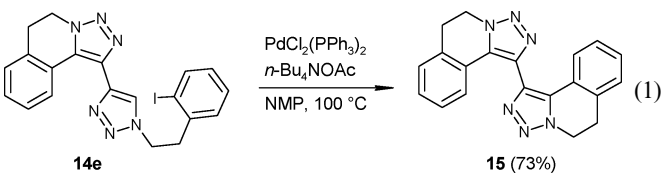
1-[2-(2-Iodophenyl)ethyl]-4-(trimethylsilyl)-1*H*-1,2,3-triazole (4). Trimethylsilylacetylene **2** (0.681 g, 6.93 mmol) was added at room temperature under nitrogen to a stirred solution of 2-iodophenylethyl azide **1a** (1.262 g, 4.62 mmol), CuI (0.880 g, 4.62 mmol) and 1,1,4,7,7-pentamethyldiethylenetriamine (0.96 mL, 4.62 mmol) in THF (16 mL). The mixture was heated at 50 °C for 2h, then quenched with a saturated aqueous solution of NH_4Cl (50 mL) and extracted with ethyl acetate (3 × 60 mL). The organic extracts were washed with an aqueous solution of NaCl (3 × 40 mL), dried over Na_2SO_4 and concentrated under vacuum. Purification by column chromatography, R_f 0.43 (30% ethyl acetate/petroleum ether), afforded 1.474 g of compound **4** (86% yield). After crystallization from petroleum ether, compound **4** was obtained as a white solid, mp = 57–58 °C. Found: C, 42.15; H, 4.86; N, 11.38. $C_{13}H_{18}IN_3Si$ requires: C, 42.05; H, 4.89; N, 11.32%. ν_{max}/cm^{-1} (KBr) 3104, 2955, 2896, 1466, 1438, 1419, 1244, 1189, 1114, 1099, 1050, 1009, 838, 749; δ_H (400 MHz, $CDCl_3$) 7.79 (dd, *J* = 7.6, 1.2 Hz, 1H), 7.21 (s, 1H), 7.16 (td, *J* = 7.6, 1.2 Hz, 1H), 6.93 (dd, *J* = 7.6, 1.6 Hz, 1H), 6.89 (td, *J* = 7.6, 1.6 Hz, 1H), 4.56 (t, *J* = 7.4 Hz, 2H), 3.27 (t, *J* = 7.4 Hz, 2H), 0.24 (s, 9H); δ_C (100.6 MHz, $CDCl_3$) 146.2, 139.6, 139.6, 130.2, 129.3, 128.8, 128.5, 100.1, 49.1, 41.5, –1.2; MS *m*/*z* 328 (2%), 244 (44), 231 (73), 217 (5), 200 (4), 126 (15), 104 (86), 98 (14), 90 (16), 86 (21), 83 (15), 77 (25), 73 (100), 59 (34), 45 (34), 43 (36).

5,6-Dihydro-1-(trimethylsilyl)-[1,2,3]triazolo[5,1-*a*] isoquinoline (5). To a solution of compound **4** (0.519 g, 1.40 mmol) in NMP (10 mL) at room temperature under nitrogen $PdCl_2(PPh_3)_2$ (0.049 g, 0.07 mmol) and *n*-Bu_4NOAc (0.844 g, 2.80 mmol) were successively added. The resulting mixture was stirred at 100 °C for 1h, then was quenched with a saturated aqueous solution of NH_4Cl (40 mL) and extracted with ethyl acetate (3 × 50 mL). The organic extracts were washed with an aqueous solution of

Table 3 Synthesis of arylethynl-1,2,3-triazole-fused dihydroisoquinilines **10** staring from compound **13**

Compound **13**	Aryliodide	Products **10** (yields %)
 **13**	Iodobenzene	 **10c** (66%)
13	*p*-Iodotoluene	 **10d** (60%)
13	*p*-Nitroiodobenzene	 **10e** (83%)
13	3-Iodopyridine	 **10f** (67%)

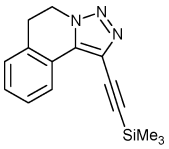
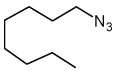
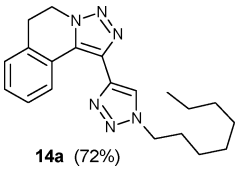
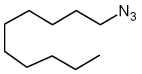
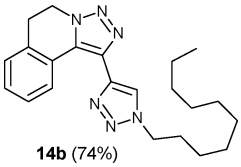
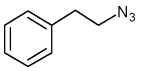
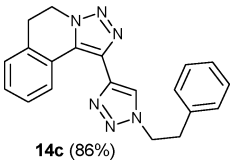
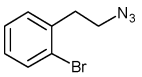
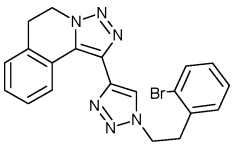
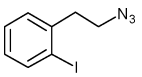
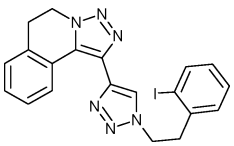
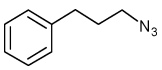
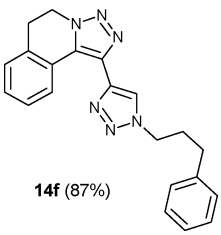
NaCl (3 × 40 mL), dried over Na_2SO_4 and concentrated under vacuum. Purification by column chromatography, R_f 0.57 (60% ethyl acetate/hexane), afforded 0.235 g of compound **5** (69% yield). After crystallization from petroleum ether, compound **5** was obtained as a white solid, mp 82–83 °C. Found: C, 64.25; H, 7.10; N, 17.19. $C_{13}H_{17}N_3Si$ requires: C, 64.15; H, 7.04; N, 17.27%. ν_{max}/cm^{-1} (KBr) 3048, 2954, 2895, 1456, 1437, 1337, 1245, 837, 756, 740, 727; δ_H (400 MHz, $CDCl_3$) 7.62 (d, J = 7.6 Hz, 1H), 7.37–7.28 (m, 3H), 4.56 (t, J = 6.8 Hz, 2H), 3.16 (t, J = 6.8 Hz, 2H), 0.43 (s, 9H); δ_C (100.6 MHz, $CDCl_3$) 141.1, 138.7, 133.0, 128.9, 128.5, 127.4, 126.0, 125.8, 44.4, 29.2, –0.9; MS: m/z 243 (M^+, 7%), 214 (28), 200 (11), 184 (5), 173 (14), 159 (4), 145 (13), 130 (11), 116 (28), 115 (32), 73 (100), 59 (25), 45 (44), 43 (30).



14e **15** (73%) (1)

5,6-Dihydro-1-iodo-[1,2,3]triazolo[5,1-*a*]isoquinoline (6). To a solution of compound **5** (0.785 g, 3.23 mmol) in CH_3CN (20 mL) under nitrogen, NIS (2.180 g, 9.69 mmol) was added. The mixture was heated at reflux for 2 h, then quenched with a saturated aqueous solution of $Na_2S_2O_3$ (50 mL) and extracted with ethyl acetate (3 × 50 mL). The organic extracts were washed with an aqueous solution of NaCl (3 × 40 mL), dried over Na_2SO_4 and concentrated under vacuum. The residue was purified by column chromatography, R_f 0.75 (60% ethyl acetate/petroleum ether), leading to 0.883 g of compound **6** (92% yield). After crystallization from ethyl acetate/petroleum ether, compound **6** was obtained as a white solid, mp 137–138 °C. Found: C, 40.50; H, 2.76; N, 14.09. $C_{10}H_8IN_3$ requires: C, 40.43; H, 2.71; N, 14.14%. ν_{max}/cm^{-1} (KBr) 3005, 2979, 2951, 2904, 1476, 1458, 1449, 1424, 1417, 1347, 1281, 1251, 1220, 1178, 1170, 1157, 1036, 994, 778, 758, 738, 713; δ_H (400 MHz, $CDCl_3$) 8.32 (dd, J = 7.8, 1.0 Hz, 1H), 7.43–7.30 (m, 3H), 4.58 (t, J = 7.0 Hz, 2H), 3.21 (t, J = 7.0 Hz, 2H); δ_C (100.6

Table 4 Synthesis of products **14** starting from compound **13**

Compound **13**	Azides	Products **14** (yields %)
 **13**		 **14a** (72%)
13		 **14b** (74%)
13		 **14c** (86%)
13	 **1b**	 **14d** (80%)
13	 **1a**	 **14e** (78%)
13		 **14f** (87%)

MHz, $CDCl_3$) 133.4, 132.5, 129.7, 128.4, 127.6, 124.0, 123.7, 83.5, 45.2, 29.1; MS: *m/z* 297 (M^+, 15%), 142 (13), 140 (12), 127 (8), 115 (100), 89 (9), 71 (11), 63 (10), 58 (10), 51 (9), 50 (8).

General procedure for the synthesis of products 7

Alkyne (2 equiv) was added at room temperature under nitrogen to a stirred suspension (0.1 N) of compound **6** (1 equiv), $Pd(PPh_3)_4$ (0.04 equiv) and CuI (0.02 equiv) in Et_3N. The mixture was heated at 50 °C and, after completion (5–7h), was quenched with a saturated aqueous solution of NH_4Cl (30 mL) and extracted with ethyl acetate (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 by crystallization.

1-(Hept-1-yn-1-yl)-5,6-dihydro-[1,2,3]triazolo[5,1-*a*]isoquinoline (7a). Compound **7a** was prepared from compound **6** (0.071 g, 0.24 mmol) and 1-heptyne (0.046 g, 0.48 mmol) in accordance with general procedure. Purification by column chromatography, R_f 0.71 (60% ethyl acetate/petroleum ether), afforded 0.053 g of compound **7a** (84% yield). After crystallization from ethyl acetate/hexane, compound **7a** was obtained as a pale yellow solid, mp 54–56 °C. Found: C, 77.00; H, 7.25; N, 15.90. $C_{17}H_{19}N_3$ requires: C, 76.95; H, 7.22; N, 15.84%. ν_{max}/cm^{-1} (KBr) 3064, 2950, 2927, 2857, 2233, 1473, 1457, 1423, 1364, 1346, 1232, 1186, 775, 745, 727; δ_H (400 MHz, $CDCl_3$) 8.16 (dd, *J* = 6.8, 2.0 Hz, 1H), 7.40–7.25 (m, 3H), 4.52 (t, *J* = 7.0 Hz, 2H), 3.19 (t, *J* = 7.0 Hz, 2H), 2.51 (t, *J* = 7.0 Hz, 2H), 1.65 (quintet, *J* = 7.0 Hz, 2H), 1.51–1.41 (m, 2H), 1.40–1.29 (m, 2H), 0.89 (t, *J* = 7.2 Hz, 3H); δ_C (100.6 MHz, $CDCl_3$) 133.3, 131.9, 129.5, 128.1, 127.6, 126.5, 124.5, 124.2, 96.6, 71.0, 44.7, 31.1, 28.7, 28.0, 22.2, 19.6, 13.9; MS: *m/z* 265 (M^+, 14%), 236 (8), 222 (14), 208 (23), 196 (35), 194 (30), 182 (100), 180 (48), 169 (54), 168 (39), 155 (30), 152 (43), 139 (14), 128 (18), 115 (32), 103 (12), 89 (12), 77 (29), 63 (16), 55 (14), 51 (22), 41 (48), 39 (39).

1-(Cyclohexylethynyl)-5,6-dihydro-[1,2,3]triazolo[5,1-*a*]isoquinoline (7b). Compound **7b** was prepared from compound **6** (0.071 g, 0.24 mmol) and cyclohexylacetylene (0.052 g, 0.48 mmol) in accordance with general procedure. Purification by column chromatography, R_f 0.74 (60% ethyl acetate/hexane), afforded 0.057 g of compound **7b** (85% yield). After crystallization from ethyl acetate/hexane, compound **7b** was obtained as a pale yellow solid, mp 94–96 °C. Found: C, 77.90; H, 6.98; N, 15.30. $C_{18}H_{19}N_3$ requires: C, 77.95; H, 6.90; N, 15.15%. ν_{max}/cm^{-1} (KBr) 3054, 2922, 2852, 2234, 1475, 1447, 1424, 1371, 1347, 1232, 948, 777, 746, 730; δ_H (400 MHz, $CDCl_3$) 8.19 (dd, *J* = 6.8, 2.0 Hz, 1H), 7.40–7.26 (m, 3H), 4.53 (t, *J* = 6.8 Hz, 2H), 3.20 (t, *J* = 6.8 Hz, 2H), 2.76–2.65 (m, 1H), 1.98–1.89 (m, 2H), 1.82–1.70 (m, 2H), 1.66–1.50 (m, 3H), 1.42–1.30 (m, 3H); δ_C (100.6 MHz, $CDCl_3$) 133.3, 132.0, 129.5, 128.2, 127.7, 126.6, 124.5, 124.3, 100.4, 71.0, 44.7, 32.3, 29.8, 28.8, 25.8, 24.8; MS: *m/z* 277 (M^+, 19%), 248 (84), 234 (12), 220 (100), 206 (49), 194 (23), 193 (21), 192 (24), 191 (22), 180 (25), 178 (29), 168 (48), 165 (34), 155 (24), 154 (23), 152 (27), 139 (22), 130 (24), 115 (43), 103 (24), 102 (22), 89 (23), 82 (21), 77 (43), 63 (24), 51 (30), 41 (65), 39 (65).

1-(3-Cyclopentylprop-1-yn-1-yl)-5,6-dihydro-[1,2,3]triazolo [5,1-*a*]isoquinoline (7c). Compound **7c** was prepared from compound **6** (0.122 g, 0.41 mmol) and 3-cyclopentyl-1-propyne (0.089 g, 0.82 mmol) in accordance with general procedure. Purification by column chromatography, R_f 0.65 (60% ethyl acetate/hexane), afforded 0.092 g of compound **7c** (81% yield) as a yellow oil. Found: C, 77.85; H, 6.95; N, 15.20. $C_{18}H_{19}N_3$ requires: C, 77.95; H, 6.90; N, 15.15%. ν_{max}/cm^{-1} (neat) 3057, 2947, 2865, 2236, 1474, 1457, 1425, 1369, 1350, 1235, 1047, 769, 745, 728; δ_H (400 MHz, $CDCl_3$) 8.16 (dd, *J* = 6.8, 2.2 Hz, 1H), 7.36–7.25 (m, 3H), 4.51 (t, *J* = 7.0 Hz, 2H), 3.18 (t, *J* = 7.0 Hz, 2H), 2.51 (d, *J* = 6.8 Hz, 2H), 2.17 (septet, *J* = 6.8 Hz, 1H), 1.90–1.80 (m, 2H), 1.70–1.48 (m, 4H), 1.43–1.30 (m, 2H); δ_C (100.6 MHz, $CDCl_3$) 133.3, 131.9, 129.4, 128.1, 127.6, 126.5, 124.5, 124.1, 96.1, 71.0, 44.7, 38.8, 32.0, 28.7, 25.4, 25.2; MS: *m/z* 277 (M^+, 10%), 248 (24), 220 (27), 208 (15), 206 (13), 182 (75), 180 (55), 168 (19), 152 (31), 103 (10), 89 (8), 77 (20), 69 (10), 67 (9), 63 (10), 51 (15), 41 (100), 39 (36).

5,6-Dihydro-1-(oct-1-yn-1-yl)-[1,2,3]triazolo[5,1-*a*]isoquinoline (7d). Compound **7d** was prepared from compound **6** (0.122 g, 0.41 mmol) and 1-octyne (0.090 g, 0.82 mmol) in accordance with general procedure. Purification by column chromatography, R_f 0.63 (50% ethyl acetate/hexane), afforded 0.084 g of compound **7d** (73% yield). After crystallization from hexane, compound **7d** was obtained as a pale brown solid, mp 42–43 °C. Found: C, 77.45; H, 7.55; N, 15.20. $C_{18}H_{21}N_3$ requires: C, 77.38; H, 7.58; N, 15.04%. ν_{max}/cm^{-1} (KBr) 3064, 2953, 2926, 2856, 2237, 1474, 1458, 1429, 1369, 1350, 1234, 1187, 769, 742, 728; δ_H (400 MHz, $CDCl_3$) 8.14 (dd, *J* = 7.2, 1.8 Hz, 1H), 7.38–7.22 (m, 3H), 4.50 (t, *J* = 7.0 Hz, 2H), 3.17 (t, *J* = 7.0 Hz, 2H), 2.49 (t, *J* = 7.0 Hz, 2H), 1.63 (quintet, *J* = 7.0 Hz, 2H), 1.50–1.41 (m, 2H), 1.33–1.23 (m, 4H), 0.85 (t, *J* = 7.0 Hz, 3H); δ_C (100.6 MHz, $CDCl_3$) 133.2, 131.9, 129.4, 128.1, 127.6, 126.4, 124.4, 124.1, 96.6, 71.0, 44.7, 31.2, 28.7, 28.6, 28.3, 22.5, 19.6, 14.0; MS: *m/z* 279 (M^+, 13%), 250 (22), 236 (7), 222 (57), 210 (23), 208 (28), 194 (27), 183 (57), 182 (100), 180 (54), 168 (39), 152 (48), 140 (10), 128 (19), 115 (31), 103 (13), 89 (11), 77 (30), 63 (14), 55 (20), 51 (21), 43 (29), 41 (65), 39 (40).

Synthesis of products 10 according to Scheme 1

1-[2-(2-Bromophenyl)ethyl]-4-(trimethylsilylethynyl)-1*H*-1,2,3-triazole (8). 1-Trimethylsilyl-1,3-butadiyne **3** (0.580 g, 4.75 mmol) and 2-bromophenylethyl azide **1b** (0.716 g, 3.17 mmol) were added at room temperature to a solution of $Cu(OAc)_2 \cdot H_2O$ (0.127 g, 0.63 mmol) in H_2O (15 mL) in a capped flask. The mixture was stirred at room temperature for 7 h, then quenched with a saturated aqueous solution of NH_4Cl (50 mL) and extracted with ethyl acetate (3 × 50 mL). The organic extracts were washed with an aqueous solution of NaCl (3 × 40 mL), dried over Na_2SO_4 and concentrated under vacuum. Purification by column chromatography, R_f 0.72 (30% ethyl acetate/petroleum ether), afforded 0.827 g of compound **8** (75% yield). After crystallization from ethyl acetate/petroleum ether, compound **8** was obtained as a white solid, mp 127–128 °C. Found: C, 51.85; H, 5.30; N, 12.15. $C_{15}H_{18}BrN_3Si$ requires: C, 51.72; H, 5.21; N, 12.06%. ν_{max}/cm^{-1} (KBr) 3136, 3044, 2961, 2177, 1472, 1458, 1436, 1352, 1250, 1220, 1055, 1026, 865, 841, 752, 655, 648; δ_H (400 MHz, $CDCl_3$) 7.54 (dd, *J* = 7.6, 1.2 Hz, 1H), 7.41 (s, 1H), 7.17 (td, *J* = 7.6, 1.2 Hz, 1H), 7.10 (td, *J* = 7.6, 1.6 Hz, 1H), 6.97 (dd, *J* = 7.6, 1.6 Hz, 1H), 4.58 (t, *J* = 7.2 Hz, 2H), 3.31 (t, *J* = 7.2 Hz, 2H), 0.21 (s, 9H); δ_C (100.6 MHz, $CDCl_3$) 135.8, 133.1, 131.1, 130.7, 129.1, 127.9, 126.5, 124.2, 98.6, 93.4, 49.6, 37.0, –0.4; MS *m/z* 268 (3%), 240 (7), 185 (55), 183 (60), 169 (13), 150

(47), 137 (6), 122 (11), 107 (23), 104 (100), 97 (22), 86 (36), 77 (45), 73 (89), 59 (81), 53 (23), 43 (51).

General procedure for the synthesis of products 9

To a solution (0.2 M) of aryl iodide (1 equiv) and compound **8** (1 equiv) in DMF at room temperature under nitrogen were successively added $Pd(PPh_3)_4$ (0.05 equiv), AgCl (0.2 equiv), K_2CO_3 (8 equiv) and MeOH (8 equiv). The mixture was stirred at 40 °C and, after reaction completion (2–3 h), was quenched with a saturated aqueous solution of NH_4Cl (40 mL) and extracted with ethyl acetate (3 × 50 mL). The organic extracts were washed with an aqueous solution of NaCl (3 × 40 mL), dried over Na_2SO_4 and concentrated under vacuum. The residue was purified by column chromatography on silica gel and by crystallization.

1-[2-(2-Bromophenyl)ethyl]-4-[(4-methoxyphenyl)ethynyl]-1*H*-1,2,3-triazole (9a). Compound **9a** was prepared from compound **8** (0.150 g, 0.43 mmol) and *p*-iodoanisole (0.101 g, 0.43 mmol) in accordance with general procedure. Purification by column chromatography, R_f 0.75 (60% ethyl acetate/petroleum ether), afforded 0.142 g of compound **9a** (86% yield). After crystallization from ethyl acetate/petroleum ether, compound **9a** was obtained as a yellow solid, mp 117–119 °C. Found: C, 59.80; H, 4.20; N, 10.94. $C_{19}H_{16}BrN_3O$ requires: C, 59.70; H, 4.22; N, 10.99%. ν_{max}/cm^{-1} (KBr) 3147, 3007, 2959, 2923, 2836, 2226, 1604, 1544, 1502, 1458, 1440, 1292, 1248, 1232, 1171, 1033, 835, 810, 754; δ_H (400 MHz, $CDCl_3$) 7.55 (dd, J = 7.6, 1.2 Hz, 1H), 7.46–7.41 (m, 3H), 7.18 (td, J = 7.6, 1.2 Hz, 1H), 7.10 (td, J = 7.6, 1.6 Hz, 1H), 6.99 (dd, J = 7.6, 1.6 Hz, 1H), 6.86–6.81 (m, 2H), 4.61 (t, J = 7.2 Hz, 2H), 3.79 (s, 3H), 3.33 (t, J = 7.2 Hz, 2H); δ_C (100.6 MHz, $CDCl_3$) 159.9, 135.9, 133.1, 131.1, 131.1, 129.1, 127.9, 127.6, 125.8, 124.2, 114.3, 114.0, 92.4, 77.1, 55.3, 49.7, 37.0; MS: m/z 274 (68%), 259 (29), 247 (39), 231 (29), 185 (26), 183 (28), 169 (61), 157 (77), 141 (64), 127 (27), 113 (63), 104 (100), 90 (38), 89 (35), 77 (84), 63 (42), 51 (47).

1-[2-(2-Bromophenyl)ethyl]-4-[(thiophen-2-yl)ethynyl]-1*H*-1,2,3-triazole (9b). Product **9b** was prepared from compound **8** (0.150 g, 0.43 mmol) and 2-iodothiophene (0.091 g, 0.43 mmol) in accordance with general procedure. Purification by column chromatography, R_f 0.48 (40% ethyl acetate/petroleum ether), afforded 0.094 g of compound **9b** (61% yield). After crystallization from ethyl acetate/petroleum ether, compound **9b** was obtained as a pale yellow solid, mp 124–126 °C. Found: C, 53.75; H, 3.45; N, 11.80; S, 8.90. $C_{16}H_{12}BrN_3S$ requires: C, 53.64; H, 3.38; N, 11.73; S, 8.95%. ν_{max}/cm^{-1} (KBr) 3131, 3095, 2952, 2932, 1437, 1231, 1218, 1182, 1050, 1042, 1016, 1009, 850, 836, 755, 707, 655; δ_H (400 MHz, $CDCl_3$) 7.51 (dd, J = 7.6, 1.2 Hz, 1H), 7.45 (s, 1H), 7.27–7.22 (m, 2H), 7.14 (td, J = 7.6, 1.2 Hz, 1H), 7.07 (td, J = 7.6, 1.6 Hz, 1H), 6.98–6.92 (m, 2H), 4.59 (t, J = 7.2 Hz, 2H), 3.30 (t, J = 7.2 Hz, 2H); δ_C (100.6 MHz, $CDCl_3$) 135.7, 133.0, 132.5, 131.0, 130.4, 129.0, 127.8, 127.8, 127.0, 126.2, 124.1, 122.0, 85.7, 82.0, 49.6, 36.9; MS: m/z 250 (54%), 223 (31), 217 (30), 185 (21), 169 (22), 160 (39), 133 (100), 116 (26), 104 (74), 89 (85), 77 (78), 69 (28), 63 (30), 51 (37), 45 (73), 39 (48).

1-[2-(2-Bromophenyl)ethyl]-4-(phenylethynyl)-1*H*-1,2,3-triazole (9c). Compound **9c** was prepared from compound **8** (0.150 g, 0.43 mmol) and iodobenzene (0.088 g, 0.43 mmol) in accordance with general procedure. Purification by column chromatography, R_f 0.87 (70% ethyl acetate/petroleum ether), afforded 0.144 g of compound **9c** (95% yield). After crystallization from ethyl acetate/petroleum ether, compound **9c** was obtained as a yellow solid, mp 86–88 °C. Found: C, 61.45; H, 3.95; N, 11.98. $C_{18}H_{14}BrN_3$ requires: C, 61.38; H, 4.01; N, 11.93%. ν_{max}/cm^{-1} (KBr) 3145, 3055, 2923, 1439, 1229, 1201, 1052, 1031, 808, 753, 746, 691; δ_H (400 MHz, $CDCl_3$) 7.56 (dd, J = 7.6, 1.2 Hz, 1H), 7.52–7.48 (m, 2H), 7.46 (s, 1H), 7.34–7.29 (m, 3H), 7.19 (td, J = 7.6, 1.2 Hz, 1H), 7.11 (td, J = 7.6, 1.6 Hz, 1H), 6.99 (dd, J = 7.6, 1.6 Hz, 1H), 4.63 (t, J = 7.2 Hz, 2H), 3.35 (t, J = 7.2 Hz, 2H); δ_C (100.6 MHz, $CDCl_3$) 135.9, 133.1, 131.6, 131.1, 130.8, 129.1, 128.7, 128.3, 127.9, 126.1, 124.2, 122.3, 92.4, 78.4, 49.7, 37.1; MS: m/z 244 (50%), 217 (23), 202 (22), 185 (53), 183 (53), 169 (12), 166 (12), 154 (20), 142 (8), 127 (100), 113 (14), 104 (88), 90 (22), 77 (71), 63 (27), 51 (34).

1-[2-(2-Bromophenyl)ethyl]-4-[(4-methylphenyl)ethynyl]-1*H*-1,2,3-triazole (9d). Product **9d** was prepared from compound **8** (0.150 g, 0.43 mmol) and *p*-iodotoluene (0.094 g, 0.43 mmol) in accordance with general procedure. Purification by column chromatography, R_f 0.67 (40% ethyl acetate/petroleum ether), afforded 0.126 g of compound **9d** (80% yield). After crystallization from ethyl acetate/petroleum ether, compound **9d** was obtained as a pale yellow solid, mp 138–139 °C. Found: C, 62.40; H, 4.25; N, 11.55. $C_{19}H_{16}BrN_3$ requires: C, 62.31; H, 4.40; N, 11.47%. ν_{max}/cm^{-1} (KBr) 3151, 3042, 2945, 2916, 1456, 1438, 1233, 1204, 1050, 1030, 820, 808, 755; δ_H (400 MHz, $CDCl_3$) 7.55 (dd, J = 7.6, 1.2 Hz, 1H), 7.44 (s, 1H), 7.42–7.37 (m, 2H), 7.18 (td, J = 7.6, 1.2 Hz, 1H), 7.15–7.08 (m, 3H), 6.99 (dd, J = 7.6, 1.6 Hz, 1H), 4.62 (t, J = 7.2 Hz, 2H), 3.34 (t, J = 7.2 Hz, 2H), 2.33 (s, 3H); δ_C (100.6 MHz, $CDCl_3$) 138.9, 135.9, 133.1, 131.4, 131.1, 131.0, 129.1, 129.1, 127.9, 125.9, 124.2, 119.2, 92.6, 77.8, 49.7, 37.0, 21.5; MS: m/z 258 (47%), 243 (20), 231 (23), 216 (19), 215 (17), 185 (35), 183 (38), 167 (36), 153 (13), 141 (59), 139 (64), 127 (20), 115 (53), 104 (100), 90 (28), 89 (31), 77 (69), 63 (26), 51 (39).

General procedure for the synthesis of products 10a–d

To a solution (0.1 M) of triazole **9** (1 equiv) in NMP at room temperature under nitrogen were successively added $PdCl_2(PPh_3)_2$ (0.05 equiv) and *n*-Bu_4NOAc (2 equiv). The resulting mixture was stirred at 100 °C and, after reaction completion (2–3h), was quenched with aqueous NH_4Cl (40 mL) and extracted with ethyl acetate (3 × 40 mL). The organic extracts were washed with an aqueous solution of NaCl (3 × 30 mL), dried over anhydrous Na_2SO_4 and concentrated under vacuum. The residue was purified by column chromatography on silica gel and by crystallization.

5,6-Dihydro-1-[(4-methoxyphenyl)ethynyl]-[1,2,3]triazolo[5,1-*a*]isoquinoline (10a). Compound **10a** was prepared from **9a** (0.130 g, 0.34 mmol) in accordance with general procedure. Purification by column chromatography, R_f 0.56 (60% ethyl acetate/petroleum ether), afforded 0.072 g of compound **10a** (70% yield). After crystallization from ethyl acetate/petroleum ether and washing with ethyl acetate, compound **10a** was obtained as a white solid, mp 132–134 °C. Found: C, 75.80; H, 5.09; N, 13.85. $C_{19}H_{15}N_3O$ requires: C, 75.73; H, 5.02; N, 13.94%. ν_{max}/cm^{-1} (KBr) 3063, 3002, 2978, 2934, 2836, 2205, 1602, 1512, 1489, 1285, 1250, 1239, 1181, 1023, 1013, 836, 770, 763, 734, 535; δ_H (400 MHz, $CDCl_3$) 8.24 (d, J = 7.2 Hz, 1H), 7.53 (d, J = 8.4 Hz, 2H), 7.44–7.28 (m, 3H), 6.90 (d, J = 8.4 Hz, 2H), 4.59 (t, J = 7.0 Hz, 2H), 3.82

(s, 3H), 3.24 (t, J = 7.0 Hz, 2H); δ_C (100.6 MHz, $CDCl_3$) 160.0, 133.7, 133.2, 132.1, 129.7, 128.3, 127.9, 126.4, 124.8, 124.2, 114.6, 114.1, 95.0, 78.5, 55.3, 44.8, 28.8; MS: m/z 301 (M^+, 21%), 273 (83), 258 (27), 245 (17), 242 (21), 241 (22), 240 (23), 230 (36), 215 (25), 202 (54), 141 (18), 136 (16), 123 (20), 115 (100), 108 (22), 101 (55), 88 (58), 77 (17), 75 (22), 63 (17), 51 (23), 39 (34).

5,6-Dihydro-1-[(thiophen-2-yl)ethynyl]-[1,2,3]triazolo[5,1-*a*]isoquinoline (10b). Compound **10b** was prepared from **9b** (0.096 g, 0.27 mmol) in accordance with general procedure. Purification by column chromatography, R_f 0.41 (40% ethyl acetate/petroleum ether), afforded 0.045 g of compound **10b** (60% yield). After crystallization from ethyl acetate/petroleum ether, compound **10b** was obtained as a pale yellow solid, mp 138–140 °C. Found: C, 69.35; H, 4.05; N, 15.28; S, 11.60. $C_{16}H_{11}N_3S$ requires: C, 69.29; H, 4.00; N, 15.15; S, 11.56%. ν_{max}/cm^{-1} (KBr) 3095, 2963, 2927, 2207, 1261, 1223, 1095, 1079, 1035, 1009, 851, 803, 775, 732, 699; δ_H (400 MHz, $CDCl_3$) 8.16 (dd, J = 7.8, 2.0 Hz, 1H), 7.42–7.30 (m, 5H), 7.03 (dd, J = 5.2, 3.6 Hz, 1H), 4.58 (t, J = 7.0 Hz, 2H), 3.24 (t, J = 7.0 Hz, 2H); δ_C (100.6 MHz, $CDCl_3$) 134.2, 132.7, 132.1, 129.9, 128.3, 128.1, 127.9, 127.2, 125.7, 124.9, 123.8, 122.3, 88.2, 83.3, 44.8, 28.7; MS: m/z 277 (M^+, 26%), 249 (93), 248 (100), 221 (49), 216 (17), 204 (22), 189 (23), 176 (24), 163 (16), 151 (16), 141 (15), 124 (25), 115 (43), 110 (45), 96 (30), 89 (31), 77 (24), 69 (18), 63 (25), 51 (32), 45 (65), 39 (49).

5,6-Dihydro-1-(phenylethynyl)-[1,2,3]triazolo[5,1-*a*]isoquinoline (10c). Compound **10c** was prepared from **9c** (0.102 g, 0.29 mmol) in accordance with general procedure. Purification by column chromatography, R_f 0.74 (70% ethyl acetate/petroleum ether), afforded 0.075 g of compound **10c** (95% yield). After crystallization from ethyl acetate/petroleum ether, compound **10c** was obtained as a pale yellow solid, mp 101–103 °C. Found: C, 79.60; H, 4.92; N, 15.58. $C_{18}H_{13}N_3$ requires: C, 79.68; H, 4.83; N, 15.49%. ν_{max}/cm^{-1} (KBr) 3050, 3024, 2922, 2844, 1486, 1472, 1438, 1373, 1344, 910, 766, 755, 738, 724, 686, 599; δ_H (400 MHz, $CDCl_3$) 8.24 (dd, J = 7.6, 1.2 Hz, 1H), 7.63–7.56 (m, 2H), 7.44–7.30 (m, 6H), 4.57 (t, J = 7.0 Hz, 2H), 3.24 (t, J = 7.0 Hz, 2H); δ_C (100.6 MHz, $CDCl_3$) 134.0, 132.1, 131.6, 129.8, 128.8, 128.4, 128.3, 127.9, 125.9, 124.8, 124.0, 122.4, 94.9, 79.8, 44.8, 28.7; MS: m/z 271 (M^+, 17%), 243 (88), 242 (80), 228 (34), 227 (28), 215 (99), 202 (16), 189 (15), 140 (17), 139 (18), 121 (67), 115 (66), 108 (66), 107 (58), 94 (100), 89 (21), 81 (19), 77 (21), 63 (30), 51 (38).

5,6-Dihydro-1-[(4-methylphenyl)ethynyl]-[1,2,3]triazolo[5,1-*a*]isoquinoline (10d). Compound **10d** was prepared from **9d** (0.100 g, 0.27 mmol) in accordance with general procedure. Purification by column chromatography, R_f 0.55 (60% ethyl acetate/petroleum ether), afforded 0.071 g of compound **10d** (91% yield). After crystallization from ethyl acetate/petroleum ether, compound **10d** was obtained as a pale yellow solid, mp 150–153 °C. Found: C, 79.88; H, 5.42; N, 14.68. $C_{19}H_{15}N_3$ requires: C, 79.98; H, 5.30; N, 14.73%. ν_{max}/cm^{-1}(KBr) 3024, 2914, 1485, 1473, 1463, 1371, 1348, 1338, 1235, 1042, 1012, 819, 774, 736, 528; δ_H (400 MHz, $CDCl_3$) 8.23 (dd, J = 8.0, 1.6 Hz, 1H), 7.47 (d, J = 8.0 Hz, 2H), 7.40–7.27 (m, 3H), 7.17 (d, J = 8.0 Hz, 2H), 4.56 (t, J = 7.0 Hz, 2H), 3.22 (t, J = 7.0 Hz, 2H), 2.36 (s, 3H); δ_C (100.6 MHz, $CDCl_3$) 139.0, 133.8, 132.0, 131.4, 129.7, 129.1, 128.2, 127.8, 126.1, 124.7, 123.9, 119.3, 95.0, 79.1, 44.7, 28.7, 21.5; MS: m/z 285 (M^+, 21%), 257 (83), 242 (60), 241 (56), 227 (35), 215 (70), 202 (22), 189 (13), 141 (22), 127 (79), 121 (46), 115 (100), 101 (62), 88 (27), 77 (22), 63 (25), 51 (35).

Alternative procedure for the synthesis of product 5 according to the Scheme 2

1-(2-Azidoethyl)-2-(trimethylsilylethynyl)benzene (11). Trimethylsilylacetylene **2** (0.719 g, 7.32 mmol) was added at room temperature under nitrogen to a stirred suspension of 2-iodophenylethyl azide **1a** (1.000 g, 3.66 mmol), $Pd(PPh_3)_4$ (0.169 g, 0.15 mmol), CuI (0.055 g, 0.29 mmol) in Et_3N (15 mL). The mixture was heated at 50 °C for 2h, then quenched with a saturated aqueous solution of NH_4Cl (50 mL) and extracted with ethyl acetate (3 × 60 mL). The organic extracts were washed with an aqueous solution of NaCl (3 × 40 mL), dried over Na_2SO_4 and concentrated under vacuum. Purification by column chromatography, R_f 0.39 (1% ethyl acetate/hexane), afforded 0.623 g of compound **11** (70% yield) as a pale yellow oil. Found: C, 64.28; H, 7.15; N, 17.20. $C_{13}H_{17}N_3Si$ requires: C, 64.15; H, 7.04; N, 17.27%. ν_{max}/cm^{-1} (neat) 3066, 3022, 2959, 2930, 2898, 2874, 2154, 2101, 1481, 1458, 1448, 1343, 1284, 1249, 1106, 867, 842, 758, 644; δ_H (400 MHz, $CDCl_3$) 7.47–7.42 (m, 1H), 7.28–7.22 (m, 1H), 7.21–7.15 (m, 2H), 3.50 (t, J = 7.4 Hz, 2H), 3.06 (t, J = 7.4 Hz, 2H), 0.25 (s, 9H); δ_C (100.6 MHz, $CDCl_3$) 140.1, 132.6, 129.4, 128.8, 126.7, 122.8, 103.0, 98.7, 51.2, 34.3, –0.1; MS: m/z 243 (M^+, 5%), 214 (21), 200 (8), 173 (12), 145 (10), 130 (8), 116 (24), 115 (25), 73 (100), 59 (21), 45 (36), 43 (27).

5,6 - Dihydro - 1 - (trimethylsilyl) - [1,2,3]triazolo[5,1-*a*]isoquinoline (5). A solution of compound **11** (0.756 g, 3.11 mmol) in toluene (20 mL) was heated at 130 °C for 2 h, then quenched with a saturated aqueous solution of NH_4Cl (40 mL) and extracted with ethyl acetate (3 × 50 mL). The organic extracts were washed with an aqueous solution of NaCl (3 × 40 mL), dried over Na_2SO_4 and concentrated under vacuum. Purification by column chromatography, R_f 0.57 (60% ethyl acetate/hexane), afforded 0.688 g of compound **5** (91% yield).

Alternative procedure for the synthesis of products 10 according to the Scheme 2

1-(2-Azidoethyl)-2-(4-trimethylsilylbuta-1,3-diyn-1-yl)- benzene (12). A solution of 1-trimethylsilyl-1,3-butadiyne **3** (0.536 g, 4.39 mmol) in Et_3N (5 mL) was added at room temperature under nitrogen to a stirred suspension of 2-iodophenylethyl azide **1a** (0.800 g, 2.93 mmol), $Pd(PPh_3)_4$ (0.139 g, 0.12 mmol), CuI (0.011 g, 0.06 mmol) in Et_3N (10 mL). The mixture was heated at 50 °C for 2 h, then quenched with a saturated aqueous solution of NH_4Cl (50 mL) and extracted with ethyl acetate (3 × 50 mL). The organic extracts were washed with an aqueous solution of NaCl (3 × 40 mL), dried over Na_2SO_4 and concentrated under vacuum. Purification by column chromatography, R_f 0.59 (2% ethyl acetate/hexane), afforded 0.642 g of compound **12** (82% yield) as a pale yellow oil. Found: C, 67.45; H, 6.45; N, 15.68. $C_{15}H_{17}N_3Si$ requires: C, 67.37; H, 6.41; N, 15.71%. ν_{max}/cm^{-1} (neat) 3066, 3023, 2959, 2202, 2100, 1450, 1280, 1250, 1014, 845, 757; δ_H (400 MHz, $CDCl_3$) 7.48 (br d, J = 7.6 Hz, 1H), 7.33–7.26 (m, 1H), 7.25–7.16 (m, 2H), 3.52 (t, J = 7.0 Hz, 2H), 3.04 (t, J = 7.0 Hz, 2H), 0.22 (s, 9H); δ_C (100.6 MHz, $CDCl_3$) 141.5, 133.8, 129.6, 129.5, 126.9, 121.1, 91.7, 87.5, 78.0, 74.6, 51.4, 34.1, –0.4; MS: m/z 267

(M$^+$, 11%), 252 (4), 239 (94), 238 (100), 224 (43), 197 (12), 195 (11), 180 (12), 169 (11), 167 (13), 155 (14), 152 (13), 115 (27), 109 (21), 105 (19), 98 (26), 86 (14), 84 (16), 83 (15), 77 (17), 59 (67), 53 (24), 45 (26), 43 (68).

5,6-Dihydro-1-(trimethylsilylethynyl)-[1,2,3]triazolo[5,1-*a*]isoquinoline (13). A solution of compound **12** (0.488 g, 1.83 mmol) in toluene (20 mL) was heated at 130 °C for 8h, then quenched with a saturated aqueous solution of NH_4Cl (40 mL) and extracted with ethyl acetate (3 × 50 mL). The organic extracts were washed with an aqueous solution of NaCl (3 × 40 mL), dried over Na_2SO_4 and concentrated under vacuum. Purification by column chromatography, R_f 0.71 (60% ethyl acetate/petroleum ether), afforded 0.395 g of compound **13** (81% yield). After crystallization from ethyl acetate/hexane, compound **13** was obtained as a white solid, mp 69–70 °C. Found: C, 67.55; H, 6.47; N, 15.68. $C_{15}H_{17}N_3Si$ requires: C, 67.37; H, 6.41; N, 15.71%. ν_{max}/cm^{-1} (KBr) 3062, 2982, 2952, 2893, 2166, 1473, 1350, 1338, 1250, 1232, 1083, 861, 837, 768, 756; δ_H (400 MHz, $CDCl_3$) 8.20–8.15 (m, 1H), 7.39–7.26 (m, 3H), 4.53 (t, J = 7.0 Hz, 2H), 3.20 (t, J = 7.0 Hz, 2H), 0.28 (s, 9H); δ_C (100.6 MHz, $CDCl_3$) 134.4, 132.1, 129.8, 128.2, 127.7, 125.9, 124.7, 123.9, 101.4, 95.0, 44.7, 28.7, –0.4; MS: m/z 267 (M$^+$, 10%), 239 (96), 238 (100), 224 (45), 197 (13), 195 (12), 180 (12), 169 (11), 167 (14), 155 (16), 153 (10), 152 (13), 115 (24), 109 (20), 104 (16), 98 (24), 86 (15), 84 (19), 83 (16), 77 (15), 67 (10), 59 (73), 53 (26), 45 (26), 43 (64).

General procedure for the synthesis of compounds 10c–f

To a solution (0.1–0.15 N) of aryliodide (1 equiv.) and compound **13** (1 equiv.) in DMF at room temperature under nitrogen were successively added $Pd(PPh_3)_4$ (0.05 equiv.), AgCl (0.2 equiv.), K_2CO_3 (8 equiv.) and MeOH (8 equiv.). The mixture was stirred at 40 °C and, after reaction completion (2–4h), was quenched with a saturated aqueous solution of NH_4Cl (40 mL) and extracted with ethyl acetate (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 by crystallization.

5,6-Dihydro-1-(phenylethynyl)-[1,2,3]triazolo[5,1-*a*]isoquinoline (10c). Compound **10c** was prepared from **13** (0.099 g, 0.37 mmol) and iodobenzene (0.076 g, 0.37 mmol) in accordance with general procedure. Purification by column chromatography afforded 0.066 g of compound **10c** (66% yield).

5,6-Dihydro-1-[(4-methylphenyl)ethynyl]-[1,2,3]triazolo[5,1-*a*]isoquinoline (10d). Compound **10d** was prepared from **13** (0.100 g, 0.37 mmol) and *p*-iodotoluene (0.081 g, 0.37 mmol) in accordance with general procedure. Purification by column chromatography afforded 0.064 g of compound **10d** (60% yield).

5,6-Dihydro-1-[(4-nitrophenyl)ethynyl]-[1,2,3]triazolo[5,1-a]isoquinoline (10e). Compound **10e** was prepared from **13** (0.130 g, 0.49 mmol) and *p*-nitroiodobenzene (0.122 g, 0.49 mmol) in accordance with general procedure. Purification by column chromatography, R_f 0.77 (80% ethyl acetate/hexane), afforded 0.128 g of compound **10e** (83% yield). After crystallization from ethyl acetate, compound **10e** was obtained as a yellow solid, mp 233–234 °C. Found: C, 68.40; H, 3.75; N, 17.68. $C_{18}H_{12}N_4O_2$ requires: C, 68.35; H, 3.82; N, 17.71%. ν_{max}/cm^{-1} (KBr) 3099, 3069, 2935, 2217, 1591, 1508, 1489, 1336, 1103, 852, 818, 767; δ_H (400 MHz, DMSO-d_6) 8.30 (d, J = 8.2 Hz, 2H), 8.14 (d, J = 7.2 Hz, 1H), 7.94 (d, J = 8.2 Hz, 2H), 7.55–7.44 (m, 3H), 4.65 (t, J = 7.0 Hz, 2H), 3.29 (t, J = 7.0 Hz, 2H); δ_C (100.6 MHz, DMSO-d_6) 147.1, 134.7, 133.4, 132.5, 130.3, 128.7, 128.2, 127.8, 124.1, 123.9, 123.5, 122.9, 92.7, 84.8, 44.4, 27.7; MS: m/z 288 (56%), 241 (100), 240 (70), 227 (59), 215 (61), 213 (56), 202 (33), 121 (24), 120 (22), 115 (79), 107 (49), 94 (39), 89 (22), 88 (20), 77 (20), 75 (18), 63 (34), 51 (33), 39 (50).

5,6-Dihydro-1-(pyridin-3-ylethynyl)-[1,2,3]triazolo[5,1-*a*]isoquinoline (10f). Compound **10f** was prepared from **13** (0.130 g, 0.49 mmol) and 3-iodopyridine (0.100 g, 0.49 mmol) in accordance with general procedure. Purification by column chromatography, R_f 0.41 (80% ethyl acetate/hexane), afforded 0.089 g of compound **10f** (67% yield). After crystallization from ethyl acetate/hexane, compound **10f** was obtained as a white solid, mp 169–171 °C. Found: C, 74.88; H, 4.42; N, 20.68. $C_{17}H_{12}N_4$ requires: C, 74.98; H, 4.44; N, 20.58%. ν_{max}/cm^{-1}(KBr) 3029, 2952, 2227, 1638, 1480, 1454, 1420, 1374, 1342, 1183, 1011, 802, 766, 724, 698; δ_H (400 MHz, $CDCl_3$) 8.75 (d, J = 1.2 Hz, 1H), 8.51 (dd, J = 4.8, 1.6 Hz, 1H), 8.12 (dd, J = 7.4, 2.0 Hz, 1H), 7.85–7.77 (m, 1H), 7.39–7.23 (m, 4H), 4.53 (t, J = 7.0 Hz, 2H), 3.20 (t, J = 7.0 Hz, 2H); δ_C (100.6 MHz, $CDCl_3$) 151.9, 148.9, 138.3, 134.3, 132.1, 130.0, 128.3, 127.8, 125.1, 124.6, 123.5, 123.0, 119.5, 91.3, 83.1, 44.7, 28.5; MS: m/z 272 (M$^+$, 16%), 243 (100), 229 (22), 216 (41), 189 (22), 163 (15), 140 (11), 122 (12), 115 (43), 109 (20), 108 (24), 94 (57), 81 (49), 77 (13), 75 (14), 63 (20), 51 (21), 39 (31).

General procedure for the synthesis of compounds 14a–f (Scheme 2)

A THF solution (0.2–0.3 M) of silylated derivative **13** (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-pentamethyldiethylene triamine (1.2 equiv.) and soon afterwards TBAF (1 M in THF, 1.2 equiv.) were added. The mixture was stirred at room temperature until reaction completion (3–6 h), then was quenched with a saturated aqueous solution of NH_4Cl (30 mL) and extracted with CH_2Cl_2 (3 × 50 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 by crystallization.

5,6-Dihydro-1-(1-octyl-1*H*-1,2,3-triazol-4-yl)-[1,2,3]triazolo- [5,1-*a*]isoquinoline (14a). Product **14a** was prepared from compound **13** (0.136 g, 0.51 mmol) and n-octyl azide (0.095 g, 0.61 mmol) in accordance with general procedure. Purification by column chromatography, R_f 0.69 (80% ethyl acetate/petroleum ether), afforded 0.129 g of product **14a** (72% yield) as a pale yellow oil. Found: C, 68.65; H, 7.42; N, 23.88. $C_{20}H_{26}N_6$ requires: C, 68.54; H, 7.48; N, 23.98%. ν_{max}/cm^{-1} (neat) 3115, 3065, 2949, 2923, 2854, 1465, 1458, 1436, 1261, 1221, 1048, 963, 771; δ_H (400 MHz, $CDCl_3$) 8.89 (d, J = 7.6 Hz, 1H), 8.08 (s, 1H), 7.39–7.30 (m, 1H), 7.29–7.20 (m, 2H), 4.55 (t, J = 7.0 Hz, 2H), 4.39 (t, J = 7.2 Hz, 2H), 3.17 (t, J = 7.0 Hz, 2H), 1.92 (quintet, J = 7.2 Hz, 2H), 1.38–1.15 (m, 10H), 0.81 (t, J = 7.0 Hz, 3H); δ_C (100.6 MHz, $CDCl_3$) 140.7, 134.6, 132.4, 130.4, 129.2, 127.8, 127.8, 127.6, 124.5, 122.3, 50.4, 45.0, 31.5, 30.1, 29.1, 28.9, 28.8, 26.4, 22.4, 13.9; MS: m/z 350

(M$^+$, 17%), 294 (12), 251 (10), 237 (32), 209 (21), 195 (19), 182 (20), 169 (30), 154 (15), 141 (16), 127 (17), 115 (20), 77 (12), 55 (27), 43 (55), 41 (100).

1-(1-Decyl-1*H*-1,2,3-triazol-4-yl)-[1,2,3]triazolo-5,6-dihydro-[5,1-*a*]isoquinoline (14b). Product **14b** was prepared from compound **13** (0.110 g, 0.41 mmol) and *n*-decyl azide (0.090 g, 0.49 mmol) in accordance with general procedure. Purification by column chromatography, R_f 0.75 (80% ethyl acetate/petroleum ether), afforded 0.115 g of product **14b** (74% yield). After crystallization from ethyl acetate/petroleum ether, product **14b** was obtained as a white solid, mp 64–65 °C. Found: C, 69.65; H, 7.90; N, 22.30. $C_{22}H_{30}N_6$ requires: C, 69.81; H, 7.99; N, 22.20%. ν_{max}/cm^{-1} (KBr) 3116, 3065, 2921, 2854, 1466, 1458, 1434, 1351, 1261, 1221, 1048, 962, 770; δ_H (400 MHz, $CDCl_3$) 8.90 (d, J = 7.6 Hz, 1H), 8.09 (s, 1H), 7.39–7.32 (m, 1H), 7.31–7.23 (m, 2H), 4.56 (t, J = 6.8 Hz, 2H), 4.40 (t, J = 7.2 Hz, 2H), 3.19 (t, J = 6.8 Hz, 2H), 1.93 (quintet, J = 7.2 Hz, 2H), 1.38–1.15 (m, 14H), 0.82 (t, J = 6.6 Hz, 3H); δ_C (100.6 MHz, $CDCl_3$) 140.6, 134.5, 132.4, 130.4, 129.3, 127.8, 127.5, 124.4, 122.3, 50.4, 45.0, 31.7, 30.1, 29.3, 29.2, 29.1, 29.1, 28.9, 26.4, 22.5, 14.0 (one coincident peak not observed); MS: m/z 378 (M$^+$, 18%), 322 (15), 237 (32), 223 (18), 209 (24), 195 (19), 182 (20), 169 (36), 156 (19), 154 (18), 141 (16), 139 (16), 128 (16), 127 (16), 115 (18), 103 (7), 77 (11), 55 (32), 43 (70), 41 (100), 39 (18).

5,6-Dihydro-1-[1-(2-phenylethyl)-1*H*-1,2,3-triazol-4-yl]-[1,2,3]-triazolo[5,1-*a*]isoquinoline (14c). Product **14c** was prepared from compound **13** (0.150 g, 0.56 mmol) and 2-phenylethyl azide (0.099 g, 0.67 mmol) in accordance with general procedure. Purification by column chromatography, R_f 0.43 (60% ethyl acetate/petroleum ether), afforded 0.165 g of product **14c** (86% yield). After crystallization from ethyl acetate/petroleum ether, compound **14c** was obtained as a white solid, mp 136–138 °C. Found: C, 70.10; H, 5.40; N, 24.62. $C_{20}H_{18}N_6$ requires: C, 70.16; H, 5.30; N, 24.54%. ν_{max}/cm^{-1} (KBr) 3114, 3063, 3046, 3024, 2943, 2905, 2879, 2830, 1472, 1449, 1422, 1357, 1259, 1223, 1057, 1027, 963, 772, 711, 690; δ_H (400 MHz, $CDCl_3$) 8.83 (d, J = 7.6 Hz, 1H), 7.93 (s, 1H), 7.39–7.34 (m, 1H), 7.33–7.17 (m, 5H), 7.13 (d, J = 7.2 Hz, 2H), 4.65 (t, J = 7.4 Hz, 2H), 4.55 (t, J = 6.8 Hz, 2H), 3.26 (t, J = 7.4 Hz, 2H), 3.18 (t, J = 6.8 Hz, 2H); δ_C (100.6 MHz, $CDCl_3$) 140.5, 136.7, 134.4, 132.5, 130.4, 129.3, 128.7, 128.5, 127.9, 127.8, 127.4, 127.0, 124.4, 122.7, 51.6, 45.0, 36.5, 29.1; MS: m/z 342 (M$^+$, 44%), 195 (84), 168 (100), 153 (27), 141 (79), 127 (30), 115 (50), 105 (23), 103 (27), 91 (89), 77 (59), 65 (35), 51 (52), 41 (22).

1-{1-[2-(2-Bromophenyl)ethyl]-1*H*-1,2,3-triazol-4-yl}-5,6-dihydro-[1,2,3]triazolo[5,1-*a*]isoquinoline (14d). Product **14d** was prepared from compound **13** (0.110 g, 0.41 mmol) and 2-bromophenylethyl azide **1b** (0.111 g, 0.49 mmol) in accordance with general procedure. Purification by column chromatography, R_f 0.61 (80% ethyl acetate/petroleum ether), afforded 0.138 g of product **14d** (80% yield). After crystallization from ethyl acetate/petroleum ether, compound **14d** was obtained as a white solid, mp 147–148 °C. Found: C, 57.15; H, 4.15; N, 19.90. $C_{20}H_{17}BrN_6$ requires: C, 57.02; H, 4.07; N, 19.95%. ν_{max}/cm^{-1} (KBr) 3115, 3062, 2952, 2889, 1467, 1449, 1437, 1262, 1224, 1057, 1044, 1024, 963, 775, 734; δ_H (400 MHz, $CDCl_3$) 8.85 (dd, J = 7.6, 1.2 Hz, 1H), 7.97 (s, 1H), 7.53 (d, J = 8.0 Hz, 1H), 7.36 (td, J = 7.6, 1.6 Hz, 1H), 7.33–7.24 (m, 2H), 7.15 (td, J = 7.6, 1.2 Hz, 1H), 7.10–7.05 (m, 2H), 4.68 (t, J = 7.2 Hz, 2H), 4.56 (t, J = 6.8 Hz, 2H), 3.39 (t, J = 7.2 Hz, 2H), 3.19 (t, J = 6.8 Hz, 2H); δ_C (100.6 MHz, $CDCl_3$) 140.6, 136.0, 134.4, 133.0, 132.5, 131.0, 130.5, 129.3, 128.9, 127.8, 127.8, 127.8, 127.5, 124.5, 124.2, 122.8, 49.6, 45.0, 37.1, 29.1.

1-{1-[2-(2-Iodophenyl)ethyl]-1*H*-1,2,3-triazol-4-yl}-5,6-dihydro-[1,2,3]triazolo[5,1-*a*]isoquinoline (14e). Product **14e** was prepared from compound **13** (0.198 g, 0.74 mmol) and 2-iodophenylethyl azide **1a** (0.242 g, 0.89 mmol) in accordance with general procedure. Purification by column chromatography, R_f 0.78 (90% ethyl acetate/petroleum ether), afforded 0.271 g of compound **14e** (78% yield). After crystallization from ethyl acetate/petroleum ether, compound **14e** was obtained as a white solid, mp 127–129 °C. Found: C, 51.15; H, 3.75; N, 17.90. $C_{20}H_{17}IN_6$ requires: C, 51.30; H, 3.66; N, 17.95%. ν_{max}/cm^{-1} (KBr) 3113, 3060, 2879, 2824, 1465, 1448, 1445, 1432, 1357, 1260, 1224, 1056, 1012, 962, 774, 734; δ_H (400 MHz, $CDCl_3$) 8.86 (dd, J = 7.6, 1.2 Hz, 1H), 7.99 (s, 1H), 7.80 (dd, J = 8.0, 1.2 Hz, 1H), 7.39–7.24 (m, 3H), 7.18 (td, J = 7.6, 1.2 Hz, 1H), 7.07 (dd, J = 7.6, 1.6 Hz, 1H), 6.89 (td, J = 7.6, 1.6 Hz, 1H), 4.64 (t, J = 7.6 Hz, 2H), 4.56 (t, J = 6.8 Hz, 2H), 3.37 (t, J = 7.6 Hz, 2H), 3.19 (t, J = 6.8 Hz, 2H); δ_C (100.6 MHz, $CDCl_3$) 140.6, 139.7, 139.3, 134.4, 132.5, 130.4, 130.1, 129.3, 129.0, 128.6, 127.8, 127.8, 127.4, 124.4, 122.8, 100.1, 49.8, 45.0, 41.4, 29.1.

5,6-Dihydro-1-[1-(3-phenylpropyl)-1*H*-1,2,3-triazol-4-yl]-[1,2,3]triazolo[5,1-*a*]isoquinoline (14f). Product **14f** was prepared from compound **13** (0.110 g, 0.41 mmol) and 3-phenylpropyl azide (0.079 g, 0.49 mmol) in accordance with general procedure. Purification by column chromatography, R_f 0.64 (80% ethyl acetate/petroleum ether), afforded 0.127 g of product **14f** (87% yield). After crystallization from ethyl acetate/petroleum ether, compound **14f** was obtained as a white solid, mp 119–120 °C. Found: C, 70.70; H, 5.70; N, 23.62. $C_{21}H_{20}N_6$ requires: C, 70.77; H, 5.66; N, 23.58%. ν_{max}/cm^{-1} (KBr) 3133, 3026, 2940, 2923, 2865, 2849, 1465, 1458, 1451, 1261, 1218, 1050, 965, 775, 757, 746, 699; δ_H (400 MHz, $CDCl_3$) 8.93 (d, J = 8.0 Hz, 1H), 8.11 (s, 1H), 7.43–7.35 (m, 1H), 7.34–7.25 (m, 4H), 7.24–7.15 (m, 3H), 4.58 (t, J = 6.8 Hz, 2H), 4.42 (t, J = 7.2 Hz, 2H), 3.21 (t, J = 6.8 Hz, 2H), 2.68 (t, J = 7.2 Hz, 2H), 2.30 (quintet, J = 7.2 Hz, 2H); δ_C (100.6 MHz, $CDCl_3$) 140.7, 140.0, 134.5, 132.5, 130.4, 129.3, 128.5, 128.4, 127.9, 127.5, 126.2, 124.4, 122.5, 49.5, 45.0, 32.3, 31.5, 29.1 (one coincident peak not observed).

Synthesis of a symmetrical bi-1,2,3-triazole-fused dihydroisoquinoline

5,5′,6,6′-Tetrahydro-1,1′-bi[1,2,3]triazolo[5,1,*a*]isoquinoline (15). To a solution of compound **14e** (0.254 g, 0.54 mmol) in NMP (6 mL) at room temperature under nitrogen were successively added $PdCl_2(PPh_3)_2$ (0.021 g, 0.03 mmol) and *n*-Bu_4NOAc (0.326 g, 1.08 mmol). The resulting mixture was stirred at 100 °C for 23h, then was quenched with a saturated aqueous solution of NH_4Cl (30 mL) and extracted with CH_2Cl_2 (3 × 50 mL). The organic extracts were washed with an aqueous solution of NaCl (3 × 40 mL), dried over Na_2SO_4 and concentrated under vacuum. Purification by column chromatography, R_f 0.66 (50% ethyl acetate/CH_2Cl_2), afforded 0.135 g of compound **15** (73% yield). After crystallization from CH_2Cl_2/petroleum ether,

compound **15** was obtained as a white solid, mp 238–240 °C. Found: C, 70.52; H, 4.68; N, 24.62. $C_{20}H_{16}N_6$ requires: C, 70.57; H, 4.74; N, 24.69%. ν_{max}/cm^{-1} (KBr) 3058, 3055, 2938, 1475, 1449, 1432, 1347, 1254, 1187, 1159, 1043, 991, 968, 760, 737, 714; δ_H (400 MHz, $CDCl_3$) 8.00 (d, J = 8.0 Hz, 2H), 7.30–7.18 (m, 6H), 4.65 (t, J = 6.8 Hz, 4H), 3.26 (t, J = 6.8 Hz, 4H); δ_C (100.6 MHz, $CDCl_3$) 134.3, 132.6, 132.0, 129.5, 128.1, 127.8, 126.2, 124.5, 45.1, 29.1; MS: m/z 340 (M^+, 33%), 283 (92), 256 (26), 167 (24), 154 (18), 141 (27), 127 (100), 115 (29), 114 (39), 113 (38), 101 (31), 89 (15), 77 (42), 63 (17), 51 (28), 39 (31).

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