Tetrahedron 66 (2010) 8846–8853

Contents lists available at ScienceDirect

Tetrahedron

journal homepage: www.elsevier.com/locate/tet

An easy synthetic approach to 1,2,3-triazole-fused heterocycles

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ARTICLE INFO

Article history:
Received 30 June 2010
Received in revised form 1 September 2010
Accepted 20 September 2010
Available online 24 September 2010

Keywords:
Cycloaddition
Click chemistry
Alkynes
Azides
Triazole-fused heterocycles

ABSTRACT

A convenient synthesis of 1,2,3-triazole-fused isoindolines and dihydroisoquinolines in good to excellent yield is reported, starting from easily available terminal alkynes and (2-haloaryl)alkylazides. The method is based upon a cycloaddition reaction, via click chemistry, followed by a transition metal-catalyzed functionalization of a C–H bond.

1. Introduction

Because of the widespread application of structurally novel heterocycles in drug development, nitrogen heterocycles, such as 1,2,3-triazoles, have received considerable attention due to their applications ranging from medicinal chemistry[1] to material science.[2] In addition, several heterocycles containing the 1,2,3-triazole ring system are reported to possess a broad spectrum of biological properties, such as antibacterial,[3] antiallergic,[4] and anti-HIV activity.[5] The most popular method for the synthesis of 1,2,3-triazoles is the Huisgen 1,3-dipolar cycloaddition reaction of azides with alkynes.[6] However, the original reactions were severely limited by the high reaction temperatures and the low regioselectivity. These limitations have been overcome by the introduction of the copper catalyzed 1,3-dipolar cycloaddition of terminal alkynes and azides, so-called 'click chemistry'.[7,8] 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. The number of publications dealing with click chemistry has grown exponentially over the last few years,[9,10] and, in particular, this methodology has been widely used by many research groups for the synthesis of several bicyclic, as well as polycyclic fused triazoles heterocycles,[11] compounds of great interest for their various biological and pharmacological activities.[11,12] Mainly, fused triazoles are prepared by an intramolecular 1,3-dipolar cycloaddition between azides and alkynes[11b,i] and a one-pot copper-[11c] or palladium-catalyzed[11d,e,l] coupling reaction followed by a [3+2] cycloaddition. An alternative approach may involve an intramolecular direct transition metal-catalyzed arylation of 1,2,3-triazoles by cleavage of C–H bonds with aryl halides,[11g,h] a methodology which has been recently shown to be a powerful synthetic tool for functionalization of heterocycles.[13]

Owing to our continuing interest in the synthesis of novel structures of biological significance,[14–16] we recently reported a straightforward synthesis of a variety of heterocyclic compounds, with an indole and benzofuran skeleton,[14a,b] and an easy and general approach[15] to more complex 4-substituted-1,2,3-triazoles,[15a] and to unsymmetrically substituted 4,4′-bi-1,2,3-triazoles,[15b] via click chemistry. During our studies, we became interested in developing an easy approach to 1,2,3-triazole-fused heterocycles. Herein we wish to report on these studies, which enabled the synthesis of the title compounds through a reaction sequence involving a preliminary cycloaddition of easily available terminal alkynes and (2-haloaryl)alkylazides, followed by an intramolecular direct transition metal-catalyzed C–H arylation.

2. Results and discussion

Our strategy is depicted in Scheme 1. We started with the cycloaddition reaction between (2-haloaryl)alkylazides, 2-iodo- or 2-bromobenzylazide (**1**, n=0) and 2-(2-iodophenyl)ethylazide or 2-(2-bromophenyl)ethylazide (**2**, n=1) and several terminal alkynes **3**. All reactions were performed in H_2O at 100 °C in the presence of $Cu(OAc)_2 \cdot H_2O$ as a catalyst[15b] (20 mol %), leading to functionalized 1,4-substituted-1,2,3-triazoles **4** (n=0) and **5** (n=1).

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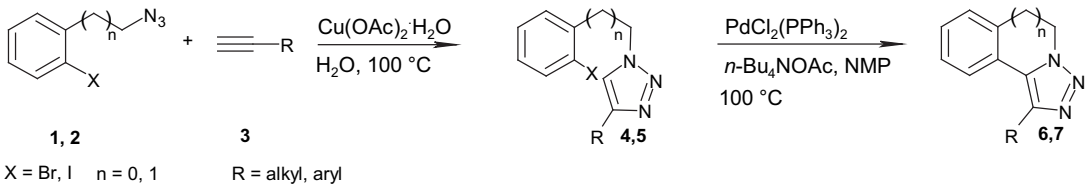
doi:10.1016/j.tet.2010.09.068



Scheme 1.

To obtain the annulated triazoles **6** and **7** we investigated the catalytic activity of various Pd catalyst and we found[17] that compounds **4** and **5** were easily cyclized in the presence of $PdCl_2(PPh_3)_2$ (5 mol %), leading respectively to 1,2,3-triazole-fused isoindolines **6** (n=0) and dihydroiso-quinolines **7** (n=1). It is noteworthy that, relatively to compounds **6**, there is only one report regarding the synthesis of triazole-fused isoindolines, obtained in fair yields employing the 2-iodobenzylazide and various terminal alkynes, in a one-pot Pd-catalyzed coupling reaction and cycloaddition.[11l] Our procedure is completely different and, as reported in Table 1, the novel compounds **4** and the 1,2,3-triazole-fused isoindolines **6** were obtained in high yields. Moreover, the reactions can be performed both with 2-iodobenzylazide **1a** (entries 1, 4, and 6) and 2-bromobenzylazide **1b** (entries 2, 3, 5, and 7), and alkyl- (entries 1–3), aryl- (entries 4–6) and heteroaryl-acetylenes (entry 7) were used. With the same strategy we were able to perform the synthesis of functionalized 1,2,3-triazole-fused 5,6-dihydroisoquinolines,[11g] simply by employment of 2-(2-iodophenyl)ethylazide **2a** and
2-(2-bromophenyl)ethyl azide **2b**. We wish to emphasize that the isoquinoline derivatives are an important class of alkaloids and many biologically active natural products contain the isoquinoline framework[18] and their biological activities have made them useful in pharmaceutical compounds.[19] The overall results are reported in Table 2. Also in this case we can use azide **2a** (entries 1, 2, 4, 5, and 7) or azide **2b** (entries 3 and 6) obtaining the novel intermediates **5** in high yields, substituted in position 4 by alkyl- (entries 1–3), or aryl- (entries 4–6), or 3-thienyl-group (entry 7). The intramolecular direct Pd-catalyzed C–H arylation of novel compounds **5** led to 1,2,3-triazole-fused 5,6-dihydroisoquinolines **7** in high yields.

In summary, the procedure described here appears to be a useful route to 1,2,3-triazole-fused heterocycles **6** and **7** and compares favorably with other methodologies. We have shown that the title compounds can be easily synthesized by simple cycloaddition reactions, via click chemistry, followed by an intramolecular direct transition metal-catalyzed C–H arylation.

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, CD_2Cl_2 or acetone-d_6 on a Varian Inova at 400 MHz. ^{13}C NMR spectra were recorded in deuterochloroform, CD_2Cl_2 or acetone-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. NMP was used as supplied.

3.2. General procedure for the synthesis of compounds 4 and 5

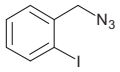
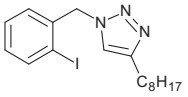
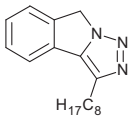
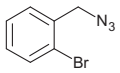
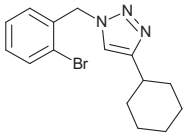
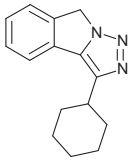
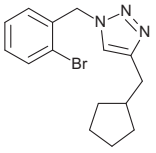
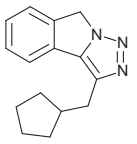
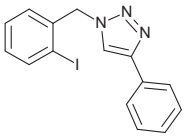
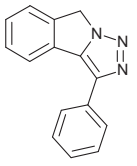
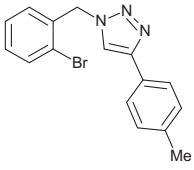
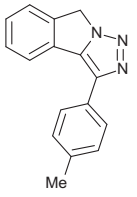
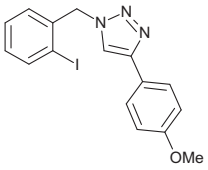
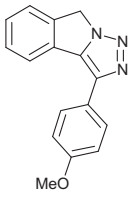
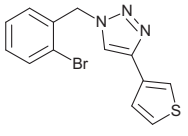
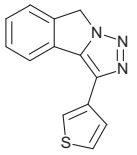
Alkyne **3** (1.2 equiv) and azide (1 equiv) were added at room temperature to a solution (0.04 M) of $Cu(OAc)_2\cdot H_2O$ (0.2 equiv) in H_2O in a capped flask. The mixture was stirred at 100 °C and, after reaction completion (1–4 h), was quenched with a saturated aqueous solution of NH_4Cl (20 mL) and extracted with ethyl acetate (3×30 mL). The organic extracts were washed with an aqueous solution of NaCl (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.

*3.2.1. 1-(2-Iodobenzyl)-4-octyl-1H-1,2,3-triazole (**4a**).* Compound **4a** was prepared from 2-iodobenzylazide (0.400 g, 1.54 mmol) and 1-decyne (0.256 g, 1.85 mmol) and the reaction was performed at 100 °C in accordance with general procedure. Purification by column chromatography (silica gel, 30% ethyl acetate/petroleum ether) afforded 0.446 g of compound **4a** (73% yield). After crystallization from ethyl acetate/petroleum ether, compound **4a** was obtained as a white solid, mp=96–98 °C. [Found: C, 47.42; H, 5.13; N, 11.90. $C_{14}H_{18}IN_3$ requires C, 47.34; H, 5.11; N, 11.83%.] ν_{max} (KBr) 3108, 3057, 2949, 2919, 2849, 1463, 1458, 1436, 1219, 1054, 1012, 750, 742; δ_H (400 MHz, $CDCl_3$) 7.88–7.84 (m, 1H), 7.30 (td, J=7.6, 1.2 Hz, 1H), 7.26 (s, 1H), 7.04–6.98 (m, 2H), 5.55 (s, 2H), 2.68 (t, J=7.6 Hz, 2H), 1.62 (quintet, J=7.6 Hz, 2H), 1.36–1.17 (m, 10H), 0.84 (t, J=7.0 Hz, 3H); δ_C (100.6 MHz, $CDCl_3$) 148.9, 139.7, 137.6, 130.2, 129.4, 129.0, 120.9, 98.4, 58.2, 31.8, 29.4, 29.3, 29.2, 29.2, 25.7, 22.6, 14.1; MS m/z 397 (M^+, 3), 299 (7), 270 (5), 217 (100), 186 (5), 152 (6), 90 (34), 69 (7), 55 (11), 43 (9), 41 (18%).

*3.2.2. 1-(2-Bromobenzyl)-4-cyclohexyl-1H-1,2,3-triazole (**4b**).* Compound **4b** was prepared from 2-bromobenzylazide (0.199 g, 0.94 mmol) and cyclohexylacetylene (0.122 g, 1.13 mmol) and the reaction was performed at 100 °C in accordance with general procedure. Purification by percolation (florisil, 50% ethyl acetate/petroleum ether) afforded 0.283 g of compound **4b** (94% yield). After crystallization from ethyl acetate/petroleum ether, compound **4b** was obtained as a white solid, mp=120–121 °C. [Found: C, 56.35; H, 5.70; N, 13.15. $C_{15}H_{18}BrN_3$ requires C, 56.26; H, 5.67; N, 13.12%.] ν_{max} (KBr) 3109, 3057, 2919, 2849, 1448, 1209, 1044, 1026, 759, 744; δ_H (400 MHz, $CDCl_3$) 7.58 (dd, J=7.6, 1.2 Hz, 1H), 7.30–7.24 (m, 2H), 7.18 (td, J=7.6, 1.6 Hz, 1H), 7.05 (dd, J=7.6, 1.6 Hz, 1H), 5.59 (s, 2H), 2.77–2.68 (m, 1H), 2.06–1.98 (m, 2H), 1.80–1.64 (m, 3H), 1.42–1.14 (m, 5H); δ_C (100.6 MHz, $CDCl_3$) 154.1, 134.6, 133.0, 130.1, 130.0, 128.1, 123.2, 119.5, 53.5, 35.3, 32.9, 26.1, 26.0; MS m/z 321 (M+2, 3), 319 (M^+, 3), 265 (4), 263 (4), 184 (7), 171 (79), 169 (100), 122 (31), 95 (14), 90 (46), 89 (36), 80 (18), 67 (21), 63 (13), 55 (16), 53 (14), 51 (12%).

*3.2.3. 1-(2-Bromobenzyl)-4-(cyclopentylmethyl)-1H-1,2,3-triazole (**4c**).* Compound **4c** was prepared from 2-bromobenzylazide (0.199 g, 0.94 mmol) and 3-cyclopentyl-1-propyne (0.123 g, 1.13 mmol) and the reaction was performed at 100 °C in accordance with general procedure. Purification by column chromatography (silica gel, 50% ethyl acetate/petroleum ether) afforded 0.283 g of compound **4c** (94% yield). After crystallization from petroleum ether, compound **4c** was obtained as a white solid, mp=62–63 °C.

Table 1
Synthesis of 1,2,3-triazoles **4** and 1,2,3-triazole-fused isoindolines **6**

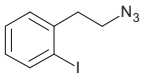
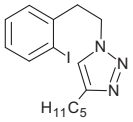
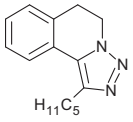
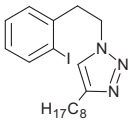
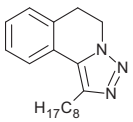
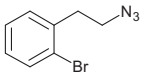
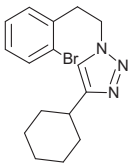
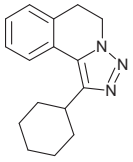
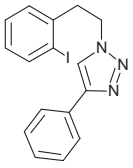
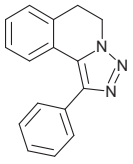
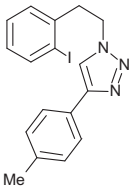
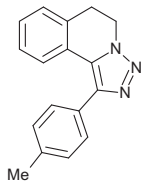
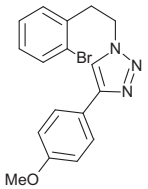
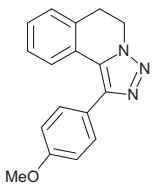
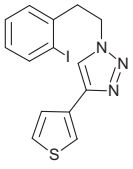
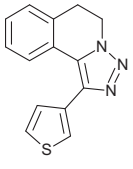
Entry	Azides **1**	Alkynes **3**	Products **4**[a], yield[b] (%)	Products **6**[c], yield[b] (%)
1	 **1a**	1-Decyne	 **4a** (73)	 **6a** (77)
2	 **1b**	Cyclohexylacetylene	 **4b** (94)	 **6b** (95)
3	**1b**	3-Cyclopentyl-1-propyne	 **4c** (94)	 **6c** (87)
4	**1a**	Phenylacetylene	 **4d** (77)	 **6d** (68)
5	**1b**	*p*-Tolylacetylene	 **4e** (95)	 **6e** (87)
6	**1a**	*p*-Methoxyphenylacetylene	 **4f** (90)	 **6f** (98)
7	**1b**	3-Ethynyltiophene	 **4g** (96)	 **6g** (95)

[a] All reactions were carried out in H_2O in a capped flask at 100 °C, according to a general procedure.
[b] Yields of purified isolated products.
[c] All reactions were carried out in NMP at 100 °C, according to a general procedure.

[Found: C, 56.30; H, 5.73; N, 13.20. $C_{15}H_{18}BrN_3$ requires C, 56.26; H, 5.67; N, 13.12%.] ν_{max} (KBr) 3115, 3063, 2936, 2862, 1439, 1212, 1141, 1046, 1031, 751, 739; δ_H (400 MHz, $CDCl_3$) 7.58 (dd, J=7.6, 1.2 Hz, 1H), 7.30–7.23 (m, 2H), 7.18 (td, J=7.6, 1.6 Hz, 1H), 7.04 (dd, J=7.6, 1.6 Hz, 1H), 5.59 (s, 2H), 2.68 (d, J=7.6 Hz, 2H), 2.14 (septet, J=7.6 Hz, 1H), 1.76–1.65 (m, 2H), 1.64–1.42 (m, 4H), 1.25–1.10 (m, 2H); δ_C (100.6 MHz, $CDCl_3$) 148.3, 134.6, 133.1, 130.1, 129.9, 128.1, 123.2, 121.2, 53.5, 39.9, 32.4, 31.7, 25.1; MS m/z 253 (8), 251 (8), 171 (79), 169 (100), 144 (11), 122 (13), 95 (15), 90 (39), 89 (31), 80 (11), 79 (11), 67 (14), 54 (11), 41 (61%).

*3.2.4. 1-(2-Iodobenzyl)-4-phenyl-1H-1,2,3-triazole (**4d**).* Compound **4d** was prepared from 2-iodobenzylazide (0.300 g, 1.16 mmol) and phenylacetylene (0.142 g, 1.39 mmol) and the reaction was performed at 100 °C in accordance with general procedure. Purification by column chromatography (silica gel, 30% ethyl acetate/

Table 2
Synthesis of 1,2,3-triazoles **5** and 1,2,3-triazole-fused 5,6-dihydroisoquinolines **7**

Entry	Azides **2**	Alkynes **3**	Product **5**[a], yield[b] (%)	Product **7**[c], yield[b] (%)
1	 **2a**	1-Heptyne	 **5a** (86)	 **7a** (94)
2	**2a**	1-Decyne	 **5b** (84)	 **7b** (91)
3	 **2b**	Cyclohexylacetylene	 **5c** (71)	 **7c** (87)
4	**2a**	Phenylacetylene	 **5d** (97)	 **7d** (82)
5	**2a**	*p*-Tolylacetylene	 **5e** (84)	 **7e** (83)
6	**2b**	*p*-Methoxyphenylacetylene	 **5f** (99)	 **7f** (74)
7	**2a**	3-Ethynylthiophene	 **5g** (97)	 **7g** (87)

[a] All reactions were carried out in H_2O in a capped flask at 100 °C, according to a general procedure.
[b] Yields of purified isolated products.
[c] All reactions were carried out in NMP at 100 °C, according to a general procedure.

petroleum ether) afforded 0.322 g of compound **4d** (77% yield). After crystallization from ethyl acetate/petroleum ether, compound **4d** was obtained as a pale yellow solid, mp=115–117 °C. [Found: C, 49.95; H, 3.38; N, 11.70. $C_{15}H_{12}IN_3$ requires C, 49.88; H, 3.35; N, 11.63%.] ν_{max} (KBr) 3112, 3076, 3028, 1459, 1437, 1419, 1228, 1090, 1051, 1015, 764, 742, 694; δ_H (400 MHz, $CDCl_3$) 7.89 (dd, J=7.6, 1.2 Hz, 1H), 7.83–7.78 (m, 2H), 7.75 (s, 1H), 7.42–7.37 (m, 2H), 7.36–7.28 (m, 2H), 7.12 (dd, J=7.6, 1.6 Hz, 1H), 7.04 (td, J=7.6, 1.6 Hz, 1H), 5.65 (s, 2H); δ_C (100.6 MHz, $CDCl_3$) 148.1, 139.9, 137.3, 130.4, 130.4, 129.6, 129.1, 128.8, 128.2, 125.7, 119.8, 98.6, 58.4; MS *m*/*z* 361

(M^+, 6), 332 (4), 217 (36), 206 (53), 178 (6), 128 (10), 116 (100), 102 (35), 90 (54), 89 (62), 77 (13), 63 (24), 51 (17%).

*3.2.5. 1-(2-Bromobenzyl)-4-(4-methylphenyl)-1H-1,2,3-triazole (**4e**).* Compound **4e** was prepared from 2-bromobenzylazide (0.199 g, 0.94 mmol) and 4-ethynyltoluene (0.131 g, 1.13 mmol) and the reaction was performed at 100 °C in accordance with general procedure. Purification by column chromatography (silica gel, 40% ethyl acetate/petroleum ether) afforded 0. 293 g of compound **4e** (95% yield). After crystallization from ethyl acetate/petroleum ether, compound **4e** was obtained as a white solid, mp=133–134 °C. [Found: C, 58.50; H, 4.28; N, 12.75. $C_{16}H_{14}BrN_3$ requires C, 58.55; H, 4.30; N, 12.80%.] ν_{max} (KBr) 3126, 3105, 2925, 1458, 1442, 1427, 1350, 1222, 1046, 1026, 820, 748; δ_H (400 MHz, $CDCl_3$) 7.72 (s, 1H), 7.71–7.67 (m, 2H), 7.60 (dd, *J*=7.6, 1.2 Hz, 1H), 7.29 (td, *J*=7.6, 1.2 Hz, 1H), 7.23–7.18 (m, 3H), 7.17–7.13 (m, 1H), 5.67 (s, 2H), 2.35 (s, 3H); δ_C (100.6 MHz, $CDCl_3$) 148.2, 138.0, 134.3, 133.1, 130.3, 130.2, 129.5, 128.2, 127.6, 125.6, 123.3, 119.4, 53.8, 21.2; MS *m*/*z* 329 (M+2, 3), 327 (M^+, 3), 300 (3), 298 (3), 220 (31), 171 (18), 169 (22), 130 (100), 110 (10), 103 (19), 90 (22), 89 (21), 77 (21), 63 (11), 51 (13%).

*3.2.6. 1-(2-Iodobenzyl)-4-(4-methoxyphenyl)-1H-1,2,3-triazole (**4f**).* Compound **4f** was prepared from 2-iodobenzylazide (0.300 g, 1.16 mmol) and *p*-methoxyphenylacetylene (0.184 g, 1.39 mmol) and the reaction was performed at 100 °C in accordance with general procedure. Purification by column chromatography (silica gel, 40% ethyl acetate/petroleum ether) afforded 0.408 g of compound **4f** (90% yield). After crystallization from ethyl acetate/petroleum ether, compound **4f** was obtained as a pale yellow solid, mp=140–141 °C. [Found: C, 49.08; H, 3.58; N, 10.75. $C_{16}H_{14}IN_3O$ requires C, 49.12; H, 3.61; N, 10.74%.] ν_{max} (KBr) 3125, 3102, 2925, 1498, 1458, 1438, 1246, 1222, 1174, 1028, 1012, 830, 750; δ_H (400 MHz, CDCl3) 7.88 (dd, *J*=7.7, 1.2 Hz, 1H), 7.75–7.70 (m, 2H), 7.67 (s, 1H), 7.31 (td, *J*=7.7, 1.2 Hz, 1H), 7.09 (dd, *J*=7.7, 1.6 Hz, 1H), 7.03 (td, *J*=7.7, 1.6 Hz, 1H), 6.94–6.89 (m, 2H), 5.62 (s, 2H), 3.81 (s, 3H); δ_C (100.6 MHz, CDCl3) 159.6, 148.0, 139.8, 137.4, 130.3, 129.5, 129.0, 127.0, 123.1, 119.0, 114.2, 98.5, 58.4, 55.3; MS *m*/*z* 391 (M+, 18), 236 (74), 221 (18), 217 (21), 193 (19), 165 (12), 146 (100), 128 (9), 119 (34), 103 (21), 90 (64), 89 (62), 76 (30), 65 (21), 63 (30), 51 (26), 50 (25%).

*3.2.7. 1-(2-Bromobenzyl)-4-(thiophen-3-yl)-1H-1,2,3-triazole (**4g**).* Compound **4g** was prepared from 2-bromobenzylazide (0.199 g, 0.94 mmol) and 3-ethynylthiophene (0.122 g, 1.13 mmol) and the reaction was performed at 100 °C in accordance with general procedure. Purification by column chromatography (silica gel, 40% ethyl acetate/petroleum ether) afforded 0.289 g of compound **4g** (96% yield). After crystallization from ethyl acetate/petroleum ether, compound **4g** was obtained as an ivory-white solid, mp=99–100 °C. [Found: C, 48.91; H, 3.22; N, 13.15; S, 10.05. $C_{13}H_{10}BrN_3S$ requires C, 48.76; H, 3.15; N, 13.12; S, 10.01%.] ν_{max} (KBr) 3123, 3094, 2923, 1436, 1216, 1044, 1029, 850, 824, 784, 739, 711, 615; δ_H (400 MHz, $CDCl_3$) 7.66 (s, 1H), 7.65 (dd, *J*=3.0, 1.2 Hz, 1H), 7.61 (dd, *J*=7.6, 1.2 Hz, 1H), 7.41 (dd, *J*=5.0, 1.2 Hz, 1H), 7.34 (dd, *J*=5.0, 3.0 Hz, 1H), 7.28 (td, *J*=7.6, 1.2 Hz, 1H), 7.21 (td, *J*=7.6, 2.0 Hz, 1H), 7.14 (dd, *J*=7.6, 2.0 Hz, 1H), 5.67 (s, 2H); δ_C (100.6 MHz, $CDCl_3$) 144.3, 134.2, 133.1, 131.6, 130.3, 130.1, 128.2, 126.3, 125.7, 123.3, 121.1, 119.6, 53.7; MS *m*/*z* 321 (M+2, 4), 319 (M^+, 4), 292 (3), 290 (3), 212 (44), 184 (6), 171 (21), 169 (24), 122 (100), 106 (14), 95 (16), 90 (36), 89 (29), 63 (16), 51 (13), 45 (79%).

*3.2.8. 1-[2-(2-Iodophenyl)ethyl]-4-pentyl-1H-1,2,3-triazole (**5a**).* Compound **5a** was prepared from 2-iodophenylethylazide (0.150 g, 0.55 mmol) and 1-heptyne (0.064 g, 0.66 mmol) and the reaction was performed at 100 °C in accordance with general procedure. Purification by column chromatography (silica gel, 30% ethyl acetate/petroleum ether) afforded 0.175 g of compound **5a** (86% yield) as a pale yellow oil. [Found: C, 48.70; H, 5.51; N, 11.49. $C_{15}H_{20}IN_3$ requires C, 48.79; H, 5.46; N, 11.38%.] ν_{max} (neat) 3131, 3063, 2953, 2927, 2856, 1466, 1459, 1436, 1217, 1048, 1013, 750; δ_H (400 MHz, $CDCl_3$) 7.80 (dd, *J*=7.7, 1.2 Hz, 1H), 7.17 (td, *J*=7.7, 1.2 Hz, 1H), 7.00 (s, 1H), 6.95 (dd, *J*=7.7, 1.6 Hz, 1H), 6.89 (td, *J*=7.7, 1.6 Hz, 1H), 4.50 (t, *J*=7.4 Hz, 2H), 3.27 (t, *J*=7.4 Hz, 2H), 2.62 (t, *J*=7.6 Hz, 2H), 1.57 (quintet, *J*=7.6 Hz, 2H), 1.35–1.18 (m, 4H), 0.84 (t, *J*=7.0 Hz, 3H); δ_C (100.6 MHz, $CDCl_3$) 148.1, 139.6, 139.6, 130.2, 128.9, 128.6, 120.9, 100.1, 49.5, 41.5, 31.2, 29.1, 25.5, 22.3, 13.9; MS *m*/*z* 242 (100), 231 (42), 217 (9), 170 (4), 158 (5), 124 (17), 117 (9), 104 (98), 95 (20), 90 (21), 77 (35), 68 (23), 55 (39), 41 (86%).

*3.2.9. 1-[2-(2-Iodophenyl)ethyl]-4-octyl-1H-1,2,3-triazole (**5b**).* Compound **5b** was prepared from 2-iodophenylethylazide (0.300 g, 1.10 mmol) and 1-decyne (0.183 g, 1.32 mmol) and the reaction was performed at 100 °C in accordance with general procedure. Purification by column chromatography (silica gel, 30% ethyl acetate/petroleum ether) afforded 0.380 g of compound **5b** (84% yield). After crystallization from petroleum ether, compound **5b** was obtained as a white solid, mp=49–51 °C. [Found: C, 50.72; H, 5.88; N, 10.70. $C_{18}H_{2.6}IN_3$ requires C, 50.78; H, 5.94; N, 10.77%.] ν_{max} (KBr) 3125, 3060, 2923, 2848, 1466, 1454, 1438, 1208, 1054, 1014, 752; δ_H (400 MHz, $CDCl_3$) 7.81 (dd, *J*=7.6, 1.2 Hz, 1H), 7.18 (td, *J*=7.6, 1.2 Hz, 1H), 7.01 (s, 1H), 6.96 (dd, *J*=7.6, 1.6 Hz, 1H), 6.91 (td, *J*=7.6, 1.6 Hz, 1H), 4.52 (t, *J*=7.2 Hz, 2H), 3.28 (t, *J*=7.2 Hz, 2H), 2.63 (t, *J*=7.6 Hz, 2H), 1.57 (quintet, *J*=7.6 Hz, 2H), 1.32–1.17 (m, 10H), 0.85 (t, *J*=7.0 Hz, 3H); δ_C (100.6 MHz, $CDCl_3$) 148.2, 139.7, 139.7, 130.3, 128.9, 128.6, 121.0, 100.1, 49.5, 41.6, 31.8, 29.5, 29.3, 29.2, 29.1, 25.5, 22.6, 14.1; MS *m*/*z* 313 (4), 284 (100), 231 (60), 217 (11), 166 (10), 110 (32), 104 (98), 103 (23), 96 (20), 82 (15), 77 (26), 68 (21), 67 (17), 55 (30), 41 (77%).

*3.2.10. 1-[2-(2-Bromophenyl)ethyl]-4-cyclohexyl-1H-1,2,3-triazole (**5c**).* Compound **5c** was prepared from 2-bromophenylethylazide (0.149 g, 0.66 mmol) and cyclohexylacetylene (0.086 g, 0.79 mmol) and the reaction was performed at 100 °C in accordance with general procedure. Purification by column chromatography (silica gel, 30% ethyl acetate/petroleum ether) afforded 0.157 g of compound **5c** (71% yield). After crystallization from ethyl acetate/petroleum ether, compound **5c** was obtained as a white solid, mp=81–82 °C. [Found: C, 57.53; H, 6.10; N, 12.65. $C_{16}H_{20}BrN_3$ requires C, 57.49; H, 6.03; N, 12.57%.] ν_{max} (KBr) 3109, 3062, 2917, 2849, 1460, 1447, 1434, 1215, 1058, 1039, 1024, 752; δ_H (400 MHz, $CDCl_3$) 7.53 (dd, *J*=7.6, 1.2 Hz, 1H), 7.16 (td, *J*=7.6, 1.2 Hz, 1H), 7.08 (td, *J*=7.6, 1.6 Hz, 1H), 6.98–6.92 (m, 2H), 4.54 (t, *J*=7.2 Hz, 2H), 3.29 (t, *J*=7.2 Hz, 2H), 2.74–2.65 (m, 1H), 2.00–1.90 (m, 2H), 1.79–1.62 (m, 3H), 1.43–1.13 (m, 5H); δ_C (100.6 MHz, $CDCl_3$) 153.5, 136.5, 133.0, 131.2, 128.8, 127.7, 124.2, 119.7, 49.3, 37.3, 35.2, 33.0, 26.1, 26.0; MS *m*/*z* 254 (78), 226 (8), 185 (29), 183 (30), 169 (9), 136 (63), 109 (33), 104 (73), 91 (25), 80 (38), 79 (38), 77 (56), 67 (64), 55 (29), 41 (100%).

*3.2.11. 1-[2-(2-Iodophenyl)ethyl]-4-phenyl-1H-1,2,3-triazole (**5d**).* Compound **5d** was prepared from 2-iodophenylethylazide (0.150 g, 0.55 mmol) and phenylacetylene (0.067 g, 0.66 mmol) and the reaction was performed at 100 °C in accordance with general procedure. Purification by column chromatography (silica gel, 30% ethyl acetate/petroleum ether) afforded 0.200 g of compound **5d** (97% yield). After crystallization from ethyl acetate/petroleum ether, compound **5d** was obtained as a white solid, mp=115–117 °C. [Found: C, 51.19; H, 3.80; N, 11.25. $C_{16}H_{14}IN_3$ requires C, 51.22; H, 3.76; N, 11.20%.] ν_{max} (KBr) 3116, 3089, 3055, 2958, 2930, 1466, 1436, 1221, 1076, 1015, 767, 751, 694; δ_H (400 MHz, $CDCl_3$) 7.85 (dd, *J*=7.6, 1.2 Hz, 1H), 7.78–7.73 (m, 2H), 7.51 (s, 1H), 7.42–7.36 (m, 2H), 7.33–7.28 (m, 1H), 7.21 (td, *J*=7.6, 1.2 Hz, 1H), 7.03 (dd, *J*=7.6, 1.8 Hz, 1H), 6.94 (td, *J*=7.6, 1.8 Hz, 1H), 4.62 (t, *J*=7.2 Hz, 2H), 3.37 (t, *J*=7.2 Hz, 2H); δ_C (100.6 MHz, $CDCl_3$) 147.3, 139.6, 139.3, 130.4, 130.1, 128.9, 128.6, 128.5, 127.9, 125.5, 119.9, 100.1, 49.7, 41.3; MS *m*/*z* 375

(M^+, 2), 248 (41), 231 (19), 220 (13), 142 (5), 130 (25), 117 (28), 104 (100), 89 (32), 77 (51), 63 (22), 51 (31%).

*3.2.12. 1-[2-(2-Iodophenyl)ethyl]-4-(4-methylphenyl)-1H-1,2,3-triazole (**5e**).* Compound **5e** was prepared from 2-iodophenylethylazide (0.200 g, 0.73 mmol) and 4-ethynyltoluene (0.102 g, 0.88 mmol) and the reaction was performed at 100 °C in accordance with general procedure. Purification by column chromatography (silica gel, 30% ethyl acetate/petroleum ether) afforded 0.239 g of compound **5e** (84% yield). After crystallization from ethyl acetate/petroleum ether, compound **5e** was obtained as a pale yellow solid, mp=118–120 °C. [Found: C, 52.53; H, 4.17; N, 10.85. $C_{17}H_{16}IN_3$ requires C, 52.46; H, 4.14; N, 10.80%.] ν_{max} (KBr) 3082, 3057, 2942, 1459, 1436, 1219, 1188, 1086, 1047, 1014, 814, 761, 744, 530; δ_H (400 MHz, $CDCl_3$) 7.83 (dd, *J*=7.6, 1.2 Hz, 1H), 7.67–7.62 (m, 2H), 7.48 (s, 1H), 7.23–7.16 (m, 3H), 7.02 (dd, *J*=7.6, 1.6 Hz, 1H), 6.92 (td, *J*=7.6, 1.6 Hz, 1H), 4.60 (t, *J*=7.4 Hz, 2H), 3.35 (t, *J*=7.4 Hz, 2H), 2.35 (s, 3H); δ_C (100.6 MHz, $CDCl_3$) 147.6, 139.7, 139.5, 137.9, 130.3, 129.4, 129.0, 128.7, 127.7, 125.5, 119.6, 100.1, 49.8, 41.5, 21.2; MS *m*/*z* 389 (M^+, 7), 262 (23), 234 (29), 231 (29), 144 (39), 130 (18), 117 (54), 115 (64), 104 (100), 91 (27), 90 (25), 89 (22), 77 (46), 65 (13), 63 (17), 51 (25%).

*3.2.13. 1-[2-(2-Bromophenyl)ethyl]-4-(4-methoxyphenyl)-1H-1,2,3-triazole (**5f**).* Compound **5f** was prepared from 2-bromophenylethylazide (0.149 g, 0.66 mmol) and 4-ethynylanisole (0.104 g, 0.79 mmol) and the reaction was performed at 100 °C in accordance with general procedure. Purification by column chromatography (silica gel, 30% ethyl acetate/petroleum ether) afforded 0.234 g of compound **5f** (99% yield). After crystallization from ethyl acetate/petroleum ether, compound **5f** was obtained as a white solid, mp=114–115 °C. [Found: C, 57.05; H, 4.45; N, 11.70. $C_{17}H_{16}BrN_3O$ requires C, 57.00; H, 4.50; N, 11.73%.] ν_{max} (KBr) 3088, 3044, 2952, 2932, 2834, 1502, 1472, 1443, 1435, 1248, 1081, 1026, 827, 758; δ_H (400 MHz, $CDCl_3$) 7.69–7.65 (m, 2H), 7.56 (dd, *J*=7.6, 1.2 Hz, 1H), 7.41 (s, 1H), 7.16 (td, *J*=7.6, 1.2 Hz, 1H), 7.09 (td, *J*=7.6, 1.8 Hz, 1H), 7.02 (dd, *J*=7.6, 1.8 Hz, 1H), 6.94–6.89 (m, 2H), 4.62 (t, *J*=7.2 Hz, 2H), 3.80 (s, 3H), 3.35 (t, *J*=7.2 Hz, 2H); δ_C (100.6 MHz, $CDCl_3$) 159.5, 147.4, 136.3, 133.0, 131.2, 128.9, 127.8, 126.9, 124.3, 123.3, 119.1, 114.2, 55.3, 49.6, 37.2; MS *m*/*z* 359 (M+2, 12), 357 (M^+, 13), 250 (32), 183 (15), 160 (74), 146 (29), 145 (27), 133 (100), 117 (60), 104 (82), 90 (40), 89 (68), 78 (22), 77 (80), 76 (23), 63 (36), 51 (40), 50 (24%).

*3.2.14. 1-[2-(2-Bromophenyl)ethyl]-4-(thiophen-3-yl)-1H-1,2,3-triazole (**5g**).* Compound **5g** was prepared from 2-iodophenylethylazide (0.200 g, 0.73 mmol) and 3-ethynylthiophene (0.095 g, 0.88 mmol) and the reaction was performed at 100 °C in accordance with general procedure. Purification by column chromatography (silica gel, 30% ethyl acetate/petroleum ether) afforded 0.270 g of compound **5g** (97% yield). After crystallization from ethyl acetate/petroleum ether, compound **5g** was obtained as a white solid, mp=92–94 °C. [Found: C, 50.35; H, 3.60; N, 12.62; S, 9.63. $C_{14}H_{12}BrN_3S$ requires C, 50.31; H, 3.62; N, 12.57; S, 9.59%.] ν_{max} (KBr) 3099, 3077, 2954, 2930, 1438, 1217, 1074, 1017, 853, 788, 754, 717, 624; δ_H (400 MHz, $CDCl_3$) 7.83 (dd, *J*=7.6, 1.2 Hz, 1H), 7.61 (dd, *J*=2.8, 1.2 Hz, 1H), 7.42 (s, 1H), 7.38 (dd, *J*=5.0, 1.2 Hz, 1H), 7.34 (dd, *J*=5.0, 2.8 Hz, 1H), 7.21 (td, *J*=7.6, 1.2 Hz, 1H), 7.02 (dd, *J*=7.6, 1.6 Hz, 1H), 6.93 (td, *J*=7.6, 1.6 Hz, 1H), 4.60 (t, *J*=7.4 Hz, 2H), 3.35 (t, *J*=7.4 Hz, 2H); δ_C (100.6 MHz, $CDCl_3$) 143.7, 139.7, 139.5, 131.8, 130.3, 129.1, 128.7, 126.2, 125.8, 121.0, 119.7, 100.1, 49.8, 41.5; MS *m*/*z* 381 (M^+, 8), 254 (35), 231 (16), 226 (17), 217 (7), 142 (15), 136 (56), 122 (23), 109 (67), 104 (100), 90 (32), 77 (53), 65 (24), 63 (25), 51 (33), 45 (90%).

3.3. General procedure for the synthesis of compounds 6 and 7

To a solution (0.1 N) of triazole (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 (1–5 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-Octyl-8H-[1,2,3]triazolo[5,1-a]isoindole (**6a**).* Compound **6a** was prepared from **4a** (0.151 g, 0.38 mmol) in accordance with general procedure. Purification by column chromatography (silica gel, 40% ethyl acetate/petroleum ether) afforded 0.079 g of compound **6a** (77% yield). After crystallization from petroleum ether, compound **6a** was obtained as a pale yellow solid, mp=79–80 °C. [Found: C, 75.87; H, 8.55; N, 15.70. $C_{17}H_{23}N_3$ requires C, 75.80; H, 8.61; N, 15.60%.] ν_{max} (KBr) 2947, 2914, 2850, 1474, 1458, 1437, 1310, 1166, 765, 726; δ_H (400 MHz, $CDCl_3$) 7.58 (br d, *J*=7.6 Hz, 1H), 7.49–7.41 (m, 2H), 7.35 (td, *J*=7.6, 1.2 Hz, 1H), 5.27 (s, 2H), 2.92 (t, *J*=7.6 Hz, 2H), 1.78 (quintet, *J*=7.6 Hz, 2H), 1.44–1.17 (m, 10H), 0.84 (t, *J*=6.8 Hz, 3H); δ_C (100.6 MHz, $CDCl_3$) 140.6, 139.3, 139.3, 128.7, 128.5, 127.6, 124.1, 120.8, 50.9, 31.8, 29.5, 29.3, 29.2, 29.2, 25.9, 22.6, 14.1; MS *m*/*z* 269 (M^+, 5), 240 (14), 198 (9), 184 (22), 170 (100), 156 (44), 144 (30), 143 (25), 131 (22), 130 (26), 129 (22), 128 (21), 115 (32), 89 (16), 77 (7), 63 (7), 51 (7), 43 (22), 41 (51%).

*3.3.2. 3-Cyclohexyl-8H-[1,2,3]triazolo[5,1-a]isoindole (**6b**).* Compound **6b** was prepared from **4b** (0.150 g, 0.47 mmol) in accordance with general procedure. Purification by column chromatography (silica gel, 50% ethyl acetate/petroleum ether) afforded 0.107 g of compound **6b** (95% yield). After crystallization from ethyl acetate/petroleum ether, compound **6b** was obtained as a pale brown solid, mp=124–125 °C. [Found: C, 75.30; H, 7.20; N, 17.63. $C_{15}H_{17}N_3$ requires C, 75.28; H, 7.16; N, 17.56%.] ν_{max} (KBr) 3072, 2919, 2849, 1448, 1421, 1340, 1258, 1156, 994, 773, 754, 729; δ_H (400 MHz, CD_2Cl_2) 7.69 (d, *J*=8.0 Hz, 1H), 7.53–7.43 (m, 2H), 7.38 (td, *J*=7.6, 1.2 Hz, 1H), 5.27 (s, 2H), 3.00 (tt, *J*=12.0, 3.6 Hz, 1H), 2.08–2.00 (m, 2H), 1.94–1.85 (m, 2H), 1.84–1.65 (m, 3H), 1.55–1.31 (m, 3H); δ_C (100.6 MHz, CD_2Cl_2) 144.4, 141.1, 138.5, 128.7, 128.6, 127.5, 124.2, 121.4, 50.9, 36.3, 32.8, 26.5, 26.1; MS *m*/*z* 239 (M^+, 8), 210 (64), 196 (15), 182 (100), 168 (36), 156 (13), 144 (15), 130 (22), 117 (15), 115 (13), 89 (19), 77 (19), 63 (14), 51 (15), 41 (33%).

*3.3.3. 3-(Cyclopentylmethyl)-8H-[1,2,3]triazolo[5,1-a]isoindole (**6c**).* Compound **6c** was prepared from **4c** (0.150 g, 0.47 mmol) in accordance with general procedure. Purification by column chromatography (silica gel, 40% ethyl acetate/petroleum ether) afforded 0.098 g of compound **6c** (87% yield). After crystallization from ethyl acetate/petroleum ether, compound **6c** was obtained as a pale brown solid, mp=104–105 °C. [Found: C, 75.32; H, 7.21; N, 17.60. $C_{15}H_{17}N_3$ requires C, 75.28; H, 7.16; N, 17.56%.] ν_{max} (KBr) 2941, 2919, 2855, 1447, 1261, 1169, 1093, 1025, 798, 771, 744, 722; δ_H (400 MHz, $CDCl_3$) 7.59 (br d, *J*=7.6 Hz, 1H), 7.50–7.41 (m, 2H), 7.35 (td, *J*=7.6, 1.2 Hz, 1H), 5.28 (s, 2H), 2.92 (d, *J*=7.6 Hz, 2H), 2.35 (septet, *J*=7.6 Hz, 1H), 1.82–1.72 (m, 2H), 1.70–1.59 (m, 2H), 1.58–1.48 (m, 2H), 1.36–1.22 (m, 2H); δ_C (100.6 MHz, $CDCl_3$) 140.7, 139.5, 138.8, 128.7, 128.6, 127.6, 124.1, 120.8, 50.9, 40.5, 32.3, 31.7, 25.0; MS *m*/*z* 239 (M^+, 17), 210 (58), 196 (13), 182 (81), 168 (63), 144 (25), 143 (34), 142 (42), 130 (49), 115 (56), 89 (33), 77 (15), 63 (19) 51 (18), 41 (100%).

*3.3.4. 3-Phenyl-8H-[1,2,3]triazolo[5,1-a]isoindole (**6d**)*[111]. Compound **6d** was prepared from **4d** (0.152 g, 0.42 mmol) in accordance with general procedure. Purification by column chromatography (silica gel, 40% ethyl acetate/petroleum ether) afforded 0.067 g of compound **6d** (68% yield). After crystallization from ethyl acetate/petroleum ether, compound **6d** was obtained as a pale brown solid, mp=153–155 °C. [Found: C, 77.30; H, 4.80; N, 17.93. $C_{15}H_{11}N_3$

requires C, 77.23; H, 4.75; N, 18.01%.] ν_{max} (KBr) 3058, 3034, 2964, 2922, 2850, 1609, 1448, 1359, 985, 760, 699, 668; δ_H (400 MHz, $CDCl_3$) 7.95–7.90 (m, 2H), 7.88 (br d, J=7.2 Hz, 1H), 7.54–7.37 (m, 6H), 5.35 (s, 2H); δ_C (100.6 MHz, $CDCl_3$) 141.1, 139.3, 139.0, 131.2, 128.9, 128.8, 128.4, 128.1, 128.1, 126.9, 124.2, 121.3, 50.9; MS m/z 233 (M^+, 7), 205 (54), 204 (100), 190 (14), 176 (20), 151 (11), 102 (68), 89 (39), 88 (39), 76 (44), 63 (25), 51 (25), 50 (19%).

*3.3.5. 3-(4-Methylphenyl)-8H-[1,2,3]triazolo[5,1-a]isoindole (**6e**).* Compound **6e** was prepared from **4e** (0.148 g, 0.45 mmol) in accordance with general procedure. Purification by column chromatography (silica gel, 40% ethyl acetate/petroleum ether) afforded 0.098 g of compound **6e** (87% yield). After crystallization from ethyl acetate/petroleum ether, compound **6e** was obtained as a white solid, mp=160–162 °C. [Found: C, 77.80; H, 5.35; N, 17.03. $C_{16}H_{13}N_3$ requires C, 77.71; H, 5.30; N, 16.99%.] ν_{max} (KBr) 3067, 3024, 2963, 2918, 2853, 1437, 1413, 1354, 1176, 1128, 984, 829, 810, 764, 714; δ_H (400 MHz, acetone-d_6) 7.95 (d, J=7.2 Hz, 1H), 7.88–7.83 (m, 2H), 7.72–7.68 (m, 1H), 7.55–7.49 (m, 1H), 7.47 (td, J=7.6, 1.2 Hz, 1H), 7.39–7.34 (m, 2H), 5.50 (s, 2H), 2.40 (s, 3H); δ_C (100.6 MHz, acetone-d_6) 144.1, 140.4, 140.2, 139.5, 131.4, 130.9, 130.4, 130.1, 129.9, 128.5, 126.5, 122.8, 52.6, 22.3; MS m/z 247 (M^+, 14), 219 (89), 218 (100), 204 (88), 203 (38), 189 (18), 176 (15), 166 (10), 116 (10), 109 (39), 102 (37), 95 (42), 94 (33), 89 (21), 82 (46), 76 (26), 63 (26), 51 (30), 50 (22%).

*3.3.6. 3-(4-Methoxyphenyl)-8H-[1,2,3]triazolo[5,1-a]isoindole (**6f**).* Compound **6f** was prepared from **4f** (0.149 g, 0.38 mmol) in accordance with general procedure. Purification by column chromatography (silica gel, 40% petroleum ether/ethyl acetate) afforded 0.098 g of compound **6f** (98% yield). After crystallization from ethyl acetate/petroleum ether, compound **6f** was obtained as a white solid, mp=154–156 °C. [Found: C, 72.85; H, 5.02; N, 16.03. $C_{16}H_{13}N_3O$ requires C, 72.99; H, 4.98; N, 15.96%.] ν_{max} (KBr) 3064, 2961, 2922, 2850, 1615, 1508, 1454, 1420, 1356, 1298, 1246, 1174, 1100, 1031, 825, 803, 768; δ_H (400 MHz, acetone-d_6) 7.93–7.86 (m, 3H), 7.69–7.65 (m, 1H), 7.52–7.47 (m, 1H), 7.44 (td, J=7.6, 1.2 Hz, 1H), 7.13–7.07 (m, 2H), 5.47 (s, 2H), 3.87 (s, 3H); δ_C (100.6 MHz, acetone-d_6) 161.5, 144.0, 140.2, 139.8, 130.3, 130.0, 129.9, 129.9, 126.4, 126.1, 122.6, 116.2, 56.6, 52.6.

*3.3.7. 3-(Thiophen-3-yl)-8H-[1,2,3]triazolo[5,1-a]isoindole (**6g**).* Compound **6g** was prepared from **4g** (0.150 g, 0.47 mmol) in accordance with general procedure. Purification by column chromatography (silica gel, 40% ethyl acetate/petroleum ether) afforded 0.107 g of compound **6g** (95% yield). After crystallization from ethyl acetate/petroleum ether, compound **6g** was obtained as a green solid, mp=178–180 °C. [Found: C, 65.32; H, 3.85; N, 17.60; S, 13.35. $C_{13}H_9N_3S$ requires C, 65.25; H, 3.79; N, 17.56; S, 13.40%.] ν_{max} (KBr) 3101, 2963, 2924, 2848, 1420, 1402, 1319, 1171, 1121, 1070, 867, 856, 793, 773, 730, 708; δ_H (400 MHz, $CDCl_3$) 7.85 (br d, J=7.6 Hz, 1H), 7.74 (dd, J=2.8, 1.2 Hz, 1H), 7.64 (dd, J=4.8, 1.2 Hz, 1H) 7.53–7.49 (m, 1H), 7.49–7.43 (m, 2H), 7.40 (td, J=7.6, 1.2 Hz, 1H), 5.33 (s, 2H); δ_C (100.6 MHz, $CDCl_3$) 140.9, 138.4, 135.0, 132.0, 128.7, 128.2, 127.8, 126.5, 126.3, 124.1, 122.0, 121.0, 50.9; MS m/z 239 (M^+, 12), 211 (99), 210 (100), 184 (27), 166 (19), 152 (10), 139 (29), 105 (14), 102 (17), 92 (61), 79 (22), 63 (25), 51 (22), 45 (60%).

*3.3.8. 1-Pentyl-5,6-dihydro[1,2,3]triazolo[5,1-a]isoquinoline (**7a**).* Compound **7a** was prepared from **5a** (0.173 g, 0.47 mmol) in accordance with general procedure. Purification by column chromatography (silica gel, 50% ethyl acetate/petroleum ether) afforded 0.107 g of compound **7a** (94% yield) as a pale yellow oil. [Found: C, 74.67; H, 7.87; N, 17.50. $C_{15}H_{19}N_3$ requires C, 74.65; H, 7.94; N, 17.41%.] ν_{max} (neat) 2953, 2923, 2857, 1476, 1466, 1456, 1373, 1351, 1338, 1306, 1196, 768, 740, 731, 682; δ_H (400 MHz, $CDCl_3$) 7.58 (d, J=7.6, 1H), 7.38–7.25 (m, 3H), 4.52 (t, J=6.8 Hz, 2H), 3.17 (t, J=6.8 Hz, 2H), 2.94 (t, J=7.6 Hz, 2H), 1.78 (quintet, J=7.6 Hz, 2H), 1.46–1.30 (m, 4H), 0.88 (t, J=7.0 Hz, 3H); δ_C (100.6 MHz, $CDCl_3$) 143.5, 132.4, 128.8, 128.5, 128.4, 127.7, 125.6, 124.0, 44.7, 31.7, 29.3, 28.6, 26.5, 22.4, 14.0; MS m/z 241 (M^+, 16), 212 (23), 198 (25), 185 (100), 184 (59), 170 (47), 156 (45), 143 (20), 130 (35), 129 (48), 128 (53), 127 (21), 115 (57), 103 (20), 91 (10), 89 (10), 77 (34), 63 (12), 51 (23), 41 (41%).

*3.3.9. 1-Octyl-5,6-dihydro[1,2,3]triazolo[5,1-a]isoquinoline (**7b**).* Compound **7b** was prepared from **5b** (0.189 g, 0.46 mmol) in accordance with general procedure. Purification by column chromatography (silica gel, 50% ethyl acetate/petroleum ether) afforded 0.118 g of compound **7b** (91% yield) as a pale yellow oil. [Found: C, 76.27; H, 8.87; N, 17.50. $C_{18}H_{25}N_3$ requires C, 76.28; H, 8.89; N, 17.63%.] ν_{max} (neat) 2923, 2854, 1476, 1466, 1439, 1371, 1190, 767, 739, 729, 682; δ_H (400 MHz, $CDCl_3$) 7.57 (d, J=7.6, 1H), 7.37–7.24 (m, 3H), 4.51 (t, J=6.8 Hz, 2H), 3.16 (t, J=6.8 Hz, 2H), 2.93 (t, J=8.0 Hz, 2H), 1.76 (quintet, J=8.0 Hz, 2H), 1.47–1.37 (m, 2H), 1.36–1.16 (m, 8H), 0.84 (t, J=7.0 Hz, 3H); δ_C (100.6 MHz, $CDCl_3$) 143.4, 132.4, 128.8, 128.5, 128.4, 127.7, 125.6, 124.0, 44.7, 31.8, 29.4, 29.3, 29.2, 29.1, 28.9, 26.5, 22.6, 14.0; MS m/z 283 (M^+, 14), 254 (18), 240 (10), 212 (10), 198 (39), 185 (100), 184 (60), 170 (42), 156 (35), 143 (16), 130 (27), 129 (29), 128 (33), 115 (35), 103 (14), 77 (14), 55 (8), 51 (8), 41 (39%).

*3.3.10. 1-Cyclohexyl-5,6-dihydro[1,2,3]triazolo[5,1-a]isoquinoline (**7c**).* Compound **7c** was prepared from **5c** (0.130 g, 0.39 mmol) in accordance with general procedure. Purification by column chromatography (silica gel, 50% ethyl acetate/petroleum ether) afforded 0.086 g of compound **7c** (87% yield). After crystallization from ethyl acetate/petroleum ether, compound **7c** was obtained as a white solid, mp=84–86 °C. [Found: C, 75.90; H, 7.63; N, 16.65. $C_{16}H_{19}N_3$ requires C, 75.85; H, 7.56; N, 16.59%.] ν_{max} (KBr) 3060, 2927, 2850, 1474, 1443, 1338, 1190, 993, 778, 756, 730, 684; δ_H (400 MHz, $CDCl_3$) 7.56 (d, J=7.6 Hz, 1H), 7.34 (td, J=7.6, 2.0 Hz, 1H), 7.31–7.23 (m, 2H), 4.49 (t, J=6.8 Hz, 2H), 3.14 (t, J=6.8 Hz, 2H), 3.01–2.91 (m, 1H), 2.02–1.92 (m, 2H), 1.91–1.70 (m, 5H), 1.48–1.26 (m, 3H); δ_C (100.6 MHz, $CDCl_3$) 147.9, 132.6, 128.4, 128.3, 127.9, 127.7, 125.7, 124.1, 44.6, 35.9, 32.2, 29.3, 26.6, 25.9; MS m/z 253 (M^+, 36), 224 (100), 196 (83), 185 (49), 182 (72), 168 (26), 167 (28), 141 (15), 130 (21), 128 (25), 115 (44), 103 (20), 91 (24), 84 (18), 77 (41), 63 (13), 55 (16), 51 (23), 41 (55%).

*3.3.11. 1-Phenyl-5,6-dihydro[1,2,3]triazolo[5,1-a]isoquinoline (**7d**).* Compound **7d** was prepared from **5d** (0.139 g, 0.37 mmol) in accordance with general procedure. Purification by column chromatography (silica gel, 50% ethyl acetate/petroleum ether) afforded 0.075 g of compound **7d** (82% yield). After crystallization from ethyl acetate/petroleum ether, compound **7d** was obtained as a yellow solid, mp=154–156 °C. [Found: C, 77.80; H, 5.35; N, 16.95. $C_{16}H_{13}N_3$ requires C, 77.71; H, 5.30; N, 16.99%.] ν_{max} (KBr) 3057, 3044, 3032, 2972, 2947, 2913, 1478, 1466, 1448, 1365, 1340, 1232, 1191, 1152, 987, 784, 764, 750, 730, 705, 682; δ_H (400 MHz, acetone-d_6) 7.72–7.67 (m, 2H), 7.56–7.53 (m, 1H), 7.52–7.41 (m, 4H), 7.33 (td, J=7.6, 1.2 Hz, 1H), 7.25–7.19 (m, 1H), 4.60 (t, J=6.8 Hz, 2H), 3.32 (t, J=6.8 Hz, 2H); δ_C (100.6 MHz, acetone-d_6) 144.2, 135.6, 134.3, 130.9, 130.8, 130.6, 130.5, 130.2, 130.1, 129.0, 127.0, 125.8, 46.6, 30.8; MS m/z 247 (M^+, 14), 219 (31), 218 (24), 204 (23), 189 (12), 165 (7), 141 (8), 116 (80), 115 (100), 109 (36), 96 (29), 94 (30), 82 (32), 63 (14), 51 (18%).

*3.3.12. 1-(4-Methylphenyl)-5,6-dihydro[1,2,3]triazolo [5,1-a]isoquinoline (**7e**).* Compound **7e** was prepared from **5e** (0.167 g, 0.43 mmol) in accordance with general procedure. Purification by column chromatography (silica gel, 50% ethyl acetate/petroleum ether) afforded 0.093 g of compound **7e** (83% yield). After crystallization from ethyl acetate/petroleum ether, compound **7e** was obtained as a yellow solid, mp=140–142 °C. [Found: C, 78.20; H, 5.75; N, 16.05. $C_{17}H_{15}N_3$ requires C, 78.13; H, 5.79; N, 16.08%.] ν_{max} (KBr) 3055, 3016,

2943, 2914, 1514, 1469, 1366, 1349, 1342, 1184, 991, 827, 773, 748, 738, 556; δ_H (400 MHz, $CDCl_3$) 7.61–7.57 (m, 3H), 7.32–7.22 (m, 4H), 7.16 (td, *J*=7.6, 1.2 Hz, 1H), 4.55 (t, *J*=6.8 Hz, 2H) 3.22 (t, *J*=6.8 Hz, 2H), 2.40 (s, 3H); δ_C (100.6 MHz, $CDCl_3$) 143.0, 138.2, 132.7, 129.3, 129.0, 128.9, 128.7, 128.4, 128.3, 127.4, 125.1, 124.3, 44.9, 29.2, 21.3; MS *m*/*z* 261 (M^+, 10), 233 (27), 218 (15), 203 (15), 189 (8), 141 (12), 116 (79), 115 (100), 109 (21), 103 (15), 102 (18), 101 (16), 94 (11), 89 (23), 77 (10), 76 (12), 63 (10), 51 (13%).

*3.3.13. 1-(4-Methoxyphenyl)-5,6-dihydro[1,2,3]triazolo [5,1-a]isoquinoline (**7f**).* Compound **7f** was prepared from **5f** (0.150 g, 0.42 mmol) in accordance with general procedure. Purification by column chromatography (silica gel, 40% petroleum ether/ethyl acetate) afforded 0.086 g of compound **7f** (74% yield). After crystallization from ethyl acetate/petroleum ether, compound **7f** was obtained as a pale yellow solid, mp=116–117 °C. [Found: C, 73.68; H, 5.49; N, 15.09. $C_{17}H_{15}N_3O$ requires C, 73.63; H, 5.45; N, 15.15%.] ν_{max} (KBr) 3067, 2956, 2923, 2838, 1610, 1508, 1466, 1458, 1366, 1297, 1246, 1228, 1190, 1178, 1023, 843, 769; δ_H (400 MHz, $CDCl_3$) 7.62–7.57 (m, 2H), 7.56–7.53 (m, 1H), 7.30–7.26 (m, 1H), 7.23 (td, *J*=7.6, 1.2 Hz, 1H), 7.14 (td, *J*=7.6, 1.2 Hz, 1H), 6.98–6.93 (m, 2H), 4.53 (t, *J*=6.8 Hz, 2H), 3.82 (s, 3H), 3.20 (t, *J*=6.8 Hz, 2H); δ_C (100.6 MHz, $CDCl_3$) 159.6, 142.7, 132.7, 129.7, 128.8, 128.7, 128.4, 127.3, 125.1, 124.1, 123.9, 114.0, 55.2, 44.9, 29.2; MS *m*/*z* 277 (M^+, 14), 249 (32), 234 (30), 219 (7), 218 (7), 206 (9), 204 (9), 178 (14), 152 (9), 141 (13), 116 (77), 115 (100), 111 (20), 103 (11), 102 (18), 94 (12), 89 (19), 88 (14), 82 (10), 76 (23), 63 (16), 51 (14%).

*3.3.14. 1-(Thiophen-3-yl)-5,6-dihydro[1,2,3]triazolo [5,1-a]isoquinoline (**7g**).* Compound **7g** was prepared from **5g** (0.130 g, 0.34 mmol) in accordance with general procedure. Purification by column chromatography (silica gel, 50% ethyl acetate/petroleum ether) afforded 0.075 g of compound **7g** (87% yield). After crystallization from ethyl acetate/petroleum ether, compound **7g** was obtained as a yellow solid, mp=160–162 °C. [Found: C, 66.32; H, 4.42; N, 16.60; S, 12.72. $C_{14}H_{11}N_3S$ requires C, 66.38; H, 4.38; N, 16.59; S, 12.66%.] ν_{max} (KBr) 3095, 3073, 2929, 1484, 1474, 1466, 1458, 1400, 1348, 1321, 1288, 1240, 1184, 1133, 857, 802, 774, 743, 640; δ_H (400 MHz, $CDCl_3$) 7.68–7.64 (m, 2H), 7.42–7.39 (m, 2H), 7.33–7.30 (m, 1H), 7.28 (td, *J*=7.6, 1.2 Hz, 1H), 7.21 (td, *J*=7.6, 1.6 Hz, 1H), 4.55 (t, *J*=6.8 Hz, 2H), 3.22 (t, *J*=6.8 Hz, 2H); δ_C (100.6 MHz, $CDCl_3$) 138.6, 132.8, 132.1, 129.2, 129.1, 128.5, 127.6, 127.5, 126.0, 125.0, 124.3, 123.8, 44.9, 29.2; MS *m*/*z* 253 (M^+, 16), 225 (38), 224 (20), 210 (17), 197 (8), 191 (6), 165 (8), 152 (11), 141 (10), 116 (77), 115 (100), 112 (16), 98 (38), 89 (11), 85 (11), 77 (12), 76 (11), 63 (13), 51 (15), 45 (36%).

Acknowledgements

This work was financially supported by the University of Bari (Italy).

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