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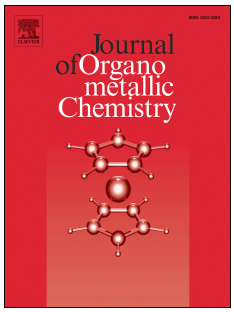

Copper-catalyzed cross-coupling reactions of 5-stibano-1,2,3-triazoles with bromoalkynes under aerobic conditions: Synthesis of 5-alkynyl-1,2,3-triazoles

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Copper-catalyzed cross-coupling reactions of 5-stibano-1,2,3-triazoles with bromoalkynes under aerobic conditions: Synthesis of 5-alkynyl-1,2,3-triazoles

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ABSTRACT

Cu-catalyzed cross-coupling of 5-stibano-1,2,3-triazoles with bromoalkynes is described. The reaction of 5-stibanotriazoles with bromoalkynes under aerobic conditions in DMF, using a combination of 10 mol% of Cu_2O and 1,10-phenanthroline, produced a variety of 5-alkynyltriazoles in moderate-to-excellent yields. This reaction is the first example of Cu-catalyzed C(Ar)–C(sp) bond formation using trivalent organoantimony compounds.

Keywords:

Copper-catalyzed cross-coupling reaction

Organoantimony

Stibane

Bromoalkyne

1,2,3-Triazole

Highlights:

Cu-catalyzed cross-coupling of 5-stibanotriazoles with bromoalkynes has been reported.

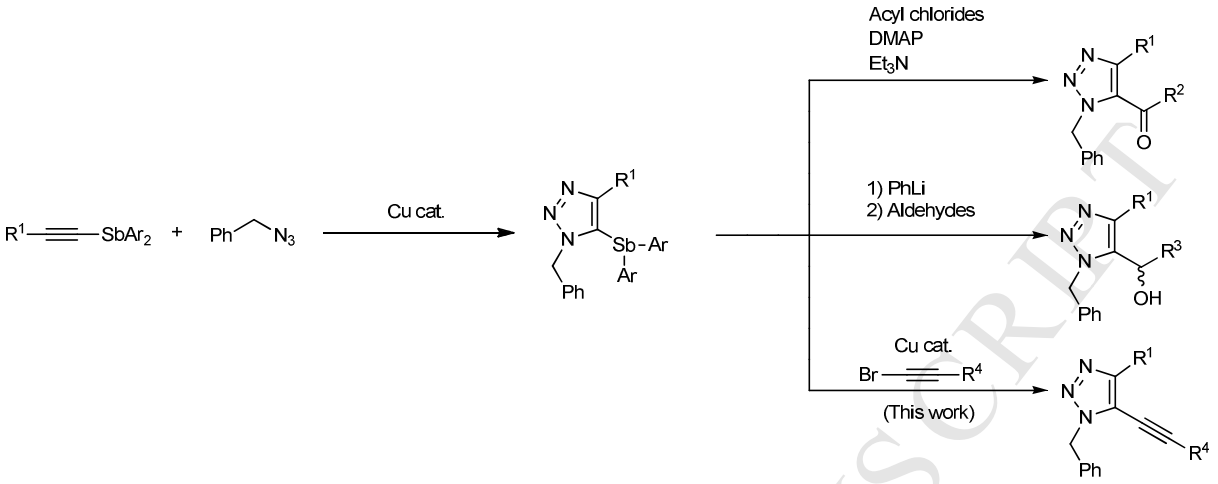
A variety of 5-alkynyltriazoles were obtained in moderate-to-excellent yields.

This reaction procced without additive such as bases under aerobic conditions.

1. Introduction

1,2,3-Triazoles constitute an important class of aromatic five-membered heterocyclic ring containing three nitrogen atoms, and are crucial in the design and synthesis of novel biologically active agents [1, 2]. Among these, fully substituted 5-alkynyl-1,2,3-triazoles have attracted widespread research interest as target compounds because of their use as reagents with biological activities, such as selective HDAC8 inhibition [3], and antileukemic properties [4]. In addition, these compounds have an alkyne moiety, which can be converted into other functional groups or cyclic compounds. They are synthesized by Cu-catalyzed regioselective [3+2] azide-alkyne cycloaddition (CuAAC), followed by cross-coupling with acetylene derivatives using two-step reaction or tandem reaction [5-13]. Zhang et al. reported the Cu-catalyzed tandem reaction of organic azides with two equivalents of terminal alkynes and isolated 5-alkynyltriazoles, which have the same functional group on the 4-position of triazole and acetylene [10]. Lautens et al. developed the three-component reaction of terminal alkynes, iodoalkynes, and organic azides using the catalytic system of palladium and copper [11]. Xu et al. also performed the three-component reaction of terminal alkynes, bromoalkynes, and organic azides using CuCl (20 mol%) and LiO^{t}Bu (2 eq.) to give the desired products [12]. However, these reactions required stoichiometric amounts of base. Stefani et al. reported the synthesis of 5-tellanyl-1,2,3-triazoles using CuAAC of azides with tellurium-substituted acetylenes and their application of Sonogashira-type reaction for the preparation of 5-alkynyltriazoles [9]. One drawback of Pd-catalyzed Sonogashira-type reaction of 5-tellanyltriazole utilizing the reactivity of the tellurium atom is the requirement of excess Cu reagent and base. Recently, we have reported the synthesis of trisubstituted 5-stibano-1,2,3-triazoles having Sb atom in the 5-position of triazole by the CuAAC of ethynylstibanes with organic azides [14-17]. Furthermore, as a chemical modification of 5-stibanotriazoles, an acyl-induced deantimonation and an Sb-Li exchange reaction were performed to functionalize triazoles (Scheme 1) [16, 17]. In this paper, as a continuation of our studies on the chemical reactivity of 5-stibanotriazoles, we report a simple Cu-catalyzed C(Ar)–C(sp) bond formation via cross-coupling of bromoalkynes and stibanotriazoles for the synthesis of 5-alkynyl-1,2,3-triazoles in the absence of additive like bases under aerobic

conditions. This reaction is the first reported example of Cu-catalyzed C(Ar)–C(sp) bond formation using trivalent organoantimony compounds.



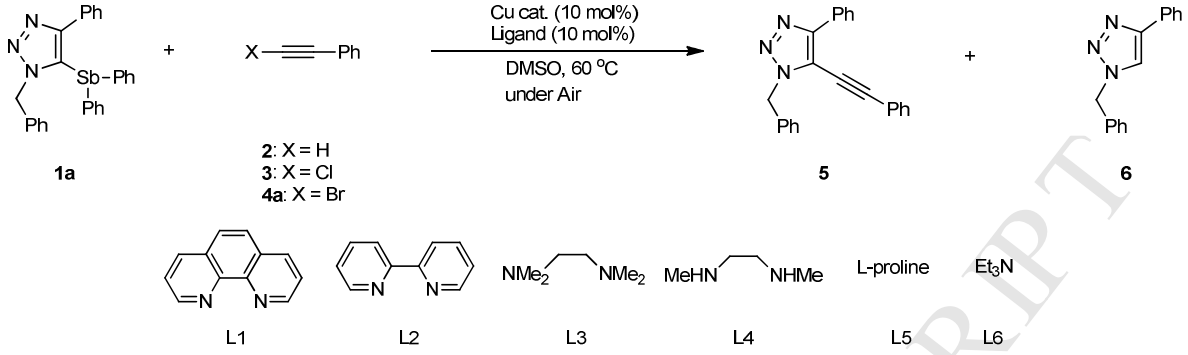
Scheme 1. Synthesis of 5-stibanotriazoles and its chemical reactivity.

2. Results and discussion

We initially investigated the optimal conditions for the synthesis of 5-phenylethynyl-1,2,3-triazole **5** *using 5-stibanotriazole* **1a** *and various alkynes* **2-4a**. *The results of the optimization experiments to identify suitable alkynes, catalysts, ligands, and solvents are summarized in Table 1. First, we performed the reaction of* **1a** *(0.5 mmol) and alkynes (0.75 mmol), such as terminal alkyne* **2**, *chloroalkyne* **3**, *and bromoalkyne* **4a**, *to compare the reactivity using CuI (0.05 mmol) as catalyst and 1,10-phenanthroline (0.05 mmol) as ligand in DMF at 60 ºC under aerobic conditions. The expected cross-coupling product* **5** *was obtained in good yields when bromoalkyne* **4a** *was employed as a substrate; however, the reaction of terminal alkyne* **2** *and chloroalkyne* **3** *were inefficient (entries 1-3). Next, several available Cu catalysts were screened for the reaction of* **1a** *with bromoalkyne* **4a** *(entries 3-12). CuI, CuOAc, Cu_2O, and $Cu(OAc)_2$ gave the coupling product* **5** *in good-to-excellent yield (60–81%). Cu_2O was identified as the best catalyst for this reaction in terms of the yields of the coupling product* **5** *(81%) and by-product* **6** *(12%) (entry 7). The reaction without a Cu catalyst gave the coupling product* **5** *in <1% yield, as determined by gas-liquid chromatography analysis (entry 13). When various ligands (***L1-6***) were screened,*

*1,10-phenanthroline (***L1***) was revealed as the most effective (entries 7, 14-18). The catalytic system of* Cu_2O *and 1,10-phenanthroline plays an important role, and the reaction without adding ligand* **L1** *show a decrease in the yield of* **5** *(entry 19). Moreover, the increase in the ratio of the ligand to the catalyst was ineffective (entry 20). A solvent screen showed that the reaction proceeds effectively in DMF, NMP,* CH_3CN*, and DMSO, among which DMF gave the highest yield of* **5** *(entries 7, 21-28). In terms of yield and reaction time, DMF was found to be best solvent for this reaction (3 h, 82%) (entry 7). On the other hand, EtOH, 1,2-DCE, THF, 1,4-dioxane, and toluene were inefficient reaction solvents. The yield of the reaction in argon atmosphere was comparable to that under aerobic condition (3 h, 72%) (entries 7, 29). This reaction was not significantly influenced by the reaction atmosphere, and is easy to operate under aerobic conditions, which are thus considered excellent reaction conditions. When the reaction was carried out at room temperature, yield of the product* **5** *was only 4% (entry 30); this showed that it is necessary to heat the reaction mixture to 60* ºC to improve the yield. *The reaction is sensitive to catalyst loading: decreasing the catalytic system loading from 10 mol% to 5 and 1 mol% gave significantly reduced yields of* **5** *(entries 31, 32). Consequently, the best result was obtained when* **1a** *and* **4a** *were treated with* Cu_2O *and 1,10-phenanthroline as catalytic system in DMF at 60 ºC without the use of any additive under aerobic conditions. We also examined the Cu-catalyzed three-component reaction using diphenyl(phenylethynyl)stibane, benzyl azide, and bromoalkyne* **4a** *under optimal reaction conditions. However, this reaction gave 1,4-diphenylbuta-1,3-diyne as the main product in 61% yield, and the cross-coupling product* **5** *was obtained in only 20% yield.*

Table 1. Cu-catalyzed reaction of 5-stibanotriazole **1a** with alkynes **2-4a**.[a]



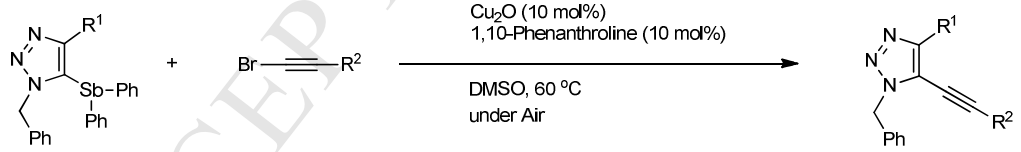
Entry	Alkyne	Cu cat.	Ligand	Solvent	Temp. (°C)	Time (h)	Yield (%)	
							5[b]	**6**[b]
1	**2**	CuI	L1	DMF	60	24	---	84
2	**3**	CuI	L1	DMF	60	24	33	58
3	**4a**	CuI	L1	DMF	60	2	61	26
4	**4a**	CuBr	L1	DMF	60	6	36	40
5	**4a**	CuCl	L1	DMF	60	6	38	50
6	**4a**	CuOAc	L1	DMF	60	24	60	38
7	**4a**	Cu_2O	L1	DMF	60	3	81(78)[c]	12
8	**4a**	$CuBr_2$	L1	DMF	60	5	48	38
9	**4a**	$CuCl_2$	L1	DMF	60	24	32	59
10	**4a**	$Cu(OAc)_2$	L1	DMF	60	1	68	30
11	**4a**	CuO	L1	DMF	60	24	< 1	< 1
12	**4a**	$CuSO_4$	L1	DMF	60	6	14	84
13	**4a**	---	---	DMF	60	24	< 1	10
14	**4a**	Cu_2O	L2	DMF	60	4	73	26
15	**4a**	Cu_2O	L3	DMF	60	24	18	33
16	**4a**	Cu_2O	L4	DMF	60	24	24	21
17	**4a**	Cu_2O	L5	DMF	60	3	52	41
18	**4a**	Cu_2O	L6	DMF	60	24	58	16
19	**4a**	Cu_2O	---	DMF	60	24	48	16
20[d]	**4a**	Cu_2O	L1	DMF	60	4	79	13
21	**4a**	Cu_2O	L1	NMP	60	24	78	20
22	**4a**	Cu_2O	L1	CH_3CN	60	24	77	21
23	**4a**	Cu_2O	L1	DMSO	60	24	60	33
24	**4a**	Cu_2O	L1	EtOH	60	2	55	41
25	**4a**	Cu_2O	L1	1,2-DCE	60	24	29	68
26	**4a**	Cu_2O	L1	THF	60	24	20	54
27	**4a**	Cu_2O	L1	1,4-Dioxane	60	24	8	90
28	**4a**	Cu_2O	L1	Toluene	60	24	5	< 1
29[e]	**4a**	Cu_2O	L1	DMF	60	3	72	24
30	**4a**	Cu_2O	L1	DMF	rt	24	4	13
31[f]	**4a**	Cu_2O	L1	DMF	60	6	62	29
32[g]	**4a**	Cu_2O	L1	DMF	60	24	41	55

[a] Condition: **1a** (0.5 mmol), alkynes (0.75 mmol), Cu cat (0.05 mmol), ligand (0.05 mmol).
[b] GC yield using 9,10-diphenylanthracene as internal standard. The yield 100% corresponds to the formation of 0.5 mmol of **5**.
[c] Isolated yield.
[d] Cu cat. (10 mol%), 1,10-phenanthroline (20 mol%).
[e] Under Ar.
[f] Cu cat. (5 mol%).

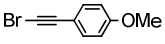
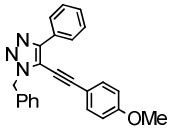
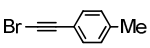
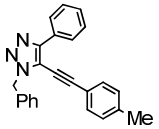
[g] Cu cat. (1 mol%).

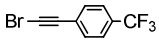
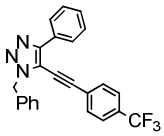
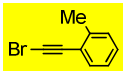
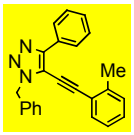
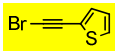
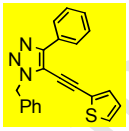
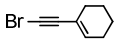
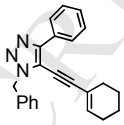
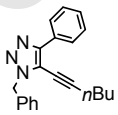
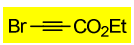
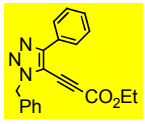
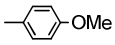
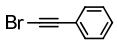
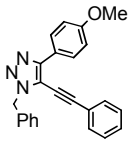
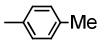
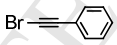
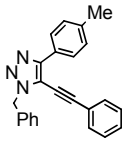
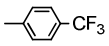
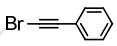
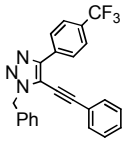
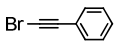
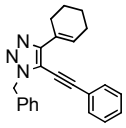
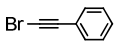
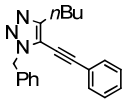
To demonstrate the efficiency and generality of this cross-coupling reaction, the reactions of various 5-stibanotriazoles **1** *with bromoalkynes* **4** *were investigated under the optimized conditions. The key starting materials, 5-stibanotriazoles* **1**, *could easily be prepared following the reported general method [15]. The Cu-catalyzed azide-alkyne cycloaddition of ethynylstibanes having aryl, vinyl, and alkyl group with benzylazide in the presence of CuBr (5 mol%) led to formation of 5-stibanotriazoles (***1a-f***) in 70–77% yields. The results of this cross-coupling reaction are summarized in Table 2. The reaction of 5-stibanotriazole* **1a** *with various bromoalkynes* **4b-f** *having aryl group gave the corresponding 5-alkynyltriazoles* **7-11** *in fair-to-high yields (45–84%) (entries 1-5). In the case of aryl alkynes* **4e** *and* **4f** *having sterically hindered ortho-substituted group and heterocyclic ring, the yield of coupling product decreased. Furthermore, the reaction of bromoalkynes* **4g** *and* **4i** *having vinyl group and ester with* **1a** *afforded the corresponding coupling products* **12** *and* **14** *in satisfactory yields respectively (entries 6, 8). However, alkyl alkyne* **4h** *showed low reactivity (entry 7). Various 5-stibanotriazoles* **1b-f** *were then treated with bromoalkynes* **4a** *under the same reaction conditions. Reaction between 5-stibanotriazoles* **1b-d** *with aryl groups also gave the coupling products* **15-17** *in moderate-to-high yields (entries 9-11). However, the vinyl and alkyl derivative* **1e** *and* **1f** *gave slight desired product or a complex mixture (entries 12, 13)*

Table 2. Reaction of 5-stibanotriazole **1** with bromoalkyne **4**.[a]



1 **4** **7-18**

Entry	**1**	R^1	**4**	Alkyne	Time (h)	Product	Yield (%)[b]
1	**1a**		**4b**		5		**7**: 84
2	**1a**		**4c**		2		**8**: 83

3	**1a**		**4d**		4		**9**: 64
4	**1a**		**4e**		3		**10**: 52
5	**1a**		**4f**		3		**11**: 45
6	**1a**		**4g**		4		**12:** 71
7	**1a**		**4h**		2		**13:** 36
8	**1a**		**4i**		2		**14**: 60
9	**1b**		**4a**		5		**15:** 81
10	**1c**		**4a**		6		**16:** 76
11	**1d**		**4a**		4		**17:** 87
12	**1e**		**4a**		4		**18:** 37
13	**1f**		**4a**		24		**19:** ---

[a] Condition: **1** (0.5 mmol), **4** (0.75 mmol), Cu_2O (0.05 mmol), 1,10-phenanthroline (0.05 mmol).
[b] Isolated yields.

At present, the mechanism of this cross-coupling reaction is unclear. We consider that the

mechanism would be similar to that of the Cu-catalyzed reaction of aryl boronic acids with bromoalkynes in the presence of CuI and 8-hydroxyquinoline, as reported by Yang et al. [18]. A possible mechanism for the present reaction is shown in Fig. 1. The initial step of the reaction would be the generation of complex **A** *from Cu(I) or Cu(II) catalysts with ligands, followed by oxidative addition of bromoalkynes* **4** *to* **A** *to form the intermediate* **B**. *Transmetallation between the 5-stibanotriazol* **1** *and* **B** *forms the intermediate* **D**, *which undergoes reductive elimination to give the desired product* **5** *and regenerated* **A**. *An alternative mechanism would involve the generation of the Cu(III) intermediate* **C** *by oxidative addition of 5-stibanotriazole* **1** *to* **A**, followed by transmetallation of **C** with **4** to give intermediate **D**.

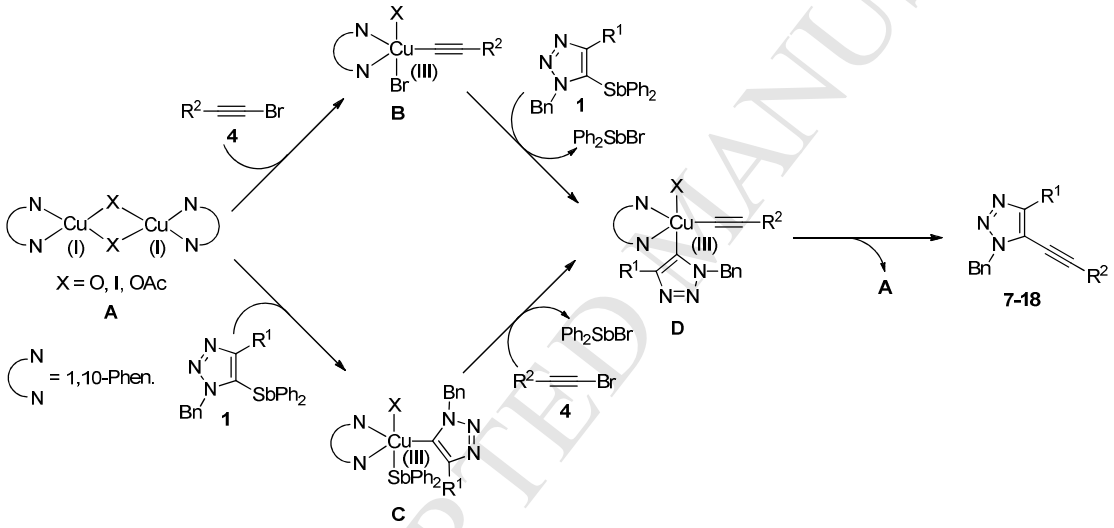


Fig. 1. Possible Mechanism

3. Conclusion

In conclusion, we found that 5-alkynyl-1,2,3-triazoles can be synthesized from *5-stibano-1,2,3-triazoles* and *bromoalkynes* without an additive under *aerobic conditions. Under mild conditions, the reaction of 5-stibanotriazoles and bromoalkynes bearing various functional groups afforded the corresponding cross-coupling products except alkyl derivatives. Trivalent organoantimony compounds having heterocyclic rings are a new class of Cu-catalyzed cross-coupling reagent. Detailed mechanistic studies of this cross-coupling and reactions of*

5-stibanotriazoles with other coupling partners are underway.

4. Experimental

4.1. General

Melting points were measured on a Yanagimoto micro melting point hot-stage apparatus (MP-S3) and reported as uncorrected values. ^{1}H-NMR (TMS: δ: 0.00 ppm as an internal standard) and ^{13}C-NMR ($CDCl_3$: δ: 77.00 ppm as an internal standard) spectra were recorded on JEOL JNM-AL400 (400 MHz and 100 MHz) spectrometers in $CDCl_3$. Mass spectra were obtained on a JEOL JMP-DX300 instrument (70 eV, 300 mA). IR spectra were recorded on a Shimadzu FTIR-8400S spectrophotometer and reported in terms of frequency of absorption (cm^{-1}). Only selected IR bands are reported. Chromatographic separations were carried out using Silica Gel 60N (Kanto Chemical Co., Inc.) under the solvent system stated. Thin-layer chromatography (TLC) was performed using Merck Pre-coated TLC plates (silica gel 60 F254). Compound **2** and each reagents were purchased from Sigma-Aldrich Japan, Wako Pure Chemical Industries and Tokyo Chemical Industry Co., Ltd. Each starting materials were prepared according to the published procedures (**1a-f** [15], **3**[19], **4a-i**[20]).

*4.2. Preparation of 5-alkynyltriazole (**5**, **7**-**18**)*

Cu_2O (7.2 mg, 0.05 mmol, 10 mol%), 1,10-phenanthroline (9.0 mg, 0.05 mmol, 10 mol%), 5-stibanotriazole (**1** : 0.5 mmol) and bromoacetylene (**4** : 0.75 mmol, 1.5 eq.) were dissolved in DMF (4 mL). The reaction mixture was stirred at 60 ºC. The reaction mixture was diluted with CH_2Cl_2 (20 mL) and water (20 mL). The phases were separated and aqueous layer was extracted with CH_2Cl_2 (20 mL × 2). The combined organic layers were washed brine (20 mL), dried over $MgSO_4$, and concentrated under reduced pressure. The residue was purified by silica gel chromatography (*n*-hexane : AcOEt = 4 : 1), affording compound **5**, **7**-**18**.

*4.2.1. 1-Benzyl-4-phenyl-5-(2-phenylethynyl)-1H-1,2,3-triazole (**5**)*[9]

Colorless needle (130.8 mg, 78% yield), mp 91-93 ˚C (*n*-hexane-CH_2Cl_2), R_f = 0.3 (*n*-hexane : AcOEt = 4 : 1). ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 8.18 (2H, dd, J = 8.3, 1.0 Hz, Ar-H), 7.51-7.25 (13H, m, Ar-H), 5.67 (2H, s, CH_2). ^{13}C-NMR (100 MHz, $CDCl_3$) δ: 148.1 (s), 134.7 (s), 131.5 (d), 130.3 (s), 130.0 (d), 128.9 (d), 128.66 (d)×2, 128.6 (d), 128.5 (d), 128.1 (d), 126.2 (d), 121.4 (s), 117.2 (s), 102.3 (s), 75.6 (s), 53.0 (t). HRMS: *m/z* [M^+] calcd for $C_{23}H_{17}N_3$: 335.1422. Found: 335.1428. FTIR (KBr) v: 2220 cm^{-1} (C≡C).

*4.2.2. 1-Benzyl-5-(4-methoxyphenylethynyl)-4-phenyl-1H-1,2,3-triazole (**7**)*

Colorless needle (153.5 mg, 84% yield), mp 99-102 ˚C (*n*-hexane-CH_2Cl_2), R_f = 0.5 (*n*-hexane : AcOEt = 3 : 1). ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 8.18 (2H, dd, J = 7.3, 1.0 Hz, Ar-H), 7.47-7.29 (10H, m, Ar-H), 6.92 (2H, d, J = 9.3 Hz, Ar-H), 5.66 (2H, s, CH_2), 3.85 (3H, s, CH_3). ^{13}C-NMR (100 MHz, $CDCl_3$) δ: 160.7 (s), 147.7 (s), 134.8 (s), 133.2 (d), 130.4 (s), 128.8 (d), 128.6 (d), 128.44 (d), 128.41 (d), 128.1 (d), 126.1 (d), 117.6 (s), 114.3 (d), 113.4 (s), 102.5 (s), 74.4 (s), 55.4 (q), 52.9 (t). HRMS: *m/z* [M^+] calcd for $C_{24}H_{19}N_3O$: 365.1528. Found: 365.1522. FTIR (KBr) v: 2218 cm^{-1} (C≡C).

*4.2.3. 1-Benzyl-4-phenyl-5-p-tolylethynyl-1H-1,2,3-triazole (**8**)*

Colorless needle (144.8 mg, 83% yield), mp 88-91 ˚C (*n*-hexane-CH_2Cl_2), R_f = 0.5 (*n*-hexane : AcOEt = 3 : 1). ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 8.18 (2H, dd, J = 7.3, 1.5 Hz, Ar-H), 7.47-7.28 (10H, m, Ar-H), 7.21 (2H, d, J = 8.5 Hz, Ar-H), 5.66 (2H, s, CH_2), 2.40 (3H, s, CH_3). ^{13}C-NMR (100 MHz, $CDCl_3$) δ: 147.9 (s), 140.1 (s), 134.7 (s), 131.4 (d), 130.3 (s), 129.4 (d), 128.8 (d), 128.6 (d), 128.5 (d), 128.4 (d), 128.1 (d), 126.1 (d), 118.3 (s), 117.4 (s), 102.6 (s), 75.0 (s), 52.9 (t), 21.6 (q). HRMS: *m/z* [M^+] calcd for $C_{24}H_{19}N_3$: 349.1579. Found: 349.1580. FTIR (KBr) v: 2220 cm^{-1} (C≡C).

*4.2.4. 1-Benzyl-4-phenyl-5-(4-trifluoromethylphenylethynyl)-1H-1,2,3-triazole (**9**)*

Colorless needle (129.6 mg, 64% yield), mp 154-156 ˚C (*n*-hexane-CH_2Cl_2), R_f = 0.8 (*n*-hexane : AcOEt = 3 : 1). ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 8.15 (2H, d, J = 7.3 Hz, Ar-H), 7.66 (2H, d, J = 7.3 Hz, Ar-H), 7.57 (2H, d, J = 8.3 Hz, Ar-H), 7.46 (2H, t, J = 7.8 Hz, Ar-H), 7.42-7.30 (6H, m, Ar-H),

5.69 (2H, s, CH_2). ^{13}C-NMR (100 MHz, $CDCl_3$) δ: 148.8 (s), 134.5 (s), 131.8 (d), 131.3 (s, $^2J_{C,F}$ = 32 Hz), 130.0 (s), 128.9 (d), 128.8 (d), 128.7 (d), 128.6 (d), 127.9 (d), 126.3 (d), 125.6 (d, $^3J_{C,F}$ = 3.3 Hz), 125.1 (s), 123.6 (s, $^1J_{C,F}$ = 272 Hz), 116.6 (s), 100.6 (s), 76.7 (s), 53.2 (t). HRMS: *m/z* [M^+] calcd for $C_{24}H_{16}F_3N_3$: 403.1296. Found: 403.1299. FTIR (KBr) *v*: 2274 cm^{-1} (C≡C).

*4.2.5. 1-Benzyl-4-phenyl-5-(o-tolylethynyl)-1H-1,2,3-triazole (**10**)*

Colorless needle (90.8 mg, 52% yield), mp 88-91 ˚C (*n*-hexane-CH_2Cl_2), R_f = 0.8 (*n*-hexane : AcOEt = 3 : 1). ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 8.20 (2H, d, *J* = 8.3 Hz, Ar-H), 7.44 (3H, t, *J* = 7.8 Hz, Ar-H), 7.40-7.26 (7H, m, Ar-H), 7.25-7.20 (2H, m, Ar-H), 5.69 (2H, s, CH_2), 2.43 (3H, s, CH_3). ^{13}C-NMR (100 MHz, $CDCl_3$) δ: 148.0 (s), 140.3 (s), 134.8 (s), 132.1 (d), 130.3 (s). 129.8 (d), 129.7 (d), 128.9 (d), 128.60 (d), 128.56 (d), 128.4 (d), 127.8 (d), 126.3 (d), 125.9 (d), 121.3 (s), 117.5 (s), 101.5 (s), 79.1 (s), 52.8 (t), 20.8 (q). HRMS: *m/z* [M^+] calcd for $C_{24}H_{19}N_3$: 349.1579. Found: 349.1562. FTIR (KBr) *v*: 2223cm^{-1} (C≡C).

*4.2.6. 1-Benzyl-4-phenyl-5-(thiophen-2-ylethynyl)-1H-1,2,3-triazole (**11**)*

Colorless plate (76.8 mg, 45% yield), mp 74-76 ˚C (*n*-hexane-Et_2O), R_f = 0.8 (*n*-hexane : AcOEt = 3 : 1). ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 8.15 (2H, dd, *J* = 8.3, 1.4 Hz, Ar-H), 7.50-7.30 (10H, m, Ar-H), 7.09 (1H, dt, *J* = 5.4, 1.5 Hz, Ar-H), 5.66 (2H, s, CH_2). ^{13}C-NMR (100 MHz, $CDCl_3$) δ: 148.2 (s), 134.6 (s), 133.4 (d), 130.2 (s), 129.3 (d), 128.9 (d), 128.7 (d), 128.6 (d), 128.5 (d), 128.2 (d), 127.5 (d), 126.2 (d), 121.1 (s), 116.9 (s), 95.7 (s), 79.1 (s), 53.1 (t). HRMS: *m/z* [M^+] calcd for $C_{21}H_{15}N_3S$: 341.0987. Found: 341.0999. FTIR (KBr) *v*: 2211 cm^{-1} (C≡C).

*4.2.7. 1-Benzyl-5-[cyclo(hexen-1-yl)ethynyl]-4-phenyl-1H-1,2,3-triazole (**12**)*

Colorless needle (121.3 mg, 71% yield), mp 87-90 ˚C (*n*-hexane-CH_2Cl_2), R_f = 0.6 (*n*-hexane : AcOEt = 3 : 1). ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 8.13 (2H, d, *J* = 7.3 Hz, Ar-H), 7.46-7.28 (8H, m, Ar-H), 6.31-6.27 (1H, m, cyclohexene), 5.59 (2H, s, CH_2), 2.24-2.15 (4H, m, cyclohexene), 1.75-1.60 (4H, m, cyclohexene). ^{13}C-NMR (100 MHz, $CDCl_3$) δ: 147.4 (s), 138.0 (d), 134.8 (s),

130.4 (s), 128.8 (d), 128.5 (d), 128.34 (d), 128.32 (d), 128.1 (d), 126.0 (d), 119.7 (s), 117.7 (s) 104.3 (s), 73.1 (s), 52.7 (t), 28.4 (t), 25.8 (t), 22.0 (t), 21.2 (t). HRMS: *m/z* [M^+] calcd for $C_{23}H_{21}N_3$: 339.1735. Found: 339.1730. FTIR (KBr) *v*: 2203 cm^{-1} (C≡C).

*4.2.8. 1-Benzyl-5-(1-hexyn-1-yl)-4-phenyl-1H-1,2,3-triazole (**13**)*[5]

Colorless oil (57.0 mg, 36% yield), R_f = 0.6 (*n*-hexane : AcOEt = 3 : 1). ^{1}H-NMR (400 MHz, $CDCl_3$) *δ*: 8.13 (2H, dd, *J* = 7.3, 1.5 Hz, Ar-H), 7.42 (2H, t, *J* = 7.6 Hz, Ar-H), 7.38-7.27 (6H, m, Ar-H), 5.59 (2H, s, CH_2), 2.53 (2H, t, *J* = 7.1 Hz, CH_2), 1.65-1.56 (2H, m, CH_2), 1.50-1.40 (2H, m, CH_2), 0.94 (3H, t, *J* = 7.3 Hz, CH_3). ^{13}C-NMR (100 MHz, $CDCl_3$) *δ*: 147.3 (s), 134.9 (s), 130.5 (s), 128.7 (d), 128.5 (d), 128.3 (d), 127.8 (d), 126.0 (d), 117.8 (s), 104.6 (s), 67.4 (s), 52.5 (t), 30.1 (t), 22.0 (t), 19.5 (t), 13.5 (q). HRMS: *m/z* [M^+] calcd for $C_{21}H_{21}N_3$: 315.1735. Found: 315.1736. FTIR (neat) *v*: 2234 cm^{-1} (C≡C).

*4.2.9. Ethyl 3-(1-benzyl-4-phenyl-1H-1,2,3-triazol-5-yl)propiolate (**14**)*

Colorless needle (99.4 mg, 60% yield), mp 49-50 ˚C (*n*-hexane), R_f = 0.6 (*n*-hexane : AcOEt = 3 : 1). ^{1}H-NMR (400 MHz, $CDCl_3$) *δ*: 8.09 (2H, d, *J* = 5.4 Hz, Ar-H), 7.50-7.30 (8H, m, Ar-H), 5.65 (2H, s, CH_2), 4.35 (2H, q, *J* = 7.2 Hz, CH_2), 1.39 (3H, t, *J* = 7.3 Hz, CH_3). ^{13}C-NMR (100 MHz, $CDCl_3$) *δ*: 152.9 (s), 151.2 (s), 133.9 (s), 129.4 (d), 129.2 (s), 129.0 (d), 128.9 (d), 128.8 (d), 128.4 (d), 126.5 (d), 114.2 (s), 93.6 (s), 71.9 (s), 62.7 (t), 53.5 (t), 14.0 (q). HRMS: *m/z* [M^+] calcd for $C_{20}H_{17}N_3O_2$: 331.1321. Found: 331.1315. FTIR (KBr) *v*: 2222 cm^{-1} (C≡C), 1710 cm^{-1} (C=O).

*4.2.10. 1-Benzyl-4-(4-methoxyphenyl)-5-phenylethynyl-1H-1,2,3-triazole (**15**)*

Colorless needle (148.3 mg, 81% yield), mp 93-95 ˚C (*n*-hexane-CH_2Cl_2), R_f = 0.4 (*n*-hexane : AcOEt = 4 : 1). ^{1}H-NMR (400 MHz, $CDCl_3$) *δ*: 8.12 (2H, d, *J* = 8.3 Hz, Ar-H), 7.52-7.29 (10H, m, Ar-H), 6.98 (2H, d, *J* = 8.3 Hz, Ar-H), 5.66 (2H, s, CH_2), 3.84 (3H, s, CH_3). ^{13}C-NMR (100 MHz, $CDCl_3$) *δ* : 159.9 (s), 148.1 (s), 134.8 (s), 131.5 (d), 129.6 (d), 128.9 (d), 128.7 (d), 128.5 (d), 128.1 (d), 127.6 (d), 122.9 (s), 121.5 (s), 116.4 (s), 114.1 (d), 102.1 (s), 75.8 (s), 55.3 (q), 53.0 (t). HRMS:

m/z [M^+] calcd for $C_{24}H_{19}N_3O$: 365.1528. Found: 365.1535. FTIR (KBr) *v*: 2218 cm^{-1} (C≡C).

*4.2.11. 1-Benzyl-5-phenylethynyl-4-p-tolyl-1H-1,2,3-triazole (**16**)*

Colorless needle (133.3 mg, 76% yield), mp 88-90 ˚C (*n*-hexane-CH_2Cl_2), R_f = 0.4 (*n*-hexane : AcOEt = 4 : 1). ^{1}H-NMR (400 MHz, $CDCl_3$) *δ*: 7.89 (2H, d, *J* = 7.8 Hz, Ar-H), 7.31 (2H, d, *J* = 7.3 Hz, Ar-H), 7.29-7.12 (8H, m, Ar-H), 7.08 (2H, d, *J* = 7.3 Hz, Ar-H), 5.49 (2H, s, CH_2), 2.21 (3H, s, CH_3). ^{13}C-NMR (100 MHz, $CDCl_3$) *δ*: 148.3 (s), 138.5 (s), 134.8 (s), 131.5 (d), 129.6 (d), 129.3 (d), 128.8 (d), 128.6 (d), 128.4 (d), 128.1 (d), 127.5 (s), 126.1 (d), 121.5 (s), 116.9 (s), 102.2 (s), 75.7 (s), 52.9 (t), 21.4 (q). HRMS: *m/z* [M^+] calcd for $C_{24}H_{19}N_3$: 349.1579. Found: 349.1574. FTIR (KBr) *v*: 2218 cm^{-1} (C≡C).

*4.2.12. 1-Benzyl-5-phenylethynyl-4-(4-trifluoromethylphenyl)-1H-1,2,3-triazole (**17**)*

Colorless needle (174.5 mg, 87% yield), mp 159-160 ˚C (*n*-hexane-CH_2Cl_2), R_f = 0.5 (*n*-hexane : AcOEt = 4 : 1). ^{1}H-NMR (400 MHz, $CDCl_3$) *δ*: 8.31 (2H, d, *J* = 8.3 Hz, Ar-H), 7.71 (2H, d, *J* = 8.8 Hz, Ar-H), 7.52 (2H, dd, *J* = 5.4, 1.7 Hz, Ar-H), 7.47-7.32 (8H, m, Ar-H), 5.70 (2H, s, CH_2). ^{13}C-NMR (100 MHz, CDCl3) *δ*: 146.6 (s), 134.4 (s), 133.7 (s), 131.6 (d), 130.2 (s, $^2J_{C,F}$ = 33 Hz), 130.0 (d), 128.9 (d), 128.8 (d), 128.6 (d), 128.1 (d), 126.2 (d), 125.6 (d, $^3J_{C,F}$ = 4.1 Hz), 124.1 (s, $^1J_{C,F}$ = 272 Hz), 121.0 (s), 118.1 (s), 103.1 (s), 75.0 (s), 53.1 (t). HRMS: *m/z* [M^+] calcd for $C_{24}H_{16}F_3N_3$: 403.1296. Found: 403.1301. FTIR (KBr) *v*: 2224 cm^{-1} (C≡C).

*4.2.13. 1-Benzyl-4-(1-cyclohexen-1-yl)-5-phenylethynyl-1H-1,2,3-triazole (**18**)*

Colorless needle (57.8 mg, 37% yield), mp 90-93 ˚C (*n*-hexane-CH_2Cl_2), R_f = 0.4 (*n*-hexane : AcOEt = 4 : 1). ^{1}H-NMR (400 MHz, $CDCl_3$) *δ*: 7.46-7.27 (10H, m, Ar-H), 6.81-6.77 (1H, m, cyclohexene), 5.60 (2H, s, CH_2), 2.67-2.60 (2H, m, cyclohexene), 2.27-2.20 (2H, m, cyclohexene), 1.81-1.74 (2H, m, cyclohexene), 1.72-1.64 (2H, m, cyclohexene). ^{13}C-NMR (100 MHz, $CDCl_3$) *δ*: 150.0 (s), 134.9 (s), 131.4 (d), 129.4 (d), 128.8 (d), 128.6 (d), 128.3 (d), 128.1 (s), 128.0 (d), 127.5 (d), 121.7 (s), 115.9 (s), 101.9 (s), 76.2 (s), 52.7 (t), 26.0 (t), 25.6 (t), 22.5 (t), 22.0 (t). HRMS: *m/z* [M^+] calcd for

$C_{23}H_{21}N_3$: 339.1735. Found: 339.1733. FTIR (KBr) *v*: 2214 cm^{-1} (C≡C).

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