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1-Iodobuta-1,3-diynes in Copper-Catalyzed Azide−Alkyne Cycloaddition: A One-Step Route to 4-Ethynyl-5-iodo-1,2,3-triazoles

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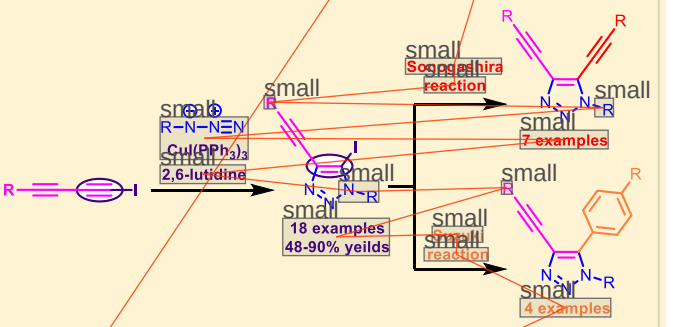
Supporting Information

ABSTRACT: Cu-catalyzed 1,3-dipolar cycloaddition of iodobutadiacetylenes with organic azides using iodotris(triphenylphosphine)copper(I) as a catalyst was found to be an efficient one-step synthetic route to 5-iodo-4-ethynyltriazoles. The reaction is tolerant to various functional groups in both butadiyne and azide moieties. The synthetic application of 5-iodo-4-ethynyl triazoles obtained was also evaluated: the Sonogashira coupling with alkynes resulted in unsymmetrically substituted triazole-fused enediyne systems, while the Suzuki reaction yielded the corresponding 5-aryl-4-ethynyl triazoles.



INTRODUCTION

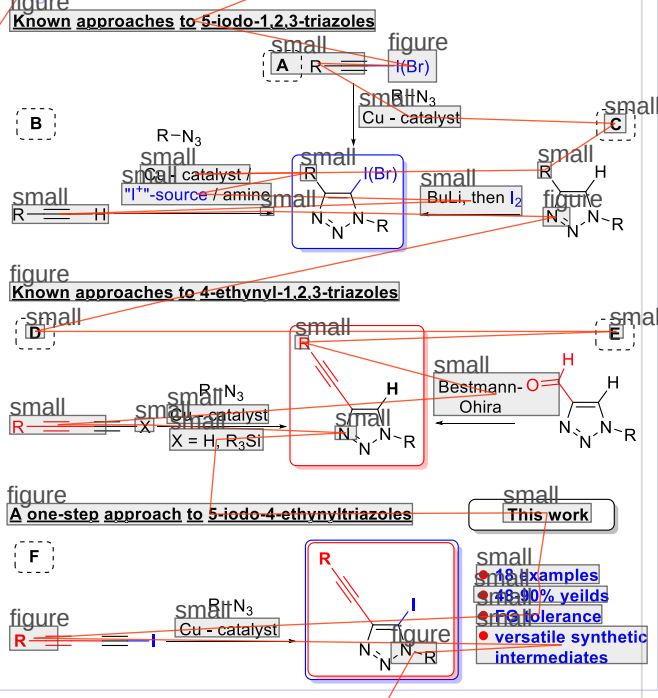
During recent years 1,2,3-triazoles have been holding a leadership in different areas of fundamental and applied research. The fields of 1,2,3-triazole application are described in numerous recent reviews. The main trends are bioorthogonal chemistry,[1,2] organic synthesis,[3,4] creation of new ligands and complexes[5−7] and using the latter as catalysts,[8] construction of functionalized macromolecules and polymeric materials,[9−13] modified nanoparticles,[14] sensors,[15] blocks for energetic materials,[16] the use in medicinal chemistry for the search of new biologically active compounds, and as approved medicines.[17−22]

Such a broad application of triazoles is a result of not only their functionality but also their synthetic accessibility.[23] Among the synthetic approaches toward 1,2,3-triazoles, four general directions could be stressed: metal-catalyzed alkyne−azide cycloaddition (AAC) including mostly Cu-catalyzed (CuAAC)[24,25] and Ru-catalyzed (RuAAC),[26,27] strain-promoted alkyne−azide cycloaddition (SPAAC),[28−30] organocatalytic synthesis of triazoles from azides and nonalkyne C3 synthones[31] using enamine-mediated[32] or enolate-mediated routes,[33] and azide/alkyne/metal-free approaches.[34,35] Among these methodologies, CuAAC, discovered by Sharpless, Fokin,[36] and Meldal[37] groups independently in 2002, remains number one for the synthesis of 1,4-disubstituted 1,2,3-triazoles due to high regioselectivity, efficiency, and tolerance in the presence of many functional groups.

Since the discovery, CuAAC has been also expanded for the regioselective synthesis of 5-iodo(bromo)-1,4-disubstituted 1,2,3-triazoles starting from iodo(bromo)alkynes[38−47] (Scheme 1A) and 1-substituted 4-ethynyl-1,2,3-triazoles from either terminal diacetylenes[48−54] or trialkylsilylbuta-1,3-diynes with a one-pot desylilation[55−57] (Scheme 1D).

Taking into account that both a halogen atom, especially iodine, and a triple bond are useful functional groups

Scheme 1. Previous and Current Work on the Synthesis of 4-Ethynyl-5-iodo-1,2,3-triazoles



responsible for special properties and possibility of further chemical modification, other methods for the synthesis of 5-iodo- and 4-ethynyltriazoles have been elaborated. CuAAC in the presence of electrophilic iodine species generated in situ and amine ligands[58−63] has been investigated for the synthesis

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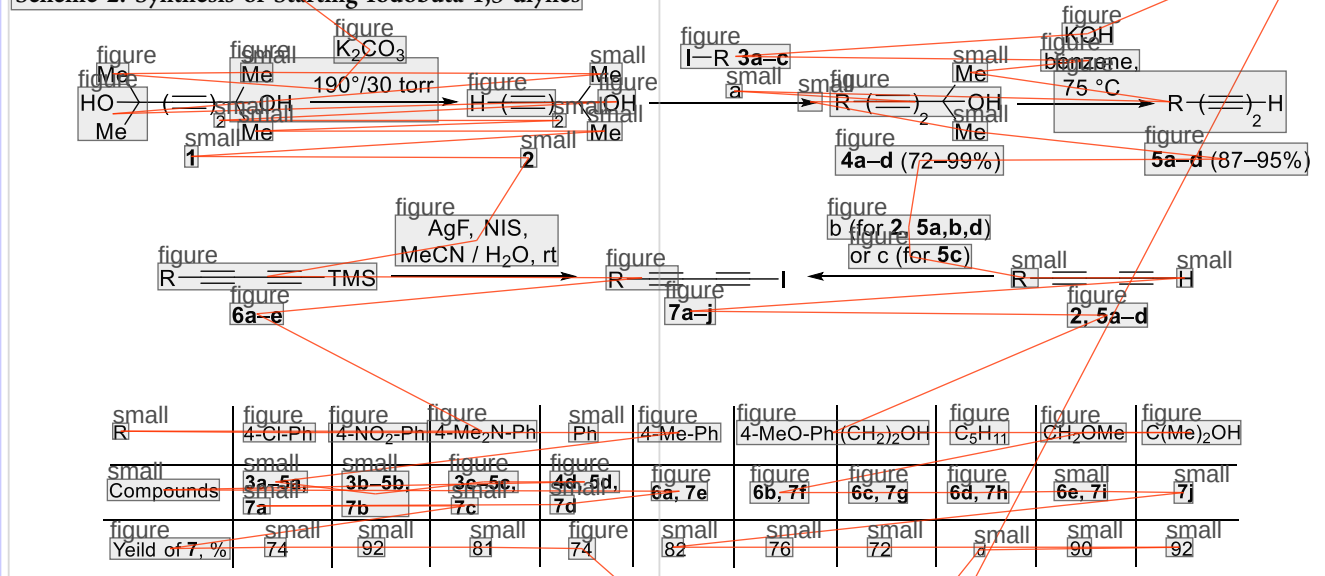
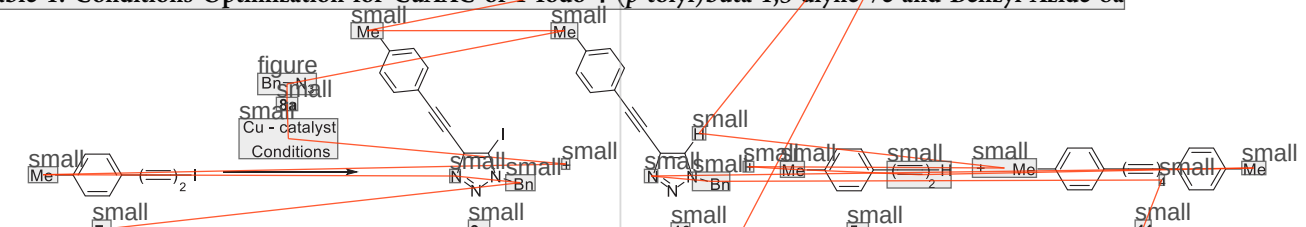
Scheme 2. Synthesis of Starting Iodobuta-1,3-diynes



imageDescription
Reagents and conditions: a) $Pd(PPh_3)_4$ 5 mol%, CuI 10 mol%, Et_3N; b) NIS, $AgNO_3$, acetone, rt; c) NIS, DBU, MeCN, rt; d) iodoalkyne **7h** was used in CuAAC without purification

Table 1. Conditions Optimization for CuAAC of 1-Iodo-4-(*p*-tolyl)buta-1,3-diyne 7e and Benzyl Azide 8a



entry	catalyst/ligand (equiv)/solvent[a]	conversion 7e (%)[b]	yield of 9a (%)[b]	yield[b] of 10, 5e, 11 (%)
1	CuI/TEA (2)/THF	33	5	**10** (–); **5e** (12); **11** (7)
2	CuI/TEA (2)/MeCN	100	10	**10** (2); **5e** (4); **11** (61)
3	CuI/TBTA (0.05) /MeCN	30	25	**10** (3); **5e** (–); **11** (2)
4	CuI/–/glycerol	0	0	
5	$CuI(PPh_3)_3$[c]/2,6-lutidine (0.04)/–	100	92	**10** (1); **5e** (–); **11** (3)
6	CuCl(IPr)/–/THF	0	0	
7	$Cu(OAc)_2$/TBTA (0.1)/*tert*-BuOH, H_2O	6	4	

[a]Conditions: **7e** (0.1 mmol), **8a** (0.1 mmol), and a catalyst (5 mol %) were used in an appropriate solvent with the addition of an appropriate ligand with a reaction time of 18 h at rt. [b]NMR conversion and yields. (1,3,5-Trimethoxybenzene was used as an internal standard.) [c]1 mol % catalyst was used; TEA, triethylamine; TBTA, tris(benzyltriazolylmethyl)amine; CuCl(IPr), chloro[1,3-bis(2,6-diisopropylphenyl)imidazol-2-ylidene]copper(I).

of 5-iodotriazoles (Scheme 1B) and was employed for the preparation of bioactive triazole derivatives.[64−68] An approach based on direct C^5 lithiation of 1,4-substituted triazoles with subsequent halogenation was also proposed for obtaining of some 5-iodo derivatives (Scheme 1C).[39,64,69−71] An alternative way for the synthesis of 4-ethynyltriazoles reported earlier used the reaction of 1,2,3-triazoles-4-carbaldehydes with the Bestmann−Ohira reagent (Scheme 1E).[72]

While some methodologies are presently available for the preparation of 5-iodo- and 4-ethynyl-1,2,3-triazoles, among 1,2,3-triazoles having both halogen and ethynyl moieties, the only example of a 5-chloro derivative accessible through a multistep synthetic sequence has been reported[73] and 4-ethynyl-5-iodo-1,2,3-triazoles still remain unknown.

We decided to study CuAAC of 1-iodobuta-1,3-diynes with organic azides as a one-step synthetic approach to 4-ethynyl-5-iodo-1,2,3-triazoles (Scheme 1F), taking into account that routes B and C being applied to the terminal buta-1,3-diynes and 4-ethynyl-1,2,3-triazoles, respectively, could be complicated with side reactions such as iodination of the second triple bond by electrophilic iodine species or acetylene−allene isomerization induced by strong bases. In the present work, we report the scope and limitation of this methodology along with the synthetic utility of 4-ethynyl-5-iodo-1,2,3-triazoles as versatile synthetic intermediates.

RESULTS AND DISCUSSION

It is of first importance that starting 1-iodobuta-1,3-diynes **7a**−**j** are synthetically available compounds and can be synthesized either by iodination of terminal buta-1,3-diynes using different iodination agents or from TMS-protected buta-1,3-diynes

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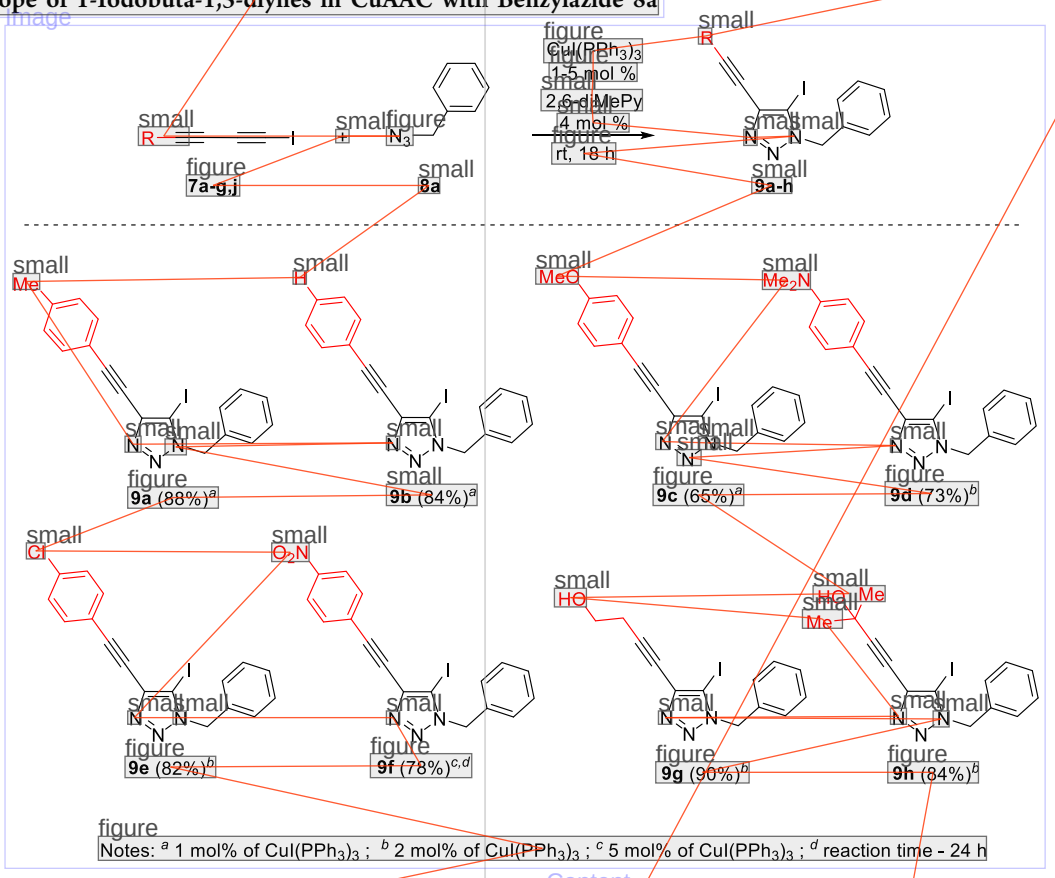
Scheme 3. Scope of 1-Iodobuta-1,3-diynes in CuAAC with Benzylazide 8a



through a one-pot desilylation/iodination approach (Scheme 2).

Terminal diacetylenes bearing aromatic substituents **5a−d** were synthesized from diacetylenic diol **1**[74] by K_2CO_3-induced selective deprotection of one carbinol group by the *retro*-Favorskii reaction[75] followed by the Sonogashira coupling[76] of resulting 2-methylhexa-3,5-diyn-2-ol (**2**) with iodoarenes and the second *retro*-Favorskii reaction (Scheme 2). TMS-Protected buta-1,3-diynes **6c−e** were prepared by the Cadiot−Chodkiewicz coupling[77] according to known procedures. TMS-Protected arylbuta-1,3-diynes **6a,b** were available through the Sonogashira coupling of corresponding bromoalkynes with TMS-acetylene.[78] Iodination of terminal buta-1,3-diynes using the *N*-iodosuccinimide/$AgNO_3$ system proceeded in high yields for diacetylenes **2** and **5a,b,d**, affording iodides **7a,b,d,j**. However, in the case of 4-(*p*-dimethylaminophenyl)-buta-1,3-diyne **5c**, iodination with the use of NIS/DBU[79] was more efficient for the synthesis of **7c**. The second approach toward iodobutadiynes based on desililation/iodination of TMS-diacetylenes **6a−e** in one-pot by NIS/AgF[80] allowed compounds **7e−i** to be obtained in high yields (Scheme 2).

Initially, CuAAC of *p*-tolylbuta-1,3-diyne **7e** with benzyl azide **8a** was studied for the search of optimal conditions. A series of Cu catalysts, ligands, and solvents employed earlier for the successful synthesis of 5-iodo-1,4-triazoles (entries 1−6)[38,46,81] and 5-unsubstituted 1,4-triazoles (entry 7)[82] were tested (Table 1).

We found that the result of the reaction strongly depends on the nature of a catalyst, a ligand, and a solvent. It was a surprise that CuI with different ligands reported as the best conditions for the synthesis of 5-iodotriazoles[38] gave unsatisfactory results with the iododiacetylene **7e** (entries 1−3). The maximal 25% yield of triazole **9a** was reached in the case of tris-(benzyltriazolylmethyl)amine (TBTA) ligand (entry 3). Moreover, when we used triethylamine (TEA) as a ligand and MeCN as a solvent instead of THF, the main reaction product detected in the reaction mixture was a tetrayne **11** (entry 2). In the presence of CuI with glycerol,[81] no conversion of the starting compound was observed (entry 4). Solvent-free conditions using the complex $CuI(PPh_3)_3$ together with 2,6-lutidine as a ligand[46] (entry 5) turned out to be the most effective catalytic system, providing a complete conversion of the starting iodobutadiyne to ethynyliodotriazole **9a** in 92% yield.

Despite the fact that the Cu(I) complex with *N*-heterocyclic carbene ligand was very efficient in the case of iodoalkyne/azide cycloaddition,[46] for iododiacetylene **7e**, no traces of any products were detected in the reaction mixture after 18 h (entry 6). When $Cu(OAc)_2$ with TBTA was used,[82] the reaction proceeded very slowly giving only traces of cycloaddition product **9a** (entry 7).

Then the scope of Cu-catalyzed 1-iodobuta-1,3-diyne/azide cycloaddition was explored with respect to the substituents effect at conjugate triple bonds (Scheme 3).

$CuI(PPh_3)_3$ in the presence of 2,6-lutidine was chosen as the best catalytic system. Iodobutadiynes bearing aromatic substituents with both electron-donating groups (EDGs) **7c,e,f** and electron-withdrawing groups (EWGs) **7a,b** and hydroxyalkyl-substituted iododiacetylenes **7g,j** were studied in CuAAC with benzylazide **8a**. It should be particularly emphasized that the reaction studied proceeds with a high chemoselectivity and regioselectivity and afforded exclusively 1-benzyl-4-ethynyl-5-iodo-1,2,3-triazoles **9a−h** in high yields.

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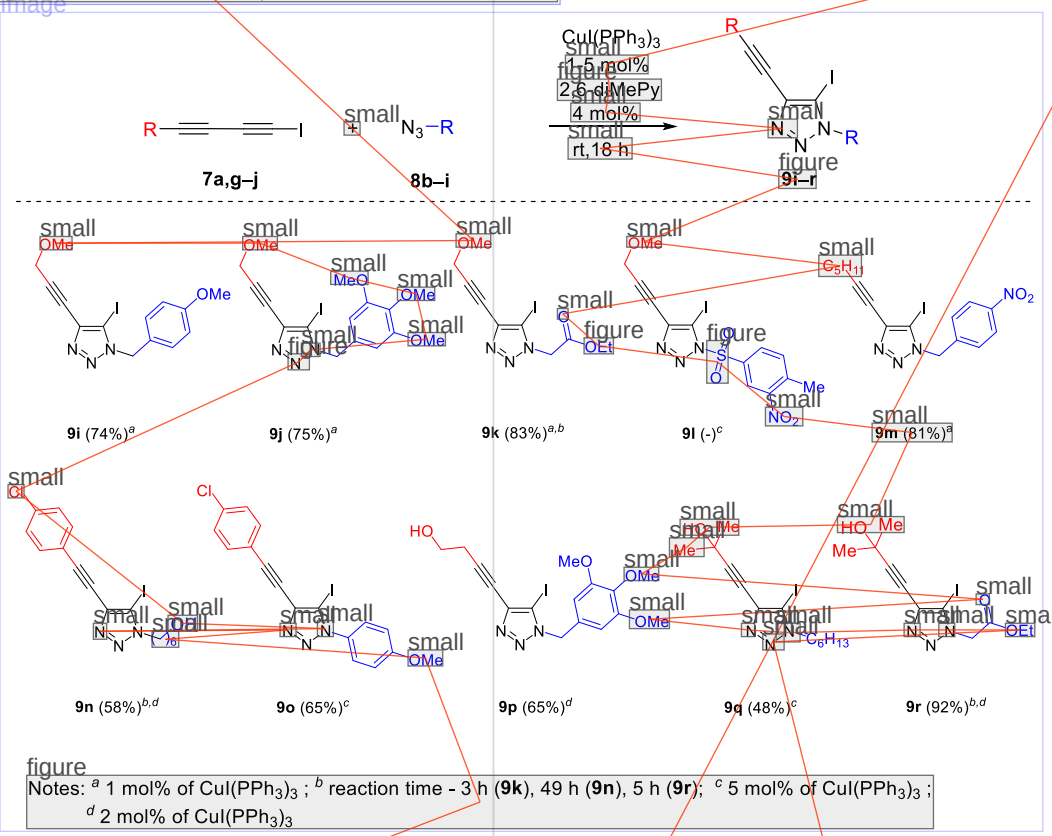
Scheme 4. Scope of 1-Iodobuta-1,3-diynes and Azides in CuAAC



Notes: [a] 1 mol% of $CuI(PPh_3)_3$; [b] reaction time - 3 h (**9k**), 49 h (**9n**), 5 h (**9r**); [c] 5 mol% of $CuI(PPh_3)_3$; [d] 2 mol% of $CuI(PPh_3)_3$

The formation of 5-iodo-4-ethynyl-1,2,3-triazoles was proved by the 2D NMR analysis of triazole **9a** and additionally by X-ray analysis of the cross-coupling products **13d** and **15a,b** of 5-iodo-4-ethynyl-1,2,3-triazoles **9a,c,d** (see below).[83]

A preferred coordination of a Cu-catalyst to an iodo-substituted triple bond compared with an internal triple bond is supposed to be a reason for the excellent chemoselectivity of azide interaction with the iodo-substituted triple bond of 1-iodobuta-1,3-diynes. On the other hand, a regioselective reaction of azides with 1-iodobutadiynes could be explained by the mechanism of CuAAC for iodoalkynes with less activation barrier values for the formation of 1,4-cycloadducts rather than for 1,5-cycloadducts[46] that is in an agreement with numerous examples of CuAAC for iodoalkynes.[38,41,43,44,46,47]

It is important to note that cycloaddition of hydroxyalkyl iododiacetylenes **7g,j** and dimethylamino derivative **7c** required 2 mol % catalyst instead of 1 mol % in order to reach full conversion of 1-iodo(buta-1,3-diyne). In the case of iodopenyldiacetylenes with an EWG, an increased catalyst loading was also essential. While 2 mol % was optimal for 4-chlorophenyl-substituted diyne **7a**, a stronger EWG (NO_2, **7b**) demanded 5 mol % catalyst.[84] The drop of reactivity for iodobutadiynes bearing an EWG could be explained in less donating ability of the iodo-substituted triple bond because of conjugation with the EWG, that would hinder the formation of π Cu-alkyne complexes,[85] which is very important in the proposed mechanism of CuAAC with iodoalkynes.[46,86]

Further reaction capabilities have been studied using a series of structurally and functionally diverse azides **8b–i** with variedly substituted 1-iodobutadiynes **7a,g–j** (Scheme 4).

Benzyl azides with donor **8b,c** and acceptor groups **8f**, alkyl azides **8d,g,i** including azides with FG **8d,g**, *p*-methoxyphenylazide **8h**, and nitrotosylazide **8e** were investigated in CuAAC with different iododiacetylenes. In all cases except nitrotosylazide **8e**, the reaction afforded 4-ethynyl-5-iodotriazoles from moderate to high yields. In the case of nitrotosylazide **8e**, only starting materials were detected in the reaction mixture after 48 h even though 5 mol % catalyst was used. Synthesis employing either OH-substituted alkylazide **8g** or iodobutadiynes **7g,j** required a higher catalyst loading (2–5 mol %). The scope of the reaction was also expanded to arylazide **8h**, which required 5 mol % $CuI(PPh_3)_3$ for the full conversion giving 1-aryl-substituted triazole **9o**.

On the next step, we evaluated a synthetic application of 4-ethynyl-5-iodotriazoles. Two types of reactions involving an iodine atom, which lead to 1,4,5-trisubstituted triazoles were explored, the Sonogashira–Hagihara[87,88] and the Suzuki–Miyaura[89] couplings.

It is important that both types of products, triazole-fused enediynes and 5-aryl-4-ethynyltriazoles, are of special importance because of possible further intramolecular cyclizations known for other types of benzene(heteroarene)-fused enediynes[90–95] and *ortho*-ethynylaryl-substituted arenes,[96–100] leading to highly conjugated polyaromatic compounds. Among such systems, polycyclic fused 1,2,3-triazoles are of particular interest.[101–103]

We started with the synthesis of enediynes. Remarkably, a triple bond has been introduced into position 5 of a triazole ring mostly using the Sonogashira coupling,[101,104–106] yet several examples for the synthesis of 4-aryl-5-ethynyl-1,2,3-triazole using one-pot CuAAC/ethynylation have also been reported.[107–113]

Common conditions for the Sonogashira reaction of 4-aryl-5-iodo-1,2,3-triazoles ($Pd(PPh_3)_4/CuI/K_2CO_3$ /THF, 65

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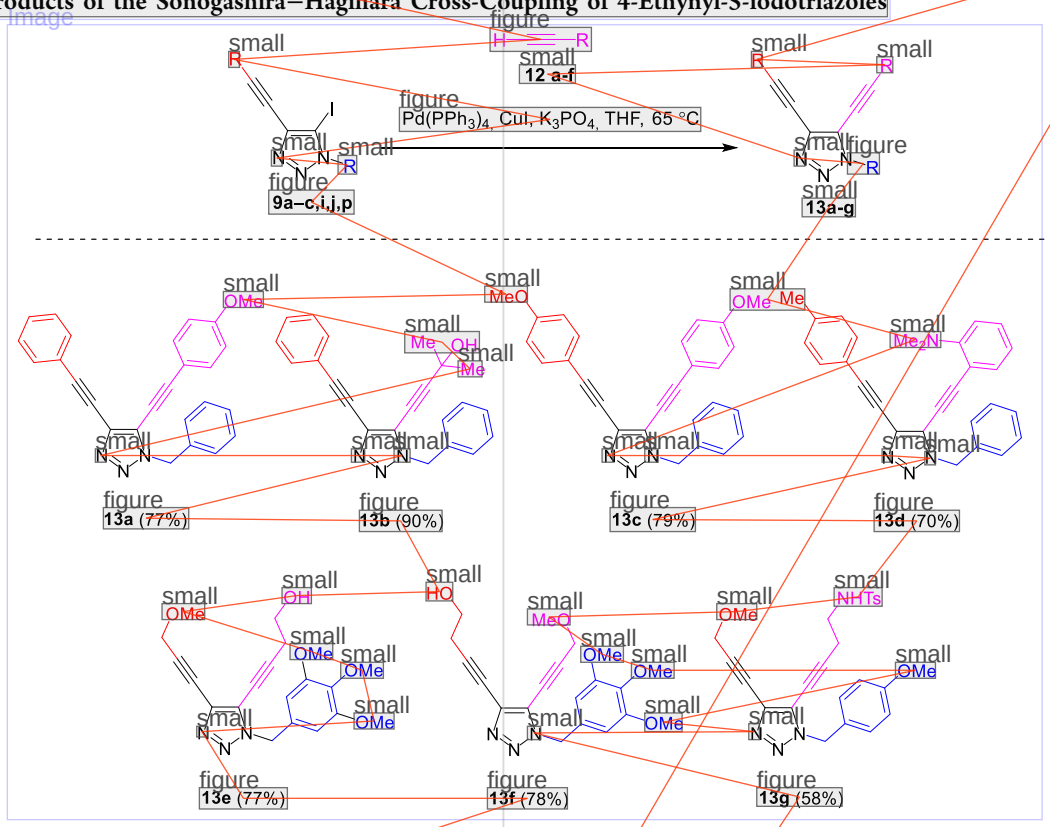
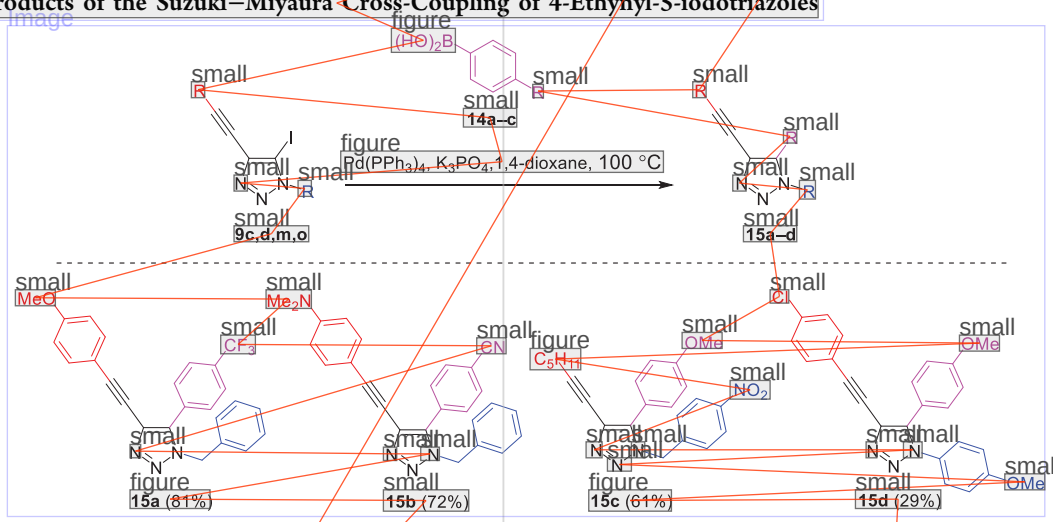
Scheme 5. Products of the Sonogashira−Hagihara Cross-Coupling of 4-Ethynyl-5-iodotriazoles



Scheme 6. Products of the Suzuki−Miyaura Cross-Coupling of 4-Ethynyl-5-iodotriazoles



°C[104] and $Pd(PPh_3)_4$/CuI/Et_3N/toluene, 80 °C[105]) were initially employed for coupling of iodotriazole **9b** with 4-MeO-phenylacetylene **12a** and 2-methylbuta-3-yn-2-ol **12b**, respectively. Surprisingly, the reaction with alkynol **12b** proceeded with a partial deiodination of iodotriazole **9b**. A mixture of the desired enediyne **13b** along with reduced 4-ethynyltriazole and a significant amount of the alkyne homocoupling byproduct was obtained. The reaction with 4-MeO-phenylacetylene **12a** reached only ~60% conversion of starting iodide to enediyne.[114] Switching to other conditions useful for the Sonogashira coupling in the synthesis of enediynes fused to hererocycles[115−117] gave either a poor conversion or mixture of target enediynes with the deiodinated starting triazole.[114] Taking into account electron-withdrawing properties of a triple bond neighbor to iodine, we analyzed examples of the Sonogashira reaction for 5-iodotriazoles bearing an EWG at the C4 position reported earlier. The literature search revealed that low conversion and reductive deiodination are common problems for the Sonogashira coupling of 5-iodo-1,2,3-triazolecarboxylates,[118] carboxamides,[119,120] nitriles,[121] and even 5-iodo-4-phenyl-triazoles.[122] It is particularly remarkable that for 5-iodotriazoles with an EWG at N^1 the Sonogashira reaction proceeded smoothly,[123] while for triazole with bulky EDG (ferrocenyl) the yields also were low.[124] The best and the simplest solution was found by David Goyard et al., who carried out both the Sonogashira and the Suzuki coupling using K_3PO_4 as a base and $Pd(PPh_3)_4$ as a catalyst in THF.[122]

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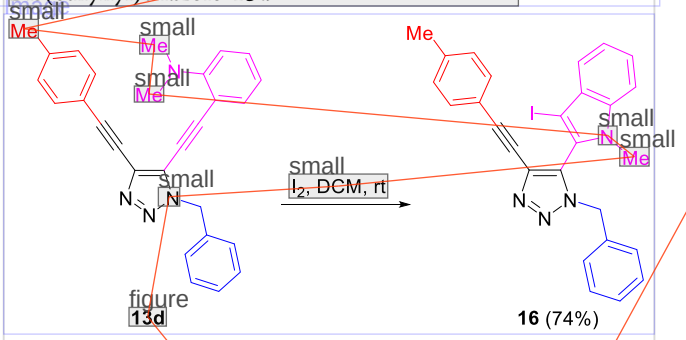
These conditions also worked perfectly for the cross-coupling of 4-ethynyl-5-iodotriazoles with acetylenes, providing unsymmetrically substituted enediynes **13a–g** fused to 1,2,3-triazole ring in high yields (Scheme 5). These conditions proved to be FG tolerant, which allowed OH functions and substituted amino groups to be introduced into an enediyne system. Unsymmetrically substituted enediynes such as **13e–g** are of crucial importance because they could be used as starting compounds for the synthesis of macrocyclic triazole-fused enediynes by the Nicholas-type macrocyclization.[116,125]

The Suzuki coupling of *N*-benzyliodotriazoles **9c,d,m** proceeded in high yields also using $Pd(PPh_3)_4$ as a catalyst and K_3PO_4 as a base providing 5-aryl-4-ethynyltriazoles **15a–c** in moderate to good yields (Scheme 6). In contrast with *N*-benzyl-substituted 5-iodotriazoles, the reaction of *N*-(4-methoxyphenyl) triazole **9o** gave the coupling product **15d** in a low yield because of a formation of an unidentified byproduct complex mixture. The possible reason for this exception could be a relatively easy 5-iodotriazole ring opening promoted by both *N*-aryl group and EWG (4-(chlorophenyl)-ethynyl) at C-4 of the triazole ring. Thus, the palladium-catalyzed denitrogenative indolization of *N*-aroylbenzotriazoles with internal alkynes has been reported previously.[126]

Additional synthetic utility of enediyne **13d** bearing ethynyl and Me_2N groups at the *ortho*-position of a benzene ring was illustrated by electrophile-induced cyclization[127] that led to 2-triazolyl-3-iodoindole **16** (Scheme 7).

Scheme 7. Electrophile-Induced Cyclization of Bis(ethynyl)triazole 13d



In summary an efficient and convenient one-step approach toward 1-substituted 4-ethynyl-5-iodo-1,2,3-triazoles was developed based on CuAAC of 1-iodobutadiynes with organic azides using a $CuI(PPh_3)_3$/2,6-lutidine catalytic system. The reaction is tolerant to various functional groups and allows alkyl, aryl, hydroxyalkyl, ethoxycarbonyl, and dialkylamino functional groups to be introduced into different positions of target triazoles. 4-Ethynyl-5-iodo-1,2,3-triazoles were demonstrated to be useful building blocks for the synthesis of triazole-fused enediyne systems and 5-aryl-4-ethynyltriazoles, which are of great interest because of their further synthetic utility.

EXPERIMENTAL SECTION

General Information and Methods. Solvents, reagents, and chemicals (2-methylbut-3-yn-2-ol, iodoarenes) used for reactions were purchased from commercial suppliers. Catalyst $Pd(PPh_3)_4$ was purchased from Sigma-Aldrich. Solvents were dried under standard conditions, and chemicals were used without further purification. Catalysts $Cu(PPh_3)_3I$[128] and CuCl(IPr), chloro[1,3-bis(2,6-diisopropylphenyl)imidazol-2-ylidene]copper(I),[129] were synthesized by known procedures without any modification. Benzyl azide (**8a**),[130] 1-(azidomethyl)-4-methoxybenzene (**8b**),[45] 5-(azidomethyl)-1,2,3-trimethoxybenzene (**8c**),[131] ethyl 2-azidoacetate (**8d**),[132] 1-(azidomethyl)-4-nitrobenzene (**8f**),[45] 6-azidohexan-1-ol (**8g**),[133] 1-azido-4-methoxybenzene (**8h**),[134] 1-azidohexane (**8i**),[45] 2,7-dimethylocta-3,5-diyne-2,7-diol (**1**),[135] buta-1,3-diyn-1-ylbenzenes (**4d, 5d**),[115] trimethyl(*p*-tolylbuta-1,3-diyn-1-yl)silane (**6a**),[78] ((4-methoxyphenyl)-buta-1,3-diyn-1-yl)trimethylsilane (**6b**),[78] 6-(trimethylsilyl)hexa-3,5-diyn-1-ol (**6c**),[115] trimethyl(penthyl)silane (**6d**),[136] and methoxymethyltrimethylsilane (**6e**)[125] were synthesized using previously reported procedures.

Evaporation of solvents and concentration of reaction mixtures were performed in vacuo at 35 °C on a rotary evaporator. Thin-layer chromatography (TLC) was carried out on silica gel plates (Silica gel 60, UV 254) with detection by UV or staining with a basic aqueous solution of $KMnO_4$. Melting points (mp) determined are uncorrected. ^1H and $^{13}C\{^1H\}$ NMR spectra were recorded at 400 and 100 MHz, respectively, at 25 °C in $CDCl_3$ without the internal standard. The ^1H NMR data are reported as chemical shifts (δ), multiplicity (s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; br, broad), coupling constants (J, given in Hz), and number of protons. The ^{13}C NMR data are reported as the chemical shifts (δ) and type of carbon (p, primary; s, secondary; t, tertiary; q, quaternary) determined from DEPT experiments with coupling constant J_{C-F} for F-containing compounds. Chemical shifts for ^1H and ^{13}C are reported as δ values (ppm) and referenced to a residual solvent (δ = 7.26 ppm for ^1H; δ = 77.16 ppm for ^{13}C). High-resolution mass spectra (HRMS) were determined using electrospray ionization (ESI) in the mode of positive ion registration with a TOF mass analyzer. High-resolution mass spectra of compound **7e** (methanol solution) were recorded on a Bruker maXis Q-TOF instrument equipped with an atmospheric pressure chemical ionization (APCI-MS) ion source in positive ion mode. IR spectra were recorded for tablets with KBr. The single-crystal X-ray diffraction studies were carried out on a diffractometer at 100 K using Cu Kα radiation (λ = 1.54180 Å). Using Olex 2,[137] the structure was solved with the Super flip structure solution program[138] using Charge Flipping and refined with the ShelXL refinement package[139] using least-squares minimization.

*2-Methylhexa-3,5-diyn-2-ol (**2**).* A modified method reported earlier[140] was used. A mixture of 2,7-dimethyl-3,5-octadiyne-2,7-diol (**1**) (9.96 g, 60.0 mmol), and potassium carbonate (1.29 g, 9.40 mmol) was placed into a vacuum distillation apparatus followed by 1 mL of a high-vacuum oil (VM-4). The pressure was reduced to 30 Torr, and the apparatus was dipped into a preheated oil bath (bath temperature 190–195 °C) and heated rapidly. After the melting of the reaction mixture, the vigorous liberation of acetone occurred and the product started to distill (95°/30 Torr). The second distillation (bp 52–54 °C/3 Torr) gave 2-methylhexa-3,5-diyn-2-ol (**2**) (3.57 g, 55% yield): lit.[140] bp 36–37 °C/0.4 Torr; ^1H NMR ($CDCl_3$, 400.13 MHz, δ) 2.20 (s, 1H), 2.02 (br s, 1H, OH), 1.54 (s, 6H).

*General Procedure for the Synthesis of Aryldiacetylenes (**4a–c**) by the Sonogashira Reaction.* To the solution of iodoarene (1.00 equiv) in triethylamine (0.1 M) were added terminal diacetylene **2** (1.50 equiv), $Pd(PPh_3)_4$ (5 mol %), and CuI (10 mol %). The resulting solution was evacuated and flushed with Ar several times and allowed to stir at room temperature. After completion of the reaction (TLC control), the reaction mixture was poured into a saturated aqueous solution of NH_4Cl, extracted with ethyl acetate, washed with saturated solution of NH_4Cl and brine, dried over anhydrous Na_2SO_4, and concentrated under reduced pressure to yield the crude product, which was purified by column chromatography on silica gel.

*6-(4-Chlorophenyl)-2-methylhexa-3,5-diyn-2-ol (**4a**).*[141] This compound was synthesized from 2-methylhexa-3,5-diyn-2-ol (**2**) (648.8 mg, 6.00 mmol) and 1-chloro-4-iodobenzene (955.0 mg, 4.00 mmol). The crude product was purified by column chromatography (eluent: hexane/EtOAc = 3:1) to afford a yellow solid (872 mg, 99% yield): ^1H NMR ($CDCl_3$, 400.13 MHz, δ) 7.40 (d, J = 8.5 Hz, 2H), 7.29 (d, J = 8.5 Hz, 2H), 1.58 (s, 6H).

*2-Methyl-6-(4-nitrophenyl)hexa-3,5-diyn-2-ol (**4b**).*[141] This compound was synthesized from 2-methylhexa-3,5-diyn-2-ol (**2**) (648.8 mg, 6.00 mmol) and 1-iodo-4-nitrobenzene (996.0 mg, 4.00 mmol).

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The crude product was purified by column chromatography (eluent: hexane/EtOAc = 3:1) to afford a yellow solid (742 mg, 81% yield): ^{1}H NMR ($CDCl_3$, 400.13 MHz, δ) 8.19 (d, J = 8.6 Hz, 2H), 7.62 (d, J = 8.6 Hz, 2H), 1.59 (s, 6H).

*6-(4-(Dimethylamino)phenyl)-2-methylhexa-3,5-diyn-2-ol (**4c**).*[142] This compound was synthesized from 2-methylhexa-3,5-diyn-2-ol (**2**) (605.4 mg, 5.60 mmol) and 4-iodo-*N*,*N*-dimethylaniline (988.0 mg, 4.00 mmol). The crude product was purified by column chromatography (eluent: hexane/EtOAc = 5:1) to afford a yellow solid (656 mg, 72% yield): ^{1}H NMR ($CDCl_3$, 400.13 MHz, δ) 7.36 (d, J = 9.0 Hz, 2H), 6.59 (d, J = 9.0 Hz, 2H), 2.98 (s, 6H), 1.57 (s, 6H).

*General Procedure for the Synthesis of Terminal (Buta-1,3-diynyl)arenes **5a−c** by the retro-Favorskii Reaction.* A round-bottom oven-dried flask equipped with a magnetic stirring bar was charged with a solution of corresponding alcohol **4a−c** (1.00 equiv) in dry benzene (10.0 mL) through the septum via syringe. Argon was bubbled through the solution for 10 min, and then well-ground anhydrous KOH (1.25 equiv for **4a**,**c** and 2.20 equiv for compound **4b**) was added in the stream of Ar. A reflux condenser was equipped, and the flask with the resulting mixture was heated on an oil bath (bath temperature 75 °C). After completion of the reaction (TLC control), the reaction mixture was cooled and a precipitate was filtered through a short pad of silica gel eluting with benzene. The solvent was removed under reduced pressure, and the crude product was purified by column chromatography on silica gel using EtOAc/hexane as the eluent.

*1-(Buta-1,3-diyn-1-yl)-4-chlorobenzene (**5a**).*[143] This compound was synthesized in accordance with the general procedure from 6-(4-chlorophenyl)-2-methylhexa-3,5-diyn-2-ol (**4a**) (316.0 mg, 1.45 mmol) and KOH (101.3 mg, 1.81 mmol). The crude product was purified by column chromatography (eluent: hexane/EtOAc = 20:1), which afforded a brown solid (221 mg, 95% yield): ^{1}H NMR ($CDCl_3$, 400.13 MHz, δ) 7.44 (d, J = 8.7, 2H, Ar), 7.31 (d, J = 8.7, 2H, Ar), 3.50 (s, 1H, C≡CH).

*1-(Buta-1,3-diyn-1-yl)-4-nitrobenzene (**5b**).*[144] This compound was synthesized in accordance with the general procedure from 2-methyl-6-(4-nitrophenyl)hexa-3,5-diyn-2-ol (**4b**) (370.0 mg, 1.61 mmol) and KOH (199.2 mg, 3.55 mmol). The crude product was purified by column chromatography (eluent: hexane/EtOAc = 5:1), which afforded a light red solid (245 mg, 89% yield): ^{1}H NMR ($CDCl_3$, 400.13 MHz, δ) 8.20 (d, J = 9.0, 2H, Ar), 7.66 (d, J = 9.0, 2H, Ar), 3.63 (s, 1H, C≡CH).

*4-(Buta-1,3-diyn-1-yl)-N,N-dimethylaniline (**5c**).*[145] This compound was synthesized in accordance with the general procedure from 6-(4-(dimethylamino)phenyl)-2-methylhexa-3,5-diyn-2-ol (**4c**) (235.0 mg, 1.03 mmol) and KOH (72.5 mg, 1.29 mmol). The crude product was purified by column chromatography (eluent: hexane/EtOAc = 30:1), which afforded a light yellow solid (152 mg, 87% yield): ^{1}H NMR ($CDCl_3$, 400.13 MHz, δ) 7.41 (d, J = 9.2, 2H, Ar), 6.62 (d, J = 9.2, 2H, Ar), 3.02 (s, 6H, $N(CH_3)_2$), 2.48 (s, 1H, C≡CH).

*Synthesis of 1-Iodobuta-1,3-diyn-1-yl (**7a−j**).* The halogenation of TMS-protected diynes[80] (method A) is described as follows: To a solution of (buta-1,3-diynyl)trimethylsilane **6** (1.00 equiv) in acetonitrile with an addition of H_2O (2 equiv) under an atmosphere of an Ar and in the dark was added AgF (1.00 equiv), and the mixture was stirred for 20 min. Then *N*-iodosuccinimide (NIS) (1.20 equiv) was added, and the mixture was stirred for several hours until the completion of the reaction (TLC control). Acetonitrile was removed under reduced pressure. EtOAc (15−20 mL) was added to the residue. The resulting mixture was washed with H_2O (3 × 15 mL), the organic layer was separated, and dried over anhydrous Na_2SO_4. Evaporation of solvents under reduced pressure gave a crude product, which was purified by column chromatography on silica gel.

The halogenation of terminal diynes (method B) is described as follows: To a solution of buta-1,3-diyne **5** (1 equiv) in 10 mL of acetone under an atmosphere of an Ar and in the dark was added $AgNO_3$ (3 mol %), and the mixture was stirred at room temperature for 20 min. Then NIS (1.1 equiv) was added, and the mixture was stirred for several hours until the completion of the reaction (TLC control). Acetone was removed under reduced pressure. EtOAc (15−20 mL) was added to the residue. The resulting mixture was washed with H_2O (3 × 15 mL), the organic layer was separated, dried over anhydrous Na_2SO_4, and evaporated under reduced pressure to yield the crude product, which was purified by column chromatography.

*1-Chloro-4-(iodobuta-1,3-diyn-1-yl)benzene (**7a**).* This compound was synthesized in accordance with method B from 1-(buta-1,3-diyn-1-yl)-4-chlorobenzene (**5a**) (200.0 mg, 1.25 mmol). The crude product was purified by column chromatography (eluent: pentane) to afford a yellow solid (323 mg, 91% yield): mp 117−118 °C; ^{1}H NMR ($CDCl_3$, 400.13 MHz, δ) 7.43−7.40 (m, 2H), 7.31−7.28 (m, 2H); ^{13}C{^{1}H} NMR ($CDCl_3$, 100.6 MHz, δ) 135.9 (q), 134.4 (t), 129.0 (t), 119.5 (q), 78.3 (q), 76.0 (q), 72.7 (q), 3.6 (q); IR (cm^{-1}) ν 1896 (C≡C), 2112 (C≡C); HRMS ESI [M + Ag]$^+$ calcd for $C_{10}H_4ClAg^+$ 392.8092, found 392.8076.

*1-(Iodobuta-1,3-diyn-1-yl)-4-nitrobenzene (**7b**).*[80] This compound was synthesized in accordance with method B from 1-(buta-1,3-diyn-1-yl)-4-nitrobenzene (**5b**) (230.0 mg, 1.34 mmol). The crude product was purified by column chromatography (eluent: hexane/EtOAc = 10:1 → 1:1) to afford a light yellow solid (366 mg, 92% yield): ^{1}H NMR (DMSO-d_6, 400.13 MHz, δ) 8.25−8.21 (m, 2H), 7.84−7.81 (m, 2H); ^{13}C{^{1}H} NMR (DMSO-d_6, 100.6 MHz, δ) 147.5 (q), 134.2 (t), 126.8 (q), 123.9 (t), 79.1 (q), 75.9 (q), 70.9 (q), 2.1 (q).

*4-(Iodobuta-1,3-diyn-1-yl)-N,N-dimethylaniline (**7c**).* This compound was prepared using the NIS/DBU (diazabicycloundecene) iodination system.[79] To a solution of 4-(buta-1,3-diyn-1-yl)-*N*,*N*-dimethylaniline (**5c**) (50 mg, 0.295 mmol) in 1 mL of MeCN under an atmosphere of an Ar were added DBU (50 mg, 0.325 mmol) and NIS (73 mg, 0.325 mmol). The reaction mixture was stirred at room temperature for 1 h. Then it was poured into water and extracted with dichloromethane (5 mL × 3). The combined organic layers were washed with brine, dried under anhydrous Na_2SO_4, and concentrated under reduced pressure to yield the crude product, which was purified by column chromatography on silica gel (eluent: hexane/EtOAc = 20:1) to afford a yellow solid (71 mg, 81% yield): ^{1}H NMR ($CDCl_3$, 400 MHz, δ) 7.36 (d, J = 8.9 Hz, 2H), 6.59 (d, J = 8.9 Hz, 2H), 2.99 (s, 6H, $N(CH_3)_2$); ^{13}C{^{1}H} NMR ($CDCl_3$, 100.6 MHz, δ) 150.9 (q), 134.5 (t), 111.7 (t), 106.8 (q), 79.2 (q), 75.8 (q), 73.6 (q), 40.2 (p), 0.4 (q); IR (cm^{-1}) ν 2101 (C≡C), 2188 (C≡C); HRMS ESI [M + H]$^+$ calcd for $C_{12}H_{11}IN^+$ 295.9931, found 295.9924.

*(Iodobuta-1,3-diyn-1-yl)benzene (**7d**).*[146] This compound was synthesized in accordance with method B from buta-1,3-diyn-1-ylbenzene (**5d**) (300.0 mg, 2.38 mmol). The crude product was purified by column chromatography (eluent: hexane/acetone = 100:1) to afford a light brown solid (443 mg, 74% yield): ^{1}H NMR ($CDCl_3$, 400.13 MHz, δ) 7.55−7.45 (m, 2H, Ar), 7.34 (m, 3H, Ar).

*1-(Iodobuta-1,3-diyn-1-yl)-4-methylbenzene (**7e**).* This compound was synthesized in accordance with method A from trimethyl(*p*-tolylbuta-1,3-diyn-1-yl)silane (**6a**) (254.4 mg, 1.20 mmol). The crude product was purified by column chromatography (eluent: hexane/acetone = 100:1) to afford a light brown solid (263 mg, 82% yield): ^{1}H NMR ($CDCl_3$, 400.13 MHz, δ) 7.39 (d, J = 8.0 Hz, 2H), 7.13 (d, J = 8.0 Hz, 2H), 2.36 (s, 3H, CH_3); ^{13}C{^{1}H} NMR ($CDCl_3$, 100.6 MHz, δ) 140.1 (q), 133.1 (t), 129.3 (t), 117.8 (q), 78.6 (q), 74.5 (q), 74.2(q), 21.8 (p), 1.9 (q); HRMS APCI [M + MeOH + H]$^+$ calcd for $C_{12}H_{12}IO^+$ 298.9927, found 298.9928.

*1-(Iodobuta-1,3-diyn-1-yl)-4-methoxybenzene (**7f**).* This compound was synthesized in accordance with method A from ((4-methoxyphenyl)buta-1,3-diyn-1-yl)trimethylsilane (**6b**) (135.0 mg, 0.592 mmol). The crude product was purified by column chromatography (eluent: hexane/acetone = 50:1) to afford a light brown solid (126 mg, 76% yield): ^{1}H NMR ($CDCl_3$, 400.13 MHz, δ) 7.45−7.41 (m, 2H), 6.85−6.82 (m, 2H), 3.93 (s, 3H, OMe); ^{13}C{^{1}H} NMR ($CDCl_3$, 100.6 MHz, δ) 160.7 (q), 134.8 (t), 114.3 (t), 112.8 (q), 78.7 (q), 74.2 (q), 74.0 (q), 55.5 (p), 1.48 (q); HRMS ESI [M + Ag]$^+$ calcd for $C_{11}H_7OIAg^+$ 388.8587, found 388.8595.

*6-Iodohexa-3,5-diyn-1-ol (**7g**).* This compound was synthesized in accordance with method A from 6-(trimethylsilyl)hexa-3,5-diyn-1-ol

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(**6c**) (315.9 mg, 1.90 mmol). The crude product was purified by column chromatography (eluent: hexane/EtOAc = 5:1) to afford a light brown solid (304 mg, 72% yield): ^{1}H NMR ($CDCl_3$, 400.13 MHz, δ) 3.75 (t, J = 6.2 Hz, 2H, CH_2), 2.57 (t, J = 6.2 Hz, 2H, CH_2), 1.80 (s, 1H, OH); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100.6 MHz, δ) 78.5 (q), 73.7 (q), 68.0 (q), 60.8 (s), 23.5 (s), −3.9 (q); HRMS ESI [M + Na]$^+$ calcd for $C_6H_5OINa^+$ 242.9277, found 242.9270.

*1-Iodonona-1,3-diyne (**7h**).* This compound was synthesized in accordance with method A from trimethyl(nona-1,3-diyn-1-yl)silane (**6d**) (51.6 mg, 0.268 mmol). The crude product (light brown liquid) was used in CuAAC without additional purification.

*1-Iodo-5-methoxypenta-1,3-diyne (**7i**).* This compound was synthesized in accordance with method A from (5-methoxypenta-1,3-diyn-1-yl)trimethylsilane (**6e**) (166.0 mg, 1.00 mmol). The crude product was purified by column chromatography (eluent: hexane/EtOAc = 20:1) to afford a light brown solid (198 mg, 90% yield): ^{1}H NMR ($CDCl_3$, 400.13 MHz, δ) 4.20 (s, 2H, CH_2), 3.38 (s, 3H, CH_3); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100.6 MHz, δ) 77.9, 72.1, 71.2, 60.0, 58.0, −0.3; HRMS ESI [M + Ag]$^+$ calcd for $C_6H_5IOAg^+$ 326.8431, found 326.8428.

*6-Iodo-2-methylhexa-3,5-diyn-2-ol (**7j**).* This compound was synthesized in accordance with method B from 2-methylhexa-3,5-diyn-2-ol (**2**) (230.0 mg, 1.34 mmol). The crude product was purified by column chromatography (eluent: hexane/EtOAc = 5:1) to afford a light brown solid (980 mg, 92% yield): ^{1}H NMR ($CDCl_3$, 400.13 MHz, δ) 1.52 (s, 6H, $2CH_3$); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100.6 MHz, δ) 79.2, 77.8, 68.1, 65.5, 31.3, 0.01; HRMS ESI: [M + Na]$^+$ calcd for $C_7H_7IONa^+$ 256.9434, found 256.9428.

*Synthesis of Marker Compounds for the Condition Optimization of CuAAC. 1-Benzyl-4-(p-tolylethynyl)-1H-1,2,3-triazole (**10**).* To the solution of 1-(buta-1,3-diyn-1-yl)-4-methylbenzene (**5e**) (30.0 mg, 0.21 mmol) and benzyl azide **8a** (28.5 mg, 0.21 mmol) in a mixture of THF/H_2O (1:1 w/w, 1.5 mL) were added $CuSO_4{\cdot}5H_2O$ (2.66 mg, 0.011 mmol) and sodium ascorbate (4.23 mg, 0.021 mmol). The reaction mixture was stirred at room temperature for 2 h. After completion of the reaction (TLC control), the reaction mixture was diluted with saturated aqueous solution of NH_4Cl (10 mL) and extracted with ethyl acetate (3 × 15 mL). The combined organic layers were dried under anhydrous Na_2SO_4 and concentrated under reduced pressure to yield the crude product, which was purified by column chromatography on silica gel (eluent: CH_2Cl_2) to afford triazole **10** as a white solid (30 mg, 52% yield): ^{1}H NMR ($CDCl_3$, 400.13 MHz, δ) 7.58 (s, 1H), 7.47−7.35 (m, 5H), 7.30−7.28 (m, 2H), 7.14 (d, J = 7.9 Hz, 2H), 5.55 (s, 2H), 2.36 (s, 3H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 125.7 MHz, δ) 139.1 (q), 134.3 (q), 131.8 (q), 131.6 (t), 129.3 (t), 129.3 (t), 129.1 (t), 128.3 (t), 125.8 (t), 119.4 (q), 92.9 (q), 77.9 (q), 54.5 (s), 21.7 (p); HRMS ESI [M + Na]$^+$ calcd for $C_{18}H_{15}N_3Na^+$ 296.1158, found 296.1155.

*1-(Buta-1,3-diyn-1-yl)-4-methylbenzene (**5e**).*[143] This compound was synthesized in accordance with the general procedure for the synthesis of terminal (buta-1,3-diynyl)arenes by the *retro*-Favorskii reaction from 2-methyl-6-(*p*-tolyl)hexa-3,5-diyn-2-ol (750.0 mg, 3.78 mmol) and KOH (424.5 mg, 7.57 mmol). The crude product was purified by column chromatography (eluent: hexane), which afforded **5e** as a light yellow solid (400 mg, 75% yield); ^{1}H NMR ($CDCl_3$, 400.13 MHz, δ) 7.41 (d, J = 8.1 Hz, 2H), 7.13 (d, J = 8.1 Hz, 2H), 2.45 (s, 1H, C≡CH), 2.36 (s, 3H, CH_3).

*1,8-Di-p-tolylocta-1,3,5,7-tetrayne (**11**).*[147] To the solution of 1-(iodobuta-1,3-diyn-1-yl)-4-methylbenzene (**7e**) (53.2 mg, 0.199 mmol) in acetonitrile (1 mL) were added triethylamine (40.5 mg, 0.399 mmol) and CuI (1.90 mg, 0.01 mmol). The reaction mixture was stirred at room temperature for 18 h. After completion of the reaction (TLC control), the reaction mixture was diluted with a saturated aqueous solution of NH_4Cl (20 mL) and extracted with EtOAc (20 mL). The organic layer was dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The crude product was purified by column chromatography (eluent: hexane/acetone = 100:1), which afforded **11** as a light yellow solid (50.0 mg, 90% yield): ^{1}H NMR ($CDCl_3$, 400.13 MHz, δ) 7.43 (d, J = 7.8 Hz, 4H), 7.15 (d, J = 7.7 Hz, 4H), 2.37 (s, 6H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100.6 MHz, δ) 140.7 (q), 133.3 (t), 129.5 (t), 117.6 (q), 78.2 (q), 74.1 (q), 67.2 (q), 63.9 (q), 21.9 (p).

*General Procedure for the Synthesis of 5-Iodo-4-ethynyl-1H-1,2,3-triazoles **9a−r**.* To an azide (1.00 equiv) in a crew vial were added 1-iodo(buta-1,3-diyne) (1.00 equiv), [CuI(PPh_3)$_3$] (1−5 mol %), and 2,6-lutidine (4 mol %). The thick resulting mixture was vigorously stirred for 4−18 h at room temperature. After completion of the reaction (TLC control), the reaction mixture was diluted with EtOAc (20 mL) and a saturated aqueous solution of NH_4Cl (20 mL). The reaction mixture was shaken; the organic layer was separated, dried over anhydrous Na_2SO_4, and concentrated under reduced pressure to yield the crude product, which was purified by column chromatography on silica gel.

*1-Benzyl-5-iodo-4-(p-tolylethynyl)-1H-1,2,3-triazole (**9a**).* This compound was prepared in accordance with the general procedure from benzyl azide **8a** (53.3 mg, 0.4 mmol), 1-iodo(buta-1,3-diyne) **7e** (106 mg, 0.4 mmol), [CuI(PPh_3)$_3$] (3.91 mg, 1 mol %), and 2,6-lutidine (1.71 mg) with a reaction time of 18 h. The crude product was purified by column chromatography (eluent: hexane/EtOAc = 5:1) to afford a beige solid (141 mg, 88% yield): mp 114−115 °C; ^{1}H NMR ($CDCl_3$, 400.13 MHz, δ) 7.47 (d, J = 8.1 Hz, 2H), 7.38−7.33 (m, 3H), 7.29−7.27 (m, 2H), 7.16 (d, J = 8.1 Hz, 2H), 5.60 (s, 2H, CH_2), 2.37 (s, 3H, CH_3); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100.6 MHz, δ) 139.4 (q), 138.9 (q), 134.0 (q), 131.8 (t), 129.3 (t), 129.1 (t), 128.8 (t), 128.0 (t), 119.2 (q), 95.3 (q), 84.1 (q), 77.8 (q), 54.8 (s), 21.7 (p); IR (cm^{-1}) ν 2224 (C≡C); HRMS ESI [M + Na]$^+$ calcd for $C_{17}H_{14}IN_3Na^+$ 422.0125, found 422.0115.

*1-Benzyl-5-iodo-4-(phenylethynyl)-1H-1,2,3-triazole (**9b**).* This compound was prepared in accordance with the general procedure from benzyl azide **8a** (117 mg, 0.88 mmol), 1-iodo(buta-1,3-diyne) **7d** (221 mg, 0.88 mmol), [CuI(PPh_3)$_3$] (8.57 mg, 1 mol %), and 2,6-lutidine (3.76 mg) with a reaction time of 18 h. The crude product was purified by column chromatography (eluent: hexane/EtOAc = 5:1 → 2:1) to afford a beige solid (285 mg, 84% yield): mp 135−136 °C; ^{1}H NMR ($CDCl_3$, 400.13 MHz, δ) 7.66−7.48 (m, 2H, Ar), 7.38−7.33 (m, 6H, Ar), 7.27−7.30 (m, 2H, Ar), 5.61 (s, 2H, CH_2); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100.6 MHz, δ) 138.8 (q), 134.0 (q), 131.9 (t), 129.1 (t), 129.1 (t), 128.8 (t), 128.5(t), 128.0 (t), 122.2 (q), 95.1 (q), 84.3 (q), 78.5 (q), 54.9 (s); IR (cm^{-1}) ν 2227 (C≡C); HRMS ESI [M + H]$^+$ calcd for $C_{17}H_{13}IN_3^+$ 386.0149, found 386.0142.

*1-Benzyl-5-iodo-4-((4-methoxyphenyl)ethynyl)-1H-1,2,3-triazole (**9c**).* This compound was prepared in accordance with the general procedure from benzyl azide **8a** (64 mg, 0.48 mmol), 1-iodo(buta-1,3-diyne) **7f** (136 mg, 0.48 mmol), [CuI(PPh_3)$_3$] (4.69 mg, 1 mol %), and 2,6-lutidine (2.03 mg) with a reaction time of 18 h. The crude product was purified by column chromatography (eluent: hexane/DCM = 1:3) to afford a white solid (130 mg, 65% yield): mp 110−111 °C; ^{1}H NMR ($CDCl_3$, 400.13 MHz, δ) 7.53−7.49 (m, 2H), 7.39−7.31 (m, 3H), 7.29−7.27 (m, 2H), 6.90−6.86 (m, 2H), 5.60 (s, 2H, CH_2), 3.82 (s, 3H, CH_3O); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100.6 MHz, δ) 160.3 (q), 139.0 (q), 134.0 (q), 133.5 (t), 129.1 (t), 128.8 (t), 127.9 (t), 114.3 (q), 114.2 (t), 95.2 (q), 83.9 (q), 77.2 (q), 55.5 (p), 54.8 (s); IR (cm^{-1}) ν 2221 (C≡C); HRMS ESI [M + Na]$^+$ calcd for $C_{18}H_{14}IN_3ONa^+$ 438.0074, found 438.0056.

*4-((1-Benzyl-5-iodo-1H-1,2,3-triazol-4-yl)ethynyl)-N,N-dimethylaniline (**9d**).* This compound was prepared in accordance with the general procedure from benzyl azide **8a** (29.3 mg, 0.220 mmol), 1-iodo(buta-1,3-diyne) **7c** (65.0 mg, 0.220 mmol), [CuI(PPh_3)$_3$] (4.30 mg, 2 mol %), and 2,6-lutidine (1.00 mg) with a reaction time of 18 h. The crude product was purified by column chromatography (eluent: hexane/acetone = 3:1) to afford a brown solid (69 mg, 73% yield): mp 171−172 °C (with decomposition); ^{1}H NMR ($CDCl_3$, 400.13 MHz, δ) 7.46−7.42 (m, 2H), 7.38−7.30 (m, 3H), 7.30−7.26 (m, 2H), 6.66−6.63 (m, 2H), 5.59 (s, 2H, CH_2), 2.99 (s, 6H, $(CH_3)_2N$); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100.6 MHz, δ) 150.7 (q), 139.5 (q), 134.2 (q), 133.1 (t), 129.1 (t), 128.7 (t), 127.9 (t), 111.8 (t), 108.8 (q), 96.6 (q), 83.5 (q), 76.4 (q), 54.8 (s), 40.3 (p); IR (cm^{-1}) ν 2218 (C≡C); HRMS ESI [M + Na]$^+$ calcd for $C_{19}H_{17}IN_4Na^+$ 451.0390, found 451.0392.

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*1-Benzyl-5-iodo-4-((4-chlorophenyl)ethynyl)-1H-1,2,3-triazole (**9e**).* This compound was prepared in accordance with the general procedure from benzyl azide **8a** (53.5 mg, 0.401 mmol), 1-iodo(buta-1,3-diyne) **7a** (115 mg, 0.401 mmol), [CuI(PPh_3)$_3$] (7.9 mg, 2 mol %), and 2,6-lutidine (1.70 mg) with a reaction time of 18 h. The crude product was purified by column chromatography (eluent: hexane/EtOAc = 1:3) to afford a light brown solid (138 mg, 82% yield): mp 136−137 °C; ^{1}H NMR ($CDCl_3$, 400.13 MHz, δ) 7.51−7.48 (m, 2H), 7.40−7.32 (m, 5H), 7.30−7.28 (m, 2H), 5.61 (s, 2H, CH_2); ^{13}C{^{1}H} NMR ($CDCl_3$, 100.6 MHz, δ) 138.5 (q), 135.3 (q), 133.9 (q), 133.1 (t), 129.1 (t), 128.9 (t), 128.8 (t), 128.0 (t), 120.7 (q), 93.9 (q), 84.4 (q), 79.5 (q), 54.9 (s); IR (cm^{-1}) ν 2223 (C≡C); HRMS ESI [M + Na]$^+$ calcd for $C_{17}H_{11}ClIN_3Na^+$ 441.9578, found 441.9572.

*1-Benzyl-5-iodo-4-((4-nitrophenyl)ethynyl)-1H-1,2,3-triazole (**9f**).* This compound was prepared in accordance with the general procedure from benzyl azide **8a** (20.0 mg, 0.151 mmol), 1-iodo(buta-1,3-diyne) **7b** (45.0 mg, 0.151 mmol), [CuI(PPh_3)$_3$] (7.40 mg, 5 mol %), and 2,6-lutidine (0.650 mg) with a reaction time of 24 h. The crude product was purified by column chromatography (eluent: hexane/EtOAc = 3:1) to afford a light yellow solid (51 mg, 78% yield): ^{1}H NMR (DMSO-d_6, 400.13 MHz, δ) 8.31−8.27 (m, 2H), 7.86−7.83 (m, 2H), 7.47−7.29 (m, 3H), 7.26−7.17 (m, 2H), 5.72 (s, 2H, CH_2); ^{13}C{^{1}H} NMR (DMSO-d_6, 100.6 MHz, δ) 147.2 (q), 136.3 (q), 134.8 (q), 132.6 (t), 128.8 (t), 128.2 (t), 127.9 (q), 127.5 (t), 124.0 (t), 92.0 (q), 91.5 (q), 83.9 (q), 53.9 (s); IR (cm^{-1}) ν 2223 (C≡C), 1592 and 1344 (NO_2); HRMS ESI [M + Na]$^+$ calcd for $C_{17}H_{11}IN_4O_2Na^+$ 452.9819, found 452.9839.

*4-(1-Benzyl-5-iodo-1H-1,2,3-triazol-4-yl)but-3-yn-1-ol (**9g**).* This compound was prepared in accordance with the general procedure from benzyl azide **8a** (60.5 mg, 0.45 mmol), 1-iodo(buta-1,3-diyne) **7g** (100 mg, 0.45 mmol), [CuI(PPh_3)$_3$] (8.88 mg, 2 mol %), and 2,6-lutidine (1.95 mg) with a reaction time of 18 h. The crude product was purified by column chromatography (eluent: DCM/MeOH = 100:1) to afford a white solid (145 mg, 90% yield): mp 124−126 °C; ^{1}H NMR ($CDCl_3$, 400.13 MHz, δ) 7.37−7.32 (m, 3H), 7.29−7.18 (m, 2H), 5.57 (s, 2H, CH_2), 3.84 (t, J = 6.2 Hz, 2H, CH_2), 2.75 (t, J = 6.2 Hz, 2H, CH_2); ^{13}C{^{1}H} NMR ($CDCl_3$, 100.6 MHz, δ) 138.7 (q), 133.9 (q), 129.1 (t), 128.8 (t), 127.9 (t), 93.3 (q), 83.8 (q), 71.7 (q), 60.9 (s), 54.8 (s), 24.1 (s); IR (cm^{-1}) ν 3307 (OH), 2250 (C≡C); HRMS ESI [M + Na]$^+$ calcd for $C_{13}H_{12}IN_3ONa^+$ 375.9917, found 375.9900.

*4-(1-Benzyl-5-iodo-1H-1,2,3-triazol-4-yl)-2-methylbut-3-yn-2-ol (**9h**).* This compound was prepared in accordance with the general procedure from benzyl azide **8a** (85.3 mg, 0.641 mmol), 1-iodo(buta-1,3-diyne) **7j** (150 mg, 0.641 mmol), [CuI(PPh_3)$_3$] (12.5 mg, 2 mol %), and 2,6-lutidine (2.75 mg) with a reaction time of 18 h. The crude product was purified by column chromatography (eluent: hexane/EtOAc = 2:1) to afford a white solid (197 mg, 84% yield): mp 133−135 °C; ^{1}H NMR ($CDCl_3$, 400.13 MHz, δ) 7.39−7.31 (m, 3H), 7.26−7.23 (m, 2H), 5.58 (s, 2H, CH_2), 2.18 (s, 1H, OH), 1.63 (s, 6H, $2CH_3$); ^{13}C{^{1}H} NMR ($CDCl_3$, 100.6 MHz, δ) 138.2 (q), 133.9 (q), 129.1 (t), 128.8 (t), 127.9 (t), 100.0 (q), 84.4 (q), 71.7 (q), 65.7 (q), 54.8 (s), 31.3 (p); IR (cm^{-1}) ν 3426 (OH), 2218 (C≡C); HRMS ESI [M + Na]$^+$ calcd for $C_{14}H_{14}IN_3ONa^+$ 390.0074, found 390.0066.

*5-Iodo-1-(4-methoxybenzyl)-4-(3-methoxyprop-1-yn-1-yl)-1H-1,2,3-triazole (**9i**).* This compound was prepared in accordance with the general procedure from 4-methoxybenzyl azide **8b** (81.5 mg, 0.5 mmol), 1-iodo(buta-1,3-diyne) **7i** (110 mg, 0.5 mmol), [CuI(PPh_3)$_3$] (4.88 mg, 1 mol %), and 2,6-lutidine (2.14 mg) with a reaction time of 18 h. The crude product was purified by column chromatography (eluent: hexane/EtOAc = 5:1) to afford a white solid (142 mg, 74% yield): mp 98.5−100 °C; ^{1}H NMR ($CDCl_3$, 400.13 MHz, δ) 7.25−7.21 (m, 2H), 6.88−6.84 (m, 2H), 5.50 (s, 2H, CH_2), 4.36 (s, 2H, CH_2), 3.79 (s, 3H, OCH_3), 3.46 (s, 3H, OCH_3); ^{13}C{^{1}H} NMR ($CDCl_3$, 100.6 MHz, δ) 160.1 (q), 138.1 (q), 129.6 (t), 126.1 (q), 114.5 (t), 91.3 (q), 84.0 (q), 75.9 (q), 60.3 (s), 57.8 (p), 55.5 (p), 54.5 (s); HRMS ESI [M + Na]$^+$ calcd for $C_{14}H_{14}IN_3O_2Na^+$ 406.0023, found 406.0028.

*5-Iodo-4-(3-methoxyprop-1-yn-1-yl)-1-(3,4,5-trimethoxybenzyl)-1H-1,2,3-triazole (**9j**).* This compound was prepared in accordance with the general procedure from 1,2,3-trimethoxybenzyl azide **8c** (63.9 mg, 0.286 mmol), 1-iodo(buta-1,3-diyne) **7i** (63 mg, 0.286 mmol), [CuI(PPh_3)$_3$] (2.80 mg, 1 mol %), and 2,6-lutidine (1.23 mg) with a reaction time of 18 h. The crude product was purified by column chromatography (eluent: hexane/EtOAc = 3:1) to afford a light beige solid (96 mg, 75% yield): mp 104−106 °C; ^{1}H NMR ($CDCl_3$, 400.13 MHz, δ) 6.53 (s, 2H), 5.49 (s, 2H, CH_2), 4.37 (s, 2H, CH_2), 3.82 (s, 9H, $3OCH_3$), 3.47 (s, 3H, OCH_3); ^{13}C{^{1}H} NMR ($CDCl_3$, 100.6 MHz, δ) 153.7 (q), 138.5 (q), 138.2 (q), 129.3 (q), 105.4 (t), 91.4 (q), 84.3 (q), 75.8 (q), 61.0 (p), 60.3 (s), 57.9 (p), 56.4 (p), 55.1 (s); HRMS ESI [M + Na]$^+$ calcd for $C_{16}H_{18}IN_3O_4Na^+$ 466.0234, found 466.0236.

*Ethyl 2-(5-Iodo-4-(3-methoxyprop-1-yn-1-yl)-1H-1,2,3-triazol-1-yl)acetate (**9k**).* This compound was prepared in accordance with the general procedure from azide **8d** (83.9 mg, 0.65 mmol), 1-iodo(buta-1,3-diyne) **7i** (143 mg, 0.65 mmol), [CuI(PPh_3)$_3$] (6.35 mg, 1 mol %), and 2,6-lutidine (2.79 mg) with a reaction time of 3 h. The crude product was purified by column chromatography (eluent: hexane/EtOAc = 2:1) to afford a white solid (189 mg, 83% yield): mp 80−81 °C; ^{1}H NMR ($CDCl_3$, 400.13 MHz, δ) 5.17 (s, 2H, CH_2), 4.39 (s, 2H, CH_2), 4.28 (q, J = 7.2 Hz, 2H, OCH_2CH_3), 3.48 (s, 3H, OCH_3), 1.30 (t, J = 7.2 Hz, 3H, OCH_2CH_3); ^{13}C{^{1}H} NMR ($CDCl_3$, 100.6 MHz, δ) 165.2 (q), 138.2 (q), 91.4 (q), 85.8 (q), 75.6 (q), 62.8 (s), 60.3 (s), 57.9 (p), 51.8 (s), 14.2 (p); IR (cm^{-1}) ν 1739 (C=O); HRMS ESI [M + Na]$^+$ calcd for $C_{10}H_{12}IN_3O_3Na^+$ 371.9816, found 371.9799.

*4-(Hept-1-yn-1-yl)-5-iodo-1-(4-nitrobenzyl)-1H-1,2,3-triazole (**9m**).* This compound was prepared in accordance with the general procedure from 4-nitrobenzyl azide **8f** (47.8 mg, 0.268 mmol), crude 1-iodo(buta-1,3-diyne) **7h** obtained from trimethyl(nona-1,3-diyn-1-yl)silane **6h** (51.6 mg, 0.268 mmol), [CuI(PPh_3)$_3$] (2.62 mg, 1 mol %), and 2,6-lutidine (1.15 mg) with a reaction time of 18 h. The crude product was purified by column chromatography (eluent: hexane/EtOAc = 5:1 → 3:1) to afford a white solid (92 mg, 81% yield): mp 81−82 °C; ^{1}H NMR ($CDCl_3$, 400.13 MHz, δ) 8.22−8.19 (m, 2H), 7.39 (d, J = 8.2 Hz, 2H), 5.66 (s, 2H, CH_2), 2.48−2.44 (m, 2H, CH_2), 1.66−1.59 (m, 2H, CH_2), 1.48−1.41 (m, 2H, CH_2), 1.37−1.31 (m, 2H, CH_2), 0.92−0.88 (m, 3H, CH_3); ^{13}C{^{1}H} NMR ($CDCl_3$, 100.6 MHz, δ) 148.2 (q), 141.0 (q), 139.6 (q), 128.7 (t), 124.4 (t), 97.5 (q), 83.7 (q), 69.6 (q), 53.8 (s), 31.1 (s), 28.1 (s), 22.3 (s), 19.5 (s), 14.1 (p); IR (cm^{-1}) ν 2251 (C≡C), 1542 and 1347 (NO_2); HRMS ESI [M + H]$^+$ calcd for $C_{16}H_{18}IN_4O_2^+$ 425.0469, found 425.0474.

*6-(4-((4-Chlorophenyl)ethynyl)-5-iodo-1H-1,2,3-triazol-1-yl)-hexan-1-ol (**9n**).* This compound was prepared in accordance with the general procedure from 5-azidohexan-1-ol **8g** (45.0 mg, 0.314 mmol), 1-iodo(buta-1,3-diyne) **7a** (90.0 mg, 0.314 mmol), [CuI-(PPh_3)$_3$] (6.10 mg, 2 mol %), and 2,6-lutidine (1.40 mg) with a reaction time of 49 h. The crude product was purified by column chromatography (eluent: hexane/acetone = 3:1 → 2:1) to afford a beige solid (78 mg, 58% yield): mp 86−87 °C; ^{1}H NMR ($CDCl_3$, 400.13 MHz, δ) 7.52−7.49 (m, 2H), 7.35−7.32 (m, 2H), 4.39 (t, J = 7.2 Hz, 2H, CH_2), 3.64 (t, J = 6.4 Hz, 2H, CH_2), 1.94 (p, J = 7.2 Hz, 2H, CH_2), 1.63−1.51 (m, 2H, CH_2), 1.48−1.34 (m, 5H, $2CH_2$, OH); ^{13}C{^{1}H} NMR ($CDCl_3$, 100.6 MHz, δ) 137.9 (q), 135.2 (q), 133.1 (t), 128.9 (t), 120.8 (q), 93.7 (q), 84.1 (q), 79.6 (q), 62.7 (s), 51.3 (s), 32.5 (s), 29.8 (s), 26.2 (s), 25.2 (s); IR (cm^{-1}) ν 3275 (OH), 2228 (C≡C); HRMS ESI [M + Na]$^+$ calcd for $C_{16}H_{17}ClIN_3ONa^+$ 451.9997, found 451.9980.

*4-((4-Chlorophenyl)ethynyl)-5-iodo-1-(4-methoxyphenyl)-1H-1,2,3-triazole (**9o**).* This compound was prepared in accordance with the general procedure from 1-azido-4-methoxybenzene **8h** (36.5 mg, 0.244 mmol), 1-iodo(buta-1,3-diyne) **7a** (70.0 mg, 0.244 mmol), [CuI(PPh_3)$_3$] (11.9 mg, 5 mol %), and 2,6-lutidine (1.00 mg) with a reaction time of 27 h. The crude product was purified by column chromatography (eluent: hexane/acetone = 3:1) to afford a reddish solid (49 mg, 65%; 71% conversion 1-iodo(buta-1,3-diyne) **7a**): mp 162−163 °C; ^{1}H NMR ($CDCl_3$, 400.13 MHz, δ) 7.56−7.51 (m, 2H),

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7.49−7.43 (m, 2H), 7.38−7.33 (m, 2H), 7.08−7.01 (m, 2H, Ar), 3.90 (s, 3H, OCH_3); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100.6 MHz, δ) 161.1 (q), 138.5 (q), 135.3 (q), 133.2 (t), 129.6 (q), 129.0 (t), 127.4 (t), 120.8 (q), 114.7 (t), 94.1 (q), 85.9 (q), 79.5 (q), 55.8 (p); IR (cm^{-1}) ν 2231 (C≡C); HRMS ESI $[M + H]^+$ calcd for $C_{17}H_{12}ClIN_3O^+$ 435.9708, found 435.9700.

4-(5-Iodo-1-(3,4,5-trimethoxybenzyl)-1H-1,2,3-triazol-4-yl)but-3-yn-1-ol (**9p**). This compound was prepared in accordance with the general procedure from 1,2,3-trimethoxybenzyl azide **8c** (52.7 mg, 0.236 mmol), 1-iodo(buta-1,3-diyne) **7g** (52 mg, 0.236 mmol), $[CuI(PPh_3)_3]$ (4.62 mg, 2 mol %), and 2,6-lutidine (1.01 mg) with a reaction time of 18 h. The crude product was purified by column chromatography (eluent: hexane/EtOAc = 3:1 → 2:1) to afford a white solid (68 mg, 65% yield): mp 161−162.5 °C; ^1H NMR ($CDCl_3$, 400.13 MHz, δ) 6.51 (s, 2H), 5.46 (s, 2H, CH_2), 3.84 (t, J = 6.2 Hz, 2H, CH_2), 3.81 (s, 9H, $3OCH_3$), 2.74 (t, J = 6.2 Hz, 2H, CH_2); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100.6 MHz, δ) 153.7 (q), 138.7 (q), 138.4 (q), 129.4 (q), 105.4 (t), 93.4 (q), 83.7 (q), 71.6 (q), 61.0 (p), 60.9 (s), 56.4 (p), 55.0 (s), 24.0 (s); IR (cm^{-1}) ν 3485 (OH), 2244 (C≡C); HRMS ESI $[M + Na]^+$ calcd for $C_{16}H_{18}IN_3O_4Na^+$ 466.0234, found 466.0233.

4-(1-Hexyl-5-iodo-1H-1,2,3-triazol-4-yl)-2-methylbut-3-yn-2-ol (**9q**). This compound was prepared in accordance with the general procedure from 1-azidohexane **8i** (81.5 mg, 0.641 mmol), 1-iodo(buta-1,3-diyne) **7j** (150 mg, 0.641 mmol), $[CuI(PPh_3)_3]$ (31.3 mg, 5 mol %), and 2,6-lutidine (2.75 mg) with a reaction time of 18 h. The crude product was purified by column chromatography (eluent: hexane/EtOAc = 5:1 → 3:1) to afford a beige solid (112 mg, 48% yield): ^1H NMR ($CDCl_3$, 400.13 MHz, δ) 4.36 (t, J = 7.3 Hz, 2H, CH_2), 2.08 (s, 1H, OH), 1.90−1.88 (m, 2H, CH_2), 1.65 (s, 6H, $2CH_3$), 1.33−1.31 (m, 6H, $3CH_2$), 0.98−0.81 (m, 3H, CH_3); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100.6 MHz, δ) 137.5 (q), 99.7 (q), 84.1 (q), 71.8 (q), 65.7 (q), 51.4 (s), 31.4 (p), 31.2 (s), 29.9 (s), 26.1 (s), 22.5 (s), 14.1 (p); IR (cm^{-1}) ν 3367 (OH), 2225 (C≡C); HRMS ESI $[M + Na]^+$ calcd for $C_{13}H_{20}IN_3ONa^+$ 384.0543, found 384.0543.

Ethyl 2-(4-(3-Hydroxy-3-methylbut-1-yn-1-yl)-5-iodo-1H-1,2,3-triazol-1-yl)acetate (**9r**). This compound was prepared in accordance with the general procedure from azide **8d** (82.7 mg, 0.641 mmol), 1-iodo(buta-1,3-diyne) **7j** (150 mg, 0.641 mmol), $[CuI(PPh_3)_3]$ (12.5 mg, 2 mol %), and 2,6-lutidine (2.75 mg) with a reaction time of 5 h. The crude product was purified by column chromatography (eluent: hexane/EtOAc = 3:1 → 2:1) to afford a light yellow oil (215 mg, 92% yield): ^1H NMR ($CDCl_3$, 400.13 MHz, δ) 5.16 (s, 2H, CH_2), 4.28 (q, J = 7.1 Hz, 2H, OCH_2CH_3), 2.12 (s, 1H, OH), 1.65 (s, 6H, $2CH_3$), 1.30 (t, J = 7.1 Hz, 3H, OCH_2CH_3); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100.6 MHz, δ) 165.2 (q), 138.2 (q), 100.1 (q), 85.7 (q), 71.5 (q), 65.7 (q), 62.7 (s), 51.8 (s), 31.3 (p), 14.2 (p); IR (cm^{-1}) ν 3381 (OH), 2244 (C≡C), 1750 (C=O); HRMS ESI $[M + Na]^+$ calcd for $C_{11}H_{14}IN_3O_3Na^+$ 385.9972, found 385.9969.

General Procedure for the Sonogashira Coupling. 5-Iodo-1*H*-1,2,3-triazoles **9a−c,i,j,p** (1 equiv), CuI (10 mol %), K_3PO_4 (1.1 equiv), and $Pd(PPh_3)_4$ (5 mol %) were placed in a vial. The vial was sealed, and the mixture was evacuated and flushed with Ar several times. THF (1 mL) was added; the mixture was stirred at room temperature for 10 min, and then an alkyne **12a−f** (1.1−2 equiv) was added. The vial with the reaction mixture was placed in a preheated oil bath (65 °C) and stirred at this temperature for 1−16 h (TLC control). After cooling to room temperature, the reaction mixture was filtered through a pad silica gel and the pad was washed with CH_2Cl_2 (3 × 10 mL). The solvent was removed under reduced pressure, and the crude product was purified by column chromatography on silica gel.

1-Benzyl-5-((4-methoxyphenyl)ethynyl)-4-(phenylethynyl)-1H-1,2,3-triazole (**13a**). This compound was prepared in accordance with the general procedure from 5-iodo-1*H*-1,2,3-triazole **9b** (19.3 mg, 0.050 mmol) and 1-ethynyl-4-methoxybenzene **12a** (13.2 mg, 0.100 mmol, 2 equiv) with a reaction time of 16 h. The crude product was purified by chromatography (eluent: hexane/EtOAc = 5:1) to afford a beige solid (15 mg, 77% yield): ^1H NMR ($CDCl_3$, 400.13 MHz, δ) 7.58−7.56 (m, 2H), 7.48−7.42 (m, 2H), 7.38−7.33 (m, 8H), 6.94−6.88 (m, 2H), 5.62 (s, 2H, CH_2), 3.85 (s, 3H, OCH_3); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100.6 MHz, δ) 161.0 (q), 134.5 (q), 133.8 (q), 133.5 (t), 131.9 (t), 129.1 (t), 129.0 (t), 128.8 (t), 128.5 (t), 128.3 (t), 124.2 (q), 122.5 (q), 114.5 (t), 113.2 (q), 103.8 (q), 95.3 (q), 78.5 (q), 72.6 (q), 55.55 (p), 53.4 (s); IR (cm^{-1}) ν 2217 (C≡C); HRMS ESI $[M + H]^+$ calcd for $C_{26}H_{20}N_3O^+$ 390.1601, found 390.1605.

4-(1-Benzyl-4-(phenylethynyl)-1H-1,2,3-triazol-5-yl)-2-methylbut-3-yn-2-ol (**13b**). This compound was prepared in accordance with the general procedure from 5-iodo-1*H*-1,2,3-triazole **9b** (19.6 mg, 0.059 mmol) and 2-methylbut-3-yn-2-ol **12b** (8.6 mg, 0.102 mmol, 2 equiv) with a reaction time of 1 h. The crude product was purified by column chromatography (eluent: benzene/acetone = 10:1 → 5:1) to afford a white solid (15.7 mg, 90% yield): ^1H NMR ($CDCl_3$, 400.13 MHz, δ) 7.64−7.48 (m, 2H), 7.41−7.27 (m, 8H), 5.54 (s, 2H, CH_2), 1.60 (s, 6H, $2CH_3$); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100.6 MHz, δ) 134.4 (q), 134.3 (q), 131.9 (t), 129.1 (t), 129.1 (t), 128.8 (t), 128.6 (t), 128.2 (t), 123.3 (q), 122.3(q), 108.5 (q), 95.4 (q), 78.1 (q), 67.1 (q), 65.8 (q), 53.5 (s), 31.1 (p); IR (cm^{-1}) ν 3367 (OH), 2229 (C≡C); HRMS ESI $[M + Na]^+$ calcd for $C_{22}H_{19}N_3ONa^+$ 364.1420, found 364.1418.

1-Benzyl-4,5-bis((4-methoxyphenyl)ethynyl)-1H-1,2,3-triazole (**13c**). This compound was prepared in accordance with the general procedure from 5-iodo-1*H*-1,2,3-triazole **9c** (21.8 mg, 0.05 mmol) and 1-ethynyl-4-methoxybenzene **12a** (13.2 mg, 0.100 mmol, 2 equiv) with a reaction time of 13 h. The crude product was purified by column chromatography (eluent: C_6H_6/Acetone = 100:1) to afford a yellowish oil (16 mg, 79% yield): ^1H NMR ($CDCl_3$, 400.13 MHz, δ) 7.53−7.47 (m, 2H), 7.46−7.41 (m, 2H), 7.39−7.30 (m, 5H), 6.94−6.89 (m, 2H), 6.89−6.84 (m, 2H), 5.61 (s, 2H, CH_2), 3.85 (s, 3H, OCH_3), 3.82 (s, 3H, OCH_3); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100.6 MHz, δ) 161.0 (q), 160.2 (q), 134.6 (q), 134.1 (q), 133.51 (t), 133.46 (t), 129.0 (t), 128.7 (t), 128.3 (t), 123.8 (q), 114.6 (q), 114.4 (t), 114.2 (t), 113.3 (q), 103.6 (q), 95.5 (q), 77.2 (q), 72.7 (q), 55.5 (p), 55.4 (p), 53.3 (s); IR (cm^{-1}) ν 2215 (C≡C); HRMS ESI $[M + Na]^+$ calcd for $C_{27}H_{21}N_3O_2Na^+$ 442.1526, found 442.1519.

2-((1-Benzyl-4-(p-tolylethynyl)-1H-1,2,3-triazol-5-yl)ethynyl)-N,N-dimethylaniline (**13d**). This compound was prepared in accordance with the general procedure from 5-iodo-1*H*-1,2,3-triazole **9a** (100 mg, 0.250 mmol) and 2-ethynyl-*N*,*N*-dimethylaniline **12c** (40.0 mg, 0.276 mmol, 1.1 equiv) with a reaction time of 5 h. The crude product was purified by column chromatography (eluent: C_6H_6) to afford a white solid (73 mg, 70% yield): ^1H NMR ($CDCl_3$, 400.13 MHz, δ) 7.46−7.42 (m, 2H), 7.41−7.29 (m, 7H), 7.17−7.13 (m, 2H), 6.97−6.85 (m, 2H), 5.63 (s, 2H, CH_2), 2.94 (s, 6H, $N(CH_3)_2$), 2.37 (s, 3H, CH_3); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100.6 MHz, δ) 155.4 (q), 139.3 (q), 134.6 (q), 134.60 (t), 134.0 (q), 131.7 (t), 131.0 (t), 129.3 (t), 129.1 (t), 128.7 (t), 128.2 (t), 124.3 (q), 120.3 (t), 119.4 (q), 117.2 (t), 112.5 (q), 103.4 (q), 95.5 (q), 78.6(q), 78.1 (q), 53.2 (s), 43.7 (p), 21.7 (p); IR (cm^{-1}) ν 2216 (C≡C); HRMS ESI $[M + H]^+$ calcd for $C_{28}H_{25}N_4^+$ 417.2074, found 417.2073. Single crystals of **13d** were grown from the solution in chloroform by the vapor exchange with hexane. Crystallographic data (excluding structure factors) for the structures reported in this work have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC 1869739 (Figure S1).

4-(4-(3-Methoxyprop-1-yn-1-yl)-1-(3,4,5-trimethoxybenzyl)-1H-1,2,3-triazol-5-yl)but-3-yn-1-ol (**13e**). This compound was prepared in accordance with the general procedure from 5-iodo-1*H*-1,2,3-triazole **9j** (66.0 mg, 0.149 mmol) and but-3-yn-1-ol **12d** (15.7 mg, 0.223 mmol, 1.5 equiv) with a reaction time of 7 h.The crude product was purified by column chromatography (eluent: hexane/EtOAc = 2:1 → 1:1) to afford a beige solid (44 mg, 77% yield): mp 73−75 °C; ^1H NMR ($CDCl_3$, 400.13 MHz, δ) 6.55 (s, 2H), 5.43 (s, 2H, CH_2), 4.35 (s, 2H, CH_2), 3.91−3.69 (m, 11H, $3OCH_3$, CH_2), 3.44 (s, 3H, OCH_3), 2.77 (t, J = 6.2 Hz, 2H, CH_2); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100.6 MHz, δ) 153.7 (q), 138.4 (q), 133.2 (q), 129.9 (q), 124.2 (q), 105.5 (t), 102.7 (q), 91.4 (q), 75.5 (q), 66.8 (q), 60.9 (p), 60.5 (s), 60.4 (s), 57.9 (p), 56.4 (p), 53.4 (s), 24.3 (s); IR (cm^{-1}) ν 3411 (OH),

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2242 (C≡C); HRMS ESI $[M + Na]^+$ calcd for $C_{20}H_{23}N_3O_5Na^+$ 408.1530, found 408.1531.

*4-(5-(3-Methoxyprop-1-yn-1-yl)-1-(3,4,5-trimethoxybenzyl)-1H-1,2,3-triazol-4-yl)but-3-yn-1-ol (**13f**).* This compound was prepared in accordance with the general procedure from 5-iodo-1*H*-1,2,3-triazole **9p** (50.0 mg, 0.113 mmol) and 3-methoxyprop-1-yne **12e** (11.9 mg, 0.169 mmol, 1.5 equiv) with a reaction time of 20 h. The crude product was purified by column chromatography (eluent: hexane/EtOAc = 2:1 → 1:1) to afford a yellowish solid (34 mg, 78% yield): ^{1}H NMR ($CDCl_3$, 400.13 MHz, δ) 6.55 (s, 2H), 5.44 (s, 2H, CH_2), 4.38 (s, 2H, CH_2), 3.84−3.81 (m, 11H, $3OCH_3$, CH_2), 3.40 (s, 3H, OCH_3), 2.73 (t, J = 6.2 Hz, 2H, CH_2); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100.6 MHz, δ) 153.7 (q), 138.5 (q), 134.5 (q), 129.7 (q), 122.8 (q), 105.5 (t), 99.7 (q), 95.8 (q), 71.2 (q), 71.1 (q), 60.95 (p), 60.9 (s), 60.4 (s), 58.2 (p), 56.3 (p), 53.6 (s), 24.1 (s); IR (cm^{-1}) ν 3421 (OH), 2246 (C≡C); HRMS ESI $[M + H]^+$ calcd for $C_{20}H_{24}N_3O_5^+$ 386.1710, found 386.1713.

*N-(4-(1-(4-Methoxybenzyl)-4-(3-methoxyprop-1-yn-1-yl)-1H-1,2,3-triazol-5-yl)but-3-yn-1-yl)-4-methylbenzenesulfonamide (**13g**).* This compound was prepared in accordance with the general procedure from 5-iodo-1*H*-1,2,3-triazole **9i** (88.0 mg, 0.230 mmol) and *N*-(but-3-yn-1-yl)-4-methylbenzenesulfonamide **12f** (51.3 mg, 0.230 mmol, 1.0 equiv) with a reaction time of 6 h. The crude product was purified by column chromatography (eluent: C_6H_6/EtOAc = 5:1), followed by recrystallization from benzene to afford a white solid (63.5 mg, 58% yield): mp 113−114 °C; ^{1}H NMR ($CDCl_3$, 400.13 MHz, δ) 7.77−7.67 (m, 2H), 7.30−7.24 (m, 2H), 7.24−7.17 (m, 2H), 6.90−6.82 (m, 2H), 5.42 (s, 2H, CH_2), 5.08 (t, J = 6.5 Hz, NH), 4.34 (s, 2H, CH_2), 3.78 (s, 3H, OCH_3), 3.42 (s, 3H, OCH_3), 3.17 (q, J = 6.5 Hz, 2H, CH_2), 2.70 (t, J = 6.5 Hz, 2H, CH_2), 2.40 (s, 3H, CH_3); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100.6 MHz, δ) 160.0 (q), 143.9 (q), 137.1 (q), 133.5 (q), 129.9 (t), 129.6 (t), 127.1 (t), 126.4 (q), 123.7 (q), 114.4 (t), 101.5 (q), 91.4 (q), 75.5 (q), 67.3 (q), 60.4 (s), 60.95 (p), 57.9 (p), 55.4 (p), 52.8 (s), 41.5 (s), 21.7 (s), 21.6 (p); IR (cm^{-1}) ν 3170 (NH), 2247 (C≡C); HRMS ESI $[M + Na]^+$ calcd for $C_{26}H_{26}N_2O_5SNa^+$ 501.1567, found 501.1563.

General Procedure for the Suzuki Coupling. 5-Iodo-1*H*-1,2,3-triazoles **9c,d,m,o** (1 equiv), $ArB(OH)_2$ **14a−c** (2 equiv), K_3PO_4 (2 equiv), and $Pd(PPh_3)_4$ (5 mol %) were placed in a vial. The vial was sealed, and the mixture was evacuated and flushed with Ar several times. 1,4-Dioxane (1 mL) was added, and the vial with the reaction mixture was placed in a preheated oil bath (100 °C) and stirred for 7−20 h (TLC control). After cooling to rt, the reaction mixture was filtered through a pad silica gel and washed with CH_2Cl_2 (3 × 10 mL). Solvents were removed under reduced pressure, and the crude product was purified by column chromatography on silica gel.

*1-Benzyl-4-((4-methoxyphenyl)ethynyl)-5-(4-(trifluoromethyl)-phenyl)-1H-1,2,3-triazole (**15a**).* This compound was prepared in accordance with the general procedure from 5-iodo-1*H*-1,2,3-triazole **9c** (72.0 mg, 0.173 mmol) and (4-(trifluoromethyl)phenyl)boronic acid **14a** (65.9 mg, 0.347 mmol) with a reaction time of 7 h. The crude product was purified by column chromatography (eluent: hexane/EtOAc = 3:1) to afford a white solid (61 mg, 81% yield): ^{1}H NMR ($CDCl_3$, 400.13 MHz, δ) 7.72 (d, J = 8.1 Hz, 2H), 7.54 (d, J = 8.1 Hz, 2H), 7.41−7.36 (m, 2H), 7.32−7.30 (m, 3H), 7.10−7.07 (m, 2H), 6.89−6.80 (m, 2H), 5.57 (s, 2H, CH_2), 3.81 (s, 3H, OCH_3); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100.6 MHz, δ) 160.3 (q), 137.8 (q), 135.0 (q), 133.3 (t), 131.9 (q), (q, $^2J_{C-F}$ = 32.8 Hz), 131.0 (q), 130.0 (q), 129.7 (t), 129.2 (t), 128.7 (t), 127.2 (t), 126.01 (t), (q, $^3J_{C-F}$ = 3.8 Hz), 123.8 (q), (q, $^1J_{C-F}$ = 272.5 Hz), 114.3 (q), 114.2 (t), 93.8 (q), 77.4 (q), 55.5 (p), 52.8 (s); HRMS ESI $[M + H]^+$ calcd for $C_{25}H_{19}N_3OF_3^+$ 434.1475, found 434.1474. Single crystals of **15a** were grown from the solution in chloroform by the vapor exchange with hexane. Crystallographic data (excluding structure factors) for the structures reported in this work have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC 1869738 (Figure S2).

*4-(1-Benzyl-4-((4-(dimethylamino)phenyl)ethynyl)-1H-1,2,3-triazol-5-yl)benzonitrile (**15b**).* This compound was prepared in accordance with the general procedure from 5-iodo-1*H*-1,2,3-triazole **9d** (60.0 mg, 0.140 mmol) and (4-cyanophenyl)boronic acid **14b** (41.2 mg, 0.280 mmol) with a reaction time of 20 h. The crude product was purified by column chromatography (eluent: hexane/acetone = 3:1) to afford a yellow pale solid (41 mg, 72% yield): ^{1}H NMR ($CDCl_3$, 400.13 MHz, δ) 7.74−7.68 (m, 2H), 7.57−7.53 (m, 2H), 7.33−7.27 (m, 5H), 7.08−7.05 (m, 2H), 6.63−6.57 (m, 2H), 5.58 (s, 2H, CH_2), 2.98 (s, 6H, $N(CH_3)_2$); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100.6 MHz, δ) 136.8 (q), 134.8 (q), 133.0 (t), 132.7 (t), 131.8 (q), 131.1 (q), 129.9 (t), 129.2 (t), 128.7 (t), 127.1 (t), 118.2 (q), 113.5 (q), 111.8 (t), 108.5 (q), 95.7 (q), 76.4 (q), 52.9 (s), 40.2 (p); IR (cm^{-1}) ν 2223 (C≡C, C≡N); HRMS ESI $[M + Na]^+$ calcd for $C_{26}H_{21}N_5Na^+$ 426.1689, found 426.1689. Single crystals of **15b** were grown from the solution in chloroform by the vapor exchange with hexane. Crystallographic data (excluding structure factors) for the structures reported in this work have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC 1869737 (Figure S3).

*4-(Hept-1-yn-1-yl)-5-(4-methoxyphenyl)-1-(4-nitrobenzyl)-1H-1,2,3-triazole (**15c**).* This compound was prepared in accordance with the general procedure from 5-iodo-1*H*-1,2,3-triazole **9m** (60.0 mg, 0.141 mmol) and (4-methoxyphenyl)boronic acid **14c** (43.0 mg, 0.283 mmol) with a reaction time of 7 h. The crude product was purified by column chromatography (eluent: hexane/EtOAc = 3:1) to afford a white solid (35 mg, 61% yield): ^{1}H NMR ($CDCl_3$, 400.13 MHz, δ) 8.18−8.10 (m, 2H), 7.28−7.19 (m, 4H), 6.98−6.92 (m, 2H), 5.59 (s, 2H, CH_2), 3.84 (s, 3H, CH_3), 2.36 (t, J = 7.1 Hz, 2H, CH_2), 1.59−1.49 (m, 2H, CH_2), 1.41−1.19 (m, 4H, $2CH_2$), 0.86 (t, J = 7.0 Hz, 3H, CH_3); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100.6 MHz, δ) 160.9 (q), 148.0 (q), 142.4 (q), 139.0 (q), 130.7 (q), 130.5 (t), 128.1 (t), 124.3 (t), 117.8 (q), 114.7 (t), 95.1 (q), 70.3 (q), 55.5 (p), 51.5 (s), 31.1 (s), 28.1 (s), 22.3 (s), 19.5 (s), 14.1 (p); IR (cm^{-1}) ν 2242 (C≡C), 1524 and 1347 (NO_2); HRMS ESI $[M + H]^+$ calcd for $C_{26}H_{28}N_5O_3^+$ 405.1921, found 405.1910.

*4-((4-Chlorophenyl)ethynyl)-1,5-bis(4-methoxyphenyl)-1H-1,2,3-triazole (**15d**).* This compound was prepared in accordance with the general procedure from 5-iodo-1*H*-1,2,3-triazole **9o** (68.0 mg, 0.156 mmol) and (4-methoxyphenyl)boronic acid **14c** (47.4 mg, 0.312 mmol) with a reaction time of 21 h. The crude product was purified by column chromatography (eluent: hexane/EtOAc = 3:1 → 2:1) to afford a light yellow solid (19 mg, 29% yield): mp 130−131 °C; ^{1}H NMR ($CDCl_3$, 400.13 MHz, δ) 7.46−7.40 (m, 2H), 7.37−7.32 (m, 2H), 7.32−7.30 (m, 2H), 7.29−7.26 (m, 2H), 6.96−6.92 (m, 2H), 6.92−6.88 (m, 2H), 3.85 (s, 3H, OCH_3), 3.83 (s, 3H, OCH_3); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100.6 MHz, δ) 160.6 (q), 160.3 (q), 138.9 (q), 134.8 (q), 132.9 (t), 130.7 (t), 129.5 (q), 129.3 (q), 128.9 (t), 126.7 (t), 121.3 (q), 118.1 (q), 114.7 (t), 114.4 (t), 92.3 (q), 80.8 (q), 55.7 (p), 55.5 (p); HRMS ESI $[M + H]^+$ calcd for $C_{24}H_{19}N_3O_2Cl^+$ 416.1160, found 416.1143.

*2-(1-Benzyl-4-(p-tolylethynyl)-1H-1,2,3-triazol-5-yl)-3-iodo-1-methyl-1H-indole (**16**).* To the solution of compound **13d** (30 mg, 0.072 mmol) in CH_2Cl_2 (1 mL) was added I_2 (0.086 mmol, 1.2 equiv), and the reaction mixture was stirred at room temperature for 2 h. The saturated aqueous solution of $Na_2S_2O_3$ was then added, and the reaction mixture was extracted with EtOAc (3 × 5 mL). The organic layers were dried over anhydrous Na_2SO_4. After filtration and removal of the solvent under reduced pressure, the residue was purified by column chromatography (eluent: benzene/acetone = 100:1) to give the 2-triazolyl-3-iodoindole **16** (28 mg, 74% yield) as a viscous oil: ^{1}H NMR ($CDCl_3$, 400.13 MHz, δ) 7.58−7.53 (m, 1H), 7.39−7.35 (m, 1H), 7.32−7.27 (m, 3H), 7.25−7.14 (m, 2H), 7.09−7.02 (m, 4H), 6.83−6.78 (m, 2H), 5.77 (d, J = 14.5 Hz, 1H), 5.33 (d, J = 14.5 Hz, 1H), 3.07 (s, 3H, NCH_3), 2.31 (s, 3H, CH_3); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100.6 MHz, δ) 139.4 (q), 138.0 (q), 134.3 (q), 133.8 (q), 131.8 (t), 130.2 (q), 130.2 (q), 129.2 (t), 128.8 (t), 128.7 (t), 128.3 (t), 126.7 (q), 124.4 (t), 121.9 (t), 121.3 (t), 119.0 (q), 110.2 (t), 95.0 (q), 77.4 (q), 63.3 (q), 54.3 (s), 31.0 (p), 21.7 (p); HRMS ESI $[M + H]^+$ calcd for $C_{27}H_{22}N_4I^+$ 529.0884, found 529.0890

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ASSOCIATED CONTENT

Supporting Information

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Conditions optimization for the Sonogashira coupling, copies of ^{1}H, $^{13}C\{^{1}H\}$, and DEPT NMR spectra, and X-ray details for compounds **13d** and **15a,b** (PDF)

Crystal data for **15b** (CIF)

Crystal data for **13d** (CIF)

Crystal data for **15a** (CIF)

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Notes

The authors declare no competing financial interest.

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