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A One-Pot Procedure for the Synthesis of "Click-Ready" Triazoles from Ketones

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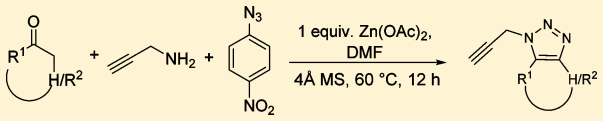
Supporting Information

ABSTRACT: A practical, straightforward, and highly regioselective $Zn(OAc)_2$-mediated method toward propargyl triazoles has been developed for the first time from commercially available enolizable ketones and propargyl amine. Postfunctionalization of this triazole leads to unique N- and C-linked bis-triazoles in excellent yields.



INTRODUCTION

The propargyl group is a key functional group that is widely used in leading-edge research for various applications in organic, medicinal, and material chemistry.[1a−d] For instance, propargyl derivatives have been used as essential starting materials to synthesize various heterocyclic moieties such as triazole, indole, imidazole, and pyrazoline via C−C or C−X (X = O and N) bond formation reactions.[1a−d] Propargyl moieties are also used as starting points in various metathesis and oligomerization reactions.[2b] In medicinal chemistry, this group has been found to be a key functionality in various biologically active molecules. Of the compounds shown in Figure 1,

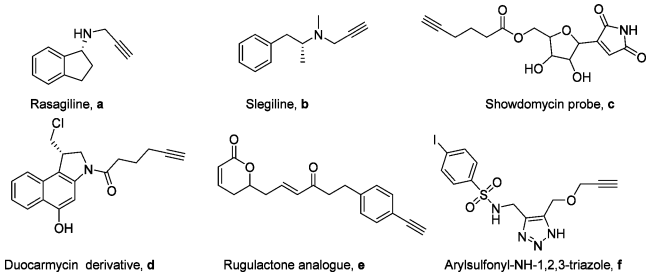
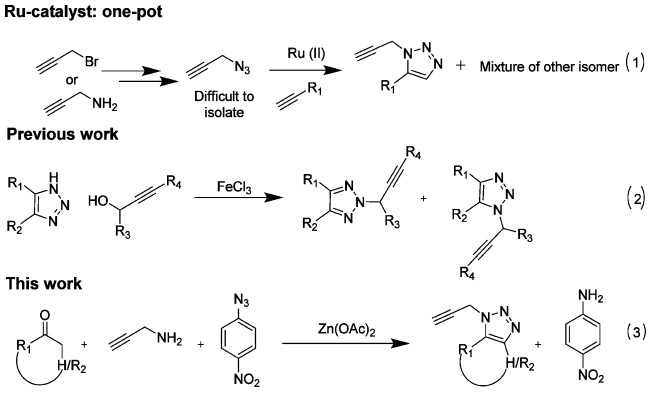


Figure 1. Illustration of pharmaceutically active propargyl moieties.

Rasagiline **a** and slegiline **b** are monoamine oxidase inhibitors and are also known as commercial drugs for Parkinson's disease,[2c] showdomycin probe **c** is attached to a fluorophore to identify diverse enzymes,[2d] duocarmycin derivative **d** exhibits antitumor activity,[2e] rugulactone analogue **e** shows antibacterial activity,[2f] and arylsulfonyl-*NH*-1,2,3-triazole **f** is a VIM-2 β-lactamase inhibitor.[2g] Moreover, propargyl group-functionalized drug molecules are widely used as bioorthogonal tags for detecting druglike activities in cells by spontaneous Raman spectroscopic techniques.[2h]

1,2,3-Triazoles are of great importance in organic synthesis because they are more stable toward biodegradation than their isosteres, such as amide bonds, are.[2a] Cu(I)- and Ru(II)-catalyzed regioselective azide alkyne cycloaddition reactions are widely used to synthesize 1,4- and 1,5-disubstituted 1,2,3-triazoles, respectively.[4] Considering the importance of the triazole moieties, several analogous methodologies have been discovered.[4,5] Interestingly, the N-substituted propargyl triazoles have been scarcely reported. This could be due to the instability of propargyl azide even at room temperature.[6] However, in 2010, Shi and co-workers reported an iron(III)-catalyzed procedure for the preparation of propargyl-substituted triazoles starting from *NH*-triazoles and propargyl alcohols (Scheme 1, eq 2).[7] Unfortunately, the scope of this

Scheme 1. Three Distinct Approaches to N-Substituted Propargyl 1,2,3-Triazole



reaction is limited because of the lack of regioselectivity. Consequently, a cost-effective and general methodology from readily available building blocks is desired to functionalize triazole heterocycles with propargyl functionalities. Such compounds would be very useful for clicking a second moiety to the triazole.

Very recently, we have developed a potent triazolization strategy toward the synthesis of 1,5-disubstituted or fused 1,2,3-triazole from commercially available ketones and amines.[3] Our initial attempts to synthesize the propargyl-substituted triazole

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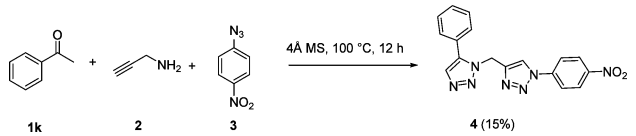
by this method resulted in a complicated reaction mixture that could be due to the elevated temperature (100 °C) used in this reaction. A careful analysis and separation of this crude reaction mixture resulted in the isolation of 15% of the bis-triazole derivative **4**, which was derived from the thermal cycloaddition reaction of 4-nitrophenyl azide with the propargyl group before or after the triazolization reaction (Scheme 2). However, from

Scheme 2. Formation of Undesired Bis-Triazole



the mechanistic study of our previous triazolization reaction, it was evident that enamine formation was the rate-determining step that usually requires 100 °C. Thus, we assumed that the presence of a Lewis acid catalyst could increase the reaction rate by activating the keto group at a comparatively lower temperature, and the subsequent triazolization reaction could also proceed under these relatively mild conditions.

RESULTS AND DISCUSSION

To prove this hypothesis, we initiated our studies with cyclohexanone (1 equiv), propargyl amine (2 equiv), and 4-nitrophenyl azide (1.4 equiv) as standard substrates. Interestingly, initial screening of 10 mol % $Sc(OTf)_3$ in CH_2Cl_2 at 40 °C afforded the triazolization product in ≤39% yield after 24 h (entry 1, Table 1). Inspired by this result, we screened several

Table 1. Optimization of Reaction Conditions[a]

entry	catalyst (mol %)	temp (°C)	solvent	time (h)	yield[b] (%)
1	$Sc(OTf)_3$ (10 mol %)	40	DCM	24	39
2	$Fe(OTf)_3$ (10 mol %)	40	DCM	24	43
3	$Zn(OTf)_3$ (10 mol %)	40	DCM	24	52
4	$BF_3{\cdot}OEt_2$ (10 mol %)	40	DCM	24	32
5	$Zn(OAc)_2$ (10 mol %)	40	DCM	24	54
6	$Zn(OAc)_2$ (50 mol %)	40	DCM	24	62
7	$Zn(OAc)_2$ (100 mol %)	40	DCM	24	67
8	$Zn(OAc)_2$ (100 mol %)	40	DMF	24	66
9	**$Zn(OAc)_2$ (100 mol %)**	**60**	**DMF**	**10**	**75**
10	$Zn(OAc)_2$ (100 mol %)	70	DMF	6	61
11	$Zn(OAc)_2$ (100 mol %)	60	ethanol	10	28
12	$Zn(OAc)_2$ (100 mol %)	60	THF	10	62
13	$Zn(OAc)_2$ (100 mol %)	60	DMSO	10	51
14	$Zn(OAc)_2$ (100 mol %)	60	EtOH	10	13
15	no	60	DMF	10	23

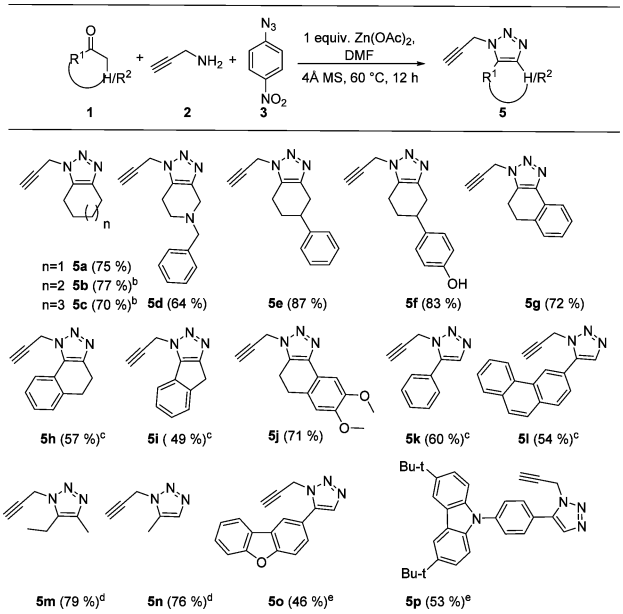
[a]Standard reaction conditions: 1 equiv of cyclohexanone **1a**, 2 equiv of propargyl amine **2a**, 1.4 equiv of 4-nitrophenyl azide **3a**, 40 mg of 4 Å MS, and 1 equiv of $Zn(OAc)_2$ were mixed in a 0.2 mL solution of DMF at 60 °C. [b]Isolated yield.

Lewis acid catalysts such as $Fe(OTf)_3$, $Zn(OTf)_2$, $BF_3{\cdot}OEt_2$, and $Zn(OAc)_2$ in our model reactions (entries 2–5, Table 1). Among these, $Zn(OAc)_2$ showed the best catalytic activity, which gave the expected product in 54% isolated yield (entry 5, Table 1). A gradual increase in the yield was observed when the amount of $Zn(OAc)_2$ was increased from 10 to 100 mol % (entries 5–7, Table 1).

Interestingly, a slight improvement in the yield was observed when we replaced CH_2Cl_2 with DMF (entry 8, Table 1). Further investigation showed that this reaction is highly temperature dependent; increasing the temperature from 40 to 60 °C in DMF resulted in a 75% yield after 10 h (entry 9, Table 1), whereas an increase in temperature from 60 to 70 °C resulted in a diminished yield of 61% (entry 10, Table 1). Among the tested solvents, DMF and CH_2Cl_2 gave the best results, whereas DMSO, THF, and ACN gave moderate yields; a protic solvent such as EtOH afforded a lower yield. As expected, a small amount of desired product was obtained while the reaction was being performed without any Lewis acid catalyst (entry 15, Table 1). We found that cyclohexanone, propargyl amine, and 4-nitrophenyl azide **3** in a respective molar ratio of 1:2:1.4 using 1 equiv of $Zn(OAc)_2$ in a 2.5 M solution of DMF over a period of 10 h at 60 °C afforded **5** in 75% yield.

With these optimized conditions in hand, the scope of this triazolization reactions was investigated. An array of cyclic ketones were employed in the optimized reaction condition, which afforded the propargyl-functionalized triazole derivatives **5a–5f** in good yields regardless of the size of the cyclic ketones (Scheme 3). Similarly, screening of different aromatic bicyclic

Scheme 3. Substrate Scope with Respect to a Variety of Ketones[a]



[a]Reaction conditions: **1** (1 equiv), **2** (2 equiv), **3** (1.4 equiv), $Zn(OAc)_2$ (1 equiv), DMF (0.4 mL), 60 °C, 10 h, isolated yields. [b]Eight hours. [c]Twenty-four hours. [d]At 40 °C for 24 h. [e]Thirty-six hours.

ketones also led to corresponding products **5g–5j** in excellent yields (Scheme 3). It is worth mentioning that high regioselectivity was observed for product **5g** derived from 2-tetralone (Scheme 3). Evidently, product formation occurs through the cycloaddition of azide with the more stable enamine conjugated to the aromatic ring.

Next, we investigated the scope of the reaction with respect to acetyl-substituted aromatic hydrocarbons such as acetophenone and 3-acetyl phenanthrene, which delivered moderate yields of the expected products under the optimized reaction

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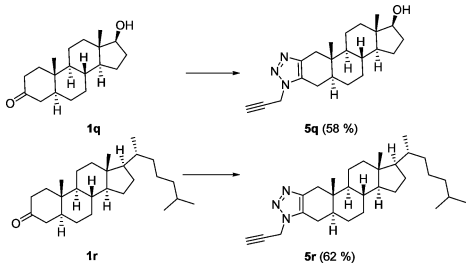
circumstances (**5k** and **5l**) (Scheme 3). The extension of this protocol to symmetrical acyclic ketones resulted in the formation of 1,4,5-trisubstituted 1,2,3-triazoles in good yields (**5m** and **5n**) (Scheme 3). The utility of this reaction is further proved in heterocycles of interest in material research such as dibenzofuran and carbazole. Thus, this triazolization strategy decorated these useful heterocycles with propargyl groups (**5o** and **5p**) (Scheme 3) in good yields even though these reactions required reaction times longer than those used with the previously optimized conditions.

Modification of natural products such as alkaloids, nucleosides, and steroids with propargyl groups for various applications such as Cu(I)-triggered immobilization is of interest in the area of medicinal chemistry.[2a] By taking into account the fact that enolizable ketones are abundantly available in various natural products, this protocol provides an easy pathway for the functionalization of natural products with a "clickable" propargyl group. The application of this methodology to dihydrotestosterone **1q**, an androgen hormone, led to highly regioselective 2,3-A-ring-fused triazole **5q** in good yield. In a similar manner, cholesterol-derived cholestan-3-one **1r** under these reaction circumstances afforded A-ring-fused triazole **5r** in good yield (Scheme 4).

Scheme 4. Substrate Scope with Respect to the Natural Products



Thus, to prove the usefulness of these propargyl-substituted triazoles, a series of bis-triazole derivatives **7a**–**7g** (Figure 2) have been prepared via CuAAc click reaction. Although there are several reports on C–C- and N–N-linked bis-triazole formation, a suitable methodology for formation of N–C-linked unsymmetrical bis-triazoles is still lacking.[8] For instance, here we report for the first time a N–C-linked bis-triazole hybrid of porphyrin and carbazole **7a** (entry 1). Barthélémy et al. reported that the rate of uptake of oligonucleotide increased many-fold across the cell membrane when it is attached with lipophilic cholesterol with a triazole linkage.[9] As a possible alternative to this previously reported synthetic strategy, we also developed a bis-triazole-linked compound **7b** derived from azidothymidine (AZT) **6b** and propargyl-derived choleston-3-one **5r** in a straightforward manner (entry 2, Figure 2). Amphiphilic cholesterol derivative **7c** has been prepared in good yield from cholesterol **5r** and triethylene glycol azide **6c** (entry 3).[10] Propargyl-substituted steroid **5q** was further functionalized with azido sugar **6d**, leading to a new type of bis-triazole hybrid system **7d** in excellent yield (entry 4). Sugar azide **6e** also coupled with propargyl triazole **4k** to give **7e** in excellent yield (entry 5).

On the basis of previously reported work, here we have proposed a plausible mechanism for this reaction (Figure 3). Initially, enamine is formed from propargyl amine and enolizable ketone in a Lewis acid-mediated reaction. Then the enamine undergoes cycloaddition with azide to form a triazoline intermediate. Subsequently, the triazoline intermediate leads to the desired product via ring opening and ring closing intermediates with the elimination of a molecule of 4-nitrophenyl aniline.

In conclusion, we have developed a highly efficient and regiospecific $Zn(OAc)_2$-mediated synthesis of propargyl-functionalized triazole derivatives in a single step from ketones and propargyl amine. Subsequently, Cu(I) reactions of these propargyl triazoles with various organic azides having supramolecular and medicinal interest lead to novel N–C-linked bis-triazole moieties in a regioselective manner in excellent yield. This newly developed method has the following advantages. (1) It gives access in a single step to propargyl triazoles, which is not possible by any other reported method. (2) It uses cheap and readily available building blocks. (3) It can be extended to natural products containing enolizable ketone groups. Considering the importance of these products, we believe that this methodology could attract attention for various applications in the field of medicinal and material chemistry. Further studies of these propargyl triazole analogues for medicinal chemistry applications as well as for metal ligand binding studies are under investigation and will be reported in due course.

EXPERIMENTAL SECTION

General Information. NMR spectra were recorded on commercial instruments, and chemical shifts (δ) are reported in parts per million referenced to tetramethylsilane (^{1}H) or the internal (NMR) solvent signal (^{13}C). Exact mass measurements were taken on a mass spectrometer in ESI mode at a resolution of 60000. For column chromatography, 70–230 mesh silica 60 was used as the stationary phase. Chemicals received from commercial sources were used without further purification. Reaction solvent DMF was used as received from a commercial source.

General Procedure for the Preparation of Propargyl-Substituted 1,2,3-Triazoles. To an oven-dried screw-capped reaction tube equipped with a magnetic stirring bar were added the ketone, propargyl amine, 4-nitrophenyl azide, $Zn(OAc)_2$, and 4 Å molecular sieves. The mixture was dissolved in DMF (0.4 mL) and stirred at 60 °C for 10–36 h. Upon completion of the reaction, the solvent was removed *in vacuo*. The crude reaction mixture was then directly purified by column chromatography (silica gel) at first with CH_2Cl_2 as the eluent to remove all the 4-nitroaniline formed during the reaction followed by using a mixture of heptane and ethyl acetate as the eluent to afford the corresponding propargyl-substituted 1,2,3-triazoles as off-white solids or semisolids.

*1-(Prop-2-yn-1-yl)-4,5,6,7-tetrahydro-1H-benzo[d][1,2,3]triazole (**5a**).* Cyclohexanone (100 mg, 1.019 mmol), propargyl amine (112 mg, 2.038 mmol), 4-nitrophenyl azide (234 mg, 1.4266 mmol), zinc acetate (187 mg, 1.019 mmol), 4 Å molecular sieves (40 mg), and DMF (0.4 mL) were used. The reaction time was 10 h. The product was purified by flash column chromatography (CH_2Cl_2 followed by a 3:2 heptane/EtOAc mixture), affording **5a** (123 mg, 75% yield) as an off-white semisolid: ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.05 (t, J = 2.1 Hz, 2H), 2.73 (dd, J = 13.3, 6.8 Hz, 4H), 2.45 (t, J = 2.6 Hz, 1H), 1.90–1.77 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 144.1, 132.23, 75.6, 74.6, 37.6, 22.6, 22.4, 21.9, 20.1; HRMS (ESI$^+$) m/z calcd for $C_9H_{11}N_3$ $[M + H]^+$ 162.1025, found 162.1034.

*1-(Prop-2-yn-1-yl)-1,4,5,6,7,8-hexahydrocyclohepta[d][1,2,3]-triazole (**5b**).* Cycloheptanone (100 mg, 0.891 mmol), propargyl amine (98 mg, 1.783 mmol), 4-nitrophenyl azide (204 mg, 1.2474 mmol), zinc acetate (164 mg, 0.891 mmol), 4 Å molecular sieves (40 mg), and DMF (0.4 mL) were used. The reaction time was 8 h. The product was purified by flash column chromatography (CH_2Cl_2 followed by a 3:2 heptane/EtOAc mixture), affording **5b** (125 mg, 77% yield) as an off-white semisolid: ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.06 (d, J = 2.6 Hz, 2H), 2.92–2.78 (m, 4H), 2.43 (t, J = 2.6 Hz, 1H),

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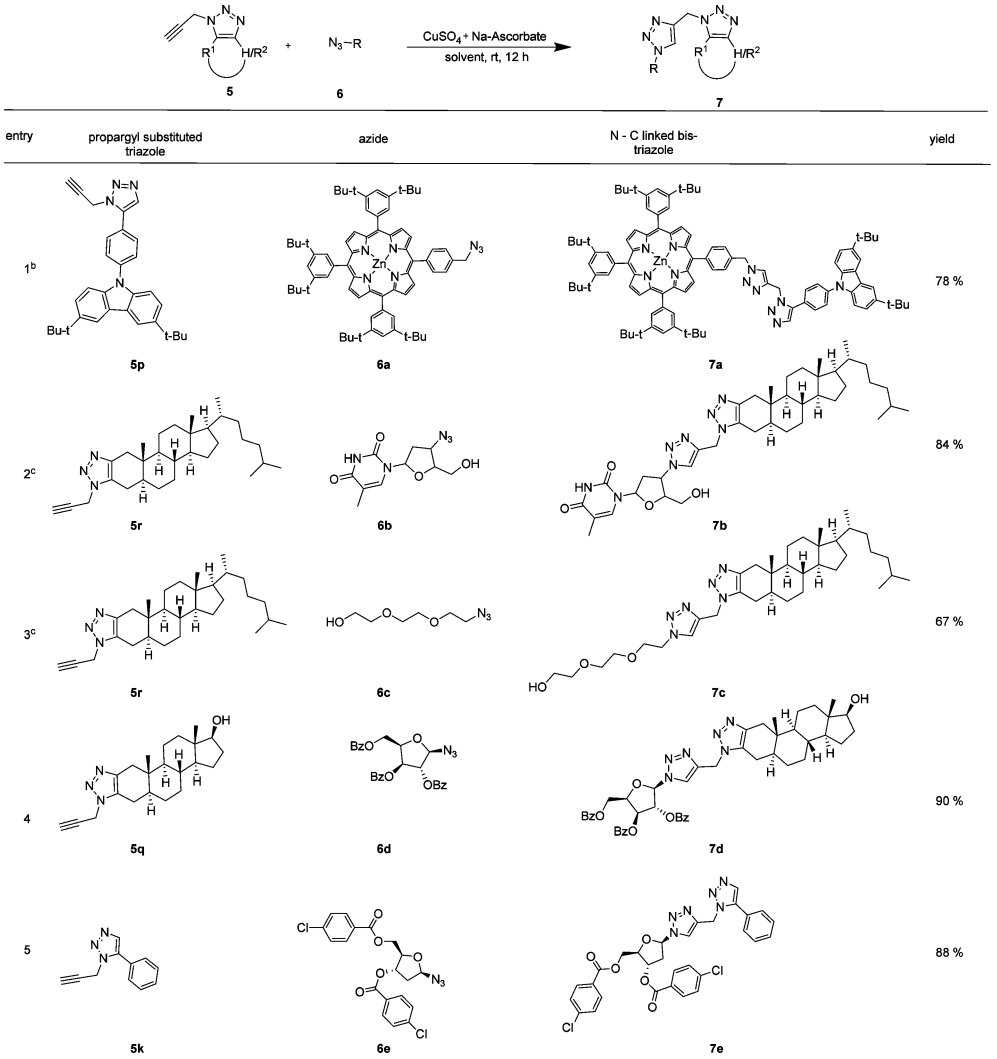

Figure 2. Synthesis of N−C-linked unsymmetrical bis-triazole derivatives. Footnote a: **4** (1 equiv), **5** (1.2 equiv), $CuSO_4$ (0.05 equiv), sodium ascorbate (0.11 equiv), rt, 12 h, isolated yield. Footnote b: *t*-BuOH/H_2O/DCM (1:1:1), 6 h. Footnote c: *t*-BuOH/H_2O/THF (1:1:1), 36 h.

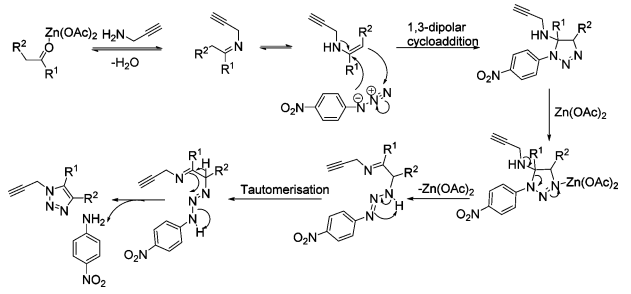

Figure 3. Proposed mechanism for the formation of propargyl triazole.

1.91−1.81 (m, 2H), 1.80−1.68 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 147.8, 135.1, 76.01, 74.4, 37.9, 30.8, 27.3, 27.2, 26.8, 24.2; HRMS (ESI$^+$) *m*/*z* calcd for $C_{10}H_{13}N_3$ [M + H]$^+$ 176.1182, found 176.1193.

*1-(Prop-2-yn-1-yl)-4,5,6,7,8,9-hexahydro-1H-cycloocta[d][1,2,3]-triazole (**5c**).* Cyclooctanone (100 mg, 0.782 mmol), propargyl amine (87 mg, 1.585 mmol), 4-nitrophenyl azide (179 mg, 1.0948 mmol), zinc acetate (145 mg, 0.792 mmol), 4 Å molecular sieves (40 mg), and DMF (0.4 mL) were used. The reaction time was 8 h. The product was purified by flash column chromatography (CH_2Cl_2 followed by a 3:2 heptane/EtOAc mixture), affording **5c** (105 mg, 70% yield) as an off-white semisolid: ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.06 (d, *J* = 2.6 Hz, 2H), 2.95−2.83 (m, 4H), 2.45 (t, *J* = 2.6 Hz, 1H), 1.92−1.84 (m, 2H), 1.80−1.71 (m, 2H), 1.59−1.41 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 145.2, 133.4, 76.1, 74.5, 37.7, 28.1, 26.0, 25.9, 24.7, 24.5, 21.7; HRMS (ESI$^+$) *m*/*z* calcd for $C_{11}H_{15}N_3$ [M + H]$^+$ 190.1338, found 190.1336.

*5-Benzyl-1-(prop-2-yn-1-yl)-4,5,6,7-tetrahydro-1H-[1,2,3]triazolo-[4,5-c]pyridine (**5d**).* 1-Benzylpiperidin-4-one (100 mg, 0.528 mmol), propargyl amine (58.2 mg, 1.057 mmol), 4-nitrophenyl azide (121 mg, 0.7392 mmol), zinc acetate (97 mg, 0.528 mmol), 4 Å molecular sieves (40 mg), and DMF (0.4 mL) were used. The reaction time was 10 h. The product was purified by flash column chromatography (CH_2Cl_2 followed by a 3:2 heptane/EtOAc mixture), affording **5d** (85 mg, 64% yield) as an off-white semisolid: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.35−7.26 (m, 5H), 5.07 (d, *J* = 2.6 Hz, 2H), 3.76 (s, 2H), 3.69 (s, 2H), 2.83 (s, 4H), 2.46 (t, *J* = 2.6 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 143.1, 138.0, 131.0, 129.1, 128.5, 127.5, 75.3, 75.0, 61.8, 49.8, 49.2, 37.9, 21.0; HRMS (ESI$^+$) *m*/*z* calcd for $C_{15}H_{16}N_4$ [M + H]$^+$ 253.1447, found 253.1451.

*5-Phenyl-1-(prop-2-yn-1-yl)-4,5,6,7-tetrahydro-1H-benzo[d]-[1,2,3]triazole (**5e**).* 4-Phenylcyclohexan-1-one (100 mg, 0.574 mmol), propargyl amine (63.2 mg, 1.148 mmol), 4-nitrophenyl azide (132 mg, 0.8036 mmol), zinc acetate (105 mg, 0.574 mmol), 4 Å molecular sieves (40 mg), and DMF (0.4 mL) were used. The reaction time was 10 h. The product was purified by flash column chromatography (CH_2Cl_2 followed by a 3:2 heptane/EtOAc mixture), affording **5e** (118 mg, 87% yield) as an off-white semisolid: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40−7.32 (m, 2H), 7.27−7.23 (m, 3H), 5.1−5.0 (m, 2H),

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3.13 (dd, J = 15.4, 4.9 Hz, 1H), 3.06−2.96 (m, 1H), 2.93−2.76 (m, 3H), 2.47 (t, J = 2.6 Hz, 1H), 2.26−2.17 (m, 1H), 2.09−1.96 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 144.93, 144.35, 132.04, 128.76, 126.98, 126.75, 75.50, 74.84, 40.61, 37.86, 30.03, 29.73, 20.12; HRMS (ESI$^+$) m/z calcd for $C_{15}H_{15}N_3$ [M + H]$^+$ 238.1338, found 238.1338.

4-[1-(Prop-2-yn-1-yl)-4,5,6,7-tetrahydro-1H-benzo[d][1,2,3]-triazol-5-yl]phenol (**5f**). 4-(4-Hydroxyphenyl)cyclohexan-1-one (100 mg, 0.526 mmol), propargyl amine (87.9 mg, 1.051 mmol), 4-nitrophenyl azide (121 mg, 0.7364 mmol), zinc acetate (96 mg, 0.526 mmol), 4 Å molecular sieves (40 mg), and DMF (0.4 mL) were used. The reaction time was 10 h. The product was purified by flash column chromatography (CH_2Cl_2 followed by a 3:2 heptane/EtOAc mixture), affording **5f** (110 mg, 83% yield) as an off-white solid: mp 186−187 °C; ^{1}H NMR (300 MHz, DMSO-d_6) δ 9.21 (s, 1H), 7.11 (d, J = 8.5 Hz, 2H), 6.71 (d, J = 8.5 Hz, 2H), 5.24 (d, J = 2.5 Hz, 2H), 3.55 (t, J = 2.6 Hz, 1H), 2.90−2.80 (m, 3H), 2.78−2.60 (m, 2H), 2.08−1.79 (m, 2H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 155.75, 143.17, 135.49, 132.04, 127.75, 115.13, 77.05, 76.69, 36.99, 29.76, 29.41, 19.29; HRMS (ESI$^+$) m/z calcd for $C_{15}H_{15}N_3O_1$ [M + H]$^+$ 254.1287, found 254.1291.

3-(Prop-2-yn-1-yl)-4,5-dihydro-3H-naphtho[1,2-d][1,2,3]triazole (**5g**). 3,4-Dihydronaphthalen-2(1*H*)-one (100 mg, 0.684 mmol), propargyl amine (75 mg, 1.368 mmol), 4-nitrophenyl azide (157 mg, 0.9576 mmol), zinc acetate (126 mg, 0.684 mmol), 4 Å molecular sieves (40 mg), and DMF (0.4 mL) were used. The reaction time was 10 h. The product was purified by flash column chromatography (CH_2Cl_2 followed by a 3:2 heptane/EtOAc mixture), affording **5g** (103 mg, 72% yield) as an off-white solid: mp 86.5−87.5 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.93 (d, J = 7.4 Hz, 1H), 7.34−7.27 (m, 1H), 7.25−7.18 (m, 2H), 5.15 (d, J = 2.6 Hz, 2H), 3.21−2.94 (m, 4H), 2.48 (t, J = 2.6 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 144.2, 133.5, 132.9, 128.5, 128.3, 127.7, 127.4, 122.1, 75.3, 75.1, 38.0, 28.5, 19.1; HRMS (ESI$^+$) m/z calcd for $C_{13}H_{11}N_3$ [M + H]$^+$ 210.1025, found 210.1026.

1-(Prop-2-yn-1-yl)-4,5-dihydro-1H-naphtho[1,2-d][1,2,3]triazole (**5h**). 3,4-Dihydronaphthalen-1(2*H*)-one (100 mg, 0.684 mmol), propargyl amine (75 mg, 1.368 mmol), 4-nitrophenyl azide (157 mg, 0.9576 mmol), zinc acetate (126 mg, 0.684 mmol), 4 Å molecular sieves (40 mg), and DMF (0.4 mL) were used. The reaction time was 10 h. The product was purified by flash column chromatography (CH_2Cl_2 followed by a 3:2 heptane/EtOAc mixture), affording **5h** (82 mg, 57% yield) as an off-white semisolid: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74 (d, J = 7.4 Hz, 1H), 7.38−7.28 (m, 3H), 5.38 (d, J = 2.2 Hz, 2H), 3.12−2.89 (m, 4H), 2.51 (s, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 145.7, 137.3, 131.5, 129.3, 128.9, 127.4, 124.8, 123.1, 76.1, 75.6, 39.7, 30.3, 20.8; HRMS (ESI$^+$) m/z calcd for $C_{13}H_{11}N_3$ [M + H]$^+$ 210.1025, found 210.1029.

3-(Prop-2-yn-1-yl)-3,8-dihydroindeno[1,2-d][1,2,3]triazole (**5i**). 2,3-Dihydro-1*H*-inden-1-one (100 mg, 0.757 mmol), propargyl amine (83 mg, 1.513 mmol), 4-nitrophenyl azide (173 mg, 1.0598 mmol), zinc acetate (139 mg, 0.757 mmol), 4 Å molecular sieves (40 mg), and DMF (0.4 mL) were used. The reaction time was 10 h. The product was purified by flash column chromatography (CH_2Cl_2 followed by a 3:2 heptane/EtOAc mixture), affording **5i** (72 mg, 49% yield) as an off-white semisolid: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.79−7.75 (m, 1H), 7.56 (dd, J = 6.6, 0.8 Hz, 1H), 7.41 (td, J = 7.3, 3.9 Hz, 1H), 7.35 (td, J = 7.5, 1.4 Hz, 1H), 5.37 (d, J = 2.6 Hz, 2H), 3.77 (s, 2H), 2.56 (t, J = 2.6 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 156.0, 147.7, 141.5, 129.5, 127. 6, 127.4, 126.7, 121.0, 75.6, 75.5, 39.2, 29.2; HRMS (ESI$^+$) m/z calcd for $C_{12}H_9N_3$ [M + H]$^+$ 196.0869, found 196.0874.

7,8-Dimethoxy-3-(prop-2-yn-1-yl)-4,5-dihydro-3H-naphtho[1,2-d][1,2,3]triazole (**5j**). 6,7-Dimethoxy-3,4-dihydronaphthalen-1(2H)-one (100 mg, 0.485 mmol), propargyl amine (53.4 mg, 0.97 mmol), 4-nitrophenyl azide (111 mg, 0.679 mmol), zinc acetate (89 mg, 0.485 mmol), 4 Å molecular sieves (40 mg), and DMF (0.4 mL) were used. The reaction time was 10 h. The product was purified by flash column chromatography (CH_2Cl_2 followed by a 3:2 heptane/EtOAc mixture), affording **5j** (92 mg, 71% yield) as an off-white solid: mp 147−148 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.48 (s, 1H), 6.77 (s, 1H), 5.15 (d, J = 2.6 Hz, 2H), 3.95 (s, 3H), 3.89 (s, 3H), 3.04 (s, 4H), 2.49 (t, J = 2.6 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 148.4, 148.4, 144.3, 131.9, 125.8, 121.2, 111.8, 105.6, 75.3, 75.1, 56.2, 56.1, 38.01, 28.1, 19.3; HRMS (ESI$^+$) m/z calcd for $C_{15}H_{15}N_3O_2$ [M + H]$^+$ 270.1236, found 270.1242.

5-Phenyl-1-(prop-2-yn-1-yl)-1H-1,2,3-triazole (**5k**). Acetophenone (100 mg, 0.832 mmol), propargyl amine (92 mg, 1.665 mmol), 4-nitrophenyl azide (191 mg, 1.165 mmol), zinc acetate (153 mg, 0.832 mmol), 4 Å molecular sieves (40 mg), and DMF (0.4 mL) were used. The reaction time was 24 h. The product was purified by flash column chromatography (CH_2Cl_2 followed by a 3:2 heptane/EtOAc mixture), affording **5k** (91 mg, 60% yield) as an off-white semisolid: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.75 (s, 1H), 7.63−7.47 (m, 5H), 5.13 (d, J = 2.6 Hz, 2H), 2.48 (t, J = 2.6 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 138.1, 133.1, 129.9, 129.3, 129.0, 128.8, 126.5, 76.6, 74.9, 38.3; HRMS (ESI$^+$) m/z calcd for $C_{11}H_9N_3$ [M + H]$^+$ 184.0869, found 184.0869.

5-(Phenanthren-3-yl)-1-(prop-2-yn-1-yl)-1H-1,2,3-triazole (**5l**). 1-(Phenanthren-3-yl)ethan-1-one (100 mg, 0.454 mmol), propargyl amine (50 mg, 0.908 mmol), 4-nitrophenyl azide (104 mg, 0.636 mmol), zinc acetate (83 mg, 0.454 mmol), 4 Å molecular sieves (40 mg), and DMF (0.4 mL) were used. The reaction time was 24 h. The product was purified by flash column chromatography (CH_2Cl_2 followed by a 3:2 heptane/EtOAc mixture), affording **5l** (70 mg, 54% yield) as an off-white solid: mp 126−127 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.81 (d, J = 8.7 Hz, 1H), 8.72 (d, J = 8.0 Hz, 1H), 8.08 (d, J = 1.8 Hz, 1H), 7.94 (dd, J = 7.7, 1.4 Hz, 1H), 7.89 (s, 1H), 7.85 (d, J = 8.9 Hz, 1H), 7.81−7.76 (m, 2H), 7.75−7.64 (m, 2H), 5.22 (d, J = 2.6 Hz, 2H), 2.51 (t, J = 2.5 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 138.0, 133.4, 132.6, 132.2, 131.0, 129.8, 128.9, 128.9, 128.5, 127.6, 127.3, 126.6, 126.4, 124.4, 123.8, 123.0, 75.1, 38.5; HRMS (ESI$^+$) m/z calcd for $C_{19}H_{13}N_3$ [M + H]$^+$ 284.1182, found 284.1187.

5-Ethyl-4-methyl-1-(prop-2-yn-1-yl)-1H-1,2,3-triazole (**5m**). Pentan-3-one (100 mg, 1.161 mmol), propargyl amine (128 mg, 2.322 mmol), 4-nitrophenyl azide (267 mg, 1.625 mmol), zinc acetate (213 mg, 1.161 mmol), 4 Å molecular sieves (40 mg), and DMF (0.4 mL) were used. The reaction time was 24 h. The product was purified by flash column chromatography (CH_2Cl_2 followed by a 4:1 heptane/EtOAc mixture), affording **5m** (137 mg, 79% yield) as an off-white semisolid: ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.06 (d, J = 2.6 Hz, 2H), 2.76 (q, J = 7.6 Hz, 2H), 2.44 (t, J = 2.6 Hz, 1H), 2.29 (s, 3H), 1.24 (t, J = 7.6 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 141.0, 134.6, 76.2, 74.5, 37.9, 16.1, 13.0, 10.5; HRMS (ESI$^+$) m/z calcd for $C_8H_{11}N_3$ [M + H]$^+$ 150.1025, found 150.1022.

5-Methyl-1-(prop-2-yn-1-yl)-1H-1,2,3-triazole (**5n**). Acetone (71 mg, 1.219 mmol), propargyl amine (47.9 mg, 0.870 mmol), 4-nitrophenyl azide (100 mg, 0.609 mmol), zinc acetate (79 mg, 0.433 mmol), 4 Å molecular sieves (40 mg), and DMF (0.4 mL) were used. The reaction time was 24 h. The product was purified by flash column chromatography (CH_2Cl_2 followed by a 4:1 heptane/EtOAc mixture), affording **5n** (56 mg, 76% yield) as an off-white semisolid: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.47 (s, 1H), 5.11 (d, J = 2.6 Hz, 2H), 2.47 (t, J = 2.6 Hz, 1H), 2.42 (d, J = 0.7 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 133.5, 133.0, 75.4, 74.8, 37.7, 8.5; HRMS (ESI$^+$) m/z calcd for $C_6H_7N_3$ [M + H]$^+$ 122.0712, found 122.0705.

5-(Dibenzo[b,d]furan-2-yl)-1-(prop-2-yn-1-yl)-1H-1,2,3-triazole (**5o**). 1-(Dibenzo[*b*,*d*]furan-2-yl)ethan-1-one (100 mg, 0.476 mmol), propargyl amine (52.4 mg, 0.951 mmol), 4-nitrophenyl azide (109 mg, 0.666 mmol), zinc acetate (87 mg, 0.476 mmol), 4 Å molecular sieves (40 mg), and DMF (0.4 mL) were used. The reaction time was 36 h. The product was purified by flash column chromatography (CH_2Cl_2 followed by a 6:4 heptane/EtOAc mixture), affording **5o** (60 mg, 46% yield) as an off-white solid: mp 93−94 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.13 (d, J = 1.4 Hz, 1H), 7.99 (dd, J = 7.7, 0.6 Hz, 1H), 7.82 (s, 1H), 7.73−7.69 (m, 1H), 7.66−7.58 (m, 2H), 7.57−7.51 (m, 1H), 7.41 (td, J = 7.6, 1.0 Hz, 1H), 5.17 (d, J = 2.6 Hz, 2H), 2.51 (t, J = 2.6 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 156.9, 156.8, 138.2, 133.3, 128.3, 127.8, 125.3, 123.5, 123.4, 121.4, 121.5, 121.0, 112.6, 112.1, 77.2, 75.0, 38.3; no mass detected via HRMS (ESI$^+$).

3,6-Di-tert-butyl-9-{4-[1-(prop-2-yn-1-yl)-1H-1,2,3-triazol-5-yl]-phenyl}-9H-carbazole (**5p**). 1-[4-(3,6-Di-*tert*-butyl-9*H*-carbazol-9-yl)-

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phenyl]ethan-1-one (100 mg, 0.252 mmol), propargyl amine (41.6 mg, 0.755 mmol), 4-nitrophenyl azide (61.9 mg, 0.377 mmol), zinc acetate (46.1 mg, 0.252 mmol), 4 Å molecular sieves (40 mg), and DMF (0.4 mL) were used. The reaction time was 24 h. The product was purified by flash column chromatography (CH_2Cl_2 followed by a 3:2 heptane/EtOAc mixture), affording **5p** (61 mg, 53% yield) as an off-white solid: mp 220−221 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.16 (d, J = 1.3 Hz, 2H), 7.86 (s, 1H), 7.76 (d, J = 2.0 Hz, 4H), 7.51−7.41 (m, 4H), 5.25 (d, J = 2.5 Hz, 2H), 2.53 (t, J = 2.5 Hz, 1H), 1.48 (s, 18H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 143.7, 139.9, 138.9, 137.5, 133.4, 130.3, 127.2, 124.7, 124.0, 123.9, 116.6, 109.2, 76.6, 75.2, 38.5, 34.9, 32.1; HRMS (ESI$^+$) m/z calcd for $C_{31}H_{32}N_4$ $[M + H]^+$ 461.2699, found 461.2692.

*(1S,3aS,3bR,5aS,10aS,10bS,12aS)-10a,12a-Dimethyl-7-(prop-2-yn-1-yl)-1,2,3,3a,3b,4,5,5a,6,7,10,10a,10b,11,12,12a-hexadecahydrocyclopenta[7,8]phenanthro[2,3-d][1,2,3]triazol-1-ole (**5q**).* 5α-Dihydrotestosterone (90 mg, 0.310 mmol), propargyl amine (34.1 mg, 0.620 mmol), 4-nitrophenyl azide (71.2 mg, 0.434 mmol), zinc acetate (56.9 mg, 0.310 mmol), 4 Å molecular sieves (40 mg), and DMF (0.4 mL) were used. The reaction time was 24 h. The product was purified by flash column chromatography (CH_2Cl_2 followed by a 3:2 heptane/EtOAc mixture), affording **5q** (63 mg, 57.5% yield) as an off-white solid: mp 198−199 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.05 (t, J = 2.5 Hz, 2H), 3.66 (t, J = 8.5 Hz, 1H), 2.86 (d, J = 15.5 Hz, 1H), 2.68 (dd, J = 15.9, 5.0 Hz, 1H), 2.45 (t, J = 2.6 Hz, 1H), 2.33−2.25 (m, 2H), 2.14−2.02 (m, 1H), 1.87 (dt, J = 12.4, 3.3 Hz, 1H), 1.79−1.72 (m, 1H), 1.72−1.57 (m, 5H), 1.53−1.36 (m, 4H), 1.34−1.22 (m, 1H), 1.12 (td, J = 12.8, 4.1 Hz, 1H), 1.04−0.85 (m, 3H), 0.77 (s, 3H), 0.74 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 144.0, 131.0, 82.0, 75.6, 74.7, 53.9, 50.9, 43.0, 42.3, 37.8, 36.9, 36.7, 36.2, 35.7, 31.3, 30.6, 29.0, 24.6, 23.6, 20.9, 11.8, 11.2; HRMS (ESI$^+$) m/z calcd for $C_{22}H_{31}N_3O_1$ $[M + H]^+$ 354.2539, found 354.2532.

*(1R,3aS,3bR,5aS,10aS,10bS,12aR)-10a,12a-Dimethyl-1-[(R)-6-methylheptan-2-yl]-7-(prop-2-yn-1-yl)-1,2,3,3a,3b,4,5,5a,6,7,10,10a,10b,11,12,12a-hexadecahydrocyclopenta[7,8]phenanthro[2,3-d][1,2,3]triazole (**5r**).* (5*S*,8*R*,9*S*,10*S*,13*R*,14*S*,17*R*)-10,13-Dimethyl-17-[(*R*)-6-methylheptan-2-yl]hexadecahydro-3*H*-cyclopenta[*a*]phenanthren-3-one (100 mg, 0.259 mmol), propargyl amine (28.5 mg, 0.517 mmol), 4-nitrophenyl azide (59.4 mg, 0.362 mmol), zinc acetate (47.4 mg, 0.259 mmol), 4 Å molecular sieves (40 mg), and DMF (0.4 mL) were used. The reaction time was 24 h. The product was purified by flash column chromatography (CH_2Cl_2 followed by a 3:2 heptane/EtOAc mixture), affording **5r** (72 mg, 62% yield) as an off-white solid: mp 132−133 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 5.11−5.01 (m, 2H), 2.85 (d, J = 15.2 Hz, 1H), 2.66 (dd, J = 15.6, 5.2 Hz, 1H), 2.44 (t, J = 2.6 Hz, 1H), 2.32−2.25 (m, 2H), 2.06−2.03 (m, 1H), 1.87−1.80 (m, 1H), 1.76−1.72 (m, 1H), 1.68−1.57 (m, 4H), 1.54−1.46 (m, 2H), 1.42−1.31 (m, 6H), 1.28−1.23 (m, 2H), 1.18−1.06 (m, 6H), 1.04−0.99 (m, 2H), 0.92 (d, J = 6.5 Hz, 3H), 0.87 (d, J = 2.6 Hz, 3H), 0.86 (d, J = 2.6 Hz, 3H), 0.73 (s, 3H), 0.68 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 144.2, 131.1, 77.4, 75.6, 74.7, 56.4, 53.8, 42.6, 42.3, 40.0, 39.6, 37.8, 36.8, 36.3, 36.2, 35.9, 35.7, 31.7, 29.1, 28.4, 28.2, 24.6, 24.4, 24.0, 23.0, 22.7, 21.3, 18.8, 12.1, 11.8; HRMS (ESI$^+$) m/z calcd for $C_{30}H_{47}N_3$ $[M + H]^+$ 450.3842, found 450.3844.

*Carbazole Porphyrin Conjugate (**7a**).* 3,6-Di-*tert*-butyl-9-{4-[1-(prop-2-yn-1-yl)-1*H*-1,2,3-triazol-5-yl]phenyl}-9*H*-carbazole (69 mg, 0.150 mmol), Zn-TPP (192 mg, 0.180 mmol), $CuSO_4$ (1.195 mg, 0.00749 mmol), sodium (*R*)-2-[(*S*)-1,2-dihydroxyethyl]-4-hydroxy-5-oxo-2,5-dihydrofuran-3-olate (3.26 mg, 0.016 mmol), and a *t*-BuOH/DCM/H_2O mixture (1:1:1) were used. The reaction time was 6 h. After the reaction had reached completion, the reaction mixture was extracted three times with DCM (3 × 100 mL), dried over $MgSO_4$, and concentrated under reduced pressure to afford desired product **7a** in 78% yield (178 mg) as an off-white solid: mp 253−254 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.10 (d, J = 4.6 Hz, 2H), 9.00 (s, 4H), 8.94 (d, J = 4.6 Hz, 2H), 8.30 (d, J = 7.9 Hz, 2H), 8.15 (d, J = 1.6 Hz, 4H), 8.11 (d, J = 1.6 Hz, 2H), 8.07 (d, J = 1.6 Hz, 2H), 7.83 (s, 2H), 7.78 (s, 1H), 7.46 (d, J = 8.4 Hz, 2H), 7.40−7.34 (m, 4H), 7.23 (d, J = 8.7 Hz, 3H), 7.03 (d, J = 7.8 Hz, 2H), 6.77 (s, 1H), 5.59 (s, 2H), 4.82 (s, 2H), 1.54 (s, 36H), 1.52 (s, 18H), 1.40 (s, 18H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 150.7, 150.5, 150.2, 149.9, 148.8, 148.5, 144.6, 143.6, 142.7, 142.6, 142.1, 139.8, 138.7, 136.0, 135.2, 133.8, 132.2, 131.4, 130.4, 129.9, 126.8, 125.3, 123.9, 123.8, 123.6, 122.8, 122.4, 122.2, 120.9, 120.8, 119.5, 116.5, 109.2, 35.3, 35.2, 34.9, 32.1, 32.0, 31.9; HRMS (ESI$^+$) m/z calcd for $C_{100}H_{109}N_{11}Zn$ $[M + H]^+$ 1528.8231, found 1528.8428.

*1-[4-(4-{[(1R,3aS,3bR,5aS,10aS,10bS,12aR)-10a,12a-Dimethyl-1-[(R)-6-methylheptan-2-yl]-2,3,3a,3b,4,5,5a,6,10,10a,10b,11,12,12a-tetradecahydrocyclopenta[7,8]phenanthro[2,3-d][1,2,3]triazol-7(1H)-yl]methyl}-1H-1,2,3-triazol-1-yl)-5-(hydroxymethyl)tetrahydrofuran-2-yl]-5-methylpyrimidine-2,4(1H,3H)-dione (**7b**).* **5r** (150 mg, 0.334 mmol), AZT (107 mg, 0.400 mmol), $CuSO_4$ (2.66 mg, 0.017 mmol), sodium (*R*)-2-[(*S*)-1,2-dihydroxyethyl]-4-hydroxy-5-oxo-2,5-dihydrofuran-3-olate (7.27 mg, 0.037 mmol), and a *t*-BuOH/H_2O mixture (1:1) were used. The reaction time was 12 h. After the reaction had reached completion, the reaction mixture was extracted three times with DCM (3 × 100 mL), dried over $MgSO_4$, and concentrated under reduced pressure to afford desired product **7b** in 84% yield (201 mg) as an off-white solid: mp 188−189 °C; ^{1}H NMR (400 MHz, DMSO) δ 11.34 (s, 1H), 8.32 (s, 1H), 7.80 (s, 1H), 6.41 (t, J = 6.5 Hz, 1H), 5.55 (s, 2H), 5.36 (dt, J = 10.4, 5.3 Hz, 1H), 5.27 (t, J = 5.0 Hz, 1H), 4.18 (d, J = 4.7 Hz, 1H), 3.73−3.57 (m, 2H), 2.62−2.50 (m, 4H), 2.20 (t, J = 14.7 Hz, 2H), 1.98 (d, J = 12.1 Hz, 1H), 1.80 (s, 4H), 1.65 (d, J = 10.8 Hz, 1H), 1.62−1.45 (m, 5H), 1.32 (s, 6H), 1.22−1.03 (m, 7H), 1.00 (d, J = 6.7 Hz, 2H), 0.90 (d, J = 6.2 Hz, 3H), 0.87−0.81 (m, 6H), 0.65 (s, 3H), 0.63 (s, 3H); ^{13}C NMR (101 MHz, DMSO) δ 163.7, 150.4, 142.1, 136.2, 130.9, 123.5, 109.6, 84.4, 83.9, 60.7, 59.4, 55.8, 54.9, 52.8, 42.4, 42.0, 41.5, 39.5, 37.1, 36.2, 35.6, 35.6, 35.2, 35.0, 31.2, 28.4, 27.8, 27.4, 23.86, 23.7, 23.2, 22.6, 22.4, 20.7, 18.5, 12.2, 11.8, 11.4; HRMS (ESI$^+$) m/z calcd for $C_{40}H_{60}N_8O_4$ $[M + H]^+$ 717.4809, found 717.4813.

*2-{2-[2-(4-{[(1R,3aS,3bR,5aS,10aS,10bS,12aR)-10a,12a-Dimethyl-1-[(R)-6-methylheptan-2-yl]-2,3,3a,3b,4,5,5a,6,10,10a,10b,11,12,12a-tetradecahydrocyclopenta[7,8]phenanthro[2,3-d][1,2,3]triazol-7(1H)-yl]methyl}-1H-1,2,3-triazol-1-yl)ethoxy]ethoxy}ethan-1-ol (**7c**).* **5r** (150 mg, 0.334 mmol), 2-[2-(2-azidoethoxy)ethoxy]ethan-1-ol (70.1 mg, 0.400 mmol), $CuSO_4$ (2.66 mg, 0.017 mmol), sodium (*R*)-2-[(*S*)-1,2-dihydroxyethyl]-4-hydroxy-5-oxo-2,5-dihydrofuran-3-olate (7.27 mg, 0.037 mmol), and a *t*-BuOH/H_2O/THF mixture (1:1:1) were used. The reaction time was 12 h. After the reaction had reached completion, the reaction mixture was extracted three times with DCM (3 × 100 mL), dried over $MgSO_4$, and concentrated under reduced pressure to afford desired product **7c** in 67% yield (143 mg) as an off-white solid: mp 101−102 °C; ^{1}H NMR (600 MHz, MeOD) δ 8.04 (s, 1H), 5.47 (s, 2H), 4.47 (s, 2H), 3.77 (d, J = 4.2 Hz, 2H), 3.56−3.52 (m, 2H), 3.48 (ddd, J = 8.2, 6.0, 2.9 Hz, 4H), 3.41−3.39 (m, 2H), 2.63 (s, 1H), 2.13 (s, 2H), 1.98 (d, J = 12.0 Hz, 1H), 1.82−1.73 (m, 1H), 1.67−1.64 (m, 1H), 1.58−1.48 (m, 3H), 1.46−1.40 (m, 3H), 1.34−1.24 (m, 6H), 1.22−1.12 (m, 2H), 1.12−0.98 (m, 6H), 0.98−0.89 (m, 2H), 0.86 (d, J = 6.4 Hz, 4H), 0.79 (d, J = 2.3 Hz, 3H), 0.78 (d, J = 2.3 Hz, 3H), 0.63 (s, 3H), 0.59 (s, 3H); ^{13}C NMR (101 MHz, MeOD) δ 126.1, 73.7, 71.4, 70.2, 62.2, 57.7, 55.0, 54.8, 51.5, 44.1, 43.6, 43.4, 41.3, 40.7, 37.7, 37.4, 37.2, 37.0, 36.9, 32.8, 29.9, 29.3, 29.2, 25.3, 25.0, 23.2, 23.0, 22.3, 19.3, 12.4, 12.0; HRMS (ESI$^+$) m/z calcd for $C_{36}H_{60}N_6O_3$ $[M + H]^+$ 625.4799, found 625.4813.

*(2R,3S,4R,5R)-2-[(Benzoyloxy)methyl]-5-(4-{[(1S,3aS,3bR,5aS,10aS,10bS,12aS)-1-hydroxy-10a,12a-dimethyl-2,3,3a,3b,4,5,5a,6,10,10a,10b,11,12,12a-tetradecahydrocyclopenta[7,8]phenanthro[2,3-d][1,2,3]triazol-7(1H)-yl]methyl}-1H-1,2,3-triazol-1-yl)tetrahydrofuran-3,4-diyl Dibenzoate (**7d**).* **4q** (100 mg, 0.283 mmol), (2*R*,3*R*,4*S*,5*R*)-2-azido-5-[(benzoyloxy)methyl]-tetrahydrofuran-3,4-diyl dibenzoate (165 mg, 0.339 mmol), $CuSO_4$ (2.483 mg, 0.016 mmol), sodium (*R*)-2-[(*S*)-1,2-dihydroxyethyl]-4-hydroxy-5-oxo-2,5-dihydrofuran-3-olate (6.16 mg, 0.031 mmol), and a *t*-BuOH/H_2O mixture (1:1) were used. The reaction time was 12 h. After the reaction had reached completion, the reaction mixture was extracted three times with DCM (3 × 100 mL), dried over $MgSO_4$, and concentrated under reduced pressure to afford desired product **7d** in 90% yield (215 mg) as an off-white solid: mp 123−124 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02 (d, J = 8.0 Hz, 2H), 7.95 (dd, J =

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13.0, 8.1 Hz, 4H), 7.81 (s, 1H), 7.56 (q, J = 7.5 Hz, 3H), 7.45−7.35 (m, 6H), 6.35 (d, J = 2.4 Hz, 1H), 6.26−6.22 (m, 1H), 6.13 (t, J = 5.7 Hz, 1H), 5.54−5.40 (m, 2H), 4.88 (dd, J = 9.3, 4.6 Hz, 1H), 4.77 (dd, J = 12.2, 3.2 Hz, 1H), 4.59 (dd, J = 12.2, 4.8 Hz, 1H), 3.65 (t, J = 8.4 Hz, 1H), 2.82 (d, J = 13.2 Hz, 1H), 2.69 (d, J = 14.8 Hz, 1H), 2.27−2.15 (m, 2H), 2.12−1.99 (m, 1H), 1.85 (d, J = 12.1 Hz, 1H), 1.75−1.52 (m, 6H), 1.48−1.22 (m, 5H), 1.10 (t, J = 11.3 Hz, 1H), 1.02−0.80 (m, 3H), 0.75 (s, 3H), 0.67 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.2, 165.2, 165.1, 143.0, 134.0, 133.8, 133.5, 130.0, 129.9, 129.9, 129.4, 128.7, 128.7, 128.6, 128.5, 122.9, 90.5, 81.9, 81.3, 77.4, 75.2, 71.7, 63.8, 53.8, 50.9, 43.2, 43.0, 42.2, 36.8, 36.7, 36.2, 35.7, 31.2, 30.6, 29.81, 28.8, 24.4, 23.5, 20.9, 11.8, 11.2; HRMS (ESI$^+$) m/z calcd for $C_{48}H_{52}N_6O_8$ $[M + H]^+$ 841.3919, found 841.3929.

*((2R,3S,5R)-3-[(4-Chlorobenzoyl)oxy]-5-{4-[(5-phenyl-1H-1,2,3-triazol-1-yl)methyl]-1H-1,2,3-triazol-1-yl}tetrahydrofuran-2-yl)methyl 4-Chlorobenzoate (**7e**).* 5-Phenyl-1-(prop-2-yn-1-yl)-1*H*-1,2,3-triazole (50 mg, 0.273 mmol), (2*R*,3*S*,5*R*)-5-azido-2-{[(4-chlorobenzoyl)oxy]-methyl}tetrahydrofuran-3-yl 4-chlorobenzoate (143 mg, 0.327 mmol), $CuSO_4$ (2.178 mg, 0.014 mmol), sodium (*R*)-2-[(*S*)-1,2-dihydroxyethyl]-4-hydroxy-5-oxo-2,5-dihydrofuran-3-olate (5.95 mg, 0.030 mmol), and a *t*-BuOH/H_2O mixture (1:1) were used. The reaction time was 12 h. After the reaction had reached completion, the reaction mixture was extracted three times with DCM (3 × 100 mL), dried over $MgSO_4$, and concentrated under reduced pressure to afford desired product **7e** in 88% yield (148 mg) as an off-white solid: mp 154−155 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.02−7.85 (m, 5H), 7.71 (s, 1H), 7.52−7.36 (m, 10H), 6.41 (t, J = 6.1 Hz, 1H), 5.80 (dd, J = 6.5, 3.3 Hz, 1H), 5.61 (s, 2H), 4.68−4.59 (m, 1H), 4.59−4.45 (m, 2H), 3.35−3.26 (m, 1H), 2.88−2.80 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.3, 165.0, 143.1, 140.3, 139.9, 131.2, 129.8, 129.3, 129.1, 129.0, 128.9, 127.8, 127.5, 126.4, 123.2, 88.8, 83.5, 75.1, 64.2, 43.4, 37.8; HRMS (ESI$^+$) m/z calcd for $C_{30}H_{24}Cl_2N_6O_5$ $[M + H]^+$ 619.1257, found 619.1264.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.6b02607.

Copies of ^{1}H and ^{13}C NMR spectra for all new compounds (PDF)

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Notes

The authors declare no competing financial interest.

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