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A Multicomponent Approach toward Angularly Fused/Linear Bitriazoles: A Cascade Cornforth Rearrangement and Triazolization

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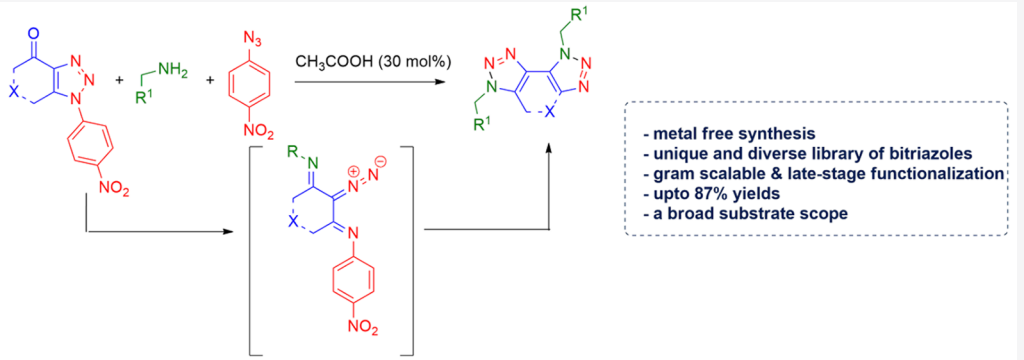

ABSTRACT: A multicomponent reaction of triazoloketones, primary amines, and 4-nitrophenyl azide was developed for the synthesis of hitherto unknown angularly fused/linear bitriazoles. The two-stage mechanism was well proven by the isolation of the intermediate. This sequential reaction consists of Cornforth rearrangement and triazolization, which has also been demonstrated in a one-pot manner.

Organic frameworks adorned with fused or linked polyheterocycles have attracted much attention due to their numerous applications in material and medicinal chemistry.[1] One of the privileged five membered heteroaromatic ring scaffolds, namely 1,2,3-triazoles, are extensively used as synthetic building blocks in both simple and complex molecular structures.[2−4] Triazole-fused polycyclic heterocycles have potential application as organometallic ligands, pharmaceuticals, and materials.[5−7]

The copper/ruthenium/iridium-catalyzed azide−alkyne cycloadditions (AACs) have been widely applied for the selective synthesis of 1,2,3-triazoles.[8−10] However, considering that these metal ions are toxic to living systems, the development of efficient greener alternatives for their synthesis has received significant attention over the last few decades. In this regard, much effort has been devoted toward the organocatalyzed synthesis of 1,2,3-triazoles.[11−15] Surprisingly, among these approaches, only limited reports dealt with azide-free synthesis.[16] The latter would undoubtedly provide a great advantage because organic azides are highly explosive and hazardous when used in large scale synthesis. Thus, we developed a metal-free three-component reaction for the synthesis of 1,5-di- and 1,4,5-trisubstituted 1,2,3-triazoles from readily available enolizable ketones, primary alkylamines and the 4-nitrophenyl azide (4-NPA).[17] Later, we explored this so-called "triazolization reaction" toward the synthesis of triazapentalenes, various heterocycles, and post functionalization and synthesis of natural products.[18−22] In light of these recent advances, we envisioned the possibility of making an extension of this methodology toward bitriazole motifs.

Apart from the great variety of applications of 1,2,3-triazoles in medicinal chemistry and other disciplines, suitably substituted derivatives have been employed as outstanding and attractive synthons due to their ability to ring open and generate α-diazoimines. The formed diazoimines always exist in equilibrium with their closed isomers, which may lead to several heterocycles through rearrangements.[23] It was also found that the amount of open form becomes larger with an increasingly electron-withdrawing character of the substituents and with increasing temperatures. It is also worth noting that the imino metallocarbene formed after the denitrogenative decomposition of electron deficient triazoles in the presence of transition metal catalysts has been well utilized for the construction of heterocycles by various research groups, as documented in recent reviews.[24,25] Herein, we report the acid catalyzed formation of an imine resulting from 1,2,3-triazolo

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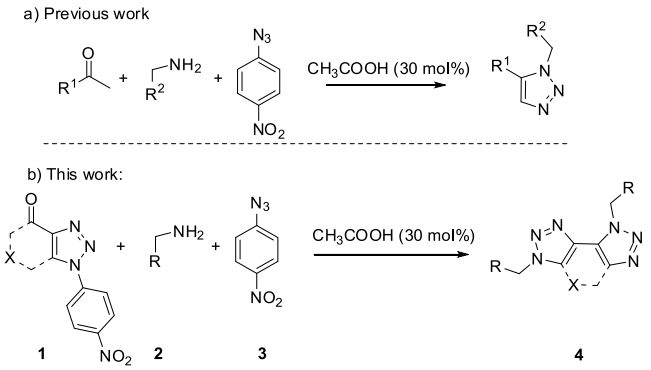
ketone **1** and the consecutive Cornforth rearrangement followed by triazolization toward the angularly fused/linear bitriazoles **4** (Scheme 1).[26]

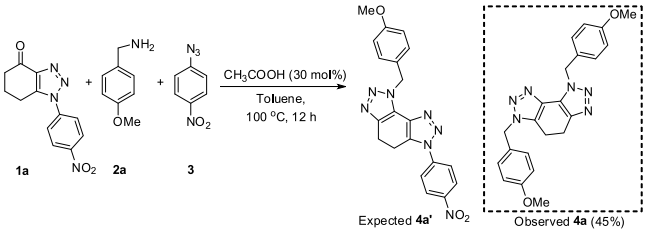
Scheme 1. Triazolization and Bitriazolization Reactions



At present, the most reliable way of synthesizing 4−4′/5−5′-linked symmetric bitriazoles and the bis-triazole is the classical copper-catalyzed Huisgen cycloaddition of dialkynes.[27−30] While there are some earlier reports from our laboratory for the metal-free synthesis of bitriazole scaffolds.[6,17] Despite these advances, alternative and nonmetal catalyzed approaches are still highly desirable and will lead to greater advancement in the exploration of bitriazoles and their fused derivatives.

Building on our previous results on the triazolization reactions, we envisioned an extension of our methodology toward the synthesis of bitriazoles (**4a′**) by utilizing triazoloketone **1a** as an enolizable ketone (Scheme 2). The

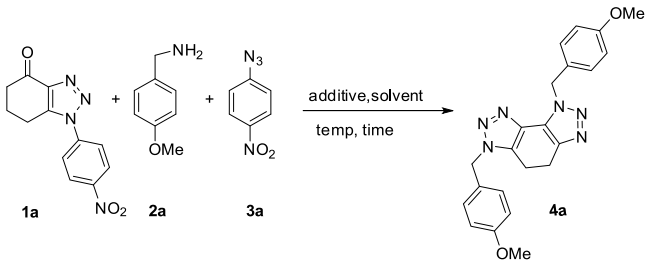
Scheme 2. Multicomponent Reaction



triazoloketone used for this reaction was obtained via the organocatalytic azide/enolate cycloaddition reaction of 1,3-diketones **5a** and *p*-nitrophenyl azide **3** (see Experimental Section, Procedure A).[31−33] Thus, we initiated our experiments by treating 1 equiv of triazoloketone **1a**, 1.2 equiv of amine **2a**, and 1 equiv of **3** in toluene at 100 °C in the presence of a catalytic amount of acetic acid for 12 h. The expected product of triazolization would be **4a′**. Surprisingly, the formation of an angularly fused tetrahydrobenzo-bis([1,2,3]-triazole) **4a** was observed in 45% yield instead (Scheme 2).

Increasing the equivalents of primary amine **2a** from 1.2 to 2 equiv concomitantly increased the yield up to 62% (Table 1, entry 2), which is due to the requirement of two equivalents of primary amine for the complete conversion of **1a** to bitriazole **4a**. Further increasing the equivalents of primary amine **2a** and nitrophenyl azide **3** from 2:1 to 2.5:1.2 resulted in a rise in yield up to 65% (Table 1, entry 3). Next, various solvents were screened, including acetonitrile, toluene, DMF, DMSO, THF, and dioxane (Table 1, entries 3−8), and dioxane proved to be superior. After investigating the effect of various acids, we

Table 1. Optimization of the Reaction Conditions[a]



Entry	Additive	Solvent	Temperature (°C)	Time (h)	Yield (%)[b]
1[c]	CH_3COOH	Toluene	100	12	45
2[d]	CH_3COOH	Toluene	100	12	62
3	CH_3COOH	Toluene	100	12	65
4	CH_3COOH	Acetonitrile	85	12	68
5	CH_3COOH	DMF	100	12	40
6	CH_3COOH	DMSO	100	12	55
7	CH_3COOH	1, 4 dioxane	100	12	81
8	CH_3COOH	THF	75	12	65
9	morpholine:TfOH	1, 4 dioxane	100	12	70
10	TfOH	1, 4 dioxane	100	12	75
11	_	1, 4 dioxane	100	12	trace
12	_	1, 4 dioxane	100	24	20
13	CH_3COOH	1, 4 dioxane	80	12	72
14	CH_3COOH	1, 4 dioxane	60	12	no reaction
15	CH_3COOH	1, 4 dioxane	60	24	no reaction

[a]Reaction conditions: triazoloketone **1a** (0.20 mmol), *p*-methoxy benzylamine **2a** (0.50 mmol), *p*-nitrophenyl azide **3** (0.24 mmol), additive (30 mol %), solvent (2.0 mL). [b]Isolated yields. [c]**1a** (0.20 mmol), *p*-**2a** (0.24 mmol), **3** (0.20 mmol). [d]**1a** (0.20 mmol), **2a** (0.40 mmol), **3** (0.20 mmol).

observed that acetic acid was optimal for the conversion, and only traces of the product were detected without organic acid. An increased reaction time for 24 h without the addition of acid delivered the product **4a** in only 20% yield, and further increase of time did not much effect the conversion (Table 1, entries 9−12). A temperature of 100 °C proved to be optimal, and decreasing the temperature drastically reduced the yield of the reaction (Table 1, entries 4, 13, and 14). Moreover, at 60 °C, no conversion of starting material was observed (Table 1, entry 15). These observations clearly indicate that an organic acid and an increased temperature are essential for complete conversion. Finally, the optimized reaction conditions were established to provide a maximum yield of 81%, which are depicted in Table 1, entry 7.

With the optimized reaction conditions in hand, we evaluated the substrate scope of this methodology (Table 2). First, the multicomponent process was found to be general with a diverse range of benzylamines substituted with both electron-donating and withdrawing substituents, which furnished the fused bitriazole **4a−4e** in good yields ranging 65−81%. Pleasingly, we also found that linear alkylamines were well tolerated and gave the products in high yields of 85% (**4f**)

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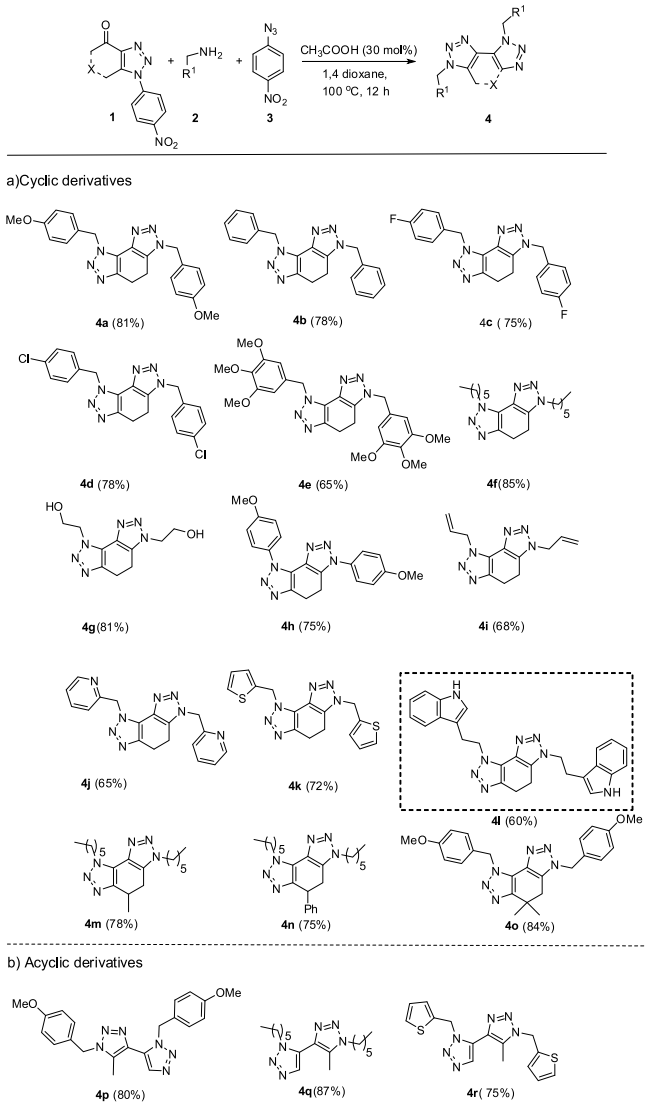
Table 2. Multicomponent Reaction[a]



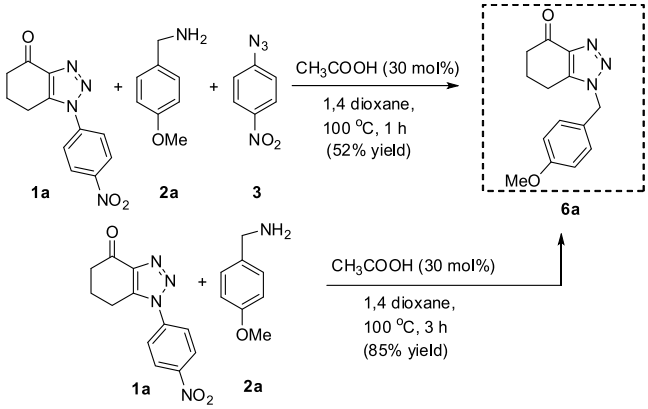
[a]Reaction conditions: **1** (0.20 mmol), **2** (0.50 mmol), **3** (0.24 mmol, acetic acid (30 mol %), 1,4-dioxane (2.0 mL), 100 °C, 12 h.

and 81% (**4g**). Moreover, the bitriazole **4g** formed from 2-hydroxyethylamine was found to be water-soluble. The aromatic amine *p*-anisidine reacted smoothly and led to **4h** in 75% yield. Next, allyl (**4i**) and heteroaryl groups (**4j** and **4k**) were efficiently incorporated in the bitriazole product. Additionally, the tryptamine was successfully converted into the fused bitriazole **4l** in 60% yield, showing that natural product derivatives can be obtained with this methodology.

Further studies were performed to evaluate the reactivity of different cyclic ketones. Gratifyingly, fused triazoloketones **1b** and **1c** derived from 1,3-cyclohexanediones substituted with methyl and phenyl at the C5 position were well tolerated under the reaction conditions, giving the corresponding products **4m** and **4n** in high yield of 78 (**4m**) and 75% (**4n**). Additionally, from the reaction of triazolodimedone **1d**, the desired product **4o** was obtained in 84% yield. Finally, we turned our attention toward acyclic triazoloketone **1e** derived from acyclic 1,3-diketone for the synthesis of linear bitriazoles. To our delight, the reaction afforded the corresponding product with aliphatic (**4p**), benzyl (**4q**), and heteroaryl (**4r**) substituents in excellent yields ranging 75−87%.

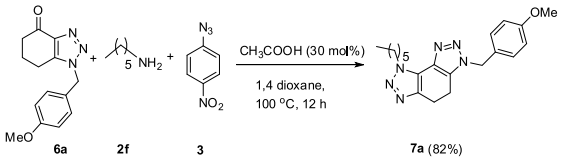
To our delight, reducing the reaction time to 1 h followed by immediate purification afforded *N*-(4-methoxybenzyl) substituted triazoloketone **6a** in 52% yield. This indicates that this compound is an intermediate on the way from the reaction of *N*-nitrophenyl triazolo ketone **1a** to compounds **4a**. The formation of **6a** could be referred to as a result of the well-known Cornforth rearrangement of the imine resulting from condensation of amine **2a** with **1a**, followed by hydrolysis of the rearranged product under the reaction circumstances.[27] To further confirm this, we performed a control experiment in the absence of 4-nitrophenyl azide **3**, and the compound **6a** was isolated in 85% yield (Scheme 3).

Scheme 3. Control Experiments



To further demonstrate the value of this methodology, we also tested the probability of formation of unsymmetrically substituted fused bitriazole by making use of the isolated triazolo ketone **6a**. Pleasingly, triazolization reaction of **6a** with hexyl amine resulted the formation of an unsymmetrically substituted fused bitriazole **7a** in 82% yield (Scheme 4).

Scheme 4. Synthesis of Unsymmetrically Substituted Fused Bitriazoles



Several insights from our synthetic work are mechanistically relevant. First, intermediate **6a** was isolated from the reaction mixture. Second, **6a** smoothly underwent triazolization toward **7a**. Thus, based on this experimental evidence and the mechanism reported in the previous work,[17] we propose a plausible mechanism which is depicted in Scheme 5. The bitriazole synthesis consists of two individual steps involving a Cornforth rearrangement and the triazolization reaction.[26,34] In the first step, the keto triazole **I** reacts with an equimolar amount of amine, resulting in the imine intermediate **II**. Subsequent ring opening of triazole furnishes the diazo intermediate **III**, which immediately cyclizes to the more stable triazole intermediate **IV**. Then, hydrolysis of the imine to ketone **V** completes the first stage of the reaction (Scheme 5a). The final product was formed by the reaction of **V** with

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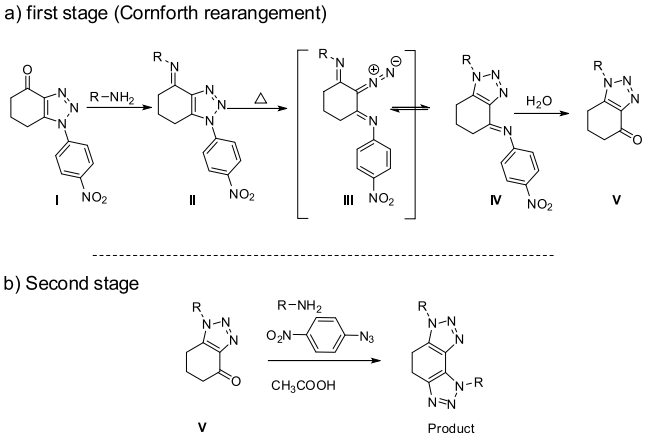
Scheme 5. Plausible Mechanism of the Reaction



another equivalent of primary amine and 4-nitrophenyl azide in the presence of acetic acid (Scheme 5b, named "triazolization"[17]). This reaction also involves the formation of an imine, which via its equilibration with enamine reacts with the 4-nitrophenyl azide and gives further ring opening, recyclization, and elimination of 4-nitroaniline, giving 1,2,3-triazoles as described earlier.[17]

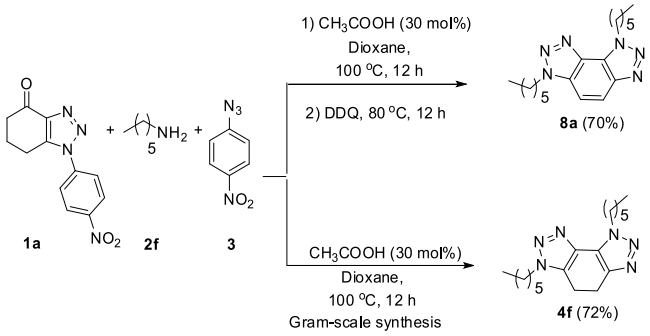
Next, our success in the bitriazole synthesis from triazoloketone prompted us to explore the same reaction in a one-pot two-step reaction starting from readily available 1,3-diketone. Thus, we treated equimolar amounts of **5a** and **3** in 1 mL of DMSO at room temperature in the presence of 5 mol % DBU. After complete consumption of diketone **5a**, 2 equiv of **2a**, an additional equivalent of **3**, and 30 mol % AcOH were added along with 1 mL of dioxane, and the mixture was left to stir at 100 °C for 12 h. Pleasingly, the expected bitriazole **4a** was isolated in 73% yield (Scheme 6).

Scheme 6. One-Pot Synthesis

To highlight the versatility of this methodology, further oxidative aromatization was executed in a one-pot strategy on triazoloketone **1a** and *n*-hexylamine **2f**. After complete conversion of **1a** to bitriazole **4f**, DDQ was added to the same reaction tube, and this was then left to stir at 80 °C for 12 h. As expected, the benzofused heteroarene **8a** was obtained in 70% yield. Additionally, the outlined methodology (Scheme 7) was applied in the gram scale synthesis of **4f** in good yield of 72% by utilizing 1.5 g of **1a**.

In conclusion, we have reported herein the synthesis of angularly fused/linear bitriazoles via the multicomponent reaction of triazoloketones, primary amines, and 4-nitrophenyl azide. This methodology was also successfully applied to one-pot two-step synthesis of bitriazole starting from readily available 1,3-diketones. Our bitriazolization strategy showed broad substrate scope and good functional group tolerance. The proposed two-stage mechanism was successfully proven by the isolation of the intermediate. The synthesized angularly fused symmetrically and unsymmetrically substituted bitriazoles have not previously been obtainable via other methods as far as we could ascertain. Further studies to broaden the scope and applications of these molecules are currently ongoing in our laboratory.

Scheme 7. Aromatization and Scale-Up



EXPERIMENTAL SECTION

Chemicals received from commercial sources were used without further purification. Reaction solvents were used as received from commercial sources. TLC was carried out on Kieselgel 60 F254 plates (Merck) and visualized with a UV lamp at 254 nm. For column chromatography, 70-230 mesh silica 60 (E. M. Merck) was used as the stationary phase. NMR spectra were recorded on a Bruker Advance III HD 400 (400 MHz) or a Bruker Advance 300 (300 MHz) instrument. Chemical shifts for ^{1}H NMR spectra are reported as δ in units of parts per million (ppm) downfield from $SiMe_4$ (δ 0.0) and relative to the signal of chloroform-d (δ 7.26 ppm) or MeOD (3.31 ppm). Multiplicities were given as s (singlet), d (doublet), t (triplet), q (quartet), dd (double doublet), and m (multiplet). Coupling constants are reported as J values in Hz. Carbon nuclear magnetic resonance spectra ($^{13}C\{^1H\}$ NMR) are reported as δ in units of parts per million (ppm) downfield from $SiMe_4$ (δ 0.0) and relative to the signal of chloroform-d (δ 77.16 ppm) or MeOD (49.0 ppm). Melting points were determined using a Reichert thermovar apparatus and are uncorrected. Exact mass spectra were acquired with a quadrupole orthogonal acceleration time-of-flight mass spectrometer (Synapt G2 HDMS, Waters, Milford, MA). Samples were infused at 3uL/min, and spectra were obtained in positive (or negative) ionization mode with a resolution of 15 000 (fwhm) using leucine enkephalin as lock mass.

Synthetic Procedure for the Multicomponent Reaction toward Bitriazoles. *Procedure A: Synthesis of Triazoloketone (**1a**–**1e**).*[31] 1,3-Diketone (1.0 mmol), a mixture of 4-nitrophenyl azide **3** (1.0 mmol), DBU (5 mol %), and DMF (1.5 mL) were added to a 25 mL round-bottomed flask and stirred at room temperature for 3 h. After completion of the reaction, the reaction mixture was quenched with water (5 mL). The precipitate formed was collected by filtration and further purified by silica gel column chromatography using ethyl acetate/petroleum ether as eluent.

*Procedure B: Synthesis of Bitriazoles (**4a**–**4r**).*[31] The triazolo ketone (0.2 mmol), primary amine (0.50 mmol), and 4-nitrophenyl azide (0.24 mmol) were weighed into a reaction tube. 1,4-Dioxane (2 mL) was added along with the addition of 30 mol % acetic acid and allowed to stir at 100 °C using oil bath for 12 h. Upon completion of the reaction, the solvent was evaporated 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 of the 4-nitroaniline formed during the reaction followed by using a mixture of petroleum ether and ethyl acetate as eluent.

*1-(4-Nitrophenyl)-5,6,7,7a-tetrahydro-1H-benzo[d][1,2,3]triazol-4(3aH)-one (**1a**).* The reaction was performed according to procedure A with 1,3-cyclohexanedione **5a** (1.12 g, 10.0 mmol) and 4-nitrophenylazide **3** (1.64 g, 10.0 mmol). The crude product was purified by silica gel column chromatography (60% ethyl acetate in hexane) to afford the product **1a** as a pale yellow solid (1.87 g, 72%).

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mp: 192−194 °C. Analytical data of **1a**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.47 (d, J = 8.7 Hz, 2H), 7.86 (d, J = 9.0 Hz, 2H), 3.14 (t, J = 6.3 Hz, 2H), 2.71 (t, J = 6.3 Hz, 2H), 2.35−2.27 (m, 2H). $^{13}C\{^1H\}$ (75 MHz, $CDCl_3$) δ 189.8, 148.0, 144.5, 143.0, 140.5, 125.6, 123.8, 38.2, 23.3, 22.3. HRMS (ESI-HRMS) (m/z): Calcd for $C_{12}H_{11}N_4O_3$, $(M+H)^+$: 259.0826; found: 259.0833. Spectroscopic data for **1a** are consistent with previously reported data.[31]

*6-Methyl-1-(4-nitrophenyl)-5,6,7,7a-tetrahydro-1H-benzo[d][1,2,3]triazol-4(3aH)-one (**1b**).* The reaction was performed according to procedure A with 5-methyl-1,3-cyclohexanedione **5b** (252 mg, 2.0 mmol) and 4-nitrophenylazide **3** (328 mg, 2.0 mmol). The crude product was purified by silica gel column chromatography (60% ethyl acetate in hexane) to afford the product **1b** as a pale yellow solid (381 mg, 70%). mp: 232−234 °C. Analytical data of **1b**: ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.48 (d, J = 9.2 Hz, 2H), 7.85 (d, J = 8.8 Hz, 2H), 3.17−3.11 (m, 1H), 2.87−2.75 (m, 2H), 2.56−2.44 (m, 2H), 1.26 (d, J = 6.4 Hz, 3H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 189.3, 148.0, 144.1, 143.0, 140.5, 125.6, 123.8, 46.6, 31.6, 30.1, 21.0. HRMS (ESI-HRMS) (m/z): Calcd for $C_{13}H_{13}N_4O_3$, $(M+H)^+$: 273.0982; found: 273.0995. Spectroscopic data for **1b** are consistent with previously reported data.[31]

*1-(4-Nitrophenyl)-6-phenyl-5,6,7,7a-tetrahydro-1H-benzo[d][1,2,3]triazol-4(3aH)-one (**1c**).* The reaction was performed according to procedure A with 5-phenyl-1,3-cyclohexanedione **5c** (376 mg, 2.0 mmol) and 4-nitrophenylazide **3** (328 mg, 2.0 mmol). The crude product was purified by silica gel column chromatography (60% ethyl acetate in hexane) to afford the product **1c** as a pale yellow solid (434 mg, 65%). mp: 172−174 °C. Analytical data of **1c**: ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.46−8.44 (m, 2H), 7.86−7.83 (m, 2H), 7.42−7.29 (m, 5H), 3.66−3.61 (m, 1H), 3.35−3.25 (m, 2H), 3.07−2.86 (m, 2H). $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$): δ 188.6, 148.0, 143.8, 143.0, 141.1, 140.3, 129.4, 128.1, 126.8, 125.6, 123.8, 45.26, 42.0, 30.3. HRMS (ESI-HRMS) (m/z): Calcd for $C_{18}H_{15}N_4O_3$, $(M+H)^+$: 335.1539; found: 335.1533.

*6,6-Dimethyl-1-(4-nitrophenyl)-5,6,7,7a-tetrahydro-1H-benzo-[d][1,2,3]triazol-4(3aH)-one (**1d**).* The reaction was performed according to procedure A with 5,5-dimethyl-cyclohexane 1,3-dione **5d** (280 mg, 2.0 mmol) and 4-nitrophenylazide **3** (328 mg, 2 mmol). The crude product was purified by silica gel column chromatography (60% ethyl acetate in hexane) to afford the product **1d** as a pale yellow solid (400 mg, 70%). mp: 204−206 °C. Analytical data of **1d**: ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.48 (d, J = 9.0 Hz, 2H), 7.85 (d, J = 9.0 Hz, 2H), 2.97 (s, 2H), 2.59 (s, 2H), 1.19 (s, 6H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 189.3, 148.0, 143.6, 142.3, 140.4, 125.6, 123.8, 52.3, 36.3, 35.9, 28.5. HRMS (ESI-HRMS) (m/z): Calcd for $C_{14}H_{14}N_4NaO_3$, $(M+Na)^+$: 309.0958; Found: 309.0958. Spectroscopic data for **1d** are consistent with previously reported data.[31]

*1-(5-Methyl-1-(4-nitrophenyl)-4,5-dihydro-1H-1,2,3-triazol-4-yl)-ethenone (**1e**).* The reaction was performed according to procedure A with pentane-2,4-dione **5e** (252 mg, 2.0 mmol) and 4-nitrophenylazide (1.64 g, 2 mmol). The crude product was purified by silica gel column chromatography (40% ethyl acetate in hexane) to afford the product **1e** as a pale yellow solid (398 mg, 81%). mp: 142−144 °C. Analytical data of **1e**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.47 (d, J = 8.4 Hz, 2H), 7.73 (d, J = 8.8 Hz, 2H), 2.77 (s, 3H), 2.69 (s, 3H). $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ 194.3, 148.4, 144.2, 140.3, 137.5, 125.9, 125.3, 28.1, 10.49. HRMS (ESI-HRMS) (m/z): Calcd for $C_{11}H_{10}N_4NaO_3$, $(M+Na)^+$: 269.0645; Found: 269.0605.

*1,6-Bis(4-methoxybenzyl)-1,4,5,6-tetrahydrobenzo[1,2-d,3,4-d′]-bis([1,2,3]triazole) (**4a**).* The reaction was performed according to procedure B with triazoloketone **1a** (52 mg, 0.2 mmol), 4-methoxy benzylamine **2a** (69 mg, 0.50 mmol), and 4-nitrophenylazide **3** (39 mg, 0.24 mmol). The crude reaction mixture was then directly purified by silica gel column chromatography (CH_2Cl_2 followed by petroleum ether/EtOAc = 3:7) to afford the product **4a** as a white semisolid (66 mg, 81%). Analytical data of **4a**: ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.54 (d, J = 8 Hz, 2H), 7.18 (d, J = 8 Hz, 2H), 6.84 (dd, $J1$ = 8 Hz, $J2$ = 16.4 Hz, 4H), 5.77 (s, 2H), 5.44 (s, 2H), 3.78 (s, 3H), 3.74 (s, 3H), 3.08 (t, J = 8.4 Hz, 2H), 2.85 (t, J = 8.4 Hz, 2H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 160.0, 159.7, 142.0, 135.9, 134.0, 130.4, 129.3, 127.5, 126.4, 125.9, 114.6, 114.1, 55.4, 55.3, 52.8, 52.4, 20.2, 19.5. HRMS (ESI-HRMS) (m/z): Calcd for $C_{22}H_{23}N_6O_2$, $(M+H)^+$: 403.1877; found: 403.1873.

*1,6-Dibenzyl-1,4,5,6-tetrahydrobenzo[1,2-d,3,4-d′]bis([1,2,3]-triazole) (**4b**).* The reaction was performed according to procedure B with triazoloketone **1a** (52 mg, 0.2 mmol), benzylamine **2b** (54 mg, 0.50 mmol), and 4-nitrophenylazide **3** (39 mg, 0.24 mmol). The crude reaction mixture was then directly purified by silica gel column chromatography (CH_2Cl_2 followed by petroleum ether/EtOAc = 3:7) to afford the product **4b** as a white semisolid (53 mg, 78%). Analytical data of **4b**: ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.59−7.57 (m, 2H), 7.36−7.28 (m, 6H), 7.23−7.21 (m, 2H), 5.85 (s, 2H), 5.52 (s, 2H), 3.10 (t, J = 8.4 Hz, 2H), 2.86 (t, J = 8.4 Hz, 2H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 142.0, 135.9, 135.3, 134.3, 134.0, 129.3, 129.0, 128.9, 128.8, 128.5, 127.7, 53.3, 52.8, 20.2, 19.5. HRMS (ESI-HRMS) (m/z): Calcd for $C_{20}H_{19}N_6$, $(M+H)^+$: 343.1666; found: 343.1664.

*1,6-Bis(4-fluorobenzyl)-1,4,5,6-tetrahydrobenzo[1,2-d:3,4-d′]bis-([1,2,3]triazole) (**4c**).* The reaction was performed according to procedure B with triazoloketone **1a** (52 mg, 0.2 mmol), 4-fluoro benzylamine **2c** (63 mg, 0.50 mmol), and 4-nitrophenylazide **3** (39 mg, 0.24 mmol). The crude reaction mixture was then directly purified by silica gel column chromatography (CH_2Cl_2 followed by petroleum ether/EtOAc = 3:7) to afford the product **4c** as a white solid (57 mg, 75%). mp: 175−177 °C. Analytical data of **4c**: ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.60−7.57 (m, 2H), 7.25−7.22 (m, 2H), 7.08−6.98 (m, 4H), 5.81 (s, 2H), 5.49 (s, 2H), 3.13 (t, J = 8.0 Hz, 2H), 2.88 (t, J = 8.0 Hz, 2H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 164.2, 164.1, 161.8, 161.7, 142.2, 136.0, 134.1, 131.1, 131.1, 130.9, 130.8, 129.7, 129.6, 126.5, 116.6, 116.3, 115.9, 115.7, 52.6, 52.1, 20.2, 19.5. HRMS (ESI-HRMS) (m/z): Calcd for $C_{20}H_{17}F_2N_6$, $(M+H)^+$: 379.1478; found: 379.1482.

*1,6-Bis(4-chlorobenzyl)-1,4,5,6-tetrahydrobenzo[1,2-d:3,4-d′]bis-([1,2,3]triazole) (**4d**).* The reaction was performed according to procedure B with triazoloketone **1a** (52 mg, 0.2 mmol), 4-chloro benzylamine **2d** (71 mg, 0.50 mmol), and 4-nitrophenylazide **3** (39 mg, 0.24 mmol). The crude reaction mixture was then directly purified by silica gel column chromatography (CH_2Cl_2 followed by petroleum ether/EtOAc = 3:7) to afford the product **4d** as a white solid (64 mg, 78%). mp: 98−100 °C. Analytical data of **4d**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.52 (d, J = 8.8 Hz, 2H), 7.36−7.34 (m, 2H), 7.30−7.28 (m, 2H), 7.17 (d, J = 8.8 Hz, 2H), 5.81 (s, 2H), 5.49 (s, 2H), 3.13 (t, J = 8.4 Hz, 2H), 2.88 (t, J = 8.4 Hz, 2H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 142.2, 135.9, 135.1, 134.6, 134.2, 133.6, 132.4, 130.3, 129.6, 129.1, 129.1, 126.5, 52.6, 52.1, 20.2, 19.5. HRMS (ESI-HRMS) (m/z): Calcd for $C_{20}H_{17}Cl_2N_6$, $(M+H)^+$: 411.0916; found: 411.0880.

*1,6-Bis(3,4,5-trimethoxybenzyl)-1,4,5,6-tetrahydrobenzo[1,2-d:3,4-d′]bis([1,2,3]triazole) (**4e**).* The reaction was performed according to procedure B with triazoloketone **1a** (52 mg, 0.2 mmol), 3,4,5 trimethoxy benylamine **2e** (99 mg, 0.50 mmol), and 4-nitrophenylazide **3** (39 mg, 0.24 mmol). The crude reaction mixture was then directly purified by silica gel column chromatography (CH_2Cl_2 followed by petroleum ether/EtOAc = 1:9) to afford the product **4e** as a white solid (68 mg, 65%). mp: 115−117 °C. Analytical data of **4e**: ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.96 (s, 2H), 6.44 (s, 2H), 5.75 (s, 2H), 5.44 (s, 2H), 3.84−3.79 (m, 18H), 3.14 (t, J = 8.0 Hz, 2H). 2.92 (t, J = 8.0 Hz, 2H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 153.9, 153.4, 142.2, 138.5, 138.1, 136.0, 134.3, 130.7, 129.4, 126.5, 106.3, 104.9, 61.0, 60.9, 56.4, 56.3, 53.8, 53.0, 20.3, 19.5. HRMS (ESI-HRMS) (m/z): Calcd for $C_{26}H_{31}N_6O_6$, $(M+H)^+$: 523.2300; found: 523.2306.

*1,6-Dihexyl-1,4,5,6-tetrahydrobenzo[1,2-d:3,4-d′]bis([1,2,3]-triazole) (**4f**).* The reaction was performed according to procedure B with triazoloketone **1a** (52 mg, 0.2 mmol), *n*-hexylamine **2f** (51 mg, 0.50 mmol), and 4-nitrophenylazide **3** (39 mg, 0.24 mmol). The crude reaction mixture was then directly purified by silica gel column chromatography (CH_2Cl_2 followed by petroleum ether/EtOAc = 1:1) to afford the product **4f** as a colorless viscous liquid (56 mg, 85%). Analytical data of **4f**: ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.68 (t, J = 7.2 Hz, 2H), 4.31 (t, J = 7.2 Hz, 2H), 3.24−3.20 (m, 2H), 3.08−3.04 (m,

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2H), 2.08−2.00 (m, 2H), 1.94−1.87 (m, 2H), 1.33−1.25 (m, 12H), 0.90−0.84 (m, 6H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 141.9, 135.5, 133.8, 126.8, 50.1, 48.8, 31.4, 31.3, 30.1, 30.0, 26.3, 26.2, 22.6, 20.5, 19.6, 14.1, 14.1. HRMS (ESI-HRMS) (m/z): Calcd for $C_{18}H_{31}N_6$, $(M+H)^+$: 331.2605; found: 331.2605.

*2,2′-(4,5-Dihydrobenzo[1,2-d:3,4-d′]bis([1,2,3]triazole)-1,6-diyl)-diethanol (**4g**).* The reaction was performed according to procedure B with triazoloketone **1a** (52 mg, 0.2 mmol), 2-aminoethanol **2g** (31 mg, 0.50 mmol), and 4-nitrophenylazide **3** (39 mg, 0.24 mmol). The crude reaction mixture was then directly purified by silica gel column chromatography (CH_2Cl_2 followed by petroleum ether/EtOAc = 2:8) to afford the product **4g** as a colorless viscous liquid (40 mg, 81%). Analytical data of **4g**: ^1H NMR (400 MHz, MeOD) δ 4.78 (t, J = 5.6 Hz, 2H), 4.49 (t, J = 4.8 Hz, 2H), 4.09 (t, J = 5.6 Hz, 2H), 3.96 (t, J = 4.8 Hz, 2H), 3.25−3.21 (m, 2H), 3.18−3.14 (m, 2H). $^{13}C\{^1H\}$ NMR (101 MHz, MeOD) δ 143.6, 137.8, 135.7, 128.8, 61.9, 61.3, 53.3, 52.3, 20.9, 20.5. HRMS (ESI-HRMS) (m/z): Calcd for $C_{10}H_{15}N_6O_2$, $(M+H)^+$: 251.1251; Found: 251.1256.

*1,6-Bis(4-methoxyphenyl)-1,4,5,6-tetrahydrobenzo[1,2-d:3,4-d′]-bis([1,2,3]triazole) (**4h**).* The reaction was performed according to procedure B with triazoloketone **1a** (52 mg, 0.2 mmol), 4-methoxy aniline **2h** (62 mg, 0.50 mmol), and 4-nitrophenylazide **3** (39 mg, 0.24 mmol). The crude reaction mixture was then directly purified by silica gel column chromatography (CH_2Cl_2 followed by petroleum ether/EtOAc = 2:8) to afford the product **4h** as a white solid (56 mg, 75%). mp: 182−184 °C. Analytical data of **4h**: ^1H NMR (400 MHz, $CDCl_3$) δ 8.00 (d, J = 9.2 Hz, 2H), 7.46−7.44 (m,2H), 7.10−7.05 (m, 4H), 3.89 (s, 6H), 3.30−3.25 (m, 2H), 3.19−3.15 (m, 2H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 160.6, 160.2, 143.0, 135.9, 134.8, 130.2, 129.1, 125.3, 124.9, 115.0, 114.6, 55.8, 55.7, 20.9, 20.5. HRMS (ESI-HRMS) (m/z): Calcd for $C_{20}H_{19}N_6O_2$, $(M+H)^+$: 375.1564; found: 375.1567.

*1,6-Diallyl-1,4,5,6-tetrahydrobenzo[1,2-d:3,4-d′]bis([1,2,3]-triazole) (**4i**).* The reaction was performed according to procedure B with triazoloketone **1a** (52 mg, 0.2 mmol), allylamine **2i** (26 mg, 0.50 mmol), and 4-nitrophenylazide **3** (39 mg, 0.24 mmol). The crude reaction mixture was then directly purified by silica gel column chromatography (CH_2Cl_2 followed by petroleum ether/EtOAc = 2:8) to afford the product **4i** as a brown viscous liquid (33 mg, 68%). Analytical data of **4i**: ^1H NMR (400 MHz, $CDCl_3$) δ 6.20−6.10 (m, 1H), 6.03−5.93 (m, 1H), 5.40−5.33 (m, 2H), 5.34−5.28 (m, 3H), 5.24−5.18 (m, 1H), 4.99−4.97 (m, 2H), 3.21 (t, J = 7.6 Hz, 2H), 3.05 (t, J = 8.8 Hz, 2H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 142.1, 135.7, 134.4, 131.5, 130.8, 126.8, 119.8, 52.1, 51.3, 20.4, 19.5. HRMS (ESI-HRMS) (m/z): Calcd for $C_{12}H_{15}N_6$, $(M+H)^+$: 243.1353; Found: 243.1350.

*1,6-Bis(pyridin-2-ylmethyl)-1,4,5,6-tetrahydrobenzo[1,2-d:3,4-d′]bis([1,2,3]triazole) (**4j**).* The reaction was performed according to procedure B with triazoloketone **1a** (52 mg, 0.2 mmol), pyridin-2-ylmethanamine **2j** (54 mg, 0.50 mmol), and 4-nitrophenylazide **3** (39 mg, 0.24 mmol). The crude reaction mixture was then directly purified by silica gel column chromatography (CH_2Cl_2 followed by petroleum ether/EtOAc = 1:9) to afford the product **4j** as a brown viscous liquid (45 mg, 65%). Analytical data of **4j**: ^1H NMR (400 MHz, $CDCl_3$) δ 8.58−8.55 (m, 2H), 7.69−7.67 (m, 1H), 7.62−7.60 (m, 2H), 7.28−7.24 (m, 2H), 7.21−7.18 (m, 2H), 6.02 (s, 2H), 5.62 (s, 2H), 3.22−3.18 (m, 2H), 3.11−3.06 (m, 2H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 154.8, 154.0, 149.9, 149.9, 142.2, 137.5, 137.1, 135.7, 135.2, 127.4, 123.6, 123.1, 122.4, 122.3, 54.7, 54.2, 20.3, 19.7. HRMS (ESI-HRMS) (m/z): Calcd for $C_{18}H_{17}N_8$, $(M+H)^+$: 345.1571; Found: 345.1580.

*1,6-Bis(thiophen-2-ylmethyl)-1,4,5,6-tetrahydrobenzo[1,2-d:3,4-d′]bis([1,2,3]triazole)(**4k**).* The reaction was performed according to procedure B with triazoloketone **1a** (52 mg, 0.2 mmol), thiophen-2-ylmethanamine **2k** (57 mg, 0.50 mmol), and 4-nitrophenylazide **3** (39 mg, 0.24 mmol). The crude reaction mixture was then directly purified by silica gel column chromatography (CH_2Cl_2 followed by petroleum ether/EtOAc = 1:9) to afford the product **4k** as a brown semisolid (51 mg, 72%). Analytical data of **4j**: ^1H NMR (400 MHz, $CDCl_3$) δ 7.36−7.35 (m, 1H), 7.32−7.30 (m, 1H), 7.24−7.23 (m, 1H), 7.09−7.07 (m, 1H), 7.00−6.98 (m, 1H), 6.93−6.91 (m, 1H), 6.02 (s, 2H), 5.70 (s, 2H), 3.17−3.13 (m, 2H), 3.01−2.97 (m, 2H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 142.1, 136.9, 135.8, 134.1, 128.6, 127.9, 127.5, 127.2, 127.1, 126.9, 47.7, 47.4, 20.3, 19.6. HRMS (ESI-HRMS) (m/z): Calcd for $C_{16}H_{15}N_6S_2$,$(M+H)^+$: 355.0794; found: 355.0794

*1,6-Bis(2-(1H-indol-3-yl)ethyl)-1,4,5,6-tetrahydrobenzo[1,2-d:3,4-d′]bis([1,2,3]triazole) (**4l**).* The reaction was performed according to procedure B with triazoloketone **1a** (52 mg, 0.2 mmol), 2-(1H-indol-3-yl)ethanamine **2l** (80 mg, 0.50 mmol), and 4-nitrophenylazide **3** (39 mg, 0.24 mmol). The crude reaction mixture was then directly purified by silica gel column chromatography (CH_2Cl_2 followed by petroleum ether/EtOAc = 1:4) to afford the product **4l** as a white semisolid (54 mg, 60%). Analytical data of **4l**: ^1H NMR (300 MHz, $CDCl_3$) δ 8.09−8.07 (m, 2H), 7.66 (d, J = 7.5 Hz, 1H), 7.40−7.28 (m, 3H), 7.20−7.04 (m, 5H), 6.71 (d, J = 2.0 Hz, 1H), 4.97 (t, J = 7.6 Hz, 2H), 4.55 (t, J = 6.5 Hz, 2H), 3.50 (t, J = 7.5 Hz, 2H), 3.36 (t, J = 6.4 Hz, 2H), 2.62 (t, J = 8.1 Hz, 2H), 2.15 (t, J = 8.1 Hz, 2H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 142.1, 142.1, 136.3, 136.2, 135.1, 134.8, 127.6, 127.0, 126.9, 122.8, 122.7, 122.1, 120.0, 119.7, 111.7, 111.6, 111.2, 111.1, 50.6, 49.5, 26.7, 26.3, 20.1, 19.1. HRMS (ESI-HRMS) (m/z): Calcd for $C_{26}H_{25}N_8$, $(M+H)^+$: 449.2197; found: 449.2193.

*1,6-Dihexyl-4-methyl-1,4,5,6-tetrahydrobenzo[1,2-d:3,4-d′]bis-([1,2,3]triazole) (**4m**).* The reaction was performed according to procedure B with triazoloketone **1b** (54 mg, 0.2 mmol), *n*-hexylamine **2f** (51 mg, 0.50 mmol), and 4-nitrophenylazide **3** (39 mg, 0.24 mmol). The crude reaction mixture was then directly purified by silica gel column chromatography (CH_2Cl_2 followed by petroleum ether/EtOAc = 3:7) to afford the product **4m** as a colorless viscous liquid (54 mg, 78%). Analytical data of **4m**: ^1H NMR (400 MHz, $CDCl_3$) δ 4.67 (t, J = 7.2 Hz, 2H), 4.35−4.27 (m, 2H), 3.52−3.42 (m, 1H), 3.15 (dd, J_1 = 16.4 Hz, J_2 = 7.6 Hz, 1H), 2.70 (dd, J_1 = 16.4, J_2 = 8.4 Hz, 1H), 2.07−2.00 (m, 2H), 1.91−1.86 (m, 2H), 1.47 (d, J = 6.8 Hz, 3H), 1.35−1.28 (m, 12H), 0.89−0.83 (m, 6H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 146.4, 135.2, 133.6, 125.9, 50.0, 48.8, 31.3, 30.1, 28.3, 27.9, 26.2, 22.6, 19.8, 14.1. HRMS (ESI-HRMS) (m/z): Calcd for $C_{19}H_{33}N_6$, $(M+H)^+$: 345.2761; found: 345.2761.

*1,6-Dihexyl-4-phenyl-1,4,5,6-tetrahydrobenzo[1,2-d:3,4-d′]bis-([1,2,3]triazole) (**4n**).* The reaction was performed according to procedure B with triazoloketone **1c** (67 mg, 0.2 mmol), *n*-hexylamine **2f** (51 mg, 0.50 mmol), and 4-nitrophenylazide **3** (39 mg, 0.24 mmol). The crude reaction mixture was then directly purified by silica gel column chromatography (CH_2Cl_2 followed by petroleum ether/EtOAc = 3:7) to afford the product **4n** as a brown viscous liquid (61 mg, 75%). Analytical data of **4n**: ^1H NMR (300 MHz, $CDCl_3$) δ 7.30−7.23 (m, 4H), 7.16−7.13 (m, 2H), 4.74 (t, J = 7.5 Hz, 2H), 4.68−4.63 (m, 1H), 4.26 (t, J = 6.9 Hz, 2H), 3.48−3.40 (m, 1H), 3.19−3.11 (m, 1H), 2.11−2.04 (m, 2H), 1.84−1.75 (m, 2H), 1.39−1.24 (m, 12H), 0.89−0.85 (m, 6H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 144.4, 142.0, 135.3, 133.1, 129.0, 127.5, 127.4, 50.2, 48.9, 38.7, 31.3, 31.2, 30.1, 30.0, 29.6, 26.3, 26.2, 22.6, 22.5, 14.1. HRMS (ESI-HRMS) (m/z): Calcd for $C_{24}H_{35}N_6$, $(M+H)^+$: 407.2918; found: 407.2915.

*1,6-Dihexyl-4,4-dimethyl-1,4,5,6-tetrahydrobenzo[1,2-d:3,4-d′]-bis([1,2,3]triazole) (**4o**).* The reaction was performed according to procedure B with triazoloketone **1d** (58 mg, 0.2 mmol), 4-methoxy benzylamine **2a** (69 mg, 0.50 mmol), and 4-nitrophenylazide **3** (39 mg, 0.24 mmol). The crude reaction mixture was then directly purified by silica gel column chromatography (CH_2Cl_2 followed by petroleum ether/EtOAc = 3:7) to afford the product **4o** as a white semisolid (72 mg, 84%). Analytical data of **4o**: ^1H NMR (400 MHz, $CDCl_3$) δ 7.53 (d, J = 8.8 Hz, 2H), 7.15 (d, J = 8.8 Hz, 2H), 6.84 (dd, J_1 = 16.6, J_2 = 8.8 Hz, 4H), 5.78 (s, 2H), 5.46 (s, 2H), 3.78 (s, 3H), 3.74 (s, 3H), 2.64 (s, 2H), 1.29 (s, 6H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 159.9, 159.7, 150.1, 135.4, 133.9, 130.4, 129.1, 127.5, 126.2, 124.5, 114.6, 114.1, 55.4, 55.3, 52.8, 52.3, 35.5, 33.6, 28.1. HRMS (ESI-HRMS) (m/z): Calcd for $C_{24}H_{27}N_6O_2$, $(M+H)^+$: 431.2190; found: 431.2189.

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*1,3′-Bis(4-methoxybenzyl)-5-methyl-1H,3′H-4,4′-bi(1,2,3-triazole) (**4p**).* The reaction was performed according to procedure B with triazoloketone **1e** (49 mg, 0.2 mmol), 4-methoxy benzylamine (69 mg, 0.50 mmol), and 4-nitrophenylazide **3** (39 mg, 0.24 mmol). The crude reaction mixture was then directly purified by silica gel column chromatography (CH_2Cl_2 followed by petroleum ether/EtOAc = 2:8) to afford the product **4p** as a semi white solid (62 mg, 80%). Analytical data of **4p**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70 (s, 1H), 7.12 (dd, J_1 = 16.8, J_2 = 8.8 Hz, 4H), 6.88 (d, J = 8.4 Hz, 2H), 6.70 (d, J = 8.8 Hz, 2H), 5.87 (s, 2H), 5.45 (s, 2H), 3.80 (s, 3H), 3.72 (s, 3H), 2.08 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 159.9, 159.4, 133.7, 132.7, 132.1, 129.7, 128.9, 127.9, 127.7, 126.2, 114.6, 114.0, 55.5, 55.3, 52.4, 52.0, 8.6. HRMS (ESI-HRMS) (m/z): Calcd for $C_{21}H_{23}N_6O_2$, $(M+H)^+$: 391.1877; found: 391.1873.

*1,3′-Dihexyl-5-methyl-1H,3′H-4,4′-bi(1,2,3-triazole) (**4q**).* The reaction was performed according to procedure B with triazoloketone **1e** (52 mg, 0.2 mmol), *n*-hexylamine **2f** (69 mg, 0.50 mmol), and 4-nitrophenylazide (39 mg, 0.24 mmol). The crude reaction mixture was then directly purified by silica gel column chromatography (CH_2Cl_2 followed by petroleum ether/EtOAc = 1:1) to afford the product **4q** as a colorless viscous liquid (55 mg, 87%). Analytical data of **4q:** ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.73 (s, 1H), 4.72−4.68 (m, 2H), 4.33−4.29 (m, 2H), 2.40 (s, 3H), 1.93−1.88(m, 4H), 1.34−1.25 (m, 12H), 0.90−0.81 (m, 6H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 133.4, 132.0, 131.4, 128.1, 49.7, 48.5, 31.3, 31.3, 30.3, 29.9, 26.3, 26.2, 22.6, 22.5, 14.1, 8.8. HRMS (ESI-HRMS) (m/z): Calcd for $C_{17}H_{31}N_6$, $(M+H)^+$: 319.2605; found: 319.2598.

*5-Methyl-1,3′-bis(thiophen-2-ylmethyl)-1H,3′H-4,4′-bi(1,2,3-triazole) (**4r**).* The reaction was performed according to procedure B with triazoloketone **1a** (52 mg, 0.2 mmol), benzylamine (69 mg, 0.50 mmol), and 4-nitrophenylazide (39 mg, 0.24 mmol). The crude reaction mixture was then directly purified by silica gel column chromatography (CH_2Cl_2 followed by petroleum ether/EtOAc = 3:7) to afford the product **4r** as a brown semisolid (51 mg, 75%). Analytical data of **4r**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.71 (s, 1H), 7.32 (dd, J = 5.1, 1.3 Hz, 1H), 7.13 (dd, J 1= 5.1, J 2= 1.2 Hz, 1H), 7.04−6.94 (m, 3H), 6.80 (dd, J = 5.1, 3.5 Hz, 1H), 6.14 (s, 2H), 5.71 (s, 2H), 2.27 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 137.2, 136.1, 133.5, 132.4, 132.2, 127.9, 127.6, 127.4, 126.9, 126.8, 126.5, 47.6, 47.3, 8.9. HRMS (ESI-HRMS) (m/z): Calcd for $C_{15}H_{14}N_6NaS_2$, $(M+Na)^+$: 365.0614; found: 365.0611.

*Synthesis and Characterization of 1-(4-Methoxybenzyl)-6,7-dihydro-1H-benzo[d][1,2,3]triazol-4(5H)-one (**6a**).* The triazolo ketone **1a** (52 mg, 0.2 mmol) and 4-methoxy benzylamine **2a** (27 mg, 0.20 mmol) were weighed into a reaction tube. After that, 30 mol % acetic acid and 1,4-dioxane (2 mL) were added and allowed to stir at 100 °C using oil bath for 3 h. Upon completion of the reaction, the solvent was evaporated 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 petroleum ether and ethyl acetate as eluent to afford the product **6a** as a white solid (44 mg, 85%). mp: 140−142 °C. Analytical data of **6a**: ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.18 (d, J = 8.8 Hz, 2H), 6.89−6.87(m, 2H), 5.47 (s, 2H), 3.79 (s, 3H), 2.72−2.69 (m, 2H), 2.55−2.52 (m, 2H), 2.16−2.13 (m, 2H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 190.2, 160.0, 144.5, 142.5, 129.3, 125.8, 114.6, 55.4, 52.1, 38.2, 23.0, 20.5. HRMS (ESI-HRMS) (m/z): Calcd for $C_{14}H_{15}N_3NaO_2$, $(M+Na)^+$: 280.1056; found: 280.1059.

*Synthesis and Characterization of 1-Hexyl-6-(4-methoxybenzyl)-1,4,5,6-tetrahydrobenzo[1,2-d:3,4-d′]bis([1,2,3]triazole) (**7a**).* The triazolo ketone **6a** (56 mg, 0.2 mmol), *n*-hexylamine **2f** (20 mg, 0.20 mmol), and 4-nitrophenyl azide **3** (33 mg, 0.20 mmol) were weighed into a reaction tube, and 1,4-dioxane (2 mL) was added along with 30 mol % acetic acid and allowed to stir at 100 °C using oil bath for 12 h. Upon completion of the reaction, the solvent was evaporated 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 petroleum ether and ethyl acetate as eluent to afford the product **7a** as a white semisolid (60 mg, 82%). Analytical data of **7a**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.19−7.17 (m, 2H), 6.88−6.85 (m, 2H), 5.46 (s, 2H), 4.65 (t, J = 7.3 Hz, 2H), 3.78 (s, 3H), 3.13−3.09 (m, 2H), 2.89−2.85 (m, 2H), 2.04−1.98 (m, 2H), 1.37−1.24 (m, 6H), 0.86−0.83 (m, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 160.0, 141.8, 136.0, 133.9, 129.2, 126.6, 126.0, 114.6, 55.4, 52.4, 50.0, 31.3, 30.0, 26.2, 22.5, 20.3, 19.6, 14.1. HRMS (ESI-HRMS) (m/z): Calcd for $C_{20}H_{27}N_6O$, $(M+H)^+$: 367.2241; found: 367.2239.

*Synthesis and Characterization of 1,6-Dihexyl-1,6-dihydrobenzo[1,2-d:3,4-d′]bis([1,2,3]triazole) (**8a**).* The triazolo ketone **1a** (52 mg, 0.2 mmol), *n*-hexylamine **2f** (20 mg, 0.20 mmol), and 4-nitrophenyl azide (33 mg, 0.20 mmol) were weighed into a reaction tube, and 1,4-dioxane (2 mL) and 30 mol % acetic acid were added and allowed to stir at 100 °C for 12 h. Upon completion of the reaction, the solvent was evaporated in vacuo. One milliliter of dioxane and DDQ were added to the same reaction tube, and this was then left to stir at 80 °C using an oil bath for 12 h. 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 petroleum ether and ethyl acetate (60% ethyl acetate in hexane) to afford the product **8a** as a colorless viscous liquid (46 mg, 70%). Analytical data of **8a**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.07 (d, J = 9.2 Hz, 1H), 7.44 (d, J = 9.2 Hz, 1H), 5.08 (t, J = 7.2 Hz, 2H), 4.71 (t, J = 7.2 Hz, 2H), 2.25−2.16 (m, 2H), 2.09−2.02 (m, 2H), 1.43−1.23 (m, 12H), 0.89−0.83 (m, 6H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 143.9, 133.1, 132.4, 125.0, 120.1, 106.9, 50.6, 49.0, 31.3, 30.0, 29.8, 26.5, 26.3, 22.6, 22.5, 14.1, 14.0. HRMS (ESI-HRMS) (m/z): Calcd for $C_{18}H_{29}N_6$, $(M+H)^+$: 329.2448; found: 329.2448.

Procedure for One-Pot Reaction. 1,3-Cyclohexanedione **5a** (112 mg, 1.0 mmol), 4-nitrophenylazide **3** (164 mg, 1.0 mmol), DBU (5 mol %), and DMSO (1.0 mL) were added to a reaction tube and stirred at room temperature for 1 h. After completion of the reaction, *n*-hexylamine **2f** (202 mg, 2 mmol) and 4-nitrophenyl azide **3** (164 mg, 1.0 mmol) were weighed into the same reaction tube, and 1,4-dioxane (1 mL) was added along with 30 mol % acetic acid and allowed to stir at 100 °C using oil bath for 12 h. Upon completion of the reaction, the solvent was evaporated in vacuo. To the reaction mixture, water was added and then extracted with ethyl acetate. The combined organic layers were thoroughly washed with water and dried over $MgSO_4$, and the solvent was removed under 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 petroleum ether and ethyl acetate as eluent to afford the product **4f** as a viscous liquid (241 mg, 73%).

Gram Scale Synthesis. The triazolo ketone **6a** (1.5 g, 5.8 mmol), *n*-hexylamine **2f** (1.5 g, 14.5 mmol), and 4-nitrophenyl azide **3** (1.1 g, 6.96 mmol) were weighed into a 100 mL round-bottom flask, and 1,4-dioxane (30 mL) was added along with 30 mol % acetic acid and allowed to stir at 100 °C using oil bath for 12 h. Upon completion of the reaction, the solvent was evaporated 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 petroleum ether and ethyl acetate as eluent to afford the product **4f** as a viscous solid (1.4 g, 72%).

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.joc.0c03014.

NMR spectra of all of the synthesized compounds (**1a**−**1e**, **4a**−**4r**, **6a**, **7a**, and **8a**) (PDF)

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Notes

The authors declare no competing financial interest.

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