Investigation of the Reactivity of 1-Azido-3-Iodobicyclo[1.1.1]pentane under "Click" Reaction Conditions

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ABSTRACT The bicyclo[1.1.1]pentane (BCP) unit exhibits special physical and chemical properties and is under scrutiny as a bioisostere in drug molecules. We employed methodologies for the synthesis of different BCP triazole building blocks from one precursor, 1-azido-3-iodobicyclo[1.1.1]pentane, by Cu(I)-catalyzed 1,3-dipolar cycloaddition ("click") reactions and integrated cycloaddition-Sonogashira coupling reactions. Thereby, we accessed three classes of substituted BCP derivatives: 1,4-disubstituted triazoles, 5-iodo-1,4,5-trisubstituted triazoles and 5-alkynylated 1,4,5-trisubstituted triazoles. This gives entry to the synthesis of multiply

substituted BCP triazoles either on a modular or a one-pot basis. These methodologies were further utilized for appending large chromophoric porphyrin moieties onto the BCP core.

INTRODUCTION The development of synthetic routes towards bicyclo[1.1.1]pentane (BCP) derivatives is a field of growing interest.[1] This rigid hydrocarbon scaffold has attracted attention as a linear linker in electron donor-acceptor systems as well as in molecular rods and rotors. Future applications require simple and robust synthetic methods for its modification. BCP derivatives have promise as bioisosteres for organic moieties, such as phenyl rings, *tert*-butyl groups and alkynes and the BCP moiety can favorably alter physicochemical and pharmacokinetic properties of drug candidate molecules.[1a,2]

In the context of using functionalized hydrocarbon cages as building blocks and molecular tectons in medicinal and materials chemistry we[3] are interested in appending BCP with chromophores for the construction of donor-acceptor systems. Searching for versatile methods for the synthesis of new BCP building blocks and BCP-chromophore arrays we reflected that the copper-catalyzed azide-alkyne 1,3-dipolar cycloaddition ("click" reaction)[4] can be a very useful tool due to its broad substrate scope, its efficiency and easily available precursors.[5] Although previously described for 1-azido-3-iodo-BCP **1** (Figure 1), "click" reactions on this facile BCP derivative have been limited to a rather narrow scope of small molecule substrates.[6]

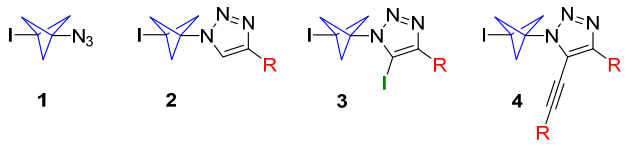


Figure 1. 1-Azido-3-iodo-BCP **1** precursor and general structures of the three triazole building blocks derived thereof.

We intended to investigate the reactivity of **1** in more detail and to broaden the range of accessible BCP-triazoles **2** to derivatives with complex chromophoric substituents. In doing so, we came across more "click"-type reactions that yielded functional BCP-triazole cores **3** and **4**.

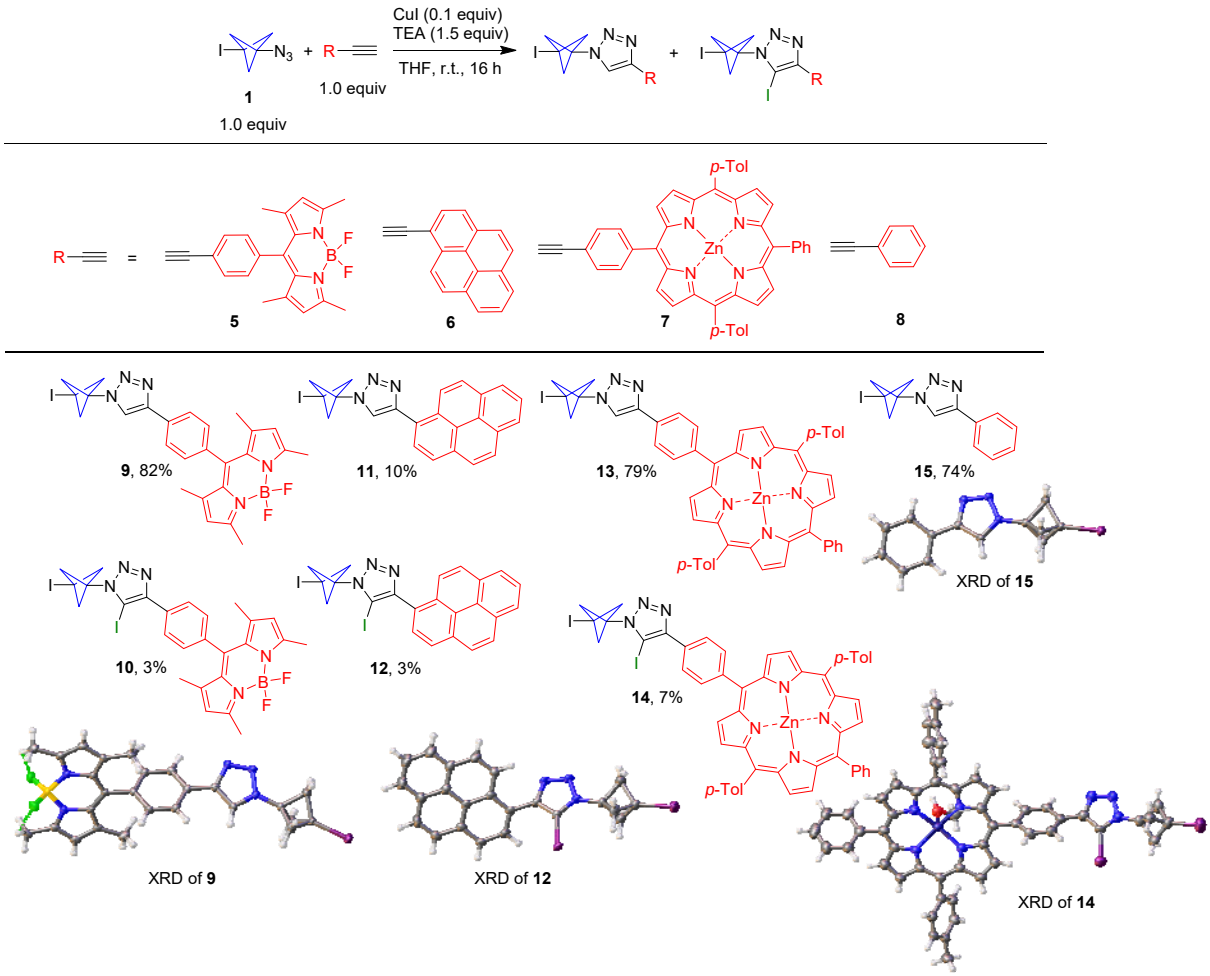
This led us to study the use of 1-azido-3-iodo-BCP as a precursor for three different "click"-type reactions, the first of which is a classical Cu(I)-catalyzed "click" reaction to obtain 5-protio-1,2,3-triazoles (**2**). Secondly, we investigated the synthesis of BCP-5-iodotriazoles (**3**). 5-Iodo-1,2,3-triazoles have attracted widespread attention as compounds for anion recognition and in biomedical applications, among others.[7] Lastly, we synthesized 1,4,5-trisubstituted BCP-triazoles (**4**) resembling molecular "tweezers" with different alkynyl-substituents in the 5-position. Similar 1,4,5-trisubstituted triazole scaffolds have previously been found to show desirable properties for biological applications,[8] such as antifungal,[9] antiviral[10] anticancer[11] and antiophidian agents,[12] receptor antagonists and binders,[13] protease inhibitors,[14] antiplatelet aggregation[15] and anti-inflammatory agents.[16] Additionally, substitution of the triazole ring in the 4- and 5-positions provides the possibility to arrange two moieties, e.g. donor-acceptor chromophores, in a defined spatial manner.

Both, the synthesis of 5-iodotriazoles (**3**) and of "tweezer"-like triazole (**4**) compounds have been unexplored so far for BCP scaffolds. The applied synthetic methods enabled us to obtain the building blocks **2**, **3** and **4** from the same precursors in single step one-pot reactions.

RESULTS AND DISCUSSION To investigate the modification of BCP *via* 1,3-dipolar cycloaddition reactions, 1-azido-3-iodo-BCP **1** was prepared according to a literature procedure.[17] Intending to append a chromophore on BCP, **1** was reacted with ethynyl-substituted BODIPY **5** under "click" reaction conditions as reported previously.[6] Stirring a solution of BCP **1** in THF with triethylamine (TEA) (1.5 equiv), CuI (0.1 equiv) and BODIPY **5**

(1 equiv) for 16 h yielded the 1,2,3-triazole product **9** in 82% (Scheme 1). Interestingly, a small fraction eluted just before 1,2,3-triazole **9**. The ^{1}H NMR spectrum showed a characteristic singlet at 3.07 ppm corresponding to the six BCP bridge protons. At the same time, the signals of the BODIPY moiety could be found but no proton signal for the 5-position of the triazole ring was apparent, pointing towards a 1,4,5-substituted triazole. Mass spectrometry gave evidence that 5-iodo-1,2,3-triazole **10** had formed as a side product of the "click" reaction with a yield of 3%. Similar reactions of BCP **1** with other chromophoric substrates, 1-ethynylpyrene **6** and alkynyl-porphyrin **7**, also gave the corresponding 5-iodo-1,2,3-triazoles **12** and **14** as minor products in 3% and 7% yield, respectively, next to 5-protio-1,2,3-triazoles **11** (10%) and **13** (79%). However, when the reaction was carried out using phenylacetylene, only the 5-protio-1,2,3-triazole product **15** was isolated (Scheme 1).

Scheme 1. "Click" reactions with 1-azido-3-iodo-BCP **1** and different substrates.



The repeated formation of BCP 5-iodo-1,2,3-triazoles in reactions with different substrates led us to investigate this side reaction in more depth. A survey of the literature revealed that the synthesis of 5-iodo-1,2,3-triazoles *via* 1,3-dipolar cycloaddition reactions can be achieved by two different routes. Either a terminal alkyne can be used in combination with an electrophilic iodine species which is added as such or generated *in situ* or an iodoalkyne is employed as a starting material.[18] In a few cases, the formation of small amounts of 5-iodo-1,2,3-triazoles as side products in "click" reactions was observed under conditions similar to the ones employed by us.[19]

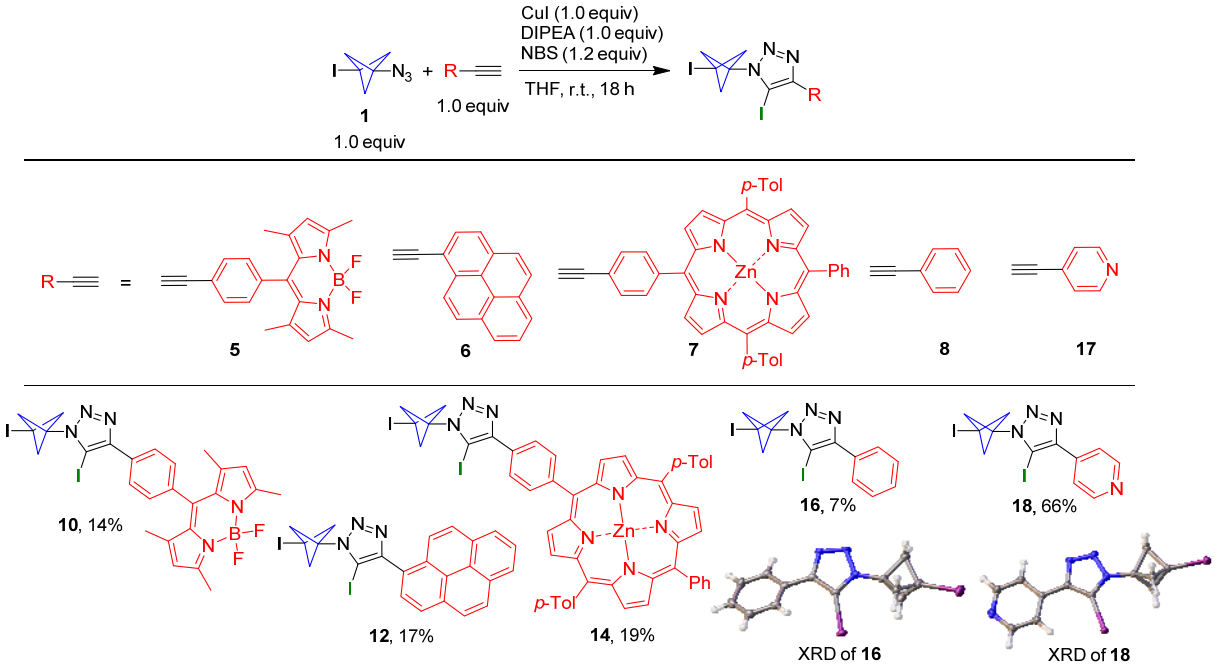
The formation of 5-iodo-1,2,3-triazoles is likely affected by the presence of residual oxygen in the reaction mixture which facilitates oxidation of I^- to an electrophilic iodine species. This assumption was supported by the results of test reactions carried out in argon-purged solvents and under air, respectively, where reactions under air showed higher yields (Table 1). An increase in the amount of CuI (1.0 equiv) used and carrying out the reaction under air led to an elevated yield of 5-iodo-1,2,3-triazole **10** of 33% along with 22% of the 5-protio-1,2,3-triazole **9**. However, formation of a considerable amount of a butadiyne-linked BODIPY dimer from a Glaser[20] coupling reaction occurring under these conditions limited the yield of **10**. To enhance the formation the new BCP-5-iodotriazole building blocks we applied a literature procedure which uses CuI (1 equiv) in combination with an oxidant, *N*-bromosuccinimide (NBS) (1.2 equiv), and a base, *N*,*N*-diisopropylethylamine (DIPEA) (1.0 equiv).[21] Compound **10** was formed in a good yield of 69% under these conditions (Scheme 2).

Table 1. Screening of reaction conditions for the formation of 5-protio-1,2,3-triazole **9** and 5-iodo-1,2,3-triazole **10** from precursors **1** and **5**.

	conditions	atmosph.[b]	yield[c] of **10**	yield[c] of **9**
1	CuI (0.2 equiv), TEA (1.5 equiv)	argon	11%	80%
2	CuI (0.3 equiv), TEA (1.5 equiv)	argon	13%	71%
3	CuI (0.2 equiv), TEA (1.5 equiv)	air	15%	54%
4	CuI (0.3 equiv), TEA (1.5 equiv)	air	17%	54%
5	CuI (1.0 equiv), TEA (3.8 equiv)	air	33%	22%
6	CuI (1.0 equiv), DIPEA (1 equiv), NBS (1.2 equiv)	argon	69%	6%

[a] All reactions were carried out with **1** (28.7 μmol) and **5** (28.7 μmol) in THF (0.67 mL) for 16 h. [b] For reactions carried out under argon atmosphere the solvent was deoxygenated by purging with argon for 15 min. [c] Yield obtained from ^{1}H NMR with an internal standard.

Scheme 2. Synthesis of 5-iodo-1,2,3-triazoles from **1**.

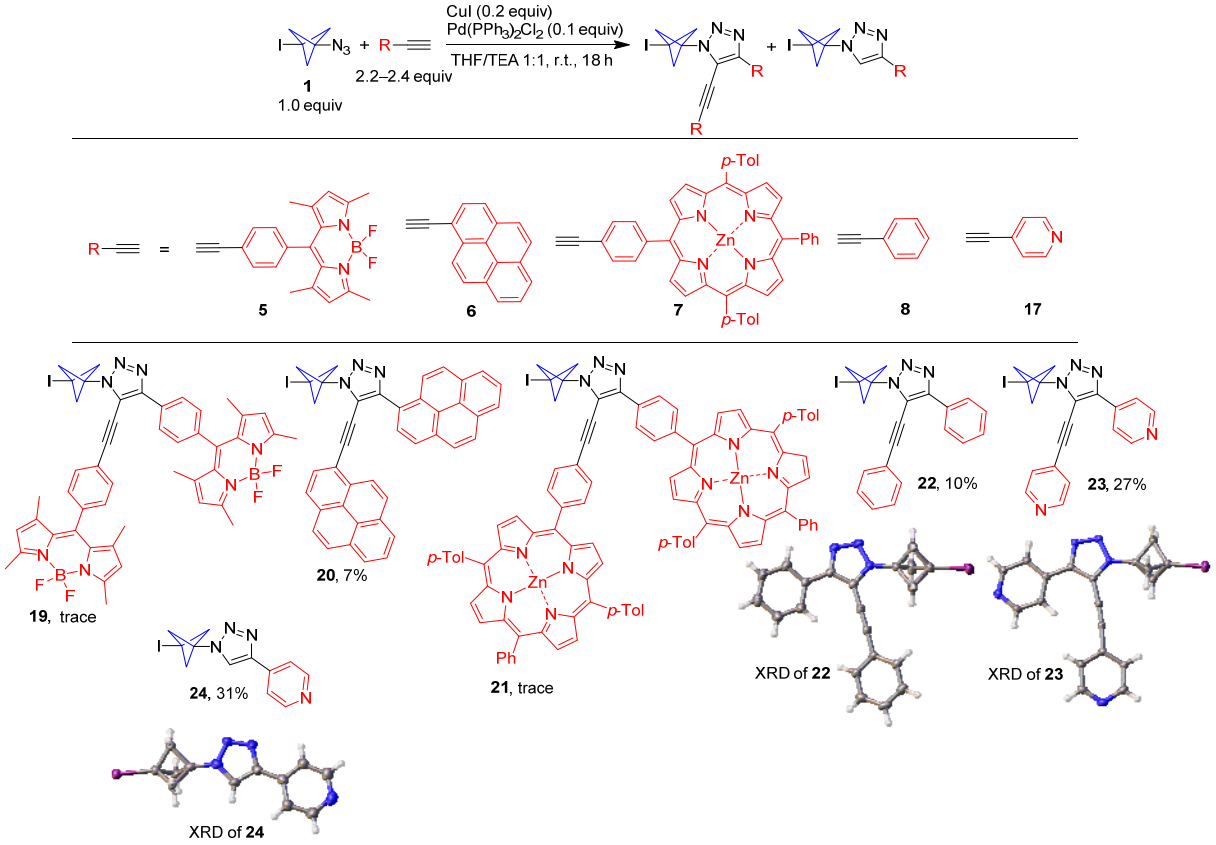


These reaction conditions proved to be promising for the synthesis of different BCP-5-iodo-1,2,3-triazoles in improved yields and were applied to other substrates. While reaction with 4-ethynylpyridine **17** proceeded in a good yield of 66%, more electron-rich substrates such as 1-ethynylpyrene **6** and phenylacetylene **8** gave low yields of 17% and 7%, respectively. Possibly, this is due to side reactions such as Glaser couplings occurring to a larger extent with these substrates. The reaction with alkynyl-BODIPY **5** and -porphyrin **7** yielded the 5-iodo-1,2,3-triazoles **10** and **14** in 14% and 19% yield, respectively.

The 5-iodo of the triazole ring is a useful synthetic handle for subsequent functionalization with a second moiety yielding tweezer-like 1,4,5-trisubstituted 1,2,3-triazoles. Such scaffolds can likewise be synthesized by several single-step procedures from the respective azide and different precursors such as terminal alkynes.[18b,22] 1,4,5-Trisubstituted 1,2,3-triazoles have been reported as compounds with promising biological activities in various fields.[17,20b] Hence, we

investigated the reactivity of 1-azido-3-iodo-BCP to produce 1,4,5-trisubstituted 1,2,3-triazoles. 5-Alkynylated triazoles can be obtained in one-pot reactions using only copper salts as catalysts in the presence of oxygen or oxidants such as *N*-methylmorpholine-*N*-oxide.[18b,22,23] The reaction proceeds *via* a triazolide intermediate with copper(I) bound in the 5-position of the triazole ring that undergoes C-C bond formation with a free terminal acetylene.[22] Another approach to 5-alkynyl-1,2,3-triazoles is the use of 5-halogenated precursors or their *in situ* generation followed by Pd-catalyzed Sonogashira[24] coupling reaction.[20b,25] Surprisingly, when we directly used 1-azido-3-iodo-BCP in a Sonogashira reaction with 1-ethynylpyrene using $Pd(PPh_3)_2Cl_2$ (0.1 equiv) and CuI (0.2 equiv) formation of the 1,4,5-trisubstituted triazole **20** in 7% yield was observed (Scheme 3). Apparently, the reaction conditions mediated the azide-alkyne 1,3-dipolar cycloaddition and C-C bond formation reaction in the 5-position of the triazole ring in a single step. The scope of this unprecedented reaction was tested using different alkynyl-substrates as reactants (Scheme 3). With phenylacetylene the 1,4,5-trisubstituted 1,2,3-triazole product **22** was obtained in 10% yield while, using 4-ethynylpyridine, 27% of the trisubstituted product **23** formed. The 5-protio-1,2,3-triazole **24** was also formed and isolated in 31% yield.

Scheme 3. One-pot procedure for the synthesis of 1,4,5-trisubstituted 1,2,3-triazoles from **1** and terminal alkynes.



We saw potential in using this reaction for the one-pot synthesis of BCP-bound chromophore tweezers and reacted **1** with alkynyl-substituted BODIPY **5** and porphyrin **7**. In both cases, formation of complex mixtures of reaction products and difficult purifications allowed only the isolation of trace amounts of the respective 1,4,5-trisubstituted 1,2,3-triazoles **19** and **21**. One such example of the formation of a 1,4,5-trisubstituted 1,2,3-triazole from azide and alkyne starting materials as a side product in Sonogashira coupling reactions was reported in the literature and it was proposed that the 5-alkynylation reaction is copper-mediated.[26] To investigate the dependence of the 5-alkynylation reaction on Pd, we carried out one reaction with 4-ethynylpyridine under the reported conditions but without addition of a Pd catalyst. No formation of product **23** was observed, indicating that Pd is required for the 5-alkynylation reaction to take place.

Due to the low yield for large chromophoric moieties in the one-pot cycloaddition-coupling reaction, a sequential approach was tested. When 5-iodo-1,2,3-triazole **10** was reacted with ethynyl-substituted BODIPY **5** under Sonogashira coupling conditions; however, only the BODIPY dimer **25** was obtained along with unreacted starting material **10**. Preliminary results in our lab showed that Suzuki coupling reactions are much more promising for the functionalization of the 5-position of 5-iodotriazoles (see SI). More detailed studies on Suzuki coupling reactions with 5-iodotriazoles are underway.

The structures of BODIPY **5** and BCP compounds **9**, **12**, **14**, **15**, **16**, **18**, **22**, **23** and **24** (see SI Figures S3-S12) were determined by single crystal X-ray diffraction analysis. We focused on the identification of prominent non-covalent interactions. Such interactions are of great importance in nature, where they determine the 3D structure of biomacromolecules and mediate ligand-receptor interactions.[27] Considering that the BCP moiety attracts growing interest as a bioisostere in drug candidates[2] it is pivotal to study the effects of the bioisosteric replacement on the weak interactions with molecules in the surroundings. The engineering of crystals with tuned non-covalent interactions is also of growing interest for the design of functional materials.[28] In the case of BCP-triazoles some interesting non-covalent interactions were observed for the different types of molecules. Halogen bonding[29] governs the molecular packing in several structures. Prominent interactions that were identified are I···N,[30] I···I,[30c,31] C-H···I[32] as well as C-H···N[33] contacts resulting in the arrangement of molecules in 2D sheets or 3D networks, respectively.

BCP **18** differs from BCP **16** only by having a pyridine in place of a phenyl substituent in the 4-position of the triazole ring. In BCP **16** a halogen bond between triazolo-nitrogen N8 and triazolo-iodine I2 fixes the molecules in a head-to-head packing pattern (Figure 2a). In BCP **18**

halogen bonding between I1 and pyridyl-nitrogen N13 is the dominant interaction (Figure 2b). In parallel, the nucleophilic site of I1 forms a type II halogen bond with the electrophilic end of I2.[30c,31] In combination with an additional C14-H14···N6 contact this results in an offset packing of parallel sheets.

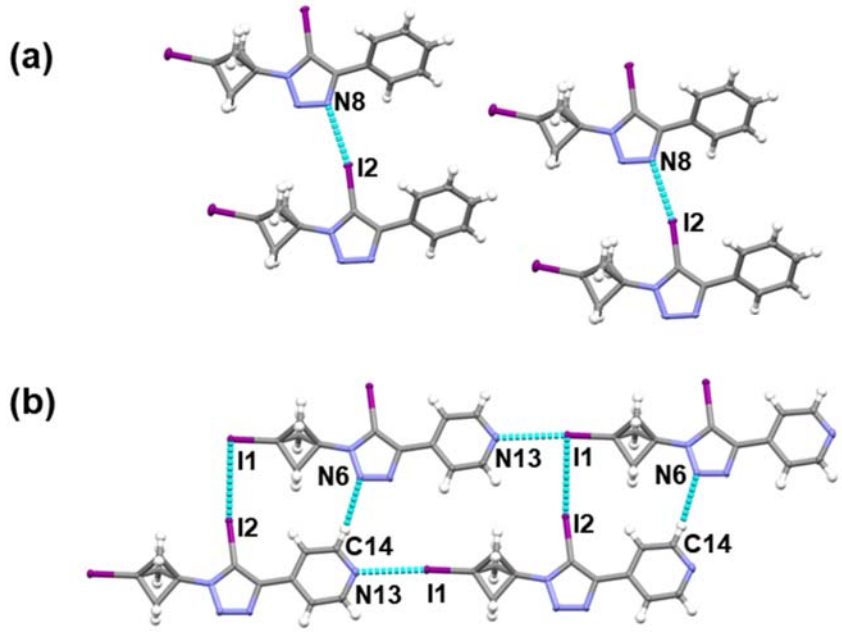


Figure 2. Non-covalent interactions in the crystals of (a) BCP **16** (N8···I2 = 2.897 (16) Å) and (b) BCP **18** (I1···N13 = 3.184 (11) Å, 176.0 (10)°; I1···I2 = 3.721 (13) Å, 172.2 (17)°, 89.1 (4)°; C14-H14···N6= 3.456 (14) Å).

In the structures of the 5-protiotriazoles BCP **15** and BCP **24** it is also observed that replacement of a phenyl ring with a pyridyl moiety results in an iodine-nitrogen interaction (Figure 3b) which dominates over the iodine-π interaction observed for the phenyl containing sample (Figure 3a). In both compounds contacts are formed between triazolo-C-H and triazolo-nitrogen which mediate the formation of parallel sheets.

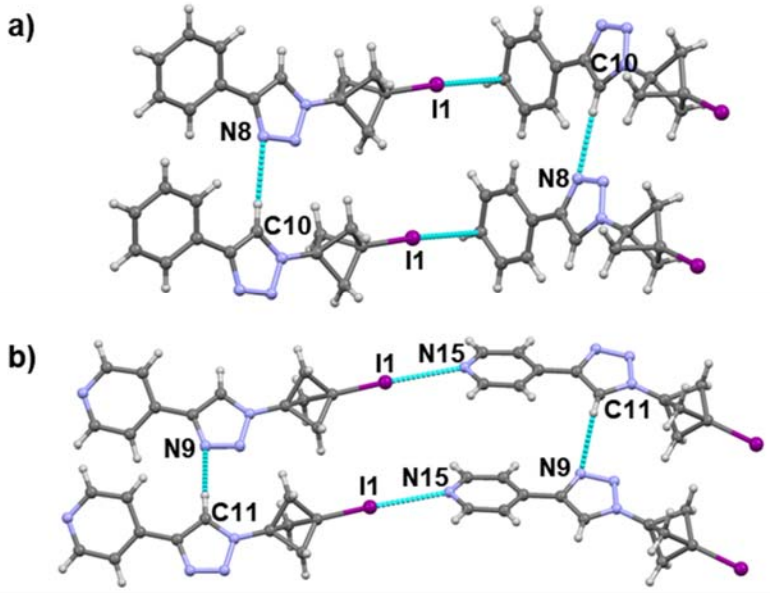


Figure 3. Non-covalent interactions in the crystals of (a) BCP **15** (I1··· π = 3.630 (2) Å; (C10-H10···N8 = 3.377 (3) Å) and (b) BCP **24** (I1···N15 = 3.107 (16) Å; C11-H11···N9 = 3.392 (18) Å).

Crystal structures of the phenyl- and pyridyl-substituted BCP tweezer compounds **22** and **23** were compared as well. BCP **22** molecules are arranged in layers that are interconnected by intermolecular C-H··· I and C-H··· N contacts (Figure S15).

In the crystal structure of compound **23** additional hydrogen bonds are formed by the two pyridine moieties. Pyridyl-nitrogen N22 forms a bifurcated bond with pyridyl-C18-H18 and pyridyl-C21-H21 of an adjacent tweezer molecule (Figure S16). Bifurcated hydrogen bond formation of pyridine-type compounds has been previously observed in solid state and in solution.[34] Additional hydrogen contacts occur between triazolo-nitrogen N7 and BCP-C3-H3 as well as between pyridyl-nitrogen N16 and BCP-C2-H2. In combination with an I···π interaction between I1 and a pyridine ring this leads to the formation of layers.

CONCLUSION In conclusion, we explored three different means to synthesize new BCP-triazole building blocks using 1,3-dipolar cycloaddition reactions. We obtained molecules that were iodinated in the 5-position of the triazole ring in moderate to good yields. Iodine in this position is a useful synthetic handle for further functionalization as well as a site for molecular interaction. We also produced BCP compounds substituted with 5-alkynylated 1,2,3-triazoles in a one-step cycloaddition-Pd-catalyzed coupling reaction to yield molecular tweezer compounds. X-ray analysis revealed notable intermolecular interactions of some of the synthesized derivatives in the solid state. Particularly noteworthy are different non-covalent interactions involving iodine moieties, indicating intermolecular binding capabilities of this class of molecules. The synthetic approaches presented herein are promising tools for the generation of BCP derivatives with different potential applications, i.e. in the fields of medicinal chemistry and materials sciences.

EXPERIMENTAL SECTION

General Information. All reagents were obtained from commercial sources and used as received unless otherwise stated. All air and/or water-sensitive materials were handled using standard high vac. procedures. Anhydrous THF and TEA were purchased from Sigma-Aldrich and anhydrous dichloromethane was obtained by distillation from P_2O_5 and stored over activated molecular sieves. The precursors 1-azido-3-iodobicyclo[1.1.1]pentane (**1**),[17] 8-(4-ethynylphenyl)-4,4-difluoro-1,3,5,7-tetramethyl-4-bora-3a,4a-diaza-*s*-indacene (**5**),[35] 1-ethynylpyrene (6),[36] and [5-(4-ethynylphenyl)-10,20-bis(4-methylphenyl)-15-phenylporphyrinato)]zinc(II) (**7**)[37] were synthesized according to literature procedures. For some reactions, a mixture of 1-azido-3-iodobicyclo[1.1.1]pentane (**1**) and 1,3-diiodobicyclo[1.1.1]pentane was used. To rule out the possibility that the use of this mixture as a

starting material for “click” reactions has an effect on the product formation, a test “click” reaction with neat 1-azido-3-iodo-BCP **1** and BODIPY **2** was performed under the conditions of general procedure A. The 5-iodo-1,2,3-triazole product **7** was isolated with a yield of 6%, alongside the 5-protio-1,2,3-triazole product **6** with a yield of 71%. This product distribution was comparable to the results obtained when a mixture of 1-azido-3-iodobicyclo[1.1.1]pentane and 1,3-diiodobicyclo[1.1.1]pentane was used, indicating that use of the mixture had no influence on the product formation. Reactions at elevated temperatures were carried out using a hot plate with oil bath as a heat source. Flash chromatography was carried out using silica gel Florisil (200 mesh; Aldrich). Preparative thin layer chromatography was performed on precoated preparative Uniplates (silica, 2000 μm, 20 × 20 cm, Analtech). Analytical thin-layer chromatography was carried out on precoated 60 F254 silica plates (0.2 mm thick, 20 × 20 cm) and visualized by UV irradiation on a Shimadzu Multispec-1501. Bruker DPX 400 and Agilent 400 were used to obtain ^{1}H (400.13 MHz), ^{13}C{H} (100.61 MHz), ^{19}F{H} (376.60 MHz) and ^{11}B (128.40 MHz) NMR spectra and a Bruker AV 600 was employed for ^{1}H (600.13 MHz) and ^{13}C{H} (150.90 MHz) NMR spectra. NMR spectroscopy was carried out at room temperature using deuterated solvent, as indicated for each synthesis. All melting points are uncorrected and determined with a Digital Stuart SMP10 melting point apparatus. UV/Vis spectra were recorded in solutions using a Specord 250 spectrophotometer from Analytik Jena (1 cm path length quartz cell). Mass spectrometry analysis (HRMS) were performed with a Q-Tof Premier Waters quadrupole time-of-flight (Q-TOF) mass spectrometer equipped with Z-spray electrospray ionization (ESI) and matrix assisted laser desorption ionization (MALDI) sources with *trans*-2-[3-(4-*tert*-butylphenyl)-2-methyl-2-propenylidene]malononitrile as the matrix and with a Bruker micrOTOF-Q-III with ESI and atmospheric pressure chemical ionization (APCI) sources.

General Procedure A for the Synthesis of 1,2,3-Triazoles **9**, **11**, **13**, **15**. 1,2,3-Triazoles were synthesized by adapting a literature procedure.[6] A microwave vial equipped with a rubber septum was evacuated and refilled with argon (3×). 1-azido-3-iodobicyclo[1.1.1]pentane (**1**) (1.0 equiv) dissolved in anhydrous THF was added to the vial, followed by TEA (1.5 equiv). Argon was bubbled through the mixture for 10 min. CuI (0.1 equiv) and the ethynyl substrate (1.0 equiv) were added and argon was bubbled for another 5 min. The mixture was stirred under argon at room temperature in the dark for 16 h. The solvent was removed under reduced pressure, the residue was dry-loaded onto silica gel and purified by column chromatography.

General Procedure B for the Synthesis of 5-Iodo-1,2,3-triazoles **10**, **12**, **14**, **16**, **18**. A modified literature procedure was used for the synthesis of 5-iodo-1,2,3-triazoles.[21] A microwave vial equipped with a rubber septum was evacuated and refilled with argon (3×). 1-Azido-3-iodobicyclo[1.1.1]pentane (**1**) (1.0 equiv) dissolved in anhydrous THF was added to the vial, followed by DIPEA (1.0 equiv). Argon was bubbled through the mixture for 10 min. CuI (1.0 equiv), the ethynyl substrate (1.0 equiv) and, at the end, NBS (1.2 equiv) were added and argon was bubbled for another 5 min. The reaction mixture was stirred under argon at room temperature in the dark for 18 h. The solvent was removed under reduced pressure, the residue was dry-loaded onto silica gel and purified by column chromatography.

General Procedure C for the Synthesis of 5-Alkynylated 1,2,3-Triazoles **19**−**23**. An oven-dried Schlenk tube equipped with a rubber septum was evacuated and refilled with argon (3×). 1-azido-3-iodobicyclo[1.1.1]pentane (**1**) (1.0 equiv) dissolved in anhydrous THF was added to the tube, followed by the same amount of anhydrous TEA. The ethynyl substrate (2.2−2.4 equiv) was added and argon was bubbled through the mixture for 15 min. CuI (0.2 equiv) and $Pd(PPh_3)_2Cl_2$ (0.1 equiv) were added and argon was bubbled for another 5 min. The reaction

mixture was stirred under argon at room temperature in the dark for 18 h. The solvent was removed under reduced pressure. The residue was dissolved in EtOAc or dichloromethane and passed through a plug of silica gel. Subsequently, the crude mixture was dry-loaded onto silica gel and further purified by silica gel column chromatography.

Screening of Reaction Conditions for the Formation of 5-Protio-1,2,3-triazole **9** *and 5-Iodo-1,2,3-triazole* **10**. Five reactions were carried out with **1** (6.7 mg, 28.7 µmol, 1.0 equiv) and **5** (10.0 mg, 28.7 µmol, 1.0 equiv) and varying amounts of reagents in 0.67 mL anhydrous THF based on general procedure A: **I)** CuI (1.1 mg, 5.78 µmol, 0.2 equiv), TEA (6 µL, 43.0 µmol, 1.5 equiv), under argon atmosphere according to general procedure A. **II)** CuI (1.6 mg, 8.4 µmol, 0.3 equiv), TEA (6 µL, 43.0 µmol, 1.5 equiv), under argon atmosphere according to general procedure A. **III)** CuI (1.1 mg, 5.78 µmol, 0.2 equiv), TEA (6 µL, 43.0 µmol, 1.5 equiv), the solvent was not deoxygenated and the reaction was carried out under air. **IV)** CuI (1.6 mg, 8.4 µmol, 0.3 equiv), TEA (6 µL, 43.0 µmol, 1.5 equiv), the solvent was not deoxygenated and the reaction was carried out under air. **V)** CuI (5.5 mg, 28.9 µmol, 1.0 equiv), TEA (15 µL, 108 µmol, 3.8 equiv), the solvent was not deoxygenated and the reaction was carried out under air. One reaction was carried out based on general procedure B with **1** (6.7 mg, 28.7 µmol, 1.0 equiv) and **5** (10.0 mg, 28.7 µmol, 1.0 equiv) in 0.67 mL THF: **VI)** CuI (5.5 mg, 28.9 µmol, 1.0 equiv), DIPEA (5 µL, 28.7 µmol, 1.0 equiv), NBS (6.1 mg, 34.2 µmol, 1.2 equiv) under argon atmosphere according to general procedure B. All reactions were left to stir for 16 h in the dark and the solvent was removed under reduced pressure. For reactions **I**−**IV** the crude solids were completely dissolved in $CDCl_3$ (~0.5 mL), the internal standard dibromomethane (20 µL) was added and ^{1}H NMR spectra of the 4 samples were recorded. For reactions **V** and **VI** a lower solubility was observed due to side product formation. Therefore, the crude solids were dissolved

in $CHCl_3$ (1 mL), aliquots of this solution (30 µL) were mixed in NMR tubes with dibromomethane (10 µL) and $CDCl_3$ (~0.5 mL) and the ^1H NMR spectra were recorded. The total amounts of compounds **9** and **10** in the reaction mixtures were calculated based on the intensity of their BCP bridge proton signals at 2.87 ppm and 3.07 ppm relative to the intensity of the signal of dibromomethane at 4.93 ppm

1-(3-Iodobicyclo[1.1.1]pentan-1-yl)-4-(8-(4-phenyl)-4,4-difluoro-1,3,5,7-tetramethyl-4-bora-3a,4a-diaza-s-indacene)-1H-1,2,3-triazole (**9**).

Compounds **1** (13.5 mg, 57.4 µmol), **5** (20 mg, 57.4 µmol), CuI (1.1 mg, 5.78 µmol) and TEA (12 µL, 86.1 µmol) were reacted in 0.7 mL THF in accordance with general procedure A. Silica gel column chromatography (hexane/EtOAc gradient 20:1 to 5:1) afforded **9** as orange crystals (27.5 mg, 47.2 µmol, 82%). M. p. = 157 °C (dec.). R_f = 0.26 (hexane/EtOAc 5:1). ^1H NMR (400 MHz, $CDCl_3$) δ = 1.42 (s, 6H, CH_3), 2.56 (s, 6H, CH_3), 2.88 (s, 6H, CH_2), 5.98 (s, 2H, pyrrole-H), 7.36 (d, *J* = 8.1 Hz, 2H, Ar-H), 7.80 (s, 1H, triazole-H), 7.96 (d, *J* = 8.1 Hz, 2H, Ar-H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ = -3.0, 14.7, 54.8, 62.0, 118.5, 121.5, 126.6, 128.8, 131.1, 131.5, 135.2, 141.2, 143.2, 147.1, 155.8 ppm. ^{19}F NMR (377 MHz, $CDCl_3$) δ = -146.29 (q, *J* = 32.7 Hz) ppm. ^{11}B NMR (128 MHz, $CDCl_3$) δ = 0.77 (t, *J* = 33.3 Hz) ppm. UV-vis (CH_2Cl_2) λ_{max} (log ε) = 349 (3.89), 474 sh, 504 (4.96). HRMS (ESI): *m/z* calcd. for $[C_{26}H_{26}BF_2IN_5]$ $[M+H]^+$ 584.1293; found 584.1303.

1-(3-Iodobicyclo[1.1.1]pentan-1-yl)-4-(1-pyrenyl)-1H-1,2,3-triazole (**11**). Compounds **1** (20.6 mg, 87.6 µmol), **6** (20 mg, 87.6 µmol), CuI (1.7 mg, 8.93 µmol) and TEA (19 µL, 0.138 mmol) were reacted in 2 mL THF in accordance with general procedure A. Silica gel column chromatography (hexane/EtOAc gradient 50:1 to 10:1) afforded **11** as a white solid (4.2 mg, 9.10 µmol, 10%). M. p. = 207 °C (dec.). R_f = 0.16 (hexane/EtOAc 10:1). ^1H NMR (600 MHz, $CDCl_3$)

δ = 2.97 (s, 6H, CH_2), 7.90 (s, 1H, triazole-H), 8.02–8.05 (t, *J* = 7.6 Hz, 1H, Ar-H), 8.11 (m, 3H, Ar-H), 8.20–8.23 (m, 4H, Ar-H), 8.65 (d, *J* = 9.2 Hz, 1H, Ar-H) ppm. ^{13}C NMR (151 MHz, $CDCl_3$) δ = -2.7, 29.9, 53.6, 54.9, 62.2, 121.2, 124.8, 124.9, 124.9, 125.0, 125.2, 125.4, 125.7, 126.3, 127.4, 127.5, 128.1, 128.5, 128.9, 131.0, 131.5, 131.6, 147.7 ppm. UV-vis (CH_2Cl_2) λ_{max} (log ε) = 273 sh, 283 (4.61), 353 (4.51). HRMS (ESI): *m/z* calcd. for [$C_{23}H_{17}IN_3$] $[M+H]^+$ 462.0462; found 462.0463.

1-(3-Iodobicyclo[1.1.1]pentan-1-yl)-4-[5-(4-phenyl)-10,20-(4-methylphenyl)-15-phenylporphyrinato]zinc(II)-1H-1,2,3-triazole (**13**). Compounds **1** (8.0 mg, 34.0 µmol), **7** (25 mg, 34.2 µmol), CuI (0.6 mg, 3.15 µmol) and TEA (6 µL, 43.0 µmol) were reacted in 1.3 mL THF in accordance with general procedure A. Silica gel column chromatography (hexane/EtOAc gradient 20:1 to 10:1) afforded **13** as purple crystals (23.2 mg, 24.0 µmol, 79%). M. p. ›300 °C. R_f = 0.22 (hexane/EtOAc 5:1). ^{1}H NMR (600 MHz, $CDCl_3$) δ = 2.71 (s, 6H, CH_3), 2.97 (s, 1H, CH_2), 7.56 (d, *J* = 7.7 Hz, 4H, Ar-H), 7.73–7.79 (m, 3H, Ar-H), 7.96 (s, 1H, triazole-H), 8.11 (d, *J* = 7.8 Hz, 4H, Ar-H), 8.16 (d, *J* = 8.0 Hz, 2H, Ar-H), 8.22–8.24 (m, 2H, Ar-H), 8.28 (d, *J* = 8.0 Hz, 2H, Ar-H), 8.95 (d, *J* = 4.6 Hz, 2H, β-H), 8.97–9.00 (m, 6H, β-H) ppm. ^{13}C NMR (151 MHz, $CDCl_3$) δ = -2.7, 21.7, 54.9, 62.1, 118.4, 120.4, 121.3, 121.5, 124.2, 126.7, 127.5, 127.6, 129.5, 131.8, 132.1, 132.2, 132.3, 134.5, 134.6, 135.1, 137.3, 140.0, 143.0, 143.2, 147.9, 150.1, 150.4, 150.5, 150.6 ppm. UV-vis (CH_2Cl_2) λ_{max} (log ε) = 406 sh, 423 (6.98), 551 (5.56), 592 (4.96) nm. HRMS (ESI): *m/z* calcd. for [$C_{53}H_{39}IN_7Zn$] $[M+H]^+$ 964.1598; found 964.1599.

1-(3-Iodobicyclo[1.1.1]pentan-1-yl)-4-phenyl-1H-1,2,3-triazole (**15**). Compounds **1** (25 mg, 0.106 mmol), **8** (12 µL, 0.106 mmol), CuI (2.0 mg, 10.6 µmol) and TEA (22 µL, 0.159 mmol) were reacted in 3 mL THF in accordance with general procedure A. Silica gel column chromatography (hexane/EtOAc gradient 200:1 to 10:1) afforded **15** as a white solid (26.5 mg,

78.6 µmol, 74%). Characterization data in accordance with the literature.[6a] R_f = 0.24 (hexane/EtOAc 10:1). ^{1}H NMR (600 MHz, $CDCl_3$) δ = 2.87 (s, 6H, CH_2), 7.32–7.36 (m, 1H, Ar-H), 7.40–7.44 (m, 2H, Ar-H), 7.80–7.82 (m, 2H, Ar-H) ppm. HRMS (ESI): *m/z* calcd. for [$C_{13}H_{13}IN_3$] $[M+H]^+$ 338.0149; found 338.0150.

1-(3-Iodobicyclo[1.1.1]pentan-1-yl)-4-(8-(4-phenyl)-4,4-difluoro-1,3,5,7-tetramethyl-4-bora-3a,4a-diaza-s-indacene)-5-iodo-1H-1,2,3-triazole (**10**). Compounds **1** (6.8 mg, 28.7 µmol), **5** (10.0 mg, 28.7 µmol), CuI (5.5 mg, 28.9 µmol), NBS (6.1 mg, 34.3 µmol) and DIPEA (5 µL, 28.7 µmol) were reacted in 2 mL THF in accordance with general procedure B. Silica gel column chromatography (hexane/DCM gradient 2:1 to 1:1) afforded **10** as an orange solid (2.8 mg, 3.95 µmol, 14%). M. p. = 224 °C (dec.). R_f = 0.33 (hexane/EtOAc 5:1). ^{1}H NMR (600 MHz, $CDCl_3$) δ = 1.43 (s, 6H, CH_3), 2.56 (s, 6H, CH_3), 3.07 (s, 6H, CH_2), 5.99 (s, 2H, pyrrole-H), 7.39 (d, J = 8.2 Hz, 2H, Ar-H), 8.05 (d, J = 8.2 Hz, 2H, Ar-H) ppm. ^{13}C NMR (151 MHz, $CDCl_3$) δ = -1.7, 14.7, 14.8, 56.9, 62.4, 73.1, 121.5, 128.4, 128.5, 130.8, 131.5, 135.6, 141.1, 143.2, 149.9, 155.9 ppm. ^{19}F NMR (377 MHz, $CDCl_3$) δ = -146.28 (q, J = 33.0 Hz) ppm. ^{11}B NMR (128 MHz, $CDCl_3$) δ = 0.78 (t, J = 33.3 Hz) ppm. UV-vis (CH_2Cl_2) λ_{max} (log ε) = 348 (4.08), 477 sh, 504 (5.10) nm. HRMS (ESI): m/z calcd. for [$C_{26}H_{23}BF_2I_2N_5$] $[M-H]^-$ 708.0114; found 708.0097.

1-(3-Iodobicyclo[1.1.1]pentan-1-yl)-4-(1-pyrenyl)-5-iodo-1H-1,2,3-triazole (**12**). Compounds **1** (11.2 mg, 47.8 µmol), **6** (11.8 mg, 47.8 µmol), CuI (9.1 mg, 47.8 µmol), NBS (10.2 mg, 57.3 µmol) and DIPEA (9 µL, 51.7 µmol) were reacted in 2 mL THF in accordance with general procedure B. Silica gel column chromatography (hexane/EtOAc gradient 200:1 to 40:1) and trituration with hexane and toluene afforded **12** as a yellow solid (4.8 mg, 8.17 µmol, 17%). M. p. = 198 °C (dec.). R_f = 0.24 (hexane/EtOAc 10:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 3.15 (s, 6H, CH_2), 8.02–8.07 (m, 2H, Ar-H), 8.09 (s, 2H, Ar-H), 8.10–8.17 (m, 2H, Ar-H), 8.20–8.27 (m, 3H,

Ar-H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ = -1.5, 53.6, 56.9, 62.5, 124.2, 124.6, 124.7, 125.1, 125.3, 125.6, 125.7, 126.4, 127.5, 128.3, 128.4, 128.5, 129.9, 131.0, 131.4, 132.1, 152.3 ppm. UV-vis (CH_2Cl_2) λ_{max} (log ε) = 271 sh, 281 (4.67), 336 sh, 348 (4.52) nm. HRMS (ESI): *m/z* calcd. for $[C_{23}H_{16}I_2N_3]$ $[M+H]^+$ 587.9428; found 587.9434.

1-(3-Iodobicyclo[1.1.1]pentan-1-yl)-4-[5-(4-phenyl)-10,20-(4-methylphenyl)-15-phenylporphyrinato]zinc(II)-5-iodo-1H-1,2,3-triazole (**14**). Compounds **1** (8.4 mg, 35.6 µmol), **7** (26.0 mg, 35.6 µmol), CuI (6.8 mg, 35.7 µmol), NBS (7.6 mg, 42.7 µmol) and DIPEA (5 µL, 28.7 µmol) were reacted in 1.4 mL THF in accordance with general procedure B. Silica gel column chromatography (hexane/EtOAc gradient 20:1 to 10:1) afforded **14** as a purple solid (7.5 mg, 6.87 µmol, 19%). ^{1}H and ^{13}C NMR spectra were recorded of **14** with pyridine as the axial ligand to prevent intermolecular interactions between porphyrins arising from zinc(II) coordination. M. p. = 272 °C (dec.). R_f = 0.32 (hexane/EtOAc 5:1). ^{1}H NMR (600 MHz, $CDCl_3$) δ = 2.70 (s, 6H, CH_3), 3.15 (s, 6H, CH_2), 4.17 (br s, 2H, pyridine-H), 5.96–6.01 (m, 2H, pyridine-H), 6.70 (t, J = 7.4 Hz, 1H, pyridine-H), 7.53 (d, J = 7.4 Hz, 4H, Ar-H), 7.70–7.75 (m, 3H, Ar-H), 8.08 (d, J = 7.5 Hz, 4H, Ar-H), 8.20 (d, J = 7.1 Hz, 2H, Ar-H), 8.24 (d, J = 7.8 Hz, 2H, Ar-H), 8.30 (d, J = 7.8 Hz, 2H, Ar-H), 8.87 (d, J = 4.4 Hz, 2H, β-H), 8.90–8.93 (m, 6H, β-H) ppm. ^{13}C NMR (151 MHz, $CDCl_3$) δ = -1.3, 21.7, 56.96, 62.5, 72.9, 119.8, 120.9, 121.0, 122.7, 125.7, 126.5, 127.2, 127.3, 128.8, 129.0, 131.1, 131.6, 131.8, 131.9, 132.0, 134.6, 134.7, 134.9, 135.9, 137.0, 139.5, 140.5, 143.6, 144.2, 145.1, 150.0, 150.2, 150.4, 150.4, 150.9 ppm. UV-vis (CH_2Cl_2) λ_{max} (log ε) = 403 sh, 423 (5.73), 551 (4.31), 592 (3.73) nm. HRMS (APCI): m/z calcd. for $[C_{53}H_{38}I_2N_7Zn]$ $[M+H]^+$ 1090.0564; found 1090.0537.

1-(3-Iodobicyclo[1.1.1]pentan-1-yl)-4-phenyl-5-iodo-1H-1,2,3-triazole (**16**). Compounds **1** (11.2 mg, 47.8 µmol), **8** (6 µL, 54.6 µmol), CuI (9.1 mg, 47.8 µmol), NBS (10.2 mg, 57.3 µmol)

and DIPEA (9 µL, 51.7 µmol) were reacted in 2 mL THF in accordance with general procedure B. Silica gel column chromatography (hexane/EtOAc gradient 200:1 to 20:1) afforded **16** as an off-white solid (1.5 mg, 3.24 µmol, 7%). M. p. = 182 °C (dec.). R_f = 0.42 (hexane/EtOAc 10:1). ^{1}H NMR (600 MHz, $CDCl_3$) δ = 3.06 (s, 6H, CH_2), 7.41 (t, *J* = 7.3 Hz, 1H, Ar-H), 7.46 (t, *J* = 7.6 Hz, 2H, Ar-H), 7.86 (d, *J* = 7.4 Hz, 2H, Ar-H) ppm. ^{13}C NMR (151 MHz, $CDCl_3$) δ = -1.4, 56.8, 62.4, 72.6, 127.9, 128.7, 128.9, 123.0, 150.8 ppm. HRMS (APCI): *m/z* calcd. for $[C_{13}H_{12}I_2N_3]$ $[M+H]^+$ 463.9115; found 463.9118.

1-(3-Iodobicyclo[1.1.1]pentan-1-yl)-4-(4-pyridinyl)-5-iodo-1H-1,2,3-triazole (**18**). Compounds **1** (14.1 mg, 60.0 µmol), **17** (6.2 mg, 60.1 µmol), CuI (11.5 mg, 60.3 µmol), NBS (12.8 mg, 71.9 µmol) and DIPEA (8 µL, 45.9 µmol) were reacted in 2 mL THF in accordance with general procedure B. The crude product was purified by silica gel column chromatography (hexane/EtOAc gradient 5:1 to 2:1). The isolated product was dissolved in DCM and washed with saturated aqueous $NaHCO_3$ solution (2x) and H_2O (1x) to afforded **18** as an off-white solid (18.3 mg, 38.8 µmol, 66%). M. p. = 137 °C (dec.). R_f = 0.40 (hexane/EtOAc 1:1). ^{1}H NMR (600 MHz, $CDCl_3$) δ = 3.07 (s, 6H, CH_2), 7.89 (br d, *J* = 3.7 Hz, 2H, Ar-H), 8.73 (br s, 2H, Ar-H) ppm. ^{13}C NMR (151 MHz, $CDCl_3$) δ = -1.9, 56.8, 62.4, 73.6, 121.6, 137.6, 147.8, 150.4 ppm. HRMS (ESI): *m/z* calcd. for $[C_{12}H_{11}I_2N_4]$ $[M+H]^+$ 464.9068; found 464.9069.

1-(3-Iodobicyclo[1.1.1]pentan-1-yl)-4-(8-(4-phenyl)-4,4-difluoro-1,3,5,7-tetramethyl-4-bora-3a,4a-diaza-s-indacene)-5-(8-(4-phenylethynyl)-4,4-difluoro-1,3,5,7-tetramethyl-4-bora-3a,4a-diaza-s-indacene)-1H-1,2,3-triazole (**19**). Compounds **1** (12.0 mg, 51.1 µmol), **5** (42.0 mg, 121 µmol), CuI (2.1 mg, 11.0 µmol) and $Pd(PPh_3)_2Cl_2$ (3.9 mg, 5.56 µmol) were reacted in a mixture of 1 mL THF and 1 mL TEA in accordance with general procedure C. Silica gel column chromatography (1. chromatography hexane/EtOAc gradient 10:1 to 5:1; 2. chromatography neat

dichloromethane and dichloromethane/EtOAc 100:1) afforded **19** as an orange solid (trace amount). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 1.43 (s, 6H, CH_3), 1.43 (s, 6H, CH_3), 2.54 (s, 6H, CH_3), 2.55 (s, 6H, CH_3), 3.04 (s, 6H, CH_2), 5.97 (s, 2H, pyrrole-H), 6.00 (s, 2H, pyrrole-H), 7.41 (dd, J = 8.0, 1.8 Hz, 4H, Ar-H), 7.67 (d, J = 8.1 Hz, 2H, Ar-H), 8.32 (d, J = 8.4 Hz, 2H, Ar-H) ppm. HRMS (MALDI): m/z calcd. for $[C_{47}H_{42}B_2F_4IN_7]$ $[M]^+$ 929.2669; found 929.2646.

1-(3-Iodobicyclo[1.1.1]pentan-1-yl)-4-(1-pyrenyl)-5-(1-pyrenylethynyl)-1H-1,2,3-triazole (**20**) Compounds **1** (25.0 mg, 0.106 mmol), **6** (57.5 mg, 0.254 mmol), CuI (4.0 mg, 21.2 µmol) and $Pd(PPh_3)_2Cl_2$ (7.4 mg, 10.6 µmol) were reacted in a mixture of 0.6 mL THF and 0.6 mL TEA in accordance with general procedure C. Two silica gel column chromatographies (hexane/EtOAc 20:1 and hexane/EtOAc 100:3) afforded **20** as a light yellow solid (5.4 mg, 7.88 µmol, 7%). M. p. = 206 °C (dec.). R_f = 0.21 (hexane/EtOAc 10:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 3.24 (s, 6H, CH_2), 7.33 (d, *J* = 9.1 Hz, 1H, Ar-H), 7.77 (d, *J* = 9.1 Hz, 1H, Ar-H), 7.96–8.12 (m, 7H, Ar-H), 8.15–8.23 (m, 5H, Ar-H), 8.29 (d, *J* = 7.5 Hz, 1H, Ar-H), 8.34 (d, *J* = 7.9 Hz, 1H, Ar-H), 8.49 (d, *J* = 7.9 Hz, 1H, Ar-H), 8.68 (d, *J* = 9.3 Hz, 1H, Ar-H) ppm. ^{13}C NMR (151 MHz, $CDCl_3$) δ =.-1.6, 55.5, 62.6, 80.3, 101.9, 115.2, 119.9, 124.1, 124.4, 124.4, 124.6, 124.7, 124.9, 124.9, 125.3, 125.6, 125.6, 125.7, 126.2, 126.4, 126.6, 127.2, 127.6, 128.1, 128.5, 128.9, 129.1, 129.2, 129.5, 130.8, 131.2, 131.3, 131.5, 132.2, 132.2, 132.4, 149.9 ppm. UV-vis (CH_2Cl_2) λ_{max} (log ε) = 282 (4.74), 297 sh, 352 (4.77), 374 sh, 398 sh. HRMS (APCI): *m/z* calcd. for $[C_{41}H_{25}IN_3]$ $[M+H]^+$ 686.1088; found 686.1101.

1-(3-Iodobicyclo[1.1.1]pentan-1-yl)-4-[5-(4-phenyl)-10,20-(4-methylphenyl)-15-phenylporphyrinato]zinc(II)-5-[5-(4-phenylethynyl)-10,20-(4-methylphenyl)-15-phenylporphyrinato]zinc(II)-1H-1,2,3-triazole (**21**). Compounds **1** (6.4 mg, 27.5 µmol), **7** (44.0 mg, 60.3 µmol), CuI (1.0 mg, 5.25 µmol) and $Pd(PPh_3)_2Cl_2$ (2.0 mg, 2.85 µmol) were reacted in

a mixture of 0.5 mL THF and 0.5 mL TEA in accordance with general procedure C. Silica gel column chromatography (dichloromethane/hexane 3:7, 2:3, neat dichloromethane, dichloromethane/EtOAc 10:1) and preparative TLC (dichloromethane/hexane 4:1) afforded **21** as a purple solid (trace amount). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 2.66 (s, 6H, CH_3), 2.67 (s, 6H, CH_3), 3.27 (s, 6H, CH_2), 7.48–7.53 (m, 4H, Ar-H), 7.70–7.76 (m, 4H, Ar-H), 8.02–8.09 (m, 6H, Ar-H), 8.16–8.20 (m, 2H, Ar-H), 8.28 (d, J = 8.4 Hz, 2H, Ar-H), 8.41 (d, J = 8.1 Hz, 2H, Ar-H), 8.69 (d, J = 8.3 Hz, 2H, Ar-H), 8.89–8.96 (m, 12H, β-H), 8.99 (d, J = 4.9 Hz, 2H, β-H), 9.05 (d, J = 4.7 Hz, 2H, β-H) ppm. HRMS (MALDI): m/z calcd. for $[C_{101}H_{68}IN_{11}Zn_2]$ $[M]^+$ 1689.3287; found 1689.3296.

1-(3-Iodobicyclo[1.1.1]pentan-1-yl)-4-phenyl-5-phenylethynyl-1H-1,2,3-triazole (**22**). Compounds **1** (20 mg, 85.1 µmol), **8** (20.9 mg, 0.205 mmol), CuI (3.2 mg, 16.8 µmol) and $Pd(PPh_3)_2Cl_2$ (6.0 mg, 8.55 µmol) were reacted in a mixture of 1 mL THF and 1 mL TEA in accordance with general procedure C. Silica gel column chromatography (hexane/EtOAc 40:1) afforded **22** as a white solid (3.8 mg, 8.69 µmol, 10%). M. p. = 173–176 °C. R_f = 0.62 (hexane/EtOAc 10:1). ^{1}H NMR (600 MHz, $CDCl_3$) δ = 3.03 (s, 6H, CH_2), 7.38 (t, *J* = 7.3 Hz, 1H, Ar-H), 7.43–7.50 (m, 5H, Ar-H), 7.55–7.59 (m, 2H, Ar-H), 8.15 (d, *J* = 7.5 Hz, 2H, Ar-H) ppm. ^{13}C NMR (151 MHz, $CDCl_3$) δ = -1.7, 55.2, 62.3, 75.6, 102.4, 116.3, 121.4, 126.5, 128.9, 128.9, 129.0, 130.1, 130.1, 131.6, 148.4 ppm. HRMS (ESI): *m/z* calcd. for $[C_{21}H_{17}IN_3]$ $[M+H]^+$ 438.0462; found 438.0456.

1-(3-Iodobicyclo[1.1.1]pentan-1-yl)-4-(4-pyridinyl)-5-(4-pyridinylethynyl)-1H-1,2,3-triazole (**23**) and *1-(3-Iodobicyclo[1.1.1]pentan-1-yl)-4-(4-pyridinyl)-1H-1,2,3-triazole* (**24**).

Compounds **1** (20 mg, 85.0 µmol), **17** (21 mg, 204 µmol), CuI (3.2 mg, 17.2 µmol) and $Pd(PPh_3)_2Cl_2$ (6.0 mg, 8.50 µmol) were reacted in a mixture of 0.4 mL THF and 0.4 mL TEA in

accordance with general procedure C. Silica gel column chromatography (hexane/EtOAc gradient 2:1, to 1:2) afforded **23** as a white solid (9.9 mg, 22.5 µmol, 27%) and **24** as a white solid (9.0 mg, 26.6 µmol, 31%). *1-(3-Iodobicyclo[1.1.1]pentan-1-yl)-4-(4-pyridyl)-5-(4-pyridinylethynyl)-1H-1,2,3-triazole* **23**: M. p. = 159 °C (dec.). R_f = 0.19 (hexane/EtOAc 1:2). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 3.02 (s, 6H, CH_2), 7.44 (dd, *J* = 4.4, 1.6 Hz, 2H, Ar-H), 8.00 (dd, *J* = 4.6, 1.6 Hz, 2H, Ar-H), 8.73 (dd, *J* = 4.6, 1.6 Hz, 2H, Ar-H), 8.77 (dd, *J* = 4.4, 1.6 Hz, 2H, Ar-H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ = -2.7, 55.2, 62.3, 78.6, 100.5, 116.9, 120.4, 125.06, 128.8, 137.1, 146.5, 150.6, 150.7 ppm. HRMS (APCI): *m/z* calcd. for $[C_{19}H_{15}IN_5]$ $[M+H]^+$ 440.0367; found 440.0369.

1-(3-Iodobicyclo[1.1.1]pentan-1-yl)-4-(4-pyridinyl)-1H-1,2,3-triazole **24**: M. p. = 219 °C (dec.). R_f = 0.33 (hexane/EtOAc 1:2). ^{1}H NMR (600 MHz, $CDCl_3$) δ = 2.88 (s, 6H, CH_2), 7.71 (br d, *J* = 3.7 Hz, 2H, Ar-H), 7.85 (s, 1H, triazole-H), 8.69 (s, 2H, Ar-H) ppm. ^{13}C NMR (151 MHz, $CDCl_3$) δ = -3.2, 54.8, 62.0, 119.5, 120.2, 137.7, 145.4, 150.6 ppm. HRMS (APCI): *m/z* calcd. for $[C_{12}H_{12}IN_4]$ $[M+H]^+$ 339.0101; found 339.0105.

ASSOCIATED CONTENT

The supporting information is available free of charge on the ACS publications website. The following files are available free of charge: Additional experimental data, X-ray crystallography data and NMR spectra (pdf).

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Notes

Any additional relevant notes should be placed here.

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ABBREVIATIONS

BCP, bicyclo[1.1.1]pentane; DCM, dichloromethane; EtOAc, ethyl acetate; TEA, triethylamine; THF, tetrahydrofuran; TLC, thin layer chromatography.

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