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Photochemical Bromination of 2,5-Dimethylbenzoic Acid as Key Step of an Improved Alkyne-Functionalized Blue Box Synthesis**

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Dedicated to Prof. Maurizio Prato on the occasion of his 70th birthday

Cyclobis(paraquat-*p*-phenylene), also known as *"blue box"*, is a highly electron-deficient macrocycle, widely used as a molecular receptor for small electron-rich molecules. Inserting a reactive functional group onto the molecular structure of this cyclophane is paramount for its inclusion into complex architectures. To this aim, including an alkyne moiety would be ideal, because it can participate in click reactions. However, the synthesis of such alkyne-functionalized cyclophane suffers from several drawbacks: the use of toxic and expensive CCl_4, the need for high-pressure reactors, and overall low yield. We have revised the existing synthesis of this cyclophane derivative bearing an alkyne moiety, to overcome all these limitations. In particular, photochemical radical bromination is adopted to obtain a sensitive intermediate. We demonstrated that the synthesized host molecule can be functionalized *via* click reactions and take part in radical-radical interactions. Our work makes a key functionalized paraquat macrocycle more accessible, facilitating the development of novel redox-responsive systems.

Introduction

Cyclobis(paraquat-*p*-phenylene) ($CBPQT^{4+}$), also referred to as *"blue box"*, is a widely employed tetracationic cyclophane synthesized for the first time four decades ago.[1] Due to the presence of electron-poor bipyridinium units, $CBPQT^{4+}$ can participate in non-covalent donor-acceptor interaction with small electron-rich molecules, forming host-guest complexes.[1,2] As a result, $CBPQT^{4+}$ is one of the privileged scaffolds to form mechanical bonds in pseudo-rotaxanes,[3] rotaxanes,[4–6] and catenanes.[7] Stoddart and co-workers have also demonstrated that in the reduced form – $CBPQT^{2(+\bullet)}$ – this macrocycle interacts efficiently with viologen radical cations, *via* radical-cation or radical-radical interaction.[8,9] This type of interaction has been extensively employed by the group of Stoddart in the last decade, in particular to control directional motion in supramolecular pumps, and related supramolecular structures.[10,11]

To include this reliable recognition motif in multifunctional structures, a necessary step is the functionalization of $CBPQT^{4+}$ macrocycle. To this aim a number of functionalized derivatives have been reported, bearing pendant functional groups such as a carboxylic acid,[12] a pyrrole,[13] an azide,[14] and an ester[15,16] that can be directly converted into alkyne moiety.[16–20] Azide- or alkyne-functionalized cyclophanes are particularly attractive because they allow exploiting "click" chemistry. Click chemistry is an elegant approach to obtain more complex molecules in a fast and efficient way.[21,22] Besides, this reaction is highly attractive due to its bioorthogonality.[23]

The synthesis of target alkyne functionalized macrocycle ($\mathbf{4}^{4+}$, Figure 1) is achieved *via* a three-step strategy.[20] The first step converts 2,5-dimethyl benzoic acid (**1**) into the halogenated intermediate **2**, which is subjected to an esterification reaction with propargyl alcohol to give **3**, employed in the final template-directed synthesis of $\mathbf{4}^{4+}$. This reaction sequence presents several drawbacks. The first step uses CCl_4 as reaction medium: a toxic, expensive, and atmosphere harmful solvent.[24–26] The second step affords compound **3** in just 12% yield.[20]

The last step is performed using a high-pressure reactor (15 kbar), which is a reaction setup unavailable in many laboratories.[20] Herein, we revised the synthesis of cyclophane $\mathbf{4}^{4+}$, overcoming all aforementioned limitations. A photochemical bromination afforded compound **2**, without using CCl_4 as solvent. Optimization of the subsequent esterification afforded a 5-fold yield increase, and the use of high-pressure reactor was

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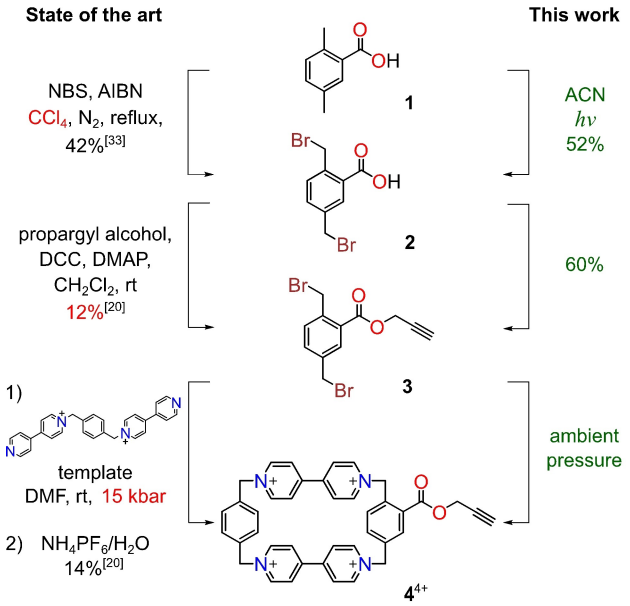
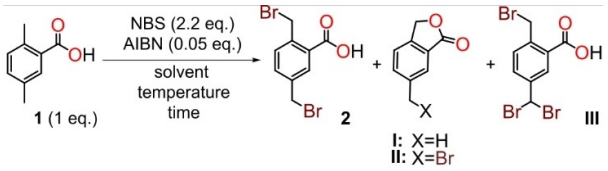


Figure 1. Reported procedure for the synthesis of alkyne functionalized cyclophane $\mathbf{4}^{4+}$ with drawbacks highlighted in red, and advancements reported in this work highlighted in green. NBS: *N*-bromosuccinimide; AIBN: azobisisobutyronitrile; DCC: *N,N'*-dicyclohexylcarbodiimide; DMAP: 4-dimethylaminopyridine; template: 2-[2-[5-[2-(2-Hydroxyethoxy)ethoxy] naphthalen-1-yl]oxyethoxy]ethanol. All positive charges are balanced by PF_6^- counterions, which are omitted for clarity.

Table 1. Radical bromination of 2,5-dimethyl benzoic acid **1** affording desired product **2** and byproducts **I–III**.



Entry	Solvent	Radical initiation	T [°C]	Time [h]	Products (ratio)[a]
1	ACN	Δ	reflux	4	**I:II** (53:47)
2	ACN	Δ	70	4	**I:II** (54:46)
3	*o*-DCB	Δ	105	4	**2:II:III** (34:55:11)
4	*o*-DCB	Δ	105	2	**2:II:III** (40:35:25)
5	benzene	Δ	70	4	**2:III** (76:24)
6	benzene	*hν*[b]	25	4	**2:III** (76:24)
7	ACN	*hν*[b]	25	4	**2**, 52%[c]
8	ACN	no light	25	4	**2**, 0%

[a] Values obtained from NMR analysis of the crude. [b] 6 W UV lamp at λ = 365 nm. [c] Isolated yield. NBS: *N*-bromosuccinimide; AIBN: azobisisobutyronitrile.

bypassed. The as-synthetized alkyne-functionalized cyclophane $\mathbf{4}^{4+}$ undergoes a Cu-catalyzed 1,3 dipolar cycloaddition, obtaining a model compound that was characterized also electrochemically, confirming its ability to participate in radical-radical interactions.

Results and Discussion

The starting point is the synthesis of brominated compound **2**, which is typically performed *via* a radical addition reaction with *N*-bromosuccinimide (NBS) as radical source and azobisisobutyronitrile (AIBN) as initiator. To get over the use of CCl_4, we screened other solvents previously employed in radical addition reactions, from the more polar acetonitrile (ACN),[27] to *o*-dichlorobenzene (*o*-DCB),[28] to the least polar benzene (Table 1).[29]

In all tested solvents, analysis of the crude reaction mixtures reveals the formation of byproducts, which could be identified *via* ^{1}H-NMR and HRMS analysis.[30] In ACN, no presence of the compound **2** was detected, whereas the formation of lactones **I** and **II** is observed. Moving to less polar solvents such as *o*-DCB and benzene, it is obtained the desired bis-brominated product **2** together with other side products. When the reaction is carried out in *o*-DCB for 4 hours, the main byproducts detected are mono-brominated lactone **II** and the overbrominated acid **III**. These side products form also when reducing the reaction time down to 2 hours, affording lactone **II** and desired compound **2** in comparable amounts. Using benzene as solvent suppresses the formation of **II**, but the desired product **2** forms together with **III** in ratio 76:24. Overall, solvent screening reveals that **2** always forms with significant amounts of byproducts, which are strongly dependent from the employed solvent.

Given the formation of multiple products, we explored several purification strategies. Despite successful literature reports,[30] recrystallization was not helpful to separate target compound **2** from mixtures obtained in our conditions. Chromatography was also not applicable since **2** converted quantitatively into lactone **II** in the silica column. Attempts to purify **2** with liquid/liquid extraction also proved unsuccessful (SI section 2).

To retrieve **2** from lactone **II**, we attempted lactone opening using hydrobromic acid (SI section 3).[31] To this aim, the isolated lactone was reacted with HBr in glacial acetic acid and the reaction crude subsequently quenched by pouring it onto ice, affording a white-off solid. While the obtained solid was still a mixture of **2:II** 64:36, this experiment revealed that in the solid state compound **2** can tolerate water.

The unsuccessful attempts highlighted why this transformation is challenging and which factors need to be considered. With this information in hand, we approached the photochemical activation of AIBN. We reasoned that light could induce radical cleavage of the AIBN at room temperature, preventing the temperature-promoted formation of lactone **II** side product, which implies the nucleophilic attack of the carboxylic acid to the nearby benzylic bromide. The photochemical activation of AIBN was previously used to functionalize *p*-toluic acid, but we are not aware of examples describing the bromination of benzylic positions having a carboxylic acid in the *o*-position, responsible of the above-mentioned problems.[32] Irradiation at 365 nm, where AIBN has an absorption band, afforded a crude reaction mixture where **2** was present as major product, with only traces of other impurities. No transformation occurs in the dark (Entry 8, Table 1), confirm-

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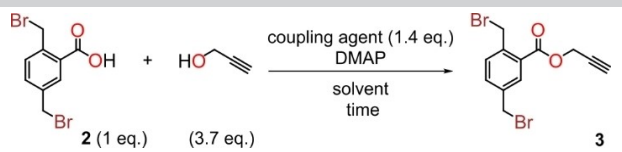
ing that the reactivity is driven by the photochemical activity of AIBN and NBS, which form Br• radicals upon light irradiation. The bromination was confirmed to be photochemically accessible also in benzene, which however promotes the formation of tris-brominated side product **III** together with the desired compound **2** with the same 76:24 ratio observed when heating (Table 1). For this reason, we focused on the purification from ACN. After drying the crude under reduced pressure, water is added to the obtained solid, removing succinimide in a solid-liquid extraction. Recrystallization afforded target compound **2** in 52% yield, which is slightly higher than previous literature reports, 42% being the highest value.[33] Importantly, the photochemical bromination can be performed from small (0.69 g, 4.6 mmol of **1**) to medium scale (5 g, 33.3 mmol of **1**), pointing out the versatility of the photochemical method. We have observed that the duration and yield of the photoreaction are rather sensitive to irradiation conditions. As an example. using an LED strip reactor, the reaction is complete in 30 minutes, but the yield drops down to 42% (SI section 4).

Having established the successful synthesis of **2** with the photochemical approach, we focused on the esterification to obtain compound **3**. Previously, the synthesis of **3** was carried out with a catalytic amount of dimethyl amino pyridine (DMAP) as a base, *N,N'*-dicyclohexylcarbodiimide (DCC) as coupling agent and excess of propargyl alcohol, affording the product in low yield (12%).[20] Attempts to use different coupling agents, such as an uronium-based coupling agents afforded at best the same 12% yield reported in the literature (Table 2 and SI section 5).[20,34] The purification attempts of **2**, clearly illustrated the sensitivity of **2** to bases. The importance of base amount was evident when performing the coupling reaction in the presence of different amounts of base: as it decreased from 0.2 eq. to 0.05 eq., the yield increased from just traces of **3** to 36%. Thus, the base strictly needs to be added in low amount, albeit necessary. Moreover, analysis of crude reaction mixtures revealed the formation of byproducts resulting from the nucleophilic substitution of benzyl bromides by propargyl alcohol. Therefore, we adjusted the reaction protocol to activate the acid adding DCC first and then the base, followed by slow addition of propargyl alcohol. These changes increased the yield of **3** from 36% up to 60%, which is five times higher than the reported literature value.[20]

The final step to obtain the alkyl functionalized macrocycle $\mathbf{4}^{4+}$ is the template-promoted cyclization of a pyridyl-pyridinium thread with **3** to form cyclophane $\mathbf{4}^{4+}$ (Figure 2a). To circumvent the use of a high-pressure reactor, we explored the use of NaI as catalyst, which was successfully employed in similar reactions.[35] The reaction mixture was monitored over time and after 10 days NMR analysis (Figure S8) clearly showed a complete conversion of **3**, affording the product $\mathbf{4}^{4+}$ in 13% yield, a value comparable with the one reported in literature (14%).[20] To corroborate the importance of NaI as catalyst, a control experiment was performed in the same conditions but without adding NaI. The reaction did not proceed to complete conversion in 10 days (Figure S8), confirming the importance of NaI. Even though cyclization takes longer than in literature procedures, no special equipment is needed to perform the reaction, making this synthetic target more accessible.[20] Having revised the synthesis of $\mathbf{4}^{4+}$, we tested its ability to participate

Table 2. Esterification between **2** and propargyl alcohol to afford **3** (SI section 5).



2 (1 eq.) (3.7 eq.) **3**

Entry	Solvent	Time [h]	Base [eq.]	Coupling agent	Yield [%]
1	DMF	48	0.1 or 2	HBTU	traces
2	CH_2Cl_2	24	0.1	EDC	12
3	CH_2Cl_2	24	2	DCC	traces
4	CH_2Cl_2	24	0.1	DCC	36
5	CH_2Cl_2	24	0.05	DCC	36
6[a]	CH_2Cl_2	24	0.05	DCC	60

[a] Base addition performed after DCC addition, followed by slow addition of propargyl alcohol (see Experimental Section). DMAP: dimethyl amino pyridine; HBTU: (2-(1H-benzotriazol-1-yl)-1,1,3,3-tetramethyluronium hexafluorophosphate; EDC: 1-Ethyl-3-(3-dimethylaminopropyl)carbodiimide; DCC: *N,N'*-dicyclohexylcarbodiimide.

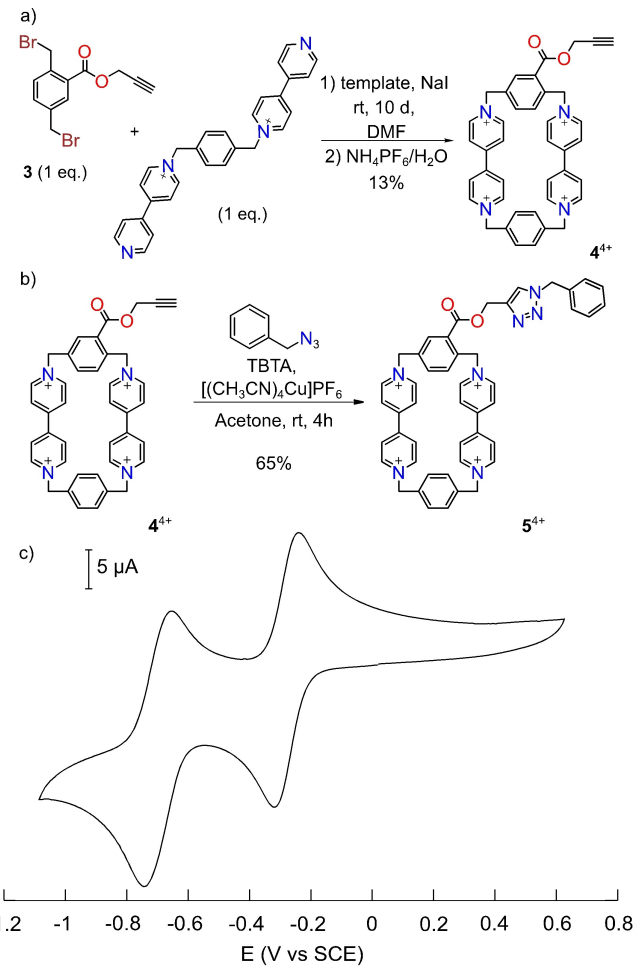


Figure 2. a) Reaction scheme for the synthesis of a) $\mathbf{4}^{4+}$ and b) $\mathbf{5}^{4+}$. TBTA: tris(benzyltriazolylmethyl)amine. All positive charges are balanced by PF_6^- counterions, which are omitted for clarity. c) CV of $\mathbf{5}^{4+}$ at 200 mV s^{-1} scan rate. Conditions: ACN, $TEAPF_6$ 100 mM.

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in Cu-promoted azide–alkyne cycloaddition. Following a modified literature protocol, $\mathbf{4}^{4+}$ was reacted with benzyl azide, which was selected as model click reaction partner to form $\mathbf{5}^{4+}$ (Figure 2b).[36] The successful synthesis of $\mathbf{5}^{4+}$ was confirmed by NMR and HRMS analysis, in particular from the disappearance of the alkyne proton peak at 3.24 ppm in the ^{1}H-NMR spectrum (Figure S9). Despite the moderate isolated yield (65%), the result is in line with similar reported structures bearing multiple cyclophanes.[17] Host $\mathbf{5}^{4+}$ has also been characterized *via* electrochemical measurements, using cyclic voltammetry (CV) and differential pulse voltammetry (DPV). The CV analysis reveals two quasi-reversible reduction processes at −0.71 and −0.28 V (Figure 2c), which are very similar to the redox processes observed for $\mathbf{CBPQT}^{4+}$ under the same experimental condition.

Finally, we confirmed that $\mathbf{5}^{4+}$ can participate in radical-radical interactions. To this aim, electrochemical characterization was performed in the presence of axle-shaped molecule $\mathbf{6}^{4+}$ (Figure 3a), which comprises a viologen unit and was already employed to demonstrate radical-radical interactions with $\mathbf{CBPQT}^{4+}$.[37] In its reduced form, $\mathbf{6}^{4+}$ will act as a guest molecule for reduced host $\mathbf{5}^{2(+\bullet)}$, forming the pseudorotaxane complex $[\mathbf{6}^{2+(+\bullet)}\subset\mathbf{5}^{2(+\bullet)}]$ (Figure 3a). The complexation is driven by radical-radical interactions between the viologen units present on both axle and cyclophane. Investigating the CV of an equimolar mixture of host $\mathbf{5}^{4+}$ and guest $\mathbf{6}^{4+}$, we observed the presence of a single first reduction peak (−0.38 V) and a stepwise second reduction peak (−0.71 V and −0.79 V). Also, in the re-oxidation scan, three peaks not observed in the isolated components appeared at less negative potentials (from ca. −0.21 to 0.28 V, Figure S14).

Considering that the observed peaks are irreversible, we employed DPV analysis to gain insights. In oxidative DPV scans it was possible to observe new peaks at −0.21, 0.04, and 0.28 V, which are not present in the DPV of the individual components (Figure 3b). The appearance of these additional peaks is coherent with the formation of inclusion complex $[\mathbf{6}^{2+(+\bullet)}\subset\mathbf{5}^{2(+\bullet)}]$, exploiting the radical-radical-radical interactions between the viologen units present in $\mathbf{6}^{4+}$ and $\mathbf{5}^{4+}$.[8,37,38] The ability to participate in radical-radical interaction was further corroborated by spectroelectrochemical measurements (Figure S15).

Conclusions

In summary, we have improved the synthesis of a versatile alkyne-functionalized cyclophane derivative, both in terms of required conditions and yield. In particular, we circumvented the use of toxic and expensive CCl_4, as well as the use of a high-pressure reactor. Key to the reported improvements was to understand the degradation pathways involving brominated benzoic acid intermediate **2**, both during its synthesis and subsequent use. By preparing **2** *via* photochemical halogenation, and reconsidering the condition of its esterification, we could increase over five-fold the overall yield of target alkyne-functionalized macrocycle $\mathbf{4}^{4+}$. We demonstrated that the obtained cyclophane can be further functionalized *via* click reaction and take part in radical-radical interactions, affording a pseudorotaxane. Our work facilitates the realization of redox-active supramolecular systems, with possible implications for bromination reactions in the presence of nucleophilic species.

Experimental Section

Materials and synthesis

All reagents and solvents were purchased from commercial sources and used as received, unless otherwise stated. All reactions were performed under an inert atmosphere with dried glassware, using standard Schlenk techniques. Photochemical reactions are carried out at 365 nm. UV lamp used was purchased from Herolab GmbH (6 W lamp), whereas realUV™ LED strip light was purchased from Waveform Lightning. A complete description of the synthetic protocols and characterization data of synthesized compounds is reported herein and in the Supporting Information.

Electrochemical experiments

Cyclic voltammetry (CV) were measured out at room temperature in Ar-purged ACN, using Autolab PGSTAT100 or PGSTAT204. A glassy carbon working electrode, a Pt wire counter electrode, and an Ag wire as electrode were employed; ferrocene was present as an internal standard. All analyses were performed in the presence of tetraethylammonium hexafluorophosphate ($TEAPF_6$) as a supporting electrolyte. Typically, in both CV and DPV, the potential range was swept from +0.8 V to −1.1 V.

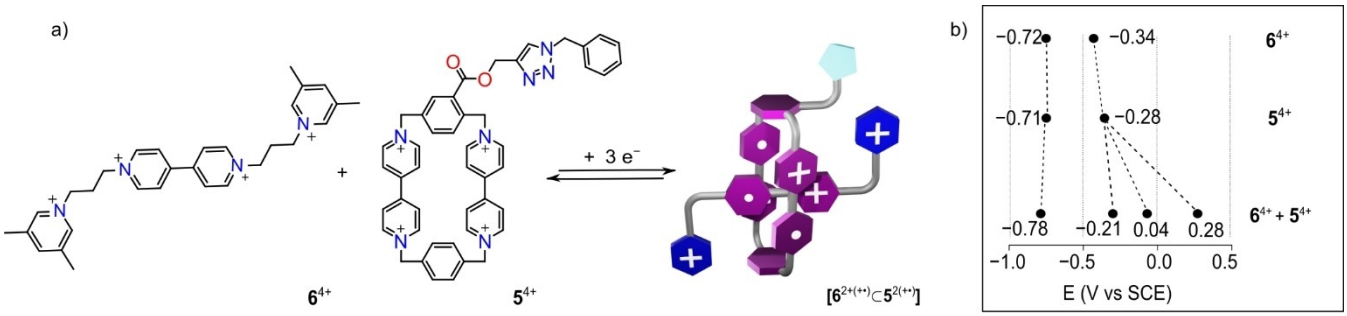

Figure 3. a) Reaction scheme to obtain $[\mathbf{6}^{2+(+\bullet)}\subset\mathbf{5}^{2(+\bullet)}]$ upon reduction and self-assembly. b) Genetic diagram displaying the redox processes observed in the DPV of $\mathbf{5}^{4+}$, $\mathbf{6}^{4+}$, and a 1 mM mixture of both. Conditions: ACN, $TBAPF_6$ 100 mM. All positive charges are balanced by PF_6^- counterions, which are omitted for clarity.

Synthetic procedures

2: Under inert atmosphere, in a 100 mL Schlenk tube, 3 g of 2,5-dimethyl benzoic acid **1** (19.9 mmol, 1 eq.) are dissolved in 60 mL of dry ACN. Then, 7.82 g of NBS (43.9 mmol, 2.2 eq.) and 180 mg of AIBN (0.055 mmol, 0.05 eq.) are added to the reaction mixture. The solution is irradiated using a 6 W UV lamp (365 nm). The solution turns from colourless to yellow in 30 minutes, becoming inhomogeneous after 2 hours. After 4 h, the solvent is removed under reduced pressure. 100 mL of water are added to the solid and the mixture is stirred for 15 minutes. The mixture is filtered, and the obtained white solid is collected and dried under vacuum. The solid is recrystallized by dissolving it in the minimal amount of CH_2Cl_2: acetone (3:1) and adding 30 mL of cyclohexane, obtaining **2** as white-off crystals, which are filtered and dried under vacuum (3.23 g, 52%). ^{1}H NMR: (400 MHz, $CDCl_3$), δ (ppm) = 8.12 (d, J = 2.0 Hz, 1H), 7.59 (dd, J = 7.9 Hz, 2.0 Hz, 1H), 7.51 (d, J = 7.9 Hz, 1H), 4.99 (s, 2H), 4.50 (s, 2H). ^{13}C NMR: (125 MHz, $CDCl_3$), δ = 170.17, 140.43, 138.67, 134.11, 132.86, 132.78, 128.06, 31.74, 30.80. HRMS: m/z calcd. for $[M–H]^-$: 305.8896, found: 305,8853. Characterization consistent with literature data.[33]

3: This molecule has been prepared according to a modified literature procedure.[17] Under inert atmosphere, in a two-neck 100 mL round bottom flask, 3.0 g (9.7 mmol, 1 eq.) of **2** are dissolved in 50 mL of dry CH_2Cl_2. Then, 2.81 g of DCC (13.6 mmol, 1.4 eq.), previously dissolved in 10 mL of dry CH_2Cl_2, are added dropwise and the reaction mixture is left stirring. After 20 minutes, 60 mg of DMAP (0.48 mmol, 0.05 eq.) are added. Finally, after 2 h, 2 mL of propargyl alcohol (35.9 mmol, 3.5 eq.) are slowly added to the reaction mixture and the solution is stirred for 24 h. The reaction mixture is filtered using a syringe filter (0.22 μm) and the filtrate is concentrated under reduced pressure at rt. Then, 60 mL of diethyl ether are added to the crude, and the formed precipitate is filtered with a syringe filter. The filtrate is concentrated and purified by column chromatography (SiO_2, CH_2Cl_2/cyclohexane 4:1) to afford **3** as a white-off solid (2 g, 60%). ^{1}H NMR: (400 MHz, 25 °C, $CDCl_3$): δ (ppm) = 8.03 (d, ^4J = 2 Hz, 1H, aryl–H *o*-CO_2R), 7.56 (dd, ^3J = 8 Hz, ^4J = 2 Hz, 1H, aryl–H *p*-CO_2R), 7.47 (d, ^3J = 8 Hz, 1H, aryl–H *m*-CO_2R), 4.96 (d, ^4J = 2 Hz, 2H, propargyl–CH_2), 4.94 (s, 2H, CH_2Br), 4.49 (s, 2H, CH_2Br), 2.55 ppm (t, ^4J = 2 Hz, 1H, alkyne–H); ^{13}C NMR (125 MHz, 25 °C, $CDCl_3$): δ = 165.17, 139.88, 138.58, 133.59, 132.56, 132.11, 128.73, 77.4, 75.60, 53.00, 31.83, 30.80 ppm. HRMS: m/z calcd. for $[M–H]^-$: 343.9008, found: 343.8933. Characterization consistent with literature data.[20]

4$(PF_6)_4$: Under inert atmosphere, in a two-neck 25 mL round bottom flask, 143 mg of **3** (0.41 mmol, 1.1 eq.), 265 mg of 1,1′-(*p*-xylylene)bis(4,4′-bipyridinium) bis(hexafluorophosphate) (0.38 mmol, 1.0 eq.), and 379 mg of 2,2′-(((naphthalene-1,5-diylbis(oxy))bis(ethane-2,1-diyl))bis(oxy))bis(ethan-1-ol) acting as template (1.13 mmol, 3 eq.) are dissolved in 7 mL of dry DMF and stirred at room temperature, then NaI (17 mg, 0.3 eq.) is added. After 10 days, 18 mL of THF are added. The precipitated purple solid is collected by filtration and dried under a vacuum. The solid is dissolved in a minimal volume of water and extracted to remove the template ($H_2O/CHCl_3$, 1 L of $CHCl_3$ used). Water is removed under vacuum. The residue is purified by filtration on a silica plug, using MeOH/$MeNO_2$/NH_4Cl (aq. 2 M) 7:1:2 as eluent. The fractions are gathered and evaporated under vacuum. The obtained solid is then dissolved in water and NH_4PF_6 is added. The mixture is filtered and washed with a copious amount of water, then with ethanol twice, diethyl ether, and dried under vacuum to afford **4**$(PF_6)_4$ as a pale-yellow solid (64 mg, 14%). ^{1}H NMR (400 MHz, 25 °C, CD_3CN) δ = 8.91–8.86 (br s, 8H), 8.23 (s, 1H, aryl–H *o*-CO_2R), 8.20–8.15 (m, 6H), 8.09 (d, J = 5 Hz, 2H), 7.69 (d, J = 7 Hz, 1H, aryl–H *p*-CO_2R), 7.57 (d, J = 7 Hz, 1H, aryl–H *m*-CO_2R), 7.54 (s, 4H, unsubstituted aryl–H), 6.14 (s, 2H, benzyl–H), 5.84 (s, 2H, benzyl–H), 5.75 (s, 4H, benzyl–H), 4.98 (d, J = 2 Hz, 2H, propargyl CH_2), 2.96 ppm (t, J = 2 Hz, 1H, alkyne–H); ^{13}C NMR (125 MHz, 25 °C, CD_3CN): δ = 166.16, 150.83, 150.62, 150.58, 150.47, 146.98, 146.39, 146.22, 146.14, 137.48, 137.08, 136.91, 135.28, 134.6, 133.57, 131.37, 131.23, 130.72, 128.51, 128.42, 128.36, 127.83, 78.20, 77.37, 65.7, 65.64, 64.94, 62.54, 54.59 ppm. HRMS: m/z calcd. for $[M–PF_6^-]^+$: 1037.1607; found: 1037.1587. Characterization consistent with literature data.[20]

5$(PF_6)_4$: In a 10 mL Schlenk tube, under inert atmosphere, 11.4 mg of benzyl azide (0.094 mmol, 1 eq) and 101 mg of **4**$(PF_6)_4$ (0.094 mmol, 1 eq) are dissolved in 6 mL of dry acetone. The solution is subsequently degassed by bubbling argon for 20 min. Then, 5.2 mg of $[(CH_3CN)_4Cu]PF_6$ (0.014 mmol, 0.15 eq) and 7.4 mg tris(benzyltriazolylmethyl)amine (0.014 mmol, 0.15 eq) are added, and the reaction mixture is stirred at rt (22–25 °C) for 4 h. The reaction mixture is evaporated and purified by column chromatography (SiO_2, 10 mg/mL of NH_4PF_6 in ACN). The fractions are gathered, evaporated under vacuum, and washed with water to precipitate the product and remove excess NH_4PF_6 in excess. After that, the solid is filtered and collected, affording **5**$(PF_6)_4$ as a white solid. (69 mg, 65% yield). ^{1}H NMR (400 MHz, 25 °C, CD_3CN) δ (ppm) = 8.87 (m, 8H,), 8.15 (m, 7H), 8.03 (m, 2H), 7.99 (s, 1H), 7.69 (dd, J = 8.1, 2 .1 Hz, 1H), 7.58 (d, J = 8.0 Hz, 1H), 7.55 (s, 4H), 7.18 (m, 5H), 6.13 (s, 2H), 5.80 (s, 2H), 5.76 (m, 4H), 5.59 (s, 2H), 5.47 (s, 2H). ^{13}C NMR (125 MHz, 25 °C, CD_3CN) δ = 166.66, 150.70, 150.39, 150.37, 150.25, 146.91, 146.32, 146.18, 146.11, 143.09, 137.51, 137.19, 137.00, 136.99, 136.71, 135.17, 134.67, 133.54, 131.44, 131.33, 131.30, 129.83, 129.32, 128.87, 128.47, 128.37, 128.29, 127.80, 125.94, 125.78, 65.74, 65.68, 64.98, 62.59, 60.19, 54.41. HRMS: m/z calcd. for $[M\text{-}2\cdot PF_6]^{2+}$: 512.6297 and for $[M\text{-}3\cdot PF_6]^{3+}$: 293.4315; found: 512.6296 $[M\text{-}2\cdot PF_6]^{2+}$; 293.4311 $[M\text{-}3\cdot PF_6]^{3+}$.

Supporting information

Additional references are cited within the Supporting Information.[39–43]

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Conflict of Interests

The authors declare no conflict of interest.

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Data Availability Statement

The data that support the findings of this study are available in the supplementary material of this article.

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