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Substituted *meta*[*n*]Cycloparaphenylenes: Synthesis, Photophysical Properties and Host–guest Chemistry

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Abstract: Breaking the centrosymmetry of [*n*]cycloparaphenylenes ([*n*]CPPs) by one *meta* connection, leads to bright emission in the typically non-fluorescent smaller derivatives, conserving their size dependent emissive properties. Using the building block strategy for [*n*]CPPs, different nitrile substituted *meta*[*n*]CPPs ($n=6$, 8, 10) have been prepared. The nitrile substituent offers a convenient handle for functional group conversions (e.g., carboxylic acid, amide, aldehyde, as well as 1*H*-tetrazole). Besides the synthetic work, the photophysical properties of these novel *m*[*n*]CPP derivatives have been characterized. Additionally, the host–guest ability of cyano-*m*[10]CPP has been explored by studying its complexation with fullerene C_{60}. These insights open new applications of *meta*[*n*]CPPs as fluorophore in synthetic organic chemistry, material sciences as well as biomedical research.

Introduction

Based on the ground-breaking studies in 1993 by Vögtle,[1] syntheses of various [*n*]cycloparaphenylenes ([*n*]CPPs) were presented over the past several years.[2] First synthesized by Jasti and Bertozzi, [*n*]CPPs have been intensively studied in organic synthesis, as well as material sciences due to their unique bent, radially arranged π-systems.[3] Interestingly, the major absorption of CPPs is entirely size independent with a maximum around 340 nm, whereas the fluorescence is shifted bathochromicly with decreasing size.[4] This shift in emission is accompanied by a reduced quantum yield as the ring size decreases, where [5]- and [6]CPP are completely non-emissive.[5]

Based on Tretiak's theoretical studies,[6] Jasti developed the synthesis of *meta*[*n*]CPPs, breaking the centrosymmetry of the smaller parent [*n*]CPP derivatives, and therefore turning-on their fluorescence.[7] However, usage of this new class of cycloparaphenylenes is scarce in literature: In 2022, Cong used a covalent template synthesis for an all-benzene catenane consisting of two unsubstituted *meta*[9]CPPs.[8] So far, only three substituted *meta*[6]CPP derivatives are published by Jasti. His group synthesized pyridine incorporated nanohoops, which are applied in the formation of different rotaxanes.[9] Additionally, Jasti could successfully use an alkyne functionalized *meta*[6]CPP for copper(I)-catalyzed azide–alkyne cycloaddition reactions to introduce *meta*[6]CPP as fluorophore into HeLa-cells for two-photon fluorescence imaging, highlighting the importance of flexible substitution for application.[10] Most recently, the same group published an alkyne-incorporated *meta*[9+1]CPP, whereas the first number describes the number of phenylene units and the second the number of incorporated alkynes.[11]

Due to the potential of *meta*[*n*]CPPs in organic synthesis, material sciences, as well as biomedical applications, we planned to develop a bottom-up synthesis of three different sized *meta*[*n*]CPPs with a functional group attached to the *meta*-unit. This unit should be readily modifiable into a variety of other functionalities and should also be stable to the synthesis conditions of the *meta*[*n*]CPP. Aryl nitriles serve in various fields of chemistry as a key motif enabling applications in pharmaceuticals, dyes, materials and agrochemicals (Figure 1).[12] Unfortunately, post-functionalization after the cycloparaphenylene assembly is usually difficult to achieve due to selectivity issues. So, installing a CN substituent as a polar unsaturated functional group, where the nitrogen atom serves as nucleophilic center, the triple bond as π-coordinator, and the carbon as electrophilic center, enables a variety of chemical transformations.[13] The combination of a flexible synthesis and the chemically robustness with the large effective Stokes shifts of CPPs,[7,14] will push *meta*[*n*]CPPs into a new focus of attention as versatile fluorophores.

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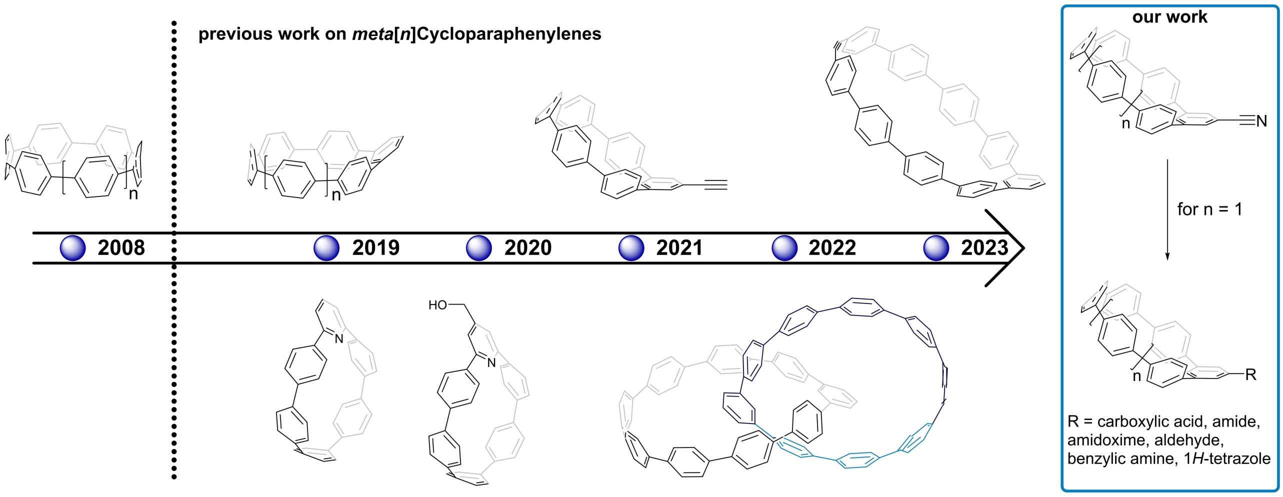
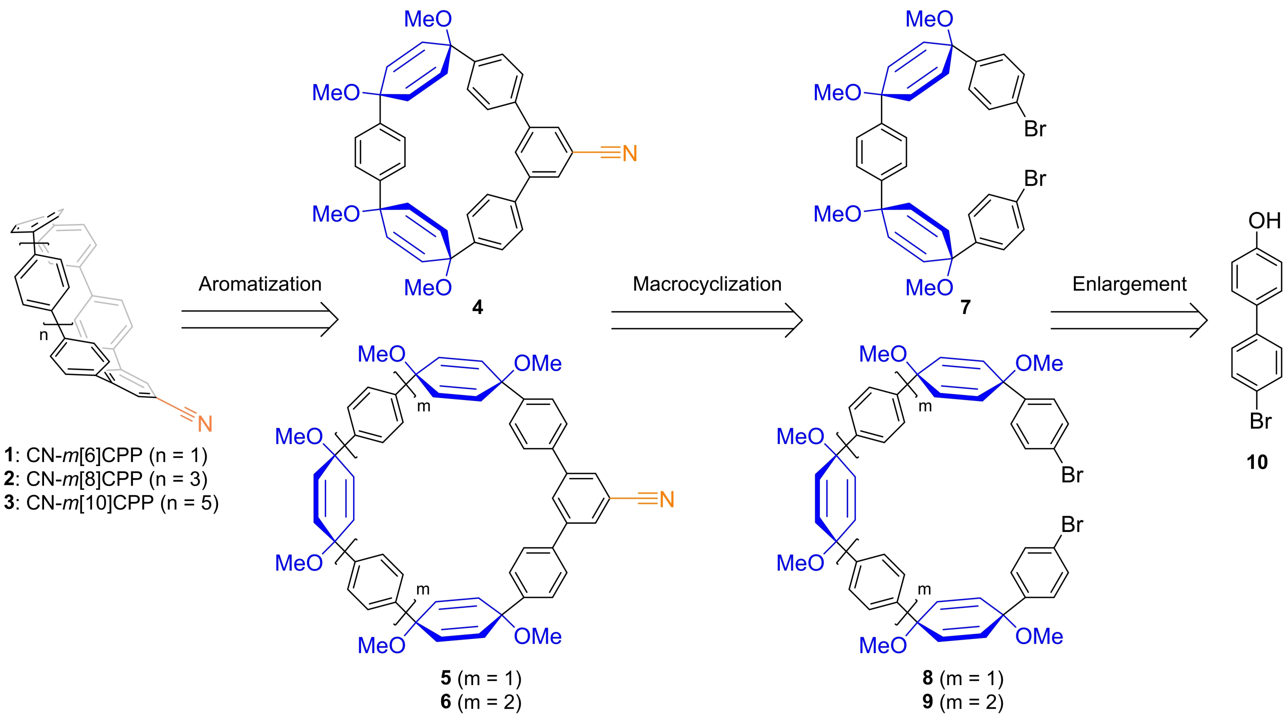


Figure 1. Towards substituted *meta*[*n*]cycloparaphenylenes. Previous described work of past years on *meta*[*n*]cycloparaphenylenes, and synthetic work described in this work.

Results and Discussion

Synthesis of cyano-*meta*[*n*]cycloparaphenylenes

Following the modular bottom-up approach for [*n*]CPPs, the synthesis of nitrile-substituted *meta*-[*n*]CPPs **1**–**3** is subdivided into three different parts. The first part proceeds according to well-established methods for an efficient and fast enlargement of the different building blocks (see Supporting Information Scheme S1). The second step tackles the formation of the unstrained macrocyclic precursors, which are aromatized within the third and final synthetic step (Scheme 1). The synthesis was initiated from 1-bromo-1′-hydroxybiphenyl (**10**) to the building blocks **7** and **8** through a combination of lithiation and regioselective addition of 1,4-diiodobenzene. Building block **9** was prepared via Suzuki-cross-coupling reaction. The *meta*-motif as well as the nitrile as functional group were introduced to the unstrained macrocycles **4**–**6** via Suzuki-cross-coupling reactions of 3,5-bis(pinacol) ester benzonitrile (**11**) and the building blocks **7**, **8**, or **9**, which resulted in good to very good



Scheme 1. Retrosynthetic analysis of cyano-*meta*[*n*]cycloparaphenylenes **1**–**3**, described in this work.

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yields. Afterwards, the unstrained macrocyclic precursors underwent reductive aromatization, using tin chloric acid as the reagent, concluding the synthesis of the targeted cyano-*meta*[*n*]CPPs (CN-*m*[*n*]CPPs), with $n=6$ (**1**, yield = 82 %), $n=8$ (**2**, yield = 43 %), and $n=10$ (**3**, yield = 43 %) (Scheme 2).

Solid-state structures of cyano-*meta*[*n*]cycloparaphenylenes (*n* = 6; 10)

Single crystals of cyano-*meta*[6]CPP **1** suitable for X-ray diffraction were obtained by evaporation of a dichloromethane solution. Similarly, crystals of cyano-*meta*[10]CPP **3** were obtained using chloroform as solvent. Both, the ORTEP plot of **1** and **3** as well as the dihedral angles together with distance measurements are depicted in Figure 2.

Both solid-state structures of **1** and **3** revealed an out-pointing position of the nitrile group. Additionally, the nearly regular shape of the macrocycles is distorted by the inwards pointing proton, which decreases the inner radius by around 0.7 Å. Furthermore, the nitrile substituent at the *meta*-phenylene widens the dihedral angle in the solid-state structure of cyano-*meta*[6]CPP **1** throughout the whole molecule compared to unsubstituted *meta*[6]CPP, prepared by Jasti.[7] The dihedral angle in **1** decreases from 56° at the *meta*-phenylene to 23° at the opposite phenyl of the macrocycle, while for **3** these angles change from 44° to 29°.

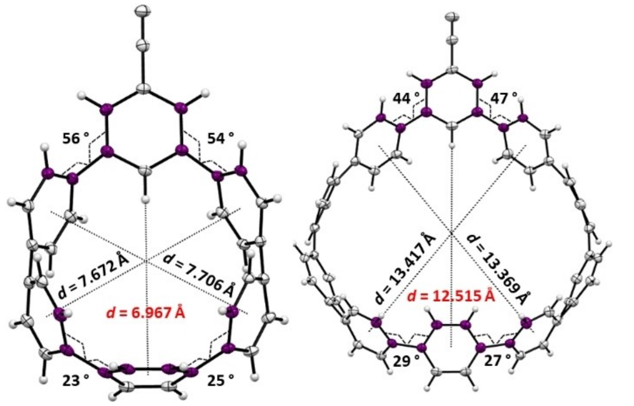


Figure 2. ORTEP plots of cyano-*meta*[6]CPP **1** (left), and cyano-*meta*[10]CPP **3** (right) depicted with their diameters and dihedral angles. Solvent molecules are omitted for clarity, thermal ellipsoids are shown at 50 % probability.

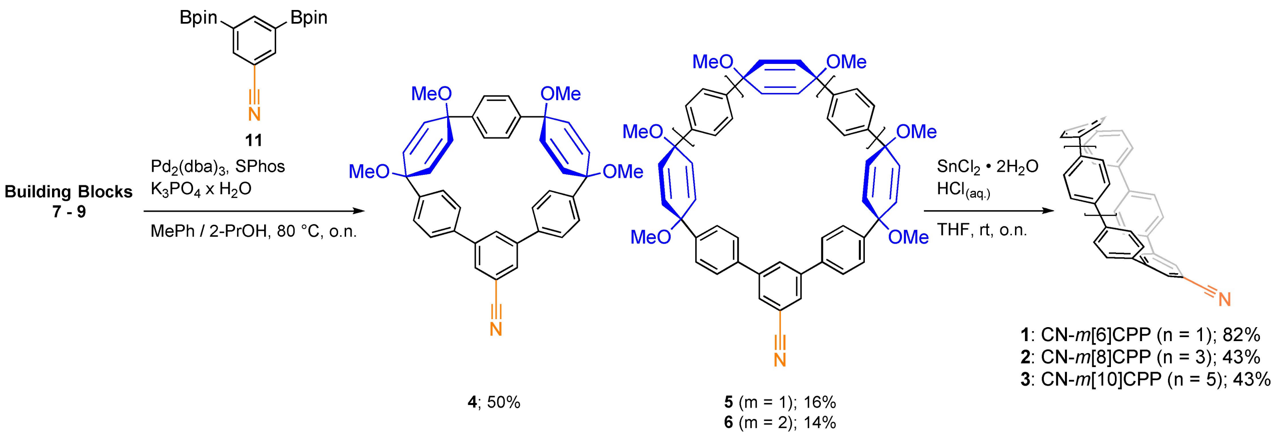
Functional group conversion of the cyano-group

As a demonstration of the nitrile group's versatility for further functionalization, cyano-*meta*[6]CPP **1** served as the key compound in the synthesis of different functionalized *meta*[*n*]CPPs (Scheme 3).

Therefore, we tested several one-step functional group conversion reactions (e.g., hydrolysis, reduction, and cycloaddition). Applying alkaline conditions for hydrolysis of the nitrile resulted in two different products dependent on the quenching conditions of the reaction. Terminating the reaction with HCl resulted in the precipitation of the carboxylic acid **12** (63 % yield), while water stopped the reaction at the amide **13** (74 % yield). Changing the base from sodium- or potassium hydroxide to hydroxylamine, results in the formation of an amidoxime **14** in 72 % yield, which is an important functional group in for example, medical chemistry. Furthermore, nitriles can be reduced with suitable reagents. Applying DIBAL-H, the nitrile group was converted to aldehyde **15** in 68 % yield. Using the stronger reducing agent $LiAlH_4$, provided the benzylic amine **16**, which can be isolated in yields of 76 %. Tetrazole **17** is formed in 74 % yield by a 1,3-dipolar cycloaddition, using sodium azide and L-proline as organocatalyst.

Photophysical properties of substituted *meta*[*n*]CPPs

The photophysical properties of the substituted *meta*[*n*]CPPs were studied via UV/Vis- and fluorescence spectroscopy. Analogous to the parent *meta*[*n*]CPPs, the cyano-*meta*[*n*]CPPs



Scheme 2. Macrocyclization and aromatization reactions towards cyano-*meta*[*n*]cycloparaphenylenes **1–3**.

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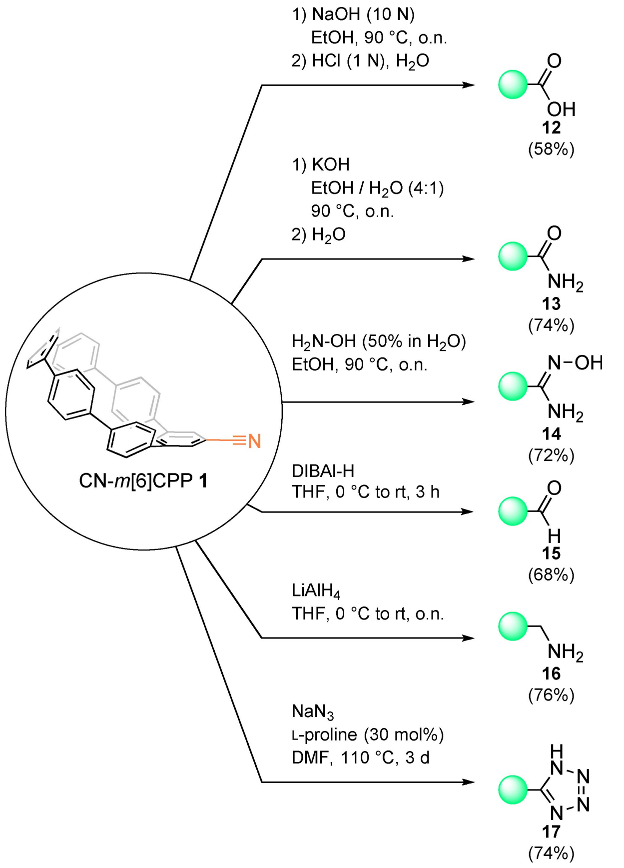

Scheme 3. One-step functional group conversion of the nitrile functionality toward different substituted-*meta*[6]cycloparaphenylenes **12**–**17**.

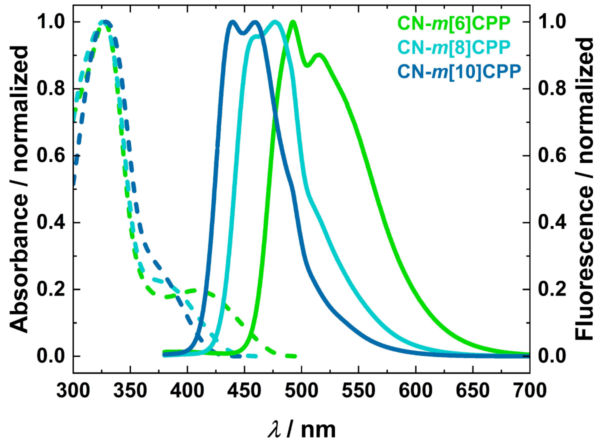

Figure 3. Absorbance (dashed, $c=3*10^{-5}$ м) and emission (bold, $c=3*10^{-6}$ м) spectra of cyano-*meta*[*n*]CPPs **1**–**3** measured in chloroform.

1–**3** share a common absorption maximum around 327 nm in chloroform. Changing the solvent from chloroform to DMSO for the different substituted *meta*[6]CPPs **1**, **12**–**17**, shifts this maximum only slightly toward 330 nm. Additionally, a red-shifted second absorption appears with decreasing ring-sizes. While for cyano-*meta*[10]CPP only a small shoulder is visible, the second absorption is clearly visible for cyano-*meta*[8]CPP and the differently substituted *meta*[6]CPPs. This observation is in accordance to the unsubstituted *meta*[*n*]CPPs, published by Jasti in 2019, where the main absorption is assigned to the transitions between HOMO-1 to LUMO and HOMO to LUMO+1, whereas the second absorption is the HOMO to LUMO transition.[7] Furthermore, the series of cyano-*meta*[*n*]CPPs **1**–**3** shows two blue shifted emission maxima with increasing ring size in the range of 440–516 nm (Figure 3).

For the substituted *meta*[6]CPPs in DMSO these two maxima are located at around 493 nm and 519 nm, respectively, and are not influenced by the type of substituent (spectra in the Supporting Information). Furthermore, the quantum yield and brightness of the different sized cyano-*meta*[*n*]CPPs **1**–**3** were determined. Confirming the trend of unsubstituted *meta*[*n*]CPPs, cyano-*meta*[*n*]CPPs **1**–**3** show an increasing extinction coefficient as well as an increasing quantum yield with increasing ring size. Consequently, the brightness increases with the number of phenyl units incorporated into the macrocyclic ring, too. The photophysical properties of cyano-*meta*[*n*]CPPs **1**–**3** are summarized in Table 1.

Furthermore, the presence of the carboxylate in molecule **12** allowed solubility studies in mixtures of water and DMSO for a first insight into the ability of using similar derivatives as bioimaging probes. For pH = 7, the absorbance started to deviate from linearity after 100 μм, and the fluorescence after 30 μм. Increasing the pH level to 8, using a mono- and dibasic potassium phosphate buffer system, shifted the maximum concentration towards 60 μм (see Supporting Information Figure S11 for more insights). At higher pH level, the carboxylic acid should be in its deprotonated form, resulting in a better solubility which fits to the obtained data. The intensity of the fluorescence can be influenced by several factors, such as aggregation, and static or dynamic fluorescence quenching, though. As a comparison, Jasti and co-workers synthesized the morpholine end-functionalized *meta*[6]CPP **18** (Figure 4), which can compete in many aspects such as solubility (150 μм), brightness (6750 $м^{-1}cm^{-1}$), self-quenching (starting at 500 μм), and cytotoxicity (50 μм) in comparison to state-of-the-art small molecule fluorophores (namely: BODIPY-FL, sulfo-Cy3, and Alexa Fluor 488). As *meta*[6]CPP **12**, is only end-functionalized without

Table 1. Photophysical properties of CN-*m*[n]CPPs **1**–**3** measured in chloroform. Absorbance maximum ($\lambda_{abs,max}$), extinction coefficient at absorbance maximum ($\varepsilon_{\lambda abs,max}$), emission maxima ($\lambda_{em,1}$; $\lambda_{em,2}$), fluorescence quantum yield at emission maximum (Φ_{max}), and brightness ($\varepsilon_{\lambda abs,max}\cdot\Phi_{max}$).

n	$\lambda_{abs,max}$/nm	$\varepsilon_{\lambda abs,max}$/(M·cm)$^{-1}$	$\lambda_{em,max1}$/nm	$\lambda_{em,max2}$/nm	Φ_{max}	$\varepsilon_{\lambda abs,max}\cdot\Phi_{max}$
6	327	$5.7\cdot10^4\pm0.1$	493	519	0.24	$1.4\cdot10^4$
8	326	$6.9\cdot10^4\pm0.4$	465	477	0.52	$3.6\cdot10^4$
10	328	$7.3\cdot10^4\pm0.3$	440	458	0.71	$5.2\cdot10^4$

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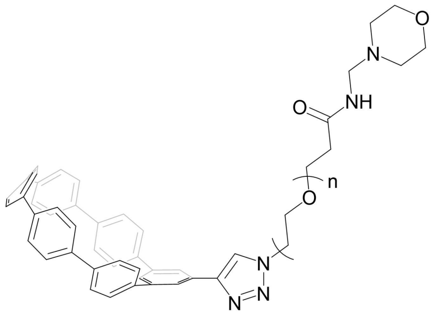

18

Figure 4. Morpholine end-functionalized *meta*[6]CPP **18**, reported by Jasti and co-workers.[10]

additional solubilizing linker, the solubility of at least 60 μM is remarkable. Especially the possibility to easily modify its solubility properties by simple chemical transformations opens great potential in the development of small molecule fluorophores.

Host–guest behavior of cyano-*meta*[10]CPP with fullerene (C_{60})

The nearly regular shape of cyano-*meta*[10]CPP **3** bears high potential as host for fullerene guests, such as C_{60}. Therefore, a ^{1}H NMR spectrum of a 1:1 mixture of **3** with C_{60} was measured in tetrachloroethane (TCE-d_2) to get a qualitative insight into the binding behavior (Figure 5). The ^{1}H NMR signal for the proton, pointing inside the macrocyclic ring, is shifted downfield by 0.184 ppm (Figure 5, Proton **a**). Here, two different effects can be considered. First, the dihedral angle should be decreased due to the complexation, and the proton **a** should be affected by the ring current which also leads to a deshielding effect. Second, the C_{60} serves as electron acceptor and therefore decreases the electron density throughout the cycloparaphenylene **3**. This effect is also visible in the ^{1}H NMR signals of the phenyl moieties between 7.7 ppm and 7.5 ppm, which show a strong downfield shift, too. The ^{1}H NMR signals of protons **b** are nearly unaffected as well as the other two protons of the *meta*-phenyl (**c**). Remarkably, the ^{1}H NMR signal of the two protons next to the nitrile-moiety at around 7.90 ppm is the only one which slightly shifted to a higher field (Figure 5, proton **c**). The binding affinity of cyano-*meta*[10]CPP **3** to C_{60} was determined by fluorescence quenching experiments, which resulted in an association constant (K_a) of $6.73*10^4$ M^{-1}. Compared to *para*-[10]cycloparaphenylene, K_a is decreased by two orders of magnitude.[15] This decline in binding affinity can be rationalized by the deviation from the regular circular shape due to the proton of the *meta*-phenyl pointing inside the macrocyclic structure. Nevertheless, the binding strength of CN-*meta*[10]CPP (**3**) with C_{60} can easily compete with other systems such as calixarenes[16] and cycloparaphenyleneacetylenes.[17]

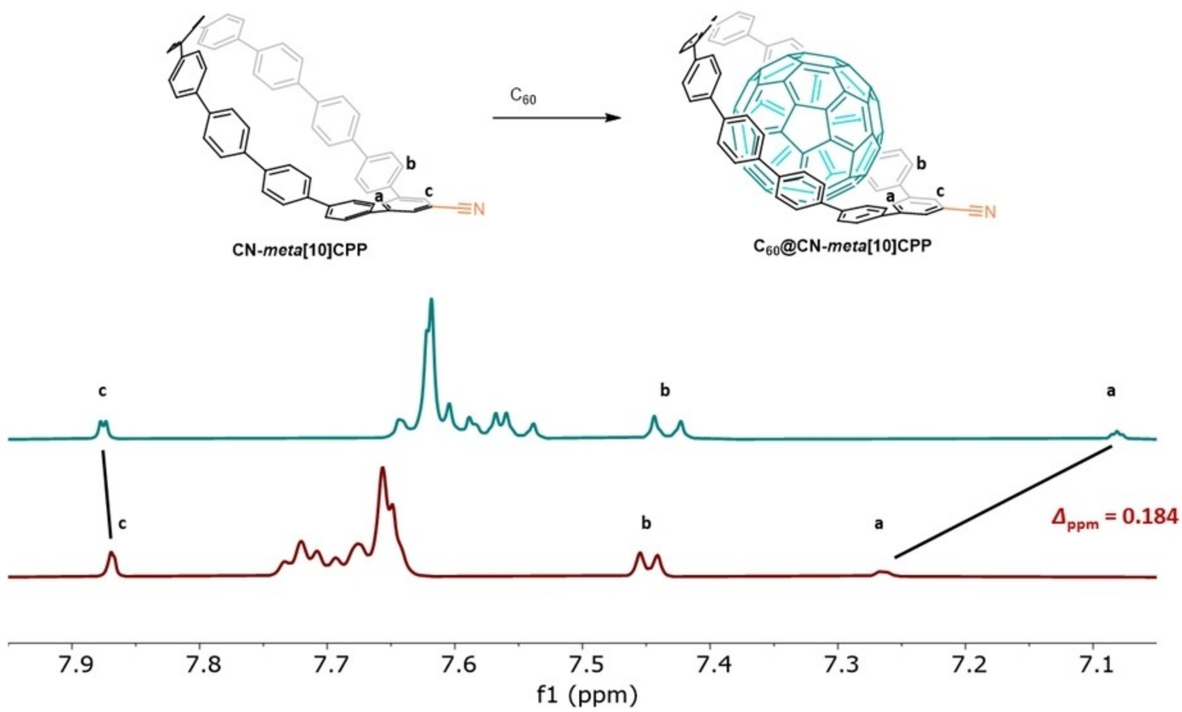

Figure 5. ^{1}H-NMR spectrum in deuterated tetrachloroethane-d_2 of a 1:1 mixture of cyano-*meta*[10]CPP **3** at room temperature before (top) and after (bottom) the addition of fullerene (C_{60}).

Conclusion

Following a modular synthesis strategy, we prepared three different sized cyano-*meta*[*n*]CPPs ($n = 6$, 8, 10). All compounds were characterized regarding their photophysical properties and confirm the earlier reported trends of unsubstituted *meta*[*n*]CPPs of a size-independent absorption maximum, a size-dependent emission maximum as well as an increasing brightness with increased ring size. In cases for cyano-*meta*[6]CPP and cyano-*meta*[10]CPP solid-state structures were obtained, revealing the outwards pointing nitrile functionality. The structural parameter of cyano-*meta*[10]CPP encouraged us to investigate the binding affinity towards C_{60}, which was quantified by fluorescence quenching experiments. Furthermore, the versatility of the nitrile group of cyano-*meta*[6]CPP could be demonstrated, using different strategies for functional group conversion. Within this work, different groups such as a carboxylic acid, amide, and aldehyde were introduced to the *meta*[6]CPP. In addition, an amidoxime could be installed at the *meta*[6]CPP as well as a benzylic amine and a 1*H*-tetrazole. Absorbance and fluorescence measurements in DMSO showed an independency of the maxima regarding the functionalities attached. In summary, our strategy towards substituted *meta*[*n*]CPPs using the nitrile functionality as versatile group can serve as general concept towards functionalized *meta*[*n*]CPPs, opening great potential for application in organic synthesis, material sciences, biomedical research, or fluorescent dyes.

Experimental Section

General Procedure for the Macrocyclization (4–6): Either dibromide **7**, **8**, or **9** (1.00 equiv.) and diboronate **11** (1.10 equiv.) were added to a round-bottomed three-neck-flask connected to the Schlenk-line. The flask was evacuated for 5 min and purged 3x with nitrogen. After adding the solvent mixture (PhMe/2-PrOH = 10:1, *c*(dibromide) = 3.6 mM), the mixture was flushed with nitrogen for 2 h at 40 °C (oil bath). Aqueous $K_3PO_4 \times H_2O$ (2.0 M, 4.0 equiv.) was purged with nitrogen in a separate flask for 2 h at rt. After 2 h, $Pd_2(dba)_3$ (10 mol%), SPhos (20 mol%) and the base were added to the flask in this order. The reaction mixture was allowed to stir at 80 °C (oil bath) overnight. After cooling to rt, the reaction mixture was then filtered through a plug of Celite®. The round bottom flask was rinsed 3x with DCM, which was filtered through the Celite® plug. The filtrate was added to a separatory funnel along with water and the organic phase was extracted 3x with DCM. The extracted layer was washed with brine, dried over sodium sulfate, and concentrated to yield the crude product. The crude product was further purified by flash silica gel chromatography.

General Procedure for the Aromatization (1–3): For aromatization of the corresponding macrocyclic precursors **4**, **5**, and **6** a stock solution of H_2SnCl_4 was prepared. Therefore, $SnCl_2 \cdot 2H_2O$ (0.040 M, 2.0 equiv./OMe) was added to a Schlenk-tube together with THF, followed by dropwise addition of concentrated HCl (4.0 equiv./OMe). This solution was allowed to stir at rt for 30 min.

(*note: if the tin chloride is too old, then the solution becomes cloudy during the addition of HCl, and the reaction does not work properly*)

The freshly prepared H_2SnCl_4 solution was added to the macrocyclic precursors **4**–**6** at rt in a Schlenk-tube. After stirring overnight, the reaction was quenched with aqueous saturated $NaHCO_3$ solution, and the product was extracted 3x with DCM. The combined organic layers were washed with water and brine, dried over magnesium sulfate, and the volatiles were removed under reduced pressure obtaining the crude product. Further purification of the addressed compounds **1**–**3** was done by flash silica gel chromatography.

Deposition Numbers 224802 (for **1**) and 224804 (for **3**) contain the supplementary crystallographic data for this paper. These data are provided free of charge by the joint Cambridge Crystallographic Data Centre and Fachinformationszentrum Karlsruhe Access Structures service.

Carboxylic acid-*meta*[6]cycloparaphenylene (12): In a 25 mL round-bottomed-flask CN-*m*[6]CPP **1** (20.0 mg, 41.5 μmol, 1.00 equiv.) was suspended in an ethanolic solution of NaOH (10 N, 2.0 mL). The mixture was stirred at 90 °C overnight. After cooling to rt, the solution was acidified by 1 N HCl (pH ~ 2) and the organic phase was extracted with ethyl acetate after stirring for 30 min at rt. The combined organic phase was washed with brine, dried over magnesium sulfate, filtrated, and the volatiles were evaporated under reduced pressure. The crude product was further purified by flash silica gel chromatography (eluent: Cy/EtOAc/MeOH = 5:1:0–4:1:1). The product was obtained as yellow solid yielding 12 mg (24.0 μmol, 58%). Mp.: > 280 °C (slow decomposition). ^1H NMR (400 MHz, DMSO-d_6): $\delta = 13.20$ (s, 1H); 8.05 (d, $J = 1.85$ Hz, 2H); 7.60–7.52 (m, 16H); 7.23–7.21 (m, 4H); 5.67 (t, $J = 1.85$ Hz, 1H) ppm. ^{13}C NMR (101 MHz, DMSO-d_6): $\delta = 167.18$ (1 C); 142.33 (2 C); 142.24 (1 C); 141.02 (2 C); 138.55 (2 C); 136.80 (2 C); 135.61 (2 C); 134.95 (2 C); 132.49 (1 C); 129.33 (4 C); 128.02 (4 C); 127.78 (4 C); 127.72 (4 C); 127.40 (4 C); 122.96 (2 C) ppm. HRMS (ESI) m/z for $C_{37}H_{24}O_2$ $[M-H^+]^-$ calculated 499.1703; found 499.1706.

Amide-*meta*[6]cycloparaphenylene (13): In a 25 mL round-bottomed-flask, CN-*m*[6]CPP **1** (20.0 mg, 41.5 μmol, 1.00 equiv.) was suspended in a solution of KOH (20.0 mg, 356 μmol, 8.59 equiv.) in $EtOH/H_2O$ (2.5 mL, v:v = 4:1) and stirred overnight at 90 °C. After cooling to rt, H_2O (20 mL) was added, and the reaction was extracted with ethyl acetate (3 × 20 mL). The combined organic layers were washed with brine (50 mL), dried over magnesium sulfate, and filtrated. The volatiles were evaporated, and the crude product was further purified by flash silica gel chromatography (eluent: Cy/EtOAc/MeOH = 5:1:1). The product was obtained as yellow solid yielding 15.3 mg (30.6 μmol, 74%). Mp.: > 280 °C (slow decomposition). ^1H NMR (400 MHz, DMSO-d_6): $\delta = 8.13$ (s, 1H); 8.00 (d, $J = 1.76$ Hz, 2H); 7.60–7.52 (m, 16H); 7.23–7.21 (m, 4H); 5.99 (t, $J = 1.76$ Hz, 1H) ppm. *(*One proton of the amide is missing most likely due to H-D exchange with water)*. ^{13}C NMR (101 MHz, DMSO-d_6): $\delta = 167.78$ (1 C); 142.06 (2 C); 141.38 (1 C); 140.56 (1 C); 138.43 (2 C); 136.76 (2 C); 136.08 (1 C); 135.62 (2 C); 135.00 (1 C); 129.25 (4 C); 128.03 (4 C); 127.78 (4 C); 127.71 (4 C); 127.44 (4 C); 121.30 (2 C) ppm. HRMS (ESI) m/z for $C_{37}H_{24}O$ $[M+Na]^+$ calculated 522.1828; found 522.1832.

Amidoxime-*meta*[6]cycloparaphenylene (14): In a 10 mL round-bottomed-flask, CN-*m*[6]CPP **1** (20.0 mg, 41.5 μmol, 1.00 equiv.) was added to a mixture of 50% aq. NH_2OH/EtOH (2.00 mL, v/v = 3:1). After stirring overnight at 90 °C, the mixture was cooled to rt and concentrated under reduced pressure to obtain the target compound as a yellow solid (15.3 mg, 29.7 μmol, 72%). Mp.: > 280 °C (slow decomposition). ^1H NMR (600 MHz, DMSO-d_6): $\delta = 9.75$ (s, 1H); 7.80 (d, $J = 1.74$ Hz, 2H); 7.59–7.52 (m, 16H); 7.23–7.21 (m, 4H); 5.98 (s, 2H); 5.47 (t, $J = 1.74$ Hz, 1H) ppm. ^{13}C NMR (151 MHz, DMSO-d_6): $\delta = 150.82$ (1 C); 141.95 (2 C); 141.74 (2 C); 138.39 (1 C); 138.32 (2 C); 136.73 (2 C); 135.63 (2 C); 135.05 (2 C); 134.96 (1 C); 129.17 (4 C); 128.05 (4 C); 127.79 (4 C); 127.70 (4 C); 127.44 (4 C); 119.23 (2 C) ppm. HRMS (ESI) m/z for $C_{37}H_{26}N_2O$ $[M+H]^+$ calculated 515.2118; found 515.2122.

Aldehyde-*meta*[6]cycloparaphenylene (15): In 10 mL Schlenk-tube, CN-*m*[6]CPP (20.0 mg, 41.5 μmol, 1.00 equiv.) was dissolved in DCM (0.5 mL), cooled to 0 °C, and treated slowly dropwise with DIBAL-H (1 M in *n*-hexanes, 0.10 mL, 0.10 mmol, 2.4 equiv.). The reaction was allowed to warm up to rt and then stirred for 3 h. To the mixture was added 6 M aqueous HCl solution (2 mL) and some ice under vigorous stirring. After stirring for 1 h at rt, the aqueous phase was extracted with DCM (3×20 mL). The combined organic phases were washed with saturated aqueous $NaHCO_3$ solution (20 mL) and distilled H_2O (50 mL), dried with magnesium sulfate, and filtrated. The volatiles were evaporated under reduced pressure and the crude product was further purified by flash silica gel chromatography (eluent: chloroform/hexanes = 4:1). The product was obtained as yellow solid yielding 13.6 mg (28.1 μmol, 68 %).

Benzylic amine-*meta*[6]cycloparaphenylene (16): In a 50 mL Schlenk-tube $LiAlH_4$ (5.20 mg, 130 μmol, 3.14 equiv.) was added in small portions to a solution of CN-*m*[6]CPP **1** (20.0 mg, 41.5 μmol, 1.00 equiv.) in THF (2.00 mL) at 0 °C. The resulting mixture was warmed to rt and stirred overnight. The next day, a saturated solution of sodium/potassium tartrate (20 mL) was added and allowed to stir for 1 h at rt. The aqueous phase was extracted with EtOAc (4×25 mL). The combined organic layers were dried over magnesium sulfate, filtrated, and the volatiles were evaporated under reduced pressure. The crude was further purified by flash silica gel chromatography (eluent: DCM/MeOH = 19:1 + 0.5 % TEA). The product was obtained as yellow solid yielding 15.3 mg (31.5 μmol, 76 %). Mp.: > 250 °C (slow decomposition). ^{1}H NMR (400 MHz, DMSO-d_6): δ = 7.60–7.51 (m, 16H); 7.48 (d, J = 1.90 Hz, 2H); 7.18–7.16 (m, 4H); 5.29 (t, J = 1.90 Hz, 1H); 3.84 (s, 2H) ppm. ^{13}C NMR (101 MHz, DMSO-d_6): δ = 145.8 (1 C); 142.31 (2 C); 142.02 (2 C); 138.05 (2 C); 136.64 (2 C); 136.09 (1 C); 135.59 (2 C); 135.07 (2 C); 129.09 (4 C); 128.01 (4 C); 127.76 (4 C); 127.60 (4 C); 127.28 (4 C); 120.89 (2 C); 45.71 (1 C) ppm. HRMS (ESI) m/z for $C_{37}H_{27}N$ $[M+H]^+$ calculated 486.2216; found 486.2213.

1*H*-Tetrazole-5-*meta*[6]cycloparaphenylene (17): In a 20 mL Schlenk-tube, the mixture of CN-*m*[6]CPP **1** (20.0 mg, 41.5 μmol, 1.00 equiv.), NaN_3 (5.00 mg, 76.1 μmol, 1.83 equiv.), and L-proline (1.50 mg, 13.0 μmol, 31.0 mol %) was stirred at 110 °C in DMF (2.00 mL) for 3 d. After completion of the reaction, the mixture was allowed to cool to rt and afterwards poured in ice water under rigorous stirring. This mixture was acidified with aqueous HCl solution (2 N). The resulting precipitate was dissolved with ethyl acetate and the organic phase was extracted with ethyl acetate (2× 20 mL). The combined organic phases were washed with water (6× 50 mL), brine (100 mL), and dried over magnesium sulfate. After filtration, the volatiles were evaporated under reduced pressure and the pure product was obtained (16.2 mg, 30.9 μmol, 74 %). Mp.: > 280 °C (slow decomposition). ^{1}H NMR (400 MHz, DMSO-d_6): δ = 8.17 (d, J = 1.75 Hz, 2H); 7.60–7.53 (m, 16H); 7.28–7.26 (m, 4H); 5.64 (t, J = 1.75 Hz, 1H) ppm. ^{13}C NMR (101 MHz, DMSO-d_6): δ = 155.47 (C_q, 1 C - HMBC); 143.05 (C_q, 2 C); 140.85 (C_q, 2 C); 140.49 (C_q, 1 C); 138.71 (C_q, 2 C); 136.85 (C_q, 2 C); 135.63 (C_q, 2 C); 134.92 (C_q, 2 C); 129.28 (C_{sp2}, 4 C); 128.04 (C_{sp2}, 4 C); 127.78 (C_{sp2}, 4 C); 127.74 (C_{sp2}, 4 C); 127.51 (C_{sp2}, 4 C); 125.67 (C_q, 1 C); 120.74 (C_q, 2 C) ppm. HRMS (ESI) m/z for $C_{37}H_{24}N_4$ $[M+Na]^+$ calculated 547.1893; found 547.1888.

Supporting Information

The data supporting the results of this study are available in the Supporting Information of this article. Furthermore, the authors have cited additional references within the Supporting Information.[18]

Author Contributions

F. B. and H. A. W. conceptualized the project. F. B. performed the organic synthesis and collected experimental data. All authors were involved in discussing the data and preparing the manuscript.

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Conflict of Interests

The authors declare no conflict of interest.

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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