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Synthesis of 1,4,5,16-tetrahydroxytetraphenylene

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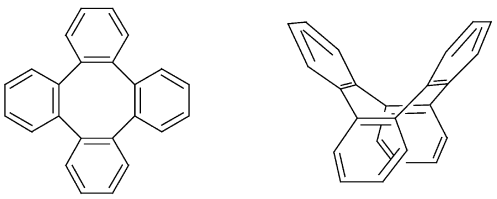
Dedicated to Professor Cheng-Ye Yuan on the occasion of his 80th birthday

Abstract—This paper concerns the synthesis of 1,4,5,16-tetrahydroxytetraphenylene, which may function as a building block for the construction of molecular scaffolds. The synthesis of 1,4,5,16-tetrahydroxytetraphenylene was realized by stepwise Diels–Alder reactions to form two benzene rings using 1,10-dimethoxydibenzo[*a*,*e*]cyclooctene as a precursor. This key intermediate, in turn, could be obtained by photo-rearrangement of its corresponding barrelene.

1. Introduction

Tetraphenylene (tetrabenzo[*a*,*c*,*e*,*g*]cyclooctatetraene) (**1**) is a structurally highly interesting molecule; it contains four benzene rings, which are disposed alternately above and below the main plane of the molecule, this molecule belongs to a D_{2d} symmetry point group (Scheme 1).[1]



Scheme 1.

Triggered by the aforementioned reasons, we have begun a research program with the aim to construct three-dimensional molecular scaffolds using tetraphenylenols as building blocks. In our program, we would like to synthesize five tetraphenylenols **2**,[2] **3**, **4**, **5** and **6**[3] (Scheme 2), as different modules which would subsequently serve to build various molecular scaffolds.

As can be seen, the hydroxyl groups of these tetraphenylenols are placing in different positions which could be interconnected with guest molecules via non-covalent interaction,[4] or with central metal linkages via covalent interaction[5] in diversified combination to form ordered linear, two- and three-dimensional scaffolds.

In this paper, we would like to report the synthesis of 1,4,5,16-tetrahydroxytetraphenylene (**4**), by employing 1,10-dimethoxydibenzo[*a*,*e*]cyclooctene (**9**) as the key intermediate.

2. Results and discussion

After the first synthesis of tetraphenylene (**1**) was reported in 1943,[6] considerable efforts has been devoted to the improved synthesis of **1** and its derivatives.[7] Because of the structural characteristics of our target molecule, we would like to utilize an eight-membered ring compound **9** as a precursor. Two benzene rings will then be introduced into the skeleton of **9** via stepwise Dieds–Alder reactions.[8] The retro-synthetic pathway is shown in Scheme 3. It is noteworthy that in our synthetic route, four hydroxyl groups could be introduced in a regiospecific manner.

As can be seen in Scheme 4, the hydroxyl groups in 1,10-dihydroxyanthraquinone (**11**) were converted to methoxy groups.[9] The protected anthraquinone **12** was then reduced smoothly to its corresponding anthracene **13** in the presence of zinc under an alkaline environment.[10] With 1,8-dimethoxyanthracene (**13**) in hand, a Diels–Alder reaction[11] between the anthracene **13** and dimethyl acetylenedicarboxylate (DMAD) provided dimethyl

Keywords: Diels–Alder reaction; Tetraphenylene; Strained acetylene; Photo-rearrangement.
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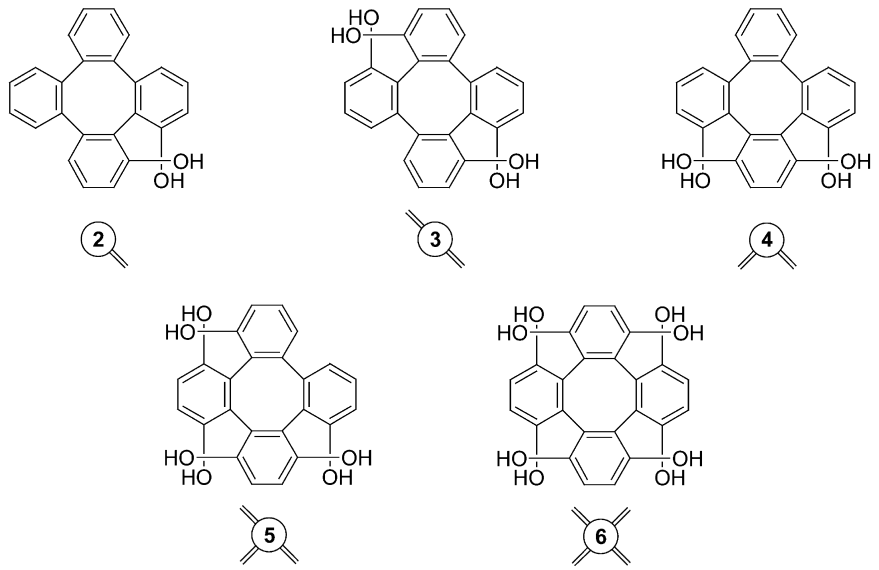
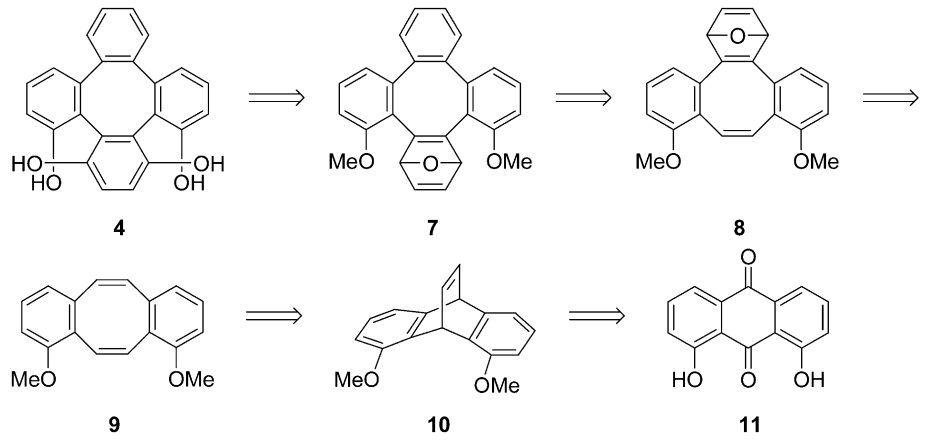
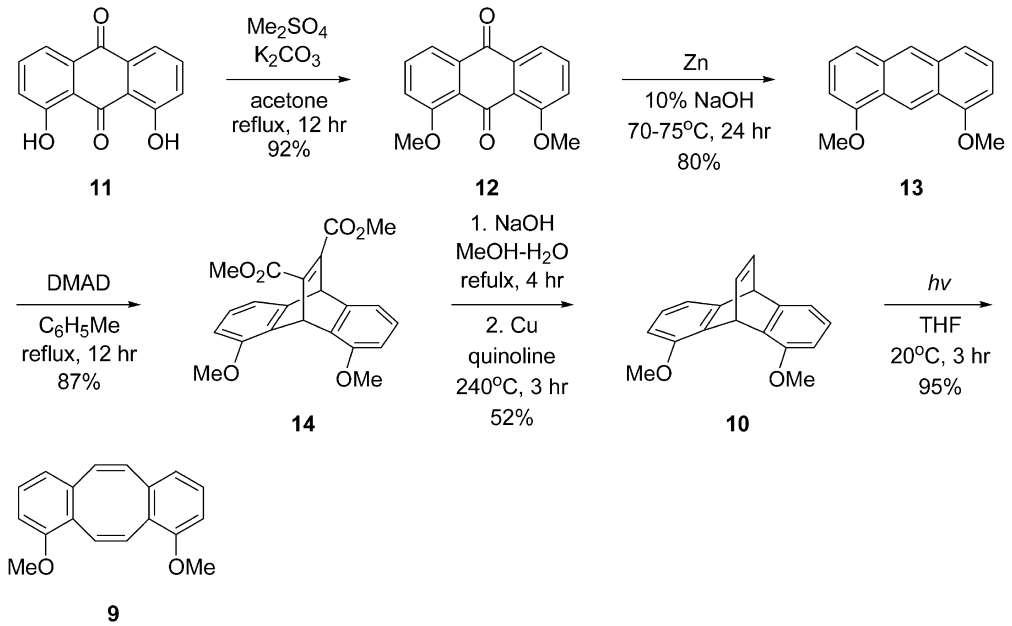


Scheme 2.



Scheme 3.



Scheme 4.

9,10-dihydro-9,10-etheno-1,8-dimethoxyanthracene-11,12-dicarboxylate (**14**) in high yield.[12] This adduct was allowed to undergo a saponification step to provide the corresponding diacid, whose reductive bisdecarboxylation yielded 1,8-dimethoxybarrelene (**10**).[12] In the proton NMR spectrum of barrelene **10**, two bridge-head protons show two sets of doublet of doublets at δ 5.17–5.19 and δ 6.10–6.13, respectively. Photoinduced isomerization of barrelene **10** furnished dibenzo[*a*,*e*]cyclooctene **9** in an excellent yield.[13] A significant difference was found in the proton NMR spectra between barrelene **10** and dibenzo[*a*,*e*]cyclooctene **9**, which is a direct evidence for the success of photo rearrangement. As mentioned above, for barrelene **10**, two bridge-head protons give two sets of doublet of doublets, while the rearrangement product show two sets of singlets at δ 6.73 and 6.74 which could be attributed to the olefinic protons in the central cyclooctene ring.

After a sufficient amount of the key intermediate, namely 1,10-dimethoxydibenzo[*a*,*e*]cyclooctene (**9**) was secured, the next step was to construct the pivotal tribenzo[*a*,*c*,*e*]-cyclooctene skeleton. The synthesis of tribenzo[*a*,*c*,*e*]cyclooctene framework was not expected to be trivial, as can be revealed by a literature survey.[14]

First, bromination[15] of dibenzo[*a*,*e*]cyclooctene **9** with one molar equivalent of bromine at 0 °C in CCl_4 gave a mixture of 5,6-dibromo-5,6-dihydro-1,10-dimethoxydibenzo[*a*,*e*]-cyclooctene (**15**) and 11,12-dibromo-11,12-dihydro-1,10-dimethoxydibenzo[*a*,*e*]cyclooctene (**16**). The two isomers were used directly without separation and purification in the next dehydrobromination step by using potassium *tert*-butoxide as the base.[16] The reactive strained alkynes, after their generation, underwent Diels–Alder reaction with furan to yield endoxide **8** and endoxide **17**, respectively. Moreover, another product was found to be 5-*tert*-butoxy-1,10-dimethoxydibenzo[*a*,*c*]cyclooctene (**18**) which was generated in only 10% yield.[17] A notable singlet at δ 1.20 was found in the proton NMR spectrum of compound **18** which was due to the absorption of the *tert*-butyl group. The structure of the major endoxide **8** was confirmed by an X-ray crystallographic study (Fig. 1). To obtain the tribenzo[*a*,*c*,*e*]cyclooctene framework, **8** was deoxygenated by the low-valent-titanium reagent,[18] yielding 1,12-dimethoxytribenzo[*a*,*c*,*e*]cyclooctene (**19**) (Scheme 5). The resonances of the proton NMR spectrum are assigned as the following. Thus, the singlet at δ 3.80 corresponds to the methoxy protons. The olefinic protons (H-13, H-14) absorb as a singlet at δ 6.73. Also, two sets of doublet of doublets belonging to the benzenoid protons (H-2, H-4, H-9, H-11) appear at δ 6.74–6.81. The multiplet due to the absorption of the two protons (H-6, H-7) overlaps with those of H-3 and H-10 in the region of δ 7.14–7.7.19. Finally, the doublet of doublets at δ 6.36–6.39 (J=5.7 Hz, 3.6 Hz) can be attributed to two protons (H-5, H-8) of the newly constructed benzene ring. The HRMS (EI) of **19** shows a molecular peak at m/z 314.1305 (Calcd for $C_{22}H_{18}O_2$: 314.1307). Furthermore, the elemental analysis result is

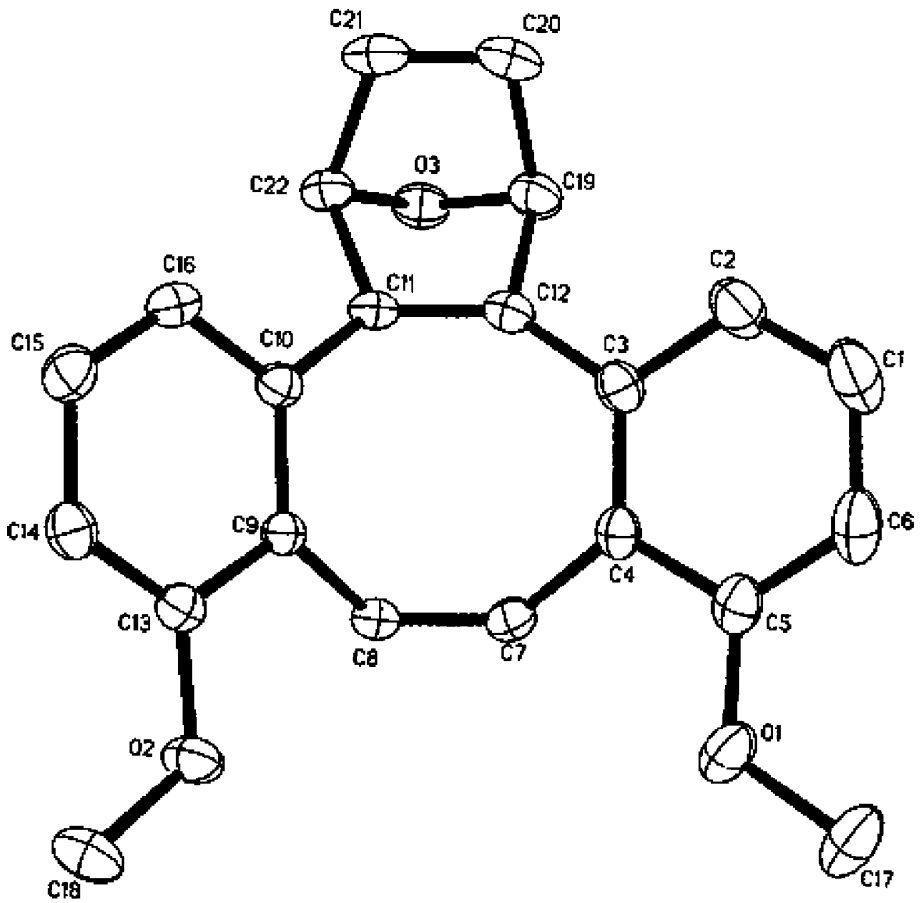
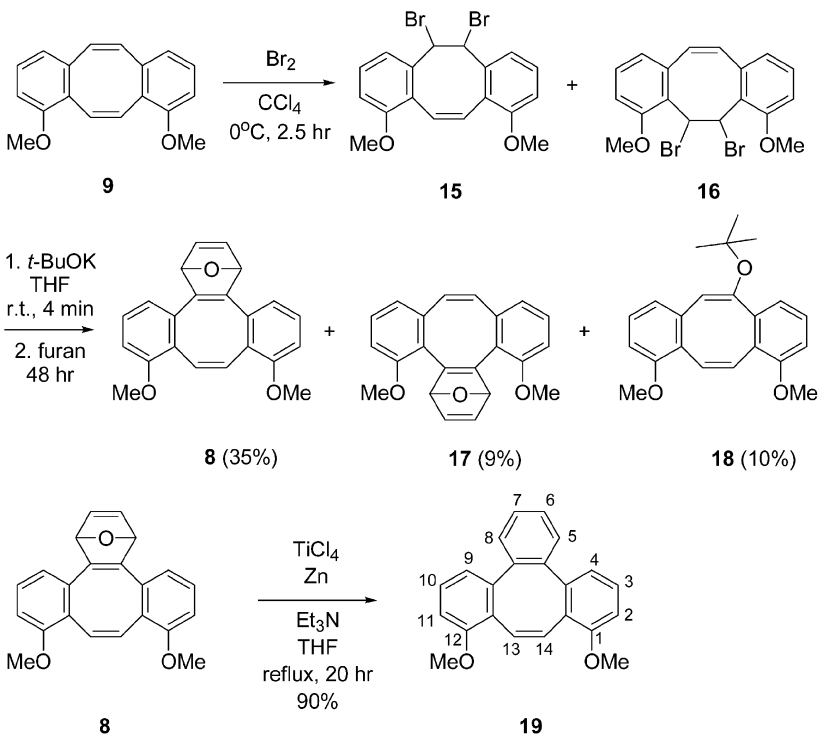
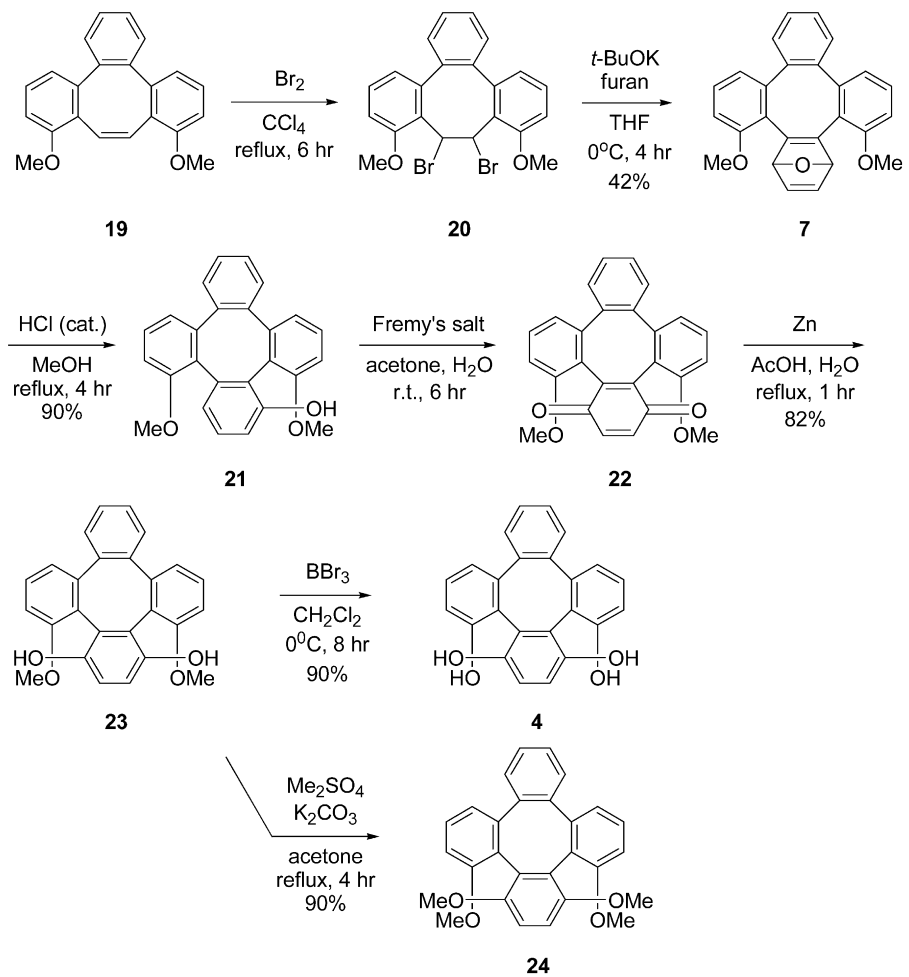


Figure 1. Molecular structure and atom labeling of **8**. H atoms have been omitted for clarity. Ellipsoids are drawn at the 30% probability level.



Scheme 5.



Scheme 6.

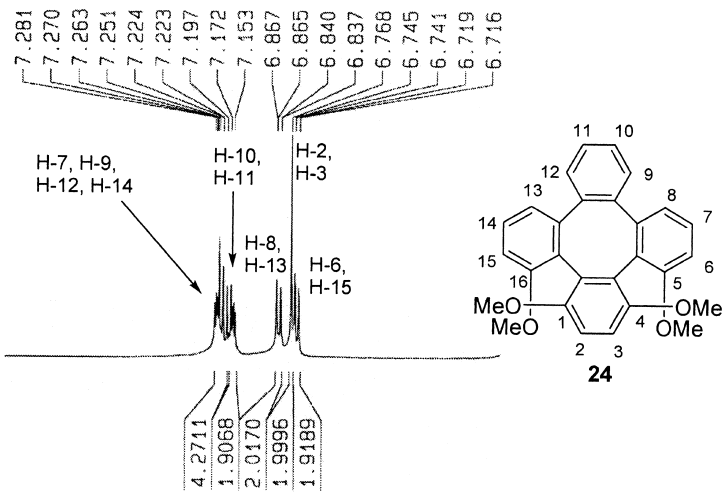


Figure 2. The proton NMR spectrum of **24** with characterization in aromatic region.

consistent with the structure of **19** (Anal. Calcd for $C_{22}H_{18}O_2$: C, 84.05; H, 5.77. Found: C, 84.28; H, 5.82).

With **19** in hand, the introduction of the remaining dihydroxybenzene ring towards the realization of our target was then preformed.

As can be seen in Scheme 6, bromine was used again to brominate the double bond of **19**. However, the solubility of dibromide **20** is generally low in common solvents and it was difficult to purify **20** by column chromatography. As a result, the crude product was directly used in the dehydrobromination step and the freshly generated strained alkyne was trapped by furan concomitantly to give endoxide **7** in 42% yield in two steps.[16,17] With endoxide **7** in hand, acid catalyzed ring opening reaction was performed to lead to phenol **21** smoothly.[19] Since the structure of phenol **21** is unsymmetrical, its proton NMR signals are quite complicated. The chemical shifts of two methoxy groups are found at δ 3.68 and 3.74, respectively. The phenolic proton resonates at δ 4.88. The benzenoid protons absorb at δ 6.74–6.86 (multiplet, 6H), and 7.12–7.26 (multiplet, 7H). The molecular peak found in its HRMS (FAB) spectrum is 380.1418 (Calcd for $C_{26}H_{20}O_3$: 380.1412).

To oxidize phenol to quinone, the typical reagent, Fremy's salt[20] was employed. Through a radical mechanism, phenol **21** was successfully oxidized to quinone **22** by Fremy's salt. Due to the low solubility and the almost identical polarities of phenol **21** and quinone **22**, it was difficult to separate **21** and **22** by column chromatography. Since phenol **21** would not affect the reduction reaction from quinone **22** to hydroquinone **23**, we directly reduced the crude products with zinc powder to form hydroquinone **23** under an acidic condition.[21] The reacted yield was found to be 82% in two steps. Finally, the remaining two methoxy groups were deprotected by BBr_3 to give our target molecule, 1,4,5,16-tetrahydroxytetraphenylene (**4**) in high yield.[22] Furthermore, the free hydroxyl groups on **23** could also be protected by dimethyl sulfate to give tetramethoxytetraphenylene **24** (Scheme 6).

As expected, tetramethoxytetraphenylene **24** is a highly stable compound with a sharp melting point (mp 204 °C). However, tetrahydroxytetraphenylene **4** is relatively unstable when it was exposed to air and light without protection.

The splitting patterns shown in the proton NMR spectra of these three tetraphenylene derivatives, namely **4**, **23** and **24** are quite similar at the downfield region (δ 6.7–7.4). However, we can still easily identify them by the number of methoxy signals at about δ 3.7 in their spectra. In Figure 2, the downfield region in the proton NMR spectrum of tetramethoxytetraphenylene **24** with full characterization is shown.

In summary, the synthesis of 1,4,5,16-tetrahydroxytetraphenylene (**4**), through 1,4-endoxo-1,4-dihydro-8,11-dimethoxytribenzo[*a*,*c*,*e*]cyclooctene (**8**) as the intermediate, was accomplished in 15 steps and the total yield was found to be 3%.

3. Experimental

3.1. General

All reagents and solvents were reagent grade. Further purification and drying by standard method[23] were employed when necessary. All evaporations of organic solvents were carried out with a rotary evaporator in conjunction with a water aspirator. The plates used for thin-layer chromatography (TLC) were E. Merck silica gel $60F_{254}$ (0.25 mm thickness) precoated on aluminum plates, and they were visualized under both long (365 nm) and short (254 nm) UV light. Compounds on TLC plates were visualized with a spray of 5% dodecamolybdophosphoric acid in ethanol and with subsequent heating. Column chromatography was performed using E. Merck silica gel (230–400 mesh).

Melting points were measured on a Reichert Microscope apparatus and were uncorrected. NMR spectra were recorded on a Bruker DPX-300 spectrometer (300.13 MHz for ^{1}H and 75.47 MHz for ^{13}C). All NMR measurements

were carried out at room temperature in deuterated chloroform solution unless otherwise stated. Chemical shifts are reported as parts per million (ppm) in δ units on the scale downfield from tetramethylsilane (TMS) or relative to the resonance of chloroform solvent (7.26 ppm in the ^{1}H, 77.0 ppm for the central line of the triplet in the ^{13}C modes, respectively). Coupling constants (*J*) are reported in hertz (Hz). Splitting pattern are described as 's' (singlet); 'd' (doublet); 't' (triplet); 'q' (quartet); 'm' (multiplet). ^{1}H NMR data are reported in this order: chemical shifts; multiplicity; coupling constant(s), number(s) of proton. Mass spectra (MS and HRMS) were obtained with a Thermofinnigan MAT95XL spectrometer, and recorded at an ionization energy of 70 eV unless otherwise stated. In all case, signals are reported as *m*/*z*. Elemental analyses were performed at Shanghai Institute of Organic Chemistry, The Chinese Academy of Sciences and MEDAC LTD at Brunel Science Centre, UK.

3.1.1. 1,8-Dimethoxyanthraquinone (12).[24] To a vigorously stirred solution of 1,8-dihydroxyanthraquinone (**11**) (20.0 g, 83 mmol) in acetone (500 mL) was added K_2CO_3 (15 g). Then the mixture was heated to reflux and dimethyl sulfate (23 mL, 250 mmol) was added through a dropping funnel in 1 h. The mixture was refluxed for a further 12 h. After cooling to room temperature, the residue was filtered off and washed with acetone (2×20 mL). The combined organic solvent was evaporated under reduced pressure. The residue was chromatographed on silica gel (500 g, hexanes/EtOAc 3:1) to afford 1,8-dimethoxyanthraquinone (**12**) (21.1 g, 92%) as a yellow solid: mp 223–224 °C (lit.[25] 223–235 °C); ^{1}H NMR ($CDCl_3$) δ 4.00 (s, 6H), 7.30 (dd, *J*=8.4 Hz, 0.6 Hz, 2H), 7.63 (dd, *J*=8.0, 8.0 Hz, 2H), 7.82 (dd, *J*=7.8, 1.2 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ 56.5, 118.0, 118.9, 124.0, 133.9, 134.7, 159.4, 182.9, 184.0.

3.1.2. 1,8-Dimethoxyanthracene (13).[26] To a 10% NaOH solution (300 mL) of 1,8-dimethoxyanthraquinone (**12**) (20.0 g, 74.6 mmol) was added zinc powder (25.0 g, 382 mmol). The mixture was stirred and heated for 24 h, and then the reaction mixture was filtered and the filtered cake was washed with CH_2Cl_2 (5×300 mL). The organic extracts were combined and evaporated. The residue was chromatographed on silica gel (1000 g, hexanes/EtOAc 9:1) to give 1,8-dimethoxyanthracene (**13**) (14.2 g, 80%) as yellow needles: mp 198–199 °C (lit.[26] 199–200 °C); ^{1}H NMR ($CDCl_3$) δ 4.09 (s, 6H), 6.74 (d, *J*=7.5 Hz, 2H), 7.40 (dd, *J*=8.1, 8.1 Hz, 2H), 7.59 (d, *J*=8.7 Hz, 2H), 8.34 (s, 1H), 9.28 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 55.4, 101.5, 115.7, 120.2, 124.4, 125.1, 125.6, 132.9, 155.9.

3.1.3. Dimethyl 9,10-dihydro-9,10-etheno-1,8-dimethoxyanthracene-11,12-dicarboxylate (14). A mixture of 1,8-dimethoxyanthracene (**13**) (10.0 g, 42.0 mmol) and dimethyl acetylenedicarboxylate (8.9 g, 63.0 mmol) in toluene (25 mL) was refluxed with stirring for 12 h. The reaction mixture was cooled with an ice water bath and filtered by suction. The filtered cake was washed with ice cooled absolute ethanol (3×5 mL), and dried at room temperature to give the crude product (13.9 g, 87%). Recrystallization from absolute ethanol afforded dimethyl 9,10-dihydro-9,10-etheno-1,8-dimethoxyanthracene-11,12-dicarboxylate (**14**) (12.8 g, 80%) as a white solid: mp 263–265 °C; ^{1}H NMR ($CDCl_3$) δ 3.77 (s, 3H), 3.80 (s, 3H), 3.85 (s, 6H), 5.49 (s, 1H), 6.36 (s, 1H), 6.61 (dd, *J*=8.1, 0.6 Hz, 2H), 6.96 (dd, *J*=7.8, 7.8 Hz, 2H), 7.03 (d, *J*=6.9 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ 39.6, 52.3, 52.3, 52.5, 55.9, 109.0, 116.6, 126.2, 131.4, 146.7, 147.0, 148.5, 154.7, 165.8, 166.3. Anal. Calcd for $C_{22}H_{20}O_6$: C, 69.46; H, 5.30. Found: C, 69.18; H, 5.42.

3.1.4. 1,8-Dimethoxybarrelene (10).[27] To a stirred solution of NaOH (15.0 g, 380 mmol) in 40% aqueous methanol (300 mL) was added dimethyl 9,10-dihydro-9,10-etheno-1,8-dimethoxyanthracene-11,12-dicarboxylate (**14**) (10.0 g, 26.3 mmol). The mixture was allowed to reflux for 4 h, and was then cooled to room temperature. The reaction mixture was acidified with 36% HCl to *p*H 2, filtered with suction filtration and dried under vacuum without further purification to give 9,10-dihydro-9,10-etheno-1,8-dimethoxyanthracene-11,12-dicarboxylic acid.

To a vigorously stirred solution of 9,10-dihydro-9,10-etheno-1,8-dimethoxyanthracene-11,12-dicarboxylic acid (vide supra) (10.0 g, 29.8 mmol) in quinoline (250 mL) was added copper powder (9.4 g, 142.0 mmol). The reaction mixture was refluxed for 3 h under N_2. After cooling to room temperature, CH_2Cl_2 (250 mL) was added to the mixture and the residue was then filtered. The filtrate was washed with 1 N HCl (4×200 mL) and dried over $MgSO_4$. After evaporation of the solvent, the residue was chromatographed on a silica gel column (600 g, hexanes/EtOAc 10:1) to afford 1,8-dimethoxybarrelene (**10**) (4.1 g, 52%) as colorless crystals: mp 210–211 °C (lit.[27] 211–212 °C); ^{1}H NMR ($CDCl_3$) δ 3.87 (s, 6H), 5.18 (dd, *J*=5.4, 1.5 Hz, 1H), 6.12 (dd, *J*=5.4, 1.8 Hz, 1H), 6.60 (dd, *J*=7.8, 0.9 Hz, 2H), 6.91–7.06 (m, 6H); ^{13}C NMR ($CDCl_3$) δ 37.4, 51.6, 55.8, 108.2, 116.1, 125.1, 133.8, 139.7, 140.3, 149.1, 154.0. Anal. Calcd for $C_{18}H_{16}O_2$: C, 81.79; H, 6.10. Found: C, 81.84; H, 6.17.

3.1.5. 1,10-Dimethoxydibenzo[*a*,*e*]cyclooctene (9). A solution of 1,8-dimethoxybarrelene (**10**) (1.0 g, 3.79 mmol) in degassed anhydrous THF (500 mL) was irradiated with a mercury lamp (125 W medium pressure) at room temperature for 3 h under a nitrogen atmosphere. After evaporation of the solvent, chromatography on silica gel (100 g, hexanes/EtOAc 7:1) afforded 1,10-dimethoxydibenzo[*a*,*e*]-cyclooctene (**9**) (0.95 g, 95%) as colorless crystals: mp 207–208 °C; ^{1}H NMR ($CDCl_3$) δ 3.78 (s, 6H), 6.65–6.70 (m, 4H), 6.73 (s, 2H), 6.74 (s, 2H) 7.14 (dd, *J*=8.0, 8.0 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ 55.5, 108.5, 121.1, 126.5, 127.8, 129.2, 133.0, 138.5, 157.3. Anal. Calcd for $C_{18}H_{16}O_2$: C, 81.79; H, 6.10. Found: C, 81.93; H, 6.16.

3.1.6. 5,6-Dibromo-5,6-dihydro-1,10-dimethoxydibenzo[*a*,*e*]cyclooctene (15); 11,12-dibromo-11,12-dihydro-1,10-dimethoxydibenzo[*a*,*e*]cyclooctene (16). To a suspension of 1,10-dimethoxydibenzo[*a*,*e*]cyclooctene (**9**) (0.60 g, 2.3 mmol) in anhydrous CCl_4 (50 mL) was added slowly a solution of bromine (0.36 g, 2.3 mmol) in anhydrous CCl_4 (10 mL) through a dropping funnel within 2 h at 0 °C under N_2. After addition, the temperature was slowly allow to rise to room temperature and the mixture was stirred for an additional 30 min. The reaction was quenched by addition of 10% $Na_2S_2O_5$ (3 mL). The mixture

was extracted with CH_2Cl_2 (2×10 mL), and the combined organic extract was dried over $MgSO_4$ and evaporated under reduced pressure to give a mixture of 5,6-dibromo-5,6-dihydro-1,10-dimethoxydibenzo[*a*,*e*]cyclooctene (**15**) and 11,12-dibromo-11,12-dihydro-1,10-dimethoxydibenzo[*a*,*e*]-cyclooctene (**16**) as a white solid. These compounds were not purified further and were used immediately in the next step.

3.1.7. 1,4-Endoxo-1,4-dihydro-8,11-dimethoxytribenzo[*a*,*c*,*e*]cyclooctene (8); 1,4-endoxo-1,4-dihydro-5,14-dimethoxytribenzo[*a*,*c*,*e*]cyclooctene (17); 5-*tert*-butoxy-1,10-dimethoxydibenzo[*a*,*c*]cyclooctene (18). To a solution of freshly sublimed KO-*t*-Bu (0.76 g 6.8 mmol) in anhydrous THF (40 mL) and furan (20 mL) under N_2 was added slowly a solution of previously prepared dibromides **15** and **16** (1.0 g, 2.3 mmol) (vide supra) in anhydrous THF (40 mL) and furan (20 mL) within 3 min. After the solution was stirred for 1 min, brine (15 mL) was added. The organic layer was separated and dried over $MgSO_4$, and the filtrate was then stirred for further 48 h under N_2. The solvent was evaporated under reduced pressure and the residue was separated by flash column chromatography on silica gel (30 g, hexanes/EtOAc 3:1) to give 1,4-endoxo-1,4-dihydro-8,11-dimethoxytribenzo[*a*,*c*,*e*]cyclooctene (**8**) (260 mg, 35%), 1,4-endoxo-1,4-dihydro-5,14-dimethoxytribenzo[*a*,*c*,*e*]cyclooctene (**17**) (70 mg, 9%) and 5-*tert*-butoxy-1,10-dimethoxydibenzoc[*a*,*c*]cyclooctene (**18**) (80 mg, 10%).

Data of **8**: mp 150–151 °C; ^{1}H NMR ($CDCl_3$) δ 3.80 (s, 6H), 5.44–5.45 (m, 2H), 6.36 (dd, *J*=7.8, 0.9 Hz, 2H), 6.62 (s, 2H), 6.71 (dd, *J*=7.8, 8.1 Hz, 2H), 7.17 (dd, *J*=8.0, 8.0 Hz, 2H), 7.40 (s, 2H); ^{13}C NMR ($CDCl_3$) δ 55.6, 87.9, 109.2, 114.8, 126.4, 128.3, 129.9, 136.4, 142.5, 151.5, 157.8. MS *m*/*z* 330 (M^+). HRMS (EI) Calcd for $C_{22}H_{18}O_3$: 330.1256. Found: 330.1250. Crystallization from 20% EtOAc in CH_2Cl_2 at room temperature gave colorless crystals, which were sufficiently good for an X-ray crystallographic analysis.

Data of **17**: mp 145–146 °C; ^{1}H NMR ($CDCl_3$) δ 3.75 (s, 6H), 5.40–5.41 (m, 2H), 6.41 (s, 2H), 6.65 (dd, *J*=8.1, 0.6 Hz, 2H), 6.70 (dd, *J*=7.8, 0.9 Hz, 2H), 7.14 (dd, *J*=7.4, 7.4 Hz, 2H), 7.16 (s, 2H); ^{13}C NMR ($CDCl_3$) δ 55.2, 87.4, 108.9, 122.0, 124.2, 128.2, 133.4, 138.6, 142.5, 152.4, 158.0. MS *m*/*z* 330 (M^+). HRMS (EI) Calcd for $C_{22}H_{18}O_3$: 330.1256. Found: 330.1247.

Data of **18**: mp 198–199 °C; ^{1}H NMR ($CDCl_3$) δ 1.20 (s, 9H), 3.77 (s, 6H), 6.37 (s, 1H), 6.61–6.86 (m, 5H), 6.99 (d, *J*=7.8 Hz, 1H), 7.07–7.16 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 29.2, 55.5, 78.4, 108.1, 109.3, 120.2, 121.8, 126.1, 126.6, 127.6, 127.8, 128.9, 130.3, 137.6, 140.0, 151.8, 156.7, 157.3. MS *m*/*z* 279 ($M^+-C_4H_9$). HRMS (EI) Calcd for $C_{22}H_{24}O_3$: 279.1021. Found: 279.1019.

3.1.8. 1,12-Dimethoxytribenzo[*a*,*c*,*e*]cyclooctene (19). Anhydrous THF (6 mL) was added to titanium(IV) chloride (1.0 mL, 9.1 mmol) dropwise under N_2 with stirring at 0 °C. Zinc powder (0.80 g, 12 mmol) was added, and was followed by triethylamine (0.30 mL, 2.2 mmol). After refluxing for 30 min, a suspension of 1,4-endoxo-1,4-dihydro-8,11-dimethoxytribenzo[*a*,*c*,*e*]cyclooctene (**8**) (0.50 g, 1.5 mmol) in anhydrous THF (30 mL) was added dropwise to the low-valent-titanium solution. The reaction mixture was then stirred at refluxing temperature for 20 h. Sat. K_2CO_3 (5 mL) was added, and was followed by extraction with CH_2Cl_2 (3×20 mL). The combined organic layer was dried over anhydrous $MgSO_4$ and evaporated. Chromatography on a column of silica gel (25 g, hexanes/EtOAc 10:1) gave 1,12-dimethoxytribenzo[*a*,*c*,*e*]cyclooctene (**19**) (0.43 g 90%) as colorless crystals: mp 212–213 °C; ^{1}H NMR ($CDCl_3$) δ 3.80 (s, 6H), 6.73 (s, 2H), 6.76 (dd, *J*=8.4, 0.9 Hz, 2H), 6.79 (dd, *J*=7.5, 0.9 Hz, 2H), 7.14–7.19 (m, 4H), 7.38 (dd, *J*=5.7, 3.6 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ 55.7, 109.0, 122.1, 126.6, 127.1, 127.9, 128.9, 129.7, 141.9, 143.0, 156.3; MS *m*/*z* 314 (M^+). HRMS (EI) Calcd for $C_{22}H_{18}O_2$: 314.1307. Found: 314.1305. Anal. Calcd for $C_{22}H_{18}O_2$: C, 84.05; H, 5.77. Found: C, 84.28; H, 5.82.

3.1.9. 13,14-Dibromo-13,14-dihydro-1,12-dimethoxytribenzo[*a*,*c*,*e*]cyclooctene (20). To a suspension of 1,12-dimethoxytribenzo[*a*,*c*,*e*]cyclooctene (**19**) (0.25 g, 0.81 mmol) in anhydrous CCl_4 (47 mL) was added bromine (0.26 g 3.2 mmol). The mixture was stirred and refluxed for 6 h, and then cooled to room temperature. The reaction was quenched by addition of 10% $Na_2S_2O_5$ (3 mL), and extracted with CH_2Cl_2 (2×10 mL). The combined organic extract was dried over $MgSO_4$ and evaporated under reduced pressure to give 13,14-dibromo-13,14-dihydro-1,12-dimethoxytribenzo[*a*,*c*,*e*]cyclooctene (**20**) as a white solid. This compound was not purified further and was used immediately in the next step.

3.1.10. 1,4-Endoxo-1,4-dihydro-5,16-dimethoxytetrabenzo[*a*,*c*,*e*,*g*]cyclooctene (7). To a solution of freshly sublimed KO-*t*-Bu (0.48 g 4.3 mmol) in anhydrous THF (15 mL) and furan (15 mL) under N_2 was added dropwise a solution of the previously prepared dibromides **20** (vide supra) in anhydrous THF (25 mL) and furan (12 mL) within 60 min. After the solution was stirred for 3 h, 0.5 N HCl (10 mL) was added. The mixture was extracted with CH_2Cl_2 (3×20 mL). The combined organic extract was washed with brine (10 mL), dried over $MgSO_4$, and evaporated under reduced pressure. The residue was chromatographed on a column of silica gel (30 g, hexanes/EtOAc 3:1) to give 1,4-endoxo-1,4-dihydro-5,16-dimethoxytetrabenzo[*a*,*c*,*e*,*g*]cyclooctene (**7**) (0.13 g, 42%) as colorless crystals: mp 251–253 °C; ^{1}H NMR ($CDCl_3$) δ 3.87 (s, 6H), 5.65 (d, *J*=0.9 Hz, 2H), 6.59 (d, *J*=0.9 Hz, 2H), 6.79–6.84 (m, 4H), 6.97 (dd, *J*=5.7, 3.3 Hz, 2H), 7.20–2.26 (m, 4H); ^{13}C NMR ($CDCl_3$) δ 55.7, 85.5, 109.3, 122.1, 123.1, 126.6, 128.8, 130.7, 140.8, 143.3, 144.0, 151.6, 157.2; MS *m*/*z* 381 (M^++1), 380 (M^+). HRMS (FAB) Calcd for $C_{26}H_{21}O_3$: 381.1491. Found: 381.1483.

3.1.11. 1-Hydroxy-5,16-dimethoxytetrabenzo[*a*,*c*,*e*,*g*]-cyclooctene (21). A mixture of 1,4-endoxo-1,4-dihydro-5,16-dimethoxytetrabenzo[*a*,*c*,*e*,*g*]cyclooctene (**7**) (0.10 g, 0.26 mmol) and 36% HCl (0.5 mL) in MeOH (30 mL) was refluxed with stirring for 4 h. After cooling to room temperature, the reaction was quenched by addition of brine (15 mL), and extracted with CH_2Cl_2 (3×20 mL). The combined organic extract was dried over $MgSO_4$ and evaporated under reduced pressure. The residue was separated by flash column chromatography on silica gel

(10 g, hexanes/EtOAc 3:1) to give 1-hydroxy-5,16-dimethoxytetrabenzo[*a*,*c*,*e*,*g*]cyclooctene (**21**) (90 mg 90%) as a white solid: mp 284–285 °C; ^{1}H NMR ($CDCl_3$) δ 3.68 (s, 3H), 3.74 (s, 3H), 4.88 (s, 1H), 6.74 (dd, *J*=2.7, 1.2 Hz, 1H), 6.77 (dd, *J*=2.7, 0.9 Hz, 1H), 6.80 (dd, *J*=8.1, 1.2 Hz, 1H), 6.84 (s, 1H), 6.86 (d, *J*=0.9 Hz, 1H), 6.90 (dd, *J*=8.4, 0.9 Hz, 1H), 7.10–7.17 (m, 3H), 7.19–7.29 (m, 4H); ^{13}C NMR ($CDCl_3$) δ 56.2, 56.5, 110.9, 114.2, 121.5, 122.6, 122.8, 123.8, 124.0, 127.1, 127.3, 127.8, 127.9, 128.0, 128.0, 128.3, 129.1, 130.2, 138.5, 140.8, 141.2, 143.1, 145.0, 152.5, 155.9, 156.1. MS *m/e* 381 (M^++1), 380 (M^+). HRMS (FAB) Calcd for $C_{26}H_{20}O_3$: 380.1412. Found: 380.1418.

3.1.12. 1,4-Dioxo-1,4-dihydro-5,16-dimethoxytetrabenzo[*a*,*c*,*e*,*g*]cyclooctene (22). To a vigorously stirred solution of 1-hydroxy-5,16-dimethoxytetrabenzo[*a*,*c*,*e*,*g*]-cyclooctene (**21**) (50 mg 0.13 mmol) in acetone (6 mL) was added a buffer solution (Na_2HPO_4, NaH_2PO_4, *p*H=5.8, 6 mL) of Fremy's salt (174 mg, 0.65 mmol). The resulting mixture was vigorously stirred for 6 h. The mixture was extracted with CH_2Cl_2 (3×10 mL). The combined organic extract was dried over $MgSO_4$ and evaporated under reduced pressure to give 1,4-dioxo-5,16-dimethoxytetrabenzo[*a*,*c*,*e*,*g*]cyclooctene (**22**), which was used in the next step without further purification and characterization.

3.1.13.1,4-Dihydroxy-5,16-dimethoxytetrabenzo[*a*,*c*,*e*,*g*]-cyclooctene (23). A mixture of 1,4-dioxo-1,4-dihydro-5,16-dimethoxytetrabenzo[*a*,*c*,*e*,*g*]cyclooctene (**22**) (vide supra) and zinc powder (60 mg, 0.92 mmol) in acetic acid: water (2:1) solution (8 mL) was refluxed with stirring for 1 h. The mixture was extracted with CH_2Cl_2 (3×15 mL). The combined organic extract was dried over $MgSO_4$ and evaporated under reduced pressure. The residue was purified by flash column chromatography on silica gel (8 g, hexanes/EtOAc 1:1) to give 1,4-dihydroxy-5,16-dimethoxytetrabenzo[*a*,*c*,*e*,*g*]cyclooctene (**23**) [17 mg, 82% (reacted yield)] as a white solid: mp 241–242 °C; ^{1}H NMR (CD_2Cl_2) δ 3.77 (s, 6H), 4.56 (s, 2H), 6.70 (s, 2H), 6.83 (dd, *J*=7.5, 0.9 Hz, 2H) 6.79 (dd, *J*=7.5, 0.9 Hz, 2H), 7.17 (dd, *J*=5.7, 2.4 Hz, 2H) 7.28–7.33 (m, 4H); ^{13}C NMR (CD_2Cl_2) δ 56.9, 111.3, 116.2, 123.1, 125.5, 128.0, 128.6, 129.4, 129.8, 141.3, 145.0, 147.1, 156.5. MS *m/e* 396 (M^+). HRMS (EI) Calcd for $C_{26}H_{20}O_4$: 396.1362. Found 396.1353.

3.1.14. 1,4,5,16-Tetrahydroxytetraphenylene (4). To a vigorously stirred solution of 1,4-dihydroxy-5,16-dimethoxytetrabenzo[*a*,*c*,*e*,*g*]cyclooctene (**23**) (10 mg 0.025 mmol) in CH_2Cl_2 (4 mL) at 0 °C was added BBr_3 (0.1 mM, 0.5 mL) in CH_2Cl_2 slowly. The mixture was stirred for 8 h at 0 °C. After that the temperature was allowed to slowly rise to room temperature. The reaction was quenched by addition of brine (2 mL), and extracted with CH_2Cl_2 (2×5 mL). The combined organic extract was dried over $MgSO_4$ and evaporated under reduced pressure. The residue was separated by flash column chromatography on silica gel (4 g, hexanes/EtOAc 1:2) to give 1,4,5,16-tetrahydroxytetraphenylene (**4**) (8.3 mg, 90%) as a white solid: mp 135 °C (dec); ^{1}H NMR (d^6-Acetone) δ 6.58 (dd, *J*=7.5, 0.9 Hz, 2H), 6.62 (s, 2H), 6.74 (dd, *J*=8.1, 1.2 Hz, 2H), 7.06 (dd, *J*=7.8, 7.8 Hz, 2H), 7.14–7.17 (m, 2H), 7.22–7.25 (m, 2H); ^{13}C NMR (d^6-Acetone) δ 144.5, 121.6, 126.7, 127.2, 128.5, 128.6, 128.6, 130.5, 136.8, 141.0, 143.1, 151.6; MS *m/z* 368 (M^+). HRMS (FAB) Calcd for $C_{24}H_{16}O_4$: 368.1049. Found 368.1038.

3.1.15. 1,4,5,16-Tetramethoxytetraphenylene (24). To a vigorously stirred solution of 1,4-dihydroxy-5,16-dimethoxytetrabenzo[*a*,*c*,*e*,*g*]cyclooctene (**23**) (10 mg 0.025 mmol) in acetone (4 mL) was added K_2CO_3 (14 mg). Then the mixture was heated to reflux and dimethyl sulfate (0.01 mL, 0.1 mmol) was added. The mixture was refluxed for a further 4 h and NaOH (0.05 g) was added. After cooling to room temperature, the residue was filtered off and washed with acetone (2 mL). The combined organic solvent was washed with brine (3 mL), dried over $MgSO_4$ and evaporated under reduced pressure. The residue was purified by flash column chromatography on silica gel (6 g, hexanes/EtOAc, 3:1) to give 1,4,5,16-tetramethoxytetraphenylene (**24**) (9.6 mg, 90%) as a white solid: mp 204 °C; ^{1}H NMR (CD_2Cl_2) δ 3.63 (s, 6H), 3.72 (s, 6H), 6.73 (dd, *J*=7.5, 0.9 Hz, 2H), 6.77 (s, 2H), 6.86 (dd, *J*=8.1, 0.9 Hz, 2H), 7.16 (dd, *J*=5.7, 3.3 Hz, 2H), 7.20–7.28 (m, 4H); ^{13}C NMR (CD_2Cl_2) δ 56.7, 56.8, 110.7, 111.0, 122.0, 126.9, 127.7, 128.6, 128.7, 128.9, 141.9, 143.6, 151.6, 157.4; MS *m/e* 424 (M^+). HRMS (EI) Calcd for $C_{28}H_{24}O_4$: 424.1675. Found: 424.1661.

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