# Expanded Cyclotetrabenzoins

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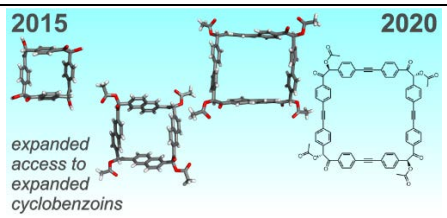


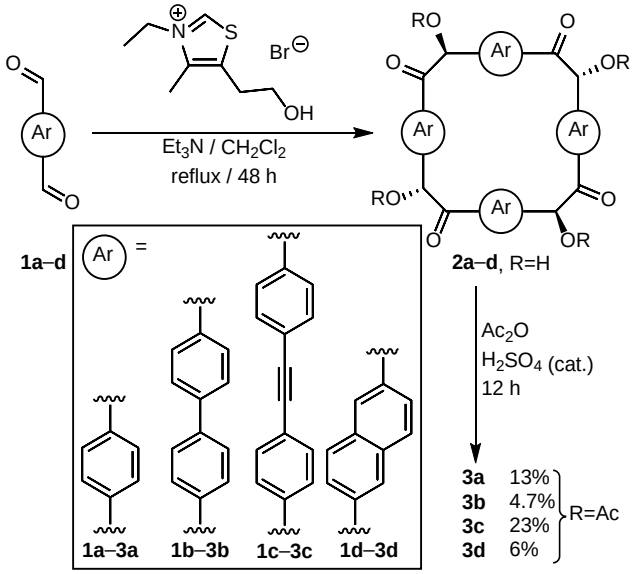

**ABSTRACT:** Cyclobenzoins are stable and shape-persistent macrocycles which offer promise as components of optoelectronic and porous materials. We report three new cyclotetrabenzoins, derived from biphenyl, naphthalene, and tolane skeletons. Their synthesis relied on the *N*-heterocyclic carbene-catalyzed benzoin condensation. Isolated as their acetic esters, these compounds are characterized by structures similar in shape, but larger in size than the parent cyclotetrabenzoin. Alkyne groups of the tolane-based cyclotetrabenzoin were post-synthetically functionalized with $Co_2(CO)_6$ moieties under mild reaction conditions.

Cyclobenzoins[1] are cyclic oligomers of aromatic dialdehydes formed by benzoin condensation.[2] These readily made macrocycles[3] bode well for applications as supramolecular hosts, porous molecular crystals,[1b] and as precursors to optoelectronic materials.[4] Cyclotetrabenzoin (**2a**, Scheme 1) was first synthesized by us via the tetramerization of terephthaldehyde (**1a**) using NaCN as the catalyst.[1b] Compound **2a** was shown to have a low surface area (~50 $m^2$ $g^{-1}$) and solubility in most organic solvents; its acetic ester derivative **3a** exhibited a much-improved solubility as well as the surface area of 570 $m^2$ $g^{-1}$ and an ability to sequentially fill its pores with solvent molecules.[5] In this Letter, we report the synthesis of three extended cyclotetrabenzoins based on larger aromatic scaffolds, the X-ray crystal structures of two of them, and the post-synthetic modification of one of them. In addition, we show that these new cyclotetrabenzoins, as well as **2a**, can be prepared using a more environmentally friendly *N*-heterocyclic carbene (NHC) catalyst.[6,2d]

After screening some potential NHC catalysts, we found that 3-ethyl-5-(2-hydroxyethyl)-4-methylthiazolium bromide[7] was the most efficient precatalyst for the conversion of **1a** into **2a**. Its exposure to **1a** and $Et_3N$ produced **2a** in 18% yield, quite comparable to the 21% observed in the cyanide-catalyzed reaction. This finding was encouraging in two ways: not only did it demonstrate that a less dangerous catalyst can be used to produce cyclobenzoins, but also showed that the cyclization can be performed in solvents of relatively low polarity, such as $CH_2Cl_2$. The latter point was important, as it allowed us to explore other, less polar, precursors to potential cyclobenzoins—which were not soluble in the originally used EtOH/$H_2O$ mixture required to dissolve the NaCN catalyst. Thus, starting from 4,4′-biphenylenedicarbaldehyde (**1b**), NHC-mediated cyclotetramerization yielded evidence of the formation of **2b**. However, efforts to purify this new cyclotetrabenzoin at this stage proved futile because of its low solubility and the high polarity of both **2b** and the obtained side products. We, therefore, proceeded to acetylate the crude material and perform the thorough purification at the stage of its acetic ester **3b**, which was ultimately isolated in an overall yield of 4.7% after two steps. Tolane-derived precursor **1c** was subjected to analogous reaction conditions and gave **3c** in 23% overall yield. Finally, a similar two-step procedure was also fruitful with 2,6-diformylnaphthalene (**1d**) as the starting material, ultimately yielding **3d** in 6% overall yield. Attempts to engage dialdehydes based on terphenylene (**4**, Figure 1),[8] functionalized biphenylene (**5a**–**c**)[9] or [2.2]paracyclophane (**6**)[10] skeletons, unfortunately, did not yield evidence of macrocycle formation.

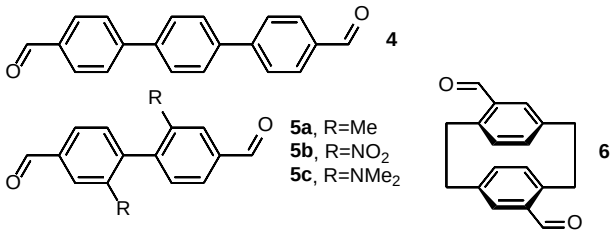
Compounds **3b**–**3d** are white powders. Their $^1$H NMR spectra are consistent with the regio- and stereoisomers shown in Scheme 1, and the diagnostic benzoin C–H peaks are clearly discernible singlets at $\delta$ 6.93 ppm for **3b**, 6.84 ppm for **3c**, and 7.10 ppm for **3d** (in $CDCl_3$). Aromatic regions of the $^{13}$C NMR spectra of **3b**–**d** and the $^1$H NMR spectrum of **3d** show two sets of peaks, suggesting somewhat restricted rotation around the long axis of the Ar groups in Scheme 1. Proton NMR spectra of **3b** and **3c** are more complex, but also show some peak broadening and overlapping which is consistent with this conclusion.[11]

**Scheme 1. Preparation of extended cyclotetrabenzoins and their acetic esters.**




Single crystals of **3b** suitable for X-ray diffraction analysis were grown by diffusion of MeOH into a solution of **3b** in THF. Compound **3b** crystallizes in the Fdd2 space group, with eight molecules of **3b** per unit cell. The obtained structure is shown in Figure 2A. Its overall shape, defined here by the four corners represented by benzoin CHOAc carbon atoms, is that of a puckered square with angles of 86.3° and 86.6°, and sides that vary in length between 10.1 and 11.9 Å. The crystal structure also confirmed the stereochemistry of **3b** to be that of the achiral *S,R,S,R* isomer[12]—analogous to **2a** and **3a**. Pairs of phenylene rings in the biphenylene moieties are distorted from coplanarity by 15.7°, 37.4°, and 36.7°. The packing diagram of **3b**, viewed along the crystallographic *a* axis (Figure 2B), shows infinite channels that appear to be filled with disordered solvent molecules which have been treated with the PLATON/SQUEEZE routine. Notable short contacts are established between the ester carbonyl oxygens and hydrogens of the benzoin functionality and those in the *ortho*-position of the biphenylene, with [C=O···H–C] distances of 2.38 Å and 2.47 Å, respectively.

**Figure 1. Aldehyde precursors that did not yield cyclobenzoin products.**




Single crystals of **3d** were fortuitously obtained after one of the column chromatography fractions (eluted with EtOAc/$CH_2Cl_2$ solvent mixture) was left to stand at room temperature overnight. Compound **3d** crystallizes in $I\bar{4}$ space group, with two molecules per unit cell. Its molecular structure is shown in Figure 3A, once again indicating the *S,R,S,R* stereochemistry of the four stereogenic centers.[12] The overall shape of **3d**, defined by the four corners represented by benzoin CHOAc carbon atoms, is that of a puckered square—but more symmetric than that observed for **3b**—with angles of 86.7° and sides of 8.63 Å. At the same time, naphthalene "walls" are very much distorted from a parallel arrangement: those on the opposite sides of the molecule form an angle of 52.2° with each other, while those on the neighboring sides stand at an angle of 78.9°. Crystal packing diagram of **3d** is shown in Figure 3B and reveals one-dimensional channels when viewed along the crystallographic *c* axis. Close contacts established between molecules of **3d** include [C–H···O] hydrogen bonds between the ester carbonyl oxygen and the benzoin hydrogen (2.69 Å) as well as the *ortho*-hydrogen on the naphthalene nucleus (2.61 Å). Despite extensive experimentation, we were unable to produce crystals of **3c** of a quality high enough for X-ray diffraction.

**Figure 2. X-ray crystal structure of 3b (A), and its packing diagram (B), viewed along the crystallographic *a* axis. Element colors: C—gray, H—white, O—red. Solvent molecules removed for clarity.**

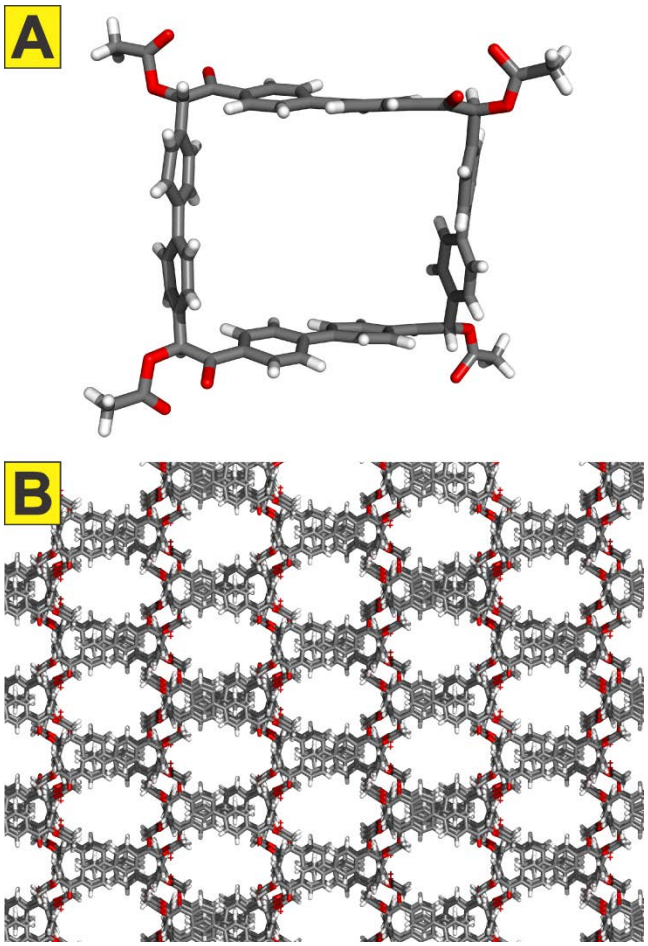
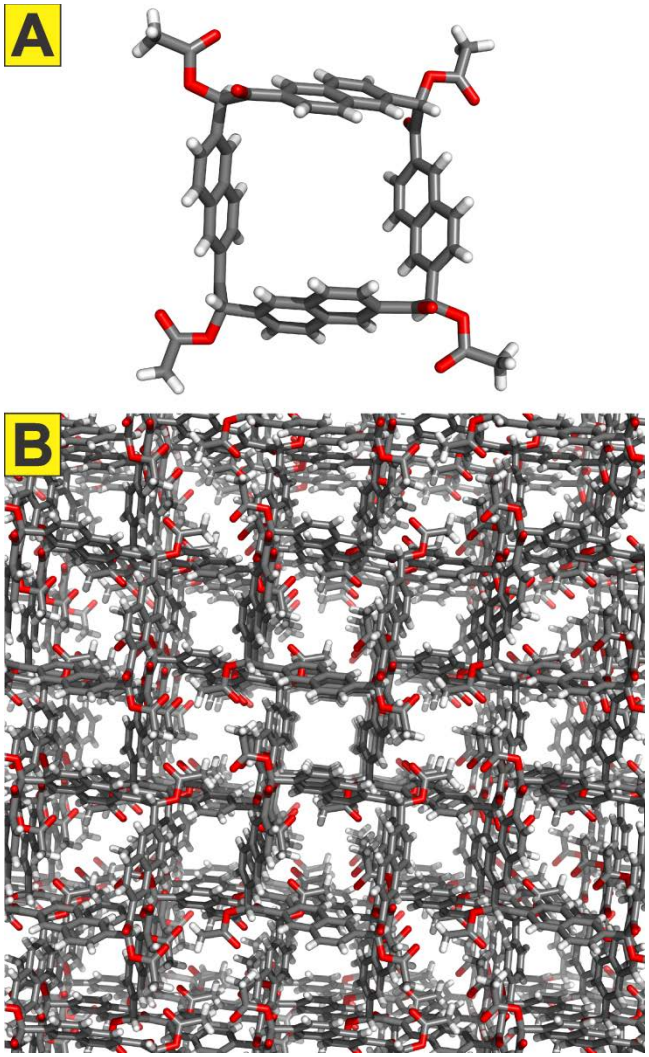


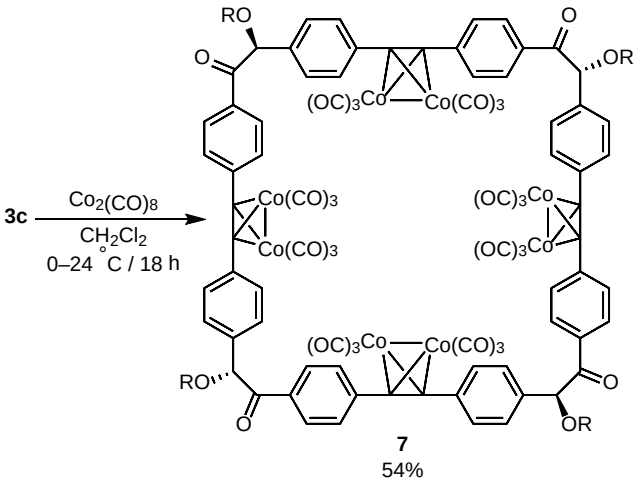
**Figure 3. X-ray crystal structure of 3d (A), and its packing diagram (B), viewed along the crystallographic *c* axis. Element colors: C—gray, H—white, O—red. Solvent molecules removed for clarity.**




Our observation of apparent pores in the crystal structure of **3d** prompted us to experimentally examine the porosity of both **3c** and **3d**. Miniscule nitrogen sorption within the pores suggested that the pores are either inaccessible to guest molecules or collapsing upon activation at 60 °C for 14 h.

The presence of alkyne moieties in the cyclotetrabenzoin **3c** opens many opportunities for further modifications. In this work, we have attempted one of them: hexacarbonyl dicobalt complexation of triple bonds in **3c**. The reaction of **3c** with $Co_2(CO)_8$ in $CH_2Cl_2$ smoothly proceeded to give complex **7**, which was isolated as a red solid in 54% yield. Compound **7** was thoroughly characterized by UV-vis, IR, and NMR spectroscopy, as well as by mass spectrometry. Complex **7** shows significant visible light absorption at ~400 nm and an additional absorption band at 260 nm in comparison with parent **3c**. IR spectra of **7** shows the appearance of diagnostic new bands at 2092, 2053, and 2003 $cm^{-1}$ related to the cobalt carbonyls,[13] and the disappearance of the low-intensity 2220 $cm^{-1}$ band, associated with the C≡C vibration in **3c**. High resolution electrospray ionization mass spectrometry (HR-ESI MS) provided strong evidence in determining the composition of **7** as $C_{96}H_{48}Co_8O_{36}$. HR-ESI MS spectra in negative mode showed a peak at $m/z$ = 2375.565, which was assigned to the $[M+I]^-$ adduct, with iodine stemming from the added CsI. Even more diagnostic was a series of fragment peaks $[M+I-28n]^-$, where $n$ indicates the number of lost CO molecules. We have observed the sequential loss of all CO molecules, i.e. up to $n$=24. In the $^1$H NMR spectra strong downfield shift of signals, corresponding to the $HC^{Ar}$ is observed, together with expected peak broadening[13c] due to the presence of the metal. Signals at ~199 ppm in the $^{13}$C NMR spectra additionally confirm the presence of CO groups. Unfortunately, our attempts to obtain single crystals of **7** were unsuccessful.

**Scheme 2. Postsynthetic modification of cyclotetrabenzoin 3c by complexation with $Co_2(CO)_6$ groups.**




In conclusion, the work presented in this contribution advances the chemistry of cyclobenzoins in three significant ways. First, we have shown that cyclobenzoins can be prepared using environmentally friendly NHC catalysts, which represents a marked improvement in safety compared to the originally used cyanide catalyst. Second, the family of cyclotetrabenzoins has been expanded with three new, larger members. Finally, we have shown that functional groups within the cyclobenzoin skeletons can be postsynthetically modified.

The roughly square-shaped cavities of **3b** and **3d** (and the presumed cavity of **3c** or even **7**) are larger than those of **2a** and **3a**. We presume that they will be able to include aromatic and other small molecular guests, and are currently investigating the use of **3b**–**d** as supramolecular hosts, as well as their further post-synthetic modifications. We will report our results in due course.

## ASSOCIATED CONTENT

**Supporting Information**. Experimental procedures and copies of $^1$H and $^{13}$C NMR spectra, Crystallographic Information Files (CIFs) for compounds **3b** and **3d**, along with their checkCIF reports. This material is available free of charge via the Internet at http://pubs.acs.org. Crystallographic data for **3b** and **3d** has been deposited with the Cambridge Crystallographic Data Center under deposition numbers 2019827 and 2019826, respectively.

## AUTHOR INFORMATION

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### Author Contributions

A. M. E. synthesized **2b**, **2d**, **3b**, and **3d**, and produced their crystals. X. W. solved the crystal structures of **3b** and **3d**. S. O. and K. V. K. prepared **2c, 3c**, and **7**, as well as provided the aldehydes **4**–**6**. P. W. performed the HR-ESI mass analysis of **7.** All authors analyzed the obtained results together. O. Š. M. wrote the manuscript with the input from all authors, who have given their approval to the final version of the manuscript.

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11. Hindered rotation in **3d** is expected, as the two C–C bonds connecting the naphthalene moiety to the rest of the molecule are offset. Simultaneous rotation around both of them would have introduced strain into the molecule. For **3b** and **3c**, the finding is a bit less expected, especially in light of the absence of similar peak doubling in **3a** (ref. 5).
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