VIP Bowl-Shaped Molecules

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Tribenzotriquinacene: A Versatile Synthesis and C_3-Chiral Platforms**

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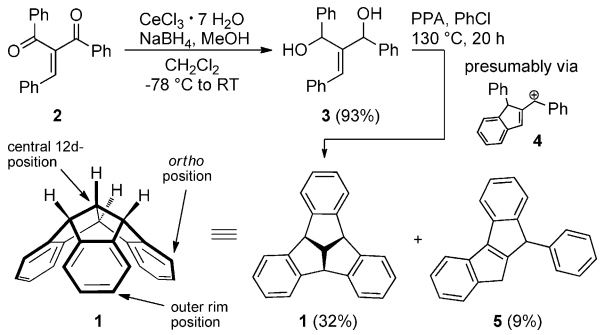
Dedicated to Professor Klaus Hafner on the occasion of his 85th birthday

Molecules belonging to point group C_3 have recently attracted much interest owing to their applications in asymmetric catalysis and chiral recognition.[1–3] Nonetheless, the number of C_3-chiral molecules is still limited compared to the numerous C_2-chiral systems, and more entries to C_3-chiral molecules are needed. One way to obtain functional C_3-chiral molecules, which is the most common in the synthesis of tripodal ligands, is to append three enantiopure handles to an otherwise achiral platform. The second approach, which is much more common in supramolecular chemistry, is to start with a C_3-chiral platform from the very beginning and to extend it with achiral recognition units. The molecular bowl tribenzotriquinacene (**1**; Scheme 1) constitutes an excellent platform for the second strategy owing to its rigidity and configurational stability.[4,5] However, the preparation of C_3-chiral derivatives is severely hampered by the lack of regioselectivity.[6] Herein we wish to report a C_3-specific entry to this class of compounds, thereby providing a new access to this novel family of C_3-chiral molecules. The work is based on a new and versatile synthesis of the parent hydrocarbon **1** and its previously only poorly accessible *ortho* derivatives. The latter furthermore provide a highly anticipated entry to extended carbon networks.[7–9]



Scheme 1. The synthesis of tribenzotriquinacene (**1**).

Our synthesis of tribenzotriquinacene **1** starts off with the benzylidene propanedione **2** (Scheme 1), which can be easily obtained by Knoevenagel condensation.[10] Reduction to the diastereomeric diols **3** had already been reported by Olah et al. (32% yield), and we improved this step by developing an optimized Luche procedure (93% yield).[10,11] Olah's motivation for accessing diols **3** was their study under superacidic conditions (FSO_3H/SO_2ClF, −80°C), whereby he observed a cyclodehydrated intermediate, presumably of form **4**. While working with diols **3**, we found that isomerizations and cyclodehydrations took place even under mildly acidic conditions (cat. *p*-toluenesulfonic acid in CH_2Cl_2, RT) and hypothesized that such cyclizations might eventually lead to tribenzotriquinacene (**1**). Application of Kuck's cyclodehydration conditions[5b] (H_3PO_4, chlorobenzene, 130°C, 20 h) to diols **3** indeed gave tribenzotriquinacene in 28% yield. Switching to polyphosphoric acid (PPA) as dehydrating agent increased the yield to 32%, making **1** available in gram quantities for the first time. Other acids were also tested, but did not prove effective (acetic acid, trifluoroacetic acid, methanesulfonic acid, Eaton's reagent, trifluoromethanesulfonic acid (TfOH), Tf_2O, H_2SO_4). The reaction presumably proceeds through a series of intramolecular Friedel–Crafts alkylations with carbocation intermediates, which is supported by the fact that the yield did not depend on the diastereomer of **3** being used. A reaction mechanism that also explains the formation of the dihydroindenoindene byproduct **5** is proposed in the Supporting Information.[12] The synthesis is higher-yielding than Kuck's synthesis of the parent hydrocarbon (over three steps: 19% vs. 5%).[5b] Moreover, as we will show below, it allows the planned introduction of aromatic substituents by varying the easily available benzaldehyde and dibenzoylmethane components of the Knoevenagel adduct.

Functionalization of the aromatic rings in tribenzotriquinacene has largely been limited to the outer rim positions, as these are easily accessible by electrophilic aromatic substitution.[7,13] *Ortho* functionalization of tribenzotriquinacenes is rare and limited in scope. One example is known in which

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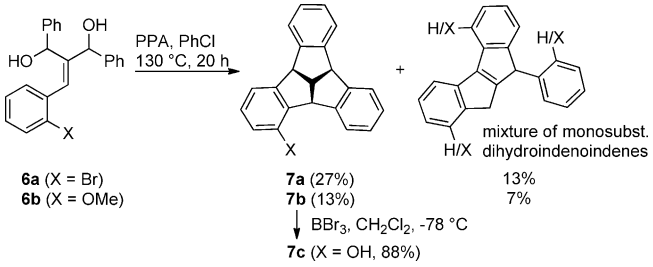
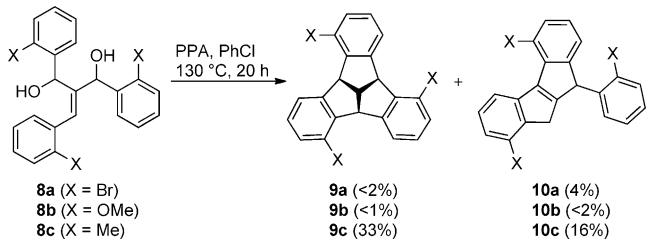
a metal carbonyl complex of 12d-methyltribenzotriquinacene was functionalized at one of the inner *ortho* positions.[14] More recently, Krüger and co-workers prepared *ortho*-methylated tribenzotriquinacenes by a variation of Kuck's procedure.[8] By a Scholl reaction, Mughal and Kuck achieved the formation of a cycloheptatriene unit between two opposing and unfunctionalized *ortho* positions.[9] By starting with Knoevenagel adducts derived from 2-bromo or 2-methoxy benzaldehyde, our Scheme allows the regiospecific synthesis of various *ortho*-functionalized tribenzotriquinacenes (**7a–c**, Scheme 2). While cyclization of the brominated diols **6a**



Scheme 2. Synthesis of *ortho*-substituted tribenzotriquinacenes.

proceeded smoothly to **7a** (27%), we were surprised to see that the yield for the methoxy derivative **7b** dropped to 13%. A control experiment demonstrated that the methoxy group is stable under the employed reaction conditions. Evidently, the electron-donating property of the methoxy group has a negative effect on the desired reaction sequence.[15] This is also reflected by the significantly reduced yield of the monosubstituted dihydroindenoindene byproducts (7% for OMe vs. 13% for Br). Deprotection of ether **7b** was achieved in 88% yield, leading to chiral phenol **7c**.

The above experiments demonstrated for the first time the installation of various functional groups in the *ortho* position of tribenzotriquinacene. We then wondered whether our strategy could also be applied to trisubstituted systems. Most importantly, this would provide a C_3-specific entry to *ortho*-functionalized tribenzotriquinacenes, a family of compounds that is not accessible by current methods. No selective entry to C_3-chiral tribenzotriquinacenes is known as yet, and is in particular unknown for the hardly accessible *ortho* positions.[6] By starting with *o*,*o*′-disubstituted dibenzoylmethanes[16] and 2-substituted benzaldehydes, we synthesized the trisubstituted diols **8a–c** (Scheme 3). Cyclization of **8a**,**b** indeed gave the C_3-chiral tribromo and trimethoxy tribenzotriquinacenes **9a**,**b** in a selective fashion; however, only in yields of less than



Scheme 3. Synthesis of C_3-chiral tribenzotriquinacenes.

2%. We therefore switched to the trimethyl-substituted diol **8c**, hoping that its electronic or steric properties might be more favorable. Notably, a yield of 33% was found for **9c**, which compares well with the result for parent hydrocarbon **1** (32%). We wish to emphasize at this point that the formation of the unsymmetric C_1-chiral derivative is intrinsically precluded. The C_3-specific nature of the cyclization and the regiospecific formation of byproducts **10a–c** can be explained by the mechanism presented in the Supporting Information.

An interesting feature of the mono- and trisubstituted tribenzotriquinacenes is their chirality: **7a–c** and **9a–c** are C_1- and C_3-chiral, respectively, and we were able to resolve their enantiomers by chiral-phase HPLC (see Supporting Information).[17,18] A crystal structure was obtained for the C_3-chiral tribenzotriquinacene **9c** (Figure 1).[19,20] The compound crys-

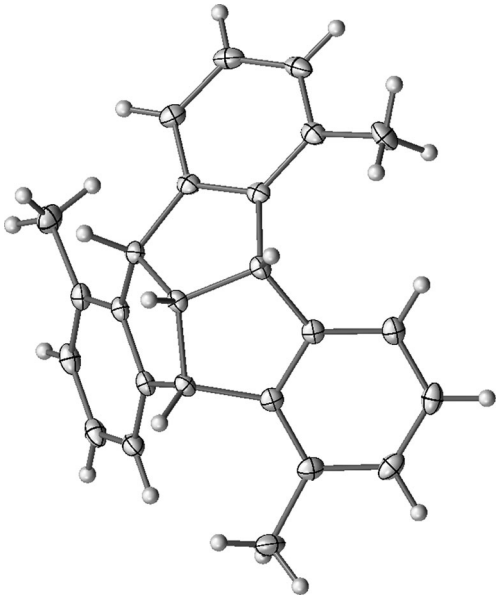


Figure 1. ORTEP of C_3-chiral tribenzotriquinacene **9c** (ellipsoids set at 50% probability).

tallized in the triclinic space group $P\bar{1}$, but C_3 symmetry was maintained to a good approximation (r.m.s. deviation from C_3 symmetry = 0.18 Å). Interestingly, **9c** did not exhibit the columnar stacking that is known for the parent hydrocarbon **1** and its 12d-methyl derivative.[4a,b,13] CH/π-mediated layers of bowls with opposite orientation were formed, and the methyl substituents, even when hidden in the *ortho* positions, seem to have a pronounced effect on the solid-state structure.[21] Crystal structures were also obtained for byproducts **5** and **10a–c**.[19]

With respect to potential applications of C_3-chiral tribenzotriquinacenes in supramolecular recognition,[22] it is interesting to compare the geometric parameters of derivative **9c** with those of other C_3-symmetric platforms. We limit our discussion to aromatic platforms that have been functionalized with recognition units, and we show crystallographic data

of relevant reference molecules in Figure 2. The distances between the sites of functionalization in these tripodal molecules range between 5.0 and 10.0 Å.[23] C_3-Chiral triben-

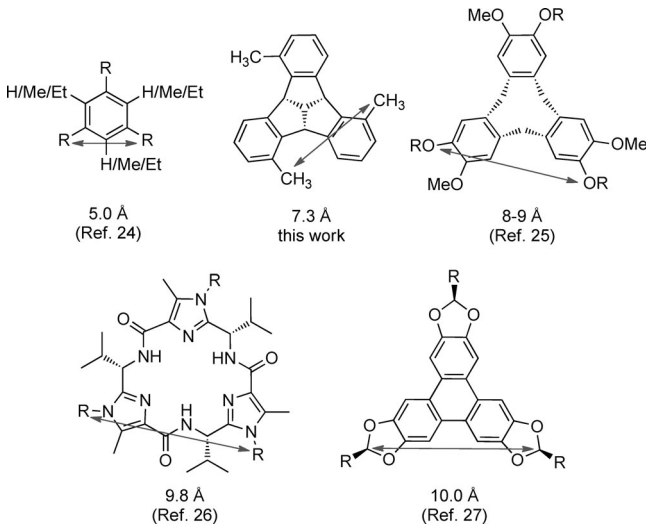


Figure 2. Structural parameters of selected platforms with threefold symmetry (X-ray data).

zotriquinacene **9c** exhibits a tripodal distance of 7.3 Å and bridges the gap between the mesitylene derivatives and the other C_3-symmetric platforms. It therefore offers new opportunities for the construction of chiral receptors.

In summary, we have developed a new preparative method by which the tricyclic core of tribenzotriquinacenes is assembled in one step from acyclic precursors. The precursors themselves are available by simple reactions using commercial starting materials. Our new route to tribenzotriquinacene is of unprecedented variability and offers direct access to C_1- and C_3-chiral derivatives that are of interest to supramolecular chemists and the asymmetric catalysis community alike. While the former might focus on the chiral binding pocket,[28] the latter might consider these chiral molecules as bulky phenyl groups. The C_3-specific cyclization is a particularly attractive feature of our synthesis, and we will shortly report extensions of this strategy and the use of functionalized and optically active tribenzotriquinacenes.

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[19] CCDC 904629 (**5**), 904630 (**9c**), 904631 (**10a**), 904632 (**10b**) and 904633 (**10c**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

[20] Crystals of monosubstituted tribenzotriquinacenes **7a** and **7c** were disordered.

[21] A crystal packing diagram for **9c** is included in the Supporting Information.

[22] Extended achiral tribenzotriquinacenes have been shown to bind C_{60}; see, for example: T. Wang, Z.-Y. Li, A.-L. Xie, X.-J. Yao, X.-P. Cao, D. Kuck, *J. Org. Chem.* **2011**, *76*, 3231 – 3323.

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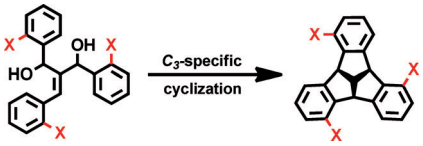
Communications

Bowl-Shaped Molecules

G. Markopoulos, L. Henneicke, J. Shen, Y. Okamoto, P. G. Jones, H. Hopf* _____ ■■■■–■■■■

Tribenzotriquinacene: A Versatile Synthesis and C_3-Chiral Platforms



Fusing rings: A new synthesis of the bowl-shaped hydrocarbon tribenzotriquinacene is presented (see scheme). The synthesis allows easy access to *ortho*-functionalized and C_3-chiral derivatives that are attractive for supramolecular chemistry and asymmetric catalysis.