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Synthesis and Study of 7,12,17-Trioxa[11]helicene

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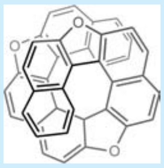
Ⓢ *Supporting Information*

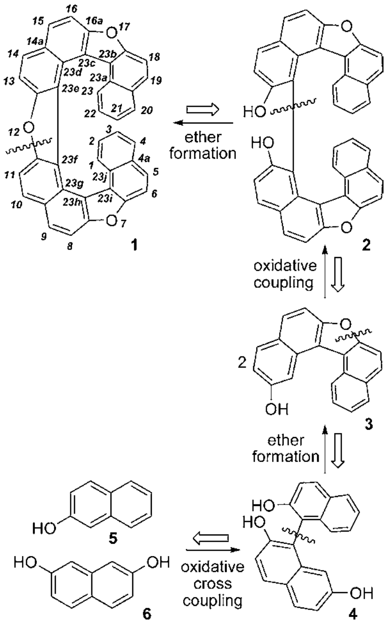
ABSTRACT: Synthesis of the title compound 7,12,17-trioxa[11]helicene, a large oxygen-containing helicene, has been reported. The 11-membered heterohelicene was synthesized by a combination of two simple reactions involving oxidative coupling and dehydrative cyclization. The final helicene was characterized by single-crystal X-ray diffraction, fluorescence spectroscopy, and differential scanning calorimetric analysis.



Screw-shaped helical molecules comprising ortho-fused aromatic rings acquire a unique shape in order to release internal strain. Such molecules have been widely studied in recent years due to the unique properties associated with their structure.[1] Basically, there are two types of helical molecules: carbahelicenes and heterohelicenes. Although early work was more focused on the former class, recently, more interesting properties have been observed for the latter type of helical molecules containing one or different heteroatoms. Polycyclic aromatic oxygen-containing molecules, particularly fused furans, are expected to provide relatively high HOMO levels[2] and are known to show interesting utility in electronic devices as organic light-emitting diodes[3] or organic field-effect transistors.[4] The synthesis and study of oligonaphthofurans has also been reported recently,[5] where the systematic correlation of the number of naphthofuran units and the physical properties is evaluated. The compounds belonging to the general class of oxahelicenes have been synthesized, and their various properties have been studied.[6] The special properties of helical molecules have been attributed to the extended conjugation of the π electrons in the framework. For larger helicenes with increasing numbers of ortho-fused rings, the π electrons start to form additional layers and contribute to the screw shape of the molecule. For [n]helicenes, a double layer is formed when $n = 7$ and a triple layer when $n = 13$. The synthesis of larger helicenes becomes more challenging due to the difficulty of releasing the internal strain. For a long time, [14]helicene, as synthesized by Martin and Baes[7] in 1975, remained the largest carba-helicene, until the very recent report of [16]helicene by Murase, Fujita, and Mori,[8] after nearly 40 years. Similarly, some of the heterohelicenes of larger size, such as hexathia[13]helicene,[9] carbon−sulfur-containing [11]helicene,[10] or poly(thiaheterohelicene),[11] were reported in the literature. In this communication, we report the design and synthesis of one such large oxygen-containing 7,12,17-trioxa[11]helicene, which is expected to form nearly 1.5 rotations of a helical twist involving a considerable delocalization of π electrons. In continuation of our work on the synthesis and study of helicene-like compounds[12a] and aza[n]helicenes,[12b,c] we present the synthesis of trioxa[11]helicene.

The retrosynthesis for the target molecule 7,12,17-trioxa[11]helicene **1** is presented in Scheme 1. The central naphthofuran ring can be built by acid-catalyzed ether formation from the corresponding binaphthol **2**, according to the procedure developed by Thongpanchang.[6d] Diol **2** can be synthesized by oxidative coupling of 2-hydroxy-7-oxa[5]helicene **3** by a standard procedure. The desired molecule **3** can be prepared by acid-promoted selective ether formation from 1,1′-binaphthalenyl-2,2′,7-triol **4**, which can be obtained by oxidative cross-coupling of 2-naphthol **5** and 2,7-dihydroxynaphthalene **6**. Proposed conversion of **3** to **2** by oxidative coupling is expected to be difficult due to the steric considerations.

Scheme 1. Retrosynthesis of 7,12,17-Trioxa[11]helicene 1



The cross-coupling of 2-naphthol **5** with other substituted naphthol derivatives is a well-studied reaction.[13] However, cross-coupling reaction between two naphthol units, both possessing electron-releasing substituents, tends to be less selective, and the desired cross-coupling products are accompanied by the

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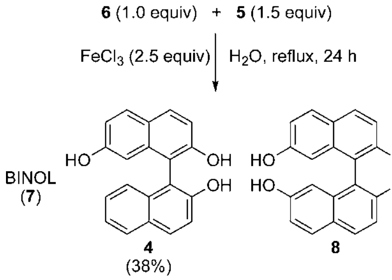
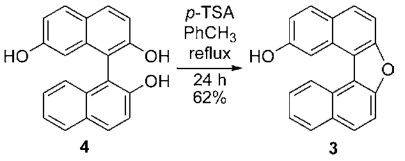
formation of the homocoupling compounds. A good selectivity can be achieved in a cross-coupling reaction between the two coupling partners possessing considerable difference in the electron density.[13a] However, in the present case, we need to couple two electron-rich naphthol derivatives, **5** and **6**, and thus we expect formation of the corresponding homocoupled products **7** and **8** (Scheme 2). The optimized condition of $FeCl_3$-catalyzed cross-coupling in aqueous medium is presented here, while the detailed investigations will be disclosed later.

Scheme 2. Oxidative Cross-Coupling of Naphthols



A pure sample of triol **4** was subjected to the acid-catalyzed ether formation by the standard procedure developed earlier.[6d] The desired product 2-hydroxy-7-oxa[5]helicene **3** was obtained in good yield from the reaction mixture by simple workup and column chromatography over silica gel (Scheme 3). The dehydration reaction of **4** appears to be difficult as it involves conversion of a nearly perpendicular structure of the binaphthyl framework to a more planar moiety of oxa[5]helicene **3**. The dihedral angle of a dinaphthofuran system similar to **4**, about 85°, changes to merely ~15° when such cyclization occurs.[5a] Due to small dihedral angle, the helical isomers of **3** are expected to possess a low isomerization barrier, resulting in fast interconversion, and hence, no attempts were made to resolve them.

Scheme 3. Synthesis of 2-Hydroxy-7-oxa[5]helicene



The oxidative homocoupling of 2-hydroxy-7-oxa[5]helicene **3** may possibly follow four different pathways (Figure 1). Out of these orientations, modes B, C, and D will lead to the steric crowding, and hence, the coupling is expected to follow the more feasible mode A. The homocoupling between two molecules of **3** should be the key step in the synthesis of the target molecule. The homocoupled product **2** (in mode A) can then be subjected to acid-catalyzed ether formation to obtain the final compound **1**. The above conversion requires interaction between the two almost perpendicularly oriented hydroxyl groups and may also pose a considerable challenge.

The homocoupling of **3** was initially screened with aqueous $FeCl_3$; however, the reaction resulted in a complex mixture, and no significant product was isolated. Hence, another routinely used catalyst system of $CuCl_2$–TMEDA was screened in dry methyl alcohol at room temperature (Scheme 4). Coupling product **2** was found to be difficult to purify on a silica gel column. However, another deep orange-colored, nonpolar crystalline compound was isolated from the reaction mixture.

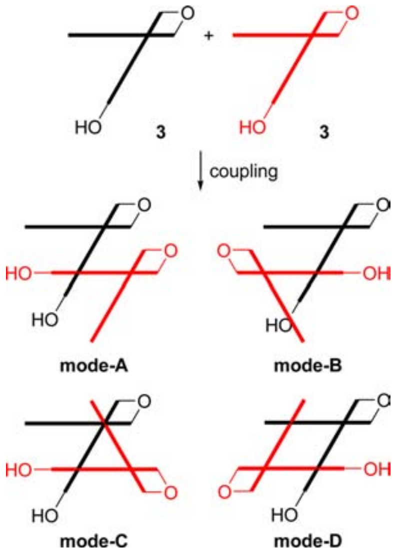
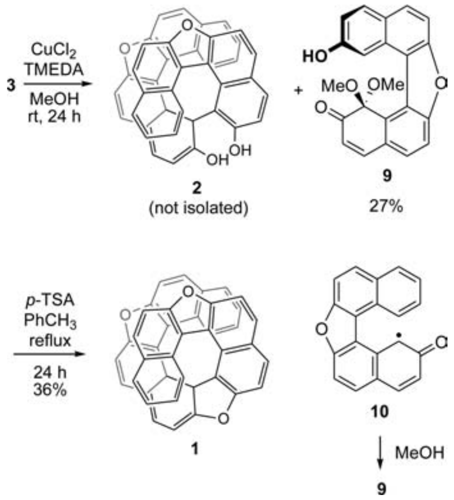


Figure 1. Possible modes of homocoupling of **3**.

Scheme 4. Coupling of 2-Hydroxy-7-oxo[5]helicene 3



This bright-colored compound was characterized to be 1,1-dimethoxy-2-oxo-12-hydroxy-7-oxo[5]helicene **9**, isolated in low yield. This unexpected compound was formed in several repeat experiments when performed in methyl alcohol. All other fractions were collected, presumably containing the required homocoupling product **2**, and subjected to acid-catalyzed ether formation. Repeated attempts to separate and access a pure sample of **2** were not successful. The above coupling reaction also failed in other solvents such as ethyl alcohol, 2-propanol, or 1,4-dioxane. Cyclization of crude **2** was performed with *p*-TSA in refluxing toluene, and the desired oxahelicene **1** was isolated in moderate yield as light yellow needles.

The structure of **9** was established by spectral analysis and confirmed by a single-crystal X-ray diffraction study. The ^1H NMR of **9** showed only one singlet at δ 3.22 for six hydrogens, indicating rapid interconversion between the two isomers during the measurement at ambient conditions. The same was observed in ^{13}C NMR when the methoxy carbon showed a single peak at δ 51.87. The α,β-unsaturated ketone system was established by observing the resonance peaks of two doublets in the ^1H NMR at δ 6.27 and 9.62. The formation of such an unexpected compound can be attributed to the trapping of a radical intermediate **10** by methyl alcohol during the coupling reaction. Formation of such keto-radical intermediate was proposed earlier.[13a] Product **9** was not observed when other alcohols were used as solvents, so probably the trapping of intermediate **10** was only feasible with the smaller methyl alcohol.

The structure of **9** was established by single-crystal X-ray analysis (Figure 2).[14] The dihedral angle in this compound was observed to be 15.4°, which was crystallized in the $Pna2_1$ space group.

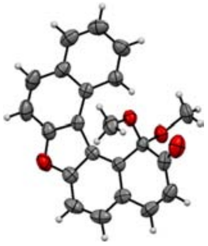


Figure 2. ORTEP diagram of **9**.

After the less polar compound **9** was isolated on the silica gel column, it was quickly further eluted with ethyl acetate and the mixture of polar compounds, presumably containing **2**, was collected. The mixture was then subjected to acid-catalyzed cyclization with *p*-TSA in refluxing toluene to obtain the desired target compound **1**, purified by careful chromatography over silica gel. Compound **1** was obtained as light yellow crystals from ethyl acetate and characterized by spectral techniques and single-crystal X-ray diffraction analysis.[14] The ^{1}H NMR showed 10 signals indicating the symmetrical nature of the molecule. Hydrogen attached to C2 (and C22) appears as typical triplet-type multiplet at δ 6.26 due to the shielding effect of the terminal ring.[8] The proton attached to the next carbon C3 (and C21) appears to have shifted downfield and shows a similar multiplet at δ 6.95, as it is in the deshielding zone of the terminal ring. All other signals appear as doublets, in agreement of the structure. Similarly, 10 signals for the aromatic carbons were seen in the ^{13}C NMR due to the symmetrical nature, while a molecular ion peak was observed at 548 *m*/*z*, which is also the base peak.

Single-crystal X-ray analysis of **1** further established the structure (Figure 3). The compound was crystallized in the $P2_1/c$ space group; its unit cell consists of two molecules, one in "*P*" conformation and the other in "*M*" conformation (see Supporting Information). This indicates the absence of any spontaneous resolution, a phenomenon occasionally observed in some helical molecules during crystallization.[15] Crystal structure is packed in the alternate *P* and *M* channels along the *a*-axis, with a helical pitch of 7.637 Å. Along each channel, consecutive molecules are connected by π-stacking (C10−C32, 3.323 Å; C10−C33, 3.360 Å; and C16−C32; 3.226 Å). Along the *b*-axis, the shape of the molecule looks like the letter "Z" with a diagonal length of about 10.1 Å, and the width is about 9.9 Å, while the intramolecular pitch of the outer helicene is about 4.8 Å (Figure 4). The interplanar angle in **1** was found to be 24.37° (angle created by the intersection of planes passing through C1−C2−C3−C4−C4a−C23j and C14a−C15−C16−C16a−C23c−C23d) and agrees well with the known observation for larger helicenes where it tends to decrease for elongated structures.[16] The torsional angle between the inner carbon atoms of **1** was found to be 4.39° (C23−C23a−C23b−C23c), 10.95° (C23a−C23b−C23c−23Cd), 23.71° (C23b−C23c−C23d−C23e), 19.30° (C23c−C23d−C23e−C23f), and 2.66° (C23d−C23e−C23f−C23g), suggesting different degrees of distortion in the aromatic rings. As a consequence of torsional strain generated due to the helical shape, the bond lengths in the skeleton are different. In comparison of the standard bond length of benzene (1.393 Å),[17] the range of carbon−carbon bond lengths of the inner helix was observed to be 1.429−1.437 Å, while the same on the outer periphery was shorter, as seen in the range of 1.347−1.360 Å. It was also interesting to see the difference between the bond lengths of the two fused furan rings. The bond length of the side furan rings C23b−C23c (and C23h−C23i) was 1.461 Å, while the same for the central furan ring C23e−C23f was found to be slightly elongated to be 1.471 Å, clearly due to much greater strain exerted in the inner portion.

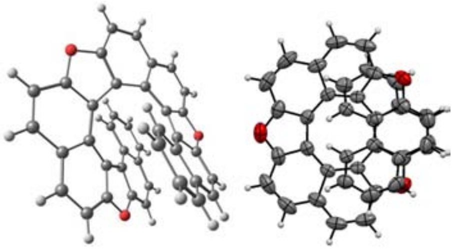


Figure 3. Stereoview and top view of the ORTEP diagram of **1**.

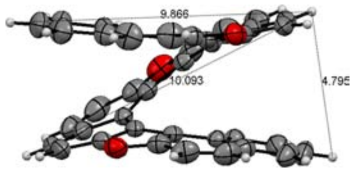


Figure 4. Side view and dimensions of **1** (distances in Å).

The optical and thermal properties of highly conjugated helicene **1** were measured. The UV−vis and fluorescence spectra indicated an absorption maxima at 352 nm and emission at 432 nm, with a shoulder peak at 450 nm (Figure 5), indicating a Stokes shift of 80 nm. The observed λ_{em} values and the nature of the peaks are in the range observed for similar oligonaphthofurans (364−486 nm).[5b] The fluorescence quantum yield (Φ) of **1** was observed to be 0.191, as determined using a standard solution of quinine sulfate (0.1 M H_2SO_4, measured at an excitation wavelength of 350 nm).

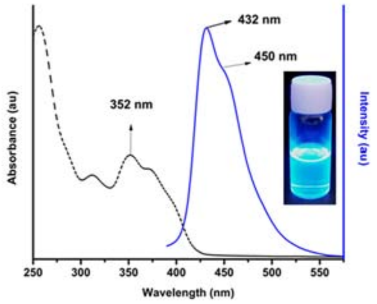


Figure 5. UV−vis and fluorescence spectra of **1** (*c* 9.12 × 10^{-5} M in acetonitrile, 25 °C).

Thermal behavior of **1** was investigated by differential scanning calorimetry, where the sample was heated at 10 °C/

min from 35 to 385 °C under an inert atmosphere (see Supporting Information). Analysis indicated that the compound showed a melting point of 345.5 °C, and the glass transition temperature was observed at 245.5 °C, indicating the high thermal stability, expected of such helicenes.[12b,18] The HPLC analysis of **1** on a Chiralpak IC column showed the presence of well-resolved peaks at 11.15 and 12.95 min (10% hexane in isopropyl alcohol; 0.5 mL/min), indicating the presence of two stable helical isomers.

In this communication, we report the synthesis of a large oxygen-containing heterohelicene, 7,12,17-trioxa[11]helicene, along with its characterization. The 11-membered helicene shows good thermal stability and fluorescence properties.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.orglett.5b02948.

X-ray data for **9** (CCDC No. 999893) (CIF)
X-ray data for **1** (CCDC No. 999892) (CIF)
Detail experimental procedures, analytical data, copies of spectra, details of crystal structures (PDF)

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Notes

The authors declare no competing financial interest.

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(14) Crystallographic data for the structures of compounds **9** (CCDC No. 999893) and **1** (CCDC No. 999892) have been deposited with the Cambridge Crystallographic Data Centre. Copies of the data can be obtained from http://www.ccdc.cam.ac.uk/conts/retrieving.html or from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CD21EZ, UK (fax: +44-1223-336-033; e-mail: deposit@ccdc.cam.ac.uk).

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