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Synthesis of Novel Acetylenic Cyclophanes with Helical Chirality: Potential New Structures for Liquid Crystals

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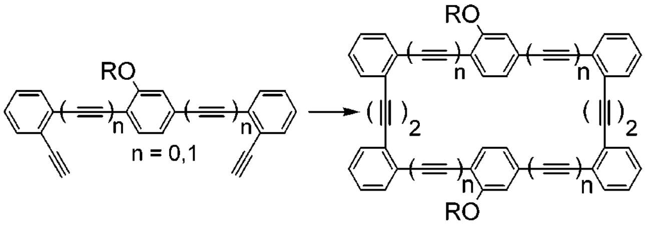
ABSTRACT



The synthesis of a series of novel acetylenic cyclophanes is described. X-ray crystallographic analysis of the core structure revealed a twisted conformation with helical chirality. Preliminary results suggest that these cyclophanes, with appropriate functionality, have the potential to act as unique liquid crystalline materials.

The synthesis and design of novel cyclophanes and assorted cage compounds with novel shapes and geometries continue to be topics of current interest.[1] Earlier, we reported the synthesis of a new class of cyclophanes connected by enediyne moieties.[2] A number of [1.4]paracyclophanes[3] are known, and recently we described the synthesis of a related class of phenyl acetylene cyclophanes in which a benzene ring replaced the double bond.[4] The combination of the number and type of unsaturated linkages in these molecules creates a twisted conformation that imparts helical chirality.[3d,5] This property, which is shared with other D_2-symmetric cyclophanes,[6] should allow these molecules to be employed as novel liquid crystalline materials.[7]

The design of liquid crystals, dopants, and optically active materials using chiral aromatic cores has attracted increased interest.[8] Enantiomerically pure optically active materials

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[†] For enquiries regarding X-ray analysis.

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containing biphenyl cores have been investigated for use as liquid crystals[9] as well as dopants.[10] The best ferroelectric liquid crystals have an aromatic core adjacent to a chiral center. Until recently, there were no examples in which the aromatic core also provided the chirality. However, Katz et al. constructed racemic helicenes containing long alkyl chains which form a liquid crystalline phase and assemble in solution to form helical columns.[11] Subsequently, they prepared the related chiral nonracemic derivatives **1** to generate the first liquid crystalline columnar mesophase molecules with a nonracemic helical aromatic core.[12] Helicenes have also been assembled with acetylene bridges to form helical cyclophanes and polymers in order to investigate their optical properties.[13]

We envisioned that modification of our acetylenic cyclophanes should also afford compounds that would exhibit interesting optical properties, and in addition, they might serve as liquid crystal dopants to induce the type of polarization observed for smectic liquid crystals.[5c,d] The parent ring system represented by the cyclic structure **2** appeared to possess the required geometric constraints to provide the desired rigid conformation (Figure 1). We wish to report the synthesis of a series of functionalized benzenoid−acetylenic cyclophanes in order to eventually access their potential optical properties.

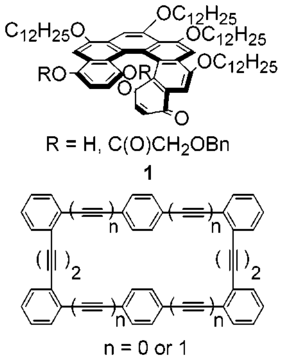
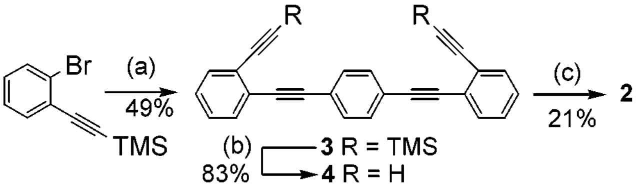


Figure 1. Helicene (above) and cyclophane (below) core structures.

Scheme 1. Synthesis of Core Structure[a]



[a] (a) (i) BuLi, THF, −78 °C, 15 min, (ii) $ZnBr_2$, THF, 0 °C, 15 min, (iii) 1,4-bis(bromoethynyl)benzene, $Pd(PPh_3)_4$, reflux, 15 h; (b) K_2CO_3, THF, MeOH, H_2O, 15 h; (c) $Cu(OAc)_2$ (6 equiv), 3:1 pyridine:Et_2O, 4 h.

Initially we prepared **2** ($n = 1$) by the route outlined in Scheme 1. Lithium−halogen exchange of (2-bromophenylethynyl)trimethylsilane followed by transmetalation with ZnBr affords an organozincate that is coupled with 1,4-bis(bromoethynyl)benzene[15] in the presence of $Pd(PPh_3)_4$ to afford **3** in 49% yield. Removal of the trimethylsilyl protecting groups with K_2CO_3 in THF/MeOH/H_2O gave the diacetylene **4** 83%. Dimerization with $Cu(OAc)_2$ in 3:1 pyridine:ether under high dilution conditions gave the expected dimer in 21% yield. The increase in separation of the terminal acetylenes eliminated the product resulting from intramolecular coupling (cf. **10**, Scheme 3).[3] X-ray crystallographic analysis of the hydrocarbon core revealed the stereoviews in Figure 2 which confirmed the twisted helical geometry that was anticipated. This differed significantly from the special orientation observed with a smaller cyclophane,[3] in which a pincer like arrangement of the aromatic rings resulted in cocrystallization of the solvent (CH_2Cl_2). As illustrated, the two central benzene rings are aligned in a slightly offset but overlapping, superimposed manner,

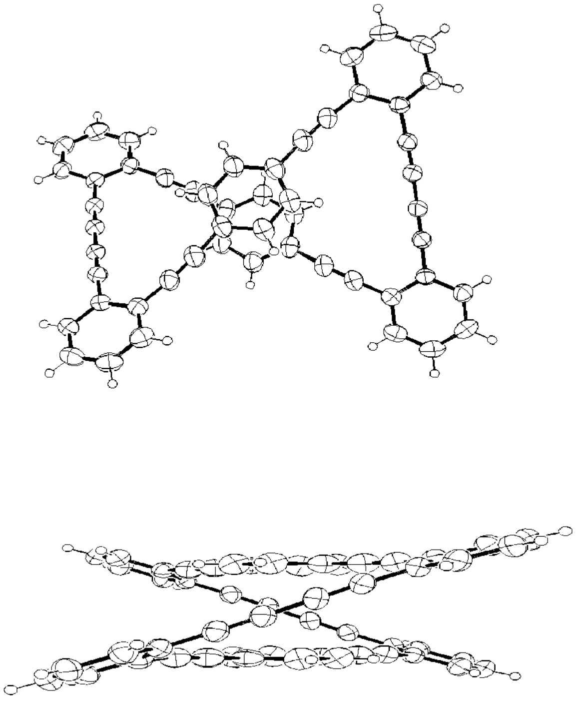


Figure 2. X-ray crystal structure of the parent cyclophane **2** ($n = 1$) displaying its twisted nature and the helical chirality inherent in these compounds. View from the top (above) and from the side (below).[14]

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(9) Solladie, G.; Hugele, P.; Bartsch, R.; Skoulios, A. *Angew. Chem., Int. Ed. Engl.* **1996**, *35*, 1533.

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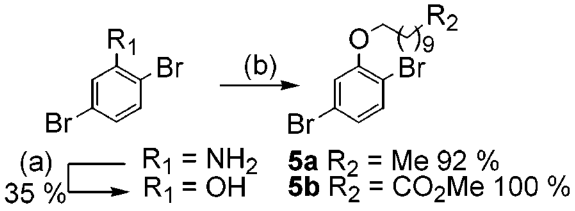
through the central axis with an inter-ring distance of 3.572 Å (Figure 2). The length of the diacetylene "arm" is 13.073 Å, while the spacial separation of the bent top and bottom phenyl rings is slightly longer at 16.371 Å.

Our strategy for the potential liquid crystalline cyclophanes was based upon the synthetic route above in which a C11-alkyl chain could be attached by an ether linkage. The first series examined were cyclophanes related to **2** ($n = 0$) in which the acetylene spacers have been deleted.

These syntheses commenced with the conversion of 2,5-dibromoaniline to the corresponding phenol via a diazonium salt intermediate. Attachment of the appropriate side chain was accomplished in greater than 90% yield by refluxing the alkyl bromide with the phenol in acetone in the presence of K_2CO_3 (Scheme 2). Compounds **5a** and **5b** were employed as starting materials for the synthesis of both the shortened ($n = 0$) and extended ($n = 1$) cyclophanes.

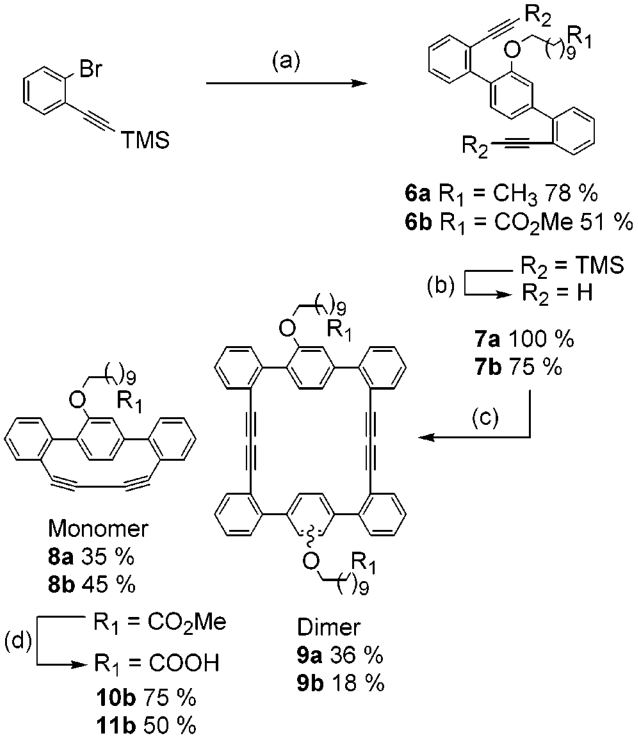
Scheme 2. Synthesis of Acetylenic Cyclophane Precursors[a]



[a] (a) H_2SO_4, $NaNO_2$, H_2O, reflux 3h; (b) for **5a**, 1-bromoundecane, K_2CO_3, acetone, reflux, 15 h; for **5b**, methyl 11-bromoundecanoate, K_2CO_3, acetone, reflux, 15 h.

Construction of the mono- and diacetylenic synthons was achieved using ZnBr-mediated palladium cross-coupling methodology described previously (Scheme 3).[3,16] Generation of the organozincate of (2-bromophenylethynyl)trimethylsilane followed by addition of **5a** or **5b** and $Pd(PPh_3)_4$ afforded the silyl-protected derivatives **6a** and **6b** in yields of 78% and 51%, respectively. Deprotection of the trimethylsilyl groups gave the diacetylenes **7a** and **7b** in 100% and 75% yields. Dimerization of **7a** or **7b** with $Cu(OAc)_2$ under pseudo high dilution conditions (syringe pump addition) gave mixtures of both the expected dimers and the "monomer" products resulting from intramolecular coupling of the terminal acetylenes.[3] Yields of the monomer compounds were similar and provided the products in 35−45% yield as yellow gums which blackened over time upon exposure to air (even when stored under nitrogen) for both series of compounds. The dimer **9a** was obtained in 36% yield, while **9b** was obtained in 18% yield. The dimers were obtained as yellow foams. In an effort to obtain solid samples, the ester-bearing compounds **8b** and **9b** were subjected to hydrolysis using LiOH in THF/MeOH/H_2O. The corresponding acids **10b** and **11b** were isolated in yields of 75% and 50%, respectively. Unfortunately **10b** rapidly decomposes to become a black tar over several hours, while **11b** remained an orange foam which could not be crystallized.

Scheme 3. Synthesis of Diacetylenic Cyclophanes[a]



[a] (a) (i) BuLi, THF, −78 °C, 15 min, (ii) $ZnBr_2$, THF, 0 °C, 15 min, (iii) **5a** or **5b**, $Pd(PPh_3)_4$, reflux, 15 h; (b) K_2CO_3, THF, MeOH, H_2O, 15 h; (c) $Cu(OAc)_2$ (6 equiv), 3:1 pyridine:Et_2O, 4 h; (d) LiOH, H_2O, THF, MeOH, 5 h.

The ^{13}C NMR spectra obtained for the dimers indicated that a mixture of compounds had been formed. Several signals appeared as pairs of equal intensity. This is a consequence of the free rotation of the central benzene ring, despite the presence of the long chains, and the formation of the statistical 1:1 mixture of isomers during the dimerization. These dimers were therefore a racemic mixture of the two different regioisomers.

The next series of compounds were generated by insertion of an additional acetylene unit between the central and outer benzene rings of the cyclophanes. Their synthesis (Scheme 4) also began with **5a** and **5b**. The reaction sequence, via Sonogashira coupling, paralleled the routes described above to provide the acetlyene monomers **15**, except the cross-coupling step required the use of (2-iodoophenylethynyl)-trimethylsilane in place of the bromide (from treatment of the lithium salt with NIS, 95%). The dimerization was accomplished under $Cu(OAc)_2$ reaction conditions identical to those used previously to provide the dimers **16a** and **16b** in similar yields of 40−41%. Dimer **16a** was a golden yellow liquid, which solidified into a brittle yellow solid when placed

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(14) X-ray data for compound **2** has been deposited with the Cambridge Crystallographic Data Centre as supplementary publication number CCDC 147868. Copies of the data may be obtained free of charge from CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (fax (+44) 1223−336−033; e-mail deposit@ccdc.cam.ac.uk).

(15) 1,4-Bis(bromoethynyl)benzene was isolated as a pale yellow solid prepared in 91% yield by treating 1,4-ethynylbenzene with NBS in acetone in the presence of a catalytic amount of $AgNO_3$ (15 h).

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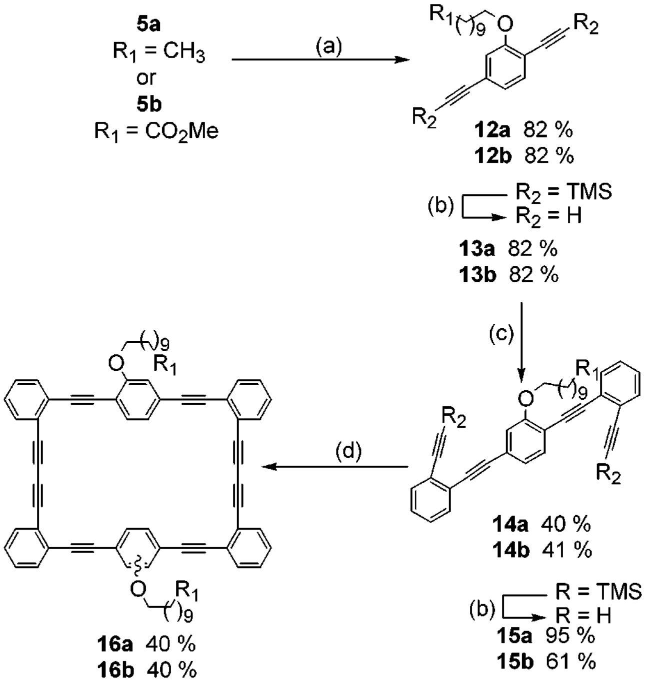
Scheme 4. Synthesis of Extended Acetylenic Cyclophanes[a]



[a] (a) $Pd(PPh_3)_2Cl_2$, CuI, TMSA, DEA, THF, reflux, 15 h; (b) K_2CO_3, THF, MeOH, H_2O, 15 h; (c) (2-iodophenylethynyl)trimethylsilane, $Pd(PPh_3)_2Cl_2$, CuI, DEA, THF, reflux, 15 h; (d) $Cu(OAc)_2$ (6 equiv), 3:1 pyridine:Et_2O, 4 h.

under vacuum, while compound **16b** was obtained as a pale orange solid. Both dimers exhibited the same ^{13}C NMR effect as was observed with the standard group of cyclophanes. Independent examination of the melting range of these compounds on a hot stage polarizing microscope did not reveal liquid crystal behavior in the case of **16a**. However, approximately 50% of the sample **16b** melted as a clear liquid, while the remaining portion melted from 48 to 66 °C to provide a gray opaque solution typical of liquid crystal behavior. This is likely due to the more polar regioisomer of **16b** but definitive proof will require an single enantiomerically pure isomer. Unfortunately, the individual isomers could not be separated. Thus, in the future, modification of the synthetic sequence to incorporate substituents into the rigid (corner) phenyl rings would eliminate the current complication from free rotation of the central benzene rings.

In summary, we have developed a short, efficient syntheses of a series of novel, functionalized acetylenic cyclophanes by Pd- and Cu-mediated coupling reactions. The X-ray analysis of the extended cyclophane has established the nature of the hydrocarbon core. This structure differs from the previously synthesized dimer and suggests that further synthetic manipulation will generate interesting solid-state geometries. The synthetic protocol above will also facilitate the preparation of new derivatives which may possess unusual optical properties. These methods allow variation of the chain length, alteration of the position of the alkyl groups, and modification of the acetylene spacers to control the helical conformation. In addition, the inclusion of heteroaromatic rings should permit the capture of metal ions.[17]

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