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# Transformations of a Macrocyclic Cyclophane Belt into Advanced [8]Cyclacene and [8]Cyclacene Triquinone Precursors[1]

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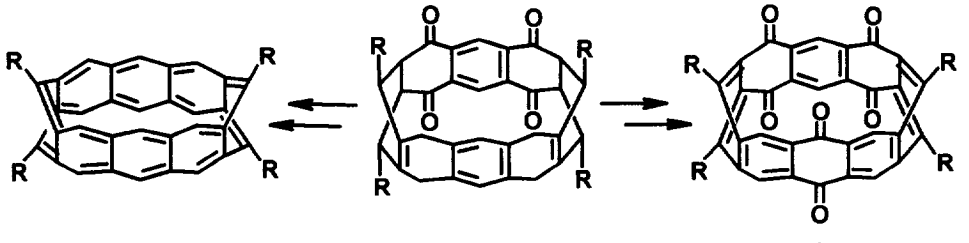
**Abstract**: Belt-shaped cyclophane **2**, is converted to a naphthalene-containing belt-shaped cyclophane by dehydrogenation, to an unexpected bisdiene-containing belt-shaped cyclophane by epoxidation and dehydration, and to an unexpected anthraquinone-containing belt-shaped cyclophane by PCC oxidation. The latter cyclophane could be functionalized further by a surprising oxidation involving sequential dehydrogenation and conjugate addition of ethoxide.

Fully unsaturated hoop-shaped cyclophanes, such as [8]cyclacene **1** (R = hexyl) and derivatives such as triquinone **3**, are as yet unknown but are of interest for a variety of reasons.[2] The cylindrical cavities of these molecular belts are predicted to allow them to act as molecular hosts to cylindrical molecular guests of the diameter of acetylene[3] and to molecules which have cylindrical end groups such as terminal acetylenes and terminal conjugated diynes. Since **1** and **3** are expected to be electronically complementary, electron-rich host **1** should preferentially complex electron-poor guests, such as dicyanoacetylene, while electron-poor host **3** should preferentially complex electron-rich guests such as terminal diynes and triynes.

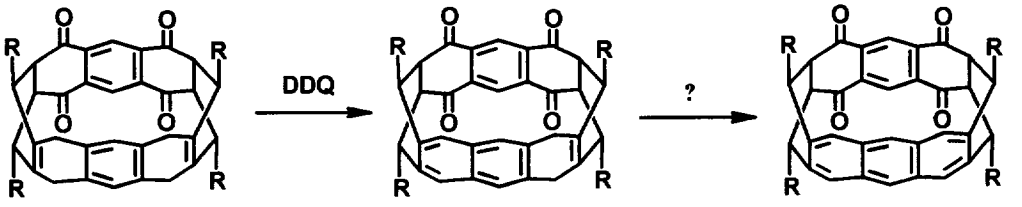


**1** **2** **3**

A convergent synthesis of belt-shaped cyclophane **2** has recently been carried out in our laboratories,[1] and we are currently investigating the conversion of this key intermediate to cyclacene **1** and derivatives, including its triquinone, **3**. Molecular modeling indicated that **2** is unstrained, but that introduction of additional unsaturation results in strained systems, which, indeed, accounts for the rigid hoop shape of **1** and **3**. This strain and the special steric and stereoelectronic requirements of the macrocyclic structures gives rise to unexpected modes of reactivity. We now report some of our most interesting observations arising from the unique nature of these cyclophane belts, which represent progress toward the synthesis of fully unsaturated molecular hoops, including **1** and **3**.

## PRECURSORS TO [8]CYCLACENE 1

***Synthesis of naphthalene-containing cyclophane 4.*** Dehydrogenation of cyclophane **2** with 2,3-dichloro-5,6-dicyano-*p*-benzoquinone in benzene at room temperature produced naphthalene **4** in 95% yield (yellow solid, mp 75-78 °C).[4,5] Although it may be possible to further aromatize **4** to anthracene **5**, an alternative potential pathway from **2** to **5** was diverted to an even more interesting cyclophane (*vide infra*).




**2** **4** **5**

***Spectroscopic evidence for the structure of cyclophane 4.*** The structure of **4** was initially inferred from its mass spectrum, which indicated that it has two fewer hydrogen atoms than the starting material. Furthermore, unlike cyclophane **2**,[1] naphthalene **4** cannot undergo facile double retro-Diels-Alder fragmentation, and, indeed, the parent peak at 806 is the base peak. The $^1$H NMR spectrum showed three distinct sets of aromatic protons (Fig. 1): $H_a$ giving rise to a singlet at 7.56, $H_b$ a singlet at 6.96, and $H_c$ a singlet at 6.65 ppm.

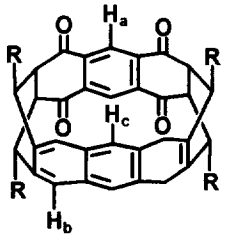
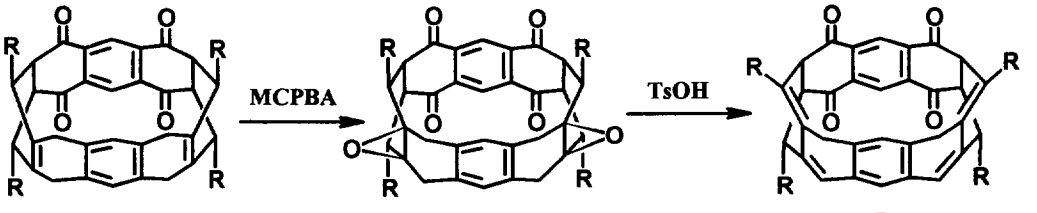


Figure 1. Labeling of protons of cyclophane **4**

***Two step conversion of cyclophane 2 to bisdiene-containing cyclophane 7.***




**2** **6** **7**

An alternative route to anthracene **5** would be via epoxidation-dehydration. Reaction of **2** with two equivalents of *m*-chloroperoxybenzoic acid generated diepoxide **6** in 90% yield (white solid, mp 169-171 °C). However, dehydration of **6** using *p*-toluenesulfonic acid in refluxing benzene did not generate the expected anthracene, **5**, but bisdiene **7** was obtained in 60% yield after short reaction times (yellow solid, mp 54-57 °C).[6] Bisdiene **7** has the same degree of unsaturation as anthracene **5**, and further dehydrogenation should lead to an [8]cyclacene diquinone, which may in turn be reduced to [8]cyclacene **1**.

***Spectroscopic evidence for the structure of bisdiene 7.*** The $^1$H NMR spectrum of **7** showed five distinct aromatic and vinylic signals (Fig. 2): singlets at 7.61 and 7.63 ppm assigned to $H_a$ and $H_b$, singlets at 6.34 and 6.46 ppm assigned to $H_c$ and $H_d$, and a singlet at 6.02 ppm assigned to $H_e$. The only major mass spectral line was the parent peak at 804.

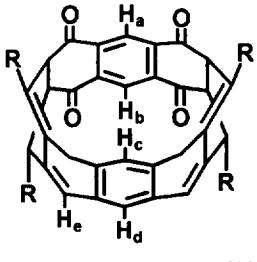
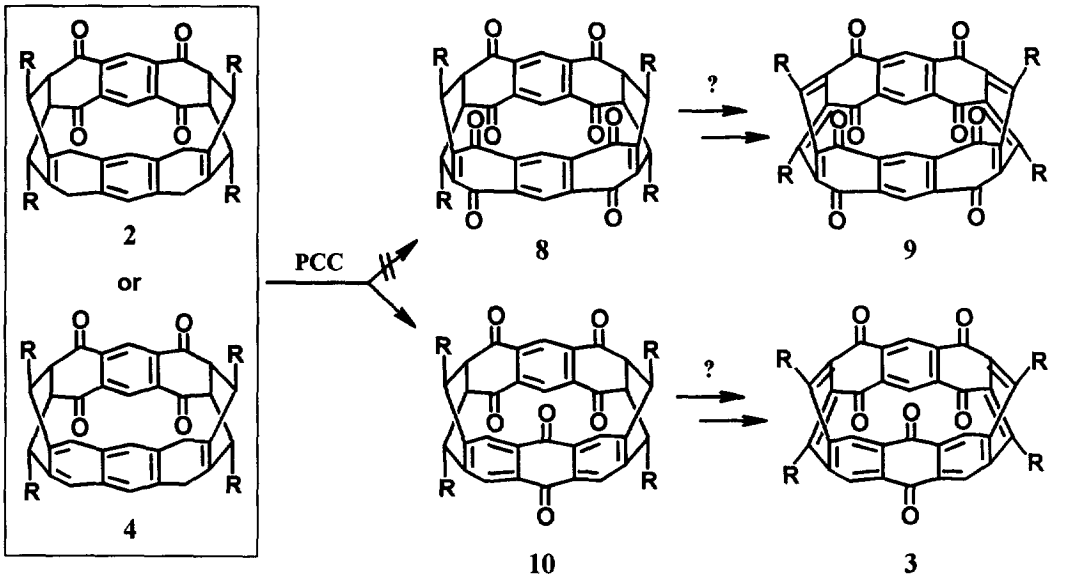


Figure 2. Labeling of protons of bisdiene **7**

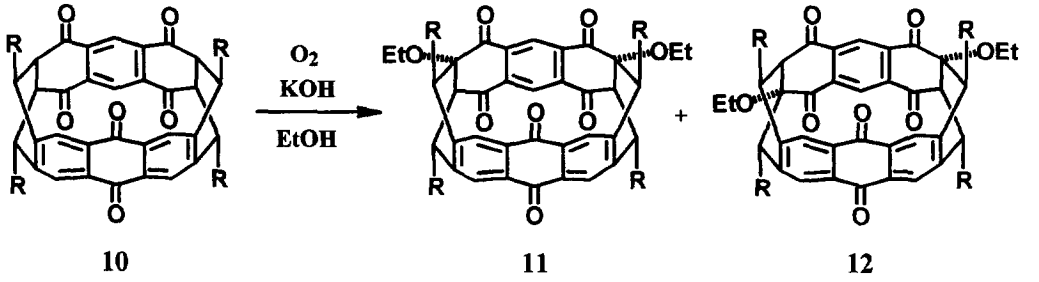
## PRECURSORS TO TRIQUINONE 3

***Oxidation of cyclophane 2 to anthraquinone-containing cyclophane 10.*** When cyclophane **2** was treated with pyridinium chlorochromate on Celite® in refluxing benzene,[7] instead of the expected diquinone **8**, which we hoped would serve as a precursor to cyclacene tetraquinone **9**, anthraquinone cyclophane **10** was obtained in 35% yield (light yellow solid, mp 103-105 °C). It is reasonable to infer that **2** was first dehydrogenated to naphthalene **4** and then to anthracene **5**, which would then be oxidized to anthraquinone **10**. Alternative mechanisms cannot be ruled out at this time, but when naphthalene **4** was subjected to the same reaction conditions, quinone **10** was obtained in 33% yield. At this point cyclacene triquinone **3** became a prime target.




***Spectroscopic evidence for the structure of quinone 10.*** Examination of the mass spectrum of quinone **10** indicated that only two new oxygen atoms had been incorporated, rather than the four expected. Its $^1$H NMR spectrum had two aromatic signals: a four proton singlet at 7.31 ppm and a two proton singlet at 7.37 ppm, as expected for **10**.

***Oxidation of anthraquinone cyclophane 10 to ethoxy ketones 11 and 12.*** In an attempt to aromatize its two remaining saturated rings, quinone **10** was treated with oxygen in alcoholic potassium hydroxide.[8] However, the product, obtained in 47% yield, was not triquinone **3**, but a mixture of two ethoxy ketones, **11** and **12** (white solid, mp 157-160 °C), in a ratio varying from 1.1:1 to 1.3:1 (individual identity not yet assigned).



***Spectroscopic evidence for the structure of ethoxy ketones 11 and 12.*** The mass spectrum of the product mixture was consistent with its having been derived from quinone **10** by replacement of two hydrogen atoms by two ethoxy groups. The mass spectral fragmentation pattern and the $^1$H NMR spectrum indicated that the ethoxy groups had been incorporated at positions α to carbonyl groups on opposite sides of the macrocycle.

***Proposed mechanism for the formation of 11 and 12.*** This mixture of compounds may be generated via conjugate addition of ethoxide to transient quinone double bonds. If this is the case, it may be possible to isolate a triquinone from a similar oxidation under modified conditions. Alternatively, the ethoxy ketones themselves may serve as stepping stones toward triquinone **3**. These possibilities are being actively investigated.

## CONCLUSIONS

The syntheses of [8]cyclacene **1** and its triquinone, **3**, are well underway. The precursors to these strained hoop-shaped molecular belts follow unexpected pathways of reaction with a variety of reagents. Bisdiene **7** and quinone **10** are the most highly unsaturated precursors to **1** and **3** that we have synthesized to date, but it seems likely that a more highly unsaturated diquinone (and perhaps even a triquinone) was formed as an intermediate in the formation of ethoxy ketones **11** and **12**. Experiments directed toward the introduction of additional unsaturation are currently underway.

## ACKNOWLEDGMENTS

Financial support of this work by the Natural Sciences and Engineering Council (NSERC) of Canada is gratefully acknowledged. CLM thanks NSERC for a Postgraduate Scholarship.

## REFERENCES AND NOTES

1. Belt-Shaped Cyclophanes. 2. For the previous paper in this series see the preceding paper in this issue.
2. Schröder, A.; Mekelburger, H.-B.; Vögtle, F. *Top. Curr. Chem.* **1994**, *172*, 179-201.
3. Molecular mechanics calculations on the corresponding [8]beltene predict a cavity of roughly the same size: Alder, R. W.; Sessions, R. B. *J. Chem. Soc., Perkin Trans. 2* **1985**, 1849-1854.
4. All compounds were purified by flash chromatography and crystallization from dichloromethane/methanol.
5. All compounds were characterized using HRMS, LRMS, IR, $^1$H NMR and $^{13}$C NMR. $^1$H-$^1$H (COSY) correlations were employed to assign absorptions for non-aromatic protons.
6. After two minutes at reflux, the reaction mixture was *immediately* subjected to flash chromatography.
7. Rathore, R.; Saxena, N.; Chandrasekaran, S. *Synth. Comm.* **1986**, *16*, 1493-1498.
8. Becker, B.; Bohner, A.; Ehrenfreud, M.; Wolfarth, W.; Sakata, Y.; Huber, W.; Müllen, K. *J. Am. Chem. Soc.* **1991**, *113*, 1121-1127.

## $^1$H NMR DATA (300 MHz)

**Naphthalene cyclophane 4**: ($C_6D_6$) δ 1.0 (m, 12H), 1.3-2.2 (m, 40 H), 2.34 (m, 2 H), 2.83 (m, 2 H), 2.94 (d, $J$ = 14 Hz, 2H), 3.04 (m, 2 H), 3.13 (m, 2 H), 3.22 (d, $J$ = 14 Hz, 2 H), 6.65 (s, 2 H), 6.96 (s, 2 H), 7.56 (s, 2 H). **Bisdiene cyclophane 7**: ($C_6D_6$) δ 0.95 (m, 12 H), 1.2-1.7 (m, 32 H), 2.0 (m, 8 H), 2.42 (m, 2 H), 2.87 (d, $J$ = 13 Hz, 2 H), 2.91 (dd, $J$ = 7, 4 Hz, 2 H), 3.16 (dd, $J$ = 13, 3 Hz, 2 H), 3.62 (dd, $J$ = 7, 3 Hz, 2 H), 5.80 (s, 2 H), 6.03 (s, 2 H), 6.32 (s, 1 H), 7.88 (s, 1 H), 7.97 (s, 1 H). **Anthraquinone cyclophane 10**: ($CDCl_3$): δ 0.92 (m, 12 H), 1.2-1.8 (m, 32 H), 1.91 (m, 8 H), 3.30 (m, 4 H), 3.54 (m, 4 H), 7.31 (s, 4 H), 7.37 (s, 2 H). **Diethoxy cyclophanes 11 + 12**: ($CDCl_3$) δ 0.92 (m, 12 H), 1.18 (m, 6 H), 1.3-1.8 (m, 34 H), 1.93 (m, 4 H), 2.31 (m, 2 H), 3.16 (m, 4 H), 3.32 (d, $J$ = 9 Hz, 2 H), 3.41 (dd, $J$ = 6, 2.5 Hz, 2 H), 3.62 (m, 2 H), 7.32 (s, 1 H), 7.35 (s, 1 H), 7.36 (s, 1 H), 7.39 (s, 1 H), 7.51 (d, $J$ = 0.5 Hz, 0.5 H), 7.58 (s, 1 H), 7.95 (d, $J$ = 0.5 Hz, 0.5 H); ($C_6D_6$) δ 0.90 (m, 18 H), 1.2-1.5 (m, 28 H), 1.60 (m, 4 H), 1.85 (m, 6 H), 2.61 (m, 2 H), 2.95 (m, 2 H), 3.22 (m, 2 H), 3.32 (m, 4 H), 3.47 (dd, $J$ = 6, 1 Hz, 2 H), 7.58 (s, 1 H), 7.60 (s, 1 H), 7.70 (s, 1 H), 7.72 (s, 1 H), 7.85 (d, $J$ = 0.5 Hz, 0.5 H), 7.90 (s, 1 H), 7.95 (d, $J$ = 0.5 Hz, 0.5 H).

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