Tetrahedron Letters, Vol. 34, No. 47, pp. 7533-7536, 1993
Printed in Great Britain

0040-4039/93 $6.00 + .00
Pergamon Press Ltd

Linearly Fused Ribbons of Carbocyclic Six-Membered Rings via Diels-Alder Cycloadditions

1. Model Studies and Key Intermediates

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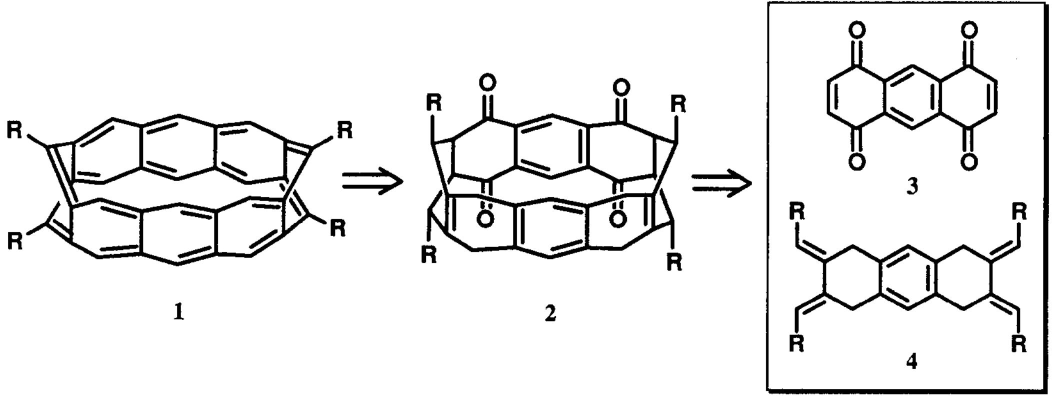
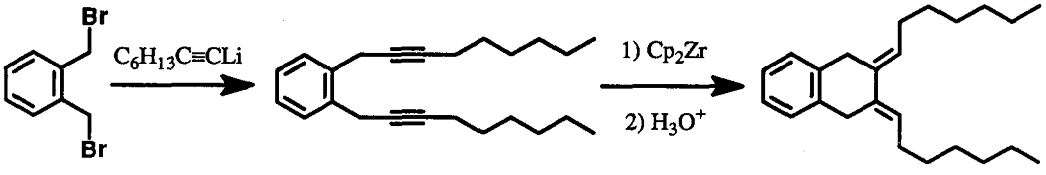
Abstract: A synthesis of 7,14-dihexyl-6,15-hexacenedione is accomplished by Diels-Alder addition followed by dehydrogenation, and the double Diels-Alder components (1,4,5,8-anthradiquinone and 2,3,6,7-tetraheptylidene-1,2,3,4,5,6,7,8-octahydroanthracene) for a proposed synthesis of a cyclacene are prepared.

As part of a synthetic program directed toward cyclacenes (cyclophanes having a core structure consisting of a rigid macrocyclic belt of fused benzene rings) we have undertaken an investigation of the potential utility of double Diels-Alder cycloadditions for the preparation of macrocyclic cyclophane precursors to cyclacenes. These studies differ from the related work of Stoddart[1,2] in the nature of both the bisdiene and bisdienophile components. For example, one can envision a synthesis of tetra-alkyl substituted [8]cyclacene **1** by reduction and aromatization of macrocyclic double Diels-Alder adduct **2**, which would be formed by macro-annulation of diquinone **3** by bisdiene **4**. This strategy also differs from the double Diels-Alder approach of Schlüter, in which a dimerization of a diene-quinone was involved.[3] The doughnut-like core structure of cyclacene **1** would have a cylindrical interior cavity, open at both ends, and it should be able to act as a host to complementary shaped small molecules and end groups. Our modeling studies indicate that it would be of just the right size to accommodate a cylindrical rod-shaped guest molecule of the diameter and length of dicyanoacetylene.[4]

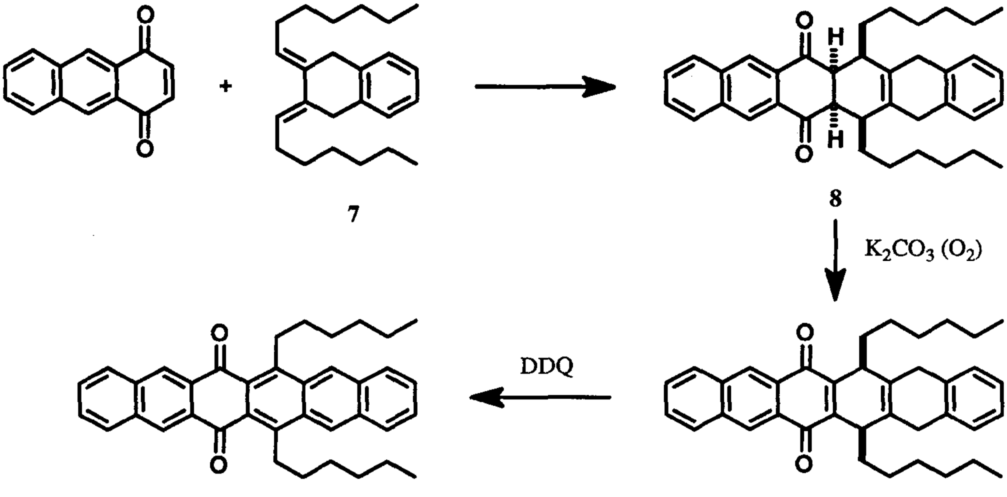


Since bisdiene **4** was of a type not prepared before, a model study, designed to test the feasibility of both the synthesis of this class of compound and also its Diels-Alder cycloadditions with quinones, was first carried out, using hexyl groups for R to increase[5] the solubility and hence the tractability of the adducts and their subsequent derivatives. Accordingly, treatment of 1,2-bis(bromomethyl)benzene (**5**) with 1-octynyllithium (THF, −78 °C to r. t.) gave diyne **6** (58%), which underwent reductive cyclization (Cp_2Zr, THF, −78 °C to r. t.)[6] to produce diene **7** in 91% yield. The stereochemistry of **7** was assigned by analogy with previous studies.



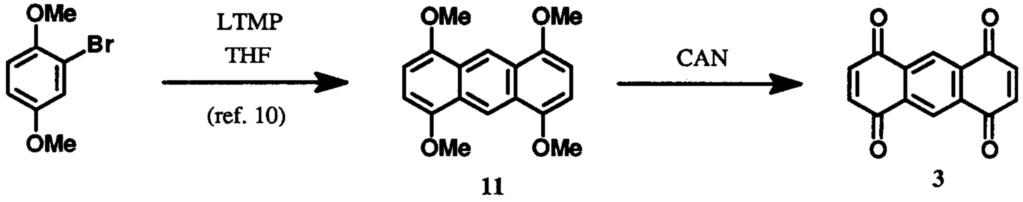
5 **6** **7**

When diene **7** was treated with 1,4-anthraquinone ($CHCl_3$, r. t.), Diels-Alder adduct **8** was obtained in 67% yield. The assumed stereochemistry shown for adduct **8** is based on an x-ray structure reported by Nugent for a related adduct[7] and is consistent with the endo rule. Further confirmation of the structure of the adduct, as well as modeling of transformations contemplated for later use with cyclophane **2**, was obtained by stepwise removal of hydrogen at stereocenters. Dehydrogenation of adduct **8** was accomplished by tautomerization (K_2CO_3, acetone, r. t.), presumably accompanied by air oxidation, giving quinone **9** (yellow, mp 126-127 °C), followed by aromatization (DDQ, benzene, reflux) to give quinone **10** (yellow, mp 217-219 °C). As expected, the two hexyl groups confer both solubility and a dramatic lowering of the melting point relative to the parent quinone corresponding to **10**, but lacking the hexyl groups (mp 391-394 °C).[8]

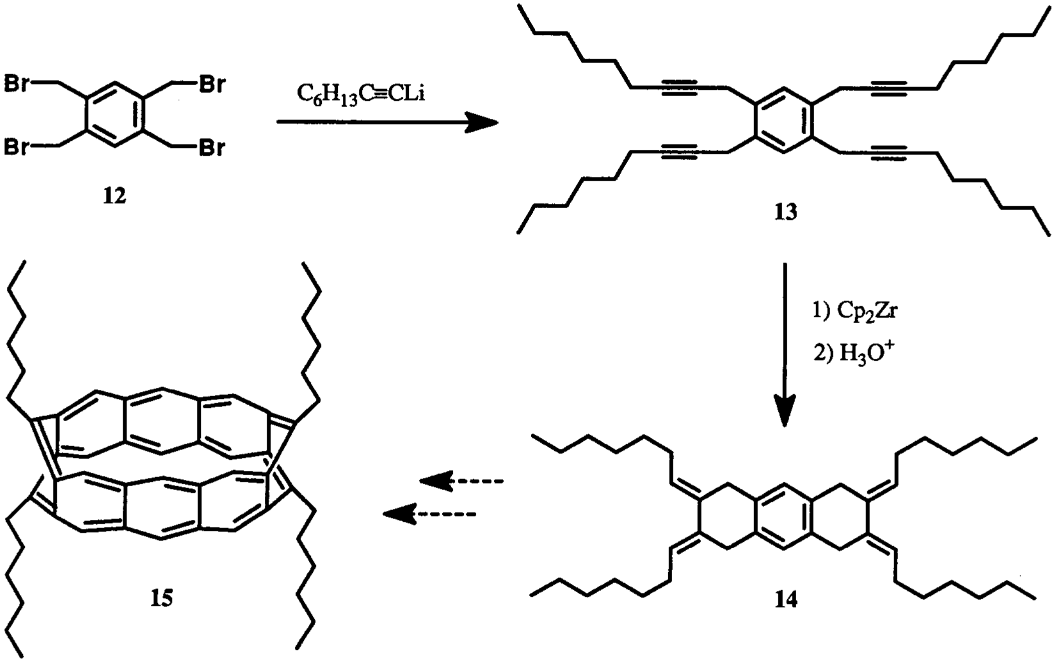


7 **8** **10** **9**

In contrast to previous lengthy and tedious syntheses of diquinone 3,[9] this potential bisdienophile was easily prepared *in a single step* from 1,4,5,8-tetramethoxyanthracene (**11**) by oxidative demethylation (ceric ammonium nitrate, H_2O/CH_3CN, r. t.), giving **3** in 45% yield. Anthracene **11** is itself derived in one step from commercially available 1-bromo-2,5-dimethoxybenzene.[10,11] Now that diquinone **3** is readily available, its reactivity in Diels-Alder reactions can be investigated for the first time, and in particular, an investigation of the double Diels-Alder reaction of **3** with diene **7** is now in progress.



By analogy with the synthesis of diene **7**, the synthesis of bisdiene **4** (R= hexyl) proceeded under similar conditions from tetrabromide **12** via tetrayne **13** to tetraene **14** (colorless oil, 42%). Studies of the double Diels-Alder addition of 1,4-anthraquinone to **14**, as well as the key reaction of **3** with **14**, are currently under investigation (with the eventual aim of converting **14** to cyclacene **15**). Preliminary indications are that both of these experiments have been successful but that some optimization of the conditions remains to be done. Details of these results will be forthcoming in future publications from these laboratories.



Acknowledgment: Financial support of this work by the Natural Sciences and Engineering Research Council of Canada is gratefully acknowledged.

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SELECTED ^{1}H NMR DATA

Diketone **8**: (300 MHz, $CDCl_3$) δ 0.8-1.4 (m, 22 H), 1.5-1.9 (m, 4 H), 2.50 (m, 2 H), 3.21 (m, 2 H), 3.4-3.7 (m, 4 H), 7.14 (s, 4 H), 7.66 (m, 2 H), 8.05 (m, 2 H), 8.53 (s, 2 H).

Quinone **9**: (200 MHz, $CDCl_3$) δ 0.90 (m, 6 H), 1.3 (m, 12 H), 1.5 (m, 4 H), 1.75 (m, 4 H), 3.34 (m, 2 H), 3.5-3.8 (m, 4 H), 7.20 (s, 4 H), 7.63 (m, 2 H), 8.02 (m, 2 H), 8.59 (s, 2 H).

(200 MHz, C_6D_6) δ 0.90 (m, 6 H), 1.3 (m, 12 H), 1.65 (m, 4 H), 1.9 (m, 4 H), 3.20 (m, 2 H), 3.60 (m, 2 H), 3.84 (t, J = 5 Hz, 2 H), 7.20 (m, 6 H), 7.55 (m, 2 H), 8.65 (m, 2 H).

Quinone **10**: (200 MHz, $CDCl_3$) δ 1.00 (m, 6 H), 1.5 (m, 8 H), 1.76 (m, 4 H), 1.93 (m, 4 H), 3.62 (m, 4 H), 7.54 (m, 2 H), 7.60 (m, 2 H), 8.0 (m, 4 H), 8.65 (s, 2 H), 8.83 (s, 2 H).

Tetrayne **13**: (200 MHz, $CDCl_3$) δ 0.90 (m, 12 H), 1.2-1.6 (m, 32 H), 2.2 (m, 8 H), 3.57 (t, J = 2 Hz, 8 H), 7.38 (s, 2 H).

Tetraene **14**: (200 MHz, $CDCl_3$) δ 0.86 (m, 12 H), 1.2-1.4 (m, 32 H), 2.09 (q, J = 7 Hz, 8 H), 3.44 (s, 8 H), 5.60 (t, J = 7 Hz, 4 H), 6.90 (s, 2 H).

(Received in USA 23 August 1993; accepted 21 September 1993)