Pergamon

*Tetrahedron Letters*, Vol. 35, No. 27, pp. 4711-4714, 1994
Elsevier Science Ltd
Printed in Great Britain
0040-4039/94 $7.00+0.00

0040-4039(94)00915-5

# Revolveneynes: Novel Eneyneparacyclophanes by Sequential Palladium Coupling

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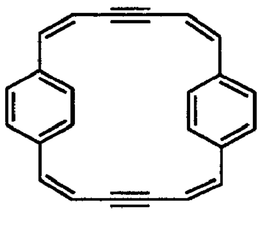
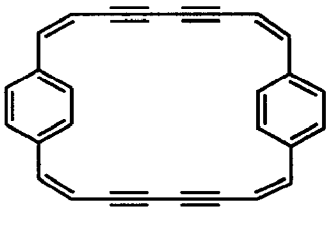
**Abstract:** The synthesis and initial study of a new series of eneyne-bridged cyclophanes (revolveneynes) are described in which the phenyl rings are free to rotate within the cavity. Either palladium coupling or oxidative dimerization provided rapid access to [14], [6.6] and [8.8] phane systems.

Diverse families of cyclophanes[1] and assorted cage compounds[2] with novel structures and properties continue to be topics of wide spread current interest.[3] Similarly, cyclic acetylenes are receiving renewed attention due to their incorporation into annulenes,[4] and their potential to act as multidentate ligands for transition metal clusters.[5] In addition, lithium-induced cyclization reactions[6] and solid state polymerization[7] of these species provide direct entry to unusual structures provided the cyclic substrates are available. Motivated by these multiple considerations and the possibility that more highly functionalized systems may serve as a direct entry to unusual host-guest combinations[8] we wish to report the synthesis of the first members **1**[9] and **2** of a new class of eneyne-bridged paracyclophanes and the related compound **3** by sequential Pd(0)-based coupling or a combination of palladium and copper-mediated oxidative ring closure. This strategy compliments existing methods and should be applicable to a variety of targets.[1,12]



**1**



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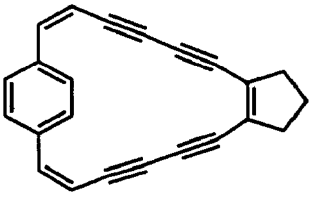
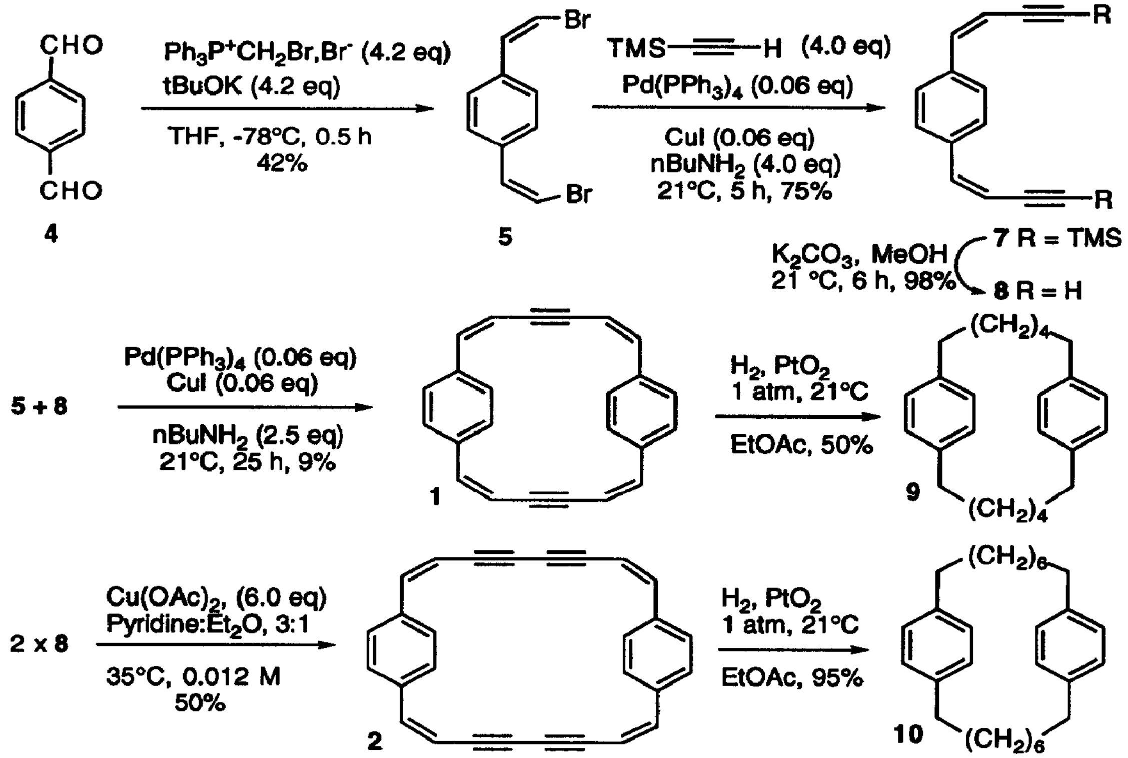


**3**

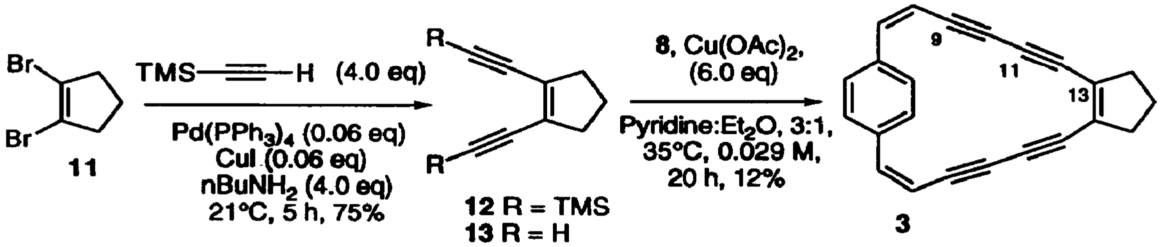
Our synthetic approach to these systems was based on the preparation of the key intermediates **5** and **8**. These were assembled from 1,4-benzenedicarboxaldehyde **4** by a double Wittig reaction, as illustrated, to afford the Z-dibromodiene **5** in 42% isolated yield. An interesting, consistent biproduct (10%), from this reaction was the bromo-epoxide (Z-4-(2-bromovinyl)styrene oxide **6**). Palladium(0)-based coupling of **5** with trimethylsilylacetylene generated the TMS protected diacetylene **7**. The silyl groups were removed with $K_2CO_3$ in methanol at 21°C over 6 h to give **8** which was used directly.

The synthesis of **1** was effected by palladium-mediated coupling of the dibromide **5** and the diacetlyene **8** in 9% yield. It was important to conduct this reaction at high dilution (0.004 M) and add a THF solution of **5** and **8** with a syringe pump over a 25 hour period. The dimer **2** was synthesized directly (50%) by oxidative coupling.[13] Compound **2** crystallized as fine red needles [m.p. 240 °C (dec) unsuitable for X-ray]. The UV spectrum ($CH_2Cl_2$) displayed intense absorptions at 346 nm ($8.95 \times 10^5$) and 382 nm ($1.85 \times 10^5$). For the orange revolveneyne **1** signals appeared at 308 ($4.33 \times 10^5$) and at 394 nm ($6.40 \times 10^4$), respectively. These spectral shifts and the variation of the relative intensities find a partial parallel in the unsaturated [4.4]paracyclophanes studied previously in which related features were ascribed to 'half-chromophore' resonance.[14] The spectra of **1** and **2** reflect the distortion of the system from planarity and the reduced intensity for **1** is a measure of the larger steric barrier necessary to achieve this. The $^1$H NMR spectrum of **1** [$\delta$ 8.72 (s, 8 H), 6.11 (dm, 4 H, J = 11.6 Hz), 5.38 (dm, 4 H, J = 11.6) ppm] remained unchanged upon cooling, indicating that the benzene rings continued to rotate freely even at -60 °C on the NMR time scale.

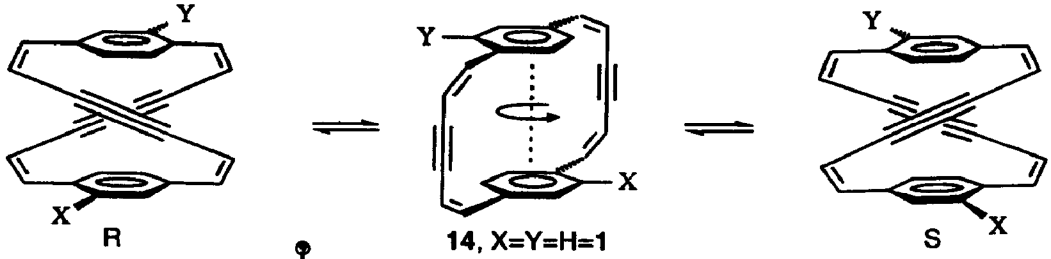


The structural assignments were firmly established by HRMS, $^{13}$C- and $^1$H NMR, as well as hydrogenation to the known [6.6]paracyclophane **9**[15] and, in a related manner, by reduction to the new [8.8]paracyclophane **10** in 95% yield. Thus, this palladium or oxidative coupling-hydrogenation sequence provides a rapid entry to these systems.

The investigation was extended to 1,2-dibromocyclopentene **11** which was coupled with trimethylsilylacetylene as before. Oxidative dimerization of the deprotected material **13** provided the diene-tetrayne system **3** (12%) accompanied by the dimer **2** (15%).[16] Hydrogenation of **3** readily afforded the corresponding [14]paracyclophane (95%). Large-ring systems of this type are frequently difficult to prepare by other routes. Revolveneyne **3** displayed UV bands at 326 nm ($1.85 \times 10^6$) and 384 ($3.07 \times 10^5$).



The flat structures drawn for 1-3 do not truly reflect the geometric relationships as revealed by the x-ray structure of 3. (Figure 1) The angle subtended between the benzene and polyeneyne macrocycle is 155.9°. The $C_9$-$C_{10}$-$C_{11}$ and $C_{11}$-$C_{12}$-$C_{13}$ angles are 173.9° and 176.0° respectively.[17] As noted above, the benzene rings in these compounds rotate freely, but this should not be the case in related molecules bearing appropriate substituents. These compounds will be chiral due to the restricted rotation imposed by bulky substituents, (X and Y in 14).[10] Rigid 'Dreiding type' molecular models suggest the unsaturated linkage imparts a helical twist to these structures similar to related $D_2$ symmetric olefinic paracyclophanes.[14,18] Thus, the strain depicted in 14 is relieved by rotation of one benzene ring with respect to the other about an axis that passes through the centre of both rings. This gyrochiral property implies that at suitable temperatures the enantiomers lacking substituents may also be resolvable. As illustrated the two rings are offset slightly with respect to each other. Preliminary calculations have not established unambiguously whether the ground state structures for 1 and 2 exhibit sufficient twist to conform to the helical structures displayed by the molecular models. At present the energy barriers for conformational inversion are unknown but the possibility of resolving some of these systems is under investigation as are synthetic approaches to related multiple bridged systems.[19] These structures possess accordion-like flexibility and yet the rigid nature of the bridge presents a large cavity for complexation (inclusion[20]) with various substrates and different reactive sites for subsequent functionalization.



14, X=Y=H=1

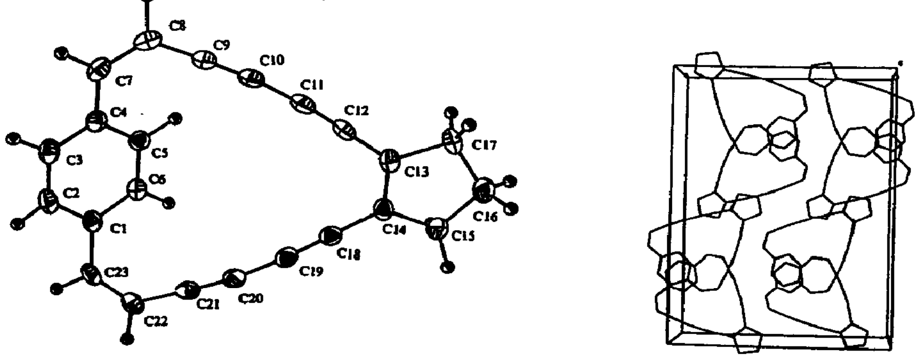


Figure 1

In conclusion, this palladium coupling sequence provides a rapid route to novel eneyne-bridged cyclophanes that possess interesting geometric features. It is anticipated that current investigations will lead to more highly functionalized systems with unique properties.

**Acknowledgment** We are grateful to the Natural Sciences and Engineering Research Council of Canada for financial support of this research.

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(9) In normal [n.m]paracyclophanes, possesing saturated methylene units between the benzene rings, rotation of the ring is usually restricted by the bridge.[10] These new compounds posses benzene rings which rotate freely. As a consequence of this 'skipping rope' property,[11] where the bridging unit and one ring may swing around the other ring, we have called these structures revolveneynes. Compound 1 can be named as 1,5-dien-3-yne-[6.6]paracyclophane or 1(1,4)-benzena-4-(1,4)-benzacyclotetradeca-2,6-dien-4-yne or recent IUPAC nomenclature 1(1,4),8(1,4)-dibenzenacyclotetradeca-2,6,9,13-tetradien-4,11-diyne.

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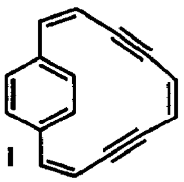
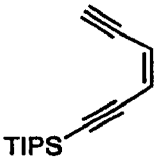
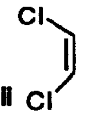
(16) Various attempts to prepare **i** by coupling **ii**[19] and **5** or **iii** and **8** were unsuccessful, and similar coupling of **11** with **8** or **5** with **13** failed to generate **iv**.

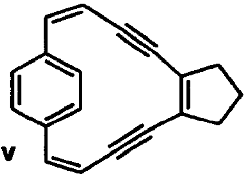

**i**



**ii**



**iii**


**iv**

(17) Crystal data for revolveneyne **3**: Crystal size 0.20 x 0.20 x 0.20 mm$^3$; Orthorombic space group P bac; Unit cell: a = 17.604(4), b = 23.824(6), c = 7.417(3) Å, Z = 8, T = 160 K, $D_c$ = 1.352 g cm$^{-3}$; Mo-K$\alpha$ radiation: 2544 reflections measured, 2544 independent and 1822 observed, $R_f$ (sign refl) 0.060; $R_w$ (sign refl) 0.049; $R_f$ (all refl) 0.089; $R_w$ (all refl) 0.049.

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(*Received in USA* 31 *March* 1994; *revised* 3 *May* 1994; *accepted* 6 *May* 1994)