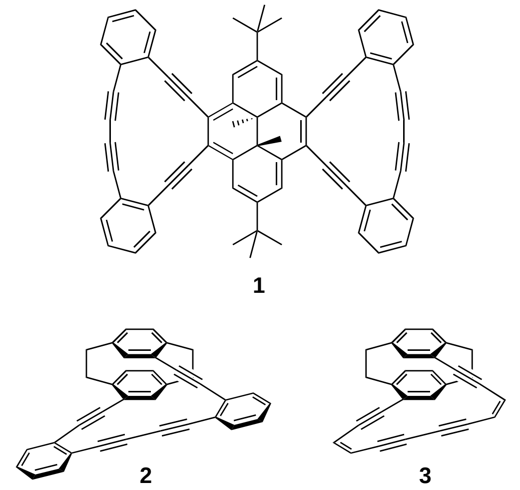
“Polyunsaturated” Cyclophanes**

Graham J. Bodwell* and Teizi Satou

Cyclophane chemistry has a long and colorful history.[1] Although this discipline has evolved in many ways, several of the fundamental sources of interest in cyclophanes remain unchanged. These include the conception of novel, aesthetically pleasing and interesting structures, the challenge of synthesizing them, and the study of their properties once they have been prepared.

As with other areas of synthetic chemistry, the development of new methodology has played a crucial role in the development of cyclophane chemistry. An early example of this is the emergence of the sulfur-based ring-contraction strategies that were developed in the 1960s and 1970s,[2] which paved the way for the synthesis of a very wide range of [2.2]cyclophanes and [2.2]cyclophanedienes. That these approaches are still in use today speaks to their lasting value. A more recent example is the advent of palladium-catalyzed cross-coupling reactions,[3] which opened the door for the design and synthesis of whole new families of cyclophanes, that is, those that have multiply unsaturated bridges. A selection of such “polyunsaturated” cyclophanes is presented in Scheme 1.

When considering compounds that are composed of aromatic units linked by unsaturated bridges, the distinction between a cyclophane and a dehydrobenzannulene (DBA) can become blurred, or even disappear entirely. A crude criterion for distinguishing these two fascinating classes of compounds is that a DBA has only 1,2-disubstituted aromatic units, whereas a cyclophane has at least one non-1,2-disubstituted aromatic unit.[4] Thus, the aptly named “dehydrobenzannulene–dimethyldihydropyrene hybrid” **1** reported by Haley, Mitchell, and co-workers[5] falls under the DBA category, whereas the “[2.2]paracyclophane-dehydrobenzannulene hybrids” **2** and **3** described by Hopf, Haley, and co-workers[6] fall under the heading of cyclophanes. Comparison of the electronic absorption spectra of **2** and **3** with appropriate DBAs and “broken” DBA analogues provided evidence of global transannular delocalization between the fully conjugated decks of the cyclophane.



Scheme 1. Some examples of cyclophanes with multiply unsaturated bridges, made by using palladium-catalyzed cross-coupling.

The use of electrocyclic reactions that result in the formation of new aromatic systems to generate strained systems is a strategy that has been successfully applied to a variety of small cyclophanes for some time.[7] More recently, this approach has been enlisted in the construction of much larger strained systems. For example, Tsuji and co-workers' syntheses of cyclophanes **4** and **5** (see Scheme 2)[8] featured tethered Dewar benzenes as precursors to the *para*-phenylene units. Their shape facilitated the palladium- or copper-catalyzed dimerization of the two halves to afford macrocyclic precursors. Removal of the tether and photochemical valence isomerization afforded the *para*-phenylene units, the substituents of which render the systems both chiral and amenable to further synthetic manipulation. Tobe et al., on the other hand, employed [4.3.2]propellane units as masked alkynes, which can be liberated by a [2+2] cycloreversion reaction. Again, their geometry permitted the construction of the comparatively unstrained precursor cyclophanes **6a** and **6b** by oxidative coupling of the two halves.[9] Photolysis of **6a** at 77 K resulted in changes in the UV/Vis spectrum that were attributed to the formation of cyclophyne **7a**. Laser-desorption time-of-flight mass spectrometry of **6b** gave rise not only to a signal caused by $C_{36}Cl_8^-$ (**7b**$^-$), but also to a relatively

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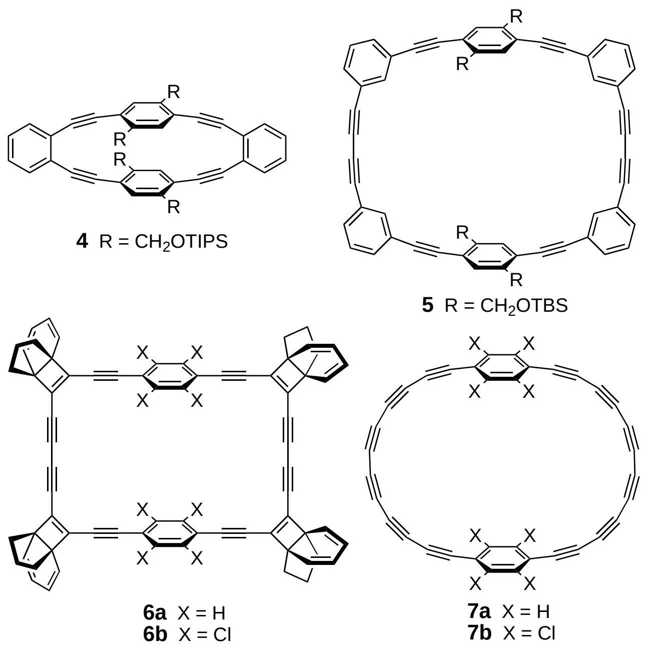


4 R = CH_2OTIPS

5 R = CH_2OTBS

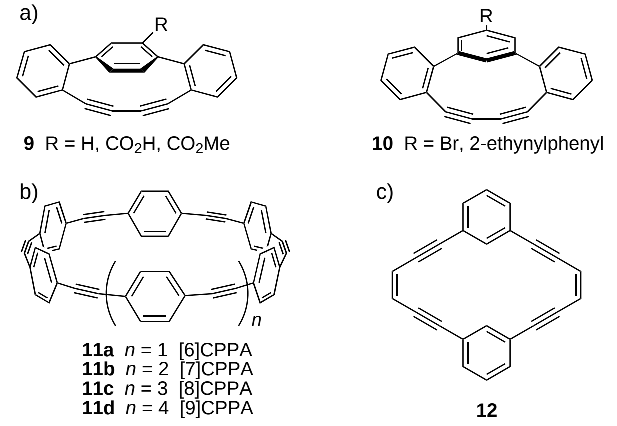
6a X = H
6b X = Cl

7a X = H
7b X = Cl

Scheme 2. Cyclophanes synthesized by a dimerization route. TIPS = triisopropylsilyl, TBS = *tert*-butyldimethylsilyl.

strong signal arising from C_{36}^-, which was speculated to correspond to the D_{6h}-symmetric carbon cluster.

Cyclophanes **6a** and **6b** are structurally related to a number of arene–alkyne cyclophanes **8a–g** (Table 1) that have been reported recently.[10–12] These consist of two linear arylene units and four angular arylene units, all linked by varying numbers of alkynyl groups. Sonogashira and copper-mediated oxidative couplings feature prominently in the syntheses of these compounds. In the case of the cyclophanes of Marsella et al., **8a–c**, the comparatively high yield of **8c** (yield of **8c** = 30% vs. 12% for **8a** and 10% for **8b**) was ascribed to favorable aryl–perfluoroaryl electrostatic interactions. This result is a rare example of such interactions being of importance in solution. The linear arylene units in Baxter's "twistophane" **8d** are 4,4′-(2,2′-bipyridyl)ene units, which allow the system to function as a sensor for Co^{2+}, Ni^{2+}, Cu^{2+}, and Zn^{2+} ions.[11] Of particular interest is that **8d** responds differently to the different analytes. Fallis and co-workers reported the synthesis of the cyclophanes **8e–g**.[12] The crystal structure of **8e** revealed the helically chiral nature of the cyclophane core. The incorporation of long side chains (**8f** and **8g**) was performed with an eye to preparing new liquid crystalline materials. Indeed, **8g** melted to provide a gray, opaque solution, which is typical of liquid crystal behavior.



a)

9 R = H, CO_2H, CO_2Me

10 R = Br, 2-ethynylphenyl

b)

11a $n = 1$ [6]CPPA
11b $n = 2$ [7]CPPA
11c $n = 3$ [8]CPPA
11d $n = 4$ [9]CPPA

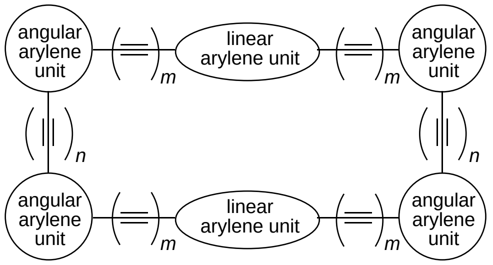
c)

12

Scheme 3. Strained cyclophanes made by a) the Fallis group;[14] b) Oda and co-workers;[15] c) Sankaraman and co-workers.[16]

The Fallis group has also produced some novel strained cyclophanes, which include **9**[13] and **10**, shown in Scheme 3.[14] These compounds can be viewed as dibenzododecadehydro[8]para- and -metacyclophanes, respectively. Oda and co-workers' cyclic *para*-phenylacetylenes (CPPA) **11a–d** stand out, not only because of their braceletlike structures, but also because their synthesis does not involve the use of palladium.[15] The precursor cyclophanepolyenes were generated by an intramolecular McMurry-type reaction and the triple

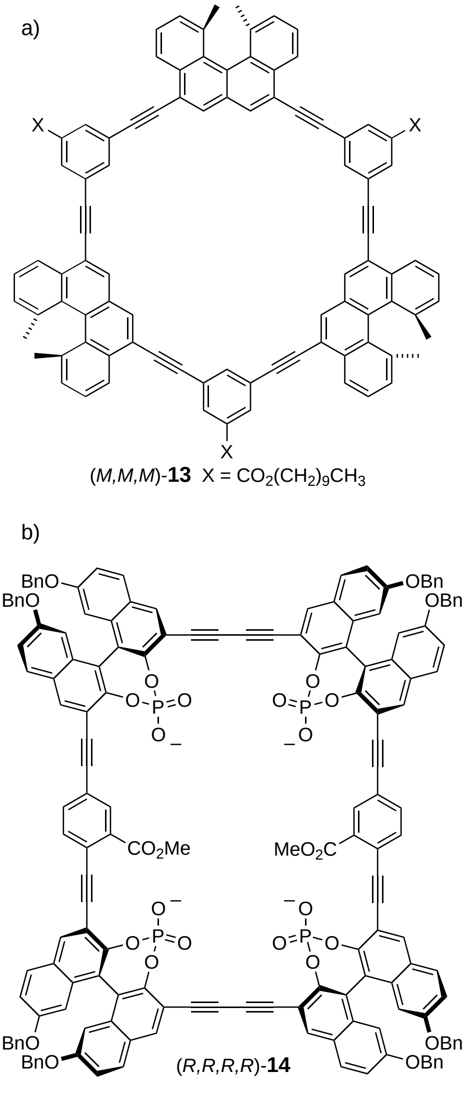
Table 1. Some structurally related arene–alkyne cyclophanes.



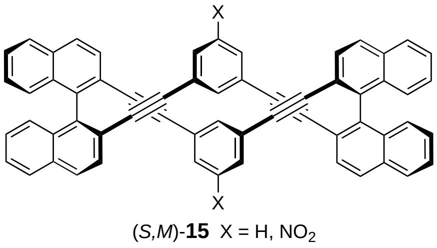
Compound	Linear arylene unit	Angular arylene unit	Alkynes	
			m	*n*
8a	1,4-phenylene	2,3-thiophendiyl	1	1
8b	1,4-perfluorophenylene	2,3-thiophendiyl	1	1
8c	1,4-phenylene and 1,4-perfluorophenylene	2,3-thiophendiyl	1	1
8d	4,4′-(2,2′-bipyridyl)ene	1,2-phenylene	1	2
8e	1,4-phenylene	1,2-phenylene	1	2
8f	1,4-(2-undecyloxyphenyl)ene	1,2-phenylene	1	2
8g	1,4-(2-(11-methoxy-11-oxoundecyloxy)phenyl)ene	1,2-phenylene	1	2

bonds were installed by an addition–elimination sequence. No evidence for cyclic conjugation in these systems has been obtained to date, but they were reported to form inclusion complexes with C_{60}, C_{70}, and hexamethylbenzene. Another interesting cyclophane is Sankararaman and co-workers' [6.6]metacyclophane **12**, which features enediyne bridges.[16] We await with interest the outcome of studies on the reactivity of the bridges in this and related systems.

A new wrinkle in the synthesis of enantiomerically pure cyclophanes is the use of enantiomerically pure chiral aromatic systems as building blocks. Yamaguchi and co-workers employed single enantiomers of a [4]helicene derivative to prepare every possible stereoisomer of **13** (Scheme 4).[17] The various stereoisomers of **13** aggregated in organic solvents (dimer formation) and the stereochemistry of the helicene units influenced the aggregation. The (*R*)-binol-derived tetraphosphate (*R*,*R*,*R*,*R*)-**14** was reported by Droz and Diederich,[18] and exhibited a high affinity for two disaccharides in the competitive solvent mixture CD_3OD-CD_3CN. Finally, Otera's group used the 1,1′-binaphthyl unit as the source of chirality for some enantiopure double-helical cyclophanes, for example, (*S*,*M*)-**15** (Scheme 5).[19] In addition to the sheer beauty of these structures, a noteworthy feature of this work is that the solution and solid-state CD spectra agree with one another. This led the authors to suggest that the structures of these cyclophanes change little on going from solution to the solid state. Once again, palladium played a key part in the syntheses of **13**–**15**.

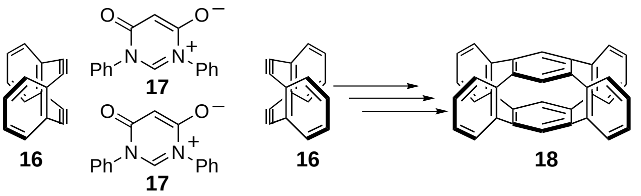


Scheme 4. a) One isomer (*M*,*M*,*M*) of the Yamaguchi[17] cyclophane; b) the cyclophane reported by Droz and Diederich.[18]



Scheme 5. Otera and co-workers' double-helical cyclophanes.[19]

Hot off the press is Wudl and co-workers' tetrabenzannulated 1,2,4,5-cyclophanetetraene (**18**), which was prepared by a remarkably short and imaginative route (Scheme 6).[20] Two units each of the DBA **16**[21] and the mesoionic heteroaromatic diene **17**[22] were united through successive hetero-Diels–Alder/retro-hetero-Diels–Alder reactions to produce **18**. This strained [2_n]cyclophane, which sets a new standard for the number of unsaturated and/or benzannulated two-carbon-atom bridges, reacts rapidly with tetracyanoethylene (TCNE) to form a Diels–Alder adduct with no apparent formation of a charge-transfer complex.



Scheme 6. A strained cyclophane made by Wudl and co-workers through a series of cycloaddition reactions.

Palladium-catalyzed cross-coupling reactions have clearly worked wonders for the field of cyclophane chemistry. We look forward with great enthusiasm to subsequent developments in this area and, of course, to the next methodological revolution and the novel, interesting, and useful cyclophanes that it will surely produce.

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Odd-Electron Bonds and Biradicals in Main Group Element Chemistry[**]

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Radicals play a crucial role in bond-forming and bond-breaking processes.[1] In hydrocarbon chemistry, however, carbon-centred radicals are usually observed as rather short-lived intermediates.[2] Some selected recent examples serve as highlights to demonstrate that in main group element chemistry (apart from C) such reactive intermediates can be stabilized even to such an extent that they can be isolated in crystalline form.

Odd-Electron Bonds

To study the generation of a new type of a genuine two-center, one-electron (2c1e) P–P bond, Geoffroy, Mathey, Le Floch et al.[3] developed the macrocyclic system **1**. Compound **1** contains two phosphinine units, PC_5R_5, which are linked by two flexible siloxane bridges to form a twelve-membered heterocycle. In the ground state conformation, the two phosphinine ring planes are almost coplanar and the two phosphorus atoms approach each other to a distance of 3.26 Å (Scheme 1).

This neutral precursor can be reversibly reduced at a potential of $E^\circ_{1/2} = -1.85$ V and $E^\circ_{1/2} = -2.10$ V (scan rate $5\,V\,s^{-1}$, THF) to give the radical anion **2** and the dianion **3**, respectively. Chemically, **1** was reduced with sodium naphthalenide. The combination of the results from X-ray analyses of the neutral precursor **1** and the fully reduced dianion **3** with the results from EPR spectroscopy and DFT calculations for the persistent phosphorus radical anion **2**, demonstrated that in this case the unpaired electron resides in the single-occupied molecular orbital (SOMO; Scheme 1). This SOMO is partially delocalized over both phosphinine rings, but mainly localized in a P–P σ bond. Notably, the P–P distance in **2** has shortened considerably and lies between that of the neutral compound **1** and that of the fully reduced form **3**, in which a 2c2e P–P bond has formed and the phosphinine rings deviate strongly from planarity.

The formation of the P–P bond in **2** and **3** resembles the creation of S–S bonds in the intensively studied radical cations of type **II** and dications of type **III** of polysulfur compounds (Scheme 1, bottom).[4] The chemical process of bond making and the electronic configuration is different in these sulfur compounds. In the neutral precursor **I**, the nonbonding electron pairs of the two –S– entities interact to

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