Toward Antikekulene: Angular 1,2-Di-, 2,3-Di-, and 1,2,15,16-Tetrachloro[6]phenylene

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Abstract: The synthesis of the first ring-functionalized heliphenes is described, comprised of angular 1,2-di-, 2,3-di-, and 1,2,15,16-tetrachloro[6]phenylene, via a series of Sonogashira couplings and cobalt-catalyzed alkyne cyclotrimerization steps. These molecules are explored as potential precursors to antikekulene and their reactivity compared to that of the parent angular [6]phenylene. An X-ray structural determination of 1,2,15,16-tetrachloro[6]phenylene reveals a structure with a considerably larger helical separation than in [6]phenylene, caused by the bulk of the appended chlorine atoms.

Key words: alkynes, cobalt, cycloaddition, helical structures, polycycles

The cyclophenylene[1] antikekulene (**1**),[2] in which the minimization of cylobutadienoid circuits enhances the relative importance of a resonance form (shown) with peripheral inside and outside antiaromatic superdelocalization, has been elusive. The hitherto most promising strategy, based on a triple $CpCo(CO)_2$-catalyzed cycloisomerization of a hexaethynyltribenzocyclyne, aimed at generating the three benzene rings indicated in red in structure **1** in a single operation, was upended by the (presumed to be kinetic) failure of the last cyclization.[3] The subsequent preparation of the helical angular phenylenes (heliphenes),[4] including [6]heliphene (**2a**),[4a] suggested an alternative approach featuring the cross-coupling of its two terminal arene units (blue bonds in **1**) in the final step (Figure 1). While this scheme is ambitious, it was thought to be facilitated by the close proximity of the carbons involved (e.g., in **2a**, H1–H15 = 2.36 Å).[4a]

Encouraged by the observation of facile 2 H and 4 H loss in the mass spectrum of **2a** (see Supporting Information),[4a] unique in the series of available heliphenes,[4] initial studies focused on this molecule. Closer scrutiny by matrix-assisted laser desorption/ionization–time-of-flight mass spectrometry (MALDI–TOF-MS)[5] revealed a pristine molecular ion ($m/z = 448$) at low laser power. Increasing the latter led to the emergence of major peaks at $m/z = 446$ and 444, accompanied by a fragment indicating loss of C_2H_2.[6] These findings suggested the preparative flash-vacuum-pyrolytic (FVP) treatment of **2a**, which might engender **1** and/or other novel structures.[7] In the event, **2a** proofed to be remarkably resilient to change on sublimation (6×10^{-7} torr) through a hot quartz tube at temperatures up to 800 °C, beyond which it decomposed to black soot. Hoping to achieve Scholl-type[8] (at least) single-bond formation across the termini, **2a** was exposed to $FeCl_3$ (H_2O, 2 equiv, 100 °C) or $Cu(SO_3CF_3)_2$–$AlCl_3$ (CS_2, 20 °C), leading only to recovered starting material. $VOCl_3$ (CH_2Cl_2, 2.5 equiv, 23 °C), caused immediate decomposition, while 30% Pd/C in boiling 1-methyl-4-(1-methylethyl)benzene (*p*-cymene, 177 °C) left **2a** largely intact (ca. 20% decomposition). Finally, simple irradiation (Rayonet, THF, 300 and 350 nm, 4 h) also had no effect.

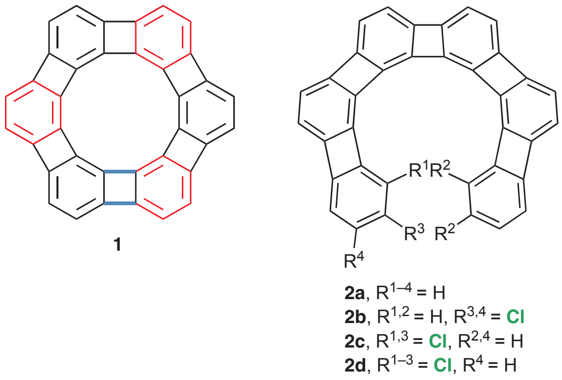

Figure 1

In view of the preceding failures, attention turned to end-ring-functionalized derivatives of **2a**, specifically chloro-substituted versions, chosen to avoid interference of the halogen with the requisite Sonogashira coupling[9] and Co-catalyzed alkyne cyclotrimerization steps[10] of the envisaged synthesis. Such ring-functionalized derivatives of the heliphenes are unknown.[1,3,4,7] For reasons of preparative ease, the (from a regiochemical stand point less desirable) angular 2,3-dichloro[6]phenylene (**2b**) frame was targeted first, assembled by appropriate modification of the approach to **2a**,[4a] shown in Scheme 1 (see Supporting Information). It commenced with 1,2-dichloro-4,5-diiodobenzene (**3**)[10] and its nonselective heterobisalkynylation to **4** and selective deprotection to **5**. Attachment of synthon **6**[3] engendered **7**, which was elaborated similarly, but now with building block **8**,[4] to assemble crucial hexayne **9**. Prototetradesilylation followed by $CpCo(CO)_2$-catalyzed double cyclization ended in **2b**. An alternative triple cyclooligomerization strategy[4] that constructed 8 of the 11 rings in the final step from an oc-

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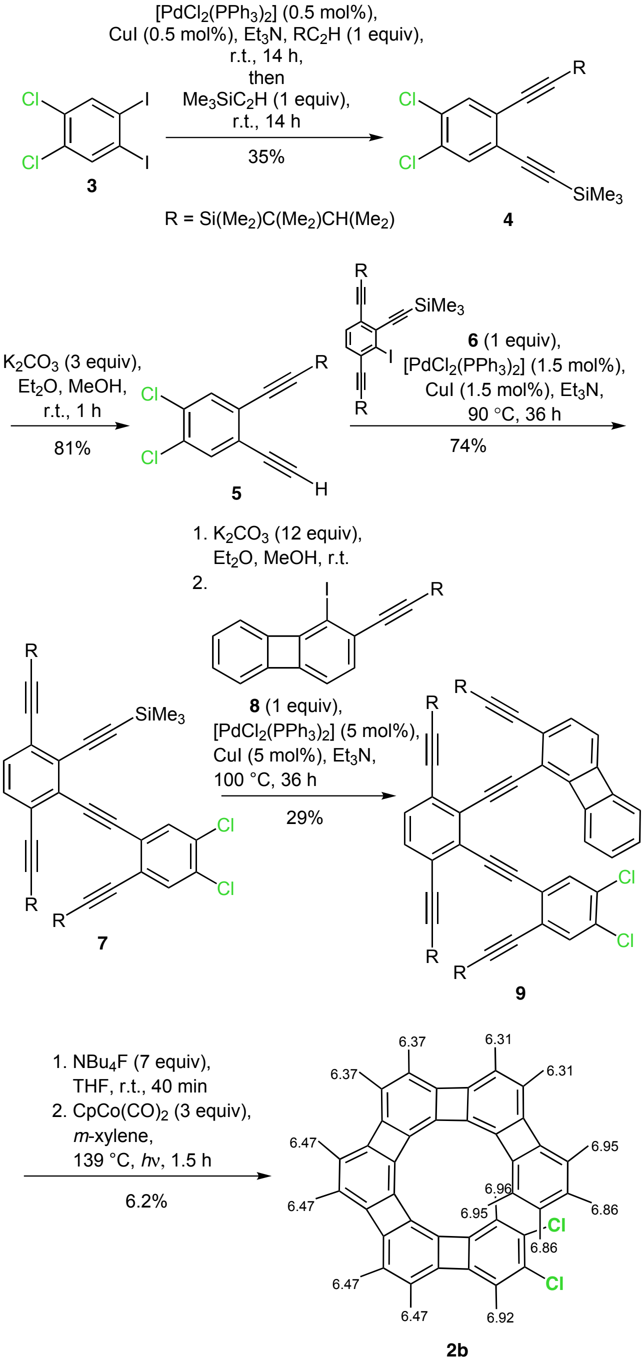
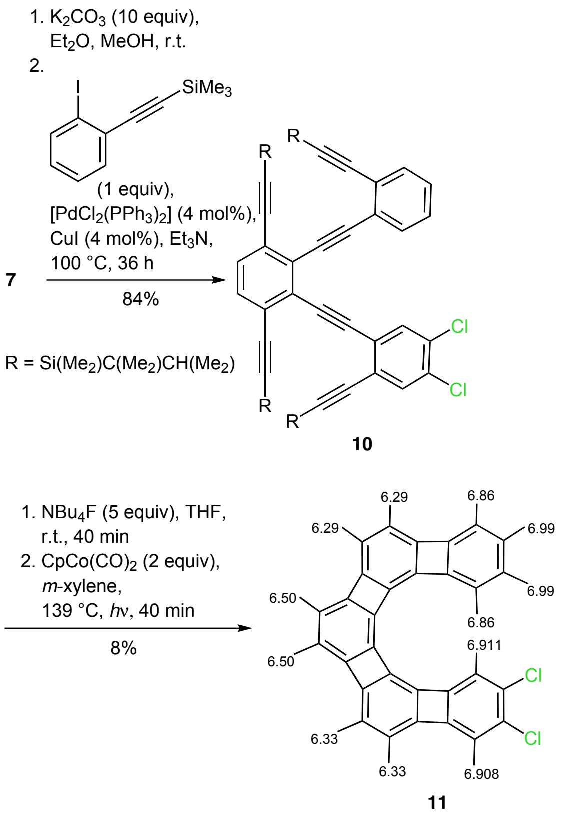
tayne pieced together from **6** and **7** was also successful but suffered from low yields (see Supporting Information). Finally, for purposes of comparison, the lower benzocyclobutadienologue 2,3-dichloro[5]phenylene (**11**) was prepared (see Supporting Information), in analogy to the double cyclization scheme depicted in Scheme 1, but substituting 1-iodo-2-(trimethylsilyl)ethynylbenzene[11] for **8**, thus accessing **10** as the framework to be subjected to the cobalt cyclization (Scheme 2).



Scheme 1 Synthesis of **2b** [with ^{1}H NMR data, δ (ppm), CD_2Cl_2]

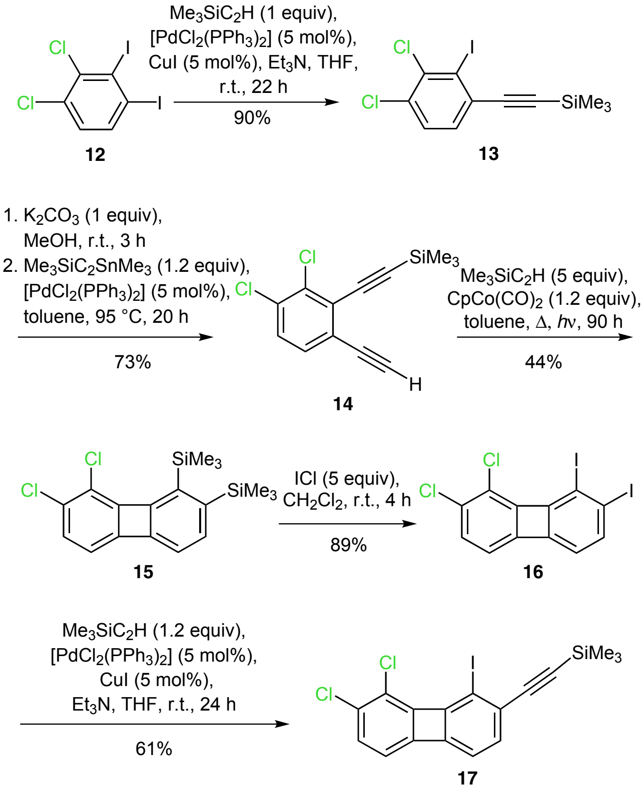


Scheme 2 Synthesis of **11** [with ^{1}H NMR data, δ (ppm), CD_2Cl_2]

The NMR and UV/vis spectral data of the chlorophenylenes **2b** and **11** (see Supporting Information) differ only slightly from those of the parent systems,[4a,12] attesting to minimal perturbation by the halo substituents. In contrast, the mass spectrum of **2b** shows, in addition to the base molecular ion peak envelope at $m/z = 516$, 518, and 520 (9:6:1), a prominent fragment ion at $m/z = 444$ ($C_{36}H_{12}$, 27%), signalling the loss of two HCl molecules. MALDI–TOF confirms this ready fissure, with the fragment ion becoming dominant at high laser power. As in the case of **2a**, it is tempting to associate this process with the generation of antikekulene **1**, now facilitated by 1,2-hydrogen shifts of the phenyl radicals arising from Cl atom extrusion.[13] That it is the close proximity of the terminal arene nuclei in **2b** which is responsible for this behavior is indicated by the corresponding mass spectrum of **11**: The parent ion at $m/z = 442$ is also the base peak, and Cl loss is relatively minor.

Armed with this information, attempts were made to access **1** from **2b** preparatively, albeit unsuccessfully. Thus, attempted FVP (850 °C, 6×10^{-6} torr) led to decomposition to soot. Similarly, **11**, while stable up to 900 °C, disintegrated at 1000 °C. Turning to a transition-metal-catalyzed C–H arylation protocol,[14] particularly inspired by the precedence for metal migration,[15] which might relocate functionality from the 2,3- to the required 1,2-loci, **2b** was exposed to $[PdCl_2(PPh_3)_2]$ (Et_3N, MeCN, 120 °C, 20 h). Surprisingly, hydrodechlorination with simultaneous complete four-membered ring hydrogenolysis[16] took place to give what appears to be a mixture of sexiphenyl isomers, as indicated by the mass spectrum (*m/z* = 458) and the replacement of the characteristically shielded phenylene signals in the ^{1}H NMR spectrum by 'normal' aromatic signals (δ = 7.1–7.8 ppm, m; see Supporting Information).[17]

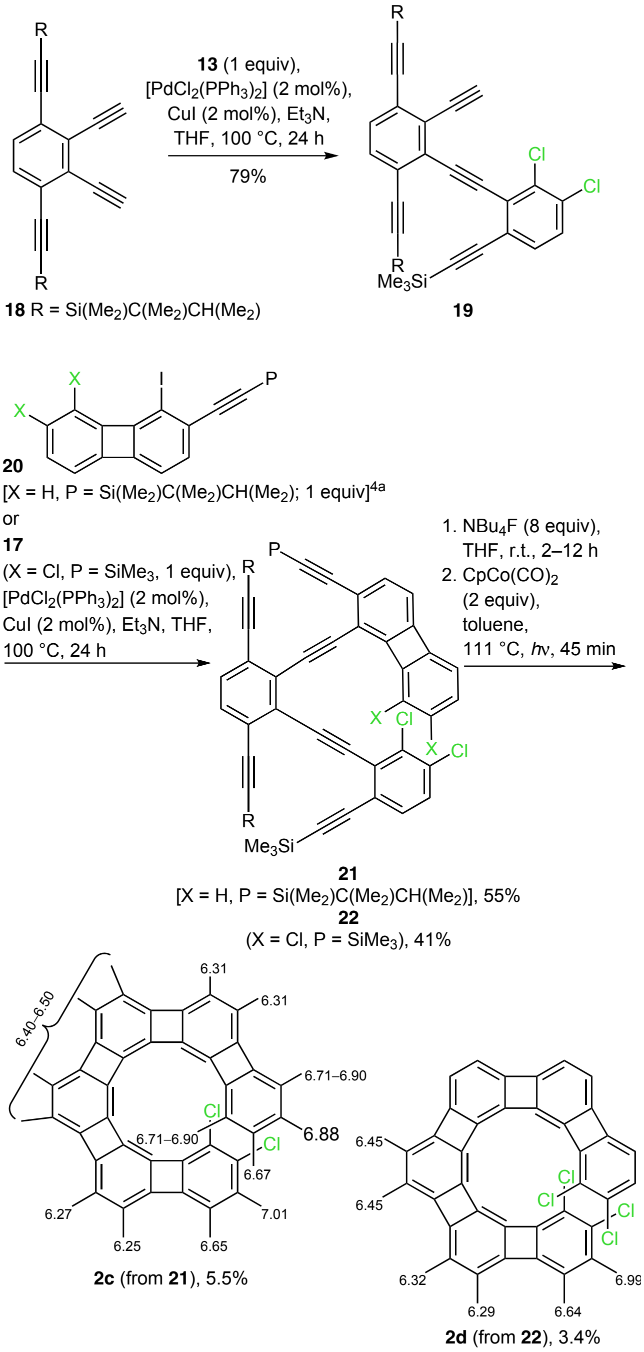
At this stage, it became apparent that the plan to utilize the 2,3-dichloro topology as a latent 1,2-functional synthon may have been too ambitious. Consequently, the identity of the targets shifted to the much more attractive 2,3-di- and 1,2,15,16-tetrachloro[6]phenylenes **2c** and **2d**, respectively. Contemplation of the alterations of Scheme 1 required to reach these structures highlights the need for 1,2-dichloro-3,4-diiodobenzene (**12**), not only to replace **3**, but also to construct a 1,2-dichloro analogue of **5** (i.e., **14**) and 7,8-dichloro derivative of **8** (i.e., **17**; Scheme 3). At the outset of this work, **12** was unknown, but convenient access was developed by us recently,[18] the yield of which was further improved here on scale-up (255 mmol; see Supporting Information).



Scheme 3 Synthesis of dichloro building blocks **14** and **17**

From **12**, the assembly of **14** and **17** proceeded as shown in Scheme 3. The sterically controlled regioselectivity of the single Sonogashira coupling[18] to **13** was crucial and confirmed by an independent synthesis of **13** from 2,3-dichloro-6-iodoaniline[19] (see Supporting Information). Desilylation of **13**, followed by Stille coupling,[20] furnished the regiodifferentiated diyne **14**, which was subjected to partly selective cobalt-catalyzed cocyclotrimerization with (trimethylsilyl)acetylene (TMSA)[21] to give **15** (in addition to its metabissilyl isomer, ratio = 3:1). Diiodination rendered 1,2-dichloro-7,8-diiodobiphenylene (**16**), which constitutes a valuable building block for the synthesis of other angular phenylenes. As observed for 1,2-diiodobiphenylene,[21a] this molecule underwent selective β-Sonogashira coupling with TMSA to provide **17**.

The utilization of **13** and **17** in the creation of the final targets is depicted in Scheme 4, starting from **18**[3] and its gratifyingly selective single coupling with **13** to give **19**. The remaining steps followed the previous strategy to the angular [6]phenylene nucleus.[4a]



Scheme 4 Assembly of **2c** and **2d** [with ^{1}H NMR data, δ (ppm), CDCl$_3$]

To determine the effect of the added chlorine atoms in **2d** on the helical structure of the parent **2a**,[4a] an X-ray structural investigation was carried out (Figure 2).[22] Compound **2d** crystallizes with two independent molecules **A** and **B** in the asymmetric unit, exhibiting very similar bond lengths and angles, but differing substantially in the degree of helical separation, the latter much more pronounced than in **2a**. Thus, the shortest intramolecular contacts in **2d** are between Cl1 and Cl4: 3.471 Å for **A**, and 3.416 Å for **B**, held roughly at van der Waals distances (ca. 3.50 Å)[23] by increasing the distance and interplanar angle of the terminal benzene nuclei to 5.885 Å and 33.40° (**A**), and 6.374 Å and 39.83° (**B**), respectively. At the B3LYP/6-311G** level, the geometries of both molecules (**A** and **B**) converged to a single symmetrical C_2 topology with a Cl1···Cl4 distance of 3.669 Å and corresponding separation and interplanar angle of the terminal benzenes of 6.302 Å and 39.61°, respectively. In contrast, the shortest contact in **2a** is between the terminal hydrogens H1 and H4 (adopting the numbering for Cl from above) at 2.364 Å, necessitating lesser distortion of the helix (terminal benzene ring distances and angles: 5.62 Å and 22.8°).

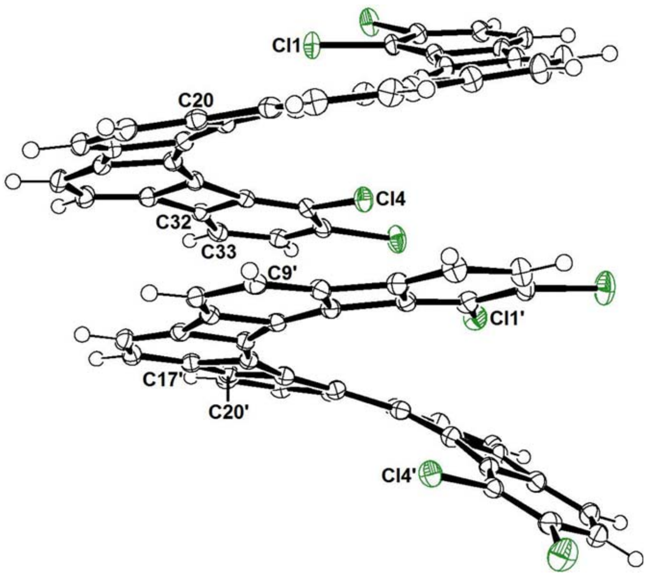


Figure 2 ORTEP plot of **2d** showing two molecules (**A**, top; **B**, bottom) in the unit cell

The data are a testament to the pronounced flexibility of the heliphenes[4] and the phenylenes in general.[24] This facet is also reflected in the variance of interplanar angles between successive fused six- and four-membered rings: for **A**, 3.01, 5.14, 3.51, 3.31, 4.76, 3.96, 5.86, 5.45, 5.68, and 2.63°; for **B**, 1.60, 1.19, 1.92, 2.74, 4.87, 4.93, 8.67, 8.51, 7.81, and 3.89° (computed for the C_2 structure: 3.60, 5.42, 4.54, 5.53, and 4.11°), revealing markedly uneven helical turns. For comparison, the (experimentally symmetrical) structure of **2a** displays values of 1.49, 3.35, 2.41, 3.28, and 3.28°.[4a] Despite these differences in topology, the computed energies of **A** and **B** (at experimental geometries) show the latter to be more energetic by only 0.12 kcal mol^{-1}. Finally, **A** and **B** form offset π-stacked pairs (Figure 2), juxtaposing two angular [4]phenylene substructures, with close contacts C33···C20′ = 3.277 Å, C20···C9′ = 3.290 Å, C32···C17′ = 3.380 Å, and Cl1′···Cl4 = 3.494 Å (see Supporting Information).

With small amounts of **2c** and **2d** in hand, their feasibility as precursors to antikekulene (**1**) was assessed. Disappointingly, inspection of the mass spectrum of **2c** showed it to be essentially identical to that of **2b**, with the molecular ion at *m*/*z* = 516 constituting the base peak, and loss of two HCl molecules [*m*/*z* (%) = 444 (37)] not being relatively accentuated. Similarly, **2d** exhibits the [M]$^+$ pattern expected for a tetrachloride [*m*/*z* (%) = 591 (4), 590 (14), 589 (19), 588 (56), 587 (39), 586 (100), 585 (31), 584 (78)], the fragment at *m*/*z* (%) = 444 (20) ([M – 4 Cl]$^+$ also not especially pronounced. For comparison, 1,2-dichlorobiphenylene (accessed by protodesilylation of **15**; see Supporting Information) displays *m*/*z* (%) = 220 (100, [M]$^+$) and single [185 (15)] and double loss of Cl [150 (40)] to a similar degree. Since these data were unencouraging with respect to pyrolytic attempts to generate **1**, a (substance) limited foray (^{1}H NMR experiments, mg scale, THF-d_8) into the intramolecular cross-coupling of **2d** was taken,[25] with mixed results. Thus, nickel-catalyzed methods[26] led to complete decomposition, while Mg; Mg–Cu(AcO)$_2$; Na; (activated)[27] Cu; or Na–CuI proved inert. Most promising was activated Cu–Na–CuI at room temperature, which led reproducibly to the clean emergence of a singlet at δ = 5.97 ppm, before complete decomposition set in, thus precluding the recording of a ^{13}C NMR spectrum. This behavior, in addition to the unique chemical shift outside the range of plausible impurities[28] and tantalizingly close to that calculated for **1** (δ = 6.20 ppm),[2e] are promising. Corroboration of this speculation will have to await large-scale syntheses of **2d** and its preparative conversion.

In conclusion, we have synthesized the first ring-functionalized heliphenes **2b**–**d**, in which the halogen should provide a general handle with respect to structural modification, particularly for materials applications.[29] Some evidence, albeit speculative, has been obtained suggesting **2d** as a hopeful precursor to antikekulene (**1**).

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Supporting Information for this article is available online at http://www.thieme-connect.com/products/ejournals/journal/10.1055/s-00000083.

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