Synthetic Strategies for Dehydrobenzo[*n*]annulenes

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In memoriam Leroy H. Klemm

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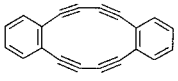
Dehydrobenzoannulenes have accrued great interest due to their potential uses such as hosts for binding guest molecules and precursors to fullerenes and other carbon-rich materials, as well as their unique properties such as conductivity or superconductivity and nonlinear optical effects. These systems have seen numerous synthetic strategies employed in their construction over the past 50 years. As alkyne chemistry has developed more recently, annulene networks with greater complexity have been possible and the field has seen a vast resurgence. This article gives an account of synthetic methods developed for the preparation of annulenic systems and describes some of the interesting observed properties.

1 Introduction

By the late 1980s dehydrobenzoannulene (DBA) chemistry was a mature field on the decline. The 35+ years of research devoted to molecules comprised primarily, if not exclusively, of benzene rings linked by carbon−carbon triple bonds (e.g., **1**) had produced a large number of macrocycles.[1] The main impetus driving these studies had been questions of whether planar examples of such ring systems were able to sustain induced ring currents, and if so, what was the strength of those ring currents. From the myriad of compounds produced, the main conclusion to the questions was that ring currents in these systems were extremely weak and, in some cases, even undetectable based on standard spectroscopic techniques. Subsequently, such research was deemed unfashionable for many years and thus new investigations came to a virtual halt.



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Grant J. Palmer (not pictured) was born in Chicago, Illinois in 1972. He received his B.S. in chemistry from the University of the South in 1996. During his undergraduate education he worked in the laboratory of Professor Timothy Blair. He received his Ph.D. from the University of Kentucky in 2001. His work there under Professor John E. Anthony dealt with the synthesis of annulenes derived from acenaphthylene. After spending a postdoctoral year in the laboratory of Professor Haley at the University of Oregon, he accepted a position at Albany Molecular Research Inc., in Albany, New York where he is currently doing custom scale-up synthesis of pharmaceutical intermediates.

Michael M. Haley (right) was born in 1965 in Lake Charles, Louisiana. After growing up in Tulsa, Oklahoma, he studied cyclopropene and cyclopropararene chemistry with Prof. W. E. Billups at the Rice University where he received both his B.A. (1987) and Ph.D. degrees (1991). In 1991 he received a National Science Foundation Postdoctoral Fellowship to work with Prof. K. P. C. Vollhardt on [N]phenylene chemistry at the University of California, Berkeley. In 1993 he joined the faculty at the University of Oregon where he is currently an Associate Professor of Chemistry and a member of the Materials Science Institute. Included among the honors and awards he has received are a National Science Foundation CAREER Award (1995), a Camille Dreyfus Teacher-Scholar Award (1998), an Alexander von Humboldt Research Fellowship (2000), and the Thomas F. Hermann Distinguished Teaching Award (2002). In addition to dehydrobenzoannulene chemistry, his current research also focuses on the formation of metallabenzenes and valence isomers using vinylcyclopropene ligands as well as the synthesis of novel heterocycles via reactive intermediates. Outside the laboratory he can be found enjoying the great state of Oregon − gardening, wine tasting, snowboarding, or whitewater kayaking.

MICROREVIEWS: This feature introduces the readers to the authors' research through a concise overview of the selected topic. Reference to important work from others in the field is included.

The last decade of the 20th century heralded a rebirth of DBA chemistry. A number of synthetic discoveries, most notably Pd-mediated cross-coupling reactions between sp- and sp^2-carbon centers, were adopted from other areas of organic chemistry. These improvements made the previously laborious task of macrocycle assembly now a quick and efficient process. The ability to create new DBAs allowed chemists to easily functionalize the annulene backbone and thus tailor the chemical reactivity and physical properties of the macrocycle. Recognition of potential materials applications for these π-electron rich systems has driven most of the DBA research conducted currently. Indeed, DBAs have been shown to exhibit nonlinear optical behavior, to polymerize giving tubular polymers, and even to explode furnishing ordered carbon nanostructures.

The purpose of this microreview is twofold. First, we will survey the two main synthetic strategies employed for dehydrobenzoannulene synthesis, highlighting the strengths and weaknesses of each technique as well as providing salient examples of molecules prepared by each methodology. Second, we will present a number of more recent studies illustrating both the synthetic advances reported over the last 6−8 years and the interesting chemical reactivity and physical properties found in the resultant macrocycles.

2 Synthetic Strategies

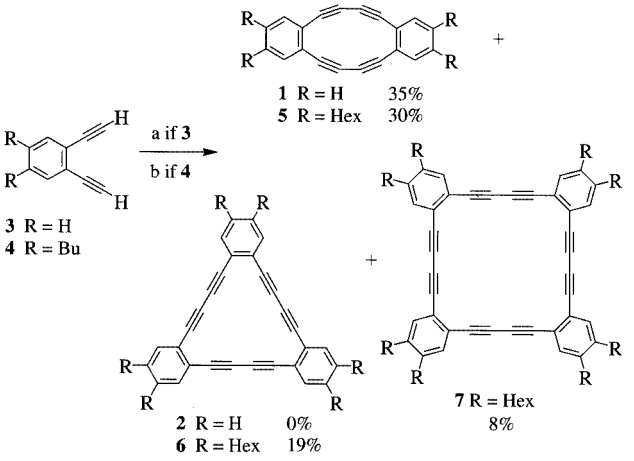
DBA synthesis can be divided into two main categories based on the method by which the ring is built, either *intermolecular* or *intramolecular*. The classical approach is by an intermolecular reaction in which the ring closure involves formation of two or more new bonds. The intramolecular approach, which has been utilized more often in recent years, involves the creation of only one new bond per ring formed. These two main headings can be subdivided further by the number of alkyne units between phenyl rings, by the number of atoms in the ring, and by whether the resultant annulene is symmetrical or unsymmetrical. The subcategory that each DBA falls into depends upon the starting materials used and the type of reaction by which cyclization occurred.

2.1 Intermolecular Approach

The cyclooligomerization technique, nX = Z, where several (n) of the same components (X) are coupled together to form the ring (Z) was the initial intermolecular approach developed. This method is still widely used today for macrocycle synthesis. The second procedure under this category is an X + Y = Z technique in which two different components (X and Y) are brought together to form the ring (Z). It should be noted that this intermolecular technique has only been used to form monoyne structures.

2.1.1 nX = Z

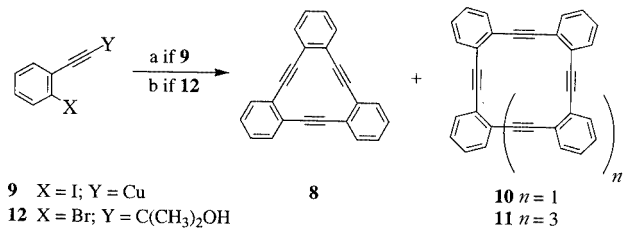
The first reported phenylacetylene macrocycle was prepared by Eglinton et al. in the late 1950s using the intermolecular nX = Z approach targeting trimeric [18]annulene **2**.[2] They later reported the correct structure of the isolated material to be that of dimer **1**,[3] with no observation of higher macrocycles such as **2** (Scheme 1). The Eglinton cyclooligomerization method is the simplest approach to a diacetylenic or larger annulene, where the synthon is coupled with itself to form the final macrocycle, and uses chemistry initially developed by their group. The Eglinton coupling[4] involves the oxidative dimerization of terminal acetylene moieties, in this case *o*-diethynylbenzene (**3**), using $Cu(OAc)_2$ under high dilution in pyridine. This procedure and numerous other variations of Cu-mediated oxidative homocoupling of alkynes[5] have been utilized for DBA synthesis.



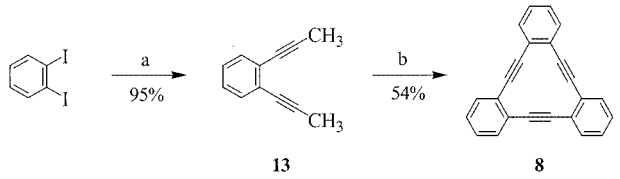
Scheme 1. Reagents: (a) $Cu(OAc)_2$, pyridine, MeOH; (b) CuCl, TMEDA, *o*-dichlorobenzene, O_2

In 1994 the Swager group repeated this procedure for annulene synthesis using arenes possessing various solubilizing groups (**4**), which produced dimer **5** as well as larger macrocycles **6** and **7** (Scheme 1).[6] This was the first time that larger diacetylenic annulenes had been reported for this type of reaction, such that $n > 2$ for nX = Z. The isolation of **6** and **7** is attributed to the greater solubilizing character of the R groups, and the importance of these substituents will be clearly demonstrated for larger planar annulenes (vide infra).

Eglinton also used a variation of the intermolecular technique to prepare macrocycles such as **8** (Scheme 2).[7] Through a Castro−Stephens reaction,[8] with a copper acetylide group *ortho* to a halogen (**9**), only monoyne-connec-



Scheme 2. Reagents: (a) pyridine, reflux; (b) $Pd(PPh_3)_4$, CuI, KOH, $BnEt_3N^+Cl^-$, PhH, 85 °C



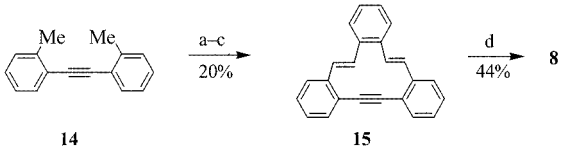
Scheme 3. Reagents: (a) propyne, $PdCl_2(PPh_3)_2$, CuI, NEt_3; (b) $(t\text{BuO})_3\text{W}{\equiv}\text{C}t\text{Bu}$, toluene, 80 °C

ted materials were produced by the cyclization. The reaction gave the desired [12]annulene **8** in a yield of 26% after isolation by preparative thin-layer chromatography. Youngs et al. repeated this work 20 years later and produced the same DBA **8** in 48% yield by purification using vacuum sublimation.[9] They also reported higher annulenes **10** and **11** isolated by column chromatography of the residue left in the sublimator. Huynh and Linstrumelle used an analogous Pd-mediated cross-coupling protocol to prepare **8** in 36% yield (Scheme 2).[10] Although not initially reported, this method also yields oligomers **10** and **11**.[11]

A recent report by Vollhardt and co-workers described the synthesis of DBA **8** by alkyne metathesis of dialkynylarene **13** (Scheme 3).[12] Through use of the catalyst $(t\text{BuO})_3\text{W}{\equiv}\text{C}t\text{Bu}$, **8** was formed in a moderate yield of 54%. This novel variation of the *n*X = Z intermolecular synthesis of DBA macrocycles is applicable to a variety of 4,5-disubstituted systems. Unfortunately, substituents *ortho* to the acetylene groups in **13** completely shut down the metathesis reaction, thus limiting the utility of this method.

2.1.2 X + Y = Z

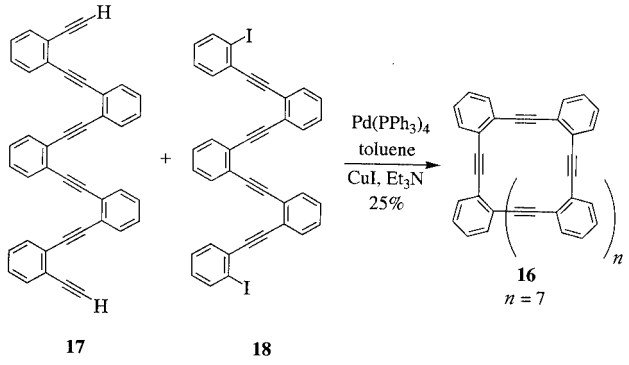
In 1966 Staab reported the first example of an X + Y = Z intermolecular reaction to produce DBA **8** (Scheme 4).[13] X and Y were the bis(ylide) derived from **14** and phthalaldehyde, which formed the ring **15** by a double Wittig reaction. Bromination of this intermediate followed by elimination afforded **8** in only 9% overall yield; however, higher oligomers such as **10** and **11** were not possible by this route.



Scheme 4. Reagents: (a) Br_2, CCl_4, NBS, BPO; (b) PPh_3, PhH; (c) i. PhLi, THF; ii. phthalaldehyde, THF; (d) Br_2, CCl_4; (e) *t*BuOK, THF

With the advent of modern Pd-catalyzed alkyne cross-coupling reactions such as those discovered by Stille[14] and Sonogashira,[15] a resurgence in annulene chemistry was seen. Alkyne groups can be more easily placed in a variety of positions on the phenyl rings under these conditions. Cross-coupling reactions in combination with existing alkyne homodimerization techniques are viable routes to compounds such as **8** and other larger annulenes according to the X + Y = Z methodology. Iyoda has used a Pd-catalyzed cross-coupling to form the parent [12]annulene **8** in 39% yield from 1,2-diiodobenzene and excess acetylene gas in a single step.[16]

Similarly, Youngs has formed larger annulenes such as **16** (Scheme 5).[17] Iterative Sonogashira cross-coupling synthesis provided coupling components **17** and **18** which ultimately formed the ring system.



Scheme 5

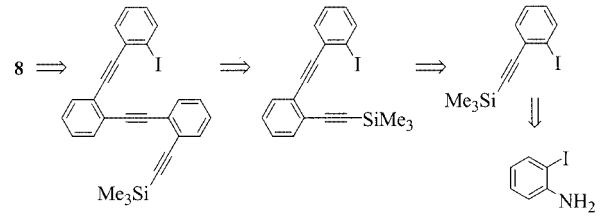
2.2 Intramolecular Approach

The main benefit to an intramolecular approach in DBA synthesis is that the likelihood for formation of oligomeric compounds is minimized. Intramolecular syntheses provide a rational route to a single product, which improves the yield of the ring-closing step and greatly facilitates purification. A much larger array of annulene topologies are possible using an intramolecular approach, and it is the only viable way to produce unsymmetrical systems and those possessing lower symmetry. A drawback of this methodology is the increased number of steps needed to assemble the precursor for cyclization. Nevertheless, a majority of recent annulene syntheses use this approach. The versatility of alkyne cross-coupling reactions for annulene systems will also be fully demonstrated by intramolecular routes.

The intramolecular class can also be divided into two main subcategories. The first involves a linear synthesis in which the molecule is built up until the ring is ready for the final intramolecular closure. The other intramolecular procedure uses a convergent synthesis of two or more components which are cross-coupled together to form the precursor to cyclization, followed by the final intramolecular closure of the ring.

2.2.1 Linear

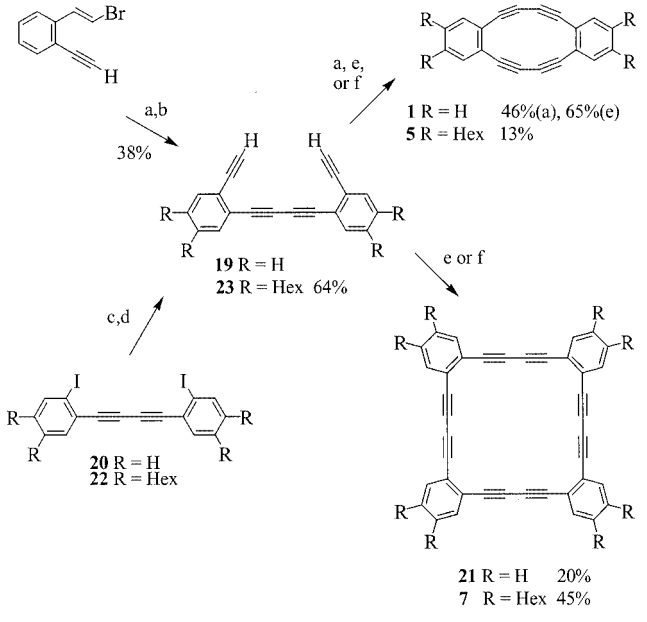
The linear methodology involves the greatest number of steps needed for the synthesis of intermediates, mostly by way of cross-coupling reactions. One of the simpler annulene syntheses by this route is that of parent [12]annulene **8** done by Haley et al., which still proceeds through 10 steps (Scheme 6).[18] For this reason examples of linear intramolecular syntheses are limited to that of **8** and a few larger [12]annulene systems, which will be described later.



Scheme 6. Linear intramolecular approach to synthesis of **8**

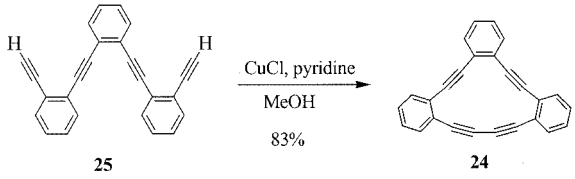
2.2.2 Convergent

The first example of a convergent synthesis of a DBA was reported in 1964 by Eglinton as a structural proof of his earlier product, strained annulene **1**.[19] Alkyne dimerization of the starting material by using $Cu(OAc)_2$ in pyridine allowed no possibility for the formation of cyclic materials (Scheme 7). Elimination on the bromo intermediate gave **19** which was intramolecularly homocoupled to form **1**. Youngs later synthesized **19** by Pd-mediated cross-coupling from **20** and repeated the cyclization (Scheme 7).[20] By using CuCl rather than $Cu(OAc)_2$ and bubbling air through the reaction mixture, Youngs was able to isolate not only **1** but also dimer **21** in 20% yield. Swager had incorporated solubilizing groups on the diacetylene **22**, and with an analogous synthesis produced [12]annulene **5** and [24]annulene **7** (Scheme 7).[6] The larger ring system **7** (45%) was favored over **5** (15%) with the hexyl chains attached. The benefit and/or drawback of these dimerization approaches are that only products with an even number of phenyl rings can be formed.



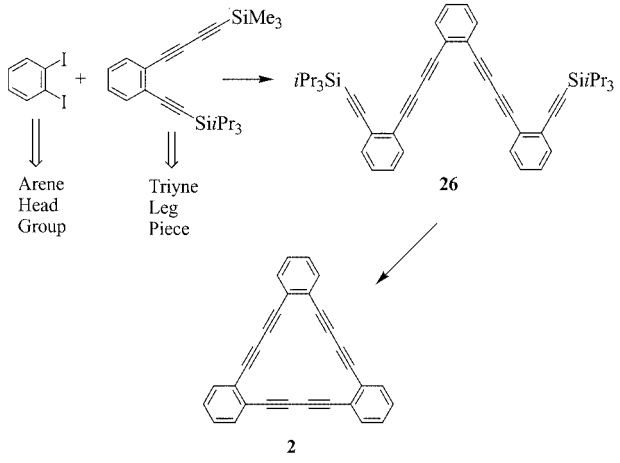
Scheme 7. Reagents: (a) $Cu(OAc)_2$, pyridine, MeOH; (b) *t*BuOK, *t*BuOH; (c) $HC{\equiv}CSiMe_3$, $PdCl_2(PPh_3)_2$, CuI; (d) KF or KOH, H_2O, THF, MeOH; (e) CuCl, pyridine, O_2; (f) CuCl, TMEDA, *o*-dichlorobenzene, O_2

With the intramolecular route, a variety of annulenes that cannot be prepared by any other method are possible. This point is exemplified by Vollhardt and Youngs' synthesis of the tribenzo[14]annulene **24** (Scheme 8).[21] Intramolecular cyclization of **25** (an intermediate in Youngs' synthesis of [40]annulene **15**) with CuCl in pyridine/MeOH afforded macrocycle **24** in excellent yield (83%). Because of the C_{2v} symmetry of **24**, only an intramolecular cyclization could furnish this molecule.



Scheme 8

The Haley group has used the convergent intramolecular approach for the vast majority of the annulenes prepared at Oregon. The key step in our syntheses of diacetylenic annulenes is an in situ deprotection/alkynylation protocol. Due to the instability of the terminal diacetylenes that are frequently employed, a selective protiodesilylation must be carried out in situ using KOH, dissolved in a minimal amount of water, under otherwise typical Sonogashira cross-coupling conditions. A second protiodesilylation and Cu-mediated oxidative dimerization of the deprotected alkynes are the ring-closing steps in DBA construction. These reactions are exemplified by the synthesis of [18]annulene **2** (Scheme 9).[22] The arene head group and the triyne leg components are cross-coupled after selective in situ deprotection of the more labile TMS group with base. The product of this reaction is **26**, upon which the triisopropylsilyl (TIPS) group is removed by a fluoride ion. The resultant terminal monoyne is then homocoupled to form annulene **2** as the sole product. This set of reactions is the cornerstone for the methodology used by the Haley group and will be described later in more detail.

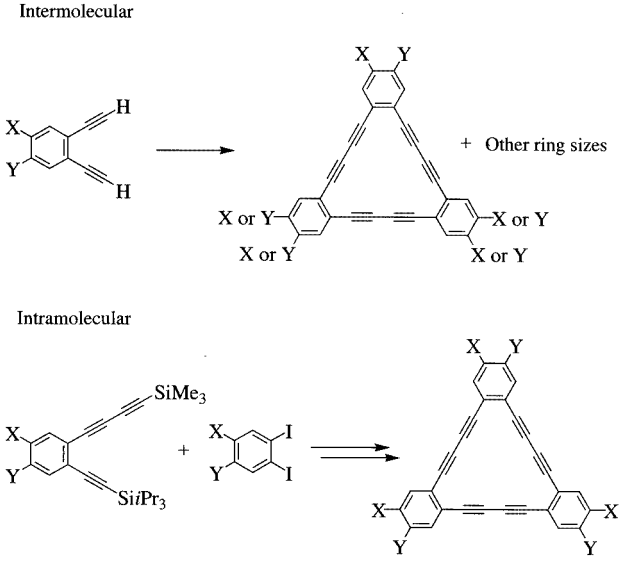


Scheme 9. Intramolecular approach to parent [18]annulene

2.3 Compare and Contrast

While annulenes can be synthesized by both intermolecular and intramolecular strategies, there are pros and cons to each method. The major drawback to the intermolecular approach is the high probability of forming numerous cyclooligomeric macrocycles, which are often difficult to separate and purify from the desired molecule. This drawback can be balanced by the ease with which the starting materials can be prepared and by the fewer overall number of steps that are needed to prepare the annulenes. This is most aptly demonstrated by Iyoda's single-step synthesis of the parent [12]annulene **8** using only two commercially available components.[16]

The main shortcoming of the intramolecular synthesis is the greater number of steps needed to assemble the more complex precursors prior to cyclization. However, the great advantage of this technique is the wide variety of new annulenes that can be prepared as the sole product of the cyclization, compounds that are otherwise impossible to prepare according to the intermolecular approach. The ability to place an assortment of functional groups at specific locations on the annulene is only possible through the intramolecular route (Scheme 10). Synthesis of these same functionalized systems by the intermolecular route would give a mixture of products with the functionalities in multiple positions, and separation of these products would be extremely difficult. An additional advantage of the intramolecular technique is the ability to assemble ring systems with unusual topologies such as molecules possessing low or no symmetry, hybrid structures with fused annulenes, and cycles containing various numbers of acetylene linkages.

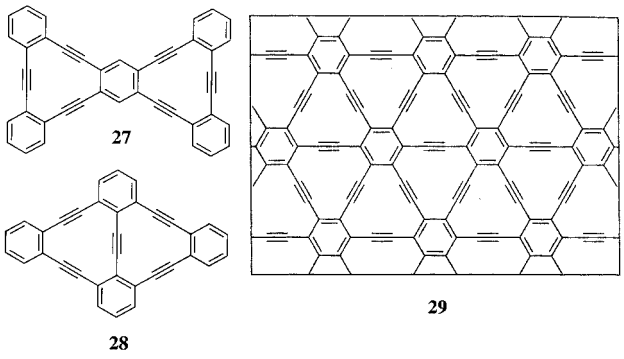


Scheme 10. Intermolecular vs. intramolecular syntheses

3 Dehydrobenzo[*n*]annulene Synthesis

3.1 Dehydrobenzo[12]annulenes

The superiority of the intramolecular route to complex macrocycles was quickly realized by the Haley group. Initial annulene syntheses were directed at the [12]annulene systems **27** and **28**, which are substructures of the theoretical all-carbon network graphyne (**29**).[23]

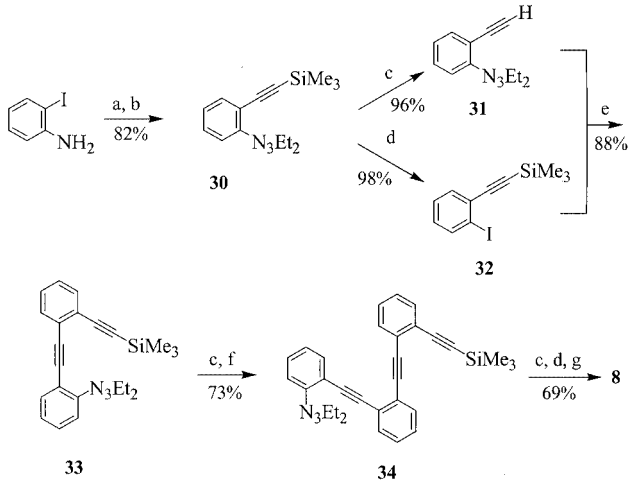


3.1.1 [12]DBA Revisited

An intermolecular approach similar to Linstrumelle's[10] was the first method attempted and yielded only polymeric material even under high-dilution conditions. At this point we decided to try a new approach by a linear intramolecular strategy comprised of alkyne protection/deprotection,[24] Pd-catalyzed alkynylation,[25] and conversion of triazenes into iodides[26] to build the system up before its final cyclization. To test the feasibility of this methodology, DBA **8**, previously prepared only by intermolecular routes, was synthesized.[27] This new approach to **8** should also improve the overall yield and eliminate the chromatographic separation of higher macrocycles. For the synthesis, 2-iodoaniline was first diazotized and quenched with Et_2NH to give the triazene, then cross-coupled with TMSA to afford **30** (Scheme 11). This important intermediate was taken into two directions. Half of the material was deprotected to form terminal alkyne **31**, while the other half was converted into iodoarene **32** by heating in MeI. These two components were then cross-coupled to give **33**, which afforded the precyclized triyne **34** after conversion into the iodoarene and cross-coupling with additional **31**. After another sequence of triazene-into-iodide conversion and deprotection of the alkyne, intramolecular cross-coupling gave the parent [12]annulene **8**. Although this route produced the desired product and no larger macrocycles, it had significantly more steps than the previous syntheses and furnished **8** in a modest 35% overall yield; thus, the ease and simplicity of Vollhardt's metathesis pathway is superior for the assembly of **8** and its 4,5-disubstituted derivatives.[12] Nevertheless, the linear intramolecular route opened the door for preparing higher annulenes **27** and **28**.

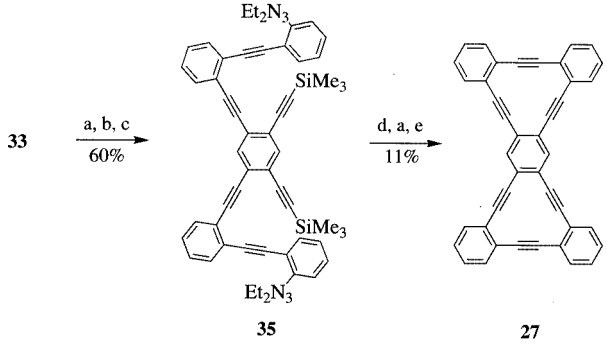
3.1.2 Bowtie [12]DBA

Using intermediate **33** from the synthesis of DBA **8** as the starting material, we set about the synthesis of "bowtie" annulene **27** (Scheme 12).[27] A series of analogous reactions developed for **8** (deprotections, alkynylations) gave the precyclized material **35**. Conversion of the triazenes to iodoarenes and sequential deprotection and cross-coupling led to



Scheme 11. Reagents: (a) i. HCl, $NaNO_2$; ii. K_2CO_3, H_2O, Et_2NH; (b) $PdCl_2(PPh_3)_2$, CuI, Et_3N, HC≡CSiMe_3; (c) MeI, 120 °C; (d) K_2CO_3, MeOH; (e) $PdCl_2(PPh_3)_2$, CuI, Et_3N; (f) **28**, $PdCl_2(PPh_3)_2$, CuI, Et_3N; (g) $Pd(dba)_2$, PPh_3, CuI, Et_3N

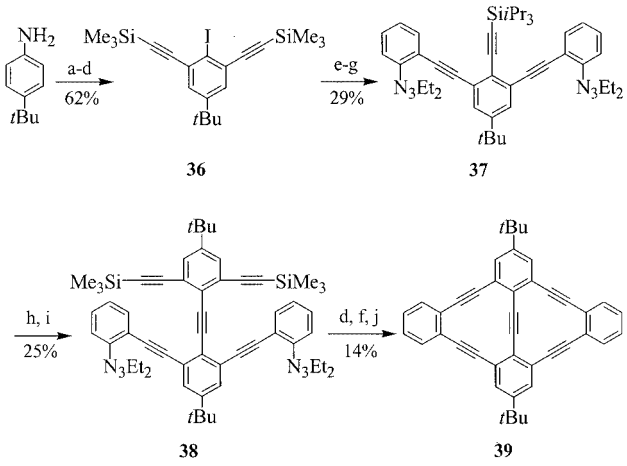
annulene **27**. Because of the purported low solubility of **27**, the ring closure proceeded in very poor yield (< 15%). NMR data was not obtained, although UV/Vis, IR, and MS data agree with the proposed structural assignment. Recently however, Vollhardt and co-workers were able to assemble **27** and secure the ^1H NMR spectrum of the compound.[12] The synthesis of **27** in 6% yield by the metathesis route is remarkable in that it required five different molecules to come together to form the two macrocyclic rings.



Scheme 12. Reagents: (a) K_2CO_3, MeOH; (b) 1,5-dibromo-2,4-diiodobenzene, $PdCl_2(PPh_3)_2$, CuI, Et_3N; (c) $PdCl_2(PPh_3)_2$, CuI, Et_3N, HC≡CSiMe_3; (d) MeI, 120 °C; (e) $Pd(dba)_2$, PPh_3, CuI, Et_3N

3.1.3 Diamond [12]DBA

The "diamond" DBA **28**, which consists of two [12]annulenes fused by a common edge, can be synthesized by previous linear methodology (Scheme 13).[27] To circumvent possible solubility problems, the starting material included *tert*-butyl groups. Iodoarene **36** was acquired in four steps from 4-*tert*-butylaniline. Part of this material was converted in three more steps into triyne **37**, upon which iodoarene **36** was cross-coupled after deprotection, affording **38**. Desilylation and double intramolecular cross-coupling of **38** furnished DBA **39** as a bright yellow solid. While the overall yield for this 13-step synthesis was only 0.6%, an intramolecular route appears to be the only viable approach for macrocycles containing two or more fused annulenes. New methodological advances and/or adaptations such as alkyne metathesis,[28] however, may make increased quantities of **39** and even larger substructures of graphyne (**29**) synthetically accessible.



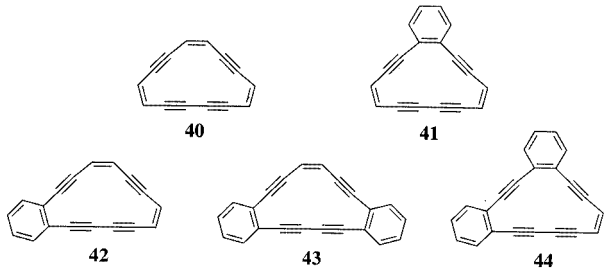
Scheme 13. Reagents: (a) $BnEt_3N^+ICl_2^-$, CH_2Cl_2, MeOH; (b) i. HCl, $NaNO_2$; ii. K_2CO_3, H_2O, Et_2NH; (c) $PdCl_2(PPh_3)_2$, CuI, Et_3N, HC≡CSiMe_3; (d) MeI, 120 °C; (e) $PdCl_2(PPh_3)_2$, CuI, Et_3N, HC≡CSiiPr_3; (f) K_2CO_3, MeOH; (g) *N*,*N*-diethyl-*N*′-(*o*-iodophenyl)triazene, $PdCl_2(PPh_3)_2$, CuI, Et_3N; (h) Bu_4NF, EtOH; (i) **36**, $PdCl_2(PPh_3)_2$, CuI, Et_3N; (j) $Pd(dba)_2$, PPh_3, CuI, Et_3N

3.2 Dehydrobenzo[14]annulenes

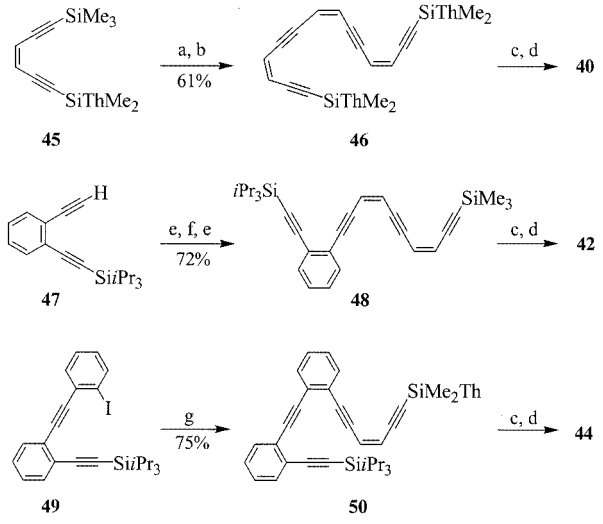
Because of the synthetic complexity, low overall yield, and poor solubility of DBAs **27** and **39**, we switched our efforts to the preparation of annulenes containing diacetylenic units. Systems with one or more butadiyne bridges had previously been synthesized, most notably DBAs **5**−**7**. The intramolecular syntheses of macrocycles with diacetylenic units are much more simplified and convergent than those of the smaller [12]annulenes. The cross-coupling of two polyyne units to an iodoarene followed by homocoupling of the terminal acetylenes closes the ring and forms the diyne unit as demonstrated by Vollhardt's synthesis of [14]annulene **24** (Scheme 8).

3.2.1 Aromaticity of Benzannelated Dehydro[14]annulenes

Although a large number of DBAs that exhibit weak induced ring currents have been prepared over the last 45+ years, the synthesis and study of a family of related structures has not been reported. Specifically, we were interested in comparing the diatropicity of a series of six octadehydro[14]annulenes (**24**, **40**−**44**) as the core was successively benzannelated.[29]



The parent octadehydro[14]annulene **40** was synthesized starting from enediyne **45** (Scheme 14). Selective deprotection followed by cross-coupling with 1,2-dichloroethene gave tetrayne **46**, which was deprotected and cyclized to give the [14]annulene. Similar 4-step strategies were used to assemble symmetrical derivatives **41** and **43**.



Scheme 14. Reagents: (a) K_2CO_3, MeOH, THF; (b) (*Z*)-1,2-dichloroethene, $Pd(PPh_3)_4$, CuI, THF, $PrNH_2$; (c) Bu_4NF, THF, MeOH; (d) $Cu(OAc)_2{\cdot}H_2O$, MeCN, 100 °C (Th = 1,1,2-trimethylpropyl); (e) (*Z*)-(4-chloro-3-buten-1-ynyl)trimethylsilane, $Pd(PPh_3)_4$, CuI, $PrNH_2$, THF; (f) NaH, MeOH, THF; (g) **45**, K_2CO_3, $PdCl_2(PPh_3)_2$, CuI, Et_3N, MeOH

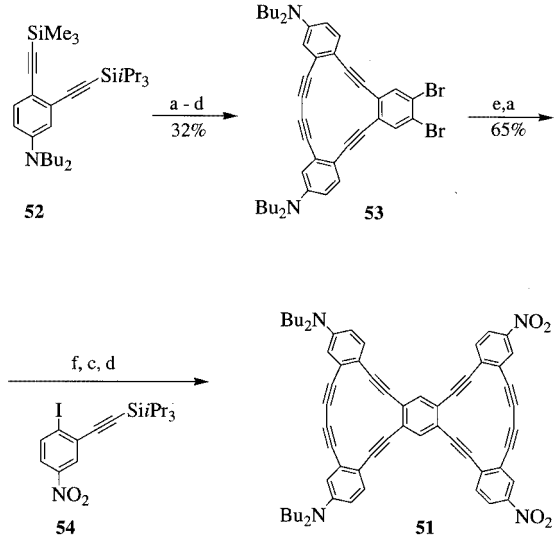
To prepare the monobenzannelated system **42**, diyne **47** was first cross-coupled with (*Z*)-(4-chloro-3-buten-1-ynyl)-trimethylsilane (Scheme 14). After deprotection of the TMS group, an identical cross-coupling gave the precyclized polyyne **48**, which was deprotected and homocoupled to afford macrocycle **42**.

Bis(benzannelated) **44** started with an in situ deprotection/alkynylation procedure from iodoarene **49** and enediyne **45** giving polyyne **50** (Scheme 14). DBA **44** was obtained from stepwise deprotection and cyclization of this key intermediate. Although DBAs **40**−**42** and **44** proved to be stable only in dilute solutions due to rapid polymerization that occurred in the solid state, ^{1}H NMR data were secured for all compounds in the series.

In the case of the parent octadehydro[14]annulene (**40**), the alkene protons exhibit large downfield shifts (δ = 7.39−7.92) typical of an aromatic compound. The ^{1}H NMR data of DBAs **41** and **42** show an average upfield shift (Δδ) of 0.67 ppm compared to **40**, demonstrating that annelation of one benzene ring significantly reduces the diatropicity of the larger ring. The ^{1}H NMR data of **43** and **44** show a smaller average Δδ of 0.38 ppm compared to the monobenzannelated systems, which is approximately half the difference of adding only one benzene ring. Fusion of one benzene ring is known to reduce the aromaticity of an annulene system by about one-half.[30] The NMR data for **41**−**44** show that fusion of a second benzene ring reduces the remaining ring current again by half. Nucleus-independent chemical shift (NICS) calculations through a collaborative study with the Williams group further corroborated these findings as the NICS values for the series of compounds were in excellent agreement with the experimentally observed trends. It follows from this study that the [14]annulenes can be used as a sensitive probe for qualitatively measuring the aromaticity of annulenic systems.[31]

3.2.2 Bowtie [14]DBAs

Another subset of [14]annulenes currently under investigation in the Haley group are prepared through an intramolecular procedure and consist of bowtie-shaped systems such as **51** (Scheme 15).[32] Discreet positioning of donor and acceptor groups leads to distinct changes in the electronic properties of the macrocycles. Donor/acceptor (D/A) acetylenic systems were studied initially with only linear π-conjugated structures[33] and subsequently with [18]annulenes,[34] which will be discussed in more detail later. The extensive polarization of the conjugated backbone from the donor to the acceptor groups should give rise to large nonlinear optical (NLO) susceptibilities; such studies are underway.



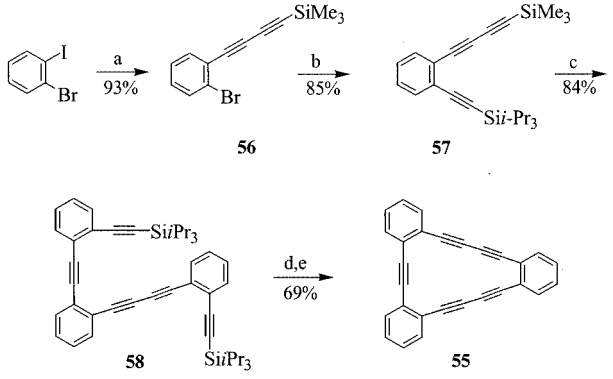
Scheme 15. Reagents: (a) K_2CO_3, MeOH, THF; (b) 1,2-dibromo-4,5-diiodobenzene, $Pd(PPh_3)_4$, CuI, iPr_2NH, THF, 50 °C; (c) Bu_4NF, MeOH, THF; (d) CuCl, TMEDA, $MeCl_2$; (e) $HC{\equiv}CSiMe_3$, $Pd(PPh_3)_4$, CuI, iPr_2NH, THF, 80 °C; (f) **54**, $Pd(PPh_3)_4$, CuI, iPr_2NH, THF

An example synthesis from these systems starts with the selective cross-coupling of electron donor diyne **52** to the iodo positions of 1,2-dibromo-4,5-diiodobenzene, followed

by deprotection and cyclization to give the intermediate [14]annulene **53**. TMSA is next cross-coupled on, deprotection and further cross-coupling of the electron acceptor component **54** give the precursor to cyclization. DBA **51** is completed by deprotection and standard intramolecular alkyne dimerization. A variety of donor/acceptor bis([14]-annulenes) and "bis([15]annulenes)" with specifically placed functional groups, as well as the corresponding monocyclic D/A-[14]DBAs are currently under construction in the Haley laboratory according to this strategy.[32]

3.3 Dehydrobenzo[16]annulene

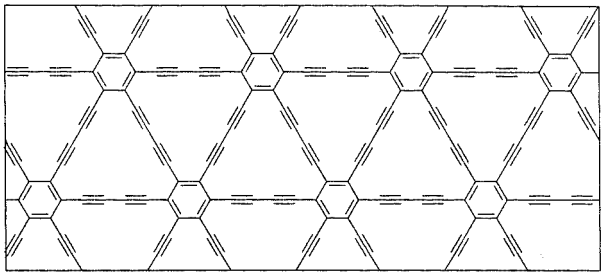
The next larger DBA, [16]annulene **55**, contains one monoacetylene and two diacetylene sides. Due to its symmetry, a different mode of construction for each diyne linkage was necessary (Scheme 16).[35] The first diacetylene was attached in one piece as trimethylsilyl-1,3-butadiyne to the more reactive iodo site of 1-bromo-2-iodobenzene by a Sonogashira reaction to give **56**. After cross-coupling triisopropylsilylacetylene (TIPSA) to the bromo position, **57** was selectively deprotected and cross-coupled to **49** furnishing precyclized α,ω-polyyne **58**. The second diacetylene unit was formed through a Cu-mediated intramolecular ring closure after deprotection to afford **55**. The [16]annulene does indeed show a distinct upfield shift of the arene proton resonances ($\Delta\delta = 0.05-0.15$ ppm), demonstrating its $4n$ π-electron antiaromatic character.



Scheme 16. Reagents: (a) HC≡CC≡CSiMe$_3$, PdCl$_2$(PPh$_3$)$_2$, CuI, Et$_3$N; (b) HC≡CSi*i*Pr$_3$, PdCl$_2$(PPh$_3$)$_2$, CuI, Et$_3$N; (c) **49**, KOH, H$_2$O, PdCl$_2$(PPh$_3$)$_2$, CuI, Et$_3$N; (d) Bu$_4$NF, EtOH, THF; (e) Cu(OAc)$_2$·H$_2$O, pyridine, MeOH

3.4 Dehydrobenzo[18]annulenes

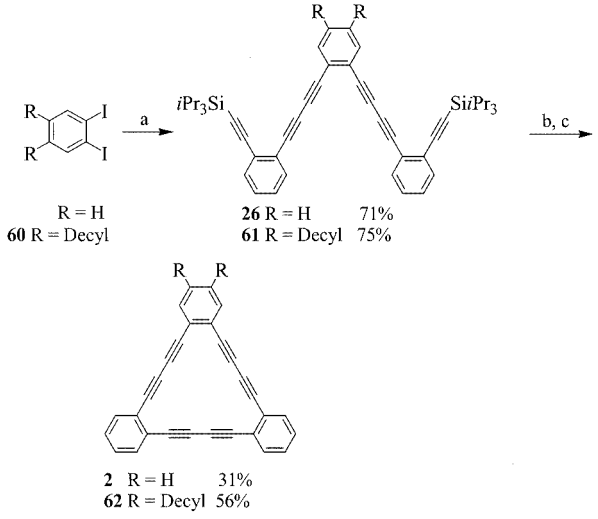
The [18]annulenes are extended versions of the [12]annulenes, with diacetylenic rather than monoacetylenic sides, yet their syntheses are (for the most part) considerably more straightforward. For this reason, [18]DBAs have been the predominant focus of the Haley group's synthetic work. Much like the [12]DBAs, the [18]annulenes are also substructures of a unique theoretical all-carbon network. Graphdiyne (**59**), much like other carbon-rich systems, is predicted to possess fascinating materials properties:[23,36] (1) because of the high degree of conjugation, a large third-order nonlinear optical susceptibility is predicted; (2) conductivity or superconductivity can be expected when doped with alkali metals; and (3) redox activity due to through-sheet transport of ions within the large pores (about 2.5 Å) of the planar sheets is possible for this network. Large substructures of the network ideally should demonstrate some, if not all, of these characteristics.



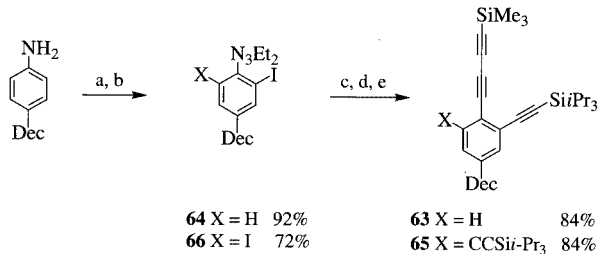
59

3.4.1 Parent [18]DBA

It is surprising that the parent [18]annulene **2**, the simplest substructure of **59,** had eluded synthetic attempts despite nearly 40 years of effort, until the Haley group used an intramolecular technique patterned off of the synthesis of **24**. If a 1-butadiynyl-2-ethynylbenzene precursor such as **57** was used in place of a 1,2-diethynylbenzene, formation of the [18]annulene occurs. An in situ deprotection/alkynylation of triyne **57** with 1,2-diiodobenzene provided hexayne **26** (Scheme 17).[22] Deprotection of the TIPS groups by fluoride ion gave the free alkyne which was homocoupled under Eglinton conditions to provide DBA **2** in 35% yield. The low yield of the final cyclization was attributable to the poor solubility of the planar system. Indeed, if two decyl groups are built into the arene head (**60**) to which **57** is cross-coupled, the yield is improved to 56% for annulene **62**. To prepare larger fused DBA networks, solubilizing chains must be attached at the building block stage.



Scheme 17. Reagents: (a) **57**, KOH, H$_2$O, Pd(PPh$_3$)$_4$, CuI, Et$_3$N, THF; (b) Bu$_4$NF, EtOH, THF; (c) Cu(OAc)$_2$·H$_2$O, pyridine, MeOH



Scheme 18. Reagents: (a) $BnEt_3N^+ICl_2^-$, CH_2Cl_2, MeOH; (b) i. HCl, $NaNO_2$, H_2O, THF, Et_2O, CH_3CN, ii. K_2CO_3, Et_2NH, H_2O, CH_3CN; (c) HC≡CSi*i*Pr$_3$, $PdCl_2(PPh_3)_2$, CuI, Et_3N; (d) MeI, 120 °C; (e) HC≡CC≡CSiMe$_3$, $PdCl_2(PPh_3)_2$, CuI, Et_3N

The poor solubility of **2** gave an important clue to why its isolation had not been previously attained. We discovered that CH_2Cl_2 was a superior solvent to Et_2O, which is most commonly used in the workup of Cu-mediated alkyne homocouplings. Repetition of Eglinton's original coupling of 1,2-diethynylbenzene, now using CH_2Cl_2 in the workup followed by column chromatography, gave dimer **1** (58%) and an inseparable 3:2 mixture of trimer **2** and tetramer **21** (20%). It is therefore likely that **2** was synthesized in the original study and discarded as insoluble by-product!

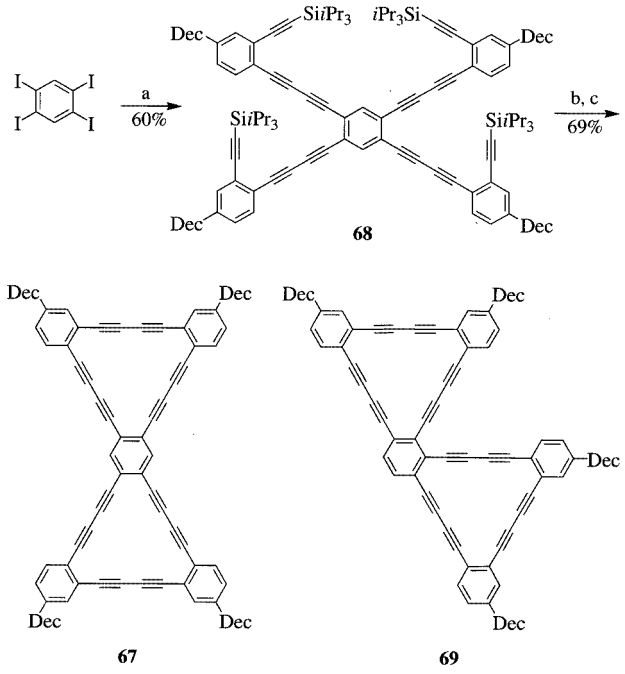
3.4.2 Expanded [18]DBAs

Solubilizing groups can easily be incorporated onto the larger [18]annulene networks through the triyne legs. These triyne components are key to the syntheses of larger networks and can be prepared in multigram quantities. The construction of **63** with a decyl solubilizing group is outlined in Scheme 18.[22,37] Iodination of 4-decylaniline followed by conversion into the diethyltriazene gave **64**. Cross-coupling of TIPSA to **64** followed by decomposition of the triazene in MeI and subsequent cross-coupling of trimethylsilylbutadiyne furnished **63**. Another important component for DBA syntheses is tetrayne **65**, which is similarly prepared with the exception of double iodination of the starting aniline and using an additional equivalent of TIPSA on subsequent cross-couplings (Scheme 18). These two components are utilized in a vast majority of the expanded [18]DBAs. Several other pendant moieties [NBu_2, *t*Oct, $(CH_2CH_2O)_4CH_3$] for increased solubility are also currently being explored.

3.4.2.1 Bowtie and Boomerang [18]DBAs

With multigram quantities of decyl triyne **63** in hand, a variety of [18]annulene networks are possible by using different halo-substituted benzenes as the central ring. The "bowtie" annulene **67** was prepared by cross-coupling **63** to 1,2,4,5-tetraiodobenzene to give dodecayne **68** (Scheme 19).[22] Removal of the silyl protecting groups with Bu_4NF followed by Cu-mediated cyclization of each ring furnished bis(annulene) **67** in 27% overall yield from triyne **63**.

The electronic absorption spectra of the [18]annulene systems display a characteristic pattern of four absorption bands, which are assigned to $\pi \rightarrow \pi^*$ and other transitions



Scheme 19. Reagents: (a) **63**, KOH, H_2O, $PdCl_2(PPh_3)_2$, CuI, Et_3N, THF; (b) Bu_4NF, EtOH, THF; (c) CuCl, $Cu(OAc)_2 \cdot H_2O$, pyridine, MeOH

(Figure 1). Compared to the parent [18]DBA **2**, a bathochromic shift of about 45 nm and a peak intensity that is approximately double are observed for **67**. These features are attributable to the longer 1,4-bis(phenylbutadiynyl)benzene chromophore and thus the increased linear π-conjugation in **67**.

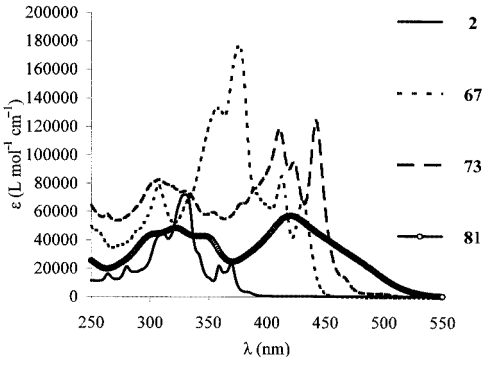


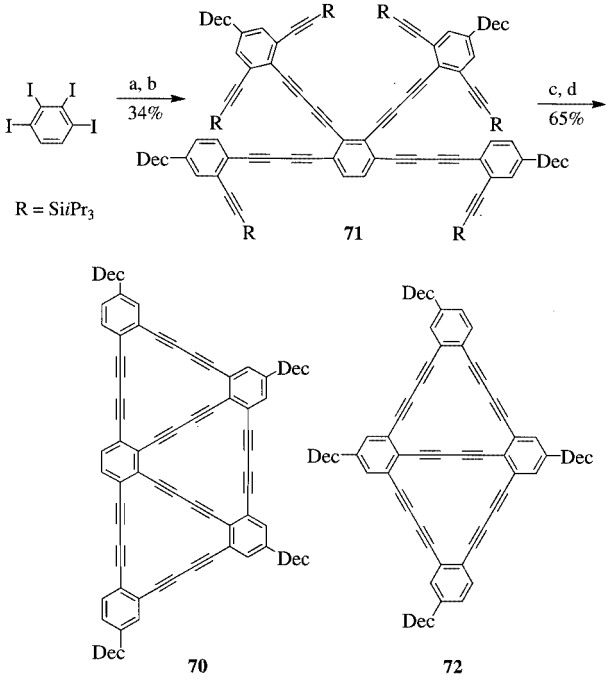
Figure 1. Electronic absorption spectra for selected annulenes

By repeating the above synthesis with 1,2,3,4-tetraiodobenzene, the "boomerang" [18]DBA **69** was prepared.[37] This structural isomer of **67** displayed a smaller bathochromic shift of only 30 nm from the parent annulene **2**, which is due to **69** containing only one of the longer 1,4-bis(phenylbutadiynyl)benzene chromophores, whereas **67** contains two of these extended units.

3.4.2.2 Half-Wheel and Diamond [18]DBAs

The "half-wheel" annulene **70** can also be prepared from 1,2,3,4-tetraiodobenzene (Scheme 20). By taking advantage

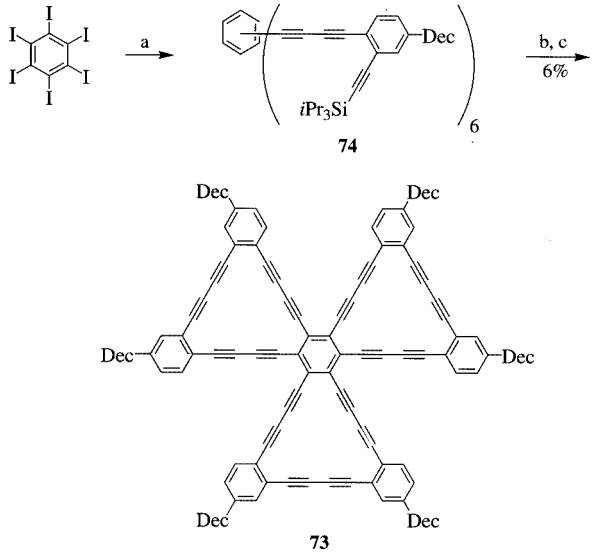
of the more reactive, sterically less congested 1,4-positions, 2 equiv. of triyne **63** were first cross-coupled, followed by tetrayne **65** to the remaining iodides to give **71**. Subsequent deprotection and cyclization furnished DBA **70** which contains three fused rings. Inclusion of the extra ring caused a red shift of only about 6 nm with respect to **67**, demonstrating that the electronic absorption behavior is more dependent on extended linear-conjugated pathways. To further exemplify this point, "diamond" subunit **72** was also synthesized using components **63** and **65** cross-coupled to **66**. This structure contains two [18]DBAs fused side-on without the extended chromophores found in **67**, **69**, and **70**, and as consequence, a hypsochromic shift of the absorption peaks of ca. 20 nm was observed compared to **67**.



Scheme 20. Reagents: (a) **63**, KOH, H_2O, $PdCl_2(PPh_3)_2$, CuI, Et_3N, THF; (b) **65**, KOH, H_2O, $PdCl_2(PPh_3)_2$, CuI, Et_3N, THF; (c) Bu_4NF, EtOH, THF; (d) CuCl, $Cu(OAc)_2{\cdot}H_2O$, pyridine, MeOH

3.4.2.3 Trefoil [18]DBA

To prepare larger subunits of graphdiyne such as the "radiation symbol" **73**, hexaiodobenzene was used for the cross-coupling reaction (Scheme 21).[38] Due to the steric congestion of cross-coupling six triyne components to the central ring, a more active palladium catalyst, Pd[P(*o*-Tol)$_3$]$_2$, was used.[39] This catalyst contains phosphane ligands with a much larger cone angle than the standard $Pd(PPh_3)_2Cl_2$ or $Pd(PPh_3)_4$ catalysts, aiding in the oxidative insertion step of the catalytic cycle. It was also necessary for the butadiyne unit of the triyne to be deprotected before coupling, rather than generation in situ. The product of this cross-coupling (**74**) was contaminated with the fivefold-coupled product where the sixth position was substituted with a proton (as determined by NMR and MS data). Despite this contamination the Cu-mediated homocoupling was carried out and DBA **73** was isolated in 6% overall yield. It



Scheme 21. Reagents: (a) **63**, Pd[P(*o*-Tol)$_3$]$_2$, CuI, Et_3N, NMP; (b) Bu_4NF, EtOH, THF; (c) CuCl, $Cu(OAc)_2{\cdot}H_2O$, pyridine, MeOH

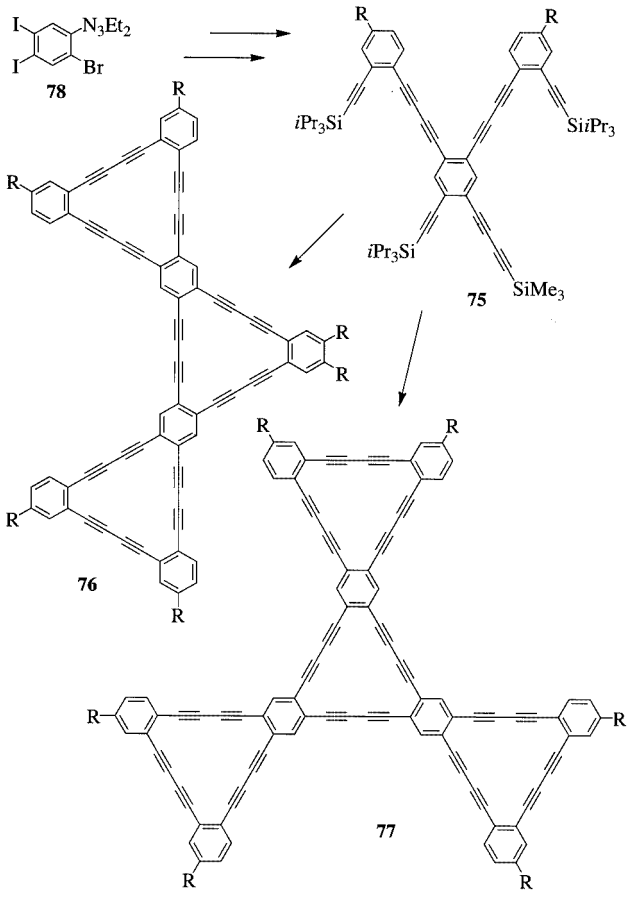
is interesting to note that the λ_{max} of **73** is red-shifted by almost 60 nm with respect to the uncyclized precursor **74**. This bathochromic shift clearly illustrates the effect of locking the system into planarity, and is most evident with large macrocycles such as **73** (Figure 1).

3.4.2.4 Super-Sized [18]DBAs

Work is in progress in the Haley group on the synthesis of larger graphdiyne substructures.[40] The common feature, that all of the [18]DBAs described thus far (**67**, **69**, **70**, **72**, and **73**) possess, is a symmetrical central benzene ring onto which the annulenes are attached. To prepare larger systems with [18]DBA rings fused in patterns other than to a central ring, the methodology must be modified. Asymmetric coupling component **75**, which contains one and a half precyclized rings, was designed to address this problem (Scheme 22). This component can be cross-coupled to a variety of central units, deprotected, and cyclized as before to give super-sized DBA substructures such as **76** and **77**. Haloarene **78**, with three different substituents suitable for Sonogashira cross-coupling, was prepared in five steps from 1,2-dinitrobenzene. To prepare nonayne **75** from **78**, triyne units were first cross-coupled to the more reactive iodo positions, TIPSA to the bromo position, and trimethylsilylbutadiyne to the remaining position after conversion of the triazene into an iodide. The new key component **75** can be deprotected, cross-coupled to a variety of central haloarenes, and then cyclized to form even larger graphdiyne subunits such as **76** and **77**.

3.4.3 Functionalized [18]DBAs

With the advent of a rational synthesis of the [18]DBA skeleton, site-specific placement of functional groups on the benzene rings was now possible. Electron-donor and -acceptor groups can be built into the rings in a variety of

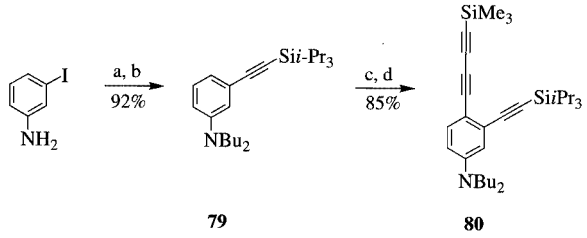


Scheme 22. Synthetic pathway for expanded graphdiyne substructures

positions. This forms various push-pull systems within the annulene and gives rise to extreme polarization of the conjugated backbone. These donor/acceptor groups can be built either into the triyne legs or the diiodoarene heads used in the cross-coupling protocol. Donor/acceptor-substituted triynes require additional synthetic transformations compared to the parent triyne **57**.

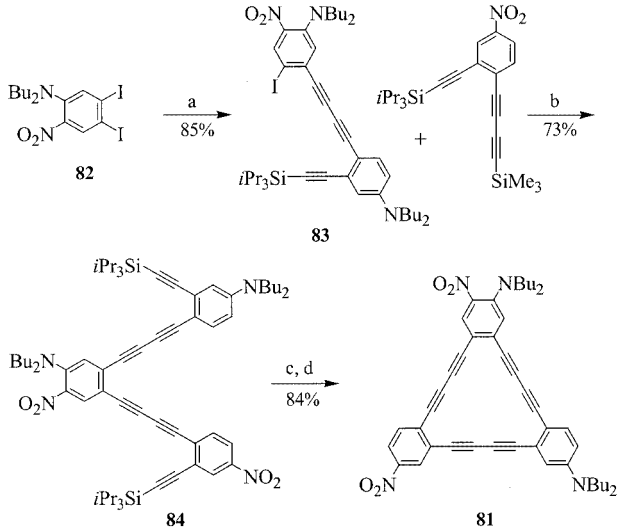
The synthesis of the donor triyne started by *N*-alkylation of 3-iodoaniline with bromobutane followed by cross-coupling to furnish **79** (Scheme 23).[34] This intermediate was iodinated and cross-coupled to yield donor triyne **80**. Triynes with an acceptor group were prepared analogously to the synthesis of **63** starting instead with either 4-nitro- or 4-cyanoaniline (Scheme 18).

These donor and acceptor components were cross-coupled to a variety of haloarenes containing a mixture of neutral, donor, donor/acceptor, or acceptor substituents in a combinatorial approach to produce an array of functionalized systems. One synthesis that should be highlighted is the assembly of the C_s-symmetric annulene **81** that shows a remarkable 52% overall yield for the four synthetic steps (Scheme 24).[34] The donor triyne **82** was first cross-coupled to the more reactive iodo position *para* to the electron-withdrawing nitro group on **82** to give **83**. The acceptor triyne was then cross-coupled to the remaining iodide to afford



Scheme 23. Reagents: (a) BuBr, $NaHCO_3$, THF, DMF; (b) $HC{\equiv}CSiiPr_3$, $PdCl_2(PPh_3)_2$, CuI, Et_3N; (c) $BnEt_3N^+ICl_2^-$, CH_2Cl_2, MeOH, CH_2Cl_2; (d) $HC{\equiv}CC{\equiv}CSiMe_3$, $PdCl_2(PPh_3)_2$, CuI, Et_3N

precursor **84**, which was deprotected and cyclized to yield substituted DBA **81**. Figure 2 illustrates a few of the numerous functionalized [18]DBAs that have been prepared.



Scheme 24. Reagent: (a) **80**, KOH, H_2O, $PdCl_2(PPh_3)_2$, CuI, Et_3N; (b) KOH, H_2O, $PdCl_2(PPh_3)_2$, CuI, Et_3N; (c) Bu_4NF, MeOH, THF; (d) $Cu(OAc)_2$, CuCl, pyridine

The donor/acceptor-substituted [18]DBAs show unique electronic absorption spectra (Figure 1). The characteristic set of four peaks typical for annulenes are present but weakened and the low energy absorption bands are greatly extended and broadened. These shifts are attributed to the increased polarization of the conjugated backbone between donor and acceptor groups, and are maximized when opposing groups are positioned at each end of the molecule such as in **81**.

The donor/acceptor [18]DBAs are good candidates for use in nonlinear optics due to the ease in placement of various groups on the benzene rings.[41] With these systems one is able to tune the physical properties of the material to enhance a specific NLO response by varying the position of substituents on the system. It has been suggested that chromophores with threefold symmetry could give a higher first hyperpolarizability (β) value than linear dipolar compounds, which is desirable for second-order NLO properties.[42] These systems are also locked into planarity, which

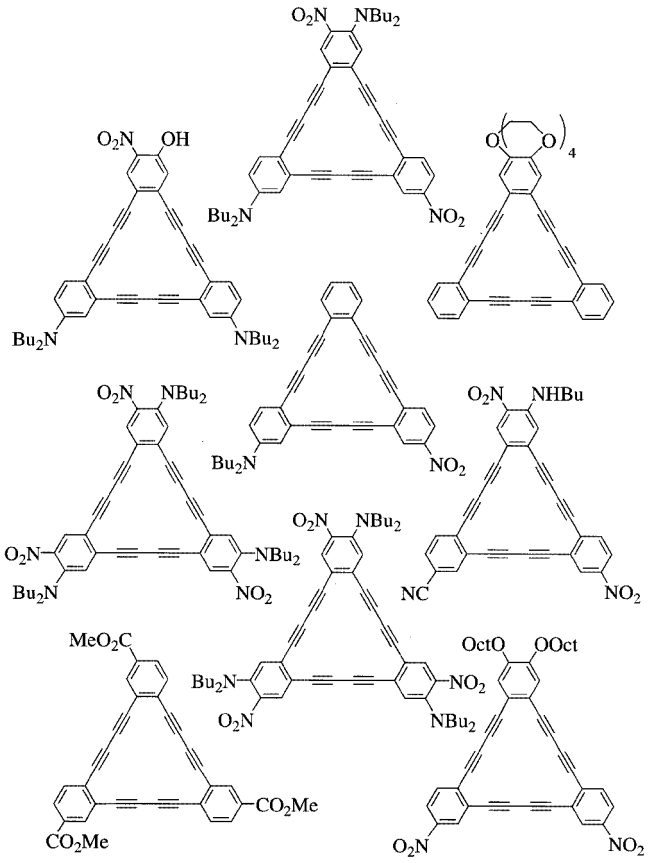
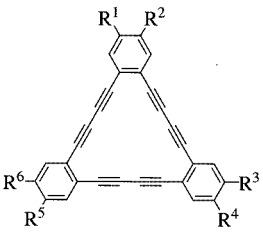


Figure 2. A plethora of functionalized DBAs

further enhances overall π-conjugation and communication between chromophores, thereby increasing NLO efficiency. With a rational synthesis of an [18]DBA, one can achieve various symmetries for NLO studies. The β values of several donor/acceptor [18]DBAs were measured using the hyper Raleigh scattering (HRS) technique. These materials demonstrated hyperpolarizability values 2−3 times greater than that of the standard 4-dimethylamino-4′-nitrostilbene (DANS) reference chromophore (Figure 3).



R^1	R^2	R^3	R^4	R^5	R^6	$\beta_0/10^{-28}$ esu	$(\beta_0/M)_{rel}$
NO_2	H	H	H	H	NBu_2	6.6	1.4
NO_2	NBu_2	H	H	H	H	6.3	1.3
NO_2	H	H	NBu_2	H	H	3.1	0.7
NO_2	NBu_2	H	NBu_2	NO_2	H	4.9	0.9
NO_2	NBu_2	NO_2	NBu_2	NO_2	NBu_2	1.7	0.3
H	H	H	H	H	H	1.7	0.5
					DANS	2.4	=1

Figure 3. NLO data of push-pull [18]DBAs

3.5 Larger Dehydrobenzoannulenes

Larger dehydrobenzoannulenes are now possible using the rational, intramolecular synthetic procedures developed for [18]- and smaller annulenes. These larger DBAs can be broken up into two major groups: planar and nonplanar. Planar annulenes have two or (typically) three phenyl rings in the system, while four or more phenyl units impart nonplanarity to the DBA backbone.

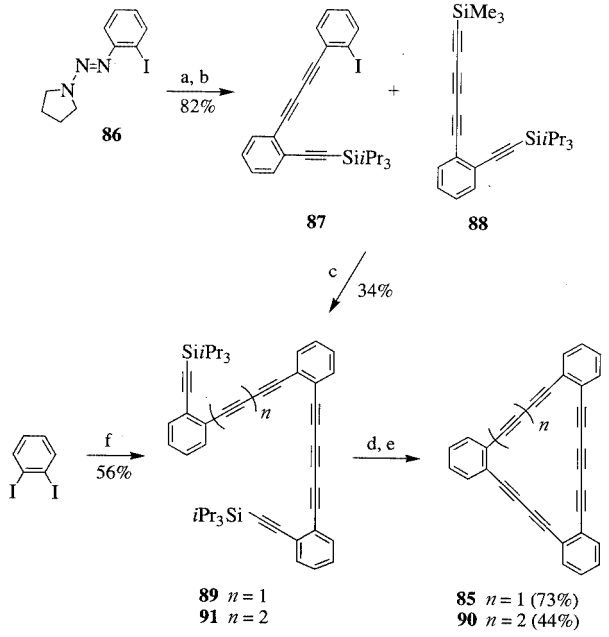
3.5.1 Large Planar DBAs

3.5.1.1 [20]DBA

The first of these larger annulenes is symmetrical [20]DBA **85** (Scheme 25).[35b,43] Starting from triazene **86**, which in turn was prepared from 2-iodoaniline, cross-coupling with triyne **57** and triazene decomposition with iodomethane afforded **87**. This intermediate was cross-coupled with tetrayne **88**, prepared by a Cadiot−Chodkiewicz[44] reaction between trimethylsilylbutadiyne and the appropriate (bromoethynyl)benzene, to give precyclized product **89**. Desilylation and cyclization furnished planar **85**. Unlike previous DBAs, **85** exhibited essentially no change in the ^{1}H NMR spectrum upon cyclization and thus can be considered atropic.

3.5.1.2 [22]DBA

The largest planar annulene that has been prepared by the Haley group is [22]DBA **90** (Scheme 25).[35b,43] Two tetrayne units **88** were first attached to 1,2-diiodobenzene.



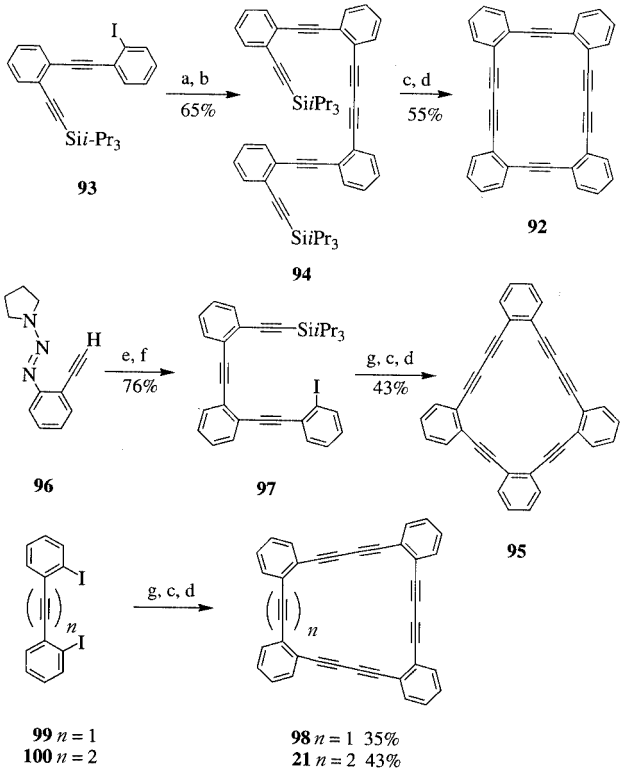
Scheme 25. Reagent: (a) **57**, KOH, H_2O, $PdCl_2(PPh_3)_2$, CuI, Et_3N, THF; (b) MeI, 120 °C; (c) KOH, H_2O, $PdCl_2(PPh_3)_2$, CuI, Et_3N, THF; (d) Bu_4NF, EtOH, THF; (e) CuCl, $Cu(OAc)_2{\cdot}H_2O$, pyridine; (f) **88**, KOH, H_2O, $PdCl_2(PPh_3)_2$, CuI, Et_3N, THF

Subsequent desilylation and cyclization of **91** gave **90**. Whereas **85** is atropic, **90** is diatropic as it exhibited a small but discernable downfield shift ($\delta\Delta = 0.10-0.15$) in the arene proton signals. Although the ring current lessens as the ring size increases, the attenuation in diatropic systems is much slower than in paratropic ones. Monoalkene and dialkene versions of **85** and **90**, respectively, can be assembled in analogous fashion using an (*E*)-enediyne in place of the triyne linkage in **88**.[43,45]

3.5.2 Nonplanar DBA

3.5.2.1 Nonplanar [20]DBAs

The synthesis of nonplanar dehydrotetrabenzo[20]annulene **92** takes advantage of two units of diyne **93** (Scheme 26).[35] The diacetelyne linkage between these components in **94** comes from trimethylsilylbutadiyne. Deprotection and cyclization of this intermediate gave **92** in 30% overall yield. Interestingly, this system had been previously prepared by Vollhardt et al. by an intermolecular *n* X = Z strategy in only 20% yield and was accompanied by higher cyclooligomers.[46]



Scheme 26. Reagents: (a) HC≡CC≡CSiMe$_3$, PdCl$_2$(PPh$_3$)$_2$, CuI, Et$_3$N; (b) **93**, KOH, H$_2$O, PdCl$_2$(PPh$_3$)$_2$, CuI, Et$_3$N, THF; (c) Bu$_4$NF, MeOH, THF; (d) CuCl, Cu(OAc)$_2$·H$_2$O, pyridine, MeOH; (e) **93**, PdCl$_2$(PPh$_3$)$_2$, CuI, Et$_3$N; (f) MeI, 120 °C; (g) **57**, KOH, H$_2$O, PdCl$_2$(PPh$_3$)$_2$, CuI, Et$_3$N, THF

One of the more unusual annulenes prepared thus far using the intramolecular methodology is **95** (Scheme 26), a structural isomer of **92**.[35] Iodoarene **93** was cross-coupled with alkyne **96** followed by conversion of the triazene to an iodide giving **97**. This precursor was then cross-coupled with triyne **57**, deprotected, and cyclized to yield DBA **95**. Like most of the nonplanar tetrabenzo-DBAs, **95** possesses a distorted saddle shape in the solid state (Figure 4).

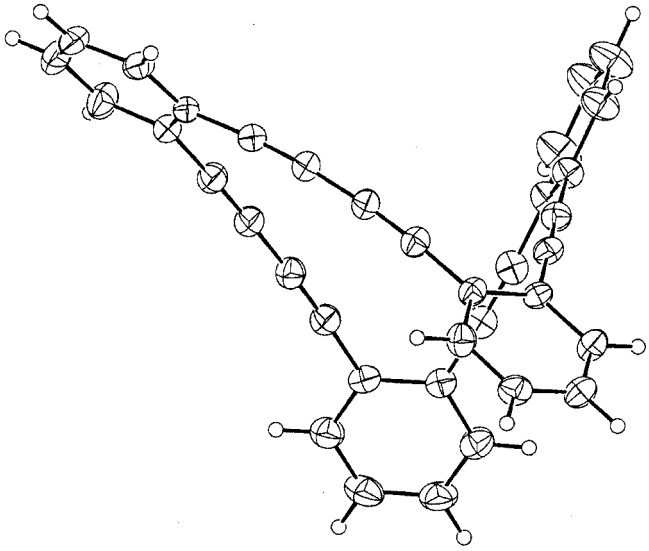


Figure 4. Crystal structure of diamond [20]annulene **95**

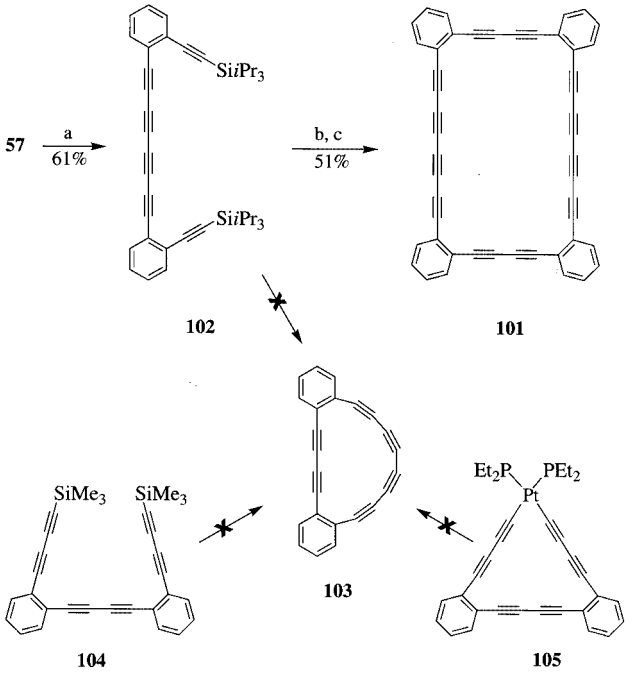
An interesting feature of dehydrobenzoannulene chemistry is thermally induced decomposition and products arising thereof. Vollhardt observed that strained [14]DBA **24** underwent topochemical 1,4-polymerization at 120 °C to give a novel polydiacetylenic tube structure.[21] The Vollhardt group also noted that compound **92** decomposed explosively at 250 °C to give a pure carbon residue which included "bucky tubes" and "bucky onions".[46] In contrast, **95** reacted nonviolently at a temperature 50 °C lower but released 50 kJ mol^{-1} more energy.[35] The difference in reactivities must be ascribed to variations in their solid-state packing. For example, both **1** and **55** exhibit π-stacking similar to **24** in the solid state;[35b,47] however, the slipped stacks are outside the parameters prescribed by Enkelmann for topochemical 1,4-polymerizations.[48]

3.5.2.2 Non-Planar [22]- and [24]DBAs

The next set of saddle-shaped annulenes, [22]DBA **98** and [24]DBA **21**, were prepared in the usual manner by cross-coupling the appropriate diiodo precursor **99** or **100** with the ever-versatile triyne **57** (Scheme 26).[35] The resultant intermediates were then deprotected and cyclized to yield either **98** or **21**. The parent [24]annulene **21** had been isolated previously by Youngs as an intermolecular byproduct in the intramolecular synthesis of **1** (Scheme 5).[20]

3.5.2.3 [32]DBA

The largest nonplanar annulene constructed by the Haley group is [32]DBA **101** (Scheme 27).[49] The intermolecular synthesis of this system involves only protiodesilylations and alkyne dimerizations. Triyne **57**, which is desilylated in situ under homocoupling conditions, avoids the free phenylbutadiyne and gives polyyne **102** containing a tetraacetyl-



Scheme 27. Reagents: (a) K_2CO_3, $Cu(OAc)_2 \cdot H_2O$, pyridine, MeOH; (b) Bu_4NF, EtOH, THF; (c) CuCl, $Cu(OAc)_2 \cdot H_2O$, pyridine

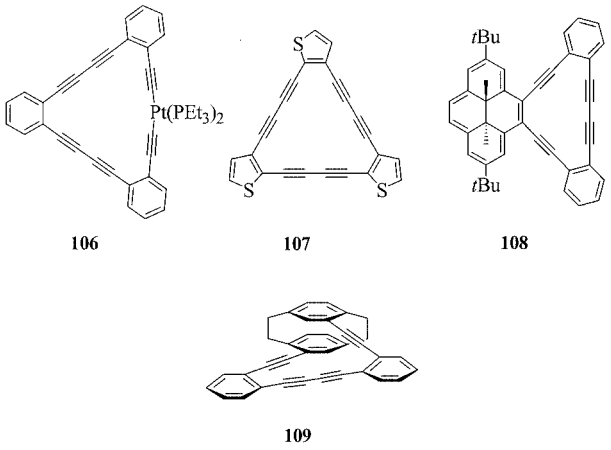
enic linkage. It was initially hoped that deprotection followed by intramolecular cyclization would give highly strained [16]annulene **103**. The only isolated product, however, was dimer **101** (51%). Another attempt at **103** involved dimerization of **104** to form the tetraacetylenic moiety last, but furnished only **101**. Similarly, reductive elimination of the Pt fragment from **105** did not lead to **103**.

3.5.2.4 [40]DBA

The largest, well-characterized DBA is the 40-membered ring system **16**, formed by the intermolecular X + Y = Z method (Scheme 6).[17] The higher derivatives of [80]-, [120]-, [160]-, and [200]DBA were also isolated in small amounts and characterized by TOFSIMS.[50]

3.6 DBA Hybrids

The versatility of these reaction sequences can be seen not only with "pure" dehydrobenzoannulenes, but also with a cornucopia of unusual structures as highlighted by DBA "hybrids" **106**−**109**. Compounds such as **106**[51] and **107**[52] have been prepared to study their optical properties and thus possibly increase the polarizability of the basic [18]annulene system. Dimethyldihyrodropyrene-fused hybrid **108** has been used as an NMR probe of aromaticity in DBAs.[53] The intramolecular route to DBAs has even been combined with paracyclophane chemistry to create unique systems such as **109** that exhibit global transannular delocalization through the fully conjugated decks of the molecules.[54] Clearly, the possibility for hybrid structures with interesting properties is virtually endless.



4 Outlook

Although dehydrobenzoannulene chemistry has been around for nearly half a century, it is only recently that it has experienced a tremendous resurgence. The development of modern alkyne cross-coupling reactions by pioneers such as Sonogashira, Stille, and Negishi made this renaissance possible. Nevertheless, Eglinton can be considered the father of DBA chemistry as he established oxidative alkyne homodimerizations to be the unrivaled foundation, even to this day, for dehydroannulene and dehydrobenzoannulene synthesis. In addition, the vast and important contributions of Staab, Nagakawa, and Sondheimer established annulenes as a field of their own and thus should not be overlooked. By combining and adapting newer Pd-catalyzed cross-coupling techniques with classical synthetic strategies, the Haley group has been able to expand the field of DBA chemistry to macrocycles possessing novel topologies and unique substitution patterns. These materials show great promise for technological applications such as nonlinear optics (NLO), liquid crystalline displays (LCD), and supramolecular chemistry, as well as other interesting properties associated with π-electron-rich/carbon-rich compounds and networks. With a large number of publications every year overcoming synthetic obstacles and advancing synthetic feasibility, the future of annulene chemistry looks to be vast and exciting.

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