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REVIEW

Alkyne Benzannulations in the Preparation of Contorted Nanographenes

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Nanographenes are a popular area of research due to their promising properties for electronics. Over the last twenty years there has been a significant increase in interest in the development of contorted nanographenes. While many top-down techniques are employed in the synthesis of these planar nanographenes, the use of alkynes in bottom-up syntheses allows for easy functionalization and the development of contorted nanographenes. The syntheses of contorted nanographenes with a focus on utilizing alkynes is reviewed here.

Introduction

For the last two decades, nanographenes (NGs) have been recognized as useful organic materials for electronic and optoelectronic devices due to their extended π-conjugation.[1] There are great advantages in using organic compounds for these applications as the molecules can be tailored in size, shape, functionality, and so on, through rational design and synthesis.[2] In turn, this allows for the electronic and optical properties to be tuned.[3] NGs are divided into two general types, planar and non-planar. Among the two types of NGs, non-planar NGs such as corannulene **1**,[4-11] helicenes **2**,[12-17] and twisted acenes **3**,[18-24] as shown in Figure 1, show a variety of fascinating properties due to their molecular packing and/or structures due to their curved π-framework.

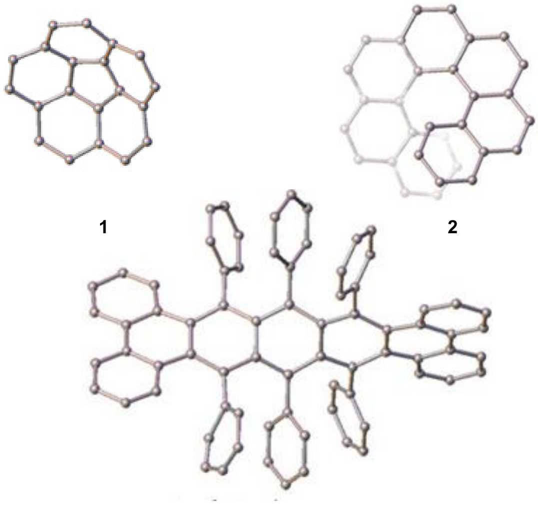

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Figure 1 - Contorted NGs. Adapted with permission from W. Yang, G. Longhi, S. Abbate, A. Lucotti, M. Tommasini, C. Villani, V. J. Catalano, A. O. Lykhin, S. A. Varganov and W. A. Chalifoux, *J. Am. Chem. Soc.*, 2017, **139**, 13102-13109. Copyright 2017 American Chemical Society.

Many non-planar NGs contain unfavourable strain which leads to contortion to a more stable conformation. This contortion can result in a stereogenic axis (right- or lefthanded corkscrew) known as helicity or axial chirality.[25] The role that chirality plays in the function of NGs is key to understanding some of the changes in properties between planar and contorted NGs. Contorted NGs are of great interest for applications in switches, sensors, and nonlinear optics due to their useful photophysical properties and dynamic behavior.[26]

Contorted NGs can be subdivided into two major categories based on the Gaussian curvature of their overall surface.[27] While planar NGs have zero Gaussian curvature, NGs with a network containing rings smaller than six-membered induce a positive Gaussian curvature (bowl-shape) and NGs containing rings larger than six-membered induce a negative Gaussian curvature (saddle shape). It is important to note that not all NGs containing non-benzenoid rings possess Gaussian curvature. If the non-benzenoid ring is on the periphery or not heavily fused to the benzenoid rings, it may still be planar in order to maximize conjugation.[28] These negatively curved NGs show promise in the synthesis of anode materials for lithium ion batteries based on computational studies.[27]

Unlike planar NGs, which tend to be very rigid and insoluble due to π-π interactions, contorted NGs are much more soluble allowing for the use of solution-based processes.[29] The effective intermolecular contact in the crystals and polycrystalline films could offer better charge transport properties required in organic materials-based devices.[29] These non-planar structures afford concave surfaces that relate to the convex surfaces of

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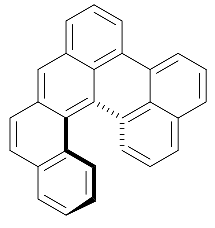
Electronic Supplementary Information (ESI) available: [details of any supplementary information available should be included here]. See DOI: 10.1039/x0xx00000x fullerenes and could be utilized in organic photovoltaics as p-n junction materials.[29] As one can see, contorted NGs have great potential across a broad area of material science, which is the main driver for the recent increase in interest for this fascinating class of molecules.

Contorted NG Syntheses

Designing syntheses of contorted NGs from commercially available starting materials is an area of high interest. This provides an easy method to functionalize the molecule as to enhance solubility or tune specific properties. As one of the oldest C-C bond forming reactions, the century old Scholl reaction is popular in the synthesis of NGs.[30, 31] A number of approaches have been reported in the literature regarding the synthesis of planar and contorted NGs in which the key step involves oxidative aryl-aryl coupling either by cyclization using the Scholl reaction (Figure 2) or a transition-metal-catalysed reaction (Figure 3).[32-35] In 2007, King and co-workers analysed the scope of the Scholl reaction to provide insight into the reaction mechanism, including the role of substitution and electronic effects..[36] In 1966, Vingiello and Ojakaar synthesized various fused NGs containing seven aromatic rings including [5]helicene **4** (Figure 2) via cyclodehydrogenation.[34] Unfortunately, the original AlCl$_3$-NaCl melt procedure of the Scholl does not afford a homogenous melt but instead a sticky semi-solid mixture that is difficult to stir.[34] There have been a number of advances in the development of the Scholl reaction, including the work from Müllen and Rathore, which has rendered it much easier to carry out and more reliable.[37] This oxidative cyclodehydrogenation reaction was used by Scott, Itami, and co-workers in 2013 in the two-step synthesis (from corannulene) of the large double-concave nanographene **5** (Figure 2).[38] This nanographene contains five seven-membered rings and is soluble in common organic solvents.

Following the first reports for the synthesis of [*n*]cycloparaphenylenes ([*n*]CPP)[39-42], many groups have used and attempted to use the Scholl reaction to extend and create a fused π system on [*n*]CPP and other related molecules.[43-45] In 2015, Müllen and co-workers reported the synthesis of hexabenzocoronene (HBC) incorporated [21]CPP **6** via Scholl reaction (Figure 2). The success of this synthesis being dependent on the large ring size of [21]CPP and the addition of strategically placed methyl groups to prevent 1,2-phenyl shifts.[45] In 2018, the Merner group showed the successful π-extension of strained benzenoid macrocycles via Scholl to afford the [5]helicene containing macrocycle **7** (Figure 2). Macrocycle **7** has an end-to-end bend (of the dibenzo[*f,j*]picene unit) of 31.8° and is the first example of successful annulation onto the *para*-phenylene unit via Scholl chemistry.[43]



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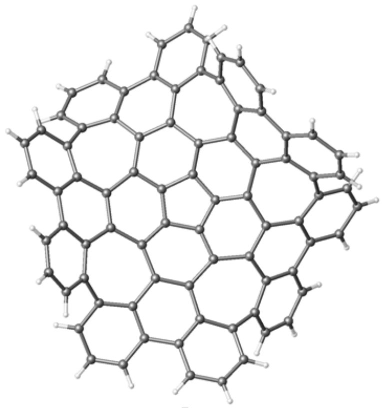
Vingiello, 1966



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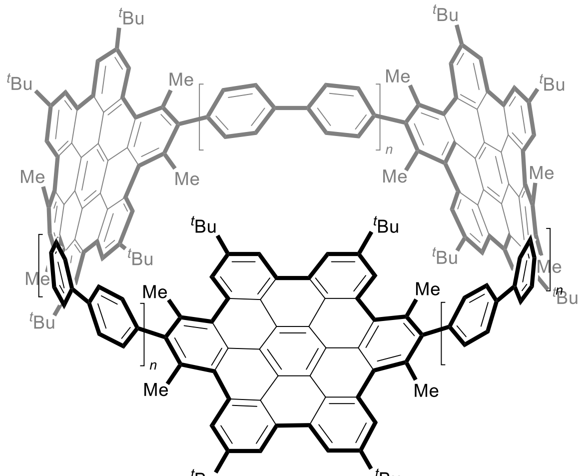
Scott & Itami, 2013



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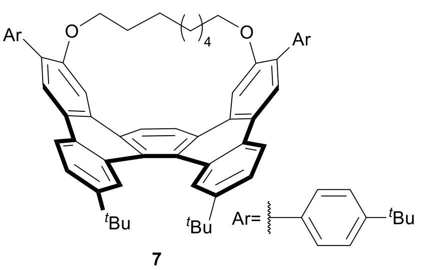
Müllen, 2015



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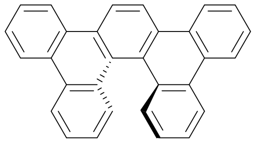
Merner, 2018

Figure 2 - Synthetic approaches to contorted NGs utilizing Scholl chemistry. Adapted by permission from Spring Nature Customer Service Centre GmbH: Springer Nature *Nature Chemistry* "A grossly warped nanographene and the consequences of multiple odd-membered-ring defects" Kawasumi, Q. Zhang, Y. Segawa, L. T. Scott, K. Itami, Copyright 2013.

As a mild alternative to the classic Scholl reaction, the use of photochemical cyclization/dehydroiodination by Alabugin[46] or cyclodehydrochlorination (CDHC) by Morin[47] have also been



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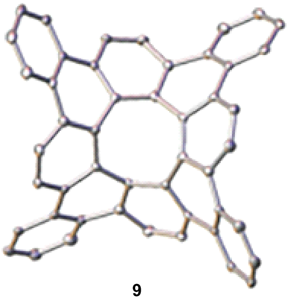
Morin, 2016



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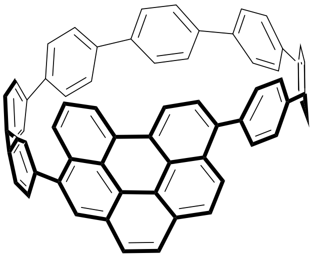
Suzuki & Sakamoto, 2013
Whalley, 2014



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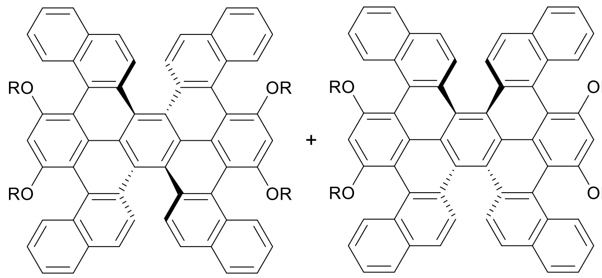
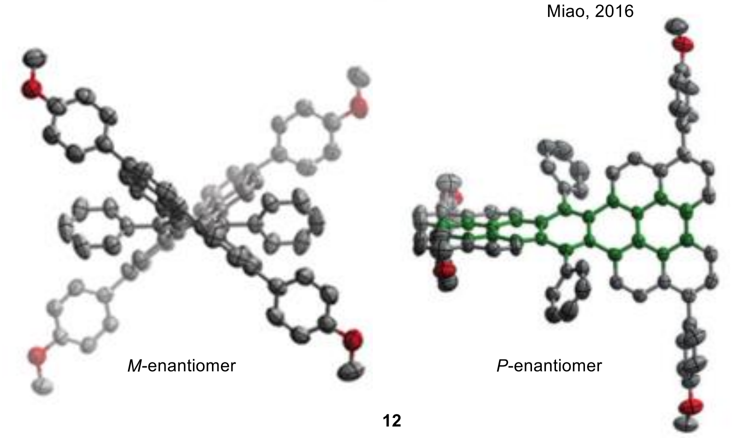
Jasti, 2016



twisted anti

11

Miao, 2016



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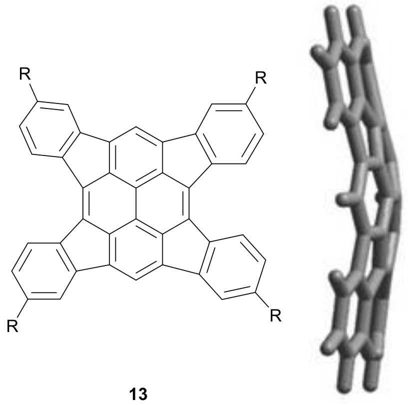
Miao, 2016



13

de Meijere & Scott, 2016 (R= ^{t}Bu)
Amsharov, 2019 (R=H)

Figure 3 - Synthetic approaches to contorted NGs utilizing transition-metal catalysed arylation. †

reported. In 2016, the Morin group showed the use of the CDHC reaction to afford contorted NGs like **8** (Figure 3). The CDHC reaction has many advantages over the classic Scholl reaction for NGs, including but not limited to: regioselectivity, better control of edge topology, does not require a metal catalyst, and the use of milder conditions.[47] Their work showed the CDHC reaction could be completed in the presence of acid-sensitive moieties, given the presence of base was neither necessary nor detrimental to the reaction.

In 2013, Suzuki and Sakamoto showed the first synthesis of tetrabenzo[8]circulene **9** (Figure 3) via oxidative cyclodehydrogenation of cyclic octaphenylene precursors in 7% yield.[11] Interestingly, in 2014, Whalley and co-workers developed another synthesis of **9** utilizing the Diels-Alder cycloaddition and Pd-catalysed C-H arylation in 24% yield.[48] While the Suzuki group generated the core 8-membered ring in the final step of their synthesis, the Whalley group opted to incorporate the ring pre-assembled.[11, 48] This product exhibited high stability in comparison to its parent structure [8]circulene given its full benzenoid structure. In 2016, Jasti and co-workers

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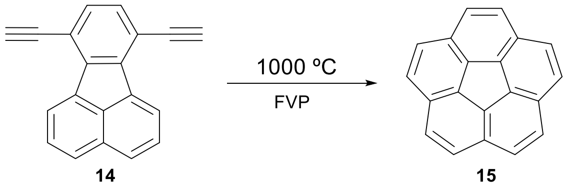
† Adapted with permission from *Synlett* "Rapid π-Extension of Aromatics via Alkyne Benzannulations" W. Yang & W. Chalifoux. © Georg Thieme Verlag KG. Adapted with permission from John Wiley and Sons: *Chemistry – A European Journal* "Twisted polycyclic Arenes from Teatranaphthyldiphenylbenzenes by Controlling the Scholl Reaction with Substituents" Y. Yang, L. Yuan, B. Shan, Z. Liu and Q. Miao, Copyright 2016.
Adapted with permission from John Wiley and Sons: *Chemistry – A European Journal* "Towards Nonalternant Nanographenes through Self-Promoted Intramolecular Indenoannulation Cascade by C—F Bond Activation" V. Akhmetov, M. Feofanov, O. Papaianina, S. Troyanov, K. Amsharov, Copyright 2019.

investigated the use of the Diels-Alder reaction in the π-extension of CPP rings containing a perylene moiety.[49] Utilizing nitroethylene as a masked acetylene, the Jasti group was able to observe desired Diels-Alder adduct **10**; however, they were unable to successfully separate **10** from starting material and concluded its presence in a 1.2:1 ratio with the starting material.[49]

Recently, the Miao group synthesized two novel types of twisted polycyclic arenes using Diels-Alder cycloaddition of alkyne precursors followed by a controlled Scholl reaction (Figure 3).[50] The multiple helicene-bearing two [5]helicene and four [4]helicene moiety **11** with six-fold helicity, has 24 stereoisomers, 10 pairs of enantiomers, and four *meso* isomers in principle. The twisted acene **12**, which is also the constitutional isomer of **11**, has uneven distribution of the twist throughout the pentacene nucleus.[50] The combination of local helicities in a multiple helicene provides molecular dynamic and structural information, and describes the molecular packing in the solid state.[50] In 2019, Amsharov and co-workers utilized C—F bond activation via Al_2O_3 indenoannulation to afford bowl-shaped tetraindenopyrene **13** (right: DFT optimized geometry; Figure 3). Unfortunately, **13** was too insoluble to extract fully from alumina and was only confirmed via HPLC and UV/Vis, albeit in full conversion following 3 days at 190 °C.[51] It should be noted that this indenoannulation to afford substituted derivatives of **13** had been previously reported by de Meijere, Scott, and co-workers in 2006 using a Pd catalyst with yields <1%.[52]

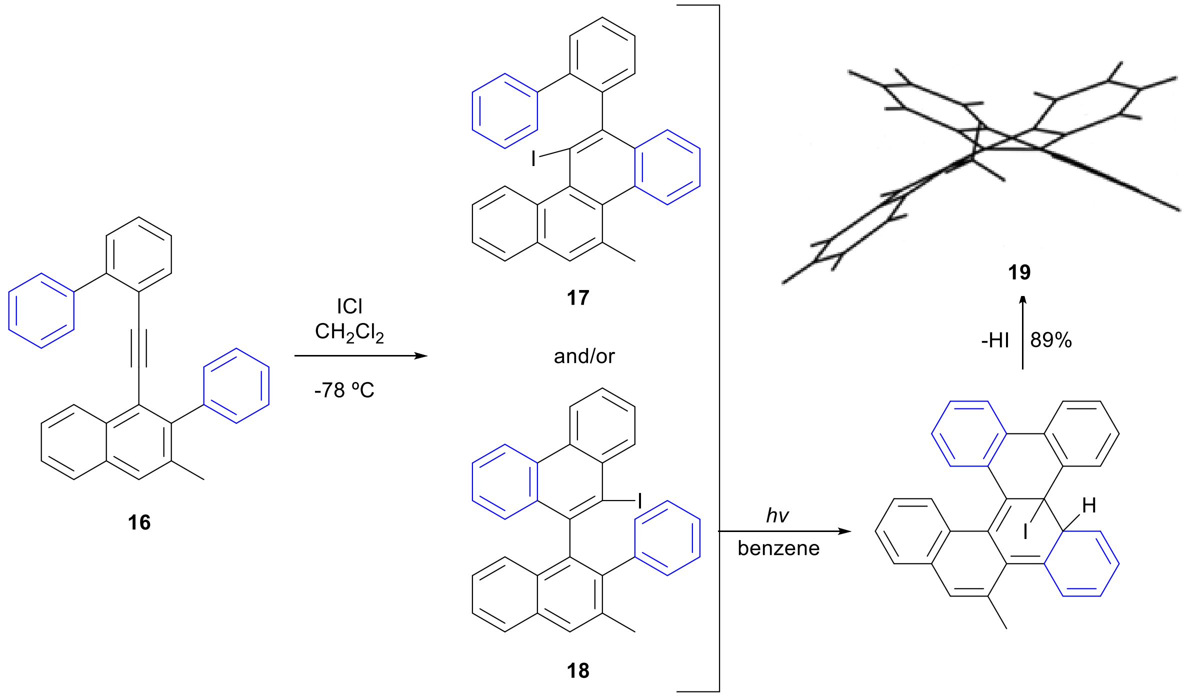


Scheme 1. FVP to afford corannulene.

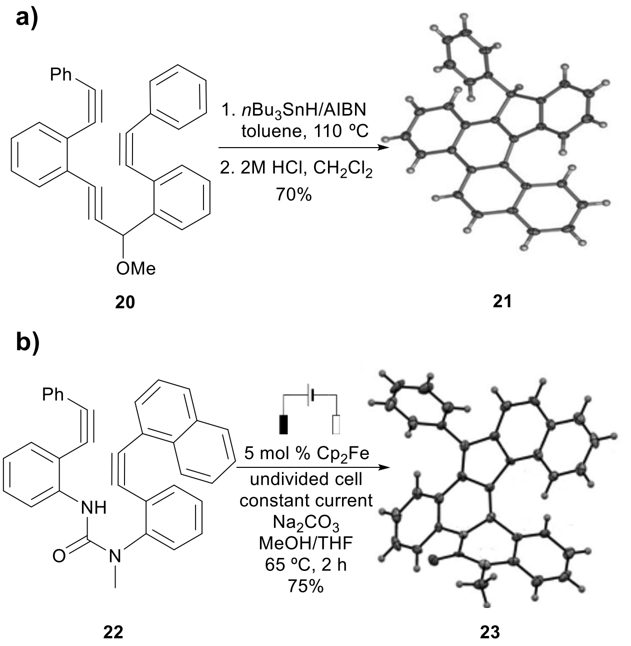
Alkynes are versatile and effective precursors for the formation of carbon-rich materials. This is owing to the fact that a large thermodynamic driving force is associated with formation of conjugated six-membered ring containing products from alkyne starting materials.[53] Alkyne benzannulation reactions have been utilized in a number of transformations using π-Lewis acids,[54-60] Brønsted acids,[61] electrophiles,[62] as well as radical reagents[63] to form planar NGs. However, reports of utilizing alkyne benzannulation, or even utilizing alkynes in the preparation of non-planar or contorted NGs, are less encountered, even with the availability of established cross-coupling reactions.[64] Thus, the aim of this paper is to summarize the scope of methods that use alkynes in building up a broad spectrum of fascinating contorted NGs.

In 1991, Scott and co-workers developed a simple procedure for the synthesis of corannulene via flash vacuum pyrolysis (FVP).[65] Utilizing 7,10-diethynylfluoranthene **14** at 1000 °C, as shown in Scheme 1, provided quantitative yields of corannulene **15** for all substrate that passed through the pyrolysis apparatus. Their work was later advanced in 1997 to afford a short three step

Alkyne Benzannulations



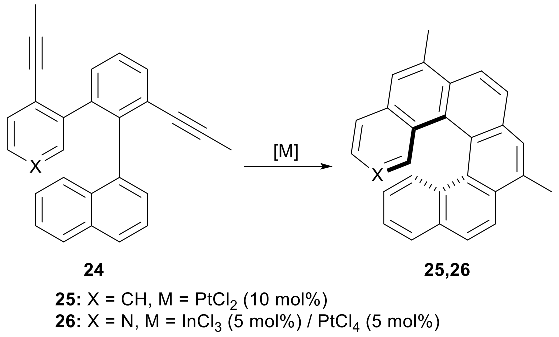
Scheme 2 - Electrophilic cyclization via ICl to afford [4,5]helicenes. Adapted with permission from John Wiley and Sons: *Angewandte Chemie International Edition* "Alkynes as Linchpins for the Additive Annulation of Biphenyls: Convergent Construction of Functionalized Fused Helicenes" R. K. Mohamed, S. Mondal, J. V. Guerrera, T. M. Eaton, T. E. Albrecht-Schmitt, M. Shatruk and I. V. Alabugin, Copyright 2016.



Scheme 3 - (a) Tin-mediated radical cyclization. Adapted with permission from K. Pati, G. dos Passos Gomes, T. Harris, A. Hughes, H. Phan, T. Banerjee, K. Hanson and I. V. Alabugin, *J. Am. Chem. Soc.*, 2015, **137**, 1165-1180. Copyright 2015 American Chemical Society. https://pubs.acs.org/doi/10.1021/ja510563d (b) Electrochemically induced radical cyclization. Adapted with permission from Z.-W. Hou, Z.-Y. Mao, J. Song and H.-C. Xu, *ACS Catal.*, 2017, **7**, 5810-5813. Copyright 2017 American Chemical Society.

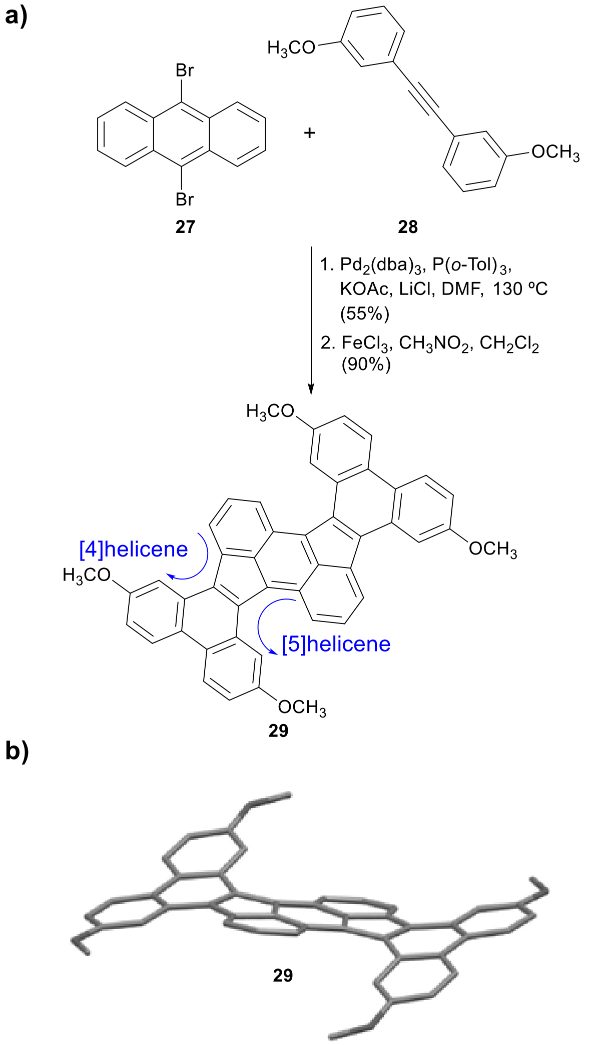
synthesis to **15**.[66] In 2004, Scott and Donovan moved on to use of Ru-catalysis in the synthesis of coronene via Ru(PPh$_3$)(cymene)Cl$_2$.[67] The synthesis of coronene derivatives was also shown by Liu and co-workers with improved yield from a more reactive Ru-catalyst.[68]

In 2016, the Alabugin group showed the use of alkynes as linchpins in a two-step conversion to obtain [4,5]helicenes.[46, 69-72] The synthesis involves building the first core of the helicene frame by treating bis(biaryl)acetylene **16** with 1.1 equiv. of ICl in CH$_2$Cl$_2$ at -78 °C for 2-3 h. Iodine monochloride induced an electrophilic cyclization to afford iodochrysene **17**, iodophenanthrene **18**, or a mixture of both (Scheme 2). However, the strategy offers the same desired helicene product **19** on the subsequent cyclization/dehydroiodination under photochemical conditions (intermediate isomer not shown). The photochemical closure allows for the formation of a variety of helicenes with diverse substituents including phenyl, tolyl, and thiophene as well as extension into [5,5]helicenes. Significant changes in crystal packing were observed for varying substituents.[46] This shows the versatility of alkynes to as effective precursors in convergent syntheses to highly functionalized NGs.

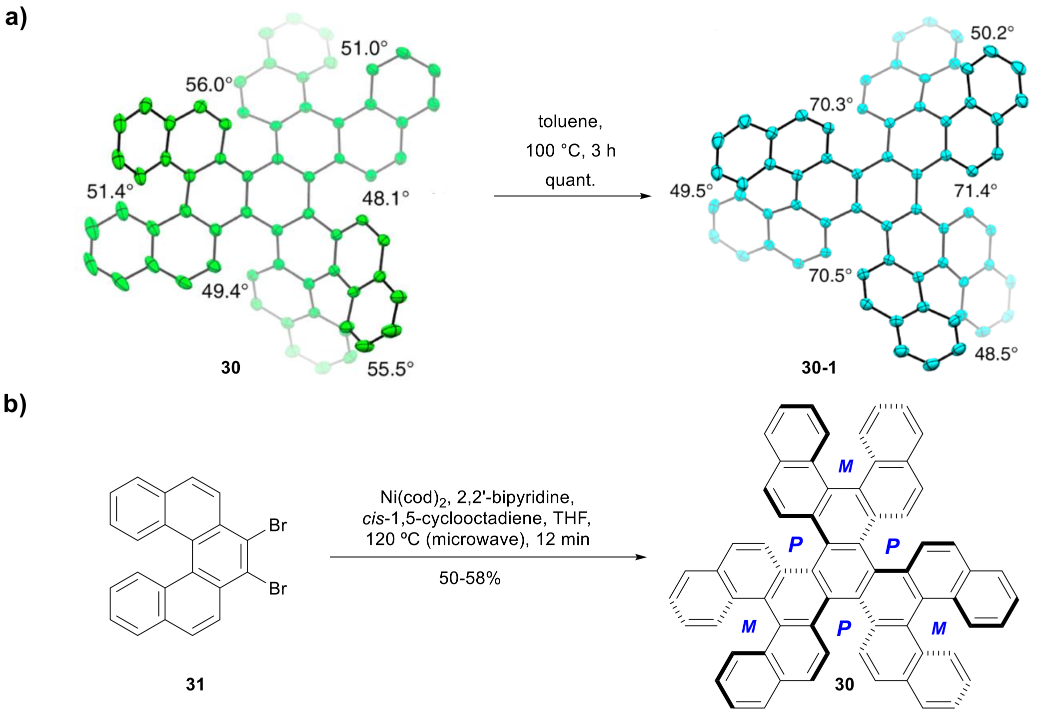


Scheme 4. Pt-catalysed two-fold alkyne benzannulation to afford [6]helicene and aza[6]helicene.

In 2015 the Alabugin group reported a highly regioselective traceless tin-mediated radical cyclization of triyne **20** to afford NG **21** (Scheme 3a).[73, 74] This method affords multiple C—C bonds in a single step and was the first example in which the directing group for the radical cascade reaction was not replaced but was instead eliminated without a second step.[73] Recently, as an approach towards achieving green radical chemistry, the Xu group reported an efficient electrolytic cyclization leading to N-doped NGs from easily available urea-tethered diynes **22**.[64] Unlike the previously reported methods, the five-membered ring remains conjugated in **23** using Xu's green electrochemical method. The general method employed by the Xu group utilized 0.05 equiv. ferrocene-catalyst, 1.0 equiv. Na$_2$CO$_3$ in MeOH/THF (1:1) at 65 °C for 2 h under constant current of 7.5 mA and provides good yields. Helical chirality was



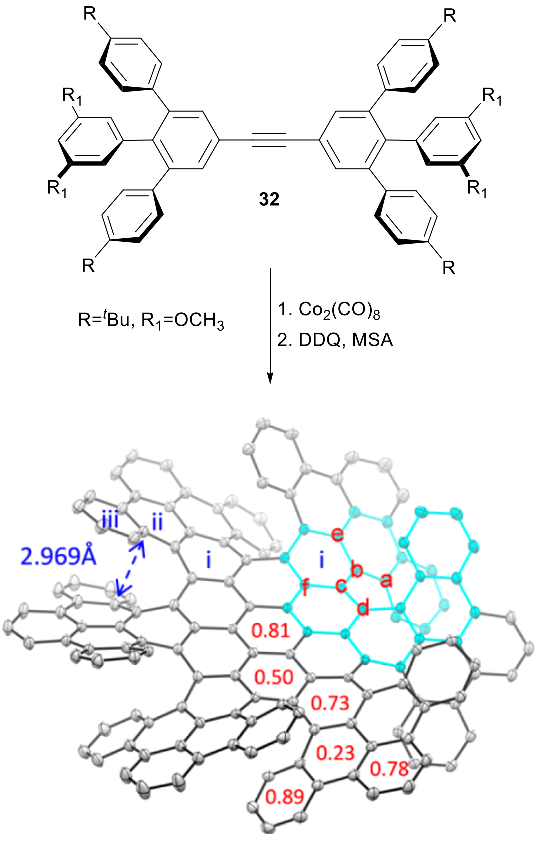
Scheme 5 - (a) Cyclopentannulation followed by Scholl oxidation to afford [4,5]helicene **29** containing five-membered rings. (b) Crystal structure of **29**. Adapted from Ref. 79 with permission from The Royal Society of Chemistry.



Scheme 6 - (a) (*P,M,P,P,M,P*) isomer of hexapole helicene **30** conversion to (*P,M,P,M,P,M*) isomer of **30-1**. Adapted with permission from T. Hosokawa, Y. Takahashi, T. Matsushima, S. Watanabe, S. Kikkawa, I. Azumaya, A. Tsurusaki and K. Kamikawa, *J. Am. Chem. Soc.*, 2017, **139**, 18512-18521. Copyright 2017 American Chemical Society. (b) Gringas 1-step synthesis to afford hexapole helicene in 3:1 to > 5:1 dr.

observed in the crystal structure as a racemic mixture of one of the molecules, as shown in the Scheme 3b. Significant molecular twisting was also observed in **23** at the urea ring, with a dihedral angle of 32.5°. The Xu group was also able to complete this radical cyclization at the gram and decagram scale with no significant loss in yield. Additionally, the reaction showed tolerance to a wide variety of electron-donating and electron-withdrawing substituents placed throughout the molecule; however, the terminal phenyl ring did not tolerate highly electron-withdrawing substituents as it resulted in alkyne hydroamidation.[64] This shows the potential of alkyne precursors in utilizing them in preparation of NGs through electrochemical processes when mild redox catalysts are used as a speedy entry into helicene-like structures.[64]

In 2002, Fürstner and co-workers reported a flexible synthesis of phenanthrenes utilizing a $PtCl_2$-catalysed cycloisomerization.[55] Their investigation showed that no desired or anticipated products were formed without the presence of metal cation, therefore the reactions were not just the result of thermal electrocyclizations at 80 °C. Additionally, they observed a significant preference for the 6-endo-dig cyclization to afford phenanthrenes over the 5-exo mode.[55] Only substrates with strongly electron-withdrawing ester groups on the alkyne overturned this bias (as well as lowered the reaction rate). This is the result of forcing the 1,4-addition process that corresponds to the 5-exo pathway. The work of Fürstner and co-workers pioneered and inspired the use of transition metals in the synthesis of both planar and contorted NGs. Similarly, in 2009 the Storch group synthesized [6]helicene



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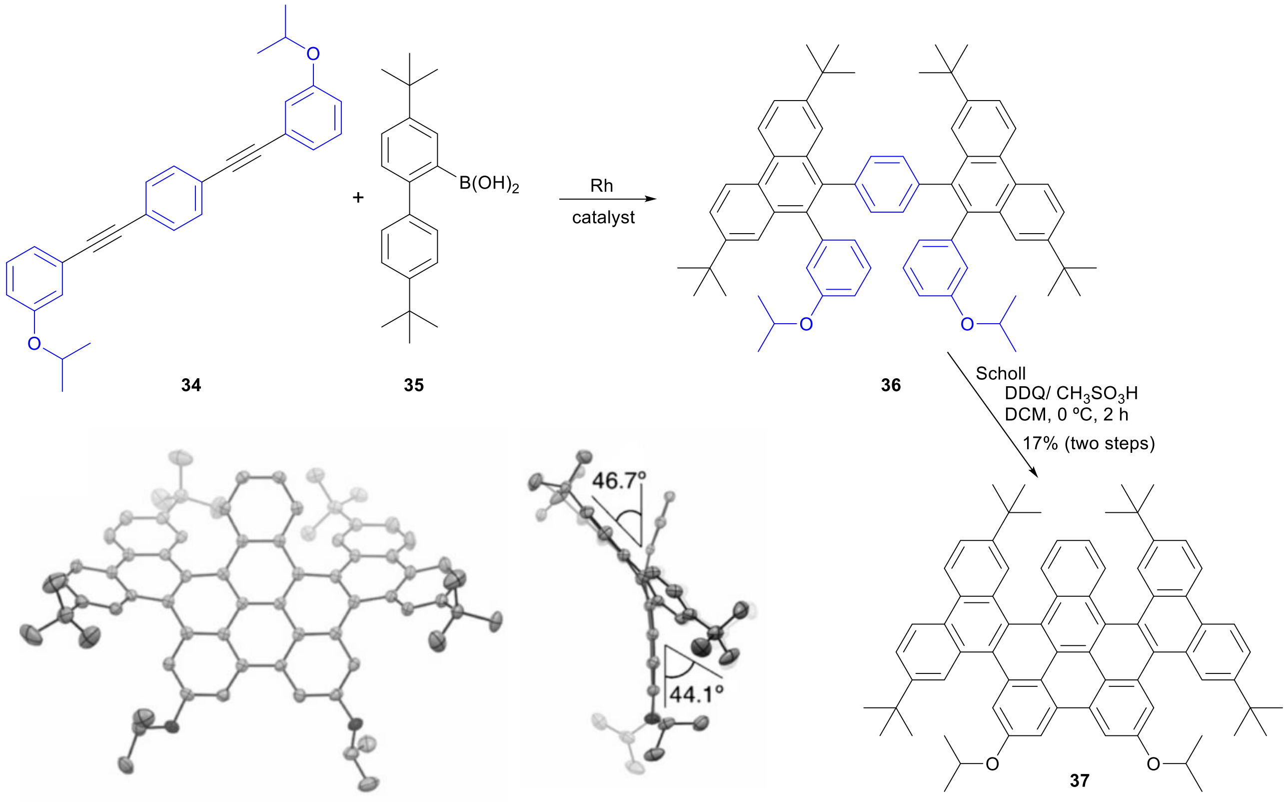
Scheme 7 - Synthesis of hexapole [7]helicene via alkyne cyclotrimerization. Adapted with permission from Y. Zhu, Z. Xia, Z. Cai, Z. Yuan, N. Jiang, T. Li, Y. Wang, X. Guo, Z. Li, S. Ma, D. Zhong, Y. Li and J. Wang, *J. Am. Chem. Soc.*, 2018, **140**, 4222-4226. Copyright 2018 American Chemical Society.



Scheme 8 - $[(\mathrm{Cp^*RhCl_2})_2]$ catalysed two-fold annulation of 2-biphenylboronic acid with bis(arylethynyl)arenes followed by subsequent Scholl reaction. Crystal structure of Scholl product containing [5]helicene moiety with thermal ellipsoids set to 50% probability. Adapted with permission from John Wiley and Sons: *Chemistry – A European Journal* "Twisted Polycyclic Aromatic Systems Prepared by Annulation of Bis(arylethynyl)arenes with Biphenylboronic Acids" Y. Tokoro, A. Oishi and S.-i. Fukuzawa, Copyright 2016.

from a two-fold $\mathrm{PtCl_2}$-catalyzed alkyne benzannulation reaction of **24** in 80% yield to afford **25** (Scheme 4). They were able to extend this work to the aza[6]helicene **26** in 2010; however, this required a mixture of In(III) and Pt(IV) to effect the two-fold alkyne benzannulation in 80% yield.[75, 76] Similarly, Stará, Starý, and co-workers have reported transition-metal-catalysed [2+2+2] alkyne cycloisomerization using Ni(0), Co(I), or Rh(I) as a catalys to afford functionalized helicenes and hetereohelicenes.[77, 78]

In 2016, Plunkett and co-workers reported a new class of contorted aromatics containing five-membered ring cores.[79] These contorted aromatics are prepared from alkyne cyclopentannulation (developed by Garcia-Garibay)[80] of dibromoanthracene **27** with biarylacetylene **28** to afford the cyclopentene ring followed by Scholl cyclodehydrogenation to yield **29**, as shown in Scheme 5. Compound **29** possesses two [5]helicene-like as well as two [4]helicene-like moieties where the [4]helicene-like moiety exhibits a splay angle of 14.34° (smaller than the splay angle of [4]helicene) and the [5]helicene-like moiety exhibits a splay angle of 36.83°. The lowered splay angle value for the [4]helicene-like moiety is believed to be induced by the [5]helicene-like counterpart of **29**.[79] Previous reports of this cyclopentannulation reaction include the work by Müllen and co-workers[81] on pyrene and perylene as well as the work by Wu and co-workers[82] on corannulene and [5]helicene moieties. These cyclopentannulation products are highly soluble, likely due to

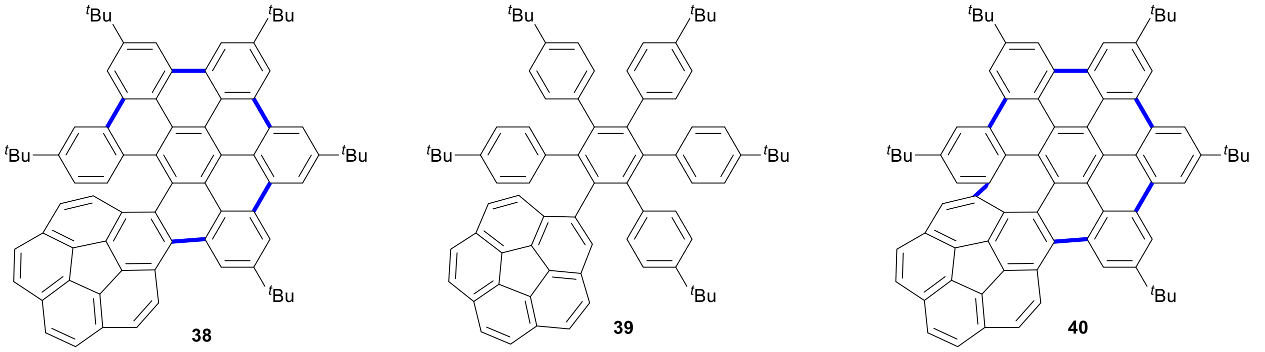
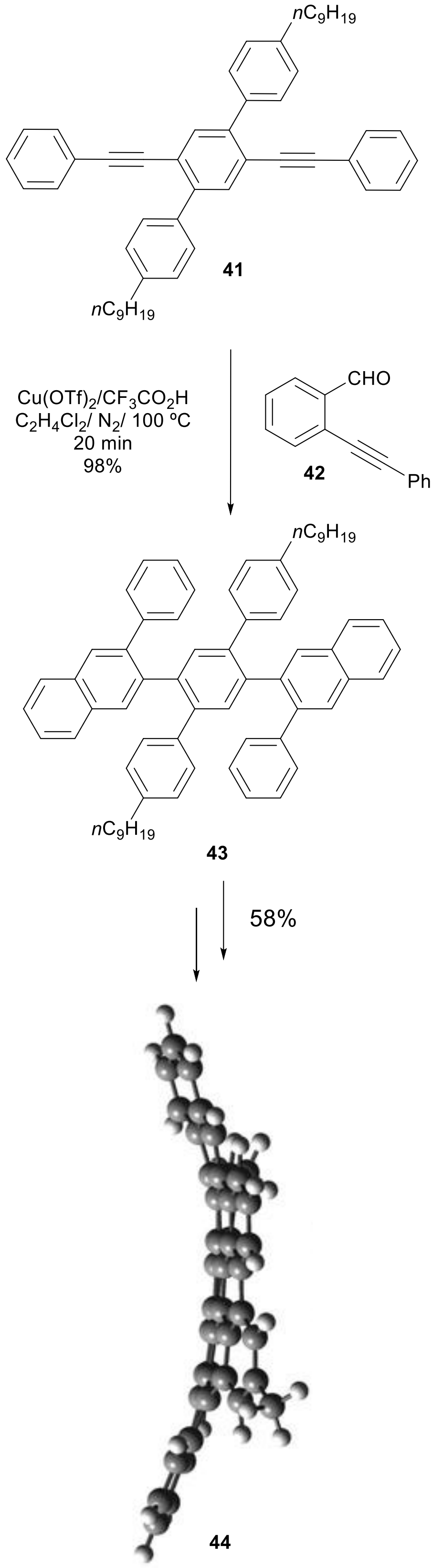


Figure 4 - [4+2] cycloaddition products.



Scheme 9 - Hexabenzocoronenes via benzannulation-cyclodehydrogenation. Alkyl chains truncated to -CH_3 in crystal structure for clarity. Adapted from Ref. 89 with permission from The Royal Society of Chemistry.

the arrangement of the aryl substituents minimizing aggregation.

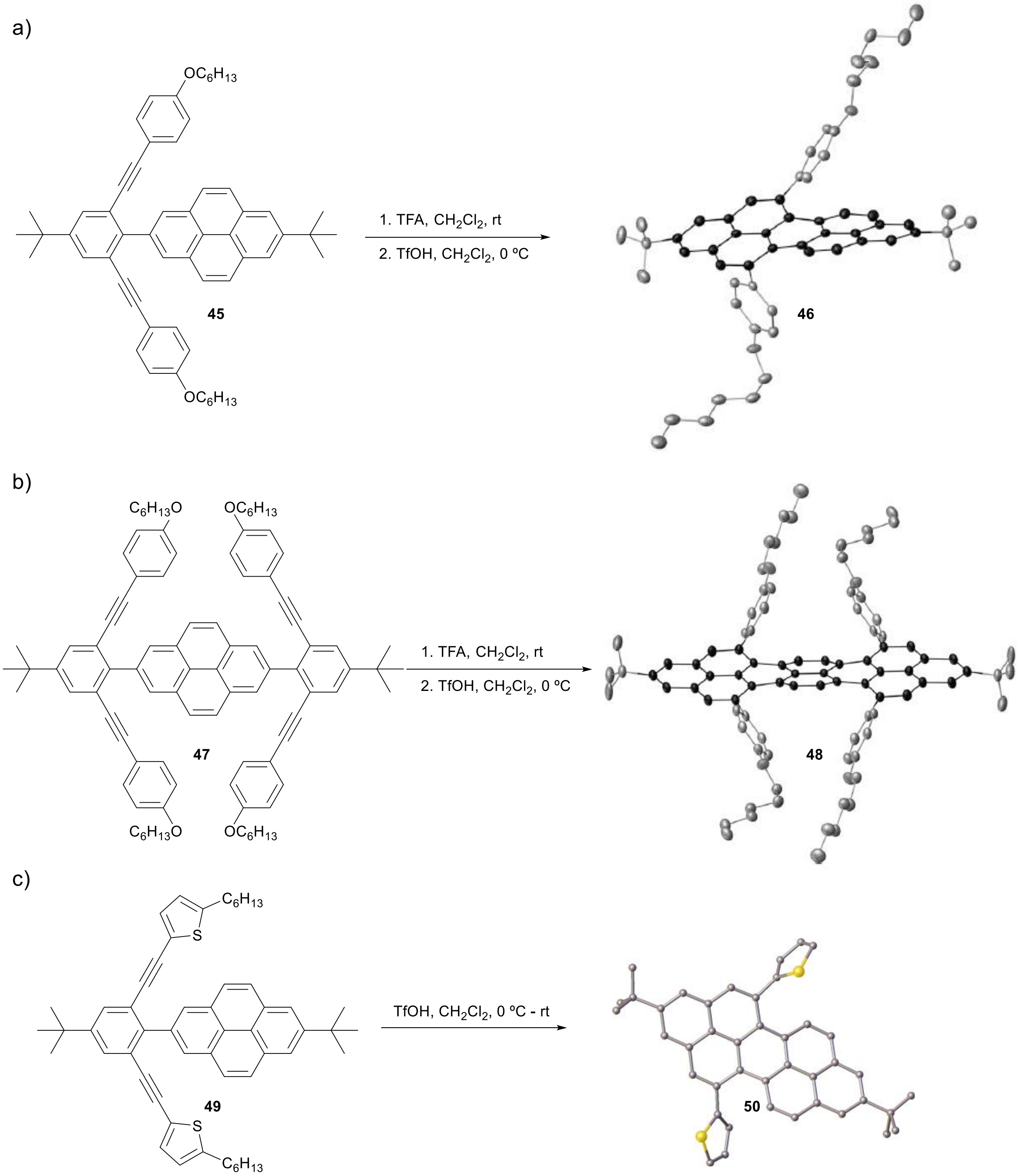
A highly twisted hexapole helicene **30** (six-[5]helicene) has been synthesized by the Kamikawa group in 2017 by Pd-catalyzed [2+2+2] cycloadditions of aryne precursors, as shown in Scheme 6.[83] The efficiency of the methodology can be understood based on the selective formation of only one pair of isomers among the 20 different ones possible (and 10 possible enantiomer pairs). The hexapole helicene was formed stereoselectively and confirmed by X-ray crystallographic analysis to be the (*P,M,P,P,M,*P) configuration (Scheme 6a); however, when heated to 100 °C in toluene for 3 h, the product isomerized into the higher symmetry (*P,M,P,M,P,M*) product, **30-1** (Scheme 6a). The aryne precursor is subjected to 6.0 equiv. of CsF, 0.1 equiv. of $Pd_2(dba)_3$•$CHCl_3$ in CH_3CN at room temperature for 24 h. Hexapole helicene **30** also possesses a twist angle of 35.7°, measured as the deformation of the benzene ring adjacent to the core benzene ring, which is the largest twist angle reported to date.[83] The synthesis of **30** was also completed in 2017 by Gingras and coworkers, utilizing a Yamamoto Ni(0) coupling of 7,8-dibromo[5]helicene **31** in one step, shown in Scheme 6b.[84] Gingras reported large interplanar angles between the two terminal rings of a helicene with 49° for the external [5]helicenes and 69.9° for the internal [5]helicenes (compared to [5]helicene with 46° and carbohelicenes ranging from 40-53°.[15, 16]

In 2018, the Wang group reported the first synthesis of two hexapole [7]helicene derivatives from hexaphenylbenzene based precursors. As shown in Scheme 7, alkyne cyclotrimerization of **32** by $Co_2(CO)_8$ in excellent yields to afford the desired hexaphenylbenzene based precursors followed by Scholl oxidation afforded the 150 conjugated carbon atoms of hexapole [7]helicene **33** in 18% yield.[85] Interestingly, **33** shows no π-π stacking in the unit cell containing both (*M*)- and (*P*)-enantiomers.[85] Compound **33** also possesses impressive thermostability. Optically pure **33** was heated to 270 °C in diphenyl ether in a sealed Schlenk tube for 12 h under inert atmosphere and showed no evidence of decomposition.[85] This work was also extended later in 2018, to hexapole [9]helicene.[86] Hexapole [9]helicene is soluble in common organic solvents and its optical activity is comparable to that of **33**.[86] Similar to **33**, hexapole [9]helicene shows both isomers within the unit cell stacking alternately to form a columnar structure.[86]

In 2016, Fukuzawa provided an efficient synthesis of twisted polycyclic aromatic systems by successive rhodium-catalysed annulation reactions of bis(arylethynyl)arenes **34** with biphenylboronic acids **35** (Scheme 8) to afford sterically crowded **36**.[87] The reaction was performed with 1.0 equiv. bis(arylethynyl)arene, 2.4 equiv. biphenylboronic acid, and 0.25 equiv. of AgOAc in dry DMF at 100 °C for 16 h in good yields. Isolated **36** was then subjected to Scholl reaction conditions (DDQ/CH_3SO_3H) which provided the double annulated product **37** as the major product. X-ray crystallographic analysis showed a large twisting angle of 46.7°, shown in Scheme 8, for the product containing two [5]helicene moieties and two fjord regions. Interestingly, the thienyl-substituted derivatives underwent further cyclizations resulting in more planar thiophene-fused fjords.[87]

In 2018, the Martín group explored the π-extension of corannulene via [4+2] cycloaddition between an alkyne-substituted corannulene and aryl-substituted cyclopentadienones followed by Scholl oxidation. They observed different, unique contorted NGs depending on the Scholl technique employed, as shown in Figure 4. Using $FeCl_3$ in CH_3NO_2 at -50 °C the [4,6]helicene containing product **38** is formed selectively from pentaphenyl benzene moiety **39**. Whereas, when **39** is treated with DDQ and TfOH at 0 °C the selectively formed product is **40** , which is both positively and negatively curved as the result of the formation of the seven-membered ring. Interestingly, [4,6]helicene containing **38** can be treated with DDQ and TfOH to quantitatively afford **40**.[88]

In 2013, the Dichtel group investigated the transition-metal-catalysed Asao-Yamamoto benzannulation of electronically polarized diarylacetylenes **41** with *ortho*-



Scheme 10 - (a) Two-fold alkyne benzannulation of **45** reaction to afford chiral peropyrene **46** (b) Four-fold alkyne benzannulation reaction of **47** to afford chiral teropyrene **48** (c) Two-fold alkyne benzannulation or **49** reaction to afford thiophene functionalized peropyrene **50**. Alkyl groups removed from crystal structure for clarity. Adapted with permission from John Wiley and Sons: *Angewandte Chemie International Edition* "Pyrenes, Peropyrenes, and Teropyrenes: Synthesis, Structures, and Photophysical Properties" W. Yang, J. H. S. K. Monteiro, A. de Bettencourt-Dias, V. J. Catalano and W. A. Chalifoux, Copyright 2016.

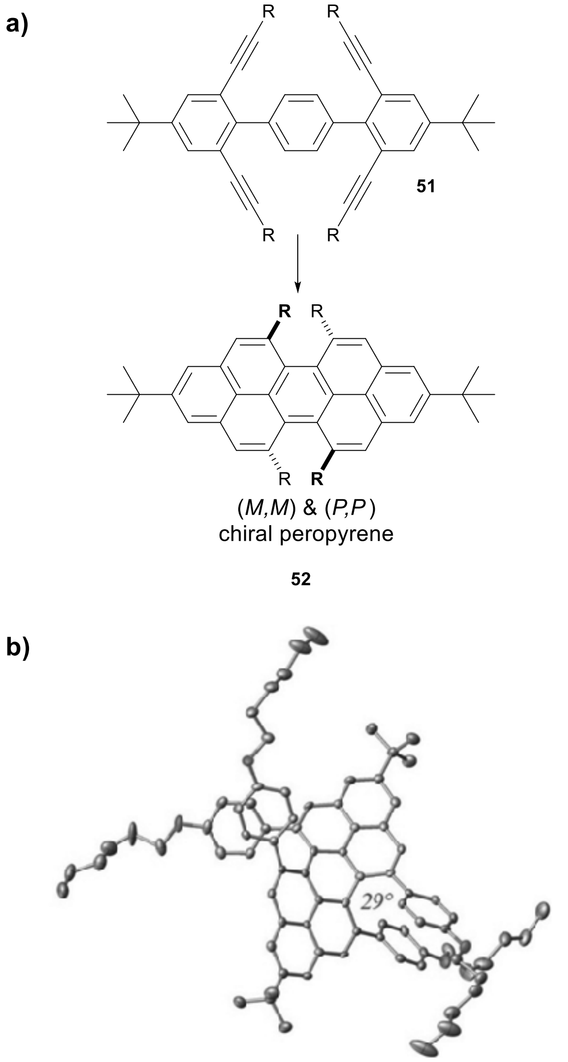


Figure 5 - (a) Chalifoux group chiral peropyrene **52** from acid catalysed four-fold alkyne benzannulation of **51**. (b) Crystal structure of chiral peropyrene **52**, where R= *p*-hexyloxyphenyl. Adapted with permission from W. Yang, G. Longhi, S. Abbate, A. Lucotti, M. Tommasini, C. Villani, V. J. Catalano, A. O. Lykhin, S. A. Varganov and W. A. Chalifoux, J. Am. Chem. Soc., 2017, 139, 13102-13109. Copyright 2017 American Chemical Society.

(phenylethynyl)benzaldehyde **42** to produce a 2,3-disubstituted naphthalene derivative **43** extending the developed method to make contorted hexabenzocoronenes **44** as shown in Scheme 9. This method utilizes $Cu(OTf)_2$ and CF_3CO_2H as catalysts in dichloroethane at 100 °C for the benzannulation followed by oxidation with $FeCl_3$ in CH_3NO_2 in dichloroethane.[89-98] It has been reported previously that the Scholl reaction is generally associated with rearrangement products;[99] however, the efficiency of the above-mentioned method lies in the fact that the extended reaction time during the cyclization step provides fully cyclized products. It should be noted that only the selected derivatives underwent the cyclization completely which was assumed to be dependent on the steric hinderance provided by respective peripheral groups on the hexabenzocoronene. This method provides both fully fused and partially fused hexabenzocoronene derivatives with differing substitution patterns from previous methods as well as an opportunity to

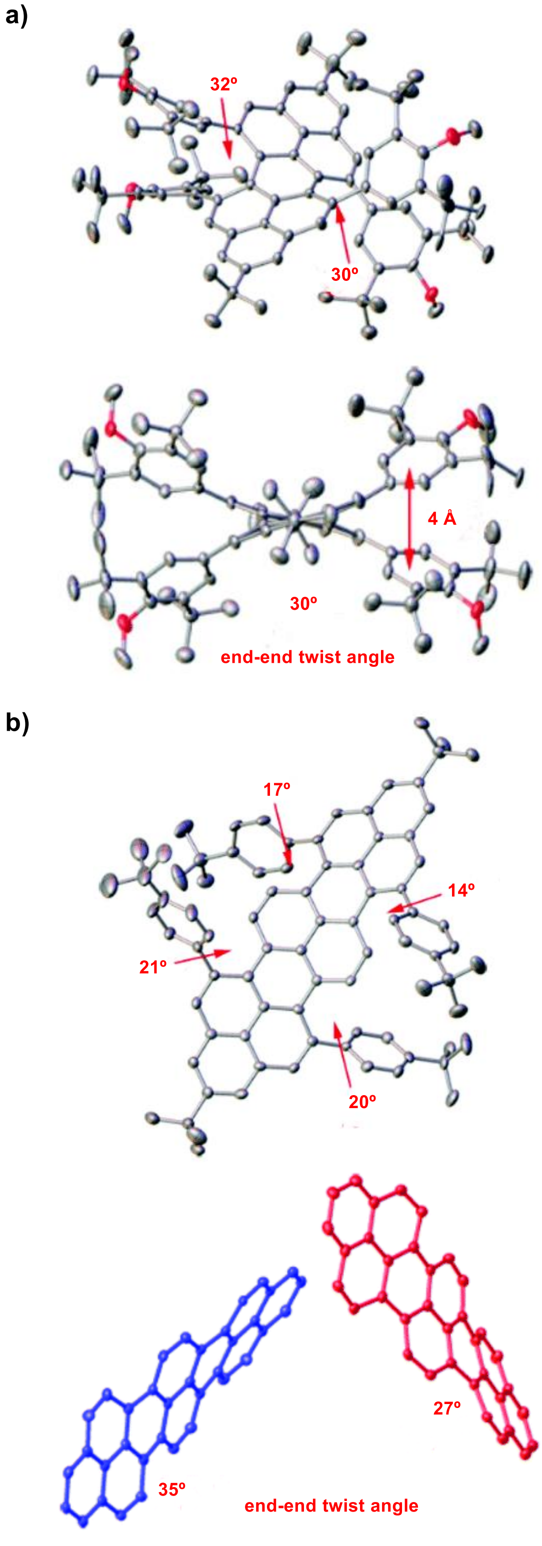


Figure 6 - (a) Crystal structure of chiral peropyrene **52** . (R=3,5-di-*tert*-butyl-4-methoxyphenyl) (b) Crystal structures of chiral teropyrene. Adapted from Ref. 53 with permission from The Royal Society of Chemistry.

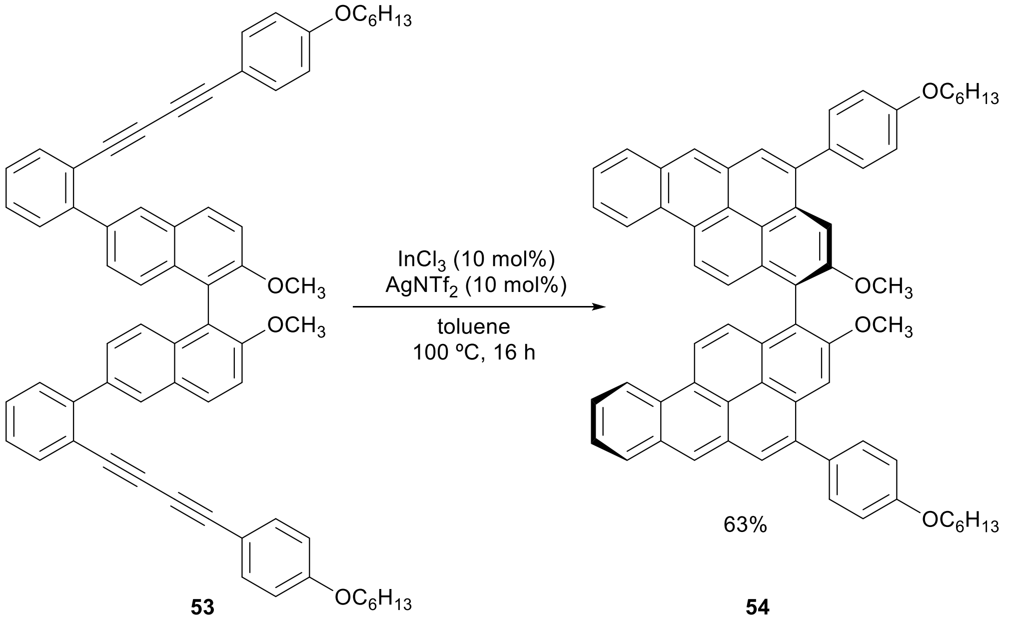
explore the solubility and electrochemical properties of partially fused intermediates.[89]

Acid-catalysed Alkyne Benzannulations

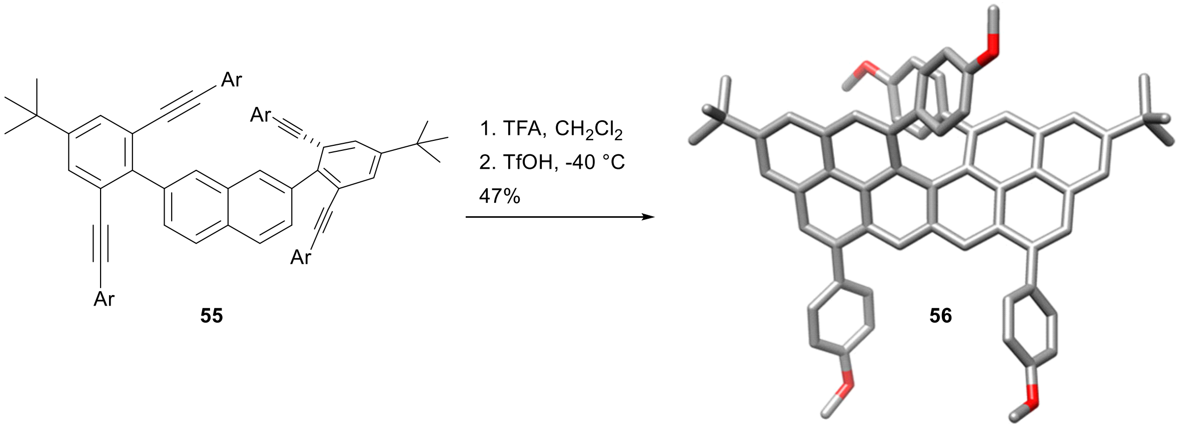
Alkyne benzannulation reactions are an effective method that can be explored in making contorted NGs. This reaction is highly favourable for the bottom-up approach to the synthesis of NGs and graphene nanoribbons.[1] This reaction was pioneered in 1994 by Swager and co-workers who utilized Brønsted acids to afford benzannulated graphene nanoribbons.[100] By incorpoarting a *p*-alkoxyphenylethynyl group, or other electron-donating group and a strong electrophile such as TFA or iodonium tetrafluoroborate, the alkyne benzannulation readily proceeded in high yields.[61]

Recently, the Chalifoux group discovered an efficient alkyne benzannulation method that employs Brønsted acids (CF_3CO_2H and TfOH) as catalysts to make pyrenes, peropyrenes, and teropyrenes.[101] In 2016, the two-fold alkyne benzannulation of **45** to afford peropyrene **46** (Scheme 10a) showed twisting in the backbone in the solid state as the result of steric repulsion and led to an end-to- end twist angle of ~18°. The four-fold alkyne benzannulation of **47** to afford teropyrene **48** (Scheme 10b) as well as the thiophene functionalized two-fold alkyne benzannulation of **49** to afford teropyrene **50** (Scheme 10c) were chiral in the solid state with end-to-end twisting observed.[101, 102] Exploration of alkyne benzannulation reactions on **51** (Figure 5), the Chalifoux group reported the first ever synthesis of chiral peropyrene **52** with two substituents in each bay region, containing two helicene-like moieties. The synthesis involves a four-fold alkyne benzannulation reaction using the same Brønsted acid methodology mentioned previously.[103] Interestingly, in the synthesis of chiral peropyrene **52**, none of the meso peropyrene product was detected. Chiral peropyrene **52** (R= *p*-hexyloxyphenyl) possessed an optical rotation value $[\alpha]^{25}_{589}$= +1438 (c = 8.69×10^{-3} g/L in CH_2Cl_2), which is comparable to that observed in other helicene systems. Additionally, X-ray crystallographic analysis showed a splay angle of the bay region is ~29° and an end-to-end twist angle of 28°, as shown in Figure 6b.[103]

The Brønsted acid catalysed alkyne benzannulation method was effective for electron-rich ethynylaryl moieties, where R is either *p*-alkoxyphenylethynyl or thiophenyl; however, neither electron-neutral, electron- deficient, nor alkyl-substituted alkyne moieties gave cyclization products when using TfOH or TFA. In search of a more efficient and widely functional group tolerant catalyst, the Chalifoux group established a Lewis acid ($InCl_3$) catalysed alkyne benzannulation after screening a variety of commonly used Lewis acids for the transformation.[53, 104] The method involves 1.0 equiv. of $InCl_3$ in toluene at 120 °C for 24 h, for the conversion of tetrayne **51** to a very sterically congested chiral peropyrene **52**. This allowed for the expansion of the scope of R to include electron-rich and electron-poor aryl groups as well as alkyl groups. The formation of chiral peropyrenes were less successful with electron-withdrawing groups like Ph-CF_3; however, introducing more sterics to the aryl ring enhanced the twisting of the peropyrene backbone of **52** (R=3,5-di-*tert*-butyl-4-methoxyphenyl) as can be seen in the crystal structures shown in Figure 6a. The Chalifoux group also worked on a scope of teropyrenes, one of which was chiral in the solid-state. This teropyrene, crystal structure shown in



Scheme 11 - "Butterfly" ligand from domino alkyne benzannulation.



Scheme 12 – Four-fold alkyne benzannulation to afford pyreno[*a*]pyrene-based helicenes. Alkyl groups truncated and hydrogens removed for clarity. Adapted with permission from R. Bam, W. Yang, G. Longhi, S. Abbate, A. Lucotti, M. Tommasini, R. Franzini, C. Villani, V. J. Catalano, M. M. Olmstead and W. A. Chalifoux, *Org. Lett.*, 2019, **21**, 8652-8656. Copyright 2019 American Chemical Society.

Figure 6b, possessed dihedral angles in the bay regions up to 21° and end-to-end twist angles ranging from 27-35°.[53]

In 2018, the Chalifoux group reported the first domino benzannulation reaction of buta-1,3-diynes catalysed by $InCl_3/AgNTf_2$.[105] This was seen to work on a number of unique substrates. Of note, the polyyne with dimethoxy-1,1'-binaphthalene core **53** affords a chiral "butterfly" ligand **54**, as shown in Scheme 11.[105] This series of irregularly sized NGs allowed for the study of optical properties for a variety of NG isomers.[105]

In 2019, the Chalifoux group reported the synthesis of pyreno[*a*]pyrene-based helicenes.[106] These helicene-based NGs become both laterally and helically π-extended in a single reaction step. The tetrayne precursor **55** was treated with TFA to afford an approximately 1:1 ratio of bis-cyclized intermediates as well as a rearranged side product (not shown) in trace quantities that was confirmed by X-ray crystallographic analysis. Treatment of these intermediates in situ with TfOH afforded a racemic mixture of pyreno[*a*]pyrene-based helicenes **56** in good yields (Figure 12).[106] This type of rearrangement has been previously reported by Swager and co-workers who also utilize acid-catalysed alkyne benzannulations and this rearrangement likely occurs to relieve steric strain.[61, 100] Based on single X-ray crystallographic analysis, the two aryl substituents present in the cove are positionally locked making these the first examples of pyreno[*a*]pyrene-based helicenes.

Conclusions

Many methods have been employed in the synthesis of contorted NGs. Of these, alkynes have been utilized in various methods as important precursors to make non-planar or chiral NGs. Whether alkynes are used in the preliminary steps, such as in cycloaddition reactions, or in key intermediate steps, alkynes are an excellent functional group for these conversions. The versatility of alkynes as reaction tools from cycloaddition reactions, radical cascades, electrochemical syntheses to alkyne benzannulation reactions, alkynes have broad potential to be exploited in the preparation of non-planar NGs. Furthermore, recently discovered highly efficient alkyne benzannulation reactions provide an effective alternative as compared to the highly utilized Scholl reaction in making NGs, which is often associated with harsh reaction conditions and the possibility of rearranged products. There are still some challenges in the use of alkynyl substrates in the development of contorted NGs. For example, work is needed in expanding the scope of heteroatom-doped substrates as they are electronically poor and thus more difficult to cyclize. Additionally, the direct alkyne benzannulation reaction to arrive at both larger (7-membered or more) and smaller (5-membered) rings, is in need of further exploration.

Alkyne benzannulation reactions provide a method of forming one or more new rings within a single reaction step while still tolerating a variety of EDG and EWGs. This allows for the potential to form even larger contorted NGs, with greater than four-fold cyclization. The development of these larger contorted NGs would create a broader scope of compounds with new and interesting properties to be studied. There is also potential for further expansion in the use of polyynes, such as **53**, in the cascade or alkyne benzannulations reactions to develop more interesting and contorted NGs. Thus, alkynes are attractive precursors that need to be explored more in the preparation of non-planar NGs.

Conflicts of interest

The authors declare no conflict of interest.

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