Twisted 4,5-Diarylphenanthrenes via Self-Terminating Cascade Radical Cyclization of Enyne-Allenes

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Abstract

Non planar aromatic hydrocarbons constitute an interesting class of compounds that have been studied for a long period of time. Steric interaction originated around the bay region of polycyclic hydrocarbons and its derivatives is considered to be the main reason behind such deformation from planarity to non-planarity. Initial studies on 4,5-dimethylsubstituted phenanthrenes have revealed intricate details about the structural distortion and opened a new avenue of research on helicene chemistry. The present review focused on the preparation of more congested 4,5-diaryl substituted phenanthrenes with a special attention on their highly twisted molecular frameworks. The synthesis is based on self-terminating cascade radical cyclization of different enyne-allenes produced from appropriately designed enediynes through prototropic tautomerization. Fully conjugated helical polyaromatics are ultimately afforded *via* effective synthetic transformation.

Keywords: Enyne-Allene, Diarylphenanthrene, Cascade-Radical Cyclization, Nonplanar

Introduction

Different planar and nonplanar polyaromatic hydrocarbons (PAH)[1-3] have attracted lots of interest among the scientific community in the last few decades due to their remarkable optoelectronic properties[4-8] and various applications in the field of supramolecular chemistry[9,10]. Between planar and nonplanar varieties, synthesis of nonplanar polyaromatics are comparatively more challenging than their planar analogues. The nonplanarity essentially occurs in a particular hydrocarbon due to the undue steric congestion within the hydrogen atoms present in the molecular bay region.[11-13] The fjord region[14] of crowded nonplanar polyaromatics plays an important role for tuning the biological reactivity of diol epoxide (DE), the crucial metabolite of PAH. Nonplanarity of DE proves helpful to adopt energetically stabilized in-quasidiequatorial geometry in which the epoxide ring situates on the same side of the distal aromatic ring of PAH.[15] The arrangement effectively shields the epoxide oxygen from acid catalyzed hydrolysis reaction in solution or near the DNA resulting the generation of more DNA bound DE than the formation of tetrol.[16] Apart from DNA binding and intercalation[17-19], nonplanarity induces some other interesting features in PAH that represents the molecules as most promising in the field of chiral recognition[20,21], asymmetric catalysis[22], designing photochromic materials[23], sensors[24], molecular level devices[25], NLO materials[26] etc.

Review of Literature

Phenanthrene, the first member of the group of *ortho*-fused polyaromatics, is a planar molecule. But, appropriate grafting on C4 and C5 can make the whole molecule contorted, owing to the huge steric destabilization along the bay region of the molecule in the planar arrangement.[27-29] Number of studies[30-32] have already been done to determine the structural strain and the consequential skeletal deformations of different 4,5-disubstituted phenanthrenes (**Figure 1**). To be more precise, 4,5-dimethylphenanthrene has been the choice of substrate for most of these studies. Processes like ozonolysis of pyrene,[33] photo-induced dehydrogenative cyclization of stilbene[34,35] are utilized for the preparation of 4,5-dimethyl analogue. Due to the most hindered positioning of the methyl substituents, they experience a severe nonbonded steric interaction which forces them to be out of the aromatic plane. The methyl groups prefer to be projected on the alternate sides of the phenanthrene

system. Such arrangement of 4,5-dimethyl substituted phenanthrenes exhibited a special type of optical isomerism that provides the basic guiding concept for future helicene chemistry.[36-38] Upon increasing the steric demand of the substituents by replacing methyl groups with phenyls, very rationally, the aromatic framework of phenanthrene would be more distorted. Consequentially, 4,5-diarylphenanthrene forms a helically twisted molecular architecture allowing a comparatively easier resolution of the resultant axial isomers.

Figure 1: **Structures of Some 4,5- Disubstituted Phenanthrenes**
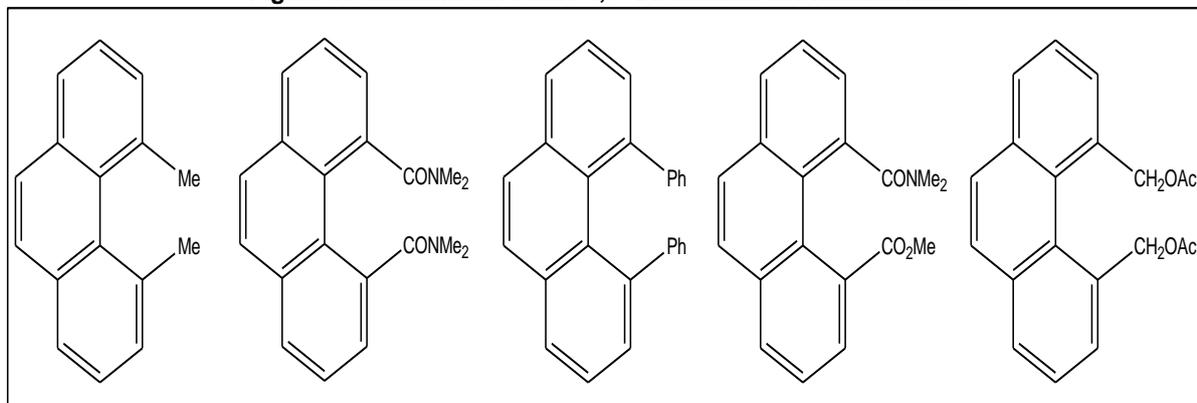
Objective of the Study

Preparation of 4,5-diaryl substituted phenanthrene and its derivatives is mostly dependent on photocyclization based methodology.[39-41] Different strategy involving tandem radical cyclization for the synthesis of distorted 4,5-diarylphenanthrenes has been documented here. Interestingly, all the radical intermediates formed during the course of reactions are intramolecularly self-quenched. This particular non-chain character again suggests to refer the relay radical reaction as self-terminating.[42,43] So, in this present review, self-terminating cascade radical cyclization based processes leading to an easy access of different 4,5-diarylphenanthrenes are represented with a highlight on their special structural features.

Scheme 1: **Synthesis of 4,5-Diarylphenanthrene**
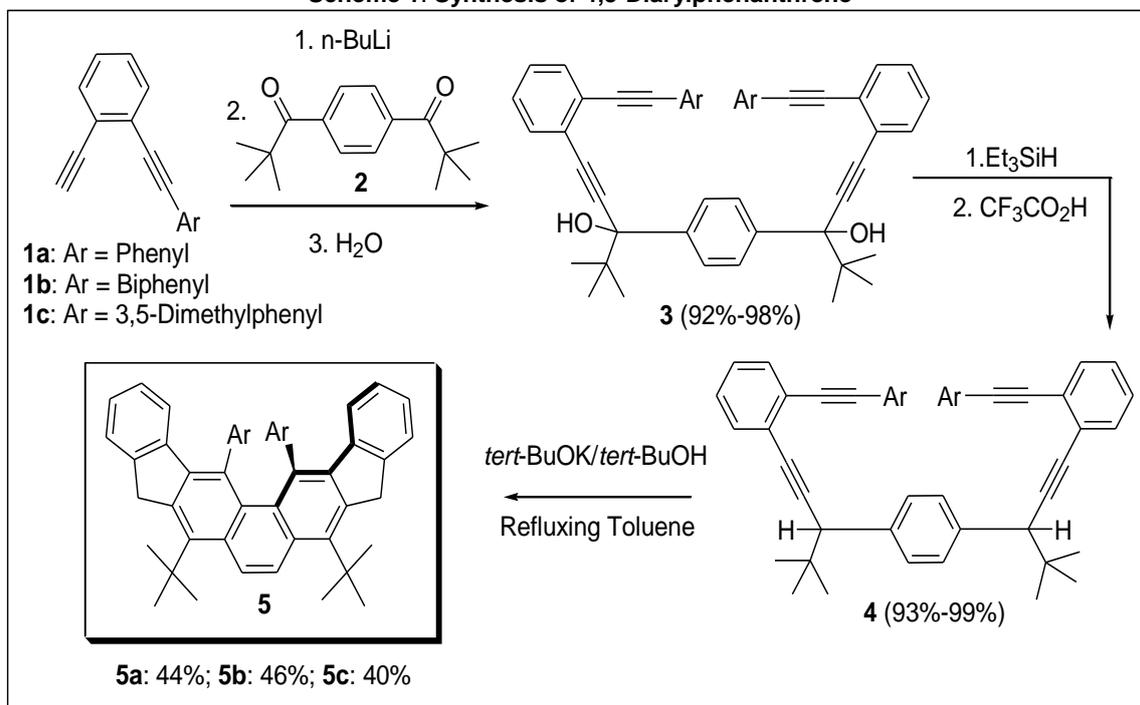
Scheme 2: Cascade Radical Cyclization
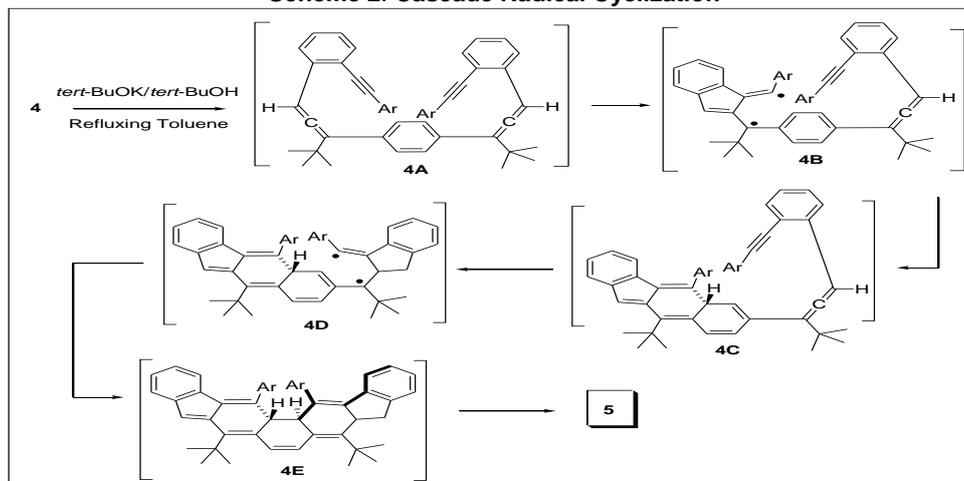
The first successful synthesis of 4,5-diarylphenanthrenes through cascade radical cyclization was demonstrated by Wang group.[44] The synthesis was started from simple diacetylene **1 (Scheme 1)**. Treatment with *n*-butyllithium followed by condensation with diketone **2** produces 1:1 diastereomeric mixtures of the propargylic alcohol **3** in 92-98% yield. Conversion of this alcohol to the corresponding hydrocarbon derivative **4** was achieved by triethylsilane in presence of trifluroacetic acid. Resulting tetraacetylene **4** was then reacted with potassium *tert*-butoxide under refluxing toluene for about 10 h to furnish 4,5-diarylphenanthrene **5** with an yield up to 46%. Mechanism for such brilliant transformation from tetraacetylene **4** to **4,5-**diarylphenanthrene **5** has been speculated to be based upon Schmittel cycloaromatization[45,46] of the *in situ* generated benzannulated enyne-allene **4A** intermediate through 1,3-prototropic isomerization **(Scheme 2).** Formation of such enyne-allene intermediate **4A** had been confirmed by kinetic NMR experiments under mild reaction condition. For, major proportion of the tetraacetylene **4**, the characteristic propargylic proton signal converted to the allenic hydrogen signal appearing at δ 6.91 within 3 h of heating at 65 °C in THF. Initial C^2-C^6 cyclization in one hand of enyne-allene **4A** generated the biradical

4B which upon intramolecular radical-radical coupling reaction with the central phenyl ring afforded intermediate **4C**. Conversion of the enyne-allene **4A** to intermediate **4C** can also be considered as a formal Diels-Alder reaction. However, based on DNA cleaving and other relevant mechanistic studies, it had been suggested to follow an alternative stepwise biradical pathway.[47-49] Similar course of C^2-C^6 cyclization and subsequent radical-radical coupling in the other part of the molecule afforded intermediate **4E**. Finally, two hydrogen atom tautomerizations furnished 4,5-diarylphenanthrene **5 (Scheme 2).**

Structure of the 4,5-diarylphenanthrene, **5a** was unambiguously established by crystallographic analysis **(Figure 2)** which revealed the distorted nature of the central aromatic ring with two severely bent phenyl substituents.[44] Two phenyl groups are actually parallelly oriented having an interplanar perpendicular distance of 2.9 Å which is much lower than the optimal van der Waals contact distance of usual π-system.[50] In addition, C4, C5 phenyl substituents of **5a** form an angle of 53.1° with respect to the central phenanthryl moiety. Two outer phenyl rings of the nonplanar phenanthrene system creates a much larger angular twisting of 46.1° as compared to 27.9° twist in case of the dimethyl derivative, reported earlier by other research teams.[51,52]

Figure 2: X-Ray Crystal Structure of Compound 5a

(a) Viewing along the axis perpendicular to the phenanthrene system

(b) Viewing along the crystalographic C_2 axis with hydrogen atoms ommitted
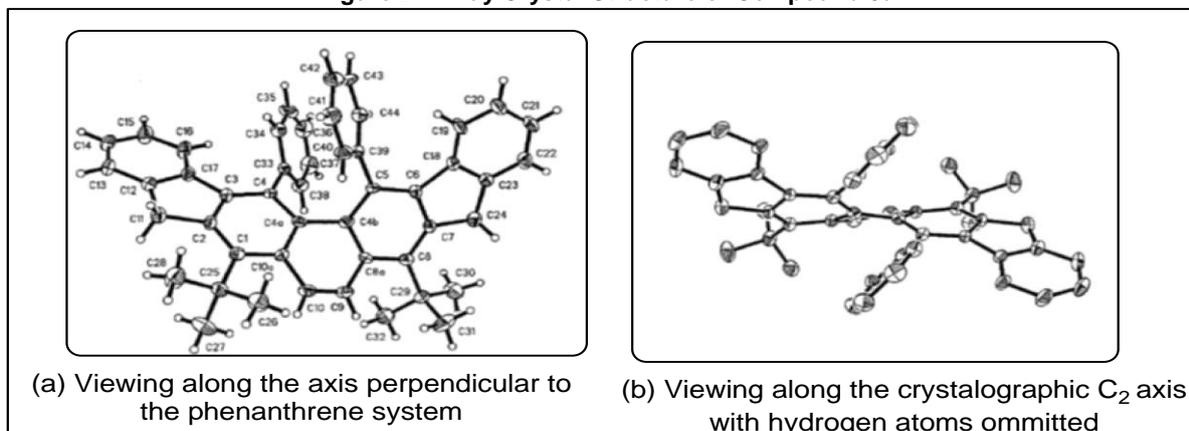
Helical twisting of **5a** was also manifested by the corresponding NMR spectroscopy. The AB pattern

of the two diastereotopic methylene hydrogens of the five membered ring of indene moiety appeared at δ

4.15 and 4.39 with a significant geminal coupling constant of 21 Hz **(Figure 3)**. Another interesting point mentioned by the author was about the appreciable upfield shift of different aromatic protons.[44] This was attributed to the particular nonplanar geometry of the molecule where C4, C5 phenyl rings are projected nearly in a perpendicular direction with respect to the central aromatic system. Now, the helical nature of the molecule forces the outer aromatic rings of the diindenophenanthrene system to be closer to these phenyl substituents. Thus, some aromatic protons fall into the shielding region of the induced aromatic ring current effect of the closely situated phenyl substituents. Due to this anisotropic effect, *ortho*-proton of the phenyl substituent appeared at 6.52 ppm whereas in case of the outer indenyl aromatic ring, two protons were upfield shifted to 6.20 and 6.74 ppm **(Figure 3).** Number and pattern of the other proton signals were fully consistent with the structure of the molecule **5a**.

Figure 3: NMR Spectra of Phenanthrene 5a
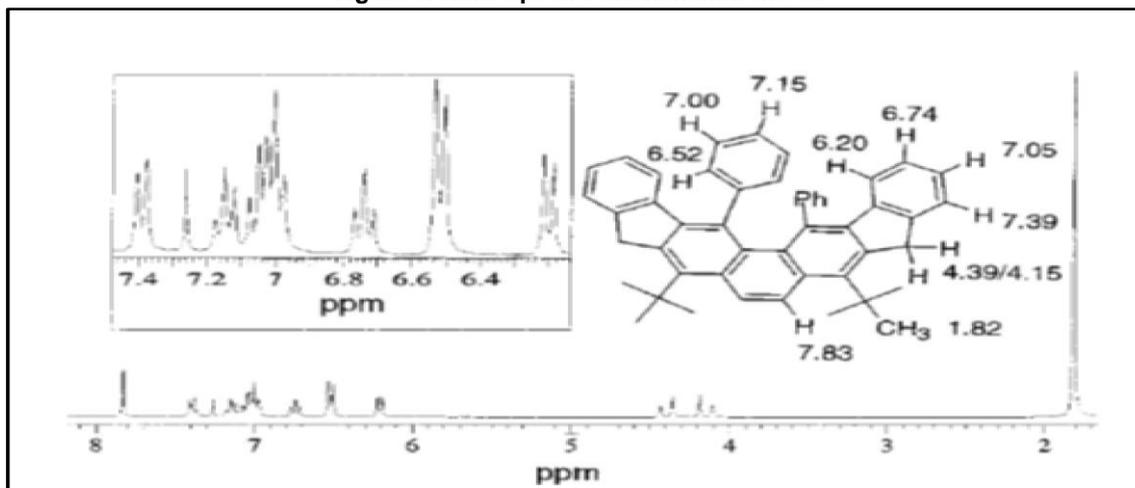
The same methodology for the construction of 4,5-diarylphenanthrene was further extrapolated towards the synthesis of structurally more congested hydrocarbon **9 (Scheme 3)** bearing two additional phenyl substituents linked to the outermost aromatic rings of diindenophenanthrene system.[53] Starting precursor was the diyne **6** which was again stepwise synthesized from 1,1'-biphenyl-2-ol **(Scheme 3).**[53,54] Reaction of two equivalents of the diyne **6** with diketone **2** in presence of butyllithium furnished the tetrayne species **7** in 94% yield. Dehydroxylative reduction of alcohol **7** with triethylsilane and trifluoroacetic acid produced hydrocarbon **8**. Now, similar to the earlier case, enyne-allene intermediate was assumed to be formed *via* prototropic rearrangement after the reaction with potassium *tert*-butoxide in refluxing *p*-xylene. Subsequent course of reactions including two self-quenched cascade radial cyclizations and two prototropic rearrangements finally afforded the unique structure of compound **9 (Scheme 3)** in only 20% yield. Lower yield of the final product compared to the earlier phenanthrene derivative **5** was attributed to the highly congested structural framework of the present compound.

Scheme 3: Synthesis of Tetraphenyl Substituted Phenanthrene Derivative
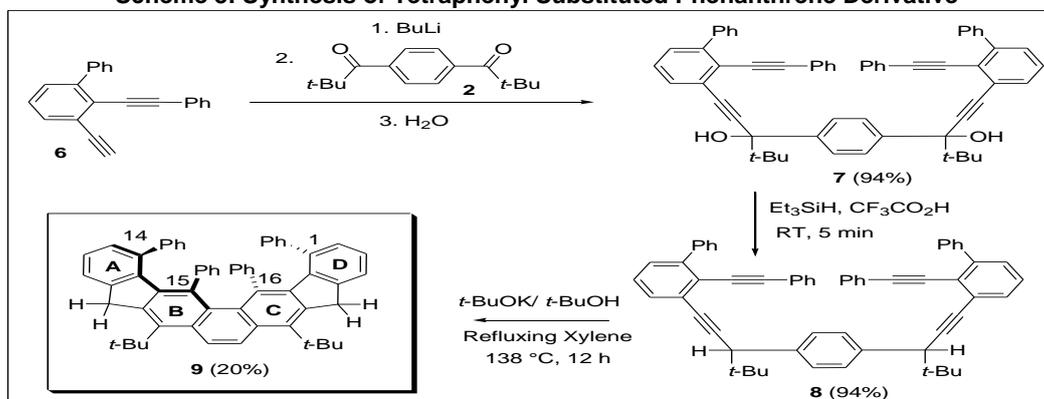
The X-ray structure of compound **9 (Figure 4)** displayed some interesting arrangement of the four phenyl rings inside the molecule. Rings were oriented vertically with respect to the central helical axis of the diindenophenanthrene framework maintaining a parallel relationship with each other at the same time. Perpendicular distance between two neighboring phenyl rings was found to be 3.1 Å. A and B phenyl rings of diindenophenanthrene system showed a interplanar twist angle of 29.3° while the mean planes of B and C rings was 59.2° twisted. Dihedral angle between the two bonds C1-phenyl and C16-phenyl

was 53.6°, whereas, bonds between C15-phenyl and C16-phenyl exhibited a much larger angle of 63.5°. In addition, vision along the C1 and C14 line revealed that the connecting bond between C14 and the phenyl substituent was rotated by 184.3° from the C1-phenyl interbond along the rotating direction of the helical twist. To avoid the intense steric interaction, four

phenyl rings were projected in a skewed fashion, they did not protrude on top of each other. Thus upon viewing from the perpendicular direction with respect to helical axis, it appeared as an exceptional arrangement of a segmented spiral staircase having four parallel steps.

Figure 4: X-ray Structure of Compound 9
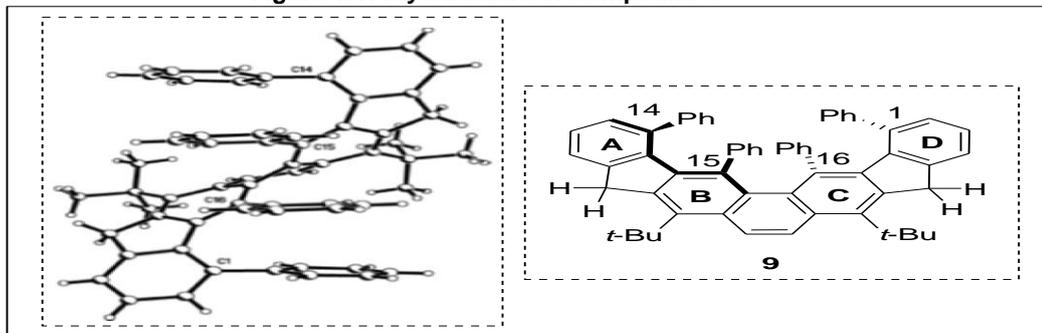
Introduction of these two extra phenyl rings in structure **9** resulted severe buttressing effect that reduced the rate of racemization of the molecule. As a consequence, a more stable conformation of compound **9** could be obtained at 25 °C compared to the previously synthesized 4,5-diarylphenanthrene system **5**. From, temperature dependent NMR study, the rotational barriers for 4,5-diphenylphenanthrene **5** were calculated to be 12.5 and 12.6 kcal/mol at -22 and -10 °C, respectively, whereas, an increased barriers of 14.3 and 14.2 kcal/mol at 25 and 30 °C respectively were found for compound **9**.[53]

Next, a vital transformation of 4,5-diarylphenanthrene **5a** was accomplished by Yang and his coworkers leading to the generation of fully aromatic hydrocarbon **11**.[55] For this purpose, a

mixture of three diastereomeric alcohols (**10a, 10b** and **10c**) was first prepared by the treatment of phenanthrene **5a** with lithium diisopropylamide (LDA) followed by the reaction with paraformaldehyde **(Scheme 4).** Presence of the bulky *tert*-butyl groups played an important role by preventing any unwanted condensation reaction of alcohol **10** with excess LDA and paraformaldehyde. 9-Fluorenylmethanol **10** (**a, b** and **c**) was reacted with phosphorous pentoxide (P$_2$O$_5$) in *p*-xylene at 110 °C to yield 73% of diphenylpentacene **11** *via* Wagner-Meerwein type rearrangement[56,57] reaction with the complete removal of *tert*-butyl groups. Heptacene **11** is highly congested due to the attachment of two phenyl substituents at the sterically most hindered C17 and C18 positions.

Scheme 4: Synthetic transformation of 4,5-diarylphenanthrene
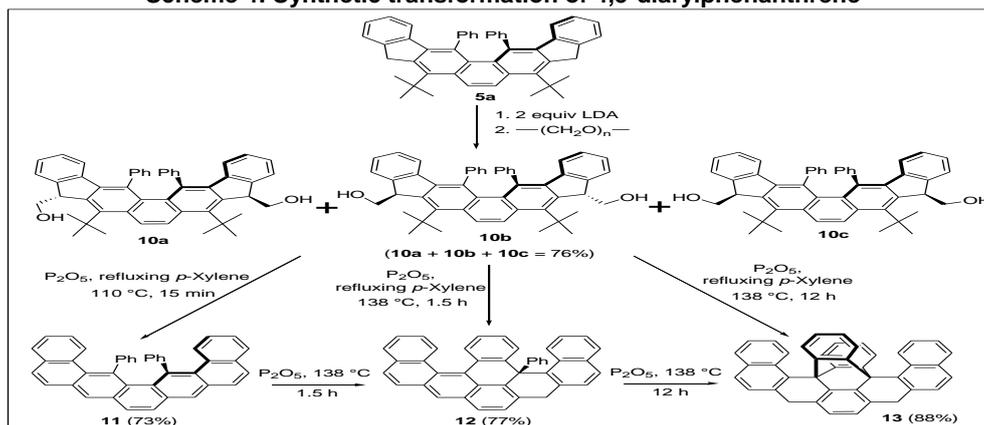
Interestingly, the previous reaction sequence exhibited some other derivational scopes too.[55] Initially formed diphenylpentacene **11** upon further heating in *p*-xylene at relatively higher temperature of 138 °C transformed into compound **12 (Scheme 4)** in 77% yield. Apparently, the conversion proceeded through C7 protonation of compound **11** followed by intramolecular electrophilic aromatic substitution involving the phenyl substituent linked to C17 position led to the generation of the crucial transition state **11b**

(Scheme 5). Subsequent deprotonation then furnished another unique hydrocarbon **12** within 1.5 h. On continuing the heating process at 138 °C for a prolong time of **12 h**, triptycene **13 (Scheme 4)** was afforded as the major compound. Conversion of compound **12** to triptycene **13** was assumed to occur by a second intramolecular electrophilic aromatic substitution reaction by C18 carbon attached phenyl substituent after the initial protonation at the C10 position.[55]

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Scheme 5: Intramolecular Electrophilic Aromatic Substitution of Compound 11
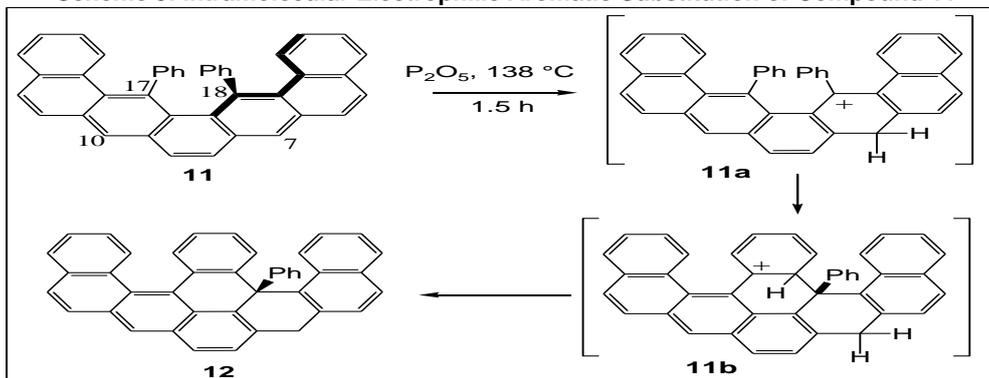
Following, similar synthetic protocol, phenanthrene **5b** was transformed into the diastereomeric mixtures of fluorenylmethanol derivative **14** (diastereomeric ratio = 55:45) in 77% yield **(Scheme 6).**[55] Phosphorous pentoxide promoted dehydroxylation reaction in refluxing *p*-xylene with ring expansion of the methyl alcohol derivative afforded highly conjugated and sterically congested aromatic system **15** in an excellent yield of 89% within a very short time period of **15** min. If the same reaction was carried out at higher temperature (138 °C) for a long time, another bridged hydrocarbon **16** was obtained in 42% yield which was otherwise difficult to prepare.

Scheme 6: Preparation of Congested Hydrocarbons
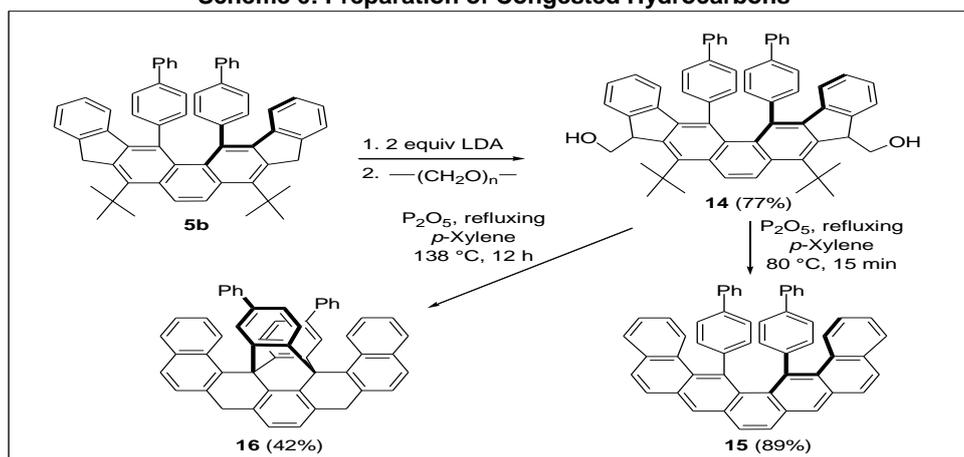
Conclusion

The review is presented with an intension to summarize all the tandem radical processes utilized for the preparation of 4,5-diarylphenanthrene derivatives. Earlier literature reports on the synthesis of this particular distorted polyaromatics were indeed very limited. So, the importance of the radical processes is noteworthy that had provided an innovative and more versatile synthetic route for the generation of various contorted 4,5-diarylphenanthrene derivatives. Appropriately substituted enediyne components upon base promoted hydrogen tautomerization directly fabricates the essential enyne-allene intermediates. Afterwards, *via* two successive tandem C2-C6 radical cyclizations, the allenes transformed into appreciably distorted skeleton of different 4,5-diarylphenanthrenes. Generality of the methodology was manifested by synthesizing profoundly twisted geometry of four phenyl ring substituted diindenophenanthrene. Furthermore, the review included an important transformation of diindenophenanthrene system to the fully aromatic hydrocarbons, useful for organo-electronics, cosmetic[58,59] and graphene chemistry[60-62]. Judging the potential of the radical cyclization, it would not be very incorrect to foretell that the similar tandem course can possibly be utilized for the construction of other intricate molecular frameworks as well in near future.

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