Polyaromatic Compounds

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Radical Alkyne *peri*-Annulation Reactions for the Synthesis of Functionalized Phenalenes, Benzanthrenes, and Olympicene

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Abstract: *Radical cyclization reactions at a peri position were used for the synthesis of polyaromatic compounds. Depending on the choice of reaction conditions and substrate, this flexible approach led to Bu_3Sn-substituted phenalene, benzanthrene, and olympicene derivatives. Subsequent reactions with electrophiles provided synthetic access to previously inaccessible functionalized polyaromatic compounds.*

Annealing of an additional benzene ring to an existing aromatic system ("benzannulation") provides a useful strategy for the controlled growth of polyaromatic nanostructures, such as open carbon nanotubes and graphene nanoribbons. In this context such transformations are often referred to as "annulative π-extension (APEX) reactions".[1] The high energy and carbon content render the alkyne moiety a perfect functionality for the benzannulative expansion of polyaromatic systems.[2] For example, Scott and co-workers introduced a Diels–Alder strategy for the growth of a carbon nanotube from the "biphenyl-like" bay regions,[3] whereas Swager and co-workers used acid- and electrophile-promoted alkyne cyclization reactions to anneal additional aromatic rings to paraphenylene polymers.[4] Recently, Chalifoux and co-workers prepared pyrene, peropyrene, and teropyrene derivatives through the benzannulation of alkynes as promoted by Brønsted acids and later expanded this approach to the bottom-up synthesis of graphene nanoribbons.[5,6] Ito, Itami, and co-workers reported the Pd/chloranil-catalyzed annealing of a biphenyl moiety at the K-region with dibenzosiloles and dibenzogermoles.[1c] Annealing of two armchair polyaromatic units with an alkyne showcases the ability of this functionality to serve as a "carbon-rich glue" that can connect two carbon nanostructures.[7]

The scope of this approach is expanding continuously. In particular, alkyne benzannulation at a biphenyl unit was accomplished through electrophile-assisted,[7] transition-metal-catalyzed,[8–10] and oxidative radical pathways.[11] However, these examples are limited to the extension of polycyclic aromatic structures at the armchair edge (bay and "K-regions"[12]). In contrast, alkyne annulations at a zigzag edge ("L-region") of carbon nanostructures remain remarkably scarce.[13]

We were interested in understanding the reasons behind this scarcity because *peri*-cyclization reactions can serve as a potential strategy for terminating *exo*-dig cyclization cascades that transform oligoalkynes into extended polyaromatics.[14,15] The "*peri*" approach, such as termination of the cascade with radical attack at a naphthalene unit, would provide pentagon-free polyaromatic systems (Figure 1c).

The kinetics and thermodynamics of the intramolecular attack of a vinyl radical at a naphthyl or biphenyl core show subtle but important differences. Addition to naphthalene is more favorable thermodynamically owing to lower loss of aromatic stabilization. However, the higher strain in the *peri*-cyclization transition state offsets the favorable thermodynamic contribution. The rigidity of a fused bicycle leads to a 2.6 kcal mol^{-1} higher activation barrier in comparison to radical attack at the more flexible biphenyl target, which can

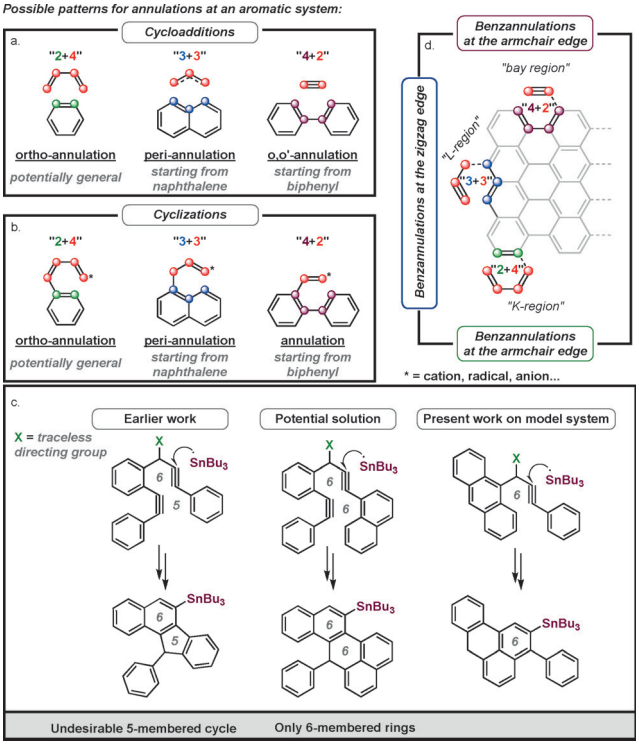

Figure 1. Possible patterns and strategies for annulations at an aromatic system: a) cycloaddition; b) cyclization; c) evolution of polyaromatic ribbon synthesis; d) benzannulative approaches to the growth of carbon nanostructures.

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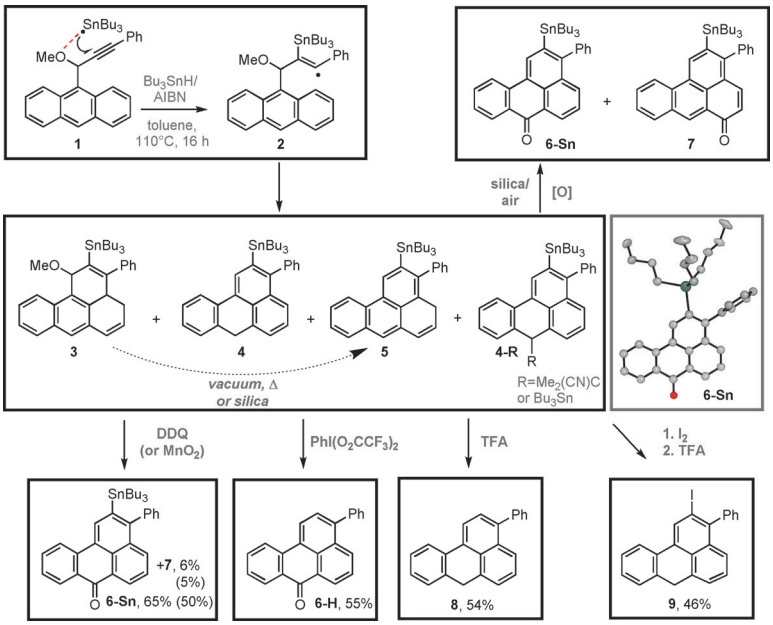
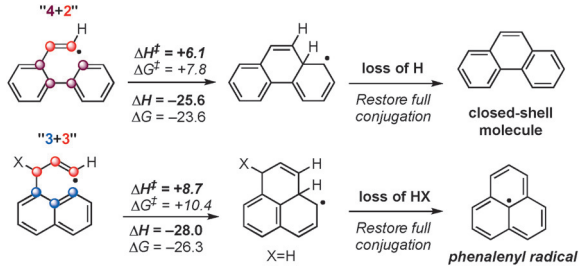
readily twist to align its aromatic system with the attacking vinyl radical.

In addition to the 2.6 kcal mol^{-1} penalty (corresponding to an approximately 100-fold slower cyclization), a unique conceptual difficulty exists for benzannulation at the zigzag edge. Whereas the radical product of the "4+2" path in Scheme 1 can be readily converted into a stable phenanthrene moiety through the loss of a single H atom at the ring junction point, a similar escape into a thermodynamically protected stable structure is not available for the "3+3" path. Even if loss of H_2 (or HX) can restore conjugation along the full polycyclic core of the "3+3" product, this change would produce an odd alternant hydrocarbon, that is, the phenalenyl radical. Although these species are remarkably interesting[16] and this new approach to phenalenyl radicals could offer valuable synthetic opportunities, the intrinsic instability associated with the open-shell structural motif necessitates an additional step that converts initially formed species into stable products.



Scheme 2. *peri*-Cyclization of a 9-anthracenyl propargylic ether in reductive and oxidative regimes. AIBN = azobisisobutyronitrile, DDQ = 2,3-dichloro-5,6-dicyano-1,4-benzoquinone, TFA = trifluoroacetic acid.



Scheme 1. Computed kinetics and thermodynamics for the intramolecular attack of a vinyl radical at the naphthyl and biphenyl core at the UM06-2X/6-31 + G(d,p) level of theory.

Herein, we disclose a general approach to benzannulation at the *peri* position of polyaromatic cores through Bu_3Sn-mediated radical cyclization of propargylic ethers. Depending on the choice of workup (reductive or oxidative), this process furnishes the corresponding tin- and iodo-substituted benzannulated phenalenes and benzanthrones, which can be readily functionalized by classic cross-coupling approaches.

Initial exploration of radical *peri*-cyclizations on the anthracene core quickly revealed that Si- and S-centered radicals react with the model alkyne sluggishly and nonselectively (see the Supporting Information). On the other hand, the directing effect of the MeO group on the addition of a Sn radical at the alkyne, used before for the preparation of expanded polyaromatic structures from oligoalkynes (Figure 1 c),[15] provided reliable assistance toward the formation of tetracyclic products **3**–**5** (Scheme 2).

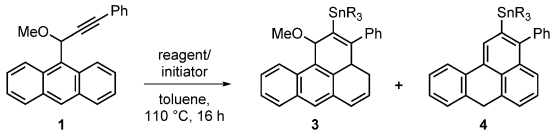
These compounds are labile, and their isolation required silica deactivated by acetone. ^{1}H NMR spectra of product **3** showed the presence of both a MeO group and the CH/CH_2 system of allylic protons. Hence, in contrast to the traceless alkoxy directing groups in Sn-promoted radical cyclizations,[15] the directing OMe group is retained in one of the products when the reaction is finished. These observations suggest that the cyclized radicals are initially reduced by H-transfer, and lose methanol later in a subsequent slower step. We have also observed minor amounts of products **4-R** formed from the recombination of a cyclized radical with the Bu_3Sn and Me_2CCN radicals present in the reaction mixture.

Additional purification attempts led to partial loss of the MeO group and the appearance of a new aromatic C–H signal in the ^{1}H NMR spectra. The newly developed NMR spectroscopy features were identical to those of the other products **4** and **5**, which in turn were slowly oxidized in the presence of air to benzanthrones **6-Sn** and **7** (see the Supporting Information for structural assignment). Finally, the structure of benzanthrone **6-Sn** was unambiguously assigned by single-crystal X-ray diffraction analysis (Scheme 2).

Having obtained these initial results, we screened for optimal reaction conditions by varying the radical source, initiator, and solvent (see the Supporting Information). The best results were obtained in toluene with 2 equivalents of Bu_3SnH and 1 equivalent of AIBN (Table 1). The large amount of AIBN indicates inefficiency of the radical propagation step, probably owing to the formation of highly stabilized radical intermediates (see below).

Treatment with TFA is highly beneficial for the transformation of the above mixtures **4** and **5** into benzanthrene **8** (up to 77 % combined yield for **8** and **6-H**; see the Supporting Information). When the reaction mixture was treated with iodine before TFA, iodobenzanthrene **9** was isolated in moderate yield. Alternatively, the cyclization step can be coupled to an oxidation step. Slow oxidation was already observed upon exposure of the reaction mixture to air, and the process can be accelerated by a variety of oxidants. Good

Table 1: Optimization of the Sn-promoted radical cyclization of alkyne **1**.[a]



Entry	Reagent (equiv)	Initiator (equiv)	Ratio by NMR spectroscopy[b] 1	3	4
1	Bu_3SnH (2)	AIBN (0.1)	71	20	9
2	Bu_3SnH (2)	AIBN (0.2)	65	22	12
3	Bu_3SnH (2)	AIBN (0.3)	38	35	27
4	Bu_3SnH (2)	AIBN (0.5)	23	45	32
5	Bu_3SnH (2)	AIBN (1)	0	66	34
6	Bu_3SnH (1)	AIBN (1)	90	10	<1

[a] See the Supporting Information for the reaction scale and reagent concentrations. [b] Compound **5** appeared after exposure of the mixtures to silica gel.

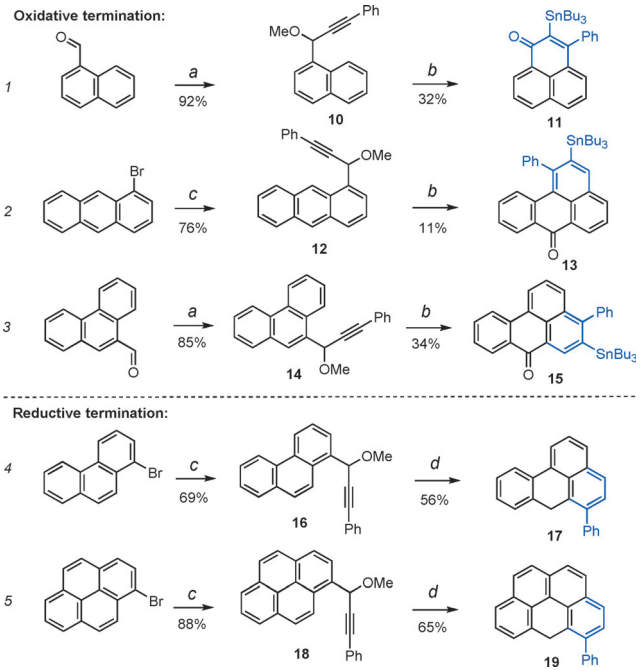
yields of the two isomeric benzanthrones **6-Sn** and **7** were observed upon treatment with MnO_2 and DDQ. These oxidants are capable of performing the target C–H oxidation while preserving the Sn substituent.

To test the scope of the reaction, we extended it to other polyaromatic cores. The propargyl ether substrates were assembled in one-pot transformations from aryl aldehydes or aryl bromides (Scheme 3). Oxidative workup with DDQ or MnO_2 could provide new polyaromatic ketones, albeit in varying yields (Scheme 3, entries 1–3),[17] whereas treatment with TFA gave rise to the destannylated hydrocarbon derivatives (entries 4 and 5 in Scheme 3). In particular, the pyrene precursor was transformed by the latter approach into a phenyl-substituted "olympicene" **19**.[18]

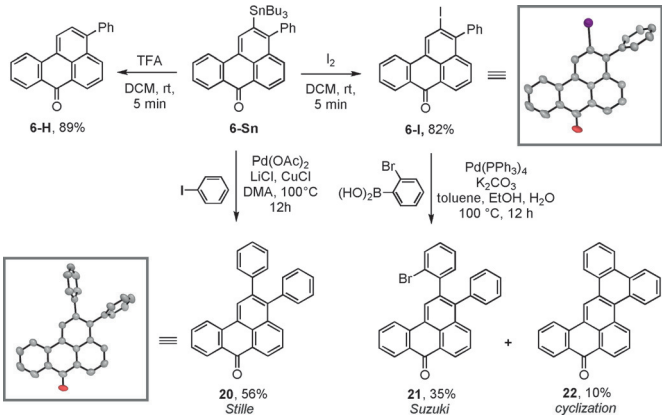
The stannylated products could be readily iodinated or destannylated in nearly quantitative yield. Subsequent Stille coupling of the stannanes or Suzuki coupling of the iodo derivatives increase the structural diversity of the final products (Scheme 4).

Computational analysis indicates that *peri*-cyclization in polyaromatics shows relatively small changes for different cyclic cores. Expansion from naphthalene to anthracene has the largest transition-state-stabilizing effect (3–5 kcal mol^{-1}), whereas the barriers for intramolecular radical attack at phenanthrene and pyrene is predicted to be only about 1 kcal mol^{-1} lower relative to that in the naphthalene derivative (Scheme 5).

On the other hand, the progression of intermediate species that evolve under the reaction conditions from the initial cyclized radical provides a complex mechanistic puzzle. We show how this complexity can be unraveled by using the 9-anthracenyl system as an example. The initially formed cyclic radical **G** is highly delocalized and potentially can abstract a hydrogen atom at six different carbon atoms to give products **A**–**F** (Scheme 6; see also the Supporting Information). However, the spin density is concentrated at only three positions. H-abstraction at these positions is more favorable thermodynamically than abstraction at the remote benzene ring (Scheme 6).

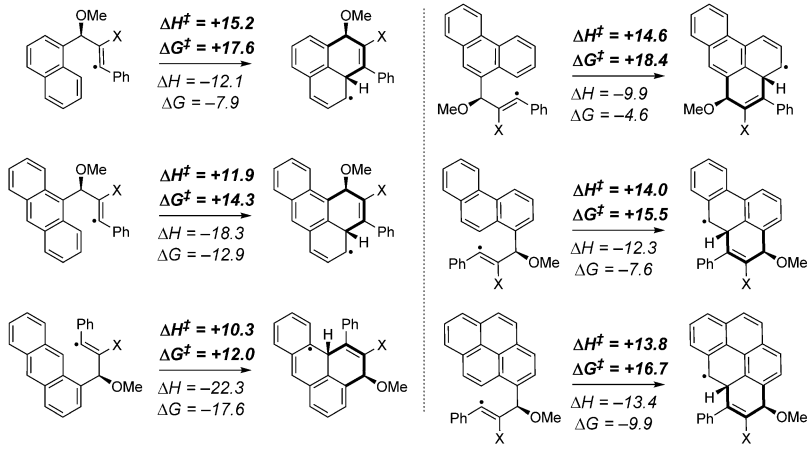


Scheme 3. Precursors (left), cyclization substrates (center), and products of radical *peri*-cyclization reactions (right). Reaction conditions: a) 1. lithium phenylacetylide (1.5 equiv), THF, −78 °C, 1 h; 2. MeI (5 equiv), THF, 0 °C→rt, 12 h; b) 1. Bu_3SnH/AIBN (2.0 equiv/1.0 equiv), toluene, 110 °C, 16 h; 2. DDQ (4 equiv), DCM, room temperature, 4 h; c) 1. *n*BuLi (1.1 equiv), THF, −78 °C, 1 h; 2. phenylpropargyl aldehyde (1.2 equiv), THF, −78 °C, 1 h; 3. MeI (5 equiv), THF, 0 °C→rt, 12 h; d) Bu_3SnH/AIBN (2.0 equiv/1.0 equiv), toluene, 110 °C, 16 h; 2. TFA (5 equiv), DCM, room temperature, 15 min; K_2CO_3, 10 min. DCM = dichloromethane.



Scheme 4. Protodestannylation (left) and iodination (right) of product **6-Sn**, and cross-coupling approaches to extended polyaromatic hydrocarbons (PAHs; bottom). DMA = dimethylacetamide.

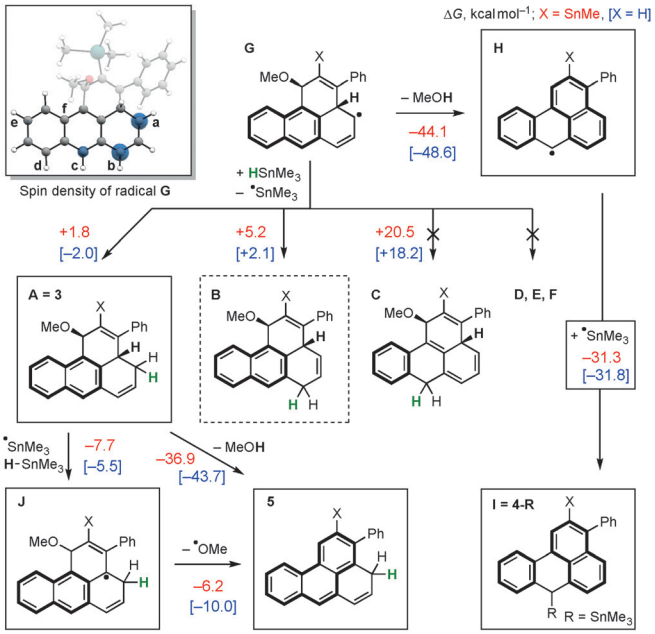
Furthermore, the Me_3Sn–H bond dissociation energy (BDE; 71.2 kcal mol^{-1} at the same UM06-2X/LanL2DZ level)[19] is less than the calculated BDE for the potentially formed C–H bond in only one of the possible products. The calculated H-transfer is thermodynamically favorable only for the formation of isomer **A** (Scheme 6), which we observe experimentally (product **3**, Scheme 2). The greater stability of this product is not surprising, considering that it preserves the



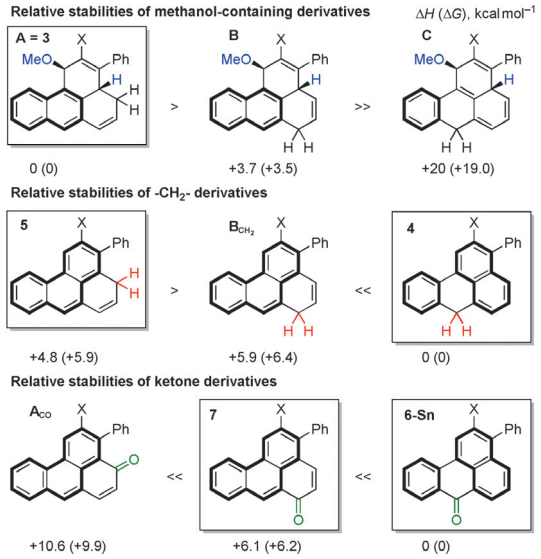
Scheme 5. Computed cyclization barriers and reaction energies at the (U)M06-2X/LanL2DZ level at 110 °C, in kcal mol^{-1} (X = $SnMe_3$).

radical **G** through the loss of MeOH (Scheme 6, top right). This elimination provides a fully delocalized benzophenalenyl radical **H**, which can abstract a hydrogen atom to provide another route to products **4** and **5** (Scheme 2). The formation of products **4-R** suggests that the highly delocalized radical **H** is likely to be persistent[20] under the reaction conditions.

Importantly, a different aromaticity pattern emerges after the loss of MeOH, leading to preferred reactions at the middle ring (position "c", Scheme 6, top left) as they provide the benzene and naphthalene subunits instead of forming a phenanthrene. The structures of the final aromatized products from both the reductive and the oxidative



Scheme 6. Selected computational results for the proposed evolution of the initially formed cyclic species. Favorable intermediates and observed products are boxed. Δ*G* values at (U)M06-2X/LanL2DZ at 110 °C, in kcal mol^{-1}. Energies of intermediates **d**–**f** and additional energy comparisons are given in the Supporting Information.



Scheme 7. Relative stabilities of benzanthrene derivatives (X = $SnMe_3$) at the (U)M06-2X/LanL2DZ level at 110 °C, in kcal mol^{-1}. Experimentally observed products are boxed.

greatest degree of aromaticity and keeps conjugation with the alkene moiety.

However, even the most stable of the initial closed-shell reduced products, **A** (Scheme 7), still has two "weak spots". The first weakness is the tertiary C–H bond; this hydrogen atom may be abstracted by the R_3Sn radical ($\Delta H \approx -5$ kcal mol^{-1}) or other transient radicals. This H-abstraction opens a path to the exergonic loss of a MeO radical with a low energy (ca. 8 kcal mol^{-1}) barrier. This step leads to aromatization of the newly formed ring and completes the benzannulation process to form the isolated product **5**.

A parallel pathway suggested by the computational analysis includes aromatization of the initially formed cyclic workup procedures follow this general preference. The same trend displays itself in the cyclization products derived from the other cores (Scheme 3).

In conclusion, *peri*-cyclization reactions of acene subunits and vinyl radicals formed from propargylic ethers provide a viable strategy for benzannulation at the L-region of acenes. The initially formed cyclic products can be trapped through a reductive or oxidative path with the concomitant loss of the alkoxy directing group. The Bu_3Sn moiety can be retained or exchanged to give iodoarenes for further cross-coupling transformations en route to extended polyaromatics.

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Conflict of interest

The authors declare no conflict of interest.

Keywords: alkyne benzannulation · cyclization · polyaromatic compounds · radical reactions · zigzag edge

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