Radical-Induced Cycloaromatization: Routes to Fluoranthenes and Acephenanthrylenes

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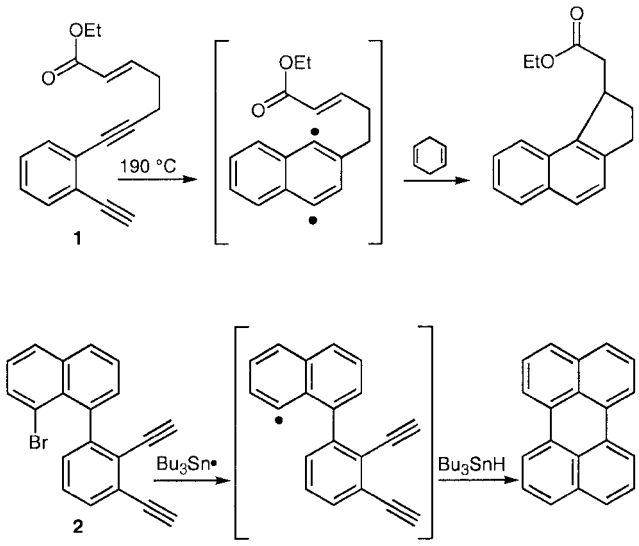
Abstract: The cycloaromatization of easily-prepared arenediynes is an efficient route to fused aromatic systems, but the requirement of very high temperatures to induce this reaction limits both scalability and generality. We demonstrate that cycloaromatization can be induced by addition of a radical species to an arenediyne unit. Tethering this radical to the enediyne leads to the formation of larger fused systems, such as fluoranthenes and acephenanthrylenes, in a single step.

Key words: polycyclic aromatic hydrocarbon, Bergman reaction, enediyne, cycloaromatization

Polycyclic aromatic hydrocarbons (PAHs) have been at the forefront of research in a significant number of disciplines. Aromatic systems with bay regions have been extensively studied by bioorganic chemists for their potential role in carcinogenesis.[1] PAHs containing five-membered rings are valued both for their unusual photophysical properties[2] as well as for their usefulness in approaches to the rational syntheses of fullerenes and carbon nanotubes.[3] The technological importance of such fused aromatic compounds to materials science is exemplified by their appearance in applications as diverse as photovoltaics for use in power generation and organic transistors fabricated for data storage.[4] Currently new applications of PAHs are based on commercially available materials such as pentacene and C_{60}. Synthetic modifications of the basic building blocks of these devices are just beginning to bear fruit. In transistors based on pentacene, the use of alkylated pentacene has improved orbital energy matching for the electrode,[5] while silylethynylated pentacene has yielded materials that can be incorporated into high performance transistors by simple solution deposition methods.[6] These results underscore the importance of developing new methods for the synthesis of novel aromatic topologies.

Our approach to the synthesis of PAHs utilizes cycloaromatization, a thermal reaction that turns easily-prepared arenediynes into linearly fused aromatic systems.[7] While this reaction has proven useful in the synthesis of simple acenes and rylenes, the limitations of cycloaromatization, including high reaction temperature, and the expense and volatility of the typical hydrogen atom source (1,4-cyclohexadiene), reduce the utility and scalability of the reaction.[8] A promising route to mediating the harsh conditions required for this reaction involves the addition of a 'trigger' to the enediyne unit to initiate cyclization. Recent reports of cycloaromatization occurring after the addition of methoxide to arenediynes,[9] or upon the simple reduction of an enediyne system,[10] have led us to investigate the feasibility of using an appended radical 'trigger' to induce cycloaromatization under mild conditions.

Our inspiration for this work is drawn from results published in the early 1990's, where Grissom and co-workers reported that fused ring systems could be prepared by trapping the diradical species formed by cyclization with an appended radical acceptor.[11] The presence of the intramolecular radical trap dramatically improved the yield of the reaction, ostensibly by preventing reversion of the intermediate *p*-benzyne to enediyne (Scheme 1, top).



Scheme 1 Two routes to fused systems involving cycloaromatization. Top: *p*-Benzyne generated by cycloaromatization reacts with appended group to form a new fused ring (see ref.[11]). Bottom: Radical generated adjacent to enediyne induces cycloaromatization.

As part of our study of parallel cycloaromatization of adjacent enediynes, we recently showed that an aryl radical generated adjacent to an enediyne would induce cyclization, forming a fused aromatic system (Scheme 1, bottom).[12] In fact, there is a strong parallel between these reactions, one providing a 'trap' to react with the radical formed by cycloaromatization, while the other generates an appended radical to induce the cycloaromatization re-

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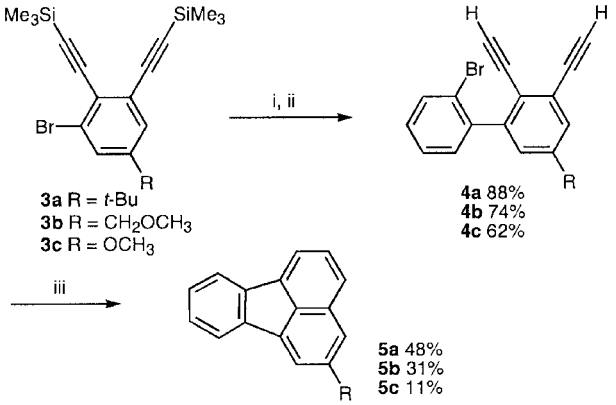
action. In this case the radical cascade involves initial *exo* attack on the triple bond, with the resulting vinyl radical performing a 6-*endo* cyclization to form the aromatic ring.[13] We report here the further investigation of this radical-induced cyclization, with the aim of producing a milder temperature, more scalable synthetic tool for the formation of fused PAHs.

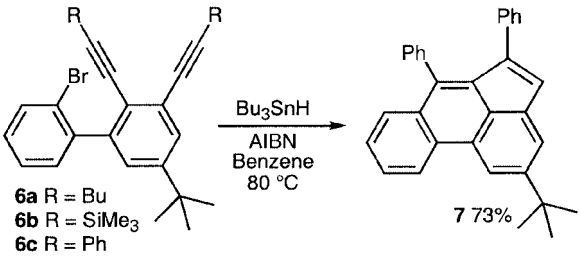
Our target molecule for this study is based on biphenyl, with one ring substituted with bromine at the *ortho*-position (the radical trigger), and the other containing the enediyne unit. The substituent at the 5-position of this ring simplifies the synthesis, and serves as a handle for the addition of further functionality. The biphenyl system is prepared by a Negishi-type coupling[14] between the known bromoenediynes **3** and commercially available 1-bromo-2-iodobenzene.[15] Desilylation of the resulting biphenyl provided the corresponding enediynes, which were used immediately in the cyclization step.



Scheme 2 (i) BuLi (Et_2O, –78 °C) then $ZnBr_2$, 1-bromo-2-iodobenzene, $(PPh_3)_2PdCl_2$ 25 °C; (ii) K_2CO_3 in MeOH/THF; (iii) Bu_3SnH/AIBN in benzene, 80 °C.

Tin-hydride mediated generation of the radical trigger led to immediate reaction at moderate temperature (80 °C, vs 180 °C required for thermal cycloaromatization). The only all-organic product of this reaction was the desired fluoranthene, with the *t*-butyl substituted derivative providing the desired product in reasonable yield. Upon careful analysis of the crude reaction mixture, we discovered that the reaction produced numerous tin-containing byproducts, suggesting that hydrostannylation of the terminal alkynes was the major competing reaction (Scheme 2). In fact, for methoxy derivative **4c**, hydrostannylation was the major reaction product (70%). In order to determine that we were not observing a simple thermal cycloaromatization reaction, a solution of enediyne **4a** was dissolved in a deoxygenated mixture of benzene and 1,4-cyclohexadiene in a sealed reaction vessel, and the temperature was raised steadily until evidence of cycloaromatization was found. No significant cycloaromatization was observed below 160 °C, and conversion was sluggish at temperatures below 180 °C. Heating enediyne **4c** at 80 °C in the presence of tributyltin hydride without a radical initiator (AIBN or light) also yielded no cycloaromatized product (although some hydrostannylated material was observed). Clearly, this reaction is a radical-induced cycloaromatization that provides a lower-temperature, more scalable version of cycloaromatization for the synthesis of fluoranthene derivatives.

In order to improve the yield of this reaction further, we sought to eliminate the undesired hydrostannylation of the alkyne. Because hydrostannylation of internal alkynes is a much slower process than for the corresponding terminal acetylene, biphenyl derivatives **6a**–**c** were prepared and subjected to radical-induced cycloaromatization (Scheme 3). Neither **6a** nor **6b** yielded characterizable cyclization products: The former underwent tin hydride mediated dehalogenation (in poor yield). While the latter did appear to cyclize, but showed only numerous products arising from hydrogen abstraction from the appended alkyl groups. Similar behavior has been observed in alkyl-substituted systems undergoing thermal cycloaromatizations.[16]



Scheme 3

In contrast, diphenyl derivative **6c** produced a single new compound **7** upon radical-induced cycloaromatization, in 73% yield. It was immediately obvious that this new pale yellow material did not possess the fluoranthene chromophore. Crystals of this new compound grown from methanol were analyzed by X-ray crystallography and were determined to be the acephenanthrylene **7** (Figure 1), the product of a 6-*endo* cyclization followed by a 5-*endo* ring closing.[17] The high yield of product is particularly impressive in comparison with the conditions required to perform thermal cycloaromatization of similarly-substituted systems: Cycloaromatization of diphenyl arenediynes typically takes place only at temperatures greater than 240 °C, and the yields are typically quite low (<20%).[18]

The shift from classic 'Bergman' type (C1-C6) cyclization to the less-common C1-C5 cyclization upon substitution of the alkynes with aryl groups is certainly not unheard of. It has been reported that photochemically-induced cyclizations of arene-substituted enediynes yields substituted fulvenes, rather than arenes.[19] Theoretical consideration of this reaction revealed that substitution can have a dramatic effect on the outcome of the cyclization of arenediyne radical anions, leading to the possibility of 'tuning' an enediyne to yield arenes or fulvenes.[20] Because of the system's resistance to hydrostannylation, the radical-induced cyclization of **6c** results in a significantly

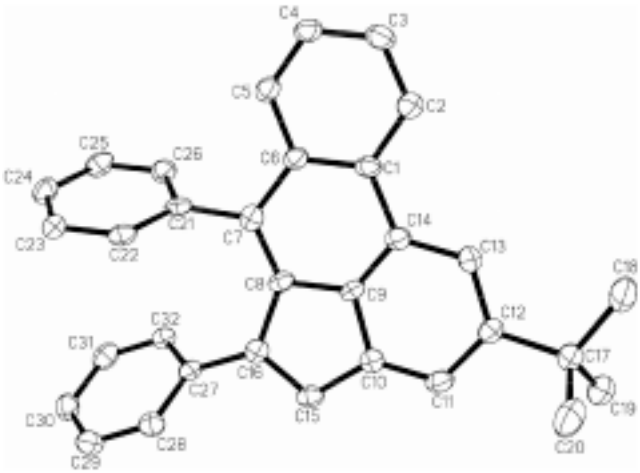


Figure 1 X-ray crystal structure of **7**.

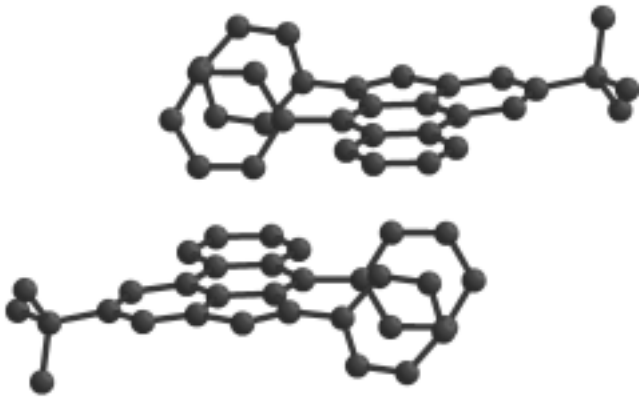


Figure 3 Solid-state packing of acephenanthrylene **7**.

higher yield than the cyclization of **4a**–**c**, making it a relatively efficient route to substituted acephenanthrylenes.

Acephenanthrylene **7** is a pale yellow material with optical absorption properties that mimic the parent hydrocarbon (substitution simply leads to a 9 nm red-shift in the absorption). Also comparable to the parent hydrocarbon, the material exhibits moderate, broad fluorescence emission centered at ca 500 nm (Figure 2).[21] Unlike the parent, this functionalized derivative is fluorescent in the solid-state, both in evaporated and solution-deposited thin films. The bright solid-state emission is most likely a function of the crystal packing (Figure 3), where the substituents prevent any close-packing of the chromophores. While there is an edge-to-face interaction between the acephenanthrylene core and the out-of-conjugation aryl substituent of an adjacent molecule, the closest interaction between chromophore is >5 Å, preventing fluorescence quenching by solid-state coupling between chromophores. Further tuning of the emission by exchanging the *t*-butyl substituent for an electron-donating group should lead to a green emission exploitable for use in a small-molecule organic light emitting diode (SMOLED).

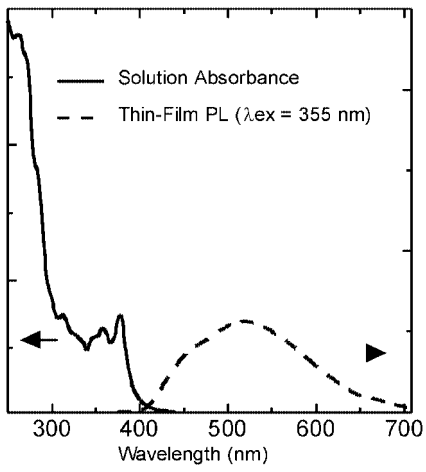


Figure 2 Solution absorbance and thin-film photoluminescence spectra of acephenanthrylene **7**.

In conclusion, radical cascade across enediyne units is a novel and exploitable method for the preparation of new topographies of fused aromatic compounds. In particular, the facility with which functionalized enediynes undergo cyclization may lead to new methods for the preparation of such highly-substituted systems.

General Procedure for Converting Bromodiyne to Biphenyl

The bromoenediyne (10.0 mmol) was dissolved in 10 mL dry Et_2O, the solution cooled to –78 °C and BuLi (4.47 mL, 1.1 equiv) was added dropwise. The solution was stirred for 10 min. Dry $ZnBr_2$ (2.0 equiv) was added and the solution was stirred for 10 min. Bis(triphenylphosphine)palladium(II) chloride (2 mol%) and 1-bromo-2-iodobenzene (1.10 equiv) were then added. The solution was allowed to warm to r.t. and stirred overnight under a blanket of dry nitrogen. The reaction mixture was extracted with 100 mL of H_2O, 10% HCl, H_2O, and brine (2 × each). The organic layer was dried with $MgSO_4$ and run through a small plug of silica using hexane as the eluent. After removal of solvent, chromatography on silica (hexanes–CH_2Cl_2, 9:1) yielded pure biphenyl.

General Procedure for Radical Cycloaromatization

For the cyclization of **4a**–**c**, the silyl groups were first removed by addition of 1 pellet of KOH to a solution of silylated enediyne (typically 2.25 mmol) in MeOH–THF (2:1) and allowing this mixture to stir for 1 h. The resulting desilylated materials were extracted into hexanes, washed with copious amounts of H_2O, dried over $MgSO_4$, and concentrated to a volume of ca 5 mL. This solution was immediately added to dry, deoxygenated benzene (ca 100 mL). The solution was heated to reflux. Bu_3SnH (0.670 mL, 2.49 mmol) and AIBN (0.15 g, 0.4 equiv) were dissolved in benzene (30 mL) and added by syringe pump over 6 h. The reaction mixture was stirred for an additional 2 h, then the solvent was removed. The residue was dissolved in hexanes and washed with 150 mL H_2O and brine (2 × each). The organic layer was dried with $MgSO_4$ and run through a thin plug of silica using hexanes as the eluent. Chromatography on silica followed by recrystallization provided the pure product.[22]

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(22) Selected characterization data. Compound **4a** (silylated): mp. 110–111 °C (EtOH). ^{1}H NMR (200 MHz, $CDCl_3$): δ = 0.08 (s, 9 H), 0.33 (s, 9 H), 1.35 (s, 9 H), 7.20–7.25 (m, 1 H), 7.30 (d, *J* = 2.2 Hz, 1 H), 7.34 (s, 1 H), 7.36 (s, 1 H), 7.56 (d, *J* = 2.2 Hz, 1 H), 7.68 (d, *J* = 7.6 Hz, 1 H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = –0.34, –0.04, 30.97, 34.75, 97.52, 101.64, 101.98, 104.04, 122.75, 123.29, 125.27, 126.58, 127.18, 128.29, 128.84, 131.43, 132.41, 141.58, 144.20, 150.68 ppm. FTIR (KBr): 3052.63, 2955.33, 2893.88, 2151.35, 1244.95, 871.12, 840.40 cm^{-1}. HRMS: *m*/*z* (%) calcd for $C_{22}H_{33}BrSi_2$: 480/482. Found: 482.1284(20) [M + 2], 480.1304(25) [M^+], 467(80) [$M^+ - CH_3$]. Compound **5a**: ^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.43 (s, 9 H), 7.34–7.45 (m, 4 H), 7.55–7.63 (m, 1 H), 7.77–7.81 (m, 1 H), 7.85–7.95 (m, 2 H), 8.06 (d, *J* = 2 Hz, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 29.69, 31.65, 119.03, 119.32, 121.37, 121.54, 121.81, 123.05, 125.47, 125.79, 126.51, 127.06, 127.37, 127.95, 128.96, 132.12, 132.81, 151.38 ppm. HRMS: *m*/*z* (%) calcd for $C_{20}H_{18}$: 258.1409. Found: 258.1403(65) [M^+], 243(100) [$M^+ - CH_3$]. Anal. Calcd for $C_{20}H_{18}$: C, 92.97%; H, 7.02%. Found: C, 92.74%; H, 7.03%. Compound **6c**: Yellow oil. ^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.75 (s, 9 H), 7.22 (m, 7 H), 7.31 (d, *J* = 7 Hz, 1 H), 7.33 (m, 5 H), 7.35 (d, *J* = 8 Hz, 1 H), 7.55 (d, *J* = .5 Hz, 1 H), 7.67 (d, *J* = 7 Hz, 1 H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 30.96, 34.76, 87.51, 89.06, 93.11, 96.38, 115.16, 120.18, 121.90, 122.81, 123.33, 123.42, 125.49, 125.55, 126.74, 126.81, 127.24, 127.87, 127.91, 128.10, 128.32, 129.04, 131.26, 131.55, 131.59, 131.77, 132.57, 141.60, 143.44, 150.67 ppm. MS (EI, 70 eV): *m*/*z* (%) = 488(10) [M^+], 473(80) [$M^+ - CH_3$]. Anal. Calcd for $C_{32}H_{25}Br$: C, 78.52%; H, 5.14%. Found: C, 78.33%; H, 4.90%. Compound **7**: mp 170–171 °C (MeOH). ^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.82 (s, 9 H), 7.25 (m, 6 H), 7.37 (m, 5 H), 7.51 (s, 1 H), 7.73 (t, *J* = 8 Hz, 1 H), 7.95 (t, *J* = 8 Hz, 1 H), 8.11 (d, *J* = 7 Hz, 1 H), 8.71 (s, 1 H), 9.03 (d, *J* = 8 Hz, 1 H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 31.81, 35.65, 116.57, 120.74, 122.85, 125.20. 125.98, 126.20, 127.02, 127.19, 127.27, 127.38, 128.34, 128.93, 131.21, 131.49, 131.56, 134.25, 136.93, 137.19, 138.50, 138.92, 145.23, 151.51 ppm. MS: *m*/*z* (%) calcd for $C_{32}H_{26}$: 410.2035. Found: 410.2035(20) [M^+], 395(100) [$M^+ - CH_3$].