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Synthesis of chryseno[1,2-*b*]heteroarenes and phenanthro[1,2-*b*:8,7-*b*']diheteroarenes by an S_NAr-anionic cyclization cascade reaction strategy

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ABSTRACT

The synthesis of [5]heterophenacenes bearing one or two indole, furan, or thiophene rings is described using an S_NAr-anionic cyclization cascade strategy. The convergent reaction sequences furnish chryseno[1,2-*b*]heteroarenes and phenanthro[1,2-*b*:8,7-*b*']diheteroarenes in only four synthetic steps. The heteroaromatic functionality is selected and installed in the final step of the syntheses from common *ortho*-fluoro-ethynylarene precursors.

[n]Phenacenes, W-shaped fused aromatic molecules, have emerged as promising compounds for the next-generation of organic electronics (Fig. 1) [1]. In contrast to the linearly fused [n]acenes, [n]phenacenes exhibit significantly higher stability to air and light owing to lower HOMO energy levels that are maintained even for extended aromatic systems [2]. Modification of the phenacene core by installation of heteroaromatic rings at interior [3] and terminal [4] positions has been explored as a means to alter and optimize molecular properties for electronic applications. For example, the thiophene-containing systems phenanthro[2,1-*b*:7,8-*b*']dithiophene (PDT) [4a,b] and piceno[4,3-*b*:9,10-*b*']dithiophene (PiDT) [4] have shown promise as organic field effect transistors and as polymer-based semiconductors in organic solar cells. However, the syntheses of these compounds are not readily adapted for incorporation of heterocycles beyond thiophene, and have thus far been limited to systems with symmetrically disposed thiophene rings. Therefore, there remains an urgent need for general and efficient methods to access diverse [n]heterophenacenes, especially those containing terminal heteroaromatic rings, to further applications development.

Our group has developed tandem nucleophilic aromatic substitution (S_NAr)-anionic cyclization cascades of *ortho*-fluoro-ethynylbenzenes with *N*- and *O*- nucleophiles to produce indoles and benzofurans (Scheme 1) [5]. These methods have also been investigated with *S*-, and *Se*-nucleophiles, for the formation of thiophene or selenophene rings [6]. The cascade reaction proceeds without the use of transition metals and allows installation of diverse heteroaromatic systems from a common synthetic precursor. Furthermore, the functionality present on the ethynyl group is incorporated at the 2-position of the resulting heterocycle, allowing facile installation of 2-aryl and 2-*tert*-butyl groups. We now report the synthesis of chryseno-systems **1** and phenanthro-systems **2** using S_NAr-anionic cyclization reactions (Fig. 1). The synthetic sequences are short and convergent, allowing the formation of heteroaromatic rings with X = N—H, *N*-Ar, O, or S in the final step of the synthesis from common *ortho*-fluoro-ethynylarene precursors.

Our route to common cyclization precursor **7** toward the synthesis of chryseno[1,2-*b*]heteroarenes **1** is shown in Scheme 2. Mizoroki-Heck coupling of 1-bromo-2-fluoro-3-iodobenzene **3**

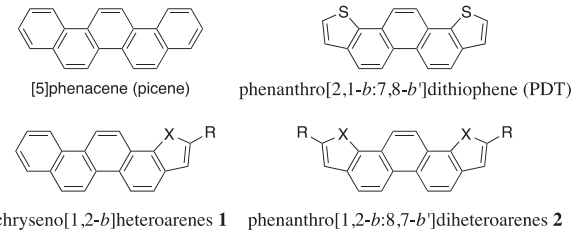

Fig. 1. Representative phenacenes and heterophenacenes.

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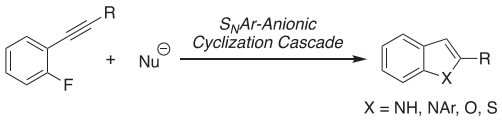
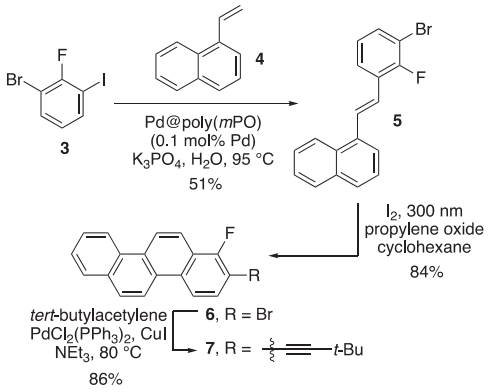


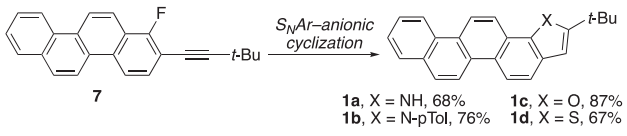
Scheme 1. General Scheme of S_NAr-Anionic Cyclization Reactions of *ortho*-fluoroethynylarenes.



Scheme 2. Synthesis of common cyclization precursor 2-(*tert*-butylethynyl)-1-fluorochrysene **7**.

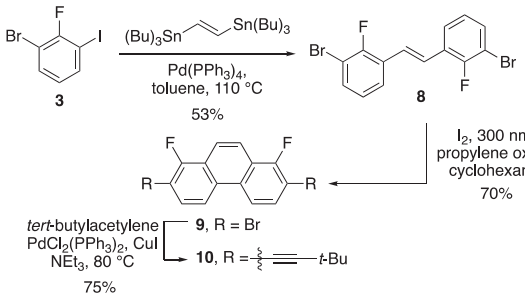
with 1-vinylnaphthalene (**4**) was carried out under aqueous conditions using our recently developed heterogenous Pd@poly(*m*PO) catalyst [7] at a Pd catalyst loading of 0.1 mol % (Pd@poly(*m*PO), K_3PO_4, H_2O, 95 °C, 48 h). The resulting stilbene **5** was then subjected to Mallory photocyclization to furnish 2-bromo-1-fluorochrysene **6** in 84% yield (I_2, cyclohexane, propylene oxide, 300 nm, 24 h) [8]. Installation of the requisite *ortho*-ethynyl group was accomplished via Sonogashira coupling of *tert*-butylacetylene to yield cyclization precursor **7** ($PdCl_2(PPh_3)_2$, CuI, NEt_3, 80 °C, 18 h). Our previous investigations [5] revealed that arylethynyl groups were most activating for substitution of aryl fluorides, leading to S_NAr-anionic cyclization cascades that proceeded at lower temperatures and in the highest yields. However, for this study we chose to utilize *tert*-butylethynyl systems to both maximize organic solubility and to generate a substitution pattern that is otherwise difficult to install by metalation or cross-coupling methods.

With a common precursor in hand, formation of chryseno[1,2-*b*]heteroarenes **1** was then investigated by reaction of 2-(*tert*-butylethynyl)-1-fluorochrysene **7** with *N*-, *O*-, and *S*- nucleophiles (Scheme 3). As we have previously reported on simple *ortho*-fluoro-ethynylarenes, use of acetamide as the nucleophile in these cascade processes proceeds with *in situ* acetate cleavage, leading to *N*—H indole products [5]. Indeed, reaction of **7** with acetamide furnished *N*—H—phenanthro[1,2-*g*]indole **1a** in 68% yield (KO*t*Bu, DMSO, 145 °C, 18 h). Changing to a *p*-toluidine nucleophile allowed for facile formation of *N*-*p*-tolyl-phenanthro[1,2-*g*]indole target **1b**,



Conditions: **1a**: 2.5 equiv acetamide, 2.5 equiv KO*t*Bu, DMSO, 145 °C, 18 h; **1b**: 2.5 equiv *p*-toluidine, 2.5 equiv KO*t*Bu, DMSO, 145 °C, 18 h; **1c**: 2.0 equiv KOH, DMSO, 150 °C, 3 d; **1d**: 2.0 equiv $Na_2S{\cdot}9H_2O$, DMSO, 120 °C, 18 h.

Scheme 3. Synthesis of chryseno[1,2-*b*]heteroarenes 1 from common precursor **7** *via* S_NAr-anionic cyclization reactions.



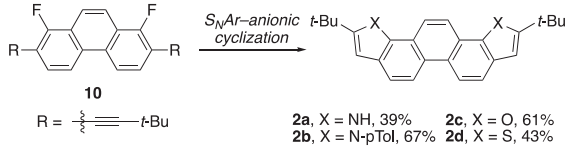
Scheme 4. Synthesis of common cyclization precursor 2-(*tert*-butylethynyl)-1-fluorochrysene **10**.

which was isolated in 76% yield (KO*t*Bu, DMSO, 145 °C, 18 h). It is notable that post-cyclization arylation of the indole nitrogen atom on **1a** to yield **1b** would be challenging due to the adjacent *tert*-butyl substituent. Reaction of 2-(*tert*-butylethynyl)-1-fluorochrysene **7** was also investigated using chalcogen nucleophiles. Hydroxide reacted smoothly with **7** (DMSO, 150 °C, 3 d), furnishing chryseno[1,2-*b*]furan **1c** in 87% yield. Surprisingly, sodium sulfide reacted rather sluggishly with chrysene **7** in comparison to our observations on related systems for the formation of thiahelicenes [6]. Nonetheless, reaction completion was observed at 120 °C for 18 h, providing chryseno[1,2-*b*]thiophene **1d** in 67% yield ($Na_2S{\cdot}9H_2O$, DMSO, 120 °C, 18 h).

With our successful generation of chryseno[1,2-*b*]heteroarenes **1a-d**, we next turned to investigating the synthesis of symmetrical phenanthro[1,2-*b*:8,7-*b'*]diheteroarenes **2**. Our synthetic sequence to the requisite bisethynylphenanthrene **10** again utilized 1-bromo-2-fluoro-3-iodobenzene **3**, which was subjected to Stille coupling using 1,2-bis(tributylstannyl)ethene ($Pd(PPh_3)_4$, toluene, 110 °C, 18 h), furnishing stilbene **8** (Scheme 4). Photocyclization of **8** to form the desired phenanthrene core then proceeded smoothly to produce dibromophenanthrene **9** in 70% yield (I_2, cyclohexane, propylene oxide, 300 nm, 24 h). Finally, Sonogashira coupling (*tert*-butylacetylene, $PdCl_2(PPh_3)_2$, CuI, NEt_3, 80 °C, 18 h) provided *tert*-butylethynyl-substituted phenanthrene **10**, functionalized for entry into S_NAr-anionic cyclization cascades.

Reaction of 2,7-bisethynyl-1,8-difluorophenanthrene **10** with *N*-, *O*-, and *S*- nucleophiles successfully furnished the desired targets, phenanthro[1,2-*b*:8,7-*b'*]diheteroarenes **2** (Scheme 5). *N*—H—benzodiindole **2a** was formed by reaction with acetamide (KO*t*Bu, DMSO, 145 °C, 18 h), while analogous reaction using *p*-toluidine led to formation of *N*-*p*-tolyl-benzodiindole **2b**. Likewise, reaction of phenanthrene **10** with potassium hydroxide provided phenanthro-difuran **2c** (DMSO, 150 °C, 3 d), while sodium sulfide generated phenanthro-dithiophene **2d** ($Na_2S{\cdot}9H_2O$, DMSO, 120 °C, 18 h).

Single crystals of phenanthro[1,2-*g*]indole **1b** were obtained by slow evaporation from chloroform, and the solid-state structure is shown in Fig. 2 [9]. Due to steric buttressing by the 2-position *tert*-butyl group, the *N*-*p*-tolyl substituent on **1b** is held nearly orthog-



Conditions: **1a**: 5.0 equiv acetamide, 5.0 equiv KO*t*Bu, DMSO, 145 °C, 18 h; **1b**: 5.0 equiv *p*-toluidine, 5.0 equiv KO*t*Bu, DMSO, 145 °C, 18 h; **1c**: 4.0 equiv KOH, DMSO, 150 °C, 3 d; **1d**: 4.0 equiv $Na_2S{\cdot}9H_2O$, DMSO, 120 °C, 18 h.

Scheme 5. Synthesis of phenanthro[1,2-*b*:8,7-*b'*]diheteroarenes **2** from common precursor **10** *via* S_NAr-anionic cyclization reactions.

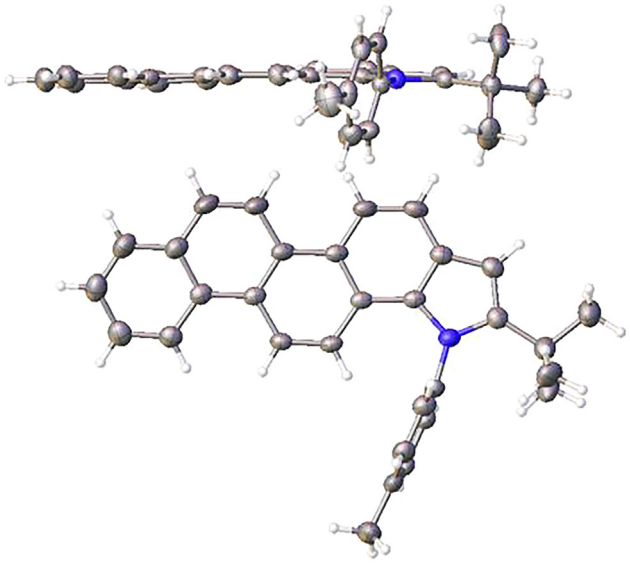


Fig. 2. Solid-state structure of phenanthro[1,2-*g*]indole 1b, showing both independent molecules in the asymmetric unit. Thermal ellipsoids drawn at the 50% probability level.

onal to the aromatic framework of the phenacene system. The angle between mean planes of the *p*-tolyl and indole rings is 86.9° and 83.6° for the two independent molecules in the asymmetric unit. Modest steric repulsion between the *N*-*p*-tolyl and *tert*-butyl substituents is also evident as the *p*-tolyl ring bends away from the *tert*-butyl functionality (the average angle observed between the *p*-tolyl plane normal and the *N*-C_{pTol} bond for the two independent molecules is 84.7°).

In conclusion, chryseno[1,2-*b*]heteroarenes **1** and phenanthro [1,2-*b*:8,7-*b'*]diheteroarenes **2** have been accessed using S_NAr-anionic cyclization cascades in short, efficient reaction sequences from common *ortho*-ethynylarene precursors. The strategy provides access to a diverse set of [5]heterophenacenes and allows installation of *tert*-butyl functionality at the 2-positons of the heteroaromatic rings. Investigations to access larger heterophenacenes and those with alternative heteroaromatic functionality are ongoing and will be reported in due course.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgments

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Appendix A. Supplementary data

Synthetic procedures, compound characterization data, and NMR spectra for compounds **1a-d**, **2a-d**, **5-10**. Absorbance and fluorescence spectra for compounds **1a-d**, **2a-d**. Crystallographic information for compound **1b** (PDF).

Supplementary data to this article can be found online at https://doi.org/10.1016/j.tetlet.2020.152663.

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[9] Crystallographic data for 1b: M = 413.53, monoclinic space group P21/c, a = 23.6799(7) Å, b = 9.5379(3) Å, c = 22.9830(7) Å, β = 115.465(3)°, V = 4686.6(3) Å3, Z = 8, R1 = 0.0460, Rw = 0.1082, GOF = 1.036. CCDC 2016643 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/data_request/cif, or by emailing data_request@ccdc.cam.ac.uk, or by contacting The Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033.