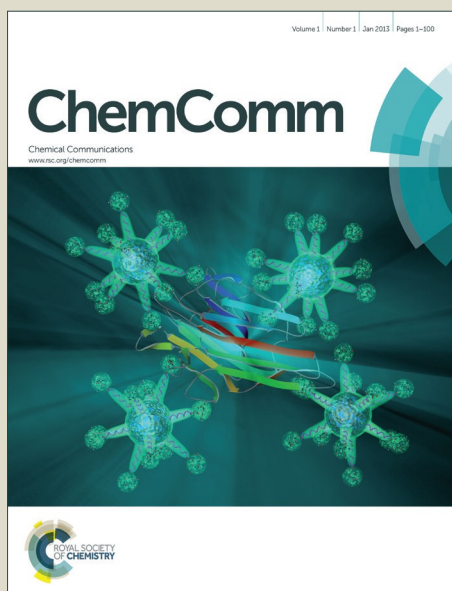


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1,7-Naphthodiyne: a new platform for the synthesis of novel, sterically congested PAHs

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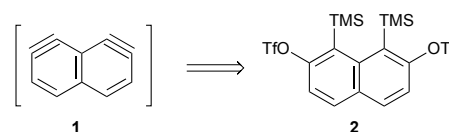
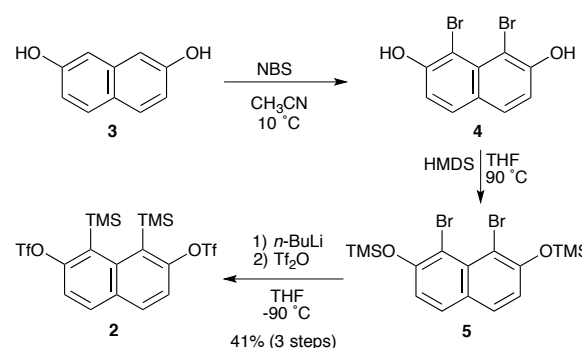
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The synthesis of an efficient precursor of the novel 1,7-naphthodiyne synthon is reported. Preliminary experiments demonstrate the usefulness of this platform for the synthesis of sterically congested polyarenes, such as helicenes and angularly fused acene derivatives. Furthermore, a novel intramolecular aryne trapping reaction is described.

Arynes are extremely reactive intermediates, widely featured in chemical literature.¹ From the first proposal of an aryne species² to the recent on-surface generation and AFM imaging of a single aryne molecule,³ these short-lived species have attracted the attention of theoretical, physical and synthetic chemists.⁴ Doubly unsaturated derivatives (bisarynes or bisaryne synthons)⁵ have been less widely studied but have a clear and increasing interest for synthetic organic chemists. The generation of these reactive species in the presence of a diene leads to two sequential cycloaddition reactions in a single synthetic operation,⁶ while the selective generation of one of the formal triple bonds and subsequent reaction with a suitable partner allows straightforward access to new structurally complex aryne precursor, as we recently demonstrated.⁷

The number of bisaryne synthons described to date is limited and 1,4-benzodiyne⁸ and 2,6-naphthodiyne^{9,6b,6e} are the most widely studied. With regard to bisarynes derived from naphthalene, the formal generation and trapping of 1,3-,^{6a} 1,5-^{6b,10} and 1,6-naphthodiyne^{6a} has also been described. We report here the efficient generation of the novel 1,7-naphthodiyne synthon (**1**), which is an interesting building block for the construction of different families of non-linearly fused polycyclic aromatic hydrocarbons (PAHs).

On the basis of our broad experience in the use of *ortho*-(trimethylsilyl)aryl triflates¹¹ to generate arynes under mild reaction conditions, we targeted bistriflate **2** as potential precursor of 1,7-naphthodiyne (**1**) (Figure 1).

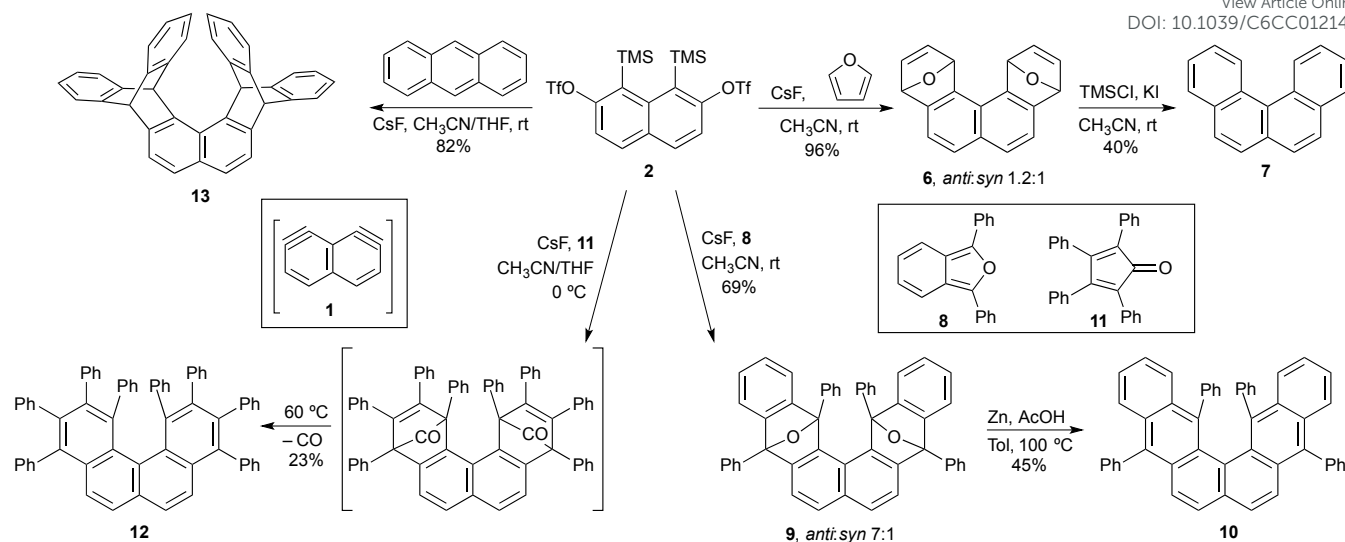
Fig. 1 1,7-Naphthodiyne (**1**) and its bistriflate formal precursor **2**Scheme 1 Synthesis of 1,8-bis(trimethylsilyl)naphthalene-2,7-diyl bistriflate (**2**)

This sterically crowded 1,2,7,8-tetrasubstituted naphthalene was successfully obtained through the reaction sequence shown in Scheme 1. Regioselective bromination¹² of 2,7-naphthalenediol (**3**) afforded 1,8-dibromonaphthalene-2,7-diol (**4**) in quantitative yield. Treatment of **4** with hexamethyldisilazane (HMDS) in refluxing THF gave bis(trimethylsilyl)ether **5**, which was sequentially treated with *n*-BuLi and Tf₂O to afford 1,8-bis(trimethylsilyl)naphthalene-2,7-diyl bistriflate (**2**) in 41% overall yield.

Reaction of **2** with CsF in acetonitrile in the presence of furan afforded cycloadducts **6** in an excellent 96% yield, as a 1.2:1 mixture of isomers. The major product resulted to be the chiral isomer *anti*-**6**, as demonstrated by the separation into enantiomers by chiral HPLC (see ESI). The formation of **6** is the result of two probably sequential [4+2] cycloaddition reactions and demonstrates the feasibility of **2** as formal precursor of 1,7-naphthodiyne. Treatment of **6** with TMSCl and KI¹³ allowed deoxygenation to afford benzo[*c*]phenanthrene (**7**) in 40% yield (Scheme 2).

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Scheme 2 Formal generation and double Diels-Alder reactions of the 1,7-naphthodiyne synthon

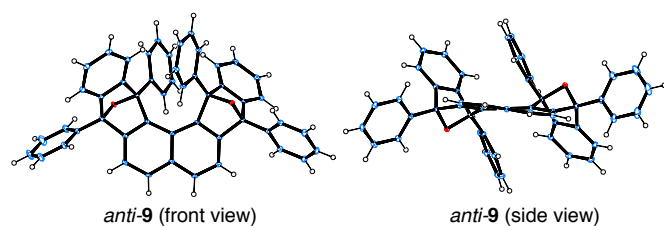


Figure 2 X-Ray structure of bisadduct *anti*-**9**

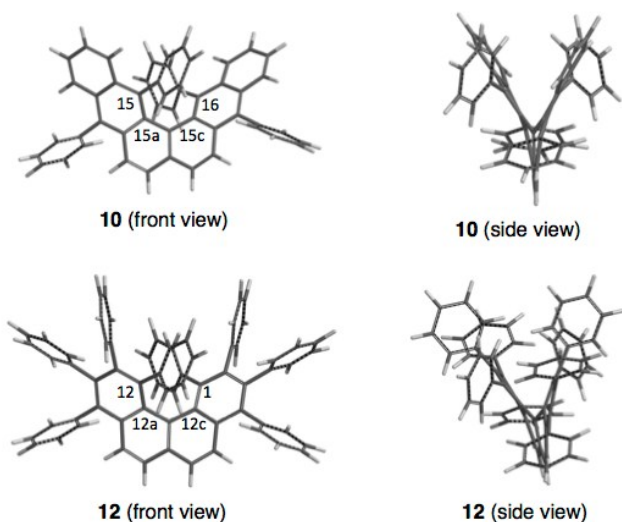
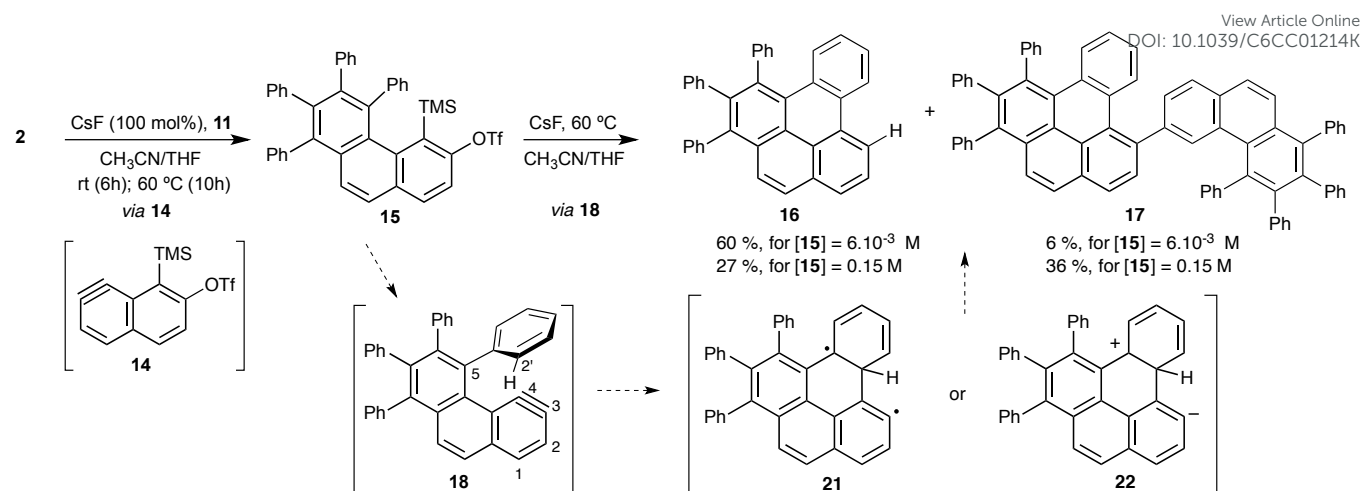


Figure 3 DFT optimized geometries for **10** and **12**

More remarkably, reaction of **2** with 1,3-diphenylisobenzofuran (**8**) under similar conditions led to the isolation of endoxides **9** in 69% overall yield as a 7:1 mixture of stereoisomers, which were separated by selective precipitation of the major product from Et₂O. Single-crystal X-ray diffraction analysis allowed the unambiguous characterization of the major isomer as *anti*-**9** (Figure 2). Reduction of **9** by treatment with Zn in AcOH afforded 5,10,15,16-tetraphenylnaphtho[2,3-*a*]tetraphene **10** in a reasonable 45% yield.

The computational DFT study of this sterically congested system showed a highly distorted structure, with a twist angle of 60° at the central [4]helicene moiety (Figure 3).¹⁴ Other dienes can successfully react with the aryne intermediate generated from **2**. Thus, treatment of **2** with CsF in the presence of 2,3,4,5-tetraphenylcyclopentadienone (**11**) gave octaphenylbenzo[*c*]phenanthrene **12**, as a result of a double Diels-Alder reaction of naphthodiyne (**1**), followed by chelotropic extrusion of CO. The yield of this reaction was moderate (23%), probably due to competing reactions which will be discussed below and also to the steric strain of this helically distorted compound, which has a twist angle of 55.9°.¹⁴ On the other hand, reaction with anthracene afforded the novel iptycene **13** in an excellent 82% yield. The unambiguous characterization of this product was achieved by X-ray diffraction analysis (see ESI for details).

Once the suitability of bistriflate **2** as 1,7-naphthodiyne equivalent had been demonstrated, it was decided to explore the synthesis of new functionalized 3-phenanthryne precursors by controlled generation of only one of the formal triple bonds from **2** and subsequent [4+2] reaction of the resulting aryne **14** with an appropriate diene.¹⁵ Thus, treatment of **2** with 100 mol% of CsF in acetonitrile/THF, in the presence of dienone **11** afforded 5,6,7,8-tetraphenyl-4-(trimethylsilyl)phenanthrene-3-yl triflate **15** in 24% yield (34% considering the starting material recovered), together with minor amounts (< 5%) of two side products which, on the basis of their mass and ¹H-NMR spectra, were identified as 1,2,3-triphenylbenzo[*e*]pyrene (**16**) and the 8-phenanthryl-substituted derivative **17** (Scheme 3), respectively. These compounds seemed to be formed as a result of an intramolecular arylation involving C–H bond activation, specifically by a formal insertion of the new triple bond generated at C(3)–C(4) positions of phenanthryne **18** into one of the C(2')–H bonds of the vicinal phenyl group located at C(5). To the best of our knowledge there is no literature precedent for the type of reaction described above, as previous reports on intramolecular aryne trapping by a pendant unactivated phenyl group are based on Diels-Alder cycloaddition processes.^{16, 17}



Scheme 3 Synthesis of 5,6,7,8-tetraphenyl-4-(trimethylsilyl)phenanthren-3-yl triflate (**15**). Generation and intramolecular trapping of aryne **18**.

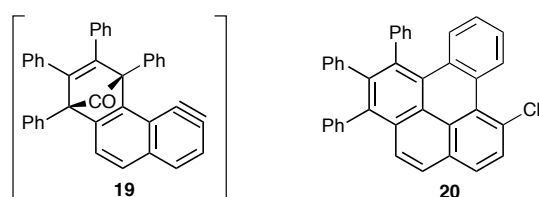


Figure 4 Aryne intermediate **19** and 8-chlorobenzo[e]pyrene **20**

The behavior of triflate **15** under aryne-forming conditions shed light on the mechanism of the cyclization reaction and also on the double cycloaddition process to obtain **12**: (1) It was proven that the generation of aryne **18** in the presence of cyclopentadienone **11** did not result in the formation of **12**, but in the isolation of **16** and **17** in significant yields, suggesting that the Diels–Alder reaction of this hindered aryne with the sterically demanding diene **11** is prevented; we therefore reasoned that the formation of **12** described above (Scheme 2) must have involved the less hindered, tetracyclic aryne **19**. (2) Compounds **16** and **17** were also obtained when **15** was treated with CsF in the absence of **11**. It was also found that the product ratio **16**:**17** is influenced by the concentration of aryne precursor **15** in the reaction mixture, as shown in Scheme 3. (3) Finally, when aryne **18** was generated using CCl₄ as co-solvent, GC-MS and NMR analysis of the reaction mixture evidenced the incorporation of chlorine at C(8) in the benzo[e]pyrene product **20**, suggesting the possibility of a radical cyclization through intermediate **21** rather than a polar, Friedel–Crafts type mechanism involving zwitterion **22**. A preliminary computational study on this new reaction supports the radical reaction pathway through a singlet diradical intermediate **21**. The electronic character of the reaction intermediate was analysed by carrying out a DFT study on the closed-shell singlet **22** and the open-shell diradical singlet **21** using the M062x functional and 6-31++G(d,p) basis set.¹⁸ For the diradical species, the broken symmetry formalism (BS-DFT) was used (see ESI for details).

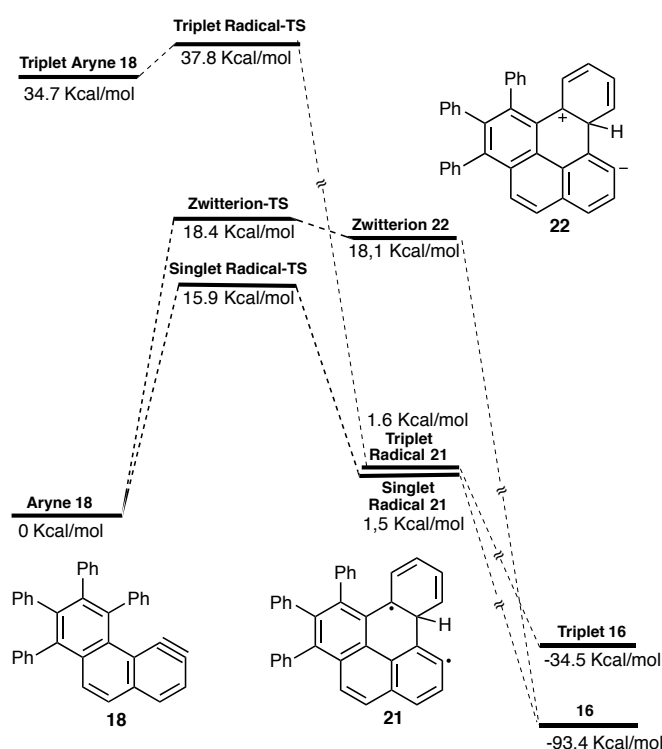


Figure 5 Energy profile for the intramolecular arylation of aryne **18**

It was found that the singlet diradical **21**¹⁹ is more stable than **22** by 16.6 kcal/mol and lies only 1.5 kcal/mol above aryne **18**. The spin-paired singlet **22** lies 18.1 kcal/mol above aryne and has zwitterionic character, as supported by the calculated electrostatic potential map (see ESI). On the other hand, the transition state that leads to the singlet diradical **21** is 15.9 kcal/mol above aryne **18** and is 2.5 kcal/mol more stable than the transition state leading to the spin-paired singlet (Figure 5).

In conclusion, it has been demonstrated that 1,8-bis(trimethylsilyl)naphthalene-2,7-diyl bistriflate (**2**) is an efficient precursor of the novel 1,7-naphthodiyne synthon **1**. The preliminary

experiments reported here show the utility of this platform for the synthesis of novel, sterically congested PAHs such as helicenes, iptycenes and angularly fused acene derivatives.

Furthermore, the selective generation of one of the aryne moieties from **2** and subsequent reaction with an appropriate partner allows straightforward access to a new structurally complex 3-phenanthryne precursor. Generation of this 5-phenyl-substituted 3-phenanthryne with CsF led to the serendipitous discovery of a novel intramolecular aryne trapping reaction.

Acknowledgements

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