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

Iago Pozo, Agustín Cobas, Diego Peña, Enrique Guitián and Dolores Pérez*

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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. From the first proposal of an aryne species to the recent on-surface generation and AFM imaging of a single aryne molecule, these short-lived species have attracted the attention of theoretical, physical and synthetic chemists. Doubly unsaturated derivatives (bisarynes or bisaryne synthons) 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, 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.

The number of bisaryne synthons described to date is limited and 1,4-benzodiyne and 2,6-naphthodiyne are the most widely studied. With regard to bisarynes derived from naphthalene, the formal generation and trapping of 1,3, 1,5 and 1,6-naphthodiyynes 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 triflates to generate arynes under mild reaction conditions, we targeted bistriflate as potential precursor of 1,7-naphthodiyne (1) (Figure 1).

[Diagram of 1,7-Naphthodiyne (1) and its bistriflate formal precursor 2]

This sterically crowded 1,2,7,8-tetrasubstituted naphthalene was successfully obtained through the reaction sequence shown in Scheme 1. Regioselective bromination of 2,7-naphthalenediol afforded 1,8-dibromonaphtho-2,7-diol 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 in 41% overall yield.

Reaction of 2 with CsF in acetonitrile in the presence of furan afforded cycloadducts 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 KI allowed deoxygenation to afford benzoc[7]phenanthrene in 40% yield (Scheme 2).

**Scheme 1**: Synthesis of 1,8-bis(trimethylsilyl)naphthalene-2,7-diyl bistriflate

[Scheme 1]

**Fig. 1**, 1,7-Naphthodiyne (1) and its bistriflate formal precursor 2
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). 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-tetraphenycyclopentadienone (11) gave octaphenyl-benzoc[1]phenanthrene 12, as a result of a double Diels–Alder reaction of naphthodiynone (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 55.5°. 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-naphthodiynone equivalent had been demonstrated, it was decided to explore the synthesis of new functionalized 3-phenanthrene 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. Thus, treatment of 2 with 100 mol% of CsF in acetonitrile/THF, in the presence of diene 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-phenanthrenyl-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 phenanthrene 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.

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-tetraphenylanthracene 10 in a reasonable 45% yield.

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

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

**Figure 3** DFT optimized geometries for 10 and 12
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.14 For the diradical species, the broken symmetry formalism (BS-DFT) was used (see ESI for details).

It was found that the singlet diradical 21 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-diyldistri fluoride (2) is an efficient precursor of the novel 1,7-naphthodyl synth 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 S-phenyl-substituted 3-phenanthryne with CsF led to the serendipitous discovery of a novel intramolecular aryne trapping reaction.

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Notes and references

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14 Measured as the dihedral angle defined by C(15)–C(15a)–C(15c)–C(16) in 10 and C(12)–C(12a)–C(12c)–C(12) in 12. See ESI for details.
15 We recently demonstrated the ability of some bis(trimethylsilyl)aryl bistriﬂates to generate both formal aryne triple bonds sequentially, allowing easy access to complex polycyclic aryne precursors, see ref. 7.
17 For reports on base-promoted sp2 C–H bond arylation involving aryne intermediates, see: (a) G. B. Bajracharya, O. Daugulis, Org. Lett., 2008, 10, 4625 (intramolecular C–arylation of phenols); (b) T. Truong, O. Daugulis, J. Am. Chem. Soc., 2011, 133, 4243 (intramolecular arylation of heteroarenes and arenes containing acidic C–H bonds).
18 Solvent effects for acetonitrile were computed using the CPCM model:

19 The calculated spin density map of the open shell singlet 21 supports a σ–π diradical character, showing separation of the π-type density, delocalized in the upper ring and a sigma-type density localized on the sp2 hybrid orbital at C(8).