

# ChemComm

Accepted Manuscript



This is an *Accepted Manuscript*, which has been through the Royal Society of Chemistry peer review process and has been accepted for publication.

*Accepted Manuscripts* are published online shortly after acceptance, before technical editing, formatting and proof reading. Using this free service, authors can make their results available to the community, in citable form, before we publish the edited article. We will replace this *Accepted Manuscript* with the edited and formatted *Advance Article* as soon as it is available.

You can find more information about *Accepted Manuscripts* in the [Information for Authors](#).

Please note that technical editing may introduce minor changes to the text and/or graphics, which may alter content. The journal's standard [Terms & Conditions](#) and the [Ethical guidelines](#) still apply. In no event shall the Royal Society of Chemistry be held responsible for any errors or omissions in this *Accepted Manuscript* or any consequences arising from the use of any information it contains.

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

Received 00th January 20xx,  
Accepted 00th January 20xx

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

DOI: 10.1039/x0xx00000x

www.rsc.org/

The synthesis of an efficient precursor of the novel 1,7-naphthodiynes 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.<sup>1</sup> From the first proposal of an aryne species<sup>2</sup> to the recent on-surface generation and AFM imaging of a single aryne molecule,<sup>3</sup> these short-lived species have attracted the attention of theoretical, physical and synthetic chemists.<sup>4</sup> Doubly unsaturated derivatives (bisarynes or bisaryne synthons)<sup>5</sup> 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,<sup>6</sup> 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.<sup>7</sup>

The number of bisaryne synthons described to date is limited and 1,4-benzodiyne<sup>8</sup> and 2,6-naphthodiyne<sup>9,6b,6e</sup> are the most widely studied. With regard to bisarynes derived from naphthalene, the formal generation and trapping of 1,3-,<sup>6a</sup> 1,5-<sup>6b,10</sup> and 1,6-naphthodiyne<sup>6a</sup> 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<sup>11</sup> to generate arynes under mild reaction conditions, we targeted bistriflate **2** as potential precursor of 1,7-naphthodiyne (**1**) (Figure 1).

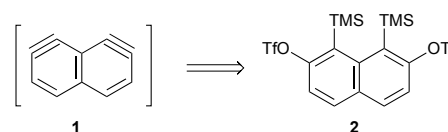
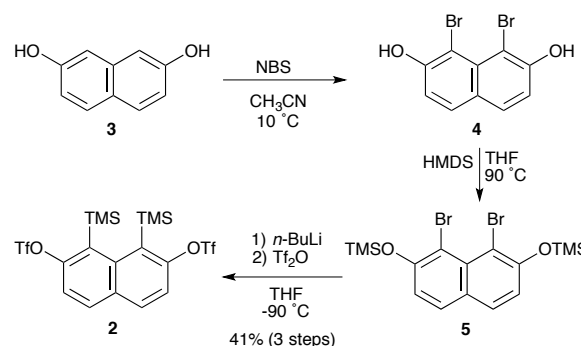


Fig. 1 1,7-Naphthodiyne (**1**) and its bistriflate formal precursor **2**



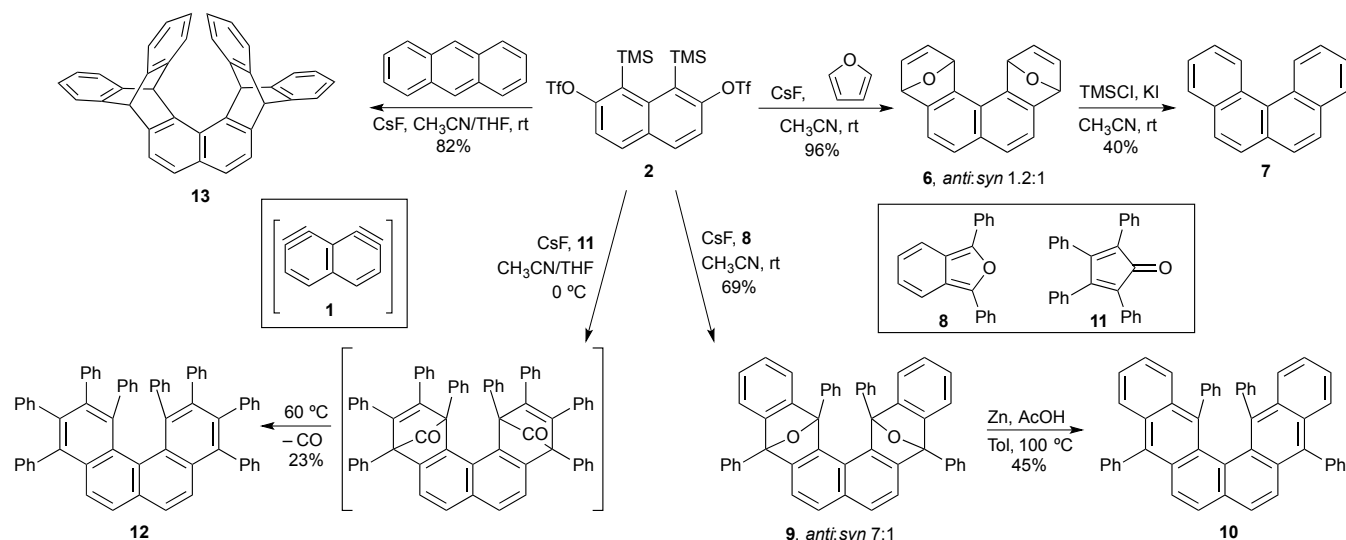
Scheme 1 Synthesis of 1,8-bis(trimethylsilyl)naphthalene-2,7-diyl bistriflate (**2**)

This sterically crowded 1,2,7,8-tetrasubstituted naphthalene was successfully obtained through the reaction sequence shown in Scheme 1. Regioselective bromination<sup>12</sup> of 2,7-naphthalenediol (**3**) afforded 1,8-dibromonaphtho-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 Tf<sub>2</sub>O to afford 1,8-bis(trimethylsilyl)naphthalene-2,7-diyl bistriflate (**2**) in 41% overall yield.

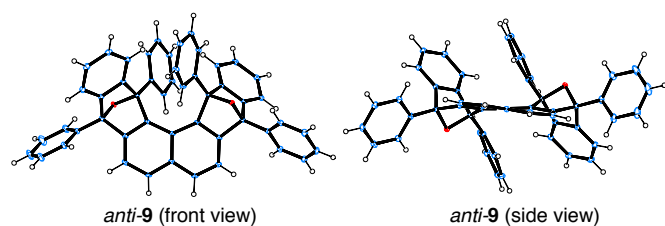
Reaction of **2** with CsF in acetonitrile in the presence of furan afforded cycloadducts **6** in an excellent 96% yield, as a 1.2:1 mixture of isomers. The major product resulted to be the chiral isomer *anti*-**6**, as demonstrated by the separation into enantiomers by chiral HPLC (see ESI). The formation 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 KI<sup>13</sup> allowed deoxygenation to afford benzo[*c*]phenanthrene (**7**) in 40% yield (Scheme 2).

Centro Singular de Investigación en Química Biolóxica e Materiais Moleculares (CIQUS) and Departamento de Química Orgánica, Universidade de Santiago de Compostela, 15782 Santiago de Compostela, Spain. E-mail: dolores.perez@usc.es.

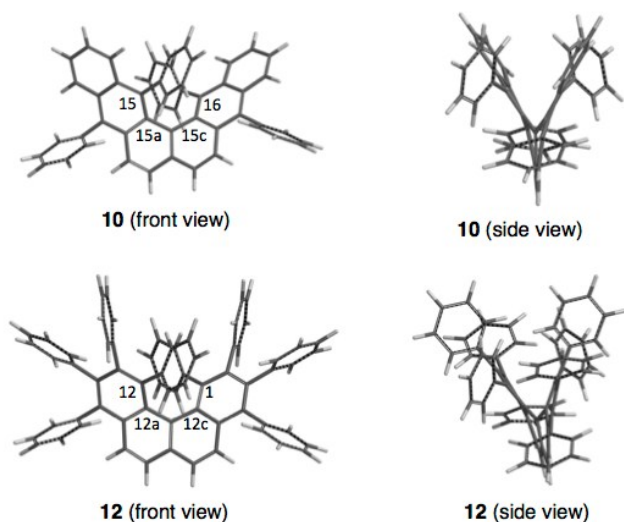
Electronic Supplementary Information (ESI) available: Experimental, spectroscopic and computational data, CCDC 1443038 and 1443039. See DOI:10.1039/x0xx00000x



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



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

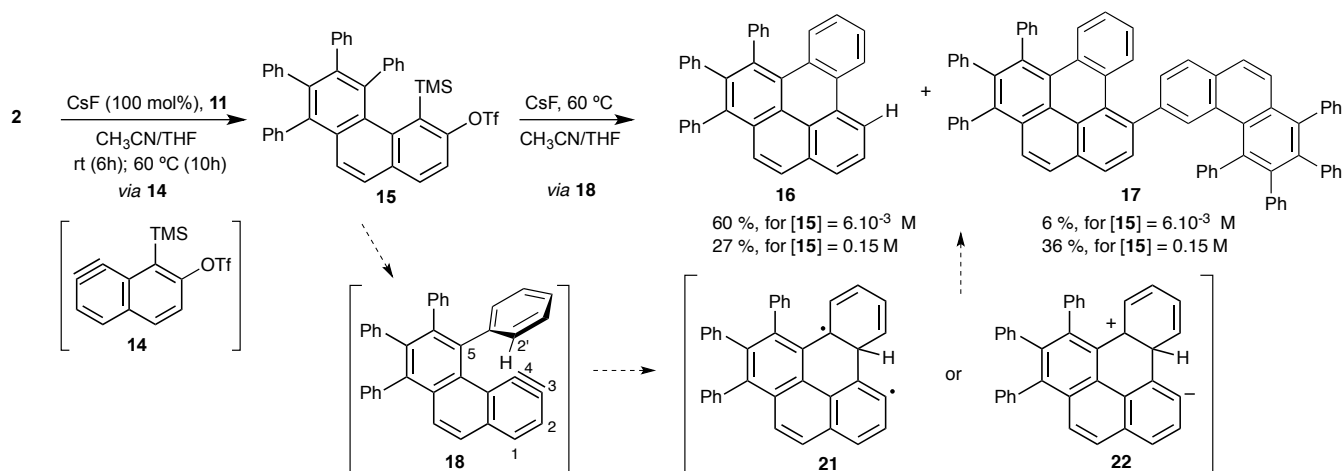


**Figure 3** DFT optimized geometries for **10** and **12**

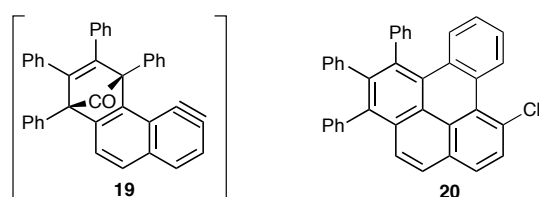
More remarkably, reaction of **2** with 1,3-diphenylisobenzofuran (**8**) under similar conditions led to the isolation of endoxides **9** in 69% overall yield as a 7:1 mixture of stereoisomers, which were separated by selective precipitation of the major product from Et<sub>2</sub>O. Single-crystal 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).<sup>14</sup> 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°.<sup>14</sup> 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.<sup>15</sup> 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 <sup>1</sup>H-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.<sup>16,17</sup>



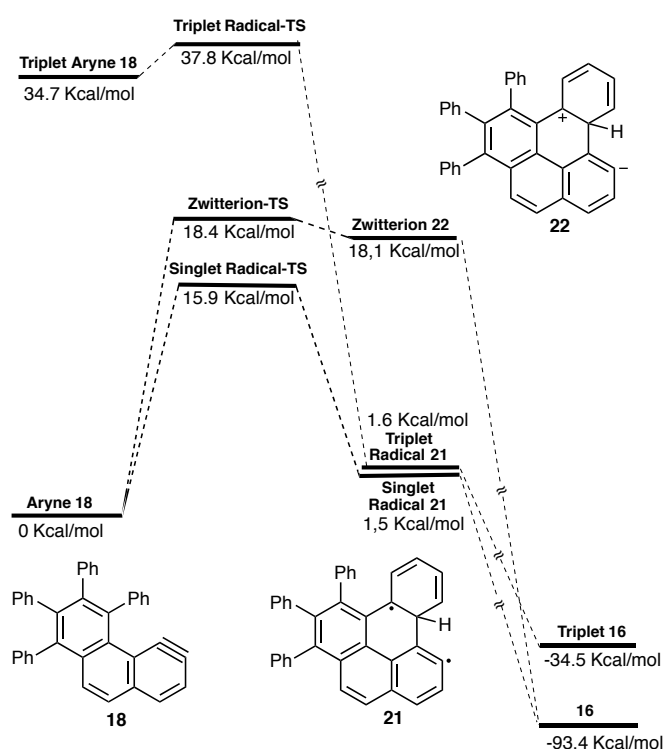
**Scheme 3** Synthesis of 5,6,7,8-tetraphenyl-4-(trimethylsilyl)phenanthren-3-yl triflate (**15**). Generation and intramolecular trapping of arylene **18**.



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

The behavior of triflate **15** under arylene-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 arylene **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 arylene 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 arylene **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 arylene precursor **15** in the reaction mixture, as shown in Scheme 3. (3) Finally, when arylene **18** was generated using  $\text{CCl}_4$  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.<sup>18</sup> 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 arylene **18**

It was found that the singlet diradical **21**<sup>19</sup> is more stable than **22** by 16.6 kcal/mol and lies only 1.5 kcal/mol above arylene **18**. The spin-paired singlet **22** lies 18.1 kcal/mol above arylene 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 arylene **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

Financial support from the Spanish Ministry of Economy and Competitiveness (MINECO, CTQ2013-44142-P and MAT2013-46593-C6-6-P), the European Union (Project PAMS, contract no. 610446), Xunta de Galicia (GPC2014/25) and FEDER is gratefully acknowledged. We also thank the Centro de Supercomputación de Galicia (CESGA) for generous allocation of computer time.

## Notes and references

† Electronic supplementary information (ESI) available: Experimental, spectroscopic and computational CCDC 1443038 and 1443039. DOI: .

§

- General reviews on aryne chemistry: (a) Hoffmann, R. W. *Dehydrobenzene and Cycloalkynes*, Academic Press, New York, 1967; (b) Hart, H. *Arynes and Heteroarynes Suppl. C2: The Chemistry of Triple-Bonded Functional Groups* (Eds.: S. Patai, Z. Rappoport), Wiley, Chichester, 1994, p. 1017; (c) Pellisier, H.; Santelli, M., *Tetrahedron*, 2003, **59**, 701; (d) R. Sanz, *Org. Prep. Proced. Int.*, 2008, **40**, 215; (e) C. Wentrup, *Aust. J. Chem.*, 2010, **63**, 979; (f) A. Bhunia, S. R. Yetra and A. T. Biju, *Chem. Soc. Rev.*, 2012, **41**, 3140.
- (a) R. Stoerme and B. Kahlert, *Ber. Dtsch. Chem. Ges.*, 1902, **35**, 1633; (b) H. H. Wenk, M. Winkler, W. Sander, *Angew. Chem. Int. Ed.*, 2003, **42**, 502.
- N. Pavlicek, B. Schuler, S. Collazos, N. Moll, D. Pérez, E. Guitián, G. Meyer, D. Peña, L. Gross, *Nat. Chem.*, 2015, **7**, 623.
- Recent reviews on synthetic applications of arynes: (a) P. M. Tadross and B. M. A. Stoltz, *Chem. Rev.*, 2012, **112**, 3550; (b) C. M. Gampe and E. M. Carreira, *Angew. Chem. Int. Ed.*, 2012, **51**, 3766; (c) D. Pérez, D. Peña and E. Guitián, *Eur. J. Org. Chem.*, 2013, 5981.
- (a) T. Sato, H. Niino, *Aust. J. Chem.*, 2010, **63**, 1048; (b) M. Winkler, W. Sander, *Aust. J. Chem.*, 2010, **63**, 1013; (c) J. Li, Q. Zhang, *Synlett*, 2013, **24**, 686.
- See, for instance: (a) G. W. Gribble, R. B. Perni, *J. Org. Chem.*, 1985, **50**, 2934; (b) J. Lu, D. M. Ho, N. J. Vogelaar, C. M. Kraml, R. A. Pascal Jr., *J. Am. Chem. Soc.*, 2004, **126**, 11168; (c) H. M. Duong, M. Bendikov, D. Steiger, Q. Zhang, G. Sonmez, J. Yamada, F. Wudl, *Org. Lett.*, 2003, **5**, 4433; (d) D. Franz, S. J. Robbins, R. T. Boeré, P. W. Dibble, *J. Org. Chem.*, 2009, **74**, 7544; (e) C. Kitamura, Y. Abe, T. Ohara, A. Yoneda, T. Kawase, T. Kobayashi, H. Naito, T. Komatsu, *Chem.–Eur. J.*, 2010, **16**, 890; (f) C. Kitamura, A. Takenaka, T. Kawase, T. Kobayashi, H. Naito, *Chem. Commun.*, 2011, **47**, 6653; (g) J. Li, Y. Zhao, J. Lu, G. Li, J. Zhang, Y. Zhao, X. Sun, Q. Zhang, *J. Org. Chem.*, 2015, **80**, 109.
- (a) B. Schuler, S. Collazos, L. Gross, G. Meyer, D. Pérez, E. Guitián, D. Peña, *Angew. Chem. Int. Ed.*, 2014, **53**, 9004; (b) D. Rodríguez-Lojo, D. Pérez, D. Peña, E. Guitián, *Chem. Commun.*, 2015, **51**, 5418; (c) D. Rodríguez Lojo, D. Peña, D. Pérez, E. Guitián, *Synlett*, 2015, **26**, 1633.

- (a) M. Masaya, A. Yabe, *Chem. Lett.*, 1998, **4**, 337; (b) T. Sato, S. Arulmozhiraja, H. Niino, S. Sasaki, T. Matsuura, A. Yabe, *J. Am. Chem. Soc.*, 2002, **124**, 4512.
- T. Sato, H. Niino, A. Yabe, *J. Photochem. Photobiol. A*, 2001, **145**, 3.
- C. S. LeHoullier, G. W. Gribble, *J. Org. Chem.*, 1983, **48**, 1682.
- (a) Y. Himeshima, T. Sonoda, H. Kobayashi, *Chem. Lett.*, 1983, 1211; (b) D. Peña, A. Cobas, D. Pérez, E. Guitián, L. Castedo, *Synthesis*, 2002, 1454.
- (a) A. Thirsk, G. Hawkes, R. Kroemer, K. Liedl, T. Loerting, R. Nasser, R. Pritchard, M. Steele, J. Warren, A. Whiting, *J. Chem. Soc., Perkin Trans.*, 2002, **2**, 1510; (b) K. Majumdar, S. Mondal, D. Ghosh, *Tetrahedron Lett.*, 2009, **50**, 4781.
- G. Thanasis, K. Masato, *J. Org. Chem.*, 1993, **58**, 7158.
- 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(1) in **12**. See ESI for details.
- 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.
- V. D. Pogula, T. Wang, T. R. Hoye, *Org. Lett.*, 2015, **17**, 856
- For reports on base-promoted sp<sup>2</sup> 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 (intermolecular arylation of heteroarenes and arenes containing acidic C–H bonds).
- Solvent effects for acetonitrile were computed using the CPCM model: (a) M. Cossi, N. Rega, G. Scalmani, V. Barone, *J. Comp. Chem.*, 2003, **24**, 669; (b) V. Barone M. Cossi, *J. Phys. Chem. A*, 1998, **102**, 1995.
- The calculated spin density map of the open shell singlet **21** supports a  $\sigma$ - $\pi$  diradical character, showing separation of the pi-type density, delocalized in the upper ring and a sigma-type density localized on the sp<sup>2</sup> hybrid orbital at C(8).