Sulfurane [S(IV)]-mediated fusion of benzynes leads to helical dibenzofurans

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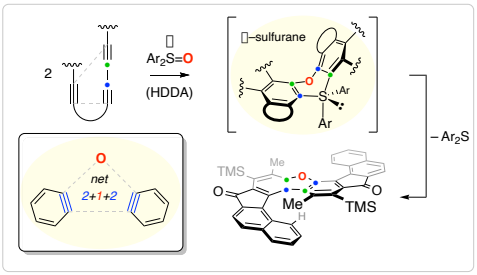
ABSTRACT: Here we disclose a sulfurane-mediated method for the formation of dimeric dibenzofuran helicenes via the reaction between diaryl sulfoxides and hexadehydro-Diels-Alder (HDDA) derived benzynes. A variety of S-shaped and U-shaped helicenes were formed under thermal conditions. Both experimental and DFT studies support a sulfur(IV)-based coupling (aka ligand coupling) mechanism involving tetracarbo-ligated S(IV) intermediates undergoing reductive elimination to afford the helicene products. This process involves the de novo generation of five new rings in a single operation and constitutes a new method for the construction of topologically interesting, polycyclic aromatic compounds.



σ–Sulfuranes (:SX_4) are a relatively rare class of functional group, especially so when all the covalent substituents are carbon atoms [S(IV)C_4].[1] These hypervalent species have only been isolated or observed in limited instances,[2] although the σ–selenurane [Se(IV)C_4] and, especially so, σ–tellurane [Te(IV)C_4] group 16 analogs are more common. The S(IV)C_4 sulfuranes are proposed as reactive intermediates that undergo reductive elimination[3] to produce products containing new C–C bonds (the first example: $Ph_3S^+Br^-$ + PhLi → Ph_2S + $PhPh$[4]). Here we describe a paradigm for [S(IV)C_4]-based coupling reactions of hexadehydro-Diels-Alder (HDDA) benzynes,[5] which leads to the formation of helical dibenzofurans. These dimerizations are mediated by simple diaryl sulfoxides that serve as the benzyne trapping partner.

Trapping of arynes with a sulfoxide was first observed in the 1970's by both Shibuya and Bunnett and their coworkers.[6] In each of those instances, the action of a strong base in DMSO solution on an aryl halide gave an *o*-methylthiophenol derivative as a byproduct. Only recently have reactions of benzynes with sulfoxides been revisited more broadly.[7] In the study most relevant to the results we disclose below, Peng and coworkers recently described the diaryl sulfoxide-promoted coupling of two molecules of *o*-benzyne (**I**)[†] to produce phenoxathiine (**3**) and biaryls **4** (Figure 1a).[8] This demonstrated the efficiency as well as selectivity of reductive elimination within the tetravalent (and trigonal pyramidal) σ–sulfurane **V**. That is to say, no diaryl sulfide (ArSAr), dibenzofuran,[9] or mixed biaryl compounds were detected among the products. The transformation was proposed to proceed via intermediates **II** (a benzoxathiete[10]), **III** (a sulfur ylide type structure) and **IV** (a 1,6-zwitterion and the adduct of **III** with **I**), in line with known reactions of arynes with sulfoxides.[7]

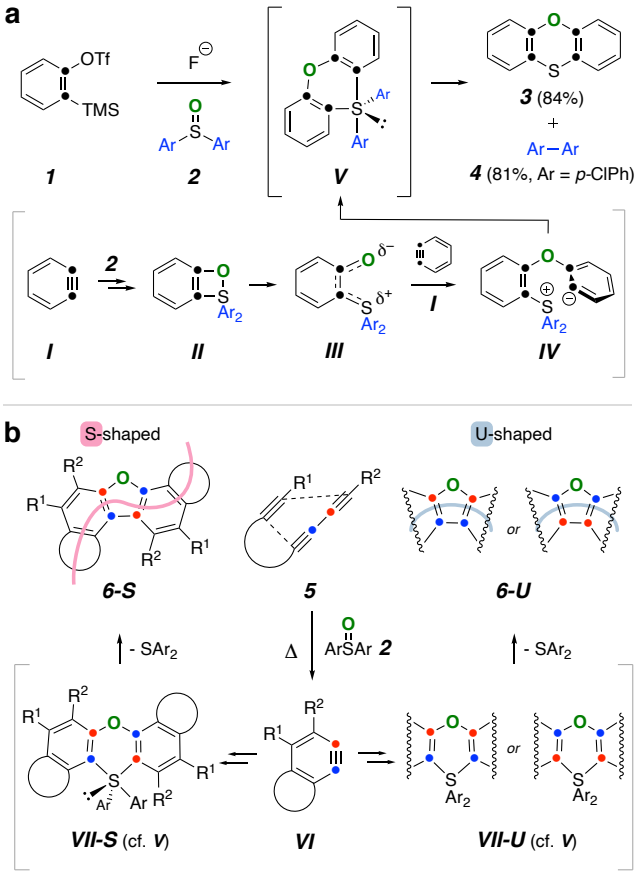


Figure 1. **a**) Prior work by Peng and coworkers trapping Kobayashi benzynes with diaryl sulfoxides.[8] **b**) Trapping HDDA-benzynes with diaryl sulfoxides to form dibenzofurans (this work).

[†] In this manuscript Roman numerals are used to designate the structures of (presumed or computed) transient intermediates or transition structures (TSs).

We report here thermal reactions between several HDDA triyne substrates **5** and various diaryl sulfoxides **2** (Figure 1b). These proceed, by way of benzynes **VI**, through previously unreported pathways to produce the polycyclic dimers **6-S** (and, on two occasions, the U-shaped analogs **6-U**). These contain a single oxygen atom, derived from the sulfoxide **2**, within the newly formed central furan ring arising via a net (2+2+1)-annulation process. We posit that this occurs by a unique type of reductive-elimination event within the σ-sulfurane **VII-S** (and **VII-U**). It is also notable that i) there is considerable interest in the structure-property relationships of helicene type molecules[11a] and ii) a number of synthetic strategies require the use transition metal-mediated processes[11b-g] and/or give rise predominantly to helicenes having a U-shaped topology.[11h]

In a first experiment we heated the triyne **7** (3 equiv) in the presence of diphenyl sulfoxide (**2a**) at 110 °C (Figure 2). To our surprise, we did not detect any products containing a phenoxathiine skeleton nor any biphenyl (cf. the parent **3** and **4**, Figure 1a). Instead, the fluorenone **8**[7d] (major) and the helical product **9-S** were formed in good overall yield. This significant difference in reaction outcome from that seen in the reactions performed under Kobayashi conditions[8,12] immediately raised interesting mechanistic questions. Products **8** and **9-S** can be

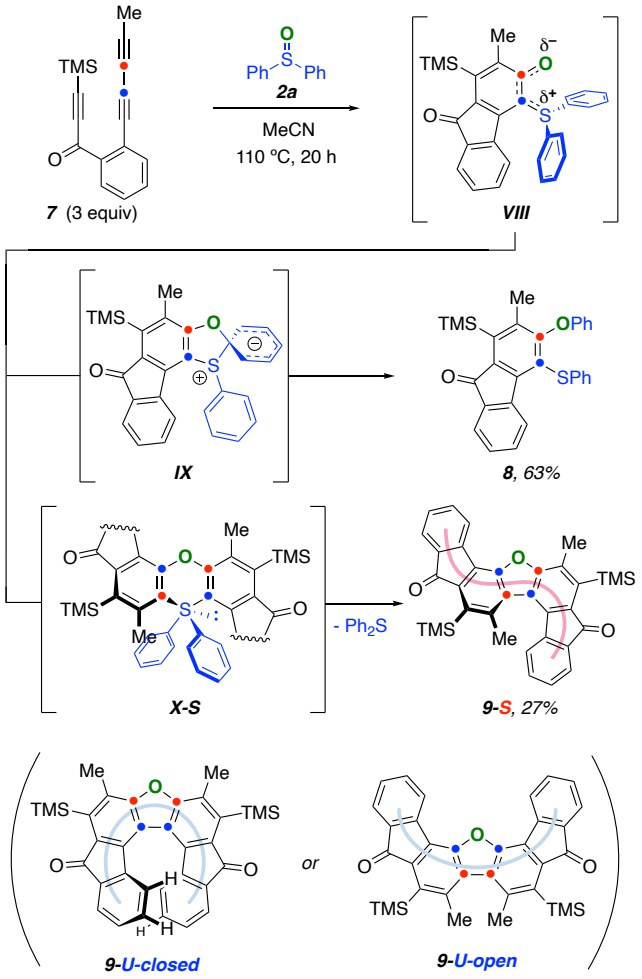


Figure 2. Reaction of triyne **7** with $Ph_2S{=}O$ gives the S_NAr product **8** along with the S-shaped helicene **9-S** and diphenyl sulfide. Surprisingly, there was no indication of formation of a phenoxathiine or biphenyl (cf. Figure 1a).

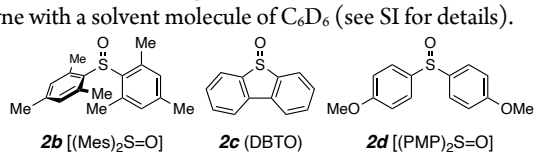
viewed as arising from their respective precursor intermediates **IX** and **X-S**, each coming from **VIII**, the initial adduct of the sulfoxide **2a** and the HDDA-benzyne. Notably even though an excess of HDDA triyne **7** was used, the major product was the 1:1 adduct **8**, accountable by way of an intramolecular S_NAr event via the zwitterionic **IX**. In contrast the product **9-S** resulted from the charge-annihilated, σ–sulfurane **X-S**. Diphenyl sulfide could also be isolated and was clearly evident by GC-MS and ^1H NMR analyses of crude product mixtures. Close examination of the chromatographed sample of **9-S** revealed the presence of a smaller amount of another (co-eluting) 2:1 adduct. Although this substance could not be obtained in pure form, it was clear from the NMR data of this mixture that the second component was one of the symmetrical isomers **9-U-closed** or **9-U-open**. Formation of these helical compounds led us to consider whether the process leading to these topologically intriguing dimers could be optimized to become the dominant pathway.

Toward that end, we felt that the choices of both the reaction solvent and of the diaryl sulfoxide could play important roles in enhancing the efficiency of production of the helicene **9-S**. We carried out the screening studies summarized in Table 1. As we surmised, changing the solvent from acetonitrile to less polar options progressively reduced the amount of the S_NAr pathway and resulting product **8**. Interestingly, the crude product mixture also now showed no sign of the minor helicene **9-U**. We screened various diaryl sulfoxides using benzene-d_6 (C_6D_6) as the solvent. The bulkier mesityl groups in **2b** proved counterproductive. A minor improvement was observed using dibenzothiophene oxide (DBTO, **2c**), possibly a reflection of an altered geometry at the sulfur in intermediate **VIII.** To our delight, we observed the sole formation of the desired compound **9-S** when diaryl sulfoxide **2d** was used. We presume that the electron-donating *p*-methoxyphenyl (PMP) substituents in **2d** disfavor formation of the Meisenheimer complex in the S_NAr pathway (cf. **IX**). With

Table 1. Optimization studies[a] to maximize the preferential formation of the S-helicene 9-S

solvent	# equiv of 7	diaryl sulfoxide[d]	product ratio (NMR): 9-S : 9-U : 8
CH_3CN (cf. Fig. 2)	3.0	$Ph_2S{=}O$ (**2a**)	3.4 : 1 : 7
$CDCl_3$[b]	4.0	$Ph_2S{=}O$ (**2a**)	5 : 1 : 11
C_6D_6[b,c]	4.0	$Ph_2S{=}O$ (**2a**)	1 : 0 : 1.5
C_6D_6[c]	4.0	$Mes_2S{=}O$ (**2b**)	1 : 0 : 3.3
C_6D_6[c]	4.0	DBTO (**2c**)	1 : 0 : 1.3
C_6D_6[c]	4.0	$PMP_2S{=}O$ (**2d**)	1 : 0 : 0
C_6D_6[c]	2.2	$PMP_2S{=}O$ (**2d**)	1 : 0 : 0 (55% isol yield)
DCE	2.2	$PMP_2S{=}O$ (**2d**)	1 : 0 : 0 (70% isol yield)

[a]Reactions performed at 120 °C for 20 h with $[\mathbf{2}]_0 = 0.1$ M. [b]Reaction at 60 °C (90 h). [c]Competitive formation of a [4+2] adduct of benzyne with a solvent molecule of C_6D_6 (see SI for details).

[d] 

conditions established for favoring formation of **9-S,** we then reduced the excess of HDDA substrate **7** from 4.0 to just 2.2 molar equivalents to afford compound **9-S** in 55% yield. Finally, after noticing that a significant portion of HDDA benzyne was being consumed by DA addition with the benzene solvent (see SI), we switched to the benign, relatively non-polar solvent dichloroethane (DCE), which resulted in an increased 70% yield of **9-S**.

We then used these optimized conditions (Figure 3a) to explore other aspects of this transformation. Changing the substituent on the terminus of the conjugated diyne moiety from a methyl group (in **7**) to a substantially larger aryl group (PMP in **10**) significantly changed the product distribution (Figure 3b). Namely, in the reaction of triyne **10** with sulfoxide **2d** the U-shaped product

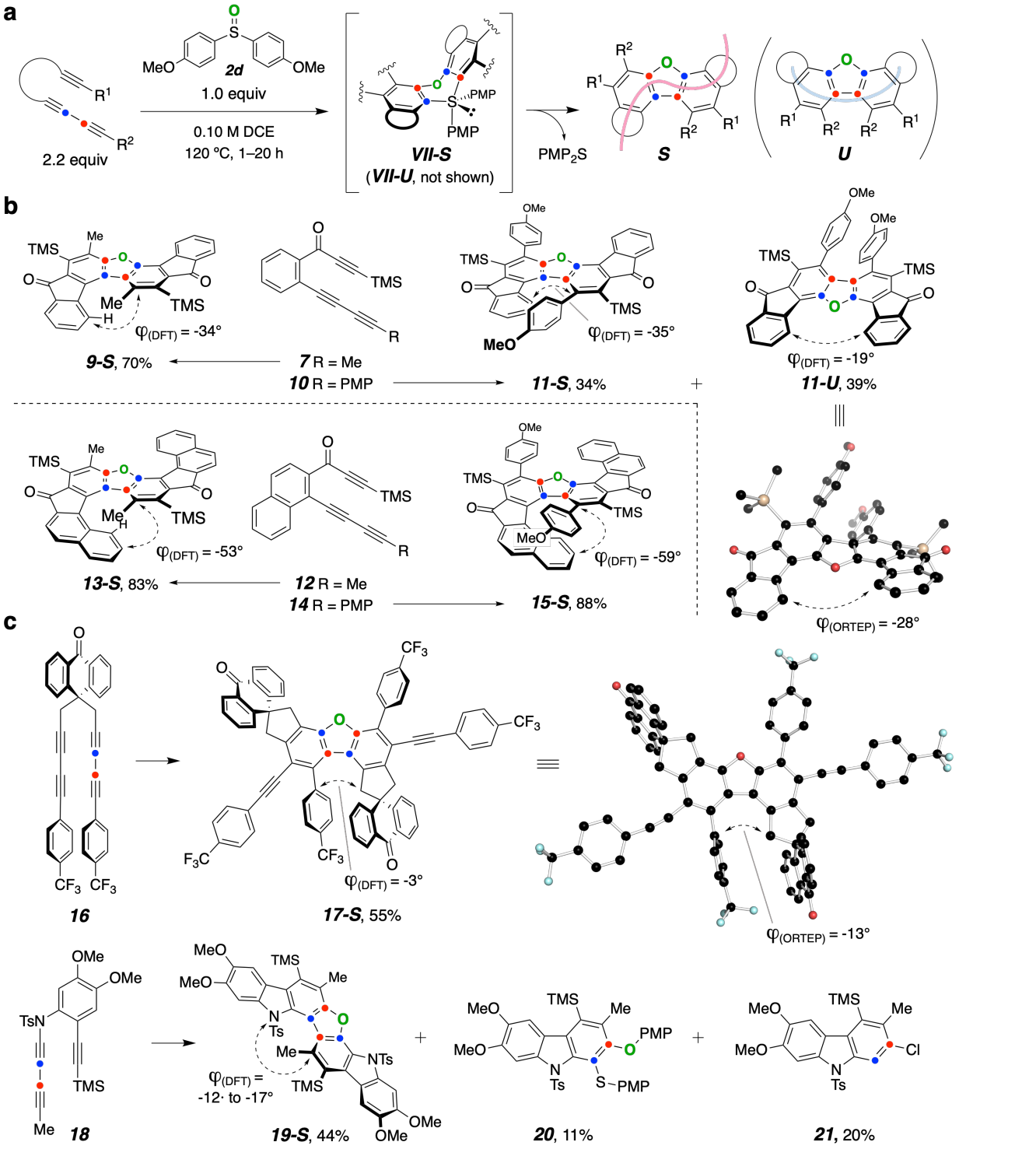


Figure 3. a) General conditions for these (2+2+1) reactions. **b)** Steric effects: size of the diyne terminal group biases the ratio of S- vs. U-shaped helicenes and a naphthalene linker (**12** and **14**) produces products with an extended helicene skeleton. **c)** Other types of HDDA polyyne substrates (**16** and **18**) are competent. The value of φ indicated in each product structure is an indicator of the degree of twist, obtained by treating the atoms at each end of the double-headed, dotted arrow and the two nearest carbon atoms within the essentially planar, central furan ring as a dihedral array.

predominated (**11-U**:**11-S** = 1.1:1). The head-to-head vs. tail-to-tail topicity of the symmetrical helicene **11-U** was confirmed by X-ray crystallographic analysis. The bulkier PMP group on the benzyne presumably is now disfavoring approach of the diarylated sulfur atom to the adjacent benzyne carbon in both the first and second steps of the process. Increasing the size of the triyne linker by replacing the 1,2-phenyl moiety (cf. **7**) for a 1,2-naphthyl subunit (cf. triyne **12**, with a methyl group terminus) led to the sole formation of helicene **13-S** in an 83% yield. Similarly, the PMP-containing HDDA substrate **14**, again having the naphthyl tether, also led to exclusive formation of the S-helicene **15-S** (88%). Thus, the size of the linker group appeared to have a significantly greater impact than that of the substituent on the diyne terminus. Notably, the products **13-S** and **15-S** each contain nine fused, fully conjugated aromatic rings. Additionally, the highly crystalline helicenes **9-S**, **11-U**, **13-S**, and **15-S** could be efficiently isolated in high purity simply by precipitation/ filtration from the cooled reaction mixture.

We next tested several other HDDA polyyne precursors having different types of diyne-diynophile linkers (Figure 3c). The anthrone-templated tetrayne **16** led to the formation of **17-S** in a 55% yield as the sole isolable product. This structure was also confirmed by X-ray crystallographic analysis. Triyne **18**, which is known to produce a benzyne that exhibits highly regioselective trapping by nucleophiles at the benzyne carbon distal to nitrogen,[13] led to a mixture comprising compounds **19-S** (44%) and carbazoles **20** (11%) and **21** (20%). No U-shaped dimer was detected. The observation of the S_NAr 1:1 adduct **20** is consistent with the fact that benzyne formation from **18** is slower than that from the previous poly-yne substrates. The longer steady state lifetime of the sulfur ylide intermediate gives more opportunity for its unimolecular conversion to the Meisenheimer intermediate (cf. **VIII** to **IX**). Twist angles (φ) of the dimeric compounds were computed using density functional theory (DFT) calculations. All these structures showed a helical twist except for **17-S**; the dibenzofurano moiety was found to be essentially planar in its computed structure.

DFT calculations were performed to gather further insight into the key σ–sulfurane reductive elimination event. The truncated analog of triyne **7** (i.e., **7-nor-TMS**) was used as a model substrate to simplify the computations. The most salient energetics are summarized in Figure 4; a fuller description of the overall potential energy surface can be found in the Supporting Information (Figure S1 and discussion there). The energy of the sulfurane **XV** has been referenced to 0; it is computed to be 31.2 kcal more stable than the precursors **XIII** and **XIV**. The key divergence lies in the pathways leading to phenoxathiine **26** via TS **XVI** vs. that to dibenzofuran **27** via **XVII**. The S-shaped σ-sulfurane **XV** was found to have a trigonal bipyramidal geometry. Reductive elimination of diphenyl sulfide from **XV** leading to the formation of **27** was favored by 11.4 kcal mol^{-1} over the biphenyl elimination pathway leading to **26**. This was consistent with experimentation during which no phenoxathiines were observed. Incidentally, an isomeric Berry pseudorotamer of **XV**, slightly lower energy, was identified; it also favored formation of **27** over **26**, now by a $\Delta\Delta G^{\ddagger}$ of 6.5 kcal mol^{-1} (see SI).

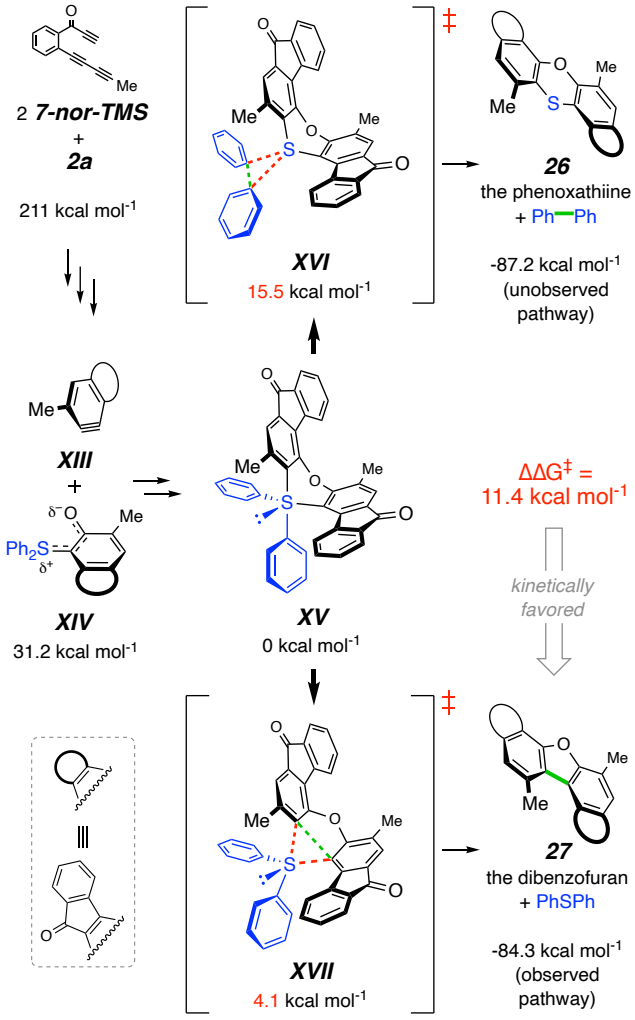


Figure 4. Computed reductive elimination pathways for the σ-sulfurane **XV** to form phenoxathiine **26** + Ph_2 (top) vs. the dibenzofuran **27** + Ph_2S (bottom). **7-nor-TMS** and **27** are the truncated analogs of triyne **7** and dibenzofuran **9-S** in which the TMS groups have been replaced by H. Calculations performed at the [(SMD:$C_2H_4Cl_2$)/M06-2X/6-311+G**//(SMD:$C_2H_4Cl_2$)/M06-2X/6-31G*] level of theory.

In summary, we have disclosed a new reaction process that fuses two copies of an HDDA benzyne into a central dibenzofuran core, the oxygen atom of the furan originating from a diaryl sulfoxide. The transformation is believed to involve a σ-sulfurane (e.g., cf. **XV**), a rare (and reactive) form of tetravalent sulfur [S(IV)]. Reductive elimination could have given either the observed dibenzofuran derivatives (cf. **27**) and diaryl sulfide or the sulfur-containing phenoxathiines (cf. **26**) and biaryl. The exclusive formation of the former is consistent with a DFT analysis of those competing events. This course of reaction complements that of Peng and coworkers in which, under CsF-induced benzyne forming conditions, only the phenoxathiine generation path was seen. This represents another example in which the reaction course of HDDA-derived (i.e., thermally generated) benzynes complements that of more classically produced i.e., (reagent-generated) benzynes.[5] It is also notable that this dibenzofuran-forming annulation reaction has not been reported in the many previous studies of reactions of arynes with sulfoxides.[12b,14]

This process constitutes a new method for the construction of topologically interesting polycyclic aromatic compounds of

potential practical utility. The overall regioselectivities, as indicated in the observed ratios of S- vs. U-shaped topology, are a reflection of a subtle interplay of the distortion-controlled, inherent preference for nucleophilic attack to the benzyne[15] and the longer range steric interactions that attend both i) the trapping of the first benzyne by the sulfoxide and ii) the addition of the second benzyne to the sulfur ylide intermediate. These two guiding influences are, no doubt, both in play, but any more definitive explanation would be speculative. Finally, it is notable that five new, fused rings are produced in this single, thermally induced operation. Exploitation of analogous processes are being explored, including the use of reagents containing various S=N, P=N, P=S, P=Se functional groups.

ASSOCIATED CONTENT

Supporting Information

"The Supporting Information (SI) is available free of charge on the ACS Publications website."

PDF: The SI provides the preparative details and the spectroscopic characterization data, which includes copies of ^{1}H and ^{13}C NMR spectra, for all new compounds.

.cif files: The x-ray diffraction structures of **11-U** and **17-S**; these have been deposited at the Cambridge Crystallographic Data Centre (CCDC Deposition Numbers 2094221 and 2094224). These data can be obtained via data_request@ccdc.cam.ac.uk.

FAIR Data (FID for Publication.zip): Raw NMR data for each type of spectrum for compounds **S3, S5, S7, S8, S9, 8, 9-S, 9-U, 10, 11-S, 11-U, 12, 13-S, 14, 15-S, 16, 17-S, 19-S, 20,** and **21**.

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Notes

The authors have no competing financial interests to declare.

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