# **ORGANIC** CHEMISTRY

**FRONTIERS** 







# **RESEARCH ARTICLE**

View Article Online
View Journal | View Issue



**Cite this:** *Org. Chem. Front.*, 2022, **9**, 929

# Planar Blatter radicals through Bu<sub>3</sub>SnH- and TMS<sub>3</sub>SiH-assisted cyclization of aryl iodides: azaphilic radical addition†

Paulina Bartos, (1) \*\* Małgorzata Celeda, (1) \*\* Anna Pietrzak (1) \*\* and Piotr Kaszyński (1) \*\* a.c.,d

Bu<sub>3</sub>SnH- and TMS<sub>3</sub>SiH-assisted cyclizations of iodoarene derivatives of benzo[e][1,2,4]triazine lead to the formation of planar Blatter radicals (2-phenyl-3*H*-[1,2,4]triazino[5,6,1-*kl*]phenoxazin-3-yls and 2-phenyl-3*H*-[1,2,4]triazino[5,6,1-*kl*]phenothiazin-3-yls) in yields of up to 96%. The cyclization step involves the thermodynamically favored (DFT:  $\Delta G^{\dagger}_{298} = 3.1$  kcal mol<sup>-1</sup> and  $\Delta H = -55.3$  kcal mol<sup>-1</sup>) unprecedented attack of a C-centered radical on the heterocyclic N atom. This method opens up access to functionalized sulfur-containing planar Blatter radicals for the first time. New radicals were characterized using spectroscopic (UV-vis, EPR), electrochemical, and single-crystal X-ray diffraction methods.

Received 22nd November 2021, Accepted 9th December 2021 DOI: 10.1039/d1qo01742j

rsc.li/frontiers-organic

# Introduction

Increasing interest in stable radicals as structural elements for advanced materials  $^{1-8}$  has resulted in increasing demand for their functional derivatives with tailored properties. Of particular interest is the benzo[e][1,2,4]triazinyl radical (Blatter radical) and its derivatives,  $^{10,11}$  which are exceptionally stable,  $^{12,13}$  and exhibit  $\pi\text{-spin}$  delocalization, a narrow electrochemical window,  $^{15,16}$  and low excitation energies. For these reasons, there is rapidly increasing interest in the exploration of this radical as a structural element for advanced materials, such as sensors,  $^{18}$  photodetectors and liquid crystalline photoconductors,  $^{20,21}$  and also for applications in spintronics  $^{22-24}$  and radical polymerization.  $^{25,26}$ 

Recent advances<sup>10,11</sup> in the chemistry of the benzo[e][1,2,4] triazinyl led to the discovery of planar Blatter radicals.<sup>27</sup> The two parent radicals, **10-a** (2-Ph-3H-[1,2,4]triazino[5,6,1-kl] phenoxazin-3-yl) containing a phenoxazine ring and **1S-a** based on phenothiazine (2-phenyl-3H-[1,2,4]triazino[5,6,1-kl]

Successful Pschorr cyclization (Method B) implies an azaphilic addition of the transient aryl radical to the [1,2,4]triazine and suggests that other processes involving aryl rad-

 $<sup>\</sup>dagger$  Electronic supplementary information (ESI) available: Additional synthetic details, NMR spectra, details of XRD, spectroscopic (UV-vis and EPR) and electrochemical analyses and archives of DFT computational results. CCDC 2107124. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/d1q001742j

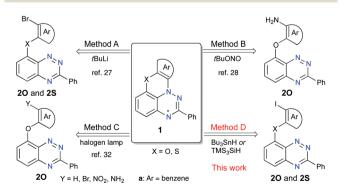


Fig. 1 Three known (A–C) methods and one new (D) method for the preparation of planar benzo[e][1,2,4]triazin-4-yl radicals 1O and 1S.

phenothiazin-3-yl), were obtained in low yields (20–25%) *via* the intramolecular azaphilic addition of ArLi, which was generated *in situ* from the appropriate derivative **2-a** (Method A, Fig. 1).<sup>27</sup> A much improved yield of **10-a** and access to its functional derivatives were demonstrated with the aza-Pschorr cyclization reaction (Method B).<sup>28–31</sup> Further progress in the synthesis of ring-fused derivatives of **10-a** involved photocyclization (Mallory-type cyclization) of C(8)-substituted benzo[*e*][1,2,4]triazines (Method C, Fig. 1).<sup>32</sup> Unfortunately, neither of the latter two methods is suitable for the preparation of sulfur-containing radicals **15**: strongly oxidative conditions are incompatible with the divalent sulfur in Method B, while in Method C the heavy atom effect causes a rapid decay of the S<sub>1</sub> state.

<sup>&</sup>lt;sup>a</sup>Faculty of Chemistry, University of Łódź, 91-403 Łódź, Poland. E-mail: piotr.kaszynski@chemia.uni.lodz.pl

<sup>&</sup>lt;sup>b</sup>Faculty of Chemistry, Łódź University of Technology, 90-924 Łódź, Poland <sup>c</sup>Centre of Molecular and Macromolecular Studies, Polish Academy of Sciences, 90-363 Łódź. Poland

 $<sup>^</sup>d$ Department of Chemistry, Middle Tennessee State University, Murfreesboro, Tennessee 37132, USA

icals,33 e.g. transformations of aryl halides in the presence of R<sub>3</sub>SnH<sup>34,35</sup> or R<sub>3</sub>SiH, <sup>36,37</sup> could also lead to N-cyclization and formation of the planar radical.

Radical chain cyclization reactions<sup>38,39</sup> of aryl halides in the presence of R<sub>3</sub>SnH<sup>34,35</sup> or R<sub>3</sub>SiH<sup>36,37</sup> are well-established and have been used for the formation of carbocyclic derivatives (e.g. phenanthrenes<sup>40-42</sup> and helicenes<sup>43,44</sup>) and for a variety of ring-fused heterocycles. 38,39,45-48 In all these reactions, the key step is the attack of the transient C-centered radical onto the ring C-atom, which is preferred over the N-attack, if the two paths are available. 49,50 Consequently, N-attack of an aryl radical has never been observed in tin- or silicon-hydrideassisted radical cyclization processes.

Herein, we present an efficient Bu<sub>3</sub>SnH- and TMS<sub>3</sub>SiHassisted radical chain cyclization of aryl iodides 2 on the [1,2,4]triazine N-atom and the formation of planar Blatter radicals 10 and 1S (Method D, Fig. 1). The new method is tested on four previously reported radicals and applied to the preparation of the first functionalized sulfur-containing planar Blatter radical, ester 1S-b, as well as 10-c. The two newly obtained radicals, 10-c and 1S-b, are characterized by spectroscopic (UV-vis and EPR) and electrochemical methods, and the structure of the former radical is determined using a single crystal XRD method.

## Results and discussion

## **Synthesis**

Research Article

Initial investigation focused on the cyclization reaction of the benzo[e][1,2,4]triazine 20-a with Bu<sub>3</sub>SnH in toluene (Fig. 2). Following a literature procedure for similar cyclization reactions, 39,44 a solution of the initiator AIBN was added to a solution of 20-a and Bu<sub>3</sub>SnH in toluene at 80 °C over a 4 h period via a syringe pump (Method D-Sn). The initially formed leuco form, 10-a-leuco, underwent slow oxidation to 10-a during workup, and more rapidly during deposition onto the passivated SiO<sub>2</sub>. The crude radical 10-a, which was isolated by filtration through passivated silica gel, contained significant

Fig. 2 Cyclization of benzo[e][1,2,4]triazines 2 to radicals 1. Reagents and conditions, Method D: 1. Bu<sub>3</sub>SnH or TMS<sub>3</sub>SiH, AIBN, toluene, 80 °C, 4 h 2. Air.

amounts of organotin impurities. Therefore, following a modified analogous procedure24 crude 10-a was oxidized with AgOTf to [10-a]<sup>+</sup>, which was purified using chromatography. The pure salt was subsequently reduced with Zn/AcOH and the resulting 10-a-leuco was exposed to air, giving pure radical 10a in 48-52% yield (Scheme 1). Using the same method, radicals 10-b, 10-c and 1S-a were obtained in comparable vields of 42-69% (Fig. 2). The yield of radical 10-d was significantly lower than those of the others in the series (13% yield), mainly due to its lower stability on silica gel and alumina during the purification process.

The difficulties with the removal of organotin byproducts prompted the investigation of an alternative method using TMS<sub>3</sub>SiH instead of Bu<sub>3</sub>SnH. Thus, treatment of benzo [e][1,2,4]triazine **20-a** with TMS<sub>3</sub>SiH in toluene in the presence of AIBN gave the desired radical 10-a in an excellent yield of 96% (Method D-Si) without the need of going through the cation [10-a]+ for purification purposes. This method allowed radicals 10-a-10-c and the parent sulfur-containing radical 18a to be obtained in higher yields of 48-94%. This method appears to be superior to Method D-Sn, and therefore was used to obtain radical 1S-b, the first functional derivative of 18-a. The same Method D-Si did not work unfortunately for the extended radical 10-d. The starting 20-d was fully consumed, and only a complex mixture of polar products was formed.

The parent radicals 10-a and 18-a show no signs of decomposition after 6 years of storage in the solid-state under ambient conditions. Derivatives of 10-a also exhibit long-term stability in the solid-state.

Precursors 2 were tested for photostability and photochemical formation of the corresponding radicals 1. The results demonstrated that all precursors 2 were stable under ambient conditions, while photocyclization of 20-a-20-c in CH<sub>2</sub>Cl<sub>2</sub> solutions gave complex reaction mixtures from which 10-a and 10-c were isolated in 7% and 5% yield, respectively. As expected, attempts at the photocyclization of 8-(2-nitrophenylsulfanyl)-3-phenylbenzo[e][1,2,4]triazine (3S) did not yield the desired radical 1S-a and most of the substrate was recovered. This is in sharp contrast to a moderately efficient photocyclization of the analogous oxygen derivative 30 to form 10-a (31% yield) under the same conditions.<sup>32</sup>

The requisite precursors 20 and 28 were obtained from 8-fluoro-3-phenylbenzo[e][1,2,4]triazine<sup>27</sup> (4) by nucleophilic aromatic substitution reactions with the appropriate ortho-

Scheme 1 Interconversion of cations 1+ and radicals 1. Reagents and conditions: (i) AgOTf, CH2Cl2/CH3CN (9:1), 50 °C, 5-10 min (ii) 1. Zn powder, AcOH, CH<sub>2</sub>Cl<sub>2</sub>/CH<sub>3</sub>CN (9:1), 50 °C, 5 min; 2. Air.

iodo phenols 50 (X = O) or thiols 5S (X = S) in the presence of NaH (Scheme 2).

The iodoarenes 50 and 58-a were obtained using modified literature procedures by iodination of the appropriate phenols diazotization of 2-iodoaniline, respectively.51 Iodomercaptan 5S-b was obtained from methyl 4-amino-3iodobenzoate as shown in Scheme 3. Thus, treatment of 4-aminobenzoate 6 with pyridine iodine monochloride in MeOH gave methyl 4-amino-2-iodobenzoate (7) in 85% yield.<sup>52</sup> To avoid the double iodination of 6 and to obtain high yields of 7, the reaction mixture was quenched with Na<sub>2</sub>S<sub>2</sub>O<sub>3</sub> before the workup. The ester 7 was diazotized and then treated with EtOCSSK, subsequently with KOH/EtOH and finally with iodine. The resulting 4,4'-disulfanediylbis(3-iodobenzoic acid) (8) was partially purified and transformed to dimethyl ester 9 with diazomethane in THF. Finally, the disulfide 9 was reduced with NaBH4 in THF/MeOH according to a general literature procedure, 53 giving methyl 3-iodo-4-mercaptobenzoate (5S-b).

#### Mechanistic considerations

The observed successful formation of 1-leuco in a radical chain process indicates that (a) the addition of the transient radical 10 to the N(1) atom is favorable and fast, and (b) the resulting radical 1 efficiently transfers an H atom from the donor R<sub>3</sub>E-H (E = Sn or Si, Fig. 3). DFT calculations at the B3LYP/6-31G(2d,p)level of theory performed in benzene dielectric medium indeed show a low barrier to the N(1) addition of radical **100-a** ( $\Delta G_{298}^{\ddagger}$  = 3.1 kcal mol<sup>-1</sup>) and high exotherm for the formation of 10-a  $(\Delta H = -55.3 \text{ kcal mol}^{-1}, \text{ Fig. 3})$ . More importantly, the H transfer takes place in spite of the relatively low N-H bond dissociation energy (BDE) in 1-leuco, calculated to be about 69 kcal mol<sup>-1</sup>, 30

Scheme 2 Synthesis of derivatives 20 and 2S. Reagents and conditions: (i) iodoarene 5, 60% NaH, DMSO, 80 °C, 6 h.

Scheme 3 Synthesis of mercaptan 5S-b. Reagents and conditions: (i) 1. pyridine iodine monochloride, MeOH, rt, 2 h; 2. Na<sub>2</sub>S<sub>2</sub>O<sub>3</sub>; 85% yield; (ii) 1. NaNO<sub>2</sub>, aq HCl, ice bath; 2. EtOCSSK; 3. KOH, EtOH, reflux, 10 h; 4. l<sub>2</sub>, H<sub>2</sub>O; 40-56% yield, crude; (iii) CH<sub>2</sub>N<sub>2</sub>, THF/Et<sub>2</sub>O, 0 °C, 10 min; 70-72% yield; (iv) NaBH<sub>4</sub>, THF/MeOH, quant.

Fig. 3 Proposed mechanism for the formation of 1-leuco in a radical chain process and DFT-derived thermochemical parameters for the N-addition step in 100-a.

which compares to the experimental BDE of 73.4  $\pm$  2 kcal mol<sup>-1</sup> for Bu<sub>3</sub>SnH in benzene.<sup>54</sup>

### Crystal and molecular structures

The structure of 10-acetyl derivative 10-c was confirmed with a single-crystal XRD analysis (Fig. 4 and the ESI†). The analysis revealed that **10-c** crystallizes in the triclinic space group  $P\bar{1}$ . The asymmetric unit of 10-c contains two molecules, for which the dimensions of the heterocyclic skeleton are consistent with those found in similar systems.27,29,30 The data showed that the heterocyclic core is nearly ideally planar. The C(2)-Ph ring is twisted from the coplanar orientation with the heterocycle by 4.2° and 5.3° in the two symmetry-independent molecules. The supramolecular system of 10-c consists of two types of slipped stacks extending along the [1 0 0] direction. Each stack is formed by symmetry-equivalent molecules with an interplanar separation of 3.183 Å (for stack A) and 3.246 Å (for stack B) and slippage angles of 27.0° (for stack A) and 62.2° (for stack B). Stacks A are stabilized by C(2)...C(7a) close contacts of 3.228 Å.

## Electronic spectroscopy and electrochemistry

The electronic properties of the new radicals 10-c and 1S-b were analyzed using spectroscopic (UV-vis and EPR) and

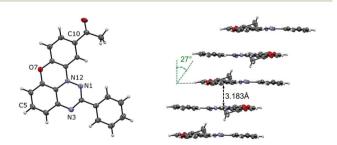


Fig. 4 A displacement ellipsoid diagram for molecule A of 10-c and slipped stack A indicating the distances between the average planes and the slippage angle. Ellipsoids are set at the 50% probability level and labelled according to the chemical structure. Selected intramolecular dimensions: N(1)-N(12), 1.360(1) Å; N(12)-C(11a), 1.399(1) Å; C(10)-Ac, 1.496(2) Å. For molecule B and other details, see the ESI.†

electrochemical methods. Data revealed that both radicals exhibit typical strong absorption in the UV region and broad, low-intensity absorption bands in the entire visible range. The absorption bands of sulfur analogues 1S-a and 1S-b are bathochromically shifted relative to those of the oxygen analogues and exhibit absorption maxima at about 680 nm and 755 (sh) nm (Fig. 5). Analysis of the spectra demonstrated that the optical band gaps, as determined from the absorption edge, are typically about 1.7 eV for radicals 10-a-10-d, while those of the sulfur analogs 1S-a and 1S-b are markedly lower at about 1.5 eV (Table 1).

Research Article

Cyclic voltammetry revealed that the oxidation and reduction processes are quasi-reversible for all derivatives (Fig. 5, Table 1). The oxidation potentials  $E_{1/2}^{0/+1}$  in the "oxo" series increase slightly from -0.15 V for the parent 10-a to -0.09 V for 10-b and to -0.075 V for the 10-acetyl derivative **10-c.** Similarly, the reduction potentials  $E_{1/2}^{-1/0}$  increase for C(10)-substituted derivatives 10-b and 10-c. This effect was recently correlated with the  $\sigma_{
m m}$  substituent parameter for a larger pool of 10 derivatives. 30 Analysis of the pair of 1S derivatives reveals the same trend: there is an anodic shift of redox potentials upon substitution of the parent with the COOMe group (Table 1). Incidentally, the magnitude of this shift in  $E_{1/2}^{0/+1}$  is exactly 0.065 eV in both pairs of radicals, while the reduction potential is affected more strongly in the sulfur pair  $(\Delta E_{1/2}^{-1/0} = 0.059 \text{ V for the } 10 \text{ pair and } 0.099 \text{ V for the } 18$ 

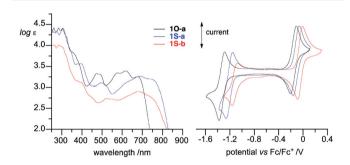


Fig. 5 Left: UV/vis spectra in CH<sub>2</sub>Cl<sub>2</sub> and right: Cyclic voltammograms  $(0.5 \text{ mM in CH}_2\text{Cl}_2 [n-\text{Bu}_4\text{N}]^+\text{PF}_6^- (50 \text{ mM}), \text{ at } \sim 20 \text{ °C}, 50 \text{ mV s}^{-1}, \text{ glassy}$ carbon working electrode) for radicals 10-a (black), 1S-a (blue), and 1Sb (red).

Table 1 Electrochemical data for planar Blatter radical derivatives 1

	Radical R	$E_{1/2}^{-1/0 a}/V$	$E_{1/2}^{0/+1 a}/V$	$E_{\rm cell}^{\ \ b}/{ m V}$	Eg c/eV
O-a	$H^d$	-1.317	-0.154	1.163	1.66
O-b	$COOMe^d$	-1.258	-0.089	1.169	1.72
О-с	Ac	-1.222	-0.075	1.147	1.68
O-d	Naphth <sup>e</sup>	-1.354	-0.212	1.142	1.67
S-a	Н	-1.202	-0.112	1.090	1.48
S-b	COOMe	-1.103	-0.047	1.056	1.51

 $<sup>^</sup>a$  Potentials vs. Fc/Fc<sup>+</sup>.  $^bE_{\rm cell}=E_{1/2}^{0/+1}-E_{1/2}^{-1/0}.$   $^c$  Optical band gap from the absorption edge.  $^d$  Ref. 28.  $^e$  Ref. 32. For details, see the ESI.†

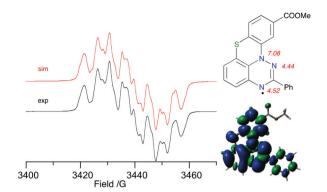


Fig. 6 Left: experimental (black) and simulated (red) EPR spectra for 1S-b recorded in benzene at ca. 20 °C. Right: assignment of the resulting hfcc and total spin density in 1S-b. Contour values are plotted at  $\pm 0.02$  (e per bohr<sup>3</sup>)<sup>1/2</sup>.

## EPR spectroscopy

Electron paramagnetic spectroscopy (EPR) revealed that the experimental hyperfine coupling constants (hfcc)  $a_N$  for 10-c and 1S-b (Fig. 6) are consistent with those for other planar benzo[e][1,2,4]triazinyl radicals.30 Analysis of the results indicates that the  $a_{\rm N(12)}$  value slightly decreases (from 7.42 G for **1S-a** to 7.08 G for **1S-b**), while the values for  $a_{N(1)}$  and  $a_{N(3)}$ increase, e.g. for  $a_{N(1)}$ , from 4.38 G for 1S-a to 4.52 G for 1S-b. This substituent effect is consistent with that observed in the oxygen analogues 10.30

## Conclusions

We have demonstrated a new and efficient method for the formation of planar Blatter radical derivatives through Bu<sub>3</sub>SnHand TMS<sub>3</sub>SiH-assisted cyclization of aryl iodides. Unlike in previous such reactions, the cyclization takes place at the heterocyclic N atom. The new method complements the existing methods A-C for the preparation of planar Blatter radicals with important advantages. Similarly to the Pschorr-type cyclization (Method B), it tolerates functional groups, such as COOMe and COMe, and allows for obtaining the desired products with significantly higher yields (Table 2). Most importantly, for the first time, it permits the preparation of functio-

Table 2 Comparison of Methods A-D in the formation of radicals 1

Radical				Method			
1	R	A	В	C	D-Sn	D-Si	
O-a O-b O-c O-d S-a S-b	H COOMe Ac c H COOMe	20-25% a,b a,b 0% 22-30% a,b	57-64% 48-55% b 0% a,b a,b	7-64% 5% 14-55% a	$48-52\%$ $69\%$ $42-47\%$ $(13\%)^d$ $48\%$	96% 87% 78% 0% 94% 49%	

<sup>&</sup>lt;sup>a</sup> Not compatible. <sup>b</sup> Not attempted. For references see the text. <sup>c</sup> Naphtho-fused radical. <sup>d</sup> Low stability on isolation.

nalized derivatives of the [1,2,4]triazino[5,6,1-kl]phenothiazinyl (radical 1S-b), which was not possible through other methods. This discovery opens up possibilities for further exploration of functionalized [1,2,4]triazino[5,6,1-kl]phenothiazinyl radicals, especially of their magnetic properties in the solid state. This work is underway in our laboratory.

The radical cyclization of aryl iodides method also gives the ring-extended derivatives, such as the naphtho-derivative 10-d, but in this case, the photocyclization Method C appears to be more efficient. The newly discovered Method D for obtaining radicals 1 makes a significant contribution to the development of new materials for molecular electronics, spintronics, and functional self-organizing materials.

#### Computational details

**Organic Chemistry Frontiers** 

Quantum-mechanical calculations were carried out using the Gaussian 09 suite of programs.<sup>55</sup> Geometry optimizations were undertaken at the UB3LYP/6-31G(2d,p) level of theory using tight convergence limits and appropriate symmetry constraints. The transition state for the cyclization of 100-a was located with the QST3 keyword. Calculations involving the cyclization of radical 100-a to form 10-a used SCF energies for reaction components in benzene dielectric medium requested with the SCRF(Solvent = Benzene) keyword (PCM model;<sup>56</sup> single point calculations at the UB3LYP/6-311++G(2d,p)// UB3LYP/6-31G(2d,p) level of theory) and thermodynamic corrections obtained with the UB3LYP/6-31G(2d,p) method.

Isotropic Fermi contact coupling constants for radical 1S-b were calculated using the UCAM-B3LYP/gen //UB3LYP/6-31G (2d,p) method in benzene dielectric medium requested with the SCRF(Solvent = Benzene) keyword (PCM model<sup>56</sup>). The basis set was requested with the GEN keyword: EPRIII basis for all light elements and 6-311 + G(2df) for the S atom.

# **Experimental section**

#### General

Reagents and solvents were obtained commercially. Heat for reactions requiring elevated temperatures was supplied using oil baths. NMR spectra were obtained at 600 MHz (1H) and 151 MHz ( $^{13}$ C) in CDCl<sub>3</sub> and referenced to the solvent ( $\delta$  = 7.26 ppm for <sup>1</sup>H and  $\delta$  = 77.16 ppm for <sup>13</sup>C) or in DMSO- $d_6$ and referenced to the solvent ( $\delta$  = 2.50 ppm for <sup>1</sup>H and  $\delta$  = 39.52 ppm for <sup>13</sup>C).<sup>57</sup> IR spectra were recorded using a Nexus FT-IR Thermo Nikolet IR spectrometer in KBr tablets. UV spectra were measured in CH2Cl2 using a PerkinElmer Lambda 45 spectrophotometer. Melting points were determined using a Stuart SMP30 Advanced Digital Melting Point Apparatus and are uncorrected. High-resolution mass spectrometry (HRMS) measurements were performed using SYNAPT G2-Si High Definition Mass Spectrometry equipped with an ESI or APCI source and Quantitative Time-of-Flight (QuanTof) mass analyzer. Other mass spectrometry measurements were performed using a Varian 500-MS LC Ion Trap Spectrometer. In all cases little or no fragmentation was

observed, and the M, [M + H] or [M - H] peaks were the most intense signals.

Et<sub>3</sub>N-passivated SiO<sub>2</sub> gel and chromatographic separation of radicals 1. The solid support was mixed with a 2% solution of Et<sub>3</sub>N in CH<sub>2</sub>Cl<sub>2</sub> and the solvent was evaporated to dryness (rotavap). For the chromatographic separation of radicals, small amounts of dry, passivated SiO2 were added to the reaction mixture, and the resulting mixture was evaporated to dryness <50 °C. The resulting solid was deposited onto a passivated SiO<sub>2</sub> plug or column (pet. ether), and the product was eluted with a CH<sub>2</sub>Cl<sub>2</sub>/pet. ether mixture.

The activity and effectiveness of the solid supports varied between suppliers and even between batches, and the exact conditions for isolation of the radicals required adjustments for each new container.

## General procedure for Method D-Sn. Bu<sub>3</sub>SnH-assisted cyclization of aryl iodides 2

To a solution of aryl iodide 2 (0.25 mmol) in dry toluene (4 mL), Bu<sub>3</sub>SnH (0.50 mmol) was added and stirred at 80 °C under an atmosphere of Ar. Then, AIBN (0.15 mmol) dissolved in dry toluene (2 mL) was added to the reaction mixture over a period of 4 h using a syringe pump. After 4 h the reaction mixture was cooled and the solvent was evaporated to dryness. The residue was re-dissolved in ethyl acetate (20 mL), saturated aqueous potassium fluoride (20 mL) was added, and the mixture was stirred vigorously for 15 min. The organic fraction was separated, washed with brine  $(2 \times 30 \text{ mL})$ , dried  $(Na_2SO_4)$ , and concentrated in vacuo. The crude product was separated using a short silica gel column passivated with Et<sub>3</sub>N (vide supra). To remove organotin impurities, the radical was oxidized to form the triflate salt 1<sup>+</sup>, purified, and subsequently reduced back to radical 1.

Formation of salts 1<sup>+</sup>[OTf] by oxidation of radicals 1. Radical 1 was dissolved in CH<sub>2</sub>Cl<sub>2</sub>/CH<sub>3</sub>CN (9:1) and AgOTf (0.30 mmol, 1.2 eq.) was added in one portion. The reaction mixture was stirred for 5-10 minutes at 50 °C until the substrate was no longer detectable by TLC (pet. ether/AcOEt, 9:1). The crude salt was purified using a short silica gel column with CH<sub>2</sub>Cl<sub>2</sub>/MeOH 9:1 as the eluent.

Formation of 1 by reduction of salts 1<sup>+</sup>[OTf]. Salt 1<sup>+</sup>[OTf] was dissolved in a 9:1 CH<sub>2</sub>Cl<sub>2</sub>/CH<sub>3</sub>CN mixture (25 mL), and 100 μL of AcOH and 150 mg of zinc powder were added. The reaction mixture was stirred at 50 °C for 5 min until the starting salt 1<sup>+</sup>[OTf] was no longer detectable by TLC analysis (pet. ether/AcOEt, 9:1). The reaction mixture was cooled, filtered through Celite, washed with H<sub>2</sub>O (2 × 30 mL), dried (Na<sub>2</sub>SO<sub>4</sub>), and concentrated in vacuo. The resulting product was recrystallized by slow evaporation of a CH<sub>2</sub>Cl<sub>2</sub>/cyclohexane solution.

# General procedure for Method D-Si. TMS<sub>3</sub>SiH-assisted cyclization of aryl iodides 2

To a solution of aryl iodide 2 (0.25 mmol) in dry toluene (4 mL), TMS<sub>3</sub>SiH (0.50 mmol) was added, and the solution was stirred at 80 °C under an atmosphere of Ar. Then, AIBN (0.15 mmol) dissolved in dry toluene (2 mL) was added to the

reaction mixture over a period of 4 h using a syringe pump. After 4 h, the reaction mixture was cooled, and the solvent was evaporated to dryness. The crude product was absorbed on passivated SiO<sub>2</sub> (vide supra), and radical 1 was isolated using a short silica gel column with passivated SiO2. The product was washed with warm cyclohexane (3×) and recrystallized from CH<sub>3</sub>CN.

Research Article

2-Phenyl-3*H*-[1,2,4]triazino[5,6,1-*kl*]phenoxazin-3-yl (10-a). (10-a). Method D-Sn: 48-52% yield, Method D-Si: 96% yield; eluent: pet. ether/AcOEt, 95:5; blue-gray crystals. Analytical data identical to those previously reported.<sup>27</sup> HRMS (ESI-TOF) m/z [M +  $H_{1}^{+}$  calcd for  $C_{19}H_{13}N_{3}O$ : 299.1059; found: 299.1055.

10-Methoxycarbonyl-2-phenyl-3*H*-[1,2,4]triazino[5,6,1-*kl*]-phenoxazin-3-vl (10-b).<sup>27</sup> Method D-Sn: 69% yield, Method D-Si: 87% yield; eluent: pet. ether/AcOEt, 95:5; blue-gray crystals. Analytical data identical to the previously reported.<sup>28</sup> HRMS (ESI-TOF) m/z [M + H]<sup>+</sup> calcd for C<sub>21</sub>H<sub>15</sub>N<sub>3</sub>O<sub>3</sub>: 357.1113; found: 357.1120.

10-Acetyl-2-phenyl-3H-[1,2,4]triazino[5,6,1-kl]phenoxazin-3-yl (10-c). Method D-Sn: 42-47% yield, Method D-Si: 78% yield; eluent: pet. ether/AcOEt, 9:1; blue-green crystals: mp 187-188 °C (MeCN); IR (KBr) ν 1680, 1567, 1383, 1348, 1266, 1210, 1162, 1031, 791, 696 cm<sup>-1</sup>; UV (CH<sub>2</sub>Cl<sub>2</sub>)  $\lambda_{\text{max}}$  (log  $\varepsilon$ ) 280 (3.58), 315(4.24), 377(3.64), 431(3.29), 514.5(3.19), 570(3.18), 618 (3.24), 673 (3.13) nm; HRMS (ESI-TOF)  $[M + H]^+$  m/z calcd for C21H15N3O2: 341.1164; found: 341.1166. Anal. Calcd for  $(C_{21}H_{14}N_3O_2)_3 \cdot H_2O$ : C, 72.82; H, 4.27; N, 12.13. Found: C, 72.99; H, 4.23; N, 12.42.

2-Phenyl-3*H*-benzo[a][1,2,4]triazino[5,6,1-kl]phenoxazin-3-yl (10-d).<sup>32</sup> Method D-Sn: 13% yield (without salt formation), Method-Si: 0% yield; eluent: pet. ether/AcOEt, 95:5; blue-gray crystals. Analytical data identical to those previously reported.<sup>32</sup> HRMS (ESI-TOF)  $[M + H]^+$  m/z calcd for  $C_{23}H_{15}N_3O$ : 349.1215; found: 349.1222.

2-Phenyl-3*H*-[1,2,4]triazino[5,6,1-*kl*]phenothiazine-3-yl (1S-a).<sup>27</sup> Method D-Sn: 48% yield, Method D-Si: 94% yield; eluent: pet. ether/AcOEt, 9:1 blue-green crystals. Analytical data identical to those previously reported.<sup>27</sup> HRMS (ESI-TOF)  $[M + H]^+ m/z$ calcd for C<sub>19</sub>H<sub>13</sub>N<sub>3</sub>S: 315.0830; found: 315.0836.

10 methoxycarbonyl-2-phenyl-3*H*-[1,2,4]triazino[5,6,1-*kl*]phenothiazin-3-yl (1S-b). Method D-Si: 49% yield; eluent: pet. ether/ AcOEt, 9:1; blue-green crystals: mp 185-186 °C (MeCN); IR (KBr) v 2956, 2925, 2854, 1728, 1470, 1436, 1404, 1249, 1080, 1013, 844, 754, 688 cm<sup>-1</sup>; UV (CH<sub>2</sub>Cl<sub>2</sub>)  $\lambda_{\text{max}}$  (log  $\varepsilon$ ) 263 (4.02), 284 (4.02), 399 (3.12 sh), 524 (2.74), 679 (2.90), 746 (2.75 sh) nm; HRMS (ESI-TOF)  $[M + H]^+$  m/z calcd for  $C_{21}H_{15}N_3O_2S$ : 373.0898; found: 373.0892. Anal. Calcd for C<sub>21</sub>H<sub>14</sub>N<sub>3</sub>O<sub>2</sub>S: C, 67.73; H, 3.79; N, 11.28. Found: C, 67.68; H, 3.93; N, 11.25.

# Synthesis of iodoarenes 2. General procedure

To a stirred solution of phenol 50 or thiophenol 5S (1.10 mmol) dissolved in DMSO (4 mL), 60% NaH (45 mg, 1.10 mmol) was added in one portion. After 15 min of stirring, 8-fluoro-3-phenylbenzo[e][1,2,4]triazine<sup>27</sup> (4,225.2 1.00 mmol) was added, and the reaction was stirred under Ar at 80 °C for 6 h. After cooling, CH<sub>2</sub>Cl<sub>2</sub> (30 mL) was added, and

the organic layer was washed well with water (3 × 25 mL) and brine (25 mL). The combined organic extracts were dried (Na2SO4), and the solvent was evaporated. The resulting solid residue was adsorbed onto passivated silica and purified by column chromatography (passivated silica). The solvent was evaporated, and the product was recrystallized from MeCN.

8-(2-Iodophenoxy)-3-phenylbenzo[e][1,2,4]triazine 368-400 mg (87-94% yield) of 20-a was obtained as yellow crystals: mp 138-139 °C (MeCN); <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>)  $\delta$  8.82-8.76 (m, 2H), 7.96 (dd,  $J_1$  = 8.0 Hz,  $J_2$  = 1.5 Hz, 1H), 7.83-7.79 (m, 2H), 7.63-7.58 (m, 3H), 7.42 (dt,  $J_1$  = 7.7 Hz,  $J_2$  = 1.5 Hz, 1H), 7.18 (dd,  $J_1$  = 8.0 Hz,  $J_2$  = 1.3 Hz, 1H), 7.03 (dt,  $J_1$  = 7.7 Hz,  $J_2 = 1.3$  Hz, 1H), 6.89 (dd,  $J_1 = 6.2$  Hz,  $J_2 = 2.7$  Hz, 1H); <sup>13</sup>C{<sup>1</sup>H} NMR (151 MHz, CDCl<sub>3</sub>)  $\delta$  160.3, 155.6, 154.2, 142.3, 140.5, 139.8, 135.8, 135.6, 131.8, 130.2, 129.15, 129.10, 127.2, 123.2, 121.6, 113.8, 89.9; IR (KBr) ν 3053, 1615, 1561, 1500, 1470, 1436, 1388, 1325, 1259, 1215, 1170, 1086, 1020, 793, 759, 691 cm<sup>-1</sup>; HRMS (ESI-TOF)  $[M + H]^+ m/z$  calcd for  $C_{19}H_{13}IN_3O$ : 426.0103; found: 426.0111. Anal. Calcd for C<sub>19</sub>H<sub>12</sub>IN<sub>3</sub>O: C, 53.67; H, 2.84; N, 9.88. Found: C, 53.67; H, 2.88; N, 10.06.

8-(2-Iodo-3-methoxycarbonylphenoxy)-3-phenylbenzo[e[1,2,4] triazine (20-b). 271 mg (56% yield) of 20-b was obtained as yellow crystals: mp 187-188 °C (MeCN); <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>)  $\delta$  8.80-8.72 (m, 2H), 8.62 (d, J = 2.0 Hz, 1H), 7.97 (dd,  $J_1 = 8.5 \text{ Hz}, J_2 = 2.0 \text{ Hz}, 1\text{H}, 7.92-7.86 (m, 2\text{H}), 7.60-7.57 (m, 2\text{H})$ 3H), 7.16 (dd,  $J_1$  = 6.6 Hz,  $J_2$  = 2.0 Hz, 1H), 6.94 (d, J = 8.7 Hz), 3.92 (s, 3H);  ${}^{13}C\{{}^{1}H\}$  NMR (151 MHz, CDCl<sub>3</sub>)  $\delta$  165.2, 160.4, 160.3, 152.6, 142.4, 141.9, 139.8, 135.7, 131.9, 131.6, 129.15, 129.10, 127.9, 125.0, 118.7, 116.8, 87.9, 52.5; IR (KBr) v 1720, 1561, 1504, 1043, 1384, 1280, 1251, 1107, 1084, 790, 701 cm<sup>-1</sup>; HRMS (ESI-TOF)  $[M + H]^+ m/z$  calcd for  $C_{21}H_{15}IN_3O_3$ : 484.0158; found: 484.0162. Anal. Calcd for C21H14IN3O3: C, 52.19; H, 2.92; N, 8.69. Found: C, 52.23; H, 2.85; N, 8.87.

8-(4-Acetyl-2-iodophenyloxy)-3-phenylbenzo[e][1,2,4]triazine (20-c). 271 mg (58% yield) of 20-c was obtained as yellow crystals: mp 204-205 °C (MeCN); <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>)  $\delta$  8.75–8.79 (m, 2H), 8.54 (d, J = 2.1 Hz, 1H), 7.88–7.94 (m, 3H), 7.58-7.61 (m, 3H), 7.21 (dd,  $J_1$  = 7.1 Hz,  $J_2$  = 1.6 Hz, 1H), 6.94 (d, J = 8.5 Hz, 1H), 2.60 (s, 3H);  ${}^{13}C{}^{1}H$  NMR (151 MHz,  $CDCl_3$ )  $\delta$  195.5, 160.5, 160.3, 152.4, 142.4, 140.9, 139.7, 135.6, 135.2, 134.8, 131.9, 130.2, 129.1, 129.0, 125.2, 118.5, 117.1, 88.2, 26.6; IR (KBr) v 1686, 1560, 1505, 1386, 1347, 1324, 1244, 1073, 847, 796, 704 cm<sup>-1</sup>; HRMS (ESI-TOF)  $[M + H]^+ m/z$  calcd for C<sub>21</sub>H<sub>15</sub>IN<sub>3</sub>O<sub>2</sub>: 468.0209; found: 468.0210. Anal. Calcd for C<sub>21</sub>H<sub>14</sub>IN<sub>3</sub>O<sub>2</sub>: C, 53.98; H, 3.02; N, 8.99. Found: C, 53.79; H, 3.05; N, 9.05.

8-((1-Iodonaphthalen-2-yl)oxy)-3-phenylbenzo[e][1,2,4]triazine (20-d). 314 mg (66% yield) of 20-d was obtained as yellow crystals: mp 204-206 °C (MeCN); <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>)  $\delta$  8.83–8.79 (m, 2H), 8.26 (d, J = 8.5 Hz, 1H), 7.91 (d, J = 8.7 Hz, 1H), 7.85 (d, J = 8.2 Hz, 1H), 7.80–7.74 (m, 2H), 7.65 (t, J = 7.7Hz, 1H), 7.62-7.59 (m, 3H), 7.56 (t, J = 7.6 Hz, 1H), 7.36 (d, J =8.7 Hz, 1H), 6.85 (d, J = 7.2 Hz, 1H);  $^{13}C\{^{1}H\}$  NMR (151 MHz,  $CDCl_3$ )  $\delta$  160.3, 154.3, 153.7, 142.3, 139.8, 135.9, 135.8, 135.6, 132.2, 131.9, 131.8, 131.2, 129.1, 129.0, 128.65, 128.60, 126.5, 122.9, 120.5, 113.4, 94.0; IR (KBr) v 1610, 1558, 1504, 1440,

1384, 1347, 1323, 1246, 1220, 1086, 819, 789, 701 cm<sup>-1</sup>; HRMS (ESI-TOF)  $[M + H]^+$  m/z calcd for  $C_{23}H_{15}IN_3O$ : 476.0260; found: 476.0268. Anal. Calcd for C<sub>23</sub>H<sub>14</sub>IN<sub>3</sub>O: C, 58.12; H, 2.97; N, 8.84. Found: C, 58.11; H, 2.93; N, 9.08.

8-((2-Iodophenyl)thio)-3-phenylbenzo[e][1,2,4]triazine (2S-a). 419 mg (95% yield) of 2S-a was obtained as yellow crystals: mp 157–159 °C (MeCN);  $^{1}$ H NMR (600 MHz, CDCl<sub>3</sub>)  $\delta$  8.80–8.75 (m, 2H), 8.10 (dd,  $J_1 = 7.9$  Hz,  $J_2 = 0.9$  Hz, 1H), 7.83-7.78 (m, 2H), 7.71 (t, J = 7.9 Hz, 1H), 7.62–7.58 (m, 3H), 7.47 (dd,  $J_1 =$ 7.6 Hz,  $J_2 = 1.1$  Hz, 1H), 7.17 (dt,  $J_1 = 7.8$  Hz,  $J_2 = 1.2$  Hz, 1H), 6.90 (dd,  $J_1$  = 7.2 Hz,  $J_2$  = 0.8 Hz, 1H); <sup>13</sup>C{<sup>1</sup>H} NMR (151 MHz,  $CDCl_3$ )  $\delta$  160.6, 143.8, 142.2, 141.15, 141.10, 137.0, 136.1, 135.7, 135.6, 131.8, 131.2, 129.9, 129.1, 129.0, 125.8, 125.4, 108.6; IR (KBr) v 1548, 1504, 1443, 1418, 1379, 1321, 1279, 1212, 1173, 1109, 1018, 981, 793, 752, 700 cm<sup>-1</sup>; HRMS (ESI-TOF)  $[M + H]^+$  m/z calcd for  $C_{19}H_{13}IN_3S$ : 441.9875; found: 441.9881. Anal. Calcd for C<sub>19</sub>H<sub>12</sub>IN<sub>3</sub>S: C, 51.71; H, 2.74; N, 9.52; S, 7.26. Found: C, 51.64; H, 2.95; N, 9.49; S, 7.06.

8-(3-Iodo-4-methoxycarbonylphylsulfanyl)-3-phenylbenzo[e]-[1,2,4]triazine (2S-b). 179 mg (36% yield) of 2S-b was obtained as yellow crystals: mp 207-208 °C (MeCN); <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>)  $\delta$  8.79–8.75 (m, 2H), 8.64 (d, J = 1.7 Hz, 1H), 7.98–7.95 (m, 2H), 7.81 (q, J = 8.3 Hz, 1H), 7.62-7.58 (m, 3H), 7.49 (d, J = 8.3 Hz, 1H), 7.62-7.58 (m, 3H), 7.49 (d, J = 8.3 Hz, 1H), 7.62-7.58 (m, 3H), 7.49 (d, J = 8.3 Hz, 1H), 7.62-7.58 (m, 3H), 7.49 (d, J = 8.3 Hz, 1H), 7.62-7.58 (m, 3H), 7.49 (d, J = 8.3 Hz, 1H), 7.62-7.58 (m, 3H), 7.49 (d, J = 8.3 Hz, 1H), 7.62-7.58 (m, 3H), 7.49 (d, J = 8.3 Hz, 1H), 7.62-7.58 (m, 3H), 7.49 (d, J = 8.3 Hz, 1H), 7.62-7.58 (m, 3H), 7.49 (d, J = 8.3 Hz, 1H), 7.62-7.58 (m, 3H), 7.49 (d, J = 8.3 Hz, 1H), 7.62-7.58 (m, 3H), 7.49 (d, J = 8.3 Hz, 1H), 7.62-7.58 (m, 3H), 7.49 (d, J = 8.3 Hz, 1H), 7.62-7.58 (m, 3H), 7.49 (d, J = 8.3 Hz, 1H), 7.62-7.58 (m, 3H), 7.49 (d, J = 8.3 Hz, 1H), 7.62-7.58 (m, 3H), 7.49 (d, J = 8.3 Hz, 1H), 7.62-7.58 (m, 3H), 7.49 (d, J = 8.3 Hz, 1H), 7.62-7.58 (m, 3H), 7.49 (d, J = 8.3 Hz, 1H), 7.62-7.58 (m, 3H), 7.49 (d, J = 8.3 Hz, 1H), 7.62-7.58 (m, 3H), 7.8.1 Hz, 1H), 7.27 (d, J = 0.8 Hz, 1H), 3.94 (s, 3H);  ${}^{13}C{}^{1}H$  NMR (151 MHz, CDCl<sub>3</sub>)  $\delta$  165.2, 160.7, 144.3, 144.0, 142.4, 141.4, 138.4, 135.7, 135.4, 133.7, 132.0, 131.3, 130.2, 129.3, 129.2, 127.7, 104.2, 52.7; IR (KBr) v 1715, 1546, 1503, 1432, 1367, 1277, 1236, 1111, 1018, 794, 765, 704 cm<sup>-1</sup>; HRMS (ESI-TOF)  $[M + H]^+$  m/z calcd for  $C_{21}H_{15}IN_3O_2S$ : 499.9930; found: 499.9933. Anal. Calcd for C<sub>21</sub>H<sub>14</sub>IN<sub>3</sub>O<sub>2</sub>S: C, 50.51; H, 2.83; N, 8.42; S, 6.42. Found C, 50.33; H, 2.68; N, 8.68; S, 6.13.

8-((2-Nitrophenyl)thio)-3-phenylbenzo[e][1,2,4]triazine (3S). Derivative 3S was obtained in 76% yield (272 mg) from 4 and 2-nitrothiphenol<sup>51</sup> as described for 2; yellow crystals: mp 211–212 °C (MeCN);  ${}^{1}$ H NMR (600 MHz, CDCl<sub>3</sub>)  $\delta$  8.77–8.73 (m, 2H), 8.26-8.23 (m, 1H), 8.19 (dd,  $J_1 = 6.4$  Hz,  $J_2 = 3.4$  Hz, 1H), 8.00-7.98 (m, 1H), 7.98 (d, J = 3.1 Hz, 1H), 7.60-7.57 (m, 3H), 7.32-7.28 (m, 2H), 6.94-6.90 (m, 1H); <sup>13</sup>C{<sup>1</sup>H} NMR (151 MHz, CDCl<sub>3</sub>)  $\delta$  160.5, 147.0, 154.4, 142.6, 136.3, 135.8, 135.7, 135.1, 134.6, 133.5, 132.1, 131.3, 130.8, 129.2, 129.1, 126.6, 126.0; IR (KBr) v 1591, 1547, 1508, 1451, 1336, 1304, 1252, 1105, 1018, 839, 783, 140, 699 cm<sup>-1</sup>; HRMS (ESI-TOF)  $[M + Na]^+$  m/z calcd for  $C_{19}H_{12}N_4O_2NaS$ : 383.0579; found: 383.0565. Anal. Calcd for C<sub>19</sub>H<sub>12</sub>N<sub>4</sub>O<sub>2</sub>S: C, 63.32; H, 3.36; N, 15.55; S, 8.90. Found: C, 63.16; H, 3.34; N, 15.42; S, 8.76.

#### Synthesis of methyl-3-iodo-4-mercaptobenzoate (5S-b)

4,4'-Disulfanediylbis(3-iodobenzoic acid) (8). A suspension of NaNO<sub>2</sub> (70.4 mg, 1 mmol) in water (500 µL) was added over 10 min to an ice-cooled solution of methyl 4-amino-2-iodobenzoate<sup>51</sup> (7, 277 mg, 1.0 mmol) in 35% aqueous HCl (167 µL, 0.02 mol) containing ice (2.0 g). After 45 min of stirring, 20% aqueous solution of sodium acetate was added until the pH of the solution was 4-5. Next, potassium methyl xanthate<sup>58</sup> (146 mg, 1 mmol) in water (1 mL) was added. The reaction mixture was slowly warmed to room temperature, and

the resulting mixture was dissolved in CH2Cl2. The organic phase was separated, dried over MgSO4, and evaporated to dryness in vacuo. The residue was refluxed with KOH (3.0 g, 85%, 0.046 mol) in absolute ethanol (10 mL) for 10 h. The solvent was removed, the resulting mixture was dissolved in H<sub>2</sub>O, and small amounts of I<sub>2</sub> were added until a permanent color change occurred. Then, the reaction mixture was acidified with HCl and the crude product precipitated. After filtration, the product was purified by crystallization with MeOH/ H<sub>2</sub>O (9:1) giving 111-156 mg (40-56% yield) of disulfide 8 as a pale solid: mp > 230 °C (MeOH/ $H_2O$ , 9:1); <sup>1</sup>H NMR (600 MHz, DMSO- $d_6$ )  $\delta$  13.27 (s, 1H), 8.33 (s, 1H), 7.96 (dd,  $J_1$  = 8.3 Hz,  $J_2$  = 1.7 Hz, 1H), 7.50 (d, J = 8.3 Hz, 1H); IR (KBr)  $\nu$ 1690, 1580, 1542, 1412, 1369, 1296, 1244, 759 cm<sup>-1</sup>; HRMS (ESI-TOF)  $[M - H]^-$  m/z calcd for  $C_{14}H_{14}I_2O_4S_2$ : 556.7875; found: 556.7883. Anal. Calcd for C<sub>14</sub>H<sub>8</sub>I<sub>2</sub>O<sub>4</sub>S<sub>2</sub>: C, 30.13; H, 1.44. Found: C, 30.32; H, 1.57.

The acid was used in the next step without further purification.

Dimethyl 4,4'-disulfanediylbis(3-iodobenzoate) (9). To a solution of 4,4'-disulfanediylbis(3-iodobenzoic acid) (8, 140 mg, 0.25 mmol) in THF (3 mL), a solution of  $CH_2N_2$  (3 eq., freshly prepared from 77 mg of N-methyl-N-nitrosourea) in diethyl ether was added at 0 °C, and the reaction mixture was stirred for 10 min. The solvent was removed, and the crude product was purified by column chromatography using silica gel (hexane/ethyl acetate = 9:1) giving 103-106 mg (70-72% yield) dimethyl ester 9 as white crystals: mp 180-181 °C (AcOEt); <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>)  $\delta$  8.45 (d, J = 1.7 Hz, 1H), 7.95 (dd,  $J_1 = 8.3$  Hz,  $J_2 = 1.8$  Hz, 1H), 7.47 (d, J = 8.3 Hz, 1H), 3.90 (s, 3H);  $^{13}\text{C}\{^1\text{H}\}$  NMR (151 MHz, CDCl<sub>3</sub>)  $\delta$  165.2, 144.9, 140.5, 130.1, 130.0, 125.6, 94.2, 52.6; IR (KBr) v 1721, 1578, 1544, 1429, 1366, 1286, 1235, 1114, 1014, 832, 758 cm<sup>-1</sup>; HRMS (ESI-TOF)  $[M + H]^+$  m/z calcd for  $C_{16}H_{13}I_2O_4S_2$ : 586.8345; found: 586.8344. Anal. Calcd for C<sub>16</sub>H<sub>12</sub>I<sub>2</sub>O<sub>4</sub>S<sub>2</sub>: C, 32.78; H, 2.06; S, 10.94. Found: C, 32.79; H, 2.18; S, 11.16.

Methyl 3-iodo-4-mercaptobenzoate (5S-b). Dimethyl 4,4'-disulfanediylbis(3-iodobenzoate) (9) was reduced with NaBH<sub>4</sub> in THF at reflux in the presence of MeOH according to a general literature procedure<sup>53</sup> to give 5S-b in essentially quant. yield, which was used for the next step without further purification: <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>)  $\delta$  8.40 (d, J = 1.7 Hz, 1H), 7.82  $(dd, J_1 = 8.2 \text{ Hz}, J_2 = 1.7 \text{ Hz}, 1H), 7.42 (d, J = 8.2 \text{ Hz}, 1H),$ 4.35 (s, 1H), 3.88 (s, 3H); <sup>13</sup>C{<sup>1</sup>H} NMR (151 MHz, CDCl<sub>3</sub>)  $\delta$  165.3, 145.4, 140.7, 129.7, 128.2, 127.6, 96.6, 52.2; HRMS (ESI-TOF)  $[M - H]^-$  m/z calcd for  $C_8H_8IO_2S$ : 292.9133; found: 292.9129.

Preparation of other intermediates is described in the ESI.†

# **Author contributions**

The manuscript was written through contributions of all authors and all authors have given approval to the final version of the manuscript.

# Conflicts of interest

The authors declare no competing financial interest.

# Acknowledgements

Support for this work was provided by the National Science Center (2019/03/X/ST4/02006 and 2017/25/B/ST5/02851). The authors thank Dr. Paweł Tokarz for helpful discussions.

# Notes and references

- 1 T. J. J. Muller and U. H. F. Bunz, Functional Organic Materials, Wiley, 2006.
- 2 I. Ratera and J. Veciana, Playing with organic radicals as building blocks for functional molecular materials, *Chem. Soc. Rev.*, 2012, **41**, 303–349.
- 3 D. A. Wilcox, V. Agarkar, S. Mukherjee and B. W. Boudouris, Stable radical materials for energy applications, *Annu. Rev. Chem. Biomol. Eng.*, 2018, **9**, 83–103.
- 4 Z. X. Chen, Y. Li and F. Huang, Persistent and stable organic radicals: Design, synthesis, and applications, *Chem.*, 2021, 7, 288–332.
- 5 S. Mukherjee and B. W. Boudouris, *Organic Radical Polymers*, Springer International Publishing, 2017.
- 6 L. Ji, J. Shi, J. Wei, T. Yu and W. Huang, Air-stable organic radicals: New-generation materials for flexible electronics?, *Adv. Mater.*, 2020, 32, 1908015.
- 7 J. M. Hudson, T. J. H. Hele and E. W. Evans, Efficient lightemitting diodes from organic radicals with doublet emission, *J. Appl. Phys.*, 2021, **129**, 180901.
- 8 M. Deumal, V. Vela, M. Fumanal, J. Ribas-Arino and J. J. Novoa, Insights into the magnetism and phase transitions of organic radical-based materials, *J. Mater. Chem. C*, 2021, **9**, 10624–10646.
- 9 H. M. Blatter and H. Lukaszewski, A new stable free radical, *Tetrahedron Lett.*, 1968, 9, 2701–2705.
- 10 F. J. M. Rogers, P. L. Norcott and M. L. Coote, Recent advances in the chemistry of benzo[*e*][1,2,4]triazinyl radicals, *Org. Biomol. Chem.*, 2020, **18**, 8255–8277.
- 11 Y. Ji, L. Long and Y. Zheng, Recent advances of stable Blatter radicals: Synthesis, properties and applications, *Mater. Chem. Front.*, 2020, 4, 3433–3443.
- 12 F. A. Neugebauer and I. Umminger, Über 1,4-dihydro-1,2,4-benzotriazinyl-radikale, *Chem. Ber.*, 1980, 113, 1205–1225.
- 13 C. P. Constantinides, P. A. Koutentis, H. Krassos, J. M. Rawson and A. J. Tasiopoulos, Characterization and magnetic properties of a "super stable" radical 1,3-diphenyl-7-trifluoromethyl-1,4-dihydro-1,2,4-benzotriazin-4-yl, J. Org. Chem., 2011, 76, 2798–2806.
- 14 F. A. Neugebauer and G. Rimmler, ENDOR and triple resonance studies of 1,4-dihydro-1,2,4-benzotriazinyl radicals and 1,4-dihydro-1,2,4-benzotriazine radical cations, *Magn. Reson. Chem.*, 1988, **26**, 595–600.

- 15 A. A. Berezin, C. P. Constantinides, S. I. Mirallai, M. Manoli, L. L. Cao, J. M. Rawson and P. A. Koutentis, Synthesis and properties of imidazolo-fused benzotriazinyl radicals, *Org. Biomol. Chem.*, 2013, 11, 6780–6795.
- 16 A. A. Berezin, G. Zissimou, C. P. Constantinides, Y. Beldjoudi, J. M. Rawson and P. A. Koutentis, Route to benzo- and pyrido-fused 1,2,4-triazinyl radicals via N'-(het) aryl-N'-[2-nitro(het)aryl]hydrazides, J. Org. Chem., 2014, 79, 314–327.
- 17 G. Karecla, P. Papagiorgis, N. Panagi, G. A. Zissimou, C. P. Constantinides, P. A. Koutentis, G. Itskos and S. C. Hayes, Emission from the stable Blatter radical, *New J. Chem.*, 2017, 41, 8604–8613.
- 18 Y. Zheng, M.-s. Miao, M. C. Kemei, R. Seshadri and F. Wudl, The pyreno-triazinyl radical magnetic and sensor properties, *Isr. J. Chem.*, 2014, 54, 774–778.
- 19 Y. Zheng, M.-s. Miao, G. Dantelle, N. D. Eisenmenger, G. Wu, I. Yavuz, M. L. Chabinyc, K. N. Houk and F. Wudl, A solid-state effect responsible for an organic quintet state at room temperature and ambient pressure, *Adv. Mater.*, 2015, 27, 1718–1723.
- 20 M. Jasiński, J. Szczytko, D. Pociecha, H. Monobe and P. Kaszyński, Substituent-dependent magnetic behavior of discotic benzo[e][1,2,4]triazinyls, J. Am. Chem. Soc., 2016, 138, 9421–9424.
- 21 M. Jasiński, K. Szymańska, A. Gardias, D. Pociecha, H. Monobe, J. Szczytko and P. Kaszyński, Tuning the magnetic properties of columnar benzo[e][1,2,4]triazin-4-yls with the molecular shape, *ChemPhysChem*, 2019, **20**, 636–644.
- 22 F. Ciccullo, A. Calzolari, K. Bader, P. Neugebauer, N. M. Gallagher, A. Rajca, J. van Slageren and M. B. Casu, Interfacing a potential purely organic molecular quantum bit with a real-life surface, ACS Appl. Mater. Interfaces, 2019, 11, 1571–1578.
- 23 F. Ciccullo, N. M. Gallagher, O. Geladari, T. Chassé, A. Rajca and M. B. Casu, A derivative of the Blatter radical as a potential metal-free magnet for stable thin films and interfaces, *ACS Appl. Mater. Interfaces*, 2016, **8**, 1805–1812.
- 24 J. Z. Low, G. Kladnik, L. L. Patera, S. Sokolov, G. Lovat, E. Kumarasamy, J. Repp, L. M. Campos, D. Cvetko, A. Morgante and L. Venkataraman, The environmentdependent behavior of the Blatter radical at the metalmolecule interface, *Nano Lett.*, 2019, 19, 2543–2548.
- 25 M. Demetriou, A. A. Berezin, P. A. Koutentis and T. Krasia-Christoforou, Benzotriazinyl-mediated controlled radical polymerization of styrene, *Polym. Int.*, 2014, 63, 674–679.
- 26 J. Areephong, K. M. Mattson, N. J. Treat, S. O. Poelma, J. W. Kramer, H. A. Sprafke, A. A. Latimer, J. Read de Alaniz and C. J. Hawker, Triazine-mediated controlled radical polymerization: new unimolecular initiators, *Polym. Chem.*, 2016, 7, 370–374.
- 27 P. Kaszyński, C. P. Constantinides and V. G. Young Jr., The planar Blatter radical: Structural chemistry of 1,4-dihydrobenzo[e][1,2,4]triazin-4-yls, *Angew. Chem., Int. Ed.*, 2016, 55, 11149–11152.

28 P. Bartos, B. Anand, A. Pietrzak and P. Kaszyński, Functional planar Blatter radical through Pschorr-type cyclization, Org. Lett., 2020, 22, 180-184.

**Organic Chemistry Frontiers** 

- 29 A. A. Hande, C. Darrigan, P. Bartos, P. Baylère, A. Pietrzak, P. Kaszyński and A. Chrostowska, UV-photoelectron spectroscopy of stable radicals: the electronic structure of planar Blatter radicals as materials for organic electronics, Phys. Chem. Chem. Phys., 2020, 22, 23637-23644.
- 30 P. Bartos, A. A. Hande, A. Pietrzak, A. Chrostowska and P. Kaszyński, Substituent effects on the electronic structure of the flat Blatter radical: Correlation analysis of experimental and computational data, New J. Chem., 2021, 45, 22876-22887.
- 31 K. I. Shivakumar, D. Pociecha, J. Szczytko, S. Kapuściński, H. Monobe and P. Kaszyński, Photoconductive bent-core liquid crystalline radicals with a paramagnetic polar switchable phase, J. Mater. Chem. C, 2020, 8, 1083-1088.
- 32 P. Bartos, V. G. Young and P. Kaszyński, Ring-fused 1,4dihydro[1,2,4]triazin-4-yls through photocyclization, Org. Lett., 2020, 22, 3835-3840.
- 33 M. Gurry and F. Aldabbagh, A new era for homolytic aromatic substitution: Replacing Bu<sub>3</sub>SnH with efficient lightinduced chain reactions, Org. Biomol. Chem., 2016, 14, 3849-3862.
- 34 A. G. Davies, Tin organometallics, Compr. Organomet. Chem. III, 2007, 3, 809-883.
- 35 A. J. Clark, Compounds of group 14 (Ge, Sn, Pb), in Science of Synthesis, ed. E. J. Thomas, Thieme, Stuttgart, 2003, vol. 5, pp. 205-274.
- 36 C. Chatgilialoglu, C. Ferreri, Y. Landais and V. I. Timokhin, Thirty years of (TMS)<sub>3</sub>SiH: A milestone in radical-based synthetic chemistry, Chem. Rev., 2018, 118, 6516-6572.
- 37 C. Chatgilialoglu and J. Lalevée, Recent applications of the (TMS)<sub>3</sub>SiH radical-based reagent, Molecules, 2012, 17, 527-555.
- 38 W. R. Bowman and J. M. D. Storey, Synthesis using aromatic homolytic substitution - recent advances, Chem. Soc. Rev., 2007, 36, 1803-1822.
- 39 W. R. Bowman, M. O. Cloonan and S. L. Krintel, Synthesis of heterocycles by radical cyclisation, J. Chem. Soc., Perkin Trans. 1, 2001, 2885-2902.
- 40 R. K. Kawade, C. Hu, N. R. Dos Santos, N. Watson, X. Lin, K. Hanson and I. V. Alabugin, Phenalenannulations: Threepoint double annulation reactions that convert benzenes into pyrenes, Angew. Chem., Int. Ed., 2020, 59, 14352-14357.
- 41 J. C. Estevez, M. C. Villaverde, R. J. Estevez and L. Castedo, Tributyltin(IV) hydride mediated free-radical syntheses of dehydrodibenzochromanones, dehydrodibenzocoumaranones and aristolactams, Tetrahedron, 1995, 51, 4075-4082.
- 42 H. Takiguchi, K. Ohmori and K. Suzuki, Synthesis and determination of the absolute configuration of cavicularin by symmetrization/asymmetrization approach, Angew. Chem., Int. Ed., 2013, 52, 10472-10476.
- 43 D. C. Harrowven, M. I. T. Nunn and D. R. Fenwick, [5] Helicenes by tandem radical cyclisation, Tetrahedron Lett., 2002, 43, 7345-7347.

- 44 D. C. Harrowven, I. L. Guy and L. Nanson, Efficient phenanthrene, helicene, and azahelicene syntheses, Angew. Chem., Int. Ed., 2006, 45, 2242-2245.
- 45 D. P. Curran and A. I. Keller, Radical additions of aryl iodides to arenes are facilitated by oxidative rearomatization with dioxygen, J. Am. Chem. Soc., 2006, 128, 13706-13707.
- 46 R. R. Castillo, C. Burgos, J. J. Vaquero and J. Alvarez-Builla, Radical intramolecular arylation of pyridinium salts: A straightforward entry to 7-hydroxypyrido[2,1-a] isoquinolinylium salts, Eur. J. Org. Chem., 2011, 619-628.
- 47 W. R. Bowman, A. J. Fletcher and G. B. S. Potts, Synthesis of heterocycles by radical cyclisation, J. Chem. Soc., Perkin Trans. 1, 2002, 2747-2762.
- 48 S. Saito, K. Matsuo and S. Yamaguchi, Polycyclic  $\pi$ -electron system with boron at its center, J. Am. Chem. Soc., 2012, **134**, 9130-9133.
- 49 S. M. Allin, W. R. S. Barton, W. R. Bowman and T. McInally, Radical cyclisation onto pyrazoles: Synthesis of withasomnine, Tetrahedron Lett., 2002, 43, 4191-4193.
- 50 F. Filace, P. A. Sańchez-Murcia, D. Sucunza, A. Perez-Redondo, J. Álvarez-Buílla, F. Gago and C. Burgos, Silyl assistance in the intramolecular addition of pyridyl radicals onto pyridines and quinolines, Eur. J. Org. Chem., 2016, 1891-1896.
- 51 For details see the ESI.†
- 52 J. Lalut, G. Santoni, D. Karila, C. Lecoutey, A. Davis, F. Nachon, I. Silman, J. Sussman, M. Weik, T. Maurice, P. Dallemagne and C. Rochais, Novel multitarget-directed ligands targeting acetylcholinesterase and σ1 receptors as lead compounds for treatment of Alzheimer's disease: Synthesis, evaluation, and structural characterization of their complexes with acetylcholinesterase, Eur. J. Med. Chem., 2019, 162, 234-248.
- 53 A. Ookawa, S. Yokoyama and K. Soai, Chemoselective reduction of diaryl bisulfides to thiols with sodium borohydride in mixed solvent containing methanol, Synth. Commun., 1986, 16, 819-825.
- 54 T. J. Burkey, M. Majewski and D. Griller, Heats of formation of radicals and molecules by a photoacoustic technique, J. Am. Chem. Soc., 1986, 108, 2218-2221.
- 55 M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, G. Scalmani, V. Barone, B. Mennucci, G. A. Petersson, H. Nakatsuji, M. Caricato, X. Li, H. P. Hratchian, A. F. Izmaylov, J. Bloino, G. Zheng, J. L. Sonnenberg, M. Hada, M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T. Nakajima, Y. Honda, O. Kitao, H. Nakai, T. Vreven, J. A. Montgomery, Jr., J. E. Peralta, F. Ogliaro, M. Bearpark, J. J. Heyd, E. Brothers, K. N. Kudin, V. N. Staroverov, R. Kobayashi, J. Normand, K. Raghavachari, A. Rendell, J. C. Burant, S. S. Iyengar, J. Tomasi, M. Cossi, N. Rega, J. M. Millam, M. Klene, J. E. Knox, J. B. Cross, V. Bakken, C. Adamo, J. Jaramillo, R. Gomperts, R. E. Stratmann, O. Yazyev, A. J. Austin, R. Cammi, C. Pomelli, J. W. Ochterski, R. L. Martin,

K. Morokuma, V. G. Zakrzewski, G. A. Voth, P. Salvador, J. J. Dannenberg, S. Dapprich, A. D. Daniels, O. Farkas, J. B. Foresman, J. V. Ortiz, J. Cioslowski and D. J. Fox, Gaussian 09, Revision A.02, Gaussian, Inc., Wallingford CT, 2009.

Research Article

- 56 M. Cossi, G. Scalmani, N. Rega and V. Barone, New developments in the polarizable continuum model for quantum mechanical and classical calculations on molecules in solution, J. Chem. Phys., 2002, 117, 43-54, and references therein.
- 57 G. R. Fulmer, A. J. M. Miller, N. H. Sherden, H. E. Gottlieb, A. Nudelman, B. M. Stoltz, J. E. Bercaw and K. I. Goldberg, NMR chemical shifts of trace impurities: Common laboratory solvents, organics, and gases in deuterated solvents relevant to the organometallic chemist, Organometallics, 2010, 29, 2176-2179.
- 58 L. Almanqur, I. Vitorica-yrezabal, G. Whitehead, D. J. Lewis and P. O'Brien, Synthesis of nanostructured powders and thin films of iron sulfide from molecular precursors, RSC Adv., 2018, 8, 29096-29103.