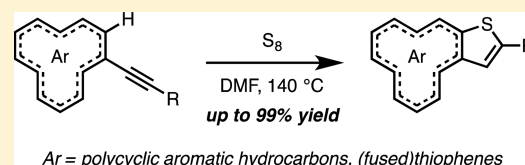


Thiophene-Fused π -Systems from Diarylacetylenes and Elemental SulfurLingkui Meng,^{†,‡} Takao Fujikawa,[‡] Motonobu Kuwayama,^{‡,§} Yasutomo Segawa,^{*,‡,§} and Kenichiro Itami^{*,†,‡,§,||}[†]Integrated Research Consortium on Chemical Sciences, Nagoya University, Chikusa, Nagoya 464-8602, Japan[‡]Graduate School of Science, Nagoya University, Chikusa, Nagoya, Japan[§]JST, ERATO, Itami Molecular Nanocarbon Project, Nagoya University, Chikusa, Nagoya, Japan^{||}Institute of Transformative Bio-Molecules (WPI-ITbM), Nagoya University, Chikusa, Nagoya, Japan

Supporting Information

ABSTRACT: A simple yet effective method for the formation of thiophene-fused π -systems is reported. When arylethynyl-substituted polycyclic arenes were heated in DMF in the presence of elemental sulfur, the corresponding thiophene-fused polycyclic arenes were obtained via cleavage of the *ortho*-C–H bond. Thus, arylethynylated naphthalenes, fluoranthenes, pyrenes, corannulenes, chrysenes, and benzo[*c*]naphtho[2,1-*p*]chrysenes were effectively converted into the corresponding thiophene-fused π -systems. Apart from polycyclic hydrocarbons, thiophene derivatives are also susceptible to this reaction. The practical utility of this reaction is demonstrated by preparations on the decagram scale, one-pot two-step reaction sequences, and multiple thiophene annulations.

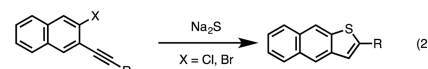
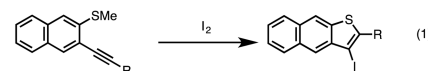


INTRODUCTION

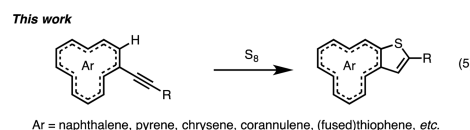
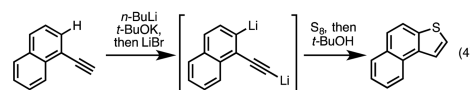
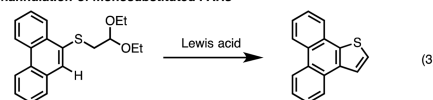
Thiophene-containing π -conjugated molecules are of great interest on account of their diverse applications in materials science. As thiophene-containing π -systems show high charge transport properties, they are widely used in organic field-effect transistors (OFETs), organic light-emitting diodes (OLEDs), and organic photovoltaics (OPVs).¹ Since thiophene-annulation reactions, the so-called thienannulations, can produce various thiophene-fused π -systems, a number of thienannulation reactions have been investigated.^{2,3} In most cases, it is necessary to introduce two functional groups (e.g., halogen, alkynyl, or sulfur-containing groups) on the arenes prior to thienannulation (Figure 1, eqs 1 and 2).² Although several examples exist, in which only one functional group is required, e.g. reactions between diethoxyethylsulfanes and Lewis acids (eq 3),^{3a} 1-ethynynaphthalene and super bases (eq 4),^{3b} and carbonyl-containing arenes and thiourea or Na₂S,^{3c–e} these methods have not been applied to the synthesis of a wide range of thiophene-fused polycyclic aromatic hydrocarbons (PAHs). As the recent C–H functionalization chemistry enables rapid synthesis and derivatization of organic materials,⁴ a simple method for the formation of thiophene rings via C–H functionalization would thus be highly attractive.

Herein, we report a simple thienannulation protocol, in which arylethynyl-substituted PAHs are heated in DMF in the presence of elemental sulfur⁵ to afford the corresponding thiophene-fused PAHs via cleavage of the *ortho*-C–H bond. This reaction requires the presence of only one functional group, i.e., an arylethynyl group on the PAHs.

Thienannulation of disubstituted PAHs



Thienannulation of monosubstituted PAHs



Ar = naphthalene, pyrene, chrysene, corannulene, (fused)thiophene, etc.

Figure 1. Thienannulation reactions.

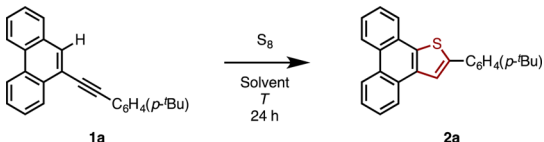
RESULTS AND DISCUSSION

Thienannulation of PAHs with Elemental Sulfur. The discovery of this thienannulation reaction was serendipitous. During the attempted Na₂S-mediated reduction⁶ of 9-arylethynylphenanthrene **1a**, we obtained not only the reduced *cis*-alkene

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but also thienannulated **2a**. As the thienannulation from **1a** to **2a** is redox-neutral and elemental sulfur is generated from Na_2S , we treated **1a** with S_8 in DMF at 140 °C under an atmosphere of argon, which resulted in the formation of **2a** in high yield. Subsequently, we screened different reaction conditions, which are summarized in Table 1. Treatment of **1a** with 1.0 equiv of S_8

Table 1. Thienannulation of 9-(Arylethynyl)phenanthrene **1a^a**



entry	S_8 [equiv]	solvent	T [°C]	yield [%] ^b
1	1.0	DMF	140	92
2	0.50	DMF	140	56
3	0.25	DMF	140	34
4	1.0	DMF	125	68
5	1.0	DMAc	140	80
6	1.0	DMSO	140	21
7	1.0	1,4-dioxane	140	19
8	1.0	mesitylene	140	trace

^aDMF = *N,N*-dimethylformamide, DMAc = *N,N*-dimethylacetamide, DMSO = dimethyl sulfoxide, mesitylene = 1,3,5-trimethylbenzene.

^bIsolated yield.

in DMF at 140 °C was identified as optimal conditions (entry 1), which afforded **2a** in 92% yield. Addition of less S_8 (0.5 or 0.25 equiv; entries 2 and 3), a lower temperature (125 °C, entry 4), or the use of other solvents (DMAc, DMSO, 1,4-dioxane, or mesitylene; entries 5–8) afforded **2a** in lower yields. This reaction can also be carried out at the decagram scale, and it also proceeds under atmospheric conditions (for details, see the Supporting Information).

Substrate Scope. Then, we investigated the scope of this simple S_8 -mediated thienannulation, using mono(arylethynyl)-PAHs (**1b–i**) and di(arylethynyl)PAHs (**1j–m**) under optimized conditions (Table 2). In order to increase the solubility of the starting materials and products, *para*-alkylphenyl groups ($\text{Ar}^1\text{--Ar}^4$) were incorporated. Thus, naphthalene (**1b–e**, **1j–l**), fluoranthene (**1f**), pyrene (**1g,h**), corannulene (**1i**), and chrysene (**1m**) derivatives could be efficiently thienannulated. In particular, pyrene, corannulene, and chrysene derivatives afforded the corresponding products in good to excellent yield. Under the applied reaction conditions, methoxy and bromo groups were tolerated well (**1d,e**). Based on the reactions of **1c,j** to **2c,j**, it can be concluded that the C1-position of the naphthalenes should be more reactive than the C3-position. In the case of di(arylethynyl)naphthalenes, not only symmetrically (**1j,k**) but also unsymmetrically substituted precursors (**1l**) could be used. To improve the reactions involving **1j–m**, 2 or 4 equiv of S_8 were used. The structures of **2e**, **2j**, and **2m** were unambiguously determined by single-crystal X-ray diffraction analysis, and all products were identified by NMR spectroscopy and high-resolution mass spectrometry. Dichloromethane solutions of **2f–2m** exhibited blue fluorescence with low to moderate quantum yields (Φ_F): 0.24 (**2g**), 0.38 (**2h**), 0.23 (**2j**), and 0.28 (**2k**).

One-Pot Two-Step Transformations Including a Thienannulation. This thienannulation could also be included in one-pot two-step transformations. Initially, we attempted a one-

pot Sonogashira coupling/thienannulation sequence (Scheme 1). After the Sonogashira coupling reaction between **4a** and a terminal alkyne in DMF, S_8 was added to the mixture without any intermediary purification step, and the resulting mixture was heated to 140 °C for 48 h. This protocol furnished thienannulated **2a** in 70% yield. We also discovered an S_8 -mediated thienannulation/reduction reaction in the presence of functional groups containing nitrogen. While dimethylamino-substituted arylethynylphenanthrene **1n** was smoothly converted into the corresponding thienophenanthrene (**2n**) in 77% yield, the reaction of a nitro-substituted derivative (**1o**) generated an amino-substituted derivative (**2o**), in which the nitro group was reduced to an amino group. Cyano or methoxycarbonyl groups on the phenyl rings also reacted to afford complex mixtures.

Multiple Thienannulations. The thienannulation described herein can also be used for the synthesis of multiply thienannulated PAHs. Tris(arylethynyl)benzo[*c*]naphtho[2,1-*p*]chrysene (**1p**) and pentakis(arylethynyl)corannulene (**1q**), which are readily available from previously reported compounds,⁷ were subjected to the optimized thienannulation conditions (Scheme 2). Threefold and fivefold thienannulations furnished triple thia[5]helicene **2p** and pentathienocorannulene **2q**, respectively. The solid-state structure of **2p** was confirmed by single-crystal X-ray diffraction analysis (Figure 2a). The C_3 -symmetric structure of **2p** is chiral on account of the presence of three thia[5]helicene moieties, and the enantioenriched fractions could be obtained by chiral HPLC (Figure 2c). The racemization barrier was determined by an analysis of the degradation of the intensity of the CD spectrum. The experimentally obtained value for the racemization barrier of **2p** ($\Delta H^\ddagger = 24.8 \text{ kcal}\cdot\text{mol}^{-1}$, $\Delta S^\ddagger = 0.44 \text{ cal}\cdot\text{mol}^{-1}\cdot\text{K}^{-1}$, and $\Delta G^\ddagger = 24.7 \text{ kcal}\cdot\text{mol}^{-1}$ (298.15 K, 1 atm)) is consistent with the value estimated from DFT calculations ($\Delta G^\ddagger = 25.8 \text{ kcal}\cdot\text{mol}^{-1}$; B3LYP/6-31G(d) level of theory^{8,9}) and slightly lower than that of a previously reported triple[5]helicene¹⁰ ($\Delta G^\ddagger = 31.0 \text{ kcal}\cdot\text{mol}^{-1}$). For pentathienocorannulene **2q**, preliminary results of an X-ray diffraction analysis suggested efficient π – π stacking between two molecules in the crystalline state (Figures 2b,d), which should enable the design of one-dimensional columnar packings.

Thienannulation of Thiophenes. Furthermore, this thienannulation can also be applied to arylethynylthiophenes: treatment of (arylbutadiynyl)phenanthrene (**1r**) with 4 equiv of S_8 afforded a thieno[3,2-*b*]thiophene-fused phenanthrene (**2r**), possibly generated by sequential thienannulations via (arylethynyl)thienophenanthrene (**3r**) as an intermediate. This result indicates that arylethynylthiophenes can be used in this thienannulation, and we therefore attempted the reaction of diarylethynylated derivatives benzo[1,2-*b*:4,5-*b'*]dithiophene (**1s**) and thiophene (**1t**), as shown in Scheme 3. As expected, thienannulated products **2s** and **2t** were obtained in 28% and 22% yields, respectively. Interestingly, (2,6-bis(4-*n*-octylphenyl)-dithieno[3,2-*b*:2',3'-*d'*]thiophene (**2t**) has recently been reported by Adachi and co-workers as a high-performance organic semiconductor that exhibits one of the highest mobilities and on/off ratios.¹¹ While our synthetic route to **2t** involves the same number of reaction steps as the previously reported one (three steps from commercially available compounds), **2t** can be produced more cheaply with our method, as it does not require the use of dithieno[3,2-*b*:2',3'-*d'*]thiophene.

Mechanistic Studies. To gain a better understanding of the mechanism of this thienannulation, the transformation of **1a** into **2a** was investigated in detail. Considering that all starting materials (**1a–t**) were synthesized by palladium-catalyzed

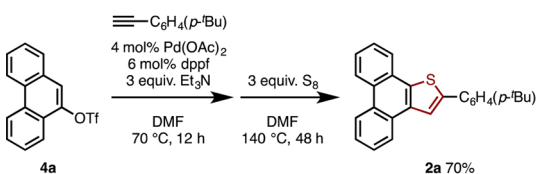
Table 2. Thienannulation of Mono- or Bis(arylethynyl)PAHs

		<p>Ar¹ = <i>p</i>-tolyl Ar² = 4-<i>n</i>-butylphenyl Ar³ = 4-<i>tert</i>-butylphenyl Ar⁴ = 4-<i>n</i>-hexylphenyl</p>	
Substrate	Product, Yield	Substrate	Product, Yield
	2b 56%		2j 25% ^b
			2k 44% ^b
			2l 59% ^c
			2m 88% ^b
	2f 50%		
	2g 50%		
	2h 72%		
	2i 99% ^a		

^a0.5 equiv of S₈, *t* = 24 h. ^b2 equiv of S₈. ^c4 equiv of S₈.

Scheme 1. Application of Thienannulations to Two-Step Transformations

(a) One-pot Sonogashira coupling/thienannulation sequence

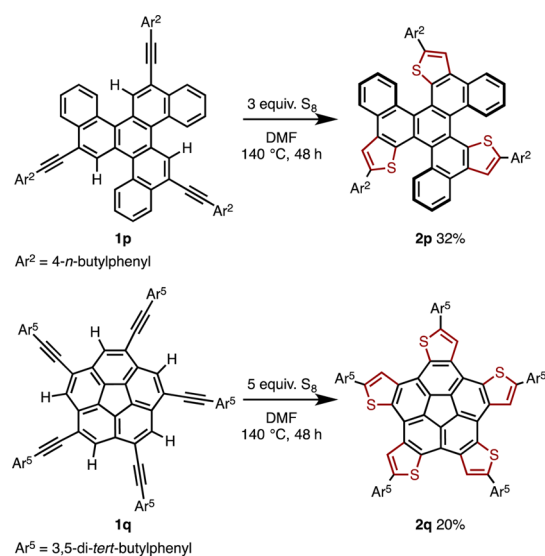


(b) Thienannulation/reduction



Sonogashira coupling reactions, we initially examined the influence of trace amounts of impurities, especially of transition metals such as palladium. However, the yield of **2a** did not change when chemicals (S₈ and DMF) from other suppliers were

Scheme 2. Synthesis of the Multiply Thienannulated PAHs 2p and 2q



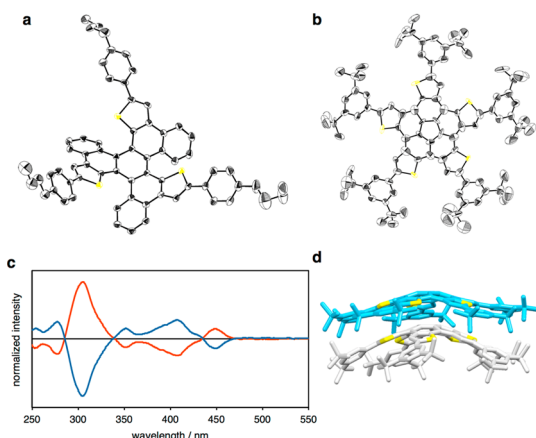
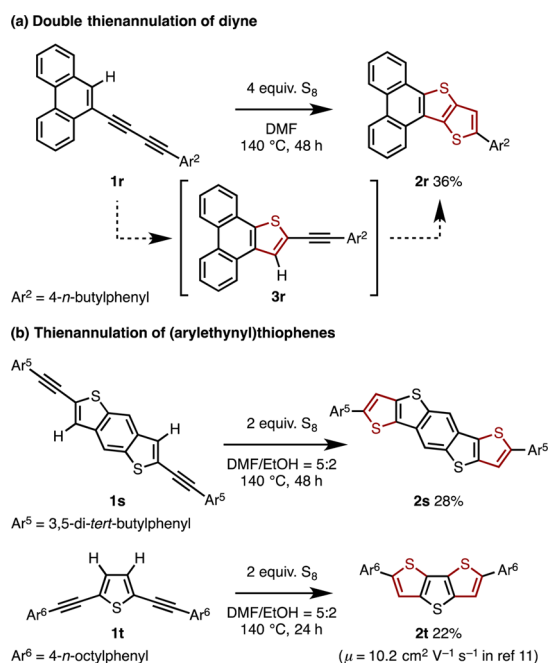


Figure 2. (a,b) ORTEP drawings of **2p** (a) and **2q** (b) with 50% probability; hydrogen atoms and minor parts of disordered atoms are omitted for clarity. (c) CD spectra of the enantiomers of **2p**. (d) Packing structure of **2q**.

Scheme 3. Thienannulation of Thiophenes



used, or when **1a** was synthesized by an alternative “palladium-free” method.¹² An inductively coupled plasma mass spectrometry (ICP-MS) analysis revealed that the contamination levels of **1a**, S_8 , and DMF with palladium were all below 1 ppm. These results suggest that this thienannulation should not be catalyzed by transition metals. Then, a model reaction was carried out under the conditions shown in **Scheme 4**. This reaction, which used 28 equiv of D_2O , afforded **2a-D**, in which the β -position of the thiophene moiety was completely deuterated. The presence of radical scavengers such as TEMPO (2,2,6,6-tetramethylpiperidine 1-oxyl) or galvinoxyl did not significantly affect the yield of **2a**, which indicates that a radical mechanism should not be operative.

Based on the substrate scope and the results of the mechanistic studies, we propose a possible reaction mechanism for the formation of the thiophene rings during this thienannulation (**Figure 3**). Initially, elemental sulfur (S_n) should react electro-

Scheme 4. Mechanistic Studies on the Thienannulation of **1a**

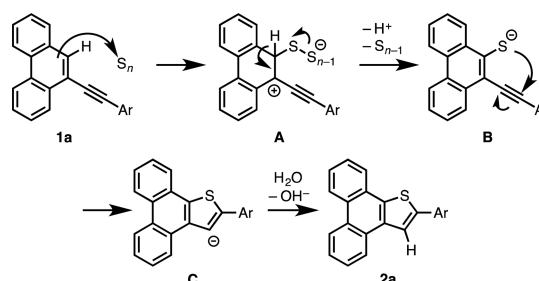
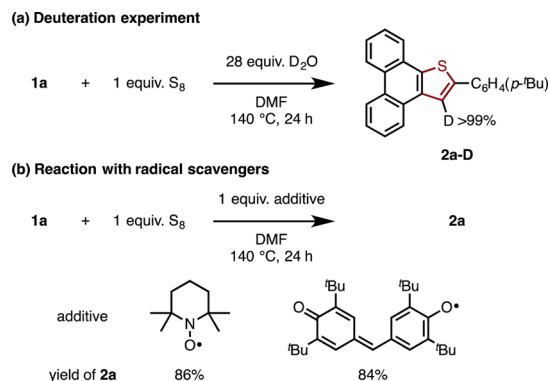


Figure 3. Proposed reaction mechanism for the formation of **2a**.

position of phenanthrene is doubly stabilized by benzylic and propargylic conjugations. The elimination of elemental sulfur (S_{n-1}) and H^+ from **A** would then produce **B**, which is a common intermediate in thienannulation reactions (cf. eq 2).² A subsequent nucleophilic attack of the sulfur anion on the alkyne would generate carboanion **C**, which would be rapidly protonated by residual H_2O in DMF to afford **2a**.

CONCLUSION

In conclusion, we have developed a simple yet effective and versatile method for the formation of thiophene-fused π -systems. Upon heating arylethynyl-substituted polycyclic arenes in DMF in the presence of elemental sulfur, the corresponding thiophene-fused polycyclic arenes are obtained via cleavage of a C–H bond. The synthetic utility of this reaction manifests in the facile generation of thiophene-fused naphthalene, fluoranthene, pyrene, corannulene, and chrysene derivatives. Not only polycyclic hydrocarbons but also thiophene derivatives are susceptible to this reaction, which greatly increases the utility of the reaction. The practical utility of this reaction is reflected in the fact that it can be carried out on a decagram scale, in one-pot two-step reaction sequences, and that multiple thienannulations are possible.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/jacs.6b06486.

Experimental procedures, characterization data for all new compounds (PDF)

Crystallographic data (CIF, CIF, CIF, CIF, CIF, CIF, CIF, CIF)

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Notes

The authors declare no competing financial interest.

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■ REFERENCES

- (1) (a) Perepichka, I. F.; Perepichka, D. F. *Handbook of Thiophene-based Materials: Applications in Organic Electronics and Photonics*; Wiley-VCH, Weinheim, 2009. (b) Anthony, J. E. *Chem. Rev.* **2006**, *106*, 5028. (c) Allard, S.; Forster, M.; Souharce, B.; Thiem, H.; Scherf, U. *Angew. Chem., Int. Ed.* **2008**, *47*, 4070. (d) Takimiya, K.; Shinamura, S.; Osaka, I.; Miyazaki, E. *Adv. Mater.* **2011**, *23*, 4347. (e) Jiang, W.; Li, Y.; Wang, Z. *Chem. Soc. Rev.* **2013**, *42*, 6113. (f) Yassar, A. *Polym. Sci., Ser. C* **2014**, *56*, 4. (g) Osaka, I.; Shinamura, S.; Abe, T.; Takimiya, K. *J. Mater. Chem. C* **2013**, *1*, 1297. (h) Cinar, M. E.; Ozturk, T. *Chem. Rev.* **2015**, *115*, 3036.
- (2) (a) Zhang, T. Y.; O'Toole, J.; Proctor, C. S. *Sulfur Rep.* **1999**, *22*, 1. (b) Takimiya, K.; Nakano, M.; Kang, M. J.; Miyazaki, E.; Osaka, I. *Eur. J. Org. Chem.* **2013**, *2013*, 217.
- (3) (a) Iwao, M.; Lee, M. L.; Castle, R. N. *J. Heterocycl. Chem.* **1980**, *17*, 1259. (b) Hanekamp, J. C.; Klusener, P. A. A.; Brandsma, L. *Synth. Commun.* **1989**, *19*, 2691. (c) Shvartsberg, M. S.; Ivanchikova, I. D. *ARKIVOC* **2003**, 87. (d) Fukutomi, Y.; Nakano, M.; Hu, J.-Y.; Osaka, I.; Takimiya, K. *J. Am. Chem. Soc.* **2013**, *135*, 11445. (e) Baranov, D. S.; Gold, B.; Vasilevsky, S. F.; Alabugin, I. V. *J. Org. Chem.* **2013**, *78*, 2074.
- (4) (a) Wencel-Delord, J.; Glorius, F. *Nat. Chem.* **2013**, *5*, 369. (b) Segawa, Y.; Maekawa, T.; Itami, K. *Angew. Chem., Int. Ed.* **2015**, *54*, 66. (c) Kuninobu, Y.; Sueki, S. *Synthesis* **2015**, *47*, 3823.
- (5) The formation of thiophene rings by reaction between alkynes and sulfur reagents such as S₈ and H₂S is well-known. For representative reports, see: (a) Bohlmann, F.; Burkhart, F. T.; Zero, C. *Naturally Occurring Acetylenes*; Academic: London, 1973. (b) Choi, K. S.; Akiyama, I.; Hoshino, M.; Nakayama, J. *Bull. Chem. Soc. Jpn.* **1993**, *66*, 623.
- (6) Chen, Z.; Luo, M.; Wen, Y.; Luo, G.; Liu, L. *Org. Lett.* **2014**, *16*, 3020.
- (7) (a) Hagen, S.; Bratcher, M. S.; Erickson, M. S.; Zimmermann, G.; Scott, L. T. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 406. (b) Seiders, T. J.; Elliott, E. L.; Grube, G. H.; Siegel, J. S. *J. Am. Chem. Soc.* **1999**, *121*, 7804.
- (8) Frisch, M. J. et al. *Gaussian 09*, revision C.01; Gaussian, Inc.: Wallingford, CT, 2010. The complete reference is given in the [Supporting Information](#).
- (9) (a) Becke, A. D. *J. Chem. Phys.* **1993**, *98*, 5648. (b) Lee, C.; Yang, W.; Parr, R. G. *Phys. Rev. B: Condens. Matter Mater. Phys.* **1988**, *37*, 785.
- (10) Barnett, L.; Ho, D. M.; Baldrige, K. K.; Pascal, R. A. *J. Am. Chem. Soc.* **1999**, *121*, 727.
- (11) Yang, Y. S.; Yasuda, T.; Kakizoe, H.; Mieno, H.; Kino, H.; Tateyama, Y.; Adachi, C. *Chem. Commun.* **2013**, *49*, 6483.
- (12) Toyota, S.; Azami, R.; Iwanaga, T.; Matsuo, D.; Orita, A.; Otera, J. *Bull. Chem. Soc. Jpn.* **2009**, *82*, 1287.
- (13) Examples of the electrophilic addition of S₈ to arenes: (a) Pichon, C.; Scott, A. I. *Tetrahedron Lett.* **1996**, *37*, 2891. (b) Filip, S. V.; Silberg, I. A.; Surducun, E.; Vlassa, M.; Surducun, V. *Synth. Commun.* **1998**, *28*, 337. (c) Lhoták, P.; Šmejkal, T.; Stibor, I.; Havlíček, J.; Tkadlecová, M.;

Petříčková, H. *Tetrahedron Lett.* **2003**, *44*, 8093. (d) Ahmed, H. H.; Elmegeed, G. A.; El-Sayed, E.-S. M.; Abd-Elhalim, M. M.; Shousha, W. G.; Shafic, R. W. *Eur. J. Med. Chem.* **2010**, *45*, 5452.