Tetrahedron 72 (2016) 2527–2534

Contents lists available at ScienceDirect

Tetrahedron

journal homepage: www.elsevier.com/locate/tet

Suzuki–Miyaura synthesis of *m*-terphenyl thioethers and their facilitated oxidation caused by through-space π···S···π interaction

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ARTICLE INFO

Article history:
Received 14 December 2015
Received in revised form 10 March 2016
Accepted 11 March 2016
Available online 29 March 2016

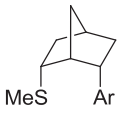
Keywords:
Regioselectivity
Unsymmetrical substitution
Electrochemistry

ABSTRACT

S-tert-Butyl *m*-terphenyl thioethers have been efficiently synthesized by Suzuki–Miyaura coupling reactions with 2,6-dibromo-*S-tert*-butylthio benzene. Selective monocoupling could be achieved with *o*-substituted boronic acids. This facilitated the synthesis of unsymmetrical *S-tert*-butyl *m*-terphenyl thioethers and bis(*S-tert*-butyl *m*-terphenyl thioether)s. The study of their electrochemistry showed facilitated oxidations resulting from through-space π···S···π interactions.

1. Introduction

Electrochemical oxidation potentials, determined by cyclic voltammetry, and ionization energies, determined by photoelectron spectroscopy, for thioethers are lowered when an aromatic ring is juxtaposed to the sulfur as in **1**.[1] This effect was ascribed to through-space S···π interaction in which an antibonding interaction between the p-type sulfur lone pair with the neighboring aromatic system becomes a new kind of three-electron S···π bond in the radical cation as shown by theoretical calculations and the absorption spectrum of the radical cation prepared under stable ion conditions.[2] To determine whether through-space S···π interactions can be extended to through-space π···S···π aromatic interactions *m*-terphenyl thioethers **2** were prepared.[3] The electrochemical oxidation potentials of **2** and ionization energy of **2b**, determined by photoelectron spectroscopy were indeed lowered, but the basis for these effects was not clearly determined.[4] Of particular concern was the conformation of the radical cation. Stabilization of the radical cation of **2** by one or both aromatic rings by



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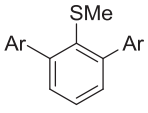
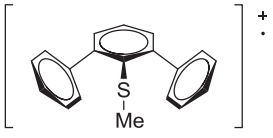


2a, Ar = 2-$MeOC_6H_4$
b, Ar = Ph
c, Ar = 4-$MeOC_6H_4$
d, Ar = 3,5-$(MeO)_2C_6H_3$



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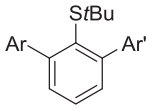
http://dx.doi.org/10.1016/j.tet.2016.03.040
0040-4020/

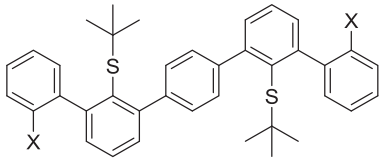
through-space S···π interaction involves conformation **3** in which the C–S–Me and flanking aromatic rings are perpendicular to the central phenyl ring. While this conformation is preferred in the *m*-terphenyl derivative **2** itself, the barrier for rotation about the aryl C–S bond is low though the barrier for rotation about the bond linking the central phenyl ring to *m*-aryl substituents in **2a** is high ($\Delta G^{\neq}$=66.9 kJ/mol) as determined by variable temperature ^{1}H NMR spectroscopic studies.[3] Since the difference in energy between the planar conformer (in which the C–S–Me moiety and central phenyl ring are coplanar) in the radical cation of thioanisole is calculated to be about 18 kcal/mol, more stable than the perpendicular conformer (in which the C–S–Me moiety is perpendicular to the central phenyl ring) owing to resonance delocalization,[5] formation of the resonance stabilized planar radical cation is a plausible alternative to the perpendicular radical cation despite steric effects, and initial studies on the radical cation of **2b**, under stable ion conditions, supported this ambiguity. To prevent planarization in **3**, i.e., the C–S–Me moiety and central phenyl ring are coplanar, the more sterically demanding *tert*-butyl-thioethers **4** were desired.

This paper reports the synthesis, characterization and electrochemistry of *tert*-butyl thioethers **4**.



4a, Ar = Ar' = Ph
b, Ar = Ar' = 3,5-$(MeO)_2C_6H_3$
c, Ar = Ar' = 4-ClC_6H_4
d, Ar = Ar' = 3-$O_2NC_6H_4$
e, Ar = Ph, Ar' = 2-$MeOC_6H_4$
f, Ar = Ph, Ar' = 2-MeC_6H_4

Furthermore, the synthetic methodology developed enabled the facile synthesis of extended systems **5** in which through-space π···S···π···S···π interactions can be assessed.

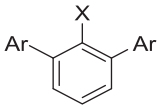


5a, X = MeO
b, X = Me

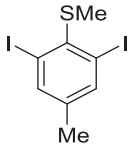
2. Results and discussion

2.1. Synthesis

Previously, we reported[3] that the most useful procedure for synthesizing *m*-terphenylmethylthioethers **2** was based on the Saednya and Hart procedure[6] in which the presumed intermediary Grignard reagent **6a** is treated with $MeSSO_2Me$. Consequently, lithio-derivative **6b**, prepared from the corresponding iodide **6c**, was treated with *t*-BuSSO_2*t*-Bu[7] or *t*-BuSSO_2*p*-Tol.[8] In neither case was **4a** formed but rather **6d**, presumably resulting from *t*-Bu elimination rather than nucleophilic substitution on sulfur. Reaction of aniline **6e** with nitrous acid and *t*-BuSS*t*-Bu also produced mainly **6d** with a small amount of **4a** in contrast to the 42% yield of **2b** obtained on performing this reaction with MeSSMe[3] instead of *t*-BuSS*t*-Bu.



6a, X = MgBr, Ar = Ph
b, X = Li, Ar = Ph
c, X = I, Ar = Ph
d, X = H, Ar = Ph
e, X = NH_2, Ar = Ph
f, X = OMe, Ar = 2-$MeOC_6H_4$



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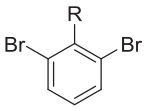
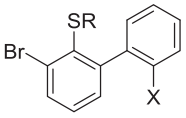
Previously, Suzuki–Miyaura[9] coupling of **7** with phenylboronic acid afforded 2,6-diphenyl-4-methylthioanisole in 27% yield.[3] Therefore, dibromide **8a**,[10] to be used in Suzuki–Miyaura couplings, was synthesized. Diazotization[11] of aniline **8c** followed by reaction with potassium ethyl xanthate and hydrolysis with KOH[12] provided thiol **8b** in an overall yield of 72%. Thiol **8b** proved susceptible to oxidative dimerization; therefore, the crude product was treated with *tert*-



8a, R = *t*-BuS
b, R = SH
c, R = NH_2
d, R = SMe
e, R = OMe



9a, R = *t*-Bu, X = OMe
b, R = Me, X = OMe
c, R = *t*-Bu, X = Me

butyl alcohol, glacial AcOH and Ac_2O followed by 70% aqueous $HClO_4$[13] to provide *tert*-butylsulfide **8a** in very high yield. Under conditions in which **7** was converted to 2,6-diphenyl-4-methylthioanisole in 27% yield, **8a** afforded a mixture of unreacted **8a**, mono- and di-substitution products. However, with excess phenylboronic acid the disubstituted product was predominantly formed. By optimizing conditions, **4a** could be formed in 81% yield without any monosubstituted byproduct. Other examples using this coupling procedure are listed in Table 1.

Table 1
Suzuki–Miyaura coupling[a] of **8a** with arylboronic acids $ArB(OH)_2$

Ar	Product	Yield (%)
Ph	**4a**	81
3,5-$(MeO)_2C_6H_3$	**4b**	61
4-ClC_6H_4	**4c**	72
4-$O_2NC_6H_4$	**4d**	77

[a] $Pd(PPh_3)_4$, LiCl, 2 M aqueous Na_2CO_3, 1,4-dioxane.

Selective Suzuki–Miyaura couplings with di- and polyhalides have been reported.[14] In this context selective monocoupling of **8a**, under our conditions by varying the equivalents of arylboronic acid could not be achieved in good yield with the arylboronic acids shown in Table 1. However, *o*-$MeOC_6H_4B(OH)_2$, under the conditions used for the reactions summarized in Table 1, gave only monocoupled product **9a** in 69% yield and none of the di-coupled product. Nevertheless mono-coupled product **9a** underwent coupling with phenylboronic acid to produce unsymmetrically coupled product **4e** in 70% yield. Steric effects[15] sometimes play a role in Suzuki–Miyaura couplings especially with di-*o*-substituted phenylboronic acids[16] and a manifestation of steric effects is suggested to account for mono-coupling with *o*-$MeOC_6H_4B(OH)_2$ in our case. Similarly selective coupling of **8a** with *o*-tolylboronic acid gave **9c** in

70% yield; although with higher concentrations of *o*-tolylboronic acid some bis-coupled product is also formed. Coupling of **9c** with phenylboronic acid produced **4f** in 95% yield.

With this improved Suzuki–Miyaura coupling condition in hand such couplings with the known[17] *S*-methyl dibromide **8d** were explored. Some examples of such couplings are listed in Table 2. In addition reaction of **8d** with *o*-$MeOC_6H_4B(OH)_2$ proved to be selective but not as selective as that with **8a**. With **8d**, **9b** was obtained in 79% yield with the balance of the material bis-coupled product. Notably anisole derivative **8e** did not undergo selective mono-coupling and the bis-coupled product **6f** was obtained in 41% yield.[18] This is an expected steric effect since it is known that the barrier for rotation about the C–C bond connecting the central ring to the lateral rings in **6f** is lower than that in **2a** (the van der Waals radius for sulfur is larger than that for oxygen).[19] Calculations on this barrier for **2a** show that the barrier height is determined by steric interaction between the *ortho* hydrogen of the rotating lateral ring and sulfur.[3] This raises an interesting question about the steric effect in the Suzuki–Miyaura coupling. That is, would the difference in steric size between the Me group in **8d** and the *t*-Bu group in **8a** affect their relative rates of reaction. Consequently a 1:1 mixture of **8a** and **8d** were treated with 1 equiv of *o*-$MeOC_6H_4B(OH)_2$ under our coupling conditions. ^1H NMR spectroscopic analysis of the resulting mixture indicated that **8d** was approximately six times more reactive than **8a** and produced some bis-coupled product whereas no bis-coupled product from **8a** is formed. Thus the Suzuki–Miyaura coupling reaction senses the difference in steric size of O versus S and the difference in alkyl groups (Me vs *t*-Bu) attached to sulfur.

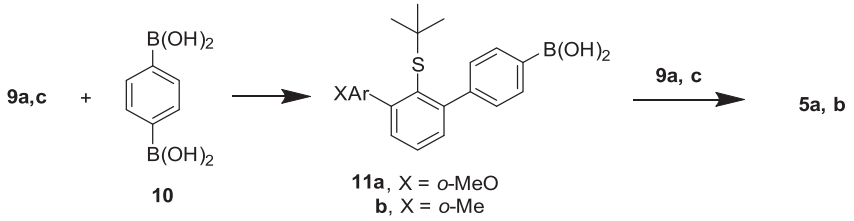
Table 2
Suzuki–Miyaura coupling[a] of **8d** with arylboronic acids $ArB(OH)_2$

Ar	Product	Yield (%)
Ph	**2b**	99
4-$(MeO)C_6H_4$	**2c**	53
3,5-$(MeO)_2C_6H_3$	**2d**	53

[a] $Pd(PPh_3)_4$, LiCl, 2 M aqueous Na_2CO_3, 1,4-dioxane.

The selective mono-coupling of **8a** with *o*-$MeOC_6H_4B(OH)_2$ and *o*-$MeC_6H_4B(OH)_2$ followed by coupling with phenylboronic acid to obtain unsymmetrical **4e** and **4f**, respectively, opened up the possibility of synthesizing more complex systems with multiple alternating thioether and aromatic π-systems arranged for through-space interaction. Morgan and co-workers[20] conjectured that alternating S···π-systems may be conduits for electron-transfer based on finding this structural motif in redox proteins. To our knowledge this conjecture has never been tested experimentally. Consequently, the syntheses shown in Scheme 1 were carried out. Compounds **5a** and **b** were both obtained in 21% overall yield on coupling **9a** and **c**, respectively, with **11a** and **b**. Both **11a** and **b** were obtained as reaction intermediates by coupling **9a** and **c**, respectively, with diboronic acid **10**.

An X-ray crystal structure study of **5a** showed its molecular structure as that in Fig. 1. Not only does the structure study unequivocally validate the assigned structure but it shows that the molecule adopts the desired conformation which allows for through space S···π interaction involving three aromatic rings and two thioethers, that is, 2-$MeOC_6H_4$···S···C_6H_4···S···2-$MeOC_6H_4$, S···π alternation and presumably, the geometry in **5b** is similar. The



Scheme 1. Synthesis of **5a** and **b**.

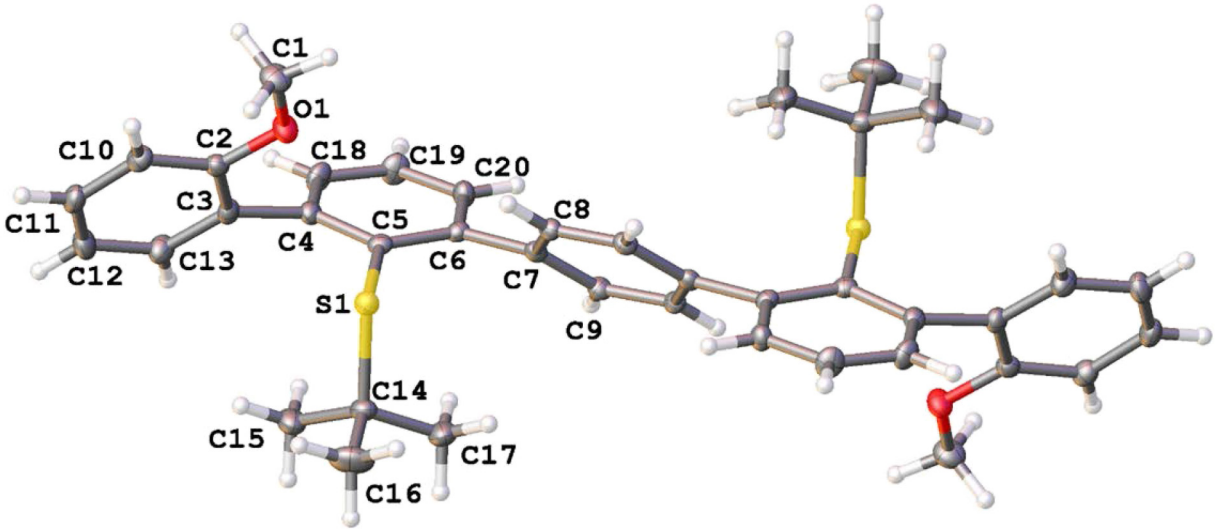


Fig. 1. The molecular structure of **5a**. One-half of the molecule is crystallographically unique and labels are shown for those atoms. A crystallographic inversion center at the center of the C7–C8–C9 containing aromatic ring generates the remainder of the molecule. Displacement ellipsoids are shown at the 50% probability level.

redox chemistry of these two compounds is reported in the following section.

As illustrated above, Suzuki–Miyaura couplings proceeded well in the presence of a thioether moiety. Other examples of such couplings illustrating the tolerance of thioether groups have been reported before.[9a,21] Thus simple aryl methylthioethers are neither substrates in the Suzuki–Miyaura reaction (although it is known[22] that heteroaromatic methylthioethers undergo Suzuki–Miyaura coupling with replacement of the MeS group, as well as other activated thioether moieties, in the presence of 1 equiv of copper (I) 2-thiophenecarboxylate and using Pd_2dba as catalyst gives the best results) nor do they act as catalyst poisons.

As pointed out above thioethers do not poison Suzuki–Miyaura catalysts. Indeed ligands used in these reactions are often appended with thioethers.[23] Although thioethers may poison heterogeneous catalysts they do not poison homogeneous catalysts. Rather, such groups are often designed into the ligand which coordinates the metal to act as a semi-labile site, that is, the thioether coordinates the metal but readily dissociates to generate an open site on the metal.

2.2. Electrochemistry

The redox chemistry of *tert*-butyl thioethers **4a**–**e** was studied in acetonitrile using cyclic voltammetry. Each compound undergoes irreversible oxidation with the peak potentials listed in Table 3. The electrochemical oxidation potential of **4a** (1.172 V) is remarkably less anodic than that reported for *t*-BuSPh (1.40 V)[24] demonstrating through-space π···S···π interaction in **4a**. This interaction is further supported by the substituent effects. That is, electron-donating substituents on the *m*-phenyl rings lower the oxidation potential; whereas, electron-withdrawing substituents raise them resulting in the series of less anodic peak potentials: **4b**<**4e**<**4a**∼**4f**<**4c**<**4d**. It is also remarkable that the oxidation potential of **4a** (1.172 V) is more anodic than that of **2b** (1.12 V)[2] by only 50 mV; whereas, those for PhSMe (1.12,[25] 1.21[24] V) and *t*-BuSPh(1.40 V)[24] differ by over 200 mV. This further demonstrates the importance of through-space π···S···π interaction in **4a**. The issues of planar versus perpendicular radical cation in **2a** and the nature of the bonding in $\mathbf{2}^{\bullet+}$ and $\mathbf{4}^{\bullet+}$ are addressed in another paper[26] in which these species were generated under stable ion conditions and their structures analyzed spectroscopically and computationally.

Table 3
Oxidation potentials for *tert*-butyl thioethers **4a**–**f**

Compound	E_p[a]
4a	1.172
4b	0.815
4c	1.191
4d	1.30
4e	1.128
4f	1.182

[a] CH_3CN, 0.1 M $NaClO_4$, reference electrode: 0.1 M $AgNO_3$ in CH_3CN, scan rate 0.1 V/s, Pt electrode.

To determine if through-space interaction in **4a** can be extended further to through-space π···S···π···S···π, the electrochemistry of **5a** and **b** was studied using cyclic voltammetry and differential pulse voltammetry. Table 4 tabulates the electrochemical results and the corresponding results for **4e** and **f**. Perusal of this table reveals that for **5a** compared with **4e** and **5b** compared with **4f** are the same within experimental error. The differential pulse voltammetry shows similar trends in the ease of oxidation as the cyclic voltammetry though potentials consistently less anodic are observed. This is likely due to less interference from product accumulation on the electrode. Consequently, through-space π···S···π···S···π does not occur.

Table 4
Oxidation potentials[a] for extended S···Ar systems **5a** and **b** and their models **4e** and **f**

Compd	CV	DPV
5a	1.144	1.076
4e	1.128	1.052
5b	1.180	1.096
4f	1.182	1.083

[a] Pt electrode, CH_3CN, 0.1 M $NaClO_4$, reference electrode: 0.1 M $AgNO_3$ in CH_3CN, scan rate 0.1 V/s.

3. Conclusions

In conclusion, Suzuki–Miyaura reactions enabled the efficient synthesis of *m*-terphenylmethyl and *tert*-butyl thioethers. In addition, highly selective monocouplings of sterically hindered *o*-methoxy and *o*-methylphenylboronic acids with *S*-*t*-Bu dibromide **8a** were found. This selective monocoupling enabled the syntheses of unsymmetrical *m*-terphenyl thioethers as well as extended systems **5a** and **b**. Electrochemical studies provided evidence for through-space π···S···π interaction in **4** and **5** but not extended through-space π···S···π···S···π interaction in **5**. Future studies are planned to further explore the possibility of extended through-space π···S···π···S···π interaction by tuning the orbital energies of the central π system (with substituents or fused aromatic rings) and alternative geometries decreasing the distance and orientation between the interacting moieties.

4. Experimental

4.1. General

Proton and carbon-13 nuclear magnetic resonance (NMR) spectra were recorded on Bruker DRX-500 and Bruker DRX-600 spectrometers. Chemical shifts are reported in parts per million using residual NMR solvent as reference. All coupling constants (*J* values) are reported in Hertz (Hz). Infrared spectra were recorded on a Nicolet Impact-410 spectrophotometer. All melting points are uncorrected and were recorded on Thomas Hoover Uni-Melt apparatus. All mass spectra were done at the University of Arizona Mass Spectrometry Facility using a JEOL HX110A high resolution mass spectrometer.

Thin layer chromatography (TLC) was carried out on EMD Chemical, Inc. TLC Plastic Sheets Si 60 F_{254}. Column chromatography was performed using Dynamic Adsorbents 32–63 micron flash silica gel. All reagents were purchased from Aldrich Chemical Co. and were used without further purification unless otherwise stated. *tert*-Butyl alcohol was purchased from J. T. Baker Inc., 200 proof ethanol was purchased from Decon Laboratories, Inc. and all other solvents were purchased from EMD Chemical, Inc. Tetrahydrofuran (THF) was purified and dried by distillation from sodium and benzophenone. All reactions were carried under argon unless otherwise indicated.

4.2. Syntheses

*4.2.1. 2,6-Dibromobenzenethiol (**8b**).* This compound was prepared by modified literature procedures.[11,12] A solution of $NaNO_2$ (0.205 g, 2.97 mmol) in H_2O (1.5 mL) was added dropwise to a suspension of

2,6-dibromoaniline, **7c**, (678 mg, 2.70 mmol) in concentrated aqueous HCl (2.6 mL, 12 M) at 0 °C. The mixture was stirred at 0 °C for 90 min. Additional $NaNO_2$ (55 mg, 0.797 mmol) was added. The mixture was stirred for an additional 45 min at 0 °C and then the resulting cold solution was added dropwise to a stirred solution of potassium ethyl xanthate (525 mg, 3.27 mmol) in H_2O (0.65 mL) at 45 °C through a glass pipet with a plug of glass wool. The reaction mixture was stirred for 30 min at this temperature and then allowed to cool to room temperature. The reaction mixture was extracted with diethyl ether (3×50 mL). The combined organic extracts were washed with 1 M NaOH solution (100 mL), water (3×50 mL), brine (50 mL), dried over anhyd $MgSO_4$, filtered and evaporated under reduced pressure. The resulting crude product was dissolved in ethanol (8 mL) and heated to reflux. Potassium hydroxide pellets (654 mg, 11.6 mmol) were added and refluxing continued overnight. After cooling to room temperature, the ethanol was evaporated under reduced pressure. The residue was dissolved in water and washed with diethyl ether (100 mL). The aqueous layer was acidified with 1 M HCl to pH 2 and extracted with diethyl ether (3×50 mL). The organic extracts were washed with water (50 mL), brine (50 mL), dried over anhyd $MgSO_4$, filtered and evaporated under reduced pressure. The residue was purified by column chromatography on silica gel using hexanes as eluent to give **8b** as a slightly yellow solid (518 mg, 72%). This compound always contains trace amounts of oxidized disulfide compound. Therefore, compound **8b** was used in next step without further purification. ^{1}H NMR (500 MHz, CD_2Cl_2) δ 5.04 (s, 1H), 6.87 (t, J=7.0 Hz, 1H), 7.52 (d, J=7.0 Hz, 2H); IR (KBr) 1400, 1421, 1543, 2553 (SH), 3064, 3458 cm^{-1}.

*4.2.2. tert-Butyl(2,6-dibromophenyl)sulfane **(8a)**.* This compound was prepared using modified procedure reported by Diéguez et al.[13] A solution of compound **8b** (180 mg, 0.671 mmol), *tert*-butyl alcohol (0.332 mL, 3.49 mmol), AcOH (2.7 mL), and acetic anhydride (0.39 mL) was stirred at 0 °C for 20 min under argon, and then 70% aqueous $HClO_4$ (0.11 mL) was added. The solution was allowed to warm to room temperature and stirred overnight. After *tert*-butyl alcohol was removed under reduced pressure, water (50 mL) was added to the solution. The solution was extracted with CH_2Cl_2 (3×50 mL). The combined organic layer was washed with 1 M NaOH (50 mL), brine (50 mL), dried with anhyd $MgSO_4$, filtered and evaporated under reduced pressure. The resulting crude product was purified by column chromatography on silica gel using hexanes as eluent to give **8a** as a slightly yellow oil (219 mg, quantitative yield): ^{1}H NMR (600 MHz, CD_2Cl_2) δ 1.41 (s, 9H), 7.02 (t, J=9.0 Hz, 1H), 7.68 (d, J=9.0 Hz, 2H); ^{13}C NMR (150 MHz, CD_2Cl_2) δ 32.2, 52.7, 131.63, 133.4, 135.5, 136.4; IR (neat) 1413, 1542, 2959 cm^{-1}; HRMS (EI) *m/z*: [M]$^+$ calcd for $C_{10}H_{12}Br_2S$, 321.9026; found: 321.9013.

*4.2.3. [1,1′:3′,1″-Terphenyl]-2′-yl(tert-butyl)sulfane **(4a)**.* To a solution of **8a** (400 mg, 1.23 mmol) in distilled 1,4-dioxane (2.0 mL) under argon, were added a 2 M aqueous solution of Na_2CO_3 (2.5 mL, 2.46 mmol), LiCl (167 mg, 3.93 mmol), phenylboronic acid (630 mg, 4.92 mmol), and $Pd(PPh_3)_4$ (142 mg, 0.123 mmol). The mixture was stirred for 24 h at reflux. H_2O (50 mL) was added to the resulting suspension and extracted with EtOAc (50 mL). The organic layer was washed successively with 1 M NaOH (50 mL), brine (50 mL), and H_2O (50 mL), dried with $MgSO_4$, filtered and evaporated under reduced pressure. The crude product was purified by column chromatography on silica gel using 1:9 chloroform/hexanes as eluent to give **4a** as a white solid (315 mg, 81% yield). The product was further purified by recrystallization twice using diethyl ether:hexanes (1:1): mp 99–100 °C; ^{1}H NMR (600 MHz, CD_2Cl_2) δ 0.66 (s, 9H), 7.32 (tt, J=7.8, 1.4 Hz, 2H), 7.38 (t, J=7.8 Hz, 4H), 7.39 (d, J=7.8 Hz, 2H), 7.45 (dd, J=7.8, 6.6 Hz, 1H), 7.50 (dd, J=7.8, 1.6 Hz, 4H); ^{13}C NMR (150 MHz, CD_2Cl_2) δ 31.5, 49.6, 127.2, 127.8, 129.3, 130.1, 130.6, 131.8, 143.7, 151.2; IR (KBr) 1448, 1560, 2965, 3054 cm^{-1}; HRMS (EI) *m/z*: [M]$^+$ calcd for $C_{22}H_{22}S$, 318.1442; found: 318.1432.

*4.2.4. . tert-Butyl(3,3″,5,5″-tetramethoxy-[1,1′:3′,1″-terphenyl]-2′-yl) sulfane **(4b)**.* Compound **4b** was synthesized by coupling compound **8a** (200 mg) with 3,5-dimethoxyphenylboronic acid using the procedure for the synthesis of **4a**. The crude product was purified by column chromatography on silica gel with dichloromethane:hexanes (4:1) as eluent to give **4b** as a white solid (166 mg, 61%). The product was further purified by recrystallization twice from diethyl ether:hexanes (1:1): mp 147–152 °C; ^{1}H NMR (600 MHz, CD_2Cl_2) δ 0.79 (s, 9H), 3.82 (s, 12H), 6.45 (t, J=2.4 Hz, 2H), 6.66 (d, J=2.4 Hz, 4H), 7.38 (dd, J=9.0, 6.0 Hz, 2H), 7.42 (dd, J=9.0, 5.4 Hz, 1H); ^{13}C NMR (150 MHz, CD_2Cl_2) δ 31.8, 49.4, 56.0, 99.3, 110.1, 129.0, 130.2, 130.4, 145.5, 150.9, 160.4; IR (KBr) 1062, 1162, 1326, 1457, 1590, 2834, 2974 cm^{-1}; HRMS (EI) *m/z*: [M]$^+$ calcd for $C_{26}H_{30}O_4S$ 438.1865; found: 438.1849.

*4.2.5. .tert-Butyl(4,4″-dichloro-[1,1′:3′,1″-terphenyl]-2′-yl)sulfane **(4c)**.* Compound **4c** was synthesized by coupling compound **8a** (300 mg) with 4-chlorophenylboronic acid using the procedure for the synthesis of **4a**. The crude product was purified by column chromatography on silica gel using chloroform/hexanes. Compound **4c** was obtained as a white solid (260 mg, 72% yield). The product was further purified by recrystallization twice from diethyl ether:hexanes (1:1): mp 168–170 °C; ^{1}H NMR (600 MHz, CD_2Cl_2) δ 0.69 (s, 9H), 7.38 (m, 6H), 7.46 (m, 5H); ^{13}C NMR (150 MHz, CD_2Cl_2) δ 30.8, 49.7, 127.3, 128.9, 129.3, 130.1, 132.6, 132.7, 141.4, 149.4; IR (KBr) 1086, 1448, 1487, 1592, 2952, 3043 cm^{-1}; HRMS (EI) *m/z*: [M]$^+$ calcd for $C_{22}H_{20}Cl_2S$ 386.0663; found: 386.0660.

*4.2.6. .tert-Butyl(3,3″-dinitro-[1,1′:3′,1″-terphenyl]-2′-yl)sulfane **(4d)**.* Compound **4d** was synthesized by coupling compound **8a** (250 mg) with 2.2 equiv of 3-nitrophenyl-boronic acid but otherwise the same procedure as that for the synthesis of **4a**. The crude product was purified by column chromatography on silica gel using chloroform/hexanes. Compound **4d** was obtained as a white solid (250 mg, 77% yield). The product was further purified by recrystallization twice from diethyl ether:hexanes (1:1): mp 225.5–227 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 0.64 (s, 9H), 7.48 (d, J=7.8 Hz, 2H), 7.55 (dd, J=7.8, 6.6 Hz, 1H), 7.57 (t, J=8.4 Hz, 2H), 7.86 (d, J=7.8 Hz, 2H), 8.20 (dd, J=7.8, 1.8 Hz, 2H), 8.38 (t, J=1.8 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 31.2, 50.9, 122.3, 126.3, 128.5, 129.8, 129.8, 131.1, 137.7, 144.1, 147.8, 148.6; IR (KBr) 1347, 1529, 2972 cm^{-1}; HRMS (EI) *m/z*: [M]$^+$ calcd for $C_{22}H_{20}N_2O_4S$ 408.1144; found:408.1125.

*4.2.7. (3-Bromo-2′-methoxy-[1,1′-biphenyl]-2-yl)(tert-butyl)sulfane **(9a)**.* Compound **9a** was synthesized by coupling compound **8a** (80 mg) with 2-methoxyphenylboronic using the procedure for the synthesis of **4a**. The crude product was purified by column chromatography on silica gel with chloroform:hexanes (1:9 ramped up to 1:1) as eluent to give **9a** as a slightly yellow oil (65 mg, 69% yield): ^{1}H NMR (600 MHz, CD_2Cl_2) δ 1.05 (s, 9H), 3.75 (s, 3H), 6.94 (d, J=8.4 Hz, 1H), 6.98 (dt, J=7.2, 0.6 Hz, 1H), 7.18 (dd, J=7.2, 1.8 Hz, 1H), 7.22 (t, J=7.8 Hz, 1H), 7.29 (dd, J=7.8, 1.2 Hz, 1H), 7.33 (dt, J=7.8, 1.8 Hz, 1H), 7.70 (dd, J=7.8, 1.2 Hz, 1H); ^{13}C NMR (150 MHz, CD_2Cl_2) δ 31.9, 50.3, 55.8, 111.1, 120.2, 129.5, 130.2, 131.1, 132.1, 132.9, 135.7, 148.9, 157.2; IR (neat) 751, 1436, 1456, 1576, 1599, 2917, 3048 cm^{-1}; HRMS (EI) *m/z*: [M]$^+$ calcd for $C_{17}H_{19}BrOS$ 350.0340; found: 350.0342.

*4.2.8. (2-Methoxy-[1,1′:3′,1″-terphenyl]-2′-yl)(tert-butyl)sulfane **(4e)**.* Compound **4e** was synthesized by coupling compound **9a**

(159 mg) with phenylboronic acid using the procedure for the synthesis of **4a**. The crude product was purified by column chromatography on silica gel using chloroform/hexanes (1:9 ramped up to 1:1) as eluent to give **4e** as a white solid (110 mg, 70% yield). The product was further purified by recrystallization twice from diethyl ether:hexanes (1:1): mp 145–146 °C; ^{1}H NMR (500 MHz, CD_2Cl_2) δ 0.67 (s, 9H), 3.80 (s, 3H), 6.95 (d, J=8.0 Hz, 1H), 6.99 (dt, J=7.5, 1.0 Hz, 1H), 7.25 (dd, J=7.5, 1.0 Hz, 1H), 7.29–7.40 (m, 6H), 7.44 (t, J=7.5 Hz, 1H), 7.53 (d, J=7.0 Hz, 2H); ^{13}C NMR (150 MHz, CD_2Cl_2) δ 31.6, 48.9, 55.8, 111.0, 120.2, 127.2, 127.8, 129.1, 130.5, 131.8, 143.7, 157.4; IR (KBr) 1231, 1460, 1596, 2833, 2956, 3056 cm^{-1}; HRMS (EI) *m/z*: [M]$^+$ calcd for $C_{23}H_{24}OS$ 348.1548; found: 348.1541.

*4.2.9. (3-Bromo-2′-methyl-[1,1′-biphenyl]-2-yl)(tert-butyl)sulfane **(9c)**.* Compound **9c** was synthesized by coupling compound **7a** (100 mg) with *o*-tolylboronic acid using the procedure for synthesis of **4a**. The crude product was purified by column chromatography on silica gel with chloroform:hexanes as eluent to give **9c** as a clear oil (73 mg, 70% yield): ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.09 (s, 9H), 2.10 (s, 3H), 7.14–7.27 (m, 6H), 7.71 (dd, J=7.0, 2.5 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 20.5, 31.9, 50.1, 124.6, 127.4, 129.5, 129.8, 129.9, 130.7, 132.5, 133.8, 135.6, 136.2, 142.1, 150.9; IR (neat) 758, 788, 1047, 1161, 1363, 1457, 1542, 2960, 3055 cm^{-1}; HRMS (EI) *m/z*: [M]$^+$ calcd for $C_{17}H_{19}BrS$ 334.0391; found: 334.0377.

*4.2.10. (2-Methyl-[1,1′:3′,1″-terphenyl]-2′-yl)(tert-butyl)sulfane **(4f)**.* Compound **4f** was synthesized by coupling compound **9c** (100 mg) with phenylboronic acid using the procedure for the synthesis of **4a**. The crude product was purified by column chromatography on silica gel using chloroform/hexanes as eluent to give **4f** as a white solid (94 mg, 95% yield). The product was further purified by recrystallization twice from diethyl ether:hexanes (1:1): mp 78–79 °C; ^{1}H NMR (500 MHz, CD_2Cl_2) δ 0.71 (s, 9H), 2.17 (s, 3H), 7.18–7.27 (m, 5H), 7.32 (tt, J=1.5, 7.5 Hz) 7.37–7.42 (m, 3H) 7.45 (t, J=7.5 Hz) 7.50–7.53 (m, 2H); ^{13}C NMR (125 MHz, CD_2Cl_2) δ 31.6, 48.8, 124.6, 126.7, 127.0, 127.3, 128.6, 129.4, 129.7, 130.0, 130.6, 130.9, 131.2, 136.5, 142.8, 142.9, 149.8, 150.1; IR (KBr) 810, 1032, 1169, 1363, 1440, 1560, 2856, 2893, 2918, 2935, 2958, 3012, 3024, 3056 cm^{-1}; HRMS (EI) *m/z*: [M]$^+$ calcd for $C_{23}H_{24}S$ 332.1599; found: 332.1585.

*4.2.11. [1,1′:3′,1″-Terphenyl]-2′-yl(methyl)sulfane **(2b)**.* Compound **2b** was synthesized by coupling (2,6-dibromophenyl)(methyl)sulfane, **8d** (100 mg), prepared using a method reported by Bryant et al.[27] with phenylboronic acid using the procedure for the synthesis of **4a**. The crude product was purified by column chromatography on silica gel using hexanes to remove a less polar impurity and then 1:4 chloroform/hexanes to isolate the compound **2b** as a white solid (99% yield): the NMR and IR spectra, and melting point of the compound were consistent with previously reported data.[3]

*4.2.12. (4,4″-Dimethoxy-[1,1′:3′,1″-terphenyl]-2′-yl)(methyl)sulfane **(2c)**.* Compound **2c** was synthesized by coupling **8d** with 4-methoxyphenylboronic acid using the procedure for the synthesis of **4a**. The crude product was purified by column chromatography on silica gel using chloroform/hexanes (1:1) as eluent to give **2c** as a white solid (53% yield). The NMR and IR spectra, and melting point of the compound were consistent with previously reported data.[3]

*4.2.13. (3,3″,5,5″-Tetramethoxy-[1,1′:3′,1″-terphenyl]-2′-yl)(methyl) sulfane **(2d)**.* Compound **2d** was synthesized by coupling **8d** with 3,5-dimethoxyphenylboronic acid using the procedure for the synthesis of **4a**. The crude product was purified by column chromatography on silica gel using dichloromethane as eluent to give **2d** as a white solid (148 mg, 53% yield). The product was further purified by recrystallization twice from diethyl ether:hexanes (1:1): mp 119–120 °C; ^{1}H NMR (600 MHz, CD_2Cl_2) δ 1.79 (s, 3H), 3.83, (s, 12H), 6.49 (t, J=2.4 Hz, 2H), 6.64 (d, J=2.4 Hz, 4H), 7.29 (dd, J=7.8, 6.6 Hz, 2H), 7.34 (dd, J=8.4, 6.6 Hz, 1H); ^{13}C NMR (150 MHz, CD_2Cl_2) δ 19.7, 55.9, 99.6, 108.3, 127.7, 130.3, 134.3, 144.6, 146.8, 160.9; IR (KBr) 1157, 1208, 1336, 1456, 1591, 2832, 2921, 3051 cm^{-1}; HRMS (EI) *m/z*: [M]$^+$ calcd for $C_{23}H_{24}O_4S$ 396.1395; found: 396.1384.

*4.2.14. (3-Bromo-2′-methoxy-[1,1′-biphenyl]-2-yl)(methyl)sulfane **(9b)**.* Compound **9b** was synthesized by coupling compound **8d** (100 mg) with 2-methoxyphenylboronic using the procedure for the synthesis of **4a**. The crude product was purified by column chromatography on silica gel with chloroform:hexanes as eluent to give **9b** as a clear oil (87 mg, 79% yield): ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.18 (s, 3H), 3.76 (s, 3H), 6.95 (d, J=8.0 Hz, 1H), 7.00 (dt, J=1.0, 7.0 Hz, 1H), 7.12 (dd, J=2.0, 7.5 Hz, 1H), 7.15–7.22 (m, 2H), 7.36 (dt, J=1.5, 6.5 Hz, 1H), 7.63 (dd, J=2.0, 7.5 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 19.3, 55.7, 110.7, 120.4, 129.4, 129.5, 130.2, 130.6, 131.3, 131.4, 132.9, 137.3, 146.0, 156.80; IR (neat) 763, 796, 1023, 1054, 1123, 1233, 1271, 1397, 1433, 1457, 1494, 2834, 2918, 2958, 3010, 3056 cm^{-1}; HRMS (EI) *m/z*: [M]$^+$ calcd for $C_{14}H_{13}BrOS$ 307.9870; found: 307.9862.

*4.2.15. (2,2‴′-Dimethoxy-[1,1′:3′,1″:4″,1‴:3‴,1‴′-quinquephenyl]-2′,2‴-diyl)bis(tert-butylsulfane) **(5a)**.* First, compound **9a** (250 mg, 0.714 mmol) was coupled with benzene-1,4-diboronic acid, **10** (472 mg, 2.85 mmol) using the procedure for the synthesis of **4a**. After 24 h, H_2O (50 mL) was added to the resulting suspension and extracted with EtOAc (50 mL). The organic layer was washed successively with brine (50 mL), and H_2O (50 mL), dried with anhyd $MgSO_4$, filtered and evaporated under reduced pressure. The crude product was purified by column chromatography on silica gel using ethyl acetate/chloroform (1:1) to remove less polar impurities and then 5% MeOH in chloroform to obtain crude (2′-(*tert*-butylthio)-2″-methoxy-[1,1′:3′,1″-terphenyl]-4-yl) boronic acid **11a** as a slightly yellow solid (184 mg). This crude product was used without further purification in next Suzuki coupling reaction with compound **9a** (41 mg, 0.117 mmol). The crude product was purified by preparative plate chromatography on silica gel using dichloromethane/hexanes (1:1) as eluent to give **5a** as a white solid (15.4 mg, 21% yield): mp 215–216 °C; ^{1}H NMR (500 MHz, CD_2Cl_2) δ 0.74 (s, 18H), 3.82 (s, 6H), 6.96 (d, J=8.5 Hz, 2H), 7.00 (dt, J=7.5, 1.0 Hz, 2H), 7.28 (d, J=6.5 Hz, 2H), 7.34 (m, 4H), 7.45 (m, 4H), 7.56 (s, 4H); ^{13}C NMR (125 MHz, CD_2Cl_2) δ 31.7, 49.2, 55.9, 111.0, 120.2, 129.0, 130.6, 130.8, 132.7, 142.1, 148.0, 150.2, 157.4; IR (KBr) 1217, 1365, 1738, 2957 cm^{-1}; HRMS (MALDI) *m/z*: [M−C_8H_{15}]$^+$ calcd for $C_{32}H_{26}O_2S_2$, 506.13687; found: 506.13733.

*4.2.16. (2,2‴′-Dimethyl-[1,1′:3′,1″:4″,1‴:3‴,1‴′-quinquephenyl]-2′,2‴-diyl)bis(tert-butylsulfane) **(5b)**.* Compound **9c** (610 mg, 1.81 mmol) was coupled with benzene-1,4-diboronic acid, **10** (301 mg, 1.81 mmol) using the procedure for the synthesis of **4a** at 90 °C. After 24 h, H_2O (50 mL) was added to the resulting suspension and extracted with EtOAc (50 mL). The organic layer was washed successively with brine (50 mL), and H_2O (50 mL), dried with anhyd $MgSO_4$, filtered and evaporated under reduced pressure. The crude product was purified by column chromatography on silica gel using chloroform/hexanes to give **5b** as a white solid (113 mg, 21% yield): mp 224.5–225.5 °C; ^{1}H NMR (500 MHz, CD_2Cl_2) δ 0.78 (s, 9H), 0.78 (s, 9H), 2.20 (s, 6H), 7.19–7.23 (m, 2H), 7.23–7.28 (m, 8H), 7.44–7.50 (m, 4H), 7.55 (s, 2H), 7.56 (s, 2H); ^{13}C NMR (125 MHz, CD_2Cl_2)δ 20.8, 31.8, 49.5, 125.0, 127.3, 129.1, 129.7, 130.2, 130.5, 130.52, 130.6, 130.7, 130.7, 136.8, 141.9, 143.2, 150.2,

150.3, 150.5; IR (KBr) 757, 798, 1165, 1363, 1457, 2856, 2895, 2918, 2962, 3012, 3044 cm^{-1}; HRMS (ICR-ESI) *m/z*: $[M-C_8H_{15}]^+$ calcd for $C_{32}H_{27}S_2$, 475.1548; found: 475.1541.

4.3. Competition experiment

*4.3.1. Competition between **8d** and **8a** in the Suzuki–Miyaura coupling reaction.* To a solution of **8d** (50 mg, 0.177 mmol) and **8a** (57 mg, 0.177 mmol) in distilled 1,4-dioxane (0.2 mL) under argon, were added a 2 M aqueous solution of Na_2CO_3 (0.35 mL, 0.70 mmol), 2-methoxyphenylboronic acid (26.9 mg, 0.177 mmol), and $Pd(PPh_3)_4$ (40.9 mg, 0.0354 mmol). The mixture was stirred overnight at reflux. H_2O (30 mL) was added to the resulting suspension and extracted with EtOAc (30 mL). The organic layer was washed successively with 1 M aqueous NaOH (30 mL), brine (30 mL), and H_2O (30 mL), dried with anhyd $MgSO_4$, filtered and evaporated under reduced pressure. The crude mixture was column chromatographed on silica gel using 1:1 chloroform/hexanes to obtain a mixture of **8a**, **8d**, **9a** and **9d** whose relative abundance was determined by ^1H NMR spectroscopic analysis.

4.4. X-ray diffraction

A clear, colorless crystal of **5a** 0.1×0.15×0.2 mm was used for data collection. Data was collected using Mo Kα radiation on a Bruker Kappa Apex II Duo diffractometer. The crystal was nonmerohedrally twinned with the two domains related by a rotation of 180° around the c* axis. The data was detwinned using CELLNOW,[28] integrated using SAINT,[29] and scaled using TWINABS.[30] After detwinning, structure solution and refinement using SHELXL97 was routine.[31] The molecule lies on an inversion center, with half of a molecule in the asymmetric unit. Table 5 lists crystallographic data and structural refinement.

Table 5
Crystal data and structure refinement of **5a**

Crystal system	Monoclinic	
Space group	P 1 21/c 1	
Unit cell dimensions	*a*=14.2500(3) Å	*α*=90°
	b=14.2983(3) Å	*β*=101.1930(10)°
	c=8.5433(2) Å	*γ*=90°
Volume	1707.59(6) $Å^3$	
Z	2	
Density (calculated)	1.204 g/cm^3	
Absorption coefficient	0.189 mm^{-1}	
F(000)	660	
Theta range for data collection	1.46–25.40°	
Reflections collected	3137	
Coverage of independent reflections	99.7%	
Absorption correction	Multi-scan	
Max. and min. transmission	0.9813 and 0.9631	
Data/restraints/parameters	3137/0/203	
Goodness-of-fit on F^2	1.065	
Δ/σ_{max}	0.001	
Final R indices	2618 data; $I>2\sigma(I)$	$R1$=0.0476, w$R2$=0.0977
	All data	$R1$=0.0615, w$R2$=0.0976
Largest diff. peak and hole	0.301 and −0.318 $eÅ^{-3}$	

Crystallographic data have been deposited with the Cambridge Crystallographic Data Centre CCDC 1049877. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK, or email: deposit@ccdc.cam.ac.uk.

4.5. Electrochemistry

All electrochemical experiments were performed using a CH Instruments Model 620C potentiostat (Austin, TX). Acetonitrile (CH_3CN), extra dry (water<10 ppm) (Acros) was used without further purification. The supporting electrolyte was $NaClO_4$ anhydrous (Alfa Aesar) which was vacuum dried prior to use. A three compartment electrochemical cell was employed with one compartment containing the working electrode Pt (2 mm od) or glassy carbon (3 mm od) obtained from CH Instruments. The counter electrode was glassy carbon and the reference electrode was 0.1 M Ag^+ in CH_3CN. Ferrocene (Sigma–Aldrich) was used for monitoring the stability of the reference electrode which had a potential of 0.028 V versus a ferrocene peak obtained by differential pulse voltammetry (DPV) (amplitude 10 mV), Cyclic voltammetry (CV) experiments were all carried out at a scan rate of 0.1 V/s. Before each experiment the working electrode was polished with 0.3 μm alumina powder, washed with the solvent and dried. All experiments were carried out in a glove box.

Acknowledgements

The authors gratefully acknowledge financial support of this work by the National Science Foundation (Grant No. 0956581).

Supplementary data

Supplementary data (Tables of crystallographic data for **5a**. Copies of NMR spectra) related to this article can be found, in the online version at http://dx.doi.org/10.1016/j.tet.2016.03.040.

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