

Aromatic Metamorphosis of Thiophenes by Means of Desulfurative Dilithiation

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Dedication ((optional))

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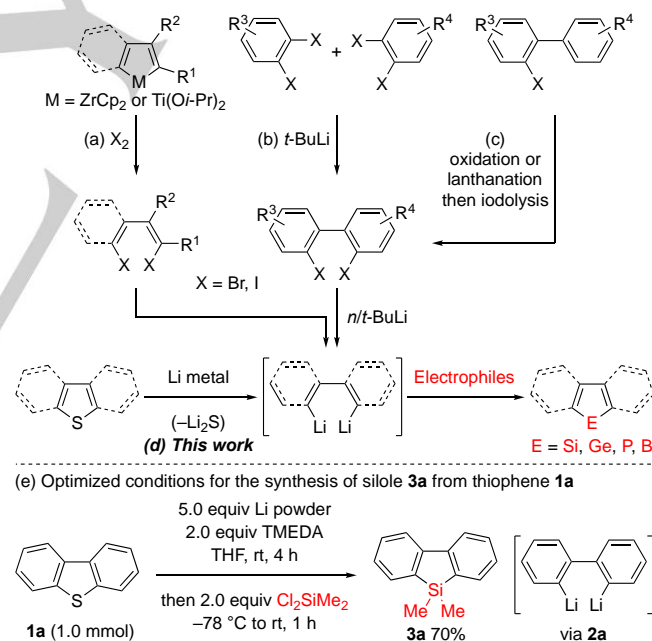
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Abstract: A new mode of aromatic metamorphosis has been developed, which allows thiophenes and their benzo-fused derivatives to be converted to a variety of exotic heteroles. This transformation involves 1) the efficient generation of key 1,4-dianions by means of desulfurative dilithiation with lithium powder and 2) the subsequent trapping of the dianions with heteroatom electrophiles in a one-pot manner. Via the desulfurative dilithiation, the sulfur atoms of thiophenes are replaced also with a carbon-carbon double bond or a 1,2-phenylene for the construction of benzene rings.

Carbanions constitute a generally useful class of intermediates for the construction of complex carbon frameworks.^[1] Among these carbanions, dianion or even polyanion species are of broad interest because they react multiply with electrophiles to significantly increase molecular complexity and diversity and/or to provide rapid accesses to target molecules.^[2] In particular, 1,4-dilithiobutadienes and their benzo-fused analogs are key intermediates for the synthesis of various cyclic molecules including heteroles.^[3]

A classical yet practical method for the generation of 1,4-dilithiobutadienes and their benzo-fused analogs is the halogen-lithium exchange reactions of the corresponding 1,4-dihalo precursors with *n*-BuLi or *t*-BuLi.^[4] Several efficient synthetic routes to the important 1,4-dihalo precursors are available. The most powerful and reliable route would currently be halogenolysis of zircona-^[5] or titanacyclopentadienes^[6] or zirconaindenes^[5,7] (Scheme 1a). However, there remain limitations in terms of substitution patterns and regioselectivity. As a typical limitation, unsymmetrical 2,3-unsubstituted 1,4-dihalobutadienes, which are not complex compounds, have not been prepared through the metallacycle-based approach. The syntheses of 2,2'-dihalobiaryl precursors, such as couplings of *ortho*-halogenated phenyl substrates (Scheme 1b)^[8] and stepwise halogenation of 2-halobiaryls (Scheme 1c)^[9], also suffer from limited substitution patterns, lack of regioselectivity, and/or cumbersome protocols. These backgrounds have encouraged us to find versatile

precursors of 1,4-dilithiobutadiene derivatives instead of dihalo compounds.



Scheme 1. Conventional and new methods for the generation of 1,4-dilithiobutadiene derivatives.

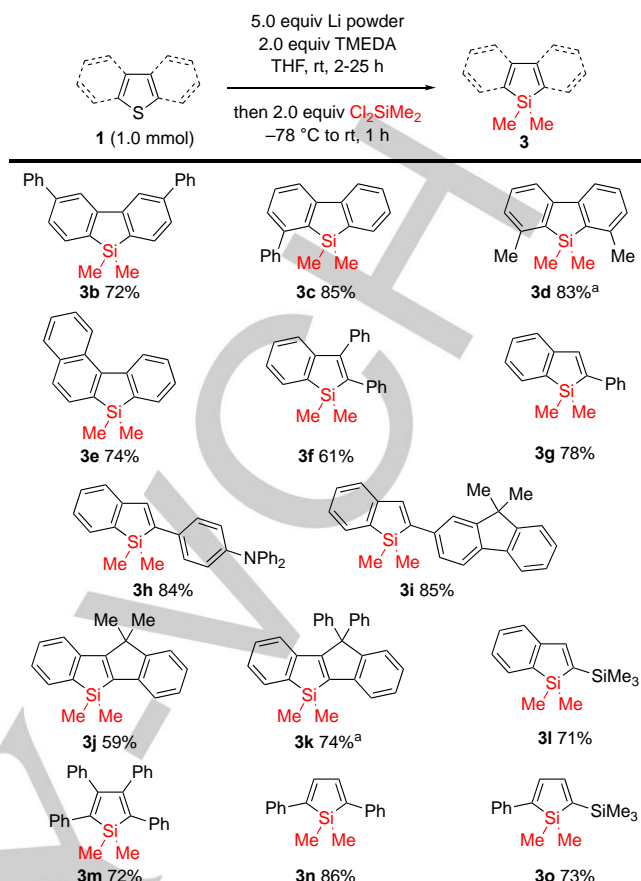
Thiophenes are sulfur-containing heteroaromatic compounds and are found widely in bioactive compounds and organic functional materials.^[10] In contrast to the facile exocyclic modifications of thiophenes,^[11] endocyclic modifications of thiophenes have been much less studied due to the robustness of thiophenes.^[12] In this context, we have been interested in 'aromatic metamorphosis' of heteroaromatic compounds, which represents a transformation of a heteroaromatic skeleton to another ring system through the

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partial disassembly of the starting aromatic core.^[13–15] Given that lithium metal can reduce organosulfur compounds to generate organolithium species,^[16] we envisioned that thiophenes are regarded as potential precursors of 1,4-dilithiobutadienes by means of desulfurative dilithiation (Scheme 1d). The dianionic species was expected to react with various electrophiles to realize diversity-oriented synthesis of interesting heteroles. This thiophene-based method has a notable advantage over the dihalobutadiene-based one: A wide range of thiophenes bearing different substitution patterns are readily available and practically stable.

Several reports on reductive desulfurization of thiophenes using alkali metals^[17] underscore the difficulty in achieving efficient and reliable generation of 1,4-dilithiobutadienes: These precedents simply focused on removal of sulfur (desulfurization) without minding the formation of dianionic species. The reduction therefore requires harsh reaction conditions such as excess amounts of alkali metals and/or high temperatures, which leads to degradations of the 1,4-dilithiobutadiene intermediates and interference with remaining alkali metals in the use of the intermediates. To our delight, we identified optimized reaction conditions for the reliable generation of 2,2'-dilithiobiphenyl (**2a**) from dibenzothiophene (**1a**), by using 5.0 equivalent of Li powder^[18] and 2.0 equivalent of TMEDA in THF at room temperature (Scheme 1e).^[19] The reaction of dianion **2a** with 2.0 equivalent of Cl_2SiMe_2 in a one-pot manner provided dibenzosilole **3a** in 70% yield along with <1% yield of biphenyl (**3a'**). The use of lithium powder is crucial: The use of Li granules required vigorous stirring for the efficient generation of **2a** and sometimes led to lack of reproducibility.

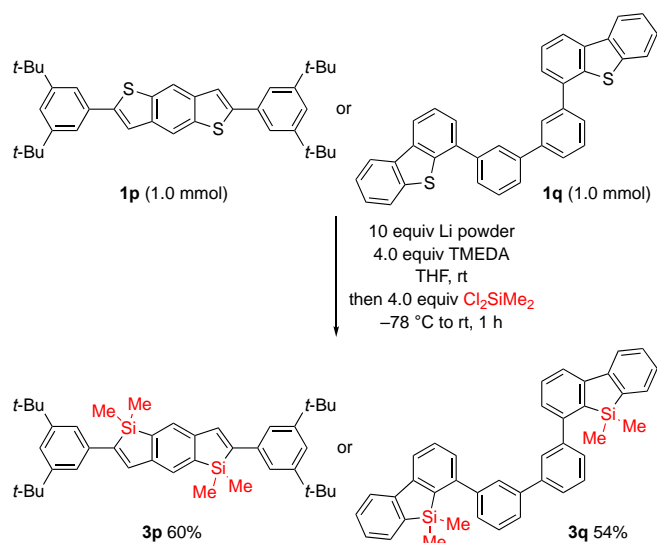
Encouraged by the efficient synthesis of dibenzosilole **3a** from dibenzothiophene (**1a**), we next investigated the scope of the aromatic metamorphosis with respect to thiophenes **1** toward the synthesis of diverse siloles **3** (Scheme 2). A variety of multi-substituted dibenzothiophenes **1b–1d** were converted to the corresponding dibenzosiloles **3b–3d** in high yields. The reductive desulfuration of **1d** was performed at 0 °C to suppress the undesired protonation of dianion **2d** by the benzylic protons, affording **3d** in 83% yield. A π -extended silole **3e** was also obtained in comparable yield. Benzothiophenes **1f–1k** having various aryl groups at their 2 positions are also suitable substrates under optimal reaction conditions. Notably, the current protocol can afford ladder-type benzosiloles **3j** and **3k** bearing dimethyl- and diphenyl-methylene bridges, respectively, which are attractive scaffolds showing intriguing photophysical properties.^[20] The protocol tolerated the trimethylsilyl group at the 2 position in **1l**, providing benzosilole **3l** in good yield. The trimethylsilyl group will be further transformed into a variety of substituents. Unfortunately, 2-methylbenzothiophene and 2,3-unsubstituted benzothiophene did not provide desired products at all along with a complex mixture of unidentified products. Interestingly, substituted thiophenes **1m–1o** bearing no fused benzene ring were efficiently converted to siloles **3m–3o** through the generations of the corresponding 1,4-dilithiobutadienes including an unsymmetrical one.



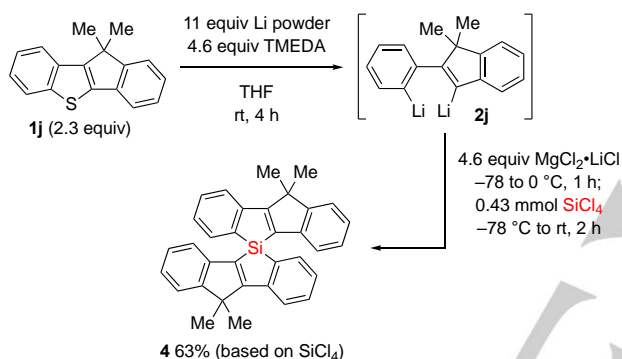
Scheme 2. Synthesis of siloles **3** from thiophenes **1**. [a] At 0 °C for 1st step.

Our protocol is sufficiently powerful and efficient to generate tetraanionic species from **1p** and **1q** and to form four C–Si bonds for the synthesis of bis-siloles (Scheme 3). In the presence of double amounts of lithium metal, TMEDA, and Cl_2SiMe_2 under optimal reaction conditions, 2,6-diarylated benzodithiophene **1p** was transformed into benzodisilole **3p** in 60% yield.^[21] Similarly, the reaction of biphenyl-linked bisdibenzothiophene **1q** leads to the formation of biphenyl-linked bisdibenzosilole **3q**, the 3,3'-difunctionalized biphenyl moiety of which would serve as an attractive scaffold in host materials of phosphorescent organic light emitting diodes.^[22]

We could also synthesize spirocyclic silole **4** from **1j** via dianion **2j** which has been an inaccessible dianion thus far (Scheme 4). The synthesis of **4** is featured by the transmetalation of dilithium species **2j** with THF-soluble $\text{MgCl}_2 \cdot \text{LiCl}$ ^[23] prior to the trapping with SiCl_4 as a limiting reagent. The spirocyclic silole **4** can be regarded as the silicon analog of Nakamura's spiro carbon-bridged *p*-phenylenevinylene that exhibits interesting physicochemical properties.^[24]

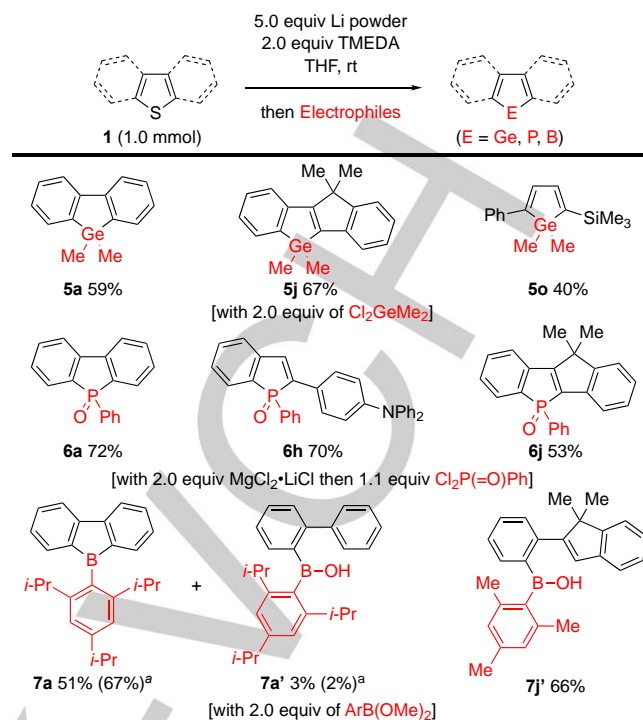


Scheme 3. Synthesis of bis-siloles **3p** and **3q** from bis-thiophenes **1p** and **1q**.



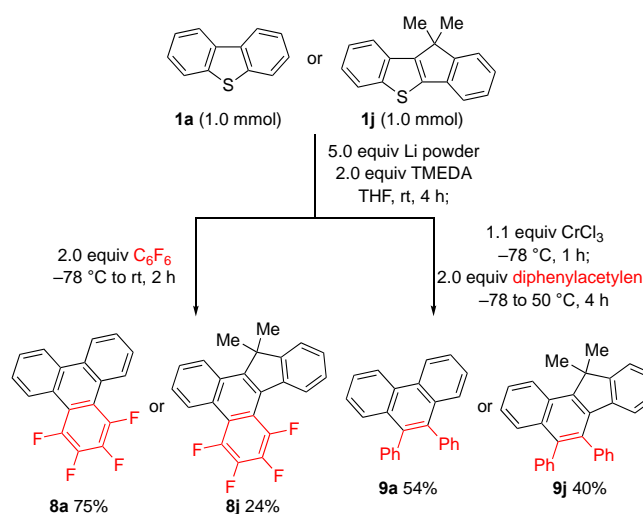
Scheme 4. Synthesis of spirocyclic silole **4**.

This protocol was naturally extended to the preparation of germales **5** and phosphole oxides **6** using suitable electrophiles (Scheme 5). The synthesis of germales **5** were carried out in a fashion similar to that of siloles **3**. The synthesis of phosphole oxides **6** was achieved through the transmetalation with $\text{MgCl}_2 \cdot \text{LiCl}$ followed by trapping with $\text{Cl}_2\text{P}(=\text{O})\text{Ph}$. Our method afforded donor-acceptor-type benzophosphole oxide **6h** having a diphenylaminophenyl group.^[25] In addition, benzophosphole oxide **6j** constrained with a dimethylmethylene bridge has become readily available, which is a promising dye for fluorescence imaging,^[26] although the construction of such a framework was laborious in previous reports.^[25,26] Borole **7a** was also obtained in high yield, albeit it was contaminated with borinic acid **7a'** via the partial decomposition of **7a**. Our attempt to isolate borole **7j** from **1j** resulted in failure, instead providing borinic acid **7j'** as a single product in our hand, probably because of the instability of the initially formed constrained **7j**. These results highlight the advantage of our synthetic strategy in terms of diversity-oriented synthesis of heteroles over the conventional synthesis starting from substrates that have pre-installed heteroatoms.^[27]



Scheme 5. Synthesis of germales **5**, phosphole oxides **6**, and boroles **7**. [a] ^1H NMR yields.

We could replace the sulfur atom of **1a** and **1j** with a two-carbon unit to achieve ring-expanding aromatic metamorphosis from a thiophene ring to a benzene ring (Scheme 6). Desulfurative dilithiation of **1a** and **1j** followed by an addition of C_6F_6 resulted in two-fold nucleophilic aromatic substitution to provide partially fluorinated polycyclic aromatic hydrocarbons **8** that have attracted much attention in the field of liquid crystalline materials.^[28] Besides, CrCl_3 -mediated annulation of the resulting dianionic species with diphenylacetylene provided phenanthrene **9a** and naphthalene **9j**.^[29]



Scheme 6. Desulfurative construction of aromatic rings from thiophenes.

Heterole-containing ladder-type π -conjugated compounds have been of interest as functional organic materials.^[30] The UV-vis absorption and fluorescence spectra of new silole-, germole-, and phosphole-containing compounds **3j**, **5j**, and **6j** and spiro-fused dimer **4** were therefore measured to evaluate their photophysical properties (Figure 1). Their photophysical data are summarized in Table 1, together with their carbon (**10a**),^[31] nitrogen (**10b**),^[15d] and sulfur (**1j** and **1j'**)^[32] analogs and the bent regioisomer **6j'**^[33] which have been reported previously (Figure 2). The longest absorption maximum (λ_{abs}) shifts to the longer wavelength region in the order of **5j** (337 nm) < **3j** (342 nm) < **6j** (363 nm). The same trend in λ_{abs} has also been observed for the dibenzoheterole derivatives.^[34] Compounds **3j** and **5j** show red-shifted absorption maxima compared to that of the carbon analog **10a** (322 nm). Such a red-shift would be attributed to the lower-lying LUMO energy levels of **3j** and **5j** induced by the $\sigma^*-\pi^*$ conjugation between the exocyclic Si/Ge-C σ^* orbitals and the endocyclic butadiene π^* orbital of the silole and germole moieties.^[35] The absorption maximum of **6j** is red-shifted by 23 nm compared to that of its regioisomer **6j'**, which indicates more effective π -conjugation in the linear structure of **6j**. In the solution-state fluorescence spectra, compounds **3j**, **5j**, and **6j** exhibit emission maxima (λ_{em}) at 406, 391, and 448 nm, respectively. The quantum yields of them are higher (0.70–0.77) than those of the related heterole-containing compounds in Table 1, but lower than that of the carbon analogue **10a**. Phosphole-containing compound **6j** exhibits a higher quantum yield than its regioisomer **6j'**. Noteworthy is that the silole- and germole-containing compounds **3j** and **5j**, respectively, maintain their high quantum yields in the solid state. The spiro-fused dimer **4** shows a red-shifted absorption spectrum compared to its substructure compound **3j**, which would be attributed to the through-space orbital interaction between the two substructure units known as spiroconjugation.^[36] The quantum yield of **4** is relatively high (0.50), while the spiro fusion was found to induce a lower quantum yield than that of its substructure **3j**.

Table 1. Photophysical Properties of Heterole-containing Ladder-type π -Conjugated Compounds.

	solution			solid	
	λ_{abs} (nm) ^[a]	λ_{em} (nm) ^[b]	Φ ^[c]	λ_{em} (nm) ^[b]	Φ ^[c]
3j	342	406	0.77	405	0.71
5j	337	391	0.73	397	0.63
6j	363	448	0.70	447	0.32
10a	322	367	0.92	---	---
10b	344	372	0.58	---	---
1j	330	354	0.11	---	---
1j'	355	444	0.46	---	---
6j'	340	412	0.52	---	---
4	356	427	0.50	432	0.12

[a] The longest absorption maximum in CH_2Cl_2 . [b] Emission maximum in CH_2Cl_2 or in the solid state. [c] Absolute quantum yield.

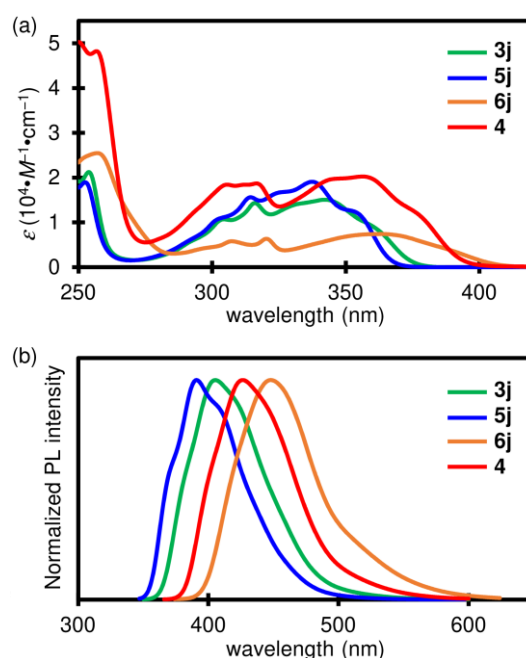


Figure 1. (a) UV-vis absorption and (b) fluorescence spectra of **3j**, **5j**, and **6j** and **4** in dichloromethane.

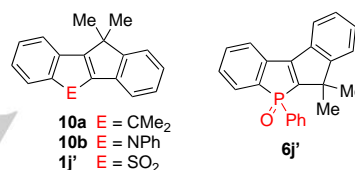


Figure 2. Structures of Known Compounds **10a**, **10b**, **1j'**, and **6j'**.

In conclusion, we have developed a new mode of aromatic metamorphosis based on desulfurative dilithiation of thiophenes using lithium powder, by generating a variety of 1,4-dilithiobutadiene intermediates. The subsequent trapping of the resulting dianions with heteroatom electrophiles provided a series of heteroles in a diversity-oriented manner. Not only benzo-fused thiophenes but also simple thiophenes are applicable to this aromatic metamorphosis. The current method allows the sulfur atoms of thiophenes to be replaced with a two-carbon unit to achieve ring-expanding aromatic metamorphosis from a thiophene ring to a benzene ring. Further extensions of this protocol toward the synthesis of novel functionalized materials are currently underway in our group.

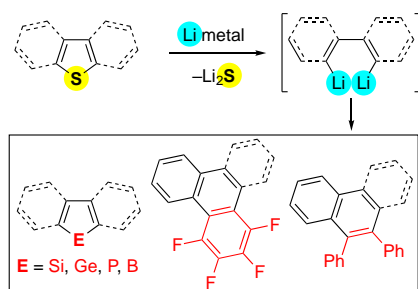
Acknowledgements

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Keywords: lithium metal • thiophene • heterole • desulfurization • dianion

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Entry for the Table of Contents



Desulfurative dilithiation of thiophenes and benzo-fused derivatives using lithium metal has been developed for the efficient generation of multi-substituted 1,4-dilithium compounds. The resulting dianions are key intermediates for the synthesis of diverse heteroles. This protocol also enables the desulfurative construction of aromatic rings from thiophene derivatives in a one-pot manner.

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