Organic LETTERS

Letter

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Catalytic [2 + 2 + 2] Cycloaddition of Benzothiophene Dioxides with α,ω-Diynes for the Synthesis of Condensed Polycyclic Compounds

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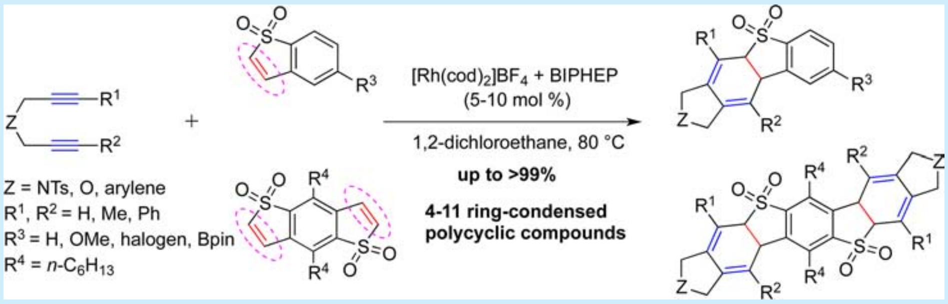
S Supporting Information



ABSTRACT: A Rh-catalyzed intermolecular [2 + 2 + 2] cycloaddition of the 2,3-double bond of benzothiophene dioxides with α,ω-diynes gave sulfone-containing cycloadducts in high yields. This is the first example of a catalytic [2 + 2 + 2] cycloaddition that uses the 2,3-double bond of a heterole as an ene moiety. The consecutive reaction of benzodithiophene tetraoxide with 2,3-naphthylene-tethered 1,7-diyne gave an 11-ring condensed polycyclic compound in one pot.

The transition-metal-catalyzed [2 + 2 + 2] cycloaddition of unsaturated motifs, such as alkynes and alkenes, is a well-established and atom-economical protocol for the construction of multicyclic six-membered ring systems, and various types of substrates have been used in this reaction.[1] For example, the intermolecular [2 + 2 + 2] cycloaddition of α,ω-diynes with 1,1-disubstituted alkenes[2] gave bicyclic 5,5-disubstituted cyclohexa-1,3-dienes, and that with 1,2-disubstituted alkenes[3] gave 5,6-disubstituted cyclohexa-1,3-dienes (paths A and B in Scheme 1). Their asymmetric variants have also been reported.

Scheme 1. Intermolecular [2 + 2 + 2] Cycloaddition of α,ω-Diynes with Various Types of Ene Moieties

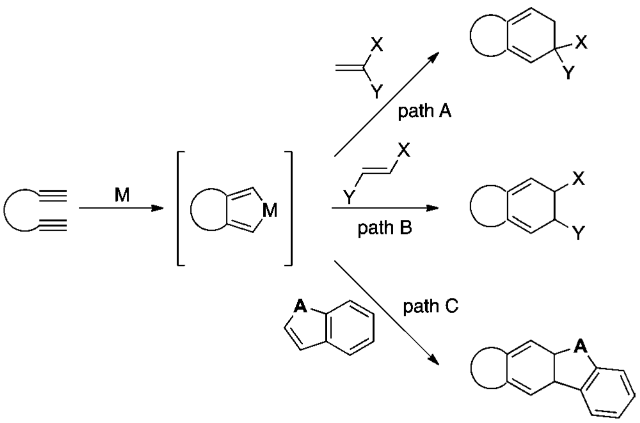
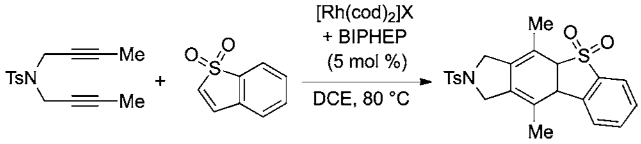


Table 1. Screening of Reaction Conditions



1a **2a** **3aa**

entry[a]	X	time (h)	yield (%)
1	BF_4	1.0	48
2	BF_4	1.0[b]	90
3	BF_4	1.5[b]	95
4	BARF	1.5[b]	93
5	OTf	1.5[b]	95

[a]Benzothiophene dioxide/diyne was 1/3. [b]Time taken for the dropwise addition of diyne **1a**.

However, to the best of our knowledge, there has been no report of catalytic cycloaddition in which the 2,3-double bond of a heterole was involved as an ene moiety (path C). This protocol could make it easy to construct a heteroatom-containing condensed multicyclic system.[4]

We have comprehensively studied the intra-[5] and inter-molecular[6] [2 + 2 + 2] cycloaddition of various types of unsaturated compounds that contain alkene motifs. We recently

Received: October 13, 2014
Published: November 10, 2014

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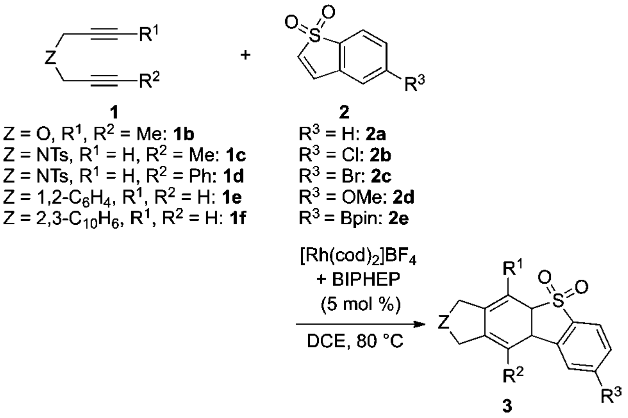
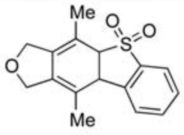
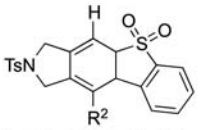
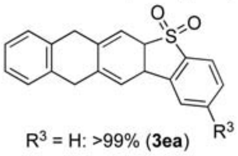
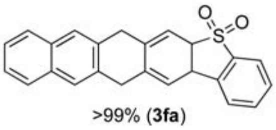
dx.doi.org/10.1021/ol5030019 | *Org. Lett.* 2014, 16, 5980−5983

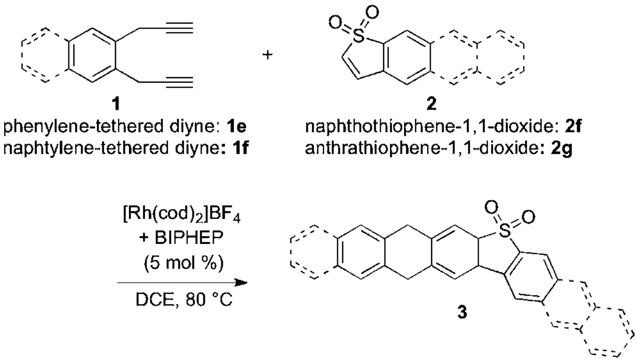
Table 2. [2 + 2 + 2] Cycloaddition of Various Diynes 1 with Substituted Benzothiophene Dioxide Derivatives 2

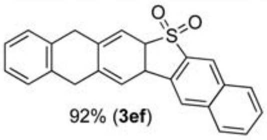
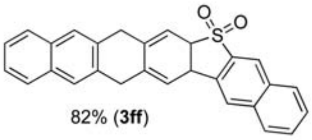
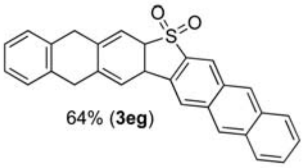
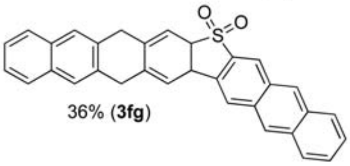


entry[a]	diyne	dioxide	product
1	1b	2a	 70% (3ba)
2	1c 1d	2a	 R^2 = Me: 85% (>20:1) (3ca) = Ph: 89% (>20:1) (3da)
3	1e	2a 2b 2c 2d 2e	 R^3 = H: >99% (3ea) = Cl: 73% (3eb) = Br: 76% (3ec) = OMe: 77% (3ed) = Bpin: 73% (3ee)
4	1f	2a	 >99% (3fa)

[a] Benzothiophene dioxide/diyne was 1/3. Diyne was added dropwise to a solution of the Rh catalyst and benzothiophene dioxide over 1.5 h.

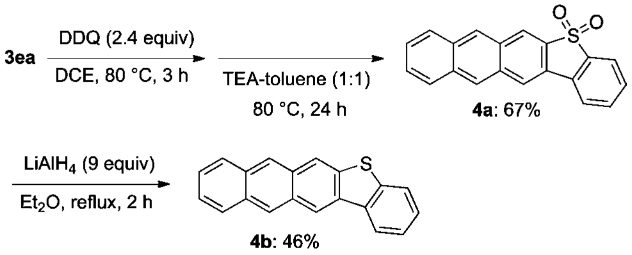
Table 3. [2 + 2 + 2] Cycloaddition of Arylene-Tethered Diynes 1 with Naphtho- and Antrathiophene Dioxide Derivatives 2



entry[a]	diyne	dioxide	product
1	1e	2f	 92% (3ef)
2	1f	2f	 82% (3ff)
3	1e	2g	 64% (3eg)
4	1f	2g	 36% (3fg)

[a] Benzothiophene dioxide/diyne was 1/3. Diyne was added dropwise to a solution of the Rh catalyst and benzothiophene dioxide over 1.5 h.

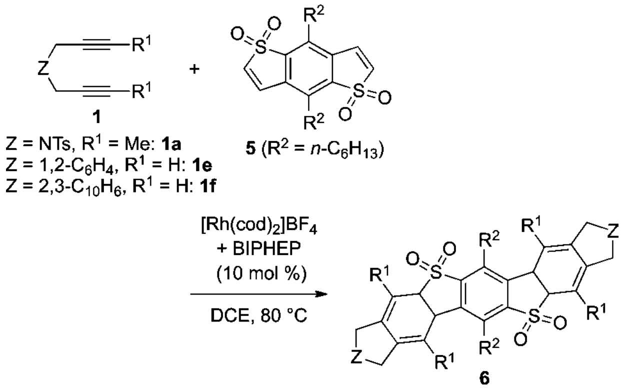
Scheme 2. Aromatization of Cycloadduct 3ea and Subsequent Reduction

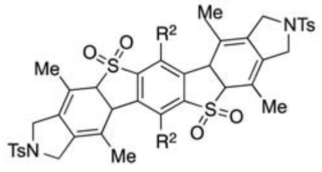
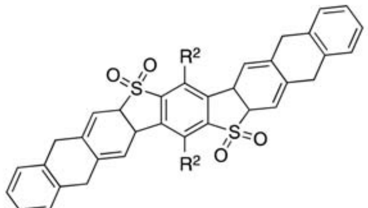
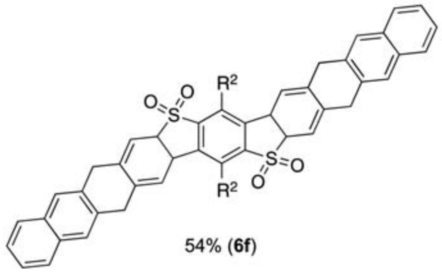


focused on sulfur-containing substrates: consecutive inter- and intramolecular cycloadditions of thiophenylene-tethered triynes gave macrocyclic heteroarylenes containing thiophene rings[7] and intermolecular cycloaddition of sulfanylbenzene-tethered diynes with alkynes gave multisubstituted dibenzothiophenes.[8] Against this background, we next considered the catalytic [2 + 2 + 2] cycloaddition of α,ω-diynes with sulfur-containing benzoheterole derivatives for the synthesis of sulfur-containing condensed polycyclic compounds.

We chose nitrogen-tethered 1,6-diyne **1a** and benzothiophene 1,1-dioxide (**2a**) as a model diyne and benzoheterole, and examined intermolecular [2 + 2 + 2] cycloaddition using Rh-2,2′-bis(diphenylphosphino)-1,1′-biphenyl (BIPHEP) catalyst at 80 °C in 1,2-dichloroethane (DCE) (Table 1).[9] The desired cycloadduct dihydrodibenzothiophene dioxide **3aa** was obtained, but the yield was moderate due to the formation of a self-cycloadduct of diyne **1a** (entry 1). When diyne **1a** was added dropwise to a heated solution of the Rh catalyst and benzothiophene 1,1-dioxide **2a** over 1 h, the yield was drastically improved to 90% (entry 2). A slower dropwise addition (1.5 h) realized an excellent yield of 95% (entry 3). This reaction was little affected by the counteranion of the cationic rhodium catalyst, and we used BF_4 for further investigations (entries 4 and 5).

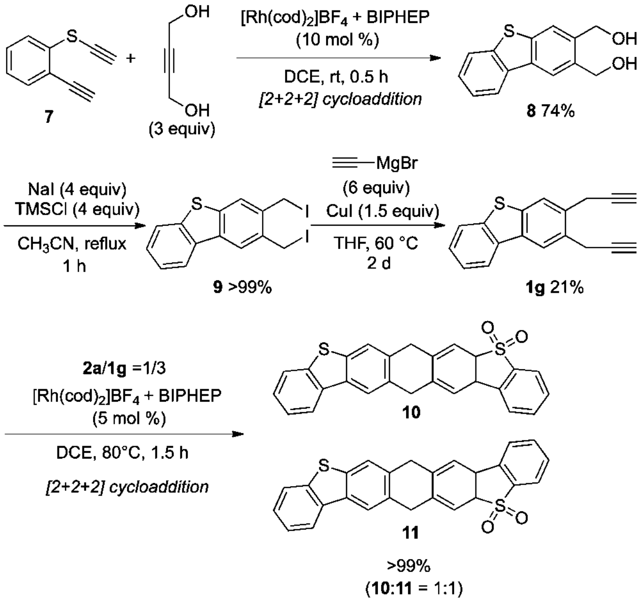
Table 4. Consecutive [2 + 2 + 2] Cycloaddition of Diynes 1 and Benzodithiophene Tetraoxide 5



entry[a]	diyne	product[b]
1	1a	 61% (**6a**)
2	1e	 81% (**6e**)
3	1f	 54% (**6f**)

[a] Benzodithiophene tetraoxide/diyne was 1/9. Diyne was added dropwise to a solution of Rh catalyst and benzodithiophene tetraoxide over 9 h. [b] The value is the total yield of cycloadducts **6** and their double bond isomers of 1,3-cyclohexadiene motif.

Scheme 3. Synthesis of a Multicyclic Compound with Sulfide and Sulfone Moieties via Two [2 + 2 + 2] Cycloadditions



Under the reaction conditions for entry 3 in Table 1, various diynes and benzothiophene dioxides were subjected to intermolecular [2 + 2 + 2] cycloaddition (Table 2). The reaction of oxygen-tethered diyne **1b** also proceeded, and the cycloadduct **3ba** was obtained in good yield (entry 1). When unsymmetrical diynes, which have a methyl or phenyl group and hydrogen on their alkyne terminus, were used, the corresponding cycloadducts **3ca** and **3da** were obtained with almost perfect regioselectivity (entry 2).[10] We next examined arylene-tethered diynes for the synthesis of condensed multicyclic compounds and first used *ortho*-phenylene-tethered diyne **1e** as a substrate (entry 3). The cycloaddition with **2a** proceeded quantitatively. The reaction of 5-substituted benzothiophene dioxide derivatives **2b–2d**, which have a chloro or bromo group as an electron-withdrawing group, and a methoxy group as an electron-donating group, also proceeded to give cycloadducts **3eb–3ed** in good yield. Notably, benzothiophene dioxide **2e** with a pinacolboryl group could also be used in this reaction: the obtained cycloadduct **3ee** can be used for further transformation. 2,3-Naphtylene-tethered diyne **1f** was also a good substrate, and hexacyclic product **3fa** was obtained quantitatively (entry 4).

Next, we examined thiophene dioxides condensed with multicyclic aromatic hydrocarbons as ene moieties (Table 3). Naphthothiophene-1,1-dioxide **2f** worked well, and the reaction with diynes **1e** and **1f** proceeded to give cycloadducts **3ef** and **3ff**, respectively, in high yields (entries 1 and 2). Furthermore, the reaction of anthrathiophene-1,1-dioxide **2g** also proceeded (entries 3 and 4). The reasons for the low yield of **3fg** are the lower reactivity of **2g** compared to **2f** and the instability of **3fg**.

We next transformed the obtained cycloadduct into a multicyclic aromatic compounds: oxidation of pentacyclic compound **3ea** using 2,3-dichloro-5,6-dicyano-*p*-benzoquinone (DDQ) gave the aromatized compound **4a** (Scheme 2).[11] Subsequent reduction gave anthra[2,3-*b*]benzo[*d*]thiophene (**4b**).

We further examined consecutive [2 + 2 + 2] cycloaddition using benzodithiophene tetraoxide (Table 4). We introduced a hexyl group at the 4 and 8 positions, respectively, to increase the solubility and used it in the reaction with diynes **1** (Table 4).[12] While excess amounts of diynes and their slower dropwise addition were required, the reactions of nitrogen-tethered diyne **1a**, phenylene- and naphthylene-tethered diynes **1e** and **1f** proceeded to give condensed polycyclic compounds. However, double isomerization of the 1,3-cyclohexadiene motif occurred under the reaction conditions, and the corresponding cycloadducts **6a**, **6e**, and **6f** could not be completely isolated.

Finally, we synthesized multicyclic compounds containing two sulfur atoms, which differ with respect to the degree of oxidation, by a stepwise protocol including two [2 + 2 + 2] cycloadditions (Scheme 3). Rh-catalyzed intermolecular [2 + 2 + 2] cycloaddition of sulfanylbenzene-tethered diyne **7** with 2-butyne-1,4-diol gave dibenzothiophene (DBT) derivative **8** in good yield.[8] Subsequent iodination and ethynylation of two hydroxyl groups gave DBT-tethered diyne **1g**. The second intermolecular [2 + 2 + 2] cycloaddition of diyne **1g** with benzothiophene 1,1-dioxide (**2a**) proceeded to give a regioisomeric mixture of cycloadducts **10** and **11** in excellent total yield.

In summary, we have developed a Rh-catalyzed intermolecular [2 + 2 + 2] cycloaddition of benzothiophene dioxides and benzodithiophene tetraoxide with α,ω-diynes. The present reaction provides a new protocol for the synthesis of condensed polycyclic compounds containing sulfone moieties. Recently, various polyaromatic systems that include thiophene dioxide moieties have been shown to exhibit unique photophysical properties that are different from those of thiophene.[13] We will further synthesize various condensed polycyclic compounds and evaluate their potential as electronic materials.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Experimental procedure, characterization, and NMR copies of all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

This work was supported by ACT-C from JST (Japan) and Grant-in-Aid for Scientific Research from the Ministry of Education, Culture, Sports, Science and Technology, Japan (No. 23655091).

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(8) Tahara, Y.; Matsubara, R.; Shibata, T. *Heterocycles, in press* (DOI: 10.3987/COM-14-S(K)78).

(9) The reaction of 1,6-diyne **1a** and benzothiophene gave no cross-cycloadduct at all under the same reaction conditions.

(10) These regioisomeric structures were determined by NOESY analyses (see Supporting Information).

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(12) The reaction of unsubstituted benzodithiophene tetraoxide with diyne **1a** proceeded, but the yield was very low and most of tetraoxide was recovered due to its poor solubility in DCE.

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