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Rhodium-catalyzed carbothiolation reaction of 1-alkylthio-1-alkynes

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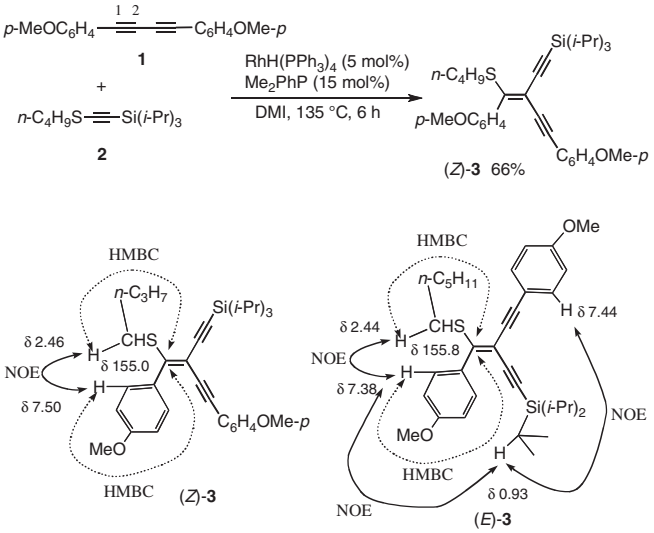
ABSTRACT

A rhodium complex derived from $RhH(PPh_3)_4$ and Me_2PhP catalyzed the carbothiolation reaction of 1-alkylthio-1-alkynes and 1,4-diaryl-1,3-butadiynes giving (*Z*)-4-alkylthio-4-aryl-3-arylethynyl-3-buten-1-ynes. Terminal alkynes such as 1-decyne and (*t*-butylthio)acetylene underwent the carbothiolation reaction using a $RhH(PPh_3)_4$-dppb catalyst. The reactions proceeded via cis-addition with C–C bond formation at the less hindered acetylene carbon.

The carbothiolation reaction[1] of alkynes is a straightforward method of synthesizing alkenylsulfur compounds starting from organosulfur compounds with the insertion of a two carbon unit. The reaction involves the formation of a C–C bond and a C–S bond at a C–C triple bond along with the C–S bond cleavage in the original organosulfur compound, and all three processes need to proceed effectively. Transition metal catalysis is an attractive method for this transformation, and the reaction of organosulfur compounds with strained or polarized C–S bonds using thiranes,[2] thiocarbonates,[3] thiocarbamates,[4] thiocyanates,[5] and thioesters[6] has been carried out. The decarboxylative carbothiolation reaction of thioesters was also reported.[7] The reaction of the less polarized C–S bond, however, was not well investigated with the exception of allyl sulfides[8] and intramolecular reactions.[9] Described in this Letter is the carbothiolation reaction of 1-alkylthio-1-alkynes with 1,3-butadiynes, 1-decyne, and 1-(*t*-butylthio)acetylene.

It was previously found in our laboratory that rhodium complexes cleave the C–S bonds of 1-organothio-1-alkynes,[10] thioesters,[11] and α-organothio ketones,[12] and that organosulfur compounds undergo the organothio exchange reaction with disulfides. It was therefore considered interesting to apply the method to the carbothiolation reaction with alkynes employing the organorhodium intermediates formed in these reactions. This method can be useful for the synthesis of novel organothio enynes.

When an equimolar mixture of 1,4-bis(*p*-methoxyphenyl)-1,3-butadiyne **1** and 1-triisopropylsilyl-2-(butylthio)acetylene **2** in dimethylimidazolidinone (DMI) was heated at 135 °C for 6 h in the presence of $RhH(PPh_3)_4$ (5 mol %) and Me_2PhP (15 mol %), (*Z*)-1-triisopropylsilyl-4-(*p*-methoxyphenyl)-3-(*p*-methoxyphenylethynyl)-4-butylthio-3-buten-1-yne (*Z*)-**3** was obtained in 66% yield (Scheme 1). The compound (*Z*)-**3** slowly isomerized to (*E*)-**3** on standing at room temperature. The structures of (*Z*)-**3** and (*E*)-**3** were determined by NMR studies. The isomer (*Z*)-**3** exhibited NOE between the methylenethio protons at δ 2.46 and the *o*-protons of the arylvinyl group at δ 7.50, and HMBC cross peaks were observed between these protons and an olefin carbon at δ 155.0. Similar NMR observations were made for the (*E*)-**3** isomer. The butylthio and *p*-methoxyphenyl groups therefore should be located on a same olefinic carbon in both isomers. NOE was observed between the isopropyl methine protons of (*E*)-**3** at δ 0.93 and the *o*-protons of arylvinyl group at δ 7.38 as well as the isopropyl methine protons at δ 0.93 and the *o*-protons of arylethynyl group at δ 7.44. The results indicated the (*E*)-stereochemistry of (*E*)-**3**, which in turn determined the (*Z*)-stereochemistry of (*Z*)-**3**.



Scheme 1.

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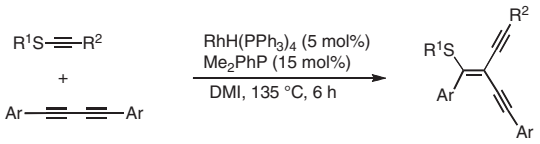
Table 1
Rhodium-catalyzed carbothiolation reaction of 1-alkylthio-1-alkynes and 1,3-butadiynes



Entry	Ar	R^1	R^2	Yield (%)
1	*p*-$MeOC_6H_4$	*n*-C_4H_9	*i*-Pr_3Si	66
2		*cyclo*-C_6H_{11}		48
3		*n*-C_6H_{13}	2,4,6-$Me_3C_6H_2$	58
4		*n*-C_6H_{13}	2,6-$Me_2C_6H_3$	55
5		*n*-C_6H_{13}	C_6H_5	30
6		*n*-C_6H_{13}	$(CH_2)_5C(OMe)$	23
7		*n*-C_6H_{13}	*t*-Bu	13
8		*n*-C_4H_9	*n*-C_4H_9	11
9	*p*-MeC_6H_4	*n*-C_4H_9	*i*-Pr_3Si	46
10	Ph	*n*-C_4H_9	*i*-Pr_3Si	43
11	*p*-ClC_6H_4	*n*-C_4H_9	*i*-Pr_3Si	Trace
12	1-Naphthyl	*n*-C_4H_9	*i*-Pr_3Si	47
13	2-Naphthyl	*n*-C_4H_9	*i*-Pr_3Si	28
14	9-Anthyl	*n*-C_4H_9	*i*-Pr_3Si	28
15	*n*-C_4H_9	*n*-C_4H_9	*i*-Pr_3Si	17

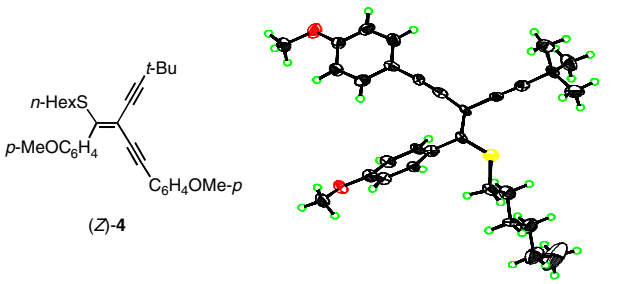


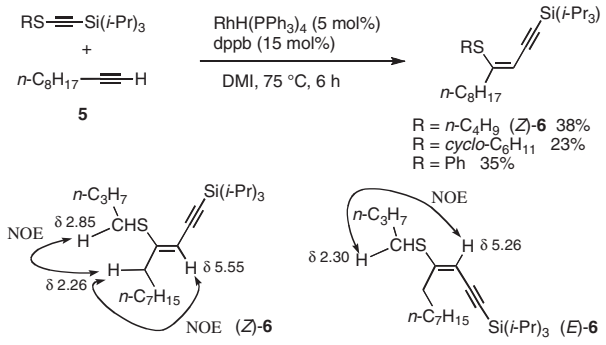
Figure 1. ORTEP view of (*Z*)-**4** (only one molecule) with thermal ellipsoid drawin at 40% probability level.

The X-ray analysis of the product (*Z*)-**4** derived from **1** and 2-(*t*-butyl)-1-(hexylthio)acetylene (Table 1, entry 7) confirmed the structure (Fig. 1).[13] The ethynylation occurred at the carbon-2 of **1** and the C–S bond formation at the carbon-1, and the carbothiolation proceeded via cis-addition.

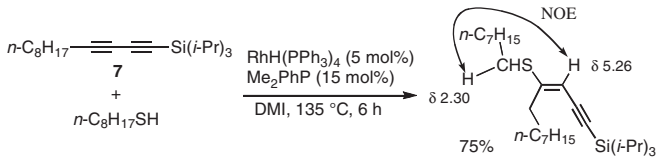
The ligand effect was substantial on the carbothiolation reaction, and only 4% yield of (*Z*)-**3** was obtained without the phosphine. Bidentate ligands such as dppe, dppb, dppBz, and dppf were not effective. The yields of (*Z*)-**3** were comparable or less than 10% using $(p\text{-}MeOC_6H_4)_3P$, $(p\text{-}ClC_6H_4)_3P$, *cyclo*-$C_6H_{11}Ph_2P$, Me_3P, and Et_3P. An elevated high reaction temperature was also required for higher yield, and the yield decreased to 35% and 8% at 125 °C and 100 °C, respectively. The reaction exhibited notable solvent effect. The reaction using aromatic solvents such as toluene and chlorobenzene gave small amounts of the product (<20%).

1-Alkylthio-1-alkynes with triisopropyl, 2,4,6-trimethylphenyl, and 2,6-dimethylphenyl groups provided good yields of the products compared with phenylacetylene (Table 1, entries 1–5). Yields lowered with aliphatic acetylenes (entries 6–8). As for the alkylthio moiety, hexylthio, and cyclohexylthio derivatives reacted smoothly but not *t*-butylthio derivatives (entries 1 and 2). The effect of the aryl substituent on the 1,3-butadiynes was observed, and those with electron donating *p*-substituents gave higher yields of the products (entries 1 and 9–11). The reaction of a dialkyl substituted 1,3-butadiyne proceeded in a low yield (entry 15).

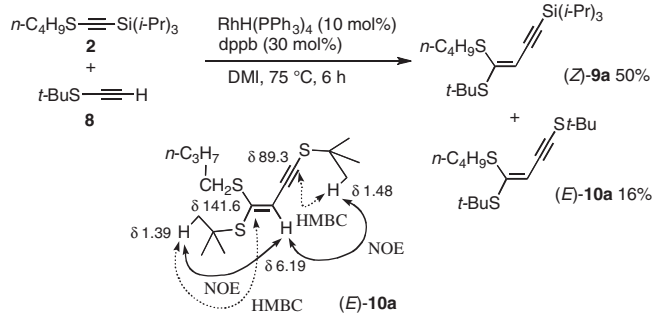
The carbothiolation reaction of 1-alkynes also proceeded under the rhodium-catalyzed conditions. The reaction of 1-decyne **5** and **2** in the presence of $RhH(PPh_3)_4$ (5 mol %) and dppb (15 mol %) in DMI at 75 °C for 6 h gave (*Z*)-4-butylthio-1-triisopropylsilyl-3-dodecen-1-yne (*Z*)-**6** in 38% yield (Scheme 2). The reaction proceeded at lower temperatures than that of 1,3-butadiynes. Isomer (*E*)-**6** was not detected. The structure of (*Z*)-**6** was determined by NOE between the vinyl proton at δ 5.55 and octyl methylene protons at δ 2.26 as well as that between the butylthio methylene proton at δ 2.85 and the methylene protons at δ 2.26. The C–C bond formation occurred at terminal carbon of **5**. Although Me_2PhP used in the reaction of 1,3-butadiynes also promoted the reaction of **5** and **2** giving (*Z*)-**6** (44%), the product was accompanied by the isomer (*E*)-**6** (21%). It was, however, noted that (*E*)-**6** was not the carbothiolation product but the addition product of 1-butanethiol to 1-triisopropylsilyl-1,3-dodecadiyne **7**, which was formed by the coupling reaction of **2** and **5**. Correspondingly, when **7** was reacted with 1-octanethiol in the presence of $RhH(PPh_3)_4$ (5 mol %) and



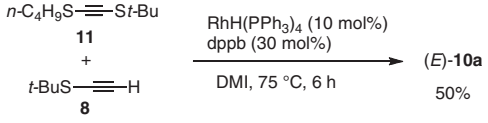
Scheme 2.



Scheme 3.

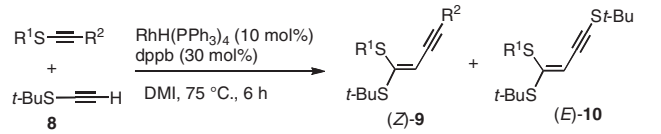


Scheme 4.



Scheme 5.

Table 2
Rhodium-catalyzed carbothiolation reaction of 1-organothio-1-alkynes and **8**



Entry	R^1	R^2	Yield (%)	
			(*Z*)-**9**	(*E*)-**10**
1	*n*-C_4H_9	*i*-Pr_3Si	50	16
2	*n*-C_6H_{13}	*i*-Pr_3Si	42	15
3	Ph	*i*-Pr_3Si	39	Trace
4	*n*-C_6H_{13}	2,4,6-$Me_3C_6H_2$	34	14
5	*n*-C_6H_{13}	1-Adamantyl	17	4

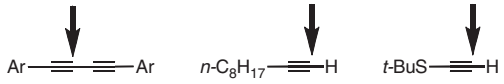


Figure 2. The C–C bond formation sites in the carbothiolation reaction.

Me_2PhP (15 mol %) in DMI at 135 °C for 6 h, the (*E*)-adduct was obtained in 75% yield without forming the (*Z*)-isomer (Scheme 3). In addition, no isomerization of (*Z*)-**6** to (*E*)-**6** was observed under the rhodium-catalyzed conditions.

1-(*t*-Butylthio)acetylene **8** was a good substrate for the carbothiolation reaction. The reaction of **2** and **8** gave (*Z*)-4-(butylthio)-4-(*t*-butylthio)-1-triisopropylsilyl-3-buten-1-yne (*Z*)-**9a** in 50% yield, which was accompanied by (*E*)-4-(butylthio)-1,4-bis(*t*-butylthio)-3-buten-1-yne (*E*)-**10a** in 16% yield (Scheme 4). The structure of (*E*)-**10a** was determined by NOE and HMBC experiments. The minor product (*E*)-**10a** was formed by the butylthio transfer from **2** to **8** giving 1-(*t*-butylthio)-2-butylthioacetylene **11**, which underwent the carbothiolation reaction with **8**. The mechanism was confirmed by an independent reaction of **11** and **8** giving (*E*)-**10a** (Scheme 5). Similarly to that of 1-decyne **5**(Scheme 2), the C–C bond formation of **8** occurred at the terminal carbon by cis-addition. The high reactivity of **8** compared with 1-decyne **5** may be partly due to the interaction of the sulfur atom with rhodium.

Several 1-alkylthio- and 1-phenylthio-1-alkynes were reacted with **8**, and the carbothiolated products (*Z*)-**9** were obtained as well as butylthio transfer products (*E*)-**10** (Table 2). Not only triisopropylsilylacetylene but also 2,4,6-trimethylphenylacetylene and (1-adamantyl)acetylene underwent the carbothiolation reaction with **8**.

In summary, in the presence of a rhodium complex and an appropriate phosphine ligand, the carbothiolation reaction of 1-alkylthio-1-alkynes proceeded with 1,3-butadiynes, 1-decyne, and (*t*-butylthio)ethyne. The carbothiolation reaction of 1-alkylthio-1-alkynes has not yet been identified. The C–C bond formation occurred at the less hindered carbon atom of alkynes (Fig. 2) with the cis-stereochemistry.

In a two-necked flask equipped with a reflux condenser were placed tetrakis(triphenylphosphine)hydriderhodium (5 mol %, 17.3 mg), dimethylphenylphosphine (15 mol %, 6.4 μL), 1-butylthio-2-(triisopropylsilyl)ethyne 2 (0.30 mmol, 81.2 mg) and 1,4-bis(4-methoxyphenyl)-1,3-butadiyne 1 (0.30 mmol, 78.7 mg) in 1,3-dimethyl-2-imidazolidinone (0.75 mL) under an argon atmosphere, and the solution was heated at 135 °C for 6 h. Then, the solvent was removed under reduce pressure, and the residue was purified by flash column chromatography on silica gel giving (*Z*)-3 (105.3 mg, 66%).

Acknowledgments

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Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2010.12.065.

References and notes

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13. Crystal Data Monoclinic Pa, Cell Dimensions: $a = 18.943(7)$, $b = 11.891(5)$, $c = 24.688(10)$ Å, $\beta = 96.535(2)°$, $Z = 8$, $T = 173$ K, Crystallographic data excluding structure factors have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication number CCDC 795726. A copy of the data can be obtained free of charge from CCDC, 12 Union Road, Cambridge CB2 1EZ, UK or e-mail: deposit@ccdc.cam.ac.uk.