Communication

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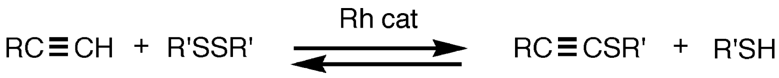

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Equilibrating C−S Bond Formation by C−H and S−S Bond Metathesis. Rhodium-Catalyzed Alkylthiolation Reaction of 1-Alkynes with Disulfides

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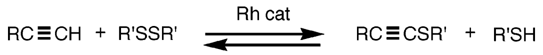
Use of transition metal catalyst for the C−H functionalization of organic molecules is a challenge in organic synthesis. For such a reaction to proceed, the catalyst must effectively be able to activate a C−H bond and form a new bond. Addition reaction to unsaturated bonds has been employed for the latter process, particularly for C−C bond formation.[1−3] In contrast, in the synthesis of heteroatom compounds such as organosulfur compounds, metathesis of C−H and S−S bonds to form C−S bonds is more important,[4,5] since a variety of S−S compounds are readily available including organic polysulfides and elemental sulfur.[6] Such catalytic synthesis of organosulfur compounds, however, is not known. Described herein is the rhodium-catalyzed alkylthiolation reaction of 1-alkynes with disulfides.[7] This is an unprecedented equilibrating oxidation reaction of hydrocarbons to organosulfur compounds involving reversible C−H, C−S, S−S, and S−H bond cleavage and metathesis (Scheme 1). Conventional syntheses of alkylthioacetylenes from 1-alkynes require stoichiometric amounts of organometallic or organic bases to promote the C−H activation or to trap the HX species generated.[8] In contrast, the present reaction employs a catalytic amount of a rhodium complex as the only activator without any added base.

Scheme 1



$$RC\equiv CH + R'SSR' \underset{}{\overset{\text{Rh cat}}{\rightleftharpoons}} RC\equiv CSR' + R'SH$$

To a mixture of triethylsilylacetylene **1**, $RhH(PPh_3)_4$ (2 mol %), and 1,1′-bis(diphenylphosphiono)ferrocene (dppf) (3 mol %) in acetone was added bis{2-(*t*-butoxycarbonylamino)}ethyl disulfide **2** (3 equiv), and the mixture was heated at reflux for 1 h. 1-{2-(*t*-Butoxycarbonylamino)ethyl}-2-triethylsilylacetylene **3** was obtained in 77% yield, which was accompanied by 2-(*t*-butoxycarbonylamino)ethanethiol **4** (69%) and a small amount of 1-{2-(*t*-butoxycarbonylamino)ethyl}-1-triethylsilylethylene **5** (4%) (Scheme 2). Other rhodium complexes such as $RhCl(PPh_3)_3$, $[RhCl(cod)_2]_2$, $[RhCl_2Cp^*]_2$, $Rh(acac)_3$, and $RhCl_3$ in the presence of dppf showed very low activities. A low yield (9%) of **3** was obtained in the absence of dppf, and the use of several other bidentate ligands revealed a high efficiency of dppf for this reaction: dppe (not detected), dppp (not detected), dppb (34%), dpppentane (29%), and dpphexane (4%). Monodentate ligands, PPh_3, $(p\text{-}ClC_6H_4)_3P$, and $(p\text{-}MeOC_6H_4)_3P$, gave small amounts (<15%) of **3**. Various dialkyl disulfides, including dimethyl disulfide, underwent alkylthiolation with silylacetylenes. In all cases, addition products of thiols to the acetylenes were obtained in less than 5% yield (Table 1, entries 1−7, 11, and 12).

Scheme 2

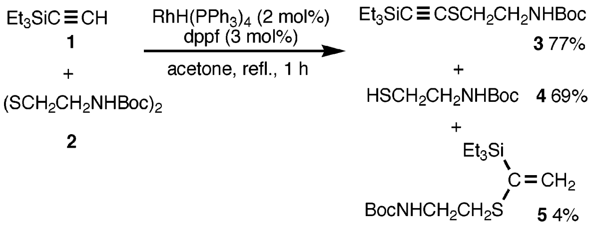
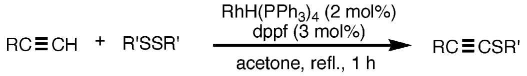


Table 1. Rh-Catalyzed Alkylthiolation of 1-Alkynes with Disulfides[a]



$$RC\equiv CH + R'SSR' \xrightarrow[\text{acetone, refl., 1 h}]{\text{RhH(PPh}_3)_4\text{ (2 mol\%)}\ \text{dppf (3 mol\%)}} RC\equiv CSR'$$

entry	R	R′	yield/%
1	Et_3Si	CH_2CH_2NHBoc	77
2		Me	74
3		$n\text{-}C_4H_9$	80
4		$i\text{-}C_5H_{11}$	81
5		$n\text{-}C_8H_{17}$	86
6		$(CH_2)_2OMe$	76
7		$(CH_2)_2CO_2Me$	83
8		Ph	86
9		$p\text{-}ClC_6H_4$	82
10		$p\text{-}MeC_6H_4$	79
11	$i\text{-}Pr_3Si$	Me	62
12		$n\text{-}C_8H_{17}$	75
13	$2,6\text{-}Me_2C_6H_3$	$n\text{-}C_8H_{17}$	54
14	$2,4,6\text{-}Me_3C_6H_2$	Me	64
15		Ph	81
16	1-adamantyl	Me	66
17		$n\text{-}C_8H_{17}$	81
18	$(CH_2)_5C(OMe)$	Ph	96
19	$(CH_2)_5C(OTBS)$	Ph	86

[a] Procedures for the reaction of dialkyl disulfide: $RhH(PPh_3)_4$ (2 mol %) and dppf (3 mol %) were used, and the mixture was heated at reflux for 1 h. Procedures for the reaction of diaryl disulfide: $RhH(PPh_3)_4$ (2 mol %) and dppf (4 mol %) were used, and the mixture was stirred at room temperature for 12 h. See SI for details.

A notable aspect of this reaction is the formation of free thiols, which does not interfere with the reaction. In addition, the thiols do not add to the silylacetylenes, although several transition metal complexes are known to catalyze such a reaction.[9] The addition products, however, were obtained by slightly modifying the conditions: When **1** and **2** were reacted at room temperature in the presence of Rh complex (2 mol %) and dppf (4 mol %), the thiol adduct **5** was obtained in 31% and **3** was obtained in 64% yield; under Rh complex (2 mol %) and dppf (2 mol %) conditions, **5** decreased to 6% and **3** to 47%. The dramatic effect of the catalyst composition may be explained by the formation of 1:1 and 1:2 complexes, of which the latter is involved in the thiol addition reaction. Under acetone refluxing conditions, 1:1 complex formation should be favored.

Alkyacetylenes were also alkylthiolated, provided that they possessed tertiary substituents (entries 16 and 17). Aromatic acetylenes exhibited similar behaviors as shown by the reactions of 2,6-dimethyl- and 2,4,6-trimethylphenylacetylene (entries 13 and 14). The need for the bulky group is partly due to competition with

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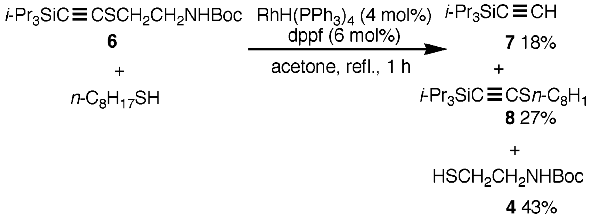
alkyne dimerization; such a byproduct was obtained in 50% yield in the reaction of *o*-tolylacetylene and dioctyl disulfide with the expected 1-octylthioacetylene in 28% yield.

Reactions of diaryl disulfides required a modification of the conditions (entries 8−10, 15, 18, and 19), since the reaction under the above conditions gave very small amounts of the arylthiolated products because of serious deactivation of the catalyst. A mixture of $RhH(PPh_3)_4$ (2 mol %) and dppf (4 mol %) was heated at reflux for 10 min to form the active catalyst. Then, **1** and diphenyl disulfide (3 equiv) were added, and the reaction was conducted at room temperature for 12 h. 2-Phenylthio-1-triethylsilylacetylene was obtained in 86% yield, although in this case, the thiol adduct was formed in 40% yield, as expected from the catalyst composition and reaction conditions.

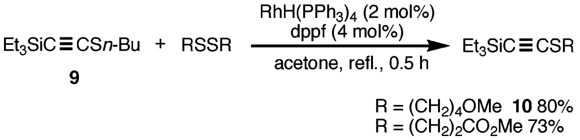
Another interesting aspect of this reaction is its equilibrating nature. Reaction of 1-octanethiol with 1-triisopropylsilyl-2-{(*t*-butoxycarbonylamino)ethylthio}ethyne **6** in the presence of $RhH(PPh_3)_4$ (4 mol %) and dppf (6 mol %) at acetone reflux for 1 h gave triisopropylsilylacetylene **7** (18%), 1-triisopropylsilyl-2-octylthioethyne **8** (27%), and **4** (43%) with the recovered **6** (41%) (Scheme 3). A mixture of disulfides possessing 1-octyl and 2-(*t*-butoxycarbonylamino)ethyl groups was also formed.

Scheme 3



In addition, alkylthio exchange reaction of disulfides and thioacetylenes took place. The treatment of 1-butylthio-2-triethylsilylethyne **9** with bis(4-methoxybutyl) disulfide (3 equiv) in refluxing acetone for 0.5 h in the presence of $RhH(PPh_3)_4$ (2 mol %) and dppf (4 mol %) gave the exchanged product **10** in 80% yield (Scheme 4). The experimental yield coincided with the yield of 80% at the equilibrium, calculated assuming the same S−S bond energies of two thioacetylenes. It is concluded that the present oxidation reaction of C−H to C−S is under equilibrium, as shown in Scheme 1.

Scheme 4



The catalyst may be involved in several reversible organometallic processes: C−H activation of acetylene, S−S bond cleavage of disulfide, C−S bond cleavage of thioacetylene, S−H activation of thiol, C−S bond formation between the alkylthio group and alkynyl sp-carbon, C−H bond formation between hydride and alkynyl sp-carbon. The catalyst can also participate in the addition reaction of thiol to acetylene. We previously reported that a catalyst system of $RhH(PPh_3)_4$, phosphine, and trifluoromethanesulfonic acid catalyzes disulfide addition to alkynes,[3] in which the presence of the acid was critical for the addition to occur. Such multiple functions and its selectivity control by judicious choice of the conditions are other notable aspects of the rhodium catalysis in organosulfur transformations.

It was shown that a rhodium catalyst can equilibrate a C−H bond and a C−S bond by lowering the activation energies of multiple organometallic processes. Such an equilibration methodology of forming C−S bonds, which requires low energy and generates minimum waste, would be a powerful tool for the synthesis of organosulfur compounds from hydrocarbons.

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Supporting Information Available: Detailed experimental procedure and characterization data. This material is available free of charge via the Internet at http://pubs.acs.org.

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