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Synthesis of Thiiranes by Rhodium-catalyzed Sulfur Addition Reaction to Reactive Alkenes

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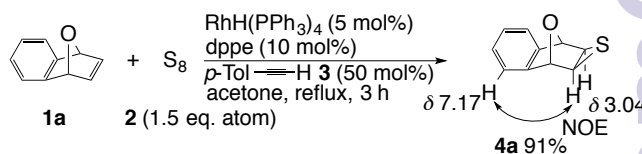
Mieko Arisawa,^{a*} Takuya Ichikawa,^a and Masahiko Yamaguchi^{a*}

A rhodium complex derived from RhH(PPh₃)₄, dppe, and 4-ethynyltoluene catalyzes the addition reaction of sulfur to norbornenes giving the corresponding thiiranes under acetone reflux conditions. The rhodium complex effectively transfers a sulfur atom to the double bond from sulfur, and *exo*-adducts are obtained. The reaction is also applicable to (*E*)-cyclooctene and cyclic allenes. The ring-opening reaction of the thiiranes with lithium aluminium hydride gives the corresponding thiols.

Thiiranes form an interesting group of heterocyclic organosulfur compounds.^[1] Generally, they are prepared by the nucleophilic addition/elimination reaction of oxiranes with reactive sulfur reagents such as thiocyanate and thiourea,^[2] and by the electrophilic addition/elimination reaction of alkenes with sulfur reagents such as sulfonyl chloride and thiocyanogen.^[3,4] The reaction of alkenes with sulfur is highly advantageous, because sulfur is inexpensive, readily available, and easy to handle. Efficient methods, however, remain undeveloped. Scattered examples of thiirane synthesis under radical conditions at high temperatures or under light irradiation were reported to give mixtures of sulfurated products containing thiiranes.^[5]

The use of transition-metal catalysis can be attractive for controlling the reaction of alkenes and sulfur. The molybdenum-catalyzed addition of sulfur to (*E*)-cyclooctene, (*E*)-cyclononene, and 1,2-cyclononadiene under refluxing acetone was reported.^[6] The reaction, however, is relatively sluggish and requires a longer reaction time. The ruthenium-catalyzed formation of cyclohexene sulfide was also reported, although it was not reproduced.^[7] A limited substrate scope is another serious issue in these synthesis. Thus, it is desirable to develop an efficient catalytic method for the synthesis of a diverse of thiiranes from alkenes and sulfur. Described here is the rhodium-catalyzed addition reaction of sulfur to alkenes, which involves various norbornene derivatives, (*E*)-cyclooctene, and cyclic allenes. The reaction is much faster than the molybdenum method, and completes in most cases within 3 h in acetone reflux. The rhodium complex effectively transfers a sulfur atom to the double bonds from sulfur.

When 7-oxabenzonorbornadiene **1a** and sulfur **2** (1.5 equiv. atom) were reacted in refluxing acetone for 3 h in the presence of RhH(PPh₃)₄ (5 mol%), dppe (10 mol%), and 4-ethynyltoluene **3** (50 mol%), *exo*-1,2,7,8-tetrahydro-2,7-epoxynaphtho[2,3-*b*]thiirane **4a** was obtained in 91% yield (Scheme 1). Alkyne **3** was recovered in 70% yield. The reaction was fast, and **4a** was obtained in 76% yield within 1 h, with a calculated TOF = 15 h⁻¹. The *exo*-configuration of **4a** was determined by NOE between the aromatic proton at δ 7.17 and the thiirane proton at δ 3.04. The rhodium complex and dppe were both essential for the reaction, and no reaction occurred in the absence of either substance. Without the addition of alkyne **3**, the yield of **4a** decreased to 53%. The yield of **4a** decreased to 68% when using 20 mol% **3** and to 76% when using 100 mol%. Other alkynes in the presence of RhH(PPh₃)₄ and dppe exhibiting similar activities include 2-ethynyltoluene (84%), 3-ethynyltoluene (81%), phenylacetylene (77%), and *p*-fluorophenylacetylene (80%) whereas 1-decyne (41%), 1-triisopropylsilylethyne (41%), 1-phenyl-1-propyne (46%), and 1,4-diphenyl-1,3-butadiyne (45%) were ineffective. Other metal complexes exhibiting activity using **1a** and sulfur (1.5 eq. atom) in the presence of dppe and **3** (50 mol%) were RhH(PPh₃)₄ (91%), RhH(CO)(PPh₃)₃ (32%), and Rh(acac)(CH₂=CH₂)₂ (20%). In contrast, RhCl(PPh₃)₃, [Rh(OAc)₂], Rh(acac)₃, and [Rh(cod)₂]BF₄ were less effective. The effect of the phosphine ligand was also substantial, and other bidentate ligands with phosphino groups separated by two carbon atoms such as 1,2-bis[di(4-methoxyphenyl)phosphino]benzene (64%), 1,2-bis(diphenylphosphino)benzene (72%), and 1,2-bis(diphenylphosphino)ethylene (65%) exhibited catalytic activity. The yield of **4a** decreased to 58, 76, and 34% when using bis(4-chlorophenyl) trisulfide, bis(4-chlorophenyl) tetrasulfide, and 1,1-dimethylthiirane in place of sulfur, respectively.



Scheme 1.

Sulfur reacted with various norbornenes giving the corresponding *exo*-thiiranes in the presence of the rhodium catalyst (Table 1). 7-Oxabenzonorbornadienes and 7-azabenzonorbornadiene **1a-d** gave *exo*-thiiranes **4a-d** in high yields (entries 1-4). Benzenorbornene, 5-acetylnorbornene, and norbornene formed *exo*-thiiranes **4e-g** in modest yields (entries 5-7). The heteroatom at the 7-position increased the yield of products, which may be due to the increased ring strain of the heteroatom-substituted benzenorbornadienes.^[8] The reaction of norbornadiene and dicyclopentadiene gave monothiiranes **4h^[9]** and **4i** (entries 7 and 8), and the second thiirane formation was slow. The addition of sulfur to 1-octene and styrene, however, did not occur. The rhodium complex transfers a sulfur atom to norbornene double bonds effectively.

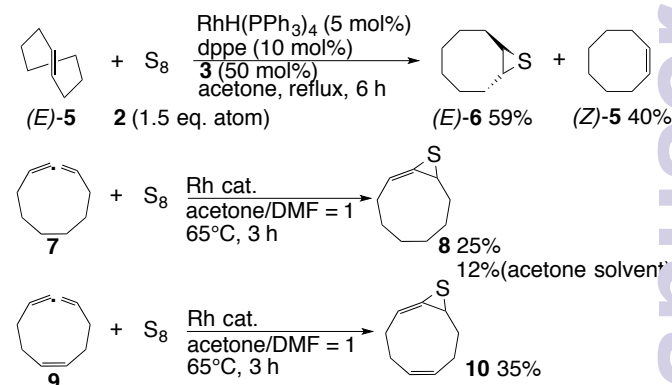
Table 1. Rhodium-catalyzed sulfur addition to various norbornenes.

Entry	Norbornenes	Thiiranes	Yield of 4/%
1			91 (4a)
2			87 (4b)
3			83 (4c)
4			75 (4d)
5			44 (4e)
6			24 ^a (4f)
7			24 ^b (4g)
8			36 ^a (4h)
9			29 ^a (4i)

^a) Using norbornenes (3 eq.) and **2** (1 eq.). ^b) Using **1g** (5 eq.).

(*E*-Cyclooctene (*E*-**5**) and cycloallenes with reactive double bonds also gave the thiiranes (Scheme 2). (*E*-**5** was converted to *trans*-

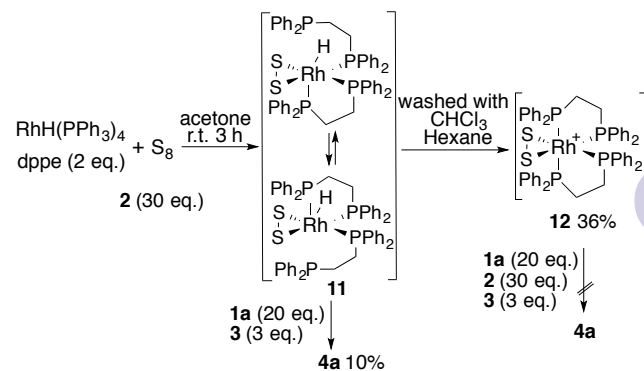
cyclooctene sulfide **6^[10]** in 59% yield, which was accompanied by the recovery of (*Z*-cyclooctene (*Z*-**5** in 40% yield. 1,2-Cyclononadiene **7** and 1,2,6-cyclononatriene **9** reacted with sulfur **2** to give the corresponding thiiranes **8** (25%) and **10** (35%), respectively. The yields of **8** and **10** were improved in acetone/DMF mixture solvent compared with in acetone.



Scheme 2

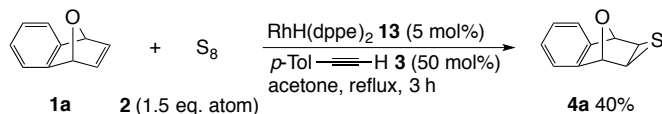
RhH(PPh₃)₄ and dppe were reacted with sulfur (30 equiv.) in acetone at r.t. for 3 h, the solvent was removed, and the mixture was washed with chloroform and hexane. Then, [RhS₂(dppe)₂]⁺ complex **12** was obtained in 36% yield as purple crystals (Scheme 3). The structure was determined by LC-MS (ESI) analysis, *m/z* 963.1222, [RhS₂(dppe)₂]⁺: calcd. for 963.1203, and elemental analysis, calcd. for C₅₂H₄₈ClP₄RhS₂: C, 62.50%; H, 4.84%; Cl, 3.55%; S, 6.42%, found: C, 62.39%; H, 4.97%; Cl, 3.46%; S, 6.42%. ³¹P-NMR analysis showed two peaks at δ 50.1 (dd, *J* = 126.7, 16.5 Hz) and 52.1 (dd, *J* = 87.0, 16.8 Hz), which were assigned to the equatorial phosphorus and apical phosphorus, respectively.^[11] The ¹H-NMR of **12** coincided with that of the known dithiorhodium complex [Rh⁺S₂(dppe)₂]Cl⁻, which was synthesized from [Rh⁺(dppe)₂]Cl⁻ and sulfur.^[12] When 7-oxabenzonorbornene **1a** (20 equiv.), **2** (30 equiv.), and alkyne **3** (3 equiv.) were reacted with the complex **12** in refluxing acetone for 3 h, thiirane **4a** was not formed.

Chloride in **12** is derived from chloroform used to wash the complex, and another rhodium complex **11** is formed before washing. ESI LC-MS analysis of the mixture provided *m/z* 963.1175, which was assigned to [RhS₂(dppe)₂]⁺: calcd. for 963.1203. ³¹P-NMR analysis showed two peaks at δ 49.4 (bs) and 50.1 (dd, *J* = 38.2, 15.2 Hz), which suggested the flipping of two phosphorus atoms.^[13] The reaction of **11**, **1a** (20 equiv.), and **3** (3 equiv.) gave thiirane **4a** in 10% yield. Thus, the dithiorhodium complex **11** may be an active species.



Scheme 3

Dppe complex **13** catalyzed the formation of **4a** from **1a** and sulfur. When **1a** and sulfur **2** (1.5 equiv. atom) were reacted in refluxing acetone for 3 h in the presence of **13** (5 mol%) and 4-ethynyltoluene **3** (50 mol%), thiirane **4a** was obtained in 40% yield (Scheme 4). The result suggests the mechanism involving the formation of **13**.



Scheme 4

A mechanism is proposed for this catalytic sulfur atom transfer reaction (Figure 1). RhH(dppe)₂ **13** is formed by the ligand exchange of RhH(PPh₃)₄. Dithiorhodium species **11**, which is coordinated with two sulfur atoms and two dppe ligands, is formed by sulfuration of **13**. Then, **11** reacts with norbornadiene **1** giving **4** and a rhodium sulfide species **14**.^[14] Subsequent sulfur atom transfer from **14** to **1** gives **4** and regenerates **13**.

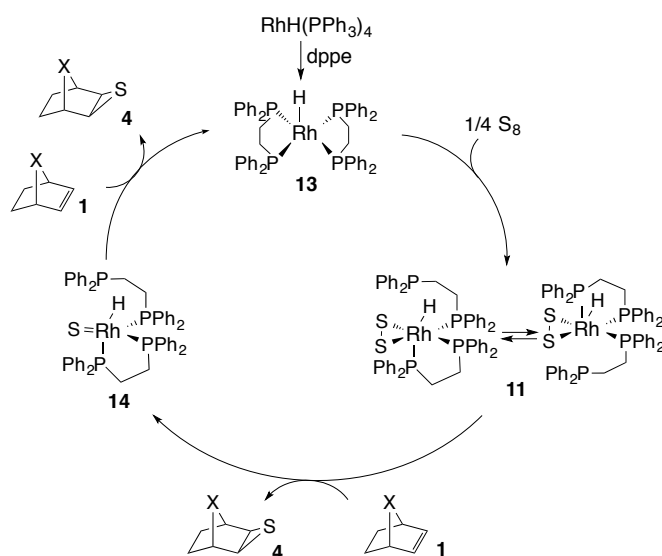
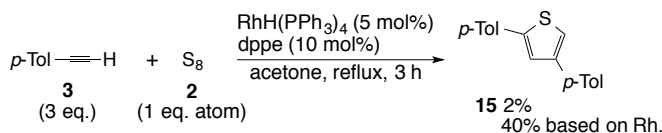


Figure 1. Possible mechanism

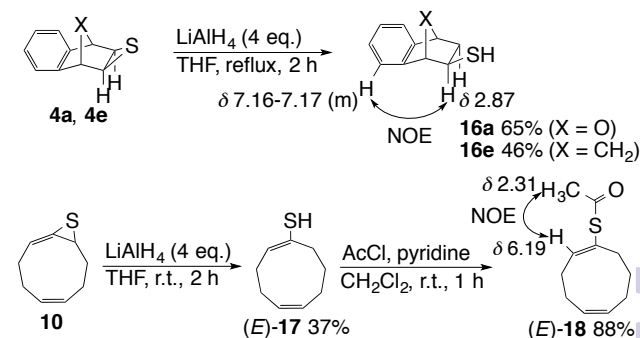
In order to probe the role of alkynes, 4-ethynyltoluene **3** (3 equiv.) and sulfur **2** (1 equiv. atom) were reacted in refluxing acetone for 3 h in the presence of RhH(PPh₃)₄ (5 mol%) and dppe (10 mol%). 2,4-Bis(*p*-tolyl)thiophene **15** was obtained in 2% yield (40% yield based on rhodium) with the recovery of **3** (93%) (Scheme 5). Alkyne probably promotes the reaction via coordination with rhodium.



Scheme 5

The reductive ring-opening reaction of thiiranes gave thiol derivatives.^[15] When **4a** was reacted with lithium aluminium hydride (4 equiv.) in refluxing THF for 2 h, *exo*-1,2,7,8-tetrahydro-2,7-

epoxynaphthalene-1-thiol **16a** was obtained in 65% yield (Scheme 6). The *exo*-configuration of **16a** was determined by NOE between the aromatic proton at δ 7.17 and the *endo*-proton at δ 2.87. **4e** was also reduced to **16e** in 46% yield. Thus, *exo*-bicyclo[2.2.1]heptane-1-thiol can readily be synthesized stereoselectively via thiiranes starting from norbornene and sulfur.^[16] The ring opening of thiirane **16** formed vinyl thiol (*E*)-**17** in 37% yield, which is a rare example of the synthesis of the organosulfur compound.^[17] The (*E*)-configuration was determined by NOE in the acetate (*E*)-**18** between the alkene proton at δ 6.19 (t) and the acetyl proton at δ 2.31 (s).



Scheme 6

Conclusions

In summary, in the presence of a rhodium complex, the addition reaction of sulfur to various norbornenes, (*E*)-cyclooctene, and cyclic allenes gave the corresponding thiiranes. The added ethynyltoluene improved the yield of the products. This reaction can be a useful synthetic method for thiiranes from reactive alkenes.

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^a Department of Organic Chemistry, Graduate School of Pharmaceutical Sciences, Tohoku University, Aoba, Sendai, 980-8578, Japan. Fax: +81-22-795-6811; Tel: +81-22-795-6812; E-mail: yama@m.tohoku.ac.jp, arisawa@m.tohoku.ac.jp

† Electronic Supplementary Information (ESI) available: [details of any supplementary information available should be included here]. See DOI: 10.1039/c000000x/

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