

# Rhodium-catalyzed sulfur atom exchange reaction between organic polysulfides and sulfur

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**Abstract**—RhH(PPh<sub>3</sub>)<sub>4</sub> and *cis*-1,2-bis(diphenylphosphino)ethylene (dppv) catalyze the exchange of sulfur atoms between sulfur and organic polysulfides. The exchange of dialkyl trisulfides with sulfur proceeds at a high efficiency within 5 min at room temperature yielding a mixture of organic polysulfides.

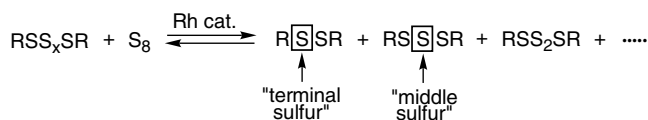
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Sulfur, one of the few elements produced in nature, is an important starting material for the synthesis of organo-sulfur compounds used in pharmaceuticals. The direct use of sulfur in organic synthesis, however, is rare, which is due to the lack of an efficient activation method for sulfur. Thermal/photochemical<sup>1</sup> or acid/base<sup>2</sup> activations require harsh reaction conditions, and are not easy to control. Often, these methods employ stoichiometric amounts of activating reagents. The catalytic activation of sulfur by transition metal complexes can provide a new approach in this field, which has an advantage of being controllable by changing metal and ligand.<sup>3</sup> The method, however, has not been well developed because of the serious deactivation of metal catalysts by sulfur.<sup>4</sup> Recent examples of the catalytic activation of organic disulfides are notable,<sup>5,6</sup> although their application to sulfur activation is not straightforward. Sulfur atoms in disulfides with C–S and S–S bonds are called the ‘terminal sulfur’, while atoms in sulfur with two S–S bonds are called the ‘middle sulfur’. The reactivities of these sulfurs are considerably different, and in particular the interaction of the latter with transition metal complexes readily leads to the formation of unreactive metal sulfides. The manipulation of middle sulfur atoms is essential for the development of effective transition metal catalysts for sulfur.

We previously reported that a rhodium complex catalyzes disulfide exchange reactions,<sup>6</sup> which proceed very rapidly at room temperature even with alkyl disulfides.

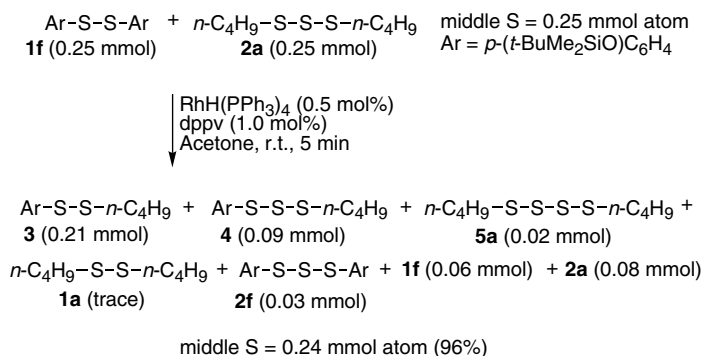
It is therefore an interesting subject whether this method can be used to control middle sulfur. In this study, the exchange reaction of sulfur atoms between organic polysulfides and sulfur is examined (Scheme 1). Such a reaction of acyclic polysulfides is generally slow even at high temperatures.<sup>7–9</sup> For example, an equilibrium was reached in a neat mixture of dimethyl disulfide and elemental sulfur after 40 days at 120 °C.<sup>8</sup> The exchange reaction between neat diethyl disulfide and sulfur was conducted at 120–128 °C for 5 h in the presence of a catalytic amount of dibutylamine.<sup>9</sup> Although some exchange reactions of sulfur and cyclic polysulfides proceed under milder conditions, they at least in some part rely on ring strain, and therefore have limitation in the substrate.<sup>10</sup> It was found here that the rhodium complex with a suitable ligand can catalyze the very rapid exchange reaction of acyclic polysulfides without deactivation.

As a preliminary study, the reaction of a trisulfide and a disulfide was examined. Bis[*p*-(*tert*-butyldimethylsilyloxy)phenyl] disulfide **1f** (0.25 mmol) and dibutyl trisulfide **2a** (0.25 mmol) were reacted in the presence of RhH(PPh<sub>3</sub>)<sub>4</sub> (0.5 mol %) and dppv (1.0 mol %) in acetone (stirring for 5 min at room temperature, and butyl *p*-(*tert*-butyldimethylsilyloxy)phenyl disulfide **3**



Scheme 1.

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Scheme 2.

(0.21 mmol), butyl *p*-(*tert*-butyldimethylsilyloxy)phenyl trisulfide **4** (0.09 mmol), dibutyl tetrasulfide **5a** (0.02 mmol), dibutyl disulfide **1a** (trace), and diaryl trisulfide **2f** (0.03 mmol) were obtained with the recovery of **1f** (0.06 mmol) and **2a** (0.08 mmol) (Scheme 2). The mass balance for terminal sulfur atoms was 98%, and that for middle sulfur atoms was 96%. This indicates that middle sulfur atoms exchange rapidly in the presence of a rhodium catalyst without loss.

Then, the method was applied to the exchange reaction of sulfur. When **2a** (0.25 mmol) was treated with sulfur (0.25 mmol atom) in the presence of RhH(PPh<sub>3</sub>)<sub>4</sub> (2.5 mol %) and dppv (5.0 mol %) in acetone with stirring, sulfur rapidly disappeared within 5 min at room temperature yielding the disulfide **1a** (0.005 mmol), tetrasulfide **5a** (0.096 mmol), pentasulfide **6a** (0.034 mmol), hexasulfide **7a** (0.021 mmol), and heptasulfide **8a** (trace) with the recovery of **2a** (0.096 mmol) (determined by <sup>1</sup>H

NMR) (Table 1, entry 1). The polysulfides were isolated by preparative reverse-phase HPLC, and higher organic polysulfides were observed by HPLC (Fig. 1). The structures of **5a**, **6a**, **7a**, and **8a** were determined by <sup>1</sup>H/<sup>13</sup>C NMR spectroscopy, and MS. The <sup>1</sup>H NMR chemical shifts of the methylene protons adjacent to the sulfur atom in the organic polysulfides showed a tendency to appear at a lower field as the sulfur atom increased in number from disulfide to heptasulfide.<sup>7</sup>

Exchange efficiency  $\Delta S = \{[\mathbf{5a}] + 2[\mathbf{6a}] + 3[\mathbf{7a}] - [\mathbf{1a}]\} / [\text{sulfur}]_0$  is defined here, where **5a**, **6a**, **7a**, and **1a** are the yields (mmol) of all products, and  $[\text{sulfur}]_0$  is the initial amount (mmol atom) of sulfur.  $\Delta S$  shows the amount of middle sulfur atoms transferred to the organic polysulfides, and  $\Delta S = 100\%$  indicates that all the sulfur atoms of sulfur are introduced into the polysulfides. The above exchange reaction occurred at a high exchange efficiency  $\Delta S = 89\%$  (entry 1). Catalyst loading

Table 1. Rhodium-catalyzed sulfur atom exchange between trisulfides and sulfur<sup>a</sup>

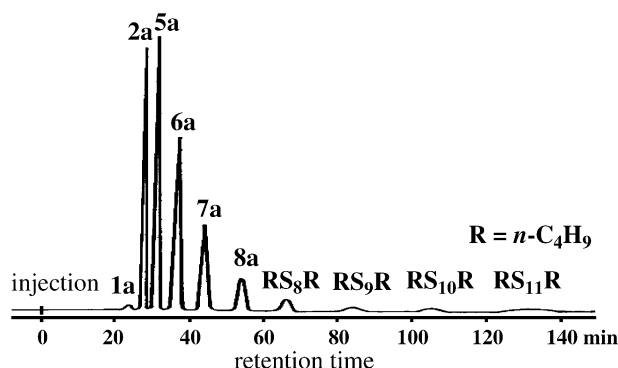
Run	R	Phosphine <sup>b</sup>	Yield/mmol					$\Delta S/\%$
			5	6	7	1	2	
1	<i>n</i> -C <sub>4</sub> H <sub>9</sub> <b>a</b>	dppv	0.096	0.034	0.021	0.005	0.096	89
2 <sup>c</sup>			0.174	0.065	0.045	0.015	0.191	85
3		dppm	0.053	0.021	0.011	0.026	0.126	50
4		dppe	0.064	0.028	0.010	0.024	0.124	50
5		dppBz	0.030	0.012	0.004	0.012	0.188	26
6		dppf	0.030	0.020	0.005	0.011	0.178	30
7	<i>n</i> -C <sub>5</sub> H <sub>11</sub> <b>b</b>	dppv	0.092	0.028	0.022	0.004	0.100	84
8	<i>i</i> -C <sub>4</sub> H <sub>9</sub> <b>c</b>		0.091	0.035	0.022	0.007	0.093	88
9	<i>s</i> -C <sub>4</sub> H <sub>9</sub> <b>d</b>		0.098	0.033	0.017	—	0.101	86
10	<i>cyclo</i> -C <sub>6</sub> H <sub>11</sub> <b>e</b>		0.097	0.058	—	—	0.097	85
11 <sup>d</sup>	<i>p</i> -( <i>t</i> -BuMe <sub>2</sub> SiO)C <sub>6</sub> H <sub>4</sub> <b>f</b>		0.027	0.010	0.003	0.031	0.030	25

<sup>a</sup> See text for reaction conditions and yield determination.

<sup>b</sup> dppv: *cis*-1,2-bis(diphenylphosphino)ethylene; dppm: 1,2-bis(diphenylphosphino)methane; dppe: 1,2-bis(diphenylphosphino)ethane; dppBz: 1,2-bis(diphenylphosphino)benzene; dppf: 1,1'-bis(diphenylphosphino)ferrocene.

<sup>c</sup> The reaction was conducted using **2a** (0.5 mmol) and sulfur (0.5 mmol atom) in the presence of RhH(PPh<sub>3</sub>)<sub>4</sub> (0.5 mol %) and dppv (1.0 mol %) for 5 min.

<sup>d</sup> The reaction was conducted using **2f** (0.1 mmol) and sulfur (0.1 mmol atom) in the presence of RhH(PPh<sub>3</sub>)<sub>4</sub> (2.5 mol %) and dppv (5.0 mol %) for 15 min.



**Figure 1.** Reverse-phase HPLC/UV (MeOH, 5 mL/min) chart of a mixture of **1a**, **2a**, **5a**, **6a**, **7a**, **8a**, and higher polysulfides obtained after silica gel treatment of reaction mixture formed from **2a** and sulfur (Table 1, entry 1). The formation of  $RS_xR$  ( $x = 8, 9, 10$ , and  $11$ ) was assumed on the basis of retention time.

could be reduced to 0.5 mol %  $RhH(PPh_3)_4$  and 1.0 mol % dppv at approximately the same efficiency  $\Delta S = 85\%$  (entry 2). The rhodium complex and dppv are essential in this reaction; no reaction takes place in the absence of either reagent under the same conditions.  $\Delta S$  decreased when other bidentate ligands such as dppe (entry 3), dppe (entry 4), dppBz (entry 5), and dppf (entry 6) were used, and dppb was not effective at all. Monodentate phosphines such as triphenylphosphine, tris(*p*-tolyl)phosphine, and tributylphosphine did not exhibit catalytic activity. It turned out that the bidentate ligand with a  $C_2$  chain was effective for the manipulation of the middle sulfur atom, while the electron-rich monodentate ligand was effective for the manipulation of the terminal sulfur atom, as previously reported.<sup>6</sup> The secondary dialkyl trisulfides **2d** and **2e** as well as the primary derivatives **2b** and **2c** undergo rapid exchange reactions with sulfur (entries 7, 8, 9, and 10). Di(*tert*-butyl) trisulfide, however, did not react under the same conditions. The aromatic trisulfide **2f** exhibited a lower  $\Delta S$  (entry 11).

The same rhodium system catalyzes the sulfur atom exchange between organic disulfides and sulfur with slightly different reaction profiles (Table 2). When **1f** (0.5 mmol) was treated with sulfur (0.5 mmol atom) in the presence of  $RhH(PPh_3)_4$  (0.5 mol %) and dppv (1.0 mol %) in acetone with stirring for 5 min at room temperature, the trisulfide **2f** (0.189 mmol), tetrasulfide **5f** (0.075 mmol), pentasulfide **6f** (0.032 mmol), and hexasulfide **7f** (0.011 mmol) were obtained with the recovery of **1f** (0.170 mmol) (by  $^1H$  NMR) at  $\Delta S = \{[2f] + 2[5f] + 3[6f] + 4[7f]\} / [sulfur]_0 = 96\%$  (entry 1). The diaryl disulfides **1g** and **1h** with electron-donating substituent showed higher  $\Delta S$  values than **1i** and **1j** (entries 2, 3, 4, and 5). The exchange reaction took place with the dialkyl disulfides **1k** and **1l** with attached methoxycarbonyl groups (entries 6 and 7); dibutyl disulfide **1a** did not undergo an exchange reaction under these conditions. The substituent effect of disulfides suggests that the balance between the stability and reactivity of the polysulfides to be important. Polysulfides with appropriate substituents may be used as mediators for the transfer of sulfur atoms from sulfur to organic molecules.

The equilibrium nature of the present reaction is shown by the following experimental results. The reaction of **1f** (0.5 mmol) and sulfur (0.25 mmol atom) in the presence of  $RhH(PPh_3)_4$  (1.0 mmol %) and dppv (2.0 mol %) at room temperature for 1 h yielded **2f**, **5f**, and **6f** at  $\Delta S = 99\%$  (Scheme 3). The addition of sulfur (0.25 mmol atom) to this mixture increased the amounts of **2f**, **5f**, **6f**, and **7f**, and decreased that of **1f** at  $\Delta S = 97\%$ . The second sulfur was almost completely incorporated in the organic disulfide, during which this catalyst maintained its activity. An analogous behavior was observed in the reaction of **2a** and sulfur.

To summarize, the exchange of sulfur atoms between an organic disulfide or trisulfide and sulfur rapidly occurs in the presence of  $RhH(PPh_3)_4$  and dppv catalyst.

**Table 2.** Rhodium-catalyzed sulfur atom exchange between disulfides and sulfur<sup>a</sup>

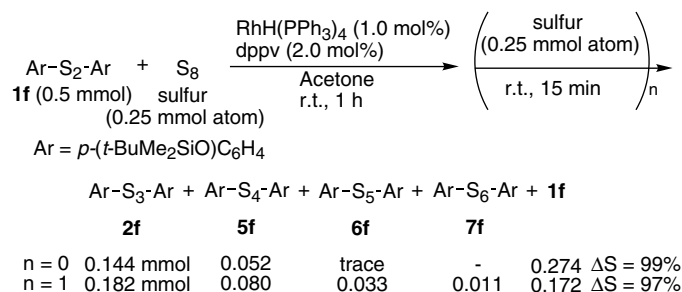
Run	Ar	Yield/mmol				$\Delta S/\%$
		2	5	6	1	
1	<i>p</i> -( <i>t</i> -BuMe <sub>2</sub> SiO)C <sub>6</sub> H <sub>4</sub> <b>f</b>	0.189	0.075	0.033 <sup>b</sup>	0.170	96
2	<i>p</i> -MeOC <sub>6</sub> H <sub>4</sub> <b>g</b>	0.185	0.083	0.040	0.184	94
3	<i>p</i> -MeC <sub>6</sub> H <sub>4</sub> <b>h</b>	0.171	0.069	0.033	0.227	82
4	C <sub>6</sub> H <sub>5</sub> <b>i</b>	0.132	0.041	0.011	0.302	49
5	<i>p</i> -ClC <sub>6</sub> H <sub>4</sub> <b>j</b>	0.171	0.005	—	0.320	36
6 <sup>c</sup>	MeO <sub>2</sub> CCH <sub>2</sub> <b>k</b>	0.159	0.045	—	0.293	50
7 <sup>c</sup>	MeO <sub>2</sub> C(CH <sub>2</sub> ) <sub>2</sub> <b>l</b>	0.123	0.065	0.034 <sup>d</sup>	0.231	85

<sup>a</sup> See text for reaction conditions and yield determination.

<sup>b</sup> Hexasulfide **7f** was also formed in 0.011 mmol amount.

<sup>c</sup> The reaction was conducted using **1** (0.5 mmol) and sulfur (0.5 mmol atom) in the presence of  $RhH(PPh_3)_4$  (2.0 mol %) and dppv (4.0 mol %) for 5 min.

<sup>d</sup> Hexasulfide **7l** was also formed in 0.017 mmol amount.



Scheme 3.

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