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Rhodium-catalyzed alkylthio exchange reaction of thioester and disulfide

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Abstract

The Wilkinson complex $RhCl(PPh_3)_3$ catalyzes equilibrating alkylthio exchange reaction of thioesters with disulfides. The treatment of a thioester and a dialkyl disulfide in refluxing diethyl ketone in the presence of $RhCl(PPh_3)_3$ (2.5 mol %) for 1.5 h gave an alkylthio exchanged thioester. The reaction of *S*-methyl ester was conducted shifting the equilibrium by removing volatile dimethyl disulfide.

Alkoxy exchange is a fundamental reaction of esters catalyzed by acid or base.[1] The reaction being under equilibrium proceeds via carbonyl addition of alcohol generating tetrahedral carbon intermediate followed by elimination. The reaction of the sulfur analog, alkylthio exchange of thioesters, however, was not known. During our investigations on the use of transition metal catalysis for the synthesis of organosulfur compounds,[2] rhodium complexes were found to catalyze alkylthio exchange reaction of organic disulfides,[3] and sulfur atom exchange reaction between sulfur and organic polysulfides.[4] The reactions were considered to proceed by the S–S bond cleavage by the metal complex followed by ligand exchange. It was also found that a rhodium complex catalyzes alkylthio exchange reaction of 1-alkylthioacetylenes, which contains S–C bond cleavage and metathesis with S–S bond.[5] It was therefore considered interesting to apply the catalytic method to the activation of other S–C bonds, since such methodology can be useful for the transformation of organosulfur compounds. Described here is the rhodium-catalyzed alkylthio exchange reaction of thioesters with disulfide (Scheme 1).

$$\mathrm{RCOSR' + R''SSR''} \xrightleftharpoons{\text{Rh cat}} \mathrm{RCOSR'' + R'SSR''}$$

$$\mathrm{RCOOR' + R''OH} \xrightleftharpoons{\text{acid or base}} \mathrm{RCOOR'' + R'OH}$$

Scheme 1.

When a mixture of *S*-octyl benzenethioate **1** and bis(2-methoxyethyl) disulfide **2** (4 equiv) in diethyl ketone was heated at reflux for 1.5 h in the presence of $RhCl(PPh_3)_3$ (2.5 mmol %), *S*-(2-methoxyethyl) benzenethioate **3** was obtained in 87% yield. The starting material **1** was recovered in 11% yield, and a mixture of disulfides was obtained containing **2** (72%), dioctyl disulfide **4** (11%), and 2-methoxyethyl octyl disulfide (77%). The mass balance regarding the octylthio group is quantitative. $RhH(PPh_3)_4$ exhibited similar reactivity, while $RhH(CO)(PPh_3)_3$ and $Pd(PPh_3)_4$ were less effective. The reaction could be conducted in various solvents such as acetone, methanol, 1,4-dioxane, xylene, chlorobenzene, 1,2-dichloroethane, acetonitrile, and DMF (Scheme 2).

Equilibrium nature of the reaction is shown by the experiments employing different amounts of **2** against **1**. The yields of **3** were 49%, 65%, and 87%, when the molar ratio **2**/**1** was changed to 0.5, 1, and 4, respectively. The yields coincided with the calculated values assuming the

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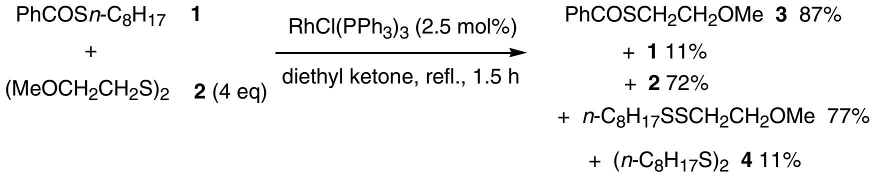


Scheme 2.

equal thermodynamical stability of **1** and **3**. The reverse reactions were conducted giving the same compositions of the products (Scheme 3). Reaction of **1** (0.5 mmol) and **2** (0.25 mmol) gave **3** in 49% yield with recovered **1** in 50%, and the reaction of **3** (0.5 mmol) with **4** (0.25 mmol) provided **1** in 48% yield with the recovered **3** in 48%.

Several thioesters were reacted with disulfides (4 equiv) in the presence of $RhCl(PPh_3)_3$ (2.5 mol %) giving the exchanged products generally in 85–90% yields (Table 1). Thioesters derived from aromatic and aliphatic acids equally reacted with dialkyl dilsulfides giving the products in comparable yields. Unsaturation as shown by the reaction of cinnamate did not interfere with the reaction (entry 8). Functional groups such as methoxycarbonyl, *t*-butoxycarbonylamino, and hydroxy did not affect the reaction (entries 10–12). An aromatic thiol ester was formed from an aliphatic thiol ester in a lower yield, which should be due to the different thermodynamic stability of the compounds (entry 4). In accordance, the reaction of *S*-phenyl thiobenzoate and **4** in 1:0.5 molar ratio gave the corresponding *S*-octyl ester and the starting material in 28 and 69% yields, respectively. The same mixture of the products was obtained from *S*-octyl benzothioate and diphenyl disulfide, which confirmed the lower thermodynamic stability of *S*-phenyl thioester under equilibrium. The formation of an apparently more reactive compound from the less reactive compound is an interesting aspect of equilibrium reaction.

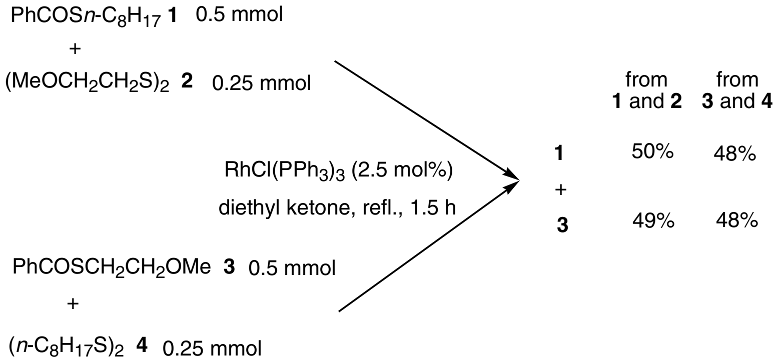
Table 1
Rhodium-catalyzed alkylthio exchange reaction

$$\underset{4\text{ eq}}{RCOSR' + R''SSR''} \xrightarrow[\text{diethyl ketone, refl., 1.5 h}]{RhCl(PPh_3)_3\text{ (2.5 mol\%)}} RCOSR'' + R'SSR''$$

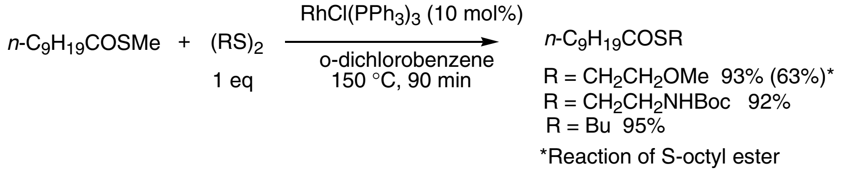
Entry	R	R′	R″	Yield (%)
1	Ph	*n*-C_8H_{17}	$(CH_2)_2OMe$	87
2			CH_2CO_2Me	86
3			$(CH_2)_2NHBoc$	85
4			Ph	41
5		*cyclo*-C_6H_{11}	$(CH_2)_2OMe$	87
6	*p*-$MeOC_6H_4$	*n*-C_8H_{17}		87
7	*p*-ClC_6H_4	*n*-C_8H_{17}		88
8	PhCH=CH	*n*-C_8H_{17}		87
9	*n*-C_7H_{15}	*n*-C_8H_{17}	$(CH_2)_2OMe$	86
10			$(CH_2)_2CO_2Me$	84
11			$(CH_2)_2NHBoc$	88
12			$(CH_2)_6OH$	90
13	$PhCH_2$	*n*-C_8H_{17}	$(CH_2)_2OMe$	86
14	*cyclo*-C_6H_{11}	*n*-C_8H_{17}	$(CH_2)_2OMe$	87

The use of *S*-methyl thioester shifts the equilibrium to the exchanged thioester using 1 equiv of disulfide, since dimethyl disulfide formed can be removed by evaporation (Scheme 4). Reaction of *S*-methyl decanethioate with **2** (1 equiv) at 150 °C for 1.5 h in *o*-dichlorobenzene with continuous bubbling of argon gave the exchanged product in 93% yield, while the use of *S*-octyl ester resulted in 63% yield of the product. It was confirmed under these high temperature conditions that the reaction did not proceed without rhodium complex. Analogously, a glutathione thioester was obtained in 85% yield from glutathione disulfide and *S*-methyl butanethioate (4 equiv) (Scheme 5). This yield is based on the two alkylthio moieties indicating both alkylthio groups to be esterificated, which is another advantage of equilibrium reaction.

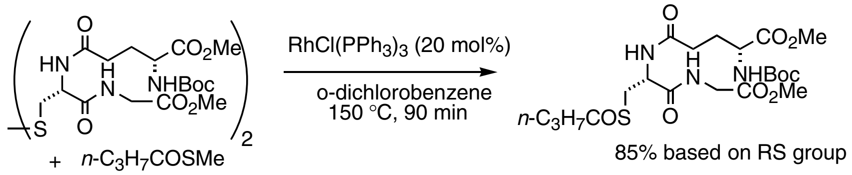
The rhodium-catalyzed alkylthio exchange reaction proceeded between two thioesters (Scheme 6).[6] Reaction



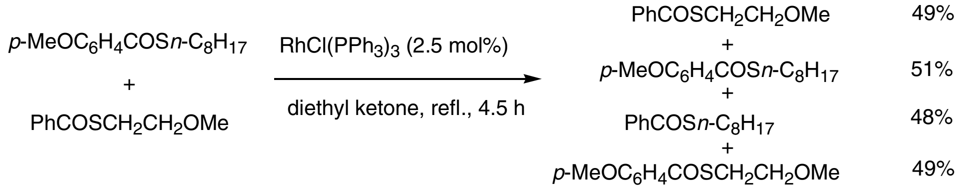
Scheme 3.



Scheme 4.



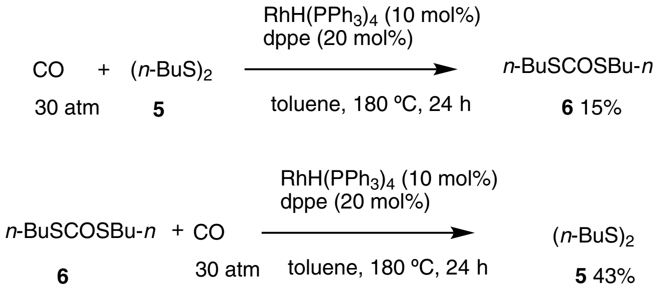
Scheme 5.



Scheme 6.

of *S*-octyl *p*-methoxybenzoate and *S*-(2-methoxyethyl) benzoate in refluxing diethyl ketone for 4.5 h in the presence of $RhCl(PPh_3)_3$ (2.5 mol %) gave a mixture of four possible exchanged thioesters in an equal amount.

The mechanism most likely involves the initial cleavage of RCO–SC bond rather than RCOS–C bond forming an acylrhodium(III) complex.[7] The alkylthio ligand exchange with disulfide on rhodium metal and reductive elimination then give the exchanged thioesters. The interpretation is supported by the experiments of dibutyl *S*,*S*′-dithiocarbonate **6** (Scheme 7). The reaction of dibutyl disulfide **5** and carbon monoxide (30 atm) in the presence of $RhH(PPh_3)_4$ (10 mol %) and dppe (20 mol %) in toluene at 180 °C for 24 h gave **6** in 15% yield with recovered **5** in 52%. The need of rhodium complex was again confirmed, which excluded the radical mechanism for the present reaction. This reaction is under equilibrium, and the treatment of **6** with the same catalyst under the same conditions gave **5** in 43% yield with recovered **6** in 16%. The reaction of **6** most likely involves the formation of BuSCO–Rh–SBu complex, and it may be reasonable that the alkylthio exchange reaction of thioesters proceeds by the similar mechanism.



Scheme 7.

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.2008.01.109.

References and notes

1. Otera, J. *Chem. Rev.* **1993**, *93*, 1449.
2. Arisawa, M.; Yamaguchi, M. *Pure Appl. Chem.*, in press; Arisawa, M.; Yamaguchi, M. *J. Synth. Org. Chem. Jpn.* **2007**, *65*, 1213.
3. Arisawa, M.; Yamaguchi, M. *J. Am. Chem. Soc.* **2003**, *125*, 6624; Arisawa, M.; Suwa, A.; Yamaguchi, M. *J. Organomet. Chem.* **2006**, *691*, 1159.
4. Arisawa, M.; Tanaka, K.; Yamaguchi, M. *Tetrahedron Lett.* **2005**, *46*, 4797.
5. Arisawa, M.; Fujimoto, K.; Morinaka, S.; Yamaguchi, M. *J. Am. Chem. Soc.* **2005**, *127*, 12226.

6. Related reaction of 1-alkylthioalkynes: Arisawa, M.; Tagami, Y.; Yamaguchi, M. *Tetrahedron Lett.*, in press.
7. Examples of transition metal-catalyzed reactions considered to contain RCO–M–SR′ intermediates: Wang, M.-D.; Calet, S.; Alper, H. *J. Org. Chem.* **1989**, *54*, 21; Khumtaveeporn, K.; Alper, H. *J. Org. Chem.* **1994**, *59*, 1414; Ogawa, A.; Kawakami, J.; Mihara, M.; Ikeda, T.; Sonoda, N.; Hirao, T. *J. Am. Chem. Soc.* **1997**, *119*, 12380; Ogawa, A.; Kuniyasu, H.; Sonoda, N.; Hirao, T. *J. Org. Chem.* **1997**, *62*, 8361; Xiao, W.-J.; Vasapollo, G.; Alper, H. *J. Org. Chem.* **1999**, *64*, 2080; Kawakami, J.; Mihara, I.; Kamiya, I.; Takeba, M.; Ogawa, A.; Sonoda, N. *Tetrahedron* **2003**, *59*, 3521.