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Ruthenium-catalyzed selective hydrosilylation reaction of allyl-functionalized PEG derivatives

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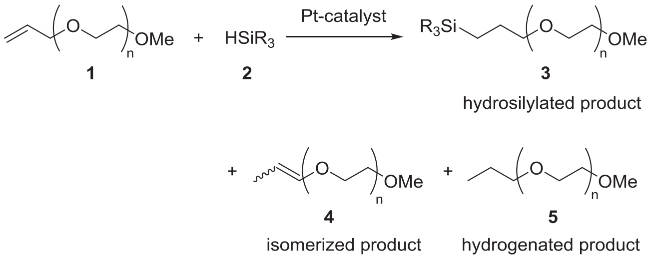
ABSTRACT

Reactions of allyl-functionalized poly(ethylene glycol) (PEG) derivatives with alkoxysilanes proceeded efficiently to furnish the corresponding hydrosilylated products in good to excellent yields using a ruthenium catalyst, $[RuCl_2(nbd)]_n$. A preliminary mechanistic study supported the pivotal role of the PEG moiety, which coordinated to the ruthenium atom during the reaction to achieve high reaction selectivity. This method may be applicable to the synthesis of various PEGs with a silyl terminus, which is useful as biocompatible and low toxic silane coupling agents.

Introduction

Poly(ethylene glycol)s (PEGs) have attracted great interest because of their high biocompatibility and low toxicity. PEGs are applicable not only for organic and biomaterials but also for inorganic materials [1]. To immobilize PEGs to various inorganic materials in a chemically stable manner, it is a powerful way to utilize PEGs with a silyl terminus (silylated PEGs) as silane coupling agents. Hydrosilylation of allyl-functionalized PEGs (**1**) can be used as one of the most common methods to synthesize such silylated PEGs [2]. For the hydrosilylation reactions, platinum catalysts such as Speier's catalyst [3] and Karstedt's catalyst [4] are efficient and normally used [5–11]. However, it is known that these platinum catalysts often undergo undesired side reactions, such as isomerization of terminal olefins to internal olefins and hydrogenation of olefins [10,11]. Indeed, platinum-catalyzed hydrosilylation reactions of **1** are known to undergo isomerization and hydrogenation as well (Scheme 1) [2]. In this respect, Moon and a coworker reported that the use of customized tris(2-methoxyethoxy)silane, which effectively stabilizes an electron–deficient intermediate, successfully improved the reaction selectivity [2a]. Meanwhile, we focused our efforts on the reaction of **1** with commercially available simple alkoxy hydrosilanes **2** in an attempt to develop a more practical and convenient method [12]. Herein, we report the selective hydrosilylation of **1** using a ruthenium catalyst precursor, $[RuCl_2(nbd)]_n$ (nbd = 2,5-norbornadiene).



Scheme 1. Pt-catalyzed hydrosilylation of allyl-functionalized PEG derivatives **1**.

Results and discussion

First, we commenced the screening of typical hydrosilylation catalysts in the reaction of diethylene glycol allyl methyl ether (**1a**) as a model compound of PEGs with 1.5 equiv of $HSi(OMe)_3$ (**2a**) at 60 °C for 16 h (Table 1). The reaction using Karstedt's catalyst gave 62% yield of desired hydrosilylated product **3a**, while alkene isomerization products **4a** and hydrogenated product **5a** were also formed in 20% and 5% yields, respectively (Table 1, entry 1). $[IrCl(cod)]_2$ [12a,13] exhibited similar catalytic performance, resulting in the formation of a mixture of **3a** (71%), **4a** (14%), and **5a** (2%) (Table 1, entry 2). The reaction catalyzed by $RhCl(PPh_3)_3$ [14] or $Ru_3(CO)_{12}$ [15] furnished **3a** in moderate 68% and 45% yields, respectively. In these reactions, slight formation of **5a** (5%) was also confirmed (Table 1, entries 3 and 4). The reaction catalyzed by $RuCl_2(dmso)_4$ (dmso = dimethyl sulfoxide) formed **3a**

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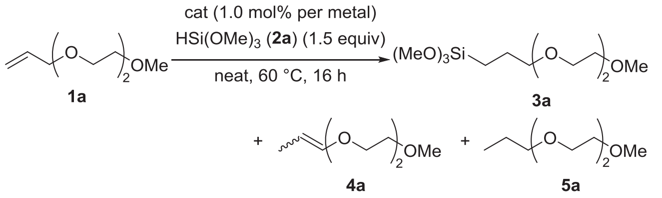
Table 1
Screening of metal catalysts.[a]



Entry	Cat.	% yield (**3a**/**4a**/**5a**)[b]
1	Karstedt's cat	62/20/5
2	$[IrCl(cod)]_2$	71/14/2
3	$RhCl(PPh_3)_3$	68/<1/5
4	$Ru_3(CO)_{12}$	45/<1/5
5	$RuCl_2(dmso)_4$	61/18/9
6	$[RuCl_2(benzene)]_2$	72/11/3
7	$[RuCl_2(mesitylene)]_2$	76/15/3
8	$[RuCl_2(p\text{-cymene})]_2$	80/6/2
9	$[RuCl_2(cod)]_n$	84/5/<1
10[c]	$[RuCl_2(nbd)]_n$	>99/<1/<1

[a] Reaction conditions: **1a** (0.5 mmol), **2a** (0.75 mmol), catalyst (0.005 mmol per metal), 60 °C, 16 h under a nitrogen atmosphere.
[b] Determined by ^1H NMR using mesitylene as an internal standard.
[c] Reaction was also performed with **2a** (1 equiv) for 1 h.

(61%), as well as the production of **4a** (18%) and **5a** (9%) (Table 1, entry 5). Further screening of metal catalysts revealed that some of the Ru(II) complexes [16] showed better selectivity than Karstedt's catalyst. The reaction using $[RuCl_2(benzene)]_2$ led to the increase in the yield of **3a** (72%) although the concomitant formation of both **4a** (11%) and **5a** (3%) was also observed (Table 1, entry 6). $[RuCl_2(mesitylene)]_2$ and $[RuCl_2(p\text{-cymene})]_2$ similarly catalyzed the reaction to form **3a** in good yields with the slight formation of both **4a** and **5a** (Table 1, entries 7 and 8). The use of $[RuCl_2(cod)]_n$ (cod = 1,5-cyclooctadiene) increased the yield of **3a** to some extent; i.e., **3a**, **4a**, and **5a** were formed in 84%, 5%, and < 1% yields, respectively (Table 1, entry 9). Interestingly, $[RuCl_2(nbd)]_n$ selectively catalyzed the hydrosilylation reaction to afford **3a** in >99% yield (Table 1, entry 10). It should be noted that the selective and quantitative hydrosilylation reaction of **1a** was also completed with 1 equiv of $HSi(OMe)_3$ within 1 h.

$[RuCl_2(nbd)]_n$ was successfully applied to other poly(ethylene glycol) allyl methyl ethers **1**. To clarify the scope of **1**, the hydrosilylation reactions of **1** with various sizes of PEG chains were performed in the presence of 1 mol% per metal of $[RuCl_2(nbd)]_n$ at 60 °C for 1 h (Table 2). The reaction of **1a**–**d** (n = 1–4) with $HSi(OMe)_3$ (**2a**) achieved the selective formation of the corresponding hydrosilylated products **3a**–**d** in 90–95% isolated yields (Table 2, entries 1–4). The reaction of **1a** with $HSiMe(OMe)_2$ (**2b**) similarly proceeded to form **3e** in 86% yield with the slight formation of **4a** and **5a** (Table 2, entry 5). The use of the bulkier $HSi(OEt)_3$ resulted in a slight decrease in the yield of **3f** (83%) (Table 2, entry 6). Next, we performed the hydrosilylation of **1e** (n = 14) and **1f** (n = 26) with a longer PEG chain. The reaction of **1e** with **2a** furnished **3g** in 90% isolated yield (Table 2, entry 7), accompanied by **4g** (7% yield). In the reaction of much longer **1f** with **2a**, the isolated yield of the hydrosilylated product **3h** further decreased to 85% (NMR) (Table 2, entry 8). The use of 3 equiv of **2a** improved the yield of **3h** to 89% (Table 2, entry 9). All the aforementioned reactions were also tested using Karstedt's catalyst for comparison. The results are also shown in Table 2, the rightmost column. Based on these results, the reactions resulted in the formation of a mixture of **3**, **4**, and **5** [16]. Thus, the superior catalytic properties of $[RuCl_2(nbd)]_n$ to Karstedt's catalyst were evidenced.

In the platinum-catalyzed hydrosilylation reactions, it has been reported that the isomerization is generally catalyzed by the *in situ*-formed Pt metal colloids [17]. To clarify this point in the case of our reactions, the reaction of **1f** with **2a** was also performed in the presence of Hg, which serves as an inhibitor of active metal-colloidal catalysts. (Table 2, entry 10). The yields of the products remained unchanged regardless of the existence of Hg. Therefore, a different reaction path from that in the platinum-catalyzed system was suggested for the formation of the isomerized products **4**. Diethylene glycol monoallyl ether with a terminal hydroxyl group (**1g**) resulted in the formation of a complex mixture (Table 2, entry 11). H_2 evolution was detected during the reaction. Thus, the occurrence of dehydrogenative coupling of **1g** with **2a** is indicated.

The addition of 10 mol% H_2O resulted in the complete suppression of the hydrosilylation reaction of **1a** (Table 2, entry 12). These results indicated that the presence of free protons impedes the hydrosilylation reaction.

To shed light on the reaction mechanism, several control experiments using allyl butyl ether (**6**) were conducted (Table 3). The reaction with **2a** in the presence of $[RuCl_2(nbd)]_n$ afforded the hydrosilylation product **7a** and the isomerized product **8** in 87% and 13% yields, respectively (Table 3, entry 1). This selectivity was similar to that in the reaction with Karstedt's catalyst (**7**/**8**/**9** = 82/17/<1). The addition of DME (10 mol%) as an external ligand did not improve the reaction selectivity (Table 3, entry 2). It was also confirmed that the use of $HSi(OCH_2CH_2OMe)_3$ (**2d**) decreased the yield of the desired **7b**, whereas the Pt-catalyzed same reaction resulted in the selective formation of **7b** as reported previously (Table 3, entry 3) [2a]. These experimental results strongly support the pivotal role of the coordination of the ethylene glycol moiety of olefin to the ruthenium center to achieve excellent reaction selectivity.

As a possible reaction path for the ruthenium-catalyzed hydrosilylation reaction of **1**, we postulated that the reaction follows the conventional (modified) Chalk–Harrod mechanism, in which the reaction starts with the oxidative addition of hydrosilane **2**, and then olefin insertion and reductive elimination successively proceed (Fig. 1). Since the control experiment using Hg excluded the possibility of the formation of ruthenium metal colloids (vide infra), the olefin isomerization is likely to proceed via *β*-H elimination of the alkyl(silyl) intermediate in the Chalk–Harrod mechanism cycle.

In summary, we have achieved highly selective hydrosilylation reactions of allyl–functionalized PEG derivatives **1** using a commercially available ruthenium catalyst, $[RuCl_2(nbd)]_n$. The

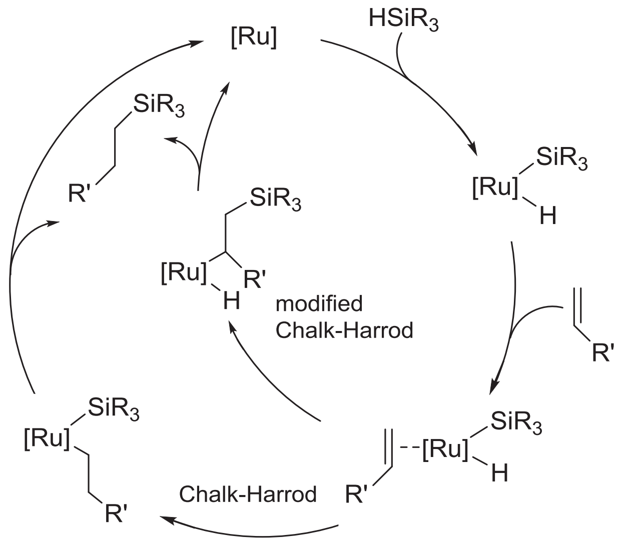


Fig 1. Possible catalytic cycles.

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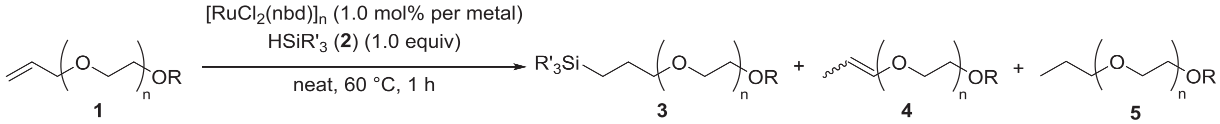
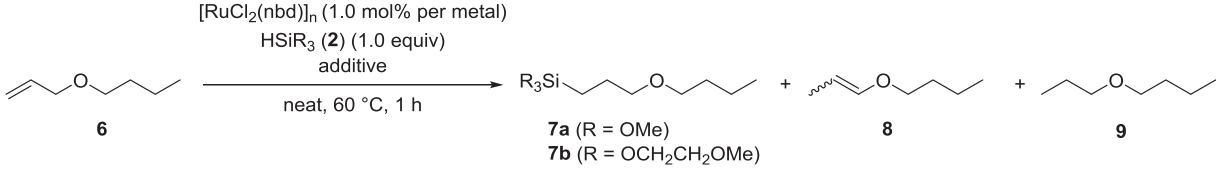
Table 2
Hydrosilylation reaction of allyl-functionalized PEGs (**1**) by $[RuCl(nbd)_2]_n$.[a]



Entry	**1**	**2**	% conv.[b] (**1**)	% conv.[b] (**2**)	% NMR yield[b] (**3**/**4**/**5**) $[RuCl_2(nbd)]_2$	% isolated yield(**3**)	% NMR yield[a],[b] (**3**/**4**/**5**) Karstedt's cat
1	n = 1, R = Me (**1b**)	$HSi(OMe)_3$ (**2a**)	>99	>99	99 /<1/<1	95 (**3b**)	76/19/5
2	n = 2, R = Me (**1a**)	**2a**	>99	>99	99/<1/<1	95 (**3a**)	62/20/5
3	n = 3, R = Me (**1c**)	**2a**	>99	>99	99/<1/<1	93 (**3c**)	69/27/5
4	n = 4, R = Me (**1d**)	**2a**	>99	>99	99/<1/<1	90 (**3d**)	64/28/6
5	**1a**	$HSiMe(OMe)_2$ (**2b**)	>99	>99	97/3/<1	86 (**3e**)	80/15/5
6	**1a**	$HSi(OEt)_3$ (**2c**)	>99	94	90/8/2	83 (**3f**)	72/25/3
7[c]	n = 14, R = Me (**1e**)	**2a**	>99	>99	92/7/<1	90[h] (**3g**)	66/29/5
8[c,d]	n = 26, R = Me (**1f**)	**2a**	>99	>99	85/15/<1	–	72/16/11
9[c,d,e]	**1f**	**2a**	>99	77	92/8/<1	89[h] (**3h**)	–
10[c,d,e,f]	**1f**	**2a**	>99	80	92/8/<1	–	–
11	n = 2, R = H (**1g**)	**2a**	n.d.	88	complex mixture	–	–
12[g]	**1a**	**2a**	3	71	<1/<1/<1	–	–

[a] Reaction conditions: **1** (0.5 mmol), **2** (0.5 mmol), catalyst (0.005 mmol per metal), 60 °C, 1 h under a nitrogen atmosphere.
[b] Determined by ^1H NMR using mesitylene as an internal standard.
[c] Reaction time (3 h).
[d] 1 mL of 1,2-dimethoxyethane (DME) was used as a solvent.
[e] **2a** (3 equiv) was used.
[f] Performed in the presence of 2.58 g of Hg.
[g] Performed in the presence of 10 mol% of H_2O.
[h] Determined by ^1H NMR of the isolated mixture containing **3** and **4**.

Table 3
Control experiments using allyl butyl ether **6**.[a]



Entry	**2**	additive	% conv.[b] (**6**)	% conv.[b] (**2**)	% yield (**7**/**8**/**9**)[b,c]
1	$HSi(OMe)_3$ (**2a**)	none	>99	>99	87/13/<1 (82/17/<1)
2	**2a**	10 mol% DME	>99	>99	89/10/<1
3	$HSi(OCH_2CH_2OMe)_3$ (**2d**)	none	29	39	<1/18/<1 (91/9/<1)

[a] Reaction conditions: **6** (0.5 mmol), **2** (0.5 mmol), catalyst (0.005 mmol per metal), 60 °C, 1 h under a nitrogen atmosphere.
[b] Determined by ^1H NMR using mesitylene as an internal standard.
[c] Results with Karstedt's catalyst were shown in the parentheses.

reactions proceeded with higher selectivity that those with the reactions with the conventional platinum catalyst. We believe that this study demonstrates a novel synthetic route that enables the utility of hydrosilylation reactions to be expanded to synthesize a variety of useful organosilicon compounds.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.tetlet.2019.151086.

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