

A Novel Synthesis of 1,3-Diol Diesters by the Reaction of Aldehydes with Oxime Esters Catalyzed by Samarium Complex

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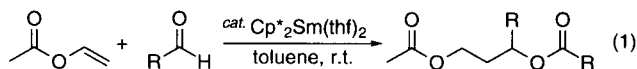
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$\text{Cp}^*_2\text{Sm}(\text{thf})_2$ was found to be an efficient catalyst for the synthesis of 1,3-diol diesters by the coupling reaction of aldehydes with oxime esters under mild conditions. For instance, the reaction of acetaldehyde with cyclohexanone oxime acetate catalyzed by $\text{Cp}^*_2\text{Sm}(\text{thf})_2$ gave 1,3-diacetoxybutane in 70% yield. Treatment of acetaldehyde with isopropenyl acetate in the presence of a small amount of cyclohexanone oxime acetate and $\text{Cp}^*_2\text{Sm}(\text{thf})_2$ resulted in the corresponding 1,3-diol diester in good yield.

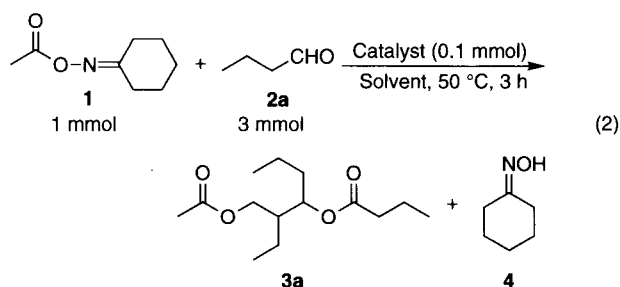
Samarium compounds have been widely used in organic synthesis. Recently, it has been reported that SmI_2 catalyzes intramolecular Tishchenko reaction,¹ epoxide rearrangements,² Michael and aldol reactions,³ and Diels-Alder reaction.⁴ Samarium complex such as $\text{Cp}^*_2\text{Sm}(\text{thf})_2$ is also a useful catalyst for hydrogenation⁵ and hydroboration of alkenes^{6,7} and hydroamination/cyclization of amines.^{5g,6}

Previously, we reported that $\text{Cp}^*_2\text{Sm}(\text{thf})_2$ and SmI_2 were efficient catalysts for a new type of 1:2 cross coupling reaction of aldehydes with vinyl esters under mild conditions to form the corresponding 1,3-diol diesters in moderate to good yields (eq. 1).⁸



Now we find that $\text{Cp}^*_2\text{Sm}(\text{thf})_2$ catalyzes the coupling reaction of oxime esters with aldehydes to form 1,3-diol diesters.

The reaction of cyclohexanone oxime acetate (**1**) with butyraldehyde (**2a**) was examined in the presence of some samarium compounds (eq. 2 and Table 1).



A typical reaction was carried out as follows: To a mixture of aldehyde (3 mmol) and oxime acetate (1 mmol) was added $\text{Cp}^*_2\text{Sm}(\text{thf})_2$ (0.1 mmol) in toluene solution (1 mL). After stirring the solution at 50 °C for 3 h, the reaction mixture was quenched with wet ether. Products were purified by column chromatography on silica gel with *n*-hexane / ethyl acetate (10 / 1 v/v).

The reaction of **1** with 3 equiv of **2a** catalyzed by $\text{Cp}^*_2\text{Sm}(\text{thf})_2$ (10 mol% with respect to **1**) at 50 °C for 3 h gave 3-acetoxymethyl-4-butanoylheptane (**3a**) in 68% yield along with cyclohexanone oxime (**4**) (60%) (run 1). The reaction proceeded smoothly even in the presence of 5 mol% of $\text{Cp}^*_2\text{Sm}(\text{thf})_2$ (run 2). **3a** was obtained in 77% yield when **1** was reacted with 2 mmol of **2a** (run 3).

Table 1. Reaction of cyclohexanone oxime acetate (**1**) with butyraldehyde (**2a**) catalyzed by Sm compounds^a

Run	Catalyst	Solvent	3a (Yield /%)
1	$\text{Cp}^*_2\text{Sm}(\text{thf})_2$	toluene	68
2 ^b	$\text{Cp}^*_2\text{Sm}(\text{thf})_2$	toluene	68
3 ^c	$\text{Cp}^*_2\text{Sm}(\text{thf})_2$	toluene	77 ^d
4	$\text{Cp}^*_2\text{Yb}(\text{thf})_2$	toluene	62
5	$\text{Sm}(\text{O}^i\text{Pr})_3$	THF	56
6	SmI_2	THF	—
7	SmI_3	THF	—
8	$\text{Sm}(\text{OTf})_3$	THF	—

^a**1** (1 mmol) was reacted with **2a** (3 mmol) in the presence of catalyst (0.1 mmol) in solvent (1 mL) at 50 °C for 3 h. ^b $\text{Cp}^*_2\text{Sm}(\text{thf})_2$ (0.05 mmol) was used. ^c**2a** (2 mmol) was used. ^dBased on **2a**.

$\text{Sm}(\text{O}^i\text{Pr})_3$ and $\text{Cp}^*_2\text{Yb}(\text{thf})_2$ also catalyzed the present reaction, but their catalytic activities were slightly lower than that of $\text{Cp}^*_2\text{Sm}(\text{thf})_2$ (runs 4 and 5). SmI_2 , SmI_3 and $\text{Sm}(\text{OTf})_3$ were inert for this reaction (runs 6-8).

On the basis of these results, a variety of aldehydes (**2b-2f**) were allowed to react with **1** in the presence of $\text{Cp}^*_2\text{Sm}(\text{thf})_2$ catalyst in toluene at 50 °C for 3 h. Representative results are shown in Table 2.

Linear aldehydes **2b** and **2c** were reacted with **1** to give the corresponding 1,3-diester **3b** and **3c** in 70% yields, respectively

Table 2. Reaction of cyclohexanone oxime acetate (**1**) with various aldehydes catalyzed by $\text{Cp}^*_2\text{Sm}(\text{thf})_2$ ^a

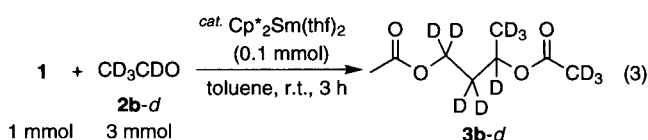
Run	Aldehyde	Product (Yield /%)
1 ^b	2b (R=H)	3b (70)
2	2c (R=Me)	3c (70)
3	2d (R= <i>i</i> Pr)	3d (54)
4	2e	3e (76)
5 ^b	2f	3f (44)

^a**1** (1 mmol) was reacted with aldehyde (3 mmol) in the presence of $\text{Cp}^*_2\text{Sm}(\text{thf})_2$ (0.1 mmol) in toluene (1 mL) at 50 °C for 3 hr.

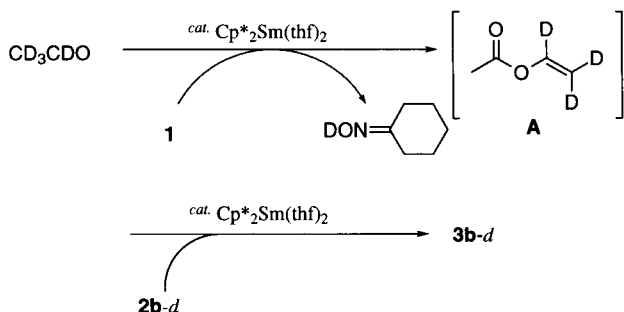
^bThe reaction was carried out at room temperature.

(runs 1 and 2). Although branched aldehyde such as 3-methylbutyraldehyde (**2d**) and isobutyraldehyde (**2e**) reacted similarly with **1** to give diester, **3d** and **3e**, in 54% and 76% yields (runs 3 and 4). However, the reaction of cyclohexanecarboxaldehyde (**2f**) with **1** resulted in **3f** in lower yield because of the concomitant formation of Tishchenko product, (cyclohexyl)methyl cyclohexanecarboxylate (21%) (run 5).

To clarify the reaction path for the present 1:3 coupling reaction of oxime ester with aldehyde, the deuterium label experiment was performed. The reaction of **1** with 3 equiv of CD₃CDO (**2b-d**) catalyzed by Cp*₂Sm(thf)₂ produced **3b-d** in which 11 deuteriums are incorporated into the molecule (eq. 3).⁹

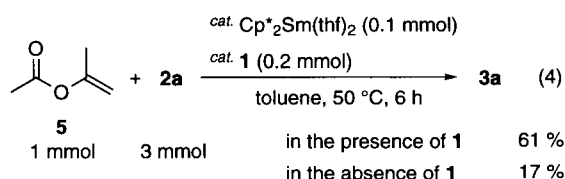


This fact shows that **1** reacts with **2b-d** to form vinyl acetate [**A**] as a transient intermediate, which then couples with **2b-d** to form 1,3-diol diester **3b-d** (Scheme 1).



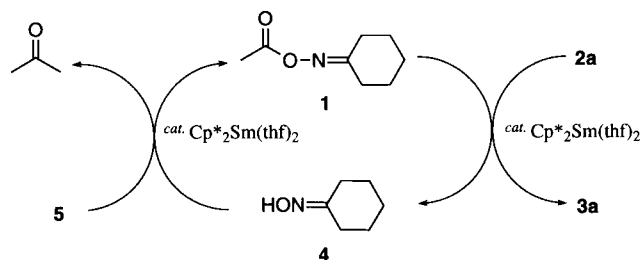
Scheme 1. A possible reaction path for the reaction of **2b-d** with **1** catalyzed by Cp*₂Sm(thf)₂

It is interesting to note that the Cp*₂Sm(thf)₂-catalyzed 1:3 coupling reaction of isopropenyl acetate (**5**) with aldehyde **2a** was enhanced by adding a small amount of oxime ester **1**. The reaction of **5** (1 mmol) with **2a** (3 mmol) in the presence of **1** (0.2 mmol) by Cp*₂Sm(thf)₂ (0.1 mmol) in toluene (1 mL) at 50 °C for 6 h formed **3a** in 61% yield, while the reaction in the absence of **1** under these conditions gave **3a** in only 17% yield (eq. 4).



The oxime ester-mediated coupling reaction of **5** with **2a** is thought to proceed as follows (Scheme 2).

Diester **3a** seems to be formed by the reaction of **2a** with **1** rather than with **5**, and the resulting oxime **4** is considered to be smoothly acylated with isopropenyl acetate **5** in the presence of Cp*₂Sm(thf)₂ to regenerate **1**. Indeed, **4** readily acylated by **5** under the influence of Cp*₂Sm(thf)₂ at room temperature giving **1** in



Scheme 2. Oxime ester-mediated coupling reaction of isopropenyl acetate (**5**) with aldehyde by Cp*₂Sm(thf)₂

quantitative yield.

In summary, a novel synthesis of 1,3-diol diesters by the coupling reaction of oxime ester with aldehydes was achieved in the presence of a catalytic amount of Cp*₂Sm(thf)₂. The coupling reaction of isopropenyl acetate **5** with aldehyde was found to be facilitated by adding a small amount of oxime ester **1**.

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- Spectral data for **3b-d** is as follows: ¹H-NMR (CDCl₃/Me₄Si) δ 1.98 (s); ¹³C-NMR (CDCl₃) δ 18.4, 18.7, 18.9, 19.2, 19.5, 19.9, 20.1, 20.4, 20.8, 21.0, 21.1, 33.0, 33.2, 33.5, 33.8, 34.1, 59.3, 59.6, 60.0, 60.2, 60.6, 66.8, 67.1, 67.4, 170.5, 170.9.