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

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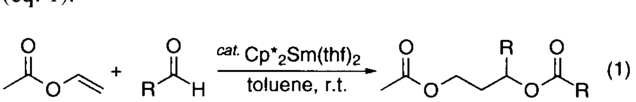
$Cp^*_2Sm(thf)_2$ was found to be an efficient catalyst for the synthesis of 1,3-diol diesters by the coupling reaction of aldehydes with oxime esters under mild conditions. For instance, the reaction of acetaldehyde with cyclohexanone oxime acetate catalyzed by $Cp^*_2Sm(thf)_2$ gave 1,3-diacetoxybutane in 70% yield. Treatment of acetaldehyde with isopropenyl acetate in the presence of a small amount of cyclohexanone oxime acetate and $Cp^*_2Sm(thf)_2$ resulted in the corresponding 1,3-diol diester in good yield.

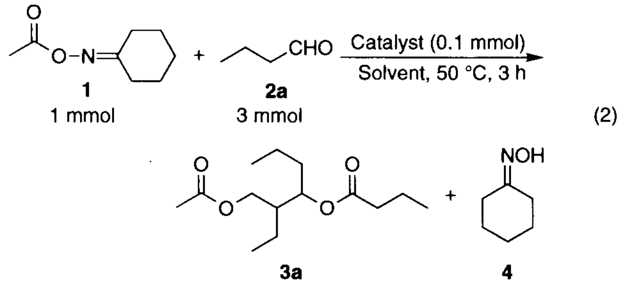
Samarium compounds have been widely used in organic synthesis. Recently, it has been reported that SmI_2 catalyzes intramolecular Tishchenko reaction,[1] epoxide rearrangements,[2] Michael and aldol reactions,[3] and Diels-Alder reaction.[4] Samarium complex such as $Cp^*_2Sm(thf)_2$ is also a useful catalyst for hydrogenation[5] and hydroboration of alkenes[6,7] and hydroamination/cyclization of amines.[5g,6]

Previously, we reported that $Cp^*_2Sm(thf)_2$ 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 $Cp^*_2Sm(thf)_2$ 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 $Cp^*_2Sm(thf)_2$ (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 $Cp^*_2Sm(thf)_2$ (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 $Cp^*_2Sm(thf)_2$ (run 2). **3a** was obtained in 77% yield when **1** was reacted with 2 mmol of **2a** (run 3). $Sm(O^iPr)_3$ and $Cp^*_2Yb(thf)_2$ also catalyzed the present reaction, but their catalytic activities were slightly lower than that of $Cp^*_2Sm(thf)_2$ (runs 4 and 5). SmI_2, SmI_3 and $Sm(OTf)_3$ were inert for this reaction (runs 6-8).

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

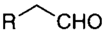
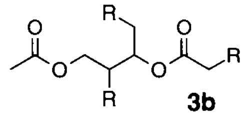
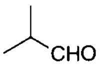
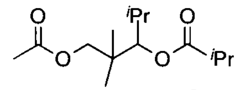
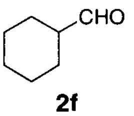
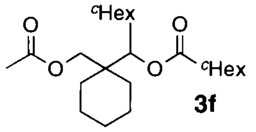
Run	Catalyst	Solvent	**3a** (Yield /%)
1	$Cp^*_2Sm(thf)_2$	toluene	68
2[b]	$Cp^*_2Sm(thf)_2$	toluene	68
3[c]	$Cp^*_2Sm(thf)_2$	toluene	77[d]
4	$Cp^*_2Yb(thf)_2$	toluene	62
5	$Sm(O^iPr)_3$	THF	56
6	SmI_2	THF	—
7	SmI_3	THF	—
8	$Sm(OTf)_3$	THF	—

[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] $Cp^*_2Sm(thf)_2$ (0.05 mmol) was used. [c] **2a** (2 mmol) was used. [d] Based on **2a**.

On the basis of these results, a variety of aldehydes (**2b**-**2f**) were allowed to react with **1** in the presence of $Cp^*_2Sm(thf)_2$ 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-diesters **3b** and **3c** in 70% yields, respectively

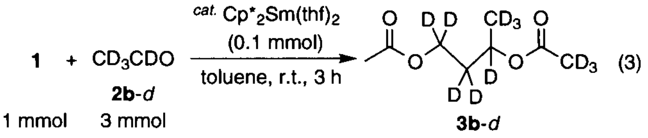
Table 2. Reaction of cyclohexanone oxime acetate (**1**) with various aldehydes catalyzed by $Cp^*_2Sm(thf)_2$ [a]

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

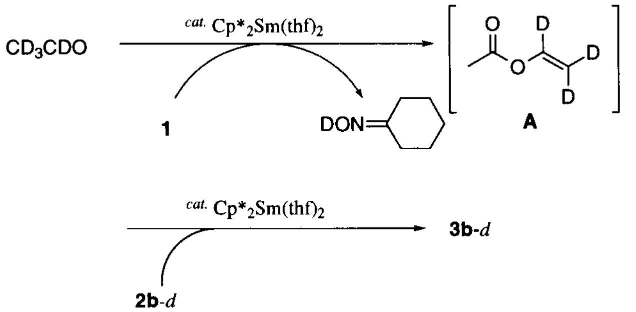
[a] **1** (1 mmol) was reacted with aldehyde (3 mmol) in the presence of $Cp^*_2Sm(thf)_2$ (0.1 mmol) in toluene (1 mL) at 50 °C for 3 hr.
[b] The reaction was carried out at room temperature.

(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 CD_3CDO (**2b**-*d*) catalyzed by $Cp^*_2Sm(thf)_2$ produced **3b**-*d* in which 11 deuteriums are incorporated into the molecule (eq. 3).[9]

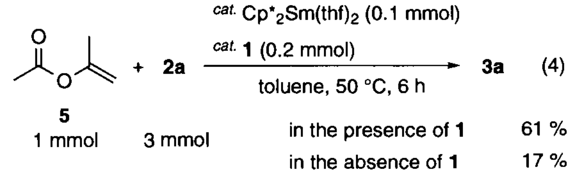


This fact shows that **1** reacts with **2b**-*d* to form vinyl acetate [**A**] as a transient intermediate, which then couples with **2b**-*d* to form 1,3-diol diester **3b**-*d* (Scheme 1).



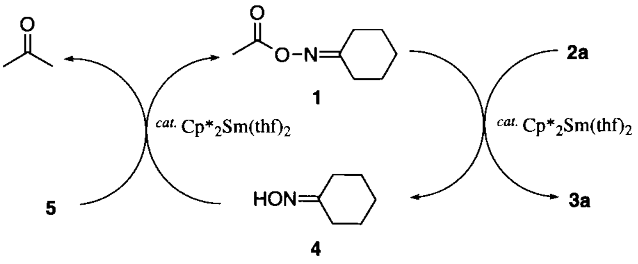
Scheme 1. A possible reaction path for the reaction of **2b**-*d* with **1** catalyzed by $Cp^*_2Sm(thf)_2$

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 quantitative yield.



Scheme 2. Oxime ester-mediated coupling reaction of isopropenyl acetate (**5**) with aldehyde by $Cp^*_2Sm(thf)_2$

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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9 Spectral data for **3b**-*d* is as follows : ^{1}H-NMR ($CDCl_3$ / Me_4Si) δ 1.98 (s) ; ^{13}C-NMR ($CDCl_3$) 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.