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Aldol Type Condensation of Imines Catalyzed by Samarium Complexes

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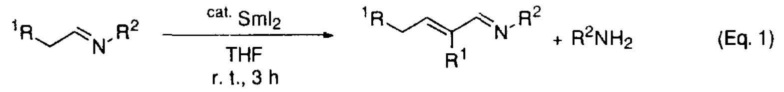
Abstract: *Aldol type condensation of imines has first been achieved via a catalytic process using samarium diiodide (SmI_2) at room temperature to form α,β-unsaturated imines in good yields. The condensation was markedly facilitated by the presence of formates or aldehydes which promote the elimination of amines from aldol adducts. It was found that the 1:2 reaction of amines with aldehydes under the influence of SmI_2 also led to α,β-unsaturated imines in satisfactory yields.*

Since the time Kagan has demonstrated a simple preparation method of samarium diiodide (SmI_2) from samarium metal and 1,2-diiodoethane,[1] SmI_2 has been widely used in synthetic reactions.[2] However, there is only a limited number of catalytic reactions using SmI_2 (e.g., the intramolecular Tishchenko reaction,[3] epoxide rearrangements,[4] Michael and aldol reactions,[5] and Diels-Alder reactions[6]).

Although the aldol reaction of carbonyl compounds is easily attained with the aid of Lewis acids or bases, an aldol-type reaction of imines is difficult to carry out because of the lower acidity of the α-proton of imines than that of carbonyl compounds. To the best of our knowledge, *N*-butylidenbutylamine (**1a**) condenses by heating at 150°C to form a condensation product, *N*-(2-ethyl-2-hexenylidene)butylamine (**2a**), in 65 % yield.[7] Recently, Kobayashi *et al.* have reported that $Sc(OTf)_3$ catalyzes the condensation of vinyl esters[8] or silyl enolates[9] with imines generated *in situ* from aldehydes and amines.

In a previous paper, we have reported that $Cp^*_2Sm(thf)_2$ and SmI_2 catalyze the 1:2 coupling reaction of vinyl esters with aldehydes[10] and the acylation of alcohols as well as amines with vinyl acetates[11] under mild conditions. In the course of our study on the catalytic use of samarium (II) compounds, we found that SmI_2 catalyzes the condensation of imines at room temperature to give the corresponding condensates, α,β-unsaturated imines, in fair to good yields (Eq. 1).

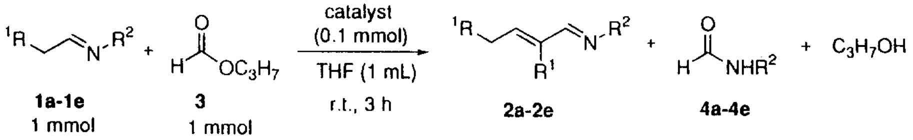


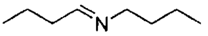
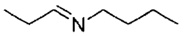
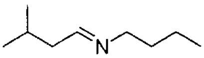
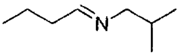
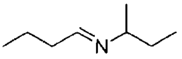
(Eq. 1)

The reaction was carried out as follows: To a THF (1 mL) solution of SmI_2 (0.1 mmol) prepared by Kagan's method was added imine (1 mmol), and the mixture was stirred at room temperature for 3 h. After removal of the samarium compounds by filtration, products were isolated by HPLC.

The aldol reaction of **1a** by SmI_2 gave **2a** in 42 % yield (Run 1 in Table 1). In contrast to the coupling reaction between aldehydes and vinyl acetates where $Cp^*_2Sm(thf)_2$ served as an efficient catalyst, the present aldol reaction was not induced by this complex (Run 2). Since the condensation of **1** to **2** takes place with the elimination of amine, the reaction is expected to be enhanced by promoting the elimination of the amine from the adduct. In a previous paper, we have shown that amines were easily acylated with formates in the presence of SmI_2.[11] Then the condensation of **1a** was carried out in the presence of propylformate (**3**) under these

Table 1. Aldol Condensation of Several Imines by Samarium Compounds in the Presence of Propylformate (3) under Various Conditions



Run	Imine	Cat. (mol%)	Product (Yield / %)
1[a]	 (1a)	SmI_2 (10)	**2a** (42)
2[a]	**1a**	$Cp^*_2Sm(thf)_2$ (10)	No reaction
3	**1a**	SmI_2 (10)	**2a** (98)
4[b]	**1a**	SmI_2 (10) / O_2	**2a** (43)
5[c]	**1a**	SmI_2 (5)	**2a** (83)
6[d]	**1a**	SmI_2 (1)	**2a** (60)
7	**1a**	SmI_3 (10)	**2a** (84)
8	**1a**	Sm(OPr-*i*)$_3$ (10)	No reaction
9	 (1b)	SmI_2 (10)	**2b** (88)
10	**1b**	SmI_3 (10)	**2b** (66)
11	 (1c)	SmI_2 (10)	**2c** (84) (*E*/*Z* = 59/41)
12	 (1d)	SmI_2 (10)	**2d** (75)
13	 (1e)	SmI_2 (10)	No reaction

a) In the absence of **3**. b) Reaction was carried out after bubbling of O_2 into the THF solution of SmI_2. c) THF (0.5 mL) was used as a solvent.
d) THF (0.1 mL) was used as a solvent.

conditions. As expected, the reaction gave **2a** in almost quantitative yield (>98 %) together with *N*-butylformamide (**4a**) and propanol (Run 3). When the quantity of SmI_2 was halved, **1a** was condensed in a slightly lower yield (83 %) to form **2a** (Run 5). The present condensation was also achieved by SmI_3, although the yield of **2a** decreased slightly (Run 7). However, Sm(OPr-*i*)$_3$ was inactive for the present condensation (Run 8). The position of the alkyl substituent on the imines influenced the yield and the geometry of condensates (Runs 9, and 11-13). 3-Alkyl substituted imine such as *N*-3-methylbutylidenbutylamine (**1c**) gave a geometrical isomer of **2c** (*E*/*Z* = 59/41) in 84 % yield (Run 11). However, in the case of 2'-alkyl substituted imine such as *N*-butyliden-2-methylpropylamine (**1d**) gave **2d** having *E*-

configuration in 75 % yield (Run 12). No reaction took place when *N*-butylidene-1-methylpropylamine was used as a substrate (Run 13).

If the amines eliminated by the condensation are trapped by aldehydes, imines would be regenerated under these reaction conditions (Scheme 1). Thus, SmI_2-catalyzed condensation of **1a** in the presence of butanal (**5a**) was carried out. As expected, **2a** was obtained in 87 % yield (Run 1 in Table 2). SmI_3 was highly effective in this reaction (Run 2). Although no condensation of **1e** was accomplished by a combination with formate **3e** (Run 12 in Table 1), the corresponding condensate, **2e**, was formed , in the presence of aldehyde **5a** instead of **3e**, in 23 % yield (Run 7). It is interesting to note that the reaction of **1a** in the presence of 2-methylpropanal (**5b**) produced exclusively **2a**, without formation of a cross condensate of **1a** with **5b** (Run 3). This fact suggests that the condensation occurs through the homo-condensation of imines rather than the cross-condensation of imines with aldehydes.

Scheme 1.

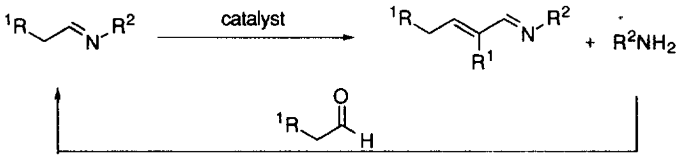
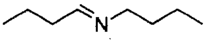
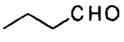
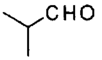
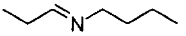
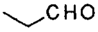
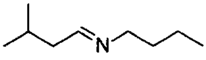
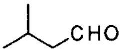
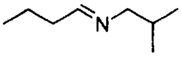
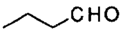
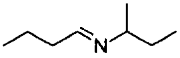
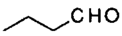
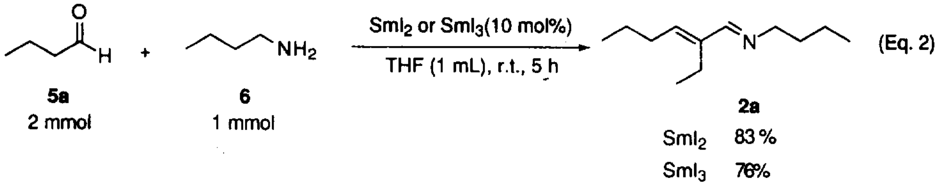


Table 2. Aldol Condensation of Several Imines by Samarium Compounds in the Presence of Aldehydes under Various Conditions[a]

Run	Imine	Aldehyde	Yield / %[b]
1	 (**1a**)	 (**5a**)	**2a** (87)
2[c]	(**1a**)	(**5a**)	**2a** (>99)
3	(**1a**)	 (**5b**)	**2a** (79)
4	 (**1b**)		**2b** (86)
5	 (**1c**)		**2c** (75) (*E*/*Z*= 39/61)
6	 (**1d**)		**2d** (80)
7	 (**1e**)		**2e** (23)

a) Imine (1 mmol) was reacted with aldehyde (1 mmol) in the presence of SmI_2 (0.1 mmol) in THF (1 mL) under a nitrogen atmosphere at r. t. for 5 h.
b) GLC yields based on imines.
c) SmI_3 (0.1 mmol) in THF (1 mL) was used as a catalyst.

Bearing in mind the possibility of a one-pot procedure from aldehyde and amine, we examined the reaction of **5a** with butylamine (**6**) under the influence of SmI_2 and SmI_3 (Eq. 2)[12]. The aldol-type condensation of imine *in situ* generated from **5a** with amine **6** to the corresponding α,β-unsaturated imine **2a** was achieved by the use of samarium compounds as catalysts. The order of addition of substrates to the THF solution of samarium compounds influenced the yield of products. The addition of aldehyde followed by amine resulted in decrease of the yield of product probably because of the occurrence of the Tishchenko reaction of the aldehyde.



Further study along this line and the utilization of α,β-unsaturated imines in synthetic reaction are now in progress.

ACKNOWLEGMENT

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12. To a THF (1 mL) solution of SmI_2 or SmI_3 (0.1 mmol) was added amine (1 mmol),then aldehyde (2 mmol) was introduced. After the stirring of the reaction mixture at room temperature for 5 h, samarium compounds were removed by filtration. Purification of the remaining solution by HPLC gave the corresponding α,β-unsaturated imines.

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