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LETTERS

Tandem Mukaiyama Michael-aldol reactions catalyzed by samarium diiodide

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Abstract

Samarium diiodide catalyzes a one pot procedure allowing to perform sequentially the Mukaiyama-Michael addition of a ketene silyl acetal on a cyclic α,β-unsaturated ketone, followed by a Mukaiyama aldol reaction of an aldehyde. The adducts are isolated as silyl ethers in good yields and in most cases with high diastereoselectivity.

Keywords : Catalysis, samarium, Michael reactions, aldol reactions.

The realization of tandem or cascade reactions allowing to carry out the consecutive formation of several carbon-carbon bonds is a fast developing area [1-3]. Transition metal derivatives have been used as catalysts to perform such reactions but in most cases they induced intramolecular bond formation reactions [1]. Three-component couplings for α,β attachment of two chains on enones by Michael-aldol sequence have found elegant applications in synthesis but they require usually either metal promotors in stoichiometric amounts, or two different promotors or catalysts [4, 5]. A one pot procedure, involving a Michael reaction of a silyl derivative on α,β-unsaturated ketones followed by reaction with a carbonyl compound, both catalyzed by trityl perchlorate has been described [6-8], and asymmetric tandem Michael aldol reactions catalyzed by aluminum derivatives have been very recently reported [9]. However, to the best of our knowledge there are no examples of tandem intermolecular carbon-carbon bonds formation catalyzed by lanthanides. We report now our results concerning the use of samarium diiodide for the tandem Mukaiyama Michael aldol reactions on cyclic α,β-unsaturated ketones.

During our previous investigations we have found that samarium diiodide is the precursor of efficient Lewis acid catalysts [10], especially for the Mukaiyama aldol and Michael reactions [11, 12]. The reactions of ketene silyl acetals with α,β-unsaturated ketones

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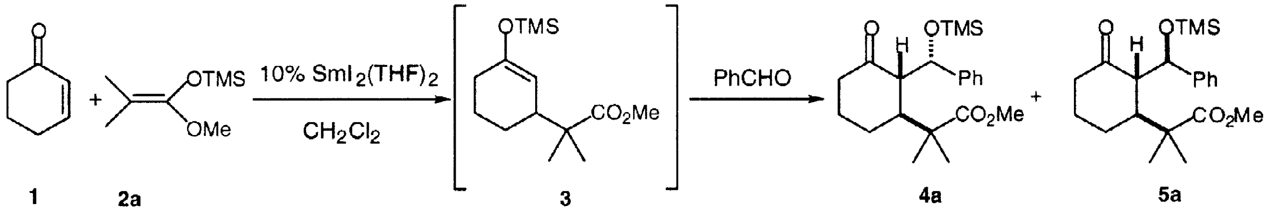
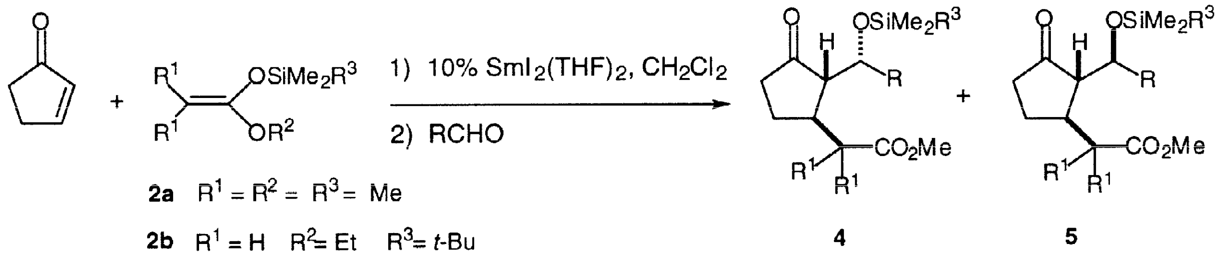
give selective Michael additions and the products are isolated as enoxysilanes. We found also examples of Mukaiyama aldol reactions of enoxysilanes with aldehydes catalyzed by samarium diiodide as well as by lanthanide iodides. This led us to examine the possibility to realize one pot tandem reactions, i.e. a Michael addition followed by a Mukaiyama aldol reaction.

In a first experiment the three-component reaction catalyzed by samarium diiodide at room temperature was carried out by the following procedure. Equimolar amounts of ketene silyl acetal **2a** and cyclohexen-2-one **1** were successively added to a suspension of $SmI_2(THF)_2$ (10 mol%) in methylene chloride (eq 1). The formation of the intermediate enoxysilane **3** was checked (GC/MS) before the addition of benzaldehyde. The crude product contains a mixture of the adducts **4a** + **5a** (and other diastereomers) and of crotonisation products, which indicates that the two reactions have been consecutively achieved (Table, entry 1). Performing the process at low temperature suppressed the formation of the crotonisation by-products and the adducts resulting of the tandem reactions were obtained with high diastereoselectivity (98/2) and satisfactory yield (entry 2).



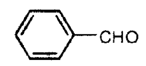
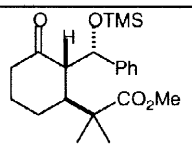
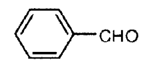
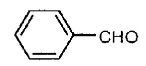
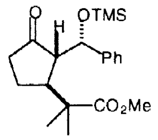
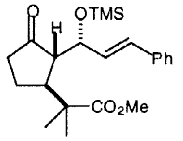
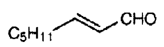
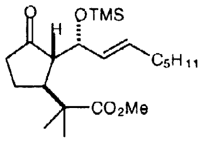
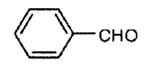
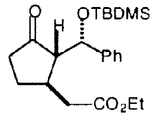
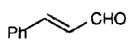
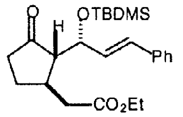
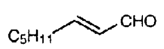
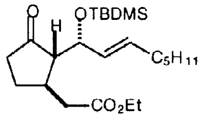
(1)

Similar samarium diiodide-catalyzed tandem reactions have been performed at low temperatures on cyclopenten-2-one using two different ketene silyl acetals and various aldehydes (eq. 2, entries 3-8). In all cases the adducts resulting from the addition of aldehyde on an intermediate enoxysilane were obtained as the silyl ethers diastereomers **4** and **5** in satisfactory yields. In the reactions involving α,β-unsaturated aldehydes, such as *trans*-cinnamaldehyde or *trans*-octen-2-al, as the electrophile, the second step gave a regioselective 1,2-addition, affording the aldol products. We have previously studied the reactions of enoxysilanes on α,β-unsaturated aldehydes catalyzed by samarium diiodide which afforded preferentially the 1,2 addition, the ratio of aldol and Michael products depending on the bulkiness of the substrates [10, 12].



(2)

Table : Tandem Mukaiyama Michael aldol reactions catalyzed by $SmI_2(THF)_2$

Entry	α,β-Unsaturated ketone	Ketene silyl acetal	Aldehyde	T °C	Major Product 4	4/5	Yield%[a]
1	Cyclohexen-2-one	**2a**		rt		60/40	75[b,c,d]
2	-	-		-60		98/2	70[e]
3	Cyclopenten-2-one	-		-30		80/20	77[d]
4	-	-		-60		95/5	72[e]
5	-	-		-		95/5	74[e]
6	-	**2b**		-30		98/2	71[d]
7	-	-		-60		60/40	63[e]
8	-	-		-		59/41	72[e,f]

[a] Isolated yield, all products are fully characterized by ^1H and ^{13}C NMR, MS, IR and elemental analysis; see [13] for experimental conditions. [b] Total yield in crude product, 50% was obtained as crotonisation product. [c] Four stereoisomers are observed in the crude product in a ratio 44/30/14/12. [d] 3 eq. aldehyde. [e] 1.5 eq. aldehyde. [f] Four stereoisomers are observed in the crude product in a ratio 47/33/12/8.

The *trans* diastereomers **4** and **5** which have the two chains fixed on the cycle in trans position are the sole stereomers isolated in all reactions but one (entry 8). Most of the tandem reactions are highly diastereoselective regarding to diastereomer **4** (entries 2-6), the structure of which has been characterized on the basis of NMR spectra (see [14,15] for data concerning **4a**). Only for the adducts resulting of the addition of cyclopenten-2-one and unsubstituted ketene silyl acetal **2b** on an α,β-unsaturated aldehyde (entries 7, 8) was the diastereoselectivity lower.

These Michael aldol reactions are the first examples of tandem carbon-carbon bonds formation catalyzed by lanthanides. The introduction of two chains in α and β-position of cyclic α,β-unsaturated ketones was realized under mild conditions by the use of samarium diiodide. The adducts were easily isolated as silyl ethers, with good yields and diastereoselectivity. We are currently studying the scope of this reaction, the origin of the diastereoselectivity and its application to enantioselective catalysis.

Acknowledgments

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References and notes

[1] Tietze, L.F. *Chem. Rev.* **1996**, *96*, 115-136.

[2] Denmark, S.E.; Thorarensen, A. *Chem. Rev.* **1996**, *96*, 137-165.

[3] Parsons, P.J.; Penkett, C.S.; Shell, A.J. *Chem. Rev.* **1996**, *96*, 195-206.

[4] Noyori, R.; Suzuki, M. *Angew. Chem. Int. Ed. Engl.* **1984**, *23*, 847-876.

[5] Marczak, S.; Michalak, K.; Urbanczyk-Lipkowska, Z.; Wicha, J. *J. Org. Chem.* **1998**, *63*, 2218-2223.

[6] Kobayashi, S.; Mukaiyama, T. *Chem. Lett.* **1986**, 1805-1808.

[7] Kobayashi, S.; Mukaiyama, T. *Chem. Lett.* **1986**, 221-224.

[8] Mukaiyama, T; Sagawa, Y.; Kobayashi, S. *Chem. Lett.* **1986**, 1821-1824.

[9] Yamada, K.; Arai, T.; Sasai, H.; Shibasaki, M. *J. Org. Chem.* **1998**, *63*, 3666-3672.

[10] Collin, J.; Giuseppone, N.; Van de Weghe, P. *Coord. Chem. Rev.* in press.

[11] Van de Weghe, P.; Collin, J. *Tetrahedron Lett.* **1993**, *34*, 3881-3884.

[12] Giuseppone, N.; Van de Weghe, P.; Mellah; M., Collin, J. *Tetrahedron.* submitted for publication.

[13] Note : A solution of SmI_2 in THF (0.1 M, 2.0 mL, 0.2 mmol) was carefully evaporated *in vacuo* to give SmI_2 (THF) $_2$ as a blue powder, suspended in CH_2Cl_2 (5 mL) and then 1-methoxy-2-methyl-1-trimethylsilyloxypropene (2 mmol, 348 mg) and cyclohexen-2-one (2 mmol, 192 mg) were added. After 0.5 h at room temperature the yellow solution was cooled at -60°C and a solution of benzaldehyde (3 mmol, 315 mg) in 5 mL CH_2Cl_2 was added at the same temperature. The reaction mixture was allowed to stand at -60°C during 36 h. The reaction was stopped by the addition of hexane (40 mL) which precipitated the samarium salts. After filtration through celite the solvents were removed under reduced pressure and the product was purified by column chromatography on desactivated silica gel (527 mg, 70% yield).

[14] Spectroscopic data for **4a** : ^{1}H NMR ($CDCl_3$, 250 MHz) δ: 7.27 (m, 5H), 5.0 (d, 1 H, *J*=5.1 Hz), 3.65 (s, 3 H), 2.63 (d, 1 H, *J*=5.1 Hz), 2.4-1.5 (m, 7H), 0.86 (s, 3 H), 0.75 (s, 3 H), -0.02 (s, 9 H). ^{13}C NMR ($CDCl_3$, 62.9 MHz) δ: 216.10, 177.80, 142.95, 128.05, 128.05, 127.55, 125.40, 77.30, 58.75, 51.40, 45.70, 41.40, 40.15, 24.50, 24.70, 22.60, 20.81, -0.20. Elemental Analysis for $C_{21}H_{32}O_4Si$: Calcd % C : 66.98, % H : 8.57; Found: % C : 67.25, % H : 8.55. HRMS Calcd for $C_{21}H_{32}O_4Si$: 376.2069, Found : 376.2070.

[15] The structure of **4a** was determined by the values of ^3J H-H (*J*=0 for the two protons on the cycle, *J*=5.1 Hz corresponding to *syn* positions on the two other asymmetric carbons) and by 2D NMR experiments.