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Imino-Diels–Alder and imino-aldol reactions catalyzed by samarium diiodide

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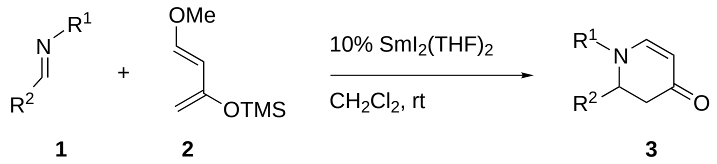
Abstract—In the presence of a catalytic amount of samarium diiodide in methylene chloride, aromatic imines react with Danishefsky diene to form tetrahydropyridine-4-ones in high yields. Under the same conditions, various imino-aldol reactions afford β-amino esters or β-amino ketones. © 2001 Elsevier Science Ltd. All rights reserved.

In our previous work, we have shown that samarium diiodide is an efficient Lewis acid-type catalyst for a variety of carbon–carbon bond-forming reactions.[1] We have performed aldol and Michael reactions,[2] Diels–Alder and hetero Diels–Alder reactions[3] and, more recently, tandem Michael-aldol reactions[4,5] by the use of catalytic amounts of samarium diiodide. Moreover, we have found that iodo samarium binaphthoxides are enantioselective catalysts for Diels–Alder reactions.[6] In all these reactions, an aldehyde or a ketone was used as the electrophile. For the lanthanide triflate-catalyzed reactions, the preferential activity of aldimines over aldehydes has been established[7] and subsequently used for the development of lanthanide triflate-catalyzed three-component reactions with in situ formation of imines.[8] This prompted us to investigate the catalytic activity of samarium diiodide for reactions involving imines, aza-Diels reactions and imino-aldol reactions, in order to evaluate the possibility of further developments for lanthanide iodides in the synthesis of heterocycles or in enantioselective catalysis.

The cycloaddition reactions of imines with various dienes or alkenes were first examined. Imines **1** react with Danishefsky diene **2** in the presence of samarium diiodide (10 mol%), in methylene chloride at room temperature (Eq. (1), Table 1) to form tetrahydropyridine-4-ones **3** which were isolated in high yields. As for reactions involving aldehydes,[2] when the imine is added to the reaction mixture, the color turns from blue to yellow or orange and remains unchanged until the end of the reaction, which is indicative of a trivalent active species. We checked that samarium triiodide can be used alternatively as a catalyst and shows the same activity as samarium diiodide (Table 1, entries 2 and 3). The presence of a chelating group on the imine increases the rate of the reaction. The activity of samarium diiodide is similar to that of ytterbium and scandium triflates in reactions involving preformed imines or in three-component reactions (in all cases reactions are carried out in acetonitrile with 10 mol% catalyst at room temperature or 0°C)[9,10] while with indium triflate[11] and bismuth chloride or triflate[12] smaller amounts of catalyst were needed.

Typical procedure: In a Schlenk tube, a samarium diiodide solution 0.1 M in THF (1 mL, 0.1 mmol) is evaporated until obtention of a blue powder of $SmI_2(thf)_2$ and after addition of CH_2Cl_2 (5 mL) under argon, a suspension 0.02 M is obtained. Then are



(1)

Keywords: samarium diiodide; catalysis; cycloadditions; imines; aldol reaction.

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Table 1. Imino Diels–Alder reactions catalyzed by samarium diiodide

Entry	R^1	R^2	*t* (h)	Yield (%)[a]
1	Ph	Ph	24	61
2	Ph	*o*-$CH_3OC_6H_4$	5	72
3	Ph	*o*-$CH_3OC_6H_4$	5	71[b]
4	Ph	*p*-$CH_3OC_6H_4$	18	82
5	*o*-$CH_3OC_6H_4$	Ph	16	86
6	*p*-$CH_3OC_6H_4$	Ph	36	86
7	*p*-$CH_3OC_6H_4$	*p*-$CH_3OC_6H_4$	36	87
8	*p*-$CH_3C_6H_4$	Ph	36	63
9	$CH_2C_6H_5$	*o*-$CH_3OC_6H_4$	6	79

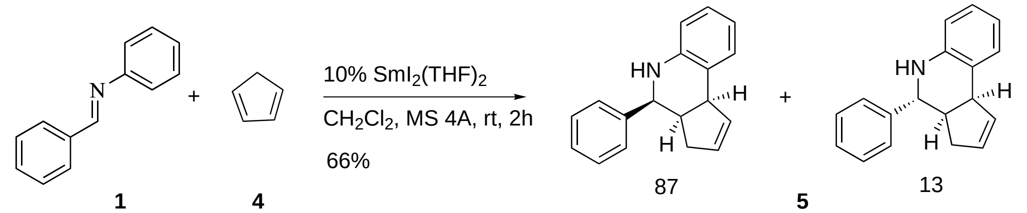
[a] Isolated yield %, all products were fully characterized by spectroscopic data.

[b] 10% $SmI_3(THF)_3$.

successively added, a solution of *N*-phenyl-2-methoxybenzaldimine (211 mg, 1 mmol) in CH_2Cl_2 (2 mL), and Danishefsky's diene (293.2 µL, 1.5 mmol). After stirring overnight, hydrolysis by HCl 0.1 M and extraction with CH_2Cl_2, the crude product is purified on silica gel (pentane/ethyl acetate: 40/60) to yield 86% of pure product.

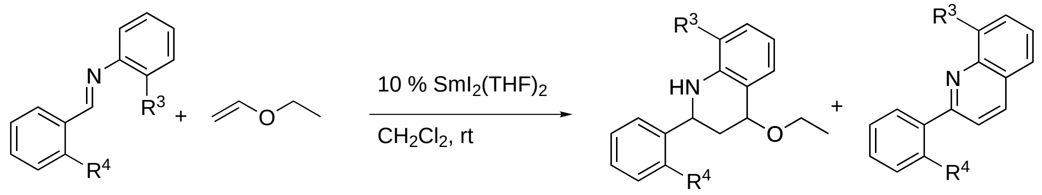
Samarium diiodide (10 mol%) also catalyzes the addition of imines to cyclopentadiene at room temperature in methylene chloride. In this reaction the imine behaves as an azadiene, and the adduct is obtained as a mixture of *cis* and *trans* isomers (Eq. (2)). Samarium diiodide shows higher activity than other catalysts such as ytterbium triflate[10] or indium chloride.[13]

The catalytic activity of samarium diiodide for the cycloaddition of imines onto ethyl vinyl ether **6** has also been studied (Eq. (3)). In this reaction, as for cyclopentadiene, the imine again works as an azadiene. With several imines crude products were mixtures of the cycloadduct **7** and of the corresponding quinoline **8**, that could be separated by column chromatography on deactivated silica (eluent pentane/ether: 80/20). In ytterbium triflate-catalyzed reactions, Fujiwara[14] and Kobayashi[9] described different conditions for the treatment of crude products which allowed them to isolate



1 **4** **5**

(2)



(3)

	1	**6**	**7**	**8**
	$R^3 = R^4 = H$		25	20
	$R^3 = OCH_3$ $R^4 = H$		3	35
	$R^3 = H$ $R^4 = OCH_3$		28	14

Table 2. Imino-aldol reactions catalyzed by samarium diiodide

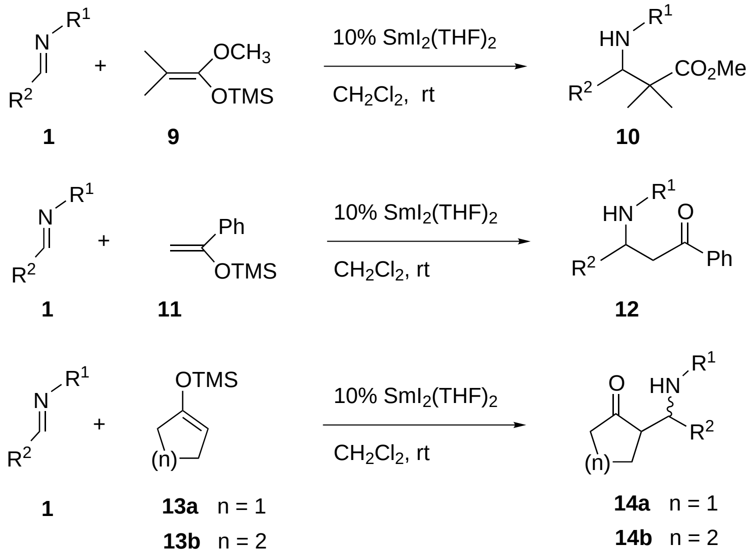
Entry	R^1	R^2	Silyl derivative	Product	Yield[a]
1	*p*-$CH_3OC_6H_4$	CO_2Et	**9**	**10**	90[b]
2	*o*-$CH_3OC_6H_4$	Ph	**9**	**10**	85[b]
3	Ph	Ph	**9**	**10**	88[b]
4	*p*-$CH_3OC_6H_4$	CO_2Et	**11**	**12**	63[b,c]
5	*o*-$CH_3OC_6H_4$	Ph	**11**	**12**	53[b,c]
6	*o*-$CH_3OC_6H_4$	*p*-CF_3	**11**	**12**	82[b,c]
7	*p*-$CH_3OC_6H_4$	CO_2Et	**13a**	**14a**	95[d]
8	*o*-$CH_3OC_6H_4$	Ph	**13a**	**14a**	95[d]
9	*o*-$CH_3OC_6H_4$	*p*-CF_3	**13a**	**14a**	93[d]
10	*p*-$CH_3OC_6H_4$	CO_2Et	**13b**	**14b**	81[d]

[a] All products were fully characterized by spectroscopic data.

[b] Isolated yield %, reaction time 18 h.

[c] Reaction performed with 1.3 equiv. enoxysilane.

[d] Yield % in crude product (decomposed by chromatography on silica).



(4)

either pure quinoline **8** or tetrahydroquinoline **7**. Both methods have been tested, always leading to mixtures of these two products.

The reaction of glyoxylic and aromatic imines with ketene silyl acetal **9** in equimolar amounts, in the presence of 10% $SmI_2(THF)_2$ in methylene chloride (Eq. (4), Table 2) gave the β-amino ester adducts in high yields at room temperature. While activity of samarium diiodide is similar to that described with samarium triiodide,[15] our procedure is much simpler, as with other catalysts such as $B(C_6F_5)$,[16] or TiI_4,[17] reactions need to be carried out at low temperature and with excess of ketene silyl acetal. Imino-aldol reactions were also observed by reaction of a glyoxylic imine as well as aromatic imines with enoxysilane **11** (Table 2, entries 4–6). In lanthanide triflate-catalyzed reactions, cycloaddition of enoxysilane **11** onto imines have been first reported,[9,14] and later on, in competitive reactions with aldehydes, the iminoaldol products were isolated.[7] Catalysis by bismuth derivatives with the same substrates yields to aza-Diels reactions,[12] while with $BF_3{\cdot}OEt_2$ Mannich reactions are observed.[18] Recently indium chloride was reported to promote Mannich reactions with enoxysilanes by three-component reactions in water, but with high amounts of catalyst (20% at least).[19] Samarium diiodide catalyzes also imino-aldol reactions with cyclic enoxysilanes **13a** and **13b** (Table 2, entries 7–10), leading to β-amino ketones.

Samarium diiodide showed high activity for different reactions involving imines such as cycloaddition reactions or Mannich reactions. These results led us to investigate the reactivity of imines in tandem Michael-aldol sequences as we have previously reported with aldehydes.[4,5] Such catalyzed tandem iminoaldol reactions have been seldom described in literature[20] and are currently under study in our laboratory.

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