



Pergamon

Tetrahedron Letters 41 (2000) 3389–3393

TETRAHEDRON
LETTERS

Synthesis of 1,3-oxazolidines from imines and epoxides catalyzed by samarium compounds

Takayuki Nishitani, Hiroyuki Shiraishi, Satoshi Sakaguchi and Yasutaka Ishii *

Department of Applied Chemistry, Faculty of Engineering and High Technology Research Center, Kansai University, Suita, Osaka 564-8680, Japan

Received 4 February 2000; revised 21 February 2000; accepted 25 February 2000

Abstract

A new method for the synthesis of 1,3-oxazolidine derivatives has been developed. Thus, a variety of 1,3-oxazolidines was prepared by the reaction of imines with epoxides in the presence of a catalytic amount of a samarium compound such as SmI_2 , SmI_3 , or $\text{Cp}^*_2\text{Sm}(\text{thf})_2$. © 2000 Elsevier Science Ltd. All rights reserved.

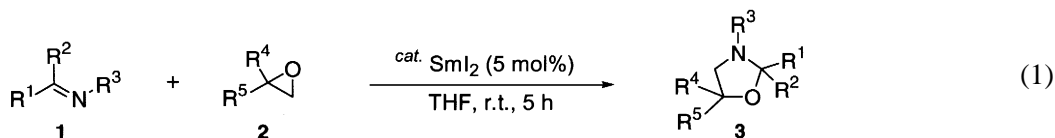
Keywords: samarium; 1,3-oxazolidines; imines; epoxides; catalytic synthesis.

1,3-Oxazolidines are useful not only as intermediates in organic synthesis¹ but also as effective ligands for metal-catalyzed asymmetric synthesis.² A general synthetic method for the synthesis of 1,3-oxazolidines is the condensation of 1,2-amino alcohols with carbonyl compounds in the presence of an acid catalyst.³ In recent years, several catalytic methods using transition metals as catalysts have been developed.⁴ For example, Yamamoto and Shim showed the Pd-catalyzed [3+2] cycloaddition of vinylic oxiranes with imines,^{4a} and the reaction of 1,2-amino alcohols with nitrile derivatives catalyzed by Pd/C or Rh/C under hydrogen atmosphere was reported by Muzart et al.^{4b,c}

Recently, we have shown that SmI_2 acts as an efficient precatalyst for the aldol-type condensation of imines to α,β -unsaturated imines.⁵ As an extension of this chemistry, a novel synthesis of pyrrole derivatives has been developed by a three-component coupling reaction of amines, aldehydes, and nitroalkanes in the presence of a catalytic amount of SmCl_3 .⁶ In addition, the reaction of imines and nitroalkenes was catalyzed by a samarium compound such as $\text{Sm}(\text{O}^i\text{Pr})_3$, producing the corresponding pyrrole derivatives.⁷ In continuation of our studies, we have now found that imines react with epoxides under mild conditions in the presence of a catalytic amount of SmI_2 to give 1,3-oxazolidine derivatives in good yields (Eq. (1)). In the patent work, it has been reported that the reaction of imine with an excess amount of alkylene oxide at 140–250 °C affords 1,3-oxazolidine derivative.⁸ To our best knowledge, no catalytic methods have been reported for the synthesis of 1,3-oxazolidines from imines and epoxides. In

* Corresponding author.

this paper, we wish to report a new route to 1,3-oxazolidine derivatives using a samarium compound as catalyst.



A typical reaction is carried out as follows. To a solution of SmI₂ (0.05 mmol) in THF (1 mL) was added *N*-(1-methyl)ethylidene benzylamine (**1a**) (1 mmol) and 2-methyl-1,2-epoxypropane (**2a**) (2 mmol), and the mixture was stirred under ambient conditions for 5 h. After quenching with wet ether, the solvent was removed under reduced pressure. Short-column chromatography on silica gel with ether, followed by distillation, gave 3-*N*-benzyl-2,2,5,5-tetramethyl-1,3-oxazolidine (**3aa**)⁹ in 93% yield.

Table 1 shows the results for the reaction of **1a** with **2a** using various samarium compounds. The reaction of **1a** with 2 equiv. of **2a** in the presence of a catalytic amount of SmI₂ (0.05 equiv. with respect to **1a**) in THF at room temperature for 5 h gave **3aa** in 98% GC yield. Cp*₂Sm(thf)₂ was less active than SmI₂ to form **3aa** in 40% yield. SmI₃ was also effective for the present reaction to give **3aa** in 85% yield, but SmCl₃ was found to be inert under these conditions (Run 4). Sm(OTf)₃ and Sm(*i*OPr)₃, which serve as Lewis acid and Lewis base, respectively, showed low activity (Runs 5 and 6).

Table 1
Reaction of **1a** and **2b** by various catalysts^a

Run	Catalyst	Yield of 3aa / % ^b
1	SmI ₂	98
2 ^c	Cp* ₂ Sm(thf) ₂	40
3	SmI ₃	85
4	SmCl ₃	3
5	Sm(OTf) ₃	24
6	Sm(<i>i</i> OPr) ₃	8





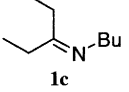

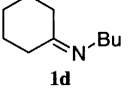

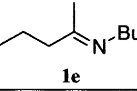
^a **1a** (1.0 mmol) was allowed to react with **2a** (2.0 mmol) in the presence of Sm catalyst (0.05 mmol) in THF (1 mL) at room temperature for 5 h under Ar atmosphere. ^b Based on GC yield.

^c Toluene (1 mL) was used as a solvent.

On the basis of these results, ketimine **1a** was allowed to react with various epoxides under the influence of SmI₂. Compound **1a** readily reacted with terminal epoxides (**2b** and **2c**) to form the corresponding 1,3-oxazolidine derivatives (**3ab** and **3ac**) in 83 and 81% yields, respectively (Table 2, Runs 2 and 3). However, the reaction of **1a** with an internal epoxide such as 1,2-epoxycyclohexane (**2d**) was difficult under these reaction conditions to form a poor yield of 1,3-oxazolidine **3ad** (Run 4). Various ketimines, **1b–1e**, were allowed to react with terminal epoxide **2a** to produce the corresponding 1,3-oxazolidine derivatives, **3ba–3ea**, in good yields (Runs 5–8).

We next tried the reaction of aldimines with epoxides. The reaction of *N*-butylidenebenzylamine (**1f**) with **2a** in the presence of the SmI₂ catalyst in THF at room temperature gave 3-*N*-benzyl-5,5-dimethyl-2-propyl-1,3-oxazolidine (**3fa**) in 32% yield along with the self-aldol condensation product (9%) of **1f** (Table 3, Run 1). Interestingly, when Cp*₂Sm(thf)₂ was used as a catalyst, the yield of **3fa** increased to 62% (Run 2).¹⁰ In a previous paper, we showed that the aldol-type condensation of aldimines is efficiently catalyzed by SmI₂, but not Cp*₂Sm(thf)₂. Therefore, it seems that SmI₂ promotes the aldol type condensation of imines rather than the reaction of aldimines with epoxide. Several aldimines,

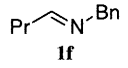
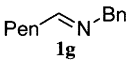
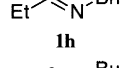
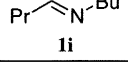
Table 2
Synthesis of 1,3-oxazolidine derivatives from ketimines and epoxides catalyzed by SmI_2^a

Run	Imine	Epoxide	Oxazolidine	Yield / % ^b	Run	Imine	Epoxide	Oxazolidine	Yield / % ^b
1			3aa	93	5		2a	3ba	88
2	1a		3ab	83	6		2a	3ca	85
3	1a		3ac	81	7		2a	3da	82
4	1a		3ad	6	8		2a	3ea	52

^a Imine (1.0 mmol) was allowed to react with epoxide (2.0 mmol) in the presence of SmI_2 (0.05 mmol) in THF (1 mL) at room temperature for 5 h under Ar atmosphere. ^b Isolated yield.

1g–1i, also reacted with **2a** by using $\text{Cp}^*\text{Sm}(\text{thf})_2$ as the catalyst (Runs 3–5). Thus, a variety of 1,3-oxazolidine derivatives could be prepared from imines and epoxides by choosing the catalyst, either SmI_2 or $\text{Cp}^*\text{Sm}(\text{thf})_2$.

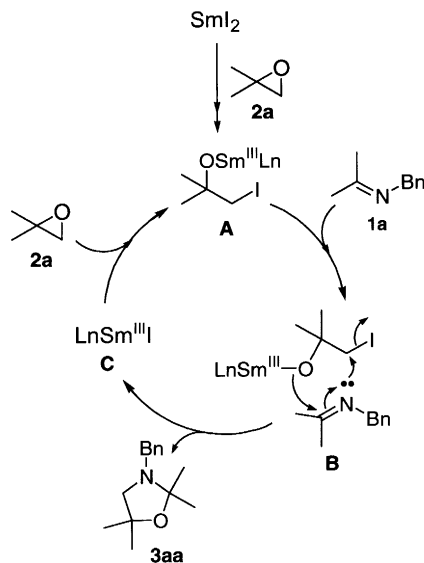
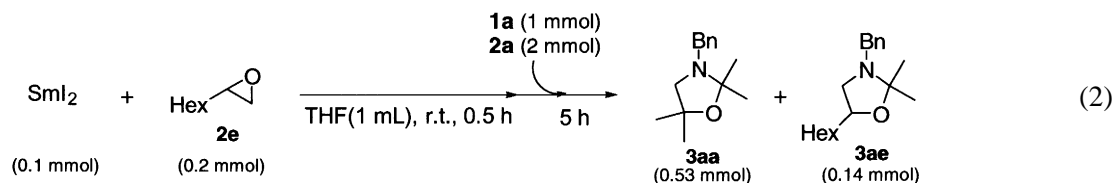
Table 3
Synthesis of 1,3-oxazolidine derivatives from the reaction of aldimines and epoxides catalyzed by $\text{Cp}^*\text{Sm}(\text{thf})_2^a$

Run	Imine	Epoxide	Oxazolidine	Yield / % ^b
1 ^c		2a	3fa	32 (9)
2	1f	2a	3fa	62 (<1)
3		2a	3ga	65
4		2a	3ha	60
5		2a	3ia	61

^a Imine (1.0 mmol) was allowed to react with epoxide (2.0 mmol) in the presence of $\text{Cp}^*\text{Sm}(\text{thf})_2$ (0.05 mmol) in toluene (1 mL) at room temperature for 5 h under Ar atmosphere. ^b Parentheses show the yield of *N*-(2-ethyl-2-hexenylidene)benzylamine. ^c SmI_2 (0.05 mmol) was used as a catalyst.

In order to obtain information on the reaction path, the following experiments were carried out. The addition of epoxide **2a** to a THF solution containing SmI_2 led to an immediate color change from blue–green to light yellow, while no color change was observed when **1a** was added to this solution. This observation suggests that the present 1,3-oxazolidine formation is initiated by the reaction of epoxides with SmI_2 to form samarium alkoxide¹¹ which then reacts with imines to give 1,3-oxazolidines. In fact, samarium iodohydrin obtained from SmI_2 (0.1 mmol) and 1,2-epoxyoctane (**2e**) (0.2 mmol) was added to a solution of **1a** (1 mmol) and **2a** (2 mmol) to give **3aa** (0.53 mmol) and 3-*N*-benzyl-2,2-dimethyl-5-

hexyl-1,3-oxazolidine (**3ae**) (0.14 mmol) (Eq. (2)). These results led to the conclusion that the real active species of the present reaction is an iodo samarium alkoxide (**A**),¹¹ which probably lies in an aggregated form through iodide, generated in situ from SmI₂ and epoxide. The **A** may readily react with imine to form oxazolidine (Scheme 1).



Scheme 1.

In conclusion, a variety of 1,3-oxazolidine derivatives was synthesized by the reaction of imines and epoxides with the use of samarium compounds. This provides a new synthetic tool for 1,3-oxazolidines, which are difficult to prepare catalytically by conventional methods.

Acknowledgements

This work is supported by a Grant-in-Aid for Scientific Research (No. 1119268) on Priority Areas (No. 283, 'Innovative Synthetic Reactions') from Monbusho.

References

1. (a) Le Bail, M.; Perard, J.; Atiken, D. J.; Bonin, M.; Husson, H.-P. *Tetrahedron Lett.* **1997**, 38, 7177–7180. (b) Heaney, H.; Papageorgiou, G.; Wilkins, R. F. *Tetrahedron* **1997**, 53, 14 381–14 396.
2. (a) Dai, W.-M.; Zhu, H. J.; Hao, X.-J. *Tetrahedron: Asymmetry* **1996**, 7, 1245–1248. (b) Prasad, K. R. K.; Joshi, N. N. *J. Org. Chem.* **1997**, 62, 3770–3771.
3. Bergman, E. D. *Chem. Rev.* **1953**, 53, 309–352. Other useful methods are as follows: (a) Yli-Kauhalauma, J. T.; Harwig, C. W.; Wentworth Jr., P.; Janda, K. D. *Tetrahedron Lett.* **1998**, 39, 2269–2272. (b) Polyak, F.; Dorofeeva, T.; Zelchans, G.; Shustov, G. *Tetrahedron Lett.* **1996**, 37, 8223–8226.

4. (a) Shim, J.-G.; Yamamoto, Y. *Tetrahedron Lett.* **1999**, *40*, 1053–1056. (b) Letinois, S.; Dumur, J.-C.; Henin, F.; Muzart, J. *Tetrahedron Lett.* **1998**, *39*, 2327–2330. (c) Henin, F.; Letinois, S.; Muzart, J. *Tetrahedron Lett.* **1997**, *38*, 7187–7190.
5. Shiraishi, H.; Kawasaki, Y.; Sakaguchi, S.; Nishiyama, Y.; Ishii, Y. *Tetrahedron Lett.* **1996**, *37*, 7291–7294.
6. Shiraishi, H.; Nishitani, T.; Sakaguchi, S.; Ishii, Y. *J. Org. Chem.* **1998**, *63*, 6234–6238.
7. Shiraishi, H.; Nishitani, T.; Nishihara, T.; Sakaguchi, S.; Ishii, Y. *Tetrahedron* **1999**, *55*, 13957–13964.
8. Frank, D.; Hee, C. European Patent Appl., 13 pp. (106:213933 CA).
9. Spectral data for **3aa**: ^1H NMR (CDCl_3/TMS) δ 7.30–7.14 (m, 5H), 3.49 (s, 2H), 2.52 (s, 2H), 1.21 (s, 6H), 1.18 (s, 6H); ^{13}C NMR (CDCl_3/TMS) δ 139.9, 128.1, 128.0, 126.7, 94.6, 77.2, 61.0, 52.6, 28.4, 24.4; IR (neat) 3447, 2960, 2934, 2874, 2806, 1461, 1360, 1086, 1034, 805 cm^{-1} ; MS (70 eV) $m/e=\text{M}^+$ 204 (100), 162 (38), 91 (82), 70 (21).
10. $\text{Cp}^*_2\text{Sm}(\text{thf})_2$ was prepared according to literature procedure: Evans, W. J.; Bloom, I.; Hunter, W. E.; Atwood, J. L. *J. Am. Chem. Soc.* **1981**, *103*, 6507–6508.
11. It was reported that the ring-opening reaction of epoxides by SmI_2 in the presence of HMPA is promoted by a catalytic amount of Sm(III) species generated by the reaction of SmI_2 with air: (a) Matsukawa, M.; Tabuchi, T.; Inanaga, J.; Yamaguchi, M. *Chem. Lett.* **1987**, 2101–2102. (b) Tabuchi, T.; Inanaga, J.; Yamaguchi, M. *Tetrahedron Lett.* **1986**, *27*, 3891–3894. (c) Girard, P.; Namy, J. L.; Kagan, H. B. *J. Am. Chem. Soc.* **1980**, *102*, 2693–2698.