Pergamon

Tetrahedron Letters, Vol. 38, No. 26, pp. 4559-4562, 1997
© 1997 Elsevier Science Ltd
All rights reserved. Printed in Great Britain
0040-4039/97 $17.00 + 0.00

PII: S0040-4039(97)00854-X

# Lewis Acid Catalysis in Micellar Systems. $Sc(OTf)_3$-Catalyzed Aqueous Aldol Reactions of Silyl Enol Ethers with Aldehydes in the Presence of a Surfactant

**Shū Kobayashi,* Takeshi Wakabayashi, Satoshi Nagayama, Hidekazu Oyamada**

Department of Applied Chemistry, Faculty of Science, Science University of Tokyo (SUT),
and CREST, Japan Science and Technology Corporation (JST)
Kagurazaka, Shinjuku-ku, Tokyo 162

***Abstract:*** *Scandium triflate ($Sc(OTf)_3$)-catalyzed aldol reactions of silyl enol ethers with aldehydes were successfully carried out in micellar systems. While the reactions proceeded sluggishly in water, remarkable enhancement of the reactivity was observed in the presence of a small amount of a surfactant. In these systems, versatile carbon-carbon bond-forming reactions proceeded in water without using any organic solvents.*

The importance of aqueous reactions is now generally recognized, and development of carbon-carbon bond-forming reactions that can be carried out in aqueous media is now one of the most challenging topics in organic synthesis.[1] As for aldol reactions of silyl enol ethers with aldehydes (Mukaiyama reaction),[2] strict anhydrous conditions are needed when typical Lewis acids such as $TiCl_4$, $SnCl_4$, $BF_3 \cdot OEt_3$, etc. are used. Recently, we have found that lanthanide and scandium triflates ($Ln(OTf)_3$, $Sc(OTf)_3$) are stable Lewis acids in water and that aldol reactions of silyl enol ethers with aldehydes proceed smoothly in aqueous media in the presence of a catalytic amount of the lanthanide salt.[3] While the reactions were successfully carried out in THF-water or toluene-ethanol-water,[4] lower yields were obtained in pure water.[3c,5,6] In the course of our investigations to develop new synthetic reactions, especially carbon-carbon bond-forming reactions, in aqueous media, we have found that such reactions proceeded smoothly in micellar systems. In this report, we describe our preliminary results on Lewis acid catalysis in micellar systems: scandium triflate-catalyzed aldol reactions of silyl enol ethers with aldehydes have been successfully carried out in aqueous solutions of surfactants.

Lewis acid catalysis in micellar systems was first found in the model reaction of the silyl enol ether of propiophenone (**1**) with benzaldehyde (Table 1). While the reaction proceeded sluggishly in the presence of 0.2 eq. $Yb(OTf)_3$ in water, remarkable enhancement of the reactivity was observed when the reaction was carried out in the presence of 0.2 eq. $Yb(OTf)_3$ in an aqueous solution of sodium dodecylsulfate (SDS, 0.2 eq., 35 mM), and the corresponding aldol adduct was obtained in a 50% yield.[7] The amounts of the surfactant also influenced the reactivity and the yield was improved when scandium triflate (Sc(OTf)$_3$) was used as a Lewis acid catalyst. Judging from the critical micelle concentration, micelles would be formed in these reactions, and it is noteworthy that the Lewis acid-catalyzed reactions proceeded smoothly in micellar systems.[8] It was also found that the surfactants influenced the yield, and that TritonX-100 was effective in the aldol reaction (but required long reaction time), while only a trace amount of the adduct was detected when using cetyltrimethylammonium bromide (CTAB) as a surfactant.[9]

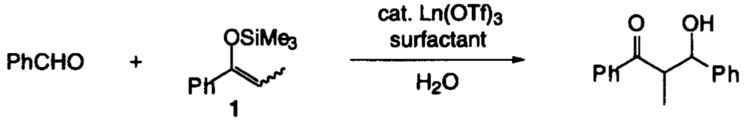
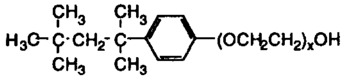


**Table 1** Effect of Ln(OTf)$_3$ and Surfactants

| Ln(OTf)$_3$/eq. | surfactant/eq. | Time/h | Yield/% |
|---|---|---|---|
| Yb(OTf)$_3$/0.2 | —— | 48 | 17 |
| Yb(OTf)$_3$/0.2 | SDS/0.04 | 48 | 12 |
| Yb(OTf)$_3$/0.2 | SDS/0.1 | 48 | 19 |
| Yb(OTf)$_3$/0.2 | SDS/0.2 | 48 | 50 |
| Yb(OTf)$_3$/0.2 | SDS/1.0 | 48 | 22 |
| Sc(OTf)$_3$/0.2 | SDS/0.2 | 17 | 73 |
| Sc(OTf)$_3$/0.1 | SDS/0.2 | 4 | 88 |
| Sc(OTf)$_3$/0.1 | TritonX-100[a]/0.2 | 60 | 89 |
| Sc(OTf)$_3$/0.1 | CTAB/0.2 | 4 | trace |

a)



Several examples of the Sc(OTf)$_3$-catalyzed aldol reactions in micellar systems are shown in Table 2. Not only aromatic, but also aliphatic and α,β-unsaturated aldehydes reacted with silyl enol ethers to afford the corresponding aldol adducts in high yields. Formaldehyde water solution also worked well. *To our great surprise, ketene silyl acetal 3, which is known to hydrolyze very easily even in the presence of a small amount of water,[10] reacted with an aldehyde in the present micellar system to afford the corresponding aldol adduct in a high yield.*

A typical experimental procedure is described for the reaction of benzaldehyde with the silyl enol ether of propiophenone (**1**): a mixture of benzaldehyde (0.5 mmol), silyl enol ether **1** (0.75 mmol), SDS (29 mg, 0.2 eq.), and Sc(OTf)$_3$ (25 mg, 0.1 eq.) in water (3 ml) was stirred at rt for 4 h. An anion exchange resin (Amberlite IRA-93ZU) was added and the mixture was stirred for 30 min.[11] The resin was filtrated, and water (15 ml) and ethyl acetate (15 ml) were added. After the organic layer was separated, the aqueous layer was

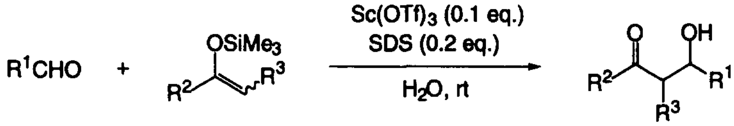
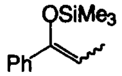
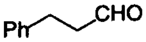
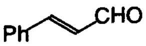
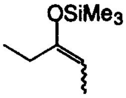
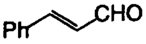
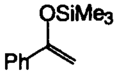
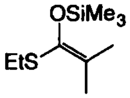
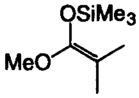


**Table 2.** Sc(OTf)$_3$-Catalyzed Aldol Reactions in Micellar Systems

| Aldehyde | Silyl Enol Ether | Yield/% |
|---|---|---|
| PhCHO |  1 | 88[a)] |
|  | 1 | 86[b)] |
|  | 1 | 88[c)] |
| HCHO | 1 | 82[d)] |
| PhCHO |  2 | 88[e)] |
|  | 2 | 80[f)] |
| PhCHO |  | 75[g,h)] |
| PhCHO |  | 94 |
| PhCHO |  3 | 84[h)] |

a) *Syn/anti* = 50/50. b) *Syn/anti* = 45/55. c) *Syn/anti* = 41/59. d) Comercially available HCHO aq. (3 ml), 1 (0.5 mmol), Sc(OTf)$_3$ (0.1 mmol), and SDS (0.1 mmol) were combined. e) *Syn/anti* = 57/43. f) *Syn/anti* = 69/31. g) Sc(OTf)$_3$ (0.2 eq.) was used. h) Additional silyl enolate (1.5 eq.) was charged after 6 h.

extracted with ethyl acetate. The combined organic layer was dried, evaporated, and the crude material was chromatographed on silica gel to afford the corresponding aldol adduct (88% yield).

In summary, we have demonstrated Lewis acid catalysis in micellar systems. The Sc(OTf)$_3$-catalyzed aldol reactions of silyl enol ethers with aldehydes proceeded smoothly in water in the presence of a surfactant to afford the corresponding aldol adducts in high yields. It should be noted that the reactions were successfully carried out in water without using any organic solvents. Use of the reusable scandium catalyst and water as a solvent would result in clean and environmentally friendly systems.

Further studies to develop other synthetic reactions in micellar systems and also to clarify the precise mechanism in these reactions are now actively in progress in our laboratories.

**Acknowledgment.** This work was partially supported by a Grant-in-Aid for Scientific Research from the Ministry of Education, Science, Sports, and Culture, Japan.

## References and Notes

(1) Review: (a) Li, C.-J. *Chem. Rev.* **1993**, *93*, 2023. (b) Lubineau, A.; Ange, J.; Queneau, Y. *Synthesis* **1994**, 741.

(2) (a) Mukaiyama, T.; Narasaka, K.; Banno, T. *Chem Lett.* **1973**, 1011. (b) Mukaiyama, T.; Banno, K.; Narasaka, K. *J. Am. Chem. Soc.* **1974**, *96*, 7503. (c) Mukaiyama, T. *Org. React.* **1982**, *28*, 203.

(3) (a) Kobayashi, S. *Chem. Lett.* **1991**, 2187. (b) Kobayashi, S.; Hachiya, I. *Tetrahedron Lett.* **1992**, 1625. (c) Kobayashi, S.; Hachiya, I. *J. Org. Chem.* **1994**, *59*, 3590. (d) Kobayashi, S. *Synlett* **1994**, 689.

(4) Kobayashi, S.; Hachiya, I.; Yamanoi, Y. *Bull Chem. Soc. Jpn.* **1994**, *67*, 2342.

(5) Lubineau reported water-promoted aldol reactions of silyl enol ethers with aldehydes, however, the yields and the substrate scope were not satisfactory. (a) Lubineau, A. *J. Org. Chem.* **1986**, *51*, 2142. (b) Lubineau, A.; Meyer, E. *Tetrahedron* **1988**, *44*, 6065.

(6) Very recently, $InCl_3$-catalyzed Mukaiyama aldol reactions in water were reported. However, these reactions could not be reproduced in our hands. Loh, T.-P.; Pei, J.; Cao, G.-Q. *J. Chem. Soc., Chem. Commun.* **1996**, 1819.

(7) In the absence of the Lewis acid and the surfactant (water-promoted conditions), only 20% yield of the aldol adduct was isolated after 48 h, while a 33% yield of the aldol adduct was obtained after 48 h in the absence of the Lewis acid in an aqueous solution of SDS.

(8) Although several organic reactions in micelles were reported, there was no report on Lewis acid catalysis in micelles, to the best of our knowledge. In addition, judging from the amount of the surfactant used in the present case, the aldol reaction would not proceed *not only in micelle*. Precise reaction mechanism is now under investigations. (a) Fendler, J. H.; Fendler, E. J. *Catalysis in Micellar and Macromolecular Systems*, Academic Press: London, 1975. (b) Holland, P. M.; Rubingh, D. N., Eds. *Mixed Surfactant Systems*, ACS: Washington, DC, 1992. (c) Cramer, C. J.; Truhlar, D. G., Eds. *Structure and Reactivity in Aqueous Solution*, ACS: Washington, DC, 1994. (d) Sabatini, D. A.; Knox, R. C.; Harwell, J. H., Eds. *Surfactant-Enhanced Subsurface Remediation*, ACS: Washington, DC, 1994.

(9) Hydrolysis of silyl enol ether **1** took place when lower yields were observed in Table 1.

(10) Cf. Kobayashi, S. Hachiya, I.; Takahori, T. *Synthesis* **1993**, 371.

(11) The anion exchange resin treatment was not needed when TritonX-100 was used as a surfactant.

(*Received in Japan* 3 *April* 1997; *revised* 28 *April* 1997; *accepted* 2 *May* 1997)