

Lanthanide Trifluoromethanesulfonates as Stable Lewis Acids in Aqueous Media.

Yb(OTf)₃ Catalyzed Hydroxymethylation Reaction of Silyl Enol Ethers with Commercial Formaldehyde Solution

Shū KOBAYASHI

Department of Applied Chemistry, Faculty of Science,
Science University of Tokyo (SUT), Kagurazaka, Shinjuku-ku, Tokyo 162

Silyl enol ethers smoothly react with commercial formaldehyde solution to give the corresponding hydroxymethylated adducts in high yields by the promotion of a catalytic amount of ytterbium(III) triflate (Yb(OTf)₃), which is a stable Lewis acid in aqueous media. Other lanthanide triflates are also found to be effective.

Formaldehyde is a versatile reagent as one of the most highly reactive C1 electrophiles in organic synthesis.¹⁾ Dry gaseous formaldehyde required for many reactions has some disadvantages because it must be generated before use from solid polymer paraformaldehyde by way of the thermal depolymerization and it is easy to self-polymerize.²⁾ On the other hand, commercial formaldehyde solution, which is an aqueous solution containing 37% of formaldehyde and 8-10% of methanol, is cheap, easy to handle, and stable even at room temperature, however the use of this reagent is strongly restricted due to the existence of a large amount of water; for example, common Lewis acids or organometallics, etc. cannot be employed. In this communication, we would like to report the hydroxymethylation reaction of silyl enol ethers with commercial formaldehyde solution as formaldehyde source by using an unprecedented unique catalyst, a lanthanide trifluoromethanesulfonate (lanthanide triflate), especially ytterbium(III) triflate (Yb(OTf)₃, Tf=CF₃SO₂), which is a stable Lewis acid in aqueous media.

We searched for some Lewis acids which can activate formaldehyde in aqueous solution and found that lanthanide triflates,^{3,4)} prepared from the corresponding lanthanide oxides (La₂O₃) and trifluoromethanesulfonic acid,⁵⁾ were quite effective for the hydroxymethylation reaction of silyl enol ethers.⁶⁾ The reaction was most effectively carried out in commercial formaldehyde solution-THF media⁷⁾ under the influence of 5-10 mol% of Yb(OTf)₃. Following is a typical experimental procedure; to commercial formaldehyde solution⁸⁾ (1 ml) and THF (3 ml) were successively added Yb(OTf)₃ (0.04 mmol, 10 mol%) and a silyl enol ether (0.4 mmol) in THF (1 ml) at rt. The mixture was stirred for 24 h at this temperature and then THF was removed under reduced pressure. Water was added and the product was extracted with dichloromethane. After usual work up, the crude product was chromatographed on silica gel to yield the pure hydroxymethylated adduct. Yb(OTf)₃ is almost quantitatively recovered from aqueous layer and can be reused.

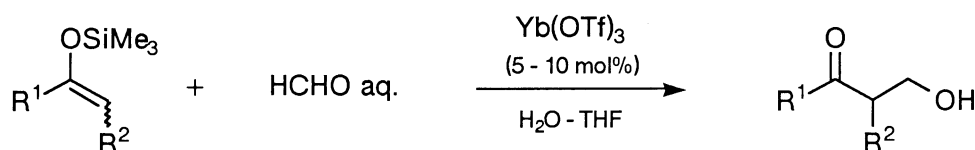
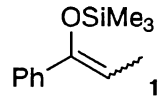
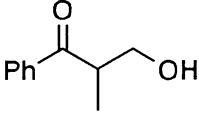
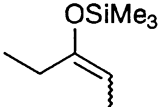
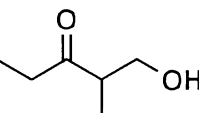
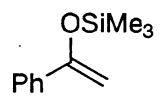
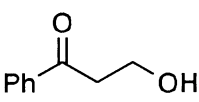
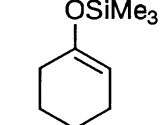
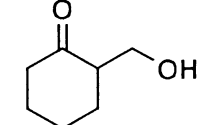
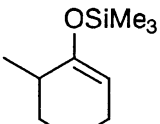
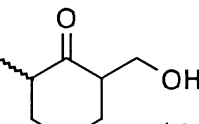
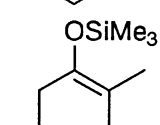
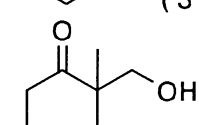
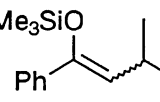
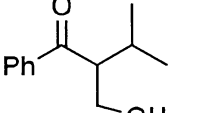
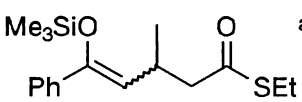
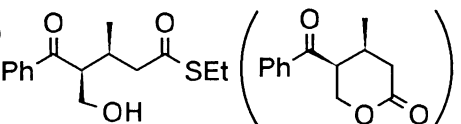
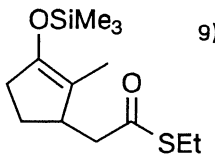
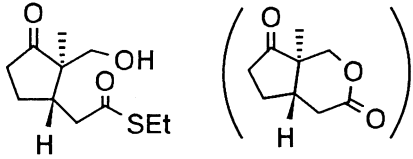
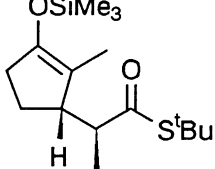
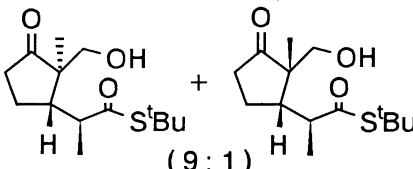


Table 1. Reaction of Silyl Enol Ethers with Commercial Formaldehyde Solution Catalyzed by $\text{Yb}(\text{OTf})_3$

Entry	Silyl enol ether	Product	Yield/%
1	 a)		94
2	 b)		85
3			77
4			82
5		 (3 : 2)	86
6			92
7	 a)		92
8	 a), 9)	 c)	88
9	 9)	 d)	83
10	 9)	 (9 : 1)	90

a) Z/E=>98/2. b) Z/E=1/4. c) The mixture of the hydroxy thioester and the lactone (2:1) was obtained. d) The mixture of the hydroxy thioester and the lactone (3:1) was obtained. Less than 3% yield of the other diastereoisomers were observed.

Several examples are listed in Table 1, and the following characteristic features of this reaction are noted. (1) In every case, the reactions smoothly proceed under extremely mild conditions (almost neutral) to give the corresponding hydroxymethylated adducts in high yields. Sterically hindered silyl enol ethers (entries 6-10) also work well and the diastereoselectivities are high. (2) Di- and poly-hydroxymethylated products were not observed.¹⁰⁾ (3) The absence of equilibrium (double bond migration) in silyl enol ethers allows for the regiospecific hydroxymethylation reaction (entry 5). (4) Only a catalytic amount of Yb(OTf)₃ is required to complete the reaction. The amount of the catalyst was examined by taking the reaction of the silyl enol ether derived from propiophenone (**1**) with commercial formaldehyde solution as a model, and the reaction was found to be catalyzed by even 1 mol% of Yb(OTf)₃; 1 mol% (90% yield); 5 mol% (90% yield); 10 mol% (94% yield); 20 mol% (94% yield); 100 mol% (94% yield). (5) Almost 100% of Yb(OTf)₃ is quite easily recovered from the aqueous layer after the reaction has completed and it can be reused. 1st use (20 mol%) in the reaction of **1** (94% yield); 2nd use (91% yield); 3rd use (93% yield). (6) Finally, it is noteworthy to refer that the present reaction can be smoothly carried out in aqueous media (water does not interfere with this reaction).

The efficient hydroxymethylation reaction by use of formaldehyde solution¹¹⁾ described here strongly depends on the unique characters of lanthanide triflates. While most Lewis acids are decomposed or deactivated under the influence of water, lanthanide triflates are stable even in aqueous media and efficiently activate formaldehyde solution as Lewis acids. Effects of some selected lanthanide triflates in the reaction of **1** with commercial formaldehyde solution are shown in Table 2. In most cases, the reactions smoothly proceed to give the corresponding adduct in high yields. Further progress to develop other synthetic reactions utilizing the unique characters of lanthanide triflates is now investigated.

Table 2. Effect of Lanthanide Triflates in the Reaction of **1** with Commercial Formaldehyde Solution

Entry	Ln(OTf) ₃	Yield/%		
		100 mol% 24 h	1 h	20 mol% 36 h
1	La(OTf) ₃	90	23	88
2	Pr(OTf) ₃	92	40	80
3	Nd(OTf) ₃	74	6	89
4	Sm(OTf) ₃	92	51	91
5	Eu(OTf) ₃	92	28	93
6	Gd(OTf) ₃	92	20	79
7	Dy(OTf) ₃	89	20	85
8	Ho(OTf) ₃	91	38	86
9	Er(OTf) ₃	90	44	83
10	Yb(OTf) ₃	94	5	94

We are grateful to Professor Teruaki Mukaiyama, Science University of Tokyo, for his kind discussion.

References

- 1) For example, Z. G. Hajos and D. R. Parrish, *J. Org. Chem.*, **38**, 3244 (1973); G. Stork and M. Isobe, *J. Am. Chem. Soc.*, **97**, 4745 (1975); D. H. Lucast and J. Wemple, *Synthesis*, **1976**, 724; N. Ono, H. Miyake, M. Fujii, and A. Kaji, *Tetrahedron Lett.*, **24**, 3477 (1983); J. Tsuji, M. Nisar, and I. Minami, *ibid.*, **27**, 2483 (1986); S. D. Larsen, P. A. Grieco, and W. F. Fobare, *J. Am. Chem. Soc.*, **108**, 3512 (1986).
- 2) Snider and Yamamoto respectively developed formaldehyde-organoaluminum complex as formaldehyde source in several reactions. B. B. Snider, D. J. Rodini, T. C. Kirk, and R. Cordova, *J. Am. Chem. Soc.*, **104**, 555 (1982); B. B. Snider, *In Selectivities in Lewis Acid Promoted Reactions*, ed by D. Schinzer, Kluwer Academic Publishers, London (1989), pp.147-167; K. Maruoka, A. B. Concepcion, N. Hirayama, and H. Yamamoto, *J. Am. Chem. Soc.*, **112**, 7422 (1990).
- 3) Lanthanide trichlorides or some organolanthanide compounds were used as Lewis acids. M. Bednarski, C. Maring, and S. Danishefsky, *Tetrahedron Lett.*, **24**, 3451 (1983); M. Ouertani, J. Collin, and H. B. Kagan, *Tetrahedron*, **41**, 3689 (1985); N. Mine, Y. Fujiwara, and H. Taniguchi, *Chem. Lett.*, **1986**, 357; A. E. Vougioukas and H. B. Kagan, *Tetrahedron Lett.*, **28**, 5513 (1987); L. Gong and A. Streitwieser, *J. Org. Chem.*, **55**, 6235 (1990).
- 4) Some of metal triflates have been used as Lewis acids. R_2BOTf : T. Mukaiyama and T. Inoue, *Chem. Lett.*, **1976**, 559; T. Inoue and T. Mukaiyama, *Bull. Chem. Soc. Jpn.*, **53**, 174 (1980). R_3SiOTf : S. Murata, M. Suzuki, and R. Noyori, *J. Am. Chem. Soc.*, **102**, 3248 (1980); S. Murata, M. Suzuki, and R. Noyori, *Tetrahedron*, **44**, 4259 (1988). $Sn(OTf)_2$: T. Mukaiyama, N. Iwasawa, R. W. Stevens, and T. Haga, *ibid.*, **40**, 1381 (1984); S. Kobayashi, H. Uchiro, Y. Fujishita, I. Shiina, and T. Mukaiyama, *J. Am. Chem. Soc.*, **113**, 4247 (1991). $R_2Sn(OTf)_2$: T. Sato, J. Otera, and H. Nozaki, *J. Am. Chem. Soc.*, **112**, 901 (1990). $Al(OTf)_3$: N. Minowa and T. Mukaiyama, *Chem. Lett.*, **1987**, 1719. $Zn(OTf)_2$: E. J. Corey and K. Shimoji, *J. Am. Chem. Soc.*, **105**, 1662 (1983).
- 5) Lanthanide(III) triflates were used as catalysts for the reaction of amines with nitriles under anhydrous conditions. J. H. Forsberg, V. T. Spaziano, T. M. Balasubramanian, G. K. Liu, S. A. Kinsley, C. A. Duckworth, J. J. Poteruca, P. S. Brown, and J. L. Miller, *J. Org. Chem.*, **52**, 1017 (1987). See also, S. Collins and Y. Hong, *Tetrahedron Lett.*, **28**, 4391 (1987); M-C. Almasio, F. Arnaud-Neu, and M.-J. Schwing-Weill, *Helv. Chim. Acta*, **66**, 1296 (1983).
- 6) Titanium tetrachloride- or TMSOTf-mediated aldol-type reaction of silyl enol ethers with trioxane or dialkoxymethanes was reported respectively. T. Mukaiyama, K. Banno, and K. Narasaka, *J. Am. Chem. Soc.*, **96**, 7503 (1974); S. Murata, M. Suzuki, and R. Noyori, *Tetrahedron Lett.*, **21**, 2527 (1980).
- 7) Water-promoted aldol reaction of silyl enol ethers with carbonyl compounds was reported. A. Lubineau and E. Meyer, *Tetrahedron*, **44**, 6065 (1988).
- 8) Purchased from Kokusan Kagaku Co., Ltd.
- 9) T. Mukaiyama, M. Tamura, and S. Kobayashi, *Chem. Lett.*, **1986**, 1817; **1987**, 743.
- 10) H. Gaut and J. Skoda, *Bull. Soc. Chim. Fr.*, **13**, 308 (1946).
- 11) Lithium enolates prepared from simple ketones react with gaseous formaldehyde to give the corresponding hydroxymethylation adducts. G. Stork and J. d'Angelo, *J. Am. Chem. Soc.*, **96**, 7114 (1974). See also, P. A. Grieco and K. Hiroi, *J. Chem. Soc., Chem. Commun.*, **1972**, 1317.

(Received September 4, 1991)