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Repeated Use of the Catalyst in Ln(OTf)$_3$-Catalyzed Aldol and Allylation Reactions

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Synopsis. The lanthanoide trifluoromethanesulfonate (lanthanoid triflate)-catalyzed aldol reactions of silyl enol ethers with aldehydes and allylation reactions of tetraallyltin with aldehydes proceeded smoothly in a water–ethanol–toluene system. The reactions proceeded much faster in the above solvent than in water–tetrahydrofuran. Repeated use of the catalyst in these reactions was realized by a very simple procedure.

Recently we found that aldol reactions of silyl enol ethers with a wide variety of aldehydes proceeded smoothly in an aqueous solution (water–tetrahydrofuran (THF)) by using a catalytic amount of lanthanoide triflate as a catalyst.[1] One feature of these reactions is that the catalyst can be quantitatively recovered after the reactions are completed and reused. However, some additional procedures to remove water were necessary in order to reuse the catalyst. We now report a new solvent system, water–ethanol–toluene, in these reactions. The reactions proceeded much faster in the above solvent than in THF–water. Furthermore, the new solvent system realized repeated use of the catalyst by a very simple procedure.

First, we examined several water–organic solvent systems in the model reaction of 1-phenyl-1-trimethylsiloxypropene with 2-pyridinecarbaldehyde under the influence of 10 mol% Yb(OTf)$_3$ (Table 1). While the reaction proceeded sluggishly in a water–toluene system, the adduct was obtained in a good yield when ethanol was added to this system. The yield increased in accordance with the amount of ethanol, and it was noted that the reaction proceeded much faster in the water–ethanol–toluene system than in the original water–THF system.

Next, we examined reuse of the catalyst. Although the water–ethanol–toluene (1:7:4) system was one phase, it easily became two phases by adding toluene after the reaction was completed. The product was isolated from the organic layer by a usual work up. On the other hand, the catalyst remained in the aqueous layer, which was used directly in the next reaction without removing water. It is noteworthy that the yields of the 2nd, 3rd, and 4th runs were comparable to that of the 1st run (Eq. 1).

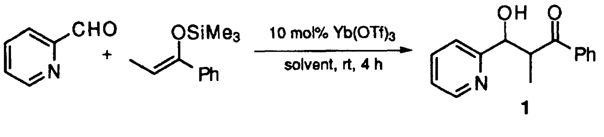
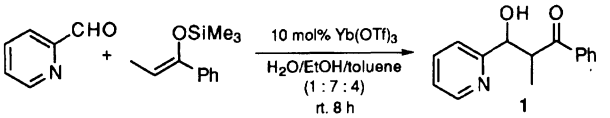


Table 1. Effect of Solvents

Solvent	Yield/%	*syn*/*anti*
H$_2$O/Toluene (1 : 4)	0	—
H$_2$O/EtOH/Toluene (1 : 3 : 4)	30	37/63
(1 : 5 : 4)	41	39/61
(1 : 7 : 4)	70	41/59
(1 : 10 : 4)	96	40/60
H$_2$O/THF (1 : 4)	12	43/57

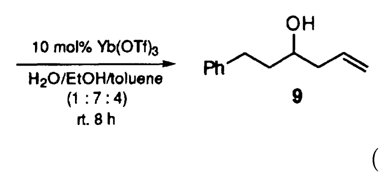


(1)

1st run : 86% (syn/anti = 38/62)
2nd run : 82% (syn/anti = 38/62)
3rd run : 90% (syn/anti = 38/62)
4th run : 82% (syn/anti = 39/61)

Several examples of the present aldol reactions of silyl enol ethers with aldehydes in water–ethanol–toluene are listed in Table 2. 3-Pyridinecarbaldehyde as well as 2-pyridinecarbaldehyde (examples of nitrogen-containing aldehydes), salicylaldehyde (an example of an aldehyde containing a free hydroxyl group), and formaldehyde water solution worked well. As for silyl enol ethers, not only ketone enol ethers but also silyl enolates derived from thioesters were used. In every case, the adducts were obtained in high yields in the presence of 10 mol% Yb(OTf)$_3$.

The water–ethanol–toluene system could be successfully applied to other lanthanoid triflate-catalyzed reactions.[2] An example of the allylation reaction of tetraallyltin with aldehyde is shown in Eq. 2, and in this case also continuous use of the catalyst was realized (Eq. 2).



(2)

1st run : 90%; 2nd run : 95%;
3rd run : 96%; 4th run : 89%

In summary, a new solvent system, water–ethanol–toluene, facilitates reuse of the catalyst in lanthanoid triflate-catalyzed reactions. Shortening of the reaction

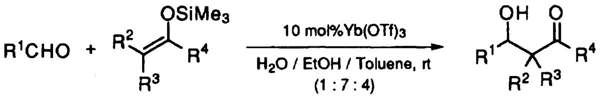
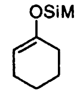
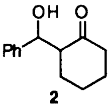
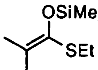
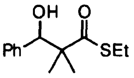
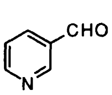
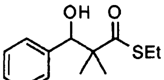
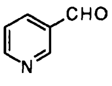
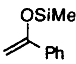
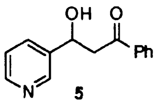
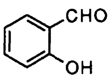
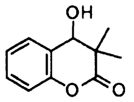
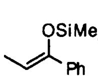
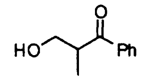


Table 2. Yb(OTf)$_3$-catalyzed Aldol Reactions of Silyl Enol Ethers with Aldehydes in Water–Ethanol–Toluene

Aldehyde	Silyl Enol Ether	Product	Yield/%
PhCHO		 2	89[a]
PhCHO	 8	 3	95
	8	 4	87
		 5	82
	8	 6	96
HCHO aq		 7	90

a) *syn*/*anti*=74/26.

time in these reactions by using the above solvent is also noteworthy.

Experimental

A typical experimental procedure for the aqueous aldol reactions follows: To a Yb(OTf)$_3$[3] (0.04 mmol, 10 mol%) solution (H_2O : EtOH=1 : 7, 1.6 ml) was added a mixture of 1-phenyl-1-trimethylsiloxypropene (0.44 mmol) and 2-pyridinecarbaldehyde (0.4 mmol) in toluene (0.8 ml) at r.t. The mixture was stirred for 4 h at this temperature. Toluene (1.5 ml) and water (1.0 ml) were then added and the organic layer was separated. The product was extracted with toluene (1.5 ml×2), and the combined organic layers were dried. After a usual work up, the crude product was chromatographed on silica gel to yield the pure aldol adduct. (The diastereomers were separated and the relative configuration assignments were made by ^{1}H NMR analyses.[4])

2nd reaction: To the aqueous layer was added ethanol (1.1 ml). A mixture of 1-phenyl-1-trimethylsiloxypropene (0.44 mmol) and 2-pyridinecarbaldehyde (0.4 mmol) in toluene (0.8 ml) was then added at r.t. The same procedure used in the 1st run gave the desired adduct in an 82% yield (*syn*/*anti*=38/62).

Similarly, 3rd and 4th reactions were carried out without reduction of the yield.

We were successfully carried out the aldol reaction starting from 20 mmol of an aldehyde.

3-Hydroxy-2-methyl-1-phenyl-3-(2-pyridyl)-1-propanone (1): (*syn*) Mp 95.0—95.2 °C; IR (KBr) 3128, 1676 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=1.16 (d, 3H, J=7.3 Hz), 4.04—4.13 (m, 1H), 4.23 (brs, 1H), 5.23 (d, 1H, J=4.0 Hz), 7.15—7.19 (m, 1H), 7.42—7.70 (m, 5H), 7.96 (d, 2H, J=7.6 Hz), 8.53—8.55 (m, 1H). Anal. Calcd for $C_{15}H_{15}NO_2$: C, 74.67; H, 6.27; N, 5.81%. Found: C, 74.90; H, 6.27; N, 5.68%.

(*anti*) IR (neat) 3433, 1680 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ= 1.22 (d, 3H, J=6.9 Hz), 4.14—4.24 (m, 1H), 4.36 (brs, 1H), 5.02 (d, 1H, J=6.0 Hz), 7.12—7.17 (m, 1H), 7.40—7.68 (m, 5H), 7.93—7.97 (m, 2H), 8.50—8.52 (m, 1H). Anal. Calcd for $C_{15}H_{15}NO_2$: C, 74.67; H, 6.27; N, 5.81%. Found: C, 74.60; H, 6.47; N, 5.68%.

2-(α-Hydroxybenzyl)cyclohexanone (2):[5] (*syn*) Mp 104.8—105.2 °C; IR (KBr) 3552, 1699 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=1.47—1.88 (m, 5H), 2.04—2.13 (m, 1H), 2.31—2.49 (m, 2H), 2.56—2.64 (m, 1H), 3.03 (d, 1H, J=3.3 Hz), 5.40 (t, 1H, J=2.6 Hz), 7.22—7.38 (m, 5H).

(*anti*) IR (neat) 3510, 1699 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ= 1.23—1.37 (m, 1H), 1.47—1.83 (m, 4H), 2.04—2.13 (m, 1H), 2.30—2.54 (m, 2H), 2.57—2.67 (m, 1H), 3.97 (s, 1H), 4.79 (d, 1H, J=8.9 Hz), 7.20—7.39 (m, 5H).

***S*-Ethyl 2,2-Dimethyl-3-hydroxy-3-phenylpropanethioate (3):** IR (neat) 3508, 1664 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=1.09 (s, 3H), 1.20—1.26 (m, 6H), 2.86 (q, 2H, J=7.3 Hz), 3.12 (s, 1H), 4.92 (s, 1H), 7.25—7.31 (m, 5H). HMRS: Calcd for $C_{13}H_{18}O_2S$: M$^+$, 238.1027. Found : m/z 238.1031.

***S*-Ethyl 3-Hydroxy-2,2-dimethyl-3-(3-pyridyl)propanethioate (4):** Mp 78.0—78.5 °C; IR (KBr) 3157, 1676 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=1.09 (s, 3H), 1.20—1.26 (m, 6H), 2.86 (q, 2H, J=7.3 Hz), 4.80 (brs, 1H), 4.98 (s, 1H), 7.21—7.31 (m, 1H), 7.66—7.71 (m, 1H), 8.37—8.39 (m, 2H). Anal. Calcd for $C_{12}H_{17}NO_2S$: C, 60.22; H, 7.16; N, 5.85; S, 13.40%. Found: C, 60.27; H, 7.21; N, 5.76; S, 13.35%.

3-Hydroxy-1-phenyl-3-(3-pyridyl)]-1-propanone (5): Mp 91.0—92.0 °C; IR (KBr) 3288, 1684 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=3.31 (dd, 1H, J=3.6, 17.5 Hz), 3.45 (dd, 1H, J=8.6, 17.5 Hz), 4.90 (brs, 1H), 5.40 (dd, 1H, J=3.6, 8.6 Hz), 7.24—7.29 (m, 1H), 7.42—7.60 (m, 3H), 7.79—7.95 (m, 3H), 8.47 (dd, 1H, J=1.7, 5.0 Hz), 8.61 (d, 1H, J=2.0 Hz). Anal. Calcd for $C_{14}H_{13}NO_2$: C, 73.99; H, 5.77; N, 6.16%. Found: C, 74.04; H, 5.78; N, 6.05%.

4-Hydroxy-3,3-dimethyl-2-chromanone (6): Mp 101.8—102.8 °C; IR (KBr) 3504, 1738 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=1.17 (s, 3H), 1.36 (s, 3H), 2.75 (brs, 1H), 4.46 (s, 1H), 7.04 (d, 1H, J=7.6 Hz), 7.13—7.19 (m, 1H), 7.28—7.37 (m, 2H). Anal. Calcd for $C_{11}H_{12}O_3$: C, 68.74; H, 6.29%. Found: C, 68.84; H, 6.28%.

3-Hydroxy-2-methyl-1-phenyl-1-propanone (7): IR (neat) 3420, 1674 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=1.24 (d, 3H, J=7.6 Hz), 2.38 (brs, 1H), 3.63—4.02 (m, 3H), 7.45—7.62 (m, 3H), 7.95—7.99 (m, 2H). Anal. Calcd for $C_{10}H_{12}O_2$: C, 73.15; H, 7.37%. Found: C, 72.50; H, 7.41%.

1-Phenyl-5-hexen-3-ol (9):[6] IR (neat) 3379 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=1.73—1.82 (m, 3H), 2.12—2.36 (m, 2H), 2.60—2.83 (m, 2H), 3.62—3.71 (m, 1H), 5.09—5.17 (m, 2H), 5.73—5.89 (m, 1H), 7.14—7.31 (m, 5H).

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