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EFFECT OF METAL HYDRIDE AND SILICA GEL ON THE SHARPLESS ASYMMETRIC EPOXIDATION

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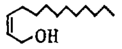
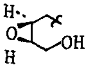
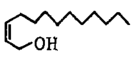
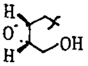
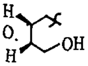
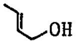
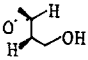
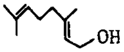
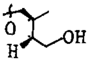
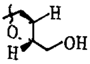
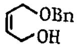
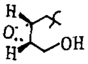
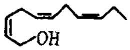
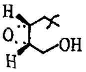
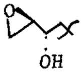
Abstract: The reaction time of asymmetric epoxidation of allylic alcohol was greatly reduced when a catalytic amount of both metal hydride and silica gel was occurred in the Sharpless reagent.

An efficient method for the asymmetric epoxidation of allylic alcohol using Sharpless reagent [Ti(OiPr)$_4$,(+)- or (-)-diethyl tartrate (DET) and tert-butylhydroperoxide (TBHP)]$^{1-3}$ is extremely useful in the synthesis of chiral compounds^4. In application of this efficient method for synthesis of insect pheromones in our laboratory^5, we discovered that addition of a catalytic amount of calcium hydride and silica gel to the Sharpless reagent can greatly reduce the reaction time. For example, the reaction time of Z-2-tridecen-1-ol in the presence of 5-10 mol% equivalent of calcium hydride and 10-15 mol% equivalent of silica gel with the Sharpless reagent can be reduced from 96 hrs to 8 hrs, while both chemical and optical yields of the epoxide product remain unchanged (Entry 1/Table 1). The reaction time of dl-1-tridecen-3-ol in the presence of 5-10 mol% equivalent of calcium hydride and 10-15% equivalent of silica gel with the Sharpless reagent via kinetic resolution can be reduced from 360 hrs to 25 hrs (Entry 9/Table 1).

Table 1:Asymmetric epoxidation of allylic alcohols by Sharpless reagent (Method A) and by the modified Sharpless reagent (Method B)

Entry	Allylic Alchols	Method[a]	Time(h)	Epoxy Alcohols	Yield(%)	$[\alpha]_D$[e]	ee%	Config.
1	 [b]	A	96		76-80	-7.6°	95[5b]	
		B	8		76	-7.8°		2R 3S
2	 [c]	A	96		76-80	+7.6°	95[5b]	
		B	10		76	+7.9°		2S 3R
3	 [c]	A	144		75	+7.3°		
		B	8		74.5	+7.4°		2S 3R
4	 [c]	A	15		43	-54.5°	95[1]	
		B	0.5		37	-54.0°		2S 3S
5	 [c]	A	18		77	-6.4°		
		B	1.5		76.7	-6.4°		2S 3S
6	 [c]	A	72		76-80	+26.5°	96[5b]	
		B	6		76.4	+25.9°		2S 3S
7	 [c]	A	24		84	-22.8°		
		B	8		82.6	-22.3°		2S 3R
8	 [c]	A	26		60.3	+8.0°		
		B	6		85			2S 3R
9	 [d]	A	360		81	+16.2°	91[5c]	
		B	25		84	+15.2°		2S 3S

a. Method A: Epoxidation using Shapless reagent[1]; Method B: Addition of 5-10% equiv. of calcium hydride and 10-15% equiv. of silica gel to the Sharpless reagent.

b. D-(-)-diethyl tartrate used.

c. L-(+)-diethyl tartrate used.

d. Via kinetic resolution.

e. Optical rotations were measured on Rudolph Research Autopol polarimeter with concentration (C) in the range of 1-3 and C_2H_5OH or $CHCl_3$ as solvent in all cases.

Table 2. Effect of metal hydride or silica gel on Sharpless asymmetric epoxidation of Z-2-tridecen-1-ol[a]

Catalyst	Amount (mol%)	Reaction Time (h)	Yield(%)	$[\alpha]_D$ (EtOH)
None	None	96	76-80	-7.6°
CaH_2-Silica Gel	5, 10	8	76	-7.8°
CaH_2	10	20	74	-4.3°
NaH	10	66	81.5	-4.2°
Silica Gel	10	96	77.7	-7.7°
KH	10	70	87	-5.0°

a. D-(-)-diethyl tartrate was used in all expriments.

The substrates investigated and the results obtained are listed in Table 1.

With the addition of calcium hydride, sodium hydride or potassium hydride alone to the Sharpless reagent for epoxidation, the reaction time can also be reduced, however the optical yield was strongly decreased (Table 2). In contrast with metal hydride, silica gel can not reduce the reaction time, but it can keep the optical yield. (Table 2.)

Experimental procedure: To a mixture of 0.79 mL (2.6 mmol) of titanium tetraisopropoxide, 10 mg(0.25 mmol) of calcium hydride, 15 mg(0.25 mmol) of silica gel in 15 mL of dry CH_2Cl_2 was injected D-(-)-diethyl tartrate (0.52 mL, 3.0 mmol) via syringe while stirring under N_2 in the cooling bath (-20°C). After the mixture was stirred for 10 min, Z-2-tridecen-1-ol (0.50 g, 2.5 mmol) was injected. The reaction mixture was stirred for further 10 min. 0.54 mL(5.04 mmol) of anhydrous TBHP (9.45 M) was then injected at-40°C. After stirring for 1 hr the reaction mixture was kept at -40°C for 7 hrs. 6 mL of 10% aqueous tartaric acid solution was added and stirred at -20°C for 30 min, and then stirred at room temp. until the aqueous layer became clear. After separation of the organic layer, the aqueous layer was extracted with CH_2Cl_2 and the combined organic layer was dried over Na_2SO_4 and concentrated. The afforded mixture was diluted with 15 mL of ether, and then 6 mL of 1N NaOH(aq.) was added at 0°C and stirred for 30 min. The aqueous layer was extracted with ether,and the combined organic layer was washed with brine, dried over Na_2SO_4, and concentrated under reduced pressure. The crude product was recrystallized from petroleum ether to give 0.4g of (2R,3S)-epoxy-tridecen-1-ol in 76% yield, $[\alpha]_D^{24}$-7.8° (c 1.28, EtOH).

The scope and mechanism of the modified Sharpless reagent are under investigation.

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