Highly Concentrated Catalytic Asymmetric Allylation of Ketones

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Experimental Section

General Methods. All reactions using titanium(IV) isopropoxide were carried out in a Vacuum Atmospheres dry box or under nitrogen using standard Schlenk techniques. NMR spectra were obtained on a Bruker 500 MHz or 300 MHz Fourier transform spectrometer at the University of Pennsylvania NMR facility. ¹H NMR spectra were referenced to tetramethylsilane in CDCl₃; ¹³C{¹H} NMR spectra were referenced to residual solvent. All reagents were purchased from Aldrich, Acros or Gelest chemical company. Titanium(IV) isopropoxide, tetraallyltin, 2-propanol and all liquid ketone substrates were distilled prior to use and stored under inert atmosphere.

Enantioselective Allylation of Ketones.

General Procedure. BINOL (17.2 mg, 0.060 mmol, 20 mol%) was weighed into the reaction vessel. After addition of titanium(IV) isopropoxide (8.94 μ L, 0.030 mmol, 10 mol%) under nitrogen, the solution turned red. Tetraallyltin (108 μ L, 0.451 mmol, 1.5 equiv.) and 2-propanol (69.0 μ L, 0.901 mmol, 3 equiv.) were then added, followed by addition of 3-methylacetophenone (40.9 μ L, 0.300 mmol). The flask was capped tightly and stirred at room temperature until the solution turned pale yellow (4-12 h). After the reaction was completed by TLC, 2 mL of CH₂Cl₂ and two spatula scoops (1.72 g) of silica (not dried) were added to the vessel to quench the reaction. All volatile materials were removed under reduced pressure and the yellow silica powder was placed on a column. The crude product was purified by column chromatography on silica gel (hexanes:EtOAc, 95:5).

One-Pot Synthesis of Epoxy Alcohols with TBHP.

General Procedure. BINOL (17.20 mg, 0.060 mmol, 20 mol%) was weighed into the reaction vessel. After addition of titanium(IV) isopropoxide (8.94 μ L, 0.030 mmol, 10 mol%) under nitrogen, the solution turned red. Tetraallyltin (108 μ L, 0.451 mmol, 1.5 equiv.) and 2-propanol (69.0 μ L, 0.901 mmol, 3 equiv.) were then added, followed by addition of 2,4,4-trimethyl-2-cyclohexen-1-one (44.9 μ L, 0.300 mmol). The flask was capped tightly and stirred at room temperature until the solution turned pale yellow (4-12 h). After the allylation was completed by TLC, TBHP (1 equiv, 5.5 M solution in decane) was added. After 12 h, the reaction was quenched with sat. aq. NH_4Cl and extracted with dichloromethane. The organic layer was dried over MgSO_4 , filtered, and the solvent was removed under reduced pressure. Hexanes was added. The solution was filtered through Celite and concentrated under reduced pressure. The residue oil was purified by silica chromatography.

The Following Homoallylic Alcohols (Table 3) Have Been Previously Characterized.

2-(*m*-tolyl)-4-penten-2-ol
2-(3-trifluoromethylphenyl)-4-penten-2-ol
2-(4-methoxyphenyl)-4-penten-2-ol
1-Naphthalenol

Waltz, K. M.; Gavenonis; Walsh, P. J. *Angew. Chem. Int. Ed.* 2002, 41, 3697-3699.

1-Allyl-2,4,4-trimethyl-cyclohex-2-enol
1-Allyl-2-benzylidene-cyclohexanol

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The Following Syn Epoxy Alcohols (Table 4) Have Been Previously Characterized.

2-Allyl-1-pentyl-6-oxa-bicyclo[3.1.0]hexan-2-ol
2-Allyl-1,5,5-trimethyl-7-oxa-bicyclo[4.1.0]heptan-2-ol
4-Allyl-2-phenyl-1-oxa-spiro[2.5]octan-4-ol

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