Manuscript No: OL0002727-21/F, Rainer Mahrwald
10-26-00

Supporting Information

Titanium (IV) Alkoxide Ligand Exchange with α-Hydroxy Acids : The Enantioselective Aldol Addition

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General Procedures: All reactions were performed using oven dried glassware under an atmosphere of dry argon. Toluene was distilled, dried and stored over molecular sieve (3A). $Ti(O\mathit{t}Bu)_4$ was purchased from Merck chemical company - BINOL was purchased from ACROS chemical company. They were used without prior purification. (*R*)-mandelic acid was purchased from FLUKA and was dried by azeotropic distillation with toluene. Aldehydes were distilled before use. Chromatographic purification of products was accomplished using flash chromatography according to the method of Still.[1]

^1H NMR and ^{13}C NMR spectra were recorded at 300 and 75 MHz, respectively using a AC-300 spectrometer. Thin layer chromatography was performed using Merck Silica Gel 60 F_{254} TLC plates.

Preparation of (1.1'-Binaphtyl-2.2'-diyloxy) bis(*tert*butoxy)titanium

BINOL-$Ti(O\mathit{t}Bu)_2$ was prepared according to the procedure of Mahrwald et al.[2]
$Ti(O\mathit{t}Bu)_4$ (3.8 ml, 10 mmol) was added under inert condidtions to 50 ml anhydrous toluene. BINOL (2.86 g, 10 mmol) was carefully added. After 10-15 min. at room temperatur a clear and deep-brown solution was obtained. Precipitation occures (after 1-3 h at room temperature) and after 10 h the crystals formed were collected by filtration and dried i. vac.
4.1 g were isolated (85.8 % yield).

General Procedure for enantioselective aldol addition reaction

BINOL-Ti(O*t*Bu)$_2$ (480 mg, 1 mmol) was suspended in 0.5 ml toluene under inert conditions. Freshly distilled aldehyde (1.5 mmol) was added and the suspension was stirred at r.t. until a clear solution appered (30 – 60 min.). (*R*)-mandelic acid (160 mg, 1 mmol) was added. The deep brown solution was stirred for 15 min. at room temperature. Diethylketone (100 µl, 1 mmol) was added. The resulting clear dark brown solution was stirred for further 5 to 8 h at room temperature. The reaction was monitored by thin-layer chromatography (dichloromethane / acetone – 99 / 1). At the end of the reaction, the mixture was diluted with diethylether and quenched successively with aq. saturated $NaHCO_3$ and NH_4Cl. The organic layer was separated, dried (Na_2SO_4), filtered, and finally concentrated i.vac. Purification by column chromatography (hexane / ethylacetate - 8 / 2) afforded the aldol adduct.

A portion of the aldol adduct was converted to the corresponding (*S*)-MTPA-ester as follows:

To the solution of the aldol adduct (0.01 mmol) and 10 mg DMAP in 1 ml abs. CH_2Cl_2 was added a CH_2Cl_2-solution of (*R*)-MTPA-Cl (0.011mmol). After 10 h at r.t. the MTPA-ester was purified by column chromatography. The enantiomeric excess of the product was determined by integration of corresponding signals in the ^{1}H NMR spectra.

(4*R*,5*R*)-1-Hydroxy-2-methyl-1-phenyl-3-pentanone (1a):[3,4,6]

^{1}H NMR ($CDCl_3$): δ = 7.4-7.2 (5H,m), 4.92 (1H, d, *J*=4.4), 2.83(1H, dq, *J*=4.4, 7.2), 2.5 (1H, dq, *J*=7.3, 18.1), 2.31 (1H, dq, *J*= 7.3, 18.0), 1.10(3H, d, *J*=7.2), 0.97(3H, t, *J*=7.3);

MTPA ester of **(4*R*,5*R*)-1a** δ = 6.06 (d, *J*=8.7), 3.36 (s,-OMe),

MTPA ester of **(4*S*,5*S*)-1a** δ = 6.02 (d, *J*=7.9), 3.43 (s, -OMe),

^{13}C NMR ($CDCl_3$): δ = 215.4, 142.5, 128.1, 127.3, 126.1, 73.9, 53.0, 35.5, 11.4, 7.3.

(4*R*,5*R*)-5-Hydroxy-4.6.6-trimethyl-3-heptanone (1b):[4]

^{1}H NMR ($CDCl_3$): δ = 3.58 (1H, d, *J*=3.5), 2.75(1H, dq, *J*=3.5, 7.0), 2.53 (1H, dq, *J*= 7.2, 17.9), 2.38 (1H, dq, *J*=7.2, 17.9), 1.13 (3H, d, *J*=7.0), 1.01(3H, tr, *J*=7.2), 0.92 (9H, s);

MTPA ester of **(4*R*,5*R*)-1b**: δ = 3.35 (s, -OMe),

MTPA ester of **(4*S*,5*S*)-1b**: δ = 3.44 (s, -OMe).

^{13}C NMR ($CDCl_3$): δ = 219.5, 77.1, 46.7, 37.4, 35.5, 26.7, 11.6, 7.4.

(4*R*,5R)-1-Hydroxy-2-methyl-1-phenylethinyl-3-pentanone (1c):[5]

^{1}H NMR ($CDCl_3$): δ = 7.2 - 7.6 (5H,m), 4.93(1H, d, *J*=4.9), 2.95 (1H, dq, *J*= 4.9, 7.3), 2,50 (2H, 2 x dq, *J*=7.5, 13.3), 1.32(2H, d, *J*= 7.2), 1.0 (3H, t, *J*=7.3);

MTPA ester of (4*R*,5*R*)-**1c**: δ = 5.88 (d, *J*=6.41), 3.55 (s, -OMe),

MTPA ester of (4S,5S)-**1c**: δ = 5.85 (d, *J*=6.78), 3.65 (s, -OMe).

^{13}C NMR ($CDCl_3$): δ = 216.8, 132.1, 128.3, 128.2, 121.9, 86.7, 84.8, 63.8, 51.1, 31.9, 11.9, 7.6.

(4*R*,5*S*)-5-Hydroxy-4.6-dimethyl-3-heptanone (1d):[4,6]

^{1}H NMR ($CDCl_3$): δ = 3.48 (1H, dd, *J*=3.8, 7.9), 2.74 (1H, dq, *J*=3.6, 7.2), 2.52 (1H, dq, *J*=7.3, 17.9), 2.49 (1H, dq, *J*=7.3, 17.9), 1.61(1H, dspt, *J*=8.2, 6.6), 1.1(3H, d, *J*=7.2), 1.04(3H, t, *J*=7.3), 0.99(3H, d, *J*=6.6), 0.84(3H, d, *J*=6.6);

MTPA ester of **(4*R*,5*S*)-1d**: δ = 3.44 (s, -OMe),

MTPA ester of **(4*S*,5*R*)-1d**: δ = 3.52 (s, -OMe).

^{13}C NMR ($CDCl_3$): δ = 216.6, 76.4, 47.5, 34.8, 30.7, 19.1, 18.9, 9.7, 7.6.

(4*R*,5*S*)-5-Hydroxy-4-methyl-3-heptanone (1e):[7]

^{1}H NMR ($CDCl_3$): δ = 3.58 (1H, ddd, *J*=3.5, 4.6, 9.1), 2.25 (1H, dq, *J*=3.5, 7.1), 2.12 (1H, dq, *J*=7.2, 18.0), 2.05 (1H, dq, *J*=7.2, 18.0), 1.45 (1H, ddq, *J*=7.4, 8.5, 13.6), 1.23 (1H, ddq, *J*=4.5, 7.4, 13.5), 0.95 (3H, d, *J*=7.2), 0.88 (3H, t, *J*=7.2), 0.81 (3H, t, *J*=7.3);

MTPA ester of **(4R,5S)-1e**: δ = 3.42 (s, -OMe),

MTPA ester of **(4S,5R)-1e**: δ = 3.48 (s, -OMe).

^{13}C NMR ($CDCl_3$): δ = 215.1, 72.9, 50.0, 34.9, 27.3, 10.9, 9.9, 7.2.

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