Catalytic Enantioselective Allylation of Ketones via a Chiral Indium(III) Complex

Yong-Chua Teo^b, Joshua-Daniel Goh and Teck-Peng Loh^{a*}

^aDivision of Chemistry and Biological Chemistry, Nanyang Technological University,
Singapore 637616

^bDepartment of Chemistry, National University of Singapore, 3 Science Drive 3,
Singapore 117543, Singapore.

Supporting Information

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General Methods

Experiments involving moisture and/or air sensitive components were performed in oven-dried glassware. Commercial solvents and reagents were used without further purification with the following exceptions: Hexane, dichloromethane, ethyl acetate were fractionally distilled. Aldehydes were distilled before used. The aldehydes can be dried over Na_2SO_4 in hexane (for reaction in hexane) before used if they are wet. Hexane for reaction purpose was distilled over CaH_2 . Azeotropic drying of starting materials or reagents was performed by the addition of the stated amount of anhydrous tetrahydrofuran, ensued by azeotropic removal of tetrahydrofuran with traces of moisture in *vacuo* followed by subsequent purging with nitrogen.

Analytical thin layer chromatography (TLC) was performed using Merck 60 F254 precoated silica gel plate (0.2 mm thickness). Subsequent to elution, plates were visualized using UV radiation (254 nm) on Spectroline Model ENF-24061/F 254 nm. Further visualization was possible by staining with basic solution of potassium permanganate or acidic solution of ceric molybdate, followed by heating on a hot plate.

Flash chromatography was performed using Merck silica gel 60 with freshly distilled solvents. Columns were typically packed as slurry and equilibrated with the appropriate solvent system prior to use.

Infrared spectra were recorded on a Bio-Rad FTS 165 FTIR spectrometer. Liquid samples were examined as film between NaCl salt plates.

Proton nuclear magnetic resonance spectra (^1H NMR) were recorded on a Bruker Avance DPX 300 and Bruker AMX 500 spectrophotometer (CDCl_3 as solvent). Chemical shifts for ^1H NMR spectra are reported as δ in units of parts per million (ppm) downfield from SiMe_4 (δ 0.0) and relative to the signal of chloroform-d (δ

7.2600, singlet). Multiplicities were given as: s (singlet); d (doublet); t (triplet); q (quartet); dd (doublets of doublet); ddd (doublets of doublets of doublet); dddd (doublets of doublets of doublets of doublet); dt (doublets of triplet); or m (multiplets). The number of protons (n) for a given resonance is indicated by nH. Coupling constants are reported as a *J* value in Hz. Carbon nuclear magnetic resonance spectra (¹³C NMR) are reported as δ in units of parts per million (ppm) downfield from SiMe₄ (δ 0.0) and relative to the signal of chloroform-d (δ 77.03, triplet). The proportion of diastereomers and geometric isomers was determined from the integration of ¹H NMR and ¹³C NMR spectra.

Mass spectral analyses were carried out on a VG 7035 micromass mass spectrophotometer at a source temperature of 200 °C and at an ion current of 70 eV. Mass spectral data were reported in units of mass to charge (m/z) and % intensity.

Experimental

General Procedure for Ketone Allylation Reactions

Representative procedure for asymmetric allylation of ketones : Preparation of (S)- 2-phenyl-pent-4-en-2-ol

To an oven dried round-bottom flask equipped with a magnetic stirring bar was added InBr_3 (0.1 mmol, 35 mg, 0.2 equiv.). The solid was azeotropically dried with anhydrous tetrahydrofuran (2 mL x 1) prior to addition of 1.0 mL of dichloromethane. (*R*)-BINOL (0.11 mmol, 31 mg, 0.22 equiv.) and 4Å molecular sieve (15 mg) were added and the mixture was stirred at room temperature for 2 hours to afford a white suspension. Allytributylstannane (1.5 mmol, 0.47 mL, 3.0 equiv.) was added to the resulting suspension and stirred for 10 minutes followed by slow addition of acetophenone (0.5 mmol, 0.06 mL in 0.5 mL dichloromethane, 1.0 equiv.). The reaction mixture was stirred for 72h at room temperature. The reaction mixture was quenched with 5 mL ammonium chloride and the aqueous layer was extracted with dichloromethane (3 X 10 mL). The combined organic extracts was washed with brine, dried over anhydrous magnesium sulphate, filtered and concentrated *in vacuo*. The residual crude product was purified via silica gel chromatography to afford the homoallylic alcohol as a colourless oil (74% yield).

Characterization of tertiary homoallylic alcohols in Table 2

(*R*)-2-Phenyl-pent-4-en-2-ol

(82 %*ee*)

Colorless oil (74 %); R_f = 0.48 (4:1 hexane/ethyl acetate)

^1H NMR (300 MHz, CDCl_3): δ 7.21-7.48 (m, 5H), 5.57-5.72 (m, 1H), 5.10-5.18 (m, 2H), 2.70 (dd, J = 13.9, 6.3 Hz, 1H), 2.51 (dd, J = 13.6, 8.0 Hz, 1H), 2.08 (s, 1H), 1.56 (s, 3H)

^{13}C NMR (75.4 MHz, CDCl_3): δ 147.6, 133.6, 128.1, 126.6, 124.7, 119.4, 73.6, 48.4, 29.8

FTIR (neat): 3415, 3075, 2974, 1640, 1445, 914, 766, 700 cm^{-1} .

HRMS Calcd for $\text{C}_{12}\text{H}_{16}\text{O}$ [$\text{M} - \text{H}_2\text{O}$]: 144.0939 Found: 144.0934

$[\alpha]_D^{25} = +37.6^\circ$ (c = 1.52 g/100 mL, CH_2Cl_2)

The enantiomeric excess was determined by HPLC analysis employing a Daicel Chiracel OJ column (Hexane: *i*-propanol 98:2, 1.0 mL/min: t_1 = 9.96 min for major enantiomer, t_2 = 12.78 min for minor enantiomer).

The absolute configuration of the product was determined by comparison of the sign of the optical rotation with the literature value¹. The *re* face of the ketone is attacked when the (*R*)-catalyst is used, in agreement with the constant preference shown by the BINOL-based catalyst.

[1] Ishizaki, M.; Soai, K.; Yokoyama, S. Chem. Lett. **1987**, 341

(R)-2-*p*-Tolyl-pent-4-en-2-ol

(84 %ee)

Colorless oil (41 %); R_f = 0.49 (4:1 hexane/ethyl acetate)

^1H NMR (300 MHz, CDCl_3): δ 7.33 (d, J = 8.0Hz, 2H), 7.15 (d, J = 8.4Hz, 2H), 5.56-5.70 (m, 1H), 5.10-5.16(m, 2H), 2.68 (dd, J = 13.6, 6.4Hz, 1H), 2.49 (dd, J = 13.6, 8.4Hz, 1H), 2.34 (s, 3H), 2.04 (s, 1H), 1.56 (s, 3H)

^{13}C NMR (75.4 MHz, CDCl_3): δ 144.8, 136.1, 133.9, 128.8, 124.7, 119.1, 73.5, 48.5, 29.8, 20.9

HRMS Calcd for $\text{C}_{12}\text{H}_{16}\text{O}$ [$\text{M} - \text{H}_2\text{O}$]: 158.1095 Found: 158.1093

$[\alpha]_D^{25} = +12.8^\circ$ (c = 2.03g/100mL, CH_2Cl_2)

The enantiomeric excess was determined by HPLC analysis employing a Daicel Chiracel OJ column (Hexane: *i*-propanol 98:2, 1.0 mL/min: t_1 = 6.98 min for major enantiomer, t_2 = 9.64 min for minor enantiomer).

The configuration was assigned by analogy with (*R*)-2-phenyl-pent-4-en-2-ol assuming a constant preference for the *re* face of the ketone.

(R)-2-Naphthalen-2-yl-pent-4-en-2-ol

(84 %*ee*)

Colorless oil (80 %); R_f = 0.54 (4:1 hexane/ethyl acetate)

^1H NMR (300 MHz, CDCl_3): δ 7.82 – 7.92 (m, 4H), 7.45 – 7.56 (M, 3H), 5.59-5.70 (m, 1H), 5.10-5.19 (m, 2H), 2.80 (dd, J = 13.6, 6.3 Hz, 1H), 2.59 (dd, J = 13.6, 8.4 Hz, 1H), 2.19 (s, 1H), 1.64 (s, 3H),

^{13}C NMR (75.4 MHz, CDCl_3): δ 142.4, 131.0, 130.5, 129.6, 125.5, 125.2, 124.8, 123.4, 123.1, 120.9, 120.6, 116.9, 71.2, 45.7, 27.3.

FTIR (neat): 3433, 3058, 2929, 2923, 2851, 1638, 1600, 1376, 916, 857, 818, 748 cm^{-1} .

HRMS Calcd for $\text{C}_{14}\text{H}_{14}\text{O}$ [$\text{M} - \text{H}_2\text{O}$]: 194.1095. Found: 194.1091

$[\alpha]_D^{25} = +39.8^\circ$ (c = 0.92g/100mL, CH_2Cl_2)

The enantiomeric excess was determined by HPLC analysis employing a Daicel Chiracel OD column (Hexane: *i*-propanol 99:1, 0.5 mL/min: t_1 = 26.28 min for minor enantiomer, t_2 = 31.30 min for major enantiomer).

The configuration was assigned by analogy with (*R*)-2-phenyl-pent-4-en-2-ol assuming a constant preference for the *re* face of the ketone.

(R)-3-Methyl-1-phenyl-hexa-1,5-dien-3-ol

(90%*ee*)

Colorless oil (82 %); R_f = 0.43 (4:1 hexane/ethyl acetate)

^1H NMR (300 MHz, CDCl_3): δ 7.19 – 7.40 (m, 5H), 6.60 (d, J = 16.1 Hz, 1H), 6.30 (d, J = 16.0 Hz, 1H), 5.77-5.91 (m, 1H), 5.14-5.19 (m, 2H), 2.45 (dd, J = 13.6, 6.4 Hz, 1H), 2.36 (dd, J = 13.6, 8.0 Hz, 1H), 1.77 (s, 1H), 1.39 (s, 3H).

^{13}C NMR (75.4 MHz, CDCl_3): δ 137.0, 136.3, 133.6, 128.6, 127.5, 127.4, 126.4, 119.3, 72.4, 47.4, 28.0.

FTIR (neat): 3410, 3078, 1640, 970, 916, 748, 693 cm^{-1} .

HRMS Calcd for $\text{C}_{10}\text{H}_{16}\text{O}$ [$\text{M} - \text{H}_2\text{O}$]: 170.1095. Found: 170.1091

$[\alpha]_D^{25} = +63.5^\circ$ (c = 1.19g/100mL, CH_2Cl_2)

The enantiomeric excess was determined by HPLC analysis employing a Daicel Chiracel OD column (Hexane: *i*-propanol 99:1, 0.5 mL/min: t_1 = 28.92min for major enantiomer, t_2 = 33.59 min for minor enantiomer).

The configuration was assigned by analogy with (*R*)-2-phenyl-pent-4-en-2-ol assuming a constant preference for the *re* face of the ketone.

(S)-3-Methyl-1-phenyl-hex-5-en-3-ol

(80 %*ee*)

Colorless oil (60%); R_f = 0.51 (4:1 hexane/ethyl acetate)

^1H NMR (300 MHz, CDCl_3): δ 7.19 – 7.31 (m, 5H), 5.82-5.96 (m, 1H), 5.12-5.19 (m, 2H), 2.68-2.74 (m, 2H), 2.30 (d, J = 7.2, 2H), 1.75-1.81 (m, 2H), 1.26 (s, 3H),

^{13}C NMR (75.4 MHz, CDCl_3): δ 142.5, 133.8, 128.4, 128.3, 125.8, 118.9, 72.1, 46.5, 43.7, 30.3, 26.8.

FTIR (neat): 3429, 3415, 2977, 1640, 912, 742, 699 cm^{-1} .

HRMS Calcd for $\text{C}_{12}\text{H}_{16}\text{O}$ [$\text{M} - \text{H}_2\text{O}$]: 172.1252. Found: 172.1252

$[\alpha]_D = +9.5^\circ$ (c = 4.30g/100mL, CH_2Cl_2)

The enantiomeric excess was determined by HPLC analysis employing a Daicel Chiracel OD column (Hexane: *i*-propanol 99:1, 0.5 mL/min: t_1 = 22.76 min for major enantiomer, t_2 = 25.54 min for minor enantiomer).

The configuration was assigned by analogy with (*R*)-2-phenyl-pent-4-en-2-ol assuming a constant preference for the *re* face of the ketone.

(R)-1-Allyl-indan-1-ol

(90 %*ee*)

Colorless oil (61 %); R_f = 0.43 (4:1 hexane/ethyl acetate)

^1H NMR (300 MHz, CDCl_3): δ 7.31 – 7.36 (m, 1H), 7.21 – 7.29 (m, 3H), 5.80-5.93 (m, 1H), 5.14-5.20 (m, 2H), 3.00 (ddd, J = 16.0, 8.7, 4.5, 1H), 2.77-2.87 (m, 1H), 2.64 (dd, J = 13.8, 7.3 1H), 2.52 (dd, J = 13.6, 7.0, 1H), 2.29-2.38 (m, 1H), 2.19 (bs, 1H), 2.03-2.12 (m, 1H).

^{13}C NMR (75.4 MHz, CDCl_3): δ 147.0, 143.0, 133.8, 128.2, 126.6, 124.9, 122.9, 118.7, 82.7, 45.0, 39.6, 29.4

FTIR (neat): 3402, 1640, 996, 914, 760 cm^{-1} .

HRMS Calcd for $\text{C}_{10}\text{H}_{18}\text{O}$ [$\text{M} - \text{H}_2\text{O}$]: 156.0939. Found 156.0934

$[\alpha]_D = -5.1^\circ$ (c = 4.03g/100mL, CH_2Cl_2)

The enantiomeric excess was determined by HPLC analysis employing a Daicel Chiracel OD column (Hexane: *i*-propanol 99:1, 1.0mL/min: t_1 = 8.34 min for major enantiomer, t_2 = 10.48 min for minor enantiomer).

The configuration was assigned by analogy with (*R*)-2-phenyl-pent-4-en-2-ol assuming a constant preference for the *re* face of the ketone.

(R)-1-Allyl-6-methyl-indan-1-ol

(92 %*ee*)

Colorless oil (50 %); R_f = 0.41 (4:1 hexane/ethyl acetate)

^1H NMR (300 MHz, CDCl_3): δ 7.08 – 7.15 (m, 3H), 5.79-5.93 (m, 1H), 5.15-5.21 (m, 2H), 2.95 (ddd, J = 16.0, 8.7, 4.5, 1H), 2.72-2.82 (m, 1H), 2.64 (dd, J = 13.6, 7.7, 1H), 2.50 (dd, J = 13.6, 7.0, 1H), 2.36 (s, 3H), 2.28-2.35 (m, 1H), 2.02-2.11 (m, 1H).

^{13}C NMR (75.4 MHz, CDCl_3): δ 147.2, 140.0, 136.3, 133.9, 129.2, 124.7, 123.4, 118.8, 82.7, 45.0, 39.9, 29.0, 21.4.

FTIR (neat): 3294, 3079, 3015, 2844, 1638, 1491, 996, 913, 812 cm^{-1} .

HRMS Calcd for $\text{C}_{10}\text{H}_{18}\text{O}$ [$\text{M} - \text{H}_2\text{O}$]: 170.1095 Found : 170.1089

$[\alpha]_D = -11.4^\circ$ (c = 3.42g/100mL, CH_2Cl_2)

The enantiomeric excess was determined by HPLC analysis employing a Daicel Chiralcel OD column (Hexane:*i*-propanol 99:1, 0.5mL/min: t_1 = 14.25 min for major enantiomer, t_2 = 17.00 min for minor enantiomer).

The configuration was assigned by analogy with (*R*)-2-phenyl-pent-4-en-2-ol assuming a constant preference for the *re* face of the ketone.