Supplementary Material for Chemical Communications

Catalytic Asymmetric Allylation of Aldehydes via a Chiral Indium(III) Complex

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Supplementary Material

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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. 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 F_{254} 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 (^{1}H 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 (^{13}C NMR) 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 77.03, triplet). The proportion of diastereomers and geometric isomers was determined from the integration of ^{1}H NMR and ^{13}C NMR spectra.

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

General Procedure for Aldehyde Allylation Reactions

Representative procedure for asymmetric allylation of aldehydes : Preparation of (*S*)-1-phenylbut-3-en-1-ol

To an oven dried 10mL round-bottom flask equipped with a magnetic stirring bar was added $InCl_3$ (22mg, 0.1mmol, 0.2 equiv.). The solid was azeotropically dried with anhydrous tetrahydrofuran twice (2 mL x 2) prior to the addition of 1.5 mL of dichloromethane. *(S)*-BINOL (31 mg, 0.11 mmol, 0.22 equiv.) and 4Å molecular sieve (15 mg) were added and the mixture was stirred under nitrogen at room temperature for 2 hours to afford a white suspension. Allyltributylstannane (0.31 mL, 1.0 mmol, 2.0 equiv.) was added to the resulting suspension and stirred for 10 minutes. The mixture was then cooled to –78°C for 15 minutes followed by slow addition of benzaldehyde (53mg in 0.5 mL dichloromethane, 0.5 mmol, 1.0 equiv). The reaction mixture was stirred at –78°C for 4h and then for 16h at room temperature. The reaction mixture was treated with 5 mL saturated sodium bicarbonate solution at room temperature for 30min., extracted with dichloromethane (3 x 10 mL), washed with brine, dried over Na_2SO_4, filtered and concentrated *in vacuo*. The residual crude product was purified via silica gel chromatography to afford the homoallylic alcohol as a colourless oil (76% yield).

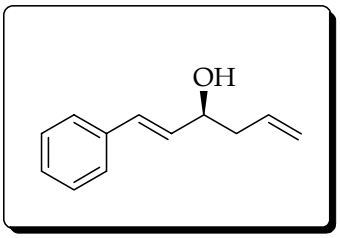
General Procedure for Aldehyde Allylation Reactions in Aqueous media

Representative procedure for asymmetric allylation of aldehydes : Preparation of (*S*)-1-phenylbut-3-en-1-ol

To an oven dried 10 mL round-bottom flask equipped with a magnetic stirring bar was added $InCl_3$ (33 mg, 0.15 mmol, 0.2 equiv.). The solid was azeotropically dried with anhydrous tetrahydrofuran twice (2 mL x 2) prior to the addition of 1.5 mL of dichloromethane. *(S)*-BINOL (47 mg, 0.33 mmol, 0.33 equiv.) was added to the mixture and stirred under nitrogen at room temperature for 2 hours. Allyltributyl stannane (0.093 mL, 0.3 mmol, 0.6 equiv.) was added to the resulting mixture and stirred for 10 minutes followed by addition of 10.5 μL H_2O to afford a white suspension. The pre-formed catalyst was further treated with allyltributyl stannane and stirred for 10 minutes followed by benzaldehyde (53mg in 0.5 mL dichloromethane, 0.5 mmol, 1.0 equiv). The reaction mixture was stirred for 16h at room temperature and treated with 5 mL saturated sodium bicarbonate solution for 30 minutes, extracted with dichloromethane (3 x 10 mL), washed with brine, dried over Na_2SO_4, filtered and concentrated *in vacuo*. The residual crude product was purified via silica gel chromatography to afford the homoallylic alcohol as a colourless oil (42% yield).

Characterization of homoallylic alcohols in Table 2

(*S*)-1-phenylhexa-1,5-dien-3-ol



(96 %*ee*)

Colorless oil (63 mg, 72 %); R_f = 0.40 (4:1 hexane/ethyl acetate)

^{1}H NMR (300 MHz, $CDCl_3$): δ 7.21-7.40 (m, 5H), 6.60 (d, *J* = 15.9 Hz, 1H), 6.25 (dd, *J* = 15.9, 6.3 Hz, 1H), 5.79-5.93 (m, 1H), 5.15-5.21 (m, 2H), 4.35-4.37 (m, 1H), 2.33-2.48 (m, 2H), 1.80 (br, 1H)

^{13}C NMR (75.4 MHz, $CDCl_3$): δ 136.6, 134.0, 131.5, 130.3, 128.5, 127.6, 126.4, 118.4, 71.6, 42.0.

FTIR (neat): 3414 cm^{-1}.

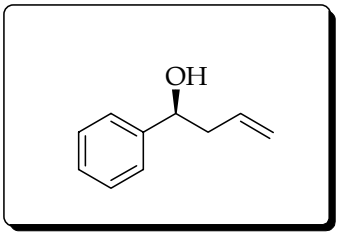
HRMS Calcd for $C_{12}H_{16}0$ [M^+]: 174.1045. Found: 176.1040.

$[\alpha]_D$ = -15.1 (c = 1.54g/100mL, CH_2Cl_2)

The enantiomeric excess was determined by HPLC analysis employing a Daicel Chiracel OD column (Hexane: *i*-propanol 98:2, 1.0 mL/min: t_1 = 13.80 min for *R* enantiomer, t_2 = 23.17 min for *S* enantiomer). It has been established that the *R* enantiomer elutes first.[6]

6. (a) Nakajima, M.; Saito, M.; Shiro, M.; Hashimoto, S. *J. Am. Chem. Soc.* **1998**, *120*, 6419 (b) C.-H.-A. Lee, T.-P. Loh. *Tetrahedron Lett.* **2004**, *45*, 5819

(*S*)-1-phenylbut-3-en-1-ol



(92 %*ee*)

Colorless oil (56 mg, 76 %); R_f = 0.38 (4:1 hexane/ethyl acetate)

^{1}H NMR (300 MHz, $CDCl_3$): δ 7.37-7.27 (m, 5H), 5.89-5.75 (m, 1H), 5.20-5.13 (m, 2H), 4.75 (t, *J* = 5.6 Hz, 1H), 2.54-2.49 (m, 2H), 2.20 (br, 1H)

^{13}C NMR (75.4 MHz, $CDCl_3$): δ 143.9, 134.5, 128.4, 127.6, 125.8, 118.4, 73.3, 43.8

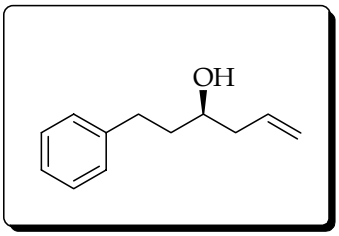
FTIR (neat): 3468, 2932, 1707, 1642, 1494, 1452, 1051, 999, 916, 758, 701 cm^{-1}.

HRMS Calcd for $C_{10}H_{12}0$ [M^+]: 148.0888. Found: 148.0899.

$[\alpha]_D$ = -42.7 ^{o} (c = 1.69g/100mL, CH_2Cl_2)

The enantiomeric excess was determined by HPLC analysis employing a Daicel Chiracel OD column (Hexane: *i*-propanol 99:1, 1.0 mL/min: t_1 = 9.72 min for *R* enantiomer, t_2 = 12.78 min for *S* enantiomer). It has been established that the *R* enantiomer elutes first.[6]

(*R*)-1-phenylhex-5-en-3-ol



(90 %*ee*)

Colorless oil (56 mg, 64 %); R_f = 0.49 (4:1 hexane/ethyl acetate)

^{1}H NMR (300 MHz, $CDCl_3$): δ 7.31-7.16 (m, 5H), 5.89-5.75 (m, 1H), 5.17-5.12 (m, 2H), 3.68 (m, 1H), 2.74 (m, 2H), 2.36-2.14 (m, 2H), 1.81-1.76 (m, 2H)

^{13}C NMR (75.4 MHz, $CDCl_3$): δ 142.0, 134.6, 128.4, 125.8, 118.2, 70.0, 42.0, 38.4, 32.0.

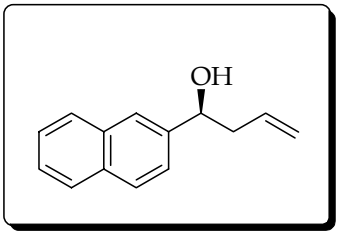
FTIR (neat): 3377, 2928, 1495 cm^{-1}.

HRMS Calcd for $C_{12}H_{16}0$ [M^+]: 176.1201. Found: 176.1199.

$[\alpha]_D$ = +15.9 ^{o} (c = 2.15g/100mL, CH_2Cl_2)

The enantiomeric excess was determined by HPLC analysis employing a Daicel Chiracel OD column (Hexane: *i*-propanol 99:1, 1.0 mL/min: t_1 = 11.35 min for *S* enantiomer, t_2 = 18.52 min for *R* enantiomer). It has been established that the *S* enantiomer elutes first.[6]

(*S*)-1-Naphthalen-2-yl-but-3-en-1-ol



(90 %*ee*)

Colorless oil (54 mg, 55 %); R_f = 0.40 (4:1 hexane/ethyl acetate)

^{1}H NMR (300 MHz, $CDCl_3$): δ 7.81-7.85 (m, 4H), 7.45-7.50 (m, 3H), 5.77-5.91 (m, 1H), 5.13-5.22 (m, 2H), 4.91 (t, *J* = 6.4 Hz, 1H), 2.53-2.68 (m, 2H), 2.14 (br, 1H)

^{13}C NMR (75.4 MHz, $CDCl_3$): δ 141.2, 134.3, 133.2, 132.9, 128.1, 127.9, 127.6, 126.0, 125.7, 124.4, 123.9, 118.4, 73.3, 43.6

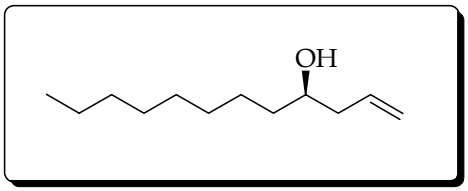
FTIR (neat): 3380cm^{-1}.

HRMS Calcd for $C_{14}H_{14}0$ [M^+]: 198.1047. Found: 198.1054.

$[\alpha]_D$ = -31.1 ^{o} (c = 1.40g/100mL, CH_2Cl_2)

The enantiomeric excess was determined by HPLC analysis employing a Daicel Chiracel OD-H column (Hexane: *i*-propanol 95:5, 0.8 mL/min: t_1 = 15.68 min (major), t_2 = 18.12 min (minor). The configuration was assigned by analogy with (*S*)-1-phenylbut-3-en-1-ol assuming a constant preference for the *Si* face of the aldehyde.

(*R*)-dodec-1-en-4-ol



(94 %*ee*)

Colorless oil (66 mg, 72 %); R_f = 0.53 (4:1 hexane/ethyl acetate)

^{1}H NMR (300 MHz, $CDCl_3$): δ 5.90-5.76 (m, 1H), 5.17-5.11 (m, 2H), 3.64 (m, 1H), 2.36 (m, 2H), 1.48-1.43 (m, 2H), 1.33-1.25 (m, 12H), 0.88 (t, *J* = 6.3 Hz, 3H)

^{13}C NMR (75.4 MHz, $CDCl_3$): δ 134.9, 118.0, 70.7, 41.9, 36.8, 31.9, 29.7, 29.3, 25.7, 22.7, 14.1.

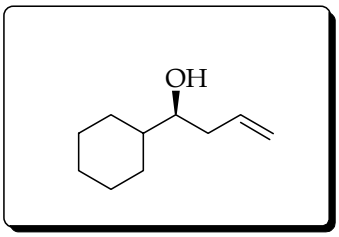
FTIR (neat): 3557, 2924, 2855, 1642, 1464, 995, 913 cm^{-1}.

HRMS Calcd for $C_{12}H_{24}0$ [M^+]: 184.1827. Found: 184.1830.

$[\alpha]_D$ = +6.4^o (c = 1.56g/100mL, CH_2Cl_2)

Chiral resolution using *R*-(+)-α-trifluoromethyl-α-methoxy-phenylacetic acid (Mosher acid). The enantiomeric excess was found to be 94 % by 500 MHz ^{1}H NMR analysis of its Mosher derivative at δ 2.40 for the *R* enantiomer and 2.33 for the *S* enantiomer.[6]

(*S*)-1-cyclohexyl-but-3-en-1-ol



(94 %*ee*)

Colorless oil (41 mg mg, 53 %); R_f = 0.43 (4:1 hexane/ethyl acetate)

^{1}H NMR (300 MHz, $CDCl_3$): δ 5.90-5.76 (m, 1H), 5.15-5.10 (m, 2H), 3.43-3.37 (m, 1H), 2.33-2.28 (m, 2H), 2.18-2.08 (m, 1H), 1.94-1.26 (m, 10H)

^{13}C NMR (75.4 MHz, $CDCl_3$): δ 135.5, 117.9, 74.8, 43.1, 38.8, 29.1, 28.1, 26.5, 26.1, 25.4.

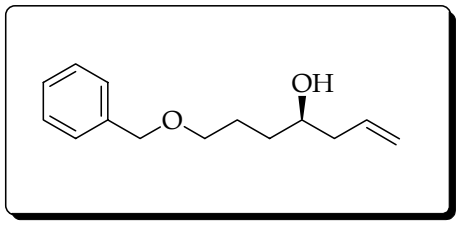
FTIR (neat) 3469, 2923, 2853, 1641, 1449, 1036, 986, 911 cm^{-1}.

HRMS Calcd for $C_{10}H_{18}0$ [M^+]: 154.1358. Found: 154.1358.

$[\alpha]_D$ = -5.4° (c = 1.13g/100mL, CH_2Cl_2)

Product was derivatized with 2,4-dinitrobenzolic chloride before the enantiometric excess was determined by HPLC analysis employing a Daicel Chiracel OD-H column (Hexane: *i*-propanol 99:1, 0.3 mL/min: t_1 = 42.32 min for the *R* enantiomer, t_2 = 46.07 min for the *S* enantiomer).[6]

(*R*)-7-(benzyloxy)hept-1-en-4-ol



(94 %*ee*)

Colorless oil (77mg, 70 %); R_f = 0.38 (4:1 hexane/ethyl acetate)

^{1}H NMR (300 MHz, $CDCl_3$): δ 7.39-7.28 (m, 5H), 5.90-5.77 (m, 1H), 5.17-5.09 (m, 2H), 4.52 (s, 2H), 3.71-3.61 (m, 1H), 3.52 (t, *J* = 5.9 Hz, 2H), 2.32-2.13 (m, 2H), 1.78-1.63 (m, 2H), 1.53-1.41 (m, 2H)

^{13}C NMR (75.4 MHz, $CDCl_3$): δ 138.2, 135.0, 128.4, 127.7, 127.6, 117.7, 73.0, 70.6, 70.4, 42.0, 34.0, 26.2

FTIR (neat): 3451, 2928, 2862, 1641, 1452, 1097, 1026, 998, 915, 740, 699 cm^{-1}.

HRMS Calcd for $C_{14}H_{20}O_2$ [M^+]: 220.1463. Found: 220.1465.

$[\alpha]_D$ = +7.4 ^{o} (c = 1.63g/100mL, CH_2Cl_2)

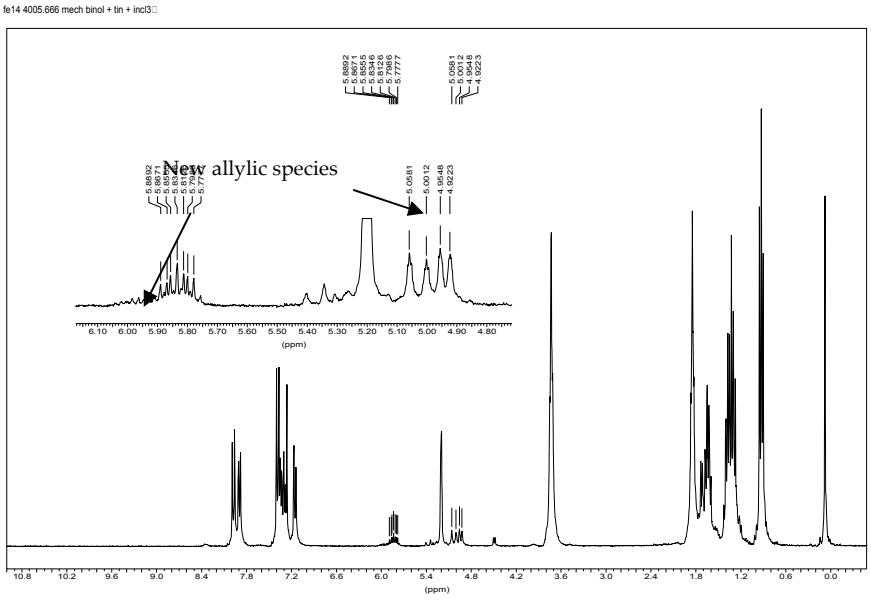
The enantiomeric excess was determined by HPLC analysis employing a Daicel Chiracel OB column (Hexane: *i*-propanol 99:1, 1.0 mL/min: t_1 = 18.84 min for the *R* enantiomer, t_2 = 27.00 min for the *S* enantiomer).[6]

Mechanism Studies

^{1}H NMR Study A: Addition of 1.0 equivalent of allyltributyl stannane

The addition of 1.0 equivalent of allyltributyl stannane to the mixture of (*S*)-BINOL-$InCl_3$ afforded the formation of new allylic species with the formation of tributyl stannane chloride. No allylic tributyl stannane was observed in the ^{1}H NMR spectrum. This study showed that indium trichloride undergo transmetallation to afford a new allylic indium species which formed a chiral indium complex with BINOL.

NMR spectrum : Equimolar of $InCl_3$ + (*S*)-BINOL + allytributyl stannane

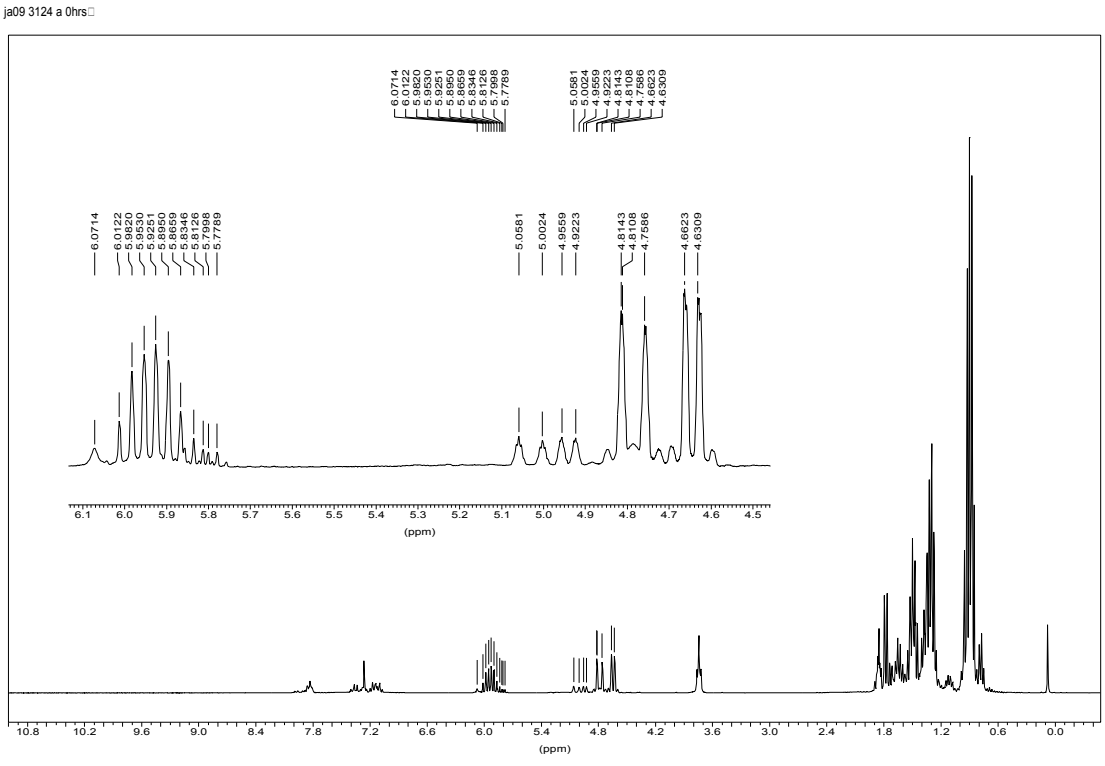


The proton chemical shift of this new set of allyl signals [(δ5.91-5.75 (m, 1H), 5.06-4.92 (m, 2H)] was significantly different from that of allytributyl stannane [(δ6.01-5.86, (m, 1H), 4.81-4.62 (m, 2H)].

^{1}H NMR Study B: Addition of 10.0 equivalent of allyltributyl stannane

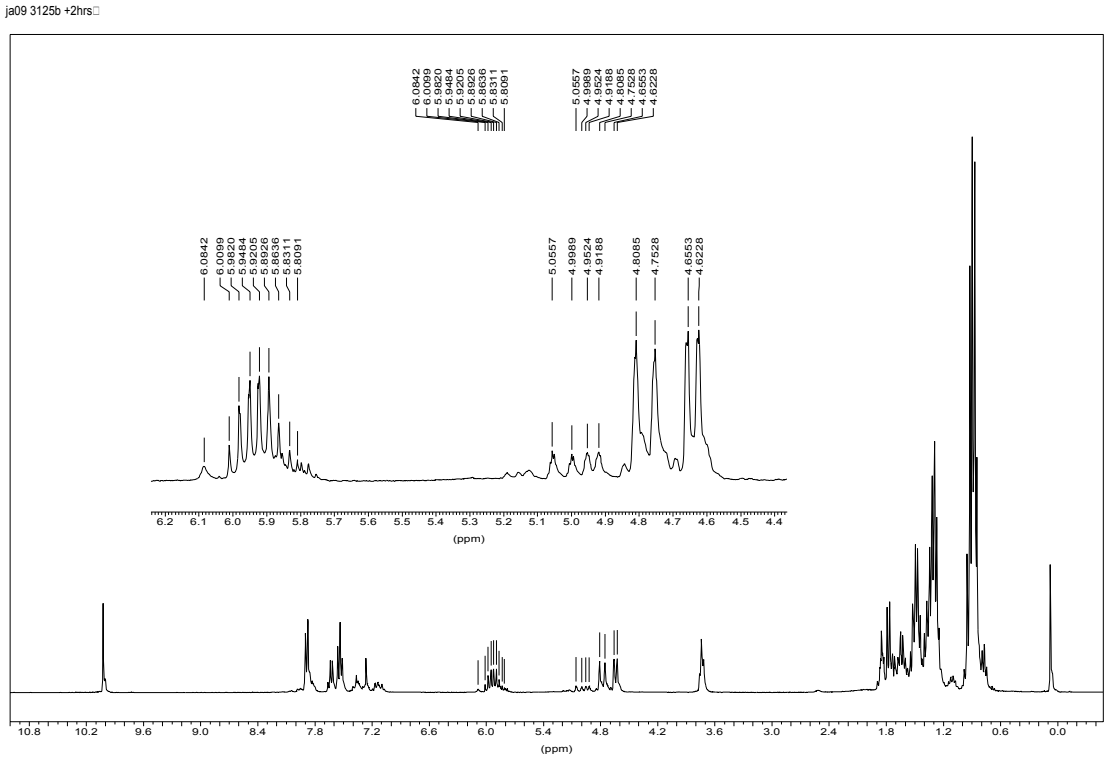
The addition of 10.0 equivalents of allyl tributyl stannane with respect to BINOL leads to the formation of new allylic species together with excess allyltributyl stannane. The formation of the tributyl stannane chloride was also evident from the ^{1}H NMR spectrum. The homoallylic alcohol started to form after 4 h upon subsequent addition of benzaldehyde. The product was eventually obtained in 52% yield with 90% *ee* after 12 h.

NMR spectrum : $InCl_3$ + (S)-BINOL + allyltributyl stannane at time = **2** hr



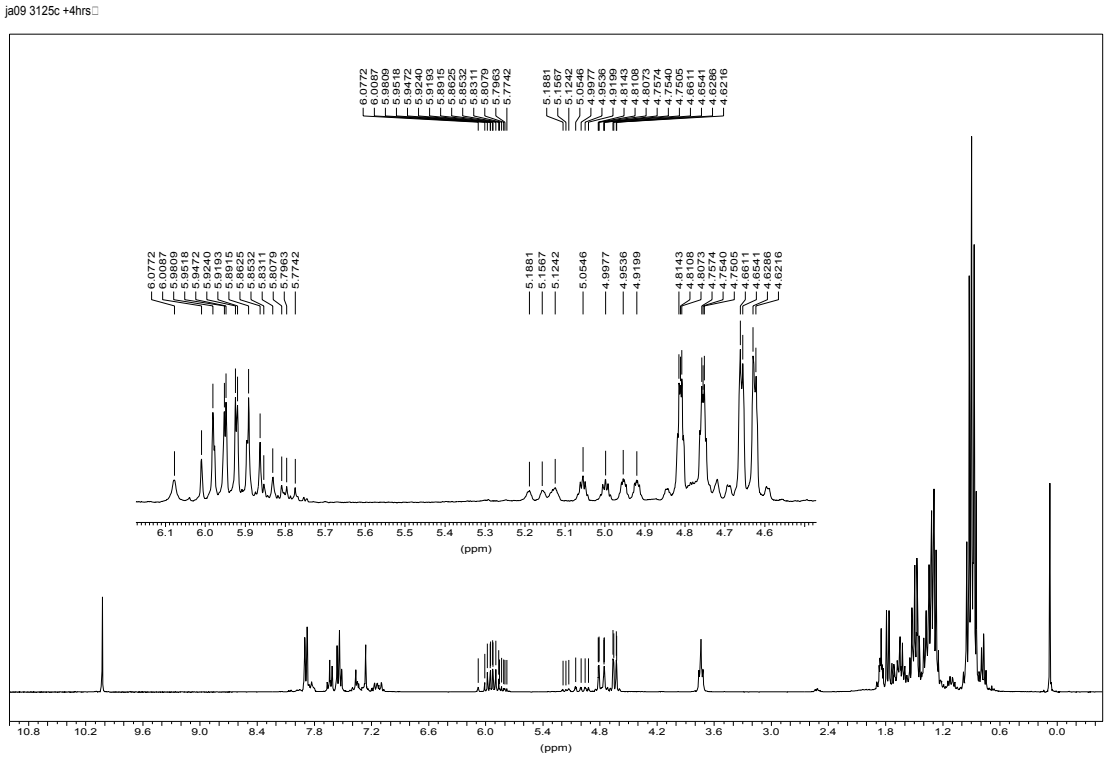
NMR indicates the formation of new allylic species together with excess allyltributyl stannane. The intensity ratio of the new allylic signal relative to allyltributyl stananes was 10:90.

NMR spectrum : $InCl_3$ + (S)-BINOL + allyltributyl stannane after initial addition of benzaldehyde



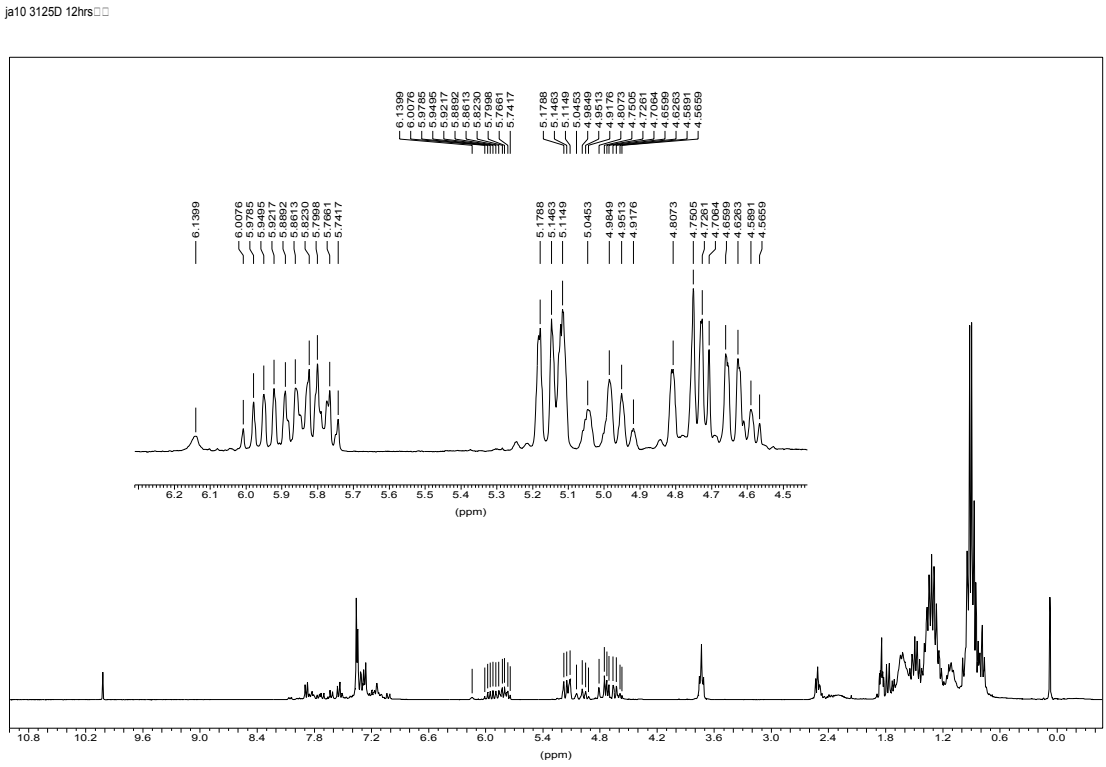
NMR indicates two sets of allylic signal together with the aldehyde signal. No product observed at this stage.

NMR spectrum : $InCl_3$ + (S)-BINOL + allyltributyl stannane after 4 hrs of reaction time



NMR indicates the presence of two allylic signals together with initial product formation.

NMR spectrum : $InCl_3$ + (S)-BINOL + allyltributyl stannane after 12 hrs of reaction time



NMR indicates significant quantity of product formation.