Electronic Supplementary Material (ESI) for ChemComm.

Toward a unified synthetic route to biselyngbyolide A and biselyngbyolide B: Rapid and enantioselective synthesis of the C1–C13 fragment

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SUPPORTING INFORMATION

Materials and Methods

Unless otherwise stated, reactions were performed in flame- or oven-dried glassware under an argon or nitrogen atmosphere using anhydrous solvents. Tetrahydrofuran (THF), dichloromethane, diethyl ether, toluene, acetonitrile, and dimethyl formamide (DMF) were dried by passage through a column of activated molecular sieves. Dioxane was purchased in anhydrous form from Sigma Aldrich. All other chemicals were purchased from commercial sources and used as received.

Unless otherwise stated, reactions were monitored using thin-layer chromatography (TLC) using glass plates precoated with silica gel XHL w/ UV254 (250 mm) purchased from *SILICYCLE®* and visualized by UV light or $KMnO_4$, phosphomolybdic acid, anisaldehyde, or 2,4-DNP stains; followed by heating. Silica gel (particle size 32–63 mm) purchased from *SILICYCLE®* was used for flash column chromatography.

^1H and ^{13}C NMR spectra are reported relative to the residual solvent peak (δ 7.26 and δ 77.0 for ^1H and ^{13}C in $CDCl_3$, δ 3.31 and δ 49.0 for ^1H and ^{13}C in CD_3OD, respectively), or tetramethylsilane (δ 0.00 for ^1H) when the residual solvent peak is obscured. Data for ^1H NMR spectra are reported as follows: (instrument field strength, solvent) δ chemical shift (ppm) (multiplicity, coupling constant (Hz), integration). Multiplicity is described using the following abbreviations: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, bs = broad singlet, app = apparent. Data for ^{13}C NMR spectra are reported in terms of chemical shift (δ ppm). Where available, DEPT data is reported immediately following the appropriate ^{13}C chemical shift using the following abbreviations: C, CH, CH_2, CH_3. Some reported spectra include minor solvent impurities of benzene (δ 7.36 ppm), water (δ 1.56 ppm), ethyl acetate (δ 4.12, 2.05, 1.26 ppm), methylene chloride (δ 5.30 ppm), grease (δ 1.26, 0.86 ppm), and/or silicon grease (δ 0.07 ppm), which do not impact product assignments.

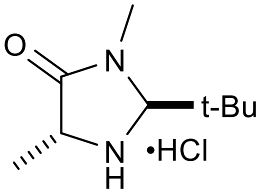
IR spectra were obtained using a Thermo Scientific Nicolet iS5 FT-IR configured with either an iD7 ATR sampling accessory or an iD1 sampling accessory (for use with thin films deposited on NaCl salt plates) and are reported in frequency of absorption (cm^{-1}). Optical rotations were obtained using Rudolph AUTOPOL®IV Automatic Polarimeter.

Analytical chiral HPLC was performed with an Agilent 1100 Series HPLC equipped with a diode array detector utilizing either a Chiralpak IA (4.6 x 250 mm, 5 micron), Chiralpak IB (4.6 x 250 mm, 5 micron), Chiralpak IC (4.6 x 250 mm, 5 micron), Chiralpak ID (4.6 x 250 mm, 5 micron), or Chiralpak IE (4.6 x 250 mm, 5 micron) column. Visualization was at 254 or 225 nm.

Experimental Procedures

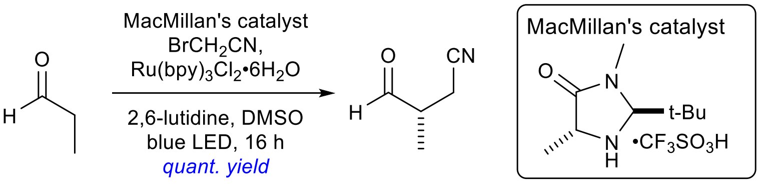
MacMillan's catalyst was synthesized Boc-D-alanine according to the procedure reported by Samulis and Tomkinson[1]. The trifluoromethane sulfonate salt was prepared fresh each time before the cyanoalkylation reaction. Spectroscopic data matches with the literature data.

(2*S*,5*R*)-5-Methyl-2-tert-butyl-3-methylimidazolidin-4-one hydrochloride (12·HCl)



^{1}H NMR (400 MHz, CD_3OD) δ 4.75 (s, 1H), 4.27 (q, *J* = 7.1 Hz, 1H), 3.06 (d, *J* = 0.4 Hz, 3H), 1.56 (d, *J* = 7.1 Hz, 3H), 1.16 (s, 9H).

^{13}C NMR (100 MHz, $CDCl_3$, DEPT) δ 170.93 (*C*O), 81.77 (C*C*H), 54.74 (CO*C*H), 37.53 (C), 32.35 (N*C*H_3), 25.26 (3 x *C*H_3), 14.65 (CH*C*H_3).



(*S*)-**8** **12·TfOH**

(*S*)-3-Methyl-4-oxobutanenitrile (8): To a aluminum foil covered round bottom flask containing (2S,5R)-2-(tert-butyl)-3,5-dimethylimidazolidin-4-one trifluoromethanesulfonate (**12·TfOH**) (0.86 g, 2.68 mmol, 0.2 eq), was added tri(bipyridine)ruthenium (II)chloride (0.1 g, 0.1339 mmol, 0.01 eq) and DMSO (4 eq. with respect to the aldehyde). The flask was purged with argon three times, followed by addition of propionaldehyde (4.8 mL, 66.96 mmol, 5 eq), 2,4-lutidine (3.10 mL, 26.78 mmol, 2 eq) and bromoacetonitrile (0.93 mL, 13.39 mmol, 1 eq). The mixture was stirred vigorously while being purged with argon for 10 mins. After the argon purge, the foil was removed and the reaction was irradiated with blue LED light for 16 hours. The light was switched off and the reaction was cooled to room temperature (during irradiation, the temperature reaches 41 °C) and saturated solution of brine (20 mL) was added to the reaction mixture. It was extracted with EtOAc (3 x 30 mL) and the combined organic layers were washed with brine (4 x 30 mL), dried with Na_2SO_4, and concentrated under reduced pressure (Caution – pressure was maintained around 50 mbar) to provide a reddish brown liquid (1.3 g, 98%). The crude product was used in the next step without further purification.

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.67 (s, 1H), 2.84-2.75 (m, 1H), 2.69 (dd, *J* = 17, 5.4 Hz, 1H), 2.47 (dd, *J* = 17, 7.7 Hz, 1H), 1.39 (d, *J* = 7.5 Hz, 3H). Note: The NMR spectrum of crude material contains peaks from 2,6-lutidine, DMSO, ethyl acetate. This was due concentration under low vacuum to avoid product loss as well as no purification of the crude.

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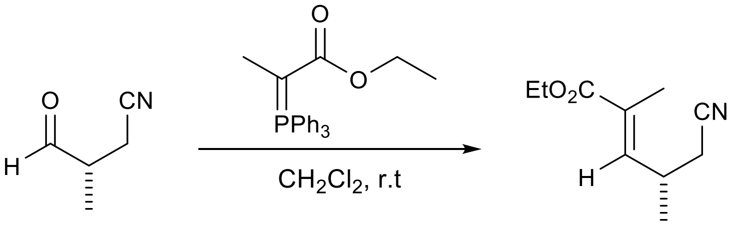
[1] Samulis, L.; Tomkinson, N.C.O. *Tetrahedron*, **2011**, *67*, 4263.



(*S*)-8 **9**

Ethyl (*S*,*E*)-5-cyano-2,4-dimethylpent-2-enoate (9): Crude aldehyde **8** (1.3 g, 13.39 mmol, 1 eq.) and ethyl 2-(triphenylphosphoranylidene)propionate (7.28 g, 20.08 mmol, 1.5 eq.) were dissolved in CH_2Cl_2 (15 mL) and stirred at room temperature for 48 hours. The reaction mixture was concentrated and the crude product was purified by flash chromatography (2:8 EtOAc:Hexane) to give a colorless oil (1.46 g, 60%).

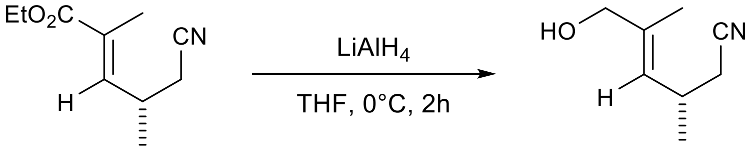
$[\alpha]_D^{25}$ = +2.1 (c 1.2, $CHCl_3$).

IR (thin film): 2970, 2934, 2249, 1707, 1652, 1255 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.53 (qd, *J* = 1.5, 9.9 Hz, 1H), 4.21 (q, *J* = 7.1 Hz, 2H), 2.94 (dddq, *J* = 6.7, 6.7, 6.7, 9.9 Hz, 1H), 2.42–2.36 (m, 2H), 1.90 (d, *J* = 1.5 Hz, 3H), 1.31 (t, *J* = 7.1 Hz, 3H), 1.21 (d, *J* = 6.7 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$, DEPT) δ 167.60 (CO), 141.9 (CH), 129.4 (C), 118.00 (C), 60.9 (CH_2), 30.4 (CH), 24.1 (CH_2), 19.5 (CH), 14.2 (CH_3), 12.7 (CH_3).

HRMS (ESI+) 204.1001 calc'd for $C_{10}H_{15}NO_2Na^+$, 204.0998 found.



9 **S1**

(*S*,*E*)-6-hydroxy-3,5-dimethylhex-4-enenitrile (S1): To an oven dried round bottom flask was added lithium aluminum hydride (0.188 g, 4.98 mmol, 1.1 eq.) and THF (5 mL). It was cooled to 0 °C followed by dropwise addition of the solution of ester (0.82 g, 4.53 mmol, 1 eq.) in THF (5 mL). The reaction was stirred at 0 °C for 2 hours (monitored by TLC) after which water (89 µL), NaOH (1.98 mL., 2.5 M soln.) and water (267 µL) were added sequentially at 15 min intervals at 0 °C. The resulting mixture was filtered and the solid residue was washed with CH_2Cl_2 (30 mL). The combined filtrates were dried (Na_2SO_4) and concentrated under reduced pressure and purified by column chromatography to provide colorless oil (0.61 g, 97%). The crude product was used further without any purification.

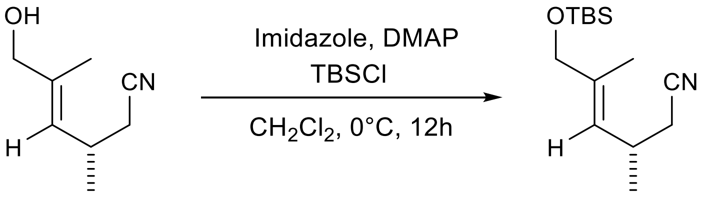
$[\alpha]_D^{25}$ = –4.9 (c 1, $CHCl_3$).

IR (thin film): 3389, 2962, 2922, 2872, 2248, 1456, 1009 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$) δ 5.28 (dt, *J* = 9.5, 1.4 Hz, 1H), 4.01 (s, 2H), 2.86 (dddq, *J* = 6.8, 6.8, 6.8, 9.5 Hz, 1H), 2.33 (dd, *J* = 13.3, 6.5 Hz, 2H), 2.05 (br s, 1H), 1.70 (s, 3H), 1.14 (d, *J* = 6.7 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$, DEPT) δ 136.8 (C), 127.0 (CH), 118.9 (C), 67.9 (CH_2), 29.4 (CH), 24.9 (CH_2), 20.4 (CH), 13.9 (CH_3).

HRMS (ESI+) 162.0895 calc'd for $C_8H_{13}ONa^+$, 162.0890 found.



S1 **10**

(*S*,*E*)-6-((*tert*-Butyldimethylsilyl)oxy)-3,5-dimethylhex-4-enenitrile (10): To the solution of the alcohol **S1** (0.6 g, 4.31 mmol, 1 eq.) in CH_2Cl_2 (10 mL) was added imidazole (0.88 g, 12.94 mmol, 3 eq.) and DMAP (0.03 g, 0.22 mmol, 0.05 eq.). The reaction mixture was stirred at room temperature for 30 mins. TBSCl (0.78 g, 5.18 mmol, 1.2 eq.) was added and reaction was stirred overnight at room temperature. It was quenched with saturated $NaHCO_3$ and extracted with CH_2Cl_2 (3 x 10 mL) combined filtrates were dried (Na_2SO_4) and concentrated under reduced pressure. The crude product was purified by flash chromatography (2:98 EtOAc:Hexane) to give a colorless oil (0.88 g, 80%).

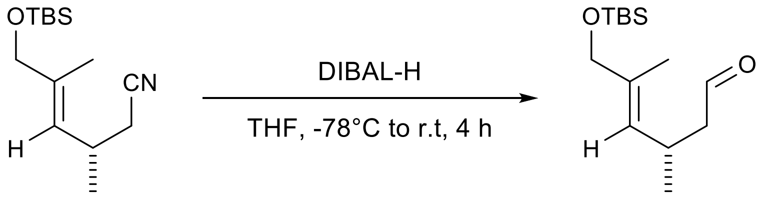
$[\alpha]_D^{25}$ = –2.9 (c 1, $CHCl_3$).

IR (thin film): 2955, 2928, 2856, 1472, 1252 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$) δ 5.22 (ddd, *J* = 9.5, 2.9, 1.5 Hz, 1H), 3.97 (s, 2H), 2.80 (dddq, *J* = 9.5, 6.7, 6.7, 6.7 Hz, 1H), 2.25 (dd, *J* = 1.2, 6.4 Hz, 2H), 1.60 (s, 3H), 1.09 (d, *J* = 6.7 Hz, 3H), 0.87 (s, 9H), 0.02 (s, 6H).

^{13}C NMR (100 MHz, $CDCl_3$, DEPT) δ 136.4 (C), 125.9 (CH), 118.70 (C), 67.8 (CH_2), 63.1 (C), 29.4 (CH), 26.0 (^{t}Bu), 25.0 (CH_2), 20.4 (CH), 13.7 (CH_3), –5.22 (CH_3), –5.24 (CH_3).

HRMS (ESI+) 276.1760 calc'd for $C_{14}H_{27}NOSiNa^+$, 276.1761 found.

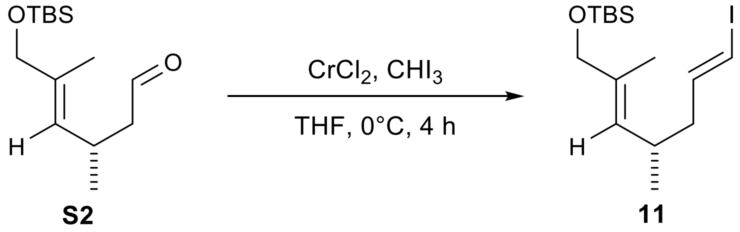


10 **S2**

(*S*,*E*)-6-((*tert*-Butyldimethylsilyl)oxy)-3,5-dimethylhex-4-enal (S2): To the solution of nitrile **10** (0.88 g, 3.47 mmol, 1 eq.) in THF (5 mL) was added the solution DIBAL-H (7.23 mL, 8.68 mmol, 2.5 eq., 1.2M in toluene) at –78 °C. The reaction was stirred at –78 °C for 2 hours after which it was warmed to room temperature over 2 hours. It was cooled to 0 °C and 10% HCl solution (1–2 mL) was added and the reaction was stirred at room temperature for 30 minutes. Layers were separated and aqueous layer was extracted with CH_2Cl_2 (3 x 10 mL), combined organic layers were dried over Na_2SO_4 and concentrated to provide yellow oil (0.64 g, 72%). It was used in the next step without further purification.

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.69 (td, *J* = 2.3, 0.6 Hz, 1H), 5.22 (d, *J* = 9.9 Hz, 1H), 3.98 (s, 2H), 2.99 (dddq, *J* = 9.7, 6.8, 6.8, 6.8 Hz, 1H), 2.36 (ddd, *J* = 7.0, 2.3, 0.6 Hz, 2H), 1.62 (s, 3H), 1.02 (d, *J* = 6.7 Hz, 3H), 0.89 (s, 9H), 0.88 (s, 3H), 0.043 (s, 6H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 202.7, 134.5, 128.2, 68.2, 63.3, 51.2, 29.5, 27.4, 26.1, 26.1, 21.1, 18.6, 18.5, 13.7, –5.11, –5.14. Note: Because no purification of the crude material was attempted, the ^{13}C NMR contains two extra peaks due to a minor impurity.



***tert*-Butyl(((*S*,2*E*,6*E*)-7-iodo-2,4-dimethylhepta-2,6-dien-1-yl)oxy)dimethylsilane (11)**: To a solution of chromium(III) chloride (1.15 g, 9.36 mmol, 6 eq.) in THF (5 mL) was added a solution of the crude aldehyde **S2** (0.4 g, 1.56 mmol, 1 eq.) and iodoform (1.23 g, 3.12 mmol, 2 eq.) in THF (15 mL) at 0 °C and reaction was stirred at 0 °C for 2 hours (monitored by TLC). Water (10 mL) was added to the reaction and layers were separated. Aqueous layer was extracted with EtOAc (3 x 15 mL), dried over Na_2SO_4 and concentrated to give brownish oily residue. The residue was purified by flash chromatography (2:98 EtOAc:Hexane) to give a colorless oil (0.35 g, 59%).

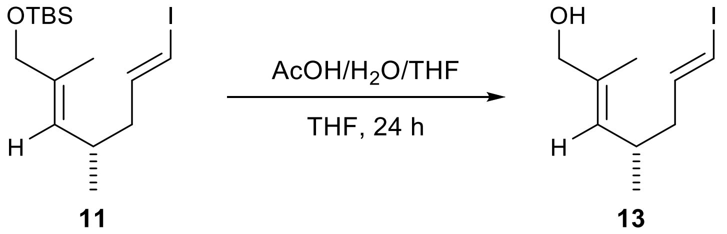
$[\alpha]_D^{25}$ = +6.4 (c 0.8, $CHCl_3$).

IR (thin film): 2956, 2923, 1721, 1455, 1157 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$) major diasteromer: δ 6.46 (td, *J* = 7.4, 14.5 Hz, 1H), 5.96 (td, *J* = 1.3, 14.3 Hz, 1H), 5.16 (ddd, *J* = 1.4, 2.8, 9.4 Hz, 1H), 4.00 (br s, 2H), 2.49 (dddq, *J* = 9.9, 6.8, 6.8, 6.8 Hz, 1H), 2.02 (ddt, *J* = 1.3, 3.3, 6.5 Hz, 2H), 1.59 (d, *J* = 1.3 Hz, 3H), 0.95 (d, *J* = 6.7 Hz, 3H), 0.91 (s, 9H), 0.06 (s, 6H).
Minor diastereomer: 6.20 (dt, *J* = 7.4, 1.2 Hz, 1H), 6.15 (td, *J* = 13.4, 6.5 Hz, 1H), 5.22 (dq, *J* = 9.6, 1.5 Hz, 1H), 2.59 (m, 1H), 2.15 (m, 2H), 1.60 (d, *J* = 1.3 Hz, 3H), 1.00 (d, *J* = 6.7 Hz, 3H).

^{13}C NMR (125 MHz, $CDCl_3$, DEPT) δ 145.1 (CH), 134.0 (C), 128.9 (CH), 82.9 (C), 75.3 (CH), 68.4 (CH_2), 43.60 (CH_2), 31.6 (CH), 26.0 (^{t}Bu), 20.4 (CH_3), 13.6 (CH_3), –5.2 (2 x CH_3).
Minor Diastereomer: 133.86, 129.50, 68.47, 42.15, 31.93, 31.35, 29.70, 22.70, 20.63, 14.14.

HRMS (ESI+) 403.0930 calc'd for $C_{15}H_{29}IOSiNa^+$, 403.0926 found.



(*S*,2*E*,6*E*)-7-Iodo-2,4-dimethylhepta-2,6-dien-1-ol (13): The vinyl iodide **11** (0.065 g, 0.171 mmol, 1 eq.) was stirred in AcOH/H_2O/THF (3:1:1, 3 mL) and stirred at room temperature for 24 hours. The reaction mixture was concentrated and neutralized (pH>10) with NaOH solution (10%), and extracted with EtOAc (3 x 15 mL). The combined organic layers were dried and concentrated to yield crude oil. The crude product was purified by flash chromatography (1:9 EtOAc:Hexane) to give a colorless oil (0.037 g, 82%).

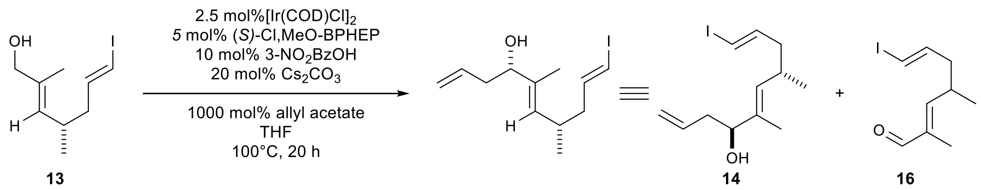
$[\alpha]_D^{25}$ = – 1.3 (c 1.13, $CHCl_3$).

IR (thin film) 3449, 2956, 2922, 2866, 1736, 1224, 1020 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.45 (ddd, *J* = 7.3, 7.3, 14.5 Hz, 1H), 5.98-5.94 (m, 1H), 5.18 (qd, *J* = 1.3, 9.5 Hz, 1H), 4.00 (d, *J* = 4.9 Hz, 2H), 2.49 (dddq, *J* = 9.4, 6.7, 6.7, 6.7 Hz, 1H), 2.09–1.96 (m, 2H), 1.67 (d, *J* = 1.4 Hz, 3H), 0.96 (d, *J* = 6.7 Hz 3H).
Minor diastereomer visible peaks: 6.22 (dt, *J* = 7.4, 1.2 Hz, 1H), 6.15 (dd, *J* = 13.9, 7.0 Hz, 1H), 5.27 (dq, *J* = 9.6, 1.4 Hz, 1H), 4.05 (d, *J* = 4.8 Hz, 1H), 2.64–2.56 (m, 1H), 2.21–2.10 (m, 2H), 1.68 (d, *J* = 1.4 Hz, 3H), 1.01 (d, *J* = 6.7 Hz 3H).

^{13}C NMR (100 MHz, $CDCl_3$, DEPT) δ 144.9 (CH), 134.3 (C), 130.5 (CH), 75.5 (CHI), 68.6 (CH_2), 43.5 (CH_2), 31.7 (CH), 20.4 (CH_3), 13.9 (CH_3).
Minor diastereomer visible peaks: 139.6 (CH), 134.1 (C), 131.54 (CH), 83.3 (CHI), 68.7 (CH_2), 42.0 (CH_2), 31.5 (CH), 20.60 (CH_3), 13.94 (CH_3).

HRMS (ESI+) 289.0065 calc'd for $C_9H_{15}IONa^+$, 289.0069 found.



(4*S*,5*E*,7*S*,9*E*)-10-Iodo-5,7-dimethyldeca-1,5,9-trien-4-ol (14): To an oven dried vial was added the alcohol **13** (30 mg, 0.112 mmol, 1 eq.), $[Ir(cod)Cl]_2$ (1.8 mg, 0.003 mmol, 0.025 eq.), (*S*)-Cl,MeO-BIPHEP (3.7 mg, 0.006 mmol, 0.05 eq.), Cs_2CO_3 (7.4 mg, 0.022 mmol, 0.2 eq.), and *m*-nitrobenzoic acid (1.9 mg, 0.011 mmol, 0.1 eq.) followed by allyl acetate (114 mg/123μL, 1.13 mmol, 10 eq.). The reaction was heated at 100 °C for 20 hr, it was then evaporated onto silica gel and purified by flash chromatography (1:9 EtOAc:Hexane) to give a colorless oil (**14**, 15 mg, 43%) and aldehyde (**16**, 16 mg, 53%).

$[\alpha]_D^{25}$ = +6.1 (c 0.4, $CHCl_3$) [lit.[2] $[\alpha]_D^{21}$ = +7.56 (c 1.0, $CHCl_3$)].

IR (thin film) 3392, 2954, 2920, 2851, 1721, 1721, 1684, 1453, 1253, 1009, 948 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.43 (ddd, *J* = 1.3, 7.6, 14.9 Hz, 1H), 5.96 (qd, *J* = 1.3, 14.4 Hz, 1H), 5.81–5.69 (m, 1H), 5.17–5.11 (m, 3H), 4.04 (t, *J* = 6.6 Hz, 1H), 2.54–2.43 (m, 1H), 2.34 – 2.30 (dt, *J* = 1.1, 6.9 Hz, 2H), 2.09–1.92 (m, 2H), 1.62 (d, *J* = 1.4, 3H), 1.57 (br s, 1H), 0.96 (d, *J* = 6.7 Hz, 3H).
Minor diastereomer visible peaks: 6.21–6.19 (m, 1H), 6.15-6.09 (m, 1H), 5.25 (d, *J* = 9.3 Hz, 1H).

^{13}C NMR (100 MHz, $CDCl_3$, DEPT) δ 145.0 (CH), 136.1 (C), 134.6 (CH), 131.5 (CH), 117.8 (CH_2), 76.6(CH), 75.40 (CH), 43.5 (CH_2), 39.9 (CH_2), 31.7 (CH), 20.5 (CH_3), 11.7 (CH_3).

HRMS (ESI+) 329.0378 calc'd for $C_{12}H_{19}IONa^+$, 329.0378 found.

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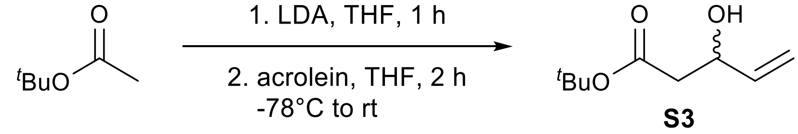
[2] Sawant, P.; Maier, M. *Synlett*, **2011**, *20*, 3002.



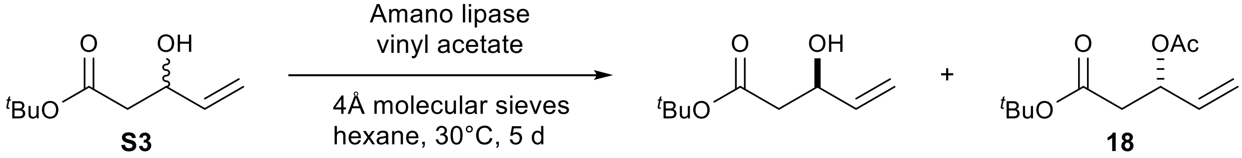
***tert*-Butyl 3-hydroxypent-4-enoate (S3)**: To a solution of lithium *N,N*-diisopropylamide (1.1 eq. prepared by adding *N,N*-diisopropylamine to the solution of *n*-butyl lithium in THF) in THF (50 mL) was added *t*-butylacetate (3.81 g, 32.8 mmol, 1 eq.) at –78 °C and it was stirred at that temperature for 1 h. After 1 h, acrolein (1.85 g, 32.9 mmol, 1 eq.) was added and reaction was stirred at –78 °C for 1 h and warmed to room temperature over 1h. the reaction was quenched with sat. NH_4Cl solution (monitored by TLC) and layers were separated. The aqueous layer was extracted with EtOAc (3 x 50 mL), combined organic layer was washed with brine, dried (over Na_2SO_4) and concentrated. The crude product (5.01 g, 88%) was used further without any purification.

IR (thin film): 3420, 2979, 2933, 1708, 1367, 1151 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$) δ 5.88 (dddd, *J* = 1.1, 5.5, 10.5, 17.2 Hz, 1H), 5.32 (ddd, *J* = 1.3, 2.6, 17.3 Hz, 1H), 5.15 (ddd, *J* = 1.3, 2.6, 10.5 Hz, 1H), 4.49 (m, 1H), 3.19 (d, *J* = 4.5 Hz, 1H), 2.52 (ddd, *J* = 1.3, 1.9, 16.3 Hz, 1H), 2.44 (ddd, *J* = 1.2, 8.3, 16.2 Hz, 1H), 1.47 (s, 9H).

^{13}C NMR (100 MHz, $CDCl_3$, DEPT) δ 171.8 (C), 138.9 (CH), 115.2 (C H_2), 81.5 (C), 69.1 (CH), 42.1 (C H_2), 28.1 (^{t}Bu).

HRMS (ESI+) 195.0997 calc'd for $C_9H_{16}O_3Na^+$, 195.0994 found.



***tert*-Butyl (*S*)-3-acetoxypent-4-enoate (18)**: To the suspension of alcohol **S3** (4.28 g, 24.87 mmol, 1 eq.) and molecular sieves (4 g) in pentane (120 mL) was added Amano lipase enzyme (2.14 g, 50 wt%) and vinyl acetate (2.3 mL, 24.87 mmol, 1 eq). The reaction was stirred at 30 °C for 5 days. It was filtered through a thin pad of silica gel wan washed with 200 mL diethyl ether. Organics were concentrated and purified by flash chromatography (1:9 EtOAC:Hexane) to provide **18** as a colorless oil (2.11 g, 40%).

$[\alpha]_D^{25}$ = –5.2 (c 1.24, $CHCl_3$); lit.[3] $[\alpha]_D^{25}$ = –5.5 (c 1.09, $CHCl_3$).

IR (thin film): 2980, 1732, 1368, 1229, 1154, 1021 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$) δ 5.83 (dddd, *J* = 1.1, 6.3, 10.5, 17.4 Hz, 1H), 5.64–5.58 (m, 1H), 5.31 (ddd, *J* = 1.2, 2.3, 17.2 Hz, 1H), 5.21 (ddd, *J* = 1.1, 2.3, 10.5 Hz, 1H), 2.60 (ddd, *J* = 1.1, 8.1, 15.3 Hz, 2H), 2.53 (ddd, *J* = 1.1, 5.8, 15.3 Hz, 2H), 2.06 (s, 3H), 1.44 (s, 9H).

^{13}C NMR (100 MHz, $CDCl_3$, DEPT) δ 169.8 (CO), 169.0 (CO), 135.2 (CH), 117.3 (CH_2), 81.1 (C), 71.1 (CH), 40.7 (CH_2), 28.0 (^{t}Bu), 21.1 (CH_3).

HRMS (ESI+) 237.1103 calc'd for $C_{11}H_{18}O_4Na^+$, 237.1103 found.

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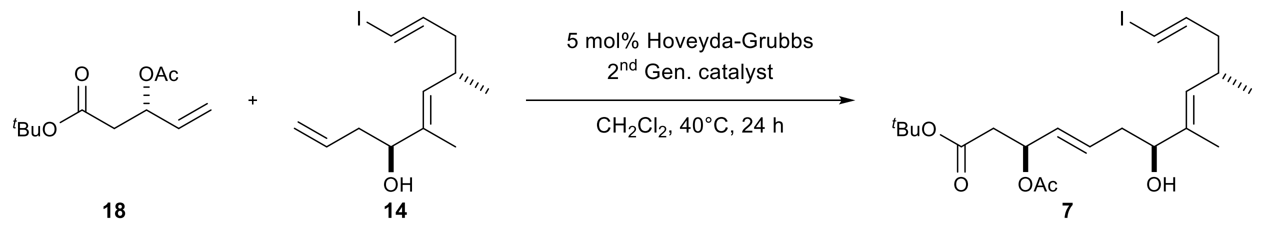
[3] Tan, C.-H.; Holmes, A. B. *Chem. Eur. J.*, **2001**, *7*, 1845.



***tert*-Butyl(3*S*,4*E*,7*S*,8*E*,10*S*,12*E*)-3-acetoxy-7-hydroxy-13-iodo-8,10-dimethyltrideca-4,8,12-trienoate (7)**: To an oven dried round bottom flask was added the compound **14** (10 mg, 0.033 mmol, 1eq.) and compound **18** (14 mg, 0.066 mmol, 2 eq.), it was evacuated and flushed with argon three times followed addition of CH_2Cl_2 (degassed for 10 mins using argon). Hoveyda–Grubbs second generation catalyst (1 mg, 0.0014 mmol, 0.005 eq.) was added to the reaction and it was flushed with argon. The reaction was heated at 40 °C for 24 hrs, TLC showed the complete consumption of the starting material, it was cooled to room temperature and ethyl vinyl ether (0.5 mL) was added to the reaction. It was stirred for 30 mins at room temperature followed by filtration through a silica plug. The filtrate was concentrated and the crude product was purified by flash chromatography (3:7 EtOAc:Hexane) to provide **7** as brownish sticky liquid (10 mg, 42%).

$[\alpha]_D^{25}$ = +1.88 (c 0.5, $CHCl_3$).

IR (thin film): 3446, 2921, 2850, 1732, 1456, 1368, 1233, 1151 cm^{-1}.

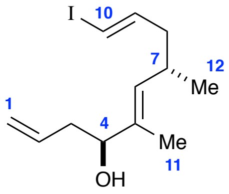
^{1}H NMR (400 MHz, $CDCl_3$) δ 6.43 (ddd, *J* = 7.2, 7.8, 14.4 Hz, 1H), 5.98 (dd, *J* = 0.8, 14.3 Hz, 1H), 5.76–5.69 (m, 1H), 5.59–5.54 (m, 2H), 5.17 (br d, *J* = 9.4 Hz, 1H), 4.01 (t, *J* = 6.4 Hz, 1H), 2.60 (dd, *J* = 6.8, 15.1 Hz, 1H), 2.55–2.44 (m, 2H), 2.28 (t, *J* = 6.8 Hz, 2H), 2.06–1.96 (m, 3H), 2.04 (s overlapped with m, 3H), 1.61 (s, 3H), 1.44 (s, 9H), 0.96 (d, *J* = 6.7 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$, DEPT) δ 169.9 (C), 169.1 (C), 144.9 (CH), 136.0 (C), 131.2 (CH), 130.3 (CH), 130.3 (CH), 81.1 (C), 76.1 (CH), 75.5 (CH), 71.0 (CH), 43.5 (CH_2), 40.9 (CH_2), 38.5 (CH_2), 31.7 (CH), 28.1 (^{t}Bu), 21.2 (CH_3), 20.4 (CH_3), 12.0 (CH_3).

HRMS (ESI+) 515.1270 calc'd for $C_{21}H_{33}IO_5Na^+$, 515.1268 found.

Comparison of NMR data for alcohol 14

Alcohol **14** was prepared by Sawant and Maier using a different synthetic route.[4] A comparison between their reported ^{1}H and ^{13}C NMR chemical shifts is given below. The carbon assignments made by Sawant and Maier are used.



14

	^{1}H NMR chemical shifts			^{13}C NMR chemical shifts	
carbon number	literature values (400 MHz)	observed values (400 MHz)		literature values (100 MHz)	observed values (100 MHz)
C1	5.08–5.17	5.11-5.17		117.7	117.79
C2	5.73	5.69-5.80		134.6	134.64
C3	2.29 & 2.31	2.32		39.9	39.93
C4	4.02	4.04		76.6	76.58
C5	--	--		136.0[a]	136.05
C6	5.08–5.17	5.11-5.17		131.5	131.52
C7	2.42–2.53	2.43-2.54		31.7	31.72
C8	1.94 & 2.04	1.92-2.09		43.5	43.51
C9	6.42	6.43		144.9	144.97
C10	5.94	5.96		75.4	75.40
C5 CH_3	1.61	1.62		20.5	20.51
C7 CH_3	0.95	0.96		11.6	11.66
C4 OH	1.61	1.57		--	--

[a] This chemical shift is not listed in the experimental section supplied by Sawant and Maier, but is clearly present in the ^{13}C NMR spectrum provided by the same authors.

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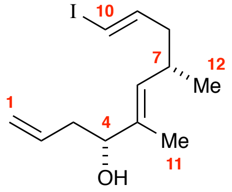
[4] Sawant, P.; Maier, M. E. *Synlett* **2011**, 3002–3004.

In an optimization reaction we also isolated compound **S4**, the C-4 epimer of alcohol **14** (shown below). The difference in the ^{1}H NMR chemical shifts are not significant while few signals in ^{13}C NMR are significant. The carbon assignments made by Sawant and Maier are used for the comparison below.

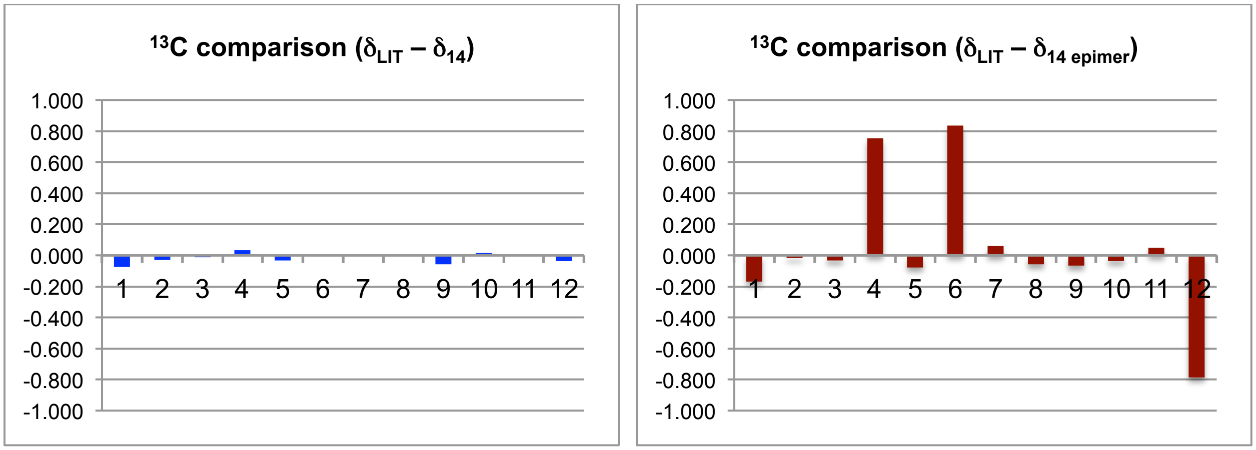


S4

	^{13}C NMR chemical shifts	
carbon number	literature values (100 MHz)	observed values (100 MHz)
C1	117.7	117.870
C2	134.6	134.617
C3	39.9	39.932
C4	76.6	75.846
C5	136.0[a]	136.077
C6	131.5	130.665
C7	31.7	31.640
C8	43.5	43.558
C9	144.9	144.967
C10	75.4	75.436
C5 CH_3	20.5	20.449
C7 CH_3	11.6	12.385
C4 OH	--	--

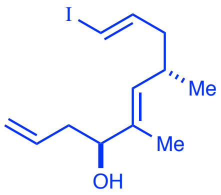
[a] This chemical shift is not listed in the experimental section supplied by Sawant and Maier, but is clearly present in the ^{13}C NMR spectrum provided by the same authors.

Graphical comparision of ^{13}C NMR data for the two diastereomers

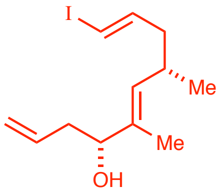


^{1}H NMR Comparision of compound 14 and S4

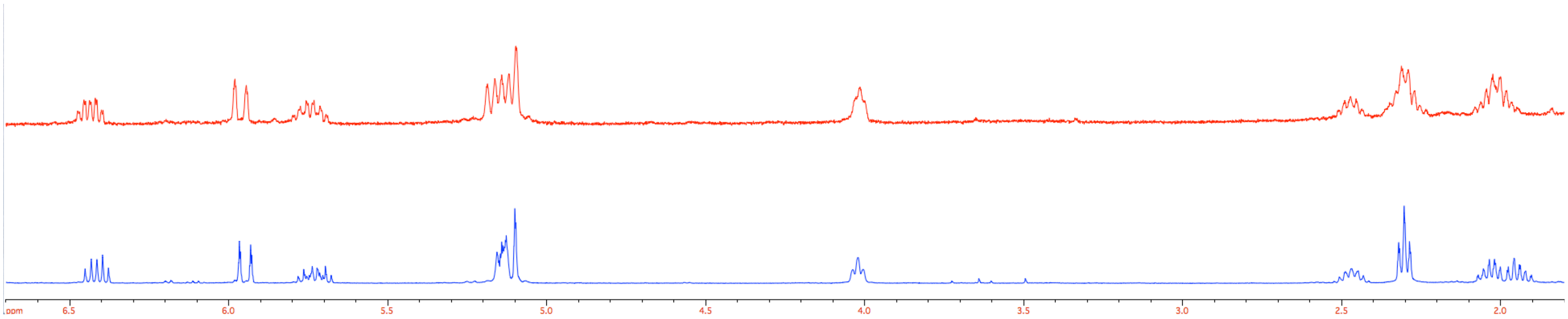
Comparision of the ^{1}H NMR spectra for compound **14** (blue) and its diastereomer **S4** (red).



14



S4



Comparision of Krische allylation with (*S*)- and (*R*)-Cl,MeO-BIPHEP

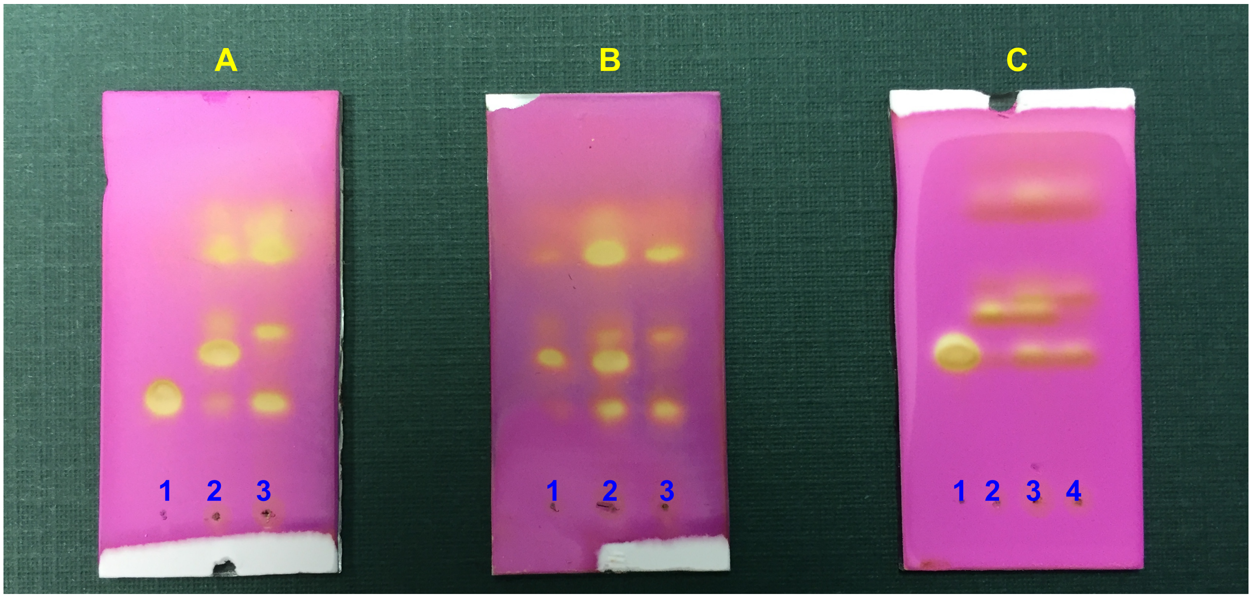


Plate A (1:9 EtOAc:Hexane, developed two times)
Lane 1: Alcohol **13**
Lane 2: Aliquot of Krische reaction using (*S*)-Cl-MeO-BIPHEP as a ligand
Lane 3: Aliquot of Krische reaction using (*R*)-Cl-MeO-BIPHEP as a ligand

Plate B (1:9 EtOAc:Hexane, developed two times)
Lane 1: Aliquot of Krische reaction using (*S*)-Cl-MeO-BIPHEP as a ligand
Lane 2: Co-spot of aliquots from (*S*)-Cl-MeO-BIPHEP and (*R*)-Cl-MeO-BIPHEP reactions
Lane 3: Aliquot of Krische reaction using (*R*)-Cl-MeO-BIPHEP as a ligand

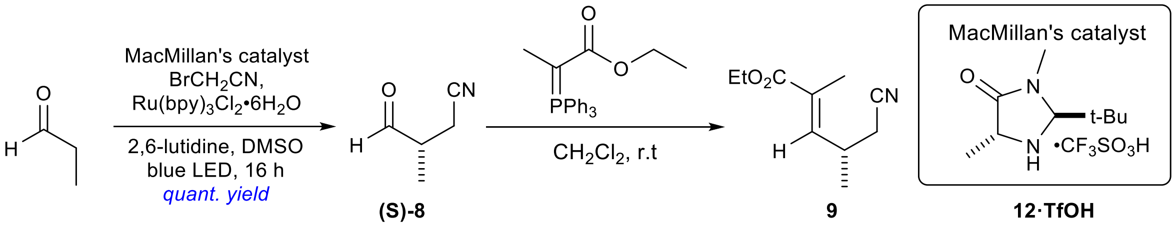
Plate C (1:9 Acetone:Hexane, developed once, 1:19 EtOAc:Hexane, developed three times)
Lane 1: Alcohol 1**3**
Lane 2: Aliquot of Krische reaction using (*S*)-Cl-MeO-BIPHEP as a ligand
Lane 3: Co-spot of aliquots from (*S*)-Cl-MeO-BIPHEP and (*R*)-Cl-MeO-BIPHEP reactions
Lane 4: Aliquot of Krische reaction using (*R*)-Cl-MeO-BIPHEP as a ligand

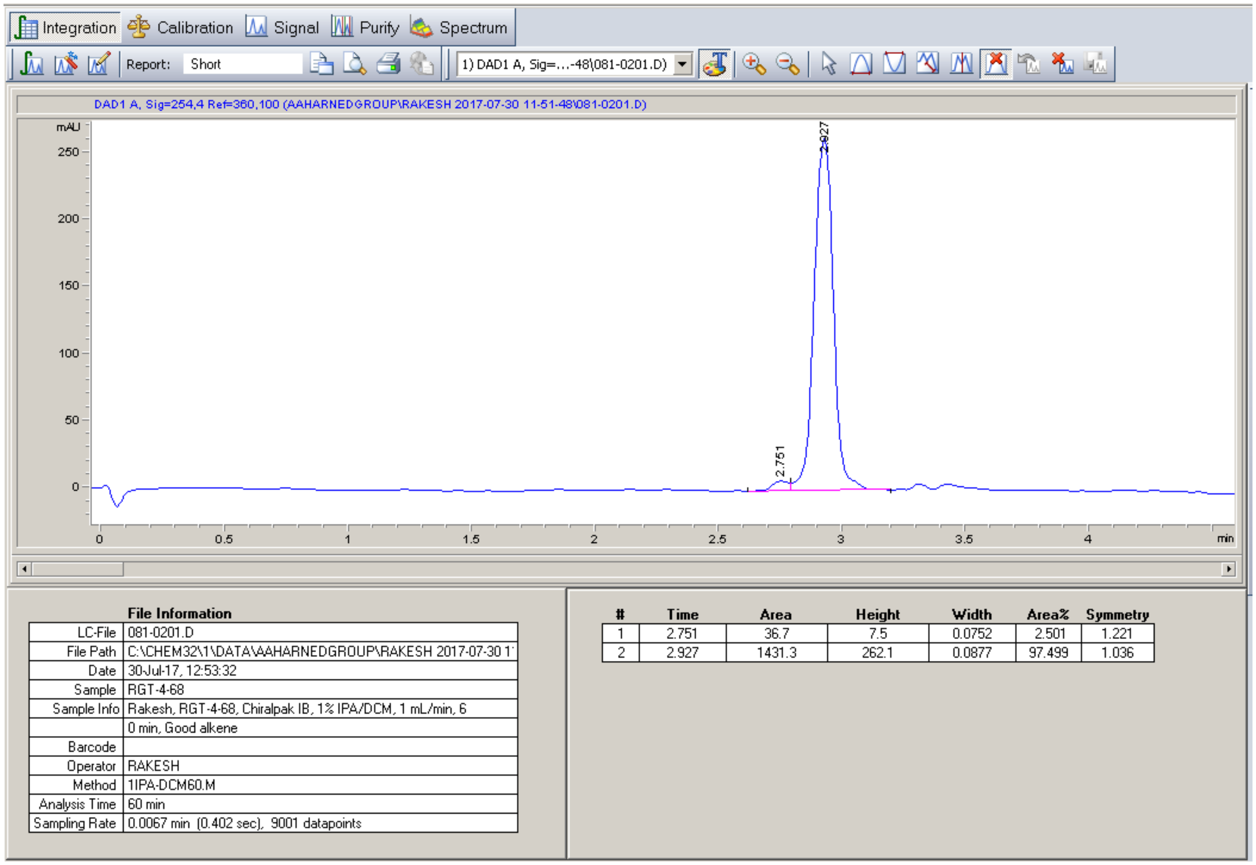
Observations –

1) Reactions have not achieved complete conversion to desired products, unreacted alcohol **13** can be seen on the lane 2 and 3 (plate **A**), lanes 1, 2 and 3 (plate **B**), lanes 2, 3 and 4 (plate **C**).
2) From the lane 2 of plate **A** and **B**, lane 3 of plate **C**, it is clear that the *syn* diastereomer did not form in the allylation reaction when (S)-Cl-MeO-BIPHEP was used as a ligand. Two distinctly separate spots can be seen in the lane 2 of plate B and lane 3 of plate C.

HPLC chromatograms

Ethyl (*S*,*E*)-5-cyano-2,4-dimethylpent-2-enoate (9)





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Barcode	
Operator	RAKESH
Method	1IPA-DCM60.M
Analysis Time	60 min
Sampling Rate	0.0067 min (0.402 sec), 9001 datapoints

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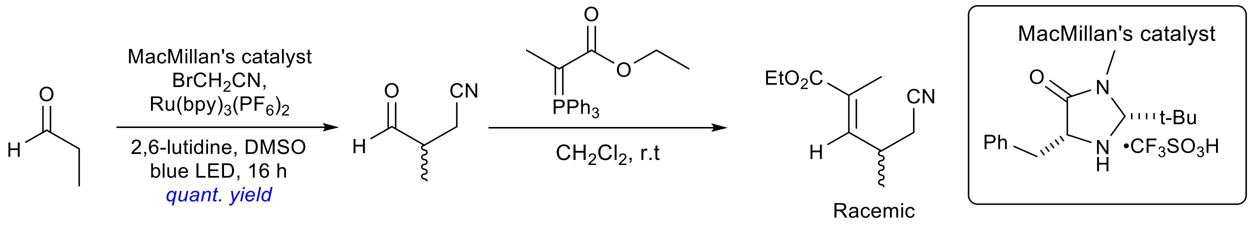
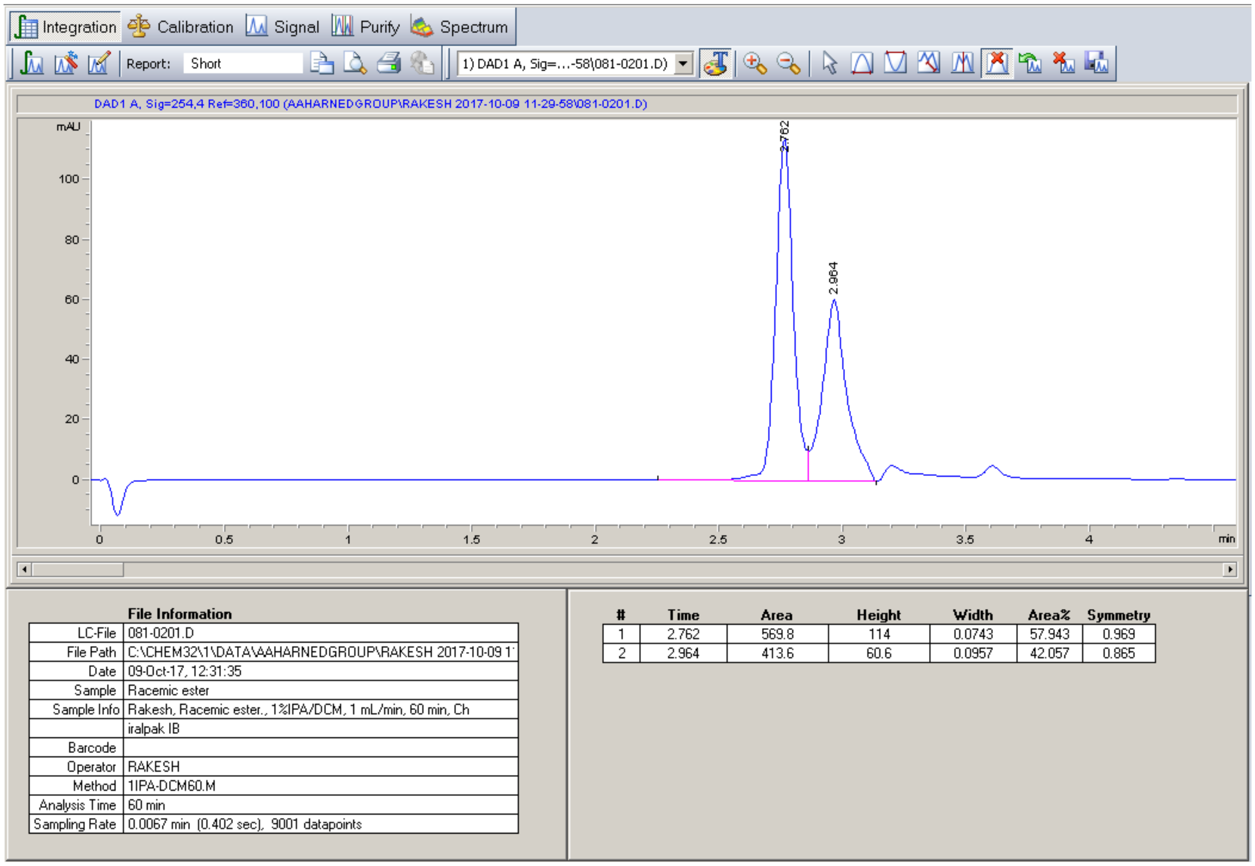
Ethyl (*S*,*E*)-5-cyano-2,4-dimethylpent-2-enoate (racemic)





DAD1 A, Sig=254,4 Ref=360,100 (AAHARNEDGROUP\RAKESH 2017-10-09 11-29-58\081-0201.D)

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	iralpak IB
Barcode	
Operator	RAKESH
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Analysis Time	60 min
Sampling Rate	0.0067 min (0.402 sec), 9001 datapoints

#	Time	Area	Height	Width	Area%	Symmetry
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