Supporting Information for:

Kinetic Resolution of Racemic Allylic Alcohols via Iridium-Catalyzed Asymmetric Hydrogenation: Scope, Synthetic Applications and Insight into the Origin of Selectivity.

Haibo Wu, a Cristiana Margarita, a Jira Jongcharoenkamol, a Mark D. Nolan, a Thishana Singh b and Pher G. Andersson*a,b

[a] Department of Organic Chemistry, Stockholm University, 106 91, Stockholm, Sweden.

[b] School of Chemistry and Physics, University of Kwazulu-Natal, Private Bag X54001, Durban, 4000, South Africa

(*pher.andersson@su.se)

Contents

1. General methods ................................................................. S2

2. General procedure for the synthesis of racemic allylic alcohols ..................... S3

3. General procedure for kinetic resolution via asymmetric hydrogenation .......... S9

4. Double stereodifferentiation and synthesis of ketone 3 ............................. S19

5. Asymmetric formal synthesis of inthomycin A and B .................................. S21

6. DFT calculation ........................................................................ S26

7. SFC and GC Chromatograms ................................................................ S38

8. $^1$H, $^{13}$C and $^{19}$F NMR spectroscopic data .............................................. S61

9. References ............................................................................. S106
1. General methods

All reactions were conducted under nitrogen atmosphere using magnetic stirring.

CH\textsubscript{2}Cl\textsubscript{2} was freshly distilled using CaH\textsubscript{2} under nitrogen atmosphere. THF was freshly distilled using sodium-benzophenone under nitrogen.

All reagents were used as supplied commercially without further purification. Chromatographic separations were performed on Kiesel gel 60 H silica gel (particle size: 0.063-0.100 mm) or Brockmann I, activated, basic Al\textsubscript{2}O\textsubscript{3} (particle size: ~150 mesh). Thin layer chromatography (TLC) was performed on aluminium plates coated with Kieselgel 60 (0.20 mm, UV254) and visualized under ultraviolet light (\(\nu = 254\) nm), or by staining with ethanolic phosphomolybdic acid and heating.

\(^1\)H NMR spectra were recorded on a Bruker 400 MHz or 500 MHz at 400/500 MHz in CDCl\textsubscript{3} and referenced internally to the residual CDCl\textsubscript{3} peak (7.26 ppm). \(^{13}\)C NMR spectra were recorded at 100/125 MHz in CDCl\textsubscript{3} and referenced to the central peak of CDCl\textsubscript{3} (77.0 ppm). Chemical shifts are reported in ppm (\(\delta\) scale).

Enantiomeric excesses were determined by either using SFC on chiral stationary phases with a diode array detector at 210 nm, 230 nm and 254 nm or using GC on chiral stationary phases with a MS detector. (Refer to the individual compounds for specific chromatographic details.) Racemic compounds were used for comparison.

HRMS data were obtained using a Bruker MicroTOF-Q II instrument operation at ambient temperature.

Optical rotations were recorded on an Autopol IV polarimeter from Rudolph Research Analytical, equipped with a sodium lamp (589 nm) and a 10 cm cell.
2. General procedure for the synthesis of racemic allylic alcohols

**General Procedure A:** The corresponding Grignard reagent (1.5 eq.) was slowly added to a solution of α-methyl-cinnamaldehyde (1.0 eq.) in dry THF at -78 °C. The reaction was stirred and monitored by TLC. Upon completion, the reaction was quenched with a saturated aqueous NH₄Cl solution, extracted with Et₂O. The combined organic phase was washed with brine and dried over Na₂SO₄. The solvent was evaporated under reduced pressure to afford the crude product, which was then purified by column chromatography on silica gel (Pentane/Et₂O 80/20) to give the corresponding product in good to excellent yield.

![Chemical structure](image)

### Table 1: Substrates and Products

| Substrate | R₁ | R₂ | R₃ | R₄ | Ref. |
|-----------|----|----|----|----|------|
| (±)-1a    | Me | Me | H  | Ph | (1)  |
| (±)-1b    | Et | Me | H  | Ph | (2)  |
| (±)-1c    | n-Bu| Me | H  | Ph | (3)  |
| (±)-1d    | i-Pr| Me | H  | Ph | (3)  |
| (±)-1e    | t-Bu| Me | H  | Ph | (4)  |
| (±)-1f    | Ph | Me | H  | Ph | New  |
| (±)-1g    | Cp | Me | H  | Ph | (3)  |
| (±)-1h    | Cy | Me | H  | Ph | (5)  |
| (±)-1i    | Bn | Me | H  | Ph | (2)  |
| (±)-1k    | CH₃TMS | Me | H  | Ph | (5)  |
| (±)-1af   | i-Pr| Et | H  | Ph | New  |
| (±)-1ag   | Et | H  | Me | Ph | (19) |
| (±)-1ah   | Cy | H  | Me | Ph | New  |
| (±)-1ai   | i-Pr| H  | Me | Me | (20) |
| (±)-1aj   | t-Bu| H  | Me | Me | (20) |
| (±)-1ak   | Cy | H  | Me | Cy | New  |

**1H NMR (400 MHz, CDCl₃) δ 7.38 – 7.18 (m, 1H), 6.45 (s, 5H), 3.90 (d, J = 8.8 Hz, 1H), 2.16 (dd, J = 16.2, 8.3 Hz, 1H), 1.93 – 1.82 (m, 4H), 1.74 – 1.42 (m, 7H), 1.30 – 1.17 (m, 1H).**

**13C NMR (101 MHz, CDCl₃) δ 140.23, 137.74, 129.14, 128.24, 126.95, 126.57, 83.54, 43.79, 29.60 (d, J = 30.4 Hz), 25.76 (d, J = 11.0 Hz), 13.11.**

**HRMS-ESI; m/z [M+Na⁺] = 239.1401, calcd. For C₁₅H₂₀NaO: 239.1406.**

### Additional Compounds

**/(E)-1-cyclopentyl-2-methyl-3-phenylprop-2-en-1-one.**

Colorless oil.

**1H NMR (400 MHz, CDCl₃) δ 7.38 – 7.18 (m, 1H), 6.45 (s, 5H), 3.90 (d, J = 8.8 Hz, 1H), 2.16 (dd, J = 16.2, 8.3 Hz, 1H), 1.93 – 1.82 (m, 4H), 1.74 – 1.42 (m, 7H), 1.30 – 1.17 (m, 1H).**

**13C NMR (101 MHz, CDCl₃) δ 140.23, 137.74, 129.14, 128.24, 126.95, 126.57, 83.54, 43.79, 29.60 (d, J = 30.4 Hz), 25.76 (d, J = 11.0 Hz), 13.11.**

**HRMS-ESI; m/z [M+Na⁺] = 239.1401, calcd. For C₁₅H₂₀NaO: 239.1406.**

**/(E)-4-benzylidene-2-methylhexan-3-ol.**

Colorless oil.

**1H NMR (400 MHz, CDCl₃) δ 7.36 – 7.27 (m, 4H), 7.22 (ddd, J = 6.4, 3.1, 1.5 Hz, 1H), 6.48 (s, 1H), 3.91 (d, J = 6.4 Hz, 1H), 2.44 – 2.14 (m, 2H), 1.93 (dq, J = 13.4, 6.7 Hz, 1H), 1.57 (s, 1H), 1.12 (t, J = 7.6 Hz, 3H), 1.01 (d, J = 6.6 Hz, 3H), 0.96 (d, J = 6.8 Hz, 3H).**
$^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 146.02, 137.88, 128.77, 128.35, 126.55, 126.26, 81.99, 31.95, 21.73, 20.11, 17.74, 14.12. HRMS-ESI; $m/z$ [M+Na$^+$] = 227.3025, calcd. For C$_{16}$H$_{20}$NaO: 227.3027.

(±)-1ah

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.45 – 7.39 (m, 2H), 7.37 – 7.30 (m, 2H), 7.29 – 7.23 (m, 1H), 5.78 (dd, $J = 9.0$, 1.3 Hz, 1H), 4.27 (dd, $J = 8.9$, 7.1 Hz, 1H), 2.10 (s, 3H), 2.03 – 1.95 (m, 1H), 1.83 – 1.65 (m, 3H), 1.56 – 1.44 (m, 2H), 1.34 – 1.13 (m, 3H), 1.12 – 0.95 (m, 2H).

$^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 143.30, 137.77, 129.76, 128.38, 127.35, 125.98, 73.39, 44.66, 29.06, 28.78, 26.70, 26.30, 26.17, 16.68. HRMS-ESI; $m/z$ [M+Na$^+$] = 253.1563, calcd. For C$_{16}$H$_{22}$NaO: 253.1567.

(E)-1-cyclohexyl-3-phenylbut-2-en-1-ol
Colorless oil.

(±)-1ak

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 5.15 (d, $J = 9.0$ Hz, 1H), 4.07 (dd, $J = 8.8$, 7.4 Hz, 1H), 1.97 – 1.88 (m, 1H), 1.88 – 1.64 (m, 9H), 1.63 (s, 3H), 1.40 – 1.07 (m, 11H), 1.03 – 0.82 (m, 2H). $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 144.40, 124.69, 72.91, 47.55, 44.55, 32.07, 31.99, 29.16, 28.71, 26.82, 26.75, 26.48, 26.34, 26.20, 15.31. HRMS-ESI; $m/z$ [M+Na$^+$] = 259.2032, calcd. For C$_{16}$H$_{28}$NaO: 259.2036.
(±)-1m  p-OMe  New
(±)-1n  p-F  New
(±)-1o  p-Cl  New
(±)-1p  p-Br  New
(±)-1q  m-Me  New
(±)-1r  p-NO₂  New
(±)-1s  3-thiophene  New
(±)-1t  2-thiophene  New

(E)-2-methyl-1-(p-tolyl)pent-1-en-3-ol.
Colorless oil.

\[ \text{H NMR (400 MHz, CDCl}_3 \text{)} \delta 7.22 - 7.11 \text{ (m, 4H), 6.45 (s, 1H), } \]
\[ 4.09 \text{ (t, } J = 6.2 \text{ Hz, 1H), 2.35 (s, 3H), 1.86 (d, } J = 1.4 \text{ Hz, 3H), 1.73} \]
\[ - 1.62 \text{ (m, 2H), 1.59 (d, } J = 3.4 \text{ Hz, 1H), 0.94 (t, } J = 7.4 \text{ Hz, 3H).} \]

\[ 1^\text{C NMR (101 MHz, CDCl}_3 \text{)} \delta 139.41, 136.24, 134.84, 129.03, \]
\[ 128.96, 126.08, 79.83, 28.08, 21.30, 13.21, 10.23. \text{ HRMS-ESI; } m/z [M+Na] = 213.1244, \]
\[ \text{calcd. For C}_{13}H_{18}NaO: 213.1250.} \]

(E)-1-(4-methoxyphenyl)-2-methylpent-1-en-3-ol.
Colorless oil.

\[ \text{H NMR (400 MHz, CDCl}_3 \text{)} \delta 7.75 - 7.19 \text{ (m, 2H), 6.91 - 6.84} \]
\[ (m, 2H), 6.42 \text{ (s, 1H), 4.08 (t, } J = 6.6 \text{, 2.9 Hz, 1H), 3.81 (s, 3H), } \]
\[ 1.85 \text{ (d, } J = 1.3 \text{ Hz, 3H), 1.73 - 1.61 \text{ (m, 2H), 1.58 (d, } J = 3.6} \]
\[ \text{Hz, 1H), 0.93 (t, } J = 7.4 \text{ Hz, 3H).} 1^\text{C NMR (101 MHz, CDCl}_3 \text{)} \delta \]
\[ 158.27, 138.52, 130.33, 130.29, 125.72, 113.70, 79.91, 55.40, 28.09, 13.16, 10.27. \text{HRMS-ESI; } \]
\[ m/z [M+Na] = 229.1194, \text{calcd. For C}_{13}H_{18}NaO_2: 229.1199.} \]

(E)-1-(4-bromophenyl)-2-methylpent-1-en-3-ol.
Colorless oil.

\[ \text{H NMR (400 MHz, CDCl}_3 \text{)} \delta 7.48 - 7.40 \text{ (m, 2H), 7.19 - 7.09 (m,} \]
\[ 2H), 6.42 \text{ (s, 1H), 4.08 (dd, } J = 6.4 \text{, 4.9 Hz, 1H), 1.83 (d, } J = 1.4 \]
\[ \text{Hz, 3H), 1.73 - 1.56 \text{ (m, 3H), 0.94 (t, } J = 7.4 \text{ Hz, 3H).} 1^\text{C NMR (101 MHz, CDCl}_3 \text{)} \delta} \]
\[ 141.14, 136.66, 131.36, 130.72, 124.87, 120.37, 79.44, 28.12, 13.38, 10.18. \text{HRMS-ESI; } m/z [M+Na] = \]
\[ 277.0200, \text{calcd. For C}_{13}H_{18}BrNaO: 277.0198.} \]

(E)-1-(4-chlorophenyl)-2-methylpent-1-en-3-ol.
Colorless oil.

\[ \text{H NMR (400 MHz, CDCl}_3 \text{)} \delta 7.32 - 7.27 \text{ (m, 2H), 7.23 - 7.17 (m,} \]
\[ 2H), 6.44 \text{ (s, 1H), 4.09 (t, } J = 6.1 \text{ Hz, 1H), 1.82 (t, } J = 5.4 \text{ Hz, 3H), } \]
\[ 1.71 - 1.56 \text{ (m, 3H), 0.94 (t, } J = 7.4 \text{ Hz, 3H).} 1^\text{C NMR (101 MHz, CDCl}_3 \text{)} \delta} \]
\[ 141.00, 136.20, 132.24, 130.38, 128.41, 124.86, 79.46, 28.13, 13.35, 10.19. \text{HRMS-ESI; } m/z [M+Na] = \]
\[ 233.0713, \text{calcd. For C}_{13}H_{18}ClNaO: 233.0704.} \]

(E)-1-(4-fluorophenyl)-2-methylpent-1-en-3-ol.
Colorless oil.

\[ \text{H NMR (400 MHz, CDCl}_3 \text{)} \delta 7.25 - 7.20 \text{ (m, 2H), 7.06 - 6.97 (m,} \]
\[ 2H), 6.44 \text{ (s, 1H), 4.13 - 4.04 (m, 1H), 1.83 (d, } J = 1.3 \text{ Hz, 3H), } \]
\[ 1.72 - 1.57 \text{ (m, 3H), 0.94 (t, } J = 7.4 \text{ Hz, 3H).} 1^\text{F NMR (377 MHz, CDCl}_3 \text{)} \delta} \]
\[ -115.86. 1^\text{C NMR (101 MHz, CDCl}_3 \text{)} \delta 161.52 \text{ (d, } J = 245.8 \text{ Hz), 140.13, 133.75 (d, } J = 3.4 \text{ Hz, 133.75 (d, } J = 3.4 \text{ Hz, 130.62 (d, } J = 7.8 \text{ Hz,} \]
\[ 125.01, 115.12 \text{ (d, } J = 21.3 \text{ Hz), 79.55, 28.12, 13.20, 10.21. \text{HRMS-ESI; } m/z [M+Na] =} \]
\[ 217.1010, \text{calcd. For C}_{13}H_{18}FNaO: 217.0999.} \]
(E)-2-methyl-1-(m-tolyl)pent-1-en-3-ol.
Colorless oil.
$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.25 – 7.20 (m, 1H), 7.12 – 7.01 (m, 3H), 6.46 (s, 1H), 4.10 (td, $J = 6.6, 2.9$ Hz, 1H), 2.36 (s, 3H), 1.86 (d, $J = 1.4$ Hz, 3H), 1.72 – 1.63 (m, 2H), 1.59 (d, $J = 3.3$ Hz, 1H), 0.95 (t, $J = 7.4$ Hz, 3H). $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 139.99, 137.78, 137.70, 129.87, 128.15, 127.33, 126.24, 126.16, 126.16, 79.76, 28.08, 21.60, 13.24, 10.23. HRMS-ESI; $m/z$ [M+Na$^+$] = 213.1240, calcd. For C$_{13}$H$_{18}$NaO: 213.1250.

(E)-2-methyl-1-(4-nitrophenyl)pent-1-en-3-ol.
Pale yellow oil.
$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.21 – 8.14 (m, 2H), 7.42 (dd, $J = 8.9, 2.0$ Hz, 2H), 6.56 (s, 1H), 4.14 (dd, $J = 9.7, 6.3$ Hz, 1H), 1.89 (d, $J = 1.4$ Hz, 3H), 1.78 – 1.60 (m, 3H), 0.97 (t, $J = 7.4$ Hz, 3H). $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 146.22, 144.70, 144.65, 129.70, 123.94, 123.64, 79.01, 28.26, 13.98, 10.11. HRMS-ESI; $m/z$ [M+Na$^+$] = 244.0927, calcd. For C$_{12}$H$_{15}$NO$_3$: 244.0950.

(E)-2-methyl-1-(p-tolyl)pent-1-en-3-ol.
Colorless oil.
$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.27 – 7.25 (m, 1H), 7.05 – 6.99 (m, 2H), 6.64 (s, 1H), 4.10 (t, $J = 6.6$ Hz, 1H), 1.97 (d, $J = 1.2$ Hz, 3H), 1.70 – 1.60 (m, 2H), 1.58 (d, $J = 7.4$ Hz, 1H), 0.92 (t, $J = 7.4$ Hz, 3H). $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 140.86, 138.53, 127.20, 126.96, 125.06, 119.33, 79.65, 28.19, 14.10, 10.21. HRMS-ESI; $m/z$ [M+Na$^+$] = 205.0649, calcd. For C$_{10}$H$_{14}$NaO: 205.0658.

(E)-2-methyl-1-(thiophen-3-yl)pent-1-en-3-ol.
Colorless oil.
$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.29 (dd, $J = 5.0, 2.9$ Hz, 1H), 7.17 (d, $J = 2.8$ Hz, 1H), 7.11 (dd, $J = 5.0, 1.2$ Hz, 1H), 6.45 (s, 1H), 4.08 (td, $J = 6.6, 3.3$ Hz, 1H), 1.90 (d, $J = 1.3$ Hz, 3H), 1.70 – 1.61 (m, 2H), 1.58 (br, 1H), 0.96 – 0.89 (m, 3H). $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 139.40, 138.78, 128.94, 124.97, 122.76, 120.39, 79.73, 28.10, 13.78, 10.23. HRMS-ESI; $m/z$ [M+Na$^+$] = 205.0656, calcd. For C$_{10}$H$_{14}$NaO: 205.0658.

General Procedure C: To a dried round-bottomed flask was added CH$_2$Cl$_2$ (5 mL), enolate precursor (1.00 mmol, 1 equiv), $i$-Pr$_2$NEt (261 μL, 1.50 mmol, 1.5 equiv), aldehyde (1.40 mmol, 1.4 equiv), and TMSOTf (217 μL, 1.20 mmol, 1.2 equiv) at 0 °C. The reaction was allowed to warm to room temperature and stirred for 24 h, then the mixture was filtered directly through a plug of silica gel (2.0 cm x 5.0 cm) and eluted with Et$_2$O. The eluent was concentrated in vacuo and the yellow residue analyzed by $^1$H NMR spectroscopy to determine conversion. The unpurified mixture was dissolved in THF (6 mL) and treated with 1.0 N HCl (2 mL). After stirring 1 h, the mixture was diluted with Et$_2$O (20 mL) and water (20 mL). The layers were separated and the organic layer was washed sequentially with saturated NaHCO$_3$ (20 mL) and brine (20 mL). The organic layer was dried over Na$_2$SO$_4$ or MgSO$_4$, then filtered and concentrated in vacuo. Flash chromatography (5-20% EtOAc in pentane) afforded the pure product.
(±)-ethyl 3-hydroxy-4-methyl-5-phenylpent-4-enoate.

Colorless oil. 

$^1$H NMR (400 MHz, CDCl$_3$) δ 7.36 – 7.30 (m, 2H), 7.29 – 7.19 (m, 3H), 6.60 (s, 1H), 4.61 (td, $J = 6.0, 3.7$ Hz, 1H), 4.20 (q, $J = 7.1$ Hz, 2H), 3.02 – 2.94 (m, 1H), 2.69 – 2.61 (m, 2H), 1.89 (d, $J = 1.3$ Hz, 3H), 1.29 (t, $J = 7.1$ Hz, 3H). 

$^{13}$C NMR (101 MHz, CDCl$_3$) δ 172.72, 138.26, 137.46, 129.12, 128.26, 126.72, 126.15, 73.71, 61.03, 40.44, 14.36, 13.99. 

HRMS-ESI; m/z [M+Na$^+$] = 257.1149, calcd. For C$_{14}$H$_{18}$NaO$_3$: 257.1148.

General Procedure D: The Grignard reagent (1.5 mmol) was added to a suspension of cerium chloride anhydrous (1.5 mmol) in THF. The mixture was stirred at room temperature for 1 h and cooled to 0 °C. The carbonyl compound (1 mmol) was added with vigorous stirring. After 30 min the reaction mixture was worked up by 10% aqueous AcOH (10 mL). The product was extracted into Et$_2$O, and the combined extracts were washed with brine, NaHCO$_3$ solution and brine and dried with MgSO$_4$. The solvent was evaporated and the residue was purified by column chromatography to give the addition product.

(E)-3-methyl-2,4-diphenylbut-3-en-2-ol.

Colorless oil.

$^1$H NMR (400 MHz, CDCl$_3$) δ 7.54 – 7.47 (m, 2H), 7.39 – 7.20 (m, 8H), 6.86 (s, 1H), 1.95 (d, $J = 1.5$ Hz, 1H), 1.81 (s, 3H), 1.72 (d, $J = 1.0$ Hz, 3H). 

$^{13}$C NMR (101 MHz, CDCl$_3$) δ 146.29, 143.05, 138.17, 129.24, 128.39, 128.23, 127.15, 126.54, 125.62, 124.54, 28.78, 15.15. 

HRMS-ESI; m/z [M+Na$^+$] = 261.1257, calcd. For C$_{17}$H$_{18}$NaO: 261.1250.

General Procedure E: The corresponding Grignard reagent (1.5 eq.) was slowly added to a solution of cyclohex-1-ene carbaldheyde or 5,6-dihydro-2H-pyran-3-carbaldehyde (1.0 eq.) in dry THF at -78 °C. The reaction was stirred and monitored by TLC. Upon completion, the reaction was quenched with a saturated aqueous NH$_4$Cl solution, extracted with Et$_2$O. The combined organic phase was washed with
brine and dried over \( \text{Na}_2\text{SO}_4 \). The solvent was evaporated under reduced pressure to afford the crude product, which was then purified by column chromatography on silica gel (Pentane/Et\(_2\)O 80/20) to give the corresponding product in good to excellent yield.

\[
\begin{align*}
\text{Y} = \text{CH}_2 \text{ or } \text{O}. \\
\end{align*}
\]

(\(\pm\)-1aa

| Substrate   | Y  | R   | Ref. |
|-------------|----|-----|------|
| (\(\pm\))-1aa | O  | \(\text{-i-Bu}\) | New  |
| (\(\pm\))-1ab | O  | \(\text{-n-Bu}\) | New  |
| (\(\pm\))-1ac | \(\text{CH}_2\) | Et   | (2)   |
| (\(\pm\))-1ad | \(\text{CH}_2\) | \(\text{-n-Bu}\) | (16)  |
| (\(\pm\))-1ae | \(\text{CH}_2\) | Cy   | (9)   |

1-(5,6-dihydro-2H-pyran-3-yl)-3-methylbutan-1-ol.

Colorless oil.

\(^1\text{H NMR (400 MHz, CDCl}_3\) \(\delta\) 5.79 (s, 1H), 4.26 – 4.05 (m, 3H), 3.80 (dt, \(J = 10.8, 5.3\) Hz, 1H), 3.69 (dd, \(J = 11.3, 6.8, 4.9\) Hz, 1H), 2.26 – 2.04 (m, 2H), 1.78 – 1.62 (m, 1H), 1.53 – 1.41 (m, 2H), 1.32 (ddd, \(J = 13.6, 7.8, 5.6\) Hz, 1H), 0.92 (d, \(J = 6.6\) Hz, 6H). \(^13\text{C NMR (101 MHz, CDCl}_3\) \(\delta\) 140.21, 119.99, 72.51, 64.82, 64.56, 44.38, 25.13, 24.89, 23.24, 22.38. HRMS-ESI; \(m/z [M+Na]^+ = 193.1201\), calcd. For \(\text{C}_{10}\text{H}_{18}\text{NaO}_2\): 193.1204.

1-(5,6-dihydro-2H-pyran-3-yl)pentan-1-ol.

Colorless oil.

\(^1\text{H NMR (400 MHz, CDCl}_3\) \(\delta\) 5.78 (s, 1H), 4.25 – 4.06 (m, 2H), 4.00 (dd, \(J = 10.1, 6.7\) Hz, 1H), 3.79 (dt, \(J = 10.8, 5.3\) Hz, 1H), 3.70 (ddd, \(J = 11.3, 6.6, 5.0\) Hz, 1H), 2.26 – 2.05 (m, 2H), 1.57 – 1.45 (m, 3H), 1.41 – 1.19 (m, 4H), 0.90 (t, \(J = 7.1\) Hz, 3H). \(^13\text{C NMR (101 MHz, CDCl}_3\) \(\delta\) 139.88, 120.07, 74.33, 64.87, 64.57, 34.99, 28.08, 25.11, 22.72, 14.17. HRMS-ESI; \(m/z [M+Na]^+ = 193.1197\), calcd. For \(\text{C}_{10}\text{H}_{18}\text{NaO}_2\): 193.1204.

Other Substrates:

1-(2H-chromen-3-yl)ethanol (\(\pm\)) 1z was prepared according to a reported procedure and has been previously characterized.\(^{11}\)
3. General procedure for kinetic resolution via asymmetric hydrogenation

A glass vial was charged with 0.2 mmol substrate, K₂CO₃ and catalyst, 1 mL dry toluene was added. The vial was placed in a hydrogenation apparatus and flushed 3 times with nitrogen. The reactor was then purged 8 times using hydrogen, before filling to the required pressure. The reaction was stirred at room temperature for the required time before the hydrogen pressure was released and the solvent was removed under vacuum. Conversions were determined by ¹H NMR spectroscopy of crude product. The crude product was then purified by column chromatography on silica gel (Pentane/Acetone 25/1 to 15/1) to yield the corresponding resolved starting material and hydrogenated product. For substrates 1b, 1c, 1d, 1f, 1g, 1h, 1i, 1j, 1l, 1m, 1o, 1p, 1q, 1r, 1s, 1t, 1v, 1w, 1x, 1y, 1ac, 1ad, 1ae, 1af, 1ag, 1ah, 1ai, 1aj, 1ak, the resolved starting materials were isolated completely, and the purity of recovered starting material were confirmed by ¹H NMR (spectra attached below). The pure resolved starting materials were used for the determinations of optical rotation and ee values. For substrates 1e, 1u, 1z, 1aa, 1ab, the separations were not complete. The yields are based on the ¹H NMR ratio of the amount of recovered starting material and hydrogenated product, and the mixtures were used for determinations of ee values. Few pure fractions were collected to obtain enantioenriched samples for the measurements of optical rotation. For substrate 1k, the crude sample was passed through a plug of silica gel (Pentane/Diethyl ether 1/1), and then solvent was removed to obtain a mixture of resolved starting material and hydrogenated product, the mixture was used for the determination of ee value, no measurement of optical rotation was performed due to instability of the compound during purification. The ee values were determined using GC or SFC on chiral stationary phase.

| Table of Hydrogenation conditions |
|----------------------------------|
| **Allylic alcohol**              | **Hydrogenation conditions** | **Conversion** |
|                                  | Cat. (mol %) | K₂CO₃ (mol %) | H₂ (Bar) | Time (min) |             |
| (±)-1b                           | 0.2          | 10            | 1        | 10         | 55%         |
| (±)-1c                           | 0.5          | 10            | 1        | 20         | 57%         |
| (±)-1d                           | 1.0          | 10            | 3        | 60         | 54%         |
| Compound   | Concentration | Time | Reaction Time | Reaction Yield |
|------------|---------------|------|---------------|----------------|
| (±)-1e     | 1.0           | 10   | 3             | 60             | 52%            |
| (±)-1g     | 1.0           | 10   | 3             | 60             | 49%            |
| (±)-1h     | 1.0           | 10   | 3             | 60             | 53%            |
| (±)-1i     | 0.5           | 10   | 3             | 60             | 52%            |
| (±)-1f     | 0.2           | 20   | 1             | 15             | 61%            |
| (±)-1k     | 1.0           | 10   | 3             | 60             | 49%            |
| (±)-1l     | 0.2           | 10   | 1             | 10             | 55%            |
| (±)-1m     | 0.2           | 10   | 1             | 10             | 55%            |
| (-)-1p | 0.2 | 10 | 1 | 10 | 54% |
|---------|-----|----|---|----|-----|
| (-)-1o | 0.2 | 10 | 1 | 10 | 53% |
| (-)-1n | 0.2 | 10 | 1 | 10 | 57% |
| (-)-1q | 0.2 | 10 | 1 | 10 | 54% |
| (-)-1r | 0.2 | 10 | 1 | 10 | 54% |
| (-)-1t | 0.2 | 10 | 1 | 10 | 52% |
| (-)-1s | 0.2 | 10 | 1 | 10 | 54% |
| (-)-1v | 1.0 | 10 | 3 | 60 | 56% |
| (-)-1w | 1.0 | 10 | 3 | 60 | 54% |
| Compounds | R1 | R2 | Method | Yield (%) |
|-----------|----|----|--------|-----------|
| (±)-1x    | 1.0| 10 | 3      | 60        | 51%       |
| (±)-1y    | 1.0| 10 | 3      | 60        | 51%       |
| (±)-1j    | 0.2| 10 | 1      | 15        | 56%       |
| (±)-1u    | 0.5| 10 | 3      | 60        | 63%       |
| (±)-1z    | 0.2| 10 | 1      | 30        | 56%       |
| (±)-1aa   | 1.0| 10 | 3      | 15        | 53%       |
| (±)-1ab   | 1.0| 10 | 3      | 15        | 53%       |
| (±)-1ac   | 1.0| 10 | 3      | 30        | 55%       |
| (±)-1ad   | 1.0| 10 | 3      | 30        | 58%       |
| Compound | R1 | R2 | R3 | R4 | Yield |
|----------|----|----|----|----|-------|
| (±)-1ae  | 1.0| 10 | 3  | 30 | 58%   |
| (±)-1af  | 1.0| 10 | 5  | 60 | 61%   |
| (±)-1ag  | 0.5| 10 | 3  | 30 | 57%   |
| (±)-1ah  | 0.5| 10 | 3  | 30 | 64%   |
| (±)-1ai  | 0.5| 10 | 3  | 30 | 53%   |
| (±)-1aj  | 0.5| 10 | 3  | 30 | 50%   |
| (±)-1ak  | 0.5| 10 | 3  | 20 | 58%   |
| Recovered Allylic Alcohol | Yield | Separation Method | ee & Optical Rotation |
|---------------------------|-------|-------------------|-----------------------|
| (R)-1b                    | 41%   | **SFC**, IC column, 5% MeOH, 2 ml/min, 254nm, t<sub>R</sub> = 7.6 min (major)/8.2 (minor) | 99% [α]<sub>D</sub><sup>25.0</sup> = -39.5 (c = 0.2 in CHCl<sub>3</sub>) Lit. 12 (90% ee for R) [α]<sub>D</sub><sup>20.0</sup> = -40.3 (c = 1.0 in CHCl<sub>3</sub>) |
| (R)-1c                    | 40%   | **SFC**, IC column, 5% MeOH, 2 ml/min, 254nm, t<sub>R</sub> = 7.6 min (major)/8.2 (minor) | 99% [α]<sub>D</sub><sup>25.0</sup> = -46.5 (c = 0.2 in CHCl<sub>3</sub>) Lit. 13 (94% ee for S) [α]<sub>D</sub><sup>25.0</sup> = +18.0 (c = 1.0 in CHCl<sub>3</sub>) |
| (R)-1d                    | 41%   | **SFC**, IC column, 5% MeOH, 2 ml/min, 230nm, t<sub>R</sub> = 6.2 min (major)/6.5 (minor) | 99% [α]<sub>D</sub><sup>25.0</sup> = -49.5 (c = 0.2 in CHCl<sub>3</sub>) |
| (R)-1e (mixture)          | 47%   | **SFC**, OJH column, 5% MeOH, 2 ml/min, 254nm, t<sub>R</sub> = 6.2 min (minor)/7.2 (major) | 99% [α]<sub>D</sub><sup>25.0</sup> = -105.5 (c = 0.2 in CHCl<sub>3</sub>) |
| (R)-1g                    | 47%   | **SFC**, OJH column, 10% MeOH, 2 ml/min, 254nm, t<sub>R</sub> = 6.3 min (minor)/6.7 (major) | 89% [α]<sub>D</sub><sup>25.0</sup> = -80.5 (c = 0.2 in CHCl<sub>3</sub>) |
| (1R,2R)-2g                | 46%   | **SFC**, OZH column, 10% MeOH, 2 ml/min, 210nm, t<sub>R</sub> = 11.5 min (minor)/12.5 (major) | 98% ee 99:1 d.r. [α]<sub>D</sub><sup>22.0</sup> = +2.6 (c = 0.3 in CHCl<sub>3</sub>) |
| (R)-1h                    | 45%   | **SFC**, ID column, 5% MeOH, 2 ml/min, 230nm, t<sub>R</sub> = 13.7 min (major)/15.2 (minor) | 99% [α]<sub>D</sub><sup>25.0</sup> = -48.5 (c = 0.2 in CHCl<sub>3</sub>) |
| Compound | Yield (%) | Method Details | Enantiomeric Purity | Optical Rotation |
|----------|-----------|----------------|---------------------|-----------------|
| (R)-1i   | 46%       | SFC, OZH column, 10% MeOH, 2 ml/min, 254nm, t<sub>R</sub> = 7.0 min (minor)/7.4 (major) | 99% | [α]<sup>25.0</sup> = -49.5 (c = 0.2 in CHCl<sub>3</sub>) |
| (R)-1f   | 37%       | SFC, IC column, 5% MeOH, 2 ml/min, 254nm, t<sub>R</sub> = 16.8 min (major)/20.3 (minor) | 99% | [α]<sup>25.0</sup> = -5.5 (c = 0.2 in CHCl<sub>3</sub>) Lit. 12 (73% ee for R) [α]<sup>25.0</sup> = -15.5 (c = 1.2 in CHCl<sub>3</sub>) |
| (S)-1k   | 45% (mixture) | SFC, IC column, 5% MeOH, 2 ml/min, 230nm, t<sub>R</sub> = 4.8 min (major)/5.1 (minor) | 87% | — |
| (R)-1l   | 40%       | SFC, IC column, 5% MeOH, 2 ml/min, 254nm, t<sub>R</sub> = 9.2 min (major)/10.0 (minor) | 99% | [α]<sup>25.0</sup> = -29.0 (c = 0.2 in CHCl<sub>3</sub>) |
| (R)-1m   | 39%       | SFC, IC column, 5% MeOH, 2 ml/min, 254nm, t<sub>R</sub> = 15.3 min (major)/16.1 (minor) | 99% | [α]<sup>25.0</sup> = -26.5 (c = 0.2 in CHCl<sub>3</sub>) |
| (R)-1p   | 44%       | SFC, IC column, 5% MeOH, 2 ml/min, 254nm, t<sub>R</sub> = 11.2 min (minor)/12.1 (major) | 99% | [α]<sup>25.0</sup> = -27.0 (c = 0.2 in CHCl<sub>3</sub>) |
| (R)-1o   | 44%       | SFC, IC column, 5% MeOH, 2 ml/min, 254nm, t<sub>R</sub> = 7.9 min (major)/7.1 (minor) | 99% | [α]<sup>25.0</sup> = -34.0 (c = 0.2 in CHCl<sub>3</sub>) |
| (R)-1n   | 40%       | SFC, IC column, 5% MeOH, 2 ml/min, 254nm, t<sub>R</sub> = 5.9 min (minor)/6.2 (major) | 99% | [α]<sup>25.0</sup> = -30.0 (c = 0.2 in CHCl<sub>3</sub>) |
| Compound | Conversion % | Method | Description | Optical Rotation |
|----------|--------------|--------|-------------|------------------|
| (R)-1q   | 43%          | SFC, IC column, 5% MeOH, 2 ml/min, 254nm, t_R = 8.6 min (major)/9.5 (minor) | 99% | [α]_D^{25.0} = -41.5 (c = 0.2 in CHCl_3) |
| (R)-1r   | 40%          | SFC, OJH column, 5% MeOH, 2 ml/min, 254nm, t_R = 6.2 min (minor)/6.7 (major) | 99% | [α]_D^{25.0} = -41.5 (c = 0.2 in CHCl_3) |
| (R)-1t   | 45%          | SFC, OJH column, 5% MeOH, 2 ml/min, 254nm, t_R = 12.1 min (minor)/14.5 (major) | 94% | [α]_D^{25.0} = -17.5 (c = 0.2 in CHCl_3) |
| (R)-1s   | 44%          | SFC, OJH column, 5% MeOH, 2 ml/min, 254nm, t_R = 12.5 min (minor)/13.8 (major) | 99% | [α]_D^{25.0} = -30.0 (c = 0.2 in CHCl_3) |
| (R)-1v   | 40%          | SFC, IC column, 5% MeOH, 2 ml/min, 254nm, t_R = 12.6 min (minor)/14.1 (major) | 99% | [α]_D^{25.0} = +3.0 (c = 0.2 in CHCl_3) |
| (R)-1w   | 42%          | SFC, OJH column, 15% MeOH, 2 ml/min, 254nm, t_R = 15.0 min (major)/16.5 (minor) | 93% | [α]_D^{25.0} = +29.0 (c = 0.2 in CHCl_3) |
| (R)-1x   | 45%          | SFC, OJH column, 10% MeOH, 2 ml/min, 254nm, t_R = 5.4 min (major)/6.0 (minor) | 89% | [α]_D^{25.0} = +13.0 (c = 0.2 in CHCl_3) |
| (S)-1y   | 47%          | SFC, IC column, 5% MeOH, 2 ml/min, 254nm, t_R = 9.9 min (minor)/10.3 (major) | 99% | [α]_D^{25.0} = -49.5 (c = 0.2 in CHCl_3) Lit. 8 (86% ee for R) [α]_D^{25.0} = +67.0 (c = 1.0 in CHCl_3) |
| (R)-1z   | 40%          | SFC, OJH column, 5% MeOH, 2 ml/min, 254nm, t_R = 11.5 min (minor)/12.5 (major) | 99% | [α]_D^{25.0} = +6.0 (c = 0.2 in CHCl_3) |
| Compound | Yield (%) | Conditions | Enantiomeric Purity | Optical Rotation |
|----------|-----------|------------|---------------------|-----------------|
| (R)-1z   | 42%       | SFC, OJH column, 10% MeOH, 2 ml/min, 254nm, \( t_R = 7.4 \text{ min} \) (minor)/8.2 (major) | 89% | \([\alpha]_D^{25.0} = +20.5 \) (c = 0.2 in CHCl₃) |
| (R)-1aa  | 45%       | SFC, IA column, 5% MeOH, 2 ml/min, 210nm, \( t_R = 7.9 \text{ min} \) (major)/9.2 (minor) | 89% | \([\alpha]_D^{25.0} = +5.0 \) (c = 0.1 in CHCl₃) |
| (R)-1ab  | 44%       | SFC, IA column, 5% MeOH, 2 ml/min, 210nm, \( t_R = 6.2 \text{ min} \) (minor)/6.7 (major) | 90% | \([\alpha]_D^{25.0} = -1.5 \) (c = 0.2 in CHCl₃) |
| (R)-1ac  | 41%       | GC-MS: column Chiraldex β-DM, 50°C to 175°C at 1°C/min. \( t_R = 55.7 \text{ min} \) (minor)/58.0 (major) | 96% | \([\alpha]_D^{25.0} = -6.5 \) (c = 0.2 in CHCl₃) |
| (R)-1ad  | 40%       | GC-MS: column Chiraldex β-DM, 50°C to 175°C at 1°C/min. \( t_R = 70.5 \text{ min} \) (minor)/74.2 (major) | 99% | \([\alpha]_D^{25.0} = -0.5 \) (c = 0.2 in CHCl₃) |
| (R)-1ae  | 39%       | SFC, OJH column, 5% MeOH, 2 ml/min, 210nm, \( t_R = 3.4 \text{ min} \) (minor)/3.6 (major) | 99% | \([\alpha]_D^{25.0} = -4.0 \) (c = 0.2 in CHCl₃) |
| (S)-1u   | 35% (below) | SFC, IC column, 5% MeOH, 2 ml/min, 254nm, \( t_R = 13.1 \text{ min} \) (major)/14.2 (minor) | 98% | \([\alpha]_D^{25.0} = -14.0 \) (c = 0.1 in CHCl₃) |
| (R)-pu   | 91%       | -- | 98% | \([\alpha]_D^{25.0} = +103.0 \) (c = 0.5 in EtOH) |
|          |           |          |                    | Lit. 14 (99% ee for R) \([\alpha]_D^{25.0} = +152.1 \) (c = 2.0 in EtOH) |
Hydrogenated product 2g

*(1R, 2R)-1-cyclopentyl-2-methyl-3-phenylpropan-1-ol.*

Colorless oil. 98% ee, 99:1 d.r.

\[
\begin{align*}
\text{1H NMR} \ (400 \text{ MHz, CDCl}_3) & \delta \ 7.32 \ - \ 7.25 \ (m, \ 2H), 7.22 \ - \ 7.15 \ (m, \ 3H), \\
& 3.42 \ - \ 3.28 \ (m, \ 1H), 2.99 \ (dd, \ J = 13.3, \ 3.6 \ Hz, \ 1H), 2.32 \ (dd, \ J = 13.3, \\
& 10.5 \ Hz, \ 1H), 2.20 \ - \ 2.06 \ (m, \ 1H), 1.92 \ - \ 1.70 \ (m, \ 3H), 1.70 \ - \ 1.49 \ (m, \\
& 4H), 1.48 \ - \ 1.18 \ (m, \ 2H), 0.87 \ (d, \ J = 6.9 \ Hz, \ 3H). \text{13C NMR} \ (101 \text{ MHz, CDCl}_3) \ \delta \ 141.71, 129.39, 128.32, 125.81, 80.24, 43.46, 39.49, 37.11, 29.45, 28.68, 25.83, \\
& 25.73, 16.82. \text{HRMS-ESI; m/z [M+Na}^+\text{]} = 241.1565, \text{calcd. For C}_{17}\text{H}_{20}\text{NaO: 241.1568.} \text{[} \alpha \text{]}_{D}^{25.0} = +2.6 \ (c = 0.3 \text{ in CHCl}_3) \end{align*}
\]
4. Double stereodifferentiation and synthesis of ketone 3

**Double stereodifferentiation:** A vial was charged with the resolved allylic alcohol \((R)-1\text{h} \ (22 \text{ mg})\) and Ir-complex \((0.4 \text{ mg})\). Dry toluene \((1 \text{ ml})\) was added and the vial was placed in a hydrogenation apparatus. The reactor was purged 3 times with \(\text{N}_2\), and then filled with \(\text{H}_2 \ (3 \text{ bar})\). The reaction was stirred at room temperature for 10 min before the \(\text{H}_2\) pressure was released and the solvent was removed \textit{in vacuo}. The crude product was purified through silica column chromatography to give the hydrogenated product \(22 \text{ mg} \) (quantitative yield).

\[
\begin{align*}
\text{(±)-1i} & \xrightarrow{KR} (R)-1\text{i} \quad + \quad (2S,3R)-2\text{i} \\
(2S,3R)-2\text{i} & \xrightarrow{} \end{align*}
\]

**\((2S,3R)-3\text{-methyl-1,4-diphenylbutan-2-ol.}\)**
Colorless oil. 96\% ee, 96:4 d.r.

\[
\begin{align*}
\text{H NMR (400 MHz, CDCl}_3\text{)} & \delta 7.40 \text{–} 7.15 \text{ (m, 10H)}, 3.70 \text{ (tt, } J = 5.6, 3.4 \text{ Hz, 1H)}, 3.06 \text{ – } 2.89 \text{ (m, 2H)}, 2.65 \text{ (dd, } J = 13.6, 9.8 \text{ Hz, 1H)}, 2.46 \text{ (dd, } J = 13.4, 9.4 \text{ Hz, 1H)}, 2.05 \text{ – } 1.90 \text{ (m, 1H)}, 1.57 \text{ – } 1.51 \text{ (m, 1H)}, 0.95 \text{ (d, } J = 6.8 \text{ Hz, 3H}). \ \\
\text{C NMR (101 MHz, CDCl}_3\text{)} & \delta 141.10, 139.06, 129.55, 129.40, 128.82, 128.39, 126.66, 125.97, 76.30, 40.61, 40.51, 38.78, 15.54. \ \\
\text{HRMS - ESI;} \ m/z \ [\text{M+Na}^+] & = 263.1409, \text{ calcd. For } C_{17}H_{20}NaO: 263.1406. [\alpha]_{D}^{25.0} = -15.0 \text{ (c = 0.2 in CHCl}_3\text{)}
\end{align*}
\]

**\((2R,3S)-3\text{-methyl-1,4-diphenylbutan-2-ol.}\)**
Colorless oil. 99\% ee, >99:1 d.r.

\[
\begin{align*}
\text{H NMR (400 MHz, CDCl}_3\text{)} & \delta 7.40 \text{ – } 7.15 \text{ (m, 10H)}, 3.70 \text{ (tt, } J = 5.6, 3.4 \text{ Hz, 1H)}, 3.06 \text{ – } 2.89 \text{ (m, 2H)}, 2.65 \text{ (dd, } J = 13.6, 9.8 \text{ Hz, 1H}), 2.46 \text{ (dd, } J = 13.4, 9.4 \text{ Hz, 1H)}, 2.05 \text{ – } 1.90 \text{ (m, 1H)}, 1.57 \text{ – } 1.51 \text{ (m, 1H)}, 0.95 \text{ (d, } J = 6.8 \text{ Hz, 3H}). \ \\
\text{C NMR (101 MHz, CDCl}_3\text{)} & \delta 141.10, 139.06, 129.55, 129.40, 128.82, 128.39, 126.66, 125.97, 76.30, 40.61, 40.51, 38.78, 15.54. \ \\
\text{HRMS - ESI;} \ m/z \ [\text{M+Na}^+] & = 263.1409, \text{ calcd. For } C_{17}H_{20}NaO: 263.1406. [\alpha]_{D}^{25.0} = +16.0 \text{ (c = 0.2 in CHCl}_3\text{)}
\end{align*}
\]
Ketone 3 was synthesized according to the following scheme:

**Step 1**, gram scale kinetic resolution: A glass vial was charged with 1.0g (5.67mmol) racemic substrate (±1b), 78mg K₂CO₃ (0.56 mmol) and 20 mg (0.011mol) catalyst, 8 ml dry toluene was added. The vial was placed in a hydrogenation apparatus and flushed 3 times with nitrogen. The reactor was then purged 8 times using hydrogen, before filling to the 1 bar. The reaction was stirred at room temperature for the 60 min before the hydrogen pressure was released and the solvent was removed under vacuum. The crude product was passed through a short silica gel layer, eluted with a mixture of Et₂O: Pentane (1:1) and remove the solvent to give the mixture of resolved alcohol and hydrogenated product (992 mg, 99% yield, 46% NMR yield for R-1b).

**Step 2**, benzylation: the obtained mixture was used without further purification. To a solution of mixture (200mg) in 5ml THF/DMF(4:1) was added 60mg (1.5 eq) NaH slowly at 0 °C. The mixture was stirred 30 min and then 0.71 ml (3.0 eq) BnBr was added. The reaction was further stirred at room temperature overnight, and then was quenched with water and extracted with Et₂O. After evaporation of the solvent, the crude extract was purified by column chromatography to afford a mixture of protected alcohols as a colorless oil (277 mg, 91%).

**Step 3**, ozonolysis: To a stirred solution of the mixture of protected alcohols (277mg) in MeOH at -78°C was bubbled through freshly generated ozone. After the color of the reaction mixture changed to light blue (ca.10min), it was quenched with dimethyl sulfide (0.3 ml, 4eq) and allowed to warm to room temperature. After 1 h, the solvent was removed under reduced pressure, and the obtained residue was purified by flash column chromatography to afford pure methyl ketone 3 (71 mg 79%).

(R)-3-(benzylxoy)pentan-2-one.

Colorless oil.

1H NMR (400 MHz, CDCl₃) δ 7.40 – 7.28 (m, 5H), 4.58 (d, J = 11.7 Hz, 1H), 4.45 (d, J = 11.7 Hz, 1H), 3.71 (dd, J = 7.0, 5.7 Hz, 1H), 2.18 (s, 3H), 1.79 – 1.66 (m, 2H), 0.96 (t, J = 7.4 Hz, 3H). 13C NMR (101 MHz, CDCl₃) δ 211.61, 137.73, 128.62, 128.05, 127.96, 86.48, 72.47, 25.61, 25.29, 9.71. [α]D25 = +58.0 (c = 0.5 in CHCl₃) Lit.15(S) [α]D25 = -113 (c = 2.6 in CHCl₃)
5. Asymmetric formal synthesis of inthomycin A and B.

(R)-methyl-3-((tert-butyldimethylsilyl)oxy)-2,2-dimethyl-4-oxopentanoate (4): kinetic resolution: A glass vial was charged with 248 mg (1.0 mmol) racemic substrate (±1y), 13.8 mg K$_2$CO$_3$ (0.1 mmol) and 16.3 mg (0.01 mmol) catalyst, 3 ml dry toluene was added. The vial was placed in a hydrogenation apparatus and flushed 3 times with nitrogen. The reactor was then purged 8 times using hydrogen, before filling to the 3 bar. The reaction was stirred at room temperature for the 1.5h before the hydrogen pressure was released and the solvent was removed under vacuum. The crude product was passed through a short silica gel layer, eluted with a mixture of Et$_2$O: Pentane (1:1) and remove the solvent to give the mixture of resolved alcohol and hydrogenated product. (4 separated reactions were set parallel in the same reactor)

To a solution of the resolved mixture (4.0 mmol) in CH$_2$Cl$_2$ were added 2,6-lutidine (1.8 ml, 16 mmol) and TBSOTf (2.3 ml, 10 mmol) at 0°C. The mixture was allowed to warm to room temperature and stirring was continued for 0.5 h. The reaction was quenched with saturated NH$_4$Cl at 0°C and extracted with Et$_2$O. The extract was washed with brine, dried over Na$_2$SO$_4$, and concentrated to give crude product. The crude product was passed through a short silica gel layer, eluted with a mixture of Et$_2$O: Pentane (5:95) and remove the solvent to give the mixture of the protected products.

To a stirred solution of the mixture of protected alcohols in a mixture of MeOH:CH$_2$Cl$_2$(1:4) 20 ml at -78°C was bubbled through freshly generated ozone. After the color of the reaction mixture changed to light blue (ca.25 min), it was quenched with dimethyl sulfide (1.2 ml, 4 eq) and allowed to worm to room temperature. After 1 h, the solvent was removed under reduced pressure, and the obtained residue was purified by flash column chromatography to afford pure methyl ketone 4 (438 mg 38%).

(R)-methyl 3-((tert-butyldimethylsilyl)oxy)-2,2-dimethyl-4-oxopentanoate

Colorless oil. R$_f$=0.3 (Et$_2$O: Pentane= 1:4)

$^1$H NMR (400 MHz, CDCl$_3$) δ 4.18 (s, 1H), 3.68 (s, 3H), 2.15 (s, 3H), 1.21 (s, 3H), 1.13 (s, 3H), 0.94 (s, 9H), 0.07 (s, 3H), 0.03 (s, 3H).

$^{13}$C NMR (101 MHz, CDCl$_3$) δ 211.45, 175.81, 82.80, 52.11, 47.66, 27.58, 25.84, 22.06, 20.81, 18.13, -4.55, -5.05. HRMS-ESI; m/z [M+Na]$^+$ = 311.1660, calcd. For C$_{14}$H$_{28}$NaO$_4$Si: 311.1649. $[\alpha]_D^{26.6} = +34.6$ (c = 0.5 in CHCl$_3$)
(S,Z)-methyl 3-((tert-butyldimethylsilyl)oxy)-2,2,4-trimethylhept-4-en-6-ynoate (5): To a solution of phosphonate (881 mg, 4.0 mmol) in THF (10 mL) was added KHMDS (4.2 mL of 1M solution in THF, 4.2 mmol) at 0 °C and the mixture was stirred at 0 °C for 30 min. Then the mixture was then cooled to -78 °C and a solution of methylketone 4 (577 mg, 2.0 mmol) in THF (3ml) was added to the mixture at -78 °C. The mixture was stirred at -78 °C for 1 h and slowly warm to 0 °C over 2h, and then quenched by the addition of H2O. The mixture was extracted with Et2O, dried over Na2SO4 and evaporated to give a mixture of TMS protected and deprotected enyl. The residue was dissolved in MeOH (10ml) and was added K2CO3 (828 mg, 6 mmol) and stirred at room temperature overnight. The reaction mixture was filtered and concentrated to give the crude product. Flash chromatography (10: 90 Et2O/Pentane) to afford the enyne 5 (503 mg, 81%) with exclusive stereoselectivity.

(E)-5-(3-bromoallyl)-2-(triisopropylsilyloxazole (7): To a solution a TIPS oxazole 6 (902mg, 4mmol) in THF (20 ml) was added n-BuLi (2.2 mL, 1.9 M in hexanes, 4.2 mmol) dropwise at -78 °C. The reaction mixture was stirred for 30 min at -78 °C and a solution of LiCl (144 mg, 3.4 mmol) and CuCN (154 mg, 1.7 mmol) in THF (6 mL) was added dropwise. After a further 2 h, trans 1,3-dibromoprop-1-ene (1.2 g, 6 mmol) was added dropwise and the reaction stirred at room temperature for 2 h. The reaction was quenched with saturated NH4Cl and extracted with Et2O. The combined organic phase was washed with brine, dried over Na2SO4 and concentrated to give the crude product. Flash chromatography (5:95 to 10:90 Et2O/Pentane) to afford the vinyl bromide 7 (1.170g, 85%).
(E)-5-(3-bromoallyl)-2-(triisopropylsilyl)oxazole

Colorless oil. Rf=0.3 (Et2O: Pentane= 1:8)

1H NMR (400 MHz, CDCl3) δ 6.86 (s, 1H), 6.37 – 6.12 (m, 2H), 3.45 (d, J = 6.7 Hz, 2H), 1.37 (dt, J = 14.4, 7.3 Hz, 3H), 1.12 (d, J = 7.4 Hz, 18H).

13C NMR (101 MHz, CDCl3) δ 168.42, 150.73, 132.15, 123.39, 107.82, 29.38, 18.50, 11.11.

HRMS-ESI; m/z [M+H+] = 344.1038, calcd. For C15H27BrNOSi: 344.1040.

(S,4Z,6E,8E)-methyl-3-((tert-butyldimethylsilyl)oxy)-2,2,4-trimethyl-10-(2-(triisopropylsilyl)oxazol-5-yl)deca-4,6,8-trienoate (8): To a solution of ZrCp2Cl2 (584 mg, 2.0 mmol) in THF (4.5 mL) was added dropwise a solution of DIBAL (2.0 mL, 1.0 M solution in hexane, 2.0 mmol) at 0 ° C in dark under argon atmosphere, and the resulting suspension was stirred at 0 ° C for 30 min followed by the addition of a solution of enyl 5 (415 mg, 1.3 mmol) in THF (2 mL). The reaction mixture was warmed to room temperature and stirred for further 30 min. To a solution of vinyl bromide (344 mg, 1.0 mmol) and PEPPSI (34 mg, 0.05 mmol) in THF (3 mL) was added the above reaction mixture, and the resulting reaction mixture was stirred at room temperature 24h. The reaction mixture was quenched with water and extracted with Et2O. The extract was dried over Na2SO4 and concentrated to give crude product. Flash chromatography (5:95 to 10:90 Et2O/Pentane) to afford the triene 8 (524 mg, 91%).

(S,Z)-methyl 3-((tert-butyldimethylsilyl)oxy)-2,2,4-trimethylhept-4-en-6-ynoate

Pale yellow oil. Rf=0.4 (Et2O: Pentane= 1:10)

1H NMR (400 MHz, CDCl3) δ 6.84 (s, 1H), 6.41 (t, J = 12.5 Hz, 1H), 6.26 – 6.04 (m, 2H), 5.98 (d, J = 11.4 Hz, 1H), 5.82 – 5.68 (m, 1H), 4.93 (s, 1H), 3.61 (s, 3H), 3.50 (d, J = 6.6 Hz, 2H), 1.78 (s, 3H), 1.45 – 1.24 (m, 6H), 1.21 (s, 3H), 1.13 (d, J = 7.4 Hz, 18H), 1.09 (s, 3H), 0.91 – 0.84 (m, 12H). 13C NMR (101 MHz, CDCl3) δ 177.14, 167.99, 152.56, 138.12, 133.22, 131.87, 129.75, 127.91, 127.64, 123.08, 74.32, 51.83, 49.60, 34.27, 29.11, 25.85, 22.48, 22.37, 21.47, 19.94, 18.53, 18.20, 14.19, 11.14, -4.72, -5.40. HRMS-ESI; m/z [M+Na+] = 578.3713, calcd. For C17H20NaO: 578.3718. [α]D27.0 = -97.6 (c = 0.5 in CHCl3)

(S,Z)-methyl 3-((tert-butyldimethylsilyl)oxy)-2,2,4-trimethylhept-4-en-6-ynoate

Pale yellow oil. Rf=0.4 (Et2O: Pentane= 1:10)

1H NMR (400 MHz, CDCl3) δ 6.84 (s, 1H), 6.41 (t, J = 12.5 Hz, 1H), 6.26 – 6.04 (m, 2H), 5.98 (d, J = 11.4 Hz, 1H), 5.82 – 5.68 (m, 1H), 4.93 (s, 1H), 3.61 (s, 3H), 3.50 (d, J = 6.6 Hz, 2H), 1.78 (s, 3H), 1.45 – 1.24 (m, 6H), 1.21 (s, 3H), 1.13 (d, J = 7.4 Hz, 18H), 1.09 (s, 3H), 0.91 – 0.84 (m, 12H). 13C NMR (101 MHz, CDCl3) δ 177.14, 167.99, 152.56, 138.12, 133.22, 131.87, 129.75, 127.91, 127.64, 123.08, 74.32, 51.83, 49.60, 34.27, 29.11, 25.85, 22.48, 22.37, 21.47, 19.94, 18.53, 18.20, 14.19, 11.14, -4.72, -5.40. HRMS-ESI; m/z [M+Na+] = 578.3713, calcd. For C17H20NaO: 578.3718. [α]D27.0 = -97.6 (c = 0.5 in CHCl3)
(S,4Z,6E,8E)-methyl-3-hydroxy-2,2,4-trimethyl-10-(oxazol-5-yl)deca-4,6,8-trienoate (9): To a solution of 8 (175mg, 0.3 mmol) in CH₃CN (4 ml) was added HF-pyridine (0.4 ml) at 0 °C. The reaction mixture was stirred at room temperature for 10 h and the basified with saturated NaHCO₃ at 0 °C and extracted with CH₂Cl₂ and dried over Na₂SO₄ and concentrated to give crude product. Flash chromatography (20:80 to 40:60 EtOAc/Pentane) to afford the alcohol 8 (68 mg, 75%), ee >99% determined by chiral SFC, OJH column, 10% MeOH, 2 ml/min, 254nm, tᵣ = 4.3 min (minor)/4.7 (major).

(S,4Z,6E,8E)-methyl 3-hydroxy-2,2,4-trimethyl-10-(oxazol-5-yl)deca-4,6,8-trienoate
Pale yellow oil.
Rᵣ=0.3 (EtOAc/Pentane = 1:2)
^1H NMR (400 MHz, CDCl₃) δ 7.78 (s, 1H), 6.79 (s, 1H), 6.43 (dd, J = 13.8, 11.5 Hz, 1H), 6.24 – 6.08 (m, 2H), 5.78 – 6.03 (d, J = 11.4 Hz, 1H), 5.78 – 5.68 (m, 1H), 4.72 (d, J = 6.1 Hz, 1H), 3.71 (s, 3H), 3.48 (d, J = 6.8 Hz, 2H), 3.26 (d, J = 6.4 Hz, 1H), 1.75 (s, 3H), 1.27 (s, 3H), 1.16 (s, 3H).

(C₁₇H₂₃N₂O₄: 328.1519, [α]D₂₇ = -87.0 (c = 0.5 in CHCl₃) Lit.^{17} (R) [α]D₂₇ = +81.9 (c = 0.99 in CHCl₃)

(S,4Z,8E)-methyl-3-((tert-butyldimethylsilyl)oxy)-2,2,4-trimethyl-10-(2-(triisopropylsilyl)oxazol-5-yl)deca-4,8-dien-6-ynoate (10): To a mixture of Pd(Ph₃P)₂Cl₂ (35 mg, 0.05mmol) and Cul (19 mg, 0.1 mmol) in THF (3ml) under argon, piperidine (0.3ml 3mmol) and vinyl bromide 7 (344mg, 1.0mmol) were added, followed by the addition of enyl 5 (341mg 1.1mmol). The reaction mixture was allowed to stirred for 30 mins at room temperature. The resulting mixture was diluted with Et₂O then filter through short pad of silica gel using Et₂O as eluent. The solution was washed with saturated NH₄Cl, dried over Na₂SO₄ and concentrated to give the crude product. Flash chromatography (5:95 to 10:90 Et₂O/Pentane) to afford the product 10 (424mg, 74%).

(S,4Z,8E)-methyl 3-((tert-butyl dimethylsilyl)oxy)-2,2,4-trimethyl-10-(2-(triisopropylsilyl)oxazol-5-yl)deca-4,8-dien-6-ynoate
Pale yellow oil.
Rᵣ=0.4 (Et₂O: Pentane= 1:10)
$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 6.87 (s, 1H), 6.19 (dt, $J$ = 15.7, 6.7 Hz, 1H), 5.74 (dd, $J$ = 15.8, 1.9 Hz, 1H), 5.53 (s, 1H), 5.14 (s, 1H), 3.63 (s, 3H), 3.55 (d, $J$ = 6.7 Hz, 2H), 1.81 (d, $J$ = 1.3 Hz, 3H), 1.58 (s, 1H), 1.45 – 1.22 (m, 6H), 1.20 (s, 3H), 1.16 (s, 3H), 1.13 (d, $J$ = 7.4 Hz, 18H), 0.90 – 0.84 (m, 12H), -0.03 (s, 3H).

$^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 177.04, 168.27, 151.52, 151.02, 136.98, 123.35, 112.92, 109.62, 92.18, 86.92, 76.62, 51.83, 49.19, 29.45, 25.81, 22.67, 20.82, 18.87, 18.51, 18.15, 11.11, -4.77, -5.54.

HRMS-ESI; $m$/z [M+Na$^+$] $=$ 596.3562, calcd. For C$_{32}$H$_{55}$NNaO$_4$Si$_2$: 596.3561.

$\left[\alpha\right]_{D}^{27.0} = -124.4$ (c = 0.5 in CHCl$_3$)

(S,4Z,8E)-methyl-3-hydroxy-2,2,4-trimethyl-10-(oxazol-5-yl)deca-4,8-dien-6-ynoate (11): To a solution of 10 (143mg, 0.25 mmol) in CH$_3$CN (10 ml) was added 47% HF (2.0 ml) at 0 °C. The reaction mixture was stirred at room temperature overnight and the basified with saturated NaHCO$_3$ at 0 °C and extracted with CH$_2$Cl$_2$ and dried over Na$_2$SO$_4$ and concentrated to give crude product. Flash chromatography (20:80 to 40:60 EtOAc/Pentane) to afford the alcohol 11 (62 mg, 82%), ee >99% determined by chiral SFC, OJH column, 10% MeOH, 2 ml/min, 254nm, $t_R$ = 3.7 min (major)/4.0 (minor)

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.79 (s, 1H), 6.82 (s, 1H), 6.11 (dt, $J$ = 15.7, 6.8 Hz, 1H), 5.73 (dd, $J$ = 15.8, 1.7 Hz, 1H), 5.57 (s, 1H), 4.83 (d, $J$ = 7.2 Hz, 1H), 3.71 (s, 3H), 3.57 (d, $J$ = 7.2 Hz, 1H), 3.50 (d, $J$ = 6.8 Hz, 2H), 1.75 (d, $J$ = 1.3 Hz, 3H), 1.32 (s, 3H), 1.18 (s, 3H). $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 178.41, 150.72, 149.84, 149.68, 136.53, 123.07, 113.25, 109.75, 91.78, 86.98, 77.30, 52.32, 46.78, 29.15, 24.64, 20.84, 18.51. HRMS-ESI; $m$/z [M+Na$^+$] $=$ 326.1368, calcd. For C$_{17}$H$_{21}$NNaO$_4$: 326.1363. $\left[\alpha\right]_{D}^{27.0} = +34.0$ (c = 0.5 in CHCl$_3$) Lit. $^{18}$ (R) $\left[\alpha\right]_{D}^{25.0} = -26.1$ (c = 0.6 in CHCl$_3$)
6. DFT calculation

Computational Details

All calculations were performed with Jaguar\textsuperscript{[1]} (version 10.1) using the B3LYP-D3\textsuperscript{[2, 3]} functional in combination with the LACVP** basis set.\textsuperscript{[4]} First, all the structures were optimized in the gas phase. The solvent energies for the optimized structures were then calculated using the Poisson-Boltzmann solver with toluene as the solvent. The energies that are shown, with the XYZ coordinates, were obtained from the optimized in the gas phase calculations. All the transition states were characterized by one negative vibrational frequency. The XYZ coordinates of the calculated structures are listed below. All computations were carried out using the computational cluster resources at the National Supercomputer Centre based at Linkoping University, Sweden.

![Energy profile depicting the transition state of the 3 diastereomers](image)

\textbf{Figure 1:} Energy profile depicting the transition state of the 3 diastereomers
XYZ coordinates of structures calculated

Start struc I (Energy = -2502.917707 Hartrees, 0 Kcal mol⁻¹)

| Atom | X (Å) | Y (Å) | Z (Å) |
|------|-------|-------|-------|
| N1   | 1.672029 | 1.440495 | 0.000000 |
| C2   | 3.980181 | 1.669586 | -1.107426 |
| C3   | 2.186959 | 3.223168 | -1.712012 |
| C4   | 3.400623 | 2.470065 | -2.322973 |
| C5   | 1.078677 | 2.173728 | -1.440395 |
| C6   | 2.992386 | 0.016527 | 0.000000 |
| H7   | 4.996249 | -0.856866 | 0.000000 |
| H8   | 3.103665 | -3.153685 | 0.000000 |
| H9   | 0.923669 | -2.316065 | 0.000000 |
| H10  | 3.303702 | 1.033269 | 0.000000 |
| H11  | 3.998596 | 1.272505 | 0.000000 |
| H12  | 1.848513 | 2.311279 | 0.000000 |
| H13  | 4.127024 | 2.710925 | 0.000000 |
| C14  | 2.695418 | 0.285022 | 0.000000 |
| H15  | 1.941734 | 0.378094 | 0.000000 |
| H16  | 3.590687 | 0.277430 | 0.000000 |
| C17  | -0.280039 | 1.049571 | 0.000000 |
| N18  | -1.210507 | 0.312790 | 0.000000 |
| C19  | -2.327911 | 0.112028 | 0.000000 |
| C20  | -2.254029 | 0.480958 | 0.000000 |
| H21  | 2.977807 | -0.282108 | 0.000000 |
| P22  | 1.055706 | 0.347071 | 0.000000 |
| H23  | -0.993258 | 0.990094 | 0.000000 |
| C24  | 0.928562 | 2.144960 | 0.000000 |
| C25  | 0.438873 | 0.749373 | 4.866203 |
| C26  | 0.717644 | 1.609385 | 2.622494 |
| C27  | 0.885346 | -0.772579 | 3.039339 |
| C28  | 0.642296 | -0.549598 | 4.393900 |
| C29  | 0.477747 | 1.827422 | 3.979742 |
| C30  | 1.055706 | 0.587106 | 0.000000 |
| H31  | 1.049500 | -1.785131 | 2.680840 |
| C32  | 0.616632 | -1.389521 | 5.082121 |
| H33  | 0.323696 | 2.838697 | 4.345277 |
| H34  | 0.253514 | 0.920340 | 5.922661 |
| S35  | -0.740445 | 4.371034 | 0.000000 |
| C36  | -3.428949 | 2.151310 | 0.688153 |
| C37  | -3.146770 | 1.584074 | 1.941452 |
| C38  | -4.756804 | 2.221488 | 0.244610 |
| C39  | -4.178415 | 1.074872 | 2.727750 |
| H40  | -2.122247 | 1.568516 | 2.304238 |
| C41  | -5.787789 | 1.714298 | 1.038091 |
| H42  | -4.976423 | 2.666369 | -0.722134 |
| C43  | -5.499854 | 1.137212 | 2.276504 |
| H44  | -3.952276 | 0.640550 | 3.697396 |
| H45  | -6.814579 | 1.767076 | 0.688598 |
| H46  | -6.303216 | 0.743308 | 2.892270 |
| C47  | 2.324476 | -1.282759 | 0.159777 |
| Atom | X Position | Y Position | Z Position |
|------|------------|------------|------------|
| C48  | 3.425756   | 0.000000   | -1.335401  |
| C49  | 2.258997   | 0.000000   | -2.166309  |
| C50  | 4.444100   | 0.000000   | -2.261680  |
| H51  | 3.483812   | 0.000000   | -0.663290  |
| C52  | 3.281491   | 0.000000   | -3.090695  |
| C53  | 4.372752   | 0.000000   | -3.139687  |
| H54  | 3.483812   | 0.000000   | -0.663290  |
| C55  | 2.258997   | 0.000000   | -2.166309  |
| C56  | 4.444100   | 0.000000   | -2.261680  |
| H57  | 3.483812   | 0.000000   | -0.663290  |
| H58  | 2.258997   | 0.000000   | -2.166309  |
| C59  | 4.444100   | 0.000000   | -2.261680  |
| H60  | 3.483812   | 0.000000   | -0.663290  |
| H61  | 2.258997   | 0.000000   | -2.166309  |
| C62  | 4.372752   | 0.000000   | -3.139687  |
| H63  | 3.483812   | 0.000000   | -0.663290  |
| H64  | 2.258997   | 0.000000   | -2.166309  |
| C65  | 4.444100   | 0.000000   | -2.261680  |
| H66  | 3.483812   | 0.000000   | -0.663290  |
| H67  | 2.258997   | 0.000000   | -2.166309  |
| C68  | 4.372752   | 0.000000   | -3.139687  |
| H69  | 3.483812   | 0.000000   | -0.663290  |
| H70  | 2.258997   | 0.000000   | -2.166309  |
| C71  | 4.372752   | 0.000000   | -3.139687  |
| H72  | 3.483812   | 0.000000   | -0.663290  |
| H73  | 2.258997   | 0.000000   | -2.166309  |
| C74  | 4.372752   | 0.000000   | -3.139687  |
| H75  | 3.483812   | 0.000000   | -0.663290  |
| H76  | 2.258997   | 0.000000   | -2.166309  |
| C77  | 4.372752   | 0.000000   | -3.139687  |
| H78  | 3.483812   | 0.000000   | -0.663290  |
| H79  | 2.258997   | 0.000000   | -2.166309  |
| C80  | 4.372752   | 0.000000   | -3.139687  |
| H81  | 3.483812   | 0.000000   | -0.663290  |
| H82  | 2.258997   | 0.000000   | -2.166309  |
| C83  | 4.372752   | 0.000000   | -3.139687  |
| H84  | 3.483812   | 0.000000   | -0.663290  |
| H85  | 2.258997   | 0.000000   | -2.166309  |
| O90  | 1.480708   | 0.000000   | -3.595390  |
| H86  | 0.738561   | 0.000000   | 2.445156  |
| H87  | 1.408248   | 0.000000   | -2.128073  |
| H88  | 1.408248   | 0.000000   | -2.128073  |
| H89  | 1.408248   | 0.000000   | -2.128073  |

Start str II (Energy = -2502.910380 Hartrees, 4.60 Kcal mol⁻¹)
Start str III (Energy = -2502.909701 Hartrees, 5.02 Kcal mol⁻¹)

N1 1.68116900000000 1.43571100000000 -0.32369600000000
C2 4.01262000000000 1.57896300000000 -1.08937000000000
C3 2.28949600000000 3.19567400000000 -1.73337800000000
C4 3.49013000000000 2.40051600000000 -2.31676800000000
C5 1.14226900000000 2.18296300000000 -0.35154700000000
C6 3.01665000000000 1.99676800000000 0.01355900000000
H7 5.03485000000000 1.86106300000000 -0.81756100000000
H8 3.19240900000000 1.76520900000000 -3.15659200000000
H9 1.00868000000000 1.53537600000000 -2.35796400000000
H10 3.01665000000000 1.99676800000000 0.01355900000000
H11 3.49013000000000 2.40051600000000 -2.31676800000000
H12 1.14226900000000 2.18296300000000 -0.35154700000000
H13 2.28949600000000 3.19567400000000 -1.73337800000000
H14 4.01262000000000 1.57896300000000 -1.08937000000000
H15 2.28949600000000 3.19567400000000 -1.73337800000000
H16 4.01262000000000 1.57896300000000 -1.08937000000000
H17 3.49013000000000 2.40051600000000 -2.31676800000000
H18 1.14226900000000 2.18296300000000 -0.35154700000000
H19 2.28949600000000 3.19567400000000 -1.73337800000000
H20 4.01262000000000 1.57896300000000 -1.08937000000000
C20 -2.1429500000000 4.1443050000000 -0.5402070000000
H21 -2.8401430000000 4.9427960000000 -0.3291580000000
P22 1.0014250000000 0.0264660000000 0.2938920000000
Ir23 -1.0396320000000 -0.2616640000000 -0.6867800000000
H24 -1.9908950000000 -0.1607960000000 0.9002490000000
C25 0.8330420000000 0.3294930000000 2.0870570000000
C26 0.2554350000000 0.7942630000000 4.7868320000000
C27 0.6561080000000 1.6387650000000 2.5558990000000
C28 0.7133584000000 -0.7475050000000 2.9792130000000
C29 0.4263600000000 -0.5126590000000 4.3231270000000
C30 0.3728730000000 1.8685750000000 3.9028520000000
H31 0.8496240000000 -1.7665390000000 2.6270860000000
H32 0.3396890000000 -1.3497080000000 5.0098480000000
H33 0.2443830000000 2.8857630000000 4.2617920000000
H34 0.0341940000000 0.9740750000000 5.8348930000000
S35 -0.6033580000000 4.4466310000000 -1.2672380000000
C36 -3.3997560000000 2.2613720000000 0.5599270000000
C37 -3.1356630000000 1.7373390000000 1.8361200000000
C38 -4.7167760000000 2.2920800000000 0.0859150000000
C39 -4.1751670000000 1.2307270000000 2.6146550000000
H40 -2.1193460000000 1.7475070000000 2.2210990000000
C41 -5.7551600000000 1.7831460000000 0.8683630000000
H42 -4.9252190000000 2.6987220000000 -0.8994580000000
C43 -5.4862550000000 1.2496000000000 2.1298310000000
H44 -3.9627010000000 0.8306800000000 3.6021070000000
H45 -6.7727650000000 1.7993980000000 0.4903110000000
H46 -6.2961680000000 0.8545930000000 2.7362850000000
C47 2.2251730000000 -1.3141230000000 0.1425790000000
C48 3.2979850000000 -1.4051160000000 1.0459910000000
C49 2.1488000000000 -2.2113000000000 -0.9330770000000
C50 4.2769110000000 -2.3814620000000 0.8736300000000
H51 3.3620270000000 -0.7252250000000 1.8905160000000
C52 3.1320890000000 -3.1857630000000 -1.1002310000000
C53 4.1945640000000 -3.2723990000000 -0.1988770000000
H54 5.1000620000000 -2.4499340000000 1.5787500000000
H55 3.0642150000000 -3.8825720000000 -1.9303160000000
H56 4.9559460000000 -4.0359020000000 -0.3283970000000
H65 -1.7096210000000 -0.9256210000000 0.8716240000000
C66 -3.8231020000000 -4.6044830000000 -0.6361930000000
C67 -3.4529860000000 -3.4429500000000 -1.3125680000000
C68 -3.6533650000000 -2.1803350000000 -0.7279990000000
C69 -4.2601770000000 -2.1281300000000 0.5422810000000
C70 -4.6251020000000 -3.2878040000000 1.2176370000000
C71 -4.3998730000000 -4.5359730000000 0.6322730000000
H72 -3.6654950000000 -5.5697220000000 -1.1089300000000
H73 -3.0352620000000 -3.5342760000000 -2.3045120000000
H74 -4.4398300000000 -1.1602100000000 1.0041360000000
H75 -5.0890400000000 -3.2197870000000 2.1978260000000
H76 -4.6827160000000 -5.4453110000000 1.1548390000000
C77 -3.3076190000000 -0.8760450000000 -1.3406290000000
TSI (Energy = -2502.89583 Hartrees, 13.71 Kcal mol⁻¹)

N1 1.6347230000000 1.5455950000000 -0.2709460000000
C2 3.8664670000000 1.8096280000000 -1.2935230000000
C3 1.9645650000000 3.2455700000000 -1.8416950000000
C4 3.1578270000000 2.5053500000000 -2.5036890000000
C5 0.9294490000000 2.1715490000000 -1.4150560000000
C6 2.9530280000000 2.2170370000000 -0.1161730000000
H7 4.8814290000000 2.1916040000000 -1.1433290000000
H8 2.8251870000000 1.7940400000000 -3.2658270000000
H9 0.7487320000000 1.4701150000000 -2.3683000000000
H10 3.3549990000000 2.0488080000000 0.8840620000000
H11 3.9284630000000 0.7254400000000 -1.3996610000000
H12 1.5439740000000 4.0395390000000 -2.4628610000000
H13 3.8179570000000 3.2262700000000 -2.9935430000000
C14 2.5666120000000 3.6594440000000 -0.4800880000000
H15 1.8452110000000 4.0991150000000 0.2146470000000
H16 3.4293130000000 4.3234710000000 -0.5803920000000
C17 -0.4290140000000 2.6968860000000 -0.9882120000000
N18 -1.3339890000000 1.9739410000000 -0.3548170000000
C19 -2.4935350000000 2.7006350000000 -0.0730290000000
C20 -2.4678880000000 3.9784490000000 -0.5520350000000
H21 -3.2302130000000 4.7356730000000 -0.4369740000000
P22 1.1595840000000 0.0761070000000 0.4008860000000
Ir23 -1.0806630000000 -0.3056600000000 -0.1987550000000
H24 -2.0843740000000 -0.4389740000000 1.1439700000000
C25 1.3593830000000 0.3241060000000 2.2012840000000
C26 1.3120040000000 0.6840750000000 4.9832730000000
C27 1.1295960000000 1.5959200000000 2.7476280000000
C28 1.5572740000000 -0.7678290000000 3.0605710000000
C29 1.5340320000000 -0.5849630000000 4.4438770000000
C30 1.1112440000000 1.7733710000000 4.1315770000000
TSII (Energy = -2502.89109 Hartrees, 16.70 Kcal mol⁻¹)

N1 1.6093260000000 1.5855550000000 -0.3250610000000
C2 3.7532660000000 1.8228080000000 -1.5202360000000
C3 1.8623520000000 3.3406110000000 -1.8483630000000
C4 2.9724680000000 2.5939210000000 -2.6374700000000
C5 0.8334370000000 2.2787370000000 -1.3849600000000
C6 2.9564880000000 2.2096800000000 0.2448110000000
H7 4.7911690000000 2.1623050000000 -1.4422730000000
H8 2.5541340000000 1.9262140000000 -3.3195430000000
H9 0.5709170000000 1.6094620000000 -2.2136060000000
H10 3.4340940000000 1.9880650000000 0.7016450000000
H11 3.7640720000000 0.7425340000000 -1.6738960000000
H12 1.4153800000000 4.1724100000000 -2.3979980000000
H13 3.6148690000000 3.3149350000000 -3.1502620000000
C14 2.5918880000000 3.6772660000000 -0.5277180000000
H15 1.9509360000000 4.1110400000000 0.2448110000000
H16 3.4663120000000 4.3164660000000 -0.6768320000000
C17 -0.4722240000000 2.8021090000000 -0.8240340000000
N18 -1.3986380000000 2.0150890000000 -0.3072590000000
C19 -2.5123570000000 2.7289580000000 0.1418420000000
C20 -2.4211740000000 4.0728600000000 -0.0721320000000
H21 -3.1475570000000 4.8279270000000 0.1929300000000
P22 1.1378890000000 0.1083420000000 0.3299670000000
Ir23 -1.1165700000000 -0.2558560000000 -0.2287770000000
H24 -2.1336900000000 -0.3348910000000 1.1091090000000
C25 1.4029110000000 0.3014610000000 2.1260240000000
C26 1.4670440000000 0.5787630000000 4.9117800000000
C27 1.2509920000000 1.5652950000000 2.7140606000000
C28 1.5815030000000 -0.8246970000000 2.9446000000000
C29 1.6137660000000 -0.6829250000000 4.3315070000000
C30 1.2870010000000 1.7014930000000 4.1074100000000
H31 1.6987010000000 -1.8093650000000 2.5008550000000
H32 1.7553050000000 -1.5583580000000 4.9583940000000
H33 1.1755980000000 2.6842330000000 4.5506400000000
H34 1.4925000000000 0.6857130000000 5.9921120000000
S35 -0.9163830000000 4.4757400000000 -0.8206540000000
C36 -3.6679220000000 2.0582040000000 0.7817780000000
C37 -3.5585350000000 1.5324170000000 2.0767510000000
C38 -4.8863520000000 1.9520910000000 0.0993620000000
C39 -4.6363414000000 0.8737470000000 2.6617750000000
H40 -2.6224790000000 1.6455790000000 2.6224350000000
C41 -5.9660900000000 1.2919710000000 0.6870190000000
TSIII (Energy = -250.88825 Hartrees) 18.48 Kcal mol⁻¹

N1 1.75015700000000 1.67058700000000 -0.20370800000000
C2 3.99214900000000 1.97019900000000 -1.20027900000000
C3 2.07083500000000 3.36013800000000 -1.79336300000000
| H54 | 5.7885970000000 -1.9134150000000 0.79530200000000 | \( -1.9134150000000 \times 10^0 \) | \( 0.79530200000000 \times 10^0 \) |
| H55 | 3.0780770000000 -3.6637960000000 -2.0505170000000 | \( -3.6637960000000 \times 10^0 \) | \( -2.0505170000000 \times 10^0 \) |
| H56 | 5.3140120000000 -3.5950020000000 -0.97090700000000 | \( -3.5950020000000 \times 10^0 \) | \( -0.97090700000000 \times 10^0 \) |
| H65 | -1.1630330000000 1.4846150000000 1.84615000000000 | \( 1.4846150000000 \times 10^0 \) | \( 1.8461500000000 \times 10^0 \) |
| C66 | -5.1799100000000 -3.1747850000000 -1.71792500000000 | \( -3.1747850000000 \times 10^0 \) | \( -1.7179250000000 \times 10^0 \) |
| C67 | -3.9828900000000 -2.1556200000000 0.20186700000000 | \( -2.1556200000000 \times 10^0 \) | \( 0.20186700000000 \times 10^0 \) |
| C68 | -5.3140120000000 -3.5950020000000 -0.97090700000000 | \( -3.5950020000000 \times 10^0 \) | \( -0.97090700000000 \times 10^0 \) |
| H76 | 6.2653840000000 -3.4121960000000 -2.47026300000000 | \( -3.4121960000000 \times 10^0 \) | \( 2.4702630000000 \times 10^0 \) |
| C77 | 2.7052450000000 0.6921480000000 3.33446600000000 | \( 0.6921480000000 \times 10^0 \) | \( 3.3344660000000 \times 10^0 \) |

References

[1] Jaguar, version 7.9, Schrodinger, LLC, New York, NY, 2011.
[2] (a) Becke, A. D. J. Chem. Phys. 1993, 98, 5648–5652. (b) Lee, C.; Yang, W.; Parr, R. G. Phys. Rev. B. 1988, 37, 785–789.
[3] Grimme, S.; Antony, J.; Ehrlich, S.; Krieg, H. J. Chem. Phys. 2010, 132, 154104.
[4] Hay, P. J.; Wadt, W. R. J. Chem. Phys. 1985, 82, 270–283.
7. SFC and GC Chromatograms
Apex: 55.712 min.
Area: 27110

Apex: 58.005 min.
Area: 1,280e+6

Apex: 55.169 min.
Area: 1,477e+6

Apex: 57.944 min.
Area: 1,482e+6

OH

(R)-1ac
8. $^1$H, $^{13}$C and $^{19}$F NMR spectroscopic data
$^1\text{H}$ and $^{19}\text{F}$ NMR of resolved allylic alcohols
9. References

1) Liu, Z.-Q.; Sun, L.; Wang, J.-G.; Han, J.; Zhao, Y.-K.; Zhou, B. Org. Lett. **2009**, 11, 1437.
2) Sudhakar, G.; Raghavaiah, J.; Mahesh, G.; Singarapu, K. K. Org. Biomol. Chem. **2016**, 14, 2866.
3) Miller, K. M.; Huang, W.-S.; Jamison, T. F. *J. Am. Chem. Soc.* **2003**, 125, 3442.
4) Ohashi, M.; Saijo, H.; Arai, T.; Ogoshi, S. Organometallics **2010**, 29, 6534.
5) Liu, J.; Krajangsri, S.; Yang, J.; Li, J.-Q.; Andersson, P. G. Nat. Catal. **2018**, 1, 438.
6) Downey, C. W.; Johnson, M. W. *Tetrahedron Lett.* **2007**, 48, 3559.
7) Abate, A.; Brenna, E.; Costantini, A.; Fuganti, C.; Gatti, F. G.; Malpezzi, L.; Serra, S. *J. Org. Chem.* **2006**, 71, 5228.
8) Balcells, S.; Haughey, M. B.; Walker, J. C. L.; Josa-Culleré, L.; Towers, C.; Donohoe, T. J. *Org. Lett.* **2018**, 20, 3583.
9) Hatano, M.; Mizuno, T.; Ishihara, K. *Chem. Commun.* **2010**, 46, 5443.
10) Lautens, M.; Maddess, M. L.; Sauer, E. L. O.; Ouellet, S. G. *Org. Lett.* **2002**, 4, 83.
11) Birman, V. B.; Jiang, H. *Org. Lett.* **2005**, 7, 3445.
12) Infante, R.; Hernández, Y.; Nieto, J.; Andrés, C. *Eur. J. Org. Chem.* **2013**, 2013, 4863.
13) Pisani, L.; Superchi, S.; D’Elia, A.; Scafato, P.; Rosini, C. *Tetrahedron* **2012**, 68, 5779.
14) Enders, D.; Lotter, H. *Angew. Chem.* **1981**, 93, 831.
15) Lin, N.-H.; Overman, L. E.; Rabinowitz, M. H.; Robinson, L. A.; Sharp, M. J.; Zablocki, J. *J. Am. Chem. Soc.* **1996**, 118, 9062.
16) Donohoe, T. J.; Johnson, P. D.; Pye, R. J.; Keenan, M. *Org. Lett.* **2004**, 6, 2583.
17) Yoshino, M.; Eto, K.; Takahashi, K.; Ishihara, J.; Hatakeyama, S. *Org. Biomol. Chem.* **2012**, 10, 8164.
18) Kumar, M.; Bromhead, L.; Anderson, Z.; Overy, A.; Burton, J. W. *Chem. Eur. J.* **2018**, 24, 16753.
19) Xiong, P.; Xu, H.-H.; Xu, H.-C. *J. Am. Chem. Soc.* **2017**, 139, 2956.
20) Adam, W.; Peters, K.; Peters, E. M.; Stegmann, V. R.; *J. Am. Chem. Soc.* **2000**, 122, 2958.
21) Infante, R.; Hernández, Y.; Nieto, J.; Andrés, C. *Eur. J. Org. Chem.* **2013**, 22, 4863.
22) Yadav, J. S.; Mysorekar, S. V.; Rao, A. V. R. *Tetrahedron* **1989**, 45, 735.