Supporting Information

Synthesis of Optically Active 2,3-Disubstituted Indoline Derivatives via a Cycloaddition between Benzynes and α,β-Unsaturated-γ-Aminobutyronitriles

Takashi Ikawa,* Yuta Sumii, Shigeaki Masuda, Ding Wang, Yuto Emi, Akira Takagi, Shuji Akai*

Graduate School of Pharmaceutical Sciences, Osaka University, 1-6 Yamadaoka, Suita, Osaka 565-0871, Japan

ikawa@phs.osaka-u.ac.jp, akai@phs.osaka-u.ac.jp

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Table S1. Chemical and optical stability of γ-tosylamino-α,β-unsaturated nitrile 3f, ester 3h and ketone 3i. a

<table>
<thead>
<tr>
<th>entry</th>
<th>R</th>
<th>3</th>
<th>er of 3b (before)</th>
<th>er of 3b (after)</th>
<th>recovery (%)</th>
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<td>&gt;99:1</td>
<td>&gt;99:1</td>
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<td>CO₂Me</td>
<td>3h</td>
<td>99:1</td>
<td>84:16</td>
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<td>3</td>
<td>COMe</td>
<td>3i</td>
<td>98:2</td>
<td>74:26</td>
<td>72</td>
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</table>

aConditions: 3 (0.10 mmol), CsF (0.30 mmol), 18-crown-6 (0.30 mmol) in THF (2.0 mL) were stirred for 12 h at rt. bEnantiomeric ratio of (S)-3 and (R)-3 determined by chiral HPLC. cDetermined by 1H NMR using 1,1,2,2-tetrachloroethane as an internal standard.

Procedure for Table S1

The test tube was charged with γ-tosylamino-α,β-unsaturated compound (S)-3f (28 mg, 0.10 mmol) [or (S)-3h (31 mg, 0.10 mmol) or (S)-3i (30 mg, 0.10 mmol)], 18-crown-6 (80 mg, 0.30 mmol) and a stirrer bar. The test tube was filled with Ar and equipped with rubber septum. THF (2.0 mL, 50 mM) was added to the mixture via a syringe. The septum was quickly opened and CsF (45 mg, 0.30 mmol) was added to the test tube and then closed with a septum. The mixture was stirred for 12 hours at room temperature. The reaction mixture was passed through a short pad of silica gel using EtOAc and solvents were removed under reduced pressure. 1,1,2,2-Tetrachloroethane (11 μL, 0.10 mmol) was added to the residue and the mixture was subjected to 1H NMR analysis for the calculation of the recovery (%) of 3 (shown in Table S1). The enantiomeric ratio (= er) of recovered 3 was determined by HPLC analysis at 20 °C, using a CHIRALCEL ID column (vide infra in details).
General considerations:

Reagents: A round-bottomed flask containing a stir-bar with a three-way stopcock and a test tube with screw cap was used as a reactor. 18-Crown-6 was recrystallized from anhydrous MeCN in a Schlenk flask. 2.3 M solutions of nBuLi in hexane were purchased from Kanto Chemical. Anhydrous THF, CH$_2$Cl$_2$ and MeCN were obtained from Kanto Chemical, and purified by Glass Contour solvent dispensing system (Nikko Hansen & Co., Ltd., Osaka, Japan) using two packed columns of activated molecular sieves. Anhydrous DMF was purchased from Kanto Chemicals, and purified by Glass Contour solvent dispensing system using a packed column of activated molecular sieves and an isocyanate column. 2-(Trimethylsilyl)phenyl trifluoromethanesulfonate 5a, 3-methoxy-2-(trimethylsilyl)phenyl trifluoromethanesulfonate 5b and 2-(tert-butyldimethylsilyl)-4-methyl-6-(trimethylsilyl)phenyl trifluoromethanesulfonate 5c were prepared according to the literature. All other reagents were purchased from Wako Pure Chemical Industries, Tokyo Chemical Industry, Aldrich Chemical, and Kishida Chemical and used without further purification. Flash chromatography was performed with Silica gel 60N, spherical neutral (40–50 μm), purchased from Kanto Chemical or Universal Column Premium (30 μm) purchased from Yamazen for automatic column chromatography system. All reactions were monitored by thin-layer chromatography (TLC) on glass-backed silica gel 60 F$_{254}$, 0.2 mm plates (Merck), and compounds were visualized under UV light (254 nm). These TLC plates were also used for preparative thin-layer chromatography (PTLC). The purification by Gel Permeation Chromatography (GPC) was carried out on LaboACE LC-5060 with JAIGEL-2H columns (Japan Analytical Industry).

Analytical methods: Melting points were recorded on a Yanagimoto melting point apparatus and are uncorrected. IR spectra were obtained on a SHIMADZU FTIR-8400S. $^1$H NMR and $^{13}$C NMR spectra were recorded on a JEOL JMN-ECA-500 ($^1$H: 500 MHz, $^{13}$C: 125 MHz) or a JEOL JMNECS-400 ($^1$H: 400 MHz, $^{13}$C: 100 MHz) or a JEOL AL-300 ($^1$H: 300 MHz, $^{13}$C: 75 MHz) instrument with chemical shifts reported in ppm relative to the residual deuterated solvent. GC spectra were taken on SHIMADZU GC-2010. The mass spectra were recorded on a JEOL JMS-S3000 (MALDI) spectrometer. HPLC analyses were carried out using a JASCO LC-2000Plus system (HPLC pump: PU-2080, UV detector: MD-4017) equipped with a Daicel CHIRALPAK AD-3 column or a Daicel CHIRALPAK ID column. All optically active compounds are detected by 254 nm wavelength absorption. “Yield” refers to the isolated yields of compounds showing at most only trace peaks in the $^1$H NMR spectra that are not attributable to the assigned structure. $^1$H NMR and melting points (where applicable) of all known compounds were taken. All new products were further characterized by high resolution mass spectrum (HRMS). The enantioselectivities (= ee) were determined by chiral HPLC analysis. The relative stereochemistry and regiochemistry were confirmed by NOESY.
General Procedure A for reactions of \(\gamma\)-tosylamino-\(\alpha,\beta\)-unsaturated compounds 3 with benzyne precursors 5 (Tables 1, 2, 4 and Scheme 2).

A test tube was charged with benzyne precursor 5 (1.5 equiv), and a magnetic stir bar. THF (not anhydrous) (1.0 mL, 50 mM) was added to the tube and stirred for a few minutes to be fully dissolved. \(\gamma\)-Amino-\(\alpha,\beta\)-unsaturated compound 3 (1.0 equiv) and 18-crown-6 (3.0 equiv) were added to the solution and the flask was equipped with a screw cap. (This solution was stirred for 10 min at indicated temperature if the reaction was conducted at 0 °C or below.) CsF (3.0 equiv) was quickly added to the test tube and then closed with a screw cap. The mixture was stirred at indicated temperature until either \(\alpha,\beta\)-unsaturated compound 3 or benzyne precursor 5 was consumed as judged by TLC analysis. The reaction mixture was passed through a short pad of silica gel using EtOAc and solvents were removed under reduced pressure. The residue was subjected to \(^1\)H NMR analysis for calculating the ratio of the two diastereomer (trans-1 or cis-1). The crude product was purified by flash column chromatography on silica gel or PTLC (a mixture of hexane and EtOAc, hexane and CH\(_2\)Cl\(_2\) and EtOAc) to afford an objective substituted indoline 1 and a single addition product 6.

![trans-1f](image)

2-((2S,3R)-2-Isopropyl-1-tosylindolin-3-yl)acetonitrile (trans-1f) (Table 2, entry 1): According to the General Procedure A, a mixture of CsF (91 mg, 0.60 mmol), 18-crown-6 (0.16 g, 0.60 mmol), 2-((trimethylsilyl)phenyl trifluoromethanesulfonate 5a\(^1\) (90 mg, 0.30 mmol) and (S,E)-N-(1-cyano-4-methylpent-1-en-3-yl)-4-methylbenzenesulfonamide 3f (56 mg, 0.20 mmol) was stirred in THF (2.0 mL, 0.10 M) for 1 hour at room temperature. The crude product (trans-1f/cis-1f = 16:1, determined by 400 MHz \(^1\)H NMR analysis) was purified by column chromatography on silica gel (hexane/EtOAc = 20:1 to 4:1) to provide the titled compound trans-1f as a colorless solid (51 mg, 72\%, >99\% ee). The relative stereochemistry was determined by NOESY spectra and the optical purity was determined by HPLC analysis at 20 °C, using a CHIRALCEL AD-3 column [hexane/2-propanol = 80:20, 1.0 mL/min; retention times 12.7 min (2S,3R), 9.1 min (2R,3S)]. \(\[\alpha\]_D^{20} = -137.4 (c 0.12, CHCl\(_3\)).\) Mp: 139–141 °C. \(\text{\(^1\)H NMR (500 MHz, CDCl\(_3\)) \(\delta\): 0.81 (3 H, d, \(J = 7.0\) Hz), 1.01 (3 H, d, \(J = 7.0\) Hz), 1.11 (1 H, dd, \(J = 17.0, 9.5\) Hz), 1.68 (1 H, dd, \(J = 17.0, 7.0\) Hz), 2.15 (1 H, septd, \(J = 7.0, 5.0\) Hz), 2.36 (3 H, s), 3.05–3.09 (1 H, m), 3.77 (1 H, dd, \(J = 5.0, 2.0\) Hz), 7.08 (1 H, dd, \(J = 7.5, 7.5\) Hz), 7.14 (1 H, d, \(J = 7.5\) Hz), 7.22 (2 H, d, \(J = 8.0\) Hz), 7.32 (1 H, ddd, \(J = 7.5, 7.5, 1.0\) Hz), 7.57 (2 H, d, \(J = 8.0\) Hz), 7.75 (1 H, d, \(J = 7.5\) Hz). \(\text{\(\text{\(^{13}\)C NMR (125 MHz, CDCl\(_3\)) \(\delta\): 16.4, 18.1, 21.5, 24.0, 33.3, 39.2, 72.1, 117.3, 117.5, 124.5, 125.1, 127.0, 129.5, 129.9, 132.9, 134.6, 141.6, 144.5. IR (neat): 3446, 2964, 2251, 1597 cm\(^{-1}\). HRMS (MALDI) Caled for C\(_{20}\)H\(_{22}\)N\(_3\)O\(_5\)S [M+Na]\(^+\): 377.1294, found 377.1291. All
spectroscopic data of the obtained product (2S,3R)-1f was in good agreement with (±)-trans-1f which was synthesized from (±)-3f.

![cis-1f](image)

**cis-1f**

2-((2S,3S)-2-Isopropyl-1-tosylindolin-3-yl)acetanitrite (cis-1f) (Table 2, entry 1) was obtained from above-mentioned crude reaction mixture as a colorless solid (2.4 mg, 3%). The relative stereochemistry was determined by NOESY spectra. $[\alpha]_{D}^{20} = -2.4$ (c 0.12, CHCl$_3$). Mp: 131–133 °C. $^1$H NMR (500 MHz, CDCl$_3$) δ: 0.51 (3 H, d, $J = 7.0$ Hz), 1.22 (3 H, d, $J = 7.0$ Hz), 1.96 (1 H, septd, $J = 7.0, 2.5$ Hz), 2.37 (3 H, s), 2.54 (1 H, dd, $J = 17.0, 9.0$ Hz), 2.68 (1 H, dd, $J = 17.0, 7.0$ Hz), 2.97–3.02 (1 H, m), 4.33 (1 H, d, $J = 8.5, 2.5$ Hz), 7.03 (1 H, d, $J = 8.0$ Hz), 7.10–7.15 (1 H, m), 7.14 (2 H, d, $J = 8.0$ Hz), 7.30 (1 H, dd, $J = 8.0, 8.0$ Hz), 7.44 (2 H, d, $J = 8.0$ Hz), 7.66 (1 H, d, $J = 8.0$ Hz).

$^{13}$C NMR (125 MHz, CDCl$_3$) δ: 15.8, 17.4, 21.0, 21.6, 29.0, 40.7, 69.3, 118.2, 119.5, 121.8, 126.1, 126.9, 128.9, 129.7, 134.9, 135.2, 142.8, 144.2. IR (neat): 2967, 2371, 1597 cm$^{-1}$. HRMS (MALDI) Calcd for C$_{20}$H$_{22}$N$_2$O$_2$S [M+Na]$^+$: 377.1294, found 377.1294.

![6f](image)

**6f**

(S,E)-N-(1-Cyano-4-methylpent-1-en-3-yl)-4-methyl-N-phenylbenzenesulfonamide (6f) (Table 2, entry 1) was obtained from above-mentioned crude reaction mixture as a colorless solid (14 mg, 20%). $[\alpha]_{D}^{21} = +23.2$ (c 0.12, CHCl$_3$). Mp: 123–126 °C. $^1$H NMR (500 MHz, CDCl$_3$) δ: 0.75 (3 H, d, $J = 7.0$ Hz), 1.14 (3 H, d, $J = 7.0$ Hz), 1.58 (1 H, septd, $J = 10.0, 7.0$ Hz), 2.42 (3 H, s), 4.38 (1 H, dd, $J = 10.0, 10.0$ Hz), 5.52 (1 H, d, $J = 16.0$ Hz), 6.38 (1 H, dd, $J = 16.0, 10.0$ Hz), 7.00 (2 H, d, $J = 7.5$ Hz), 7.23 (2 H, d, $J = 8.5$ Hz), 7.33–7.40 (3 H, m), 7.46 (2 H, d, $J = 8.5$ Hz). $^{13}$C NMR (125 MHz, CDCl$_3$) δ: 19.5, 20.3, 21.5, 29.8, 67.5, 102.9, 116.4, 127.6, 129.2, 129.2, 129.4, 132.0, 135.4, 137.0, 143.8, 151.6. IR (neat): 2965, 2225, 1595, 1489 cm$^{-1}$. HRMS (MALDI) Calcd for C$_{20}$H$_{22}$N$_2$O$_2$S [M+Na]$^+$: 377.1294, found 377.1293.
According to the General Procedure A, a mixture of CsF (23 mg, 0.15 mmol), 18-crown-6 (40 mg, 0.15 mmol), 2-(trimethylsilyl)phenyl trifluoromethanesulfonate 5a (22 mg, 75 μmol) and (S,E)-N-(1-cyano-4-methylpent-1-en-3-yl)-2,4,6-trimethylbenzenesulfonamide 3g (15 mg, 50 μmol) was stirred in THF (2.0 mL, 0.10 M) for 1 hour at room temperature. The crude product (trans-1g/cis-1g = 6.9:1, determined by 400 MHz 1H NMR analysis) was purified by PTLC (hexane/EtOAc = 3:1) to provide the titled compound trans-1g as a colorless oil (13 mg, 69%). The relative stereochemistry was determined by NOESY spectra. [α]D 20 = −2.0 (c 0.12, CHCl₃). 1H NMR (500 MHz, CDCl₃) δ: 0.60 (3 H, d, J = 7.0 Hz), 0.82 (3 H, d, J = 7.0 Hz), 1.77–1.84 (1 H, m), 2.33 (3 H, s), 2.36 (1 H, dd, J = 16.5, 9.0 Hz), 2.47 (1 H, dd, J = 16.5, 7.0 Hz), 2.64 (6 H, s), 3.15–3.20 (1 H, m), 3.82 (1 H, dd, J = 5.0, 2.0 Hz), 7.00 (2 H, s), 7.08 (1 H, dd, J = 7.5, 7.5 Hz), 7.21 (1 H, dd, J = 8.0, 7.5 Hz), 7.24–7.28 (2 H, m). 13C NMR (125 MHz, CDCl₃) δ: 16.3, 18.1, 21.2, 23.3, 24.2, 32.5, 39.6, 118.1, 118.6, 124.6, 125.2, 129.2, 132.2, 132.5, 134.1, 140.8, 142.6, 143.8. IR (neat): 2958, 2249, 1324 cm⁻¹. HRMS (MALDI) Calcd for C₂₂H₂₆N₂O₂S [M+Na]⁺: 405.1607, found 405.1602.

2-(2S,3R)-2-Isopropyl-1-(mesitylsulfonyl)indolin-3-yl)acetonitrile (trans-1g) (Table 1, entry 14) was obtained from above-mentioned crude reaction mixture as a colorless oil (3.8 mg, 20%). The relative stereochemistry was determined by NOESY spectra. [α]D 20 = −8.3 (c 0.15, CHCl₃). 1H NMR (500 MHz, CDCl₃) δ: 0.44 (3 H, d, J = 6.5 Hz), 0.83 (3 H, d, J = 7.0 Hz), 1.88–1.97 (1 H, m), 2.31 (3 H, s), 2.57–2.64 (7 H, m), 2.83 (1 H, dd, J = 17.0, 7.0 Hz), 2.97–3.02 (1 H, m), 3.92–3.99 (1 H, m), 4.31 (1 H, dd, J = 8.0, 2.5 Hz), 6.96 (1 H, s), 7.06–7.18 (3 H, m). 13C NMR (125 MHz, CDCl₃) δ: 16.2, 17.6, 20.9, 21.1, 23.4, 29.0, 41.8, 68.7, 118.3, 120.2, 121.9, 126.1, 128.5, 132.4, 140.9. IR (neat): 2959, 2249, 1326 cm⁻¹. HRMS (MALDI) Calcd for C₂₂H₂₆N₂O₂S [M+Na]⁺: 405.1607, found 405.1605.

S6
**trans-1k**

2-((2S,3R)-2-Methyl-1-tosylindolin-3-yl)acetanilide (trans-1k) (Table 4, entries 1 and 2)

**For entry 1:** According to the General Procedure A, a mixture of CsF (22 mg, 0.15 mmol), 18-crown-6 (40 mg, 0.15 mmol), 2-(trimethylsilyl)phenyl trifluoromethanesulfonate 5a1 (23 mg, 75 μmol) and (S,E)-N-(1-cyano-4-methylbut-1-en-3-yl)-4-methylbenzenesulfonamide 3k (13 mg, 50 μmol) was stirred in THF (2.0 mL, 0.10 M) for 1 hour at room temperature. The crude product (trans-1k/cis-1k = 1.1:1) was purified by PTLC (hexane/EtOAc = 2:1) to provide the titled compound trans-1k as a colorless oil (1.6 mg, 10%).

The relative stereochemistry was determined by NOESY spectra. [α]$_{D}^{20}$ = −21.8 (c 0.10, CHCl$_3$). $^1$H NMR (500 MHz, CDCl$_3$) δ: 1.37 (1 H, dd, $J$ = 17.0, 9.0 Hz), 1.47 (3 H, d, $J$ = 6.5 Hz), 1.74 (1 H, dd, $J$ = 17.0, 7.0 Hz), 2.38 (3 H, s), 2.92 (1 H, td, $J$ = 8.0, 1.5 Hz), 4.03 (1 H, qd, $J$ = 6.5, 1.5 Hz), 7.09 (1 H, td, $J$ = 7.5, 1.0 Hz), 7.19 (1 H, d, $J$ = 7.5 Hz), 7.24 (2 H, d, $J$ = 7.5 Hz), 7.34 (1 H, td, $J$ = 7.5, 1.0 Hz), 7.62 (2 H, d, $J$ = 8.0 Hz), 7.74 (1 H, d, $J$ = 7.5 Hz). $^{13}$C NMR (125 MHz, CD$_2$OD) δ: 21.6, 22.9, 23.7, 45.2, 63.5, 117.2, 117.3, 124.9, 125.3, 127.0, 129.8, 130.0, 131.3, 135.0, 140.5, 144.6. IR (neat): 2927, 2247, 1354 cm$^{-1}$. HRMS (MALDI) Calcd for C$_{13}$H$_{14}$N$_2$O$_3$S [M+Na]$^+$: 349.0981, found 349.0975.

**trans-1l**

2-((2S,3R)-2-Benzyl-1-tosylindolin-3-yl)acetanilide (trans-1l) (Table 4, entry 3): According to the General Procedure A, a mixture of CsF (91 mg, 0.60 mmol), 18-crown-6 (0.16 g, 0.60 mmol), 2-(trimethylsilyl)phenyl trifluoromethanesulfonate 5a1 (90 mg, 0.30 mmol) and (S,E)-N-(1-cyano-4-phenylbut-1-en-3-yl)-4-methylbenzenesulfonamide 3l (65 mg, 0.20 mmol) was stirred in THF (2.0 mL, 0.10 M) for 1 hour at room temperature. The crude product (trans-1l/cis-1l = 5.0:1, determined
by 400 MHz $^1$H NMR analysis) was purified by column chromatography on silica gel (hexane/EtOAc = 20:1 to 4:1) to provide the titled compound trans-1l as a yellow solid (62 mg, 77%). The relative stereochemistry was determined by NOESY spectra. $[\alpha]_{D}^{20} = -86.1$ ($c$ 0.09, CHCl$_3$). Mp: 135–138 °C. $^1$H NMR (500 MHz, CDCl$_3$) $\delta$: 1.24 (1 H, dd, $J = 17.0, 8.0$ Hz), 1.45 (1 H, dd, $J = 17.0, 8.0$ Hz), 2.37 (3 H, s), 2.80 (1 H, dd, $J = 13.5, 10.5$ Hz), 3.05 (1 H, td, $J = 8.0, 1.5$ Hz), 3.39 (1 H, dd, $J = 13.5, 4.5$ Hz), 4.11 (1 H, ddd, $J = 10.5, 4.5, 1.5$ Hz), 7.07 (1 H, dd, $J = 7.5, 7.5, 1.0$ Hz), 7.17 (1 H, d, $J = 7.5$ Hz), 7.23–7.27 (5 H, m), 7.31–7.35 (3 H, m), 7.65 (2 H, d, $J = 8.0$ Hz), 7.75 (1 H, d, $J = 8.0$ Hz). $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$: 21.5, 23.8, 41.3, 41.9, 68.4, 116.8, 124.9, 125.3, 126.9, 127.1, 128.8, 129.6, 129.9, 131.2, 134.7, 135.6, 140.7, 144.6. IR (neat): 2922, 2249, 1356, 1167 cm$^{-1}$. HRMS (MALDI) Calcd for C$_{24}$H$_{22}$N$_2$O$_2$S [M+Na]$^+$: 425.1294, found 425.1294.

 cis-1l

2-((2S,3S)-2-Benzyl-1-tosylindolin-3-yl)acetonitrile (cis-1l) (Table 4, entry 3) was obtained from above-mentioned crude reaction mixture as a yellow oil (13 mg, 16%). The relative stereochemistry was determined by NOESY spectra. $[\alpha]_{D}^{20} = -30.1$ ($c$ 0.14, CHCl$_3$). $^1$H NMR (500 MHz, CDCl$_3$) $\delta$: 2.36 (3 H, s), 2.54 (1 H, dd, $J = 17.0, 8.0$ Hz), 2.64 (1 H, dd, $J = 17.0, 7.5$ Hz), 2.94 (2 H, d, $J = 7.5$ Hz), 3.16–3.22 (1 H, m), 4.62 (1 H, dd, $J = 13.5, 4.5$ Hz), 7.14–7.37 (10 H, m), 7.45 (2 H, d, $J = 8.0$ Hz), 7.70 (1 H, d, $J = 8.0$ Hz). $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$: 16.8, 21.7, 36.0, 41.1, 66.3, 118.0, 119.2, 123.6, 125.9, 127.1, 128.7, 129.3, 129.6, 129.9, 133.3, 135.4, 136.6, 141.2, 144.3. IR (neat): 2924, 2247, 1477, 1355 cm$^{-1}$. HRMS (MALDI) Calcd for C$_{24}$H$_{22}$N$_2$O$_2$S [M+Na]$^+$: 425.1294, found 425.1294.

trans-1m

2-((2S,3R)-2-Isobutyl-1-tosylindolin-3-yl)acetonitrile (trans-1m) (Table 4, entries 4 and 5)

For entry 4: According to the General Procedure A, a mixture of CsF (91 mg, 0.60 mmol), 18-crown-6 (0.16 g, 0.60 mmol), 2-(trimethylsilyl)phenyl trifluoromethanesulfonate 5a (90 mg, 0.30 mmol) and (S,E)-N-(1-cyano-5-methylhexa-1-en-3-yl)-4-methylbenzenesulfonamide 3m (58 mg, 0.20 mmol) was stirred in THF (2.0 mL, 0.10 M) for 1 hour at room temperature. The crude product (trans-1m/cis-1m = 2.3:1, determined by 400 MHz $^1$H NMR analysis) was purified by column chromatography on
silica gel (hexane/EtOAc = 20:1 to 4:1) to provide the titled compound *trans-1m* as a colorless solid (37 mg, 51%).

**For entry 5:** According to the General Procedure A, a mixture of CsF (91 mg, 0.60 mmol), 18-crown-6 (0.16 g, 0.60 mmol), 2-(trimethylsilyl)phenyl trifluoromethanesulfonate 5a (90 mg, 0.30 mmol) and (S,E)-N-(1-cyano-5-methylhexa-1-en-3-yl)-4-methylbenzenesulfonamide 3m (58 mg, 0.20 mmol) was stirred in THF (2.0 mL, 0.10 M) for 24 hours at −40 °C. The crude product (*trans-1m/cis-1m* = 3.2:1, determined by 400 MHz 1H NMR analysis) was purified by column chromatography on silica gel (hexane/EtOAc = 20:1 to 4:1) to provide the titled compound *trans-1m* as a colorless solid (38 mg, 51%). The relative stereochemistry was determined by NOESY spectra. $\alpha_{D}^{20} = −128.6$ (c 0.11, CHCl3).

Mp: 105–107 °C. 1H NMR (500 MHz, CDCl3) δ: 0.99 (3 H, d, $J = 7.0$ Hz), 1.03 (3 H, d, $J = 7.0$ Hz), 1.16 (1 H, dd, $J = 17.0, 9.5$ Hz), 1.47 (1 H, ddd, $J = 14.0, 8.5, 5.5$ Hz), 1.60–1.73 (2 H, m), 1.80–1.90 (1 H, m), 2.95–2.98 (1 H, m), 3.99 (1 H, dd, $J = 8.0, 6.5$ Hz), 7.09 (1 H, dd, $J = 7.5, 7.5$ Hz), 7.17 (1 H, d, $J = 7.5$ Hz), 7.24 (2 H, d, $J = 8.5$ Hz), 7.33 (1 H, dd, $J = 7.5, 7.5$ Hz), 7.60 (2 H, d, $J = 8.5$ Hz), 7.74 (1 H, d, $J = 7.5$ Hz). 13C NMR (125 MHz, CDCl3) δ: 21.5, 22.0, 23.1, 23.6, 24.0, 43.4, 45.2, 65.8, 117.4, 117.8, 125.0, 125.2, 126.9, 129.5, 129.9, 132.1, 134.9, 140.6, 144.5. IR (neat): 2958, 1597 cm$^{-1}$. HRMS (MALDI) Calcd for C21H24N2O2S [M+Na]$^+$: 391.1451, found 391.1455.

The relative stereochemistry was determined by NOESY spectra. $\alpha_{D}^{20} = −126.6$ (c 0.10, CHCl3). Mp: 114–117 °C. 1H NMR (500 MHz, CDCl3) δ: 0.93 (3 H, d, $J = 7.0$ Hz), 1.09 (3 H, d, $J = 7.0$ Hz), 1.35–1.41 (1 H, m), 2.10–2.18 (1 H, m), 2.37 (3 H, s), 2.41 (1 H, dd, $J = 17.0, 9.0$ Hz), 2.59 (1 H, dd, $J = 17.0, 7.0$ Hz), 2.92–2.97 (1 H, m), 4.42–4.47 (1 H, m), 7.06 (1 H, d, $J = 8.0$ Hz), 7.13–7.16 (3 H, m), 7.32 (1 H, dd, $J = 8.0, 8.0$ Hz), 7.44 (2 H, d, $J = 8.0$ Hz), 7.68 (1 H, d, $J = 8.0$ Hz). 13C NMR (125 MHz, CDCl3) δ: 16.2, 21.2, 21.6, 23.8, 23.9, 37.7, 40.8, 58.8, 63.8, 118.0, 120.4, 123.0, 126.0, 126.9, 129.0, 129.7, 134.3, 135.3, 141.1, 144.2. IR (neat): 2957, 1598 cm$^{-1}$. HRMS (MALDI) Calcd for C21H24N2O2S [M+Na]$^+$: 391.1451, found 391.1459.

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**cis-1m**

2-((2S,3S)-2-Isobutyl-1-tosylindolin-3-yl)acetonitrile (cis-1m) (Table 4, entries 4, 5) was obtained from above-mentioned crude reaction mixture as a colorless solid [16 mg, 22% (entry 4) and 15 mg, 21% (entry 5)]. The relative stereochemistry was determined by NOESY spectra. $\alpha_{D}^{20} = −128.6$ (c 0.11, CHCl3). Mp: 114–117 °C. 1H NMR (500 MHz, CDCl3) δ: 0.93 (3 H, d, $J = 7.0$ Hz), 1.09 (3 H, d, $J = 7.0$ Hz), 1.35–1.41 (1 H, m), 2.10–2.18 (1 H, m), 2.37 (3 H, s), 2.41 (1 H, dd, $J = 17.0, 9.0$ Hz), 2.59 (1 H, dd, $J = 17.0, 7.0$ Hz), 2.92–2.97 (1 H, m), 4.42–4.47 (1 H, m), 7.06 (1 H, d, $J = 8.0$ Hz), 7.13–7.16 (3 H, m), 7.32 (1 H, dd, $J = 8.0, 8.0$ Hz), 7.44 (2 H, d, $J = 8.0$ Hz), 7.68 (1 H, d, $J = 8.0$ Hz). 13C NMR (125 MHz, CDCl3) δ: 16.2, 21.2, 21.6, 23.8, 23.9, 37.7, 40.8, 58.8, 63.8, 118.0, 120.4, 123.0, 126.0, 126.9, 129.0, 129.7, 134.3, 135.3, 141.1, 144.2. IR (neat): 2957, 1598 cm$^{-1}$. HRMS (MALDI) Calcd for C21H24N2O2S [M+Na]$^+$: 391.1451, found 391.1459.


2-((2S,3R)-2-Isobutyl-1-((4-nitrophenyl)tosyl)indolin-3-yl)acetonitrile (trans-1n) (Table 4, entries 6 and 7)

For entry 6: According to the General Procedure A, a mixture of CsF (23 mg, 0.15 mmol), 18-crown-6 (40 mg, 0.15 mmol), 2-(trimethylsilyl)phenyl trifluoromethanesulfonate 5a1 (18 mg, 75 µmol) and (S,E)-N-(1-cyano-5-methylhex-1-en-3-yl)-4-methylbenzenesulfonamide 3n (16 mg, 50 mmol) was stirred in THF (1.0 mL, 50 mM) for 1 hour at room temperature. The crude product (trans-1n cis-1n = 4.2:1, determined by 400 MHz 1H NMR analysis) was purified by PTLC (hexane/EtOAc = 2:1) to provide the titled compound trans-1n as a colorless solid (9.4 mg, 47%).

For entry 7: According to the General Procedure A, a mixture of CsF (91 mg, 0.60 mmol), 18-crown-6 (0.16 g, 0.60 mmol), 2-(trimethylsilyl)phenyl trifluoromethanesulfonate 5a1 (90 mg, 0.30 mmol) and (S,E)-N-(1-cyano-5-methylhex-1-en-3-yl)-4-methylbenzenesulfonamide 3n (65 mg, 0.20 mmol) was stirred in THF (2.0 mL, 0.10 M) for 1 hour at room temperature. The crude product (trans-1n cis-1n = 4.8:1, determined by 400 MHz 1H NMR analysis) was purified by PTLC (hexane/EtOAc = 2:1) to provide the titled compound trans-1n as a colorless solid (14 mg, 20%).

The relative stereochemistry was determined by NOESY spectra. [α]D = -126.7 (c 0.10, CHCl3).

Mp: 79–82 °C. 1H NMR (500 MHz, CDCl3) δ: 0.96 (3 H, d, J = 6.5 Hz), 1.03 (3 H, d, J = 6.5 Hz), 1.50–1.57 (1 H, m), 1.76–1.72 (1 H, m), 1.74–1.83 (1 H, m), 1.94 (1 H, dd, J = 16.5, 8.0 Hz), 2.26 (1 H, dd, J = 16.5, 7.0 Hz), 3.10–3.15 (1 H, m), 4.44 (1 H, dd, J = 9.0, 5.0 Hz), 7.14 (1 H, dd, J = 7.5, 7.5 Hz), 7.34 (1 H, dd, J = 7.5, 7.5 Hz), 7.57–7.64 (3 H, m), 7.70 (1 H, dd, J = 8.0, 8.0, 1.0 Hz), 7.92 (1 H, d, J = 8.0 Hz). 13C NMR (125 MHz, CDCl3) δ: 21.9, 23.4, 23.6, 24.4, 43.1, 44.8, 66.4, 116.7, 117.4, 124.1, 125.4, 126.0, 129.8, 130.8, 131.2, 131.7, 131.8, 134.5, 139.6, 148.2, 22.5, 22.7, 25.4, 42.2, 59.8, 103.6, 117.7, 128.9, 130.2, 130.3, 133.3, 136.5, 138.6, 145.5, 153.7. IR (neat): 2958, 2251, 1545 cm⁻¹. HRMS (MALDI) Calcd for C20H21N3O2S [M+Na]⁺: 422.1145, found 422.1139.

2-((2R,3R)-2-(((tert-Butyldimethylsilyl)oxy)methyl)-1-tosylindolin-3-yl)acetonitrile (trans-1o') and 2-((2R,3S)-2-(((tert-Butyldimethylsilyl)oxy)methyl)-1-tosylindolin-3-yl)acetonitrile (cis-1o') (Table 4, entries 8 and 9)

For entry 8: According to the General Procedure A, a mixture of CsF (91 mg, 0.60 mmol), 18-crown-
6 (0.16 g, 0.60 mmol), 2-(trimethylsilyl)phenyl trifluoromethanesulfonate 5a\(^1\) (90 mg, 0.30 mmol) and (S,E)-N-[1-cyano-4-(tert-butyldimethylsilyloxy)but-1-en-3-yl]-4-methylbenzenesulfonamide 3o\(^1\) (76 mg, 0.20 mmol) was stirred in THF (4.0 mL, 50 mM) for 24 hours at –40 °C. The crude product (trans-1o’/cis-1o’ = 2.5:1, determined by 300 MHz \(^1\)H NMR analysis) was purified by column chromatography on silica gel (hexane/EtOAc = 3:1) to provide the titled compound 1o\(^1\) as a colorless oil (64 mg, 70%).

**For entry 9:** According to the General Procedure A, a mixture of CsF (91 mg, 0.60 mmol), 18-crown-6 (0.16 g, 0.60 mmol), 2-(trimethylsilyl)phenyl trifluoromethanesulfonate 5a\(^1\) (90 mg, 0.30 mmol) and (S,E)-N-[1-cyano-4-(tert-butyldimethylsilyloxy)but-1-en-3-yl]-4-methylbenzenesulfonamide 3o\(^1\) (76 mg, 0.20 mmol) was stirred in THF (4.0 mL, 0.050 M) for 24 hours at –40 °C. The crude product (trans-1o’/cis-1o’ = 4:0:1, determined by 300 MHz \(^1\)H NMR analysis) was purified by column chromatography on silica gel (hexane/EtOAc =3:1) to provide the titled compound 1o\(^1\) as a colorless oil (59 mg, 65%). The relative stereochemistry was determined by NOESY spectra. \(^1\)H NMR (500 MHz, CDCl\(_3\)) \(\delta\): –0.05 (3/5 H, s), 0.02 (12/5 H, s), 0.05 (3/5 H, s), 0.08 (12/5 H, s), 0.66 (9/5 H, s), 0.80 (36/5 H, s), 1.44 (3/4 H, dd, \(J = 17.0, 8.5\) Hz), 1.71 (3/4 H, dd, \(J = 17.0, 7.5\) Hz), 2.80 (1/4 H, dd, \(J = 17.0, 7.5\) Hz), 2.38 (15/5 H, s), 2.98 (1/4 H, dd, \(J = 17.0, 8.0\) Hz), 3.29–3.40 (5/5 H, m), 3.64 (4/5 H, dd, \(J = 10.5, 7.5\) Hz), 3.87–3.90 (4/5 H, m), 3.96 (4/5 H, dd, \(J = 10.5, 4.0\) Hz), 3.98–4.06 (2/5 H, m), 4.25–4.30 (1/5 H, m), 7.03–7.10 (5/5 H, m), 7.12 (1/5 H, d, \(J = 7.5\) Hz), 7.17–7.26 (15/5 H, m), 7.29–7.32 (1 H, m), 7.53 (2/5 H, d, \(J = 8.5\) Hz), 7.61 (8/5 H, d, \(J = 8.5\) Hz), 7.64 (1/5 H, d, \(J = 8.0\) Hz), 7.72 (4/5 H, d, \(J = 8.5\) Hz). \(^13\)C NMR (125 MHz, CDCl\(_3\)) \(\delta\): –5.8, –5.7, –5.6, –5.4, 16.2, 18.0, 21.5, 23.8, 25.4, 25.7, 29.7, 39.7, 40.0, 63.9, 65.0, 67.8, 116.9, 117.1, 117.2, 119.0, 122.6, 124.9, 125.0, 126.7, 126.9, 132.0, 133.5, 134.4, 135.1, 141.3, 141.9, 144.3, 144.7. IR (neat): 2929, 2249, 1478, 1361 cm\(^{-1}\). HRMS (MALDI) Calcd for C\(_{32}\)H\(_{25}\)N\(_2\)O\(_3\)SSi [M+Na\(^+\)]: 479.1795, found 479.1794.

![](image)

2-((2R,3R)-2-(Hydroxymethyl)-1-tosylindolin-3-yl)acetonitrile (trans-1o) and 2-((SR,3R)-2-(hydroxymethyl)-1-tosylindolin-3-yl)acetonitrile (cis-1o) (Table 4, entry 10): According to the General Procedure A, a mixture of CsF (91 mg, 0.60 mmol), 18-crown-6 (0.16 g, 0.60 mmol), 2-(trimethylsilyl)phenyl trifluoromethanesulfonate 5a\(^1\) (90 mg, 0.30 mmol) and (S,E)-N-(1-cyano-4-hydroxybut-1-en-3-yl)-4-methylbenzenesulfonamide 3o (53 mg, 0.20 mmol) was stirred in THF (2.0 mL, 0.10 M) for 1 hour at room temperature. The crude product (trans-1o/cis-1o = 2:4:1, determined by 300 MHz \(^1\)H NMR analysis) was purified by column chromatography on silica gel (hexane/EtOAc = 20:1 to 4:1) to provide the mixture of trans-1o, cis-1o and 6o (trans-1o/cis-1o/6o = 2.4:1:1.6). Then
the mixture was purified by GPC to obtained the mixture of trans-1p, cis-1p (trans-1p/cis-1p = 76:24, 22 mg, 32%) as a colorless oil and trans-1o, cis-1o (trans-1o/cis-1o = 42:58, 17 mg, 25%) as a colorless oil. The relative stereochemistry was determined by NOESY spectra. 1H NMR (500 MHz, CDCl3) δ: 1.43 (3/4 H, dd, J = 16.5, 8.5 Hz), 1.77 (3/4 H, dd, J = 16.5, 7.0 Hz), 2.03 (1/4 H, brs), 2.09 (3/4 H, brs), 2.39 (12/4 H, s), 2.77 (1/4 H, dd, J = 17.0, 7.0 Hz), 2.87 (1/4 H, dd, J = 17.0, 8.0 Hz), 3.25–3.36 (4/4 H, m), 3.77 (3/4 H, dd, J = 11.5, 5.5 Hz), 3.85 (3/4 H, dd, J = 11.5, 5.0 Hz), 3.91–3.98 (4/4 H, m), 4.06 (1/4 H, dd, J = 12.0, 4.0 Hz), 4.32 (1/4 H, ddd, J = 9.5, 4.0, 4.0 Hz), 7.00–7.14 (4/4 H, m), 7.16–7.22 (6/4 H, m), 7.24–7.27 (6/4 H, m), 7.29–7.37 (4/4 H, m), 7.53 (2/4 H, d, J = 8.5 Hz), 7.61 (6/4 H, d, J = 8.5 Hz), 7.72 (1/4 H, d, J = 8.0 Hz), 7.77 (3/4 H, d, J = 8.0 Hz). 13C NMR (125 MHz, CDCl3) δ: 16.8, 21.7, 23.7, 39.8, 40.3, 62.6, 65.0, 65.4, 68.2, 117.1, 117.5, 117.7, 118.7, 123.4, 125.1, 125.5, 125.7, 127.1, 127.2, 129.3, 129.6, 129.8, 130.0, 130.1, 131.8, 133.9, 141.1, 145.1. IR (neat): 3504, 2925, 2251, 1597 cm⁻¹. HRMS (MALDI) Calcd for C18H16N2O4S [M+Na]⁺: 365.0930, found 365.0926.

**trans-1p**

**cis-1p**

tert-Butyl (4-((2S,3R)-3-(cyanomethyl)-1-tosylindolin-2-yl)butyl)carbamate (trans-1p) and tert-buty (4-((2S,3S)-3-(cyanomethyl)-1-tosylindolin-2-yl)butyl)carbamate (cis-1p) (Table 4, entry 11): According to the General Procedure A, a mixture of CsF (91 mg, 0.60 mmol), 18-crown-6 (0.16 g, 0.60 mmol), 2-(trimethylsilyl)phenyl trifluoromethanesulfonate 5a¹ (90 mg, 0.30 mmol) and (S,E)-N-[1-cyano-7-(tert-butoxycarbonylamino)hept-1-en-3-yl]-4-methylbenzenesulfonamide 3p (81 mg, 0.20 mmol) was stirred in THF (2.0 mL, 0.10 M) for 1 hour at room temperature. The crude product (trans-1p/cis-1p = 3:5.1) was purified by column chromatography on silica gel (hexane/EtOAc = 20:1 to 4:1) to provide the titled compound **trans-1p** and **cis-1p** as a colorless oil (60 mg, 63%). The relative stereochemistry was determined by NOESY spectra. 1H NMR (500 MHz, CDCl3) δ: 1.12–1.86 (64/4 H, m), 2.36 (12/4 H, s), 2.43 (1/4 H, dd, J = 16.5, 9.0 Hz), 2.59 (1/4 H, dd, J = 16.5, 7.0 Hz), 2.91–3.17 (11/4 H, m), 3.88 (3/4 H, m), 4.31–4.41 (1/4 H, m), 4.55 (3/4 NH, brs), 4.62 (1/4 NH, brs), 7.03–7.11 (4/4 H, m), 7.12–7.17 (5/4 H, m), 7.22 (6/4 H, d, J = 8.5 Hz), 7.26–7.35 (5/4 H, m), 7.43 (2/4 H, d, J = 8.5 Hz), 7.58 (6/4 H, d, J = 8.5 Hz), 7.66 (1/4 H, d, J = 8.5 Hz), 7.73 (3/4 H, d, J = 8.5 Hz). 13C NMR (125 MHz, CDCl3) δ: 1.1, 14.2, 16.2, 21.6, 21.9, 22.7, 22.9, 23.8, 28.5, 29.8, 29.9, 31.7, 35.9, 40.3, 40.9, 43.1, 65.3, 67.2, 79.2, 117.4, 117.8, 118.1, 120.2, 123.1, 125.2, 126.2, 126.9, 127.0, 129.2, 129.7, 129.9, 130.0, 132.1, 134.0, 134.9, 135.4, 140.9, 144.4, 144.7, 156.1. IR (neat): 3430, 2928, 2249, 1695 cm⁻¹. HRMS (MALDI) Calcd for C26H33N3O5S [M+Na]⁺: 506.2084, found 506.2080.
2-((2S,3R)-2-Isopropyl-4-methoxy-1-tosylindolin-3-yl)acetonitrile (trans-1q) (Table 4, entry 12): According to the General Procedure A, a mixture of CsF (91 mg, 0.60 mmol), 18-crown-6 (0.16 g, 0.60 mmol), 3-methoxy-2-(trimethylsilyl)phenyl trifluoromethanesulfonate 5b (98 mg, 0.30 mmol) and (S,E)-N-(1-cyano-4-methylpent-1-en-3-yl)-4-methylbenzenesulfonamide 3f (56 mg, 0.20 mmol) was stirred in THF (4.0 mL, 50 mM) for 24 hours at −40 °C. The crude product (trans-1q/cis-1q = >98:2, determined by 300 MHz 1H NMR analysis) was purified by column chromatography on silica gel (hexane/EtOAc = 2:1 to 4:1) then PTLC (CHCl3/MeOH/H2O = 200:3:1) to provide the titled compound trans-1q as a colorless solid (51 mg, 72%). The relative stereochemistry was determined by NOESY spectra. [α]D 20 = −3.1 (c 0.06, CHCl3). Mp: 170–172 °C. 1H NMR (500 MHz, CDCl3) δ: 0.83–0.90 (1 H, m), 0.82 (3 H, d, J = 7.0 Hz), 0.95 (3 H, d, J = 7.0 Hz), 1.13 (3 H, d, J = 7.0 Hz), 1.24–1.28 (2 H, m), 2.34 (3 H, s), 2.59–2.67 (1 H, m), 3.85 (1 H, d, J = 4.0 Hz), 3.88 (3 H, s), 6.60 (1 H, d, J = 8.0 Hz), 7.16 (1 H, d, J = 8.0 Hz), 7.53–7.62 (4 H, m). 13C NMR (125 MHz, CDCl3) δ: 16.6, 17.2, 21.3, 32.7, 55.7, 71.3, 106.2, 109.4, 115.0, 127.0, 129.6, 133.1, 138.1, 144.6, 154.8, 157.6, 196.4. IR (neat): 2924, 1713, 1489 cm⁻¹. HRMS (MALDI) Calcd for C21H26N2O3S [M+Na]+: 407.1400, found 407.1396.

2-((2S,3R)-4-(tert-Butyldimethylsilyl)-2-isopropyl-1-tosylindolin-3-yl)acetonitrile (trans-1r) (Table 4, entry 13): According to the General Procedure A, a mixture of CsF (91 mg, 0.60 mmol), 18-crown-6 (0.16 g, 0.60 mmol), 2-(tert-butyldimethylsilyl)-4-methyl-6-(trimethylsilyl)phenyl trifluoromethanesulfonate 5e (98 mg, 0.30 mmol) and (S,E)-N-(1-cyano-4-methylpent-1-en-3-yl)-4-methylbenzenesulfonamide 3f (56 mg, 0.20 mmol) was stirred in THF (4.0 mL, 50 mM) for 24 hours at room temperature. The crude product (trans-1r/cis-1r = 98:2, determined by 300 MHz 1H NMR analysis) was purified by column chromatography on silica gel (hexane/EtOAc = 20:1 to 4:1) to provide the titled compound trans-1r as a colorless solid (65 mg, 68%). The relative stereochemistry was determined by NOESY spectra. [α]D 20 = −25.0 (c 0.13, CHCl3). Mp: 163–165 °C. 1H NMR (500 MHz, CDCl3) δ: 0.26 (3 H, s), 0.27 (3 H, s), 0.48 (1 H, dd, J = 17.5, 12.5 Hz), 0.81 (9 H, s), 0.85 (3
(±)-2-((4αβ9αα)-9-Tosyl-1,2,3,4,9,9a-hexahydro-4aH-carbazol-4a-yl)acetonitrile (trans-1s)

(Scheme 2): According to the General Procedure A, a mixture of CsF (25 mg, 0.15 mmol), 18-crown-6 (39 mg, 0.15 mmol), 2-(trimethylsilyl)phenyl trifluoromethanesulfonate 5a1 (22 mg, 75 μmol) and (E)-N-(2-(cyanomethylene)cyclohexyl)-4-methylbenzenesulfonamide 3q (15 mg, 50 μmol) was stirred in THF (1.0 mL, 0.050 M) for 0.5 hours at 50 °C. The crude product (trans-1s/cis-1s = 98:2, determined by 400 MHz 1H NMR analysis) was purified by column chromatography on silica gel (hexane/EtOAc = 4:1) to provide the titled compound trans-1s as a colorless solid (24 mg, 33%). The relative stereochemistry was determined by NOESY spectra. Mp: 132–135 °C. 1H NMR (400 MHz, CDCl3) δ 1.17–1.12 (1 H, m), 1.27 (2 H, m), 1.45–1.39 (1 H, m), 1.50–1.57 (3 H, m), 1.77 (1 H, td, J = 13.5, 4.6 Hz), 2.26–2.24 (2 H, m), 2.38 (3 H, s), 4.08 (1 H, dd, J = 9.2, 6.3 Hz), 7.07 (1 H, dd, J = 7.5, 7.5 Hz), 7.12 (1 H, dd, J = 7.5, 1.0 Hz), 7.27 (2 H, m), 7.29–7.31 (1 H, m), 7.67 (1 H, d, J = 7.5 Hz), 7.75 (2 H, d, J = 8.0 Hz). 13C NMR (125 MHz, CDCl3) δ: 20.9, 21.3, 21.7, 29.5, 30.4, 31.3, 45.8, 67.2, 116.2, 117.0, 123.0, 124.3, 126.6, 129.6, 130.1, 134.0, 136.5, 139.0, 140.1, 144.4. IR (neat): 2934, 2860, 1599 cm⁻¹. HRMS (MALDI) Calcd for C22H38N2O2Si [M+Na⁺]: 389.1294, found 389.1290.

Methyl 2-((2S,3R)-2-isopropyl-1-tosylindolin-3-yl)acetate (trans-1h) (Table 2, entry 2): According to the General Procedure A, a mixture of CsF (91 mg, 0.6 mmol), 18-crown-6 (0.16 g, 0.60 mmol), 2-(trimethylsilyl)phenyl trifluoromethanesulfonate 5a1 (90 mg, 0.30 mmol) and (S,E)-N-(1-cyano-4-methylpent-1-en-3-yl)-4-methylbenzenesulfonamide 3h (62 mg, 0.20 mmol) was stirred in THF (2.0 mL, 0.10 M) for 1 hour at room temperature. The crude product (trans-1h/cis-1h = 19:1,
determined by 400 MHz $^1$H NMR analysis) was purified by PTLC (hexane/toluene/EtOAc = 15:15:1) to provide the titled compound trans-1h as a colorless solid (56 mg, 76%, 94% ee). The relative stereochemistry was determined by NOESY spectra and the optical purity was determined by HPLC analysis at 20 °C, using a CHIRALCEL AD-3 column [hexane/2-propanol = 85:15, 1.0 mL/min; retention times 7.9 min (2S,3R), 8.7 min (2R,3S)]. Mp: 87–89 °C. [α]$_D^{20}$ = −141.2 (c 0.12, CHCl$_3$).

$^1$H NMR (500 MHz, CDCl$_3$) δ: 0.81 (3 H, d, $J$ = 7.0 Hz), 0.92 (3 H, d, $J$ = 7.0 Hz), 1.22 (1 H, dd, $J$ = 15.0, 9.0 Hz), 1.75 (1 H, dd, $J$ = 15.0, 6.0 Hz), 2.11 (1 H, septd, $J$ = 7.0, 5.5 Hz), 2.35 (3 H, s), 3.20 (1 H, ddd, $J$ = 9.5, 6.0, 1.5 Hz), 3.62 (3 H, s), 3.79 (1 H, dd, $J$ = 5.5, 1.5 Hz), 7.01–7.02 (2 H, m), 7.18 (2 H, d, $J$ = 8.0 Hz), 7.22–7.26 (1 H, m), 7.57 (2 H, d, $J$ = 8.0 Hz), 7.71 (1 H, d, $J$ = 8.0 Hz). $^{13}$C NMR (125 MHz, CDCl$_3$) δ: 16.7, 18.0, 21.5, 33.7, 39.4, 41.1, 51.6, 72.4, 117.1, 124.4, 124.7, 127.1, 128.5, 129.5, 134.9, 135.3, 141.6, 144.0, 171.4. IR (neat): 3451, 2962, 1736 cm$^{-1}$.

HRMS (MALDI) Calcd for C$_{21}$H$_{23}$NO$_3$S [M+Na$^+$]: 410.1397, found 410.1408. All spectroscopic data of the obtained product (2S,3R)-1h was in good agreement with (±)-trans-1h which was synthesized from (±)-3h.

![cis-1h](image)

**Methyl 2-((2S,3S)-2-isopropyl-1-tosylindolin-3-yl)acetate (cis-1h) (Table 2, entry 2)** was obtained from above-mentioned crude reaction mixture as a colorless solid (3.3 mg, 4%). [α]$_D^{20}$ = −178.7 (c 0.03, CHCl$_3$). $^1$H NMR (500 MHz, CDCl$_3$) δ: 0.48 (3 H, d, $J$ = 7.0 Hz), 1.17 (3 H, d, $J$ = 7.0 Hz), 2.77 (1 H, septd, $J$ = 6.5, 2.5 Hz), 2.34 (3 H, s), 2.54 (1 H, dd, $J$ = 17.5, 10.5 Hz), 2.75 (1 H, dd, $J$ = 17.5, 5.0 Hz), 3.06–3.11 (1 H, m), 3.71 (3 H, s), 4.44 (1 H, dd, $J$ = 8.5, 2.5 Hz), 6.82 (1 H, d, $J$ = 7.5 Hz), 7.06 (1 H, dd, $J$ = 7.5, 7.5 Hz), 7.13 (2 H, d, $J$ = 8.0 Hz), 7.23 (1 H, dd, $J$ = 7.5, 7.5 Hz), 7.48 (2 H, d, $J$ = 8.0 Hz), 7.63 (1 H, d, $J$ = 8.0 Hz). $^{13}$C NMR (125 MHz, CDCl$_3$) δ: 17.3, 21.0, 21.5, 29.1, 31.7, 39.9, 52.0, 69.9, 119.2, 121.7, 125.6, 127.0, 128.1, 129.4, 135.6, 136.9, 142.8, 143.7, 172.5. IR (neat): 2966, 1736 cm$^{-1}$. HRMS (MALDI) Calcd for C$_{21}$H$_{23}$NO$_3$S [M+Na$^+$]: 410.1397, found 410.1403.

![trans-1i](image)

**1-((2S,3R)-2-Isopropyl-1-tosylindolin-3-yl)propan-2-one (trans-1i) (Table 2, entry 3):** According to the General Procedure A, a mixture of CsF (91 mg, 0.60 mmol), 18-crown-6 (0.16 g, 0.60 mmol), 2-(trimethylsilyl)phenyl trifluoromethanesulfonate 5a (90 mg, 0.30 mmol) and (S,E)-N-(1-cyano-4-methylpent-1-en-3-yl)-4-methylbenzenesulfonamide 3i (56 mg, 0.20 mmol) was stirred in THF (2.0
mL, 0.10 M) for 1 hour at room temperature. The crude product (trans-1i/cis-1i = 13:1, determined by 300 MHz $^1$H NMR analysis) was purified by column chromatography on silica gel (hexane/EtOAc = 20:1 to 4:1) to provide the titled compound trans-3i as a colorless solid (56 mg, 75%, 84% ee). The relative stereochemistry was determined by NOESY spectra and the optical purity was determined by HPLC analysis at 20 °C, using a CHIRALCEL AD-3 column [hexane/2-propanol = 85:15, 1.0 mL/min; retention times 14.5 min (2S,3R), 15.2 min (2R,3S)]. [α]$_{D}^{20}$ = –3.93 (c 0.03, CHCl$_3$). Mp: 104–105 °C. $^1$H NMR (500 MHz, CDCl$_3$) δ: 0.86 (3 H, d, J = 7.0 Hz), 0.91 (3 H, d, J = 7.0 Hz), 1.38 (1 H, dd, J = 18.0, 8.0 Hz), 1.73 (1 H, dd, J = 18.0, 6.5 Hz), 1.80 (3 H, s), 2.08 (1 H, septd, J = 7.0, 5.0 Hz), 2.38 (3 H, s), 3.23–3.26 (1 H, m), 3.61 (1 H, dd, J = 5.0, 1.5 Hz), 6.99–7.03 (2 H, m), 7.21–7.25 (3 H, m), 7.56 (2 H, d, J = 8.5 Hz), 7.71 (1 H, d, J = 8.0 Hz). $^{13}$C NMR (125 MHz, CDCl$_3$) δ: 15.8, 17.4, 21.0, 21.6, 29.0, 40.7, 69.3, 118.2, 119.6, 121.8, 126.1, 126.9, 129.0, 129.7, 134.9, 135.2, 142.8, 144.2. IR (neat): 2963, 1716 cm$^{-1}$. HRMS (MALDI) Calcd for C$_{21}$H$_{25}$NO$_3$S [M+Na]$^+$: 394.1447, found 394.1444. All spectroscopic data of the obtained product (2S,3R)-1i was in good agreement with (+)-trans-1i which was synthesized from (+)-3i.

1-((2S,3S)-2-Isopropyl-1-tosylindolin-3-yl)propan-2-one (cis-1i) (Table 2, entry 3) was obtained from above-mentioned crude reaction mixture as a colorless solid (4.6 mg, 6%). [α]$_{D}^{20}$ = –122.4 (c 0.05, CHCl$_3$). $^1$H NMR (500 MHz, CDCl$_3$) δ: 0.46 (3 H, d, J = 7.0 Hz), 1.15 (3 H, d, J = 7.0 Hz), 1.54–1.64 (1 H, m), 2.18 (3 H, s), 2.33 (3 H, s), 2.70 (1 H, dd, J = 19.0, 10.0 Hz), 2.86 (1 H, dd, J = 19.0, 4.5 Hz), 3.03–3.09 (1 H, m), 4.47 (1 H, dd, J = 8.0, 2.5 Hz), 6.78 (1 H, d, J = 7.5 Hz), 7.04 (1 H, td, J = 7.5, 7.5, 1.0 Hz), 7.12 (2 H, d, J = 8.0 Hz), 7.20–7.14 (1 H, m), 7.49 (2 H, d, J = 8.0 Hz), 7.63 (1 H, d, J = 7.5 Hz). $^{13}$C NMR (125 MHz, CDCl$_3$) δ: 17.4, 20.9, 21.5, 29.2, 30.0, 38.9, 41.4, 69.7, 119.3, 121.6, 125.5, 127.1, 129.4, 135.6, 137.4, 142.8, 143.6, 206.5. IR (neat): 2966, 1717 cm$^{-1}$. HRMS (MALDI) Calcd for C$_{21}$H$_{25}$NO$_3$S [M+Na]$^+$: 394.1447, found 394.1444.
General Procedure B for telescoping synthesis of $\gamma$-tosylamino-$\alpha,\beta$-unsaturated nitriles 3 (Table 3): A round-bottom flask was charged with $\ell$-amino acid methyl ester hydrochloride (1.0 equiv) and a stirrer bar. The flask was equipped with a three-way stopcock and evacuated and back-filled with N$_2$. CH$_2$Cl$_2$ (0.50 M) was added into the flask, and TsCl (1.1 equiv) was quickly added to the flask, and stirred at 0 °C. After stirring for 10 min at 0 °C, Et$_3$N (2.5 equiv) was quickly added to the mixture. After 10 min at 0 °C, the mixture was stirred at room temperature for indicated time. The end of the reaction was judged by TLC analysis. The reaction mixture was concentrated under reduced pressure, and diluted with EtOAc (0.10 M). The organic phase was washed water and brine, dried over MgSO$_4$ and concentrated under reduced pressure. The residue was used for the next step without further purification. The obtained material was evacuated and back-filled with Ar. The flask was added CH$_2$Cl$_2$ (0.50 M) via a syringe, and the solution was cooled to –78 °C. DIBAL (1.0 M in hexane, 2.5 equiv) was slowly added to the flask, and the mixture was stirred at –78 °C for 2 h. MeOH (2.5 mL/mmol) was slowly added into the flask at –78 °C. After stirring for 30 min 30% aq. Rochelle salt (3.3 mL/mmol) was added to the reaction mixture at –78 °C, and the mixture was stirred at room temperature for 1 hour, the mixture was separated to organic and aqueous phase, and organic phase was washed twice with 30% aq. Rochelle salt (1.8 mL/mmoll and 1.3 mL/mmol). The combined aqueous phase was extracted three times with Et$_2$O, and the combined organic extracts were washed with brine, dried over MgSO$_4$ and concentrated under reduced pressure. The residue was used for the next step without further purification. The crude product was dissolved in MeCN (1.0 M), and added diethyl cyanomethylphosphonate (1.0 equiv) and LiCl [or NaCl] (1.5 equiv), and cooled to 0 °C. iPr$_2$NEt (1.0 equiv) was added to the mixture, and the mixture was stirred at room temperature. After stirred for indicated time, the mixture was concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel (EtOAc/hexane) to provide the $\gamma$-tosylamino-$\alpha,\beta$-unsaturated nitrile 3.

![3f](image)

(S,E)-N-(1-Cyano-4-methylpent-1-en-3-yl)-4-methylbenzenesulfonamide (3f) (Table 1, entry 6–12; Table 3, entry 1): According to the General Procedure B, a mixture of methyl $\ell$-valinate hydrochloride (S)-4a (1.7 g, 10 mmol), TsCl (2.1 g, 12 mmol) and Et$_3$N (3.5 mL, 25 mmol) was stirred in CH$_2$Cl$_2$ (20 mL, 0.50 M) for 24 hours at room temperature. The mixture of the obtained crude product (2.8 g) and DIBAL (25 mL, 25 mmol) in CH$_2$Cl$_2$ (25 mL, 0.50 M) was stirred for 20 hours at –78 °C. The mixture of the crude product (2.2 g), diethyl cyanomethylphosphonate (1.6 mL, 10 mmol), LiCl (0.42 g, 10 mmol) and iPr$_2$NEt (1.8 mL, 10 mmol) in MeCN (50 mL, 0.25 M) was stirred for 20 hours at room temperature. The crude product was purified by column chromatography on silica gel
(hexane/EtOAc = 3:1) to provide the titled compound 3f (1.8 g, 63%, >99% ee) as a colorless solid. [α]D30 = −66.6 (c 0.10, CHCl3). Mp: 175–177 °C. 1H NMR (500 MHz, CDCl3) δ: 0.82 (3 H, d, J = 7.0 Hz), 0.85 (3 H, d, J = 7.0 Hz), 1.79 (1 H, sept, J = 7.0, 6.0 Hz), 2.44 (3 H, s), 3.72–3.76 (1 H, m), 4.97 (1 H, d , J = 8.0 Hz), 5.32 (1 H, dd, J = 16.5, 2.0 Hz), 6.41 (1 H, dd, J = 16.5, 6.0 Hz), 7.33 (2 H, d, J = 8.5 Hz), 7.72 (2 H, d, J = 8.5 Hz). 13C NMR (125 MHz, CDCl3) δ: 17.9, 18.4, 21.6, 32.4, 60.4, 101.6, 116.4, 127.0, 129.9, 137.2, 144.2, 152.1. IR (neat): 3232, 2231 cm−1. HRMS (MALDI) Calcd for C14H18N2O2S [M+Na]+: 301.0981, found 301.0983. Optical purity was determined by HPLC analysis at 20 °C, using a CHIRALCEL ID column [hexane/2-propanol = 80:20, 1.0 mL/min; retention times 10.6 min (S), 13.2 min (R)].

The corresponding racemic (±)-3f was obtained by the same procedure with (S)-3f shown above using a racemic methyl DL-valinate hydrochloride (±)-4a (67% overall yield in 3-step). The racemic (±)-3f was used to determine enantiomeric excess (ee) % of 3f shown above.

(S,E)-N-(1-Cyano-4-methylpent-1-en-3-yl)-2,4,6-trimethylbenzenesulfonamide (3g) (Table 2, entry 2): According to the General Procedure B, a mixture of methyl L-valinate hydrochloride (0.84 g, 5.0 mmol), MesSO2Cl (1.2 g, 5.5 mmol) and Et3N (1.8 mL, 13 mmol) was stirred in CH2Cl2 (10 mL, 0.50 M) for 16 hours at room temperature. The mixture of the obtained crude product (1.6 g) and DIBAL (13 mL, 13 mmol) in CH2Cl2 (10 mL, 0.50 M) was stirred for 2 hours at −78 °C. The mixture of the crude product (1.5 g), diethyl cyanomethylphosphonate (0.79 mL, 5.0 mmol), LiCl (0.32 g, 7.5 mmol) and iPr2NEt (1.4 mL, 7.5 mmol) in MeCN (5 mL, 1.0 M) was stirred for 16 hours at room temperature. The crude material was purified by column chromatography on silica gel (hexane/EtOAc = 5:1 to 2:1) to provide the titled compound 3g (0.84 g, 55%) as a colorless solid. [α]D30 = −57.8 (c 0.11, CHCl3). Mp: 128–130 °C. 1H NMR (300 MHz, CDCl3) δ: 0.82 (3 H, d, J = 6.5 Hz), 0.88 (3 H, d, J = 6.5 Hz), 1.71–1.87 (1 H, m), 2.30 (3 H, s), 2.60 (6 H, s), 3.63–3.72 (1 H, m), 4.62 (NH, brd, J = 7.5 Hz), 5.23 (1 H, dd, J = 16.0, 1.5 Hz), 6.33 (1H, dd, J = 16, 6.5 Hz), 6.96 (2 H, s). 13C NMR (75 MHz, CDCl3) δ: 18.2, 18.4, 21.0, 23.2, 32.6, 60.6, 101.8, 116.4, 132.3, 134.2, 138.8, 143.0, 151.9. IR (neat): 3286, 2966, 2226, 1324 cm−1. HRMS (MALDI) Calcd for C16H22N2O2S [M+Na]+: 329.1294, found 329.1290.
(S,E)-N-(4-Cyanobut-3-en-2-yl)-4-methylbenzenesulfonamide (3k) (Table 3, entry 3): According to the General Procedure B, a mixture of methyl l-alanine hydrochloride (4.2 g, 30 mmol), TsCl (6.3 g, 33 mmol) and Et3N (9.2 mL, 66 mmol) was stirred in CH2Cl2 (30 mL, 1.0 M) for 15 hours at room temperature. The crude product (7.4 g) was obtained. The mixture of the crude mixture (5.2 g) and DIBAL (50 mL, 50 mmol) in CH2Cl2 (40 mL, 0.50 M) was stirred for 2 hours at −78 °C. The mixture of obtained crude product, MS 4A (5.0 g), N-methylmorpholine oxide (2.6 mg, 22 mmol) and Pr2NRuO4 (0.35 g, 1.0 mmol) in CH2Cl2 (100 mL, 0.20 M) was stirred for 1 hour at room temperature. The mixture of crude product, diethyl cyanomethylphosphonate (3.8 mL, 24 mmol), LiCl (1.0 g, 24 mmol) and iPr2NEt (4.2 mL, 24 mmol) in MeCN (20 mL, 1.0 M) was stirred for 18 hours at room temperature. The crude product was purified by flash column chromatography on silica gel (EtOAc/hexane = 2:1) to provide the titled compound 3k (1.8 g, 36%) as a colorless oil. [α]D21 = −15.6 (c 0.14, CHCl3). [α]D21 = −15.6 (c 0.14, CHCl3). 1H NMR (500 MHz, CDCl3) δ: 1.20 (3 H, d, J = 7.0 Hz), 2.45 (3 H, s), 4.01–4.08 (1 H, m), 4.59–4.62 (1 H, m), 5.45 (1 H, dd, J = 16.0, 2.0 Hz), 6.45 (1 H, dd, J = 16.0, 5.0 Hz), 7.34 (2 H, d, J = 8.0 Hz); 7.73 (2 H, d, J = 8.0 Hz). 13C NMR (125 MHz, CDCl3) δ: 20.7, 21.6, 50.6, 100.6, 116.4, 127.0, 130.0, 137.1, 144.2, 154.1. IR (neat): 3266, 2226, 1597 cm−1. HRMS (MALDI) Calcd for C12H14N2O2S [M+Na]+: 273.0663, found 273.0663.

\[ \begin{array}{c}
\text{Ts} \\
\text{N} \\
\text{H} \\
\text{Bn} \\
\text{CN} \\
\end{array} \]

(S,E)-N-(4-Cyano-1-phenylbut-3-en-2-yl)-4-methylbenzenesulfonamide (3l) (Table 3, entry 4): According to the General Procedure B, a mixture of methyl l-phenylalaninate hydrochloride (4.3 g, 20 mmol), TsCl (4.2 g, 22 mmol) and Et3N (6.1 mL, 44 mmol) was stirred in CH2Cl2 (40 mL, 0.50 M) for 5 hours at room temperature. The mixture of the crude product (6.8 g) and DIBAL (25 mL, 25 mmol) in CH2Cl2 (20 mL, 0.50 M) was stirred for 2 hours at −78 °C. The mixture of the crude product (3.1 g), diethyl cyanomethylphosphonate (2.4 mL, 15 mmol), NaCl (0.88 g, 15 mmol) and iPr2NEt (2.7 mL, 15 mmol) in MeCN (10 mL, 1.0 M) was stirred for 10 hours at room temperature. The mixture was purified by flash column chromatography on silica gel (EtOAc/hexane = 2:1) to provide the titled compound 3l (2.7 g, 82%) as a colorless solid. [α]D21 = −58.9 (c 0.11, CHCl3). Mp: 89–92 °C. 1H NMR (500 MHz, CDCl3) δ: 2.43 (3 H, s), 2.73 (1 H, dd, J = 14.0, 7.0 Hz), 2.78 (1 H, dd, J = 14.0, 7.0 Hz), 4.11–4.16 (1 H, m), 4.87 (1 H, d, J = 7.5 Hz), 5.43 (1 H, dd, J = 16.5, 1.5 Hz), 6.51 (1 H, dd, J = 16.5, 5.5 Hz), 6.94–6.96 (2 H, m), 7.20–7.26 (5 H, m), 7.57 (2 H, d, J = 8.5 Hz). 13C NMR (125 MHz, CDCl3) δ: 21.5, 40.7, 55.8, 101.4, 116.5, 126.9, 127.4, 128.9, 129.2, 129.8, 124.4, 136.6, 144.0, 152.6. IR (neat): 3274, 2226, 1635, 1598 cm−1. HRMS (MALDI) Calcd for C18H18N2O2S [M+Na]+: 349.0981, found 349.0977.
(S,E)-N-(1-Cyano-5-methylhex-1-en-3-yl)-4-methylbenzenesulfonamide (3m) (Table 3, entry 5): According to the General Procedure B, a mixture of methyl L-leucinate hydrochloride (3.6 g, 20 mmol), TsCl (4.2 g, 22 mmol) and Et3N (6.1 mL, 44 mmol) was stirred in CH2Cl2 (40 mL, 0.50 M) for 4 hours at room temperature. The mixture of crude product (6.5 g) and DIBAL (25 mL, 25 mmol) in CH2Cl2 (20 mL, 0.50 M) was stirred for 2 hours at –78 °C. The mixture of crude product (3.0 g), diethyl cyanomethylphosphonate (2.4 mL, 15 mmol), NaCl (0.88 g, 15 mmol) and iPr2NEt (2.7 mL, 15 mmol) in MeCN (10 mL, 1.0 M) was stirred for 16 hours at room temperature. The mixture was purified by flash column chromatography on silica gel (EtOAc/hexane = 2:1) to provide the titled compound 3m (2.0 g, 67%) as a yellow oil. [α]D21 = –63.8 (c 0.13, CHCl3). 1H NMR (500 MHz, CDCl3) δ: 0.74 (3 H, d, J = 7.0 Hz), 0.82 (3 H, d, J = 7.0 Hz), 1.24–1.36 (2 H, m), 1.50–1.61 (1 H, m), 2.44 (3 H, s), 3.88–3.94 (1 H, m), 5.03 (1 H, d, J = 7.5 Hz), 5.36 (1 H, dd, J = 16.0, 1.5 Hz), 6.37 (1 H, dd, J = 16.0, 6.5 Hz), 7.33 (2 H, d, J = 8.5 Hz), 7.72 (2 H, d, J = 8.5 Hz). 13C NMR (125 MHz, CDCl3) δ: 21.5, 21.6, 22.4, 24.2, 43.7, 53.4, 100.5, 116.5, 127.1, 129.8, 137.2, 144.2, 153.6. IR (neat): 3259, 2224, 1635, 1597 cm⁻¹. HRMS (MALDI) Calcd for C15H26N2O3S [M+Na]+: 315.1138, found 315.1133.

(S,E)-N-(1-Cyano-5-methylhex-1-en-3-yl)-4-nitrobenzenesulfonamide (3n) (Table 3, entry 6): According to the General Procedure B, a mixture of methyl L-leucinate hydrochloride (0.91 g, 5.0 mmol), NsCl (1.2 g, 5.3 mmol) and Et3N (1.5 mL, 11 mmol) was stirred in CH2Cl2 (10 mL, 0.50 M) for 11 hours at room temperature. The mixture of the crude product and DIBAL (13 mL, 13 mmol) in CH2Cl2 (10 mL, 0.50 M) was stirred for 3 hours at –78 °C. The mixture of the crude product, diethyl cyanomethylphosphonate (0.77 mL, 5.0 mmol), NaCl (0.44 g, 7.5 mmol) and iPr2NEt (0.90 mL, 5.0 mmol) in MeCN (7.0 mL, 0.70 M) was stirred for 21 hours at room temperature. The mixture was purified by Yamazen automatic flash column chromatography on silica gel (EtOAc/hexane = 4:1 to 1:1) to provide the titled compound 3n (2.8 g, 55%) as a white solid. [α]D21 = –57.3 (c 0.13, CHCl3). [α]D31 = –57.3 (c 0.13, CHCl3). Mp: 119–121 °C. 1H NMR (300 MHz, CDCl3) δ: 0.78 (3 H, d, J = 6.5 Hz), 0.87 (3 H, d, J = 7.0 Hz), 1.31–1.51 (2 H, m), 1.53–1.69 (1 H, m), 2.44 (3 H, s), 4.11–4.22 (1 H, m), 5.38 (NH, brd, J = 8.0 Hz), 5.50 (1 H, dd, J = 16.0, 1.5 Hz), 6.43 (1 H, dd, J = 16.0, 6.0 Hz), 7.74–7.80 (2 H, m), 7.86–7.93 (1 H, m), 8.04–8.10 (1 H, m). 13C NMR (75 MHz, CDCl3) δ: 21.6, 22.6, 24.4, 43.7, 54.6, 101.2, 116.3, 125.7, 130.7, 133.1, 134.2, 134.4, 147.8, 153.2. IR (neat) 3327, 2960, 2227, 1540 cm⁻¹. HRMS (MALDI) Calcd for C14H17N3O4S [M+Na]+: 346.0832, found
According to the General Procedure B, a mixture of methyl L-serinate hydrochloride (1.6 g, 10 mmol), TsCl (2.1 g, 11 mmol) and Et3N (3.1 mL, 22 mmol) was stirred in CH2Cl2 (0.50 L, 0.020 M) for 24 hours at 0 °C. The mixture of crude product, tBuMe2SiCl (2.3 g, 15 mmol) and imidazole (1.4 g, 20 mmol) in DMF (30 mL, 0.33 M) was stirred for 4.5 hours at room temperature. The mixture of the crude product (2.9 g) and DIBAL (19 mL, 19 mmol) in CH2Cl2 (15 mL, 0.50 M) was stirred for 2 hours at –78 °C. The crude product (2.2 g) was obtained. The mixture of the crude material (2.2 g), diethyl cyanomethylphosphonate (1.2 mL, 7.5 mmol), NaCl (0.44 g, 7.5 mmol) and iPr2NEt (1.3 mL, 7.5 mmol) in MeCN (7 mL, 1.0 M) was stirred for 22 hours at room temperature. The mixture was purified by flash column chromatography on silica gel (EtOAc/hexane = 5:1) to provide the titled compound 3o* (1.1 g, 39%) as a colorless solid. 

\[\begin{align*}
\text{Ts}^+ \quad \text{N} & \quad (R,E)-N-(1-((\text{tert-Butyldimethylsilyl})oxy)-4-cyanobut-3-en-2-yl)-4-methylbenzenesulfonamide \\
\text{3o}^* & \quad (\text{Table 3, entry 7; Table 4, entries 10 and 11}): \quad \text{According to the General Procedure B, a mixture of methyl } L\text{-serinate hydrochloride (1.6 g, 10 mmol), TsCl (2.1 g, 11 mmol) and Et}_3\text{N (3.1 mL, 22 mmol) was stirred in CH}_2\text{Cl}_2 (0.50 L, 0.020 M) for 24 hours at 0 °C. The mixture of crude product, tBuMe}_2\text{SiCl (2.3 g, 15 mmol) and imidazole (1.4 g, 20 mmol) in DMF (30 mL, 0.33 M) was stirred for 4.5 hours at room temperature. The mixture of the crude product (2.9 g) and DIBAL (19 mL, 19 mmol) in CH}_2\text{Cl}_2 (15 mL, 0.50 M) was stirred for 2 hours at –78 °C. The crude product (2.2 g) was obtained. The mixture of the crude material (2.2 g), diethyl cyanomethylphosphonate (1.2 mL, 7.5 mmol), NaCl (0.44 g, 7.5 mmol) and iPr}_2\text{NEt (1.3 mL, 7.5 mmol) in MeCN (7 mL, 1.0 M) was stirred for 22 hours at room temperature. The mixture was purified by flash column chromatography on silica gel (EtOAc/hexane = 5:1) to provide the titled compound 3o* (1.1 g, 39%) as a colorless solid.}
\end{align*}\]

\[\begin{align*}
\text{Ts}^+ \quad \text{N} & \quad (R,E)-N-(4-\text{Cyano-1-hydroxybut-3-en-2-yl)-4-methylbenzenesulfonamide (3o)} (\text{Table 4, entry 12}): \quad \text{A round bottom flask was charged with (R,E)-N-(1-((\text{tert-butyldimethylsilyl})oxy)-4-cyanobut-3-en-2-yl)-4-methylbenzenesulfonamide (3o*) (0.38 g, 1.0 mmol) and stirrer bar. The flask was evacuated and back-filled with N}_2. \text{ THF (10 mL, 0.10 M) was added to the flask and the mixture was cooled to 0 °C. Bu}_4\text{NF (1.0 M in THF, 1.1 mL, 1.1 mmol) was added into the flask via a syringe. After stirring for 8 hours at 0 °C, saturated NH}_4\text{Cl (ca. 5 mL) was added and the mixture was extracted with EtOAc (this process was repeated three times). The combined organic extracts were dried over MgSO}_4 \text{ and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (EtOAc/hexane = 5:1) to provide the titled compound 3o (1.0 g, 36%) as a colorless solid.}
\end{align*}\]

\[\begin{align*}
\text{Ts}^+ \quad \text{N} & \quad (R,E)-N-(1-((\text{tert-Butyldimethylsilyl})oxy)-4-cyanobut-3-en-2-yl)-4-methylbenzenesulfonamide (3o*) (0.38 g, 1.0 mmol) and stirrer bar. The flask was evacuated and back-filled with N}_2. \text{ THF (10 mL, 0.10 M) was added to the flask and the mixture was cooled to 0 °C. Bu}_4\text{NF (1.0 M in THF, 1.1 mL, 1.1 mmol) was added into the flask via a syringe. After stirring for 8 hours at 0 °C, saturated NH}_4\text{Cl (ca. 5 mL) was added and the mixture was extracted with EtOAc (this process was repeated three times). The combined organic extracts were dried over MgSO}_4 \text{ and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (EtOAc/hexane = 5:1) to provide the titled compound 3o (1.0 g, 36%) as a colorless solid.}
\end{align*}\]
silica gel (hexane/EtOAc = 1:1) to provide the titled compound 3 (0.23 mg, 88%) as a colorless solid. 

\[ \alpha \] D 21 = -72.8 (c 0.12, CHCl3). Mp: 68–71 °C. \(^1\)H NMR (500 MHz, CDCl3) \( \delta \): 1.92 (1 H, t, \( J = 5.0 \) Hz), 2.45 (3 H, s), 3.61–3.67 (2 H, m), 4.03–4.07 (1 H, m), 5.24 (1 H, d, \( J = 8.0 \) Hz), 5.53 (1 H, dd, \( J = 16.0, 1.5 \) Hz), 6.51 (1 H, dd, \( J = 16.0, 5.0 \) Hz), 7.34 (2 H, d, \( J = 8.0 \) Hz), 7.74 (2 H, d, \( J = 8.0 \) Hz).

\(^1\)C NMR (125 MHz, CDCl3) \( \delta \): 21.6, 56.1, 63.5, 102.8, 116.3, 127.1, 130.0, 136.9, 144.4, 150.4.

IR (neat): 3500, 3260, 2228, 1637, 1597 cm\(^{-1}\).


\[ \text{S1} \]

**tert-Butyl (S,E)-(7-cyano-5-((4-methylphenyl)sulphonamido)hept-6-en-1-yl)carbamate (S1):** To the solution of N\(^2\)-(((9H-fluoren-9-yl)methoxy)carbonyl)-N\(^6\)-(tert-butoxycarbonyl)-L-lysine (2.8 g, 6.0 mmol) in DMF (12 mL, 0.50 M) was added MEI (1.5 mL, 24 mmol) and Na\(_2\)CO\(_3\) (1.3 g, 12 mmol) at 0 °C. After stirring for 22 hours, the mixture was passed through a short pad of celite, and diluted with EtO and water. The mixture was extracted twice with EtO and concentrated under reduced pressure. The crude product (4.0 g) was obtained. To the solution of the crude mixture in CH\(_2\)Cl\(_2\) (12 mL, 0.50 M) was added pipperidine (0.71 mL, 7.2 mmol) at 0 °C. After stirring 13 h, the mixture was concentrated under reduced pressure. The crude product (5.0 g) was obtained. The mixture of the crude product, TsCl (1.4 g, 7.2 mmol) and Et\(_3\)N (1.3 mL, 9.0 mmol) was stirred in CH\(_2\)Cl\(_2\) (12 mL, 0.50 M) for 8 hours at room temperature. The crude material was purified by automatic column chromatography on silica gel to provide the titled compound S1 (2.2 g, 88%) as a colorless solid. \[ \alpha \] D 21 = +26.6 (c 0.10, CHCl3). Mp: 83–86 °C. \(^1\)H NMR (500 MHz, CDCl3) \( \delta \): 1.38–1.31 (2 H, m), 1.42 (11 H, m), 1.65–1.59 (1 H, m), 1.76–1.69 (1 H, m), 2.41 (3 H, s), 3.05 (2 H, d, \( J = 6.3 \) Hz), 3.48 (3 H, s), 3.88 (1 H, m), 4.51 (1 H, s), 5.13 (1 H, d, \( J = 8.6 \) Hz), 7.28 (2 H, d, \( J = 8.0 \) Hz), 7.70 (2 H, d, \( J = 8.0 \) Hz). \(^1\)C NMR (125 MHz, CDCl3) \( \delta \): 21.5, 22.0, 28.4, 29.3, 32.8, 40.1, 52.4, 55.5, 127.3, 129.6, 136.7, 143.7, 156.0, 172.1. IR (neat): 3391, 3286, 2952, 2952, 1742, 1695 cm\(^{-1}\). HRMS (MALDI) Calcd for C19H30N3O6S [M+Na]^+: 437.1717, found 437.1711.
tert-Butyl (S,E)-(7-cyano-5-(4-methylphenyl)sulfonamido)hept-6-en-1-yl)carbamate (3p) (Table 3, entry 8): According to the General Procedure B, the mixture of the S1 (2.2 g) and DIBAL (19 mL, 19 mmol) in CH2Cl2 (11 mL, 0.50 M) was stirred for 2 hours at –78 °C. The mixture of the crude product (2.2 g), diethyl cyanomethylphosphonate (0.83 mL, 5.3 mmol), NaCl (0.46 g, 7.9 mmol) and iPr₂NEt (1.4 mL, 7.9 mmol) in MeCN (5.3 mL, 1.0 M) was stirred for 20 hours at room temperature. The mixture was purified by Yamazen automatic column chromatography on silica gel (hexane/EtOAc = 4 : 1 to 3 : 2) to provide the titled compound 3p (1.7 g, 78%) as a colorless solid. [α]21D = –42.3 (c 0.11, CHCl3). Mp: 134–137 °C. 1H NMR (500 MHz, CDCl3) δ: 1.10–1.63 (13 H, m), 2.43 (3 H, s), 2.97–3.12 (2 H, m), 4.54 (1 H, brs), 5.10 (1 H, d, J = 4.5 Hz), 5.45 (1 H, d , J = 21.0 Hz), 6.40 (1 H, dd, J = 21, 6.5 Hz), 7.27 (2 H, d, J = 8.5 Hz), 7.72 (2 H, d, J = 8.5 Hz). 13C NMR (125 MHz, CDCl3) δ: 21.6, 28.5, 29.7, 29.8, 33.4, 39.3, 54.9, 79.8, 101.0, 116.6, 127.2, 129.9, 137.4, 143.9, 153.6, 156.6. IR (neat): 3425, 2942, 2226, 1653 cm⁻¹. HRMS (MALDI) Calcd for C15H21NO3S [M+Na]+: 318.1134, found 318.1135.

S2

2-(p-Toluenesulfonylamino)cyclohexanone (S2) (Scheme 2): 1-(Trimethylsiloxy)cyclohexene (1.7 mL, 9.0 mmol) was dissolved in MeCN (12 mL). PhINTs (2.3 g, 6.0 mmol) was added to the solution and the mixture was cooled to –20 °C. Cu(OTf)2 (0.22 g, 0.6 mmol) was added to the mixture and it was stirred at 0 °C for 1 hour. Then, the mixture was warmed to room temperature and stirred for 30 min. The reaction mixture was passed through a short pad of silica gel using EtOAc and the solvents were removed under reduced pressure. The residue was purified by column chromatography on silica gel (hexane/EtOAc = 5:1) to provide the titled compound S2 (0.62 g, 39%) as a colorless solid. Mp: 130–133 °C. 1H NMR (500 MHz, CDCl3) δ: 1.47–1.73 (3 H, m), 1.81–1.88 (1 H, m), 2.02–2.10 (1 H, m), 1.87–2.26 (1 H, m), 2.40 (3 H, s), 2.42–2.56 (2 H, m), 3.72–3.77 (1 H, m), 5.77 (1 H, d, J = 5.0 Hz), 7.27 (2 H, d, J = 8.0 Hz), 7.71 (2 H, d, J = 8.0 Hz). 13C NMR (125 MHz, CDCl3) δ: 21.5, 23.9, 27.4, 36.9, 40.7, 60.6, 127.0, 129.7, 137.0, 143.5. IR (neat): 3298, 2943, 1716 cm⁻¹. HRMS (MALDI) Calcd for C13H17NO3S [M+Na]+: 290.0821, found 290.0820.
(E)-N-(2-(Cyanomethylene)cyclohexyl)-4-methylbenzenesulfonamide (3q) (Scheme 2): The round bottomed flask was charged with LiCl (9.3 mg, 0.22 mmol) and stir bar. MeCN (1.0 mL), diethyl cyanomethylphosphonate (35 μL, 0.22 mmol) and iPr₂NEt (1.0 equiv) was sequentially added to the flask and it was cooled to 0 °C. Then MeCN (1.0 mL) solution of 2(p-toluenesulfonamido)cyclohexanone (S2) (53 mg, 0.20 mmol) was added via a cannula and the mixture was stirred at room temperature for 15 hours. Water (ca. 2.0 mL) was added to the reaction mixture and the mixture was extracted with EtOAc three times. Combined organic phase was dried over MgSO₄. Solvents were removed under reduced pressure. The residue was purified by flash column chromatography on silica gel (EtOAc/hexane = 2:1) to provide the titled compound 3q (32 mg, 56%) as a white solid. Mp: 130–133 °C. ¹H NMR (500 MHz, CDCl₃) δ: 1.29–1.52 (3 H, m), 1.70–1.84 (3 H, m), 2.07–2.14 (1 H, m), 2.44 (3 H, s), 2.82–2.88 (1 H, m), 3.78–3.84 (1 H, m), 5.04 (1 H, brd, J = 8.0 Hz), 5.34 (1 H, s), 7.32 (2 H, d, J = 8.0 Hz), 7.73 (2 H, d, J = 8.0 Hz). ¹³C NMR (125 MHz, CDCl₃) δ: 21.5, 24.3, 26.7, 32.0, 35.4, 56.3, 93.2, 119.4, 126.9, 129.9, 137.3, 144.0, 165.3. IR (neat): 3264, 2942, 2219 cm⁻¹. HRMS (MALDI) Calcd for C₁₅H₁₈N₂O₂S [M+Na]⁺: 313.0981, found 313.0979.

Methyl N-tosyl-L-valinate (S3): A solution of methyl L-valinate hydrochloride (5.6 g, 40 mmol) in CH₂Cl₂ (0.20 L, 0.20 M) was added TsCl (8.0 g, 42 mmol). The solution was stirred for 10 min at 0 °C. Then Et₃N was added to the mixture and the mixture was stirred for 30 min at room temperature. Water was added to the mixture was extracted with EtOAc three times. Combined organic phase was washed with brine and dried over MgSO₄ and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel (EtOAc/hexane = 3:1) to provide the titled compound S3 (7.7 g, 67%) as a colorless solid. Mp: 75–77 °C. ¹H NMR (300 MHz, CDCl₃) δ: 0.86 (3 H, d, J = 7.0 Hz), 0.93 (3 H, d, J = 7.0 Hz), 2.23 (1 H, septd, J = 7.0, 5.0 Hz), 2.40 (3 H, s), 3.43 (3 H, s), 3.72 (1 H, dd, J = 10.5 Hz, 5.0 Hz), 5.02 (NH, brd , J = 10.5 Hz), 7.27 (2 H, d, J = 8.5 Hz), 7.69 (2 H, d, J = 8.5 Hz).
(S)-4-Methyl-N-(3-methyl-1-oxobutan-2-yl)benzenesulfonamide (S4): A solution of methyl N-tosyl-L-valinate S3 (2.9 g, 10 mmol) in CH₂Cl₂ (20 mL, 0.50 M) was added DIBAL in hexane (25 mL, 25 mmol) for 10 min at –78 °C. After stirring for 2 hour, MeOH (17.5 mL) and 30% aq. Rochelle salt (33 mL) was added slowly to the mixture and stirred for 40 min at room temperature. The mixture was washed twice with 30% aq. Rochelle salt (18 mL and 13 mL), and the aqueous phase was extracted with Et₂O three times. The combined organic extracts were washed with brine, dried over MgSO₄ and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel (EtOAc/hexane = 3:1) to provide the titled compound S4 (1.9 g, 74%) as a colorless solid. [α]ᵢ₀⁺ = +91.2 (c 0.13, CHCl₃). Mp: 54–57 °C. ¹H NMR (500 MHz, CDCl₃) δ: 0.89 (3 H, d, J = 7.0 Hz), 1.02 (3 H, d, J = 7.0 Hz), 2.23 (1 H, septd, J = 7.0, 4.0 Hz), 2.41 (3 H, s), 3.81 (1 H, d, J = 7.5 Hz), 4.26 (1 H, d, J = 7.5 Hz), 7.28 (2 H, d, J = 8.0 Hz), 7.71 (2 H, d, J = 8.0 Hz), 9.43 (1 H, s). ¹³C NMR (125 MHz, CDCl₃) δ: 17.2, 18.9, 21.5, 29.3, 66.7, 127.2, 129.7, 136.5, 143.8, 198.5. IR (neat): 3277, 2968, 1733 cm⁻¹. HRMS (MALDI) Calcd for C₁₂H₁₀NO₃S [M+Na]⁺: 278.0821, found 278.0825.

Methyl (S,E)-5-methyl-4-((4-methylphenyl)sulfonamido)hex-2-enoate (3h) (Table 2, entry 2): A solution of (S)-4-methyl-N-(3-methyl-1-oxobutan-2-yl)benzenesulfonamide (S4) (0.77 g, 3.0 mmol) in MeCN (3.0 mL, 1.0 M) was added methyl (diethoxyphosphophyl)acetate (0.54 mL, 3.0 mmol), iPr₂NEt (0.54 mL, 3.0 mmol) and LiCl (0.15 g, 3.0 mmol) at room temperature. After stirring for 12 hours, water (3.0 mL) was added to the mixture and the mixture was extracted with EtOAc three times. Combined organic phase was washed twice with brine, dried over MgSO₄ and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel (hexane/EtOAc = 2:1) to provide the titled compound 3h (0.66 g, 71%) as a colorless solid. [α]ᵢₒ⁺ = +18.1 (c 0.14, CHCl₃). Mp: 85–87 °C. ¹H NMR (500 MHz, CDCl₃) δ: 0.83 (3 H, d, J = 7.0 Hz), 0.85 (3 H, d, J = 7.0 Hz), 1.80 (1 H, septd, J = 7.0, 5.5 Hz), 2.40 (3 H, s), 3.67 (3 H, s), 3.72–3.76 (1 H, m), 4.85 (1 H, d, J = 8.5 Hz), 5.67 (1 H, dd, J = 16.0, 1.5 Hz), 6.59 (1 H, dd, J = 16.0, 6.5 Hz), 7.27 (2 H, d, J = 8.5 Hz), 7.71 (2 H, d, J = 8.5 Hz). ¹³C NMR (125 MHz, CDCl₃) δ: 18.0, 18.4, 21.5, 32.6, 51.6, 60.1, 122.3, 127.1, 129.6, 137.6, 143.5, 145.4, 166.1. IR (neat): 3280, 1725, 1660 cm⁻¹. HRMS (MALDI) Calcd for C₁₂H₁₂NO₃S [M+Na]⁺: 334.1083, found 334.1082. Optical purity was determined by HPLC analysis at 20 °C, using a CHIRALCEL ID column [hexane/2-propanol = 80:20, 1.0
mL/min; retention times 17.3 min (S), 22.3 min (R)].

The corresponding racemic (±)-3h was obtained by the same procedure with (S)-3h shown above using a racemic methyl DL-valinate hydrochloride (±)-4a. The racemic (±)-3h was used to determine enantiomeric excess (ee) % of 3h shown above.

(S,E)-4-Methyl-N-(2-methyl-6-oxohept-4-en-3-yl)benzenesulfonamide (3i) (Table 2, entry 3): A solution of dimethyl acetonylphosphonate (0.18 mL, 1.3 mmol) in MeCN (1.0 mL) was added LiCl (97 mg, 2.3 mmol) and iPr₂NEt (0.31 mL, 1.8 mmol) at 0 °C. After stirring for 20 min at 0 °C, (S)-4-methyl-N-(3-methyl-1-oxobutan-2-yl)benzenesulfonamide (S4) (0.26 g, 1.0 mmol) in MeCN (1.5 mL) was added to the mixture via a cannula and the mixture was stirred for 2 hours at room temperature. Water (3.0 mL) was added to the mixture and the mixture was extracted with EtOAc three times. Combined organic phase was washed twice with brine, dried over MgSO₄ and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel (hexane/EtOAc = 1:1) to provide the titled compound 3i (0.29 g, 97%) as a colorless solid. [α]D²¹ = −35.9 (c 0.10, CHCl₃). Mp: 114–117 °C. ¹H NMR (500 MHz, CDCl₃) δ: 0.84 (3 H, d, J = 7.0 Hz), 0.87 (3 H, d, J = 7.0 Hz), 1.80 (1 H, septd, J = 7.0, 5.5 Hz), 2.06 (3 H, s), 2.40 (3 H, s), 5.05 (1 H, d, J = 8.0 Hz), 5.88 (1 H, dd, J = 16.0, 1.0 Hz), 6.38 (1 H, dd, J = 16.0, 7.0 Hz), 7.27 (2 H, d, J = 8.5 Hz), 7.72 (2 H, d, J = 8.5 Hz). ¹³C NMR (125 MHz, CDCl₃) δ: 18.0, 18.5, 21.4, 27.3, 32.7, 60.3, 127.2, 129.6, 131.3, 137.6, 143.6, 143.9, 197.4. IR (neat): 3272, 2357, 1674, 1629 cm⁻¹. HRMS (MALDI) Calcd for C₁₅H₂₁NO₃S [M+Na]+: 318.1134, found 318.1135. Optical purity was determined by HPLC analysis at 20 °C, using a CHIRALCEL ID column [hexane/2-propanol = 80:20, 1.0 mL/min; retention times 17.5 min (S), 24.0 min (R)].

The corresponding racemic (±)-3i was obtained by the same procedure with (S)-3i shown above using a racemic methyl DL-valinate hydrochloride (±)-4a. The racemic (±)-3i was used to determine enantiomeric excess (ee) % of 3i shown above.
Experimental References

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0

X : parts per Million : Carbon13

190.0 180.0 170.0 160.0 150.0 140.0 130.0 120.0 110.0 100.0 90.0 80.0 70.0 60.0 50.0 40.0 30.0 20.0 10.0 0.0

-10.0

151.191
144.154
137.069
129.918
127.040
116.428
102.336
77.430
77.000
76.579
63.931
56.053
25.678
21.520
18.145
-5.633

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Filename         = Ymsd09-059-02_proton-1-5.jxp
Author           = delta
Experiment       = proton.jxp
Sample_Id        = Ymsd09-059-02
Solvent          = CHLOROFORM-D
Creation_Time    = 29-JUL-2017 15:58:54
Revision_Time    = 29-JUL-2017 17:09:42
Current_Time     = 22-AUG-2017 22:34:42
Comment          = single_pulse
Data_Format      = 1D COMPLEX
Dim_Size         = 13107
Dim_Title        = Proton
Dim_Units        = [ppm]
Dimensions       = X
Site             = JNM-ECA500
Spectrometer     = DELTA2_NMR
Field_Strength   = 11.7473579[T] (500[MHz])
X_Acq_Duration   = 1.74587904[s]
X_Domain         = 1H
X_Freq           = 500.15991521[MHz]
X_Offset         = 5.0[ppm]
X_Points         = 16384
X_Prescans       = 1
X_Resolution     = 0.57277737[Hz]
X_Sweep          = 9.38438438[kHz]
X_Sweep_Clipped  = 7.50750751[kHz]
Irr_Domain       = Proton
Irr_Freq         = 500.15991521[MHz]
Irr_Offset       = 5.0[ppm]
Tri_Domain       = Proton
Tri_Freq         = 500.15991521[MHz]
Tri_Offset       = 5.0[ppm]
Clipped          = FALSE
Scans            = 16
Total_Scans      = 16
Relaxation_Delay = 5[s]
Recvr_Gain       = 38
Temp_Get         = 25.1[dc]
X_90_Width       = 13[us]
X_Acq_Duration   = 1.74587904[s]
X_Angle          = 45[deg]
X_Atn            = 3.6[db]
X_Pulse          = 6.5[us]
Irr_Mode         = Off
Tri_Mode         = Off
Dante_Preset     = FALSE
Initial_Wait     = 1[s]
Repetition_Time  = 6.74587904[s]