

Supplemental materials for:

**Pt(II)-Catalyzed Synthesis of 1,2-Dihydropyridines from Aziridinyl Propargylic Esters**

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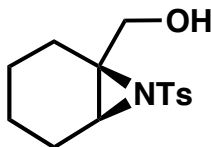
**Table of contents:**

|   |    |
|---|----|
| Materials and Methods   | 2  |
| Representative Procedure for the Formation of Aziridines                    | 3  |
| Representative Procedure for the Formation of Azyridinyl Aldehydes          | 5  |
| Representative Procedure for the Formation of Azyridinyl Propargylic Esters | 7  |
| Representative Procedure for the Formation of Dihydropyridines              | 17 |
| Representative Procedure for the Formation of Hydroxypyridines              | 26 |
| References  | 27 |
| HPLC Traces   | 28 |
| ORTEP Structure and Refinement Data   | 31 |
| Selected NMR spectra  | 33 |

**Materials and Methods.** All air or moisture sensitive reactions were conducted in flame-dried glassware under an atmosphere of nitrogen using dry, deoxygenated solvents. Toluene, methylene chloride, and acetonitrile were distilled under nitrogen from calcium hydride immediately prior to use and tetrahydrofuran (THF) was distilled under nitrogen from sodium benzophenone ketyl. Alumina was washed with water (3 mL per 100 g) prior to use. Dess-Martin periodinane was prepared according to literature precedent.<sup>1</sup> PtCl<sub>2</sub> was purchased from Strem or obtained by donation from Johnson Matthey. All other reagents were purchased from Aldrich, Acros, or Lancaster and used without further purification. Reaction temperatures were controlled by an IKAmag<sup>®</sup> temperature modulator. Thin-layer chromatography (TLC) was performed using E. Merck silica gel 60 F254 precoated plates (0.25 mm) and visualized by UV indication and anisaldehyde stain. Fisher silica gel 240-400 mesh (particle size 0.032-0.063) and Aldrich neutral alumina oxide 150 mesh were used for flash chromatography. <sup>1</sup>H and <sup>13</sup>C NMR spectra were recorded on a Bruker AV-500 (at 500 MHz (<sup>1</sup>H) and 125 MHz (<sup>13</sup>C)), on a Bruker DRX-500 (at 500 MHz (<sup>1</sup>H) and 125 MHz (<sup>13</sup>C)), or on a Bruker AVB-400 (at 400 MHz (<sup>1</sup>H) and 100 MHz (<sup>13</sup>C)) in chloroform-*d*, benzene-*d*<sub>6</sub> or methanol-*d*<sub>4</sub> at 23 °C. Chemical shifts were referenced to the residual chloroform-H peak, which was set at 7.26 ppm for <sup>1</sup>H and 77.0 ppm (center peak) for <sup>13</sup>C spectra; to the residual methanol-H peak, which was set at 3.34 ppm for <sup>1</sup>H and 49.9 ppm (center peak) for <sup>13</sup>C spectra; or to the residual benzene-H peak, which was set at 7.15 ppm for <sup>1</sup>H and 128.6 ppm (center peak) for <sup>13</sup>C spectra. Data for <sup>1</sup>H NMR are reported as follows: chemical shifts (δ ppm), multiplicity, (s = singlet, d = doublet, t = triplet, q = quartet, dd = doublet of doublets, dt = doublet of

triplets, dq = doublet of quartets, qd = quartet of doublets, m = multiplet, br = broad resonance), coupling constants (Hz) and integration. Data for  $^{13}\text{C}$  NMR are reported in terms of chemical shift. IR spectra were recorded on a Nicolet MAGNA-IR 850 spectrometer and are reported in frequency of absorption ( $\text{cm}^{-1}$ ). Low and high resolution mass spectral data were obtained from the University of California, Berkeley Mass Spectral Facility, on a VG 70-Se Micromass spectrometer for FAB (120 kV), and a VG Prospec Micromass spectrometer for EI (70 eV). Enantiomeric excesses were obtained utilizing a Shimadzu 10 A VP series chiral HPLC. Polarization data was obtained on a Perkin-Elmer 241 Polarimeter with a 59 nm sodium lamp.

#### Procedure for Synthesis of Propargylic Esters:

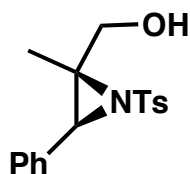


S1

#### Representative Procedure A for the Formation of Aziridines:<sup>2</sup>

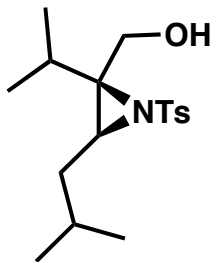
**(7-tosyl-7-aza-bicyclo[4.1.0]heptan-1-yl)methanol (S1).** Cyclohexenylmethanol was synthesized by a known method.<sup>3</sup> A flame-dried 50 mL round-bottom flask equipped with a stir bar was charged with cyclohexenylmethanol (1 g, 9.3 mmol, 1 equiv) and acetonitrile (30 mL). To the flask, anhydrous Chloramine-T (2.2 g, 9.7 mmol, 1.05 equiv) was added. To the stirring cloudy white mixture, *N*-bromosuccinimide (329 mg, 1.85 mmol, 0.2 equiv) was added. The resulting cloudy yellow mixture was stirred overnight at room temperature, and the solids were removed by filtration. The resulting yellow solution was concentrated under reduced pressure (rotary evaporation) and then

purified by column chromatography (100 mL silica gel, 4:1 hexanes:ethyl acetate) to yield 1.86 g (58%) of **S1** as a white semi-solid.  $R_f = 0.23$  (4:1 hexanes:ethyl acetate);  $^1\text{H NMR}$  (500 MHz,  $\text{CDCl}_3$ )  $\delta$  ppm 7.82 (d,  $J = 8.3$  Hz, 2H), 7.32 (d,  $J = 8.1$  Hz, 2H), 4.05 (m, 2H), 3.24 (dd,  $J = 5.0, 0.7$  Hz, 1H), 3.02 (s, 1H), 2.44 (s, 3H), 2.26 (td,  $J = 12.0, 5.8, 5.8$  Hz, 1H), 1.79 (m, 2H), 1.65 (m, 2H), 1.35 (m, 3H), 1.23-1.14 (m, 1H);  $^{13}\text{C NMR}$  (125 MHz,  $\text{CDCl}_3$ )  $\delta$  ppm 143.8, 138.1, 129.5, 126.8, 65.8, 56.4, 45.4, 27.4, 22.7, 21.5, 19.6, 19.3; **IR** (film) 3424, 2940, 1644  $\text{cm}^{-1}$ ; **HRMS** ( $\text{FAB}^+$ ) calc'd for  $[\text{C}_{14}\text{H}_{19}\text{NO}_3\text{S}]^+$ :  $m/z$  282.1164, found 282.1161.



**S2**

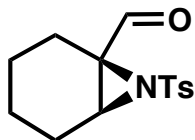
**(2-methyl-3-phenyl-1-tosylaziridin-2-yl)methanol (S2).** 2-methyl-3-phenylprop-2-en-1-ol, the aziridine precursor, was purchased from Aldrich. Following procedure A, a yellow gel was obtained in 82% yield following purification by column chromatography (silica gel, 6:1 hexanes:ethyl acetate).  $R_f = 0.18$  (4:1 hexanes:ethyl acetate);  $^1\text{H NMR}$  (500 MHz,  $\text{CDCl}_3$ )  $\delta$  ppm 7.87 (d,  $J = 8.3$  Hz, 2H), 7.33 (d,  $J = 8.1$  Hz, 2H), 7.25 (dd,  $J = 6.4, 2.9$  Hz, 3H), 7.03 (dd,  $J = 6.5, 3.0$  Hz, 2H), 4.24 (s, 1H), 4.18 (m, 2H), 3.20 (m, 1H), 2.45 (s, 3H), 1.18 (s, 3H);  $^{13}\text{C NMR}$  (125 MHz,  $\text{CDCl}_3$ )  $\delta$  ppm 144.2, 137.4, 133.0, 129.6, 128.3, 127.8, 127.1, 126.9, 65.5, 59.2, 51.3, 21.6, 16.0; **IR** (film) 3441, 1644  $\text{cm}^{-1}$ ; **HRMS** ( $\text{FAB}^+$ ) calc'd for  $[\text{C}_{17}\text{H}_{19}\text{NO}_3\text{S}]^+$ :  $m/z$  318.1164, found 318.1162.



S3

**(3-isobutyl-2-isopropyl-1-tosylaziridin-2-yl)methanol (S3).** 2-isopropyl-5-methyl-2-hexenol, the aziridine precursor, was obtained by reduction of the corresponding aldehyde using a known procedure<sup>4</sup> and was utilized crude. Following procedure A, a yellow gel was obtained in 48% yield following purification by column chromatography (silica gel, 6:1 hexanes:ethyl acetate).  $R_f = 0.36$  (4:1 hexanes:ethyl acetate);  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  ppm 7.88 (d,  $J = 8.3$  Hz, 2H), 7.36 (d,  $J = 8.0$  Hz, 2H), 4.41 (dd,  $J = 14.0, 9.0$  Hz, 1H), 3.93 (dd,  $J = 14.0, 6.1$  Hz, 1H), 3.25 (m, 2H), 2.49 (s, 3H), 1.69 (td,  $J = 14.1, 7.1, 7.1$  Hz, 1H), 1.63 (s, 1H), 1.49-1.35 (m, 2H), 1.24 (d,  $J = 7.1$  Hz, 3H), 1.08 (d,  $J = 7.1$  Hz, 3H), 0.95 (d,  $J = 6.2$  Hz, 3H), 0.84 (d,  $J = 6.4$  Hz, 3H);  $^{13}\text{C NMR}$  (125 MHz,  $\text{CDCl}_3$ )  $\delta$  ppm 143.9, 137.6, 129.4, 127.2, 63.4, 61.1, 49.4, 35.5, 31.4, 26.9, 22.9, 21.9, 21.5, 19.7, 18.0; **IR** (film) 3519, 2961, 1599  $\text{cm}^{-1}$ ; **HRMS** (FAB<sup>+</sup>) calc'd for  $[\text{C}_{17}\text{H}_{27}\text{NO}_3\text{S}]^+$ :  $m/z$  326.1802, found 326.1800.

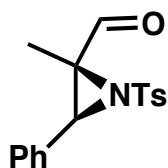
**Representative Procedure B for the Formation of Aziridinyl Aldehydes:**



S4

**7-tosyl-7-aza-bicyclo[4.1.0]heptane-1-carbaldehyde (S4).** A flame-dried 50 mL round-bottom flask equipped with a stir bar was charged with **S1** (1.5 g, 4.2 mmol, 1 equiv) and

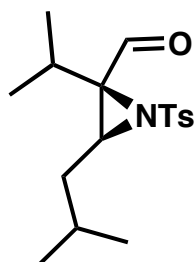
methylene chloride (15 mL). The resulting clear solution was cooled to 0 °C and then stirred for an additional 10 min. Sodium bicarbonate (689 mg, 8.4 mmol, 2 equiv) and Dess-Martin periodinane (1.9 g, 4.6 mmol, 1.1 equiv) were then added. The resulting cloudy white mixture was then warmed to room temperature and until all the starting material was consumed as judged by TLC analysis (1 h). The white mixture was washed with sat. aq. sodium bicarbonate and extracted with methylene chloride (2 x 15 mL). The combined organic extracts were dried over MgSO<sub>4</sub> and concentrated under reduced pressure (rotary evaporation). The crude white oil was purified by column chromatography (150 mL silica gel, 4:1 hexanes:ethyl acetate) to yield 1.2 g (80%) of **S4** as a white semi-solid.  $R_f = 0.35$  (4:1 hexanes:ethyl acetate); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ ppm 9.53 (s, 1H), 7.83 (d, *J* = 8.3 Hz, 2H), 7.34 (d, *J* = 8.0 Hz, 2H), 3.70 (dd, *J* = 3.9, 2.1 Hz, 1H), 2.51-2.41 (m, 4H), 1.87-1.73 (m, 3H), 1.48-1.38 (m, 1H), 1.38-1.29 (m, 1H), 1.28-1.14 (m, 2H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ ppm 194.7, 144.5, 136.9, 129.8, 127.2, 56.9, 46.2, 23.0, 21.6, 21.15, 19.07, 19.05; IR (film) 3423, 1643 cm<sup>-1</sup>; HRMS (FAB<sup>+</sup>) calc'd for [C<sub>14</sub>H<sub>17</sub>NO<sub>3</sub>S]<sup>+</sup>: *m/z* 280.1007, found 280.1007.



**S5**

**2-methyl-3-phenyl-1-tosylaziridine-2-carbaldehyde (S5).** Obtained following Procedure B, a white semi-solid was obtained in quantitative yield following purification by column chromatography (silica gel, 6:1 hexanes:ethyl acetate).  $R_f = 0.38$  (4:1 hexanes:ethyl acetate); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ ppm 9.76 (s, 1H), 7.93 (d, *J* = 8.2 Hz, 2H), 7.40 (d, *J* = 8.1 Hz, 2H), 7.37-7.27 (m, 3H), 7.16-7.09 (m, 2H), 4.73 (s, 1H),

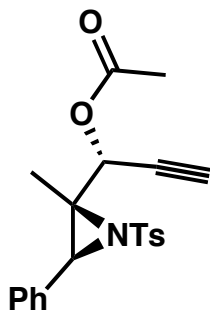
2.51 (s, 3H), 1.21 (s, 3H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  ppm 194.1, 144.8, 136.2, 131.1, 129.8, 128.6, 128.6, 127.4, 127.1, 59.8, 52.1, 21.6, 11.3; IR (film) 3064, 1721, 1598  $\text{cm}^{-1}$ ; HRMS (FAB $^+$ ) calc'd for  $[\text{C}_{17}\text{H}_{17}\text{NO}_3\text{S}]^+$ :  $m/z$  316.1007, found 316.1004.



**S6**

**3-isobutyl-2-isopropyl-1-tosylaziridine-2-carbaldehyde (S6).** Following procedure B, the product was obtained and the crude material was taken on directly.

**Representative Procedure C for the Formation of Aziridinyl Propargylic Esters:**

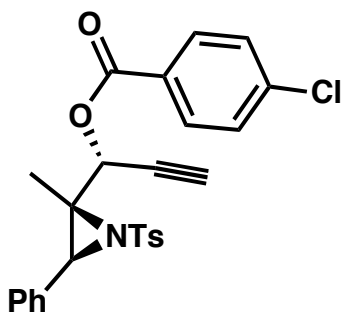


**1a**

**1-(2-methyl-3-phenyl-1-tosylaziridin-2-yl)prop-2-ynyl acetate (1a).** A flame-dried 50 mL round-bottom flask equipped with a stir bar was charged with **S5** (500 mg, 1.6 mmol, 1 equiv) and THF (7 mL). To the stirred clear solution, cooled to  $-78\text{ }^\circ\text{C}$  was added ethynylmagnesium bromide (0.5M in THF, 9.5 mL, 4.7 mmol, 3 equiv). After stirring at room temperature for 1 h, acetyl chloride (0.41 mL, 5.3 mmol, 3.3 equiv) was added dropwise over 10 min to the orange solution. The resulting red solution was stirred until all the starting material was consumed as judged by TLC analysis (20 min) and

subsequently quenched with sat. aqueous NH<sub>4</sub>Cl (15 mL) and extracted with ethyl acetate (2 x 7mL). The combined organic extracts were dried over MgSO<sub>4</sub> and concentrated under reduced pressure (rotary evaporation). The crude yellow oil was purified by column chromatography (50 mL silica gel, 4:1 hexanes:ethyl acetate) to yield 498 mg (81% yield) of **1a** as a white gel.  $R_f = 0.41$  (4:1 hexanes:ethyl acetate); <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>) δ ppm 7.86 (d,  $J = 8.2$  Hz, 2H), 7.31 (d,  $J = 8.1$  Hz, 2H), 7.28-7.22 (m, 3H), 7.04 (dd,  $J = 6.5, 2.6$  Hz, 2H), 6.07 (d,  $J = 2.0$  Hz, 1H), 4.16 (s, 1H), 2.62 (d,  $J = 2.1$  Hz, 1H), 2.43 (s, 3H), 2.13 (s, 3H), 1.28 (s, 3H); <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>) δ ppm 169.2, 144.4, 137.0, 132.1, 129.6, 128.4, 128.1, 127.5, 127.0, 78.7, 75.1, 64.9, 56.5, 50.4, 21.6, 20.7, 14.0; IR (film) 3279, 2983, 1752 cm<sup>-1</sup>; HRMS (FAB<sup>+</sup>) calc'd for [C<sub>21</sub>H<sub>21</sub>NO<sub>4</sub>S]<sup>+</sup>:  $m/z$  384.1270, found 384.1279.

**Enriched sample:**  $[\alpha]_D^{23} = -12.7^\circ$  ( $c = 0.7$  in CHCl<sub>3</sub>). A racemic sample of **1a** was resolved using a HPLC system with Rainin SD-1 pumps, Sonntek UV detector and a 2 X 25 cm Chiraplak OD-H column (using a solvent system of 20% ethanol in hexane at 3mL/min). Analysis of enantiomers by chiral HPLC (Chiraplak OD-H, 20% ethanol in hexane at 3mL/min,  $T_r$  major 3.68, minor 2.52 at > 99.9% ee. Enantiomeric excess was determined using HPLC analysis, which was conducted by Ms. Christina Kraml (AccelaPure Corp., Princeton, NJ, USA). HPLC traces are provided on pages 27-28.

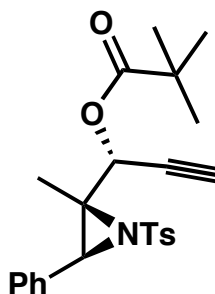


**1b**



**1-(2-methyl-3-phenyl-1-tosylaziridin-2-yl)prop-2-ynyl 4-chlorobenzoate (1b).**

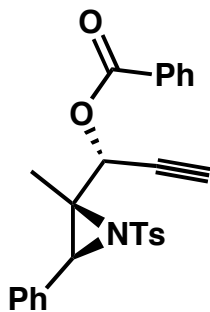
Following procedure C, a clear semi-solid was obtained in 75% yield following purification by column chromatography (silica gel, 4:1 hexanes:ethyl acetate).  $R_f = 0.47$  (4:1 hexanes:ethyl acetate);  $^1\text{H NMR}$  (500 MHz,  $\text{CDCl}_3$ )  $\delta$  ppm 7.94 (d,  $J = 8.4$  Hz, 2H), 7.82 (d,  $J = 8.1$  Hz, 2H), 7.42 (d,  $J = 8.4$  Hz, 2H), 7.34-7.30 (m, 3H), 7.22-7.15 (m, 4H), 6.30 (d,  $J = 1.4$  Hz, 1H), 4.28 (s, 1H), 2.68 (d,  $J = 1.7$  Hz, 1H), 2.34 (s, 3H), 1.39 (s, 3H);  $^{13}\text{C NMR}$  (125 MHz,  $\text{CDCl}_3$ )  $\delta$  ppm 164.2, 144.9, 140.2, 137.1, 132.537, 131.8, 130.0, 129.1, 128.9, 128.7, 128.4, 127.9, 127.6, 78.8, 76.1, 65.8, 56.6, 50.2, 22.0, 14.6; **IR** (film) 3284, 2980, 1733  $\text{cm}^{-1}$ ; **HRMS** (FAB $^+$ ) calc'd for  $[\text{C}_{26}\text{H}_{22}\text{ClNO}_4\text{S}]^+$ :  $m/z$  480.1045, found 480.1043.



**1c**

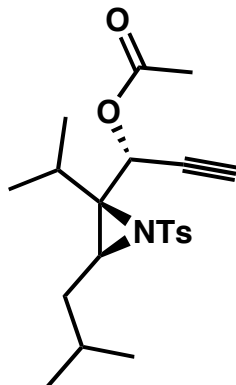
**1-(2-methyl-3-phenyl-1-tosylaziridin-2-yl)prop-2-ynyl pivalate (1c).** Following procedure C, a clear oil was obtained in 81% yield following purification by column chromatography (silica gel, 6:1 hexanes:ethyl acetate).  $R_f = 0.54$  (4:1 hexanes:ethyl acetate);  $^1\text{H NMR}$  (500 MHz,  $\text{CDCl}_3$ )  $\delta$  ppm 7.87 (d,  $J = 8.3$  Hz, 2H), 7.30 (d,  $J = 8.0$  Hz, 2H), 7.27-7.24 (m, 3H), 7.03 (dd,  $J = 6.4, 2.6$  Hz, 2H), 6.08 (d,  $J = 2.0$  Hz, 1H), 4.15 (s, 1H), 2.60 (d,  $J = 2.1$  Hz, 1H), 2.43 (s, 3H), 1.30 (s, 12H);  $^{13}\text{C NMR}$  (125 MHz,

CDCl<sub>3</sub>)  $\delta$  ppm 176.3, 144.3, 137.1, 132.2, 129.6, 128.3, 128.0, 127.5, 126.9, 78.9, 74.6, 64.8, 56.8, 50.3, 38.9, 27.0, 21.6, 14.0; **IR** (film) 3279, 2978, 1742 cm<sup>-1</sup>; **HRMS** (FAB<sup>+</sup>) calc'd for [C<sub>24</sub>H<sub>27</sub>NO<sub>4</sub>S]<sup>+</sup>:  $m/z$  426.1751, found 426.1747.



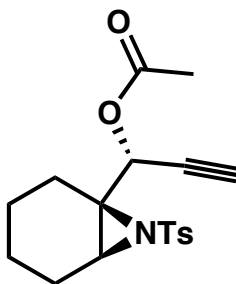
**1d**

**1-(2-methyl-3-phenyl-1-tosylaziridin-2-yl)prop-2-ynyl benzoate (1d).** Following procedure C, a clear viscous oil was obtained in 79% yield following purification by column chromatography (silica gel, 4:1 hexanes:ethyl acetate).  $R_f$  = 0.49 (4:1 hexanes:ethyl acetate); **<sup>1</sup>H NMR** (500 MHz, CDCl<sub>3</sub>)  $\delta$  ppm 7.98 (d,  $J$  = 7.3 Hz, 2H), 7.81 (d,  $J$  = 8.2 Hz, 2H), 7.59 (dd,  $J$  = 7.4, 7.4 Hz, 1H), 7.44 (dd,  $J$  = 7.8, 7.8 Hz, 2H), 7.35-7.30 (m, 3H), 7.25-7.21 (m, 2H), 7.12 (d,  $J$  = 8.1 Hz, 2H), 6.31 (d,  $J$  = 1.9 Hz, 1H), 4.30 (s, 1H), 2.66 (d,  $J$  = 2.0 Hz, 1H), 2.28 (s, 3H), 1.39 (s, 3H); **<sup>13</sup>C NMR** (125 MHz, CDCl<sub>3</sub>)  $\delta$  ppm 164.5, 144.3, 136.5, 133.2, 132.1, 129.9, 129.5, 129.4, 128.4, 128.2, 128.1, 127.4, 127.2, 78.6, 75.3, 64.9, 56.1, 49.4, 21.5, 14.1; **IR** (film) 3284, 1731 cm<sup>-1</sup>; **HRMS** (FAB<sup>+</sup>) calc'd for [C<sub>26</sub>H<sub>23</sub>NO<sub>4</sub>S]<sup>+</sup>:  $m/z$  446.1426, found 446.1430.



12c

**1-(3-isobutyl-2-isopropyl-1-tosylaziridin-2-yl)prop-2-ynyl acetate (12c).** Following procedure C, a white foam was obtained in 75% yield after purification by column chromatography (silica gel, 6:1 hexanes:ethyl acetate).  $R_f = 0.62$  (4:1 hexanes:ethyl acetate);  $^1\text{H NMR}$  (500 MHz,  $\text{C}_6\text{D}_6$ )  $\delta$  ppm 7.85 (d,  $J = 8.2$  Hz, 2H), 6.66 (d,  $J = 8.1$  Hz, 2H), 6.56 (d,  $J = 2.3$  Hz, 1H), 3.15 (dd,  $J = 7.0, 5.8$  Hz, 1H), 2.02 (d,  $J = 2.4$  Hz, 1H), 1.88 (td,  $J = 14.4, 7.1, 7.1$  Hz, 1H), 1.77 (s, 3H), 1.76 (s, 3H), 1.47 (d,  $J = 7.1$  Hz, 3H), 1.39-1.31 (m, 4H), 1.24-1.19 (m, 2H), 0.75 (d,  $J = 6.6$  Hz, 3H), 0.66 (d,  $J = 6.6$  Hz, 3H);  $^{13}\text{C NMR}$  (125 MHz,  $\text{C}_6\text{D}_6$ )  $\delta$  ppm 167.8, 143.2, 138.4, 129.0, 127.6, 127.6, 78.0, 75.4, 65.2, 59.9, 50.0, 35.5, 32.6, 26.7, 22.5, 21.8, 21.2, 20.7, 19.5; **IR** (film) 3268, 2963, 1752  $\text{cm}^{-1}$ ; **HRMS** (EI) calc'd for  $[\text{C}_{21}\text{H}_{29}\text{NO}_4\text{S}]^+$ :  $m/z$  392.1851, found 392.1852.

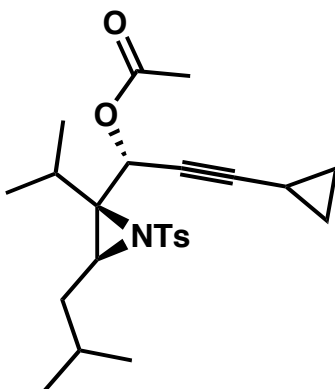


14

**1-(7-tosyl-7-aza-bicyclo[4.1.0]heptan-1-yl)prop-2-ynyl acetate (14).** Following

procedure C, a yellow gel was obtained in 69% yield after purification by column chromatography (silica gel, 4:1 hexanes:ethyl acetate).  $R_f = 0.20$  (4:1 hexanes:ethyl acetate);  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  ppm 7.80 (d,  $J = 8.3$  Hz, 2H), 7.30 (d,  $J = 8.0$  Hz, 2H), 5.87 (d,  $J = 2.2$  Hz, 1H), 3.16 (dd,  $J = 4.8, 1.0$  Hz, 1H), 2.54 (d,  $J = 2.2$  Hz, 1H), 2.43 (s, 3H), 2.32-2.22 (m, 1H), 2.12-2.06 (m, 1H), 2.04 (s, 3H), 1.87-1.76 (m, 1H), 1.68-1.59 (m, 2H), 1.54-1.41 (m, 1H), 1.40-1.20 (m, 3H);  $^{13}\text{C NMR}$  (125 MHz,  $\text{CDCl}_3$ )  $\delta$  ppm 169.2, 144.0, 137.8, 129.6, 127.2, 78.9, 74.9, 65.1, 54.0, 44.0, 25.0, 22.6, 21.6, 20.7, 19.8, 19.3; IR (film) 3424, 2942, 1750, 1644  $\text{cm}^{-1}$ ; HRMS (FAB $^+$ ) calc'd for  $[\text{C}_{18}\text{H}_{21}\text{NO}_4\text{S}]^+$ :  $m/z$  348.1262, found 348.1261.

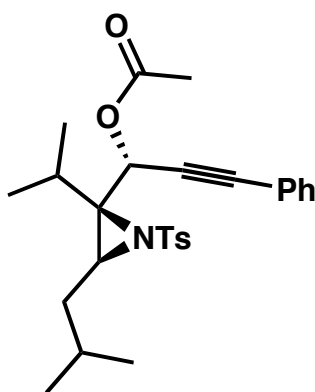
#### Representative Procedure D for the Formation of Aziridinyl Propargylic Esters:



12a

**3-cyclopropyl-1-(3-isobutyl-2-isopropyl-1-tosylaziridin-2-yl)prop-2-ynyl acetate (12a).** A flame-dried 50 mL round-bottom flask equipped with a stir bar was charged with ethynylcyclopropane (197 mg, 3 mmol, 1.3 equiv) and THF (20 mL). To the stirred clear solution, cooled to  $-78$   $^{\circ}\text{C}$ , was added butyllithium (2.5M in hexanes, 1 mL, 2.5 mmol, 1.1 equiv) dropwise over 15 min, and the resulting mixture was stirred for an additional 10 min. To the faint yellow solution, **S6** (750 mg, 2.3 mmol, 1 equiv) in THF

(1 mL) was added dropwise over 10 min. The yellow solution was stirred at 23 °C for 2 h, then acetyl chloride (0.30 mL, 4.6 mmol, 2 equiv) was added dropwise over 10 min and then stirred until all the starting material was consumed as judged by TLC analysis (20 min). The reaction was then quenched with sat. aqueous NH<sub>4</sub>Cl (15 mL) and extracted with ethyl acetate (2 x 7mL). The combined organic extracts were dried over MgSO<sub>4</sub> and concentrated under reduced pressure (rotary evaporation). The crude red oil was purified by column chromatography (50 mL silica gel, 6:1 hexanes:ethyl acetate) to yield 725 mg (73 % yield) of a yellow gel.  $R_f$  = 0.43 (4:1 hexanes:ethyl acetate); <sup>1</sup>H NMR (500 MHz, C<sub>6</sub>D<sub>6</sub>) δ ppm 7.87 (d,  $J$  = 8.3 Hz, 2H), 6.68 (d,  $J$  = 8.0 Hz, 2H), 6.55 (d,  $J$  = 1.5 Hz, 1H), 3.18 (dd,  $J$  = 6.5, 6.5 Hz, 1H), 1.91 (td,  $J$  = 14.3, 7.2, 7.2 Hz, 1H), 1.80 (s, 3H), 1.78 (s, 3H), 1.50 (d,  $J$  = 7.1 Hz, 3H), 1.42-1.38 (m, 1H), 1.36 (d,  $J$  = 7.3 Hz, 3H), 1.27-1.23 (m, 2H), 0.90 (dq,  $J$  = 8.2, 5.0, 5.0, 5.0, 2.0 Hz, 1H), 0.76 (d,  $J$  = 6.6 Hz, 3H), 0.68 (d,  $J$  = 6.6 Hz, 3H), 0.50 (m, 2H), 0.26 (m, 2H); <sup>13</sup>C NMR (125 MHz, C<sub>6</sub>D<sub>6</sub>) δ ppm 168.1, 143.2, 138.7, 129.1, 127.6, 90.7, 72.4, 66.0, 60.8, 50.1, 35.6, 32.6, 26.8, 22.5, 21.9, 21.3, 20.8, 20.3, 19.7, 7.7, 7.7, -0.4; IR (film) 2962, 1754 cm<sup>-1</sup>; HRMS (FAB<sup>+</sup>) calc'd for [C<sub>24</sub>H<sub>33</sub>NO<sub>4</sub>S]<sup>+</sup>:  $m/z$  432.2209, found 432.2208.

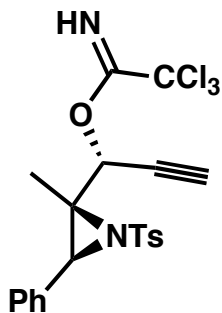


12b

1-(3-isobutyl-2-isopropyl-1-tosylaziridin-2-yl)-3-phenylprop-2-ynyl acetate (12b).

Following procedure D, a clear semi-solid was obtained in 70% yield after purification by column chromatography (silica gel, 8:1 hexanes:ethyl acetate).  $R_f = 0.55$  (4:1 hexanes:ethyl acetate);  $^1\text{H NMR}$  (400 MHz,  $\text{C}_6\text{D}_6$ )  $\delta$  ppm 7.92 (d,  $J = 8.3$  Hz, 2H), 7.40-7.33 (m, 2H), 6.93-6.89 (m, 3H), 6.86 (s, 1H), 6.72 (d,  $J = 8.0$  Hz, 2H), 3.30 (dd,  $J = 6.5, 6.5$  Hz, 1H), 2.00 (td,  $J = 14.2, 7.1, 7.1$  Hz, 1H), 1.86 (s, 3H), 1.81 (s, 3H), 1.59 (d,  $J = 7.0$  Hz, 3H), 1.49 (d,  $J = 7.2$  Hz, 3H), 1.42 (td,  $J = 13.1, 6.6, 6.6$  Hz, 1H), 1.33-1.26 (m, 2H), 0.77 (d,  $J = 6.5$  Hz, 3H), 0.70 (d,  $J = 6.6$  Hz, 3H);  $^{13}\text{C NMR}$  (100 MHz,  $\text{C}_6\text{D}_6$ )  $\delta$  ppm 168.0, 143.3, 138.5, 131.6, 129.1, 128.5, 128.2, 127.6, 122.3, 86.9, 86.0, 66.0, 60.5, 50.1, 35.5, 32.6, 26.8, 22.4, 21.8, 21.3; 20.734, 20.201, 19.615; **IR** (film) 2962, 1755, 1598  $\text{cm}^{-1}$ ; **HRMS** ( $\text{FAB}^+$ ) calc'd for  $[\text{C}_{27}\text{H}_{33}\text{NO}_4\text{S}]^+$ :  $m/z$  468.2209, found 468.2209.

#### Representative Procedure E for the Formation of Aziridinyl Propargylic Esters:

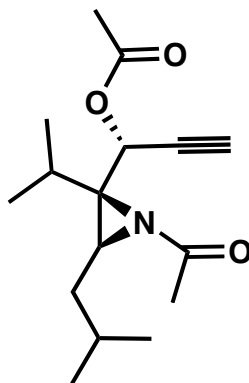


10

**1-(2-methyl-3-phenyl-1-tosylaziridin-2-yl)prop-2-ynyl 2,2,2-trichloroacetate (10).** A flame-dried 50 mL round-bottom flask equipped with a stir bar was charged with **S5** (500 mg, 1.6 mmol, 1 equiv) and THF (8 mL). To the stirred clear solution, cooled to  $-78$   $^{\circ}\text{C}$ , was added ethynylmagnesium bromide (0.5M in THF, 9.6 mL, 4.7 mmol, 3 equiv). The resulting red solution was warmed to  $23$   $^{\circ}\text{C}$  and stirred for 1 h. To the solution, 2,2,2-trichloroacetonitrile (0.52 mL, 5.2 mmol, 3.3 equiv) was added dropwise over 10 min.

The black solution was stirred until all the starting material was consumed as judged by TLC analysis (6 h), and then quenched with water (15 mL) and extracted with ethyl acetate (2 x 7mL). The combined organic extracts were dried over MgSO<sub>4</sub> and concentrated under reduced pressure (rotary evaporation). The crude red product was used without further purification.  $R_f = 0.33$  (4:1 hexanes:ethyl acetate); <sup>1</sup>H NMR (500 MHz, C<sub>6</sub>D<sub>6</sub>) δ ppm 8.67 (s, 1H), 7.85 (d,  $J = 8.3$  Hz, 2H), 7.06 (m, 2H), 6.97-6.89 (m, 3H), 6.80 (d,  $J = 2.0$  Hz, 1H), 6.61 (d,  $J = 8.1$  Hz, 2H), 4.23 (s, 1H), 2.01 (d,  $J = 2.1$  Hz, 1H), 1.73 (s, 3H), 1.45 (s, 3H); <sup>13</sup>C NMR (125 MHz, C<sub>6</sub>D<sub>6</sub>) δ ppm 160.0, 143.6, 137.9, 132.5, 129.3, 128.2, 127.9, 127.0, 91.0, 78.2, 75.2, 69.1, 56.7, 49.8, 20.7, 13.67 (16 of 17 observed).

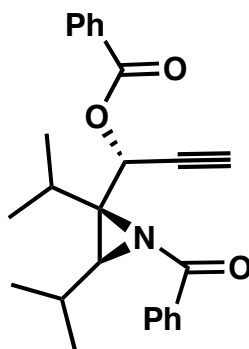
#### Representative Procedure F for the Formation of Aziridinyl Propargylic Esters:



16a

**1-(1-acetyl-3-isobutyl-2-isopropylaziridin-2-yl)prop-2-ynyl acetate (16a).** A 20 mL oven-dried vial was charged with **12c** (500 mg, 1.3 mmol, 1 equiv) and methanol (5 mL). Freshly ground magnesium (153 mg, 6.4 mmol, 5 equiv) was then added to the vial. The resulting clear mixture with the magnesium settled to the bottom was sonicated for 90 min at power 9 using a VWR model 75D sonicator to yield a cloudy green mixture without observable magnesium. This mixture was quenched with sat. aqueous NH<sub>4</sub>Cl (20

mL) and extracted with ethyl acetate (3 x 20 mL). The combined organic extracts were dried over MgSO<sub>4</sub> and concentrated under reduced pressure (rotary evaporation). A 20 mL oven-dried vial, equipped with a stir bar, was charged with the crude amino alcohol and methylene chloride (5 mL). To the resulting solution was added acetic anhydride (0.29 mL, 3.1 mmol, 2.4 equiv), triethylamine (0.46 mL, 3.4 mmol, 2.6 equiv) and dimethylaminopyridine (DMAP) (5 mg). The pale red solution was stirred overnight, then quenched with sat. aqueous NH<sub>4</sub>Cl (5 mL) and extracted with methylene chloride (2 x 5 mL). The combined organic extracts were dried over MgSO<sub>4</sub> and concentrated under reduced pressure (rotary evaporation). The crude clear oil was purified by column chromatography (50 mL silica gel, 8:1 hexanes:ethyl acetate) to yield 289 mg (81% yield) of **16a** as a clear oil. **R<sub>f</sub>** = 0.27 (4:1 hexanes:ethyl acetate); **<sup>1</sup>H NMR** (500 MHz, C<sub>6</sub>D<sub>6</sub>) δ ppm 6.00 (d, *J* = 2.3 Hz, 1H), 2.83 (dd, *J* = 7.9, 4.8 Hz, 1H), 1.98 (d, *J* = 2.3 Hz, 1H), 1.93 (s, 3H), 1.73 (m, 2H), 1.60 (s, 3H), 1.37-1.24 (m, 2H), 1.20 (dd, *J* = 7.8, 7.8 Hz, 3H), 0.99-0.92 (m, 10H); **<sup>13</sup>C NMR** (125 MHz, C<sub>6</sub>D<sub>6</sub>) δ ppm 177.3, 168.0, 78.5, 76.6, 64.1, 50.9, 42.1, 36.4, 31.3, 27.3, 24.1, 22.5, 22.2, 19.8, 19.4, 18.7; **IR** (film) 3249, 2961, 2122, 1751, 1686 cm<sup>-1</sup>; **HRMS** (EI) calc'd for [C<sub>16</sub>H<sub>25</sub>NO<sub>3</sub>]<sup>+</sup>: *m/z* 281.1933, found 281.1938.



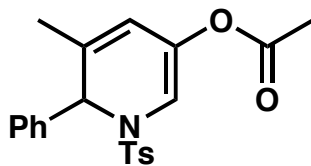
**16b**



**1-(1-benzoyl-3-isobutyl-2-isopropylaziridin-2-yl)prop-2-ynyl benzoate (16b).**

Following procedure F, a white foam was obtained in 78% yield following purification by column chromatography (silica gel, 9:1 hexanes:ethyl acetate).  $R_f = 0.84$  (4:1 hexanes:ethyl acetate);  $^1\text{H NMR}$  (500 MHz,  $\text{C}_6\text{D}_6$ )  $\delta$  ppm 8.02 (dd,  $J = 7.9, 1.6$  Hz, 2H), 7.92 (m, 2H), 7.01-6.96 (m, 1H), 6.94-6.84 (m, 5H), 5.98 (d,  $J = 2.3$  Hz, 1H), 3.08 (dd,  $J = 7.2, 5.5$  Hz, 1H), 2.14 (td,  $J = 14.3, 7.2, 7.2$  Hz, 1H), 1.84-1.74 (m, 2H), 1.56-1.44 (m, 2H), 1.40 (d,  $J = 7.0$  Hz, 3H), 1.20 (d,  $J = 7.3$  Hz, 3H), 0.95 (dd,  $J = 6.6, 4.2$  Hz, 6H);  $^{13}\text{C NMR}$  (125 MHz,  $\text{C}_6\text{D}_6$ )  $\delta$  ppm 176.8, 164.2, 135.6, 132.7, 131.5, 129.7, 129.4, 129.0, 128.0, 127.7, 78.8, 76.4, 65.8, 54.0, 43.2, 36.6, 31.7, 27.4, 22.5, 22.3, 20.0, 19.9; IR (film) 2959, 1727, 1667  $\text{cm}^{-1}$ ; HRMS (EI) calc'd for  $[\text{C}_{26}\text{H}_{29}\text{NO}_3]^+$ :  $m/z$  404.2252, found 404.2252.

**Representative Procedure G for the Formation of Dihydropyridines:**

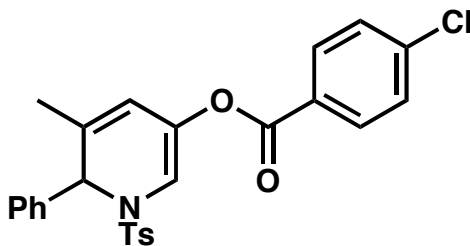


**5a**

**5-methyl-6-phenyl-1-tosyl-1,6-dihydropyridin-3-yl acetate (5a).** A 4 mL oven-dried vial equipped with a stir bar was charged with  $\text{PtCl}_2$  (6.2 mg, 0.023 mmol, 0.1 equiv). To the vial, **1a** (90 mg, 0.23 mmol, 1 equiv) and toluene (1.1 mL) were added. The vial was purged with nitrogen and then tightly sealed with a Teflon<sup>®</sup>-coated cap. The resulting pale yellow mixture was stirred at 100 °C until all the starting material was consumed as judged by TLC analysis (3 h). The resulting black mixture was concentrated under reduced pressure (rotary evaporation). Purification of the crude oil by column chromatography (20 mL neutral deactivated alumina, 16:1 hexanes:ethyl acetate) yielded

68 mg (76%) of a clear gel.  $R_f = 0.39$  (4:1 hexanes:ethyl acetate);  $^1\text{H NMR}$  (500 MHz,  $\text{CDCl}_3$ )  $\delta$  ppm 7.72 (d,  $J = 7.5$  Hz, 2H), 7.70-7.67 (m, 2H), 7.17-7.14 (m, 2H), 7.03 (dd,  $J = 7.3, 7.3$  Hz, 1H), 6.69 (d,  $J = 7.9$  Hz, 2H), 6.42 (s, 1H), 5.53-5.51 (m, 1H), 5.33 (s, 1H), 1.76 (s, 3H), 1.51 (s, 3H), 1.16 (s, 3H);  $^{13}\text{C NMR}$  (125 MHz,  $\text{CDCl}_3$ )  $\delta$  ppm 169.2, 143.7, 139.9, 136.7, 136.0, 132.0, 129.4, 128.5, 128.5, 127.9, 126.6, 117.5, 112.1, 60.7, 21.6, 20.7, 20.71; **IR** (film) 3396, 2451, 1764  $\text{cm}^{-1}$ ; **HRMS** ( $\text{FAB}^+$ ) calc'd for  $[\text{C}_{21}\text{H}_{21}\text{NO}_4\text{S}]^+$ :  $m/z$  384.1270, found 384.1279.

**Enriched sample:**  $[\alpha]_D^{26} = -467.9^\circ$  ( $c = 0.7$  in  $\text{CHCl}_3$ ). Analysis of enantiomers by chiral HPLC (Chiraplak OD-H, 10% isopropanol in hexane at 1mL/30 min,  $T_r$  major 17.34, minor 8.67 at 99% ee. HPLC traces are provided on pages 28-29.

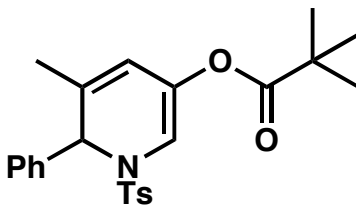


**5b**

**5-methyl-6-phenyl-1-tosyl-1,6-dihydropyridin-3-yl 4-chlorobenzoate (5b).**

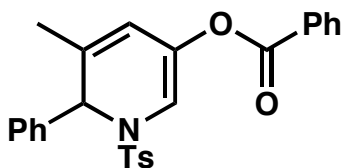
Following procedure G, a clear semi-solid was obtained in 72% yield following purification by column chromatography (20 mL neutral deactivated alumina, 16:1 hexanes:ethyl acetate).  $R_f = 0.56$  (4:1 hexanes:ethyl acetate);  $^1\text{H NMR}$  (500 MHz,  $\text{C}_6\text{D}_6$ )  $\delta$  ppm 7.82 (d,  $J = 7.3$  Hz, 2H), 7.77 (d,  $J = 8.3$  Hz, 2H), 7.68 (m, 2H), 7.22 (dd,  $J = 7.7, 7.7$  Hz, 2H), 7.11 (s, 1H), 6.94 (m, 2H), 6.76 (d,  $J = 8.0$  Hz, 2H), 6.56 (s, 1H), 5.61 (s, 1H), 5.42 (m, 1H), 1.81 (s, 3H), 1.21 (s, 3H);  $^{13}\text{C NMR}$  (125 MHz,  $\text{C}_6\text{D}_6$ )  $\delta$  ppm 163.6, 143.1, 139.8, 139.7, 137.2, 136.9, 131.7, 131.2, 129.2, 128.6, 128.6, 128.5, 128.1, 126.7, 117.7, 113.0, 60.8, 20.7, 20.2 (19 of 20 observed); **IR** (film) 3399, 1736, 1730  $\text{cm}^{-1}$ ;

**HRMS** (FAB<sup>+</sup>) calc'd for [C<sub>26</sub>H<sub>22</sub>ClNO<sub>4</sub>S]<sup>+</sup>: *m/z* 480.1036, found 480.1038.



**5c**

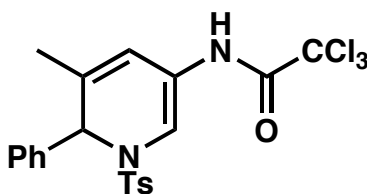
**5-methyl-6-phenyl-1-tosyl-1,6-dihydropyridin-3-yl pivalate (5c).** Following procedure G, a yellow gel was obtained in 76% yield after purification by column chromatography (20 mL neutral deactivated alumina, 25:1 hexanes:ethyl acetate). **R<sub>f</sub>** = 0.67 (4:1 hexanes:ethyl acetate); **<sup>1</sup>H NMR** (500 MHz, CDCl<sub>3</sub>) δ ppm 7.68 (d, *J* = 8.3 Hz, 2H), 7.53 (d, *J* = 6.7 Hz, 2H), 7.36-7.29 (m, 3H), 7.25 (s, 2H), 6.27 (s, 1H), 5.56 (s, 1H), 5.36 (s, 1H), 2.41 (s, 3H), 1.55 (s, 3H), 1.26 (s, 9H); **C<sup>13</sup> NMR** (125 MHz, CDCl<sub>3</sub>) 177.1, 143.7, 139.8, 136.8, 136.1, 131.9, 129.5, 128.6, 128.5, 127.9, 126.7, 117.6, 111.9, 60.7, 38.9, 27.0, 21.6, 20.7; **IR** (film) 3419, 2974, 1751 cm<sup>-1</sup>; **HRMS** (FAB<sup>+</sup>) calc'd for [C<sub>24</sub>H<sub>27</sub>NO<sub>4</sub>S]<sup>+</sup>: *m/z* 425.1661, found 425.1669.



**5d**

**5-methyl-6-phenyl-1-tosyl-1,6-dihydropyridin-3-yl benzoate (5d).** Following procedure G, a clear viscous oil was obtained in 76% yield after purification by column chromatography (20 mL neutral deactivated alumina, 16:1 hexanes:ethyl acetate). **R<sub>f</sub>** = 0.58 (4:1 hexanes:ethyl acetate); **<sup>1</sup>H NMR** (400 MHz, C<sub>6</sub>D<sub>6</sub>) δ ppm 8.01 (dd, *J* = 8.3, 1.3

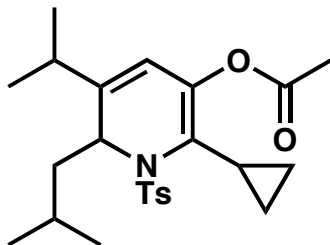
Hz, 2H), 7.84 (d,  $J = 7.4$  Hz, 2H), 7.77 (d,  $J = 8.3$  Hz, 2H), 7.21 (dd,  $J = 7.7, 7.7$  Hz, 2H), 7.11-7.05 (m, 2H), 7.00-6.94 (m, 2H), 6.74 (d,  $J = 8.0$  Hz, 2H), 6.58 (s, 1H), 5.61 (s, 1H), 5.44 (m 1H), 1.80 (s, 3H), 1.20 (s, 3H);  $^{13}\text{C}$  NMR (400 MHz,  $\text{C}_6\text{D}_6$ )  $\delta$  ppm 164.5, 143.0, 140.0, 137.2, 136.9, 133.1, 131.6, 129.9, 129.3, 129.2, 128.6, 128.5, 128.2, 128.1, 126.8, 118.0, 112.9, 60.8, 20.7, 20.1; IR (film) 3415, 1737  $\text{cm}^{-1}$ ; HRMS (FAB<sup>+</sup>) calc'd for  $[\text{C}_{26}\text{H}_{23}\text{NO}_4\text{S}]^+$ :  $m/z$  445.1348, found 445.1352.



11

**2,2,2-trichloro-N-(5-methyl-6-phenyl-1-tosyl-1,6-dihydropyridin-3-yl)acetamide**

(11). Following procedure G, a red gel was obtained in 56% yield after purification by column chromatography (20 mL neutral deactivated alumina, 16:1 hexanes:ethyl acetate).  $R_f = 0.33$  (4:1 hexanes:ethyl acetate);  $^1\text{H}$  NMR (500 MHz,  $\text{C}_6\text{D}_6$ )  $\delta$  ppm 8.00 (d,  $J = 8.3$  Hz, 2H), 7.10 (m, 2H), 7.02-6.94 (m, 3H), 6.77 (d,  $J = 8.0$  Hz, 2H), 6.23 (dd,  $J = 2.6, 2.6$  Hz, 1H), 5.28 (dd,  $J = 2.9, 1.4$  Hz, 1H), 4.56 (dd,  $J = 2.3, 1.5$  Hz, 1H), 4.17 (s, 1H), 1.83 (s, 3H), 0.84 (s, 3H);  $^{13}\text{C}$  NMR (125 MHz,  $\text{C}_6\text{D}_6$ )  $\delta$  ppm 167.1, 155.5, 144.0, 137.0, 132.3, 129.4, 128.3, 128.1, 127.9, 127.5, 104.0, 86.6, 85.8, 56.5, 48.0, 20.8, 11.6; IR (film) 3442, 1607  $\text{cm}^{-1}$ ; HRMS (FAB<sup>+</sup>) calc'd for  $[\text{C}_{21}\text{H}_{19}\text{Cl}_3\text{N}_2\text{O}_3\text{S}]^+$ :  $m/z$  485.0244, found 485.0243.

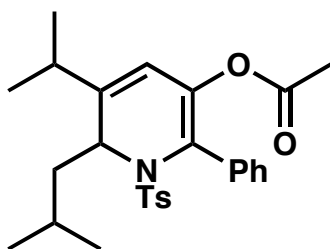


13a

**2-cyclopropyl-6-isobutyl-5-isopropyl-1-tosyl-1,6-dihydropyridin-3-yl acetate (13a).**

Following procedure G, a yellow oil was obtained in 62% yield after purification by column chromatography (20 mL neutral deactivated alumina, 16:1 hexanes:ethyl acetate).

$R_f = 0.51$  (4:1 hexanes:ethyl acetate);  $^1\text{H NMR}$  (400 MHz,  $\text{C}_6\text{D}_6$ )  $\delta$  ppm 8.05 (d,  $J = 8.2$  Hz, 2H), 6.91 (d,  $J = 8.2$  Hz, 2H), 5.17 (s, 1H), 4.70 (dd,  $J = 11.4, 2.1$  Hz, 1H), 2.30-2.04 (m, 2H), 1.93 (s, 3H), 1.80 (s, 3H), 1.23 (d,  $J = 6.4$  Hz, 3H), 1.09-0.97 (m, 4H), 0.94 (d,  $J = 6.8$  Hz, 4H), 0.81 (d,  $J = 6.8$  Hz, 4H), 0.65 (d,  $J = 6.9$  Hz, 4H);  $^{13}\text{C NMR}$  (100 MHz,  $\text{C}_6\text{D}_6$ )  $\delta$  ppm 167.4, 146.9, 143.5, 142.5, 137.4, 128.7, 128.6, 124.4, 113.7, 55.7, 38.9, 31.2, 23.4, 22.8, 21.0, 20.7, 20.7, 20.4, 19.8, 12.3, 7.6, 6.2; **IR** (film) 2959, 1764, 1348  $\text{cm}^{-1}$ ; **HRMS** (FAB $^+$ ) calc'd for  $[\text{C}_{24}\text{H}_{33}\text{NO}_4\text{S}]^+$ :  $m/z$  431.2144, found 431.2138.



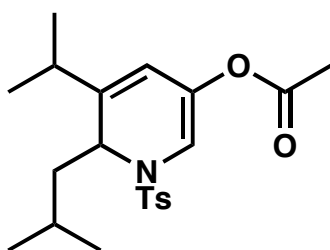
13b

**6-isobutyl-5-isopropyl-2-phenyl-1-tosyl-1,6-dihydropyridin-3-yl acetate (13b).**

Following procedure G, a clear oil was obtained in 69% yield after purification by column chromatography (20 mL neutral deactivated alumina, 18:1 hexanes:ethyl acetate).

$R_f = 0.62$  (4:1 hexanes:ethyl acetate);  $^1\text{H NMR}$  (500 MHz,  $\text{C}_6\text{D}_6$ )  $\delta$  ppm 7.76 (d,  $J = 7.8$

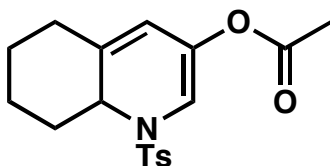
Hz, 2H), 7.73 (d,  $J = 7.9$  Hz, 2H), 7.25 (dd,  $J = 7.5, 7.5$  Hz, 2H), 7.13-7.09 (m, 1H), 6.76 (d,  $J = 7.9$  Hz, 2H), 5.35 (s, 1H), 4.97 (d,  $J = 10.4$  Hz, 1H), 2.46-2.37 (m, 1H), 2.28 (m, 1H), 1.96 (m, 1H), 1.85 (s, 3H), 1.48 (s, 3H), 1.21 (d,  $J = 6.31$  Hz, 3H), 1.10 (m, 1H), 0.96 (d,  $J = 6.7$  Hz, 3H), 0.85 (d,  $J = 6.8$  Hz, 3H), 0.77 (d,  $J = 6.8$  Hz, 3H);  $^{13}\text{C}$  NMR (125 MHz,  $\text{C}_6\text{D}_6$ )  $\delta$  ppm 167.8, 148.5, 142.7, 141.3, 137.1, 135.3, 129.2, 128.7, 123.3, 114.3, 56.4, 39.4, 31.5, 23.6, 23.5, 21.2, 21.0, 20.7, 20.4, 19.8 (20 of 23 peaks observed); IR (film) 2960, 1765, 1350  $\text{cm}^{-1}$ ; HRMS (FAB $^+$ ) calc'd for  $[\text{C}_{27}\text{H}_{33}\text{NO}_4\text{S}]^+$ :  $m/z$  467.2130, found 467.2137.



13c

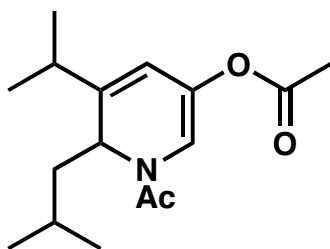
**6-isobutyl-5-isopropyl-1-tosyl-1,6-dihydropyridin-3-yl acetate (13c).** Following procedure G, a white gel was obtained in 70% yield after purification by column chromatography (20 mL neutral deactivated alumina, 16:1 hexanes:ethyl acetate).  $R_f = 0.43$  (4:1 hexanes:ethyl acetate);  $^1\text{H}$  NMR (500 MHz,  $\text{C}_6\text{D}_6$ )  $\delta$  ppm 7.78 (d,  $J = 8.3$  Hz, 2H), 6.70 (d,  $J = 8.0$  Hz, 2H), 6.64 (dd,  $J = 1.1, 1.1$  Hz, 1H), 5.26 (dd,  $J = 1.3, 1.3$  Hz, 1H), 4.58 (m, 1H), 2.20 (dtdd,  $J = 13.2, 9.8, 6.6, 6.6, 3.1$  Hz, 1H), 2.03 (ddd,  $J = 14.2, 11.1, 3.1$  Hz, 1H), 1.83-1.77 (m, 1H), 1.76 (s, 3H), 1.57 (s, 3H), 1.14 (d,  $J = 6.4$  Hz, 3H), 0.97-0.92 (m, 1H), 0.89 (d,  $J = 6.8$  Hz, 3H), 0.66 (d,  $J = 6.8$  Hz, 3H), 0.51 (d,  $J = 6.9$  Hz, 3H);  $^{13}\text{C}$  NMR (125 MHz,  $\text{C}_6\text{D}_6$ )  $\delta$  ppm 168.1, 144.5, 142.8, 141.1, 137.5, 129.1, 127.0, 113.1, 112.4, 54.7, 40.1, 31.3, 23.4, 23.1, 21.2, 21.1, 20.7, 20.2, 19.8; IR (film) 2961,

2870, 1766, 1598  $\text{cm}^{-1}$ ; **HRMS** (EI) calc'd for  $[\text{C}_{21}\text{H}_{29}\text{NO}_4\text{S}]^+$ :  $m/z$  391.1739, found 391.1816.



15

**1-tosyl-1,5,6,7,8,8a-hexahydroquinolin-3-yl acetate (15).** Following procedure G, a white foam was obtained in 76% yield after purification by column chromatography (20 mL neutral deactivated alumina, 16:1 hexanes:ethyl acetate).  $R_f = 0.40$  (4:1 hexanes:ethyl acetate);  $^1\text{H NMR}$  (500 MHz,  $\text{C}_6\text{D}_6$ )  $\delta$  ppm 7.89 (d,  $J = 8.0$  Hz, 2H), 6.83 (s, 1H), 6.77 (d,  $J = 8.0$  Hz, 2H), 5.11 (s, 1H), 4.42 (dd,  $J = 11.9, 3.9$  Hz, 1H), 2.05 (m, 1H), 1.93 (ddd,  $J = 24.4, 12.2, 3.5$  Hz, 1H), 1.76 (s, 3H), 1.72-1.66 (m, 1H), 1.59 (s, 3H), 1.46 (d,  $J = 15.4$  Hz, 1H), 1.42-1.31 (m, 2H), 1.24 (m, 1H), 1.08-0.98 (m, 1H);  $^{13}\text{C NMR}$  (125 MHz,  $\text{C}_6\text{D}_6$ )  $\delta$  ppm 168.2, 143.2, 140.8, 136.6, 135.7, 129.6, 127.0, 113.6, 112.7, 59.9, 37.4, 35.0, 29.9, 25.8, 20.8, 19.9; **IR** (film) 3214, 2885, 1721  $\text{cm}^{-1}$ ; **HRMS** ( $\text{FAB}^+$ ) calc'd for  $[\text{C}_{18}\text{H}_{21}\text{NO}_4\text{S}]^+$ :  $m/z$  347.1185, found 347.1187.

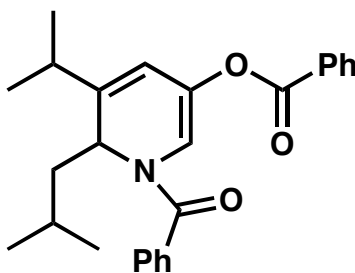


17a

**1-acetyl-6-isobutyl-5-isopropyl-1,6-dihydropyridin-3-yl acetate (17a).**

Following procedure G, a white foam was obtained in 71% yield after purification by column chromatography (20 mL neutral deactivated alumina, 16:1 hexanes:ethyl acetate).

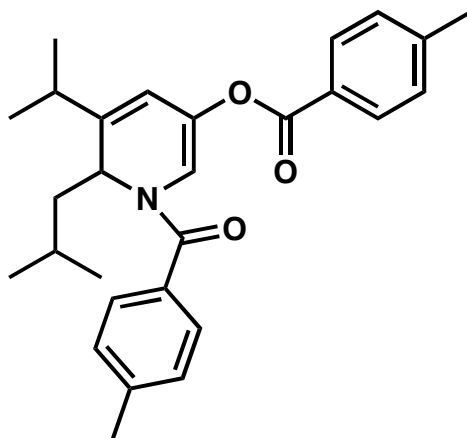
$R_f = 0.73$  (4:1 hexanes:ethyl acetate);  $^1\text{H NMR}$  (500 MHz,  $\text{C}_6\text{D}_6$ )  $\delta$  ppm 6.07 (s, 1H), 5.68 (s, 1H), 5.55 (dd,  $J = 10.9, 1.7$  Hz, 1H), 2.11 (m, 1H), 2.03 (ddd,  $J = 14.1, 10.9, 3.4$  Hz, 1H), 1.71 (s, 3H), 1.63-1.61 (m, 4H), 1.16 (d,  $J = 6.4$  Hz, 3H), 1.06 (ddd,  $J = 13.3, 10.1, 2.9$  Hz, 1H), 0.97-0.89 (m, 9H);  $^{13}\text{C NMR}$  (125 MHz,  $\text{C}_6\text{D}_6$ )  $\delta$  ppm 168.654, 168.282, 147.154, 137.673, 112.966, 112.653, 49.199, 39.847, 31.730, 24.386, 23.516, 21.950, 21.739, 20.380, 20.001, 19.939; **IR** (film) 2962, 1754, 1681  $\text{cm}^{-1}$ ; **HRMS** (EI) calc'd for  $[\text{C}_{16}\text{H}_{25}\text{NO}_3]^+$ :  $m/z$  280.1854, found 280.1859.



**17b**

**1-benzoyl-6-isobutyl-5-isopropyl-1,6-dihydropyridin-3-yl benzoate (17b).** Following procedure G, an oil was obtained in 74% yield after purification by column chromatography (20 mL neutral deactivated alumina, 25:1 hexanes:ethyl acetate).  $R_f = 0.80$  (4:1 hexanes:ethyl acetate);  $^1\text{H NMR}$  (500 MHz,  $\text{C}_6\text{D}_6$ )  $\delta$  ppm 8.02 (d,  $J = 7.5$  Hz, 2H), 7.55 (d,  $J = 3.4$  Hz, 2H), 7.04 (dd,  $J = 7.4, 7.4$  Hz, 1H), 6.97-6.94 (m, 5H), 6.22 (s, 1H), 5.78 (s, 1H), 5.68 (d,  $J = 9.6$  Hz, 1H), 2.27-2.20 (m, 1H), 2.15 (m, 1H), 1.91-1.82 (m, 1H), 1.29-1.21 (m, 4H), 0.98 (dd,  $J = 6.4, 6.4$  Hz, 6H), 0.92 (d,  $J = 6.7$  Hz, 3H);  $^{13}\text{C NMR}$  (125 MHz,  $\text{C}_6\text{D}_6$ )  $\delta$  ppm 169.0, 164.7, 146.8, 137.1, 135.2, 133.0, 130.0, 129.9, 129.5, 128.6, 128.3, 128.0, 114.8, 113.4, 50.7, 39.9, 31.9, 24.8, 23.6, 22.3, 21.9, 20.1; **IR** (film) 2961, 1735, 1669  $\text{cm}^{-1}$ ; **HRMS** (EI) calc'd for  $[\text{C}_{26}\text{H}_{29}\text{NO}_3]^+$ :  $m/z$  404.2185, found 404.2187.

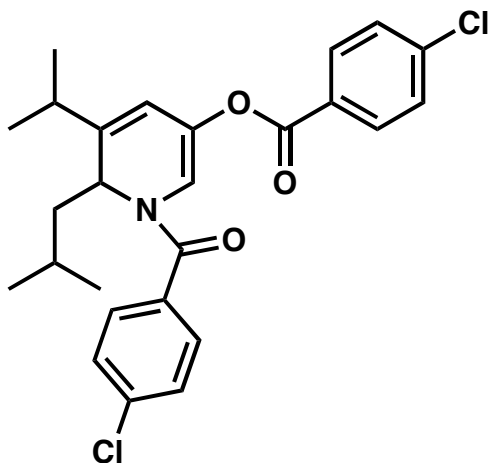




17c

**6-isobutyl-5-isopropyl-1-(4-methylbenzoyl)-1,6-dihydropyridin-3-yl**

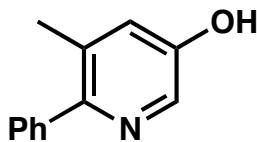
**4-methylbenzoate (17c).** Following procedure G, clear crystals were obtained in 69% yield after purification by column chromatography (20 mL neutral deactivated alumina, 25:1 hexanes:ethyl acetate).  $R_f = 0.85$  (4:1 hexanes:ethyl acetate); **MP** 67 °C- 69 °C;  $^1\text{H NMR}$  (500 MHz,  $\text{C}_6\text{D}_6$ )  $\delta$  ppm 8.02 (d,  $J = 7.9$  Hz, 2H), 7.54 (d,  $J = 7.2$  Hz, 2H), 6.81 (dd,  $J = 8.1, 8.1$  Hz, 4H), 6.33 (s, 1H), 5.81 (s, 1H), 5.66 (d,  $J = 9.5$  Hz, 1H), 2.23 (m, 1H), 2.17 (m, 1H), 1.91 (d,  $J = 3.9$  Hz, 6H), 1.29-1.20 (m, 4H), 0.97 (d,  $J = 6.3$  Hz, 6H), 0.92 (d,  $J = 6.7$  Hz, 4H);  $^{13}\text{C NMR}$  (125 MHz,  $\text{C}_6\text{D}_6$ )  $\delta$  ppm 169.0, 164.8, 146.7, 143.9, 140.2, 137.0, 132.4, 130.0, 129.1, 128.8, 128.7, 126.9, 115.1, 113.6, 50.7, 39.9, 31.9, 24.8, 23.6, 22.4, 22.0, 21.0, 20.8, 20.1; **IR** (film) 3425, 1734, 1658  $\text{cm}^{-1}$ ; **HRMS** ( $\text{FAB}^+$ ) calc'd for  $[\text{C}_{28}\text{H}_{33}\text{NO}_3]^+$ :  $m/z$  432.2539, found 432.2539.



17d

**1-(4-chlorobenzoyl)-6-isobutyl-5-isopropyl-1,6-dihydropyridin-3-yl 4-chlorobenzoate (17d).** Following procedure G, a yellow dense oil was obtained in 65% yield after purification by column chromatography (20 mL neutral deactivated alumina, 25:1 hexanes:ethyl acetate).  $R_f = 0.85$  (4:1 hexanes:ethyl acetate);  $^1\text{H NMR}$  (500 MHz,  $\text{C}_6\text{D}_6$ )  $\delta$  ppm 7.74 (d,  $J = 8.5$  Hz, 2H), 7.27 (d,  $J = 8.2$  Hz, 2H), 6.90 (d,  $J = 8.4$  Hz, 4H), 6.06 (s, 1H), 5.74 (s, 1H), 5.60 (d,  $J = 10.1$  Hz, 1H), 2.21-2.08 (m, 2H), 1.85-1.76 (m, 1H), 1.25 (d,  $J = 6.2$  Hz, 3H), 1.22-1.17 (m, 1H), 0.97 (dd,  $J = 7.1, 7.1$  Hz, 6H), 0.92 (d,  $J = 6.7$  Hz, 3H);  $^{13}\text{C NMR}$  (125 MHz,  $\text{C}_6\text{D}_6$ )  $\delta$  ppm 167.8, 163.8, 147.4, 139.8, 137.2, 136.3, 133.2, 131.2, 130.1, 129.4, 128.7, 128.3, 114.5, 113.1, 50.8, 39.9, 34.6, 31.9, 24.8, 23.6, 21.9, 20.1; **IR** (film) 2960, 1738, 1666  $\text{cm}^{-1}$ ; **HRMS** ( $\text{FAB}^+$ ) calc'd for  $[\text{C}_{26}\text{H}_{27}\text{Cl}_2\text{NO}_3]^+$ :  $m/z$  427.1433, found 427.1433.

**Representative Procedure H for the Formation of Hydroxypyridines:**



20

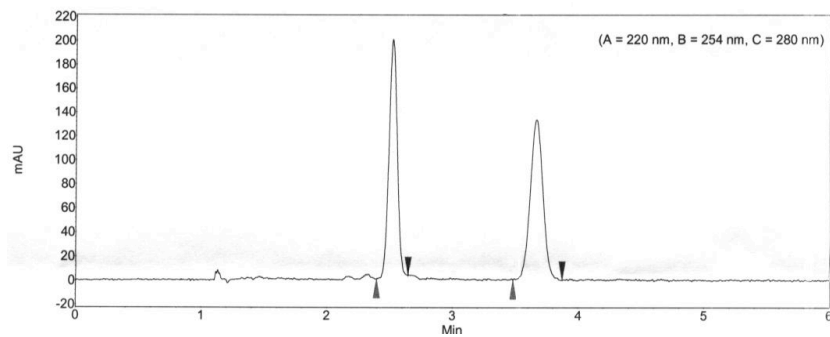
**5-methyl-6-phenylpyridin-3-ol (20).** A 10 mL flame-dried round-bottom flask was charged with **5b** (100 mg, 0.2 mmol, 1 equiv) and THF (2 mL). Potassium trimethylsilanolate (27 mg, 0.2 mmol, 1 equiv) was then added to the flask in one portion. The resulting cloudy brown mixture was stirred under a nitrogen atmosphere until all the starting material was consumed as judged by TLC analysis (3 h) and subsequently quenched with acetic acid (12.5 mg, 0.2 mmol, 1 equiv). The brown solution was concentrated under reduced pressure (rotary evaporation). The crude cloudy brown oil was purified by column chromatography (50 mL deactivated neutral alumina, 4:1 hexanes:ethyl acetate then ethyl acetate) to yield 39 mg (79%) of **20** as a white foam.  $R_f$  = 0.0 (4:1 hexanes:ethyl acetate);  $^1\text{H NMR}$  (500 MHz,  $\text{CD}_3\text{OD}$ )  $\delta$  ppm 7.95 (d,  $J$  = 2.4 Hz, 1H), 7.42 (m, 5H), 7.17 (d,  $J$  = 2.4 Hz, 1H), 2.24 (s, 3H);  $^{13}\text{C NMR}$  (500 MHz,  $\text{CD}_3\text{OD}$ )  $\delta$  ppm 153.3, 149.7, 139.9, 133.7, 132.4, 128.7, 127.8, 127.4, 125.1, 18.6;  $\text{IR}$  (film) 3423, 2528, 1647  $\text{cm}^{-1}$ ;  $\text{HRMS}$  (EI) calc'd for  $[\text{C}_{12}\text{H}_{11}\text{NO}]^+$ :  $m/z$  185.0827, found 185.0833.

#### References:

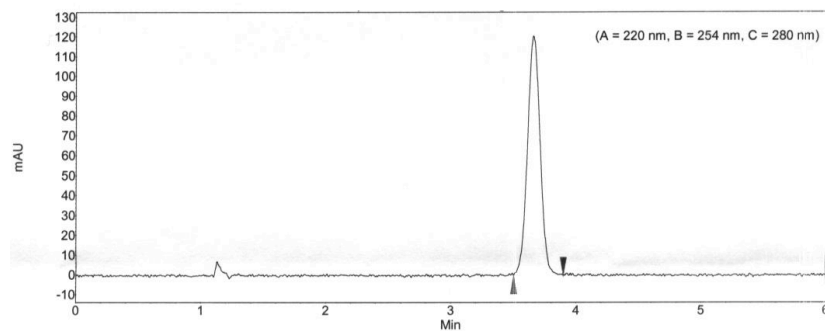
- (1) K. W. Henderson, J. K. William, M. H. Jennifer, *Tetrahedron* **2002**, 58, 4573- 4587.
- (2) J. U. Jeong, I. Sagasser, K. B. Sharpless, *J. Am. Chem. Soc.* **1998**, 120, 6844- 6845.
- (3) M. Kimura, M. Shimizo, S. Tanaka, Y. Tamaru, *Tetrahedron* **2005**, 61, 3709- 3718.
- (4) A. G. Kallianos, A. H. Warfield, M. I. Simpson, U.S. Patent 3, 704, 714, December 5, 1972.

## HPLC Traces:

### Propargylic Ester (1a) racemic and enriched HPLC traces:

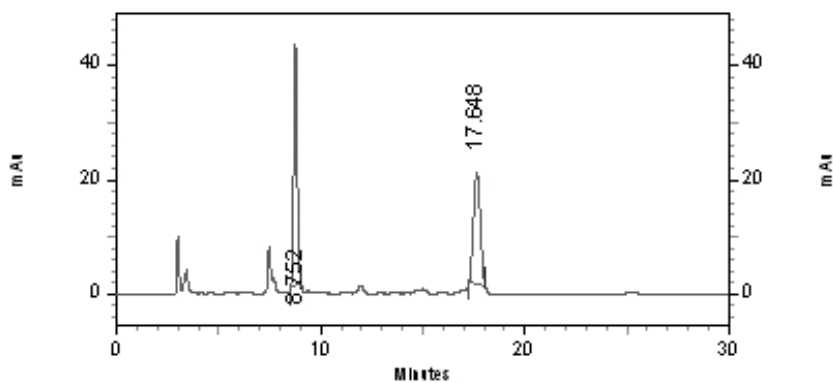


| Index | Time<br>[Min] | Res. HW | Selectivity | Height<br>[mAU] | Area<br>[mAU*min] | Area<br>[%] |
|-------|---------------|---------|-------------|-----------------|-------------------|-------------|
| 1     | 2.52          | 0.00    | 0.00        | 200.84          | 15.64             | 49.658      |
| 2     | 3.66          | 7.45    | 1.45        | 133.70          | 15.85             | 50.342      |
| Total |               |         |             |                 | 31.49             | 100.000     |



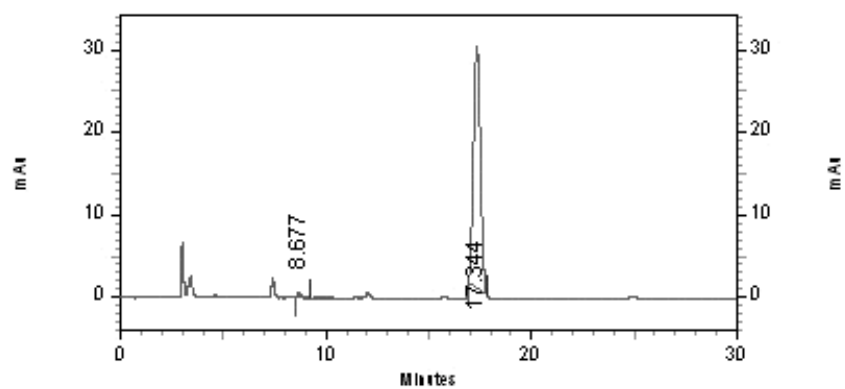
| Index | Time  | Res. HW | Selectivity | Height | Area      | Area    |
|-------|-------|---------|-------------|--------|-----------|---------|
|       | [Min] |         |             | [mAU]  | [mAU*min] | [%]     |
| 1     | 3.66  | 0.00    | 0.00        | 121.24 | 14.46     | 100.000 |
| Total |       |         |             |        | 14.46     | 100.000 |

**Dihydropyridine (5a) racemic and enriched HPLC traces:**



2: 254 nm, 4 nm Results

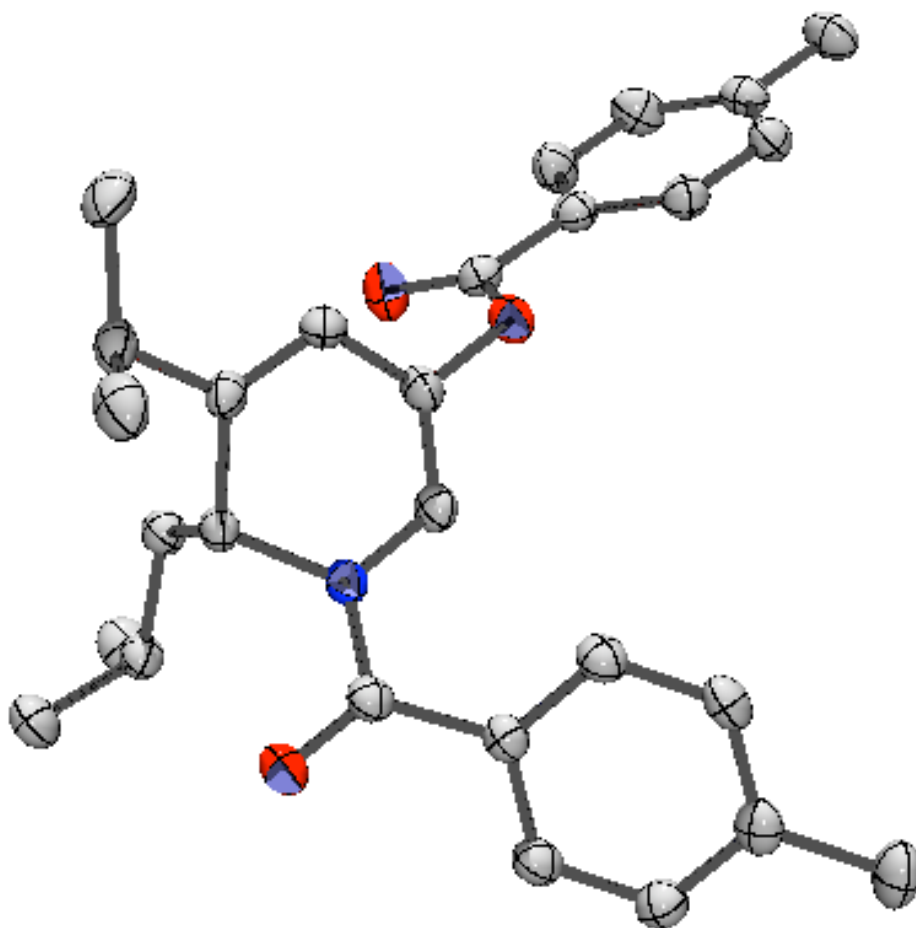
| Retention Time | Area   | Area Percent |
|----------------|--------|--------------|
| 8.752          | 492897 | 52.195       |
| 17.648         | 451448 | 47.805       |



2: 256 nm, 4 nm Results

| Retention Time | Area   | Area Percent |
|----------------|--------|--------------|
| 8.677          | 6997   | 1.009        |
| 17.344         | 686344 | 98.991       |

### X-ray Structure of 17c:



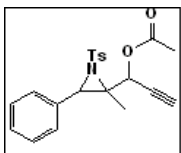
### 17c

Table 1. Crystal data and structure refinement for  $C_{28}H_{33}NO_3$  (**17c**).

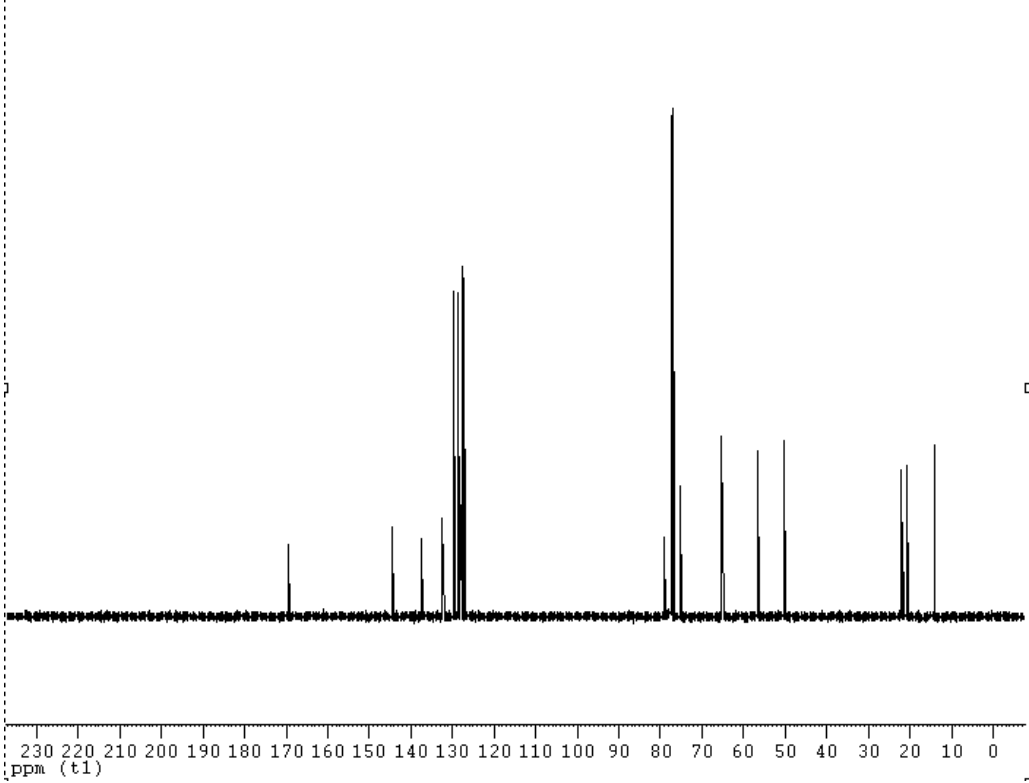
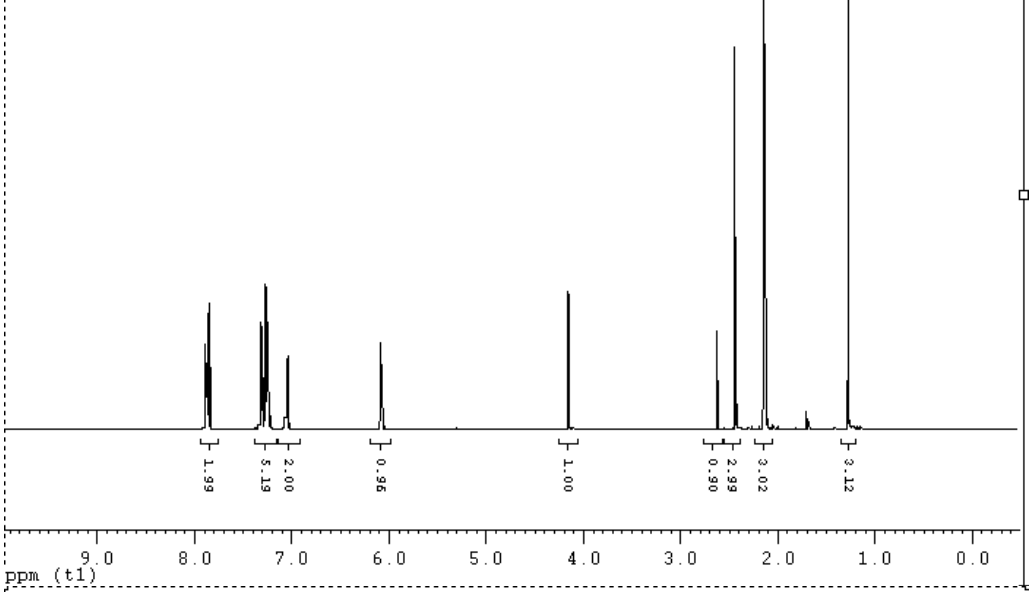
|                      |                            |                         |
|----------------------|----------------------------|-------------------------|
| Identification code  | $C_{28}H_{33}NO_3$         |                         |
| Empirical formula    | $C_{28}H_{33}NO_3$         |                         |
| Formula weight       | 431.55                     |                         |
| Temperature          | 155(2) K                   |                         |
| Wavelength           | 0.71073 Å                  |                         |
| Crystal system       | Monoclinic                 |                         |
| Space group          | P2(1)/c                    |                         |
| Unit cell dimensions | $a = 20.270(3)$ Å          | $a = 90^\circ$ .        |
|                      | $b = 8.1071(12)$ Å         | $b = 96.360(3)^\circ$ . |
|                      | $c = 14.964(2)$ Å          | $c = 90^\circ$ .        |
| Volume               | $2443.8(6)$ Å <sup>3</sup> |                         |
| Z                    | 4                          |                         |

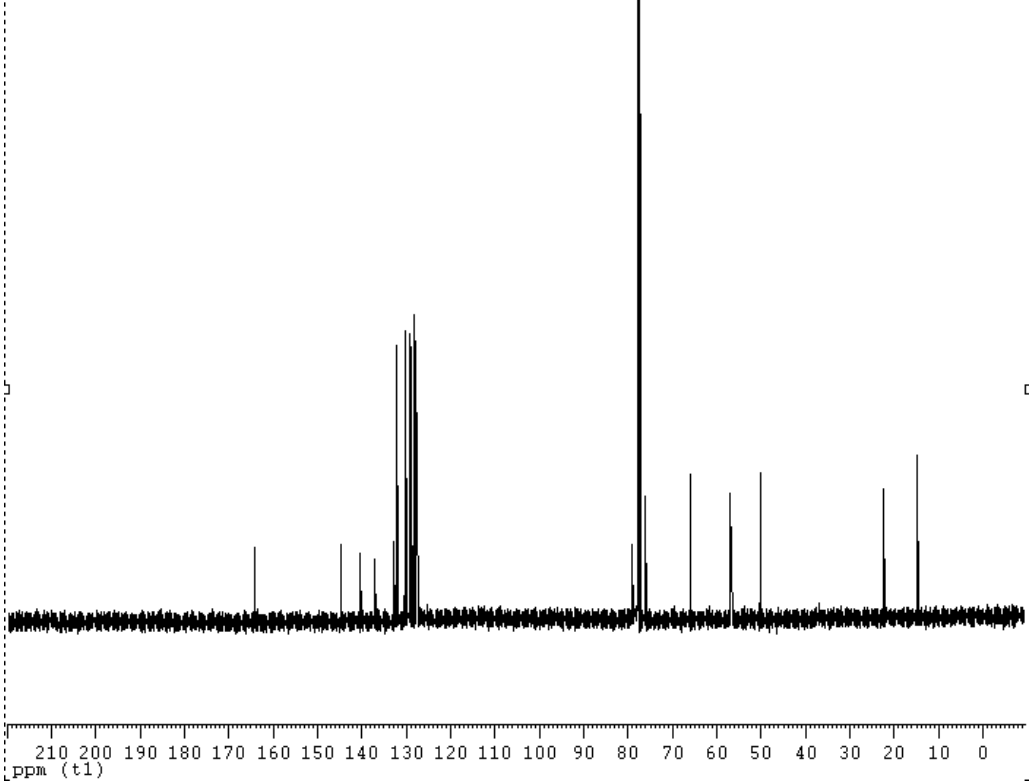
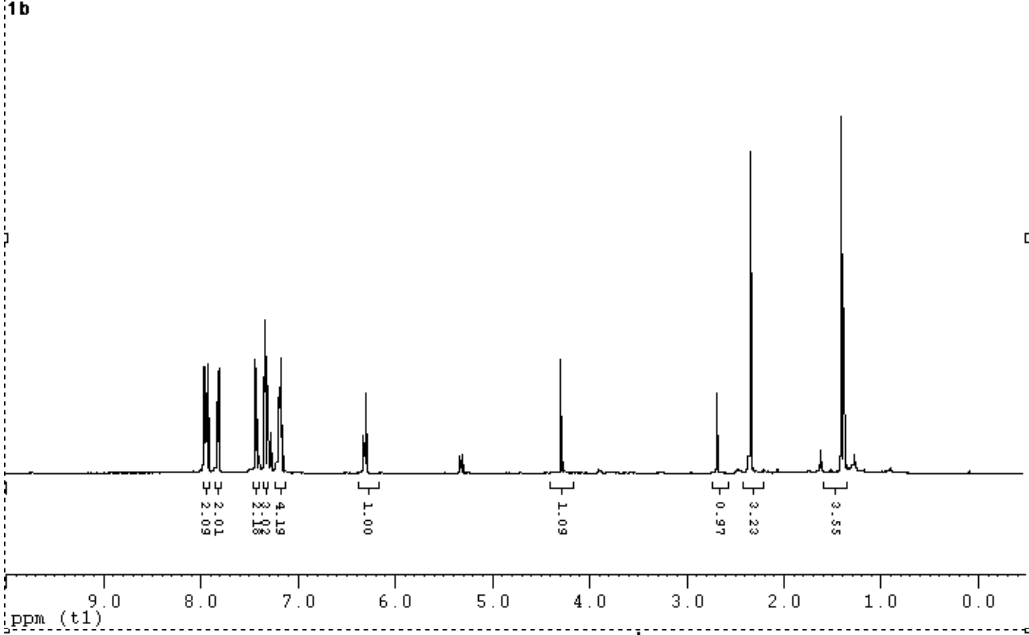
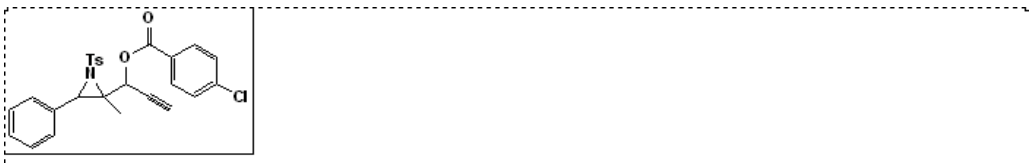
|                                   |   |
|-----------------------------------|---|
| Density (calculated)              | 1.173 Mg/m <sup>3</sup>                     |
| Absorption coefficient            | 0.075 mm <sup>-1</sup>                      |
| F(000)                            | 928   |
| Crystal size                      | 0.27 x 0.20 x 0.12 mm <sup>3</sup>          |
| Theta range for data collection   | 1 to 23.5°.                                 |
| Index ranges                      | -21<=h<=25, -9<=k<=9, -18<=l<=10            |
| Reflections collected             | 4932  |
| Independent reflections           | 3410 [R(int) = 0.0341]                      |
| Completeness to theta = 26.41°    | 98.9 %                                      |
| Absorption correction             | Empirical                                   |
| Max. and min. transmission        | 1 and 0.8311                                |
| Refinement method                 | Full-matrix least-squares on F <sup>2</sup> |
| Data / restraints / parameters    | 4932 / 0 / 421                              |
| Goodness-of-fit on F <sup>2</sup> | 0.886                                       |
| Final R indices [I>2sigma(I)]     | R1 = 0.0450, wR2 = 0.1203                   |
| R indices (all data)              | R1 = 0.0733, wR2 = 0.1373                   |
| Largest diff. peak and hole       | 0.232 and -0.158 e.Å <sup>-3</sup>          |

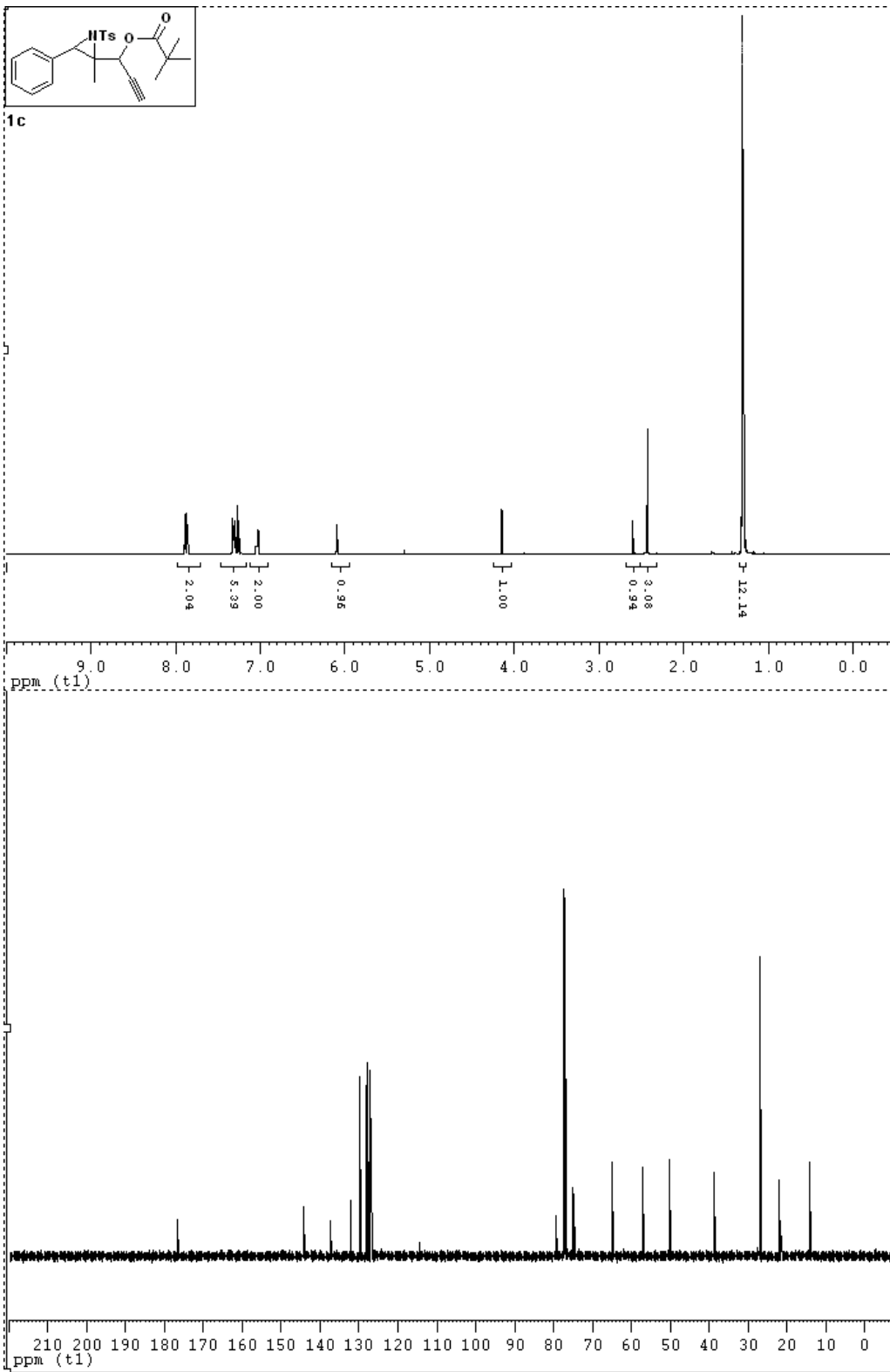


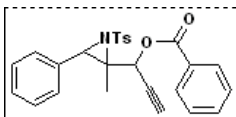


1a









1d

