Supporting Information

An attempt to construct indole-fused azabicyclo[3.3.1]nonane framework via radical cyclization

Vipin Kumar Singh, Uttam Ghosh and Tushar Kanti Chakraborty*

Department of Organic Chemistry, Indian Institute of Science, Bengaluru 560012, India.

E-mail: tushar@iisc.ac.in

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General Experimental Details:

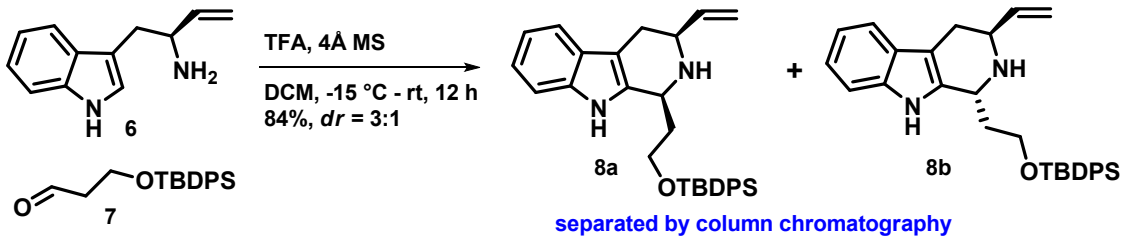
Unless otherwise stated, all the reactions were carried out in an inert atmosphere in oven-dried glassware using dry solvents. All chemicals purchased from commercial suppliers were used as received unless otherwise stated. Reactions and chromatography fractions were monitored by Merck silica gel 60 F-254 glass TLC plates and visualized using UV light, 7% ethanolic phosphomolybdic acid-heat, or 2.5% methanolic anisaldehyde (with 1% AcOH and 3.3% conc. H_2SO_4)-heat as developing agents. Flash column chromatography was performed with 100-200 mesh silica gel and yields refer to chromatographically and spectroscopically pure compounds.

Instrumentation:

All NMR spectra were recorded in $CDCl_3$ on 400 MHz instruments at 300 K and are calibrated to residual solvent peaks ($CHCl_3$ 7.26 ppm and 77.0 ppm). For ^{1}H-NMR, data are reported as follows: chemical shift, multiplicity (s = singlet, br s = broad singlet, d = doublet, dd = double of doublet, ddd = doublet of doublet of doublet, t = triplet, td = triplet of doublet, q = quartet, dq = doublet of quartet, quint = quintet, sext = sextet, m = multiplet), coupling constants (Hz) and integration. Infrared (FT-IR) spectra were recorded on the PerkinElmer Spectrum BX spectrophotometer and reported in ν_{max} in cm^{-1}. High-resolution mass spectrometric analysis (HRMS) was performed on a Micromass Q-TOF Micro instrument. Optical rotations were measured on JASCO P-2000 polarimeter.

Experimental procedures and characterization data:

Preparation of 8a and 8b:



In a flame dried round bottom flask containing 4Å molecular sieves (5.36 g, 200 mg/mmol) was added a solution of **6** (J. R. Ragains and J. D. Winkler, *Org. Lett.*, 2006, **8**, 4437–4440) (5 g, 26.84 mmol, 1 equiv) in 120 mL dry DCM. The aldehyde **7** (10.9 g, 34.89 mmol, 1.3 equiv) in 80 mL dry DCM was canulated into the amine solution. The reaction was cooled to -15 °C, then TFA (2.25 mL, 29.52 mmol, 1.1 equiv) was added, and the resulting mixture was stirred for 3 h. After 3 h stirring at -15 °C, the TFA (4.51 mL, 69.04 mmol, 2.2 equiv) was again added, and the reaction was slowly warmed up to room temperature. The reaction was stirred for 10 h at room temperature. The completion of the reaction was confirmed using TLC. The reaction mixture was diluted with DCM, and the solid molecular sieves were separated by filtering through a thin Celite pad and washed with DCM. The filtrate and washings were combined and treated with 3N NaOH solution until the solution was basic in nature. The combined organic layer was washed with water and brine and dried over anhydrous Na_2SO_4. The organic layer was filtered and concentrated in *vacuo*. The residue was purified using flash column chromatography (15% ethyl acetate in hexane, silica gel) to afford **8a** (8.15 g, 63%) and **8b** (2.17 g, 21%) with *dr* = 3:1.

^{1}H NMR (400 MHz, $CDCl_3$) of 8a (*cis* isomer): δ 8.93 (s, 1H), 7.70 (ddd, *J* = 12.8, 7.3, 1.6 Hz, 4H), 7.51 – 7.36 (m, 7H), 7.12 – 7.08 (m, 3H), 6.08 (ddd, *J* = 17.3, 10.5, 6.1 Hz, 1H), 5.34 (dt, *J* = 17.4, 1.3 Hz, 1H), 5.18 (dt, *J* = 10.5, 1.3 Hz, 1H), 4.38 – 4.36 (m, 1H), 3.99 – 3.96 (m, 2H), 3.63 – 3.58 (m, 1H), 2.89 (ddd, *J* = 15.1, 4.2, 1.6 Hz, 1H), 2.63 (ddd, *J* = 15.0, 10.9, 2.3 Hz, 1H), 2.24 (dq, *J* = 14.3, 6.9 Hz, 1H), 1.92 (bs, 1H) 1.9 – 1.88 (m, 1H), 1.16 (s, 9H).

^{13}C NMR (100 MHz, $CDCl_3$) of 8a (*cis* isomer): δ 141.0, 136.0, 135.9, 135.7, 135.7, 133.0, 132.9, 130.2, 130.1, 128.1, 128.1, 127.5, 121.4, 119.3, 118.1, 114.9, 111.0, 108.4, 77.5, 77.2, 76.8, 63.2, 57.3, 53.8, 38.1, 28.6, 27.2, 19.4.

HRMS (ESI) of 8a (*cis* isomer): calculated for $C_{31}H_{37}N_2OSi$: 481.2675 ([M + H]$^+$), found 481.2678.

IR ν_{max} (neat, cm^{-1}) of 8a (*cis* isomer): 3431, 3287, 3062, 2933.9, 2704, 2557, 2344, 1641.66, 1460, 1215, 1099, 919, 780, 734, 699.

Optical rotation $[\alpha]_D^{22}$: -28.4 (c 1.48, $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$): of 8b (*trans* isomer): δ 8.33 (s, 1H), 7.73 (ddt, *J* = 6.6, 5.2, 1.3 Hz, 4H), 7.51 – 7.40 (m, 7H), 7.19 – 7.07 (m, 3H), 6.05 (ddd, *J* = 17.2, 10.5, 6.0 Hz, 1H), 5.30 (dd, *J* = 17.2, 1.5 Hz, 1H), 5.15 (dd, *J* = 10.5, 1.5 Hz, 1H), 4.45 (t, *J* = 6.3 Hz, 1H), 4.02 – 3.97 (m, 1H), 3.95 – 3.90 (m, 1H), 3.75 – 3.70 (m, 1H), 2.92 (dd, *J* = 15.4, 4.5 Hz, 1H), 2.62 (ddd, *J* = 15.4, 8.5, 1.5 Hz, 1H), 2.09 (bs, 1H), 2.06 – 1.99 (m, 2H), 1.16 (s, 9H).

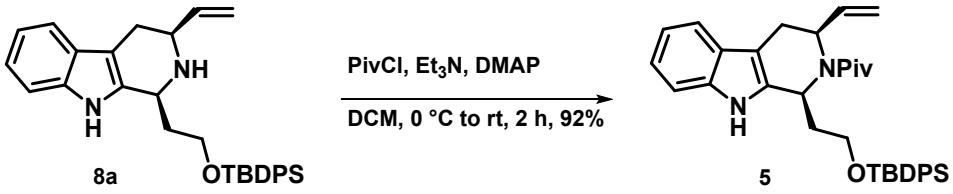
^{13}C NMR (100 MHz, $CDCl_3$): of 8b (*trans* isomer): δ 140.7, 135.9, 135.8, 135.7, 135.7, 133.5, 133.2, 130.1, 130.1, 128.1, 128.0, 127.4, 121.5, 119.3, 118.1, 115.0, 110.9, 108.0, 77.5, 77.2, 76.8, 62.5, 51.8, 49.1, 38.0, 30.6, 27.1, 19.4.

HRMS (ESI) of 8b (*trans* isomer): calculated for $C_{31}H_{37}N_2OSi$: 481.2675 ([M + H]$^+$), found 481.2673.

IR ν_{max} (neat, cm^{-1}) of 8b (*trans* isomer): 3421, 3302, 3063, 2936, 2693, 2548, 2327, 1647, 1458, 1334, 1213, 1093, 914, 730, 596.

Optical rotation $[\alpha]_D^{22}$: -11.4 (c 1.58, $CHCl_3$).

<u>Preparation of 5:</u>



In a round bottom flask containing amine **8a** (7 g, 14.58 mmol, 1 equiv) in dry DCM (70 mL) was added pivaloyl chloride (2.67 mL, 21.86 mmol, 1.5 equiv), Et_3N (4.47 mL, 32.07 mmol, 2.2 equiv) and DMAP (355 mg, 2.91 mmol, 0.2 eq), and the reaction mixture was stirred for 2 h at room temperature. After 2 h, the reaction was quenched with a saturated solution of NH_4Cl and extracted with DCM. The organic layer was washed with water and brine; then, the combined organic layer was dried over anhydrous Na_2SO_4. The organic layer was

filtered, and the solvent was evaporated in *vacuo* in a rotary evaporator. The residue was purified using flash column chromatography (8% ethyl acetate in hexane, silica gel) to afford **5** (7.58 g, 92%) as a viscous liquid.

^{1}H NMR (400 MHz, $CDCl_3$) of 5: δ 9.60 (s, 1H), 7.75 – 7.70 (m, 4H), 7.49 – 7.39 (m, 7H), 7.10 – 7.04 (m, 2H), 6.87 – 6.85 (m, 1H), 5.89 (ddd, *J* = 17.4, 10.6, 5.4 Hz, 1H), 5.5 (d, *J* = 7.8, 1H), 5.28 (t, *J* = 5.4, 1H), 5.15 (d, *J* = 17.4, 1H), 5.06 (d, *J* = 10.6, 1H), 4.30 (td, *J* = 10.6, 1.5 Hz, 1H), 3.98 (dt, *J* = 10.3, 3.6 Hz, 1H), 3.13 (ddd, *J* = 15.1, 5.3, 1.6 Hz, 1H), 3.04 (d, *J* = 15.1 Hz, 1H), 2.32 – 2.23 (m, 1H), 1.98 (dd, *J* = 14.7, 1.5 Hz, 1H), 1.39 (s, 9H), 1.23 (s, 9H).

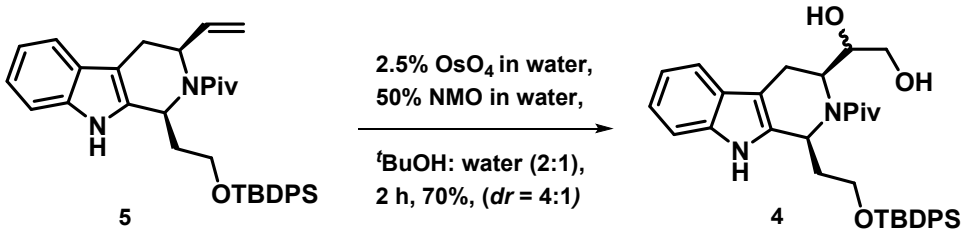
^{13}C NMR (100 MHz, $CDCl_3$) of 5: δ 177.2, 138.3, 136.0, 135.8, 135.6, 134.8, 133.2, 132.7, 130.2, 130.2, 128.2 (2C), 127.1, 121.3, 119.1, 117.8, 117.1, 111.1, 103.7, 65.7, 53.8, 52.5, 40.7, 39.4, 28.8, 27.5, 26.0, 19.6.

IR ν_{max} (neat, cm^{-1}) of 5: 3386, 3065, 2940, 2866, 1615, 1471, 1399, 1370, 1302.95, 1194, 1100, 985, 924, 820, 745, 702.

Optical rotation $[\alpha]_D^{22}$: +48.7 (c 0.7, $CHCl_3$).

Preparation of 4:

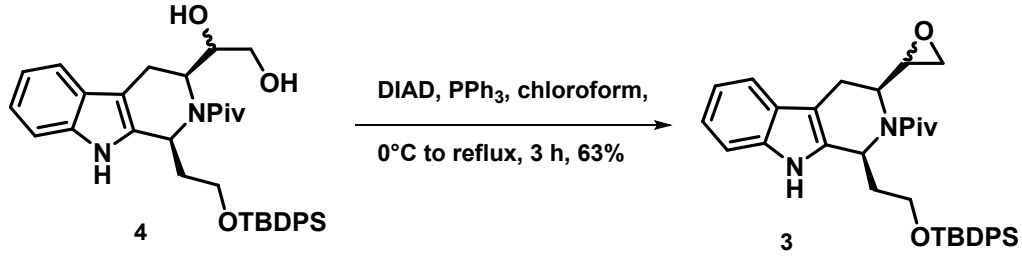
In a round bottom flask containing olefin **5** (5 g, 8.85 mmol, 1 equiv) in THF (10 mL), ^{t}BuOH (25 mL) was added. An aqueous solution of NMO (4.37 M, 6.07 mL, 26.5 mmol, 3 equiv) and aqueous solution of OsO_4 (0.08 M, 11 mL, 0.89 mmol, 0.1 equiv) were sequentially added at room temperature. The reaction was stirred for 2 h, then quenched with 20% solution of sodium metabisulphite ($Na_2S_2O_5$) and stirred for 30 m.



The aq. layer was extracted with ethyl acetate; the combined organic layers were washed with water and brine and dried over anhydrous Na_2SO_4. After filtration, the solvent was evaporated in *vacuo* using a rotary evaporator, and the residue was purified using flash column chromatography (25% ethyl acetate in hexane, silica gel) afforded **4** (3.7 g, 70%) as a solid in 4:1 diastereomeric ratio. The diol **4** was used directly in the next step.

Preparation of 3:

In a flame dried round bottom flask containing the diol **4** (3.5 g, 5.84 mmol, 1 equiv) in dry chloroform (30 mL) was added with PPh_3 (2.60 g, 9.9 mmol, 1.7 equiv) at 0 °C; then DIAD (1.30 mL, 6.42 mmol, 1.1 equiv) was added dropwise using a glass syringe at the same temperature.



The reaction was gradually warmed up to room temperature. Then it was refluxed for 3 h. After that, the reaction mixture was cooled to rt, and the solvent was evaporated in *vacuo* using a rotary evaporator. The residue was purified using flash column chromatography (10% ethyl acetate in hexane, silica gel) to afford the epoxide **3** (2.15 g, 63%) as a gummy liquid.

^{1}H NMR (400 MHz, $CDCl_3$) of 3 (mixture of diastereomers): δ 9.53 (s, 1H), 7.75– 7.69 (m, 4H), 7.43 – 7.37 (m, 7H), 7.09 – 7.05 (m, 2H), 6.83 – 6.81 (m, 1H), 5.63 – 5.62 (m, 1H), 4.53 (t, *J* = 5.93 Hz, 1H), 4.38 (td, *J* = 10.1, 2.7 Hz, 1H), 4.02 (dt, *J* = 10.1, 3.4Hz, 1H), 3.11 – 3.04 (m, 2H), 2.83 (d, *J* = 15.8 Hz, 1H), 2.73 (t, *J* = 4.2 Hz, 1H), 2.56 (dd, *J* = 4.9, 2.3 Hz, 1H), 2.29 – 2.15 (m, 2H), 1.35 (s, 9H), 1.23 (s, 9H).

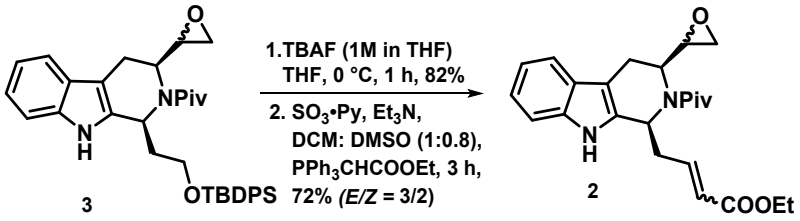
^{13}C NMR (100 MHz, $CDCl_3$) of 3 (mixture of diastereomers): δ 177.8, 136.0, 135.7, 135.6, 134.9, 133.2, 132.6, 130.2, 130.2, 128.2, 127.8, 126.7, 121.6, 119.3, 117.9, 111.2, 103.4, 65.4, 53.9, 53.0, 51.6, 47.8, 40.7, 39.4, 28.9, 27.5, 26.7, 19.6.

HRMS (ESI) of 3 (mixture of diastereomers): calculated for $C_{36}H_{45}N_2O_3Si$: 581.3199 ($[M + H]^+$), found 581.3196.

Preparation of 2:

In a round bottom flask containing epoxide **3** (2.0 g, 3.44 mmol, 1 equiv) in dry THF (20 mL) was added a solution of TBAF in THF (1M, 5.2 mL, 5.0 mmol, 1.5 equiv) at room temperature. The reaction mixture was stirred for 1 h and then quenched with aqueous

NH_4Cl solution. The organic layer was separated, and the aqueous layer was extracted with ethyl acetate.



The combined organic layers were washed with water, brine, dried over anhydrous Na_2SO_4, and filtered. The solvent was evaporated in *vacuo* using a rotary evaporator, and the residue was purified (30% ethyl acetate in hexane, silica gel) to afford the corresponding primary alcohol (960 mg, 82%) as a colourless gummy liquid.

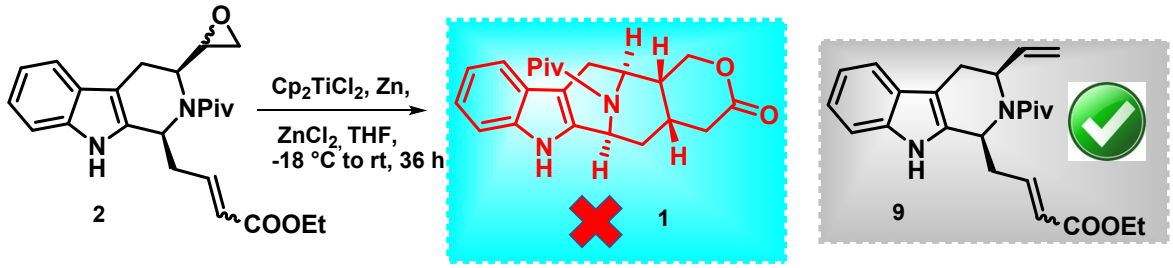
In a flame dried round bottom flask containing the alcohol (800 mg, 2.33 mmol, 1 equiv) in DCM: DMSO (7:3, 10 mL) was added by SO_3.Py (1.13 g, 7.0 mmol, 3 equiv) and Et_3N (2.0 mL, 14.4 mmol, 6 equiv) at rt, stirred the reaction for 30 m; then Ph_3PCHCO_2Et (2.0 g, 3.51 mmol, 1.5 equiv) was added. After stirring for 3 h, the reaction mixture was diluted with diethyl ether. The combined organic layers were washed with water, brine, dried over anhydrous Na_2SO_4, filtered, and concentrated in *vacuo*. The residue was purified using flash column chromatography (silica gel, 15 % ethyl acetate in hexane) to afford α,β-unsaturated ester **2** (690 mg, 72%, *E/Z* = 3/2) as a colourless gel.

^{1}H NMR (400 MHz, $CDCl_3$) of 2 (mixture of isomers): δ 8.01 (s, 1H), 7.45 (d, *J* = 7.7 Hz, 1H), 7.34 (d, *J* = 8.0 Hz, 1H), 7.25 – 7.17 (m, 2H), 7.12 (t, *J* = 7.0 Hz, 1H), 6.04 (d, *J* = 15.6 Hz, 1H), 5.75 – 5.71 (m, 1H), 4.71 (t, *J* = 5.6 Hz, 1H), 4.24 (q, *J* = 7.1 Hz, 2H), 3.15 – 3.12 (m, 1H), 3.01 – 2.94 (m, 2H), 2.81 – 2.73 (m, 3H), 2.57 – 2.55 (m, 1H), 1.36 (s, 9H), 1.32 (t, *J* = 7.1 Hz, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) of 2 (mixture of isomers): δ 188.5, 177.7, 145.2, 135.5, 130.9, 127.8, 126.1, 124.4, 122.4, 118.0, 111.2, 105.2, 60.6, 52.6, 49.5, 39.5, 31.9, 29.4, 28.8, 22.7, 21.4, 14.1

HRMS (ESI) of 2 (mixture of isomers): calculated for $C_{24}H_{30}N_2O_4Na$: 433.2103 ($[M + Na]^+$), found 433.2102.

Attempted preparation of 1:



In a flame dried round bottom flask containing freshly fused $ZnCl_2$ (72 mg, 0.53 mmol, 2.2 equiv) were added dry THF (8 mL), activated zinc dust (100 mg, 1.46 mmol, 6 equiv), and Cp_2TiCl_2 (145 mg, 0.58 mmol, 2.4 equiv) under inert atmosphere at room temperature and stirred for 1 h with the colour of the solution changing from deep red to green. Then the solution was warmed to -18 °C, and the epoxy ester **2** (100 mg, 0.24 mmol, 1 equiv) in dry THF (4 mL) was cannulated into it at -18 °C in positive pressure of nitrogen. The reaction mixture was allowed to slowly warm up to room temperature and stirred for 36 h at the same temperature. The reaction mixture was diluted with diethyl ether and quenched by saturated aqueous solution of NH_4Cl and stirred for an additional 30 m and allowed to settle down. The supernatant organic layer was separated and passed through a small pad of Celite, and the process was repeated three to four times using diethyl ether. The combined organic layers were concentrated in *vacuo,* and the residue was subjected to column chromatography (silica gel 100-200, 15% ethyl acetate in hexane) which afforded deoxygenated products **9** instead of the cyclized product **1** in 30% yield.

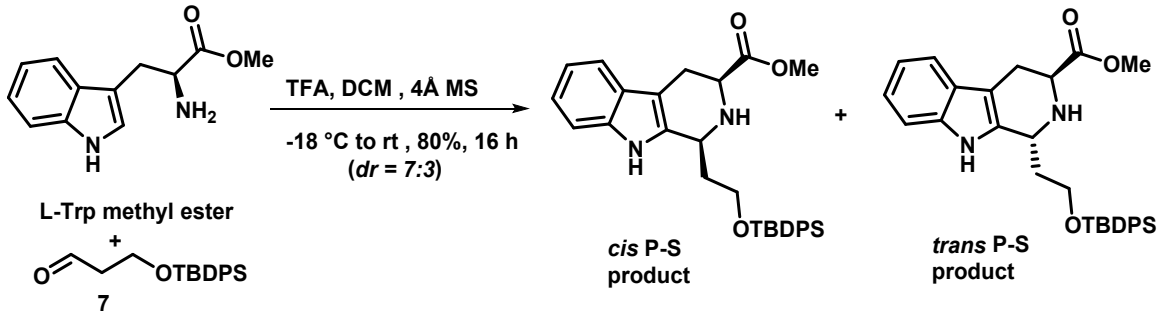
^{1}H NMR (400 MHz, $CDCl_3$) of 9 (mixture of isomers): δ 8.10 (s, 1H), 7.49 (d, *J* = 7.6 Hz, 1H), 7.33 (d, *J* = 8.0 Hz, 1H), 7.24 – 7.15 (m, 2H), 7.11 (dd, *J* = 7.6, 7.0 Hz, 1H), 6.01 – 5.90 (m, 2H), 5.75 – 5.70 (m, 1H), 5.32 – 5.29 (m, 1H), 5.19 – 5.10 (m, 2H) 4.22 (q, *J* = 7.2 Hz, 2H), 3.13 (d, *J* = 15.1 Hz, 1H), 3.05 (ddd, *J* = 15.1, 5.0, 1.4 Hz, 1H), 2.86 – 2.75 (m, 2H), 1.39 (s, 9H), 1.31 (t, *J* = 7.2 Hz, 1H).

HRMS (ESI) of 9 (mixture of isomers): calculated for $C_{24}H_{30}N_2O_3Na$: 417.2154 ($[M + Na]^+$), found 417.2153.

Preparation of *cis* and *trans* Pictet-Spengler (P-S) products:

In a flame dried round bottom flask containing a solution of L-tryptophan methyl ester (8 g, 36.66 mmol, 1 equiv) in dry DCM (75 mL) was added activated 4Å MS (7.33 g, 200

mg/mmol). The aldehyde **7** (14.9 g, 47.66 mmol, 1.3 equiv) in dry DCM (90 mL) was canulated into the stirring solution.



The reaction mixture was cooled to -15 °C; subsequently, TFA (3.4 mL, 44 mmol, 1.2 equiv) was added dropwise. The reaction mixture was stirred for 3 h at the same temperature. Then additional TFA (6.8 mL, 88 mmol, 2.4 eq) was added, and the reaction mixture was gradually warmed up to rt and stirred for 16 h. The reaction mixture was filtered using a short pad of Celite. The filtrate and washings were combined and treated with 1N NaOH till it was basic in nature. The combined organic layers were washed with water, brine, dried over anhydrous Na_2SO_4, filtered, and concentrated in *vacuo*. The residue was purified by flash column chromatography (silica gel, 20% ethyl acetate in hexane) to afford the *cis* P-S product (10.5 g, 56%) and the *trans* isomer (4.5 g, 24%) as brown gummy liquids.

^{1}H NMR (400 MHz, $CDCl_3$) of *trans* P-S product: δ 8.51 (s, 1H), 7.76 – 7.73 (m, 4H), 7.52 – 7.41 (m, 7H), 7.17 – 7.15 (m, 2H), 7.13 – 7.09 (m, 1H), 4.56 (t, *J* = 6.5 Hz, 1H), 4.04 – 3.98(m, 1H), 3.96 – 3.85 (m, 2H), 3.77 (s, 3H), 3.14 (dd, *J* = 15.5, 5.2 Hz, 1H), 3.00 (dd, *J* = 15.5, 7.6, 1H), 2.01 (q, *J* = 6.0 Hz, 2H), 1.18 (s, 9H).

^{13}C NMR 100 MHz, $CDCl_3$) of *trans* P-S product: δ 174.2, 135.8, 135.7, 135.7, 135.3, 133.4, 133.1, 130.1, 130.1, 128.1, 128.1, 127.2, 121.7, 119.4, 118.1, 110.9, 106.7, 62.4, 52.9, 52.3, 48.9, 38.1, 27.2, 25.2, 19.4.

IR ν_{max} (neat, cm^{-1}) of *trans* P-S product: 3396, 3059, 2937, 2859, 2354, 1736, 1632, 1442, 1333, 1269, 1214, 1102, 1005, 939, 822, 769, 700, 609, 520.

Optical rotation of *trans* P-S product $[\alpha]_D^{22}$: -5.8 (c 0.59, $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$) of *cis* P-S product: δ 9.03 (s, 1H), 7.74 – 7.68 (m, 4H), 7.52 – 7.37 (m, 8H), 7.16 – 7.09 (m, 3H), 4.37 – 4.35 (m, 1H), 3.99 (dd, *J* = 7.3, 3.6 Hz, 2H), 3.85 (dd, *J* =

12.04, 4.3 Hz, 1H), 3.84 (s, 3H), 3.18 (ddd, *J* = 15.0, 4.24, 1.4 Hz, 1H), 2.88 (ddd, *J* = 15.0, 12.04, 2.4 Hz, 1H), 2.26 (dq, *J* = 14.3, 7.1 Hz, 1H), 1.97 (dq, *J* = 14.3, 3.7 Hz, 1H), 1.18 (s, 9H).

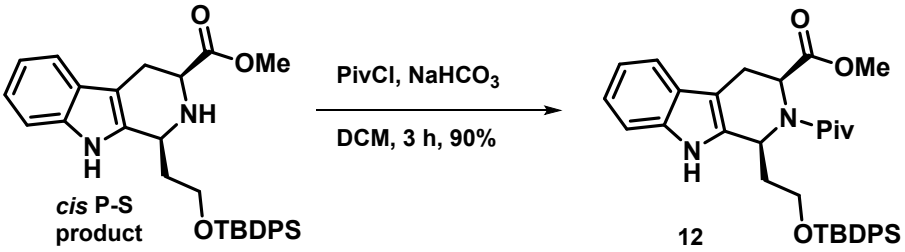
^{13}C NMR (100 MHz, $CDCl_3$) of *cis* P-S product: δ 173.3, 135.8, 135.7, 135.7, 132.9, 132.9, 130.2, 130.1, 128.1, 128.0, 127.2, 125.6, 121.6, 119.4, 118.1, 111.1, 107.5, 63.1, 57.0, 53.4, 52.3, 37.8, 27.1, 26.0, 19.4.

IR ν_{max} (neat, cm^{-1}) of *cis* P-S product: 3391, 3058, 2936, 2858, 2354, 1738, 1584, 1439, 1355, 1324, 1269, 1215, 1167, 1102, 1001, 939, 821, 743, 701, 611.

Optical rotation of *cis* P- product S$[\alpha]_D^{22}$: –38.2 (c 2.02, $CHCl_3$).

HRMS (ESI) (mixture of diastereomers): calculated for $C_{31}H_{37}N_2O_3Si$: 513.2573 ($[M + H]^+$), found 513.2576.

Preparation of 12:



To a solution of the amino ester ***cis* P-S product** (6 g, 11.72 mmol, 1 equiv) in dry DCM (50 mL) was added PivCl (2.0 mL, 16.38 mmol, 1.4 equiv) and $NaHCO_3$ (2.84 g, 35.1 mmol, 3 equiv) at room temperature. The reaction mixture was stirred for 2 h, the colour of the reaction changed brown to colourless, indicating the completion of the reaction. The reaction was diluted with DCM and washed with water, brine, dried over anhydrous Na_2SO_4, and concentrated in *vacuo*. The residue was purified (silica gel, 10% ethyl acetate in hexane) to afford the protected amine **12** (6.30 g, 90% yield) as a colourless oil.

^{1}H NMR (400 MHz, $CDCl_3$) of 12: δ 9.81 (s, 1H), 7.78 – 7.73 (m, 4H), 7.54 – 7.41 (m, 7H), 7.12 – 7.06 (m, 2H), 6.88 – 6.85 (m, 1H), 5.51 – 5.49 (m, 1H), 5.42 – 5.41 (m, 1H), 4.39 – 4.33 (m, 1H), 4.08 – 4.03 (m, 1H), 3.63 (s, 3H), 3.61 (d, *J* = 15.3 Hz, 1H), 3.10 (ddd, *J* = 15.3, 5.9, 2.0 Hz, 1.3 Hz, 1H), 2.33 – 2.28 (m, 2H), 1.37 (s, 9H), 1.26 (s, 9H).

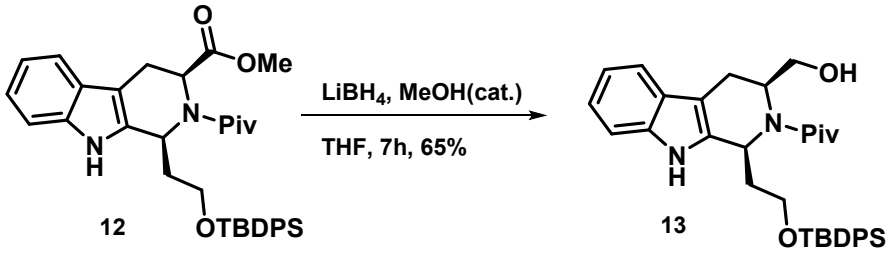
^{13}C NMR (100 MHz, $CDCl_3$) of 12: δ 177.6, 172.1, 136.1, 135.8, 135.7, 134.5, 133.17, 132.8, 130.3, 130.3, 128.3, 126.7, 121.5, 119.3, 118.1, 111.2, 103.6, 66.0, 55.8, 53.7, 52.7, 40.0, 39.4, 28.6, 27.5, 27.2, 19.7.

IR ν_{max} (neat, cm^{-1}) of 12: 3375, 3058, 2948, 2865, 2354, 1745, 1627, 1469, 1401, 1312, 1193, 1103, 1034, 977, 748, 702, 607.

HRMS (ESI) calculated for $C_{36}H_{44}N_2O_4SiNa$: 619.2968 ($[M + Na]^+$), found 619.2969.

Optical rotation $[\alpha]_D^{22}$: +58.6 (c 1.0, $CHCl_3$).

Preparation of 13:



In a flame dried round bottom flask containing ester **12** (5 g, 8.38 mmol, 1 equiv) in dry THF (40 mL) was added lithium borohydride (456 mg, 20.94 mmol, 2.5 equiv) portion-wise at 0 °C; two to four drops dry MeOH (catalytic amount) was added in the reaction mixture. The reaction mixture was slowly warmed up to room temperature and stirred for 7 h at the same temperature. The reaction was quenched with water, ethyl acetate (200 mL) was added, and the organic layer was washed with brine. The combined organic layers were dried over anhydrous Na_2SO_4, and the solvent was evaporated in *vacuo*. The residue was subjected to purification (silica gel, 10 % ethyl acetate in hexane) to afford alcohol **13** (3.10 g, 65% yield) as a colourless oil.

^{1}H NMR (400 MHz, $CDCl_3$) of 13: δ 9.58 (s, 1H), 7.77 – 7.72 (m, 4H), 7.52 – 7.47 (m, 3H), 7.45 – 7.41(m, 4H), 7.11 – 7.06 (m, 2H), 6.86 – 6.83 (m, 1H), 5.52 (d, *J* = 7.6 Hz, 1H), 4.82 – 4.78 (m, 1H), 4.37 (td, *J* = 10.6, 2.3 Hz, 1H), 4.00 (dt, *J* = 10.4, 3.5 Hz, 1H), 3.71 (dd, *J* = 10.4, 8.4 Hz, 1H), 3.59 (dd, *J* = 10.4, 5.6 Hz, 1H), 3.07 (d, *J* = 15.5 Hz, 1H), 3.00 (dd, *J* = 15.5, 4.4 Hz, 1H), 2.16 – 2.07 (m, 1H), 1.97 – 1.93 (m, 1H), 1.39 (s, 9H), 1.25 (s, 9H).

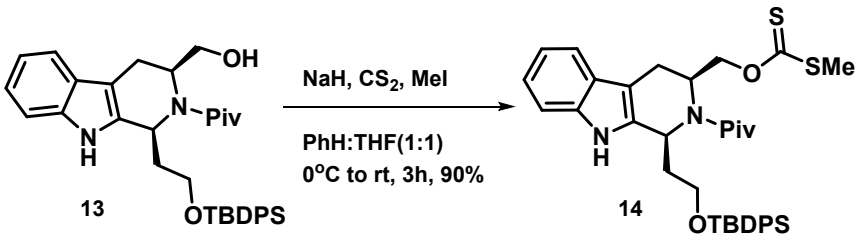
^{13}C NMR (100 MHz, $CDCl_3$) of 13: δ 177.9, 136.0, 135.7, 135.6, 133.9, 133.1, 132.6, 130.2, 130.2, 128.2, 127.1, 121.5, 119.2, 118.0, 111.1, 103.1, 65.5, 63.4, 53.6, 51.8, 40.7, 39.5, 28.7, 27.4, 22.0, 19.6.

IR ν_{max} (neat, cm^{-1}) of 13: 3394, 3062, 2939, 2868, 2355, 1598, 1469, 1411, 1372, 1312, 1197, 1078, 983, 926, 822, 747, 701, 606.

HRMS (ESI) calculated for $C_{35}H_{44}N_2O_3SiNa$: 591.3019 ([M + Na]$^+$), found 519.3017.

Optical rotation $[\alpha]_D^{22}$: +28.5 (c 1.24, $CHCl_3$).

<u>Preparation of xanthate ester 14</u>:



To a solution of the alcohol **13** (3.6 g, 6.3 mmol, 1 equiv) in THF:benzene (1:1, 40 mL) was added 55% NaH in mineral oil (760 mg, 15.83 mmol, 2.5 equiv) at 0 °C portion-wise. The reaction mixture was stirred for 20 m, then CS_2 (1.3 mL, 200 µL/mmol) was added. The reaction was stirred for 15 m, then methyl iodide (2.0 mL, 31.5 mmol, 5 equiv) was added, and the reaction was again stirred for 3 h at the same temperature. The reaction was quenched with water and extracted with ethyl acetate. The combined organic layers were washed with an aqueous solution of sodium thiosulfate, water, and brine, dried over anhydrous Na_2SO_4, and the solvent was evaporated under reduced pressure in a rotary evaporator. The residue was purified by flash column chromatography (silica gel, 7% ethyl acetate in hexane) to afford the xanthate ester **14** (3.7 g, 90%) as a yellow gel.

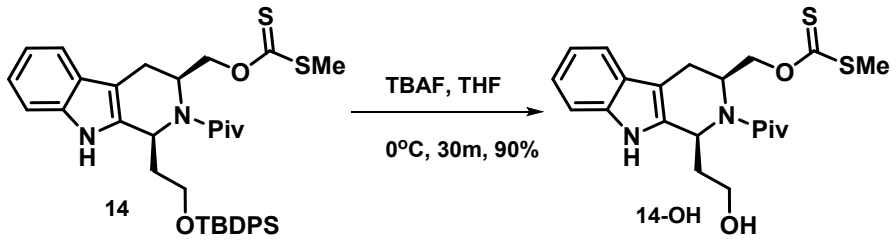
^{1}H NMR (400 MHz, $CDCl_3$) of 14: δ 9.59 (s, 1H), 7.75 – 7.69 (m, 4H), 7.50 – 7.46 (m, 3H), 7.43 – 7.38 (m, 4H), 7.10 – 7.05 (m, 2H), 6.84 – 6.80 (m, 1H), 5.56 (d, *J* = 7.6 Hz, 1H), 5.13 (q, *J* = 6.7 Hz, 1H), 4.60 (d, *J* = 7.3 Hz, 2H), 4.35 (td, *J* = 10.4, 1.6 Hz, 1H), 3.99 (dt, *J* = 10.4, 3.7 Hz, 1H), 3.15 (ddd, *J* = 15.8, 5.7, 1.6 Hz, 1H), 2.96 (d, *J* = 15.8 Hz, 1H), 2.53 (s, 3H), 2.18 – 2.09 (m, 1H), 1.99 (d, *J* = 14.5 Hz, 1H), 1.40 (s, 9H), 1.24 (s, 9H).

^{13}C NMR (100 MHz, $CDCl_3$) of 14: δ 215.6, 177.8, 136.0, 135.7, 135.6, 133.9, 133.1, 132.6, 130.2, 130.2, 128.2, 126.9, 121.6, 119.3, 117.9, 111.2, 102.8, 73.4, 65.6, 51.8, 50.7, 40.0, 39.7, 28.9, 27.5, 23.3, 19.6, 19.5.

IR ν_{max} (neat, cm^{-1}) of 14: 3391, 3058, 2936, 2858, 2354, 1738, 1584, 1439, 1324, 1296, 1215, 1167, 1102, 1001, 939, 821, 743, 701, 611.

Optical rotation $[\alpha]_D^{22}$: +51.9 (c 0.86, $CHCl_3$).

<u>Deprotection of 14 (preparation of 14-OH intermediate)</u>:



To a solution of the methyl xanthate ester **14** (3.4 g, 5.16 mmol, 1 equiv) in THF (20 mL) was added TBAF (7.8 mL, 1 M in THF, 1.5 equiv) at 0 °C dropwise. The reaction mixture was stirred for 30 m, then quenched with an aq solution of NH_4Cl. Ethyl acetate (100 mL) was added, and the organic layer was washed with water, brine, dried over anhydrous Na_2SO_4, filtered, and the solvent was evaporated under reduced pressure in a rotary evaporator. The crude residue was purified by flash column chromatography (silica gel, 25% ethyl acetate in hexane) to afford the intermediate alcohol **14-OH** (1.95 g, 90%) as a yellow gel.

^{1}H NMR (400 MHz, $CDCl_3$) of 14-OH: δ 9.31 (s, 1H), 7.46 (d, *J* = 7.7 Hz, 1H), 7.37 (d, *J* = 7.7 Hz, 1H), 7.17 (t, *J* = 7.4 Hz, 1H), 7.11 (t, *J* = 7.4 Hz, 1H), 5.72 (t, 6.4 Hz, 1H), 5.18 (q, *J* = 6.9 Hz, 1H), 4.68 – 4.59 (m, 2H), 3.92 – 3.84 (m, 2H), 3.14 (ddd, *J* = 15.7, 5.7, 1.4 Hz, 1H), 2.91 (d, *J* = 15.7 Hz, 1H), 2.55 (s, 3H), 2.26 – 2.17 (m, 1H), 1.81 – 1.75 (m, 1H), 1.44 (s, 9H).

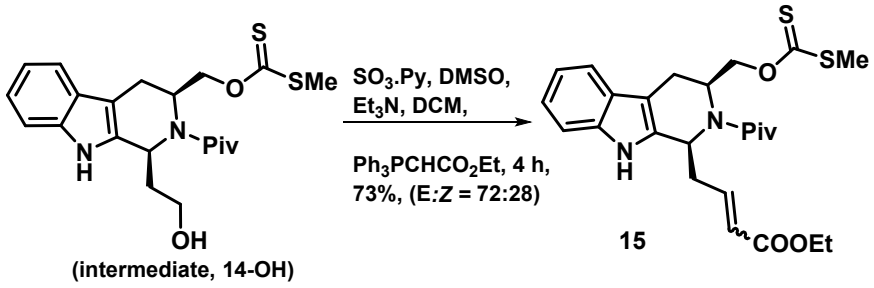
^{13}C NMR (100 MHz, $CDCl_3$) of 14-OH): δ 215.6, 179.3, 136.4, 133.1, 126.8, 121.9, 119.5, 117.9, 111.4, 103.4, 73.1, 60.1, 50.7, 49.0, 40.0, 39.2, 29.0, 23.4, 19.6.

IR ν_{max} (neat, cm^{-1}) of 14-OH: 3283, 3059, 2962, 2244, 1603, 1468, 1410, 1367, 1322, 1199, 1072, 1013, 967, 911, 838, 747.

HRMS (ESI) calculated for $C_{21}H_{30}N_2O_3S_2$: 421.1620 ([M + H]$^+$), found 421.1622.

Optical rotation $[\alpha]_D^{22}$: +88.5 (c 1.38, $CHCl_3$).

Preparation of 15:



In a flame dried round bottom flask containing the alcohol intermediate **14-OH** (1.8 g, 4.29 mmol, 1 equiv) in DCM:DMSO (7:3, 20 mL) was added SO_3.Py (2.0 g, 12.86 mmol, 3 equiv) and Et_3N (3.58 mL, 25.74 mmol, 6 equiv) at room temperature, stirred the reaction for 30 m, then Ph_3PCHCO_2Et (2.24 g, 6.44 mmol, 1.5 equiv) was added. The reaction mixture was stirred for 4 h, then diluted with diethyl ether. The organic layer was washed with water, and brine, dried over anhydrous Na_2SO_4, and filtered. The solvent was evaporated under reduced pressure in a rotatory evaporator. The crude was purified using flash column chromatography (silica gel, 20 % ethyl acetate in hexane) to afford the α,β-unsaturated ester **15** (1.53 g, 73%, *E/Z* = 72/28) as a yellow gummy liquid which was used as a mixture in the next step.

Small amounts of both *cis* and *trans* isomers in pure forms were collected during the chromatographic purification for the data.

^{1}H NMR (400 MHz, $CDCl_3$) of 15 (*cis*): δ 9.02 (s, 1H), 7.46 (d, *J* = 7.6 Hz, 1H), 7.37 (d, *J* = 8.0 Hz, 1H), 7.18 (dd, *J* = 8.0, 7.6 Hz, 1H), 7.11 (dd, *J* = 8.0, 7.6 Hz, 1H), 6.66 (ddd, *J* = 11.3, 9.5, 6.8 Hz, 1H), 5.97 (dt, *J* = 11.3, 1.3 Hz, 1H), 5.60 – 5.57 (m, 1H), 5.14 (q, *J* = 6.7 Hz, 1H), 4.68 (qd, *J* = 11.1, 7.1 Hz, 2H), 4.19 (q, *J* = 7.1 Hz, 2H), 3.66 – 3.59 (m, 1H), 3.09 (ddd, *J* = 15.6, 5.8, 2.0 Hz, 1H), 2.95 (d, *J* = 15.8 Hz, 1H), 2.67 (dt, *J* = 13.2, 6.6 Hz, 1H), 2.55 (s, 3H), 1.41 (s, 9H), 1.25 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) of 15 (*cis*): δ 215.5, 178.3, 167.1, 147.4, 136.6, 133.1, 126.8, 122.1, 121.1, 119.6, 118.0, 111.4, 104.2, 60.5, 51.2, 50.7, 39.9, 36.3, 28.9, 23.4, 19.5, 14.3.

IR ν_{max} (neat, cm^{-1}) of 15 (*cis*): 3315, 3059, 2976, 2923, 2353, 1709, 1613, 1467, 1407, 1311, 1194, 1072, 965, 819, 748, 673.

Optical rotation of 15 (*cis*) $[\alpha]_D^{22}$: +94.0 (c 0.93, $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$) of 15 (*trans*): δ 8.11 (s, 1H), 7.47 (d, *J* = 7.7 Hz, 1H), 7.34 (d, *J* = 8.0 Hz, 1H), 7.30 – 7.23 (m, 1H), 7.19 (ddd, *J* = 8.2, 7.0, 1.3 Hz, 1H), 7.14 – 7.10 (m, 1H), 6.06 (dd, *J* = 15.4, 1.3 Hz, 1H), 5.68 – 5.66 (m, 1H), 5.15 (q, *J* = 7.0 Hz, 1H), 4.66 – 4.62 (m, 2H), 4.24 (q, *J* = 7.1 Hz, 2H), 3.09 (ddd, *J* = 15.9, 6.0, 2.1 Hz, 1H), 2.94 (d, *J* = 15.9 Hz, 1H), 2.90 – 2.84 (m, 1H), 2.62 – 2.57 (m, 1H), 2.55 (s, 3H), 1.41 (s, 9H), 1.32 (t, *J* = 7.2 Hz, 3H).

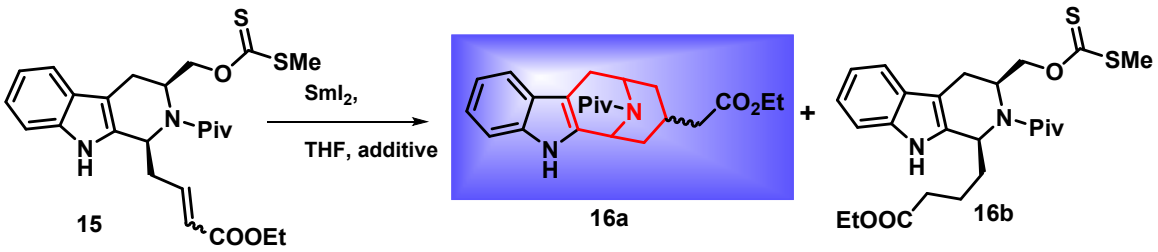
^{13}C NMR (100 MHz, $CDCl_3$) of 15 (*trans*): δ 215.6, 177.9, 166.4, 145.5, 136.4, 132.4, 126.6, 124.6, 122.5, 119.9, 118.2, 111.3, 104.6, 60.7, 50.5, 49.8, 39.6, 39.3, 28.8, 23.2, 19.6, 14.4.

IR ν_{max} (neat, cm^{-1}) of 15 (*trans*): 3323, 2975, 2962, 2353, 1711, 1616, 1466, 1404, 1368, 1316, 1271, 1196, 1074, 969, 767, 675.

Optical rotation of 15 (*trans*) $[\alpha]_D^{22}$: +105.1 (c 0.73, $CHCl_3$).

HRMS (ESI) (mixture of diastereomers): calculated for $C_{25}H_{33}N_2O_4S_2$: 489.1882 ($[M + H]^+$), found 489.1880.

Preparation of 16a and 16b:



In a flame dried round bottom flask containing methyl xanthate ester **15** (100 mg, 0.20 mmol, 1 equiv) in THF:HMPA (3:1, 4 mL), the SmI_2 solution in THF (3.7 mL of 0.07M solution, 0.26 mmol, 1.3 equiv) was added dropwise at -15°C until the blue colour was persisting. The reaction was stirred for 30 m to 1 h at -15 °C; then the reaction mixture was quenched by adding NH_4Cl solution, diethyl ether was added and the organic layer was washed with saturated aqueous solution of sodium potassium tartrate. The combined organic layer was washed with water, dried over Na_2SO_4, filtered, and the solvent was evaporated under reduced pressure in a rotatory evaporator. The crude mixture was subjected to column chromatography (silica gel, 20% ethyl acetate in hexane) to afford the cyclized product **16a** (21 mg, 28% yield) along with double bond reduced products **16b** (41.3 mg, 42%).

^{1}H NMR (400 MHz, $CDCl_3$) of 16a (mixture of rotamers and diastereomers): δ 8.62 (s, 1H), 7.47 (d, *J* = 7.5 Hz, 1H), 7.39 (d, *J* = 8.3 Hz, 1H), 7.18 (t, *J* = 7.5 Hz, 1H), 7.10 (t, *J* = 7.5 Hz, 1H), 5.49 (t, *J* = 6.4 Hz, 1H), 4.86 – 4.81 (m, 1H), 4.16 (q, *J* = 6.5 Hz, 1H), 3.02 – 2.89 (m, 2H), 2.58 – 2.52 (m, 1H), 2.47 - 2.34 (m, 2H), 2.042 – 1.99 (m, 2H), 1.82 – 1.76 (m, 2H), 1.26 (s, 9H), 0.88 (t, *J* = 6.5 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) of 16a: δ177.7, 174.4, 136.5, 133.5, 126.7, 122.0, 119.6, 117.9, 111.2, 103.7, 70.2, 60.7, 51.5, 50.2, 50.0, 39.7, 36.6, 33.5, 28.7, 22.8, 14.2.

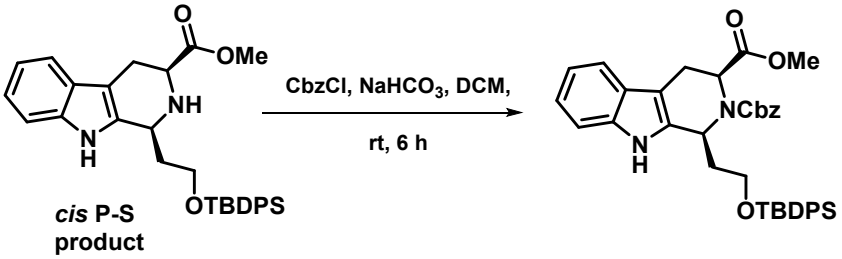
HRMS (ESI) of 16a (mixture of rotamers and diastereomers): calculated for $C_{23}H_{31}N_2O_3$: 383.2335 ($[M + H]^+$), found 383.2332.

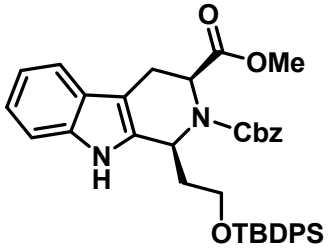
^{1}H NMR (400 MHz, $CDCl_3$) of 16b: δ 8.75 (s, 1H), 7.46 (d, *J* = 7.6 Hz, 1H), 7.39 (d, *J* = 8.0 Hz, 1H), 7.18 (t, *J* = 7.5 Hz, 1H), 7.11 (t, *J* = 7.5 Hz, 1H), 5.56 (t, *J* = 6.1 Hz, 1H), 5.13 (q, *J* = 6.3 Hz, 1H), 4.65 – 4.62 (m, 2H), 4.15 (q, *J* = 7.1 Hz, 1H), 3.08 (ddd, *J* = 15.8, 6.2, 1.3 Hz, 1H), 2.92 (d, *J* = 15.8 Hz, 1H), 2.59 – 2.51 (m, 1H), 2.55 (s, 3H), 2.43 - 2.35 (m, 1H), 2.07 – 1.98 (m, 2H), 1.85 – 1.77 (m, 2H), 1.40 (s, 9H), 1.26 (t, *J* = 7.1 Hz, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) of 16b: δ 215.6, 177.9, 174.5, 136.6, 133.7, 126.8, 126.1, 119.7, 118.0, 116.3, 111.3, 103.9, 73.5, 60.8, 50.5, 50.1, 39.8, 36.6, 33.7, 23.4, 23.0, 19.5, 14.4.

HRMS (ESI) of 16b: calculated for $C_{25}H_{35}N_2O_4S_2$: 491.2038 ($[M + H]^+$), found 491.2037.

<u>Cbz-protection of N4 of *cis* P-S product:</u> Followed the same procedure for the preparation of **12.**





<u>Data:</u> Scale of reaction 5 g, 9.77 mmol; yield 5.8 g, 92% as a light brown viscous oil.

^{1}H NMR (400 MHz, $CDCl_3$) (mixture of rotamers, 63:27): δ 9.7 – 9.48 (s, 1H), 7.79 – 7.68 (m, 4H), 7.55 – 7.39 (m, 10H), 7.32 –

7.29 (m, 2H), 7.12 – 7.09 (m, 2H), 6.93 – 6.88 (m, 1H), 5.62 – 5.45(m, 1H), 5.37 – 5.14 (m, 3H), 4.30 – 4.02 (m, 1H), 3.86 – 3.82 (m, 1H), 3.62 – 3.61 (s, 3H), 3.59 – 3.51 (m, 1H), 3.12 – 3.07 (m, 1H), 2.46 – 2.31(m, 2H), 1.26 – 1.18 (s, 9H).

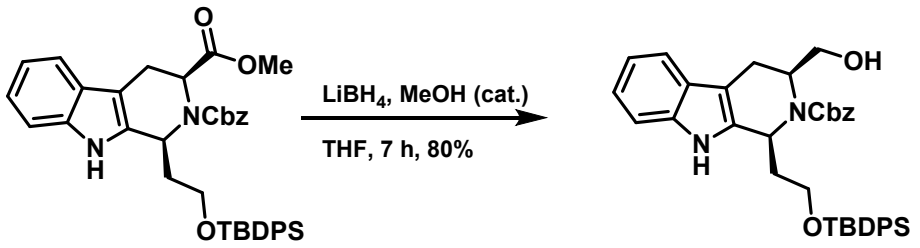
^{13}C NMR (100 MHz, $CDCl_3$) (mixture of rotamers, 63:37): δ 172.4, 172.3, 156.3, 156.3, 155.5, 155.4, 136.6, 136.2, 135.9, 135.7, 135.6, 133.2, 132.9, 132.7, 130.2, 129.0, 128.7, 128.6, 128.5, 128.2, 128.2, 127.8, 127.8, 127.1, 126.6, 121.7, 121.6, 119.3, 119.2, 118.3, 118.2, 111.1, 111.1, 104.7, 68.4, 67.7, 67.6, 65.6, 65.5, 64.8, 53.3, 53.2, 53.1, 52.4, 40.5, 39.6, 27.4, 27.4, 23.5, 23.1, 19.5.

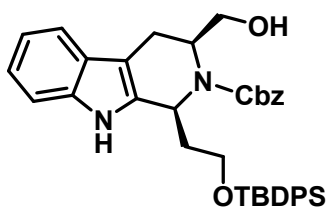
IR ν_{max} (neat, cm^{-1}) (mixture of rotamers): 3372, 3054, 2941, 2860, 2238, 1979, 1711, 1428, 1310, 1198, 1087, 729, 597.

HRMS (ESI) (mixture of rotamers): calculated for $C_{39}H_{43}N_2O_5Si$: 647.2941 ($[M + H]^+$), found 647.2942.

Optical rotation $[\alpha]_D^{22}$ (mixture of rotamers, 63:37): +22.1 (c 1.91, $CHCl_3$).

<u>Reduction of Cbz-protected ester to alcohol</u>: Followed the same procedure for the preparation of **13**.





<u>Data:</u> Scale of reaction 5.5 g, 8.51 mmol; yield 4.21 g, 80% as a colourless gel.

^{1}H NMR (400 MHz, $CDCl_3$) (mixture of rotamers): δ 9.11 (s, 1H), 7.65 – 7.62 (m, 4H), 7.43 – 7.29 (m, 11H), 7.24 – 7.21 (m, 1H), 7.09 – 7.02 (m, 2H), 6.96 – 6.93 (m, 1H), 4.83 (d, *J* = 3.5 Hz, 1H), 4.61 (s, 2H), 4.42 (t, *J* = 5.5 Hz, 1H), 4.05 – 3.83 (m, 4H), 3.00 – 2.96 (m, 1H), 2.88 – 2.81 (m, 1H), 2.63 – 2.57 (m, 1H), 2.15 – 2.06 (m, 1H), 1.12 (s, 9H).

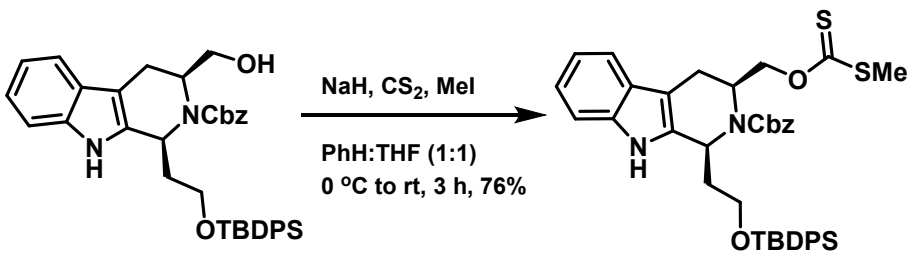
^{13}C NMR (100 MHz, $CDCl_3$) (mixture of rotamers): δ 158.4, 141.0, 136.5, 135.6, 135.6, 134.2, 133.2, 132.7, 130.2, 130.1, 128.6, 128.1, 127.6, 127.0, 126.2, 122.1, 119.6, 118.0, 111.3, 105.7, 68.2, 65.3, 63.2, 56.1, 51.9, 35.9, 27.2, 25.1, 19.4.

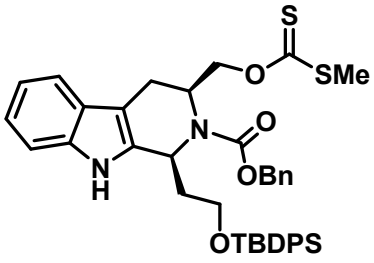
IR ν_{max} (neat, cm^{-1}) (mixture of rotamers): 3389, 3302, 3054, 2934, 2868, 2343, 1736, 1430, 1241, 1058, 731.

HRMS (ESI) (mixture of rotamers): calculated for $C_{38}H_{43}N_2O_4Si$: 619.2992 ($[M + H]^+$), found 619.2995.

Optical rotation $[\alpha]_D^{22}$ (mixture of rotamers): -30.2 (c 2.02, $CHCl_3$).

<u>Synthesis of methyl xanthate from Cbz-protected alcohol</u>: Followed the same procedure for the preparation of **14**.





<u>Data:</u> Scale of reaction 4.0 g, 6.47 mmol; yield 3.47 g, 76% as a yellow gel.

^{1}H NMR (400 MHz, $CDCl_3$) (mixture of rotamers, 52:48): δ 9.55 – 9.32 (s, 1H), 7.77 – 7.67 (m, 4H), 7.52 – 7.39 (m, 10H), 7.36 – 7.27 (m, 2H), 7.12 – 7.07 (m, 2H), 6.92 – 6.88 (m, 1H), 5.43 – 5.39 (m, 1H), 5.35 – 5.07 (m, 4H), 4.68 – 4.48 (m, 2H), 4.30 – 4.03 (m, 1H), 3.86 – 3.83 (m, 1H), 3.14 – 3.07 (m, 1H), 2.92 – 2.86 (m, 1H), 2.46 – 2.45 (s, 3H), 2.26 – 1.96 (m, 2H), 1.25 – 1.17 (m, 9H).

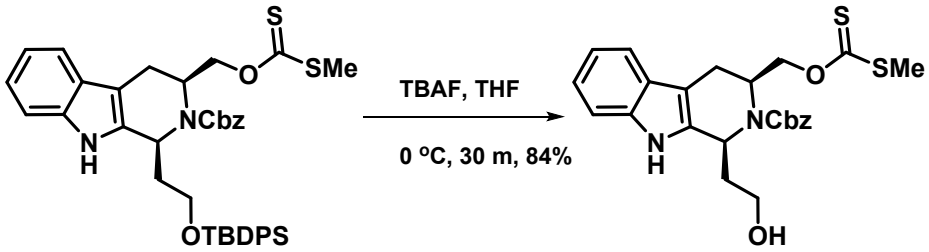
^{13}C NMR (100 MHz, $CDCl_3$) (mixture of rotamers, 52:48): δ 215.5, 215.0, 155.9, 155.8, 136.5, 136.2, 135.7, 135.6, 133.0, 132.9, 132.8, 132.6, 132.4, 130.3, 130.3, 128.7, 128.5, 128.4, 128.2, 128.2, 128.0, 126.9, 121.9, 121.8, 119.4, 118.2, 118.1, 111.2, 111.1, 104.3, 103.7, 73.6, 68.0, 67.8, 65.4, 64.4, 51.6, 50.8, 48.5, 48.2, 40.7, 40.2, 29.8, 27.5, 27.4, 27.0, 22.6, 22.3, 19.6, 19.5, 19.1, 18.9.

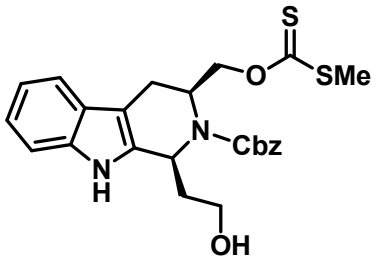
IR ν_{max} (neat, cm^{-1}) (mixture of rotamers, 52:48): 3387, 3060, 2935, 2859, 1698.23, 1454, 1416, 1326, 1201, 1073, 959, 819, 746, 701.

HRMS (ESI) (mixture of rotamers, 52:48): calculated for $C_{40}H_{44}N_2O_4S_2SiNa$: 731.2409 ([M + Na]$^+$), found 731.2406.

Optical rotation $[\alpha]_D^{22}$ (mixture of rotamers, 52:48): +7.89 (c 1.25, $CHCl_3$).

Deprotection of TBDPS group of the xanthate of Cbz-protected compound: Followed the same procedure for the deprotection of **14** (preparation of intermediate **14-OH**).





Data: Scale of reaction 3.5 g, 4.94 mmol; yield 1.95 g, 84% as a light-yellow gel.

^{1}H NMR (400 MHz, $CDCl_3$) (mixture of rotamers): δ 9.38 – 9.13 (s, 1H), 7.52 – 7.46 (m, 1H), 7.43 – 7.31 (m, 6H), 7.18 (t, *J* = 7.5 Hz, 1H), 7.11 (t, *J* = 7.5 Hz, 1H), 5.51 – 5.42 (m, 1H), 5.38 – 5.15 (m, 3H), 4.67 – 4.62 (m, 1H), 4.57 – 4.51 (m, 1H), 3.97 – 3.80 (m, 2H), 3.09 – 3.04 (m, 1H), 2.91 – 2.80 (m, 1H), 2.5 – 2.48 (s, 3H), 2.32 – 2.19 (m, 1H), 1.95 – 1.84 (m, 1H).

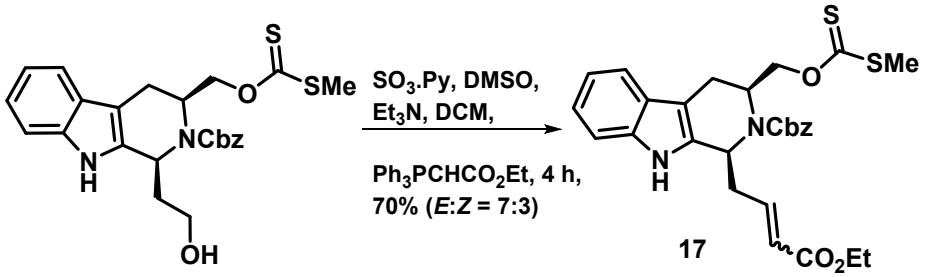
^{13}C NMR (100 MHz, $CDCl_3$) (mixture of rotamers): δ 215.5, 157.2, 136.4, 136.2, 132.1, 128.8, 128.5, 128.4, 128.0, 126.8, 122.0, 119.5, 118.1, 111.3, 104.4, 73.1, 68.2, 59.8, 48.9, 48.5, 39.4, 22.5, 19.3.

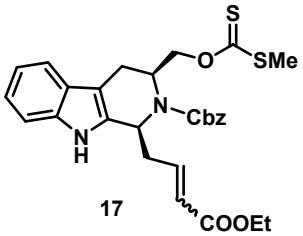
IR ν_{max} (neat, cm^{-1}) (mixture of rotamers): 3328, 3055, 2928, 2858, 2354, 1674, 1420, 1335, 1201, 1062, 964, 887, 750, 693, 601.

HRMS (ESI) (mixture of rotamers): calculated for $C_{24}H_{26}N_2O_4S_2Na$: 493.1232 ([M + Na]$^+$), found 493.1230.

Optical rotation $[\alpha]_D^{22}$ (mixture of rotamers): + 51.3 (c 0.8, $CHCl_3$).

Synthesis of 17, the α,β-unsaturated ester of xanthate: Followed the same procedure for the preparation of **15**.





Data: Scale of reaction 1.8 g, 3.82 mmol; 4 h; yield 1.44 g, 70% as a light-yellow gel (*E/Z* = 7/3).

^{1}H NMR (400 MHz, $CDCl_3$) of *cis* olefin (mixture of rotamers): δ 9.03 – 8.89 (s, 1H), 7.49 – 7.46 (m, 1H), 7.41 – 7.32 (m, 6H), 7.21–7.17 (m, 1H), 7.11 (t, *J* = 7.5 Hz, 1H), 6.58 – 6.31 (bs, 1H), 5.96 – 5.72 (m, 1H), 5.41 – 5.24 (m, 3H), 4.71 – 4.50 (m, 2H), 4.19 (q, *J* = 7.3 Hz, 2H), 3.67 – 3.49 (m, 1H), 3.07 – 3.02 (m, 1H), 2.93 – 2.72 (m, 2H), 2.48 (s, 3H), 1.75 – 1.64 (m, 1H), 1.28 (t, *J* = 7.0 Hz, 3H).

^{13}C NMR (100 MHz, DMSO-d_6) of *cis* isomer (mixture of rotamers): δ 215.3, 177.0, 167.3, 156.2, 146.7, 136.6, 132.1, 131.6, 128.7, 128.1, 126.8, 122.2, 121.7, 119.6, 118.2, 111.3, 104.7, 68.0, 60.6, 51.8, 48.6, 35.6, 29.8, 22.6, 19.1, 14.3.

IR ν_{max} (neat, cm^{-1}) of *cis* olefin (mixture of rotamers): 3360.01, 3044.64, 2931.32, 2851.40, 2647.91, 2516.31, 2352.70, 1696.85, 1414.59, 1328.80, 1274.69, 1201.19, 1068.76, 967.75, 873.79, 821.45, 765.48, 689.20.

HRMS (ESI) of *cis* olefin (mixture of rotamers): calculated for $C_{28}H_{30}N_2O_5S_2Na$: 561.1494 ([M + Na]$^+$), found 561.1492.

Optical rotation $[\alpha]_D^{22}$ of *cis* olefin (mixture of rotamers): +60.3 (c 0.8, $CHCl_3$).

^{1}H NMR (400 MHz, DMSO-d_6) of *trans* isomer (mixture of rotamers): δ 11.0 – 10.91 (s, 1H), 7.45 – 7.34 (m, 7H), 7.10 (t, *J* = 7.4 Hz, 1H), 7.02 – 6.94 (m, 2H), 5.83 (d, *J* = 15.6 Hz, 1H), 5.49 – 5.45(s, 1H), 5.28 – 5.20 (m, 2H), 5.10 – 5.05 (s, 1H), 4.64 – 4.60 (m, 1H), 4.53 – 4.48 (m, 1H), 4.08 (q, *J* = 7.1 Hz, 2H), 3.12 – 3.01 (s, 1H), 2.98 - 2.86 (m, 2H), 2.43 (s, 1H), 1.18 (t, *J* = 7.1 Hz, 3H).

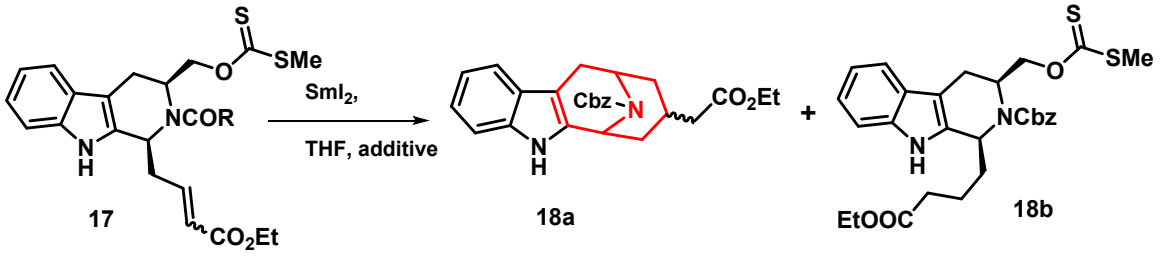
^{13}C NMR (100 MHz, DMSO-d_6) of *trans* isomer (mixture of rotamers): δ 214.73, 165.21, 155.35, 144.82, 136.37, 131.15, 128.39, 127.89, 127.37, 126.20, 122.98, 121.44, 118.75, 111.24, 104.18, 79.15, 73.68, 67.23, 66.85, 59.71, 49.83, 47.70, 21.4, 18.13, 14.10.

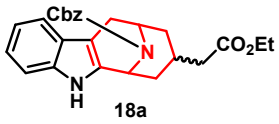
IR ν_{max} (neat, cm^{-1}) of *trans* isomer (mixture of rotamers): 3344.39, 3053.65, 2920.95, 2851.58, 1697.70, 1451.76, 1413.69, 1324.92, 1269.64, 1206.95, 1149.43, 1071.38, 970.43, 851.51, 746.01, 694.95.

HRMS (ESI) of *trans* isomer (mixture of rotamers): calculated for $C_{28}H_{30}N_2O_5S_2Na$: 561.1494 ([M + Na]$^+$), found 561.1494.

Optical rotation $[\alpha]_D^{22}$ of *trans* isomer (mixture of rotamers): +84.5 (c 0.48, $CHCl_3$).

<u>SmI_2-mediated radical cyclization of 17</u>: Followed the same procedure for the preparation of **16a** and **16b**.



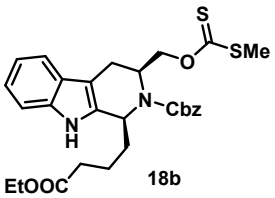


<u>Data</u>: Scale of reaction 80 mg; yield of **18a** 30 mg (48%).

^{1}H NMR (400 MHz, $CDCl_3$) (mixture of rotamers and diastereomers): δ 8.39- 7.88 (s, 1H), 7.48 – 7.45 (m, 1H), 7.40 – 7.31 (m, 6H), 7.20 – 7.15 (m, 1H), 7.13 – 7.10 (m, 1H), 5.40 – 4.92 (m, 4H), 4.26 – 4.10 (m, 2H), 3.72 - 3.51 (m, 2H), 3.0 – 2.81 (m, 2H), 2.77 – 2.67 (m, 1H), 2.48 – 2.27 (m, 1H), 1.93 – 1.75 (m, 3H), 1.32 (t, *J* = 6.5 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) (mixture of rotamers and diastereomers): δ 166.4, 156.2, 155.8, 145.1, 144.87, 136.47, 128.78, 128.71, 128.40, 126.73, 124.67, 122.48, 122.10, 119.9, 119.7, 118.4, 118.2, 111.2, 68.2, 64.3, 60.8, 52.2, 51.8, 50.7, 50.4, 40.5, 33.4, 29.8, 22.31, 22.03, 14.4.

HRMS (ESI) (mixture of rotamers and diastereomers): calculated for $C_{26}H_{28}N_2O_4Na$: 455.1947 ([M + Na]$^+$), found 455.1943.



18b

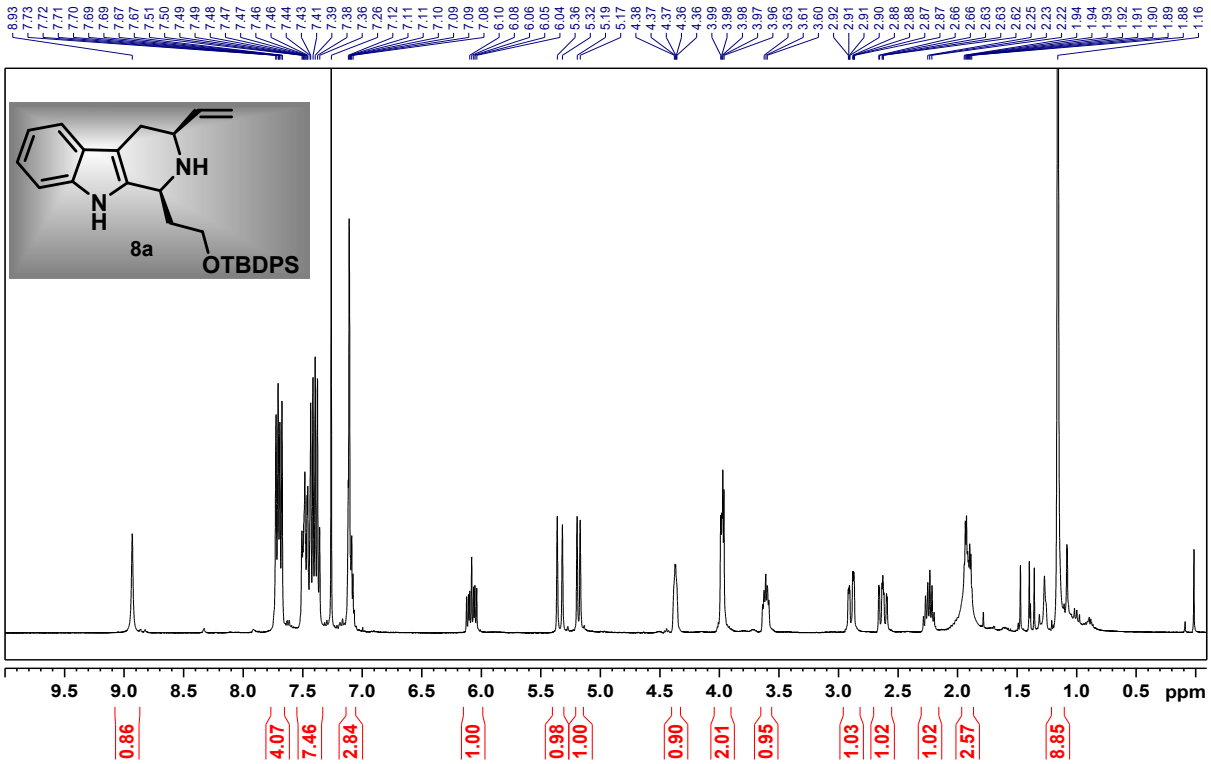
Data: Scale of reaction 80 mg; yield of **18b** 9 mg (12%).

^{1}H NMR (400 MHz, $CDCl_3$) (mixture of rotamers) δ 8.65 – 8.51 (s, 1H), 7.42 (d, *J* = 8.0 Hz, 1H), 7.42– 7.33 (m, 6H), 7.19 (td, *J* = 7.6, 1.0 Hz, 1H), 7.12 (td, *J* = 7.6, 1.0 Hz, 1H), 5.45 – 5.19 (m, 4H), 4.64 – 4.49 (m, 2H), 4.16 (q, *J* = 7.3 Hz, 2H), 3.10 – 3.0 (m, 1H), 2.89 – 2.82 (m, 1H), 2.50 (s, 3H), 2.43 – 2.29 (m, 2H), 2.00 – 1.84 (m, 4H), 1.27 (t, *J* = 7.3 Hz, 3H).

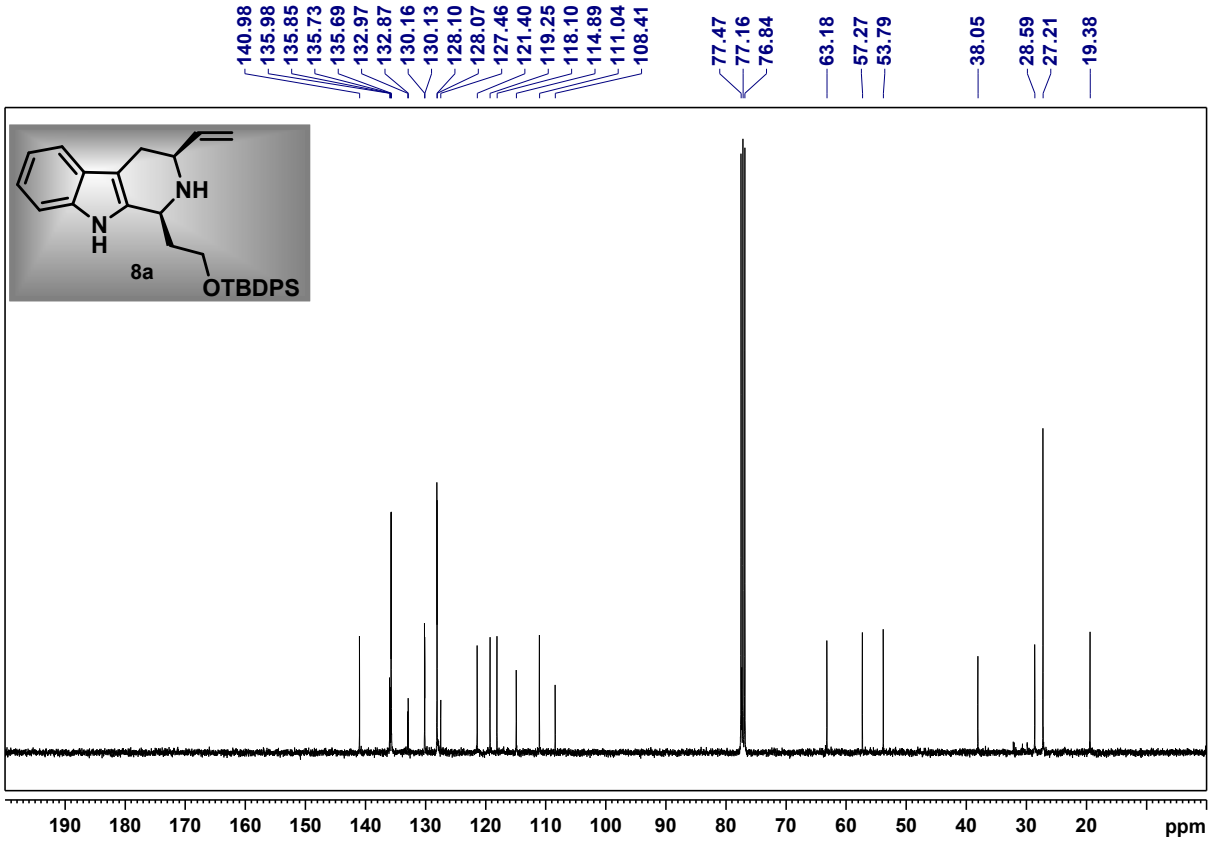
HRMS (ESI) (mixture of rotamers): calculated for $C_{28}H_{32}N_2O_5S_2Na$: 563.1650 ($[M + Na]^+$), found 563.1655.

Spectra (^{1}H and ^{13}C NMR) of Compounds

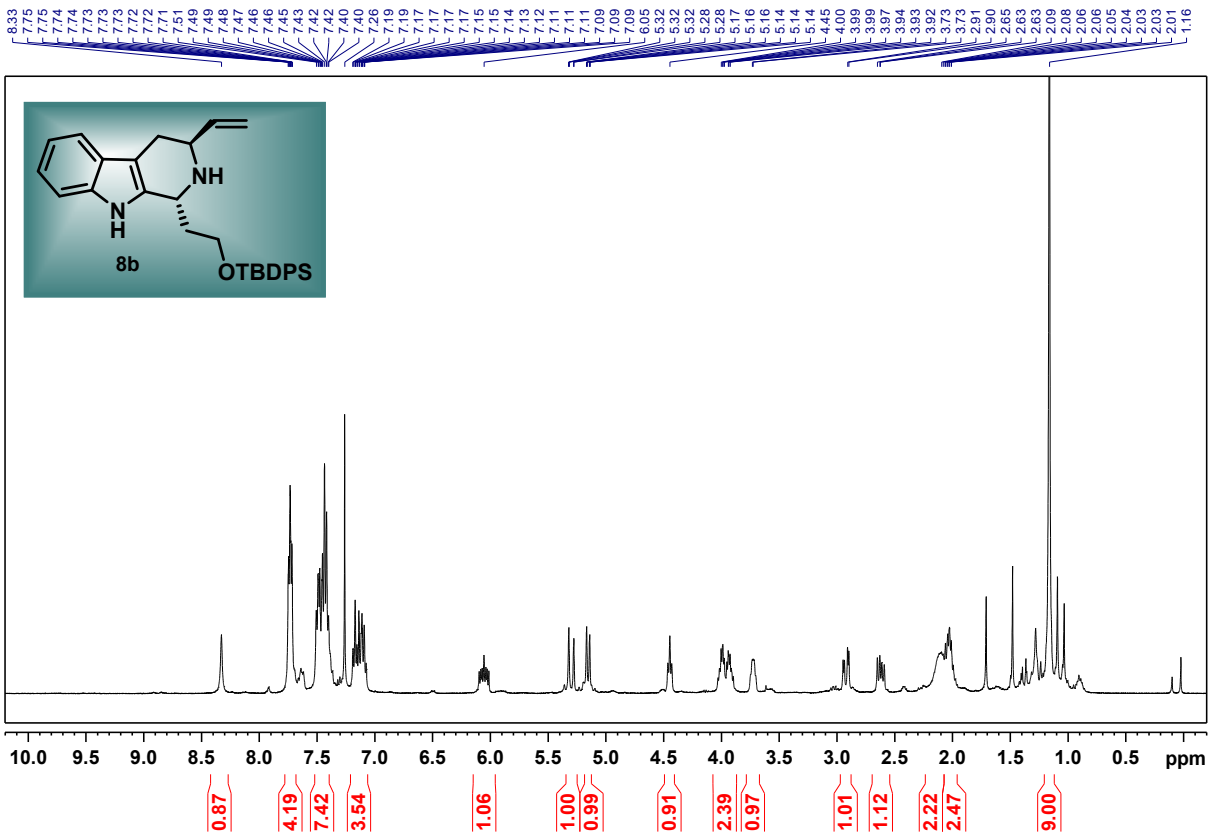
- **^{1}H NMR (400 MHz, $CDCl_3$) of 8a**



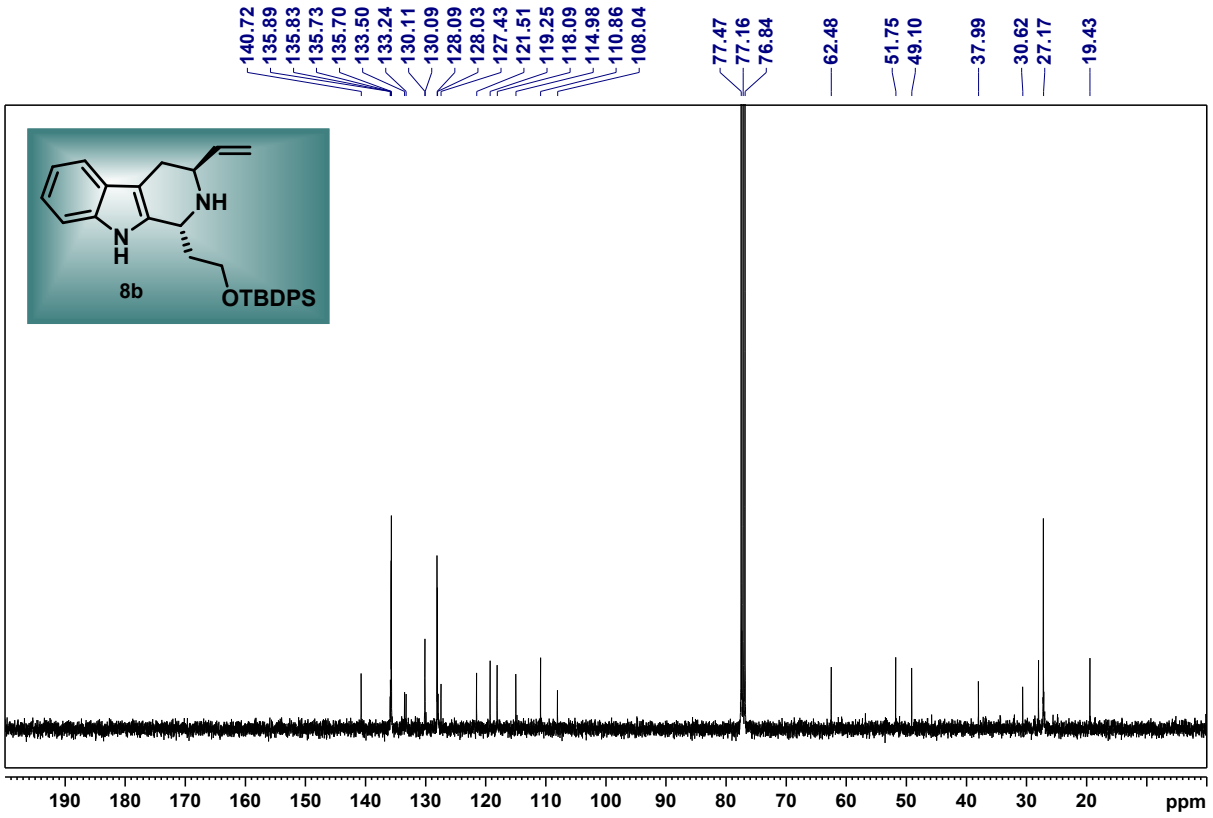
- **^{13}C NMR (100 MHz, $CDCl_3$) of 8a**



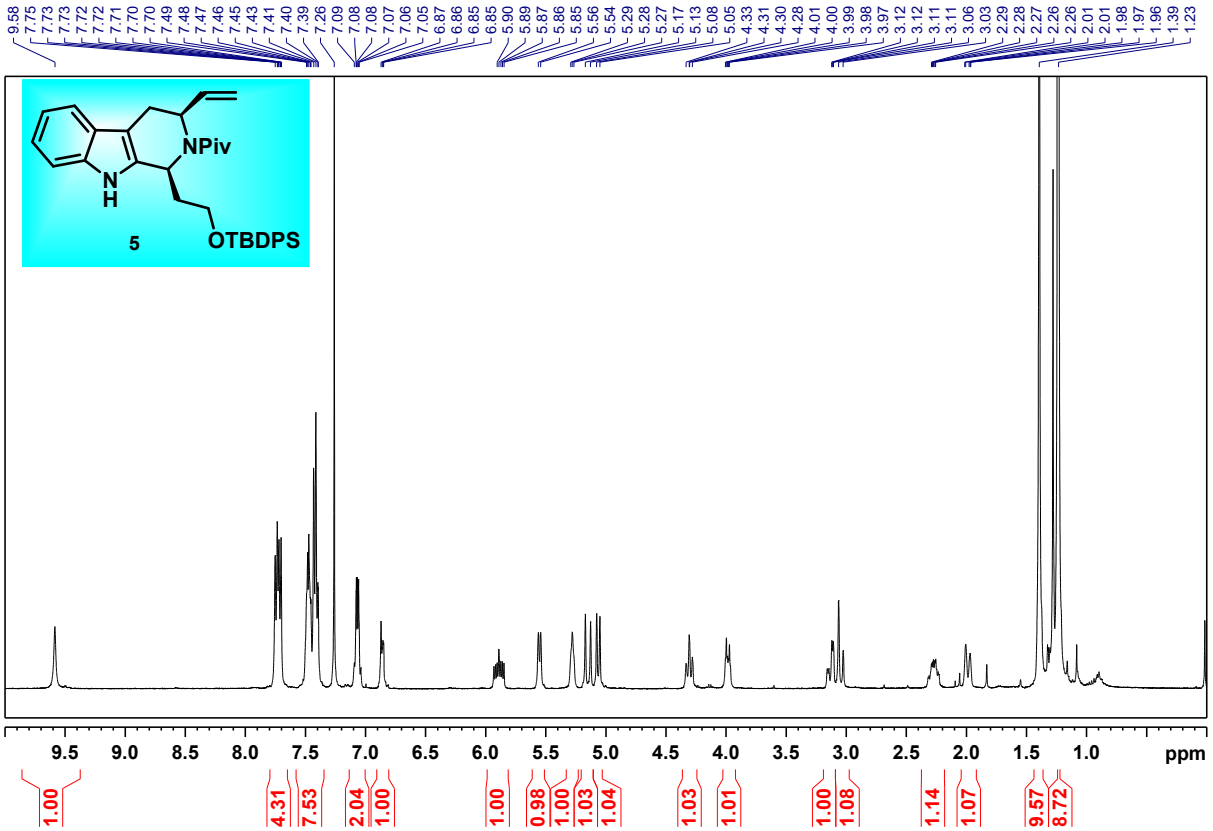
- **^{1}H NMR (400 MHz, $CDCl_3$) of 8b**



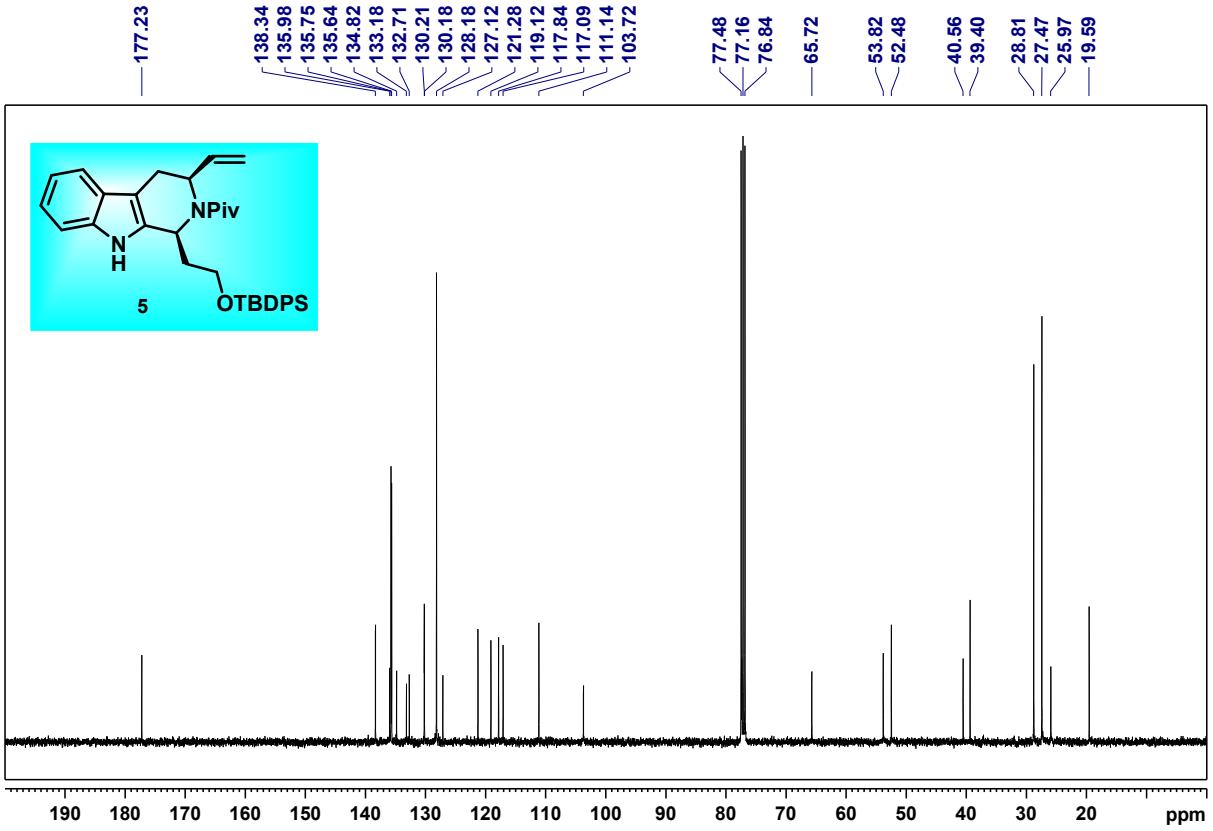
- **^{13}C NMR (100 MHz, $CDCl_3$) of 8b**



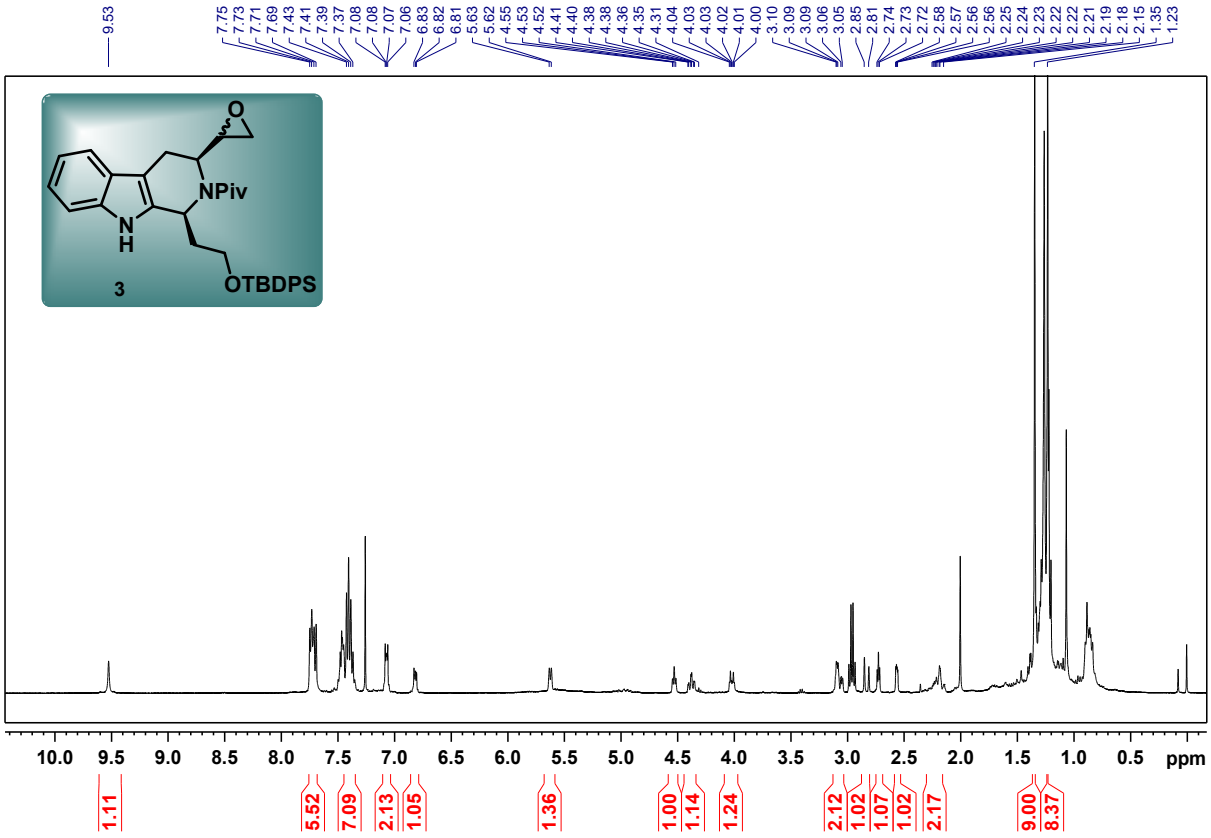
- **^{1}H NMR (400 MHz, $CDCl_3$) of 5**



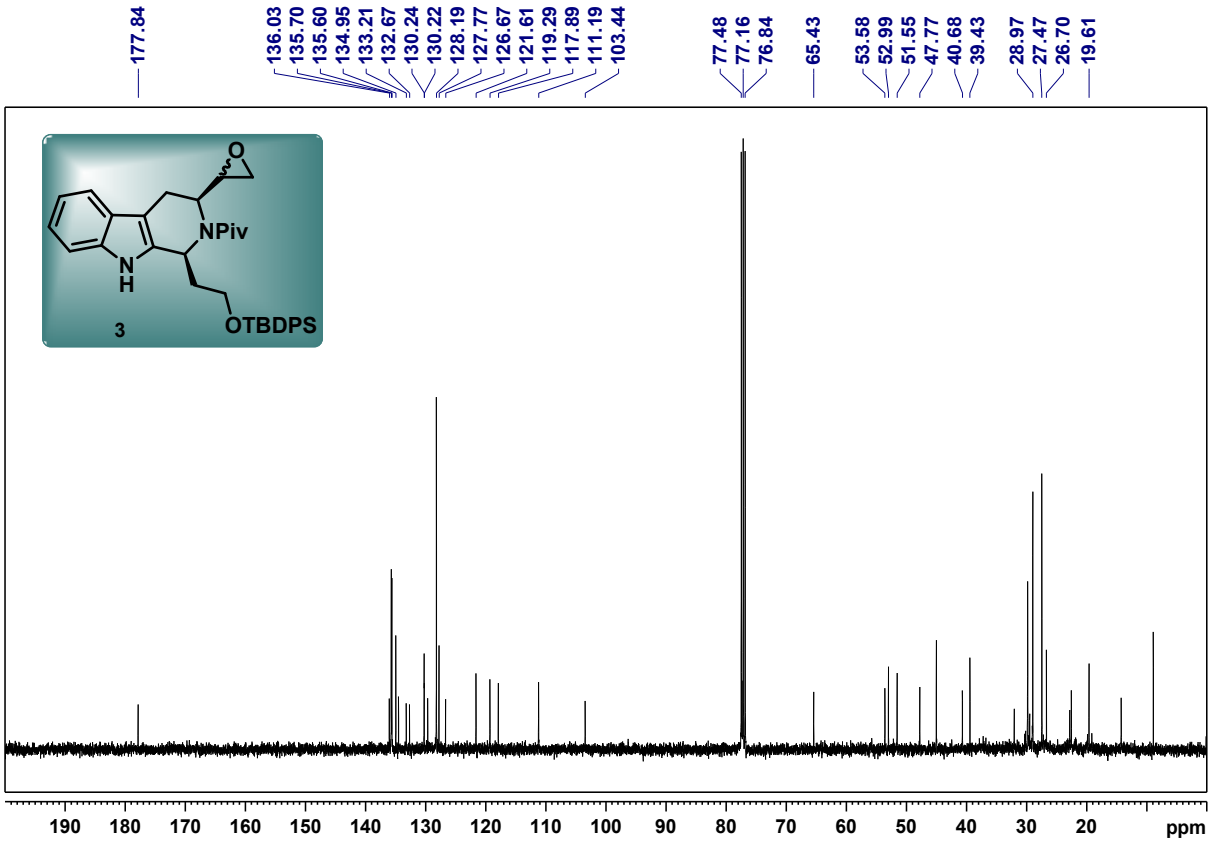
- **^{13}C NMR (100 MHz, $CDCl_3$) of 5**



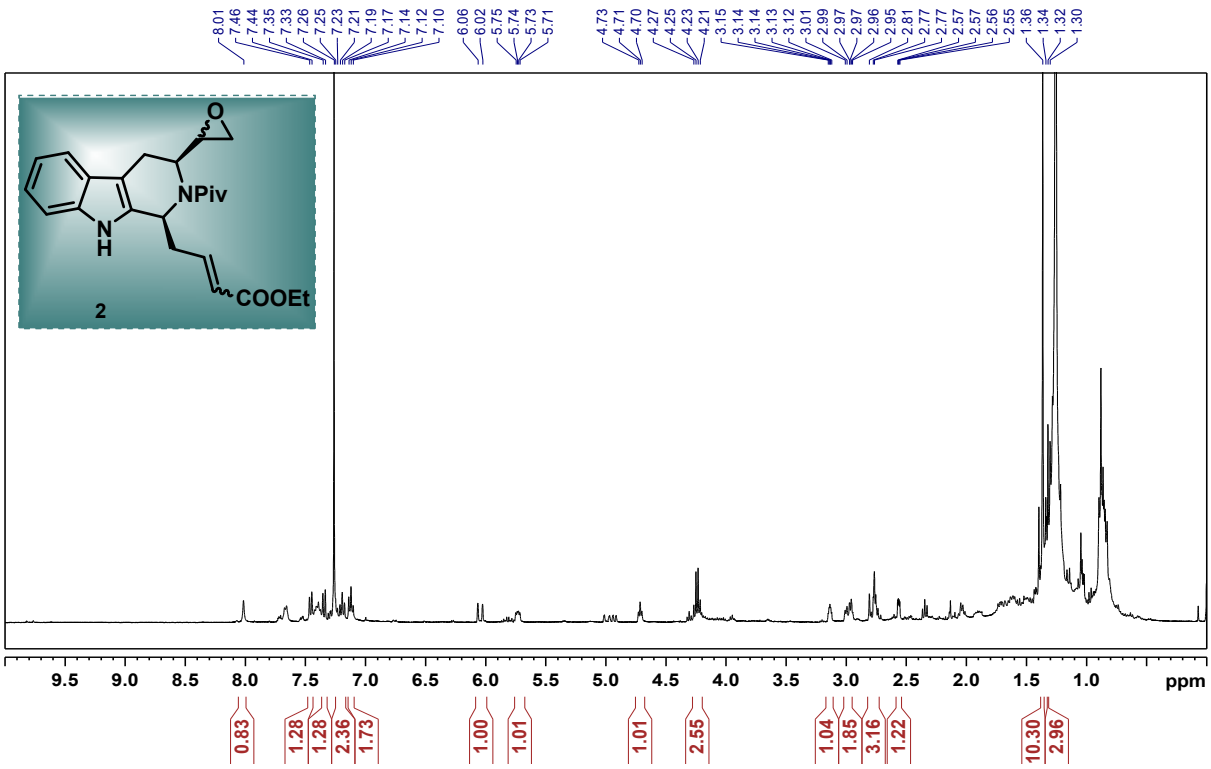
- **^{1}H NMR (400 MHz, $CDCl_3$) of 3**



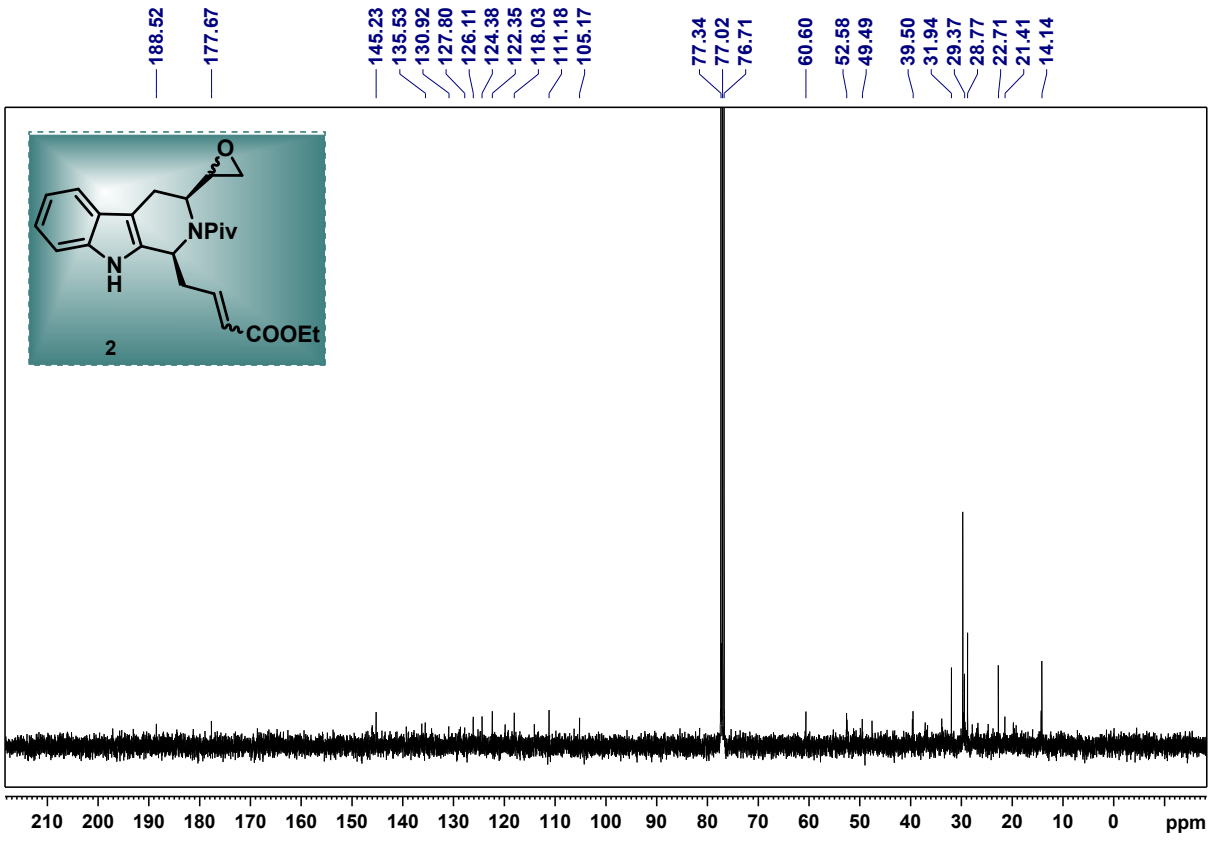
- **^{13}C NMR (100 MHz, $CDCl_3$) of 3**



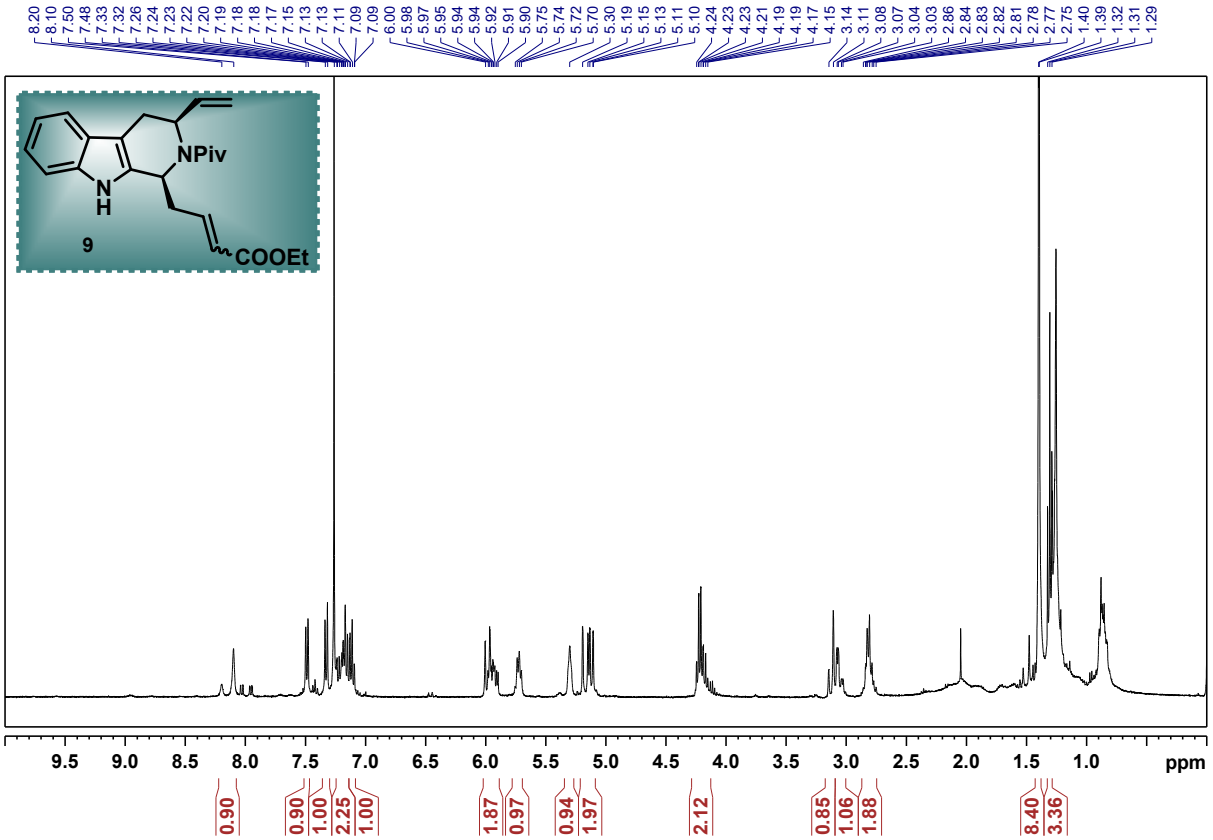
- **^{1}H NMR (400 MHz, $CDCl_3$) of 2**



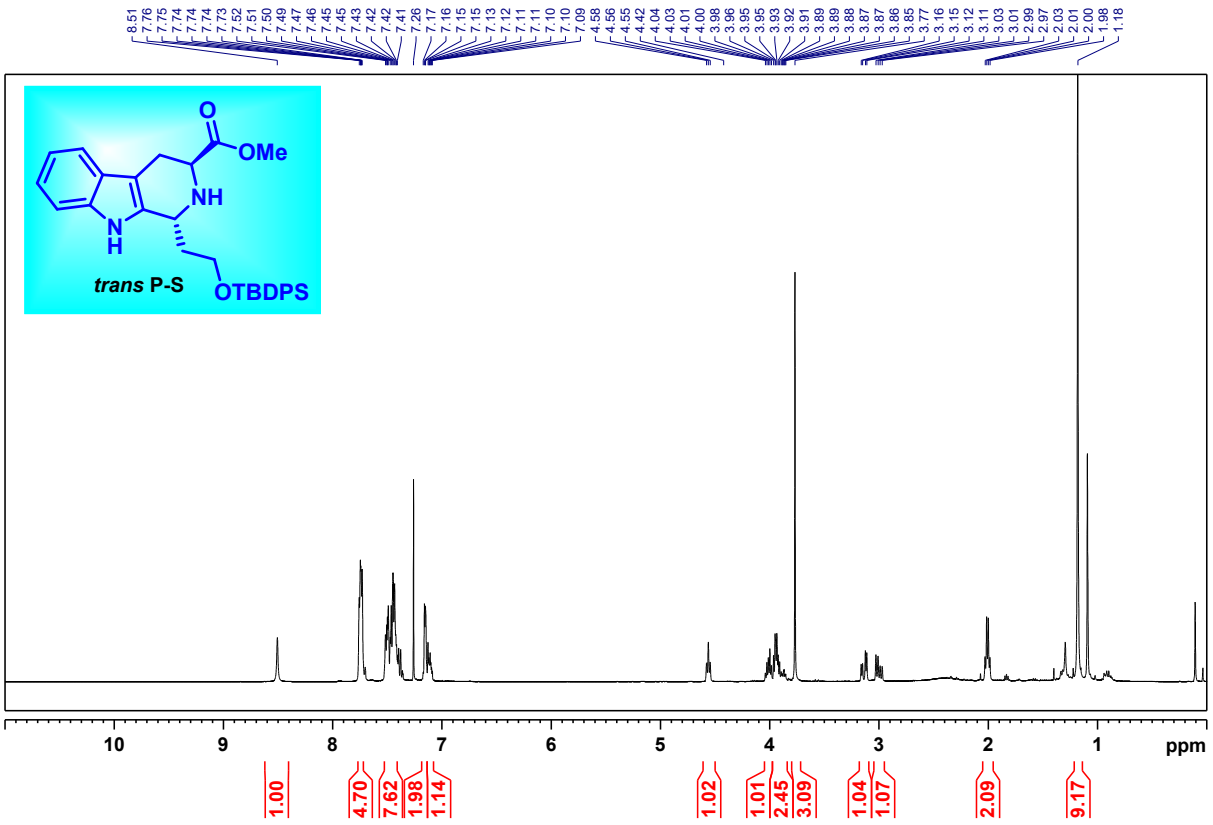
- **^{13}C NMR (100 MHz, $CDCl_3$) of 2**



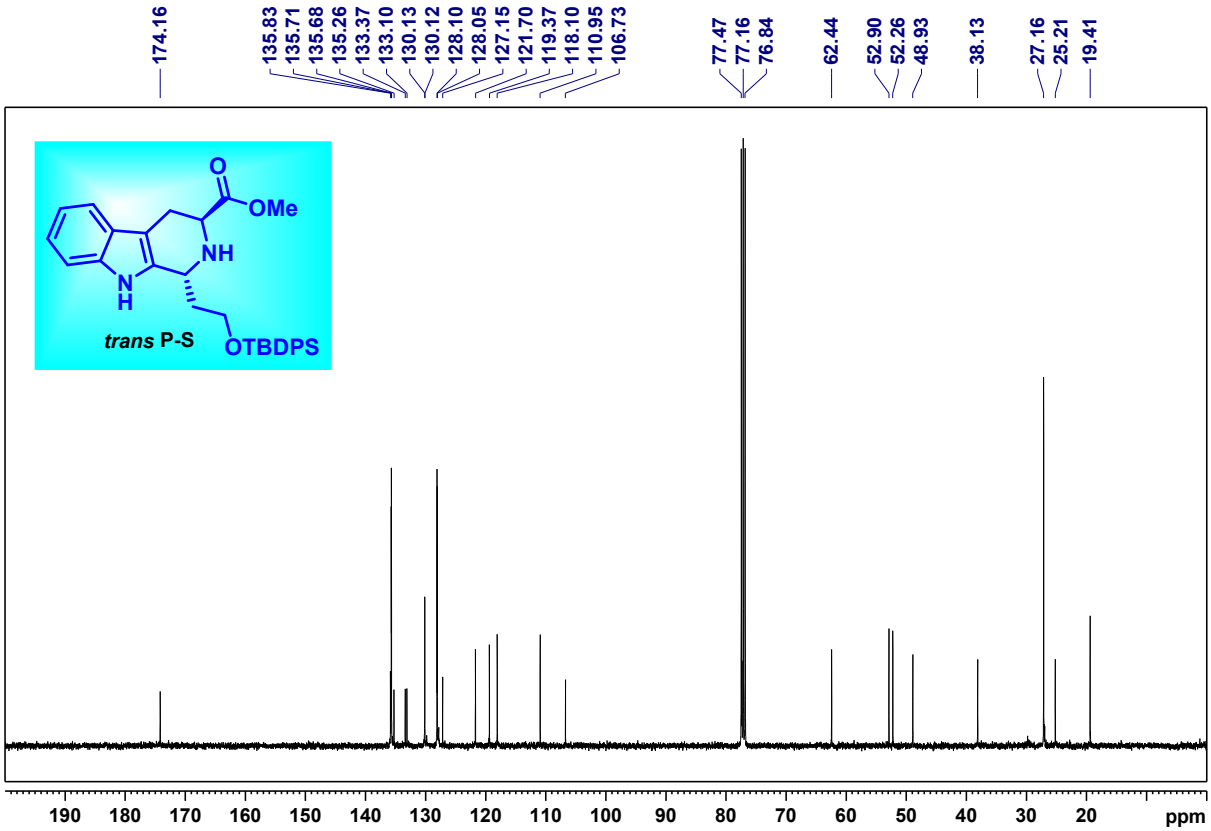
- **^{1}H NMR (400 MHz, $CDCl_3$) of 9**



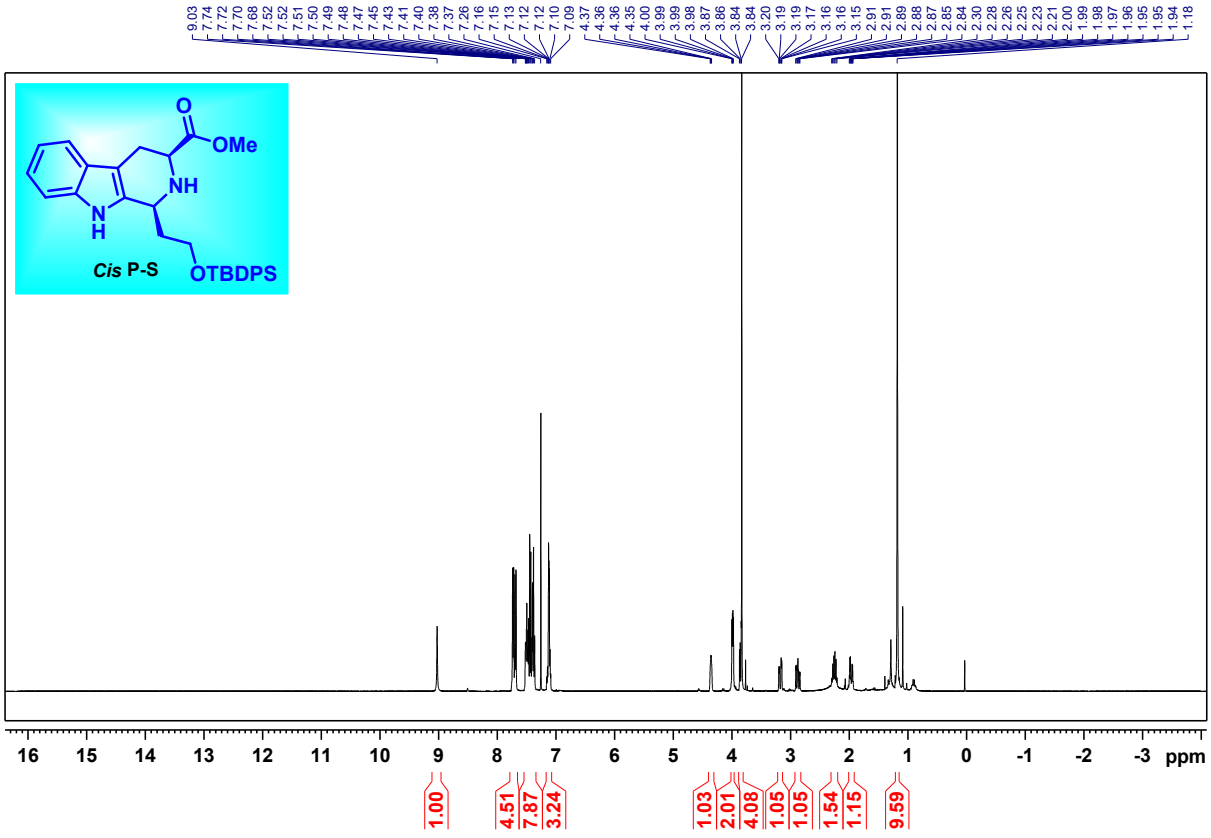
- **^{1}H NMR (400 MHz, $CDCl_3$) of *trans* P-S Product**



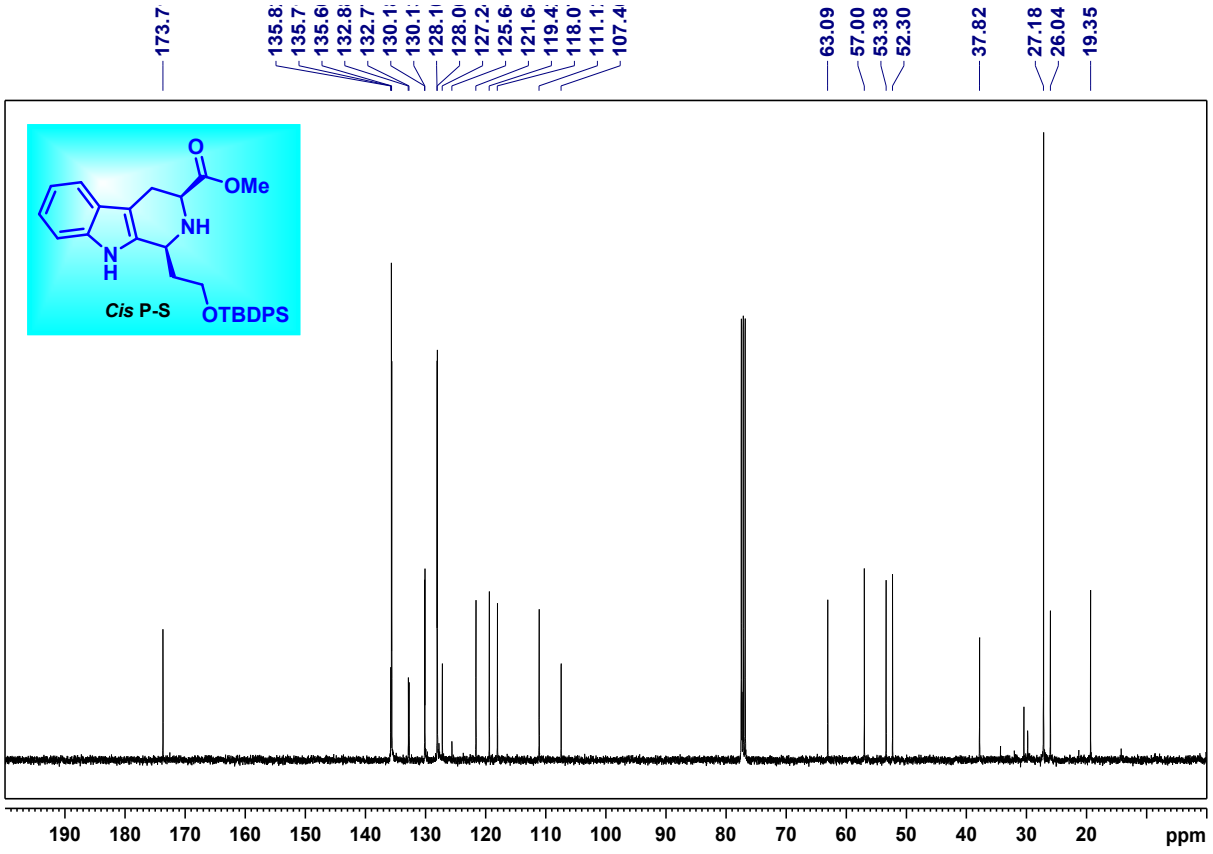
- **^{13}C NMR (100 MHz, $CDCl_3$) of *trans* P-S Product**



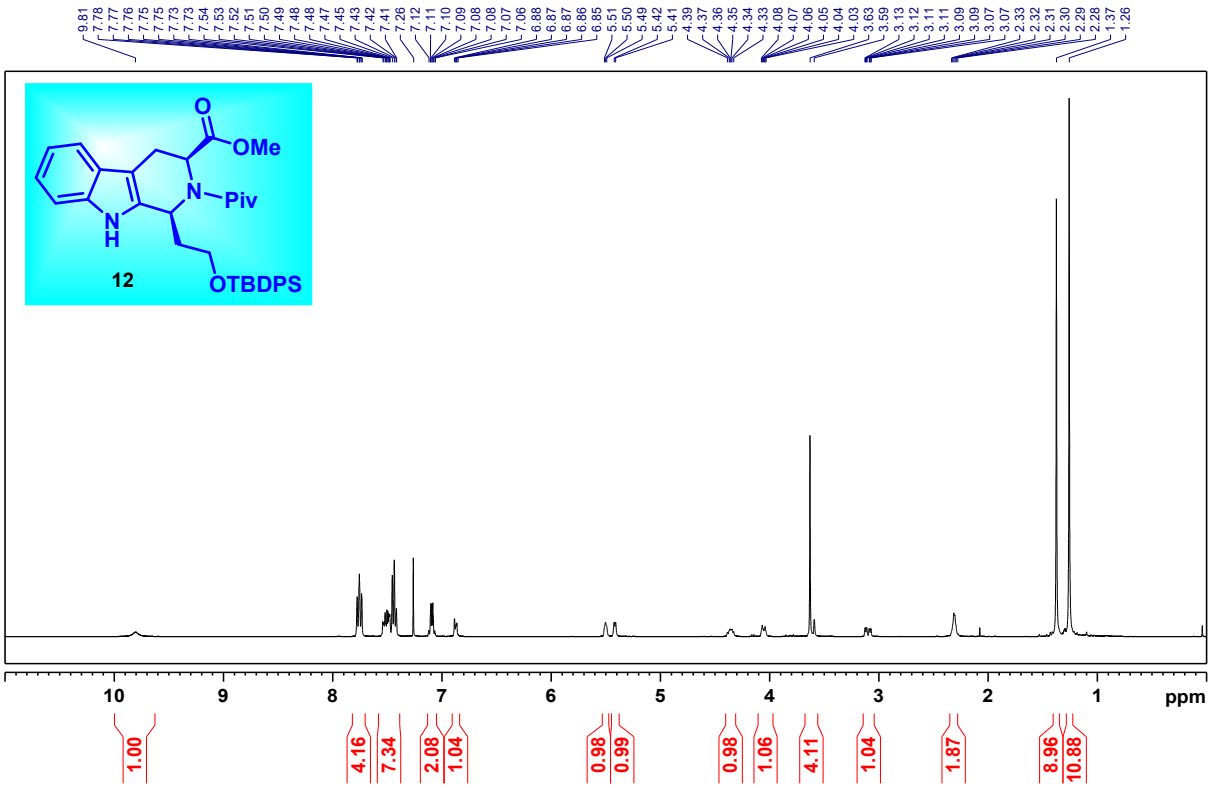
- **^{1}H NMR (400 MHz, $CDCl_3$) of *cis* P-S Product**



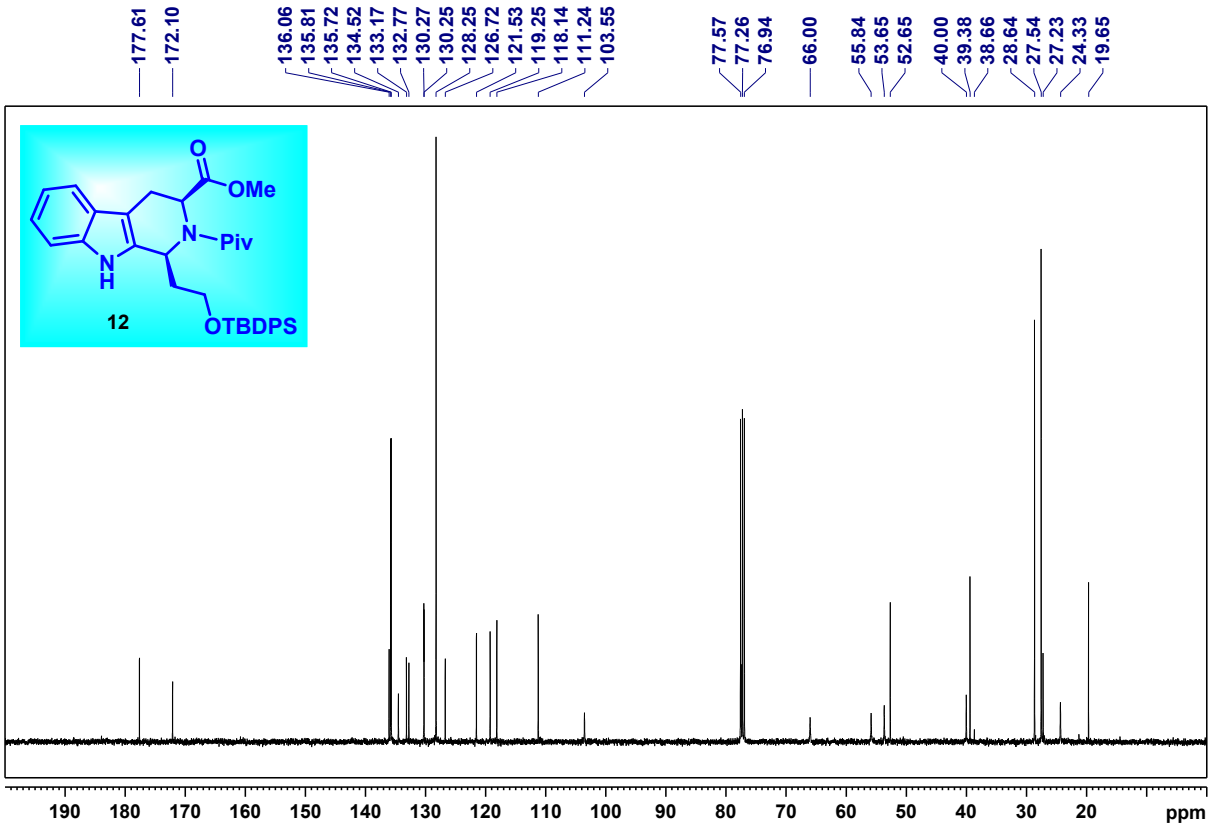
- **^{13}C NMR (100 MHz, $CDCl_3$) of c*is* P-S Product**



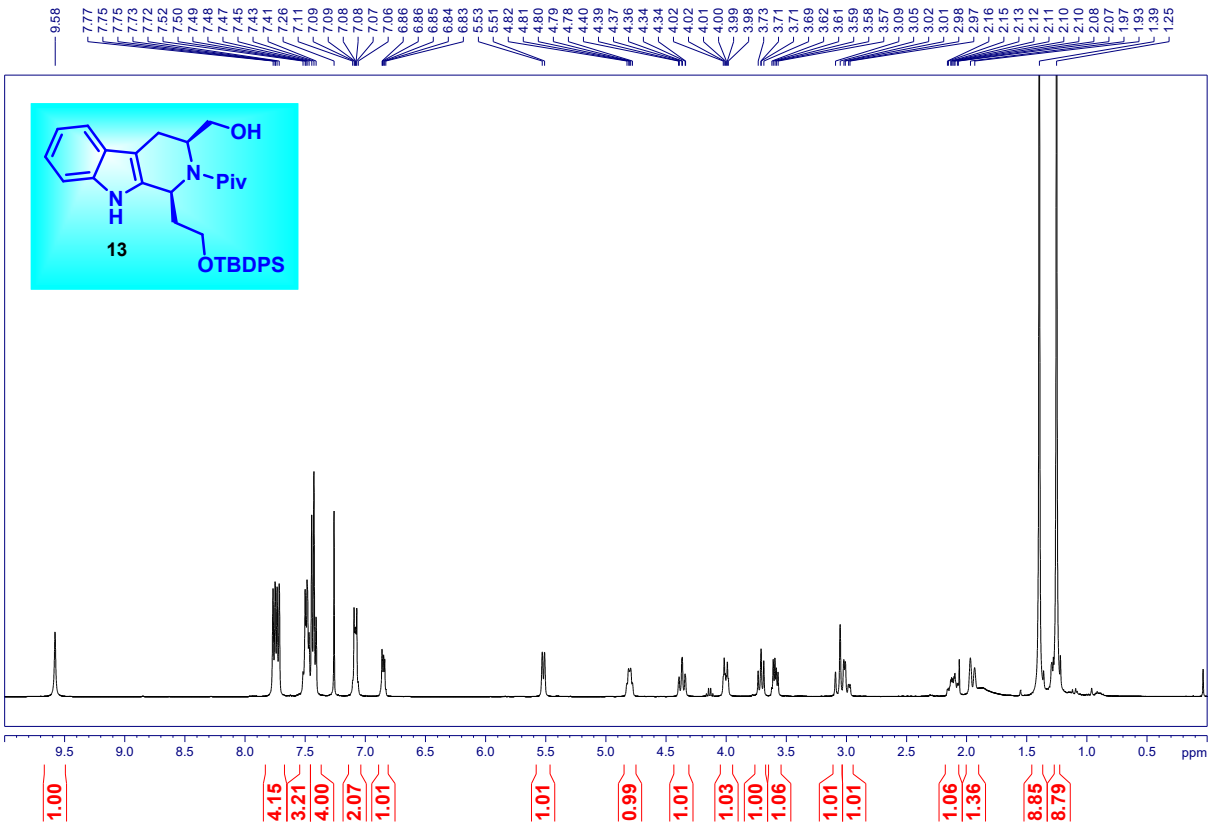
- **^{1}H NMR (400 MHz, $CDCl_3$) of 12**



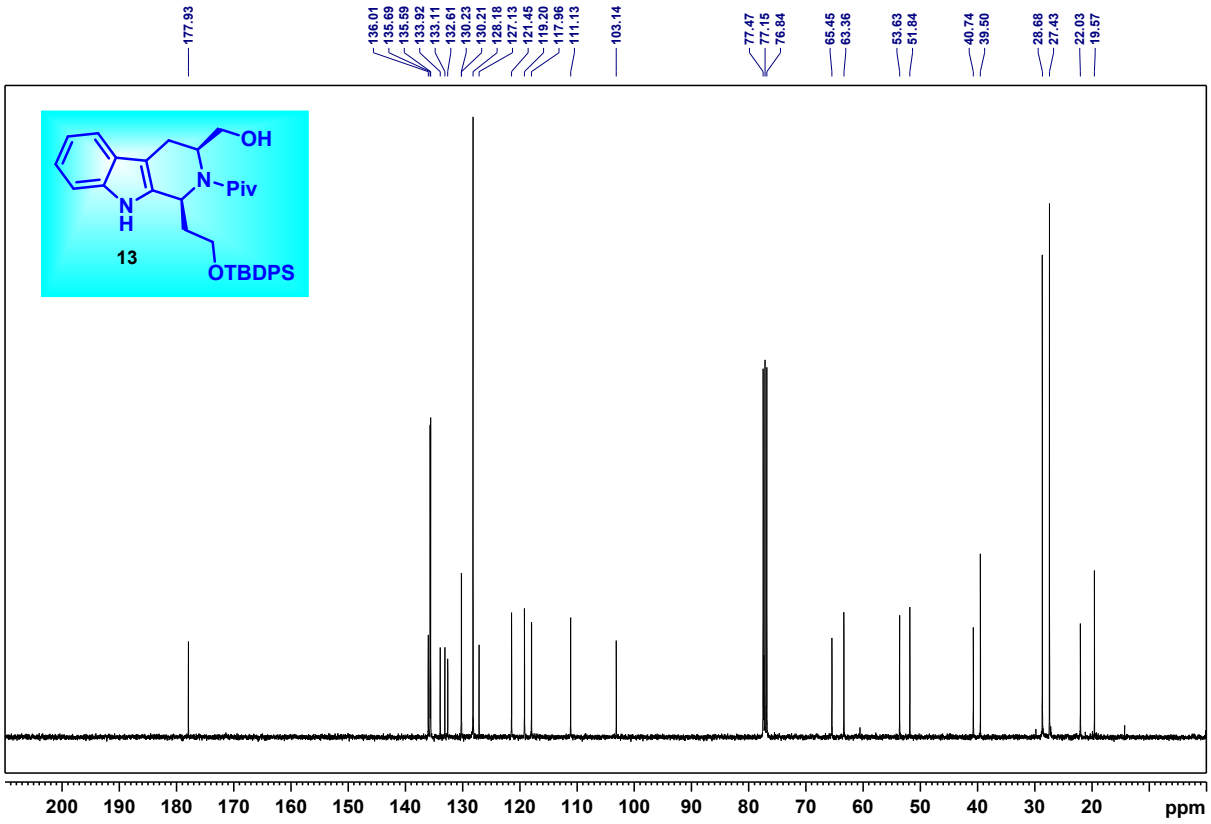
- **^{13}C NMR (100 MHz, $CDCl_3$) of 12**



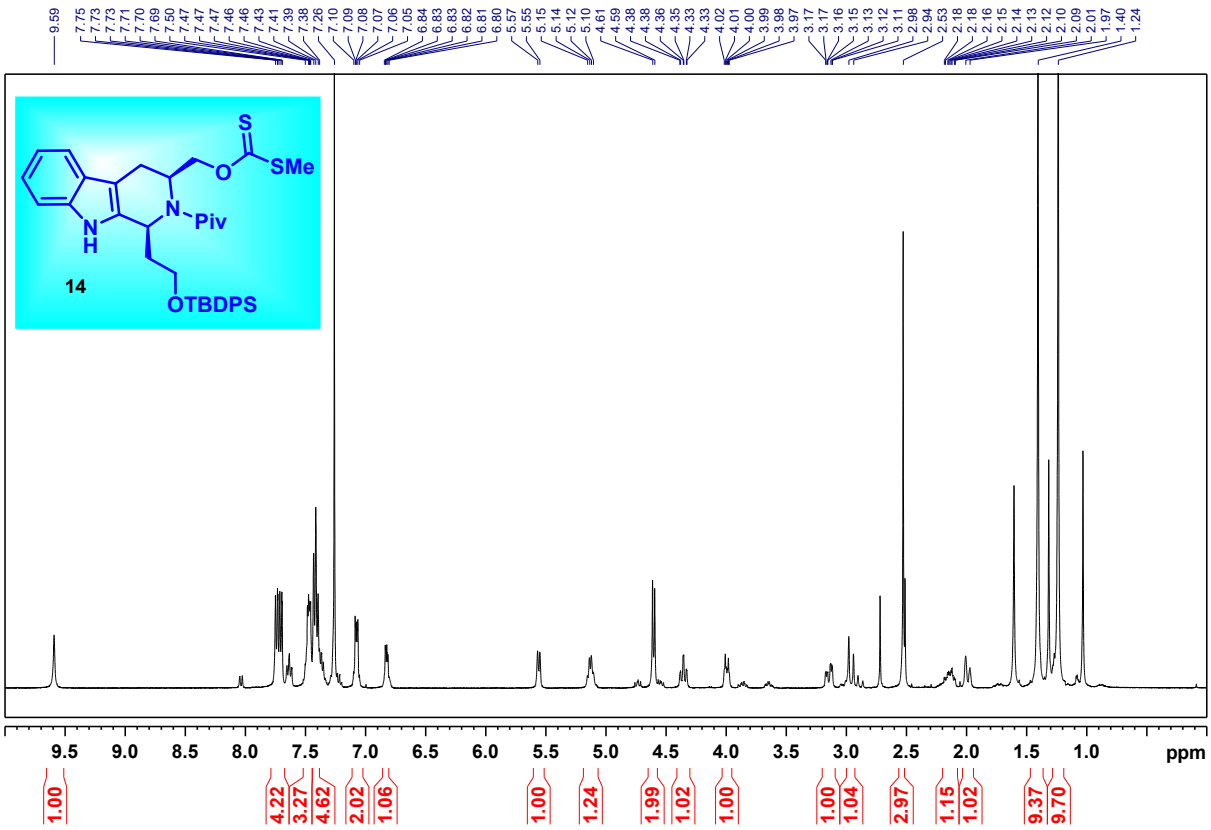
- **^{1}H NMR (400 MHz, $CDCl_3$) of 13**



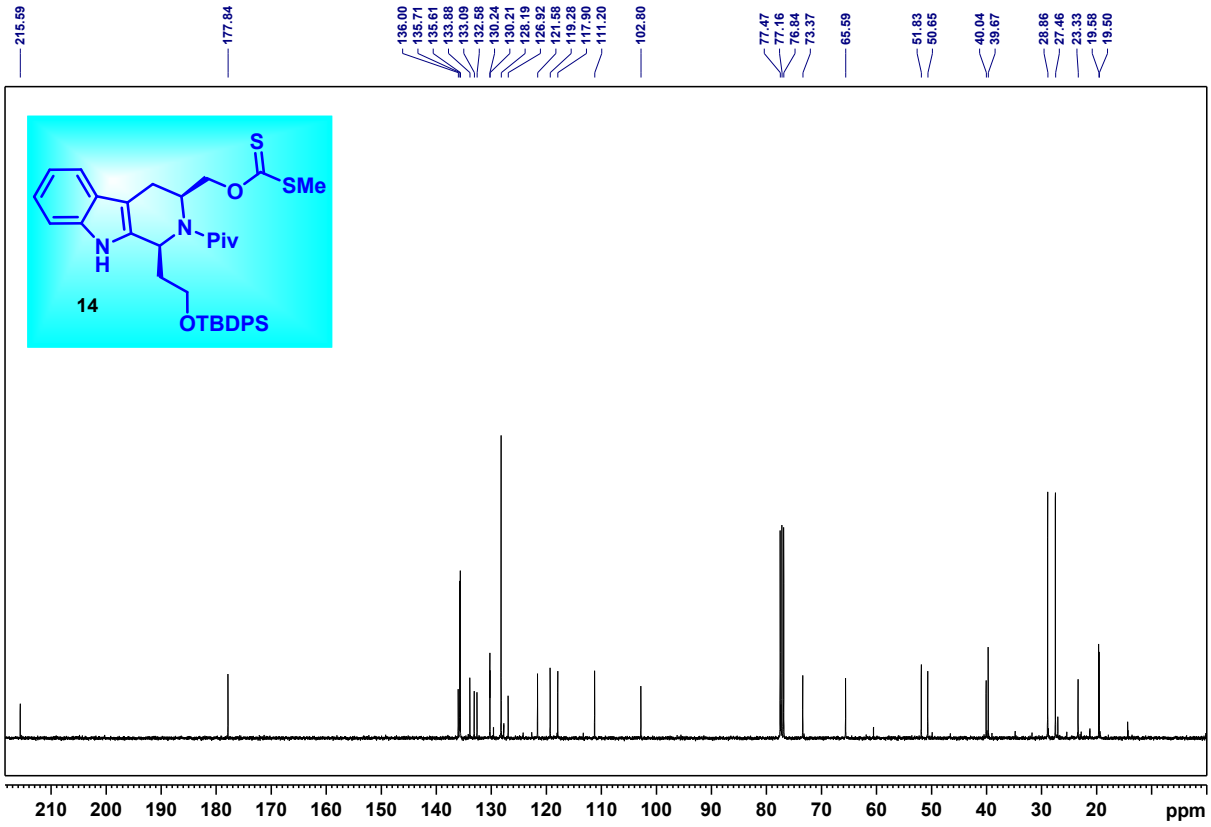
- **^{13}C NMR (100 MHz, $CDCl_3$) of 13**



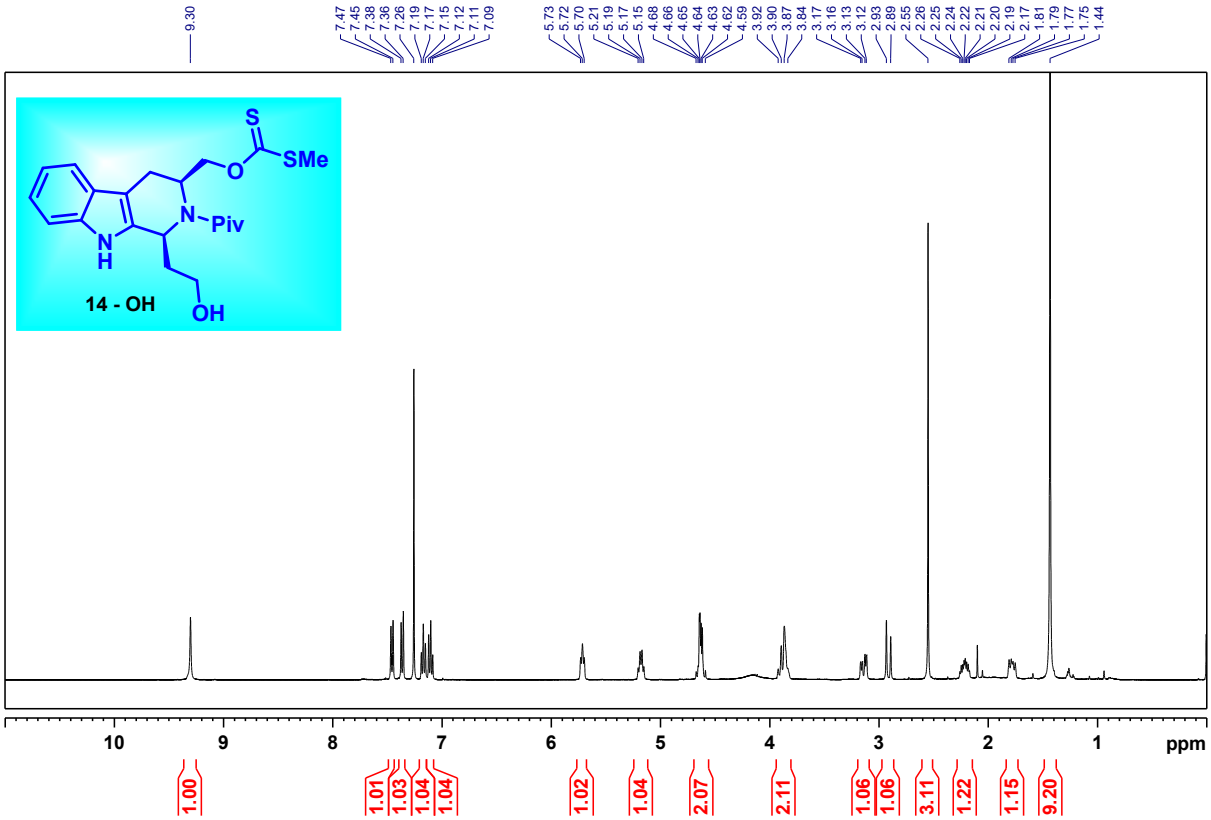
- **^{1}H NMR (400 MHz, $CDCl_3$) of 14**



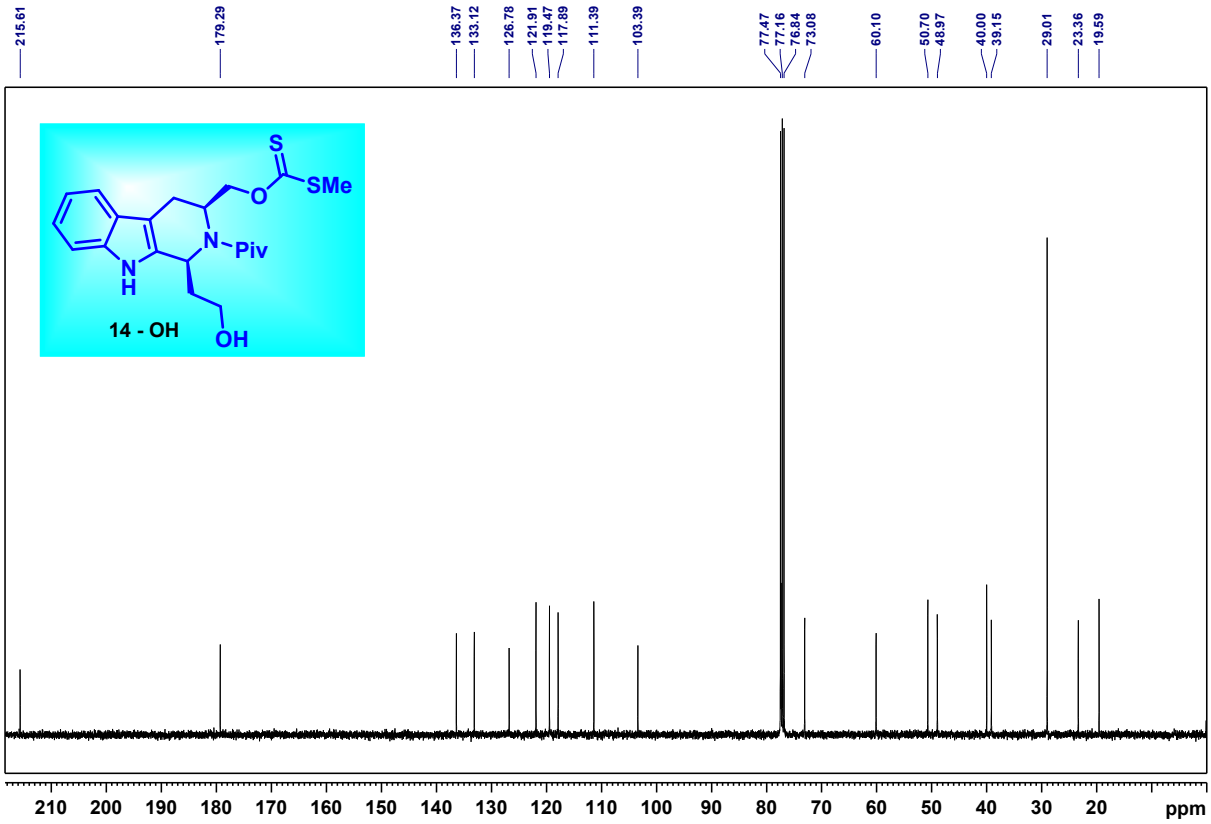
- **^{13}C NMR (100 MHz, $CDCl_3$) of 14**



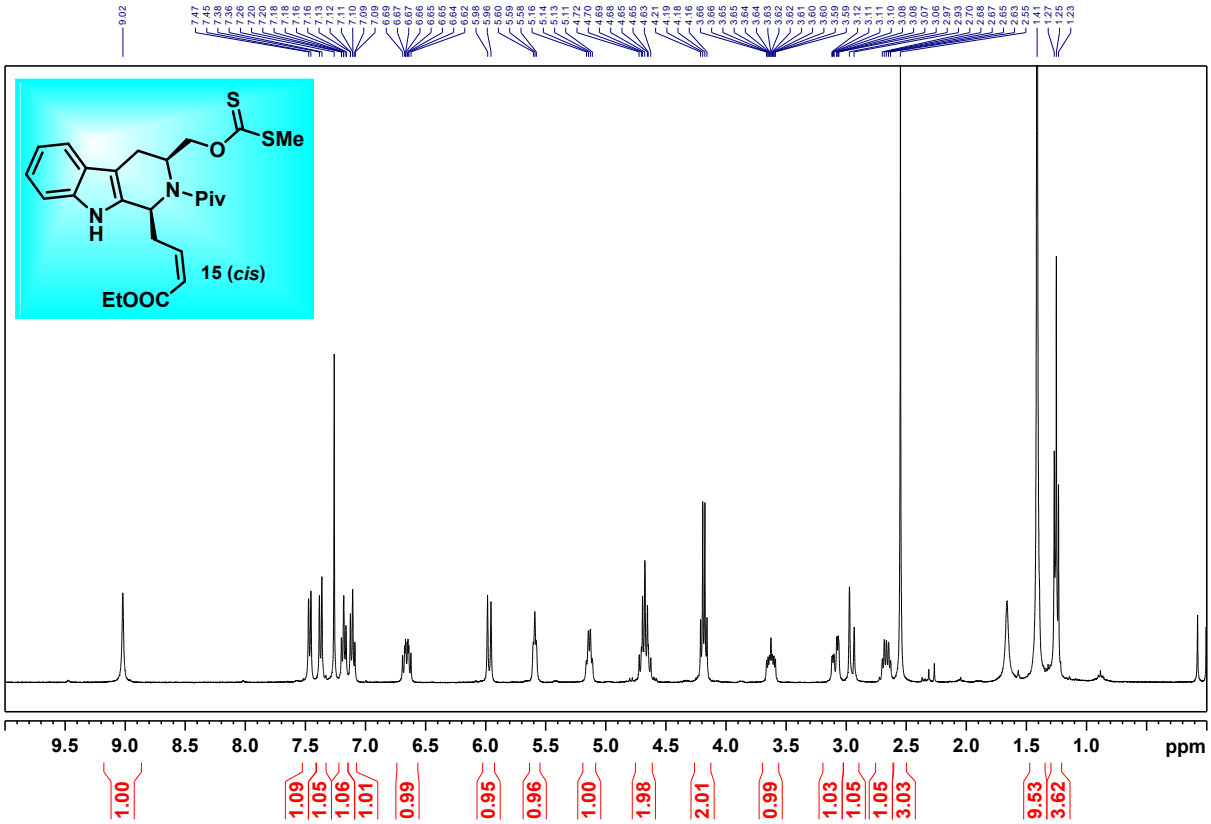
- **^{1}H NMR (400 MHz, $CDCl_3$) of 14-OH intermediate**



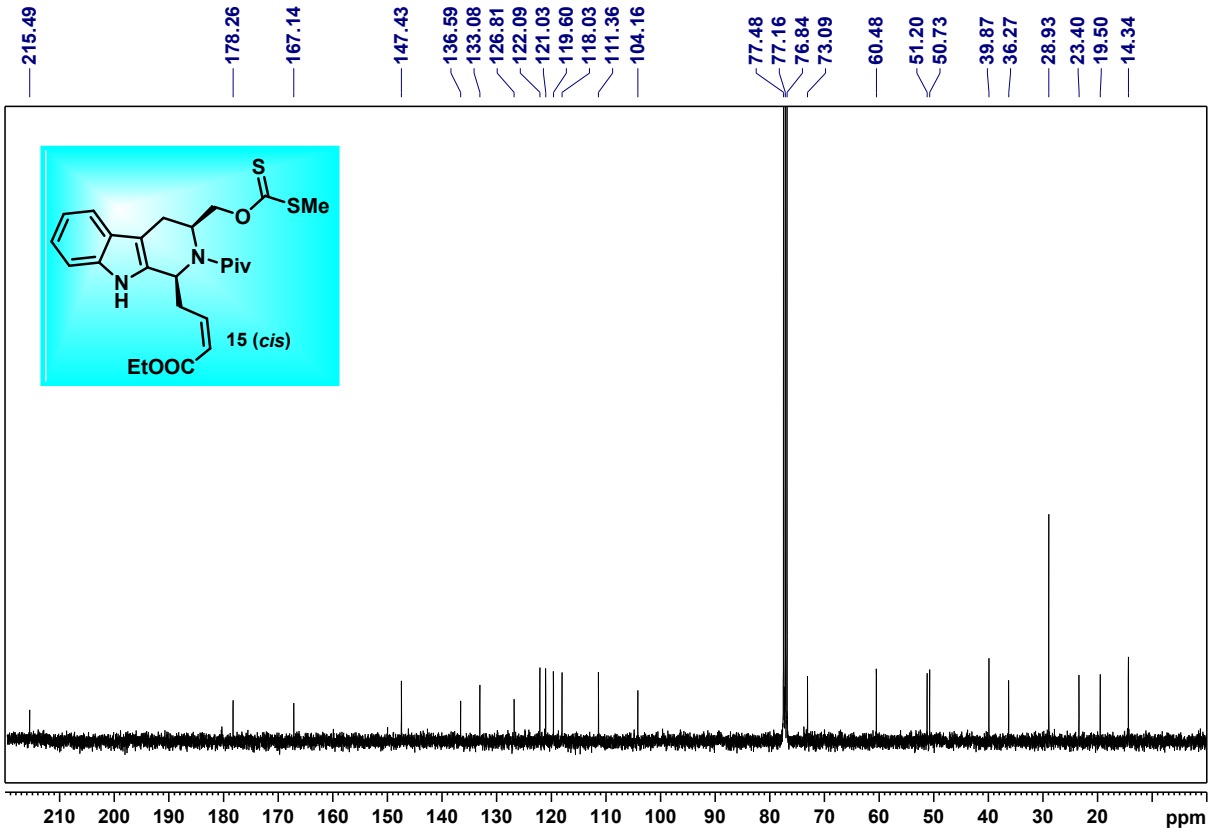
- **^{13}C NMR (100 MHz, $CDCl_3$) of 14-OH intermediate**



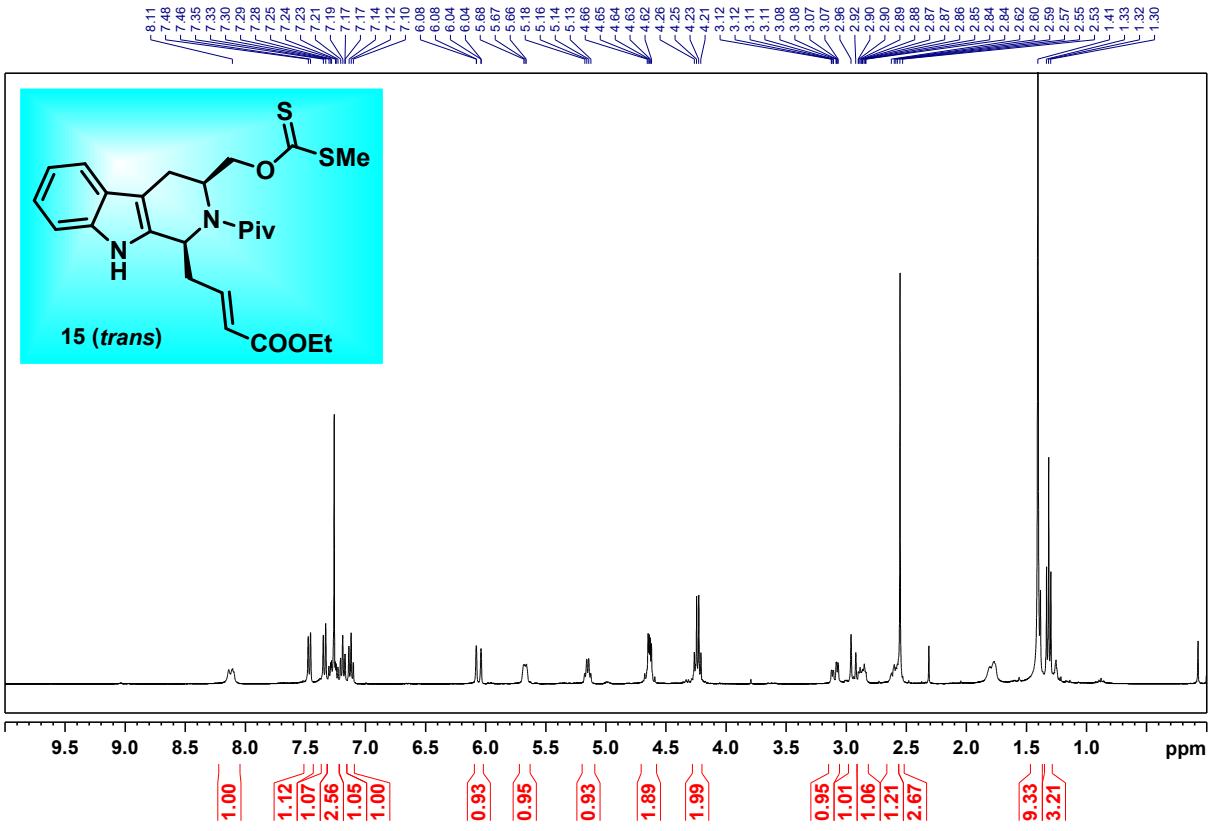
- **^{1}H NMR (400 MHz, $CDCl_3$) of 15 (*cis*)**



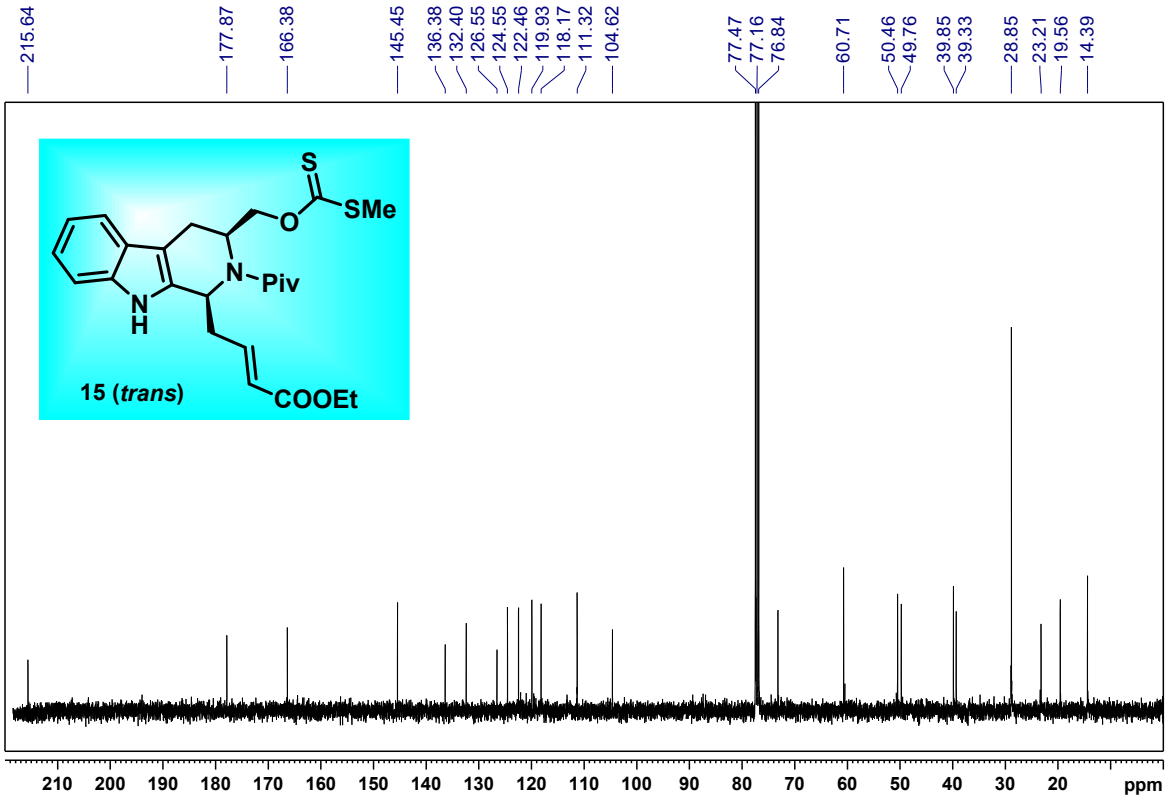
- **^{13}C NMR (100 MHz, $CDCl_3$) of 15 (*cis*)**



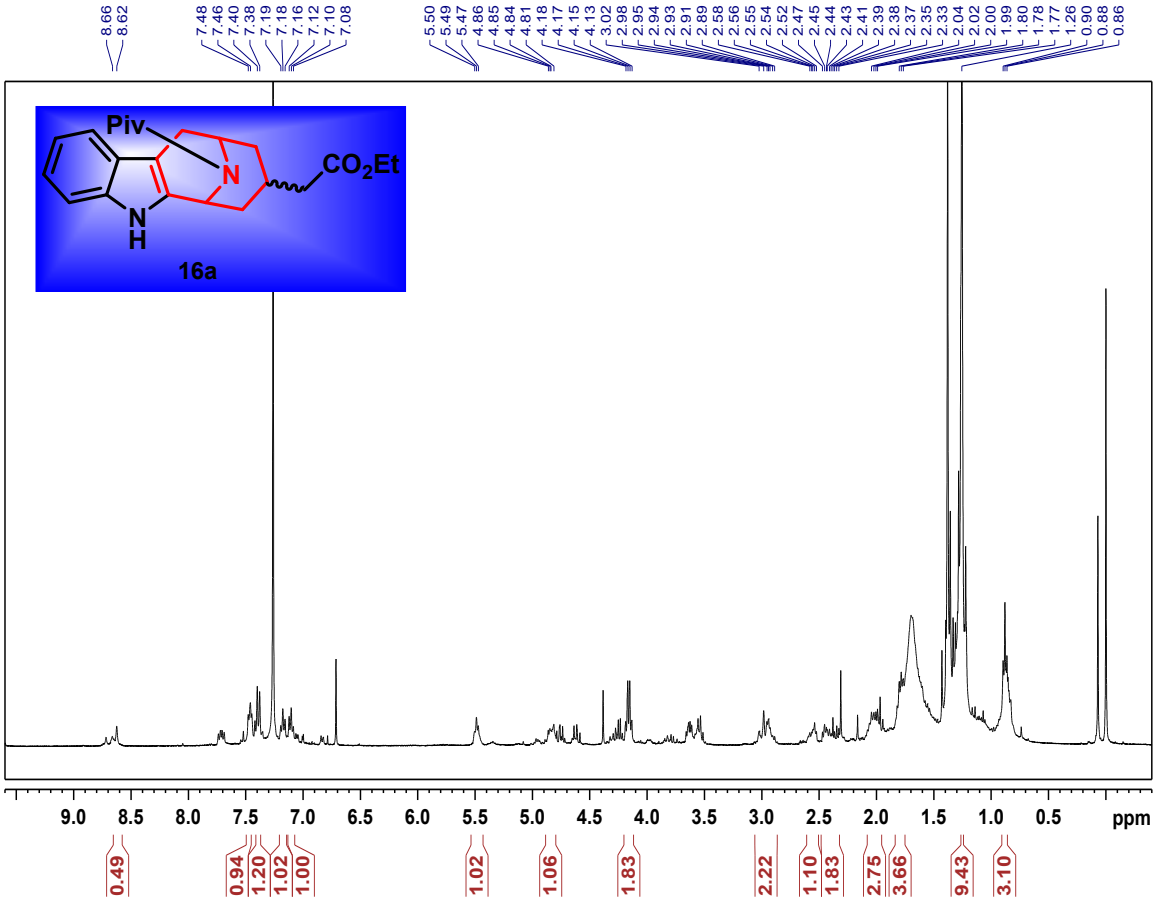
- **^{1}H NMR (400 MHz, $CDCl_3$) of 15 (*trans*)**



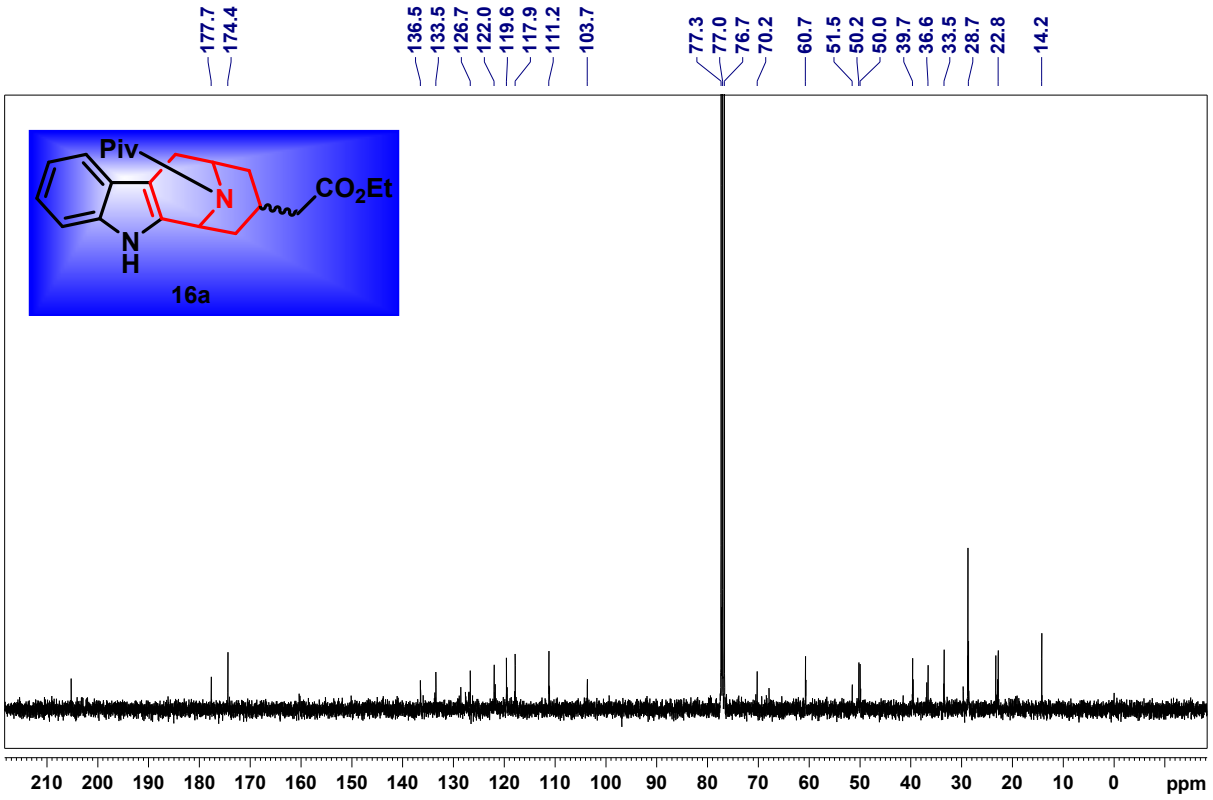
- **^{13}C NMR (100 MHz, $CDCl_3$) of 15 (*trans*)**



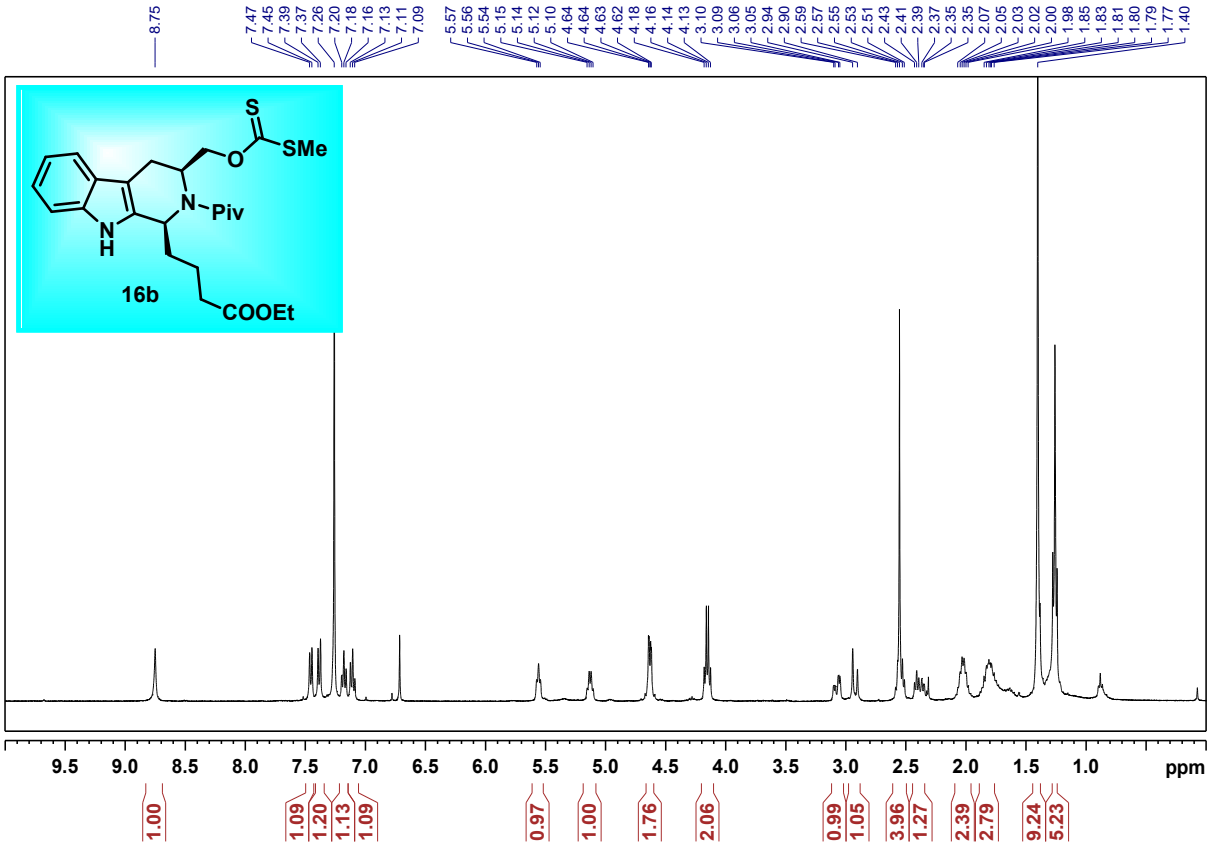
- **^{1}H NMR (400 MHz, $CDCl_3$) of 16a (mixture of rotamers and diastereomers)**



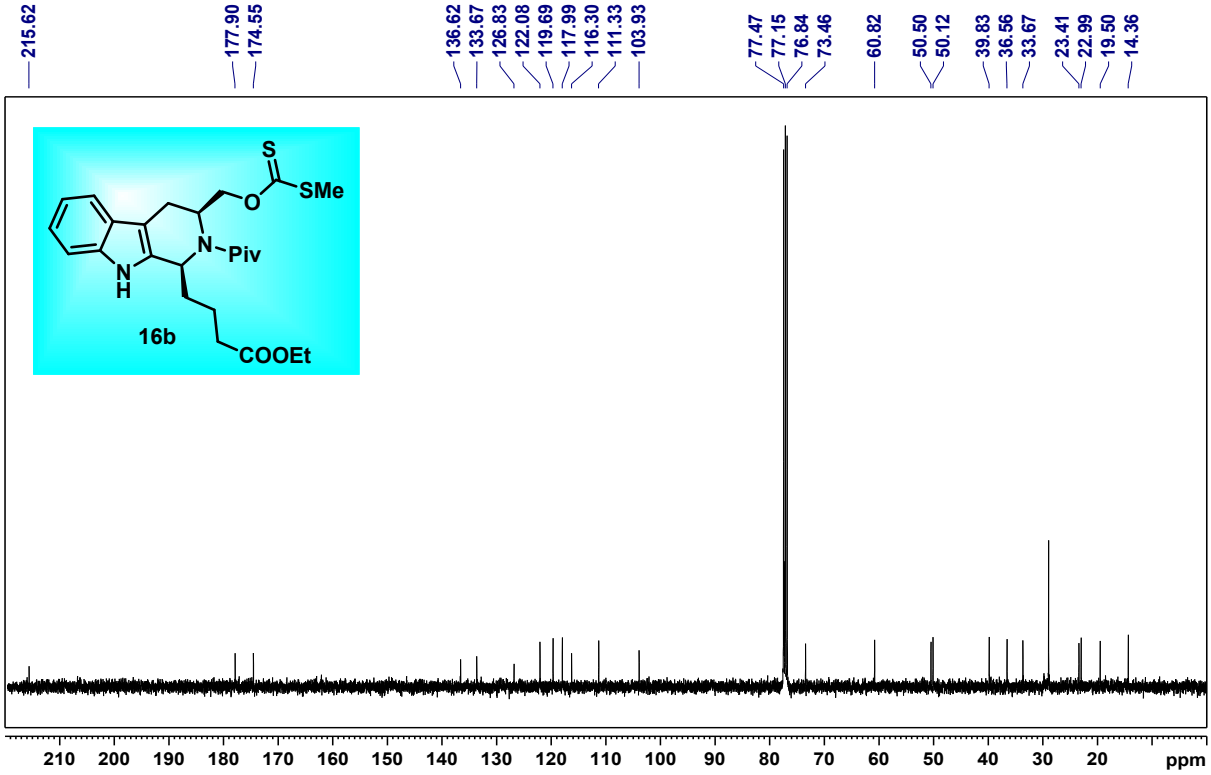
- **^{13}C NMR (100 MHz, $CDCl_3$) of 16a**



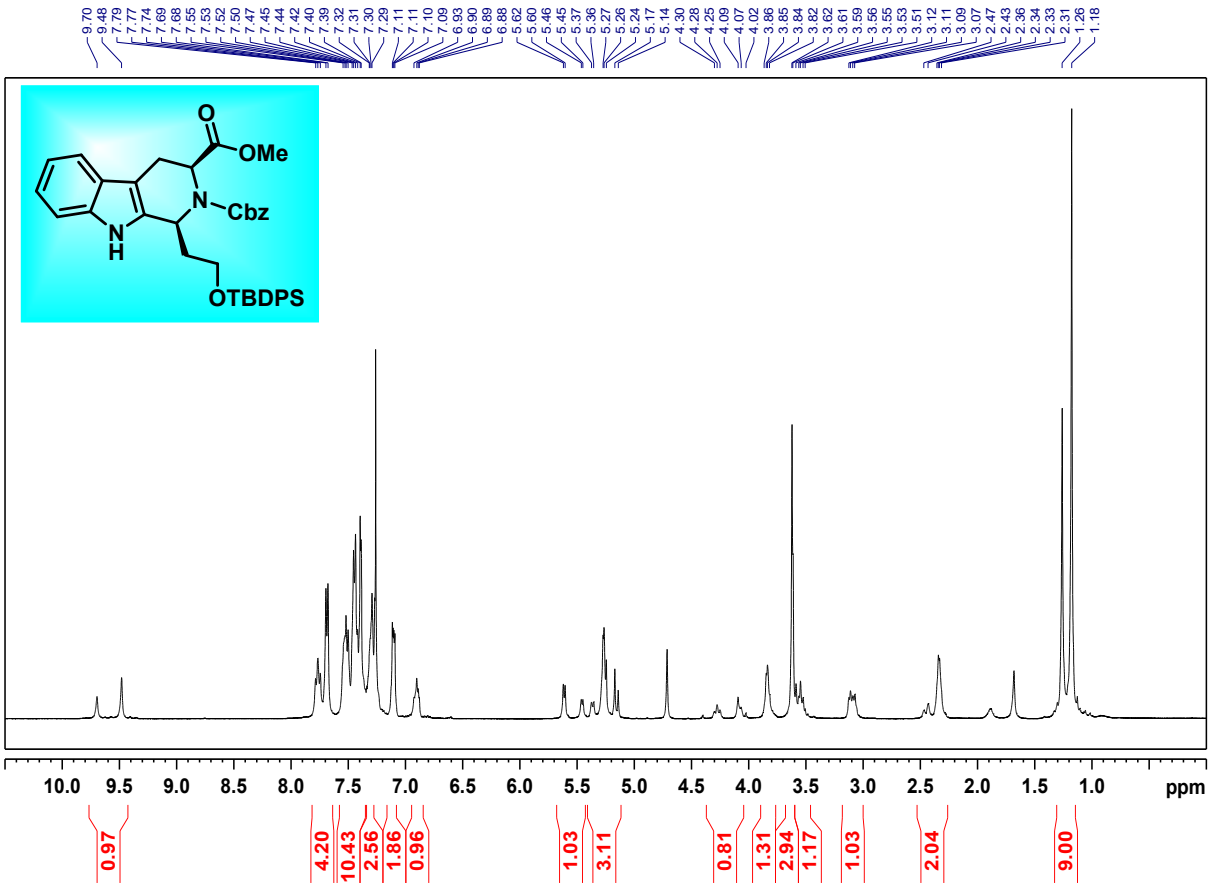
^{1}H NMR (400 MHz, $CDCl_3$) of 16b



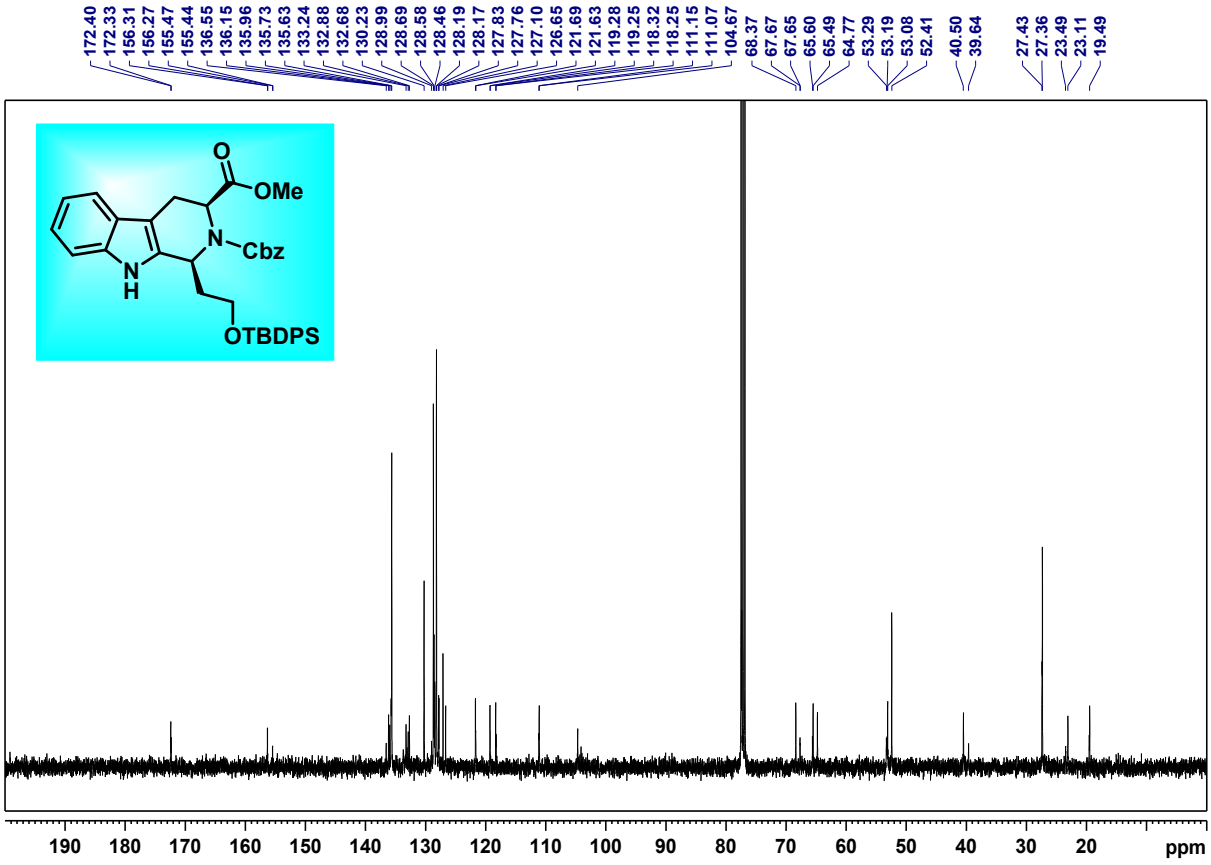
^{13}C NMR (100 MHz, $CDCl_3$) of 16b



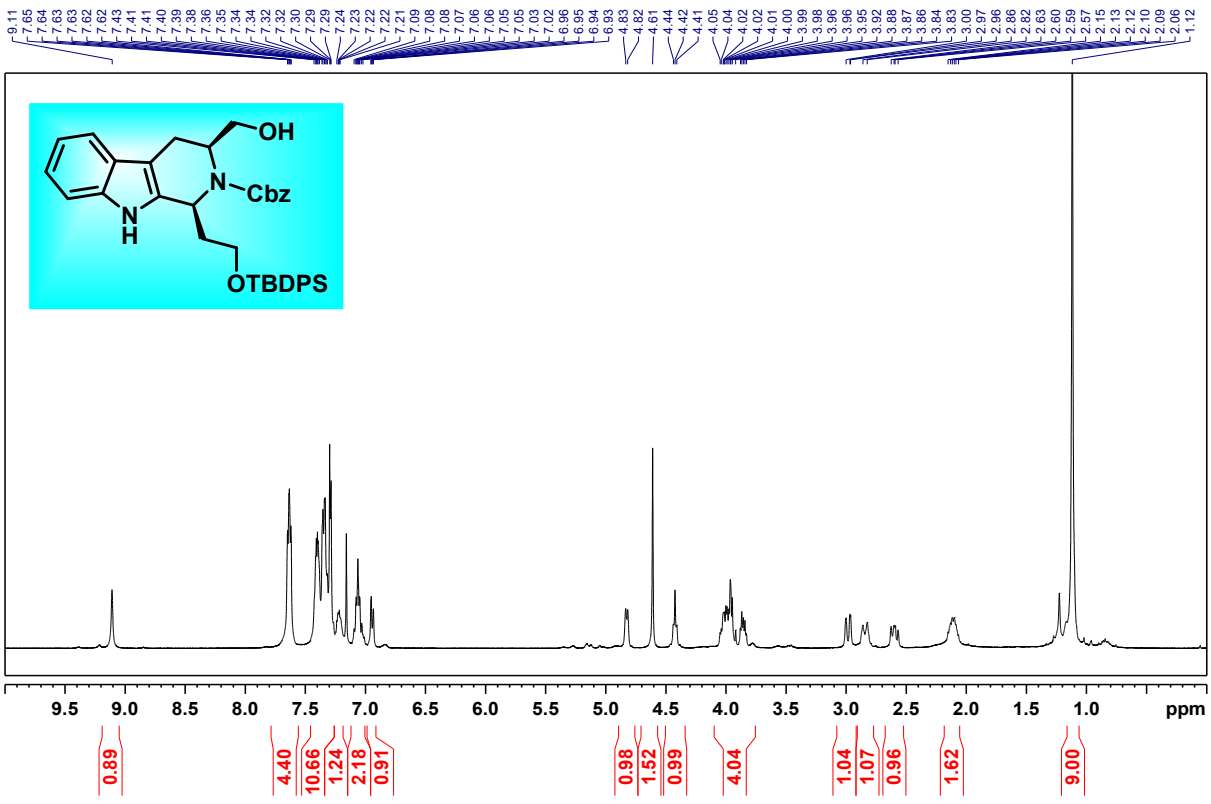
- **^{1}H NMR (400 MHz, $CDCl_3$) of Cbz-protected derivative of *cis* P-S product**



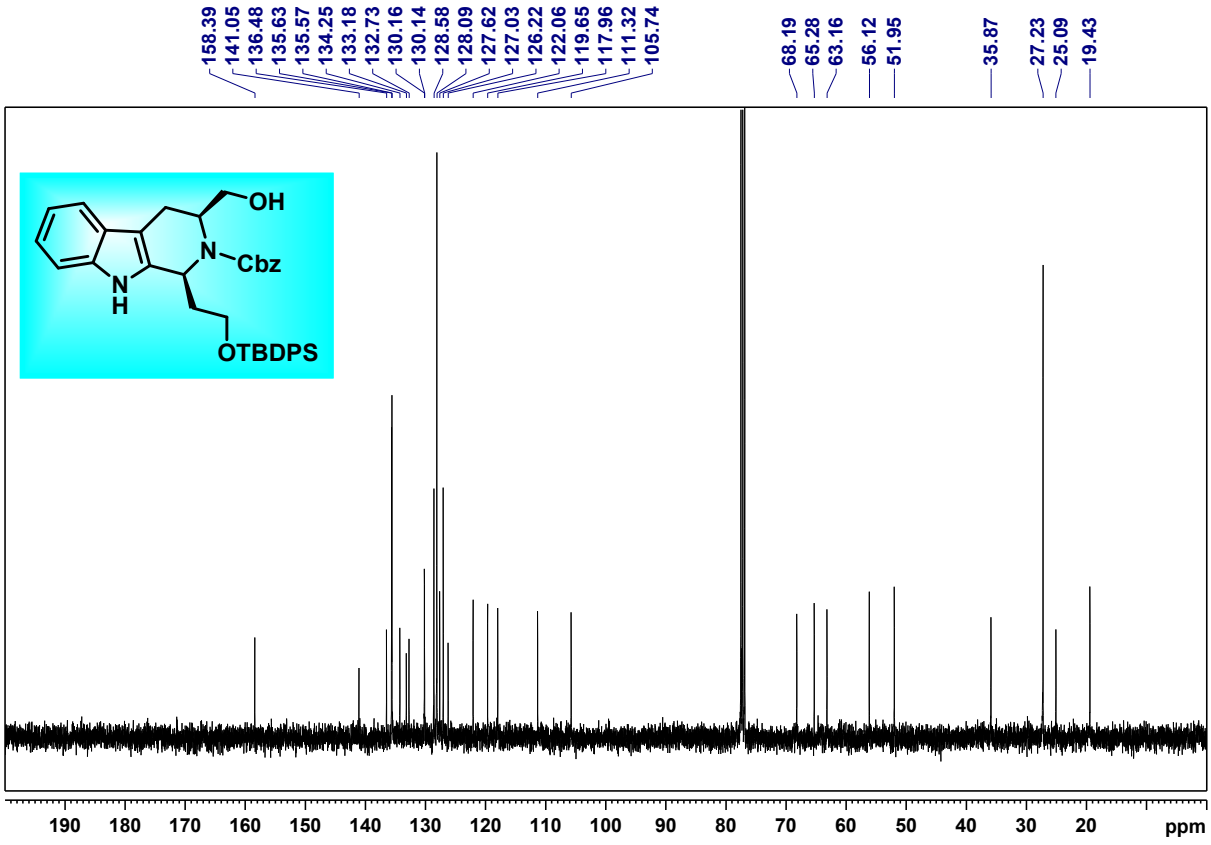
- **^{13}C NMR (100 MHz, $CDCl_3$) of Cbz-protected derivative of *cis* P-S product**



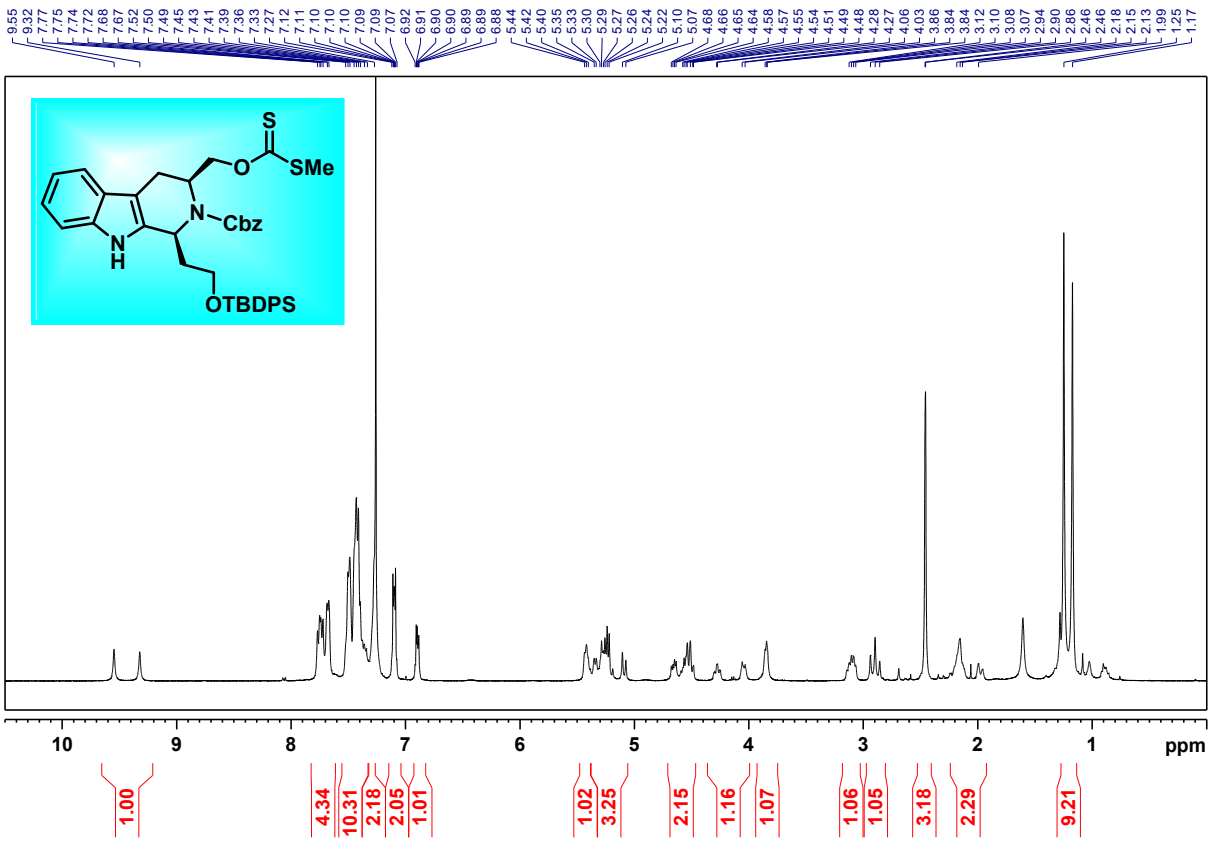
- **^{1}H NMR (400 MHz, $CDCl_3$) of Cbz-derivative of the alcohol intermediate**



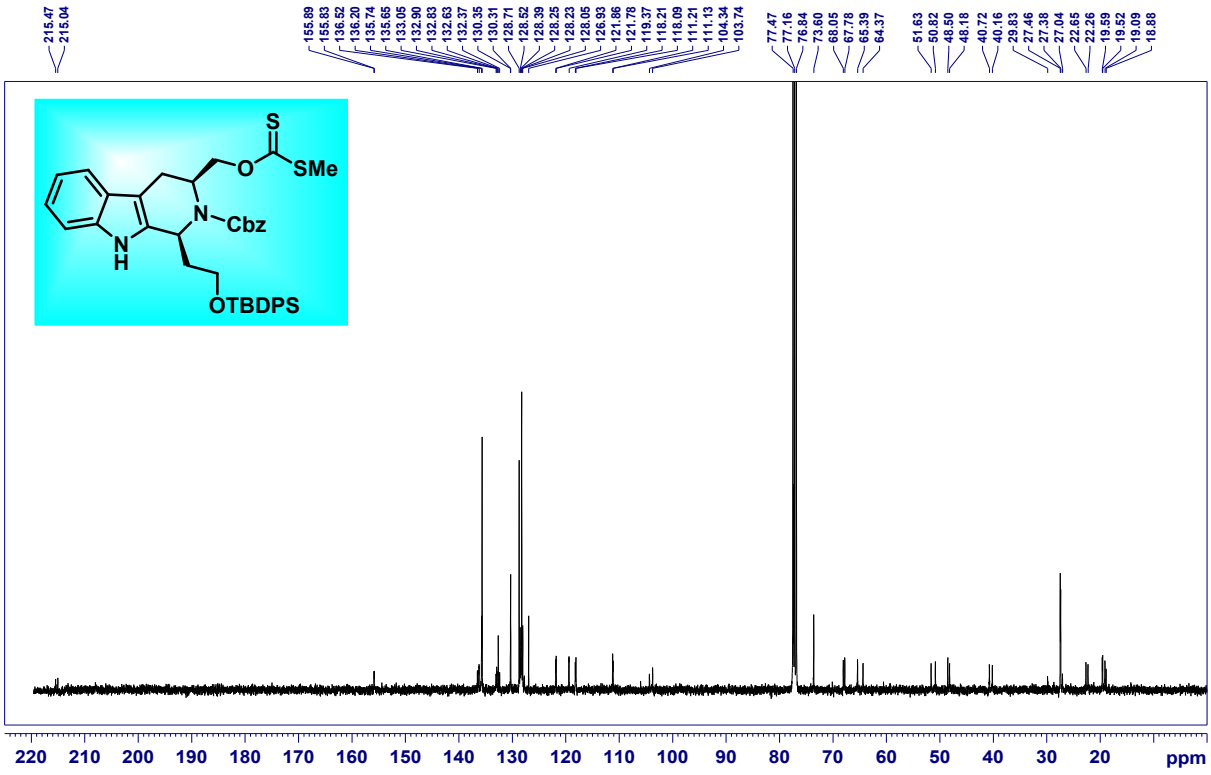
- **^{13}C NMR (100 MHz, $CDCl_3$) of Cbz-derivative of the alcohol intermediate**



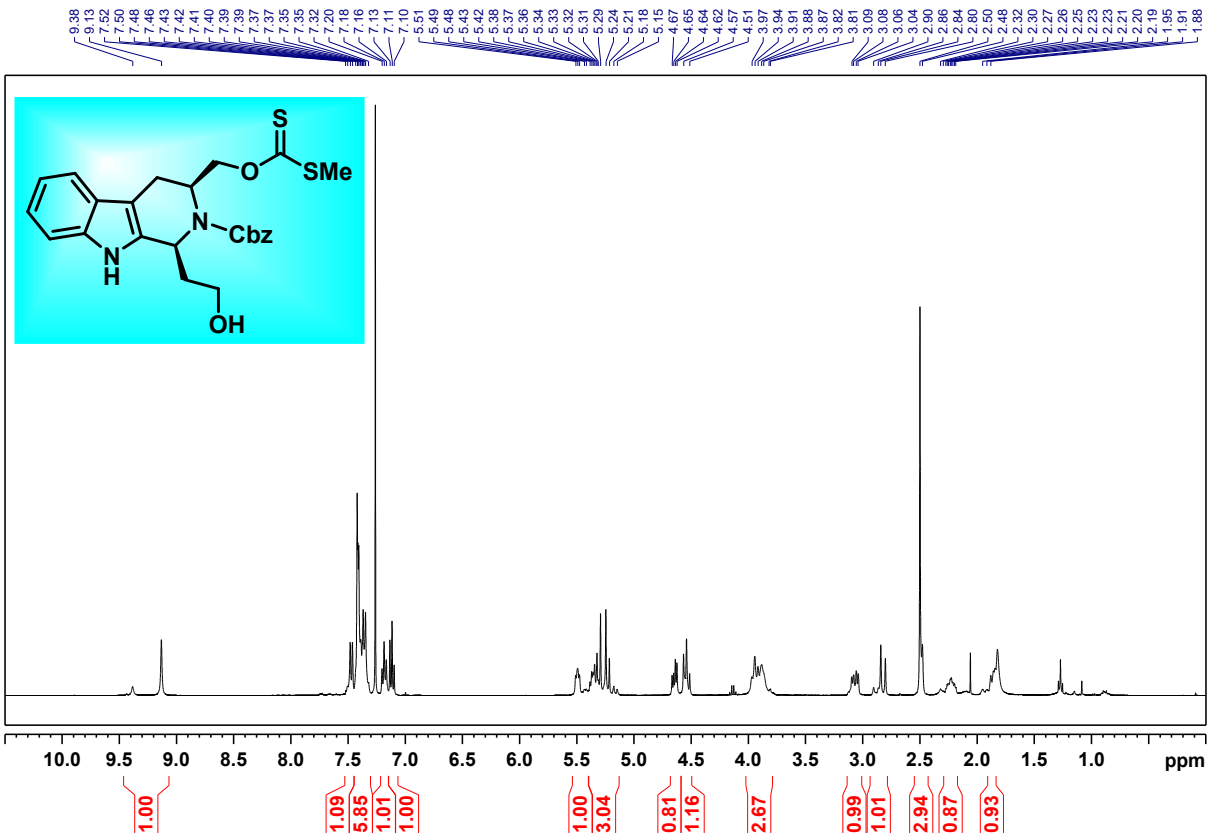
- **^{1}H NMR (400 MHz, $CDCl_3$) of the xanthate (mixture of rotamers 54:46):**



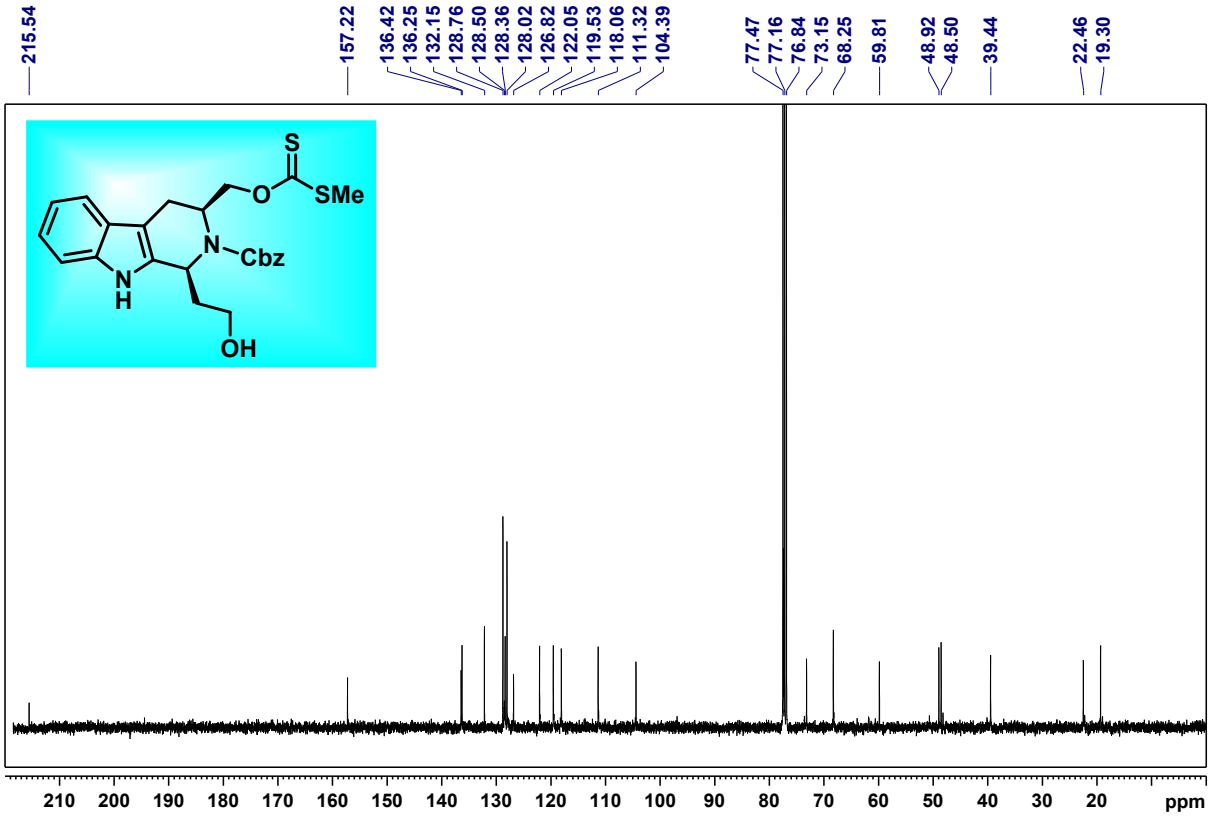
- **^{13}C NMR (100 MHz, $CDCl_3$) of the xanthate (mixture of rotamers 54:46):**



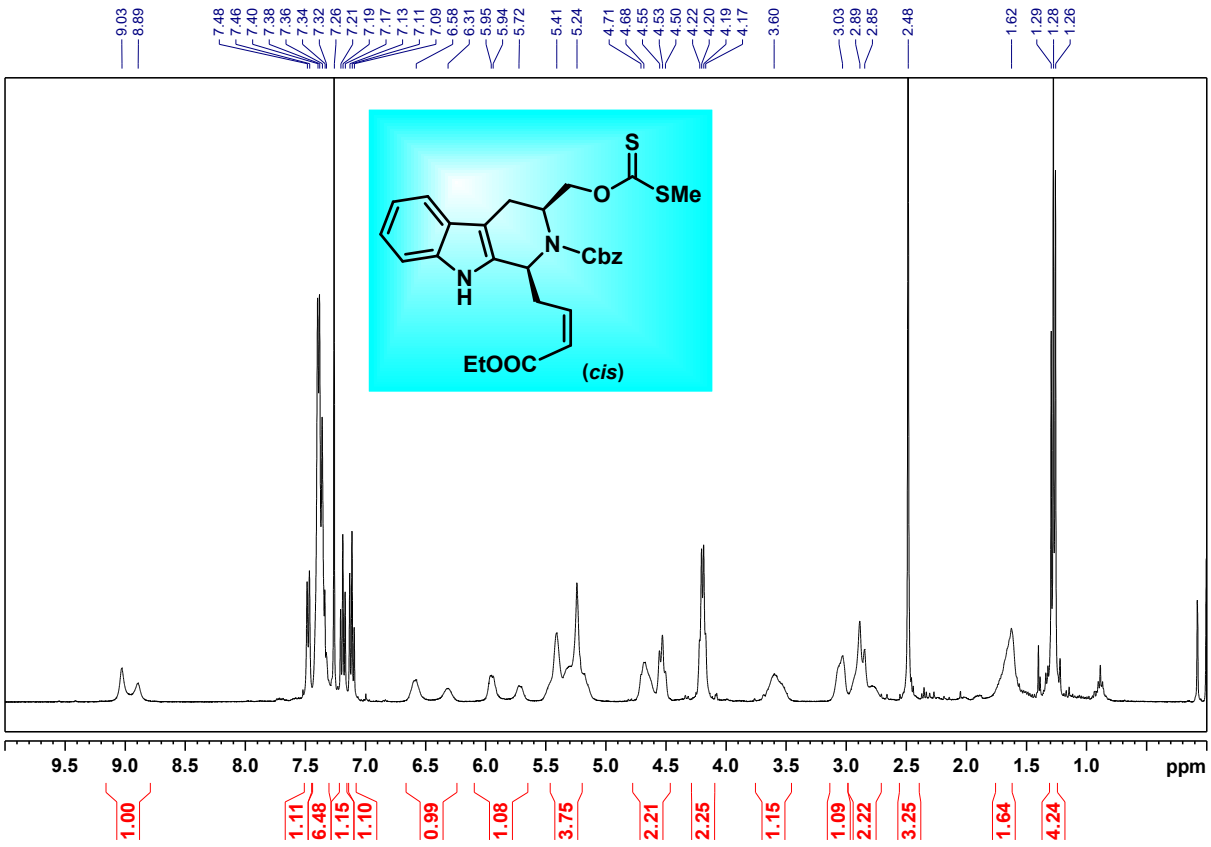
- **^{1}H NMR (400 MHz, $CDCl_3$) of the deprotected alcohol (mixture of rotamers):**



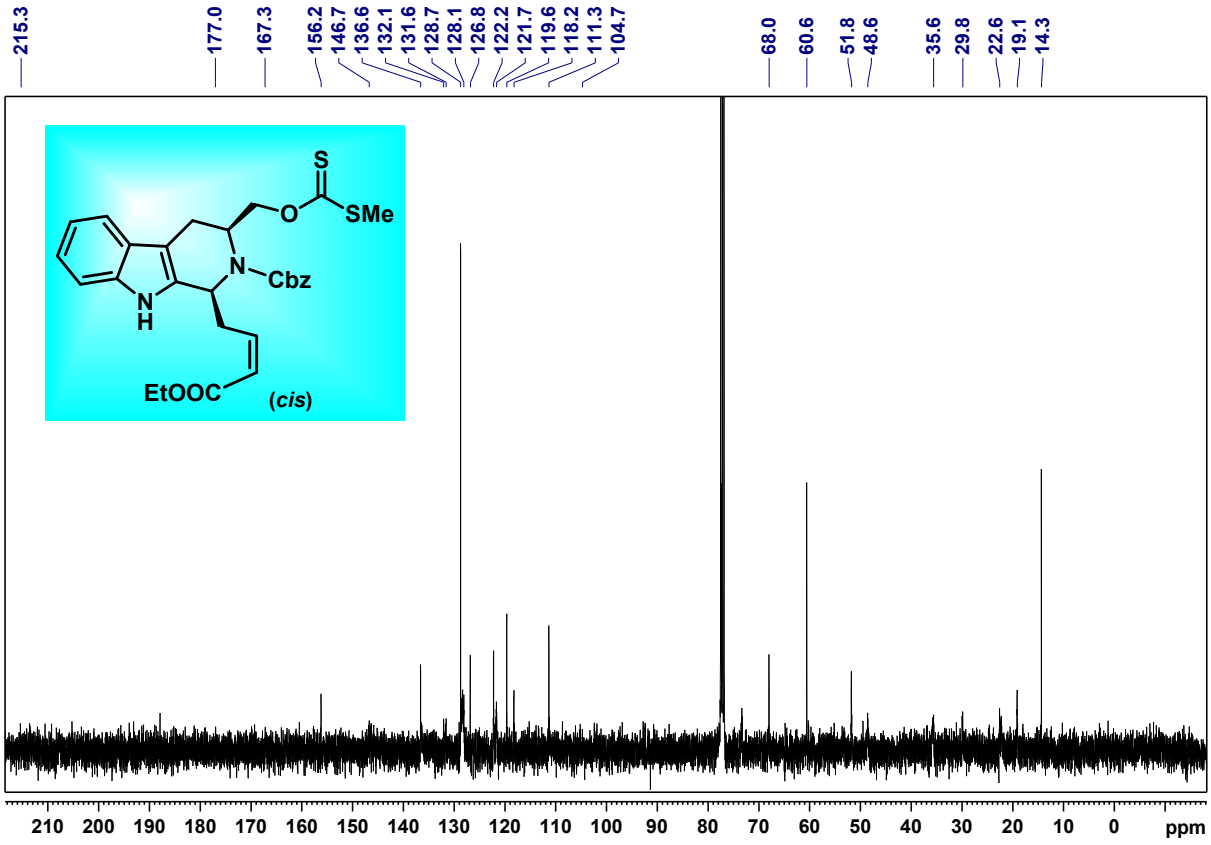
- **^{13}C NMR (100 MHz, $CDCl_3$) of the deprotected alcohol (mixture of rotamers):**



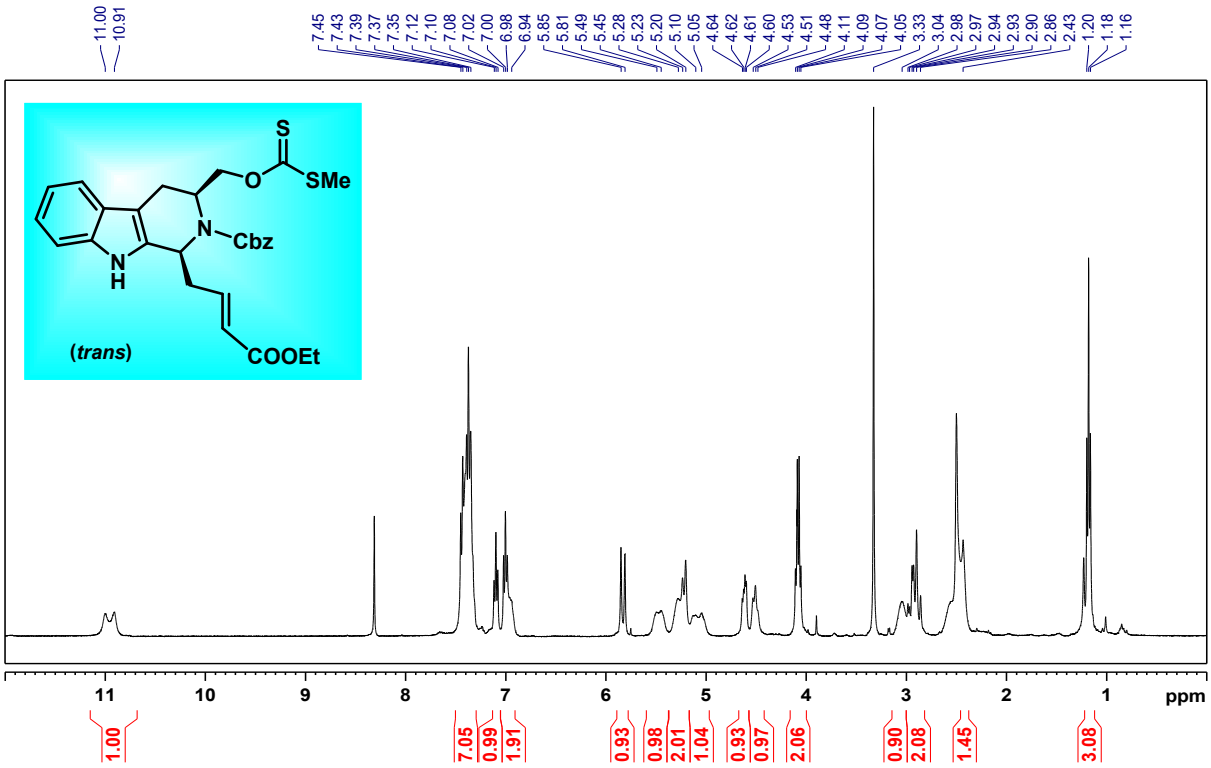
- **^{1}H NMR (400 MHz, $CDCl_3$) of 17 (*cis* isomer) (mixture of rotamers):**



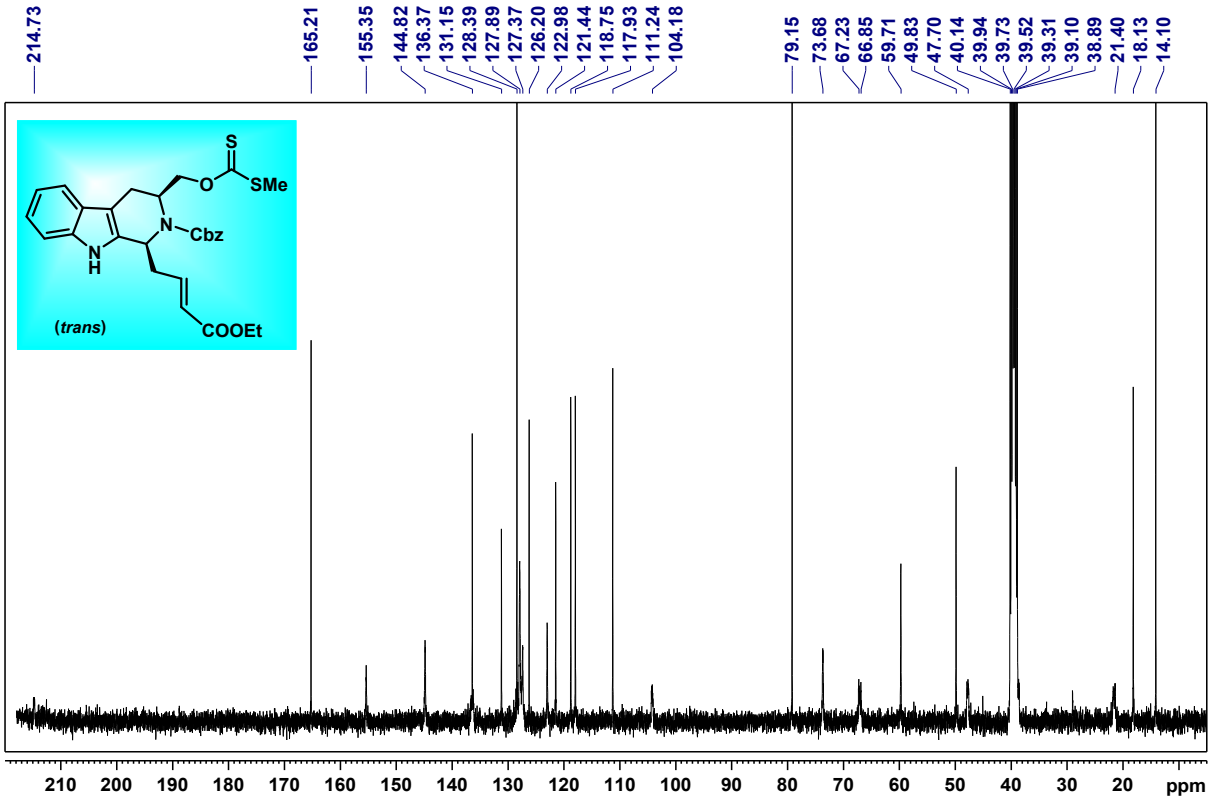
- **^{13}C NMR (100 MHz, $CDCl_3$) of 17 (*cis* isomer) (mixture of rotamers):**



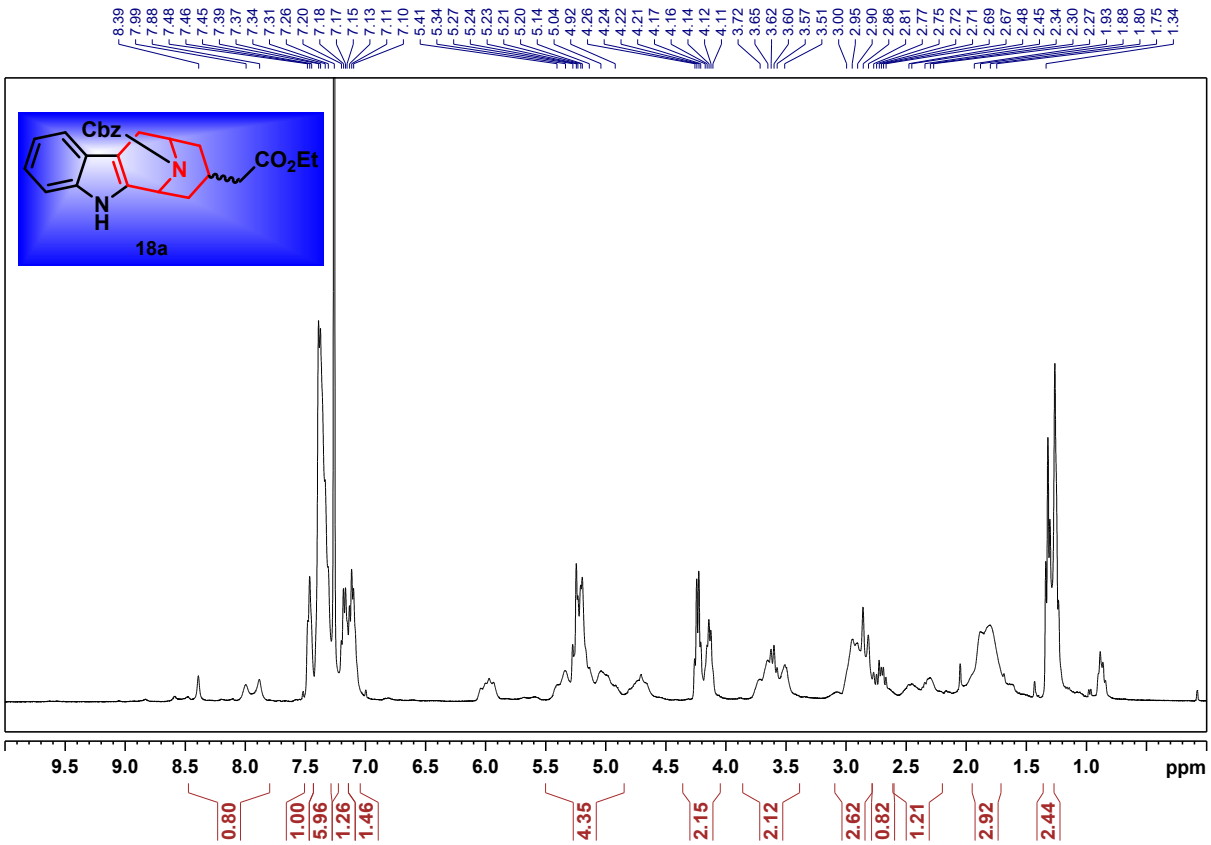
- **^{1}H NMR (400 MHz, $CDCl_3$) of 17 (*trans* isomer) (mixture of rotamers):**



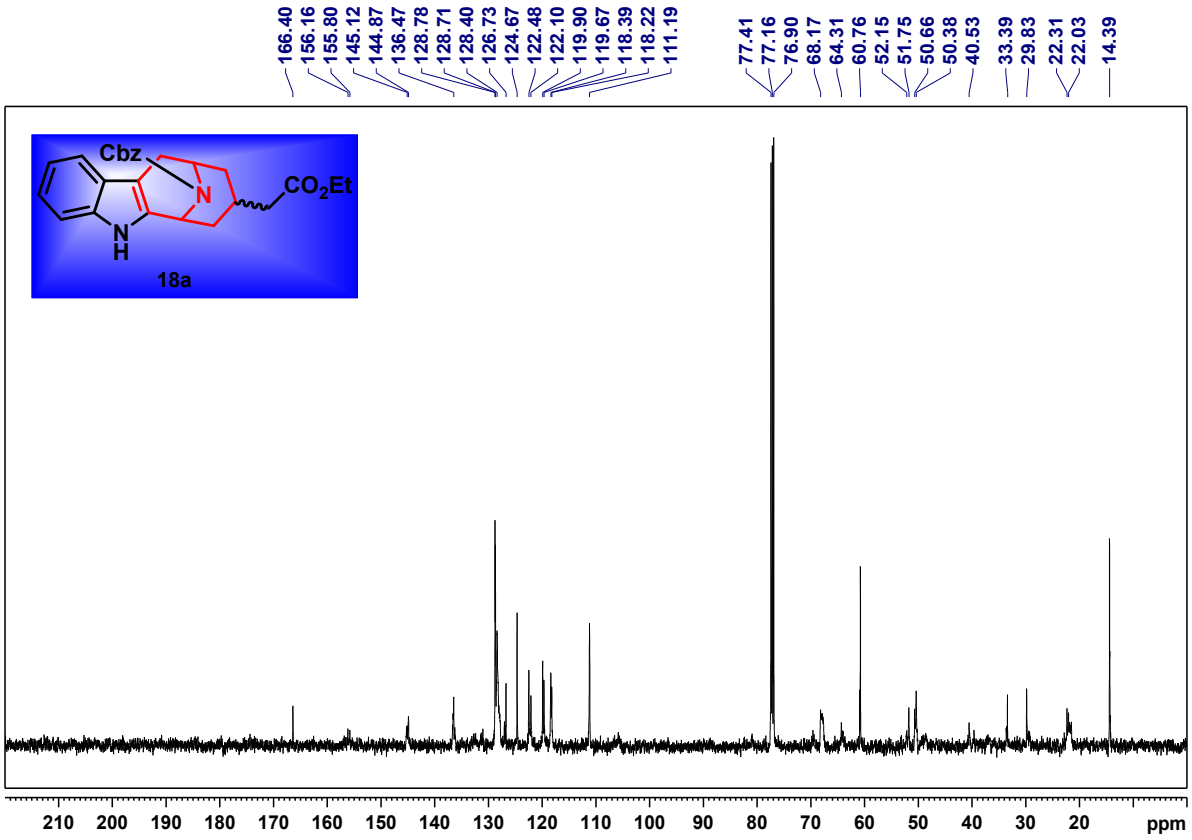
- **^{13}C NMR (100 MHz, $CDCl_3$) of 17 (*trans* isomer) (mixture of rotamers):**



- **^{1}H NMR (400 MHz, $CDCl_3$) of 18a (mixture of rotamers, diastereomers).**



- **^{13}C NMR (100 MHz, $CDCl_3$) of 18a (mixture of rotamers, diastereomers).**



- **^{1}H NMR (400 MHz, $CDCl_3$) of 18b (mixture of rotamers).**