Supporting Information

Asymmetric Total Synthesis of Lepadiformine C Using Memory of Chirality in an Intramolecular Ester Enolate Michael Addition

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Contents

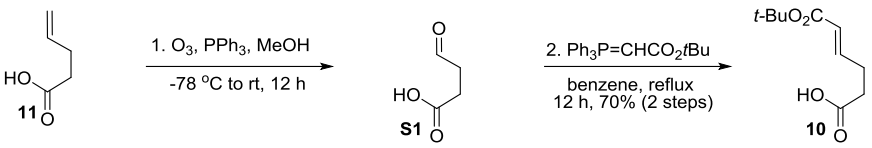
A. General

All of the chemicals were of reagent grade and were used as received. All of the reactions were performed under an inert atmosphere consisting of dry nitrogen using distilled dry solvents. The reactions were monitored by thin layer chromatography (TLC) analysis using silica gel 60 F-254 TLC plates. Flash column chromatography was performed on silica gel (230-400 mesh). The optical rotations were measured using sodium light (D line 589.3 nm) at 20 °C. ^{1}H NMR (300, 400, 500, 600 or 800 MHz) and ^{13}C NMR (100, 125, 150 or 200 MHz) spectra were recorded in δ units relative to the non-deuterated solvent as the internal reference. The IR spectra were recorded on a Fourier Transform Infrared spectrometer. High-resolution mass spectra (HRMS) were recorded using fast atom bombardment (FAB). HPLC was performed on an Agilent 1200 series instrument with a diode array detector (DAD) and CHIRALCEL OD-H column (0.46 × 25 cm, 5 μm).

B. Experimental procedure and spectroscopic data analysis

B-1. Synthesis of Michael substrate 9

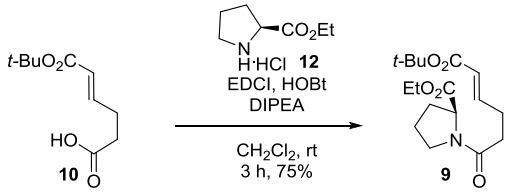
(*E*)-6-(*tert*-butoxy)-6-oxohex-4-enoic acid (10)



A solution of **11** (12.5 g, 125 mmol) in MeOH (400 mL) was cooled to –78 °C. Ozone was bubbled through the solution until blue color persisted. When TLC indicated the absence of the starting material, the ozone inlet tube was replaced with nitrogen, which was bubbled through the solution for 30 min to remove any excess ozone. Triphenylphosphine (65.5 g, 245 mmol) was added in one portion, the cooling bath was removed, and the mixture was stirred for 6 h at room temperature. The reaction mixture was filtered, and the filtrate was concentrated under reduced pressure to afford **S1** as a colorless oil, which was used in the subsequent step without further purification.

To a solution of **S1** in benzene (400 mL) was added *tert*-butyl 2-(triphenyl-λ^5-phosphanylidene)acetate (61.1 g, 162 mmol) at room temperature. The reaction mixture was heated to reflux for 12 h and then cooled to room temperature. The mixture was thrice extracted with saturated aqueous Na_2CO_3. The combined aqueous layers were thrice washed with EtOAc, and then acidified with 1N HCl (pH = 2). The aqueous solution was thrice extracted with EtOAc. The combined organic layers were dried over $MgSO_4$ and concentrated in vacuo to afford known compound **10** (17.5 g, 70%, 2 steps) as a colorless oil, which was used in the subsequent step without further purification.

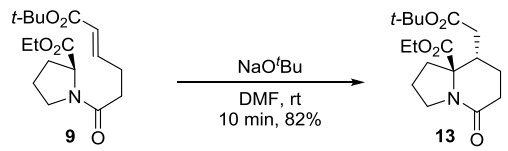
Ethyl (*E*)-(6-(*tert*-butoxy)-6-oxohex-4-enoyl)-L-prolinate (9)



To a solution of acid **10** (7.95 g, 39.7 mmol) in CH_2Cl_2 (50 mL) were added EDCI (9.25 g, 59.6 mmol), HOBt (8.05 g, 59.6 mmol) and DIPEA (27.7 mL, 159 mmol) at 0 ℃. The resulting mixture was stirred for 10 min, and then a solution of L-proline ethyl ester[1] (**12**, 8.56 g, 47.6 mmol) in CH_2Cl_2 (50 mL) was added at 0 ℃. The reaction mixture was stirred at room temperature for 3 h and then, diluted with CH_2Cl_2. The combined organic layers were washed with 1N HCl, saturated $NaHCO_3$, and brine, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel (hexane/EtOAc, 1:1) to yield **9** (9.69 g, 75%) as a colorless oil: $[\alpha]^{20}_D$ –41.6 (*c* 1.00, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 800 MHz; two rotamers in a 4:1 ratio) δ 6.86–6.78 (m, 1H), 5.75–5.70 (m, 1H), 4.43 (dd, *J* = 8.84 Hz, 3.80 Hz, 0.8H), 4.43 (dd, *J* = 8.64 Hz, 2.56 Hz, 0.2H), 4.19–4.11 (m, 2H), 3.62–3.57 (m, 1H), 3.54–3.51 (m, 0.2H), 3.46–3.43 (m, 0.8H), 2.54–2.47 (m, 2H), 2.46–2.43 (m, 1H), 2.41–2.35 (m, 0.8H), 2.30–2.26 (m, 0.2H), 2.25–2.19 (m, 0.2H), 2.17–2.12 (m, 0.8H), 2.06–2.01 (m, 1H), 1.97–1.92 (m, 1.6H), 1.88–1.85 (m, 0.4H) 1.43 (s, 9H), 1.25 (t, *J* = 7.12 Hz, 0.6H), 1.23 (t, *J* = 7.16 Hz, 2.4H); ^{13}C NMR (200 MHz, $CDCl_3$; rotamer 1/ rotamer 2) δ 172.2, 170.2, 165.8, 146.22/146.2, 123.6, 80.1, 61.6/61.0, 59.4/58.8, 46.9/46.4, 32.6/32.5, 31.4/29.15, 28.1 (3C), 27.1/26.8, 24.7/22.5, 14.14/14.10; IR (neat, cm^{-1}) υ_{max} 2980, 1743, 1712, 1652, 1432, 1369, 1320, 1294, 1257, 1243, 1186, 1149; HRMS (FAB) calcd. for $C_{17}H_{28}NO_5$ ($[M+H]^+$) 326.1967, found 326.1961.

B-2. Intramolecular Michael addition of 9

Representative procedure for the intramolecular Michael addition of 9



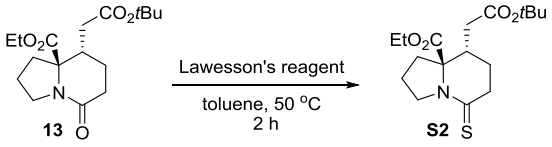
To a solution of NaO^tBu (17.0 mg, 0.169 mmol) in DMF (8 mL) was added a solution of **9** (50.0 mg, 0.154 mmol) in DMF (7 mL) dropwise at room temperature, and the mixture was stirred for 10 min at

1 Nazarova, L. S.; Rozonov, Yu. B.; Likhosherstov, A. M.; Morozova, T. V.; Skoldinov, A. P.; Kaverina N. V.; Markin, V. A. *Pharm. Chem. J.* **1984**, *18*, 811.

room temperature. The reaction was quenched by the addition of a saturated NH_4Cl aqueous solution and concentrated in vacuo. The residue was dissolved in EtOAc and water, and extracted twice with EtOAc. The organic extracts were dried over $MgSO_4$ and concentrated under reduced pressure. The yield was determined by ^1H NMR analysis of the crude reaction mixture using CH_2Br_2 as internal standard.

13: $[\alpha]^{22}_D$ –38.6 (*c* 0.5, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 4.19 (q, *J* = 6.21 Hz, 2H), 3.60–3.53 (m, 2H), 2.97–2.92 (m, 1H), 2.41–2.31 (m, 3H), 2.22–2.18 (m, 1H), 2.08 (dd, *J* = 15.5 Hz, 8.22 Hz, 1H), 1.86–1.58 (m, 5H), 1.43 (s, 9H), 1.25 (t, *J* = 7.12 Hz, 3H); ^{13}C NMR (200 MHz, $CDCl_3$) δ 173.6, 171.1, 168.7, 81.1, 72.3, 61.9, 45.1, 33.8, 33.5, 33.1, 27.9 (3C), 26.8, 23.5, 20.4, 14.1; IR (neat, cm^{-1}) υ_{max} 2979, 1729, 1650, 1447, 1412, 1369, 1269, 1226, 1208, 1090, 1023; HRMS (FAB): calcd. for $C_{17}H_{28}NO_5$ ($[M+H]^+$) 326.1967, found 326.1958.

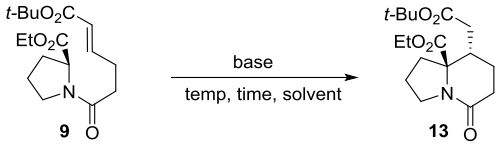
Representative procedure for synthesis of thioamide derivative S2



Crude product **13** (10.0 mg) was dissolved in toluene (0.5 mL) and Lawesson's reagent (12.0 mg, 0.0307 mmol) was added. The reaction mixture was heated to 50 ℃ for 2 h and then cooled to room temperature. The mixture was concentrated, and the residue was purified by flash column chromatography on silica gel (hexane/EtOAc, 3:1) to yield **S2** (7.0 mg) as a yellow oil. The enantiomeric purity of **S2** was determined by chiral HPLC analysis. The spectral data for **S2** was in good agreement with **15**, with the exception of optical rotation (see page S10).

S2: $[\alpha]^{20}_D$ –20.2 (*c* 0.5, $CHCl_3$).

Table S1. Additional conditions tested to optimize the intramolecular Michael addition of **9** (see Table 1 in the main text).[a]

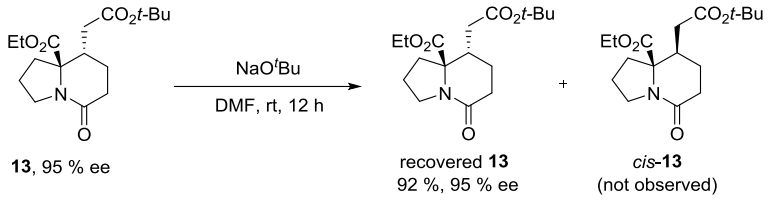


entry	solvent	base (equiv)	temp	time	yield (%)[b]	ee (%)[c]
1	THF	NaO^{t}Bu (3.0)	rt	12 h	0	-
2	CH_3CN	NaO^{t}Bu (3.0)	rt	12 h	49	83

[a]Reactions were performed with **9** (50 mg, 0.15 mmol) at a substrate concentration of 0.01 M. [b]Yield was estimated from the ^{1}H analysis. [c]Enantiomeric excess was determined by chiral HPLC analysis of thioamide derivative from **13**.

B-3 Exploratory studies to determine the mechanism of Michael addition.

B-3-a. Re-exposure of Michael product 13



Michael product **13** (9.0 mg, 0.028 mol, 95% ee), which was synthetized at –20 ℃, was dissolved in DMF (2.8 mL) and NaO^{t}Bu (3.0 mg, 0.030 mmol) was added. The reaction mixture was stirred for 12 h at room temperature. The reaction was quenched by the addition of a saturated NH_4Cl aqueous solution and concentrated in vacuo. The residue was dissolved in EtOAc and water, and extracted twice with EtOAc. The organic extracts were dried over $MgSO_4$ and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel (hexane/EtOAc, 3:1) to yield **13** (8.3 mg, 92%) as a yellow oil. The enantiomeric purity of obtained product **13** was determined to be 95% by chiral HPLC analysis after the conversion to the thioamide derivative.

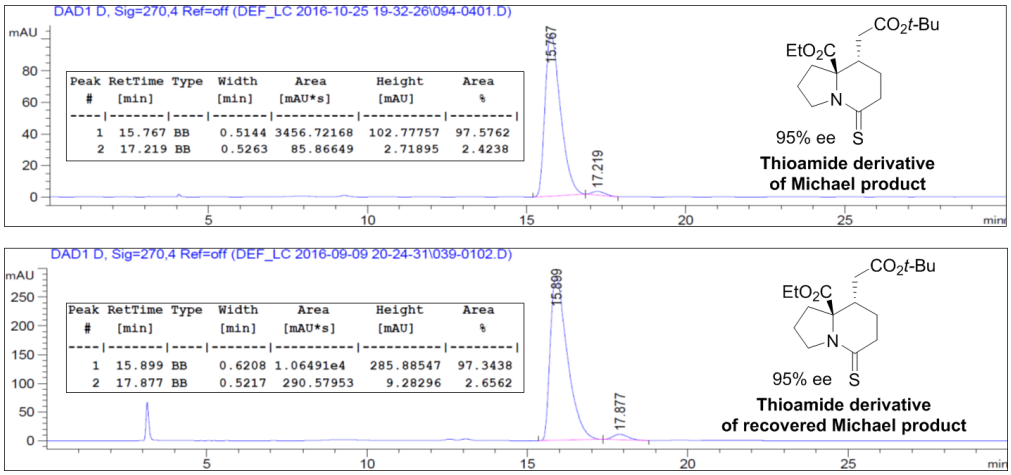
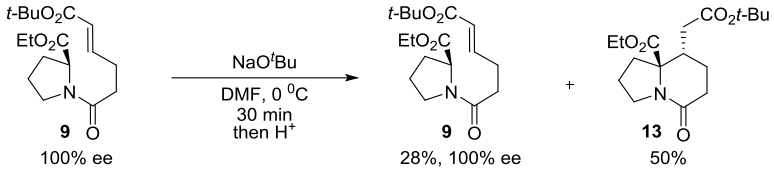


Figure S1. Chiral HPLC chromatograms of thioamide derivatives.

B-3-b. Incomplete reaction of intramolecular Michael addition



To a solution of NaO^{t}Bu (17.0 mg, 0.169 mmol) in DMF (8 mL) was added a solution of **9** (50.0 mg, 0.154 mmol, 100% ee) in DMF (7 mL) dropwise at 0 ℃, and the mixture was stirred for 30 min at 0 ℃. The reaction was quenched by the addition of a saturated NH_4Cl aqueous solution and concentrated in vacuo. The residue was dissolved in EtOAc and water, and extracted twice with EtOAc. The organic extracts were dried over $MgSO_4$ and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel (hexane/EtOAc, 3:1) to yield **9** (14.0 mg, 28%, 100% ee) and **13** (25.0 mg, 50%). The enantiomeric purity of **9** was determined using chiral HPLC analysis.

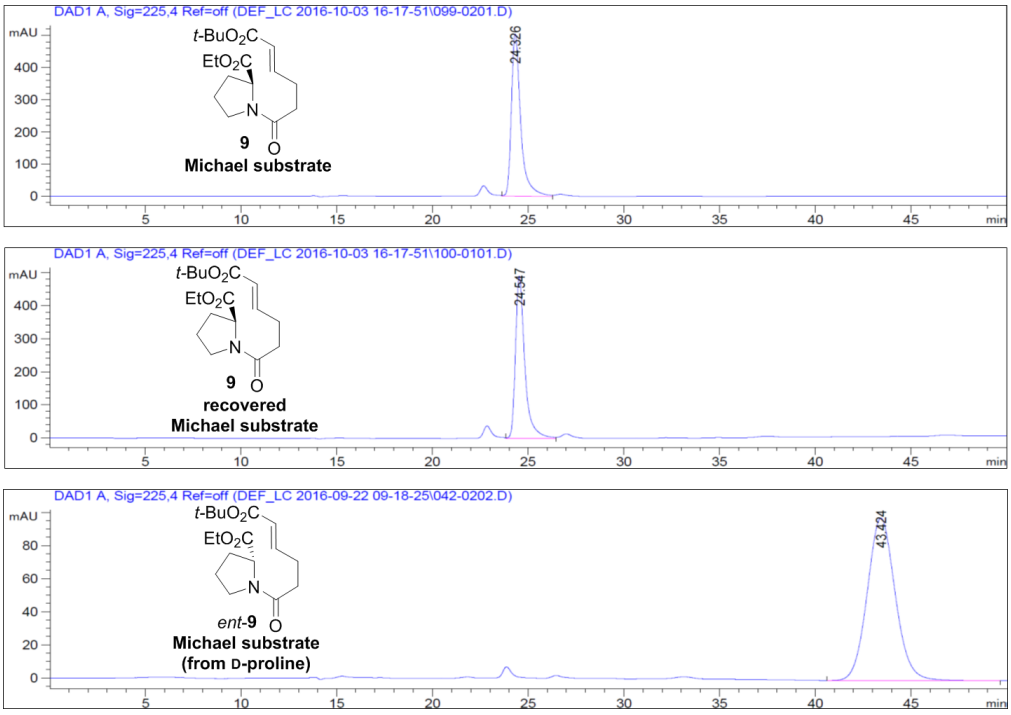
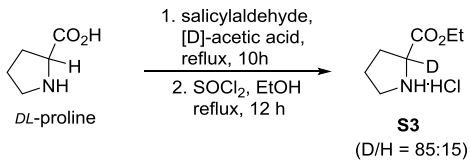


Figure S2. Chiral HPLC chromatograms of Michael substrates.

B-3-c. Deuterium study of intramolecular Michael addition

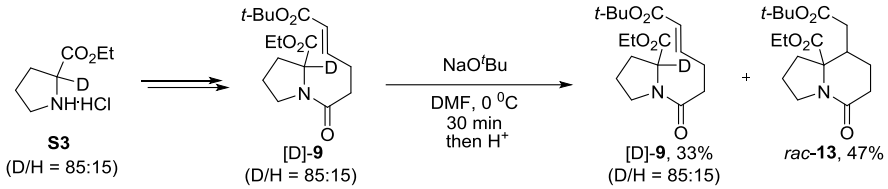
Preparation of S3



To a solution of DL-proline (2.00 g, 17.4 mmol) in [D]-acetic acid (37 mL) was added salicylaldehyde (0.164 mL, 1.54 mmol), and the mixture was heated to reflux for 10 h. The reaction mixture was concentrated under reduced pressure. To afford known compound [D]-proline as a colorless oil, which was used in the subsequent step without further purification.

To a solution of [D]-proline in EtOH (44 mL) was added $SOCl_2$ (1.41 mL, 19.3 mmol) dropwise at 0 ℃, and the mixture was heated to reflux for 12 h. The reaction mixture was concentrated under reduced pressure. To afford **S3** (D/H = 85:15) as a light yellow oil, which was used in the subsequent step without further purification.

The intramolecular Michael addition of [D]-9.



[D]-**9** was prepared according to the procedure described above for **9** using **S3** instead of **12**. To a solution of NaO^{t}Bu (4.0 mg, 0.051 mmol) in DMF (2.6 mL) was added a solution of [D]-**9** (15.0 mg, 0.0461 mmol, D/H = 85:15) in DMF (2 mL) dropwise at 0 ℃, and the mixture was stirred for 30 min at 0 ℃. The reaction was quenched by the addition of a saturated NH_4Cl aqueous solution and concentrated in vacuo. The residue was dissolved in EtOAc and water, and extracted twice with EtOAc. The organic extracts were dried over $MgSO_4$ and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel (hexane/EtOAc, 3:1) to yield [D]-**9** (5.0 mg, 33%, D/H = 85:15) and *rac*-**13** (7.0 mg, 47%).

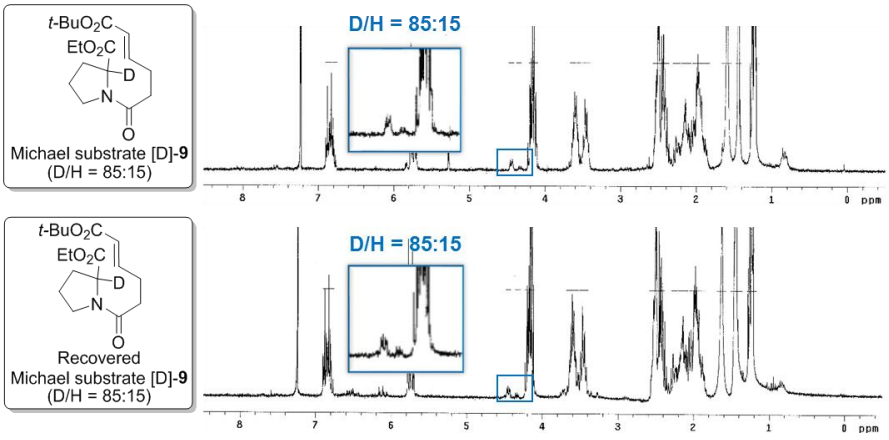
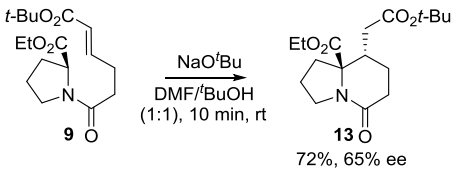


Figure S3. ^{1}H NMR spectra of [D]-**9** and recovered [D]-**9** after the Michael reaction.

B-3-d. The intramolecular Michael addition of 9 in the presence of protic solvent



To a solution of NaO^{t}Bu (17.0 mg, 0.169 mmol) in DMF (8 mL) was added a solution of **9** (50.0 mg, 0.154 mmol) in DMF (7 mL) dropwise at room temperature, and the mixture was stirred for 10 min at

room temperature. The reaction was quenched by the addition of a saturated NH_4Cl aqueous solution and concentrated in vacuo. The residue was dissolved in EtOAc and water, and extracted twice with EtOAc. The organic extracts were dried over $MgSO_4$ and concentrated under reduced pressure. The yield was determined by ^1H NMR analysis of the crude reaction mixture using CH_2Br_2 as internal standard (72%). Enantiomeric excess was determined by chiral HPLC analysis of thioamide derivative **S2** (65% ee).

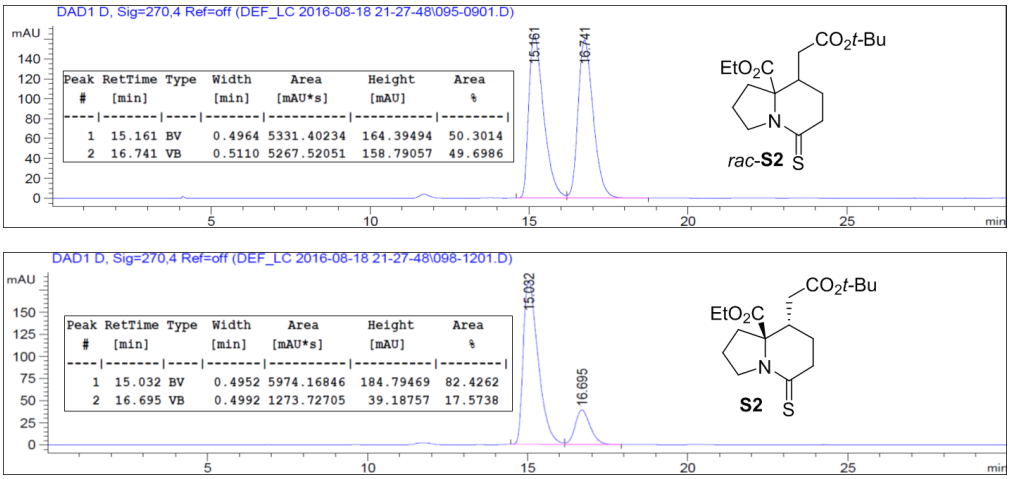
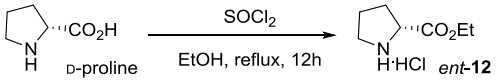


Figure S4. Chiral HPLC chromatograms of *rac*-**S2** and **S2** which was synthesized with NaO^{t}Bu at rt in DMF/^{t}BuOH (1:1).

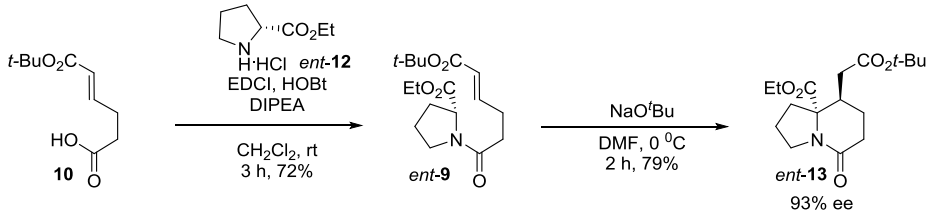
B-4 Synthesis of lepadiformine C (1)

Ethyl D-prolinate hydrochloride (*ent*-12)



To a solution of D-proline (10.0 g, 86.9 mmol) in EtOH (200 mL) was added $SOCl_2$ (7.00 mL, 96.0 mmol) dropwise at 0 ℃, and the mixture was heated to reflux for 12 h. The reaction mixture was concentrated under reduced pressure. To afford *ent*-**12** as a light yellow oil, which was used in the subsequent step without further purification.

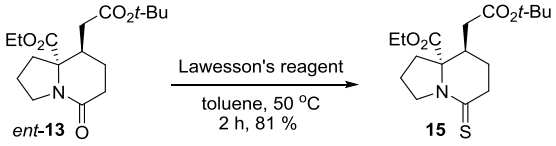
Ethyl (*8R*,8a*S*)-8-(2-(*tert*-butoxy)-2-oxoethyl)-5-oxohexahydroindolizine-8a(1*H*)-carboxylate (*ent*-13)



Ent-**9** was prepared according to the procedure described above for **9** using *ent*-**12**[1] instead of **12** (9.30g, 72%). The spectral data for *ent*-**9** were in good agreement with **9** excepting optical rotation (See pase S3): *ent*-**9**: $[\alpha]^{20}_{D}$ 52.7 (*c* 1.0, $CHCl_3$).

To a solution of NaO^tBu (844 mg, 8.78 mmol) in DMF (400 mL) was added a solution of **9** (2.60 g, 8.00 mmol) in DMF (400 mL) dropwise, and the mixture was stirred for 2 h at 0 ℃. The reaction was quenched by the addition of a saturated NH_4Cl aqueous solution and concentrated in vacuo. The residue was dissolved in EtOAc and water, and extracted twice with EtOAc. The organic extracts were dried over $MgSO_4$ and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel (EtOAc/CH_2Cl_2, 1:1) to yield *ent*-**13** (2.05 g, 79%) as a light yellow oil. Enantiomeric excess was determined by chiral HPLC analysis of thioamide derivative (93% ee). The spectral data for *ent*-**13** were in good agreement with **13** with the exception of optical rotation (see pase S4): *ent*-**13**: $[\alpha]^{20}_{D}$ 38.2 (*c* 0.1, $CHCl_3$).

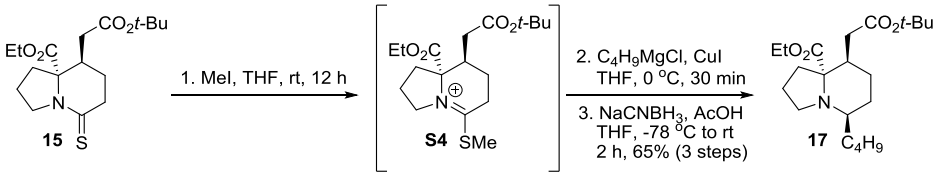
Ethyl (8*R*,8a*S*)-8-(2-(tert-butoxy)-2-oxoethyl)-5-thioxohexahydroindolizine-8a(1*H*)-carboxylate (15)



To a solution of *ent*-**13** (2.00 g, 6.15 mmol) in toluene (60 mL) was added Lawesson's reagent (1.49 g, 3.69 mmol). The reaction mixture was heated to 50 ℃ for 2 h and then cooled to room temperature. The mixture was concentrated, and the residue was purified by flash column chromatography on silica gel (hexane/EtOAc, 3:1) to yield **15** (1.70 g, 81%) as a yellow oil: $[\alpha]^{20}_{D}$ 19.8 (*c* 0.5, $CHCl_3$); ^1H

NMR ($CDCl_3$, 800 MHz) δ 4.23–4.17 (m, 2H), 3.92 (dd, J = 9.64 Hz, 5.16 Hz, 2H), 3.04 (ddd, J = 10.4 Hz, 7.82 Hz, 3.86 Hz, 1H), 3.00–2.97 (m, 1H), 2.91–2.86 (m, 1H), 2.34 (dd, J = 15.8 Hz, 6.40 Hz, 1H), 2.31 (ddd, J = 6.44 Hz, 1.04 Hz, 1H), 2.05 (dd, J = 15.8 Hz, 8.04 Hz, 1H), 1.95–1.91 (m, 1H), 1.88–1.84 (m, 1H), 1.72–1.63 (m, 3H), 1.42 (s, 9H), 1.25 (t, J = 7.12 Hz, 3H); ^{13}C NMR ($CDCl_3$, 200 MHz) δ 197.3, 171.9, 170.8, 81.3, 74.2, 62.3, 53.1, 36.2, 34.2, 33.6, 33.2, 28.0(3C), 23.4, 19.8, 14.1; IR (neat, cm^{-1}) υ_{max} 2976, 2936, 1726, 1477, 1454, 1413, 1368, 1267, 1209, 1148, 1107, 1070, 1015, 844; HRMS (FAB) calcd. for $C_{17}H_{28}NO_4S$ ([M+H]$^+$) 342.1739, found 342.1729.

Ethyl (5*R*,8*R*,8a*S*)-8-(2-(tert-butoxy)-2-oxoethyl)-5-butylhexahydroindolizine-8a(1*H*)-carboxylate (17)

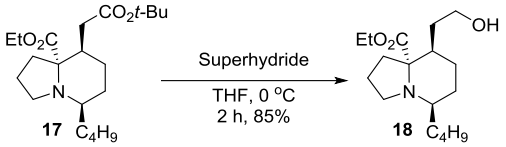


To a solution of **15** (1.00 g, 2.93 mmol) in THF (15 mL) was added iodomethane (0.910 mL, 14.6 mmol), and the mixture was stirred for 12 h at room temperature. The mixture was evaporated to dryness in vacuo to yield iminium salt **S4** as a yellow oil.

To a slurry of copper iodide (558 mg, 2.93 mmol) in anhydrous THF (14 mL) was added a solution of butylmagnesium chloride (2.20 mL, 4.39 mmol, 2.0 M solution in THF) at 0 ℃ under a N_2 atmosphere. The resulting mixture was stirred for 30 min at 0 ℃, and then a solution of iminium salt **S4** in anhydrous THF (15 mL) was added at 0 ℃. The reaction mixture was stirred for 30 min at 0 ℃ and then cooled to –78 ℃. $NaCNBH_3$ (184 mg, 2.93 mmol) was added to the mixture at –78 ℃. The reaction mixture was stirred for 15 min and then glacial AcOH (3.00 mL) was added at –78 ℃. After 15 min, the resulting mixture was allowed to slowly warm to rt and stirred for 2 h at room temperature. The reaction was quenched by the slow addition of a saturated Na_2CO_3 aqueous solution at 0 ℃, and stirred for 30 min at room temperature. Then, the mixture was extracted twice with EtOAc. The combined organic layers were washed with brine, dried over $MgSO_4$, and concentrated in vacuo. The residue was purified by flash chromatography on silica gel (hexane/EtOAc, 10:1) to yield **17** (700 mg,

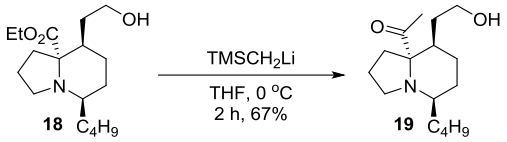
65%) as a light yellow oil: $[\alpha]^{24}_D$ –11.9 (*c* 0.5, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 800 MHz) δ 4.15–4.09 (m, 2H), 3.06–3.04 (m, 1H), 3.00–2.97 (m, 1H), 2.91–2.89 (m, 1H), 2.82–2.79 (m, 1H), 2.49 (dd, *J* = 15.9 Hz, 6.68 Hz, 1H), 2.20 (dd, *J* = 15.9 Hz, 6.92 Hz, 1H), 1.80–1.76 (m, 1H), 1.69–1.53 (m, 5H), 1.43 (s, 9H), 1.40–1.34 (m, 2H), 1.32–1.15 (m, 9H), 0.87 (t, *J* = 7.08 Hz, 3H); ^{13}C NMR ($CDCl_3$, 200 MHz) δ 175.6, 173.2, 80.0, 71.4, 59.9, 54.8, 47.3, 34.7, 34.5, 33.3, 33.0, 28.1(C3), 27.2, 27.0, 25.5, 23.2, 20.2, 14.3, 14.1; IR (neat, cm^{-1}) υ_{max} 2958, 2924, 2862, 1728, 1368, 1149, 1098; HRMS (FAB) calcd. for $C_{21}H_{38}NO_4$ ($[M+H]^+$) 368.2801, found 368.2796.

Ethyl (5*R*,8*R*,8a*S*)-5-butyl-8-(2-hydroxyethyl)hexahydroindolizine-8a(1*H*)-carboxylate (18)



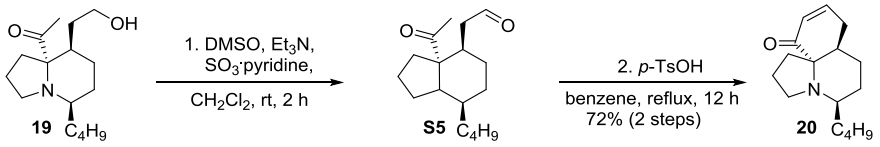
To a solution of this acid **17** (500 mg, 1.36 mmol) in THF (14 mL) was added Superhydride (3.40 mL, 3.40 mmol, 1.0 M solution in THF) at 0 ℃, and the resulting mixture was stirred for 2 h at 0 ℃. The reaction was quenched by the addition of a saturated NH_4Cl aqueous solution, and extracted twice with EtOAc. The organic extracts were dried over $MgSO_4$ and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel (EtOAc/acetone, 1:1) to yield **18** (344 mg, 85%) as a light yellow oil: $[\alpha]^{20}_D$ –24.5 (*c* 0.5, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 800 MHz) δ 4.12 (dd, *J* = 14.2 Hz, 7.12 Hz, 2H), 3.73–3.70 (m, 1H), 3.61 (td, *J* = 11.3 Hz, 5.72 Hz, 1H), 3.19 (brs, 1H, OH), 3.06 (td, *J* = 8.48 Hz, 5.44 Hz, 1H), 3.04–3.01 (m, 1H), 2.95 (td, *J* = 9.14 Hz, 4.88 Hz, 1H), 2.47 (td, *J* = 9.63 Hz, 4.90 Hz, 1H), 2.00 (td, *J* = 12.5 Hz, 9.90 Hz, 1H), 1.84 (td, *J* = 14.6 Hz, 6.53 Hz, 1H), 1.79–1.76 (m, 1H), 1.75–1.71 (m, 1H), 1.67–1.59 (m, 5H), 1.51 (ddd, *J* = 12.9 Hz, 8.58 Hz, 4.02 Hz, 1H), 1.43–1.38 (m, 1H), 1.32–1.25 (m, 4H), 1.24 (t, *J* = 7.12 Hz, 3H), 1.21–1.17 (m, 1H), 0.87 (t, *J* = 7.16 Hz, 3H); ^{13}C NMR ($CDCl_3$, 200 MHz) δ 175.9, 71.7, 61.1, 60.0, 54.7, 47.4, 34.8, 33.7, 32.2, 31.4, 27.5, 26.5, 25.7, 23.1, 20.2, 14.3, 14.1; IR (neat, cm^{-1}) υ_{max} 3387, 3342, 2933, 2861, 1725, 1461, 1379, 1175, 1144, 1097, 1052, 1022; HRMS (FAB) calcd. for $C_{17}H_{32}NO_3$ ($[M+H]^+$) 298.2382, found 298.2379.

1-((5*R*,8*R*,8a*S*)-5-butyl-8-(2-hydroxyethyl)hexahydroindolizin-8a(1*H*)-yl)ethan-1-one (19)



To a solution of this acid **18** (300 mg, 1.01 mmol) in THF (10 mL) was added (Trimethylsilyl)methyllithium (2.02 mL, 2.02 mmol, 1.0 M solution in pentane) at 0 ℃, and the resulting mixture was stirred for 2 h at 0 ℃. The reaction was quenched by the slow addition of MeOH at 0 ℃, and stirred for 1 h at room temperature. Then, the mixture was diluted with water, and extracted twice with EtOAc. The combined organic layers were washed with brine, dried over $MgSO_4$, and concentrated in vacuo. The residue was purified by flash chromatography on silica gel (EtOAc/acetone, 1:1) to yield **19** (180 mg, 62%) as a light yellow oil: $[\alpha]^{20}_D$ –33.2 (*c* 0.5, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 3.64–3.52 (m, 2H), 2.94–2.80 (m, 3H), 2.27–2.22 (m, 1H), 2.14 (s, 3H), 1.85–1.63 (m, 3H), 1.60–1.37 (m, 7H), 1.31–1.18 (m, 6H), 0.846 (t, *J* = 6.72 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 213.3, 74.7, 61.0, 52.2, 46.3, 34.6, 33.1, 31.3, 29.9, 28.2, 25.1, 24.5, 24.1, 22.9, 22.7, 14.1; IR (neat, cm^{-1}) υ_{max} 2932, 2860, 1702, 1461, 1348, 1158, 1141, 1091, 1055; HRMS (FAB) calcd. for $C_{16}H_{30}NO_2$ ($[M+H]^+$) 268.2277, found 268.2287.

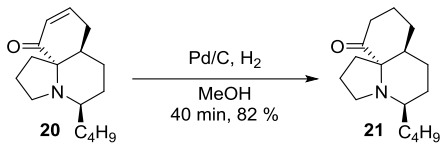
(5*R*,7a*R*,11a*S*)-5-butyl-2,3,6,7,7a,8-hexahydro-1*H*-pyrrolo[2,1-*j*]quinolin-11(5*H*)-one (20)



To a solution of **19** (120 mg, 0.449 mmol) in CH_2Cl_2 (9 mL) were added DMSO (0.700 mL, 9.86 mmol), SO_3·pyridine (547 mg, 3.36 mmol) and Et_3N (0.940 mL, 6.74 mmol) at 0 ℃, and the resulting mixture was stirred for 2 h at room temperature. The reaction was quenched by the slow addition of a saturated $NaHCO_3$ aqueous solution, water and brine at 0 ℃ and the mixture was extracted once with EtOAc. The organic layer was dried over $MgSO_4$ and concentrated in vacuo to afford **S5** as a brown oil, which was used in the subsequent step without further purification.

To a solution of crude **S5** in dry benzene (6 mL) was added *p*-TsOH (77.0 mg, 0.449 mmol) at room temperature. The reaction mixture was heated to reflux under a Dean-Stark trap for 12 h. The reaction mixture was then allowed to cool to room temperature, and the solvent was removed under reduced pressure. The residue was diluted with CH_2Cl_2 and washed with saturated $NaHCO_3$ aqueous solution and water. The organic layer was dried over $MgSO_4$ and concentrated in vacuo. The residue was purified by flash column chromatography on silica gel (CH_2Cl_2/MeOH, 5:1) to afford **20** (80.0 mg, 72%) as a light brown oil: $[\alpha]^{20}_D$ –77.7 (*c* 0.5, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 6.74 (ddd, J = 9.98 Hz, 5.62 Hz, 2.02 Hz, 1H), 5.89 (dd, J = 10.0 Hz, 2.36 Hz, 1H), 3.03 (t, J = 7.24 Hz, 1H), 2.86 (s, 1H), 2.70 (ddd, J = 12.1 Hz, 7.72 Hz, 4.96 Hz, 1H), 2.34–2.31 (m, 1H), 2.21 (td, J = 19.0 Hz, 4.48 Hz, 1H), 2.11–2.01 (m, 1H), 1.97 (td, J = 12.9 Hz, 6.72 Hz, 1H), 1.71–1.56 (m, 4H), 1.54–1.48 (m, 3H), 1.28–1.21 (m, 6H), 0.83 (t, J = 8.48 Hz, 3H); ^{13}C NMR ($CDCl_3$, 200 MHz) δ 203.0, 147.0, 128.4, 71.2, 51.3, 47.3, 35.8, 34.5, 31.7, 29.0, 28.5, 22.8, 22.6, 22.3, 21.1, 14.0; IR (neat, cm^{-1}) υ_{max} 2932, 2862, 1692, 1461, 1380, 1148; HRMS (FAB) calcd. for $C_{16}H_{26}NO$ ($[M+H]^+$) 248.2014, found 248.2012.

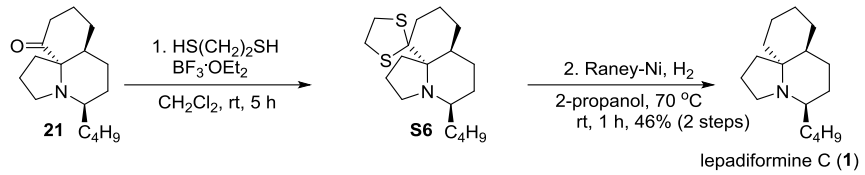
(5*R*,7a*S*,11a*S*)-5-butyloctahydro-1H-pyrrolo[2,1-j]quinolin-11(5H)-one (21)



To a solution of **20** (40.0 mg, 0.162 mmol) in MeOH (1.5 mL) was added HCl 2.0 M in ether solution (2.0 mL) at 0 ℃, and the resulting mixture was stirred for 15 min at room temperature. The mixture was evaporated to dryness in vacuo to yield HCl salt of **20** as a light brown oil. To a solution of HCl salt of **20** was added 10% Pd/C (40.0 mg, 100% wt. of **20**). The flask was evacuated, filled with H_2, and stirred at room temperature for 40 min. The mixture was then filtered through Celite, and the filtrate was concentrated. The residue was diluted with CH_2Cl_2 and washed with saturated $NaHCO_3$ aqueous solution and water. The organic layer was dried over $MgSO_4$ and concentrated in vacuo. The residue was purified by flash column chromatography on silica gel (CH_2Cl_2/MeOH, 7:1) to afford the **21** (33.0 mg, 82%) as a brown oil: $[\alpha]^{20}_D$ –33.1 (*c* 0.5, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 800

MHz) δ 2.99 (t, J = 7.68 Hz, 1H), 2.88–2.87 (m, 1H), 2.68 (ddd, J = 11.8 Hz, 8.44 Hz, 5.40 Hz, 1H), 2.59 (ddd, J = 15.1 Hz, 12.9 Hz, 7.42 Hz, 1H), 2.39–2.36 (m, 1H), 1.97–1.88 (m, 4H), 1.71–1.64 (m, 3H), 1.59–1.55 (m, 2H), 1.54–1.46 (m, 4H), 1.30–1.24 (m, 4H), 1.23–1.20 (m, 2H), 0.86 (t, J = 7.00 Hz, 3H); ^{13}C NMR ($CDCl_3$, 200 MHz) δ 212.0, 75.1, 51.6, 46.8, 39.3, 38.2, 34.4, 31.3, 29.1, 28.4, 25.6, 23.0, 22.89 22.86, 21.7, 14.1; IR (neat, cm^{-1}) υ_{max} 3414, 2955, 2934, 2869, 1715, 1642, 1460, 1180, 1122, 1034, 1012, 684, 657; HRMS (FAB) calcd. for $C_{16}H_{28}NO$ ([M+H]$^+$) 250.2171, found 250.2179.

Lepadiformine C (1)



To a solution of **21** (30.0 mg, 0.120 mmol) in CH_2Cl_2 (0.1 mL) were added 1,2-ethanedithiol (0.154 mL, 1.80 mmol) and $BF_3{\cdot}OEt_2$ (0.178 mL, 1.44 mmol) at 0 ℃, and the resulting mixture was stirred for 5 h at room temperature. The mixture was diluted with toluene and evaporated to dryness in vacuo. The mixture was filtered through a short pad of silica using CH_2Cl_2, and the filtrate was concentrated in vacuo to afford **S6** as a yellow oil, which was used in the subsequent step without further purification.

To a solution of **S6** was added Raney-Nickel (0.8 mL). The flask was evacuated, filled with H_2, and stirred at 70 ℃ for 1 h. The mixture was then filtered through PTFE filter, and the filtrate was concentrated and purified by flash column chromatography on silica gel (CH_2Cl_2/MeOH, 7:1) to yield lepadiformine C (**1**) (13.0 mg, 46%) as a colorless oil. The free base **1** was dissolved in MeOH (0.5 mL). To this solution was added HCl 2.0 M in ether solution (2 mL) at 0 ℃, and the resulting mixture was stirred for 20 min at room temperature. The solution was then evaporated to dryness in vacuo to afford **1**·HCl as a white gum. The spectral data matched those previously reported in the literature: $[\alpha]^{20}_D$ –10.7 (*c* 0.3, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 600 MHz) δ 3.67 (td, J = 11.4 Hz, 5.96 Hz, 1H), 3.52–3.49 (m, 1H), 2.85 (ddd, J = 18.3 Hz, 11.7 Hz, 6.65 Hz, 1H), 2.43–2.40 (m, 1H), 2.20 (d, J = 13.7 Hz,

1H), 2.11–2.06 (m, 1H), 2.05–1.91 (m, 5H), 1.86–1.84 (m, 1H), 1.75–1.72 (m, 1H), 1.69–1.63 (m, 2H), 1.60–1.46 (m, 2H), 1.41–1.20 (m, 8H), 1.20–1.04 (m, 1H), 0.88 (t, J = 7.11 Hz, 3H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 74.8, 55.4, 47.0, 37.8, 35.5, 30.8, 29.9, 28.4, 27.7, 25.2, 23.8, 22.4, 22.4, 20.9, 20.0, 13.9; IR (neat, cm^{-1}) υ_{max} 2935, 2866, 2708, 2631, 2579, 2524, 2490, 1467, 1449, 1347; HRMS (FAB) calcd. for $C_{16}H_{30}N$ ($[M+H]^+$) 236.2378, found 236.2377.

D. Computational study

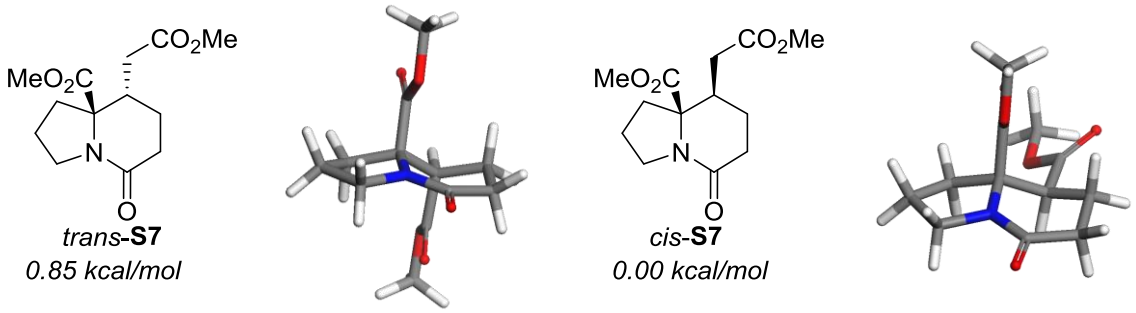
General procedure for molecular energy calculations

Computational energy minimization was performed on system of **13** using the DMol3 program[2] in Material Studio 2017 (Accelrys software, Inc., San Diego, CA). A generalized gradient approximation (GGA) for the Perdew, Burke and Ernzerhof (PBE)[3] exchange-correlation function was applied with double-numerical plus d-functions polarization (DNP), as implemented in DMol3. All molecules were modeled in the gas phase.

Geometry optimization and energy minimization of the compounds

The compounds were calculated to compare their energy levels using the method described above. This computational energy minimization demonstrated that *cis*-**S7** is thermodynamically more stable than *trans*-**S7**. The energy differences are 0.85 kcal/mol.

Table S2. Molecular energies of **S7**.



compound	Hartree (Ha)[a]	kcal/mol	Relative energy (kcal/mol)
trans-**S7**	–897.7160481	–563325.2506	0.8527
cis-**S7**	–897.717407	–563326.1034	0

[a]1Ha = 627.509391 kcal/mol.

2 (a) Delley, B. *J. Chem. Phys.* **1990**, *92*, 508. (b) Delley, B. *J. Chem. Phys.* **2000**, *113*, 7756.
3 Perdew, J. P.; Burke K.; Ernzerhof, M. *Phys. Rev. Lett.* **1996**, *77*, 3865.

Calculation input

All calculations are performed under following conditions.
Task parameters

Calculate	optimize
Opt_energy_convergence	1.0000e–005
Opt_gradient_convergence	2.0000e–003 A
Opt_displacement_convergence	5.0000e–003 A
Opt_iterations	50
Opt_max_displacement	0.3000 A
Initial_hessian	improved
Scf_density_convergence	1.0000e–006
Scf_charge_mixing	2.0000e–001
Scf_diis	6 pulay
Scf_iterations	50

Electronic parameters

Spin_polarization	restricted
Charge	0
Basis	dnp
Pseudopotential	none
Functional	pbe
Aux_density	hexadecapole
Integration_grid	fine
Occupation	fermi
Cutoff_Global	3.7000 angstrom

Calculated properties

Calculation output

trans-**S7**

Atom	X	Y	Z	Atom	X	Y	Z
C	17.42437	-9.30988	15.04145	H	19.63313	-12.8365	16.19837
C	16.83511	-10.1331	13.88153	H	17.90105	-14.3736	15.50367
N	17.27417	-11.5079	14.14083	H	19.35119	-14.7681	14.58815
C	18.03841	-11.6579	15.3721	H	17.0592	-14.6212	13.25905
C	18.49242	-10.2066	15.69173	H	18.4724	-13.8674	12.53692
C	19.18986	-12.6804	15.20679	O	15.8876	-12.3721	16.23664
C	18.56926	-14.0041	14.71053	O	17.62482	-12.2836	17.6981
C	17.79216	-13.8149	13.39923	C	15.04909	-12.8033	17.33767
C	17.0556	-12.4912	13.20971	H	15.02925	-12.0362	18.12255
O	16.35774	-12.2859	12.21394	H	15.43008	-13.7402	17.76251
H	16.63614	-9.06756	15.7692	O	20.16244	-11.8362	13.1233
H	17.84677	-8.3591	14.69465	O	21.49614	-12.2308	14.92271
H	15.73847	-10.0773	13.8377	C	22.62363	-11.829	14.10728
H	17.21703	-9.82458	12.89712	H	14.05592	-12.9467	16.90283
C	17.17794	-12.142	16.5731	H	23.49997	-11.9365	14.75405
H	19.46836	-10.0325	15.21712	H	22.5062	-10.7883	13.78026
H	18.611	-10.0503	16.77033	H	22.70676	-12.4749	13.22415
C	20.29082	-12.192	14.28051				

Total energy = –897.7160481 Ha

cis-**S7**

Atom	X	Y	Z	Atom	X	Y	Z
C	16.10405	-12.9753	17.00904	H	19.81128	-14.0222	17.18356
C	16.12808	-14.5106	16.91829	H	19.54602	-15.3689	19.93848
N	17.33289	-14.9094	17.65763	H	20.95075	-15.538	18.90515
C	18.01074	-13.7862	18.30757	H	19.13484	-17.4319	18.68565
C	17.50272	-12.5635	17.50058	H	19.74349	-16.7357	17.19517
C	19.55026	-14.0181	18.25451	O	16.765	-14.5778	20.23374
C	19.86432	-15.378	18.88566	O	17.91886	-12.6319	20.45202
C	19.17181	-16.4985	18.1082	C	16.34139	-14.4241	21.61247
C	17.75969	-16.2139	17.61353	H	17.21288	-14.42	22.27788
O	17.06959	-17.0923	17.08992	H	15.69941	-15.2866	21.81255
H	15.33886	-12.6507	17.7301	O	21.02806	-13.0522	19.93328
H	15.8566	-12.5105	16.04678	O	20.33603	-11.7655	18.19083
H	15.23375	-14.9736	17.35963	C	21.05562	-10.66	18.78916
H	16.20935	-14.8865	15.8879	H	15.78885	-13.4844	21.73867
C	17.57632	-13.5925	19.78524	H	20.60857	-10.4045	19.75781
H	18.18346	-12.4107	16.65181	H	20.95391	-9.83077	18.08217
H	17.51269	-11.6499	18.10256	H	22.11017	-10.9234	18.93584
C	20.37405	-12.9158	18.91796				

Total energy = –897.717407 Ha

E. Chiral HPLC chromatograms of S2

Using **S2**, we determined enantiomeric excess by chiral HPLC (see Table 1 in the main text). The chromatograms were compared with the chromatogram obtained from *rac*-**S2**, which was prepared from DL-proline.

HPLC conditions : CHIRALCEL OD-H (0.46 × 25 cm, 5 μm), hexane/2-propanol = 96:4, flow rate 1.0 mL/min, λ = 270 nm.

Ref. *rac*-**S2**

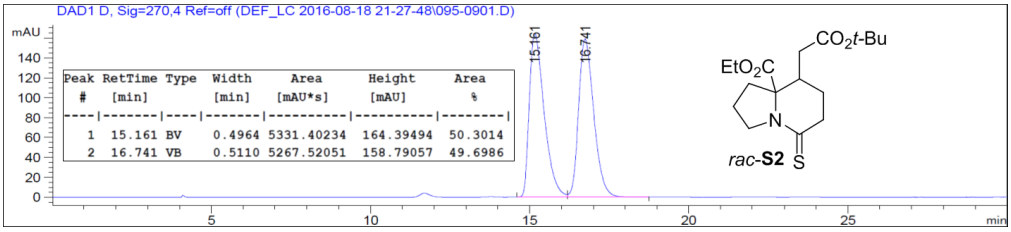


Table 1 (entry 1, NaO^{t}Bu (1.1 equiv), rt, 10 min)

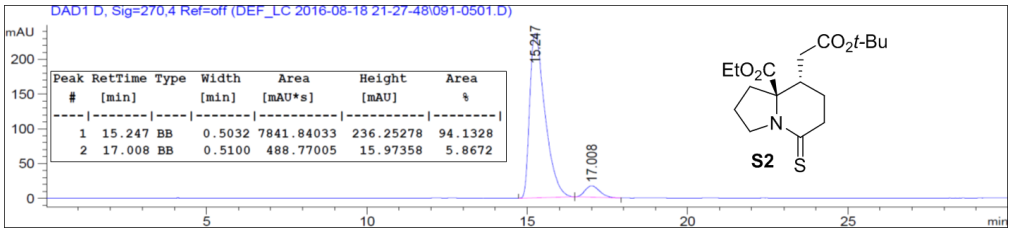


Table 1 (entry 2, KO^{t}Bu (1.1 equiv), rt, 3 h)

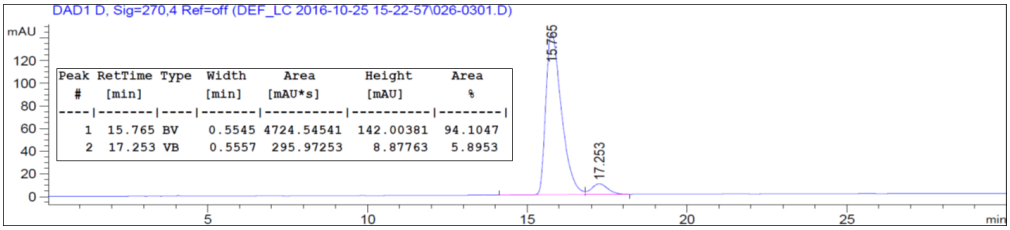


Table 1 (entry 4, NaO^{t}Bu (3 equiv), rt, 10 min)

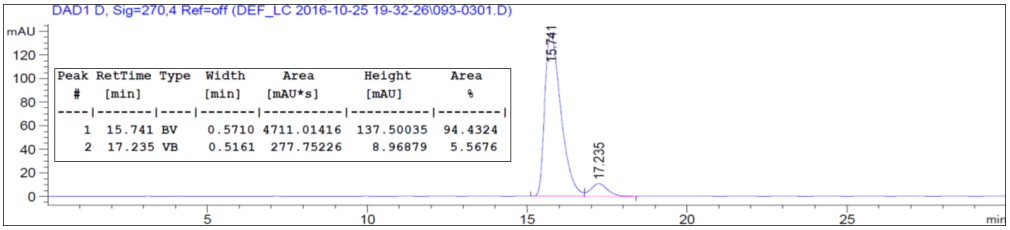


Table 1 (entry 5, NaO^{t}Bu (0.5equiv), rt, 2 h)

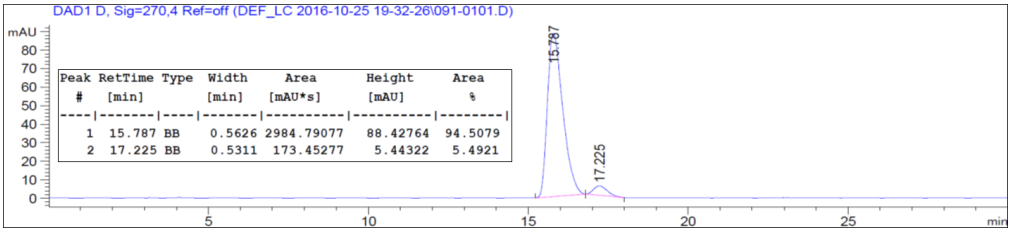


Table 1 (entry 6, NaO^{t}Bu (1.1equiv), 0 ℃, 2 h)

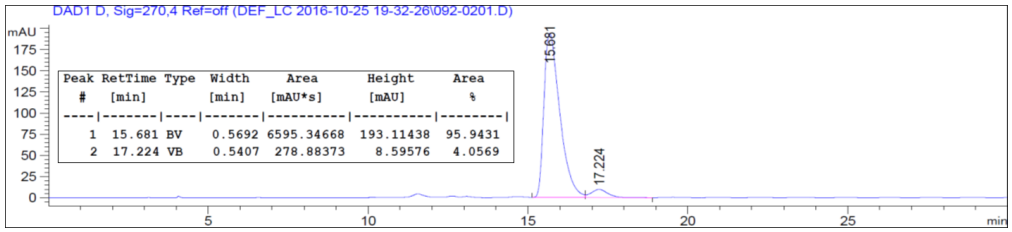


Table 1 (entry 7, NaO^{t}Bu (1.1equiv), –20 ℃, 12 h)

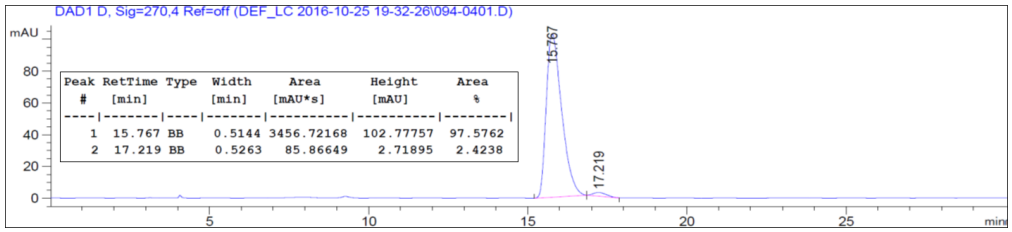


Table 1 (entry 8, NaO^{t}Bu (1.1equiv), –40 ℃, 72 h)

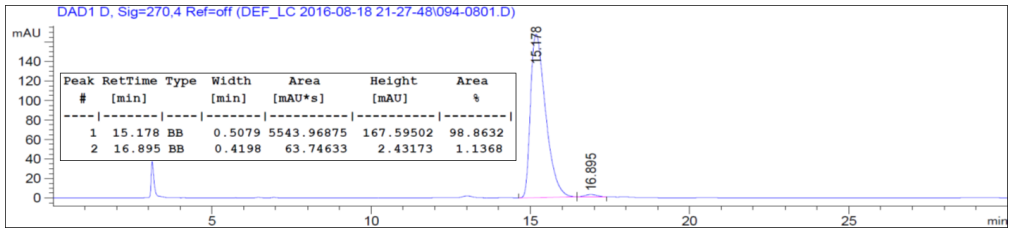


Table 1 (entry 9, NaOEt (1.1equiv), rt, 12 h)

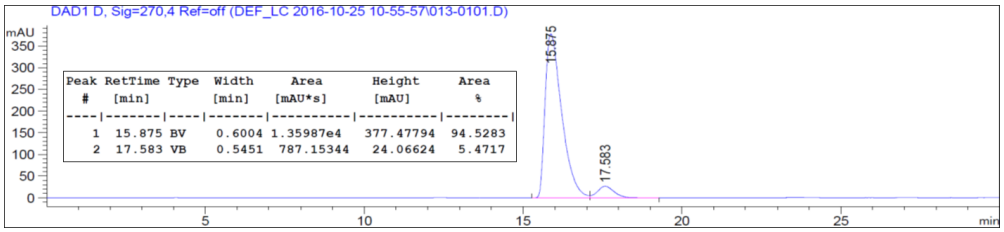
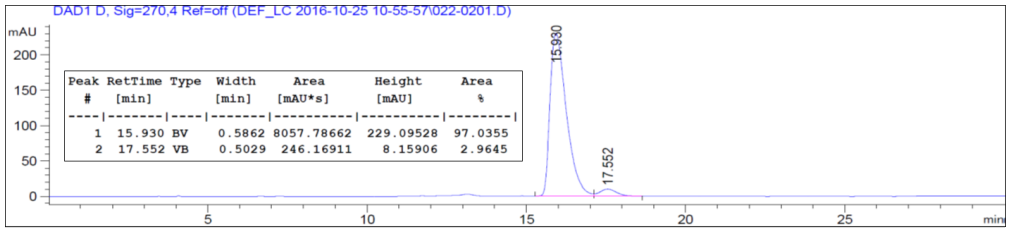
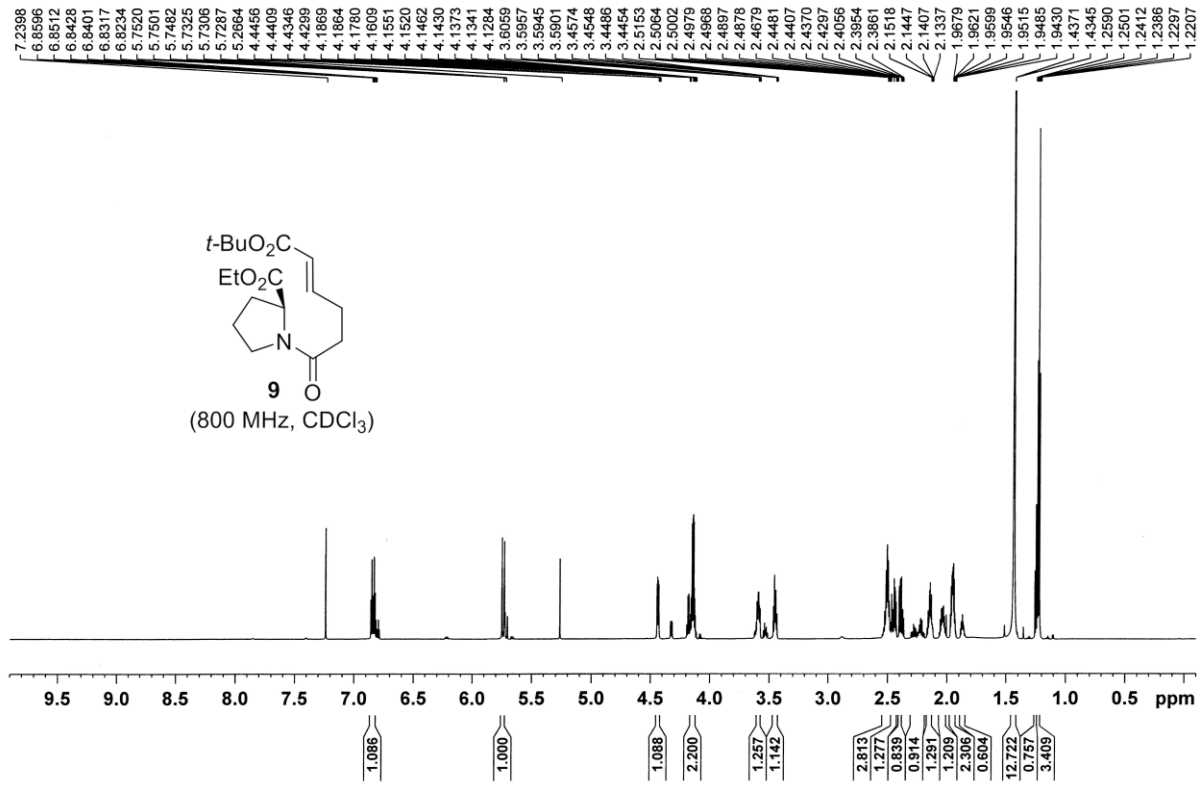
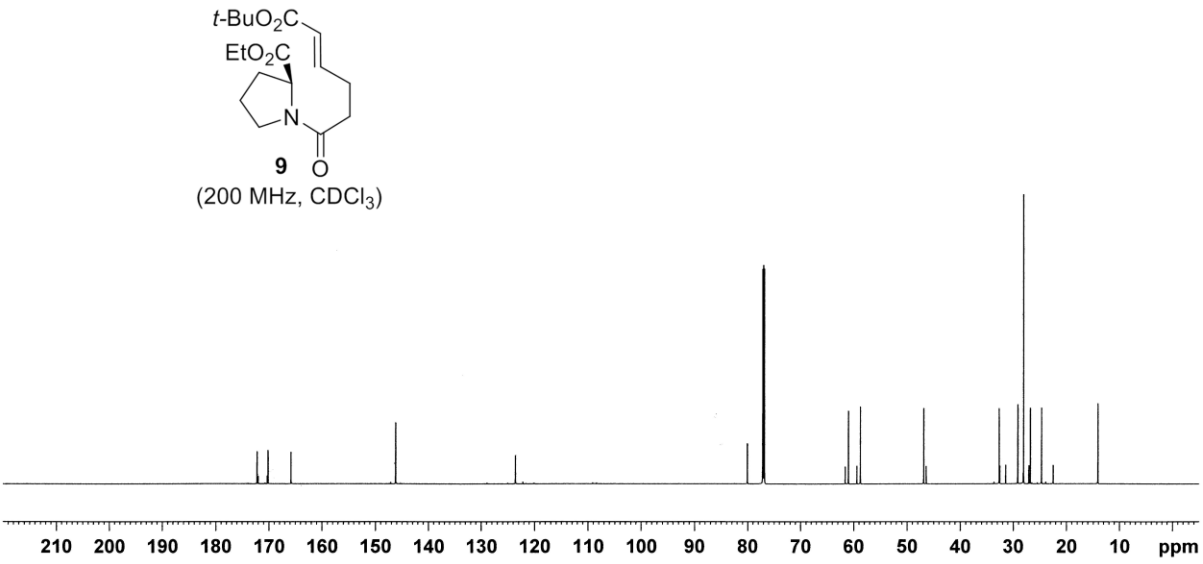


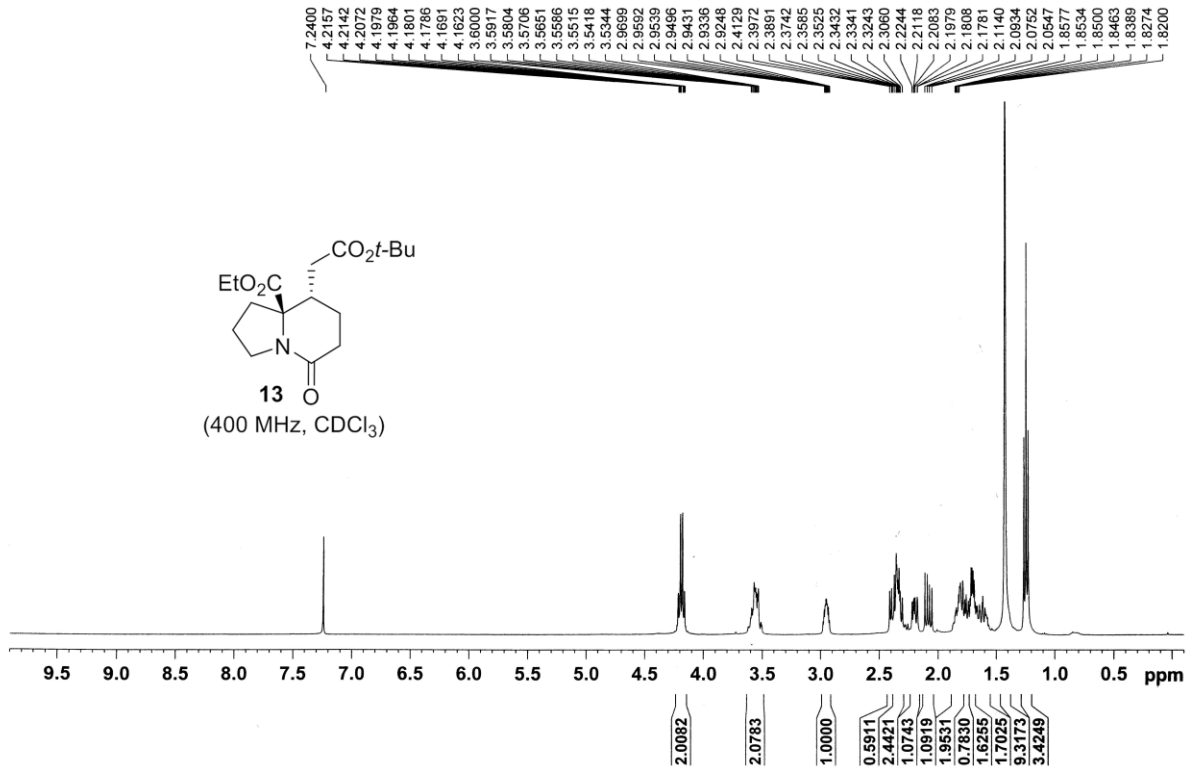
Table 1 (entry 10, NaHMDS (3 equiv), –78 ℃, 1 h)

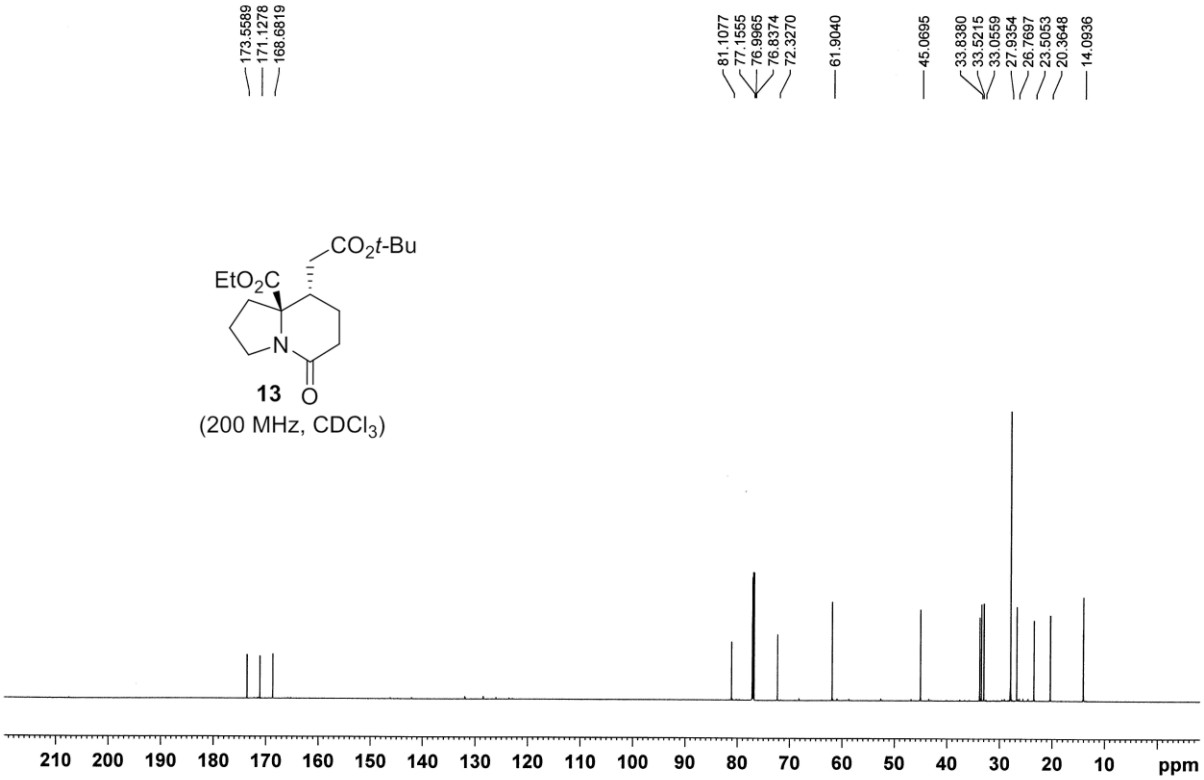


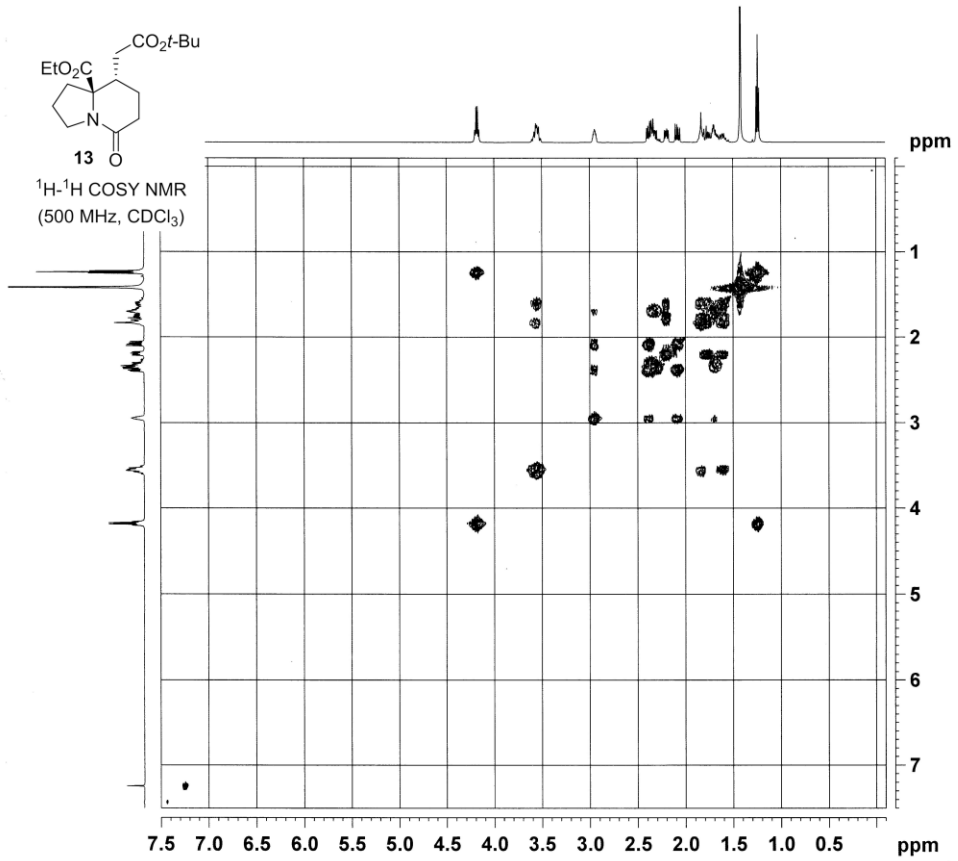
E. Copies of spectra



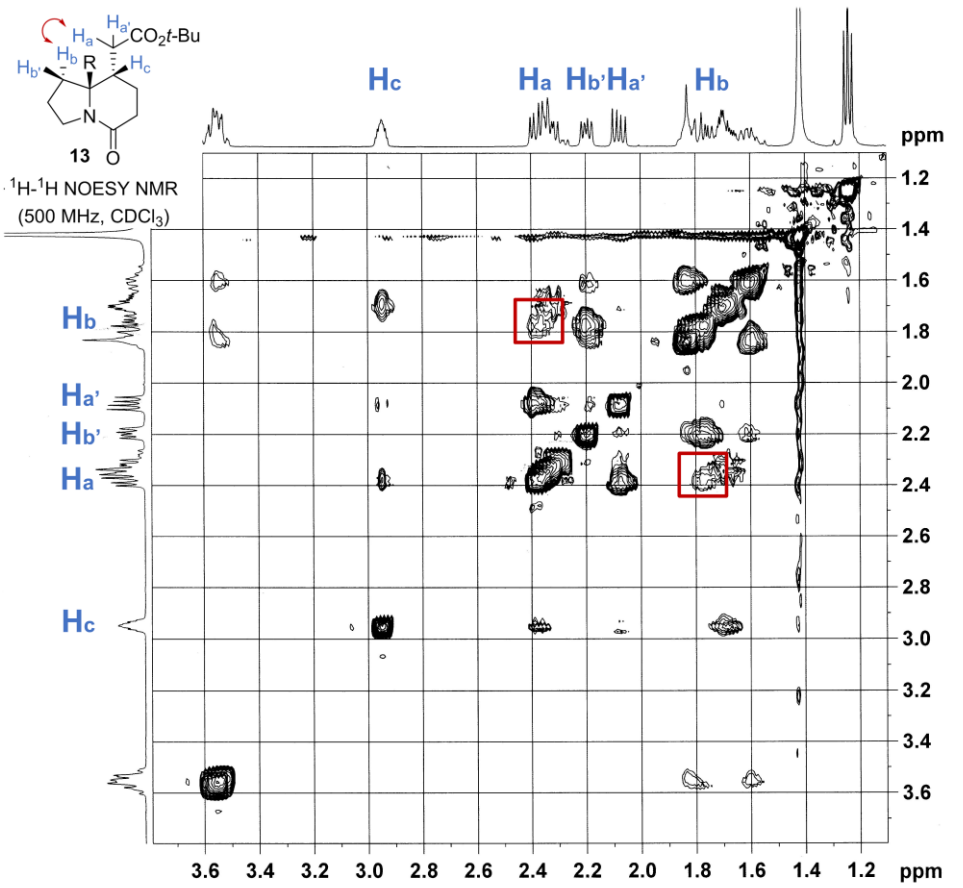



7.2400
4.2157
4.2142
4.2072
4.1979
4.1964
4.1801
4.1786
4.1691
4.1623
3.6000
3.5917
3.5804
3.5706
3.5651
3.5586
3.5515
3.5418
3.5344
2.9699
2.9592
2.9539
2.9496
2.9431
2.9336
2.9248
2.4129
2.3972
2.3891
2.3742
2.3585
2.3525
2.3432
2.3341
2.3243
2.3060
2.2244
2.2118
2.2083
2.1979
2.1808
2.1781
2.1140
2.0934
2.0752
2.0547
1.8577
1.8534
1.8500
1.8463
1.8389
1.8274
1.8200
CO2t-Bu
EtO2C
N
O
13
(400 MHz, CDCl3)
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm
2.0082
2.0783
1.0000
0.5911
2.4421
1.0743
1.0919
1.9531
0.7830
1.6255
1.7025
9.3173
3.4249

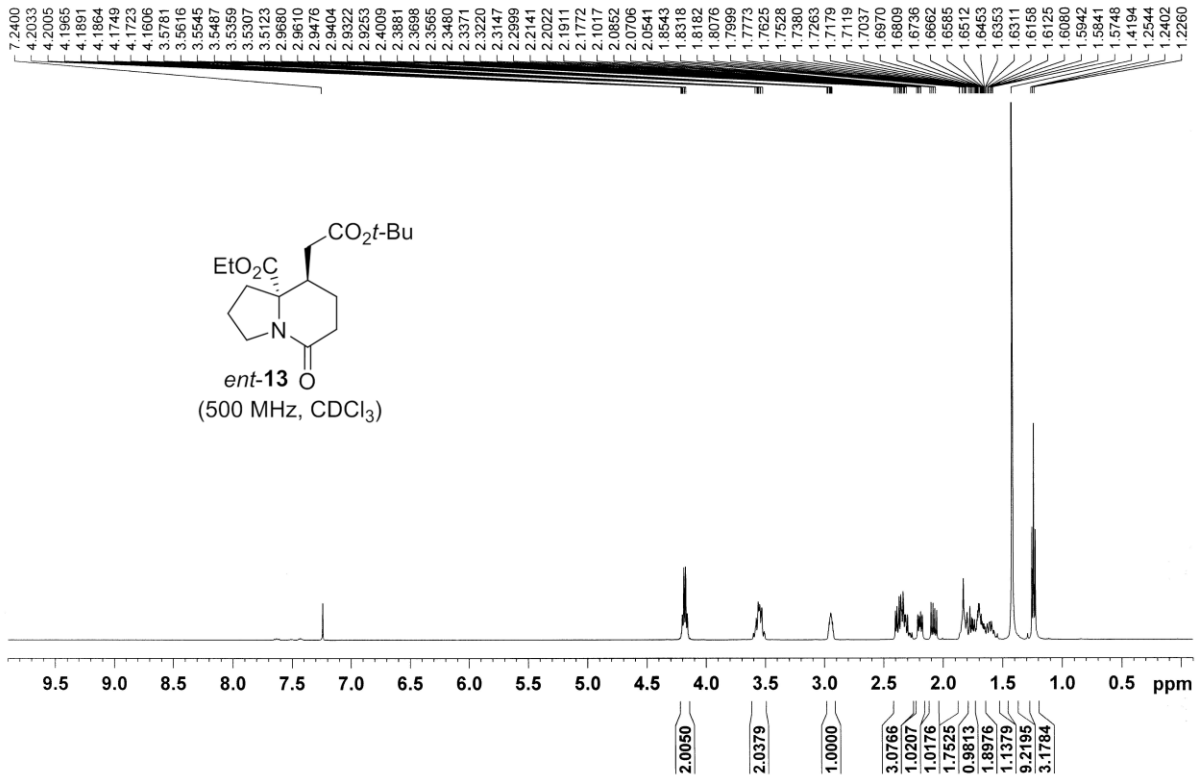

173.5589
171.1278
168.6819
81.1077
77.1555
76.9965
76.8374
72.3270
61.9040
45.0695
33.8380
33.5215
33.0559
27.9354
26.7697
23.5053
20.3648
14.0936
CO2t-Bu
EtO2C
N
O
13
(200 MHz, CDCl3)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

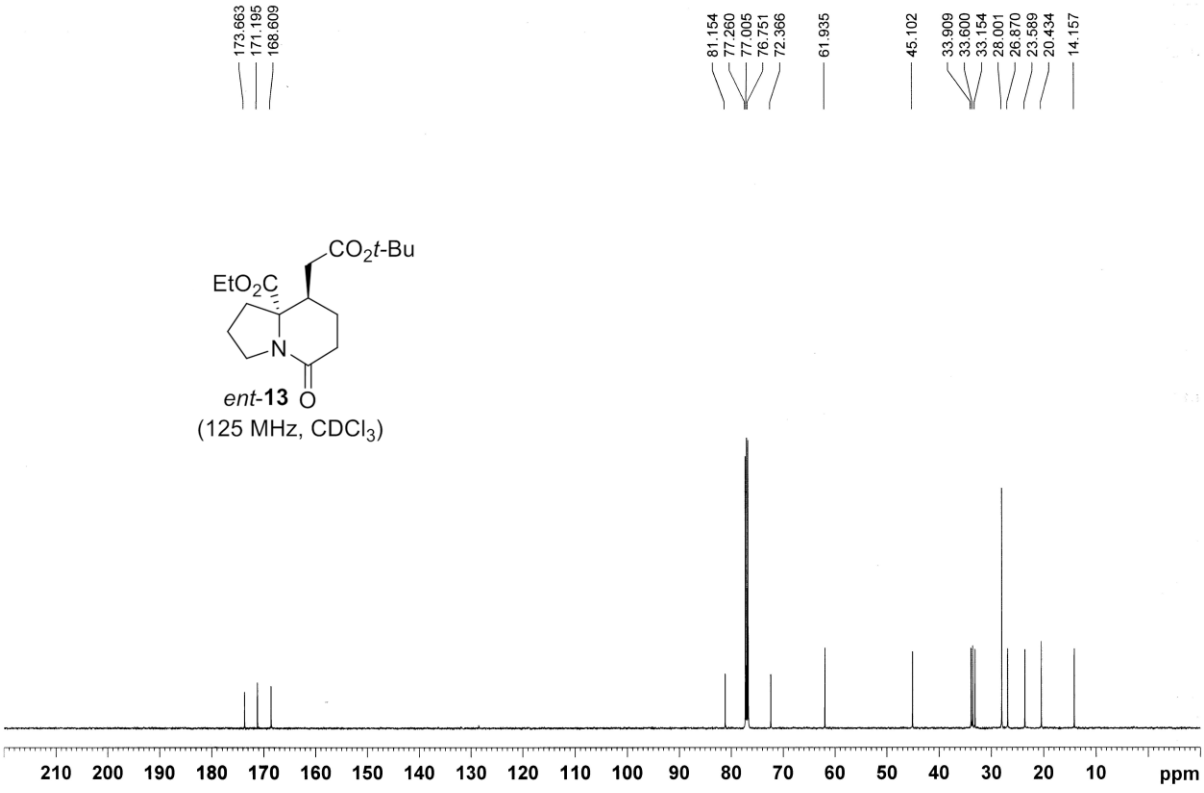


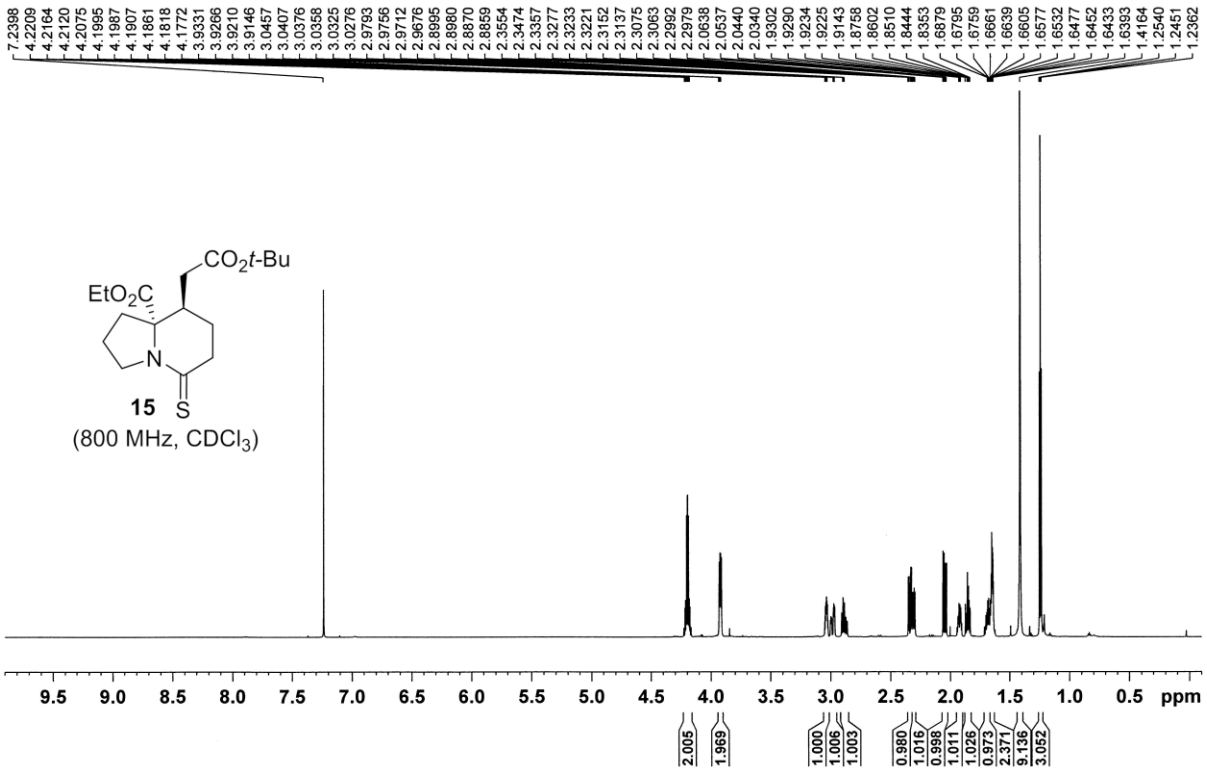

```
Current Data Parameters
NAME                  KSHee-A
EXPNO                      11
PROCNO                      1

F2 - Acquisition Parameters
Date_              20161025
Time                   0.11
INSTRUM                spect
PROBHD   5 mm TXI 13C/1
PULPROG          cosygpqf
TD                      2048
SOLVENT              CDCl3
NS                        16
DS                        16
SWH                7002.801 Hz
FIDRES             3.419337 Hz
AQ                 0.1463486 sec
RG                      90.5
DW                   71.400 usec
DE                    6.50 usec
TE                   296.7 K
D0                 0.00000300 sec
D1                 1.48689198 sec
D13                0.00000300 sec
D16                0.00020000 sec
IN0                0.00014280 sec

======== CHANNEL f1 ========
NUC1                      1H
P0                     10.00 usec
P1                     10.30 usec
PL1                    -1.80 dB
SFO1            500.1324949 MHz

====== GRADIENT CHANNEL =====
GPNAM1               SINE.100
GPNAM2               SINE.100
GPX1                    0.00 %
GPX2                    0.00 %
GPY1                    0.00 %
GPY2                    0.00 %
GPZ1                   10.00 %
GPZ2                   10.00 %
P16                  1000.00 usec

F1 - Acquisition parameters
ND0                        1
TD                       256
SFO1             500.1325 MHz
FIDRES          27.354692 Hz
SW                  14.002 ppm
FnMODE                  QF

F2 - Processing parameters
SI                       2048
SF             500.1300183 MHz
WDW                    SINE
SSB                       0
LB                     0.00 Hz
GB                        0
PC                     1.00

F1 - Processing parameters
SI                        512
MC2                        QF
SF             500.1300187 MHz
WDW                    SINE
SSB                       0
LB                     0.00 Hz
GB                        0
```

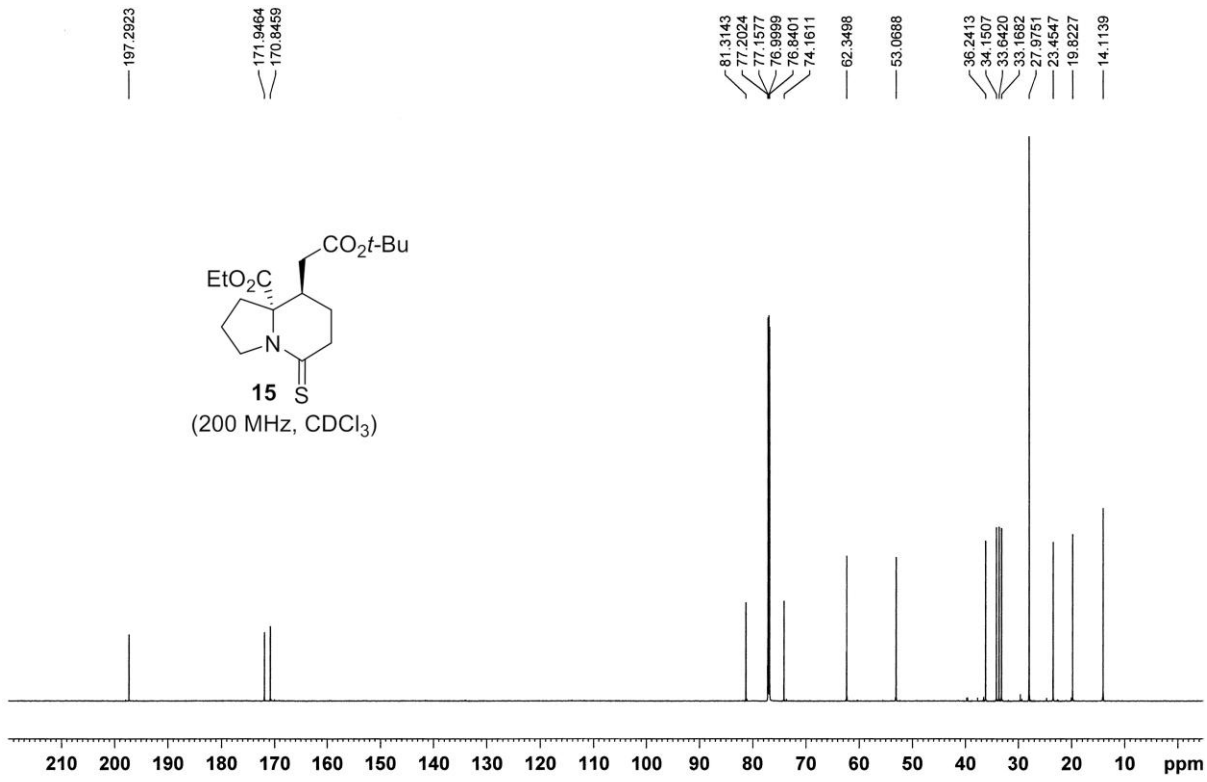


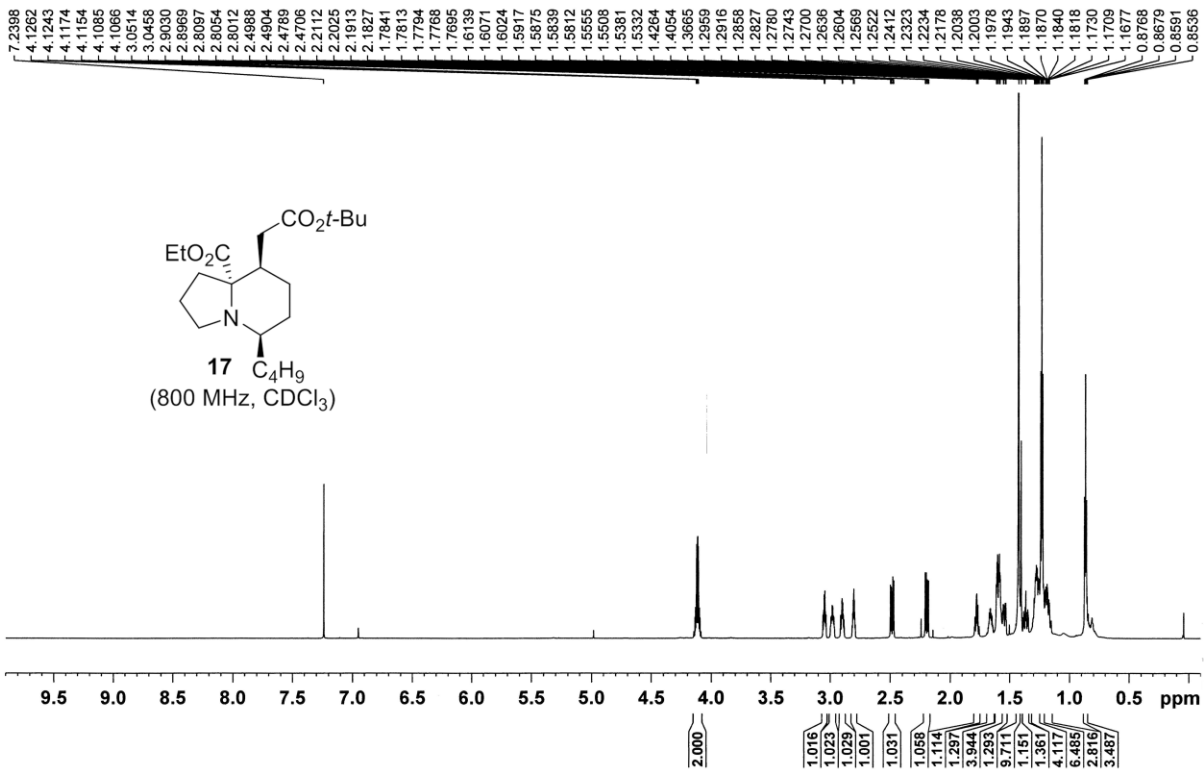

```
Current Data Parameters
NAME                  KSHee-A
EXPNO                      14
PROCNO                      1

F2 - Acquisition Parameters
Date_              20161024
Time                   20.49
INSTRUM                spect
PROBHD   5 mm TXI 13C/1
PULPROG          noesygpph
TD                      2048
SOLVENT              CDCl3
NS                        16
DS                        16
SWH                7002.801 Hz
FIDRES             3.419337 Hz
AQ                 0.1463486 sec
RG                      71.8
DW                   71.400 usec
DE                    6.00 usec
TE                   296.7 K
d0                 0.00005829 sec
D1                 2.00000000 sec
D8                 0.80000001 sec
D16                0.00020000 sec
IN0                0.00014280 sec
ST1CNT                   128
TAU                0.39880002 sec

======== CHANNEL f1 ========
NUC1                      1H
P1                     10.30 usec
P2                     20.00 usec
PL1                    -1.80 dB
SFO1            500.1324949 MHz

====== GRADIENT CHANNEL =====
GPNAM1               SINE.100
GPNAM2               SINE.100
GPX1                    0.00 %
GPX2                    0.00 %
GPY1                    0.00 %
GPY2                    0.00 %
GPZ1                   20.00 %
GPZ2                   20.00 %
P16                  1000.00 usec

F1 - Acquisition parameters
ND0                        1
TD                       256
SFO1             500.1325 MHz
FIDRES          27.354692 Hz
SW                  14.002 ppm
FnMODE          States-TPPI

F2 - Processing parameters
SI                       2048
SF             500.1300236 MHz
WDW                    QSINE
SSB                       2
LB                     0.00 Hz
GB                        0
PC                     1.00

F1 - Processing parameters
SI                       1024
MC2             States-TPPI
SF             500.1300208 MHz
WDW                    QSINE
SSB                       2
LB                     0.00 Hz
GB                        0
```

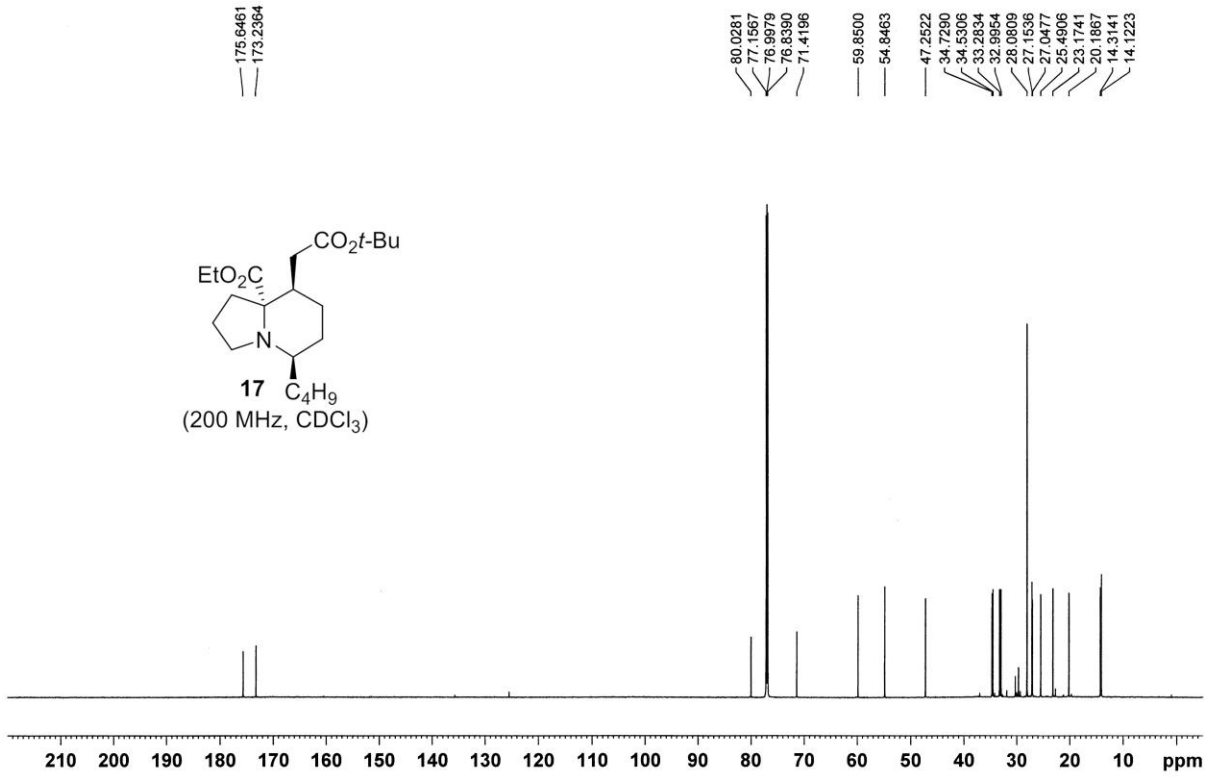

7.2400
4.2033
4.2005
4.1965
4.1891
4.1864
4.1749
4.1723
4.1606
3.5781
3.5616
3.5545
3.5487
3.5359
3.5307
3.5123
2.9680
2.9610
2.9476
2.9404
2.9322
2.9253
2.4009
2.3881
2.3698
2.3565
2.3480
2.3371
2.3220
2.3147
2.2999
2.2141
2.2022
2.1911
2.1772
2.1017
2.0852
2.0706
2.0541
1.8543
1.8318
1.8182
1.8076
1.7999
1.7773
1.7625
1.7528
1.7380
1.7263
1.7179
1.7119
1.7037
1.6970
1.6809
1.6736
1.6662
1.6585
1.6512
1.6453
1.6353
1.6311
1.6158
1.6125
1.6080
1.5942
1.5841
1.5748
1.4194
1.2544
1.2402
1.2260
CO2t-Bu
EtO2C
N
O
ent-13
(500 MHz, CDCl3)
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm
2.0050
2.0379
1.0000
3.0766
1.0207
1.0176
1.7525
0.9813
1.8976
1.1379
9.2195
3.1784

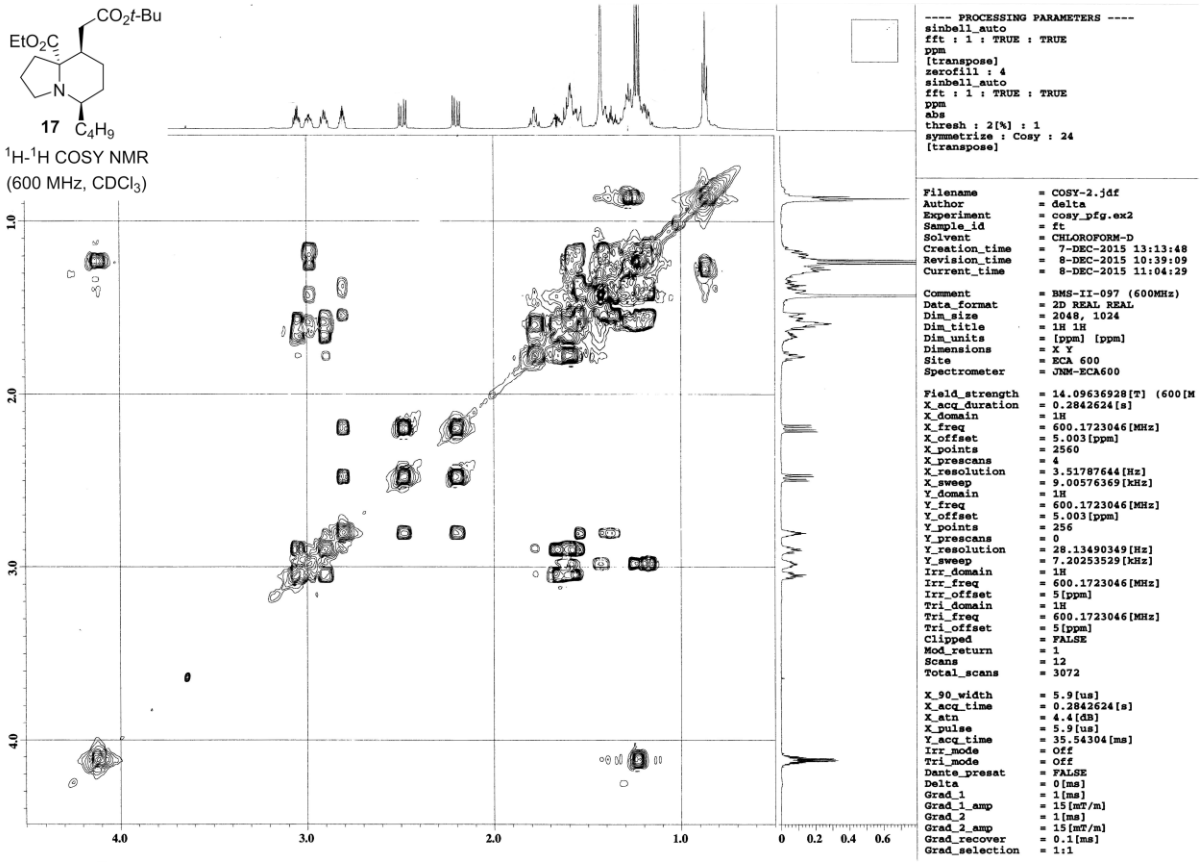

173.663
171.195
168.609
81.154
77.260
77.005
76.751
72.366
61.935
45.102
33.909
33.600
33.154
28.001
26.870
23.589
20.434
14.157
CO2t-Bu
EtO2C
N
O
ent-13
(125 MHz, CDCl3)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm


CO2t-Bu
EtO2C
N
S
15
(800 MHz, CDCl3)
ppm

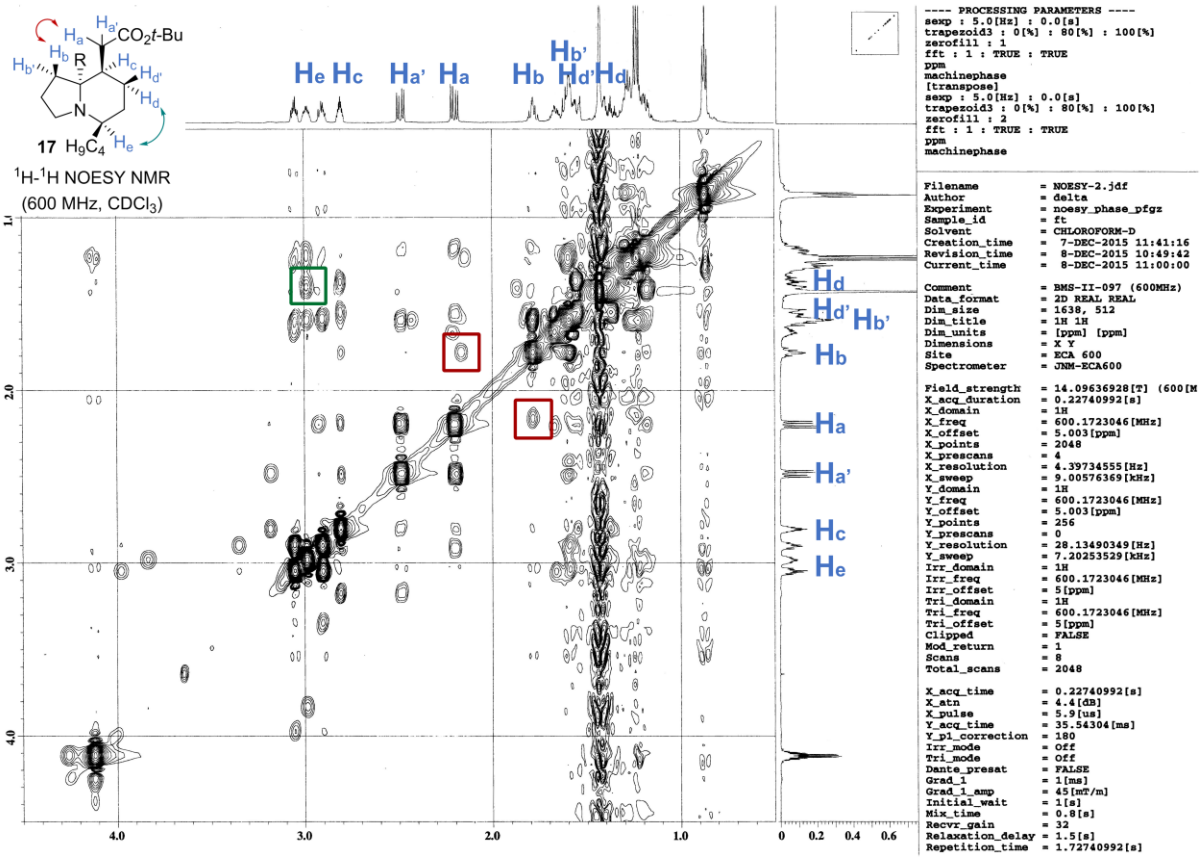

CO2t-Bu
EtO2C
N
S
15
(200 MHz, CDCl3)
ppm


7.2398
4.1262
4.1243
4.1174
4.1154
4.1085
4.1066
3.0514
3.0458
2.9030
2.8969
2.8097
2.8054
2.8012
2.4988
2.4904
2.4789
2.4706
2.2112
2.2025
2.1913
2.1827
1.7841
1.7813
1.7794
1.7768
1.7695
1.6139
1.6071
1.6024
1.5917
1.5875
1.5839
1.5812
1.5555
1.5508
1.5381
1.5332
1.4264
1.4054
1.3665
1.2959
1.2916
1.2858
1.2827
1.2780
1.2743
1.2700
1.2636
1.2604
1.2569
1.2522
1.2412
1.2323
1.2234
1.2178
1.2038
1.2003
1.1978
1.1943
1.1897
1.1870
1.1840
1.1818
1.1730
1.1709
1.1677
0.8768
0.8679
0.8591
0.8536
CO2t-Bu
EtO2C
N
17 C4H9
(800 MHz, CDCl3)
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm
2.000
1.016
1.023
1.029
1.001
1.031
1.058
1.114
1.297
3.944
1.293
9.711
1.151
1.361
4.117
6.485
2.816
3.487

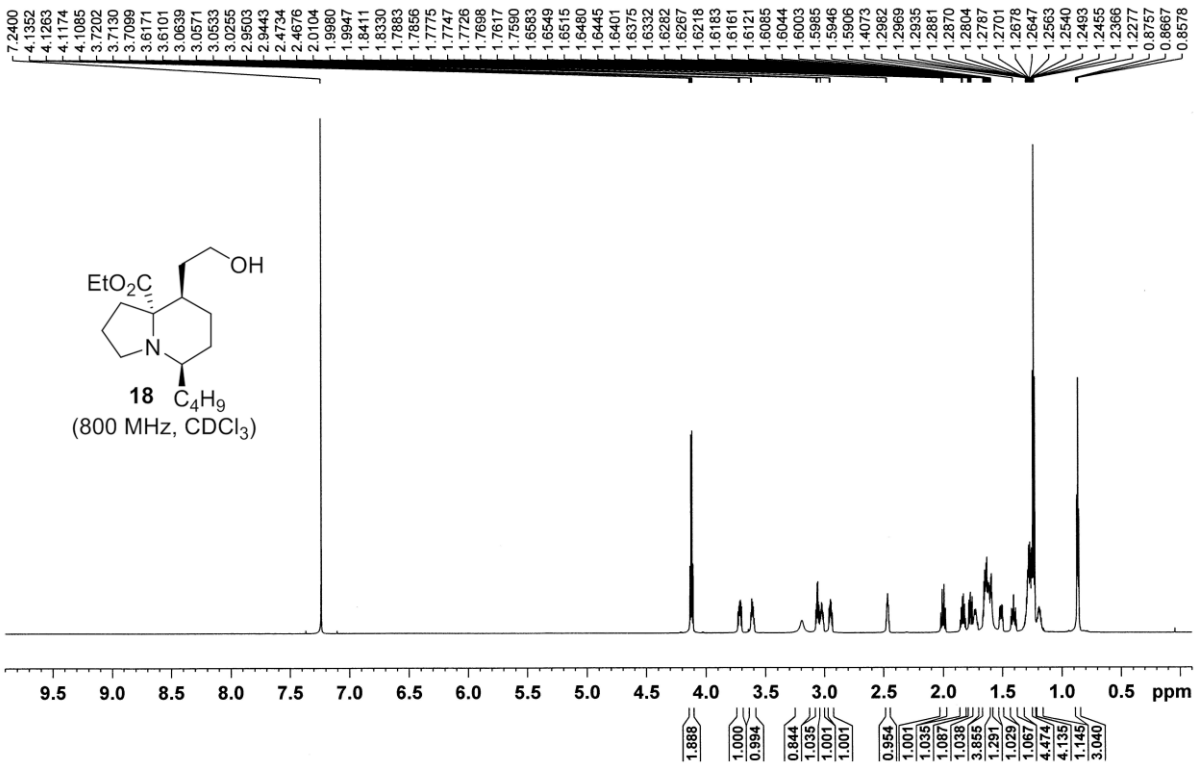

175.6461
173.2364
80.0281
77.1567
76.9979
76.8390
71.4196
59.8500
54.8463
47.2522
34.7290
34.5306
33.2834
32.9954
28.0809
27.1536
27.0477
25.4906
23.1741
20.1867
14.3141
14.1223
CO2t-Bu
EtO2C
N
17 C4H9
(200 MHz, CDCl3)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

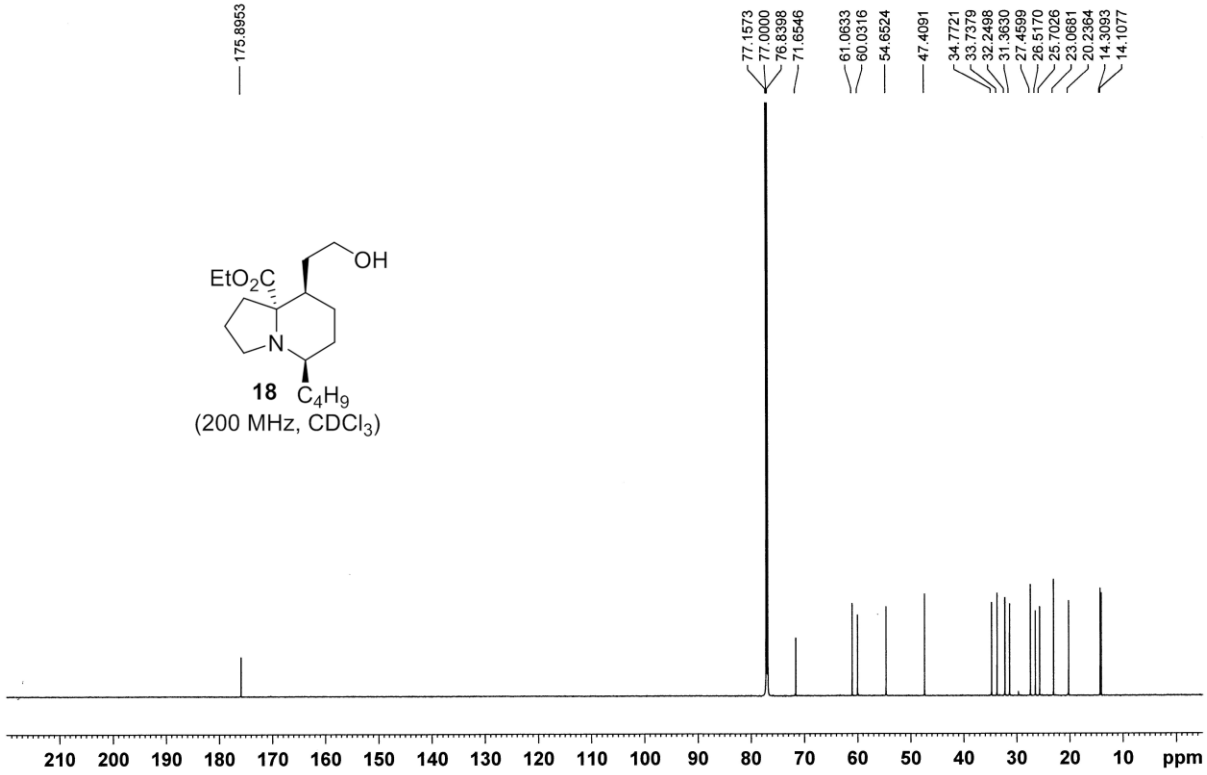


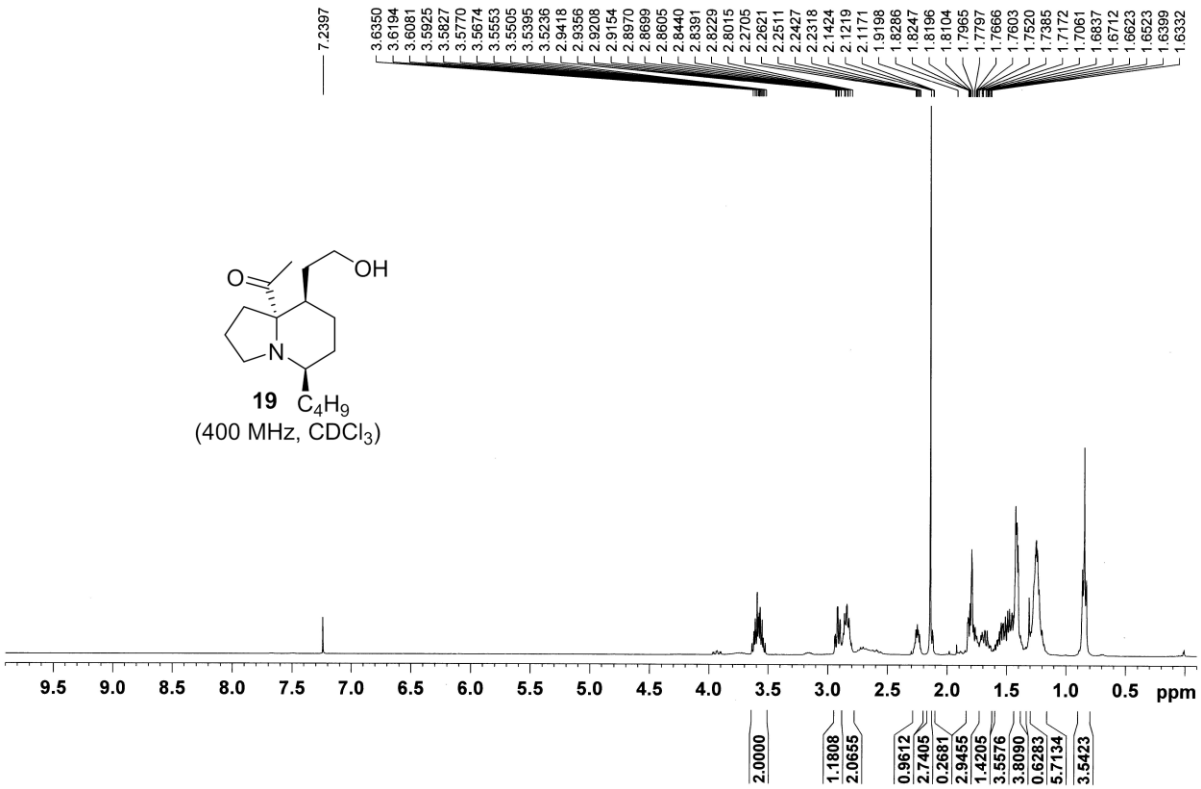

```
---- PROCESSING PARAMETERS ----
sinbell_auto
fft : 1 : TRUE : TRUE
ppm
[transpose]
zerofill : 4
sinbell_auto
fft : 1 : TRUE : TRUE
ppm
abs
thresh : 2[%] : 1
symmetrize : Cosy : 24
[transpose]

Filename          = COSY-2.jdf
Author            = delta
Experiment        = cosy_pfg.ex2
Sample_id         = ft
Solvent           = CHLOROFORM-D
Creation_time     =  7-DEC-2015 13:13:48
Revision_time     =  8-DEC-2015 10:39:09
Current_time      =  8-DEC-2015 11:04:29

Comment           = BMS-II-097 (600MHz)
Data_format       = 2D REAL REAL
Dim_size          = 2048, 1024
Dim_title         = 1H 1H
Dim_units         = [ppm] [ppm]
Dimensions        = X Y
Site              = ECA 600
Spectrometer      = JNM-ECA600

Field_strength    = 14.09636928[T] (600[M
X_acq_duration    = 0.2842624[s]
X_domain          = 1H
X_freq            = 600.1723046[MHz]
X_offset          = 5.003[ppm]
X_points          = 2560
X_prescans        = 4
X_resolution      = 3.51787644[Hz]
X_sweep           = 9.00576369[kHz]
Y_domain          = 1H
Y_freq            = 600.1723046[MHz]
Y_offset          = 5.003[ppm]
Y_points          = 256
Y_prescans        = 0
Y_resolution      = 28.13490349[Hz]
Y_sweep           = 7.20253529[kHz]
Irr_domain        = 1H
Irr_freq          = 600.1723046[MHz]
Irr_offset        = 5[ppm]
Tri_domain        = 1H
Tri_freq          = 600.1723046[MHz]
Tri_offset        = 5[ppm]
Clipped           = FALSE
Mod_return        = 1
Scans             = 12
Total_scans       = 3072

X_90_width        = 5.9[us]
X_acq_time        = 0.2842624[s]
X_atn             = 4.4[dB]
X_pulse           = 5.9[us]
Y_acq_time        = 35.54304[ms]
Irr_mode          = Off
Tri_mode          = Off
Dante_presat      = FALSE
Delta             = 0[ms]
Grad_1            = 1[ms]
Grad_1_amp        = 15[mT/m]
Grad_2            = 1[ms]
Grad_2_amp        = 15[mT/m]
Grad_recover      = 0.1[ms]
Grad_selection    = 1:1
```

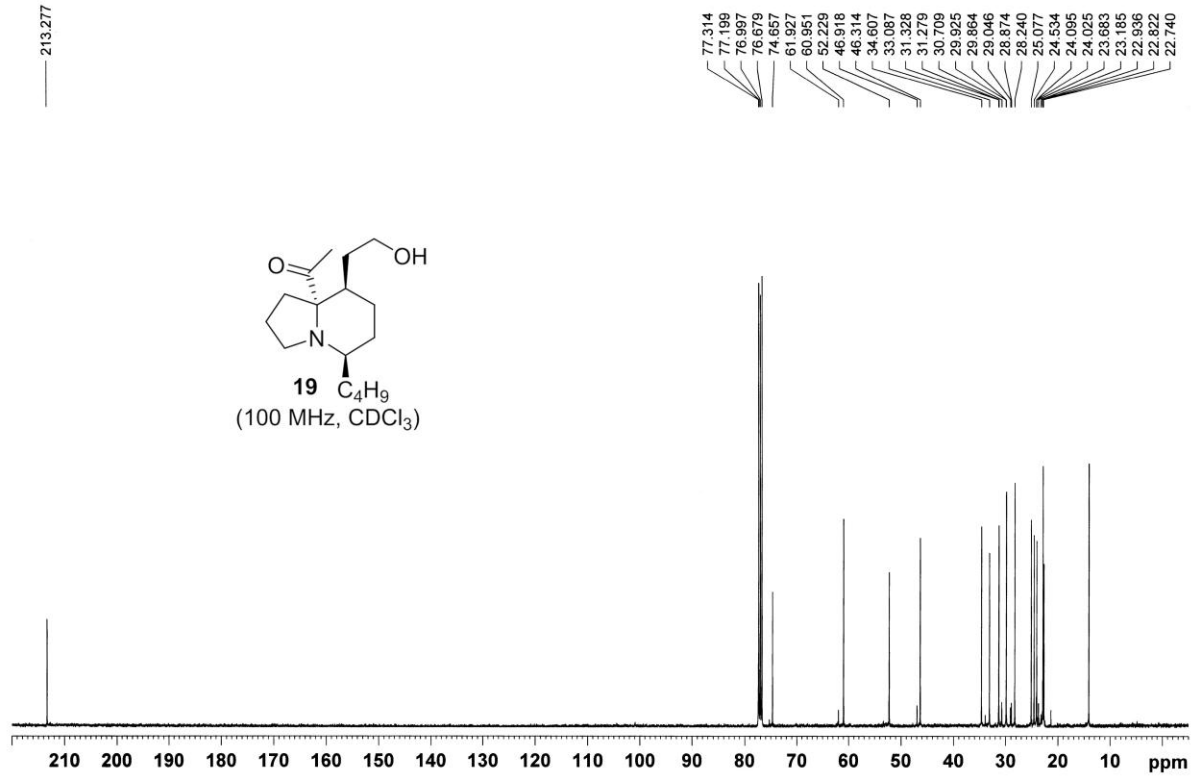


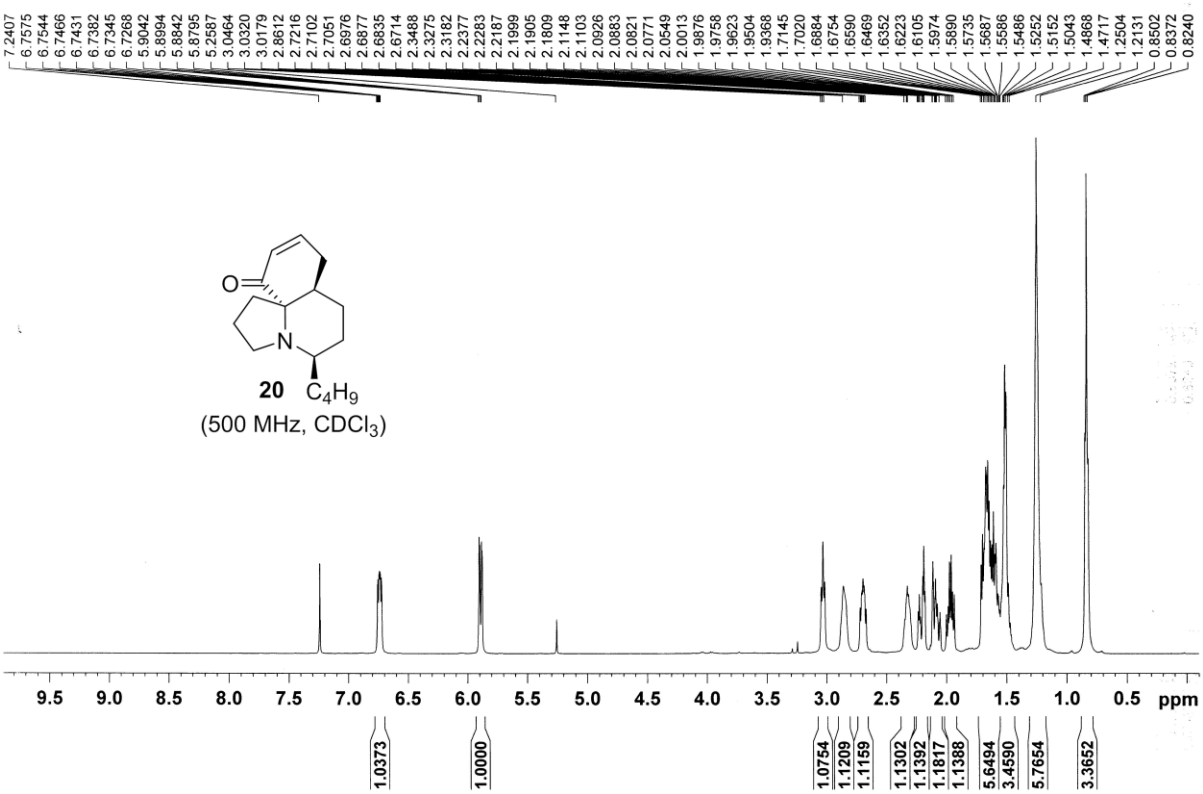

```
---- PROCESSING PARAMETERS ----
sexp : 5.0[Hz] : 0.0[s]
trapezoid3 : 0[%] : 80[%] : 100[%]
zerofill : 1
fft : 1 : TRUE : TRUE
ppm
machinephase
[transpose]
sexp : 5.0[Hz] : 0.0[s]
trapezoid3 : 0[%] : 80[%] : 100[%]
zerofill : 2
fft : 1 : TRUE : TRUE
ppm
machinephase

Filename          = NOESY-2.jdf
Author            = delta
Experiment        = noesy_phase_pfgz
Sample_id         = ft
Solvent           = CHLOROFORM-D
Creation_time     =  7-DEC-2015 11:41:16
Revision_time     =  8-DEC-2015 10:49:42
Current_time      =  8-DEC-2015 11:00:00

Comment           = BMS-II-097 (600MHz)
Data_format       = 2D REAL REAL
Dim_size          = 1638, 512
Dim_title         = 1H 1H
Dim_units         = [ppm] [ppm]
Dimensions        = X Y
Site              = ECA 600
Spectrometer      = JNM-ECA600

Field_strength    = 14.09636928[T] (600[M
X_acq_duration    = 0.22740992[s]
X_domain          = 1H
X_freq            = 600.1723046[MHz]
X_offset          = 5.003[ppm]
X_points          = 2048
X_prescans        = 4
X_resolution      = 4.39734555[Hz]
X_sweep           = 9.00576369[kHz]
Y_domain          = 1H
Y_freq            = 600.1723046[MHz]
Y_offset          = 5.003[ppm]
Y_points          = 256
Y_prescans        = 0
Y_resolution      = 28.13490349[Hz]
Y_sweep           = 7.20253529[kHz]
Irr_domain        = 1H
Irr_freq          = 600.1723046[MHz]
Irr_offset        = 5[ppm]
Tri_domain        = 1H
Tri_freq          = 600.1723046[MHz]
Tri_offset        = 5[ppm]
Clipped           = FALSE
Mod_return        = 1
Scans             = 8
Total_scans       = 2048

X_acq_time        = 0.22740992[s]
X_atn             = 4.4[dB]
X_pulse           = 5.9[us]
Y_acq_time        = 35.54304[ms]
Y_pl_correction   = 180
Irr_mode          = Off
Tri_mode          = Off
Dante_presat      = FALSE
Grad_1            = 1[ms]
Grad_1_amp        = 45[mT/m]
Initial_wait      = 1[s]
Mix_time          = 0.8[s]
Recvr_gain        = 32
Relaxation_delay  = 1.5[s]
Repetition_time   = 1.72740992[s]
```

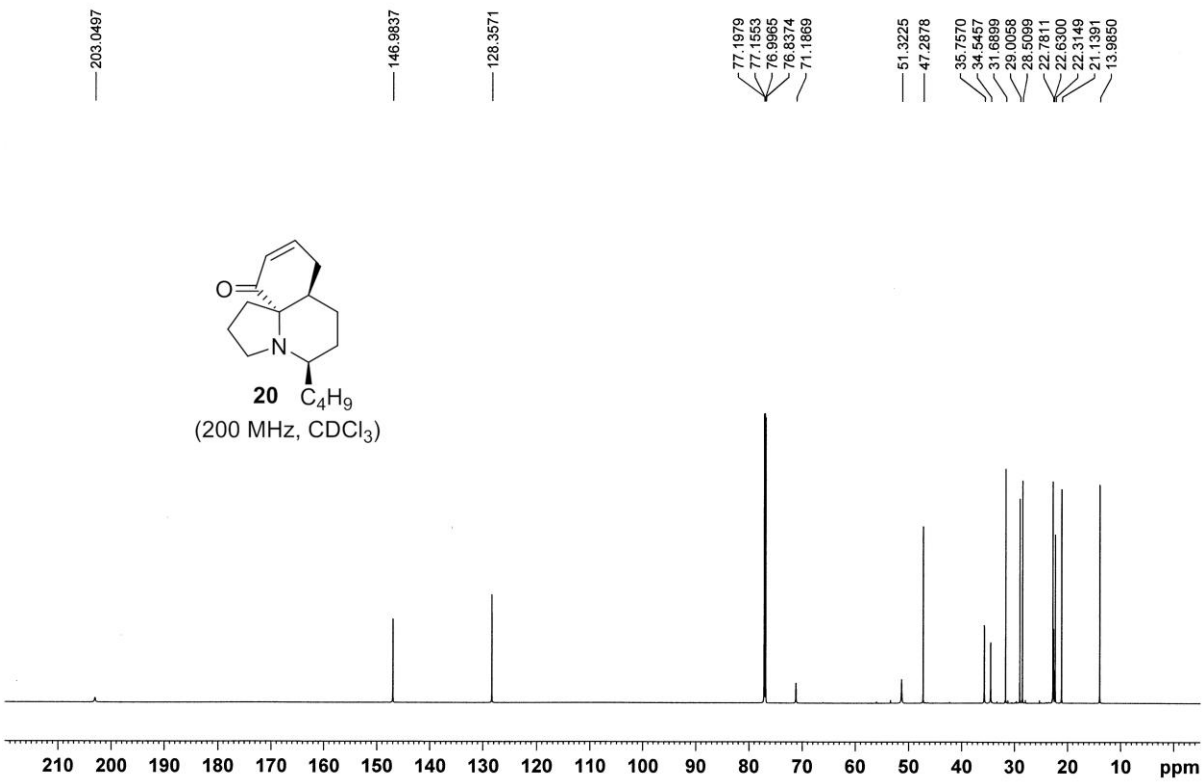

7.2400
4.1352
4.1263
4.1174
4.1085
3.7202
3.7130
3.7099
3.6171
3.6101
3.0639
3.0571
3.0533
3.0255
2.9503
2.9443
2.4734
2.4676
2.0104
1.9980
1.9947
1.8411
1.8330
1.7883
1.7856
1.7775
1.7747
1.7726
1.7698
1.7617
1.7590
1.6583
1.6549
1.6515
1.6480
1.6445
1.6401
1.6375
1.6332
1.6282
1.6267
1.6218
1.6183
1.6161
1.6121
1.6085
1.6044
1.6003
1.5985
1.5946
1.5906
1.4073
1.2982
1.2969
1.2935
1.2881
1.2870
1.2804
1.2787
1.2701
1.2678
1.2647
1.2563
1.2540
1.2493
1.2455
1.2366
1.2277
0.8757
0.8667
0.8578
EtO2C
OH
N
18 C4H9
(800 MHz, CDCl3)
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm
1.888
1.000
0.994
0.844
1.035
1.001
1.001
0.954
1.001
1.035
1.087
1.038
3.855
1.291
1.029
1.067
4.474
4.135
1.145
3.040

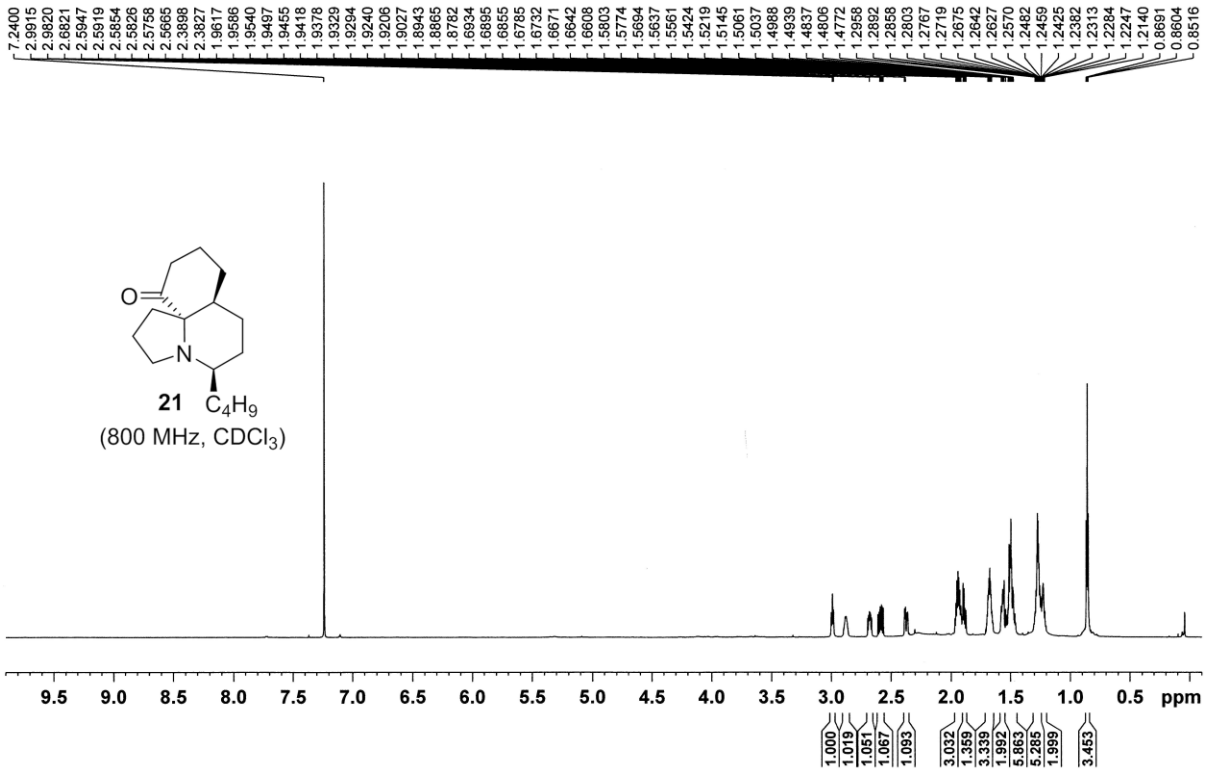

175.8953
77.1573
77.0000
76.8398
71.6546
61.0633
60.0316
54.6524
47.4091
34.7721
33.7379
32.2498
31.3630
27.4599
26.5170
25.7026
23.0681
20.2364
14.3093
14.1077
EtO2C
OH
N
18 C4H9
(200 MHz, CDCl3)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

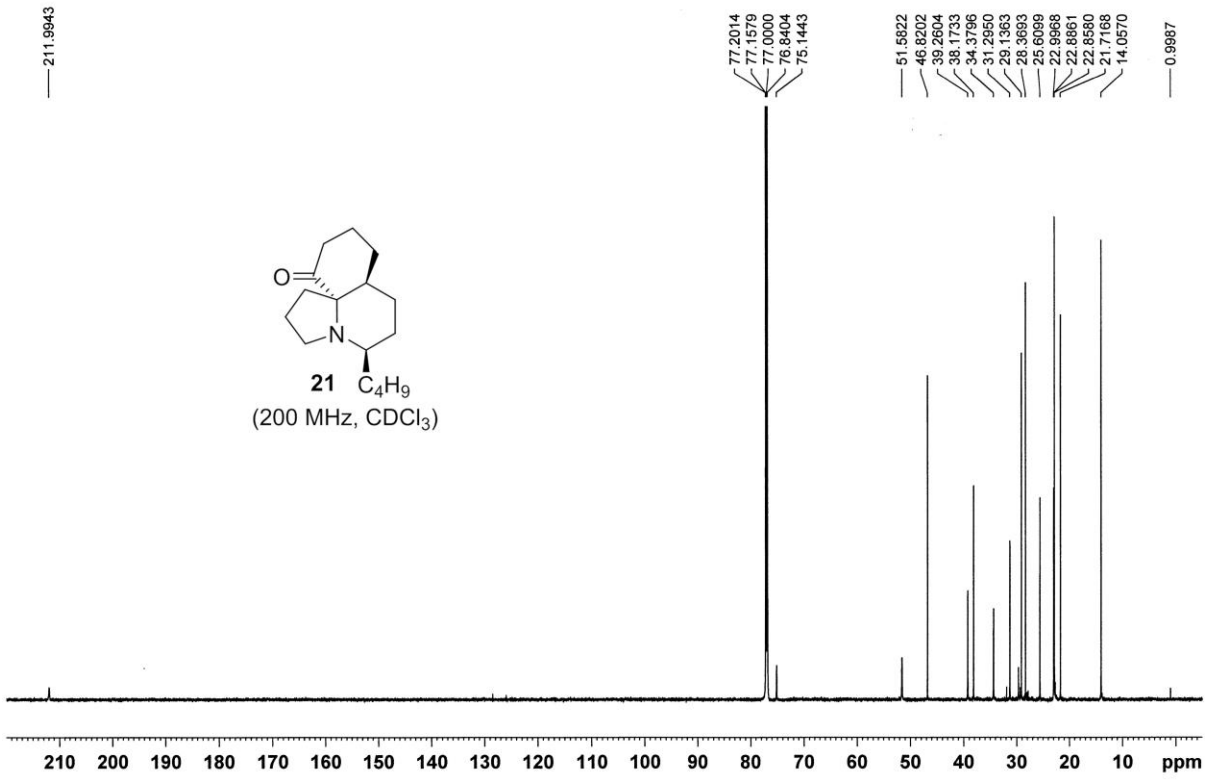

7.2397
3.6350
3.6194
3.6081
3.5925
3.5827
3.5770
3.5674
3.5553
3.5505
3.5395
3.5236
2.9418
2.9356
2.9208
2.9154
2.8970
2.8699
2.8605
2.8440
2.8391
2.8229
2.8015
2.2705
2.2621
2.2511
2.2427
2.2318
2.1424
2.1219
2.1171
1.9198
1.8286
1.8247
1.8196
1.8104
1.7965
1.7797
1.7666
1.7603
1.7520
1.7385
1.7172
1.7061
1.6837
1.6712
1.6623
1.6523
1.6399
1.6332
O
OH
N
19 C4H9
(400 MHz, CDCl3)
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm
2.0000
1.1808
2.0655
0.9612
2.7405
0.2681
2.9455
1.4205
3.5576
3.8090
0.6283
5.7134
3.5423

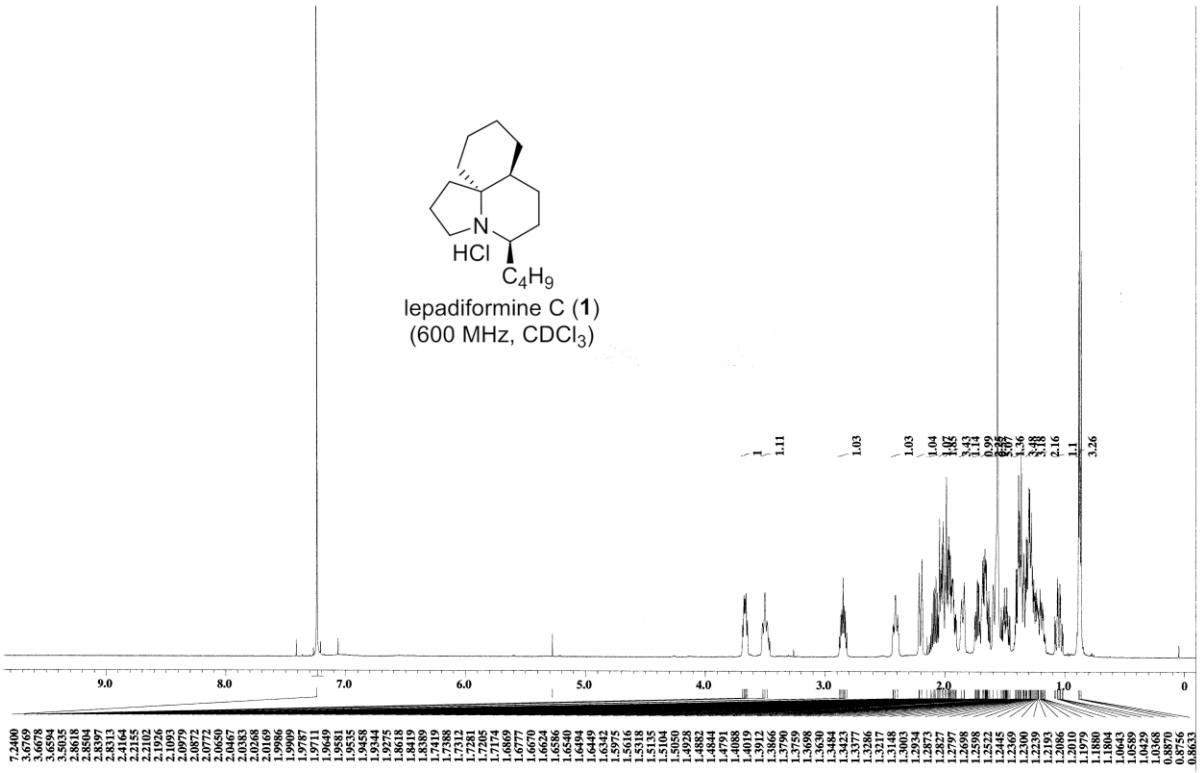

213.277
77.314
77.199
76.997
76.679
74.657
61.927
60.951
52.229
46.918
46.314
34.607
33.087
31.328
31.279
30.709
29.925
29.864
29.046
28.874
28.240
25.077
24.534
24.095
24.025
23.683
23.185
22.936
22.822
22.740
O
OH
N
19 C4H9
(100 MHz, CDCl3)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

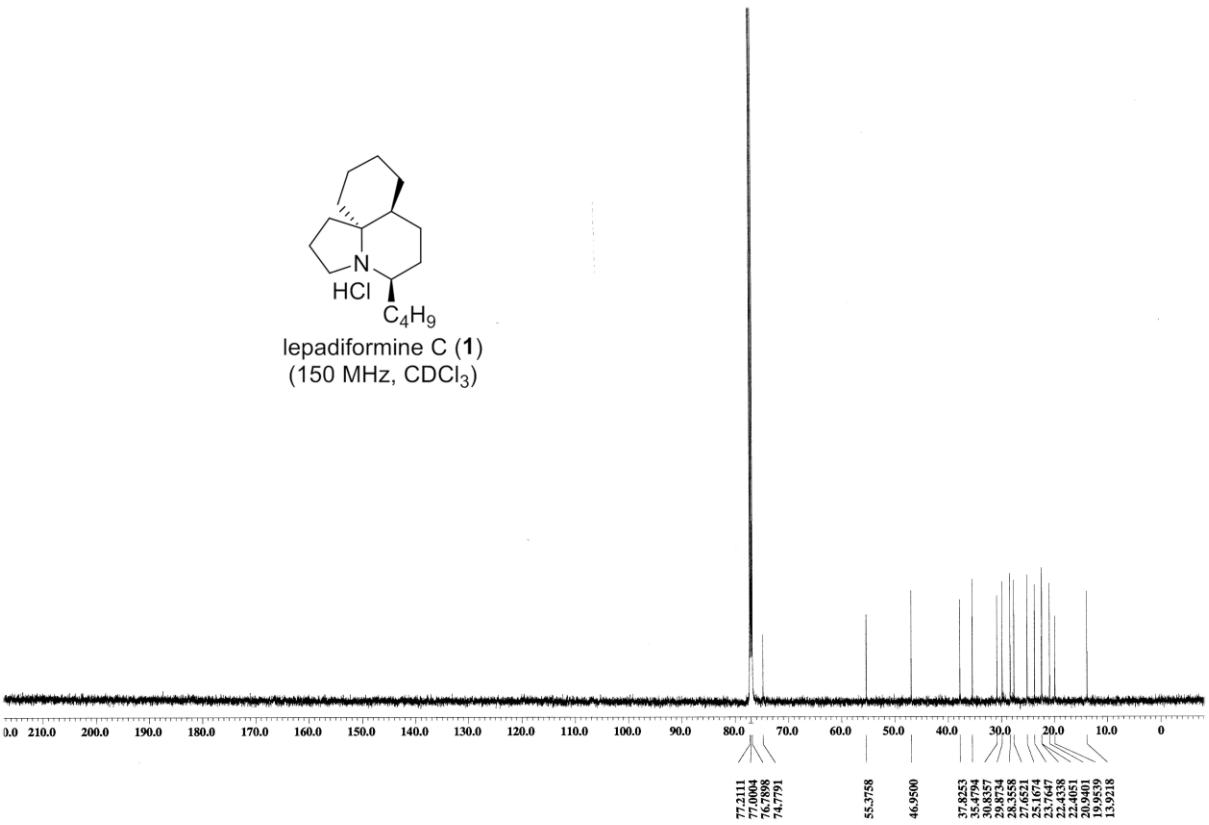

7.2407
6.7575
6.7544
6.7466
6.7431
6.7382
6.7345
6.7268
6.7102
6.7051
6.6976
6.6877
6.6835
6.6714
6.3488
6.3275
6.3182
6.2377
6.2283
6.2187
6.1999
6.1905
6.1809
6.1148
6.1103
6.0926
6.0883
6.0821
6.0771
6.0549
6.0013
5.9876
5.9758
5.9623
5.9504
5.9368
5.8842
5.8795
5.2587
3.0464
3.0320
3.0179
2.8612
2.7216
2.7102
2.7051
2.6976
2.6877
2.6835
2.6714
2.3488
2.3275
2.3182
2.2377
2.2283
2.2187
2.1999
2.1905
2.1809
2.1148
2.1103
2.0926
2.0883
2.0821
2.0771
2.0549
2.0013
1.9876
1.9758
1.9623
1.9504
1.9368
1.7145
1.7020
1.6884
1.6754
1.6590
1.6469
1.6352
1.6223
1.6105
1.5974
1.5890
1.5735
1.5687
1.5586
1.5486
1.5252
1.5152
1.5043
1.4868
1.4717
1.2504
1.2131
0.8502
0.8372
0.8240
O
N
20 C4H9
(500 MHz, CDCl3)
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm
1.0373
1.0000
1.0754
1.1209
1.1159
1.1302
1.1392
1.1817
1.1388
5.6494
3.4590
5.7654
3.3652


203.0497
146.9837
128.3571
77.1979
77.1553
76.9965
76.8374
71.1869
51.3225
47.2878
35.7570
34.5457
31.6899
29.0058
28.5099
22.7811
22.6300
22.3149
21.1391
13.9850
O
N
20 C4H9
(200 MHz, CDCl3)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm


7.2400
2.9915
2.9820
2.6821
2.5947
2.5919
2.5854
2.5826
2.5758
2.5665
2.3898
2.3827
1.9617
1.9586
1.9540
1.9497
1.9455
1.9418
1.9378
1.9329
1.9294
1.9240
1.9206
1.9027
1.8943
1.8885
1.8782
1.6934
1.6895
1.6855
1.6785
1.6732
1.6671
1.6642
1.6608
1.5803
1.5774
1.5694
1.5637
1.5561
1.5424
1.5219
1.5145
1.5061
1.5037
1.4988
1.4939
1.4837
1.4806
1.4772
1.2958
1.2892
1.2858
1.2803
1.2767
1.2719
1.2675
1.2642
1.2627
1.2570
1.2482
1.2459
1.2425
1.2382
1.2313
1.2284
1.2247
1.2140
0.8691
0.8604
0.8516
O
N
21 C_4H_9
(800 MHz, $CDCl_3$)
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm
1.000
1.019
1.051
1.067
1.093
3.032
1.359
3.339
1.992
5.863
5.285
1.999
3.453


211.9943
77.2014
77.1579
77.0000
76.8404
75.1443
51.5822
46.8202
39.2604
38.1733
34.3796
31.2950
29.1363
28.3693
25.6099
22.9968
22.8861
22.8580
21.7168
14.0570
0.9987
O
N
21 C_4H_9
(200 MHz, $CDCl_3$)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm


HCl
C_4H_9
lepadiformine C (**1**)
(600 MHz, $CDCl_3$)


HCl
C_4H_9
lepadiformine C (**1**)
(150 MHz, $CDCl_3$)