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Electronic Supplementary Information

A short total synthesis of (±)-mersicarpine via visible light-induced cascade photooxygenation

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1 General information

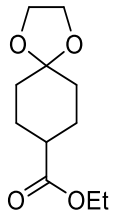
Commercially available chemicals were used as received from suppliers unless otherwise noted. Dry solvents used were obtained from suppliers in serum-cap quality. Unless otherwise noted, reactions were performed under an atmosphere of argon. Solvents for chromatographic separation were distilled twice prior to use. Thin-layer chromatography was carried out using silica-coated aluminium plates, silica 60 F_{254}, *Merck*. Column chromatography was performed with silica 60 (230-400 mesh, *Macherey-Nagel*). NMR spectra were recorded on *Bruker AVANCE 500 NEO*, *Bruker AVANCE 300 III* and *Bruker AVANCE 250 II* instruments. Spectra were calibrated against the solvent resonances of $CHCl_3$ (δ^H = 7.26 ppm) and $CDCl_3$ (δ^C = 77.0 ppm), as well as CD_3OH (δ^H = 3.31 ppm) and CD_3OD (δ^C = 49.0 ppm). ^{1}H- and ^{13}C-NMR peak assignments were made based on 2D NMR spectra. IR spectra were obtained using a *Nicolet 380 FT-IR* spectrometer by *Thermo Fisher Scientific*. ESI-TOF HRMS spectrometry was performed using an *Agilent* 1200/6210 Time-of-Flight LC-MS instrument. Optical rotation was measured with a *Gyromat-HP* polarimeter by *Anton Paar OptoTec*.

2 Experimental procedures

2.1 Synthesis of tetrahydrocarbazole 11

The synthesis of nitrile **8** starting from ethyl 4-oxocyclohexane-1-carboxylate (**2**) was performed along literature protocols.[1] Nitrile **8** was then further elaborated into ketone **9** and tetrahydrocarbazole **11**.

Ethyl 1,4-dioxaspiro[4.5]decane-8-carboxylate (3)



3

A mixture of ethyl 4-oxocyclohexane-1-carboxylate (**2**, 4.63 mL, 4.94 g, 29.05 mmol), (+)-10-camphorsulfonic acid (682.0 mg, 2.93 mmol) and ethylene glycol (8.30 mL, 9.24 g, 148.8 mmol) in toluene (67 mL) was heated to reflux with a Dean-Stark apparatus for 10 h. The mixture was cooled to r.t., and diluted with Et_2O. The mixture was washed with saturated aq. $NaHCO_3$ (2×) and brine (1×). The layers were separated and the organic layer was dried over $MgSO_4$, filtered and concentrated to dryness. Column chromatography (silica gel, heptane/Et_2O 2:1) gave compound **3** (5.50 g, 88%) as a colorless oil.

$\mathbf{R_f}$ = 0.34 (heptane/Et_2O 2:1).

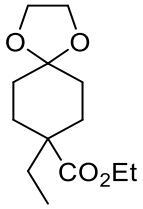
[1] J. Bergès, B. García and K. Muñiz, *Angew. Chem. Int. Ed.*, 2018, **57**, 15891-15895.

^{1}H NMR (300 MHz, $CDCl_3$) δ = 1.23 (t, *J* = 7.1 Hz, 3 H, CH_3), 1.47–1.60 (m, 2 H, CH_2), 1.71–1.81 (m, 4 H, 2 × CH_2), 1.86–1.97 (m, 2 H, CH_2), 2.31 (tt, *J* = 3.9, 10.3 Hz, 1 H, CH), 3.92 (s, 4 H, 2 × CH_2), 4.10 (d, *J* = 7.1 Hz, 2 H, CH_2) ppm.

^{13}C NMR (125 MHz, $CDCl_3$) δ = 14.2 (CH_3), 26.2 (CH_2), 33.7 (CH_2), 41.6 (CH), 60.2 (CH_2), 64.2 (2 × CH_2), 108.0 (C^{tert}), 175.1 (CO) ppm.

Analytical data are in agreement with the literature.[1]

Ethyl 8-ethyl-1,4-dioxaspiro[4.5]decane-8-carboxylate (4)



4

Diisopropylamine (3.39 mL, 24.27 mmol) was dissolved in THF (30 mL) and the mixture was cooled to –78 °C. *n*-BuLi (10.29 mL, 25.73 mmol, 2.5 M in hexanes) was added dropwise and the mixture was stirred at –78 °C for further 30 min. The mixture was allowed to warm to 0 °C and stirred for 30 min. The mixture was again cooled to –78 °C and ethyl carboxylate **3** (2.50 g, 11.67 mmol, dissolved in 8 mL THF) was added dropwise. The mixture was allowed to warm to r.t. and stirred for 30 min. The mixture was again cooled to –78 °C and a solution of iodoethane (1.40 mL, 16.5 mmol) in THF (10 mL) was added dropwise. The mixture was stirred at –78 °C for 1 h and then allowed to reach r.t. overnight. The mixture was diluted with Et_2O and washed with NH_4Cl aq. (2×) and NaCl aq. (1×). The layers were separated and the organic layer was dried over $MgSO_4$, filtered and concentrated to dryness. Column chromatography (silica gel, heptane/Et_2O 2:1) gave compound **4** (2.60 g, 92%) as a colorless oil.

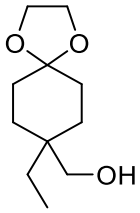
R_f = 0.33 (heptane/Et_2O 2:1).

^{1}H NMR (300 MHz, $CDCl_3$) δ = 0.75 (t, *J* = 7.5 Hz, 3 H, CH_3), 1.19 (t, *J* = 7.1 Hz, 3 H, CH_3), 1.33-1.64 (m, 8 H, 4 × CH_2), 2.08 (m_c, 2 H, CH_2), 3.86 (m_c, 4 H, 2 × CH_2), 4.09 (q, *J* = 7.1 Hz, 2 H, CH_2) ppm.

^{13}C NMR (75 MHz, $CDCl_3$) δ = 8.7 (CH_3), 14.2 (CH_3), 30.9 (2 × CH_2), 32.0 (2 × CH_2), 32.7 (CH_2), 46.3 (C^{tert}), 60.0 (CH_2), 64.1 (2 × CH_2), 108.6 (C^{tert}), 175.8 (CO) ppm.

Analytical data are in agreement with the literature.[1]

(8-Ethyl-1,4-dioxaspiro[4.5]decan-8-yl)methanol (5)



5

Ethyl carboxylate **4** (1.65 g, 6.81 mmol) was dissolved in THF (30 mL) and at 0 °C, $LiAlH_4$ (1.04 g, 27.40 mmol) was added. The mixture was warmed to r.t. and stirred for 2 h. H_2O, 40% NaOH aq. and 1 M potassium sodium tartrate aq. were successively added and the mixture was vigorously stirred overnight. The mixture was filtered through Celite, the layers were separated and the aqueous layer was extracted with CH_2Cl_2 (4×). The combined organic layers were dried over $MgSO_4$, filtered and concentrated to dryness. Column chromatography (silica gel, heptane/Et_2O 2:1) gave compound **5** (1.35 g, 99%) as a colorless oil.

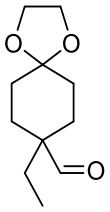
R_f = 0.29 (heptane/EtOAc 1:1).

^{1}H NMR (300 MHz, $CDCl_3$) δ = 0.80 (t, *J* = 7.6 Hz, 3 H, CH_3), 1.34–1.48 (m, 6 H, 3 × CH_2), 1.55–1.62 (m, 4 H, 2 × CH_2), 1.74 (br. s, OH), 3.41 (s, 2 H, CH_2), 3.91 (s, 4 H, 2 × CH_2) ppm.

^{13}C NMR (75 MHz, $CDCl_3$) δ = 7.6 (CH_3), 25.7 (CH_2), 29.2 (2 × CH_2), 30.3 (2 × CH_2), 36.2 (C^{tert}), 64.1 (2 × CH_2), 67.0 (CH_2), 109.1 (C^{tert}) ppm.

Analytical data are in agreement with the literature.[1]

8-Ethyl-1,4-dioxaspiro[4.5]decane-8-carbaldehyde (6)



6

Oxalyl chloride (1.16 mL, 1.72 g, 13.55 mmol) was dissolved in CH_2Cl_2 (17 mL) and the solution was cooled to –60 °C. A solution of DMSO (1.92 mL, 2.11 g, 27.03 mmol) in CH_2Cl_2 (17 mL) was added slowly and the mixture was stirred for 15 min. A solution of alcohol **5** (1.35 g, 6.74 mmol) in CH_2Cl_2 (17 mL) was added slowly, and the mixture was stirred for 45 min at the same temperature. Et_3N (6.58 mL, 4.78 g, 47.21 mmol) was added and the mixture was warmed to r.t. overnight. The mixture was washed with H_2O (3×), the layers were separated and the organic layer was dried over $MgSO_4$, filtered and evaporated to dryness. Column chromatography (silica gel, heptane/EtOAc 2:1) gave compound **6** (1.21 g, 90%) as a colorless oil.

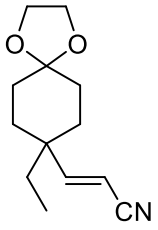
R_f = 0.55 (heptane/EtOAc 2:1).

^{1}H NMR (300 MHz, $CDCl_3$) δ = 0.76 (t, *J* = 7.6 Hz, 3 H, CH_3), 1.42–1.55 (m, 6 H, 3 × CH_2), 1.58–1.70 (m, 2 H, CH_2), 1.88–2.03 (m, 2 H, CH_2), 3.89 (s, 4 H, 2 × CH_2), 9.40 (s, 1 H, CHO) ppm.

^{13}C NMR (125 MHz, $CDCl_3$) δ = 8.1 (CH_3), 27.7 (2 × CH_2), 28.3 (CH_2), 31.3 (2 × CH_2), 49.0 (C^{tert}), 64.2 (2 × CH_2), 108.4 (C^{tert}), 206.2 (CHO) ppm.

Analytical data are in agreement with the literature.[1]

(*E*)-3-(8-Ethyl-1,4-dioxaspiro[4.5]decan-8-yl)acrylonitrile (7)



7

Aldehyde **6** (1.21 g, 6.10 mmol) and diethyl cyanomethylphosphonate (1.67 mL, 1.83 g, 10.32 mmol) were dissolved in THF (64 mL). Powdered 4 Å molecular sieves were added (3.50 g) followed by solid LiOH (291.7 mg, 12.18 mmol). The mixture was heated to reflux for 21 h, then cooled to r.t. The solvent was removed under reduced pressure, and the residue was suspended in Et_2O. The mixture was washed with H_2O (2×) and NaCl aq. (1×). The layers were separated and the organic layer was dried over $MgSO_4$, filtered and concentrated to dryness. Column chromatography (silica gel, heptane/EtOAc 2:1) gave compound **7** (1.27 g, 94%) as a yellowish oil.

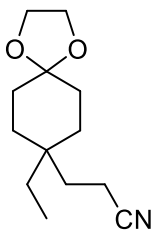
R_f = 0.63 (heptane/EtOAc 2:1).

^{1}H NMR (500 MHz, $CDCl_3$) δ = 0.77 (t, *J* = 7.5 Hz, 3 H, CH_3), 1.44 (q, *J* = 7.5 Hz, 2 H, CH_2), 1.51–1.70 (m, 8 H, 2 × CH_2), 3.92 (s, 4 H, 2 × CH_2), 5.27 (d, *J* = 16.9 Hz, 1 H, CH), 6.57 (d, *J* = 16.9 Hz, 1 H, CH) ppm.

^{13}C NMR (75 MHz, $CDCl_3$) δ = 7.9 (CH_3), 30.8 (2 × CH_2), 31.4 (2 × CH_2), 31.6 (CH_2), 40.5 (C^{tert}), 64.11 (CH_2), 64.15 (CH_2), 99.0 (CH), 108.2 (C^{tert}), 117.6 (CN), 162.1 (CH) ppm.

Analytical data are in agreement with the literature.[1]

3-(8-Ethyl-1,4-dioxaspiro[4.5]decan-8-yl)propanenitrile (8)



8

Pd/C (10 wt-% Pd, 69.6 mg, 65.4 µmol) was weighed into a 2-neck flask, which was then fitted with a septum and a hose connector. The flask was evacuated and back-filled with argon (5×). Alkene **7** (669.7 mg, 3.03 mmol) was dissolved in EtOH (7 mL) and this solution was added to the flask. A balloon filled with H_2 was fitted to the hose connector and the mixture was stirred vigorously for 50 h at r.t. The mixture was filtered through a pad of Celite with the aid of EtOH, and the solvent was evaporated under reduced pressure. Column chromatography (silica gel, heptane/EtOAc 2:1) gave compound **8** (494.5 mg, 73%) as a colorless oil.

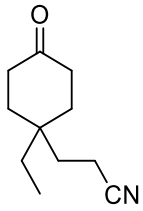
$\mathbf{R_f}$ = 0.61 (heptane/EtOAc 1:1).

^{1}H NMR (300 MHz, $CDCl_3$) δ = 0.79 (t, *J* = 7.5 Hz, 3 H, CH_3), 1.33 (q, *J* = 7.5 Hz, 2 H, CH_2), 1.38–1.47 (m, 4 H, 2 × CH_2), 1.55–1.63 (m, 4 H, 2 × CH_2), 1.63–1.72 (m, 2 H, CH_2), 2.17–2.25 (m, 2 H, CH_2), 3.91 (s, 4 H, 2 × CH_2) ppm.

^{13}C NMR (75 MHz, $CDCl_3$) δ = 7.4 (CH_3), 11.5 (CH_2), 27.0 (CH_2), 30.2 (2 × CH_2), 31.7 (CH_2), 31.8 (2 × CH_2), 34.0 (C^{tert}), 64.10 (CH_2), 64.13 (CH_2), 108.5 (C^{tert}), 120.3 (CN) ppm.

Analytical data are in agreement with the literature.[1]

3-(1-Ethyl-4-oxocyclohexyl)propanenitrile (9)



9

To a solution of ketal **8** (512.2 mg, 2.29 mmol) in acetone (25 mL) was added 10% aq. HCl (10 mL). To the resulting cloudy mixture, additional acetone was added dropwise until the solution became clear. The mixture was stirred at room temperature for 25 h. The mixture was diluted with NaCl aq., then it was extracted with CH_2Cl_2/Et_2O (1:2, 3×). The organic layer was washed with $NaHCO_3$ aq. (2×) and NaCl aq. (1×). The organic layer was dried over $MgSO_4$, filtered, and concentrated under reduced pressure. Column chromatography (silica gel, heptane/EtOAc 2:1) gave compound **9** (407.6 mg, 99%) as colorless oil.

$\mathbf{R_f}$ = 0.39 (heptane/EtOAc 1:1).

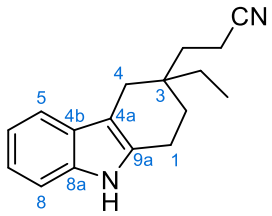
^{1}H NMR (500 MHz, $CDCl_3$) δ = 0.90 (t, *J* = 7.5 Hz, 3 H, CH_3), 1.49 (q, *J* = 7.5 Hz, 2 H, CH_2), 1.62–1.70 (m, 2 H, CH_2), 1.70–1.78 (m, 2 H, CH_2), 1.82 (m_c, 2 H, CH_2), 2.28–2.38 (m, 6 H, 3 × CH_2) ppm.

^{13}C NMR (75 MHz, $CDCl_3$) δ = 7.5 (CH_3), 11.7 (CH_2), 26.9 (CH_2), 31.6 (CH_2), 34.1 (2 × CH_2), 34.3 (C^{tert}), 36.8 (2 × CH_2), 119.9 (CN), 210.9 (CO) ppm.

IR: $\tilde{\nu}$ = 2935, 2245, 1705, 1465, 1425, 1135, 750, 505, 415 cm^{-1}.

HRMS (ESI-TOF) m/z: calc. for $C_{11}H_{18}NO^+$, $[M+H]^+$: 180.1388, found: 180.1392.

3-(3-Ethyl-2,3,4,9-tetrahydro-1*H*-carbazol-3-yl)propanenitrile (11)



11

In a 10 mL crimp cap vial, phenylhydrazine (**10**, 244.8 µL, 2.49 mmol) was dissolved in glacial acetic acid (3.00 mL). Ketone **9** (445.8 mg, 2.49 mmol) was added and the vial was sealed. The mixture was heated to 125 °C with rapid stirring for 22 h. After cooling to r.t., the vial was fitted directly to a rotary evaporator and the mixture was concentrated to dryness. Column chromatography (silica gel, heptane/EtOAc 5 :1) provided compound **11** (461.1 mg, 73%) as a colorless solid.

R_f = 0.60 (heptane/EtOAc 1:1), **m.p.**: 67-72 °C.

^{1}H NMR (500 MHz, $CDCl_3$) δ = 0.92 (t, *J* = 7.6 Hz, 3 H, CH_3), 1.39 (m_c, 1 H, CH_2), 1.48 (m_c, 1 H, CH_2), 1.69–1.89 (m, 4 H, 2-H, CH_2), 2.34 (dd, *J* = 7.8, 8.2 Hz, 2 H, CH_2), 2.53 (m_c, 2 H, 4-H), 2.72 (m_c, 2 H, 1-H), 7.08 (td, *J* = 1.1, 7.5 Hz, 1 H, 6-H), 7.13 (td, *J* = 1.1, 7.5 Hz, 1 H, 7-H), 7.29 (dd, *J* = 1.1, 7.5 Hz, 1 H, 8-H), 7.43 (dd, *J* = 1.1, 7.5 Hz, 1 H, 5-H), 7.74 (br. s, 1 H, N-H).

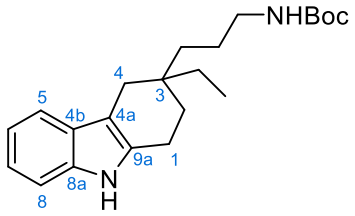
^{13}C NMR (125 MHz, $CDCl_3$) δ = 7.7 (CH_3), 11.9 (CH_2), 19.9 (C-1), 28.3 (CH_2), 31.0 (C-4), 31.4 (C-2), 31.6 (CH_2), 35.2 (C-3), 108.1 (C-4a), 110.5 (C-8), 117.5 (C-5), 119.2 (C-6), 120.4 (CN), 121.3 (C-7), 127.8 (C-4b), 132.4 (C-9a), 136.2 (C-8a) ppm.

IR: $\tilde{\nu}$ = 3390, 2920, 2245, 1465, 1325, 735, 635, 430 cm^{-1}.

HRMS (ESI-TOF) m/z: calc. for $C_{17}H_{21}N_2^+$, $[M+H]^+$: 253.1704, found: 253.1705.

2.2 Completion of the synthesis of (±)-mersicarpine (1)

tert-Butyl [3-(3-ethyl-2,3,4,9-tetrahydro-1*H*-carbazol-3-yl)propyl]carbamate (12)



12

Tetrahydrocarbazole **11** (63.1 mg, 250.0 µmol) was dissolved in EtOH (5.00 mL) in a round-bottomed flask equipped with magnetic stirrer and a three-way valve. $CHCl_3$ (4 drops) and Pt_2O

(8.5 mg, 37.4 µmol) were added. A balloon filled with H_2 was fitted to the three-way valve, and the headspace was evacuated, then purged with H_2 (5×). The reaction mixture was stirred vigorously for 24 h at r.t. A second portion of Pt_2O (8.5 mg, 37.4 µmol) was added and the mixture was stirred for 16 h. A third portion of Pt_2O (8.5 mg, 37.4 µmol) was added and the mixture was stirred for 2 h, whereupon TLC showed complete consumption of the starting material. The mixture was filtered through Celite with the aid of EtOH and EtOAc. The filtrate was concentrated to dryness and the crude product was dried in high vacuum. The crude product was dissolved in CH_2Cl_2 (2.00 mL). A solution of Boc_2O (632 mg, 2.90 mmol) in CH_2Cl_2 (1.00 mL) was added followed by Et_3N (69.3 µL, 500 µmol). The mixture was stirred at r.t. for 4 h, then poured into 5% HCl aq. and extracted with CH_2Cl_2 (3×). The combined organic layers were washed with NaCl aq. (3×), dried over $MgSO_4$, filtered, and concentrated to dryness. Column chromatography (silica gel, heptane/EtOAc 5:1 + 1 vol-% Et_3N) gave compound **12** (86.4 mg, 97%) as a yellowish solid.

R_f = 0.65 (heptane/EtOAc 1:1), **m.p.**: 63-66°C

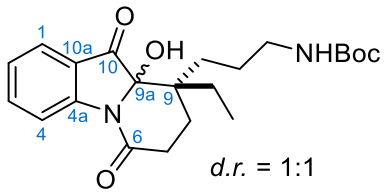
^{1}H NMR (500 MHz, CD_3OD) δ = 0.92 (t, *J* = 7.4 Hz, 3 H, CH_3), 1.25–1.34 (m, 2 H, CH_2), 1.40 (s, 9 H, *t*-Bu), 1.43–1,54 (m, 4 H, 2 × CH_2), 1.70 (t, *J* = 6.4 Hz, 2 H, 2-H), 2.46 (m_c, 2 H, 4-H), 2.64–2.70 (m, 2 H, 1-H), 2.98 (t, *J* = 6.7 Hz, 2 H, CH_2), 3.09 (br. s, 1 H, N-H), 6.91 (t, *J* = 7.5 Hz, 1 H, 6-H), 6.98 (t, *J* = 7.5 Hz, 1 H, 7-H), 7.21 (d, *J* = 7.5 Hz, 1 H, 8-H), 7.31 (d, *J* = 7.5 Hz, 1 H, 5-H), 7.89 (s, 1 H, NH) ppm.

^{13}C NMR (125 MHz, $CDCl_3$) δ = 7.8 (CH_3), 20.0 (C-1), 24.1 (CH_2), 28.4 (*t*-Bu), 28.8 (CH_2), 31.6 (C-4), 31.9 (C-2), 32.9 (CH_2), 35.0 (C-3), 41.4 (CH_2), 79.0 (*t*-Bu), 108.9 (C-4a), 110.4 (C-8), 117.5 (C-5), 118.9 (C-6), 120.9 (C-7), 128.1 (C-4b), 133.0 (C-9a), 136.1 (C-8a), 155.9 (CO) ppm.

IR: $\tilde{\nu}$ = 3325, 2925, 1685, 1510, 1455, 1365, 1240, 1160, 735 cm^{-1}.

HRMS (ESI-TOF) m/z: calc. for $C_{22}H_{33}N_2O_2^+$, $[M+H]^+$: 357.2542, found: 357.2543.

tert-Butyl [3-(9-ethyl-9a-hydroxy-6,10-dioxo-6,7,8,9,9a,10-hexahydropyrido[1,2-*a*]indol-9-yl)propyl]carbamate (13)



13

In a Pyrex tube (length ca. 15 cm, Ø = 3.0 cm), tetrahydrocarbazole **12** (45.9 mg, 128.7 µmol) and rose bengal disodium salt (2.6 mg, 2.57 µmol, 2 mol-%) were dissolved in MeOH (2.60 mL). 40% NaOH aq. (108.0 µL, 12 equiv.) was added, and the vial was sealed with a septum. An O_2 balloon was fitted (septum pierced by needle), and the mixture was irradiated with green LEDs (λ_{em} = 530 nm, 10 W total power) with rapid stirring, at r.t. for 36 h. H_2O (10 mL) and 1 M HCl aq. (ca. 2 mL, until the mixture was pH neutral) were added and the mixture was extracted with CH_2Cl_2 (4×). The combined organic layers were dried with $MgSO_4$, filtered and

evaporated. Column chromatography (silica gel, heptane/EtOAc 3:2→0:1) provided compound **13** (31.4 mg, 61%) as a colorless solid, as a 1:1 mixture of diastereomers. As a byproduct, *tert*-butyl [3-(1-ethyl-9-oxo-2,3,4,9-tetrahydro-1*H*-cyclopenta[*b*]quinolin-1-yl)propyl]carbamate was isolated (8.0 mg, 17%) as a colorless solid.

R_f = 0.37+0.31 (heptane/EtOAc 1:1), **m.p.**: 58-60 °C.

^{1}H NMR (300 MHz, $CDCl_3$), 1:1 mixture of diastereomers, δ = 0.64 (t, *J* = 7.7 Hz, 3 H, CH_3), 0.93 (t, *J* = 7.5 Hz, 3 H, CH_3), 1.16–1.23 (m, 4 H, CH_2), 1.33 (s, 9 H, *t*-Bu), 1.39 (s, 9 H, *t*-Bu), 1.46–1.72 (m, 8 H, 8-H, CH_2), 1.76–1.90 (m, 2 H, CH_2), 1.96–2.10 (m, 2 H, CH_2), 2.13–2.32 (m, 4 H, 8-H, CH_2), 2.41–2.57 (m, 2 H, 7-H), 2.67–2.84 (m, 4 H, 7-H, CH_2), 3.00–3.24 (m, 2 H, CH_2), 4.25 (m_c, 1 H, N-H), 4.73 (br. s, 1 H, N-H), 7.17 (td, *J* = 0.7, 7.5 Hz, 1 H, 2-H), 7.18 (td, *J* = 0.7, 7.5 Hz, 1 H, 2-H), 7.58-7.65 (m, 2 H, 3-H), 7.65–7.70 (m, 2 H, 1-H), 8.36 (dt, *J* = 0.7, 8.3 Hz, 1 H, 4-H), 8.37 (dt, *J* = 0.7, 8.3 Hz, 1 H, 4-H) ppm.

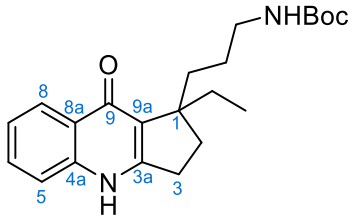
^{13}C NMR (75 MHz, $CDCl_3$), 1:1 mixture of diastereomers, δ = 8.18, 9.43 (CH_3), 24.00 (CH_2), 24.45 (CH_2), 24.50 (CH_2), 25.66 (CH_2), 26.35, 26.59 (C-8), 28.27, 28.35 (*t*-Bu), 28.48 (CH_2), 29.39, 29.47 (C-7), 35.31, 35.39 (C-9), 42.92, 43.03 (CH_2), 79.20 (*t*-Bu), 89.88, 89.95 (C-9a), 117.85, 117.89 (C-4), 121.36, 121.52 (C-10a), 124.31, 124.38 (C-1), 124.46, 124.57 (C-2), 137.81, 137.98 (C-3), 151.11, 151.15 (C-4a), 155.74, 156.15 (CO), 169.75, 169.83 (C-6), 197.82, 197.86 (C-10) ppm.

IR: $\tilde{\nu}$ = 2925, 1675, 1465, 1365, 1160, 755 cm^{-1}.

HRMS (ESI-TOF) m/z: calc. for $C_{22}H_{30}N_2O_5^+$, $[M]^+$: 402.2149, found: 402.2147.

The NMR spectroscopic data are in agreement with the literature.[2]

Analytical data for *tert*-butyl [3-(1-ethyl-9-oxo-2,3,4,9-tetrahydro-1*H*-cyclopenta[*b*]quinolin-1-yl)propyl]carbamate:



R_f = 0.65 (EtOAc/MeOH 10:1), **m.p.**: 330 °C (decomp.).

^{1}H NMR (500 MHz, CD_3OD) δ = 0.80 (t, *J* = 7.4 Hz, 3 H, CH_3), 1.20–1.27 (m, 1 H, 2-H), 1.40 (s, 9 H, *t*-Bu), 1.41–1.52 (m, 1 H, 2-H), 1.63–1.75 (m, 2 H, 3-H, CH_2), 1.95–2.12 (m, 4 H, 3-H, CH_2), 2.93–3.04 (m, 4 H, CH_2), 7.35 (ddd, *J* = 1.4, 7.0, 8.2 Hz, 1 H, 7-H), 7.50 (dd, *J* = 1.4, 8.2 Hz, 1 H, 5-H), 7.63 (ddd, *J* = 1.4, 7.0, 8.2 Hz, 1 H, 6-H), 8.24 (dd, *J* = 1.4, 8.2 Hz, 1 H, 8-H) ppm.

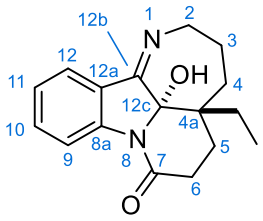
[2] J. Magolan, C. A. Carson, M. A. Kerr, *Org. Lett.*, 2008, **10**, 1437–1440.

^{13}C NMR (126 MHz, CD_3OD) δ = 9.6 (CH_3), 26.6 (C-2), 28.8 (*t*-Bu), 31.2 (CH_2), 32.3 (CH_2), 32.4 (CH_2), 37.1 (C-3), 42.1 (CH_2), 52.8 (C-1), 79.7 (*t*-Bu), 118.9 (C-5), 124.3 (C-7), 124.7 (C-9a), 126.1 (C-8), 126.9 (C-8a), 132.4 (C-6), 141.7 (C-4a), 157.3 (CO), 158.5 (C-3a), 177.6 (C-9) ppm.

IR: $\tilde{\nu}$ = 2935, 1685, 1630, 1565, 1505, 1470, 1365, 1165, 1020, 760 cm^{-1}.

HRMS (ESI-TOF) m/z: calc. for $C_{22}H_{31}N_2O_3^+$, $[M+H]^+$: 371.2335, found: 371.2338.

(±)-Mersicarpine (1)



(±)-**1**

Numbering for:

(4a*R**,12c*S**)-4a-Ethyl-3,4,4a,5,6,12c-hexahydro-12c-hydroxyazepino[4,3,2-*hi*]benz[*b*]indolizin-7(2*H*)-one

Compound **13** (30.0 mg, 74.5 µmol) was dissolved in CH_2Cl_2 (3.50 mL) and the mixture was cooled to 0 °C. 2,6-Lutidine (432.0 µL, 399.6 mg, 3.73 mmol) and TBSOTf (342.0 µL, 393.3 mg, 1.49 mmol) were added and the mixture was stirred at r.t. for 25 h. The reaction was quenched by the addition of 5% HCl aq., the layers were separated and the aqueous layer was extracted with CH_2Cl_2 (4×). The combined organic layers were dried with $MgSO_4$, filtered and evaporated to dryness. The crude product was dried in high vacuum, then dissolved in THF (3.50 mL). A solution of TBAF (1 M in THF, 223.6 µL, 223.6 µmol,) was added and the mixture was stirred at r.t. for 20 h. The mixture was evaporated onto silica, and column chromatography (heptane/EtOAc 1:1 provided (±)-mersicarpine (**1**) as a colorless solid (11.7 mg, 55%).

R_f = 0.23 (heptane/ EtOAc 1:1), **m.p.**: 232-235 °C (lit.: 150 °C decomp.)[3].

^{1}H NMR (500 MHz, $CDCl_3$) δ = 0.74 (t, *J* = 7.4 Hz, 3 H, CH_3), 1.04-1.15 (m, 1 H, CH_2), 1.25–1.35 (m, 1 H, CH_2), 1.60–1.71 (m, 3 H, 3-H, 5-H), 1.75 (dt, *J* = 3.4, 14.7 Hz, 1 H, 4-H), 1.86–1.96 (m, 1 H, 5-H), 2.00–2.11 (m, 1 H, 4-H), 2.38 (ddd, *J* = 8.7, 8.7, 18.1 Hz, 1 H, 6-H), 2.57 (ddd, *J* = 1.5, 9.5, 18.1 Hz, 1 H, 6-H), 3.76–3.90 (m, 2 H, 2-H), 5.59 (br. s, 1 H, OH), 7.06 (t, *J* = 7.8 Hz, 1 H, 11-H), 7.37 (t, *J* = 7.8 Hz, 1 H, 10-H), 7.60–7.73 (m, 1 H, 12-H), 8.11 (d, *J* = 7.8 Hz, 1 H, 9-H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$) δ = 6.8 (CH_3), 21.0 (CH_2), 22.8 (C-3), 25.5 (C-5), 29.1 (C-6), 34.2 (C-4), 39.4 (C-4a), 50.0 (C-2), 94.0 (C-12c), 116.8 (C-9), 122.7 (C-12), 123.6 (C-12a), 124.4 (C-11), 134.0 (C-10), 146.9 (C-8a), 169.4 (C-7), 169.8 (C-12b) ppm.

The signals at 122.7, 123.6, 134.0, 146.9, 169.8 ppm were of low intensity. Their presence was unambiguously confirmed by an HMBC experiment.

[3] Z. Lv, Z. Li, G. Liang, *Org. Lett.*, 2014, **16**, 1653–1655.

IR: $\tilde{\nu}$ = 2920, 1600, 1500, 1215, 1155, 900, 810, 755, 575, 500 cm^{-1}.

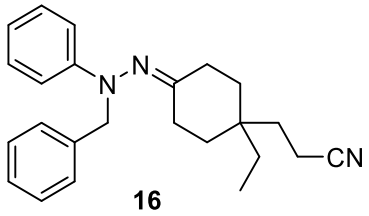
HRMS (ESI-TOF) m/z: calc. for $C_{17}H_{21}N_2O_2^+$, $[M+H]^+$: 285.1603, found: 285.1596.

The NMR spectroscopic data are in agreement with the literature.[2],[4]

3 Chiral Brønsted acid-catalyzed Fischer indolization of hydrazones 16 and 17 to enantioenriched tetrahydrocarbazoles 19 and 20

3.1 Preparation of hydrazones 16 and 17

3-(4-(2-Benzyl-2-phenylhydrazineylidene)-1-ethylcyclohexyl)propanenitrile (16)



16

1-Benzyl-1-phenylhydrazine (**14**, 99.1 mg, 0.50 mmol) and ketone **9** (90.0 mg, 0.50 mmol) were dissolved in EtOH (1.00 mL). One drop of glacial AcOH was added and the mixture was stirred at 60 °C for 3 h. The mixture was concentrated to dryness and the crude product was purified by column chromatography on silica gel (heptane/Et_2O 1:1) to give compound **16** (161.0 mg, 90%) as a colorless oil.

$\mathbf{R_f}$ = 0.25 (heptane/Et_2O 1:1).

^{1}H NMR (250 MHz, $CDCl_3$) δ = 0.76 (t, *J* = 7.6 Hz, 3 H, CH_3), 0.91–1.01 (m, 1 H, CH_2), 1.07–1.18 (m, 1 H, CH_2), 1.30 (qd, *J* = 1.2, 7.9 Hz, 2 H, CH_2), 1.37–1.55 (m, 2 H, CH_2), 1.61 (m_c, 2 H, CH_2), 2.10–2.21 (m, 3 H, CH_2), 2.28–2.34 (m, 1 H, CH_2), 2.40 (t, *J* = 6.7 Hz, 2 H, CH_2), 4.49–4.62 (m, 2 H, CH_2), 6.82–6.90 (m, 3 H, Ar-H), 7.19–7.28 (m, 3 H, Ar), 7.28–7.34 (m, 4 H, Ar) ppm.

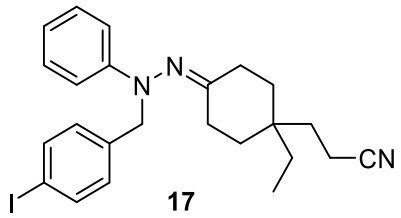
^{13}C NMR (63 MHz, $CDCl_3$) δ = 7.4 (CH_3), 11.5 (CH_2), 24.9 (CH_2), 27.0 (CH_2), 30.1 (CH_2), 31.6 (CH_2), 33.4 (CH_2), 34.5 (CH_2), 34.6 (C^{tert}), 60.6 (CH_2), 115.9 (Ar), 120.1 (CN), 120.2 (Ar), 126.9 (Ar), 128.2 (Ar), 128.7 (Ar), 128.9 (Ar), 138.8 (Ar), 150.5 (Ar), 175.8 (CN) ppm.

IR: $\tilde{\nu}$ = 3085, 3060, 2960, 2930, 1710, 1635, 1545, 1455, 1215, 1200, 910, 750 cm^{-1}.

HRMS (ESI-TOF) m/z: calc. for $C_{24}H_{30}N_3^+$, $[M+H]^+$: 360.2440, found: 360.2433.

[4] Z. Xu, Q. Wang and J. Zhu, *J. Am. Chem. Soc.*, 2013, **135**, 19127-19130.

3-(1-Ethyl-4-(2-(4-iodobenzyl)-2-phenylhydrazineylidene)cyclohexyl)propanenitrile (17)



17

1-(4-Iodobenzyl)-1-phenylhydrazine[5] (**15**, 97.3 mg, 0.30 mmol) and ketone **9** (54.0 mg, 0.30 mmol) were dissolved in EtOH (1.00 mL). One drop of glacial AcOH was added and the mixture was stirred at 60 °C for 5 h. The mixture was concentrated to dryness and the crude product was purified by column chromatography on silica gel ($PhCH_3$/ EtOAc 8:1) to give compound **17** (93.0 mg, 63%) as a colorless solid.

R_f = 0.33 ($PhCH_3$/ EtOAc 5:1), **m.p.**: 104-106 °C.

^{1}H NMR (300 MHz, $CDCl_3$) δ = 0.81 (t, *J* = 7.6 Hz, 3 H, CH_3), 0.97–1.06 (m, 1 H, CH_2), 1.13–1.22 (m, 1 H, CH_2), 1.33 (qd, *J* = 2.9, 7.7 Hz, 2 H, CH_2), 1.42–1.58 (m, 2 H, CH_2), 1.67 (m_c, 2 H, CH_2), 2.14–2.23 (m, 3 H, CH_2), 2.29–2.38 (m, 1 H, CH_2), 2.24 (t, *J* = 6.7 Hz, 2 H, CH_2), 4.46–4.56 (m, 2 H, CH_2), 6.85 (m_c, 2 H, Ar-H), 6.90 (tt, *J* = 1.1, 7.3 Hz, 1 H, Ar-H), 7.10 (dt, *J* = 1.8, 8.4 Hz, 2 H, Ar-H), 7.25 (dd, *J* = 7.3, 8.6 Hz, 2 H, Ar-H), 7.65 (dt, *J* = 1.8, 8.4 Hz, 2 H, Ar-H) ppm.

^{13}C NMR (75 MHz, $CDCl_3$) δ = 7.4 (CH_3), 11.6 (CH_2), 24.9 (CH_2), 27.0 (CH_2), 30.1 (CH_2), 31.6 (CH_2), 33.5 (CH_2), 34.56 (CH_2), 34.64 (C^{tert}), 60.3 (CH_2), 92.3 (Ar), 116.1 (Ar), 120.0 (Ar), 120.6 (Ar), 129.0 (Ar), 130.7 (Ar), 137.3 (Ar), 138.5 (Ar), 150.3 (Ar), 175.6 (CN) ppm.

IR: $\tilde{\nu}$ = 3060, 3035, 2930, 2835, 1710, 1635, 1595, 1490, 1200, 1010, 790 cm^{-1}.

HRMS (ESI-TOF) m/z: calc. for $C_{24}H_{29}IN_3^+$, $[M+H]^+$: 486.1406, found: 486.1414.

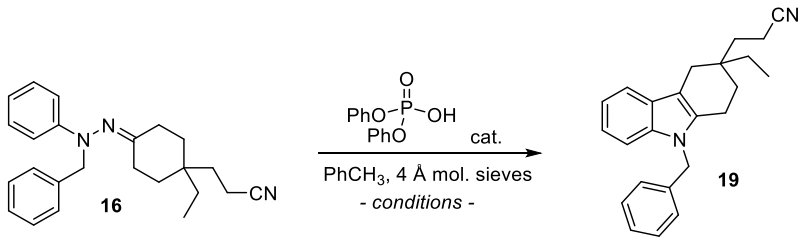
[5] S. Müller, M. J. Webber and B. List, *J. Am. Chem. Soc.*, 2011, **133**, 18534-18537.

3.2 Fischer indole synthesis

Note: Prior to their use, all commercially available phosphoric acid catalysts were dissolved in CH_2Cl_2 and the solutions were washed with 4 M HCl aq. After phase separation, the organic layers were immediately evaporated and the respective catalyst was dried in high vacuum.

The cyclization of hydrazone **16** to *N*-benzyl tetrahydrocarbazole **19** was first investigated utilizing diphenyl phosphate (DPP) as the Brønsted acid catalyst (Table ESI-1).

Table ESI-1. Fischer indolization of hydrazone **16** catalyzed by diphenyl phosphate (DPP).



entry	mol-% DPP	additive	T (°C)	t (h)	conversion of **16** (%)[a]	NMR yield (%)[b]	isolated yield (%)
1	15	none	40	48	12	10	-/-
2	30	none	40	48	25	21	-/-
3	100	none	40	48	94	86	79
4	0	Amberlite® CG 50 H^+	40	48	12	5	-/-
5	0	Amberlite® IR-120 H^+	40	48	100	87	72
6	0	Amberlite® IR-120 H^+	25	48	16	11	-/-
7	15	Amberlite® CG 50 H^+	40	48	12	10	-/-
8	15	Amberlite® CG 50 H^+	40	168	21	21	-/-
9	15	Amberlite® IR-120 H^+ + $ZnCl_2$ (15 mol-%)	25	48	38	25	-/-
10	30	Amberlite® IR-120 H^+	25	48	100	48	44

All reactions were performed on 0.10 mmol scale. a) Conversion determined by ^{1}H NMR analysis. b) NMR yield determined against 1,3,5-trimethoxybenzene standard.

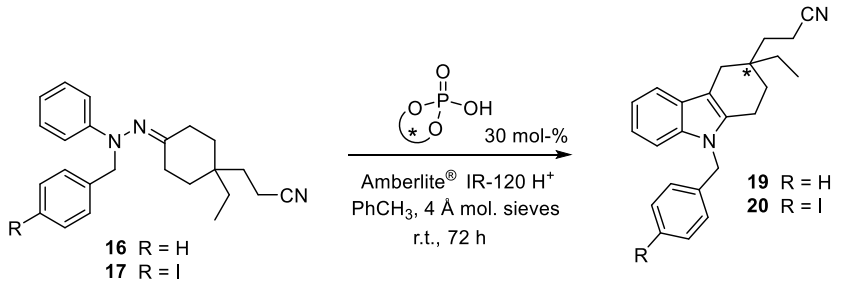
As can be seen from Table ESI-1, DPP alone showed no catalytic turnover even at 40 °C. Amberlite® CG 50 H^+ resin alone at 40 °C does induce the cyclization of **16** to **19** only to a very minor extend. However Amberlite® IR-120 H^+ resin alone efficiently promotes the reaction at 40 °C, but to a much lesser extend at 25 °C. Combining DPP with Amberlite® CG 50 H^+ resin[5] was not successful. Combining DPP with Amberlite® IR-120 H^+ resin[6] led to a catalytic

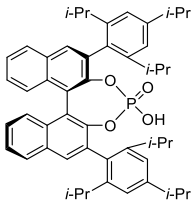
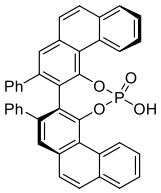
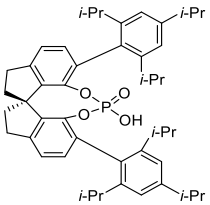
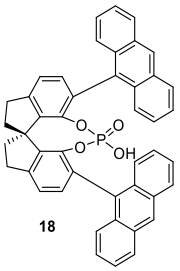
[6] B. Gosh, R. Balhara, G. Jindal, S. Mukherjee, *Angew. Chem. Int. Ed.*, 2021, **60**, 9086-9092.

turnover and full conversion at r.t., when using 30 mol-% of DPP. The addition of $ZnCl_2$[6] did not lead to further improvements.

Subsequently, the cyclizations of **16** to **19** and **17** to **20** were attempted using chiral phosphate catalysts, under the conditions of entry 10 in Table ESI-1. The results are summarized in Table ESI-2.

Table ESI-2. Asymmetric Fischer indolization of hydrazones **16** and **17** catalyzed by chiral phosphoric acids.



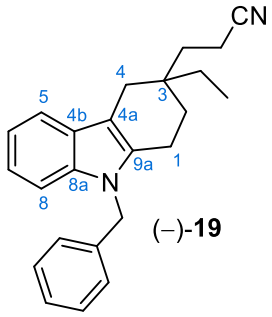
catalyst	 CAS 791616-63-2	 CAS 871130-18-6	 CAS 1372719-95-3	 CAS 1345628-08-1
substrate **16**				
conversion (%)[a]	35	16	100	100
NMR yield (%)[b]	14	17	23	50
isolated yield of **19** (%)	14	17	15	56
e.r. of **19**[c]	50:50	50:50	50:50	68:32
substrate **17**				
conversion (%)[a]	12	9	decomp.	100
NMR yield (%)[b]	6	9	0	46
isolated yield of **20** (%)	3	13	0	52
e.r. of **20**[c]	50:50	50:50	-/-	66:34

a) Conversion determined by ^{1}H NMR analysis. b) NMR yield determined against 1,3,5-trimethoxybenzene standard. c) Determined by chiral HPLC.

As can be seen from Table ESI-2, only catalyst **18** offers any asymmetric induction and acceptable product yields.

3.2.1 Synthetic procedures and analytical data

3-(9-Benzyl-3-ethyl-2,3,4,9-tetrahydro-1*H*-carbazol-3-yl)propanenitrile (–)-(19)



(–)-**19**

In a 5 mL Schlenk flask, hydrazone **16** (36.0 mg, 0.10 mmol) was dissolved in $PhCH_3$ (1 mL). Powdered 4Å molecular sieves (50 mg) were added, followed by catalyst **18** (CAS 1345628-08-1, 20.0 mg, 30.0 µmol) and Amberlite® IR 120 H^+ (CAS 39389-20-3, 200 mg). The mixture was stirred at 25 °C for 72 h (TLC showed complete consumption of starting material), then filtered through a small bed of Celite with the aid of EtOAc. The filtrate was concentrated to dryness and the crude product was purified by column chromatography on silica gel (heptane/EtOAc 5:1) to give compound (–)-**19** (19.2 mg, 56%) as a colorless oil. HPLC on chiral stationary phase showed *e.r.* = 68:32.

R_f = 0.33 (heptane/EtOAc 5:1).

$[\alpha]^{22}_D$ = –4.80° (*c* 0.8, $CHCl_3$).

^{1}H NMR (250 MHz, $CDCl_3$) δ = 0.82 (t, *J* = 7.6 Hz, 3 H, CH_3), 1.33 (dq, *J* = 7.6, 10.6 Hz, 2 H, CH_2), 1.56–1.80 (m, 4 H, 2-H, CH_2), 2.23 (t, *J* = 8.2 Hz, 2 H, CH_2), 2.43–2.59 (m, 4 H, 1-H, 4-H), 5.17 (s, 2 H, CH_2), 6.85–6.92 (m, 2 H, Ar-H), 6.97–7.07 (m, 2 H, 6-H, 8-H), 7.07–7.22 (m, 4 H, 7-H, Ar-H), 7.35–7.43 (m, 1 H, 5-H) ppm.

^{13}C NMR (63 MHz, $CDCl_3$) δ = 7.7 (CH_3), 11.9 (CH_2), 18.9 (C-1), 28.2 (CH_2), 31.1 (C-4), 31.4 (C-2), 31.6 (CH_2), 35.1 (C-3), 46.3 (CH_2), 107.7 (C-4a), 109.1 (C-8), 117.6 (C-5), 119.0 (C-6), 120.3 (CN), 121.1 (C-7), 126.0 (Ar), 127.3 (Ar), 127.5 (C-4b), 128.7 (Ar), 133.9 (C-9a), 137.0 (C-8a), 138.0 (Ar) ppm.

IR: $\tilde{\nu}$ = 3085, 3050, 2960, 1615, 1465, 1455, 1355, 1180, 735, 705, 695 cm^{-1}.

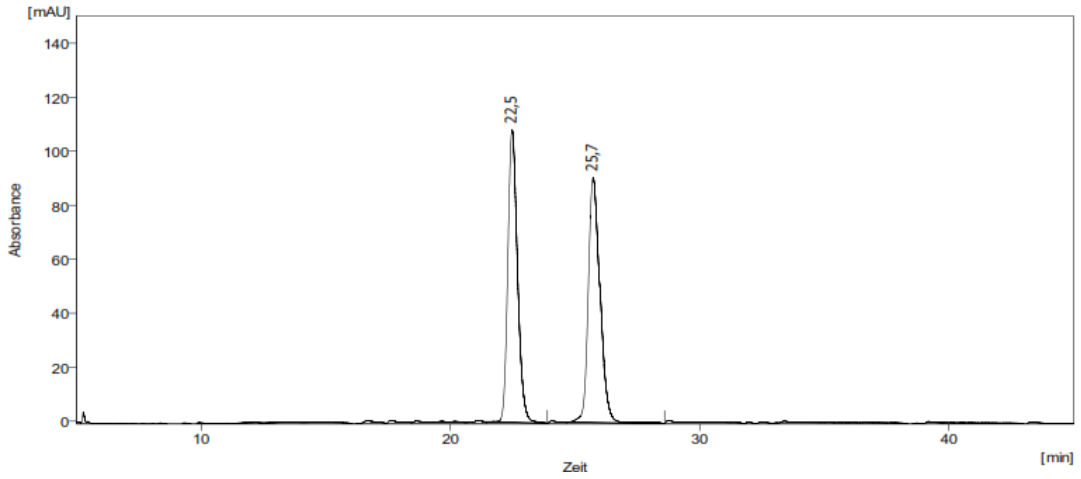
HRMS (ESI-TOF) m/z: calc. for $C_{24}H_{27}N_2^+$, $[M+H]^+$: 343.2174, found: 343.2175.

HPLC traces:

Methode	: C:\ClarityChrom\DataFiles\18314_155859_ Uni Rostock\Alice_Voß\Alice-Chiral\Alice 2 für S9b (Cellulose)	durch	: Administrator
Beschreibung	: Alice-Chiral		
Erstellt	: 20.06.2018 16:56	Geändert	: 30.11.2021 12:14
Säule	: Lux Cellulose-1, 3µm 250 x 4.6mm SNo: H21-350519, PartNr: 00G-4458-E0,	Detektor	: UV CH1:259 nm;
Mobile Phase	: Ethanlo / n- heptan 5:95	Temperatur	: 25°C
Flussrate	: 1,0 ml/min	Druck	: 120mbar
Notizen	: partial loop mit 100µl Porbeschleife /60min/ kein Gradient / standby Fluss. 1,0 ml/min, Inj. Volumen immer 10µl, Gelöst in Heptan/Ethanol. 95:5, 1mg auf 1ml		
Autostop	: 60,00 min	Externes Startsignal	: Nur externer Start, Absteigend
Detektor 1	: DAD 2.1L: Channel 1	Bereich 1	: Bipolar, 10000 mAU, 20 Proben pro Sek.
Abzuziehendes Chromatogramm	: (Keine)	Anpassung	: Keine Änderung

The racemic reference sample (±)-**19** could be base-line separated by using a Lux Cellulose-1 column, EtOH/heptane 5:95, flow rate 1.0 mL/min. The individual enantiomers eluted at retention times of 23 and 26 min, respectively.

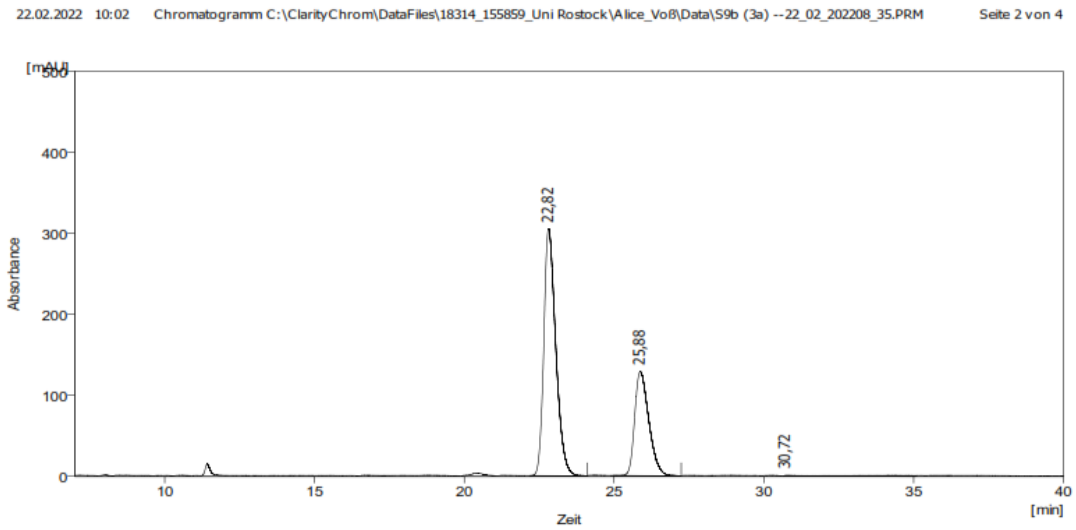
Racemate (±)-**19**



	Signalname	Retentionsz. [min]	Fläche [mAU.sek]	Höhe [mAU]	Fläche [%]	Höhe [%]
1	DAD 2.1L: Channel 1	22,478	2915,513	108,303	49,3	54,4
2	DAD 2.1L: Channel 1	25,726	2994,281	90,765	50,7	45,6
		Alle Signale Gesamt	5909,794	199,068	100,0	100,0

Lux Cellulose-1 column, EtOH/heptane 5:95, flow rate 1.0 mL/min.

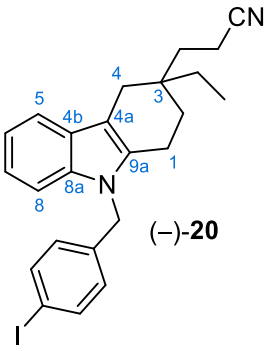
Reaction product (–)-**19**, *e.r.* 68:32



	Signalname	Retentionsz. [min]	Fläche [mAU.sek]	Höhe [mAU]	Fläche [%]	Höhe [%]
1	DAD 2.1L: Channel 1	22,818	8473,930	305,691	63,6	70,2
2	DAD 2.1L: Channel 1	25,878	4230,894	128,901	31,7	29,6
3	DAD 2.1L: Channel 1	30,721	628,282	0,770	4,7	0,2
		Alle Signale Gesamt	13333,106	435,362	100,0	100,0

Lux Cellulose-1 column, EtOH/heptane 5:95, flow rate 1.0 mL/min.

3-(3-Ethyl-9-(4-iodobenzyl)-2,3,4,9-tetrahydro-1*H*-carbazol-3-yl)propanenitrile (–)-(20)



(–)-**20**

In a 5 mL Schlenk flask, hydrazone **17** (48.0 mg, 0.10 mmol) was dissolved in $PhCH_3$ (1 mL). Powdered 4Å molecular sieves (50 mg) were added, followed by catalyst **18** (CAS 1345628-08-1, 20.0 mg, 30.0 µmol) and Amberlite® IR 120 H^+ (CAS 39389-20-3, 200 mg). The mixture was stirred at 25 °C for 48 h (TLC showed complete consumption of starting material), then filtered through a small bed of Celite with the aid of EtOAc. The filtrate was concentrated to dryness and the crude product was purified by column chromatography on silica gel (heptane/EtOAc 5:1) to give compound (–)-**20** (26.0 mg, 56%) as a colorless oil. HPLC on chiral stationary phase showed *e.r.* = 66:34.

R_f = 0.34 (heptane/EtOAc 5:1).

$[\alpha]^{22}_D$ = –4.63° (*c* 1.0, $CHCl_3$).

^{1}H NMR (250 MHz, $CDCl_3$) δ = 0.91 (t, *J* = 7.6 Hz, 3 H, CH_3), 1.42 (dq, *J* = 7.6, 10.6 Hz, 2 H, CH_2), 1.65–1.90 (m, 4 H, 2-H, CH_2), 2.34 (t, *J* = 8.2 Hz, 2 H, CH_2), 2.52–2.65 (m, 4 H, 1-H, 4-H), 5.19 (s, 2 H, CH_2), 6.71 (dt, *J* = 2.0, 8.3 Hz, 2 H, Ar-H), 7.07–7.20 (m, 3 H, 6-H, 7-H, 8-H), 7.45–7.51 (m, 1 H, 5-H), 7.59 (dt, *J* = 2.0, 8.3 Hz, 2 H, Ar-H) ppm.

^{13}C NMR (63 MHz, $CDCl_3$) δ = 7.7 (CH_3), 11.9 (CH_2), 18.9 (C-1), 28.1 (CH_2), 31.1 (C-4), 31.4 (C-2), 31.6 (CH_2), 35.1 (C-3), 45.9 (CH_2), 92.6 (Ar), 108.0 (C-4a), 109.0 (C-8), 117.7 (C-5), 119.2 (C-6), 120.3 (CN), 121.2 (C-7), 127.5 (C-4b), 127.9 (Ar), 133.7 (C-9a), 136.9 (C-8a), 137.7 (Ar), 137.8 (Ar) ppm.

IR: $\tilde{\nu}$ = 3050, 3030, 2960, 1465, 1180, 1005, 740 cm^{-1}.

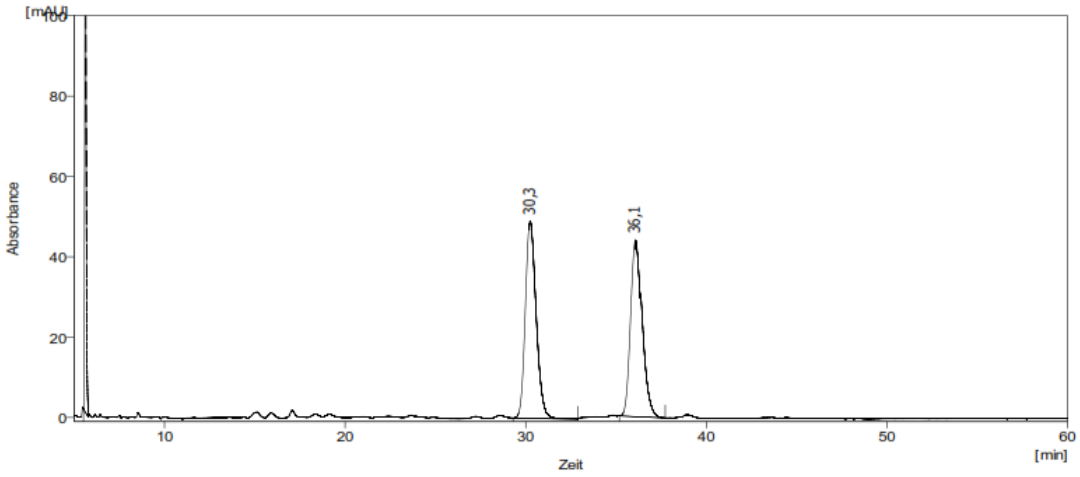
HRMS (ESI-TOF) m/z: calc. for $C_{24}H_{26}IN_2^+$, $[M+H]^+$: 469.1141, found: 469.1140.

HPLC traces:

Methode	: C:\ClarityChrom\DataFiles\18314_155859_ Uni Rostock\Alice_Voß\Alice-Chiral\Alice 2 für S9b (Cellulose)	durch	: Administrator
Beschreibung	: Alice-Chiral		
Erstellt	: 20.06.2018 16:56	Geändert	: 30.11.2021 12:14
Säule	: Lux Cellulose-1, 3µm 250 x 4.6mm SNo: H21-350519, PartNr: 00G-4458-E0,	Detektor	: UV CH1:259 nm;
Mobile Phase	: Ethanlo / n- heptan 5:95	Temperatur	: 25°C
Flussrate	: 1,0 ml/min	Druck	: 120mbar
Notizen	: partial loop mit 100µl Porbeschleife /60min/ kein Gradient / standby Fluss. 1,0 ml/min, Inj. Volumen immer 10µl, Gelöst in Heptan/Ethanol. 95:5, 1mg auf 1ml		
Autostop	: 60,00 min	Externes Startsignal	: Nur externer Start, Absteigend
Detektor 1	: DAD 2.1L: Channel 1	Bereich 1	: Bipolar, 10000 mAU, 20 Proben pro Sek.
Abzuziehendes Chromatogramm	: (Keine)	Anpassung	: Keine Änderung

The racemic reference sample (±)-**20** could be base-line separated by using a Lux Cellulose-1 column, EtOH/heptane 5:95, flow rate 1.0 mL/min. The individual enantiomers eluted at retention times of 30 and 36 min, respectively.

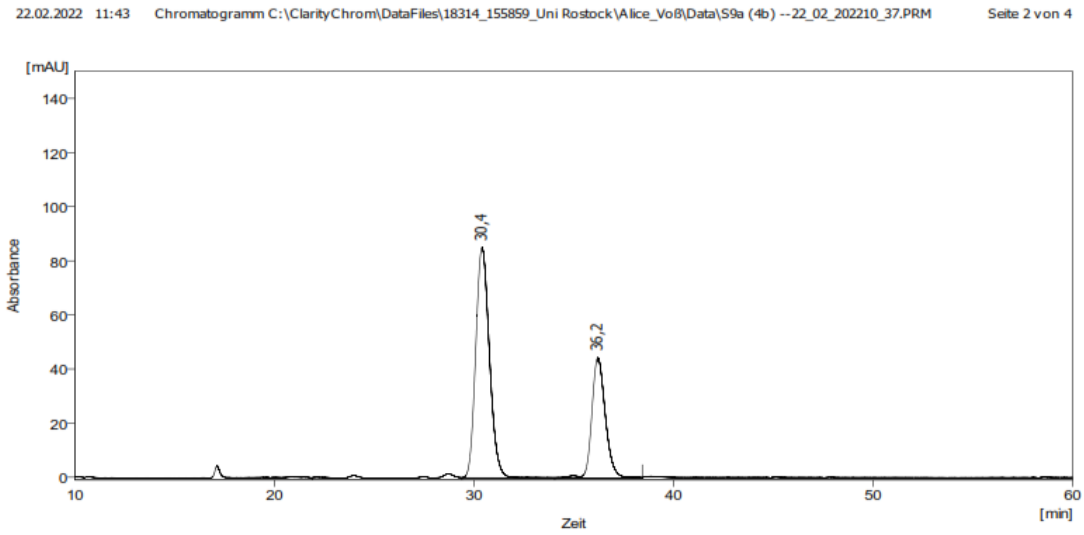
Racemate (±)-**20**



	Signalname	Retentionsz. [min]	Fläche [mAU.sek]	Höhe [mAU]	Fläche [%]	Höhe [%]
1	DAD 2.1L: Channel 1	5,619	720,588	128,301	15,2	57,9
2	DAD 2.1L: Channel 1	30,254	2058,724	49,231	43,3	22,2
3	DAD 2.1L: Channel 1	36,074	1971,259	44,068	41,5	19,9
		Alle Signale Gesamt	4750,571	221,600	100,0	100,0

Lux Cellulose-1 column, EtOH/heptane 5:95, flow rate 1.0 mL/min.

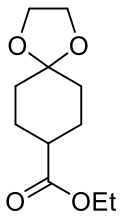
Reaction product (–)-**20**, *e.r.* 66:34



	Signalname	Retentionsz. [min]	Fläche [mAU.sek]	Höhe [mAU]	Fläche [%]	Höhe [%]
1	DAD 2.1L: Channel 1	30,399	4060,101	85,116	66,0	65,7
2	DAD 2.1L: Channel 1	36,197	2092,398	44,514	34,0	34,3
		Alle Signale Gesamt	6152,499	129,630	100,0	100,0

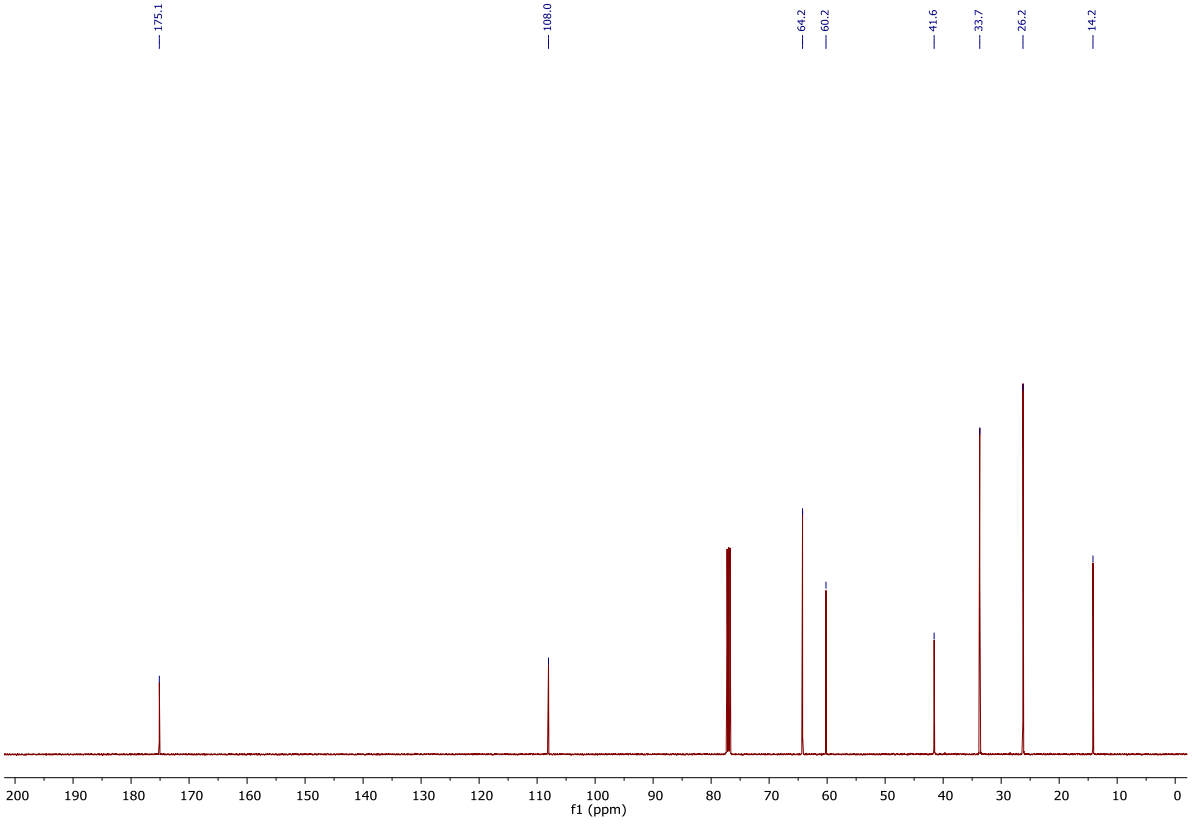
Lux Cellulose-1 column, EtOH/heptane 5:95, flow rate 1.0 mL/min.

4 NMR spectra

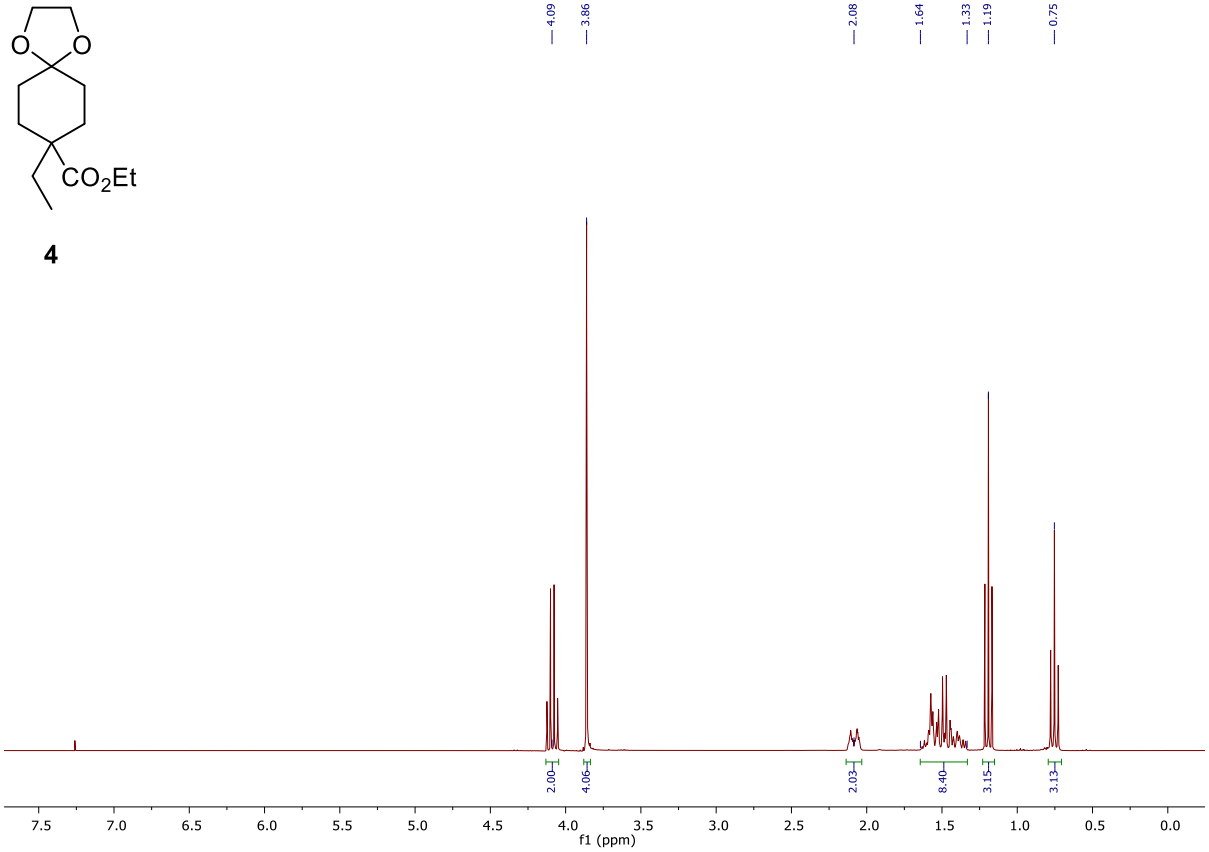


3

300 MHz, $CDCl_3$

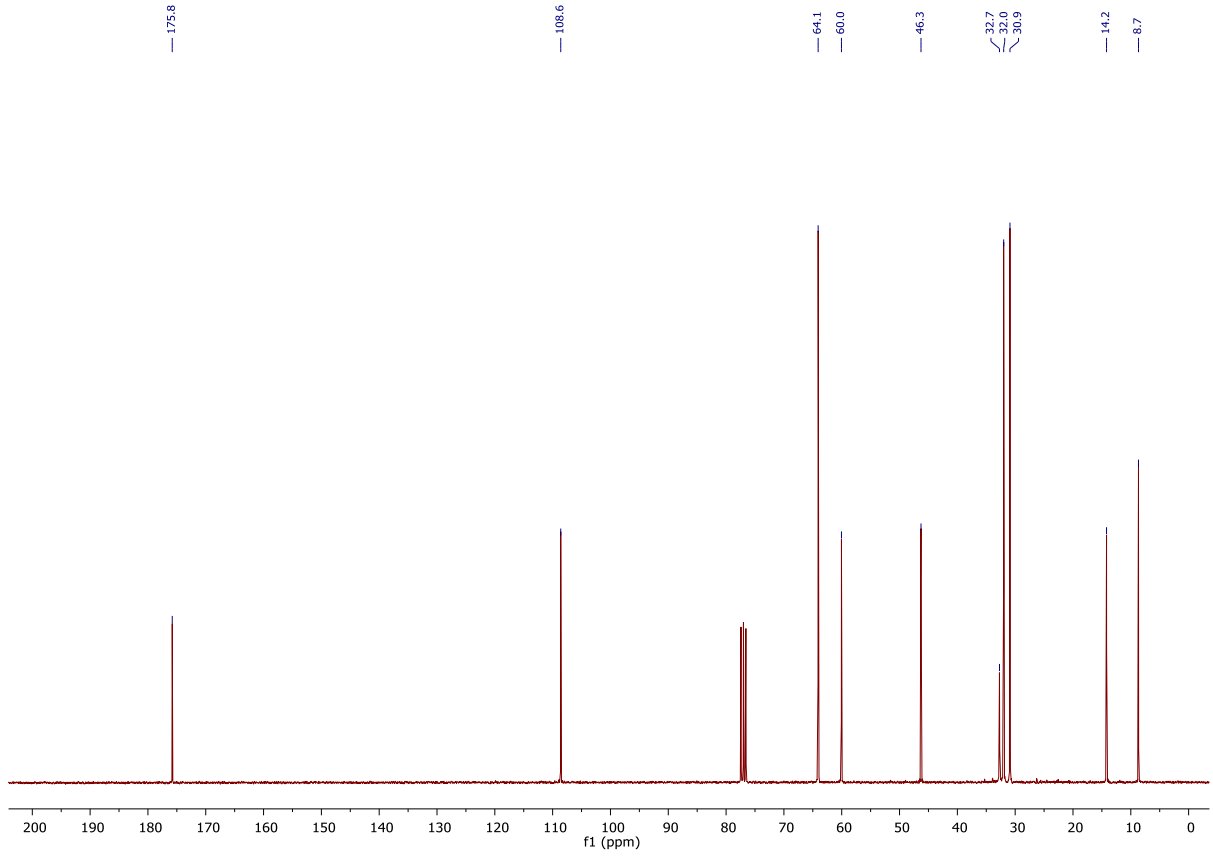


125 MHz, $CDCl_3$

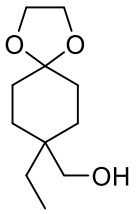


4

300 MHz, $CDCl_3$

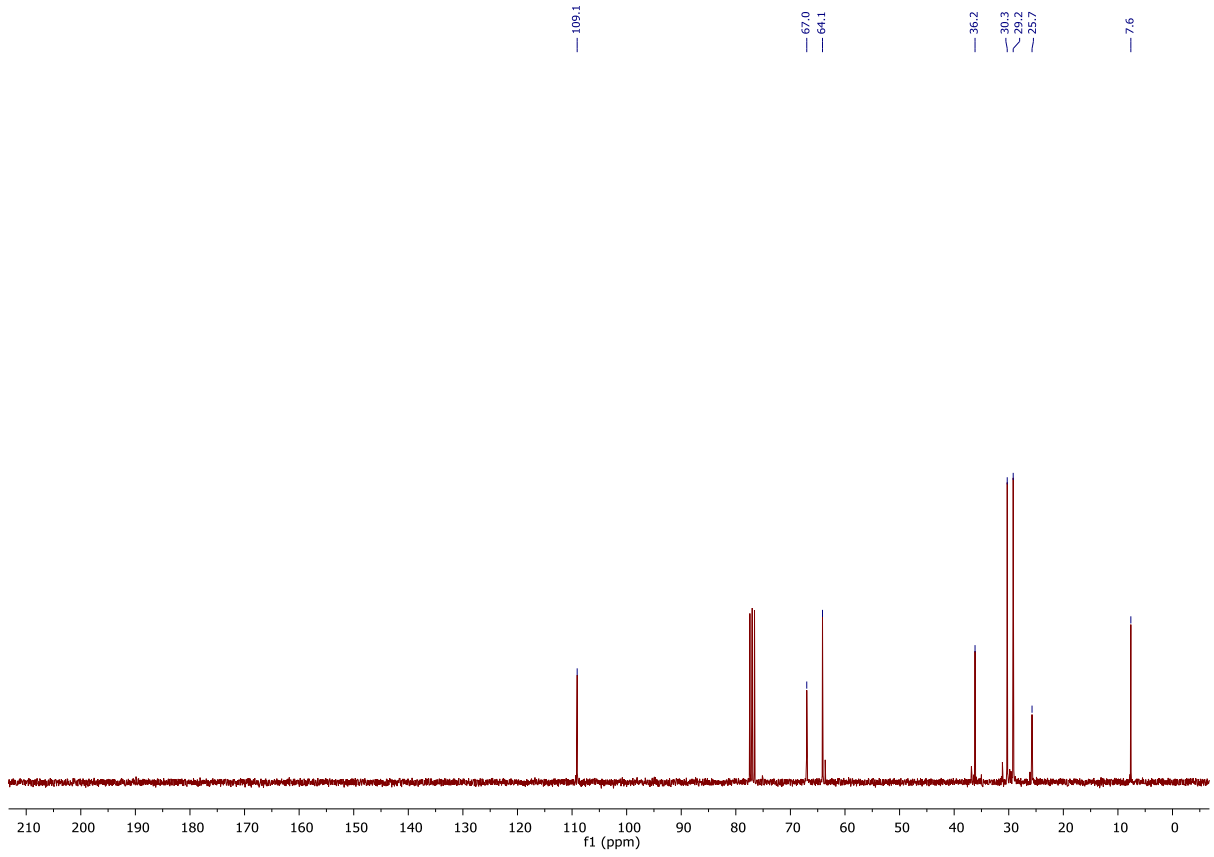


75 MHz, $CDCl_3$

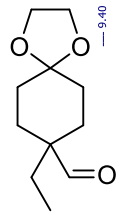


5

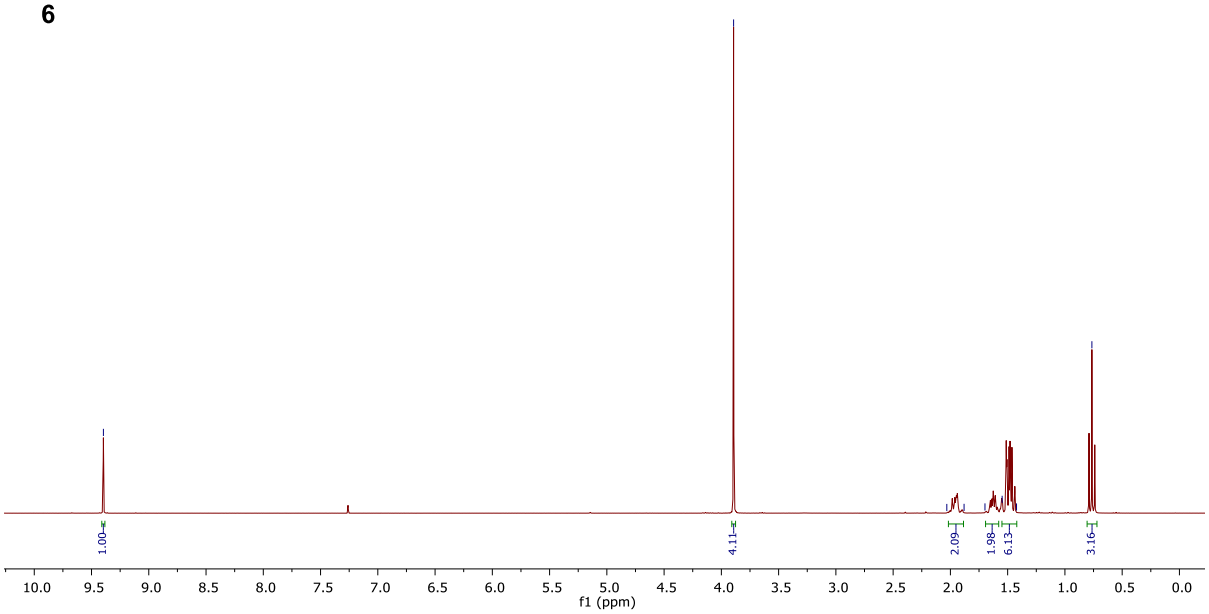
300 MHz, $CDCl_3$



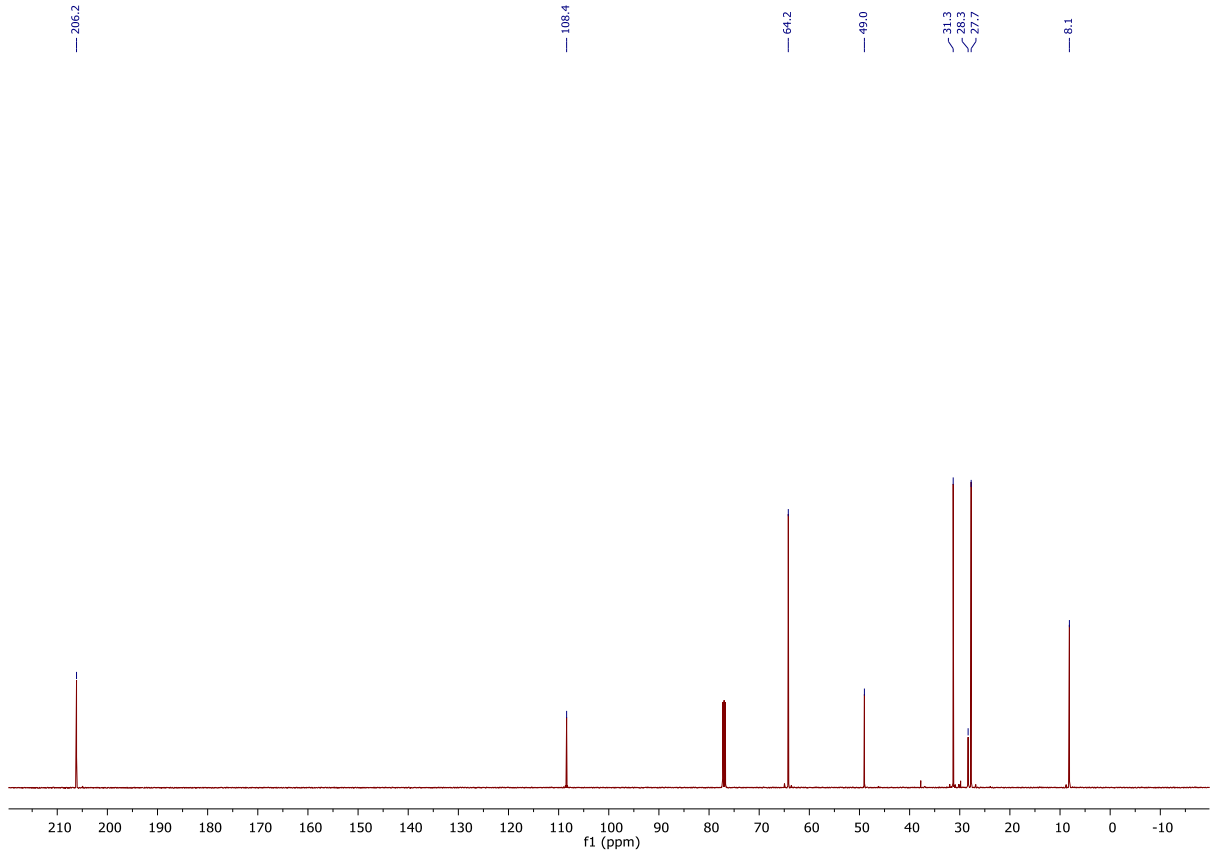
75 MHz, $CDCl_3$



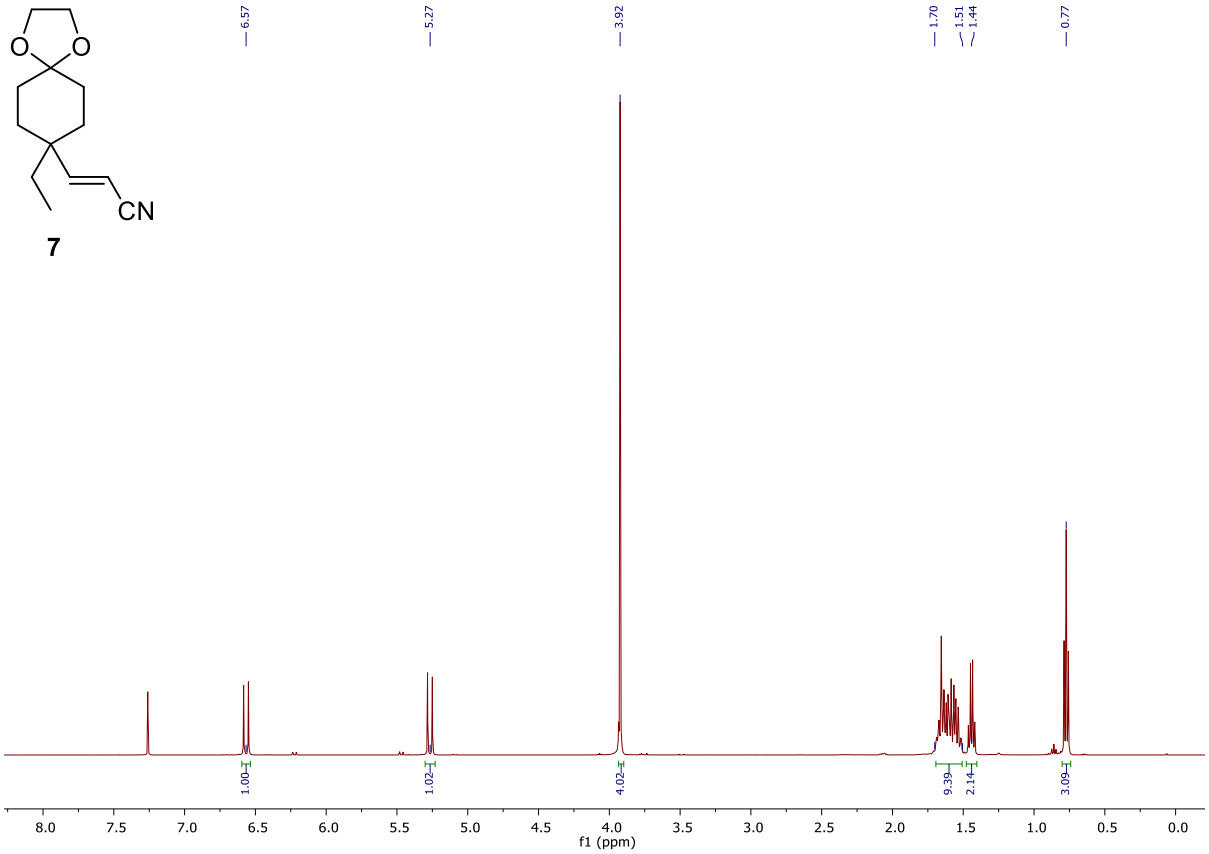
6



300 MHz, $CDCl_3$

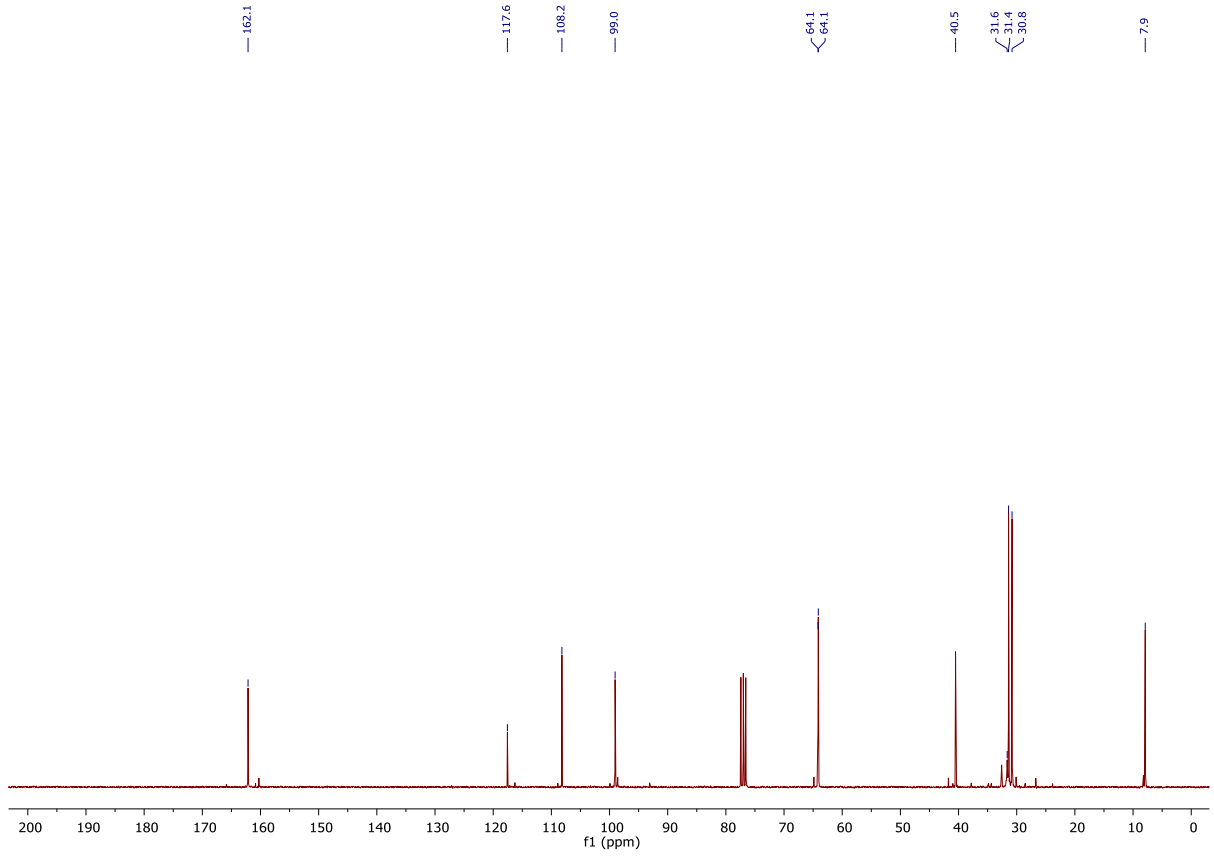


125 MHz, $CDCl_3$

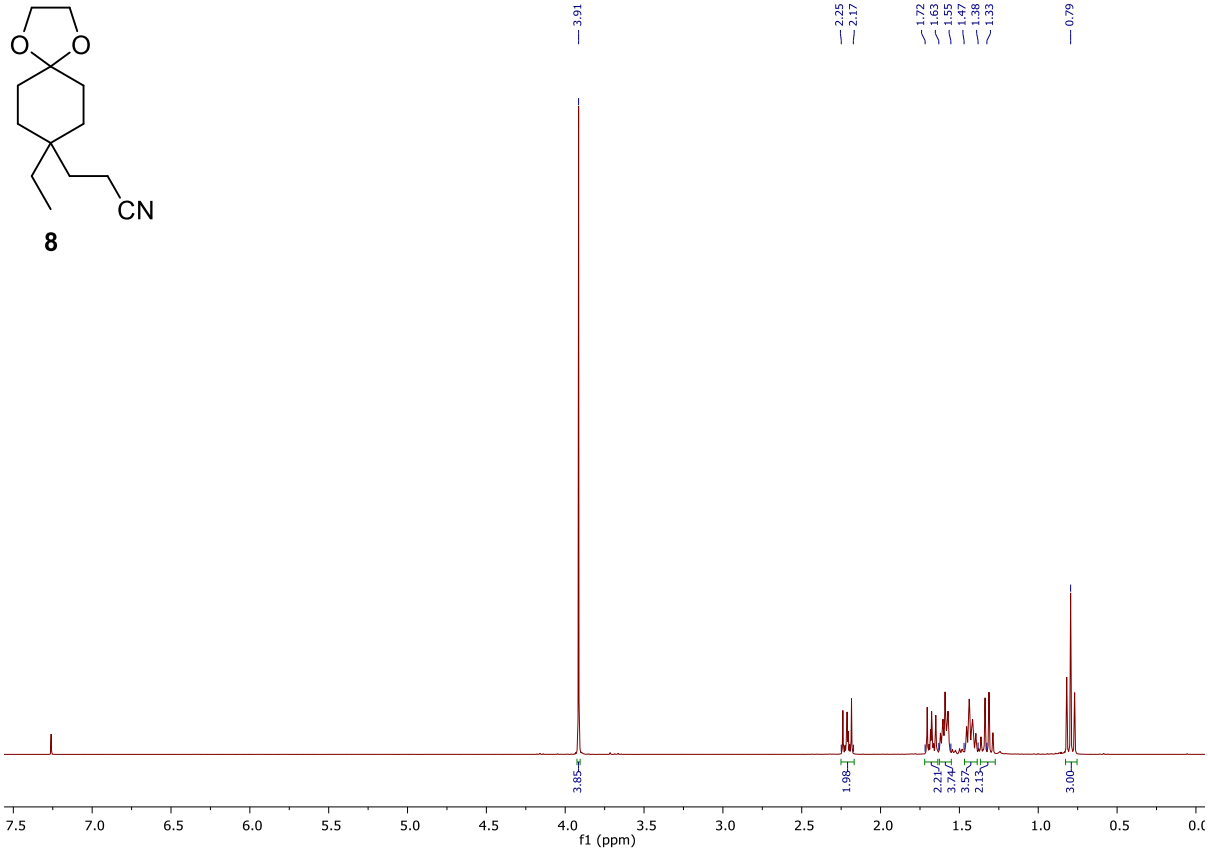


7

500 MHz, $CDCl_3$

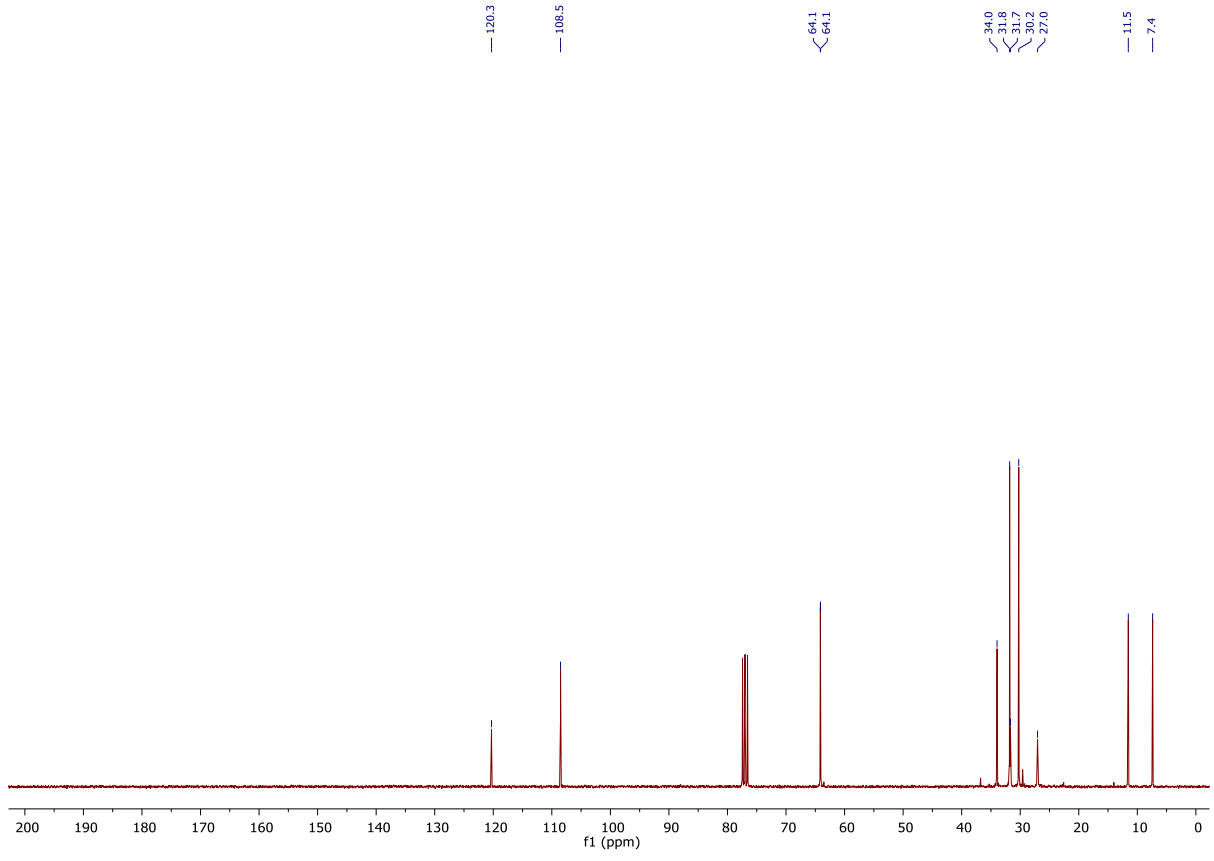


75 MHz, $CDCl_3$

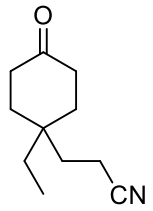


8

300 MHz, $CDCl_3$

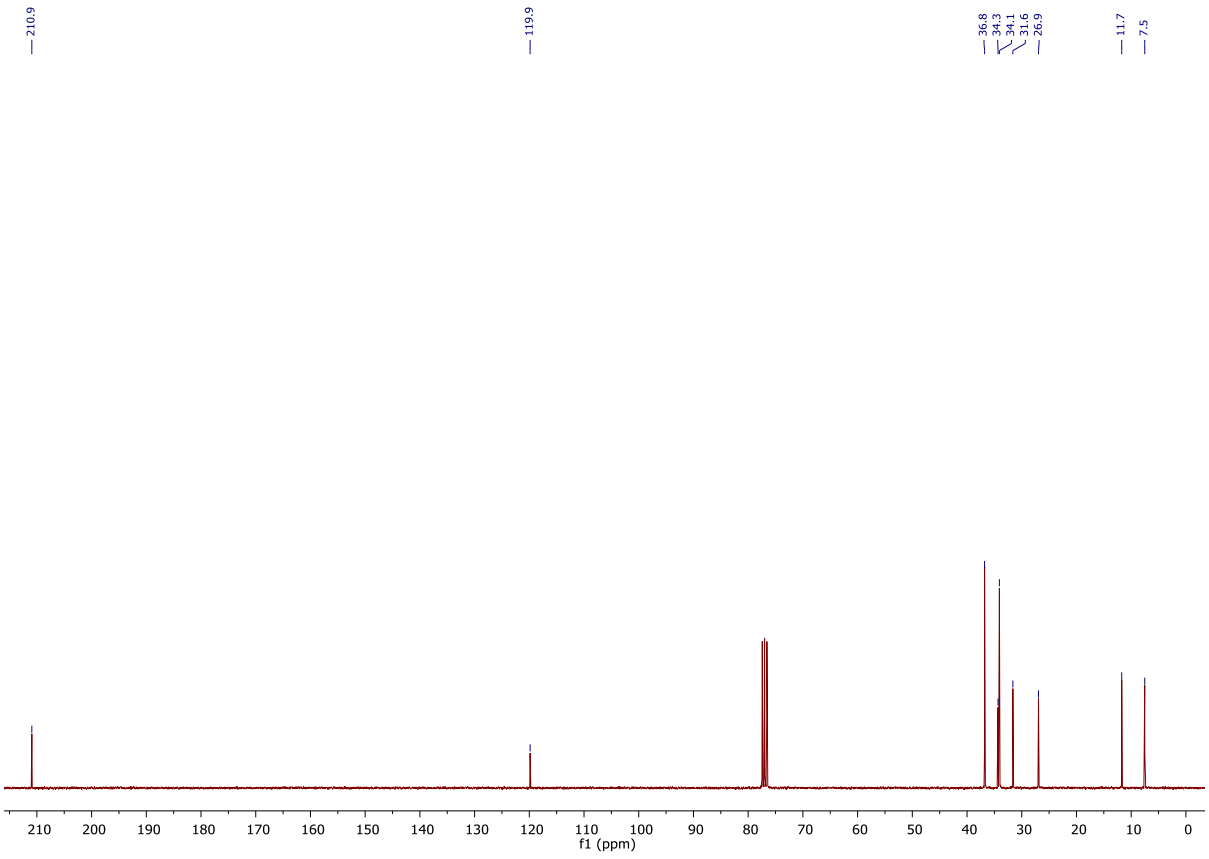


75 MHz, $CDCl_3$

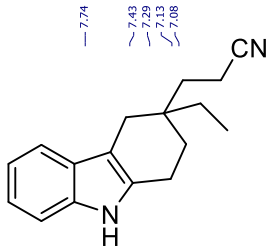


9

500 MHz, $CDCl_3$

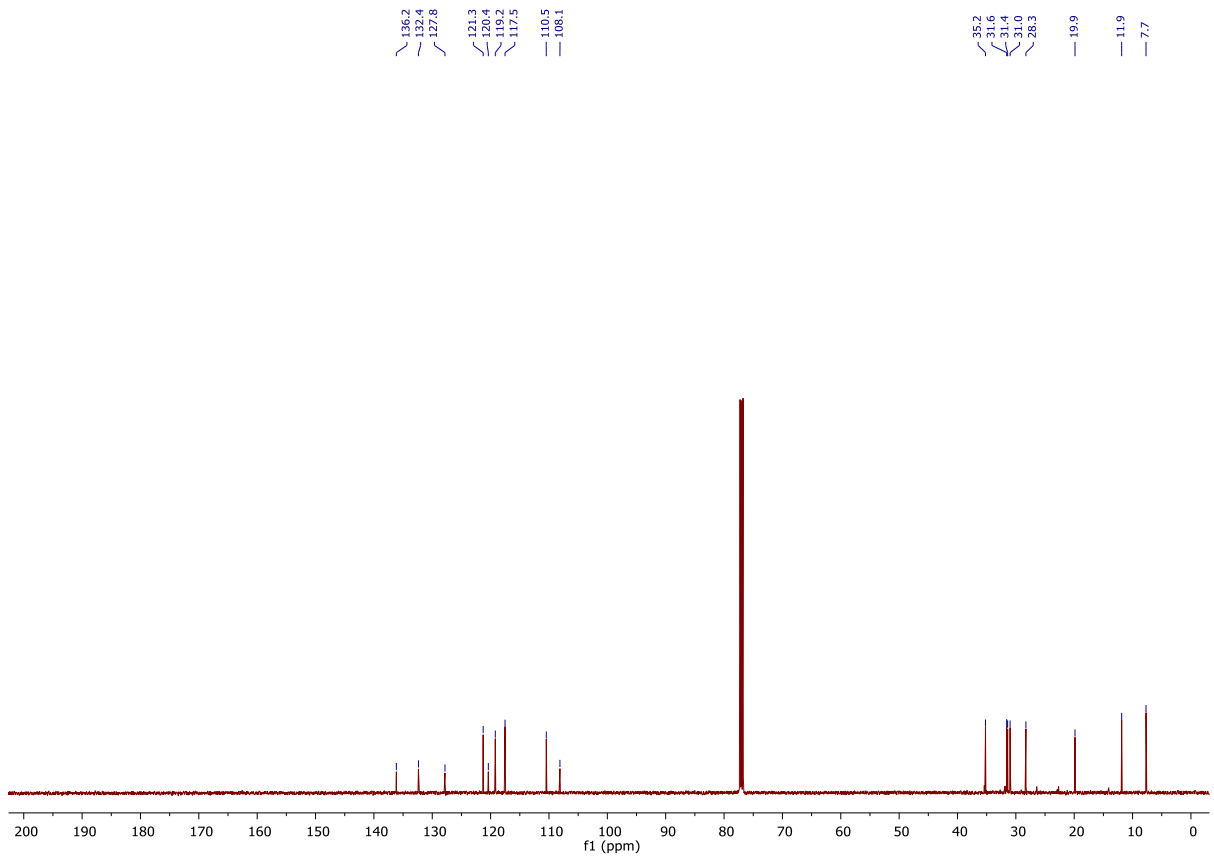


75 MHz, $CDCl_3$

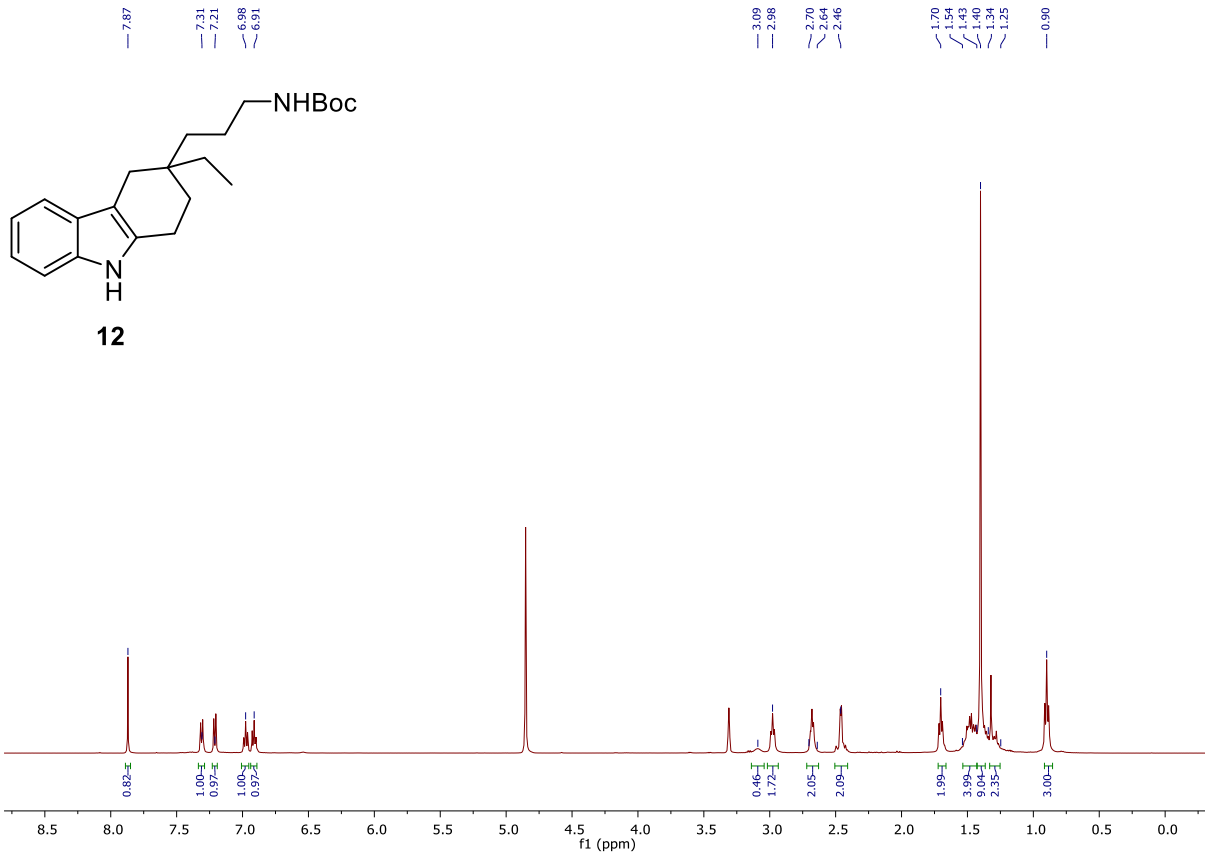


11

500 MHz, $CDCl_3$

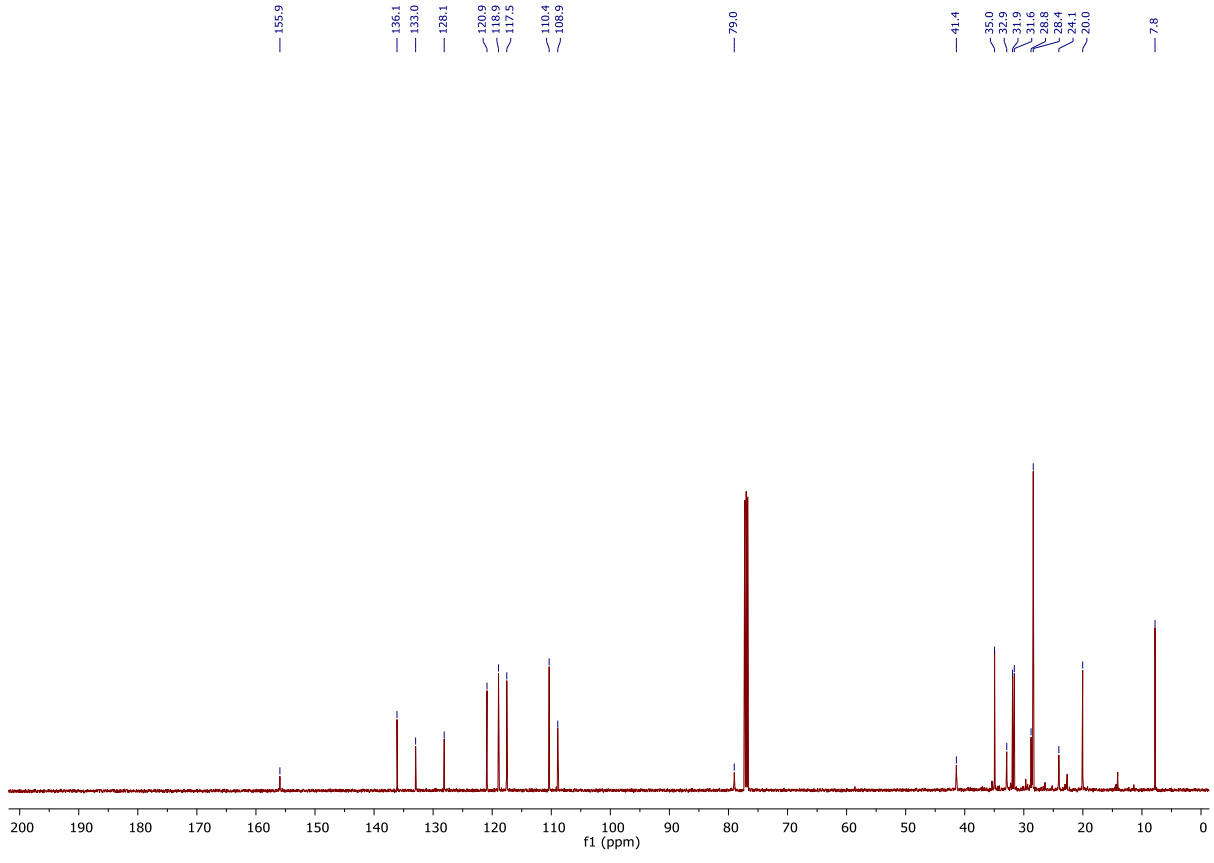


125 MHz, $CDCl_3$

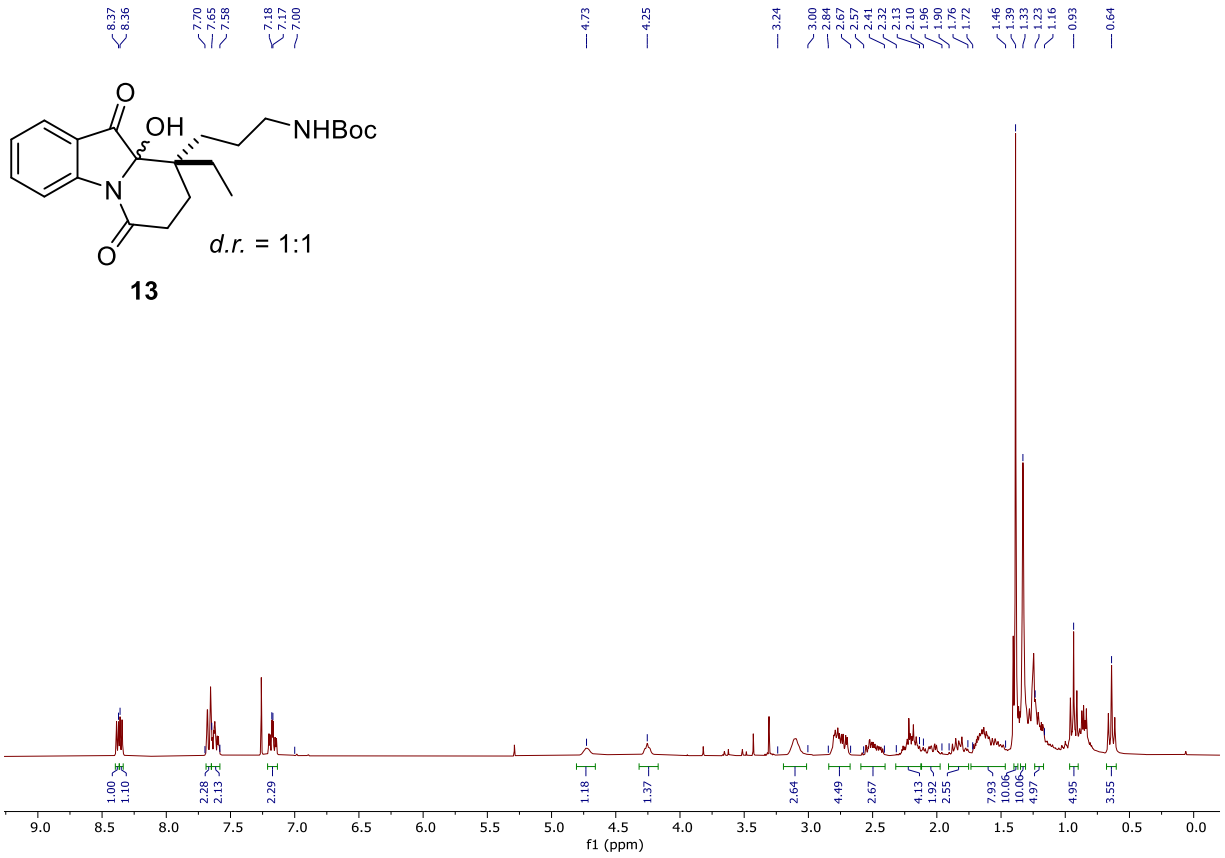


12

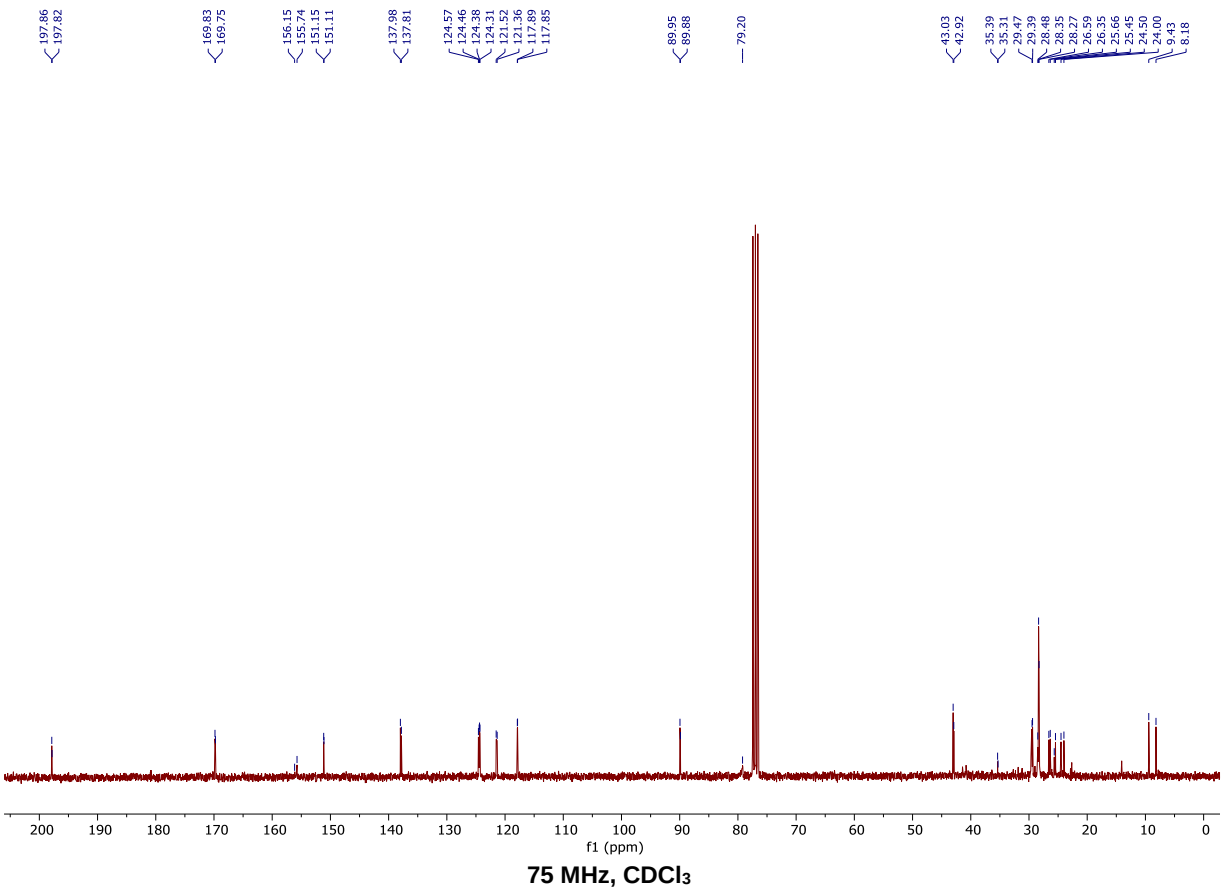
500 MHz, CD_3OD



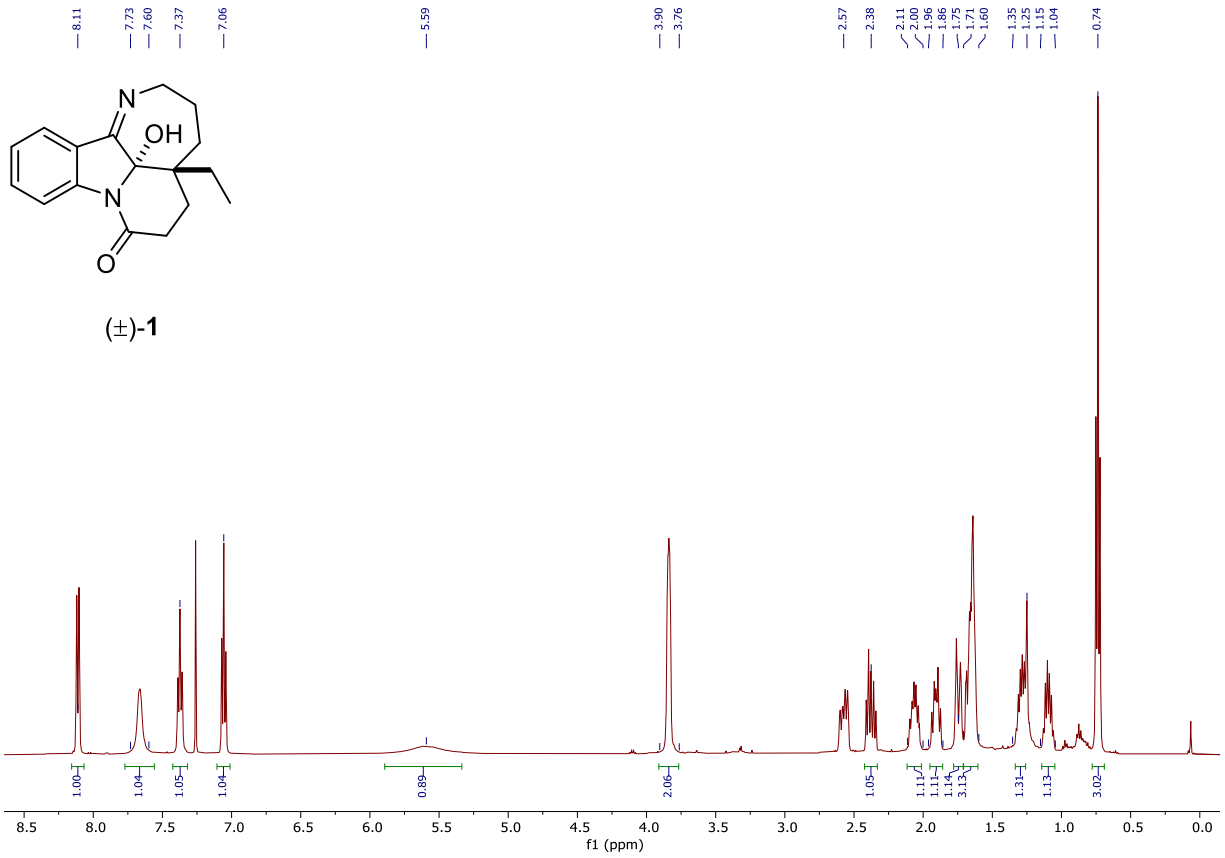
125 MHz, $CDCl_3$



300 MHz, $CDCl_3$

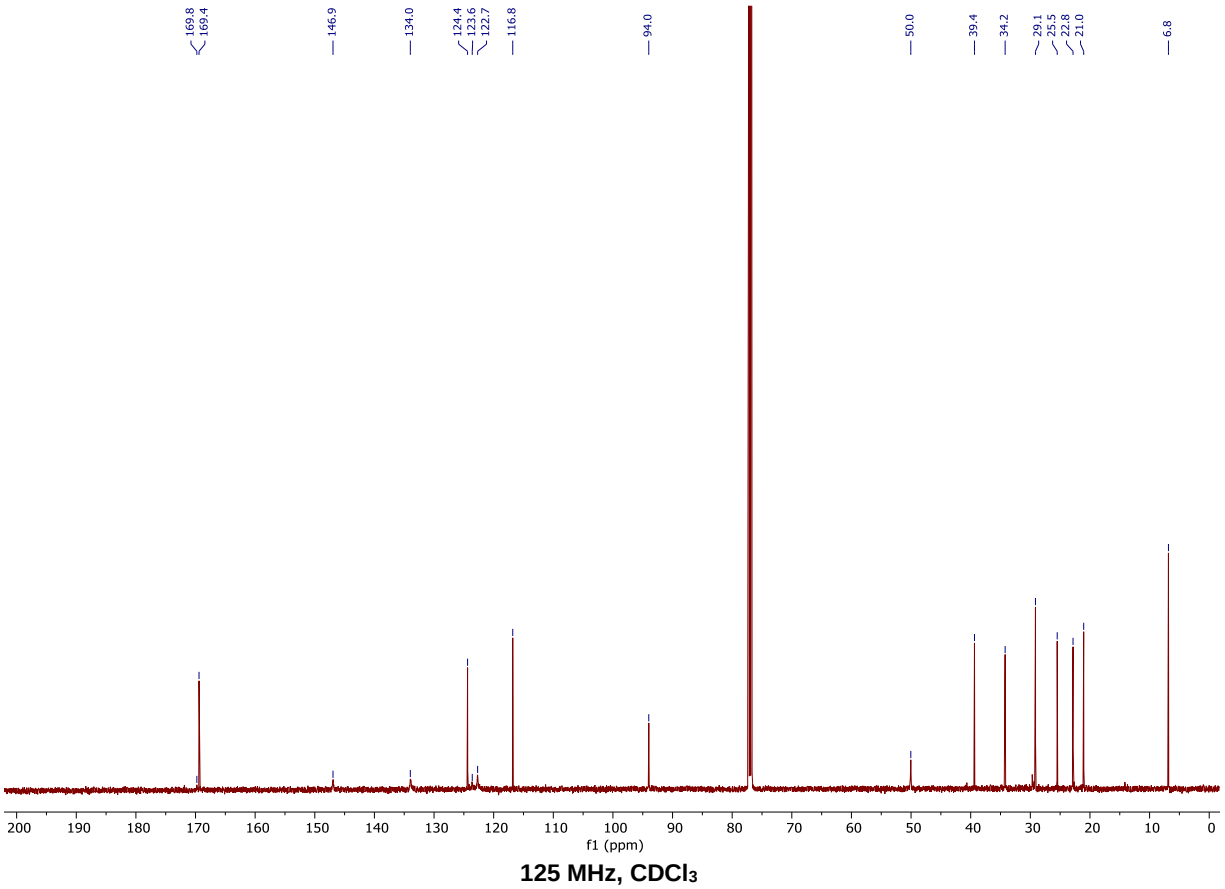


75 MHz, $CDCl_3$

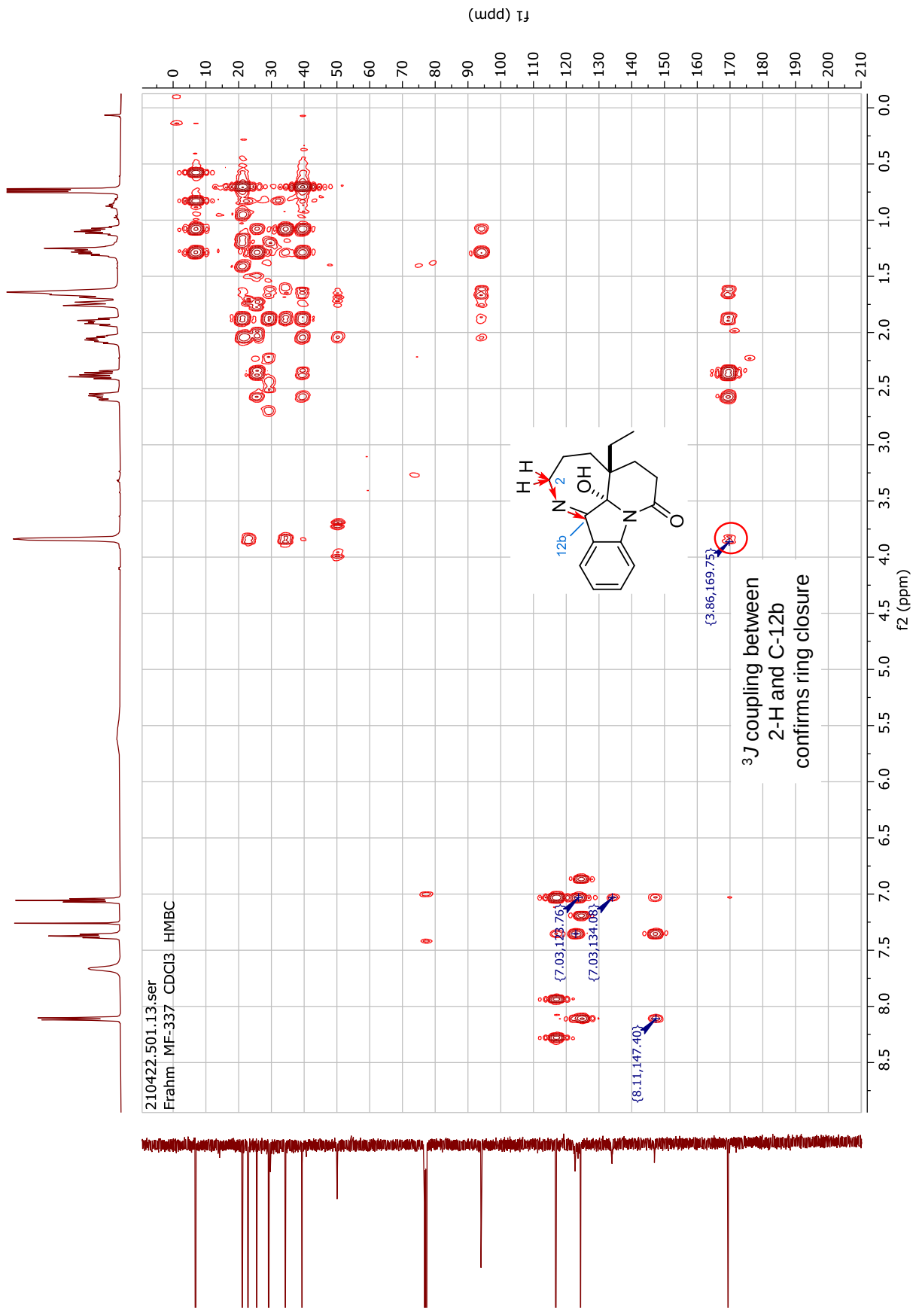


(±)-**1**

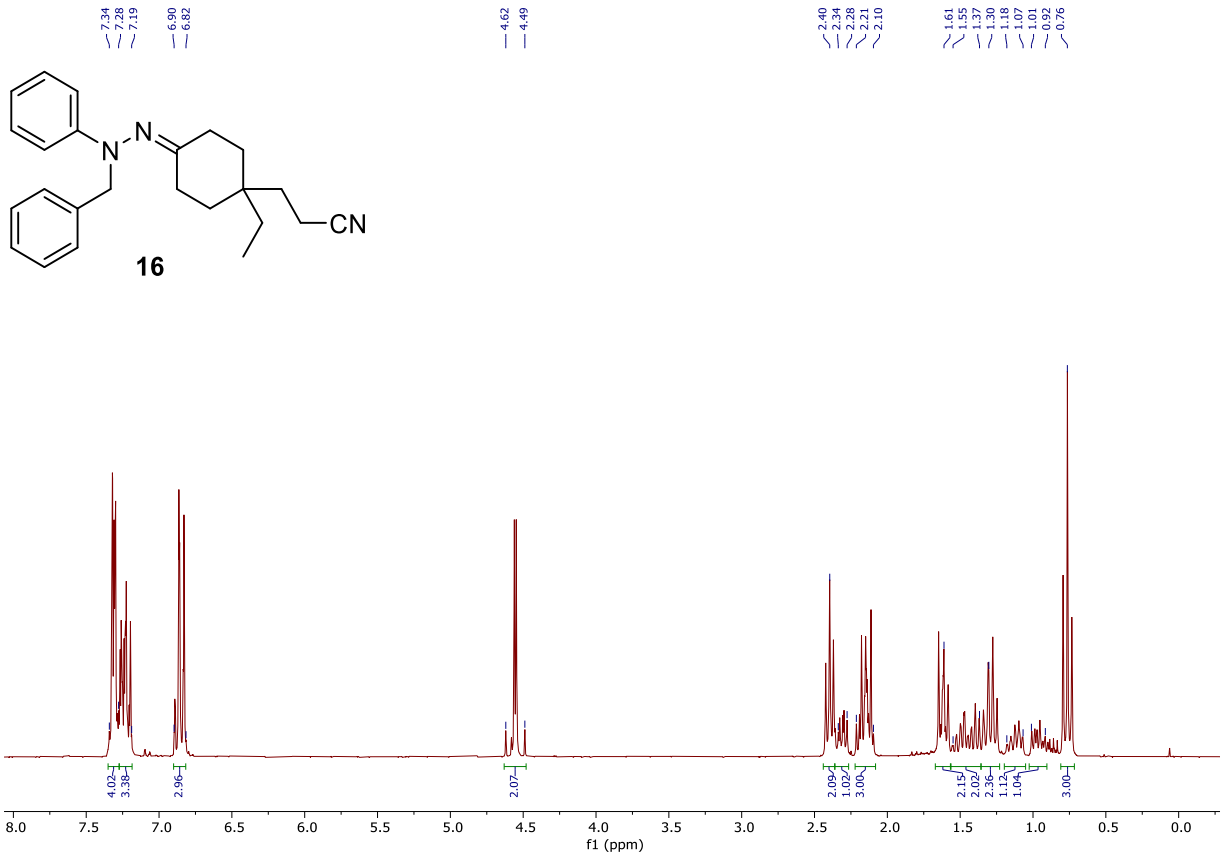
500 MHz, $CDCl_3$



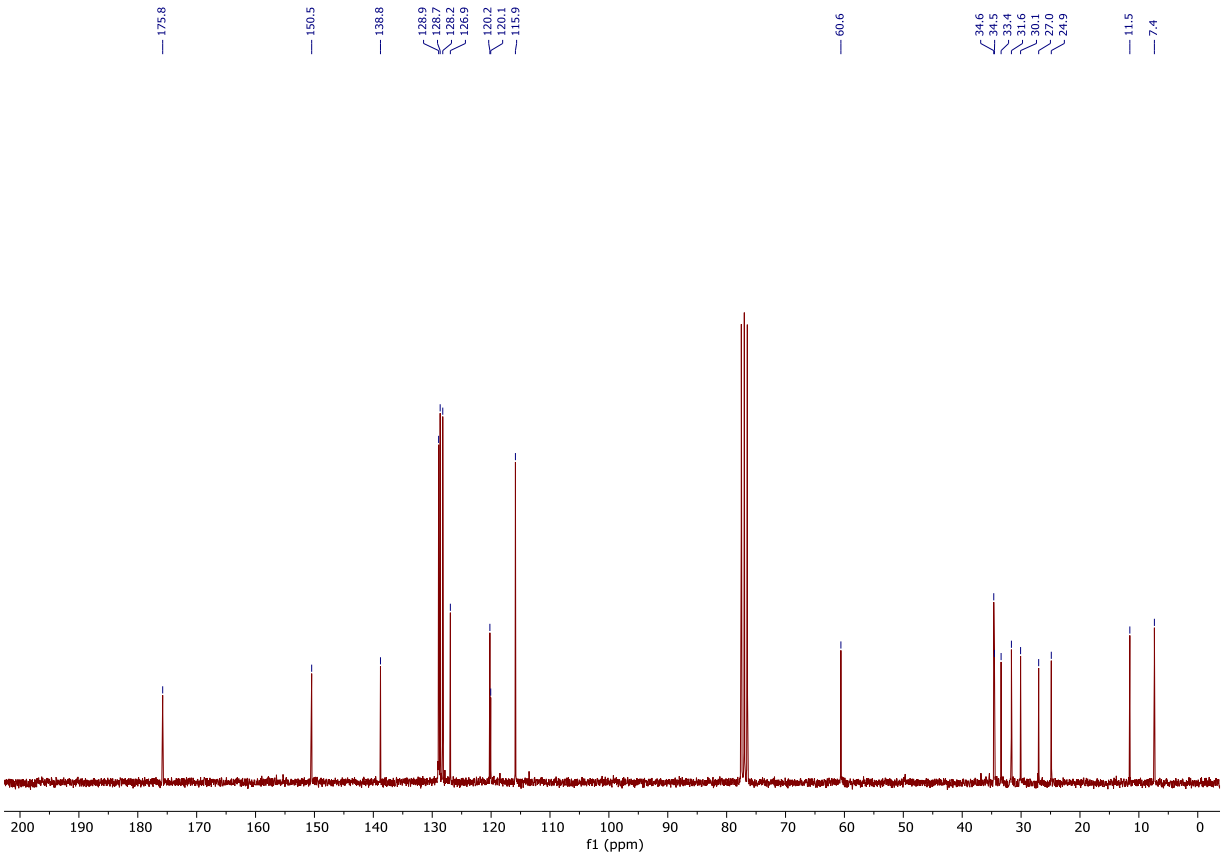
125 MHz, $CDCl_3$


210422.501.13.ser
Frahm MF-337 CDCl3 HMBC
f1 (ppm)
f2 (ppm)
{3.86,169.75}
{7.03,128.76}
{7.03,134.08}
{8.11,147.40}
12b
2
OH
H H
N
N
O
^3J coupling between
2-H and C-12b
confirms ring closure

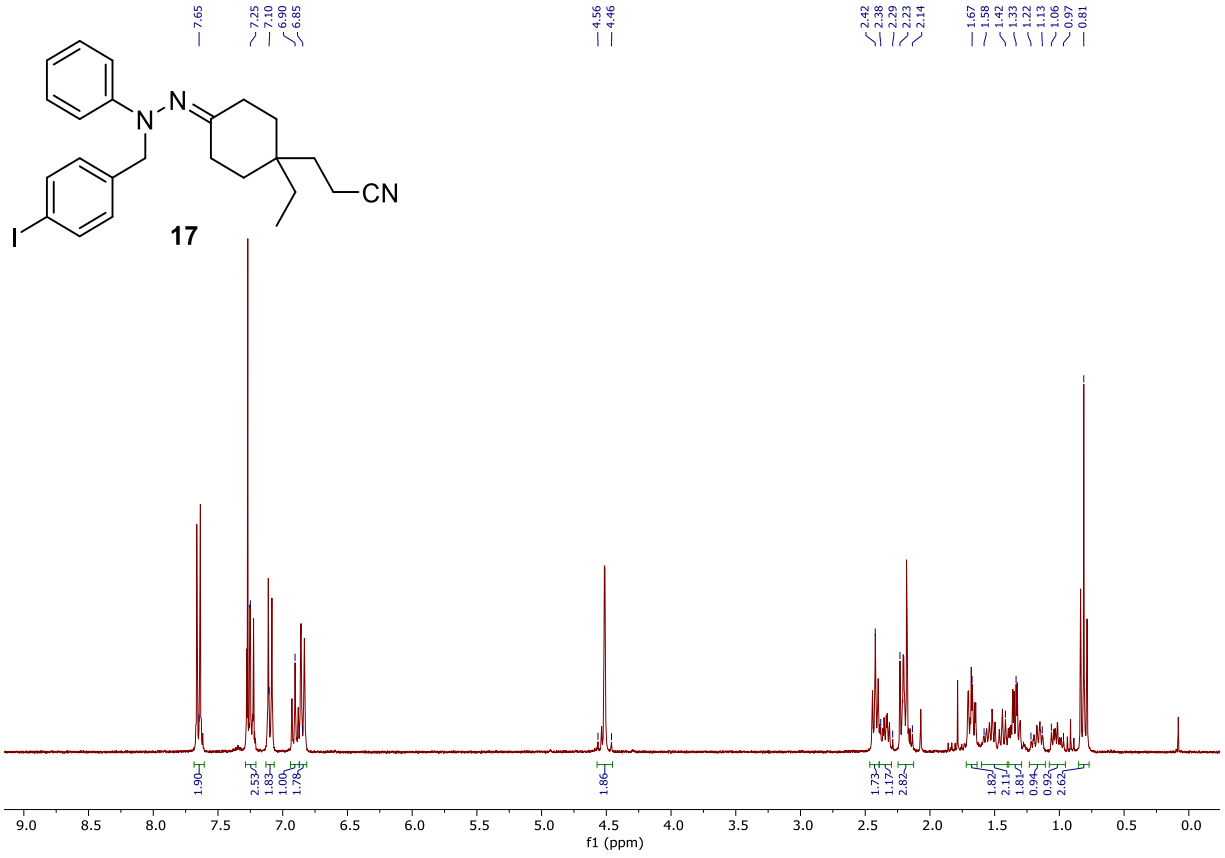
HMBC, $CDCl_3$



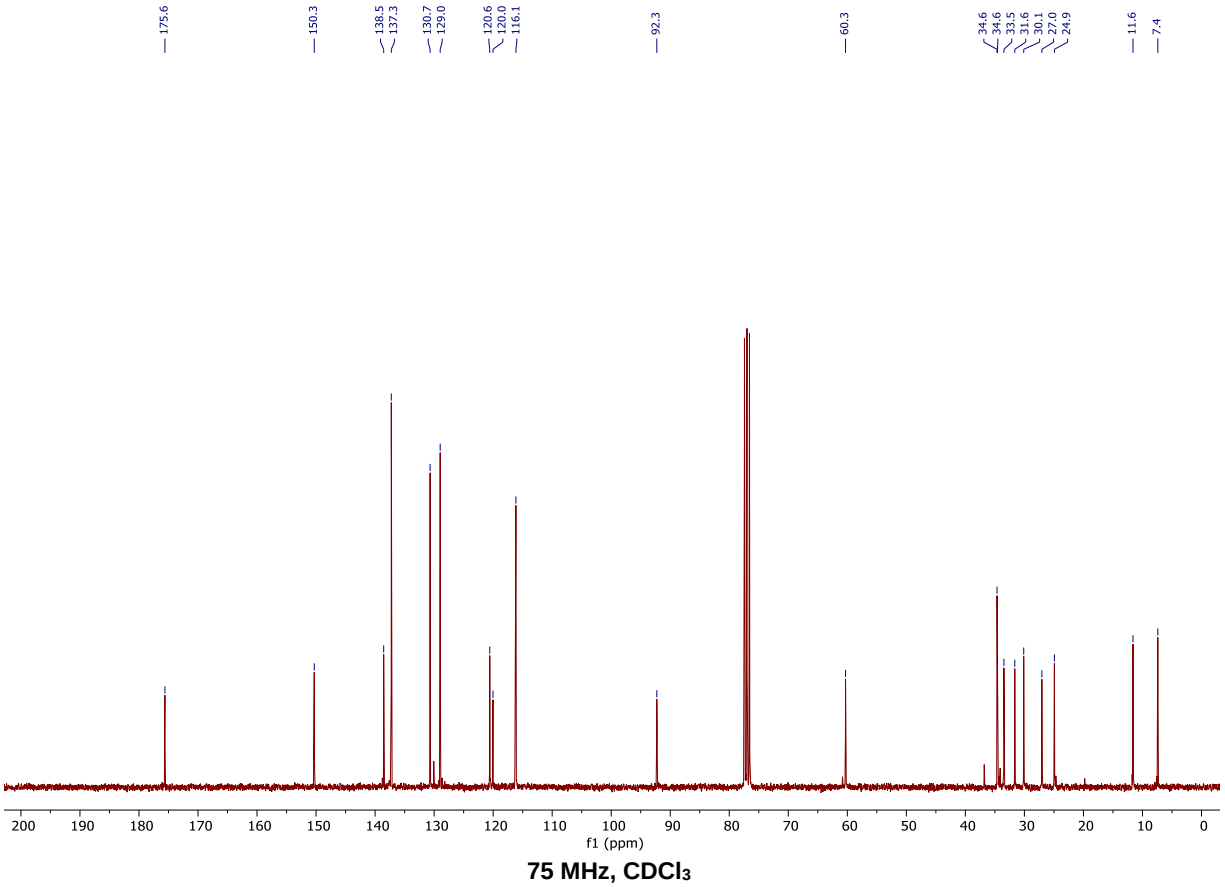
250 MHz, $CDCl_3$



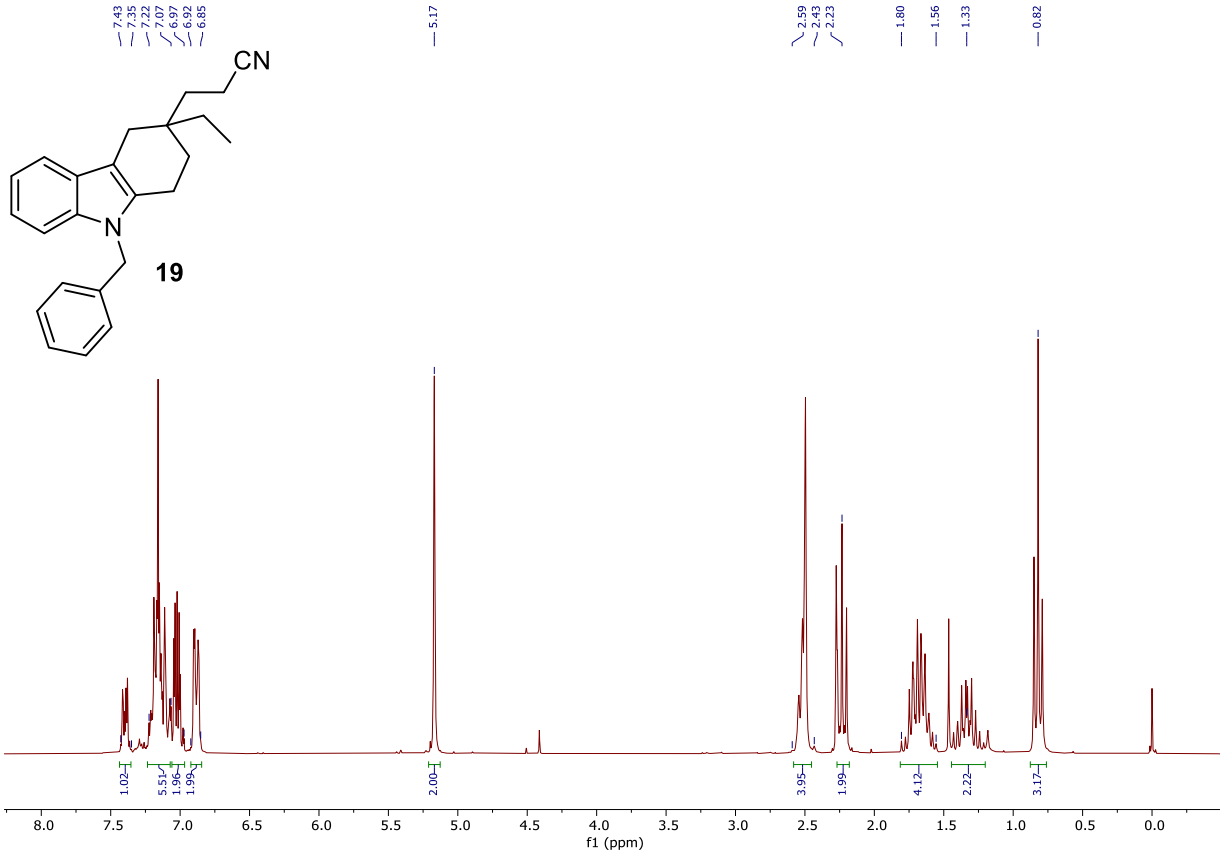
63 MHz, $CDCl_3$



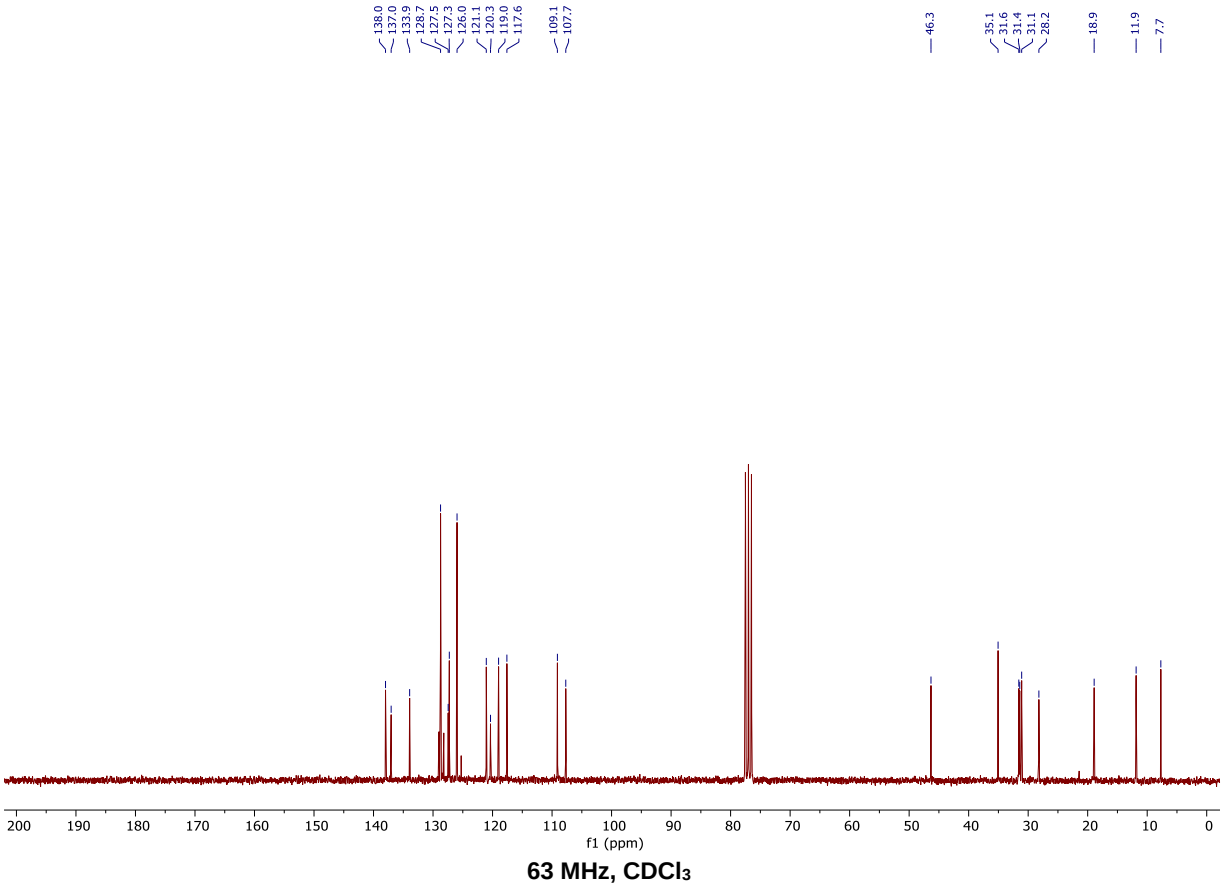
300 MHz, $CDCl_3$



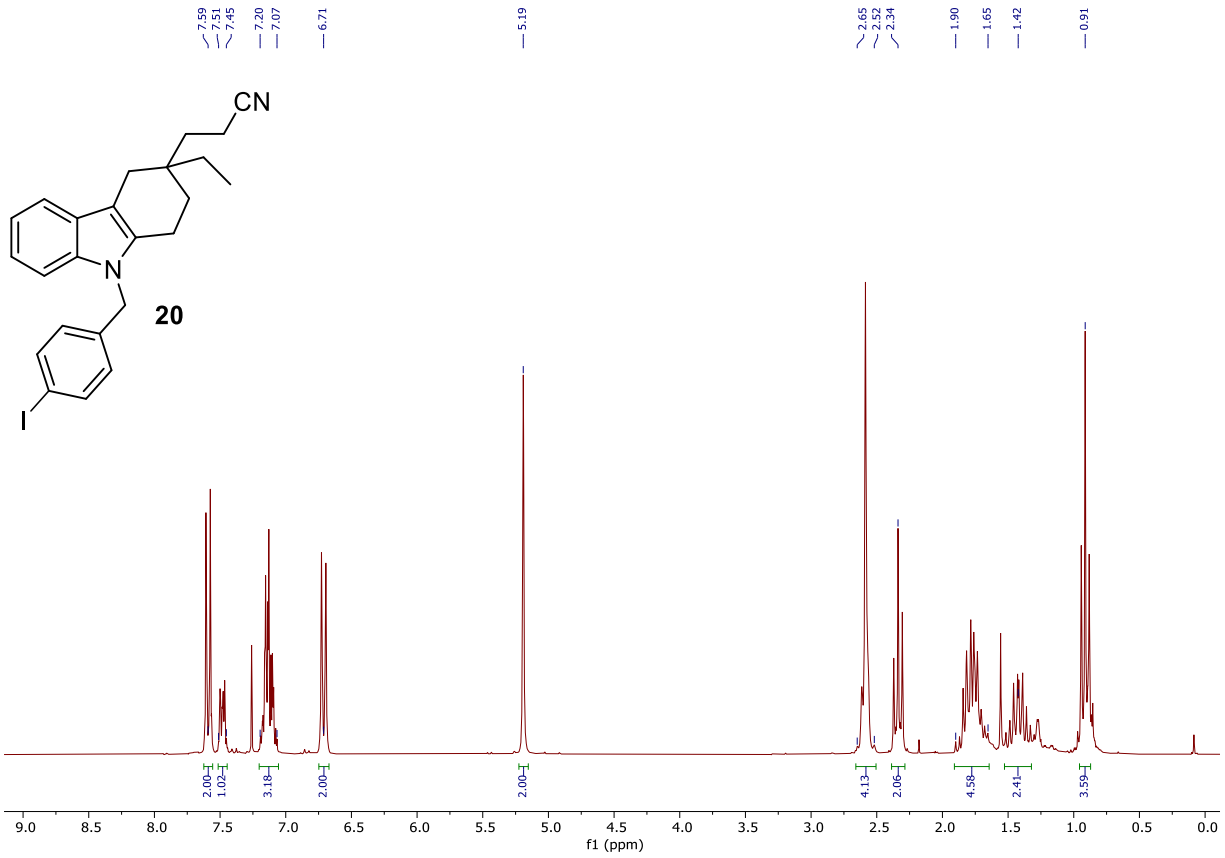
75 MHz, $CDCl_3$



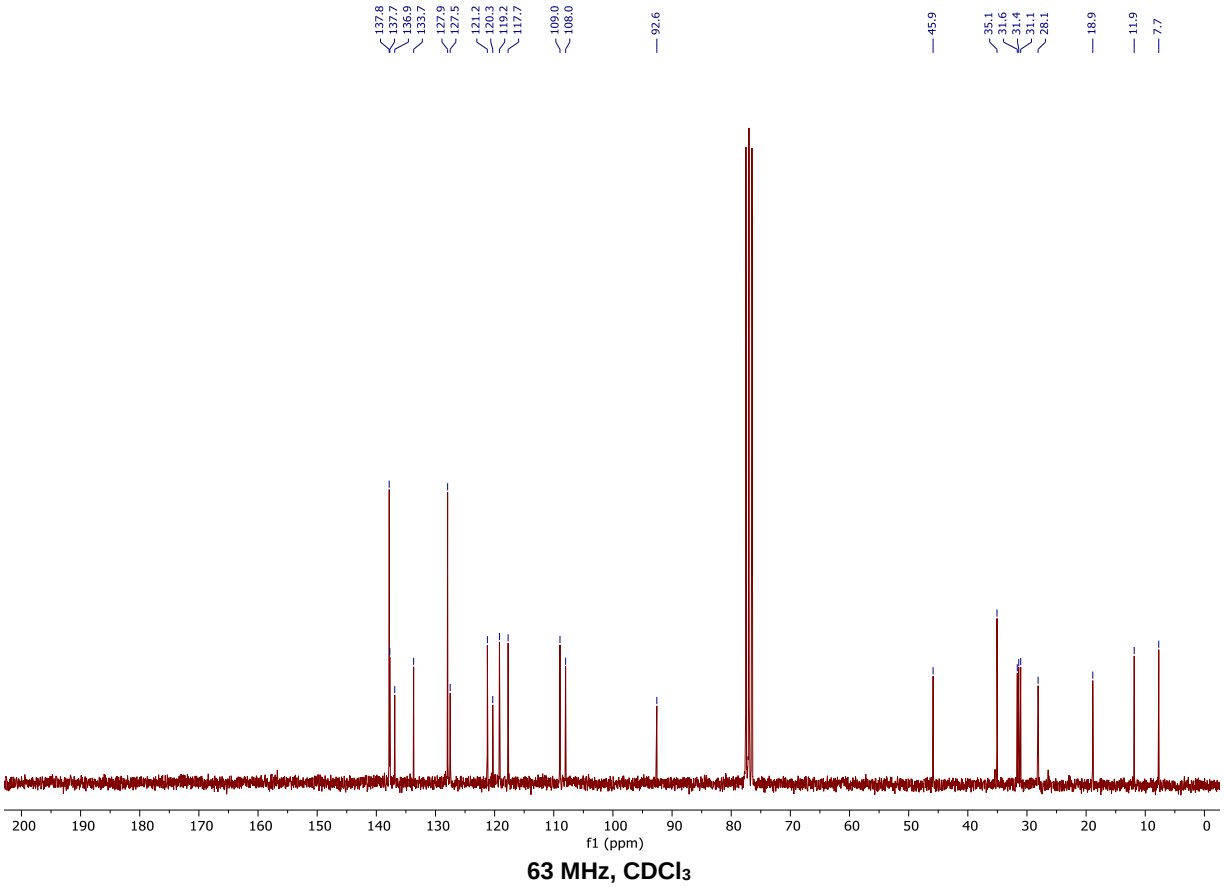
250 MHz, $CDCl_3$



63 MHz, $CDCl_3$



250 MHz, $CDCl_3$



63 MHz, $CDCl_3$