Supporting Information

A General Catalytic Reaction Sequence to Alkaloid-Inspired Indole Polycycles

Adithi Danda[a,b], Kamal Kumar[a,b]* and Herbert Waldmann[a,b]*

[a] Max Planck Institute of Molecular Physiology, Department of Chemical Biology, Otto-Hahn Str. 11, 44227-Dortmund, Germany

[b]Fakultät Chemie, Chemische Biologie, Technische Universität Dortmund, Otto-Hahn Str. 6, 44227-Dortmund, Germany.

Fax: +49-231-133-2499

email: kamal.kumar@mpi-dortmund.mpg.de; Herbert.waldmann@mpi-dortmund.mpg.de.

Table of Contents:

1. General

Unless otherwise noted, all commercially available compounds were used as provided without further purifications. Solvents for chromatography were technical grade. Analytical thin-layer chromatography (TLC) was performed on Merck silica gel aluminium plates with F-254 indicator. Compounds were visualized by irradiation with UV light or potassium permanganate staining. Column chromatography was performed using silica gel Merck 60 (particle size 0.040-0.063 mm). Solvent mixtures are understood as volume/volume. ^{1}H-NMR and ^{13}C-NMR were recorded on a Bruker DRX400 (400 MHz) and Bruker DRX600 (600 MHz), using $CDCl_3$ or DMSO-d_6 or CD_2Cl_2 as solvent. Data are reported in the following order: chemical shift (δ) values are reported in ppm with the solvent resonance as internal standard (CDCl3: δ = 7.26 ppm for 1H, δ = 77.16 ppm for 13C), (DMSO-d_6: δ = 2.50 ppm for 1H, δ = 39.52), (CD_2Cl: δ = 5.32 ppm for 1H, δ = 53.84), multiplicities are indicated br s (broadened singlet), s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet), dd (doublet of doublet), dt (doublet of triplet); coupling constants (*J*) are given in Hertz (*Hz*). High resolution mass spectra were recorded on a LTQ Orbitrap mass spectrometer coupled to an Acceka HPLC-System (HPLC column: Hypersyl GOLD, 50 mm x 1 mm, particle size 1.9 µm, ionization method: electron spray ionization. Microwave reactions were performed using CEM Intellivent Explorer 541416 machine at the desired temperature using 300 W power and 14 mbar pressure.

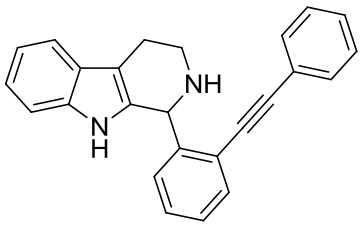
2. Synthesis of Indoloquinolizines 4 :

The various **o-alknyl benzaldehydes** were prepared according to the procedure described in *Org. Lett.* 2014, *16*, 4570-4573

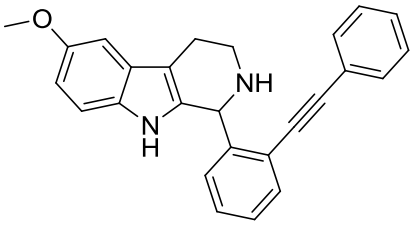
2a. General Procedure A for the synthesis of Pictet-Spengler Derivatives 3.[a]

To a mixture of the corresponding tryptamine/5-substituted tryptamine **1** (0.36 mmol), o-alkynyl benzaldehyde **2** (1.2 equiv, 0.43 mmol) and $Yb(OTf_3)$ (10 mol%, 22.51 mg) was added dry DCM (1.2 mL) under an argon atmosphere with stirring, followed by the addition of ionic liquid [bmim]Cl (0.32 ml/mmol). The reaction mixture was then subjected to microwave irradiation for 60 min at 120 ^oC. The crude reaction mixture was directly purified by column chromatography using basified silica gel with Methanol and Dichloromethane as eluents.

2b. Characterization of the Pictet-Spengler Products 3:-

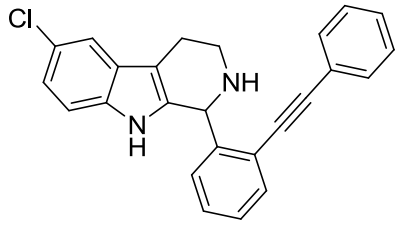


Compound **3a** was synthesized according to the general procedure **A** as a reddish-brown solid in 74% yield; ^1H NMR (400 MHz, 25 °C, $CDCl_3$): δ 7.75(s, 1H, NH), 7.54(m, 1H), 7.47(m, 1H), 7.40(m, 2H), 7.28-7.23(m, 3H), 7.23-7.15(m, 2H), 7.15-7.09(m, 2H), 7.07-7.01(m, 2H), 5.74(s, 1H), 3.23(m, 1H), 3.07(m, 1H), 2.81(m, 2H), 2.20(bs, 1H, NH); ^{13}C NMR (100 MHz, 25 °C, $CDCl_3$): δ 143.7, 136.0, 134.0, 132.8, 131.7, 128.8, 128.69, 128.67, 128.5, 127.9, 127.4, 122.9, 122.6, 121.7, 119.4, 118.2, 110.9, 110.4, 94.5, 87.1, 55.4, 42.2, 22.5; HRMS (ESI): Calculated for $C_{25}H_{21}N_2$ $[M+H^+]$: 349.16993, Found: 349.17088.

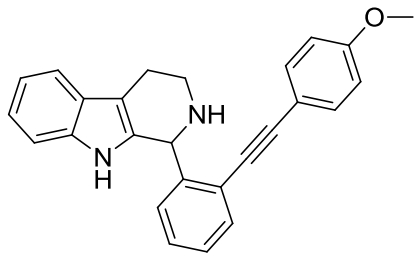


Compound **3b** was synthesized according to the general procedure **A** as a reddish-brown solid in 70% yield; ^1H NMR (400 MHz, 25 °C, $CDCl_3$): δ 7.61(m, 1H), 7.57(s, 1H, NH), 7.47(m, 2H), 7.35-7.27(m, 5H), 7.23(m, 1H), 7.13(dd, *J* = 8.7, 0.5 *Hz*, 1H), 7.0(d, *J* = 2.4 *Hz*, 1H), 6.8(dd, *J* = 8.7, 2.5 *Hz*, 1H), 5.81(s, 1H), 3.87(s, 3H), 3.33(m, 1H), 3.18(m, 1H), 2.86(m, 2H), 2.05(bs, 1H, NH); ^{13}C NMR (100 MHz, 25 °C, $CDCl_3$): δ 154.2, 143.6, 134.9, 132.9,

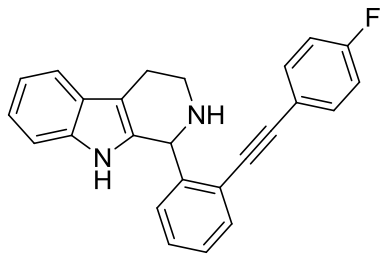
131.7, 131.1, 128.8, 128.73, 128.70, 128.5, 127.9, 127.8, 122.9, 122.7, 111.64, 111.61, 110.2, 100.6, 94.5, 87.1, 56.1, 55.6, 42.4, 22.6; HRMS (ESI): Calculated for $C_{26}H_{23}N_2O$ [M+H$^+$]: 379.18049, Found: 379.18026 .



Compound **3c** was synthesized according to the general procedure **A** as a reddish-brown solid in 60% yield; ^{1}H NMR (400 MHz, 25 °C, CD_2Cl_2): δ 8.14(s, 1H, NH), 7.63(m, 1H), 7.49(d, *J* = 1.4 *Hz*, 1H), 7.45(m, 2H), 7.37-7.24(m, 5H), 7.20(dd, *J* = 7.2, 0.6 *Hz*, 1H), 7.11(dd, *J* = 8.6, 0.6 *Hz*, 1H), 7.04(m, 1H), 5.76(s, 1H), 3.27(m, 1H), 3.09(m, 1H), 2.84(m, 1H), 2.75(m, 1H), 2.23(bs, 1H, NH); ^{13}C NMR (100 MHz, 25 °C, CD_2Cl_2): δ 143.9, 136.4, 134.7, 133.1, 131.9, 129.1, 129.0, 128.9, 128.89, 128.85, 128.2, 125.1, 123.1, 122.9, 121.8, 117.9, 112.2, 110.3, 94.7, 87.3, 55.8, 42.5, 22.6; HRMS (ESI): Calculated for $C_{25}H_{20}N_2Cl$ [M+H$^+$]: 383.13095, Found: 383.13142.

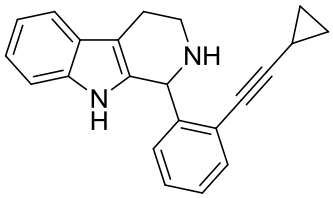


Compound **3d** was synthesized according to the general procedure **A** as a reddish-brown solid in 71% yield; ^{1}H NMR (400 MHz, 25 °C, CD_2Cl_2): δ 7.92(s, 1H, NH), 7.61(m, 1H), 7.42(m, 2H), 7.29(m, 2H), 7.26-7.18(m, 3H), 7.08(m, 2H), 6.87(m, 2H), 5.80(s, 1H), 3.81(s, 3H) 3.30(m, 1H), 3.13(m, 1H), 2.85(m, 2H), 2.03(bs, 1H, NH); ^{13}C NMR (100 MHz, 25 °C, CD_2Cl_2): δ 160.2, 143.8, 136.1, 134.5, 133.2, 132.6, 128.6, 128.5, 127.8, 123.0, 121.6, 119.3, 118.2, 115.0, 114.2, 113.7, 110.9, 110.2, 94.5, 86.0, 55.63, 55.53, 42.4, 22.6; HRMS (ESI): Calculated for $C_{26}H_{23}N_2O$ [M+H$^+$]: 379.18049, Found: 379.18131.



Compound **3e** was synthesized according to the general procedure **A** as a reddish-brown solid in 70% yield; ^{1}H NMR (400 MHz, 25 °C, $CDCl_3$): δ 7.8(s, 1H, NH), 7.61(m, 1H), 7.55(m, 1H), 7.42(m, 2H), 7.28(m, 2H), 7.23-7.18(m, 2H), 7.13(m, 2H), 7.02(m, 2H), 5.78(s, 1H),

3.32(dt, *J* = 12.2, 5.1 *Hz*, 1H), 3.16(m, 1H), 2.88(m, 2H), 2.24(bs, 1H, NH); ^{13}C NMR (100 MHz, 25 °C, $CDCl_3$): δ 162.7(d, *J* = 250.2 *Hz*, CF), 143.6, 136.0, 133.9, 133.6(d, *J* = 8.4 *Hz*, 2CH), 132.8, 128.9, 128.7, 127.9, 127.4, 122.5, 121.8, 119.5, 119.0(d, *J* = 3.5 *Hz*), 118.3, 115.8(d, *J* = 22.1 *Hz*, 2CH), 110.9, 110.4, 93.4, 86.8, 86.7, 55.6, 42.3, 22.5; HRMS (ESI): Calculated for $C_{25}H_{20}N_2F$ [M+H$^+$]: 367.16050, Found: 367.16184.



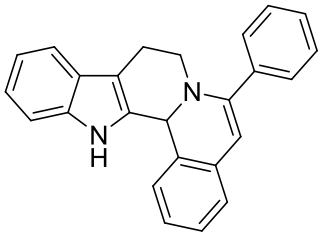
Compound **3f** was synthesized according to the general procedure **A** as a reddish-brown solid in 70% yield; ^{1}H NMR (400 MHz, 25 °C, CD_2Cl_2): δ 7.96 (s, 1H, NH), 7.52(m, 1H), 7.47(dd, *J* = 7.5, 1.1 *Hz*, 1H), 7.26-7.12(m, 5H), 7.07(m, 2H), 5.65(s, 1H), 3.26(dt, *J* = 12.1, 5 *Hz*, 1H), 3.10(m, 1H), 2.88(m, 1H), 2.80(m, 1H), 2.22(bs, 1H, NH), 1.48(m, 1H), 0.88(m, 2H), 0.76(m, 2H); ^{13}C NMR (100 MHz, 25 °C, CD_2Cl_2): δ 144.2, 136.3, 134.8, 133.0, 128.6, 128.1, 127.9, 127.7, 123.6, 121.7, 119.4, 118.3, 111.1, 110.2, 99.1, 73.7, 55.5, 42.5, 22.8, 9.02, 8.97, 0.58; HRMS (ESI): Calculated for $C_{22}H_{21}N_2$ [M+H$^+$]: 313.16993, Found: 313.17066.

[a] A.Ganesan. *et. al*. *Chem. Commun*., 2003, 916-917

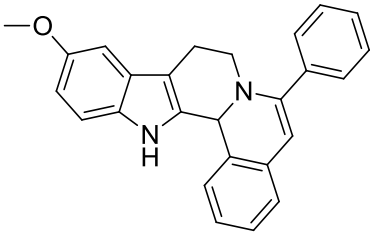
2c. General Procedure B for the gold catalyzed hydroamination reaction:

To a solution of the corresponding pictet compound **3** (0.1 mmol) in dry DCE (2 mL) under argon atmosphere was added the gold catalyst Y (10 mol%, 7.72 mg) and the reaction mixture was stirred at RT until the completion of the reaction monitored via TLC. The solvent was then removed in vacuo and the crude reaction mixture was purified by flash chromatography using silica gel with Petroleum ether and ethyl acetate as eluents.

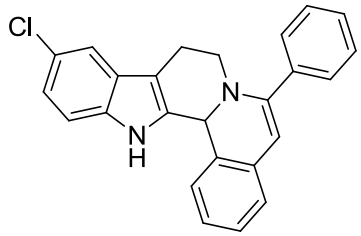
2d. Characterization of the Indoloquinolizine Products 4:



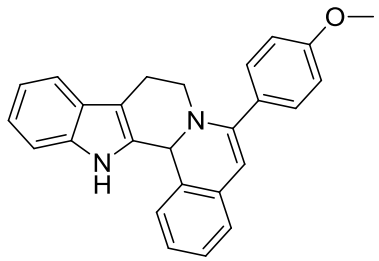
Compound **4a** was synthesized according to the general procedure **B** as a orangish-red solid in 62% yield; ^{1}H NMR (400 MHz, 25 °C, CD_2Cl_2): δ 8.03(bs, 1H, NH),7.68(m, 2H), 7.52(d, *J* = 7.8 *Hz*, 1H), 7.4(m, 4H), 7.26(m, 1H), 7.21(m, 2H), 7.13(dd, *J* = 13, 4.7 *Hz*, 2H), 7.11(m, 1H), 6.25(s, 1H), 5.53(s, 1H), 3.23(m, 1H), 3.14(m, 1H), 2.86 (m, 1H), 2.66(m, 1H); ^{13}C NMR (100 MHz, 25 °C, CD_2Cl_2): δ 149.9,137.4, 136.6 134.5, 132, 129.6, 128.9, 128.8, 128.3, 128, 127.7, 126.7, 125.2, 124.2,122.1,119.8, 118.5, 111.3, 109.6, 108.3, 57.3,43.1, 22.2 ; HRMS (ESI): Calculated for $C_{25}H_{21}N_2$ [M+H$^+$]: 349.16993, Found: 349.17038.



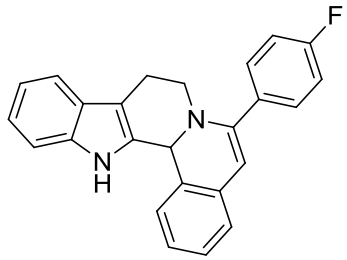
Compound **4b** was synthesized according to the general procedure **B** as a orangish-red solid in 62% yield; ^{1}H NMR (400 MHz, 25 °C, CD_2Cl_2): δ 8.07(bs, 1H, NH), 7.64(d, *J* = 8.7 *Hz*, 2H), 7.53(d, *J* = 7.5 *Hz*,1H), 7.41(d, *J* = 8 *Hz*, 1H), 7.29-7.08(m, 6H), 6.95(d, *J* = 8.6 *Hz*, 2H), 6.26(s, 1H), 5.45(s, 1H), 3.85(s, 3H), 3.13(m, 2H), 2.89(m, 1H), 2.67(dd, *J* = 15.3, 3.9 *Hz*, 1H); ^{13}C NMR (100 MHz, 25 °C, CD_2Cl_2): δ 160.6, 149.7, 136.6, 134.8, 131.9, 129.7, 129.6, 129.3, 128.1, 127.7, 126.4, 125.1, 124.0, 122.1, 119.8, 118.6, 114.2, 111.3, 109.7, 107.5, 57.1, 55.7, 42.7, 22.3; HRMS (ESI): Calculated for $C_{26}H_{23}ON_2$ [M+H$^+$]: 379.18049, Found: 379.18127.



Compound **4c** was synthesized according to the general procedure **B** as a yellowish-orange solid in 53% yield; ^{1}H NMR (400 MHz, 25 °C, $(CD_3)_2SO$): δ 11.37(s, 1H, NH), 7.74(dd, *J* = 8.1, 1.3 *Hz*, 2H), 7.51(d, *J* = 2.0 *Hz*, 1H), 7.48-7.38(m, 4H), 7.31-7.20(m, 3H), 7.11(dd, *J* = 8.6, 2.1 *Hz*, 2H), 6.62(s, 1H), 5.35(s, 1H), 3.00-2.79(m, 3H), 2.62(m, 1H); ^{13}C NMR (100 MHz, 25 °C, $(CD_3)_2SO$): δ 148.4, 135.9, 134.7, 133.3, 133.2, 129.6, 128.7, 128.6, 127.6, 127.5, 127.0, 126.6, 125.2, 123.8, 123.1, 120.8, 117.1, 112.6, 109.2, 107.5, 55.8, 41.3, 21.4; HRMS (ESI): Calculated for $C_{25}H_{20}N_2Cl$ [M+H$^+$]: 383.13095, Found: 383.12930.

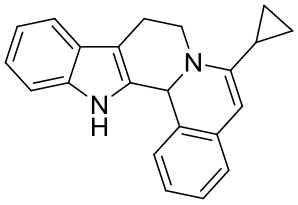


Compound **4d** was synthesized according to the general procedure **B** as a orangish-yellow solid in 60% yield**,** ^{1}H NMR (400 MHz, 25 °C, CD_2Cl_2): δ 7.88(bs, 1H, NH), 7.68(dd, *J* = 8, 1.6 *Hz*, 2H), 7.45-7.36(m, 3H), 7.29-7.24(m, 2H), 7.2(m, 2H), 7.14(d, *J* = 7.3 *Hz*, 1H), 6.97(d, *J* = 2.4 *Hz*,1H), 6.82(dd, *J* = 8.8, 2.5 *Hz*, 1H), 6.22(s, 1H), 5.51(s, 1H), 3.84(s, 3H), 3.24(m, 1H), 3.14(m, 1H), 2.81(m, 1H), 2.62(m, 1H); ^{13}C NMR (100 MHz, 25 °C, CD_2Cl_2): δ 154.3, 149.7, 137.2, 134.2, 132.7, 131.4, 129.3, 128.7, 128.6, 128, 127.9,127.8,126.4, 125, 124, 111.7,111.6, 109.2, 107.9, 100.6, 57.2, 55.9, 43, 22; HRMS (ESI): Calculated for $C_{26}H_{23}ON_2$ [M+H$^+$]: 379.18049, Found: 379.18130.



Compound **4e** was synthesized according to the general procedure **B** as a orangish-red solid in 58% yield**;** ^{1}H NMR (400 MHz, 25 °C, CD_2Cl_2): δ 8.03(bs, 1H, NH), 7.69(m, 2H), 7.53(dd, *J* = 7.8, 0.5 *Hz*, 1H), 7.40(m, 1H), 7.28(m, 1H), 7.24-7.15(m, 4H), 7.15-7.09(m, 3H), 6.27(s, 1H), 5.47(s, 1H), 3.12(m, 1H), 2.87(m, 1H), 2.66(dt, *J* = 15.4,4.3 *Hz*, 1H); ^{13}C NMR (100 MHz, 25 °C, CD_2Cl_2): δ 163.4(d, *J* = 247.2 *Hz*, CF), 148.9, 136.6, 134.4, 133.5(d, *J* = 3.2 *Hz*), 131.8, 129.8(d, *J* = 8.2 *Hz*, 2CH), 129.7, 128.3, 127.7, 126.8, 125.2, 124.2, 122.1,

119.8, 118.6, 115.7(d, *J* = 21.6 *Hz*, 2CH), 111.3, 109.6, 108.6, 57.1, 42.8, 22.2 ; HRMS (ESI): Calculated for $C_{25}H_{20}N_2F$ [M+H^+]: 367.16050, Found: 367.16107.



Compound **4f** was synthesized according to the general procedure **B** as a red solid in 50% yield**;** ^{1}H NMR (400 MHz, 25 °C, CD_2Cl_2): δ 7.56(s, 1H, NH), 7.46(m, 1H), 7.25-7.15(m, 3H), 7.13-7.02(m, 3H), 6.84(d, *J* = 7.6 *Hz*, 1H), 5.82(s, 1H), 5.18(s, 1H), 4.48(m, 1H), 3.46(m, 1H), 3.12(m, 1H), 2.78(m, 1H), 1.66(m, 1H), 0.82(m, 2H), 0.71(m, 1H), 0.56(m, 1H); ^{13}C NMR (100 MHz, 25 °C, CD_2Cl_2): δ 150.1, 135.9, 134.8, 134.0, 128.7, 128.2, 126.9, 125.5, 125.0, 123.4, 121.8, 119.7, 118.2, 111.3, 108.8, 97.7, 59.0, 45.2, 21.7, 12.9, 6.5, 6.2; HRMS (ESI): Calculated for $C_{22}H_{21}N_2$ [M+H^+]: 313.16993, Found: 313.16868.

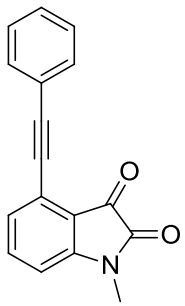
3. Synthesis of Hexacyclic Indoloquinolizines 7:

4-Iodo-*N*-Methylisatin was prepared according to the procedure described in *J. Med. Chem.* 2004, *47*, 935- 946.

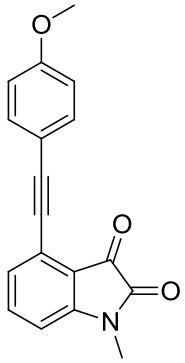
3a. General Procedure C for the synthesis of Sonogashira Products 5:

To a mixture of 4-Iodo-*N*-Methylisatin(500 mg, 1.74 mmol) and $PdCl_2(PPh_3)_2$ (15 mol%, 182.49 mg) under an argon atmosphere was added anhydrous Et_3N (12 mL), anhydrous Toulene (12 mL), anhydrous THF (12 mL) followed by the addition of the corresponding terminal alkyne (1.4 eq, 2.43 mmol). The above reaction mixture was stirred at RT for 10 mins before the addition of CuI (10 mol%, 33.13 mg). The resulting reaction mixture was heated to 50 ^oC and stirred at that temperature until the completion of the reaction monitored *via* TLC. The solvent was then removed *in vacuo* and the residue was purified by flash chromatography using silica gel to yield the corresponding sonogashira product as orange or red solids.

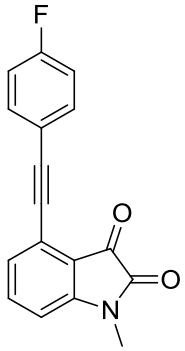
3b. Characterization of the Sonogashira Products 5:



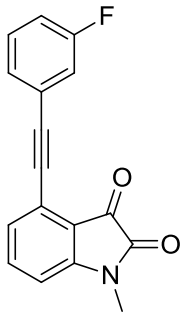
Compound **5a** was synthesized according to the general procedure **C** as a red solid in 80% yield**;** ^1H NMR (400 MHz, 25 °C, $CDCl_3$): δ 7.68 (m, 2H), 7.54 (m, 1H), 7.39 (m,1H), 7.20 (dd, *J* = 7.9, 0.8 *Hz*, 1H), 6.82 (dd, *J* = 7.9, 0.7 *Hz*, 1H), 3.26 (s, 3H); ^{13}C NMR (100 MHz, 25 °C, $CDCl_3$): δ 181.2, 158.1, 151.3, 137.3, 132.5, 129.5, 128.6, 127.4, 122.3, 122.1, 117.2, 109.1, 98.26, 85.6, 26.3; HRMS (ESI): Calculated for $C_{17}H_{12}O_2N$ $[M+H^+]$: 262.08626, Found: 262.08669.



Compound **5b** was synthesized according to the general procedure **C** as a reddish-orange solid in 74% yield; ^{1}H NMR (400 MHz, 25 °C, $CDCl_3$): δ 7.63(m, 2H), 7.51(m, 1H), 7.16(dd, *J* = 8.0, 0.8 *Hz*, 1H), 6.91(m, 2H), 6.78(dd, *J* = 7.9, 0.7 *Hz*, 1H), 3.84(s, 3H), 3.25(s, 3H); ^{13}C NMR (100 MHz, 25 °C, $CDCl_3$): δ 181.3, 160.8, 158.3,151.5, 137.3, 134.3, 127.2, 122.7, 117.1, 114.5, 114.4, 108.7, 99.0, 85.0, 55.58, 26.4; HRMS (ESI): Calculated for $C_{18}H_{14}O_3N$ [M+H$^+$]: 314.07876, Found: 314.07906.

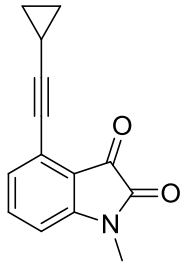


Compound **5c** was synthesized according to the general procedure **C** as a red solid in 80% yield; ^{1}H NMR (400 MHz, 25 °C, $CDCl_3$): δ 7.68(m, 2H), 7.54(td, *J* = 7.9, 1.0 *Hz*, 1H), 7.18(dd, *J* = 7.9, 0.7 *Hz*, 1H), 7.09(m, 2H), 6.83(m, 1H), 3.26(d, *J* = 0.9 *Hz*, 3H); ^{13}C NMR (100 MHz, 25 °C, $CDCl_3$): δ 181.33, 163.47(d, *J* = 251.6 *Hz*, CF), 158.16, 151.6, 137.4, 134.6(d, *J* = 8.6 *Hz*, 2CH), 127.3, 122.0, 118.6(d, *J* = 3.6 *Hz*), 117.3, 116.1(d, *J* = 22.2 *Hz*, 2CH), 109.2, 97.2,85.4, 26.4; HRMS (ESI): Calculated for $C_{17}H_{11}O_2NF$ [M+H$^+$]: 280.07683, Found: 280.07728.

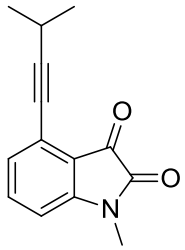


Compound **5d** was synthesized according to the general procedure **C** as a reddish-orange solid in 65% yield**;** ^{1}H NMR (400 MHz, 25 °C, $CDCl_3$): δ 7.56(td, *J* = 7.9, 1.1 *Hz*, 1H),

7,47(m, 1H), 7.36(m, 2H), 7.21(dd, *J* = 7.9, 0.8 *Hz*, 1H), 7.11(m, 1H), 6.86(dd, *J* = 7.9, 0.7 *Hz*, 1H), 3.27(d, *J* = 1.0 *Hz*, 3H); ^{13}C NMR (100 MHz, 25 °C, $CDCl_3$): δ 181.2, 162.5(d, *J* = 247.1 *Hz*, CF), 158.0, 151.6, 137.5, 130.3,(d, *J* = 8.5 *Hz*), 128.53(d, *J* = 3.1 *Hz*), 127.5, 124.2(d, *J* = 9.5 *Hz*), 121.6, 119.2(d, *J* = 22.1 *Hz*), 117.4, 117.0(d, *J* = 21.2 *Hz*), 109.6, 96.6, 86.2, 26.4; HRMS (ESI): Calculated for $C_{17}H_{14}O_2NF$ [M+H$^+$]: 280.07683, Found: 280.07705.



Compound **5e** was synthesized according to the general procedure **C** as a reddish-orange solid in 70% yield; ^{1}H NMR (400 MHz, 25 °C, $CDCl_3$): δ 7.46(m, 1H), 7.02(dt, *J* = 10.8, 5.4 *Hz*, 1H), 6.74(dd, *J* = 7.9, 0.7 *Hz*, 1H), 3.22(s, 3H), 1.54(m, 1H), 0.99(m, 4H); ^{13}C NMR (100 MHz, 25 °C, $CDCl_3$): δ 181.2, 158.2, 151.3, 137.1, 127.6, 123.2, 117.5, 108.2, 104.5, 72.4, 26.3, 9.7, 0.9; HRMS (ESI): Calculated for $C_{14}H_{12}O_2N$ [M+H$^+$]: 226.08626, Found: 226.08631.

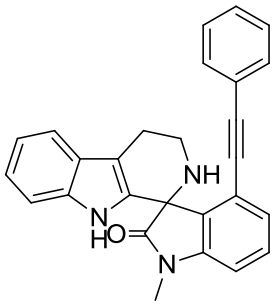


Compound **5f** was synthesized according to the general procedure **C** as a reddish-orange solid in 67% yield ^{1}H NMR (400 MHz, 25 °C, $CDCl_3$): δ 7.47(m, 1H), 7.06(m, 1H), 6.76(dd, *J* = 7.9, 0.7 *Hz*, 1H), 3.23(s, 3H), 2.88(dt, *J* = 13.8, 6.9 *Hz*, 1H), 1.32(m, 6H); ^{13}C NMR (100 MHz, 25 °C, $CDCl_3$): δ 181.2, 158.1, 151.3, 137.1, 127.8, 123.1, 117.5, 108.5, 105.8, 76.2, 26.3, 22.6, 21.7; HRMS (ESI): Calculated for $C_{14}H_{14}O_2N$ [M+H$^+$]: 228.10191, Found: 228.10232.

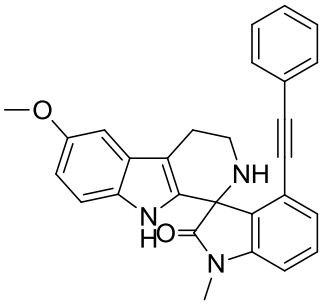
3c. General Procedure D for the synthesis of Pictet-Spengler Derivatives 6:-

To a mixture of Tryptamine/5-OMe Tryptamine **1** (0.25 mmol) and the corresponding Sonogashira product **5** (0.25 mmol) under an argon atmosphere was added 5 mL of Toulene and the reaction mixture was stirred at RT followed by the addition of TFA (1equiv, 0.25 mmol) . The resulting reaction mixture was heated to 50 ^{o}C for 24 h. The solvent was then removed in vacuo and the residue was purified by flash chromatography using basified silica gel with Methanol and dichloromethane as eluents.

3d. Characterization of the Pictet-Spengler Products 6:-

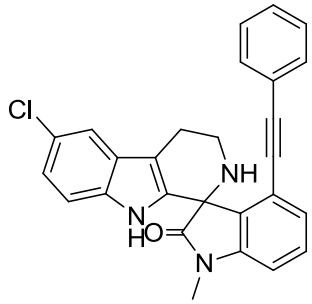


Compound **6a** was synthesized according to the general procedure **D** as a reddish-brown solid in 81% yield; ^{1}H NMR (400 MHz, 25 °C, $CDCl_3$): δ 7.57(m, 1H), 7.48(s, 1H, NH), 7.36(dd, *J* = 10.4, 5.4 *Hz*, 1H), 7.25-7.11(m, 7H), 6.87(dd, *J* = 8.3, 1.3 *Hz*, 3H), 3.95(m, 1H), 3.31(m, 1H), 3.24(s, 3H), 2.92(m, 1H), 2.78(m, 1H), 2.35(bs, 1H, NH); ^{13}C NMR (100 MHz, 25 °C, $CDCl_3$): δ 175.9, 144.7, 136.3, 131.7, 131.1, 130.1, 129.3, 128.7, 128.2, 127.6, 126.6, 122.4, 122.0, 120.0, 119.7, 118.5, 113.4, 111.2, 108.5, 95.4, 83.9, 61.2, 39.9, 26.6, 22.5; HRMS (ESI): Calculated for $C_{27}H_{22}ON_3$ [M+H^{+}]: 404.17574, Found: 404.17563.

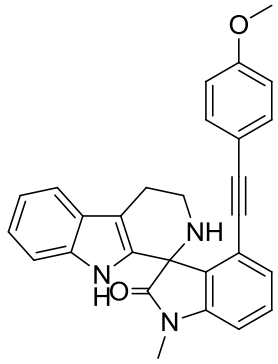


Compound **6b** was synthesized according to the general procedure **D** as a reddish-brown solid in 71% yield; ^{1}H NMR (400 MHz, 25 °C, $CDCl_3$): δ 7.29(m, 1H), 7.26(s, 1H, NH), 7.15(m, 1H), 7.06(m, 3H), 7(dd, *J* = 8.7, 0.5 *Hz*, 1H), 6.94(d, *J* = 2.4 *Hz*, 1H), 6.81(m, 3H),

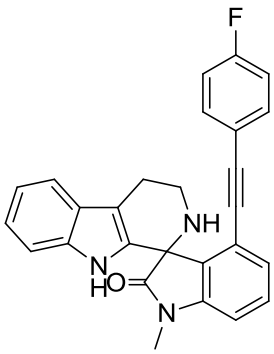
6.71(dt, *J* = 8.8, 2.2 *Hz*, 1H), 3.88(m, 1H), 3.81(s, 3H), 3.25(m, 1H), 3.17(s, 1H), 2.8(m, 1H), 2.66(m, 1H), 1.95(bs, 1H, NH); ^{13}C NMR (100 MHz, 25 °C, $CDCl_3$): δ 175.9, 154.3, 144.7, 131.7, 131.5, 131.2, 130.2, 130.1, 128.7, 128.2, 128.0, 126.6, 122.0, 120.1, 113.3, 112.3, 111.7, 108.5, 100.6, 95.4, 83.9, 61.3, 56.1, 39.9, 26.6, 22.6; HRMS (ESI): Calculated for $C_{28}H_{24}O_2N_3$ [M+H$^+$]: 434.18630, Found: 434.18655.



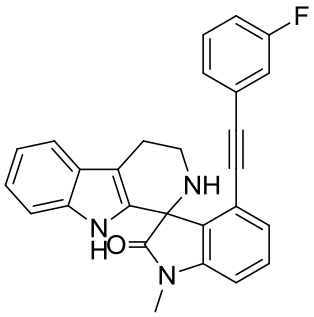
Compound **6c** was synthesized according to the general procedure **A** as a reddish-brown solid in 57% yield; ^{1}H NMR (400 MHz, 25 °C, CD_2Cl_2): δ 7.95(s, 1H, NH), 7.53(m, 1H), 7.37(m, 1H), 7.28(m, 1H), 7.19(m, 3H), 7.07(m, 2H), 6.91(m, 3H), 3.81(m, 1H), 3.23(m, 1H), 3.18(s, 3H), 2.83(m, 1H), 2.72(m, 1H), 2.30(bs, 1H, NH); ^{13}C NMR (100 MHz, 25 °C, CD_2Cl_2): δ 175.9, 145.1, 134.8, 131.77, 131.75, 131.2, 130.5, 129.1, 128.8, 128.6, 126.8, 125.5, 122.7, 122.2, 120.2, 118.1, 113.3, 112.5, 109.0, 95.4, 84.3, 61.4, 39.9, 26.7, 22.6; HRMS (ESI): Calculated for $C_{27}H_{21}ON_3Cl$ [M+H$^+$]: 438.13677, Found: 438.13722.



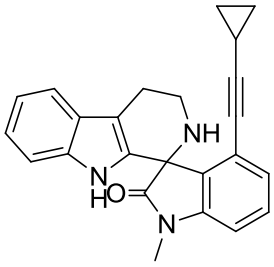
Compound **6d** was synthesized according to the general procedure **D** as a reddish-brown solid in 70% yield; ^{1}H NMR (400 MHz, 25 °C, $CDCl_3$): δ 7.57(m, 1H), 7.43(s, 1H, NH), 7.34(t, *J* = 7.9 *Hz*, 1H), 7.2(m, 1H), 7.13(m, 3H), 6.86(dd, *J* = 7.9, 0.8 *Hz*, 1H), 6.8(m, 2H), 6.65(m, 2H), 3.96(m, 1H), 3.77(s, 3H), 3.33(m ,1H), 3.25(s, 3H), 2.93(m, 1H), 2.78(m, 1H), 1.99(bs, 1H, NH); ^{13}C NMR (100 MHz, 25 °C, $CDCl_3$): δ 175.9, 160.0, 144.7, 136.3, 133.2, 130.8, 130.1, 129.4, 127.6, 126.5, 122.4, 120.5, 119.7, 118.4, 114.1, 113.9, 113.4, 111.2, 108.2, 95.7, 82.8, 61.2, 55.4, 39.9, 26.6, 22.5; HRMS (ESI): Calculated for $C_{28}H_{24}O_2N_3$ [M+H$^+$]: 434.18630, Found: 434.18640.



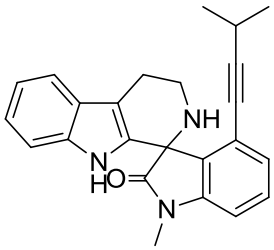
Compound **6e** was synthesized according to the general procedure **D** as a reddish-brown solid in 80% yield; ^{1}H NMR (400 MHz, 25 °C, $CDCl_3$): δ 7.55(m, 1H), 7.48(s, 1H, NH), 7.36(t, *J* = 7.9 *Hz*, 1H), 7.19(m , 1H), 7.16-7.11(m, 3H), 6.88(dd, *J* = 7.9, 0.8 *Hz*, 1H), 6.83-6.78(m, 3H), 3.95(m, 1H), 3.32(m, 1H), 3.25(s, 3H), 2.93(m, 1H), 2.74(m, 1H), 2.09(bs, 1H, NH); ^{13}C NMR (100 MHz, 25 °C, $CDCl_3$): δ 175.8, 162.7 (d, *J* = 250.5 *Hz*, CF), 144.8, 136.3, 133.6(d, *J* = 8.5 *Hz*, 2CH), 131.1, 130.2, 129.3, 127.5, 126.5, 122.5, 120.0, 119.7, 118.4, 118.1(d, *J* = 3.4 *Hz*), 115.6 (d, *J* = 22.1 *Hz*, 2CH), 113.3, 111.2, 108.6, 94.3, 83.6, 61.2, 39.8, 26.7, 22.5; HRMS (ESI): Calculated for $C_{27}H_{21}ON_3F$ [M+H$^+$]: 422.16632, Found: 422.16615.



Compound **6f** was synthesized according to the general procedure **D** as a reddish-brown solid in 75% yield; ^{1}H NMR (400 MHz, 25 °C, CD_2Cl_2): δ 7.75(s, 1H, NH), 7.60(m, 1H), 7.38(dd, *J* = 10.3, 5.5 *Hz*, 1H), 7.20-7.10(m, 5H), 6.97(m, 1H), 6.92(dd, *J* = 7.9, 0.9 *Hz*, 1H), 6.72(m, 1H), 6.62(m, 1H), 3.85(m, 1H), 3.26(m, 1H), 3.21(s, 3H), 2.91(m, 1H), 2.78(m, 1H), 2.09(bs, 1H, NH); ^{13}C NMR (100 MHz, 25 °C, CD_2Cl_2): δ 175.9, 162.3(d, *J* = 246.2 *Hz*, CF), 145.0, 136.3, 131.6, 130.2, 130.0(d, *J* = 8.6 *Hz*), 129.7, 127.6(d, *J* = 3 *Hz*), 127.3, 126.6, 124.0(d, *J* = 9.5 *Hz*), 122.5, 119.8, 119.5, 118.5, 118.2(d, *J* = 23.0 *Hz*), 116.1(d, *J* = 21.2 *Hz*), 113.2, 111.1, 109.1, 93.6(d, *J* = 3.4 *Hz*), 85.1, 61.3, 39.8, 26.5, 22.6; HRMS (ESI): Calculated for $C_{27}H_{21}ON_3F$ [M+H$^+$]: 422.16632, Found: 422.16617.

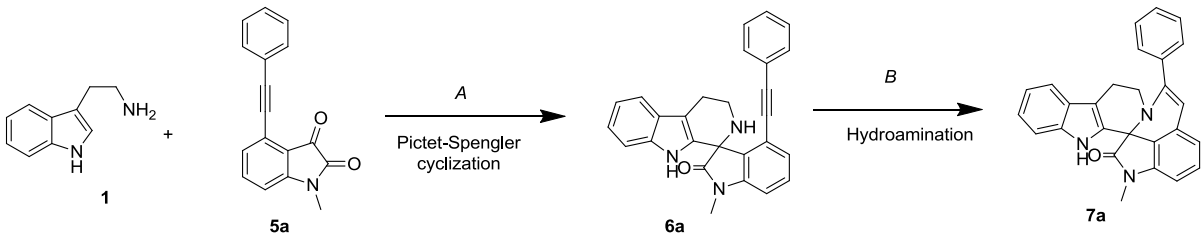


Compound **6g** was synthesized according to the general procedure **D** as a reddish-brown solid in 65% yield; ^{1}H NMR (400 MHz, 25 °C, $CDCl_3$): δ 7.54(m, 1H), 7.29(m, 2H), 7.18-7.06(m, 3H), 7.01(d, *J* = 7.9 *Hz*, 1H), 6.81(d, *J* = 7.9 *Hz*, 1H), 3.97(m, 1H), 3.36(m, 1H), 3.21(s, 3H), 2.96(m, 1H), 2.88(m, 1H), 2.03(bs, 1H, NH), 1.06(m, 1H), 0.54(m, 2H), 0.22(m, 1H), -0.01(m, 1H); ^{13}C NMR (100 MHz, 25 °C, $CDCl_3$): δ 175.9, 144.5, 136.3, 131.0, 129.9, 129.5, 127.4, 126.8, 122.2, 120.9, 119.5, 118.5, 113.0, 111.0, 107.7, 100.3, 70.6, 61.1, 39.7, 26.6, 22.4, 8.5, 8.4, 0.05; HRMS (ESI): Calculated for $C_{24}H_{22}ON_3$ [M+H$^+$]: 368.17574, Found: 368.17656.



Compound **6h** was synthesized according to the general procedure **D** as a reddish-brown solid in 76% yield; ^{1}H NMR (400 MHz, 25 °C, CD_2Cl_2): δ 7.73(s, 1H, NH), 7.55(m, 1H), 7.31(m, 1H), 7.11(m, 3H), 7.04(m, 1H), 6.82(dd, *J* = 7.9, 0.9 *Hz*, 1H), 3.84(m, 1H), 3.29(m, 1H), 3.15(s, 3H), 2.90(m, 2H), 2.41(dt, *J* = 13.8, 6.9 *Hz*, 1H), 2.24(bs, 1H, NH), 0.80(d, *J* = 6.9 *Hz*, 6H); ^{13}C NMR (100 MHz, 25 °C, CD_2Cl_2): δ 176.2, 144.9, 136.5, 131.3, 130.1, 127.6, 126.9, 122.4, 121.0, 119.6, 118.6, 113.1, 111.2, 108.2, 102.4, 74.9, 61.4, 39.9, 26.6, 22.6, 22.45, 22.41, 21.3; HRMS (ESI): Calculated for $C_{24}H_{24}ON_3$ [M+H$^+$]: 370.19139, Found: 370.19219.

3e. Supplementary Table 1 - Optimization for the gold catalyzed hydroamination.



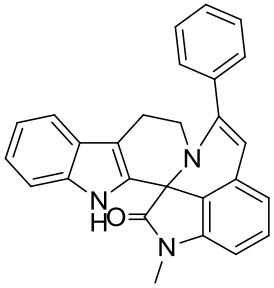
Entry	Catalyst (mol%)	Solvent	Temp (^{o}C)	Time (h)	Yield[a] (%)	
					6a	7a
1	TFA (1eq)	DCE	50	24	76	-
2	$Yb(OTf_3)$ (10mol%),	DCE	120, MW	1	55	-
3	TFA (1eq)	Toluene	50	24	81[b]	-
4	$Au(PPh_3)OTf$ (10)	DCE	RT	2	-	43
5	$Au(PPh_3)SbF_6$ (10)	DCE	RT	2	-	30
6	$AuCl_3$ (10)	DCE	RT	2	-	50
7	$AuCl(SMe_2)$ (10)	DCE	RT	2	-	76
9	$AuCl(SMe_2)$ (10)	Toluene	RT	2	-	65
10	$AuCl(SMe_2)$ (10)	AcN	RT	2	-	50

[a]isolated yield, [b]the optimized condition for the Pictet Spengler reaction, MW: Microwave, DCE: 1,2-dichloroethane, RT: Room Temperature, IL: Ionic Liquid ([bmim]Cl-$AlCl_3$(0.32 mL/mmol), unless and otherwise specified all the reactions for the hydroamination step *B* were performed at 0.1mmol scale in 2 mL of the solvent.

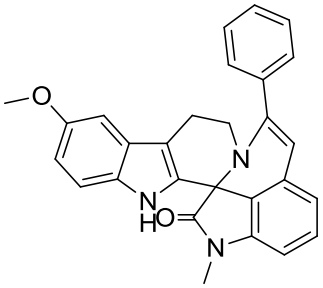
3f. General Procedure E for the gold catalyzed hydroamination:-

To a solution of the Pictet-Spengler compound **6** (0.1 mmol) in dry DCE (2 mL) under an argon atmosphere was added the gold catalyst $AuCl(SMe_2)$ (10 mol%, 0.01 mmol). The reaction mixture was stirred at RT until the completion of the reaction monitored via TLC. The solvent was then removed in vacuo and the crude reaction mixture was purified by flash chromatography (silica gel) using petroleum ether and ethyl acetate as eluents.

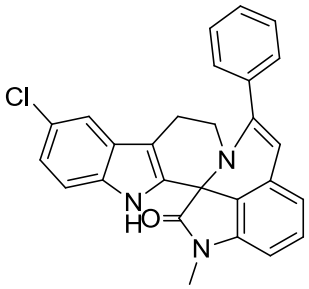
3g. Characterization of the Spirooxindole fused hexacyclic indoloquinolizines (7):



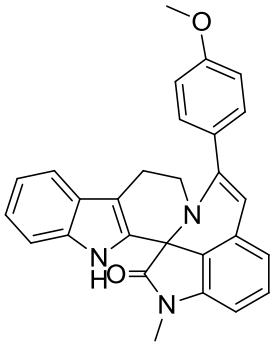
Compound **7a** was synthesized according to the general procedure **E** as a white solid in 76% yield; ^{1}H NMR (400 MHz, 25 °C, $(CD_3)_2SO$): δ 10.51(s, 1H, NH),7.44-7.35(m, 4H), 7.35-7.27(m, 3H), 7.22(dd, *J* = 8.1, 0.8 *Hz*, 1H), 7.04(m, 1H), 6.96(m, 2H), 6.64(d, *J* = 7.8 *Hz*, 1H), 5.39(s, 1H), 4.39(m, 1H), 3.63(dd, *J* = 13.6, 3.9 *Hz*, 1H), 3.18(s, 3H), 2.43(m, 2H); ^{13}C NMR (150 MHz, 25 °C, $(CD_3)_2SO$): δ 176.3, 151.6, 141.9, 137.5, 136.0, 130.9, 130.5, 129.8, 127.9, 126.6, 121.4, 118.6, 117.6, 116.9, 115.7, 111.4, 109.4, 106.5, 104.5, 61.2, 42.7, 26.3, 19.8; HRMS (ESI): Calculated for $C_{27}H_{22}ON_3$ [M+H$^+$]: 404.17574, Found: 404.17552.



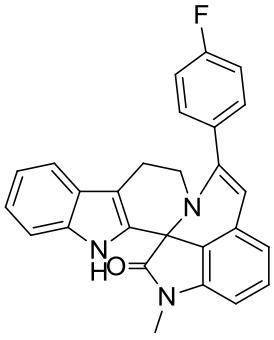
Compound **7b** was synthesized according to the general procedure **E** as a white solid in 76% yield; ^{1}H NMR (400 MHz, 25 °C, $(CD_3)_2SO$): δ 10.33(s, 1H, NH), 7.41(m, 3H), 7.35-7.25(m, 3H), 7.11(d, *J* = 8.7 *Hz*, 1H), 6.95(d, *J* = 7.8 *Hz*, 1H), 6.87(d, *J* = 2.3 *Hz*, 1H), 6.69(dd, *J* = 8.8, 2.5 *Hz*, 1H), 6.64(d, *J* = 7.8 *Hz*, 1H), 5.38(s, 1H), 4.39(m, 1H), 3.72(s, 3H), 3.62(m, 1H), 3.17(s,3H), 2.42(m, 2H); ^{13}C NMR (100 MHz, 25 °C, $(CD_3)_2SO$): δ 177.0, 153.9, 152.3, 142.6, 138.2, 131.7, 131.6, 131.2, 131.0, 128.6, 128.1, 127.6, 117.7, 116.3, 112.7, 112.1, 109.8, 107.1, 105.1, 100.3, 62.0, 56.0, 43.4, 27.0, 20.6; HRMS (ESI): Calculated for $C_{28}H_{24}O_2N_3$ [M+H$^+$]: 434.18630, Found: 434.18653.



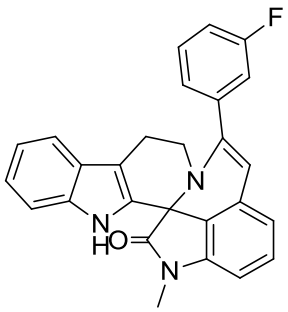
Compound **7c** was synthesized according to the general procedure **E** as a white solid in 60% yield; ^{1}H NMR (400 MHz, 25 °C, $(CD_3)_2SO$): δ 10.75(s, 1H, NH), 7.46-7.37(m, 4H), 7.35-7.27(m, 3H), 7.22(d, *J* = 8.6 *Hz*, 1H), 7.05(dd, *J* = 8.6, 2.1 *Hz*, 1H), 6.98(d, *J* = 7.8 *Hz*, 1H), 6.65(d, *J* = 7.7 *Hz*, 1H), 5.4(s, 1H), 4.38(m, 1H), 3.62(dd, *J* = 14.0, 4.7 *Hz*, 1H), 3.18(s, 3H), 2.4(m, 2H); ^{13}C NMR (150 MHz, 25 °C, $(CD_3)_2SO$): δ 176.1, 151.5, 141.9, 137.4, 134.5, 131.7, 130.9, 130.6, 128.0, 127.7, 123.3, 121.3, 117.1, 116.6, 115.8, 112.9, 109.4, 106.6, 104.6, 61.1, 42.5, 26.4, 19.7; HRMS (ESI): Calculated for $C_{27}H_{21}ON_3Cl$ [M+H$^+$]: 438.1367, Found: 438.13728.



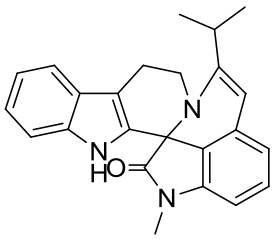
Compound **7d** was synthesized according to the general procedure **E** as a white solid in 74% yield; ^{1}H NMR (600 MHz, 25 °C, $(CD_3)_2SO$): δ 10.51(s, 1H, NH), 7.37(d, *J* = 7.9 *Hz*, 1H), 7.32-7.20(m, 4H), 7.04(m, 1H), 6.96(m, 4H), 6.62(m, 1H), 5.33(s, 1H), 4.38(m, 1H), 3.79(s, 3H), 3.62(m,1H), 3.18(s, 3H), 2.44(m, 2H); ^{13}C NMR (150 MHz, 25 °C, $(CD_3)_2SO$): δ 176.4, 158.8, 151.4, 141.9, 136.0, 131.1 130.5, 129.8, 129.6, 126.6, 121.4, 118.6, 117.6, 116.8, 115.5, 113.6, 111.4, 109.4, 106.3, 103.9, 61.2, 55.1, 42.7, 26.3, 19.8; HRMS (ESI): Calculated for $C_{28}H_{24}O_2N_3$ [M+H$^+$]: 434.18630, Found: 434.18621.



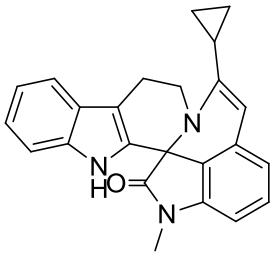
Compound **7e** was synthesized according to the general procedure **E** as a white solid in 72% yield; ^{1}H NMR (600 MHz, 25 °C, $(CD_3)_2SO$): δ 10.53(s, 1H, NH), 7.38(d, *J* = 7.7 *Hz*, 3H), 7.3(t, *J* = 7.8 *Hz*, 1H), 7.23(m, 3H), 7.04(m, 1H), 6.96(m, 1H), 6.64(m, 1H), 5.38(s, 1H), 4.4(m, 1H), 3.57(dd, *J* = 14.2, 4.9 *Hz*, 1H), 3.18(s, 3H), 2.44(m, 2H); ^{13}C NMR (150 MHz, 25 °C, $(CD_3)_2SO$): δ 176.3, 161.6(d, *J* = 244.9 *Hz*, CF), 150.5, 141.9, 136.0, 133.8(d, *J* = 3.1 *Hz*), 130.8, 130.5, 129.7, 126.6, 121.4, 118.6, 117.6, 116.9, 115.7, 111.4, 109.3, 106.6, 104.7, 61.2, 42.6, 26.3, 19.8; HRMS (ESI): Calculated for $C_{27}H_{21}ON_3F$ [M+H$^+$]: 422.16632, Found: 422.16647.



Compound **7f** was synthesized according to the general procedure **E** as a white solid in 71% yield; ^{1}H NMR (600 MHz, 25 °C, $(CD_3)_2SO$): δ 10.54(s, 1H, NH), 7.46(m, 1H), 7.39(d, *J* = 7.9 *Hz*, 1H), 7.3(m, 1H), 7.25- 7.15(m, 4H), 7.04(m, 1H), 6.99(m, 1H), 6.96(m, 1H), 6.66(m, 1H), 5.46(s, 1H), 4.41(m, 1H), 3.64(m, 1H), 3.18(s, 3H), 2.51(m, 1H), 2.44(m, 1H); ^{13}C NMR (100 MHz, 25 °C, $CDCl_3$): δ 176.2, 150.23, 150.22, 141.9, 139.8(d, *J* = 8.0 *Hz*), 136.0, 130.6(d, *J* = 4.9 *Hz*), 129.7, 126.6, 123.6, 121.4, 118.6, 117.7, 117.0, 115.8, 114.8, 111.4, 109.4, 106.8, 105.2, 61.2, 42.7, 26.3, 19.9; HRMS (ESI): Calculated for $C_{27}H_{21}ON_3F$ $[M+H^+]$: 422.16632, Found: 422.16645.



Compound **7g** was synthesized according to the general procedure **E** as a white solid in 65% yield; ^{1}H NMR (400 MHz, 25 °C, $(CD_3)_2SO$): δ 10.41(s, 1H, NH), 7.41(d, *J* = 7.7 *Hz*, 1H), 7.25(dd, *J* = 12.4, 4.7 *Hz*, 1H), 7.19(m, 1H), 7.02(m, 1H), 6.96(m, 1H), 6.87(d, *J* = 7.8 *Hz*, 1H), 6.59(d, *J* = 7.8 *Hz*, 1H), 5.39(s, 1H), 4.58(m, 1H), 3.81(dd, *J* = 14.4, 4.9 *Hz*, 1H), 3.12(s, 3H), 2.86(m, 2H), 2.75(dd, *J* = 16, 4.6 *Hz*, 1H), 1.06(dd, *J* = 21.4, 6.6 *Hz*, 6H), ^{13}C NMR (100 MHz, 25 °C, $(CD_3)_2SO$): δ 176.7, 156.7, 141.7, 135.8, 131.7, 130.5, 130.2, 126.6, 121.2, 118.5, 117.5, 116.8, 115.1, 111.3, 109.6, 105.4, 96.2, 61.4, 40.8, 27.5, 26.2, 24.5, 20.5, 20.3; HRMS (ESI): Calculated for $C_{24}H_{24}ON_3$ $[M+H^+]$: 370.19139, Found: 370.19153.

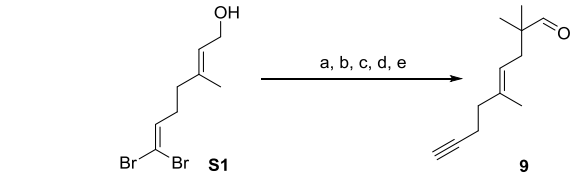


Compound **7h** was synthesized according to the general procedure **E** as a white solid in 68% yield; ^{1}H NMR (400 MHz, 25 °C, $(CD_3)_2SO$): δ 10.43(s, 1H, NH), 7.43(d, *J* = 7.6 *Hz*, 1H), 7.22(m, 2H), 7.03(dd, *J* = 11.0, 4.0 *Hz*, 1H), 6.97(t, *J* = 7.4 *Hz*, 1H), 6.85(d, *J* = 7.7 *Hz*, 1H), 6.54(d, *J* = 7.8 *Hz*, 1H), 5.27(s, 1H), 4.53(m, 1H), 4.30(dd, *J* = 14.2, 5.7 *Hz*, 1H), 3.11(m, 4H), 2.78(dd, *J* = 16.1, 4.7 *Hz*, 1H), 1.76(m, 1H), 0.79(m, 2H), 0.66(m, 1H), 0.34(m, 1H); ^{13}C

NMR (100 MHz, 25 °C, $(CD_3)_2SO$): δ 176.6, 151.8, 142.0, 135.8, 131.7, 130.3, 130.2, 126.8, 121.3, 118.5, 117.5, 116.8, 115.1, 111.3, 109.5, 105.5, 98.0, 61.3, 40.1, 26.2, 20.1, 12.5, 6.6, 6.1; HRMS (ESI): Calculated for $C_{24}H_{22}ON_3$ $[M+H^+]$: 368.17574, Found: 368.17698.

4. Cascade Polycyclization to the Hexahydro-1H-indolizino[8,7-b]indoles

4a. Synthesis of the *trans* Ene-yne-aldehyde

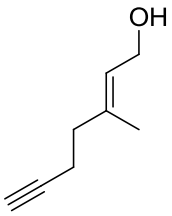


(*E*)-7,7-dibromo-3-methylhepta-2,6-dien-1-ol

a) *n*-BuLi (3.1 eq) , THF, -78 ^{o}C; b) NCS (1.2 eq), Me_2S (1.3 eq), DCM, -30 ^{o}C to RT; c) Diisopropyl amine (1.2 eq), *n*-BuLi (1.19 eq), Methylisobutyrate (1.2 eq), THF, -78 ^{o}C to RT; d) DIBAL-H (2.2 eq), DCM , 0 ^{o}C to RT e) DMSO (2.5 eq), oxalyl chloride (1.2 eq), Et_3N (5.0 eq), DCM, -78 ^{o}C to RT.

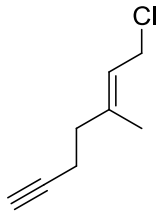
Compound **S1** was prepared according the procedure described in Max Malacria. *et. al*. *Eur. J. Org. Chem*. **2000**, 155-163.

Compound **S2**:



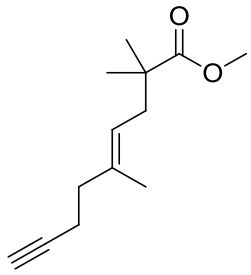
To a solution of **S1** (24 mmol, 6.7 g), in dry THF (35 mL) was added a solution of *n*-BuLi (2.5 M, 74.4 mmol) at -78 ^{o}C. After 0.5 h, the mixture was allowed to reach room temperature and then quenched with a saturated solution of NH_4Cl (35 mL) and extracted with ether (2×30 mL). The organic layer was washed twice with brine (60 mL) and dried with $MgSO_4$ and the solvent was removed under reduced pressure, the residue was then subjected to flash chromatography using silica gel; Yield: 60%, obtained as a light yellow oil, ^{1}H NMR (400 MHz, 25 °C, $CDCl_3$): δ 5.46 (m, 1H), 4.15 (d, *J* = 6.8 Hz, 2H), 2.31 (m, 2H), 2.24 (m, 2H), 1.95 (m, 1H), 1.68 (s, 3H) ppm; ^{13}C NMR (100 MHz, 25 °C, $CDCl_3$): δ: 137.6, 124.8, 83.9, 68.8, 59.3, 38.1, 17.3, 16.2 ppm; HRMS (ESI): Calculated for $C_8H_{13}O$ $[M+H^+]$:125.09609, Found: 125.09577.

Compound **S3**:



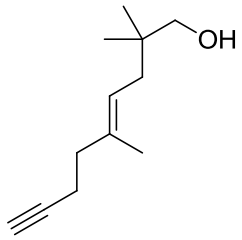
To a solution N-Chlorosuccinimide (7.57 mmol, 1.0 g) in dry DCM (31 mL) at -30 ^{o}C was added freshly distilled Dimethyl sulfide (8.20 mmol, 0.6 mL) dropwise with a syringe. The mixture was warmed to 0 ^{o}C and maintained at that temperature for 5 mins and then again cooled to -40 ^{o}C. To the resulting milky white suspension was added **S2** (6.31 mmol, 0.78 g) dissolved in dry DCM (3 mL). The suspension is warmed to 0 ^{o}C and stirred at that temperature for 2 h, then the suspension is allowed to warm to room temperature, and stirring is continued for additional 15 mins. The resulting clear colorless solution is washed with NaCl (30 mL) and extracted with pentane (2 × 50 mL), the pentane extracts are further washed with NaCl (60 mL) and dried over $MgSO_4$. The residue was directly used for the next step. Yield: 74%, obtained as yellow oil, ^{1}H NMR (400 MHz, 25 °C, $CDCl_3$): δ 5.51 (m, 1H), 4.10(dd, *J* = 7.9, 0.5 Hz, 2H), 2.36-2.25 (m, 4H), 1.96 (t, *J* = 2.5 Hz, 1H), 1.75 (m, 3H) ppm; ^{13}C NMR (100 MHz, 25 °C, $CDCl_3$): δ 140.7, 121.7, 83.6, 69.0, 40.8, 38.1, 17.2, 16.0 ppm.

Compound **S4**:



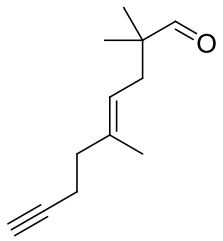
To a solution of diisopropylamine (6.5 mmol, 0.91 mL) in dry THF (12 mL) was added *n*-BuLi (2.5 M in hexane, 6.45 mmol, 2.58 mL) dropwise at 0 ^{o}C . After stirring for 10 mins the reaction mixture was cooled to -78 ^{o}C and a solution of methyl isobutyrate (6.5 mmol, 0.74 mL) in dry THF (4.5 mL) was added dropwise. The temperature was allowed to reach 0 ^{o}C for 15 mins and then decreased again to -78 ^{o}C. To the resulting reaction mixture was added a solution of **S3** (5.42 mmol, 0.77 g) in dry THF (2.5 mL) and the temperature was allowed to warm to RT. The reaction mixture was diluted with ether (20 mL) and washed with NH_4Cl (2 × 30 mL) and then brine (2 × 30 mL). The organic layer was dried over $MgSO_4$ and the solvent was removed under reduced pressure and the crude mixture was purified by Flash Chromatography using silica gel. Yield: 75%, obtained as light yellow oil, ^{1}H NMR (400 MHz, 25 °C, $CDCl_3$): δ 5.16 (m, 1H), 3.65 (s, 3H), 2.32-2.17 (m, 6H), 1.93 (t, *J* = 2.5 Hz, 1H), 1.61 (m, 3H), 1.17 (s, 6H) ppm; ^{13}C NMR (100 MHz, 25 °C, $CDCl_3$): δ 178.4, 136.0, 121.4, 84.3, 68.6, 51.8, 43.2, 38.8, 38.6, 24.9, 17.7, 16.0 ppm.

Compound **S5**:



To a solution of the **S4** (5.3 mmol, 1.1 g) in dry DCM (53 mL) at 0 ^{o}C was added DIBAL-H (1 M in THF, 13.2 mmol, 13.2 mL), the reaction mixture was stirred for 1 h. The reaction mixture was then diluted with ether, followed by the addition of MeOH (0.5 mL) and (0.5 mL) H_2O and was warmed to room temperature and stirred for 30 mins. A saturated solution of Na^+/K^+ Tartrate (55 mL) was added to the reaction mixture and stirred for 1 h at room temperature. The mixture was then extracted with DCM (2 × 40 mL) and the organic layers were washed with brine (80 mL) and dried over $MgSO_4$, the solvent was removed under reduced pressure and the compound purified by flash chromatography using silica gel. Yield: 90%, obtained as light yellow oil, ^{1}H NMR (400 MHz, 25 °C, $CDCl_3$): δ 5.31 (m, 1H), 3.34 (s, 2H), 2.31 (m, 2H), 2.24 (t, *J* = 7.1 Hz, 2H), 1.98 (d, *J* = 7.8 Hz, 2H), 1.95 (m, 1H), 1.64 (s, 3H), 0.90 (s, 6H) ppm; ^{13}C NMR (100 MHz, 25 °C, $CDCl_3$): δ 135.2, 122.4, 84.4, 72.0, 68.7, 38.8, 37.0, 36.4, 24.0, 17.6, 15.9 ppm; HRMS (ESI): Calculated for $C_{12}H_{21}O$ [M+H$^+$]: 181.15869, Found:181.15858.

Compound **9**:



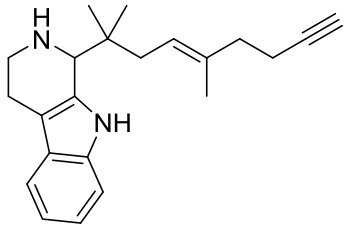
To a solution of oxalyl chloride (6 mmol, 0.51 mL) in dry DCM (39 mL) at -78 ^{0}C was added DMSO (12.5 mmol, 0.88 mL) dropwise. After stirring for 15 mins the reaction mixture was treated slowly with the compound h (5 mmol, 0.9 g) dissolved in dry DCM (7 mL), stirred for 20mins and treated slowly with treithylamine (25 mmol, 0.58 mL). After 5 min the reaction was warmed to RT and stirred for additional 1 h.The reaction mixture was poured into water (45 mL) and extracted using DCM (2 × 40 mL), the organic layer was dried using $MgSO_4$ and solvent removed under reduced pressure and the reaction mixture was purified by flash chromatography using silica gel. Yield: 89%, obtained as light yellow oil, ^{1}H NMR (400 MHz, 25 °C, $CDCl_3$): δ 9.49 (m, 1H), 5.17 (m, 1H), 2.28 (m, 2H), 2.20 (dd, *J* = 16.3, 7.1 Hz, 4H), 1.94 (m, 1H), 1.62 (s, 3H), 1.06 (s, 6H) ppm; ^{13}C NMR (100 MHz, 25 °C, $CDCl_3$): δ 206.4, 136.5, 120.3, 84.2, 68.8, 46.7, 38.7, 35.4, 21.3, 17.6, 16.1 ppm; HRMS (ESI): Calculated for $C_{12}H_{19}O$ [M+H$^+$]: 179.14304, Found:179.14268.

4b. <u>General Procedure F for the synthesis of the Pictet- Spengler Derivatives 10:</u>

To a solution of the corresponding amine **1** (0.28 mmol) and $Yb(OTf)_3$ (10 mol%, 0.028 mmol) in dry DCE (0.6 mL), was added the aldehyde **9** (0.28 mmol) dissolved in (0.4 mL) of dry DCE followed by the addition of the Ionic liquid [bmim]Cl-$AlCl_3$ (0.32 mL/mmol of aldehyde) to the mixture at room temperature. The resulting suspension was heated to 120 ^oC under microwave irradiation for 60 minutes. The solvent was removed in vacuo and the crude reaction mixture was purified by flash chromatography using basified silica gel with Dichloromethane and methanol as elutants.

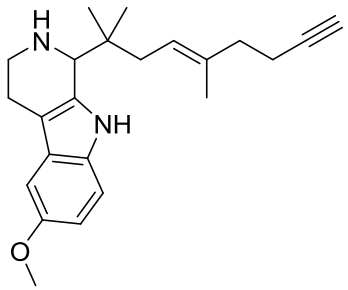
4c. <u>Characterization of the Pictet-Spengler products 10:</u>

Compound :**10a**



Compound **10a** was synthesized according to the general procedure **F** as a reddish-brown thick oil in 84% yield; ^1H NMR (400 MHz, 25 °C, CD_2Cl_2): δ 7.98 (*br* s, 1H) , 7.48 (d, *J* = 7.7 Hz, 1H), 7.33 (d, *J* = 8 Hz, 1H), 7.13 (t, *J* = 7.5 Hz, 1H), 7.07 (m, 1H), 5.43 (t, *J* = 7.2 Hz, 1H), 4.02 (s, 1H), 3.36 (dt, *J* = 12.0, 4.0 Hz, 1H) , 2.90 (m, 1H), 2.74 (m, 2H), 2.59 (*br* s, 1H), 2.36-2.23 (m, 5H), 2.13 (dd, *J* = 14.8, 7.6 Hz, 1H) , 1.98 (m, 1H), 1.68 (s, 3H), 1.14 (s, 3H), 1.08 (s, 3H) ppm; ^{13}C NMR (100 MHz, 25 °C, , CD_2Cl_2): δ 136.1, 135.9, 134.7, 127.6, 122.5, 121.7, 119.4, 118.1, 112.1, 110.9, 84.7, 68.9, 60.8, 43.8, 39.8, 39.0, 38.2, 25.5, 24.9, 23.2, 17.8, 16.2 ppm; HRMS (ESI): Calculated for $C_{22}H_{29}N_2$ $[M+H^+]$: 321.23253, Found: 321.23308.

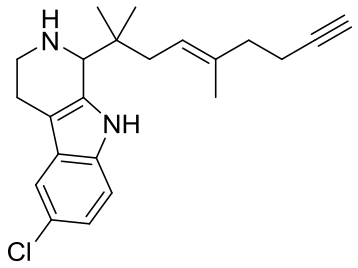
Compound: **10b**



Compound **10b** was synthesized according to the general procedure **F** as a reddish-brown thick oil in 75% yield; ^1H NMR (400 MHz, 25 °C, CD_2Cl_2): δ 7.86 (*br* s, 1H) , 7.20 (d, *J* = 8.8 Hz, 1H), 6.93 (d, *J* = 2.4 Hz, 1H), 6.76 (dd, *J* = 8.8, 2.4 Hz, 1H), 5.40 (t, *J* = 7.2 Hz, 1H), 4.04 (s, 1H), 3.82 (s, 3H), 3.39 (dt, *J* = 12.0, 4.0 Hz, 1H), 3.10 (*br* s, 1H), 2.92 (m, 1H), 2.72

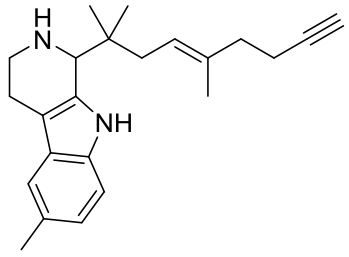
(m, 2H), 2.35-2.21 (m, 5H), 2.12 (dd, *J* = 14.4, 7.2 Hz, 1H), 1.98 (t, *J* = 2.4 Hz, 1H), 1.66 (s, 3H), 1.13 (s, 3H), 1.09 (s, 3H) ppm; ^{13}C NMR (100 MHz, 25 °C, CD_2Cl_2): δ 154.4, 136.1, 134.9, 131.2, 127.9, 122.3, 111.8, 111.64, 111.63, 100.4, 84.6, 68.9, 60.9, 56.1, 43.8, 39.8, 39.0, 38.1, 25.4, 24.9, 22.8, 17.8, 16.2 ppm; HRMS (ESI): Calculated for $C_{23}H_{31}N_2O$ [M+H$^+$]: 351.24309, Found: 351.24369.

Compound: **10c**



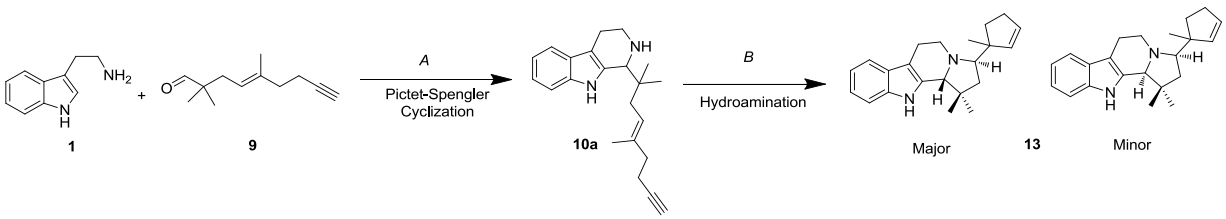
Compound **10c** was synthesized according to the general procedure **F** as a reddish-brown thick oil in 65% yield; ^{1}H NMR (400 MHz, 25 °C, CD_2Cl_2): δ 8.01 (*br* s, 1H) , 7.43 (d, *J* = 2.0 Hz, 1H), 7.24 (m, 1H), 7.07 (dd, *J* = 8.6, 2.0 Hz, 1H), 5.40 (td, *J* = 7.4, 1.2 Hz, 1H), 3.96 (t, *J* = 1.7 Hz , 1H), 3.31 (m, 1H) , 2.86 (m, 1H), 2.65 (m, 2H), 2.34-2.21 (m, 5H), 2.09 (dd, *J* = 14.4, 7.2 Hz, 1H), 1.95 (t, *J* = 2.6 Hz, 1H), 1.87 (*br* s, 1H), 1.66 (s, 3H), 1.12 (s, 3H), 1.05 (s, 3H) ppm; ^{13}C NMR (100 MHz, 25 °C, CD_2Cl_2): δ 136.9, 135.9, 134.4, 128.8, 124.9, 122.4, 121.6, 117.6, 112.1, 111.9, 84.6, 68.8, 60.7, 43.6, 39.8, 39.0, 38.2, 25.6, 25.0, 23.3, 17.8, 16.1 ppm; HRMS (ESI): Calculated for $C_{22}H_{28}N_2Cl$ [M+H$^+$]: 355.19355, Found: 355.19429.

Compound:**10d**



Compound **10d** was synthesized according to the general procedure **F** as a reddish-brown thick oil in 71% yield; ^{1}H NMR (400 MHz, 25 °C, CD_2Cl_2): δ 7.88 (*br* s, 1H) , 7.26 (s, 1H), 7.21 (d, *J* = 8.2 Hz, 1H), 6.96 (d, *J* = 8.0 Hz, 1H), 5.41 (t, *J* = 7.3 Hz, 1H), 4.02 (s, 1H), 3.37 (dt, *J* = 12.1, 4.1 Hz, 1H), 3.02 (*br* s, 1H), 2.90 (m, 1H), 2.70 (m, 2H), 2.44 (s, 3H), 2.35-2.22 (m, 5H), 2.12 (dd, *J* = 14.5, 7.3 Hz, 1H) , 1.98 (m, 1H), 1.67 (s, 3H), 1.13 (s, 3H), 1.08 (s, 3H) ppm; ^{13}C NMR (100 MHz, 25 °C, CD_2Cl_2): δ 135.8, 134.9, 134.4, 128.6, 127.8, 123.2, 122.5, 117.8, 111.6, 110.5, 84.7, 68.8, 60.9, 43.8, 39.8, 39.1, 38.2, 25.5, 24.9, 23.3, 21.5, 17.8, 16.2; HRMS (ESI): Calculated for $C_{23}H_{31}N_2$ [M+H$^+$]: 335.24818, Found: 335.24877.

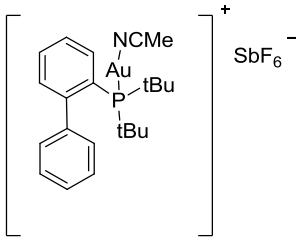
4d. Supplementary Table 2 : Optimization of the gold catalyzed hydroamination



Entry	Catalyst (mol%)	Solvent	Temp (^{o}C)	Time (h)	Yield[a] (%)	dr[b]
1	$Au(PPh_3)OTf$ (10)	DCE	80	24	30	1 : 1.5
2	$AuCl_3$ (10)	DCE	80	24	20	1 : 1.4
3	$Au(PPh_3)NTf_2$ (10)	DCE	80	24	33	1 : 1.4
4	$AuCl(SMe_2)$ (10)	DCE	80	24	43	1 : 1.4
5	$AuCl(SMe_2)$ (10)	*i*-PrOH	80	24	15	1 : 1.2
6	$AuCl(SMe_2)$ (10)	AcN	80	24	30	1 : 1.3
7	$AuCl(SMe_2)$ (10)	1.4-dioxne	80	24	24	1 : 1.2
8	Catalyst Y (10)	DCE	80	24	53	1 : 2
9	Catalyst Y (10)	DCE	80, MW	1	70	1 : 1.6
10	Catalyst Y (10)	DCE	120, MW	1	68	1 : 1.4
11	Catalyst Y (10)	DCE: Ethanol(5eq)	80, MW	1	43	1 : 1.2

[a] isolated yield of 14 (both the diastereomers together), [b] diastereoselectivity (minor : major) determined using proton NMR, MW: Microwave, DCE: 1,2-dichloroethane, IL: Ionic Liquid ([bmim]Cl-$AlCl_3$(0.32 mL/mmol of aldehyde), unless and otherwise specified all the reactions were carried out at 0.1 mmol scale in 1 mL of the solvent.

Catalyst Y :-

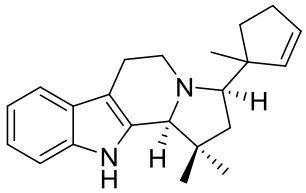


4e. General Procedure G for the gold-catalyzed reaction:-

To a solution of the catalyst Y (10 mol%, 0.01 mmol) in dry DCE (1 mL) was added the corresponding Pictet-Spengler compound (0.1 mmol) dissolved in 2 mL of dry DCE. The suspension was heated to 80 ^{o}C under microwave irradiaton for 60 mins. The solvent was removed in vacuo and the crude reaction mixture was purified using flash chromatography with petroleum ether and ethyl acetate as eluents.

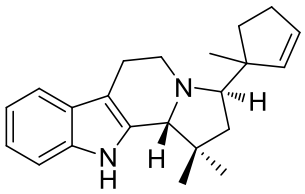
4f. Characterization of Indolizinoindoles 13:

Compound 13a: Yield: 70%, dr 1:1.6, synthesized using the general procedure **G**



Minor Diastereomer:

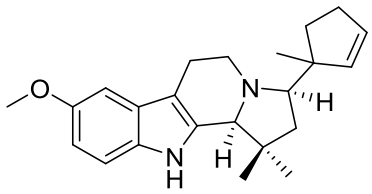
Obtained as a light yellow oil**;** ^{1}H NMR (400 MHz, 25 °C, CD_2Cl_2): δ 7.79 (*br* s, 1H), 7.44 (d, *J* = 7.6 Hz, 1H), 7.32 (d, *J* = 8.0 Hz, 1H), 7.10 (m, 1H), 7.04 (m, 1H), 5.64 (m, 1H), 5.58 (m, 1H), 3.62 (dd, *J* = 11.1, 5.8 Hz, 1H), 3.23 (s, 1H), 2.83 (m, 1H), 2.65 (m, 2H), 2.41 (m, 2H), 2.27-2.12 (m, 2H), 1.78 (dd, *J* = 12.8, 9.2 Hz, 1H), 1.7 (m, 1H), 1.56 (dd, *J* = 12.8, 8.0 Hz, 1H), 1.37 (s, 3H), 1.03 (s, 3H), 0.97 (s, 3H) ppm; ^{13}C NMR (100 MHz, 25 °C, CD_2Cl_2): δ 140.9, 136.3, 134.9, 128.6, 127.6, 121.3, 119.5, 118.2, 111.0, 110.7, 71.8, 69.9, 52.1, 48.8, 45.2, 37.5, 34.6, 32.1, 29.1, 26.3, 23.4, 23.1 ppm; HRMS (ESI): Calculated for $C_{22}H_{29}N_2$ [M+H$^+$]: 321.23253, Found: 321.23253.



Major Diastereomer:

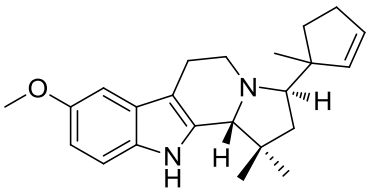
Obtained as a yellow oil; ^{1}H NMR (400 MHz, 25 °C, CD_2Cl_2): δ 7.79 (*br* s, 1H), 7.47 (d, *J* =7.8 Hz, 1H), 7.33 (d, *J* = 7.9 Hz, 1H), 7.11 (m, 1H), 7.05 (m, 1H), 5.68 (m, 1H), 5.60 (m, 1H), 3.92 (s, 1H), 3.14 (m, 3H), 2.71 (m, 2H), 2.36 (m, 2H), 1.97 (m, 1H), 1.86 (dd, *J* = 12.5, 7.3 Hz, 1H), 1.55 (m, 2H), 1.32 (s, 3H), 1.09 (s, 3H), 0.84 (s, 3H) ppm; ^{13}C NMR (100 MHz, 25 °C, CD_2Cl_2): δ 139.5, 136.7, 134.2, 129.4, 127.1, 121.5, 119.4, 118.3, 111.0, 110.9, 71.6, 67.4, 54.7, 51.4, 44.6, 43.4, 33.3, 32.3, 27.9, 25.0, 23.9, 22.1 ppm; HRMS (ESI): Calculated for $C_{22}H_{29}N_2$ [M+H$^+$]: 321.23253, Found: 321.23280.

Compound 13b: Yield: 67%, dr 1:1.7, synthesized using the general procedure **G**



Minor Diastereomer:

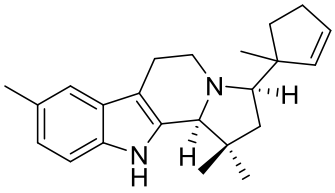
Obtained as a yellow oil; ^{1}H NMR (400 MHz, 25 °C, CD_2Cl_2): δ 7.67 (*br* s, 1H), 7.20 (dd, *J* = 8.8, 0.4 Hz, 1H), 6.90 (d, *J* = 2.4 Hz, 1H), 6.73 (dd, *J* = 8.8, 2.4 Hz, 1H), 5.64 (m, 1H), 5.57 (m, 1H), 3.82 (d, 3H, *J* = 0.7 Hz, 3H), 3.61 (m, 1H), 3.21 (s, 1H), 2.80 (m, 1H), 2.61 (m, 2H), 2.40 (m, 2H), 2.26-2.11 (m, 2H), 1.77 (dd, *J* = 12.9, 9 Hz, 1H), 1.69 (m, 1H), 1.55 (dd, *J* = 12.9, 7.9 Hz, 1H), 1.35 (s, 3H), 1.02 (s, 3H), 0.96 (s, 3H) ppm; ^{13}C NMR (100 MHz, 25 °C, CD_2Cl_2): δ 154.4, 140.8, 135.8, 131.3, 128.6, 128.0, 111.5, 110.9, 110.5, 100.7, 71.9, 69.9, 56.1, 52.1, 48.8, 45.2, 37.5, 34.6, 32.1, 29.1, 26.3, 23.4, 23.2 ppm; HRMS (ESI): Calculated for $C_{23}H_{31}N_2O$ [M+H$^+$]: 351.24309, Found: 351.24360.



Major Diastereomer:

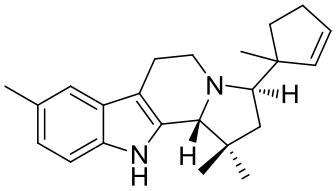
Obtained as a yellow oil; ^{1}H NMR (400 MHz, 25 °C, CD_2Cl_2): δ 7.67 (*br* s, 1H), 7.21 (d, *J* =.8.7 Hz, 1H), 6.94 (d, *J* = 2.4 Hz, 1H), 6.75 (dd, *J* = 8.7, 2.5 Hz, 1H), 5.68 (m, 1H), 5.60 (m, 1H), 3.89 (s, 1H), 3.83 (s, 3H), 3.14 (m, 3H), 2.67 (dd, *J* = 6.3, 4.5 Hz, 2H), 2.36 (m, 2H), 1.96 (m, 1H), 1.85 (dd, *J* = 12.5, 7.3 Hz, 1H), 1.54 (m, 2H), 1.30 (s, 3H), 1.09 (s, 3H), 0.84 (s, 3H) ppm; ^{13}C NMR (100 MHz, 25 °C, CD_2Cl_2): δ 154.4, 139.5, 135.2, 131.7, 129.4, 127.6, 111.5, 111.1, 110.7, 100.7, 71.6, 67.5, 56.1, 54.7, 51.4, 44.6, 43.4, 33.3, 32.3, 27.9, 25.0, 23.9, 22.2 ppm; HRMS (ESI): Calculated for $C_{23}H_{31}N_2O$ [M+H$^+$]: 351.24309, Found: 351.24357.

Compound 13c: Yield: 62%, dr 1:1.7, synthesized using the general procedure **G**



Minor Diastereomer:

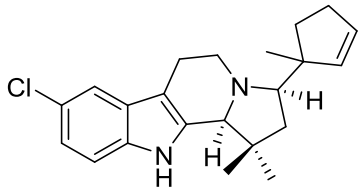
Obtained as a yellow oil; ^{1}H NMR (400 MHz, 25 °C, CD_2Cl_2): δ 7.68 (*br* s, 1H), 7.20 (m, 2H), 6.92 (d, *J* = 8.3 Hz, 1H), 5.64 (d, *J* = 5.6 Hz, 1H), 5.57 (d, *J* = 5.5 Hz, 1H), 3.60 (dd, *J* = 10.7, 5.9 Hz, 1H), 3.21 (s, 1H), 2.79 (m, 1H), 2.61 (m, 2H), 2.40 (m, 5H), 2.25-2.11 (m, 2H), 1.77 (dd, *J* = 12.9, 9.0 Hz, 1H), 1.70 (m, 1H), 1.55 (dd, *J* = 12.9, 7.8 Hz, 1H), 1.35 (s, 3H), 1.02 (s, 3H), 0.96 (s, 3H) ppm; ^{13}C NMR (100 MHz, 25 °C, CD_2Cl_2): δ 140.9, 135.0, 134.6, 128.7, 128.6, 127.9, 122.8, 118.0, 110.6, 110.2, 71.9, 69.9, 52.1, 48.8, 45.2, 37.5, 34.6, 32.1, 29.1, 26.3, 23.4, 23.1, 21.5 ppm; HRMS (ESI): Calculated for $C_{23}H_{31}N_2$ [M+H$^+$]: 335.24818, Found: 335.24871.



Major Diastereomer:

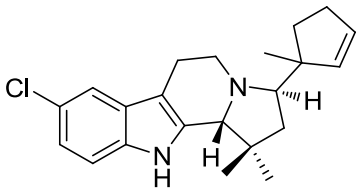
Obtained as a yellow oil; ^{1}H NMR (400 MHz, 25 °C, CD_2Cl_2): δ 7.68 (*br* s, 1H), 7.26 (s, 1H), 7.21(d, *J* = 8.2 Hz, 1H), 6.94 (d, *J* = 8.2 Hz, 1H), 5.68 (m, 1H), 5.60 (m, 1H), 3.89 (s, 1H), 3.13 (m, 3H), 2.67 (m, 2H), 2.43 (s, 3H), 2.36 (m, 2H), 1.96 (m, 1H), 1.85 (dd, *J* = 12.5, 7.3 Hz, 1H), 1.55 (m, 2H), 1.30 (s, 3H), 1.09 (s, 3H), 0.83 (s, 3H) ppm; ^{13}C NMR (100 MHz, 25 °C, CD_2Cl_2): δ 139.5, 135.0, 134.4, 129.4, 128.7, 127.4, 123.0, 118.1, 110.5, 110.4, 71.6, 67.5, 54.7, 51.4, 44.6, 43.5, 33.3, 32.3, 27.9, 25.0, 23.9, 22.1, 21.5 ppm; HRMS (ESI): Calculated for $C_{23}H_{31}N_2$ [M+H$^+$]: 335.24818, Found: 335.24844.

Compound 13d: Yield: 49%, dr 1: 1.5, synthesized using the general procedure **G**



Minor Diastereomer:

Obtained as a yellow oil; ^{1}H NMR (400 MHz, 25 °C, CD_2Cl_2): δ 7.85 (*br* s, 1H), 7.41 (s, 1H), 7.25 (d, *J* = 8.5 Hz, 1H), 7.05 (dd, *J* = 8.6, 1.7 Hz, 1H), 5.64 (m, 1H), 5.56 (m, 1H), 3.61 (dd, *J* = 11.0, 6.1 Hz, 1H), 3.21 (s, 1H), 2.79 (m, 1H), 2.62 (m, 2H), 2.40 (m, 2H), 2.26-2.09 (m, 2H), 1.78 (dd, *J* = 12.9, 9.1 Hz, 1H), 1.69 (m, 1H), 1.56 (dd, *J* = 14.2, 6.6 Hz, 1H), 1.36 (s, 3H), 1.02 (s, 3H), 0.96 (s, 3H) ppm; ^{13}C NMR (100 MHz, 25 °C, CD_2Cl_2): δ 140.8, 136.7, 134.6, 128.8, 128.7, 125.1, 121.3, 117.8, 112.0, 110.6, 71.7, 69.8, 52.1, 48.6, 45.1, 37.5, 34.5, 32.1, 29.1, 26.3, 23.4, 23.0 ppm; HRMS (ESI): Calculated for $C_{22}H_{28}N_2Cl$ [M+H$^+$]: 355.19355, Found: 355.19403.



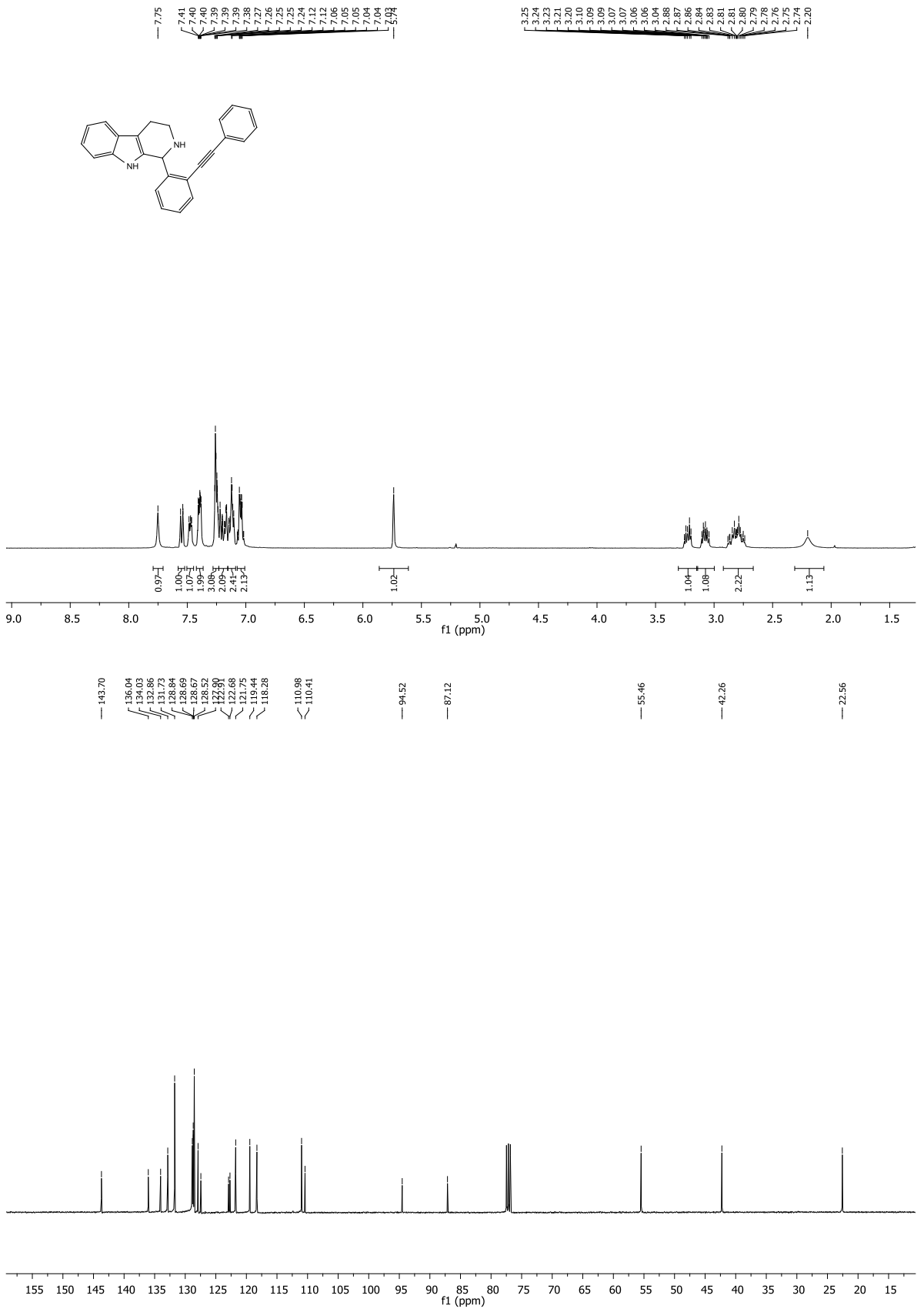
Major Diastereomer:

Obtained as a yellow oil; ^{1}H NMR (400 MHz, 25 °C, CD_2Cl_2): δ 7.86 (*br* s, 1H), 7.44 (s, 1H), 7.26(dd, *J* = 8.5, 0.5 Hz, 1H), 7.07 (m, 1H), 5.68 (m, 1H), 5.59 (m, 1H), 3.90 (s, 1H), 3.13 (m, 3H), 2.67 (m, 2H), 2.36 (m, 2H), 1.94 (m, 1H), 1.85 (dd, *J* = 12.5, 7.4 Hz, 1H), 1.54 (m, 2H), 1.31 (s, 3H), 1.08 (s, 3H), 0.83 (s, 3H) ppm; ^{13}C NMR (100 MHz, 25 °C, CD_2Cl_2): δ

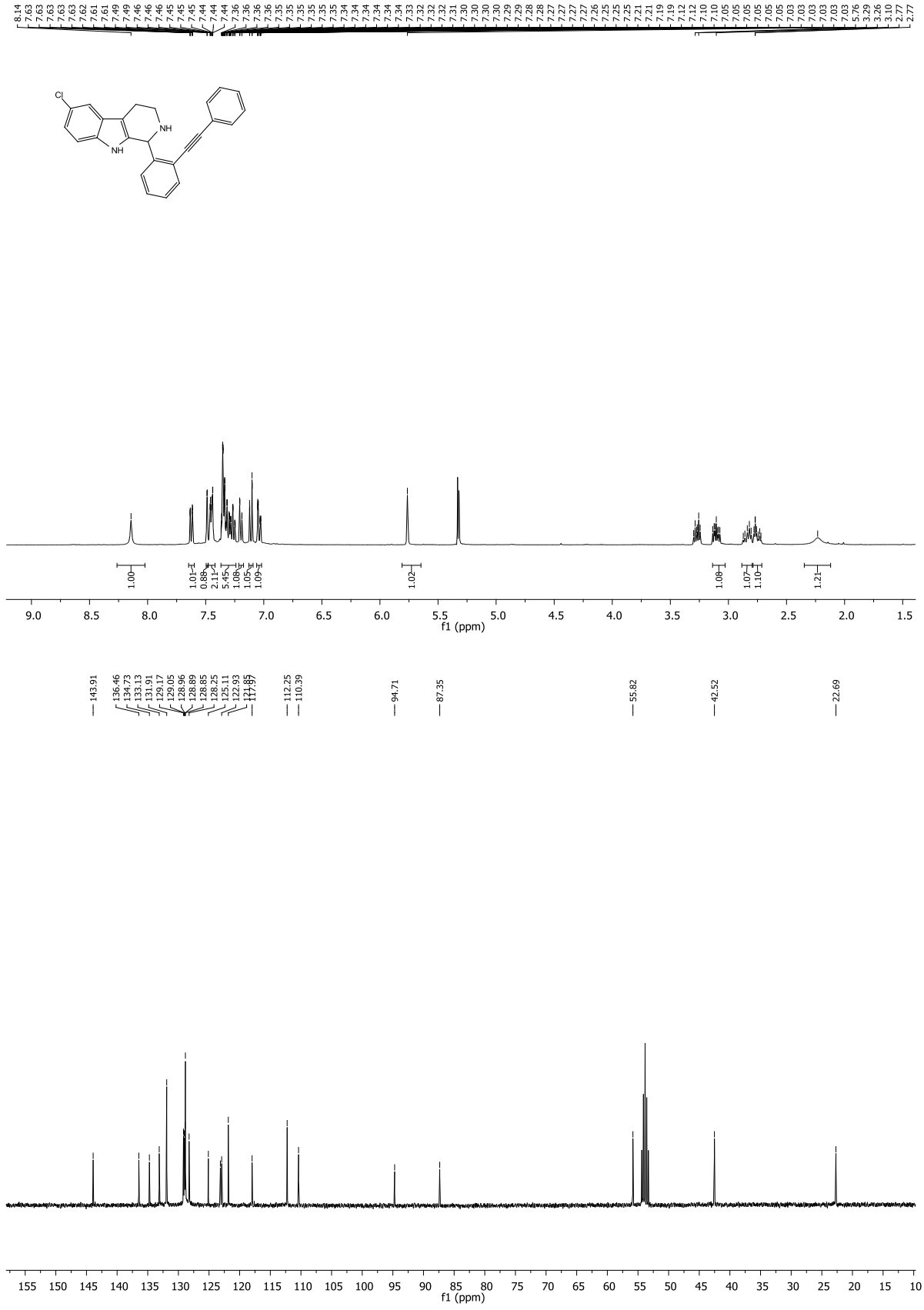
139.4, 136.1, 135.0, 129.6, 128.3, 125.0, 121.5, 117.8, 112.0, 110.8, 71.5, 67.3, 54.6, 51.1, 44.6, 43.4, 33.3, 32.3, 27.9, 24.9, 23.9, 22.0; HRMS (ESI): Calculated for $C_{22}H_{28}N_2Cl$ $[M+H^+]$: 355.19355, Found: 355.19399

5. NMR Spectra for representative compounds 3:

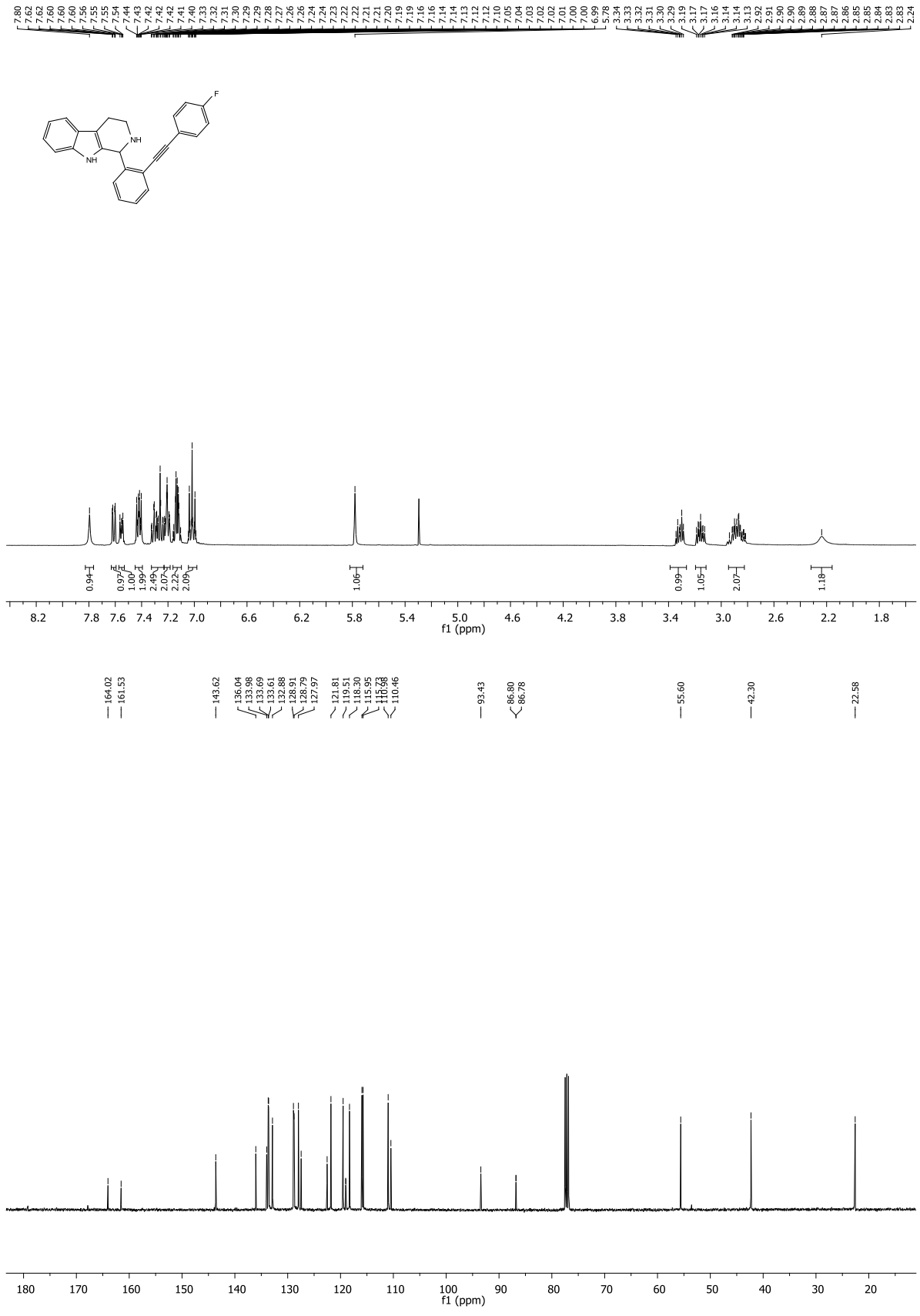
NMR of compound **3a** measured in $CDCl_3$ as solvent, 400MHz



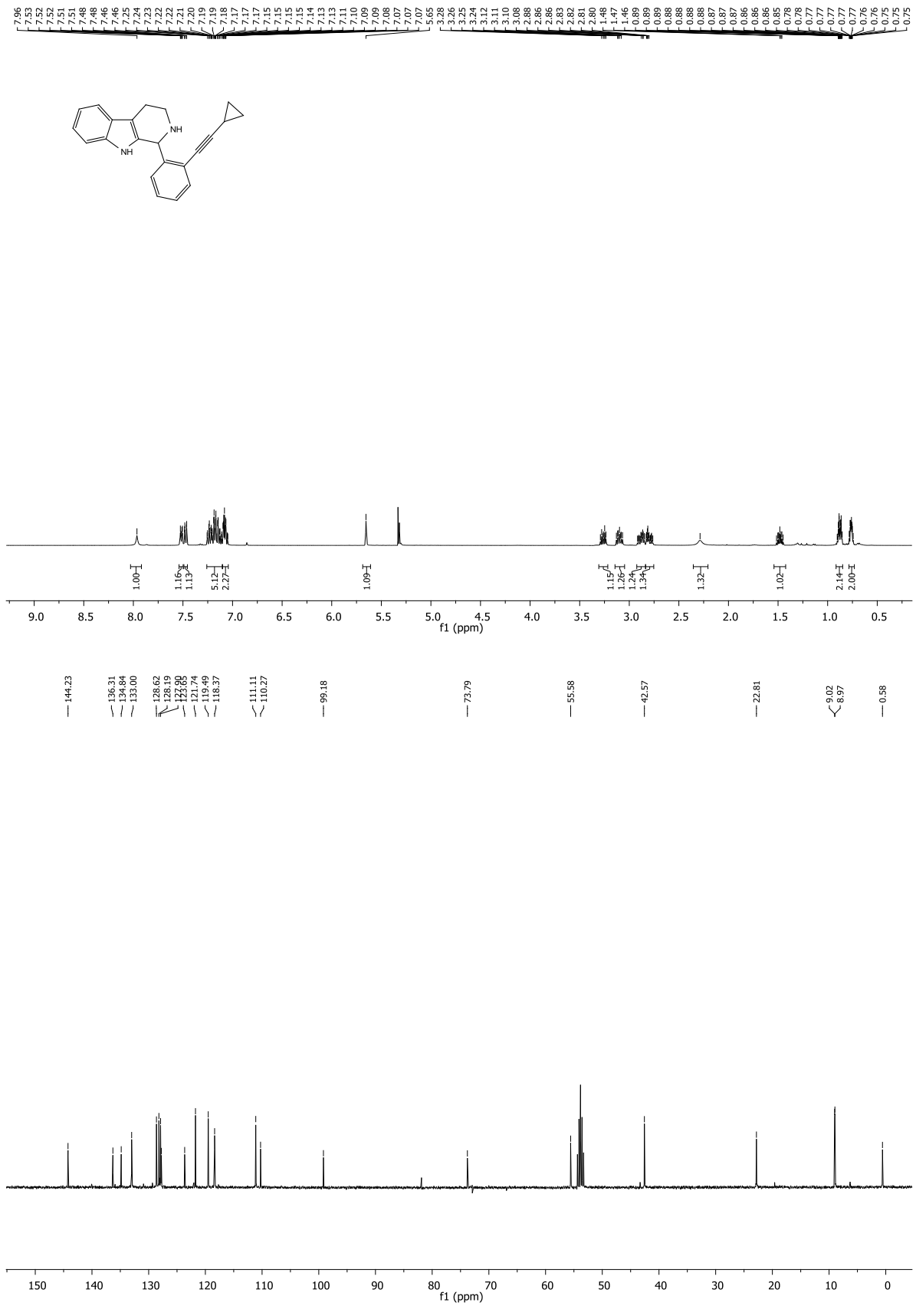
NMR of compound **3c** measured in DCM as solvent, 400MHz



NMR of compound **3e** measured in $CDCl_3$ as solvent, 400MHz

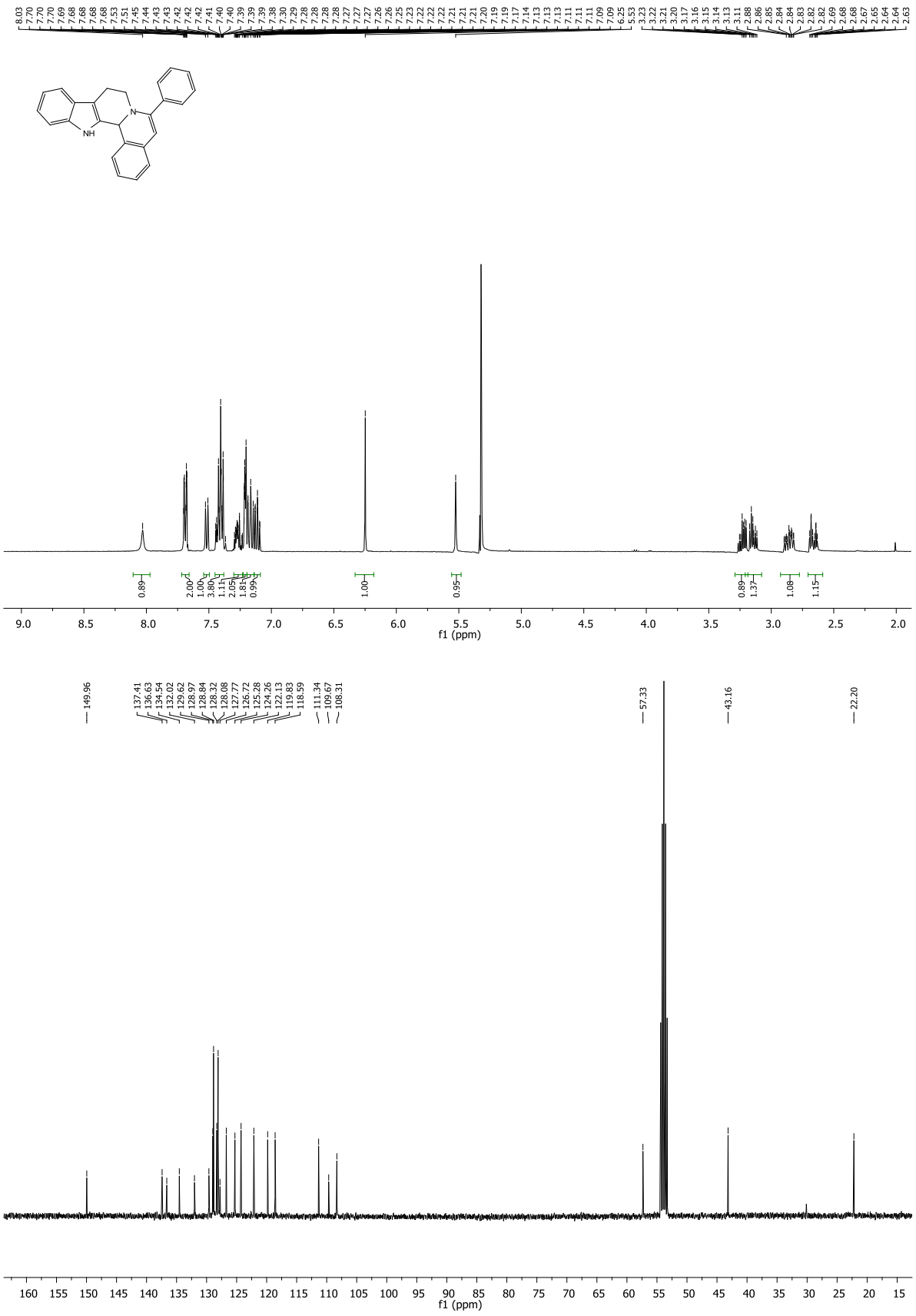


NMR of compound **3f** measured in DCM as solvent, 400MHz

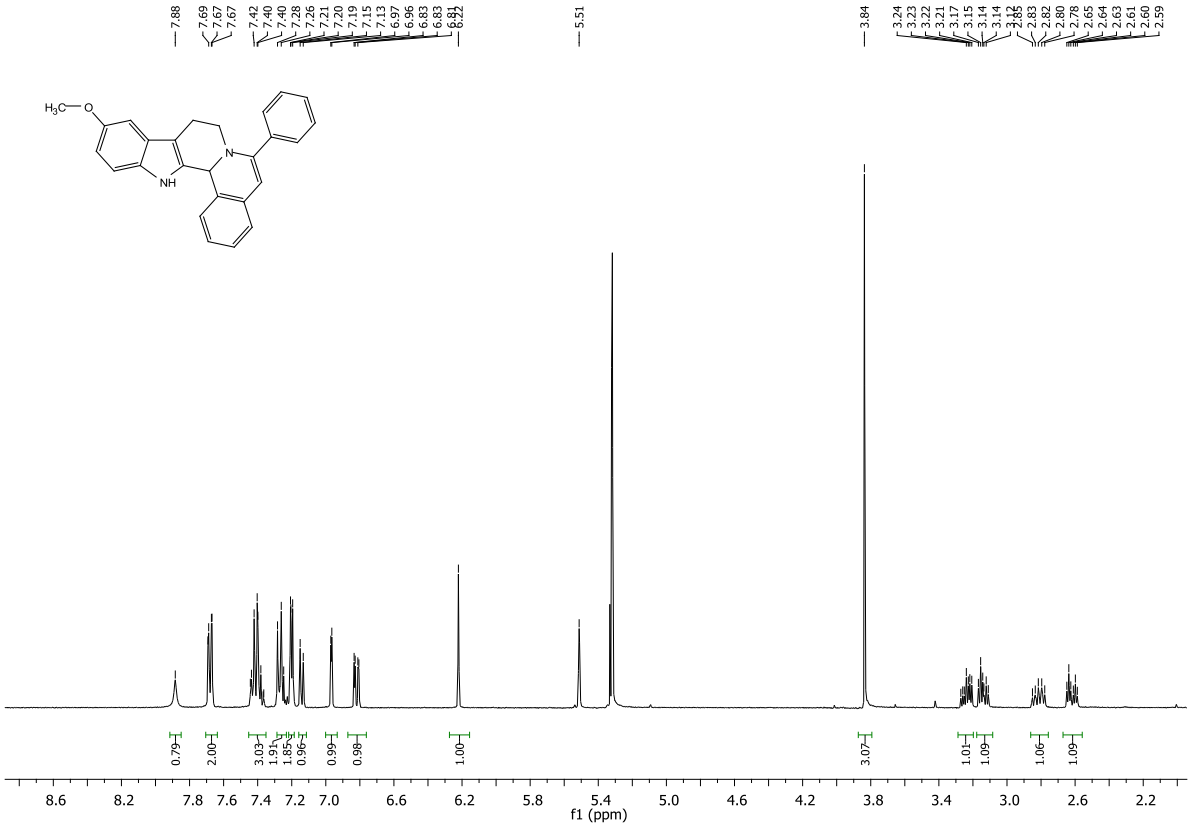


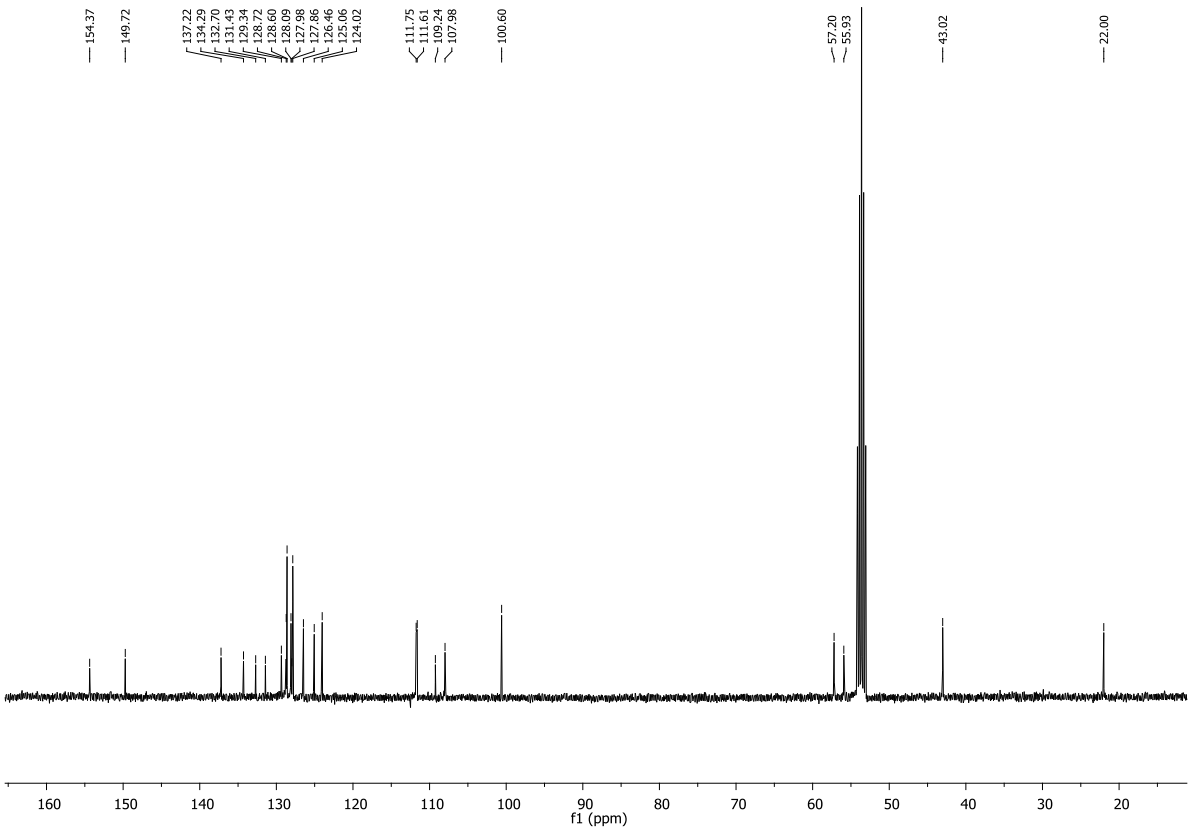
6. NMR Spectra of Products 4:

NMR of compound **4a** measured in DCM as solvent, 400MHz

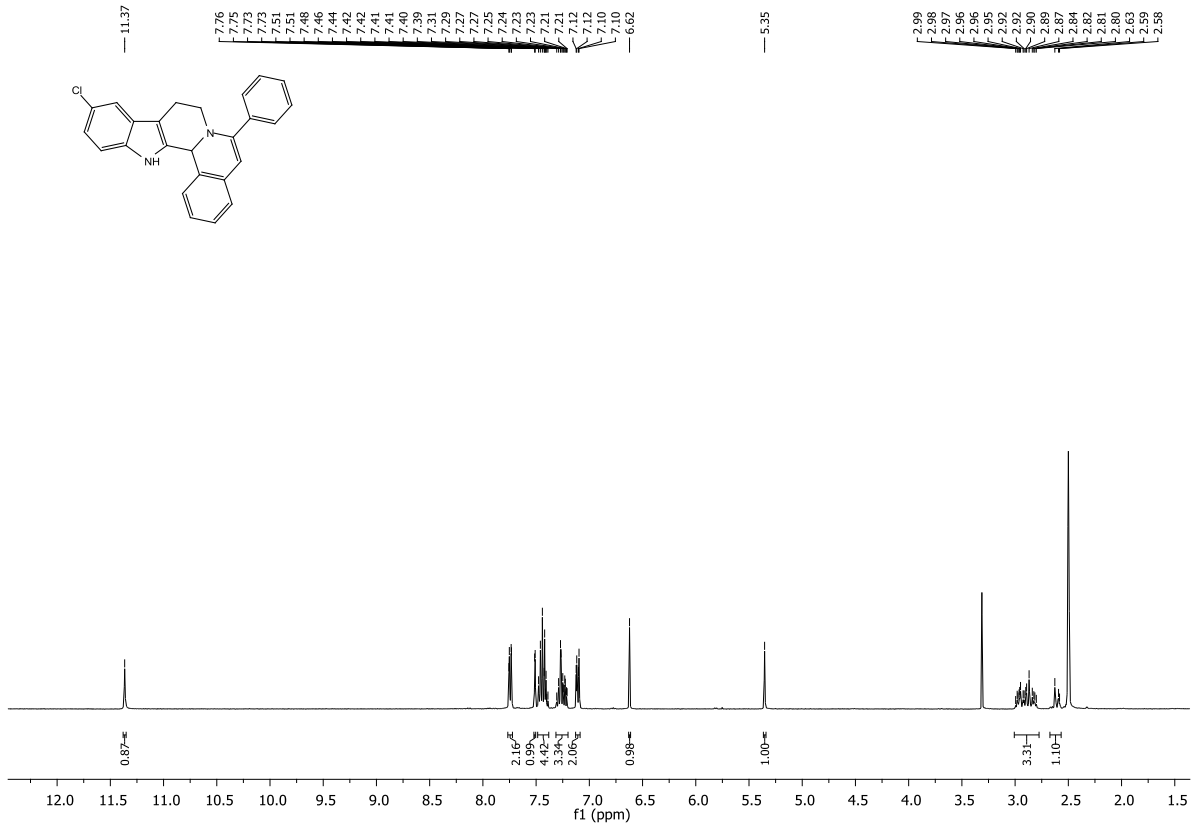


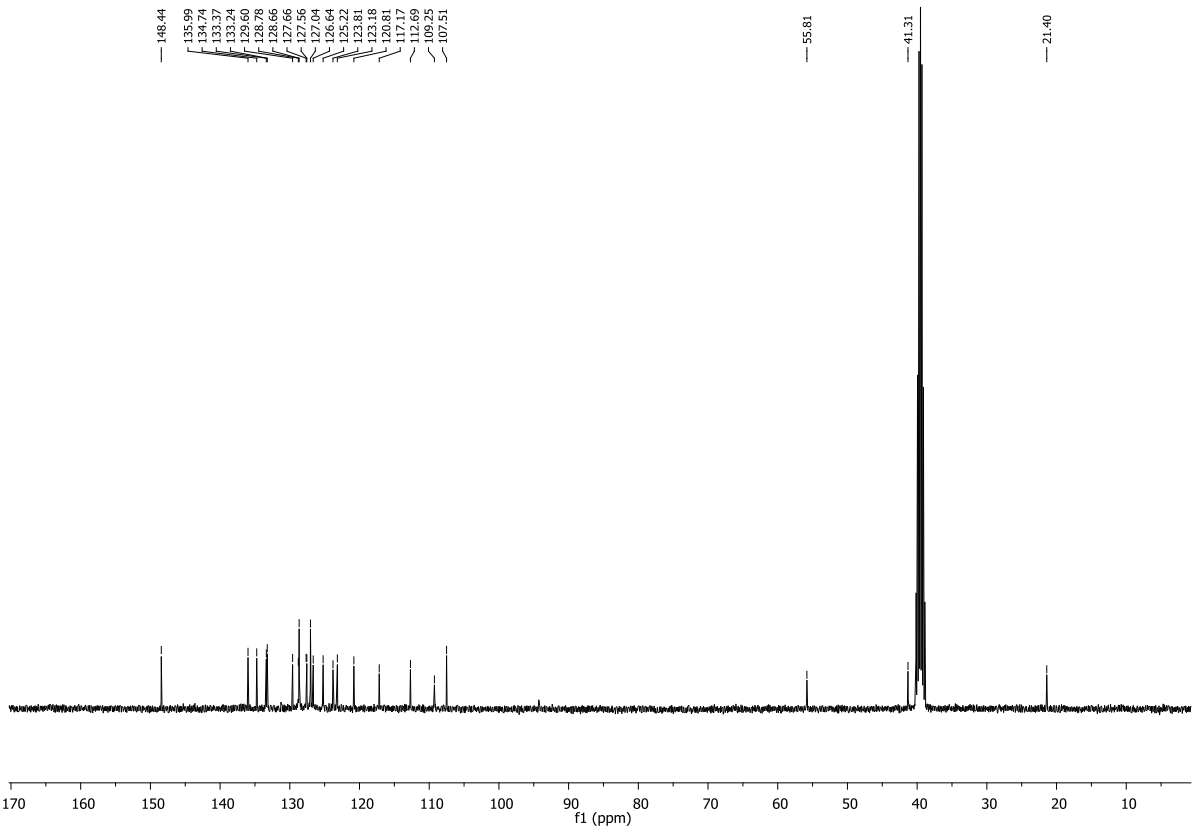
NMR of compound **4b** measured in DCM as solvent, 400MHz



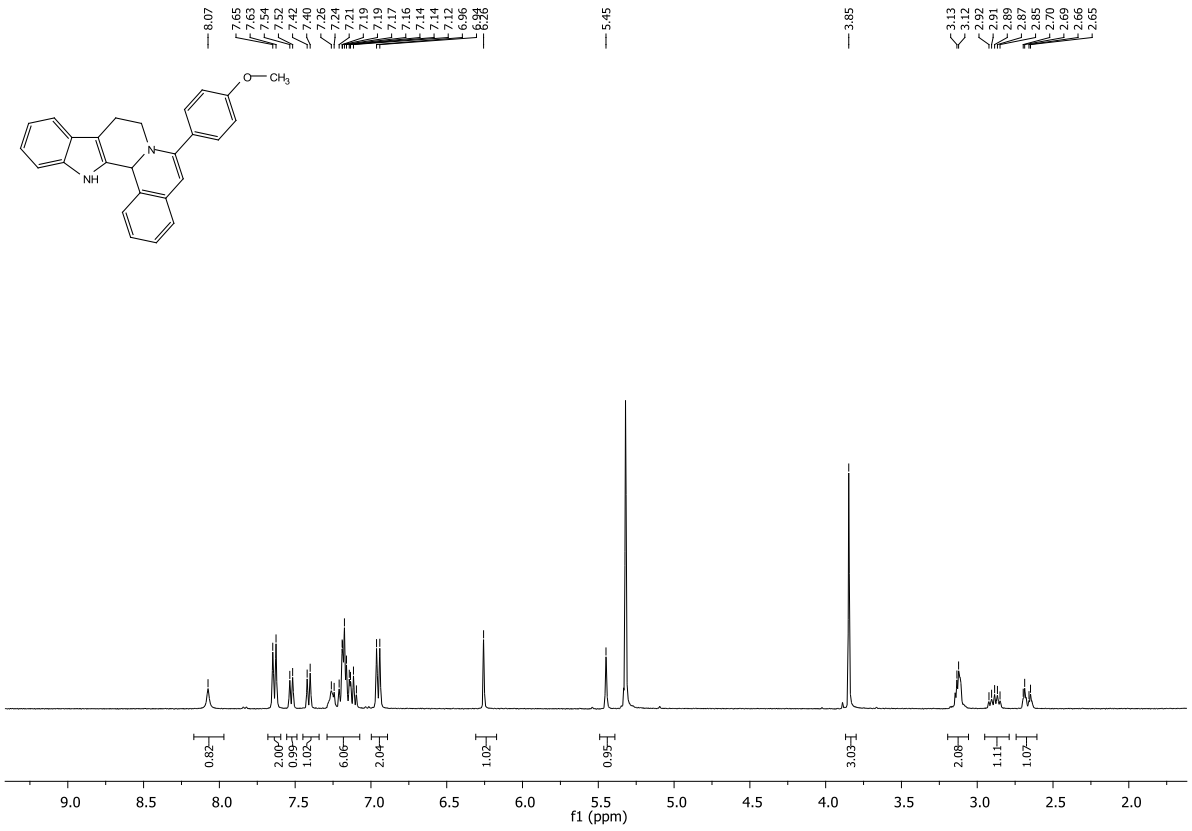


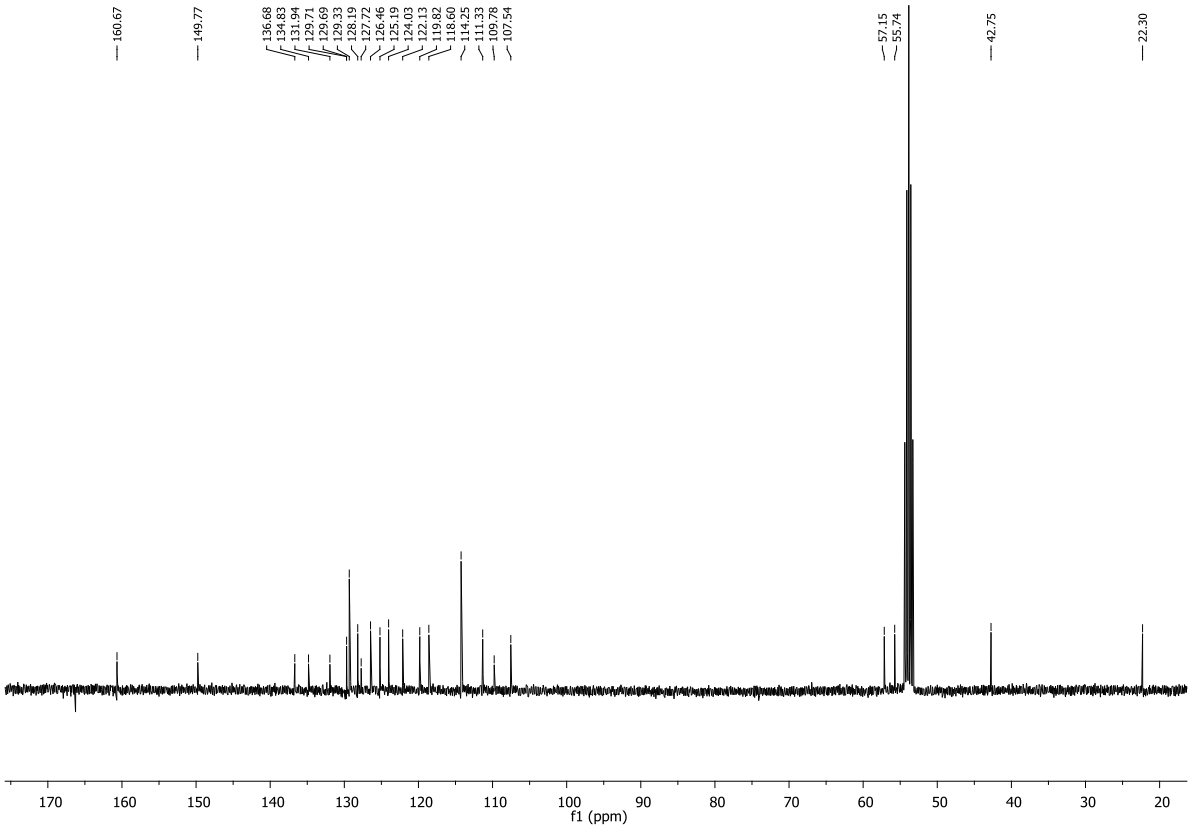
NMR of compound **4c** measured in DMSO as solvent, 400MHz



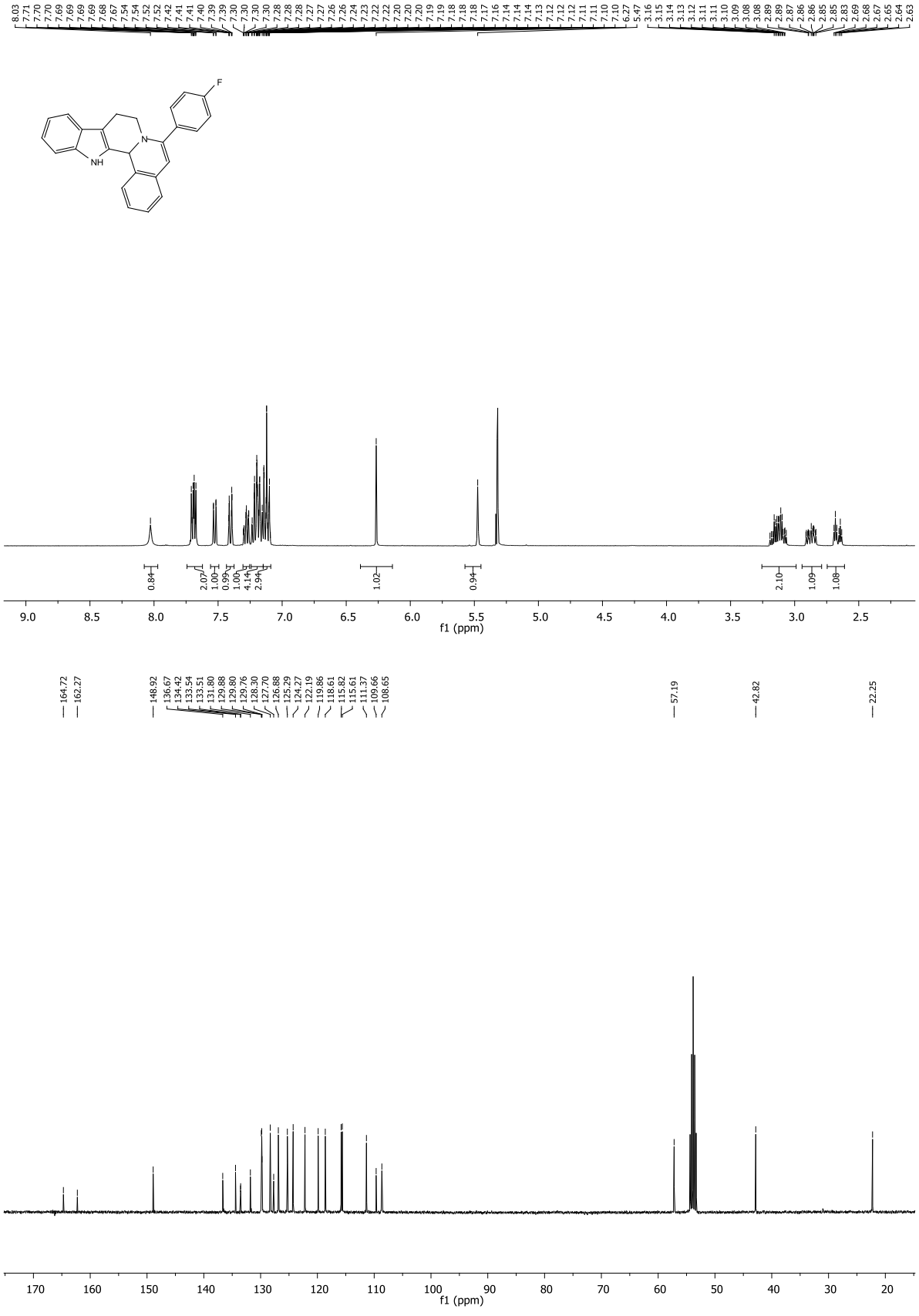


NMR of compound **4d** measured in DCM as solvent, 400MHz

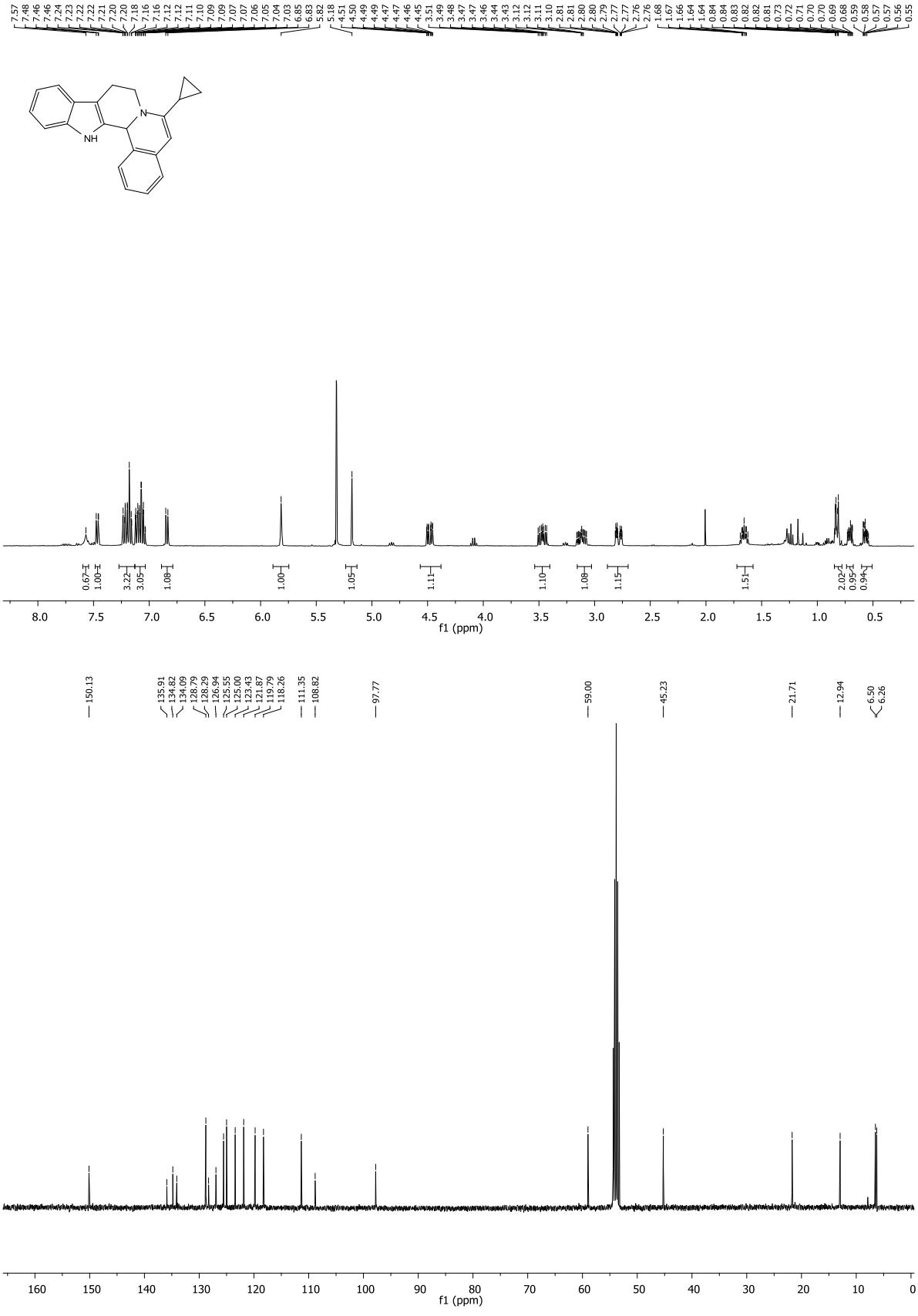




NMR of compound **4e** measured in DCM as solvent, 400MHz

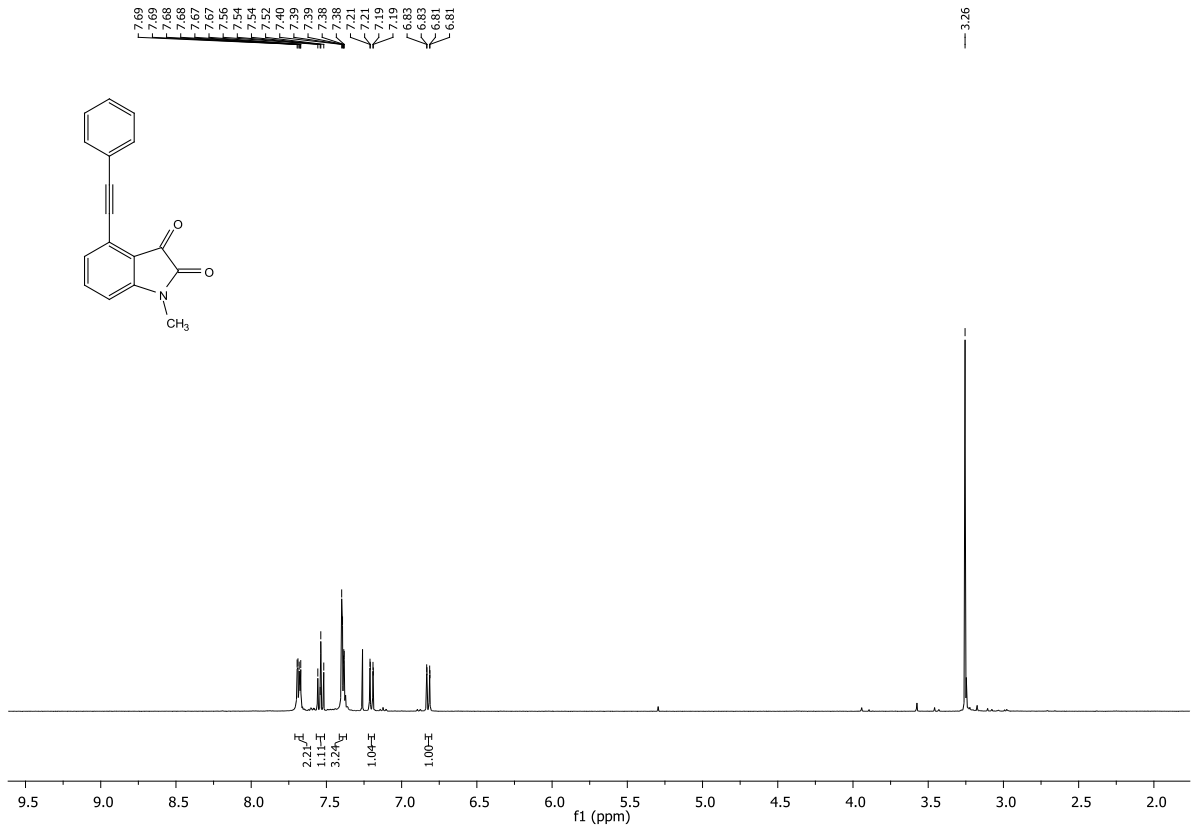


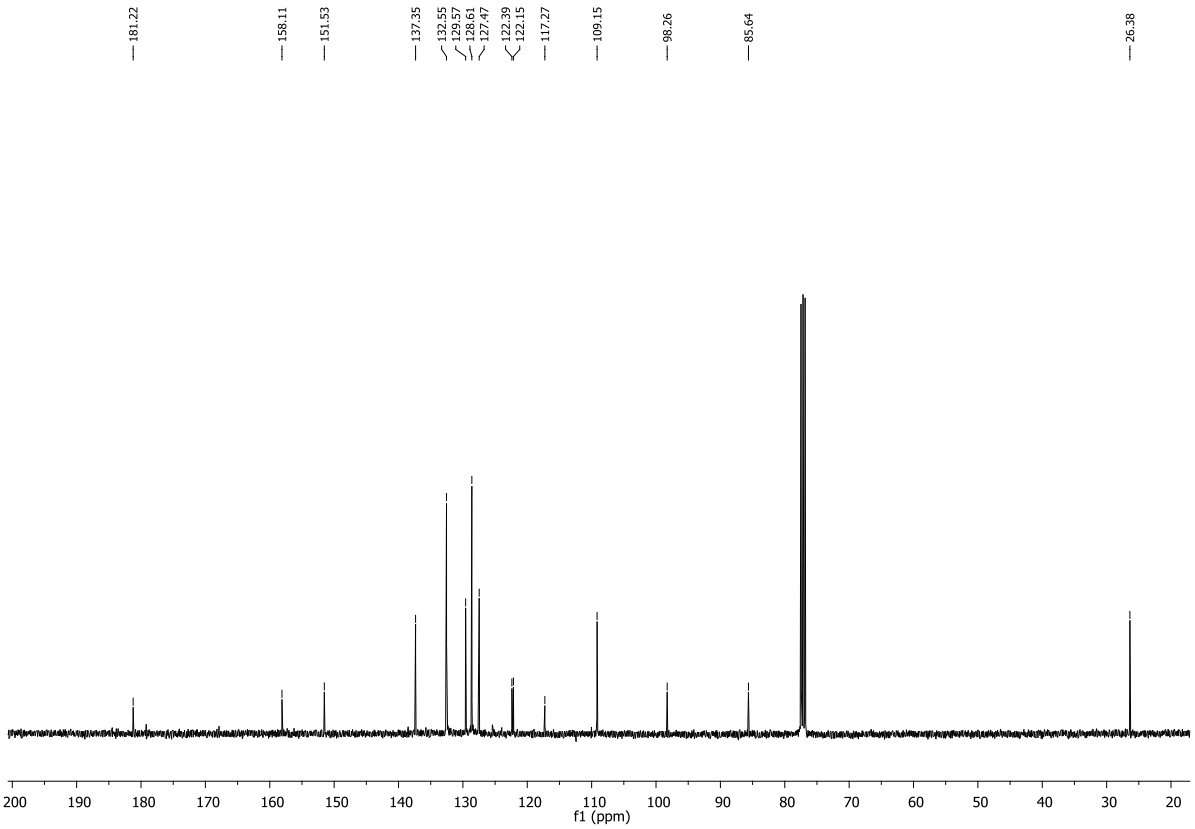
NMR of compound **4f** measured in DCM as solvent, 400MHz



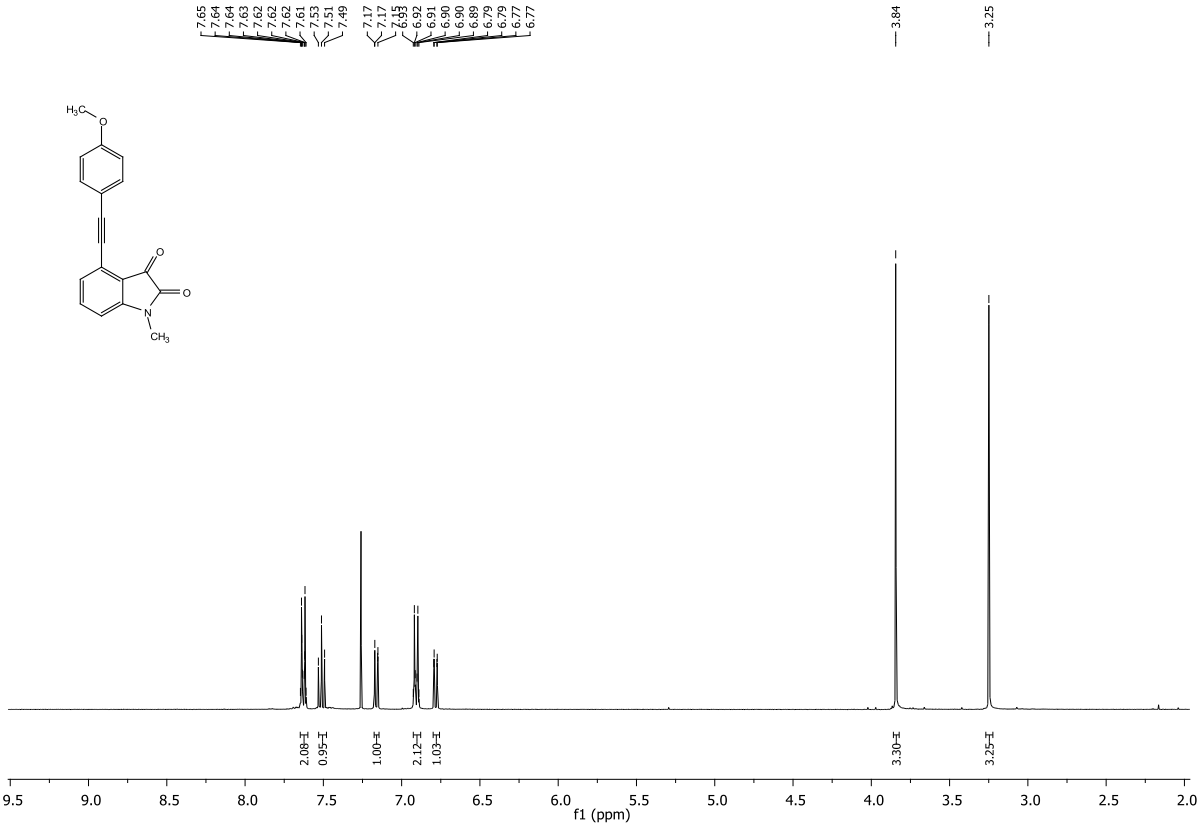
7. **NMR spectra of Sonogashira Products 5:**

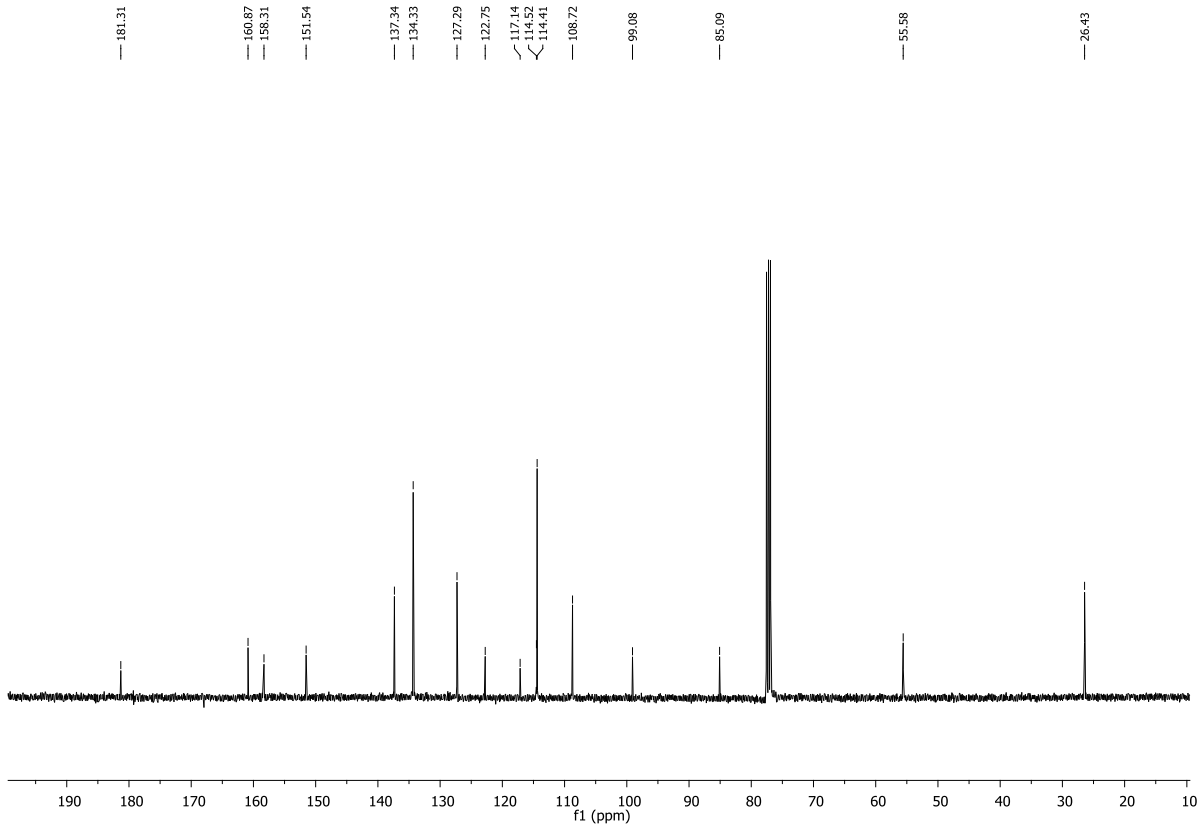
NMR of compound **5a** measured in $CDCl_3$ as solvent, 400MHz



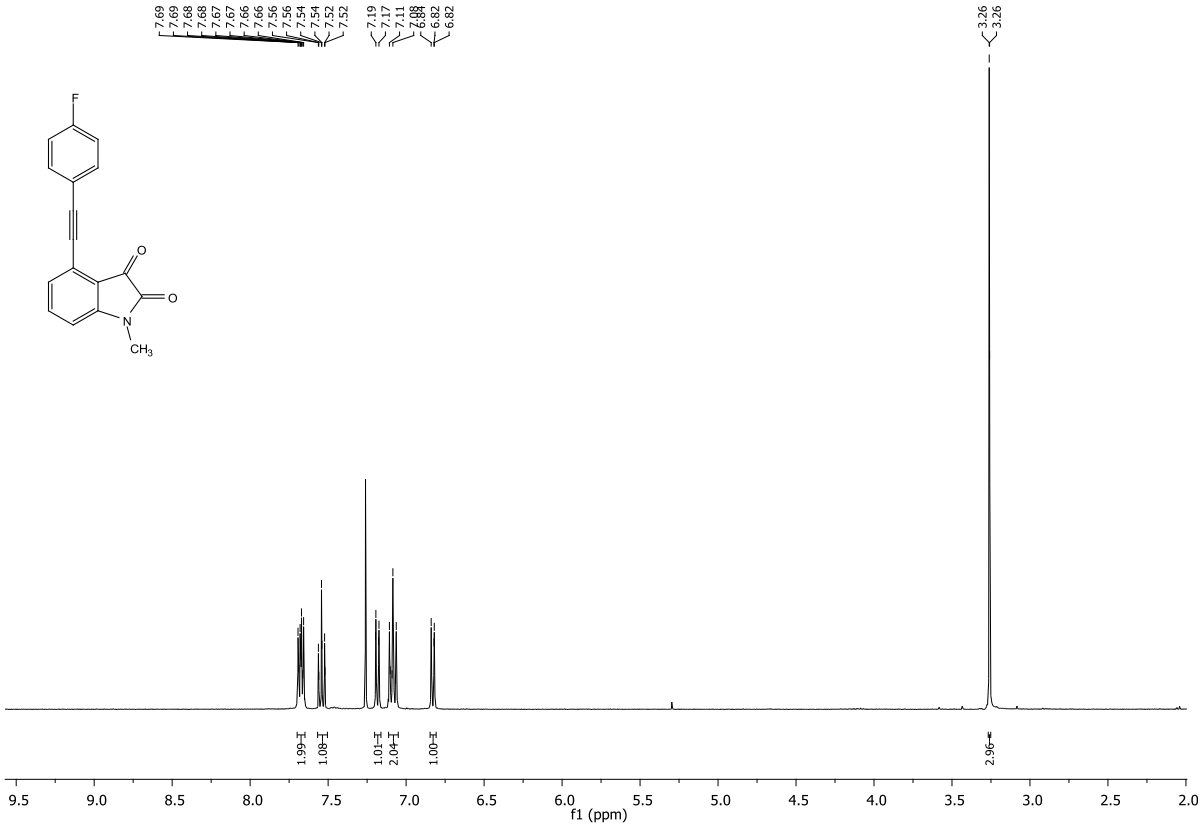


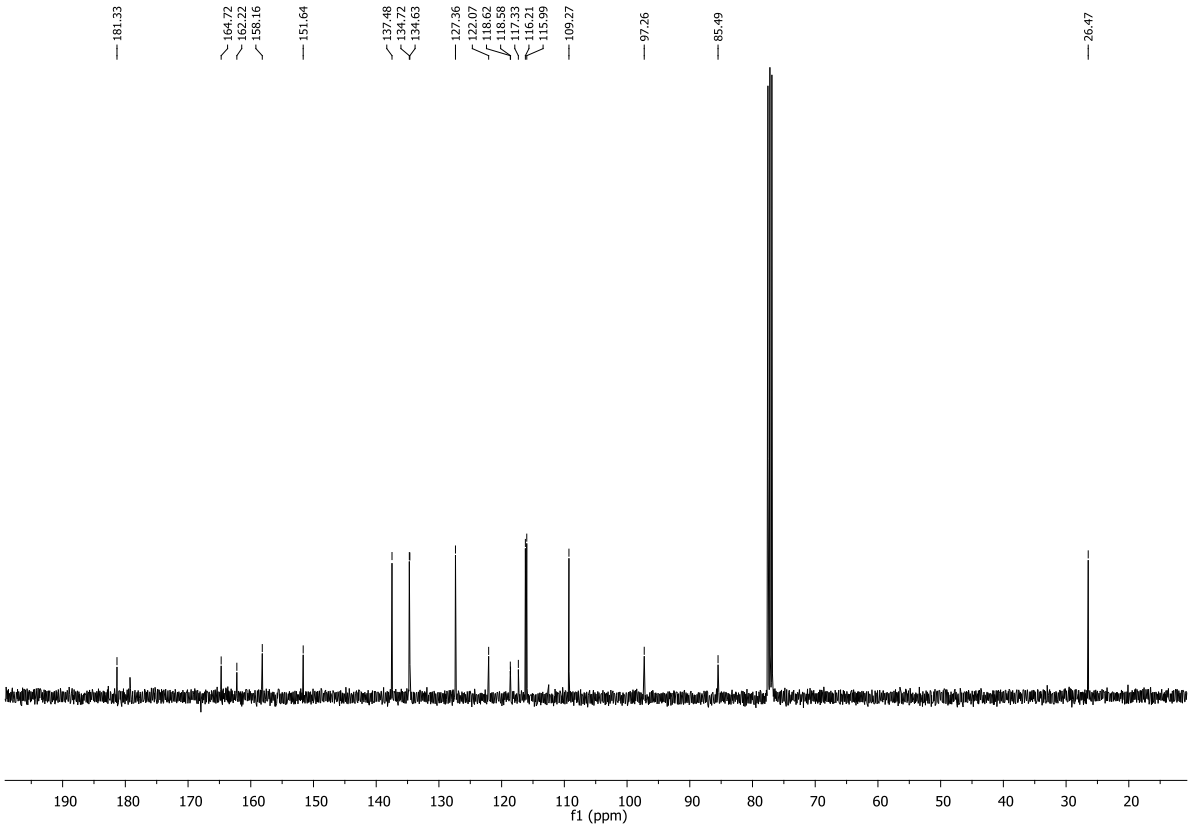
NMR of compound **5b** measured in $CDCl_3$ as solvent, 400MHz



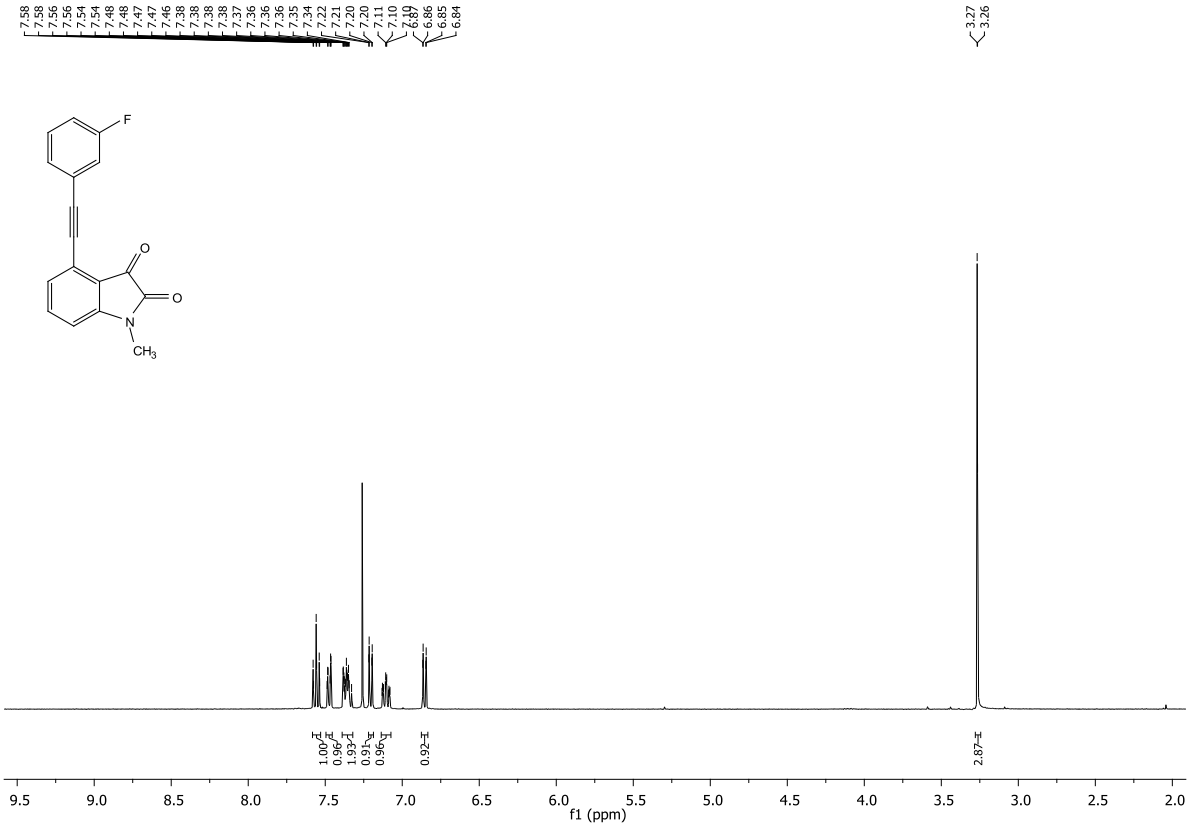


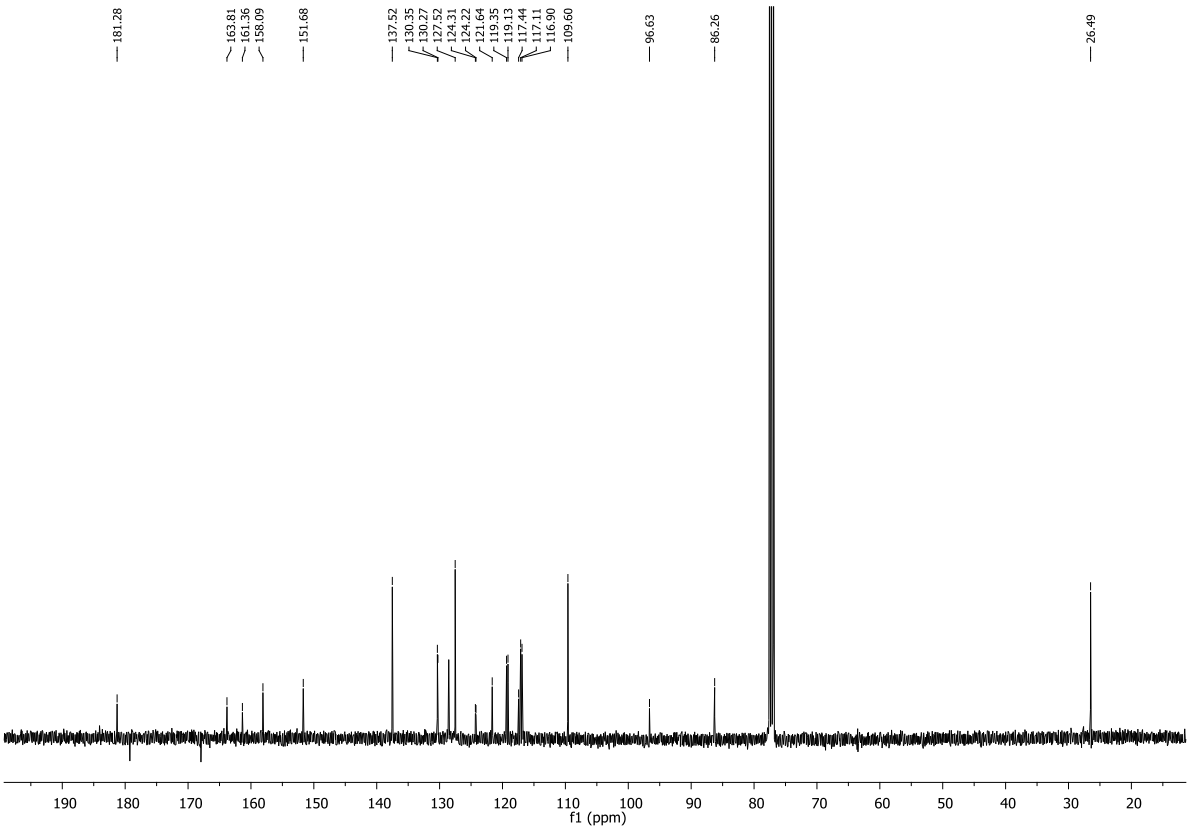
NMR of compound **5c** measured in $CDCl_3$ as solvent, 400MHz



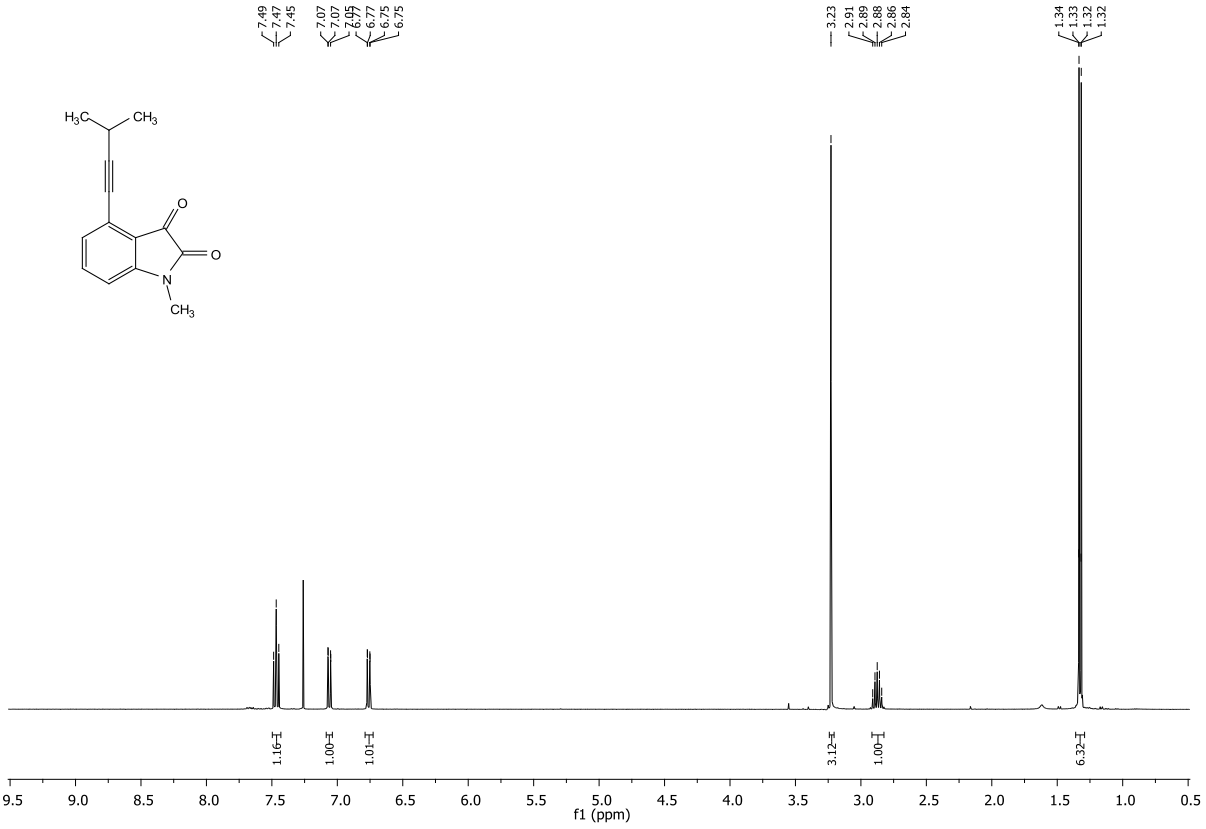


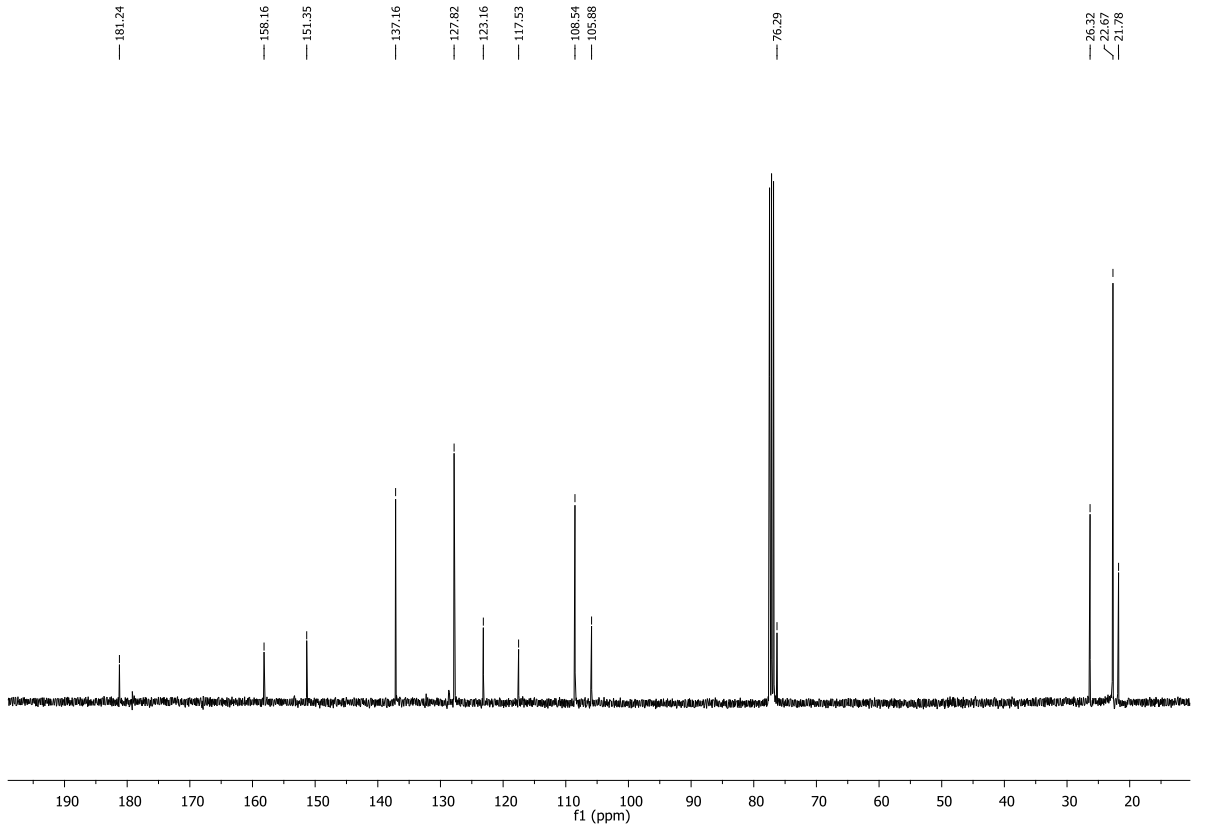
NMR of compound **5d** measured in $CDCl_3$ as solvent, 400MHz



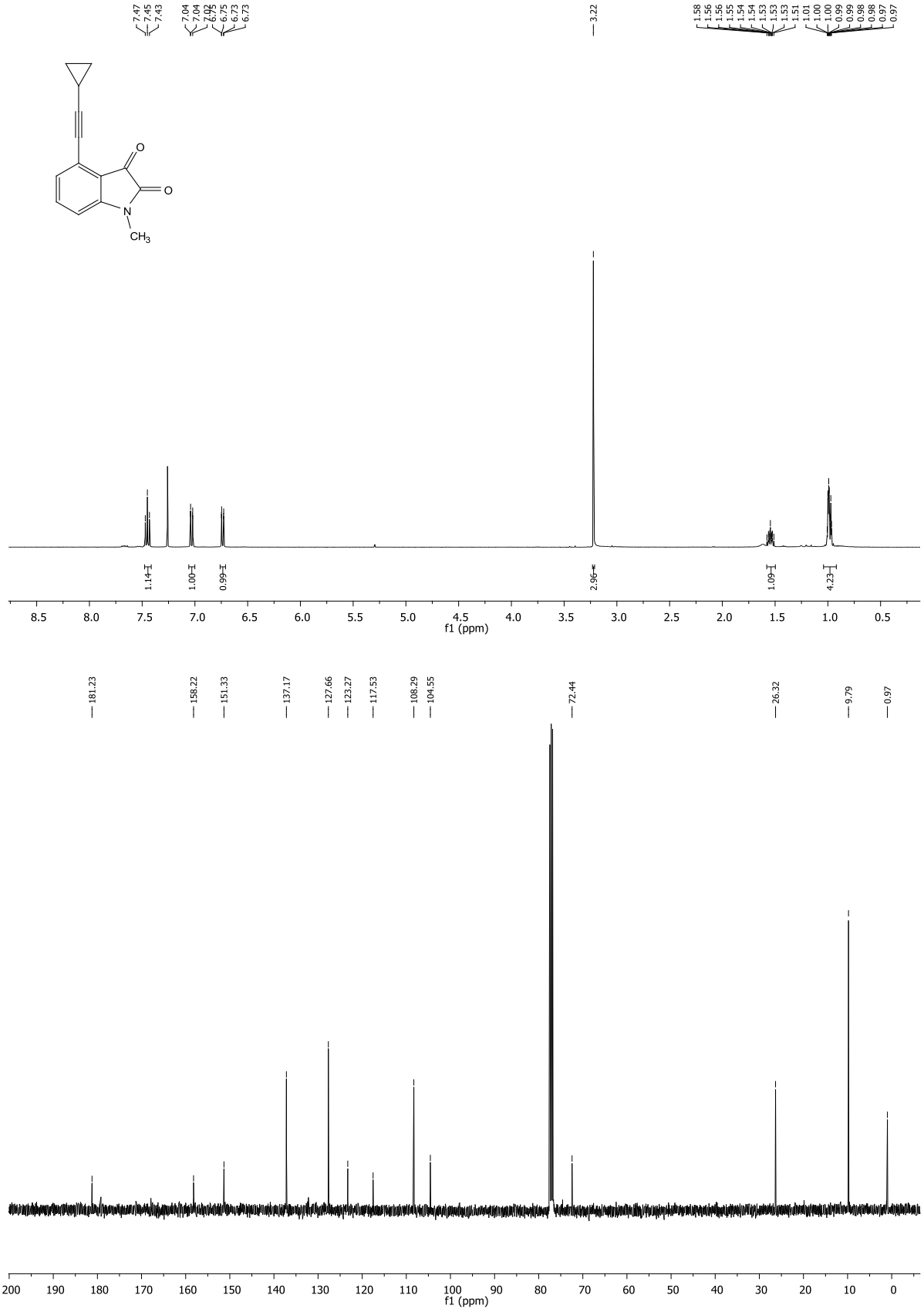


NMR of compound **5e** measured in $CDCl_3$ as solvent, 400MHz



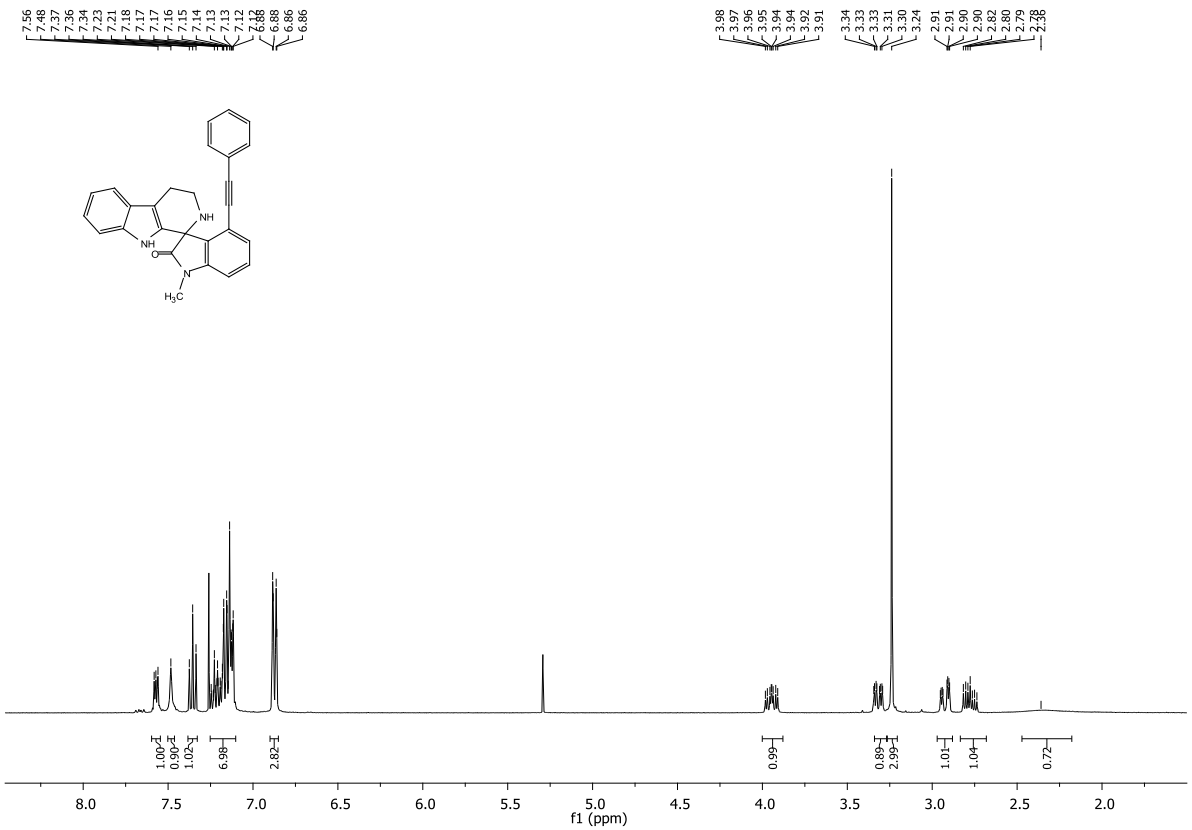


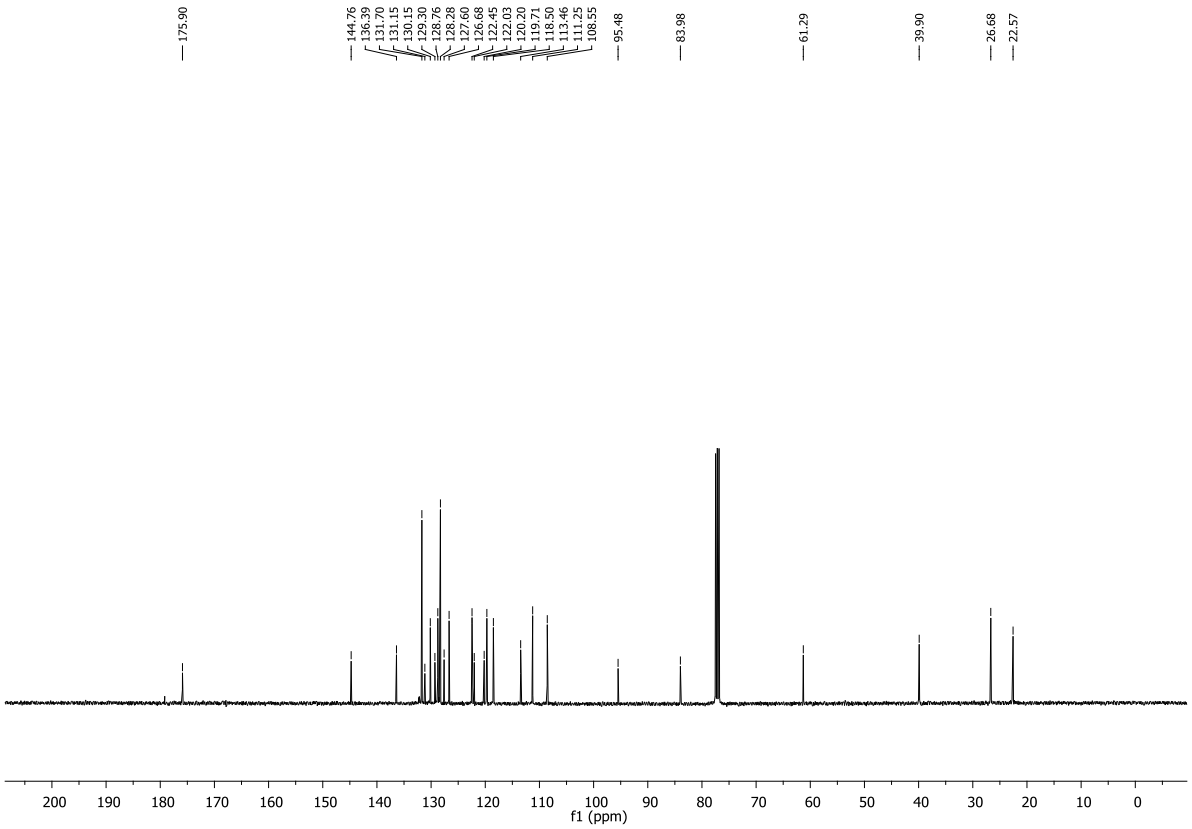
NMR of compound **5f** measured in $CDCl_3$ as solvent, 400MHz



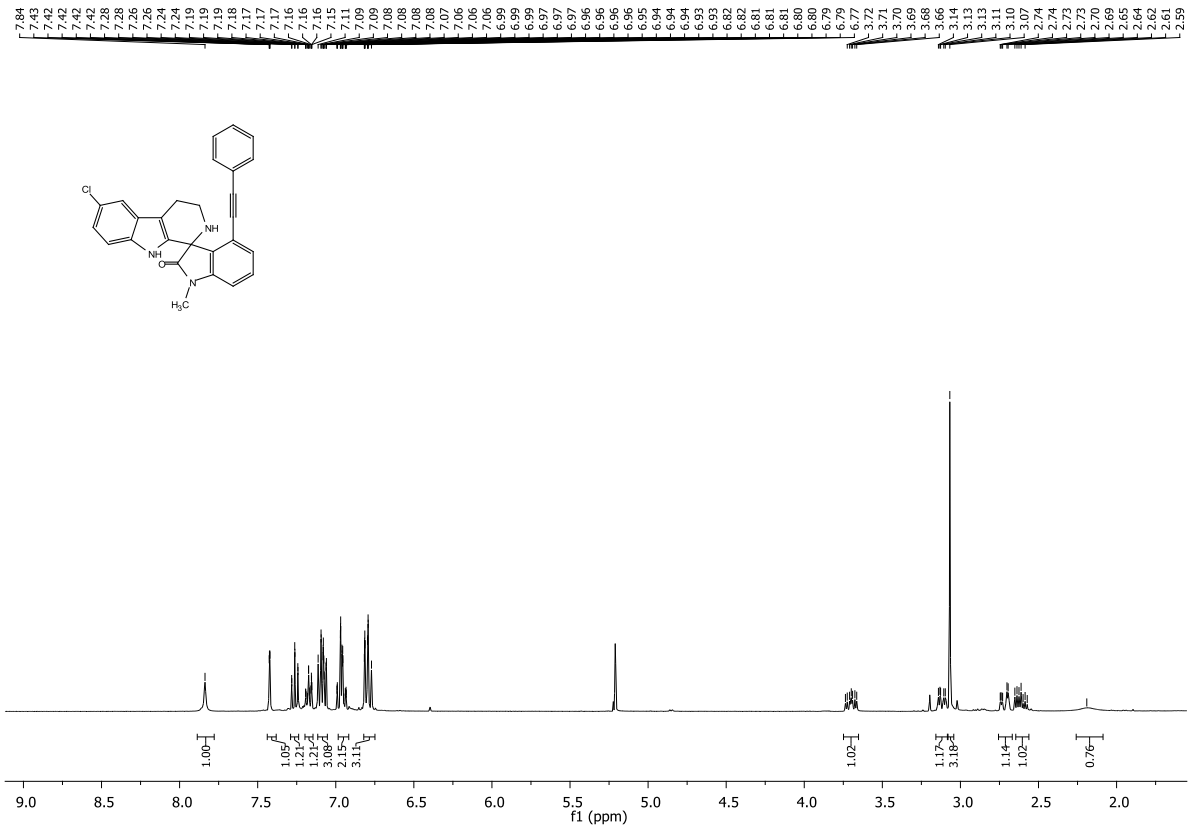
8. Represntative NMR Spectra of Compounds 6:

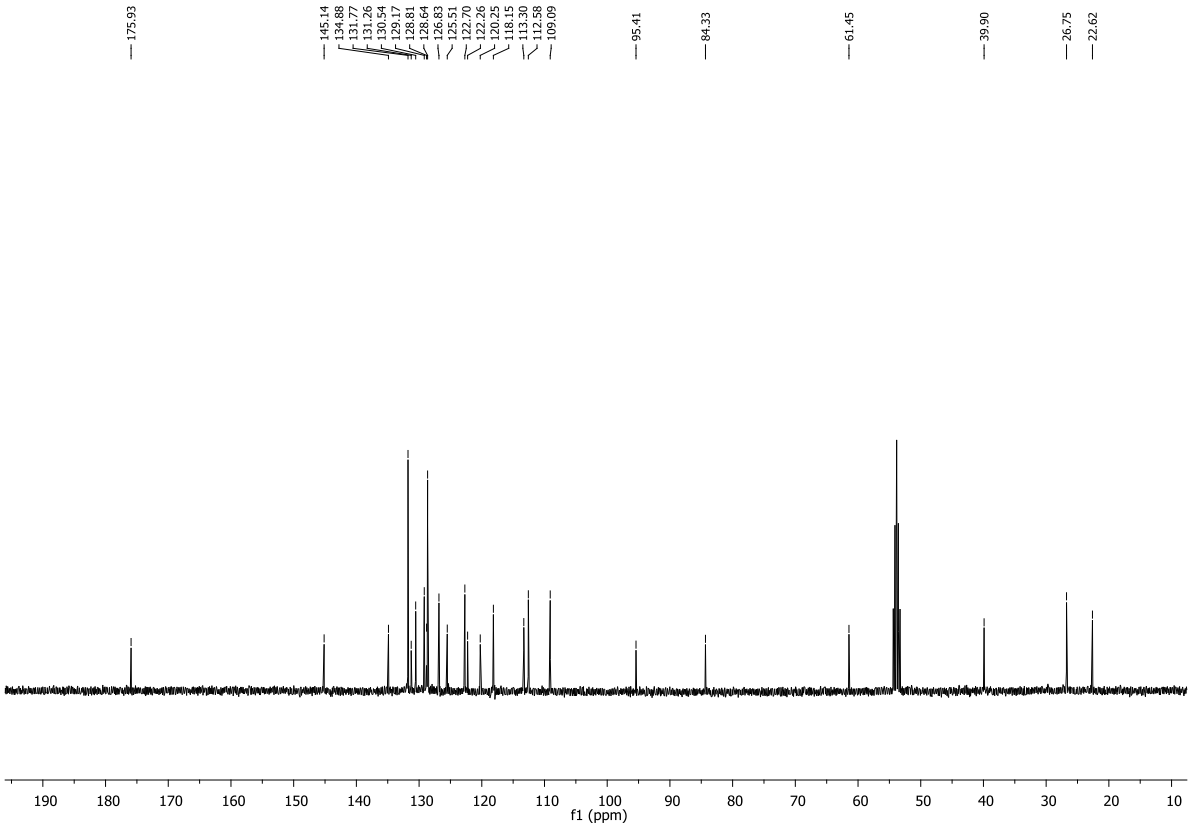
NMR of compound **6a** measured in $CDCl_3$ as solvent, 400MHz



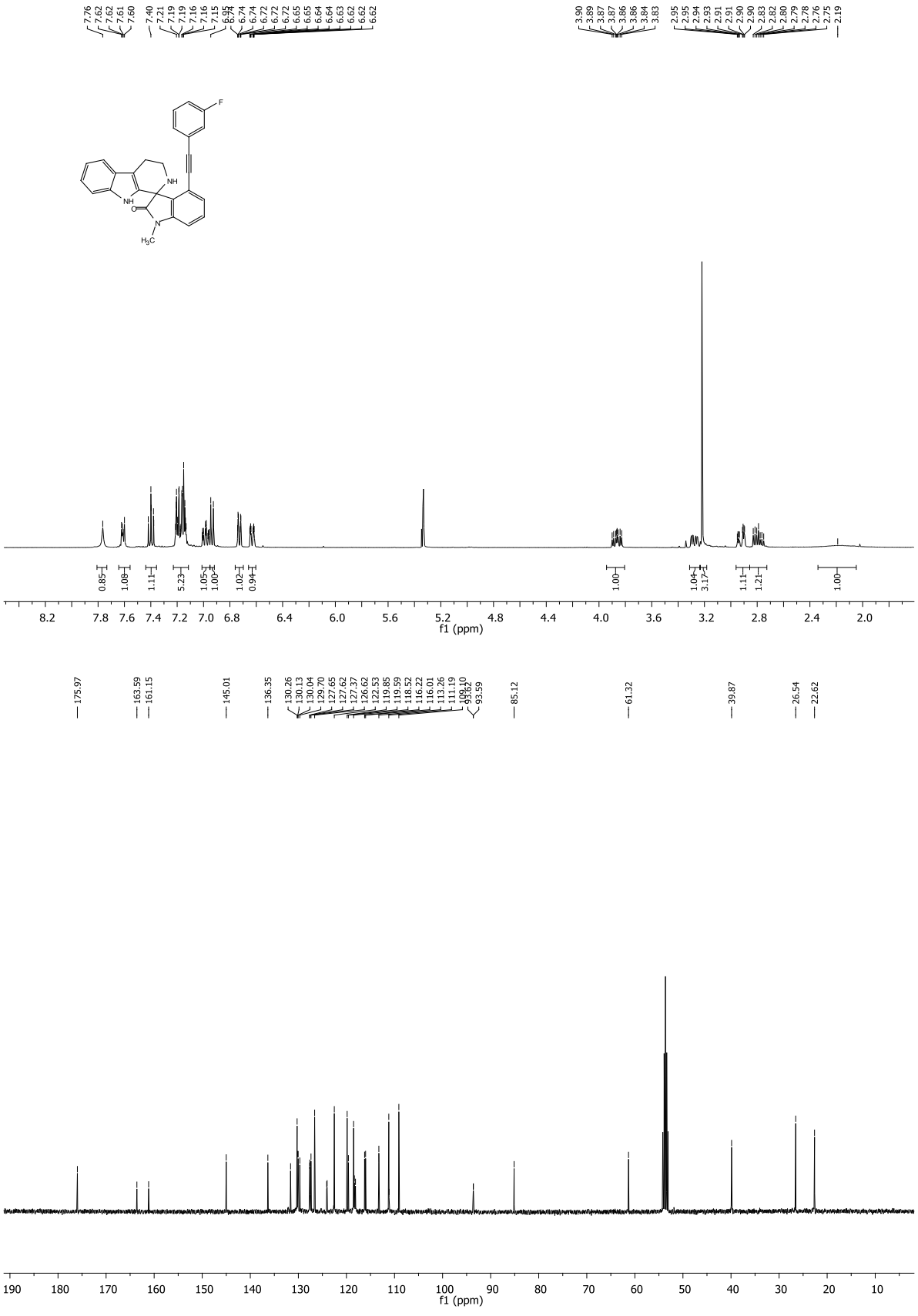


NMR of compound **6c** measured in DCM as solvent, 400MHz

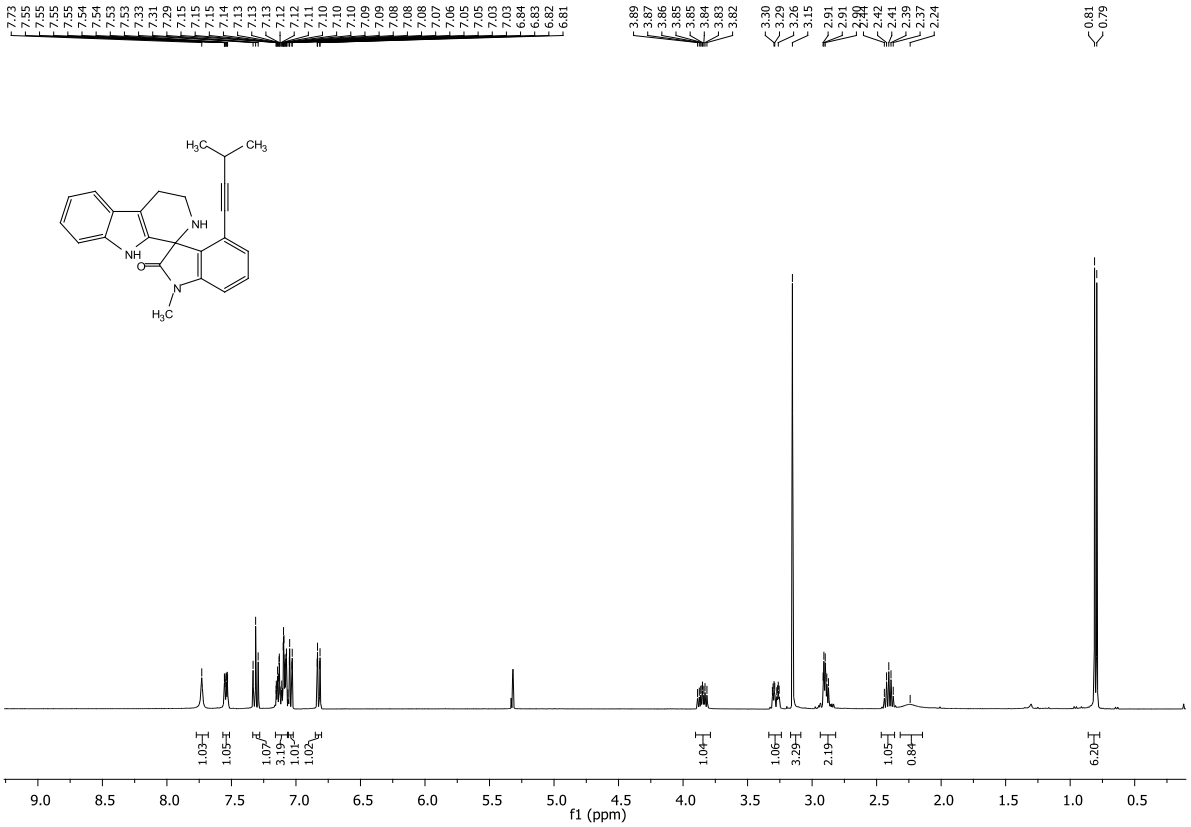


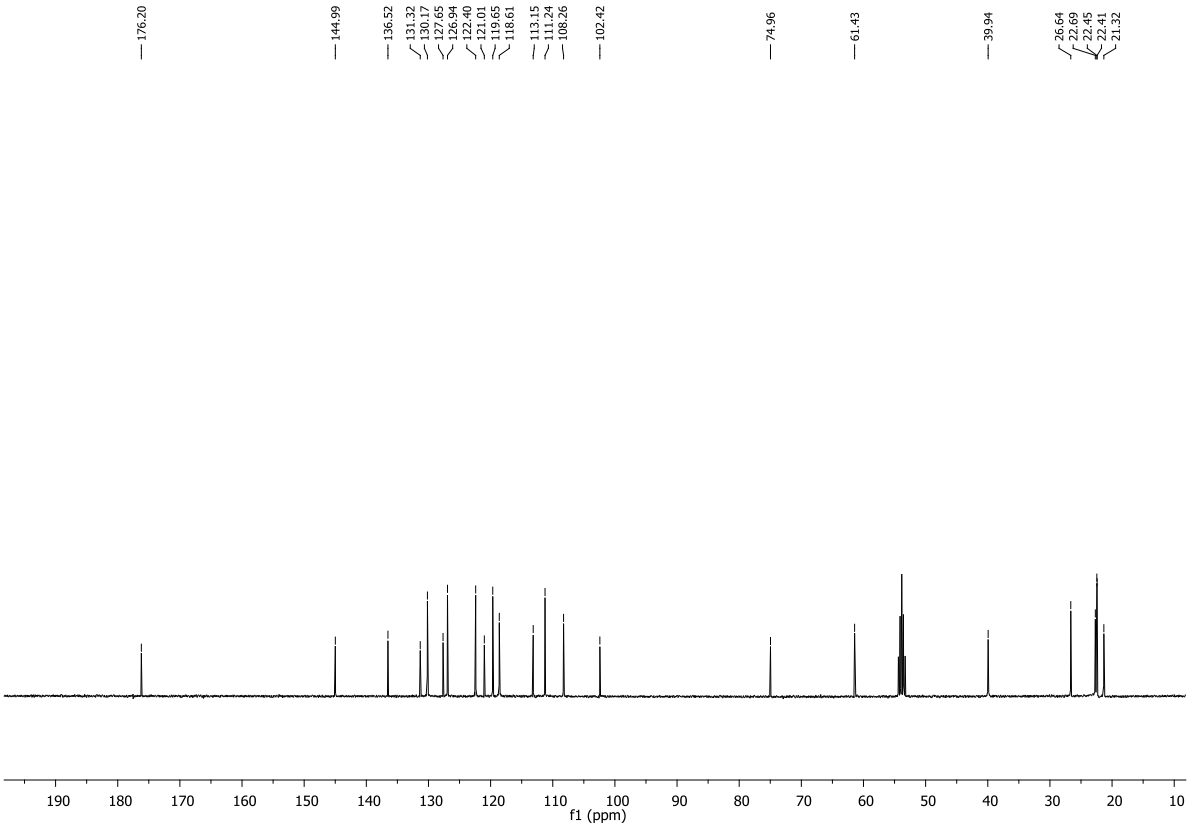


NMR of compound **6f** measured in DCM as solvent, 400MHz



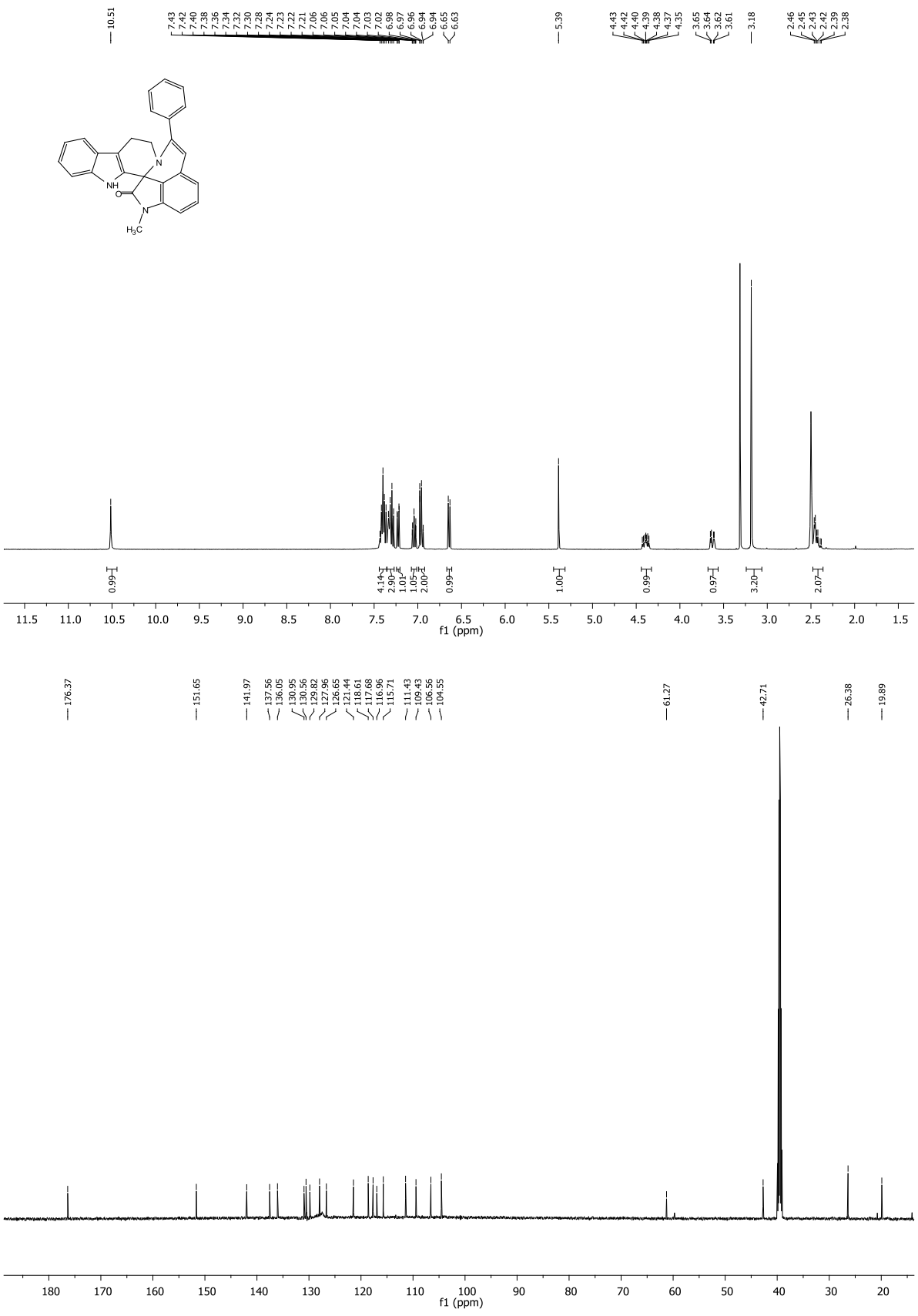
NMR of compound **6h** measured in DCM as solvent, 400MHz



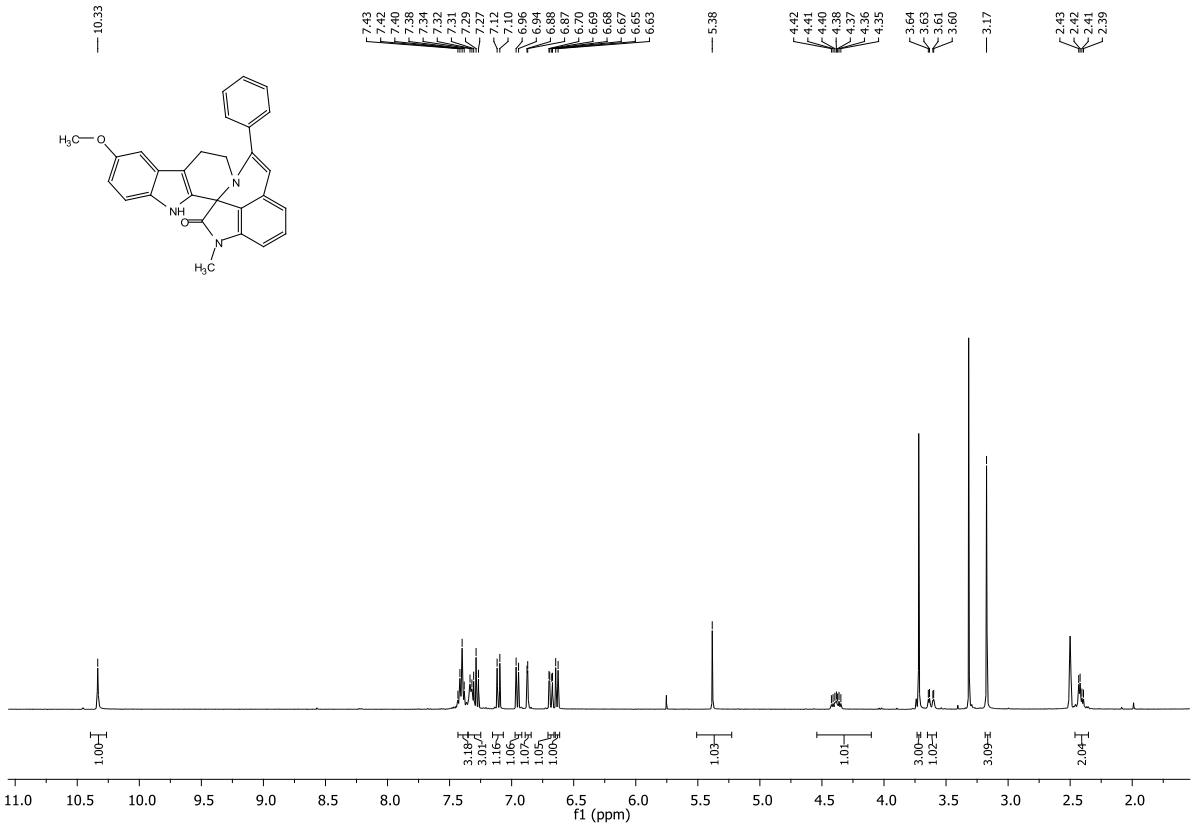


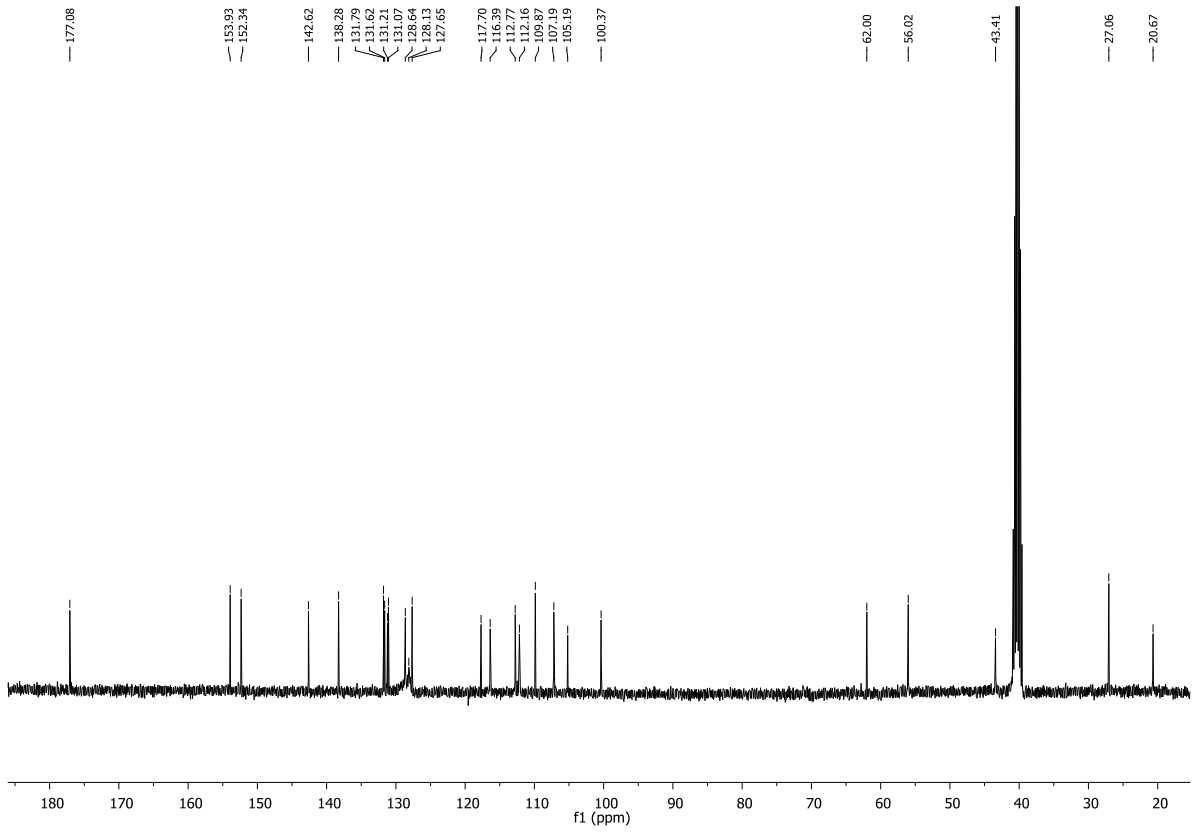
9. NMR spectra of Products 7:

NMR of compound **7a** measured in DMSO as solvent 400MHz (^{1}H) and 600MHz (^{13}C).

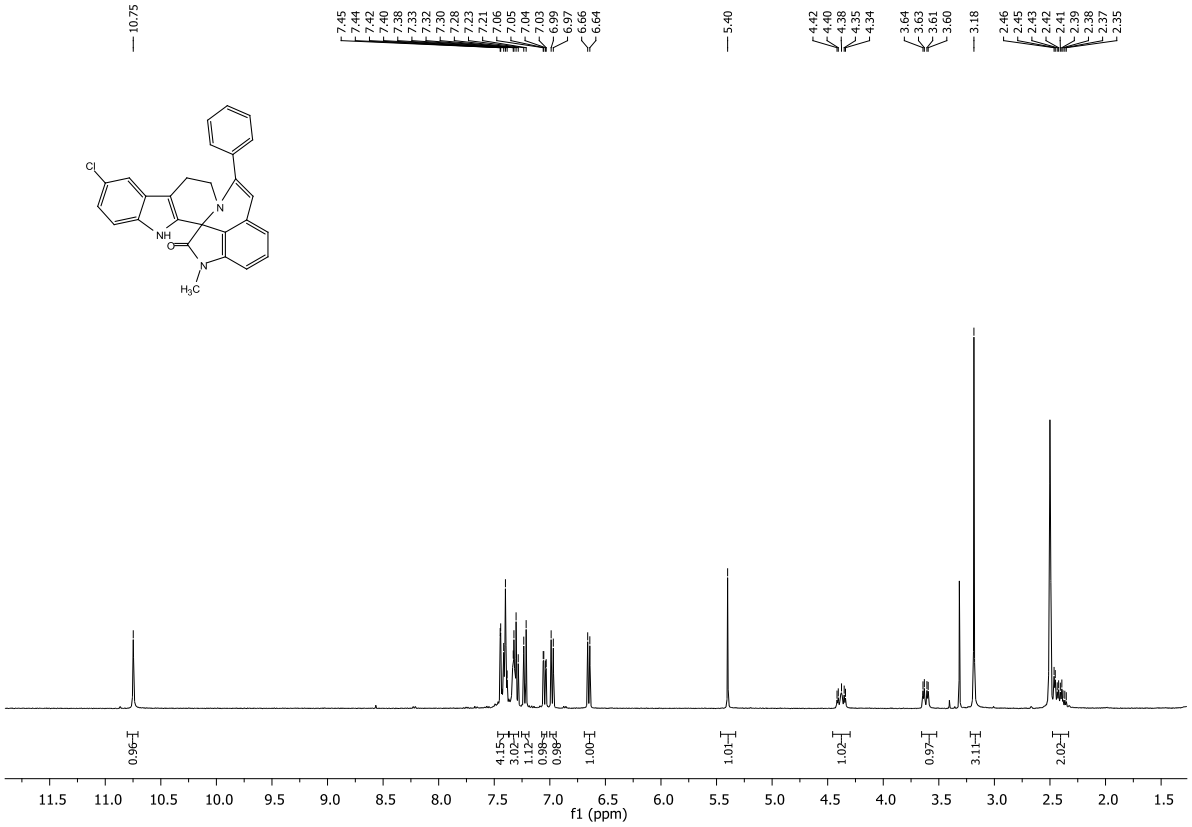


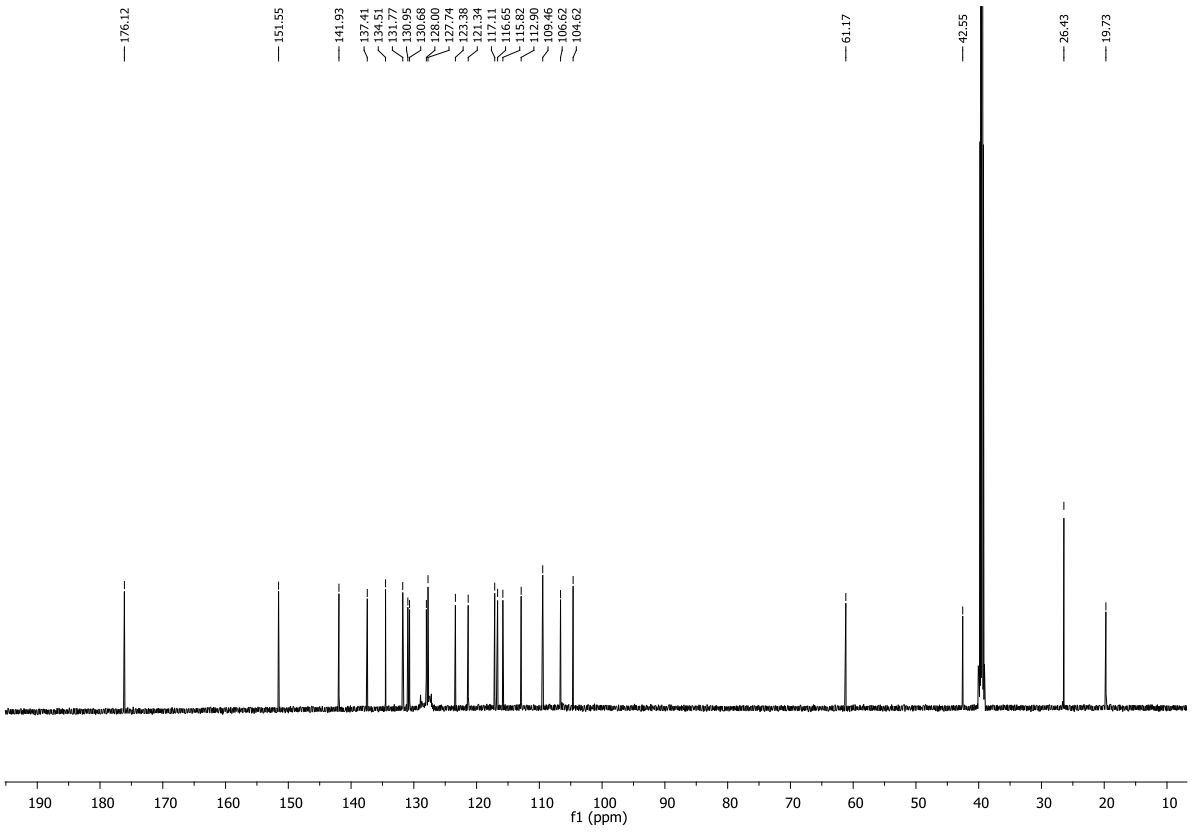
NMR of compound **7b** measured in DMSO as solvent, 400MHz



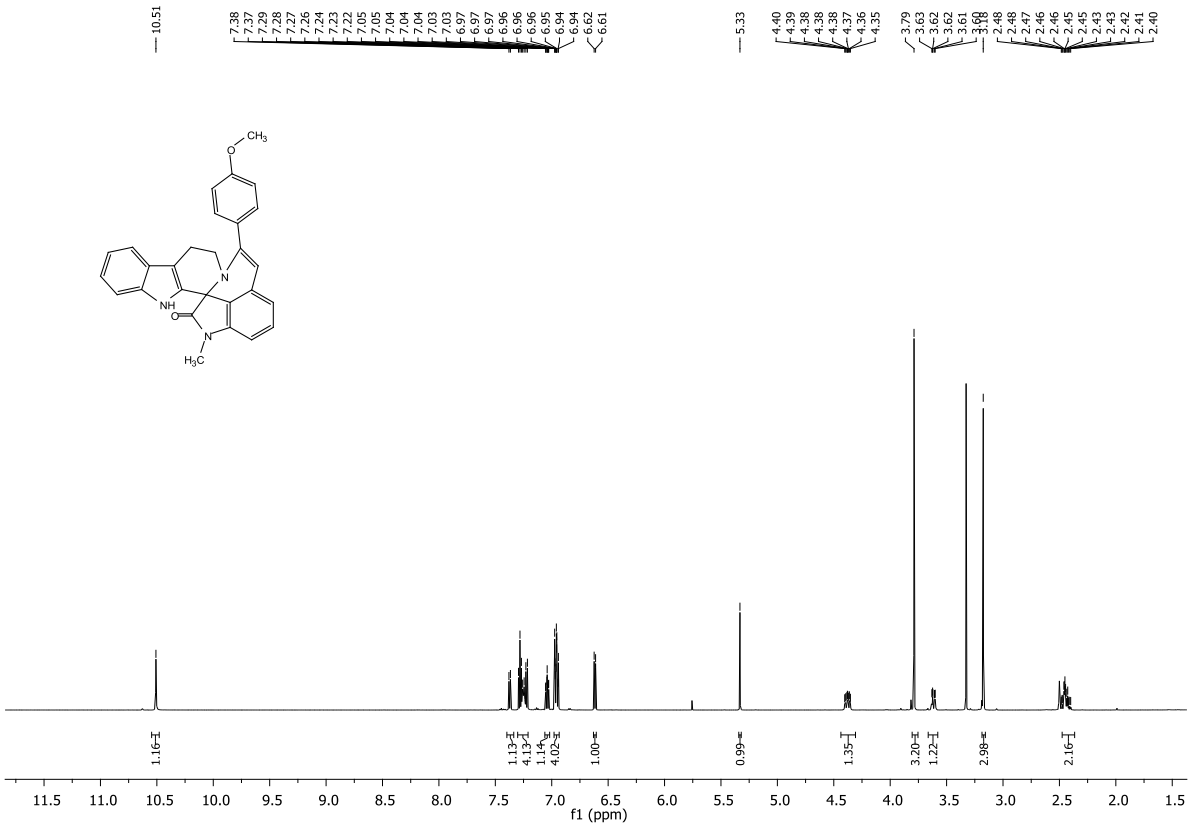


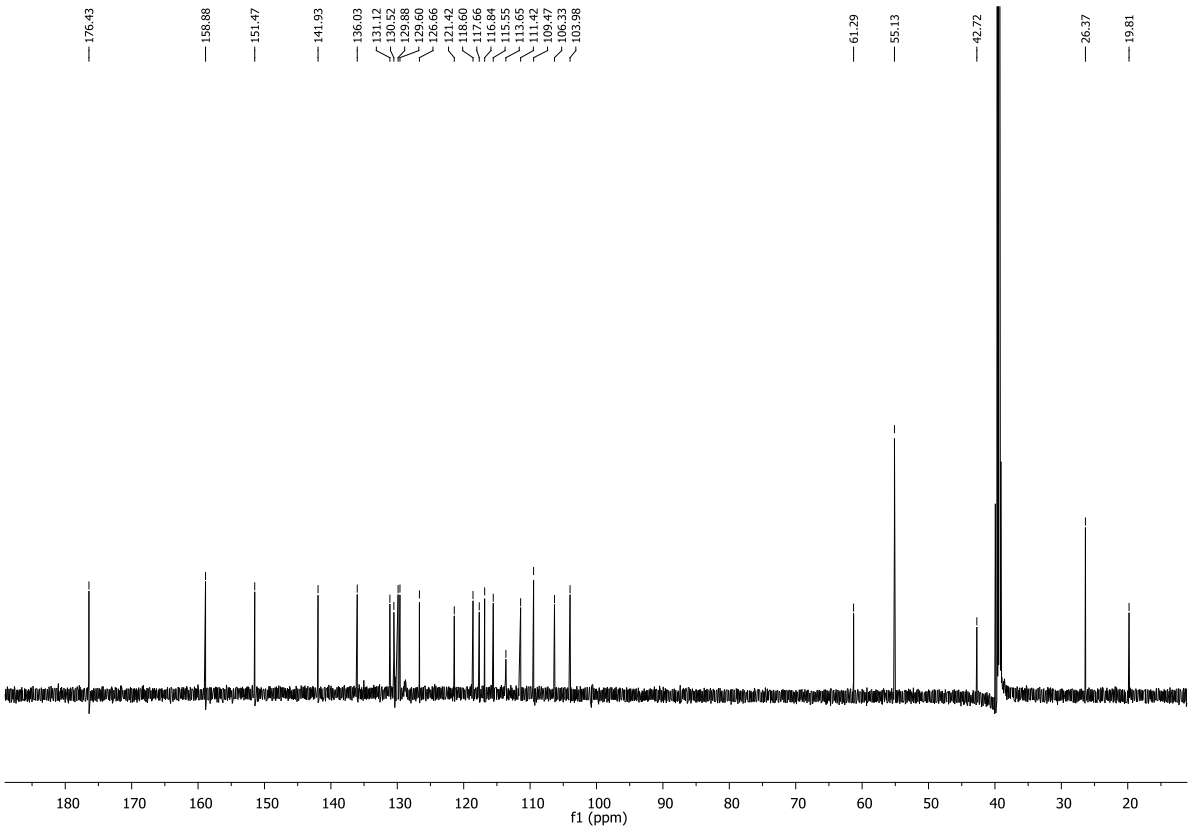
NMR of compound **7c** measured in DMSO as solvent, 400 MHz (^{1}H) and 600 MHz (^{13}C).



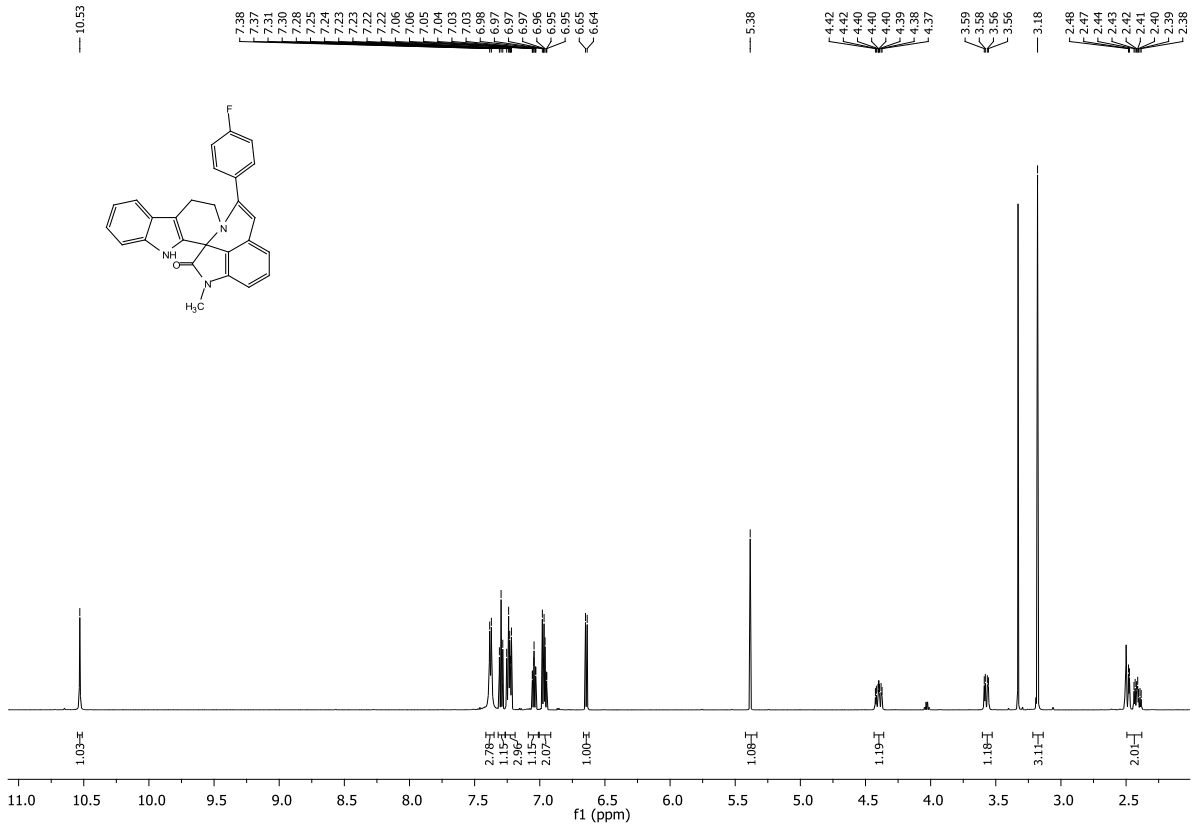


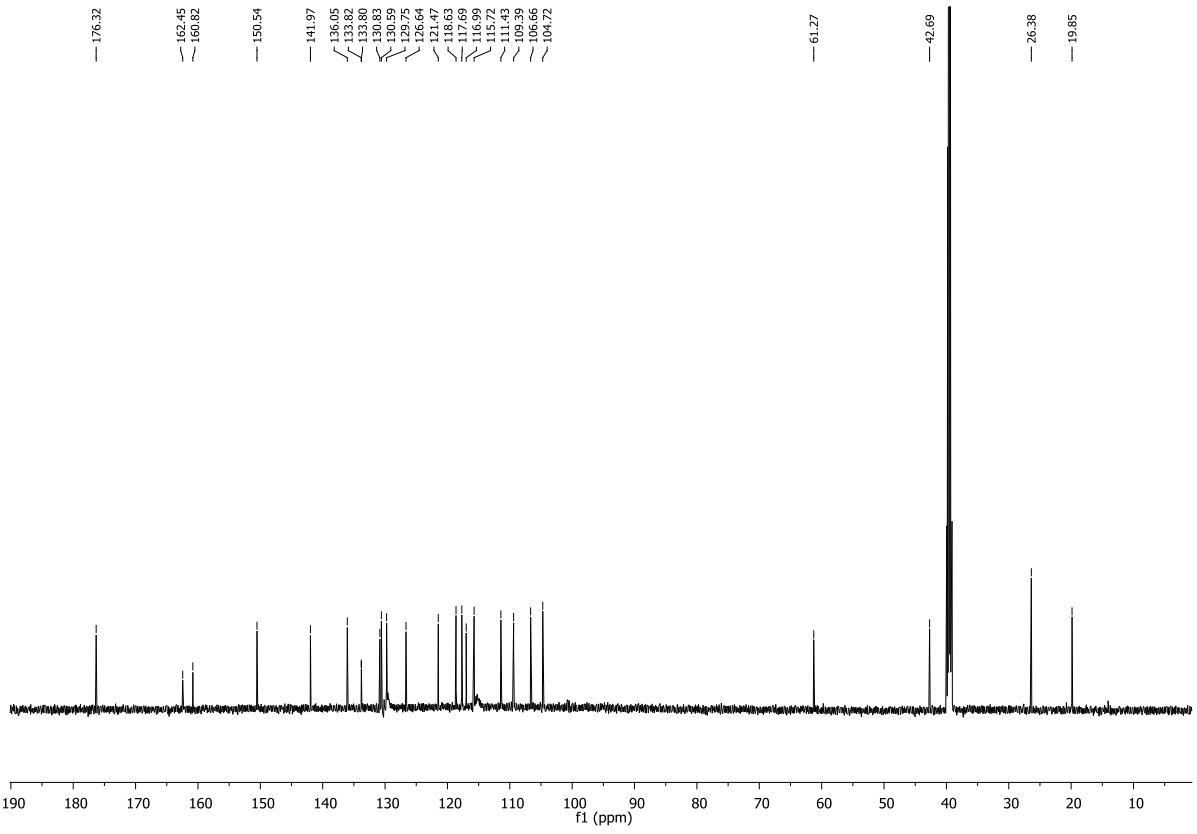
NMR of compound **7d** measured in DMSO as solvent, 600MHz



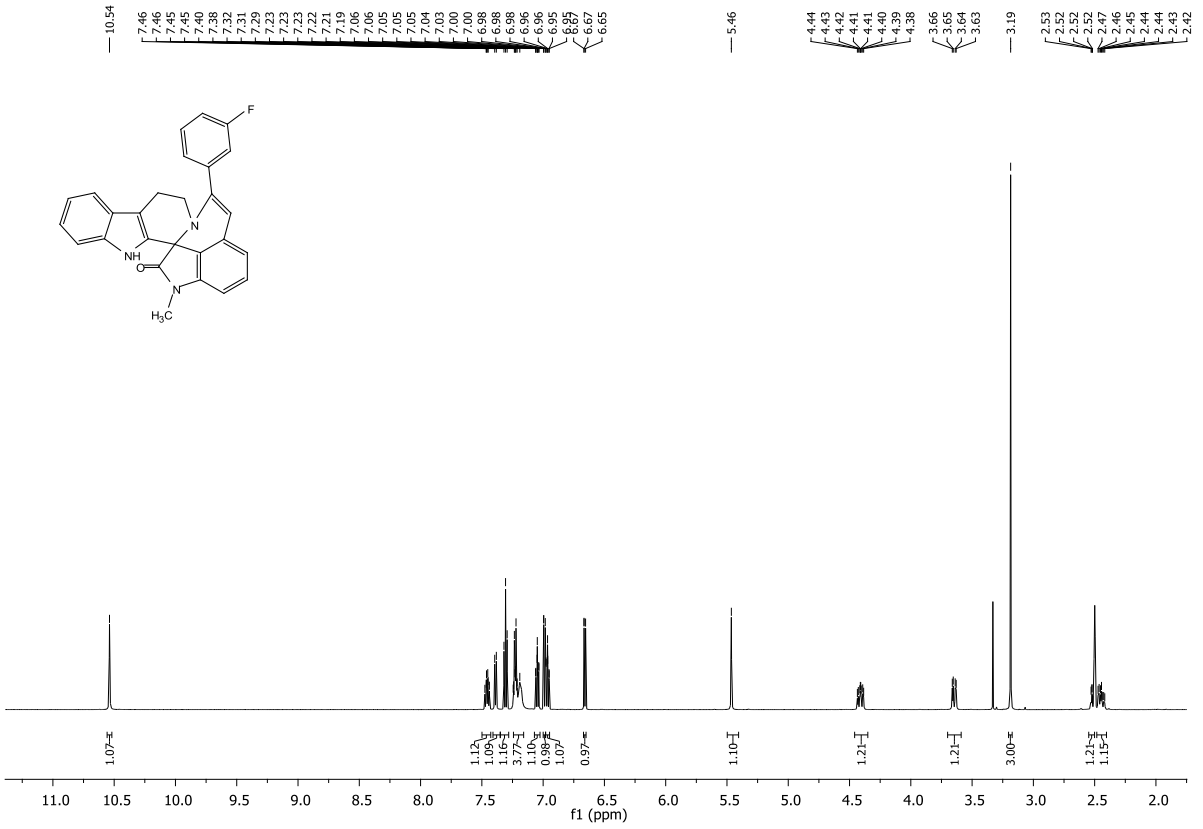


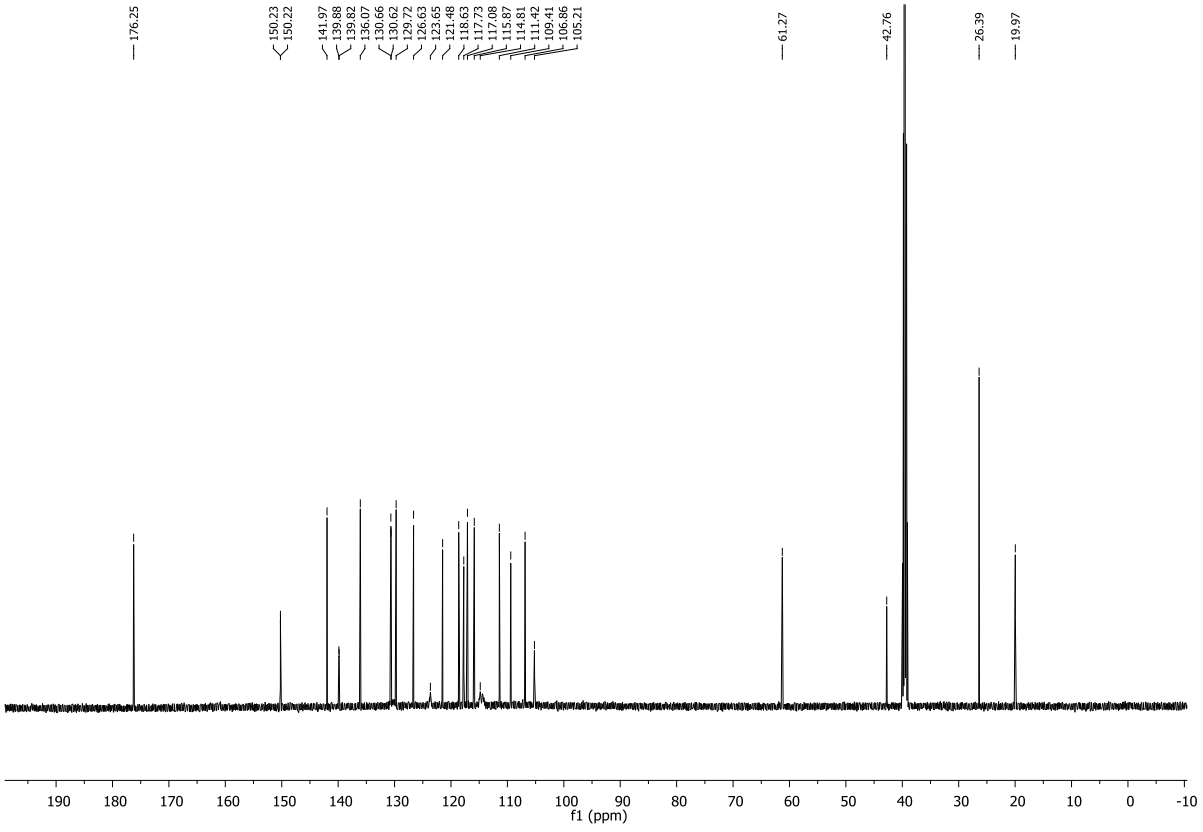
NMR of compound **7e** measured in DMSO as solvent, 600MHz



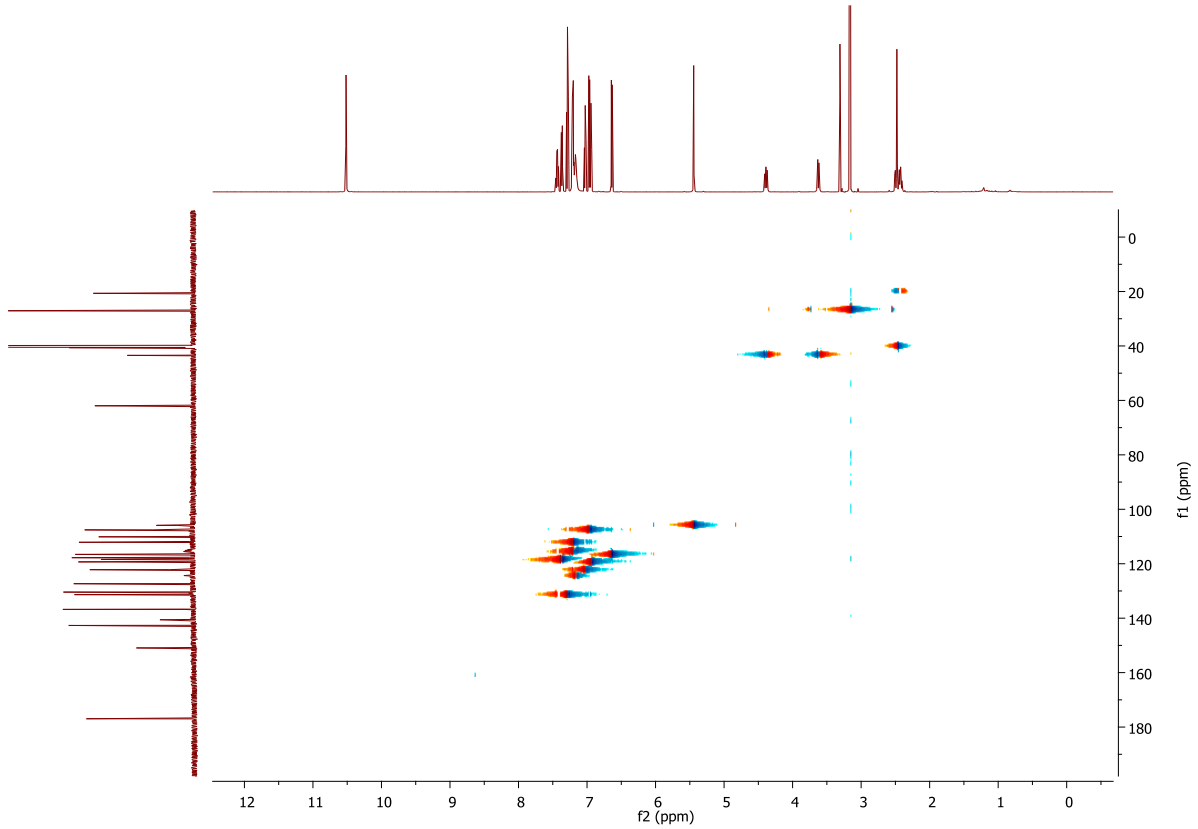


NMR of compound **7f** measured in DMSO as solvent, 600MHz

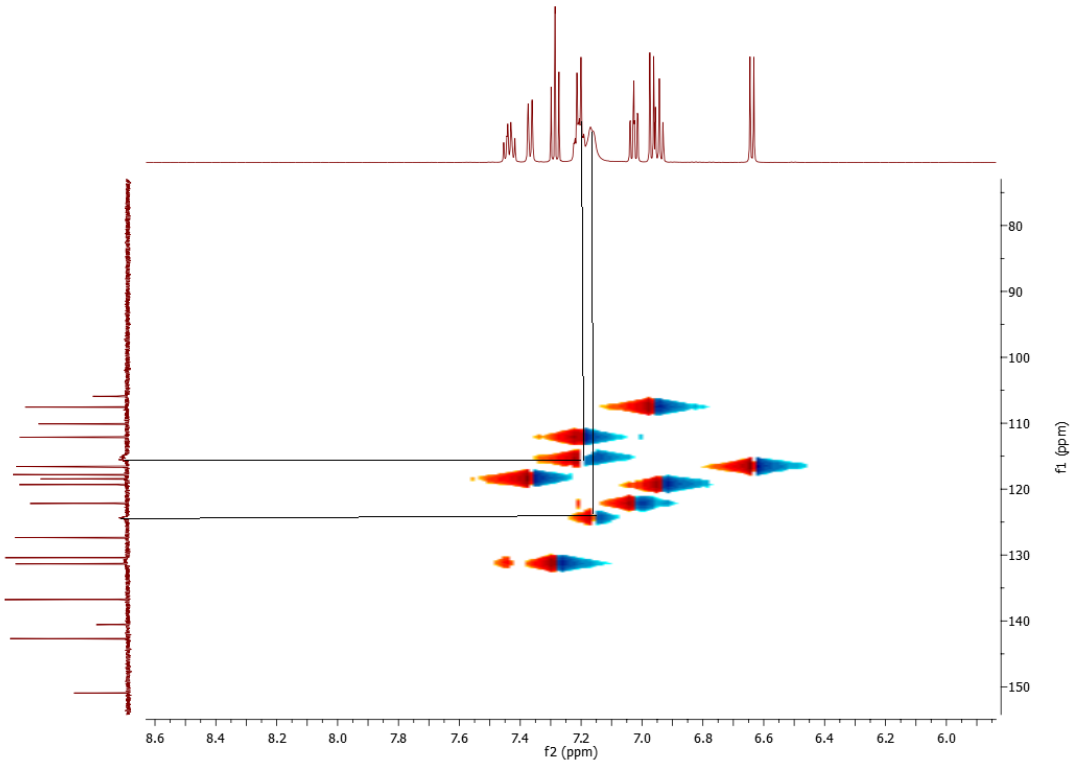




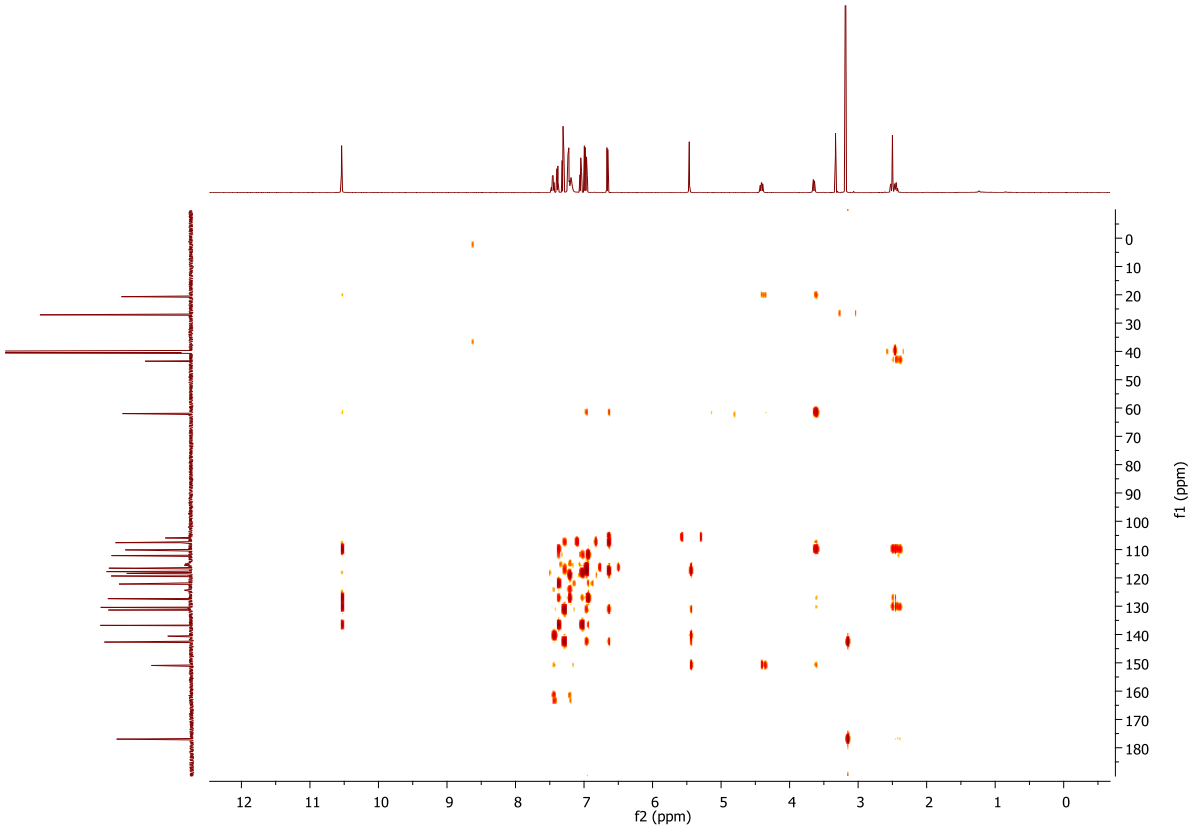
2D NMRs of , gHSQC



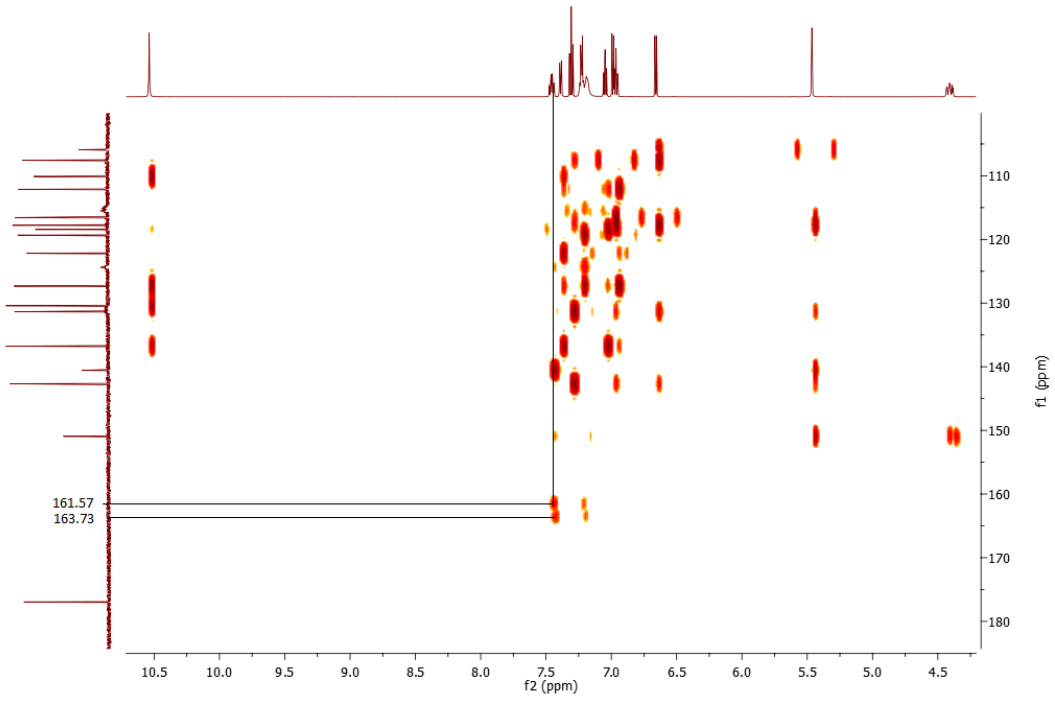
Zoomed version of the gHSQC spectra, shows that some carbons are coming as humps in the spectra in the aromatic region.



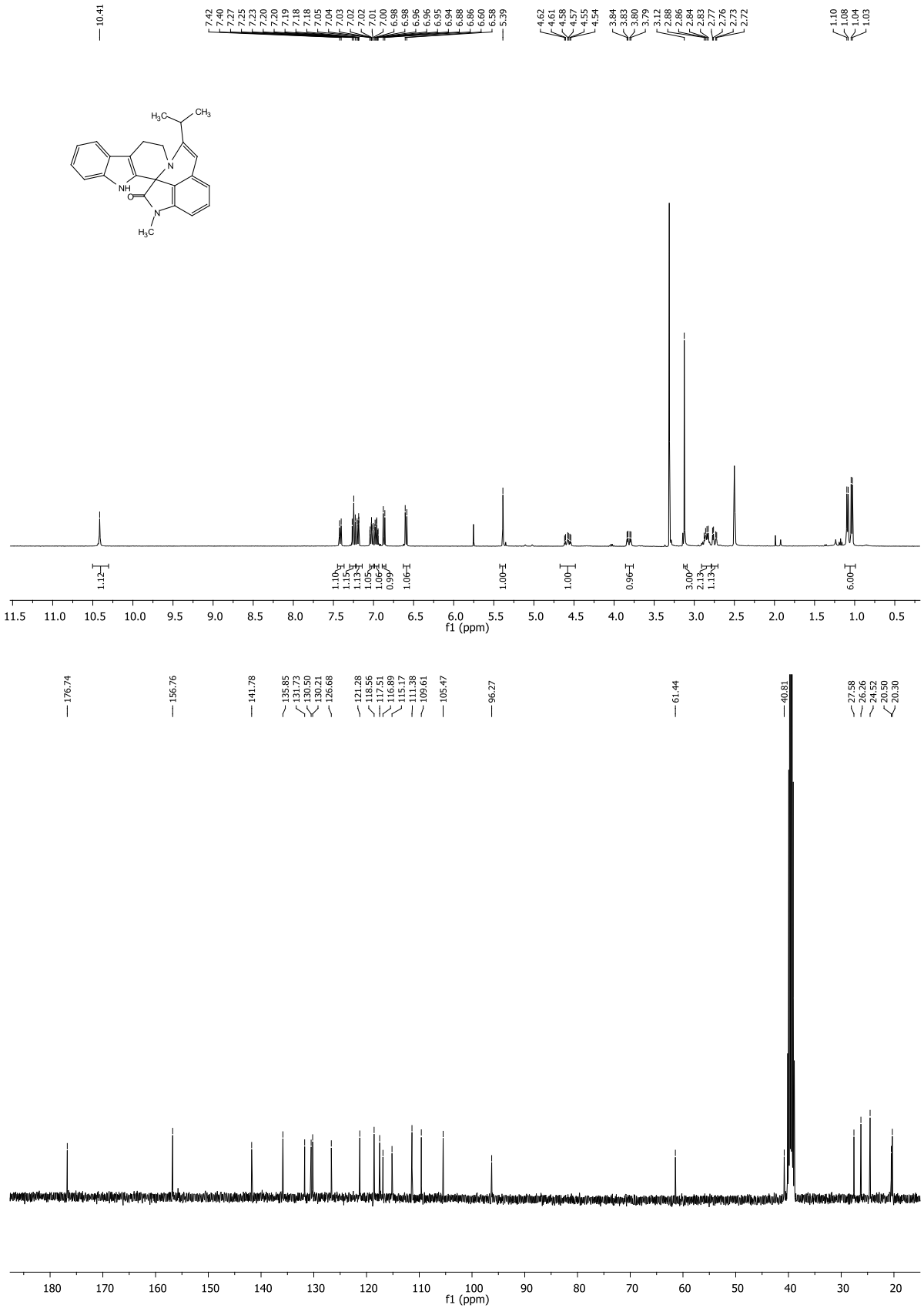
gHMBC



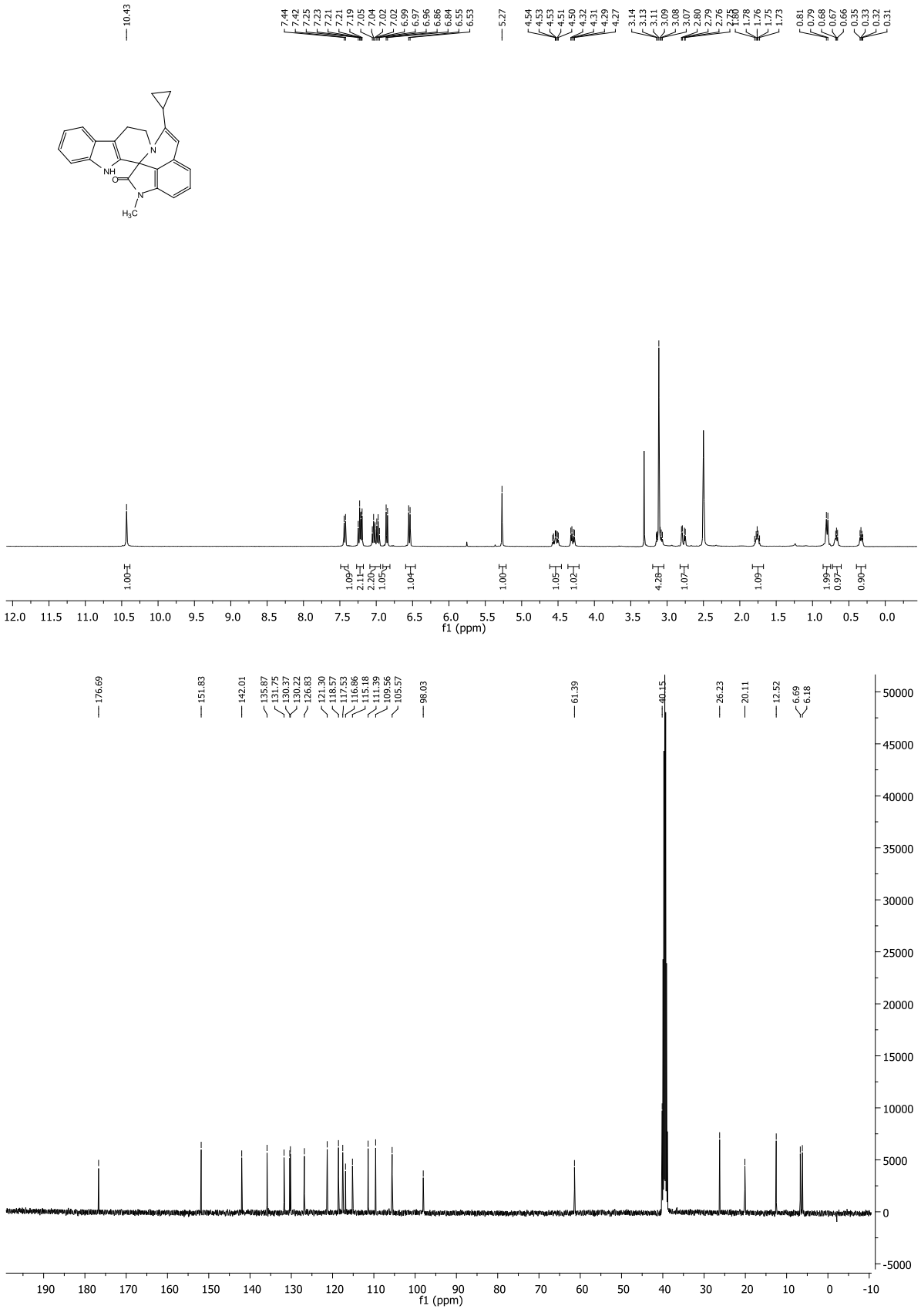
Zoomed version of the gHMBC spectra, shows the presence of the doublet because of C-F carbon



NMR of compound **7g** measured in DMSO as solvent, 400MHz

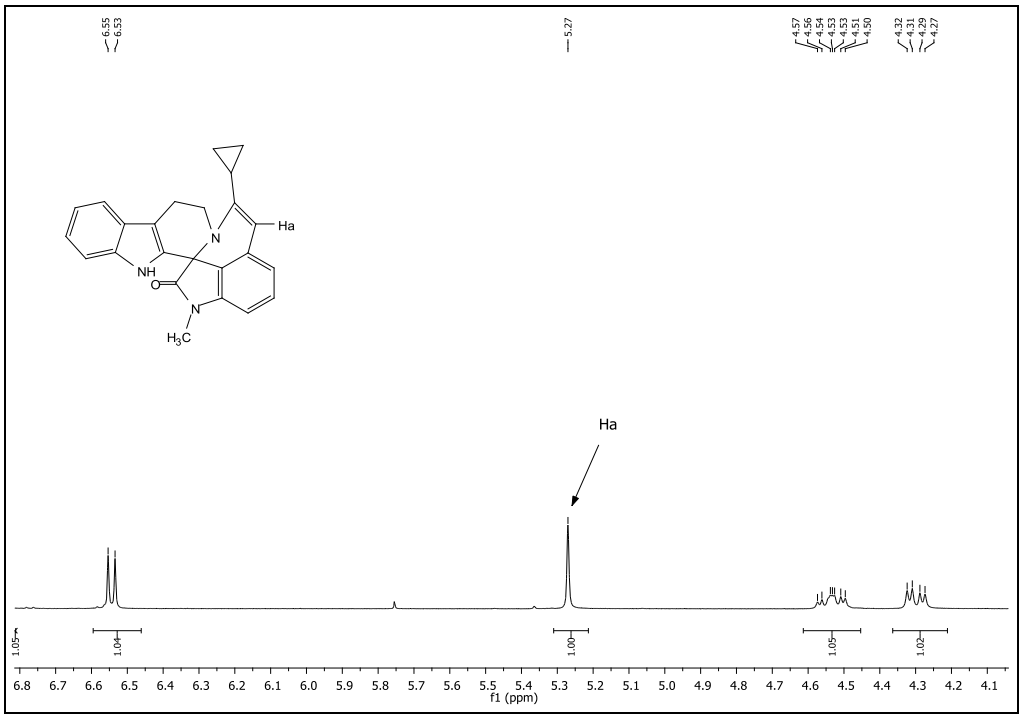


NMR of compound **7h** measured in DMSO as solvent, 400MHz

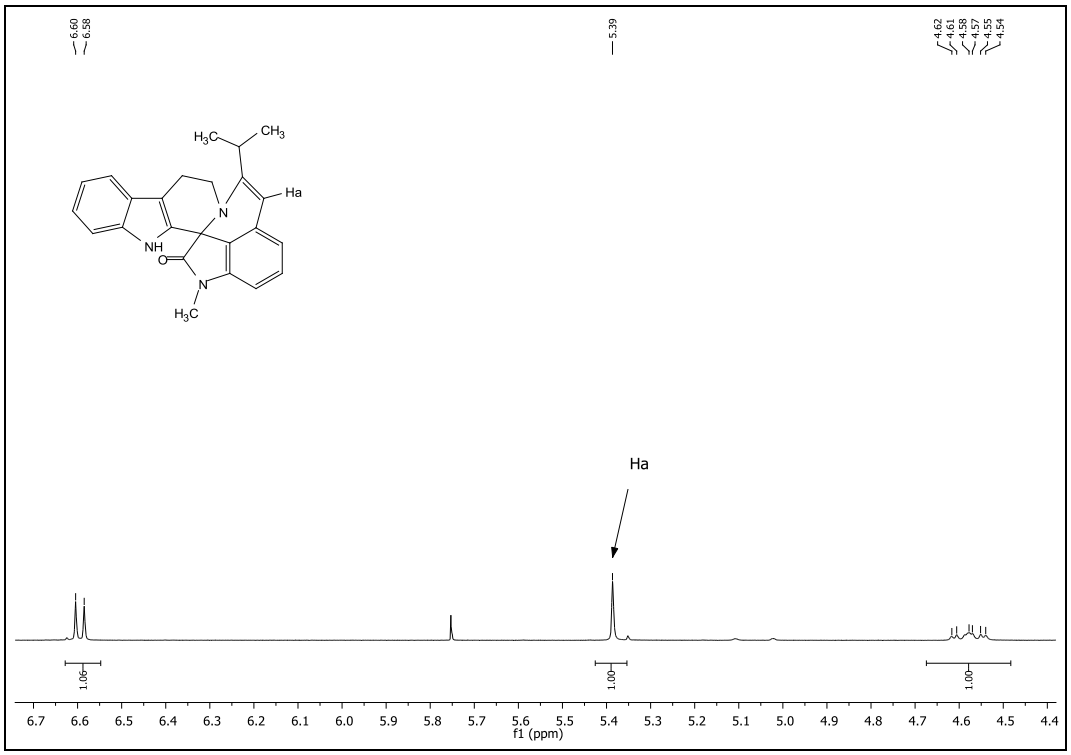


Zoomed version of the NMR spectra of **7g** and **7h** showing the enamine proton as a singlet:-

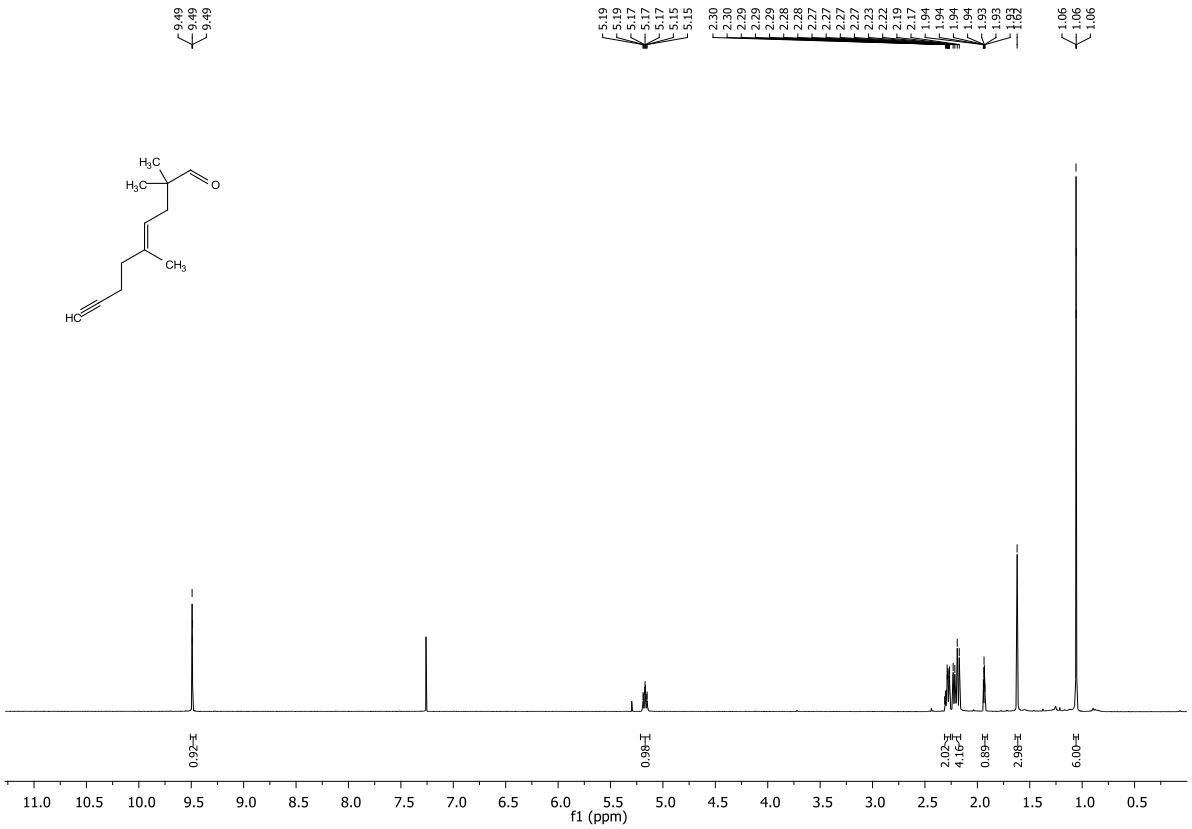
a) Zoomed spectra of 7h

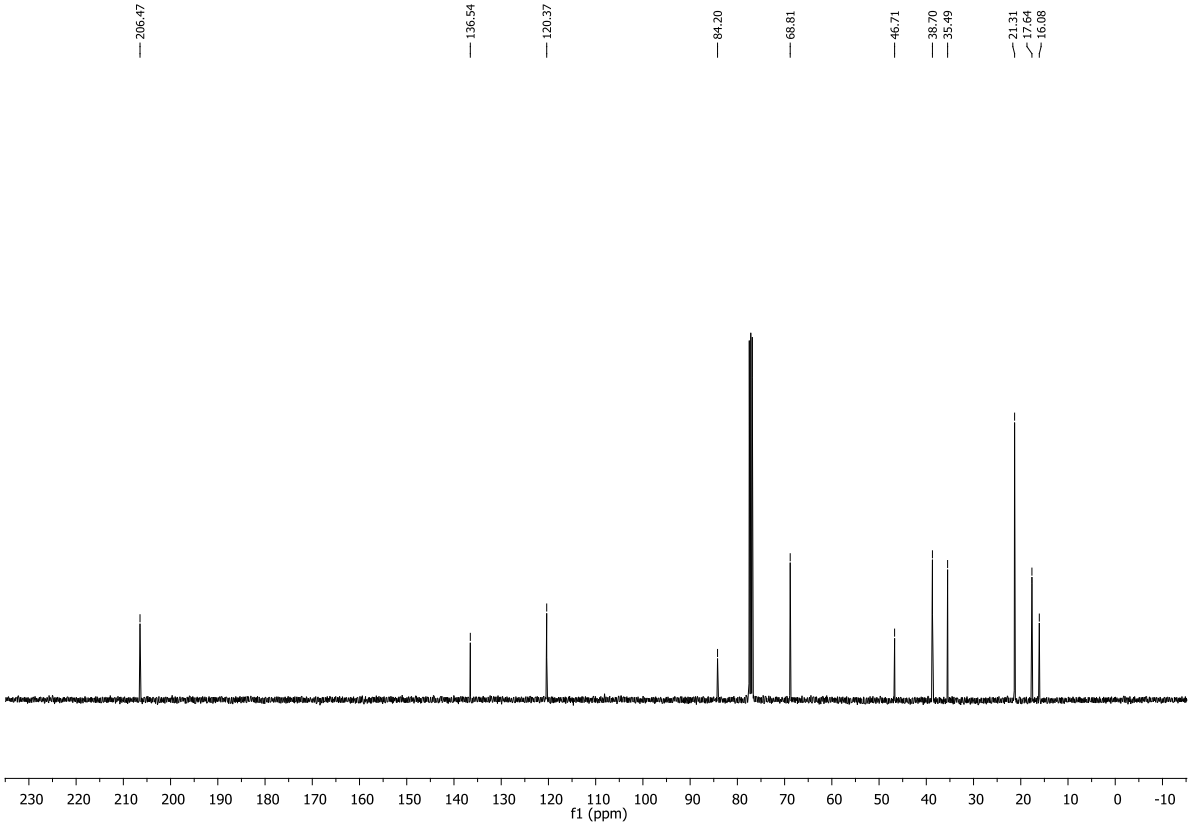


b) Zoomed spectra of 7g



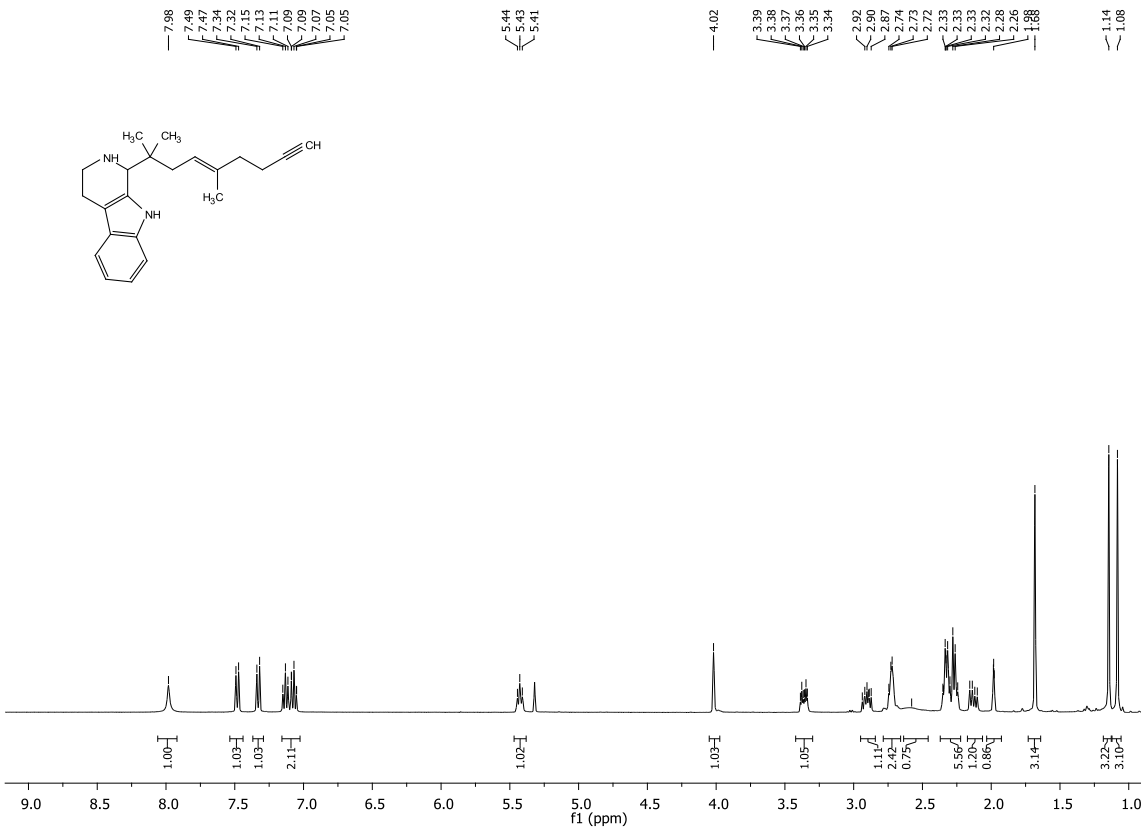
NMR of compound **9** measured in $CDCl_3$ as solvent, 400MHz

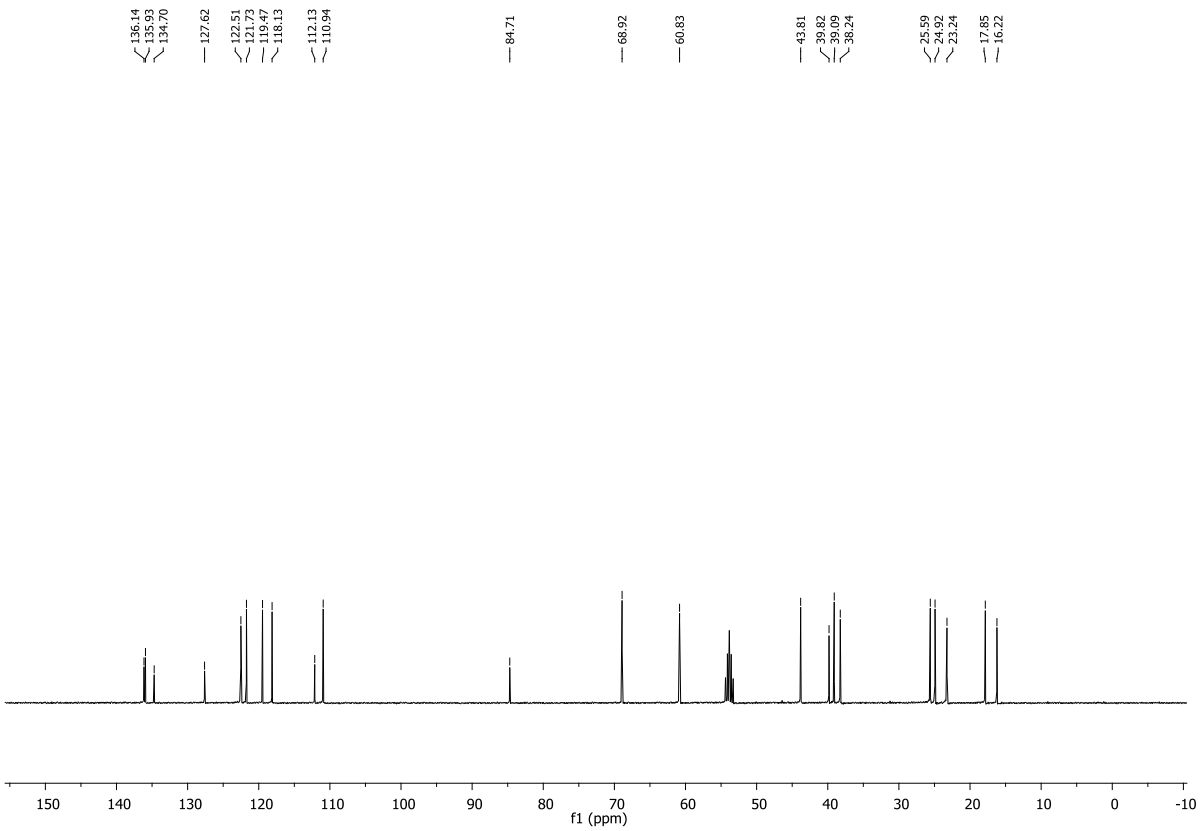




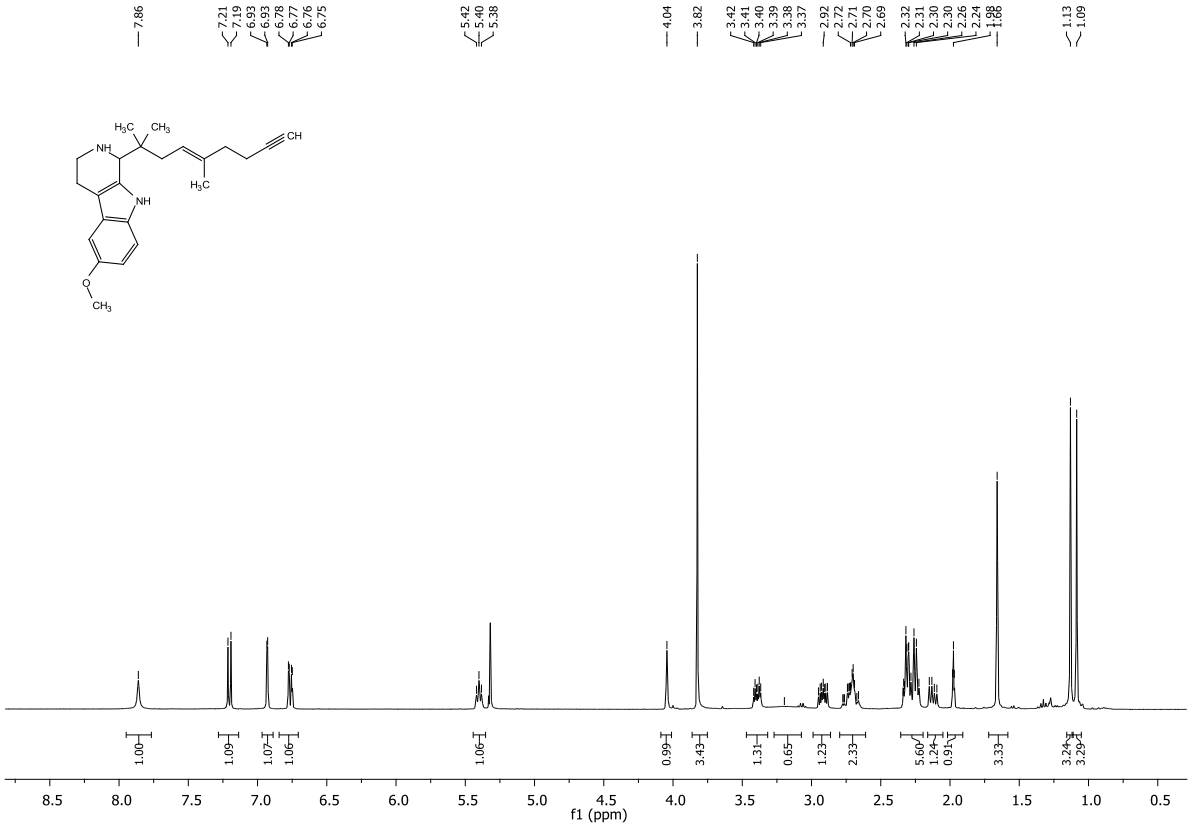
10. 8. <u>Representative NMR Spectra of compounds 10:</u>

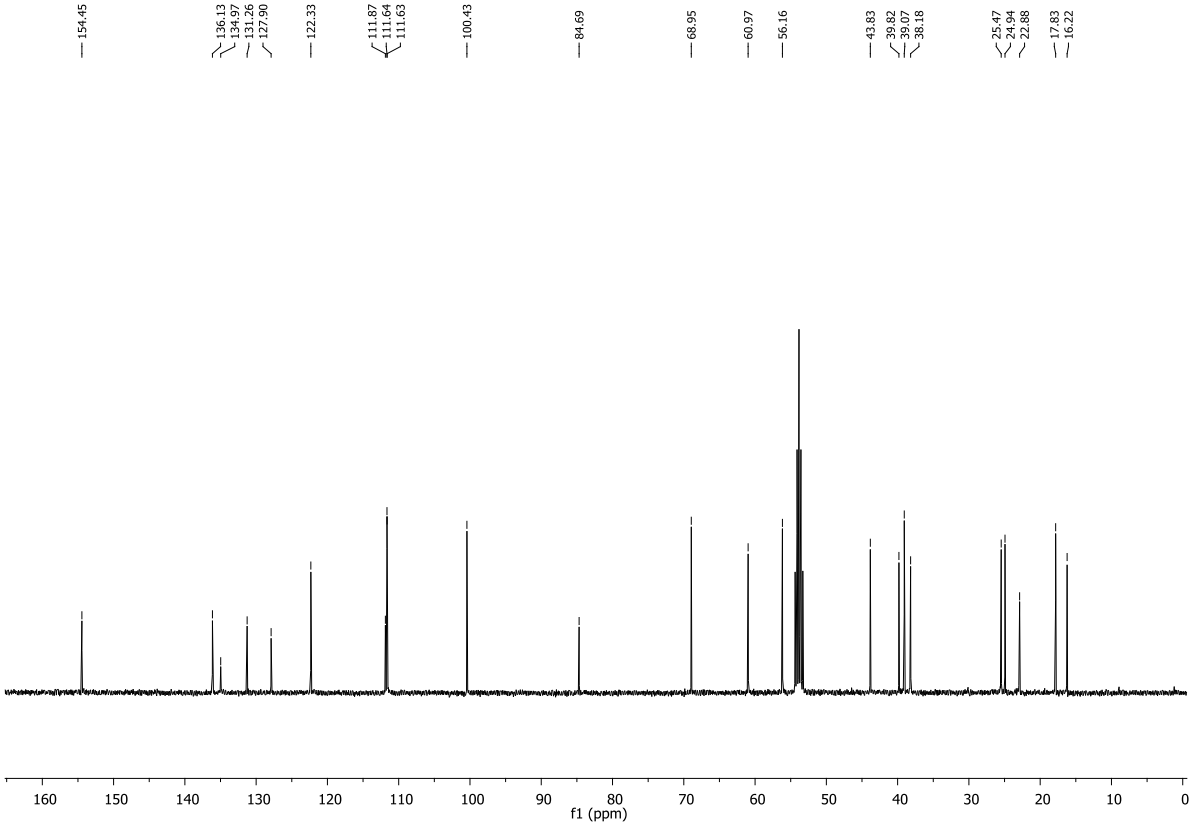
NMR of compound **10a** measured in DCM as solvent, 400MHz



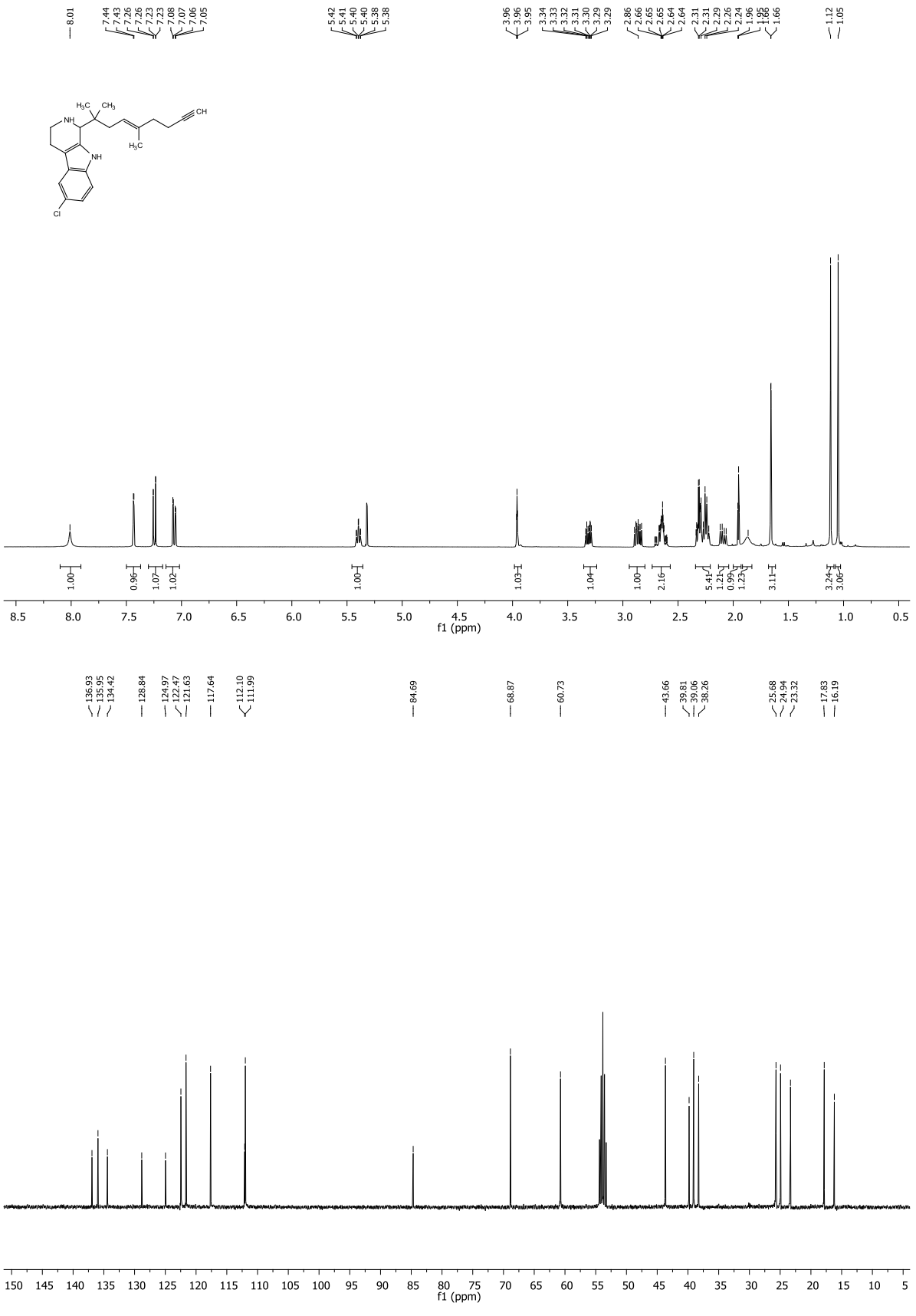


NMR of compound **10b** measured in DCM as solvent, 400MHz



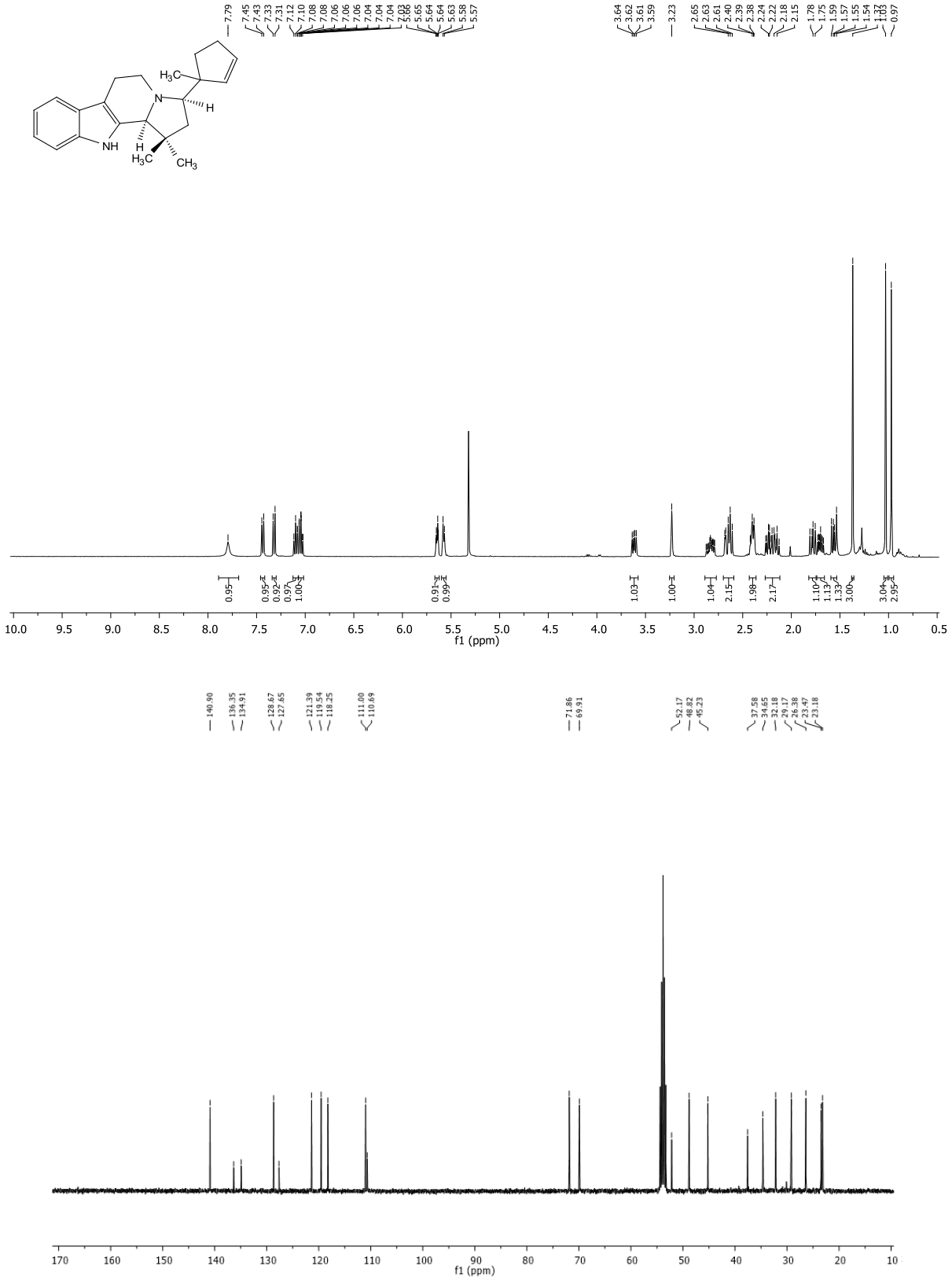


NMR of compound **10d** measured in DCM as solvent, 400MHz

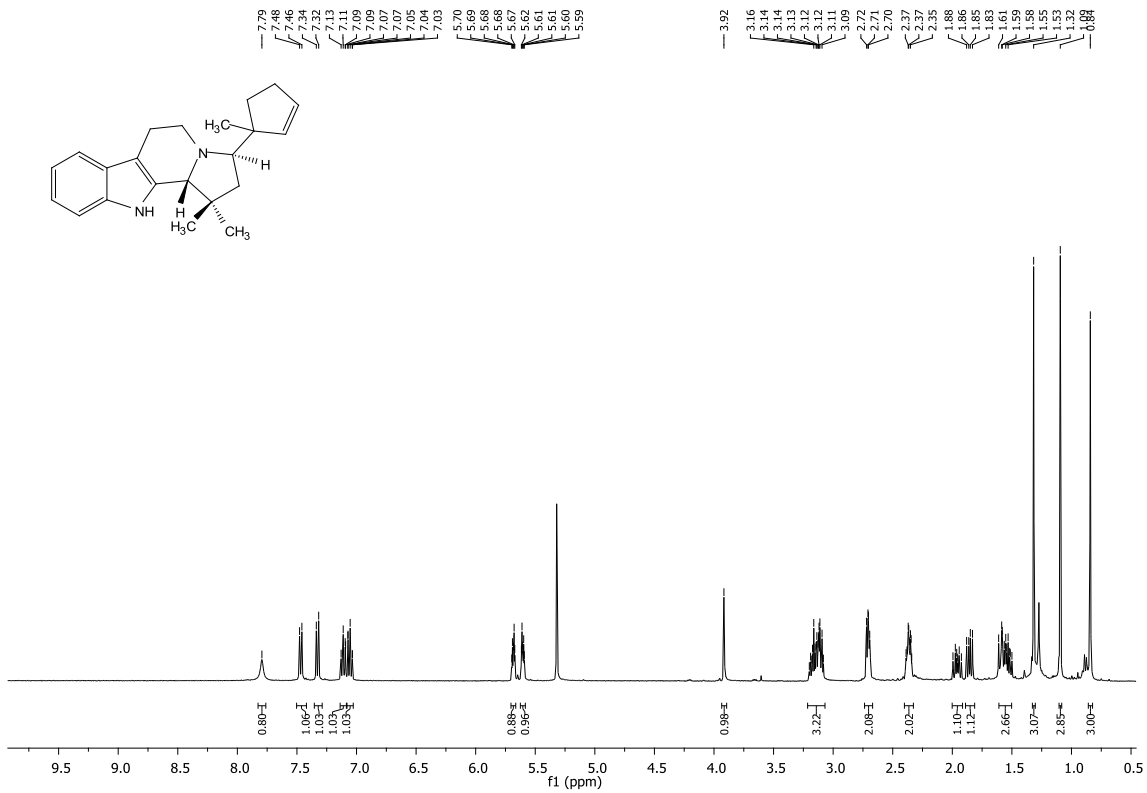


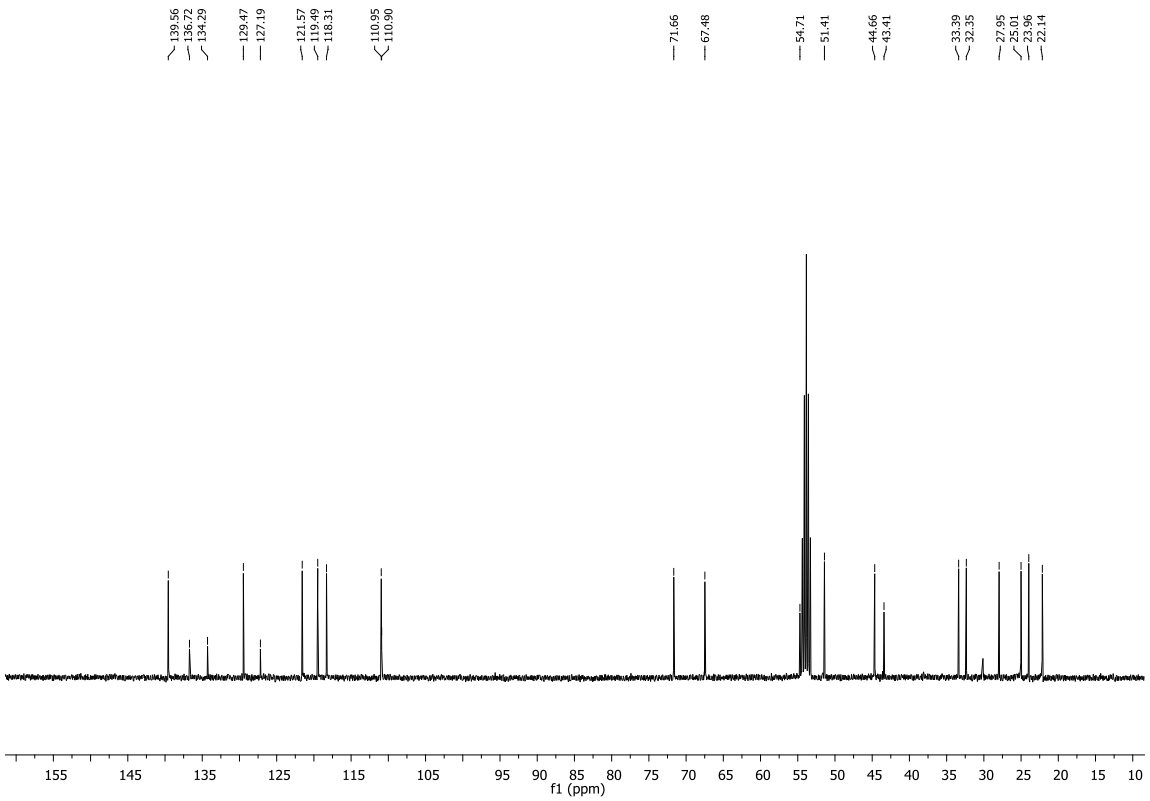
11. <u>NMR spectra of product 13:-</u>

NMR of compound **13a,**
(Minor Diastereomer), NMRs measured in CD_2Cl_2 as solvent, 400 MHz

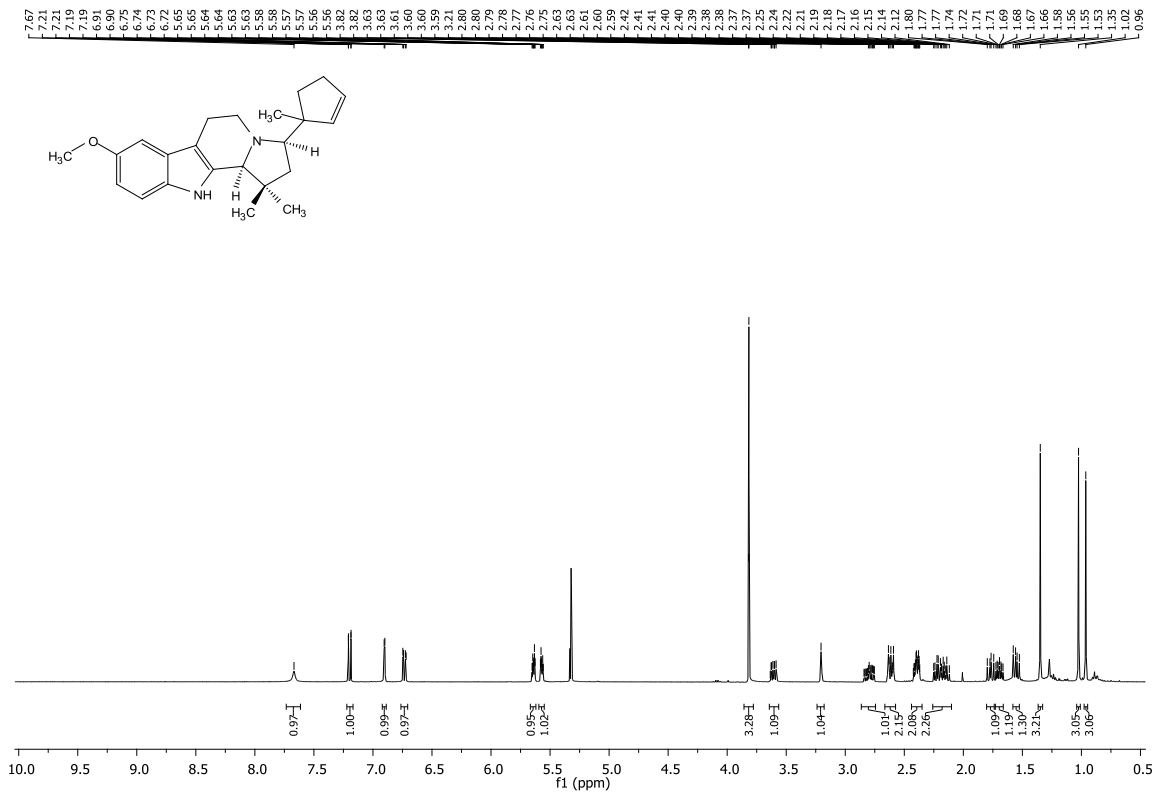


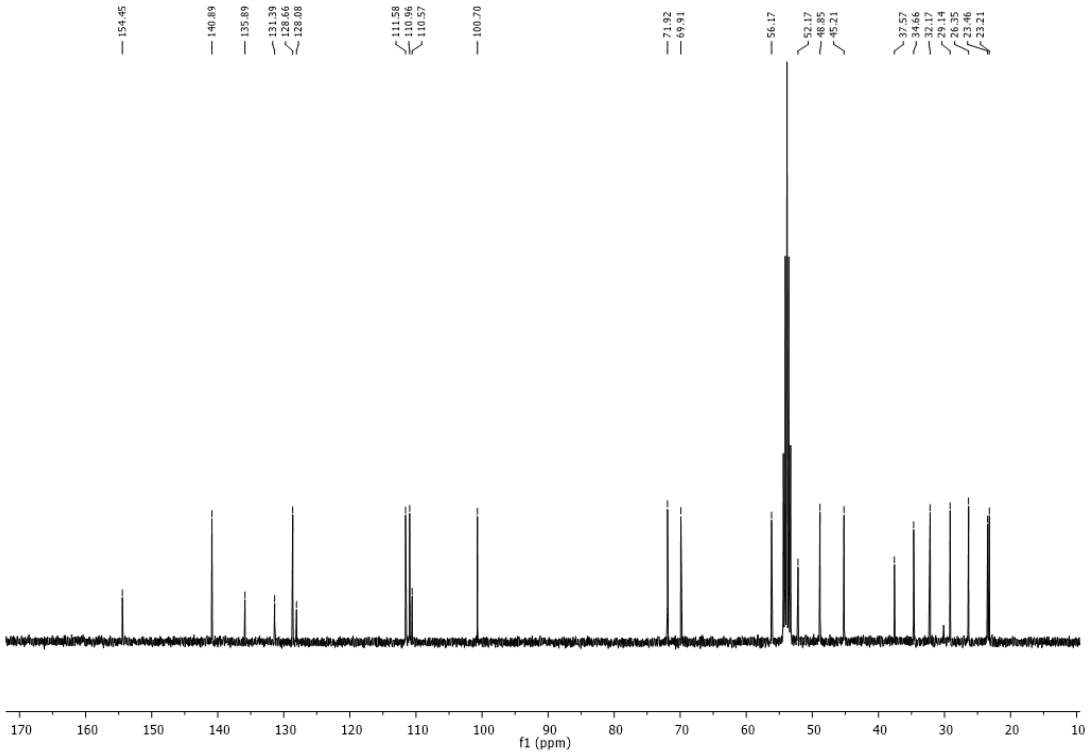
(Major Diastereomer), NMRs measured in CD_2Cl_2 as solvent, 400 MHz



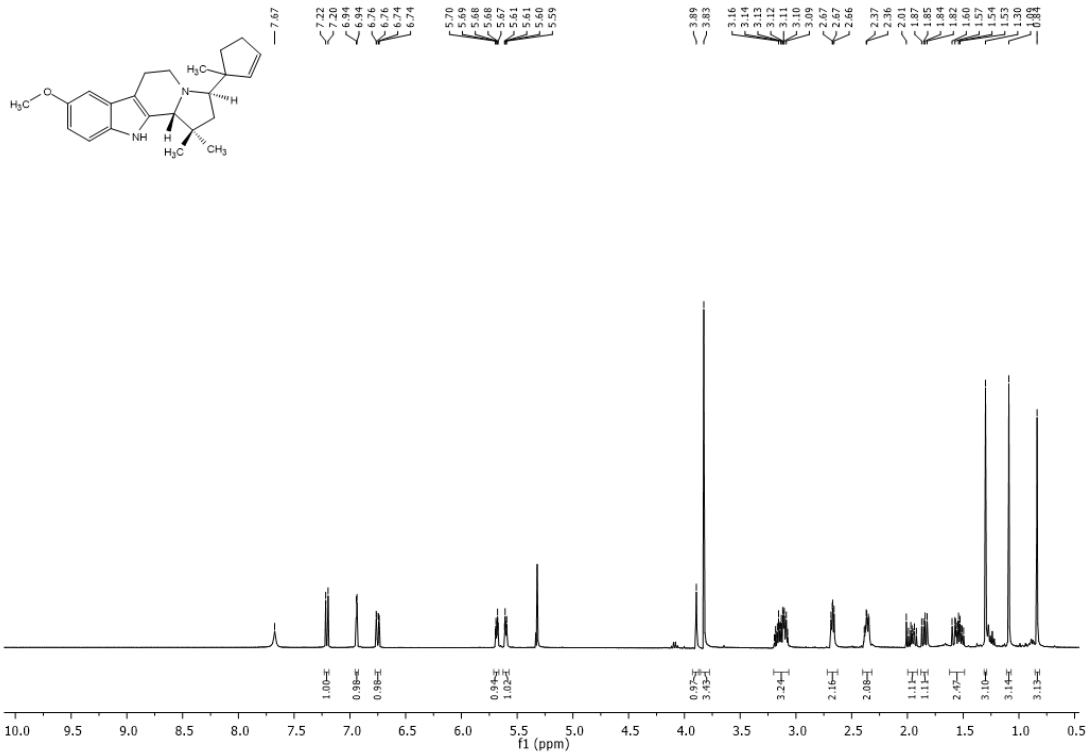


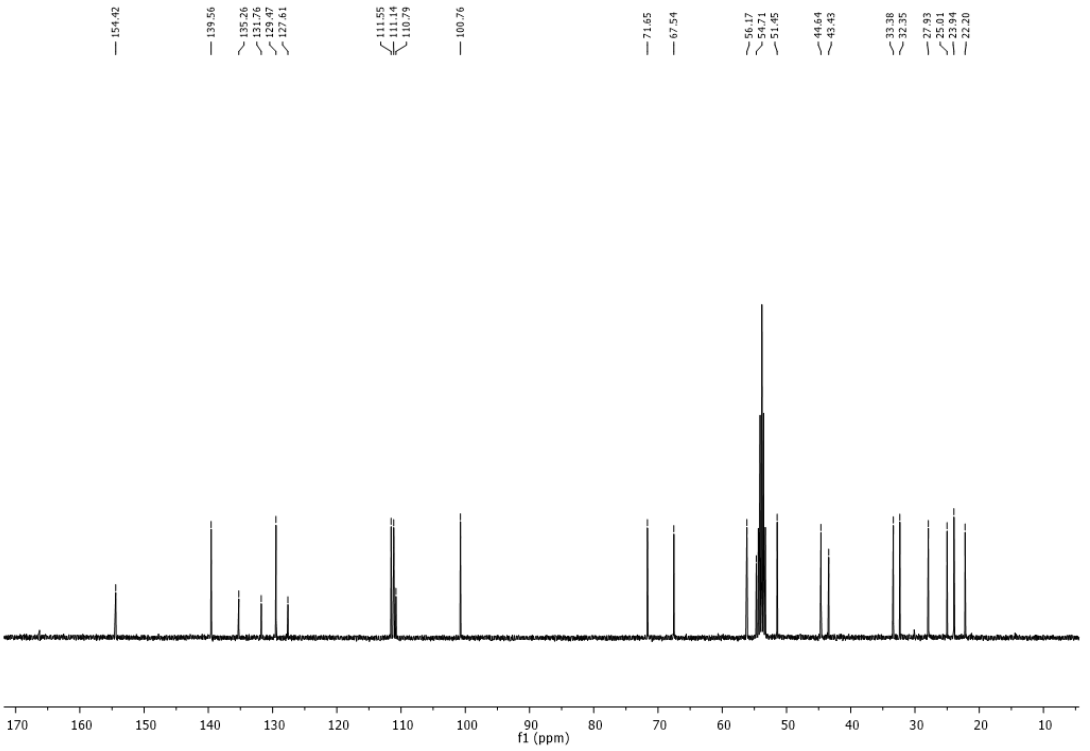
NMR of compound **13b**
(Minor Diastereomer), NMRs measured in CD_2Cl_2 as solvent, 400 MHz



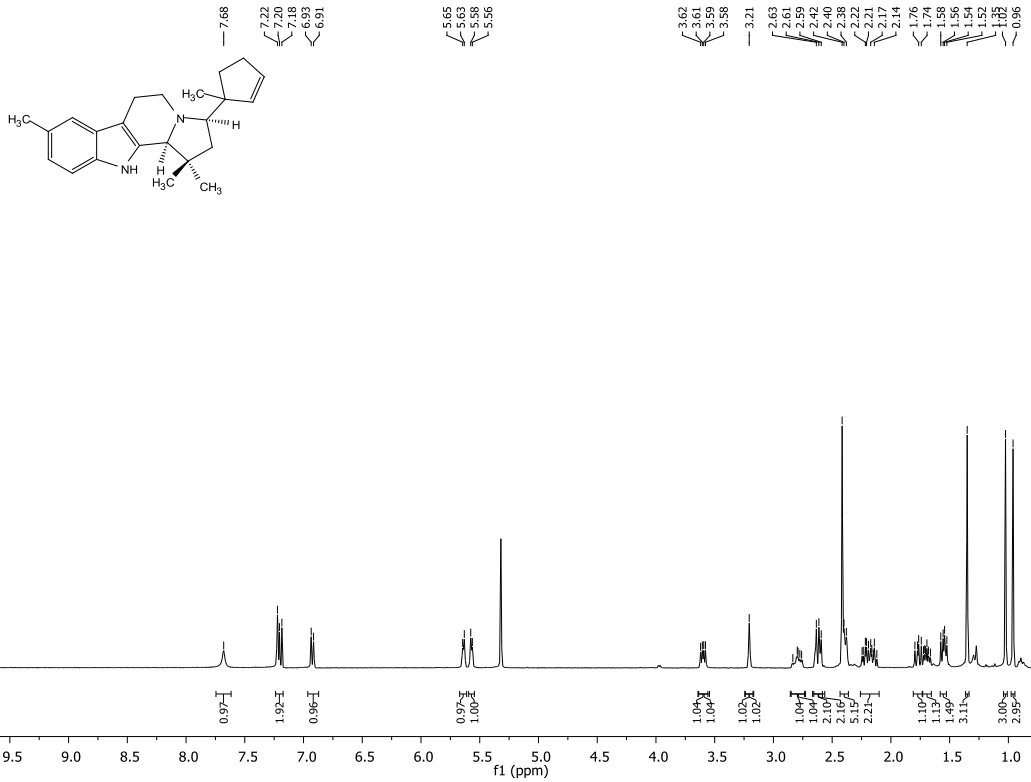


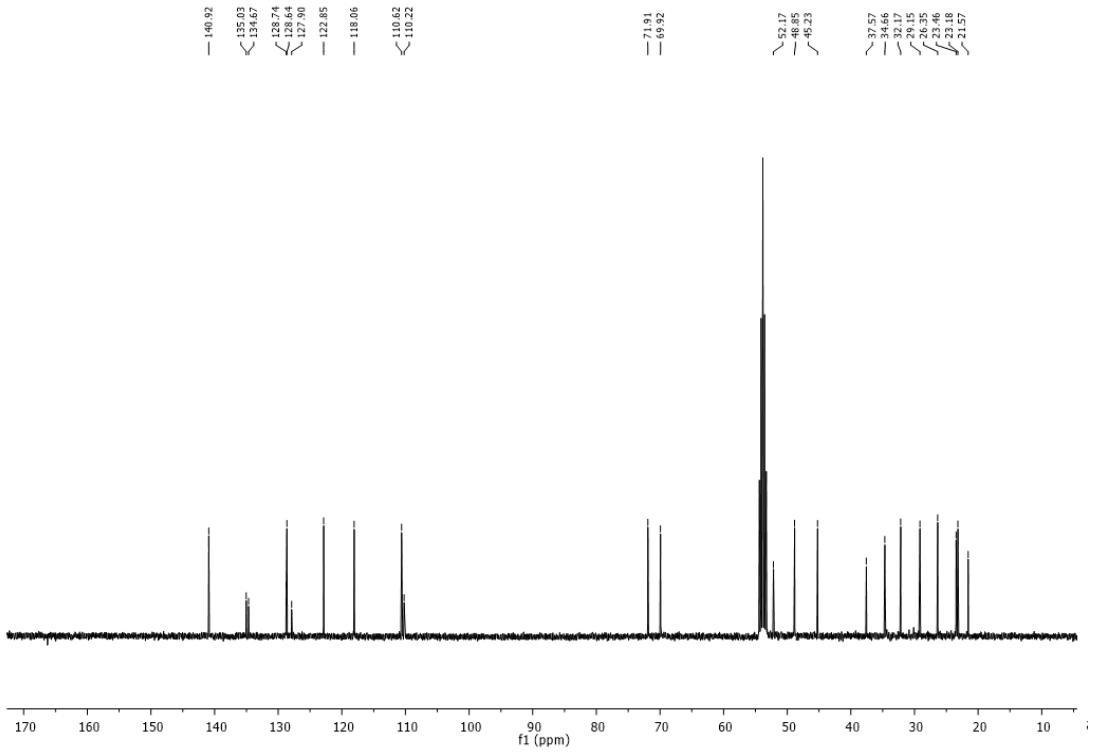
(Major Diastereomer), NMRs measured in CD_2Cl_2 as solvent, 400 MHz



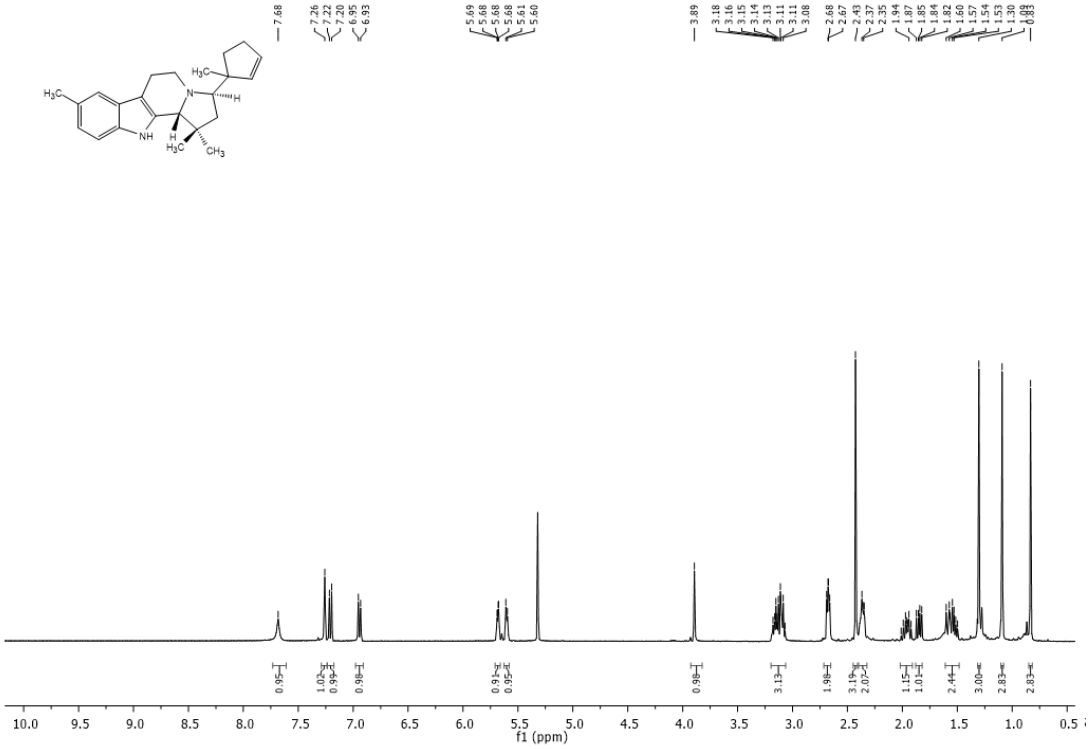


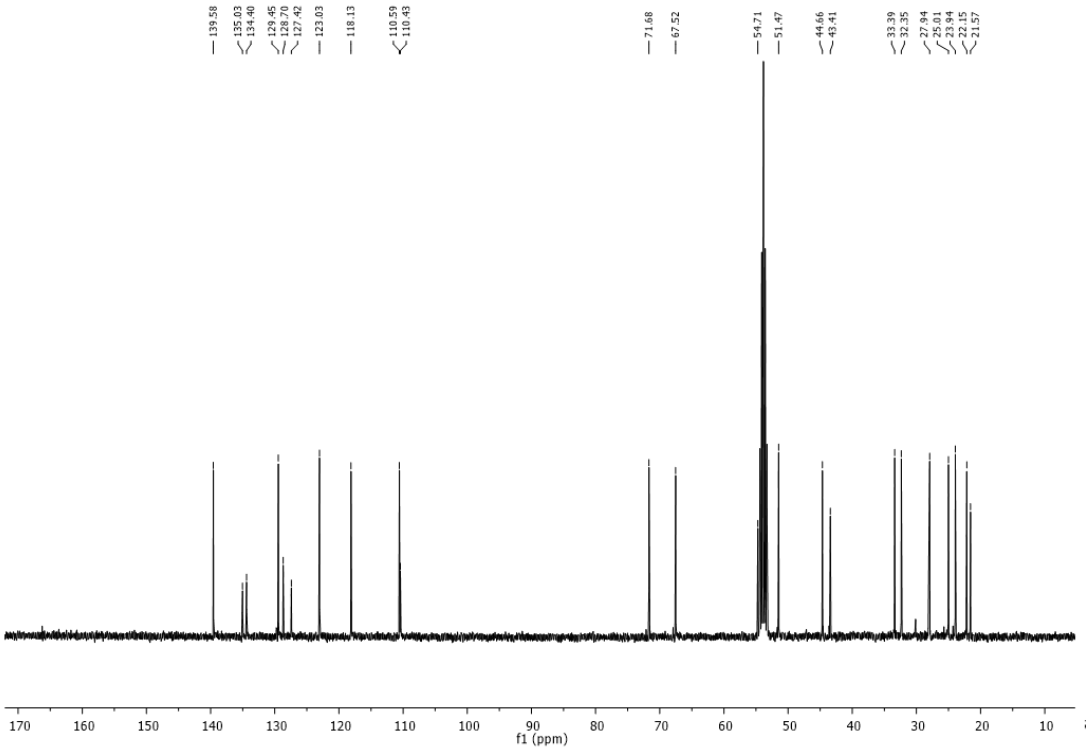
NMR of compound **13c**
(Minor Diastereomer), NMRs measured in CD_2Cl_2 as solvent, 400 MHz



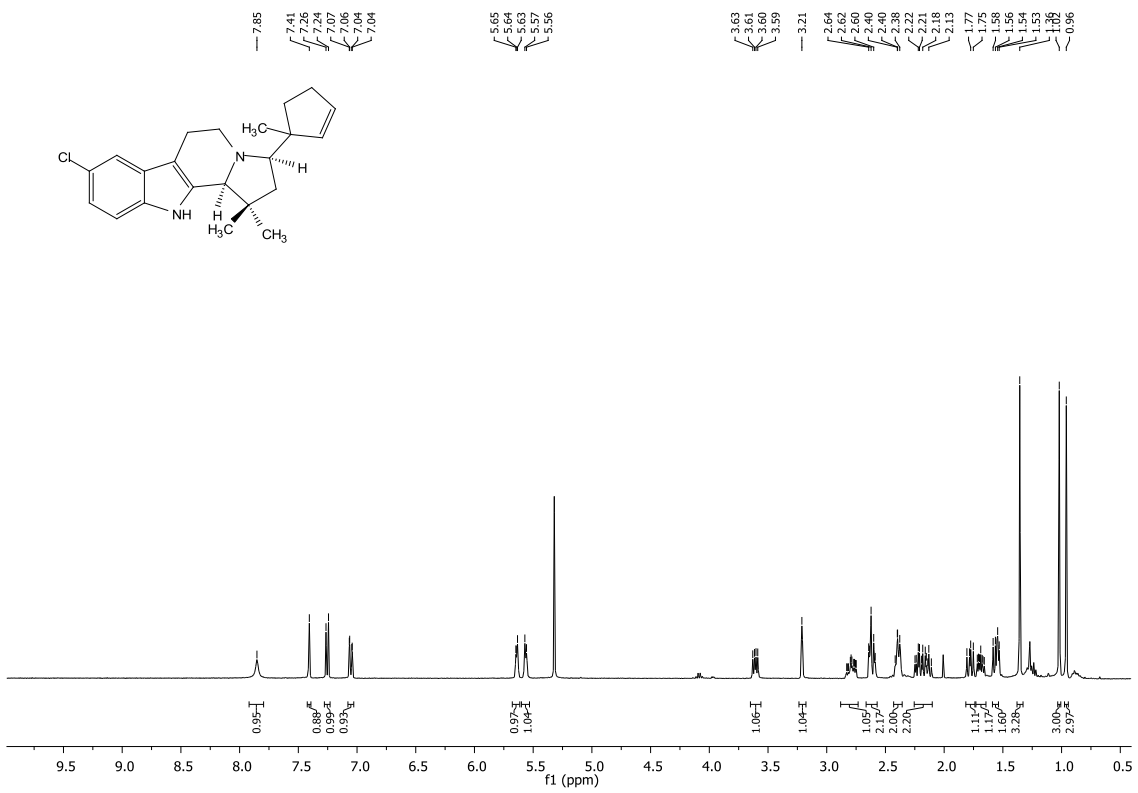


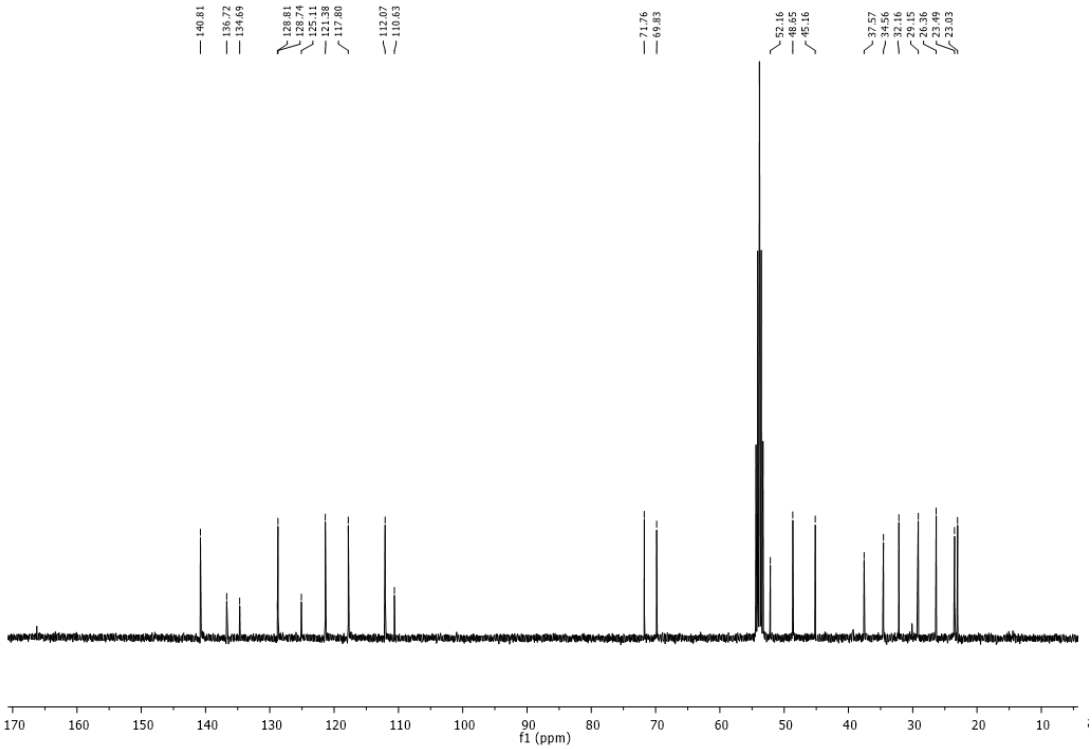
(Major Diastereomer), NMRs measured in CD_2Cl_2 as solvent, 400 MHz



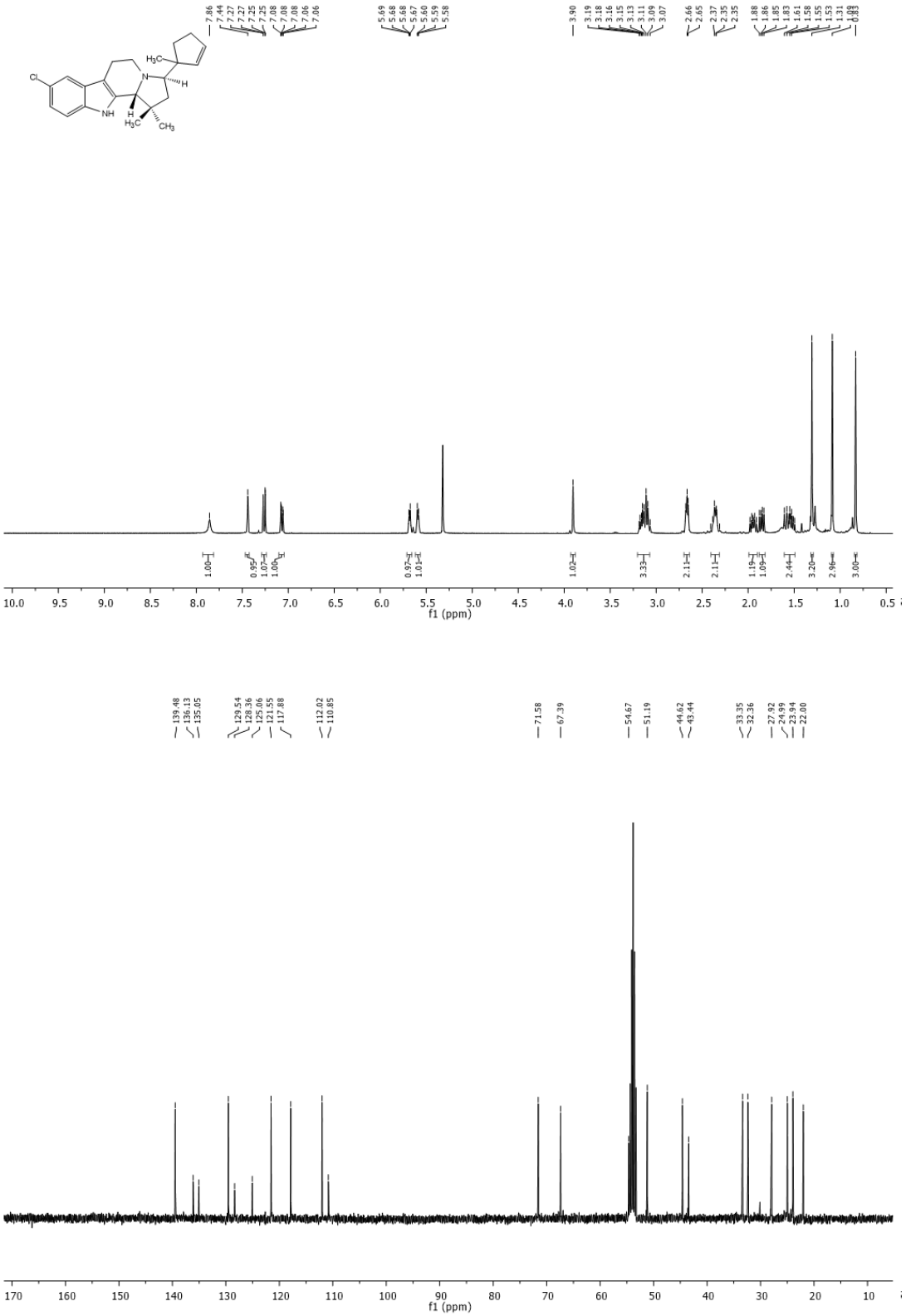


NMR of compound **13d**
(Minor Diastereomer), NMRs measured in CD_2Cl_2 as solvent, 400 MHz

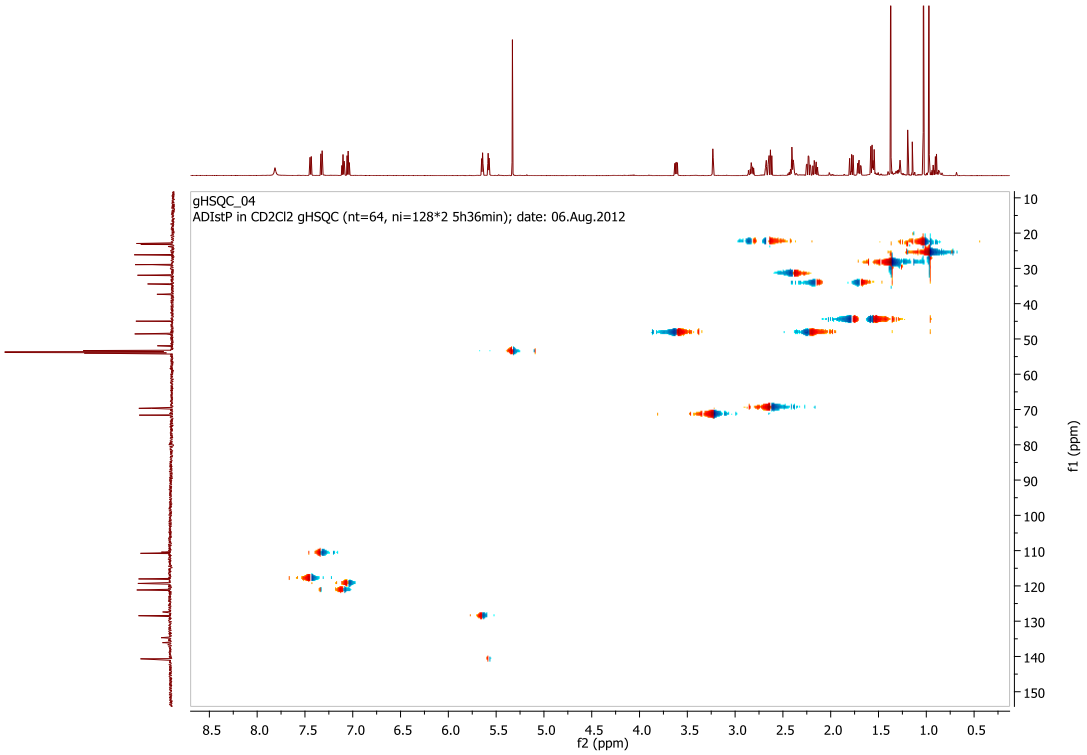


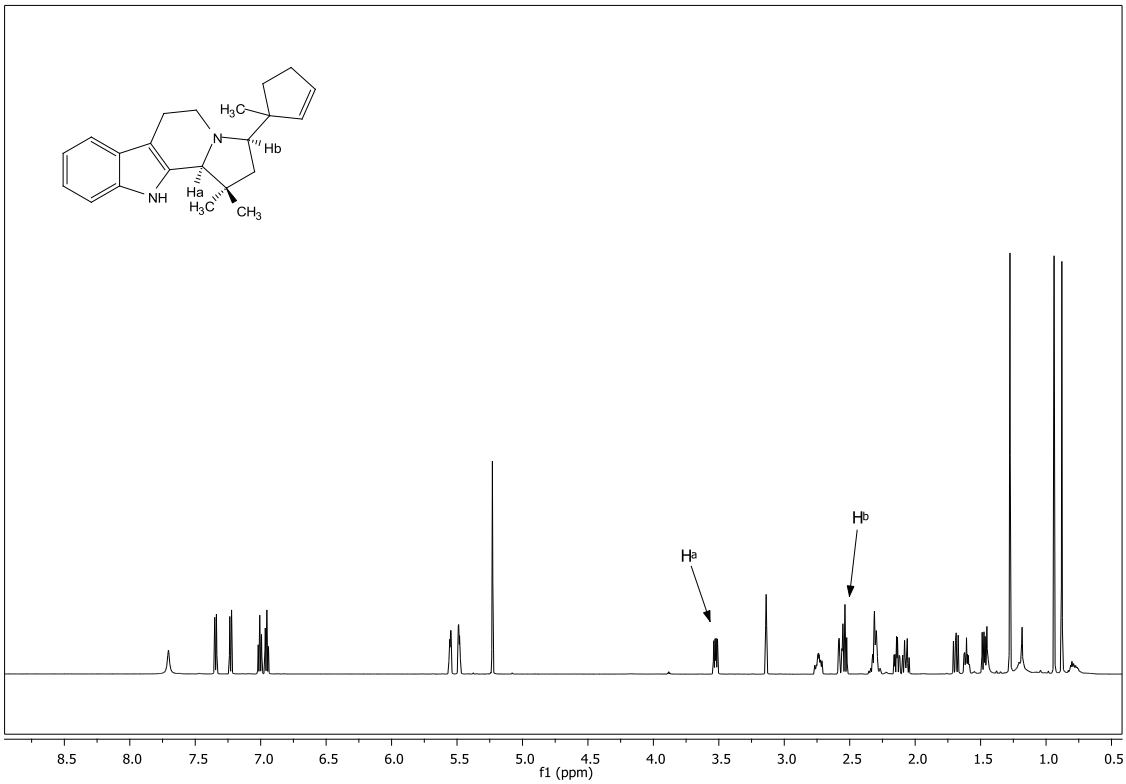


(Major Diastereomer), NMRs measured in CD_2Cl_2 as solvent, 400 MHz

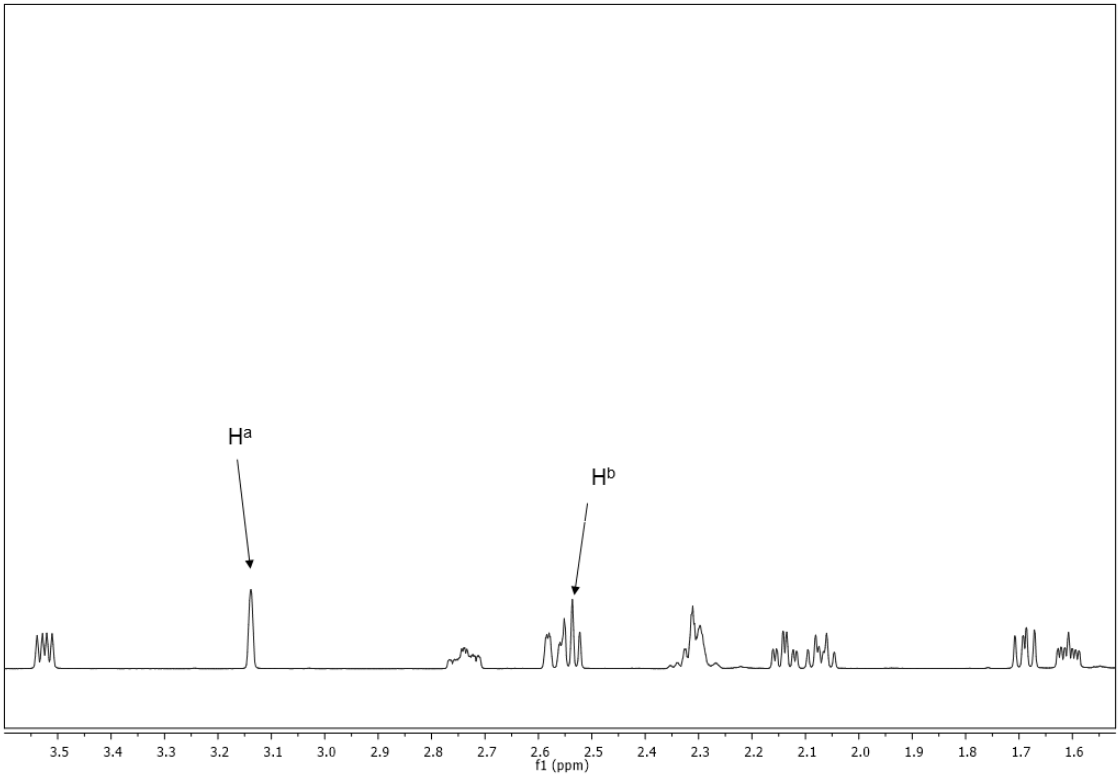


12. NOE Coupling: 13a
Minor Diastereomer:

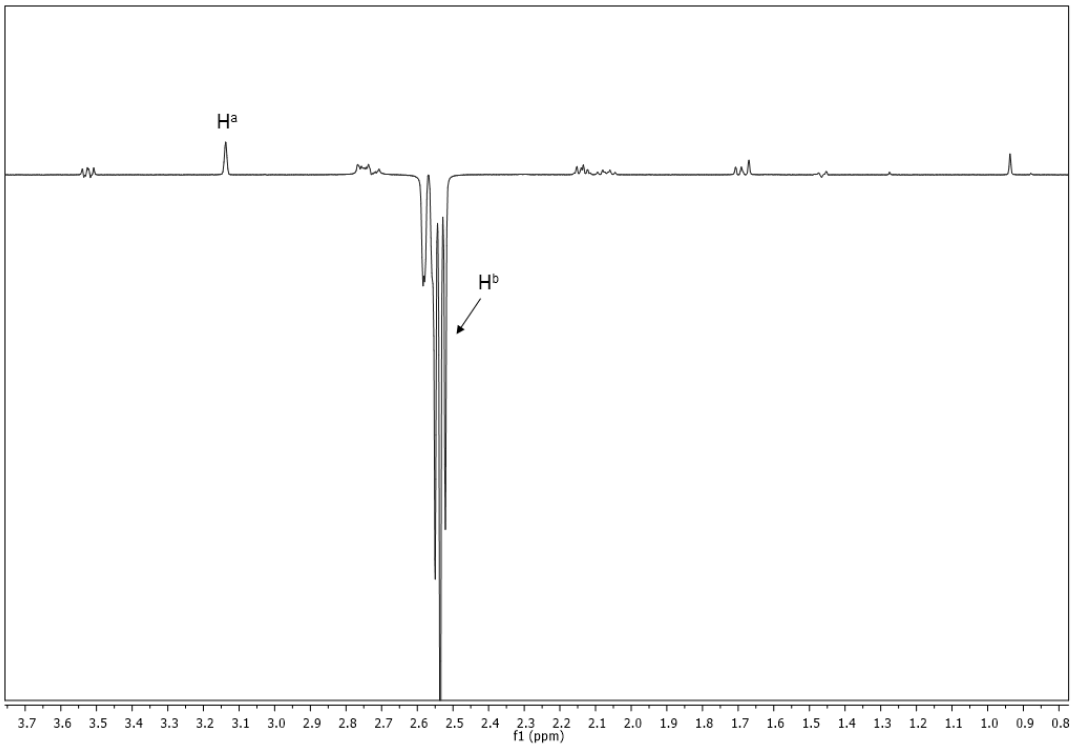




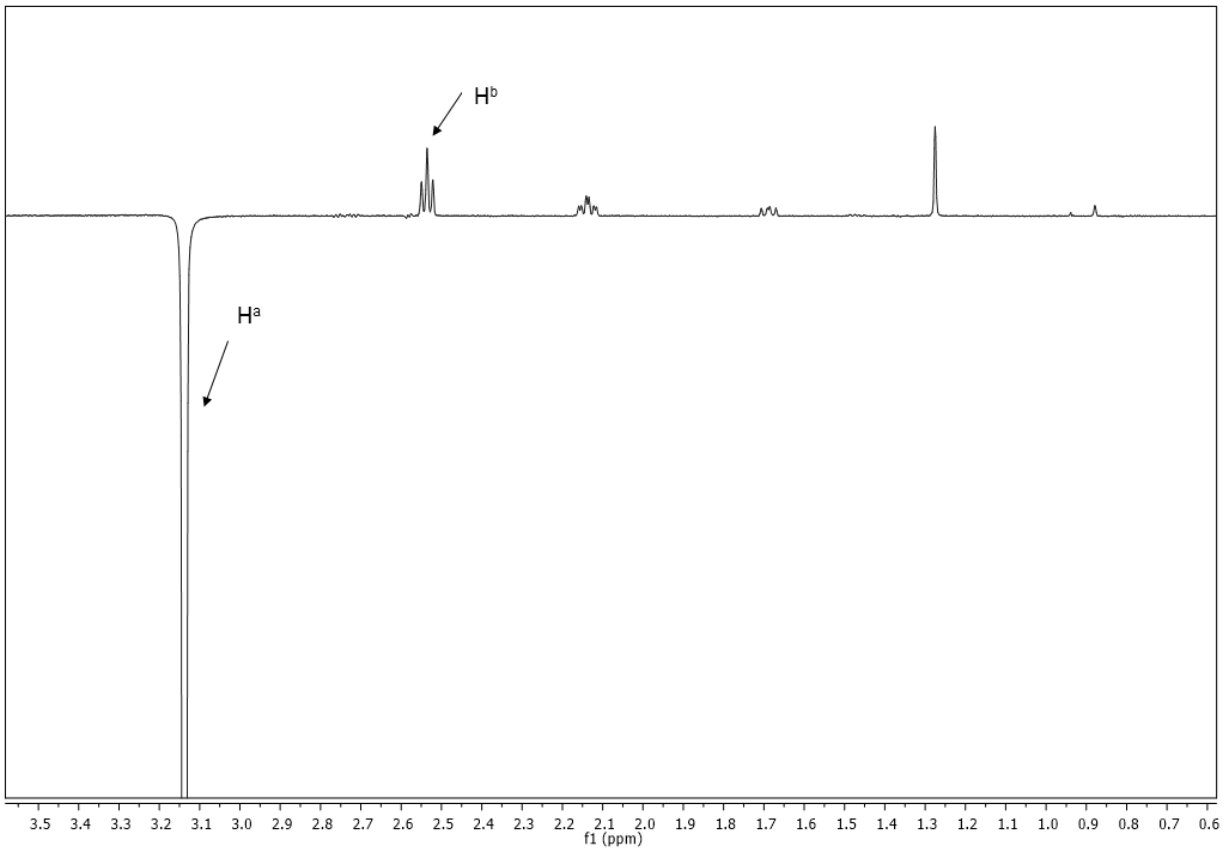
Zoomed version of the NMR spectrum



Irradiated Proton H^b

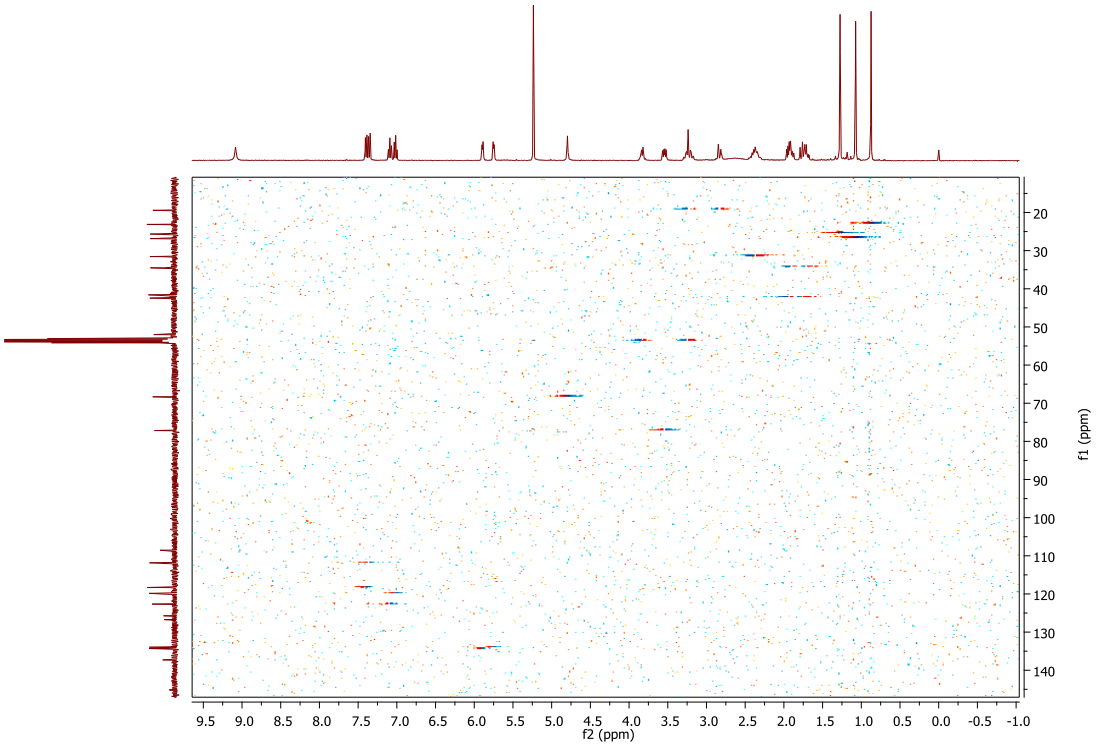


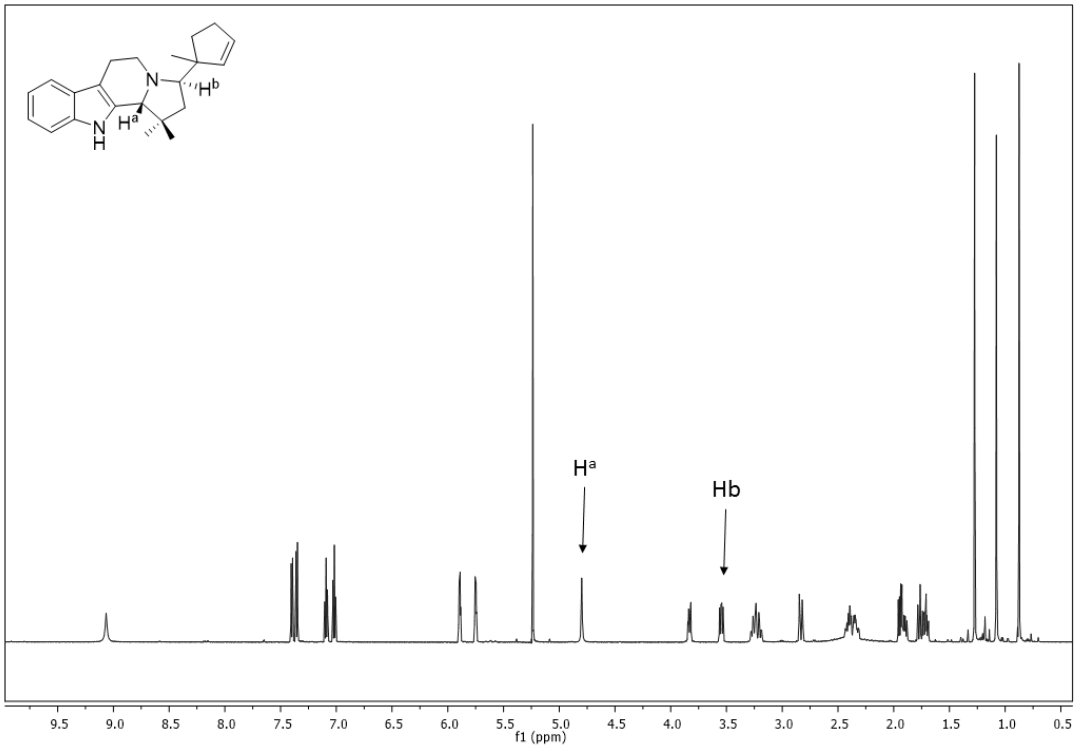
Irradiated Proton H^a



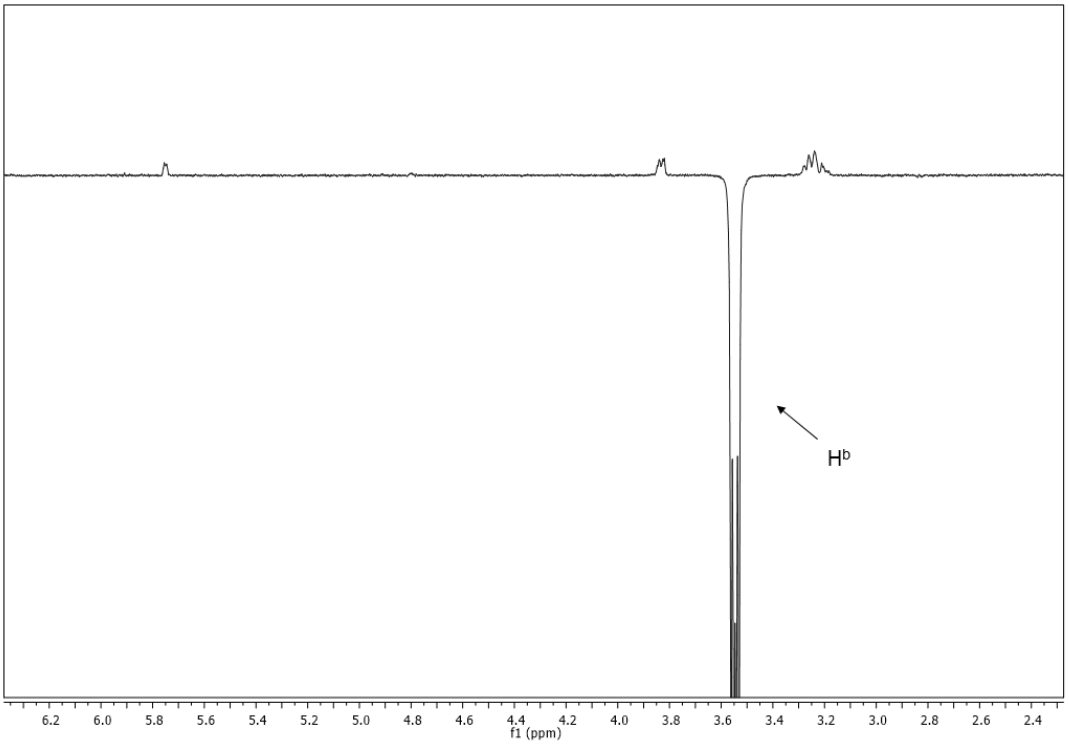
Major Diastereomer:

A TFA salt of the major diastereomer was used to determine the NOE coupling between the protons. 1D NOE was measured in CD_2Cl_2 as solvent, 600 MHz

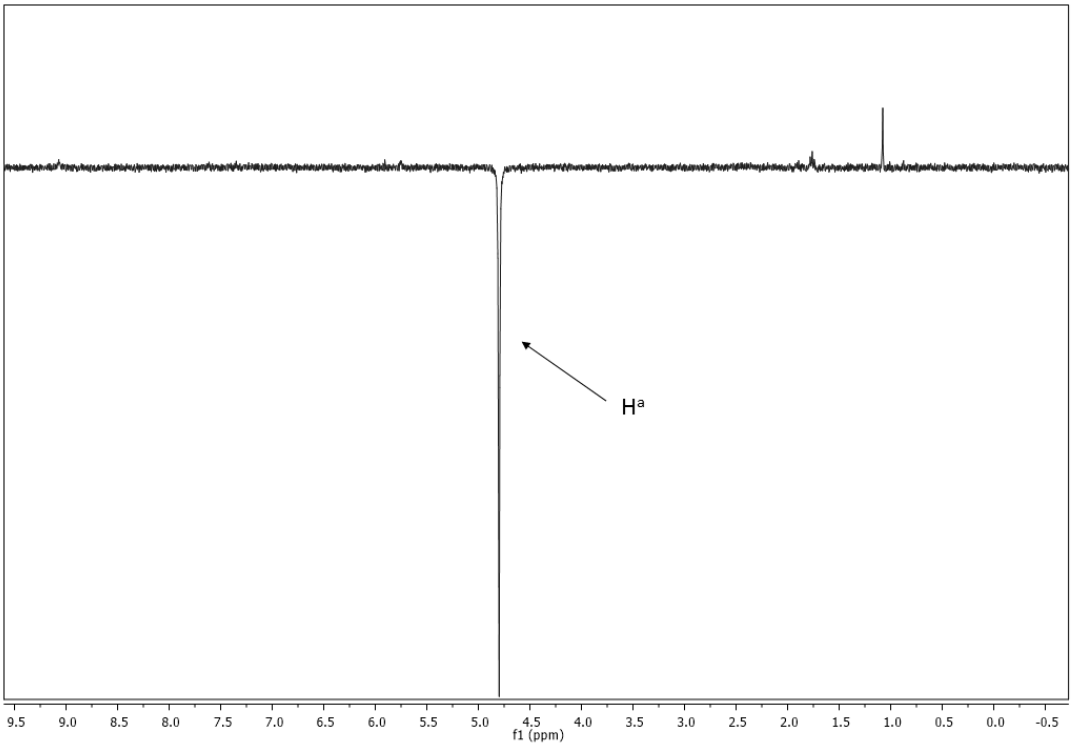




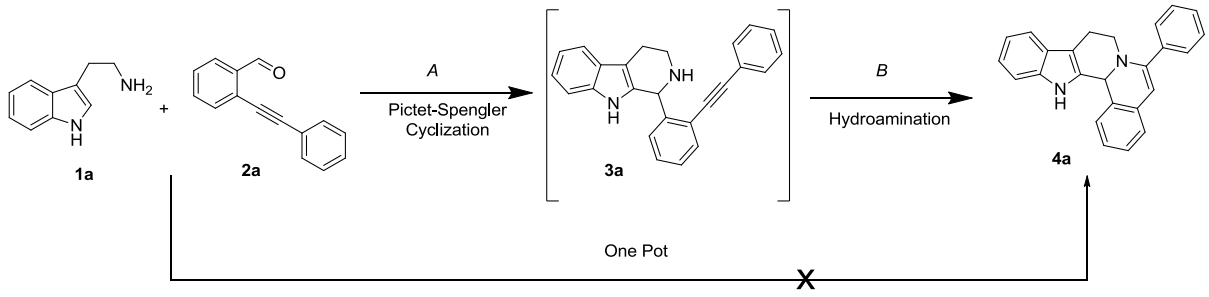
Irradiated Proton H^b



Irradiated Proton H^a



13. Efforts for the one pot cascade synthesis of indoloquinolizines 4a.



Entry	Catalyst (mol %)	Solvent	Temp (^oC)	Time (h)	Yield[h] (%)	
					3a	4a
1[a]	$Yb(OTf_3)$ (10)+ IL[c]	DCM	MW, 120	1	74	-
2[b]	Cat Y (10)	DCE	RT	1	-	62
3	$Yb(OTf_3)$ (10)+IL[c] + Cat Y (10)	DCM	RT	24	50	-
4	$Yb(OTf_3)$ (10)+IL[c] + Cat Y (10)	DCE	reflux	24	30	-
5[e]	$Yb(OTf_3)$ (10)+IL[c] + Cat Y (10)	DCE	MW, 120	1.5	28	-
6[e]	$Yb(OTf_3)$ (10)+IL[c] + Cat Y (10)	DCE: EtOH (5 equiv.)	MW, 120	1.5	20	-
7[e]	$Yb(OTf_3)$ (10)+IL[c] + Cat Y (10)	*i*-PrOH	MW, 120	1.5	15	-
8[d]	$Yb(OTf_3)$ (10)+IL[c] + $Au(PPh_3)OTf$ (10)	DCE	RT to reflux	24	20	-
9[f]	$Yb(OTf_3)$ (10)+TMSCl (1 equiv)	DCM:THF (4:1)	RT	24	75	-
10[d,g]	$Yb(OTf_3)$ (10)+ TMSCl (1 equiv) + Cat Y (10)	DCM:THF (4:1)	RT to reflux	24	30	-

[a]Optimized condition for Pictet-spengler reaction (step A), [b]Optimized condition for hydroamination reaction(step B) using pure compound 3a, [c]IL-Ionic liquid [bmim]Cl (0.32 mL/mmol of 2a), [d]the reaction was run at RT for 12h followed by reflux, unless or otherwise specified the reactions were run at 0.2mmol scale, MW- Microwave reaction, RT= Room temperature, DCE= 1,2-dicloroethane, *i*-PrOH= isopropanol, DCM= dichloromethane,[e]All the reactions were performed at room temperature as well giving only the pictet Spengler product, [f]TMSCl was used as an additive in place of IL for the pictet Spengler reaction, [g]TMSCl was used as an additive in place of IL in the one pot reaction, [h]isolated yield