Spirocyclic dihydropyridines by electrophile-induced dearomatizing cyclization of *N*-alkenyl pyridinecarboxamides

Jemma Senczyszyn, Heloise Brice and Jonathan Clayden

SUPPORTING INFORMATION

1. General Information 2
2. Experimental Procedures
    2.1 Synthesis of Cyclisation Precusors 3
    2.2 Dearomatising Cyclisations 10
4. NMR Spectra 40

General Information

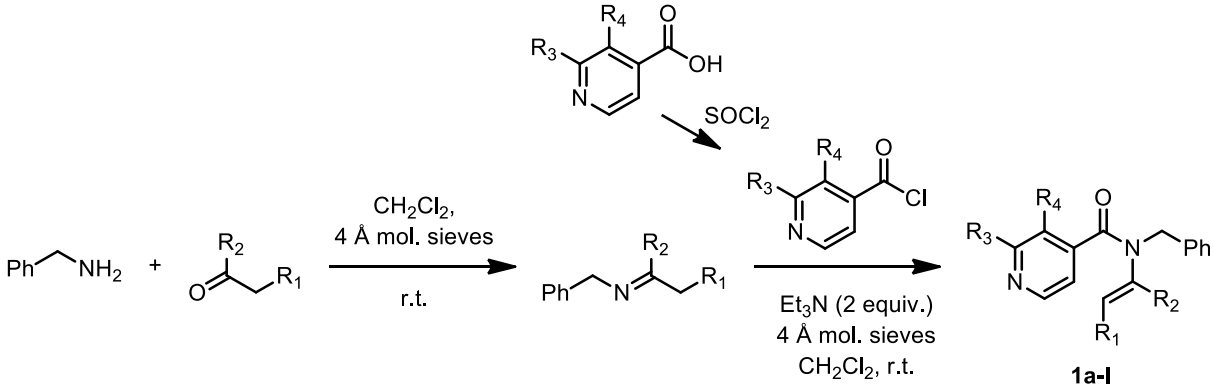
NMR spectra were recorded on a Bruker Ultrashield 300, 400 or 500 MHz spectrometer. The chemical shifts (δ) are reported in ppm downfield of trimethylsilane and coupling constants (*J*) reported in hertz and rounded to 0.5 Hz. Splitting patterns are abbreviated as follows: singlet (s), doublet (d), triplet (t), quartet (q), quintet (qn), septet (sept), multiplet (m), broad (br) and apparent (ap) or a combination of these. Aromatic protons (Ar) are assigned where possible using the following abbreviations: Phenyl (Ph), pyridine (Py) and quinoline (Qu). Where mixtures of diastereomers or rotamers have been observed, they are described as major (maj) or minor (min) where possible and as A and B where diastereomeric/ rotamer ratios are 1:1. Solvents were used as an internal standard when assigning NMR spectra (δ_H: $CDCl_3$ 7.26 ppm; δ_C: $CDCl_3$ 77.16 ppm; δ_H: CD_3OD 3.31 δ_C: CD_3OD 49.00 and δ_H: DMSO-d_6 2.50 ppm; δ_C: DMSO-d_6 39.4 ppm). Coupling constants were calculated using MestReNova LITE 5.2.5 or by ACDLabs 9.0 1D NMR processor software.

Low and high resolution mass spectra were recorded by staff at the University of Manchester. ES spectra were recorded on a Micromass Platform II spectrometer and high resolution mass spectra (HRMS) were recorded on a Kratos Concept-IS mass spectrometer, and are accurate to ± 0.001. Infrared spectra were recorded as on a Perkin Elmer Spectrum RX 1 FTIR or a on a Thermo Scientfic iD5 ATR spectrometer. Only absorption maxima of interest are reported. Melting points (m.p.) were determined on a GallenKamp apparatus.

Thin layer chromatography (TLC) was performed using commercially available pre-coated plates (Macherey-Nagel alugram. Sil G/$_{UV254}$) was visualised with UV light at 254nm or a phosphomolybdic acid dip (5% in ethanol). Flash chromatography was carried out using Fluorochem Davisil 40-63u 60 Å.

All reactions were conducted under a nitrogen atmosphere unless otherwise stated. Where a nitrogen atmosphere was employed, oven or flame dried glassware was used. Tetrahydrofuran (THF) and diethyl ether were distilled under nitrogen from sodium, using a benzophenone indicator. Dichloromethane and THF were obtained by distillation from calcium hydride under nitrogen. Toluene was obtained from the Innovative Technology Puresolve P5-mp-5 solvent purification system. Petrol refers to the fraction of light petroleum ether boiling between 40 and 65 °C. All other solvents and commercially obtained reagents were used as received or purified using standard procedures.

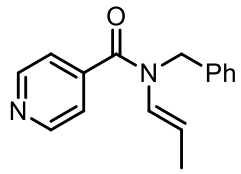
General Procedure A for Imine Acylations



Thionyl chloride (5 eq) was added to a flask containing the pyridyl carboxylic acid. The reaction was stirred under a nitrogen atmosphere for 2 hours until a clear solution was obtained. Excess thionyl chloride was removed under reduced pressure and dried under vacuum.

Aldehyde or ketone was added to a flame-dried flask under a nitrogen atmosphere containing dry dichloromethane (2.0 mL) and molecular sieves (4 Å). Benzylamine (1 eq) was added dropwise and the reaction was left to stir at room temperature. Acyl chloride (1.1 eq) was suspended in dry dichloromethane in a flame-dried flask containing molecular sieves (4 Å). The suspension was cooled to 0 °C, triethylamine (2.2 eq) was added dropwise and the solution was stirred for 2 minutes. Imine (1.0 eq) was added dropwise to the solution. The ice bath was removed and the reaction mixture was allowed to heat to room temperature. After stirring for 3-6 hours, saturated sodium hydrogen carbonate solution (20 mL) was added and the solution extracted with dichloromethane (2 × 20 mL), dried with $MgSO_4$, filtered and evaporated under reduced pressure. The residue was purified by flash chromatography (SiO_2, EtOAc:petrol 1:3) to yield the enamide.

_N_-Benzyl-_N_-((_E_)-propenyl)-isonicotinamide (1a)

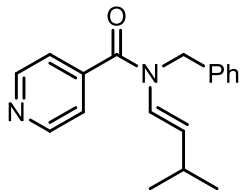


Following general procedure A, (*E*)-1-phenyl-*N*-propylidenemethanamine (2.0 mmol) (from benzylamine (0.22 mL) and propionaldehyde (0.13 mL)) was acylated with isonicotinoyl chloride (311 mg). After purification the title compound was yielded as a colourless gum (72% over 2 steps).

R_f **:** 0.29 (EtOAc:petrol 1:2); **IR:** (υmax(film)/cm^{-1}) 1641 (C=O); **^{1}H-NMR:** (400 MHz, $CDCl_3$, 2 rotamers (3:1)) δ 8.75 (d, J = 5.5 Hz, 2H$_{maj}$, Py), 8.60 (d, J = 3.5 Hz, 2H$_{min}$, Py), 7.46-7.10 (m, 7H, Ar), 6.28 (d, J = 14.0 Hz, 1H$_{maj}$, NC*H*) 5.09 (dt, J = 14.0, 7.0 Hz, 1H, CH=C*H*), 5.01 (s, 2H$_{maj}$, PhCH_2), 4.60 (s, 2H$_{min}$, PhCH_2) 1.70 (d, J = 5.5 Hz, 3H$_{min}$, CH_3), 1.51 (d, J = 6.0 Hz, 3H$_{maj}$, CH_3); **^{13}C-NMR:** (100 MHz, $CDCl_3$) δ 167.8 (*C*O), 150.3 (Py), 143.2 (Py), 136.6 (Ph$_{maj}$), 136.0 (Ph$_{min}$), 129.0 (Ph$_{min}$), 128.7 (Ph$_{maj}$), 127.3 (Ph$_{maj}$), 126.9

(Ph_{maj}), 125.9 (Ph_{min}), 125.7 (NCH=CH), 125.6 (Ph_{min}), 122.0 (Py_{maj}), 120.6 (Py_{min}), 110.8 (NCH=CH_{min}), 110.1 (NCH=CH_{maj}), 50.8 (PhCH_{2min}) 47.4 (PhCH_{2maj}), 15.5 (CH_{3min}), 15.4 (CH_{3maj}); **m/z (ES^+):** 253.1 (20%, MH^+), 275.1 (100%, MNa^+); **HRMS:** found 275.1151 (MNa^+), $C_{16}H_{16}ON_2Na$ requires 275.1155.

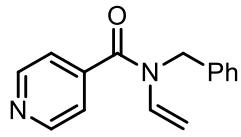
_N_-Benzyl-_N_-((_E_)-3-methyl-but-1-enyl)-isonicotinamide (1b)



Following general procedure A, (_E_)-_N_-(3-methylbutylidene)-1-phenylmethanamine (1.0 mmol) (from 3-methyl-butraldehyde (0.11 mL) and benzylamine (0.11 mL)) was acylated with isonicotinoyl chloride (155 mg). After purification, the title compound was yielded as a colourless gum (72% over 2 steps).

R_f **:** 0.21 (EtOAc:petrol 1:1); **IR:** (υmax(film)/cm^{-1}) 1641 (C=O); **^{1}H-NMR:** (300 MHz, $CDCl_3$, 2 rotamers (3:1)) δ 8.73 (d, _J_ = 5.5 Hz, $2H_{maj}$, Py), 8.58 (d, _J_ = 4.5 Hz, $2H_{min}$, Py), 7.40-7.09 (m, 7H, Ar), 6.23 (d, _J_ = 14.0 Hz, 1H, NC_H_), 5.07 (dd, _J_ = 14.0, 7.0 Hz, 1H, NCH=C_H_), 5.00 (s, $2H_{maj}$, PhCH_2), 4.66 (s, $2H_{min}$, PhCH_2), 2.36 (m, $1H_{min}$, C_H_(CH_3)$_2$), 2.11 (q, _J_ = 7.0 Hz, $1H_{maj}$, C_H_(CH_3)$_2$), 0.96 (d, _J_ = 6.5 Hz, $6H_{min}$, CH_3), 0.81 (d, _J_ = 7.0 Hz, $6H_{maj}$, CH_3); **^{13}C-NMR:** (400 Hz, $CDCl_3$) δ 168.1 (_C_O), 150.4 (Py), 143.4 (Py), 136.6 (Ph_{maj}), 136.0 (Ph_{min}) 128.8 (Ph_{min}), 128.7 (Ph_{maj}) 127.4 (Ph_{maj}), 127.2 (Ph_{maj}), 126.1 (N_C_H), 125.7 (Ph_{min}), 123.7 (NCH=_C_H), 123.4 (Ph_{min}),122.0 (Py_{maj}), 120.7 (Py_{min}), 50.8 (PhCH_{2min}), 47.6 (PhCH_{2maj}), 29.7 (CH(_C_H_3)$_{2min}$), 29.4 (CH(_C_H_3)$_{2maj}$), 23.0 (CH_{3min}), 22.8 (CH_{3maj}); **m/z (ES^+):** 303.1 (100%, MNa^+); **m/z (ES^-):** 279.8 (100%, M^-), **HRMS:** found 303.1471 (MNa^+), $C_{18}H_{20}N_2ONa$ requires 303.1473.

_N_-Benzyl-_N_-vinylisonicotinamide (1c)



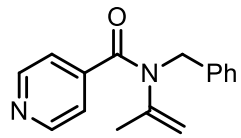
Following general procedure B, but using 2.5 eq of pyridine rather than triethylamine, _N_-benzyl-2-chloroethanamine hydrochloride[1] (3.0 mmol) was acylated with isonicotinoyl chloride (3.3 mmol). Saturated sodium hydrogen carbonate solution was added (10 mL) and the solution extracted with dichloromethane (3 x 10 mL), dried ($MgSO_4$) and evaporated under reduced pressure. The residue was purified by flash chromatography (SiO_2; EtOAc-petrol 1:3) to yield the amide, as colourless oil (0.664 g, 81%).

Potasium _tert_-butoxide (1.0 mmol) was added to stirred solution of _N_-benzyl-_N_-(2-chloroethyl)isonicotinamide (0.274 g, 1.0 mmol) in _tert_-butanol (5 mL) at room temperature. The solution was stirred for 60 hours then water (15 mL) was added and the solution extracted with EtOAc (3 x 15 mL), dried ($MgSO_4$) and evaporated under reduced pressure. The residue was purified by flash chromatography (SiO_2; EtOAc-hexane 2:3 to EtOAc) to yield the title compound as a white waxy solid (0.040 g, 17%).

[1] Mansour, A.; Portnoy, M. *J. Chem. Soc., Perkin Trans. 1* **2001**, 952 - 954.

***R*$_f$:** 0.28 (EtOAc:petrol 1:1); **^{1}H-NMR:** (400 MHz; $CDCl_3$) δ 8.75 (br s, 2H, Py), 7.28-7.45 (m, 7H, Ph, Py), 6.59 (dd, *J* = 15.0, 9.0 Hz, 1H, NCH), 5.06 (s, 2H, $PhCH_2$), 4.57 (d, *J* = 15.0 Hz, 1H, CH=C*H*$_a$H$_b$), 4.31 (d, *J* = 8.5 Hz, 1H, CH=CH$_a$*H*$_b$); **^{13}C-NMR:** (400 Hz, $CDCl_3$) δ 168.4 (C=O), 150.4 (Py), 142.7 (Py), 136.2 (Ph), 133.9 (NCH), 128.5 (Ph), 127.4 (Ph), 126.9 (Ph), 121.9 (Py), 96.5 (CH=*C*H_2), 46.2 (N*C*H_2); **m/z (ES$^+$):** 239.1 (18%, MH^+); **HRMS:** found 239.1180 (MH^+), $C_{15}H_{14}N_2O$ requires 239.1179.

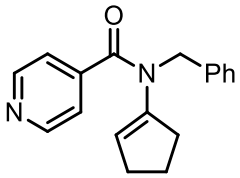
_N_-Benzyl-_N_-isopropenyl-isonicotinamide (1d)



Following general procedure A, benzyl-isoproplidene-amine (2.1 mmol) from benzylamine (0.23 mL) and acetone (0.16 mmol) was acylated with isonicotinoyl chloride (288 mg). After purification, the title compound was yielded as a colourless gum (65% over 2 steps).

***R*$_f$:** 0.30 (EtOAc:petrol 2:1); **IR:** (υmax(film)/cm^{-1}) 1636 (C=O); **^{1}H-NMR:** (400 MHz, $CDCl_3$) δ 8.26 (d, *J* = 5.5 Hz, 2H, Py), 7.35-7.26 (m, 7H, Ar), 4.84 (s, 2H, PhC*H*$_2$), 4.80 (s, 1H,NC=C*H*$_2$), 4.50 (s, 1H, NC=C*H*$_2$), 1.79 (s, 3H, C*H*$_3$); **^{13}C-NMR:** (100 MHz, $CDCl_3$) 168.1 (*C*O), 150.1 (Py), 144.3 (N*C*=CH_2 or Py), 143.5 (N*C*CH_2 or Py), 137.1 (Ph), 128.7 (Ph), 128.5 (Ph), 127.7 (Ph), 121.7 (Py), 116.6 (NC=*C*H_2), 50.1 (PhC*H*$_2$), 21.5 (C*H*$_3$); **m/z (ES$^+$):** 275.1 (100%, MNa^+); **HRMS:** found 275.1161 (MNa^+), $C_{16}H_{16}ON_2Na$ requires 275.1155.

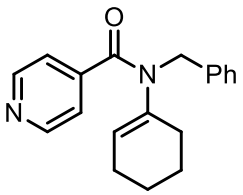
_N_-Benzyl-_N_-cyclopent-1-enyl-isonicotinamide (1e)



Following general procedure A, *N*-cyclopentylidene-1-phenylmethanamine (6.5 mmol) from cyclopentanone (0.42 mL) and benzylamine (0.71 mL) was acylated with isonicotinoyl chloride (1.00 g). After purification, the title compound was yielded as a colourless gum (78% over 2 steps).

***R*$_f$:** 0.38 (2:1 EtOAc:petrol); **IR:** (υmax(film)/cm^{-1}) 1643 (C=O); **^{1}H-NMR:** (400 MHz, $CDCl_3$) δ 8.63 (d, *J* = 8.5 Hz, 2H, Py), 7.38-7.26 (m, 7H, Ar), 5.13 (br s, 1H, NC=C*H*), 4.84 (s, 2H, PhC*H*$_2$), 2.29 (m, 2H, C*H*$_2$), 2.09 (m, 2H, C*H*$_2$) 1.74 (m, 4H, C*H*$_2$); **^{13}C-NMR:** (100 MHz, $CDCl_3$) δ 168.2 (*C*=O), 149.9 (Py), 144.5 (N*C*=CH or Py), 142.2 (N*C*=CH or Py), 137.2 (Ph), 128.6 (Ph), 128.0 (Ph), 127.6 (NC=*C*H), 127.5 (Ph), 121.6 (Py), 50.3 (Ph*C*H_2) 33.2 (*C*H_2), 30.1 (*C*H_2), 22.3 (*C*H_2); **m/z (ES$^+$):** 301.1 (100%, MNa^+); **HRMS:** found 301.1315 (MNa^+), $C_{18}H_{18}ON_2Na$ requires 301.1311.

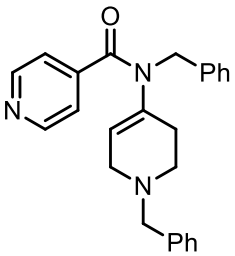
***N*-Benzyl-*N*-cyclohex-1-enyl-isonicotinamide (1f)**



Following general procedure A, *N*-cyclohexylidene-1-phenylmethanamine (1.1 mmol) from cyclohexanone (0.11 mL) and benzylamine (0.12 mL) was acylated with isonicotinoyl chloride (163 mg). After purification the title compound was yielded as a colourless gum (89% over 2 steps).

***R*$_f$:** 0.26 (EtOAc:petrol 3:1); **IR:** (υmax(film)/cm^{-1}) 1640 (C=O); **^{1}H-1H-NMR**(400 MHz, $CDCl_3$) δ 8.61 (d, *J* = 6.0 Hz, 2H, Py), 7.35-7.26 (m, 7H, Ar), 5.21 (m, 1H, NC=C*H*), 4.80 (s, 2H, PhCH_2), 1.93 (m, 2H, CH_2), 1.77 (m, 2H, CH_2), 1.47 (t, *J* = 6.0 Hz, 2H, CH_2), 1.31 (t, *J* = 6.0 Hz, 2H, CH_2); **^{13}C-NMR:** (100 MHz, $CDCl_3$) δ 168.2 (*C*O), 149.7 (Py), 144.8 (N*C*=CH or Py), 137.8 (N*C*=CH or Py), 137.2 (Ph), 129.9 (NC=*C*H), 128.7 (Ph), 128.6 (Ph), 127.6 (Ph), 121.6 (Py), 50.0 (Ph*C*H$_2$), 28.6 (*C*H$_2$), 24.6 (*C*H$_2$), 22.4 (*C*H$_2$), 21.1 (*C*H$_2$); **m/z (ES$^+$):** 293.1 (100%, MH$^+$); **HRMS:** found 315.1477 (MNa$^+$), $C_{19}H_{20}ON_2Na$ requires 315.1468.

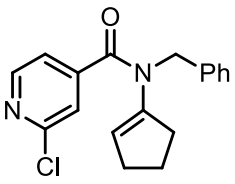
***N*-benzyl-*N*-(1-benzyl-1,2,3,6-tetrahydropyridin-4-yl)isonicotinamide (1g)**



Following general procedure A, *N*-(1-benzylpiperidin-4-ylidene)-1-phenylmethanamine (2.5 mmol) from 1-benzylpiperidin-4-one (0.44 mL) and benzylamine (0.27 mL) was acylated with isonicotinoyl chloride (388 mg). After purification, the title compound was yielded as a colourless gum (42% over 2 steps).

***R*$_f$:** 0.11 (EtOAc:petrol 2:1); **IR:** (υmax(film)/cm^{-1}) 1645 (C=O); **^{1}H-NMR:** (400 MHz, $CDCl_3$) δ 8.57 (dd, *J* = 4.5, 1.5 Hz, 2H, Py), 7.30 (dd, *J* 4.5, 1.5 Hz, 2H, Py), 7.27-7.12 (m, 10H, Ph), 5.10 (br s, 1H, NC=C*H*), 4.75 (s, 2H, PhCH_2), 3.35 (s, 2H, PhCH_2), 2.67 (m, 2H, CH_2), 2.36 (m, *J* = 5.5 Hz, 2H, CH_2), 2.02 (m, 2H, CH_2); **^{13}C-NMR:** (100 MHz, $CDCl_3$) δ 168.1 (*C*=O), 149.8 (Py or N*C*=CH), 144.4 (Py or N*C*=CH), 140.5 (Py), 138.0 (Ph), 137.2 (Ph), 136.5 (Ph), 128.8 (Ph), 128.6 (Ph), 128.4 (Ph), 128.3 (Ph), 127.6 (Ph), 127.2 (NC=*C*H), 121.6 (Py), 61.6 (Ph*C*H$_2$), 51.6 (*C*H$_2$), 49.1 (Ph*C*H$_2$), 29.1 (*C*H$_2$); **m/z (ES$^+$):** 40% (M$^+$ 384), 100% (MNa$^+$ 406); **HRMS:** found 384.2078 (MH$^+$), $C_{25}H_{26}N_3O$ requires 384.2071.

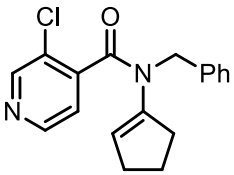
***N*-benzyl-2-chloro-*N*-(cyclopent-1-en-1-yl)isonicotinamide (1h)**



Following general procedure A, *N*-cyclopentylidene-1-phenylmethanamine (2.2 mmol) from cyclopentanone (0.18 mL) and benzylamine (0.31 mL) was acylated with 2-chloroisonicotinoyl chloride (432 mg). The title compound was yielded as a colourless gum after purification (546 mg, 78% over 2 steps).

***R*$_f$:** 0.47 (EtOAc:petrol 1:2); **IR:** (υmax(film)/cm^{-1}) 1648 (C=O); **^{1}H-NMR:** (400 MHz, $CDCl_3$) δ 8.40 (d, *J* = 5.0 Hz, 1H, Py), 7.43 (s, 1H, Py), 7.36-7.28 (m, 6H, Ar), 5.15 (m, 1H, NC=C*H*), 4.83 (s, 2H, PhCH_2), 2.22 (m, 2H, CH_2), 2.13 (m, 2H, CH_2), 1.78 (m, 2H, CH_2); **^{13}C-NMR:** (100 MHz, $CDCl_3$) δ 166.7 (C=O), 151.7 (Py), 149.7 (Py), 147.3 (Py or N*C*=CH), 141.9 (Py or N*C*=CH), 136.8 (Ph), 128.6 (Ph), 128.1 (Ph or NC=*C*H), 127.7 (Ph), 127.4 (Ph or NC=*C*H), 122.5 (Py), 120.4 (Py), 50.3 (Ph*C*H$_2$), 33.1 (*C*H$_2$), 30.1 (*C*H$_2$), 22.3 (*C*H$_2$); **m/z (ES$^+$):** 313 (M(^{35}Cl)$^+$), 315 (M(^{37}Cl)$^+$), 335 (M(^{35}Cl)Na$^+$), 337 (M(^{37}Cl)Na$^+$); **HRMS:** found 335.0923 (MNa$^+$), $C_{18}N_{17}N_2O^{35}ClNa$ requires 335.0923.

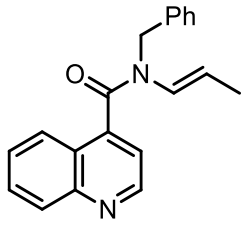
_N_-benzyl-3-chloro-_N_-(cyclopent-1-en-1-yl)isonicotinamide (1i)



Following general procedure A, *N*-cyclopentylidene-1-phenylmethanamine (1.6 mmol) (from cyclopentanone (0.13 mL) and benzylamine (0.23 mL)) was acylated with 3-chloroisonicotinoyl chloride (300 mg). The title compound was yielded as a colourless gum after purification (394 mg, 81% over 2 steps).

***R*$_f$:** 0.28 (EtOAc:petrol 1:1); **IR:** (υmax(film)/cm^{-1}) 1646 (C=O); **^{1}H-NMR:** (400 MHz; $CDCl_3$) δ 8.44 (s, 1H, Py), 8.34 (d, *J* = 5.0 Hz, 1H, Py), 7.22 – 7.12 (m, 5H, Ar), 7.06 (d, *J* = 5.0 Hz, 1H, Ar), 5.06 (t, *J* = 2.0 Hz, 1H, NC=C*H*), 4.72 (s, 2H, PhCH_2), 2.05 (m, 2H, CH_2), 1.86 (m, 2H, CH_2), 1.54 (m, *J* = 7.5 Hz, 2H, CH_2); **^{13}C-NMR:** (100 MHz, $CDCl_3$) δ 165.2 (*C*=O), 149.8 (Py), 147.6 (Py), 144.3 (Py), 140.8 (Py or N*C*=CH), 136.8 (Ph), 128.6 (Py or N*C*=CH), 128.3 (Ph), 128.2 (Ph or NC=*C*H), 128.1 (Ph or NC=*C*H), 127.6 (Ph), 121.7 (Py), 49.2 (Ph*C*H$_2$), 32.6 (*C*H$_2$), 30.1 (*C*H$_2$), 22.2 (*C*H$_2$); **m/z (ES$^+$):** 335 (M(^{35}Cl)Na$^+$), 337(M(^{37}Cl)Na$^+$); **HRMS:** found 313.1104 (MH$^+$), $C_{18}H_{17}N_2O^{35}Cl$ requires 313.1103.

(*E*)-2-Benzyl-1-quinolin-4-yl-pent-3-en-1-one (1j)

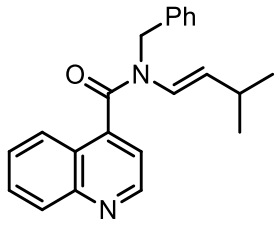


Following general procedure A, benzyl-prop-(*E*)-ylidene amine (1.5 mmol) (from benzylamine (0.17 mL) and propionaldehyde (0.10 mL)) was acylated with quinolone-4-carbonyl chloride (315 mg). The title compound was yielded as a colourless gum after purification (286 mg, 63% over 2 steps).

***R*$_f$:** 0.42 (EtOAc:petrol 1:1); **IR:** (υmax(film)/cm^{-1}) 1643 (C=O); **^{1}H-NMR:** (500 MHz, $CDCl_3$, 2 rotamers (3:1)) δ 9.02 (d, *J* = 4.5 Hz, 1H$_{maj}$, Qu), 8.80 (d, *J* = 4.5 Hz, 1H$_{min}$, Qu), 8.20 (d, *J* = 8.5 Hz, 1H$_{maj}$, Qu), 8.14 (d, *J* = 8.5 Hz, 1H$_{min}$, Qu), 7.85-7.75 (m, 2H$_{maj}$, 2H$_{min}$, Qu,), 7.63-7.58 (m, 1H$_{maj}$, 1H$_{min}$, Qu), 7.44-7.22 (m, 6H$_{maj}$, 4H$_{min}$, Ar), 7.16 (d, *J* = 4.5 Hz, 1H$_{min}$, Ar), 7.04-7.03 (m, 2H$_{min}$, Ar), 6.09 (dd, *J* = 14.0, 1.0 Hz, 1H$_{maj}$, NC*H*=CH), 5.21 (m, 1H$_{min}$, NCH=C*H*), 5.17 (s, 2H$_{maj}$, 2H$_{min}$, PhCH_2,), 5.12 (dq, *J* = 14.0, 6.5 Hz, 1H$_{maj}$, NCH=C*H*,), 1.77 (dd, *J* = 6.5, 1.5 Hz, 3H$_{min}$, CH_3,), 1.38 (dd, *J* = 6.5, 1.5 Hz, 1H$_{maj}$, CH_3,); **^{13}C-NMR:** (125 MHz; $CDCl_3$) δ 167.5 (C=O$_{maj}$), 167.2 (C=O$_{min}$), 150.0 (Qu$_{maj}$), 149.8 (Qu$_{min}$), 148.6 (Qu$_{maj}$), 148.3 (Qu$_{min}$), 141.9 (Qu$_{maj}$), 141.8 (Qu$_{min}$) 136.7 (Ph$_{maj}$), 136.0

(Ph_{min}) 130.2 (Qu_{maj}), 130.2 (Qu_{min}), 130.1 (Qu_{maj}), 130.1 (Qu_{min}) 128.8 (Ar_{maj}), 128.8 (Ar_{min}), 128.1 (N*C*H=CH), 127.9 (Ar_{maj}), 127.8 (Ar_{min}), 127.4 (Ar_{min}), 127.2 (Ar_{maj}), 125.7 (Qu_{maj}), 125.6 (Qu_{min}), 124.9 (Qu_{maj}), 124.7 (Qu_{min}), 124.2 (Qu_{maj}), 124.0 (Qu_{min}) 118.7 (Qu_{maj}), 117.5 (Qu_{min}), 110.9 (NCH=*C*H_{min}), 109.6 (NCH=*C*H_{maj}), 50.6 (Ph*C*H_{2min}), 46.7 (Ph*C*H_{2maj}), 15.6 (*C*H_{3min}), 15.3 (*C*H_{3maj}); **m/z (ES^+):** 303 (20%, MH^+), 325 (100%, MNa^+); **HRMS:** found 303.1468 (MH^+) and 325.1315 (MNa^+), $C_{20}H_{19}ON_2$ requires 303.1468 and $C_{20}H_{18}ON_2Na$ requires 325.1311.

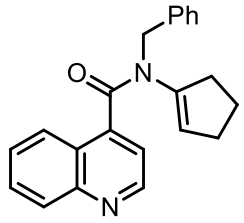
(*E*)-2-Benzyl-5-methyl-1-quinolin-4-yl-hex-3-en-1-one (1k)



Following general procedure A, benzyl-[3-methyl-but-(*E*)-ylidene]-amine (1.6 mmol) from 3-methyl-butraldehyde (0.18 mL) and benzylamine (0.18 mL), was acylated with quinolone-4-carbonyl chloride (336 mg). The title compound was isolated as a by-product as a pale yellow gum (322 mg, 61% over 2 steps).

***R_f* :** 0.43 (EtOAc:petrol 1:1); **IR:** (υmax(film)/cm^{-1}) 1643 (C=O); **^{1}H-NMR:** (500 MHz, $CDCl_3$, 2 rotamers (3:1)) δ 9.0 (d, *J* = 4.5 Hz, $1H_{maj}$, Qu), 8.78 (d, *J* = 4.5 Hz, $1H_{min}$, Qu), 8.18 (d, *J* = 8.5 Hz, $1H_{maj}$, Qu), 8.13 (d, *J* 8.5 Hz, $1H_{min}$, Qu), 7.85-7.75 (m, $2H_{maj}$, $2H_{min}$, Qu), 7.62-7.57 (m, $1H_{maj}$, $1H_{min}$, Qu), 7.41-7.23 (m, $6H_{maj}$, $4H_{min}$, Ar), 7.12 (d, *J* = 4.5 Hz, $1H_{min}$, Ar), 7.02-7.03 (m, $2H_{min}$, Ar), 6.02 (dd, *J* = 14.0, 1.0 Hz, $1H_{maj}$, NC*H*=CH), 5.15 (s, 2H, PhCH_2), 5.13 (dd, *J* = 14.0, 7.0 Hz, $1H_{min}$, NCH=C*H*), 5.11 (dd, *J* = 14.0, 7.0 Hz, $1H_{maj}$, NCH=C*H*), 2.43 (q, *J* = 7.0 Hz, $1H_{min}$, C*H*$(CH_3)_2$), 1.94 (q, *J* = 7.0 Hz, $1H_{maj}$, C*H*$(CH_3)_2$), 1.02 (d, *J* = 6.5 Hz, $6H_{min}$, CH_3), 0.67 (d, *J* = 6.5 Hz, $6H_{maj}$, CH_3); **^{13}C-NMR:** (100 MHz, $CDCl_3$) δ 167.6 (*C*=O_{maj}), 167.4 (C=O_{min}), 149.9 (Qu_{maj}), 149.8 (Qu_{min}), 148.5 (Qu_{maj}), 148.3 (Qu_{min}), 142.0 (Qu_{maj}), 141.9 (Qu_{min}), 136.7 (Ph_{maj}), 136.0 (Ph_{min}), 130.2 (Qu_{maj}) 130.1 (Qu_{maj}), 30.1 (Qu_{min}), 128.7 (Ar_{maj}), 128.7 (Ar_{min}), 127.9 (Ar_{min}), 127.8 (Ar_{maj}), 127.4 (Ar_{min}), 127.4 (Ar_{maj}), 125.8 (Ar_{min}), 125.5 (N*C*H=CH), 125.0 (Ar_{maj}), 124.7 (Ar_{min}), 124.2 (Ar_{maj}), 124.0 (Ar_{min}), 123.5 (Qu_{maj}), 123.4 (Qu_{min}), 122.9 ((*C*)CH$(CH_3)_2$), 118.8 (Qu_{maj}), 117.5 (Qu_{min}), 50.5 (Ph*C*H_{2min}), 47.0 (Ph*C*H_{2maj}), 29.7 (CH$(CH_3)_2$), 29.2 (*C*H$(CH_3)_2$), 22.6 (*C*H_3), 22.5 (*C*H_3); **m/z (ES^+):** 331 (100%, MH^+); **HRMS:** found 331.1808 (MH^+), $C_{22}H_{23}N_2O$ requires 331.1805.

***N*-Benzyl-*N*-cyclopent-1-enyl-2-((1Z,3Z)-penta-1,3-1,3-dienyl)-isonicotinamide (1l)**

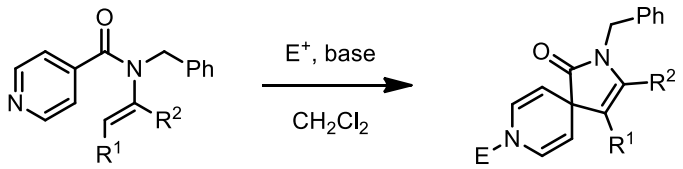


Following general procedure A, benzyl-cyclopentylidene-amine (1.7 mmol) (from cyclopentanone (0.14 mL) and benzylamine (0.24 mL)) was acylated with quinolone-4-carbonyl chloride (357 mg, 1.9 mmol). The title compound was isolated as a by-product as a colourless gum (354 mg, 63%).

***R_f* :** 0.39 (EtOAc:petrol 1:1); **IR:** (υmax(film)/cm^{-1}) 1644 (C=O); **^{1}H-NMR:** (400 MHz, $CDCl_3$, 2 rotamers (8:1)) δ 8.89 (d, *J* = 4.0 Hz, $1H_{maj}$, Qu), 8.84 (m, $1H_{min}$, Qu), 8.12 (d, *J* =

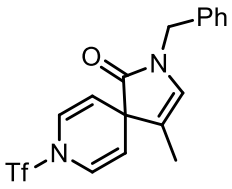
8.0 Hz, 1H$_{maj}$, 1H$_{min}$, Qu), 7.96 (d, J = 8.0 Hz, 1H$_{maj}$, Qu), 7.91 (m, 1H$_{min}$, Qu), 7.74 (dd, J = 7.5, 7.0 Hz, 1H$_{maj}$, 1H$_{min}$, Qu), 7.51 (dd, J = 7.5, 7.0 Hz, 1H$_{maj}$, 1H$_{min}$, Qu), 7.45-7.30 (m, 6H$_{maj}$, 4H$_{min}$, Ar), 7.23 (m, 1H$_{min}$, Ar), 7.03 (m, 1H$_{min}$, Ar), 5.74 (m, 1H$_{min}$, NC=C*H*), 5.02 (s, 1H$_{maj}$, NC=C*H*), 4.99 (s, 2H$_{maj}$, PhC*H*$_2$), 4.56 (m, 2H$_{min}$, PhC*H*$_2$), 2.87 (m, 2H$_{min}$, C*H*$_2$), 2.40 (m, 2H$_{min}$, C*H*$_2$), 2.07 (m, 2H$_{maj}$, C*H*$_2$), 1.98 (m, 2H$_{min}$, C*H*$_2$), 1.84 (m, 2H$_{maj}$, C*H*$_2$), 1.55 (m, 2H$_{maj}$, C*H*$_2$); **^{13}C-NMR:** (100 MHz, $CDCl_3$, only 1 rotamer observed): 167.7 (C=O), 149.5 (Qu), 148.3 (N*C*=CH), 143.4 (Qu), 141.5 (Qu), 137.3 (Ph), 129.9 (Qu), 129.8 (Qu), 128.6 (Ph), 128.3 (Ph), 127.6 (Qu), 127.6 (NC=*C*H), 127.4 (Ar), 125.2 (Qu), 124.9 (Qu) 117.8 (Qu), 49.7 (Ph*C*H$_2$), 32.8 (*C*H$_2$), 30.0 (*C*H$_2$), 22.2 (*C*H$_2$); **m/z (ES$^+$):** 351 (100%, MNa$^+$); **HRMS:** found 329.1657 (MH$^+$), $C_{22}H_{20}ON_2$ requires 329.1649.

General Procedure B for Dearomatising Cyclisations



Cyclisation precursor was dissolved in dichloromethane (0.05M). The solution was cooled to 0 °C and 2,6-lutidine *or* 2,6-di-tert-butyl-4-methylpyridine (1-3 eqiuv.) and triflic anhydride *or* methylchloroformate *or* 2,2,2-trichloroethylchloroformate *or* (*1R*)-(-)-menthyl chloroformate (1 equiv.) were added sequentially. After 30 minutes the solution was quenched by saturated sodium hydrogen carbonate solution (0.2M) and extracted twice using dichloromethane (0.2M). Organic layers were dried with $MgSO_4$, filtered and evaporated under reduced pressure. The residue was purified by flash chromatography (SiO_2, EtOAc:petrol 1:19) to yield the spirocyclic dihydropyridine.

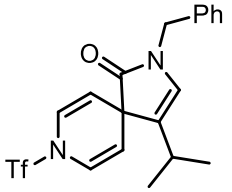
2-Benzyl-4-methyl-1-oxo-2,8-diaza-spiro [4.5] deca-3,6,9-triene-8-carboxylic acid trifluoro-methyl ester (2a)



Following general procedure B, the title compound was obtained from *N*-benzyl-*N*-((*E*)-propenyl)-isonicotinamide **1a** (0.41 mmol) using 2,6-di-*tert*-butyl-4-methylpyridine (1.23 mmol) after purification as an amorphous solid (59%).

***R*$_f$:** 0.68 (EtOAc:petrol 1:2); **IR:** (υmax(film)/cm^{-1}) 1701 (C=O); **^{1}H-NMR:** (400 MHz, $CDCl_3$) δ 7.38-7.23 (m, 5H, Ph), 6.84 (d, *J* = 8.0 Hz, 2H, NC*H*=CH), 5.96 (s, 1H, NC*H*), 4.83 (d, *J* = 8.0 Hz, 2H, NCH=C*H*), 4.58 (s, 2H, PhCH_2), 1.66 (s, 3H, CH_3); **^{13}C-NMR:** (100 MHz; $CDCl_3$) δ 178.5 (*C*O), 136.2 (Ph), 132.9 ((*C*)CH_3), 128.9 (Ph), 128.0 (Ph), 127.8 (Ph), 124.8 (N*C*H), 124.3 (N*C*H=CH), 108.3 (NCH=*C*H), 52.2 (*C*), 46.0 (Ph*C*H_2), 10.7 (*C*H_3); **m/z (ES$^+$):** 385.1 (100%, MH$^+$), 407.1 (30%, HNa$^+$); **HRMS:** found 407.0648 (MNa$^+$), $C_{17}H_{15}N_2O_3F_3SNa$ requires 407.0647.

2-Benzyl-4-isopropyl-1-oxo-2,8-diaza-spiro[4.5]deca-3,6,9-triene-8-carboxylic acid trifluoro-methyl ester (2b)

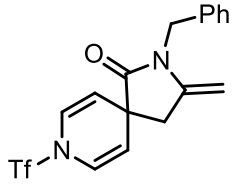


Following general procedure B, the title compound was obtained from *N*-benzyl-*N*-((*E*)-3-methyl-but-1-enyl)-isonicotinamide **1b** (0.41 mmol) using 2,6-di-*tert*-butyl-4-methylpyridine (1.23 mmol) as white amorphous solid after purification (49%).

***R*$_f$:** 0.70 (EtOAc:petrol 1:2); **IR:** (υmax(film)/cm^{-1}) 1698 (C=O); **^{1}H-NMR:** (400 MHz, $CDCl_3$) δ 7.32-7.14 (m, 5H, Ph), 6.72 (d, *J* = 8.0 Hz, 2H, NC*H*=CH), 5.88 (d, *J* = 1.5 Hz, 1H, NC*H*), 4.78 (d, *J* = 8.0 Hz, 2H, NCH=C*H*), 4.50 (s, 2H, PhCH_2), 2.30 (dq,

J = 7.0, 1.5 Hz 1H, C*H*), 0.98 (d, *J* = 7.0 Hz, 6H, CH_3); **^{13}C-NMR:** (100 MHz, $CDCl_3$) δ 178.1 (*C*=O), 136.2 (Ph), 134.1 ((*C*)CH_3), 128.9 (Ph), 127.9 (Ph), 127.8 (Ph), 124.4 (NCH), 123.8 (N*C*H=CH), 109.4 (NCH=*C*H), 52.4 (*C*), 46.1 (Ph*C*H_2), 26.1 (*C*H(CH_3)$_2$), 22.5 (2 × *C*H_3); **m/z (ES$^+$):** 413.4 (5%, MH^+), 435.2 (100%, MNa^+); **HRMS:** found 453.0934 (MNa^+), $C_{19}H_{19}N_2O_3SF_3Na$ requires 435.0936.

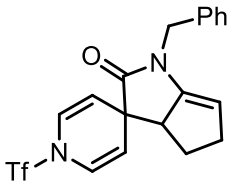
3-Methylene-8-trifluoromethanesulfonyl-1,8-diaza-spiro[4.5]deca-6,9-diene-2-one (2d)



Following general procedure B, the title compound was obatained from *N*-benzyl-*N*-isopropenyl-isonicotinamide **1d** (0.55 mmol), using 2,6-di-*tert*-butyl-4-methylpyridine (0.55 mmol), as a white amorphous solid after purification (74%).

***R*$_f$:** 0.89 (EtOAc:petrol 1:1); **IR:** (υmax(film)/cm^{-1}) 1685 (C=O); **^{1}H-NMR:** (400 MHz, $CDCl_3$) δ 7.29-7.13 (m, 5H, Ph), 6.62 (d, *J* = 8.5 Hz, 2H, NC*H*=CH), 4.98 (d, *J* = 8.5 Hz, 2H, NC*H*=CH), 4.63 (s, 2H, PhCH_2), 4.26 (dd, *J* = 8.5, 2.0 Hz, 1H, NC=CH_2), 4.14 (m, 1H, NC=CH_2), 2.65 (s, 2H, CH_2); **^{13}C-NMR:** (100 MHz, $CDCl_3$) δ 178.2 (C=O), 141.8 (N(*C*)=CH_2), 135.7 (Ph), 128.8 (Ph), 127.7 (Ph), 127.3 (Ph), 124.3, 122.7 (N*C*H=CH), 110.8 (NCH=*C*H), 87.6 (NC=*C*H_2), 44.4 (*C*), 43.8 (Ph*C*H_2), 42.9 (*C*H_2); **m/z (ES$^+$):** 407.2 (100%, MNa^+); **HRMS:** found 407.0641 (MNa^+), $C_{17}H_{15}O_3N_2F_3NaS$ requires 407.0648.

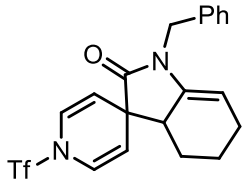
1-Benzyl-1'-(trifluoromethylsulfonyl)-4,5-dihydro-1H,1'Hspiro[cyclopenta[b]pyrrole -3,4'-pyridin]-2(3aH)-one (2e)



Following procedure B, the title compound was obtained from *N*-benzyl-cyclopent-1-enyl-isonicotinamide **1e** (0.47 mmol), using 2,6-di-*tert*-butyl-4-methylpyridine (1.41 mmol), as a whit amorphous solid after purification (77%).

***R*$_f$:** 0.75 (EtOAc:petrol 1:2); **IR:** (υmax(film)/cm^{-1}) 1676 (C=O); **^{1}H-NMR:** (400 MHz, $CDCl_3$) δ 7.29 (m, 5H, Ph), 6.69 (d, *J* = 8.5 Hz, 1H, NC*H*=CH), 6.63 (d, *J* = 8.5 Hz, 1H, NC*H*=CH), 5.01 (dd, *J* = 8.5, 2.0 Hz, 1H, NCH=C*H*), 4.82 (dd, *J* = 8.5, 2.0 Hz, 1H, NCH=C*H*), 4.66 (dd, *J* = 3.0, 1.5 Hz, 1H, NC=C*H*), 4.57 (d, *J* = 15.0 Hz, 1H, PhCH_2), 4.53 (d, *J* = 15.0 Hz, 1H, PhCH_2), 2.83 (dt, *J* = 8.0, 2.0 Hz, 1H, C*H*), 2.50-2.35 (m, 2H, CH_2), 1.79 (m, 1H, CH_2), 1.56 (m, 1H, CH_2); **^{13}C-NMR:** (100 MHz, $CDCl_3$) δ 177.4 (C=O), 143.4 (N(*C*)=CH), 135.9 (Ph), 128.7 (Ph), 127.9 (Ph), 127.8 (Ph), 123.7 (N*C*H=CH), 123.4 (N*C*H=CH), 111.7 (NCH=*C*H), 107.3 (NCH=*C*H), 98.8 (N(C)=*C*H), 55.4 (*C*), 48.7 (*C*H), 45.9 (Ph*C*H_2), 33.0 (*C*H_2), 23.8 (*C*H_2); **m/z (ES$^+$):** 433.3 (100%, MNa^+); **HRMS:** found 433.0811 (MNa^+), $C_{19}H_{17}O_3N_2F_3NaS$ requires 433.0804.

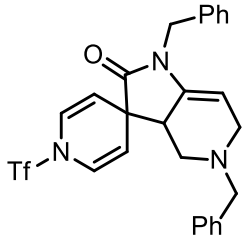
1-Benzyl-1'-(trifluoromethylsulfonyl)-4,5-dihydro-1H,1'Hspiro[cyclohexa[b]pyrrole-3,4'-pyridin]-2(3aH)-one (2f)



Following general procedure B, the title compound was obtained from *N*-benzyl-*N*-cyclohex-1-enyl-isonicotinamide **1f** (0.77 mmol), using 2,6-di-*tert*-butyl-4-methylpyridine (0.77 mmol), as a white amorphous solid after purification (81%).

***R*$_f$:** 0.85 (EtOAc: petrol 1:1); **IR:** (υmax(film)/cm^{-1}) 1678 (C=O); **^{1}H-NMR:** (400 MHz, $CDCl_3$) δ 7.27-7.15 (m, 5H, Ph), 6.72 (dd, *J* = 8.5, 1.0 Hz, 1H, NC*H*=CH), 6.59 (dd, *J* = 8.5, 1.0 Hz, 1H, NC*H*=CH), 4.98 (dd, *J* = 8.5, 2.5 Hz, 1H, NCH=C*H*), 4.95 (dt, *J* = 5.0, 2.5 Hz, 1H, NC=C*H*), 4.86 (d, *J* = 8.5, 2.5 Hz, 1H, NCH=C*H*), 4.60 (d *J* = 15.0 Hz, 1H, PhCH_2) 4.55 (d, *J* = 15.0 Hz, 1H, PhCH_2), 2.36 (m, 1H, C*H*), 2.04-1.97 (m, 2H, CH_2), 1.85 (m, 1H, CH_2), 1.68 (m, 1H, CH_2), 1.43 (m, 1H, CH_2), 1.31 (m, 1H, CH_2); **^{13}C-NMR:** (100 MHz, $CDCl_3$) δ 174.0 (*C*=O), 137.5 (N(*C*)=CH), 136.3 (Ph), 128.7 (Ph), 127.6 (Ph), 127.4 (Ph), 124.2 (N*C*H=CH), 123.1 (N*C*H=CH), 110.8 (NCH=*C*H), 108.2 (NCH=*C*H), 101.0 (N(C)=*C*H), 48.4 (*C*), 47.4 (*C*H), 44.2 (Ph*C*H$_2$), 23.3 (*C*H$_2$), 22.4 (*C*H$_2$), 21.7 (*C*H$_2$); **m/z (ES$^+$):** 447.0 (20%, MNa$^+$); **HRMS:** found 447.0972 (MNa$^+$), $C_{20}H_{19}N_2O_3F_3SNa$ requires 447.0961.

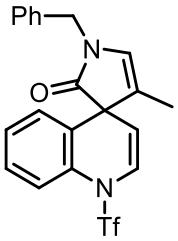
1',5'-Dibenzyl-1-((trifluoromethyl)sulfonyl)-3a',4',5',6'-tetrahydro-1H-spiro[pyridine-4,3'-pyrrolo[3,2-c]pyridin]-2'(1'H)-one (2g)



Following general procedure B, the title compound was obtained from *N*-benzyl-*N*-(1-benzyl-1,2,3,6-tetrahydropyridin-4-yl)isonicotin-amide **1g** (0.27 mmol), using 2,6-lutidine (0.27 mmol), as a white amorphous solid after purification (38%).

***R*$_f$:** (EtOAc:Petrol 1:1): 0.90; **IR:** (υmax(film)/cm^{-1}) 1699 (C=O); **^{1}H-NMR:** (400 MHz, $CDCl_3$) δ 7.33-7.21 (m, 10H, Ph), 6.75 (d, *J* = 8.0 Hz, 1H, NC*H*=CH), 6.61 (d, *J* = 8.0 Hz, 1H, NC*H*=CH), 5.05 (dd, *J* = 8.0, 2.0 Hz, 1H, NCH=C*H*), 4.93 (ap t, *J* = 2.0 Hz, 1H, NC=C*H*), 4.88 (dd, *J* = 8.0, 2.0 Hz, 1H, NCH=C*H*), 4.67 (d, *J* = 15.0 Hz, 1H, PhCH_2), 4.50 (d, *J* = 15.0 Hz, 1H, PhCH_2), 3.66 (d, *J* = 13.0 Hz, 1H, PhCH_2), 3.58 (d, *J* = 13.0 Hz, 1H, PhCH_2), 3.34 (ap dt, *J* = 15.5, 2.0 Hz, 1H, NC=CHCH_2), 2.90 (dd, *J* = 10.0, 4.5 Hz, 1H, CHCH_2), 2.82 (ap dt, *J* = 15.5, 2.0 Hz, 1H, NC=CHCH_2), 2.74 (m, 1H, CHCH_2), 2.23 (t, *J* = 10.0 Hz, 1H, C*H*); **^{13}C-NMR:** (125 MHz, $CDCl_3$) δ 173.8 (*C*=O), 137.6 (N*C*=CH), 136.5 (Ph), 136.0 (Ph), 129.0 (Ph), 128.8 (Ph), 128.4 (Ph), 127.7 (Ph), 127.5 (Ph), 127.4 (Ph), 124.4 (N*C*H=CH), 123.1 (N*C*H=CH), 110.6 (NCH=*C*H), 107.5 (NCH=*C*H), 99.0 (NC=*C*H), 62.4 (Ph*C*H$_2$), 51.4 (*C*H$_2$), 49.4 (*C*), 47.5 (*C*H$_2$), 47.0 (*C*H), 44.5 (Ph*C*H$_2$); **m/z (ES$^-$):** 550 (50% M^{35}Cl$^-$). Mass cannot be seen in ES$^+$.

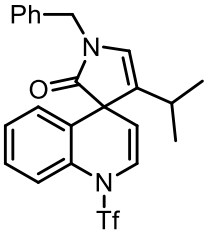
1-Benzyl-4-methyl-1'-(trifluoromethane)sulfonyl-1,2-dihyro-1'H-spiro{pyrrole-3,4'-quinoline]-2-one (2j)



Following general procedure B, the title compound was obtained from (*E*)-2-benzyl-1-quinolin-4-yl-pent-3-en-1-one **1j** (0.36 mmol) using 2,6-di-*tert*-butyl-4-methylpyridine (0.36 mmol), as a pale yellow gum after purification (87 mg, 56%).

R_f **:** 0.81 (EtOAc:petrol 1:1); **IR:** (υmax(film)/cm^{-1}) 1706 (C=O); **^{1}H-NMR:** (300 MHz, $CDCl_3$) δ 7.95 (d, *J* = 8.5 Hz, 1H, Ph), 7.42-7.18 (m, 7H, Ph), 7.09 (d, *J* = 8.0 Hz, 1H, NC*H*=CH), 6.86 (dd, *J* = 7.5, 1.5 Hz, 1H, Ph), 6.14 (d, *J* = 1.5 Hz, 1H, NC*H*), 5.12 (d, *J* = 8.0 Hz, 1H, NCH=C*H*), 4.69 (d, *J* = 15.0 Hz, 1H, PhCH_2), 4.55 (d, *J* = 15.0 Hz, 1H, PhCH_2), 1.58 (d, *J* = 1.5 Hz, 3H, CH_3); **^{13}C-NMR:** (75 MHz, $CDCl_3$) δ 178.3 (*C*=O), 136.4 (Ph), 133.9 (NCH=(*C*)Me), 129.0 (Ph), 128.7 (Ph), 128.0 (Ph), 127.9 (Ph), 127.4 (Ph), 127.3 (Ph), 127.2 (NC*H*=CH), 126.0 (Ph), 125.2 (NC*H*), 123.9 (Ph), 120.3 (Ph), 111.3 (NCH=*C*H), 55.8 (*C*), 46.0 (Ph*C*H$_2$), 10.7 (*C*H$_3$); **m/z (ES$^+$):** 435 (20%, MH$^+$), 457 (100%, MNa$^+$); **HRMS:** found 435.0972 (MH$^+$), $C_{21}H_{18}N_2O_3F_3S$ requires 435.0985.

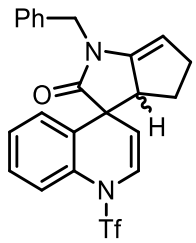
1-Benzyl-4-(propan-2-yl)-1'-(trifluoromethane)sulfonyl-1,2-dihyro-1'H-spiro{pyrrole-3,4'-quinoline]-2-one (2k)



Following general procedure B, the title compound was obtained from (*E*)-2-benzyl-5-methyl-1-quinolin-4-yl-hex-3-en-1-one **1k** (0.23 mmol) and 2,6-di-*tert*-butyl-4-methylpyridine (0.23 mmol), as an orange gum after purification (58 mg, 53%).

R_f **:** 0.72 (EtOAc:petrol 1:2); **IR:** (υmax(film)/cm^{-1}) 1710 (C=O); **^{1}H-NMR:** (500 MHz, $CDCl_3$) δ 7.96 (d, *J* = 8.0 Hz, 1H, Ph), 7.40-7.27 (m, 6H, Ph), 7.18 (dd, *J* = 8.0, 1.0 Hz, 1H, Ph), 7.07 (d, *J* = 8.0 Hz, 1H, NC*H*=CH), 6.85 (dd, *J* = 8.0, 1.5 Hz, 1H, Ph), 6.15 (d, *J* = 1.5 Hz, 1H, NC*H*), 5.12 (d, *J* = 8.0 Hz, 1H, NCH=C*H*), 4.70 (d, *J* = 15.0 Hz, 1H, PhCH_2), 4.55 (d, *J* = 15.0 Hz, 1H, PhCH_2), 2.23 (dq, *J* = 7.0, 1.5 Hz, 1H, C*H*(CH$_3$)$_2$), 0.94 (d, *J* = 6.5 Hz, 3H, CH_3), 0.73 (d, *J* = 6.5 Hz, 3H, CH_3); **^{13}C-NMR:** (125 MHz, $CDCl_3$): 178.3 (*C*=O), 136.4 (Ph), 135.2 (Ph or (*C*)CH(CH$_3$)$_2$), 133.6 (Ph or (*C*)CH(CH$_3$)$_2$),), 129.0 (Ph), 128.8 (Ph), 128.0 (Ph), 127.9 (Ph), 127.8 (Ph), 127.0 (Ph), 126.4 (NC*H*=CH), 125.4 (Ph), 125.3 (N*C*H), 120.1 (Ph), 111.3 (NCH=C*H*), 55.8 (*C*), 46.1 (Ph*C*H$_2$), 26.1 (*C*H(CH$_3$)$_2$), 22.7 (CH(*C*H$_3$)$_2$), 22.1 (CH(*C*H$_3$)$_2$); **m/z (ES):** 463 (80%, MH$^+$), 480 (100%, MNa$^+$); **HRMS:** found 463.1288 (MH$^+$), $C_{23}H_{22}O_3F_3S$ requires 463.1298.

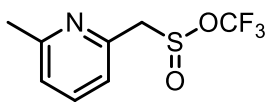
3-Benzyl-1'-(trifluoromethane)sulfonyl-1,2-dihydro-1'H,2H-spiro[cyclopenta[b]pyrrole-1,4'-quinoline]-2-one (2l)



Following general procedure B, the title compound was obtained from *N*-benzyl-*N*-cyclopent-1-enyl-2-((*1Z*,*3Z*)-penta-1,3-1,3-dienyl)-isonicotinamide **1l** (0.37 mmol) (using and 2,6-lutidine (0.37 mmol) as an unstable orange gum, containing 2 diastereoisomers (122 mg, 72%, d.r. 3:2).

***R*$_f$:** 0.92 (EtOAc:petrol 1:1); **IR:** (υmax(film)/cm^{-1}) 1673 (C=O); **^{1}H-NMR:** (400 MHz, $CDCl_3$, tentatively assigned due to compound's instability) δ 7.87 (m, 1H$_{maj}$, Qu), 7.84 (m, 1H$_{min}$, Qu), 7.38-7.31 (m, 9H$_{maj}$, 7H$_{min}$, Ar), 7.19 (m, 1H$_{maj}$, Qu), 7.17 (m, 1H$_{min}$, Qu), 7.08 (m, 1H$_{min}$, Qu), 6.98 (d, *J* = 8.0 Hz, 1H$_{maj}$, NC*H*=CH), 6.94 (d, *J* = 8.0 Hz, 1H$_{min}$, NC*H*=CH), 6.58 (m, 1H$_{min}$, Qu), 5.62 (d, *J* = 8.0 Hz, 1H$_{min}$, NCH=C*H*), 5.09 (m, 1H$_{maj}$, NCH=C*H*), 4.89 (m, 1H$_{min}$, C*H*), 4.83 (d, *J* = 15.0 Hz, 1H$_{min}$, PhCH_2), 4.81 (m, 1H, C*H*), 4.79 (d, *J* = 15.0 Hz, 1H$_{maj}$, PhCH_2), 4.75 (d, *J* = 15.0 Hz, 1H$_{min}$, PhCH_2), 4.68 (d, *J* = 15.0 Hz, 1H$_{maj}$, PhCH_2), 3.35 (m, 1H$_{maj}$, NC=C*H*), 3.16 (m, 1H$_{min}$, NC=C*H*), 2.50 (m, 2H$_{maj}$, CH_2), 2.33 (m, 2H$_{min}$, CH_2), 1.85 (m, 1H$_{maj}$, CH_2), 1.76-1.58 (m, 1H$_{maj}$, 2H$_{min}$, CH_2); **^{13}C-NMR:** (100 MHz, $CDCl_3$): 177.8 (*C*=O), 143.5 (Ar), 136.0 (Ar), 133.9 (Ar), 128.8 (Ar), 128.8 (Ar), 128.7 (Ar), 128.3 (Ar), 127.9 (Ar),127.3 (Ar), 126.6 (N*C*H=CH), 120.0 (Ar), 111.0 (NCH=*C*H), 98.7 (*C*H), 57.5 (NC=*C*H), 52.8 (*C*), 46.1 (Ph*C*H$_2$), 33.0 (*C*H$_2$), 24.9 (*C*H$_2$); **m/z (ES$^+$):** 943 (100%, 2MNa$^+$); **HRMS:** found 483.0967 (MNa$^+$), $C_{23}H_{19}O_3N_2F_3NaS$ requires 483.0961.

Trifluoro-methanesulfonic acid-6-methyl pyridine-2-ylmethyl ester (5)

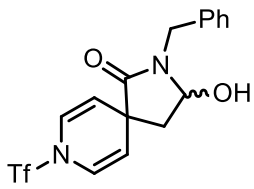


Following general procedure B, the title compound was obtained from *N*-benzyl-*N*-((*E*)-propenyl)-isonicotinamide **1a** (0.45 mmol), using 2,6-lutidine (0.45 mmol), as a by-product. The yield was not calculated.

***R*$_f$:** 0.72 (EtOAc: petrol 1:2); **^{1}H-NMR:** (300 MHz, $CDCl_3$) δ 7.57 (t, *J* = 7.5 Hz, 1H, Py), 7.17 (d, *J* = 7.5 Hz, 1H, Py), 7.10 (d, *J* = 7.5 Hz, 1H, Py), 5.34 (d, *J* = 12.5 Hz, 1H, CH_2), 5.10 (d, *J* = 12.5 Hz, 1H, CH_2), 2.52 (s, *J* = 2.5 Hz, 3H, CH_3); **^{13}C-NMR:** (75 MHz, $CDCl_3$) δ 158.6 (Ar), 153.11 (Ar), 137.4 (Ar), 123.4 (Ar), 119.1 (Ar), 70.2 (*C*H_2OSOCF_3), 24.3 (*C*H_3); **m/z (ES):** 262.0 (100%, MNa$^+$), 501.1 (10%, M_2Na$^+$); **HRMS:** found 262.0129 (MNa$^+$), $C_8H_8F_3NO_2SNa$ requires 262.0126. All data is in accordance with those previously reported.[2]

[2] Binkley, R. W.; Ambrose, M. G., *J. Org. Chem*., **1983**, *48*, 1776.

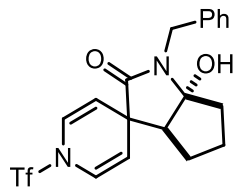
2-Benzyl-3-hydroxy-8-((trifluoromethyl)sulfonyl)-2,8-diazaspiro[4.5]deca-6,9-dien-1-one (6c)



Following general procedure B, the title compound was obtained from *N*-benzyl-*N*-vinylisonicotinamide **1c** (0.18 mmol) (using 2,6-lutidine (0.18 mmol)) compound as a colourless oil (0.034 g, 49%).

***R*$_f$:** 0.56 (EtOAc:hexane 1:1); **IR:** (υmax(film)/cm^{-1}) 3356 (OH), 1674 (C=O); **^{1}H-NMR:** (400 MHz, $CDCl_3$) δ 7.25-7.36 (m, 5H, Ph), 6.67 (dd, *J* = 8.5, 1.0 Hz, 1H, NC*H*=CH), 6.58 (dd, *J* = 8.5, 1.0 Hz, 1H, NC*H*=CH), 5.27 (dd, *J* = 8.5, 1.0 Hz, 1H, NCH=C*H*), 5.08 (dd, *J* = 6.0, 2.0 Hz, 1H, C*H*OH), 4.87 (dd, *J* = 8.5, 1.0 Hz, 1H, NCH=C*H*), 4.79 (d, *J* 15.0, 1H, PhCH_2), 4.26 (d, *J* 15.0, 1H, PhCH_2), 3.29 (1H, br s, OH), 2.17 (1H, dd, 14.0, 6.0, CH_2), 2.03 (1H, dd, 14.0, 2.0, CH_2); **^{13}C-NMR:** (400 MHz, $CDCl_3$) δ 174.0 (C=O), 136.0 (Ph), 129.0 (Ph), 128.3 (Ph), 128.0 (Ph), 123.1 (N*C*H=CH), 121.7 (N*C*H=CH), 112.6 (NCH=*C*H), 111.3 (NCH=*C*H), 79.6 (N*C*HOH), 46.1, (*C*H_2), 44.4 (Ph*C*H_2), 44.1 (C); **m/z (ES$^+$):** 389.0 (100%, MH$^+$); **HRMS:** found 389.0769 (MH$^+$), $C_{16}H_{15}N_2O_4F_3S$ requires 389.0777.

1-Benzyl-6a-hydroxy-1'-((trifluoromethyl)sulfonyl)-4,5,6,6a-tetrahydro-1H,1'H-spiro[cyclopenta[b]pyrrole-3,4'-pyridin]-2(3aH)-one (6e)



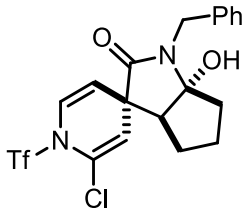
Following procedure B, the title compound was obtained from *N*-benzyl-cyclopent-1-enyl-isonicotinamide **1e** (0.53 mmol), using 2, *tert*-butyl-4-methylpyridine (0.53 mmol), as a white solid after purification (76%).

***R*$_f$:** 0.37 (EtOAc:petrol 1:2); **m.p:** 167-169 °C (EtOAc); **IR:** (υmax(film)/cm^{-1}) 3350 (O-H), 1667 (C=O); **^{1}H-NMR:** (300 MHz, $CDCl_3$) δ 7.36-7.29 (m, 5H, Ph), 6.77 (d, *J* = 8.5 Hz, 1H, NC*H*=CH), 6.58 (d, *J* = 8.5 Hz, 1H, NC*H*=CH), 5.23 (dd, *J* = 8.5, 2.5 Hz, 1H, NCH=C*H*), 4.98 (dd, *J* = 8.5, 2.5 Hz, 1H, NCH=C*H*), 4.66 (d, *J* = 15.0 Hz, 1H, PhCH_2), 4.46 (d, *J* = 15.0 Hz, 1H, PhCH_2), 2.30 (dd, *J* = 8.5, 7.0 Hz, 1H, C*H*), 2.25 (s, 1H, O*H*), 1.90 (m, 2H, CH_2), 1.77 (m, 2H, CH_2), 1.57 (m, 2H, CH_2); **^{13}C-NMR:** (75 MHz, $CDCl_3$) δ 174.2 (*C*=O), 137.8 (Ph), 128.9 (Ph), 128.2 (Ph), 127.8 (Ph), 123.7 (N*C*H=CH), 121.1 (N*C*H=CH), 113.7 (NCH=*C*H), 108.7 (NCH=*C*H), 99.2 (*C*), 59.7 (*C*OH), 46.3 (*C*H), 43.7 (Ph*C*H_2), 38.4 (*C*H_2), 26.2 (*C*H_2), 24.6 (*C*H_2); **m/z (ES$^+$):** 429 (50%, MH$^+$), 451 (100%, MNa$^+$); **HRMS:** found 429.1097 (MH$^+$), $C_{19}H_{20}N_2O_4F_3S$ requires 429.1091.

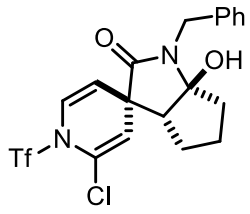
1-Benzyl-2'-chloro-6a-hydroxy-1'-((trifluoromethyl)sulfonyl)-4,5,6,6a-tetrahydro-1H,1'H-spiro[cyclopenta[b]pyrrole-3,4'-pyridin]-2(3aH)-one (6h)

Following general procedure B, the triene compound was obtained from *N*-benzyl-2-chloro-*N*-(cyclopent-1-en-1-yl)isonicotinamide **1h** (0.65 mmol) using 2,6-lutidine (0.76 mL, 0.65 mmol). The resultant gum (after removal of the solvent) was stirred in 1M HCl/diethylether

(3.25 mL). The title compound was yielded as a mixture of diastereoisomers (A:B) and isolated as a white solid (217 mg, 73% combined yield, d.r. 1:1).



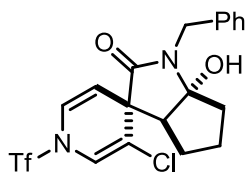
Diastereoisomer A (6h): R_f **:** 0.44 (EtOAc:petrol 1:2); **IR:** (υmax(film)/cm^{-1}) 3338 (O-H), 1668 (C=O); **^{1}H-NMR:** (400 MHz, $CDCl_3$) δ 7.35-7.29 (m, 5H, Ar), 6.81 (d, *J* = 7.5 Hz, 1H, NC*H*=CH), 5.59 (d, *J* = 2.0 Hz, 1H, NCCl=C*H*), 5.21 (d, *J* = 7.5, 2.0 Hz, 1H, NCH=C*H*), 4.60 (d, *J* = 15.0 Hz, 1H, PhCH_2), 4.46 (d, *J* = 15.0 Hz, 1H, PhCH_2), 2.60 (s, 1H, O*H*), 2.36 (dd, *J* = 9.0, 7.0 Hz, 1H, C*H*COH), 1.93 (m, 2H, CH_2), 1.74 (m, 2H, CH_2), 1.53 (m, 2H, CH_2); **^{13}C-NMR** (100 MHz, $CDCl_3$) δ 173.5 (*C*=O), 137.5 (Ph), 128.9 (Ph), 128.1 (Ph), 127.9 (N*C*Cl=CH), 127.6 (Ph), 123.6 (N*C*H=CH), 118.5 (NCCl=*C*H), 112.4 (NCH=*C*H), 99.4 (*C*), 58.2 (*C*OH), 49.3 (*C*H), 43.7 (Ph*C*H_2), 38.1 (*C*H_2), 26.7 (*C*H_2), 24.4 (*C*H_2); **m/z (ES$^+$):** 485 (M(^{35}Cl)Na$^+$), 487 (M(^{37}Cl)Na$^+$); **HRMS:** found 463.0694 (M(^{35}Cl)H$^+$), $C_{19}H_{18}N_2O_4F_3{}^{35}ClS$ requires 463.0701.



Diastereoisomer B (6h'): R_f **:** 0.36 (EtOAc:petrol 1:2); **IR:** (υmax(film)/cm^{-1}) 3338 (O-H), 1669 (C=O); **^{1}H-NMR:** (400 MHz, $CDCl_3$) δ 7.34-7.28 (m, 5H, Ph), 6.64 (d, *J* = 7.5 Hz, 1H, NC*H*=CH), 5.48 (dd, *J* = 7.5, 2.0 Hz, 1H, NCCl=C*H*), 5.40 (d, *J* = 2.0 Hz, 1H, NCH=C*H*), 4.66 (d, *J* = 15.0 Hz, 1H, PhCH_2), 4.43 (d, *J* = 15.0 Hz, 1H, PhCH_2), 2.33 (dd, *J* = 9.0, 7.0 Hz, 1H, C*H*), 2.29 (s, 1H, OH), 1.94 (m, 2H, CH_2), 1.76 (m, 2H, CH_2), 1.53 (m, 2H, CH_2); **^{13}C-NMR:** (100 MHz, $CDCl_3$) δ 173.4 (*C*=O), 137.5 (Ph), 129.0 (Ph), 128.1 (Ph), 127.9 (Ph), 125.4 (N*C*Cl=CH), 125.1 (N*C*H=CH), 117.5 (NCCl=*C*H), 114.6 (NCH=*C*H), 99.4 (*C*), 58.4 (*C*OH), 49.5 (*C*H), 43.7 (Ph*C*H_2), 38.2 (*C*H_2), 27.0 (*C*H_2), 24.3 (*C*H_2); **m/z (ES):** 485 (M(^{35}Cl)Na$^+$), 487 (M(^{37}Cl)Na$^+$); **HRMS:** found 463.0694 (M(^{35}Cl)H$^+$), $C_{19}H_{18}N_2O_4F_3{}^{35}ClS$ requires 463.0701.

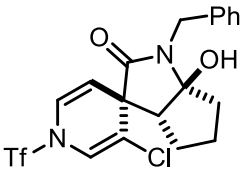
1-Benzyl-3'-chloro-6a-hydroxy-1'-((trifluoromethyl)sulfonyl)-4,5,6,6a-tetrahydro-1H,1'H-spiro[cyclopenta[b]pyrrole-3,4'-pyridin]-2(3aH)-one (6i)

Following general procedure B, the triene compound was obtained from *N*-benzyl-3-chloro-*N*-(cyclopent-1-en-1-yl)isonicotinamide **1i** (1.6 mmol) and 2,6-lutidine (1.6 mmol). The resultant gum (after removal of the solvent) was stirred in 1M HCl/diethylether (4.80 mL). The title compound was yielded as a mixture of diastereoisomers (A:B) and isolated as a white solid (495 mg, 67% combined yield, d.r. 3:2).



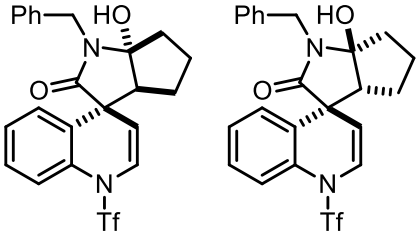
Diastereoisomer A (6i): R_f **:** 0.56 (EtOAc:petrol 1:2); **IR:** (υmax(film)/cm^{-1}) 3324 (O-H), 1675 (C=O); **^{1}H-NMR:** (400 MHz, $CDCl_3$) δ 7.37-7.27 (m, 5H, Ph), 6.90 (s, 1H, NC*H*=CCl), 6.77 (d, *J* = 8.0 Hz, 1H, NC*H*=CH), 4.97 (d, *J* = 8.0 Hz, 1H, NCH=C*H*), 4.62 (d, *J* = 15.0 Hz, 1H, PhCH_2), 4.54 (d, *J* = 15.0 Hz, 1H, PhCH_2), 2.62 (dd, *J* = 9.5, 4.0 Hz, 1H, C*H*COH), 2.50 (s, 1H, CO*H*), 1.82 (m, 1H, CH_2), 1.75-1.63 (m, 1H, CH_2), 1.30 (m, 1H, CH_2); **^{13}C-NMR:** (125 MHz, $CDCl_3$) δ 171.8 (CO), 137.9 (Ph), 128.6 (Ph), 128.2 (Ph), 127.6 (Ph), 122.4 (N*C*H=CCl), 120.5 (NC*H*=CH or NCH=*C*Cl), 120.3

(NC*H*=CH or NCH=*C*Cl), 108.8 (NCH=*C*H), 99.2 (*C*), 56.1 (*C*H), 52.3 (*C*OH), 44.1 (Ph*C*H_2), 37.6 (*C*H_2), 26.9 (*C*H_2), 24.9 (*C*H_2); **m/z (ES):** 485 (M(^{35}Cl)Na^+), 487 (M(^{37}Cl)Na^+); **HRMS:** found 463.0696 (M(^{35}Cl)H^+) $C_{19}H_{18}N_2O_4F_3ClS$ requires 463.0701.



Diastereoisomer B (6i'): (Characterised contaminated with diastereoisomer A) ***R*$_f$:** 0.52 (EtOAc:petrol 2:1); **IR:** (υmax(film)/cm^{-1}) 3348 (O-H), 1672 (C=O); **^{1}H-NMR:** (400 MHz, $CDCl_3$) δ 7.39-7.27 (m, 5H, Ph), 7.01 (s, 1H, NC*H*CCl), 6.56 (d, *J* = 8.0 Hz, 1H, NC*H*CH), 5.30 (d, *J* = 8.0 Hz, 1H, NCHC*H*), 4.77 (d, *J* = 15.0 Hz, 1H, PhCH_2), 4.43 (d, *J* = 15.0 Hz, 1H, PhCH_2), 2.75 (s, 1H, CO*H*), 2.32 (dd, *J* = 9.5, 7.0 Hz, 1H, C*H*), 1.99-1.65 (m, 6H, CH_2); **^{13}C-NMR:** (125 MHz, $CDCl_3$) δ 171.7 (*C*O), 137.3 (Ph), 128.7 (Ph), 128.5 (Ph), 127.8 (Ph), 122.9 (N*C*H=CCl), 120.5 (NC*H*=CH or NCH=*C*Cl), 120.3 (NC*H*=CH or NCH=*C*Cl), 109.0 (NCH=*C*H), 99.3 (*C*), 61.0 (*C*H), 52.7 (COH), 44.0 (Ph*C*H_2), 38.7 (*C*H_2), 25.6 (*C*H_2), 25.3 (*C*H_2); **m/z (ES):** 485 (M(^{35}Cl)Na^+), 487 (M(^{37}Cl)Na^+); **HRMS:** found 463.0696 (M(^{35}Cl)H^+), $C_{19}H_{18}N_2O_4F_3ClS$ requires 463.0701.

1-Benzyl-6a-hydroxy-1'-((trifluoromethyl)sulfonyl)-4,5,6,6a-tetrahydro-1H,1'H-spiro[cyclopenta[b]pyrrole-3,4'-quinolin]-2(3aH)-one (6l)



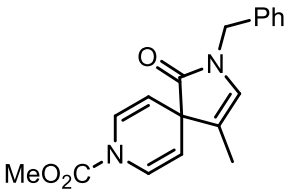
Following general procedure B, the title compound was obtained from *N*-benzyl-*N*-cyclopent-1-enyl-2-((*1Z*,*3Z*)-penta-1,3-1,3-dienyl)-isonicotinamide **1l** (0.54 mmol) and 2,6-di-*tert*-butyl-4-methyl-pyridine (0.54 mmol), as a mixture of two diastereoisomers and a clear gum (197 mg, 76%, d.r. 1.3:1).

The two diasteroisomers could not be separated by flash chromatography.

***R*$_f$:** 0.28 (EtOAc:petrol 1:2); **IR:** (υmax(film)/cm^{-1}) 3360 (O-H), 1667 (C=O); **^{1}H-NMR:** (500 MHz, $CDCl_3$) δ 7.84 (dd, *J* = 8.0, 1.5 Hz, 1H$_{min}$, Ph), 7.82 (dd, *J* = 8.0, 1.5 Hz, 1H$_{maj}$, Ph), 7.49-7.47 (m, 2H$_{maj}$, 2H$_{min}$, Ph), 7.40-7.19 (m, 5H$_{maj}$, 5H$_{min}$, Ph), 7.15 (dd, *J* = 7.5, 1.5 Hz, 1H$_{maj}$, Ph), 7.02 (dd, *J* = 7.5, 1.5 Hz, 1H$_{min}$, Ph) 7.00 (d, *J* = 7.5 Hz, 1H$_{maj}$, NC*H*=CH), 6.81 (d, *J* = 7.5 Hz, 1H$_{min}$, NC*H*=CH), 5.81 (d, *J* = 7.5 Hz, 1H$_{min}$, NCH=C*H*), 5.53 (d, *J* = 7.5 Hz, 1H$_{maj}$, NCH=C*H*), 4.75 (d, *J* = 14.5 Hz, 1H$_{min}$, PhCH_2), 4.68 (s, 2H$_{maj}$, PhCH_2) , 2.46-2.42 (m, 1H$_{maj}$, 1H$_{min}$, C*H*), 2.31 (s, 1H, O*H*), 2.25 (s, 1H, O*H*), 1.96-1.12 (m, 6H$_{maj}$, 6H$_{min}$, CH_2); **^{13}C-NMR:** (125 MHz, $CDCl_3$) δ 174.9 (*C*=O$_{maj\ or\ min}$), 174.8 (C=O$_{maj\ or\ min}$), 138.0 (Ph$_{maj\ or\ min}$), 137.8 (Ph$_{maj\ or\ min}$), 134.8 (Ph$_{maj\ or\ min}$), 133.3 (Ph$_{maj\ or\ min}$), 133.2 (Ph$_{maj\ or\ min}$), 129.6 (Ph$_{maj\ or\ min}$), 128.9 (Ph$_{maj\ or\ min}$), 128.9 (Ph$_{maj\ or\ min}$), 128.7 (Ph$_{maj\ or\ min}$), 128.5 (Ph$_{maj\ or\ min}$), 128.4 (Ph$_{maj\ or\ min}$), 128.1 (Ph$_{maj\ or\ min}$), 127.9 (Ph$_{maj\ or\ min}$), 127.9 (Ph$_{maj\ or\ min}$), 127.9 (Ph$_{maj\ or\ min}$), 127.8 (Ph$_{maj\ or\ min}$), 126.8 (N*C*H=CH$_{maj}$), 126.7 (Ph$_{maj\ or\ min}$), 126.5 (Ph$_{maj\ or\ min}$), 124.8 (N*C*H=CH$_{min}$), 122.2 (NCH=*C*H$_{min}$), 121.4 (Ph$_{min}$), 121.3 (Ph$_{maj}$), 116.3 (NCH=*C*H$_{maj}$), 100.0 (*C*$_{maj\ or\ min}$), 99.6 (*C*$_{maj\ or\ min}$), 59.7 (*C*H$_{maj}$), 59.7 (CH$_{min}$), 50.9 (*C*OH$_{maj\ or\ min}$), 49.9 (*C*OH$_{maj\ or\ min}$), 44.2 (Ph*C*H$_{2min}$), 44.0 (Ph*C*H$_{2maj}$), 39.0 (*C*H$_{2maj\ or\ min}$), 38.3 (*C*H$_{2maj\ or\ min}$), 28.4 (*C*H$_{2maj\ or}$

min), 28.3 (*C*H$_{2maj\ or\ min}$), 24.4 (*C*H$_{2maj\ or\ min}$), 24.3 (*C*H$_{2maj\ or\ min}$); **m/z (ES$^+$):** 479 (50%, MH$^+$), 501 (100%, MNa$^+$); **HRMS:** found 479.1234 (MH$^+$), $C_{23}H_{22}N_2O_4F_3S$ requires 479.1247.

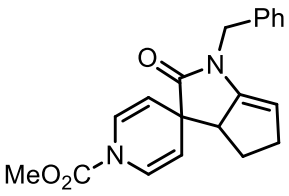
2-Benzyl-4-isopropyl-1-oxo-2,8-diaza-spiro[4.5]deca-3,6,9-triene-8-carboxylic acid methyl ester (7a)



Following general procedure B, the title compound was obtained from *N*-benzyl-*N*-((*E*)-propenyl)-isonicotinamide **1a** (0.44 mmol) using 2,6-lutidine (0.44 mmol) and methyl chloroformate (0.44 mmol), as a colourless oil after purification (69%).

***R$_f$* :** 0.26 (EtOAc:petrol 1:2); **IR:** (υmax(film)/cm^{-1}) 1729 (C=O), 1699 (C=O); **^{1}H-NMR:** (400 MHz, $CDCl_3$, 2 rotamers (A:B 1:1)) δ 7.36-7.21 (m, 5H, Ph), 7.20 (m, 2H$_{A\ or\ B}$, NC*H*=CH), 7.11 (br d, *J* = 7.0 Hz, 2H$_{A\ or\ B}$, NC*H*=CH), 5.86 (d, *J* = 1.5 Hz, 1H, NC*H*), 4.58 (d, *J* = 7.0 Hz, 2H$_{A\ or\ B}$, NCH=C*H*), 4.56 (s, 2H, PhC*H*$_2$), 4.50 (d, *J* = 7.0 Hz, 2H$_{A\ or\ B}$, NCH=C*H*), 3.84 (s, 3H, OC*H*$_3$), 1.63 (d, *J* = 1.5 Hz, 3H, C*H*$_3$); **^{13}C-NMR:** (100 MHz, $CDCl_3$) δ 180.0 (*C*=O), 151.6 (*C*=O), 136.6 (Ph), 128.8 (Ph), 127.8 (Ph), 125.8 (N*C*H=CH), 125.6 (N*C*H=CH), 124.4 (Ph), 123.6 (N*C*H), 104.7 (NCH=*C*H), 104.2 (NCH=*C*H), 53.7 (O*C*H$_3$), 53.4 (*C*), 45.9 (Ph*C*H$_2$), 11.1 (*C*H$_3$); **m/z (ES$^+$):** 311 (20%, MH$^+$), 333 (100%, MNa$^+$); **HRMS:** found 311.1393 (MH$^+$), $C_{18}H_{19}N_2O_3$ requires 311.1391.

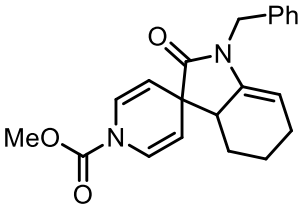
Methyl-1-benzyl-2-oxo-2,3a,4,5-tetrahydro-1H,1'H-spiro[cyclopenta[b]pyrrole-3,4'-pyridine]-1'carboxylate (7e)



Following general procedure B, the title compound was obtained as the major isomer from *N*-benzyl-*N*-cyclopent-1-enyl-isonicotinamide **1e** (0.42 mmol), using methyl chloroformate (0.42 mmol) and 2,6-lutidine (0.42 mmol), as a colourless oil after purification (67% (84% with minor isomer)).

***R$_f$* :** 0.81 (EtOAc:petrol 1:1); **IR:** (υmax(film)/cm^{-1}) 1721 (C=O), 1668 (C=O); **^{1}H-NMR:** (400 MHz, $CDCl_3$, 2 rotamers (A:B 1:1)) δ 7.33-7.24 (m, 5H, Ph), 7.16 (d, *J* = 8.0 Hz, 1H$_{A\ or\ B}$, NC*H*=CH), 7.10 (d, *J* = 8.0 Hz, 1H$_{A\ or\ B}$, NC*H*=CH), 7.04 (d, *J* = 8.0 Hz, 1H$_{A\ or\ B}$, NC*H*=CH), 6.97 (d, *J* = 8.0 Hz, 1H$_{A\ or\ B}$, NC*H*=CH), 4.85 (d, *J* = 8.0 Hz, 1H$_{A\ or\ B}$, NCH=C*H*), 4.78 (d, *J* = 8.0 Hz, 1H$_{A\ or\ B}$, NCH=C*H*), 4.66 (m, 1H, NC=C*H*), 4.62 (s, 2H, PhC*H*$_2$), 4.58 (d, *J* = 8.0 Hz, 1H$_{A\ or\ B}$, NCH=C*H*), 4.51 (d, *J* = 8.0 Hz, 1H$_{A\ or\ B}$, NCH=C*H*), 3.82 (s, 3H, OMe), 2.84 (t, *J* = 7.5 Hz, 1H, C*H*), 2.39 (m, 2H, C*H*$_2$), 1.81 (m, 1H, C*H*$_2$), 1.69 (m, 1H, C*H*$_2$); **^{13}C-NMR:** (100 MHz, $CDCl_3$) δ 178.9 (C=O), 144.1 (C=O), 140.4 (N*C*=CH), 136.2 (Ph), 128.6 (Ph), 127.9 (Ph), 127.7 (Ph), 125.0 (N*C*H=CH), 124.1 (N*C*H=CH), 107.6 (NCH=*C*H), 103.3 (NCH=*C*H), 98.0 (NC=*C*H), 55.7 (*C*H), 53.7 (O*C*H$_3$), 49.5 (*C*), 45.8 (Ph*C*H$_2$), 33.1 (*C*H$_2$), 23.9 (*C*H$_2$); **m/z (ES$^+$):** 337.1 (10%, MH$^+$), 359.2 (100%, MNa$^+$); **HRMS:** found 359.1354 (MNa$^+$), $C_{20}H_{20}O_3N_2Na$ requires 359.1366.

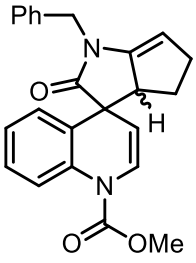
Methyl 1-benzyl-2-oxo-1,2,3a,4,5,6-hexahydro-1'H-spiro[indole-3,4'-pyridine]-1'-carboxyl-ate (7f)



Following general procedure B, the title compound was obtained as the major isomer from *N*-benzyl-*N*-cyclohex-1-enyl-isonicotinamide **1f** (0.79 mmol) using methyl chloroformate (0.79 mmol) and 2,6-lutidine (0.79 mmol), as a clear gum after purification (198 mg, 72% (91% with minor isomer)).

***R*$_f$:** 0.40 (EtOAc:petrol 1:2); **IR:** (υmax(film)/cm^{-1}) 1721 (C=O), 1677 (C=O); **^{1}H-NMR:** (500 MHz, $CDCl_3$, 2 rotamers (A:B 1:1)) δ 7.33-7.22 (m, 5H, Ph), 7.21 (m, 1H$_{A\ or\ B}$, NC*H*=CH), 7.08 (m, 1H$_A$, 1H$_B$, NC*H*=CH), 6.94 (m, 1H$_{A\ or\ B}$, NC*H*=CH), 4.90 (m, 1H, N(C)=C*H*), 4.82 (m, 1H$_{A\ or\ B}$, NCH=C*H*), 4.74 (m, 1H$_{A\ or\ B}$, NCH=C*H*), 4.70 (d, *J* = 15.5 Hz, 1H, PhC*H*$_2$), 4.64 (m, 1H$_{A\ or\ B}$, NCH=C*H*), 4.58 (d, *J* = 15.5 Hz, 1H, PhC*H*$_2$), 4.56 (m, 1H$_{A\ or\ B}$, NCH=C*H*), 3.84 (s, 3H, OC*H*$_3$), 2.37 (m, 1H, C*H*), 2.12 (m, 1H, C*H*$_2$), 2.03 (m, 1H, C*H*$_2$), 1.89 (m, 1H, C*H*$_2$), 1.75 (m, 1H, C*H*$_2$), 1.51 (m, 1H, C*H*$_2$), 1.46 (m, 1H, C*H*$_2$); **^{13}C-NMR:** (125 MHz, $CDCl_3$) δ 175.4 (*C*=O), 151.6 (*C*=O), 138.3 (N*C*=CH), 136.7 (Ph), 128.6 (Ph), 127.4 (Ph), 127.3 (Ph), 125.6 (N*C*H=CH), 124.4 (N*C*H=CH), 107.2 (NCH=*C*H), 106.8 (NCH=*C*H), 100.2 (N(C)=*C*H), 53.7 (O*C*H$_3$), 49.1 (*C*), 47.8 (*C*H), 44.1 (Ph*C*H$_2$), 23.4 (*C*H$_2$), 22.6 (*C*H$_2$), 21.4 (*C*H$_2$); **m/z (ES$^+$):** 351 (80%, MH$^+$), 373 (100%, MNa$^+$); **HRMS:** found 351.1706 (MH$^+$), $C_{21}H_{23}N_2O_3$ requires 351.1706.

Methyl 1-benzyl-2-oxo-2,3a,4,5-tetrahydro-1H,1'H-spiro[cyclopenta[b]pyrrole-3,4'-quinoline]-1'-carboxylate (7l)



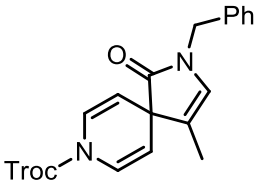
Following general procedure B, the title compound was obtained from *N*-benzyl-*N*-cyclopent-1-enyl-2-((*1Z*,*3Z*)-penta-1,3-1,3-dienyl)-isonicotinamide **1l** (0.43 mmol) (using methyl chloroformate (0.43 mmol) and 2,6-lutidine (0.43 mmol)) as a colourless gum containing 2 diastereoisomers (132 mg, 79%, d.r 1:1).

Diastereoisomer A: *R*$_f$: 0.60 (EtOAc:petrol 1:2); **IR:** (υmax(film)/cm^{-1}) 1716 (C=O), 1641 (C=O); **^{1}H-NMR:** (500 MHz, $CDCl_3$ 2 rotamers (9:1)) δ 8.16 (d, *J* 8.5, 1H$_{maj}$, NC*H*=CH), 8.09 (d, *J* 8.0, 1H$_{min}$, NC*H*=CH), 7.41-7.16 (m, 9H$_{maj}$, 7H$_{min}$, Ar), 7.00 (m, 1H$_{min}$, Ar), 6.56 (m, 1H$_{min}$, Ar), 5.44 (d, *J* = 8.0 Hz, 1H$_{min}$, NCH=C*H*), 4.90 (d, *J* = 14.5 Hz, 1H$_{min}$, PhC*H*$_2$), 4.83 (d, *J* = 8.5 Hz, 1H$_{maj}$, NCH=C*H*), 4.82 (d, *J* = 14.5 Hz, 1H$_{maj}$, PhC*H*$_2$), 4.79 (m, 1H$_{min}$, NCH=C*H*), 4.74 (m, 1H$_{maj}$, 1H$_{min}$, C*H*), 4.69 (m, 1H$_{min}$, PhC*H*$_2$), 4.67 (d, *J* = 14.5 Hz, 1H$_{maj}$, PhC*H*$_2$), 3.90 (s, 3H, OC*H*$_3$), 3.26 (m, 1H$_{maj}$, NC=C*H*), 3.04 (m, 1H$_{min}$, NC=C*H*), 2.49-2.40 (m, 2H$_{maj}$, 1H$_{min}$, C*H*$_2$), 2.26 (m, 1H$_{min}$, C*H*$_2$), 1.79 (m, 1H$_{maj}$, C*H*$_2$), 1.75-1.62 (m, 1H$_{maj}$, 2H$_{min}$, C*H*$_2$); **^{13}C-NMR:** (125 MHz, $CDCl_3$) δ 152.8 (*C*O), 144.1 (*C*O), 136.3 (Ar), 136.1 (Ar), 128.7 (Ar), 128.3 (Ar), 128.0 (Ar), 127.9 (Ar), 127.7 (Ar), 127.5 (Ar), 127.4 (Ar), 125.4 (Ar), 120.8 (N*C*H=CH), 105.9 (NCH=*C*H), 97.8 (*C*H), 57.4 (NC=*C*H),

53.5 (OMe), 52.9 (*C*), 45.9 (Ph*C*H_2), 33.1 (*C*H_2), 24.7 (*C*H_2); **m/z (ES$^+$):** 387 (50%, MH^+), 409 (100%, MNa^+);

Diastereoisomer B: Could not be separated from diastereoisomer A.

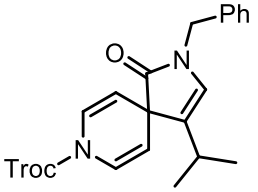
2-Benzyl-4-methy1-oxo-2,8-diaza-spiro[4.5]deca-3,6,9-triene-8-carboxylic acid 2,2,2-trichloro-ethyl ester (8a)



Following procedure B, the title compound was obtained from *N*-benzyl-*N*-((*E*)-propenyl)-isonicotinamide **1a** (0.40 mmol), using 2,2,2-trichloroethyl chloroformate (0.40 mmol) and 2,6-lutidine (0.40 mmol) as a colourless oil after purification (69%).

***R*$_f$:** 0.70 (EtOAc:petrol 1:2); **IR:** (υmax(film)/cm^{-1}) 1736 (C=O), 1690 (C=O); **^{1}H-NMR:** (400 MHz, $CDCl_3$, 2 rotamers (A:B 1:1)) δ 7.36-7.21 (m, 5H, Ph), 7.36-7.21 (m, 2H$_A$, 2H$_B$, NC*H*=CH), 5.90 (s, 1H, NC*H*),4.85 (s, 2H, PhC*H*$_2$), 4.70 (dd, *J* = 8.5, 2.0 Hz, 2H$_{A\ or\ B}$, NCH=C*H*), 4.62 (d, *J* = 8.5, 2.0 Hz, 2H$_{A\ or\ B}$, NCH=C*H*), 4.57 (s, 2H, Cl_3CCH_2), 1.65 (s, 3H, C*H*$_3$); **^{13}C-NMR:** (100 MHz, $CDCl_3$) δ 179.5 (C=O), 149.6 (C=O), 136.5 (Ph), 128.9 (Ph), 127.8 (Ph), 125.6 (N*C*H=CH), 125.1 (N*C*H=CH), 124.0 (Ph or NC*H*), 123.9 (Ph or NC*H*), 106.2 (NCH=*C*H), 105.6 (NCH=*C*H), 94.5 ((*C*)CH_3), 76.8 (*C*Cl_3), 75.7 (Cl_3CCH_2), 53.4 (*C*), 45.9 (Ph*C*H_2), 11.2 (*C*H_3); **m/z (ES$^+$):** 449 (100%, M(^{35}Cl)Na^+), 451 (80%, M(^{37}Cl)Na^+); **HRMS:** found 449.0205 (M(^{35}Cl)Na^+), $C_{19}H_{17}N_2O_3{}^{35}Cl_3Na$ requires 449.197.

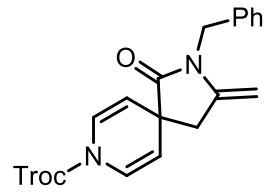
2-Benzyl-4-isopropyl-oxo-2,8-diaza-spiro[4.5]deca-3,6,9-triene-8-carboxylic acid 2,2,2-trichloro-ethyl ester (8b)



Following general procedure B, the title compound was obtained from *N*-benzyl-*N*-((*E*)-3-methyl-but-1-enyl)-isonicotinamide **1b** (0.46 mmol), using 2,2,2-trichloroethyl chloroformate (0.46 mmol) and 2,6-lutidine (0.46 mmol), as a white amorphous solid after purification (44%).

***R*$_f$:** 0.70 (EtOAc:petrol 1:1); **IR:** (υmax(film)/cm^{-1}) 1735 (C=O), 1688 (C=O); **^{1}H-NMR:** (400 MHz, $CDCl_3$, 2 rotamers (A:B 1:1)) δ 7.29-7.13 (m, 5H, Ph), 7.29-7.13 (m, 2H$_A$, 2H$_B$, NC*H*=CH), 5.85 (s, 1H, NC*H*), 4.78 (s, 2H, PhC*H*$_2$), 4.68 (dd, *J* = 8.0, 2.0 Hz, 2H$_{A\ or\ B}$, NCH=C*H*), 4.59 (dd, *J* = 8.0, 2.0 Hz, 2H$_{A\ or\ B}$, NCH=C*H*), 4.51 (s, 2H, Cl_3CCH_2), 2.34 (q, *J* = 7.0 Hz, 1H, C*H*(CH_3)), 0.99 (d, *J* = 7.0 Hz, 6H, CH(C*H*$_3$)); **^{13}C-NMR:** (100 MHz, $CDCl_3$) δ 178.5 (C=O), 149.5 (C=O), 136.5 (Ph), 135.0 ((*C*)CH(CH_3)$_2$), 128.9 (Ph), 127.8 (Ph), 127.7 (Ph), 125.1 (N*C*H=CH), 124.6 (N*C*H), 123.7 (N*C*H=CH), 107.3 (NCH=*C*H), 106.7 (NCH=*C*H), 77.1 (*C*Cl_3), 75.7 (Cl_3CCH_2), 53.4 (*C*), 46.0 (Ph*C*H_2), 26.2 (CH(*C*H_3)$_2$), 22.7 (2 × *C*H_3); **m/z (ES$^+$):** 477 (100%, M(^{35}Cl)Na^+); **HRMS:** found 477.0513 (M(^{35}Cl)Na^+), $C_{21}H_{21}N_2O_3{}^{35}Cl_3Na$ requires 477.0515.

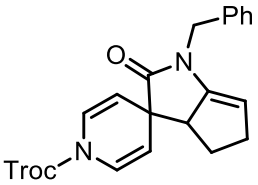
2-Benzyl-3-methylene-1-oxo-2,8-diaza-spiro[4.5]deca-6,9-diene-8-carboxylic acid 2,2,2-trichloro-ethyl ester (8d)



Following general procedure B, the title compound was obtained as the major isomer from *N*-benzyl-*N*-isopropenyl-isonicotinamide **1d** (0.49 mmol) (using 2,2,2-trichloroethyl chloroformate (0.49 mmol) and 2,6-lutidine (0.49 mmol)) as an unstable colourless oil which was tentatively assigned as the title compound after purification (152 mg, 73%).

R_f **:** 0.89 (EtOAc:petrol 1:1); **IR:** (υmax(film)/cm^{-1}) 1733 (C=O), 1691 (C=O); **^{1}H-NMR:** (400 MHz, $CDCl_3$, 2 rotamers (A:B 1:1)) δ 7.28-7.12 (m, 5H, Ph), 7.03 (d, *J* = 8.0 Hz, 2H$_{A\ or\ B}$, NC*H*=CH), 7.01 (d, *J* = 8.0 Hz, 2H$_{A\ or\ B}$, NC*H*=CH), 4.87 (dd, *J* = 8.0, 3.0 Hz, 2H$_{A\ or\ B}$, NCH=C*H*), 4.82 (d, *J* = 12.0 Hz, 1H, PhC*H*$_2$), 4.78 (dd, *J* = 8.0, 3.0 Hz, 2H$_{A\ or\ B}$, NCH=C*H*), 4.74 (d, *J* = 12.0 Hz, 1H, PhC*H*$_2$), 4.63 (s, 2H, Cl_3CCH_2), 4.22 (d, *J* = 2.0 Hz, 1H, NC=C*H*$_2$), 4.12 (d, *J* = 2.0 Hz, 1H, NC=C*H*$_2$), 2.63 (d, *J* =2.0 Hz, 1H, N(C)C*H*$_2$), 2.62 (d, *J* = 1.5 Hz, 1H, N(C)C*H*$_2$); **^{13}C-NMR:** (100 MHz, $CDCl_3$) δ 176.0 (*C*=O), 149.5 (C=O), 142.4 (N(*C*)=CH_2), 135.8 (Ph), 128.7 (Ph), 127.6 (Ph), 127.3 (Ph), 124.0 (N*C*H=CH), 123.5 (N*C*H=CH), 108.7 (NCH=*C*H), 108.1 (NCH=*C*H), 87.2 (N(C)=*C*H$_2$), 76.3 (Cl_3C), 75.6 (Cl_3CCH_2), 44.6 (*C*), 44.3 (Ph*C*H$_2$), 43.3 (N(C)*C*H$_2$); **m/z (ES$^+$):** 449.2 (100%, M(^{35}Cl)Na$^+$), 451.2 (80%, M(^{37}Cl)Na$^+$); **HRMS:** found 449.0197(M(^{35}Cl)Na$^+$), $C_{19}H_{17}O_3N_2{}^{35}Cl_3Na$ requires 449.0197.

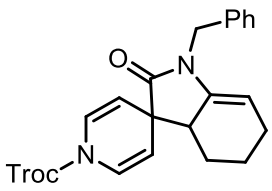
2,2,2-Trichloroethyl-1-benzyl-2-oxo-2,3a,4,5-tetrahydro-1H,1'H-spiro[cyclopenta [b]pyrrole -3,4'-pyridine]-1'carboxylate (8e)



Following general procedure B, the title compound was obtained from *N*-benzyl-*N*-cyclopent-1-enyl-isonicotinamide **1e** (0.42 mmol) (using 2,2,2-trichloroethyl chloroformate (0.42 mmol) and 2,6-lutidine (0.42 mmol)) as a colourless oil after purification (138 mg, 73%).

R_f **:** 0.88 (EtOAc:petrol 1:1); **IR:** (υmax(film)/cm^{-1}) 1731 (C=O), 1671 (C=O); **^{1}H-NMR:** (400 MHz, $CDCl_3$, 2 rotamers (A:B 1:1)) δ 7.35-7.25 (m, 5H, Ph), 7.17 (d, *J* = 8.0 Hz, 1H$_{A\ or\ B}$, NC*H*=CH), 7.16 (d, *J* = 8.0 Hz, 1H$_{A\ or\ B}$, NC*H*=CH), 7.10 (d, *J* = 8.0 Hz , 1H$_{A\ or\ B}$, NC*H*=CH), 7.08 (d, *J* = 8.0 Hz, 1H$_{A\ or\ B}$, NC*H*=CH), 4.97 (dd, *J* = 8.0, 2.0 Hz, 1H$_{A\ or\ B}$,NCH=C*H*), 4.88 (dd, *J* = 8.0, 2.0 Hz, 1H$_{A\ or\ B}$, NCH=C*H*), 4.84 (s, 2H, Cl_3CCH_2), 4.71 (m, 1H$_{A or\ B}$, NCH=C*H*), 4.70 (br m, 1H, NC=C*H*), 4.64 (s, 2H, PhC*H*$_2$), 4.63 (m, 1H$_{A\ or\ B}$, NCH=C*H*), 2.89 (m, 1H, C*H*), 1.53-1.42 (m, 2H, C*H*$_2$), 1.86 (m, 1H, C*H*$_2$), 1.68 (m, 1H, C*H*$_2$); **^{13}C-NMR:** (100 MHz, $CDCl_3$) δ 178.6 (C=O), 149.5 (*C*=O), 144.0 (N*C*=CH), 136.1 (Ph), 128.7 (Ph), 127.9 (Ph), 127.7 (Ph), 125.1 (N*C*H=CH), 124.8 (N*C*H=CH), 124.6 (N*C*H=CH), 124.3 (N*C*H=CH), 109.5 (NCH=*C*H), 108.9 (NCH=*C*H), 104.8 (NCH=*C*H), 104.2 (NCH=*C*H), 98.2 (NC=*C*H), 94.5 (*C*), 77.2 (Cl_3CCH_2), 75.7 (Cl_3CCH_2), 55.6 (NC=*C*H), 49.5 (*C*), 45.8 (Ph*C*H$_2$) 33.0 (*C*H$_2$) 24.5 (*C*H$_2$); **m/z (ES$^+$):** 453 (M(^{35}Cl)Na$^+$), 455 (M(^{37}Cl)Na$^+$); **HRMS:** found 453.0529 (M(^{35}Cl)H$^+$), $C_{21}H_{20}N_2O_3{}^{35}Cl_3$ requires 453.0535.

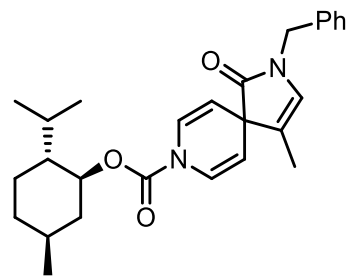
2,2,2-Trichloroethyl-1-benzyl-2-oxo-2,3a,4,5-tetrahydro-1H,1'H-spiro[cyclohexa[b] pyrrole -3,4'-pyridine]-1'carboxylate (8f)



Following general procedure B, the title compound was obtained from *N*-benzyl-*N*-cyclohex-1-enyl-isonicotinamide **1f** (.52 mmol) (using 2,2,2-trichloroethyl chloroformate (0.52 mmol) and 2,6-lutidine (0.52 mmol)) as a white amorphous solid after purification (191 mg, 79%).

***R*$_f$:** 0.85 (EtOAc:petrol 1:1); **IR:** (υmax(film)/cm^{-1}) 1732 (C=O), 1672 (C=O); **^{1}H-NMR:** (400 MHz, $CDCl_3$, 2 rotamers (A:B 1:1)) δ 7.27-7.10 (m, 5H, Ph), 7.27-7.10 (m, 1H$_A$, 1H$_B$, NC*H*=CH), 7.08 (dd, *J* = 8.0, 1.5 Hz, 1H$_{A\ or\ B}$, NC*H*=CH), 7.04 (dd, *J* = 8.0, 1.5 Hz, 1H$_{A\ or\ B}$, NC*H*=CH), 4.94 (m, 1H$_{A\ or\ B}$, NCH=C*H*), 4.93 (m, 1H, NC=C*H*), 4.88-4.83 (m, 1H$_{A\ or\ B}$, NCH=C*H*), 4.84 (s, 2H, Cl_3CCH_2), 4.76 (m, 1H$_{A\ or\ B}$, NCH=C*H*), 4.71 (d, *J* = 15.5 Hz, 1H, PhC*H*$_2$), 4.67 (m, 1H$_{A\ or\ B}$, NCH=C*H*), 4.57 (d, *J* = 15.5 Hz, 1H, PhC*H*$_2$), 2.42 (m, 1H, C*H*$_2$), 2.15-2.07 (m, 2H, C*H*$_2$), 1.91 (m, 1H, C*H*$_2$), 1.77 (m, 1H, C*H*$_2$), 1.53 (m, 1H, C*H*$_2$), 1.43 (m, 1H, C*H*$_2$); **^{13}C-NMR:** (100 MHz, $CDCl_3$) δ 175.1 (C=O), 149.5 (C=O), 138.1 (N*C*=CH), 136.5 (Ph), 128.7 (Ph), 127.5 (Ph), 127.4 (Ph), 125.6 (N*C*H=CH), 125.1 (NCH=*C*H), 124.4 (N*C*H=CH), 123.9 (NCH=*C*H), 108.7 (NCH=*C*H), 108.1 (NCH=*C*H), 105.8 (NCH=*C*H), 105.2 (NCH=*C*H), 100.6 (NC=*C*H), 76.3 (Cl_3C), 75.6 (Cl_3CCH_2), 49.2 (*C*H), 47.7 (*C*), 44.1 (Ph*C*H$_2$), 23.4 (*C*H$_2$), 22.7 (*C*H$_2$), 21.8 (*C*H$_2$); **m/z (ES$^+$):** 489.3 (60%, M(^{35}Cl)Na$^+$), 491.3 (100%, M(^{37}Cl)Na$^+$); **HRMS:** found 489.0518 (M(^{35}Cl)H$^+$) $C_{22}H_{21}O_3N_2{}^{35}Cl_3Na$ requires 489.0510.

(*1R,2S,5R*)-2-Isopropyl-5-methylcyclohexyl 2-benzyl-4-methyl-1-oxo-2,8-diazaspiro[4.5] deca-3,6,9-triene-8-carboxylate (9a)

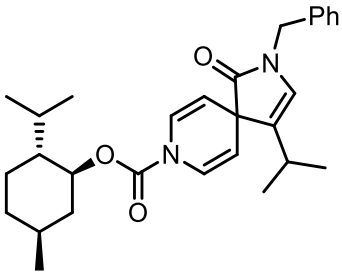


Following general procedure B, the title compound was obtained from *N*-benzyl-*N*-((*E*)-propenyl)-isonicotinamide **1a** (0.53 mmol) (using (*1R*)-(-)-menthylchloroformate (0.53 mmol) and 2,6-lutidine (0.53 mmol)) as a colourless oil after purification (87 mg, 38%).

***R*$_f$:** 0.52 (EtOAc:petrol 1:2); **IR:** (υmax(film)/cm^{-1}) 1716 (C=O); 1693 (C=O); **^{1}H-NMR:** (500 MHz, $CDCl_3$, 2 rotamers (A:B 1:1)) δ 7.36-7.22 (m, 5H, Ph), 7.36-7.22 (m, 2H$_{A\ or\ B}$, NC*H*=CH), 7.11 (d, *J* = 7.5 Hz, 2H$_{A\ or\ B}$, NC*H*=CH), 5.86 (s, 1H, NC*H*), 4.72 (dt, *J* = 11.0, 4.0 Hz, 1H, OC*H*), 4.59 (d, *J* = 15.0 Hz, 1H, PhC*H*$_2$), 4.56 (m, 2H$_{A\ or\ B}$, NCH=C*H*), 4.55 (d, *J* = 15.0 Hz, 1H, PhC*H*$_2$), 4.48 (d, *J* = 7.5 Hz, 2H$_{A\ or\ B}$, NCH=C*H*), 2.11 (br m, 1H, C*H*$_2$), 1.92 (br m, 1H, C*H*), 1.71-1.69 (m, 2H, 2 × C*H*$_2$) 1.65 (s, 3H, C*H*$_3$), 1.52 (br m, 1H, C*H*), 1.44 (br m, 1H, C*H*), 1.07 (m, 1H, C*H*$_2$), 1.06 (m, 1H, C*H*$_2$), 0.93 (d, *J* = 6.5 Hz, 3H, CH(C*H*$_3$)), 0.91 (d, *J* = 6.5 Hz, 3H, CH(C*H*$_3$)), 0.87 (m, 1H, C*H*$_2$), 0.80 (br s, 3H, C*H*$_3$); **^{13}C-NMR:** (125 MHz, $CDCl_3$) δ 180.1 (*C*=O), 150.8 (*C*=O), 136.7 (Ph), 128.8 (Ph), 127.8 (Ph), 126.0 (N*C*H=CH), 125.7 (N*C*H=CH), 124.6 (Ph), 123.4 (N*C*H), 104.3 (NCH=*C*H), 103.8 (NCH=*C*H), 77.1 (O*C*H), 53.6 (*C*), 47.3 (*C*), 45.9 (Ph*C*H$_2$), 41.1 (*C*H$_2$), 34.2 (*C*H$_2$), 31.4 (*C*H$_2$), 26.1 (*C*H), 23.5 (*C*H), 22.0 (CH(*C*H$_3$)$_2$), 20.8 (CH(*C*H$_3$)$_2$), 16.2 (*C*H), 14.2 (*C*H$_3$),

11.2 (CH_3); **m/z (ES$^+$):** 457 (100%, MNa^+); **HRMS:** found 435.2646 (MH^+), $C_{27}H_{35}N_2O_3$ requires 435.2643.

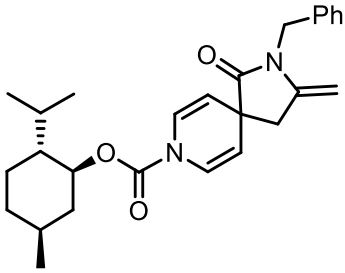
(1R,2S,5R)-2-Isopropyl-5-methylcyclohexyl 2-benzyl-4-isopropyl-1-oxo-2,8-diazaspiro[4.5]deca-3,6,9-triene-8-carboxylate (9b)



Following general procedure B, the title compound was obtained from *N*-benzyl-*N*-((*E*)-3-methyl-but-1-enyl)-isonicotinamide **1b** (0.51 mmol) (using (*1R*)-(-)-menthylchloroformate (0.51 mmol) and 2,6-lutidine (0.51 mmol)) as a colourless oil after purification (58%).

***R*$_f$:** 0.55 (EtOAc:petrol 1:2); **^{1}H-NMR:** (500 MHz, $CDCl_3$, 2 rotamers (A:B 1:1)) δ 7.30-7.19 (m, 5H, Ph), 7.30-7.19 (m, 2H$_{A\ or\ B}$, NC*H*=CH), 7.02 (m, 2H$_{A\ or\ B}$, NC*H*=CH), 5.81 (s, 1H, NC*H*), 4.65 (dt, *J* = 11.5, 4.0 Hz, 1H, OC*H*), 4.65 (m, 2H$_{A\ or\ B}$, NCH=C*H*), 4.51 (m, 2H, PhCH_2), 4.46 (d, *J* = 7.5 Hz, 2H$_{A\ or\ B}$, NCH=C*H*), 2.35 (m, 1H, C*H*), 2.05 (br m, 1H, CH_2), 1.86 (br m, 1H, C*H*), 1.64-1.06 (m, 6H, 3 × CH_2, 3 × C*H*), 0.98 (m, 6H, CH(CH_3)$_2$), 0.94 (d, *J* = 6.0 Hz, 3H, CH(CH_3)), 0.91 (d, *J* = 6.0 Hz, 3H, CH(CH_3)), 0.87 (m, 1H, CH_2), 0.80 (br s, 3H, CH_3); **m/z (ES$^+$):** 485 (100%, MNa^+).

(*1R,2S,5R*)-5-methyl-2-(propan-2-yl)cyclohexyl-2-benzyl-3-methylidene-1-oxo-2,8-diazaspiro[4.5]deca-6,9-diene-8-carboxylate (9d)

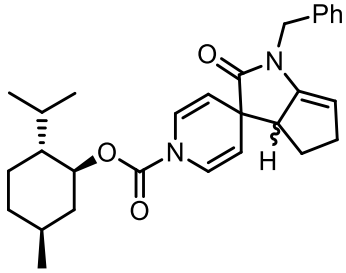


Following general procedure B, the title compound was obtained as the major double bond regioisomer from *N*-benzyl-*N*-isopropenyl-isonicotinamide **1d** (0.56 mmol) (using (*1R*)-(-)-menthyl chloroformate (0.56 mmol) and 2,6-lutidine (0.56 mmol)) as a colourless oil after purification (177 mg, 73% (80% with minor isomer)).

***R*$_f$:** 0.68 (EtOAc:petrol 1:4); **IR:** (υmax(film)/cm^{-1}) 1716 (C=O), 1683 (C=O); **^{1}H-NMR:** (400 MHz, $CDCl_3$, 2 rotamers (A:B 1:1)) δ 7.34-7.23 (m, 5H, Ph), 7.13 (d, *J* = 7.5 Hz, 2H$_{A\ or\ B}$, NC*H*=CH), 6.99 (d, *J* = 7.5 Hz, 2H$_{A\ or\ B}$, NC*H*=CH), 4.83 (d, *J* = 7.5 Hz, 2H$_{A\ or\ B}$, NCH=C*H*), 4.65 (m, 1H, OC*H*) , 4.66-4.61 (m, 2H$_{A\ or\ B}$, NCH=C*H*), 4.70 (s, 2H, PhCH_2), 4.27 (s, 1H, C=CH_2), 4.16 (s, 1H, C=CH_2), 2.68 (s, 2H, NCCH_2), 2.08 (m, 1H, CH_2), 1.91 (m, 1H, C*H*), 1.71-1.69 (m, 2H, 2 × CH_2), 1.50-1.41 (m, 2H, 2 × C*H*), 1.09-1.00 (m, 2H, 2 × CH_2), 0.93 (d, *J* 6.5, 3H, CH(CH_3)$_2$), 0.92 (d, *J* 6.5, 3H, CH(CH_3)$_2$), 0.87 (m, 1H, CH_2), 0.79 (br s, 3H, CH_3); **^{13}C-NMR:** (100 MHz, $CDCl_3$) δ 180.3 (C=O), 149.7 (C=O), 136.5 (Ph), 127.8 (Ph), 126.4 (Ph), 125.8 (Ph), 123.7 (N*C*H=CH$_{A\ or\ B}$), 123.4 (N*C*H=CH$_{A\ or\ B}$), 103.7 (NCH=*C*H$_{A\ or\ B}$), 103.4 (NCH=CH$_{A\ or\ B}$), 86.5 (N(C)=*C*H$_2$), 76.7 (O*C*H), 49. 1 (*C*), 46.1 (*C*H), 43.2 (N(C)*C*H$_2$), 42.5 (Ph*C*H$_2$), 40.0 (*C*H$_2$), 33.1 (*C*H$_2$), 30.4 (*C*H), 25.0 (*C*H), 21.7

(CH_2), 21.0 ($CH(CH_3)_2$), 20.8 ($CH(CH_3)_2$), 12.5 (CH_3); **m/z (ES$^+$):** 457 (20%, MNa^+); **HRMS:** found 435.2645 (MH^+), $C_{27}H_{35}N_2O_3$ requires 435.2643.

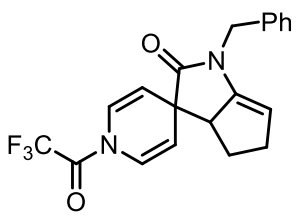
(*1R,2S,5R*)-5-methyl-2-(propan-2-yl)cyclohexyl-3-benzyl-2-oxo-3,5,6,6a-tetrahydro-1'H,2H-spiro[cyclopenta[b]pyrrole-1,4'-pyridine]-1'-carboxylate (9e)



Following general procedure B, the title compound was obtained as the major double bond regioisomers from *N*-benzyl-cyclopent-1-enyl-isonicotinamide **1e** (0.49 mmol) (using (*1R*)-(-)-menthyl chloroformate (0.49 mmol) and 2,6-lutidine (0.057 mL, 0.49 mmol)) as a colourless oil after purification (169 mg, 75% (92% with minor isomer).

R_f **:** 0.50 (EtOAc:petrol 1:5); **IR:** (υmax(film)/cm^{-1}) 1715 (C=O), 1683 (C=O); **^{1}H-NMR:** (400 MHz, $CDCl_3$, 2 rotamers (A:B 1:1)) δ 7.35-7.25 (5H, m, Ph), 7.20 (m, 1H$_{A\ or\ B}$, NC*H*=CH), 7.13 (m, 1H$_{A\ or\ B}$, NC*H*=CH), 7.07 (m, 1H$_{A\ or\ B}$, NC*H*=CH), 7.00 (m, 1H$_{A\ or\ B}$, NC*H*=CH), 4.83 (m, 1H$_{A\ or\ B}$, NCH=C*H*), 4.77 (m, 1H$_{A\ or\ B}$, NCH=C*H*), 4.71 (dt, *J* 11.0, 4.5, 1H, OC*H*), 4.67 (s, 1H, NC=C*H*), 4.64 (s, 2H, PhCH_2), 4.57 (m, 1H$_{A\ or\ B}$, NCH=C*H*), 4.49 (m, 1H$_{A\ or\ B}$, NC*H*=CH), 2.85 (m, 1H, C*H*), 2.47 (m, 2H, CH_2), 2.08 (m, 1H, CH_2), 1.89-1.83 (m, 2H, C*H*, CH_2), 1.73-1.64 (m, 3H, 3 × CH_2), 1.47 (m, 2H, 2 × C*H*), 1.14-1.01 (m, 2H, 2 × CH_2), 0.92 (d, *J* = 7.0 Hz, 3H, CH(CH_3)$_2$), 0.91 (d, *J* = 7.0 Hz, 3H, CH(CH_3)$_2$), 0.87 (m, 1H, CH_2), 0.79 (d, *J* = 7.0 Hz, 3H, CH_3); **^{13}C-NMR:** (100 MHz, $CDCl_3$) δ 179.1 (C=O), 150.7 (C=O), 144.2 (N*C*=CH), 136.3 (Ph), 128.6 (Ph), 127.9 (Ph), 127.6 (Ph), 125.4 (N*C*H=CH$_{A\ or\ B}$), 125.2 (N*C*H=CH$_{A\ or\ B}$), 125.1 (N*C*H=CH$_{A\ or\ B}$), 124.9 (N*C*H=CH$_{A\ or\ B}$), 107.5 (NCH=*C*H$_{A\ or\ B}$), 107.1 (NCH=*C*H$_{A\ or\ B}$), 102.8 (NCH=*C*H$_{A\ or\ B}$), 102.3 (NCH=*C*H$_{A\ or\ B}$), 97.8 (NC=*C*H), 77.2 (O*C*H), 55.9 (*C*H), 49.6 (*C*), 47.2 (*C*H), 45.8 (Ph*C*H_2), 41.1 (*C*H_2), 34.2 (*C*H_2), 33.0 (*C*H_2), 31.4 (*C*H), 26.1 (*C*H), 24.0 (*C*H_2), 23.3 (*C*H_2), 22.0 (CH(*C*H_3)$_2$, 20.8 (CH(*C*H_3)$_2$), 16.3 (*C*H$_{3A\ or\ B}$), 16.2 (*C*H$_{3A\ or\ B}$); **m/z (ES$^+$):** 501 (MCH_3CN^+); **HRMS:** found 461.2815 (MH^+), $C_{29}H_{37}N_2O_3$ requires 461.2809.

1-Benzyl-1'-(2,2,2-trifluoroacetyl)-4,5-dihydro-1H,1'H-spiro[cyclopenta[b]pyrrole-3,4'-pyridin]-2(3aH)-one (10e).

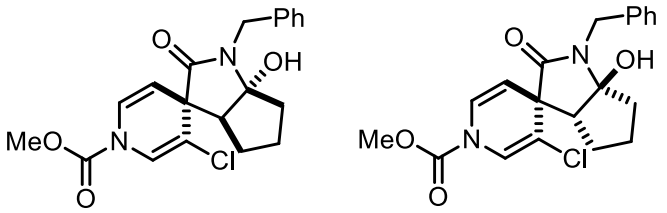


Following general procedure B, the title compound was obtained from *N*-benzyl-*N*-cyclohex-1-enyl-isonicotinamide **1e** (0.40 mmol) (using trifluoroacetic anhydride (0.80 mmol) and 2,6-lutidine (0.40 mmol)) as a white amorphous solid after purification (67 mg, 45%).

R_f **:** 0.81 (EtOAc:petrol 1:2); **^{1}H-NMR:** (400 MHz, $CDCl_3$, 2 rotamers (A:B 1:1)) δ 7.44 (d, *J* = 8.5 Hz, 1H$_{A\ or\ B}$, NC*H*=CH), 7.39 (d, *J* = 8.5 Hz, 1H$_{A\ or\ B}$,

NC*H*=CH), 7.32-7.15 (m, 5H, Ph), 7.04 (d, *J* = 8.5 Hz, 1H$_{A\ or\ B}$, NC*H*=CH), 6.98 (d, *J* = 8.5 Hz, 1H$_{A\ or\ B}$, NC*H*=CH), 5.37 (d, *J* = 14.5 Hz, 1H, PhCH_2), 5.31 (d, *J* = 14.5 Hz, 1H, PhCH_2), 5.22 (dd, *J* = 8.5, 2.5 Hz, 1H$_{A\ or\ B}$, NCH=C*H*), 5.03 (dd, *J* = 8.5, 2.5 Hz, 1H$_{A\ or\ B}$, NCH=C*H*), 4.97 (dd, *J* = 8.5, 2.5 Hz, 1H$_{A\ or\ B}$, NCH=C*H*), 4.78 (dd, *J* = 8.5, 2.5 Hz, 1H$_{A\ or\ B}$, NCH=C*H*), 3.05, (m, 2H, CH_2, C*H*), 2.93 (m, 1H, CH_2), 1.98 (m, 1H, CH_2), 1.78 (m, 1H, CH_2); **m/z (ES$^+$):** 375 (50%, MH$^+$), 397 (60%, MNa$^+$); **m/z (ES$^-$):** 373 (40%, M$^-$); **HRMS:** found 375.1314 (MH$^+$), $C_{20}H_{18}N_2O_2F_3$ requires 375.1315.

(3aS,6aR)-Methyl-1-benzyl-3'-chloro-6a-hydroxy-2-oxo-2,3a,4,5,6,6a-hexahydro-1H,1'H-spiro[cyclopenta[b]pyrrole-3,4'-pyridine]-1'-carboxylate (11i)

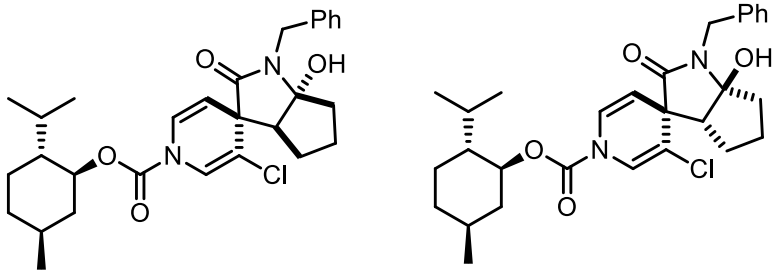


Following general procedure B, the triene compound was obtained from *N*-benzyl-3-chloro-*N*-(cyclopent-1-en-1-yl)isonicotinamide **1i** (0.57 mmol) using methyl chloroformate (0.57 mmol) and 2,6-lutidine (0.57 mmol). The resultant gum (after removal of the solvent) was stirred in 1M HCl/diethylether (2.85 mL). The title compound was yielded as a mixture of diastereoisomers (A:B) and isolated as a white solid (141 mg, 64% combined yield, d.r. 1:1).

Diastereoisomer A (11i): R_f **:** 0.23 (EtOAc:petrol 1:2); **IR:** (υmax(film)/cm^{-1}) 3331 (O-H), 1728 (C=O), 1672 (C=O); **^{1}H-NMR:** (400 MHz, $CDCl_3$, 2 rotamers (A:B 1:1)) δ 7.38-7.25 (m, 5H, Ph), 7.33 (m, 1H$_{A\ or\ B}$, NC*H*=CH or NC*H*=CCl), 7.20 (m, 1H$_{A\ or\ B}$, NC*H*=CH or NC*H*=CCl), 7.21 (m, 1H$_{A\ or\ B}$, NC*H*=CH or NC*H*=CCl), 7.05 (m, 1H$_{A\ or\ B}$, NC*H*=CH or NC*H*=CCl), 4.76 (m, 1H$_{A\ or\ B}$, NCH=C*H*), 4.68 (m, 1H$_{A\ or\ B}$, NCH=C*H*), 4.62 (d, *J* = 15.0 Hz, 1H, PhCH_2), 4.55 (d, *J* = 15.0 Hz, 1H, PhCH_2), 3.87 (s, 3H, OCH_3), 2.57 (m, 1H, C*H*), 2.50 (br s, 1H, O*H*), 1.91-1.67 (m, 5H, CH_2), 1.34 (m, 1H, CH_2); **^{13}C-NMR:** (100 MHz, $CDCl_3$) δ 173.2 (*C*=O), 150.8 (*C*=O), 138.3 (Ph), 128.5 (Ph), 128.2 (Ph), 127.4 (Ph), 104.9 (NCH=*C*H $_{(A\ or\ B)}$), 104.4 (NCH=*C*H $_{(A\ or\ B)}$), 99.0 (*C*), 56.5 (*C*H), 54.1 (O*C*H$_3$), 52.8 (*C*OH), 44.0 (Ph*C*H$_2$), 37.4 (*C*H$_2$), 27.0 (*C*H$_2$), 24.9 (*C*H$_2$); **m/z (ES$^+$):** 411 ((M(^{35}Cl)Na$^+$), 413 (M(^{37}Cl)Na$^+$).

Diastereoisomer B (11i'): Could not be purified.

(*1R,2S,5R*)-2-Isopropyl-5-methylcyclohexyl-1-benzyl-3'-chloro-2-oxo-2,3a,4,5-tetra-hydro-1H,1'H-spiro[cyclopenta[b]pyrrole-3,4'-pyridine]-1'-carboxylate (12i)

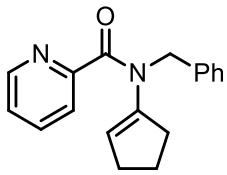


Following general procedure B, the triene compound was obtained from *N*-benzyl-3-chloro-*N*-(cyclopent-1-en-1-yl)isonicotinamide **1j** (0.37 mmol) using (*1R*)-(□)-menthyl chloroformate (0.37 mmol) and 2,6-lutidine (0.37 mmol). The resultant gum (after removal of the solvent) was stirred in 1M HCl/diethylether (1.85 mL). The title compound was yielded as a mixture of diastereoisomers (A:B) and isolated as a white solid (125 mg, 66% combined yield, d.r. 1:1).

The two diastereoisomers could not be separated by flash chromatography.

***R*$_f$:** 0.81 (EtOAc:petrol 1:1); **IR:** (υmax(film)/cm^{-1}) 3398 (O-H), 1722 (C=O), 1684 C=O); **^{1}H-NMR:** (400 MHz, $CDCl_3$; 2 rotamers (rot A:rot B 1:1)) δ 7.38 (br s, 1H$_{rotA}$, 1H$_{rotB}$, NC*H*=CCl), 7.36 (m, 1H, Ph), 7.34 (m, 1H$_{rotA\ or\ B}$, NC*H*=CH), 7.33-7.23 (m, 4H, Ph), 7.21 (m, 1H$_{rotA\ or\ B}$, NC*H*=CH), 7.18 (m, 1H$_{rotA\ or\ B}$, NC*H*=CH), 7.07 (m, 1H$_{rotA\ or\ rotB}$, NC*H*=CH), 4.73 (m, 1H$_{diaA}$, 1H$_{diaB}$, OC*H*), 4.70 (m, 1H$_{rotA\ or\ B}$, NCH=C*H*), 4.66 (m, 1H$_{rotA\ or\ B}$, NCH=C*H*), 4.63 (d, *J* = 15.0 Hz, 1H$_{diaA\ or\ B}$, PhCH_2), 4.61 (d, *J* = 15.0 Hz, 1H$_{diaA\ or\ B}$, PhCH_2), 4.56 (d, *J* = 15.0 Hz, 1H$_{diaA\ or\ B}$, PhCH_2), 4.54 (d, *J* = 15.0 Hz, 1H$_{diaA\ or\ B}$, PhCH_2), 2.58-2.52 (m, 2H$_{diaA}$, 2H$_{diaB}$, C*H*, O*H*), 2.07 (m, 1H, CH_2), 1.91-1.63 (m, 8H, 7 × CH_2, C*H*), 1.56-1.41 (m, 2H, 2 × C*H*), 1.34 (m, 1H$_A$, CH_2), 1.13-1.00 (m, 2H$_A$, 2 × CH_2), 0.92 (br. d, *J* = 6.5 Hz, 6H, CH(CH_3)$_2$), 0.87 (m, 1H, CH_2), 0.79 (d, *J* = 6.5 Hz, 3H, CH_3); **^{13}C-NMR:** (400 MHz, $CDCl_3$) δ 173.4 (*C*=O), 149.9 (*C*=O), 138.3 (Ph), 128.5 (Ph), 128.2 (Ph), 127.4 (Ph), 124.0 (N*C*H=CCl), 123.7 (N*C*H=CCl), 122.5 (N*C*H=CH), 122.2 (N*C*H=CH), 106.5 (NCH=*C*Cl), 105.8 (NCH=*C*Cl), (104.5 (NCH=*C*H), 104.2 (NCH=*C*H), 99.0 (*C*), 78.0 (O*C*H), 56.5 (*C*H), 52.9 (*C*), 47.1 (*C*H), 43.9 (Ph*C*H$_2$), 40.9 (*C*H$_2$), 37.4 (*C*H), 34.1 (*C*H$_2$), 31.4 (*C*H), 27.0 (*C*H$_2$), 26.2 (*C*H$_2$), 24.9 (*C*H$_2$), 23.3 (*C*H$_2$), 22.0 (CH(*C*H$_3$)$_2$), 20.8 (CH(*C*H$_3$)$_2$), 16.3 (*C*H$_3$); **m/z (ES$^+$):** 535 (100%, M(^{35}Cl)Na$^+$); **HRMS:** found 513.2509 (M(^{35}Cl)H$^+$), $C_{29}H_{38}N_2O_4Cl$ requires 513.2515.

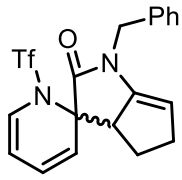
Pyridine-2-carboxylic acid benzyl-cyclopent-1-enyl-amide (13)



Following general procedure A, benzyl-cyclopentylidiene-amine (2.0 mmol) (from cyclopentanone (0.13 mL) and benzylamine (0.22 mL)) was acylated using picolinoyl chloride (341 mg, 2.2 mmol). The title compound was yielded as a yellow/brown gum after purification (261 mg, 47% over 2 steps).

R_f **:** 0.62 (EtOAc:petrol 3:1); **IR:** (υmax(film)/cm^{-1}) 1668; **^{1}H-NMR:** (500 MHz, $CDCl_3$) δ 8.49 (d, *J* = 5.0 Hz, 1H, Py), 7.66 (dt, *J* = 7.5, 2.0 Hz, 1H, Py), 7.53 (d, *J* = 7.5 Hz, 1H, Py), 7.30 - 7.16 (m, 6H, Ph and Py), 5.02 (br s, 1H, NC=C*H*), 4.84 (s, 2H, PhC*H*$_2$), 2.16 (m, 2H, C*H*$_2$), 1.97 (m, 2H, C*H*$_2$), 1.66 (m, 2H, C*H*$_2$); **^{13}C-NMR:** (125 MHz, $CDCl_3$) δ 168.7 (*C*=O), 154.9 (N(*C*)=CH), 148.5 (Py), 137.5 (Ph), 136.5 (Py), 128.7 (Ph), 128.4 (Ph), 127.9 (Ph), 127.2 (Py or N(C)=*C*H), 124.4 (Py or N(C)=*C*H), 123.1 (Py), 122.4 (Py), 50.1 (Ph*C*H$_2$), 33.0 (*C*H$_2$), 30.1 (*C*H$_2$), 22.5 (*C*H$_2$); **m/z (ES$^+$):** 279.1 (50%, MH$^+$), 301.1 (100%, MNa$^+$); **HRMS:** found 279.1493 (MH$^+$), $C_{18}H_{18}N_2O$ requires 279.1492.

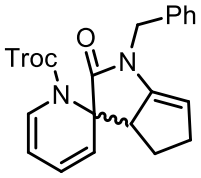
3-Benzyl-1'-(trifluoromethane)sulfonyl-3,5,6,6a-tetrahydro-1'H,2H-spiro[cyclopenta[b] pyrrole-1,2'-pyridine]-2-one (14a)



Following general procedure B, the title compound was obtained from pyridine-2-carboxylic acid benzyl-cyclopent-1-enyl-amide **13** (0.48 mmol), (using triflic anhydride (0.48 mmol) and 2,6-lutidine (0.48 mmol)) as a yellow gum and a mixture of diastereomers after purification (64 mg, 33%, d.r. 5:1).

R_f **:** 0.90 (EtOAc:petrol 1:1); **^{1}H-NMR:** (300 MHz, $CDCl_3$) δ 7.31-7.10 (m, 5H, Ph), 6.45 (d, *J* = 8.0 Hz, 1H$_{maj}$, NC*H*=CHCH=CH), 6.35 (m, 1H$_{min}$, NCH=CHC*H*=CH), 6.13 (m, 1H$_{min}$, NCH=CHC*H*=CH), 6.02 (dd, *J* = 9.5, 5.5 Hz, 1H$_{maj}$, NCH=CHC*H*=CH), 5.29 (br m, 1H, NCH=C*H*CH=CH), 5.31-4.65 (m, 3H$_{maj}$, 3H$_{min}$, NCH=C*H*CH=CH, NCH=CHCH=C*H*, NC=C*H*), 4.99 (d, *J* = 9.5 Hz, 1H, NCH=CHCH=C*H*), 4.70 (d, *J* = 15.0 Hz, 1H, PhC*H*$_2$), 4.61 (m, 1H, NC=C*H*), 4.50 (d, *J* = 15.0 Hz, 1H, PhC*H*$_2$), 3.49 (br m, 1H, C*H*), 2.39 (m, 2H, C*H*$_2$), 1.89 (m, 1H, C*H*$_2$), 1.69 (m, 1H, C*H*$_2$); **^{13}C-NMR:** (75 MHz, $CDCl_3$) δ 150.0 (C=O), 141.3 (N*C*=CH), 137.6 (Ph), 135.5 (N*C*H), 128.8 (Ph), 128.2 (Ph), 127.8 (Ph), 124.8 (*C*H=CH), 122.5 (CH=*C*H), 117.8 (*C*H), 107.2 (*C*), 98.9 (CH), 72.0 (NC=*C*H), 46.0 (Ph*C*H$_2$), 32.9 (*C*H$_2$), 24.8 (*C*H$_2$), 23.2 (*C*H$_2$); **m/z (ES$^+$):** 411 (30%, MH$^+$), 433 (100%, MNa$^+$). No further characterisation was performed on this compound due to its instability.

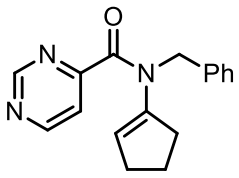
[2,2,2-tricholoroethyl-3-benzyl-2-oxo-3,5,6,6a-tetrahydro-1'H,2H-spiro[cyclopenta[b] pyrrole - 1,2'-pyridine]-2-one (14b)



Following general procedure B, the title compound was obtained from pyridine-2-carboxylic acid benzyl-cyclopent-1-enyl-amide **13** (0.52 mmol) (using 2,2,2-trichloroethyl chloroformate (0.52 mmol) and 2,6-lutidine) as yellow oil and a mixture of diastereoisomers (186 mg, 79%, d.r. 9:1).

R_f **:** 0.92 (EtOAc:petrol 1:1); **^{1}H-NMR:** (300 MHz, $CDCl_3$) δ 7.33-7.06 (m, 5H, Ph), 6.85 (d, *J* = 7.5 Hz, $1H_{maj}$, NC*H*=CHCH=CH), 6.79 (d, *J* = 7.5 Hz, $1H_{min}$, NC*H*=CHCH=CH), 6.08 (dd, *J* = 9.5, 7.0 Hz, $1H_{min}$, NCH=CHC*H*=CH), 6.03 (dd, *J* = 9.5, 7.0 Hz, $1H_{maj}$, NCH=CHC*H*=CH), 5.21-4.54 (m, $3H_{maj}$, $3H_{min}$, NCH=C*H*CH=CH, NCH=CHCH=C*H* , NC=C*H*), 4.78 (s, 2H, Cl_3CCH_2), 4.70 (d, *J* = 15.0 Hz, 1H, PhCH_2), 4.46 (d, *J* = 15.0 Hz, 1H, PhCH_2), 3.58 (m, 1H, C*H*), 2.40 (m, 2H, CH_2), 1.89 (m, 1H, CH_2), 1.70 (m, 1H, CH_2); **m/z (ES$^+$):** 493 (100%, MCH_3CN^+). No further characterisation was performed on this compound due to its instability.

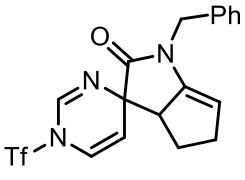
***N*-Benzyl-*N*-(cyclopent-1-en-1-yl)pyrimidine-4-carboxamide (15)**



Following general procedure A, benzyl-cyclopentylidene-amine (1.9 mmol) (from cyclopentanone (0.12 mL) and benzylamine (0.21 mL)) was acylated with pyrimidine-4-carbonyl chloride (298 mg, 2.1 mmol). The title compound was yielded as a yellow gum after purification (352 mg, 61%).

R_f **:** 0.34 (EtOAc:petrol 1:1); **IR:** (υmax(film)/cm^{-1}) 1646 (C=O); **^{1}H-NMR:** (400 MHz, $CDCl_3$) δ 9.20 (s, 1H, Py), 8.82 (d, *J* = 5.0 Hz, 1H, Py), 7.56 (d, *J* = 5.0 Hz, 1H, Py), 7.35-7.27 (m, 5H, Ph), 5.00 (br m, 1H, NC=C*H*), 4.86 (s, 2H, PhCH_2), 2.36 (br m, 2H, CH_2), 2.02 (br m, 2H, CH_2), 1.79 (br m, 2H, CH_2); **^{13}C-NMR:** (100 MHz, $CDCl_3$) δ 166.5 (*C*=O), 161.9 (Py), 158.0 (Py), 157.9 (Py), 142.4 (N*C*=CH), 136.8 (Ph), 128.5 (Ph), 128.1 (Ph), 127.8 (Py), 127.5 (Ph), 119.7 (NC=*C*H), 49.8 (Ph*C*H_2), 32.5 (*C*H_2), 30.1 (*C*H_2), 22.4 (*C*H_2); **m/z (ES$^+$):** 280 (50%, MH^+), 202 (30%, MNa^+); **HRMS:** found 280.1439 (MH^+), $C_{17}H_{18}N_3O$ requires 280.1145.

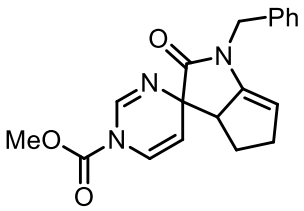
1-Benzyl-1'-((trifluoromethyl)sulfonyl)-4,5-dihydro-1H,1'H-spiro[cyclopenta[b]pyrrole-3,4'-pyrimidin]-2(3aH)-one (16a)



Following general procedure B, from *N*-benzyl-*N*-(cyclopent-1-en-1-yl)pyrimidine-4-carboxamide **15** (0.40 mmol), triflic anhydride (0.40 mmol) and 2,6-di-tert-butyl-4-methylpyridine, the resulting colourless gum was tentatively assigned as the title compound in approximately 30% yield.

^{1}H-NMR: ($CDCl_3$, 400 MHz): 8.02 (m, 1H, NC*H*), 7.23-7.19 (m, 5H, Ph), 6.97 (m, 1H, NC*H*CH), 4.74 (d, 1H, *J* = 14.0 Hz, PhCH_2), 4.45 (d, 1H, *J* = 14.0 Hz, PhCH_2).

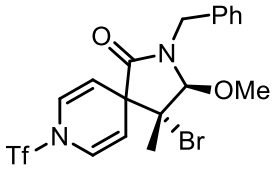
Methyl 1-benzyl-2-oxo-2,3a,4,5-tetrahydro-1H,1'H-spiro[cyclopenta[b]pyrrole-3,4'-pyrimidine]-1'-carboxylate (16b).



Following general procedure B, from *N*-benzyl-*N*-(cyclopent-1-en-1-yl)pyrimidine-4-carboxamide **15** (0.34 mmol), methyl chloroformate (0.34 mmol) and 2,6-lutidine (0.34 mmol), the resulting colourless gum was tentatively assigned as the title compound in approximately 55% yield.

^{1}H-NMR: ($CDCl_3$, 400 MHz): 7.36-7.26 (m, 5H, Ph), 4.76 (d, 1H, *J* = 15.0 Hz, PhCH_2), 4.52 (d, 1H, *J* = 15.0 Hz, PhCH_2).

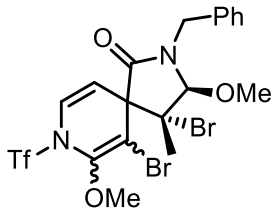
2-Benzyl-4-bromo-3-methoxy-4-methyl-8-trifluoromethanesulfonyl-2,8-diaza-spiro[4.5]deca-6,9-dien-1-one (17)



N-Bromosuccinimide (0.005 g, 0.3 mmol) was added in one portion to a solution of 2-benzyl-4-methyl-1-oxo-2,8-diaza-spiro [4.5] deca-3,6,9-triene-8-carboxylic acid tri-fluoro-methyl ester **2a** (0.010 g, 0.026 mmol) in methanol (0.50 mL) at 0 °C. The solution was stirred for 30 minutes at 0 °C then concentrated under reduced pressure and the crude purified by flash chromatography (SiO_2; EtOAc:petrol) to yield the title compound (5 mg, 39%).

***R_f* :** 0.46 (EtOAc:petrol 1:4); **IR:** (υmax(film)/cm^{-1}) 1718 (C=O); **^{1}H-NMR:** ($CDCl_3$, 400 MHz) δ 7.29-7.37 (m, 5H, Ph), 6.86 (d, *J* = 8.5 Hz, 1H, N*C*H=CH), 6.72 (d, *J* = 8.5 Hz, 1H, NC*H*=CH), 5.40 (dd, *J* = 8.5, 2.5 Hz, 1H, NCH=*C*H), 5.28 (dd, *J* 8.5, 2.5, 1H, NCH=*C*H), 5.02 (d, *J* = 14.5 Hz, 1H, PhCH_2), 4.71 (s, 1H, C*H*OMe), 4.12 (d, *J* 15.0, 1H, PhCH_2), 3.43 (s, 3H, OMe), 1.77 (s, 3H, Me); **^{13}C-NMR:** ($CDCl_3$, 100 MHz) δ 172.3 (C=O), 134.9 (Ph), 128.7 (Ph), 128.1 (Ph), 124.7 (N*C*H=CH), 123.2 (N*C*H=CH), 119.4 (q, *J* = 324 Hz, *C*F_3), 109.9 (NCH=*C*H), 108.9 (NCH=*C*H), 97.4 (*C*OMe), 72.0 (*C*MeBr), 59.5 (OMe), 53.3 (*C*), 45.4 (Ph*C*H_2), 22.3 (*C*H_3); **m/z (ES$^+$):** 517.0 (90% MNa^+), 519.1 (100%, MNa^+). **HRMS:** found 517.0041 (MH^+), $C_{18}H_{18}O_4N_2BrF_3S$ requires 517.0026.

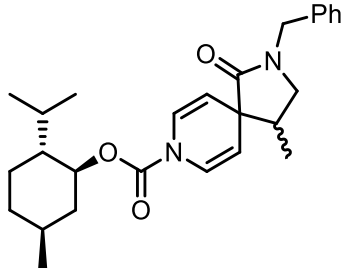
2-Benzyl-4,10-dibromo-3,9-dimethoxy-4-methyl-8-trifluoromethanesulfonyl-2,8- diaza-spiro[4.5]dec-6-en-1-one (18)



N-Bromosuccinimide (0.039 g, 0.22 mmol) was added in one portion to a solution of 2-benzyl-4-methyl-1-oxo-2,8-diaza-spiro [4.5] deca-3,6,9-triene-8-carboxylic acid tri-fluoro-methyl ester **2a** (0.077 g, 0.20 mmol) in methanol (2 mL) at 0 °C. The solution was stirred for 2 ½ hours at 0 °C and *N*-bromosuccinimide (0.005 g, 0.03 mmol) was added. The solution was stirred for a further 2 hours then a final portion of *N*-bromosuccinimide (0.010 g, 0.06 mmol) was added and the solution stirred at room temperature for 16 hours and concentrated under reduced pressure. The residue was dissolved in dichloromethane (3 mL), washed with water (5 mL), dried ($MgSO_4$) and concentrated under reduced pressure. The resultant oil was purified by flash chromatography (SiO_2; EtOAc:petrol 1:9) to yield the title compound as white prisms (72 mg, 59%).

***R*$_f$:** 0.68 (EtOAc:petrol 1:4); **m.p.:** 149-152 °C (EtOAc); **IR:** (υmax(film)/cm^{-1}) 1725 (C=O); **^{1}H-NMR:** ($CDCl_3$, 300 MHz) δ 7.30-7.39 (m, 5H, Ph), 6.58 (d, *J* = 8.5 Hz, 1H, NC*H*=CH), 5.52 (br s, 1H, C*H*Br), 5.40 (d, *J* = 8.5 Hz, 1H, NCH=C*H*), 4.96 (d, *J* = 14.5 Hz, 1H, PhCH_2), 4.81 (dd, *J* = 4.0, 1.0 Hz, 1H, C*H*OCH$_3$), 4.77 (br s, 1H, C*H*OCH$_3$), 4.14 (d, *J* = 4.5 Hz, 1H, PhCH_2), 3.64 (s, 3H, OCH_3), 3.45 (s, 3H, OCH_3), 1.95 (s, 3H, CH_3); **^{13}C-NMR:** ($CDCl_3$, 75 MHz) δ 170.3 (C=O), 134.7 (Ph), 129.1 (Ph), 128.7 (Ph), 128.1 (Ph), 124.0 (N*C*H=CH), 119.3 (q, *J* = 323 Hz, CF_3), 107.8 (NCH=*C*H), 98.0 (*C*HOCH$_3$), 90.4 (*C*HOCH$_3$), 59.9 (O*C*H$_3$), 58.1 (O*C*H$_3$), 55.2 (C), 46.8 (*C*HBr), 45.6 (Ph*C*H$_2$), 23.6 (*C*H$_3$); **m/z (ES$^+$):** 628.9 (100%, MNa$^+$). **HRMS:** found 628.9381 (MNa$^+$), $C_{19}H_{21}O_5N_2Br_2F_3S$ requires 626.9382.

(*1R,2S,5R*)-2-isopropyl-5-methylcyclohexyl-2-benzyl-4-methyl-1-oxo-2,8-diazaspiro [4.5]deca-6,9-diene-8-carboxylate (19)

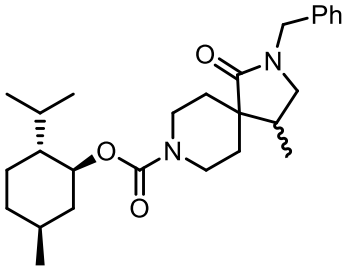


(*1R,2S,5R*)-2-Isopropyl-5-methylcyclohexyl-2-benzyl-4-methyl-1-oxo-2,8-diazaspiro [4.5]deca-3,6,9-triene-8-carboxylate **9a** (460 mg, 1.06 mmol) was dissolved in 2:1 EtOH:EtOAc (10 mL) and passed through the H-Cube (CatCart Pd/C 10% cartridge) at 40 bar pressure, 30 °C and a flow rate of 0.8 mL.min^{-1}. The solvent was evaporated under reduced pressure and the crude product was purified by flash chromatography (SiO_2, EtOAc:petrol 1:5). The title compound was yielded as a colourless gum (440 mg, 95%).

***R*$_f$:** 0.55 (EtOAc:petrol 1:2); **IR:** (υmax(film)/cm^{-1}) 1715 (C=O), 1688 (C=O); **^{1}H-NMR:** (400 MHz, $CDCl_3$, 2 rotamers (A:B 1:1)) δ 7.36-7.23 (m, 5H, Ph), 7.17 (d, *J* = 8.0 Hz, 1H$_{A\ or\ B}$, NC*H*=CH), 7.13 (d, *J* = 8.0 Hz, 1H$_{A\ or\ B}$, NC*H*=CH), 7.05 (d, *J* = 8.0 Hz, 1H$_{A\ or\ B}$, NC*H*=CH), 7.00 (d, *J* = 8.0 Hz, 1H$_{A\ or\ B}$, NC*H*=CH), 4.70 (td, *J* = 11.0, 4.5 Hz, 1H, OC*H*), 4.70-4.62 (m, 2H$_A$, 2H$_B$, NCH=C*H*), 4.53 (d, *J* = 14.5 Hz, 1H, PhCH_2), 4.38 (d, *J* = 14.5 Hz,

1H, PhCH_2), 3.20 (ap t, J = 9.0 Hz, 1H, NCH_2), 2.84 (ap t, J = 9.0 Hz, 1H, NCH_2), 2.09-1.88 (m, 3H, 2 × CH, CH_2), 1.72-1.68 (m, 2H, 2 × CH_2), 1.53-1.40 (m, 2H, 2 × CH_2), 1.11-1.00 (m, 2H, 2 × CH), 0.96 (d, J = 7.0 Hz, 3H, CH_3), 0.90 (d, J = 6.5 Hz, 3H, CH(CH_3)), 0.89 (d, J = 6.5 Hz, 3H, CH(CH_3)), 0.87 (m, 1H, CH_2), 0.77 (s, 3H, CH_3); **^{13}C-NMR:** (100 MHz, $CDCl_3$) δ 175.4 (*C*=O), 150.8 (*C*=O), 136.4 (Ph), 128.7 (Ph), 128.2 (Ph), 127.7 (Ph), 125.5 (N*C*H=CH$_{A\ or\ B}$), 125.4 (N*C*H=CH$_{A\ or\ B}$), 125.3 (N*C*H=CH$_{A\ or\ B}$), 125.0 (N*C*H=CH$_{A\ or\ B}$), 106.5 (NCH=*C*H$_{A\ or\ B}$), 105.9 (NCH=*C*H$_{A\ or\ B}$), 102.8 (NCH=*C*H$_{A\ or\ B}$), 102.3 (NCH=*C*H$_{A\ or\ B}$), 77.2 (O*C*H), 49.9 (N*C*H$_{2A\ or\ B}$), 49.8 (N*C*H$_{2A\ or\ B}$), 47.3 (*C*H), 47.1 (Ph*C*H$_2$), 41.1 (*C*H$_{2A\ or\ B}$), 40.8 (*C*H$_{2A\ or\ B}$), 34.2 (*C*H$_2$), 31.4 (*C*H), 26.4 (*C*H$_{A\ or\ B}$), 26.1 (*C*H$_{A\ or\ B}$), 23.5 (*C*H$_{2A\ or\ B}$), 23.3 (*C*H$_{2A\ or\ B}$), 22.0 (CH(*C*H$_3$)), 20.8 (CH(*C*H$_3$)), 16.5 (*C*H$_{3A\ or\ B}$), 16.3 (*C*H$_{3A\ or\ B}$), 12.9 (*C*H$_3$); **m/z (ES$^+$):** 437 (50%, MH$^+$), 459 (100%, MNa$^+$); **HRMS:** found 437.2790 (MH$^+$), $C_{27}H_{37}N_2O_3$ requires 437.2799.

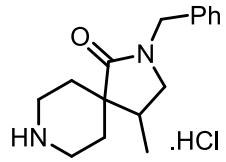
(1R,2S,5R)-2-isopropyl-5-methylcyclohexyl-2-benzyl-4-methyl-1-oxo-2,8-diazaspiro [4.5]decane-8-carboxylate (20)



(*1R*,*2S*,*5R*)-2-Isopropyl-5-methylcyclohexyl-2-benzyl-4-methyl-1-oxo-2,8-diazaspiro [4.5]deca-6,9-diene-8-carboxylate **9a** (73 mg, 0.18 mmol) was dissolved in 2:1 EtOH:EtOAc (2 mL) and run through the H-Cube (CatCart Pd/C 10% cartridge) at 90 bar, 30 °C and a flow rate of 0.8 mL.min^{-1}. The solvent was evaporated under reduced pressure and the crude product was purified by flash chromatography (SiO_2, EtOAc: petrol 1:5). The title compound was yielded as an amorphous white solid (72 mg, 91%).

R$_f$ **:** 0.50 (EtOAc:Petrol 1:1); **IR:** (υmax(film)/cm^{-1}) 1673 (C=O); **^{1}H-NMR:** (400 MHz, $CDCl_3$, 2 rotamers (A:B 1:1)) δ 7.33-7.21 (m, 5H, Ph), 4.58 (dt, J = 11.0, 4.5 Hz, 1H, O*C*H), 4.46 (d, J = 14.5 Hz, 1H, PhCH_2), 4.41 (d, J = 14.5 Hz, 1H, PhCH_2), 3.90-3.63 (m, 4H$_A$, 4H$_B$, NCH_2NCH_2), 3.28 (t, J = 8.5 Hz, 1H, NCH_2), 2.77 (dd, J = 9.5, 6.0 Hz, 1H, NCH_2), 2.12-2.07 (m, 2H, CH, CH_2), 1.92 (m, 1H, CH), 1.68-1.51 (m, 7H, 6 × CH_2, CH), 1.34 (m, 1H, CH), 1.11-1.00 (m, 2H, 2 × CH_2)), 0.94 (d, J = 7.0 Hz, 3H, CH_3), 0.90 (d, J = 7.0 Hz, 6H, CH(CH_3)$_2$), 0.88 (m, 1H, CH_2), 0.79 (d, J = 7.0 Hz, 3H, CH_3); **^{13}C-NMR:** (100 MHz, $CDCl_3$) δ 177.8 (*C*=O), 155.5 (*C*=O), 136.6 (Ph), 128.7 (Ph), 128.1 (Ph), 127.6 (Ph), 75.0 (O*C*H), 50.6 (N*C*H$_2$), 47.4 (*C*H), 46.5 (Ph*C*H$_2$), 44.4 (*C*), 41.6 (*C*H$_2$), 40.3 (N*C*H$_2$CH$_2$), 40.0 (N*C*H$_2$CH$_2$), 36.5 (*C*H), 34.4 (*C*H$_2$), 31.8 (*C*H), 31.4 (*C*H$_2$), 27.0 (*C*H$_2$), 26.5 (*C*H), 23.7 (*C*H$_2$), 22.1 (CH(*C*H$_3$)$_2$), 20.8 (CH(*C*H$_3$)$_2$), 16.7 (*C*H$_3$), 13.8 (*C*H$_3$); **m/z (ES$^+$):** 441 (10%, MH$^+$), 463 (100%, MNa$^+$); **HRMS:** found 441.3116 (MH$^+$), $C_{27}H_{41}N_2O_3$ requires 411.3112.

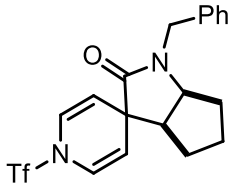
2-Benzyl-4-methyl-2,8-diazaspiro[4.5]decan-1-one hydrochloride (21)



Following Liebeskind,[3] (*1R,2S,5R*)-2-isopropyl-5-methylcyclohexyl 2-benzyl-4-methyl-1-oxo-2,8-diazaspiro[4.5]decane-8-carboxylate **20** (45 mg, 0.10 mmol) was dissolved in EtOH (1 mL) in a reusable sealed tube. KOH (2.0 M solution in EtOH, 1.5 mL) was added. The tube was sealed and the reaction mixture was stirred at 150 °C for 24 hours, and diluted with EtOAc (10 mL) and water (10 mL). The aqueous layer was washed with EtOAc (2 × 25 mL) and the organic layers were combined. The combined organics were washed with brine, dried over $MgSO_4$ and concentrated under reduced pressure. The free amine was acidified with 1M HCl in diethylether (5 mL) for 5 minutes and concentrated to give the title compound as a white solid (19 mg, 63%).

IR: (υmax(film)/cm^{-1}) 1637 (C=O); **^{1}H-NMR:** (400 MHz, $CDCl_3$, Tentatively assigned crude product) δ 9.49 (m, 2H, H_2N^+), 7.35-7.18 (m, 5H, Ph), 4.42 (br m, 2H, NCH_2), 3.96 (br m, 1H, NCH_2), 3.66 (br m, 1H, NCH_2), 3.38 (br m, 1H, CH_2), 3.28 (br m, 1H, NCH_2), 2.80 (br m, 1H, NCH_2), 2.20-1.38 (m, C*H*, 5H, 4 × CH_2), 0.81 (d, *J* = 7.0 Hz, 3H, CH_3); **m/z (ES$^+$):** 259 (100%, MH$^+$); **HRMS:** found 259.1817 (MH$^+$), $C_{16}H_{23}N_2O$ requires 259.1805.

3-Benzyl-1'-(trifluoromethane)sulfonyl-3,3^a,4,5,6,6^a-hexahydro-1'H,2H-spiro[cyclopenta[b]pyrrole-1,4'-pyridine]-2-one (22)

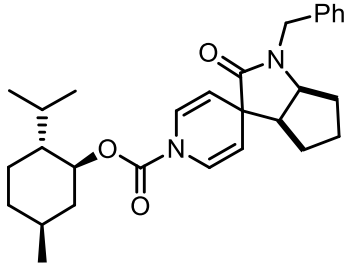


N-Benzyl-*N*-cyclopent-1-enyl-isonicotinamide **2e** (130 mg, 0.47 mmol) was dissolved in 2:1 EtOH:EtOAc (5 mL) and run through the H-Cube (CatCart Pd/C 10% cartridge) at 50 bar pressure, 30 °C at a flow rate of 0.8 mL.min^{-1}. The residue was evaporated under reduced pressure and the crude product was purified by flash chromatography (SiO_2, EtOAc:petrol 1:5) yielding a colourless oil (107 mg, 55%).

***R$_f$* :** 0.42 (EtOAc:petrol 1:2); **IR:** (υmax(film)/cm^{-1}) 1672; **^{1}H-NMR:** (400 MHz, $CDCl_3$) δ 7.26-7.19 (m, 5H, Ph), 6.69 (d, *J* = 8.5 Hz, 1H, NC*H*=CH), 6.51 (d, *J* = 8.5 Hz, 1H, NC*H*=CH), 5.15 (dd, *J* = 8.5, 2.5 Hz, 1H, NCH=C*H*), 4.91 (dd, *J* = 8.5, 2.5 Hz, 1H, NCH=C*H*), 4.55 (d, *J* = 15.0 Hz, 1H, PhCH_2), 4.40 (d, *J* = 15.0 Hz, 1H, PhCH_2), 2.31 (br m, 1H, NC*H*), 2.22 (dd, *J* = 8.5, 7.0 Hz, (1H, C)C*H*), 1.81 (m, 2H, CH_2), 1.68 (m, 2H, CH_2), 1.49 (m, 2H, CH_2); **^{13}C-NMR:** (100 MHz, $CDCl_3$) δ 177.5 (*C*=O), 137.7 (Ph), 128.9 (Ph), 128.1 (Ph), 127.8 (Ph), 123.7 (N*C*H=CH), 121.1 (N*C*H=CH), 113.7 (NCH=*C*H), 108.7 (NCH=*C*H), 99.2 (*C*H), 59.6 (*C*H), 46.3 (*C*), 43.6 (Ph*C*H$_2$), 38.4 (*C*H$_2$), 26.2 (*C*H$_2$), 24.6 (*C*H$_2$); **m/z (ES$^+$):** 413 (100%, MH$^+$).

[3] Shu, C.; Liebeskind, L. S. *J. Am. Chem*. **2003**, *125*, 2878.

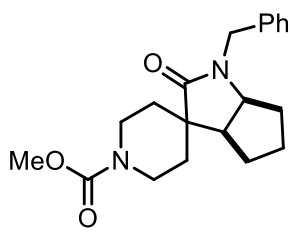
(*1R,2S,5R*)-2-isopropyl-5-methylcyclohexyl-1-benzyl-2-oxo-2,3a,4,5,6,6a-hexahydro -1H,1'H-spiro[cyclopenta[b]pyrrole-3,4'-pyridine]-1'-carboxylate (23)



(*1R,2S,5R*)-5-Methyl-2-(propan-2-yl)cyclohexyl-3-benzyl-2-oxo-3,5,6,6a-tetrahydro-1'H,2H-spiro[cyclopenta[b]pyrrole-1,4'-pyridine]-1'-carboxylate **9e** (396 mg, 0.86 mmol), was dissolved in 2:1 EtOH:EtOAc (9 mL) and run through the H-Cube (CatCart Pd/C 10% cartridge) at 75 bar, 30 °C and a flow rate of 0.8 mL.min^{-1}. The solvent was evaporated under reduced pressure and the crude product was purified by flash chromatography (SiO_2, EtOAc:petrol 1:5). The title compound was yielded as an amorphous white solid (346 mg, 87%).

***R*$_f$:** 0.41 (EtOAc:petrol 1:3); **^{1}H-NMR:** (400 MHz, $CDCl_3$, 2 rotamers (A:B 1:1)) δ 7.34-7.26 (m, 5H, Ph), 7.20 (m, 1H$_{A\ or\ B}$, NC*H*=CH), 7.08 (d, *J* = 7.5 Hz, 1H$_{A\ or\ B}$, NC*H*=CH), 7.02 (d, *J* = 7.5 Hz, 1H$_{A\ or\ B}$, NC*H*=CH), 6.90 (d, *J* = 7.5 Hz, 1H$_{A\ or\ B}$, NC*H*=CH), 5.02 (d, *J* = 15.0 Hz, 1H, PhC*H*$_2$), 4.84 (d, *J* = 7.5 Hz, 1H$_{A\ or\ B}$, NCH=C*H*), 4.76 (d, *J* = 7.5 Hz, 1H$_{A\ or\ B}$, NCH=C*H*), 4.73 (m, 1H$_{A\ or\ B}$, NCH=C*H*), 4.69 (dt, *J* = 11.0, 4.0 Hz, 1H, OC*H*), 4.63 (m, 1H$_{A\ or\ B}$, NCH=C*H*), 3.90 (d, *J* = 15.0 Hz, 1H, PhC*H*$_2$), 3.81 (m, 1H, NC*H*), 2.34 (m, 1H, NCHC*H*), 2.07 (m, 1H, C*H*$_2$), 1.91 (m, 1H, C*H*), 1.73 (m, 2H, C*H*$_2$), 1.70 (m, 1H, C*H*$_2$), 1.68 (m, 1H, C*H*$_2$), 1.62 (m, 2H, 2 × C*H*$_2$), 1.55 (m, 1H, C*H*), 1.51 (m, 1H, C*H*), 1.43 (m, 1H, C*H*), 1.07 (m, 1H, C*H*$_2$), 1.00 (m, 1H, C*H*$_2$), 0.92 (d, *J* = 6.5 Hz, 3H$_{A\ or\ B}$, CH(C*H*$_3$)$_2$), 0.90 (d, *J* = 6.5 Hz, 3H$_{A\ or\ B}$, CH(C*H*$_3$)$_2$), 0.86 (m, 1H, C*H*$_2$), 0.78 (s, 3H, C*H*$_3$); **^{13}C-NMR:** (125 MHz, $CDCl_3$) δ 175.5 (*C*=O), 150.8 (*C*=O), 136.5 (Ph), 128.7 (Ph), 128.3 (Ph), 127.6 (Ph), 125.1 (N*C*H=CH$_{A\ or\ B}$), 124.8 (N*C*H=CH$_{A\ or\ B}$), 122.7 (N*C*H=CH$_{A\ or\ B}$), 122.4 (N*C*H=CH$_{A\ or\ B}$), 109.3 (NCH=*C*H$_{A\ or\ B}$), 108.8 (NCH=*C*H$_{A\ or\ B}$), 105.0 (NCH=*C*H$_{A\ or\ B}$), 104.4 (NCH=*C*H$_{A\ or\ B}$), 76.8 (O*C*H), 58.9 (N*C*H), 51.7 (NCH*C*H), 47.8 (*C*), 47.1 (*C*H), 44.9 (Ph*C*H$_2$), 41.0 (*C*H$_2$), 34.2 (*C*H$_2$), 31.4 (*C*H), 30.2 (*C*H$_2$), 26.1 (CH$_2$), 24.5 (*C*H), 23.2 (CH$_2$), 22.0 (CH(*C*H$_3$)), 20.8 (CH(*C*H$_3$)), 16.2 (*C*H$_3$); **m/z (ES$^+$):** 485 (100%, MNa$^+$).

Methyl 1-benzyl-2-oxohexahydro-1H-spiro[cyclopenta[b]pyrrole-3,4'-piperidine]-1'-carboxylate (24)

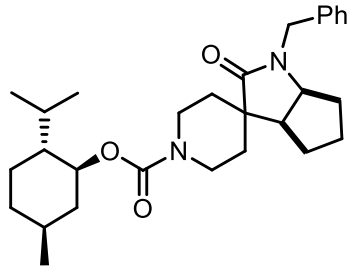


Methyl-1-benzyl-2-oxo-2,3a,4,5-tetrahydro-1H,1'H-spiro[cyclopenta[b]pyrrole-3,4'-pyridine]-1'carboxylate **7e** (228 mg, 0.68 mmol) was dissolved in 2:1 EtOH:EtOAc (7 mL) and run through the H-Cube (CatCart Pd/C 10% cartridge) at 60 bar, 30 °C and a flow rate of 0.8 mL.min^{-1}. The solvent was evaporated under reduced pressure and the crude product was purified by flash chromatography (SiO_2, EtOAc:petrol 1:5). The title compound was yieldied as an amorphous white solid (213 mg, 91%).

***R*$_f$:** 0.33 (EtOAc:petrol 1:1); **IR:** (υmax(film)/cm^{-1}) 1688 (C=O), 1676 (C=O); **^{1}H-NMR:** (400 MHz, $CDCl_3$, 2 rotamers (A:B 1:1)) δ 7.33-7.17 (m, 5H, Ph), 5.03 (d, *J* = 14.5 Hz, 1H,

PhCH_2), 4.09 (br m, 2H$_{A\ or\ B}$, NCH_2CH$_2$), 3.94 (br m, 2H$_{A\ or\ B}$, NCH_2CH$_2$), 3.81 (d, J = 14.5 Hz, 1H, PhCH_2), 3.71 (m, 1H, NCH) 3.70 (s, 3H, OCH_3), 3.18 (m, 2H$_{A\ or\ B}$, NCH_2CH$_2$), 3.08 (m, 2H$_{A\ or\ B}$, NCH_2CH$_2$), 2.38 (m, 1H, NCHCH), 2.00 (m, 1H, CH_2), 1.71-1.43 (m, 8H, CH_2), 1.27 (m, 1H, CH_2); **^{13}C-NMR:** (100 MHz, $CDCl_3$) δ 177.2 (*C*=O), 156.0 (*C*=O), 136.5 (Ph), 128.7 (Ph), 128.2 (Ph), 127.6 (Ph), 58.9 (N*C*H), 52.6 (O*C*H$_3$), 45.2 (*C*), 45.1 (NCH*C*H), 44.0 (Ph*C*H$_2$), 40.8 (N*C*H$_2$), 40.4 (N*C*H$_2$), 33.8 (*C*H$_2$), 29.8 (*C*H$_2$), 28.5 (*C*H$_2$), 27.3 (*C*H$_2$), 25.2 (*C*H$_2$); **m/z (ES$^+$):** 343 (80%, MH$^+$), 365 (100%, MNa$^+$).

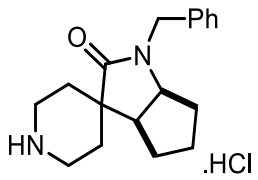
(1R,2S,5R)-2-isopropyl-5-methylcyclohexyl-1-benzyl-2-oxohexahydro-1H-spiro[cyclopenta[b]pyrrole-3,4'-piperidine]-1'-carboxylate (25)



(*1R,2S,5R*)-5-Methyl-2-(propan-2-yl)cyclohexyl-3-benzyl-2-oxo-3,5,6,6a-tetrahydro-1'H,2H-spiro[cyclopenta[b]pyrrole-1,4'-pyridine]-1'-carboxylate **9e** (104 mg, 0.23 mmol) was dissolved in 2:1 EtOH:EtOAc (3 mL) and run through the H-Cube (CatCart Pd/C 10% cartridge) at 90 bar, 30 °C and at a flow rate of 0.8 mL.min^{-1}. A flow system was set up. After 3 hours, the solvent was evaporated under reduced pressure and the crude product was purified by flash chromatography (SiO_2, EtOAc:petrol 1:5) to yield the title compound as as a white solid (95 mg, 90%).

***R$_f$* :** 0.28 (EtOAc:petrol 1:3); **m.p.:** 100 °C (EtOAc); **IR:** (υmax(film)/cm^{-1}): 1717 (C=O), 1686 (C=O); **^{1}H-NMR:** (400 MHz, $CDCl_3$, 2 rotamers (A:B 1:1)) δ 7.34-7.18 (m, 5H, Ph), 5.06 (d, J = 14.5 Hz, 1H, PhCH_2), 4.58 (m, 1H, OCH), 4.11 (br m, 2H$_{A\ or\ B}$, NCH_2CH$_2$), 3.98 (br m, 2H$_{A\ or\ B}$, NCH_2CH$_2$), 3.80 (d, J = 14.5 Hz, 1H, PhCH_2), 3.72 (m, 1H, NCH), 3.15 (ddd, J = 13.5, 10.5, 3.0 Hz, 2H$_{A\ or\ B}$, NCH_2CH$_2$), 3.04 (m, 2H$_{A\ or\ B}$, NCH_2CH$_2$), 2.40 (q, J = 7.5 Hz, 1H, NCHCH), 2.07 (m, 1H, CH_2), 1.99 (m, 1H, CH_2), 1.91 (m, 1H, CH), 1.77-1.47 (m, 10H, CH, 9 × CH_2), 1.34 (m, 2H, CH, CH_2), 1.07 (m, 1H, CH_2), 0.90 (d, J = 7.0 Hz, 6H, CH(CH_3)$_2$), 0.89 (m, 1H, CH_2), 0.80 (d, J = 7.0 Hz, 3H, CH_3); **^{13}C-NMR:** (100 MHz, $CDCl_3$) δ 177.3 (*C*=O), 157.5 (*C*=O), 135.0 (Ph), 128.7 (Ph), 128.2 (Ph), 127.5 (Ph), 75.1 (O*C*H), 58.9 (N*C*H), 47.4 (*C*H), 45.0 (NCH*C*H), 44.0 (Ph*C*H$_2$), 41.6 (*C*H$_2$), 40.6 (N*C*H$_2$CH$_2$), 40.2 (N*C*H$_2$CH$_2$), 34.4 (*C*H$_2$), 33.8 (*C*H$_2$), 31.4 (*C*H), 29.8 (*C*H$_2$), 28.4 (*C*H$_2$), 27.3 (*C*H$_2$), 26.5 (*C*H), 25.1 (*C*H$_2$), 23.7 (*C*H$_2$), 22.0 (*C*H(CH$_3$)), 20.8 (2 × CH(*C*H$_3$)), 16.7 (*C*H$_3$); **m/z (ES$^+$):** 489 (100%, MNa$^+$); **HRMS:** found 489.3085 (MNa$^+$), $C_{29}H_{42}N_2O_3Na$ requires 489.3088.

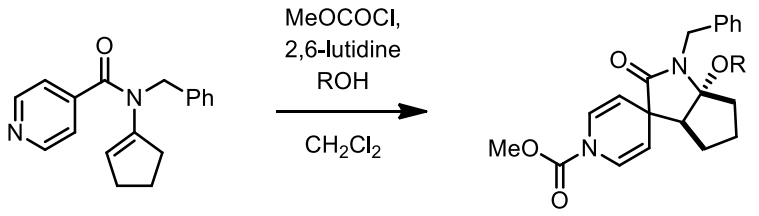
1-Benzyltetrahydro-1H-spiro[cyclopenta[b]pyrrole-3,4'-piperidin]-2(3aH)-one hydrochloride (26)



Following Liebeskind,[3] (*1R,2S,5R*)-2-isopropyl-5-methylcyclohexyl-1-benzyl-2-oxohexahydro-1H-spiro[cyclopenta[b]pyrrole-3,4'-piperidine]-1'-carboxylate **25** (104 mg, 0.23 mmol) was dissolved in EtOH (2 mL) in a reusable sealed tube. KOH in ethanol (2.0 M, 3 mL) was added. The tube was sealed and the reaction mixture was stirred at 150 °C for 24 hours, and diluted with EtOAc (10 mL) and water (10 mL). The aqueous layer was washed with EtOAc (2 × 25 mL) and the organic layers were combined. The combined organics were washed with brine, dried over $MgSO_4$ and concentrated under reduced pressure. The free amine was acidified with 1M HCl in diethylether (5 mL) for 5 minutes and concentrated to give the title compound as a white solid (52 mg, 71%).

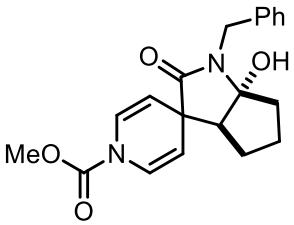
IR: (υmax(film)/cm^{-1}) 1626 (C=O); **^{1}H-NMR:** (400 MHz, $CDCl_3$) δ 9.56 (br d, m, 2H, H_2N^+), 7.33-7.16 (m, 5H, Ph), 4.98 (d, J = 14.5 Hz, 1H, PhCH_2), 4.02 (br m, 1H, NCH_2), 3.82 (d, J = 14.5 Hz, 1H, PhCH_2), 3.76 (br m, 1H, NCH_2), 3.51 (m, 1H, NCH_2), 3.27 (m, 2H, NCH_2, NCH), 2.26 (m, 11H, CH, 10 × CH_2); **m/z (ES$^+$):** 100% (MH^+ 285); **HRMS:** found 285.1958 (MH^+), $C_{18}H_{25}N_2O$ requires 285.1962.

General Procedure C for Dearomatising Cyclisations (with the addition of a nucleophile)



Cyclisation precursor was dissolved in dichloromethane (0.05M). The solution was cooled to 0 °C and 2,6-lutidine (1 equiv.), ROH (1-3 equiv.) and methyl chloroformate (1 equiv.) were added sequentially. After 30 minutes the solution was quenched by saturated sodium hydrogen carbonate solution (0.2M) and extracted twice using dichloromethane (0.2M). Organic layers were dried with $MgSO_4$, filtered and evaporated under reduced pressure. The residue was purified by flash chromatography (SiO_2, EtOAc:petrol 1:19) to yield the spirocyclic dihydropyridine.

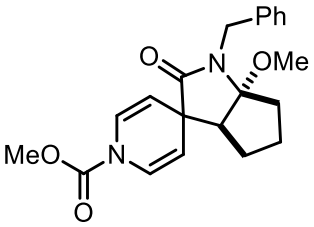
Methyl-1-benzyl-6a-hydroxy-2-oxo-2,3a,4,5,6,6a-hexahydro-1H,1'H-spiro [cyclo-penta[b]pyrrole-3,4'-pyridine]-1'-carboxylate (27a)



Following general procedure C, the racemic title compound was obtained from *N*-benzyl-cyclopent-1-enyl-isonicotinamide **1e** (212 mg, 0.76 mmol) (using methylchloroformate (0.76 mmol) and 2,6-lutidine (0.76 mmol) and distilled water (2.28 mmol) in dichloromethane: acetone (1:1 rather than dichloromethane)) as a white solid after purification (242 mg, 90%).

***R_f*:** 0.32 (EtOAc:petrol 1:1); **m.p.:** 143-145 °C (EtOAc); **IR:** (υmax(film)/cm^{-1}) 3339 (O-H), 1726 (C=O), 1687 (C=O); **^{1}H-NMR:** (400 MHz, $CDCl_3$, 2 rotamers (A:B 1:1)) δ 7.34-7.23 (m, 5H, Ph), 7.17 (d, *J* = 7.5 Hz, $1H_{A\ or\ B}$, NC*H*=CH), 7.04 (d, *J* = 7.5 Hz, $1H_{A\ or\ B}$, NC*H*=CH), 6.98 (d, *J* = 7.5 Hz, $1H_{A\ or\ B}$, NC*H*=CH), 6.84 (d, *J* = 7.5 Hz, $1H_{A\ or\ B}$, NC*H*=CH), 5.00 (d, *J* = 7.5 Hz, $1H_{A\ or\ B}$, NCH=C*H*), 4.90 (d, *J* = 7.5 Hz, $1H_{A\ or\ B}$, NCH=C*H*), 4.74 (d, *J* = 7.5 Hz, $1H_{A\ or\ B}$, NCH=C*H*), 4.65 (d, *J* = 7.5 Hz, $1H_{A\ or\ B}$, NCH=C*H*), 4.55 (d, *J* = 15.0 Hz, 1H, PhCH_2), 4.50 (d, *J* = 15.0 Hz, 1H, PhCH_2), 3.82 (s, 3H, OCH_3), 2.94 (m, 1H, O*H*), 2.25 (m, 1H, C*H*), 1.87-1.64 (m, 5H, CH_2), 1.46 (m, 1H, CH_2); **^{13}C-NMR:** (100 MHz, $CDCl_3$) δ 175.8 (*C*=O), 151.7 (*C*=O), 138.2 (Ph), 128.7 (Ph), 128.1 (Ph), 127.5 (Ph), 125.2 (N*C*H=$CH_{A\ or\ B}$), 124.9 (N*C*H=$CH_{A\ or\ B}$), 122.6 (N*C*H=$CH_{A\ or\ B}$), 122.4 (N*C*H=$CH_{A\ or\ B}$), 110.5 (NCH=*C*$H_{A\ or\ B}$), 110.0 (NCH=*C*$H_{A\ or\ B}$), 105.0 (NCH=*C*$H_{A\ or\ B}$), 104.6 (NCH=*C*$H_{A\ or\ B}$), 99.2 (*C*), 60.1 (*C*H), 53.7 (O*C*H_3), 47.0 (*C*OH), 43.5 (Ph*C*H_2), 38.4 (*C*H_2), 26.2 (*C*H_2), 24.7 (*C*H_2); **m/z (ES):** 377 (100%, MNa^+); **HRMS:** found 355.1657 (MH^+), $C_{20}H_{23}N_2O_4$ requires 355.1653.

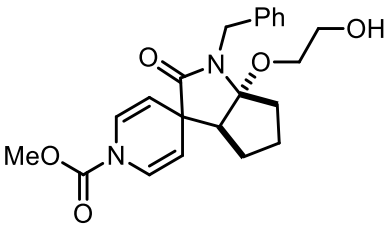
Methyl-1-benzyl-6a-methoxy-2-oxo-2,3a,4,5,6,6a-hexahydro-1H,1'H-spiro [cyclopenta[b]pyrrole-3,4'-pyridine]-1'-carboxylate (27b)



Following procedure C, the racemic title compound was obtained from *N*-benzyl-cyclopent-1-enyl-isonicotinamide **1e** (115 mg, 0.41 mmol), (using methyl chloroformate (0.41 mmol), 2,6-lutidine (0.41 mmol) and methanol (0.017 mL)) as a white solid after purification (113 mg, 75%).

***R*$_f$:** 0.61 (EtOAc:petrol 1:1); **m.p.:** 164-166 °C (EtOAc); **IR:** (υmax(film)/cm^{-1}) 1728 (C=O), 1690 (C=O); **^{1}H-NMR:** (400 MHz, $CDCl_3$, 2 rotamers (A:B 1:1)) δ 7.36-7.24 (m, 5H, Ph), 7.23 (m, 1H$_{A\ or\ B}$, NC*H*=CH), 7.14 (m, 1H$_A$, 1H$_B$, NC*H*=CH), 7.01 (m, 1H$_{A\ or\ B}$, NC*H*=CH), 4.87 (m, 1H$_{A\ or\ B}$, NCH=C*H*), 4.80 (m, 1H$_{A\ or\ B}$, NCH=C*H*), 4.70 (d, *J* = 15.0 Hz, 1H, PhC*H*$_2$), 4.69 (m, 1H$_{A\ or\ B}$, NCH=C*H*), 4.64 (m, 1H$_{A\ or\ B}$, NCH=C*H*), 4.16 (d, *J* = 15.0 Hz, 1H, PhC*H*$_2$), 3.84 (s, 3H, OMe), 3.02 (s, 3H, OMe), 2.27 (m, 1H, C*H*), 1.88-1.58 (m, 5H, C*H*$_2$), 1.34 (m, 1H, C*H*$_2$); **^{13}C-NMR:** (100 MHz; $CDCl_3$) δ 176.7 (*C*=O), 151.6 (*C*=O), 137.9 (Ph), 128.5 (Ph), 128.2 (Ph), 127.4 (Ph), 124.9 (N*C*H=CH$_{A\ or\ B}$), 124.6 (N*C*H=CH$_{A\ or\ B}$), 123.3 (N*C*H=CH$_{A\ or\ B}$), 123.2 (N*C*H=CH$_{A\ or\ B}$), 108.9 (NCH=*C*H$_{A\ or\ B}$), 108.4 (NCH=*C*H$_{A\ or\ B}$), 105.5 (NCH=*C*H$^{A\ or\ B}$), 105.0 (NCH=*C*H$_{A\ or\ B}$), 104.1 (*C*), 53.7 (COO*C*H$_3$), 52.3 (*C*H or O*C*H$_3$), 50.2 (*C*H or O*C*H$_3$), 47.1 (*C*OH), 43.6 (Ph*C*H$_2$), 37.4 (*C*H$_2$), 26.4 (*C*H$_2$), 24.6 (*C*H$_2$); **m/z (ES$^+$):** 369 (10%, MH$^+$), 391 (100%, MNa$^+$); **HRMS:** found 369.1806 (MH$^+$), $C_{21}H_{25}N_2O_4$ requires 369.1806.

Methyl-1-benzyl-6a-(2-hydroxyethoxy)-2-oxo-2,3a,4,5,6,6a-hexahydro-1H,1'H-spiro[cyclopenta[b]pyrrole-3,4'-pyridine]-1'-carboxylate (27c)

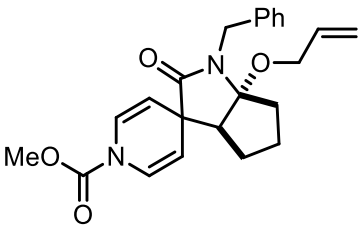


Following general procedure C, the racemic title compound was obtained from *N*-benzyl-cyclopent-1-enyl-isonicotinamide **1e** (133 mg, 0.48 mmol) (using methyl chloroformate (0.48 mmol), 2,6-luitidine (0.48 mmol) and ethylene glycol (0.48 mmol)) as a white solid after purification (172 mg, 76%).

***R*$_f$:** 0.24 (EtOAc:petrol 1:1); **m.p.:** 113-115 °C (EtOAc); **IR:** (υmax(film)/cm^{-1}) 3445 (O-H), 1727 (C=O), 1688 (C=O); **^{1}H-NMR:** (400 MHz, $CDCl_3$, 2 rotamers (A:B 1:1)) δ 7.34-7.26 (m, 5H, Ph), 7.24 (m, 1H$_{A\ or\ B}$, NC*H*=CH), 7.15 (m, 1H$_A$, 1H$_B$, NC*H*=CH), 7.01 (m, 1H$_{A\ or\ B}$, NC*H*=CH), 4.95 (m, 1H$_{A\ or\ B}$, NCH=C*H*), 4.85 (m, 1H$_{A\ or\ B}$, NCH=C*H*), 4.68 (m, 1H$_{A\ or\ B}$, NCH=C*H*), 4.62 (d, *J* = 15.0 Hz, 1H, PhC*H*$_2$), 4.61 (m, 1H$_{A\ or\ B}$, NCH=C*H*), 4.29 (d, *J* = 15.0 Hz, 1H, PhC*H*$_2$), 3.85 (s, 1H, OC*H*$_3$), 3.63 (m, 2H, OC*H*$_2$), 3.36 (dt, *J* = 5.5, 4.5 Hz, 1H, OC*H*), 3.13 (dt, *J* = 8.5, 4.5 Hz, 1H, OC*H*), 2.32 (dd, *J* = 9.0, 4.0 Hz, 1H, C*H*), 1.85-1.72 (m, 5H, C*H*$_2$), 1.64 (dd, ap q, *J* = 6.0 Hz, 1H, O*H*), 1.35 (m, 1H, C*H*$_2$); **^{13}C-NMR:** (125 MHz, $CDCl_3$) δ 176.7 (*C*=O), 151.6 (*C*=O), 138.0 (Ph), 128.6 (Ph), 128.1 (Ph), 127.5 (Ph), 124.7 (N*C*H=CH$_{A\ or\ B}$), 124.5 (N*C*H=CH$_{A\ or\ B}$), 123.8 (N*C*H=CH$_{A\ or\ B}$), 123.5 (N*C*H=CH$_{A\ or\ B}$), 108.2 (NCH=*C*H$_{A\ or\ B}$), 107.7 (NCH=*C*H$_{A\ or\ B}$), 104.8 (NCH=*C*H$_{A\ or\ B}$), 104.1 (NCH=*C*H$_{A\ or}$

$_B$), 103.9 (*C*), 64.0 (*O*CH_2), 61.6 (CH_2OH), 53.8 (COO*C*H_3), 53.2 (*C*H), 47.0 (*C*OCH_2), 43.7 (Ph*C*H_2), 37.0 (*C*H_2), 26.4 (*C*H_2), 24.6 (*C*H_2); **m/z (ES$^+$):** 399 (10%, MH^+), 421 (100%, MNa^+); **HRMS:** found 399.1913 (MH^+), $C_{22}H_{27}N_2O_5$ requires 399.1915.

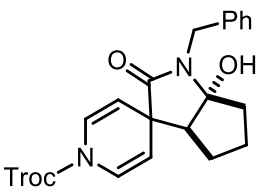
Methyl-6a-(allyloxy)-1-benzyl-2-oxo-2,3a,4,5,6,6a-hexahydro-1H,1'H-spiro[cyclopenta[b]pyrrole-3,4'-pyridine]-1'-carboxylate (27d)



Following general procedure C, the racemic title compound was obtained from *N*-benzyl-cyclopent-1-enyl-isonicotinamide **1e** (106 mg, 0.38 mmol) (using methyl chloroformate (0.38 mmol) 2,6-lutidine (0.38 mmol) and allylalcohol (0.38 mmol)) as a white solid after purification (112 mg, 63%).

***R*$_f$:** 0.56 (EtOAc:petrol 1:1); **m.p.:** 83-86 °C (EtOAc); **IR:** (υmax(film)/cm^{-1}) 1728 (C=O), 1690 (C=O); **^{1}H-NMR:** (400 MHz, $CDCl_3$, 2 rotamers (A:B 1:1)) δ 7.35-7.23 (m, 5H, Ph), 7.20 (m, 1H$_{A\ or\ B}$, NC*H*=CH), 7.15 (m, 1H$_A$, 1H$_B$, NC*H*=CH), 7.01 (m, 1H$_{A\ or\ B}$, NC*H*=CH), 5.81 (ddt, *J* = 17.0, 10.5, 5.5 Hz, 1H, C*H*=CH_2), 5.26 (dd, *J* = 17.0, 2.5 Hz, 1H, CH=CH_2^{trans}), 5.17 (dd, *J* = 10.5, 2.5 Hz, 1H, CH=CH_2^{cis}), 4.95 (m 1H$_{A\ or\ B}$, NCH=C*H*), 4.88 (m, 1H, NCH=C*H*), 4.68 (m, 1H, NCH=C*H*), 4.66 (d, *J* = 15.0 Hz, 1H, PhCH_2), 4.63 (m, 1H$_{A\ or\ B}$, NCH=C*H*), 4.20 (d, *J* = 15.0 Hz, 1H, PhCH_2), 3.84 (s, 3H, OCH_3), 3.76 (dd, *J* = 12.0, 5.5 Hz, 1H, OCH_2), 3.57 (dd, *J* = 12.0, 5.5 Hz, 1H, OCH_2), 2.32 (dd, *J* = 9.0, 4.0 Hz, 1H, C*H*), 1.86-1.62 (m, 5H, CH_2), 1.35 (m, 1H, CH_2); **^{13}C-NMR:** (100 MHz: $CDCl_3$) δ 176.6 (C=O), 151.6 (C=O), 137.9 (Ph), 133.8 (*C*H=CH_2), 128.5 (Ph), 128.2 (Ph), 127.4 (Ph), 124.8 (N*C*H=CH$_{A\ or\ B}$), 124.5 (N*C*H=CH$_{A\ or\ B}$), 123.9 (N*C*H=CH$_{A\ or\ B}$), 123.7 (N*C*H=CH$_{A\ or\ B}$), 117.0 (CH=*C*H_2), 108.3 (NCH=*C*H$_{A\ or\ B}$), 107.8 (NCH=*C*H$_{A\ or\ B}$), 104.8 (NCH=*C*H$_{A\ or\ B}$), 104.1 (NCH=*C*H$_{A\ or\ B}$), 103.9 (*C*), 63.9 (OCH_2), 53.7 (OCH_3), 53.1 (*C*H), 47.2 (*C*OCH_2), 43.7 (Ph*C*H_2), 37.5 (*C*H_2), 26.4 (*C*H_2), 24.6 (*C*H_2); **m/z (ES$^+$):** 395 (30%, MH^+), 417 (100%, MNa^+); **HRMS:** found 395.1975 (MH^+), $C_{23}H_{27}N_2O_4$ requires 395.1966.

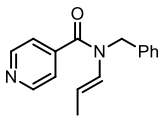
2,2,2-Trichloroethyl 1-benzyl-6a-hydroxy-2-oxo-2,3a,4,5,6,6a-hexahydro-1H,1'H-spiro[cyclopenta[b]pyrrole-3,4'-pyridine]-1'-carboxylate (27e)



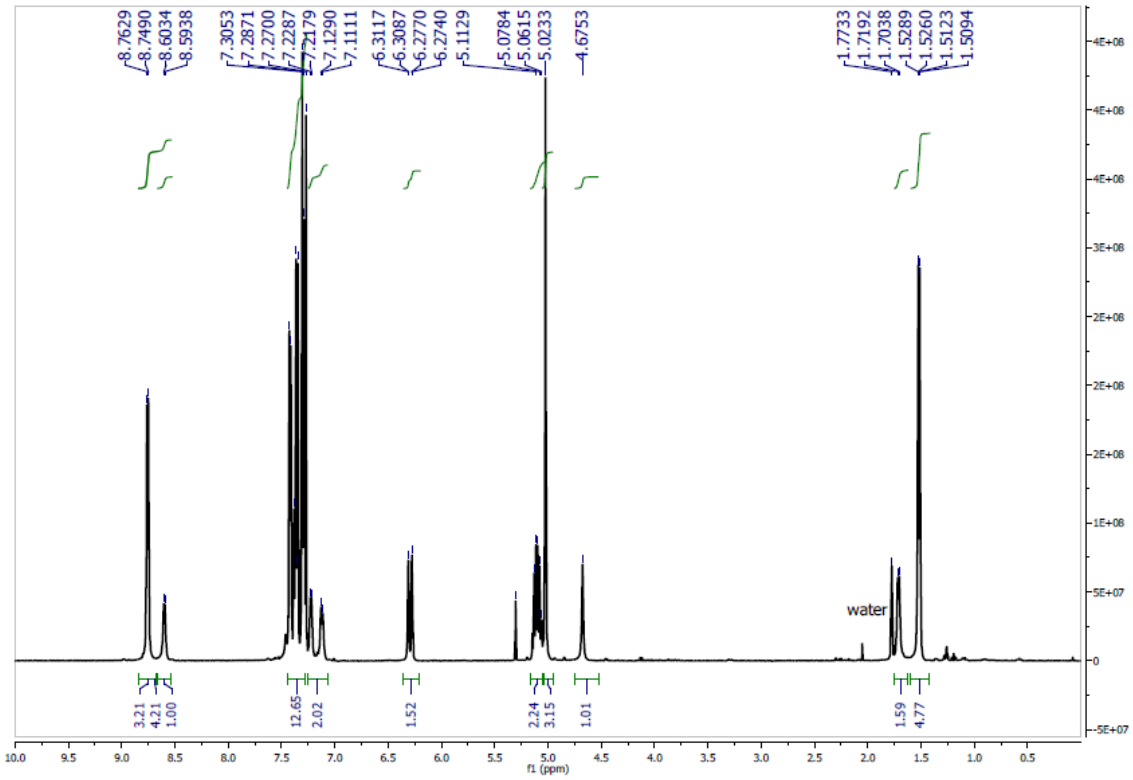
Following general procedure B, the racemic title compound was obtained from *N*-benzyl-cyclopent-1-enyl-isonicotinamide **1e** (123 mg, 0.44 mmol), using 2,2,2-trichloroethyl chloroformate (0.44 mmol) 2,6-lutidine (0.44 mmol) and distilled water (0.023 mL, 1.32 mmol) and dichloromethane:acetone (1:1) (12 mL), as a white solid after purification (83%).

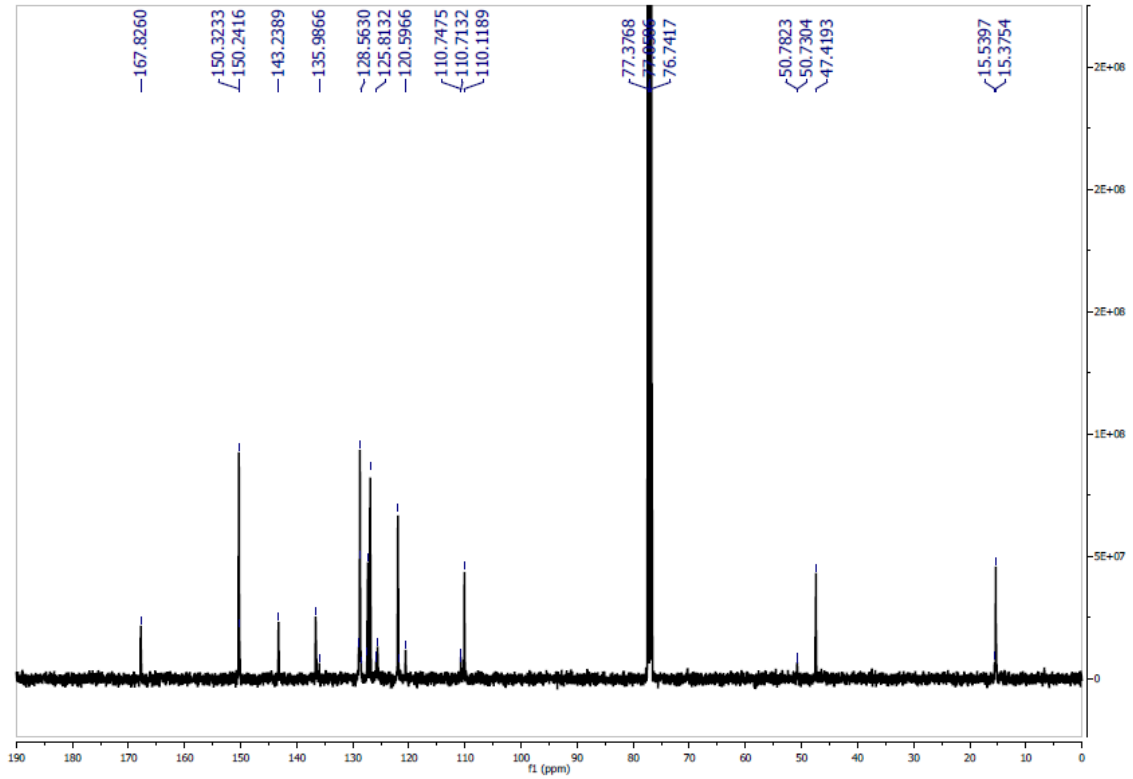
***R*$_f$:** 0.42 (EtOAc:petrol 1:1); **m.p.:** 162-164 °C ($CHCl_3$); **IR:** (υmax(film)/cm^{-1}) 3342 (O-H), 1733 (C=O); 1690 (C=O); **^{1}H-NMR:** (400 MHz, $CDCl_3$, 2 rotamers (A:B 1:1)) δ 7.37-7.27 (m, 5H, Ph), 7.18 (d, *J* = 8.5 Hz, 1H$_{A\ or\ B}$, NC*H*=CH), 7.17 (d, *J* = 8.5 Hz, 1H$_{A\ or\ B}$, NC*H*=CH), 7.00 (m, 1H$_{A\ or\ B}$, NC*H*=CH), 6.99 (m, 1H$_{A\ or\ B}$, NC*H*=CH), 5.08 (dd, *J* = 8.5, 1.5

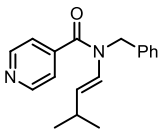
Hz, 1H$_{A\ or\ B}$, NCH=C*H*), 5.01 (dd, *J* = 8.5, 1.5 Hz, 1H$_{A\ or\ B}$, NCH=C*H*), 4.86 (m, 1H$_{A\ or\ B}$, NCH=C*H*), 4.82 (s, 2H, Cl_3CCH_2), 4.79 (m, 1H$_{A\ or\ B}$, NCH=C*H*), 4.66 (d, *J* = 15.0 Hz, 1H, PhCH_2), 4.46 (d, *J* = 15.0 Hz, 1H, PhCH_2), 2.28-2.25 (m, 2H, C*H*, CO*H*), 1.88 (m, 2H, CH_2), 1.77 (m, 2H, CH_2), 1.65 (m, 1H, CH_2), 1.53 (m, 1H, CH_2); **^{13}C-NMR:** (100 MHz, $CDCl_3$) δ 175.3 (C=O), 153.8 (*C*=O), 138.1 (Ph), 128.8 (Ph), 128.2 (Ph), 127.7 (Ph), 125.0 (N*C*H=CH$_{A\ or\ B}$), 124.5 (N*C*H=CH$_{A\ or\ B}$), 122.4 (N*C*H=CH$_{A\ or\ B}$), 122.0 (N*C*H=CH$_{A\ or\ B}$), 111.7 (NCH=*C*H$_{A\ or\ B}$), 111.1 (NCH=*C*H$_{A\ or\ B}$), 106.3 (NCH=*C*H$_{A\ or\ B}$), 99.2 (*C*), 77.2 (Cl_3C), 75.6 (Cl_3CCH_2), 60.0 (C*H*), 47.0 (*C*OH), 43.6 (Ph*C*H$_2$), 38.4 (*C*H$_2$), 26.3 (*C*H$_2$), 24.7 (*C*H$_2$); **m/z (ES$^+$):** 493 (50%, MNa$^+$).


O
N
Ph
N

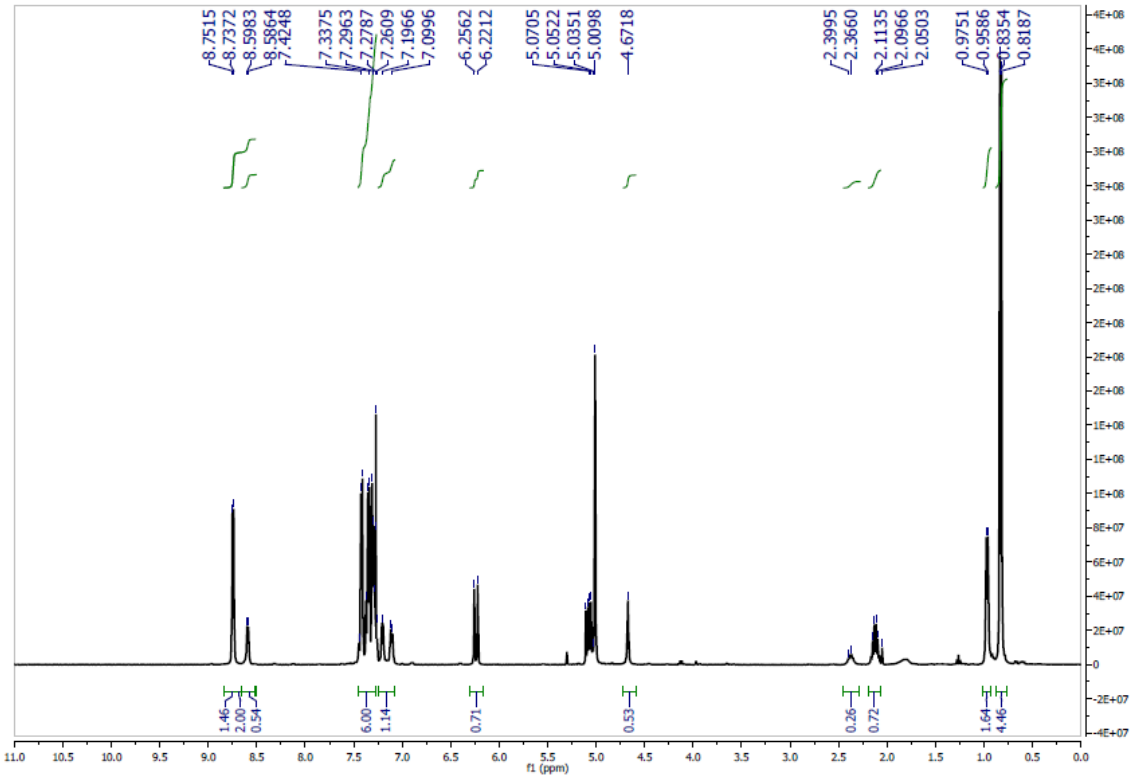
1a

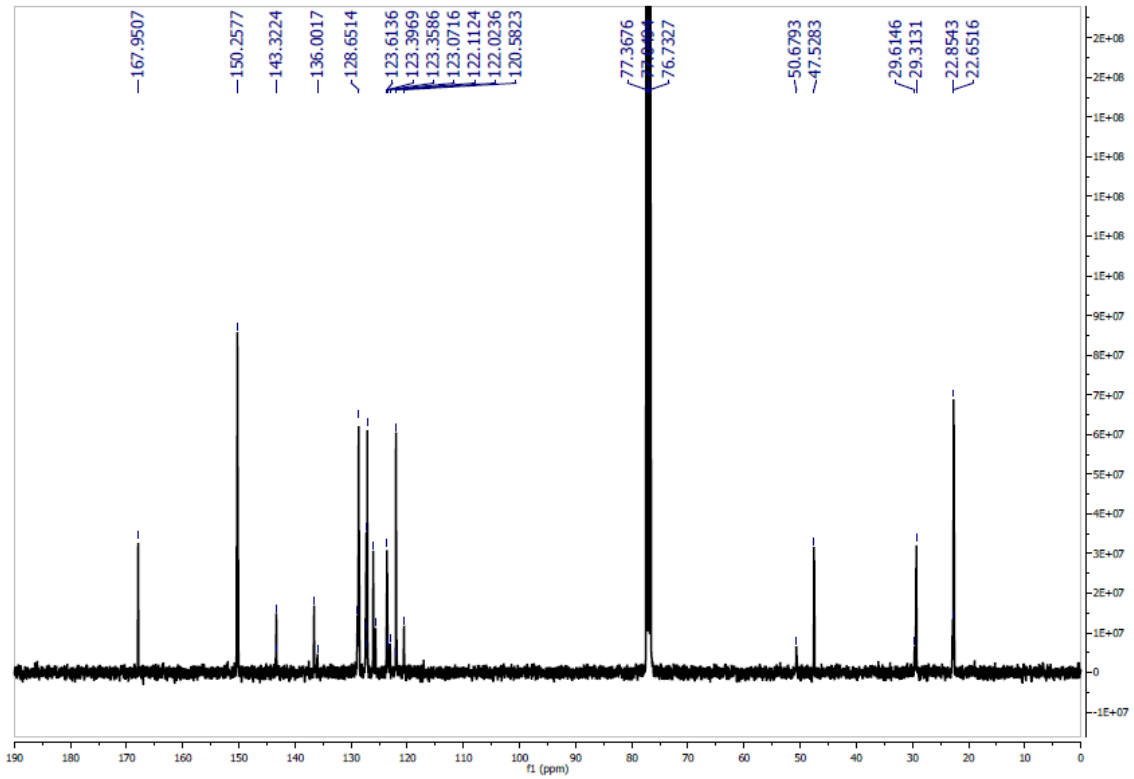

8.7629
8.7490
8.6034
8.5938
7.3053
7.2871
7.2700
7.2287
7.2179
7.1290
7.1111
6.3117
6.3087
6.2770
6.2740
5.1129
5.0784
5.0615
5.0233
4.6753
1.7733
1.7192
1.7038
1.5289
1.5260
1.5123
1.5094
water
3.21
4.21
1.00
12.65
2.02
1.52
2.24
3.15
1.01
1.59
4.77
f1 (ppm)

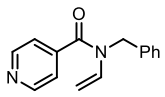

167.8260
150.3233
150.2416
143.2389
135.9866
128.5630
125.8132
120.5966
110.7475
110.7132
110.1189
77.3768
77.0586
76.7417
50.7823
50.7304
47.4193
15.5397
15.3754
f1 (ppm)


O
N
Ph
N

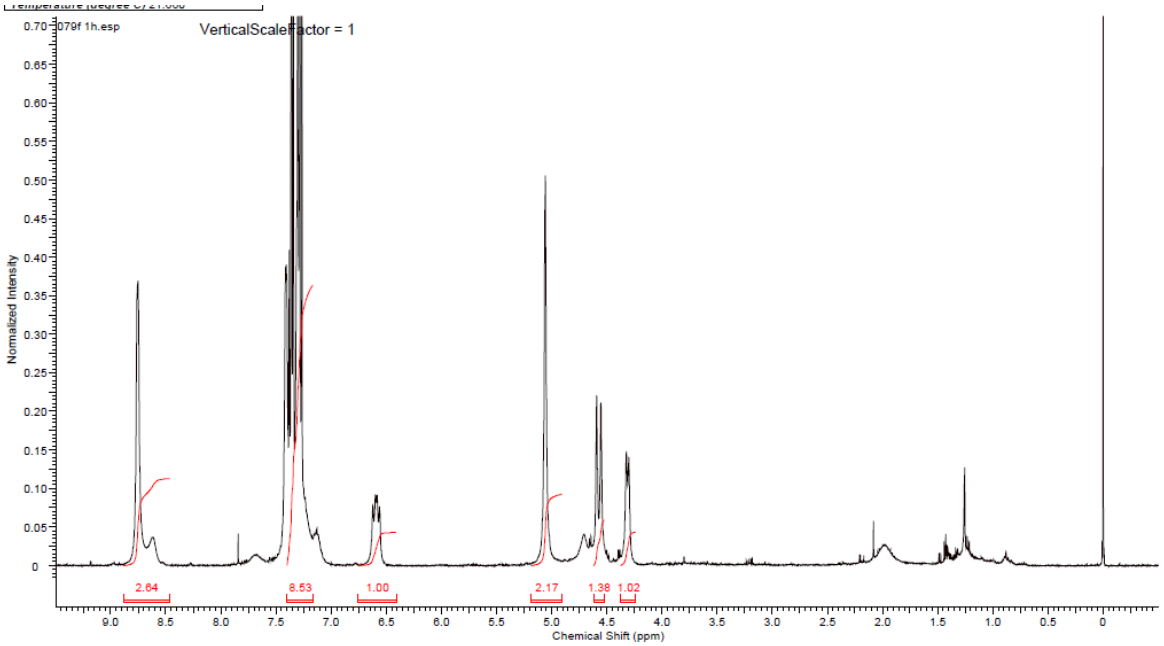
1b

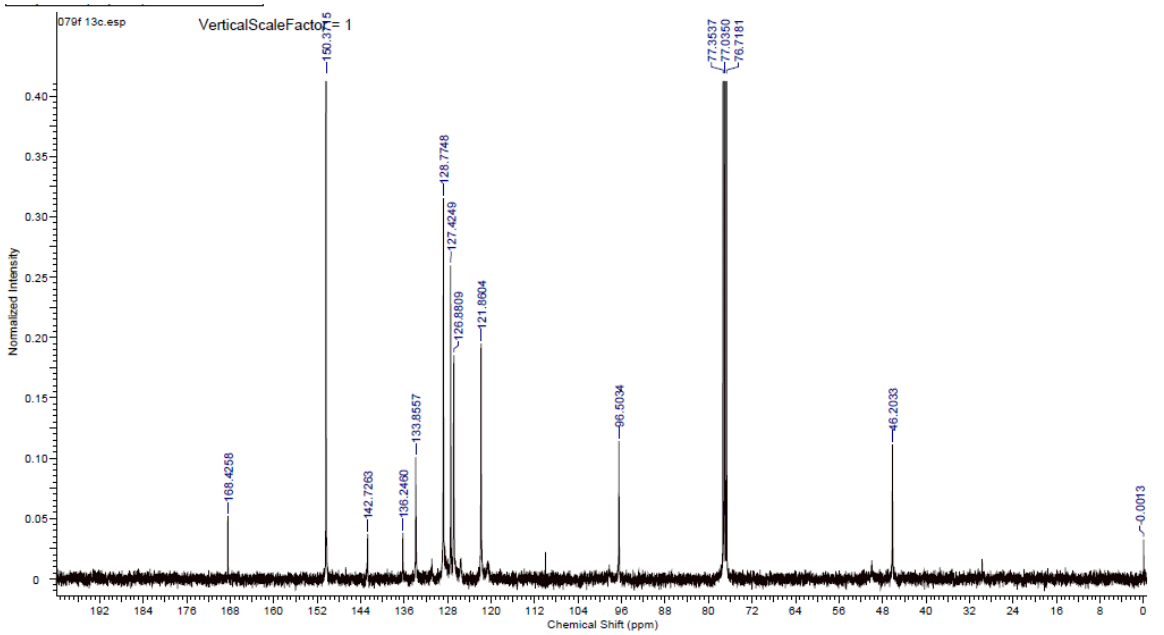

8.7515
8.7372
8.5983
8.5864
7.4248
7.3375
7.2963
7.2787
7.2609
7.1966
7.0996
6.2562
6.2212
5.0705
5.0522
5.0351
5.0098
4.6718
2.3995
2.3660
2.1135
2.0966
2.0503
0.9751
0.9586
0.8354
0.8187
1.46
2.00
0.54
6.00
1.14
0.71
0.53
0.26
0.72
1.64
4.46
f1 (ppm)

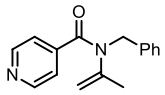

167.9507
150.2577
143.3224
136.0017
128.6514
123.6136
123.3969
123.3586
123.0716
122.1124
122.0236
120.5823
77.3676
76.7327
50.6793
47.5283
29.6146
29.3131
22.8543
22.6516
f1 (ppm)


O
N
Ph
N

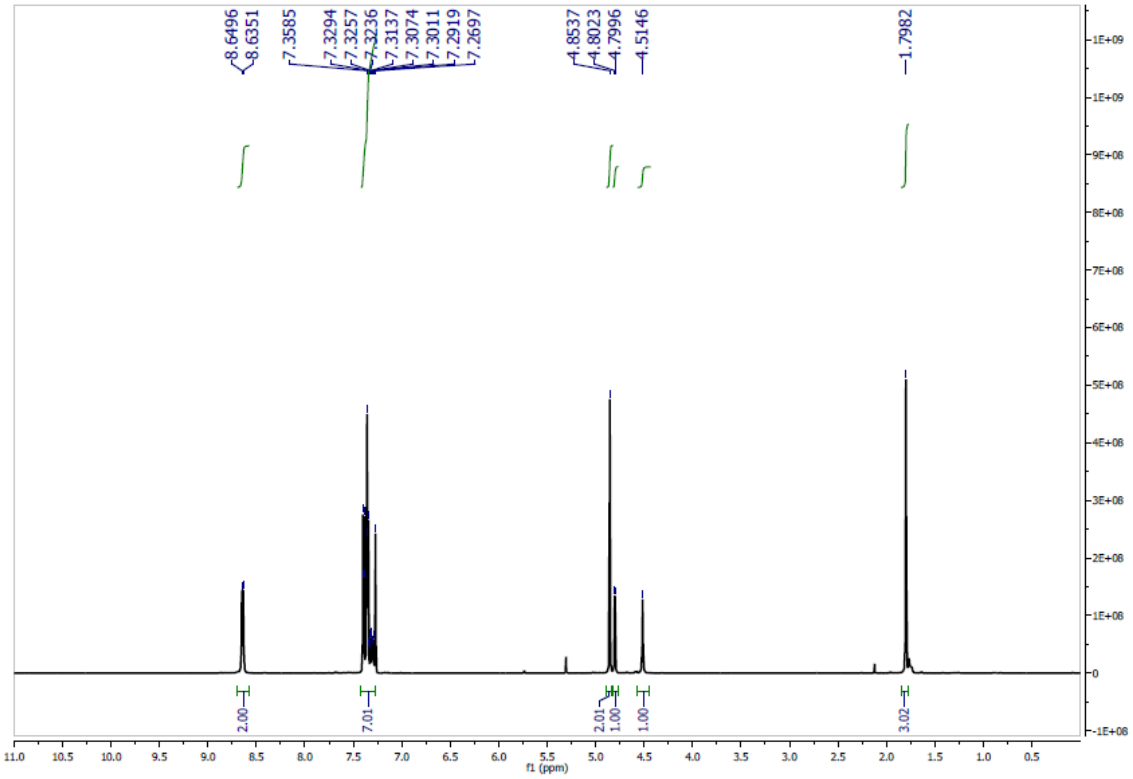
1c

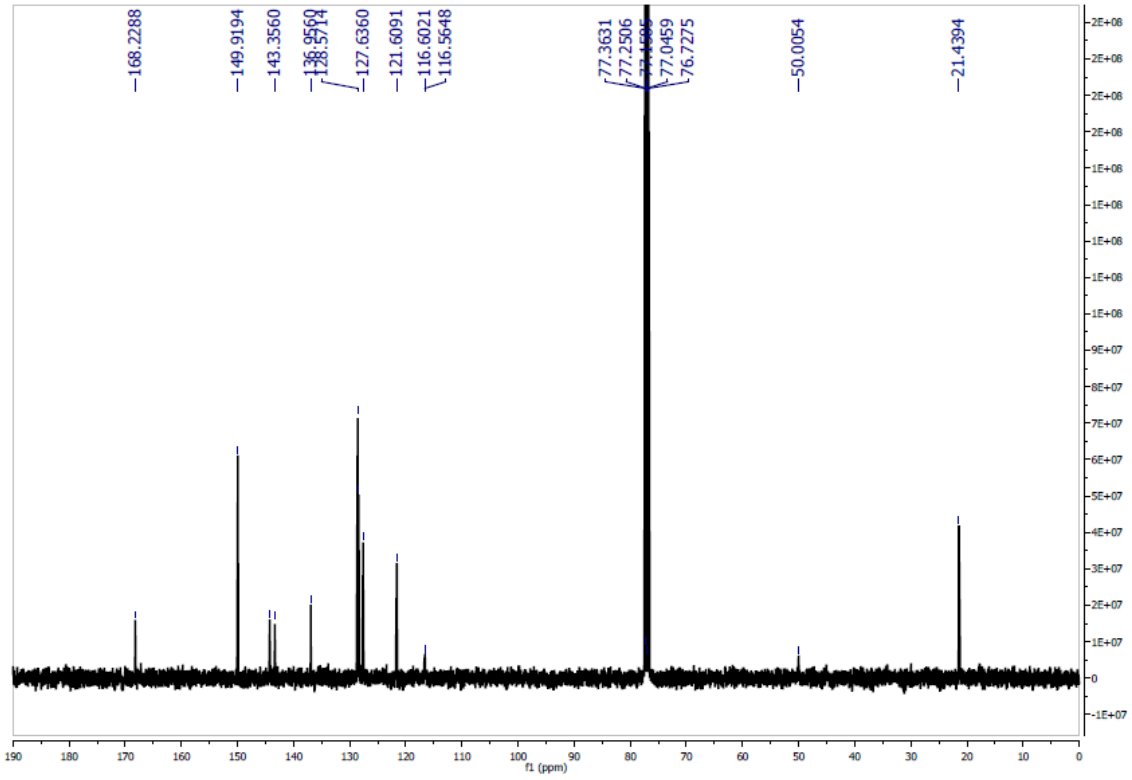

079f 1h.esp
VerticalScaleFactor = 1
Normalized Intensity
2.64
8.53
1.00
2.17
1.38
1.02
Chemical Shift (ppm)

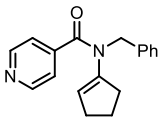

079f 13c.esp
VerticalScaleFactor = 1
Normalized Intensity
150.3715
77.3537
77.0350
76.7181
128.7748
127.4249
126.8809
121.8604
168.4258
142.7263
136.2480
133.8557
96.5034
46.2033
0.0013
Chemical Shift (ppm)


O
N
Ph
N

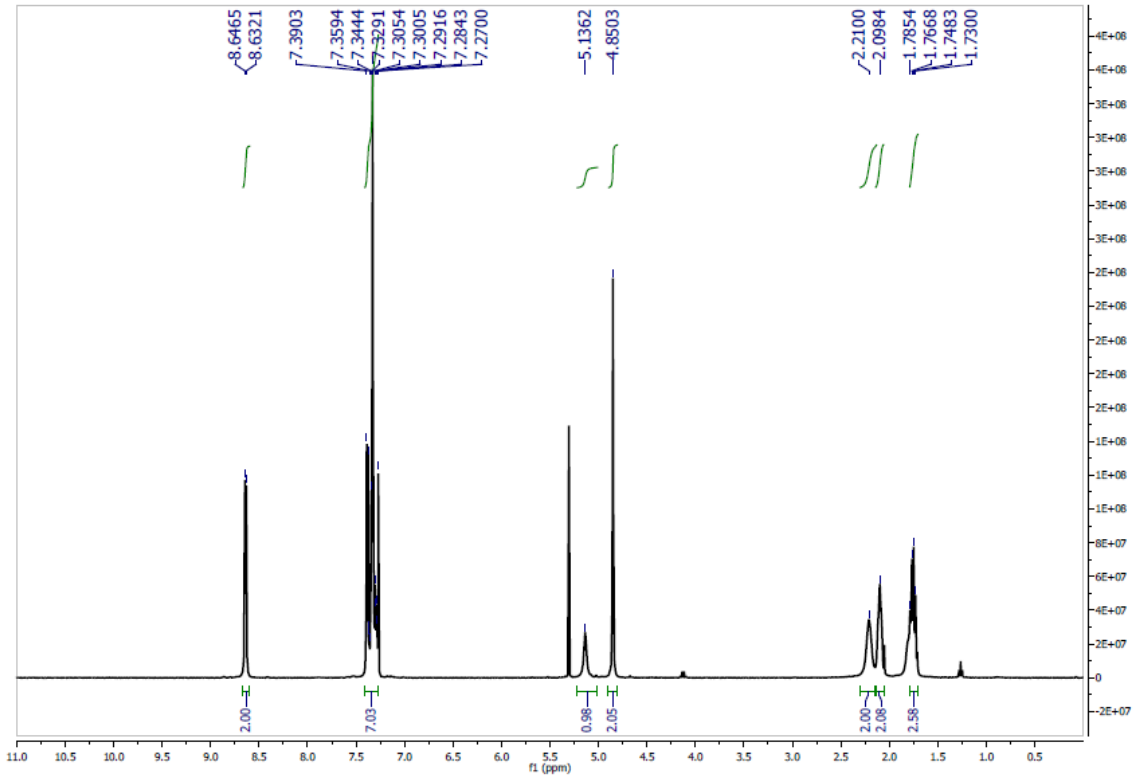
1d

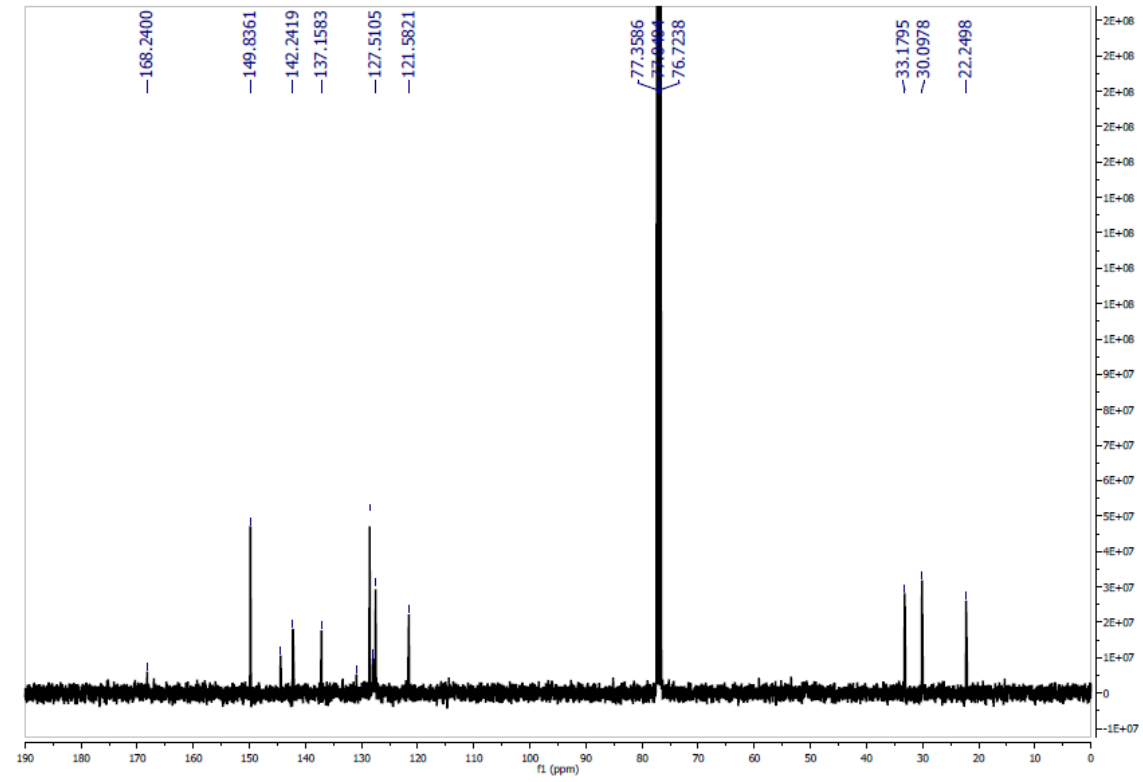

8.6496
8.6351
7.3585
7.3294
7.3257
7.3236
7.3137
7.3074
7.3011
7.2919
7.2697
4.8537
4.8023
4.7996
4.5146
1.7982
2.00
7.01
2.01
1.00
1.00
3.02
f1 (ppm)

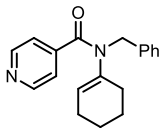

168.2288
149.9194
143.3560
136.9560
128.5714
127.6360
121.6091
116.6021
116.5648
77.3631
77.2506
77.0459
76.7275
50.0054
21.4394
f1 (ppm)



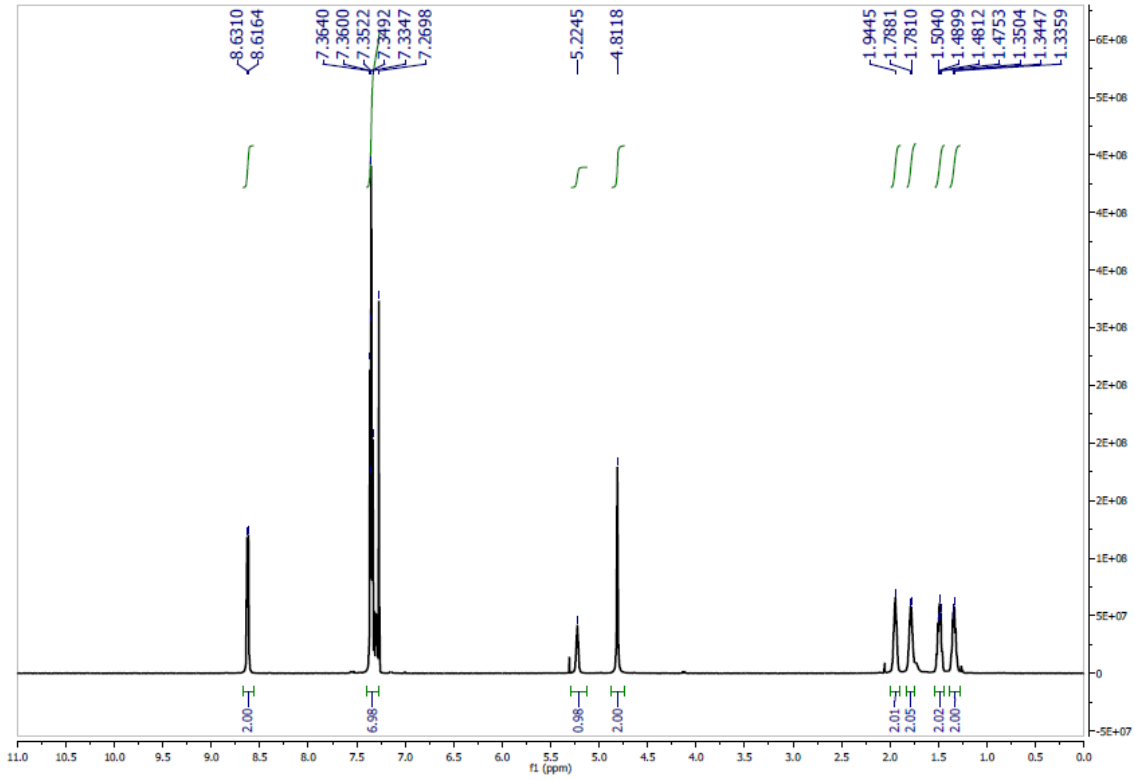
1e

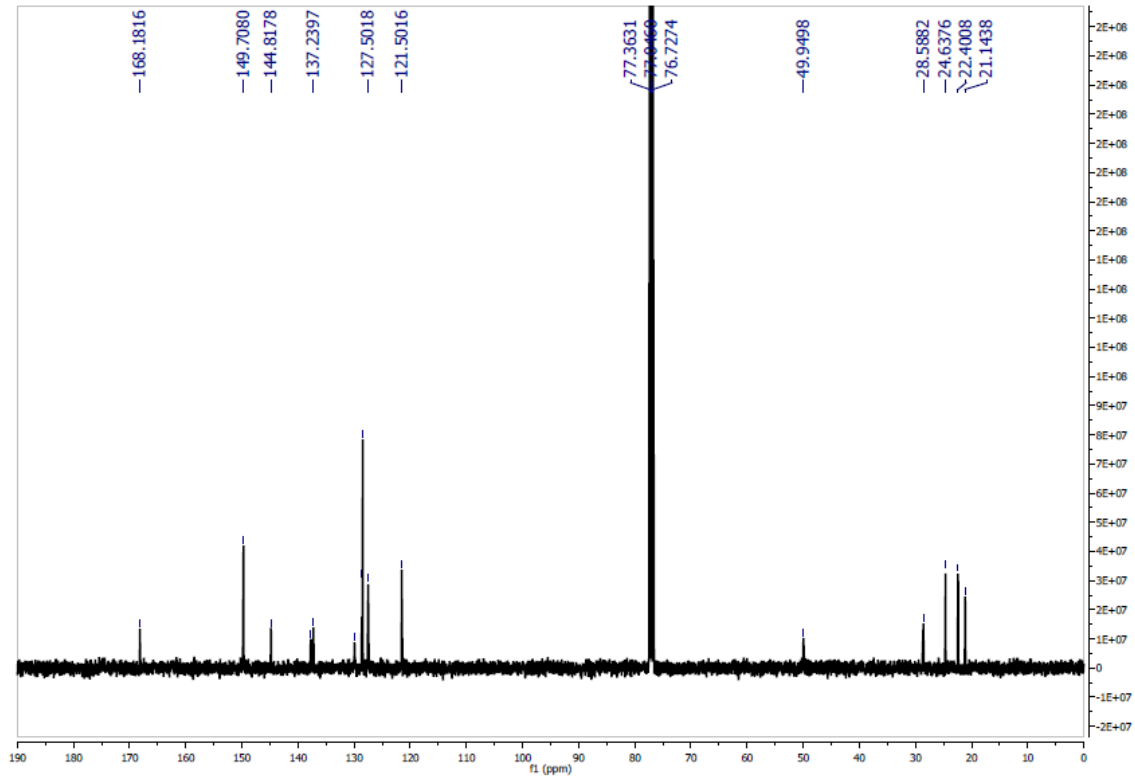

8.6465
8.6321
7.3903
7.3594
7.3444
7.3291
7.3054
7.3005
7.2916
7.2843
7.2700
5.1362
4.8503
2.2100
2.0984
1.7854
1.7668
1.7483
1.7300
2.00
7.03
0.98
2.05
2.00
2.08
2.58
f1 (ppm)

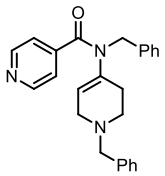

168.2400
149.8361
142.2419
137.1583
127.5105
121.5821
77.3586
77.0484
76.7238
33.1795
30.0978
22.2498
f1 (ppm)


O
N
Ph
N

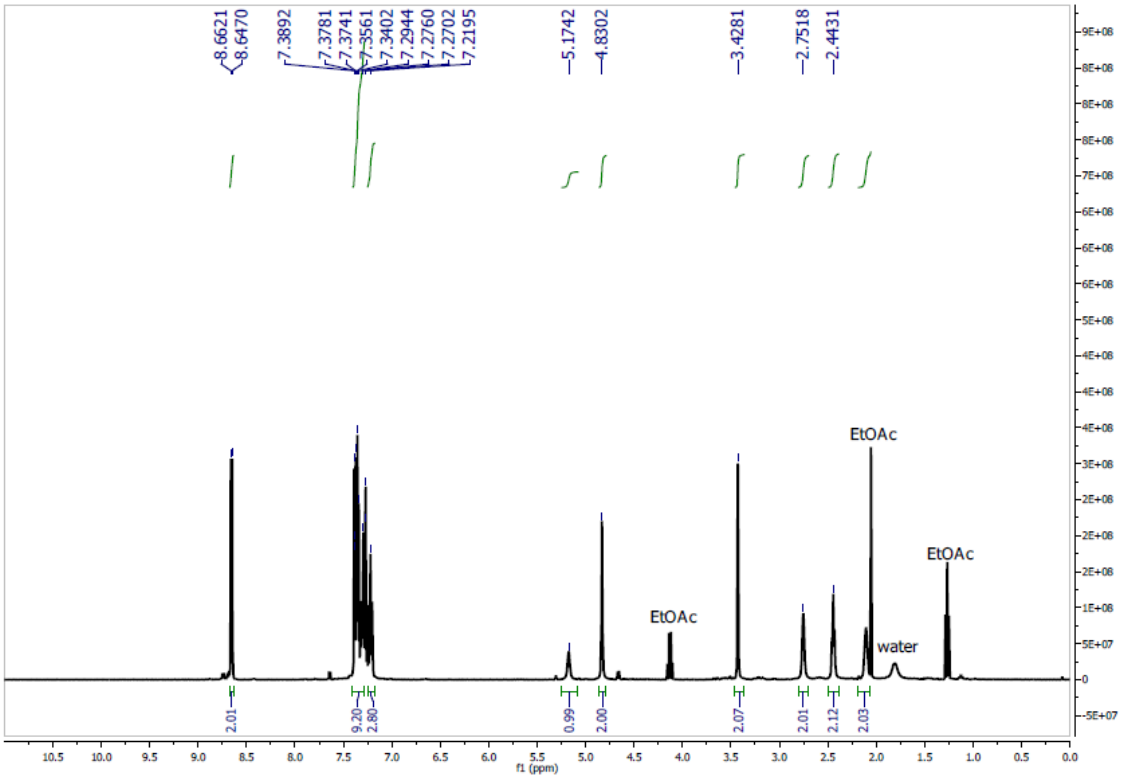
1f

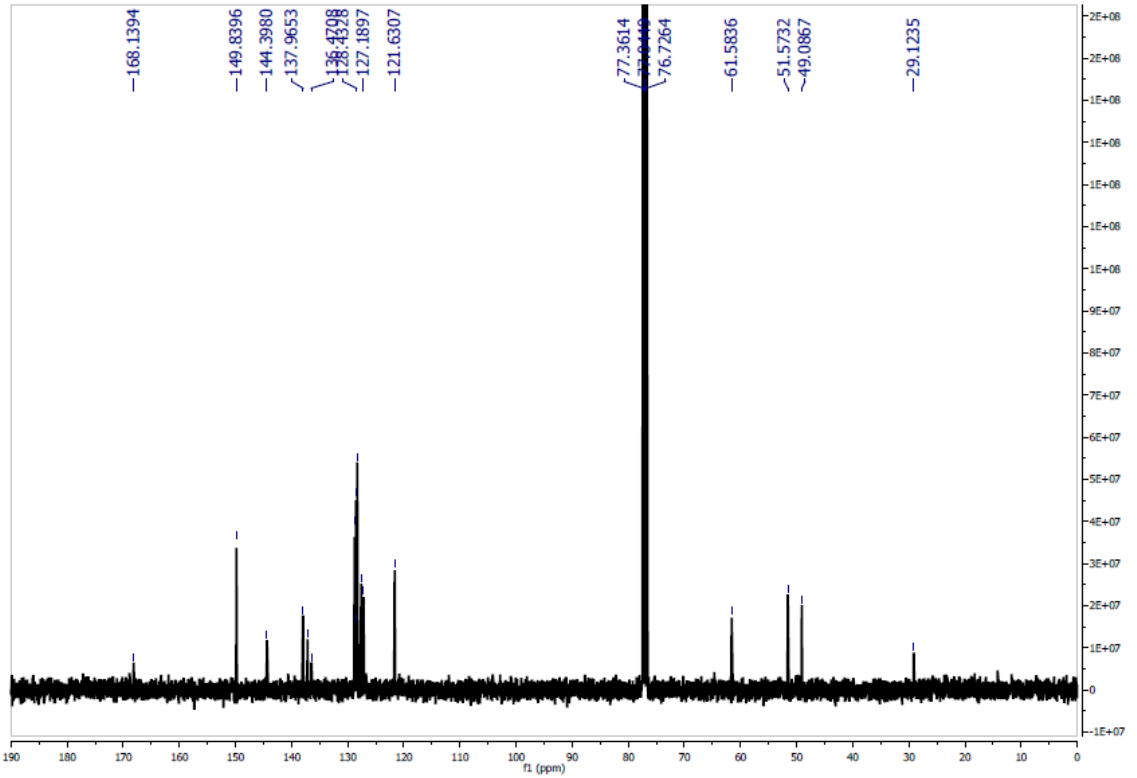

8.6310
8.6164
7.3640
7.3600
7.3522
7.3492
7.3347
7.2698
5.2245
4.8118
1.9445
1.7881
1.7810
1.5040
1.4899
1.4812
1.4753
1.3504
1.3447
1.3359
2.00
6.98
0.98
2.00
2.01
2.05
2.02
2.00
f1 (ppm)

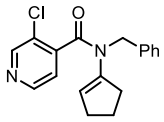

168.1816
149.7080
144.8178
137.2397
127.5018
121.5016
77.3631
77.0460
76.7274
49.9498
28.5882
24.6376
22.4008
21.1438
f1 (ppm)


O
N
Ph
N
N
Ph

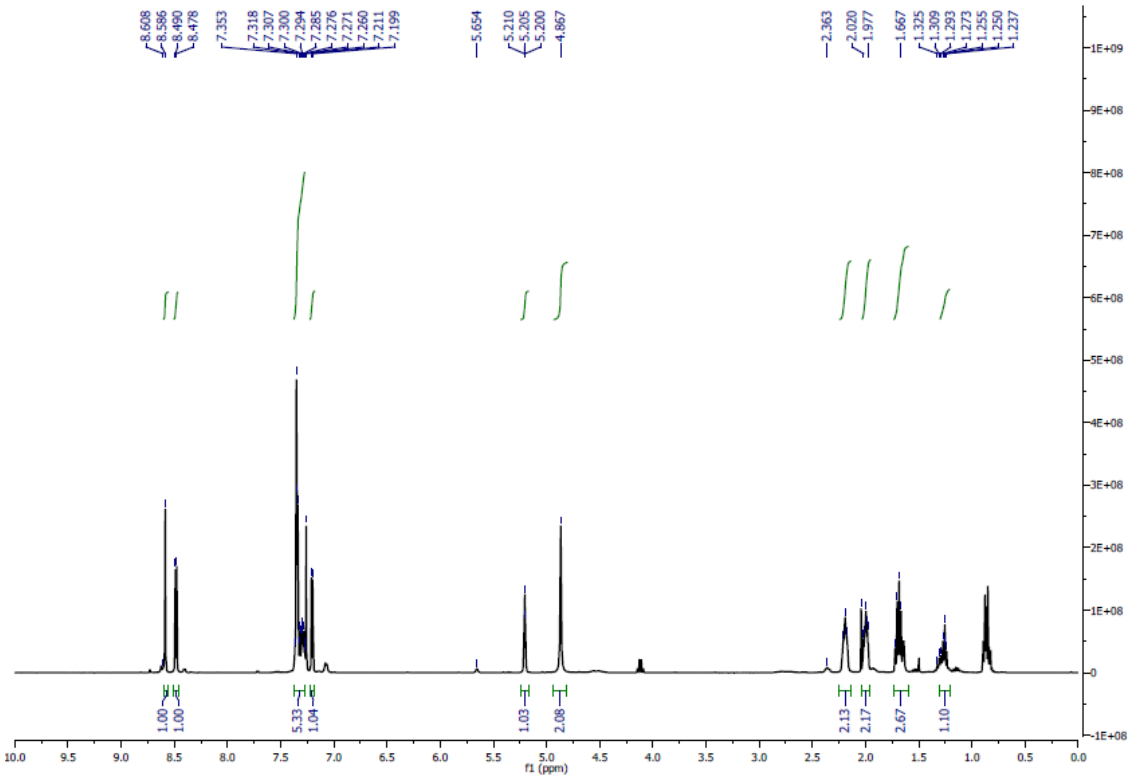
1g

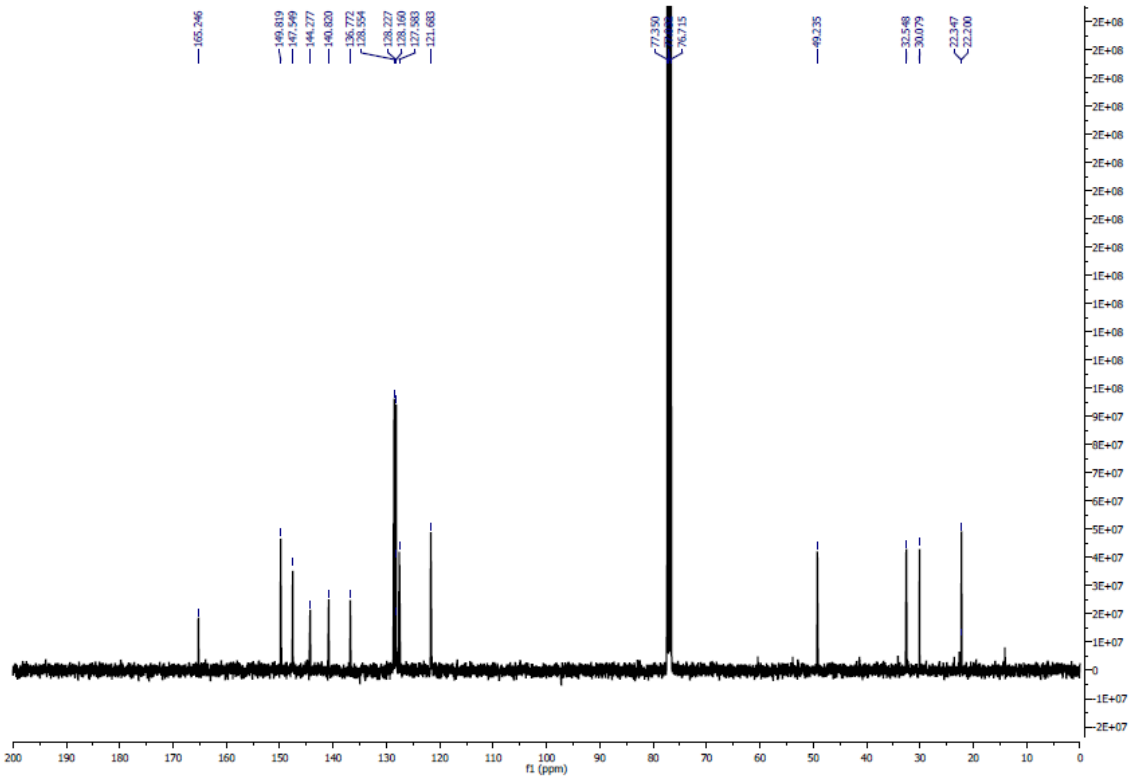

8.6621
8.6470
7.3892
7.3781
7.3741
7.3561
7.3402
7.2944
7.2760
7.2702
7.2195
5.1742
4.8302
3.4281
2.7518
2.4431
EtOAc
EtOAc
EtOAc
water
2.01
9.20
2.80
0.99
2.00
2.07
2.01
2.12
2.03
f1 (ppm)

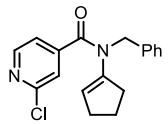

168.1394
149.8396
144.3980
137.9653
136.4708
128.4328
127.1897
121.6307
77.3614
76.7264
61.5836
51.5732
49.0867
29.1235
f1 (ppm)


Cl
O
N
Ph
N

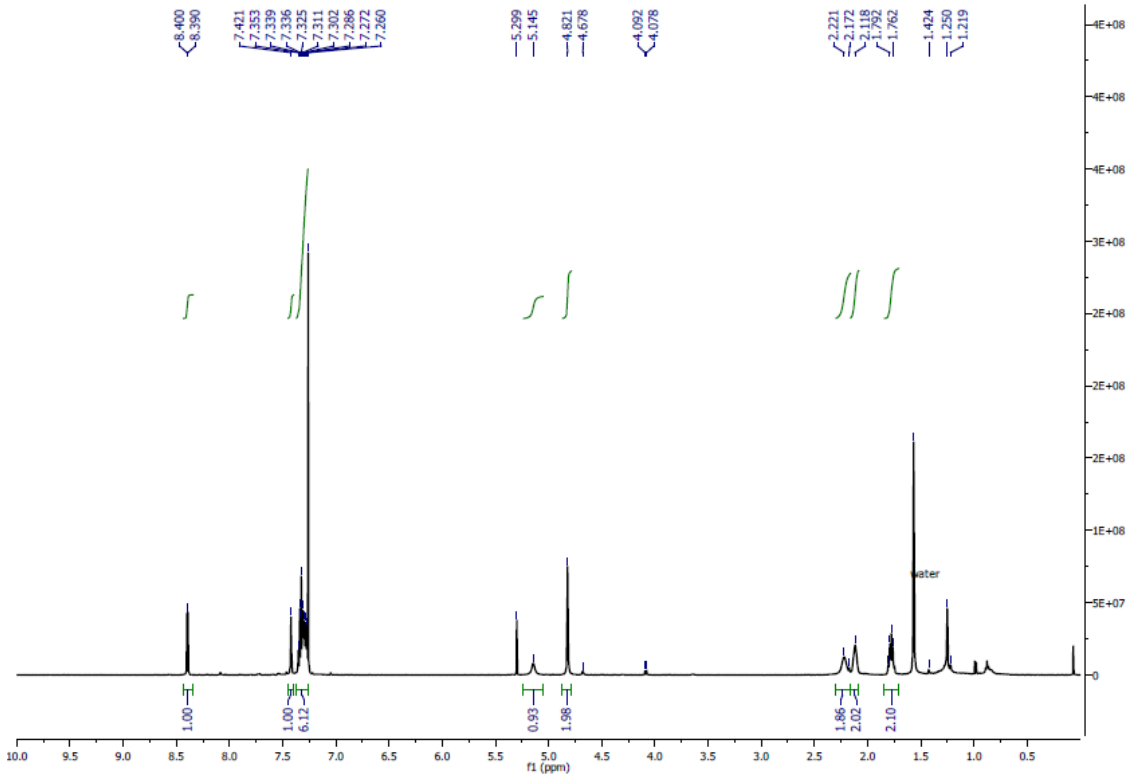
1i

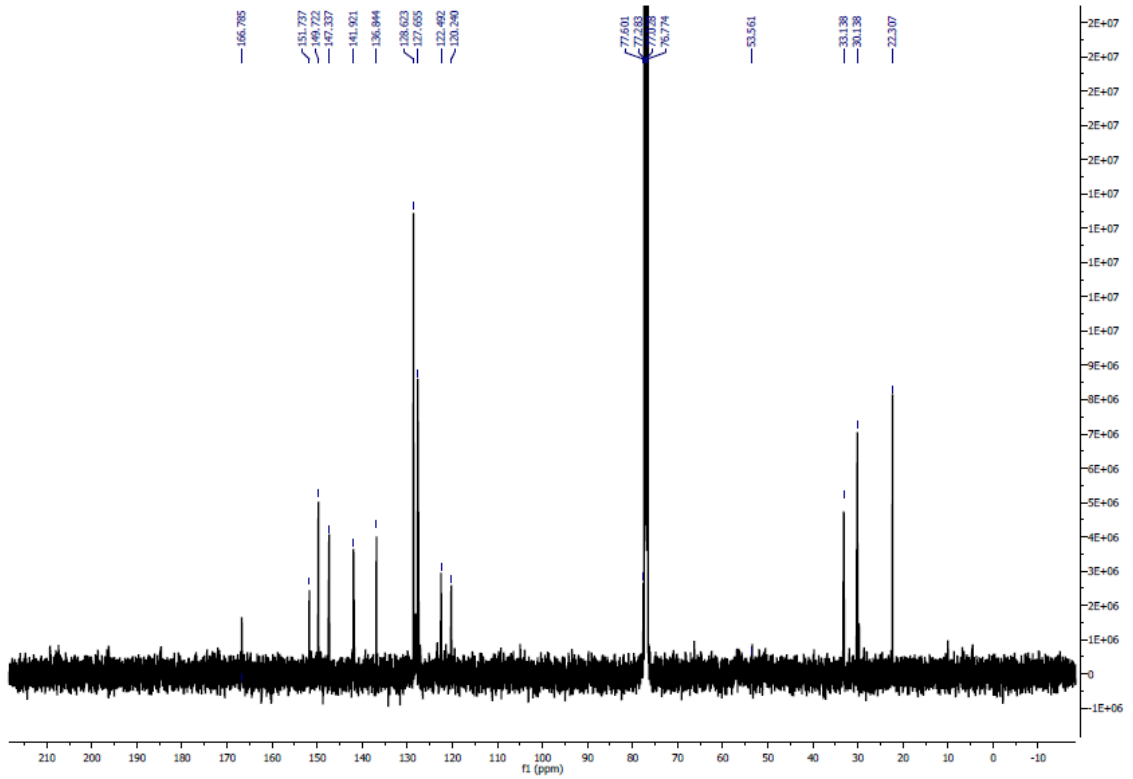

8.608
8.586
8.490
8.478
7.353
7.318
7.307
7.300
7.294
7.285
7.276
7.271
7.260
7.211
7.199
5.654
5.210
5.205
5.200
4.867
2.363
2.020
1.977
1.667
1.325
1.309
1.293
1.273
1.255
1.250
1.237
1.00
1.00
5.33
1.04
1.03
2.08
2.13
2.17
2.67
1.10
f1 (ppm)

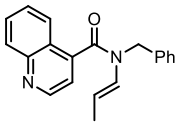

165.246
149.819
147.549
144.277
140.820
136.772
128.554
128.227
128.160
127.583
121.683
77.350
77.035
76.715
69.235
32.548
30.079
22.347
22.200
f1 (ppm)


O
N
Ph
N
Cl

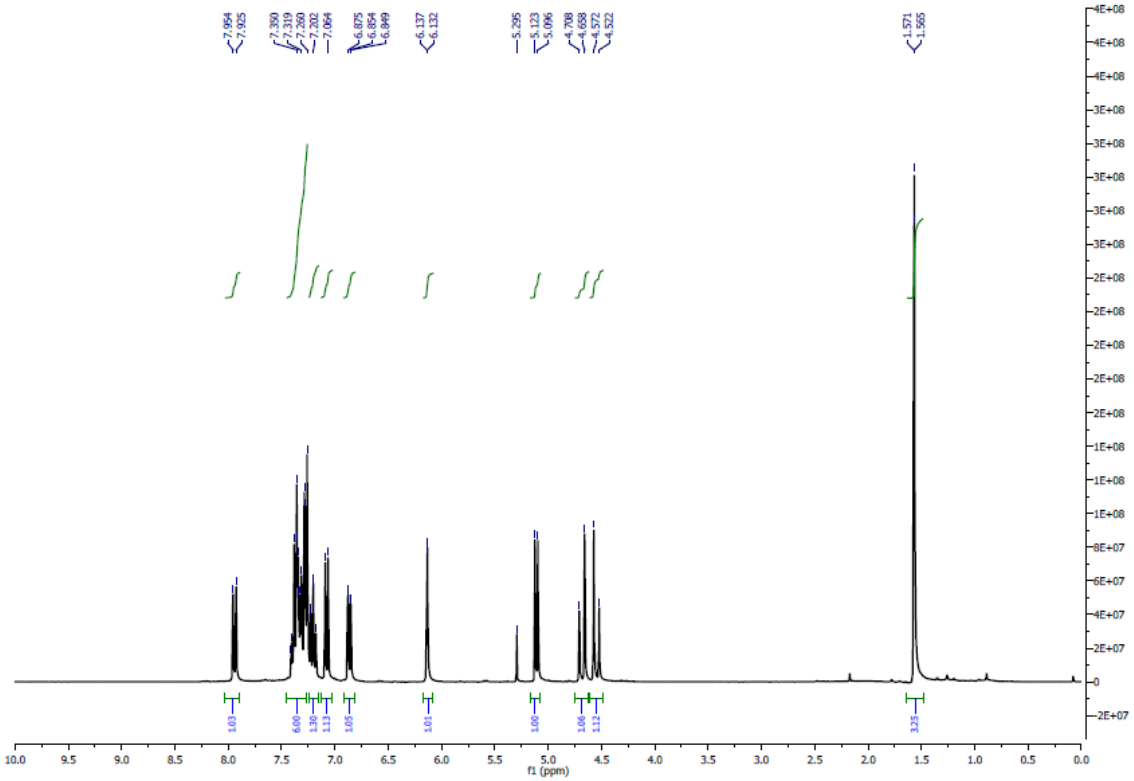
1h

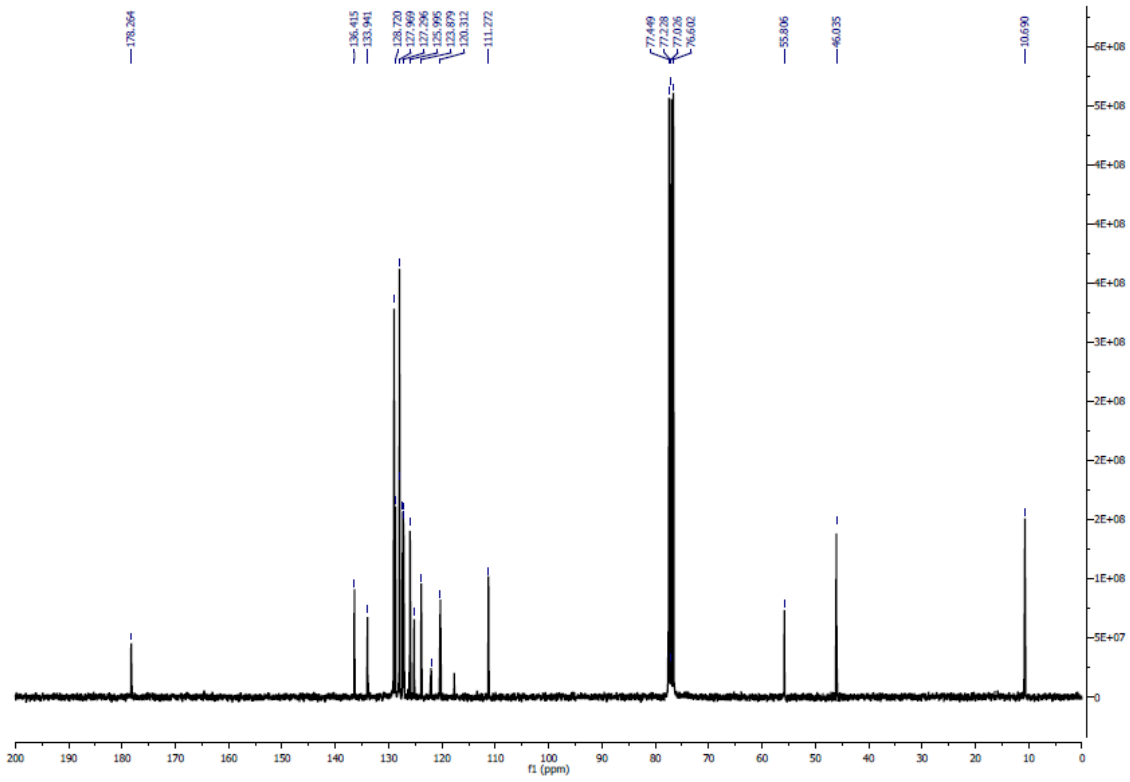

8.400
8.390
7.421
7.353
7.339
7.336
7.325
7.311
7.302
7.286
7.272
7.260
5.299
5.145
4.821
4.678
4.092
4.078
2.221
2.172
2.118
1.792
1.762
1.424
1.250
1.219
water
1.00
1.00
6.12
0.93
1.98
1.86
2.02
2.10
f1 (ppm)

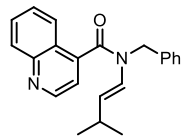

166.785
151.737
149.722
147.337
141.921
136.844
128.623
127.655
122.492
120.240
77.601
77.283
77.028
76.774
53.561
33.138
30.138
22.307
f1 (ppm)


O
N
Ph
N

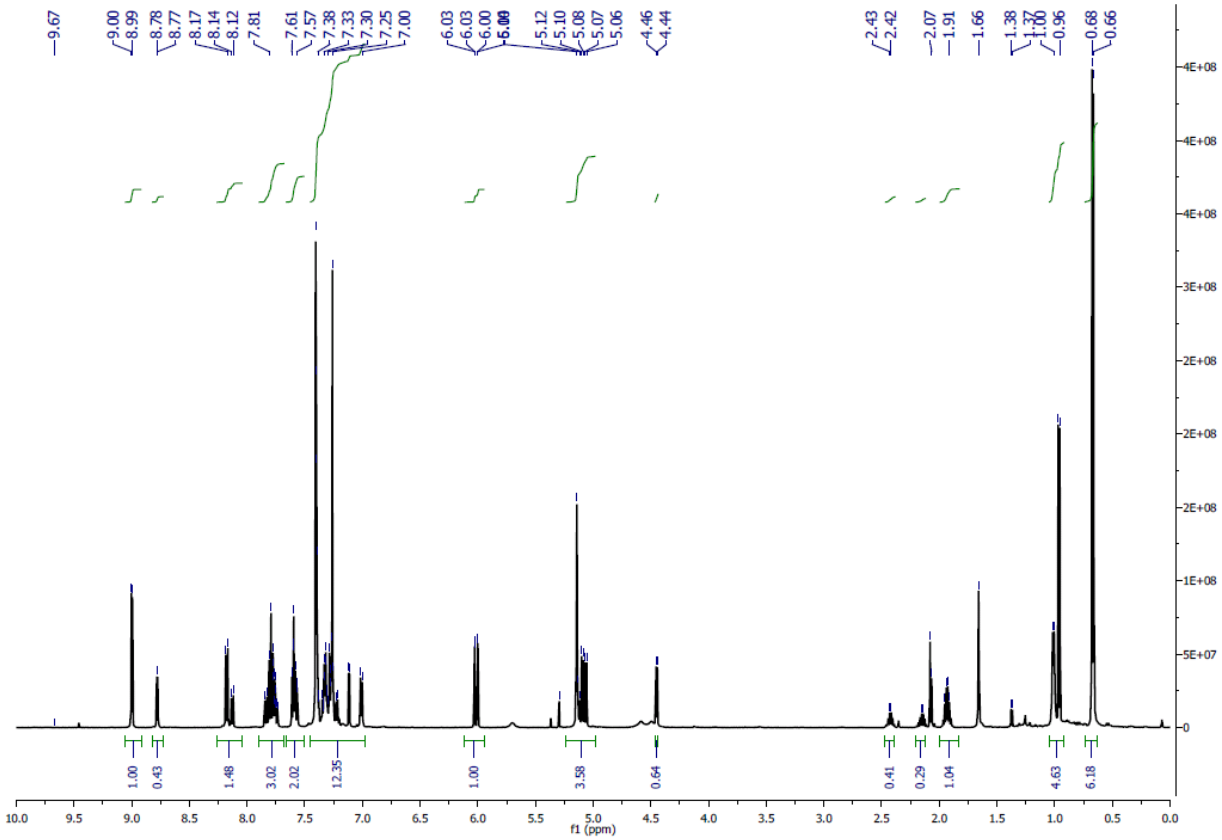
1j

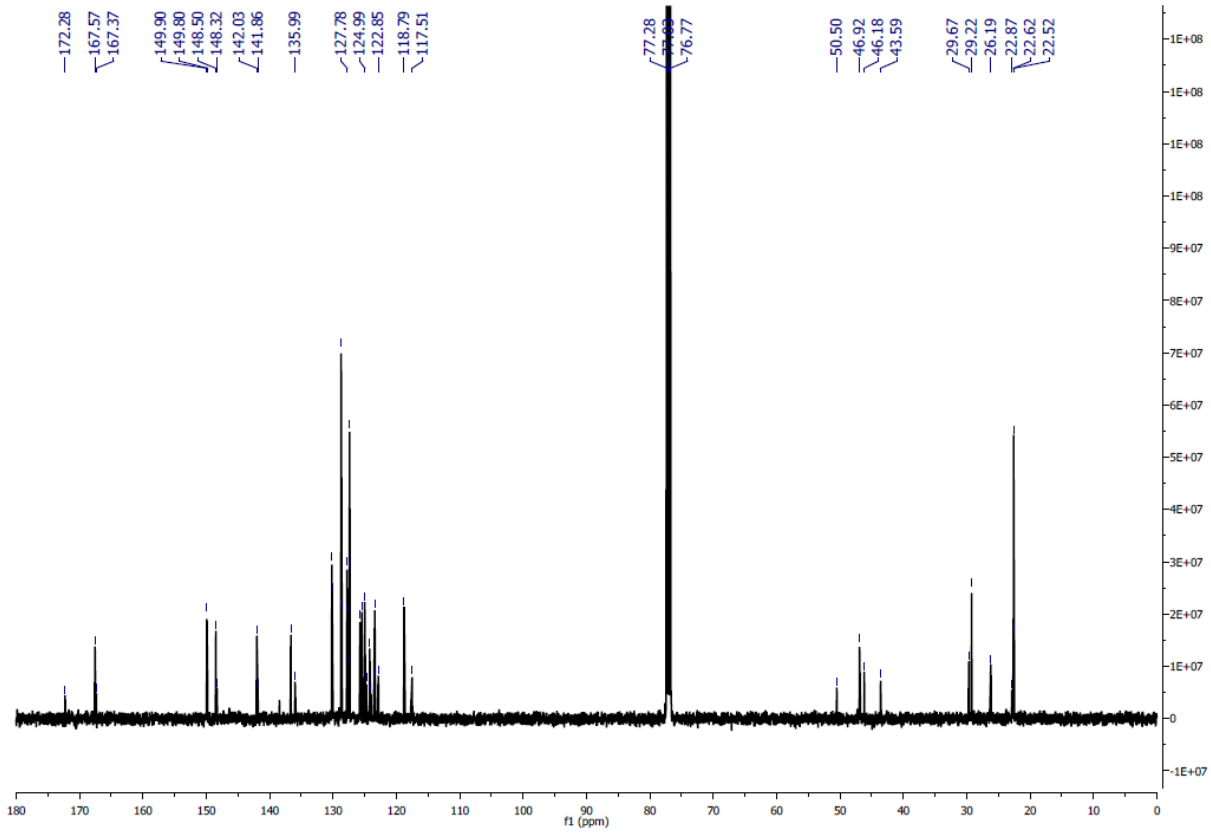

7.964
7.925
7.390
7.319
7.269
7.202
7.064
6.875
6.854
6.649
6.137
6.132
5.295
5.123
5.096
4.708
4.658
4.572
4.522
1.571
1.565
1.03
6.00
1.30
1.13
1.05
1.01
1.00
1.06
1.12
3.25
f1 (ppm)

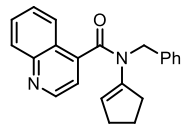

178.264
136.415
133.941
128.720
127.469
127.296
125.995
123.879
120.312
111.272
77.449
77.228
77.026
76.602
55.806
46.035
10.690
f1 (ppm)


O
N
Ph
N

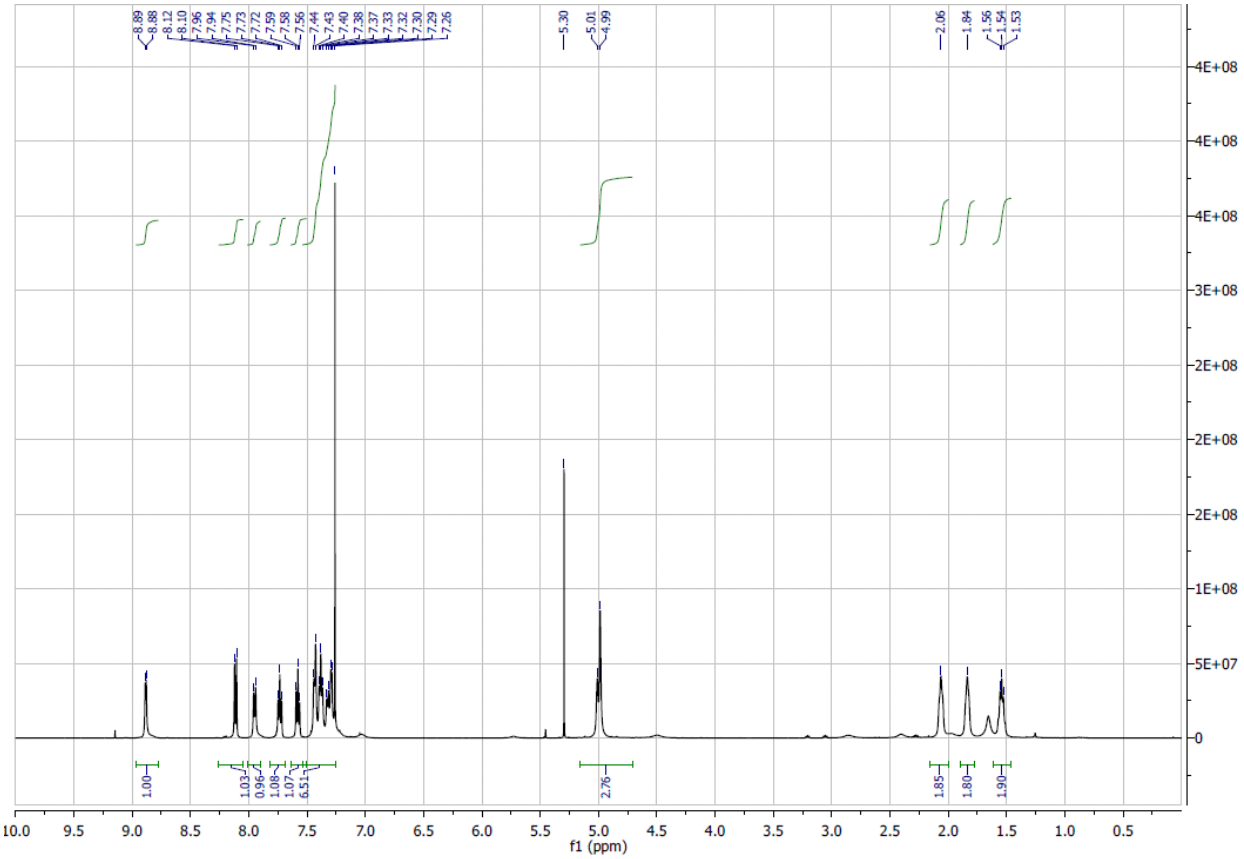
1k

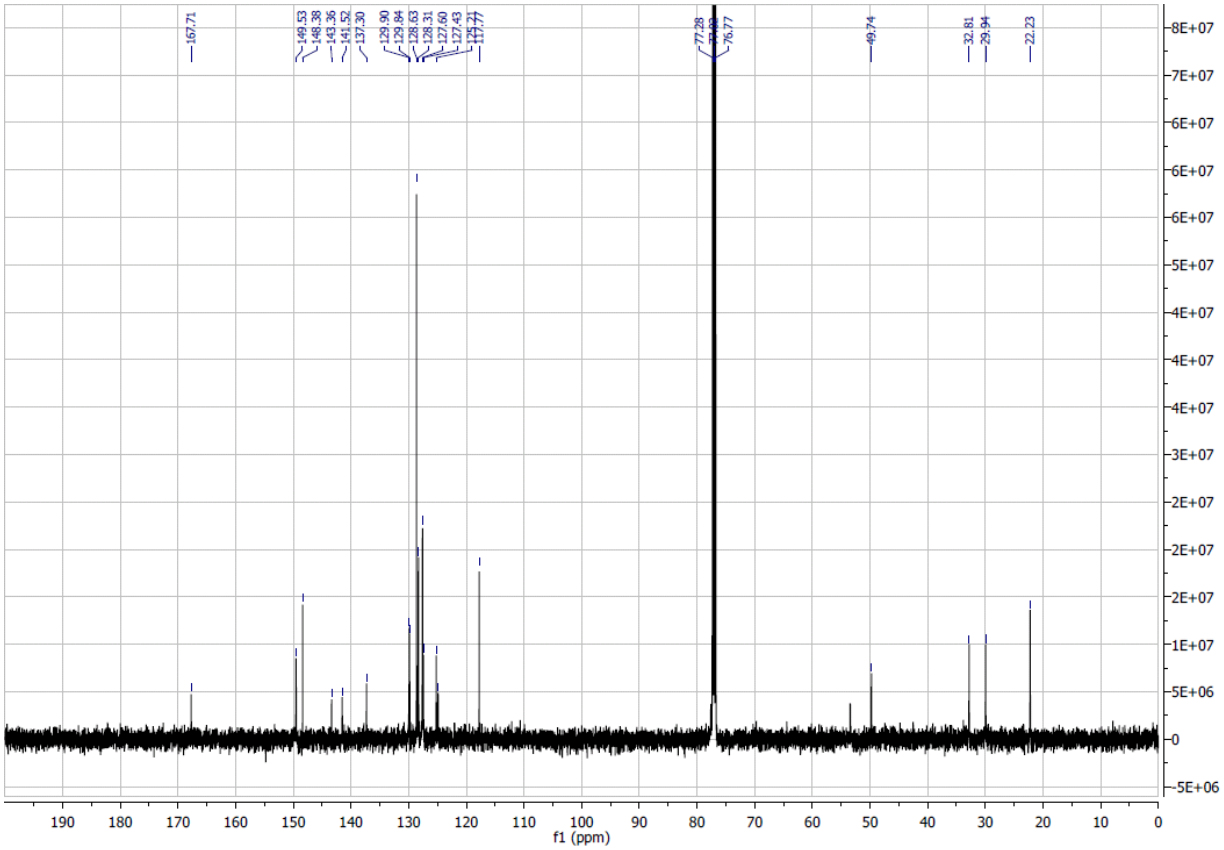

9.67
9.00
8.99
8.78
8.77
8.17
8.14
8.12
7.81
7.61
7.57
7.38
7.33
7.30
7.25
7.00
6.03
6.03
6.00
5.12
5.10
5.08
5.07
5.06
4.46
4.44
2.43
2.42
2.07
1.91
1.66
1.38
1.37
1.00
0.96
0.68
0.66
1.00
0.43
1.48
3.02
2.02
12.35
1.00
3.58
0.64
0.41
0.29
1.04
4.63
6.18
f1 (ppm)

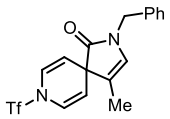

172.28
167.57
167.37
149.90
149.80
148.50
148.32
142.03
141.86
135.99
127.78
124.99
122.85
118.79
117.51
77.28
77.03
76.77
50.50
46.92
46.18
43.59
29.67
29.22
26.19
22.87
22.62
22.52
f1 (ppm)


O
N
Ph
N

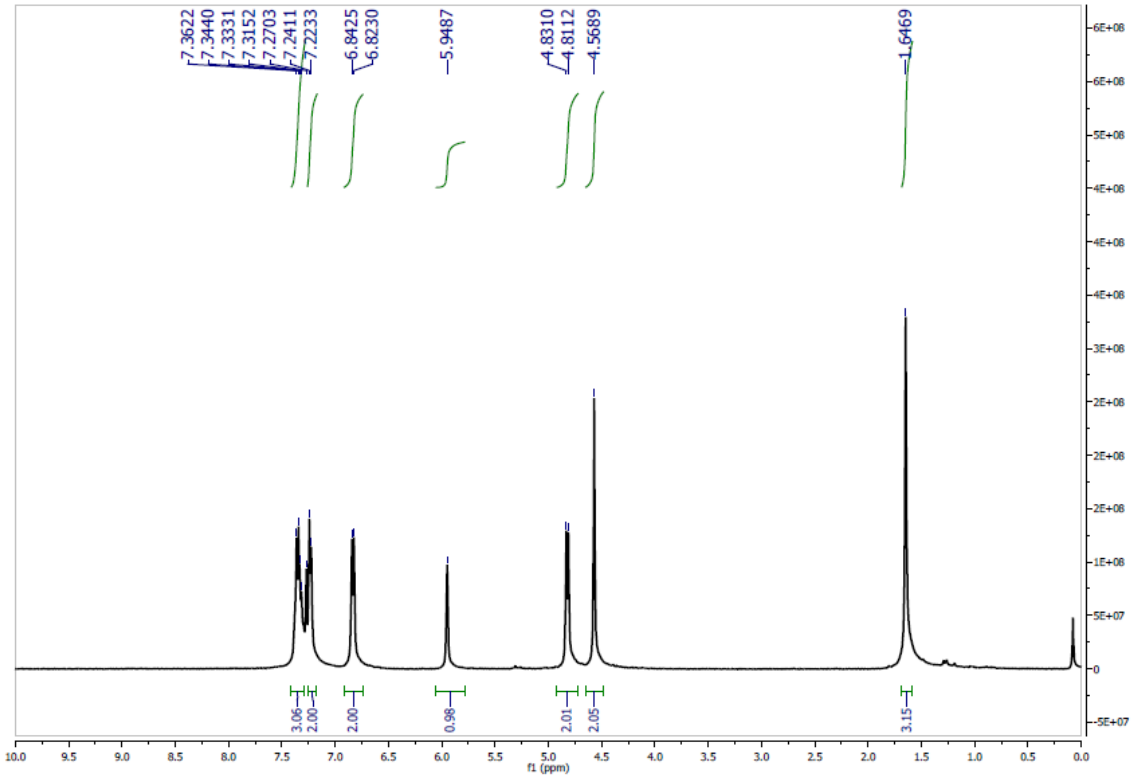
1l

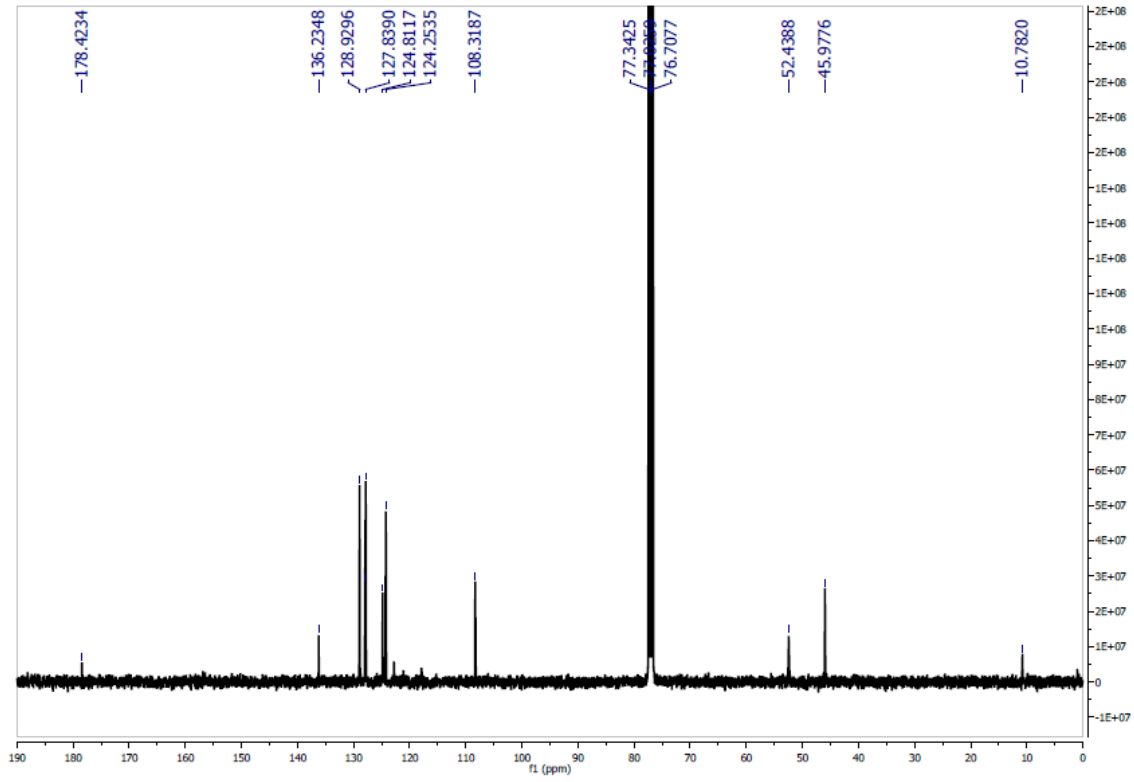

8.89
8.88
8.12
8.10
7.96
7.94
7.75
7.73
7.72
7.59
7.58
7.56
7.44
7.43
7.40
7.38
7.37
7.33
7.32
7.30
7.29
7.26
5.30
5.01
4.99
2.06
1.84
1.56
1.54
1.53
1.00
1.03
0.96
1.08
1.07
6.51
2.76
1.85
1.80
1.90
f1 (ppm)

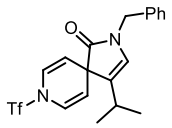

167.71
149.53
148.38
143.36
141.52
137.30
129.90
129.84
128.63
128.31
127.60
127.43
77.28
77.03
76.77
49.74
32.81
29.94
22.23
f1 (ppm)


O
N
Ph
Tf
N
Me

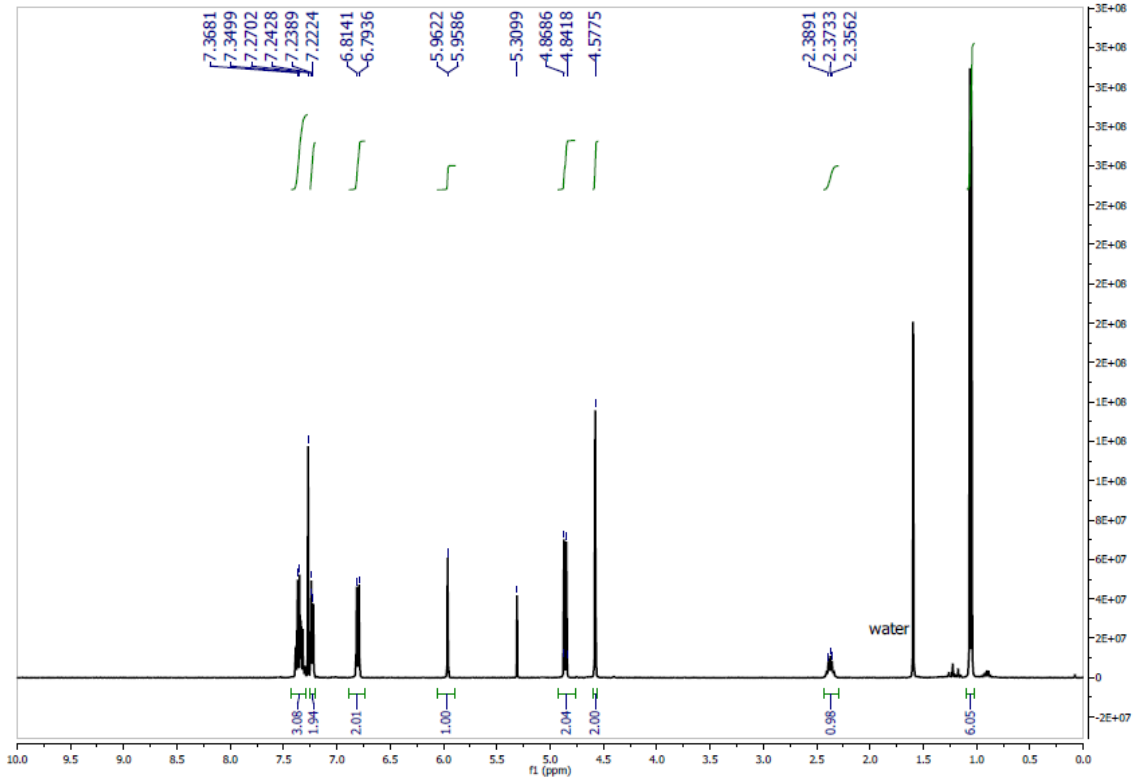
2a

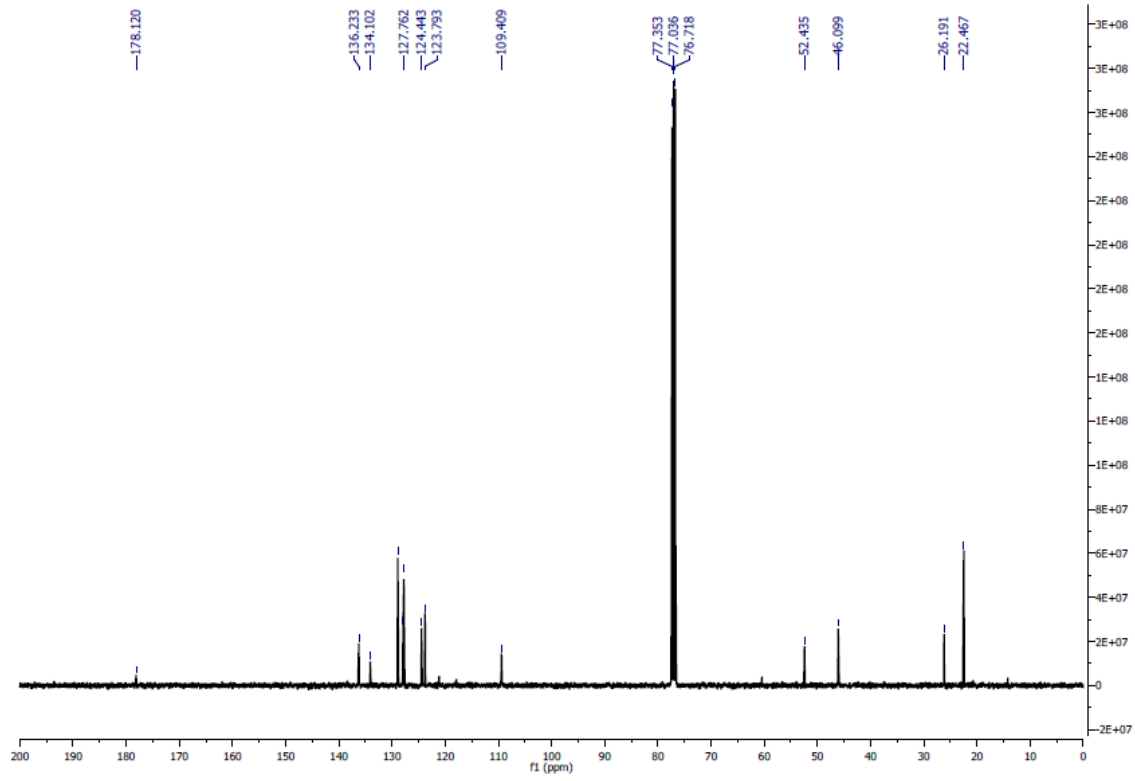

7.3622
7.3440
7.3331
7.3152
7.2703
7.2411
7.2233
6.8425
6.8230
5.9487
4.8310
4.8112
4.5689
1.6469
3.06
2.00
2.00
0.98
2.01
2.05
3.15
f1 (ppm)

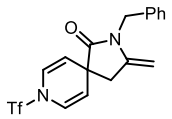

178.4234
136.2348
128.9296
127.8390
124.8117
124.2535
108.3187
77.3425
76.7077
52.4388
45.9776
10.7820
f1 (ppm)


Ph
O
N
Tf
N

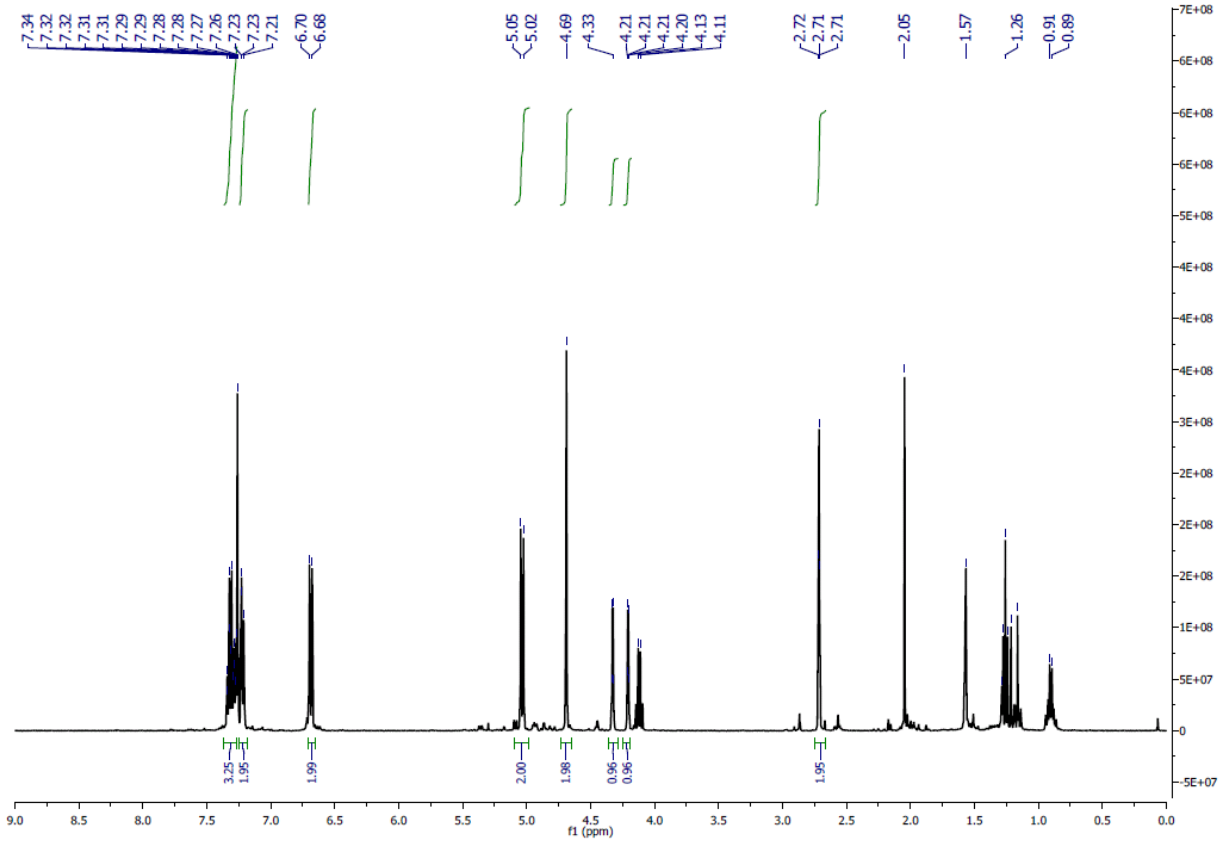
2b

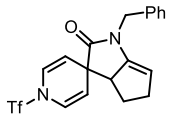

7.3681
7.3499
7.2702
7.2428
7.2389
7.2224
6.8141
6.7936
5.9622
5.9586
5.3099
4.8686
4.8418
4.5775
2.3891
2.3733
2.3562
water
3.08
1.94
2.01
1.00
2.04
2.00
0.98
6.05
f1 (ppm)


178.120
136.233
134.102
127.762
124.443
123.793
109.409
77.353
77.036
76.718
52.435
46.099
26.191
22.467
f1 (ppm)

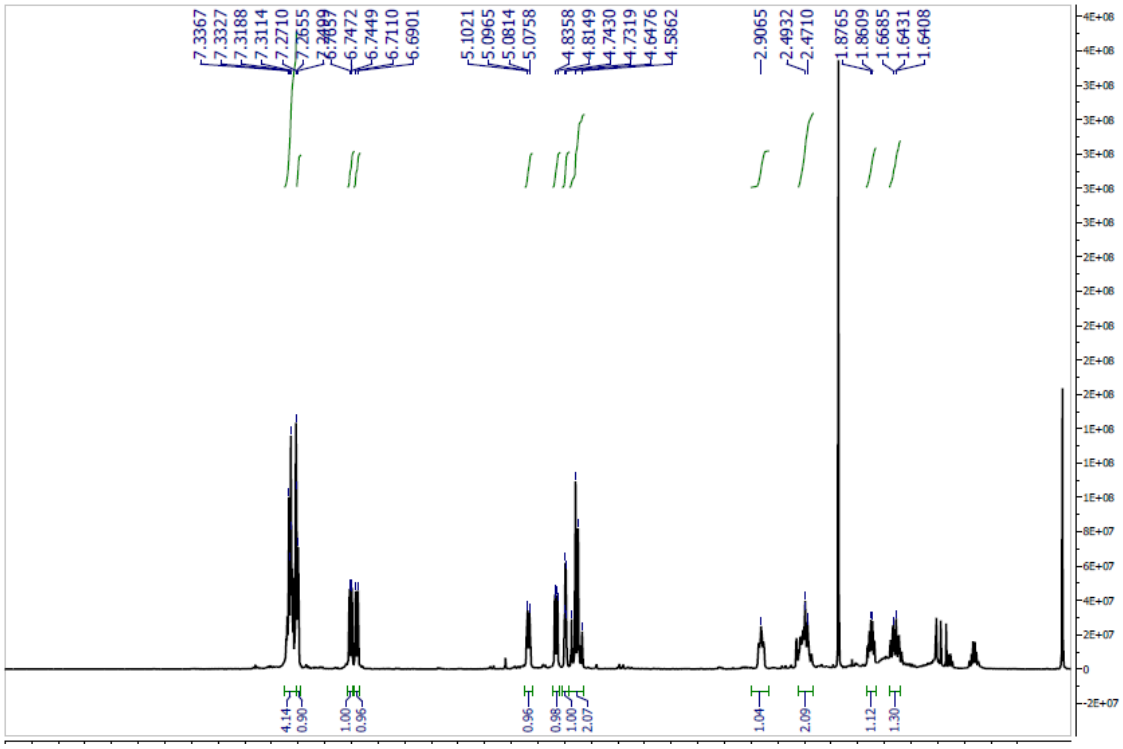

Ph
O
N
Tf
N

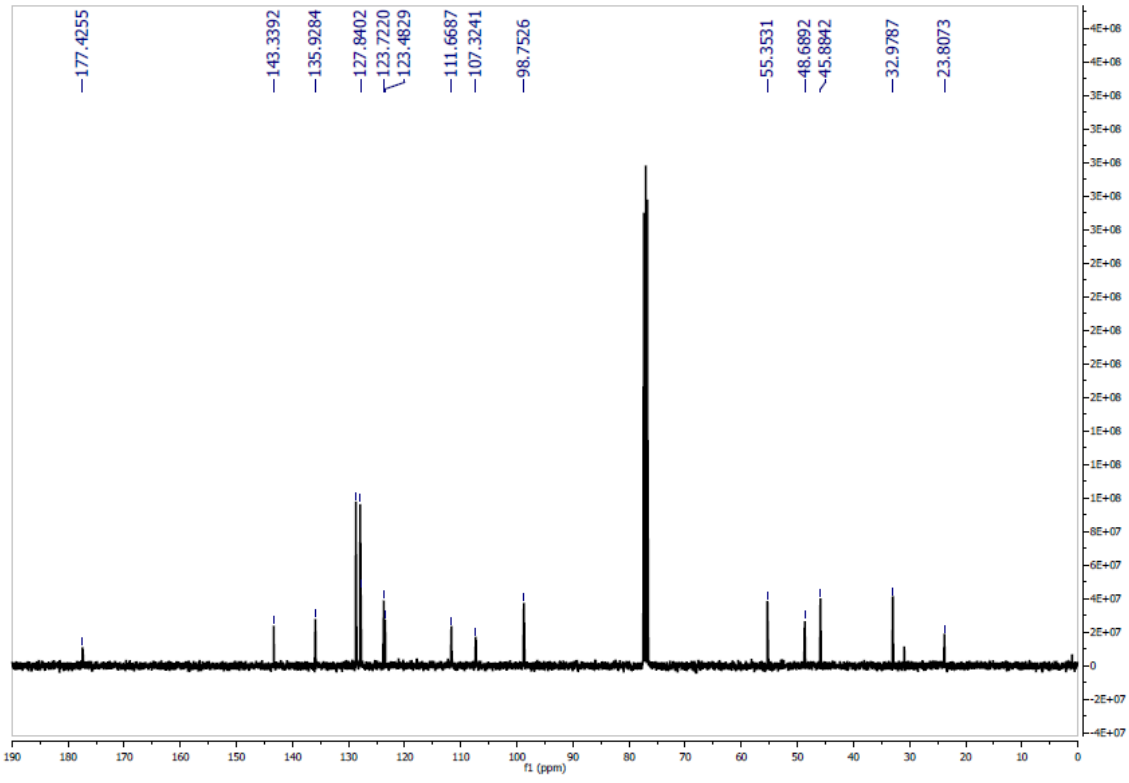
2d

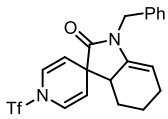

7.34
7.32
7.32
7.31
7.31
7.29
7.29
7.28
7.28
7.27
7.26
7.23
7.23
7.21
6.70
6.68
5.05
5.02
4.69
4.33
4.21
4.21
4.21
4.20
4.13
4.11
2.72
2.71
2.71
2.05
1.57
1.26
0.91
0.89
3.25
1.95
1.99
2.00
1.98
0.96
0.96
1.95
f1 (ppm)


Ph
O
N
Tf
N

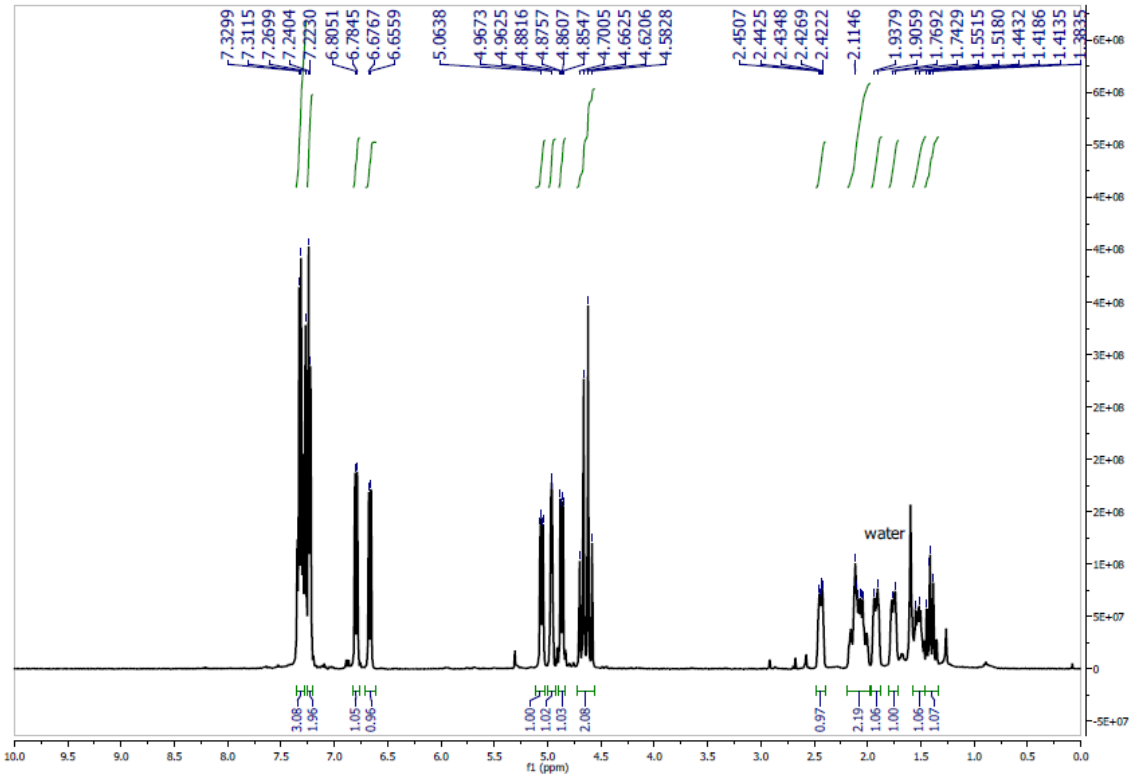
2e

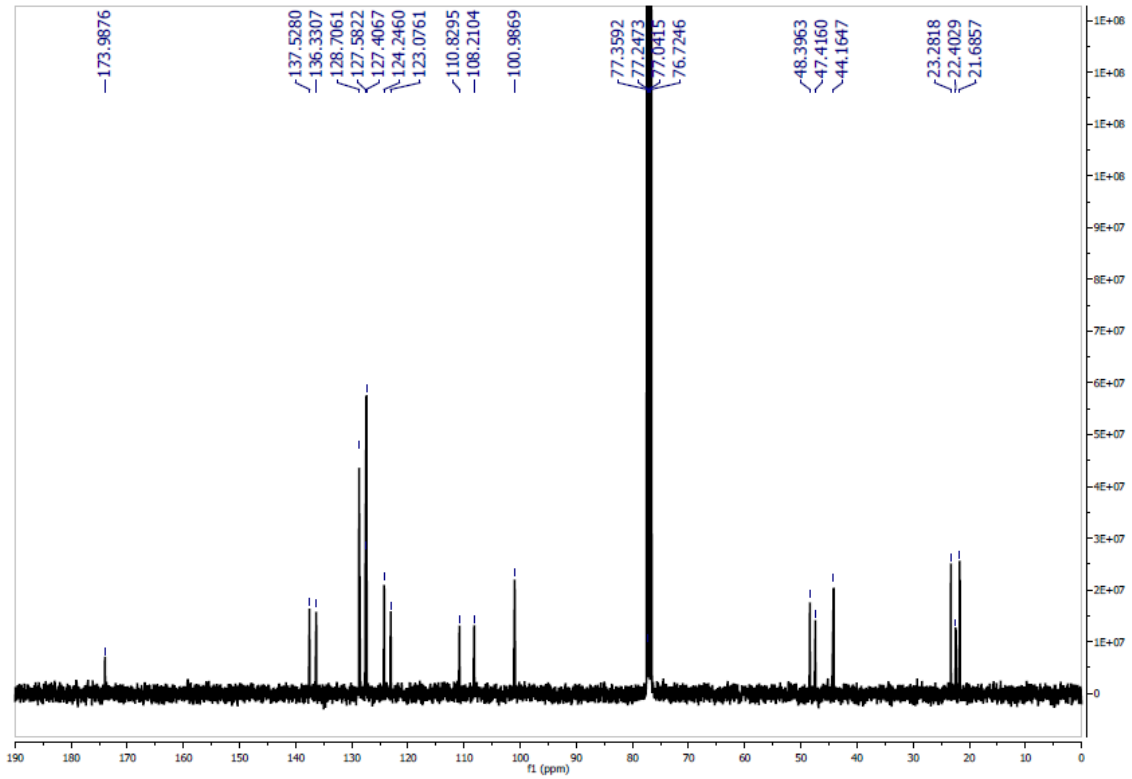

7.3367
7.3327
7.3188
7.3114
7.2710
7.2655
6.7472
6.7449
6.7110
6.6901
5.1021
5.0965
5.0814
5.0758
4.8358
4.8149
4.7430
4.7319
4.6476
4.5862
2.9065
2.4932
2.4710
1.8765
1.8609
1.6685
1.6431
1.6408
4.14
0.90
1.00
0.96
0.96
0.98
1.00
2.07
1.04
2.09
1.12
1.30

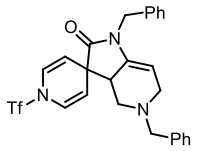

177.4255
143.3392
135.9284
127.8402
123.7220
123.4829
111.6687
107.3241
98.7526
55.3531
48.6892
45.8842
32.9787
23.8073
f1 (ppm)


Ph
O
N
N
Tf

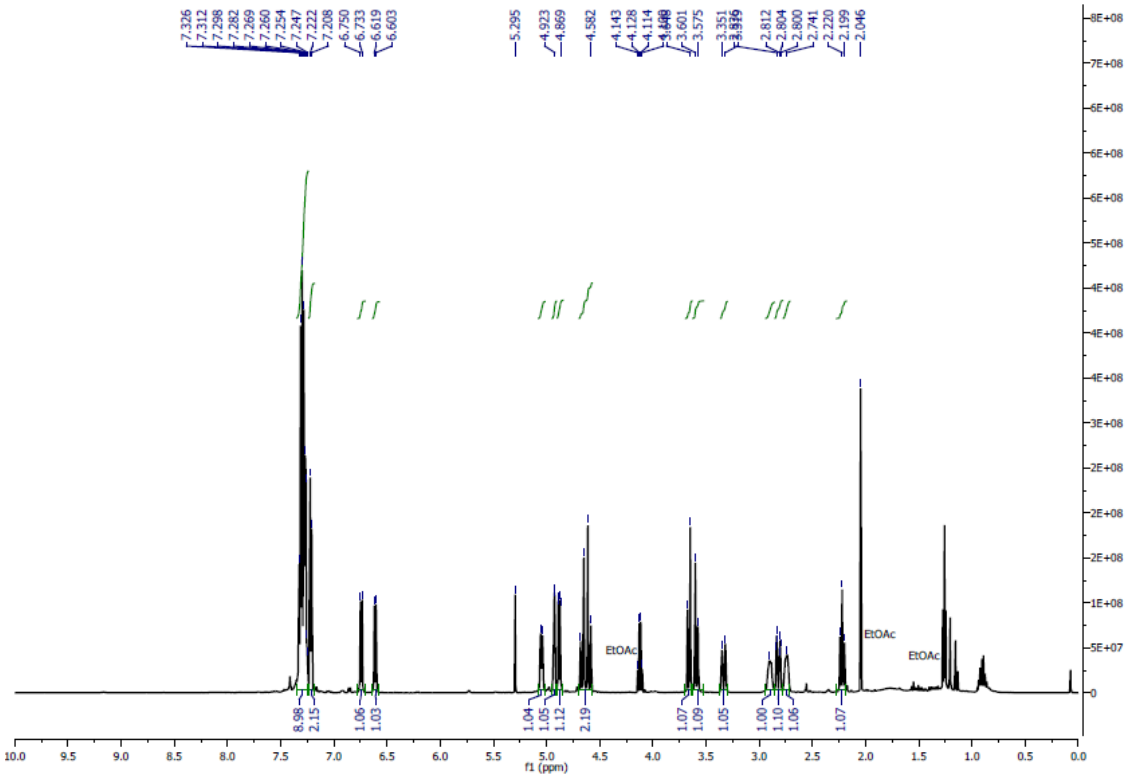
2f

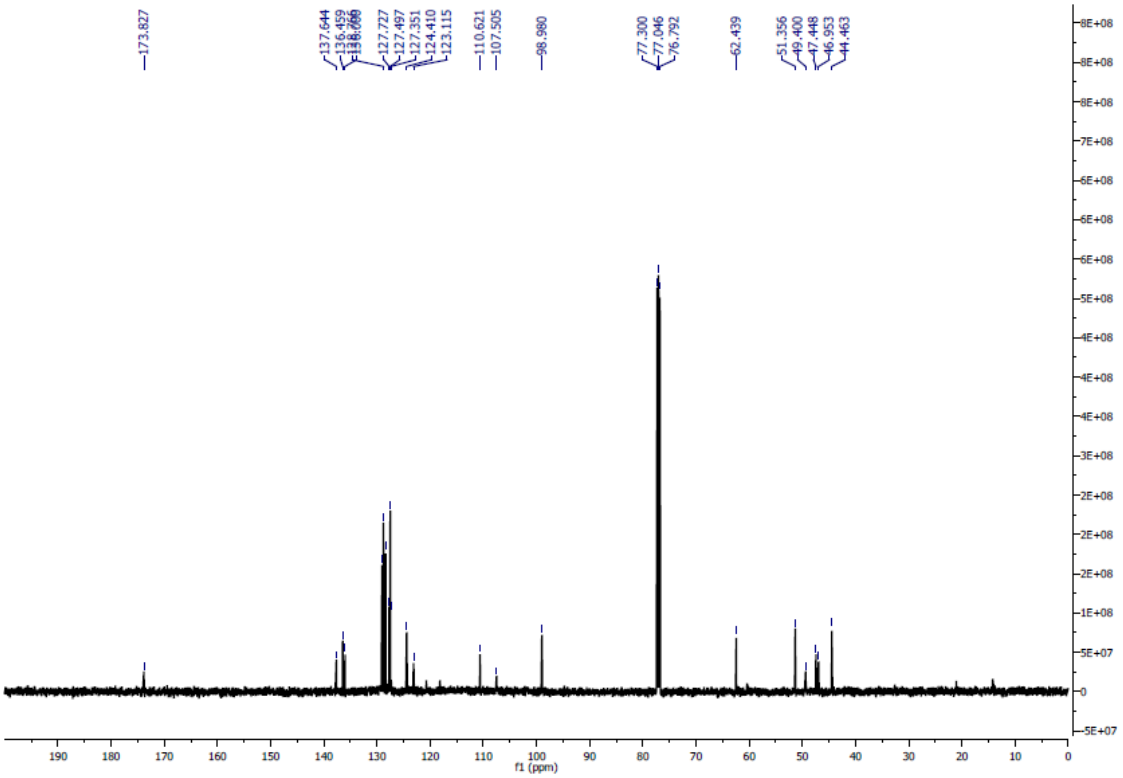

7.3299
7.3115
7.2699
7.2404
7.2230
6.8051
6.7845
6.6767
6.6559
5.0638
4.9673
4.9625
4.8816
4.8757
4.8607
4.8547
4.7005
4.6625
4.6206
4.5828
2.4507
2.4425
2.4348
2.4269
2.4222
2.1146
1.9379
1.9059
1.7692
1.7429
1.5515
1.5180
1.4432
1.4186
1.4135
1.3835
water
3.08
1.96
1.05
0.96
1.00
1.02
1.03
2.08
0.97
2.19
1.06
1.00
1.06
1.07
f1 (ppm)

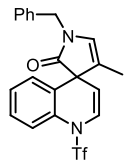

173.9876
137.5280
136.3307
128.7061
127.5822
127.4067
124.2460
123.0761
110.8295
108.2104
100.9869
77.3592
77.2473
77.0415
76.7246
48.3963
47.4160
44.1647
23.2818
22.4029
21.6857
f1 (ppm)


Ph
O
N
Tf
N
Ph

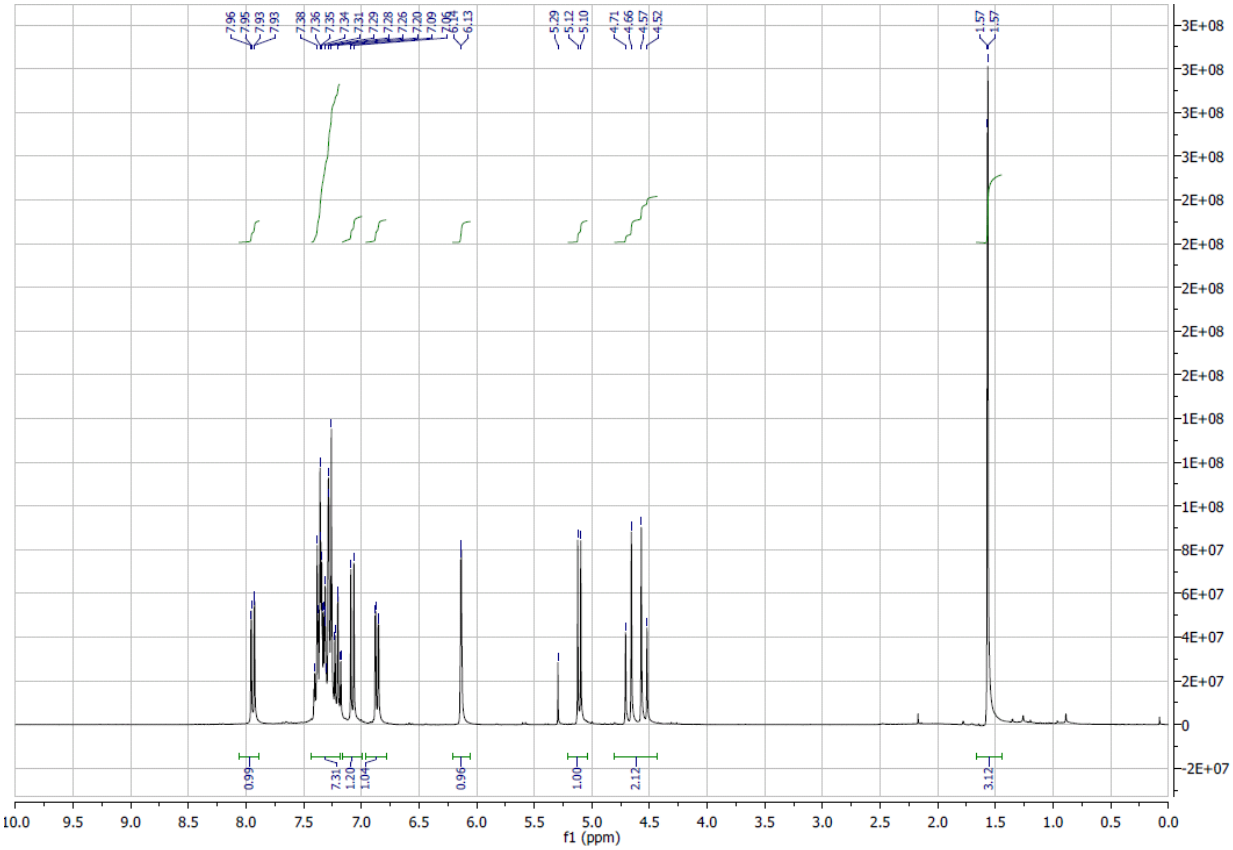
2g

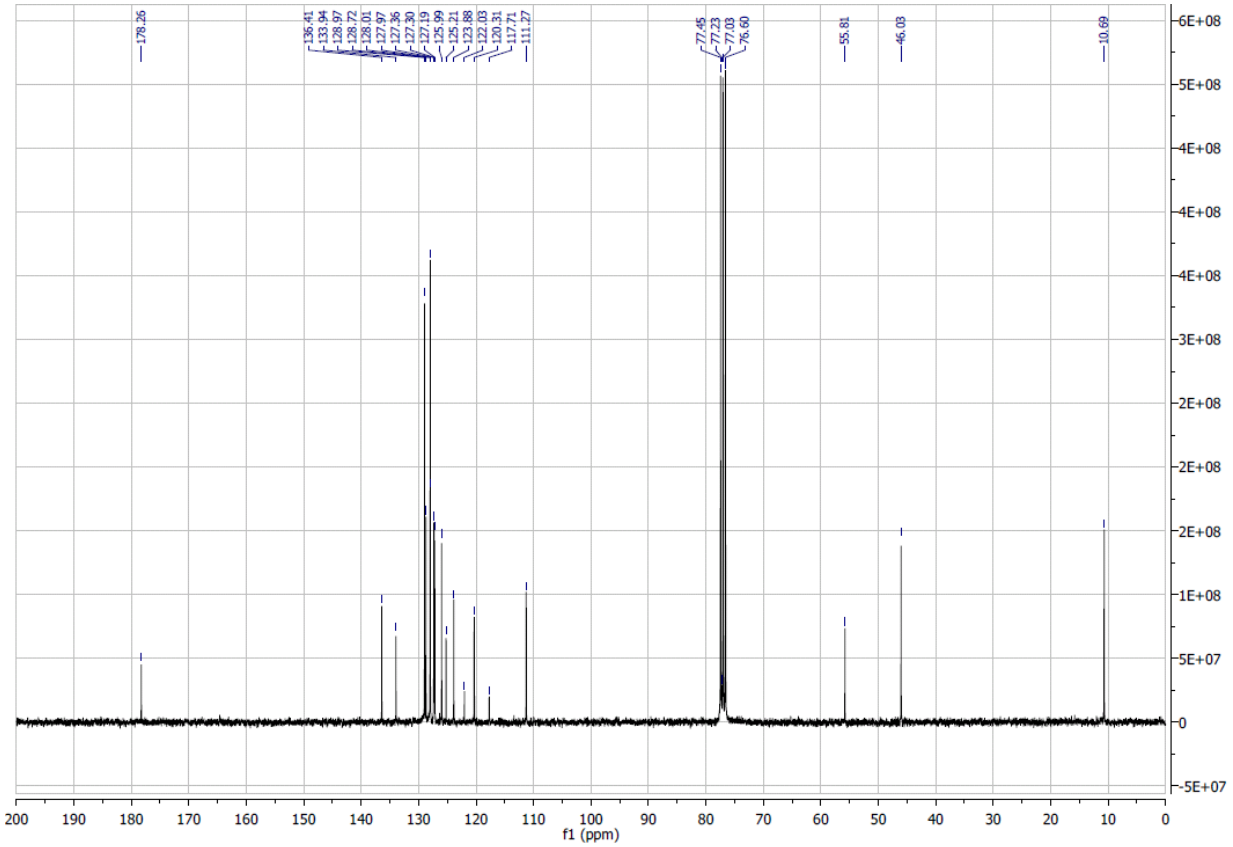

7.326
7.312
7.298
7.282
7.269
7.260
7.254
7.247
7.222
7.208
6.750
6.733
6.619
6.603
5.295
4.923
4.869
4.582
4.143
4.128
4.114
3.601
3.575
3.351
2.812
2.804
2.800
2.741
2.220
2.199
2.046
EtOAc
EtOAc
EtOAc
8.98
2.15
1.06
1.03
1.04
1.05
1.12
2.19
1.07
1.09
1.05
1.00
1.10
1.06
1.07
f1 (ppm)

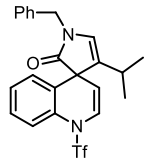

173.827
137.644
136.459
127.727
127.497
127.351
124.410
123.115
110.621
107.505
98.980
77.300
77.046
76.792
62.439
51.356
49.400
47.448
46.953
44.463
f1 (ppm)


Ph
N
O
N
Tf

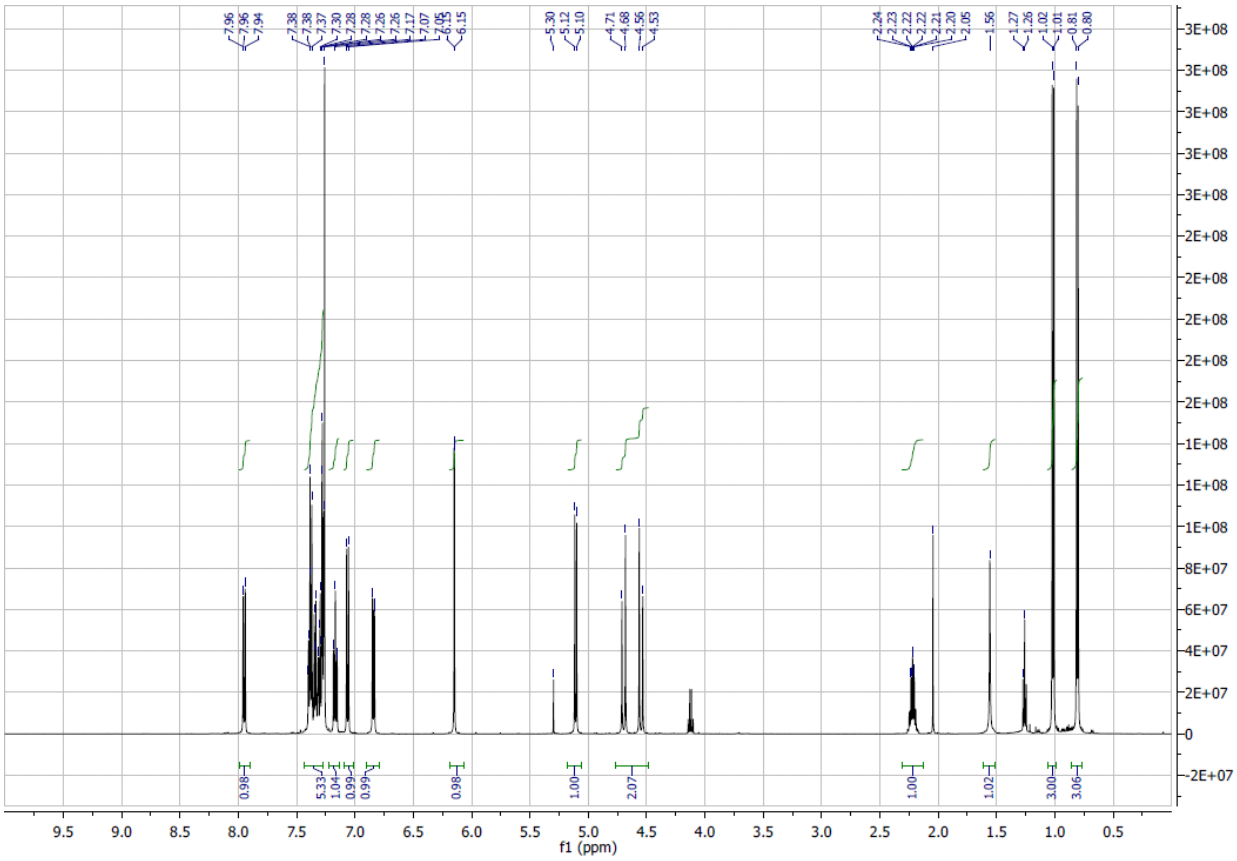
2j

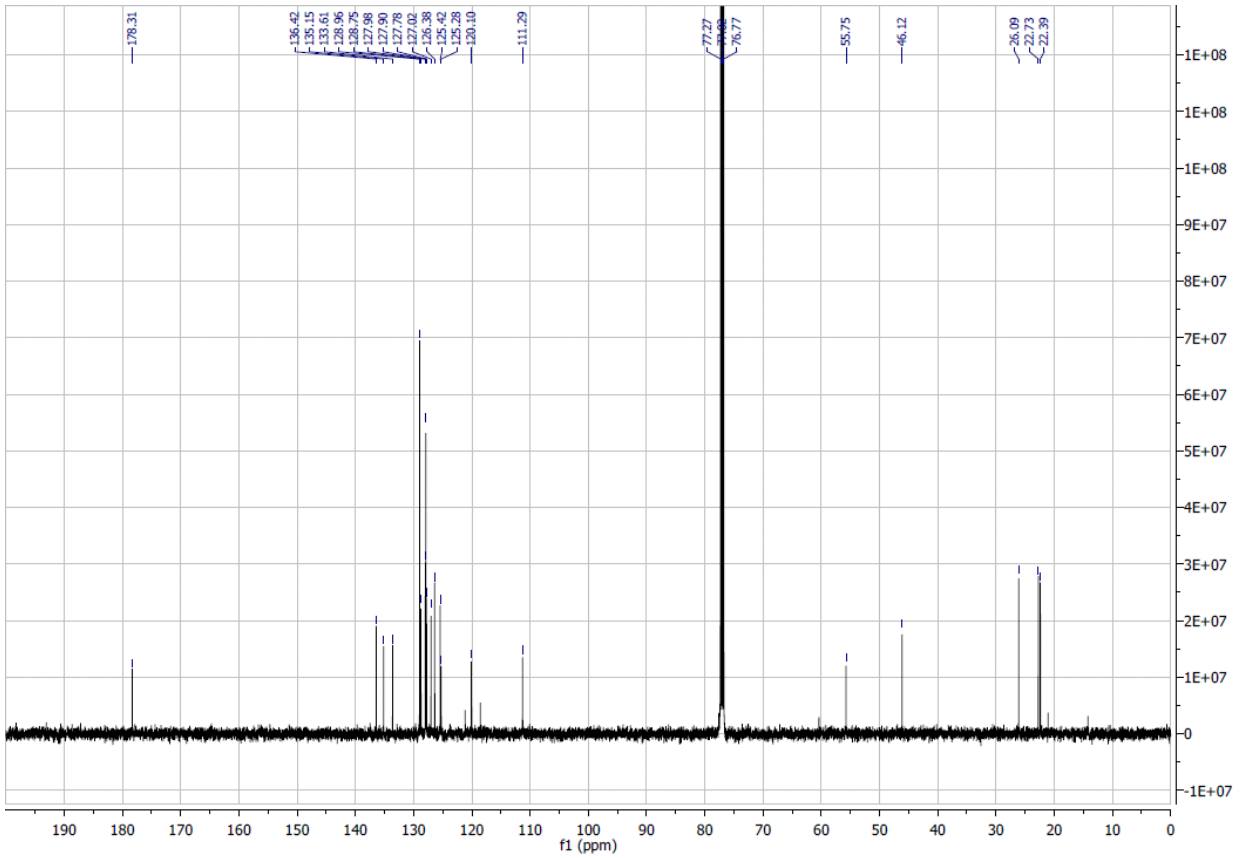

7.96
7.95
7.93
7.93
7.38
7.36
7.35
7.34
7.31
7.29
7.28
7.26
7.20
7.09
7.05
6.14
6.13
5.29
5.12
5.10
4.71
4.66
4.57
4.52
1.57
1.57
0.99
7.31
1.20
1.04
0.96
1.00
2.12
3.12
f1 (ppm)

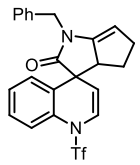

178.26
136.41
133.94
128.97
128.72
128.01
127.97
127.36
127.30
127.19
125.99
125.21
123.88
122.03
120.31
117.71
111.27
77.45
77.23
77.03
76.60
55.81
46.03
10.69
f1 (ppm)


Ph
N
O
N
Tf

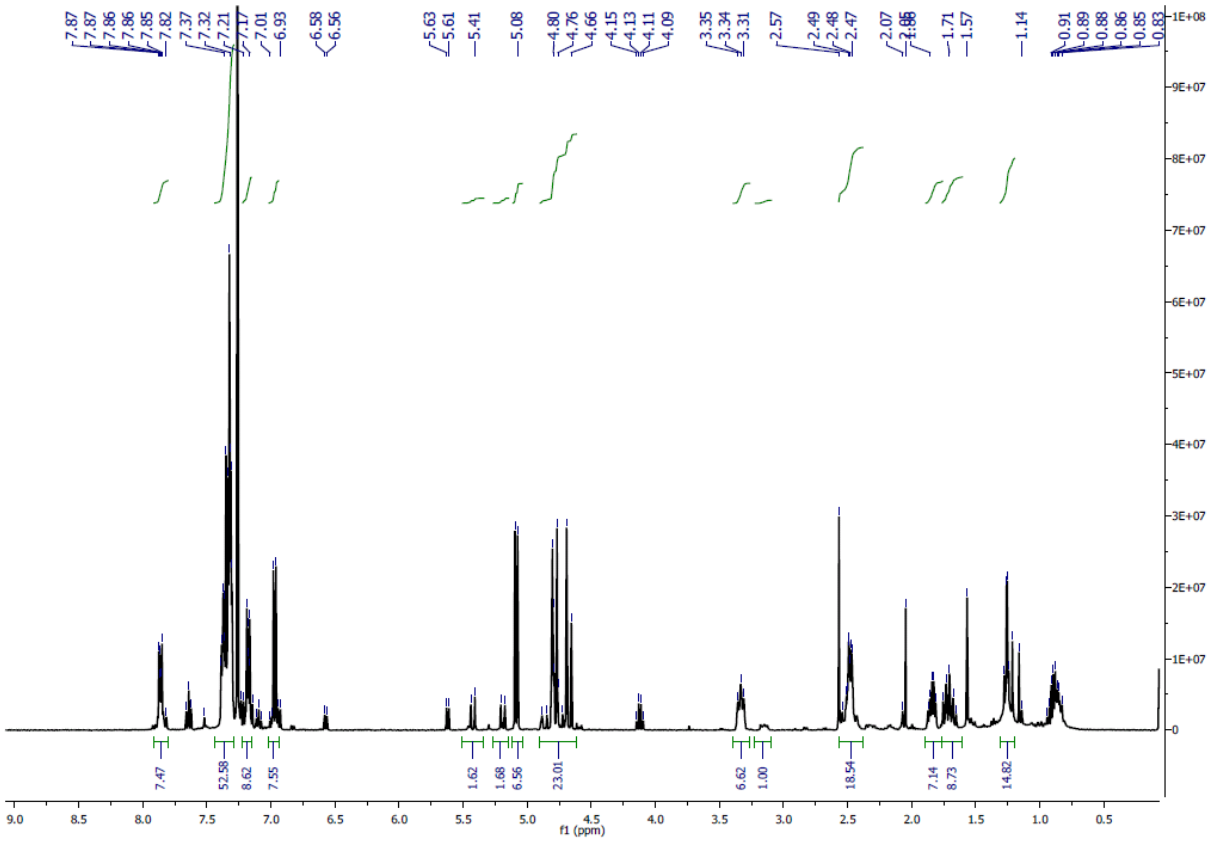
2k

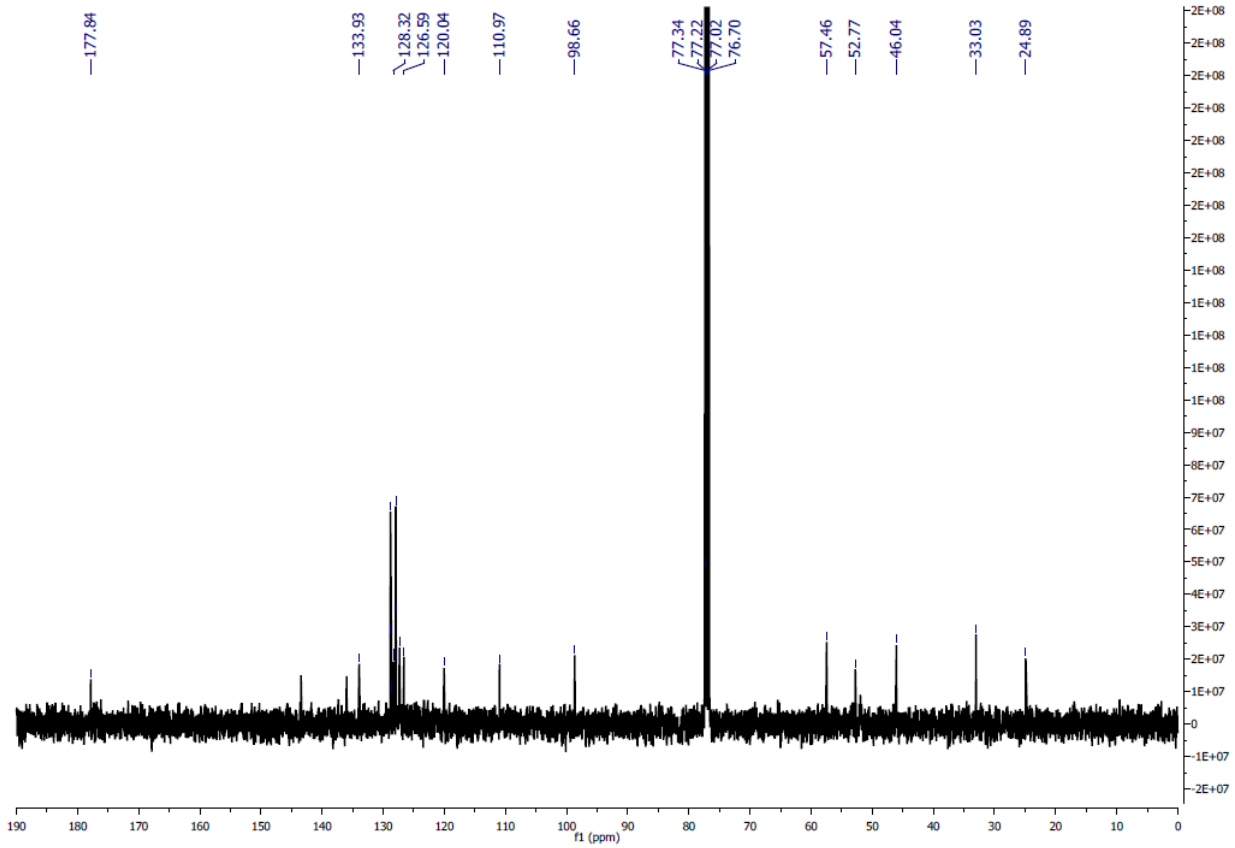

7.96
7.95
7.94
7.38
7.38
7.37
7.30
7.28
7.28
7.26
7.26
7.17
7.07
6.15
6.15
5.30
5.12
5.10
4.71
4.68
4.56
4.53
2.24
2.23
2.22
2.22
2.21
2.20
2.05
1.56
1.27
1.26
1.02
1.01
0.81
0.80
0.98
5.33
1.04
0.99
0.99
0.98
1.00
2.07
1.00
1.02
3.00
3.06
f1 (ppm)

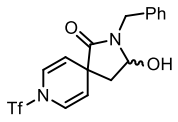

178.31
136.42
135.15
133.61
128.96
128.75
127.98
127.90
127.78
127.02
126.38
125.42
125.28
120.10
111.29
77.27
76.77
55.75
46.12
26.09
22.73
22.39
f1 (ppm)


Ph
N
O
N
Tf

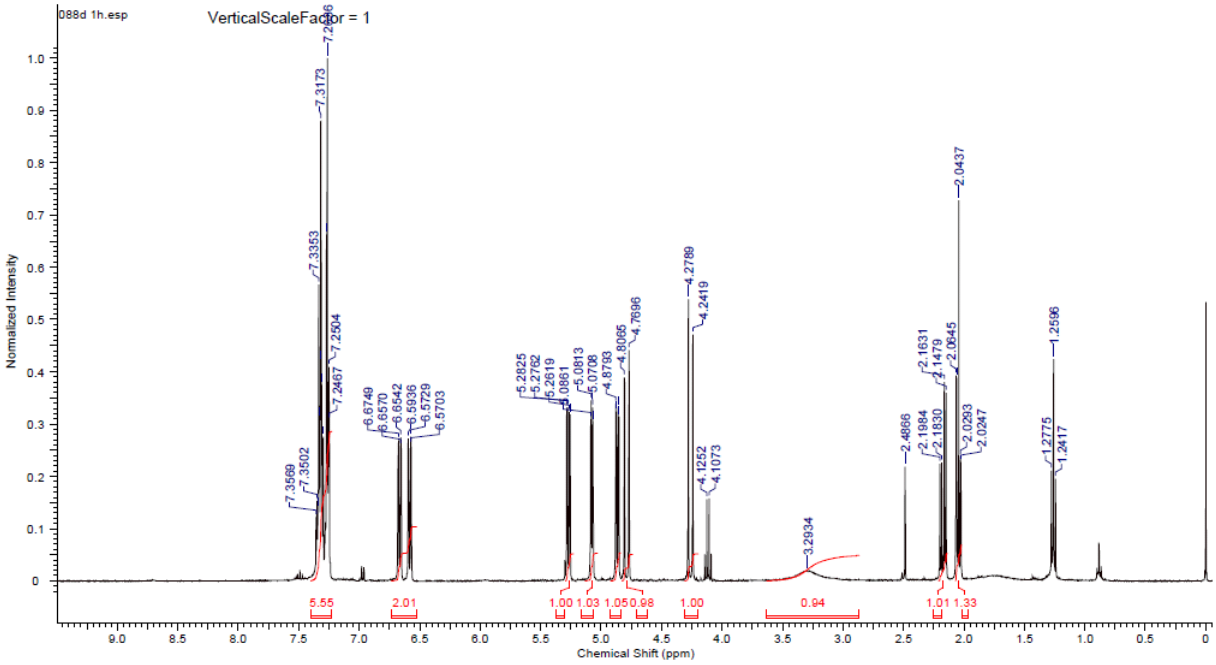
2l

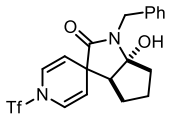

7.87
7.87
7.86
7.86
7.85
7.82
7.37
7.32
7.21
7.17
7.01
6.93
6.58
6.56
5.63
5.61
5.41
5.08
4.80
4.76
4.66
4.15
4.13
4.11
4.09
3.35
3.34
3.31
2.57
2.49
2.48
2.47
2.07
1.71
1.57
1.14
0.91
0.89
0.88
0.86
0.85
0.83
7.47
52.58
8.62
7.55
1.62
1.68
6.56
23.01
6.62
1.00
18.54
7.14
8.73
14.82
f1 (ppm)


177.84
133.93
128.32
126.59
120.04
110.97
98.66
77.34
77.22
77.02
76.70
57.46
52.77
46.04
33.03
24.89
f1 (ppm)

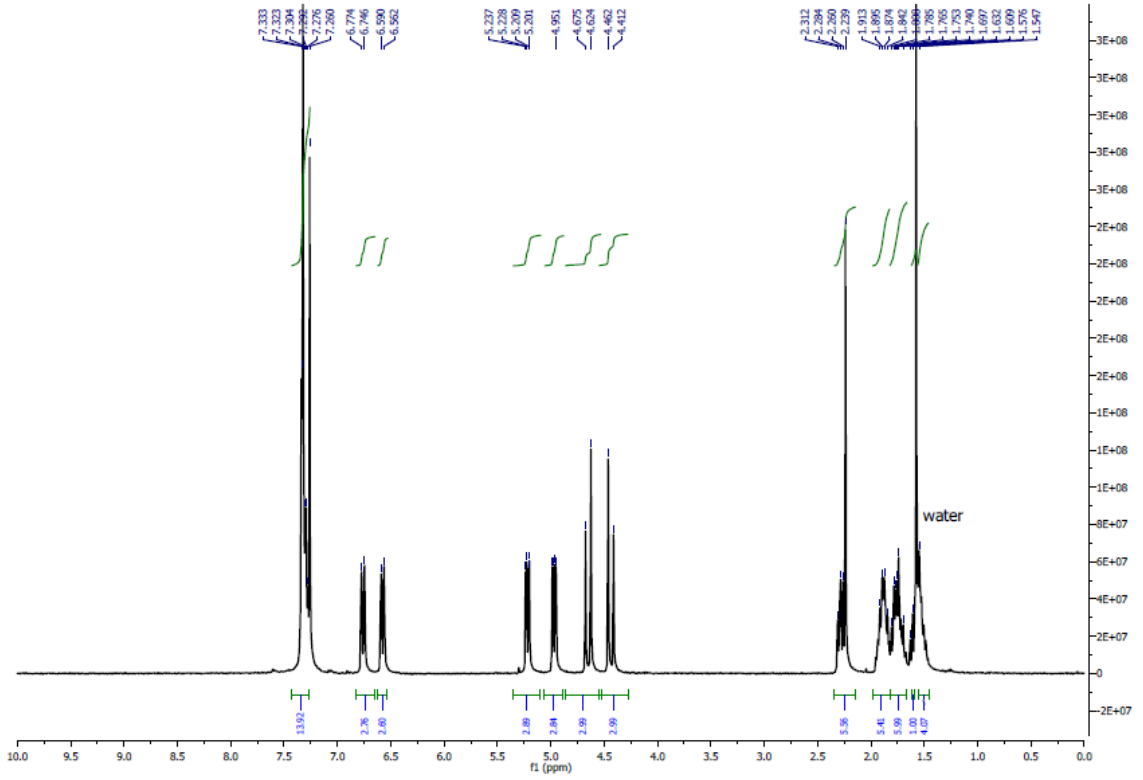

Ph
N
O
OH
Tf
N

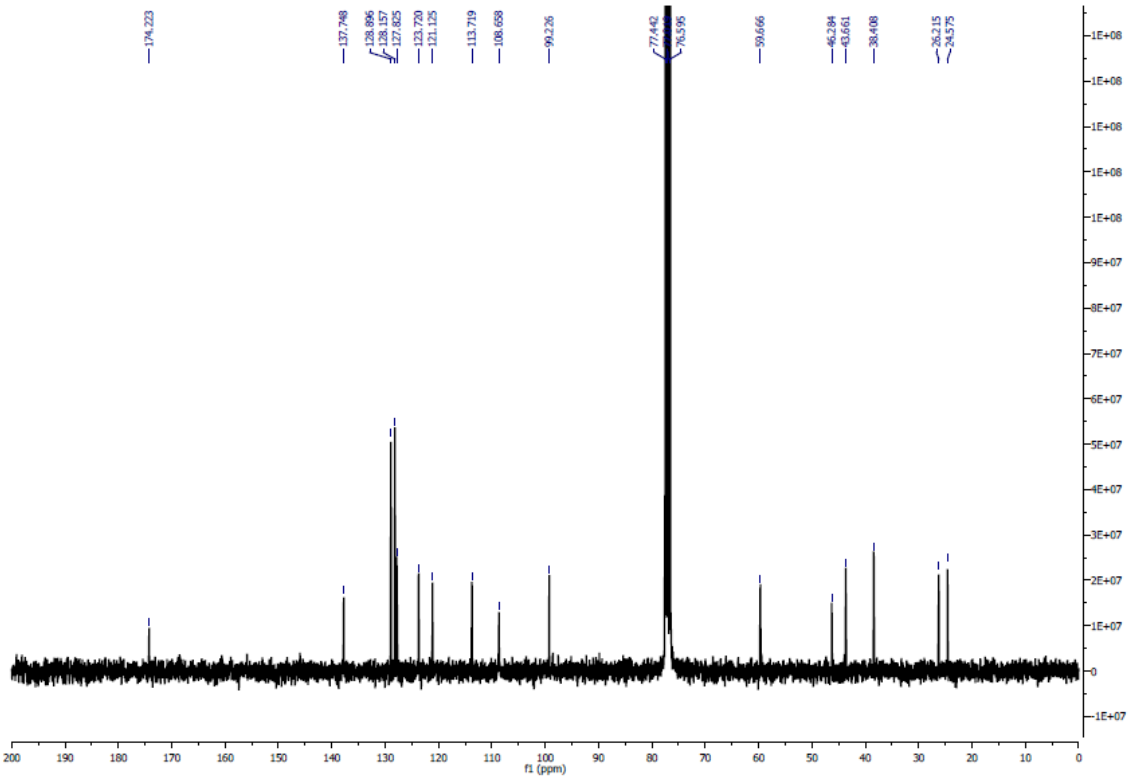
6c

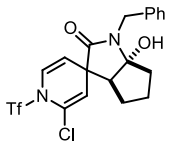

088d 1h.esp
VerticalScaleFactor = 1
Normalized Intensity
Chemical Shift (ppm)
7.3569
7.3502
7.3353
7.3173
7.2926
7.2504
7.2467
6.6749
6.6570
6.6542
6.5936
6.5729
6.5703
5.2825
5.2762
5.2619
5.0861
5.0813
5.0708
4.8793
4.8065
4.7696
4.2789
4.2419
4.1252
4.1073
3.2934
2.4866
2.1984
2.1830
2.1631
2.1479
2.0645
2.0437
2.0293
2.0247
1.2775
1.2596
1.2417
5.55
2.01
1.00
1.03
1.05
0.98
1.00
0.94
1.01
1.33


Ph
O
N
OH
Tf
N

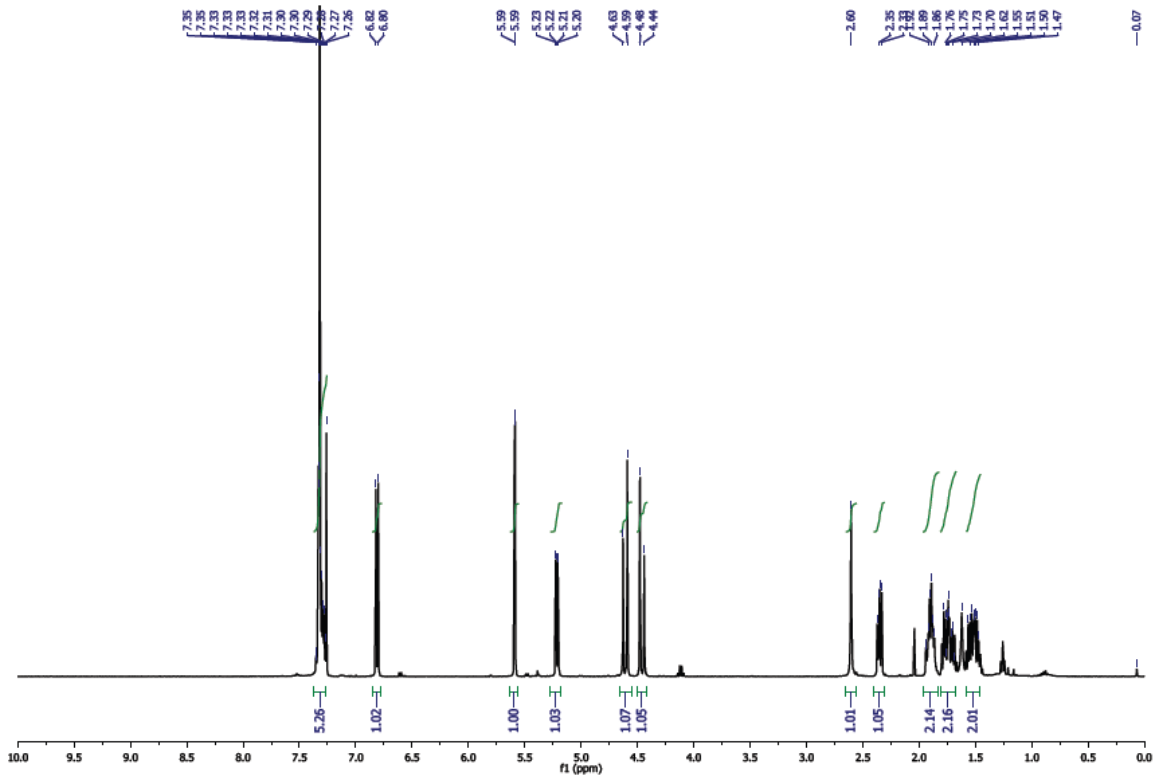
6e

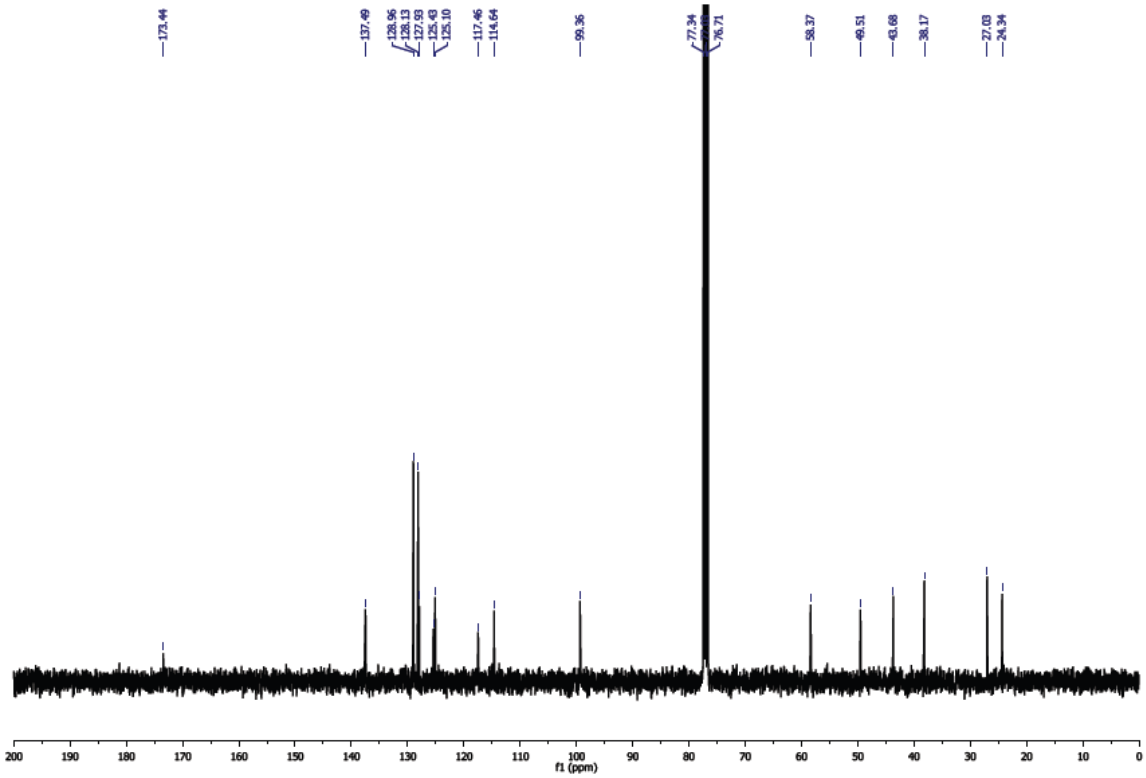

water
f1 (ppm)

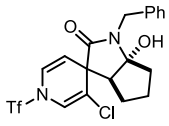

174.223
137.748
128.896
128.157
127.825
123.730
121.125
113.719
108.658
99.226
77.442
76.595
59.666
46.284
43.661
38.408
26.215
24.575
f1 (ppm)


Ph
O
N
OH
Tf
N
Cl

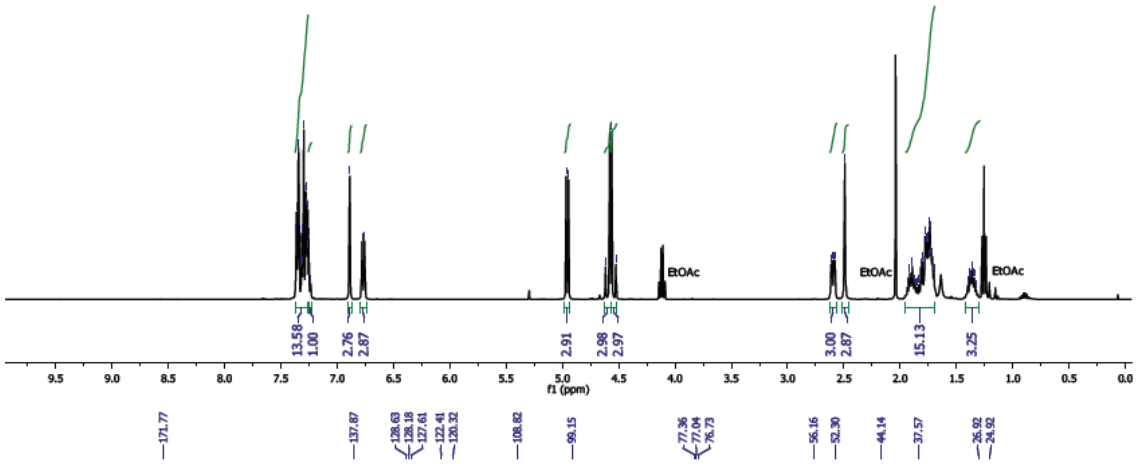
6h

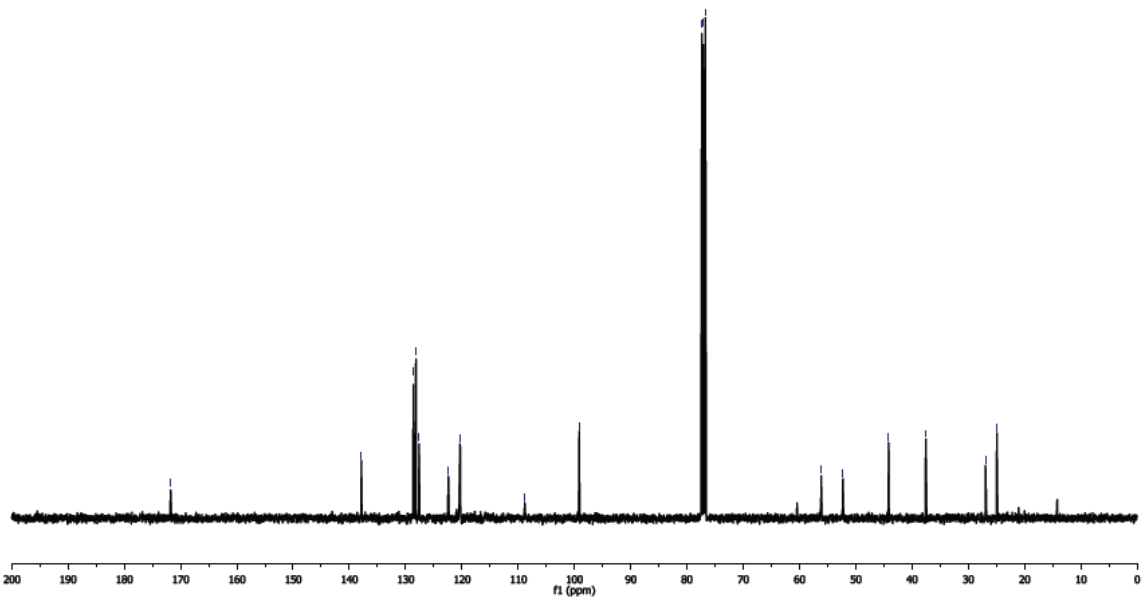

7.35
7.35
7.33
7.33
7.33
7.32
7.31
7.30
7.29
7.28
7.27
7.26
6.82
6.80
5.59
5.59
5.23
5.22
5.21
5.20
4.63
4.59
4.48
4.44
2.60
2.35
1.89
1.86
1.76
1.75
1.73
1.70
1.62
1.55
1.51
1.50
1.47
0.07
5.26
1.02
1.00
1.03
1.07
1.05
1.01
1.05
2.14
2.16
2.01
f1 (ppm)

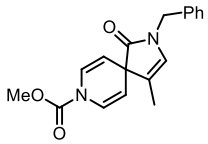

173.44
137.49
128.96
128.13
127.93
125.43
125.10
117.46
114.64
99.36
77.34
76.71
58.37
49.51
43.68
38.17
27.03
24.34
f1 (ppm)


Ph
O
N
OH
Tf
N
Cl

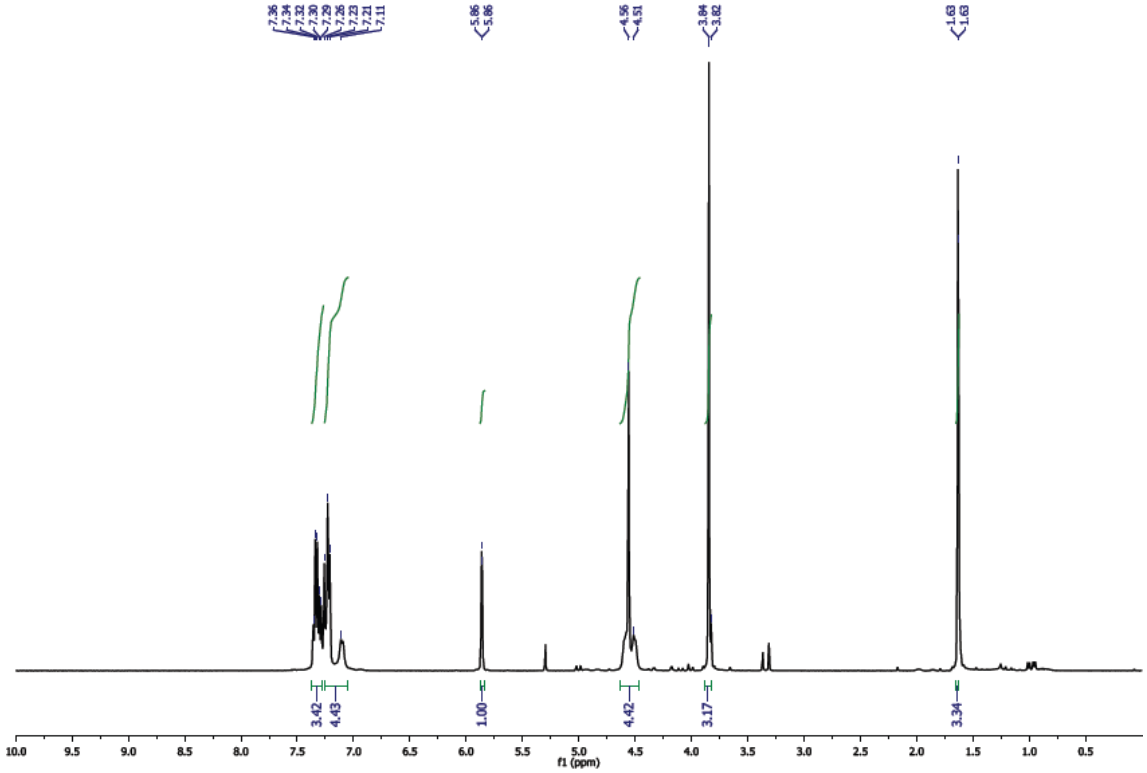
6i

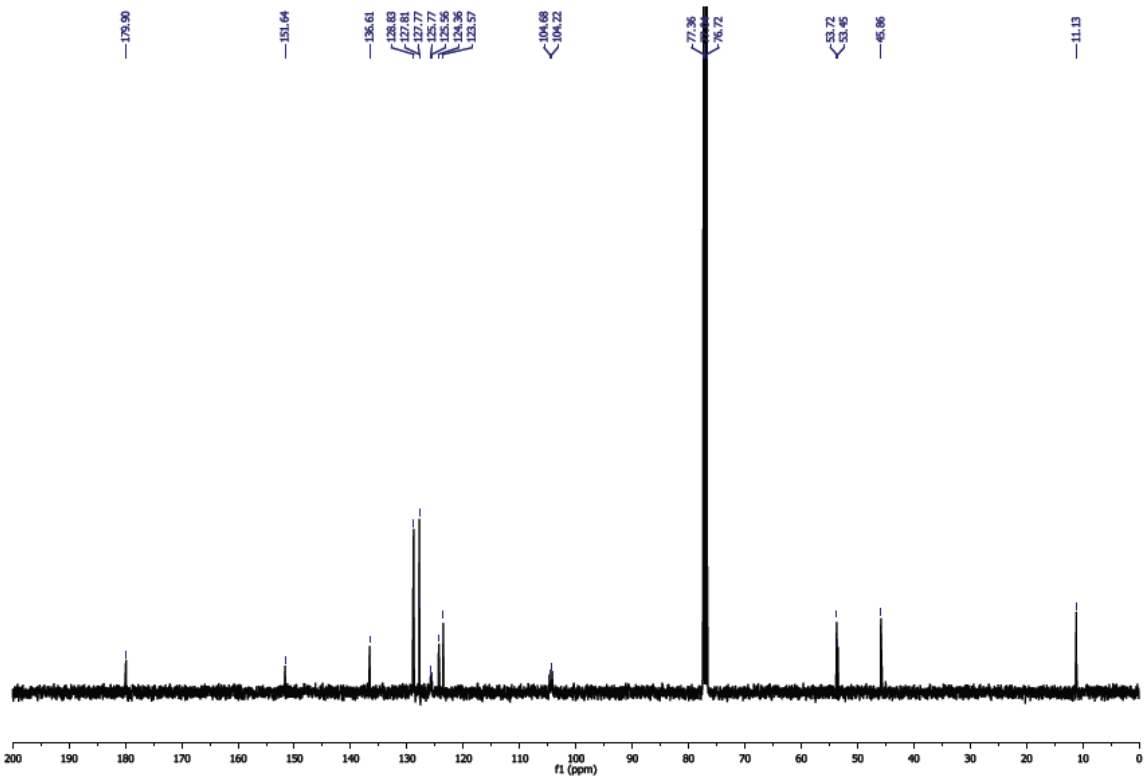

EtOAc
EtOAc
EtOAc
13.58
1.00
2.76
2.87
2.91
2.98
2.97
3.00
2.87
15.13
3.25
f1 (ppm)

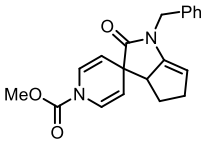

f1 (ppm)


Ph
O
N
MeO
N
O

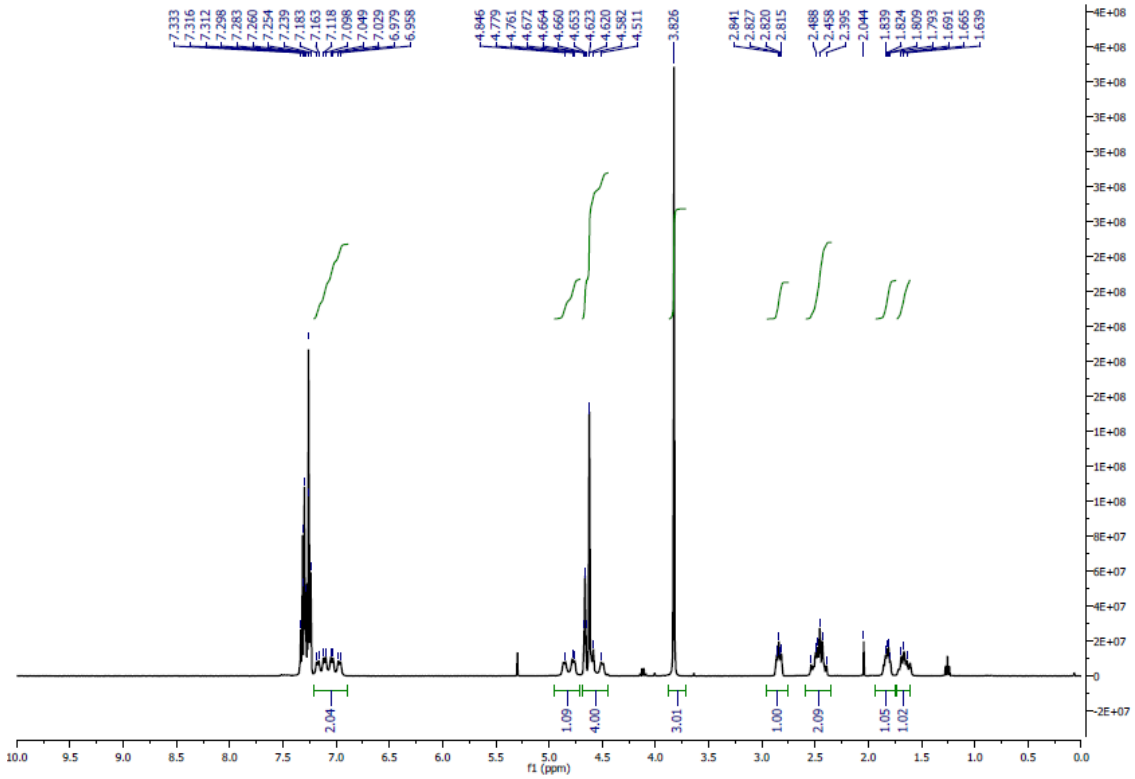
7a

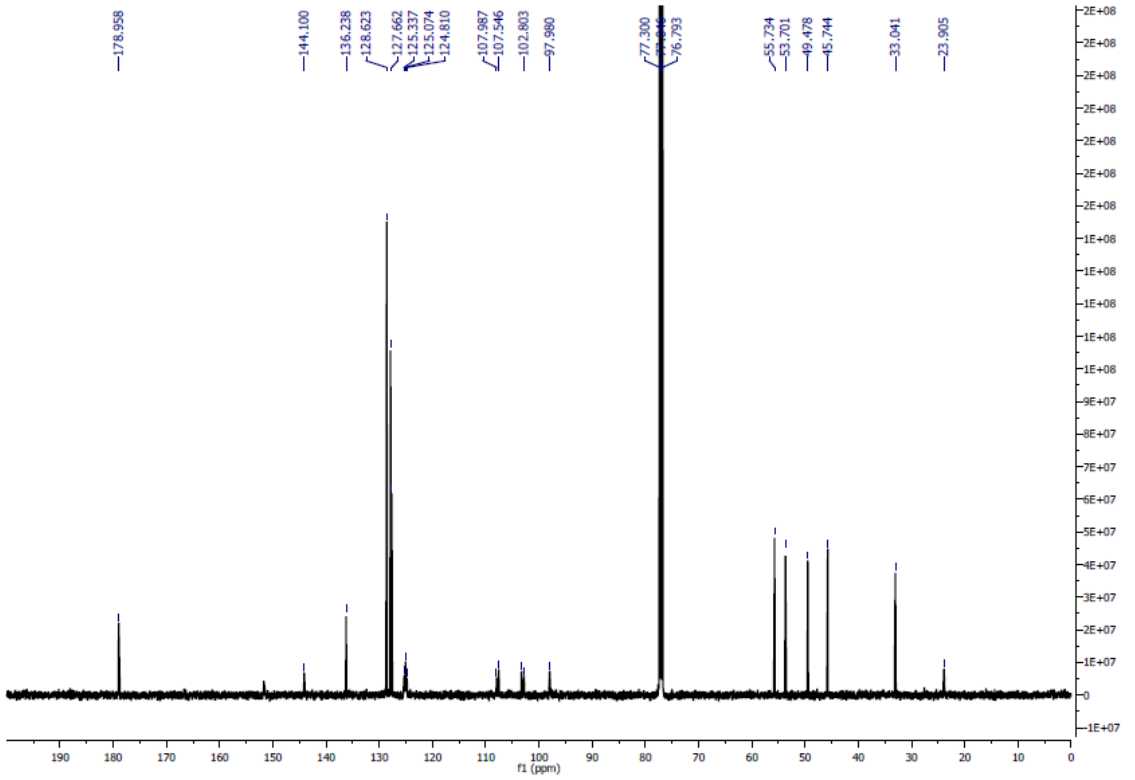

7.36
7.34
7.32
7.30
7.29
7.26
7.23
7.21
7.11
5.86
5.86
4.56
4.51
3.84
3.82
1.63
1.63
3.42
4.43
1.00
4.42
3.17
3.34
f1 (ppm)

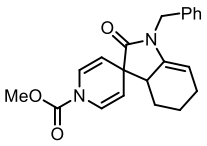

179.90
151.64
136.61
128.83
127.81
127.77
125.77
125.56
124.36
123.57
104.68
104.22
77.36
76.72
53.72
53.45
45.86
11.13
f1 (ppm)


Ph
O
N
MeO
N
O

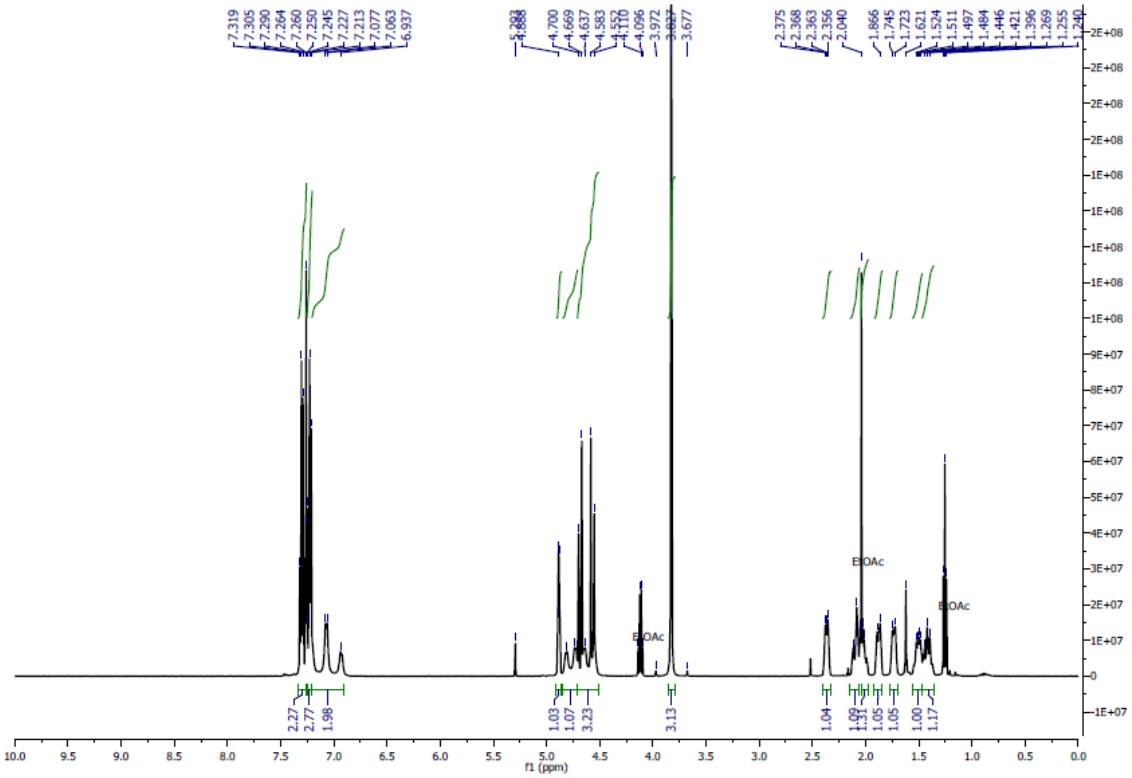
7e

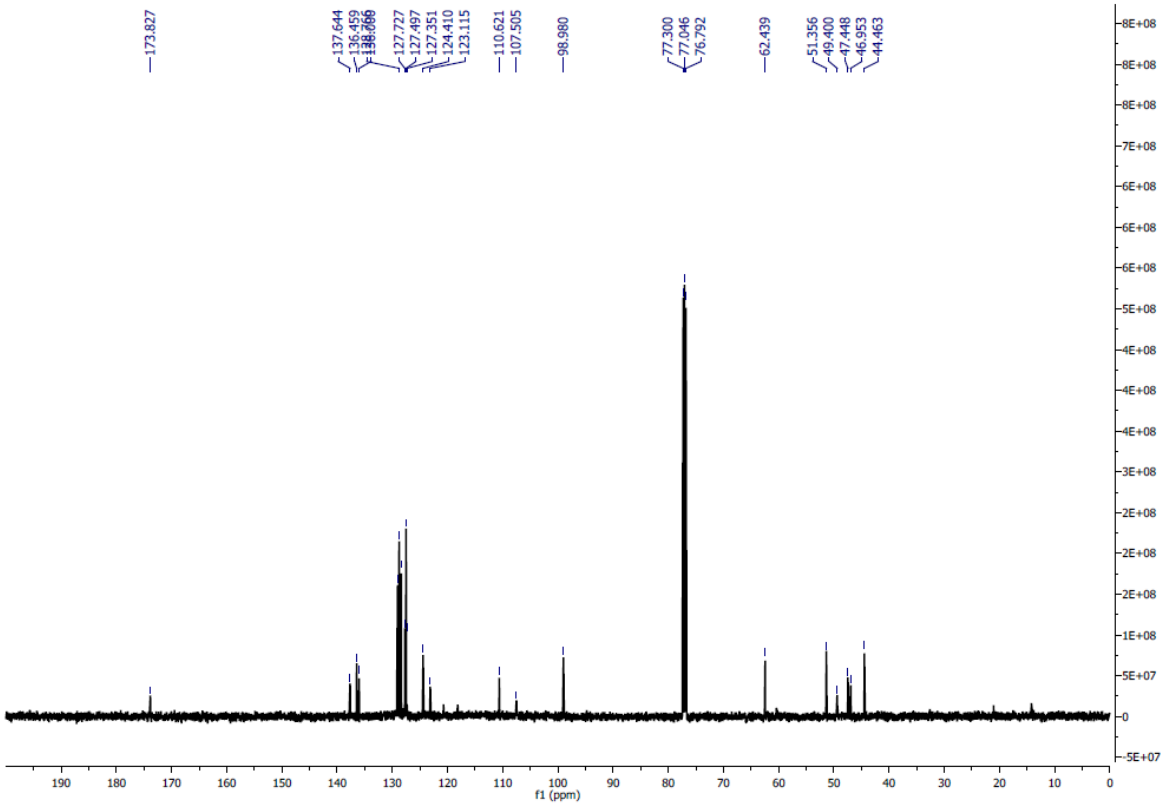

7.333
7.316
7.312
7.298
7.283
7.260
7.254
7.239
7.183
7.163
7.118
7.098
7.049
7.029
6.979
6.958
4.846
4.779
4.761
4.672
4.664
4.660
4.653
4.623
4.620
4.582
4.511
3.826
2.841
2.827
2.820
2.815
2.488
2.458
2.395
2.044
1.839
1.824
1.809
1.793
1.691
1.665
1.639
2.04
1.09
4.00
3.01
1.00
2.09
1.05
1.02
f1 (ppm)

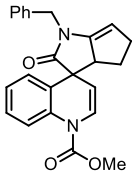

178.958
144.100
136.238
128.623
127.662
125.337
125.074
124.810
107.987
107.546
102.803
97.980
77.300
76.793
55.734
53.701
49.478
45.744
33.041
23.905
f1 (ppm)



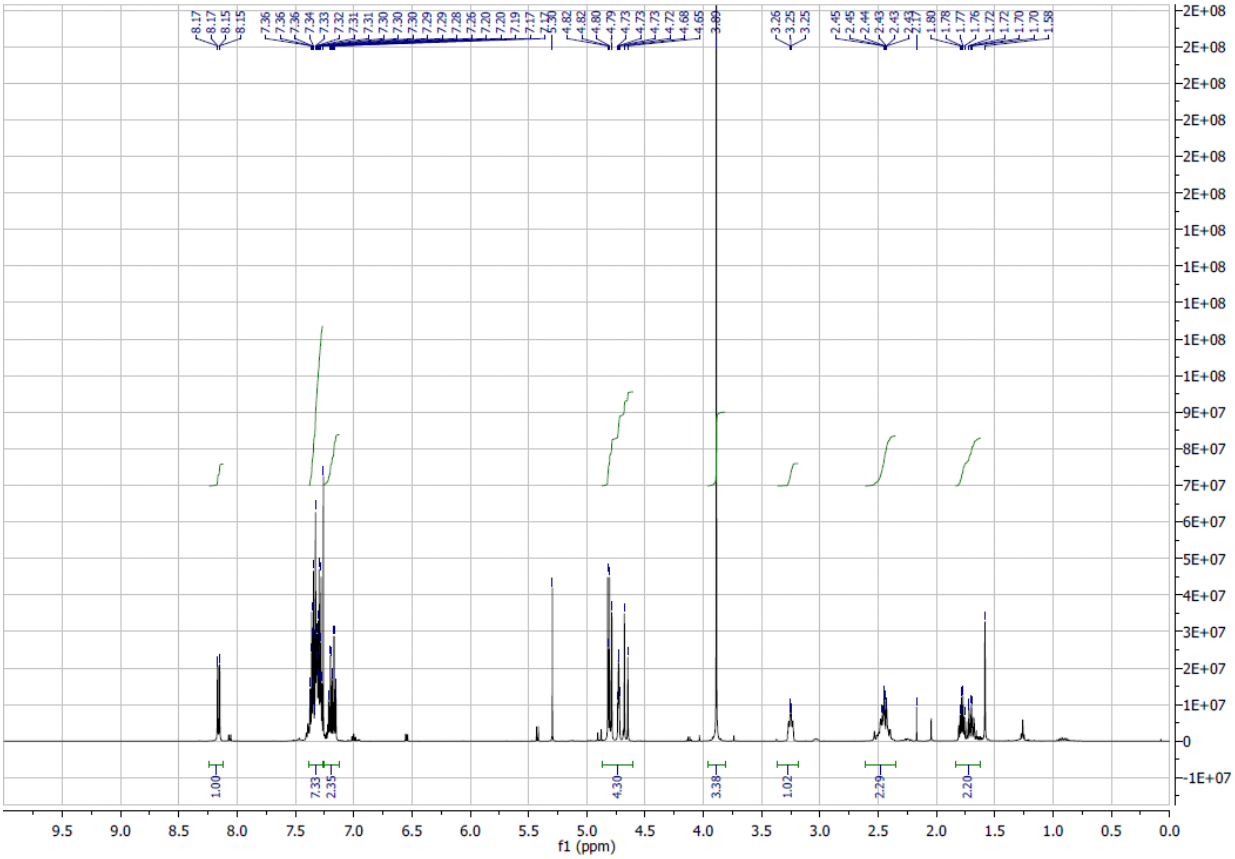
7f

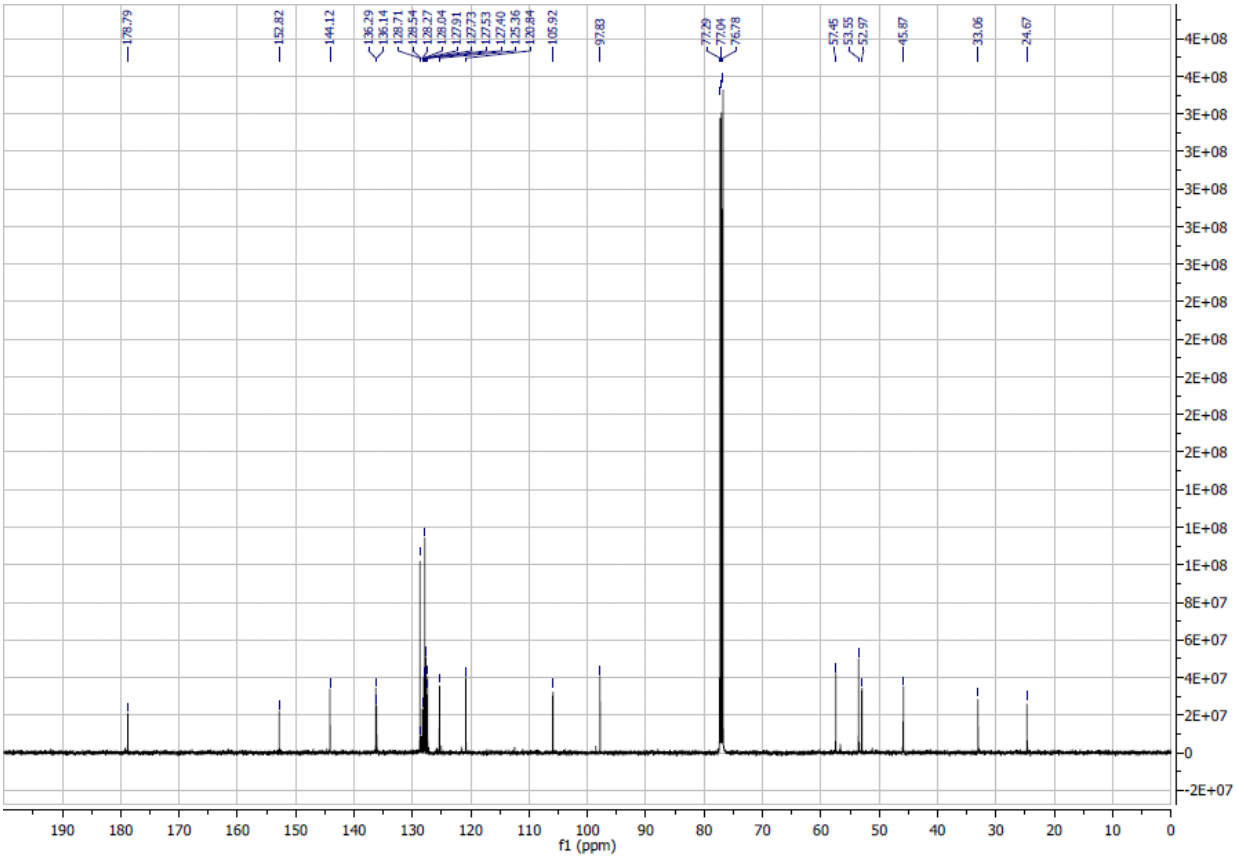


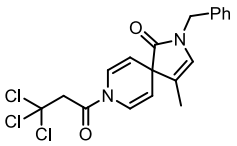




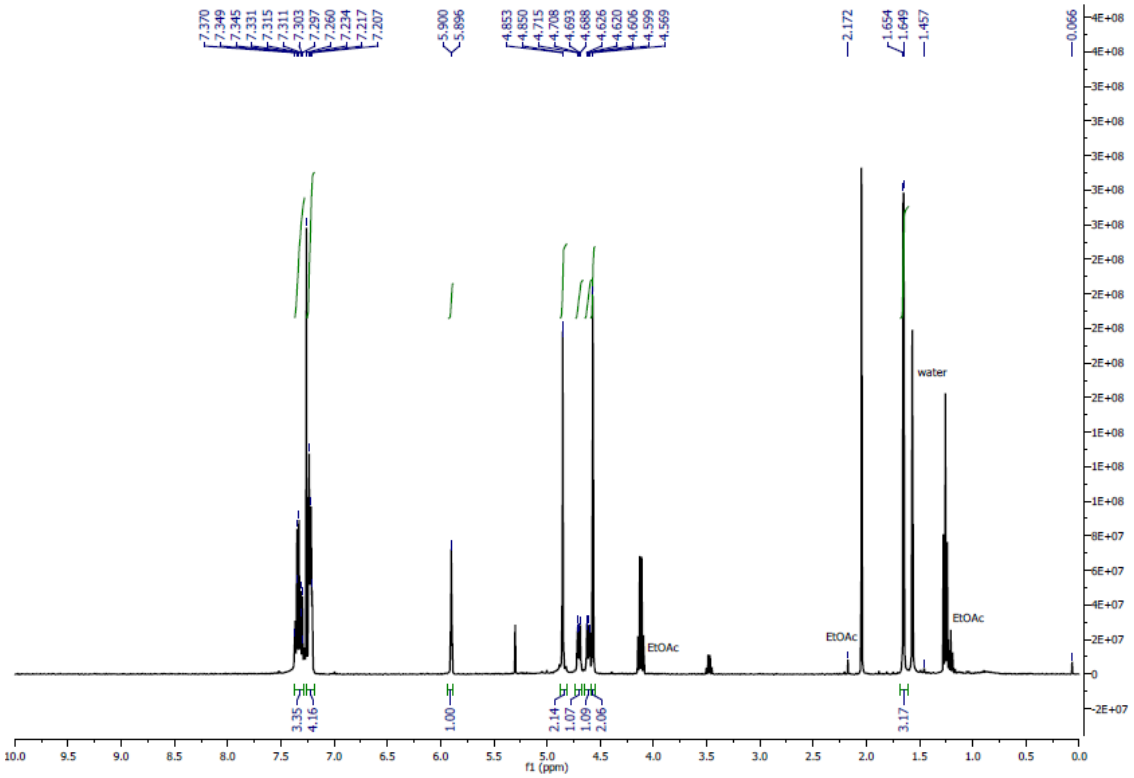
7l

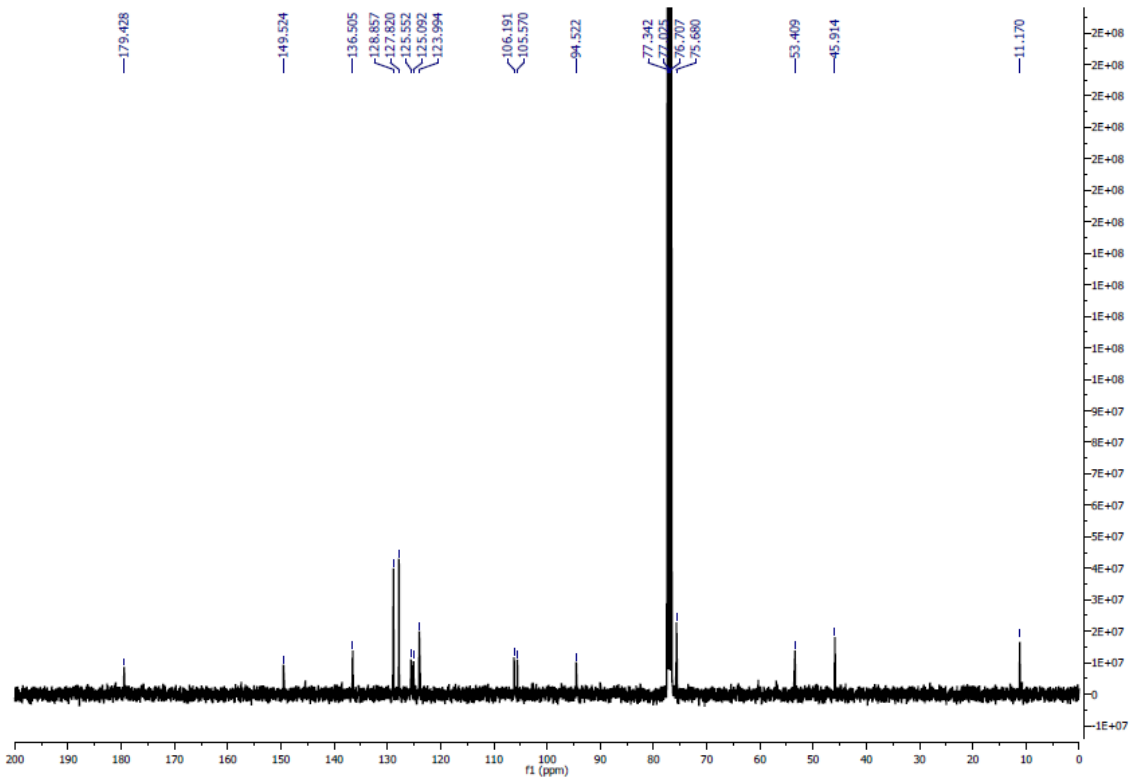


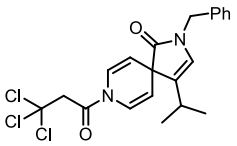



Ph
O
N
Cl
Cl
Cl
N
O

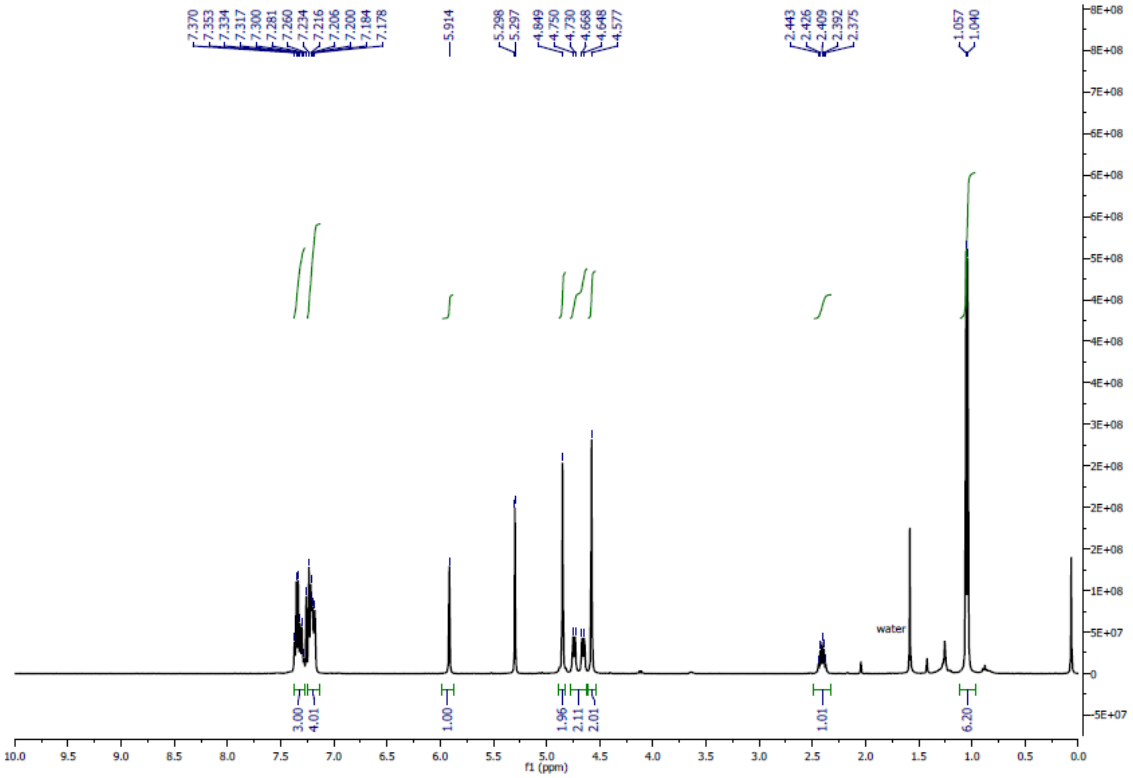
8a

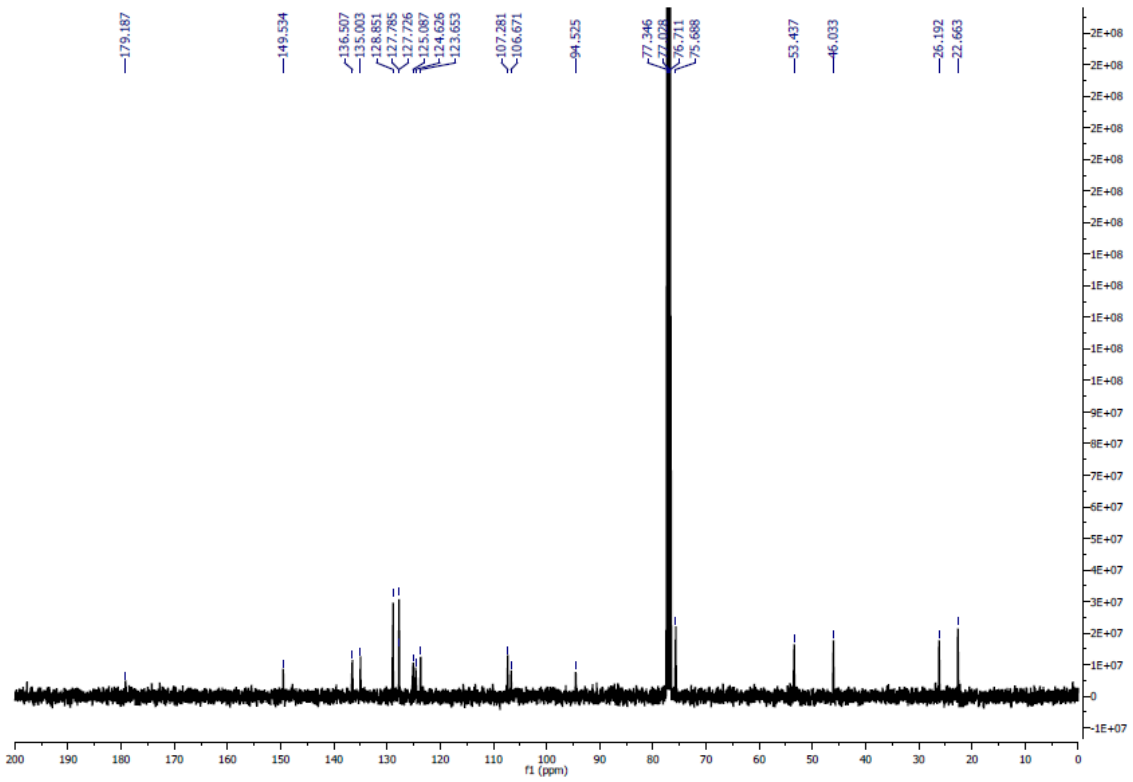

7.370
7.349
7.345
7.331
7.315
7.311
7.303
7.297
7.260
7.234
7.217
7.207
5.900
5.896
4.853
4.850
4.715
4.708
4.693
4.688
4.626
4.620
4.606
4.599
4.569
2.172
1.654
1.649
1.457
0.066
water
EtOAc
EtOAc
EtOAc
3.35
4.16
1.00
2.14
1.07
1.09
2.06
3.17
f1 (ppm)

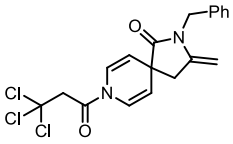

179.428
149.524
136.505
128.857
127.820
125.552
125.092
123.994
106.191
105.570
94.522
77.342
77.025
76.707
75.680
53.409
45.914
11.170
f1 (ppm)


Ph
O
N
Cl
Cl
Cl
N
O

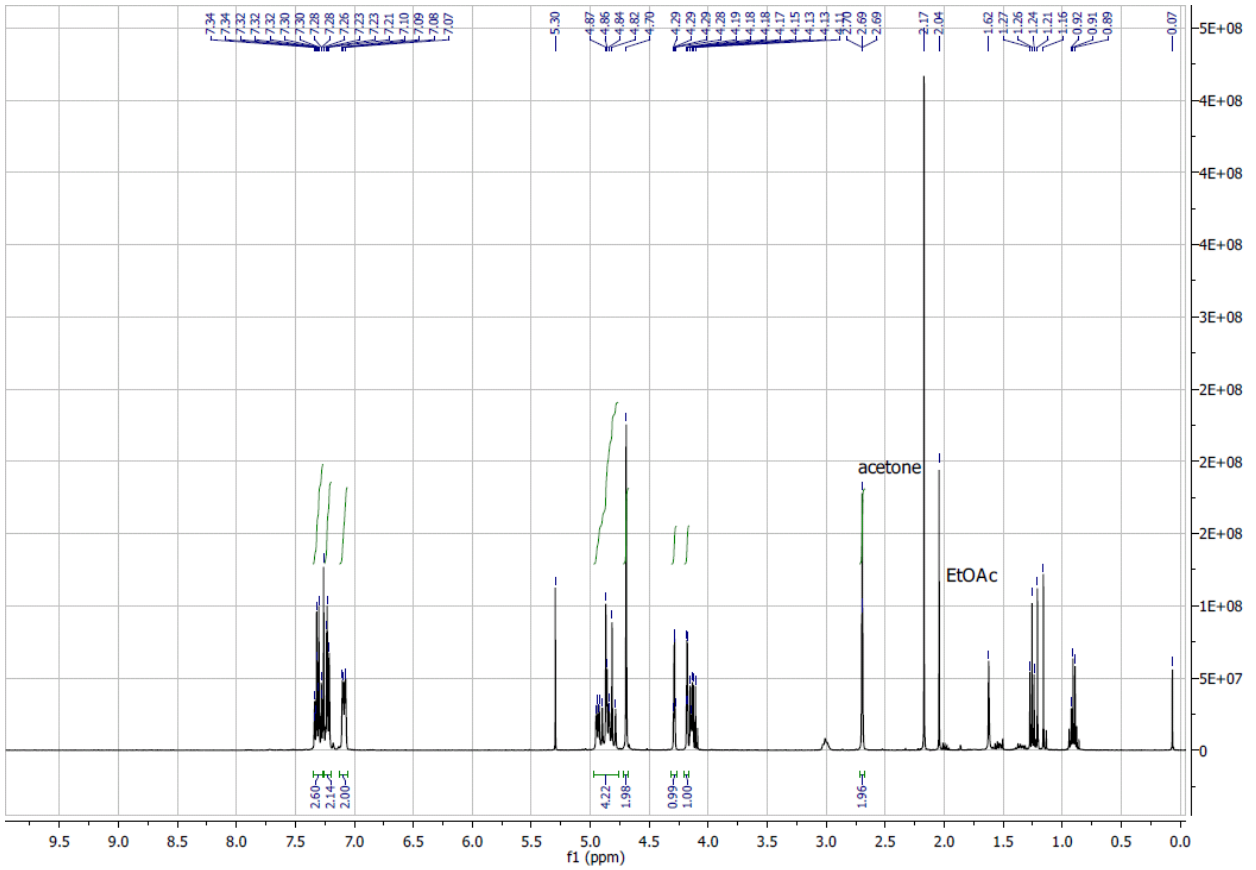
8b

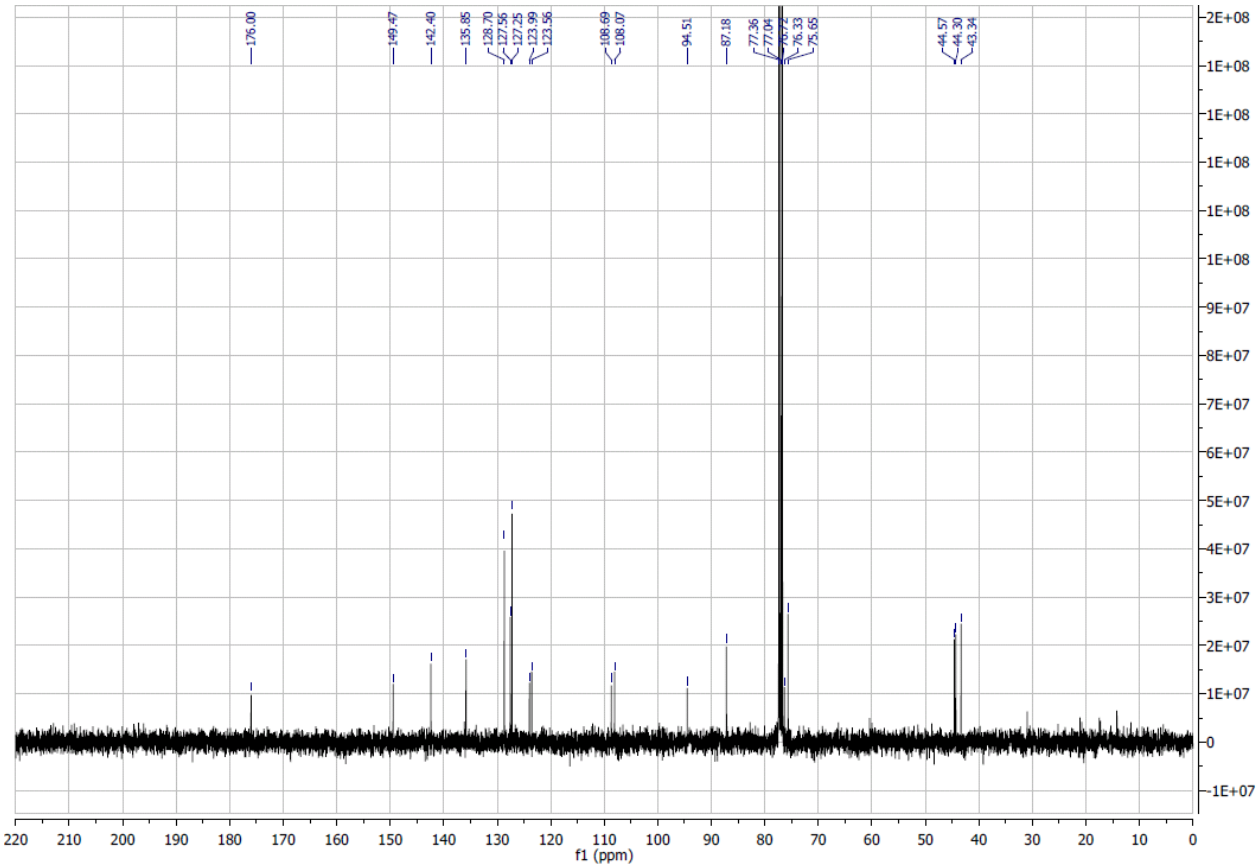

7.370
7.353
7.334
7.317
7.300
7.281
7.260
7.234
7.216
7.206
7.200
7.184
7.178
5.914
5.298
5.297
4.849
4.750
4.730
4.668
4.648
4.577
2.443
2.426
2.409
2.392
2.375
1.057
1.040
water
3.00
4.01
1.00
1.96
2.11
2.01
1.01
6.20
f1 (ppm)

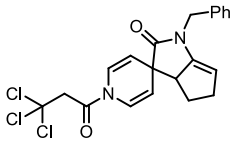

179.187
149.534
136.507
135.003
128.851
127.785
127.726
125.087
124.626
123.653
107.281
106.671
94.525
77.346
77.028
76.711
75.688
53.437
46.033
26.192
22.663
f1 (ppm)



8d

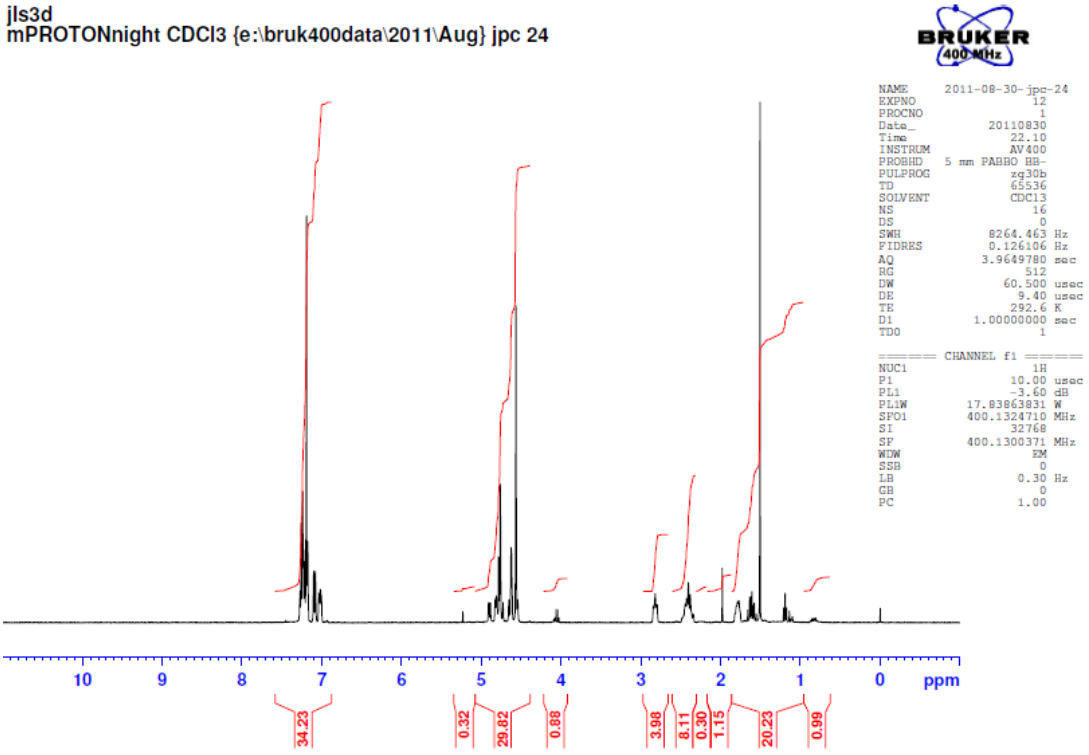




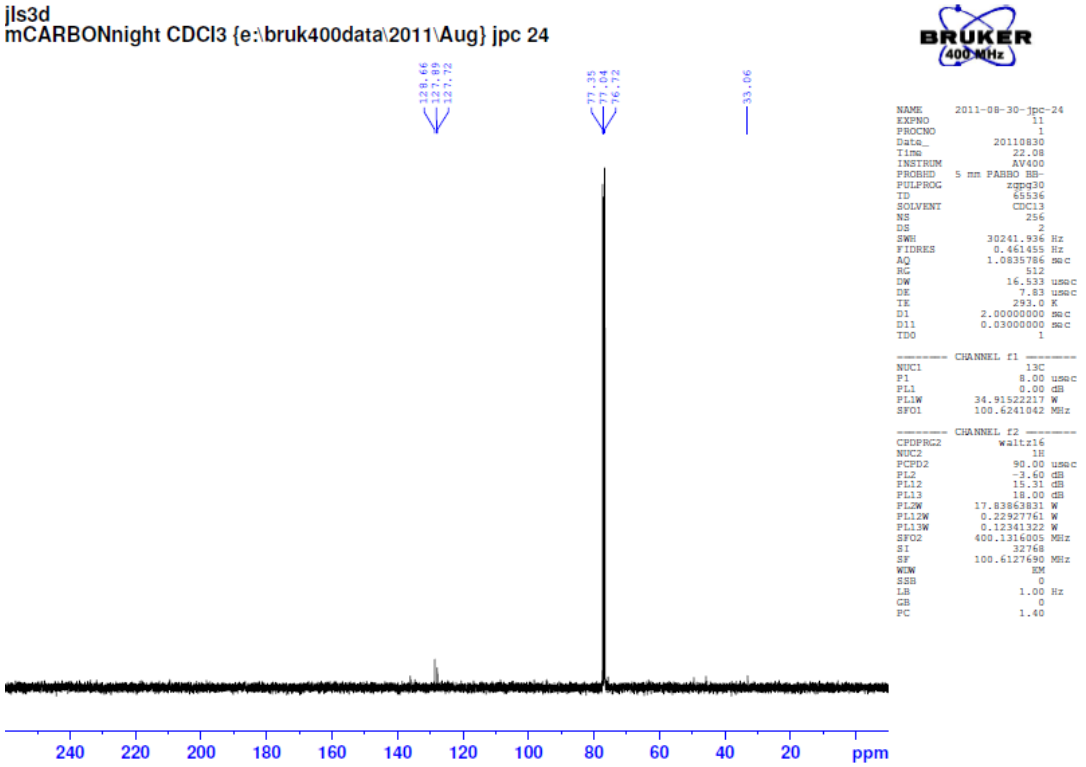


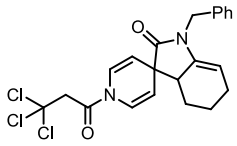
8e

jls3d
mPROTONnight CDCl3 {e:\bruk400data\2011\Aug} jpc 24

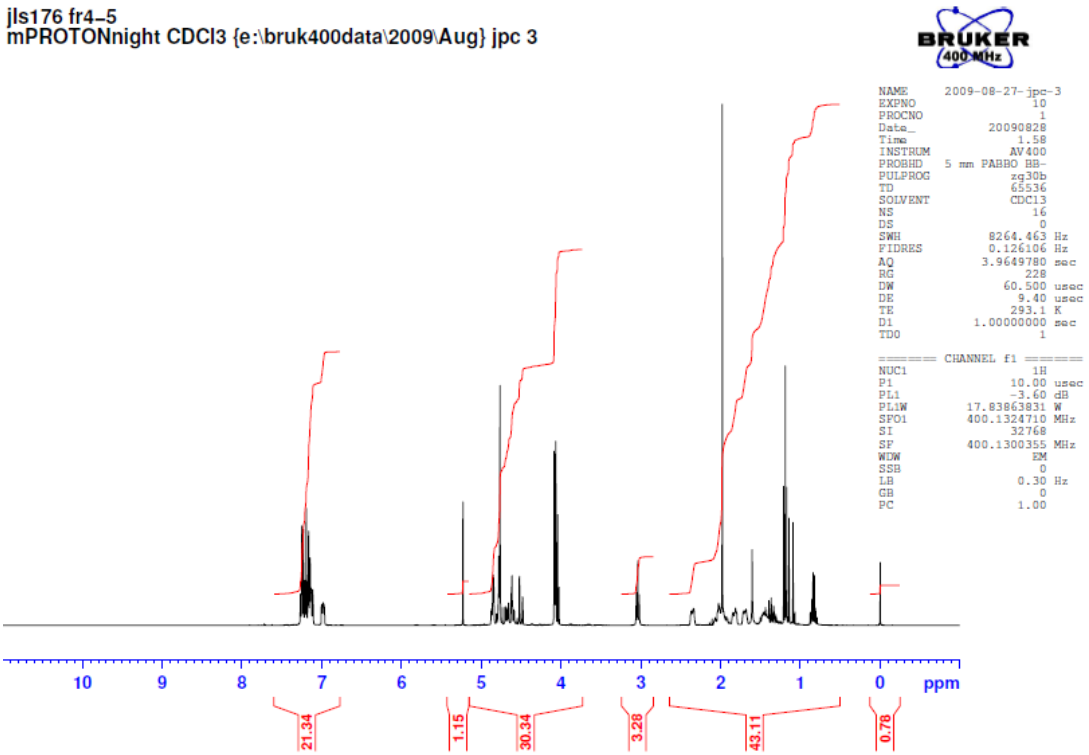


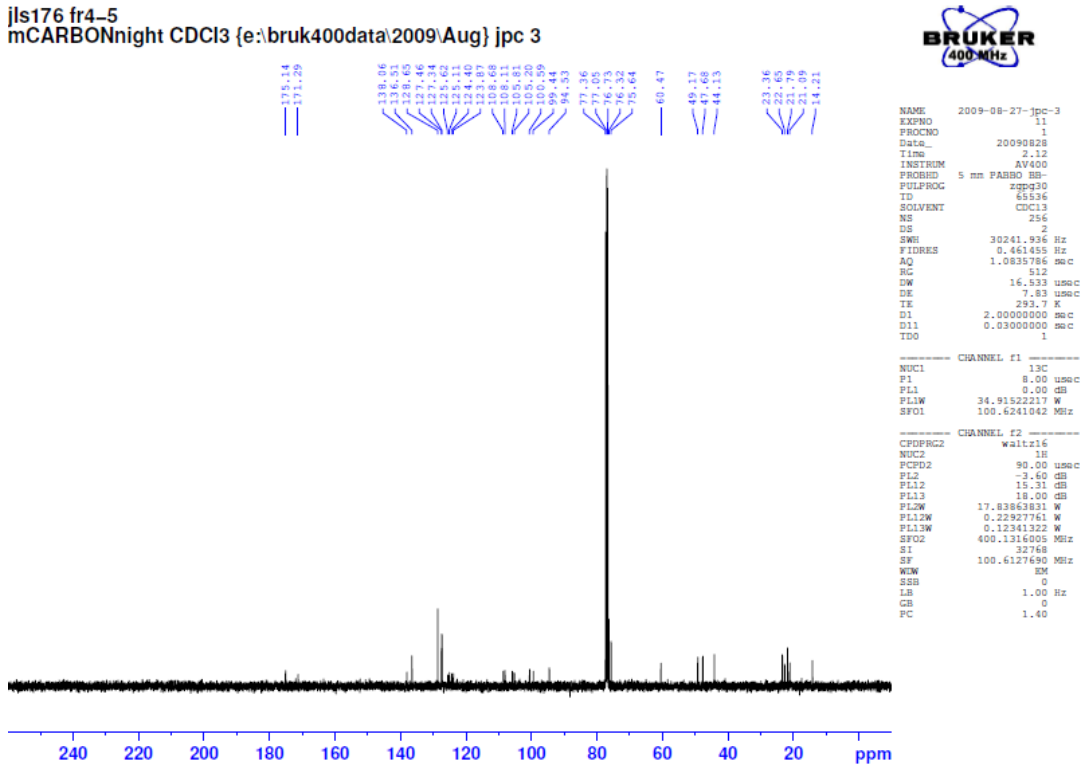
jls3d
mCARBONnight CDCl3 {e:\bruk400data\2011\Aug} jpc 24

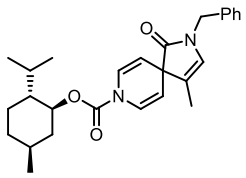



Ph
O
N
Cl
Cl
Cl
N
O

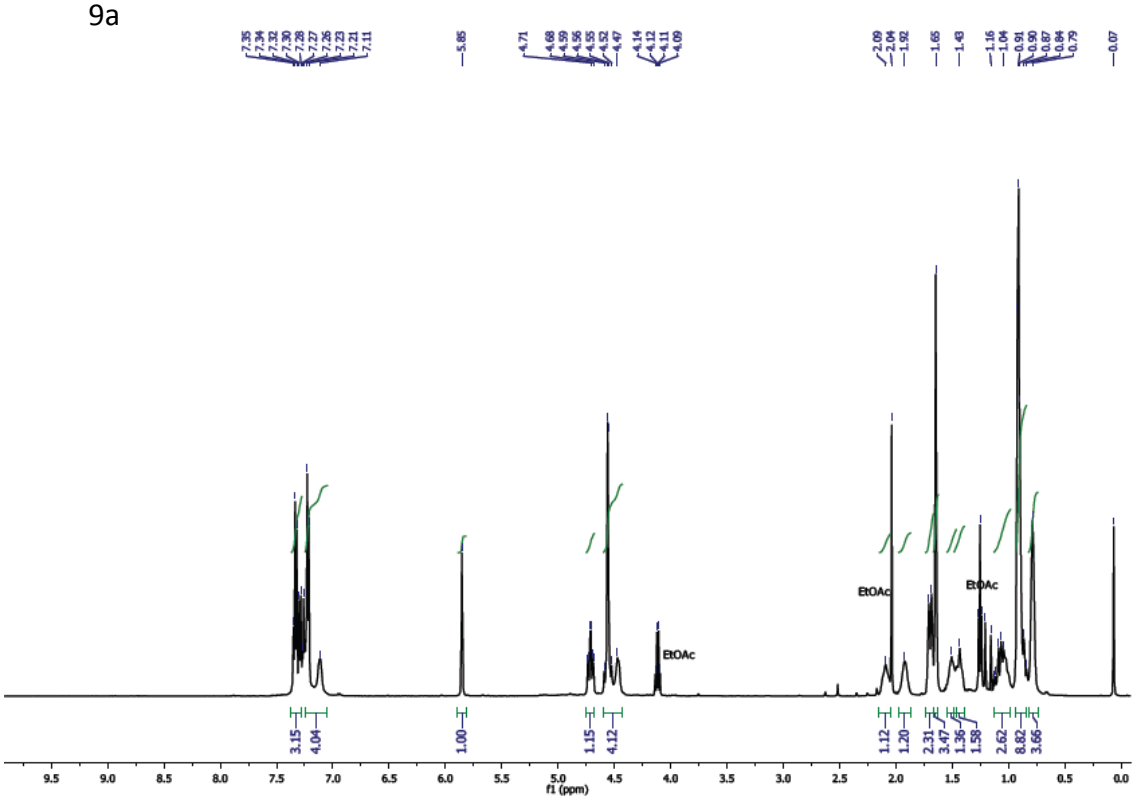
8f

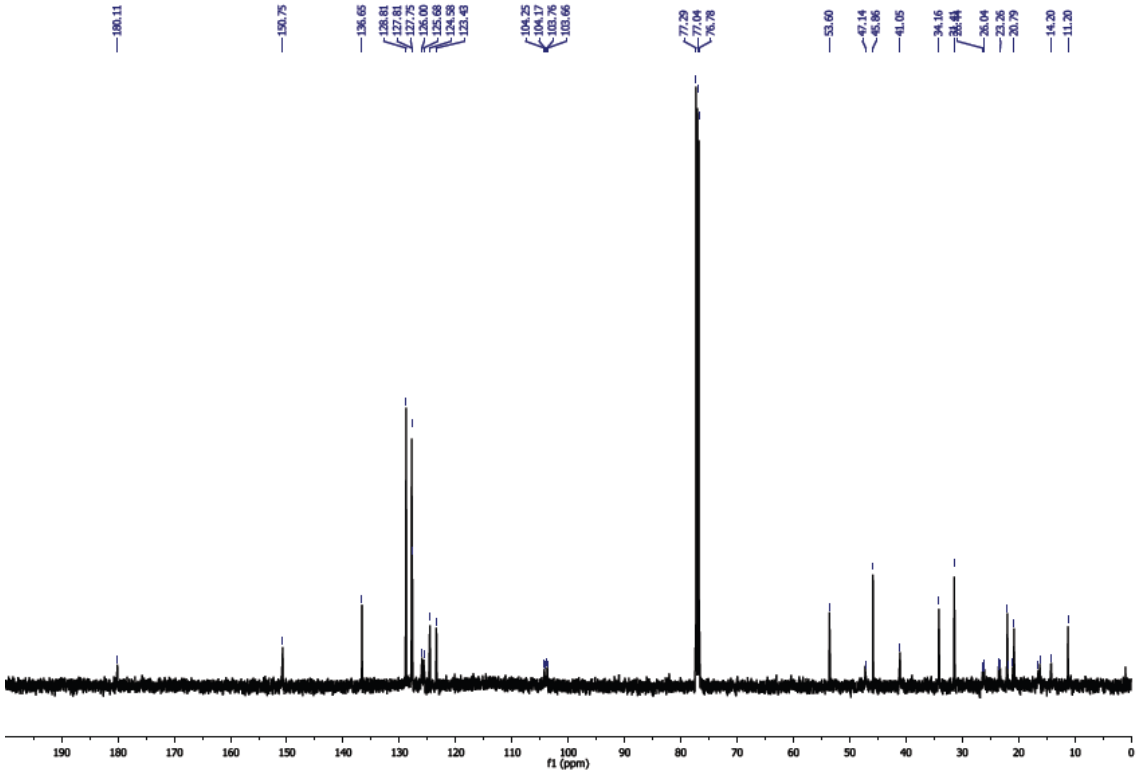

jls176 fr4–5
mPROTONnight CDCl3 {e:\bruk400data\2009\Aug} jpc 3
BRUKER
400 MHz
NAME 2009-08-27-jpc-3
EXPNO 10
PROCNO 1
Date_ 20090828
Time 1.58
INSTRUM AV400
PROBHD 5 mm PABBO BB-
PULPROG zg30b
TD 65536
SOLVENT CDCl3
NS 16
DS 0
SWH 8264.463 Hz
FIDRES 0.126106 Hz
AQ 3.9649780 sec
RG 228
DW 60.500 usec
DE 9.40 usec
TE 293.1 K
D1 1.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 10.00 usec
PL1 -3.60 dB
PL1W 17.83863831 W
SFO1 400.1324710 MHz
SI 32768
SF 400.1300355 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
10
9
8
7
6
5
4
3
2
1
0
ppm
21.34
1.15
30.34
3.28
43.11
0.78

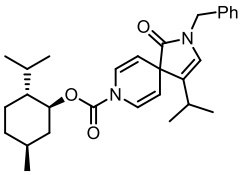

jls176 fr4–5
mCARBONnight CDCl3 {e:\bruk400data\2009\Aug} jpc 3
BRUKER
400 MHz
175.14
171.29
138.06
136.53
128.63
127.46
127.34
125.62
125.11
124.40
123.87
123.68
108.11
105.81
105.20
100.59
99.44
94.53
77.36
77.05
76.73
76.32
75.64
60.47
49.17
47.68
44.13
23.36
22.65
21.79
21.09
14.21
NAME 2009-08-27-jpc-3
EXPNO 11
PROCNO 1
Date_ 20090828
Time 2.12
INSTRUM AV400
PROBHD 5 mm PABBO BB-
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 256
DS 2
SWH 30241.936 Hz
FIDRES 0.461455 Hz
AQ 1.0835786 sec
RG 512
DW 16.533 usec
DE 7.83 usec
TE 293.7 K
D1 2.00000000 sec
D11 0.03000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 13C
P1 8.00 usec
PL1 0.00 dB
PL1W 34.91522217 W
SFO1 100.6241042 MHz
======== CHANNEL f2 ========
CPDPRG2 waltz16
NUC2 1H
PCPD2 90.00 usec
PL2 -3.60 dB
PL12 15.31 dB
PL13 18.00 dB
PL2W 17.83863831 W
PL12W 0.22927761 W
PL13W 0.12341322 W
SFO2 400.1316005 MHz
SI 32768
SF 100.6127690 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40
240
220
200
180
160
140
120
100
80
60
40
20
ppm



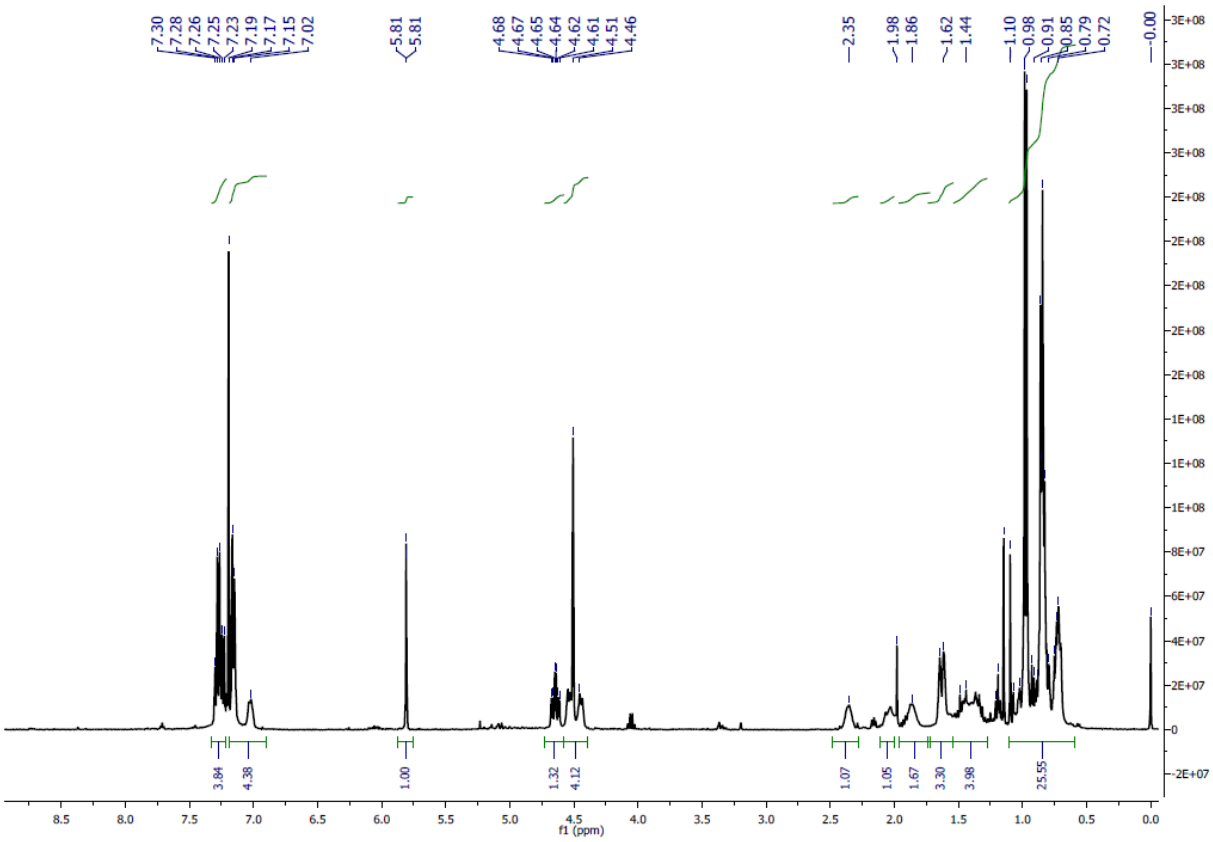
9a

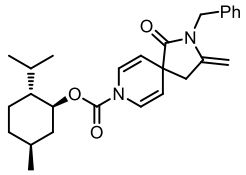




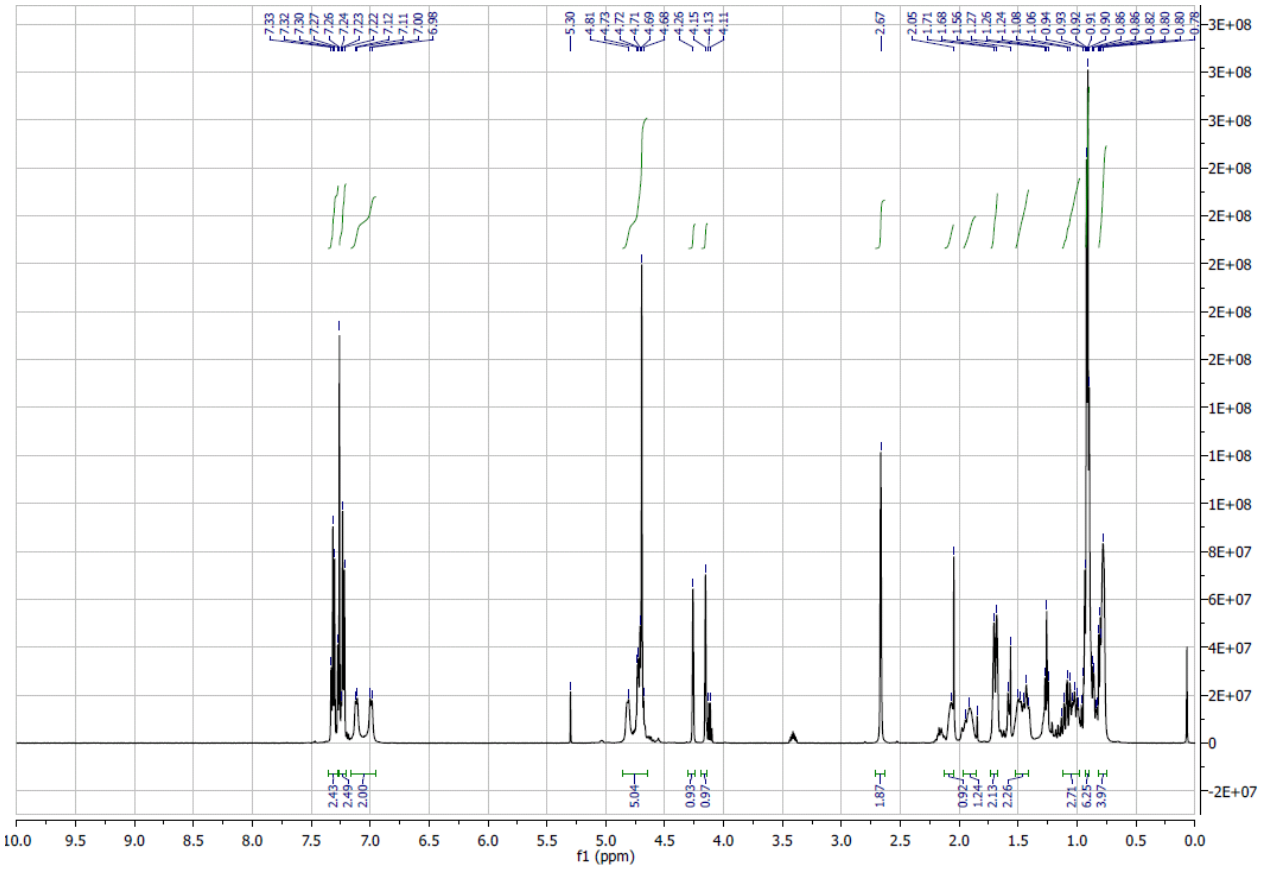

Ph
O
N
O
N
O
O

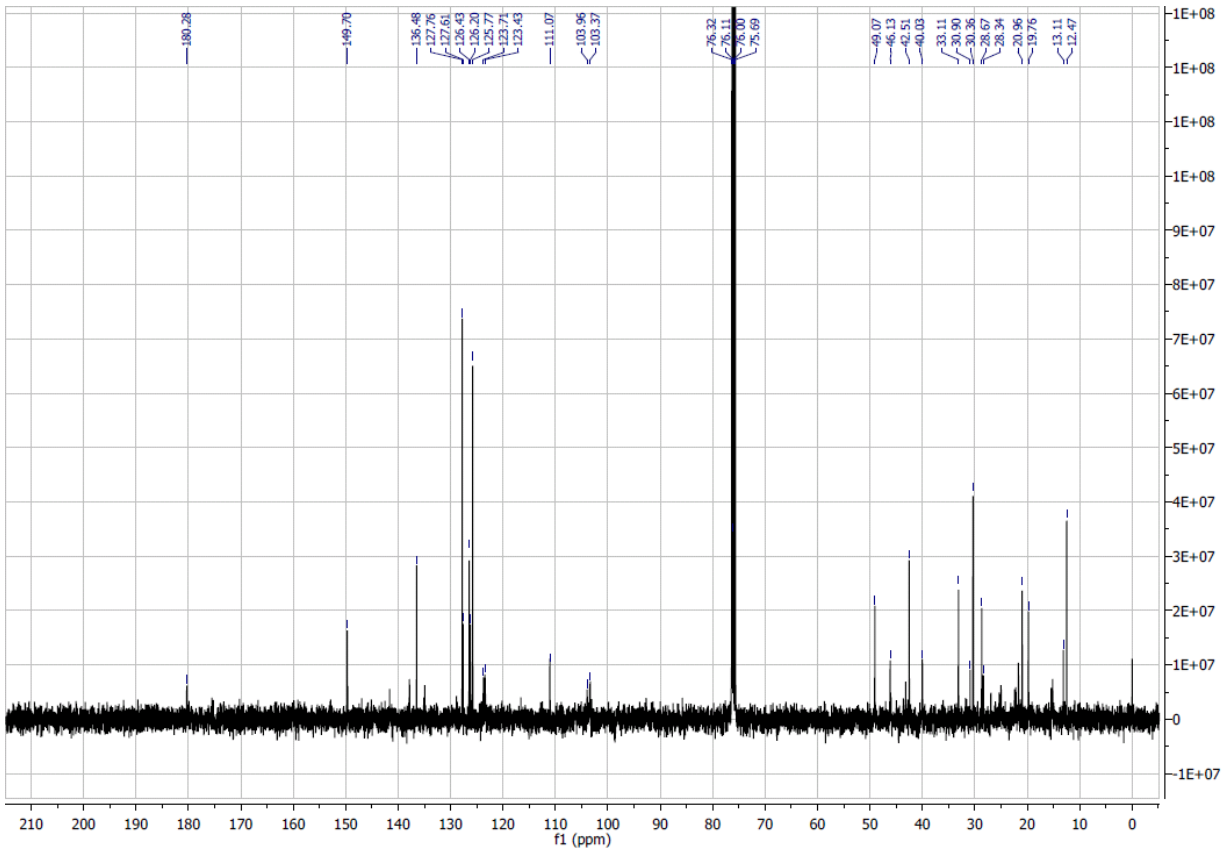
9b

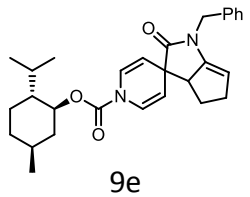

7.30
7.28
7.26
7.25
7.23
7.19
7.17
7.15
7.02
5.81
5.81
4.68
4.67
4.65
4.64
4.62
4.61
4.51
4.46
2.35
1.98
1.86
1.62
1.44
1.10
0.98
0.91
0.85
0.79
0.72
0.00
3.84
4.38
1.00
1.32
4.12
1.07
1.05
1.67
3.30
3.98
25.55
f1 (ppm)


Ph
O
N
O
N
O

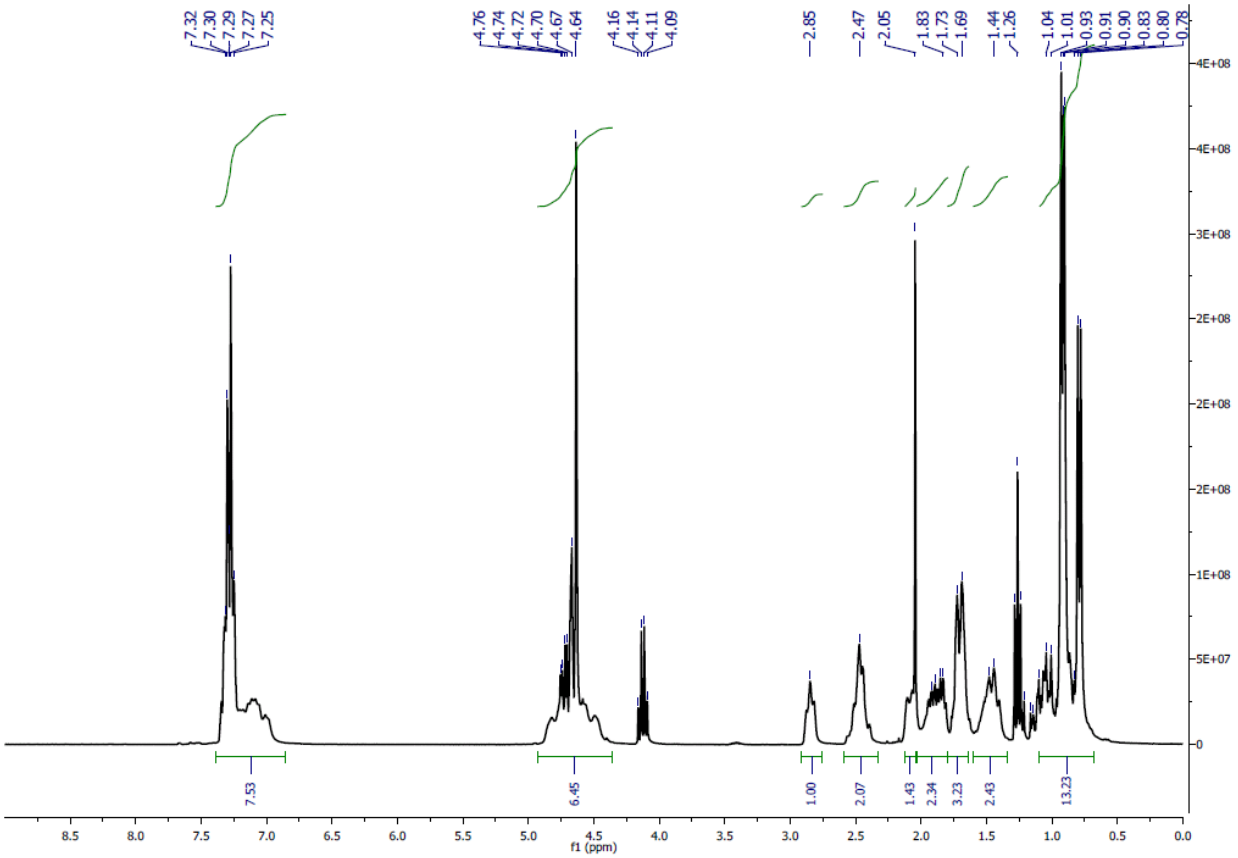
9d

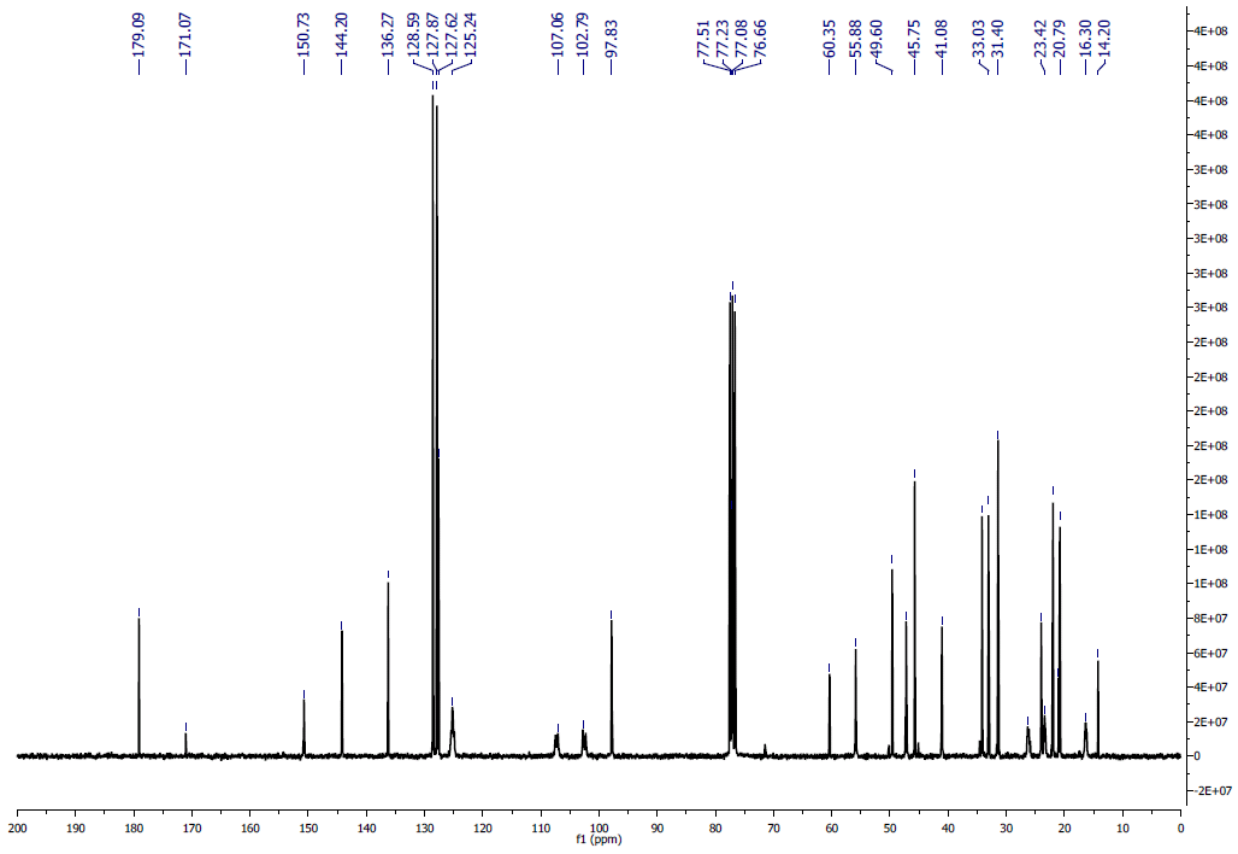

7.33
7.32
7.30
7.27
7.26
7.24
7.23
7.22
7.12
7.11
7.00
6.98
5.30
4.81
4.73
4.72
4.71
4.69
4.68
4.26
4.15
4.13
4.11
2.67
2.05
1.71
1.68
1.56
1.27
1.26
1.24
1.08
1.06
0.94
0.93
0.92
0.91
0.90
0.86
0.86
0.82
0.80
0.80
0.78
2.43
2.49
2.00
5.04
0.93
0.97
1.87
0.92
1.24
2.13
2.26
2.71
6.25
3.97
f1 (ppm)

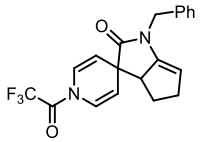

180.28
149.70
136.48
127.76
127.61
126.43
126.20
125.77
123.71
123.43
111.07
103.96
103.37
76.32
76.11
76.00
75.69
49.07
46.13
42.51
40.03
33.11
30.90
30.36
28.67
28.34
20.96
19.76
13.11
12.47
f1 (ppm)


Ph
O
N
O
N
O
O

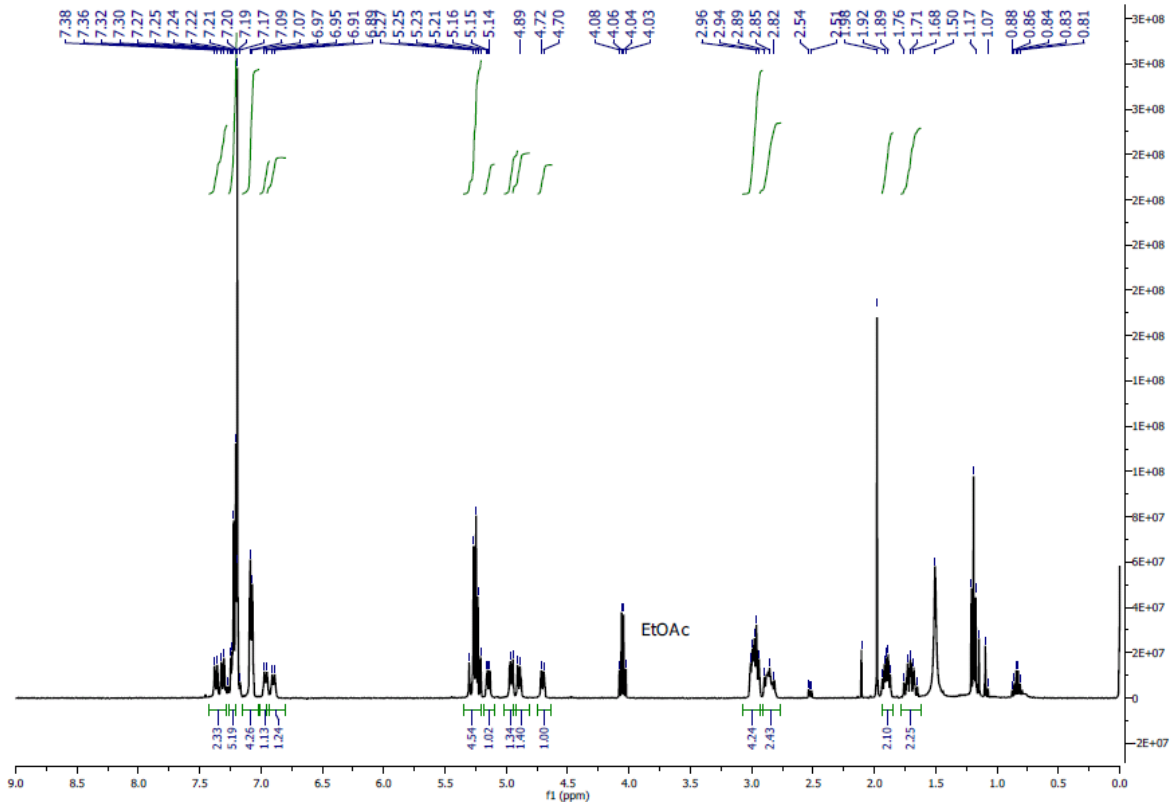
9e

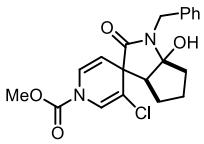

7.32
7.30
7.29
7.27
7.25
4.76
4.74
4.72
4.70
4.67
4.64
4.16
4.14
4.11
4.09
2.85
2.47
2.05
1.83
1.73
1.69
1.44
1.26
1.04
1.01
0.93
0.91
0.90
0.83
0.80
0.78
7.53
6.45
1.00
2.07
1.43
2.34
3.23
2.43
13.23
f1 (ppm)


179.09
171.07
150.73
144.20
136.27
128.59
127.87
127.62
125.24
107.06
102.79
97.83
77.51
77.23
77.08
76.66
60.35
55.88
49.60
45.75
41.08
33.03
31.40
23.42
20.79
16.30
14.20
f1 (ppm)

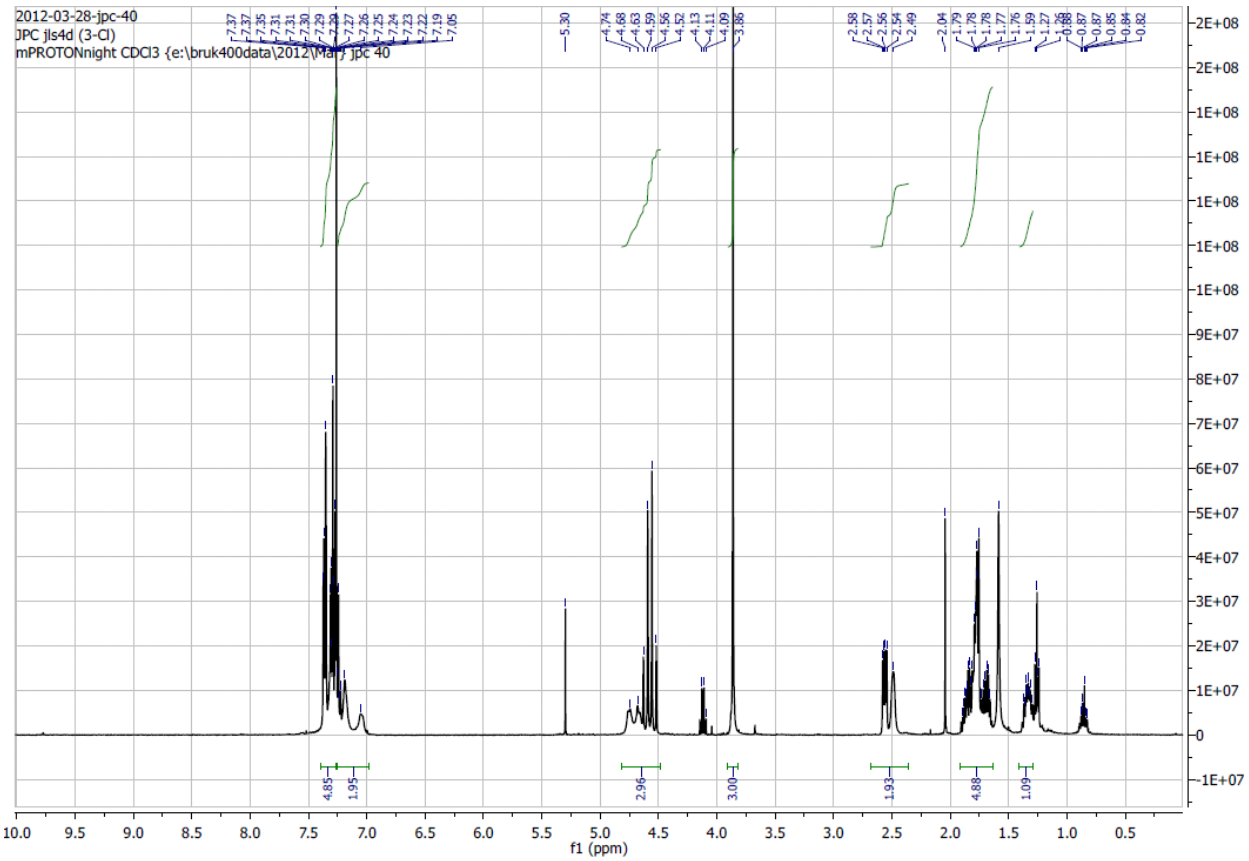


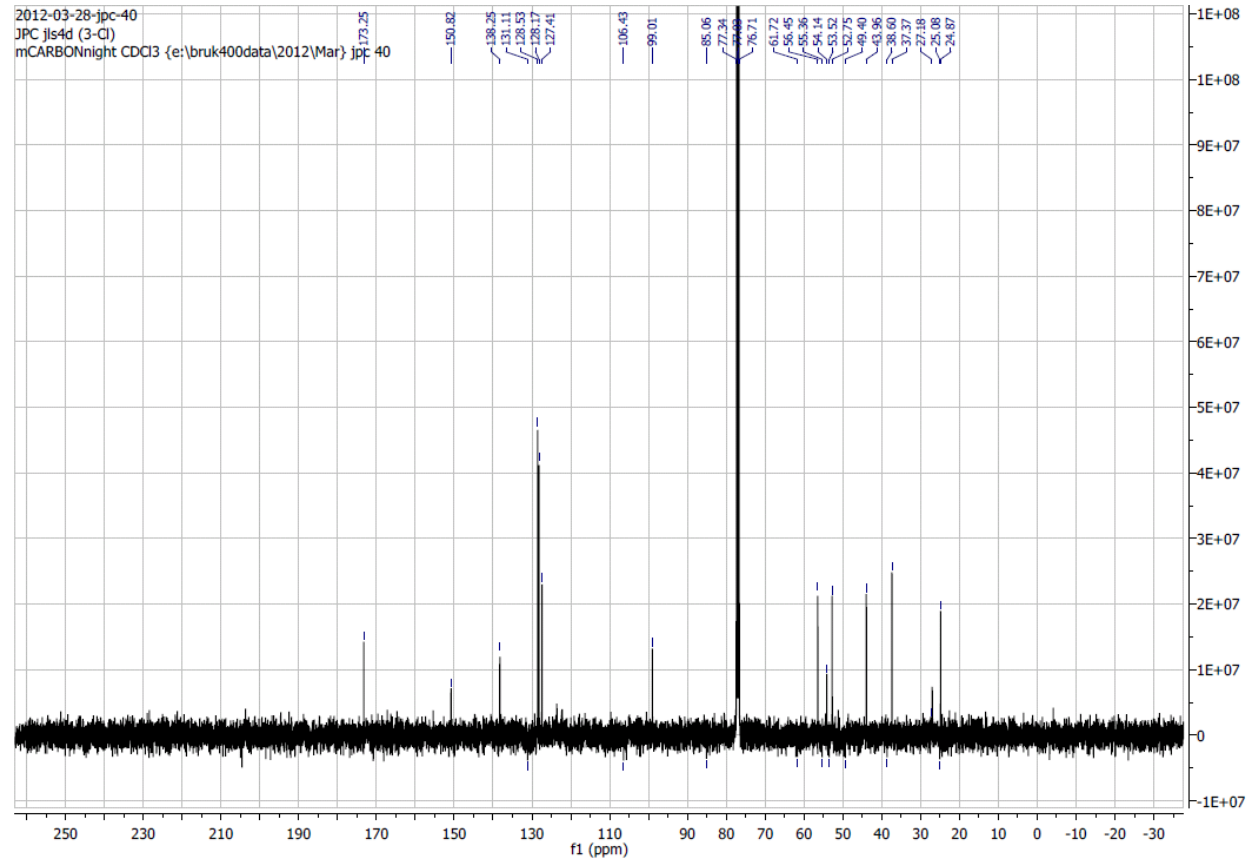
10e

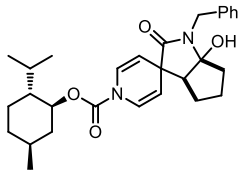



Ph
O
N
OH
MeO
N
Cl
O

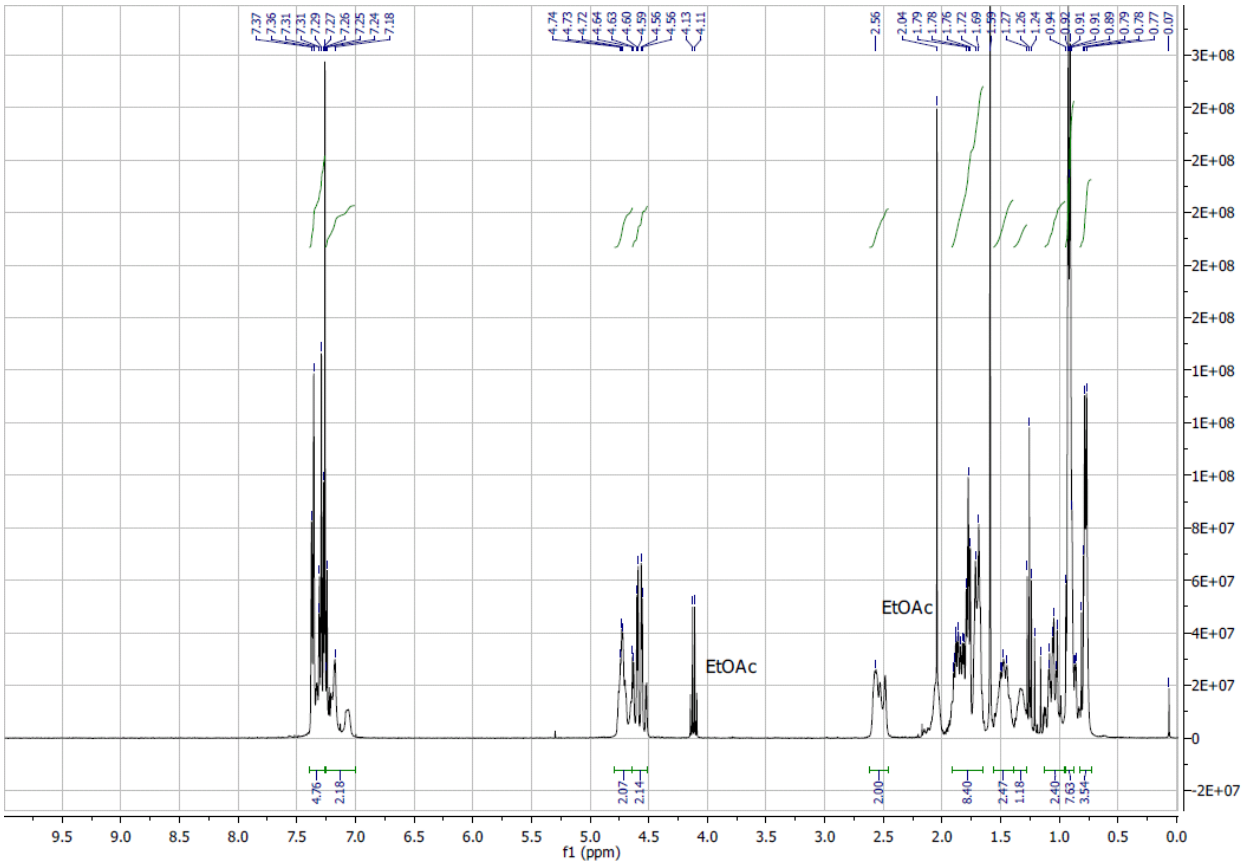
11i

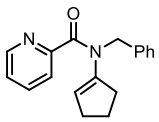

2012-03-28-jpc-40
JPC jls4d (3-Cl)
mPROTONnight CDCl3 {e:\bruk400data\2012\Mar} jpc 40
f1 (ppm)


2012-03-28-jpc-40
JPC jls4d (3-Cl)
mCARBONnight CDCl3 {e:\bruk400data\2012\Mar} jpc 40
f1 (ppm)



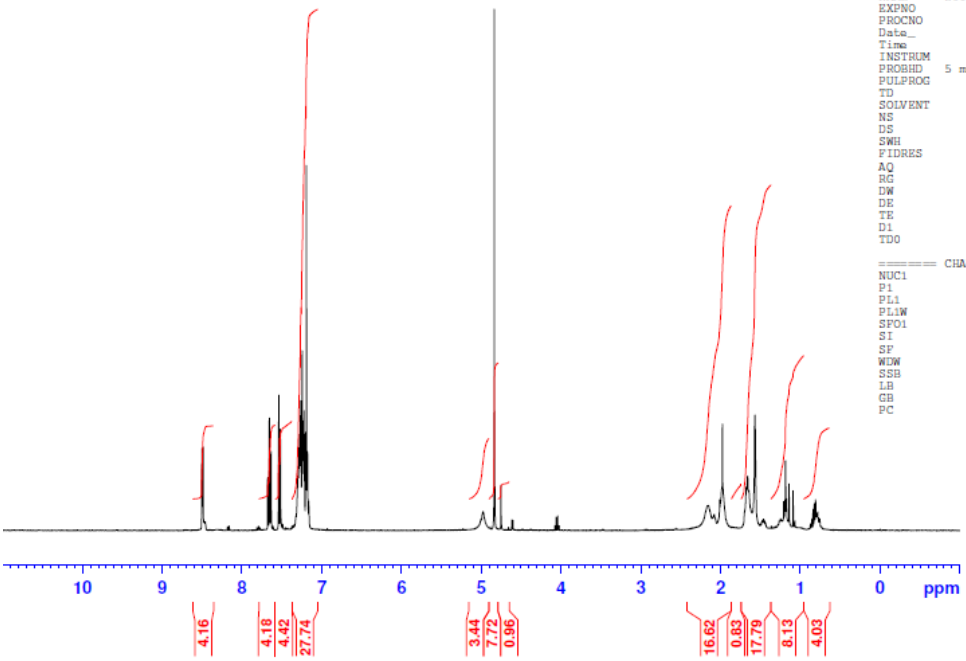
12i





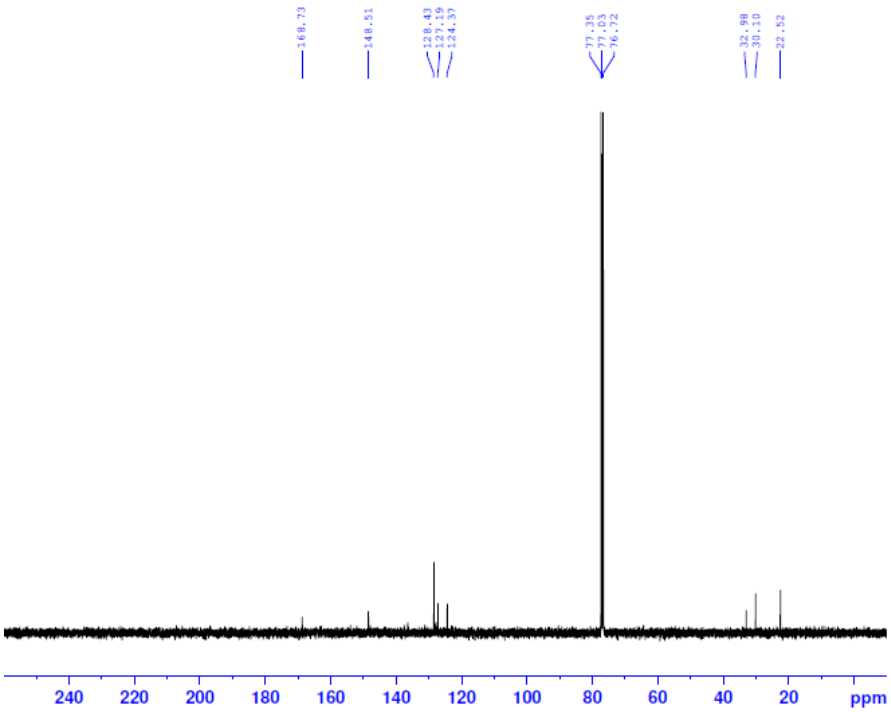
13

jls198
mPROTON CDCl3 {e:\bruk400data\2009\Oct} jpc 36

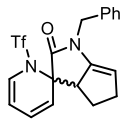



```
NAME          2009-10-20-jpc-36
EXPNO                       10
PROCNO                       1
Date_                 20091020
Time                     11.13
INSTRUM                  AV400
PROBHD   5 mm PABBO BB-
PULPROG                  zg30b
TD                       65536
SOLVENT                  CDCl3
NS                          16
DS                           0
SWH                   8264.463 Hz
FIDRES                0.126106 Hz
AQ                    3.9649780 sec
RG                         287
DW                      60.500 usec
DE                       9.40 usec
TE                      293.0 K
D1                    1.00000000 sec
TD0                          1

====== CHANNEL f1 ======
NUC1                        1H
P1                       10.00 usec
PL1                      -3.60 dB
PL1W                17.83863831 W
SFO1                400.1324710 MHz
SI                       32768
SF                  400.1300363 MHz
WDW                         EM
SSB                          0
LB                        0.30 Hz
GB                           0
PC                        1.00
```

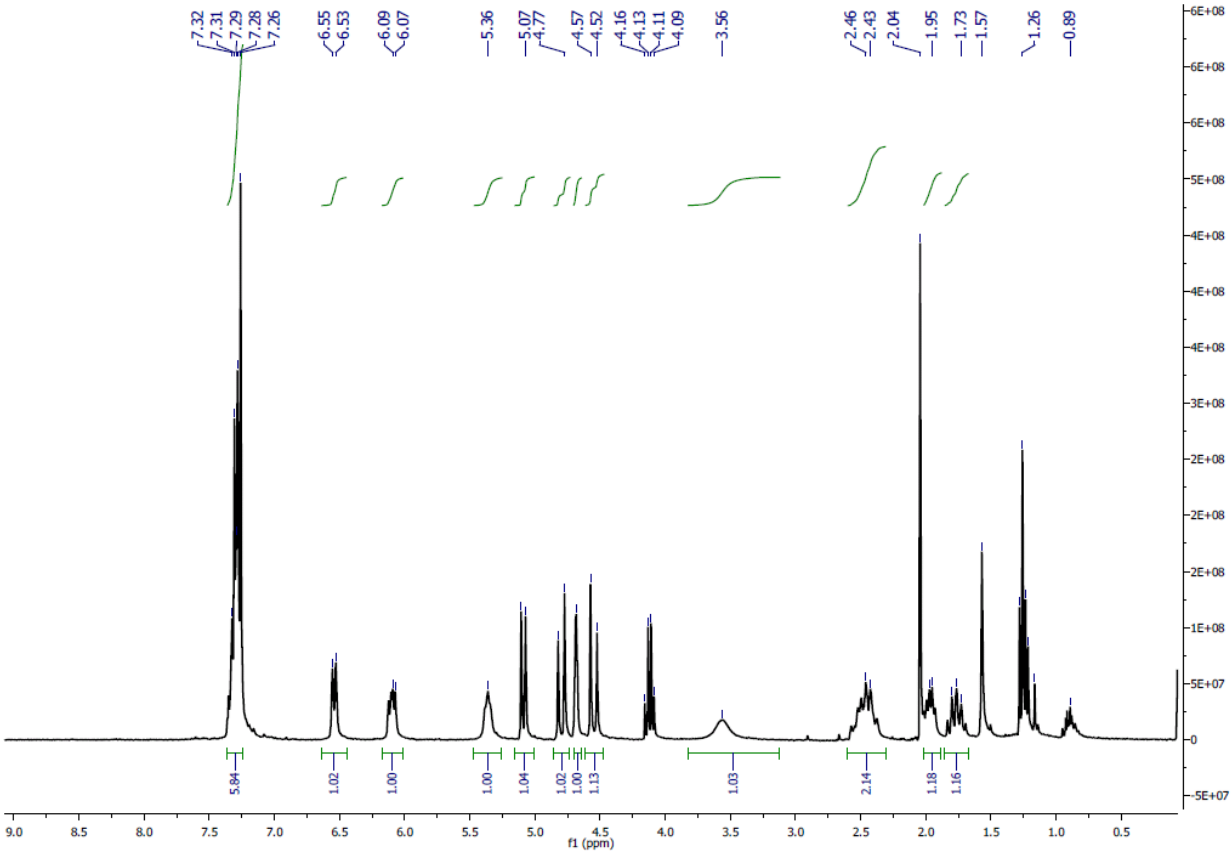
jls198
mCARBONnight CDCl3 {e:\bruk400data\2009\Oct} jpc 36

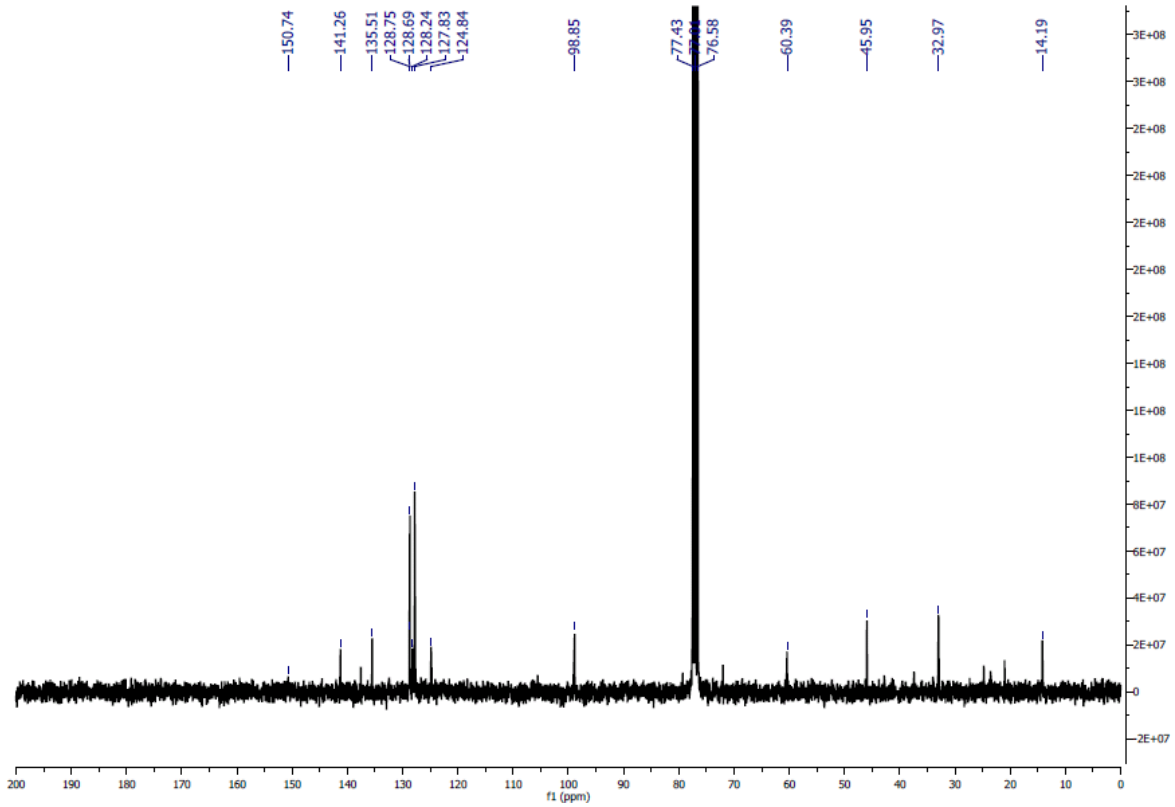


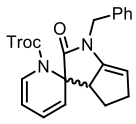

```
NAME          2009-10-20-jpc-36
EXPNO                       12
PROCNO                       1
Date_                 20091021
Time                      6.52
INSTRUM                  AV400
PROBHD   5 mm PABBO BB-
PULPROG                 zgpg30
TD                       65536
SOLVENT                  CDCl3
NS                         256
DS                           2
SWH                  30241.936 Hz
FIDRES                0.461455 Hz
AQ                    1.0835786 sec
RG                         512
DW                      16.533 usec
DE                       7.83 usec
TE                      294.6 K
D1                    2.00000000 sec
D11                   0.03000000 sec
TD0                          1

====== CHANNEL f1 ======
NUC1                       13C
P1                       8.00 usec
PL1                      0.00 dB
PL1W                34.91522217 W
SFO1                100.6241042 MHz

====== CHANNEL f2 ======
CPDPRG2                waltz16
NUC2                        1H
PCPD2                    90.00 usec
PL2                      -3.60 dB
PL12                     15.31 dB
PL13                     18.00 dB
PL2W                17.83863831 W
PL12W                0.22927761 W
PL13W                0.12341322 W
SFO2                400.1316005 MHz
SI                       32768
SF                  100.6127690 MHz
WDW                         EM
SSB                          0
LB                        1.00 Hz
GB                           0
PC                        1.40
```


Ph
Tf
O
N
N

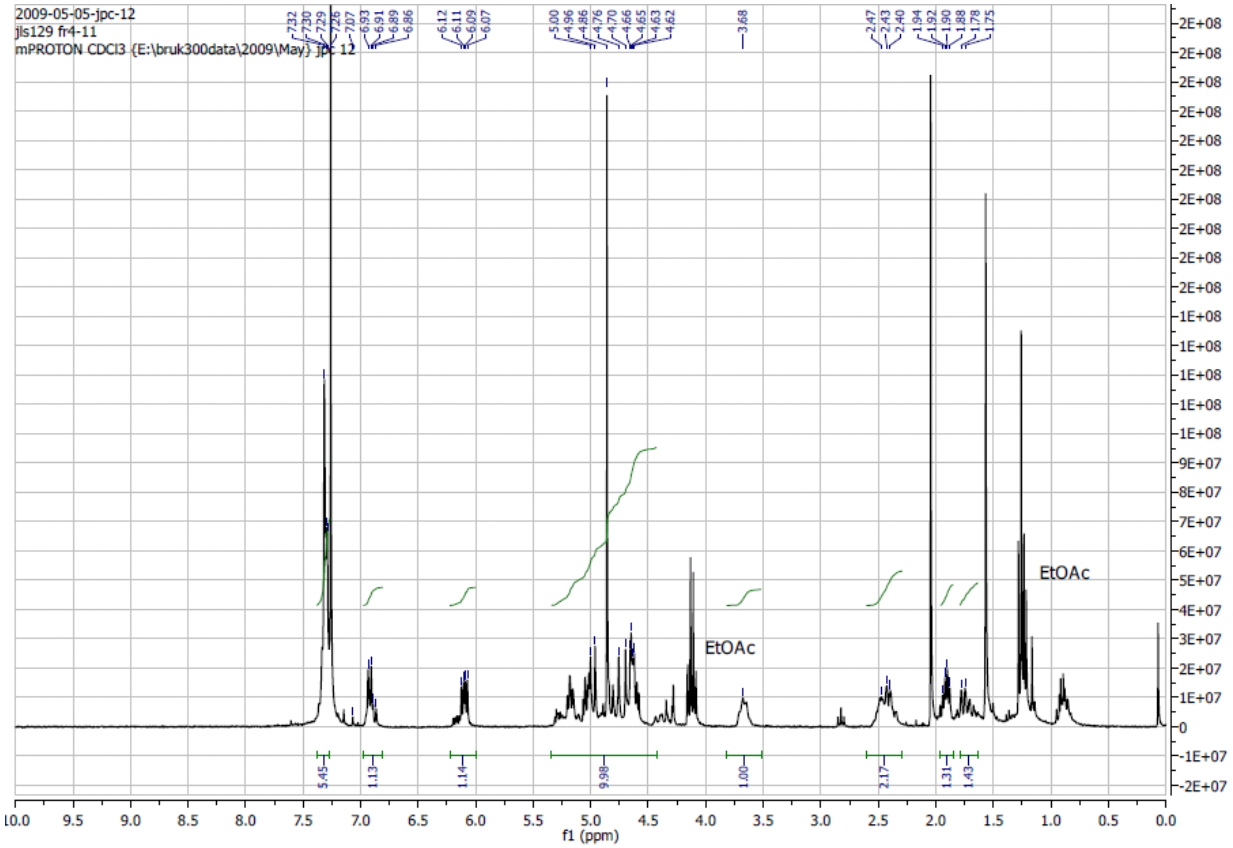
14a

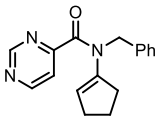

7.32
7.31
7.29
7.28
7.26
6.55
6.53
6.09
6.07
5.36
5.07
4.77
4.57
4.52
4.16
4.13
4.11
4.09
3.56
2.46
2.43
2.04
1.95
1.73
1.57
1.26
0.89
5.84
1.02
1.00
1.00
1.04
1.02
1.00
1.13
1.03
2.14
1.18
1.16
f1 (ppm)


150.74
141.26
135.51
128.75
128.69
128.24
127.83
124.84
98.85
77.43
76.58
60.39
45.95
32.97
14.19
f1 (ppm)


Troc
O
N
N
Ph

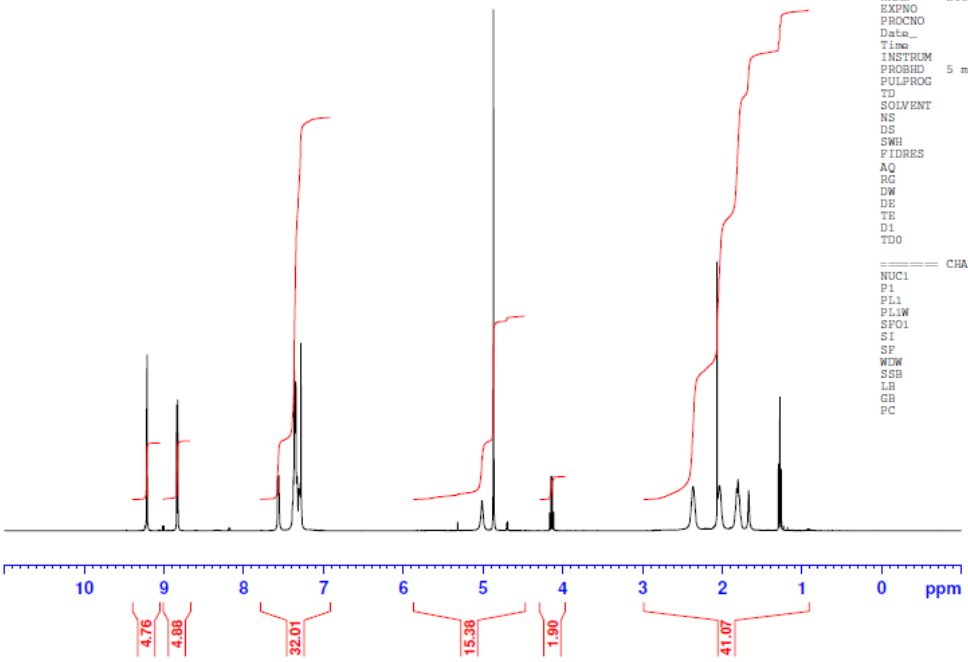
14b


2009-05-05-jpc-12
jls129 fr4-11
mPROTON CDCl3 {E:\bruk300data\2009\May} jpc 12
EtOAc
EtOAc
f1 (ppm)



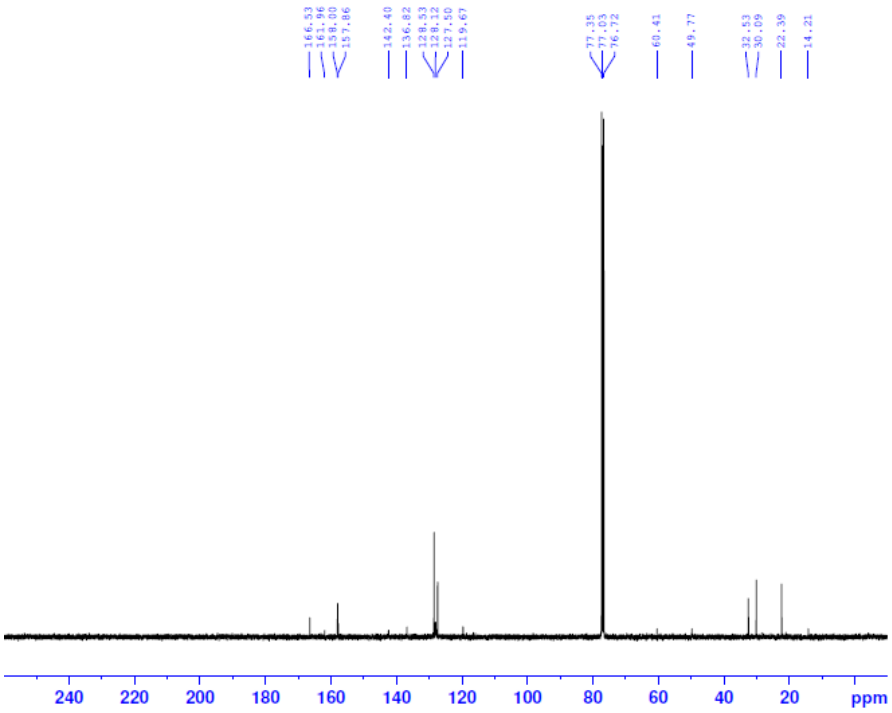
15

jpc–jls pyrimidine
mPROTONnight CDCl3 {e:\bruk400data\2012\Feb} jpc 31

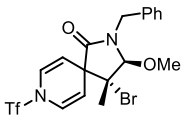



```
NAME          2012-02-21-jpc-31
EXPNO                       10
PROCNO                       1
Date_                 20120222
Time                      1.04
INSTRUM                 AV400
PROBHD   5 mm PABBO BB-
PULPROG                 zg30b
TD                        65536
SOLVENT                 CDCl3
NS                           32
DS                            0
SWH                  8264.463 Hz
FIDRES               0.126106 Hz
AQ                   3.9649780 sec
RG                          287
DW                     60.500 usec
DE                      9.40 usec
TE                     294.9 K
D1                  1.00000000 sec
TD0                          1

======== CHANNEL f1 ========
NUC1                        1H
P1                      10.00 usec
PL1                     -3.60 dB
PL1W                17.83863831 W
SFO1                400.1324710 MHz
SI                        32768
SF                  400.1300000 MHz
WDW                         EM
SSB                          0
LB                      0.30 Hz
GB                           0
PC                      1.00
```

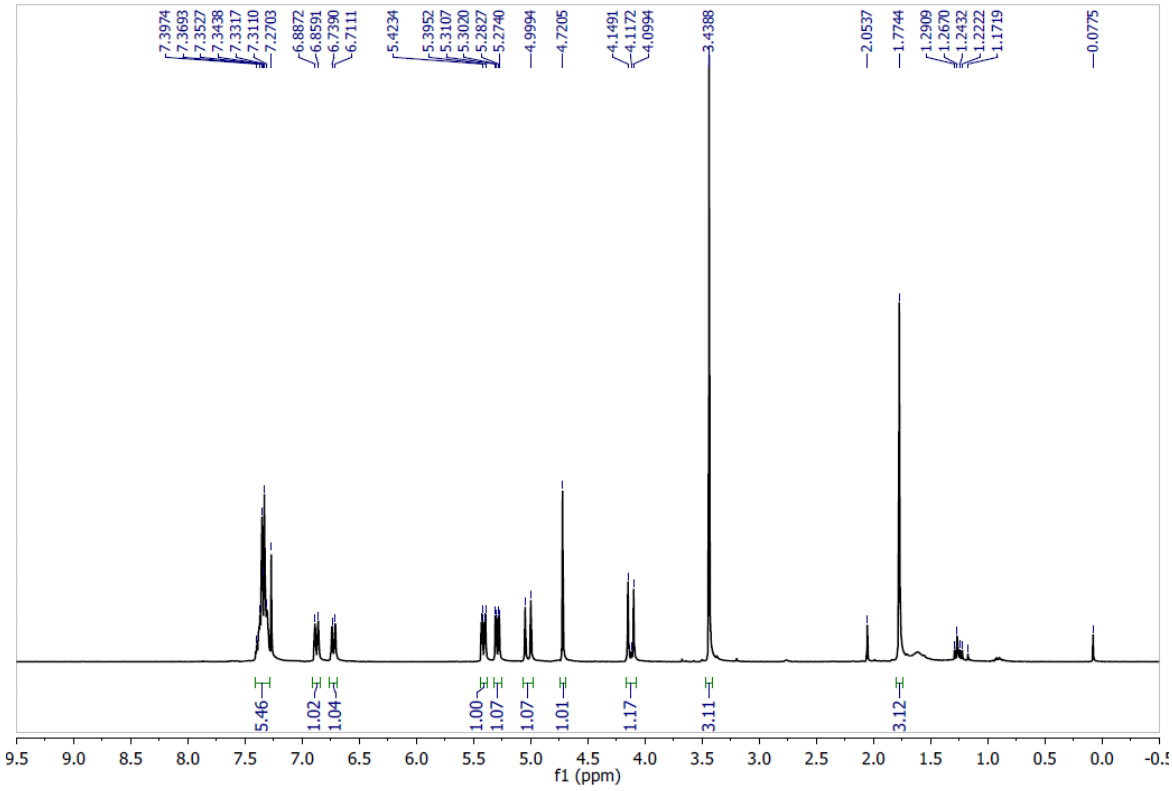
jpc–jls pyrimidine
mCARBONnight CDCl3 {e:\bruk400data\2012\Feb} jpc 31

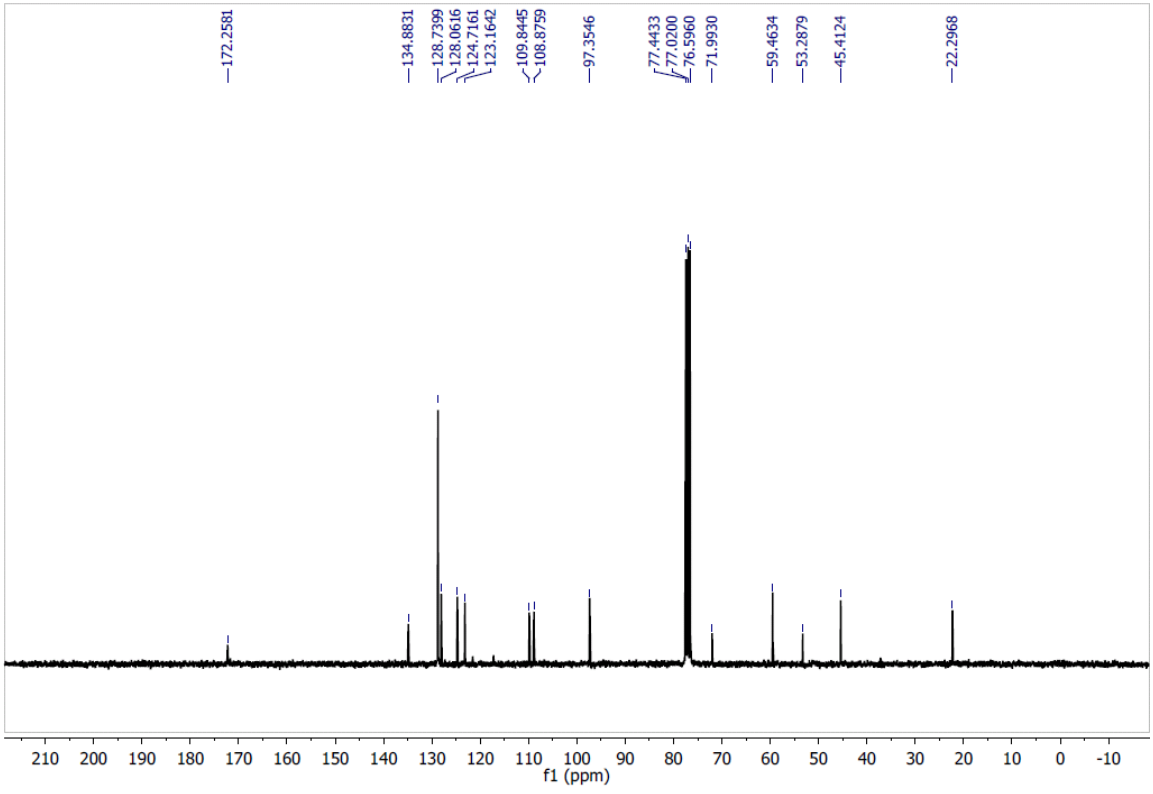


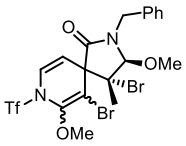

```
NAME          2012-02-21-jpc-31
EXPNO                       11
PROCNO                       1
Date_                 20120222
Time                      1.59
INSTRUM                 AV400
PROBHD   5 mm PABBO BB-
PULPROG                 zgpg30
TD                        65536
SOLVENT                 CDCl3
NS                         1024
DS                            2
SWH                 30241.936 Hz
FIDRES               0.461455 Hz
AQ                   1.0835786 sec
RG                          512
DW                     16.533 usec
DE                      7.83 usec
TE                     295.6 K
D1                  2.00000000 sec
D11                 0.03000000 sec
TD0                          1

======== CHANNEL f1 ========
NUC1                       13C
P1                      8.00 usec
PL1                     0.00 dB
PL1W                34.91522217 W
SFO1                100.6241042 MHz

======== CHANNEL f2 ========
CPDPRG2                waltz16
NUC2                        1H
PCPD2                   90.00 usec
PL2                     -3.60 dB
PL12                    15.31 dB
PL13                    18.00 dB
PL2W                17.83863831 W
PL12W                0.22927761 W
PL13W                0.12341322 W
SFO2                400.1316005 MHz
SI                        32768
SF                  100.6127690 MHz
WDW                         EM
SSB                          0
LB                      1.00 Hz
GB                           0
PC                      1.40
```


Ph
O
N
OMe
Tf
N
Br

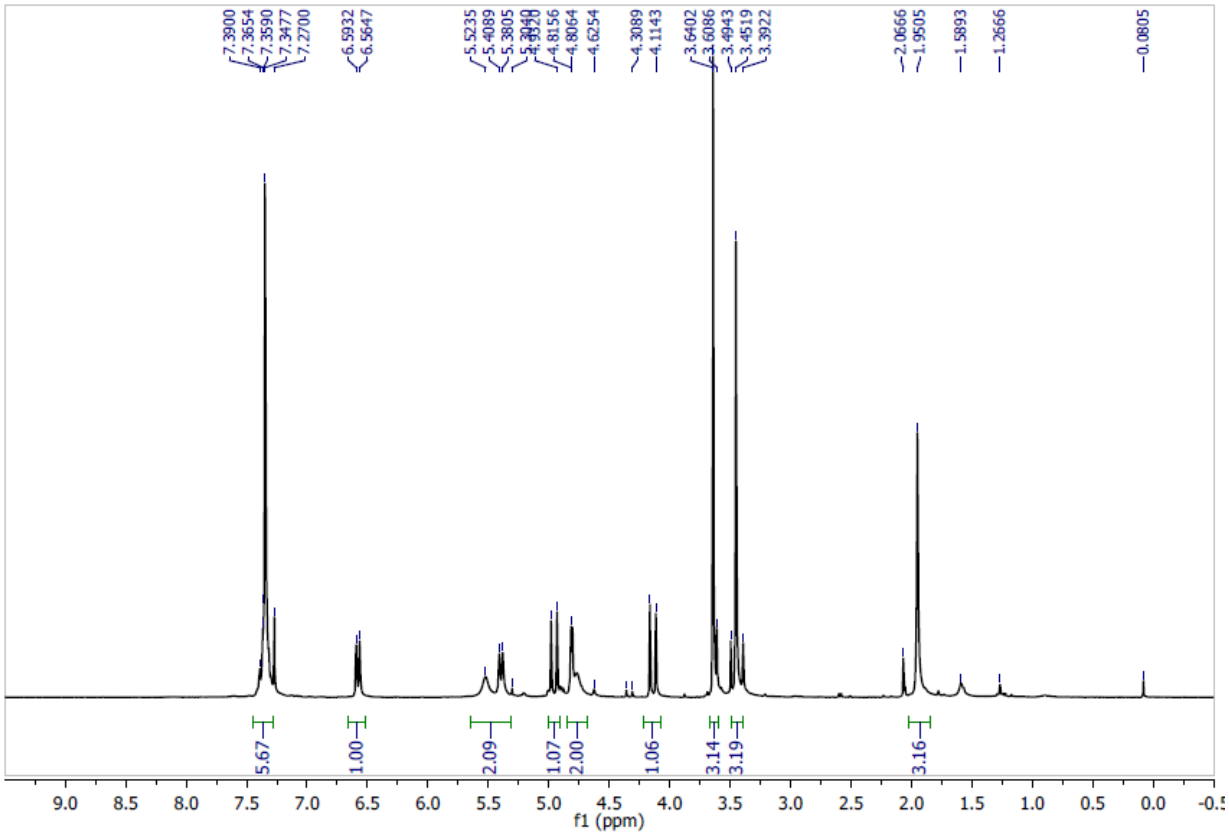
17

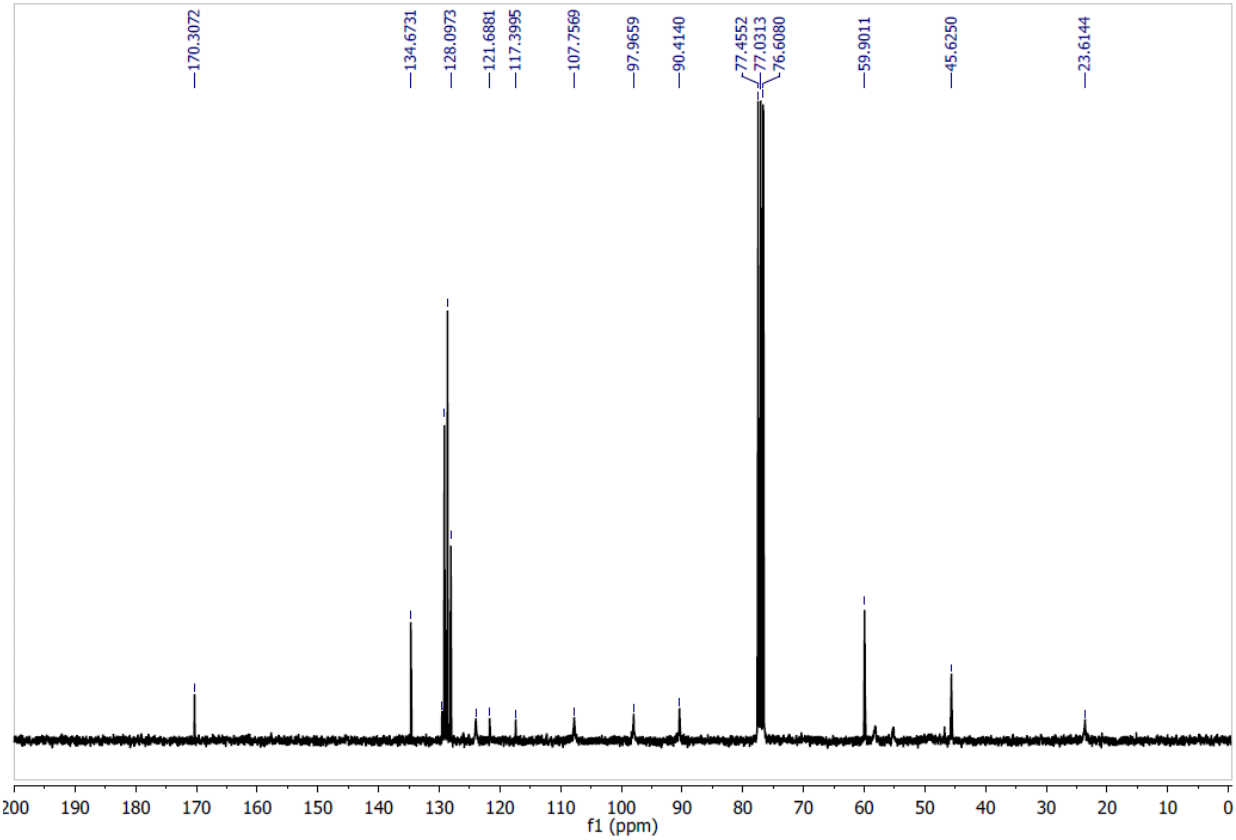

7.3974
7.3693
7.3527
7.3438
7.3317
7.3110
7.2703
6.8872
6.8591
6.7390
6.7111
5.4234
5.3952
5.3107
5.3020
5.2827
5.2740
4.9994
4.7205
4.1491
4.1172
4.0994
3.4388
2.0537
1.7744
1.2909
1.2670
1.2432
1.2222
1.1719
0.0775
5.46
1.02
1.04
1.00
1.07
1.07
1.01
1.17
3.11
3.12
f1 (ppm)

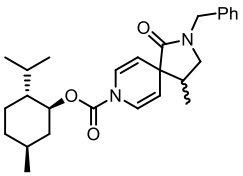

172.2581
134.8831
128.7399
128.0616
124.7161
123.1642
109.8445
108.8759
97.3546
77.4433
77.0200
76.5960
71.9930
59.4634
53.2879
45.4124
22.2968
f1 (ppm)


Ph
O
N
OMe
Br
Tf
N
Br
OMe

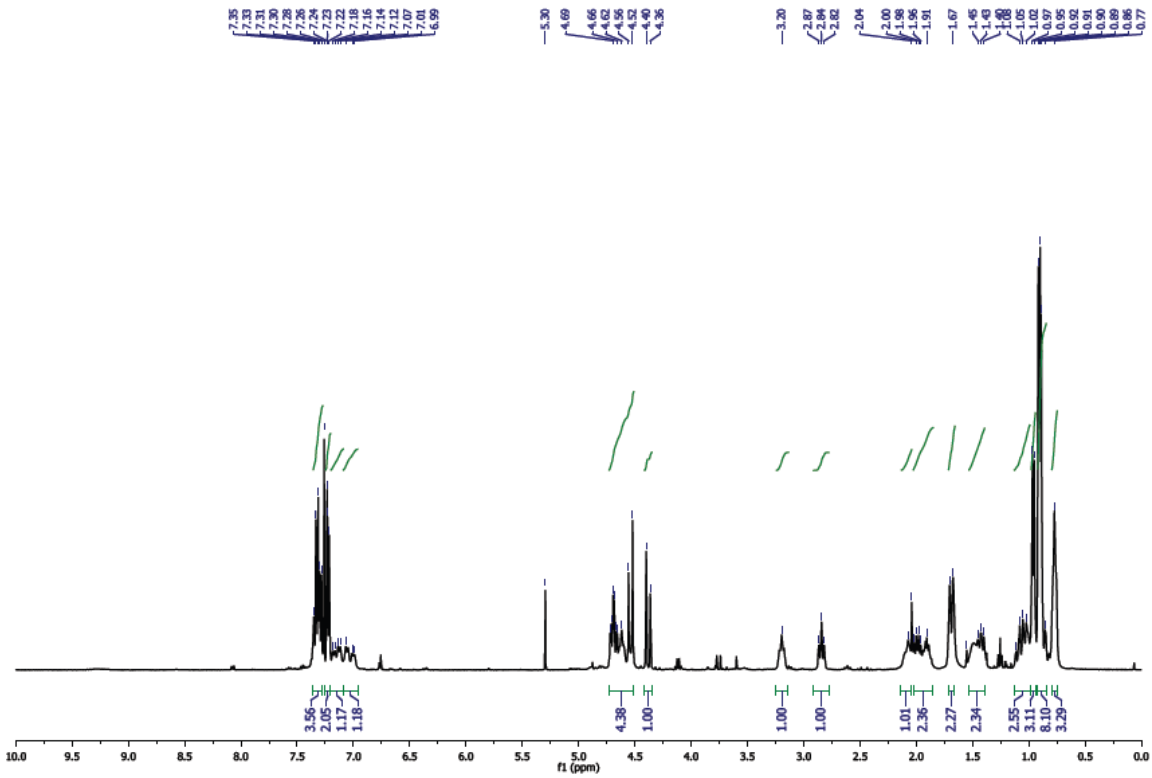
18

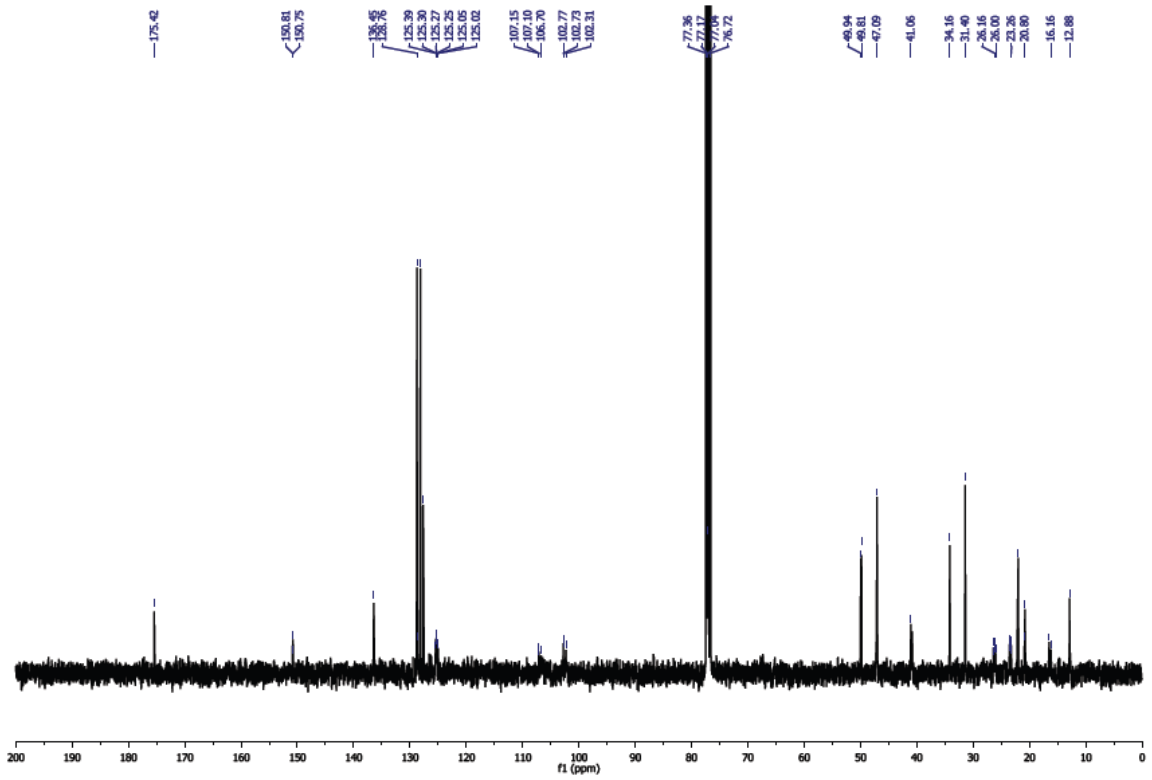

7.3900
7.3654
7.3590
7.3477
7.2700
6.5932
6.5647
5.5235
5.4089
5.3805
4.8156
4.8064
4.6254
4.3089
4.1143
3.6402
3.6086
3.4943
3.4519
3.3922
2.0666
1.9505
1.5893
1.2666
0.0805
5.67
1.00
2.09
1.07
2.00
1.06
3.14
3.19
3.16
f1 (ppm)

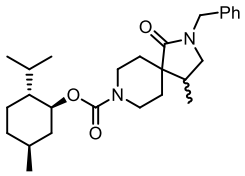

170.3072
134.6731
128.0973
121.6881
117.3995
107.7569
97.9659
90.4140
77.4552
77.0313
76.6080
59.9011
45.6250
23.6144
f1 (ppm)



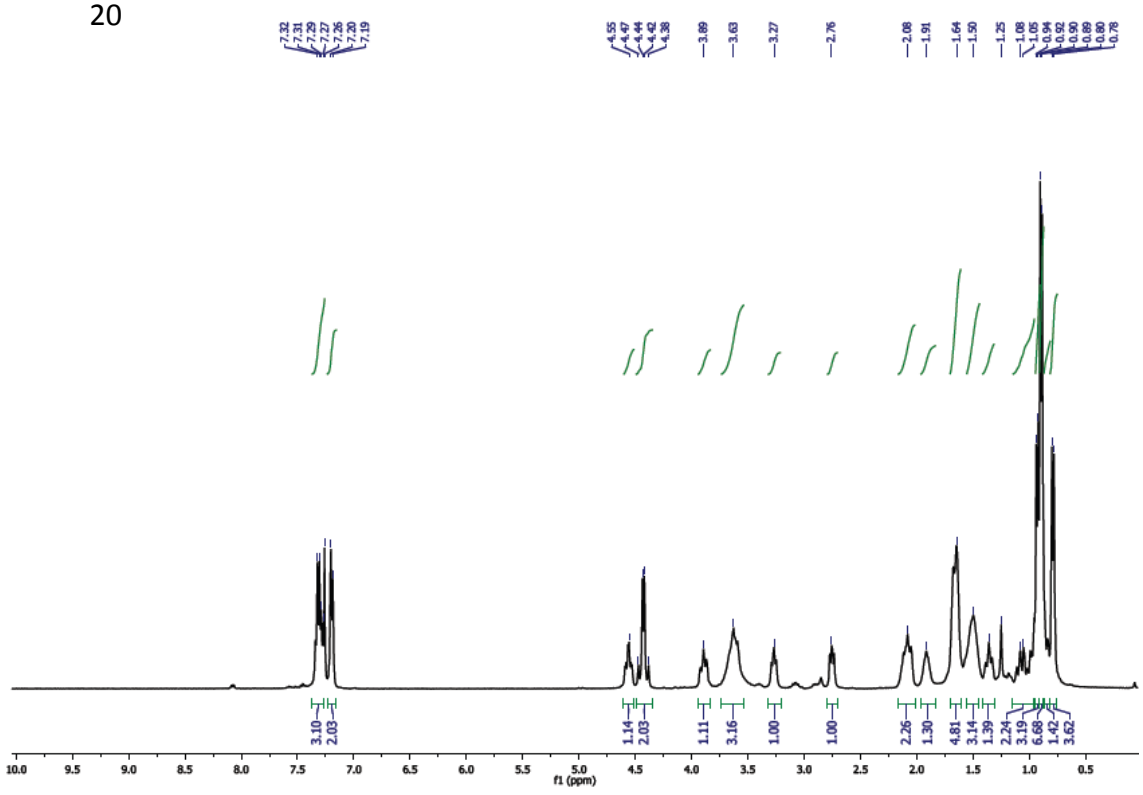
19

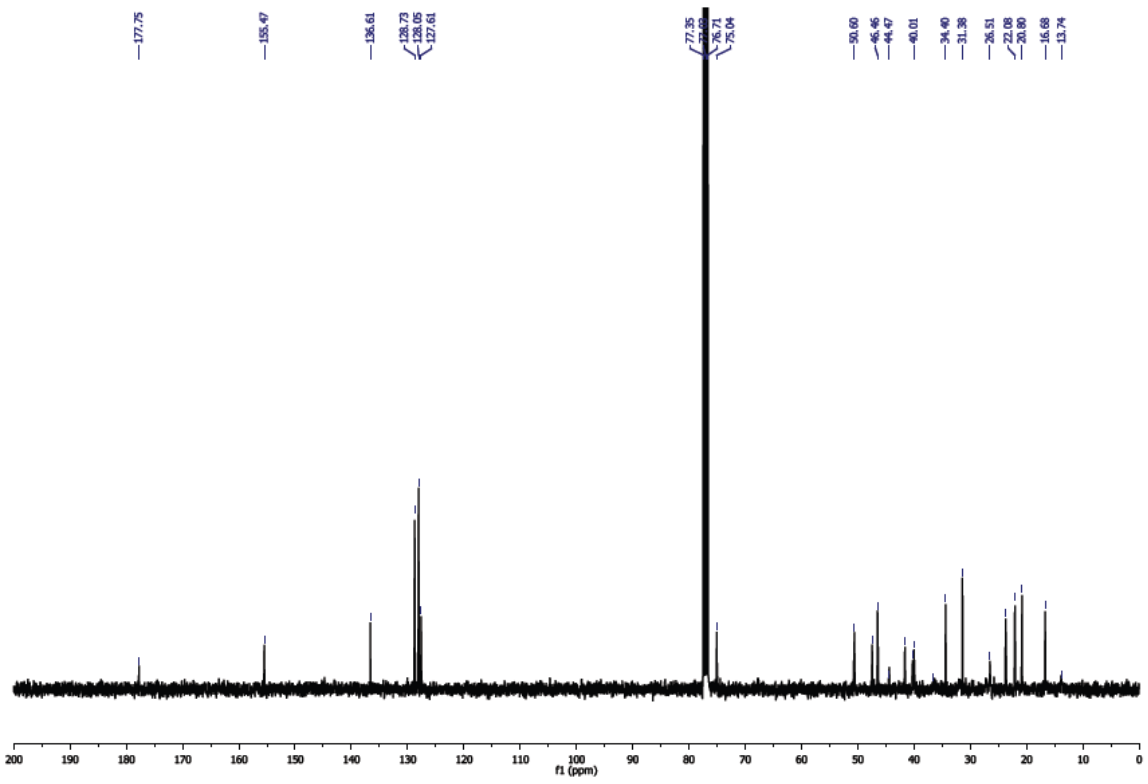


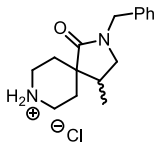



Ph
O
N
O
N
O
O

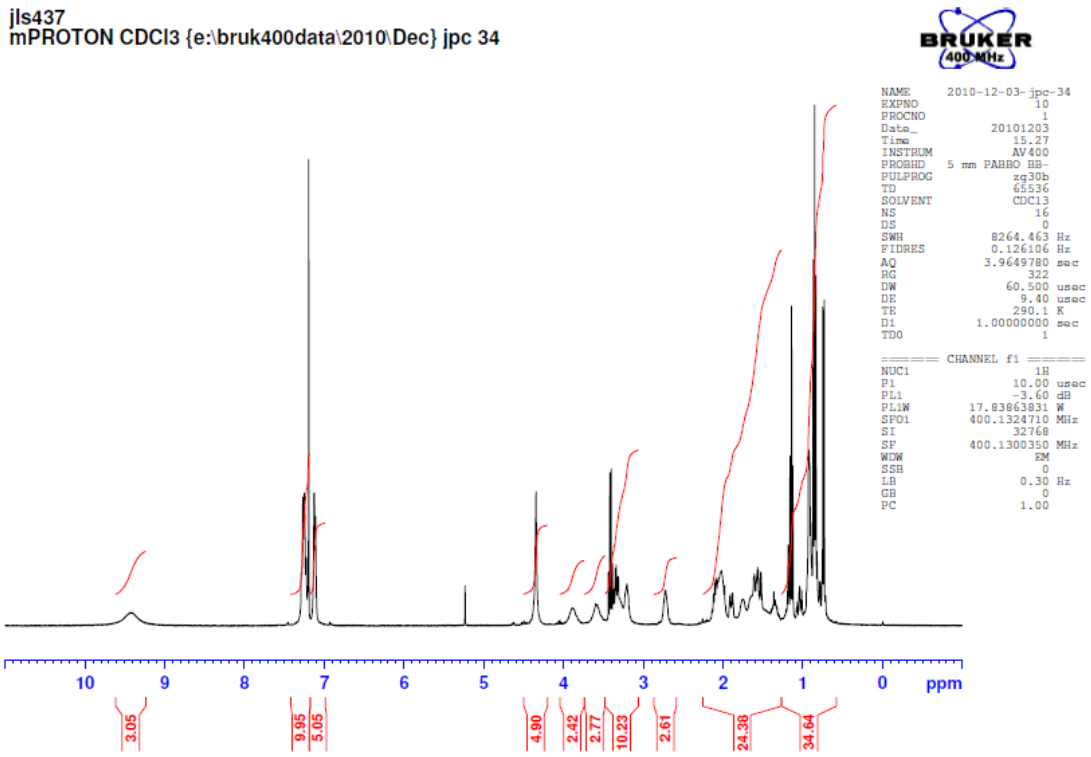
20

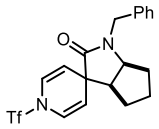

7.32
7.31
7.29
7.27
7.26
7.20
7.19
4.55
4.47
4.44
4.42
4.38
3.89
3.63
3.27
2.76
2.08
1.91
1.64
1.50
1.25
1.08
1.05
0.94
0.92
0.90
0.89
0.80
0.78
3.10
2.03
1.14
2.03
1.11
3.16
1.00
1.00
2.26
1.30
4.81
3.14
1.39
2.24
3.19
6.68
1.42
3.62
f1 (ppm)


177.75
155.47
136.61
128.73
128.05
127.61
77.35
77.03
76.71
75.04
50.60
46.46
44.47
40.01
34.40
31.38
26.51
22.08
20.80
16.68
13.74
f1 (ppm)


Ph
O
N
H_2N
Cl

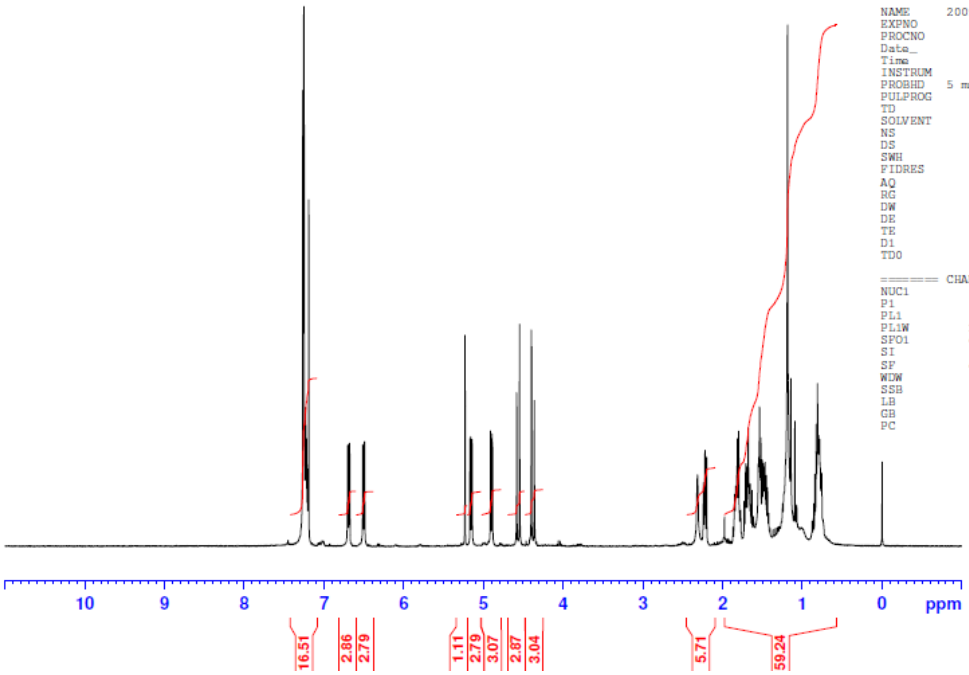
21


jls437
mPROTON CDCl3 {e:\bruk400data\2010\Dec} jpc 34
BRUKER
400 MHz
NAME 2010-12-03-jpc-34
EXPNO 10
PROCNO 1
Date_ 20101203
Time 15.27
INSTRUM AV400
PROBHD 5 mm PABBO BB-
PULPROG zg30b
TD 65536
SOLVENT CDCl3
NS 16
DS 0
SWH 8264.463 Hz
FIDRES 0.126106 Hz
AQ 3.9649780 sec
RG 322
DW 60.500 usec
DE 9.40 usec
TE 290.1 K
D1 1.00000000 sec
TD0 1
====== CHANNEL f1 ======
NUC1 1H
P1 10.00 usec
PL1 -3.60 dB
PL1W 17.83863831 W
SFO1 400.1324710 MHz
SI 32768
SF 400.1300350 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
10
9
8
7
6
5
4
3
2
1
0
ppm
3.05
9.95
5.05
4.90
2.42
2.77
10.23
2.61
24.38
34.64



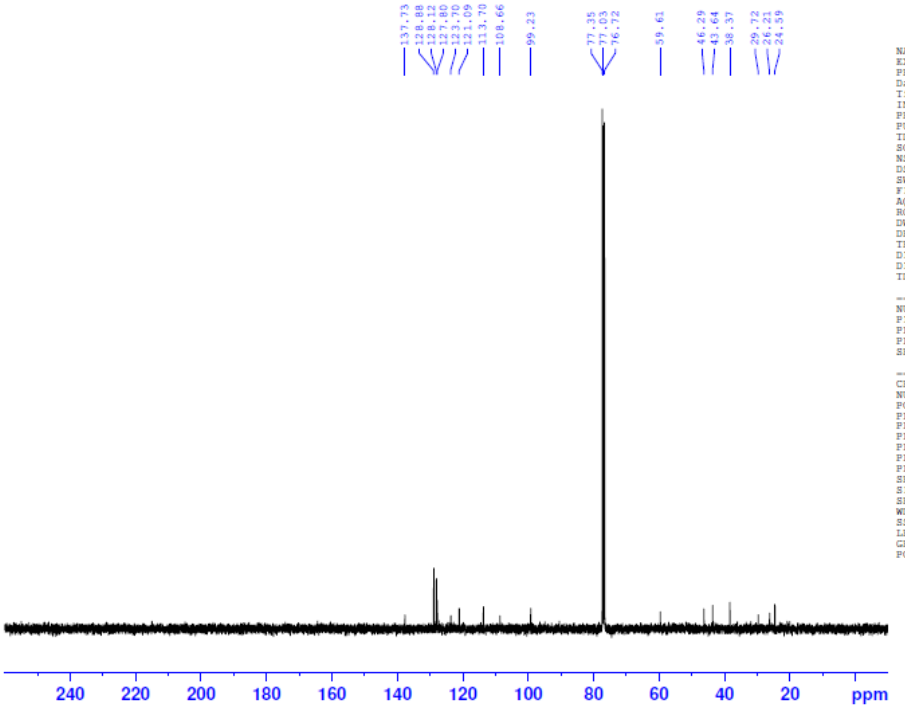
22

jls173 fr25–31
mPROTON CDCl3 {e:\bruk400data\2009\Aug} jpc 23

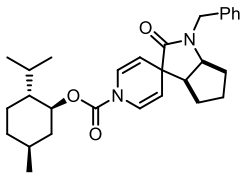



```
NAME          2009-08-25-jpc-23
EXPNO                       10
PROCNO                       1
Date_              20090825
Time                    16.25
INSTRUM                 AV400
PROBHD     5 mm PABBO BB-
PULPROG                 zg30b
TD                      65536
SOLVENT                 CDCl3
NS                          16
DS                           0
SWH                  8264.463 Hz
FIDRES               0.126106 Hz
AQ                   3.9649780 sec
RG                         256
DW                      60.500 usec
DE                       9.40 usec
TE                      292.9 K
D1                   1.00000000 sec
TD0                          1

====== CHANNEL f1 ======
NUC1                        1H
P1                       10.00 usec
PL1                      -3.60 dB
PL1W                17.83863831 W
SFO1               400.1324710 MHz
SI                       32768
SF                 400.1300364 MHz
WDW                         EM
SSB                          0
LB                        0.30 Hz
GB                           0
PC                        1.00
```

jls173 fr25–31
mCARBONnight CDCl3 {e:\bruk400data\2009\Aug} jpc 23

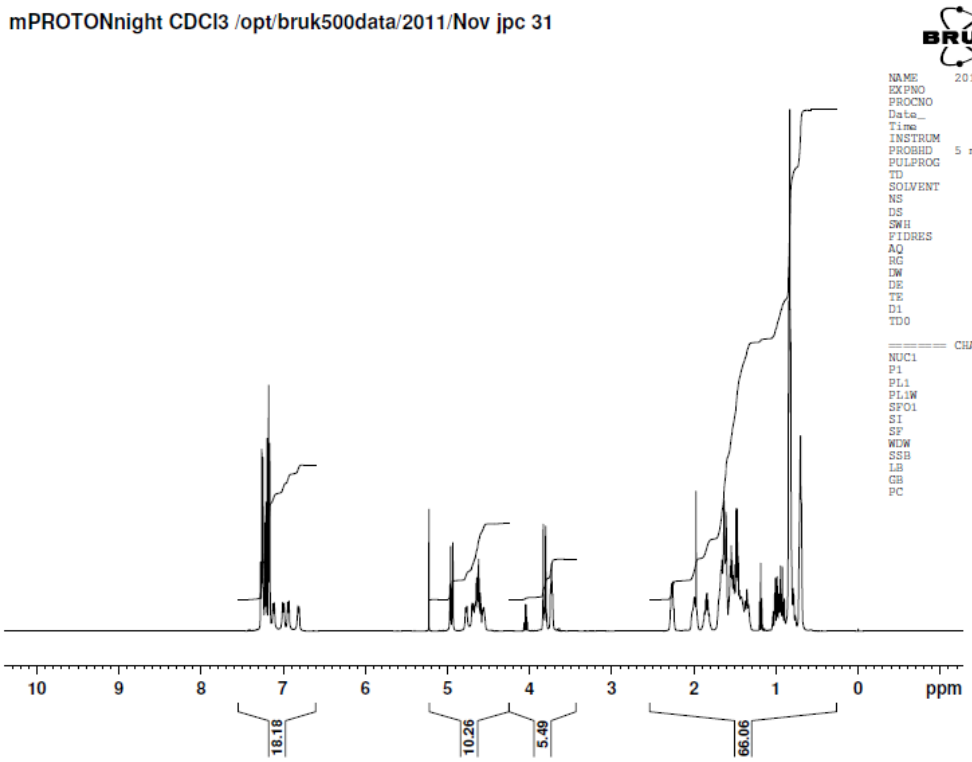



```
NAME          2009-08-25-jpc-23
EXPNO                       11
PROCNO                       1
Date_              20090826
Time                     1.14
INSTRUM                 AV400
PROBHD     5 mm PABBO BB-
PULPROG                 zgpg30
TD                      65536
SOLVENT                 CDCl3
NS                         256
DS                           2
SWH                 30241.936 Hz
FIDRES               0.461455 Hz
AQ                   1.0835786 sec
RG                         512
DW                      16.533 usec
DE                       7.83 usec
TE                      293.7 K
D1                   2.00000000 sec
D11                  0.03000000 sec
TD0                          1

====== CHANNEL f1 ======
NUC1                       13C
P1                       8.00 usec
PL1                      0.00 dB
PL1W                34.91522217 W
SFO1               100.6241042 MHz

====== CHANNEL f2 ======
CPDPRG2                waltz16
NUC2                        1H
PCPD2                    90.00 usec
PL2                      -3.60 dB
PL12                     15.31 dB
PL13                     18.00 dB
PL2W                17.83863831 W
PL12W                0.22927761 W
PL13W                0.12341322 W
SFO2               400.1316005 MHz
SI                       32768
SF                 100.6127690 MHz
WDW                         EM
SSB                          0
LB                        1.00 Hz
GB                           0
PC                        1.40
```



23

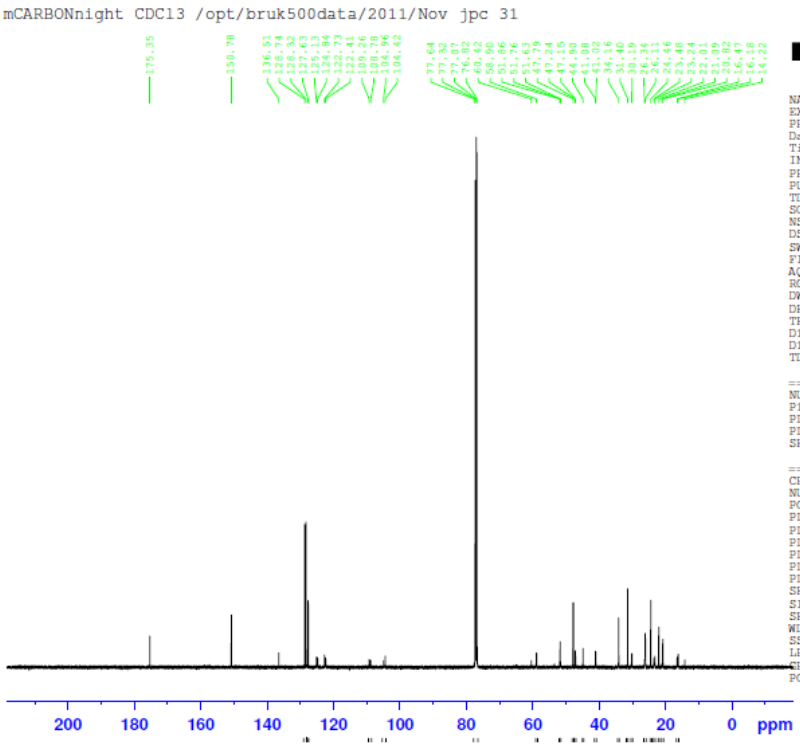
mPROTONnight CDCl3 /opt/bruk500data/2011/Nov jpc 31



BRUKER

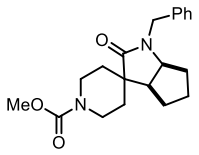
```
NAME          2011-11-11-jpc-31
EXPNO                       10
PROCNO                       1
Date_              20111111
Time                    17.11
INSTRUM                 spect
PROBHD   5 mm PABBO BB-
PULPROG                 zg30b
TD                      65536
SOLVENT                 CDCl3
NS                          16
DS                           0
SWH              10330.578 Hz
FIDRES            0.157632 Hz
AQ                3.1719923 sec
RG                        90.5
DW                   48.400 usec
DE                   13.00 usec
TE                   292.8 K
D1               1.00000000 sec
TD0                          1

====== CHANNEL f1 ======
NUC1                        1H
P1                       10.00 usec
PL1                      -0.10 dB
PL1W            26.21803665 W
SFO1           500.1330885 MHz
SI                       32768
SF             500.1300446 MHz
WDW                         EM
SSB                          0
LB                        0.30 Hz
GB                           0
PC                        1.00
```

mCARBONnight CDCl3 /opt/bruk500data/2011/Nov jpc 31



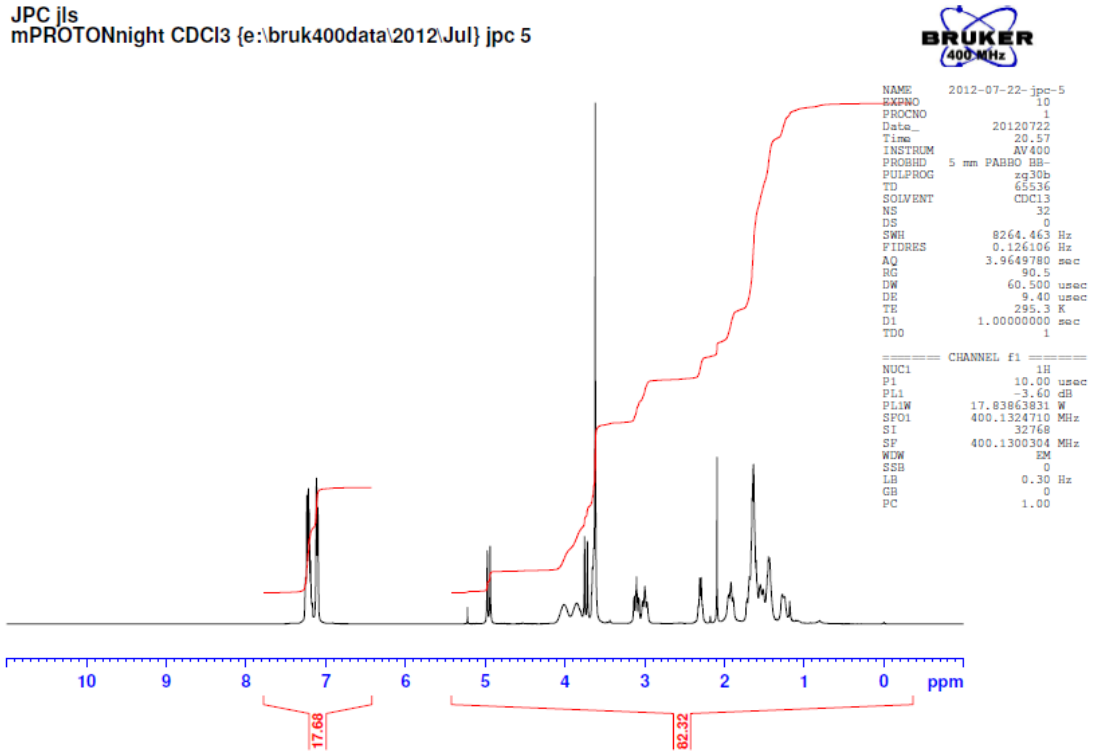
BRUKER

```
NAME          2011-11-11-jpc-31
EXPNO                       11
PROCNO                       1
Date_              20111111
Time                    21.04
INSTRUM                 spect
PROBHD   5 mm PABBO BB-
PULPROG                 zgpg30
TD                      65536
SOLVENT                 CDCl3
NS                       1024
DS                          2
SWH              29761.904 Hz
FIDRES            0.454131 Hz
AQ                1.1010548 sec
RG                        512
DW                   16.800 usec
DE                   32.78 usec
TE                   293.3 K
D1               2.00000000 sec
D11              0.03000000 sec
TD0                          1

====== CHANNEL f1 ======
NUC1                       13C
P1                        8.80 usec
PL1                      -1.00 dB
PL1W           104.35516357 W
SFO1           125.7703643 MHz

====== CHANNEL f2 ======
CPDPRG2                 waltz16
NUC2                        1H
PCPD2                    80.00 usec
PL2                       0.00 dB
PL12                     17.23 dB
PL13                    120.00 dB
PL2W            25.62124252 W
PL12W            0.48484197 W
PL13W            0.00000000 W
SFO2           500.1320005 MHz
SI                       32768
SF             125.7577890 MHz
WDW                         EM
SSB                          0
LB                        1.00 Hz
GB                           0
PC                        1.40
```

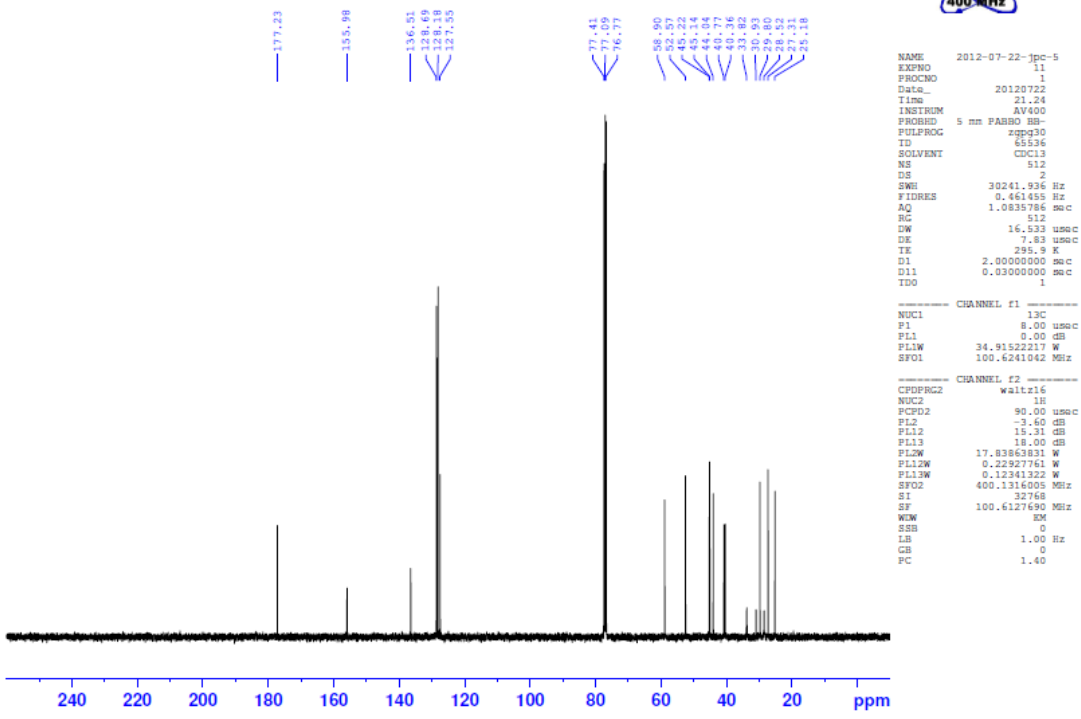


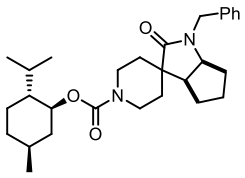
24

JPC jls
mPROTONnight CDCl3 {e:\bruk400data\2012\Jul} jpc 5

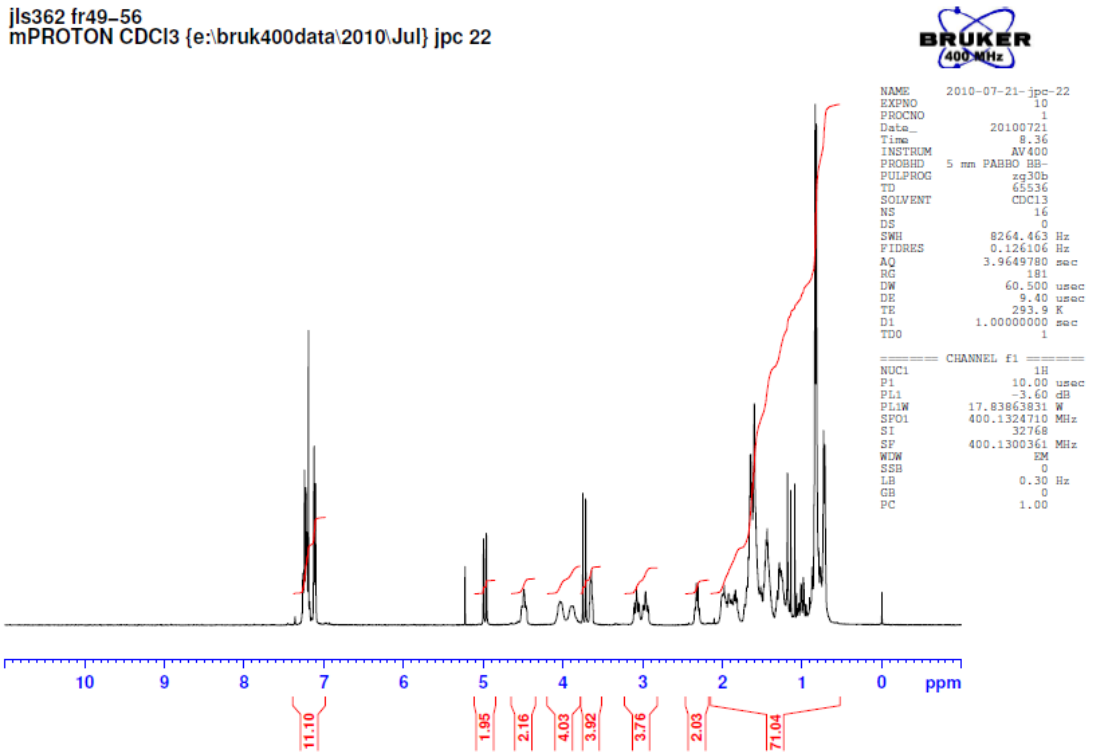


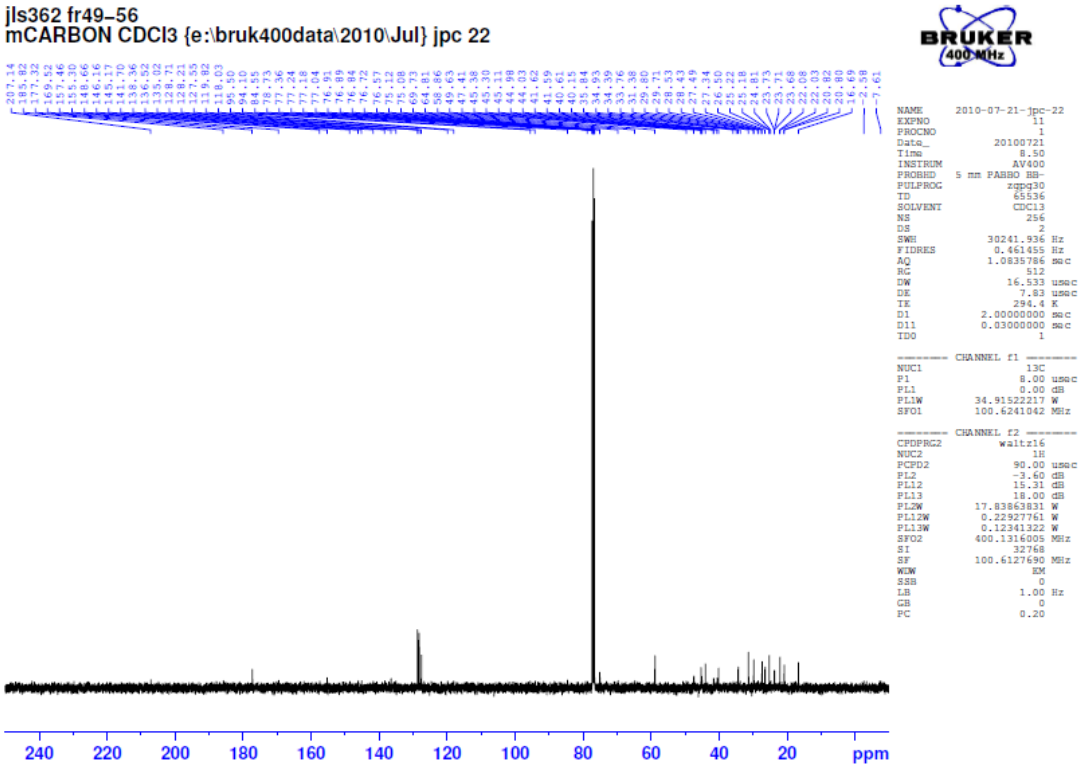
JPC jls
mCARBONnight CDCl3 {e:\bruk400data\2012\Jul} jpc 5

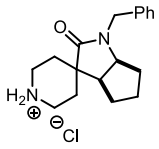



Ph
N
O
O
N
O
O

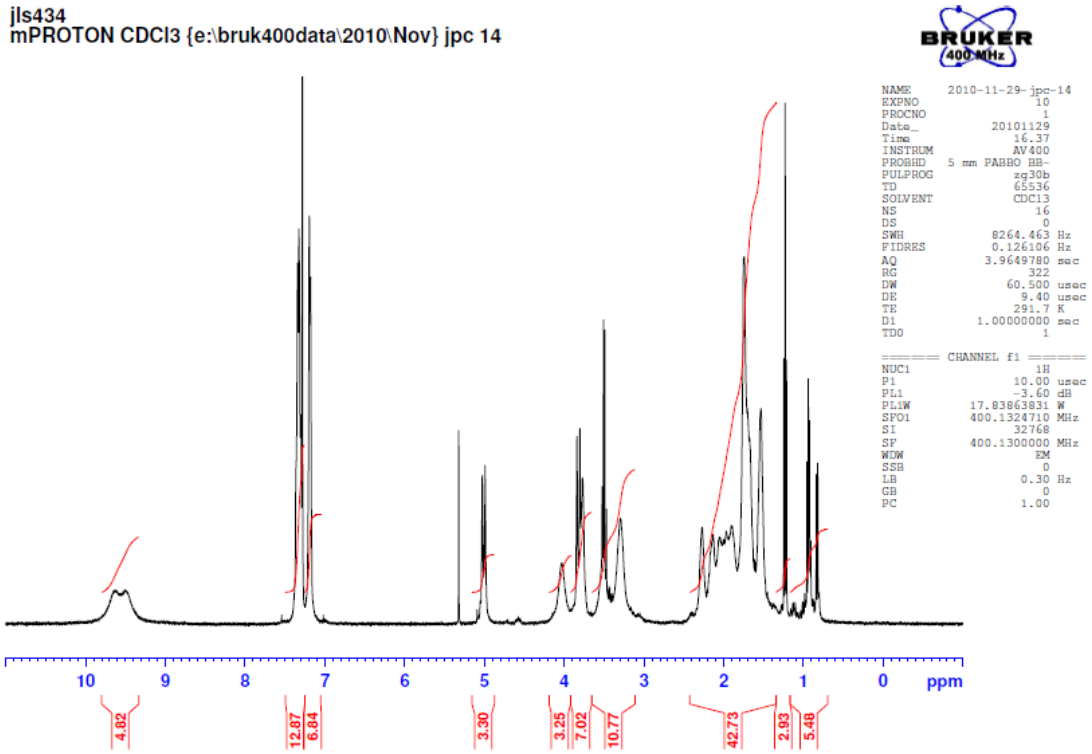
25

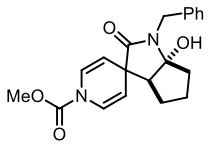

jls362 fr49–56
mPROTON CDCl3 {e:\bruk400data\2010\Jul} jpc 22
BRUKER
400 MHz
NAME 2010-07-21-jpc-22
EXPNO 10
PROCNO 1
Date_ 20100721
Time 8.36
INSTRUM AV400
PROBHD 5 mm PABBO BB-
PULPROG zg30b
TD 65536
SOLVENT CDCl3
NS 16
DS 0
SWH 8264.463 Hz
FIDRES 0.126106 Hz
AQ 3.9649780 sec
RG 181
DW 60.500 usec
DE 9.40 usec
TE 293.9 K
D1 1.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 10.00 usec
PL1 -3.60 dB
PL1W 17.83863831 W
SFO1 400.1324710 MHz
SI 32768
SF 400.1300361 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
10 9 8 7 6 5 4 3 2 1 0 ppm
11.10
1.95
2.16
4.03
3.92
3.76
2.03
71.04


jls362 fr49–56
mCARBON CDCl3 {e:\bruk400data\2010\Jul} jpc 22
BRUKER
400 MHz
NAME 2010-07-21-jpc-22
EXPNO 11
PROCNO 1
Date_ 20100721
Time 8.50
INSTRUM AV400
PROBHD 5 mm PABBO BB-
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 256
DS 2
SWH 30241.936 Hz
FIDRES 0.461455 Hz
AQ 1.0835786 sec
RG 512
DW 16.533 usec
DE 7.83 usec
TE 294.4 K
D1 2.00000000 sec
D11 0.03000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 13C
P1 8.00 usec
PL1 0.00 dB
PL1W 34.91522217 W
SFO1 100.6241042 MHz
======== CHANNEL f2 ========
CPDPRG2 waltz16
NUC2 1H
PCPD2 90.00 usec
PL2 -3.60 dB
PL12 15.31 dB
PL13 18.00 dB
PL2W 17.83863831 W
PL12W 0.22927761 W
PL13W 0.12341322 W
SFO2 400.1316005 MHz
SI 32768
SF 100.6127690 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 0.20
240 220 200 180 160 140 120 100 80 60 40 20 ppm

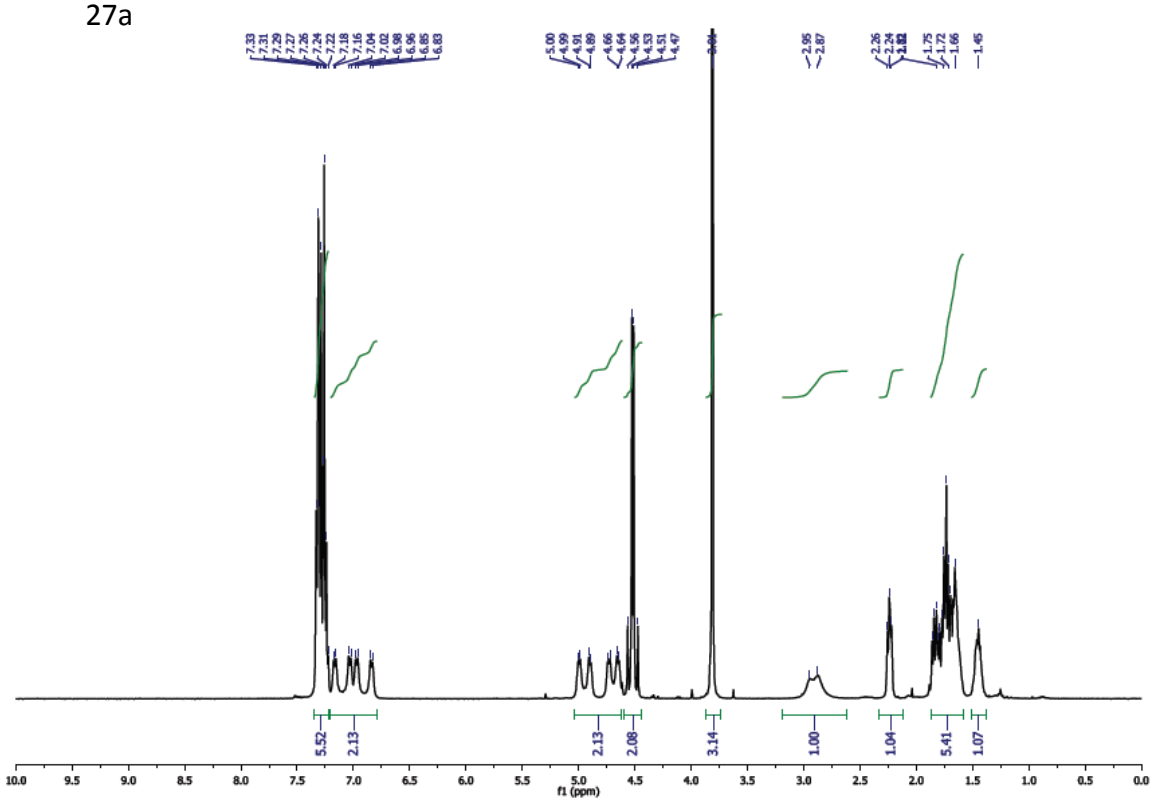

Ph
O
N
H2N
Cl

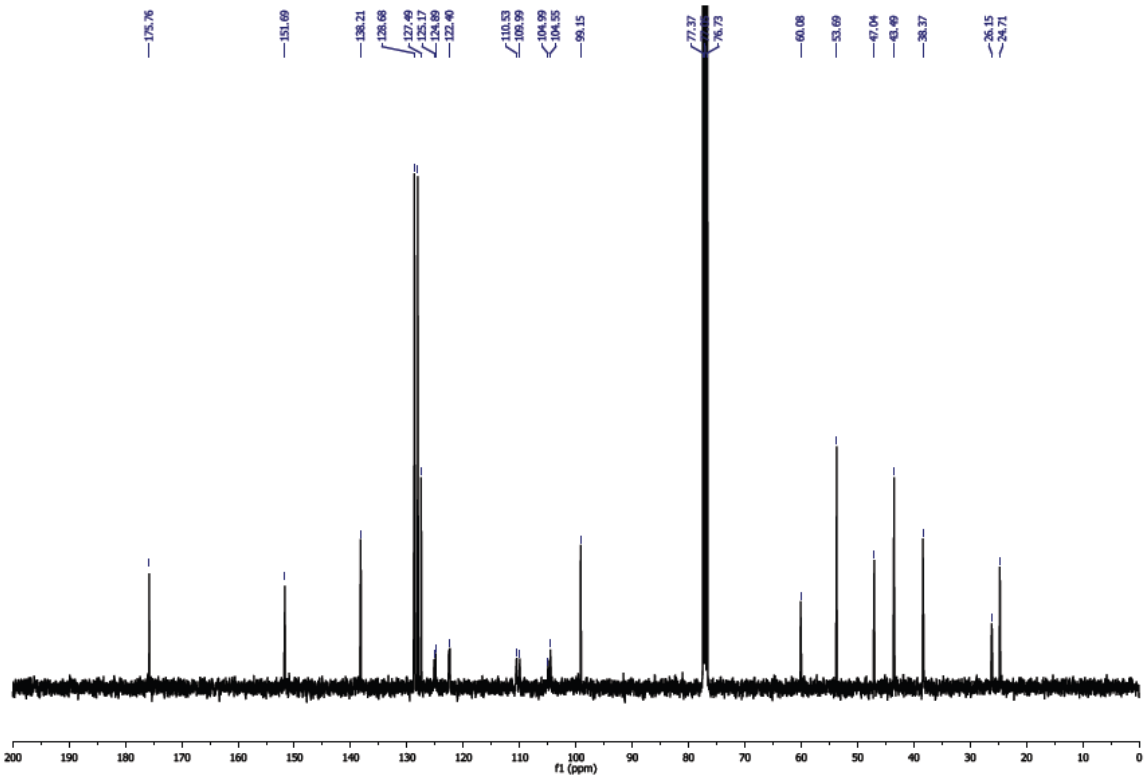
26

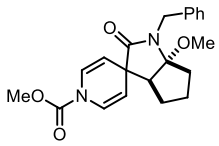

jls434
mPROTON CDCl3 {e:\bruk400data\2010\Nov} jpc 14
BRUKER
400 MHz
NAME 2010-11-29-jpc-14
EXPNO 10
PROCNO 1
Date_ 20101129
Time 16.37
INSTRUM AV400
PROBHD 5 mm PABBO BB-
PULPROG zg30b
TD 65536
SOLVENT CDCl3
NS 16
DS 0
SWH 8264.463 Hz
FIDRES 0.126106 Hz
AQ 3.9649780 sec
RG 322
DW 60.500 usec
DE 9.40 usec
TE 291.7 K
D1 1.00000000 sec
TD0 1
======= CHANNEL f1 =======
NUC1 1H
P1 10.00 usec
PL1 -3.60 dB
PL1W 17.83863831 W
SFO1 400.1324710 MHz
SI 32768
SF 400.1300000 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
10
9
8
7
6
5
4
3
2
1
0
ppm
4.82
12.87
6.84
3.30
3.25
7.02
10.77
42.73
2.93
5.48


Ph
O
N
OH
MeO
N
O

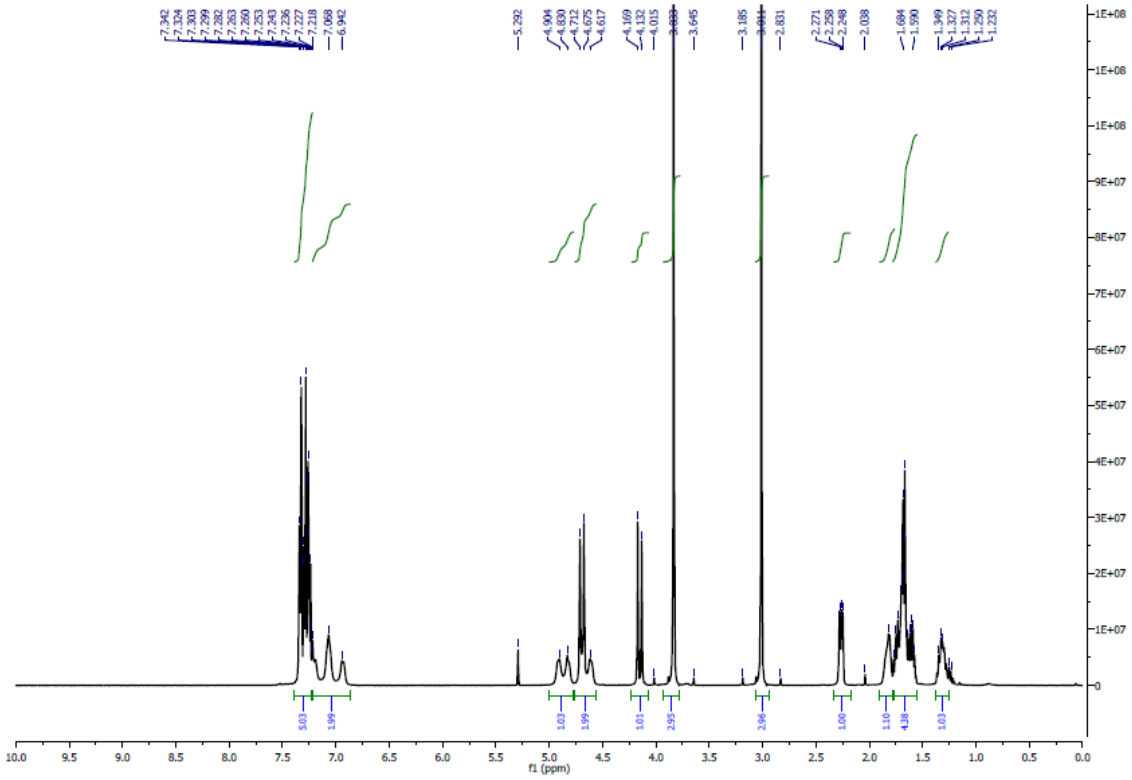
27a

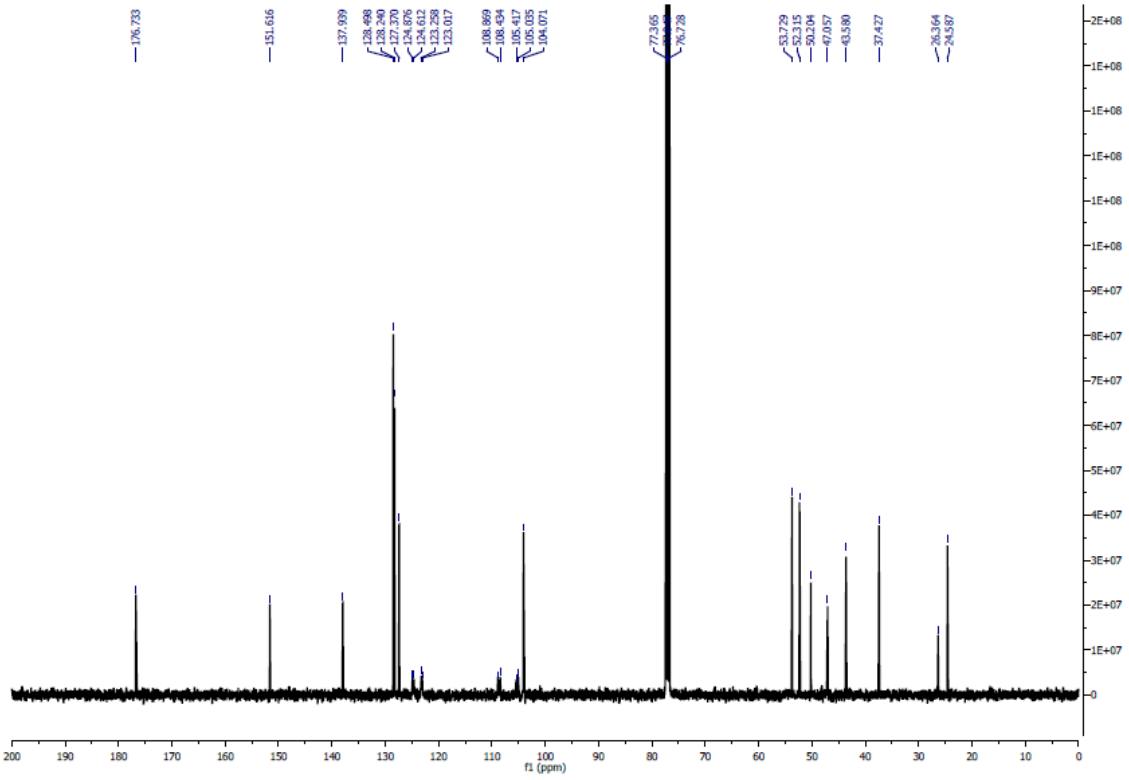

7.33
7.31
7.29
7.27
7.26
7.24
7.22
7.18
7.16
7.04
7.02
6.98
6.96
6.85
6.83
5.00
4.99
4.91
4.89
4.66
4.64
4.56
4.53
4.51
4.47
2.95
2.87
2.26
2.24
1.75
1.72
1.66
1.45
5.52
2.13
2.13
2.08
3.14
1.00
1.04
5.41
1.07
f1 (ppm)

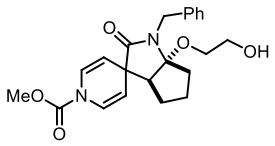

175.76
151.69
138.21
128.68
127.49
125.17
124.89
122.40
110.53
109.99
104.99
104.55
99.15
77.37
76.73
60.08
53.69
47.04
43.49
38.37
26.15
24.71
f1 (ppm)



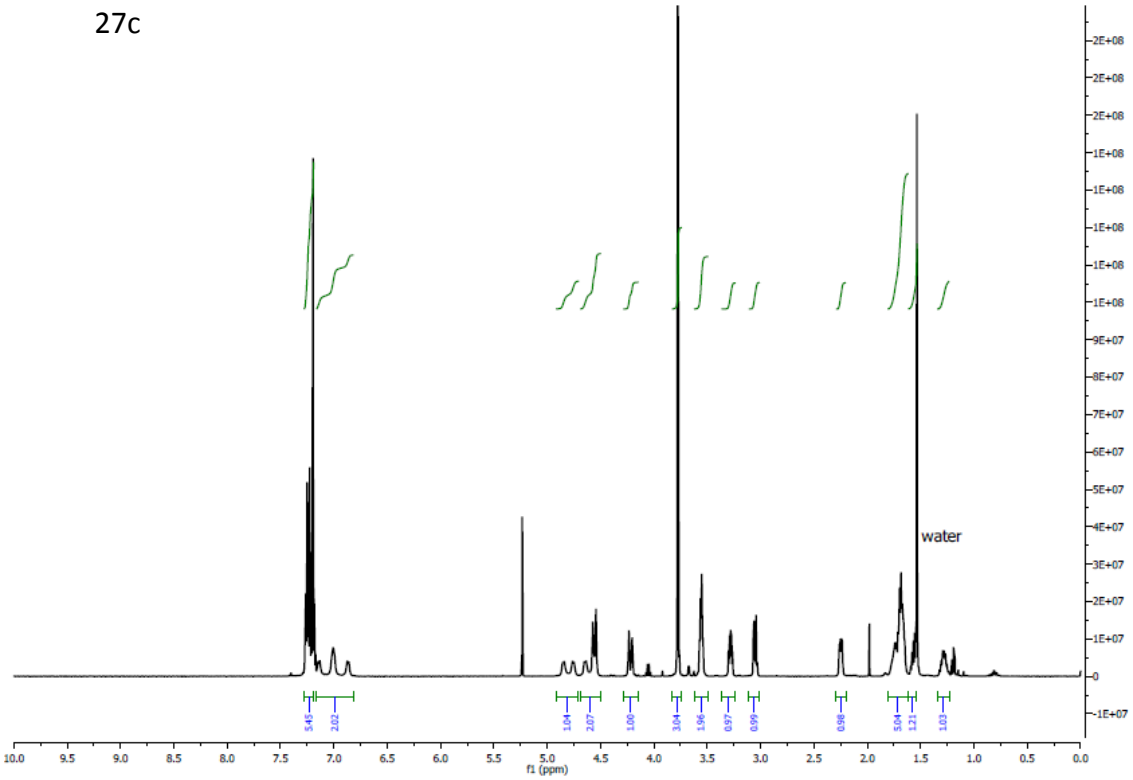
27b

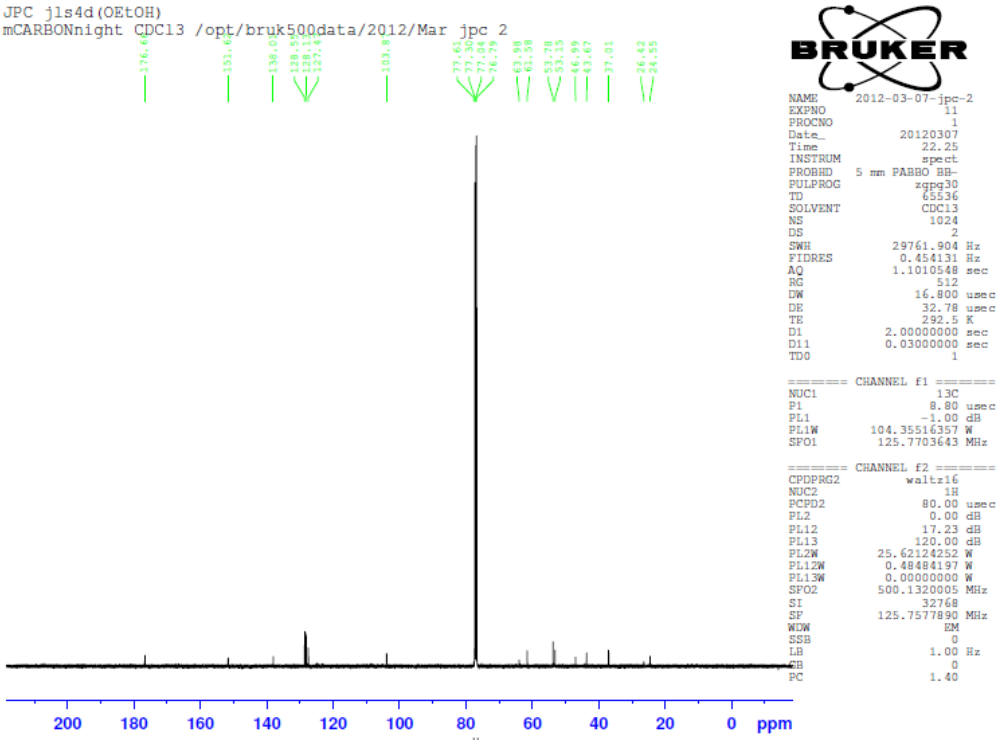


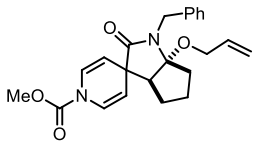



Ph
O
N
O
OH
MeO
N
O

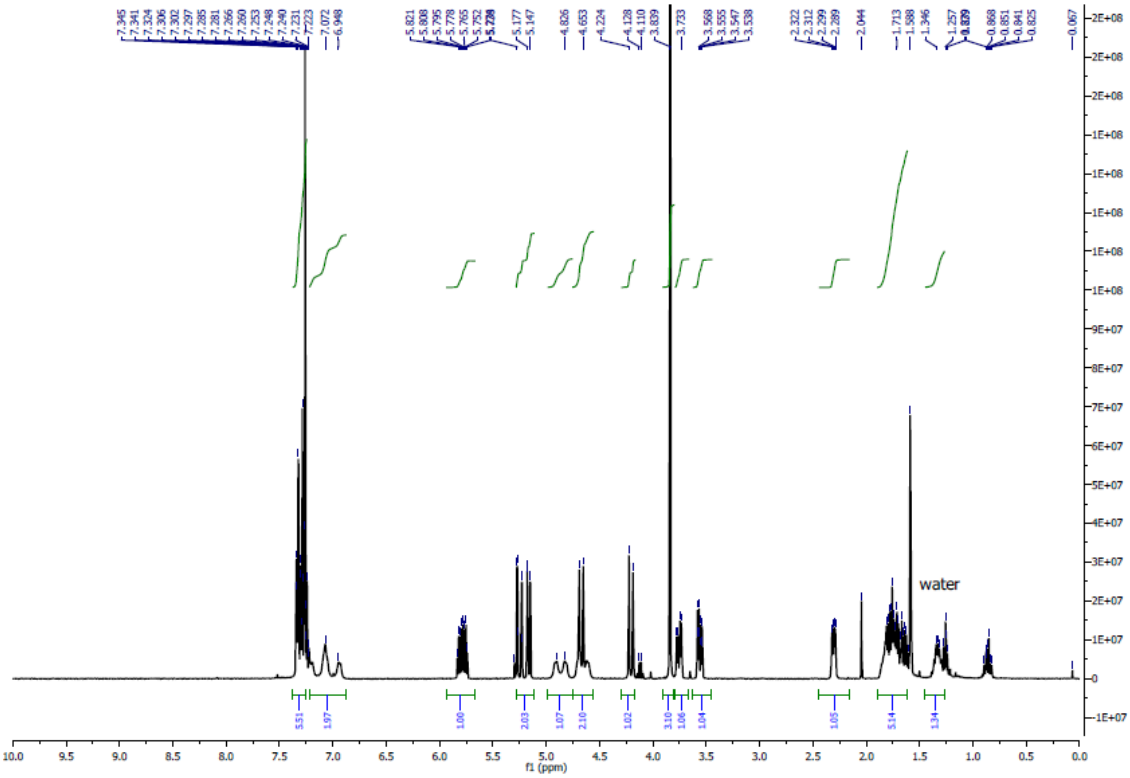
27c

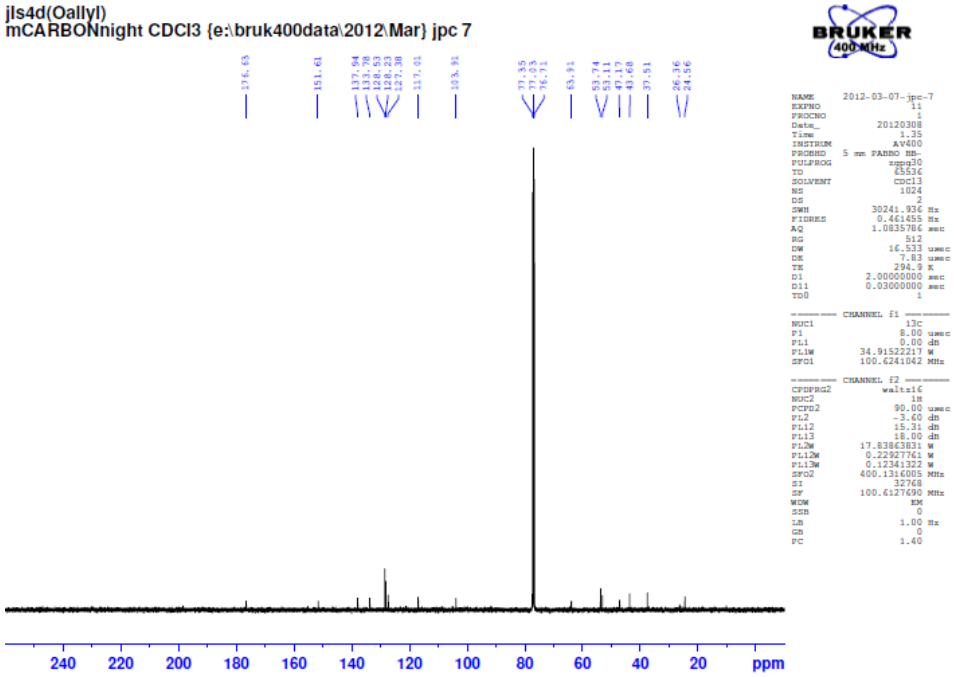

water
5.45
2.02
1.04
2.07
1.00
3.04
1.96
0.97
0.99
0.98
5.64
1.21
1.03
f1 (ppm)

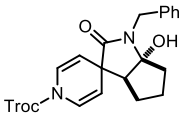

JPC jls4d(OEtOH)
mCARBONnight CDCl3 /opt/bruk500data/2012/Mar jpc 2
BRUKER
NAME 2012-03-07-jpc-2
EXPNO 11
PROCNO 1
Date_ 20120307
Time 22.25
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 1024
DS 2
SWH 29761.904 Hz
FIDRES 0.454131 Hz
AQ 1.1010548 sec
RG 512
DW 16.800 usec
DE 32.78 usec
TE 292.5 K
D1 2.00000000 sec
D11 0.03000000 sec
TD0 1
======= CHANNEL f1 =======
NUC1 13C
P1 8.80 usec
PL1 -1.00 dB
PL1W 104.35516357 W
SFO1 125.7703643 MHz
======= CHANNEL f2 =======
CPDPRG2 waltz16
NUC2 1H
PCPD2 80.00 usec
PL2 0.00 dB
PL12 17.23 dB
PL13 120.00 dB
PL2W 25.62124252 W
PL12W 0.48484197 W
PL13W 0.00000000 W
SFO2 500.1320005 MHz
SI 32768
SF 125.7577890 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40
200
180
160
140
120
100
80
60
40
20
0
ppm


Ph
O
N
O
MeO
N
O

27d


water
f1 (ppm)


jls4d(Oallyl)
mCARBONnight CDCl3 {e:\bruk400data\2012\Mar} jpc 7
BRUKER
400 MHz
ppm



27e