Supplementary Material for

Synthesis and sequential diastereoselective incorporation of hydroxyl groups into hexahydrofuro[2,3-*f*]indolizin-7(2*H*)-one to give mono-, di- and tetra-hydroxyfuroindolizidines

Peter Šafář,[a] Štefan Marchalín,*[a,b] Matej Cvečko,[a] Ján Moncol,[c] Viera Dujnič,[d] Michal Šoral,[e] and Adam Daïch*[b,†]

[a.] Department of Organic Chemistry, Faculty of Chemical & Food Technology, Slovak University of Technology, Radlinského 9, SK-81237 Bratislava, Slovakia
[b,] Normandie Univ, UNILEHAVRE, CNRS, URCOM, 76600 Le Havre, France.
[c,] Department of Inorganic Chemistry, Faculty of Chemical & Food Technology, Slovak University of Technology, Radlinského 9, SK-81237 Bratislava, Slovakia
[d,] Institute of Chemistry, Slovak Academy of Sciences, Dúbravská cesta 9, SK-845 38, Bratislava, Slovakia
[e,] Central Laboratories, Faculty of Chemical and Food Technology, Slovak University of Technology in Bratislava, 81237 Bratislava, Slovak Republic

† Corresponding author. Tel.: (+33) 02-32-74-44-03; *adam.daich@univ-lehavre.fr*; ORCID AD: orcid.org/0000-0002-6942-0519

Complete address: Normandie Univ, UNILEHAVRE, URCOM EA 3221, INC3M CNRS-FR 3038, UFR des Sciences et Techniques, Université Le Havre Normandie, BP : 1123, 25 rue Philipe Lebon, F-76063 Le Havre Cedex, France.

Peter Šafář ORCID: https://orcid.org/0000-0002-9502-3365
Štefan Marchalin ORCID: https://orcid.org/0000-0003-0680-3771; E-Mail: stefan.marchalin@stuba.sk
Jan Moncol ORCID: https://orcid.org/0000-0003-2153-9753

Table of contents

General methods

Melting points were obtained using a Boetius apparatus and are corrected. Commercial reagents were used without further purification. All solvents were distilled before use. Flash column liquid chromatography (FLC) was performed on silica gel Kieselgel pore size 60 Å (40–63 μm particle size, 230–400 mesh particlesize) and analytical thin-layer chromatography (TLC) was performed on aluminium plates pre-coated with either 0.2 mm (DC-Alufolien, Merck) or 0.25 mm silica gel 60 F254 (ALUGRAM-SIL G/UV254, Macherey–Nagel). The compounds were visualized by UV fluorescence and by dipping the plates in anaqueous H_2SO_4 solution of cerium sulfate/ammonium molybdate followed by charring with a hea tgun (250 °C). HPLC analyses were performed on Varian system 9012 with diodearray Varian 9065 polychrom UV detector: column CC 250/3 Nucleosil 120–5 C18, 250x3 mm (Macherey–Nagel). Mobile phase: solvent A: water-acetonitrile-methanesulfonic acid (1000:20:1), solvent B: water-acetonitrile-methanesulfonic acid (20/1000/1), elution mode: gradient with 5–50% solvent B, flow rate: 0.65 mL/min, UV detection: 210 nm (DAD), 35 °C, 20 minutes. GC–MS analyses were performed on GC–MS Varian Saturn 2100 T, ion trap MS detector, 70 eV. Column: Varian, Factor Four capillary column VF-5ms 30mx0.25 mm ID, DF = 0.25. Optical rotations were measured with a POLAR L-lP polarimeter (IBZ Messtechnik) with a water jacketed 10 cm cell at the wave length of the sodium line D (λ = 589 nm). Specific rotations are given in units of 10^{-1} deg cm.g^{-1} and concentrations are given in g/100 mL. Infrared spectra were recorded on a Nicolet 5700 FT-IR spectrometer as ATR discs (ATR) or as thin films on ATR plates(film). NMR spectra were recorded on a VNMRS 600 NMR spectrometer (Varian) with operating frequencies 599.76 MHz for ^{1}H and 150.82 MHz for ^{13}C. NMR spectra from all samples were measured in $CDCl_3$, d_6-Acetone or CD_3OD at 25 °C. Chemical shifts (δ) are quoted in ppm; the chemical shift axes were calculated using the reference signals of TMS (for ^{1}H and ^{13}C NMR). Depending on the possibilities and amount of information needed to provide the best possible structural proof ^{1}H, standard ^{13}C, quantitative ^{13}C,^{13}C-attached proton test, within versegated ^{1}H decoupling, supported by ^{1}H-^{1}HCOSY (with gradient coherence selection and with/without zero quantum filtering), ^{1}H-^{13}C HSQC (with varied use of gradient coherence selection, adiabatic 180° pulses on the ^{13}C channel and non-uniform sampling), ^{1}H-^{13}CHMBC (with gradient coherence selection and varied use of adiabatic 180° pulses on the ^{13}C channel and semi-selective ^{13}C excitation with WURST2 ipulses), ^{13}C-^{13}C INADEQUATE (withan adiabatic 180° pulse). For the precise extraction of chemical shift and *J*-coupling values manual spin simulation was preformed if needed in the spin simulation package built in the MestReNova software (version 11.0.2–18153). MS analysis was performed using a Thermo Scientific LTQ Orbitrap with ETD, mass spectrometer, a syringe pump, and an ESI source in the positive ion source mode, run by Xcalibur 2.0 software (Thermo Electron Corporation). The spray needle voltage was set at 5.0 kV and the spray was stabilized with a nitrogen sheath gas (30 psi). The capillary temperature was 275 °C. A syringe pump delivering 6 μl/min was used for the direct injections of compounds diluted in methanol (c = 1 mg/ml). Mass spectra were acquired in full mass scan mode and recorded with a limited mass range from m/z 80-600. All the samples were diluted in methanol (LC-MS quality, Sigma Aldrich). High-resolution spectrometry was performed on Micromass Q-Tof Micro MS system with ESI^{+}ionization (measured mass represents $M+1^{+}$) and LC-MS chromatographic separation

was performed on Agilent 1260B LC-MS system using HALO C18 column (2.1 × 50 mm, 5.0 µm particle size). A 10 min gradient elution was performed at 1.5 mL/min flow rate as follows: maintain H_2O/MeOH with 0.1% formic acid from 5% to 100%. MS detector used combine dionization (ESI + APCI) in positive mode, 50% scan and 50% SIM. All samples for analysis and NMR spectroscopy were dried at room temperature for 48 hours at Laboratory Freeze Dryer Alpha 2–4 LD plus Lyophilizer.

Synthetic experiments

(*3S,3aS,4aS,9aR*)-3,3a-Dihydroxyoctahydrofuro[2,3-*f*]indolizin-7(2*H*)-one (8c)

Method A: *Upjohn dihydroxylation with OsO_4 and NMO.*

A solution of NMO (10.35 g, 88.2 mmol) in water (10 ml) was added to a mixture of *t*-BuOH, acetone and water (500 ml, 1:5:1) at 0 °C. DHF-**5** (15.8 g, 88.2 mmol) was then added in one portion, the mixture allowed to stirred for 10 minutes and then OsO_4 (125 mg, 0.5 mmol) in *t*-BuOH (10 ml) was added dropwise over 10 minutes. The mixture could continue stirring and warm slowly to room temperature (TLC monitoring, 18 hours). The reaction was quenched by the addition of sodium sulfite (25 g) and was stirred at room temperature 15 minutes, 75 g of SiO_2 was added and concentrated *in vacuo*. [*The crude mixture (30 mg) was redissolved in 1 : 1 acetic anhydride and Et_3N (~1.0 ml) and DMAP (1 mg) was added. The mixture was stirred at room temperature overnight and concentrated in vacuo on a hot bath (~65 °C). An ^1H NMR spectrum was obtained on the crude mixture of diastereomeric acetonides endo/exo in the ratio 99:1*]. The crude solid was purified by flash chromatography (CH_2Cl_2, CH_2Cl_2:MeOH 5:1) to afford the diol as a white solid (17.1 g, 91%), which was recrystallized from isopropanol to afford white needles (14.7 g, 78%); mp 114.7-116.1 °C. $[\alpha]_D^{22}$ = -10.9 (*c* 1, MeOH). TLC (Silica gel): R_f = 0.21 (CH_2Cl_2:isopropanol 5:1). IR (ATR): ν = 3375, 3283, 2952, 2907, 2862, 1680, 1651, 1465, 1439, 1411, 1357, 1330, 1290, 1254, 1296, 1204, 1175, 1133, 1111, 1067, 1041, 1024, 977, 968, 947, 931, 880, 837, 807, 749, 623, 500, 480, 438. ^1H NMR (600 MHz, CD_3OD): δ 4.33 (t, *J* = 7.4 Hz, 1H, H-3), 4.11 (dd, *J* = 8.6, 7.3 Hz, 1H, H-2), 3.96 (dd, *J* = 13.8, 6.6 Hz, 1H, H-9_{eq}), 3.81 (dd, *J* = 8.0, 6.6 Hz, 1H, H-9a), 3.72 (dddd, *J* = 12.0, 7.4, 6.4, 3.6 Hz, 1H, H-4a), 3.69 (dd, *J* = 8.6, 7.6 Hz, 1H, H-2´), 2.85 (tdd, *J* = 13.8, 8.0, 0.8 Hz, 1H, H9_{ax}), 2.44 – 2.35 (m, 2H, 2xH-6), 2.27(tdd, *J* = 12.8, 7.5, 6.4 Hz, 1H, H-5), 2.22 (dd, *J* = 13.6, 3.6 Hz, 1H, H-4_{eq}), 1.69 (dtd, *J* = 12.8, 9.0, 6.3 Hz, 1H, H-5´), 1.56 (dd, *J* = 13.6, 12.0 Hz, 1H). ^{13}C NMR (150 MHz, CD_3OD): δ 176.6 (s, C-7), 80.5 (d, C-9a), 77.0 (d, C-3a), 73.2 (d, C-3), 72.1 (t, C-2), 54.3 (d, C-4a), 42.4 (t, C-9), 40.33 (t, C-4), 31.3 (t-C-6), 25.8 (t, C-5) ppm. HRMS (ESI): *m/z* calcd. for $C_{10}H_{15}NO_4$ $[M+H]^+$ 214.1074, found 214.1073.

Method B: *Sharpless dihydroxylation with AD-mix α.*

The crude diol was prepared from a solution of DHF-**5** (1.27 g, 7.1 mmol), AD-mix *α* (9,94 g) and methylsulfonamide (675 mg, 7.1 mmol) in a mixture of 3:1 *t*-BuOH/water (75 ml) according to the procedure and work-up described above (method A). Purification by flash chromatography (CH_2Cl_2, CH_2Cl_2:MeOH 5:1) afforded the desired diol **8c** as a white solid (968 mg, 64%). *The crude mixture (25 mg) was redissolved in 1:1 acetic anhydride/Et_3N (~1.0 ml) and DMAP (1 mg) was added. The mixture was stirred at room temperature overnight and concentrated in vacuo on a hot bath (~70 °C). An NMR spectrum was obtained on the crude mixture of diastereomeric acetonides endo/exo (99:1) from ^1H NMR analysis).*

Method C: *Sharpless dihydroxylation with AD-mix β.*

The crude diol was prepared from a solution of DHF-**5** (1.27 g, 7.1 mmol), AD-mix *β* (9.94 g) and methyl sulfonamide (675 mg, 7.1 mmol) in a mixture of 3:1 *t*-BuOH:water (75 ml) according to the procedure and work-up described above (method A). Purification by flash chromatography (CH_2Cl_2, CH_2Cl_2:MeOH 5:1) afforded the desired diol **8c** as a white solid (1.03 g, 68%). *The crude mixture (22*

mg) was redissolved in 1:1 acetic anhydride/Et_3N (~1.0 ml) and DMAP (1 mg) was added. The mixture was stirred at room temperature overnight and concentrated in vacuo on a hot bath (~70 °C). An NMR spectrum was obtained on the crude mixture of diastereomeric acetonides endo/exo (99:1) from ^1H NMR analysis).

(*3S,3aR,4aS,9aR*)-7-Oxooctahydrofuro[2,3-*f*]indolizine-3,3a(*4H*)-diyl diacetate (18c)

To a stirred solution of optically active (*3S,3aS,4aS,9aR)*-3,3a-dihydroxy-octahydrofuro[2,3-*f*] indolizin-7(*2H*)-one **(8c)** (1.10 g, 5.2 mmol) in dry CH_2Cl_2 (50 mL) was added acetic anhydride (1.33 g, 1.44 mL, 13 mmol, 2.5 eq.), DMAP (85 mg, 0.7 mmol) and triethylamine (1.32 g, 1.82 mL, 13 mmol, 2.5 eq.). The reaction mixture was stirred until disappearance of the starting material (monitored by TLC CH_2Cl_2:acetone, 3:1). The mixture was quenched with a saturated aqueous $NaHCO_3$ solution. The aqueous layer was extracted with diethyl ether and the organic layers were washed with a saturated aqueous $CuSO_4$ solution and water, dried over $MgSO_4$ and concentrated under vacuum. The yellow oil was purified by flash chromatography on silica gel column (CH_2Cl_2, CH_2Cl_2/acetone 10:1 to afford diacetyl **18c** (838 mg, 54.6%) and CH_2Cl_2:acetone 5:1 to afford monoacetyl **19c** (305 mg, 23%) as an oil, which quickly crystallized on standing in a fridge. Analytically pure compound of diacetate-**18c** was obtained by crystallization from cyclohexane; mp 116.8-117.6 °C. $[\alpha]_D^{20.3}$= +48.7 (*c* 0.95, acetone). TLC (Silica gel): R_f = 0.42 (CH_2Cl_2:isopropanol 15/1). IR (ATR): ν =2930, 1737, 1661, 1473, 1453, 1426, 1367, 1346, 1302, 1233, 1175, 1120, 1083, 1064, 1040, 998, 976, 942, 922, 904, 856, 770, 735, 684, 656, 599, 578, 566, 512, 499, 485, 451. ^{1}H NMR (600 MHz, $CDCl_3$): δ 5.47 (t, *J* = 4.6 Hz, 1H, H-3), 4.32- 4.24 (m, 2H, H-2 and H-9a), 3.87 - 3.74 (m, 3H, H-2′, H-4a and H-9_{ax}), 3.50 (dd, *J* = 14.4, 1.5 Hz, 1H, H-9_{eq}), 2.66 (dd, *J* = 14.4 Hz, 1H, H-4_{eq}), 2.46 - 2.32 (m, 2H, 2xH-6), 2.30 – 2.23 (m, 1H, H-5), 2.08 (s, 6H, 2xCH_3), 1.92 (t, *J* = 12.7 Hz, 1H, H-4_{ax}), 1.59 (qd, *J* = 11.9, 9.4Hz, 1H H-5′). ^{13}C NMR (150 MHz, $CDCl_3$): δ 174.3 (s, C-7), 169.8 (s, $CH_3\underline{CO}$) 169.6 (s, $CH_3\underline{CO}$), 81.2 (d, C-3a), 75.7 (d, C-3), 70.3 (t, C-2), 50.7 (d, C-4a), 40.2 (t, C-4), 40.0 (t, C-9), 30.3 (t-C-6), 26.3 (t, C-5), 21.3 (q, CH_3), 20.7 (q, CH_3) ppm. HRMS (ESI): *m/z* calcd. for $C_{14}H_{19}NO_6$ $[M+H]^+$ 298.1285, found 298.1285.

(*3S,3aR,4aS,9aR*)-3a-Hydroxy-7-oxodecahydrofuro[2,3-*f*]indolizin-3-yl acetate (19c); mp 215.6-217.7 °C. $[\alpha]_D^{20.4}$ = +3.79 (c 0.85, acetone); TLC (Silica gel): R_f = 0.16 (CH_2Cl_2/isopropanol 15/1). IR (ATR): ν = 3174, 2985, 2946, 2895, 2871, 1743, 1661, 1473, 1453, 1426, 1367, 1346, 1302, 1266, 1233, 1175, 1120, 1083, 1064, 1040, 998, 976, 942, 922, 904, 856, 770, 735, 684, 656, 599, 579, 566, 512, 499, 485, 451. ^{1}H NMR (600 MHz, $CDCl_3$): δ 5.25 (t, *J* = 7.3 Hz, 1H. H-3), 4.27 (dd, *J* = 9.4, 7.4 Hz, 1H, H-2), 4.01 (dd, *J* = 14.1, 6.1 Hz, 1H, H-9_{eq}), 3.89 (dd, 1H, *J* = 7.2, 6.3 Hz, H-9a), 3.84 (dd, *J* = 9.4, 7.2 Hz, 1H, H-2′), 3.75 (ddt, *J* = 10.8, 7.0, 3.5 Hz, 1H, H-4a), 2.96 (dd, *J* = 14.1, 7.3 Hz, 1H, H-9_{ax}), 2.48 – 2.38 (m, 2H, 2xH-6), 2.33 – 2.25 (m, 1H, H-5), 2.28 (dd, *J* = 14.0, 3.5 Hz, 1H, H-4_{eq}), 2.17 (s, 3H, CH_3), 1.69 (tq, *J* = 9.2, 6.6 Hz ,1H, H-5′), 1.63 (dd, *J* = 13.7, 11.8 Hz, 1H, H-4_{ax}). ^{13}C NMR (150 MHz, $CDCl_3$): δ 175.2 (s, C-7), 171.4 (s, $CH_3\underline{CO}$), 79.4 (d, C-9a), 75.9 (d, C-3a), 74.5 (d, C-3), 68.8 (t, C-2), 52.6 (d, C-4a), 40.9 (t, C-9), 40.0 (t, C-4), 30.6 (t, C-6), 25.2 (t, C-5), 20.7 (q, CH_3) ppm. HRMS (ESI): *m/z* calcd. for $C_{12}H_{17}NO_5$ $[M+H]^+$ 256.1179, found 256.1178.

(*3aS,5aR,10aS,11aR*)-2,2-Dimethyloctahydro-8*H*-[1,3]dioxolo[4',5':3,4]furo[2,3-*f*]indolizin-8-one (20)

Freshly distilled (dried with molecular sieves) 2,2-dimethoxypropane (31 mL, 0.245 mol, 5.0 eq.) and PTSA (172 mg, 1.0 mmol) were added to a solution of *cis*-dihydroxy-THF (**8c)** (10.67 g, 50.0 mmol) in dry acetone (300 mL) under argon at room temperature. After stirring for 18 h, the reaction mixture was quenched with 5% Na_2CO_3(10 mL) and the solvent was removed under reduced pressure. The solid

residue was purified by column chromatography on silica gel eluted with CH_2Cl_2 and then CH_2Cl_2:acetone (5:1) to provide **20** (11.46 g, 90.42%) as a white solid. Recrystallization from a mixture of EtOAc:*i*-hexane gave material (10.26 g, 81%) as colorless needles, mp 113.8-115.2 °C. $[\alpha]_D^{20.2}$ = + 25.9 (*c* 1.0, acetone). TLC (Silica gel): R_f = 0.35 (CH_2Cl_2:isopropanol 15:1). IR (ATR): ν = 2979, 2940, 2871, 1681, 1444, 1422, 1373, 1310, 1270, 1231, 1217, 1153, 1113, 1094, 1074, 1051, 1033, 922, 877, 858, 816, 729, 678, 662, 611, 563, 527, 496, 427. ^{1}H NMR (600 MHz, $CDCl_3$): δ 4.63 (dd, *J* = 5.5, 2.3 Hz, 1H, H-3a), 4.09 (dd, *J* = 11.0, 5.4 Hz, 1H, H-4), 4.08 (t, *J* = 6.1 Hz, 1H, H-5a), 3.98 (dd, *J* = 14.2, 6.5 Hz, 1H, H-6_{eq}), 3.92 (dd, *J* = 11.1, 2.3 Hz, 1H, H-4′), 3.56 (dtd, *J* = 11.0, 7.0, 3.2 Hz, 1H), 3.00 (dd, *J* = 14.2, 7.2 Hz, 1H, H-6_{ax}), 2.44 – 2.40 (m, 2H, 2xH-9), 2.30 (dd, *J* = 13.7, 3.2 Hz, 1H, H-11_{eq}), 2.25 (dd, *J* = 12.8, 7.0 Hz, 1H, H-10), 1.85 (dd, *J* = 13.6, 11.9 Hz, 1H, H-11_{ax}), 1.69 (qt, *J* = 9.2, 6.7 Hz, 1H), 1.52 (s, 3H, CH_3), 1.41 (s, 3H, CH_3). ^{13}C NMR (150 MHz, $CDCl_3$): δ 174.1 (s, C-8), 113.4 (s, C-2), 89.5 (d, C-11a), 85.3 (d, C-3a), 78.9 (d, C-5a), 72.2 (t, C-4), 52.9 (d, C-10a), 40.2 (t, C-11), 38.9 (t, C-6), 30.4 (t, C-9), 28.6 (q, CH_3), 27.9 (q, CH_3), 25.2 (t, C-10) ppm. HRMS (ESI): *m/z* calcd. for $C_{13}H_{19}NO_4$ $[M+H]^+$ 254.1387, found 254.1386.

(*3aS,5aR,10aS,11aR*)-2,2-Dimethyloctahydro-8*H*-[1,3]dioxolo[4',5':3,4]furo[2,3-*f*]indolizine (21)

$Me_2S{\cdot}BH_3$ (2.0 M solution in THF, 5.4 mL, 11.0 mmol) was added to a stirred solution of DMP-protected *cis*-diol **20** (317 mg, 1.25 mmol) in dry THF (10 mL) under argon and the mixture was stirred at room temperature for 30 minutes, then heated at reflux 5 h. The mixture was then cooled to room temperature, quenched by the careful addition of MeOH (15 mL) and concentrated under vacuum. The crude colorless oil of the borane–tetrahydrofuran complex **21**·BH_3·THF (290 mg, 97%) [^{13}C NMR (150 MHz, $CDCl_3$): 113.2, 92.4, 86.5, 81.8, 73.8, 65.0 (THF), 62.8, 54.9, 52.8, 39.7, 31.2, 30.2 (THF), 29.5, 28.1, 23.1] was dissolved in MeOH (25 mL) and water (5 mL) was added. The resulting mixture was heated at reflux for 30 h. After cooling to room temperature, the reaction mixture was filtered through Celite and the filtrate was concentrated to afford free base **21** (266 mg, 89 %) as a colorless oil. Subjection of this oil to flash chromatography (CH_2Cl_2, CH_2Cl_2:acetone 8:1) gave a free base **21** (218 mg, 73%) as a colorless needles, mp 42.6-46.8 °C. $[\alpha]_D^{24}$ = +18.6 (*c* 1.03, acetone); TLC (Silica gel): R_f = 0.48 (CH_2Cl_2:isopropanol 1:2). IR (ATR): ν = 2984, 2958, 2931, 2860, 2807, 2787, 1479, 1453, 1379, 1369, 1333, 1296, 1229, 1218, 1155, 1109, 1072, 1059, 1032, 971, 943, 906, 873, 833, 788, 734, 681, 604, 537, 524, 497, 443. ^{1}H NMR (600 MHz, CD_3OD): δ 4.65 (dd, *J* = 5.3, 1.2 Hz, 1H, H-3a), 4.14 (dd, *J* = 10.1, 7.3 Hz, 1H, H-5a), 4.03 (dd, *J* = 11.1, 5.3 Hz, 1H, H-4), 3.82 (dd, *J* = 11.0, 1.5 Hz, 1H, H-4′), 3.12 (dd, *J* = 11.6, 7.3 Hz, 1H, H-6_{eq}), 2.98 (td, *J* = 9.0, 2.7 Hz, 1H, H-8), 2.37 (dd, *J* = 13.4, 2.8 Hz, 1H, H-11_{eq}), 2.19 (q, *J* = 9.1 Hz, 1H, H-8′), 2.09 (dd, *J* = 11.6, 10.3 Hz, 1H, H-6_{ax}), 2.09 - 2.03 (m, 1H, H-10a), 1.97 (dddd, *J* = 12.4, 9.6, 6.6, 3.9 Hz, 1H, H-10), 1.92 - 1.78 (m, 2H, 2xH-9), 1.71 (dd, *J* = 13.3, 12.1 Hz, 1H, H-11_{ax}), 1.48 – 1.40 (m, 1H, H-10′), 1.45 (s, 3H, CH_3), 1.38 (s, 3H, CH_3). ^{13}C NMR (151 MHz, CD_3OD): δ 113.3 (s, C-2), 92.5 (d, C-11a), 86.5 (d, C-3a), 81.9 (d, C-5a), 73.9 (t, C-4), 62.8 (d, C-10a), 55.0 (t, C-8), 52.8 (t, C-6), 39.7 (t, C-11), 31.3 (t, C-10), 29.6 (q, CH_3), 28.2 (q, CH_3), 23.1 (t, C-9) ppm. HRMS (ESI): *m/z* calcd. for $C_{13}H_{21}NO$ $[M+H]^+$ 240.1594, found 240.1591.

(*3S,3aS,4aS,9aR*)-Octahydrofuro[2,3-*f*]indolizine-3,3a(4*H*)-diol (9c)

DOWEX 50W x 8 (200-400 mesh) (2 g) was washed with MeOH (3 x 15 mL), free base of DMP-protected *cis*-diol **21** (750 mg, 3.1 mmol) was added in MeOH (35 mL) and reaction mixture was stirred overnight. After complete disappearance of the starting material (TLC monitored) and full deprotection (LC-MS analysis), the MeOH was decanted, DOWEX was washed with MeOH (2 x 10 mL) and aqueous ammonia (25%, 15 mL) was added, the mixture was stirred for 2 h at room

temperature, filtered, and water was removed in vacuo. This crude diol was subjection to flash chromatography (CH_2Cl_2, CH_2Cl_2:MeOH 5:1) gave a free base **9c** (517 mg, 82.8%) as a colorless needle. Recrystallization from *n*-heptane gave material (431 mg, 68%) as colorless needles; mp 166.2-167.6 °C. $[\alpha]_D^{24}$ = +29.38 (*c* 0.5, MeOH). TLC (Silica gel): R_f = 0.15 (CH_2Cl_2:isopropanol 1:2). IR (ATR): ν = 3491, 3085, 2994, 2939, 2881, 2840, 2822, 2740, 1455, 1439, 1384, 1327, 1241, 1205, 1136, 1111, 1057, 1022, 964, 934, 904, 858, 787, 752, 689, 661, 558, 443. ^{1}H NMR (600 MHz, CD_3OD): δ 4.36 (t, *J* = 8.2 Hz, 1H, H-3), 4.04 (t, *J* = 8.0 Hz, 1H, H-2), 4.00 (dd, *J* = 10.0, 6.9 Hz, 1H, H-9a), 3.69 (t, *J* = 8.4 Hz, 1H, H-2´), 3.15 (dd, *J* = 11.4, 6.9 Hz, 1H, H-9_{eq}), 2.97 (dt, *J* = 8.7, 2.5 Hz, 1H, H-7),2.24 (dd,*J* = 13.3, 3.0 Hz, 1H, H-4_{eq}), 2.20 (q, *J* = 9.1 Hz, 1H, H-7), 2.19 – 2.12 (m, 1H, H-4a), 1.95 (dd, *J* = 11.3, 10.1 Hz, 1H, H-9_{ax}), 1.94 - 1.76 (m, 3H, H-5 and 2x H-6), 1.47 (dd, *J* = 13.3, 11.8 Hz, 1H, H-4_{ax}), 1.46 - 1.40 (m, 1H,H-5´). ^{13}C NMR (151 MHz, CD_3OD): δ 82.8 (d, C-9a), 77.6 (s, C-3a), 72.2 (d, C-3), 71.6 (t, C-2), 61.8 (d, C-4a), 56.1 (t, C-9), 54.6 (t, C-7), 37.5 (t, C-4), 31.1 (t, C-5), 23.0 (t, C-6). HRMS (ESI): *m/z* calcd. for $C_{10}H_{17}NO_3$ $[M+H]^+$ 200.1281, found 200.1281.

(*3aS,5aR,10aR,11aR*)-2,2-Dimethyl-3*a*,4,5*a*,6,10*a*,11-hexahydro-8*H*-[1,3]dioxolo[4',5':3,4]furo-[2,3-*f*]indolizin-8-one (28)

n-BuLi (2.5 M in hexanes, 15.0 mL, 35.0 mmol) was added dropwise to freshly distilled *i*-Pr_2NH (4.94 mL, 35.0 mmol) in THF (25 mL) at 0° C (Ar). After stirring for 15 min at 0 °C, the solution was cooled to -78° C and *cis*-acetonide **20** (3.64 g, 14.4 mmol) in dry THF (25 mL) at -78 °C was added dropwise under Ar. The resulting solution was stirred at -78 °C for 45 minutes before being transferred dropwise *via* cannula (45 minutes) to PhSeBr (3.66 g, 14.4 mmol) in THF (80 mL) at -78 °C under Ar. After stirring at -78 °C for 45 minutes. (TLC monitoring, two products are formed, R_f = 0.36 polar *cis*-selanyl and R_f = 0.57 *trans*-selanyl less polar, EtOAc:*n*-hexane 2:1), saturated aqueous NH_4Cl (50 mL) and Et_2O (100 ml) were added, the layers were separated, and the aqueous phase was further extracted with Et_2O (2 x 35 mL). The combined organic extracts were washed with brine, dried ($MgSO_4$), filtered, rotary evaporated and chromatographed (EtOAc:hexanes 3:1) to give the two mono(phenylselanyl)-acetonide **27** (5.25 g, 89.5%, 55:45 from ^{1}H NMR analysis) as a light-yellow oil.

Elimination of phenylselanyl-acetonides 27. H_2O_2 (19.5 ml, 0.25 mmol, 30%) was added dropwise to the diastereomeric mixture of phenylselanyl-acetonides **27** (5.1 g, 12.5 mmol) in CH_2Cl_2 (250 mL) at -10 °C. The light-yellow reaction mixture became colorless and temperature rises slowly to +10 °C. After stirring for 3 hours at 10 °C, the reaction was carefully quenched by the addition of saturated Na_2CO_3 (35 ml) and stirred for 15 minutes. The layers were separated, and the aqueous phase was further extracted with CH_2Cl_2 (2 x 35 mL). The combined organic extracts were washed with brine, dried ($MgSO_4$), filtered and after rotary evaporated (3.05 g, 97%) purified by column chromatography (CH_2Cl_2, CH_2Cl_2:MeOH 15:1) to provide alkene-amide **28** (2.72 g, 87%) as a white solid. Recrystallization from *n*-heptane gave alkene-amide (2.34 g, 75%) as colorless needles, mp 106.1-108.2 °C. $[\alpha]_D^{20.2}$ = +7.1 (*c* 1.0, acetone). TLC (Silica gel): R_f = 0.71 (CH_2Cl_2:isopropanol 5:1). IR (ATR): ν = 2982, 2948, 2879, 1662, 1581, 1457, 1424, 1379, 1370, 1310, 1260, 1233, 1213, 1151, 1090, 1064, 1052, 1034, 4022, 972, 934, 918, 883, 862, 805, 748, 735, 705, 674, 637, 566, 525, 496, 432. ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.24 (dd, *J* = 5.9, 1.7 Hz, 1H, H-10), 6.05 (dd, *J* = 5.9, 1.7 Hz, 1H, H-9), 4.89 (dd, *J* = 5.4, 1.8 Hz, 1H, H-3a), 4.19 (tdd, *J* = 12.7, 3.5, 1.7 Hz, 1H, H-10a), 4.15 (dd, *J* = 11.0, 5.9 Hz, 1H, H-4), 4.06 - 3.99 (m, 2H, H-6_{eq} and H-5), 3.84 (dd, *J* = 11.0, 1.9 Hz, 1H, H-4´), 3.06 (ddd, *J* = 12.9, 6.7, 0.8 Hz, 1H, H-6_{ax}), 2.60 (dd, *J* = 13.4, 3.6 Hz, 1H, H-11_{eq}), 1.51 (t, *J* = 13.0 Hz, 1H, H-11_{ax}), 1.45 (s, 3H, CH_3), 1.37 (m, 3H, CH_3). ^{13}C NMR (150 MHz, $CDCl_3$): δ 169.8 (s, C-8), 148.7 (d, C-10), 128.1 (d, C-9), 113.4 (s, C-2), 91.1 (d, C-11a), 85.7 (d, C-3a), 79.9 (d, C-5a), 73.2 (t, C-4), 58.3

(d, C-10a), 38.8 (t, C-6), 37.6 (t, C-11), 29.2 (q, CH_3), 28.3 (q, CH_3) ppm. HRMS (ESI): *m/z* calcd. for $C_{13}H_{17}NO_4$ $[M+H]^+$ 252.1230, found 252.1233.

(*3aS,4aS,9aS*)-Hexahydrofuro[2,3-*f*]indolizine-3,7(*2H,3aH*)-dione (14)

To a well stirred solution of PPh_3 (20 g, 76.3 mmol, 2.56 eq.) and iodine (9.7 g, 76.3 mmol, 2.56 eq.) in dry THF (250 ml, yellow solution was formed) was added in four portions imidazole (5.2 g, 76.3 mmol, 2.56 eq.) at 0 °C. After 30 minutes, a solution of *cis*-diol **8c** (6.35 g, 29.8 mmol) in THF (5 mL) was added. Reaction was allowed to warm slowly to room temperature and stirred overnight (colorless solution). Reaction mixture was poured into CH_2Cl_2 (300 mL) and treated with aqueous $Na_2S_2O_3$ solution (50 mL). Organic layer was separated, and aqueous phase was extracted with CH_2Cl_2 (3x20 mL), the combined organic layer was dried over anhydrous Na_2SO_4, filtered and concentrated. A mixture (12.5 g) containing unreacted triphenylphosphine, triphenylphosphine oxide and ketone are obtained. This mixture was purified by slow column chromatography (EtOAc:*i*-hexane 1:1 removed PPh_3 and EtOAc:*i*-hexane 4:1 removed PPh_3=O), and finally using a mixture of CH_2Cl_2:acetone 3:1 afforded ketone **14** (4.68 g, 80.5%). Recrystallization from a mixture of THF:*n*-heptane gave material (4.13 g, 71%) as colorless needles, mp 148.0-148.6 °C. $[\alpha]_D^{24}$ = +150,13 (*c* 1, CH_2Cl_2). TLC (Silica gel): R_f = 0.56 (CH_2Cl_2:isopropanol 10:1). IR (ATR): ν = 2971, 2952, 2881, 2849, 1748, 1669, 1468, 1435, 1379, 1344, 1307, 1290, 1251, 1230, 1212, 1183, 1124, 1037, 987, 927, 912, 859, 815, 754, 742, 715, 669, 654, 608, 559, 538, 484, 465, 442. ^{1}H NMR (600 MHz, $CDCl_3$): δ4.66 (td, *J* = 8.3, 6.8 Hz, 1H, H-9a), 4.20 (dd, *J* = 13.9, 6.5 Hz, 1H, H-9_{eq}), 4.15 (dd, *J* = 17.7, 1.2 Hz, 1H, H-2), 4.00 (d, *J* = 17.7 Hz, 1H, H-2´), 3.36 (dddd, *J* = 11.9, 7.4, 6.2, 3.7 Hz, 1H, H-4a), 2.84 (t, *J* = 7.4 Hz, 1H, H-3a), 2.80 (dd, *J* = 14.0, 8.8 Hz, 1H, H-9_{ax}), 2.46 – 2.35 (m, 3H, 2xH-6 and H-4_{eq}), 2.24 (dddd, *J* = 13.1, 9.3, 7.6, 5.6 Hz, 1H, H-5), 1.64 -1.57 (m, 2H, H-5´and H-4_{ax}). ^{13}C NMR (150 MHz, $CDCl_3$): δ 214.2 (s, C-3), 174.0 (s, C-7), 72.9 (d, C-9a), 69.1 (t, C-2), 52.7 (d, C-4a), 45.7 (d, C-3a), 40.0 (t, C-9), 30.3 (t, C-6), 29.5 (t, C-4), 24.8 (t, C-5) ppm. HRMS (ESI): *m/z* calcd. for $C_{10}H_{13}NO_3$ $[M+H]^+$ 196.0968, found 196.0968.

(*3S,3aR,4aS,9aS*)-3-Hydroxyoctahydrofuro[2,3-*f*] indolizin-7(*2H*)-one (23a)

The freshly crystallized keto-lactam **14** (585 mg, 3 mmol) was dissolved in dry THF (30 mL) and cooled to -45° C with stirring. K-Selectride (4 mL of a 1.0 M solution in THF) was added (5 minutes) dropwise *via* a syringe and the reaction mixture was stirred for 45 minutes at -45° C, then was quenched at the same temperature by addition of MeOH (3 mL), NaOH (1.5 mL, 25%) and 30% aqueous H_2O_2 (1.5 mL) and stirred for 30 minutes. The mixture was concentrated to dryness and extracted with hot AcOEt (3 x 30 mL). The combined organic solvents were washed with water, dried over anhydrous $MgSO_4$ and concentrated *in vacuo*. Recrystallization of the solid (564 mg, 95.2%) from toluene gave *cis*-alcohol **23a** (473 mg, 84%) as a colorless crystal; mp 164.5-165.3 °C. $[\alpha]_D^{24}$ = +22,6 (*c* 1, MeOH). TLC (Silica gel): R_f = 0.56 (CH_2Cl_2:isopropanol 10:1). IR (ATR): ν = 3312, 2986, 2908, 1651, 1455, 1446, 1421, 1361, 1305, 1264, 1248, 1217, 1161, 1115, 1092, 1064, 1002, 989, 970, 921, 822, 793, 765, 750, 694, 656, 603, 560, 529, 452, 422. ^{1}H NMR (600 MHz, CD_3OD): δ4.42 (t, *J* = 5.0 Hz, 1H, H-3), 4.06 (q, *J* = 7.8 Hz, 1H, H-9a), 4.03 – 3.96 (m, 1H, H-4a), 4.01 (dd, *J* = 9.6, 4.6 Hz, 1H, H-2), 3.93 (dd, *J* = 12.5, 6.6 Hz, 1H, H-9_{eq}), 3.85 (d, *J* = 9.7 Hz, 1H, H-2´), 3.82 - 3.76 (m, 1H, H-4a), 3.05 (dd, *J* = 12.5, 9.6 Hz, 1H, H-9_{ax}), 2.45 – 2.32 (m, 3H, 2xH-6 and H-3a), 2.28 (dd, *J* = 13.6, 3.9 Hz, 1H, H-4_{eq}), 2.27 – 2.20 (m, 1H, H-5), 1.67 (ddd, *J* = 13.6, 12.2, 7.2 Hz, 1H, H-4_{ax}), 1.61 – 1.53 (m, 1H, H-5´). ^{13}C NMR (150 MHz, CD_3OD): δ 176.6 (s, C-7), 77.4 (t, C-2), 75.0 (d, C-3), 74.9 (d, C-9a), 55.8 (d, C-4a), 43.6 (t, C-9), 42.3 (d, C-3a), 31.7 (t, C-6), 31.2 (t, C-4), 26.3 (t, C-5) ppm. HRMS (ESI): *m/z* calcd. for $C_{10}H_{15}NO_3$ $[M+H]^+$ 198.1125, found 198.1122. Reduction of the ketone **14** with $NaBH_4$ at -40 °C or 0 °C provided a mixture of *cis/trans* alcohols in a ratio 96:4 (from ^{1}H NMR analysis), finally when the reduction was carried out under reflux in methanol, a mixture of *cis/trans* alcohols in a ratio 9:1 was obtained.

(*3S,3aS,4aS,9aS*)-7-Oxodecahydrofuro[2,3-*f*]indolizin-3-yl acetate (24)

To a stirred solution of *secondary*-alcohol **23a** (513 mg, 2.6 mmol) in of dry CH_2Cl_2 (30 mL) was added acetic anhydride (0.67 g, 0.72 mL, 6.5 mmol, 2.5 eq.), 4-(dimethylamino)pyridine (DMAP, 43 mg, 0.35 mmol) and triethylamine (0.66 g, 0.91 mL, 6.5 mmol, 2.5 eq.). The reaction mixture was stirred until disappearance of the starting material (monitored by TLC CH_2Cl_2:acetone 4:1). The mixture was quenched with a saturated aqueous $NaHCO_3$ solution (10 mL). The aqueous layer was extracted with diethyl ether and the organic layers were washed with a saturated aqueous $CuSO_4$ solution and water, dried over $MgSO_4$ and concentrated under vacuum. The yellow oil was purified by flash chromatography on silica gel column (CH_2Cl_2, CH_2Cl_2:acetone 12:1) to afford acetyl **24** (590 mg, 95%) as an oil, which quickly crystallized on standing in a fridge. Analytically pure compound was obtained by crystallization from *n*-hexane (491 mg, 79%); mp 67.2-67.9 °C. $[\alpha]_D^{24}$ = -4.17 (*c* 1.0, acetone); TLC (Silica gel): R_f = 0.33 (CH_2Cl_2:isopropanol 15:1). IR (ATR): ν = 2977, 2943, 2877, 1732, 1680, 1434, 1422, 1373, 1349, 1283, 1227, 1160, 1089, 1077, 1060, 1043, 1020, 998, 957, 932, 908, 855, 819, 763, 725, 655, 631, 601, 565, 536, 525, 509, 442, 428. ^{1}H NMR (600 MHz, CD_3OD): δ 5.37 (ddd, *J* = 6.1, 4.8, 1.3 Hz, 1H, H-3), 4.08 (dd, *J* = 10.7, 4.9 Hz, 1H, H-2), 4.05 (dt, *J* = 9.5, 7.3 Hz, 1H, H-9a), 3.94 (dd, *J* = 12.8, 6.8 Hz, 1H, H-9_{eq}), 3.85 (dd, *J* = 10.7, 1.4 Hz, 1H, H-2′), 3.82 - 3.76 (m, 1H, H-4a), 2.81 (dd, *J* = 12.7, 9.7 Hz, 1H, H-9_{ax}), 2.65 (q, *J* = 6.7 Hz, 1H, H-3a), 2.30 – 2.19 (m, 3H, 2xH-6 and H-5), 2.17 (ddd, *J* = 14.3, 4.1, 1.2 Hz, 1H, H-4_{eq}), 1.70 (dd, *J* = 14.3, 11.5, 7.4 Hz, 1H, H-4_{ax}), 1.59 – 1.48 (m, 1H, H-5′). ^{13}C NMR (150 MHz, CD_3OD): δ 173.7 (s, C-7), 170.9 (s, $CH_3\underline{CO}$), 77.3 (d, C-3), 74.5 (t, C-2), 74.4 (d, C-9a), 53.9 (d, C-4a), 42.3 (d, C-9), 40.3 (t, C-3a), 30.9 (t, C-6), 30.7 (t, C-4), 26.2 (t, C-5), 21.3 (q, CH_3) ppm. HRMS (ESI): *m/z* calcd. for $C_{12}H_{17}NO_4$ $[M+H]^+$ 240.1230, found 240.1232.

(*3S,4aS,9aS*)-Decahydrofuro[2,3-*f*]indolizin-3-ol (25)

LAH (320 mg, 8.4 mmol, 4 eq.) was added to a solution of a freshly crystallized secondary acetyl-THF **24** (501 mg, 2.1 mmol) in dry THF (25 mL) at room temperature and the mixture then heated at reflux for 2.5 h. The slurry was then warmed to ambient temperature and after an additional 40 minutes was carefully quenched with 2:1 w:w $Na_2SO_4.10H_2O$:Celite (10 g). The reaction mixture was diluted with THF (50 mL) and NaOH (1 g) in H_2O (50 mL) was added. After 30 minutes, the solid was filtered, washed with hot THF (2 x 50 mL), and the combined organic layers were dried with $MgSO_4$, filtered and concentrated in vacuo to give a solid (323 mg, 84%). Recrystallization of the solid from anhydrous *n*-hexane gave **25** as white crystals; mp 112.3-113.8 °C. $[\alpha]_D^{24}$ = +27.3 (*c* 0.50, MeOH). TLC (Silica gel): R_f = 0.31 (CH_2Cl_2:isopropanol 3:1). IR (ATR): ν = 3143, 2904, 2832, 1458, 1429, 1387, 1345, 1314, 1271, 1159, 1116, 1080, 1068, 1029, 1010, 931, 914, 880, 851, 759, 735, 508, 453, 422. ^{1}H NMR (600 MHz, CD_3OD): δ 4.42 (t, *J* = 5.0 Hz, 1H, H-3), 4.06 (q, *J* = 7.8 Hz, 1H, H-9a), 4.03 – 3.96 (m, 1H, H-4a), 4.01 (dd, *J* = 9.6, 4.6 Hz, 1H, H-2), 3.93 (dd, *J* = 12.5, 6.6 Hz, 1H, H-9_{eq}), 3.85 (d, *J* = 9.7 Hz, 1H, H-2′), 3.82 - 3.76 (m, 1H, H-4a), 3.05 (dd, *J* = 12.5, 9.6 Hz, 1H, H-9_{ax}), 2.45 – 2.32 (m, 3H, 2xH-6 and H-3a), 2.28 (dd, *J* = 13.6, 3.9 Hz, 1H, H-4_{eq}), 2.27 – 2.20 (m, 1H, H-5), 1.67 (ddd, *J* = 13.6, 12.2, 7.2 Hz, 1H, H-4_{ax}), 1.61 – 1.53 (m, 1H, H-5′). ^{13}C NMR (151 MHz, CD_3OD): δ 176.6 (s, C-7), 77.4 (t, C-2), 75.0 (d, C-3), 74.9 (d, C-9a), 55.8 (d, C-4a), 43.6 (t, C-9), 42.3 (d, C-3a), 31.7 (t, C-6), 31.2 (t, C-4), 26.3 (t, C-5) ppm. HRMS (ESI): *m/z* calcd. for $C_{10}H_{17}NO_2$ $[M+H]^+$ 184.1332, found 184.1331.

(*3aS,5aR,9R,10R,10aR,11aR*)-9,10-Dihydroxy-2,2-dimethyloctahydro-8*H*-[1,3]dioxolo-[4',5':3,4]-furo[2,3-*f*]indolizin-8-one (29a)

A solution of NMO (586 mg, 5.0 mmol) in water (1 mL) was added to a mixture of acetone and water (50 ml, 5:1) at 0° C. Olefin **20** (1.25 g, 5.0 mmol) was then added in one portion, the mixture allowed

to stirred for 10 minutes and then OsO_4 (64 mg, 0.3 mmol) in *t*-BuOH (2 mL) was added dropwise over 5 minutes. The mixture was allowed to continue stirring and warm slowly to room temperature (TLC monitoring, 14 hours). The reaction was quenched by the addition of sodium sulfite (10 g) and was stirred at room temperature 15 minutes, 45 g of SiO_2 was added and concentrated *in vacuo*. The resulting solid was purified by flash chromatography (CH_2Cl_2, CH_2Cl_2:MeOH 5:1) to afford the diastereomeric mixture of *endo*/*exo*-diols (28:72 from ^{1}H NMR analysis) as white solid (1.14 g, 80.3%). This mixture was redissolved in CH_2Cl_2 and converted to acetonide **30a** (see experiment below). The small amount (100 mg) of crude diols was separated by slow column chromatography (CH_2Cl_2, CH_2Cl_2:MeOH 10:1 to CH_2Cl_2:MeOH 5:1) to yield *exo*-diol **29a** (62 mg). Analytically pure compound was obtained by crystallization from isopropanol:*n*-heptane (47 mg was obtained from 62 mg); mp 144.1-146.9 °C. $[\alpha]_D^{20.3}$ = +17.8 (*c* 1.0, MeOH). TLC (Silica gel): R_f = 0.27 (CH_2Cl_2:isopropanol 3:1). IR (ATR): ν = 3330, 3250, 3020, 2937, 1668, 1575, 1416, 1370, 1297, 1139, 1105, 1064, 987, 933, 877, 771, 673, 522, 489, 430. ^{1}H NMR (600 MHz, CD_3OD): δ 4.82 (dd, *J* = 5.4, 1.3 Hz, 1H, H-3a), 4.20 (t, *J* = 5.9 Hz, 1H, H-9), 4.14 (dd, *J* = 11.0, 5.3 Hz, 1H, H-4), 4.00 (ddd, *J* = 8.9, 5.8, 3.2 Hz, 1H, H-10), 3.93 (t, *J* = 7.5 Hz, 1H, H-5a), 3.88 (dd, *J* = 13.5, 7.1 Hz, 1H, H-6_{eq}), 3.81 (dd, *J* = 10.9, 1.9 Hz, 1H, H-4), 3.46 (dd, *J* = 12.4, 3.2 Hz, 1H, H-10a), 2.95 (dd, *J* = 13.5, 7.6 Hz, 1H, H-6_{ax}), 2.43 (dd, *J* = 13.6, 3.5 Hz, 1H, H-11_{eq}), 1.81 (dd, *J* = 13.4, 12.7 Hz, 1H, H-11_{ax}), 1.43 (s, 3H, CH_3), 1.38 (s, 3H, CH_3). ^{13}C NMR (150 MHz, CD_3OD): δ 171.7 (s, C-8), 113.3 (s, C-2), 91.0 (d, C-11a), 85.8 (d, C-3a), 79.6 (d, C-5a), 72.9 (t, C-4), 59.2 (d, C-10a), 39.3 (t, C-6), 36.7 (t, C-11), 29.1 (q, CH_3), 28.2 (q, CH_3) ppm. HRMS (ESI): *m/z* calcd. for $C_{13}H_{19}NO_6$ $[M+H]^+$ 286.1285, found 286.1287.

Preparation of diacetonides (30a,b) from a mixture of *cis*- and *trans*-dioles (29a,b)

2,2-Dimethoxypropane (6.9 mL, 56.0mmol, 10 eq.) and PTSA (50 mg, 0.3 mmol) were added to a crude mixture of diols **(29a,b)** (1.59 g, 5.6 mmol), prepared above, in dry acetone (100 mL) under argon at room temperature. After stirring for 18 h, the reaction mixture was quenched with 15% Na_2CO_3 (5 mL) and the solvent was removed under reduced pressure. The solid residue was purified by column chromatography on silica gel (CH_2Cl_2, CH_2Cl_2:acetone 15:1, CH_2Cl_2:acetone 5:1) and provided three products: less polar *endo*-diacetonid-olefin **30b** (74mg, 4.1%) as a white solid, polar *exo*-diacetonide **30a** (1.29 g, 71.2 %) as a white solid and most polar *endo*-diacetonide **31** (199 mg, 11%) as a white solid.

(*3aS,5aR,8aS,11aS,12aR*)-2,2,10,10-Tetramethyl-3*a*,4,5*a*,6,8*a*,11*a*-hexahydro-8*H*-[1,3]-dioxolo [4',5':3,4]furo[2,3-*f*][1,3]dioxolo[4,5-*a*]indolizin-8-one (31); mp 158.4-159.6 °C. $[\alpha]_D^{20.3}$ = + 56.7 (*c* 0.5, acetone). TLC (Silica gel): R_f = 0.53 (CH_2Cl_2:acetone 5:1). IR (ATR): ν = 2987, 2939, 2910, 1728, 1675, 1451, 1419, 1381, 1371, 1309, 1249, 1238, 1215, 1173, 1149, 1092, 1054, 1028, 1003, 965, 941, 905, 865, 833, 821, 800, 759, 700, 691, 662, 625, 607, 516, 504, 474, 414.^{1}H NMR (600 MHz, CD_3COCD_3): δ 4.91 (dd, *J* = 5.4, 1.5 Hz, 1H, H-3a), 4.72 (d, *J* = 6.4 Hz, 1H, H-8a), 4.51 (d, *J* = 6.4 Hz, 1H, H-11a), 4.15 (dd, *J* = 11.1, 5.5 Hz, 1H, H-4), 4.04 (dd, *J* = 13.8, 8.0 Hz, 1H, H-6_{eq}), 3.91 (dd, *J* = 8.9, 8.3 Hz, 1H, H-5a), 3.81 (dd, *J* = 11.1, 1.7 Hz, 1H, H-4´), 3.64 (ddd, *J* = 13.1, 3.5, 0.6 Hz, 1H, H-11b), 2.82 (dd, *J* = 14.3, 5.9 Hz, 1H, H-6_{ax}), 2.48 (dd, *J* = 13.4, 3.5 Hz, 1H, H-12_{eq}), 1.73 (t, *J* = 13.3 Hz, 1H, H-12_{ax}), 1.42 (s, 3H, CH_3), 1.37 (s, 3H, CH_3), 1.33 (s, 3H, CH_3), 1.32 (s, 3H, CH_3). ^{13}C NMR (151 MHz, CD_3COCD_3): δ 169.4 (s, C-8), 112.9 (s, C-2), 112.7 s, (C-10), 91.5 (d, C-12a), 85.1 (d, C-3a), 78.6 (d, C-5a), 78.2 (d, C-8a), 77.8 (d, C-11a), 73.0 (t, C-4), 58.3 (d, C-11b), 38.9 (t, C-6), 37.9 (t, C-12), 29.5 (q, CH_3), 28.1 (q, CH_3), 27.1 (q, CH_3), 25.6 (q, CH_3) ppm. HRMS (ESI): *m/z* calcd. for $C_{16}H_{21}NO_6$ $[M+H]^+$ 324.1442, found 324.1442.

(*3aS,5aR,8aR,11aR,11bR,12aR*)-2,2,10,10-Tetramethyloctahydro-8*H*-[1,3]dioxolo[4',5':3,4]-furo-[2,3-*f*][1,3]dioxolo[4,5-*a*]indolizin-8-one (30a); mp 226.1–226.9 °C. $[\alpha]_D^{24}$ = + 24.1 (*c* 0.5, acetone). TLC (Silica gel): R_f = 0.53 (CH_2Cl_2:acetone 5:1). IR (ATR): ν = 2988, 2947, 1702, 1683, 1456, 1380,

1369, 1331, 1270, 1214, 1157, 1111, 1089, 1076, 1043, 980, 968, 943, 866, 823, 803, 762, 732, 709, 633, 604, 573, 523, 492, 424. ^{1}H NMR (600 MHz, CD_3OD): δ =4.91 (dd, *J* = 5.4, 1.3 Hz, 1H), 4.72 (d, *J* = 6.3 Hz, 1H), 4.51 (d, *J* = 6.3 Hz, 1H), 4.15 (dd, *J* = 11.1, 5.4 Hz, 1H), 4.04 (dd, *J* = 13.8, 8.0 Hz, 1H), 3.91 (dd, *J* = 8.87 Hz, 1H), 3.81 (dd, *J* = 11.1, 1.6 Hz, 1H), 3.64 (dd, *J* = 13.1, 3.4 Hz, 1H), 2.82 (dd, *J* = 13.8, 9.3 Hz, 1H), 2.48 (dd, *J* = 13.4, 3.5 Hz, 1H), 1.73 (t, *J* = 13.3 Hz, 1H), 1.42 (s, 3H), 1.37 (s, 3H), 1.33 (s, 3H), 1.32 (s, 3H). ^{13}C NMR (150 MHz, CD_3OD): δ 169.4 (s, C-8), 112.9 (s, C-2), 112.7 s, (C-10), 91.5 (d, C-12a), 85.1 (d, C-3a), 78.6 (d, C-5a), 78.2 (d, C-8a), 77.8 (d, C-11a), 73.0 (t, C-4), 58.3 (d, C-11b), 38.9 (t, C-6), 37.9 (t, C-12), 29.5 (q, CH_3), 28.1 (q, CH_3), 27.1 (q, CH_3), 25.6 (q, CH_3) ppm. HRMS (ESI): *m/z* calcd. for $C_{16}H_{23}NO_6$ $[M+H]^+$ 326.1598, found 326.1598.

(*3aS,5aR,8aS,11aS,12aR*)-2,2,10,10-Tetramethyloctahydro-8*H*-[1,3]dioxolo-[4',5':3,4]-furo-[2,3-*f*][1,3]dioxolo[4,5-*a*]indolizin-8-one (30b); mp 154-156.8 °C. $[\alpha]_D^{20.2}$ = +47.8 (*c* 0.75, acetone). TLC (Silica gel): R_f = 0.38 (CH_2Cl_2:acetone 5:1). IR (ATR): ν = 3330, 3250, 3020, 2937, 1668, 1575, 1416, 1370, 1297, 1139, 1105, 1064, 987, 933, 877, 771, 673, 522, 489, 430. ^{1}H NMR (600 MHz, CD_3COCD_3): δ 4.80 (dd, *J* = 5.6, 2.5 Hz, 1H, H-3a), 4.73 (dd, *J* = 5.6, 4.7 Hz, 1H, H-11a), 4.67 (d, *J* = 5.7 Hz, 1H, H-8a), 4.15 (dd, *J* = 10.7, 5.6 Hz, 1H, H-4), 4.03 (t, *J* = 5.6 Hz, 1H, H-5a), 3.80 (dd, *J* = 10.7, 2.5 Hz, 1H, H-4´), 3.77 (ddd, *J* = 12.8, 4.7, 3.0 Hz, 1H, H-11b), 3.65 (dd, *J* = 14.3, 5.3 Hz, 1H, H-6_{eq}), 3.18 (dd, *J* = 14.3, 5.9 Hz, 1H, H-6_{ax}), 2.28 (dd, *J* = 13.9, 3.0 Hz, 1H, H-12_{eq}), 2.17 (dd, *J* = 13.8, 12.9 Hz, 1H, H-12_{ax}), 1.46 (s, 3H, CH_3), 1.39 (s, 3H, CH_3), 1.34 (s, 3H, CH_3), 1.33 (s, 3H, CH_3). ^{13}C NMR (151 MHz, acetone): δ 170.9 (s, C-8), 113.7, 112.7 (s, C-2 and C-10), 90.5 (s, C-12a), 86.5 (d, C-3a), 80.0 (d, C-5a), 79.2 (d, C-8a), 75.6 (d, C-11a), 72.6 (t, C-4), 53.4 (d, C-11b), 40.0 (t, C-6), 33.9 (t, C-12), 28.5 (q, CH_3), 28.3 (q, CH_3), 27.3 (q, CH_3), 26.3 (q, CH_3) ppm. HRMS (ESI): *m/z* calcd. for $C_{16}H_{23}NO_6$ (325,3610) $[M+H]^+$ 326.1598, found 326.1597.

Epoxidation of DHF-5 under various conditions (Methods A–E)

Method A: *Epoxidation with m-CPBA.*

To a stirred and cooled (0 °C) solution of the DHF-**5** (896 mg, 5.0 mmol) in dry CH_2Cl_2 (30 mL) was added portion wise 68% *m*-CPBA (1.52 g, 6.0 mmol, 1,2 eq.). After standing at room temperature overnight the suspension was filtered, organic layer was washed with saturated Na_2CO_3, dried and evaporated in vacuum. The solid (838 mg, 86%) was a mixture of *endo*:*exo*-epoxide (25:75 from ^{1}H NMR analysis) as a non-separable mixture of two diastereomers.

Method B: *Epoxidation with HCO_2H and H_2O_2.*

(*1aS,3aR,8aS,9aR*)-Octahydro-6*H*-oxireno[2',3':3,4]furo[2,3-*f*]indolizin-6-one (6). To concentrated formic acid (3.91 mL, 0.10 mol) was added hydrogen peroxide (30% aqueous solution, 2.29 mL, 0.13 mol). After 15 minutes DHF-**5** (896 mg, 5.0 mmol) was added at cooling (0 °C). The reaction mixture was stirred for 20 h (TLC monitoring), diluted with water (10 mL), extracted with CH_2Cl_2 (3×50 mL), and combined organic layers were dried over $MgSO_4$ and concentrated to give a mixture of *endo*:*exo*-epoxide (78:22 from ^{1}H NMR analysis) as a pale yellow solid (732 mg, 75%). This mixture of epoxides was heated in dry Et_2O (50 ml) 10 minutes, cooled to 0 °C and after 30 minutes the solid was filtered off. Recrystallization from DIPE gave **6** (549 mg, 56.3%) as colorless needles; mp 114.5-116.2 °C. $[\alpha]_D^{24}$ = -10.9 (*c* 1, MeOH). TLC (Silica gel): R_f = 0.71 (CH_2Cl_2:isopropanol 5:1). IR (ATR): ν = 2974, 2930, 2875, 1669, 1444, 1425, 1368, 1308, 1297, 1260, 1224, 1191, 1174, 1149, 1086, 1072, 1055, 1014, 994, 937, 907, 874, 843, 818, 764, 726, 659, 650, 621, 567, 556, 493, 481, 429. ^{1}H NMR (600 MHz, CD_3OD): δ 4.34 (dd, *J* = 13.0, 7.2 Hz, 1H, H-4_{eq}), 4.08 (d, *J* = 10.9 Hz 1H, H-2), 4.05 (d, *J* = 10.9 Hz 1H, H-2), 4.02 – 3.97 (m, 2H, H-1a and H-8a), 3.97 (dd, *J* = 10.1, 6.9 Hz, 1H, H-3a), 2.77 (ddd, *J* = 14.2, 10.2, 1.2 Hz, 1H, H-7), 2.66 (ddd, *J* = 17.3, 10.1, 5.5 Hz, 1H), 2.58 (dddd, *J* = 17.3, 10.1, 6.8, 1.6 Hz, 1H, H-7´), 2.48 (dddd, *J* = 12.9, 10.1, 7.9, 5.5

Hz, 1H, H-8), 2.24 (t, J = 12.5 Hz, 1H, H-9_{ax}), 2.16 (dd, J = 13.2, 4.2 Hz, 1H, H-9_{eq}), 1.92 (dddd, J = 12.9, 10.1, 6.6, 5.4 Hz, 1H, H-8′). ^{13}C NMR (151 MHz, CD_3OD): δ 176.7 (s, C-6), 73.6 (d, C-3a), 68.1 (t, C-2), 67.6 (d, C-9a), 62.2 (d, C-1a), 57.4 (d, C-8a), 42.2 (t, C-4), 34.8 (t, C-9), 31.1 (t, C-7), 25.0 (t, C-8) ppm. HRMS (ESI): *m/z* calcd. for $C_{10}H_{13}NO_3$ $[M+1]^+$ 196.0968, found 196.0968.

Method C: *Epoxidation with CH_3CO_3H.*
To commercially available concentrated peracetic acid (6.73 mL, 0.10 mol) DHF-**5** (896 mg, 5.0 mmol) was added at cooling (0 °C). The reaction mixture was stirred for 32 h (TLC monitoring), diluted with water (10 ml), extracted with CH_2Cl_2 (3×50 mL). Combined organic layers were washed with saturated Na_2CO_3, dried with $MgSO_4$ and concentrated to give a mixture of *endo*- and exo-epoxide (70:30 from ^{1}H NMR spectra) as pale yellow solid (693 mg, 71%). Worked-up the solid as above gives a *endo*-epoxide (497 mg, 51%) as colorless needles with the same physico-chemical date as above.

Method D: *Epoxidation with CF_3CO_2H and H_2O_2.*
Using the procedure described in method B, from DHF-**5** (896 mg, 5.0 mmol), CF_3CO_2H (7.65 mL, 0.1 mol) and hydrogen peroxide (30% aqueous solution, 2.29 mL, 0.13 mol) was stirred 8 hours. Worked-up the solid (702 mg, 71%, *endo:exo*-epoxide (27:73 from ^{1}H NMR analysis) as above gives a *endo*-epoxide (547 mg, 56%) as colorless needles with the same physico-chemical date as above.

Method E: *Epoxidation with $Na_2WO_4.10H_2O$ and H_2O_2.*
To hydrogen peroxide (30% aqueous solution, 2.5 mL, 0.105 mol) was added $Na_2WO_4.10H_2O$ (330 mg, 1.0 mmol) at 0 °C. After 15 minutes DHF-**5** (360 mg, 2.0 mmol) was added at cooling (0 °C). The light-yellow reaction mixture was stirred for 13 h (TLC monitoring), diluted with water (10 mL), extracted with CH_2Cl_2 (3×50 mL), combined organic layers were dried over $MgSO_4$ and concentrated to give a mixture of *endo*:*exo*-epoxide (23/77 from ^{1}H NMR analysis) as a pale yellow solid (315 mg, 80.3%). Worked-up the solid as above gives a *endo*-epoxide (239 mg, 61%) as colorless needles with the same physico-chemical date as above.

(*3R,3aS,4aS,9aR*)-3,3a-Dihydroxyoctahydrofuro[2,3-*f*] indolizin-7(2*H*)-one (8a)
Method A: *Preparation of trans-diol **8a** from a mixture of epoxides (**6,7**).*
A mixture of *endo*:*exo*-diols (ratio 25:75 from epoxidation of DHF-**5** with *m*-CPBA) (585 mg, 3 mmol) was heated at 60 °C in a mixture of CF_3CO_2H:H_2O (10 mL, 3:1) for 12 hours. The mixture was cooled to 15 °C and concentrated under reduced pressure. The residue was dissolved in MeOH (45 mL), SiO_2 (15 g) was added, again concentrated and the remaining solid purified by flash chromatography (CH_2Cl_2, CH_2Cl_2:MeOH 5:1) to give **8a** (518 mg, 81%). Recrystallization from a mixture of THF:*n*-heptane gave *trans*-diol **8a** (441 mg, 69%) as colorless needles, mp 87.6-91.8 °C. $[\alpha]_D^{20.3}$ = + 93.2 (*c* 1.15, H_2O). TLC (Silica gel): R_f = 0.09 (CH_2Cl_2:isopropanol 3:1). IR (ATR): ν = 3372, 3260, 2982, 2945, 2898, 1648, 1470, 1443, 1422, 1357, 1283, 1270, 1186, 1174, 1120, 1091, 1070, 1049, 1035, 1003, 987, 922, 899, 872, 812, 788, 736, 629, 606, 561, 523, 482, 464, 443. ^{1}H NMR (600 MHz, CD_3OD): δ 4.25 (dd, J = 9.5, 4.8 Hz, 1H, H-2), 4.07 (d, J = 4.3 Hz, 1H, H-3), 4.06 - 4.02 (m, 1H, H-4a), 4.03 (dd, J = 12.9, 7.3 Hz, 1H, H-9_{eq}), 3.83 (dd, J = 9.5, 1.0 Hz, 1H, H-2), 3.73 (dd, J = 9.6, 7.3 Hz, 1H, H-9a), 3.03 (dd, J = 12.8, 10.3 Hz, 1H, H-9_{ax}), 2.56 (dd, J = 13.7, 4.2 Hz, 1H, H-4_{eq}), 2.47 - 2.36 (m, 2H, 2xH-6), 2.25 (dddd, J = 12.8, 9.2, 7.8, 6.1 Hz, 1H, H-5), 1.61 (dddd, J = 12.8, 9.8, 7.4, 5.7 Hz, 1H, H-5′), 1.60 (dd, J = 13.7, 11.4 Hz,1H, H-4_{ax}). ^{13}C NMR (151 MHz, CD_3OD): δ 176.6 (s, C-7), 81.1 (d, C-9a), 80.7 (d, C-3), 80.3 (d, C-3a), 76.6 (t, C-2), 56.0 (d, C-4a), 42.7 (t, C-9), 41.4 (t, C-4), 31.4 (t, C-6), 26.0 (t, C-5) ppm. HRMS (ESI): *m/z* calcd. for $C_{10}H_{15}NO_4$ $[M+H]^+$ 214.1074, found 214.1070.

Method B: *Preparation of trans-diol **8a** from exo-epoxide **6**.*
A *exo*-epoxide **6** (586 mg, 3 mmol) was added at room temperature to a mixture of CF_3CO_2H:H_2O (10 mL, 3:1). The mixture was heated at 55 °C (TLC monitoring), cooled and concentrated under reduced pressure. The residue was dissolved in MeOH (45 mL), SiO_2 (10 g) was added, again concentrated and the remaining solid purified by flash chromatography (CH_2Cl_2, CH_2Cl_2:MeOH 5:1) to give a *trans*-diol (498.7 mg, 78%). Recrystallization from a mixture of THF:*n*-heptane gave *trans*-diol **8a** (435 mg, 68%) as colorless needles, mp 87.7-91.6 °C. TLC (Silica gel): R_f = 0.09 (CH_2Cl_2:isopropanol 3:1).

Method C: *Preparation of trans-diol **8a** from DHF-**5** without isolation of epoxide **6**.*
To CF_3COOH (7.65 ml, 0.1 mol) was added hydrogen peroxide (30% aqueous solution, 2.29 mL, 130 mmol). After 15 minutes DHF-5 (896 mg, 5.0 mmol) was added at cooling (0 °C). The reaction mixture was stirred for 6h at room temperature, then the temperature was raised to 60 °C, stirred 12 h (TLC monitoring), cooled and concentrated. The residue was dissolved in MeOH (50 ml), SiO_2 (20 g) was added, concentrated and the remaining solid purified by flash chromatography (CH_2Cl_2, CH_2Cl_2/MeOH 5/1) to give a *trans*-diole (864 mg, 81%). Recrystallization from a mixture of THF/*n*-heptane gave *trans*-diole **8a** (757 mg, 71%) as colorless needles, mp 87.9 - 91.5°C.

(*3aS,4aS,9aR*)-Octahydrofuro[2,3-*f*]indolizin-3a(4*H*)-ol (26)
To a solution of dry THF (50 mL) and LAH (350 mg, 9.2 mmol) a solution of epoxide **6** (586 mg, 3 mmol) in dry THF (10 mL) was added dropwise at room temperature. After 15 minutes, the reaction was heated to reflux for 90 minutes. The resulting mixture was cooled, Celite (10 g) was added, then $Na_2SO_4.10H_2O$ (10 g) cautiously until the lithium complex was destroyed. The mixture was then diluted with THF (25 mL) and NaOH (3 g, 75 mmol, in 5 mL H_2O) was added. White precipitate was filtered off and heated again in THF (2 x 25 mL). The combined THF extracts were dried over $MgSO_4$, concentrated in vacuo to give a colorless oil (489 mg, 89%). Distillation bulb-to-bulb on Kugelrohr (215 °C/0.4 mbar) gave alcohol-free base **26** as a colorless oil, which immediately solidifies. Crystallization from dry *n*-hexane under argon atmosphere (hygroscopic) furnished **26** (417 mg, 76%) as a white crystal, mp 112.4-113.1 °C. $[\alpha]_D^{20.3}$ = +21.73 (*c* 1.0 MeOH). TLC (Silica gel): R_f = 0.32 (CH_2Cl_2:isopropanol 1:2). IR (ATR): ν = 3095, 2958, 2980, 2923, 2889, 2815, 1462, 1444, 1412, 1337, 1321, 1297, 1272, 1136, 1118, 1080, 1060, 1034, 989, 908, 874, 785, 697, 559, 509, 469. ^{1}H NMR (600 MHz, CD_3OD): δ 4.06 (dt, *J* = 10.1, 7.6 Hz, 1H, H-2), 3.98 (ddd, *J* = 10.0, 8.1, 2.2 Hz, 1H, H-2′), 3.86 (dd, *J* = 9.2, 6.7 Hz, 1H), 3.10 (dd, *J* = 11.3, 6.7 Hz, 1H, H-9_{eq}), 2.97 (td, *J* = 8.8, 2.5 Hz, 1H, H-7), 2.30 – 2.25 (m, 1H, H-3), 2.24 (dd, *J* = 13.2, 3.0 Hz, 1H, H-4), 2.19 (q, *J* = 9.1 Hz, 1H, H-7′), 2.15 – 2.08 (m, 1H, H-4a), 1.93 (dddd, *J* = 12.2, 8.7, 6.4, 3.8 Hz, 1H, H-5), 1.87 (dd, *J* = 11.0, 10.1 Hz, 1H, H-9′), 1.87 - 1.79 (m, 2H, 2x H-6), 1.77 (ddd, *J* = 13.0, 7.1, 1.7 Hz, 2H, H-3′), 1.59 (dd, *J* = 13.0, 11.9 Hz, 1H, H-4′), 1.42 (ddt, *J* = 11.3, 7.4, 7.0 Hz, 1H, H-5′). ^{13}C NMR (151 MHz, CD_3OD): δ 82.9 (d, C-9a), 79.8 (s, C-3a) , 67.4 (t, C-2), 62.6 (d, C-4a), 56.2 (t, C-9), 54.6 (t, C-7), 40.1 (t, C-4), 36.1 (t, C-5), 31.0 (d, C-9a), 23.0 (t, C-6) ppm. HRMS (ESI): *m/z* calcd. for $C_{10}H_{17}NO_2$ $[M+H]^+$ 184.1332, found 184,1333.

(*3R,3aR,4aS,9aR*)-7-Oxodecahydrofuro[2,3-*f*] indolizine-3,3a-diyl diacetate(18a)
To a stirred solution of *trans*-diol **8a** (2.13 g, 10.0 mmol) in of dry CH_2Cl_2 (50 mL) was added Ac_2O (3.9 mL, 35 mmol, 3.5 eq.), DMAP (43 mg, 0.35 mmol) and Et_3N (5.6 mL, 40.0 mmol, 4.0 eq.). The reaction mixture was heated at reflux until disappearance of the starting material (monitored by TLC, CH_2Cl_2:acetone 10:1). The mixture was cooled and quenched with a saturated aqueous Na_2CO_3 solution (10 mL). The aqueous layer was extracted with CH_2Cl_2 (3 x 30 mL). The organic layers were washed with water, dried over $MgSO_4$ and concentrated under vacuum. The light-yellow oil was purified by flash chromatography on silica gel column (CH_2Cl_2, CH_2Cl_2:acetone 12:1) to afford *trans*-

diacetyl **18a** (2.47 g, 83%) as an oil, which quickly crystallized on standing. Recrystallization from a mixture of EtOAc/*n*-heptane furnished **18a** (2.2 g, 74%) as a white crystal; mp 181,8-183,1 °C. $[\alpha]_D^{20.3}$ = -78.3 (*c* 1.05, acetone). TLC (Silica gel): R_f = 0.59 (CH_2Cl_2:isopropanol 5:1). IR (ATR): ν = 2934, 2913, 2892, 1737, 1665, 1440, 1427, 1372, 1362, 1305, 1226, 1178, 1087, 1067, 1048, 1022, 977, 954, 938, 927, 899, 874, 853, 799, 757, 714, 659, 641, 603, 567, 528, 487, 441, 413. ^{1}H NMR (600 MHz, CD_3COCD_3): δ 5.59 (dd, *J* = 5.1, 1.3 Hz, 1H, H-3), 4.19 (dd, *J* = 10.8, 5.1 Hz, 1H, H-2), 4.08 (dd, *J* = 8.1, 6.7 Hz, 1H, H-9a), 3.95 (dd, *J* = 13.4, 6.6 Hz, 1H, H-9_{eq}), 3.86 (dd, *J* = 10.8, 1.4 Hz, 1H, H-2), 3.88 – 3.81 (m, 1H, H-4a), 3.04 (dd, *J* = 13.4, 8.3 Hz, 1H, H-9_{ax}), 3.00 (dd, *J* = 13.9, 3.9 Hz, 1H, H-4_{eq}), 2.29 - 2.21 (m, 3H, 2xH-6 and H-5), 2.14 (s, 3H, CH_3), 2.01 (s, 3H, CH_3), 1.80 (dd, *J* = 13.9, 11.6 Hz, 1H, H-4_{ax}), 1.64 – 1.56 (m, 1H, H-5). ^{13}C NMR (151 MHz, CD_3COCD_3): δ 174.7 (s, C-7), 171.5 (s, $CH_3\underline{CO}$), 171.1 (s, $CH_3\underline{CO}$), 88.9 (d, C-3a), 80.5 (d, C-9a), 79.5 (d, C-3), 74.3 (t, C-2), 54.3 (d, C-4a), 42.1 (t, C-9), 38.3 (t, C-4), 31.6 (t, C-6), 27.1 (t, C-5), 22.9 (q, CH_3), 21.9 (q, CH_3) ppm. HRMS (ESI): *m/z* calcd. for $C_{14}H_{19}NO_6$ $[M+H]^+$ 298.1285, found 298.1285.

(*3R,3aS,4aS,9aR*)-Octahydrofuro[2,3-*f*]indolizine-3,3a(4*H*)-diol (9a)

LAH (570 mg, 15 mmol, 6 eq.) was added to a solution of a freshly crystallized *trans*-diacetyl-THF **18a** (742 mg, 2.5 mmol) in dry THF (35 mL) at room temperature and the mixture then heated under reflux for 2.5 h. The slurry was then warmed to ambient temperature and after an additional 40 minutes was carefully quenched with 2:1 w:w $Na_2SO_4.10H_2O$:Celite (20 g). The reaction mixture was diluted with THF (75 mL) and NaOH (1.5 g) in H_2O (5 mL) was added (a white precipitate is formed). After 30 minutes, the solid was filtered, washed with hot THF (2 x 75 mL), and the combined organic layers were dried over $MgSO_4$, filtered and concentrated in vacuo to give a solid (453 mg, 91%). Recrystallization of the solid from anhydrous *n*-heptane gave *trans*-dihydroxy-THF **9a** (386 mg, 79%) as a white crystal; mp 139.1-139.7 °C. $[\alpha]_D^{24}$ = +31.65 (*c* 1.0, MeOH). TLC (Silica gel): R_f = 0.17 (CH_2Cl_2/isopropanol 1/2). IR (ATR): ν=3492, 2940, 2881, 2840, 2822, 2741, 1455, 1384, 1327, 1241, 1205, 1136, 1112, 1056, 1022, 965, 934, 904, 858, 788, 752, 689, 661, 558, 443. ^{1}H NMR (600 MHz, CD_3OD) δ 4.24 (dd, *J* = 9.4, 4.7 Hz, 1H, H-2), 4.00 (d, *J* = 4.4Hz, 1H, H-3), 3.97 (dd, *J* = 10.4, 7.2 Hz, 1H, H-9a), 3.79 (dd, *J* = 9.4, 1.1 Hz, 1H, H-2´), 3.11 (dd, *J* = 10.7, 7.1 Hz, 1H, H-9_{eq}), 2.98 (dt, *J* = 9.0, 2.4 Hz, 1H, H-7),2.59 (ddt,*J* = 10.8, 6.3, 3.6 Hz, 1H, H-4a), 2.53 (dd, *J* = 13.5, 3.5 Hz, 1H, H-4_{eq}), 2.35 (t,*J* = 10.6 Hz, 1H, H-9_{ax}), 2.19 (q, *J* = 9.1 Hz, 1H, H-7´), 1.94 - 1.76 (m, 3H, H-5 and 2x H-6), 1.57 (dd, *J* = 13.4, 11.7 Hz, 1H, H-4_{ax}), 1.31 (tq,*J* = 11.3, 6.8 Hz, 1H, H-5´). ^{13}C NMR (151 MHz, CD_3OD) δ 83.6 (d, 9a), 81.3 (d, C-3), 80.5 (s, C-3a), 76.3 (t, C-2), 62.9 (d, C-4a), 55.5 (t, C-9), 54.3 (t, C-7), 39.7 (t, C-4), 31.6 (t, C-5), 22.9 (t, C-6) ppm. HRMS (ESI): *m/z* calcd. for $C_{10}H_{17}NO_3$ $[M+H]^+$ 200.1281, found 200.1279.

(*3aS,5aR,8aS,11aR,11bR,12aR*)-2,2,10,10-Tetramethyloctahydro-8*H*-[1,3]dioxolo[4',5':3,4]-furo[2,3-f][1,3]dioxolo[4,5-a]indolizine (32a)

Method A: LAH (750 mg, 2 mmol) was added to a solution of lactam **30a** (325 mg, 1 mmol) in dry THF (30 mL) at room temperature and the mixture was then heated at reflux for 2 h. The resulting mixture was cooled, Celite (5 g) and $Na_2SO_4.10H_2O$ (5 g) were added cautiously until the lithium complex was destroyed. The mixture was then diluted with THF (25 mL) and NaOH (2 g in 5 mL H_2O) was added. White precipitate was filtered off and heated again twice in THF (2 x 25 mL). The combined THF extracts were dried over $MgSO_4$, concentrated in vacuo to give a white residue (300 mg, 88%) as THF complex (from ^{1}H NMR analysis) which was refluxed in a mixture of MeOH (50 ml) and water (5 mL) for 48 h. To cooled mixture, SiO_2 (10 g) was added and concentrated *in vacuo*. The resulting solid was purified by flash chromatography (CH_2Cl_2, CH_2Cl_2:acetone 10:1) to afford the free base as a white solid (218 mg, 70%).

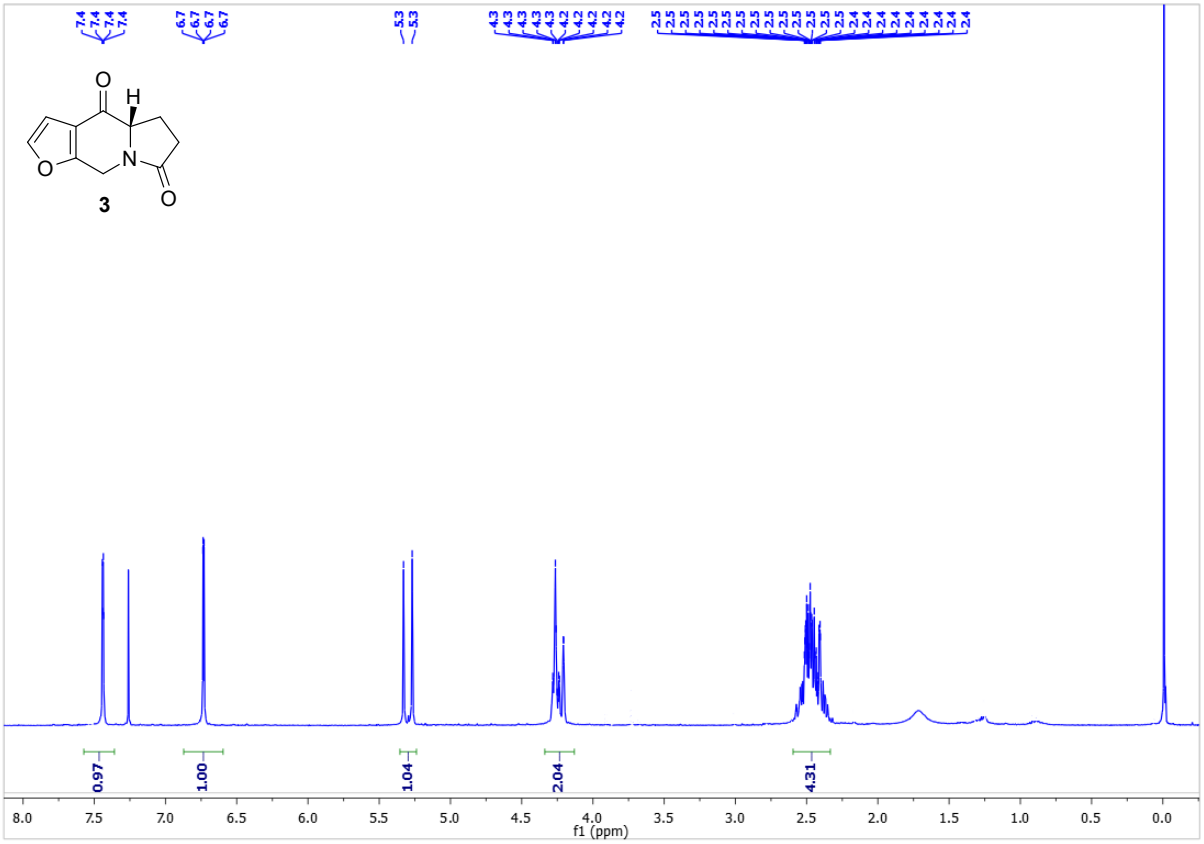
Method B: $Me_2S{\cdot}BH_3$ (2.0 M solution in THF, 10.8 mL, 22.0 mmol) was added to a stirred solution of lactam **30a** (813 mg, 2.5 mmol) in dry THF (15 mL) under argon and the mixture was stirred at room temperature for 30 minutes, then heated at reflux 4 h. The mixture was quenched by the careful addition of MeOH (20 mL) and concentrated under vacuum. The crude colorless residue of the borane–tetrahydrofuran complex **32a**$\cdot BH_3\cdot$THF (805 mg) [^{13}C NMR ($CDCl_3$): δ 114.2, 112.3, 90.9, 84.5, 84.2, 79.5, 78.5, 72.9, 66.6, 62.8 t (CH_2O-THF), 62.2 t (CH_2O-THF), 59.6, 51.5, 30.3 t (CH_2CH_2-THF), 29.9 t (CH_2CH_2-THF), 29.4 (q), 27.9 (q), 27.2 (q), 25.1 (q) ppm, TLC (Silica gel): R_f = 0.87 (CH_2Cl_2:isopropanol 3:1)] was dissolved in MeOH (35 mL) and water (10 mL) was added. The resulting mixture was heated at reflux for 5 days. The reaction mixture was filtered through Celite and the filtrate was concentrated to afford free base **32a** (669 mg, 86 %) as a colorless oil. Subjection of this oil to flash chromatography (CH_2Cl_2, CH_2Cl_2:acetone 12:1) gave a free base **32a** (520.6 mg, 67%) as a white solid; mp 81.9-82.7 °C. $[\alpha]_D^{24}$ = +43.9 (*c* 0.75, acetone); TLC (Silica gel): R_f = 0.31 (CH_2Cl_2:isopropanol 3:1). IR (ATR): ν = 2863, 2838, 2812, 1482, 1441, 1381, 1368, 1301, 1285, 1208, 1147, 1101, 1057, 1048, 1018, 978, 918, 892, 853, 841, 813, 781, 718, 701, 603, 532, 504, 491, 426. ^{1}H NMR (600 MHz, $CDCl_3$): δ 4.74 (dt, *J* = 6.8, 5.3 Hz, 1H, H-8a), 4.64 (dd, *J* = 5.4, 1.2 Hz, 1H, H-3a), 4.22 (dd, *J* = 6.9, 6.0 Hz, 1H, H-11a), 4.13 (dd, *J* = 10.1, 7.5 Hz, 1H, H-5a), 4.00 (dd, *J* = 11.1, 5.5 Hz, 1H, H-4), 3.88 (dd, *J* = 11.1, 1.6 Hz, 1H, H-4′), 3.33 (dd, *J* = 9.6, 6.4 Hz, 1H, H-8), 3.08 (dd, *J* = 11.6, 7.5 Hz, 1H, H-6_{eq}), 2.48 (dd, *J* = 13.1, 3.0 Hz, 1H, H-12_{eq}), 2.32 (dd, *J* = 9.6, 5.1 Hz, 1H, H-8), 2.12 (dd, *J* = 11.3, 10.4 Hz, 1H, H-6_{ax}), 2.10 (ddd, *J* = 12.0, 5.8, 2.9 Hz, 1H, H-11b), 1.78 (dd, *J* = 13.0, 12.3 Hz, 1H, H-12_{ax}), 1.51 (s, 3H, CH_3), 1.49 (s, 3H, CH_3), 1.42 (s, 3H, CH_3), 1.32 (s, 3H, CH_3). ^{13}C NMR (151 MHz, $CDCl_3$): δ 114.2 (s, C-2) 112.2 (s, C-10), 90.9 (s, C-12a), 84.5 (d, C-3a) 84.2 (d, C-11a), 79.5 (d, C-5a), 78.5 (d, C-8a), 72.9 (t, C-4), 66.5 (d, C-11b), 59.6 (t, C-8), 51.4 (t, C-6), 36.7 (t, C-12), 29.4 (q, CH_3), 27.9 (q, CH_3), 27.1 (q, CH_3), 25.0 (q, CH_3) ppm. HRMS (ESI): *m/z* calcd. for $C_{16}H_{25}NO_5$ $[M+H]^+$ 312.1805, found 312.1807.

(*3S,3aS,4aR,5R,6S,9aR*)-Octahydrofuro[2,3-*f*]indolizine-3,3a,5,6(4*H*)-tetraol (33a)

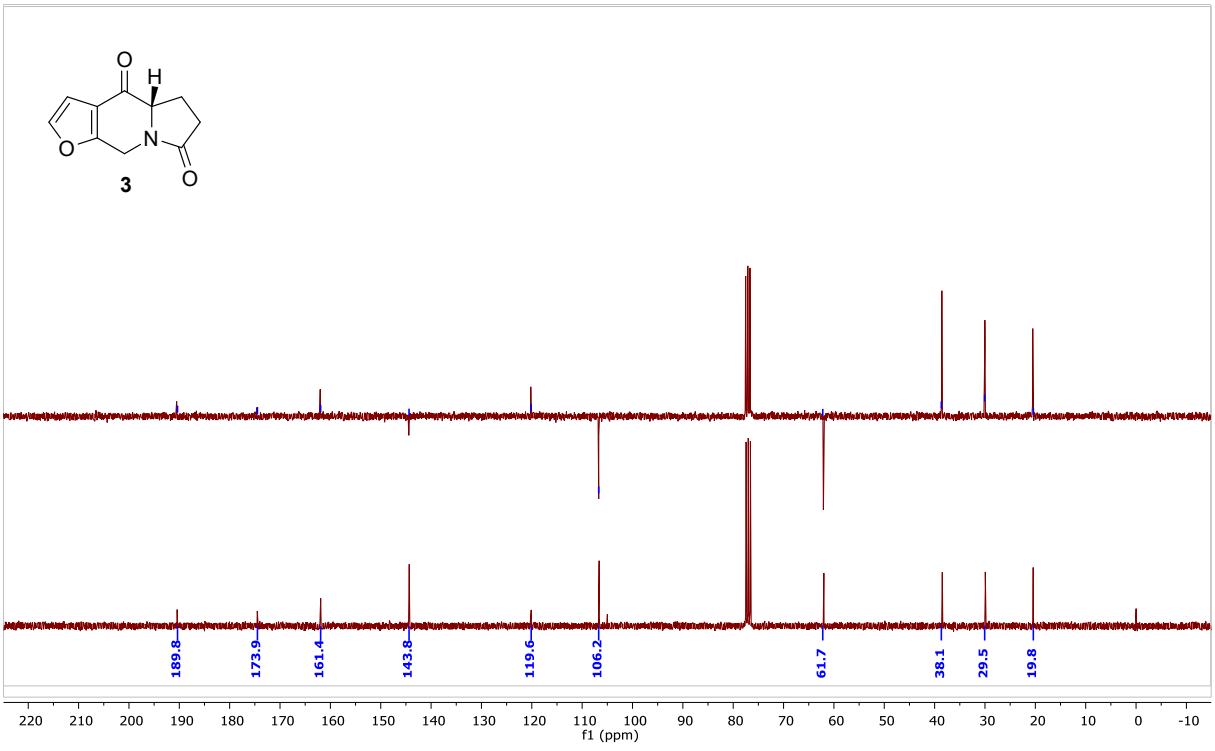
To DOWEX 50W x 8 (200-400 mesh) (1 g) washed with MeOH (3 x 10 ml), free base of di-DMP protected tetraol (467 mg, 1.5 mmol) was added in MeOH (25 mL) and the reaction mixture was stirred overnight. After complete disappearance of the starting material (TLC monitored) and full deprotection (LC-MS analysis), the MeOH was decanted, DOWEX was washed with MeOH (2 x 5 mL) and aqueous ammonia (25%, 10 mL) was added. The mixture was stirred for 1 h at 40 °C, cooled, filtered, and water was removed in *vacuo*. This crude tetraol was subjection to flash chromatography (CH_2Cl_2, CH_2Cl_2:MeOH 3:1) and gave a free base **33a** (246 mg, 71%) as a very hydroscopic white foam. $[\alpha]_D^{24}$= + 261.3 (*c* 1.03, MeOH). TLC (Silica gel): R_f = 0.48 (CH_2Cl_2:MeOH 1:1 + 0.05% 7 M NH_3:MeOH). IR (ATR): ν = 3319, 2933, 2907, 2819, 1392, 1336, 1259, 1164, 1107, 1041, 967, 928, 885, 845, 755, 565, 432. ^{1}H NMR (600 MHz, CD_3OD): δ 4.35 (t, *J* = 8.2 Hz, 1H, H-3), 4.14 (td, *J* = 6.6, 5.1 Hz, 1H, H-6), 4.04 (t, *J* = 8.0 Hz, 1H, H-2), 3.93 (dd, *J* = 9.6, 6.8 Hz, 1H, H-9a), 3.68 (t, *J* = 8.4 Hz, 1H, H-2′), 3.60 (dd, *J* = 8.0, 7.0 Hz, 1H), 3.33 (dd, *J* = 10.4, 6.7 Hz 1H, H-7), 3.07 (dd, *J* = 11.3, 6.8 Hz, 1H, H-9_{eq}), 2.39 (dd, *J* = 13.2, 3.2 Hz, 1H, H-4_{eq}), 2.25 (dd, *J* = 10.4, 4.9 Hz 1H, H-7′), 2.23 (ddd, *J* = 11.7, 8.2, 3.1 Hz, 1H, H-4a), 2.03 (t, *J* = 10.6 Hz, 1H, H-9_{ax}), 1.48 (dd, *J* = 13.1, 11.9 Hz, 1H, H-4_{ax}). ^{13}C NMR (151 MHz, CD_3OD): δ 82.6 (d, C-9a), 77.3 (s, C-3a), 76.8 (d, C-5), 72.1 (d, C-3), 71.6 (t, C-2), 69.8 (d, C-6), 64.8 (d, C-4a), 61.8 (t, C-7), 56.2 (d, C-9), 35.8 (t, C-4) ppm. HRMS (ESI): *m/z* calcd. for $C_{10}H_{17}NO_5$ $[M+H]^+$ 232.1179, found 232.1179.

Note: When di-DMP-protected free base of tetraol was retained on a column packed with DOWEX 50Wx8 (200-400 mesh), washed with MeOH, water, and then with 1N NH_4OH, a mixture of tetraol and monoacetonide was obtained (from ^{1}H NMR analysis).

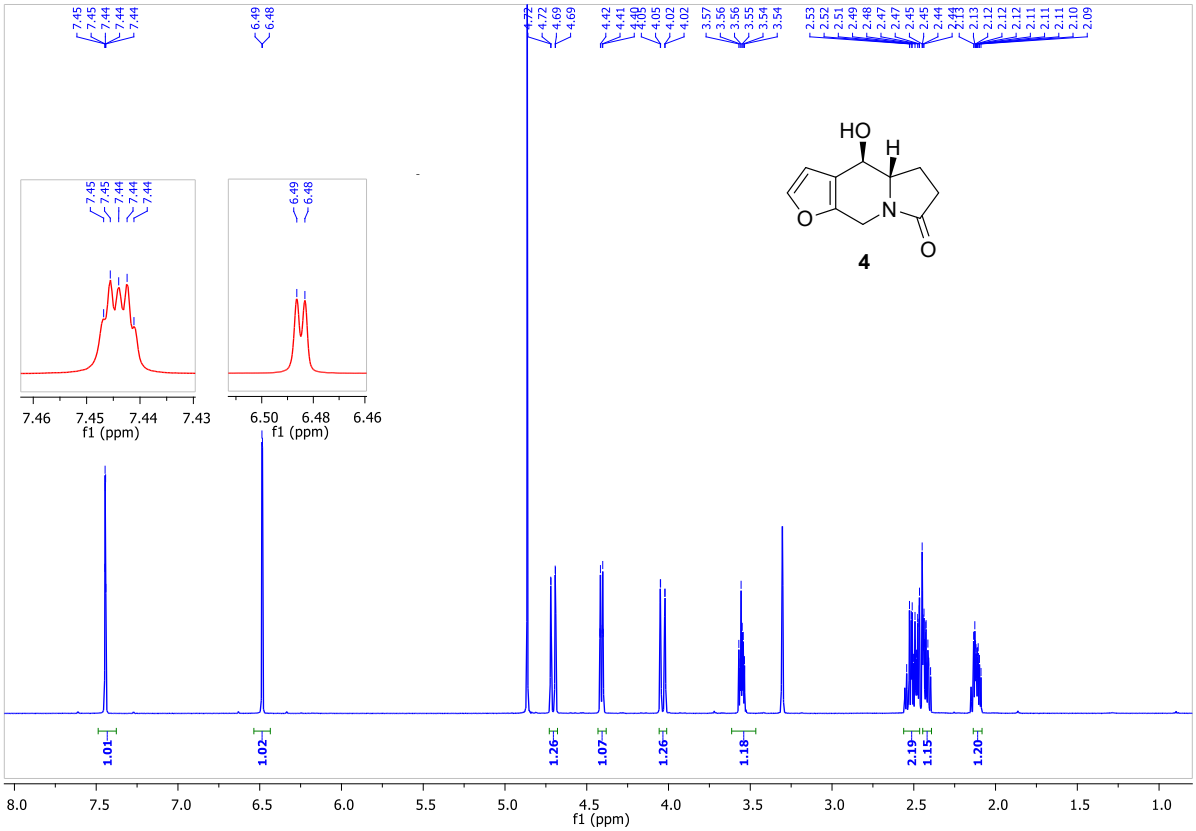
^{1}H and ^{13}C NMR, HMBC, HSQC, COSY and NOESY spectra



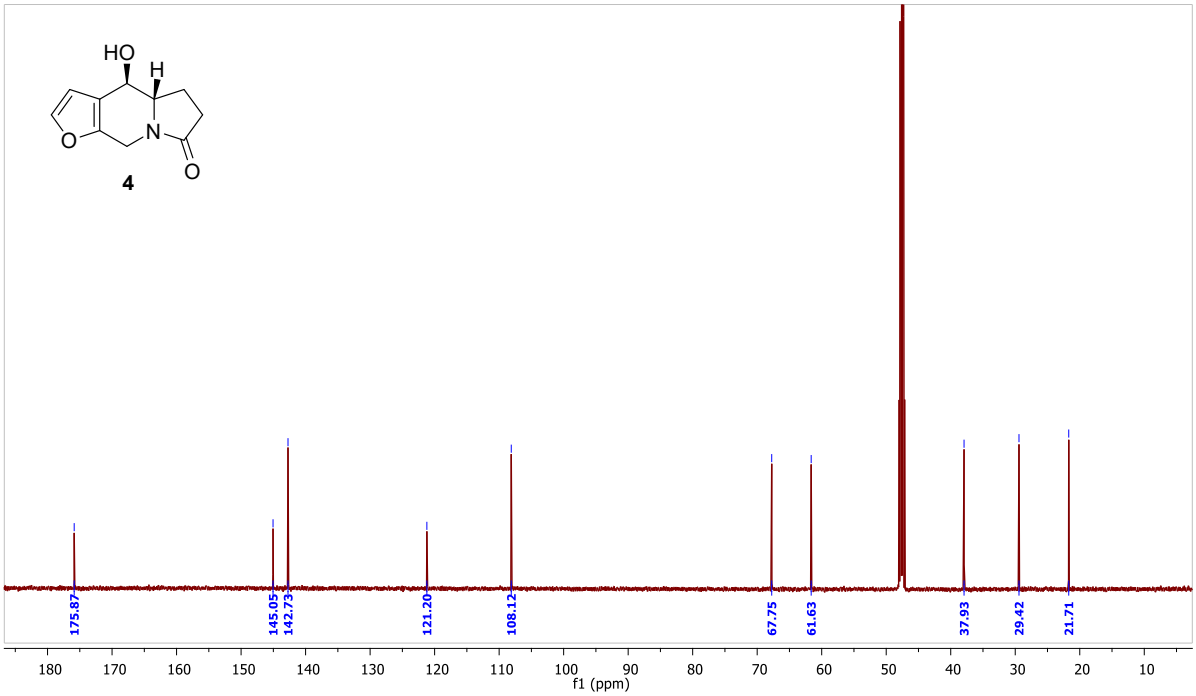
^{1}H NMR of **3**



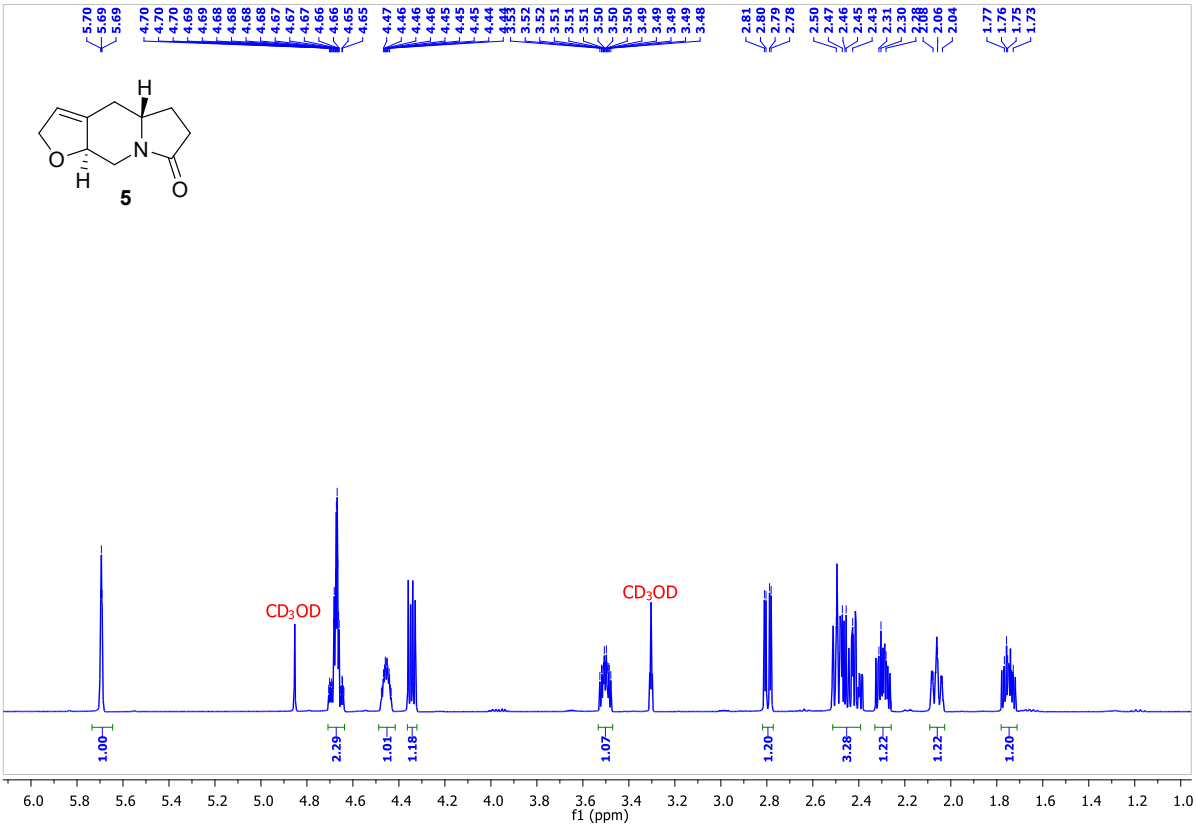
^{13}C NMR of **3**



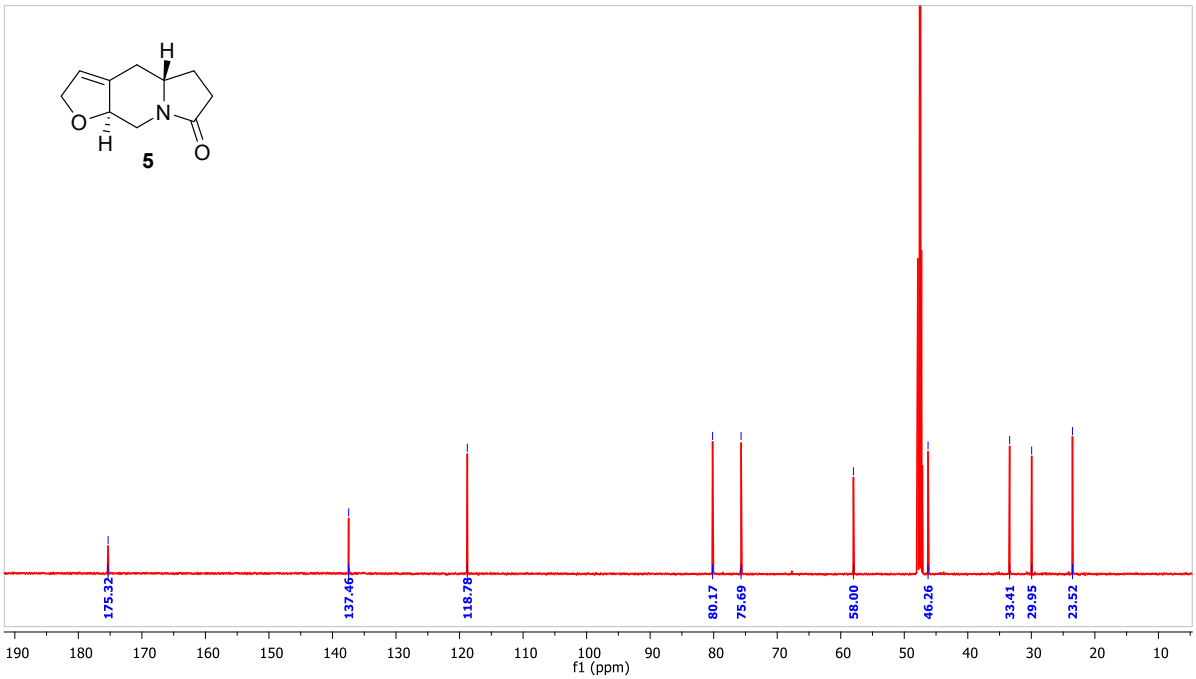
^{1}H NMR of **4**



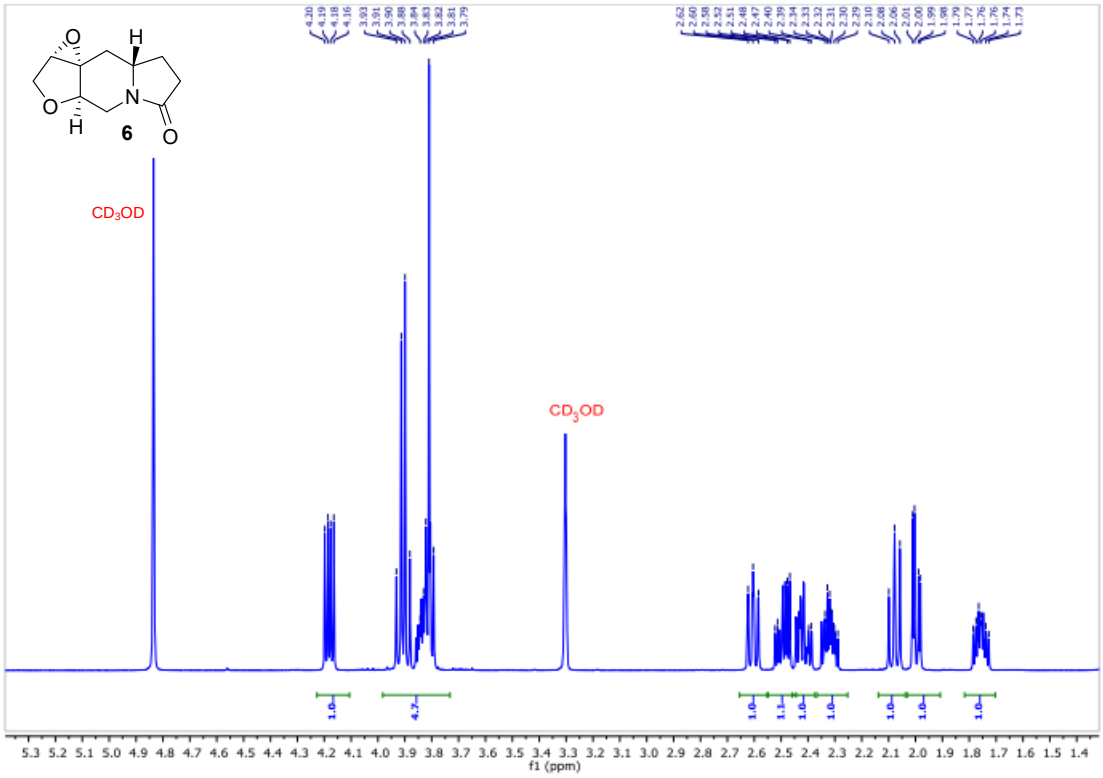
^{13}C NMR of **4**



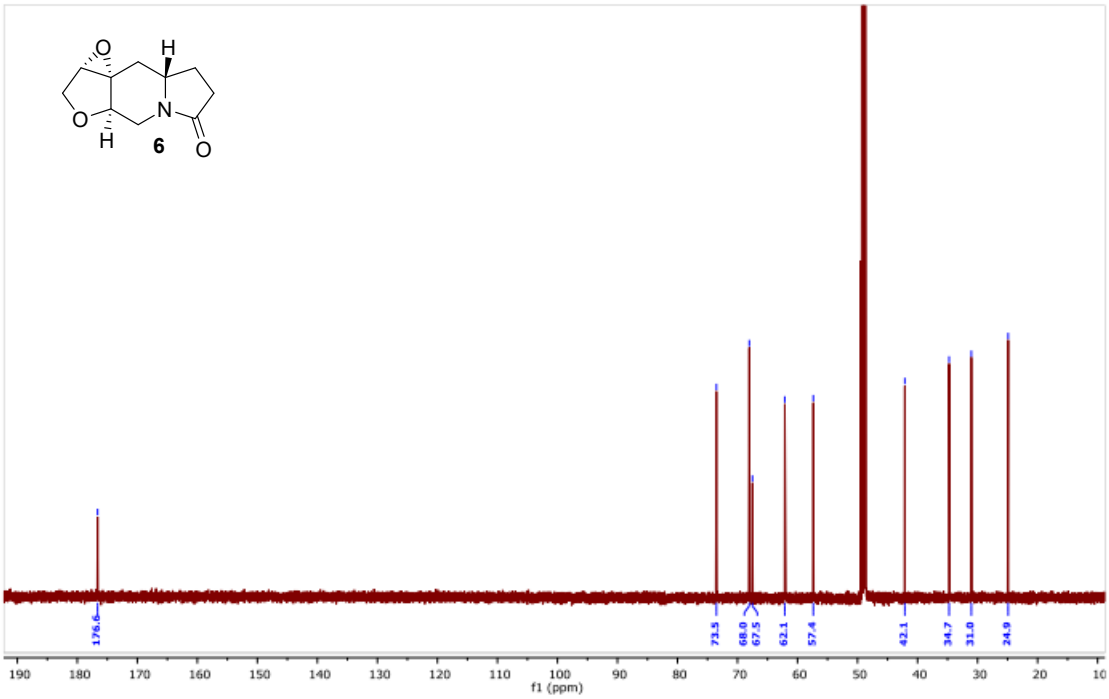
^{1}H NMR of **5**



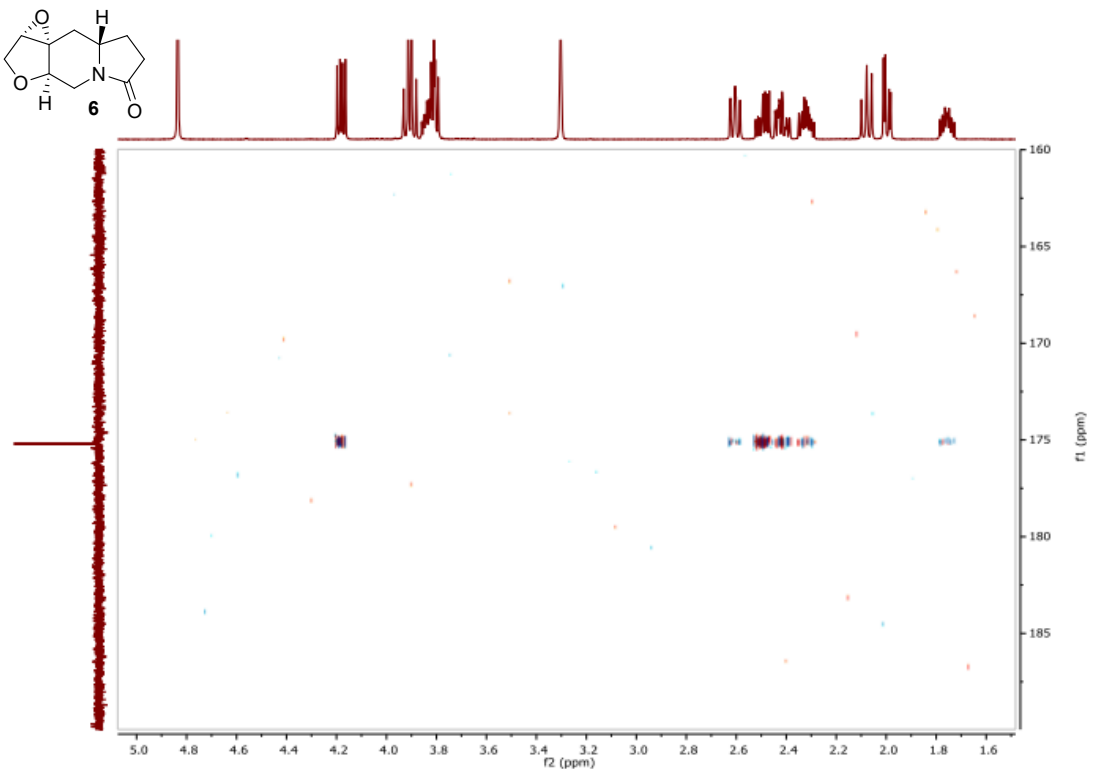
^{13}C NMR of **5**



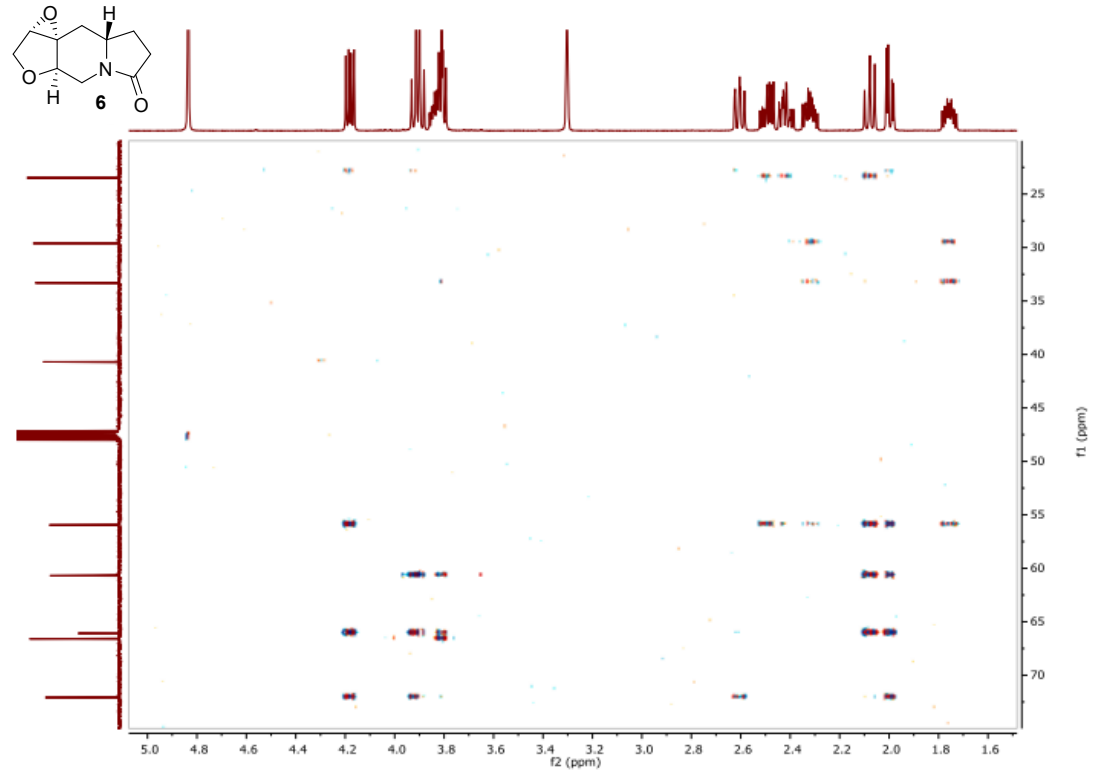
^{1}H NMR of **6**



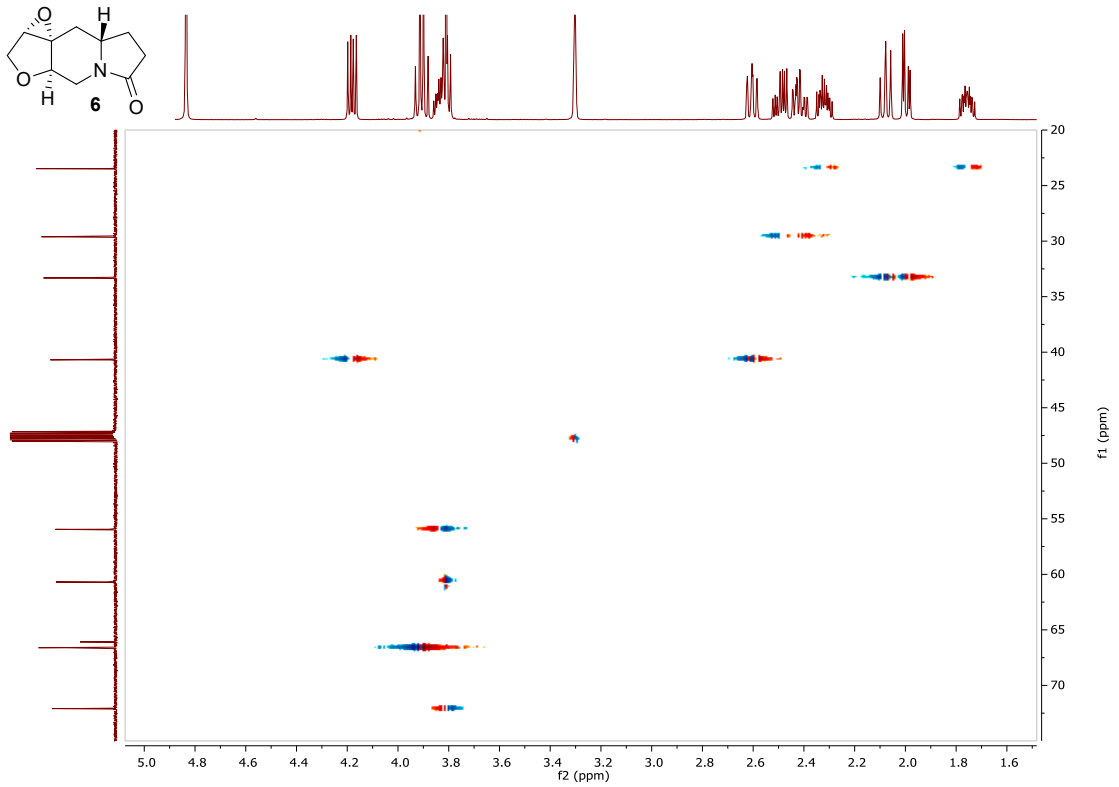
^{13}C NMR of **6**



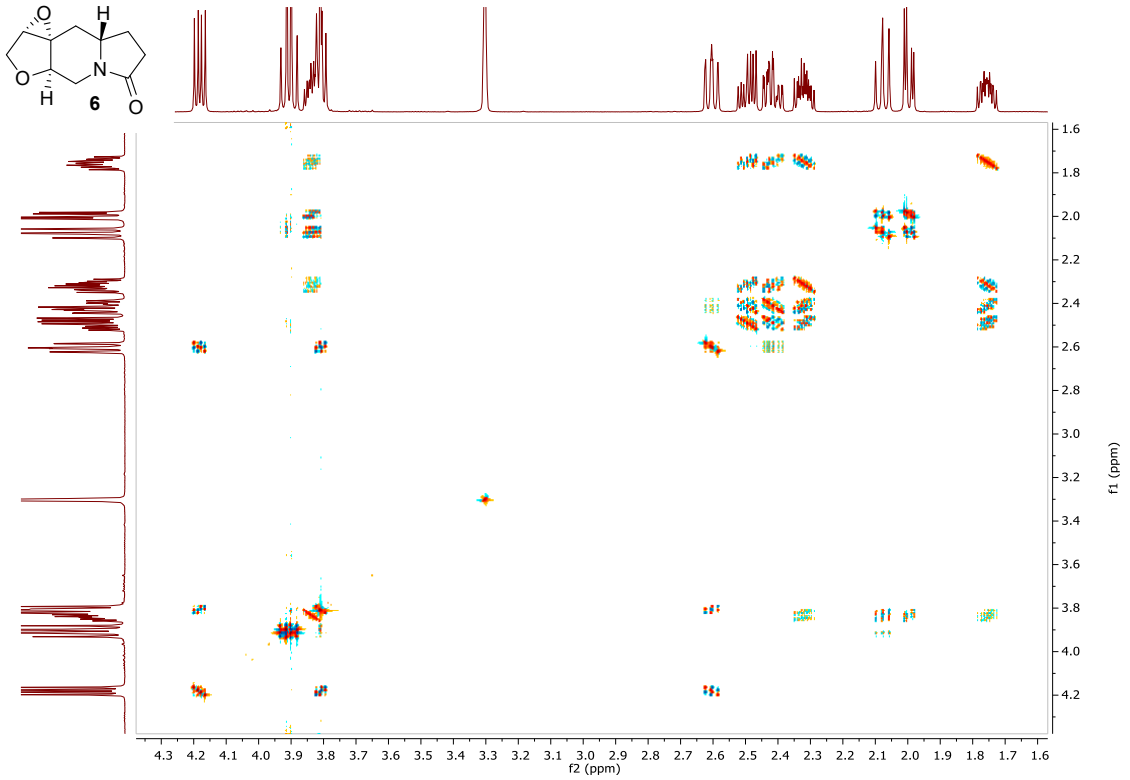
HMBC of **6**



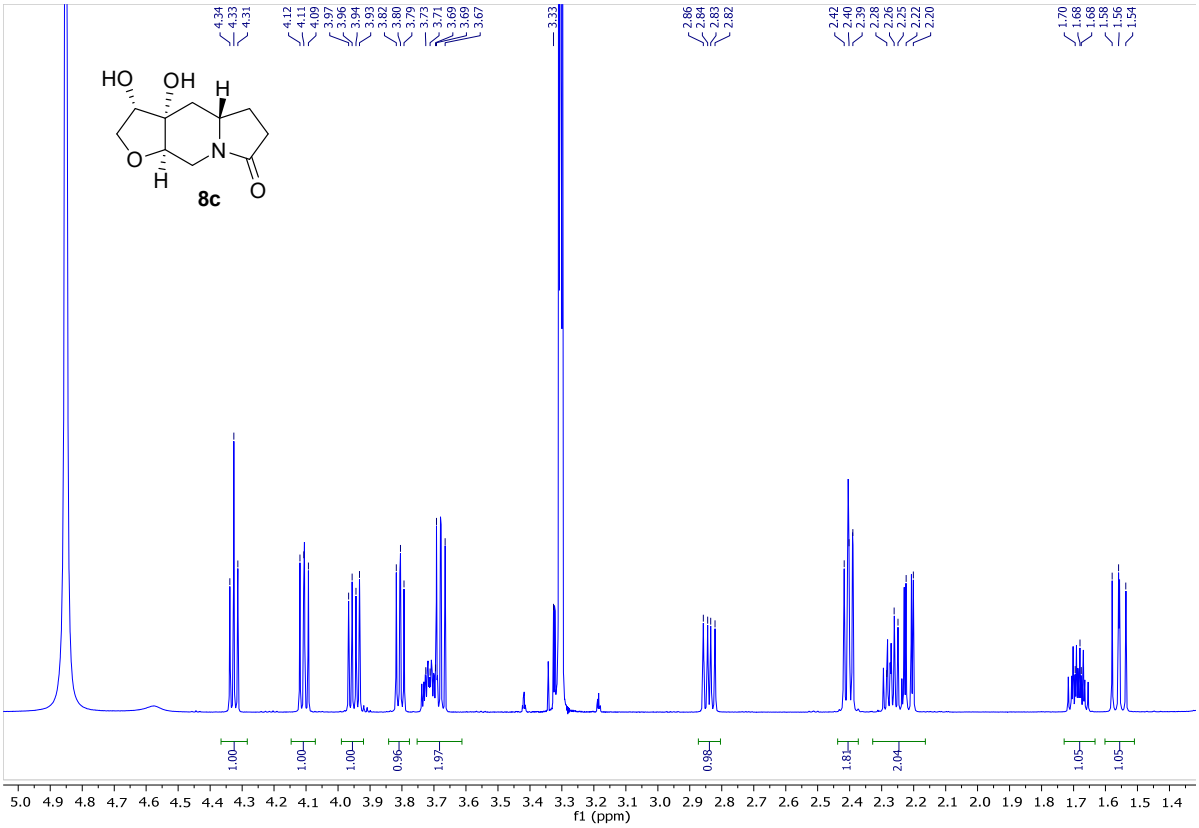
HMBC of **6**



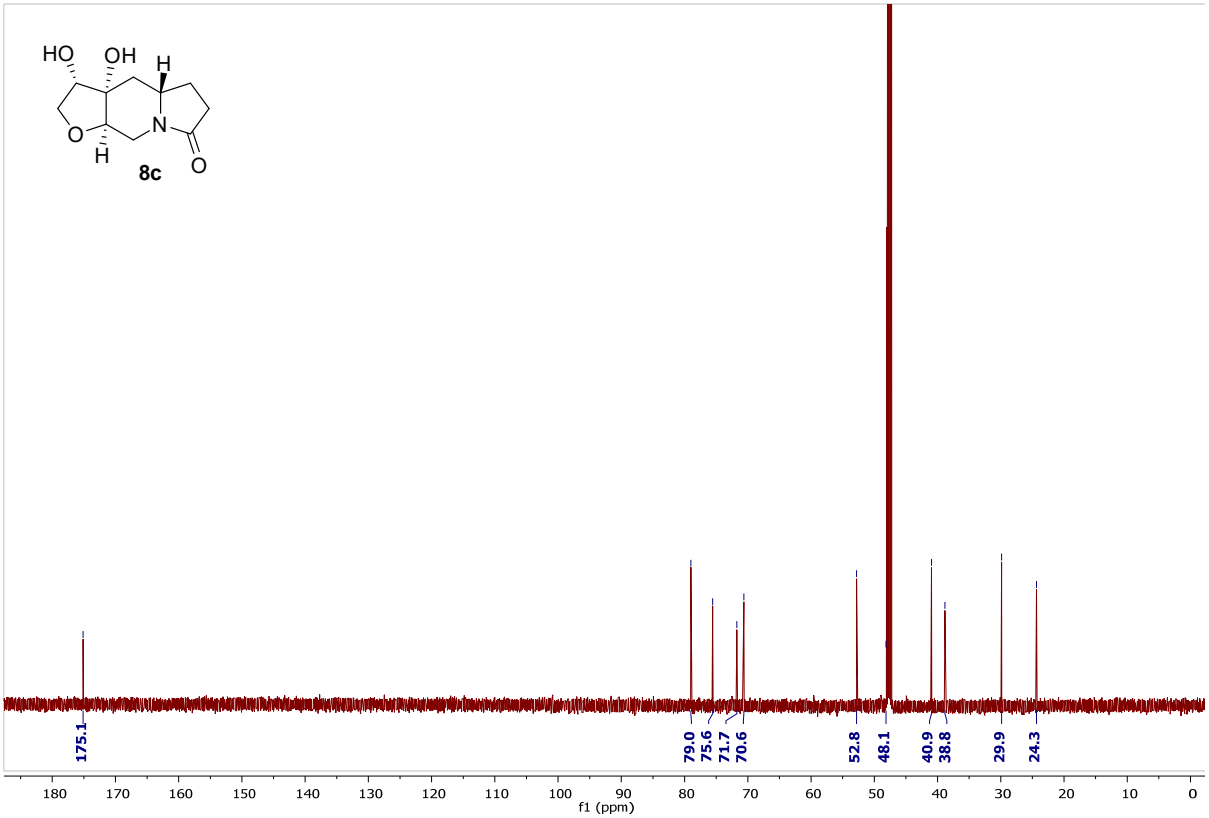
HSQC of **6**



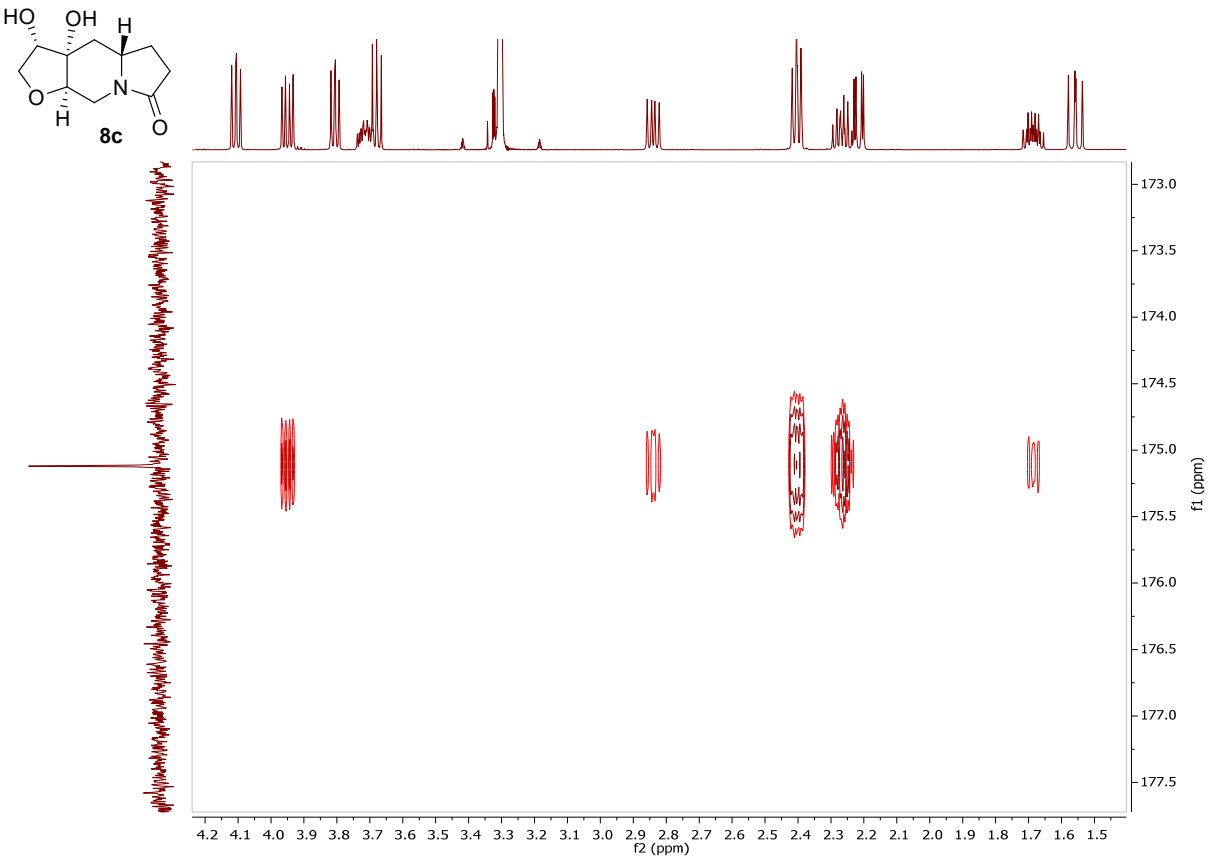
COSY of **6**



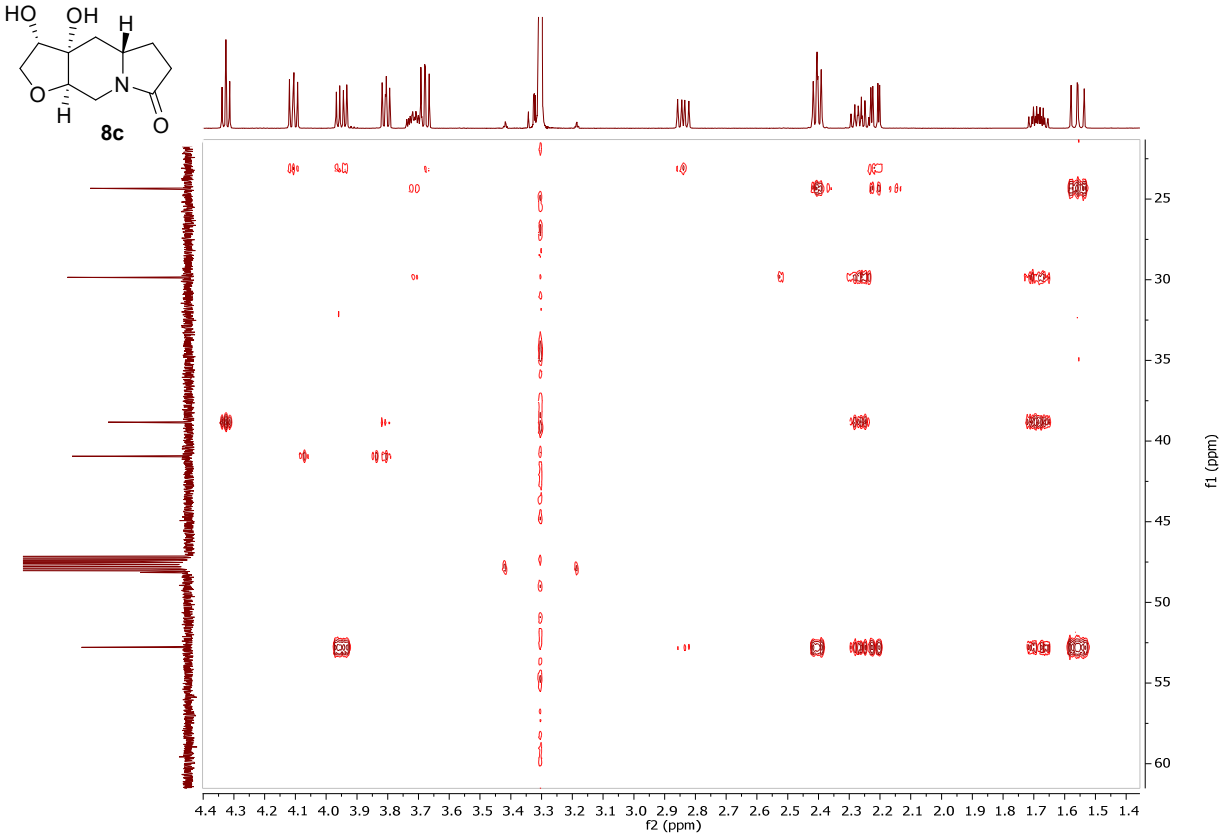
^{1}H NMR of **8c**



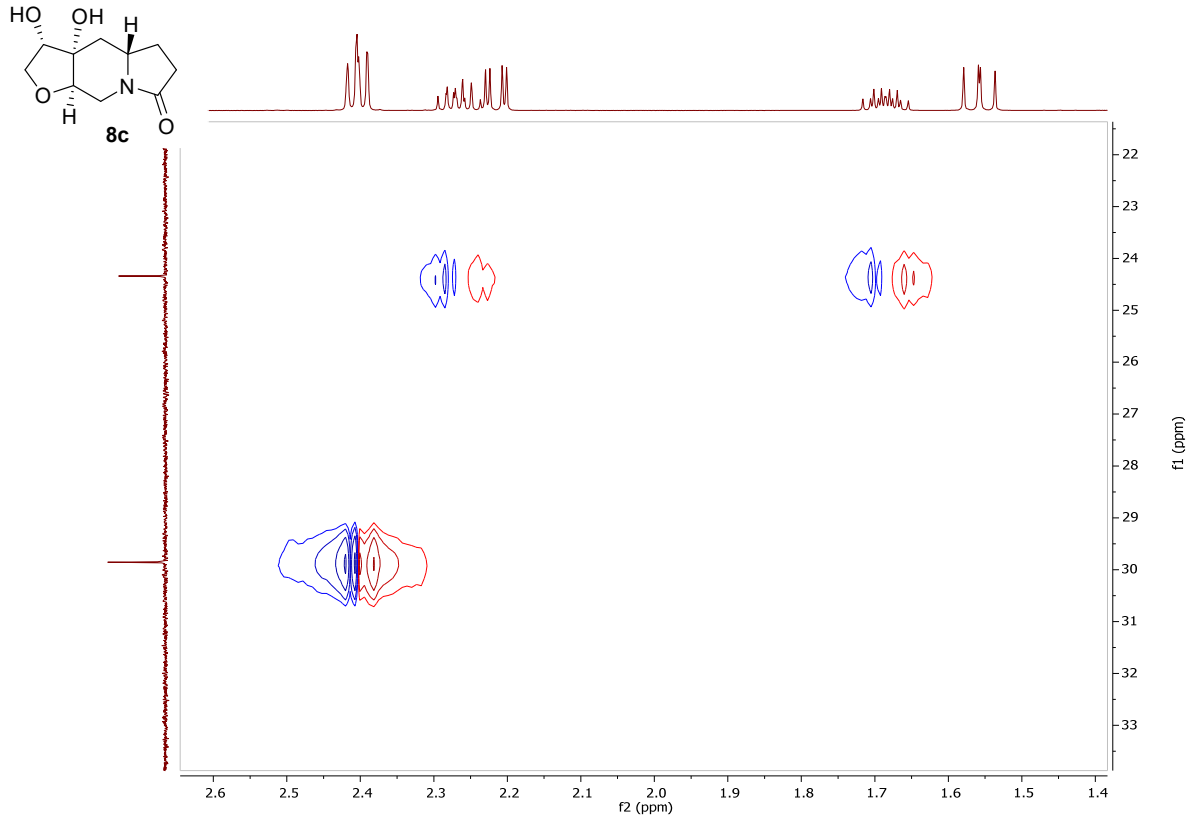
^{13}C NMR of **8c**



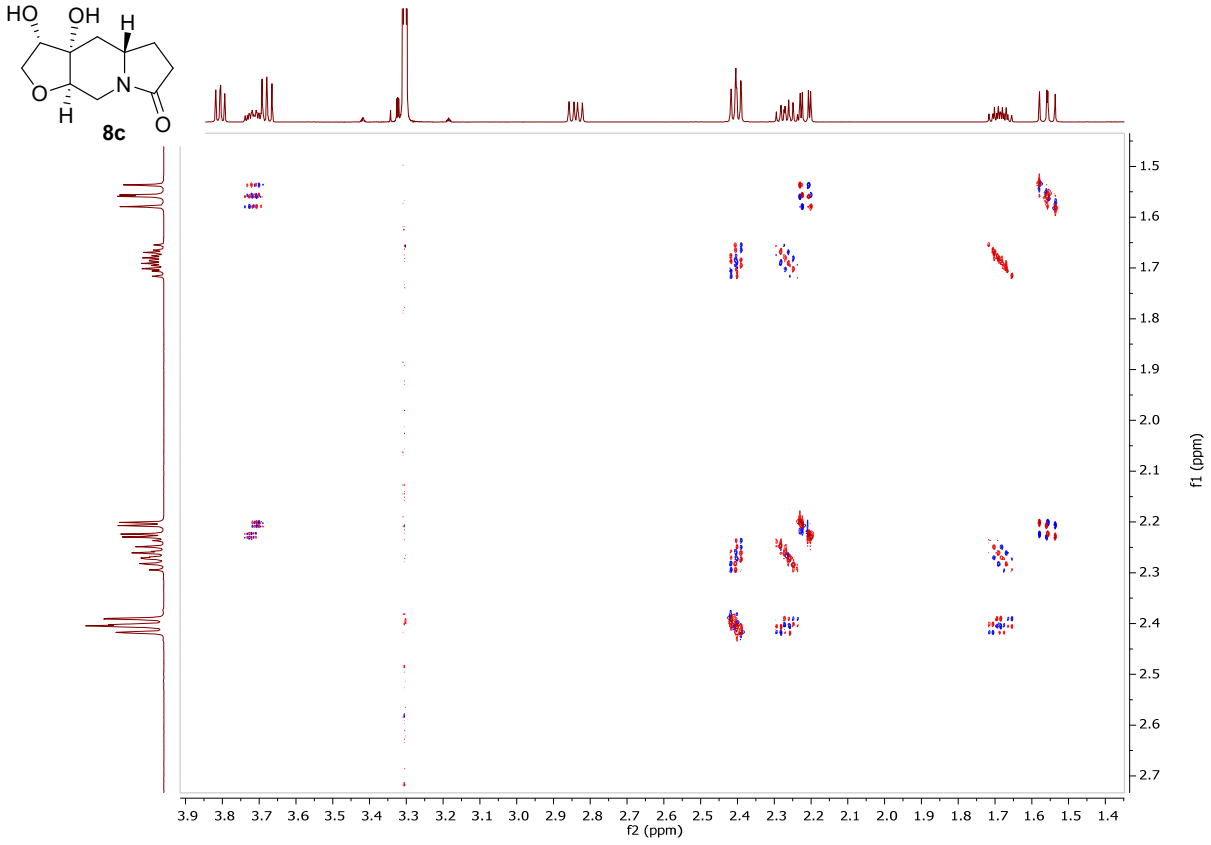
HMBC of **8c**



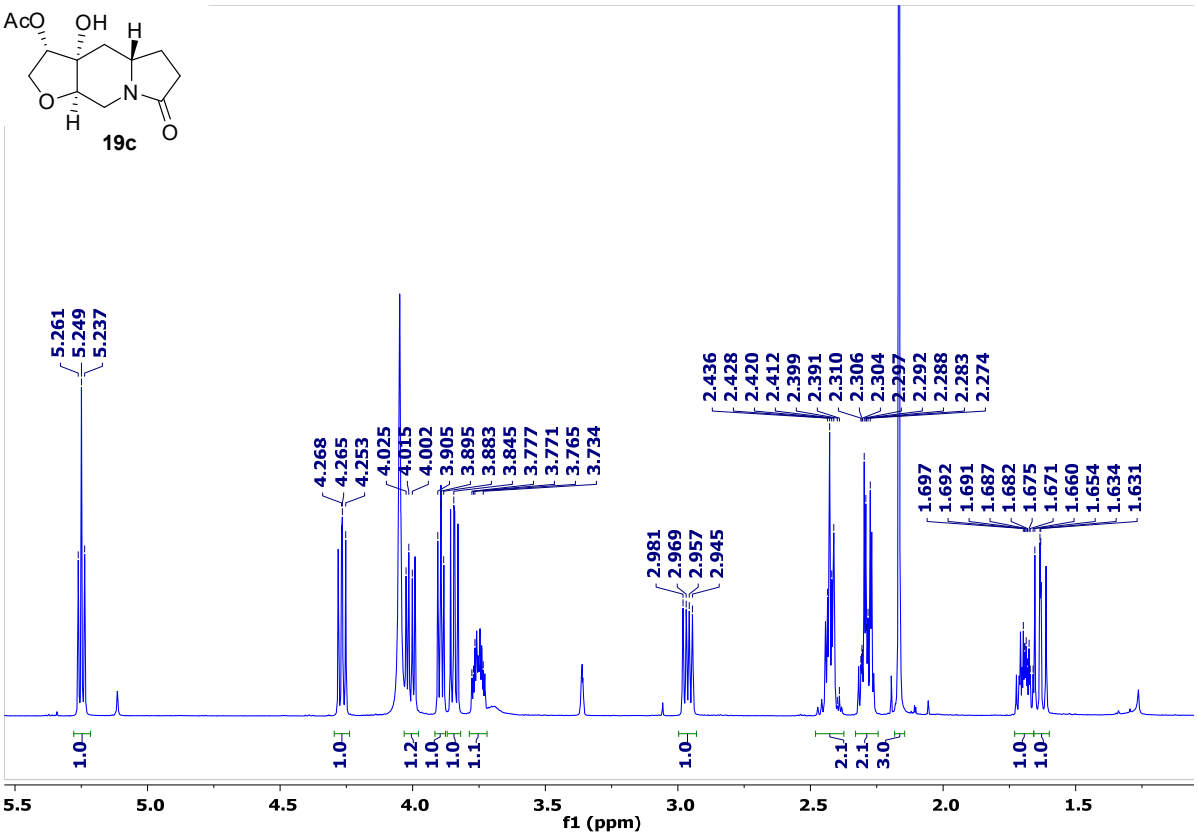
HMBC of **8c**



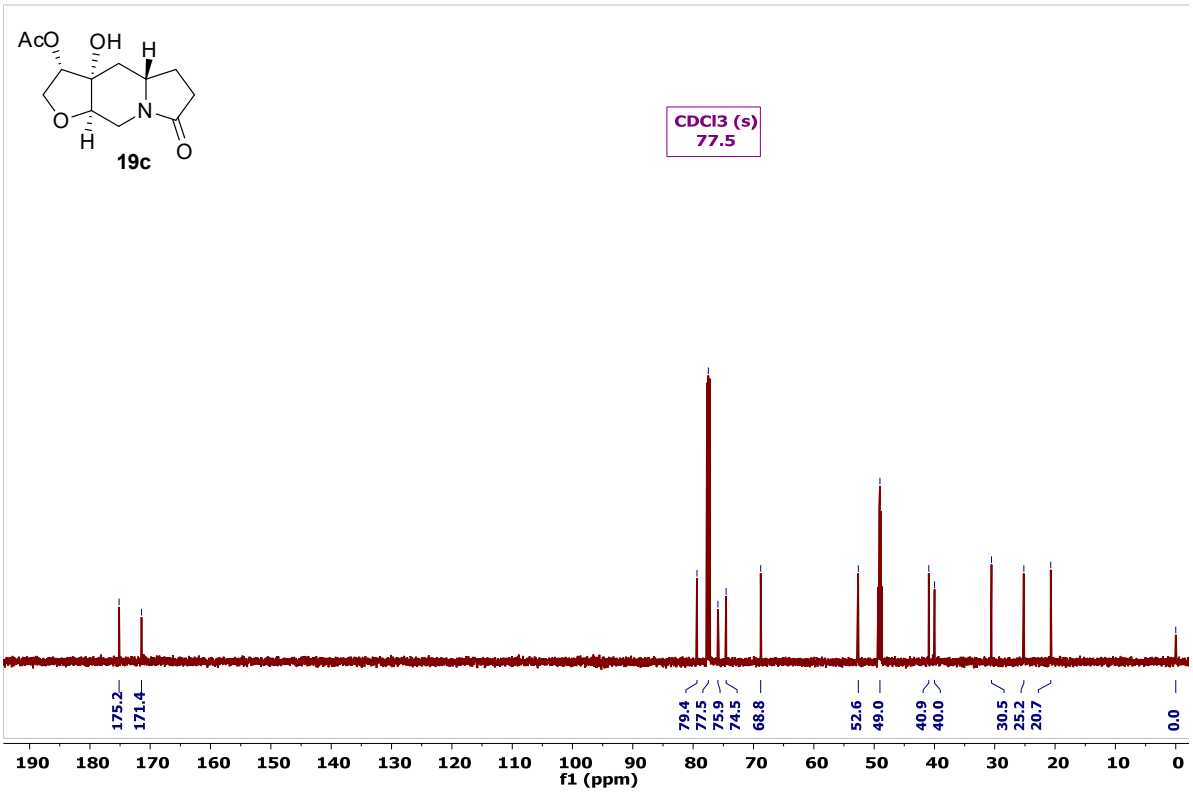
HSQC of **8c**



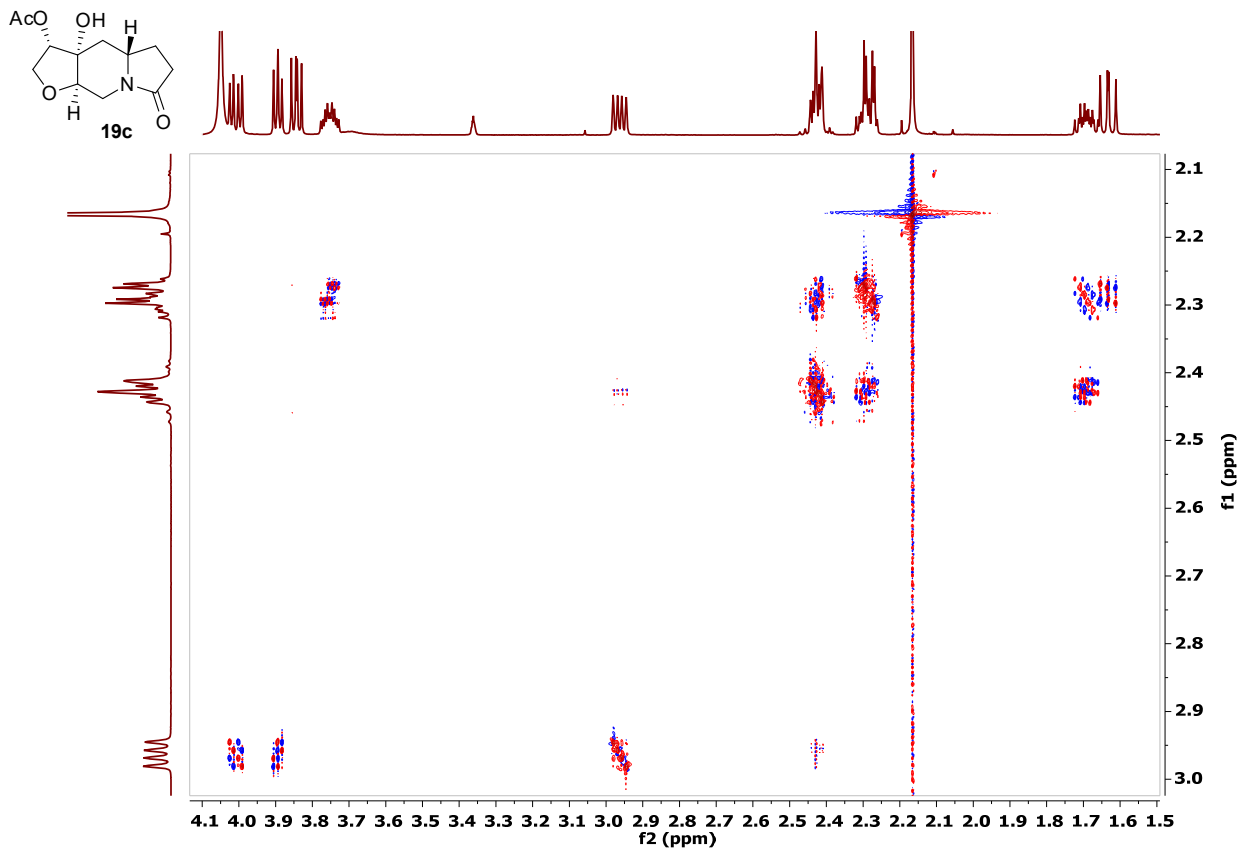
COSY of **8c**



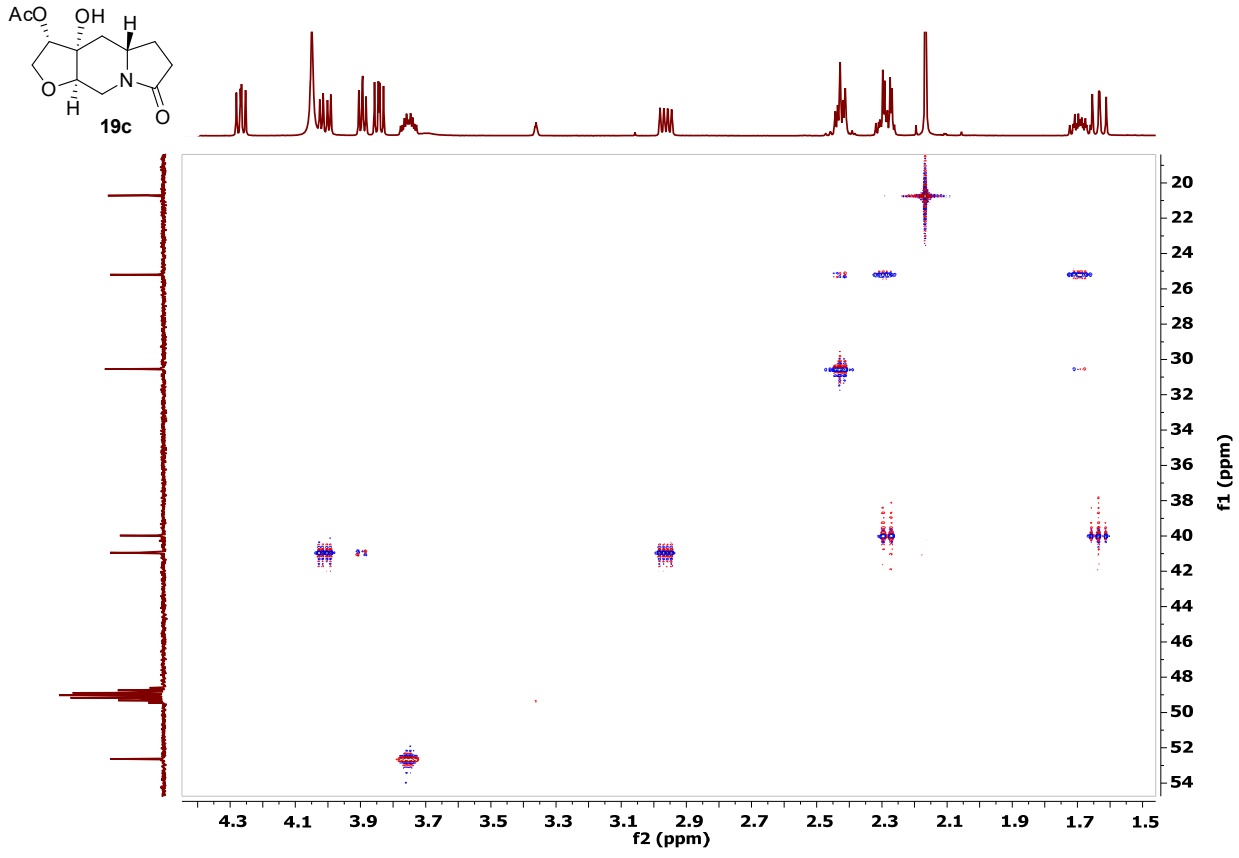
^{1}H NMR of **19c**



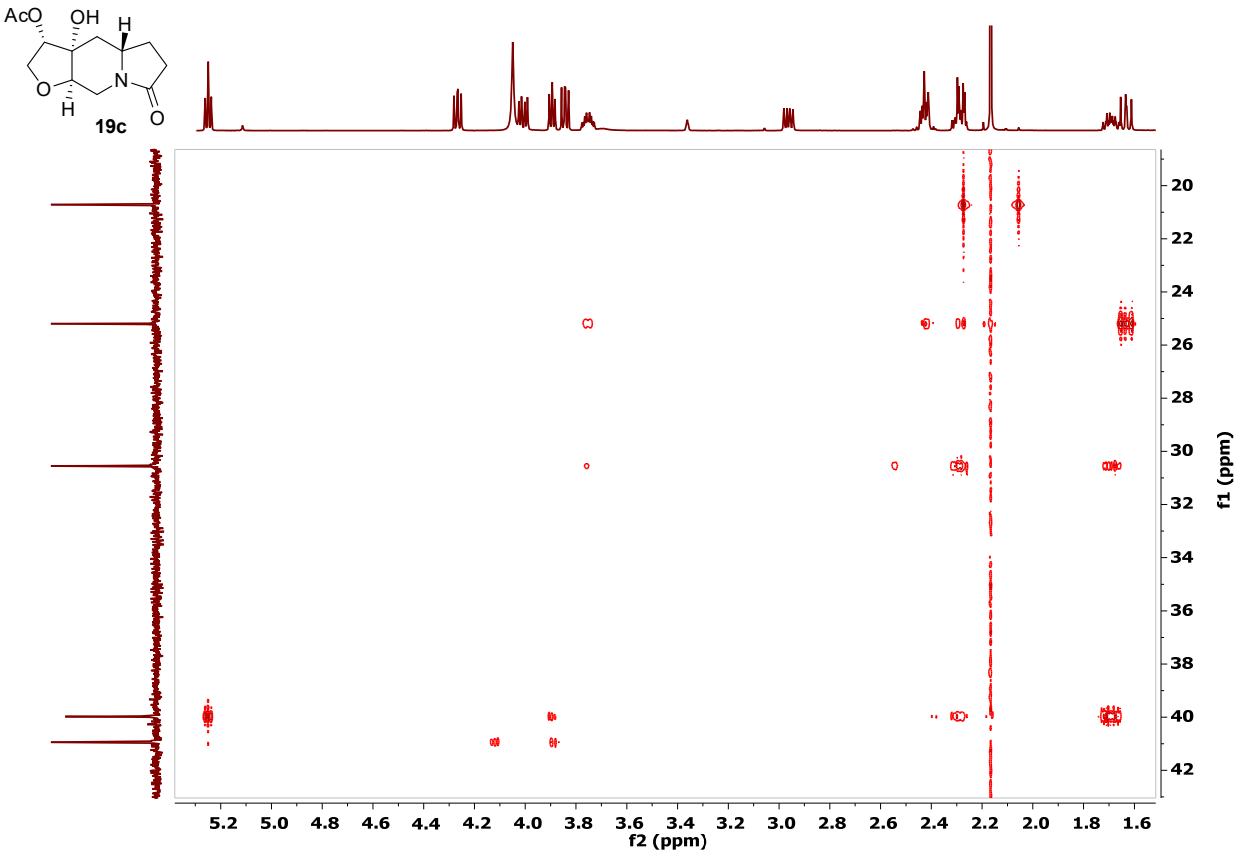
^{13}C NMR of **19c**



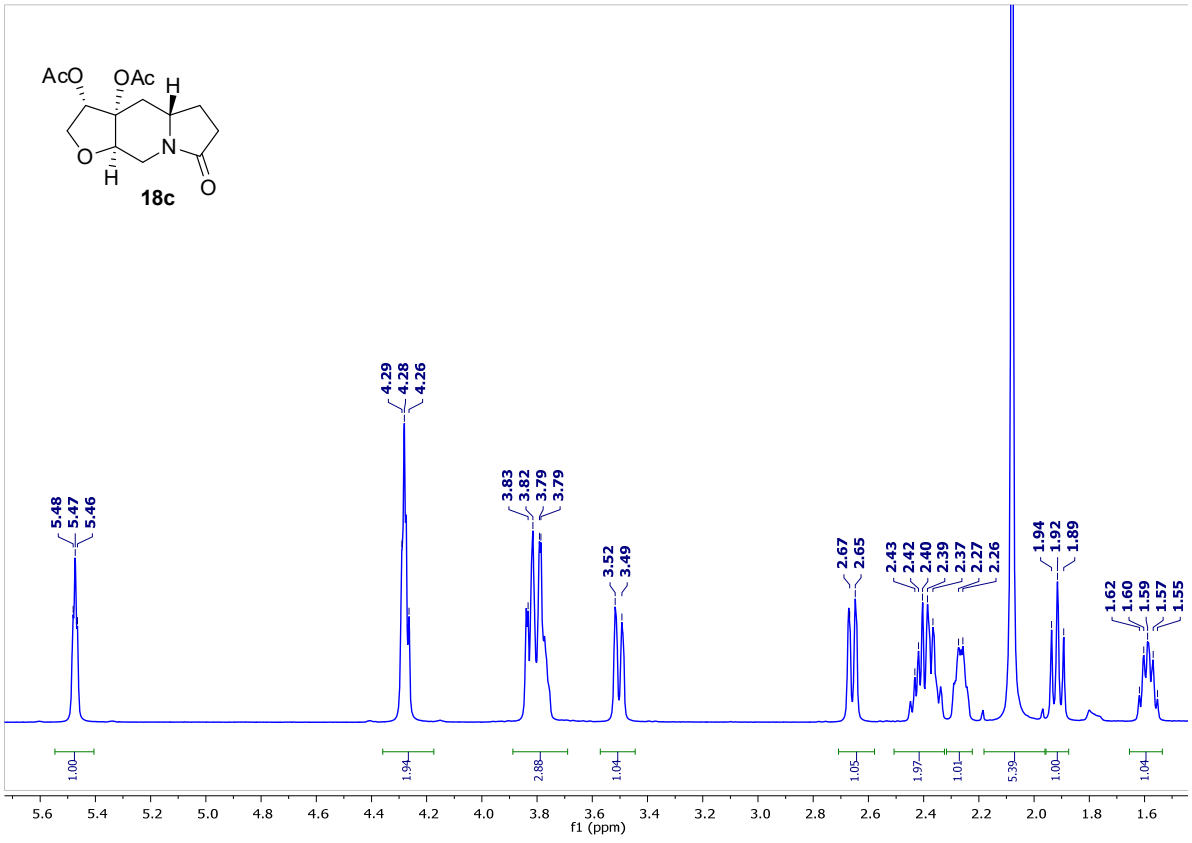
COSY of **19c**



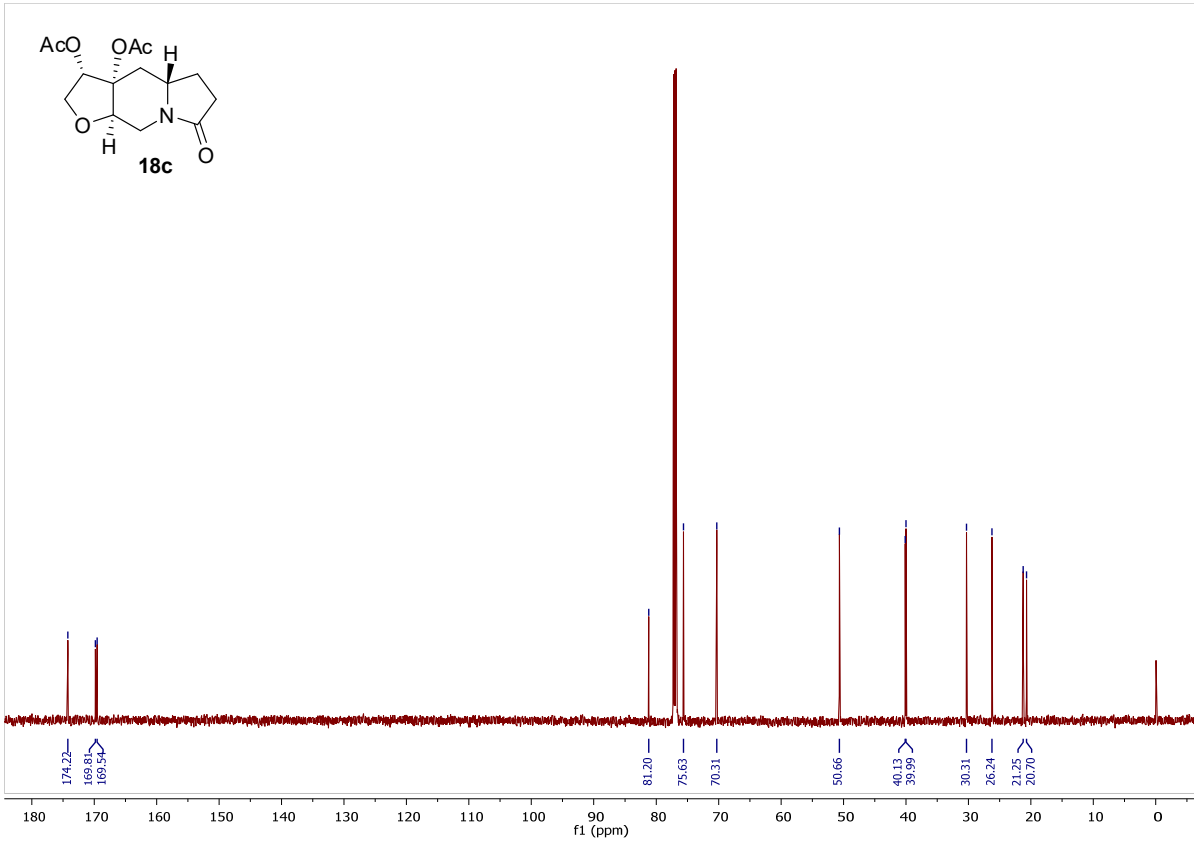
HMBC of **19c**



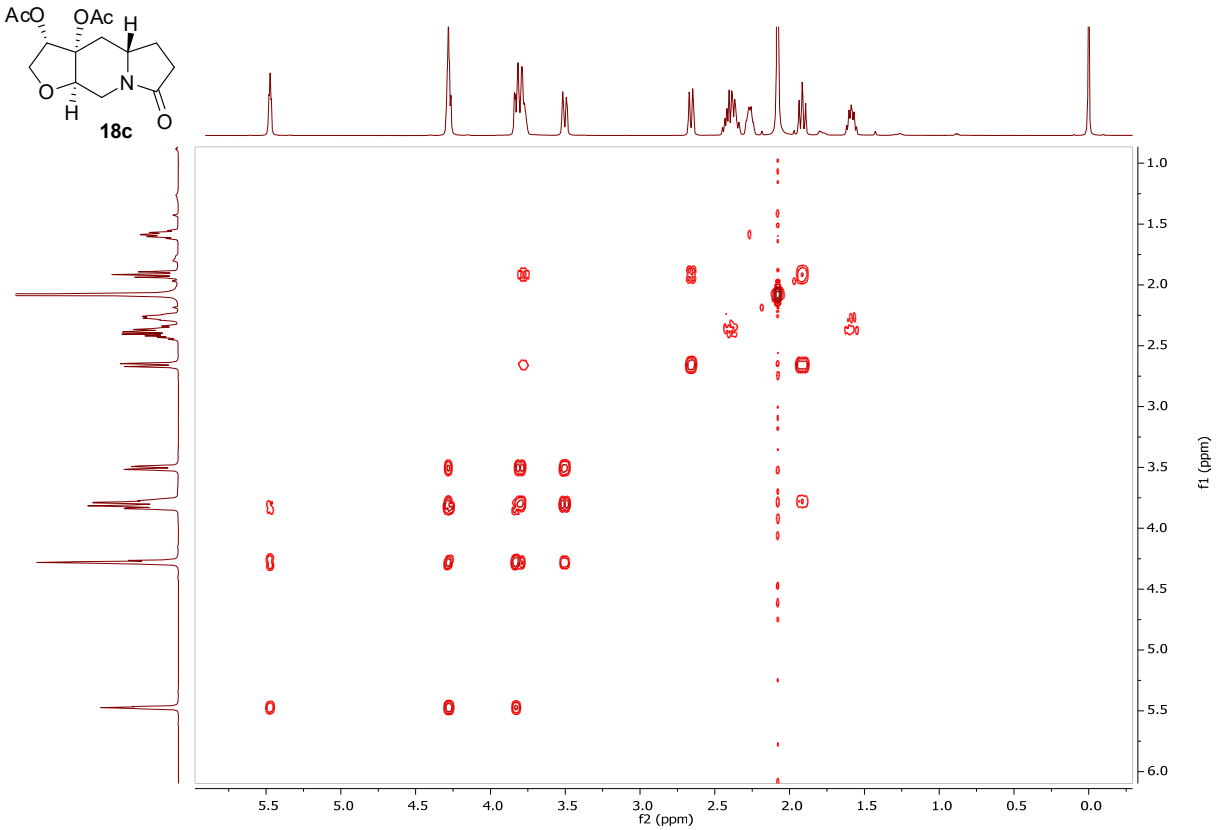
HSQC of **19c**



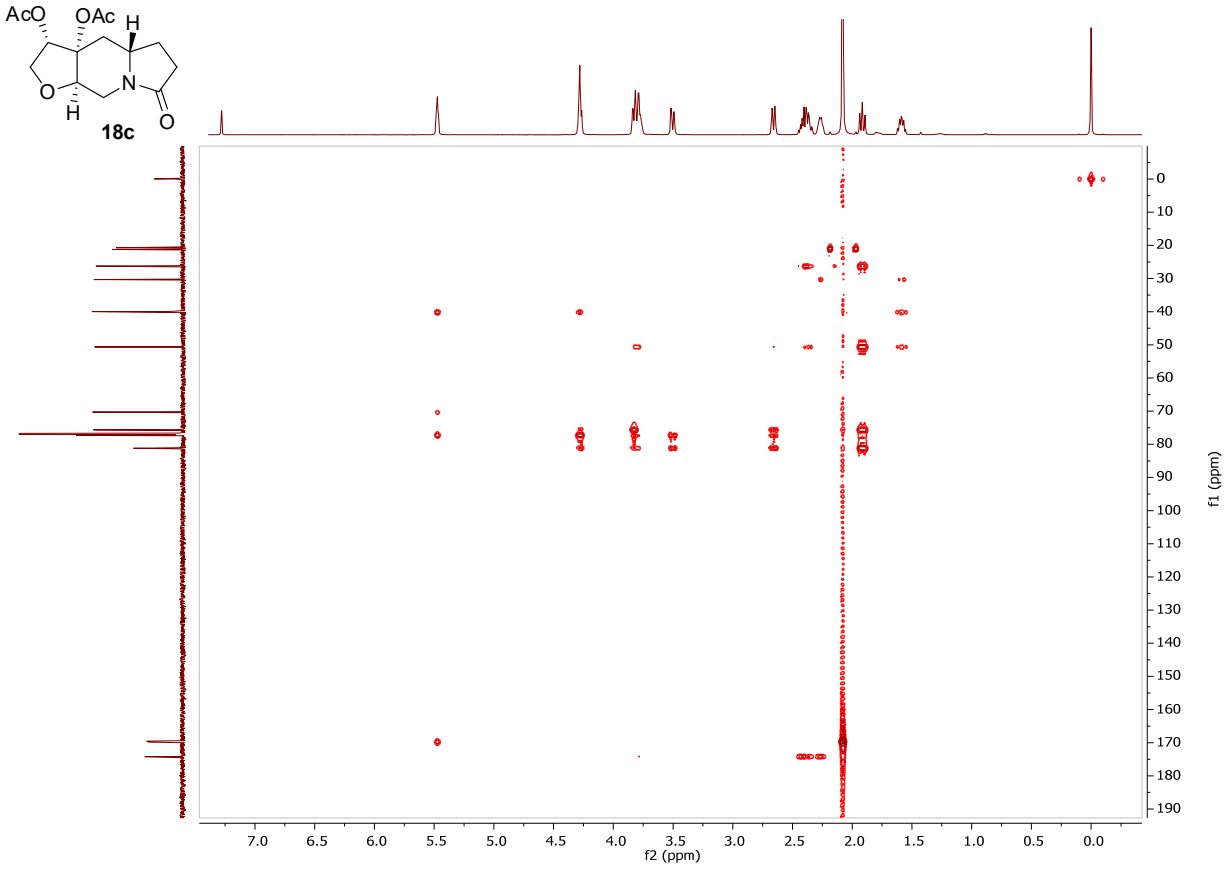
^{1}H NMR of **18c**



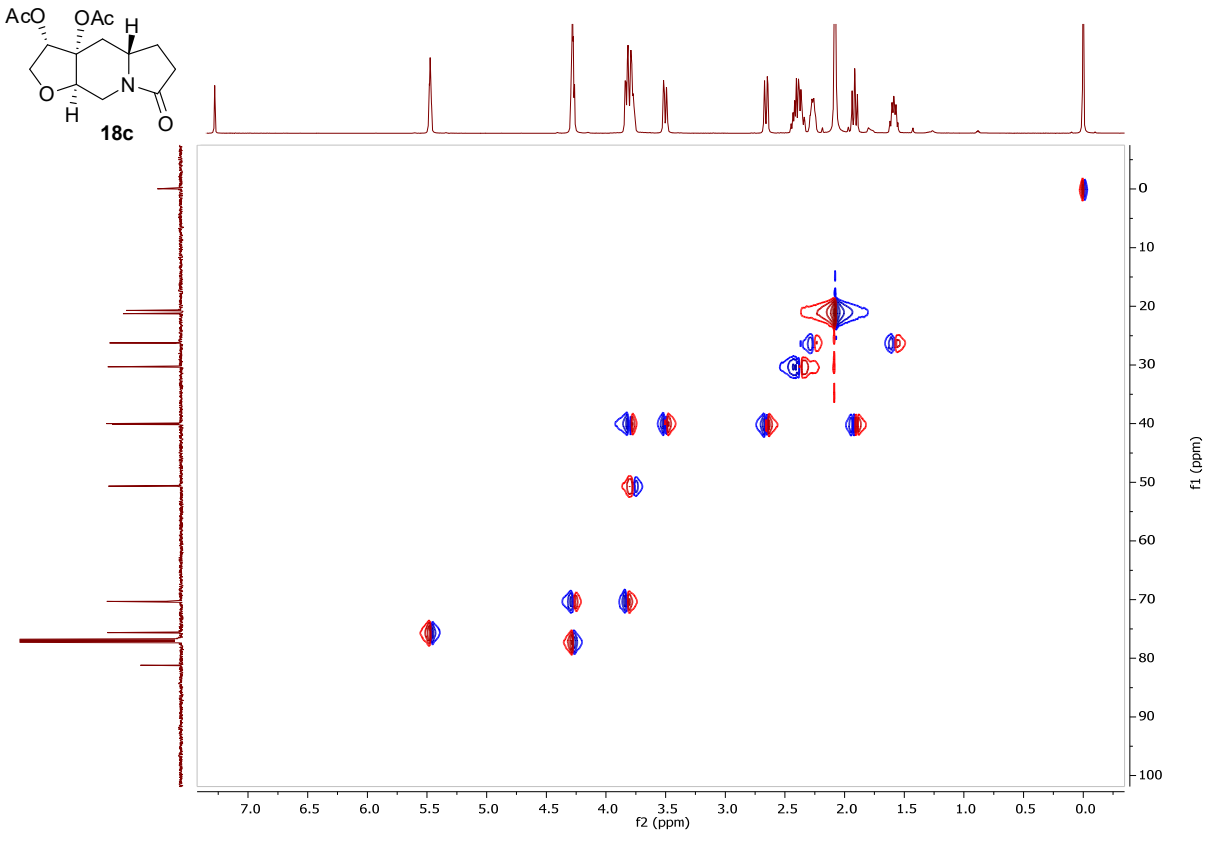
^{13}C NMR of **18c**



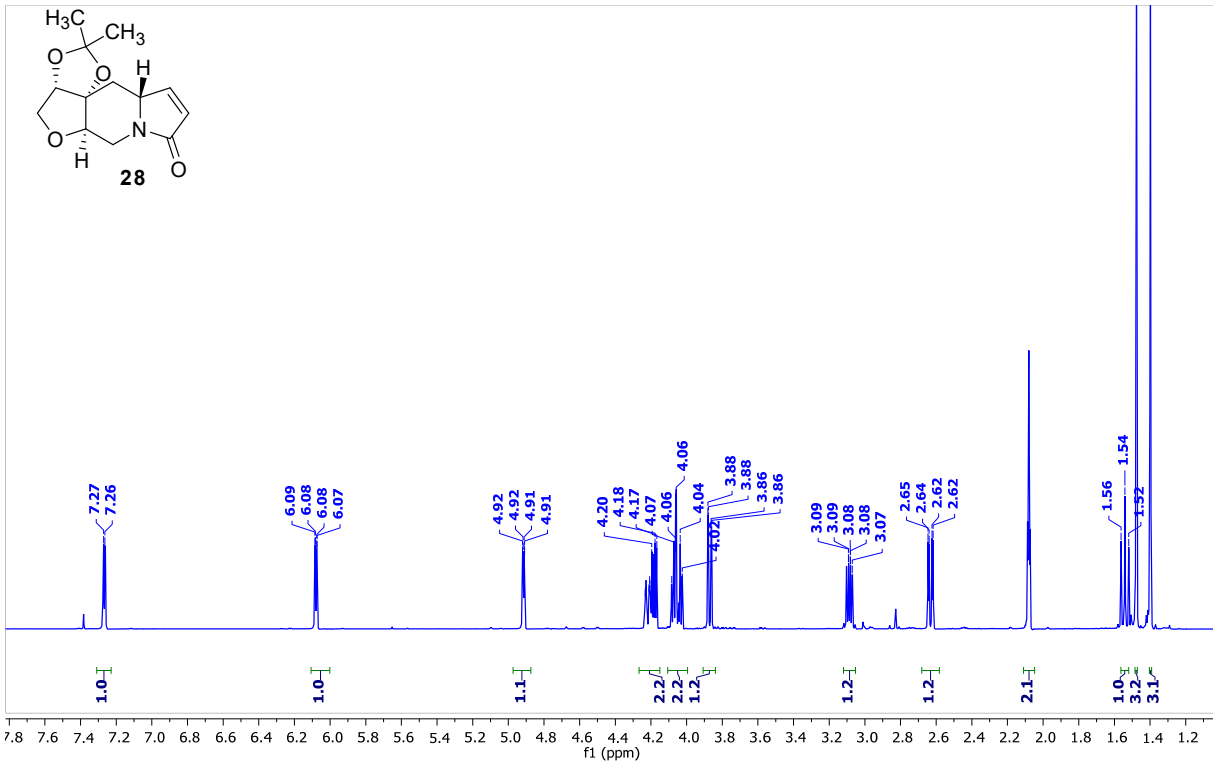
COSY of **18c**



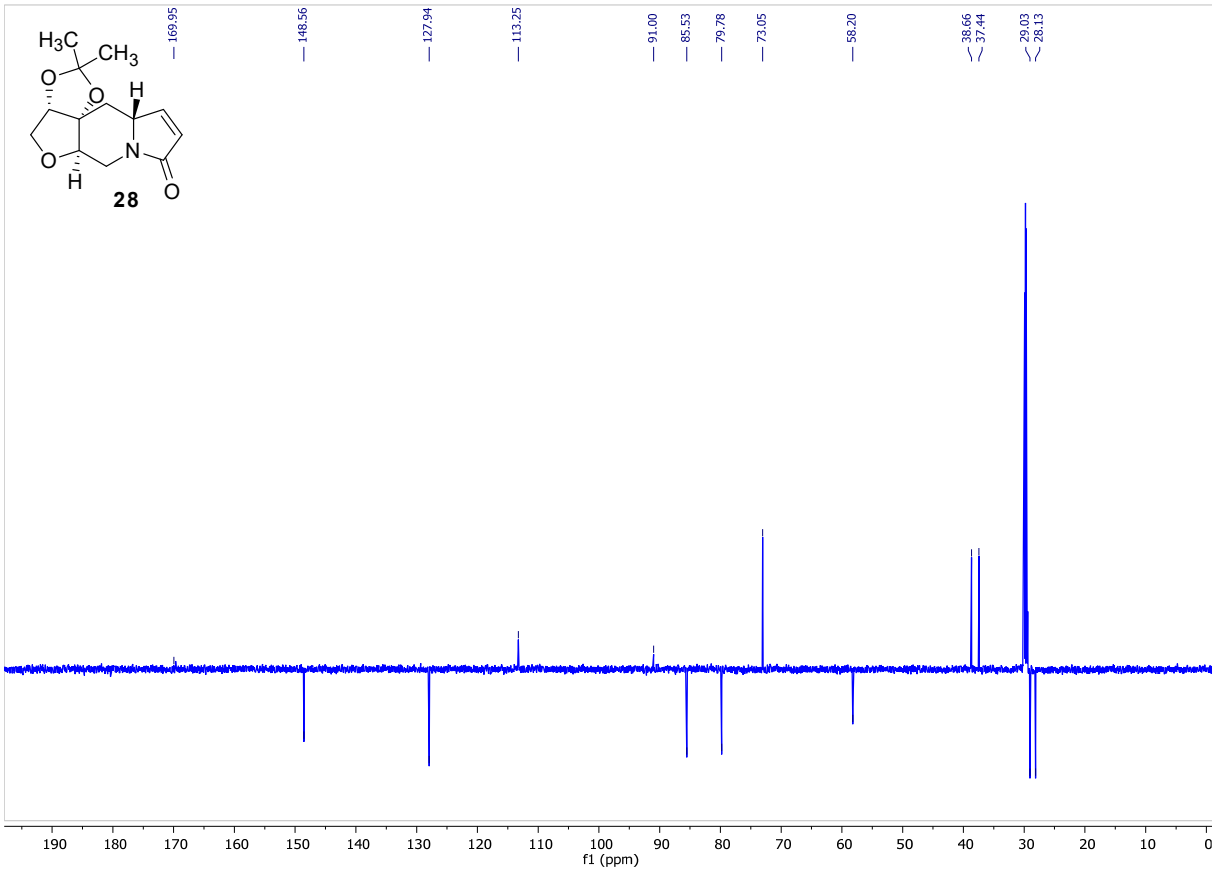
HMBC of **18c**



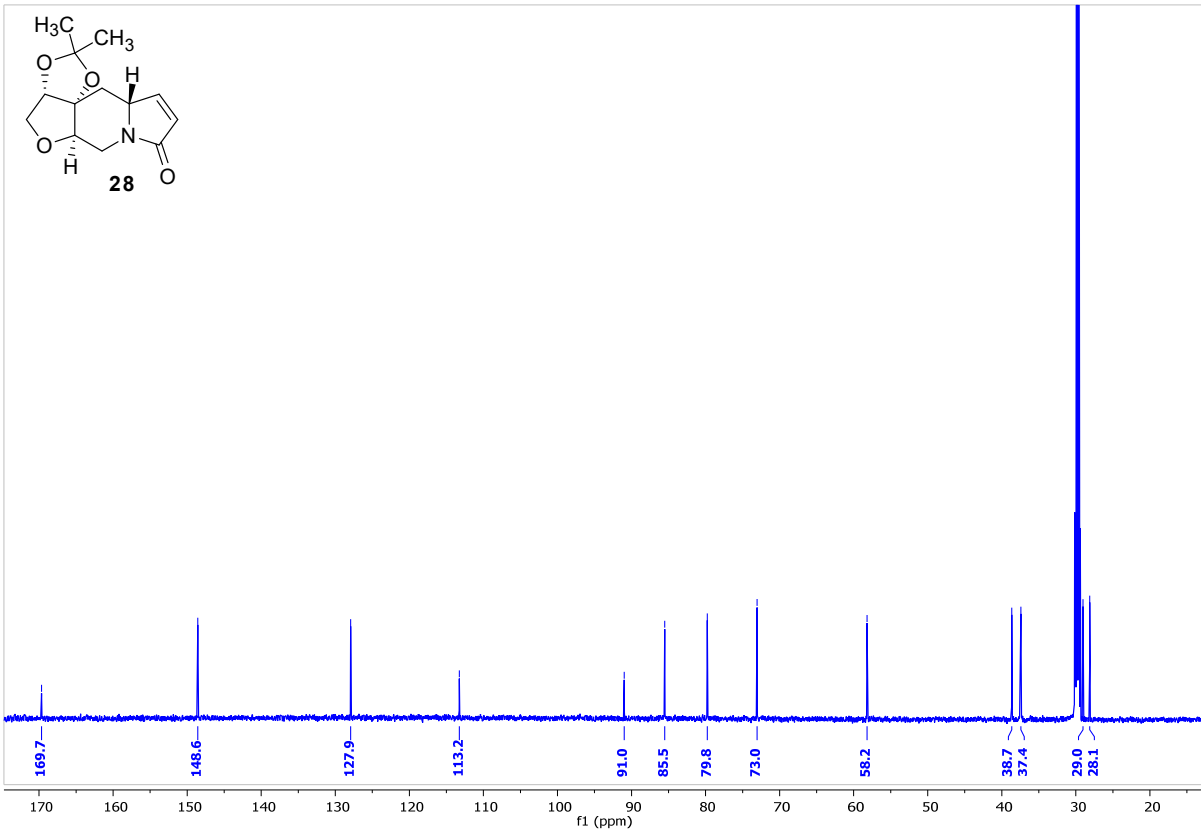
HSQC of **18c**



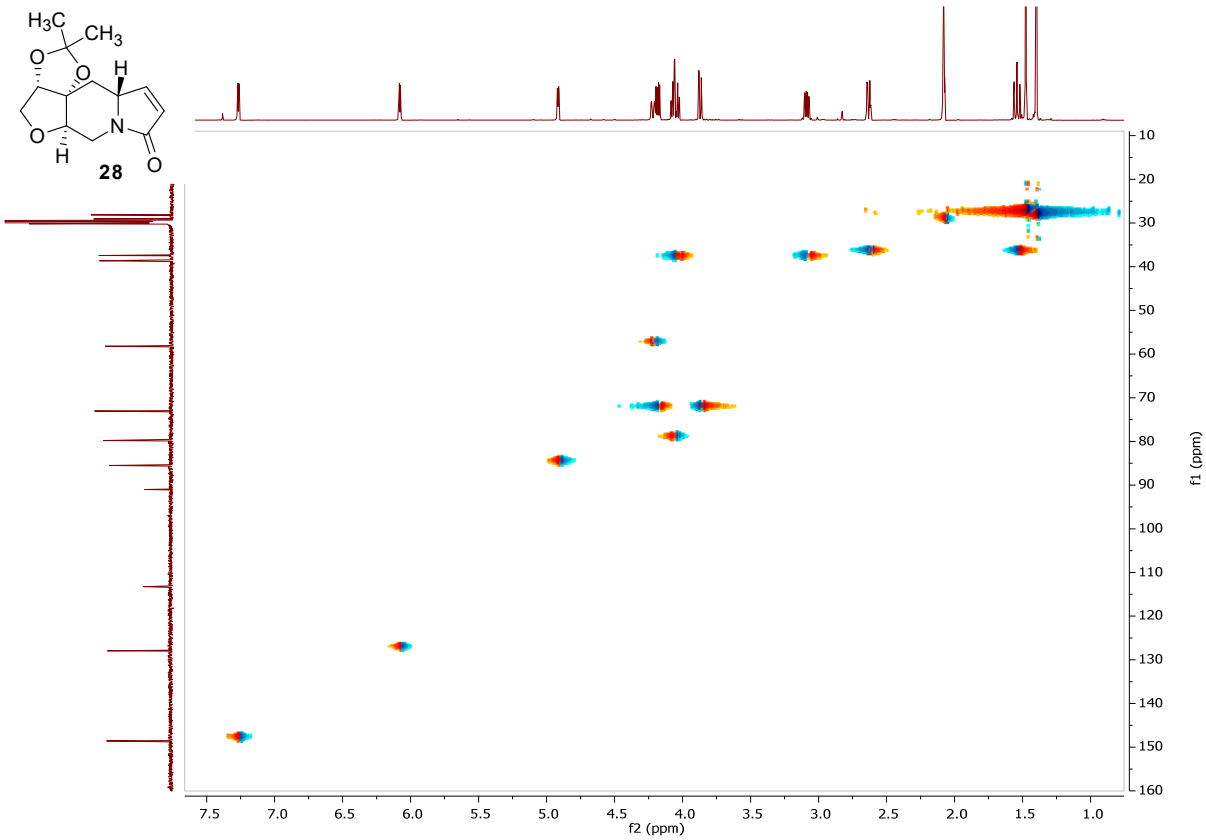
^{1}H NMR of **28**



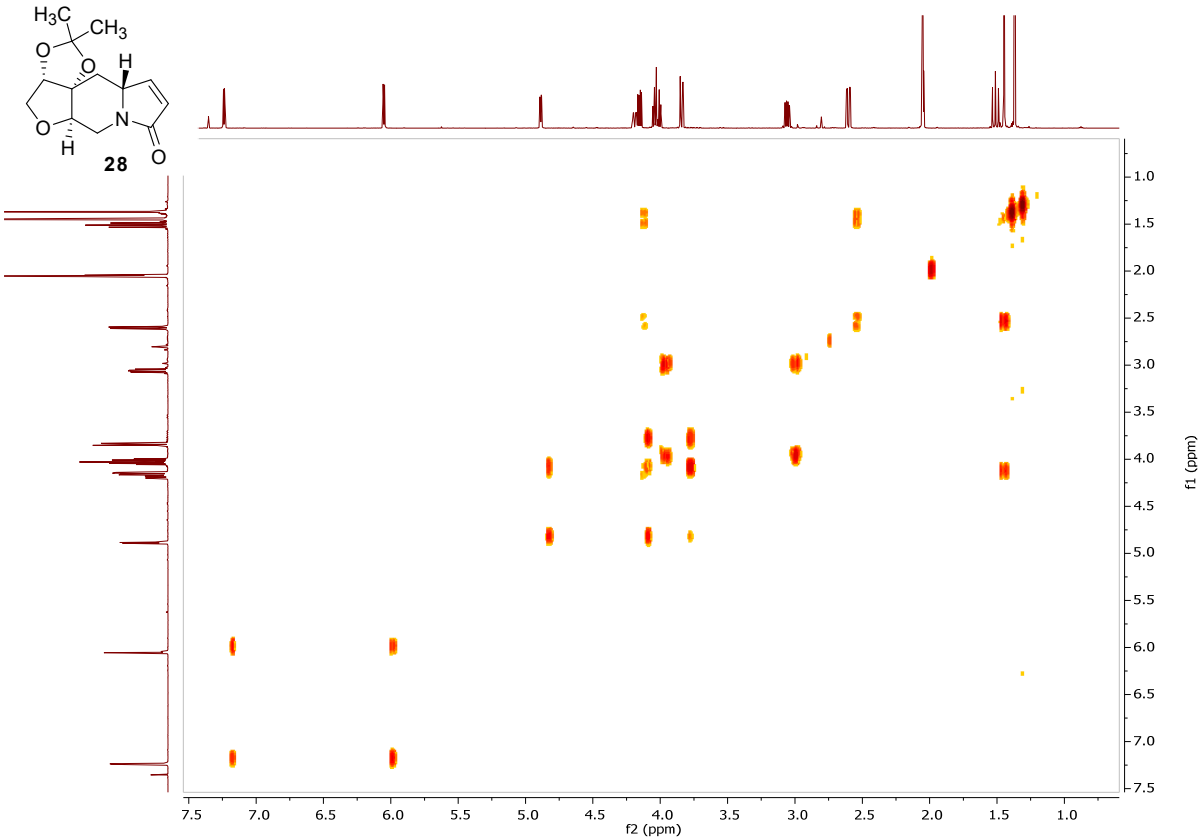
^{13}C NMR (APT) of **28**



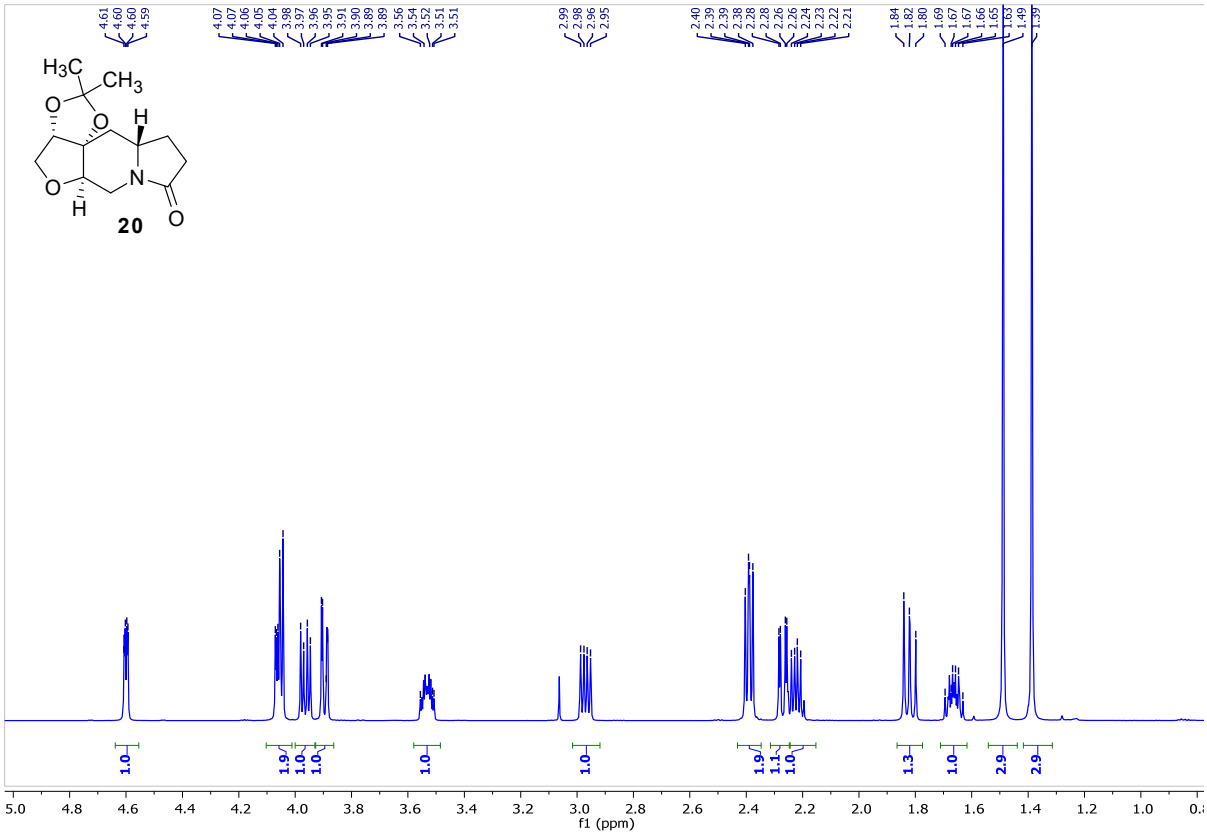
^{13}C NMR of **28**



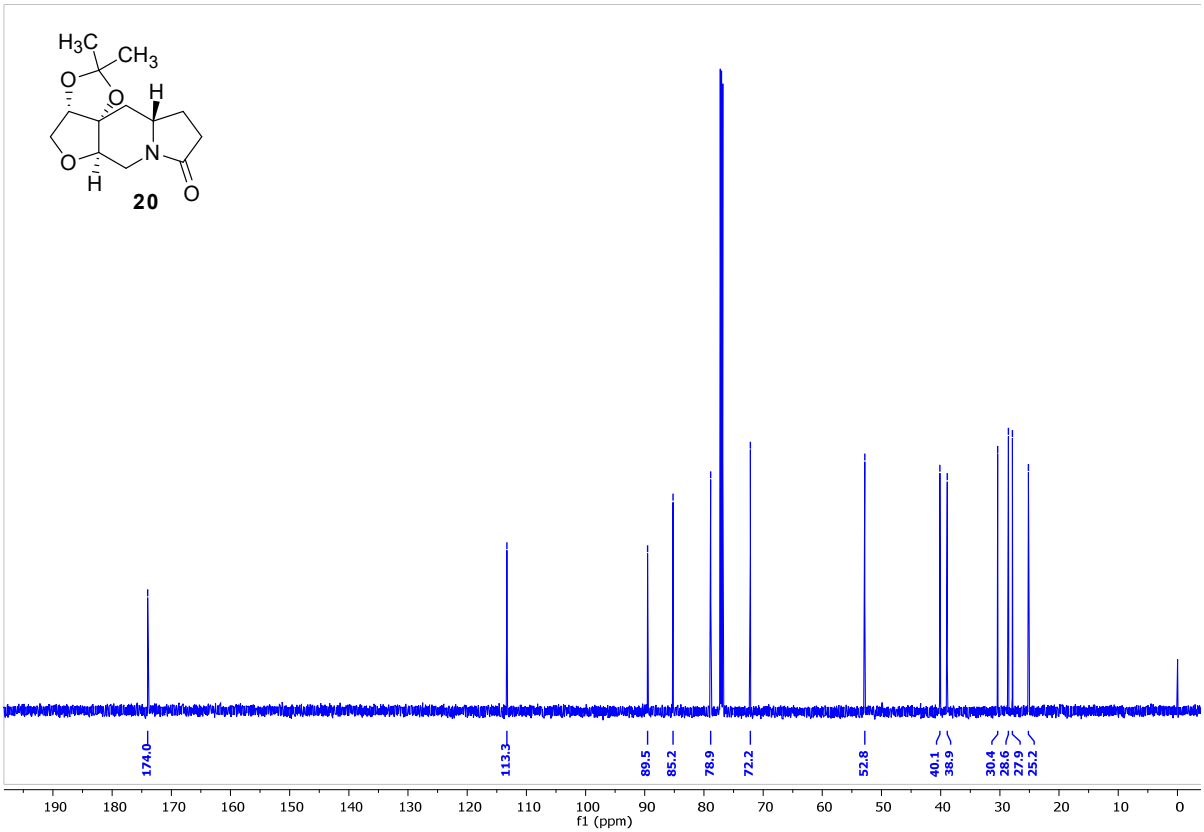
HSQC of **28**



COSY of **28**

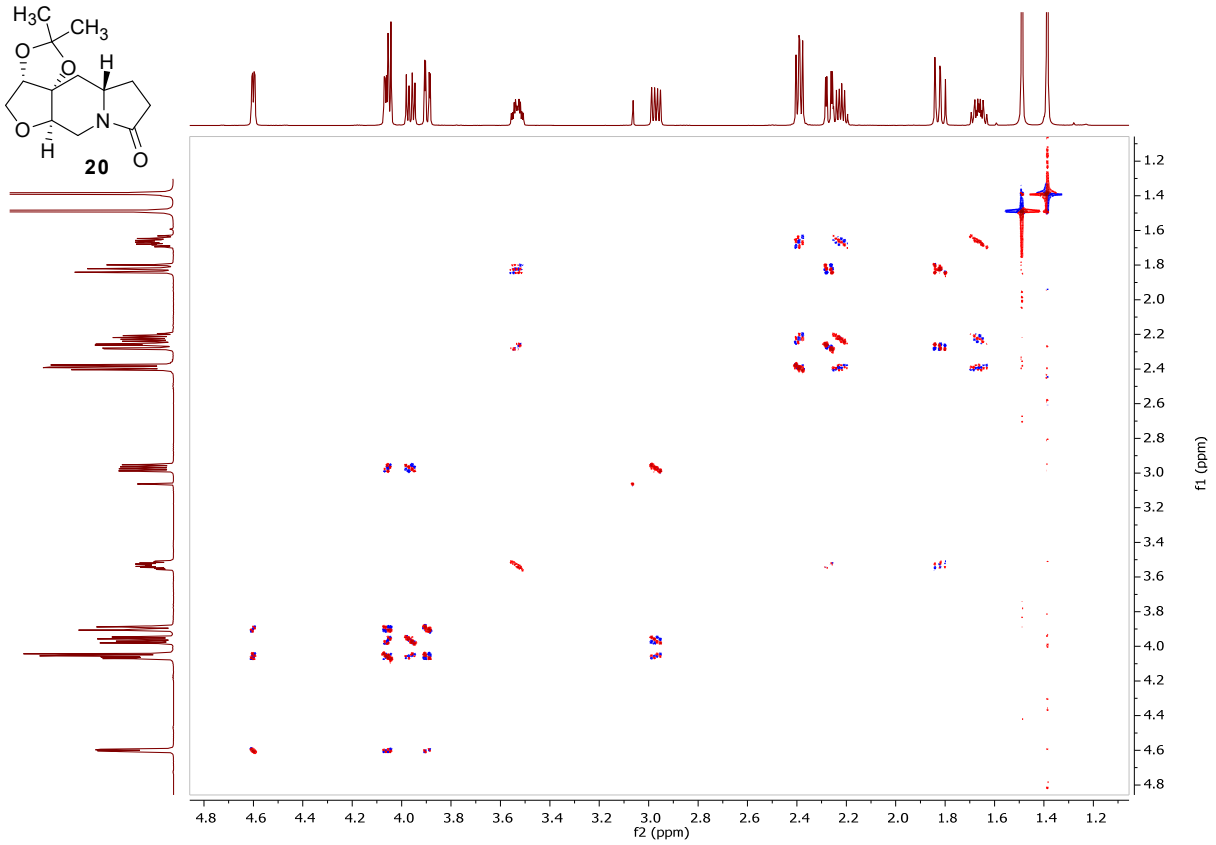


^{1}H NMR of **20**

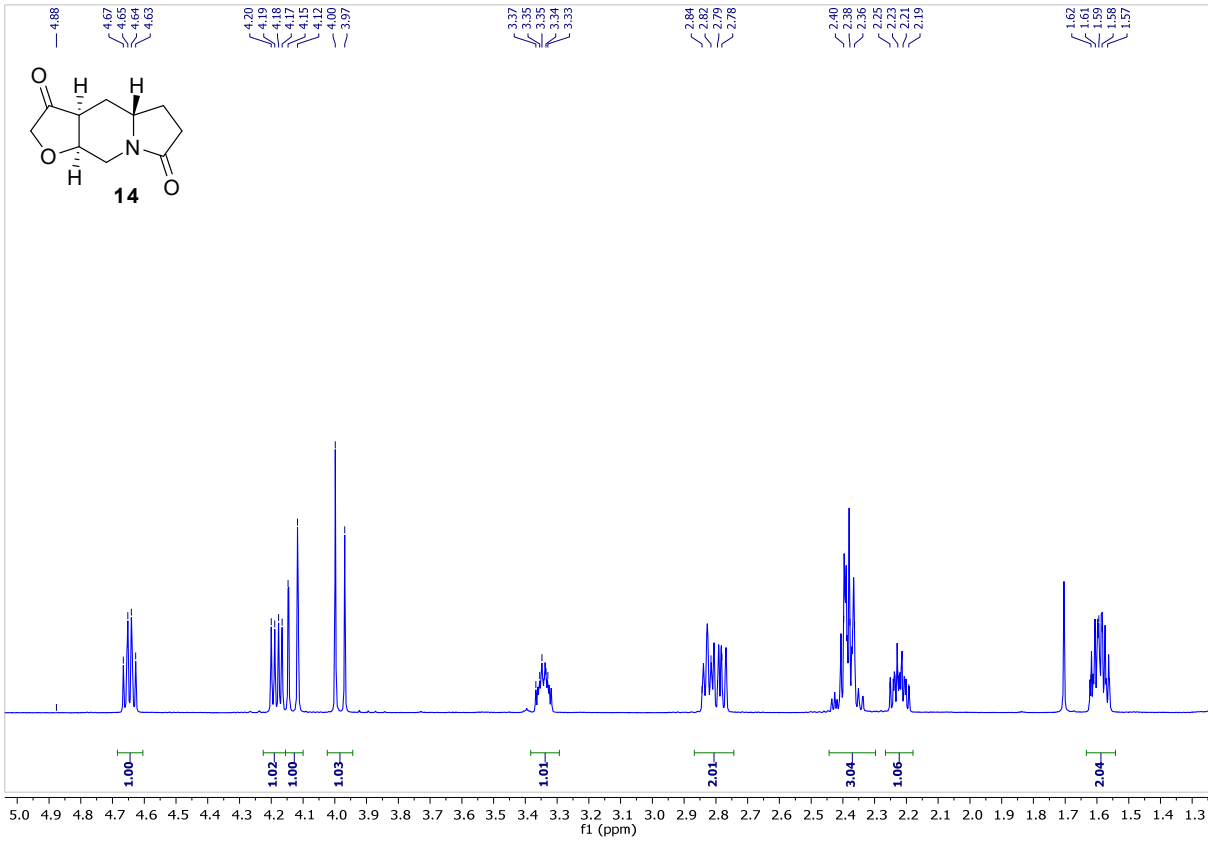


^{13}C NMR of **20**

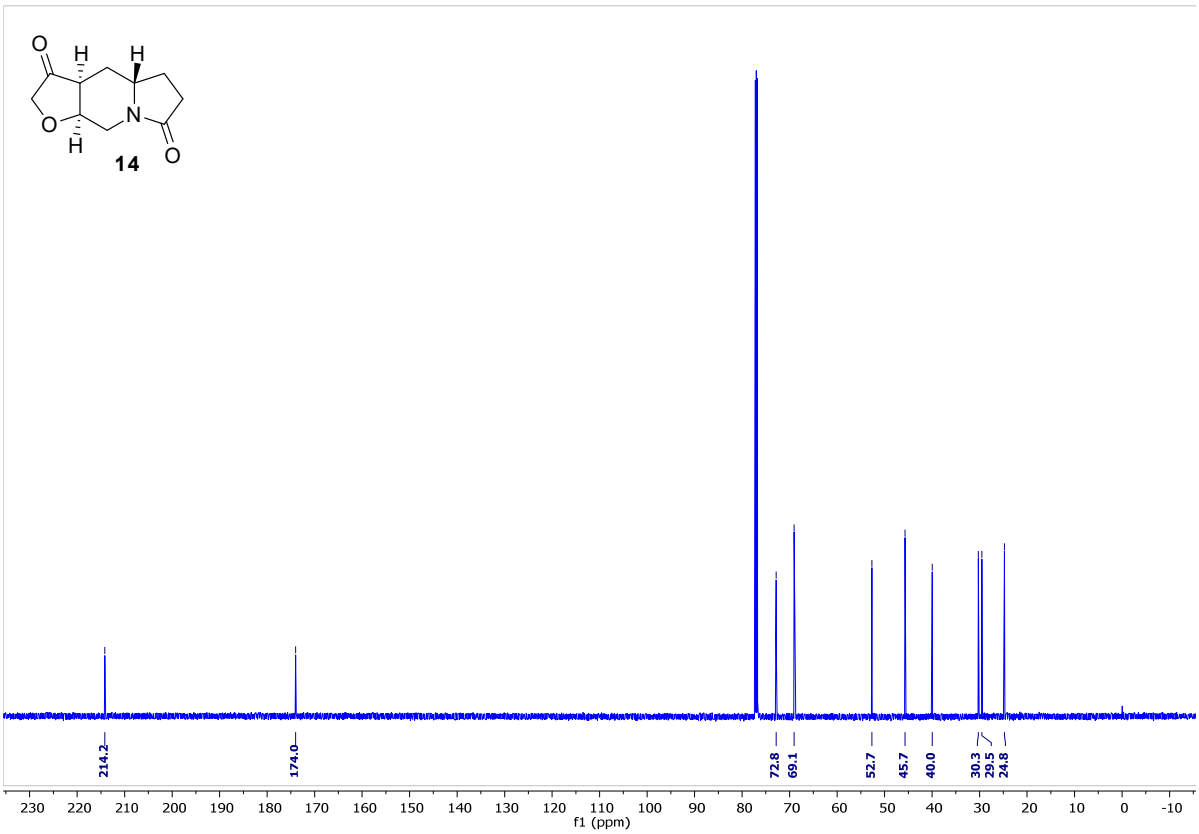
HMBC of **20**



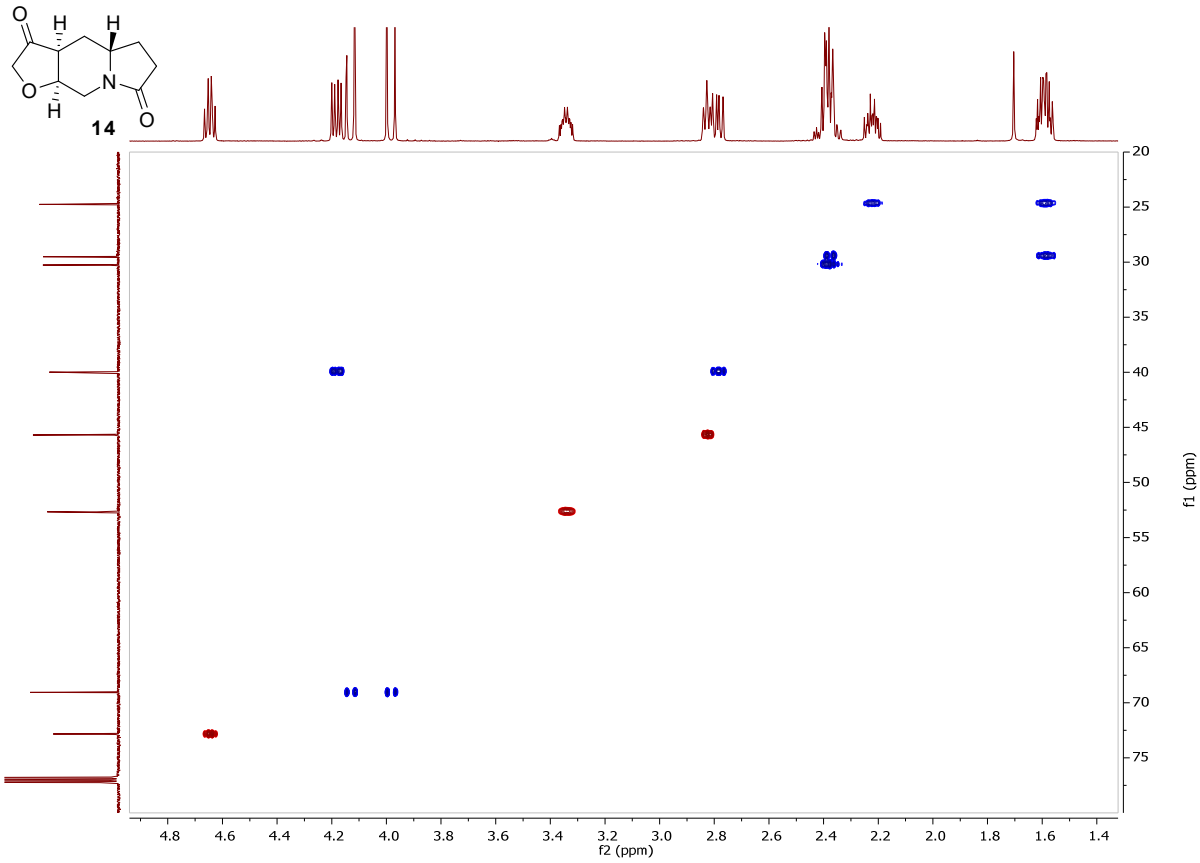
COSY of **20**



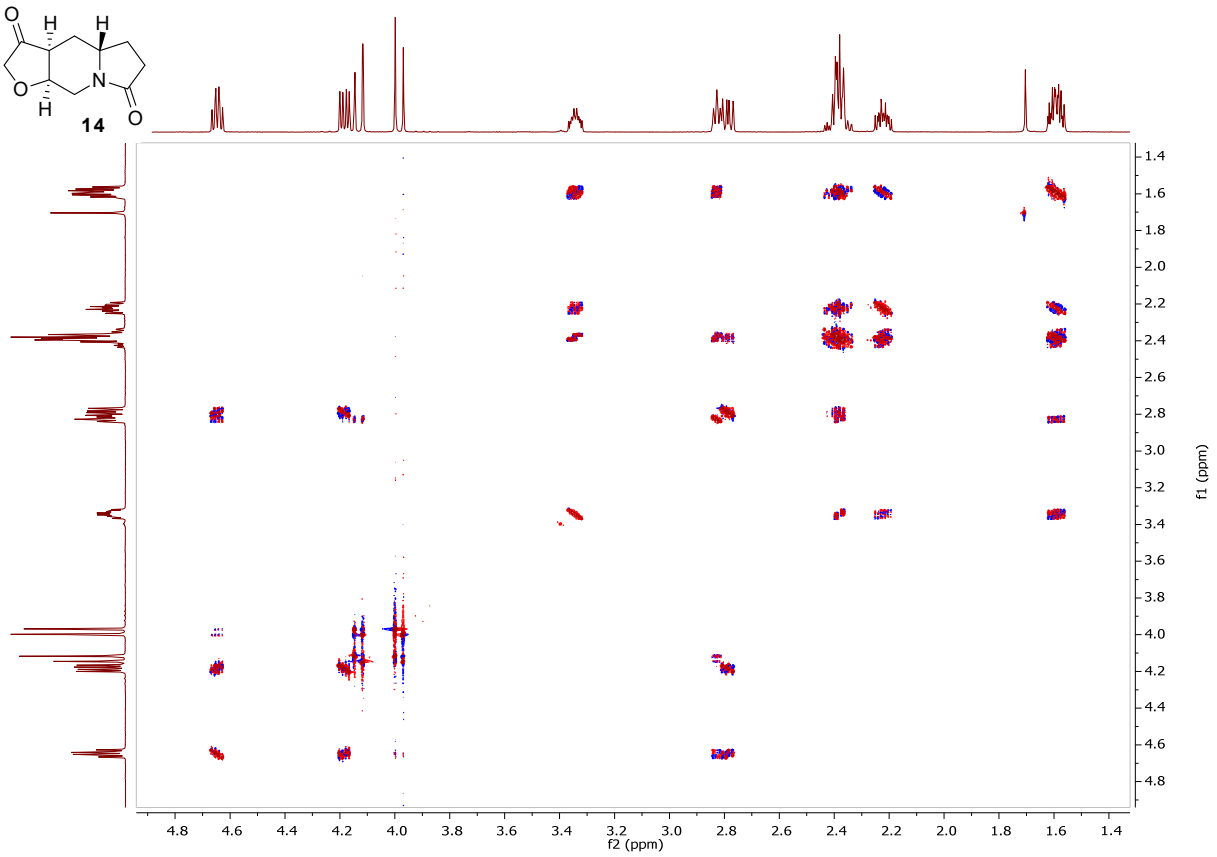
^{1}H NMR of 14



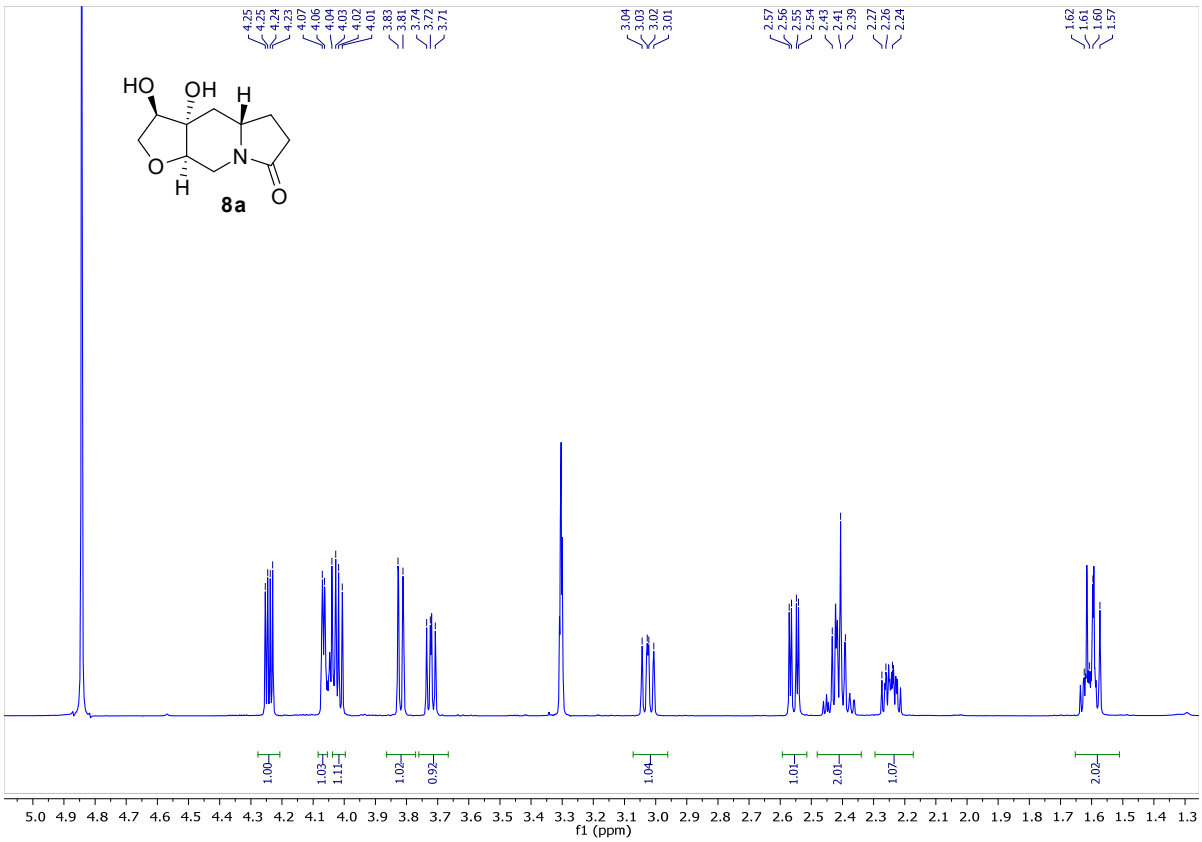
^{13}C NMR of 14



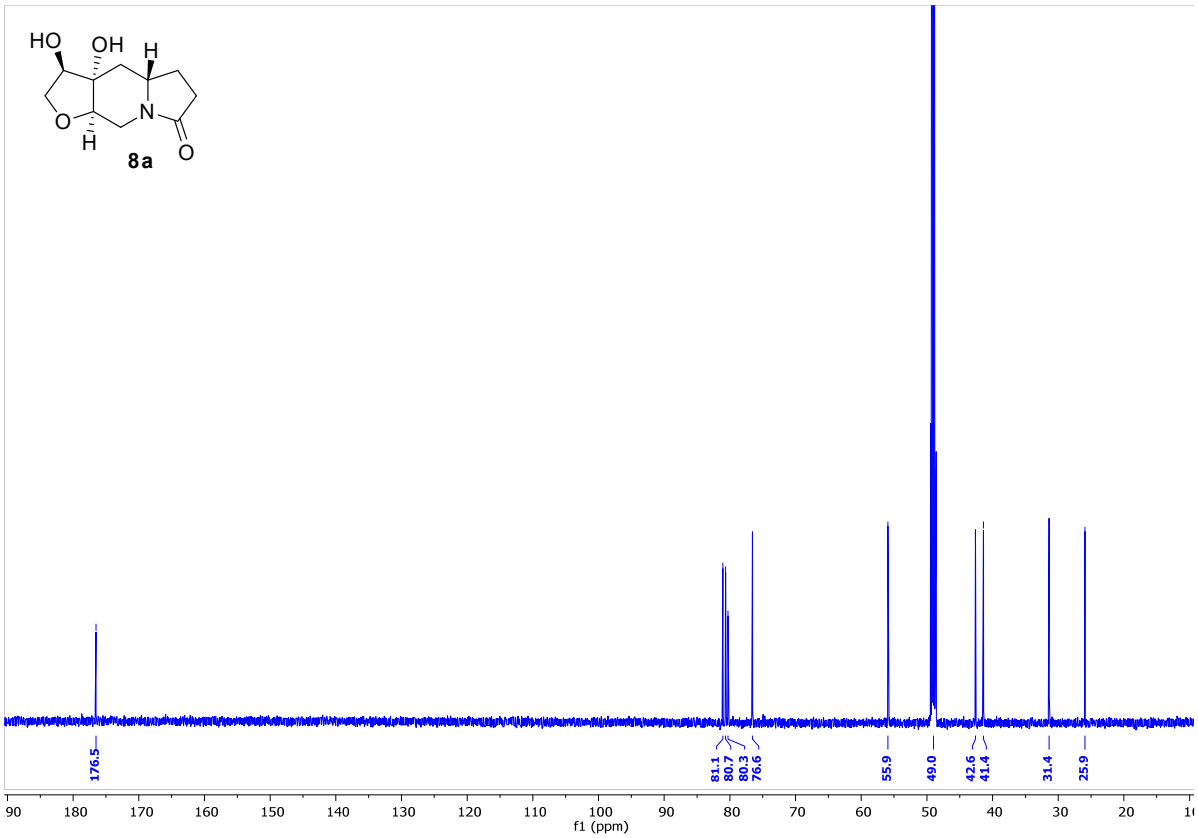
HSQC of 14



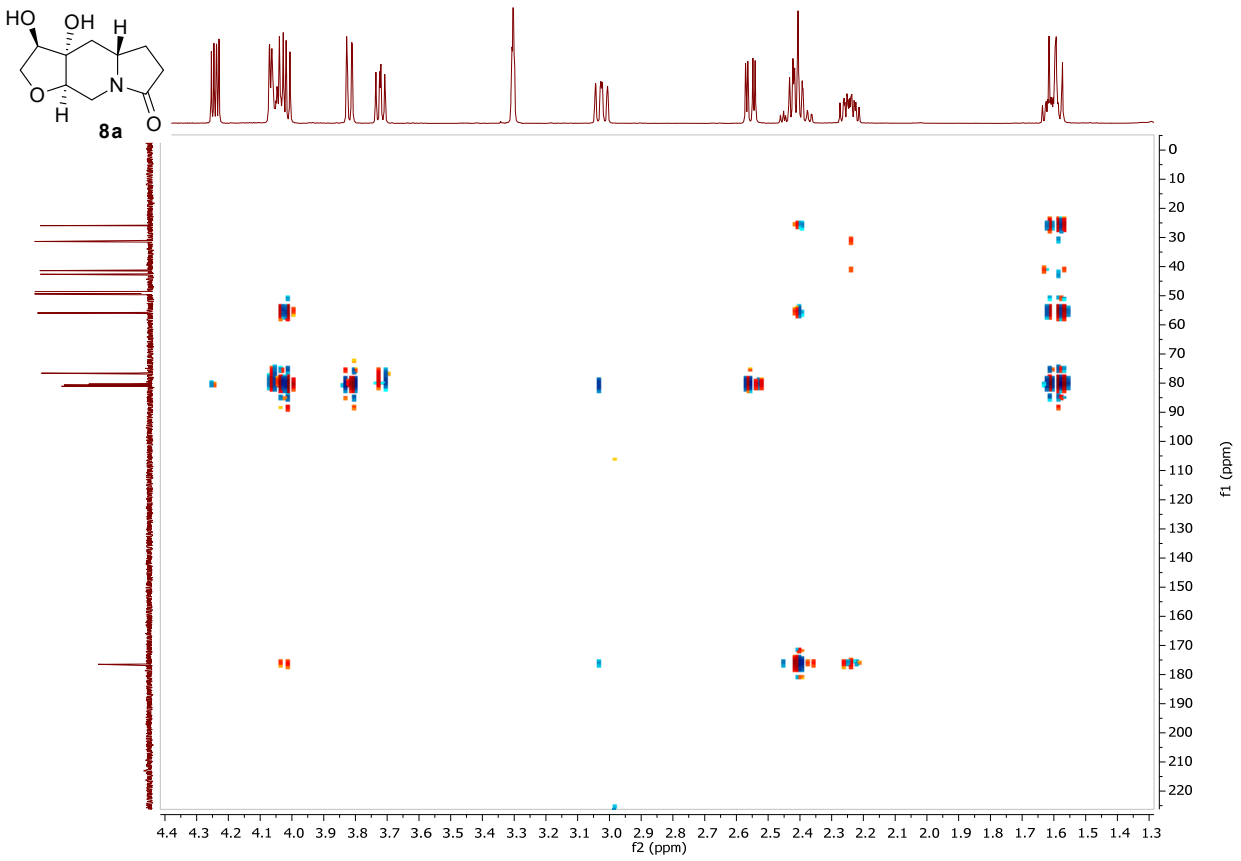
COSY of 14



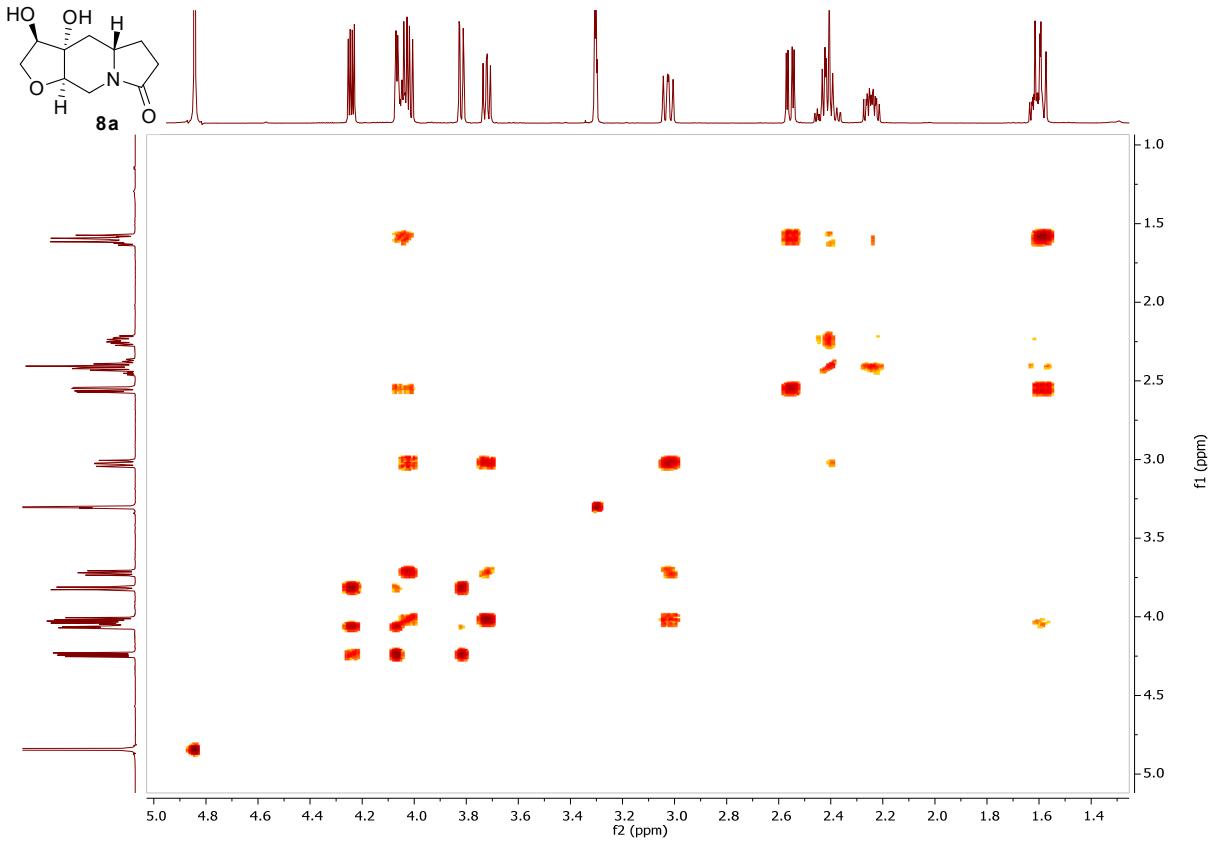
^{1}H NMR of **8a**



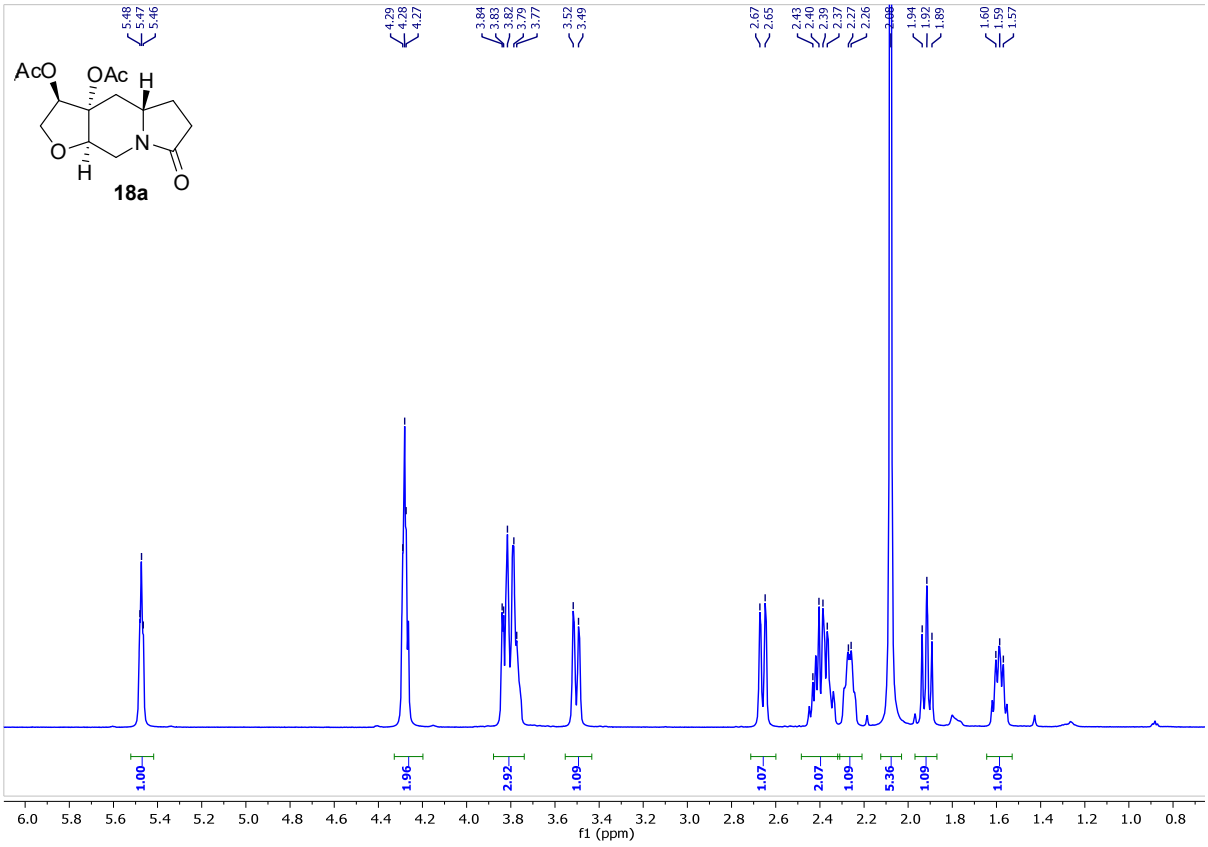
^{13}C NMR of **8a**



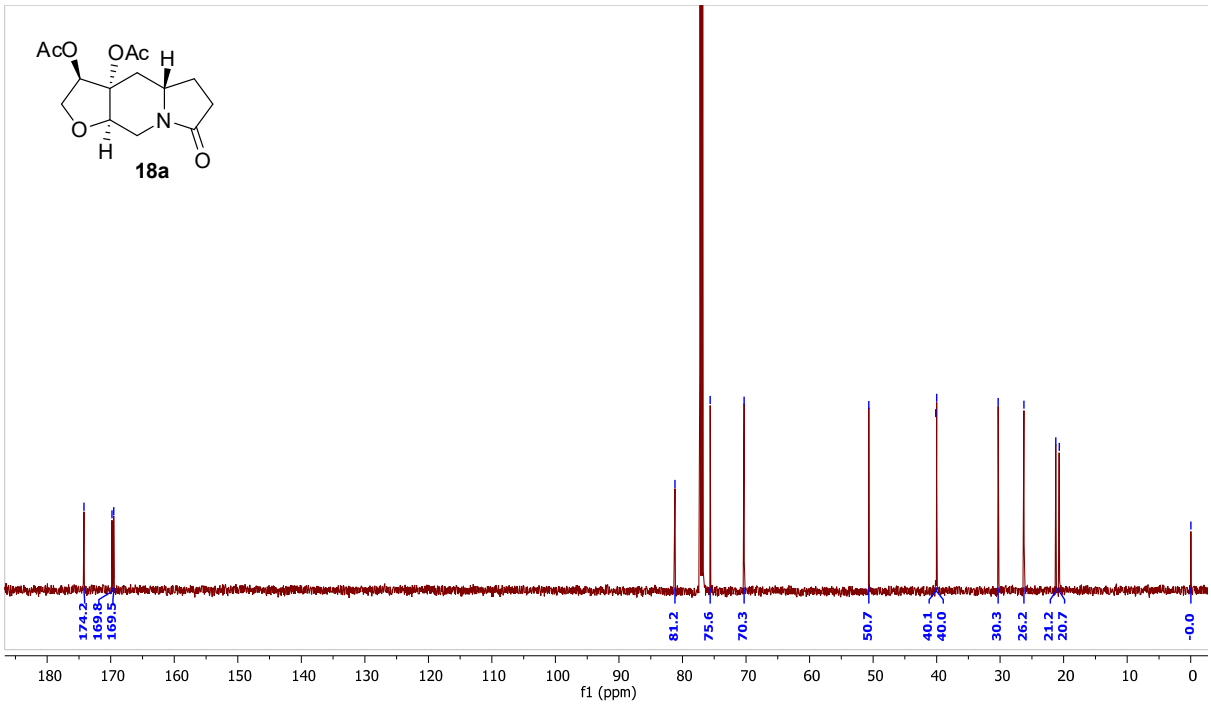
HMBC of **8a**



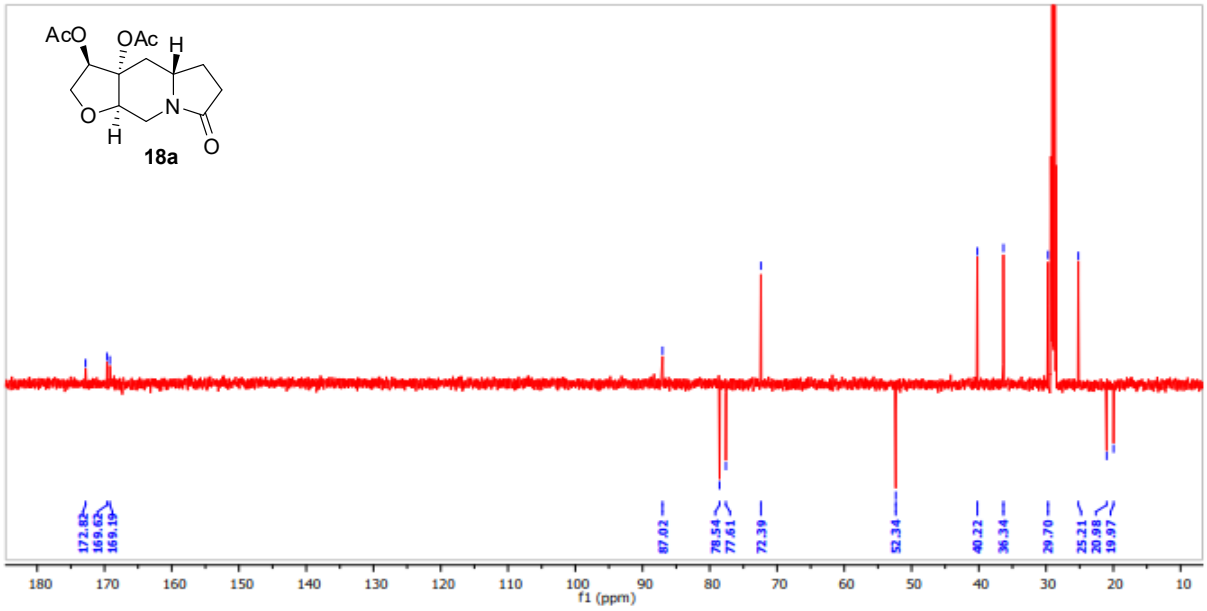
COSY of **8a**



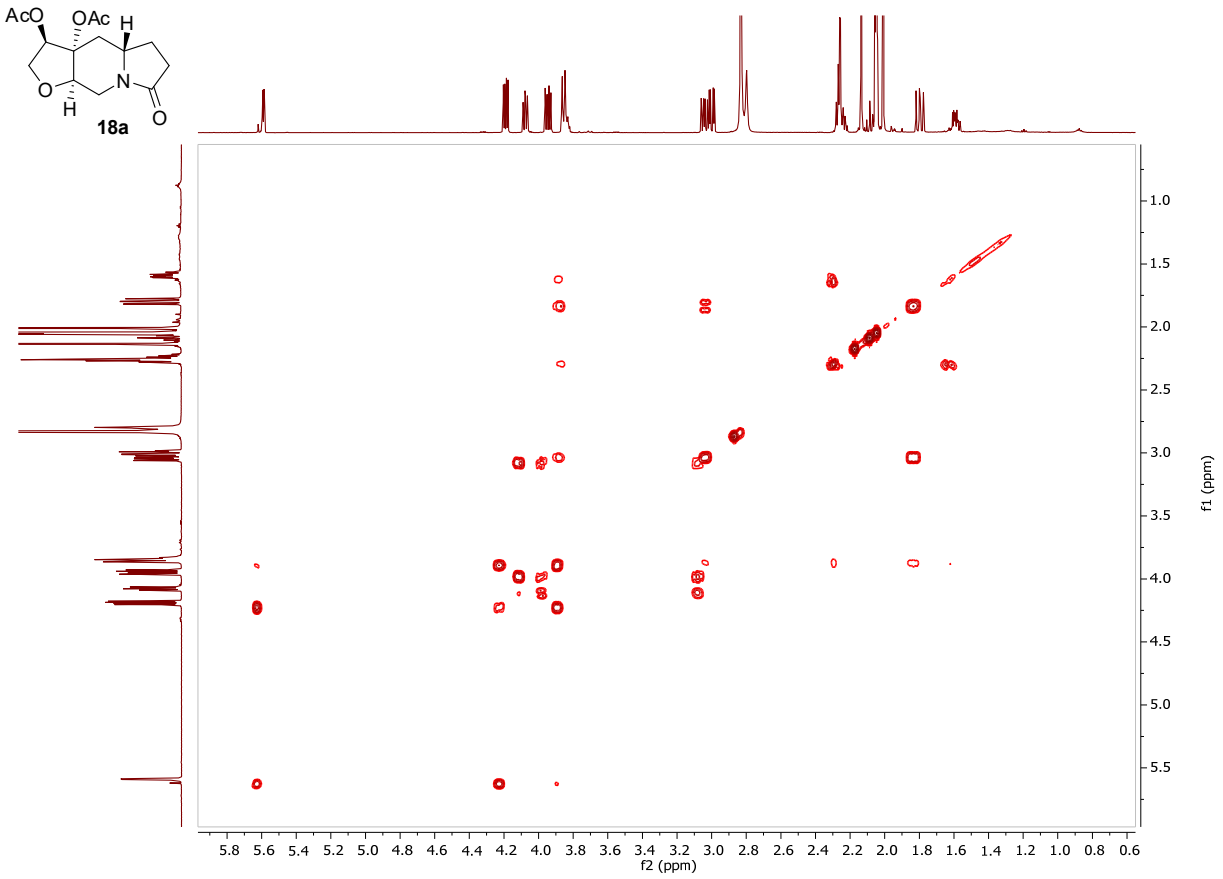
^{1}H NMR of **18a**



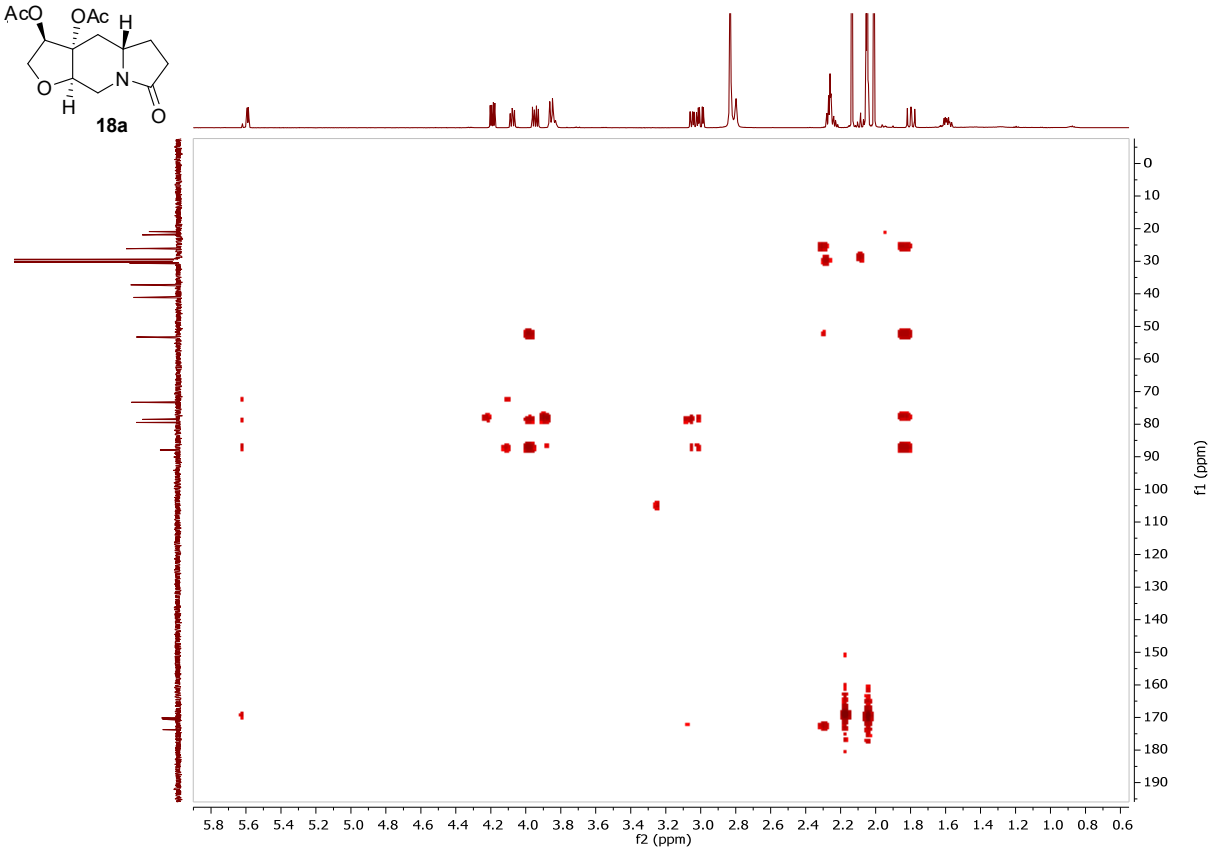
^{13}C NMR of **18a**



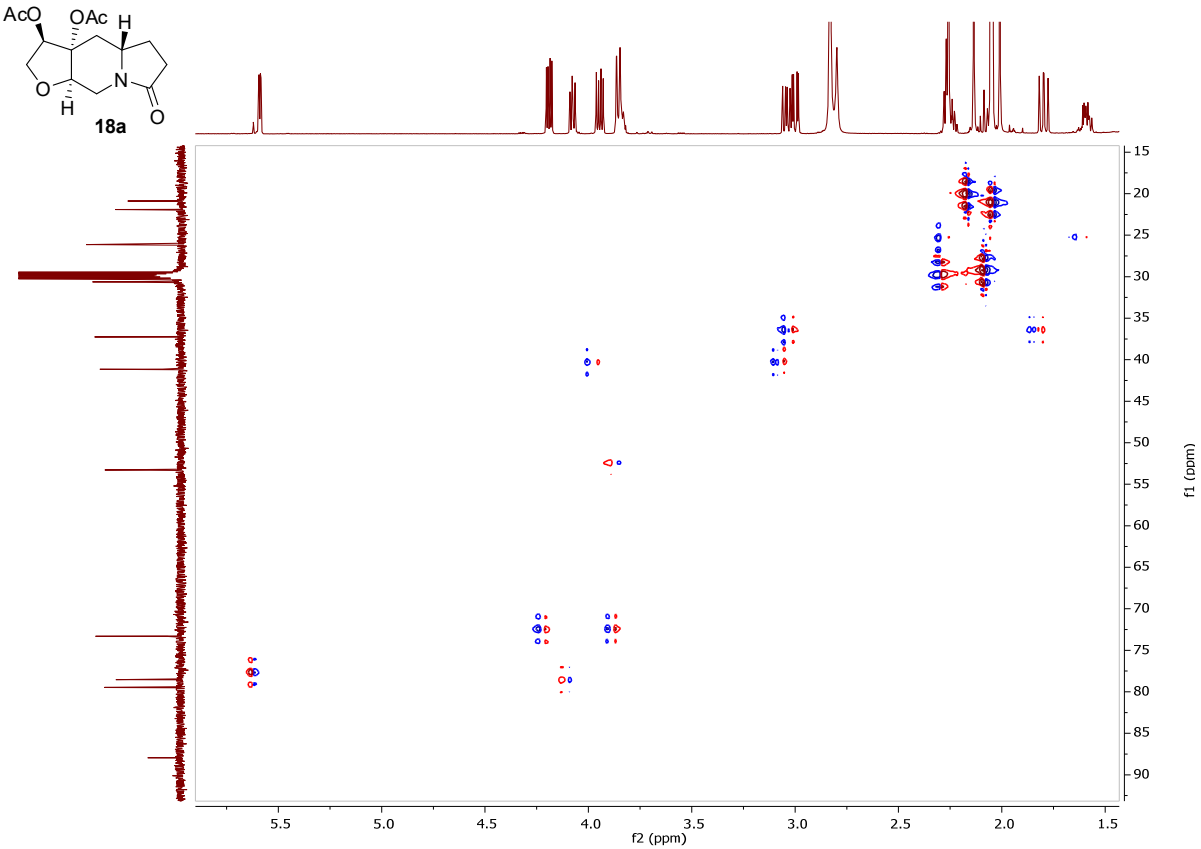
^{13}C NMR (APT) of **18a**



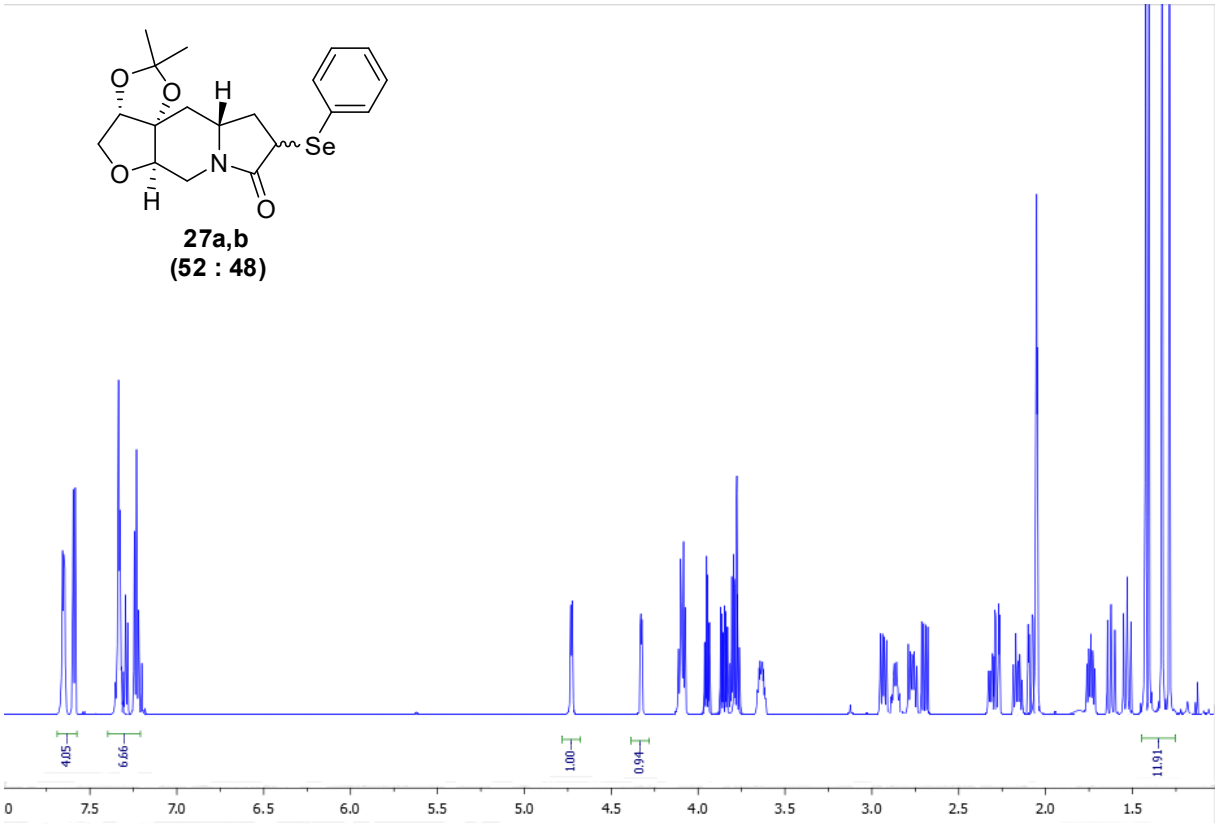
COSY of **18a**



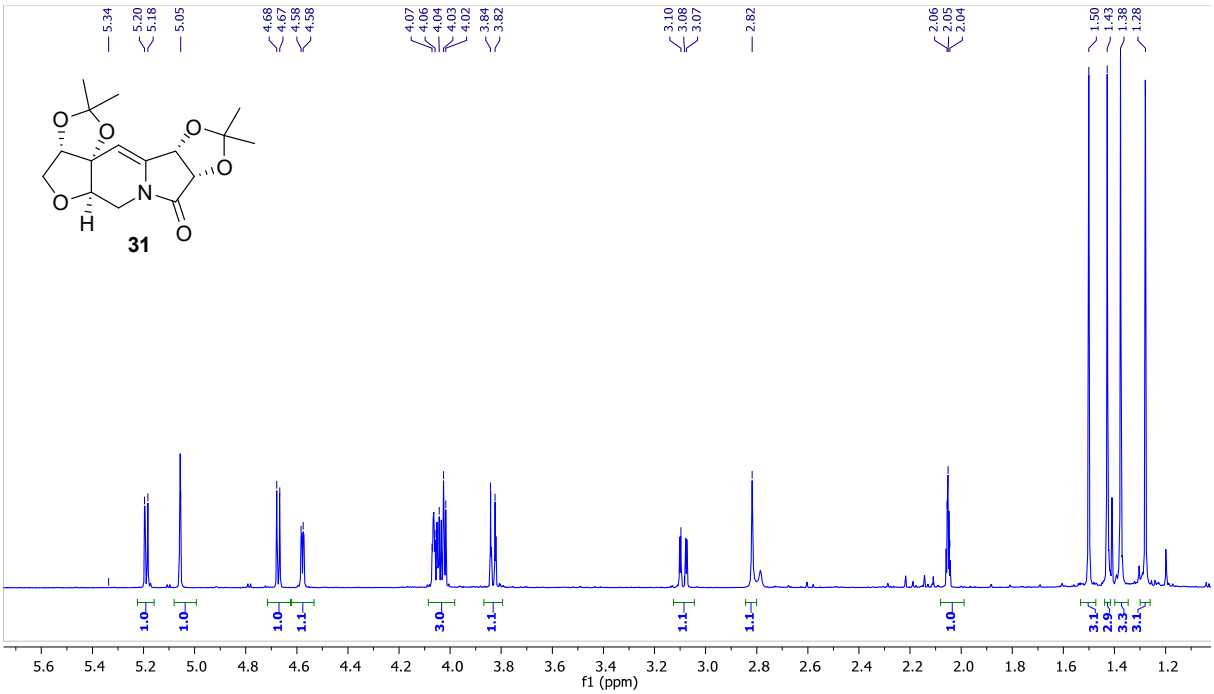
HMBC of **18a**



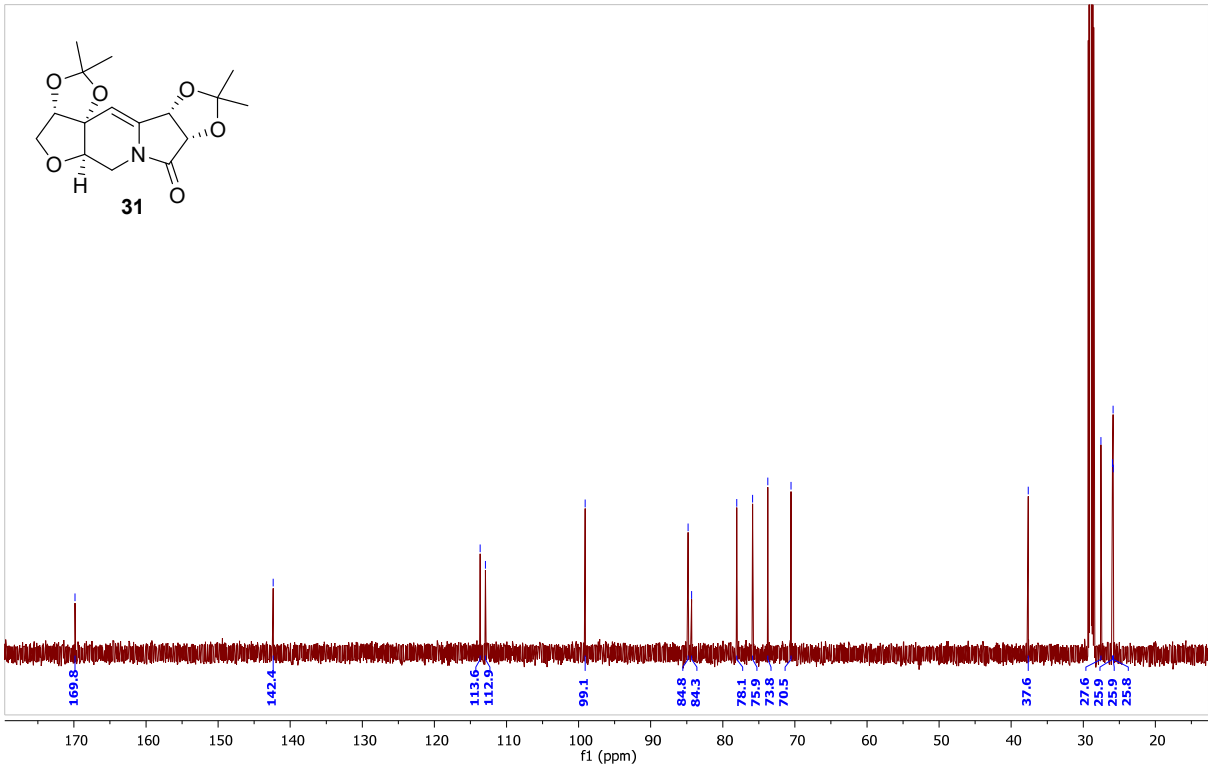
HSQC of **18a**



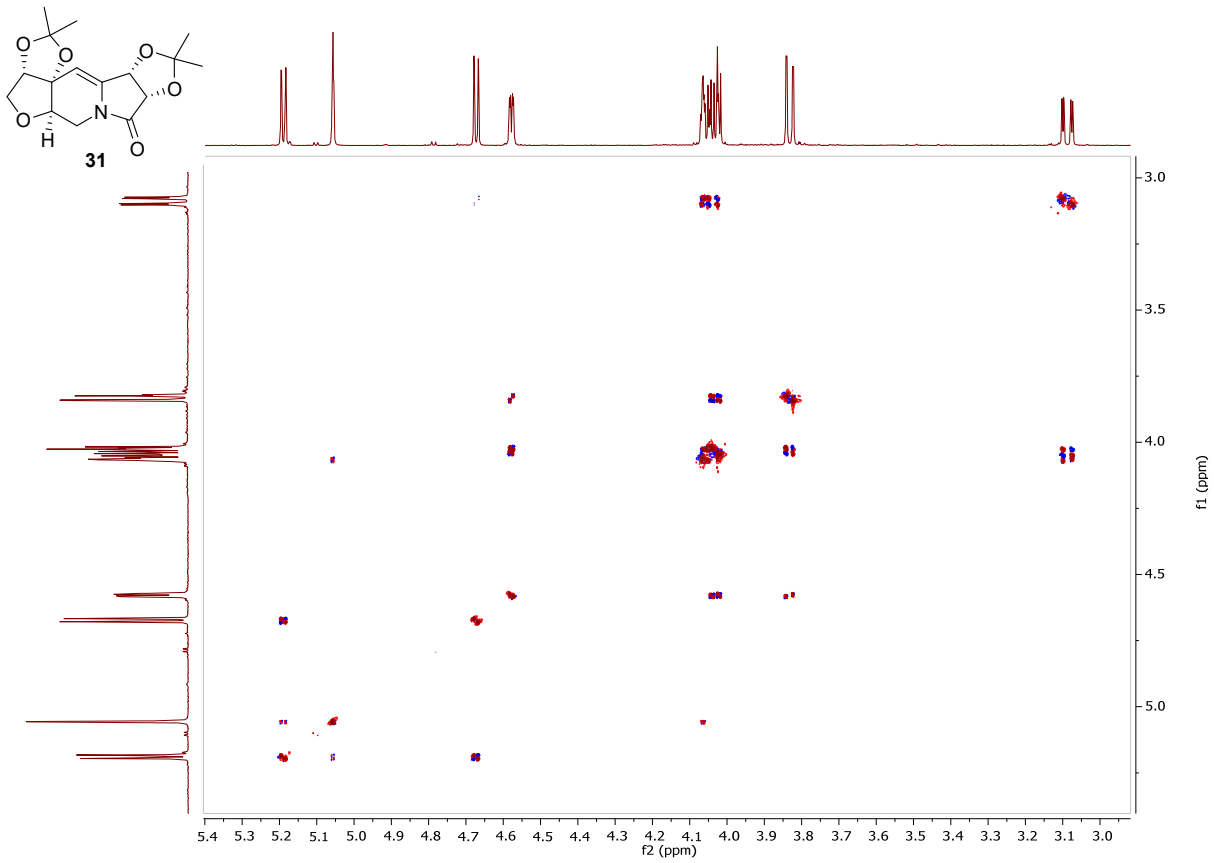
^{1}H NMR of **27a,b**



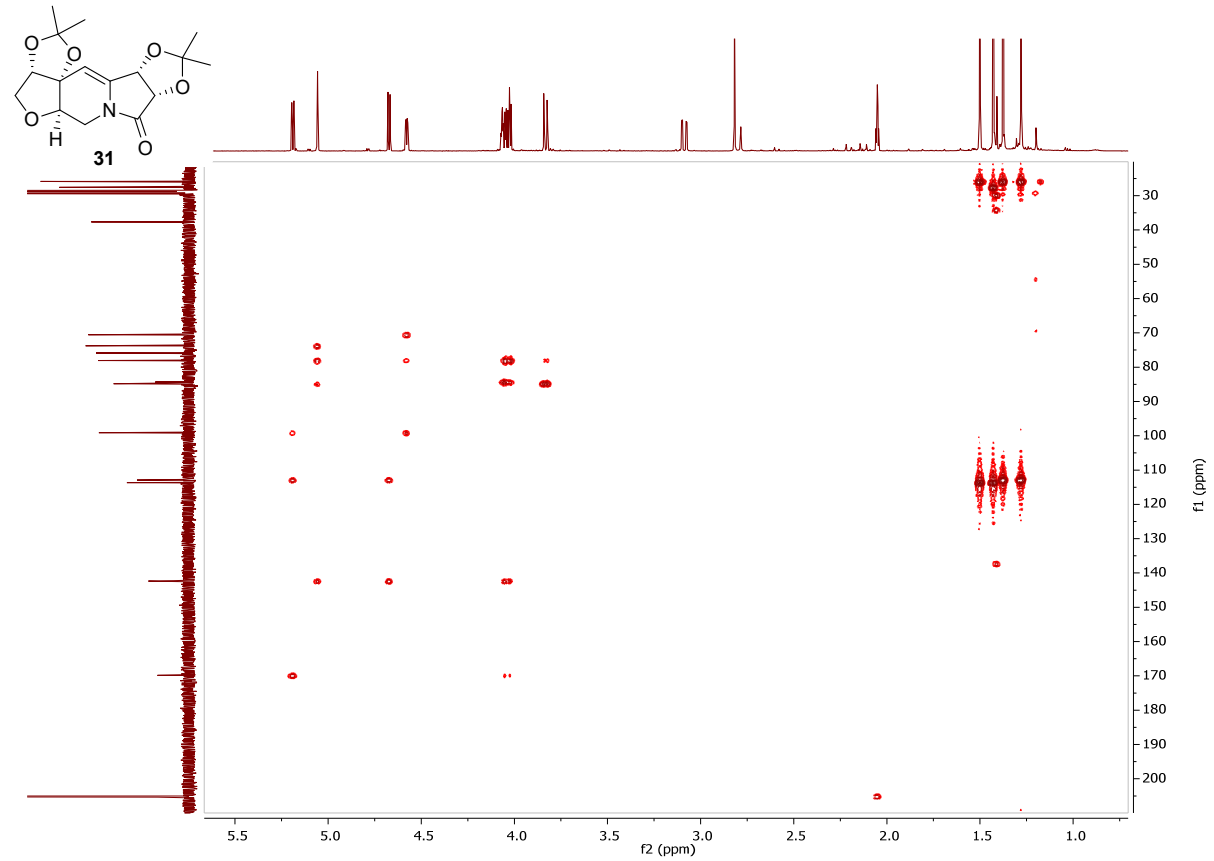
^{1}H NMR of **31**



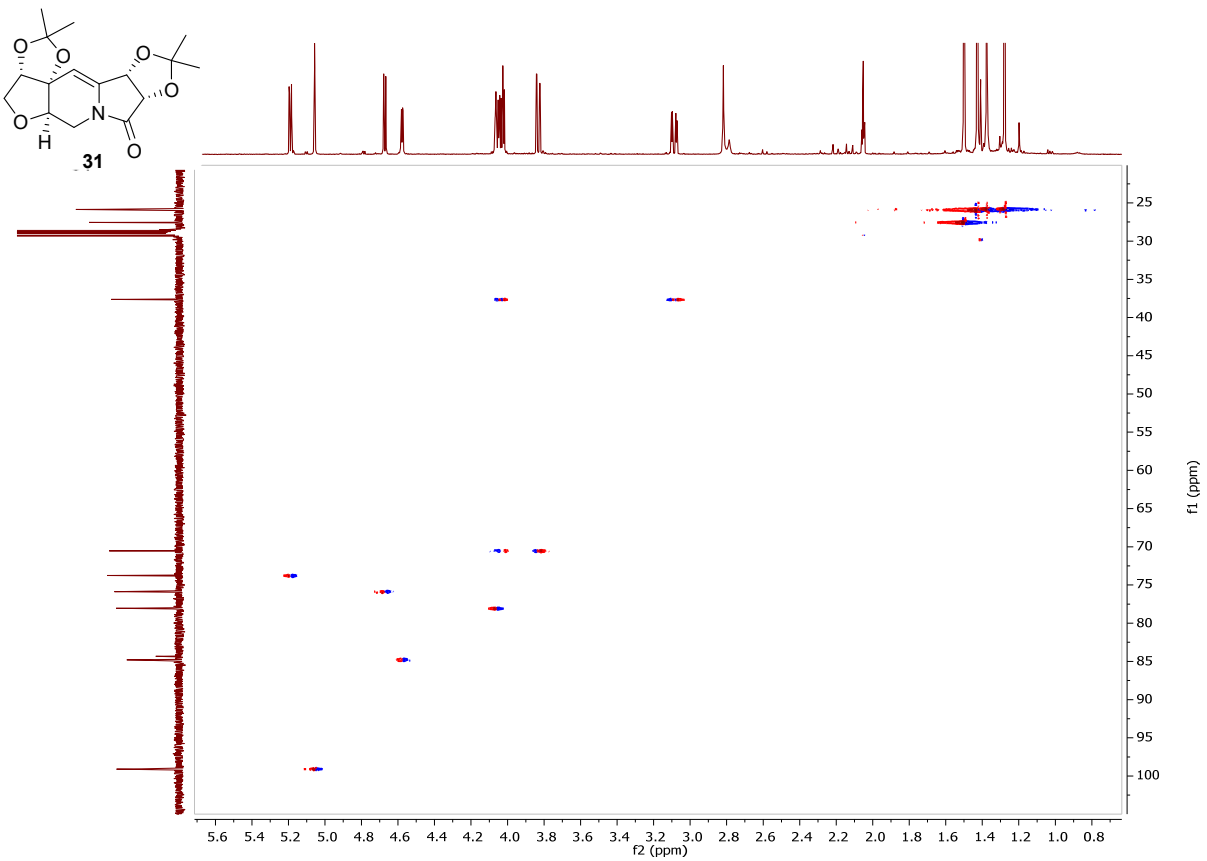
^{13}C NMR of **31**



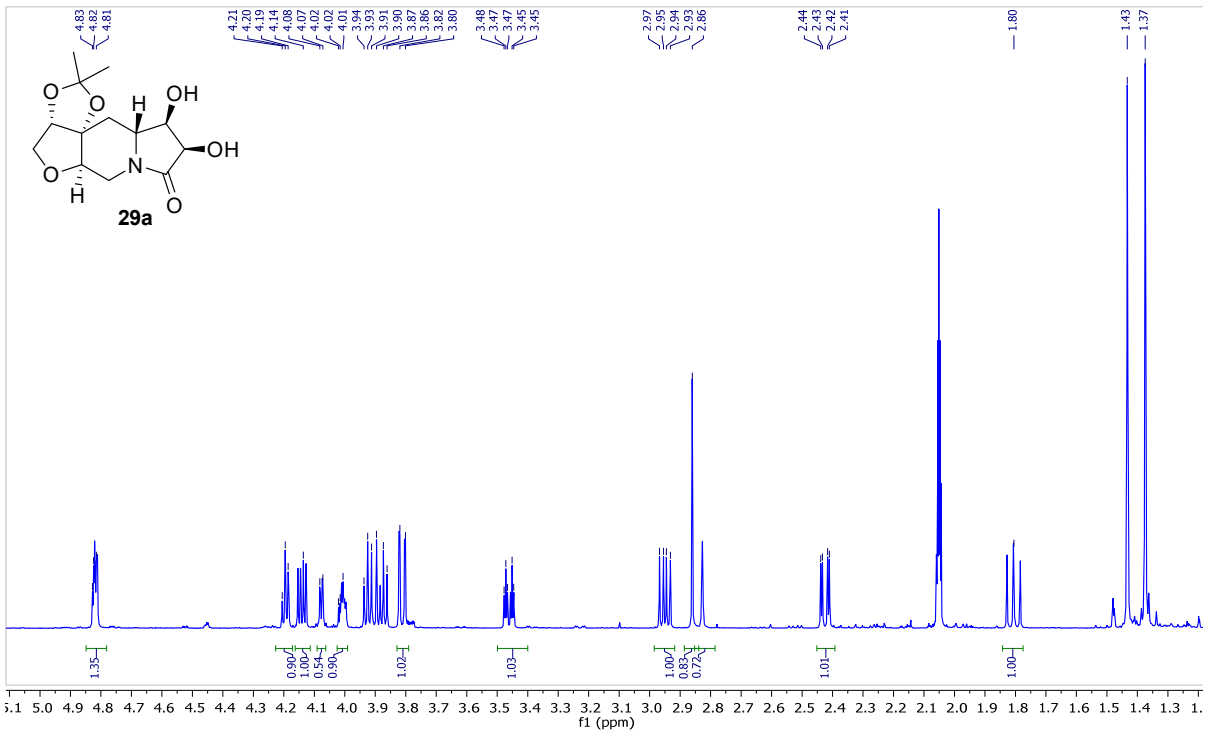
COSY of **31**



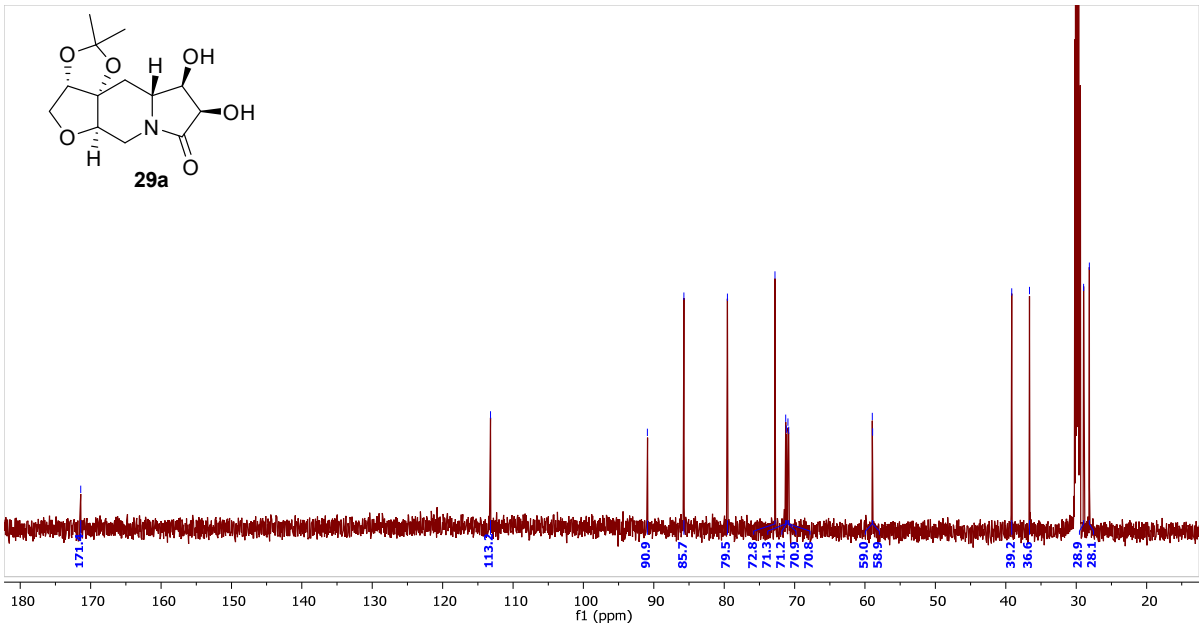
HMBC of **31**



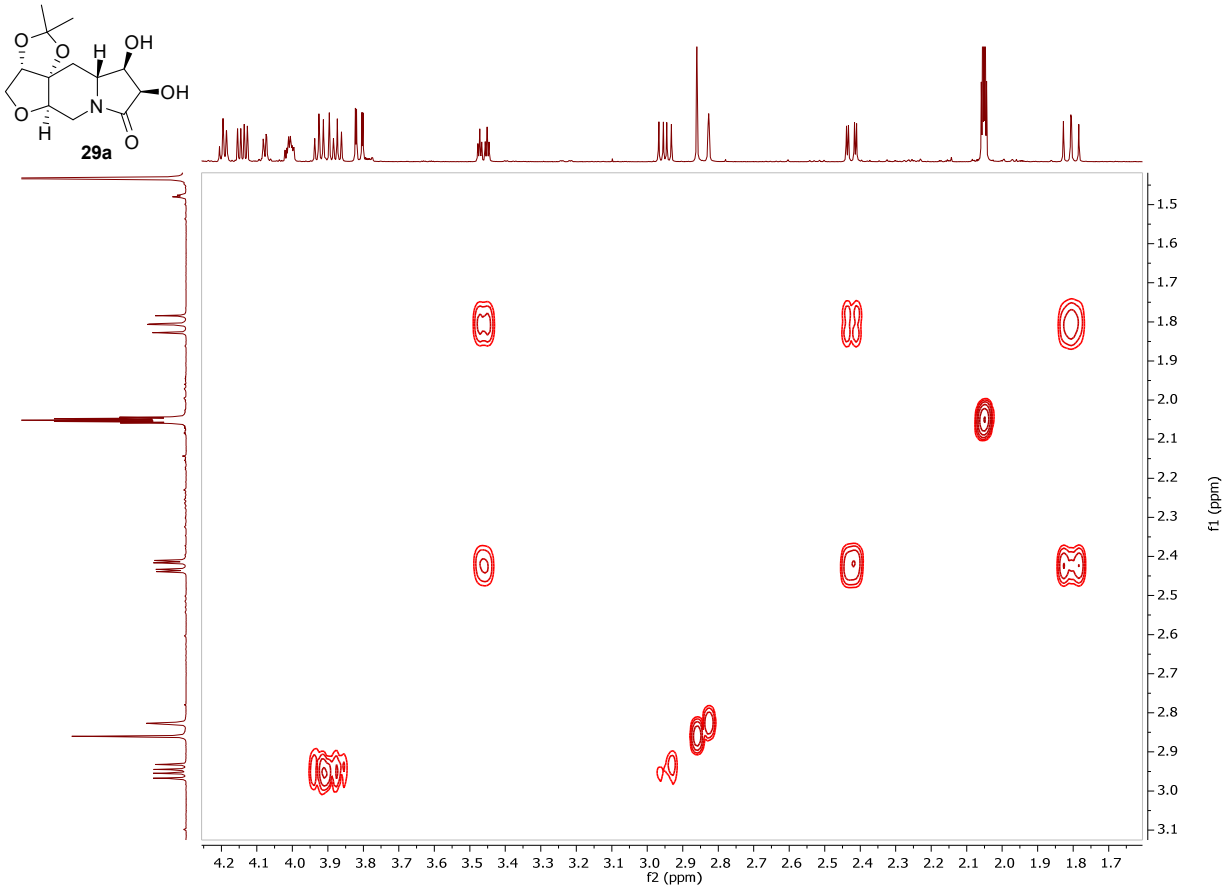
HSQC of **31**



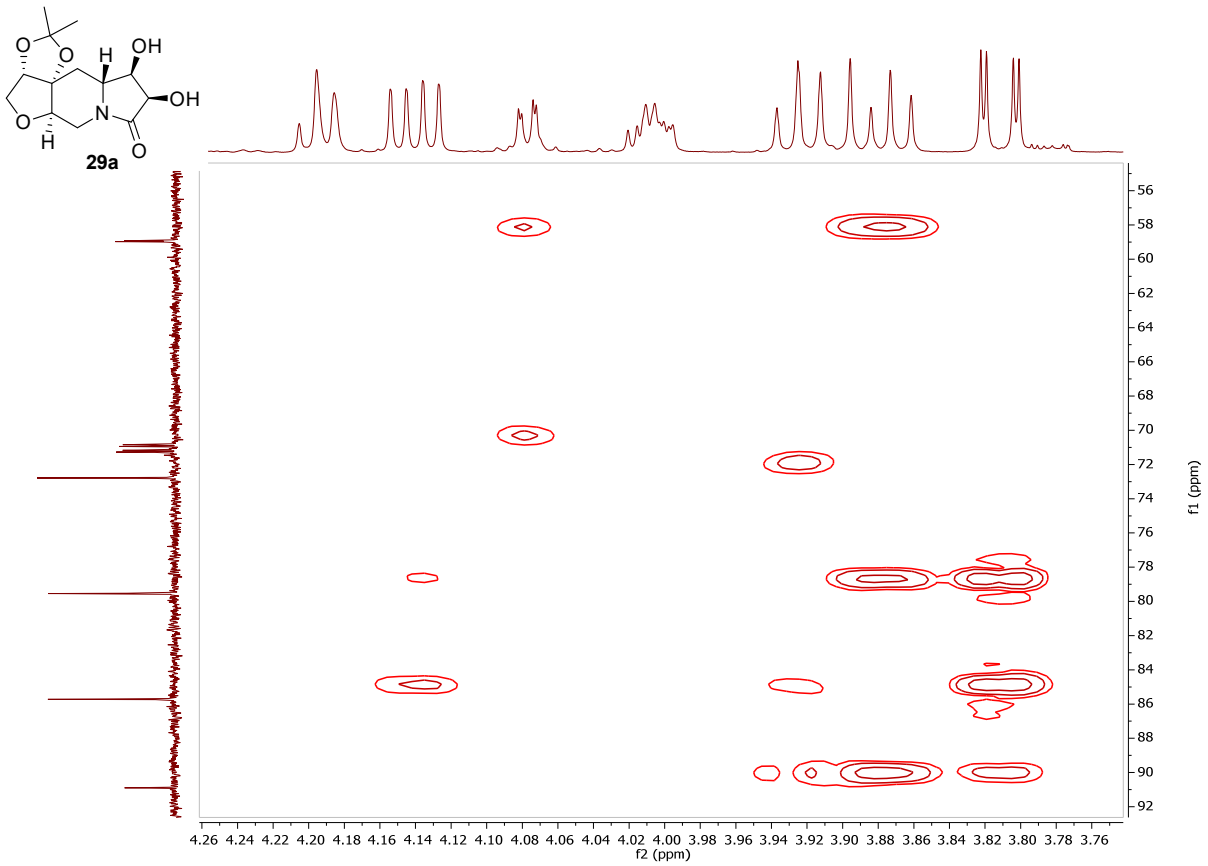
^{1}H NMR of **29a**



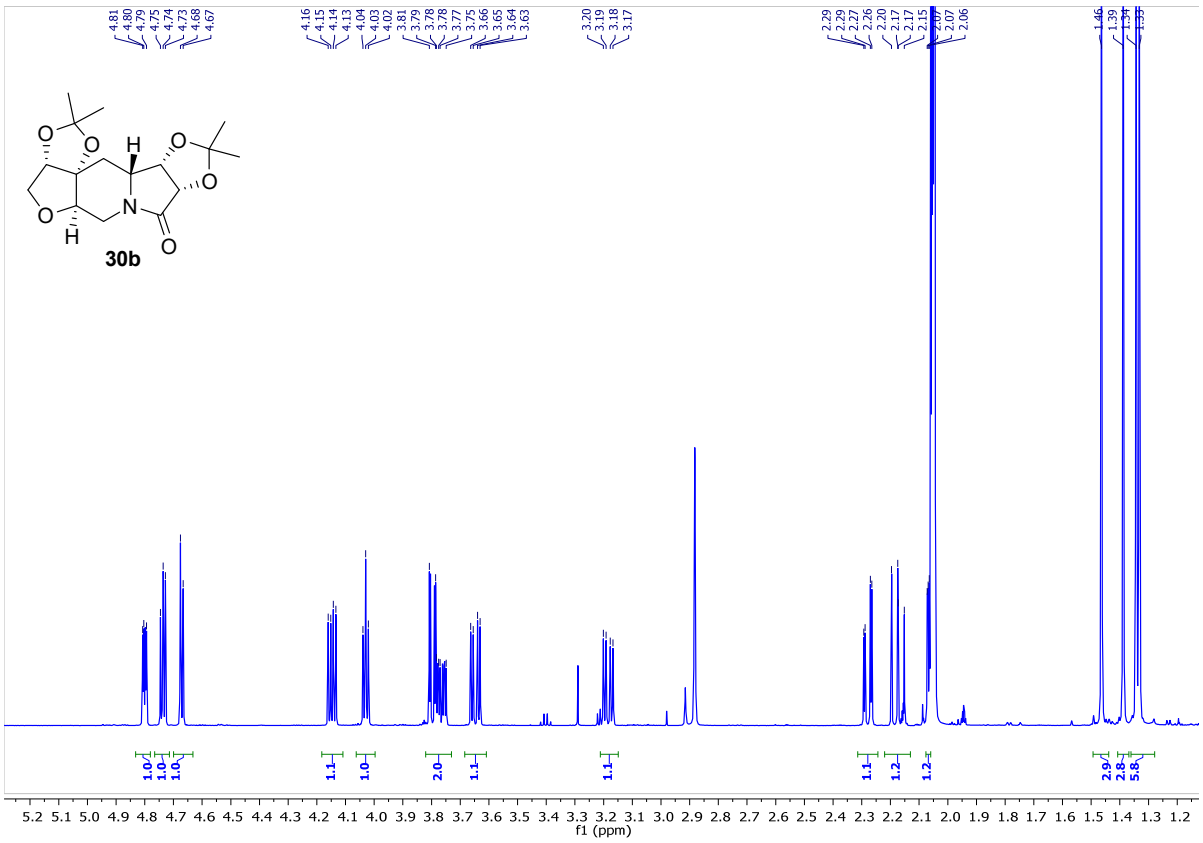
^{13}C NMR of **29a**



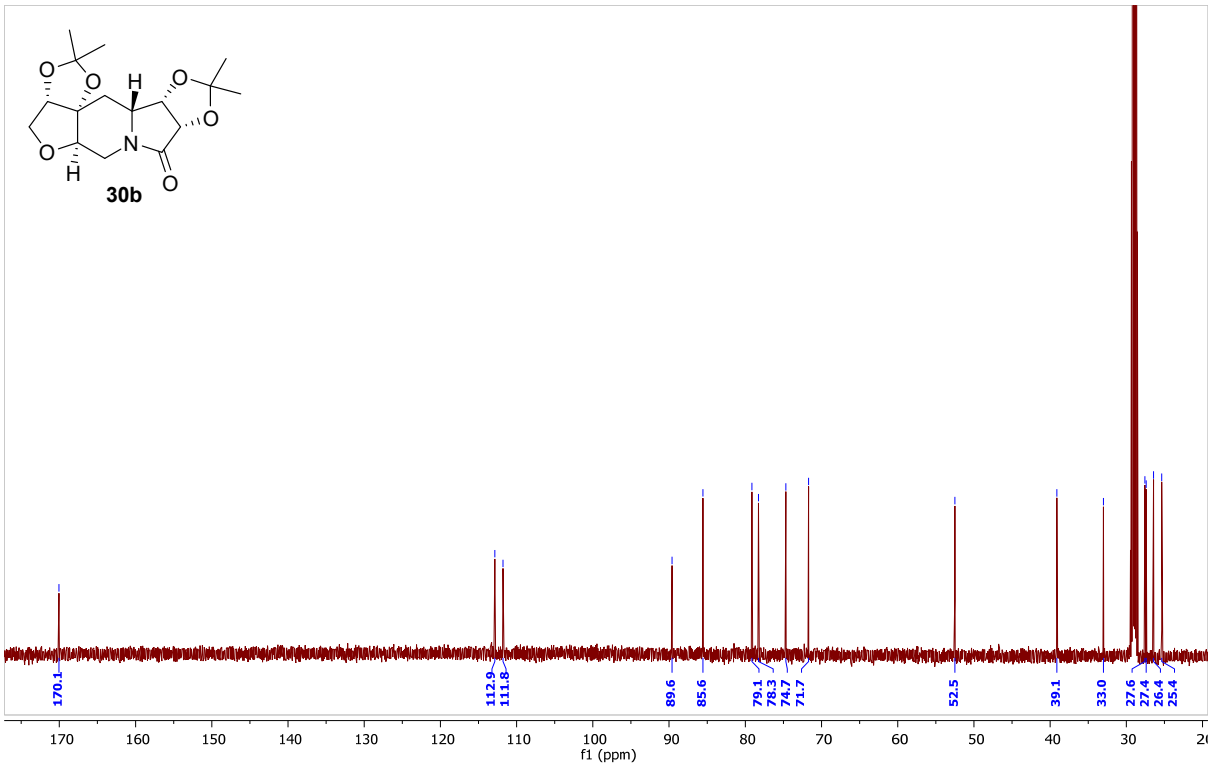
COSY of **29a**



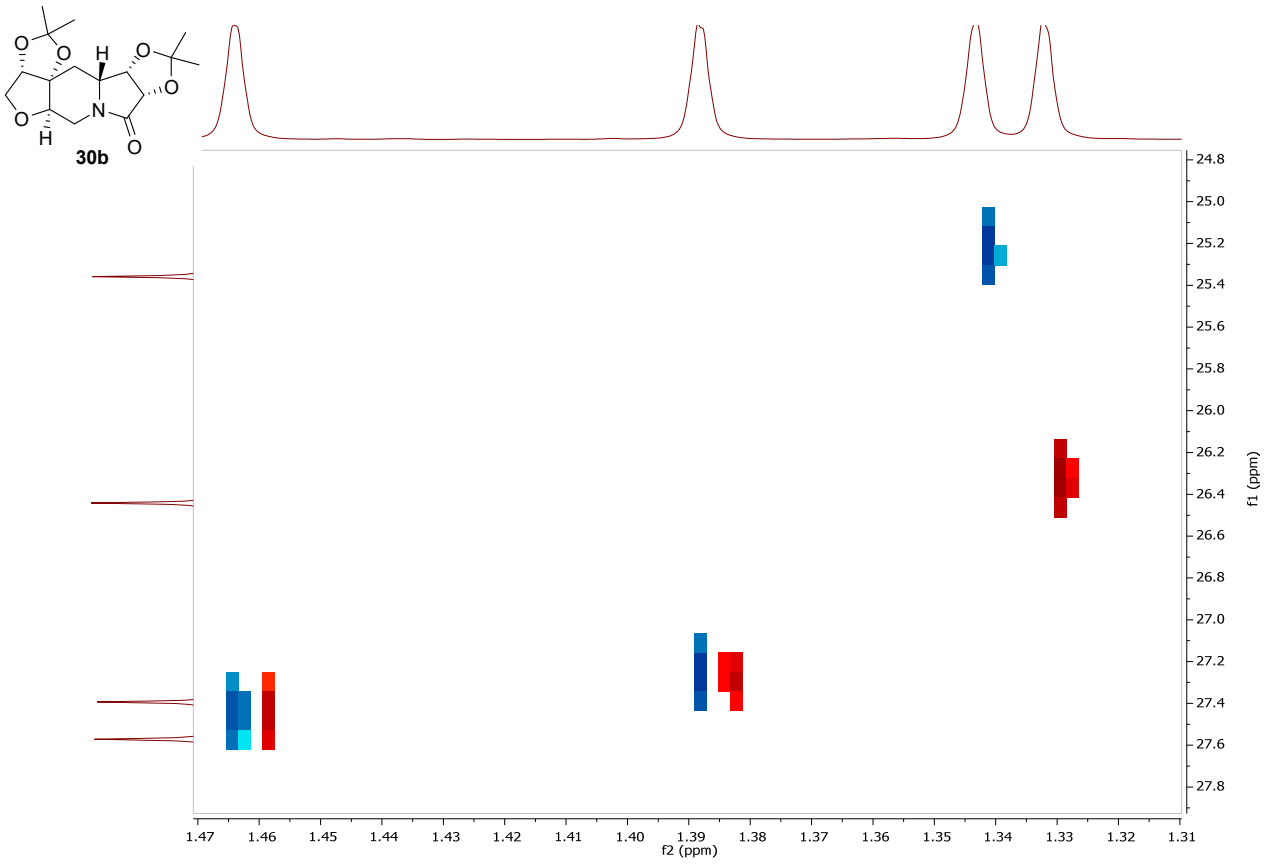
HMBC of **29a**



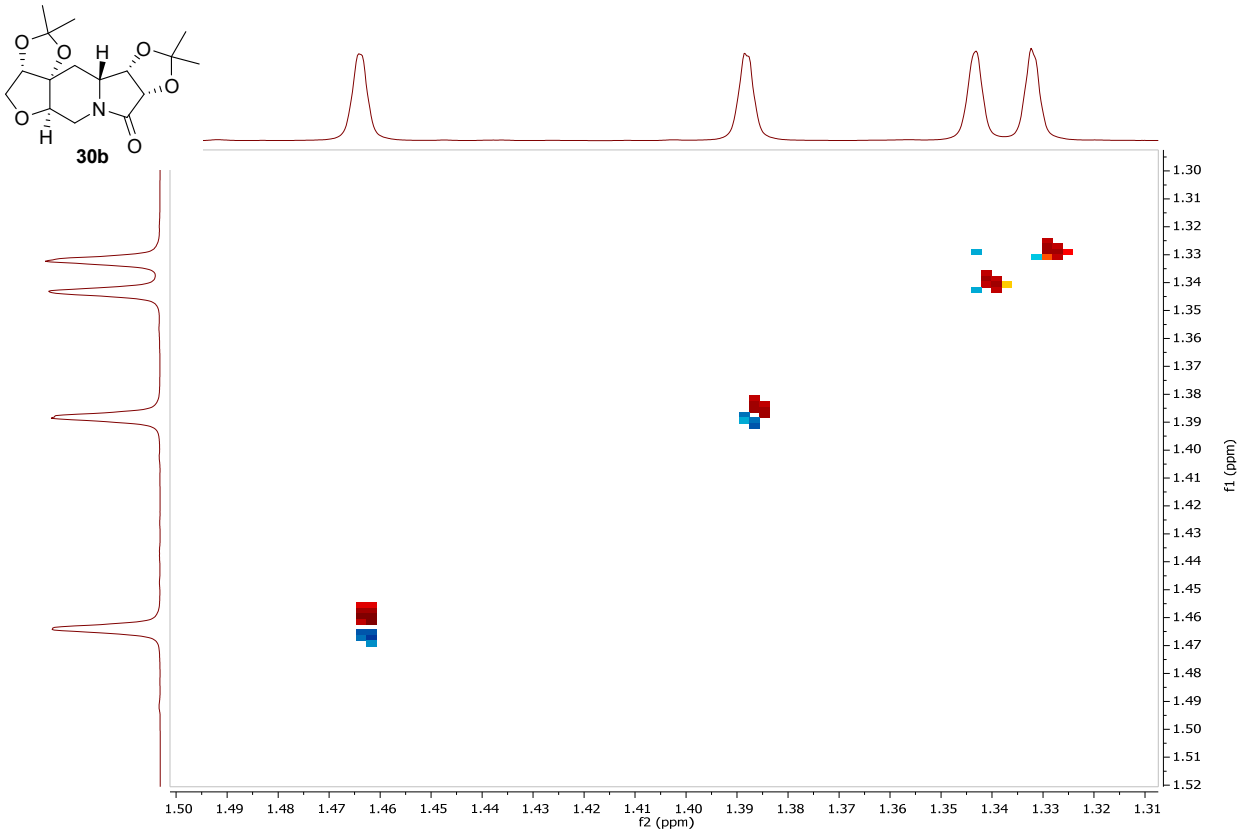
^{1}H NMR of **30b**



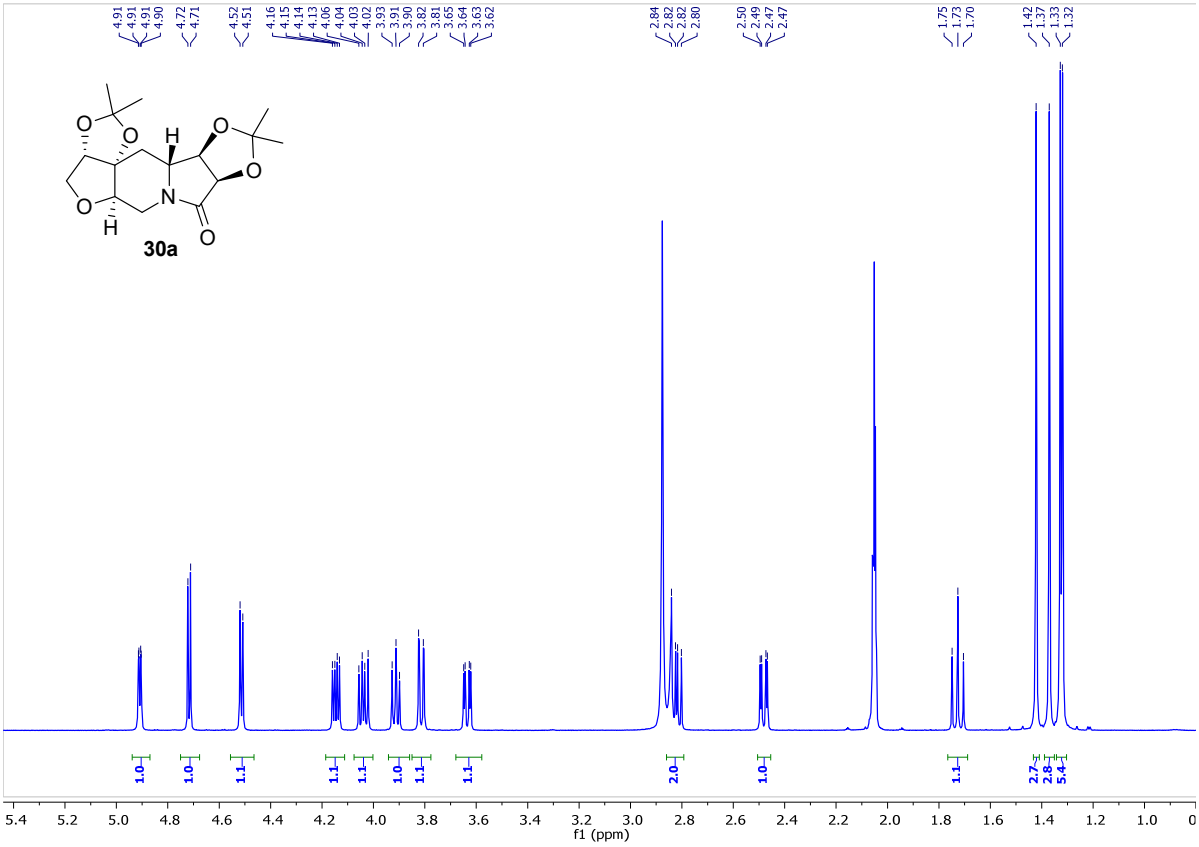
^{13}C NMR of **30b**



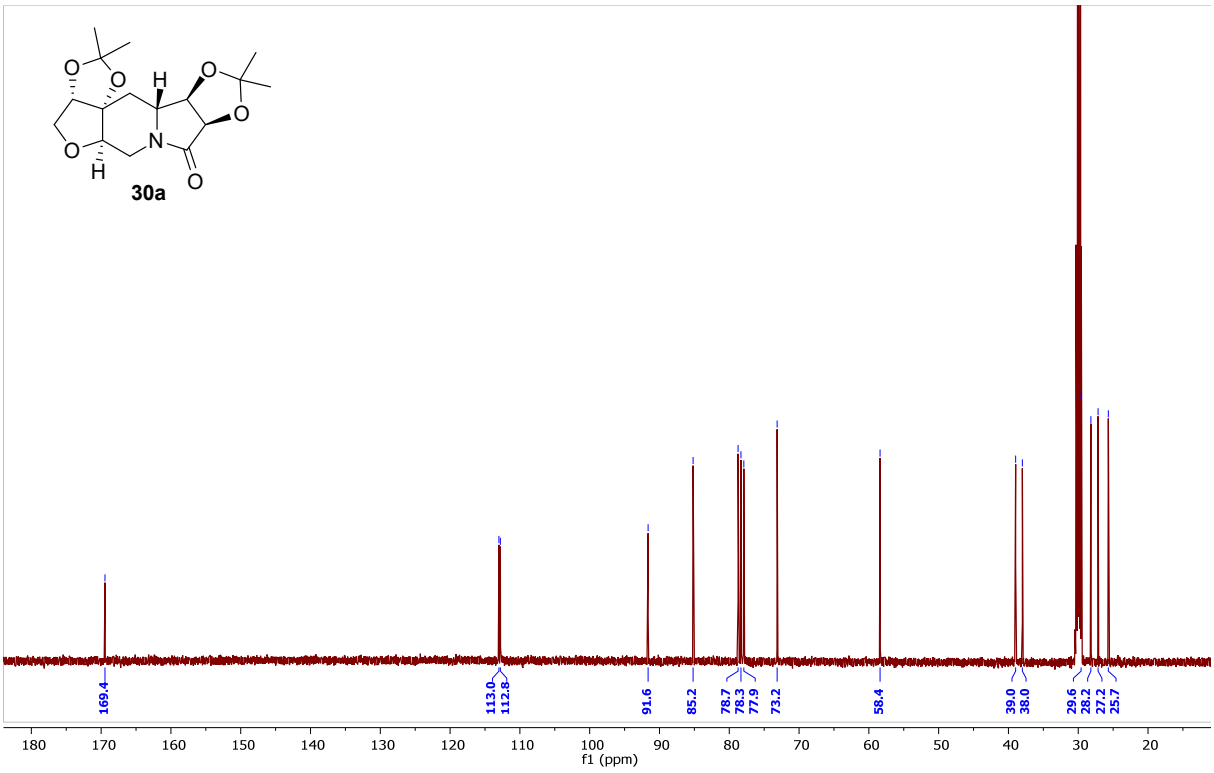
HMBC of **30b**



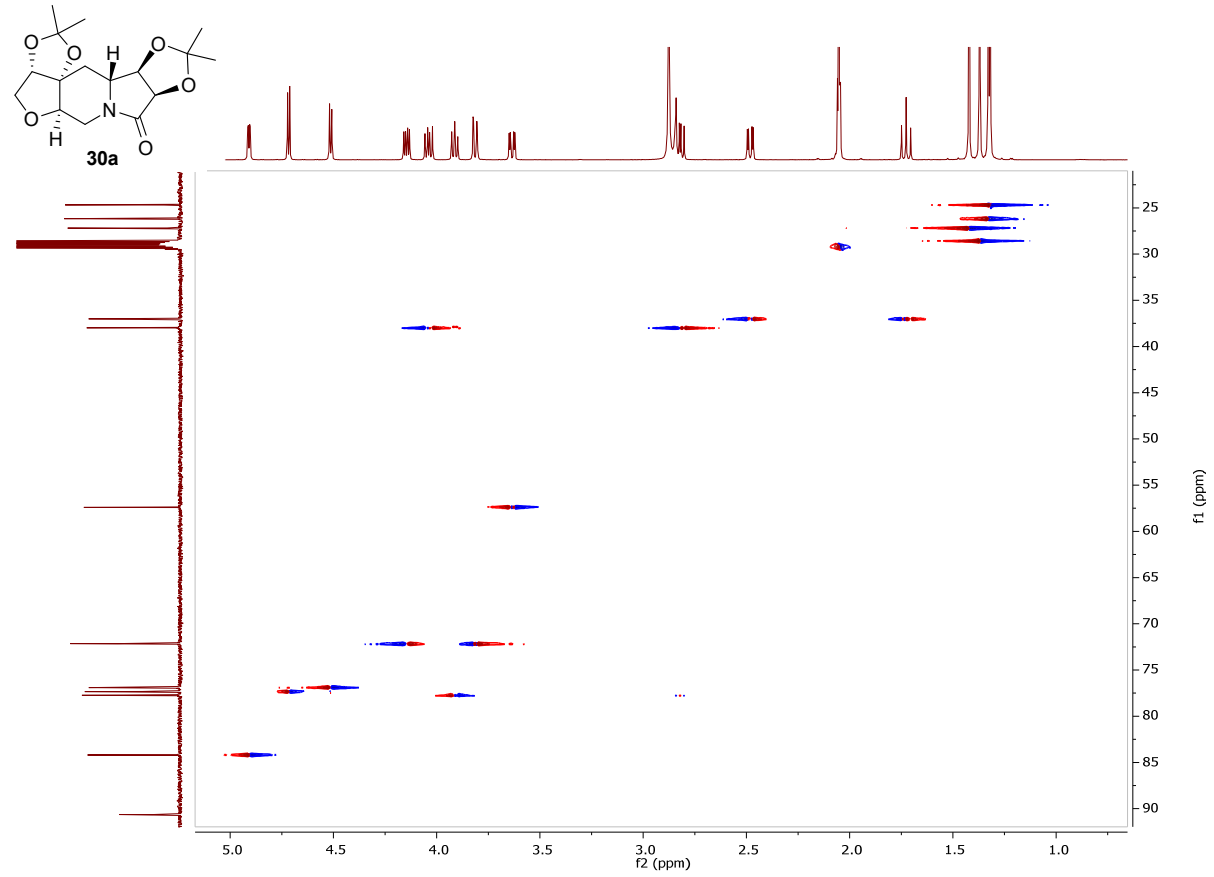
COSY of **30b**



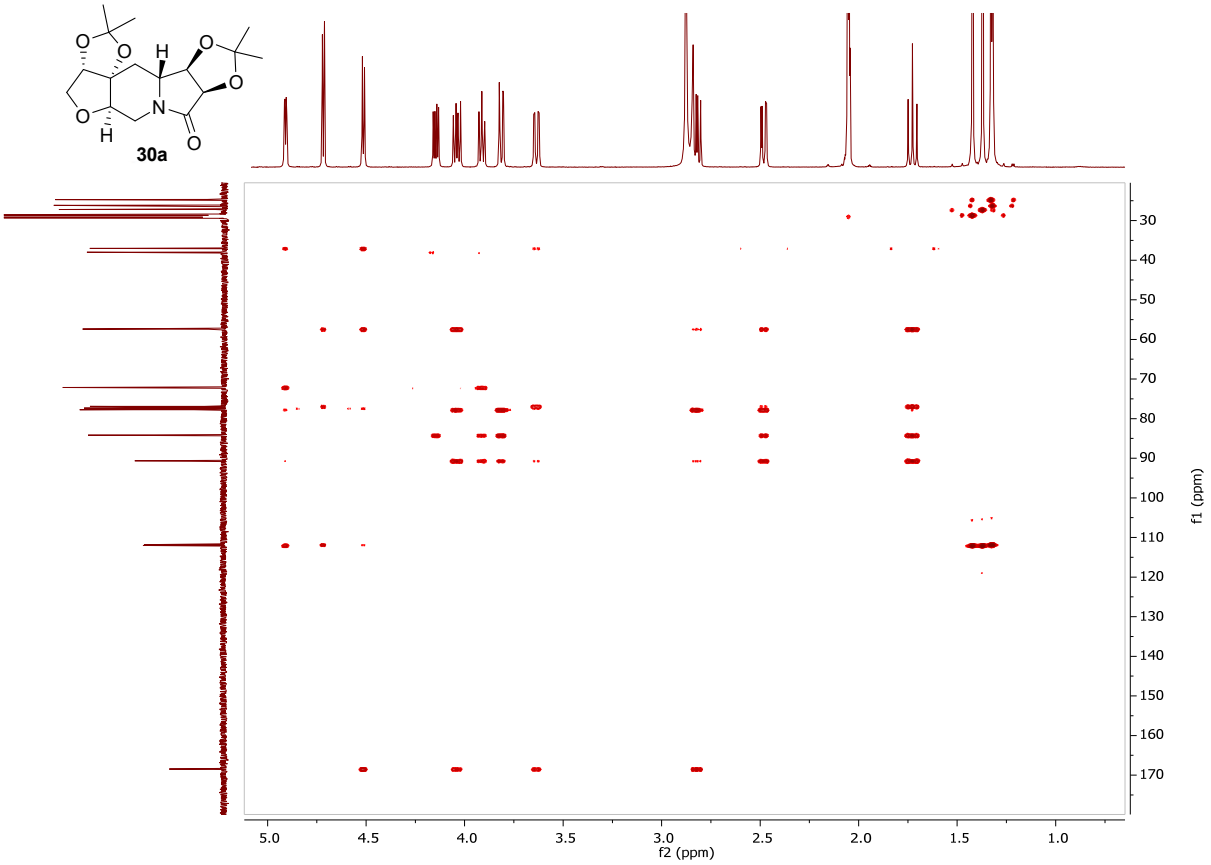
^{1}H NMR of **30a**



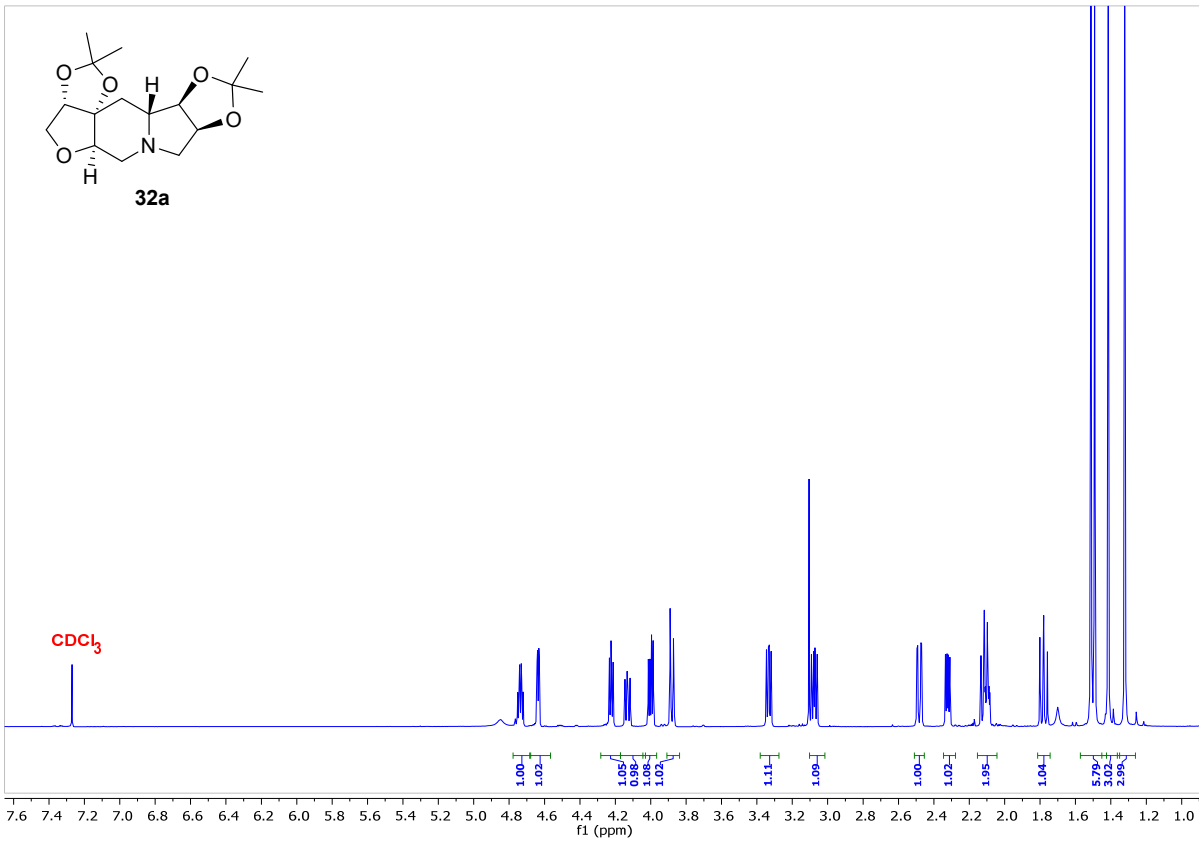
^{13}C NMR of **30a**



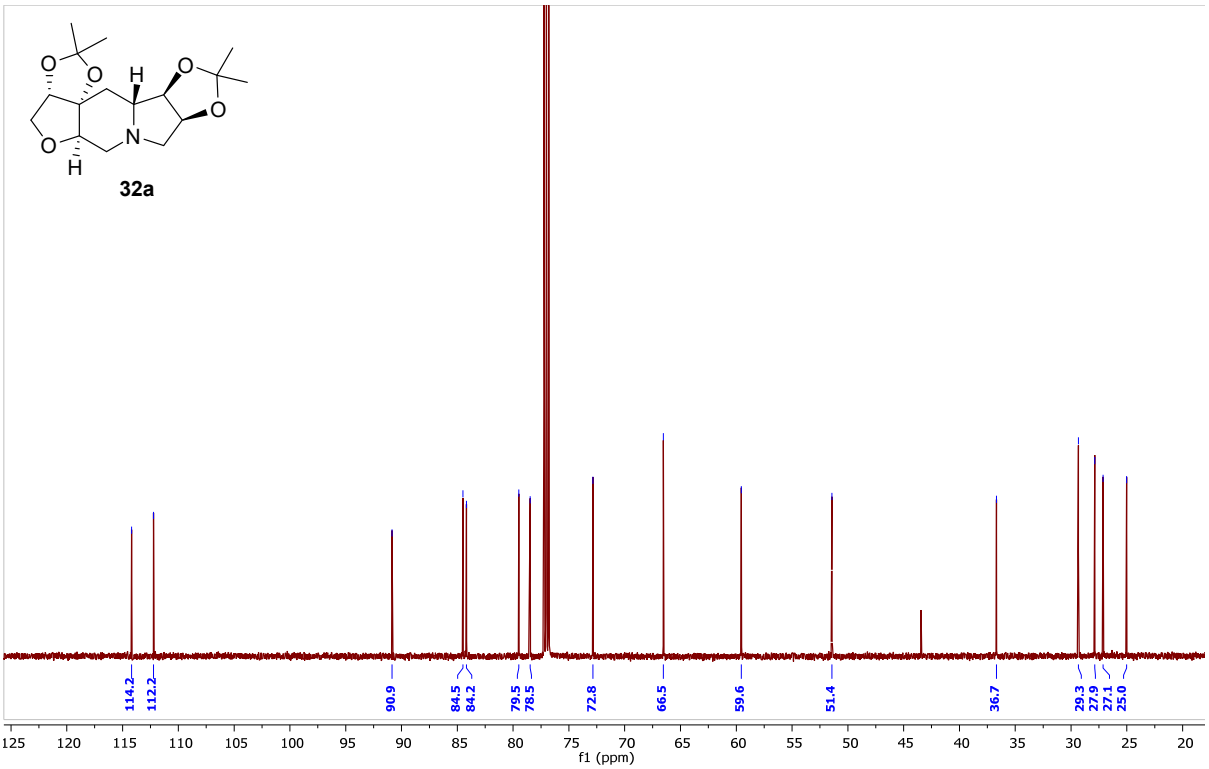
HSQC of **30a**



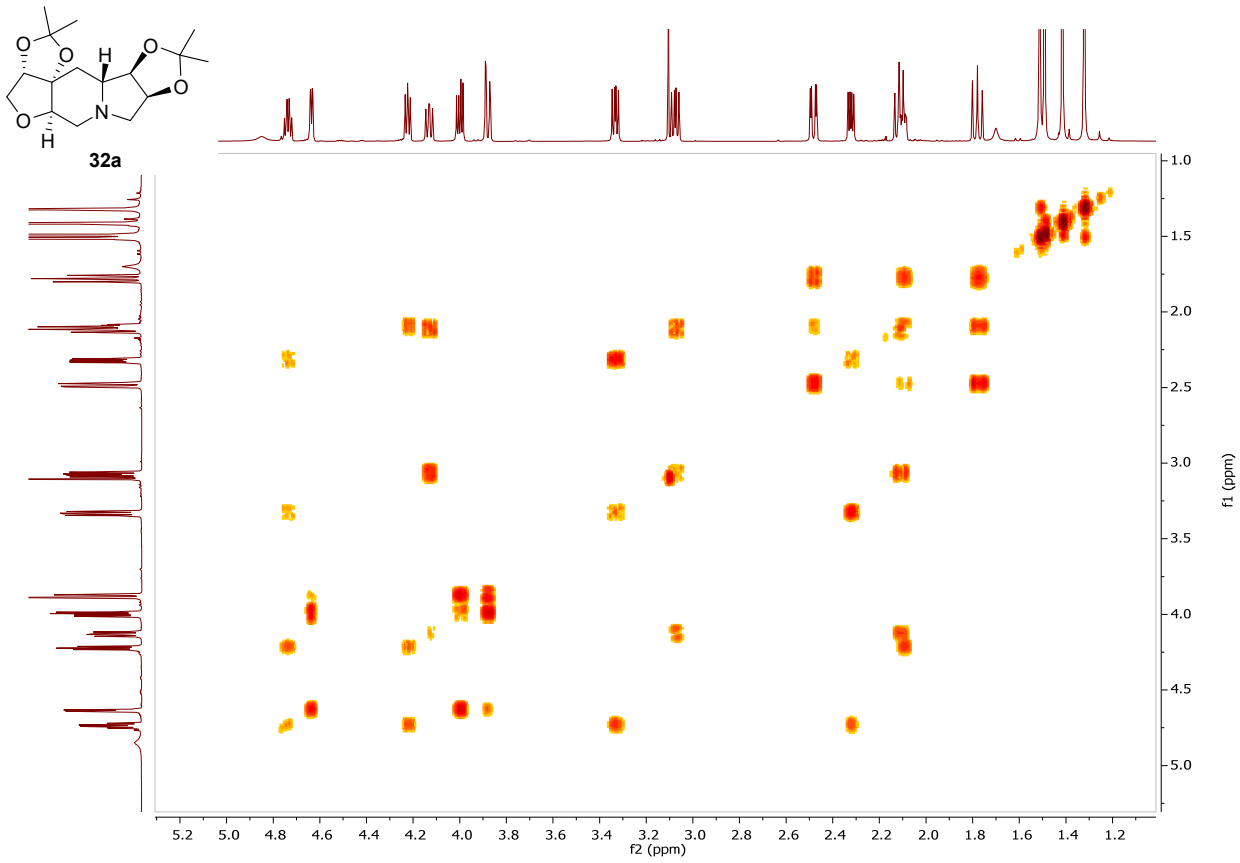
HMBC of **30a**



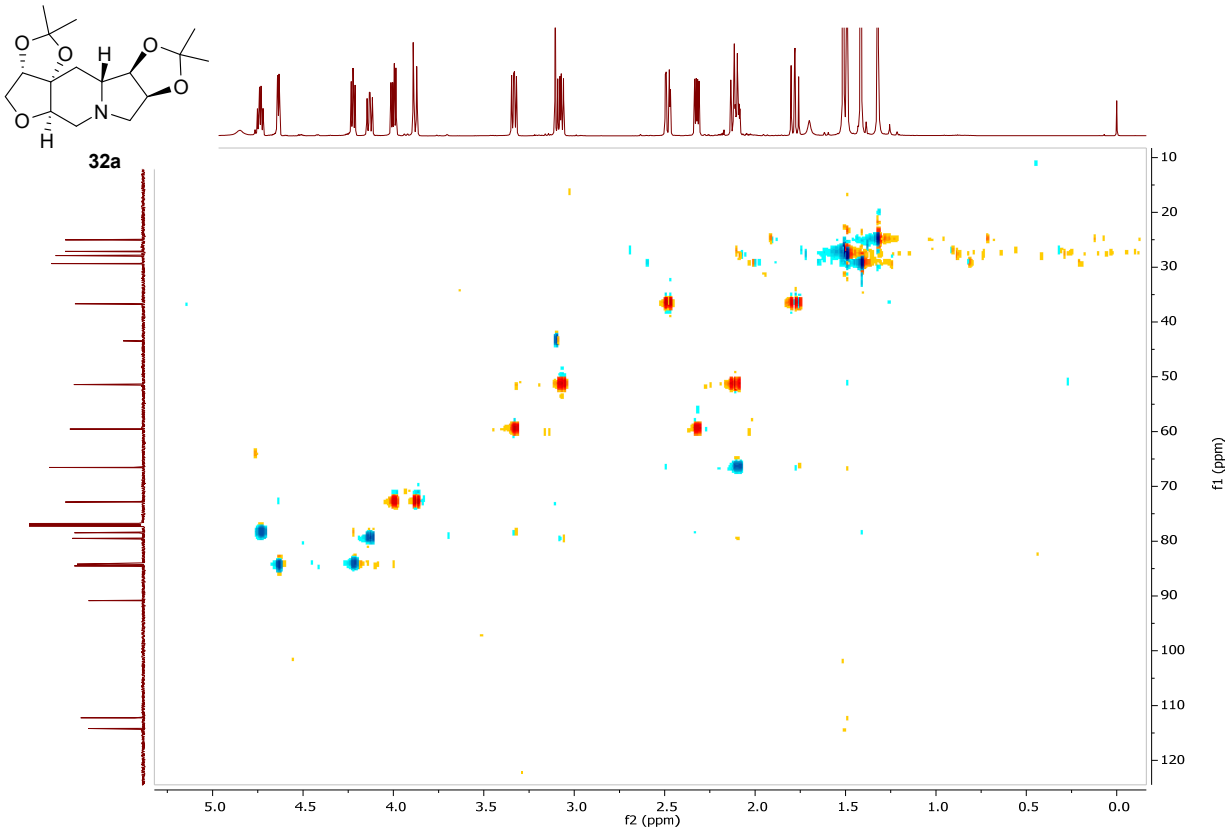
^{1}H NMR of **32a**



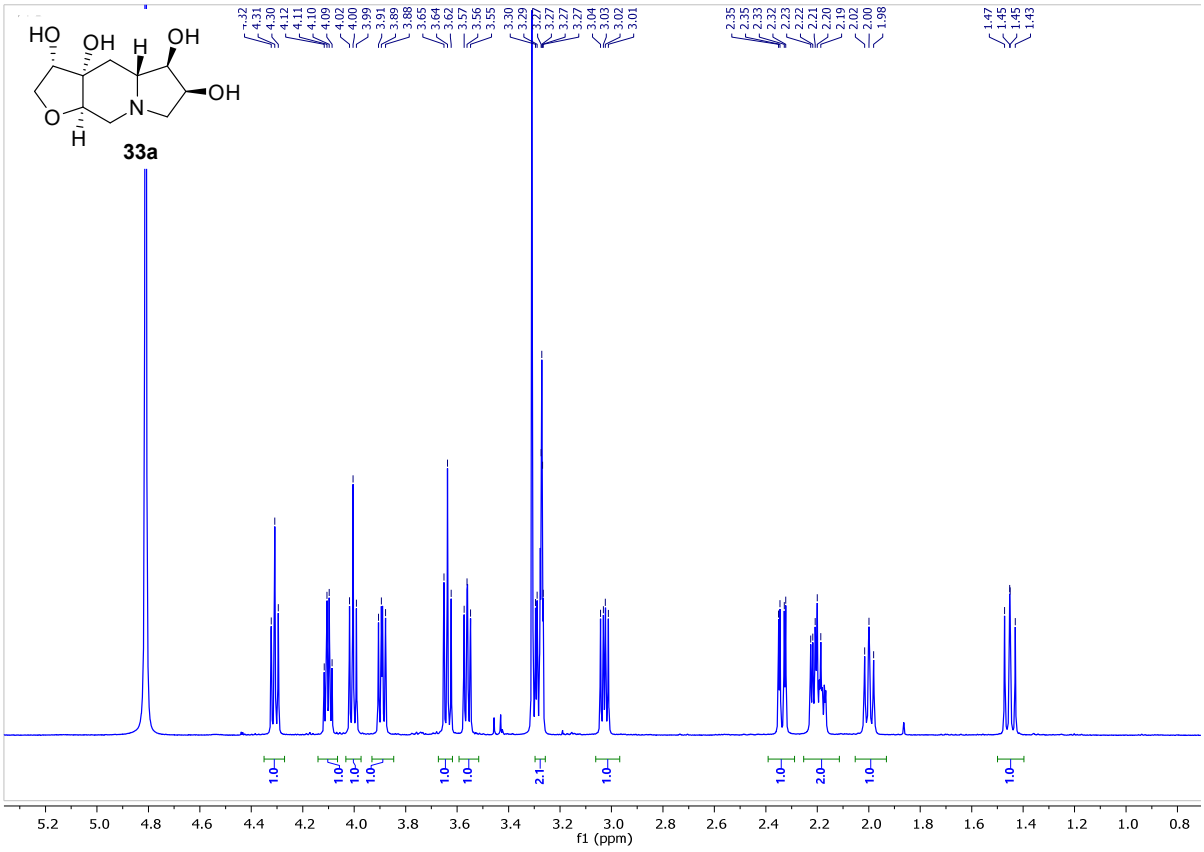
^{13}C NMR of **32a**



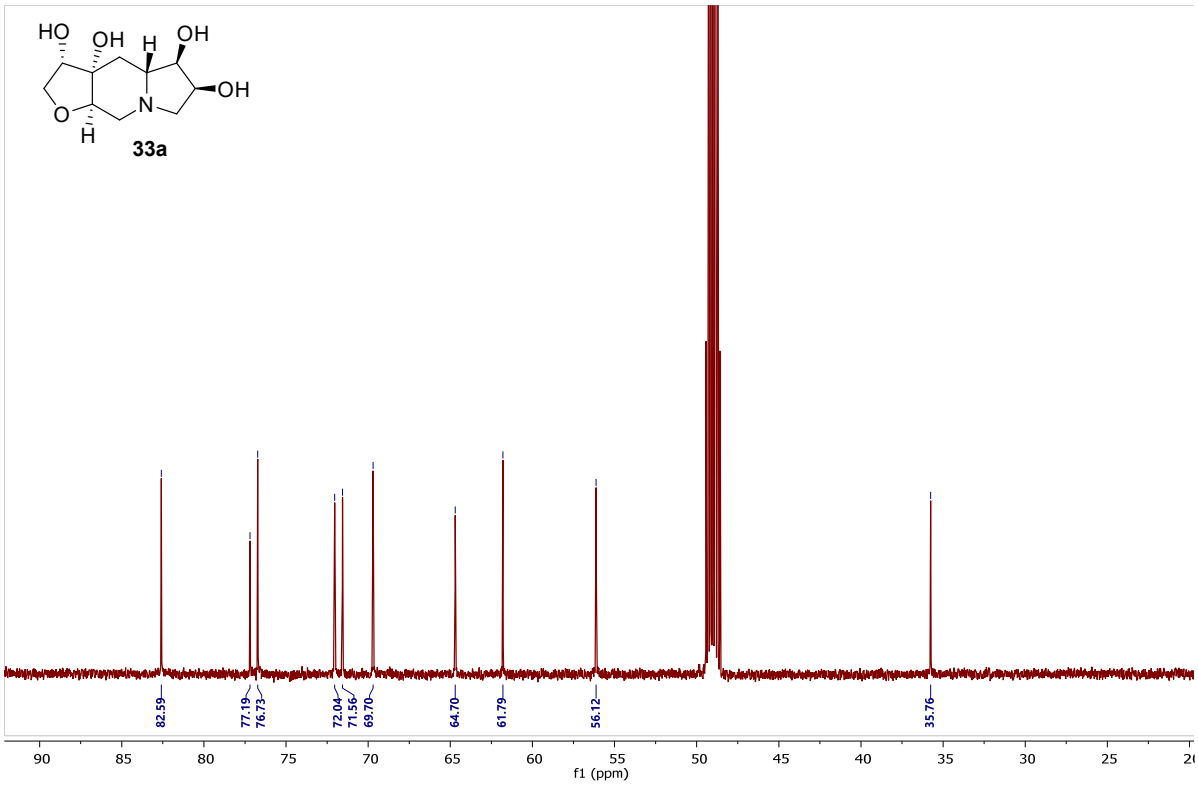
COSY of **32a**



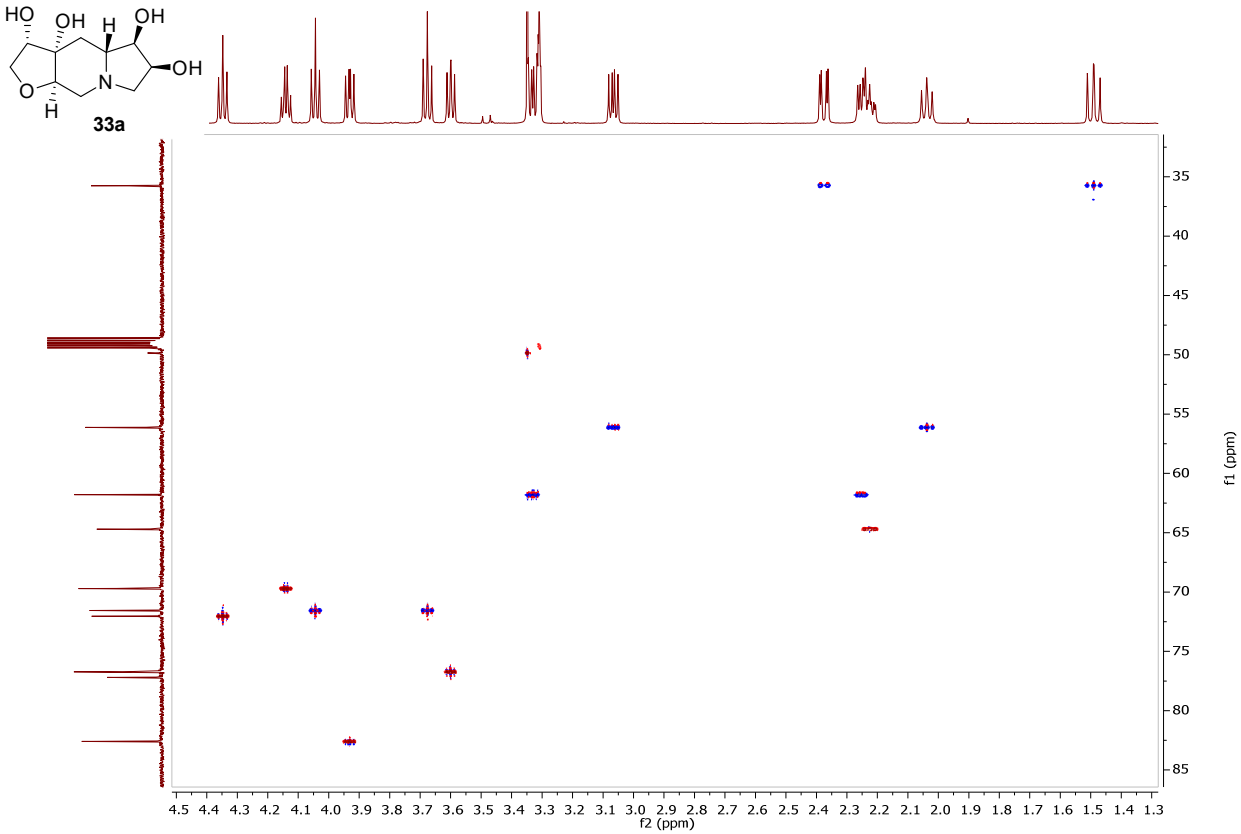
HSQC of **32a**



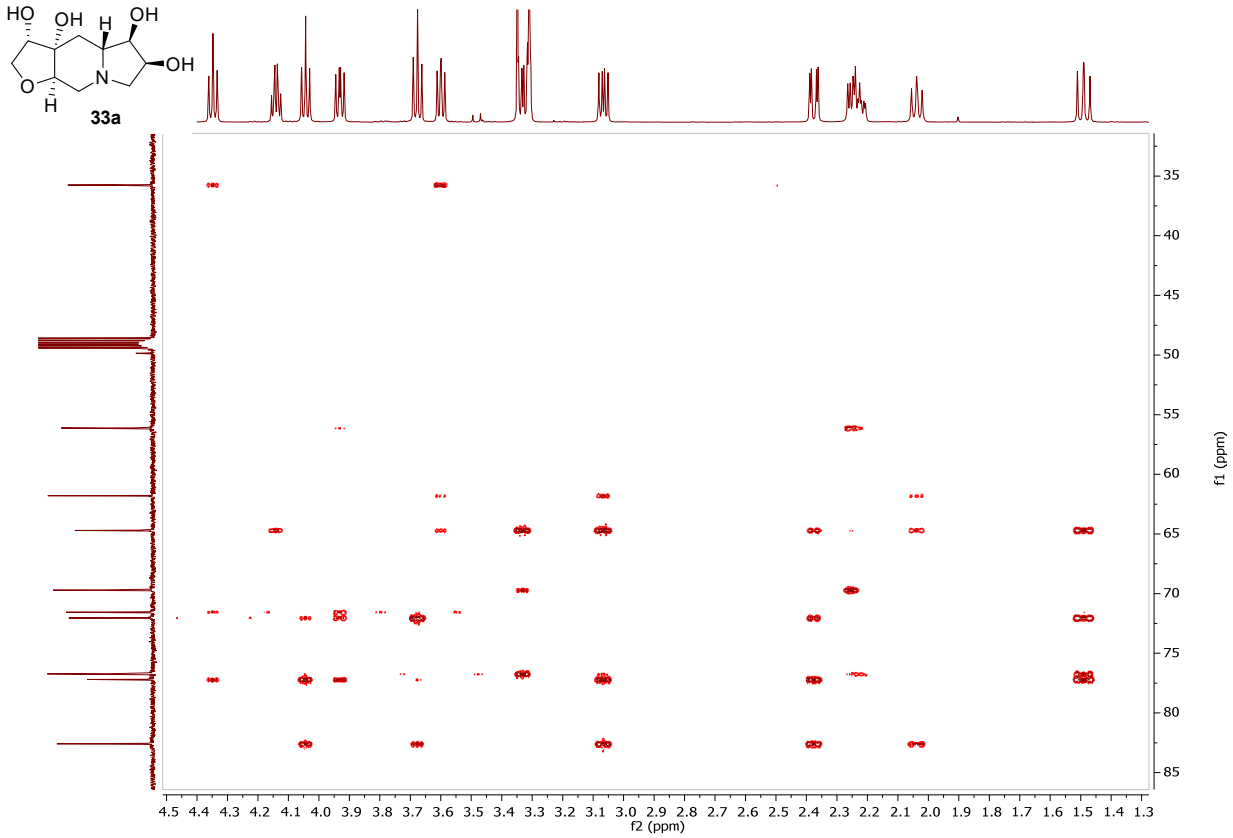
^{1}H NMR of **33a**



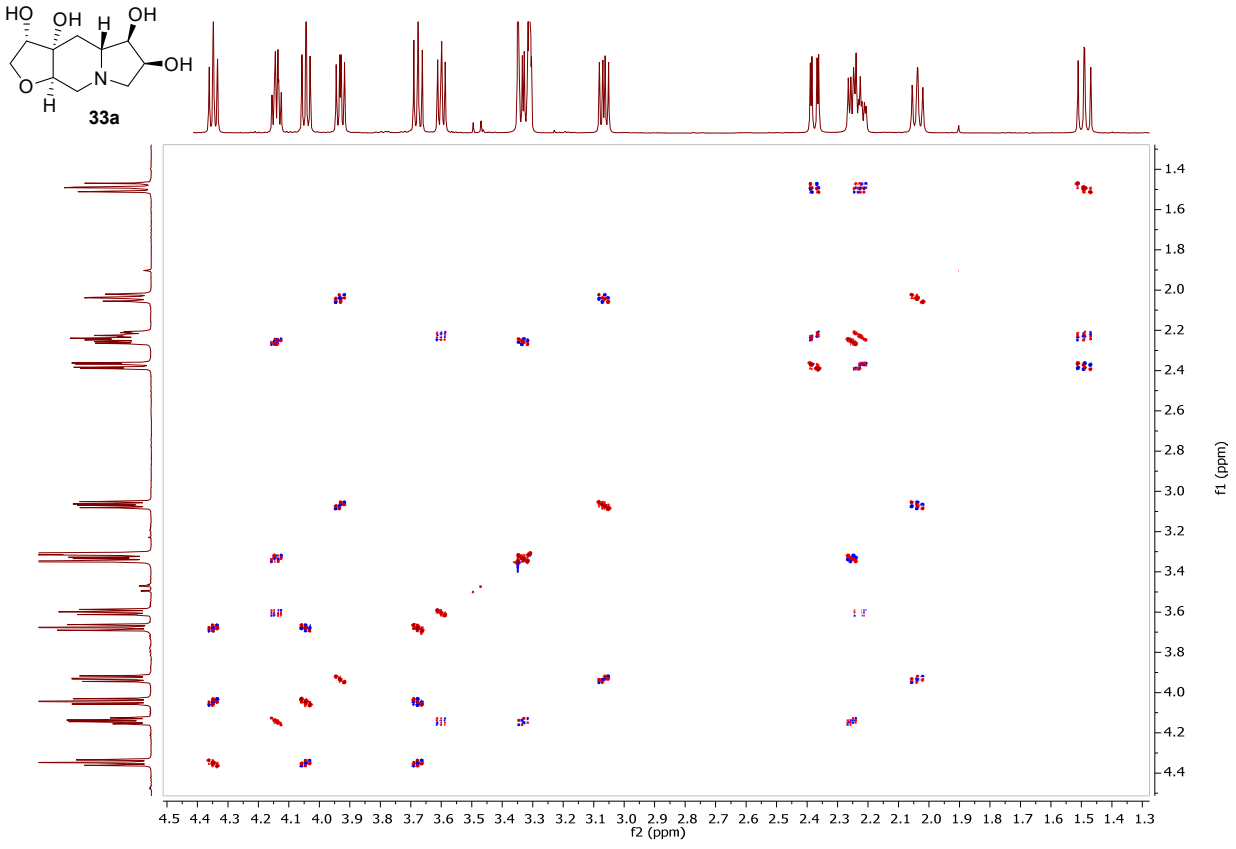
^{13}C NMR of **33a**



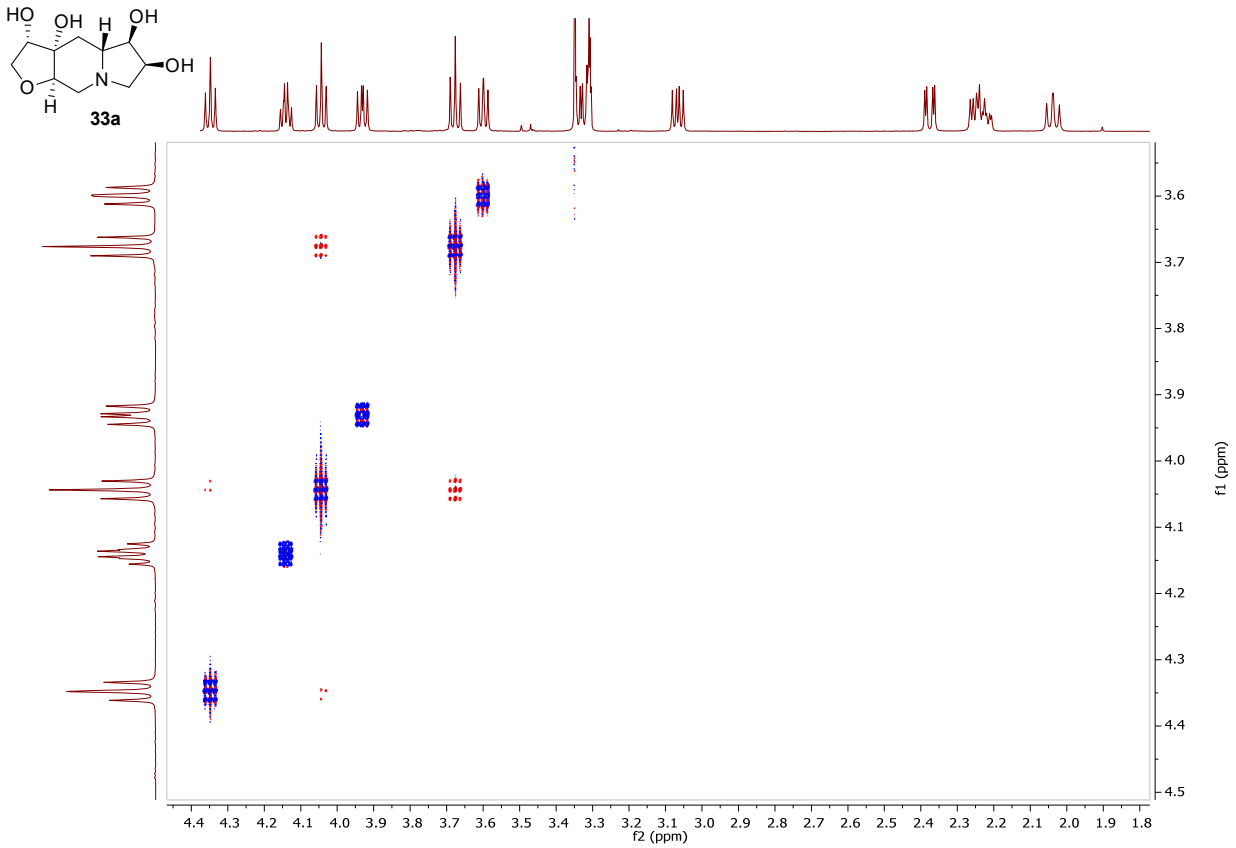
HSQC of **33a**



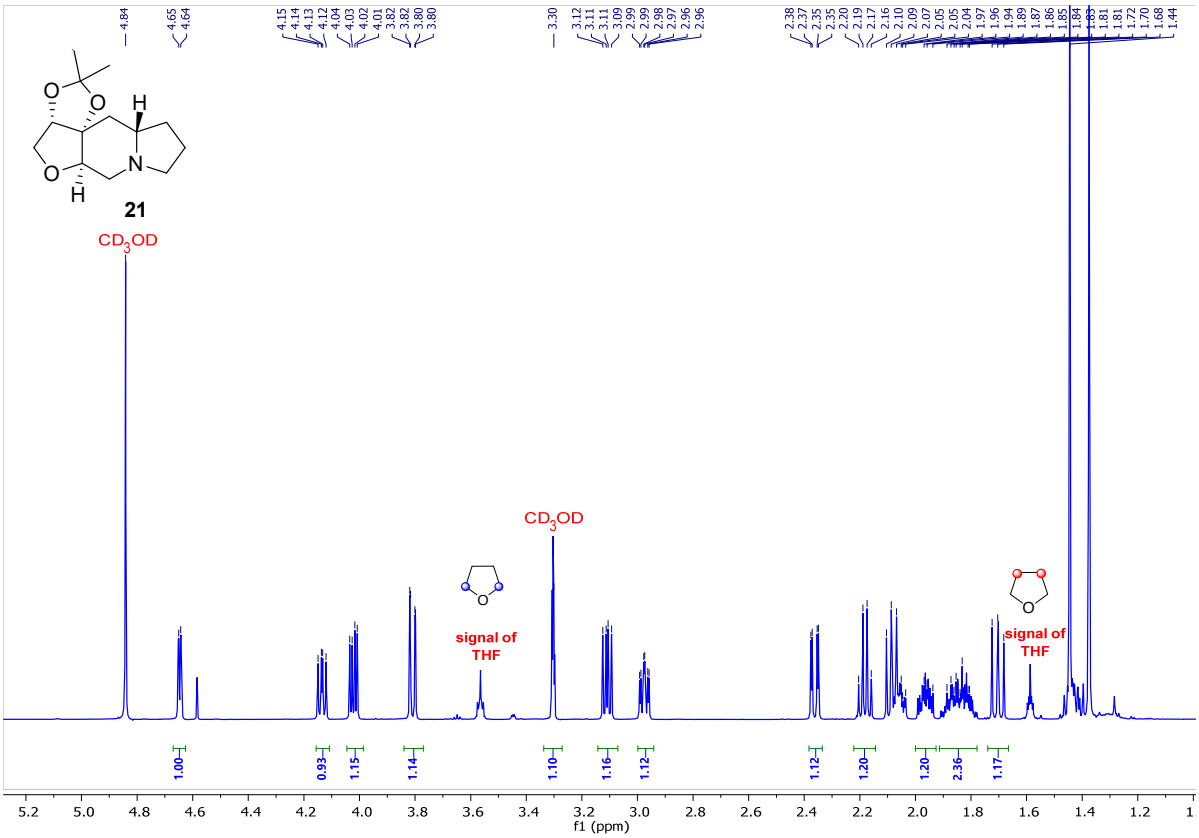
HMBC of **33a**



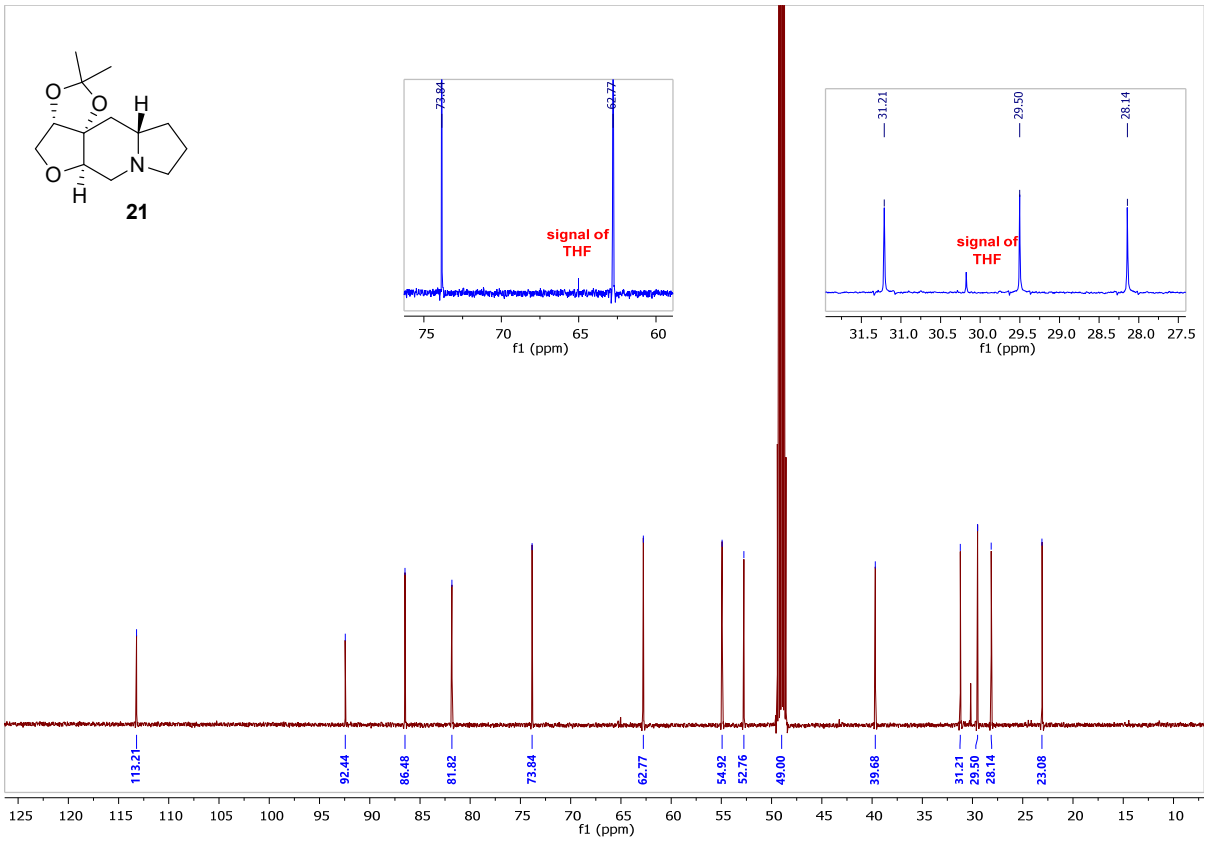
COSY of **33a**



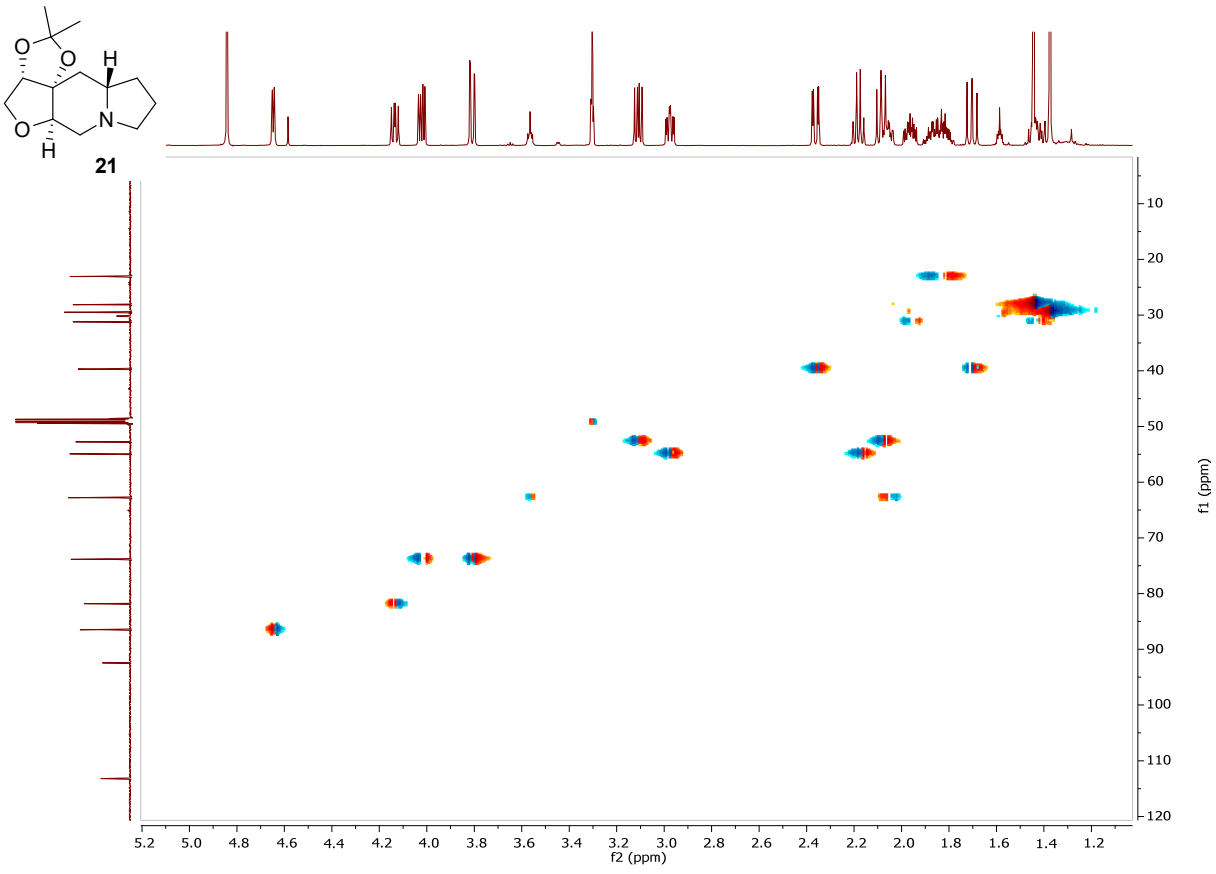
NOESY of **33a**



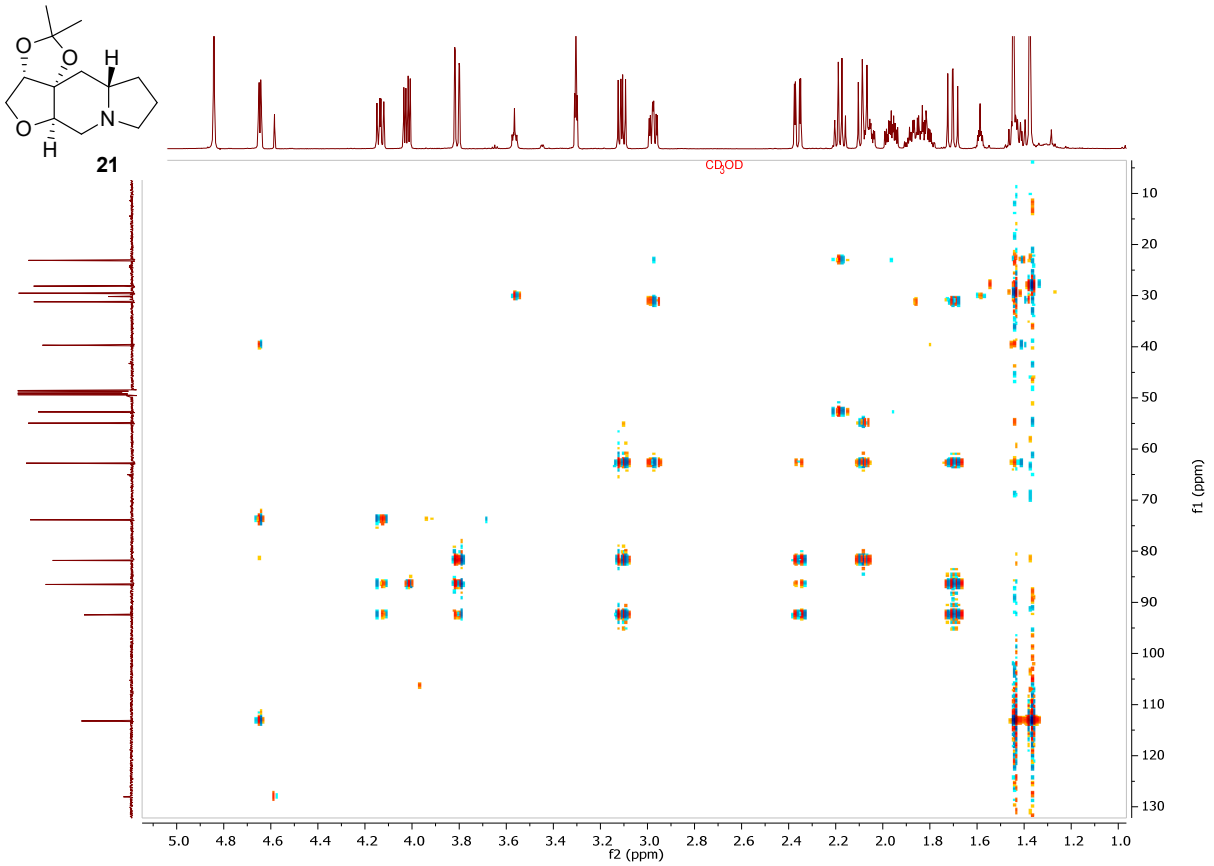
^{1}H NMR of **21**



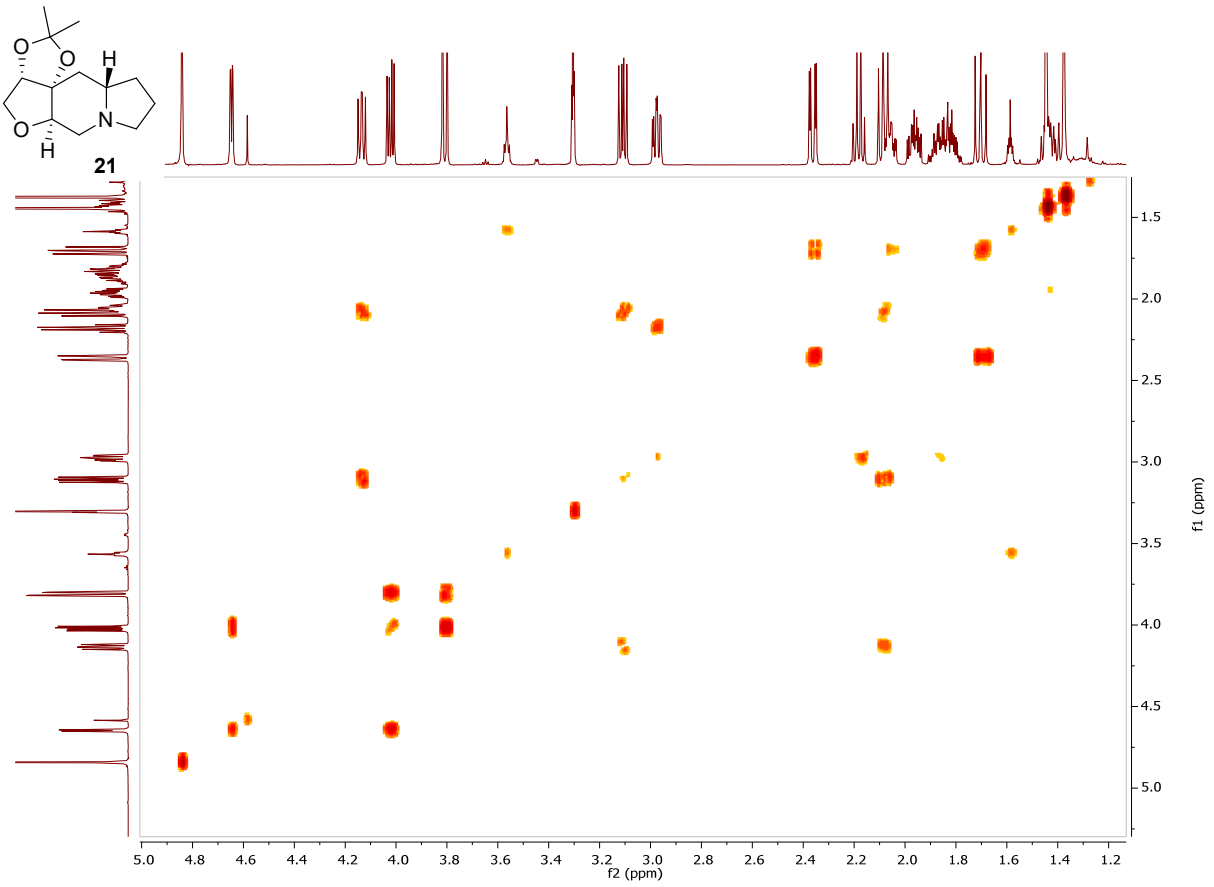
^{13}C NMR of **21**



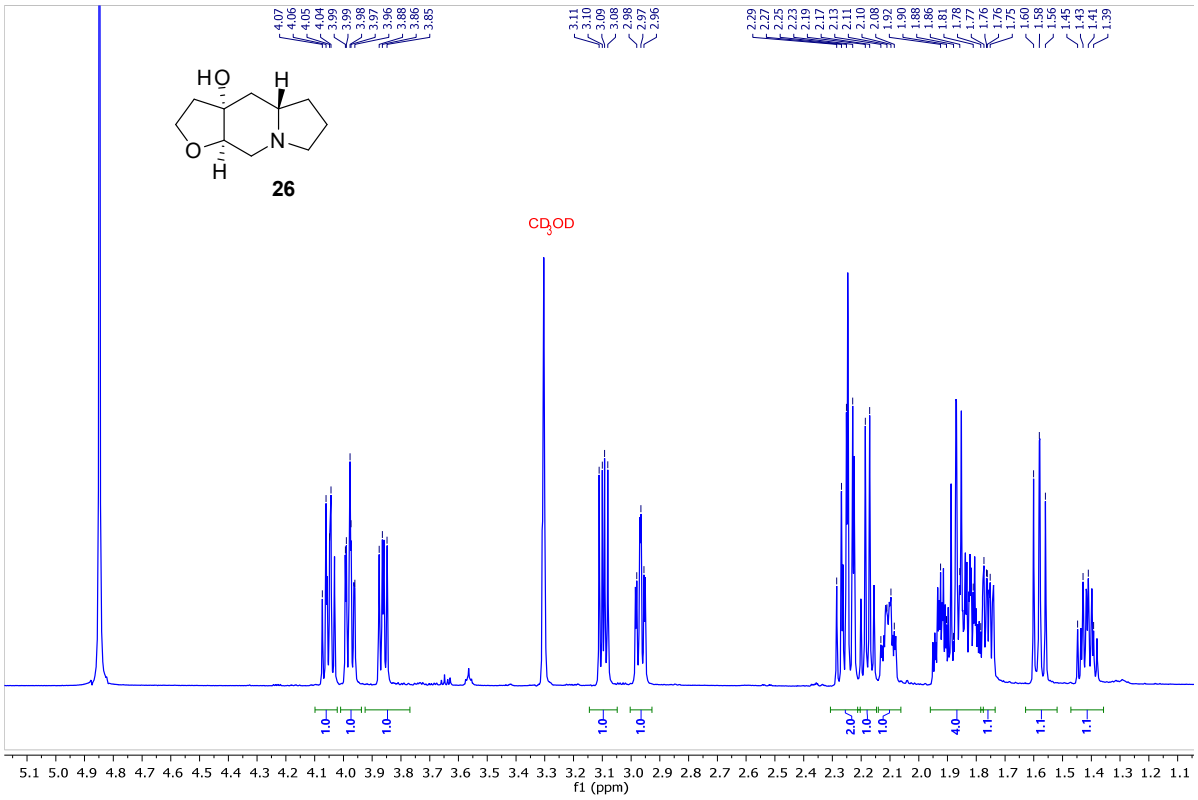
HSQC of **21**



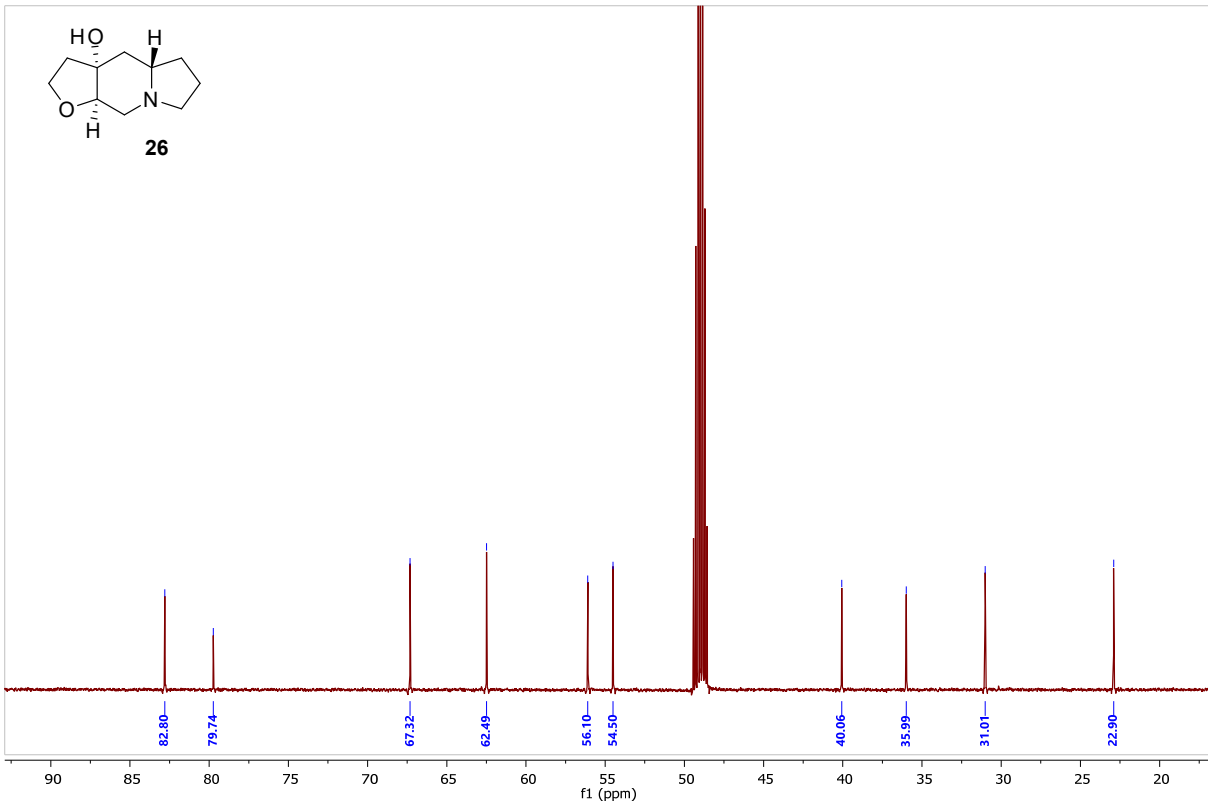
HMBC of **21**



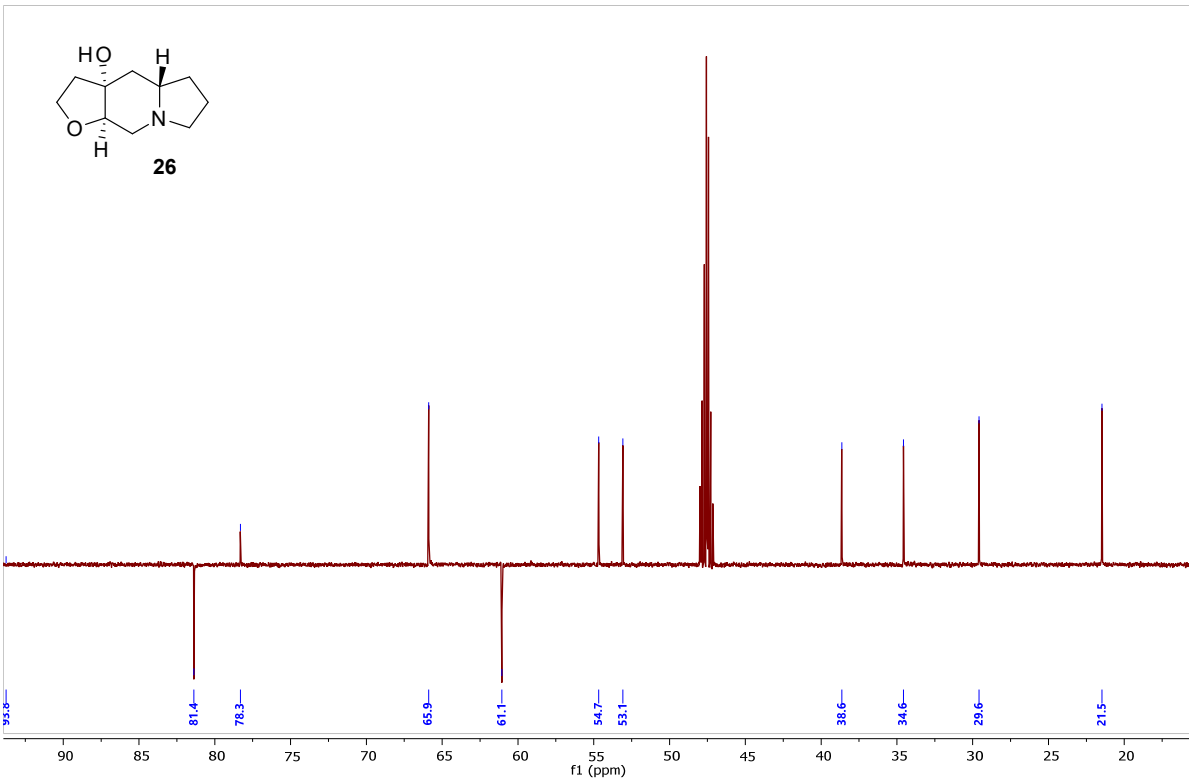
COSY of **21**



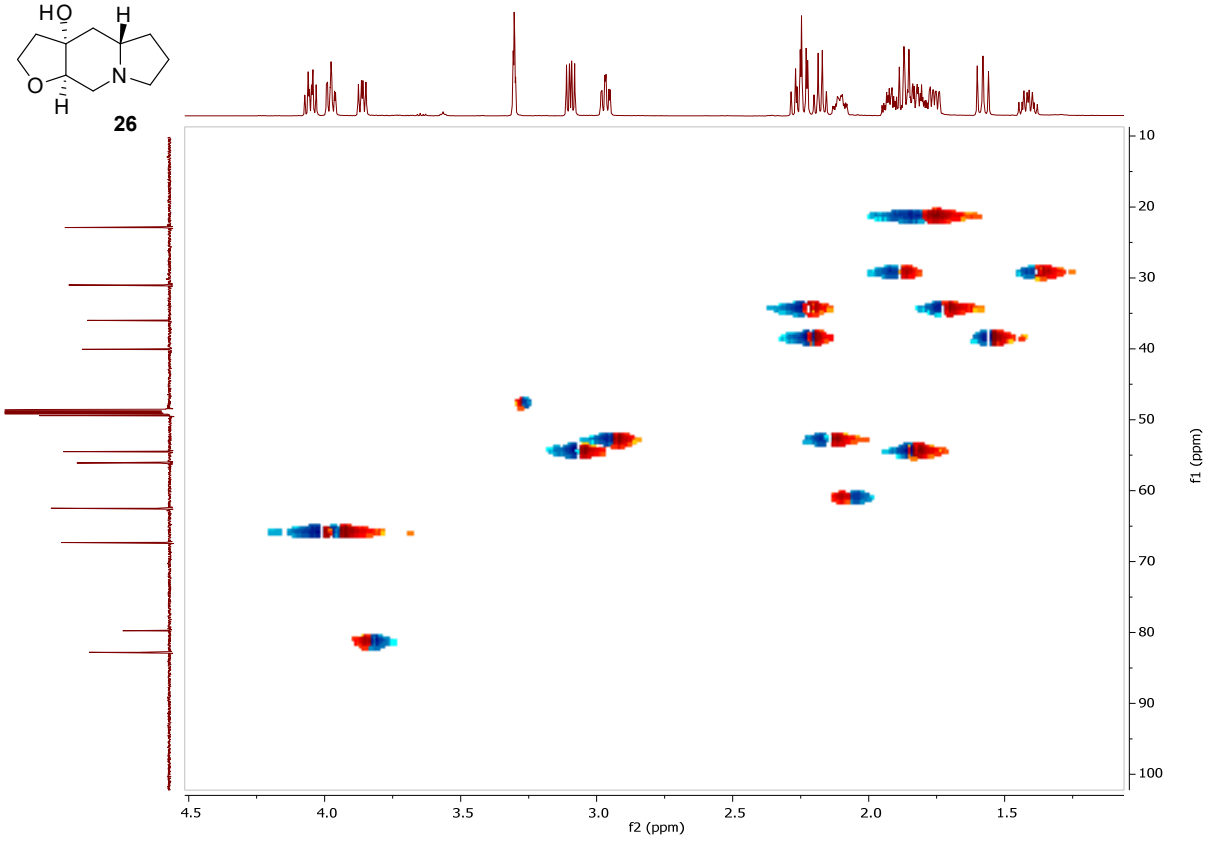
^{1}H NMR of **26**



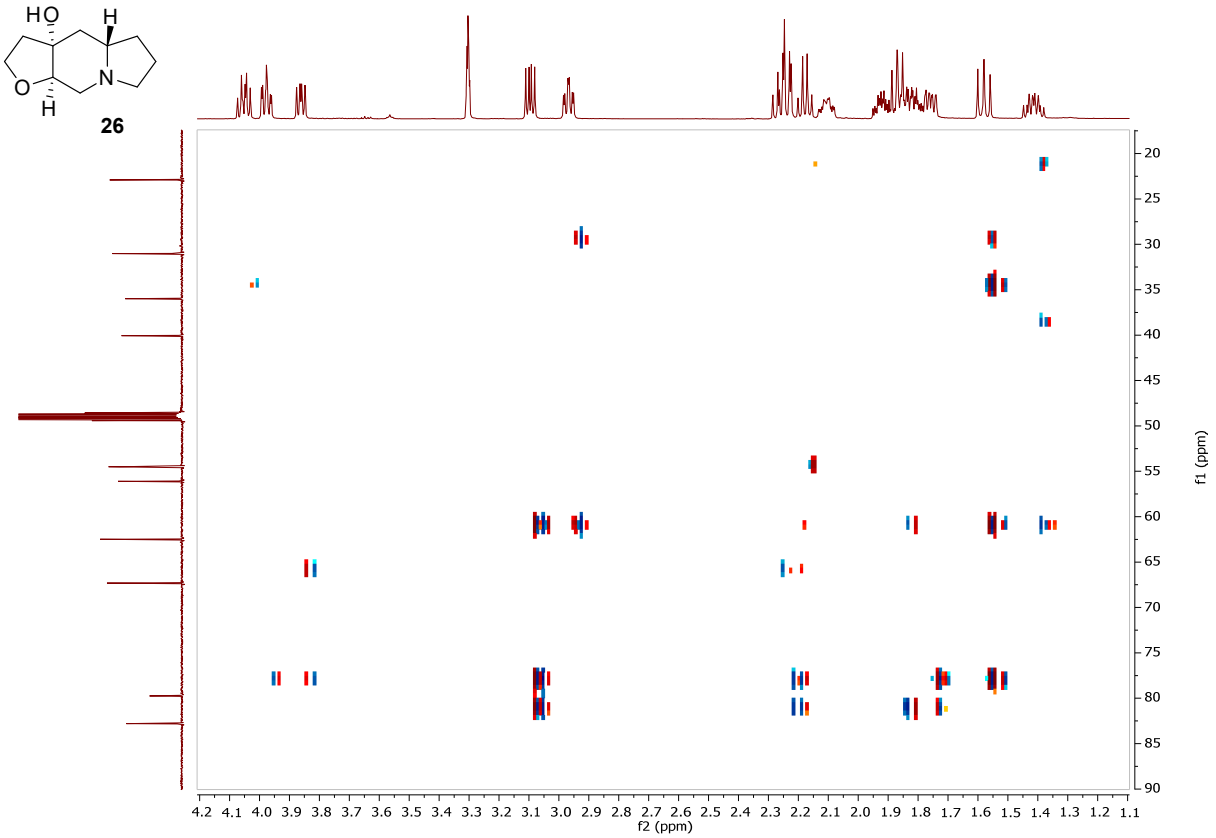
^{13}C NMR of **26**



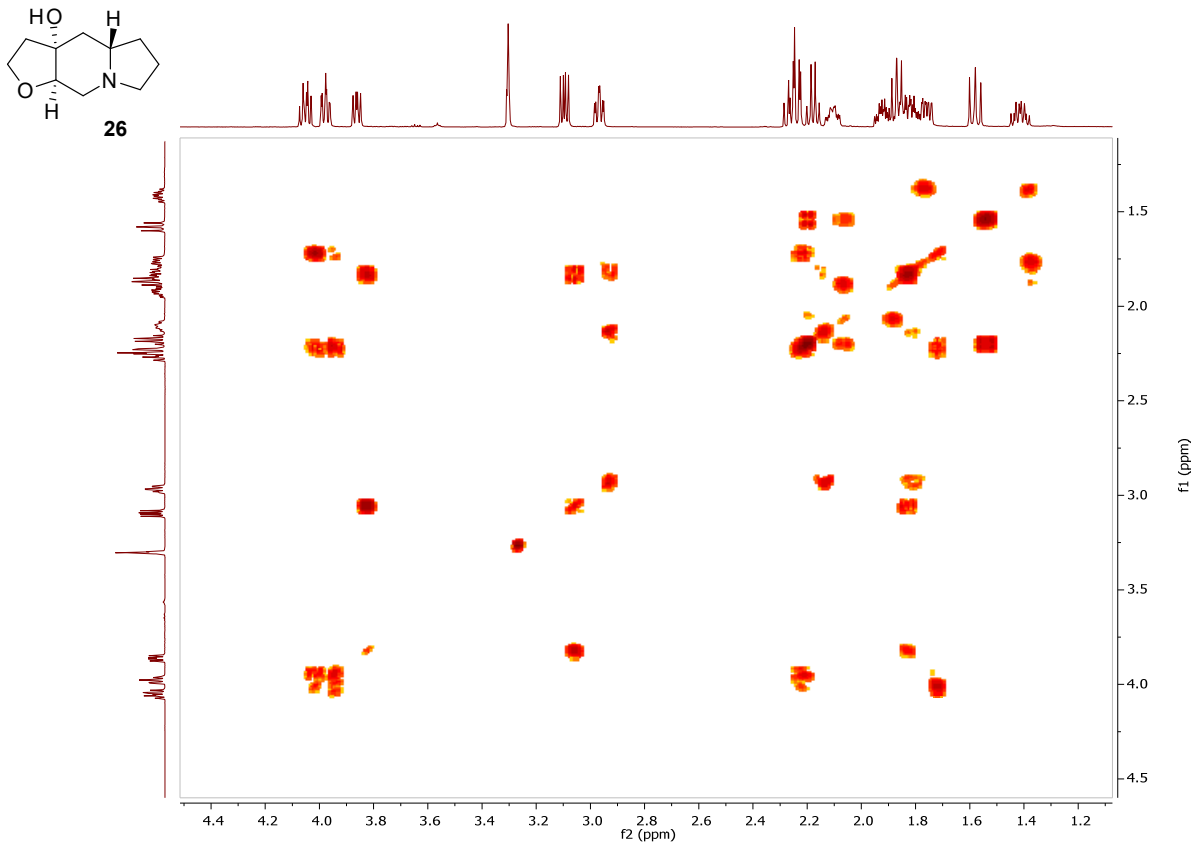
^{13}C NMR (APT) of **26**



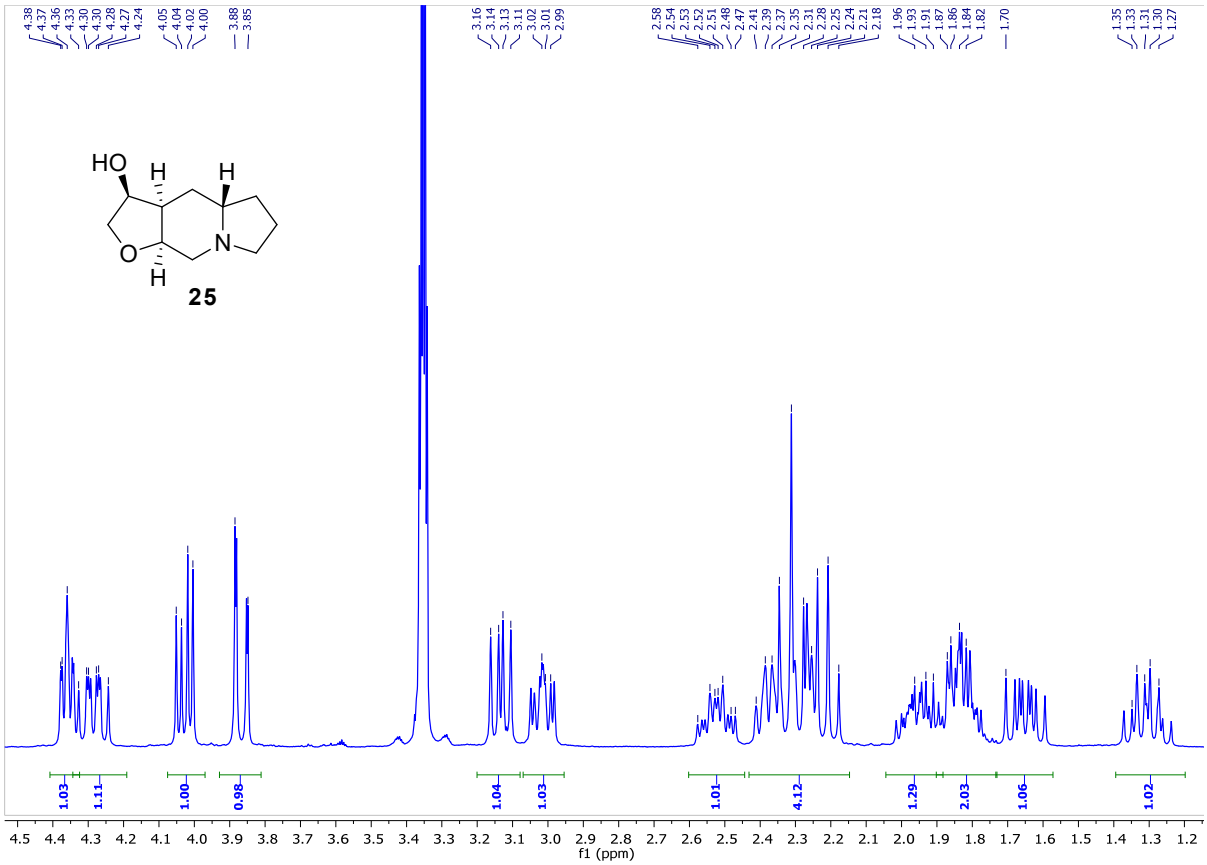
HSQC of **26**



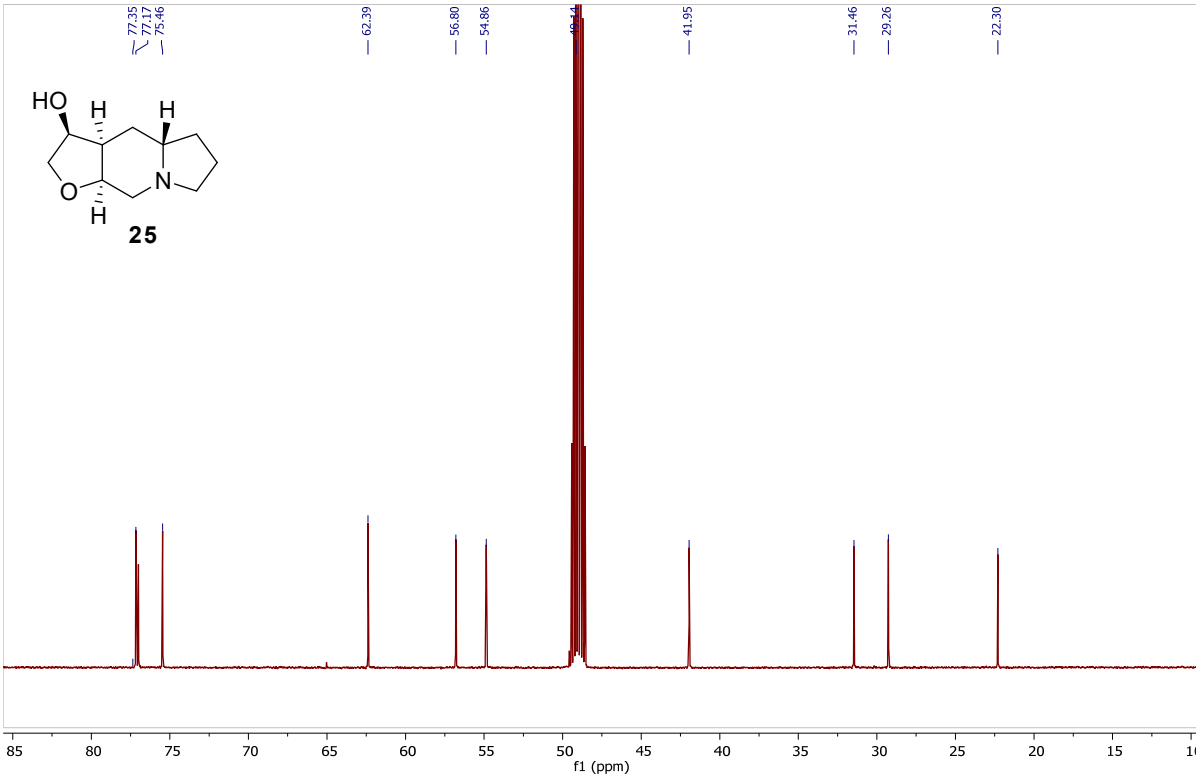
HMBC of **26**



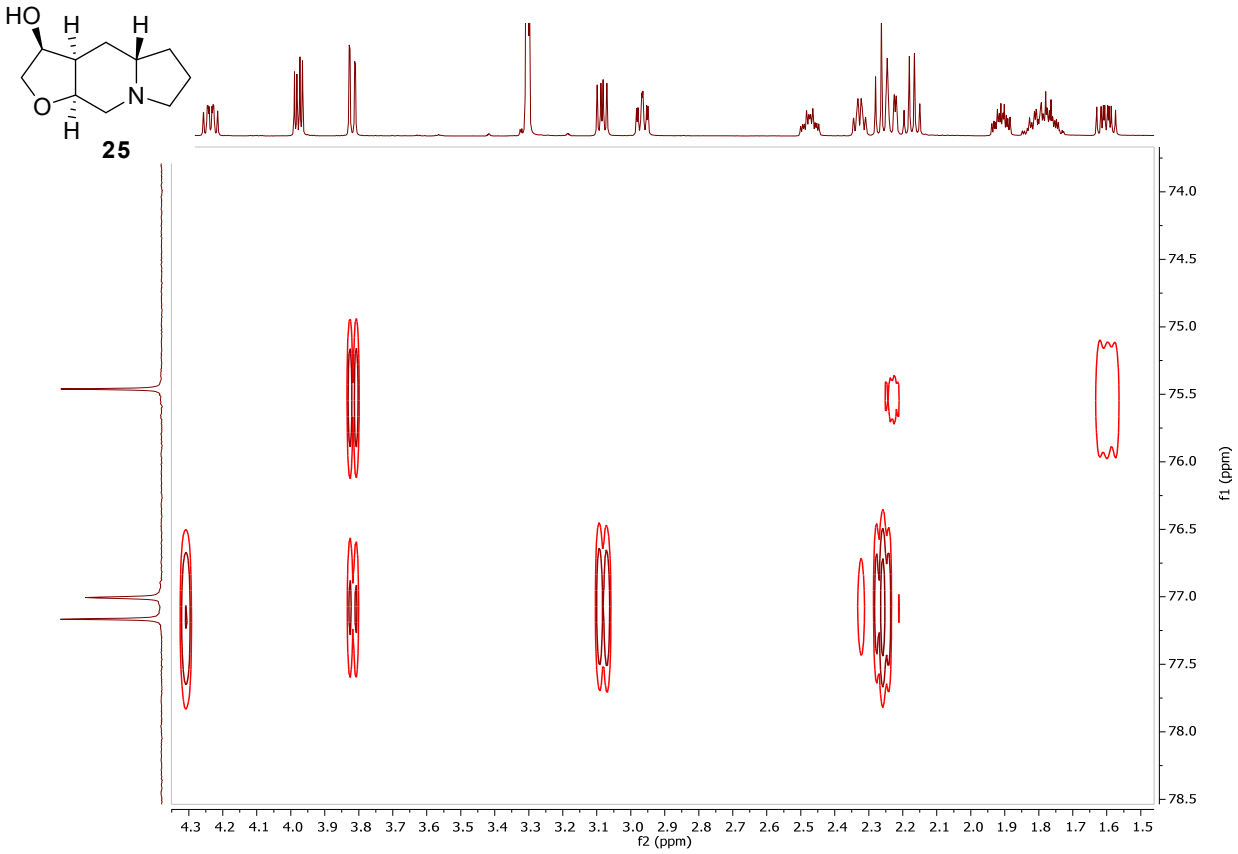
COSY of **26**



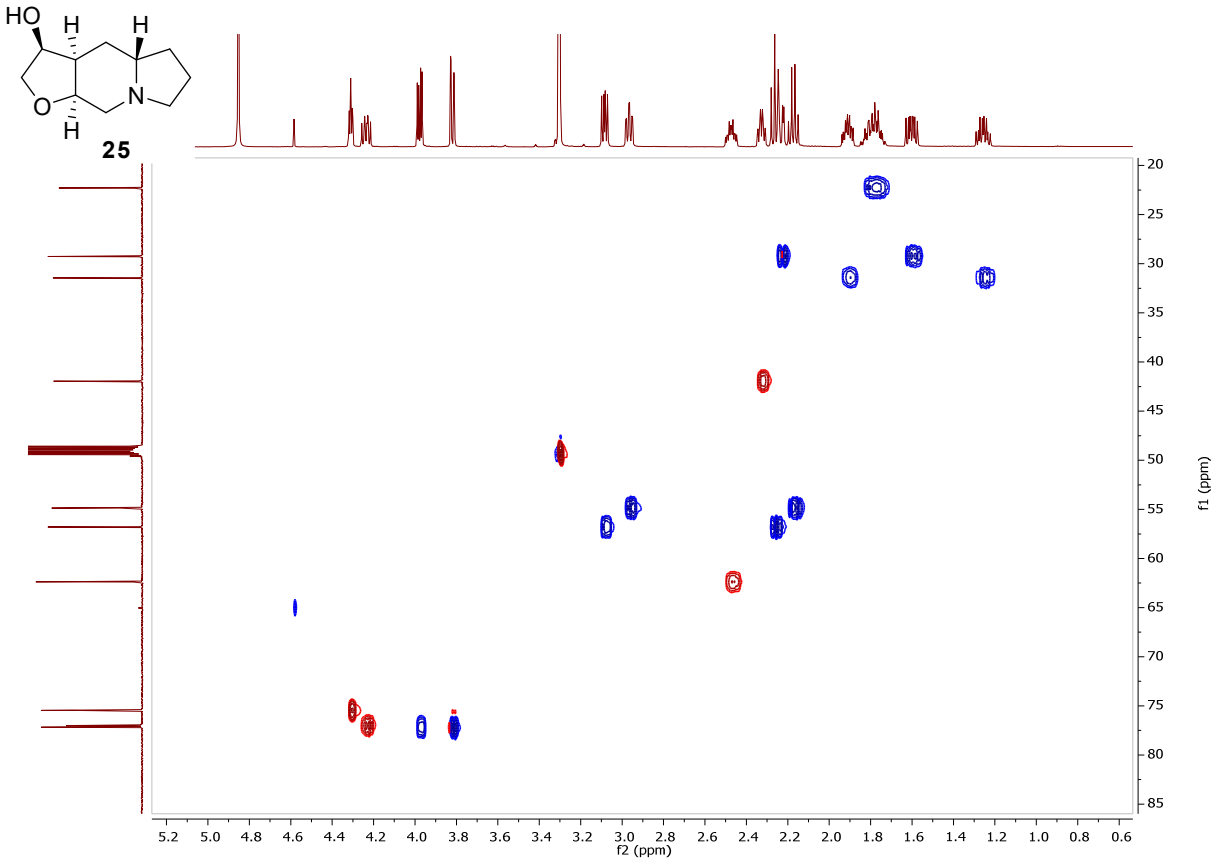
^{1}H NMR of **25**



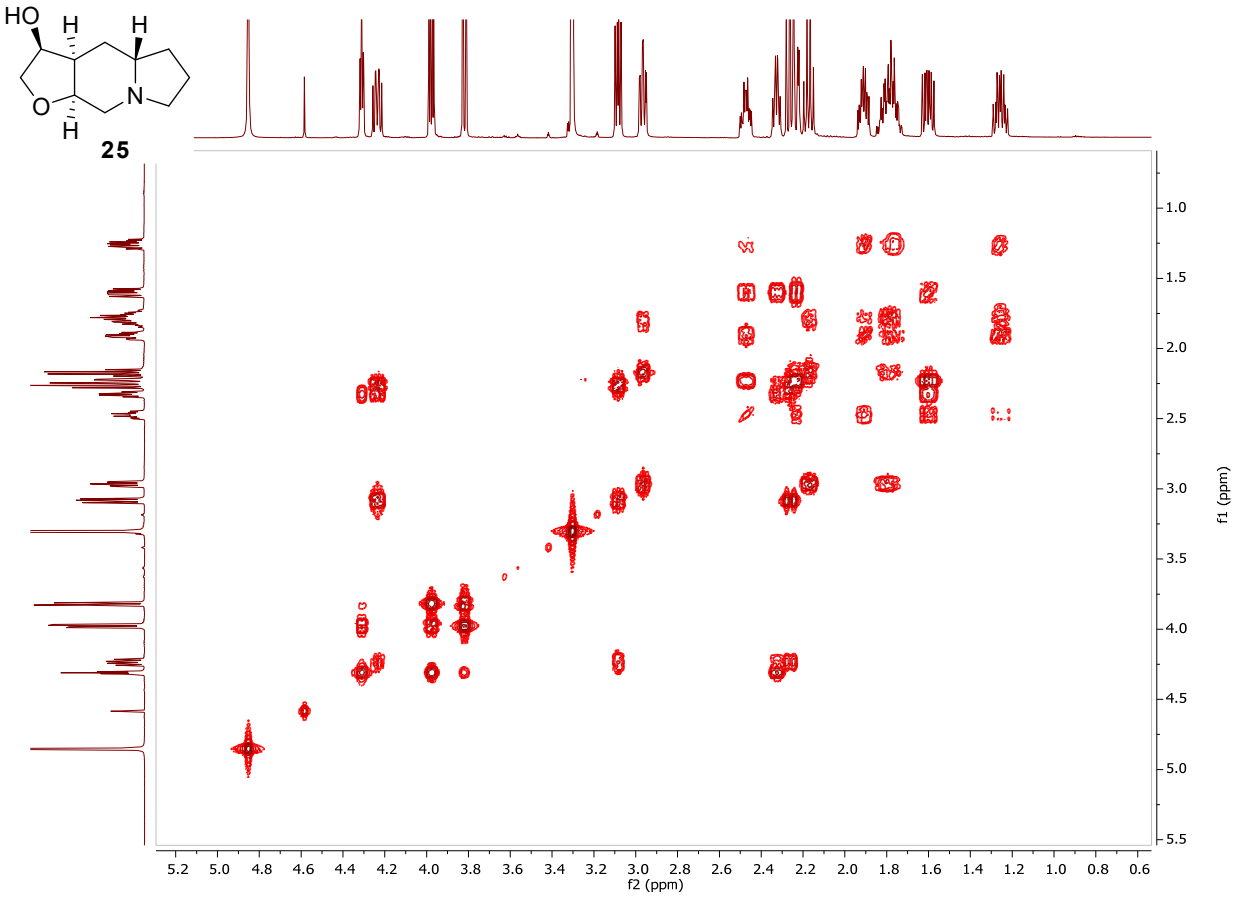
^{13}C NMR of **25**



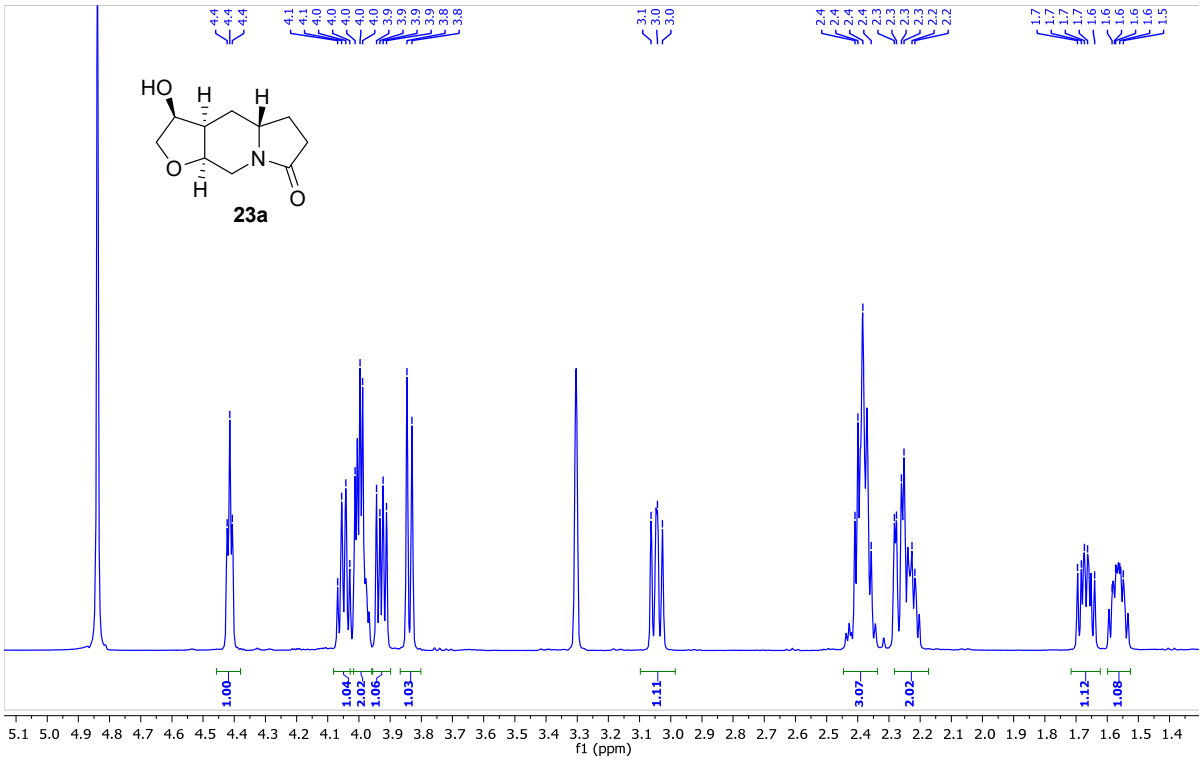
HMBC of **25**



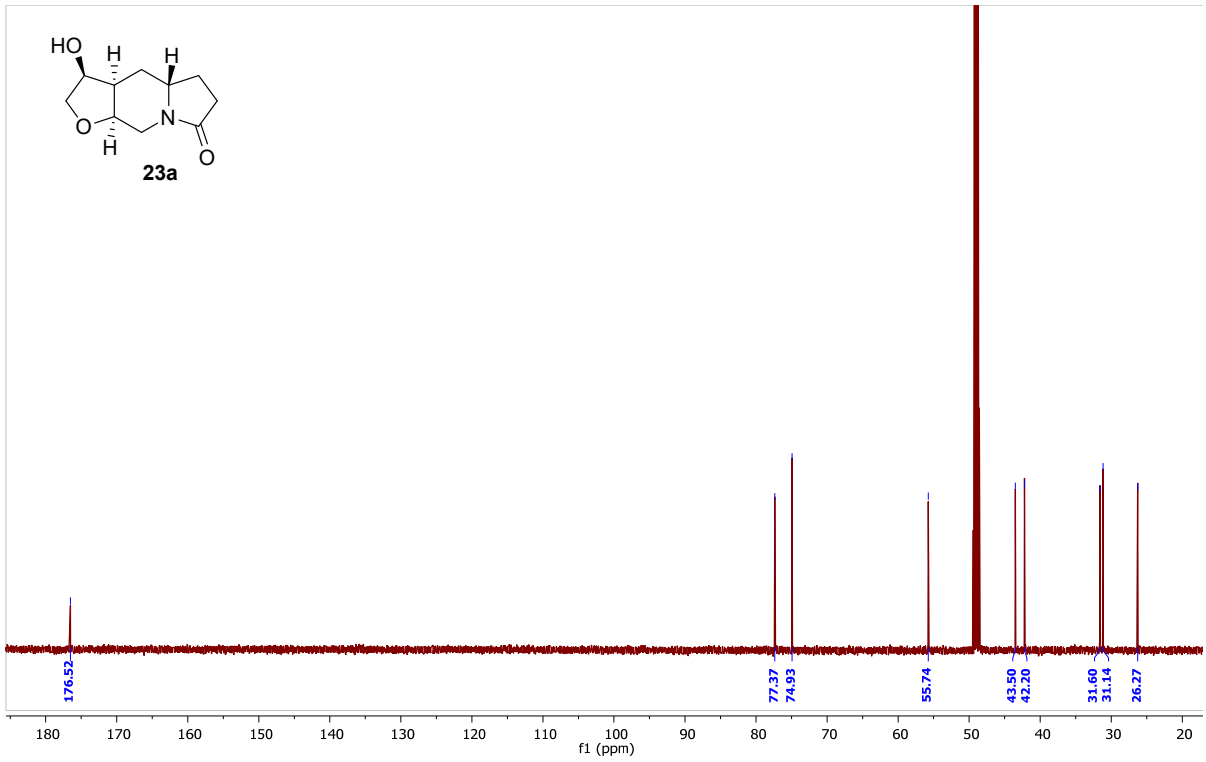
HSQC of **25**



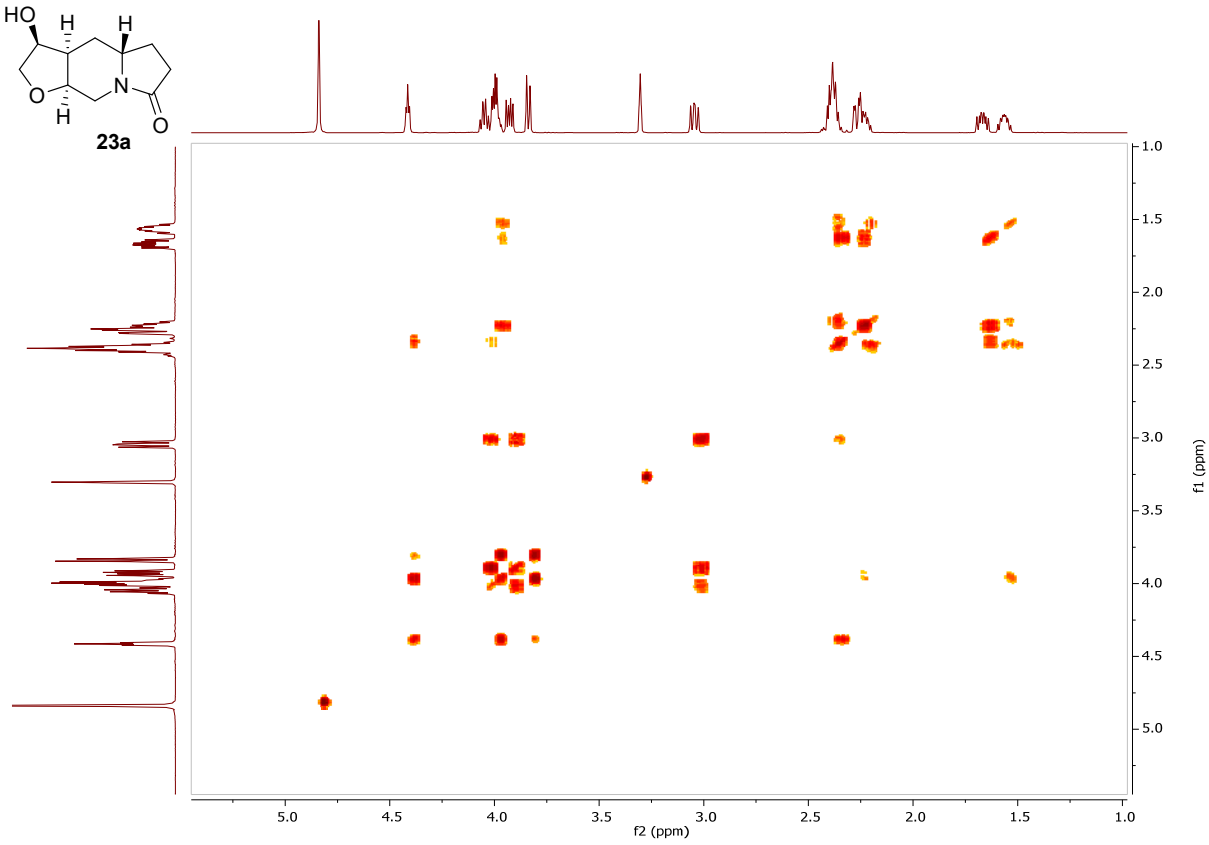
COSY of **25**



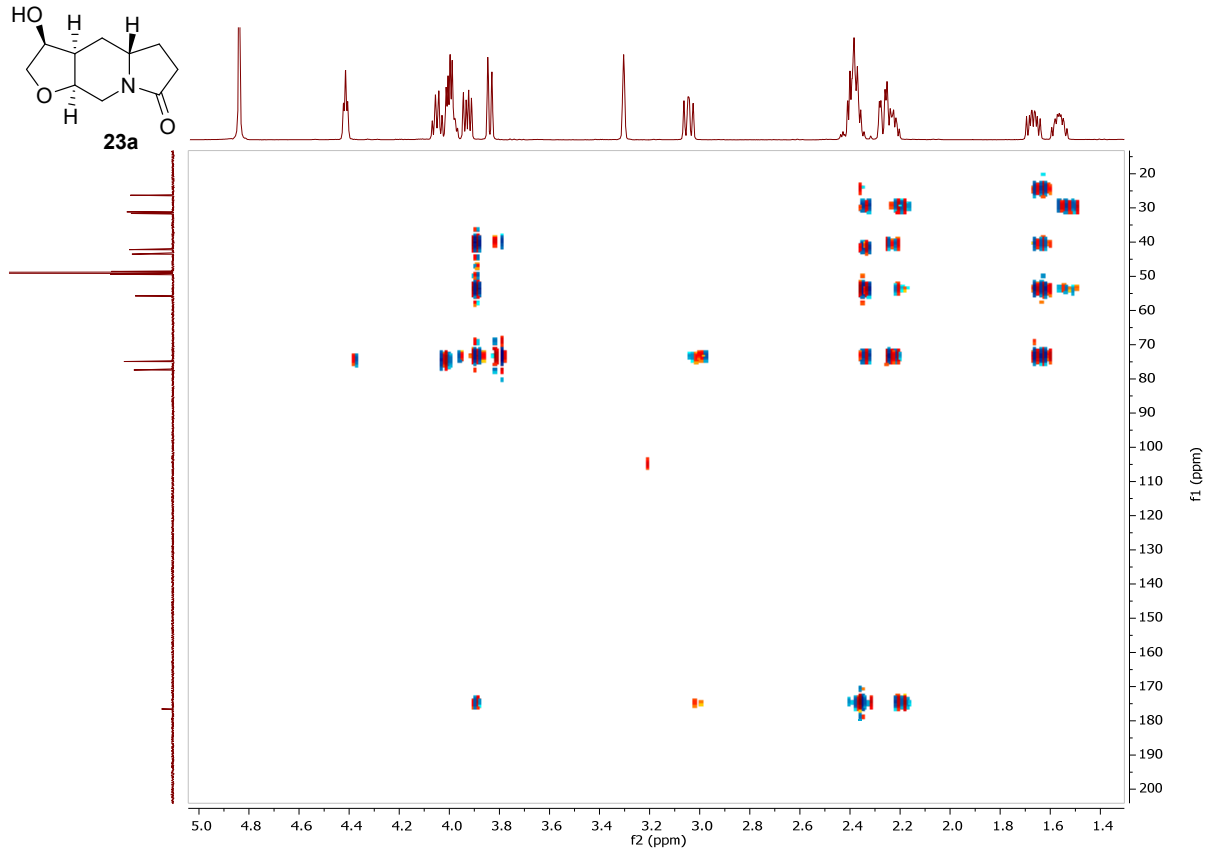
^{1}H NMR of **23a**



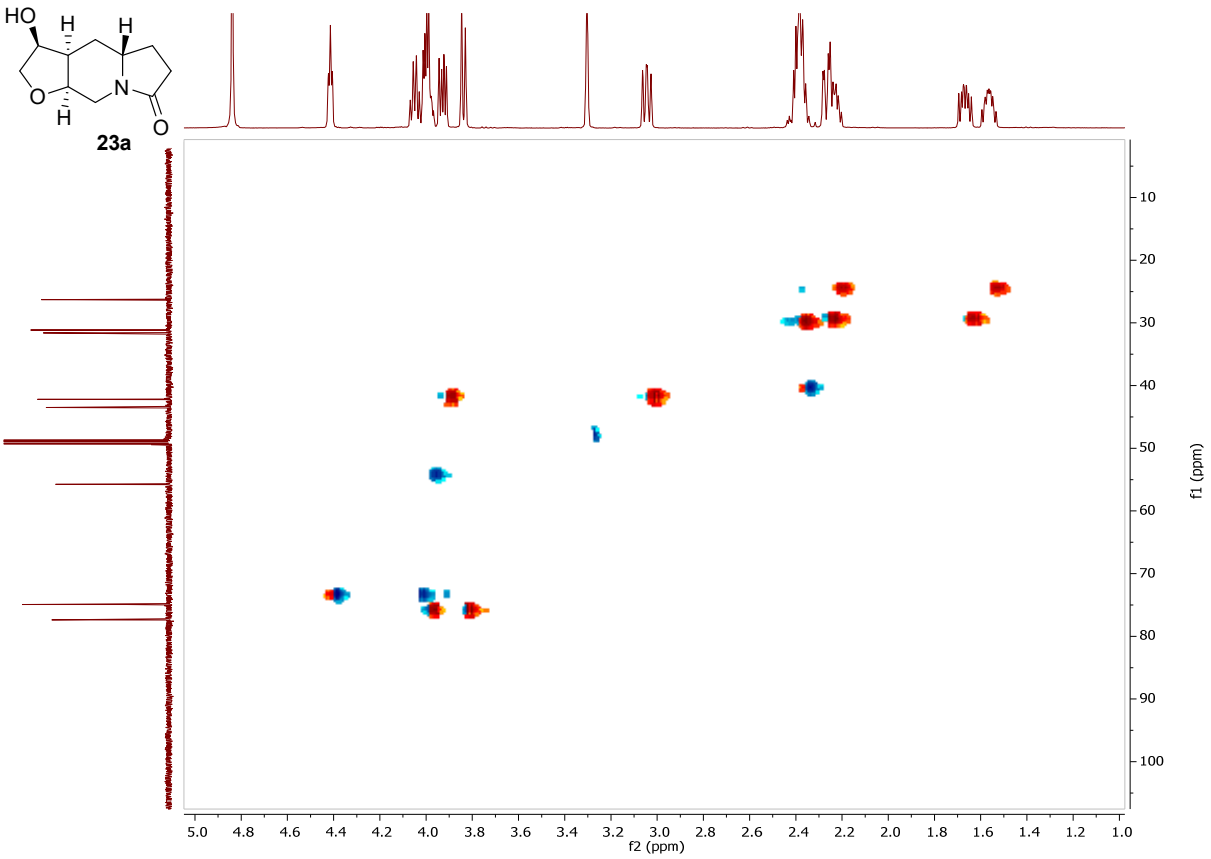
^{13}C NMR of **23a**



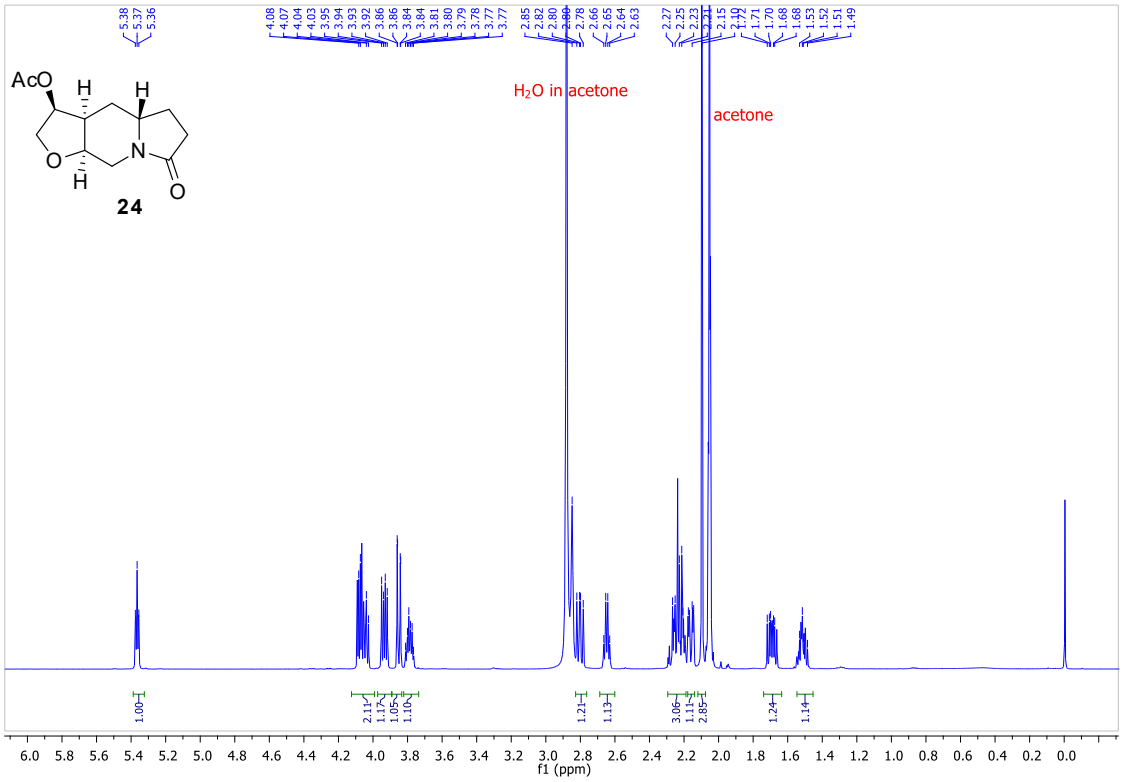
COSY of **23a**



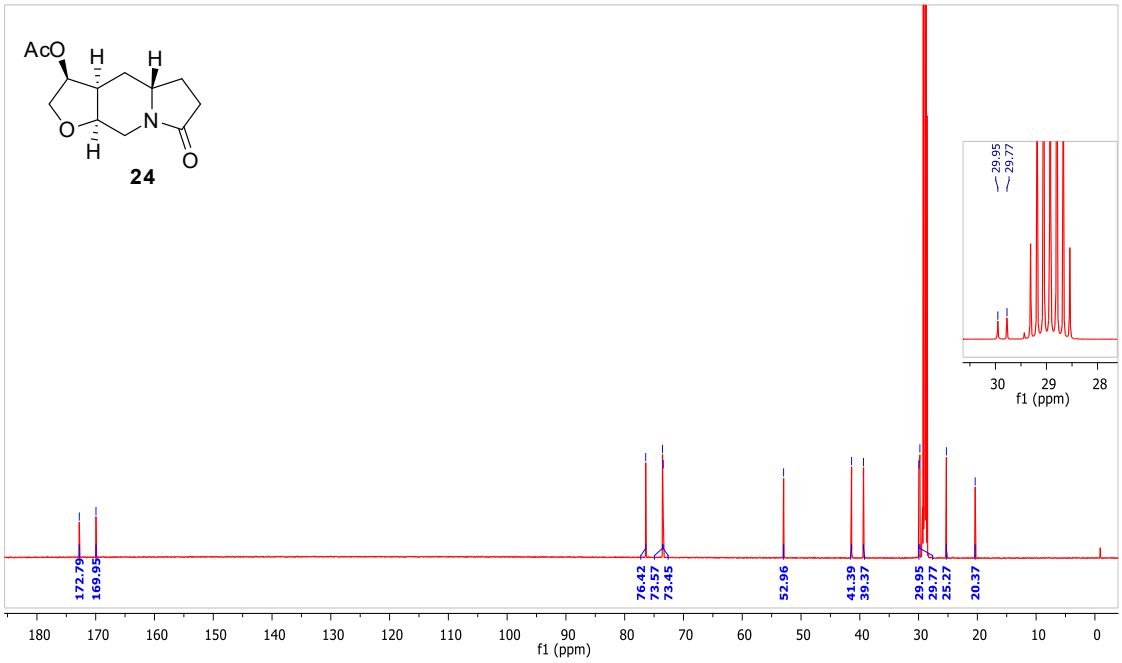
HMBC of **23a**



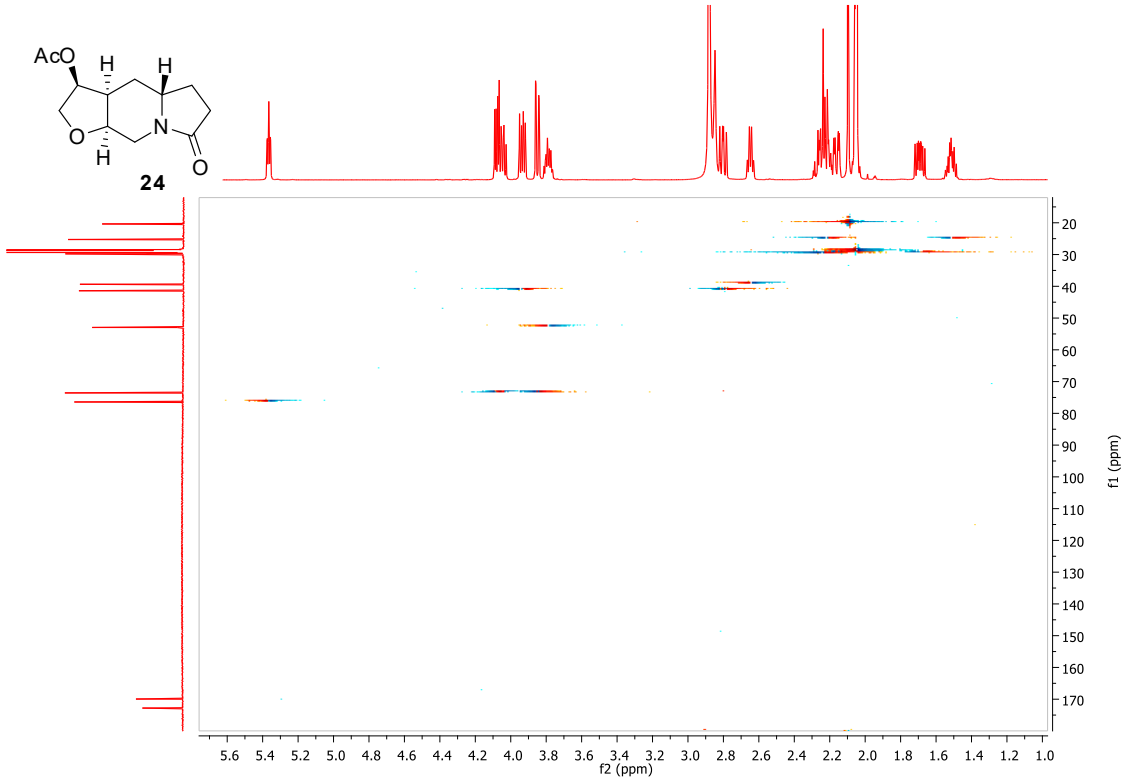
HSQC of **23a**



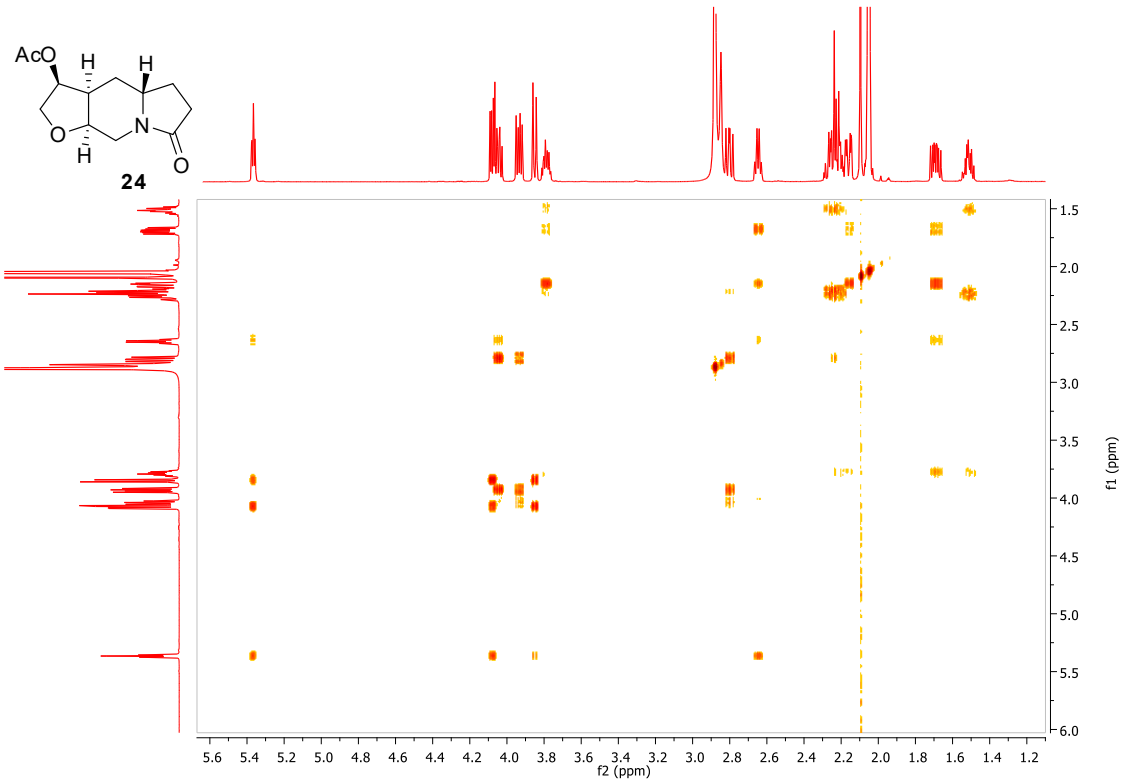
^{1}H NMR of **24**



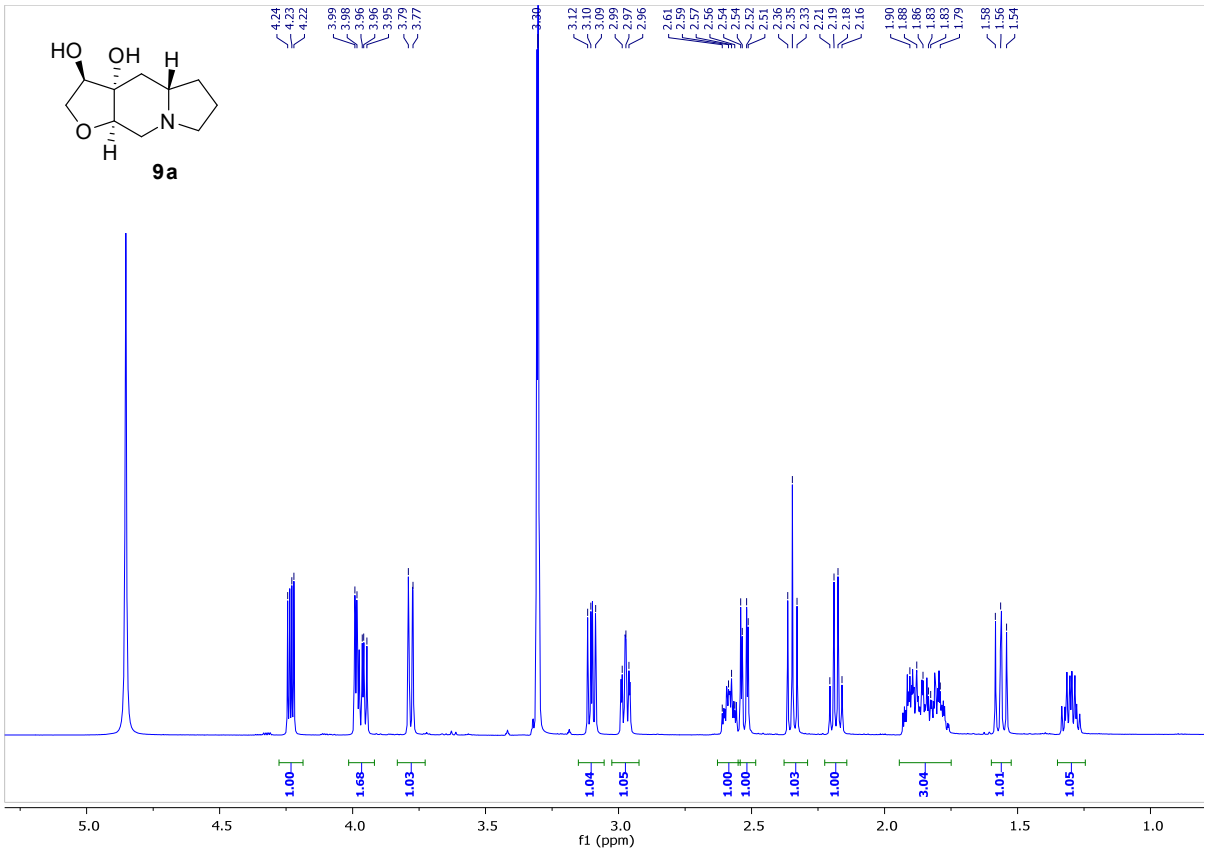
^{13}C NMR of **24**



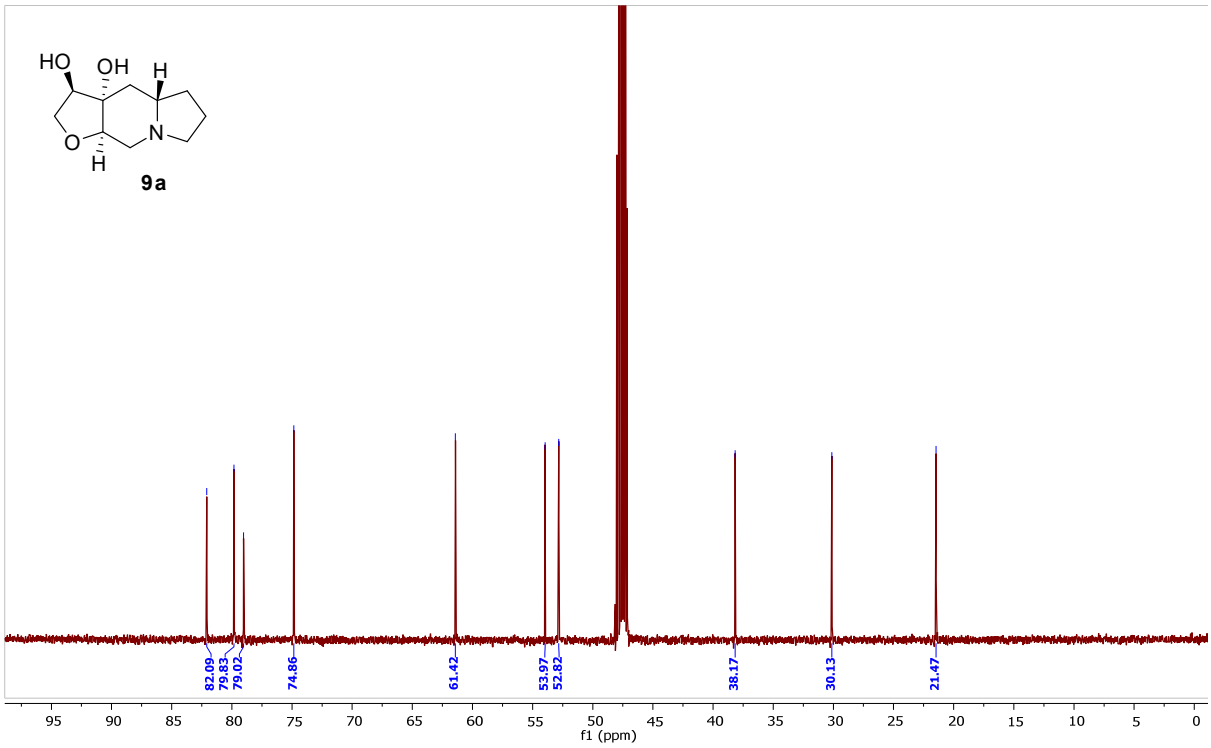
HSQC of **24**



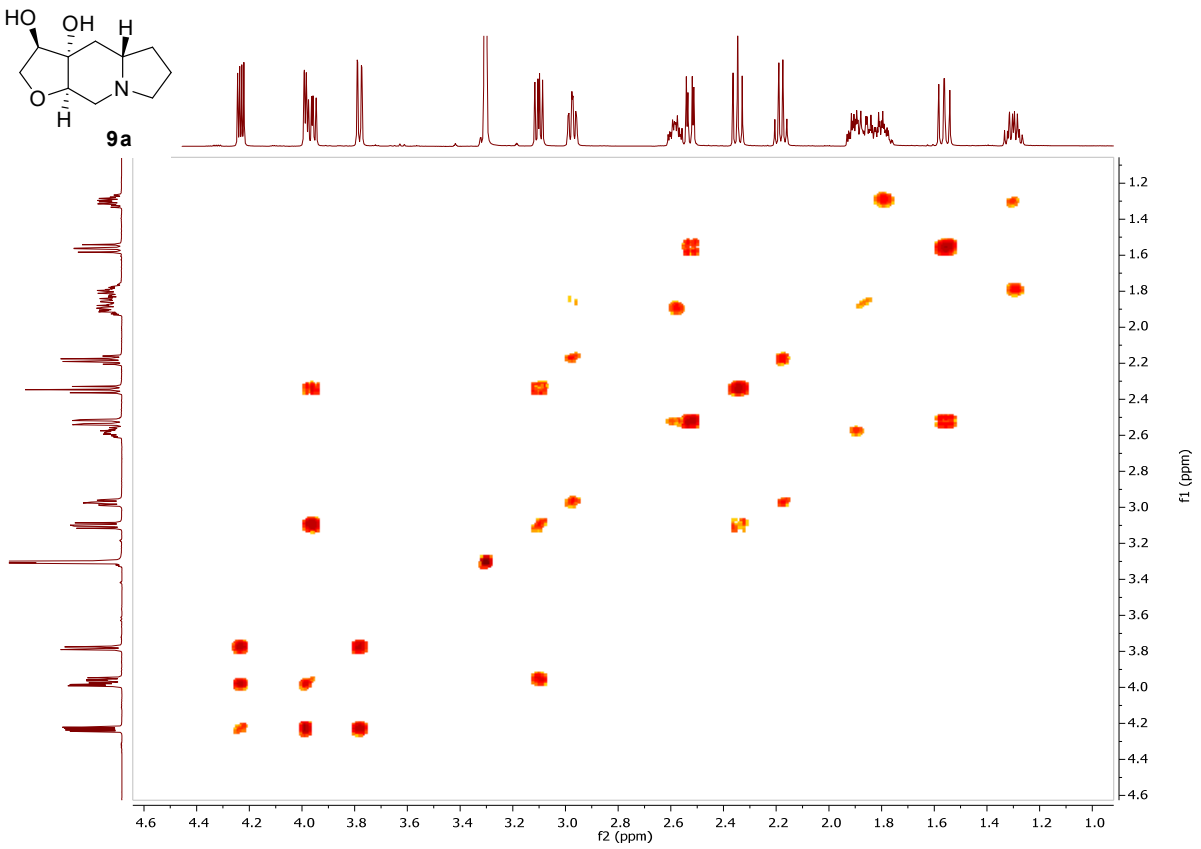
COSY of **24**



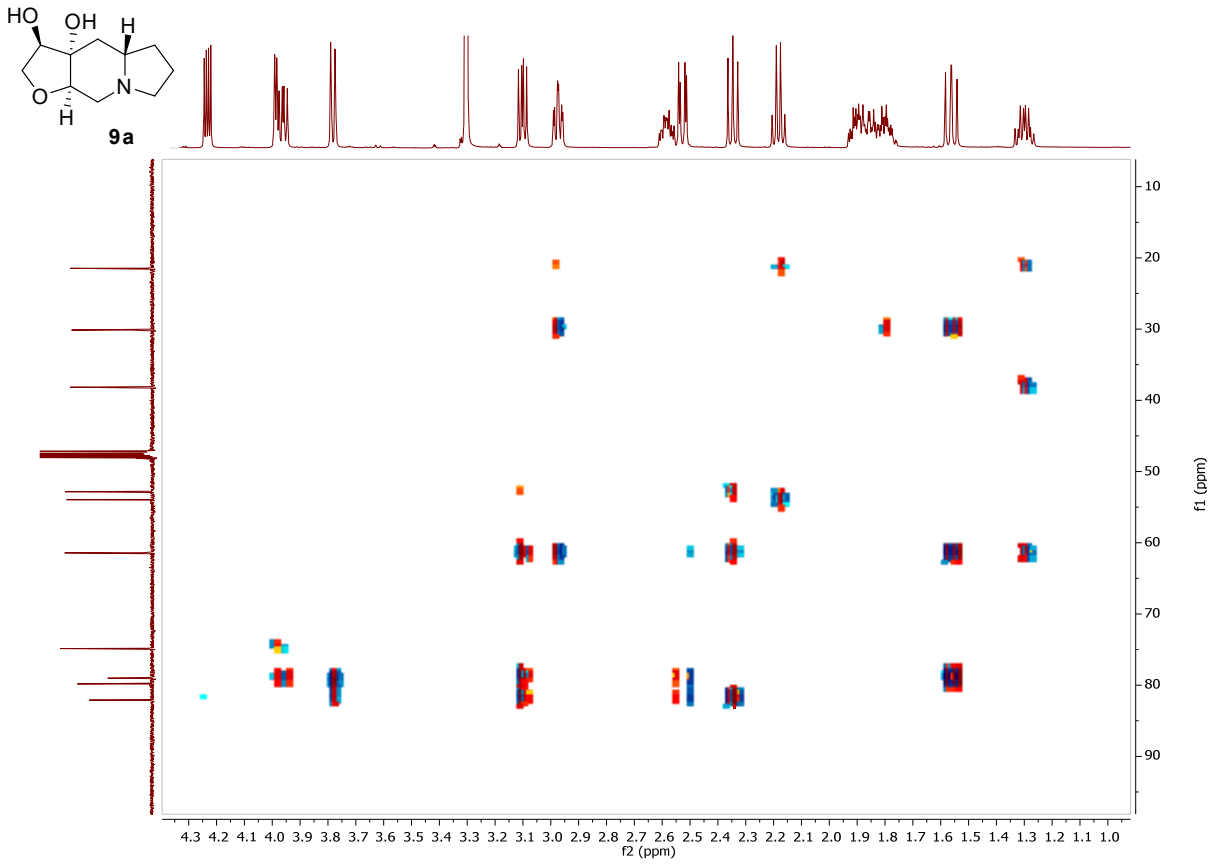
^{1}H NMR of **9a**



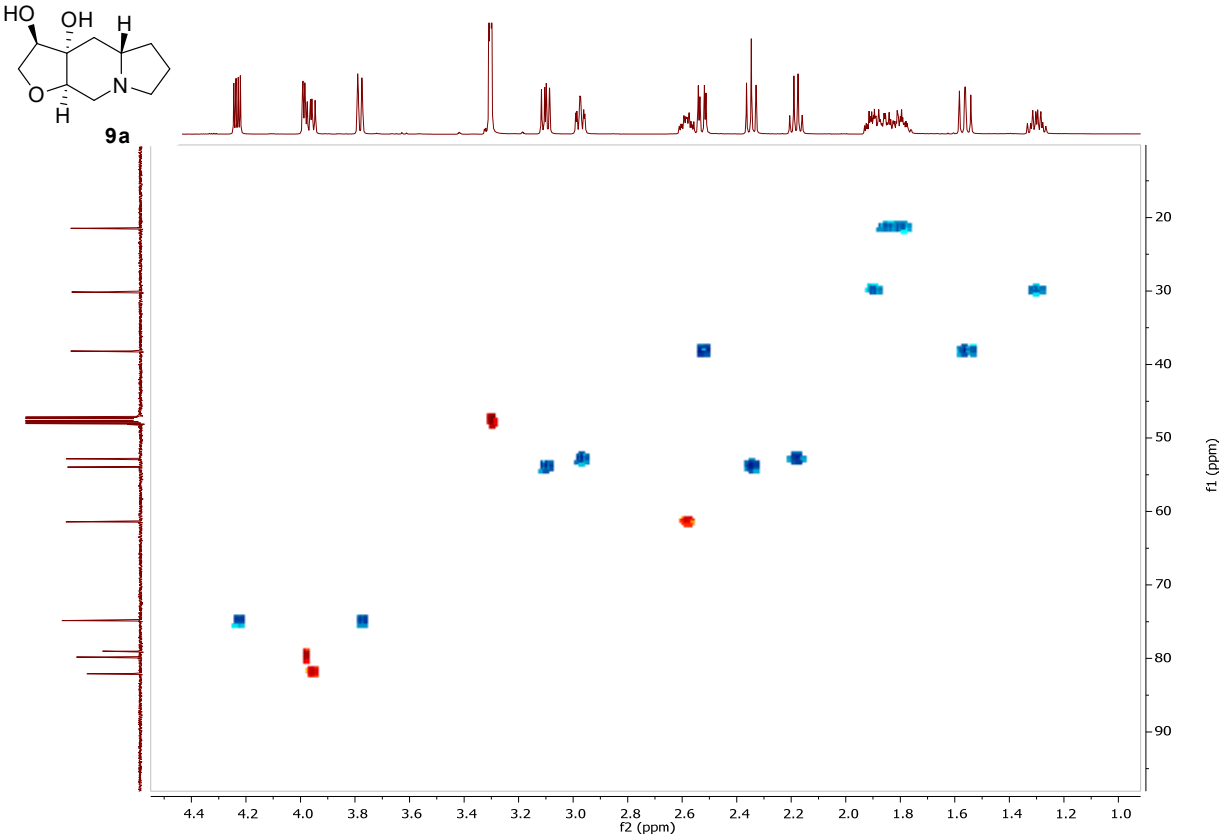
^{13}C NMR of **9a**



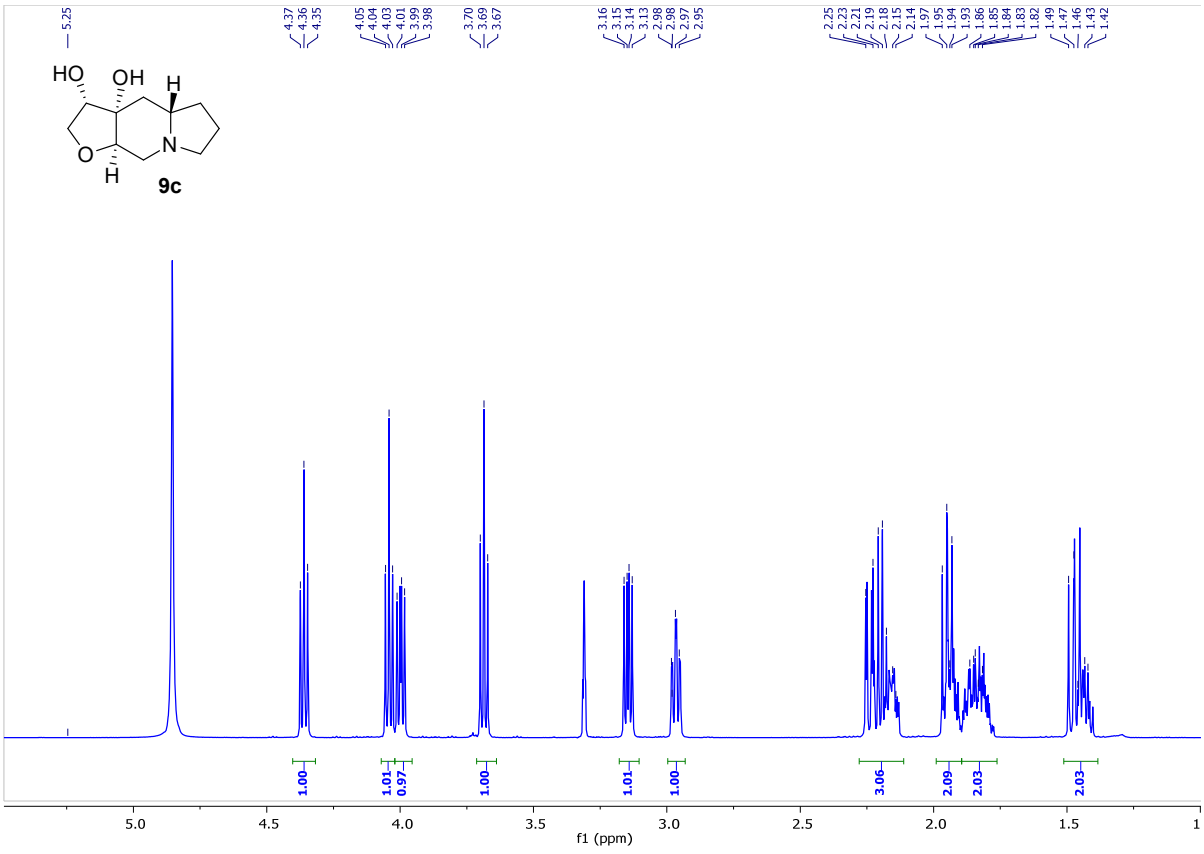
COSY of **9a**



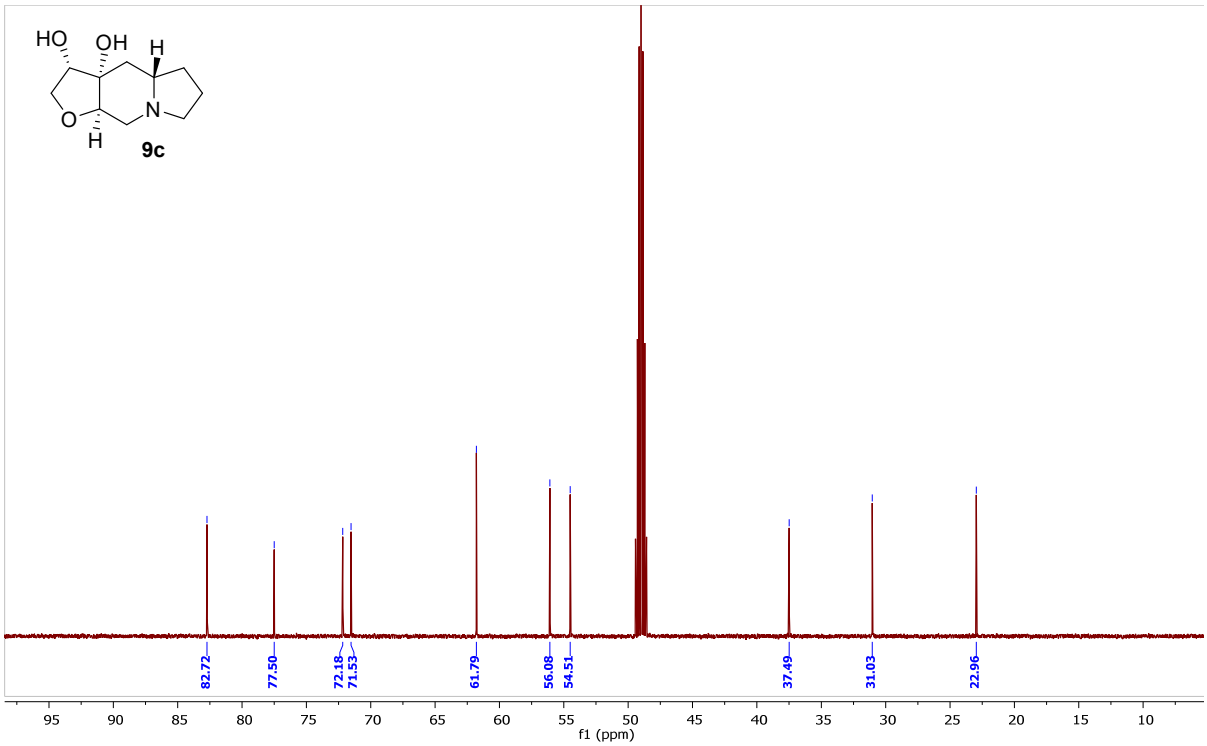
HMBC of **9a**



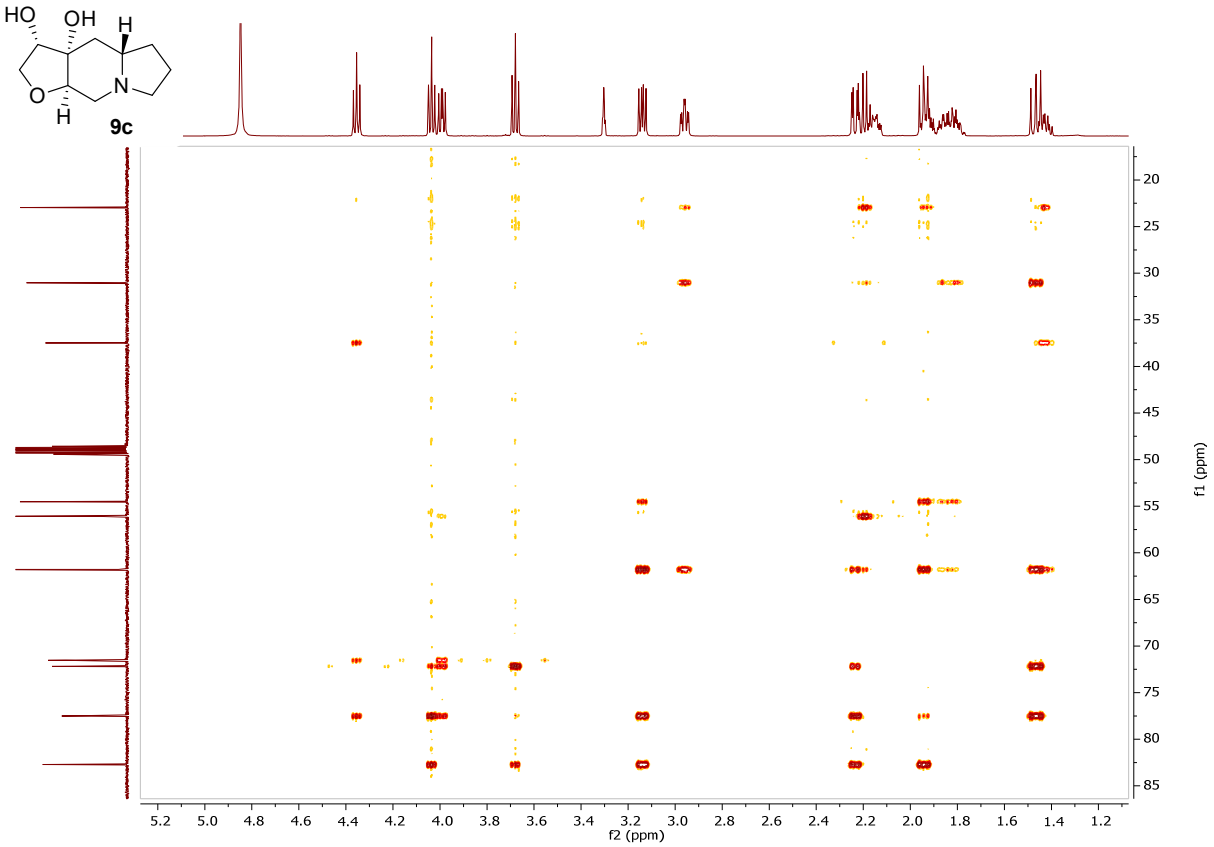
HSQC of **9a**



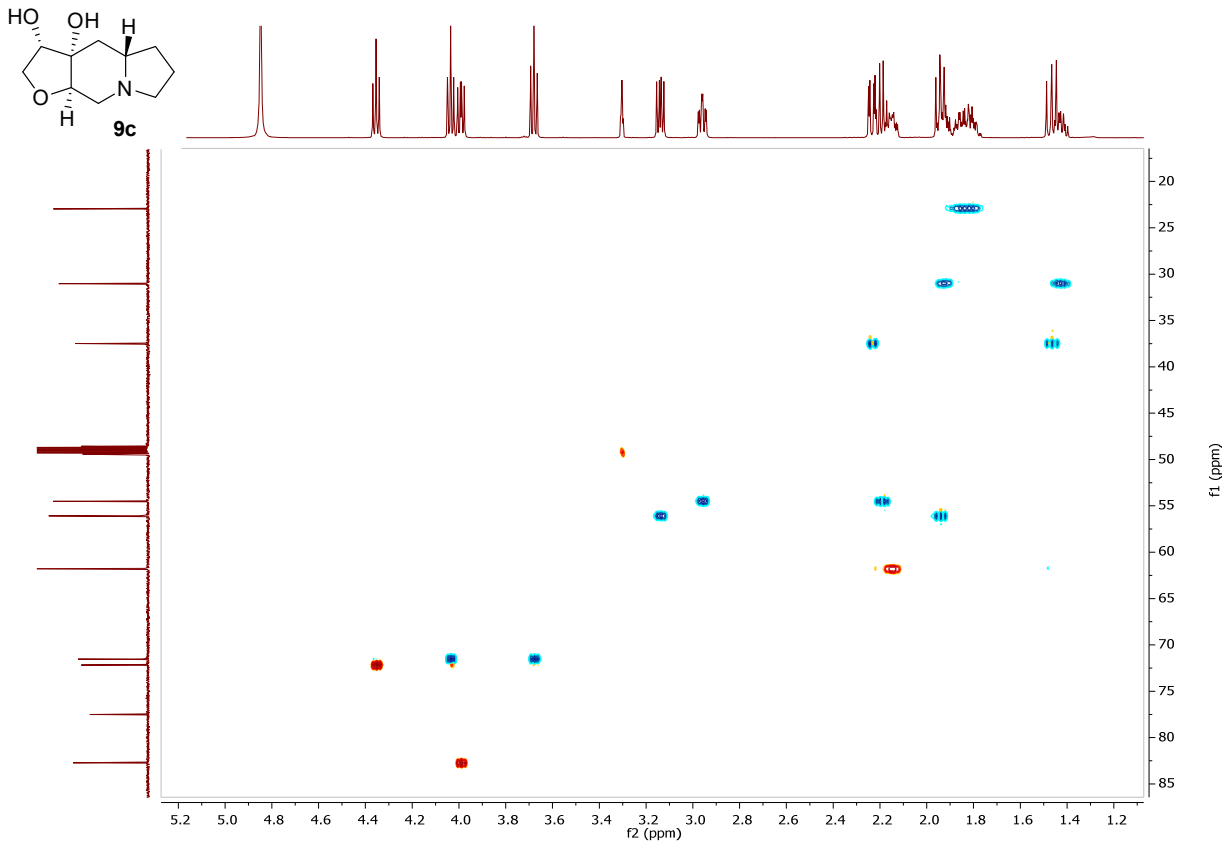
^{1}H NMR of **9c**



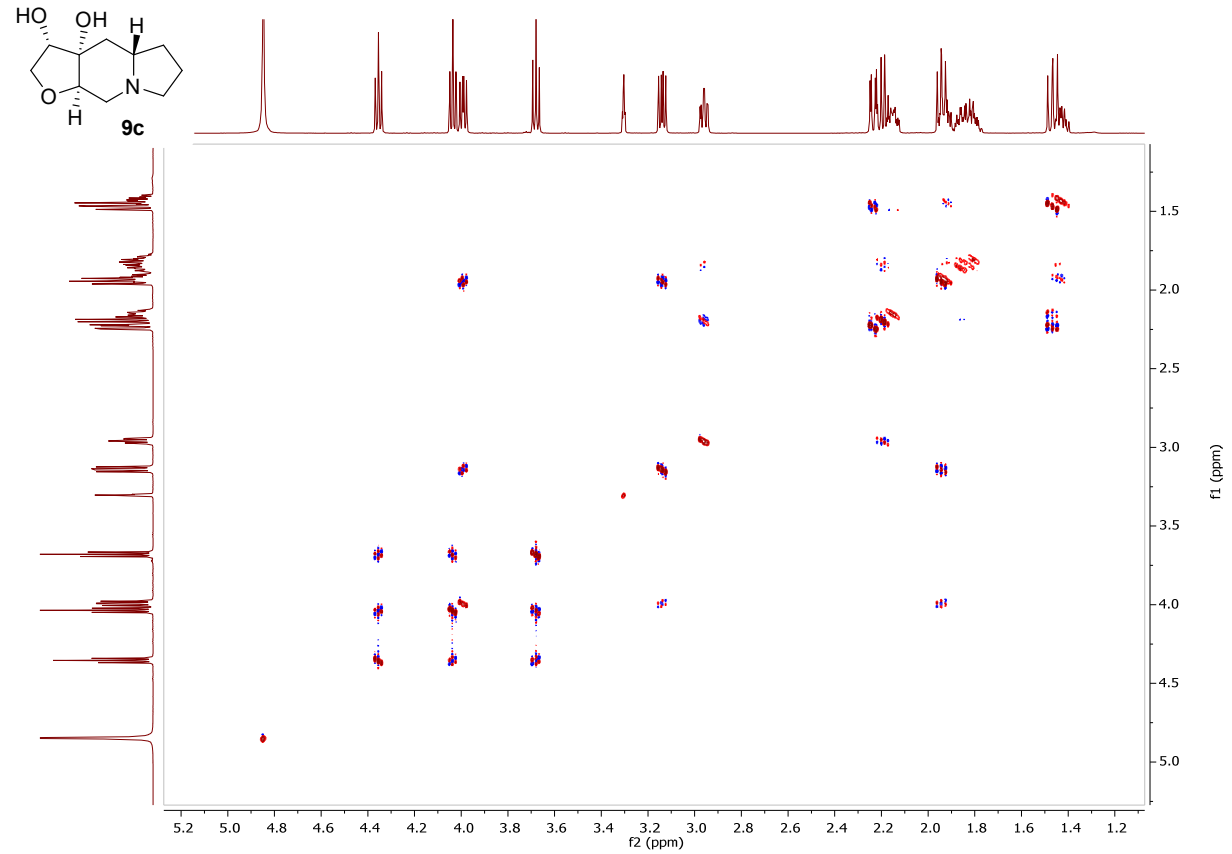
^{13}C NMR of **9c**



HMBC of **9c**



HSQC of **9c**



COSY of **9c**

X-ray Crystallographic Data of compound 6, 8a, 14, 18c, 19c, 20, 23a and 30a.

Crystallographic data: single-crystals were mounted on Stoe StadiVari diffractometer possessing PILATUS3R 300K detector and microfocused sealed tube Xenocs Genix3D Cu HD (λ = 1.54186 Å) at 100K. The structures were solved by SUPERFLIP, SHELXTL or SIR-2011 and refined by SHELXL (ver. 2018/3).[37] The structures were drawn using OLEX2 program.[38] The absolute structures were confirmed by two methods (Parsons and Hooft methods).[39]

Crystal data for **6**: $C_{10}H_{13}NO_3$ (M = 195.21 g/mol), orthorhombic space group $P2_12_12_1$ (no. 19), a = 5.8779(2), b = 9.4102(2), c = 16.0947(3) Å, V = 890.23(4) Å^3, Z = 4, D_c = 1.457 g/cm^3, μ = 0.895 mm^{-1}, R_1 = 0.0239 [$I > 2\sigma(I)$], and wR_2 = 0.0622, S = 1.059 for all 23493 reflections. Flack parameter x = 0.05(5). Hooft parameter y = 0.09(3). ***CCDC reference number 1976231.***

Crystal data for **8a**: $C_{10}H_{15}NO_4$ (M = 213.23 g/mol), orthorhombic space group $P2_12_12_1$ (no. 19), a = 19.1607(4), b = 7.5467(1), c = 6.7883(1) Å, V = 981.59(3) Å^3, Z = 4, D_c = 1.443 g/cm^3, μ = 0.936 mm^{-1}, R_1 = 0.0255 [$I > 2\sigma(I)$], and wR_2 = 0.0666, S = 1.062 for all 28016 reflections. Flack parameter x = 0.00(5). Hooft parameter y = –0.04(2). ***CCDC reference number 1976232.***

Crystal data for **14**: $C_{10}H_{13}NO_3$ (M = 195.21 g/mol), orthorhombic space group $P2_12_12_1$ (no. 19), a = 8.3442(2), b = 9.0461(2), c = 12.1350(3) Å, V = 915.98(4) Å^3, Z = 4, D_c = 1.416 g/cm^3, μ = 0.870 mm^{-1}, R_1 = 0.0245 [$I > 2\sigma(I)$], and wR_2 = 0.0656, S = 1.072 for all 48750 reflections. Flack parameter x = 0.03(7). Hooft parameter y = 0.05(6). ***CCDC reference number 1976233.***

Crystal data for **18c**: $C_{14}H_{19}NO_6$ (M = 297.30 g/mol), monoclinic space group $P2_1$ (no. 4), a = 12.2148(2), b = 6.8618(1), c = 17.7152(3) Å, β = 103.182(2)°, V = 1445.68(4) Å^3, Z = 4, D_c = 1.366 g/cm^3, μ = 0.904 mm^{-1}, R_1 = 0.0346 [$I > 2\sigma(I)$], and wR_2 = 0.0960, S = 1.086 for all 88404 reflections. Flack parameter x = –0.07(9). Hooft parameter y = –0.07(3). ***CCDC reference number 1976234.***

Crystal data for **19c**: $C_{12}H_{17}NO_5$ (M = 255.26 g/mol), orthorhombic space group $P2_12_12_1$ (no. 19), a = 7.1742(1), b = 11.1860(1), c = 14.6964(2) Å, V = 1179.39(3) Å^3, Z = 4, D_c = 1.438 g/cm^3, μ = 0.944 mm^{-1}, R_1 = 0.0233 [$I > 2\sigma(I)$], and wR_2 = 0.0593, S = 1.059 for all 71524 reflections. Flack parameter x = 0.00(2). Hooft parameter y = 0.005(14). ***CCDC reference number 1976235***.

Crystal data for **20**: $C_{13}H_{19}NO_4$ (M = 253.29 g/mol), monoclinic space group $P112_1$ (no. 4), a = 5.9193(1), b = 11.8539(1), c = 17.5843(3) Å, β = 89.986(1)°, V = 1233.83(3) Å^3, Z = 4, D_c = 1.364 g/cm^3, μ = 0.833 mm^{-1}, R_1 = 0.0225 [$I > 2\sigma(I)$], and wR_2 = 0.0581, S = 1.038 for all 72818 reflections. Flack parameter x = –0.01(5). Hooft parameter y = –0.01(3). ***CCDC reference number 1976236.***

Crystal data for **23a**: $C_{10}H_{15}NO_3$ (M = 197.23 g/mol), monoclinic space group $P2_12_12_1$ (no. 4), a = 6.72543(6), b = 9.3824(1), c = 7.51677(6) Å, β = 97.6836(8)°, V = 470.056(8) Å^3, Z = 2, D_c = 1.393 g/cm^3, μ = 0.848 mm^{-1}, R_1 = 0.0263 [$I > 2\sigma(I)$], and wR_2 = 0.0707, S = 1.057 for all 21792 reflections. Flack parameter x = –0.03(12). Hooft parameter y = –0.04(5). ***CCDC reference number 1976237.***

Crystal data for **30a**: $C_{16}H_{23}NO_6$ (M = 325.35 g/mol), monoclinic space group $P2_1$ (no. 4), a = 6.9165(6), b = 9.3607(6), c = 12.8322(9) Å, β = 97.410(6)°, V = 823.86(11) Å^3, Z = 2, D_c = 1.312

g/cm^3, μ = 0.838 mm^{-1}, R_1 = 0.0266 [$I > 2\sigma(I)$], and wR_2 = 0.0701, S = 1.081 for all 49488 reflections. Flack parameter x = –0.02(6). Hooft parameter y = –0.02(3). CCDC reference number 1976238.

Crystallographic data for the reported compounds

Fig. X1 Molecular structure of **6** with the thermal ellipsoids shown at a 50% probability level.

Fig. X2 Molecular structure of **8a** with the thermal ellipsoids shown at a 50% probability level.

Fig. X3 Molecular structure of **14** with the thermal ellipsoids shown at a 50% probability level.

Fig. X4 Two crystallographic independent molecules of **18c** with the thermal ellipsoids shown at a 50% probability level. The disordered acetyl group is drawn by green and violet lines.

Fig. X5 Molecular structure of **19c** with the thermal ellipsoids shown at a 50% probability level.

Fig. X6 Two crystallographic independent molecules of **20** with the thermal ellipsoids shown at a 50% probability level.

Fig. X7 Molecular structure of **23a** with the thermal ellipsoids shown at a 50% probability level.

Fig. X8 Molecular structure of **30a** with the thermal ellipsoids shown at a 50% probability level.

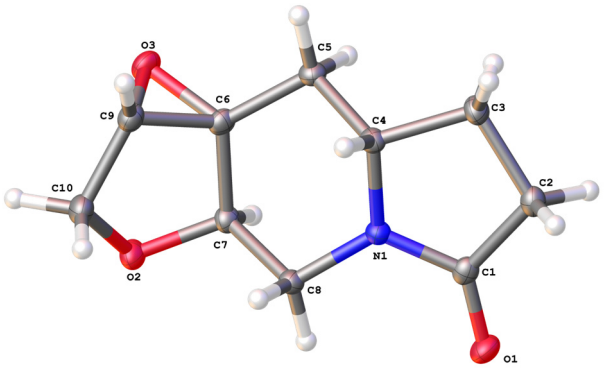


Fig. X1 Molecular structure of **6** with the thermal ellipsoids shown at a 50% probability level

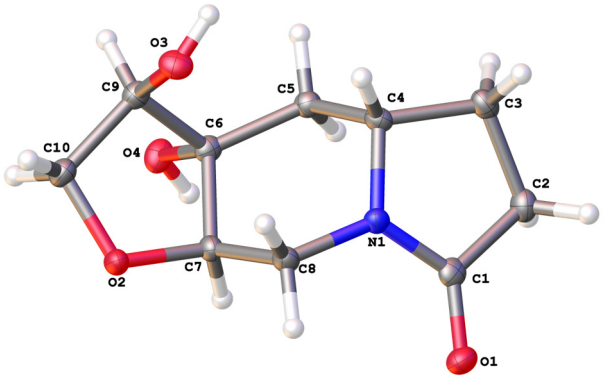


Fig. X2 Molecular structure of **8a** with the thermal ellipsoids shown at a 50% probability level.

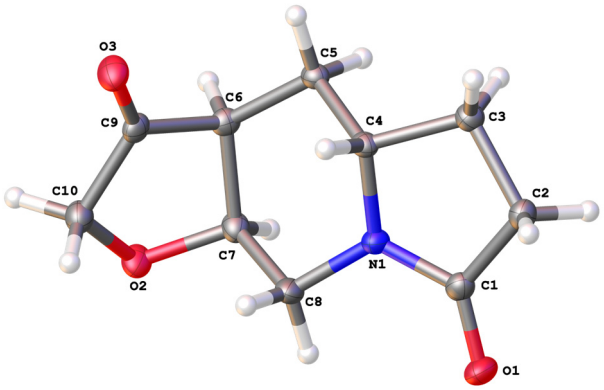


Fig. X3 Molecular structure of **14** with the thermal ellipsoids shown at a 50% probability level.

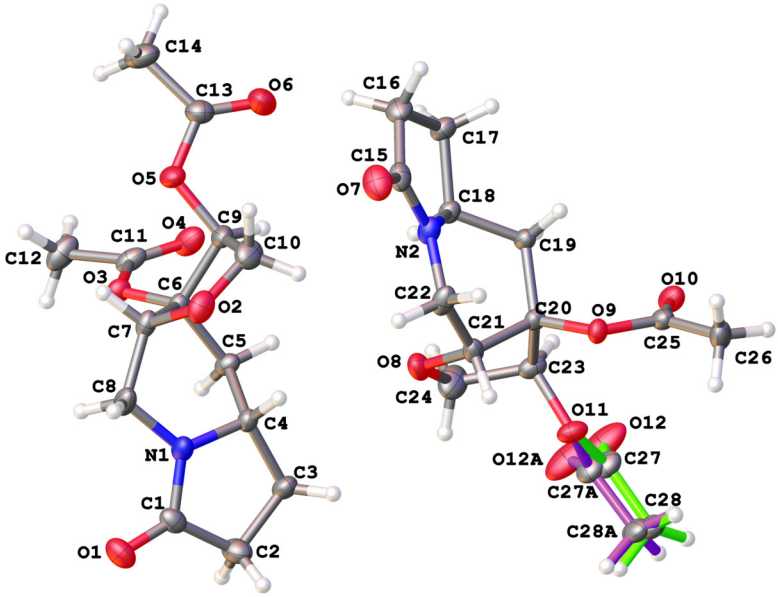


Fig. X4 Two crystallographic independent molecules of **18c** with the thermal ellipsoids shown at a 50% probability level. The disordered acetyl group is drawn by green and violet lines.

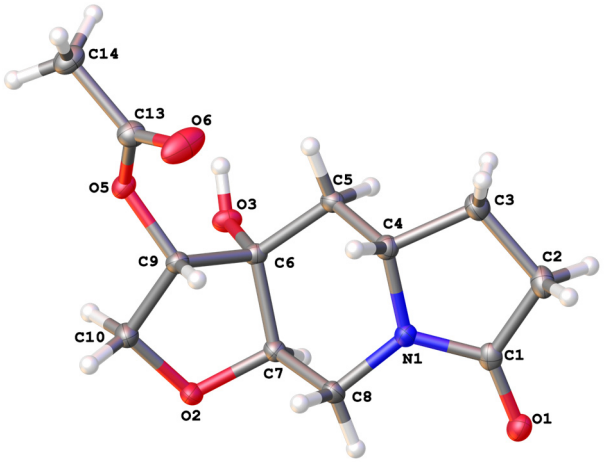


Fig. X5 Molecular structure of **19c** with the thermal ellipsoids shown at a 50% probability level.

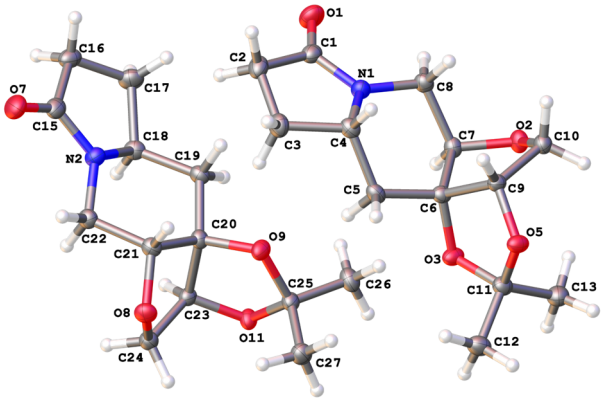


Fig. X6 Two crystallographic independent molecules of **20** with the thermal ellipsoids shown at a 50% probability level.

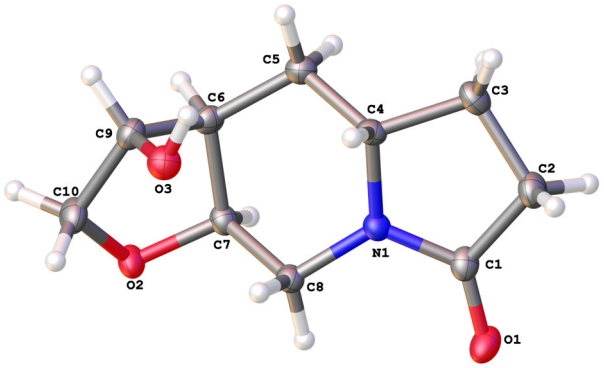


Fig. X7 Molecular structure of **23a** with the thermal ellipsoids shown at a 50% probability level.

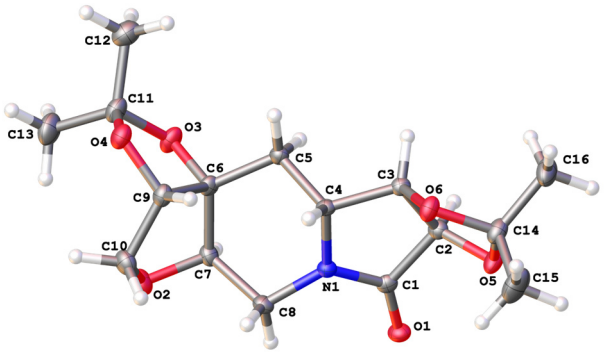


Fig. X8 Molecular structure of **30a** with the thermal ellipsoids shown at a 50% probability level.

Notes and references

37 a) L. Palatinus and G. Chapuis, *J. Appl. Crystallogr.* 2007, **40**, 786-790; b) G. M. Sheldrick, *Acta Crystallogr.* 2015, **A71**, 3-8; c) M. C. Burla, R. Caliandro, M. Camalli, B. Carrozzini, G. L. Cascarano, C. Giacovazzo, M. Mallamo, A. Mazzone, G. Polidori and R. Spagna, *J. Appl. Crystallogr.* 2012, **45**, 357-361; d) G. M. Sheldrick, *Acta Crystallogr.* 2015, **C71**, 3-8.

38 O. Dolomanov, L. J. Bourhis, R. I. Gildea and J. A. K. Howard, *J. Appl. Crystallogr.* 2009, **42**, 339-341.

39 a) S. Parsons, H. D. Flack and T. Wagner, *Acta Crystallogr.* 2013, **B69**, 249-259.; b) R. W. W. Hooft, L. H. Straver and A. L. Spek, *J. Appl. Crystallogr.* 2008, **41**, 96-103.

checkCIF/PLATON report

Structure factors have been supplied for datablock(s) 14, 18c, 19c, 20, 23a, 30a, 6, 8a

THIS REPORT IS FOR GUIDANCE ONLY. IF USED AS PART OF A REVIEW PROCEDURE FOR PUBLICATION, IT SHOULD NOT REPLACE THE EXPERTISE OF AN EXPERIENCED CRYSTALLOGRAPHIC REFEREE.

No syntax errors found. CIF dictionary Interpreting this report

Datablock: 6

```
Bond precision:  C-C = 0.0020 A          Wavelength=1.54186

Cell:             a=5.8779(2)     b=9.4102(2)     c=16.0947(3)
                  alpha=90        beta=90         gamma=90
Temperature:      100 K

                 Calculated                Reported
Volume           890.23(4)                 890.23(4)
Space group      P 21 21 21                P 21 21 21
Hall group       P 2ac 2ab                 P 2ac 2ab
Moiety formula   C10 H13 N O3              C10 H13 N O3
Sum formula      C10 H13 N O3              C10 H13 N O3
Mr               195.21                    195.21
Dx,g cm-3        1.457                     1.457
Z                4                         4
Mu (mm-1)        0.895                     0.895
F000             416.0                     416.0
F000'            417.38
h,k,lmax         7,11,19                   7,11,19
Nref             1745[ 1043]               1719
Tmin,Tmax        0.851,0.898               0.201,0.580
Tmin'            0.731

Correction method= # Reported T Limits: Tmin=0.201 Tmax=0.580
AbsCorr = MULTI-SCAN

Data completeness= 1.65/0.99      Theta(max)= 71.716

R(reflections)= 0.0239( 1692)     wR2(reflections)= 0.0622( 1719)

S = 1.059                  Npar= 128
```

The following ALERTS were generated. Each ALERT has the format
test-name_ALERT_alert-type_alert-level.
Click on the hyperlinks for more details of the test.

Alert level G

```
PLAT398_ALERT_2_G Deviating  C-O-C    Angle From 120 for O2            108.4 Degree
PLAT398_ALERT_2_G Deviating  C-O-C    Angle From 120 for O3             60.4 Degree
PLAT791_ALERT_4_G Model has Chirality at C4          (Chiral SPGR)        S Verify
PLAT791_ALERT_4_G Model has Chirality at C6          (Chiral SPGR)        R Verify
PLAT791_ALERT_4_G Model has Chirality at C7          (Chiral SPGR)        R Verify
PLAT791_ALERT_4_G Model has Chirality at C9          (Chiral SPGR)        S Verify
PLAT912_ALERT_4_G Missing # of FCF Reflections Above STh/L=  0.600        5 Note
PLAT978_ALERT_2_G Number C-C Bonds with Positive Residual Density.        7 Info
```

0 **ALERT level A** = Most likely a serious problem - resolve or explain
0 **ALERT level B** = A potentially serious problem, consider carefully
0 **ALERT level C** = Check. Ensure it is not caused by an omission or oversight
8 **ALERT level G** = General information/check it is not something unexpected

0 ALERT type 1 CIF construction/syntax error, inconsistent or missing data
3 ALERT type 2 Indicator that the structure model may be wrong or deficient
0 ALERT type 3 Indicator that the structure quality may be low
5 ALERT type 4 Improvement, methodology, query or suggestion
0 ALERT type 5 Informative message, check

Datablock: 8a

Bond precision: C-C = 0.0021 A Wavelength=1.54186

Cell:	a=19.1607(4)	b=7.5467(1)	c=6.7883(1)
	alpha=90	beta=90	gamma=90
Temperature:	100 K		

	Calculated	Reported
Volume	981.59(3)	981.59(3)
Space group	P 21 21 21	P 21 21 21
Hall group	P 2ac 2ab	P 2ac 2ab
Moiety formula	C10 H15 N O4	C10 H15 N O4
Sum formula	C10 H15 N O4	C10 H15 N O4
Mr	213.23	213.23
Dx,g cm-3	1.443	1.443
Z	4	4
Mu (mm-1)	0.936	0.936
F000	456.0	456.0
F000’	457.57	
h,k,lmax	23,9,8	23,9,8
Nref	1930[1150]	1919
Tmin,Tmax	0.874,0.981	0.543,0.895
Tmin’	0.822	

Correction method= # Reported T Limits: Tmin=0.543 Tmax=0.895
AbsCorr = MULTI-SCAN

Data completeness= 1.67/0.99 Theta(max)= 71.706

R(reflections)= 0.0255(1883) wR2(reflections)= 0.0666(1919)

S = 1.062 Npar= 138

The following ALERTS were generated. Each ALERT has the format
test-name_ALERT_alert-type_alert-level.
Click on the hyperlinks for more details of the test.

Alert level G

PLAT007_ALERT_5_G	Number of Unrefined Donor-H Atoms	2	Report
PLAT398_ALERT_2_G	Deviating C-O-C Angle From 120 for O2	109.5	Degree
PLAT791_ALERT_4_G	Model has Chirality at C4 (Chiral SPGR)	S	Verify
PLAT791_ALERT_4_G	Model has Chirality at C6 (Chiral SPGR)	S	Verify
PLAT791_ALERT_4_G	Model has Chirality at C7 (Chiral SPGR)	R	Verify
PLAT791_ALERT_4_G	Model has Chirality at C9 (Chiral SPGR)	R	Verify
PLAT850_ALERT_4_G	Check Flack Parameter Exact Value 0.00 and s.u.	0.05	Check
PLAT912_ALERT_4_G	Missing # of FCF Reflections Above STh/L= 0.600	6	Note
PLAT978_ALERT_2_G	Number C-C Bonds with Positive Residual Density.	8	Info

---

0 **ALERT level A** = Most likely a serious problem - resolve or explain
0 **ALERT level B** = A potentially serious problem, consider carefully
0 **ALERT level C** = Check. Ensure it is not caused by an omission or oversight
9 **ALERT level G** = General information/check it is not something unexpected

0 ALERT type 1 CIF construction/syntax error, inconsistent or missing data
2 ALERT type 2 Indicator that the structure model may be wrong or deficient
0 ALERT type 3 Indicator that the structure quality may be low
6 ALERT type 4 Improvement, methodology, query or suggestion
1 ALERT type 5 Informative message, check

Datablock: 14

Bond precision: C-C = 0.0020 A Wavelength=1.54186

Cell: a=8.3442(2) b=9.0461(2) c=12.1350(3)
alpha=90 beta=90 gamma=90
Temperature: 100 K

	Calculated	Reported
Volume	915.98(4)	915.98(4)
Space group	P 21 21 21	P 21 21 21
Hall group	P 2ac 2ab	P 2ac 2ab
Moiety formula	C10 H13 N O3	C10 H13 N O3
Sum formula	C10 H13 N O3	C10 H13 N O3
Mr	195.21	195.21
Dx,g cm-3	1.416	1.416
Z	4	4
Mu (mm-1)	0.870	0.870
F000	416.0	416.0
F000’	417.38	
h,k,lmax	10,11,14	10,11,14
Nref	1796[1060]	1779
Tmin,Tmax	0.829,0.957	0.236,0.780
Tmin’	0.700	

Correction method= # Reported T Limits: Tmin=0.236 Tmax=0.780
AbsCorr = MULTI-SCAN

Data completeness= 1.68/0.99 Theta(max)= 71.812

R(reflections)= 0.0245(1672) wR2(reflections)= 0.0656(1779)

S = 1.072 Npar= 127

The following ALERTS were generated. Each ALERT has the format
test-name_ALERT_alert-type_alert-level.
Click on the hyperlinks for more details of the test.

Alert level G

PLAT398_ALERT_2_G Deviating C-O-C Angle From 120 for O2 108.2 Degree
PLAT791_ALERT_4_G Model has Chirality at C4 (Chiral SPGR) S Verify
PLAT791_ALERT_4_G Model has Chirality at C6 (Chiral SPGR) S Verify
PLAT791_ALERT_4_G Model has Chirality at C7 (Chiral SPGR) S Verify
PLAT912_ALERT_4_G Missing # of FCF Reflections Above STh/L= 0.600 5 Note
PLAT978_ALERT_2_G Number C-C Bonds with Positive Residual Density. 4 Info

---

0 **ALERT level A** = Most likely a serious problem - resolve or explain
0 **ALERT level B** = A potentially serious problem, consider carefully
0 **ALERT level C** = Check. Ensure it is not caused by an omission or oversight
6 **ALERT level G** = General information/check it is not something unexpected

0 ALERT type 1 CIF construction/syntax error, inconsistent or missing data
2 ALERT type 2 Indicator that the structure model may be wrong or deficient
0 ALERT type 3 Indicator that the structure quality may be low
4 ALERT type 4 Improvement, methodology, query or suggestion
0 ALERT type 5 Informative message, check

Datablock: 18c

Bond precision: C-C = 0.0030 A Wavelength=1.54186

Cell: a=12.2148(2) b=6.8618(1) c=17.7152(3)
alpha=90 beta=103.182(1) gamma=90
Temperature: 100 K

	Calculated	Reported
Volume	1445.69(4)	1445.68(4)
Space group	P 21	P 1 21 1
Hall group	P 2yb	P 2yb
Moiety formula	C14 H19 N O6	C14 H19 N O6
Sum formula	C14 H19 N O6	C14 H19 N O6
Mr	297.30	297.30
Dx,g cm-3	1.366	1.366
Z	4	4
Mu (mm-1)	0.904	0.904
F000	632.0	632.0
F000’	634.24	
h,k,lmax	14,8,21	14,8,21
Nref	5613[3054]	5157
Tmin,Tmax	0.888,0.973	0.192,0.851
Tmin’	0.636	

Correction method= # Reported T Limits: Tmin=0.192 Tmax=0.851
AbsCorr = MULTI-SCAN

Data completeness= 1.69/0.92 Theta(max)= 71.163

R(reflections)= 0.0346(4804) wR2(reflections)= 0.0960(5157)

S = 1.086 Npar= 394

The following ALERTS were generated. Each ALERT has the format
test-name_ALERT_alert-type_alert-level.
Click on the hyperlinks for more details of the test.

Alert level B

PLAT112_ALERT_2_B ADDSYM Detects New (Pseudo) Symm. Elem B 92 %Fit

---

Alert level C

PLAT790_ALERT_4_C Centre of Gravity not Within Unit Cell: Resd. # 1 Note
C14 H19 N O6
PLAT915_ALERT_3_C No Flack x Check Done: Low Friedel Pair Coverage 83 %

Alert level G

PLAT002_ALERT_2_G Number of Distance or Angle Restraints on AtSite 6 Note
PLAT003_ALERT_2_G Number of Uiso or Uij Restrained non-H Atoms ... 6 Report

```
PLAT171_ALERT_4_G The CIF-Embedded .res File Contains EADP Records          3 Report
PLAT175_ALERT_4_G The CIF-Embedded .res File Contains SAME Records          1 Report
PLAT187_ALERT_4_G The CIF-Embedded .res File Contains RIGU Records          1 Report
PLAT301_ALERT_3_G Main Residue  Disorder .............(Resd  1  )        14% Note
PLAT398_ALERT_2_G Deviating  C-O-C    Angle From 120 for O8             108.7 Degree
PLAT398_ALERT_2_G Deviating  C-O-C    Angle From 120 for O2             109.4 Degree
PLAT790_ALERT_4_G Centre of Gravity not Within Unit Cell: Resd.  #           2 Note
             C14 H19 N O6
PLAT791_ALERT_4_G Model has Chirality at C4          (Chiral SPGR)          S Verify
PLAT791_ALERT_4_G Model has Chirality at C6          (Chiral SPGR)          R Verify
PLAT791_ALERT_4_G Model has Chirality at C7          (Chiral SPGR)          R Verify
PLAT791_ALERT_4_G Model has Chirality at C9          (Chiral SPGR)          S Verify
PLAT791_ALERT_4_G Model has Chirality at C18         (Chiral SPGR)          S Verify
PLAT791_ALERT_4_G Model has Chirality at C20         (Chiral SPGR)          R Verify
PLAT791_ALERT_4_G Model has Chirality at C21         (Chiral SPGR)          R Verify
PLAT791_ALERT_4_G Model has Chirality at C23         (Chiral SPGR)          S Verify
PLAT860_ALERT_3_G Number of Least-Squares Restraints .............         22 Note
PLAT910_ALERT_3_G Missing # of FCF Reflection(s) Below Theta(Min).          1 Note
PLAT912_ALERT_4_G Missing # of FCF Reflections Above STh/L=  0.600          9 Note
PLAT978_ALERT_2_G Number C-C Bonds with Positive Residual Density.          2 Info
```

```
   0 ALERT level A = Most likely a serious problem - resolve or explain
   1 ALERT level B = A potentially serious problem, consider carefully
   2 ALERT level C = Check. Ensure it is not caused by an omission or oversight
  21 ALERT level G = General information/check it is not something unexpected

   0 ALERT type 1 CIF construction/syntax error, inconsistent or missing data
   6 ALERT type 2 Indicator that the structure model may be wrong or deficient
   4 ALERT type 3 Indicator that the structure quality may be low
  14 ALERT type 4 Improvement, methodology, query or suggestion
   0 ALERT type 5 Informative message, check
```

Datablock: 19c

```
Bond precision:  C-C = 0.0020 A          Wavelength=1.54186

Cell:            a=7.1742(1)     b=11.1860(1)     c=14.6964(2)
                 alpha=90        beta=90          gamma=90
Temperature:     100 K
```

	Calculated	Reported
Volume	1179.40(3)	1179.39(3)
Space group	P 21 21 21	P 21 21 21
Hall group	P 2ac 2ab	P 2ac 2ab
Moiety formula	C12 H17 N O5	C12 H17 N O5
Sum formula	C12 H17 N O5	C12 H17 N O5
Mr	255.27	255.26
Dx,g cm-3	1.438	1.438
Z	4	4
Mu (mm-1)	0.944	0.944
F000	544.0	544.0
F000’	545.90	
h,k,lmax	8,13,18	8,13,18
Nref	2291[1341]	2260
Tmin,Tmax	0.844,0.893	0.331,0.930
Tmin’	0.654	

Correction method= # Reported T Limits: Tmin=0.331 Tmax=0.930
AbsCorr = MULTI-SCAN

Data completeness= 1.69/0.99 Theta(max)= 71.216

R(reflections)= 0.0233(2255) wR2(reflections)= 0.0593(2260)

S = 1.059 Npar= 166

The following ALERTS were generated. Each ALERT has the format
test-name_ALERT_alert-type_alert-level.
Click on the hyperlinks for more details of the test.

Alert level C

PLAT790_ALERT_4_C Centre of Gravity not Within Unit Cell: Resd. # 1 Note
C12 H17 N O5

Alert level G

PLAT007_ALERT_5_G Number of Unrefined Donor-H Atoms ..... 1 Report
PLAT142_ALERT_4_G s.u. on b - Axis Small or Missing ..... 0.00010 Ang.
PLAT398_ALERT_2_G Deviating C-O-C Angle From 120 for O2 109.5 Degree
PLAT791_ALERT_4_G Model has Chirality at C4 (Chiral SPGR) S Verify
PLAT791_ALERT_4_G Model has Chirality at C6 (Chiral SPGR) R Verify
PLAT791_ALERT_4_G Model has Chirality at C7 (Chiral SPGR) R Verify
PLAT791_ALERT_4_G Model has Chirality at C9 (Chiral SPGR) S Verify
PLAT850_ALERT_4_G Check Flack Parameter Exact Value 0.00 and s.u. 0.02 Check
PLAT912_ALERT_4_G Missing # of FCF Reflections Above STh/L= 0.600 3 Note
PLAT961_ALERT_5_G Dataset Contains no Negative Intensities ..... Please Check
PLAT978_ALERT_2_G Number C-C Bonds with Positive Residual Density. 8 Info

---

0 **ALERT level A** = Most likely a serious problem - resolve or explain
0 **ALERT level B** = A potentially serious problem, consider carefully
1 **ALERT level C** = Check. Ensure it is not caused by an omission or oversight

11 **ALERT level G** = General information/check it is not something unexpected

0 ALERT type 1 CIF construction/syntax error, inconsistent or missing data
2 ALERT type 2 Indicator that the structure model may be wrong or deficient
0 ALERT type 3 Indicator that the structure quality may be low
8 ALERT type 4 Improvement, methodology, query or suggestion
2 ALERT type 5 Informative message, check

Datablock: 20

Bond precision: C-C = 0.0023 A Wavelength=1.54186

Cell: a=5.9193(1) b=11.8539(1) c=17.5843(3)
alpha=90 beta=89.986(1) gamma=90
Temperature: 100 K

	Calculated	Reported
Volume	1233.83(3)	1233.83(3)
Space group	P 1 1 21	P 1 1 21
Hall group	P 2c	P 2c
Moiety formula	C13 H19 N O4	C13 H19 N O4
Sum formula	C13 H19 N O4	C13 H19 N O4
Mr	253.29	253.29
Dx,g cm-3	1.364	1.364
Z	4	4
Mu (mm-1)	0.833	0.833
F000	544.0	544.0
F000’	545.78	
h,k,lmax	7,14,21	7,14,21
Nref	4783[2476]	4529
Tmin,Tmax	0.779,0.959	0.421,0.861
Tmin’	0.687	

Correction method= # Reported T Limits: Tmin=0.421 Tmax=0.861
AbsCorr = MULTI-SCAN

Data completeness= 1.83/0.95 Theta(max)= 71.292

R(reflections)= 0.0225(4438) wR2(reflections)= 0.0581(4529)

S = 1.038 Npar= 330

The following ALERTS were generated. Each ALERT has the format
test-name_ALERT_alert-type_alert-level.
Click on the hyperlinks for more details of the test.

Alert level C
PLAT157_ALERT_4_C Non-standard Monoclinic Beta Angle less 90 Deg 89.99 Degree

```
PLAT790_ALERT_4_C Centre of Gravity not Within Unit Cell: Resd.  #          1 Note
            C13 H19 N O4
PLAT915_ALERT_3_C No Flack x Check Done: Low Friedel Pair Coverage         90 %
```

Alert level G

```
PLAT128_ALERT_4_G Alternate Setting for Input Space Group  P1121          P21 Note
PLAT142_ALERT_4_G s.u. on b - Axis Small or Missing ..............    0.00010 Ang.
PLAT398_ALERT_2_G Deviating  C-O-C    Angle From 120 for O2             106.6 Degree
PLAT398_ALERT_2_G Deviating  C-O-C    Angle From 120 for O5             108.9 Degree
PLAT398_ALERT_2_G Deviating  C-O-C    Angle From 120 for O8             106.5 Degree
PLAT398_ALERT_2_G Deviating  C-O-C    Angle From 120 for O11            109.2 Degree
PLAT790_ALERT_4_G Centre of Gravity not Within Unit Cell: Resd.  #          2 Note
            C13 H19 N O4
PLAT791_ALERT_4_G Model has Chirality at C4          (Chiral SPGR)          S Verify
PLAT791_ALERT_4_G Model has Chirality at C6          (Chiral SPGR)          R Verify
PLAT791_ALERT_4_G Model has Chirality at C7          (Chiral SPGR)          R Verify
PLAT791_ALERT_4_G Model has Chirality at C9          (Chiral SPGR)          S Verify
PLAT791_ALERT_4_G Model has Chirality at C18         (Chiral SPGR)          S Verify
PLAT791_ALERT_4_G Model has Chirality at C20         (Chiral SPGR)          R Verify
PLAT791_ALERT_4_G Model has Chirality at C21         (Chiral SPGR)          R Verify
PLAT791_ALERT_4_G Model has Chirality at C23         (Chiral SPGR)          S Verify
PLAT912_ALERT_4_G Missing # of FCF Reflections Above STh/L=  0.600         11 Note
PLAT978_ALERT_2_G Number C-C Bonds with Positive Residual Density.         13 Info
```

```
   0 ALERT level A = Most likely a serious problem - resolve or explain
   0 ALERT level B = A potentially serious problem, consider carefully
   3 ALERT level C = Check. Ensure it is not caused by an omission or oversight
  17 ALERT level G = General information/check it is not something unexpected

   0 ALERT type 1 CIF construction/syntax error, inconsistent or missing data
   5 ALERT type 2 Indicator that the structure model may be wrong or deficient
   1 ALERT type 3 Indicator that the structure quality may be low
  14 ALERT type 4 Improvement, methodology, query or suggestion
   0 ALERT type 5 Informative message, check
```

Datablock: 23a

```
Bond precision:  C-C = 0.0027 A          Wavelength=1.54186

Cell:            a=6.72543(6)    b=9.38242(10)       c=7.51677(6)
                 alpha=90        beta=97.6836(8)     gamma=90
Temperature:     100 K
```

	Calculated	Reported
Volume	470.056(8)	470.056(8)
Space group	P 21	P 1 21 1
Hall group	P 2yb	P 2yb
Moiety formula	C10 H15 N O3	C10 H15 N O3
Sum formula	C10 H15 N O3	C10 H15 N O3
Mr	197.23	197.23
Dx,g cm-3	1.393	1.393
Z	2	2
Mu (mm-1)	0.848	0.848
F000	212.0	212.0
F000’	212.69	
h,k,lmax	8,11,9	8,11,9
Nref	1838[979]	1464
Tmin,Tmax	0.960,0.987	0.532,0.935
Tmin’	0.809	

Correction method= # Reported T Limits: Tmin=0.532 Tmax=0.935
AbsCorr = MULTI-SCAN

Data completeness= 1.50/0.80 Theta(max)= 71.501

R(reflections)= 0.0263(1438) wR2(reflections)= 0.0707(1464)

S = 1.057 Npar= 128

The following ALERTS were generated. Each ALERT has the format
test-name_ALERT_alert-type_alert-level.
Click on the hyperlinks for more details of the test.

Alert level C

PLAT915_ALERT_3_C No Flack x Check Done: Low Friedel Pair Coverage 57 %

Alert level G

PLAT007_ALERT_5_G Number of Unrefined Donor-H Atoms ..... 1 Report
PLAT143_ALERT_4_G s.u. on c - Axis Small or Missing ..... 0.00006 Ang.
PLAT398_ALERT_2_G Deviating C-O-C Angle From 120 for O2 109.0 Degree
PLAT791_ALERT_4_G Model has Chirality at C4 (Chiral SPGR) S Verify
PLAT791_ALERT_4_G Model has Chirality at C6 (Chiral SPGR) R Verify
PLAT791_ALERT_4_G Model has Chirality at C7 (Chiral SPGR) S Verify
PLAT791_ALERT_4_G Model has Chirality at C9 (Chiral SPGR) S Verify
PLAT912_ALERT_4_G Missing # of FCF Reflections Above STh/L= 0.600 6 Note
PLAT978_ALERT_2_G Number C-C Bonds with Positive Residual Density. 6 Info
PLAT992_ALERT_5_G Repd & Actual _reflns_number_gt Values Differ by 1 Check

---

0 **ALERT level A** = Most likely a serious problem - resolve or explain
0 **ALERT level B** = A potentially serious problem, consider carefully
1 **ALERT level C** = Check. Ensure it is not caused by an omission or oversight
10 **ALERT level G** = General information/check it is not something unexpected

```
   0 ALERT type 1 CIF construction/syntax error, inconsistent or missing data
   2 ALERT type 2 Indicator that the structure model may be wrong or deficient
   1 ALERT type 3 Indicator that the structure quality may be low
   6 ALERT type 4 Improvement, methodology, query or suggestion
   2 ALERT type 5 Informative message, check
```

Datablock: 30a

```
Bond precision:  C-C = 0.0028 A          Wavelength=1.54186

Cell:            a=6.9165(6)     b=9.3607(6)        c=12.8322(9)
                 alpha=90        beta=97.410(6)     gamma=90
Temperature:     100 K
```

	Calculated	Reported
Volume	823.86(11)	823.86(11)
Space group	P 21	P 1 21 1
Hall group	P 2yb	P 2yb
Moiety formula	C16 H23 N O6	C16 H23 N O6
Sum formula	C16 H23 N O6	C16 H23 N O6
Mr	325.35	325.35
Dx,g cm-3	1.312	1.312
Z	2	2
Mu (mm-1)	0.838	0.838
F000	348.0	348.0
F000’	349.19	
h,k,lmax	8,11,15	8,11,15
Nref	3236[1722]	2353
Tmin,Tmax	0.834,0.967	0.290,0.873
Tmin’	0.686	

```
Correction method= # Reported T Limits: Tmin=0.290 Tmax=0.873
AbsCorr = MULTI-SCAN

Data completeness= 1.37/0.73      Theta(max)= 71.560

R(reflections)= 0.0266( 2329)     wR2(reflections)= 0.0701( 2353)

S = 1.081                  Npar= 213
```

The following ALERTS were generated. Each ALERT has the format
test-name_ALERT_alert-type_alert-level.
Click on the hyperlinks for more details of the test.

Alert level B

PLAT915_ALERT_3_B No Flack x Check Done: Low Friedel Pair Coverage 43 %

Alert level C

```
PLAT094_ALERT_2_C Ratio of Maximum / Minimum Residual Density ....       4.00 Report
PLAT911_ALERT_3_C Missing FCF Refl Between Thmin & STh/L=    0.600          7 Report
PLAT918_ALERT_3_C Reflection(s) with I(obs) much Smaller I(calc) .          1 Check
PLAT939_ALERT_3_C Large Value of Not (SHELXL) Weight Optimized S .      10.25 Check
```

Alert level G

```
PLAT398_ALERT_2_G Deviating  C-O-C    Angle From 120 for O2            106.3 Degree
PLAT398_ALERT_2_G Deviating  C-O-C    Angle From 120 for O4            108.7 Degree
PLAT398_ALERT_2_G Deviating  C-O-C    Angle From 120 for O5            107.5 Degree
PLAT398_ALERT_2_G Deviating  C-O-C    Angle From 120 for O6            107.0 Degree
PLAT791_ALERT_4_G Model has Chirality at C2          (Chiral SPGR)          R Verify
PLAT791_ALERT_4_G Model has Chirality at C3          (Chiral SPGR)          R Verify
PLAT791_ALERT_4_G Model has Chirality at C4          (Chiral SPGR)          R Verify
PLAT791_ALERT_4_G Model has Chirality at C6          (Chiral SPGR)          R Verify
PLAT791_ALERT_4_G Model has Chirality at C7          (Chiral SPGR)          R Verify
PLAT791_ALERT_4_G Model has Chirality at C9          (Chiral SPGR)          S Verify
PLAT912_ALERT_4_G Missing # of FCF Reflections Above STh/L=  0.600         14 Note
PLAT961_ALERT_5_G Dataset Contains no Negative Intensities .......     Please Check
PLAT978_ALERT_2_G Number C-C Bonds with Positive Residual Density.         10 Info
PLAT992_ALERT_5_G Repd & Actual _reflns_number_gt Values Differ by          1 Check
```

```
   0 ALERT level A = Most likely a serious problem - resolve or explain
   1 ALERT level B = A potentially serious problem, consider carefully
   4 ALERT level C = Check. Ensure it is not caused by an omission or oversight
  14 ALERT level G = General information/check it is not something unexpected

   0 ALERT type 1 CIF construction/syntax error, inconsistent or missing data
   6 ALERT type 2 Indicator that the structure model may be wrong or deficient
   4 ALERT type 3 Indicator that the structure quality may be low
   7 ALERT type 4 Improvement, methodology, query or suggestion
   2 ALERT type 5 Informative message, check
```

It is advisable to attempt to resolve as many as possible of the alerts in all categories. Often the minor alerts point to easily fixed oversights, errors and omissions in your CIF or refinement strategy, so attention to these fine details can be worthwhile. In order to resolve some of the more serious problems it may be necessary to carry out additional measurements or structure refinements. However, the purpose of your study may justify the reported deviations and the more serious of these should normally be commented upon in the discussion or experimental section of a paper or in the "special_details" fields of the CIF. checkCIF was carefully designed to identify outliers and unusual parameters, but every test has its limitations and alerts that are not important in a particular case may appear. Conversely, the absence of alerts does not guarantee there are no aspects of the results needing attention. It is up to the individual to critically assess their own results and, if necessary, seek expert advice.

Publication of your CIF in IUCr journals

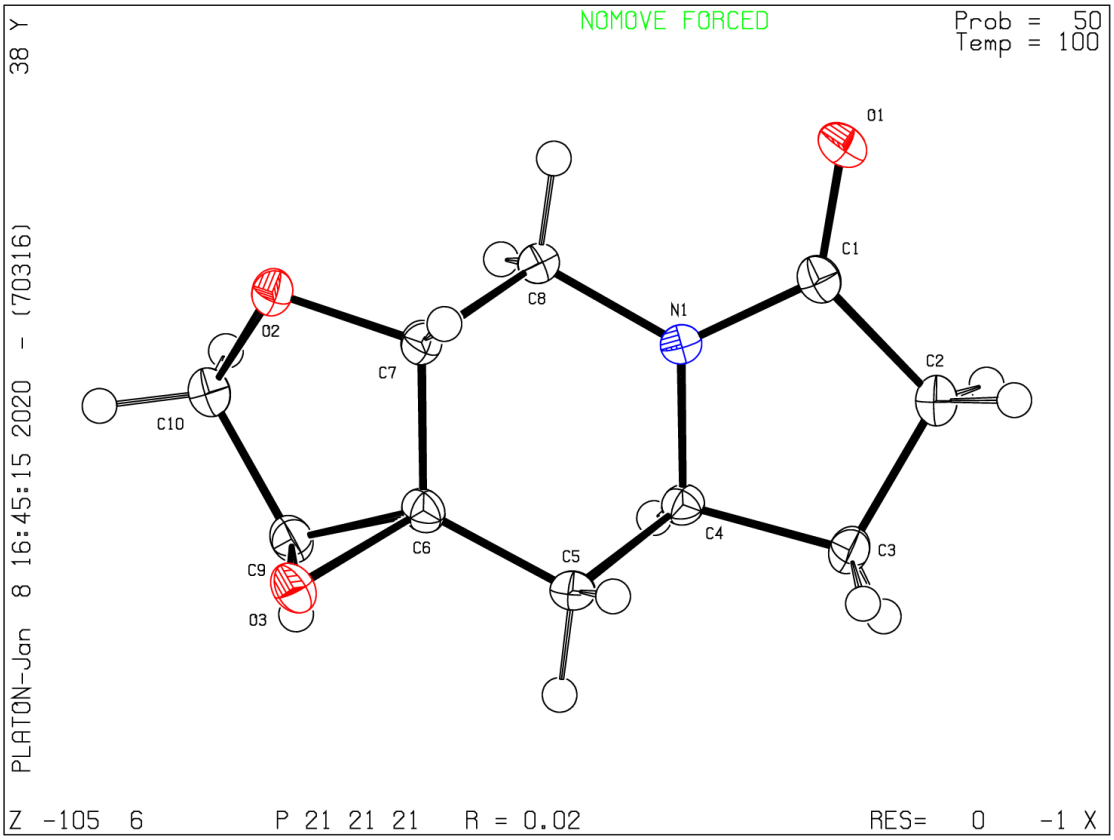
A basic structural check has been run on your CIF. These basic checks will be run on all CIFs submitted for publication in IUCr journals (*Acta Crystallographica*, *Journal of Applied Crystallography*, *Journal of Synchrotron Radiation*); however, if you intend to submit to *Acta Crystallographica Section C* or *E* or *IUCrData*, you should make sure that full publication checks are run on the final version of your CIF prior to submission.

Publication of your CIF in other journals

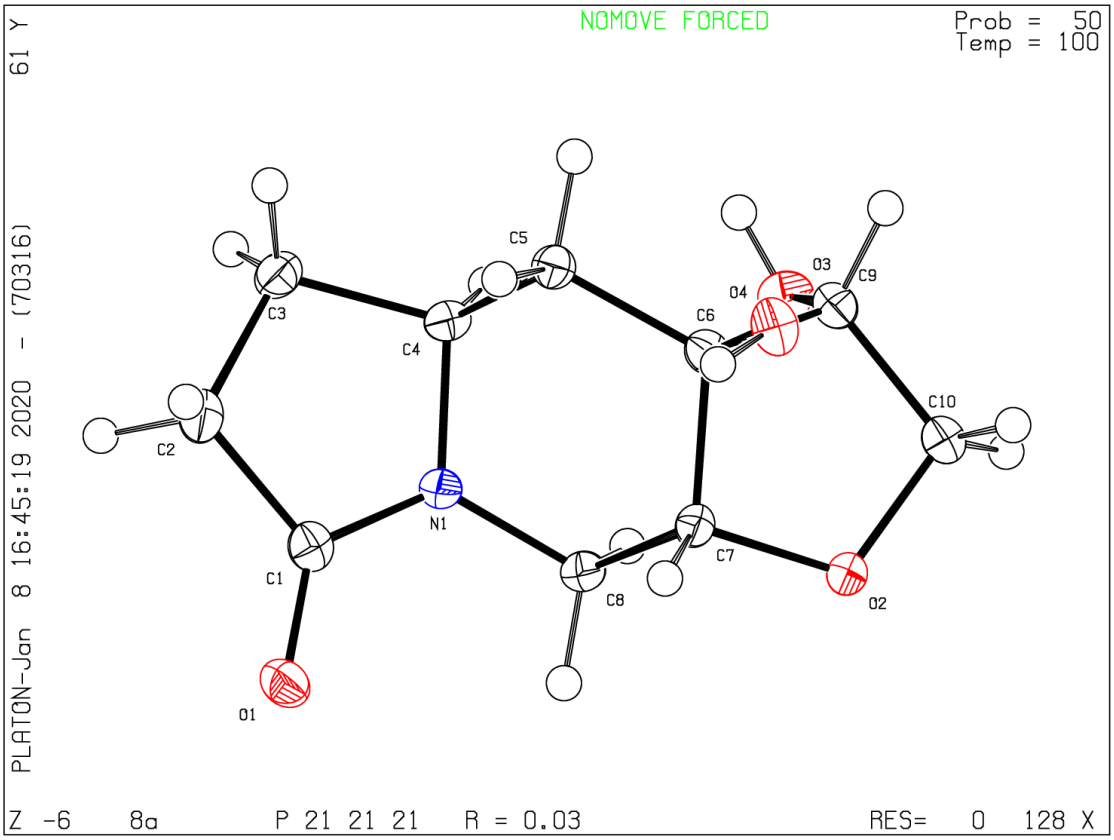
Please refer to the *Notes for Authors* of the relevant journal for any special instructions relating to CIF submission.

PLATON version of 22/12/2019; check.def file version of 13/12/2019

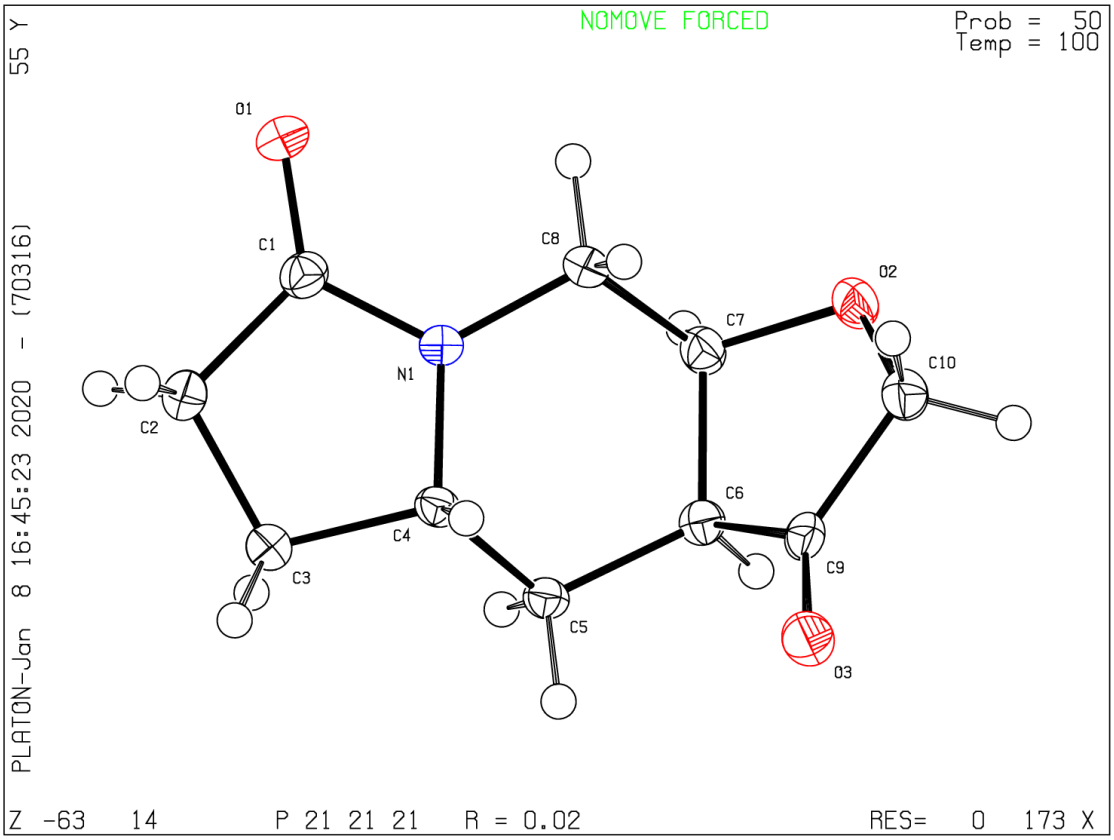
Datablock 6 - ellipsoid plot



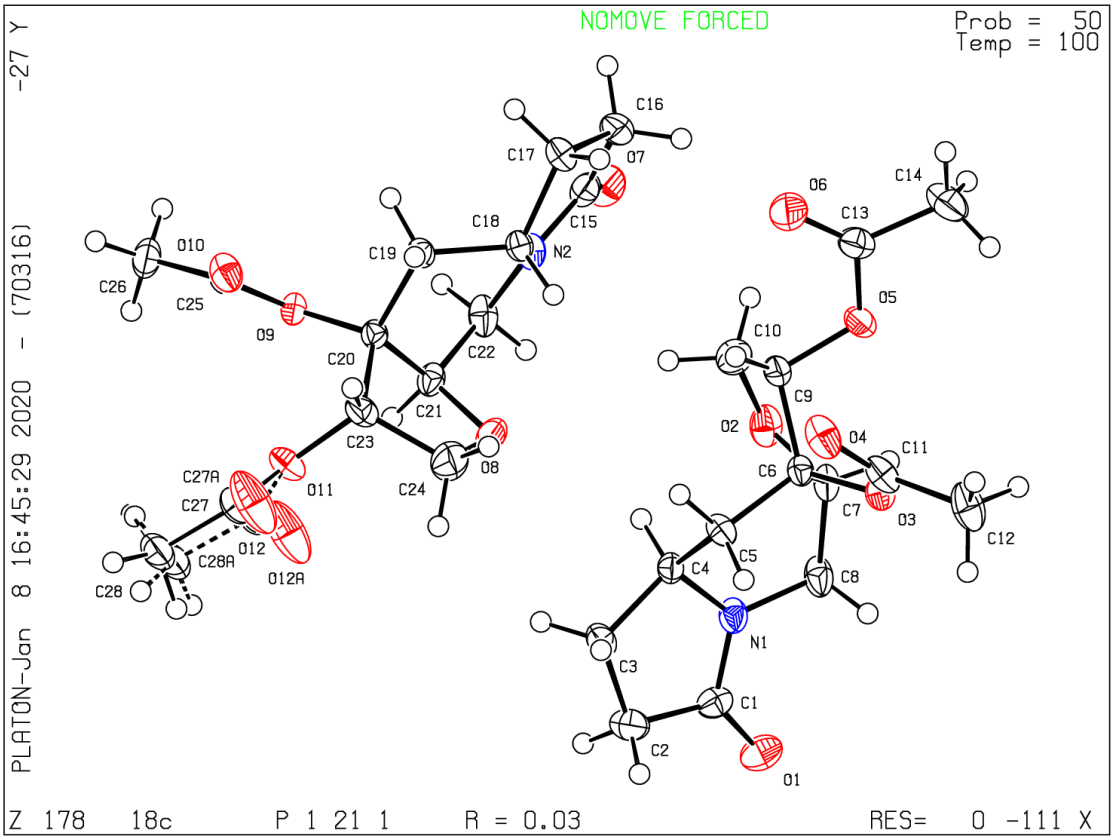
Datablock 8a - ellipsoid plot



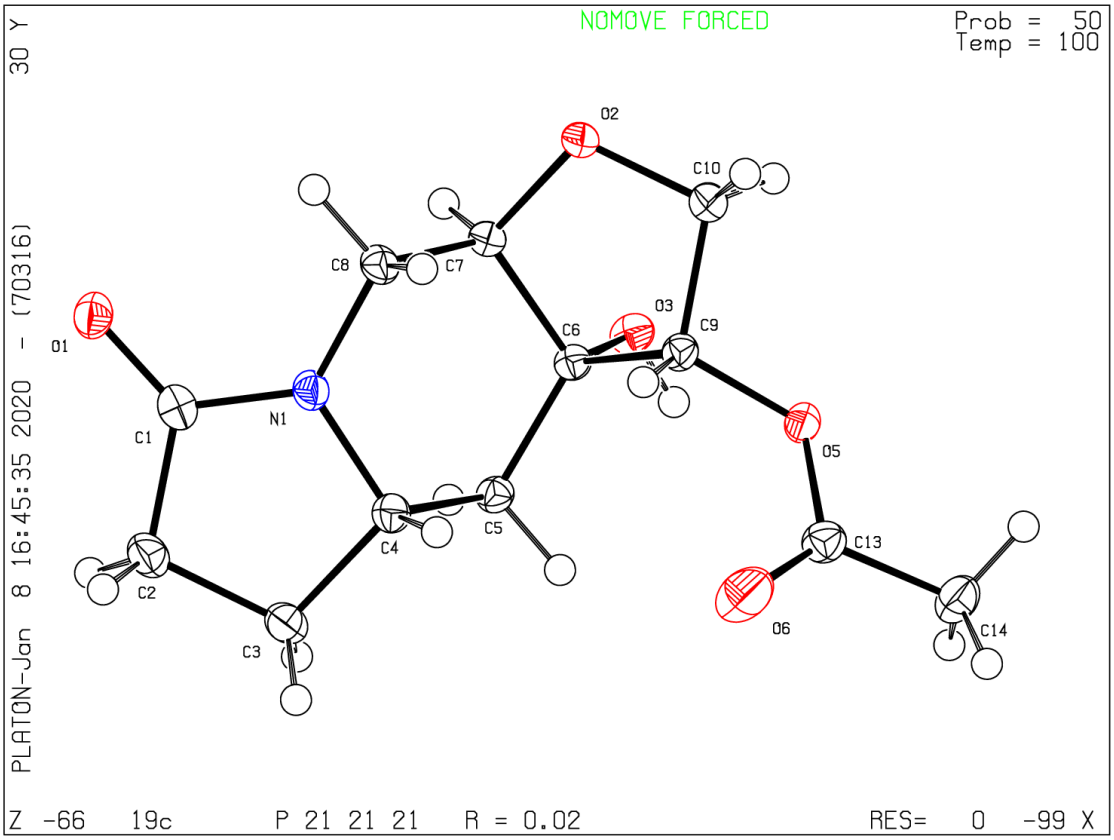
Datablock 14 - ellipsoid plot



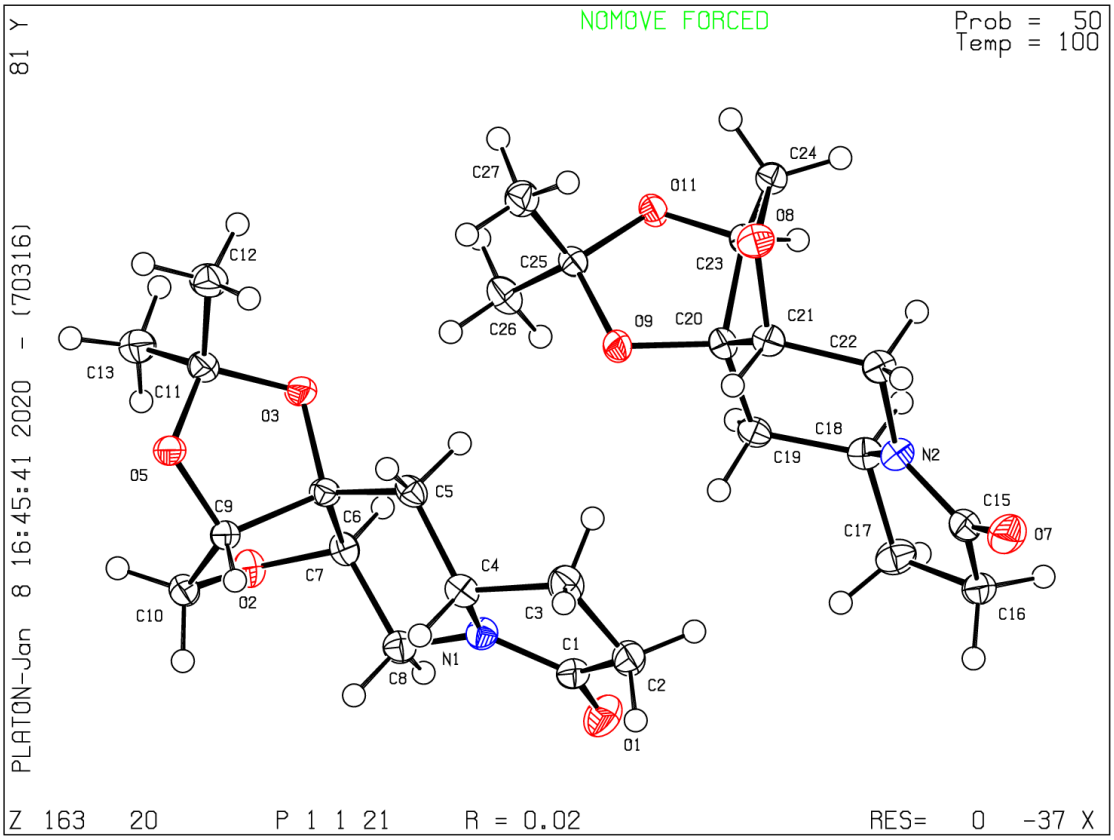
Datablock 18c - ellipsoid plot



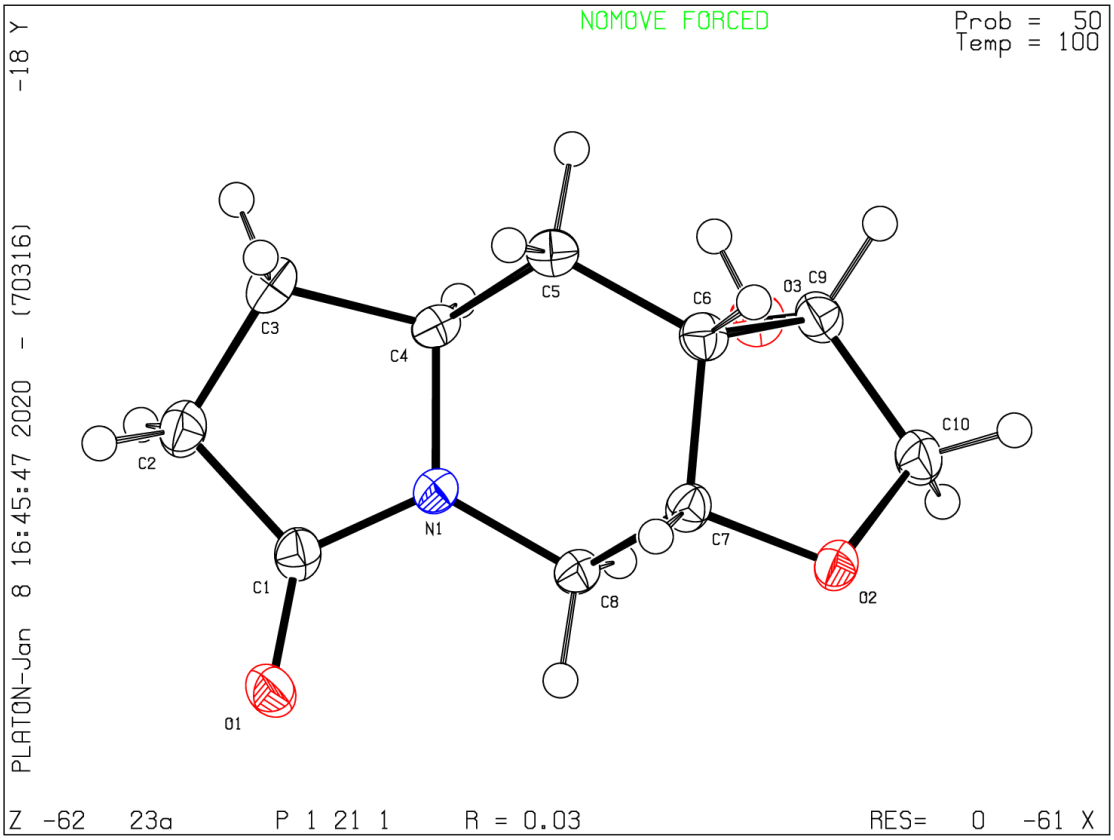
Datablock 19c - ellipsoid plot



Datablock 20 - ellipsoid plot



Datablock 23a - ellipsoid plot



Datablock 30a - ellipsoid plot