Supporting Information

First Total Synthesis of *ent*-Asperparaline C and Assignment of the Absolute Configuration of Asperparaline C

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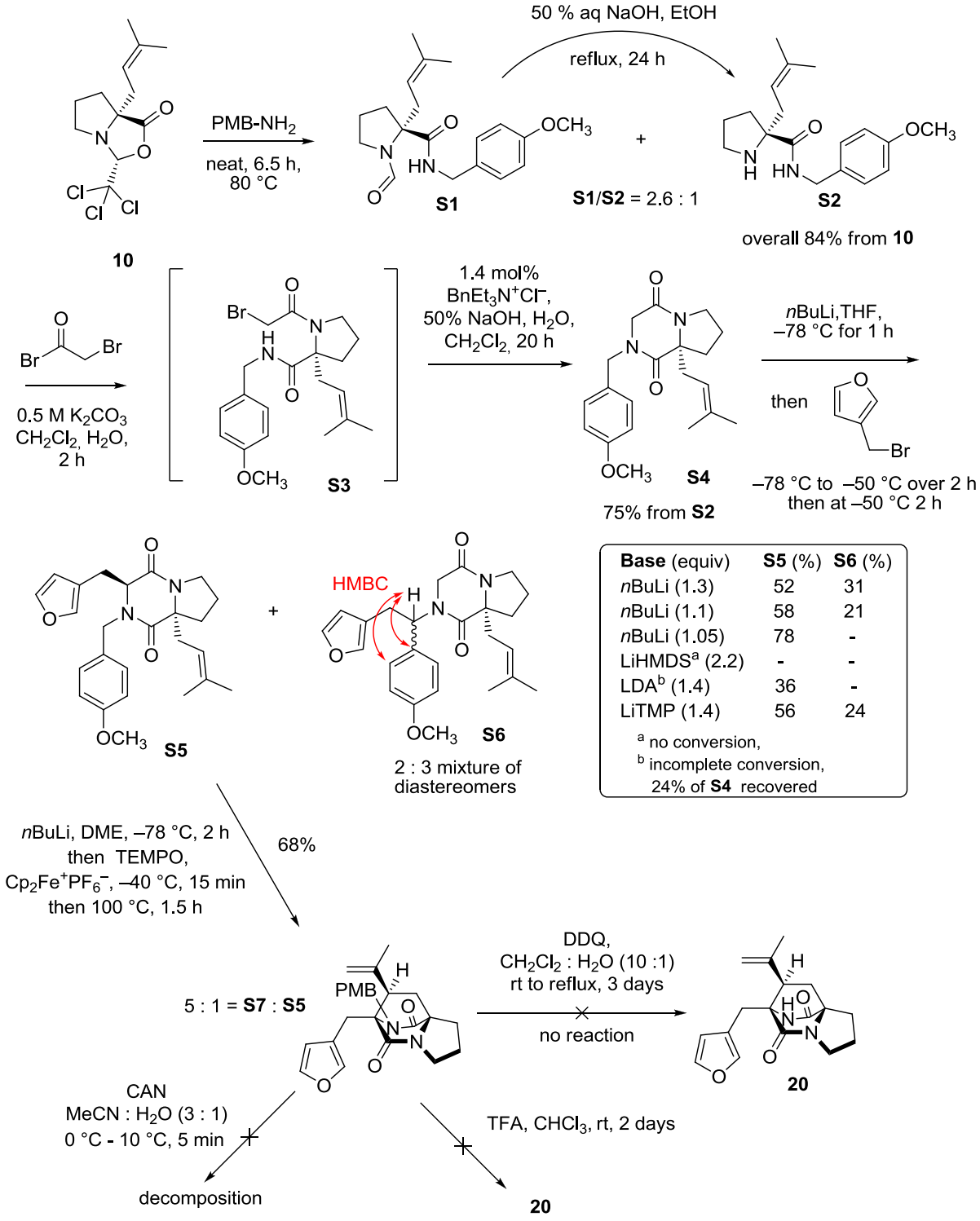
Attempted approach to asperparaline C using the PMB protecting group

Initially, a synthetic sequence using the *p*-methoxybenzyl (PMB) as protecting group was explored (Scheme S1). Oxazolidinone **10** was reacted with *p*-methoxybenzyl amine to provide an inseparable mixture of amide **S2** and *N*-formylated byproduct **S1** in a ratio of 1:2.6 respectively. The best results were obtained by heating the neat mixture at 80 °C for 6.5 h. The **S1/S2** mixture was subjected to saponification of the formyl group using a 50% aqueous NaOH in ethanol, and pure amide **S2** was obtained in 84% overall yield. Amide **S2** was converted to diketopiperazine **S4** by a two-step/one-pot protocol via bromoacetamide intermediate **S3**, which was without isolation immediately cyclized under phase-transfer catalytic conditions to provide **S4** in 75% yield. DKP **S4** was alkylated with 3-(bromomethyl)furan in THF using *n*BuLi at –78 °C providing radical cyclization precursor **S5** in up to 78% yield as a *trans* stereoisomer. The reaction also yielded compound **S6** in up to 31% yield depending on the amount of base that was used (Scheme S1). With 1.3 equiv. of *n*BuLi, 56% of the product **S5** was isolated together with 31% of **S6**. With 1.1 equiv. of *n*BuLi 58% of **S5** and 21% of **S6** were obtained. Lowering the amount of *n*BuLi to 1.05 equiv. gave **S5** in 78% yield, and no **S6** was observed in the mixture. Other bases were also tested: with LHDMS no conversion was observed and the starting material was recovered; with LDA a mixture of alkylated DKP **S5** and recovered starting material **S4** was obtained. With 1.4 equiv. of LiTMP unselective alkylation was observed giving 56% of **S5** and 24% of **S6**. Compound **S6** was identified to be a 2:3 mixture of diastereoisomers resulting from the reaction at the benzylic position of the PMB group. The subsequent oxidative cyclization reaction was performed by deprotonation of the compound **S5** with *n*BuLi at –78 °C, followed by oxygenation with ferrocenium hexafluorophosphate and TEMPO at –40 °C. The resulting solution was directly subjected to radical cyclization at 100 °C giving an inseparable 5:1 mixture of **S7** with starting **S5** in 68% yield under optimized conditions. The reaction optimization proved to be difficult. If less than 1.5 equiv. of base were used, starting material was recovered in up to 40% yield; if a larger excess of base was applied, side products presumably resulting from deprotonation at the benzylic positions of the PMB group of both **S5** and product **S7** formed. The subsequent deprotection of the PMB group failed under a variety of conditions. Deprotection with CAN led to fast decomposition of **S7**, whereas no reaction was observed with DDQ, and partial addition to the

double bond occurred with TFA in $CHCl_3$ at room temperature. Therefore, this approach was not further investigated and a different protecting group was employed (s. Scheme 3).

Scheme S1. Attempted synthesis using *p*-methoxybenzyl (PMB) protected precursors.

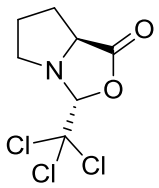


General Information

All reactions were conducted in flame or oven dried glassware under a nitrogen atmosphere. DME, THF, toluene and CH_2Cl_2 were dried following standard methods under an argon atmosphere. TLC plates POLYGRAM SIL G/UV_{254} (Macherey-Nagel) were used for monitoring reactions. Flash column chromatographic separations were performed on silica gel 60 (Fluka, 230-400 mesh). ^{1}H and ^{13}C NMR spectra were recorded on Bruker Avance instruments at 400.1 MHz, 500.1 MHz and 600.1 MHz for ^{1}H NMR or 100.6 MHz, 125.8 MHz and 150.9 MHz for ^{13}C NMR, respectively. Connectivity was determined by ^{1}H-^{1}H COSY and HMBC experiments. ^{13}C NMR assignments were obtained from APT and HSQC experiments. The stereochemistry of critical intermediates of the total synthesis was assigned using ^{1}H-^{1}H ROESY experiments. IR spectra were taken on a Bruker ALPHA FT-IR spectrometer as neat samples using an ATR device. EI mass spectra were recorded on a Waters GCT Premier spectrometer at 70 eV. ESI mass spectra were obtained on a Thermo Fisher Scientific LCQ Fleet spectrometer, sample concentration approx. 1 µg/mL, spray voltage pos. mode: 3.3 kV. HRMS spectra were measured on a Waters Q-Tof micro spectrometer, resolution: 100000. Optical rotations were measured on an Autopol IV instrument (Rudolf Research Analytical, Flanders, USA).

Experimental procedures and analytical data of all compounds

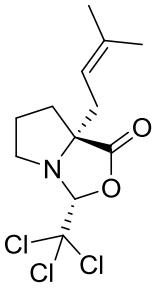
(3*R*,7a*S*)-7a-(3-Methylbut-2-en-1-yl)-3-(trichloromethyl)tetrahydropyrrolo[1,2-c]oxazol-1(3*H*)-one (9)



To a suspension of L-proline **8** (10 g, 86.8 mmol) in chloroform (120 mL), chloral hydrate (21.6 g, 0.130 mol) was added. A reverse Dean–Stark trap and a reflux condenser were attached to the reaction vessel and the reaction mixture was heated at reflux until L-proline was no longer visibly suspended (approx. 6 h). The reaction mixture was washed with water, the combined organic extracts were dried over Na_2SO_4, filtered and evaporated under reduced pressure. The resulting brown solid was recrystallized from ethanol (90 mL) to give **9** (14.6 g, 69%) as colorless crystals. **M.p.** 110–111 °C. **$[\alpha]^{20}_D$** = –2.5 (*c* 2.246, $CHCl_3$), **$[\alpha]^{20}_D$** = +33.3 (*c* 2.011, C_6H_6), lit.[1] **$[\alpha]_D$** = +33 (*c* 2, C_6H_6). **IR: *ν* (cm^{-1})** 2962, 2920, 2853, 1800, 1784, 1322, 1176, 1108, 1083, 1002, 959, 899, 839, 814. **MS ESI+ *m/z*, (%)**: 265

(100, $[M+Na]^+$), 244 (42, $[M+H]^+$). **HRMS ESI+ *m/z,*** ($[M+H]^+$): calcd. for $C_7H_9O_2NCl_3$: 243.9693, found: 243.9692. **^{1}H NMR (400 MHz, $CDCl_3$)**: δ = 1.68-1.80 (m, 1H, $NCH_2\underline{CH_2}CH_2$), 1.87-2.00 (m, 1H, $NCH_2\underline{CH_2}CH_2$), 2.06-2.15 (m, 1H, $NCH_2CH_2\underline{CH_2}$), 2.17-2.29 (m, 1H, $NCH_2CH_2\underline{CH_2}$), 3.10-3.16 (m, 1H, $N\underline{CH_2}CH_2CH_2$), 3.39-3.44 (m, 1H, $N\underline{CH_2}CH_2CH_2$), 4.12 (dd, *J* = 8.8, 4.6 Hz, 1H, NCHCO), 5.16 (s, 1H, NCHO). **^{13}C NMR (101 MHz, $CDCl_3$)**: δ = 25.4 (t, $NCH_2\underline{C}H_2CH_2$), 29.9 (t, $NCH_2CH_2\underline{C}H_2$), 57.9 (t, $N\underline{C}H_2CH_2CH_2$), 62.4 (d, $N\underline{C}HCO$), 100.7 (s, CCl_3), 103.7 (d, NCHO), 175.5 (s, C=O).

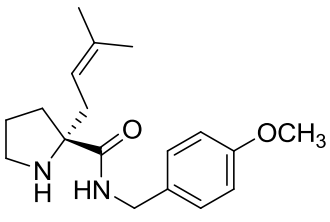
(3*R*,7a*R*)-7a-(3-Methylbut-2-en-1-yl)-3-(trichloromethyl)tetrahydro-1*H*,3*H*-pyrrolo[1,2-c]oxazol-1-one (10)



N,*N*-Diisopropylamine (2.27 mL, 16.2 mmol) was dissolved in THF (30 mL) under an N_2 atmosphere and cooled to –78 °C. *n*BuLi (10.1 mL, 16.2 mmol, 1.6M in hexanes) was added and the reaction mixture was stirred at –78 °C for 30 min. In a separate flask under N_2, oxazolidinone **9** (3.0 g, 12.3 mmol) was dissolved in THF (10 mL). This solution was added via cannula to the above LDA solution at –78 °C. The resulting brown solution was stirred at –78 °C for 30 min and prenyl bromide (1.87 mL, 16.2 mmol) was added in a single portion. The reaction mixture was warmed to –40 °C over 1 h, where it was maintained for additional 30 min. The reaction mixture was poured into a separation funnel containing 50 mL of water. The layers were separated and the aqueous was extracted with chloroform (3 x 50 mL). The combined organic layers were dried over Na_2SO_4, filtered and concentrated to give a brown oil, which was purified by column chromatography (hexane/EtOAc = 15/1) to give **10** (2.72 g, 79%) as colorless oil. **R*f*** = 0.5 (hexane/EtOAc = 5/1); **$[\alpha]^{20}_D$** = +30.2 (*c* 0.926, $CHCl_3$); lit.[2] **$[\alpha]^{20}_D$** = +31.5 (c 1.586, $CHCl_3$), **IR: *ν* (cm^{-1})** 2916, 1796, 1449, 1377, 1352, 1322, 1276, 1249, 1190, 1130, 1101, 1076, 1019, 983, 835. **MS ESI+ *m/z,* (%)**: 334 (100, $[M+Na]^+$), 312 (47, $[M+H]^+$). **HRMS ESI+ *m/z,*** ($[M+H]^+$): calcd. for $C_{12}H_{17}{}^{35}Cl_3NO_2$: 312.0319, found: 312.0321. **^{1}H NMR (400 MHz, $CDCl_3$)**: δ = 1.60-1.67 (m, 1H, $NCH_2\underline{CH_2}CH_2$), 1.65 (s, 3H, CH_3), 1.74 (s, 3H, CH_3), 1.83-1.92 (m, 1H, $NCH_2\underline{CH_2}CH_2$), 1.92-1.99 (m, 1H, $NCH_2CH_2\underline{CH_2}$), 2.06-2.15 (m, 1H, $NCH_2CH_2\underline{CH_2}$), 2.54 (dd, *J* = 14.4, 6.6 Hz, 1H, $\underline{CH_2}CH$=), 2.60 (dd, *J* = 14.4, 8.5 Hz, 1H, $\underline{CH_2}CH$=), 3.14-3.25 (m, 2H, $N\underline{CH_2}CH_2CH_2$), 4.96 (s, 1H, NCHO), 5.25 (ddt, *J* = 8.2, 6.7, 1.5 Hz, 1H, $CH_2\underline{CH}$=); **^{13}C NMR (101 MHz, $CDCl_3$)**: δ = 18.3 (q, CH_3), 25.4 (t, $NCH_2\underline{C}H_2CH_2$), 26.2 (q, CH_3), 35.4 (t, $NCH_2CH_2\underline{C}H_2$), 35.8 (t, $\underline{C}H_2CH$=), 58.5 (t,

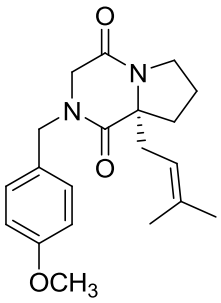
N<u>C</u>H$_2$CH$_2$CH$_2$), 72.2 (s, C$_{Pro}$), 100.7 (s, CCl$_3$), 102.5 (d, NCHO), 117.8 (d, CH$_2$<u>C</u>H=), 136.4 (s, =C(CH$_3$)$_2$), 176.7 (s, C=O).

(*R*)-*N*-(4-Methoxybenzyl)-2-(3-methylbut-2-en-1-yl)pyrrolidine-2-carboxamide (S2)



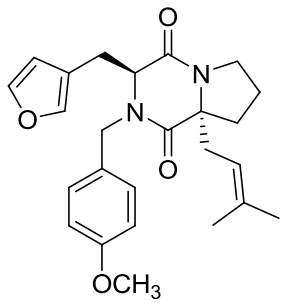
Oxazolidinone **10** (860 mg, 2.75 mmol) was mixed with *p*-methoxybenzylamine (0.75 mL, 5.78 mmol) and the reaction was stirred at 80 °C for 6.5 h. After cooling, the reaction mixture was purified by column chromatography (EtOAc) to give an inseparable 1:2.6 mixture of **S2** and *N*-formylpyrrolidine **S1** (820 mg). The mixture was dissolved in EtOH (4.5 mL), 50% aq. NaOH solution (1.5 mL) was added, and the reaction mixture was heated at reflux for 24 h. The solvent was evaporated, water was added (20 mL) and the mixture was extracted with CH$_2$Cl$_2$ (3 x 15 mL). The combined organic layers were dried over Na$_2$SO$_4$, filtered and concentrated to give 698 mg (84 %) of **S2** as colorless oil. **R*f*** = 0.2 (EtOAc). **[*α*]$^{20}_D$** = –21.1 (*c* 0.971, CHCl$_3$). **IR: *ν* (cm^{-1})** 3328, 2916, 1654, 1612, 1510, 1457, 1244, 1174, 1033, 817. **MS ESI+ *m/z*, (%)**: 303 (100, [M+H]$^+$). **HRMS ESI+ *m/z*,** ([M+H]$^+$): calcd. for C$_{18}$H$_{27}$O$_2$N$_2$: 303.2067, found: 303.2068. **^{1}H NMR (400 MHz, CDCl$_3$)**: δ = 1.62 (s, 3H, CH$_3$), 1.70 (s, 3H, CH$_3$), 1.66-1.80 (m, 4H, NCH$_2$<u>CH$_2$</u>CH$_2$, NCH$_2$CH$_2$<u>CH$_2$</u>, NH$_{Pro}$), 2.14-2.22 (m, 1H, NCH$_2$CH$_2$<u>CH$_2$</u>), 2.32 (dd, *J* = 14.4, 8.3 Hz, 1H, <u>CH$_2$</u>CH=), 2.69 (ddt, *J* = 14.4, 6.7, 1.2 Hz, 1H, <u>CH$_2$</u>CH=), 2.81 (dt, *J* = 10.4, 6.2 Hz, 1H, N<u>CH$_2$</u>CH$_2$CH$_2$), 3.00 (dt, *J* = 10.5, 6.4 Hz, 1H, N<u>CH$_2$</u>CH$_2$CH$_2$), 3.79 (s, 3H, OCH$_3$), 4.31 (dd, *J* = 14.7, 5.8 Hz, 1H, NH<u>CH$_2$</u>Ar), 4.40 (dd, *J* = 14.7, 6.2 Hz, 1H, NH<u>CH$_2$</u>Ar), 5.06 (ddt, *J* = 8.2, 6.7, 1.4 Hz, 1H, CH$_2$<u>CH</u>=), 6.85 (d, *J* = 8.6 Hz, 2H, CH$_{Ar}$), 7.18 (d, *J* = 8.6 Hz, 2H, CH$_{Ar}$), 8.17 (bs, 1H, CONH). **^{13}C NMR (101 MHz, CDCl$_3$)**: δ = 18.1 (q, CH$_3$), 26.2 (q, CH$_3$), 26.4 (t, NCH$_2$<u>C</u>H$_2$CH$_2$), 36.2 (t, NCH$_2$CH$_2$<u>C</u>H$_2$), 36.8 (t, <u>C</u>H$_2$CH=), 42.7 (t, NH<u>C</u>H$_2$Ar), 47.2 (t, N<u>C</u>H$_2$CH$_2$CH$_2$), 55.4 (q, OCH$_3$), 69.7 (s, C$_{Pro}$), 114.1 (d, CH$_{Ar}$), 119.2 (d, CH$_2$<u>C</u>H=), 128.9 (d, CH$_{Ar}$), 131.3 (s, C$_{Ar}$), 135.9 (s, =<u>C</u>(CH$_3$)$_2$), 158.9 (s, C$_{Ar}$), 176.8 (s, C=O).

(*R*)-2-(4-Methoxybenzyl)-8a-(3-methylbut-2-en-1-yl)hexahydropyrrolo[1,2-a]pyrazine-1,4-dione (S4)



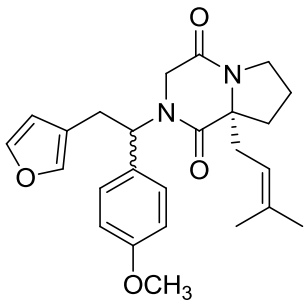
Amide **S2** (300 mg, 0.99 mmol) was dissolved in CH_2Cl_2 (10 mL), a 0.5 M K_2CO_3 solution (2.6 mL, 1.29 mmol) was added and the mixture was cooled to 0 °C. Bromoacetyl bromide (112 µL, 1.29 mmol) was added in one portion to the vigorously stirred biphasic solution. The reaction mixture was stirred at room temperature until the starting material disappeared as indicated by TLC (ca. 2 h, **R*f*** (**S3**) = 0.8 (EtOAc)). The layers were separated and the aqueous was extracted with CH_2Cl_2 (3 x 10 mL). The combined organic layers were evaporated and the residue was dissolved in CH_2Cl_2 (5 mL). A 50% NaOH solution (0.23 mL, 4.4 mmol) was added followed by benzyl(triethyl)ammonium chloride (3 mg, 1.4 mol%) and the reaction mixture was vigorously stirred for 20 h. The mixture was diluted with water (10 mL) and extracted with CH_2Cl_2 (3 x 10 mL). The combined organic layers were dried over Na_2SO_4, filtered and evaporated. Purification of the residue by column chromatography (EtOAc) gave 254 mg (75%) **S4** as a colorless solid. **R*f*** = 0.3 (EtOAc). **M.p.** 138-139 °C. **$[\alpha]^{20}_D$** = –39.8 (*c* 0.646, $CHCl_3$). **IR: *ν* (cm^{-1})** 2982, 2899, 1646, 1611, 1511, 1451, 1338, 1304, 1241, 1176, 1032, 816. **MS ESI+ *m/z*, (%)**: 381 (7, $[M+K]^+$), 365 (100, $[M+Na]^+$), 343 (20 $[M+H]^+$). **HRMS ESI+ *m/z*,** ($[M+Na]^+$): calcd. for $C_{20}H_{26}O_3N_2Na$: 365.1836, found: 365.1836. **^{1}H NMR (400 MHz, $CDCl_3$)**: δ = 1.51 (s, 3H, CH_3), 1.52 (s, 3H, CH_3), 1.93-2.07 (m, 2H, $NCH_2\underline{CH_2}CH_2$), 2.13-2.25 (m, 2H, $NCH_2CH_2\underline{CH_2}$), 2.39 (dd, *J* = 14.1, 8.4 Hz, 1H, $\underline{CH_2}CH$=), 2.51 (dd, *J* = 14.0, 7.8 Hz, 1H, $\underline{CH_2}CH$=), 3.47 (ddd, *J* = 12.5, 8.6, 4.4 Hz, 1H, $N\underline{CH_2}CH_2CH_2$), 3.66 (d, *J* = 16.9 Hz, 1H, $N\underline{CH_2}Ar$), 3.76-3.85 (m, 1H, $N\underline{CH_2}CH_2CH_2$), 3.79 (s, 3H, OCH_3), 3.84 (d, *J* = 17.0 Hz, 1H, $N\underline{CH_2}Ar$), 4.18 (d, *J* = 14.1 Hz, 1H, $N\underline{CH_2}CO$), 4.81 (d, *J* = 14.2 Hz, 1H, $N\underline{CH_2}CO$), 4.90-4.96 (m, 1H, $CH_2\underline{CH}$=), 6.86 (d, *J* = 8.7 Hz, 2H, CH_{Ar}), 7.20 (d, *J* = 8.6 Hz, 2H, CH_{Ar}). **^{13}C NMR (101 MHz, $CDCl_3$)**: δ = 17.8 (q, CH_3), 20.5 (t, $NCH_2\underline{C}H_2CH_2$), 25.9 (q, CH_3), 35.5 (t, $NCH_2CH_2\underline{C}H_2$), 36.8 (t, $\underline{C}H_2CH$=), 44.9 (t, $N\underline{C}H_2CH_2CH_2$), 49.1 (t, $N\underline{C}H_2CO$), 51.0 (t, $N\underline{C}H_2Ar$), 55.5 (q, OCH_3), 68.3 (s, C_{Pro}), 114.3 (d, CH_{Ar}), 117.2 (d, $CH_2\underline{C}H$=), 127.8 (s, C_{Ar}), 130.3 (d, CH_{Ar}), 137.8 (s, =$\underline{C}(CH_3)_2$), 159.6 (s, C_{Ar}), 163.1 (s, C=O), 169.4 (s, C=O).

(3*S*,8a*R*)-3-(Furan-3-ylmethyl)-2-(4-methoxybenzyl)-8a-(3-methylbut-2-en-1-yl)hexahydropyrrolo[1,2-a]pyrazine-1,4-dione (S5)



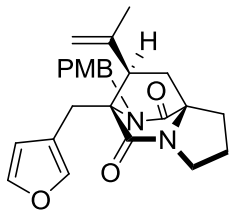
Diketopiperazine **S3** (182 mg, 0.53 mmol) was dissolved in dry THF (14 mL) and cooled to –78 °C. *n*BuLi (0.37 mL, 0.55 mmol, 1.6 M in hexane) was added dropwise and the resulting pale yellow solution was stirred at –78 °C for 1 h. 3-(Bromomethyl)furan[3] (102 mg, 0.637 mmol) was added, the temperature was raised to –50 °C over 2 h and the mixture was stirred at –50 °C for another 1.5 h. The reaction mixture was quenched with saturated NH_4Cl solution and extracted with ethyl acetate (3x). The combined organic layers were dried over Na_2SO_4, filtered and evaporated. The residue was purified by column chromatography on silica gel (hexane/EtOAc = 1/1) to give 174 mg (78%) of **S5** as a colorless solid. **R*f*** = 0.3 (hexane/EtOAc = 1/1). **M.p.** 127-129 °C. **$[\alpha]^{20}_D$** = –20.3 (*c* 1.003, $CHCl_3$). **IR: *ν* (cm^{-1})** 2931, 1646, 1512, 1438, 1247, 1176, 1024, 874. **MS ESI+ *m/z*, (%)**: 445 (100, $[M+Na]^+$), 423 (14 $[M+H]^+$). **HRMS ESI+ *m/z*,** ($[M+Na]^+$): calcd. for $C_{25}H_{30}O_4N_2Na$: 445.2098; found: 445.2098. **^{1}H NMR (400 MHz, $CDCl_3$)**: δ = 1.43 (dt, *J* = 12.3, 10.1 Hz, 1H, $NCH_2CH_2\underline{CH_2}$), 1.52 (s, 6H, CH_3), 1.66-1.79 (m, 1H, $NCH_2\underline{CH_2}CH_2$), 1.82-1.93 (m, 1H, $NCH_2\underline{CH_2}CH_2$), 2.01 (ddd, *J* = 12.5, 8.1, 1.8 Hz, 1H, $NCH_2CH_2\underline{CH_2}$), 2.27 (dd, *J* = 14.2, 7.9 Hz, 1H, $\underline{CH_2}CH$=), 2.51 (dd, *J* = 14.2, 7.5 Hz, 1H, $\underline{CH_2}CH$=), 3.05 (dd, *J* = 14.9, 4.4 Hz, 1H, $\underline{CH_2}$Fur), 3.24 (dd, *J* = 14.9, 2.7 Hz, 1H, $\underline{CH_2}$Fur), 3.31 (ddd, *J* = 12.4, 10.2, 4.5 Hz, 1H, $N\underline{CH_2}CH_2CH_2$), 3.76 (ddd, *J* = 12.5, 9.5, 6.4 Hz, 1H, $N\underline{CH_2}CH_2CH_2$), 3.81 (s, 3H, OCH_3), 3.84 (d, *J* = 14.7 Hz, 1H, $N\underline{CH_2}$Ar), 4.03 (dd, *J* = 4.4, 2.7 Hz, 1H, $N\underline{CH}CO$), 4.78–4.83 (m, 1H, $CH_2\underline{CH}$=), 5.62 (d, *J* = 14.6 Hz, 1H, $N\underline{CH_2}$Ar), 6.17 (dd, *J* = 1.8, 0.9 Hz, 1H, CH_{Fur}), 6.88 (d, *J* = 8.7 Hz, 2H, CH_{Ar}), 7.17-7.19 (m, 1H, CH_{Fur}), 7.24-7.28 (m, 2H, CH_{Ar}), 7.32 (t, *J* = 1.7 Hz, 1H, CH_{Fur}). **^{13}C NMR (101 MHz, $CDCl_3$)**: δ = 18.1 (q, CH_3), 19.8 (t, $NCH_2\underline{C}H_2CH_2$), 26.0 (q, CH_3), 26.2 (t, $\underline{C}H_2$Fur), 35.3 (t, $NCH_2CH_2\underline{C}H_2$), 36.8 (t, $\underline{C}H_2CH$=), 44.2 (t, $N\underline{C}H_2CH_2CH_2$), 45.4 (t, $N\underline{C}H_2$Ar), 55.5 (q, OCH_3), 58.7 (d, $N\underline{C}HCO$), 67.7 (s, C_{Pro}), 111.6 (d, CH_{Fur}), 114.4 (d, CH_{Ar}), 117.3 (d, $CH_2\underline{C}H$=), 118.0 (s, C_{Fur}), 127.3 (s, C_{Ar}), 130.4 (d, CH_{Ar}), 137.4 (s, =$\underline{C}(CH_3)_2$), 141.0 (d, CH_{Fur}), 143.0 (d, CH_{Fur}), 159.6 (s, C_{Ar}), 164.1 (s, C=O), 169.0 (s, C=O).

(*R*)-2-(2-(Furan-3-yl)-1-(4-methoxyphenyl)ethyl)-8a-(3-methylbut-2-enyl)hexahydropyrrolo[1,2-a]pyrazine-1,4-dione (S6)



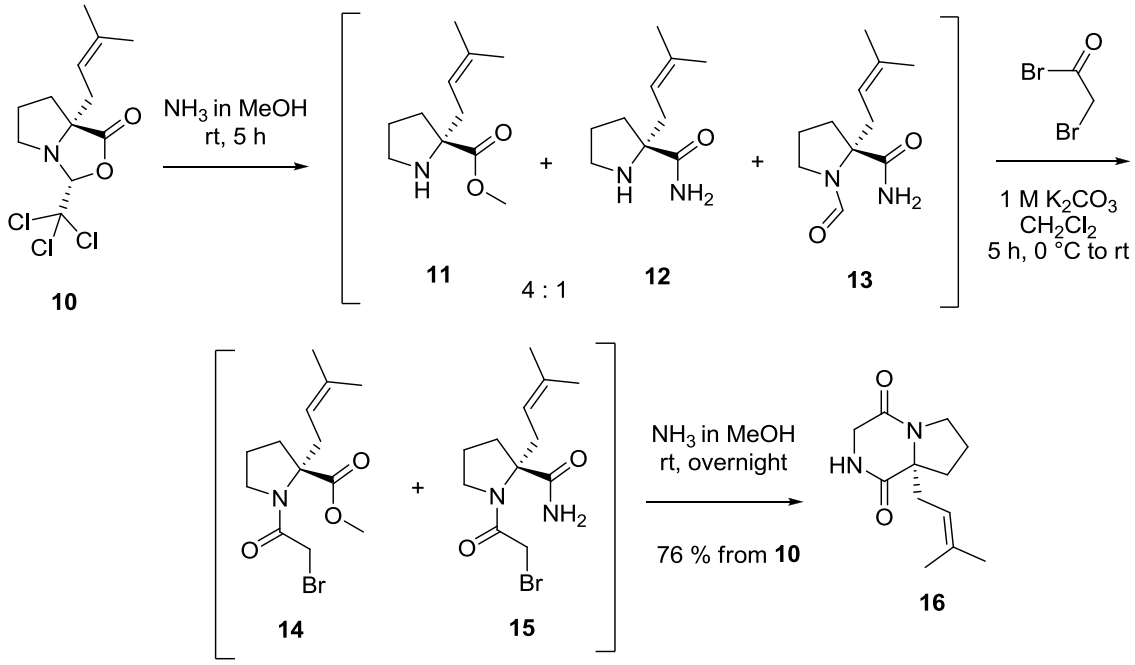
Following the above procedure for preparation of **S5** but using 1.3 equiv of *n*BuLi, **S5** was isolated in 52% yield together with 31% of **S6** as a 2:3 mixture of unassigned diasteroisomers as a colorless foam. **R*f*** = 0.2 (hexane/EtOAc = 1/1). **IR: *ν* (cm^{-1})** 2935, 1646, 1510, 1430, 1247, 1175, 1032, 870. **MS ESI+ *m/z*, (%)**: 445 (100, $[M+Na]^+$), 423 (15, $[M+H]^+$), **HRMS ESI+ *m/z*,** ($[M+Na]^+$): calcd. for $C_{25}H_{30}O_4N_2Na$: 445.2098; found: 445.2096. **^{1}H NMR (400 MHz, $CDCl_3$)**: δ = 1.38 (s, 3H, CH_3*), 1.48 (s, 3H, CH_3*), 1.52 (s, 3H, CH_3), 1.60 (s, 3H, CH_3), 1.84-2.01 (m, 5H, $NCH_2\underline{CH_2}CH_2$, $NCH_2\underline{CH_2}CH_2$*, $NCH_2CH_2\underline{CH_2}$*), 2.01-2.18 (m, 3H, $NCH_2CH_2\underline{CH_2}$, $NCH_2CH_2\underline{CH_2}$*), 2.23-2.28 (m, 2H, $\underline{CH_2}CH$=), 2.32 (dd, *J* = 14.0, 8.6 Hz, 1H, $\underline{CH_2}CH$=*), 2.45 (dd, *J* = 14.0, 7.5 Hz, 1H, $\underline{CH_2}CH$=*), 3.00 (dd, *J* = 15.3, 10.9 Hz, 1H, $\underline{CH_2}$Fur), 3.03 (d, *J* = 8.3 Hz, 2H, $\underline{CH_2}$Fur*), 3.08 (ddd, *J* = 15.2, 5.9, 1.4 Hz, 1H, $\underline{CH_2}$Fur), 3.37-3.43 (m, 2H, $N\underline{CH_2}CH_2CH_2$, $N\underline{CH_2}CH_2CH_2$*), 3.43 (d, *J* = 16.9 Hz, 1H, $N\underline{CH_2}CO$*), 3.57 (d, *J* = 16.7 Hz, 1H, $N\underline{CH_2}CO$), 3.62 (d, *J* = 16.9 Hz, 1H, $N\underline{CH_2}CO$*), 3.65-6.74 (m, 2H, $N\underline{CH_2}CH_2CH_2$, $N\underline{CH_2}CH_2CH_2$*), 3.77 (d, *J* = 16.7 Hz, 1H, $N\underline{CH_2}CO$), 3.79 (s, 3H, OCH_3), 3.80 (s, 3H, OCH_3*), 4.55-4.60 (m, 1H, $CH_2\underline{CH}$=), 4.79-4.84 (m, 1H, $CH_2\underline{CH}$=*), 6.07 (t, *J* = 8.3 Hz, 1H, $FurCH_2\underline{CH}N$*), 6.14 (dd, *J* = 10.8, 5.9 Hz, 1H, $FurCH_2\underline{CH}N$), 6.27 (dd, *J* = 1.8, 0.9 Hz, 1H, CH_{Fur}*), 6.42 (dd, *J* = 1.8, 0.9 Hz, 1H, CH_{Fur}), 6.86 (d, *J* = 8.8 Hz, 2H, CH_{Ar}), 6.89 (d, *J* = 8.8 Hz, 2H, CH_{Ar}*), 7.19-7.21 (m, 1H, CH_{Fur}*), 7.22-7.25 (m, 2H, CH_{Ar}), 7.26-7.28 (m, 2H, CH_{Ar}*), 7.29 (t, *J* = 1.7 Hz, 1H, CH_{Fur}*), 7.33-7.35 (m, 1H, CH_{Fur}), 7.36 (t, *J* = 1.7 Hz, 1H, CH_{Fur}). The minor diastereomer is marked by an *. **^{13}C NMR (101 MHz, $CDCl_3$)**: δ = 17.79 (q, CH_3), 17.81 (q, CH_3*), 20.5 (t, $NCH_2\underline{C}H_2CH_2$*), 20.7 (t, $NCH_2\underline{C}H_2CH_2$), 25.2 (t, $\underline{C}H_2$Fur*), 25.7 (t, $\underline{C}H_2$Fur), 25.8 (q, CH_3*), 25.9 (q, CH_3), 35.2 (t, $NCH_2CH_2\underline{C}H_2$), 35.7 (t, $NCH_2CH_2\underline{C}H_2$*), 36.4 (t, $\underline{C}H_2CH$=), 36.6 (t, $\underline{C}H_2CH$=*), 44.8 (t, $N\underline{C}H_2CH_2CH_2$*), 45.1 (t, $N\underline{C}H_2CH_2CH_2$), 45.7 (t, $N\underline{C}H_2CO$), 46.1 (t, $N\underline{C}H_2CO$*), 53.4 (d, $FurCH_2\underline{C}HN$*), 54.1 (d, $FurCH_2\underline{C}HN$), 55.4 (q, OCH_3), 55.5 (q, OCH_3*), 68.3 (s, C_{Pro}), 68.5 (s, C_{Pro}*), 111.2 (d, CH_{Fur}), 111.3 (d, CH_{Fur}*), 114.2 (d, CH_{Ar}*), 114.4 (d, CH_{Ar}), 117.1 (d, $CH_2\underline{C}H$=), 117.2 (d, $CH_2\underline{C}H$=*), 120.5 (s, C_{Fur}*), 120.9 (s, C_{Fur}), 128.9 (d, CH_{Ar}), 129.3 (d, CH_{Ar}*), 129.5 (s, C_{Ar}*), 129.9 (s, C_{Ar}), 137.5 (s, $=\underline{C}(CH_3)_2$), 137.6 (s, $=\underline{C}(CH_3)_2$*), 139.9 (d, CH_{Fur}), 140.2 (d, CH_{Fur}*), 143.0 (d, CH_{Fur}*), 143.3 (d, CH_{Fur}), 159.5 (s, C_{Ar}), 159.6 (s, C_{Ar}*), 163.1 (s, C=O), 163.5 (s, C=O*), 169.6 (s, C=O), 169.7 (s, C=O*).

(6*R*,7*R*,8a*R*)-6-(Furan-3-ylmethyl)-10-(4-methoxybenzyl)-7-(prop-1-en-2-yl)tetrahydro-1*H*-6,8a-(epiminomethano)indolizine-5,9(6*H*)-dione (S7)



Compound **S5** (100 mg, 0.24 mmol) was dissolved in dry DME (8 mL) and cooled to –78 °C. *n*BuLi (0.24 mL, 0.38 mmol, 1.6 M in hexane) was added dropwise, the resulting pale yellow solution was stirred at –78 °C for 1.5 h, and warmed to –40 °C over 30 min. TEMPO (47 mg, 0.3 mmol) was added to the reaction mixture followed by portionwise addition of $Cp_2Fe^+PF_6^-$ until the color of the oxidant persisted (ca 126 mg, 0.38 mmol) and stirring was continued for 10 min. The cooling bath was removed, the reaction flask was equipped with a reflux condenser and immersed to an oil bath preheated to 100 °C and the mixture was refluxed for 1.5 h. After cooling, the mixture was evaporated and the residue was immediately passed through a short column of silica gel eluting with EtOAc. The eluate was evaporated and further purified by column chromatography on silica gel (hexane/EtOAc = 1/1) to give 68 mg (68%) of an inseparable 5:1 mixture of **S7** and **S5** as a colorless solid. **R*f*** = 0.3 (hexane/EtOAc = 1/1). **^{1}H NMR (400 MHz, $CDCl_3$)**: δ = 1.57 (s, 1H, CH_3), 1.77 (dd, J = 13.4, 5.4 Hz, 1H, $\underline{CH}_{2bridge}$), 1.86-1.93 (m, 1H, $NCH_2CH_2\underline{CH_2}$), 2.01-2.09 (m, 2H, $NCH_2\underline{CH_2}CH_2$), 2.20 (dd, J = 13.4, 10.4 Hz, 1H, $\underline{CH}_{2bridge}$), 2.76 (dd, J = 10.3, 5.4 Hz, 1H, CH_{bridge}), 2.88 (dt, J = 13.0, 7.0 Hz, 1H, $NCH_2CH_2\underline{CH_2}$), 2.96 (d, J = 17.0 Hz, 1H, $\underline{CH_2}$Fur), 3.20 (dd, J = 17.3, 1.5 Hz, 1H, $\underline{CH_2}$Fur), 3.58 (t, J = 6.8 Hz, 2H, $N\underline{CH_2}CH_2CH_2$), 3.78 (s, 3H, OCH_3), 4.43 (d, J = 15.5 Hz, 1H, $N\underline{CH_2}$Ar), 4.53 (bs, 1H, $\underline{CH_2}$=), 4.73-4.82 (m, 2H, $N\underline{CH_2}$Ar, $\underline{CH_2}$=), 6.37 (dd, J = 1.9, 0.9 Hz, 1H, CH_{Fur}), 6.80 (d, J = 8.7 Hz, 1H, CH_{Ar}), 7.05 (d, J = 8.6 Hz, 1H, CH_{Ar}), 7.33-7.36 (m, 1H, CH_{Fur}), 7.37 (t, J = 1.7 Hz, 1H, CH_{Fur}). **^{13}C NMR (101 MHz, $CDCl_3$)**: δ = 19.1 (q, CH_3), 24.2 (t, $NCH_2\underline{C}H_2CH_2$), 25.6 (t, $\underline{C}H_2$Fur), 29.9 (t, $NCH_2CH_2\underline{C}H_2$), 36.4 (t, $CH_{2bridge}$), 44.4 (t, $N\underline{C}H_2CH_2CH_2$), 45.2 (t, $N\underline{C}H_2$Ar), 51.9 (d, CH_{bridge}), 55.3 (q, OCH_3), 66.1 (s, C_{Pro}), 68.6 (s, $C_{bridgehead}$), 112.4 (d, CH_{Fur}), 114.0 (d, CH_{Ar}), 116.1 (t, $\underline{C}H_2$=), 119.8 (s, C_{Fur}), 128.5 (d, CH_{Ar}), 130.4 (s, C_{Ar}), 140.9 (d, CH_{Fur}), 142.5 (d, CH_{Fur}), 142.9 (s, $=\underline{C}CH_3$), 158.9 (s, C_{Ar}), 167.5 (s, C=O), 173.6 (s, C=O).

(*R*)-8a-(3-Methylbut-2-en-1-yl)hexahydropyrrolo[1,2-a]pyrazine-1,4-dione (16)

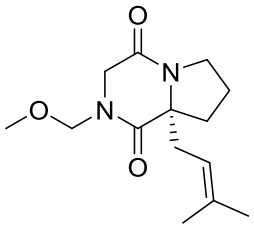


Oxazolidinone **10** (4.32 g, 13.8 mmol) was dissolved in 4M ammonia solution in methanol (34.5 mL, 138 mmol) and the mixture was stirred for 5 h. The solvent was evaporated and the crude mixture was used directly in the next step. In one experiment, the mixture was purified by column chromatography on silica gel with EtOAc providing ester **11** in 76% yield, followed by elution with EtOAc/MeOH = 95/5 giving an inseparable mixture of amide **12** and formylated compound **13** in 15% yield.

(*R*)-Methyl 2-(3-methylbut-2-en-1-yl)pyrrolidine-2-carboxylate (11): $[\alpha]^{20}_{D}$ = –59.8 (c 0.403, $CHCl_3$,); **IR: *ν* (cm^{-1})** 3350**,** 2951, 2915, 2873, 1728, 1435, 1376, 1223, 1192, 1172, 1097, 1044, 789. **MS ESI+ m/z, (%)**: 198 (100, $[M+H]^+$); **HRMS ESI+ *m/z,*** ($[M+H]^+$): calcd. for $C_{11}H_{20}O_2N$: 198.1488, found: 198.1488. **^{1}H NMR (400 MHz, $CDCl_3$)**: δ = 1.60 (s, 3H, CH_3), 1.68 (d, J = 1.4 Hz, 3H, CH_3), 1.68-1.82 (m, 3H, $NCH_2\underline{CH_2}CH_2$, $NCH_2CH_2\underline{CH_2}$), 2.12-2.19 (m, 1H, $NCH_2CH_2\underline{CH_2}$), 2.27-2.33 (m, 2H, $\underline{CH_2}CH$=, NH), 2.53 (ddd, J = 14.2, 7.6, 3.7 Hz, 1H, $\underline{CH_2}CH$=), 2.95-2.99 (m, 2H, $N\underline{CH_2}CH_2CH_2$), 3.69 (s, 3H, OCH_3), 5.08 (ddq, J = 7.5, 7.0, 1.4 Hz, 1H, CH=). **^{13}C NMR (101 MHz, $CDCl_3$)**: δ = 17.9 (q, CH_3), 25.0 (t, $NCH_2\underline{C}H_2CH_2$), 25.9 (q, CH_3), 35.2 (t, $NCH_2CH_2\underline{C}H_2$), 38.1 (t, $\underline{C}H_2CH$=), 46.4 (t, $N\underline{C}H_2CH_2CH_2$), 52.1 (q, OCH_3), 69.6 (s, C_{Pro}), 119.2 (d, $CH_2\underline{C}H$=), 134.8 (s, =$\underline{C}(CH_3)_2$), 177.4 (s, C=O).

The crude mixture of the previous step was dissolved in dichloromethane (60 mL), a 1M K_2CO_3 solution (18 mL, 17.9 mmol) was added and the mixture was cooled to 0 °C. Bromoacetyl bromide (1.56 mL, 17.9 mmol) was added in one portion to the vigorously stirred biphasic solution. The reaction mixture was stirred at room temperature until the starting material was consumed as indicated by TLC (ca. 5 h). The organic layer was separated and the aqueous extracted with CH_2Cl_2 (2 x 30 mL). The combined organic layers were dried over Na_2SO_4, filtered, and evaporated. The crude mixture was redissolved in 4M ammonia solution in methanol (17 mL, 68 mmol) and stirred at room temperature for 20 h. The volatiles were removed under reduced pressure, the residue was suspended in $CHCl_3$ and filtered. The filtrate was evaporated and purified by column chromatography (EtOAc/acetone = 1/1 gradient to 1/2) to obtain 2.34 g (76% from **10**) of **16** as a colorless oil. **R*f*** = 0.4 (EtOAc/acetone = 1/2). **$[\alpha]^{20}_D$** = –98.3 (*c* 0.901, $CHCl_3$); **IR: *ν* (cm^{-1})** 3230, 3053, 2981, 1652, 1446, 1324, 1265, 1107, 730. **MS ESI+ m/z, (%)**: 223 (100, $[M+H]^+$). **HRMS EI *m/z*,** ($[M]^+$): calcd. for $C_{12}H_{18}O_2N_2$: 222.1368, found: 222.1366. **^{1}H NMR (400 MHz, $CDCl_3$)**: δ = 1.61 (s, 3H, CH_3), 1.71 (s, 3H, CH_3), 1.95-2.05 (m, 2H, $NCH_2\underline{CH_2}CH_2$), 2.13-2.22 (m, 2H, $NCH_2CH_2\underline{CH_2}$), 2.43 (dd, *J* = 14.2, 8.2 Hz, 1H, $\underline{CH_2}CH$=), 2.52 (dd, *J* = 14.3, 7.7 Hz, 1H, $\underline{CH_2}CH$=), 3.52 (ddd, *J* = 12.8, 8.7, 4.6 Hz, 1H, $N\underline{CH_2}CH_2CH_2$), 3.75-3.89 (m, 2H, $N\underline{CH_2}CO$, $N\underline{CH_2}CH_2CH_2$), 4.03 (d, *J* = 16.8 Hz, 1H, $N\underline{CH_2}CO$), 5.16 (t, *J* = 8.0 Hz, 1H, $CH_2\underline{CH}$=), 6.61 (br. s, 1H, NH). **^{13}C NMR (101 MHz, $CDCl_3$)**: δ = 17.8 (q, CH_3), 20.2 (t, $NCH_2\underline{C}H_2CH_2$), 26.0 (q, CH_3), 34.6 (t, $NCH_2CH_2\underline{C}H_2$), 36.2 (t, $\underline{C}H_2CH$=), 45.0 (t, $N\underline{C}H_2CH_2CH_2$), 46.6 (t, $\underline{C}H_2NH$), 67.8 (s, C_{Pro}), 116.9 (d, $CH_2\underline{C}H$=), 138.0 (s, =$\underline{C}(CH_3)_2$), 163.2 (s, C=O), 171.9 (s, C=O).

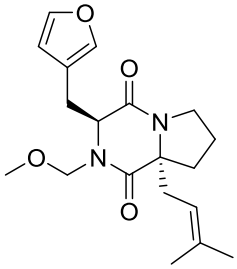
(*R*)-2-(Methoxymethyl)-8a-(3-methylbut-2-en-1-yl)hexahydropyrrolo[1,2-a]pyrazine-1,4-dione (17)



Diketopiperazine **16** (1.02 g, 4.6 mmol) was dissolved in dry THF (30 mL) under an N_2 atmosphere and the solution was cooled to 0 °C. NaH (257 mg, 6.4 mmol, 60% suspension in mineral oil) was added and stirring was continued at 0 °C for 1 h. Chloromethyl methyl ether (0.7 mL, 9.2 mmol) was added dropwise at 0 °C and the reaction mixture was stirred at room temperature for 20 h. The reaction mixture was quenched with saturated NH_4Cl solution and extracted with EtOAc (3 x 30 mL). The combined organic layers were dried over anhydrous $MgSO_4$, filtered and concentrated. The residue was purified by column chromatography (EtOAc/acetone = 1/1) to obtain 1.08 g (89%)

of compound **17** as a colorless oil. **R*f*** = 0.6 (EtOAc/acetone = 1/1). **[α]$^{20}_{D}$** = –72.8 (*c* 0.589, $CHCl_3$); **IR: *ν* (cm^{-1})** 2922, 1655, 1442, 1385, 1327, 1283, 1176, 1093, 1047, 912. **MS ESI+ m/z, (%)**: 289 (100, $[M+Na]^+$). **HRMS ESI+ *m/z,*** ($[M+Na]^+$): calcd. for $C_{14}H_{22}O_3N_2Na$: 289.1522, found: 289.1523. **^{1}H NMR (400 MHz, $CDCl_3$)**: δ = 1.60 (s, 3H, =C$\underline{C}H_3$), 1.71 (s, 3H, =C$\underline{C}H_3$), 1.92-2.05 (m, 2H, NCH$_2\underline{CH_2}$CH$_2$), 2.10-2.23 (m, 2H, NCH$_2$CH$_2\underline{CH_2}$), 2.43 (dd, *J* = 14.2, 8.0 Hz, 1H, $\underline{CH_2}$CH=), 2.54 (dd, *J* = 14.2, 7.8 Hz, 1H, $\underline{CH_2}$CH=), 3.46-3.56 (m, 1H, N$\underline{CH_2}$CH$_2$CH$_2$), 3.51 (s, 3H, OCH_3), 3.80-3.85 (m, 1H, N$\underline{CH_2}$CH$_2$CH$_2$), 3.87 (d, *J* = 17.0 Hz, 1H, N$\underline{CH_2}$CO), 4.09 (d, *J* = 17.1 Hz, 1H, N$\underline{CH_2}$CO), 4.67 (d, *J* = 10.0 Hz, 1H, N$\underline{CH_2}$O), 4.93 (d, *J* = 10.0 Hz, 1H, N$\underline{CH_2}$O), 5.13 (tdt, *J* = 7.6, 2.6, 1.2 Hz, 1H, CH=). **^{13}C NMR (101 MHz, $CDCl_3$)**: δ = 17.8 (q, =$\underline{C}CH_3$), 20.5 (t, NCH$_2\underline{C}$H$_2$CH$_2$), 26.0 (q, =CCH_3), 35.0 (t, NCH$_2$CH$_2\underline{C}$H$_2$), 36.4 (t, $\underline{C}H_2$CH=), 45.0 (t, N$\underline{C}$H$_2$CH$_2$CH$_2$), 50.0 (t, N$\underline{C}$H$_2$CO), 56.4 (q, OCH_3), 68.4 (s, C_{Pro}), 76.6 (t, NCH$_2$O), 116.9 (d, CH$_2\underline{C}$H=), 137.8 (s, =$\underline{C}(CH_3)_2$), 163.1 (s, C=O), 170.6 (s, C=O).

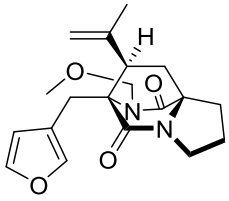
(3*S*,8a*R*)-3-(Furan-3-ylmethyl)-2-(methoxymethyl)-8a-(3-methylbut-2-en-1-yl)hexahydropyrrolo[1,2-a]pyrazine-1,4-dione (7)



Compound **17** (0.63 g, 2.38 mmol) was dissolved in dry THF (40 mL) and cooled to –78 °C. *n*BuLi (1.9 mL, 3.1 mmol, 1.6 M in hexane) was added dropwise and the resulting pale yellow solution was stirred at –78 °C for 1 h. 3-(Bromomethyl)furan[3] (575 mg, 3.6 mmol) was added, the temperature was raised to –50 °C over 2 h and the mixture was stirred for another 1.5 h at –50 °C. The reaction mixture was quenched with saturated NH_4Cl solution (30 mL) and extracted with ethyl acetate (3 x 30 mL). The combined organic layers were dried over Na_2SO_4, filtered and evaporated. The residue was purified by column chromatography on silica gel (hexane/EtOAc = 1/1) to give 0.67 g (82%) of **7** as a colorless solid. **R*f*** = 0.3 (hexane/EtOAc = 1/1). **M.p.** 94-95 °C. **[α]$^{20}_{D}$** = –24.1 (*c* 0.536, $CHCl_3$). **IR: *ν* (cm^{-1})** 2930, 1649, 1431, 1384, 1094, 1022, 873, 782. **MS ESI+ m/z, (%)**: 369 (100, $[M+Na]^+$). **HRMS ESI+ *m/z,*** ($[M+Na]^+$): calcd. for $C_{19}H_{26}O_4N_2Na$: 369.1784, found: 369.1785. **^{1}H NMR (400 MHz, $CDCl_3$)**: δ = 1.53-1.60 (m, 1H, NCH$_2$CH$_2\underline{CH_2}$), 1.56 (s, 3H, =$\underline{C}CH_3$), 1.66 (s, 3H, =$\underline{C}CH_3$), 1.73-1.82 (m, 1H, NCH$_2\underline{CH_2}$CH$_2$), 1.87-1.95 (m, 1H, NCH$_2\underline{CH_2}$CH$_2$), 2.03 (ddd, *J* = 12.4, 8.0, 1.9 Hz, 1H, NCH$_2$CH$_2\underline{CH_2}$), 2.31 (dd, *J* = 14.2, 7.5 Hz, 1H, $\underline{CH_2}$CH=), 2.53 (dd, *J* = 14.2, 8.1 Hz, 1H, $\underline{CH_2}$CH=), 3.06 (dd, *J* = 15.0, 4.4 Hz, 1H, $\underline{CH_2}$Fur), 3.35-3.43 (m, 2H, $\underline{CH_2}$Fur, N$\underline{CH_2}$CH$_2$CH$_2$), 3.38 (s, 3H, OCH_3), 3.79 (ddd, *J* = 12.5, 9.5, 6.8 Hz,

1H, N$\underline{CH_2}CH_2CH_2$), 4.23-4.31 (m, 1H, NCH), 4.64 (d, *J* = 10.2 Hz, 1H, N$\underline{CH_2}$O), 4.97-5.04 (m, 1H, $\underline{CH}$=), 5.23 (d, *J* = 10.1 Hz, 1H, N$\underline{CH_2}$O), 6.16 (dd, *J* = 1.8, 0.9 Hz, 1H, CH_{Fur}), 7.13-7.17 (m, 1H, CH_{Fur}), 7.28 (t, *J* = 1.7 Hz, 1H, CH_{Fur}). **^{13}C NMR (101 MHz, $CDCl_3$)**: δ = 18.1 (q, =C$\underline{C}H_3$), 19.9 (t, NCH$_2\underline{C}H_2$CH$_2$), 26.2 (t+q, CH$_2$Fur, =C$\underline{C}H_3$), 35.2 (t, NCH$_2$CH$_2\underline{C}H_2$), 36.7 (t, $\underline{C}H_2$CH=), 44.4 (t, N$\underline{C}H_2$CH$_2$CH$_2$), 57.0 (q, OCH_3), 58.8 (d, NCH), 68.0 (s, C_{Pro}), 75.1 (t, NCH$_2$O), 111.8 (d, CH_{Fur}), 117.2 (d, CH$_2\underline{C}$H=), 118.5 (s, C_{Fur}), 137.7 (s, =$\underline{C}(CH_3)_2$), 141.1 (d, CH_{Fur}), 142.7 (d, CH_{Fur}), 164.2 (s, C=O), 170.4 (s, C=O).

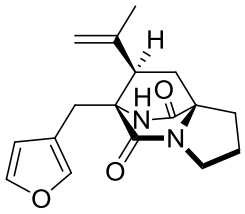
(6*R*,7*R*,8a*R*)-6-(Furan-3-ylmethyl)-10-(methoxymethyl)-7-(prop-1-en-2-yl)tetrahydro-1*H*-6,8a-(epiminomethano)indolizine-5,9(6*H*)-dione (6)



Compound **7** (340 mg, 0.98 mmol) was dissolved in dry DME (20 mL) and cooled to –78 °C. *n*BuLi (0.98 mL, 1.57 mmol, 1.6 M in hexane) was added dropwise, the resulting pale yellow solution was stirred at –78 °C for 1.5 h, and warmed to –40 °C over 30 min. TEMPO (192 mg, 1.23 mmol) was added to the reaction mixture followed by portionwise addition of $Cp_2Fe^+PF_6^-$ until the color of the oxidant persisted (ca 520 mg, 1.57 mmol) and stirring was continued for 10 min. The cooling bath was removed, the reaction flask was equipped with a reflux condenser and immersed to an oil bath preheated to 100 °C and refluxed for 1.5 h. The reaction mixture was cooled, evaporated and the residue was immediately passed through a short column of silica gel eluting with EtOAc. The eluate was evaporated and further purified by column chromatography on silica gel (hexane/EtOAc = 1/1) to give 295 mg (87%) of **6** as a colorless solid. The compound was crystallized from DCM for X-ray analysis. **R*f*** = 0.3 (hexane/EtOAc = 1/1). **M.p.** 137-138 °C. **$[\alpha]^{20}_D$** = –10.2 (*c* 0.609, $CHCl_3$); **IR: *ν* (cm^{-1})** 2931, 1694, 1674, 1644, 1363, 1304, 1142, 1082, 1045, 901, 874. **MS ESI+ m/z, (%)**: 367 (100, $[M+Na]^+$). **HRMS ESI+ *m/z*,** ($[M+Na]^+$)**:** calcd. for $C_{19}H_{24}O_4N_2Na$: 367.1628, found: 367.1629. **^{1}H NMR (400 MHz, $CDCl_3$)**: δ = 1.65 (s, 3H, =CCH_3), 1.78-1.90 (m, 2H, $\underline{CH_{2bridge}}$, NCH$_2$CH$_2\underline{CH_2}$), 1.97-2.08 (m, 2H, NCH$_2\underline{CH_2}$CH$_2$), 2.27 (dd, *J* = 13.5, 10.4 Hz, 1H, $\underline{CH_{2bridge}}$), 2.79-2.86 (m, 1H, NCH$_2$CH$_2\underline{CH_2}$), 3.05-3.12 (m, 1H, CH_{bridge}), 3.12 (d, *J* = 16.9 Hz, 1H, $\underline{CH_2}$Fur), 3.23 (s, 3H, OCH_3), 3.36 (dd, *J* = 17.1, 1.3 Hz, 1H, $\underline{CH_2}$Fur), 3.53-3.63 (m, 2H, N$\underline{CH_2}$CH$_2$CH$_2$), 4.72-4.82 (m, 2H, =$\underline{CH_2}$, N$\underline{CH_2}$O), 4.84-4.86 (m, 1H, =$\underline{CH_2}$), 4.92 (d, *J* = 10.7 Hz, 1H, N$\underline{CH_2}$O), 6.34-6.36 (m, 1H, CH_{Fur}), 7.32-7.36 (m, 2H, CH_{Fur}). **^{13}C NMR (101 MHz, $CDCl_3$)**: δ = 19.3 (q, =C$\underline{C}H_3$), 24.2 (t, NCH$_2\underline{C}$H$_2$CH$_2$), 24.8 (t, CH$_2$Fur), 29.8 (t,

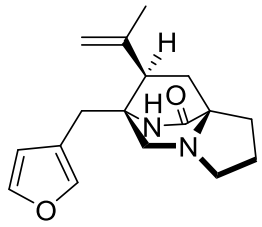
$NCH_2CH_2\underline{C}H_2$), 36.5 (t, $\underline{C}H_{2bridge}$), 44.3 (t, $N\underline{C}H_2CH_2CH_2$), 51.8 (d, CH_{bridge}), 56.6 (q, OCH_3), 66.0 (s, C_{Pro}), 67.6 (s, $C_{bridgehead}$), 73.4 (t, NCH_2O), 112.5 (d, CH_{Fur}), 116.0 (t, $=\underline{C}H_2$), 119.8 (s, C_{Fur}), 141.0 (d, CH_{Fur}), 142.3 (d, CH_{Fur}), 143.2 (s, $CH_3\underline{C}=$), 167.6 (s, C=O), 174.2 (s, C=O).

(6*R*,7*R*,8a*R*)-6-(Furan-3-ylmethyl)-7-(prop-1-en-2-yl)tetrahydro-1*H*-6,8a-(epiminomethano)indolizine-5,9(6*H*)-dione (19)



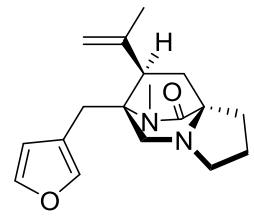
Compound **6** (180 mg, 0.52 mmol) was dissolved in dry CH_2Cl_2 (20 mL) under N_2 and cooled to –20 °C. A solution of *B*-bromocatecholborane (135 mg, 0.68 mmol) in CH_2Cl_2 (3 mL) was added dropwise. The mixture was stirred allowing the temperature to rise to 0 °C over 1 h. NaOH (20 mL, 2M in H_2O) was added and the mixture was stirred for 1 h. The layers were separated and the aqueous was extracted with CH_2Cl_2 (3 x 20 mL). The combined organic layers were dried over anhydrous $MgSO_4$, filtered and concentrated. The residue was purified by column chromatography on silica gel (EtOAc) to obtain 151 mg (96%) of **19** as a colorless oil. **R*f*** = 0.3 (EtOAc). **IR: *ν* (cm^{-1})** 3250, 2977, 1674, 1440, 1396, 1161, 1024, 908, 872. **MS ESI+ *m/z*, (%)**: 323 (100, $[M+Na]^+$). **HRMS ESI+ *m/z*,** ($[M+Na]^+$): calcd. for $C_{17}H_{20}O_2N_2Na$: 323.1366, found: 323.1367. **^{1}H NMR (400 MHz, $CDCl_3$)**: δ = 1.71 (s, 3H, CH_3), 1.78-1.86 (m, 2H, $\underline{CH_2}_{bridge}$, $NCH_2CH_2\underline{CH_2}$), 2.00-2.09 (m, 2H, $NCH_2\underline{CH_2}CH_2$), 2.30 (dd, *J* = 13.5, 10.3 Hz, 1H, $\underline{CH_2}_{bridge}$), 2.69-2.78 (m, 1H, $NCH_2CH_2\underline{CH_2}$), 2.72 (d, *J* = 15.3 Hz, 1H, $\underline{CH_2}Fur$), 2.90 (dd, *J* = 10.3, 5.5 Hz, 1H, CH_{bridge}), 3.30 (d, *J* = 15.3 Hz, 1H, $\underline{CH_2}Fur$), 3.49-3.63 (m, 2H, $N\underline{CH_2}CH_2CH_2$), 4.93-4.95 (m, 1H, $=CH_2$), 4.96-4.99 (m, 1H, $=CH_2$), 5.82 (bs, 1H, NH), 6.43 (dd, *J* = 1.8, 0.9 Hz, 1H, CH_{Fur}), 7.37-7.40 (m, 1H, CH_{Fur}), 7.42 (t, *J* = 1.7 Hz, 1H, CH_{Fur}). **^{13}C NMR (101 MHz, $CDCl_3$)**: δ = 19.2 (q, CH_3), 24.5 (t, $NCH_2\underline{C}H_2CH_2$), 25.0 (t, CH_2Fur), 29.1 (t, $NCH_2CH_2\underline{C}H_2$), 36.6 (t, $\underline{C}H_{2bridge}$), 44.1 (t, $N\underline{C}H_2CH_2CH_2$), 52.7 (d, CH_{bridge}), 62.8 (s, C_{Pro}), 66.7 (s, $C_{bridgehead}$), 112.3 (d, CH_{Fur}), 116.2 (t, $=\underline{C}H_2$), 118.1 (s, C_{Fur}), 141.5 (d, CH_{Fur}), 142.8 (s, $CH_3\underline{C}=$), 143.8 (d, CH_{Fur}), 168.3 (s, C=O), 172.7 (s, C=O).

(6*R*,7*R*,8a*R*)-6-(Furan-3-ylmethyl)-7-(prop-1-en-2-yl)hexahydro-1*H*-6,8a-(epiminomethano)indolizin-9-one (20)



DIBAL-H (1.62 mL, 1.62 mmol, 1M in toluene) was added dropwise to a solution of **19** (128 mg, 0.43 mmol) in dry toluene (10 mL) at 0 °C. The mixture was stirred at r.t. for 5 h, cooled to 0 °C and quenched with H_2O (70 µL) and 15% NaOH (70 µL). Na_2SO_4 was added, the mixture was stirred for 30 min, and filtered over celite, which was thoroughly washed with EtOAc. The filtrate was concentrated and purified by column chromatography on silica gel (EtOAc) to obtain 96 mg (79%) of **20** as a colorless oil**. R*f*** = 0.25 (EtOAc). **$[\alpha]^{20}_D$** = –15.0 (*c* 0.409, $CHCl_3$). **IR: *ν* (cm^{-1})** 3200, 3068, 2978, 1672, 1505, 1456, 1374, 1318, 1242, 1164, 1025, 908, 897, 873. **MS ESI+ *m/z*, (%)**: 309 (35, $[M+Na]^+$), 287 (100, $[M+H]^+$). **HRMS ESI+ *m/z*,** ($[M+H]^+$)**:** calcd. for $C_{17}H_{23}O_2N_2$: 287.1754, found: 287.1752. **^{1}H NMR (400 MHz, $CDCl_3$)**: δ = 1.38 (dt, *J* = 12.5, 8.7 Hz, 1H, $NCH_2CH_2\underline{CH_2}$), 1.79-1.91 (m, 3H, $NCH_2\underline{CH_2}CH_2$, $\underline{CH_{2bridge}}$), 1.92 (s, 3H, CH_3), 2.09-2.18 (m, 2H, $\underline{CH_{2bridge}}$, $N\underline{CH_2}CH_2CH_2$), 2.30 (dd, *J* = 10.2, 1.9 Hz, 1H, $C\underline{CH_2}N$), 2.44-2.54 (m, 2H, CH_{bridge}, $NCH_2CH_2\underline{CH_2}$), 2.58 (d, *J* = 15.0 Hz, 1H, $\underline{CH_2}Fur$), 2.66 (d, *J* = 15.1 Hz, 1H, $\underline{CH_2}Fur$), 3.08 (dt, *J* = 8.9, 5.5 Hz, 1H, $N\underline{CH_2}CH_2CH_2$), 3.41 (d, *J* = 10.2 Hz, 1H, $C\underline{CH_2}N$), 5.03 (s, 1H, $=CH_2$), 5.07 (s, 1H,$=CH_2$), 5.98 (bs, 1H, NH), 6.23-6.26 (m, 1H, CH_{Fur}), 7.31 (s, 1H, CH_{Fur}), 7.41 (t, *J* = 1.7 Hz, 1H, CH_{Fur}). **^{13}C NMR (101 MHz, $CDCl_3$)**: δ = 21.7 (q, CH_3), 22.5 (t, $NCH_2\underline{C}H_2CH_2$), 27.1 (t, $NCH_2CH_2\underline{C}H_2$), 29.5 (t, CH_2Fur), 37.4 (t, $\underline{C}H_{2bridge}$), 50.2 (d, CH_{bridge}), 54.2 (t, $N\underline{C}H_2CH_2CH_2$), 56.9 (t, $C\underline{C}H_2N$), 58.3 (s, C_{Pro}), 65.4 (s, $C_{bridgehead}$), 111.9 (d, CH_{Fur}), 115.9 (t, $=CH_2$), 118.1 (s, C_{Fur}), 140.8 (d, CH_{Fur}), 143.8 (d, CH_{Fur}), 144.2 (s, $CH_3\underline{C}=$), 174.2 (s, C=O).

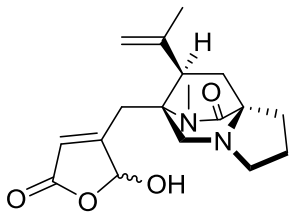
(6*R*,7*R*,8a*R*)-6-(Furan-3-ylmethyl)-10-methyl-7-(prop-1-en-2-yl)hexahydro-1*H*-6,8a-(epiminomethano)indolizin-9-one (21)



Compound **20** (95 mg, 0.33 mmol) was dissolved in dry THF (8 mL) under N_2 and the solution was cooled to 0 °C. NaH (23 mg, 0.56 mmol, 60% suspension in mineral oil) was added and stirring was continued at 0 °C for 1 h. Iodomethane (62 µL, 0.99 mmol) was added dropwise at 0 °C and the reaction mixture was stirred at room temperature for 20 h. The reaction mixture was quenched with H_2O (10 mL) and extracted with EtOAc (3 x 10 mL). The combined organic layers were dried over anhydrous $MgSO_4$, filtered and concentrated. The residue was

purified by column chromatography (EtOAc) to obtain 80 mg (80%) of compound **21** as a colorless oil. **R*f*** = 0.25 (EtOAc). **[α]$^{20}_{D}$** = +18.6 (*c* 0.263, $CHCl_3$). **IR: *ν* (cm^{-1})** 2979, 2927, 1664, 1457, 1419, 1391, 1323, 1166, 1072, 1026, 902, 873. **MS ESI+ *m/z*, (%)**: 301 (100, $[M+H]^+$). **HRMS ESI+ *m/z*, ([M+H]$^+$)**: Calcd. for $C_{18}H_{25}O_2N_2$: 323.1730, found: 323.1730. **^{1}H NMR (400 MHz, $CDCl_3$)**: δ = 1.32-1.45 (m, 1H, $NCH_2CH_2\underline{CH_2}$), 1.74-1.90 (m, 3H, $NCH_2\underline{CH_2}CH_2$, $\underline{CH_{2bridge}}$), 1.86 (s, 3H, $=CCH_3$), 2.05 (dd, *J* = 13.2, 11.4 Hz, 1H, $\underline{CH_{2bridge}}$), 2.15 (q, *J* = 8.8 Hz, 1H, $N\underline{CH_2}CH_2CH_2$), 2.43-2.52 (m, 2H, $C\underline{CH_2}N$, CH_{bridge}), 2.54-2.67 (m, 1H, $NCH_2CH_2\underline{CH_2}$), 2.75 (d, *J* = 16.3 Hz, 1H, $\underline{CH_2}Fur$), 2.83 (d, *J* = 16.5 Hz, 1H, $\underline{CH_2}Fur$), 3.04 (s, 3H, CH_3N), 3.04-3.13 (m, 1H, $N\underline{CH_2}CH_2CH_2$), 3.35 (d, *J* = 10.7 Hz, 1H, $C\underline{CH_2}N$), 4.96 (s, 1H, $=CH_2$), 5.00 (s, 1H, $=CH_2$), 6.27 (dd, *J* = 1.9, 0.9 Hz, 1H, CH_{Fur}), 7.28 (dd, *J* = 1.6, 0.9 Hz, 1H, CH_{Fur}), 7.37 (t, *J* = 1.7 Hz, 1H, CH_{Fur}). **^{13}C NMR (101 MHz, $CDCl_3$)**: δ = 21.2 (q, $=C\underline{C}H_3$), 22.4 (t, $NCH_2\underline{C}H_2CH_2$), 27.3 (q, CH_3N), 27.9 (t, $NCH_2CH_2\underline{C}H_2$), 28.6 (t, CH_2Fur), 37.6 (t, $\underline{C}H_{2bridge}$), 49.4 (d, CH_{bridge}), 54.8 (t, $N\underline{C}H_2CH_2CH_2$), 56.4 (t, $C\underline{C}H_2N$), 62.5 (s, C_{Pro}), 64.9 (s, $C_{bridgehead}$), 112.3 (d, CH_{Fur}), 115.9 (t, $CH_2=$), 118.9 (s, C_{Fur}), 141.1 (d, CH_{Fur}), 142.7 (d, CH_{Fur}), 144.7 (s, $CH_3\underline{C}=$), 175.4 (s, C=O).

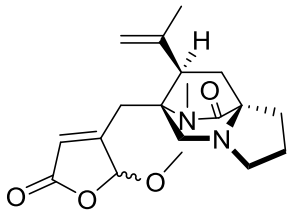
(6*R*,7*R*,8a*R*)-6-((2-Hydroxy-5-oxo-2,5-dihydrofuran-3-yl)methyl)-10-methyl-7-(prop-1-en-2-yl)hexahydro-1*H*-6,8a-(epiminomethano)indolizin-9-one (5)



Furan **21** (30 mg, 0.10 mmol) was dissolved in dry CH_2Cl_2 (10 mL) and cooled to –78 °C. Rose bengal (5 mg, 0.005 mmol) and *i*Pr_2NEt (35 µL, 0.20 mmol) were added. Oxygen gas was bubbled through the solution at –78 °C for 20 min and the mixture was subsequently irradiated with a tungsten flood light at –78 °C under constant bubbling of oxygen gas for 6 h until full consumption of **27** as indicated by TLC. The reaction mixture was warmed to r.t. and evaporated. The residue was purified by column chromatography (CH_2Cl_2/MeOH = 95/5) to give 28 mg (85%) of γ-hydroxybutenolide **5** as an inseparable diastereomeric mixture as a pale red oil, contaminated with rose bengal residues, which was directly used in the next step. The ratio could not be determined because of signal averaging by the present amine function.[4] **R*f*** = 0.2 (CH_2Cl_2/MeOH = 95/5). **IR: *ν* (cm^{-1})** 3280 (br.), 2956, 2926, 1759, 1650, 1456, 1394, 1133, 952, 907, 727. **MS ESI+ *m/z*, (%)**: 355 (65, $[M+Na]^+$), 333 (100, $[M+H]^+$). **HRMS ESI+ *m/z*,** ($[M+Na]^+$)**:** calcd. for $C_{18}H_{24}O_4N_2Na$: 355.1628, found: 355.1630. **^{1}H NMR (400 MHz, $CDCl_3$)**: δ = 1.34-1.51 (m, 1H, $NCH_2CH_2\underline{CH_2}$), 1.75-1.94 (m, 3H, $NCH_2\underline{CH_2}CH_2$, $\underline{CH_{2bridge}}$), 1.88 (s, 3H,

=CCH_3), 1.98-2.12 (m, 1H, $\underline{CH}_{2bridge}$), 2.14-2.27 (m, 1H, N$\underline{CH}_2CH_2CH_2$), 2.49-2.83 (m, 5H, C$\underline{CH}_2$N, CH_{bridge}, =C$\underline{CH}_2$, NCH$_2$CH$_2$$\underline{CH}_2$), 2.96 (s, 3H, N$CH_3$), 3.07-3.18 (m, 1H, N$\underline{CH}_2CH_2CH_2$), 3.27-3.38 (m, 1H, C$\underline{CH}_2$N), 4.99 (s, 2H, =$CH_2$), 5.97 (s, 1H, $\underline{CH}$OH), 6.05 (s, 1H, =CH). The signals of the OH protons are not visible. **^{13}C NMR (101 MHz, CDCl$_3$)**: δ = 20.8 (q, =C$\underline{C}H_3$), 22.4 (t, NCH$_2$$\underline{CH}_2CH_2$), 27.8 (t, NCH$_2CH_2$$\underline{CH}_2$), 27.9 (q, CH_3N), 31.2 (t, $\underline{C}H_2$C=), 36.5 (t, $\underline{C}H_{2bridge}$), 48.5 (d, CH_{bridge}), 54.7 (t, N$\underline{C}H_2CH_2CH_2$), 55.9 (t, C$\underline{C}H_2$N), 61.9 (s, C_{Pro}), 65.0 (s, $C_{bridgehead}$), 99.7 (d, $\underline{C}$HOH), 116.9 (t, CH_2=), 120.4 (d, =CH), 143.7 (s, $CH_3\underline{C}$=), 163.6 (s, =$\underline{C}CH_2$), 170.5 (s, NC=O), 176.1 (s, COO).

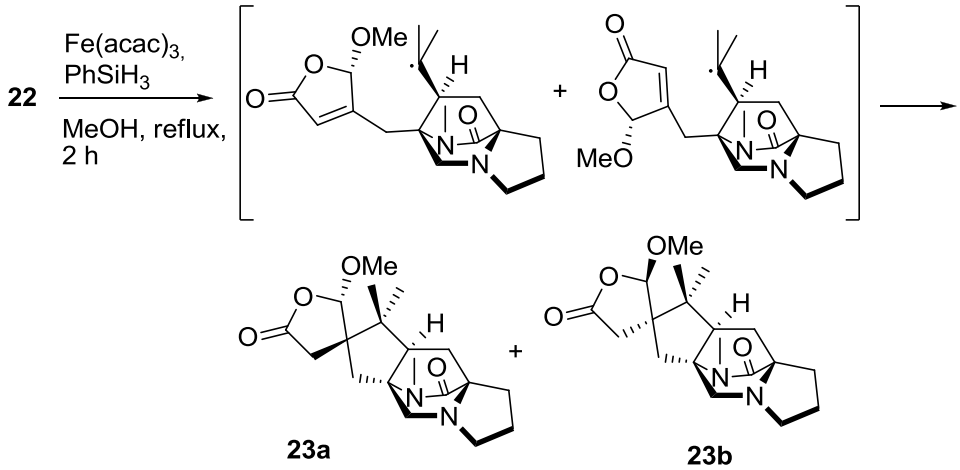
(6*R*,7*R*,8a*R*)-6-((2-Methoxy-5-oxo-2,5-dihydrofuran-3-yl)methyl)-10-methyl-7-(prop-1-en-2-yl)hexahydro-1*H*-6,8a-(epiminomethano)indolizin-9-one (22)



γ-Hydroxybutenolide **5** (54 mg, 0.162 mmol) was dissolved in dry methanol (3 mL). (+)-CSA (42 mg, 0.178 mmol) was added and the reaction mixture was stirred at reflux for 20 h. The reaction mixture was cooled to r.t., evaporated and the residue was redissolved in CH_2Cl_2 (10 mL). Saturated $NaHCO_3$ solution (10 mL) was added, the mixture was stirred for 15 min and extracted with CH_2Cl_2 (3 x 10 mL) The combined organic layers were dried over $MgSO_4$, filtered and evaporated. The residue was purified by column chromatography (CH_2Cl_2/MeOH = 95/5) to give 42 mg (75%) of **22** as an inseparable 1:1 mixture as a colorless oil. **R*f*** = 0.3 (CH_2Cl_2/MeOH = 95/5) **IR: *ν* (cm^{-1})** 2940, 1765, 1665, 1456, 1362, 1325, 1203, 1119, 972, 940, 902. **MS ESI+ m/z, (%)**: 347 (100, $[M+H]^+$). **HRMS ESI+ *m/z,*** ($[M+H]^+$): calcd. for $C_{19}H_{27}O_4N_2$: 347.1965, found: 347.1966. **^{1}H NMR (400 MHz, CDCl$_3$),** mixture of epimers: δ = 1.35-1.45 (m, 2H, NCH$_2$CH$_2$$\underline{CH}_2$, NCH$_2CH_2$$\underline{CH}_2$*), 1.77-1.94 (m, 6H, NCH$_2$$\underline{CH}_2CH_2$, $\underline{CH}_{2bridge}$, NCH$_2$$\underline{CH}_2CH_2$*, $\underline{CH}_{2bridge}$*), 1.87 (s, 6H, =CCH_3, =CCH_3*), 2.04-2.10 (m, 2H, $CH_{2bridge}$, $CH_{2bridge}$*), 2.15-2.22 (m, 2H, N$\underline{CH}_2CH_2CH_2$, N$\underline{CH}_2CH_2CH_2$*), 2.43-2.80 (m, 10H, =C$\underline{CH}_2$, NCH$_2$CH$_2$$\underline{CH}_2$, CH_{bridge}, C$\underline{CH}_2$N, =C$\underline{CH}_2$*, NCH$_2CH_2$$\underline{CH}_2$*, CH_{bridge}*, C$\underline{CH}_2$N*), 2.92 (s, 3H, NCH_3), 2.94 (s, 3H, NCH_3*), 3.09-3.12 (m, 2H, N$\underline{CH}_2CH_2CH_2$, N$\underline{CH}_2CH_2CH_2$*), 3.28-3.34 (m, 2H, C$\underline{CH}_2$N, C$\underline{CH}_2$N*), 3.59 (s, 3H, OCH_3), 3.61 (s, 3H, OCH_3*), 4.94 (s, 1H, =CH_2), 4.97 (s, 1H, =CH_2), 5.01 (s, 1H, =CH_2*), 5.04 (s, 1H, =CH_2*), 5.57 (s, 1H, $\underline{CH}$OCH_3), 5.58 (s, 1H, $\underline{CH}$OCH_3*), 6.06 (s, 1H, =CH), 6.09 (s, 1H, =CH*). **^{1}H NMR (500 MHz, CD$_3$CN)**: δ = 1.31-1.37 (m, 2H, NCH$_2$CH$_2$$\underline{CH}_2$, NCH$_2CH_2$$\underline{CH}_2$*), 1.72-1.81 (m, 6H, NCH$_2$$\underline{CH}_2CH_2$, $\underline{CH}_{2bridge}$, NCH$_2$$\underline{CH}_2CH_2$*,

$\underline{CH}_{2bridge}$*), 1.84 (s, 3H, =CCH$_3$), 1.85 (s, 3H, =CCH$_3$*), 1.98-2.00 (m, 1H, $\underline{CH}_{2bridge}$), 2.01-2.02 (m, 1H, $\underline{CH}_{2bridge}$*), 2.11-2.16 (m, 2H, N$\underline{CH}_2CH_2CH_2$, N$\underline{CH}_2CH_2CH_2$*), 2.45-2.57 (m, 5H, =C$\underline{CH}_2$, NCH$_2$CH$_2\underline{CH}_2$, CH$_{bridge}$, C$\underline{CH}_2$N, NCH$_2$CH$_2\underline{CH}_2$*, CH$_{bridge}$*, C$\underline{CH}_2$N*), 2.64 (d, *J* = 1.9 Hz, 2H, =C$\underline{CH}_2$*), 2.69-2.80 (m, 3H, =C$\underline{CH}_2$, CH$_{bridge}$, CH$_{bridge}$*), 2.86 (s, 3H, NCH$_3$), 2.87 (s, 3H, NCH$_3$*), 3.00-3.07 (m, 2H, N$\underline{CH}_2CH_2CH_2$, N$\underline{CH}_2CH_2CH_2$*), 3.24 (d, *J* = 10.8 Hz, 1H, C$\underline{CH}_2$N), 3.30 (d, *J* = 10.7 Hz, 1H, C$\underline{CH}_2$N*), 3.51 (s, 3H, OCH$_3$), 3.52 (s, 3H, OCH$_3$*), 4.92-5.04 (m, 4H, =CH$_2$, =CH$_2$*), 5.69 (s, 1H, $\underline{CH}$OCH$_3$), 5.71 (s, 1H, $\underline{CH}$OCH$_3$*), 6.13 (td, *J* = 1.9, 0.9 Hz, 1H, =CH), 6.16 (td, *J* = 1.9, 1.0 Hz, 1H, =CH). **^{13}C NMR (126 MHz, CD$_3$CN)**: δ = 20.6 (q, =C$\underline{C}$H$_3$), 20.8 (q, =C$\underline{C}$H$_3$*), 23.11 (t, NCH$_2\underline{C}$H$_2$CH$_2$*), 23.13 (t, NCH$_2\underline{C}$H$_2$CH$_2$), 27.9 (q, CH$_3$N), 28.0 (q, CH$_3$N*), 28.5 (t, NCH$_2$CH$_2\underline{C}$H$_2$, NCH$_2$CH$_2\underline{C}$H$_2$*), 31.7 (t, =C$\underline{C}$H$_2$), 32.1 (t, =C$\underline{C}$H$_2$*), 37.5 (t, $\underline{C}$H$_{2bridge}$), 37.9 (t, $\underline{C}$H$_{2bridge}$*), 48.6 (d, CH$_{bridge}$), 48.8 (d, CH$_{bridge}$*), 55.0 (t, N$\underline{C}$H$_2$CH$_2$CH$_2$), 55.1 (t, N$\underline{C}$H$_2$CH$_2$CH$_2$*), 56.76 (t, C$\underline{C}$H$_2$N), 56.79 (t, C$\underline{C}$H$_2$N*), 57.3 (q, OCH$_3$), 57.6 (q, OCH$_3$*), 62.37 (s, C$_{Pro}$), 62.43 (s, C$_{Pro}$*), 65.4 (s, C$_{bridgehead}$), 65.5 (s, C$_{bridgehead}$*), 105.8 (d, $\underline{C}$HOCH$_3$), 106.1 (d, $\underline{C}$HOCH$_3$*), 116.71 (t, CH$_2$=), 116.73 (t, CH$_2$=*), 121.3 (d, =CH), 121.4 (d, =CH*), 145.6 (s, CH$_3\underline{C}$=, CH$_3\underline{C}$=*), 163.2 (s, =$\underline{C}$CH$_2$), 163.6 (s, =$\underline{C}$CH$_2$*), 171.10 (s, NC=O), 171.11 (s, NC=O*), 175.7 (s, COO), 175.9 (s, COO*).

(2*S*,3*R*,5a'*R*,8a'*R*,9a'*R*)-2-Methoxy-8',8',11'-trimethyltetrahydro-1'*H*,2*H*,5'*H*,6'*H*,8'*H*-spiro[furan-3,7'-[5a,9a](epiminomethano)cyclopenta[*f*]indolizine]-5,10'(4*H*)-dione (23a)

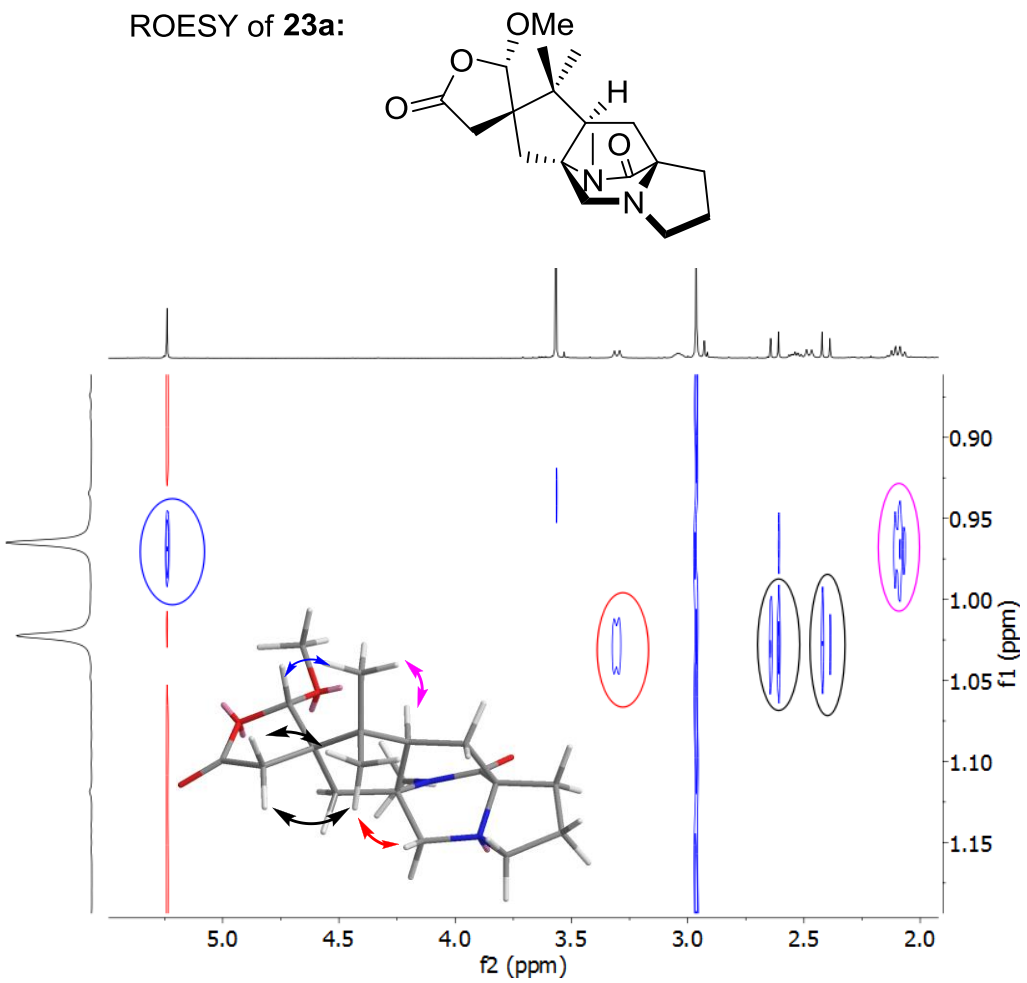


Compound **22** (30 mg, 0.087 mmol) was dissolved in dry methanol (4 mL). Fe(acac)$_3$ (30 mg, 0.087 mmol) was added followed by PhSiH$_3$ (27 μL, 0.097 mmol) at r.t. Vigorous gas evolution was observed. The reaction mixture was immersed to an oil bath preheated to 65 °C and refluxed

for 2 h. The reaction mixture was cooled to r.t., evaporated to dryness and the residue was purified by column chromatography (CH_2Cl_2/MeOH = 50/1 gradient to 20/1) to obtain first 13 mg (43%) of **23b** as colorless oil, 3 mg (10%) of a 4:1 mixure of **23a** and **23b**, followed by 9 mg (30%) of **23a** as colorless oil. Overall yield 83%.

Compound 23a: **R*f*** = 0.4 (CH_2Cl_2/MeOH = 8/1). **IR: *ν* (cm^{-1})** 2950, 2840, 1785, 1647, 1457, 1380, 1201, 1145, 940, 722. **MS ESI+ m/z, (%):** 371 (30, $[M+Na]^+$), 349 (100, $[M+H]^+$). **HRMS ESI+ *m/z,*** ($[M+Na]^+$): calcd. for $C_{19}H_{28}O_4N_2Na$: 371.1941, found: 371.1941. **^{1}H NMR (400 MHz, $CDCl_3$)**: δ = 0.97 (s, 3H, CCH_3), 1.02 (s, 3H, CCH_3), 1.34-1.45 (m, 2H, $NCH_2CH_2\underline{CH_2}$, $\underline{CH}_{2cyclopentane}$), 1.57-1.67 (m, 1H, $\underline{CH}_{2bridge}$), 1.82-1.91 (m, 3H, $NCH_2\underline{CH_2}CH_2$, $\underline{CH}_{2bridge}$), 2.04-2.17 (m, 2H, $N\underline{CH_2}CH_2CH_2$, CH_{bridge}), 2.41 (d, J = 17.0 Hz, 1H, $\underline{CH_2}C{=}O$), 2.48 (d, 1H, J = 11.0 Hz, $C\underline{CH_2}N$), 2.50-2.57 (m, 1H, $NCH_2CH_2\underline{CH_2}$), 2.63 (d, J = 17.0 Hz, 1H, $\underline{CH_2}C{=}O$), 2.94 (d, 1H, J = 15.0 Hz, $\underline{CH}_{2cyclopentane}$), 2.96 (s, 3H, NCH_3), 3.00-3.08 (m, 1H, $N\underline{CH_2}CH_2CH_2$), 3.30 (d, J = 11.1 Hz, 1H, $C\underline{CH_2}N$), 3.57 (s, 3H, OCH_3), 5.24 (s, 1H, $O\underline{CH}OCH_3$). **^{13}C NMR (101 MHz, $CDCl_3$)**: δ = 20.3 (q, $C\underline{C}H_3$), 22.2 (t, $NCH_2\underline{C}H_2CH_2$), 24.4 (q, $C\underline{C}H_3$), 25.7 (q, NCH_3), 28.1 (t, $NCH_2CH_2\underline{C}H_2$), 28.9 (t, $\underline{C}H_{2bridge}$), 34.5 (t, $CH_{2cyclopentane}$), 38.0 (t, $\underline{C}H_2C{=}O$), 41.3 (s, $\underline{C}(CH_3)_2$), 53.8 (t, $N\underline{C}H_2CH_2CH_2$), 55.9 (d, CH_{bridge}), 57.7 (q, OCH_3), 57.8 (s, C_{spiro}), 58.2 (t, $C\underline{C}H_2N$), 63.9 (s, C_{Pro}), 66.9 (s, $C_{bridgehead}$), 108.1 (d, $O\underline{C}HOCH_3$), 173.02 (s, NC=O), 173.05 (s, OC=O).

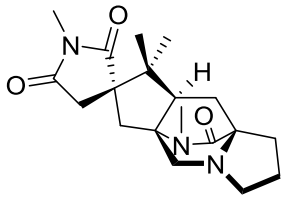
Compound 23b: **R*f*** = 0.45 (CH_2Cl_2/MeOH = 8/1). **MS ESI+ m/z, (%)**: 371 (30, $[M+Na]^+$), 349 (100, $[M+H]^+$). **HRMS ESI+ *m/z,*** ($[M+Na]^+$): calcd. for $C_{19}H_{28}O_4N_2Na$: 371.1941, found: 371.1938. **IR: *ν* (cm^{-1})** 2946, 2843, 1785, 1657, 1457, 1390, 1205, 1132, 946, 732. **^{1}H NMR (400 MHz, $CDCl_3$)**: δ = 0.93 (s, 3H, CCH_3), 1.11 (s, 3H, CCH_3), 1.33-1.42 (m, 1H, $NCH_2CH_2\underline{CH_2}$), 1.63 (dd, J = 12.2, 8.8 Hz, 1H, $\underline{CH}_{2bridge}$), 1.83-1.93 (m, 4H, $NCH_2\underline{CH_2}CH_2$, CH_{bridge}, $\underline{CH}_{2bridge}$), 1.95 (d, J = 15.4 Hz, 1H, $\underline{CH}_{2cyclopentane}$), 2.06-2.15 (m, 1H, $N\underline{CH_2}CH_2CH_2$), 2.26 (d, J = 15.4 Hz, 1H, $\underline{CH}_{2cyclopentane}$), 2.43-2.58 (m, 3H, $NCH_2CH_2\underline{CH_2}$, $\underline{CH_2}C{=}O$, $C\underline{CH_2}N$), 2.71 (d, J = 17.0 Hz, 1H, $\underline{CH_2}C{=}O$), 2.91 (s, 3H, NCH_3), 2.99-3.07 (m, 1H, $N\underline{CH_2}CH_2CH_2$), 3.29 (d, J = 11.3 Hz, 1H, $C\underline{CH_2}N$), 3.53 (s, 3H, OCH_3), 5.24 (s, 1H, $O\underline{CH}OCH_3$). **^{13}C NMR (101 MHz, $CDCl_3$)**: δ = 19.4 (q, $C\underline{C}H_3$), 22.2 (t, $NCH_2\underline{C}H_2CH_2$), 24.9 (q, $C\underline{C}H_3$), 26.0 (q, NCH_3), 28.1 (t, $NCH_2CH_2\underline{C}H_2$), 28.4 (t, $\underline{C}H_{2bridge}$), 35.5 (t, $CH_{2cyclopentane}$), 40.0 (t, $\underline{C}H_2C{=}O$), 41.8 (s, $\underline{C}(CH_3)_2$), 53.7 (t, $N\underline{C}H_2CH_2CH_2$), 56.1 (d, CH_{bridge}), 57.1 (q, OCH_3), 57.2 (s, C_{spiro}), 57.6 (t, $C\underline{C}H_2N$), 63.5 (s, C_{Pro}), 66.9 (s, $C_{bridgehead}$), 107.2 (d, $O\underline{C}HOCH_3$), 173.5 (s, NC=O), 174.2 (s, OC=O).



Scheme S2. Excerpt from ROESY spectra of compound **23a**

(3'*R*,5a*R*,8a*R*,9a*R*)-Tetrahydro-1',8,8,11-tetramethylspiro[5*H*,6*H*-5a,9a-(iminomethano)-1*H*-cyclopenta[*f*]indolizine-7(8*H*),3'-pyrrolidine]-2',5',10-trione (*ent*-4)

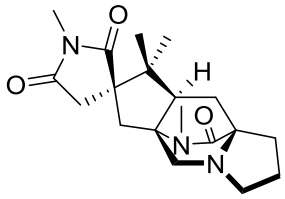
(+)-*ent*-Asperparaline C



Compound **23a** (9.0 mg, 0.026 mmol) was dissolved in dry methanol (1 mL) and $MeNH_2$ solution (129 µL, 0.26 mmol, 2M in MeOH) was added at r.t. under Ar. The reaction mixture was stirred for 3 h and evaporated. The residue was dissolved in dry CH_2Cl_2 (1 mL), PCC was added (0.08 mmol, 17 mg), and the mixture was stirred at r.t. for 1 h. The reaction mixture was filtered through a pad of Celite®, which was thoroughly washed with CH_2Cl_2. The filtrates were evaporated to dryness and the residue was purified first by column chromatography (CH_2Cl_2/MeOH = 19/1

gradient to 10/1) followed by passing through a pad of Amberlite IRN-78 eluting with MeOH to obtain 5.9 mg (66%) of *ent*-**4** as colorless oil. **R*f*** = 0.4 (CH_2Cl_2/MeOH = 10/1). **[α]$^{20}_{D}$** = + 26.3 (*c* 0.316, MeOH). Lit.[4] $[\alpha]^{20}_{D}$ = – 20 (*c* 0.05, MeOH). **IR: *ν* (cm^{-1})** 2942, 1772, 1697, 1656, 1435, 1384, 1283, 1114, 696. **MS ESI+ m/z, (%)**: 713 (15, $[2M+Na]^+$), 368 (65, $[M+Na]^+$), 346 (100, $[M+H]^+$). **HRMS ESI+ *m/z,*** ($[M+H]^+$): calcd. for $C_{19}H_{28}O_3N_3$ = 346.2125, found: 346.2126. **MS EI m/z, (%)**: 345 (M^+, 8), 317 ($[M–CO]^+$, 10), 302 ($[M–CH_3–CO]^+$, 25), 286 ($[M–CONHCH_3–H]^+$, 90), 285 (100), 273 ($[M–CH_3–CH_3NCO]^+$, 221 (5), 163 (5), 149 (10), 133 (80). **^{1}H NMR (600 MHz, C_5D_5N)**: *δ* = 0.80 (s, 3H, CCH_3), 1.01 (s, 3H, CCH_3), 1.39-1.47 (m, 1H, $NCH_2CH_2\underline{CH_2}$), 1.59-1.62 (m, 1H, $\underline{CH_{2bridge}}$), 1.65 (d, *J* = 15.5 Hz, 1H, $\underline{CH_{2cyclopentane}}$), 1.65-1.71 (m, 1H, $\underline{CH_{2\ bridge}}$), 1.76-1.85 (m, 1H, $NCH_2\underline{CH_2}CH_2$), 1.88-1.96 (m, 1H, $NCH_2\underline{CH_2}CH_2$), 2.18-2.25 (m, 1H, $N\underline{CH_2}CH_2CH_2$), 2.47 (d, *J* = 11.0 Hz, 1H, $C\underline{CH_2}N$), 2.71 (d, *J* = 18.2 Hz, 1H, $\underline{CH_2}C{=}O$), 2.78 (d, *J* = 15.5 Hz, 1H, $\underline{CH_{2cyclopentane}}$), 2.78-2.85 (m, 1H, $NCH_2CH_2\underline{CH_2}$), 2.92-2.96 (m, 1H, CH_{bridge}), 2.97 (s, 3H, $N_{imide}CH_3$), 2.97-3.04 (m, 1H, $N\underline{CH_2}CH_2CH_2$), 3.09 (d, *J* = 18.2 Hz, 1H, $\underline{CH_2}C{=}O$), 3.19 (s, 3H, NCH_3), 3.33 (d, *J* = 11.0 Hz, 1H, $C\underline{CH_2}N$). **^{13}C NMR (151 MHz, C_5D_5N)**: *δ* = 19.7 (q, $C\underline{C}H_3$), 22.9 (t, $NCH_2\underline{C}H_2CH_2$), 23.6 (q, $C\underline{C}H_3$), 24.6 (q, $N_{imide}CH_3$), 26.1 (q, NCH_3), 28.6 (t, $NCH_2CH_2\underline{C}H_2$), 29.4 (t, $\underline{C}H_{2bridge}$), 38.5 (t, $CH_{2succinimide}$), 38.8 (t, $CH_{2cyclopentane}$), 44.6 (s, $\underline{C}(CH_3)_2$), 53.8 (t, $N\underline{C}H_2CH_2CH_2$), 54.7 (d, CH_{bridge}), 58.3 (s, C_{spiro}), 58.8 (t, $C\underline{C}H_2N$), 65.0 (s, C_{Pro}), 67.1 (s, $C_{bridgehead}$), 173.0 (s, NC=O), 175.8 (s, $CH_2\underline{C}{=}O_{imide}$), 182.3 (s, $C\underline{C}{=}O_{imide}$).

(3'*S*,5a*R*,8a*R*,9a*R*)-Tetrahydro-1',8,8,11-tetramethylspiro[5*H*,6*H*-5a,9a-(iminomethano)-1*H*-cyclopenta[*f*]indolizine-7(8*H*),3'-pyrrolidine]-2',5',10-trione (25)



Prepared according to the procedure for *ent*-**4** from **23b** (12.0 mg, 0.034 mmol). Purification by column chromatography (CH_2Cl_2/MeOH = 95/5 gradient to 10/1) followed by passing through a pad of Amberlite IRN-78 eluting with MeOH gave 9.1 mg (77%) of compound **25** as a colorless oil. **R*f* =** 0.4 (CH_2Cl_2/MeOH = 10/1). **[α]$^{20}_{D}$** = + 1.5 (*c* 0.340, MeOH). **IR: *ν* (cm^{-1})** 2933, 1773, 1699, 1655, 1434, 1381, 1320, 1278, 1153, 1106. **MS ESI+ m/z, (%)**: 346 (100, $[M+H]^+$). **MS EI m/z, (%)**: 345 (M^+, 5), 317 ($[M–CO]^+$, 8), 302 ($[M–HNCO]^+$,15), 286 ($[M–CONHCH_3–H]^+$, 100), 285 (98), 273 ($[M–CH_3–CH_3NCO]^+$, 10), 221 (18), 163 (5), 149 (8), 133 (65). **HRMS ESI+ *m/z,*** ($[M+H]^+$): Calcd. for $C_{19}H_{28}O_3N_3$ = 346.2125, found: 346.2124. **^{1}H NMR (600 MHz, C_5D_5N)**: *δ*

= 0.85 (s, 3H, CCH_3), 1.16 (s, 3H, CCH_3), 1.40-1.47 (m, 1H, $NCH_2CH_2\underline{CH_2}$), 1.61-1.72 (m, 2H, $\underline{CH_{2bridge}}$), 1.75-1.84 (m, 1H, $NCH_2\underline{CH_2}CH_2$), 1.86-1.93 (m, 1H, $NCH_2\underline{CH_2}CH_2$), 1.96-2.03 (m, 1H, CH_{bridge}), 2.15-2.22 (m, 2H, $\underline{CH_2}C{=}O$, $N\underline{CH_2}CH_2CH_2$), 2.46 (d, *J* = 11.0 Hz, 1H, $C\underline{CH_2}N$), 2.51 (d, *J* = 14.7 Hz, 1H, $\underline{CH_2}C{=}O$), 2.70 (d, *J* = 17.4 Hz, 1H, $\underline{CH_{2cyclopentane}}$), 2.77-2.83 (m, 1H, $NCH_2CH_2\underline{CH_2}$), 2.89-3.02 (m, 1H, $N\underline{CH_2}CH_2CH_2$), 3.01 (s, 6H, NCH_3, $N_{imide}CH_3$), 3.22 (d, *J* = 17.4 Hz, 1H, $\underline{CH_{2cyclopentane}}$), 3.69 (d, *J* = 11.0 Hz, 1H, $C\underline{CH_2}N$). **^{13}C NMR (151 MHz, C_5D_5N)**: δ = 20.9 (q, $\underline{C}H_3$), 23.4 (t, $NCH_2\underline{C}H_2CH_2$), 24.6 (q, $\underline{C}H_3$), 25.2 (q, $N_{imide}CH_3$), 26.4 (q, NCH_3), 29.0 (t, $NCH_2CH_2\underline{C}H_2$), 29.3 (t, $\underline{C}H_{2bridge}$), 38.7 (t, $CH_{2succinimide}$), 42.9 (t, $CH_{2cyclopentane}$), 45.9 (s, $\underline{C}(CH_3)_2$), 54.2 (t, $N\underline{C}H_2CH_2CH_2$), 56.6 (d, CH_{bridge}), 58.1 (s, C_{spiro}), 58.2 (t, $C\underline{C}H_2N$), 65.3 (s, C_{Pro}), 67.6 (s, $C_{bridgehead}$), 173.8 (s, NC=O), 176.0 (s, $CH_2\underline{C}{=}O_{imide}$), 180.2 (s, $C\underline{C}{=}O_{imide}$).

Comparison of NMR data for isolated asperparaline C and synthesized *ent*-asperparaline C (*ent*-4) (numbering according to Hayashi *et al.*[5])

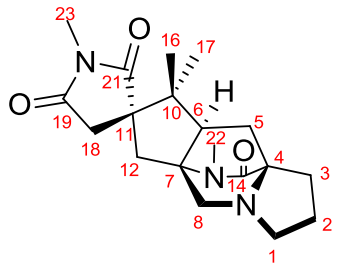


Table S1. ^{1}H NMR data in C_5D_5N

Position	asperparaline C/ppm	*ent*-asperparaline (*ent*-**4**)/ppm
1	2.21 (1H, m) 3.00 (1H, m)	2.22 (1H, m) 3.01 (1H,m)
2	1.80 (1H, m) 1.92 (1H, m)	1.80 (1H, m) 1.92 (1H, m)
3	1.42 (1H, m) 2.81 (1H, m)	1.42 (1H, m) 2.81 (1H, m)
5	1.60 (1H, dd, 12.5 Hz, 9.5 Hz) 1.76 (1H, dd, 12.5 Hz, 11.0 Hz)	1.60 (1H, m) 1.69 (1H, m)
6	2.94 (1H, ddd, 11.0 Hz, 9.5 Hz, 1.5 Hz)	2.94 (1H, m)
8	2.47 (1H, dd, 11.0 Hz, 1.5 Hz) 3.32 (1H, d, 11.0 Hz)	2.47 (1H, d, 11.0 Hz) 3.33 (1H, d, 11.0 Hz)
12	1.65 (1H, d, 15.0 Hz) 2.78 (1H, d, 15.0 Hz)	1.65 (1H, d, 15.5 Hz) 2.78 (1H, d, 15.5 Hz)
16	1.00 (3H, s)	1.01 (3H, s)
17	0.80 (3H, s)	0.80 (3H, s)
18	2.70 (1H, d, 18.3 Hz) 3.08 (1H, d, 18.3 Hz)	2.71 (1H, d, 18.2 Hz) 3.09 (1H, d, 18.2 Hz)
22	3.18 (3H, s)	3.19 (3H, s)
23	2.97 (3H, s)	2.97 (3H, s)

Table S2. ^{13}C NMR data in C_5D_5N

Position	asperparaline C/ppm	*ent*-asperparaline C (*ent*-**4**)/ppm
1	53.8 (t)	53.8 (t)
2	22.9 (t)	22.9 (t)
3	28.6 (t)	28.6 (t)
4	67.1 (s)	67.1 (s)
5	29.4 (t)	29.4 (t)
6	54.7 (d)	54.7 (d)
7	65.0 (s)	65.0 (s)
8	58.8 (t)	58.8 (t)
10	44.6 (s)	44.6 (s)
11	58.3 (s)	58.3 (s)
12	38.8 (t)	38.8 (t)
14	173.0 (s)	173.0 (s)
16	19.7 (q)	19.7 (q)
17	23.6 (q)	23.6 (q)
18	38.5 (t)	38.5 (t)
19	175.8 (s)	175.8 (s)
21	182.3 (s)	182.3 (s)
22	26.1 (q)	26.1 (q)
23	24.6 (q)	24.6 (q)

X-ray crystallography

Single-crystal diffraction data of **6** were collected on an Xcalibur X-ray diffractometer with $Cu_{K\alpha}$ (λ = 1.54180 Å) at 180 K. CrysAlisProCCD[6] was used for data collection, cell refinement and data reduction. The structure was solved by direct methods with SIR92[7] and refined by full-matrix least-squares on F with CRYSTALS.[8] The hydrogen atoms were located on a difference Fourier map; they were recalculated into idealized positions and refined with riding constraints. All non-hydrogen atoms were refined with anisotropic displacement parameters.

Crystal data for compound 6 (dimension 0.09 x 0.26 x 0.42 mm)**:**

$C_{19}H_{24}N_2O_4$, orthorhombic, space group $P2_12_12_1$, a = 8.2195(2) Å, b = 11.0955(3) Å, c = 18.8126(5) Å, V = 1715.70(8) Å^3, Z = 4, M = 344.41, 27100 reflections measured, 3244 independent reflections. Final R = 0.025, wR = 0.027, GoF = 1.073 for 3196 reflections with $I > 2\sigma(I)$ and 228 parameters, Flack parameter x = 0.09(13). The structure has been deposited at the Cambridge Crystallographic Database under the number CCDC 1875571.

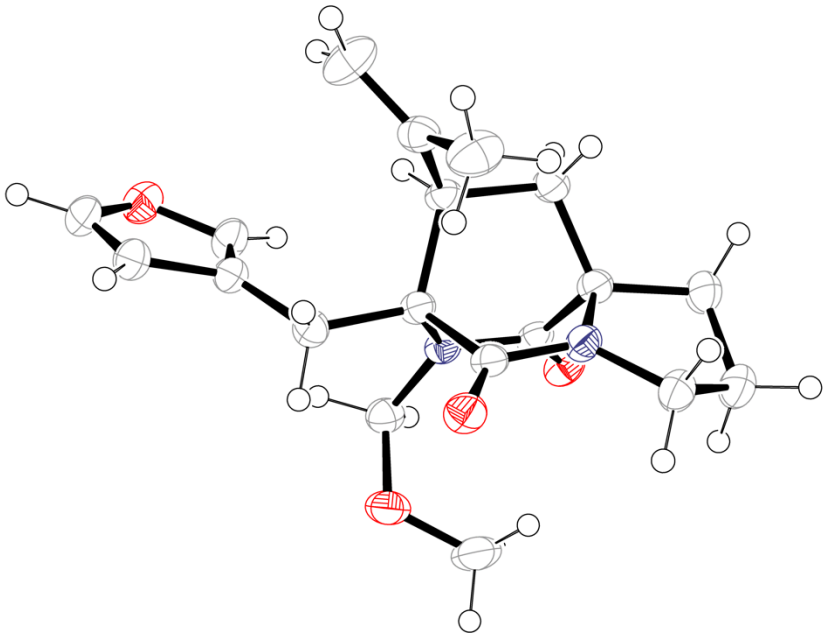


Figure S1: ORTEP[9] view of **6**, displacement ellipsoids shown at 50 % probability level.

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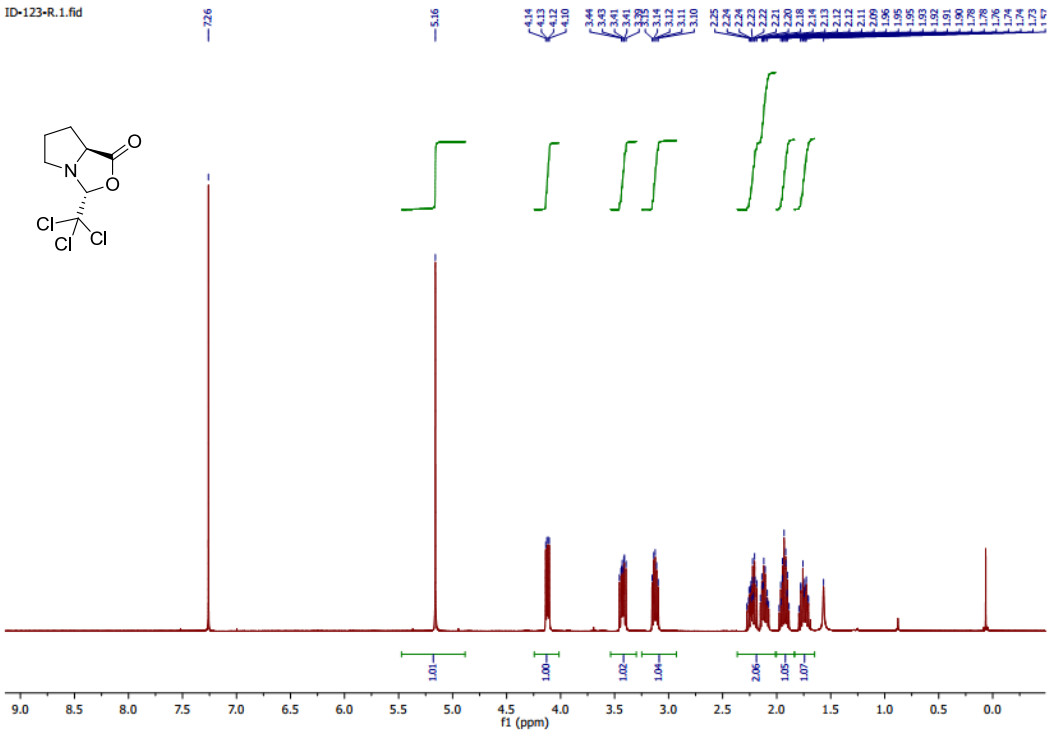
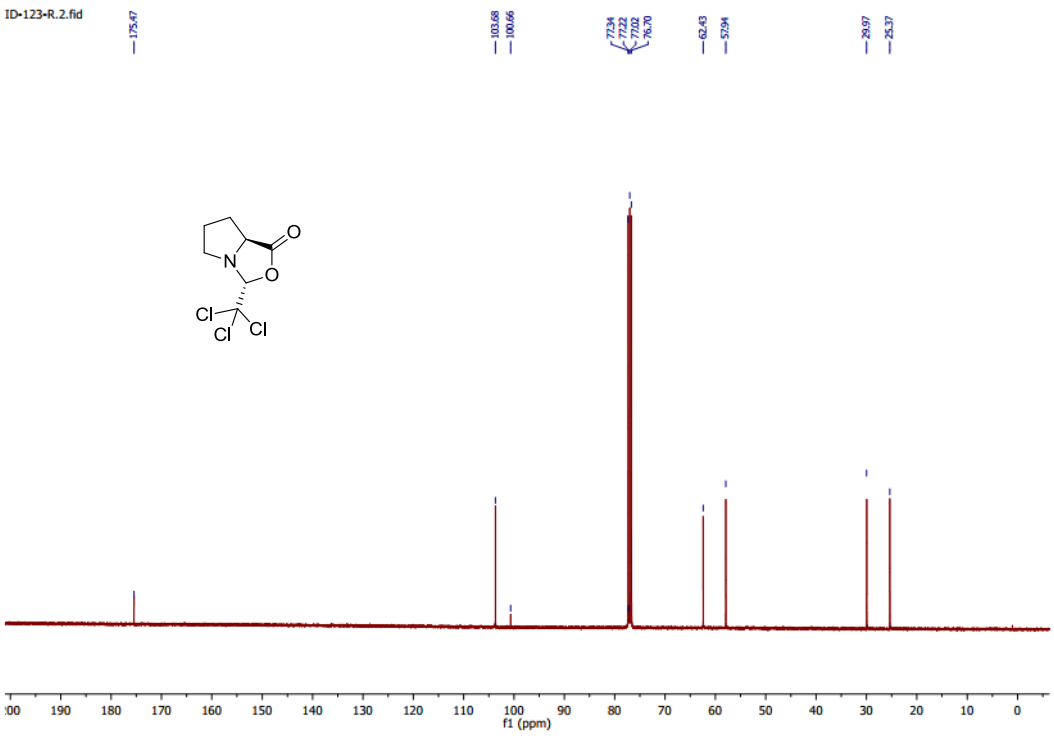
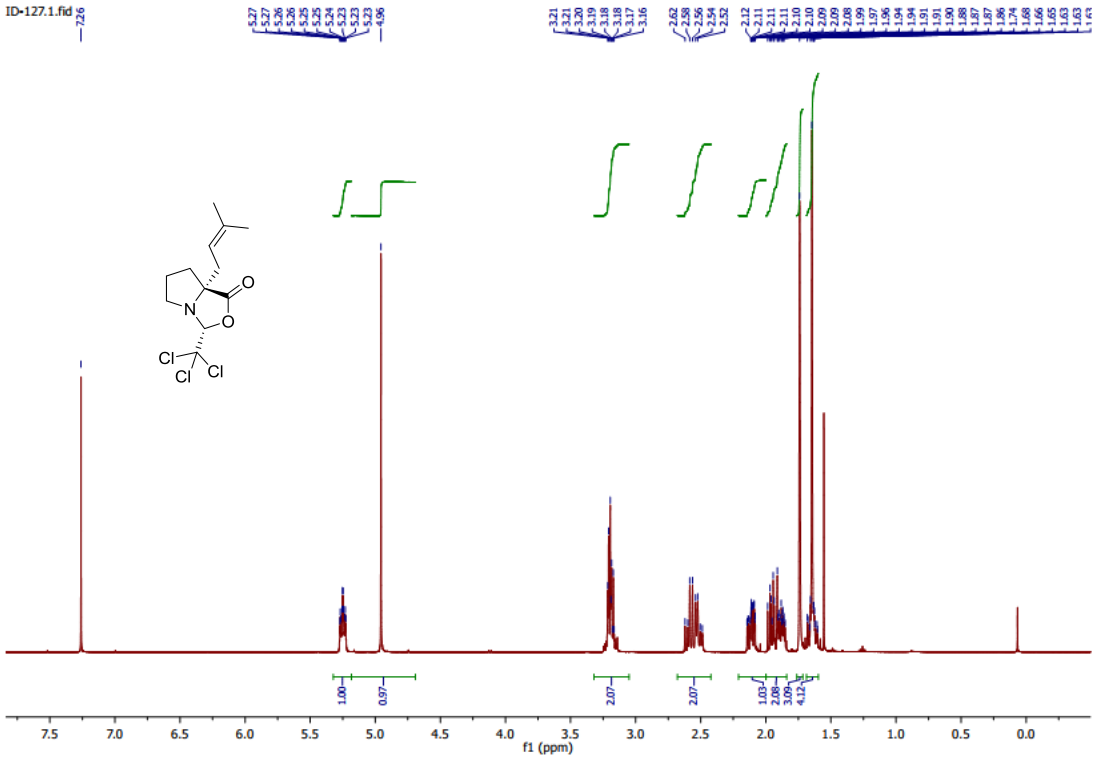
Copies of ^{1}H NMR and ^{13}C NMR spectra

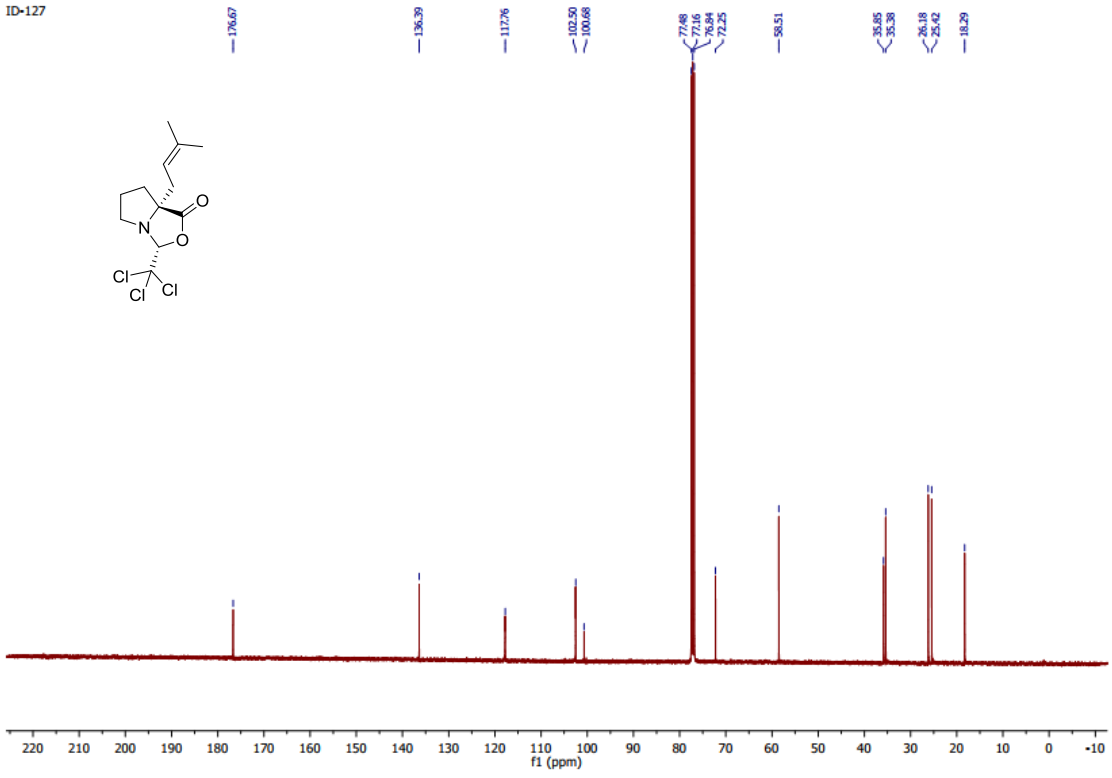
(3*R*,7a*S*)-7a-(3-Methylbut-2-en-1-yl)-3-(trichloromethyl)tetrahydropyrrolo[1,2-c]oxazol-1(3*H*)-one (9)



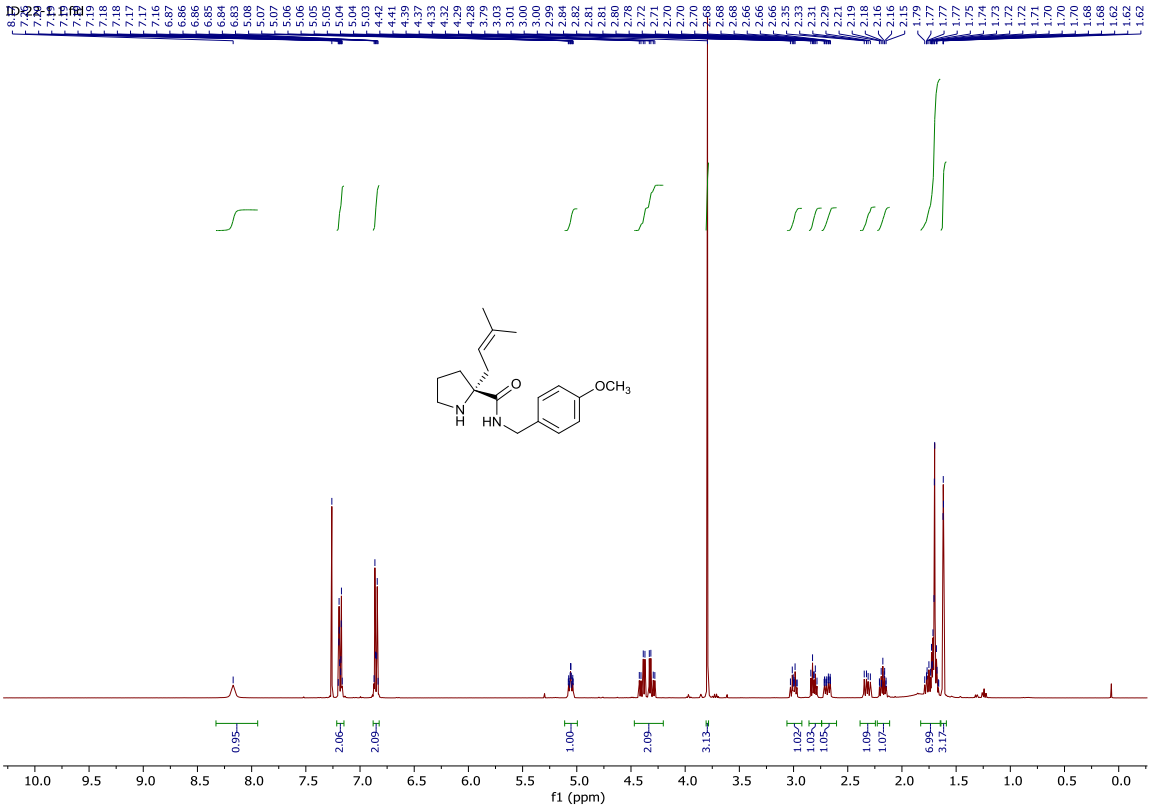


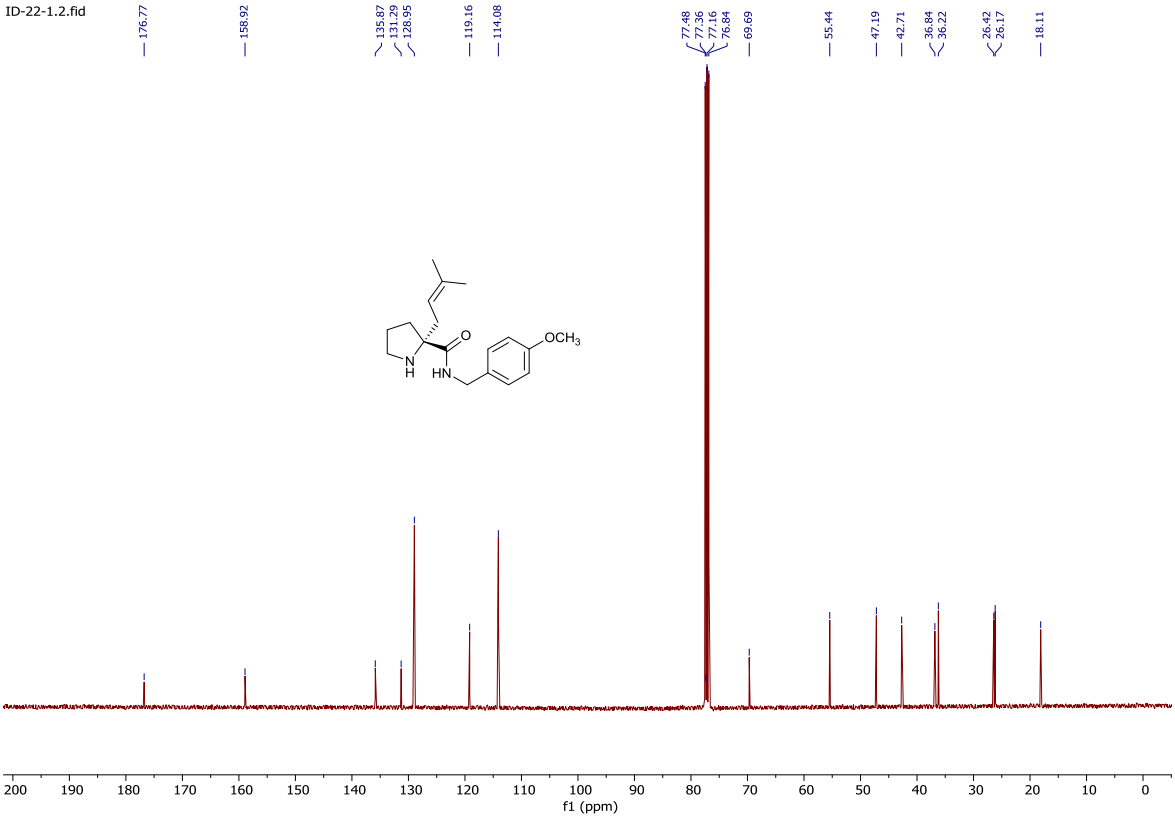
(3*R*,7a*R*)-7a-(3-Methylbut-2-en-1-yl)-3-(trichloromethyl)tetrahydro-1*H*,3*H*-pyrrolo[1,2-c]oxazol-1-one (10)



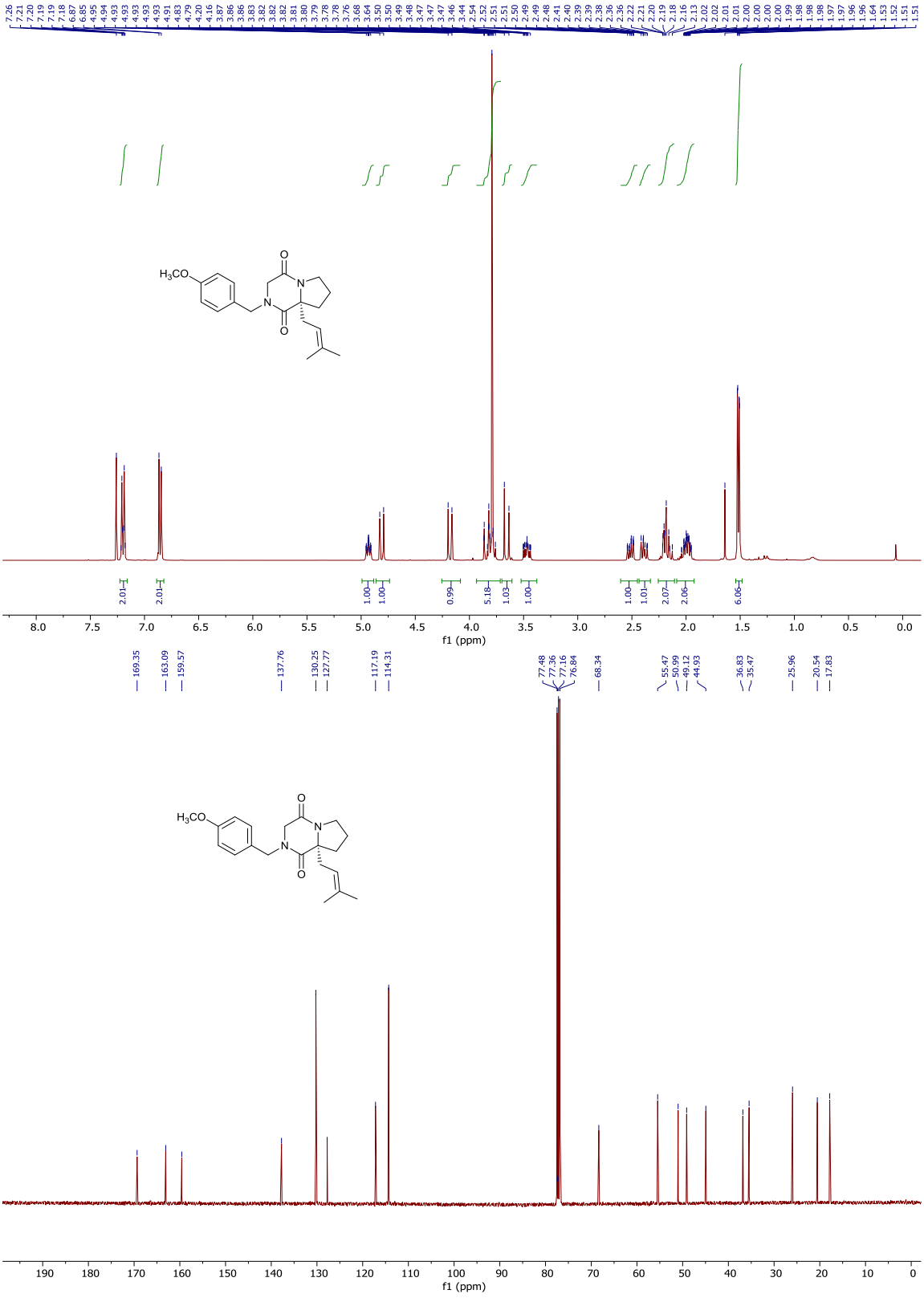


(*R*)-*N*-(4-methoxybenzyl)-2-(3-methylbut-2-en-1-yl)pyrrolidine-2-carboxamide (S2)

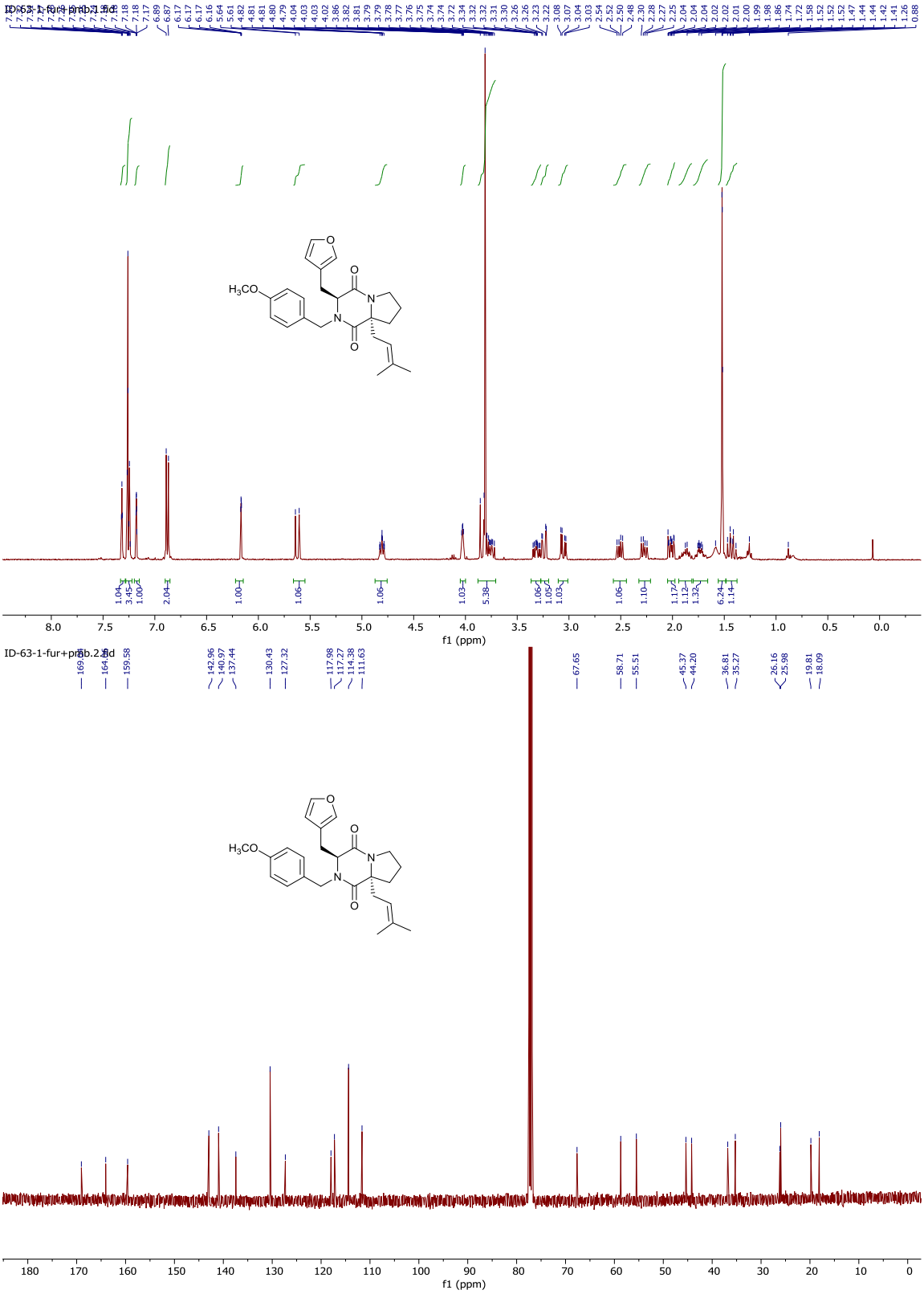




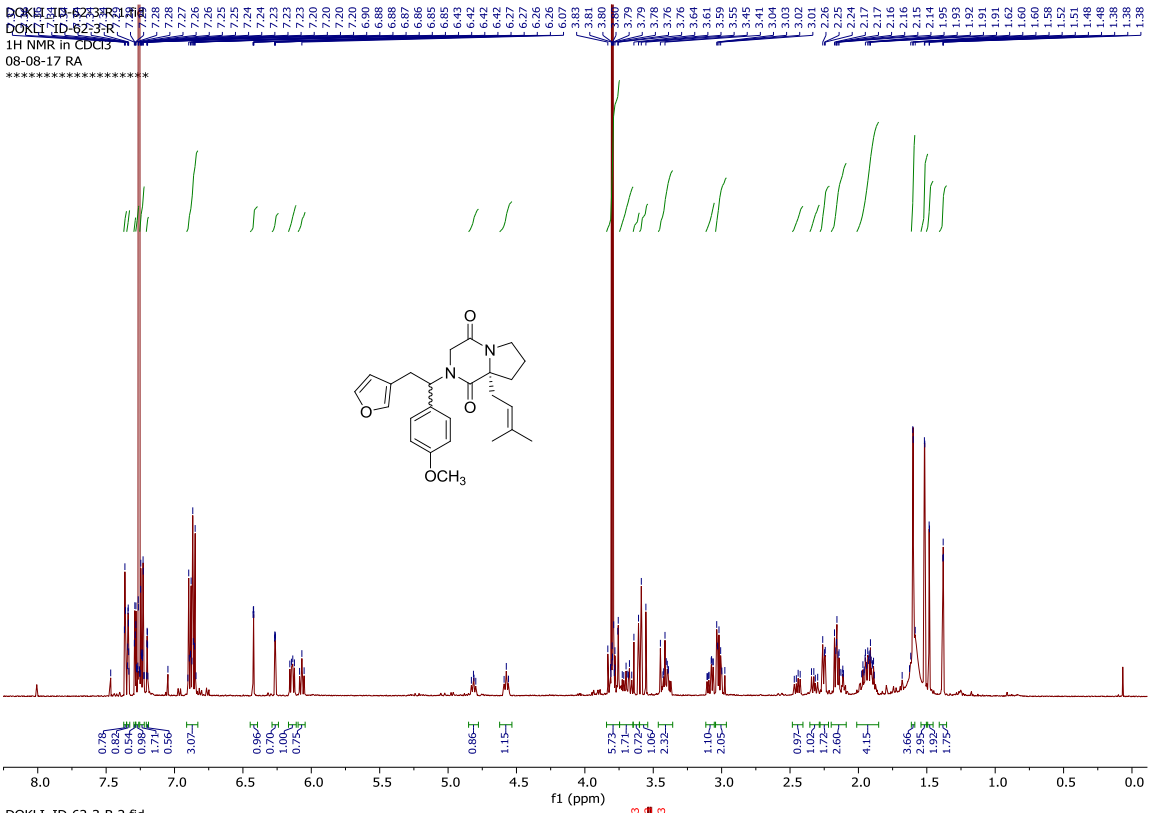
(*R*)-2-(4-Methoxybenzyl)-8a-(3-methylbut-2-en-1-yl)hexahydropyrrolo[1,2-a]pyrazine-1,4-dione (S4)

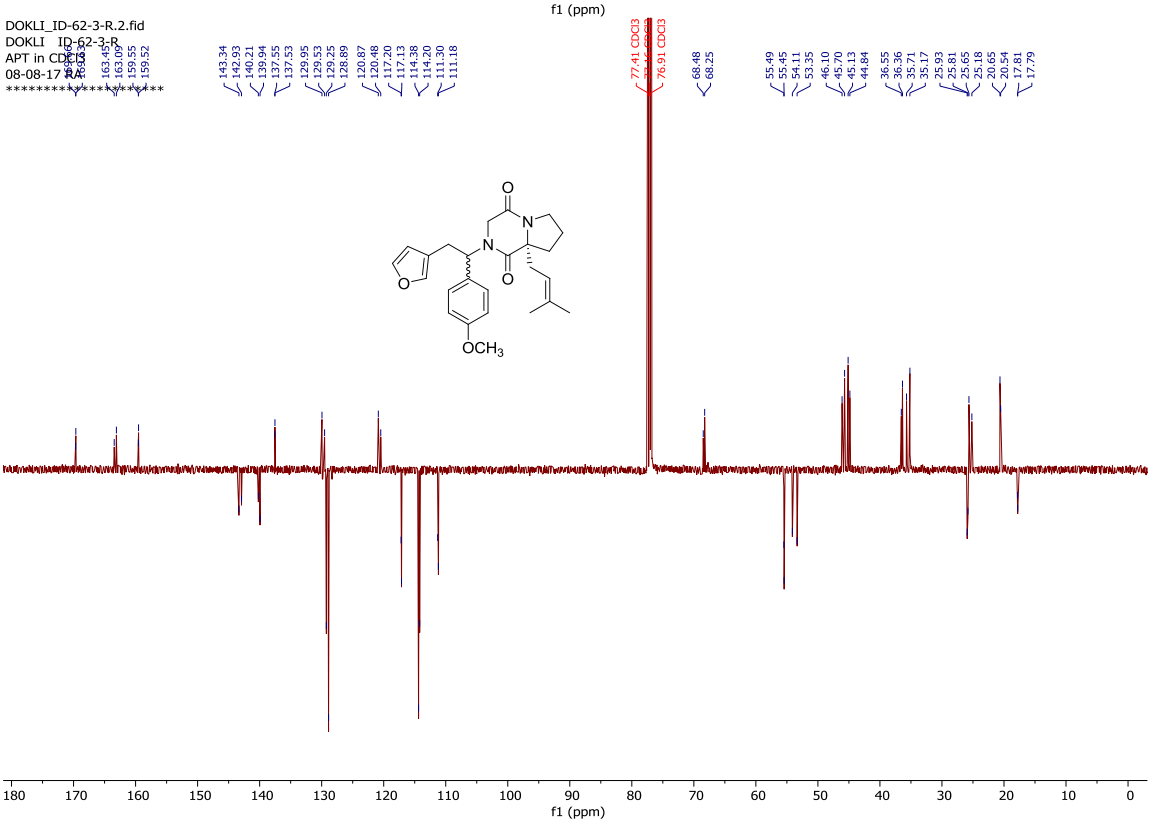


(3*S*,8a*R*)-3-(Furan-3-ylmethyl)-2-(4-methoxybenzyl)-8a-(3-methylbut-2-en-1-yl)hexahydropyrrolo[1,2-a]pyrazine-1,4-dione (S5)

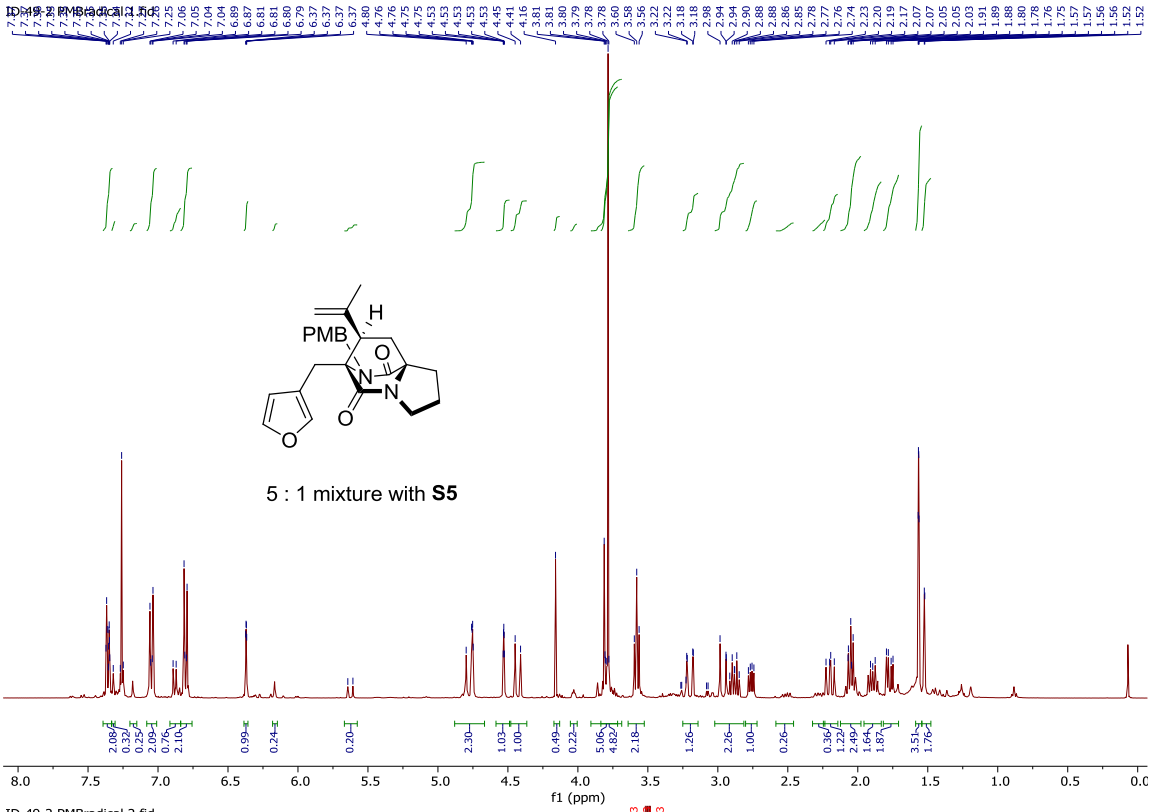


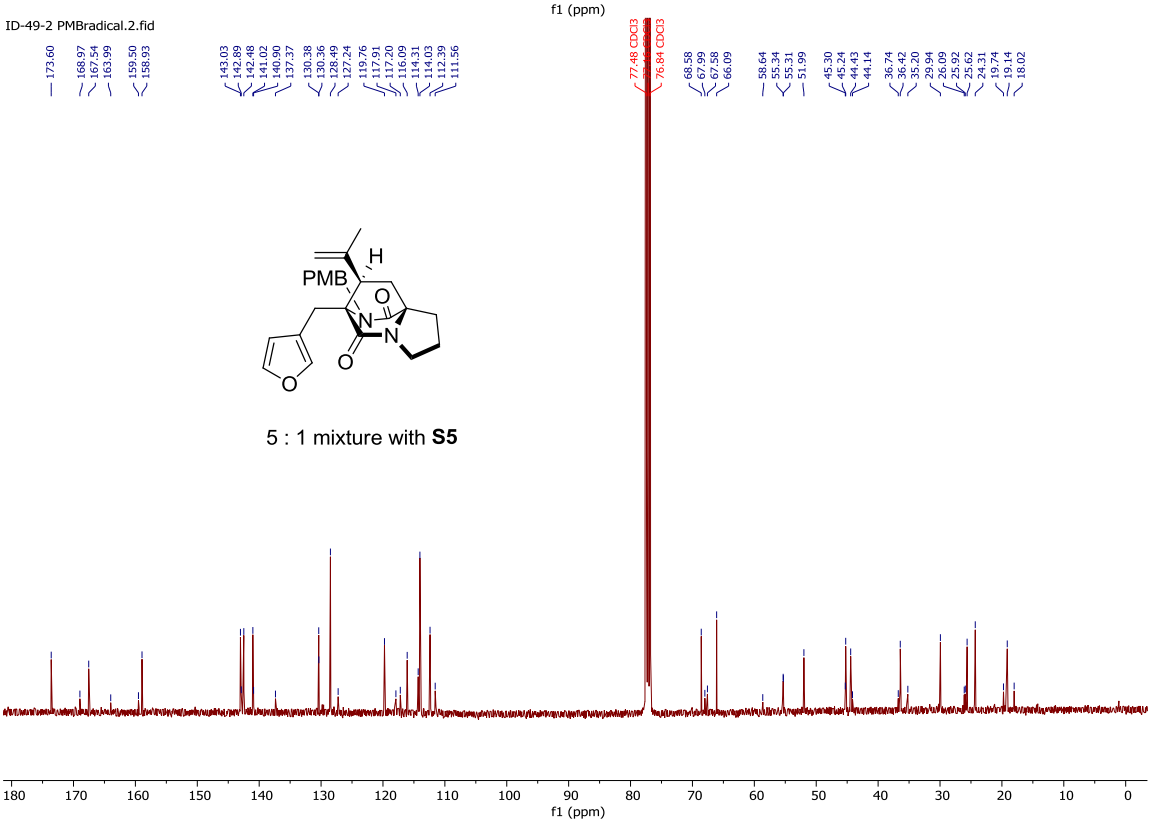
(*R*)-2-(2-(Furan-3-yl)-1-(4-methoxyphenyl)ethyl)-8a-(3-methylbut-2-enyl)hexahydropyrrolo[1,2-a]pyrazine-1,4-dione (S6)



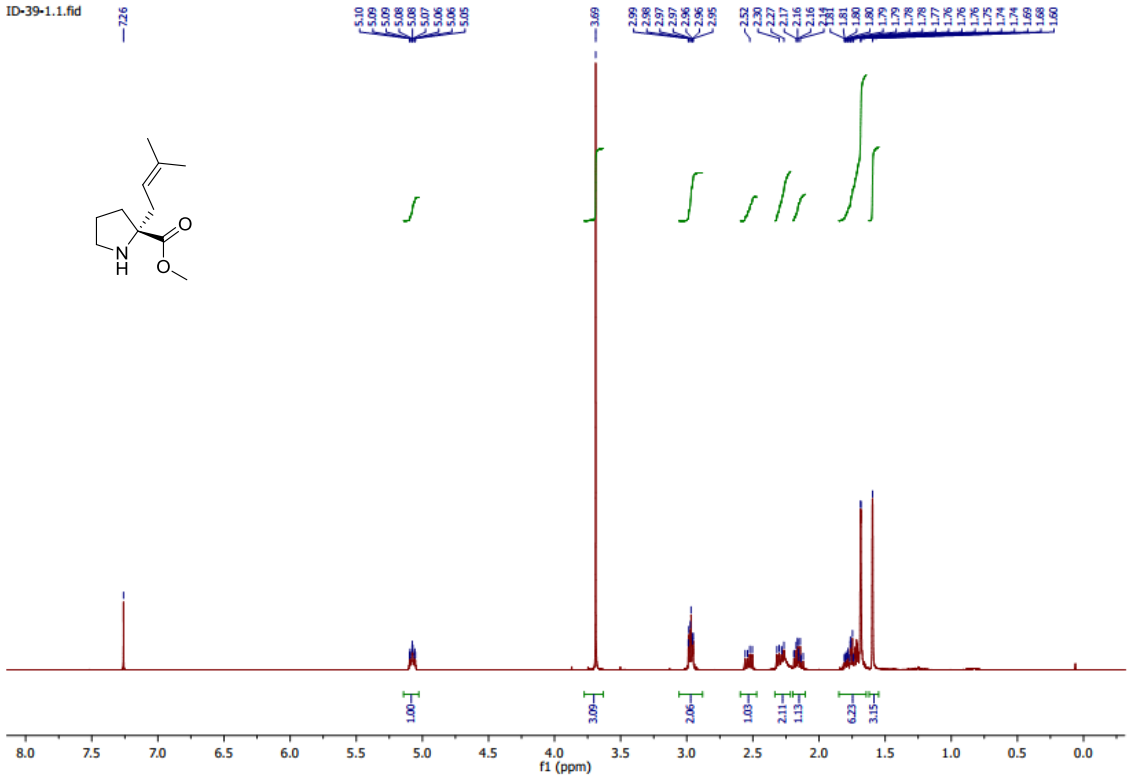


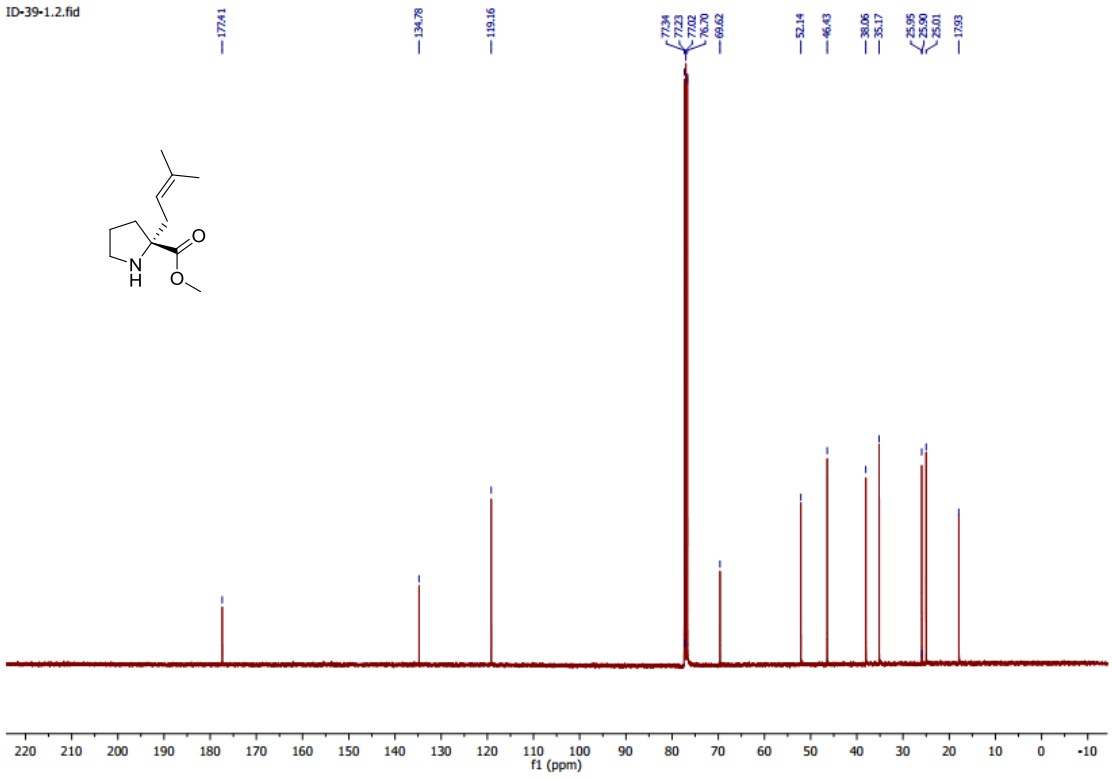
(6*R*,7*R*,8a*R*)-6-(Furan-3-ylmethyl)-10-(4-methoxybenzyl)-7-(prop-1-en-2-yl)tetrahydro-1*H*-6,8a-(epiminomethano)indolizine-5,9(6*H*)-dione (S7)



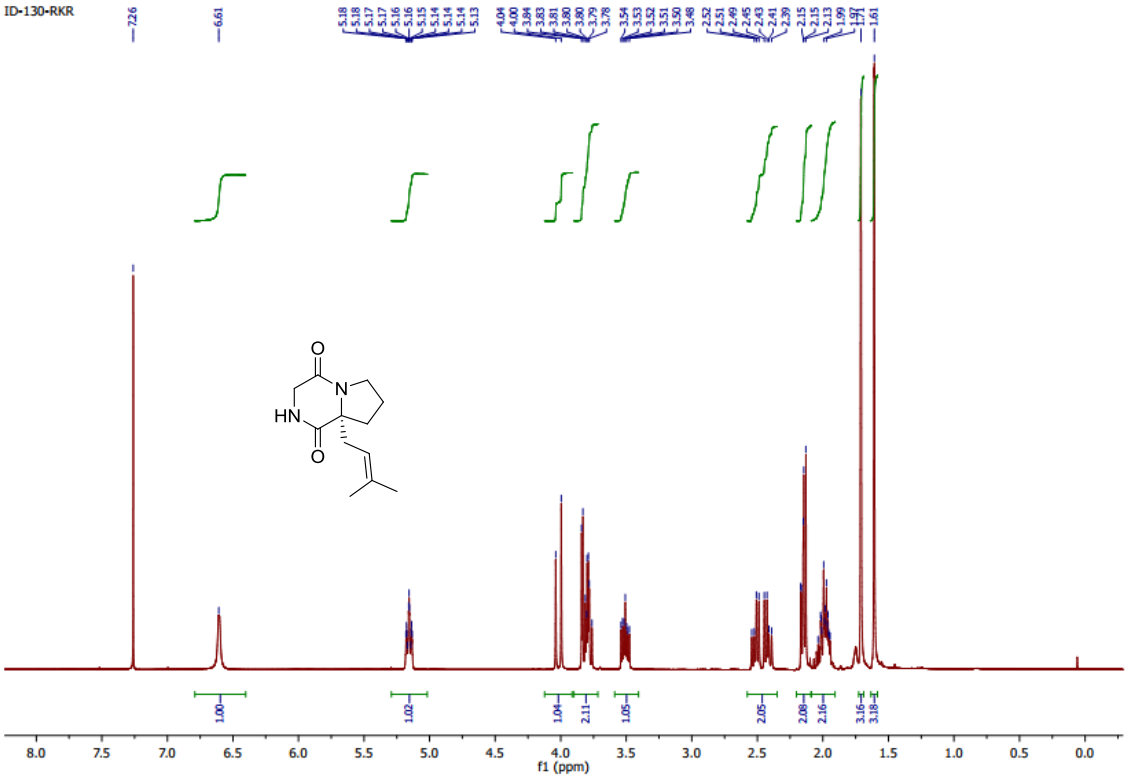


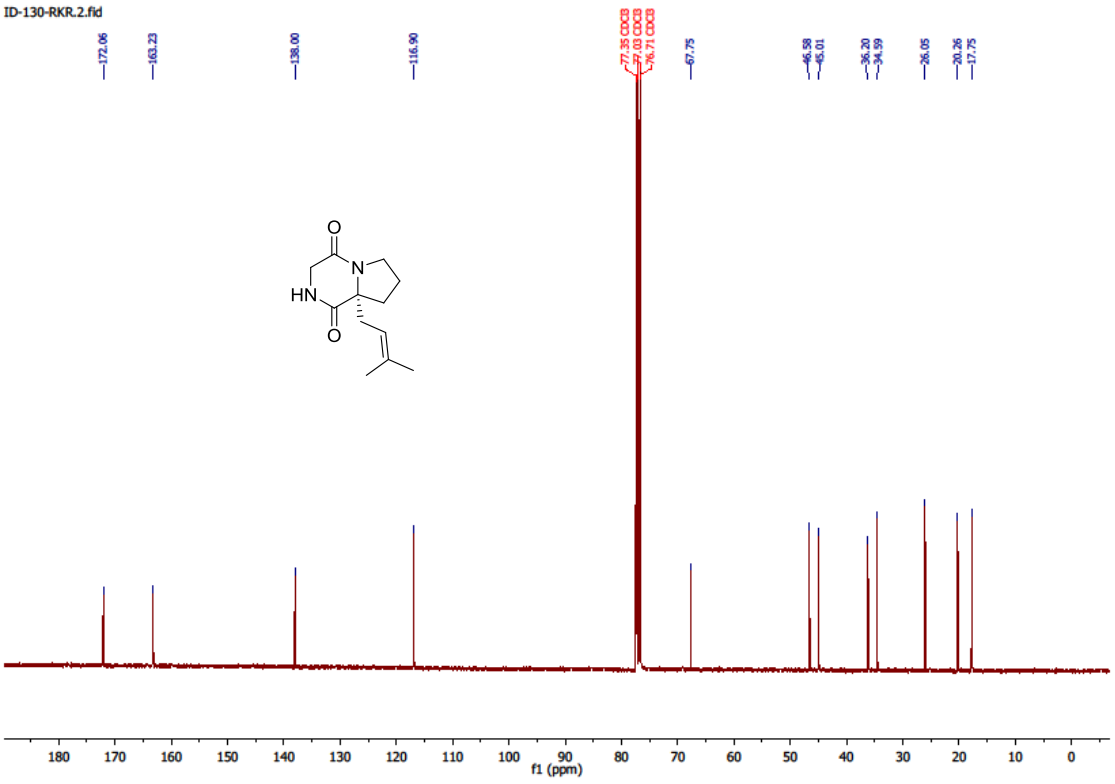
(*R*)-Methyl 2-(3-methylbut-2-en-1-yl)pyrrolidine-2-carboxylate (11)



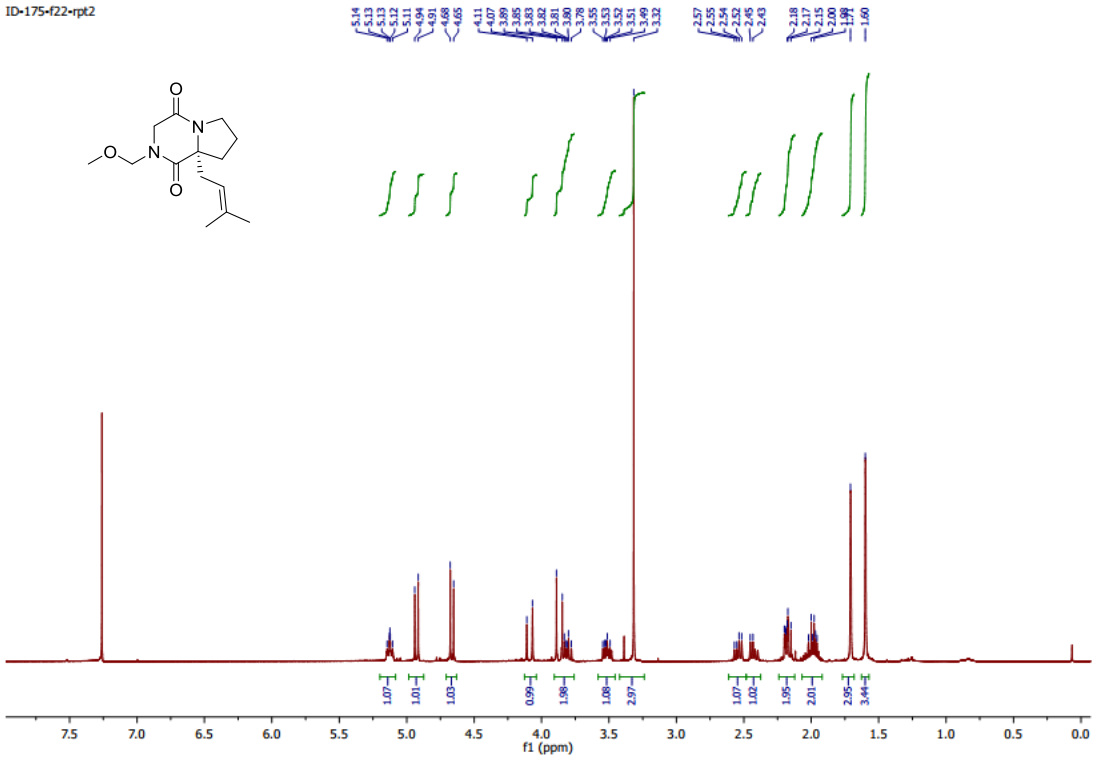


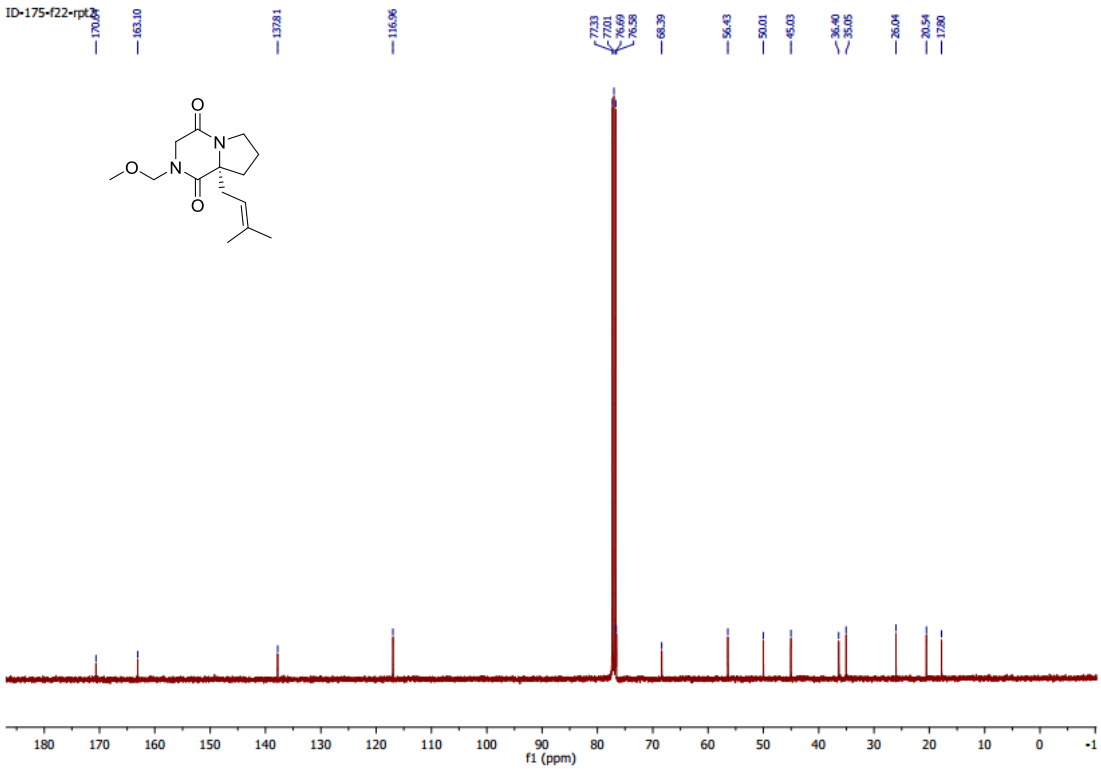
(*R*)-8a-(3-Methylbut-2-en-1-yl)hexahydropyrrolo[1,2-a]pyrazine-1,4-dione (16)



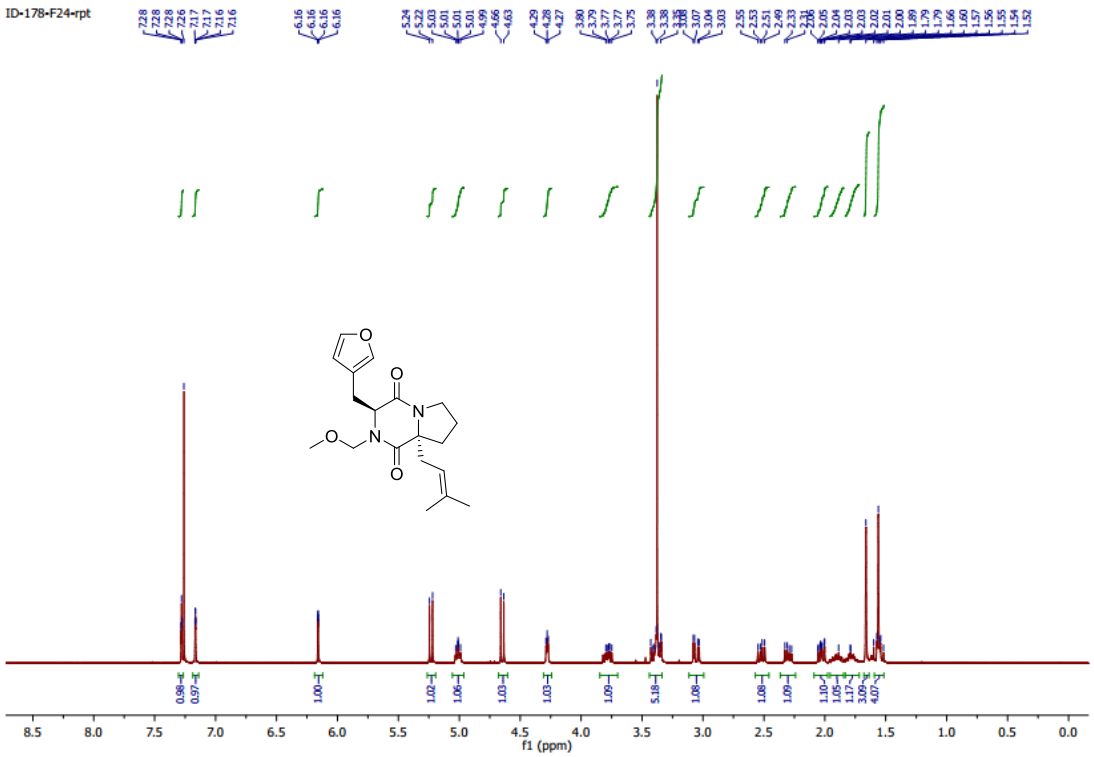


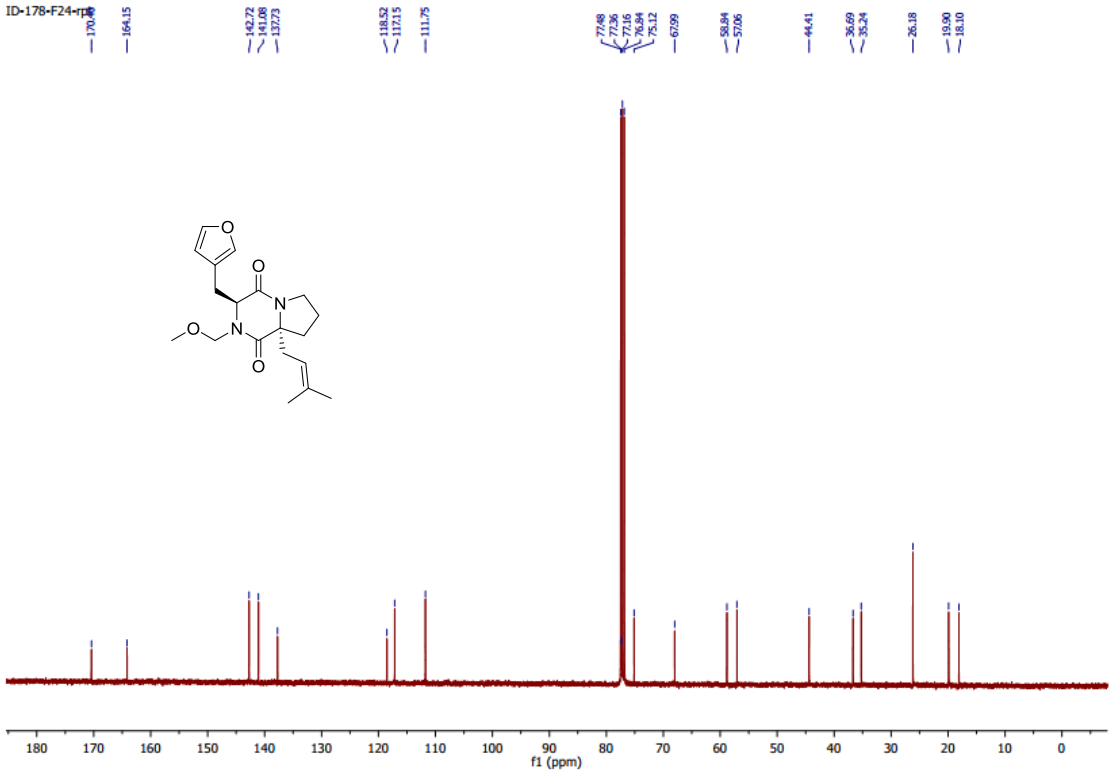
(*R*)-2-(Methoxymethyl)-8a-(3-methylbut-2-en-1-yl)hexahydropyrrolo[1,2-a]pyrazine-1,4-dione (17)



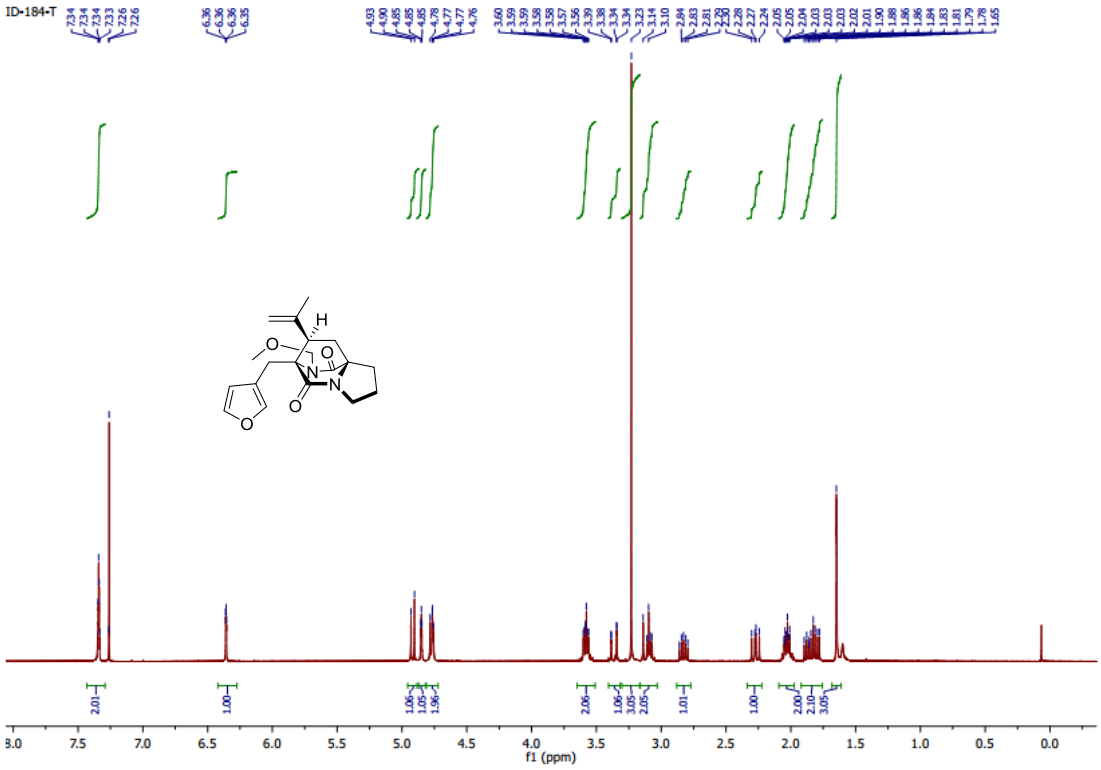


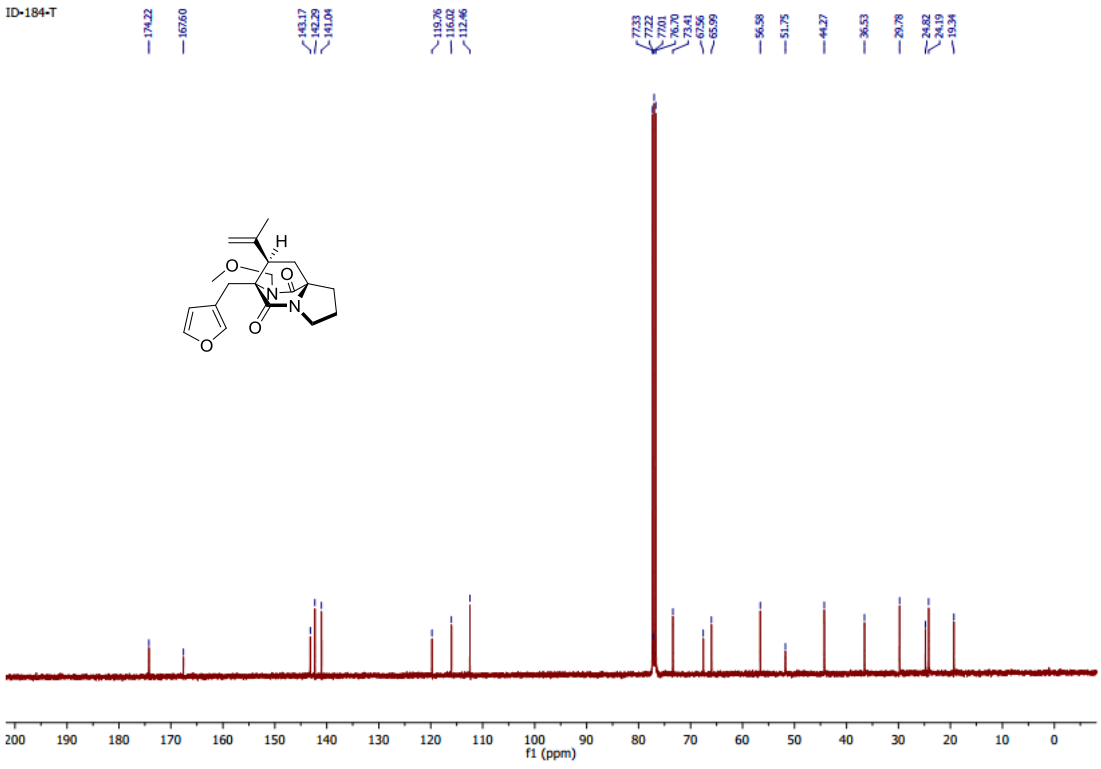
(3*S*,8a*R*)-3-(Furan-3-ylmethyl)-2-(methoxymethyl)-8a-(3-methylbut-2-en-1-yl)hexahydropyrrolo[1,2-a]pyrazine-1,4-dione (7)



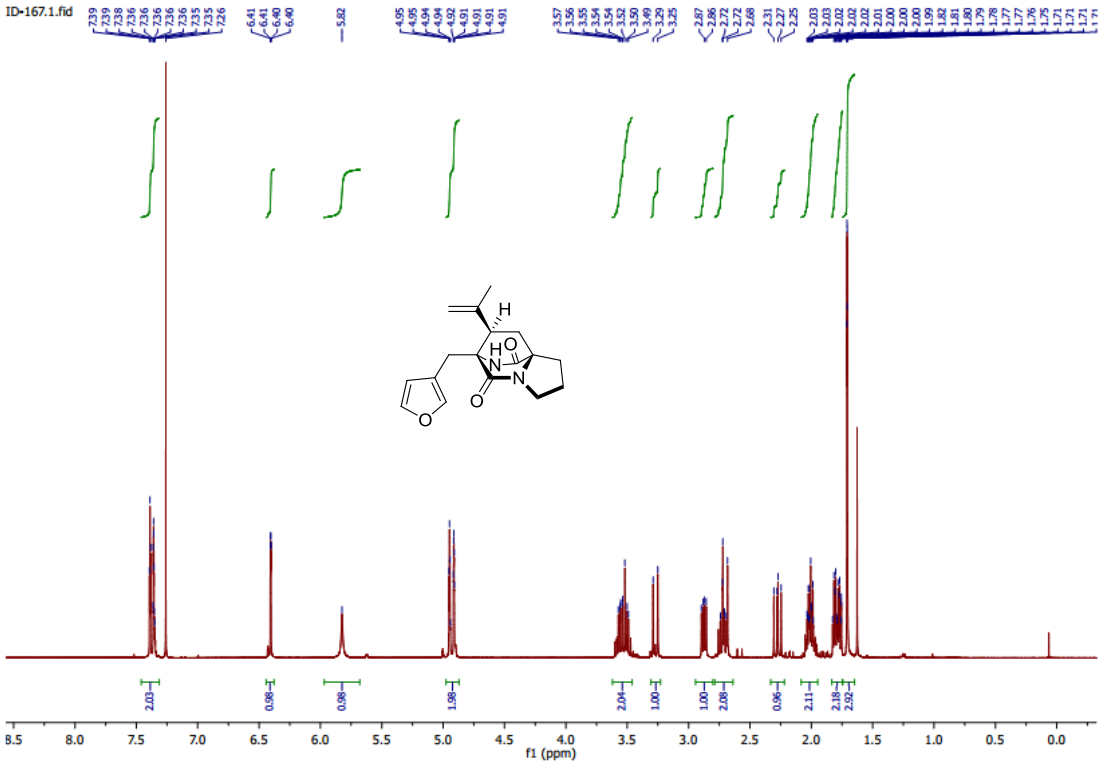


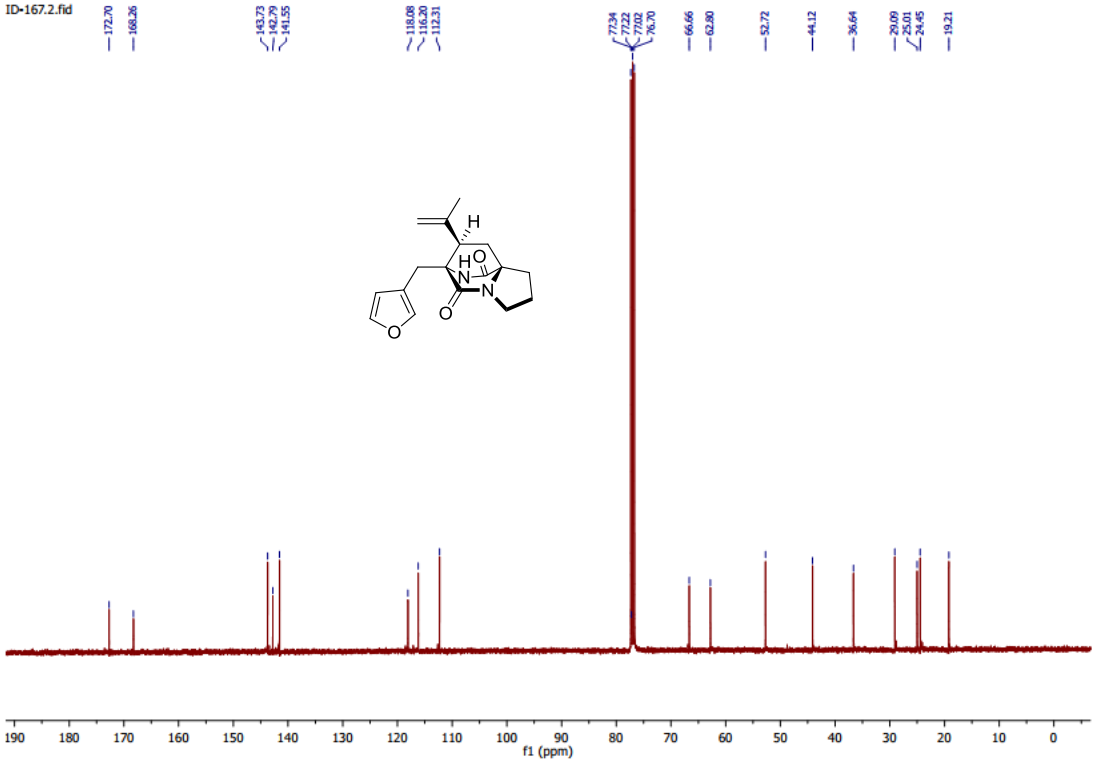
(6*R*,7*R*,8a*R*)-6-(Furan-3-ylmethyl)-10-(methoxymethyl)-7-(prop-1-en-2-yl)tetrahydro-1*H*-6,8a-(epiminomethano)indolizine-5,9(6*H*)-dione (6)



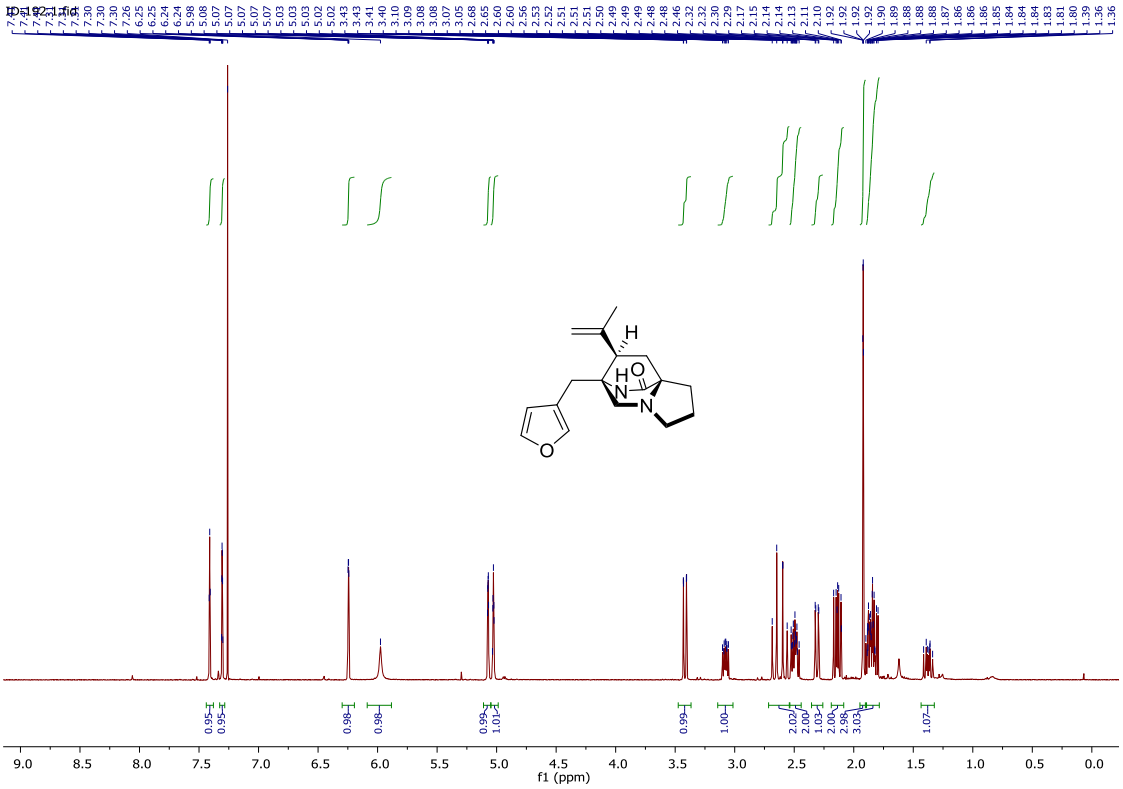


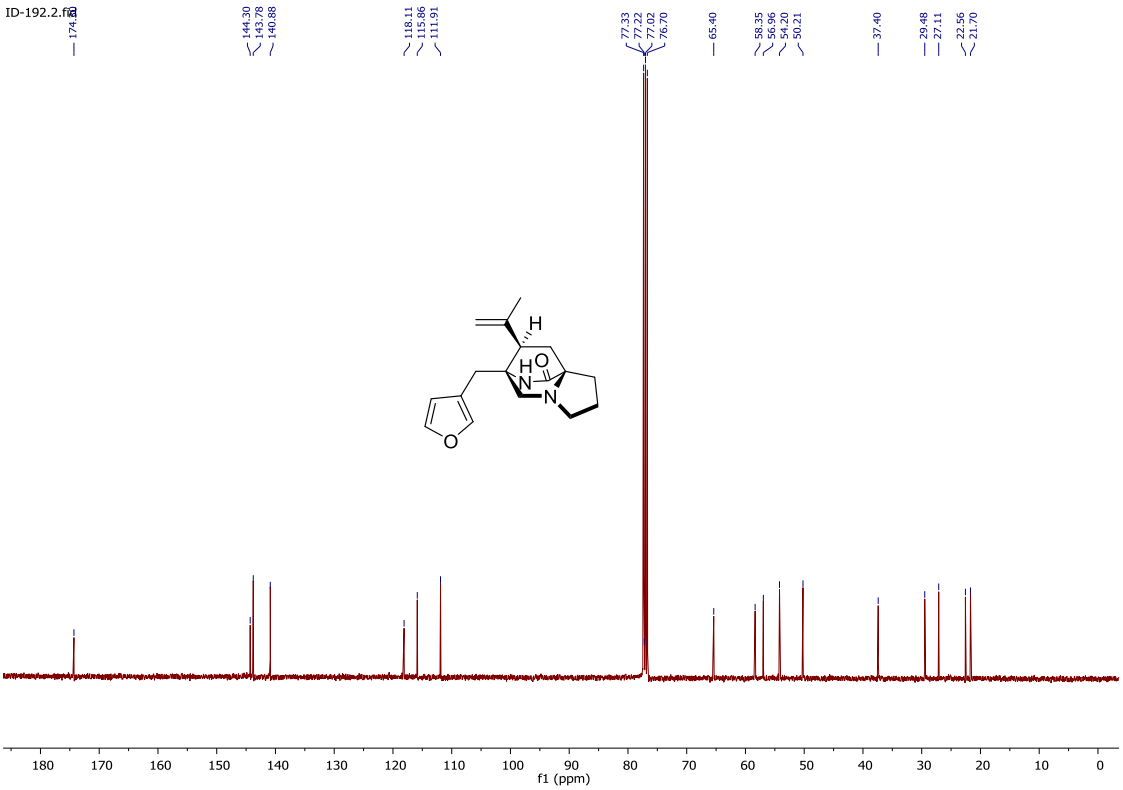
(6*R*,7*R*,8a*R*)-6-(Furan-3-ylmethyl)-7-(prop-1-en-2-yl)tetrahydro-1*H*-6,8a-(epiminomethano)indolizine-5,9(6*H*)-dione (19)



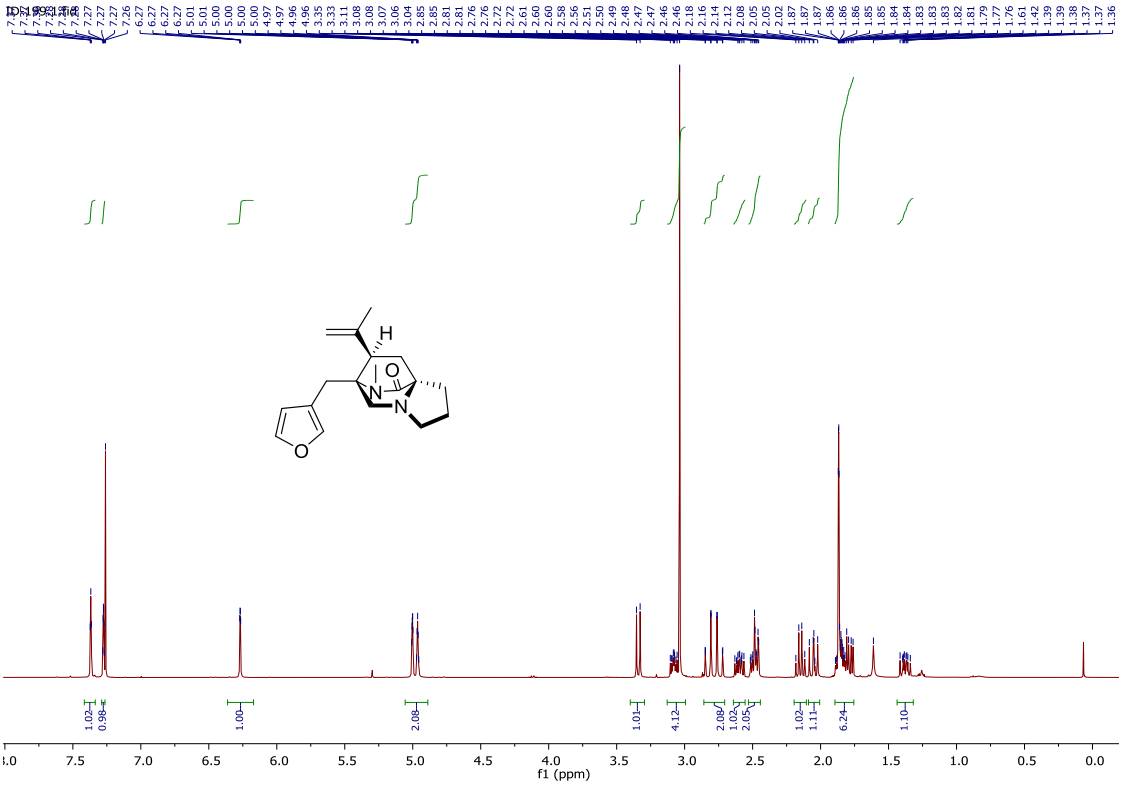


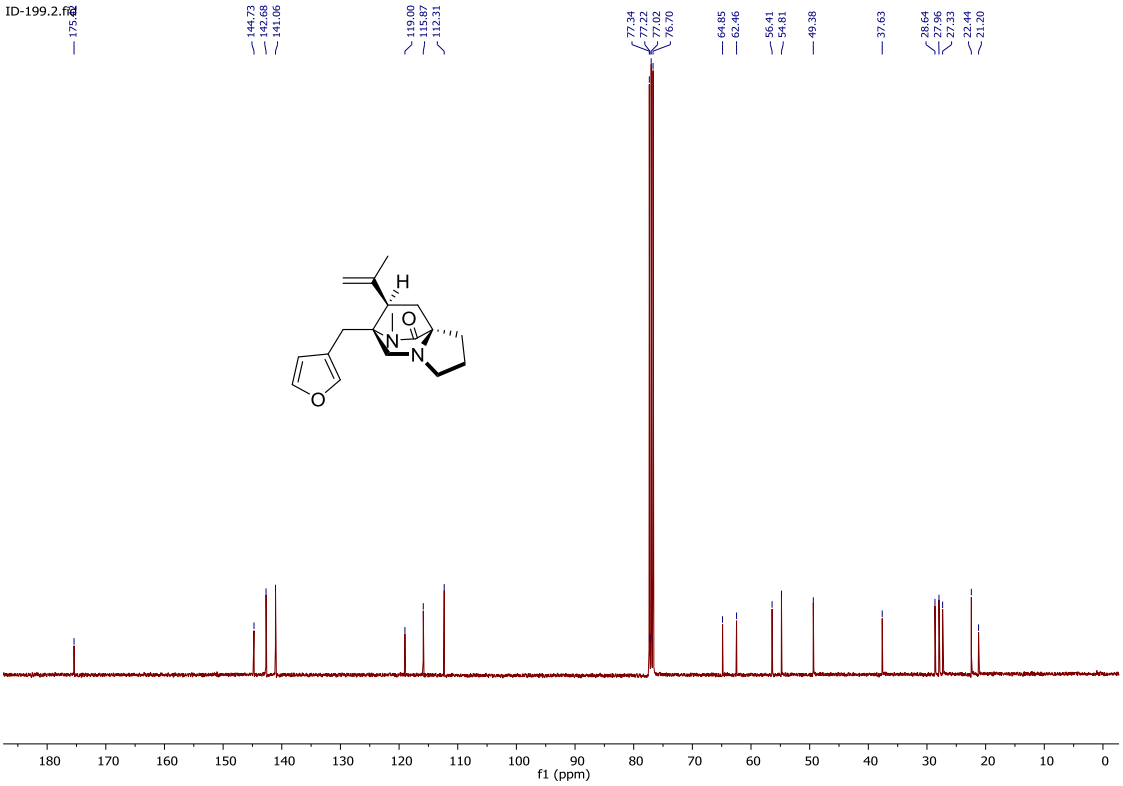
(6*R*,7*R*,8a*R*)-6-(Furan-3-ylmethyl)-7-(prop-1-en-2-yl)hexahydro-1*H*-6,8a-(epiminomethano)indolizin-9-one (20)



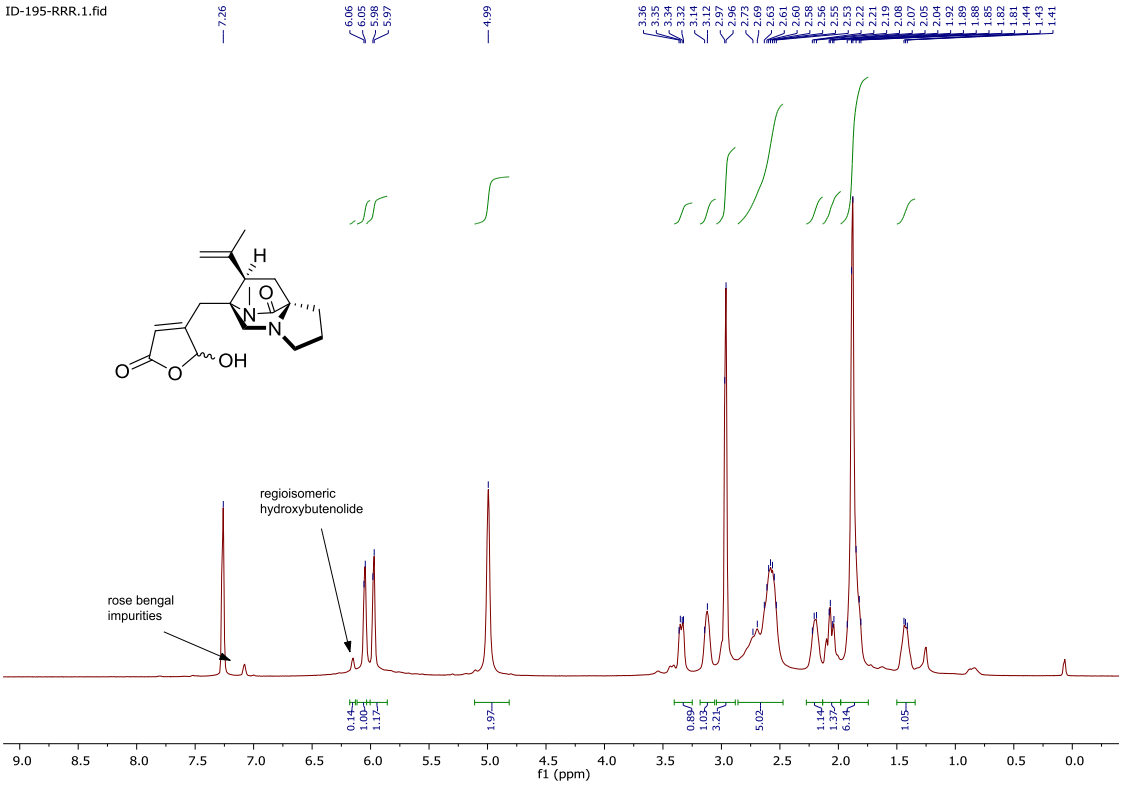


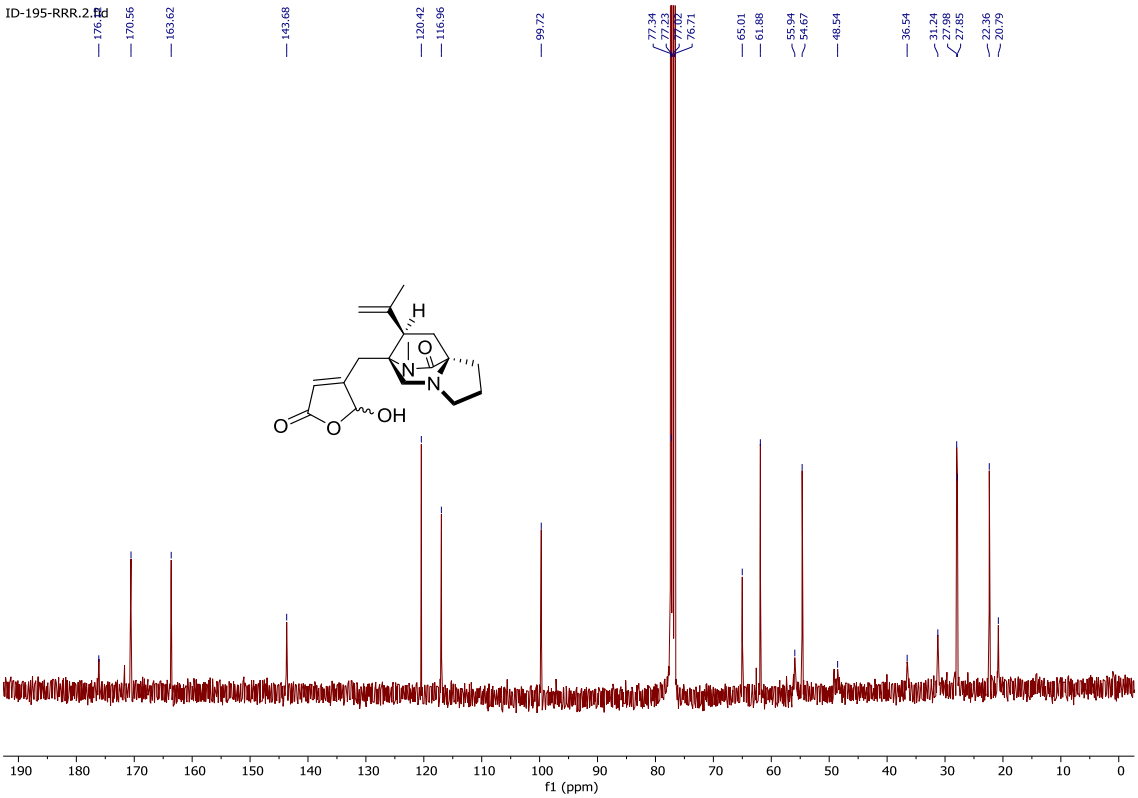
(6*R*,7*R*,8a*R*)-6-(Furan-3-ylmethyl)-10-methyl-7-(prop-1-en-2-yl)hexahydro-1*H*-6,8a-(epiminomethano)indolizin-9-one (21)



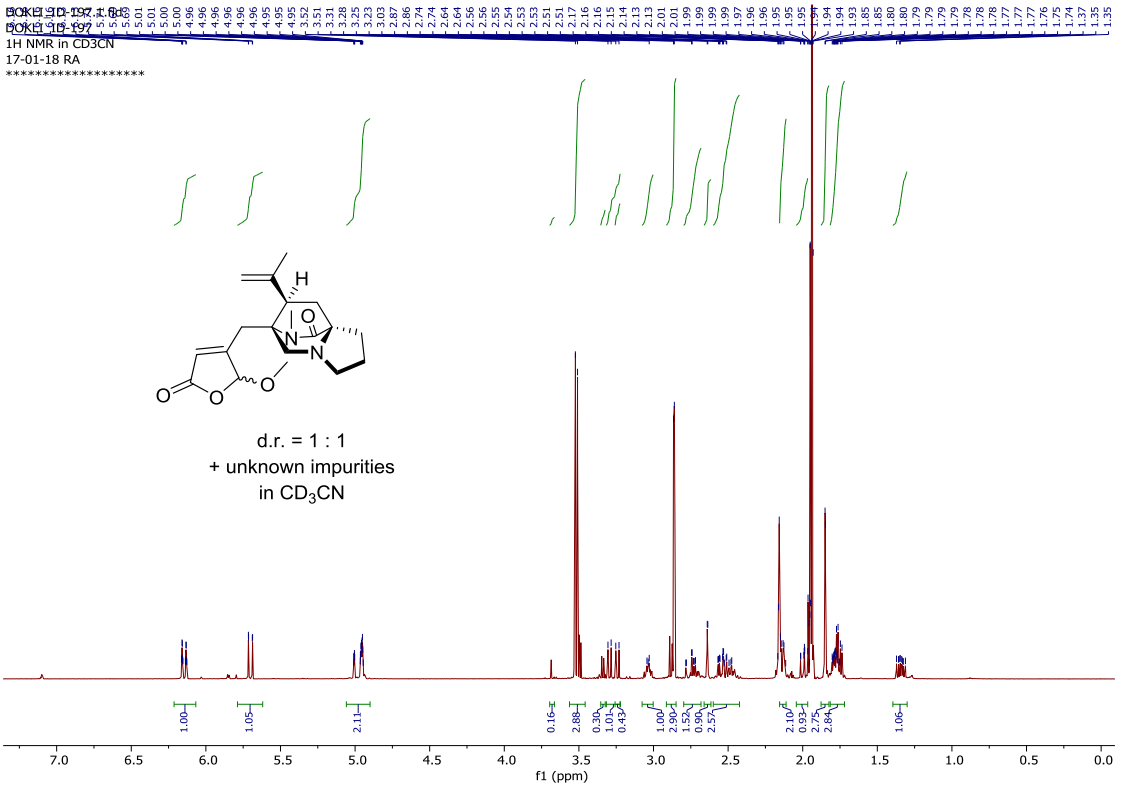


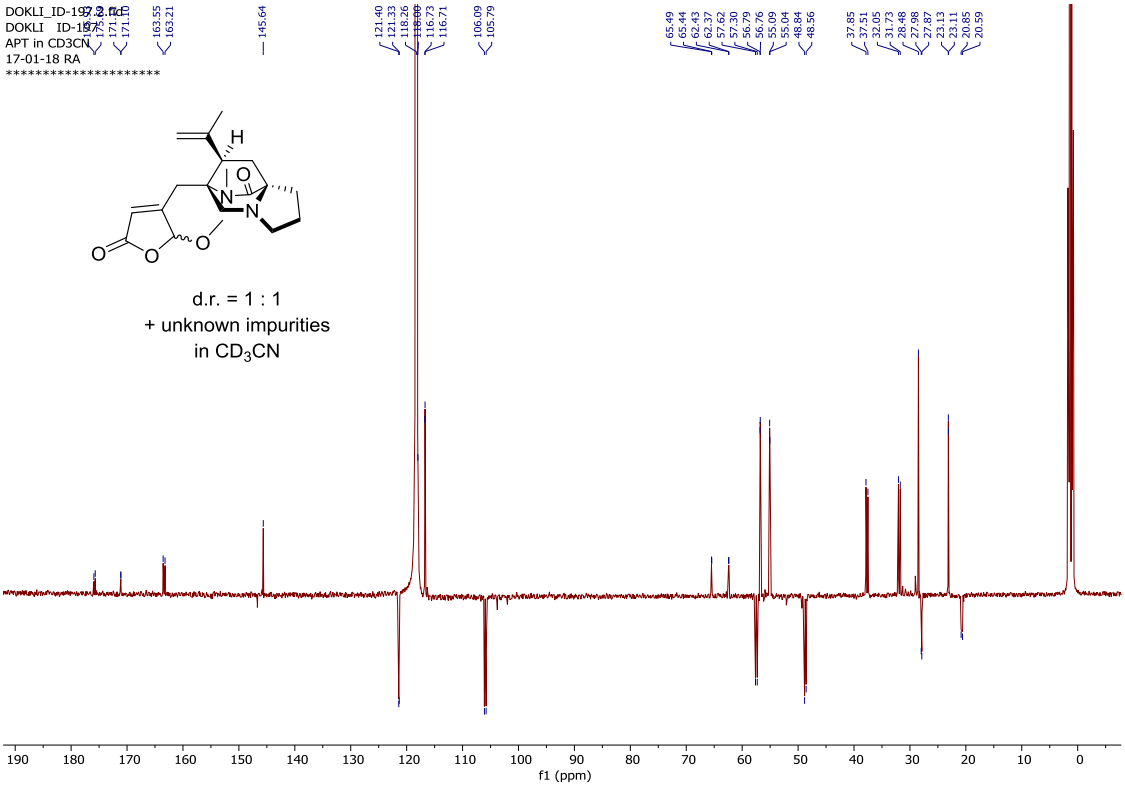
(6*R*,7*R*,8a*R*)-6-((2-Hydroxy-5-oxo-2,5-dihydrofuran-3-yl)methyl)-10-methyl-7-(prop-1-en-2-yl)hexahydro-1*H*-6,8a-(epiminomethano)indolizin-9-one (5)



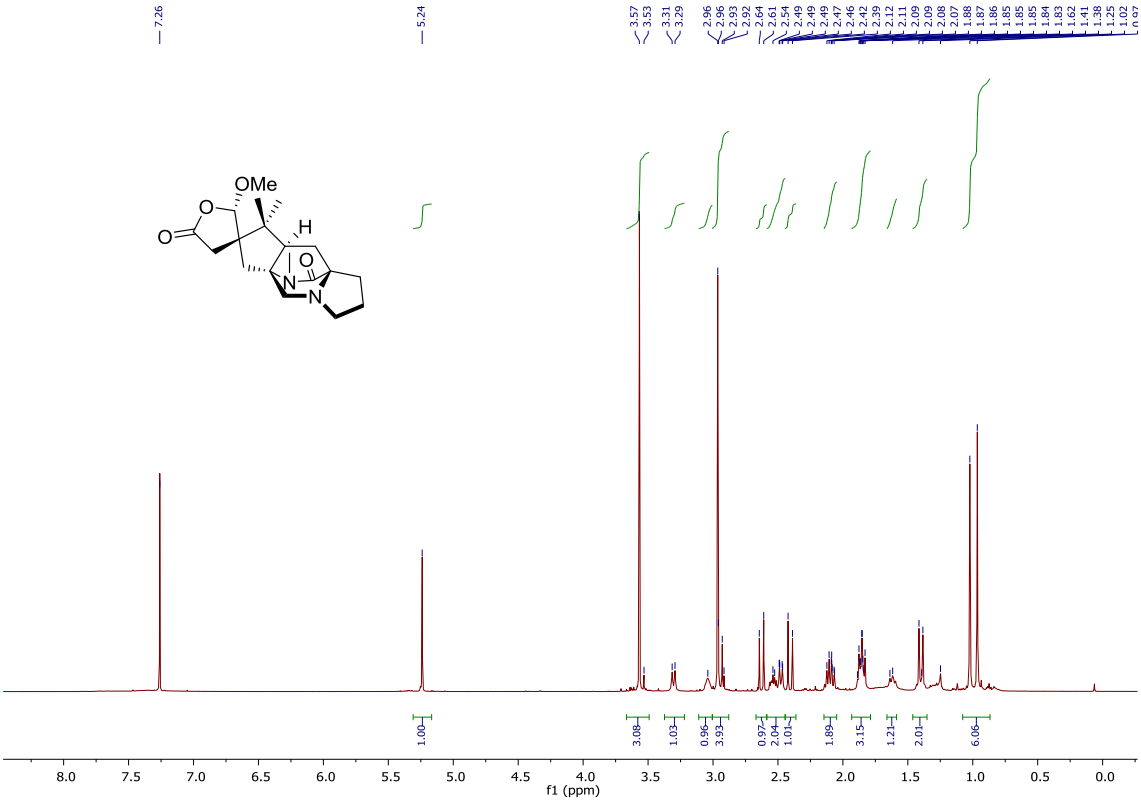


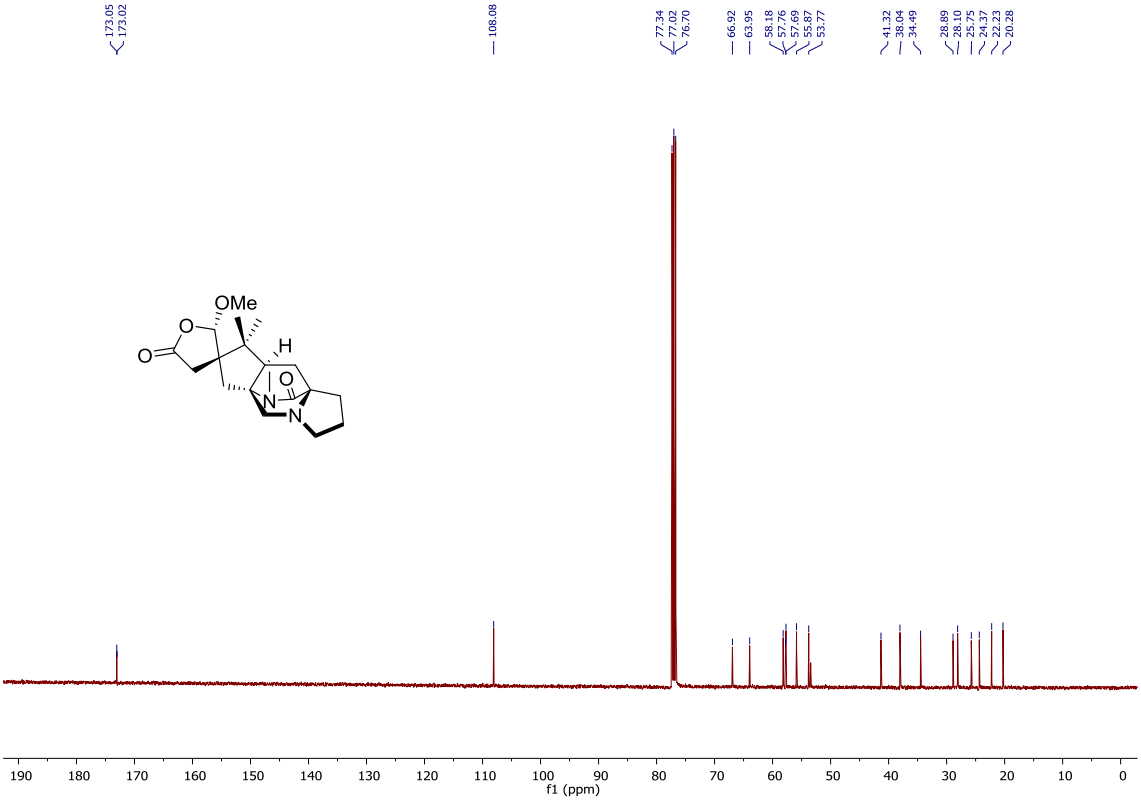
(6*R*,7*R*,8a*R*)-6-((2-Methoxy-5-oxo-2,5-dihydrofuran-3-yl)methyl)-10-methyl-7-(prop-1-en-2-yl)hexahydro-1*H*-6,8a-(epiminomethano)indolizin-9-one (22)



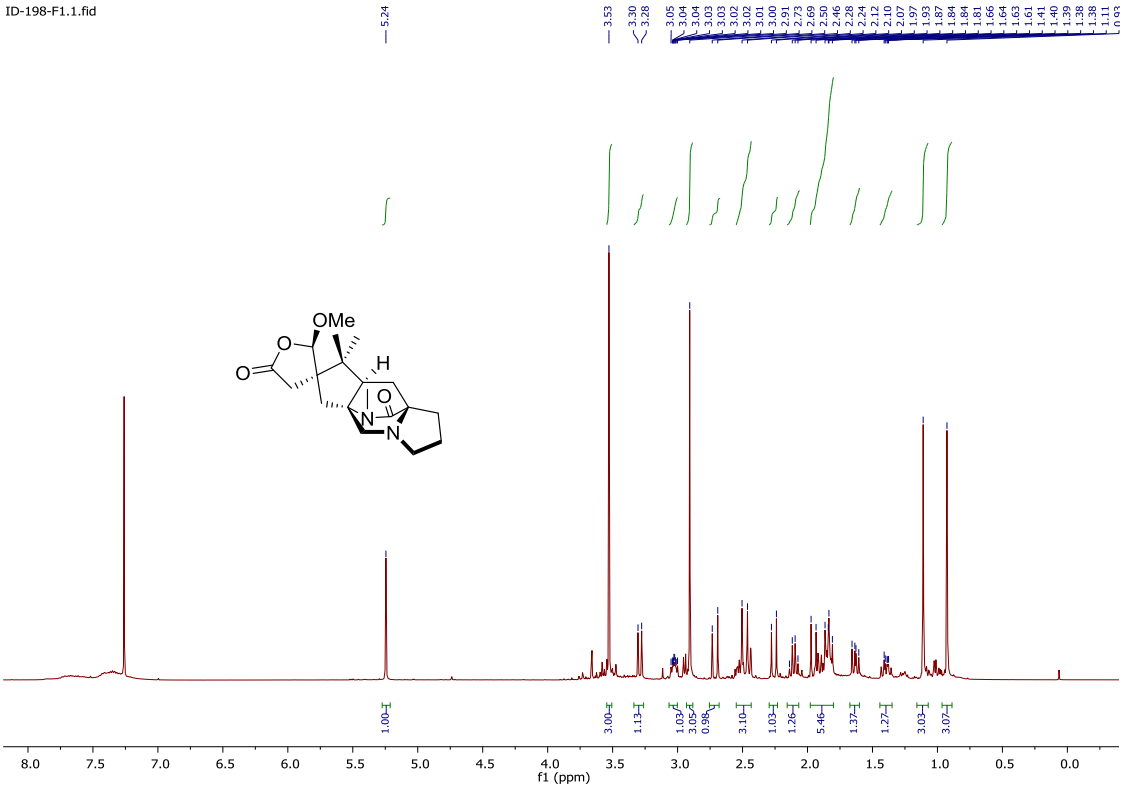


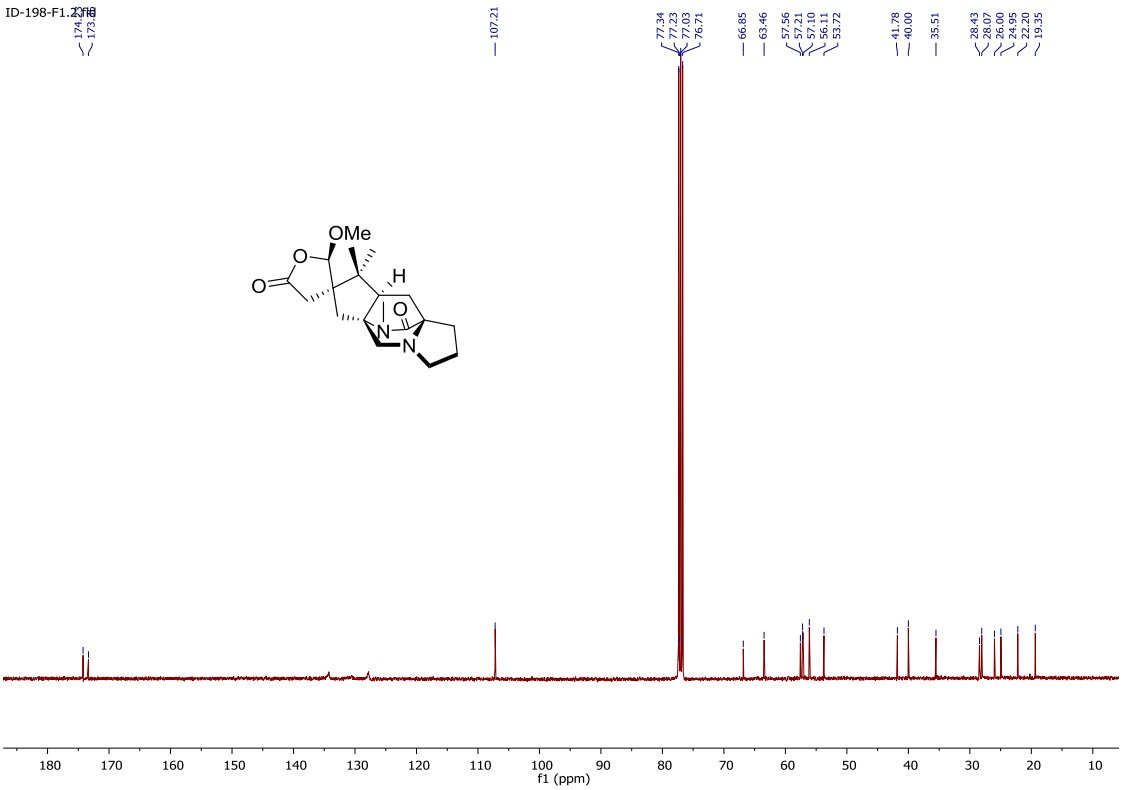
(2*S*,3*R*,5a'*R*,8a'*R*,9a'*R*)-2-Methoxy-8',8',11'-trimethyltetrahydro-1'*H*,2*H*,5'*H*,6'*H*,8'*H*-spiro[furan-3,7'-[5a,9a](epiminomethano)cyclopenta[f]indolizine]-5,10'(4*H*)-dione (23a)



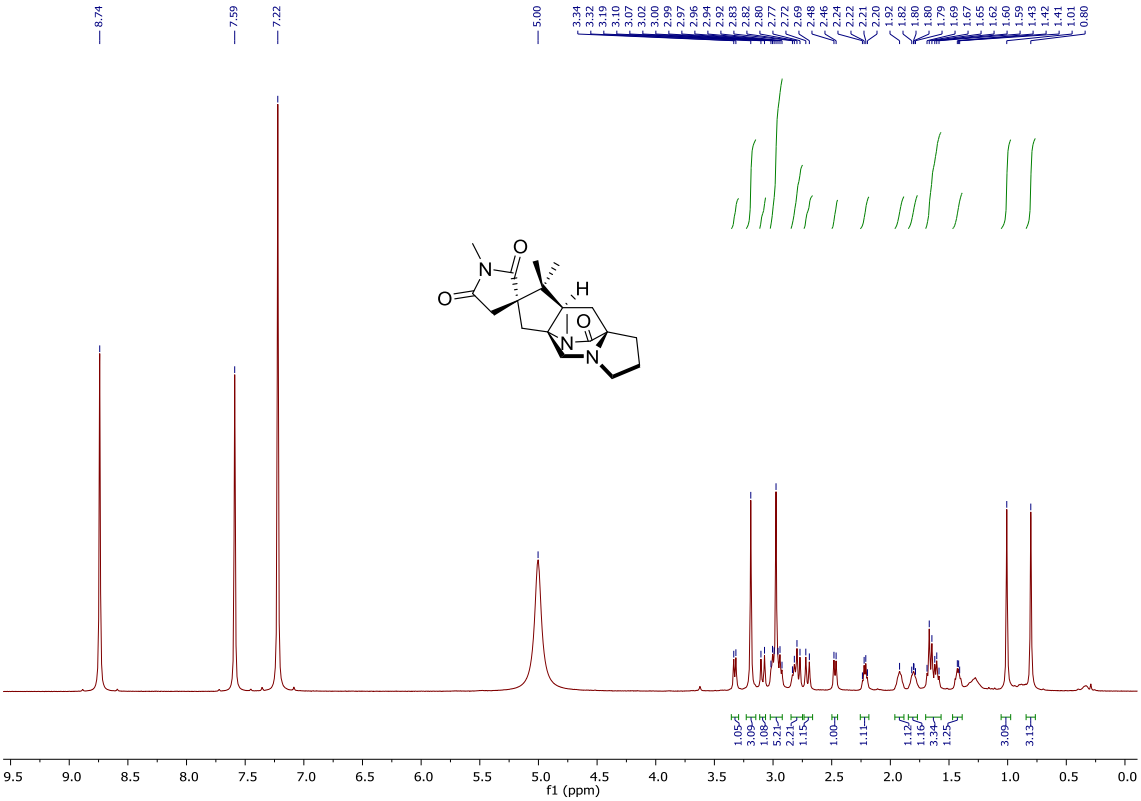


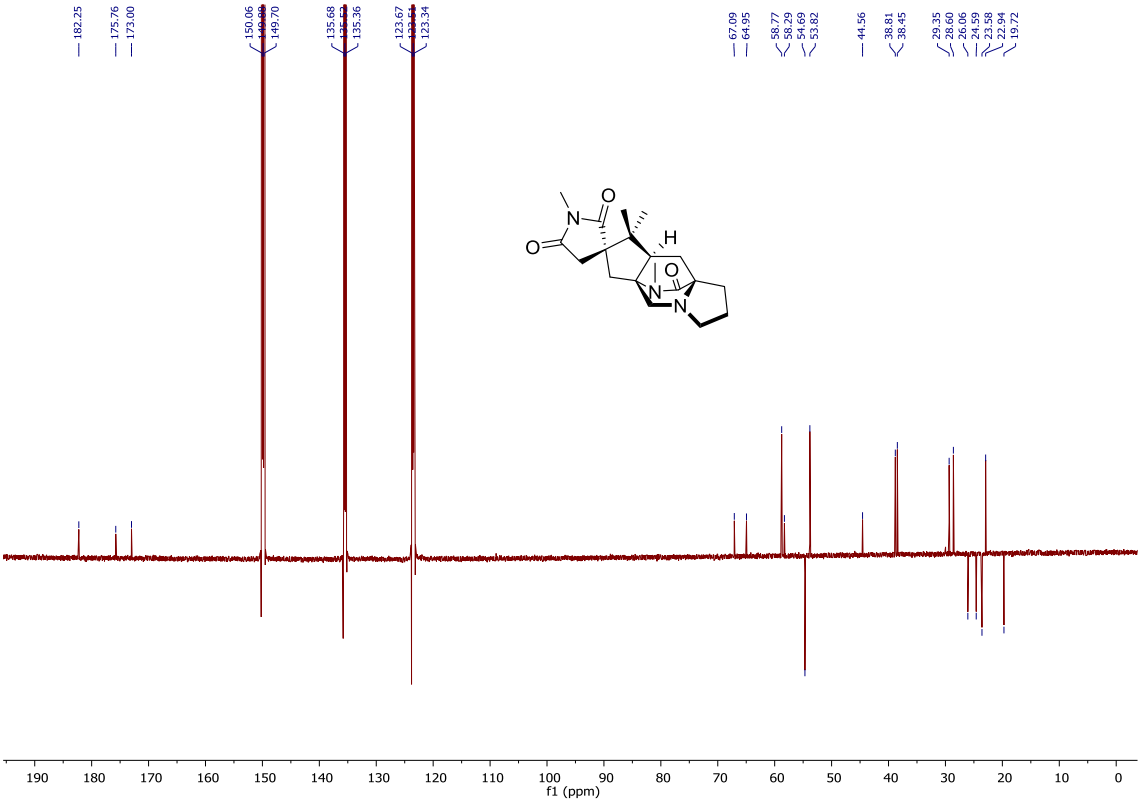
(2*R*,3*S*,5a'*R*,8a'*R*,9a'*R*)-2-Methoxy-8',8',11'-trimethyltetrahydro-1'*H*,2*H*,5'*H*,6'*H*,8'*H*-spiro[furan-3,7'-[5a,9a](epiminomethano)cyclopenta[*f*]indolizine]-5,10'(4*H*)-dione (23b)





(3'*R*,5a*R*,8a*R*,9a*R*)-Tetrahydro-1',8,8,11-tetramethylspiro[5*H*,6*H*-5a,9a-(iminomethano)-1*H*-cyclopenta[*f*]indolizine-7(8*H*),3'-pyrrolidine]-2',5',10-trione (*ent*-4)





(3'*S*,5a*R*,8a*R*,9a*R*)-Tetrahydro-1',8,8,11-tetramethylspiro[5*H*,6*H*-5a,9a-(iminomethano)-1*H*-cyclopenta[*f*]indolizine-7(8*H*),3'-pyrrolidine]-2',5',10-trione (25)