SUPPORTING INFORMATION

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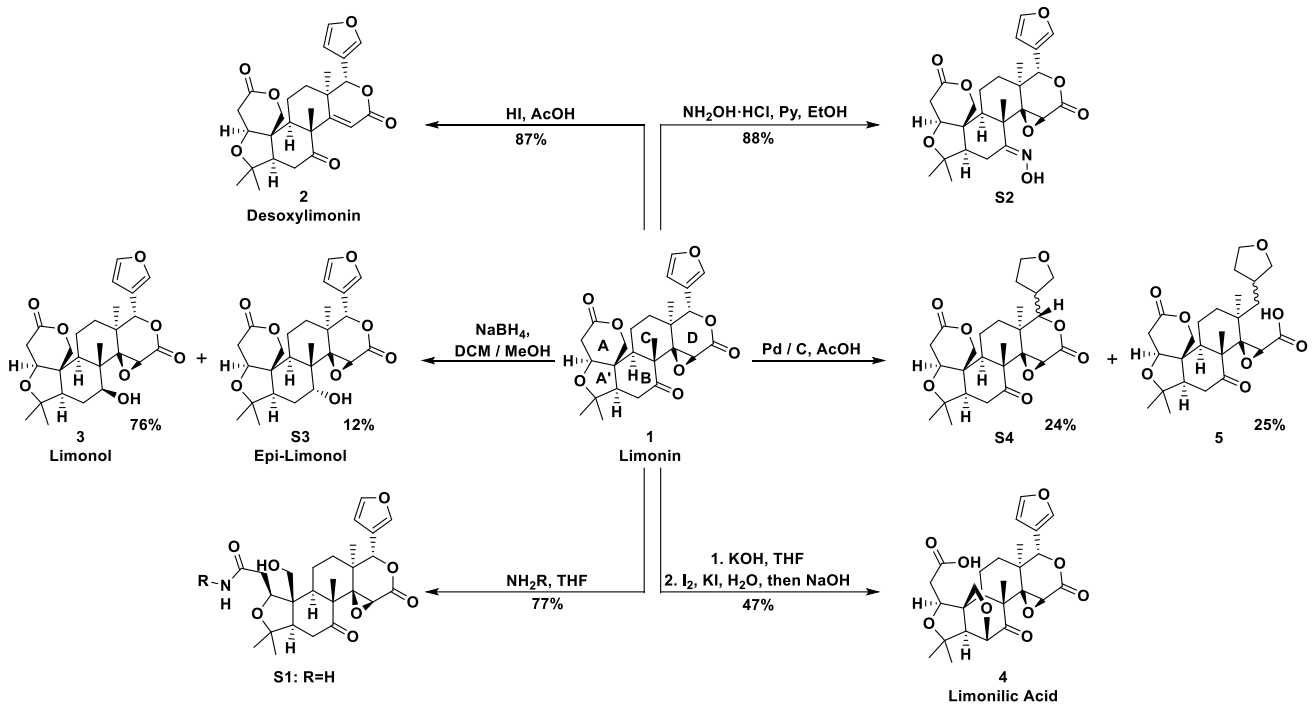
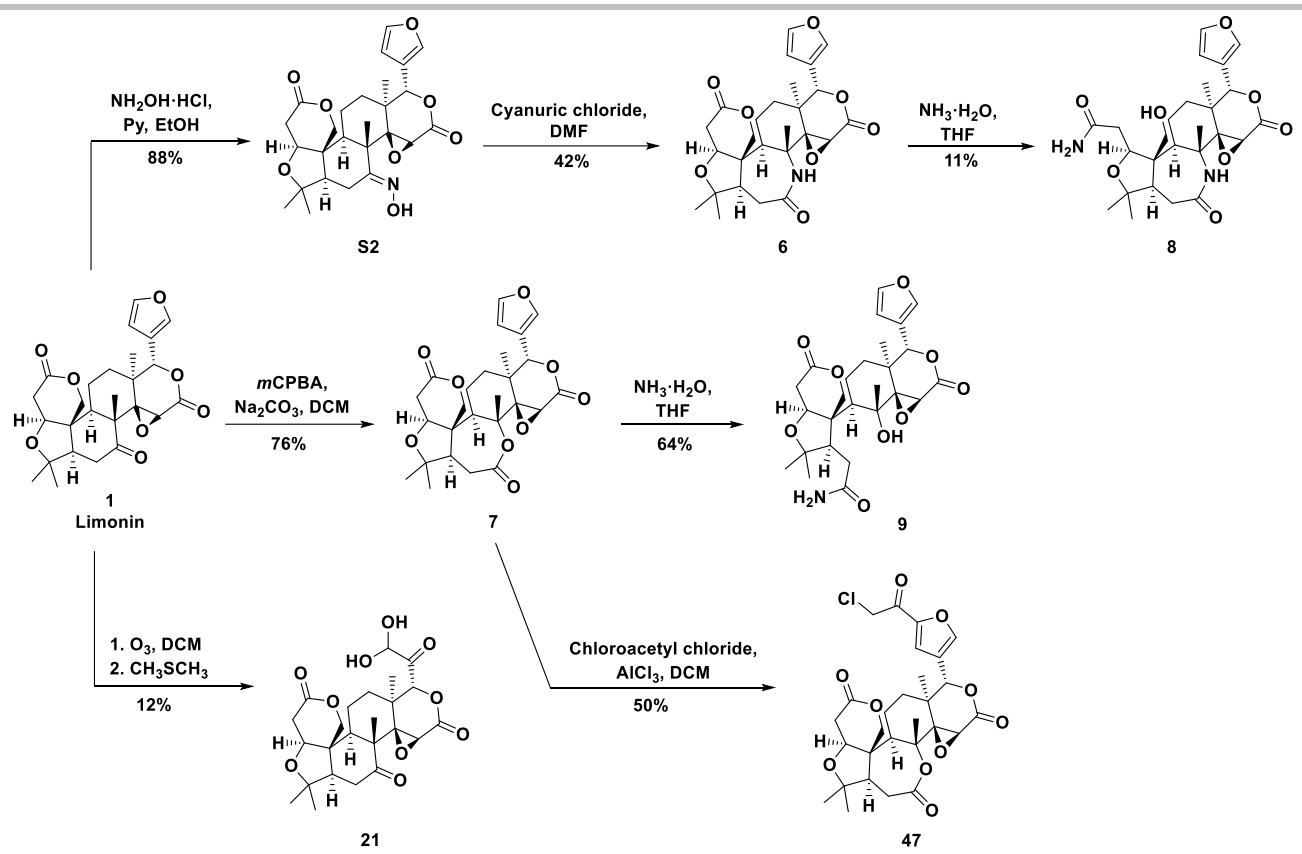
Overview Schemes

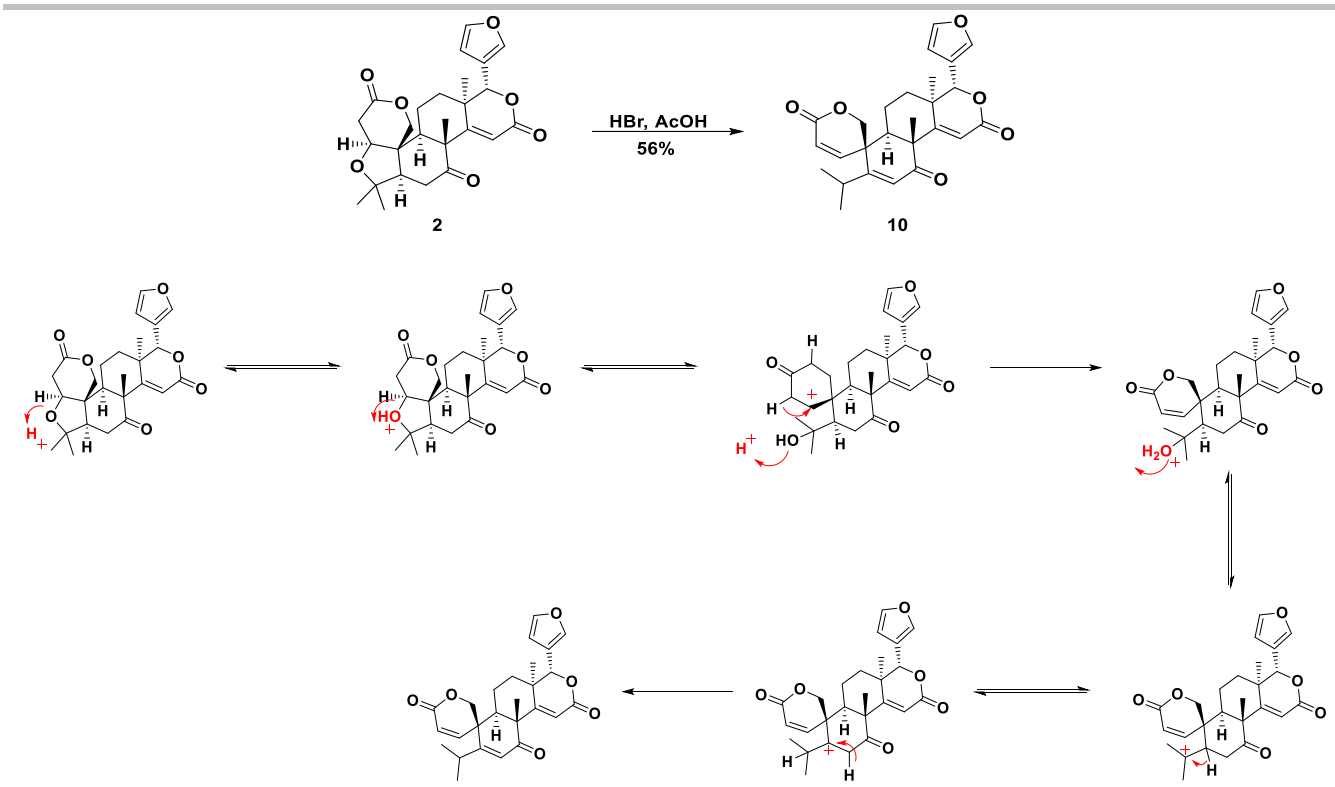
Synthesis and Proposed Mechanisms of Limonin Ring Distorted Derivatives



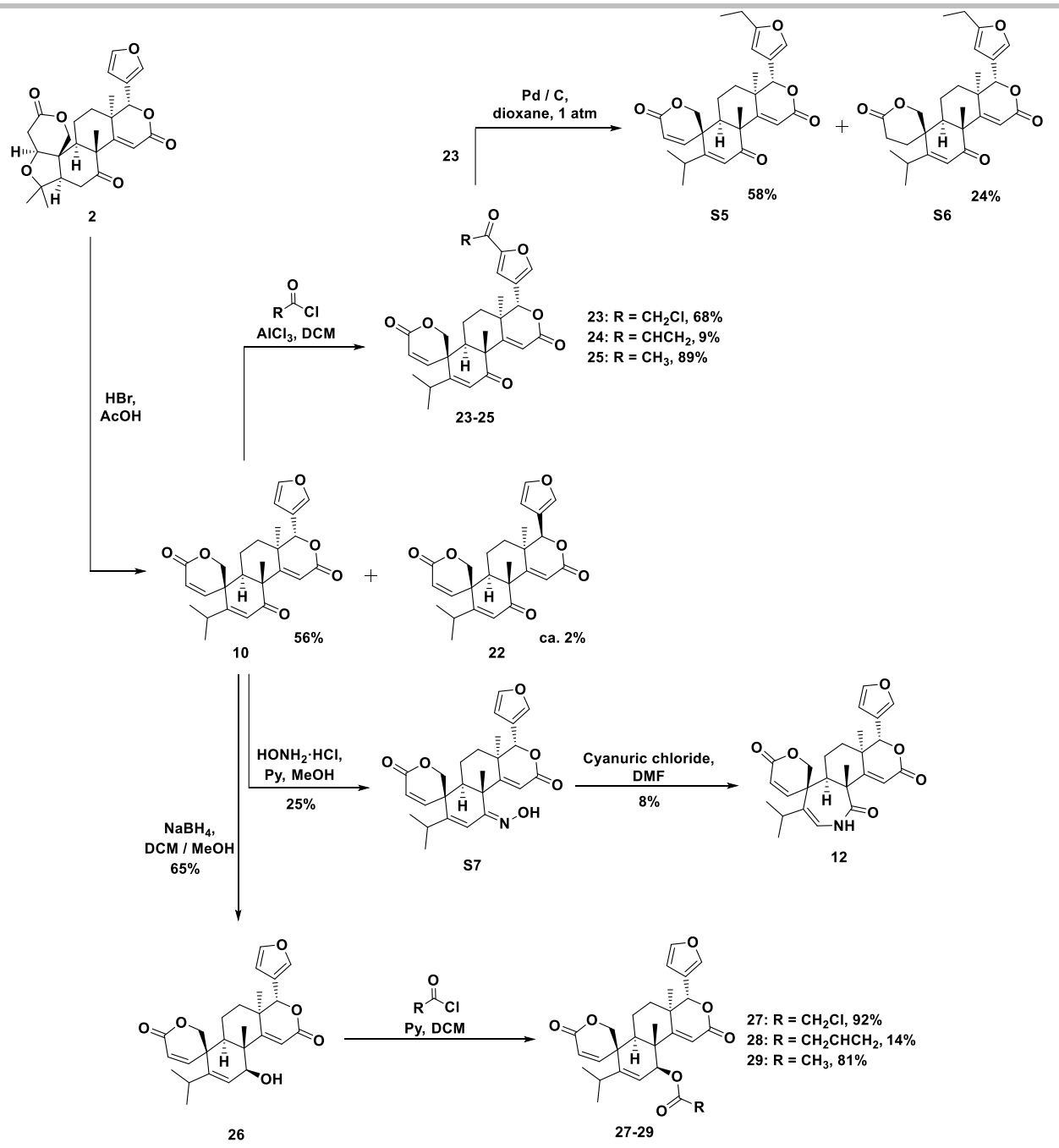
Scheme S1. Some known transformations from limonin (**2-5, S1-S4**).



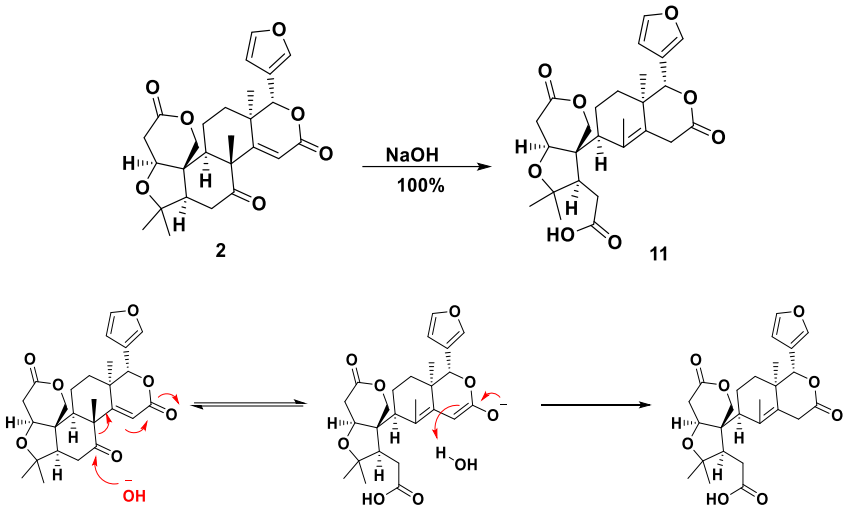
Scheme S2. Limonin Rings B and E manipulations.



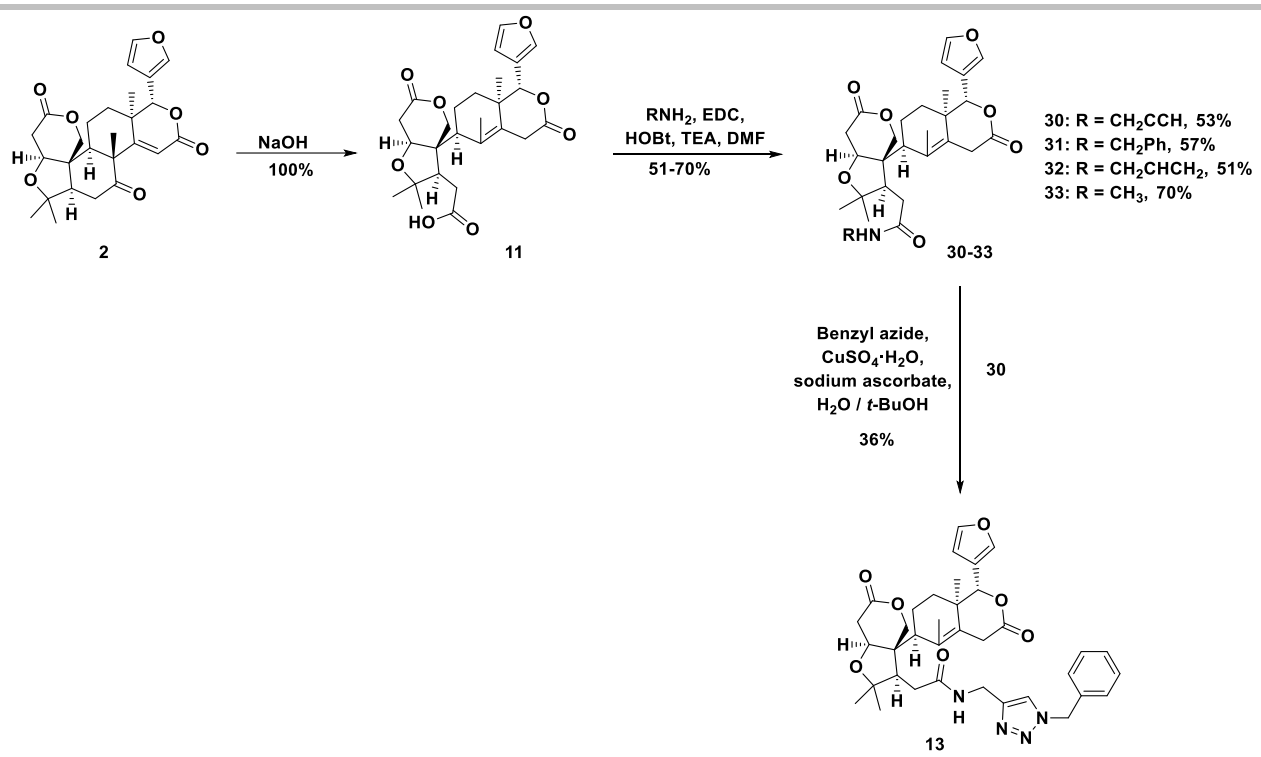
Scheme S3. Proposed mechanism for compound **10** synthesis.



Scheme S4. Desoxylimonin (**2**) ring A'-cleavage and further manipulations.



Scheme S5. Proposed mechanism for compound **11** synthesis.



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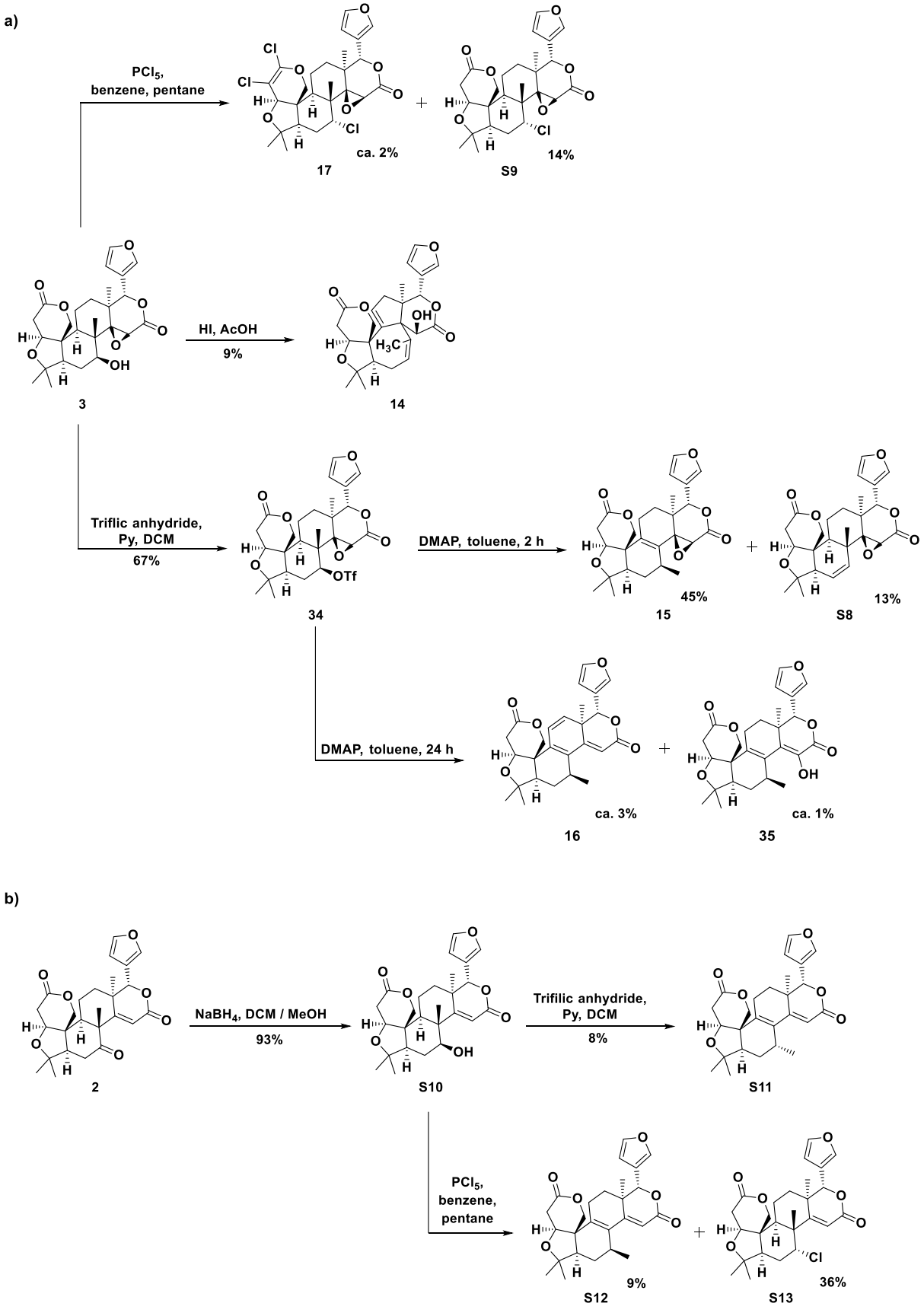

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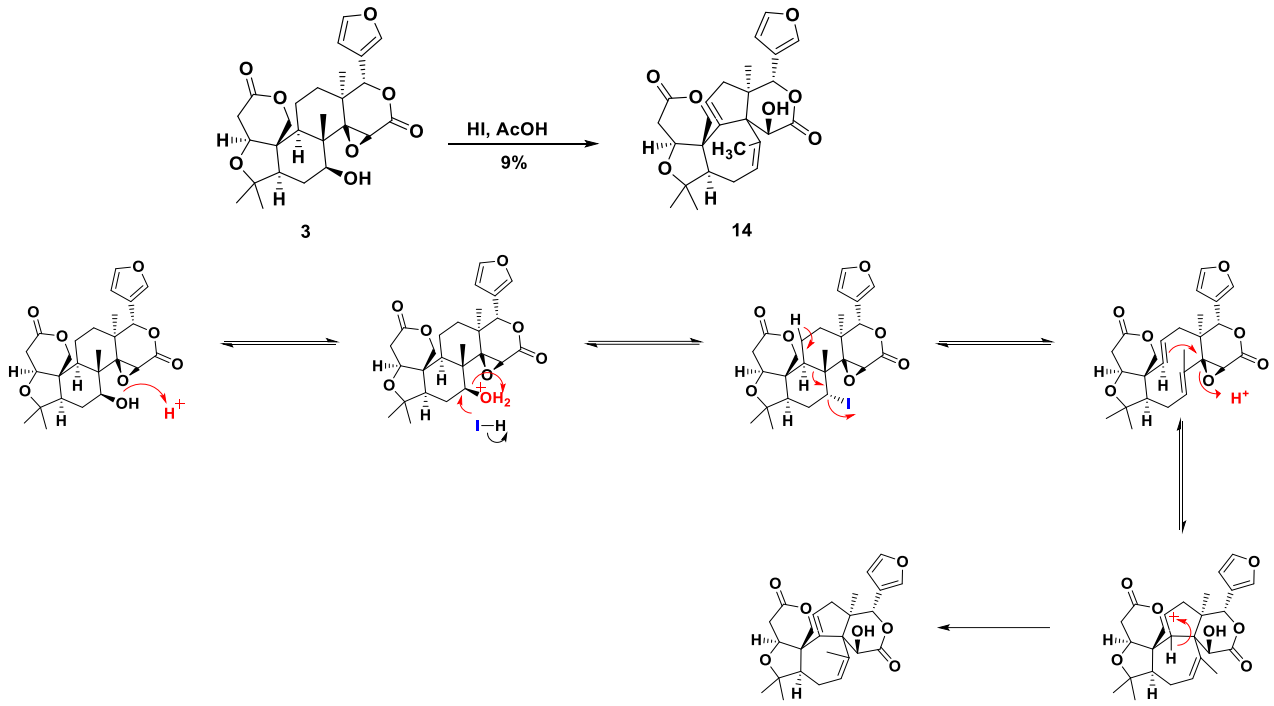
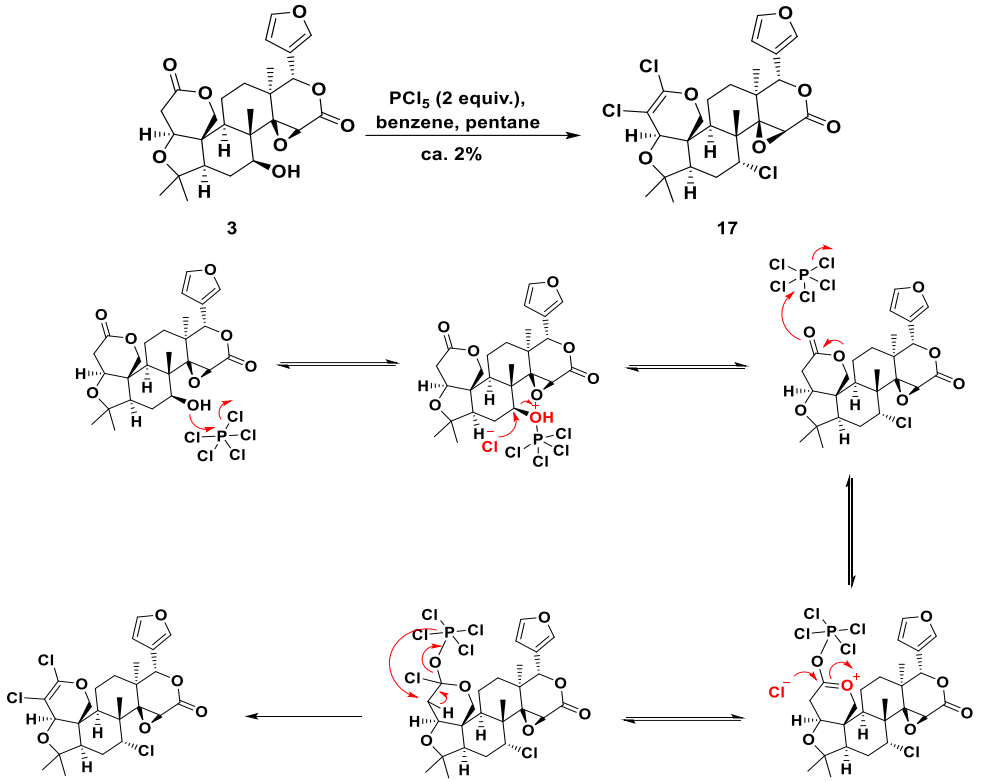


Scheme S8. Proposed mechanism for compound **14** synthesis.



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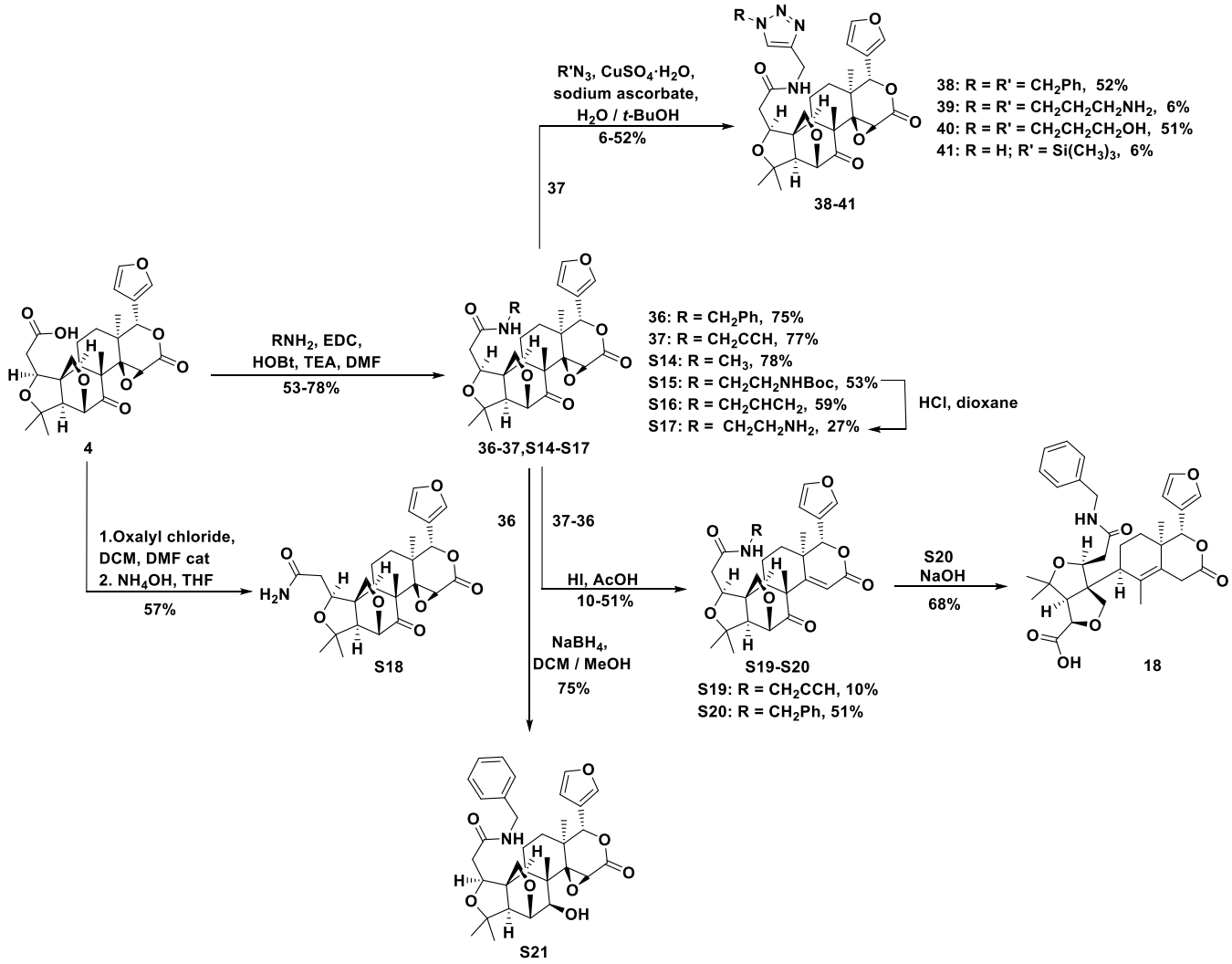

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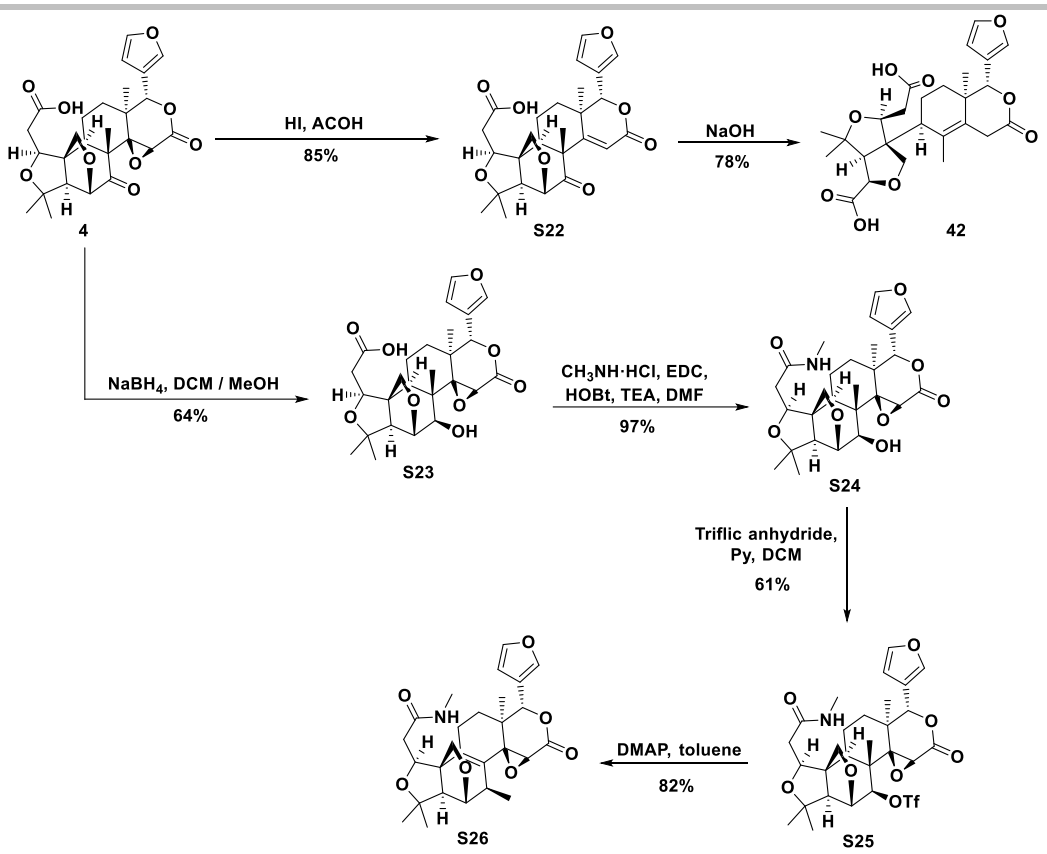
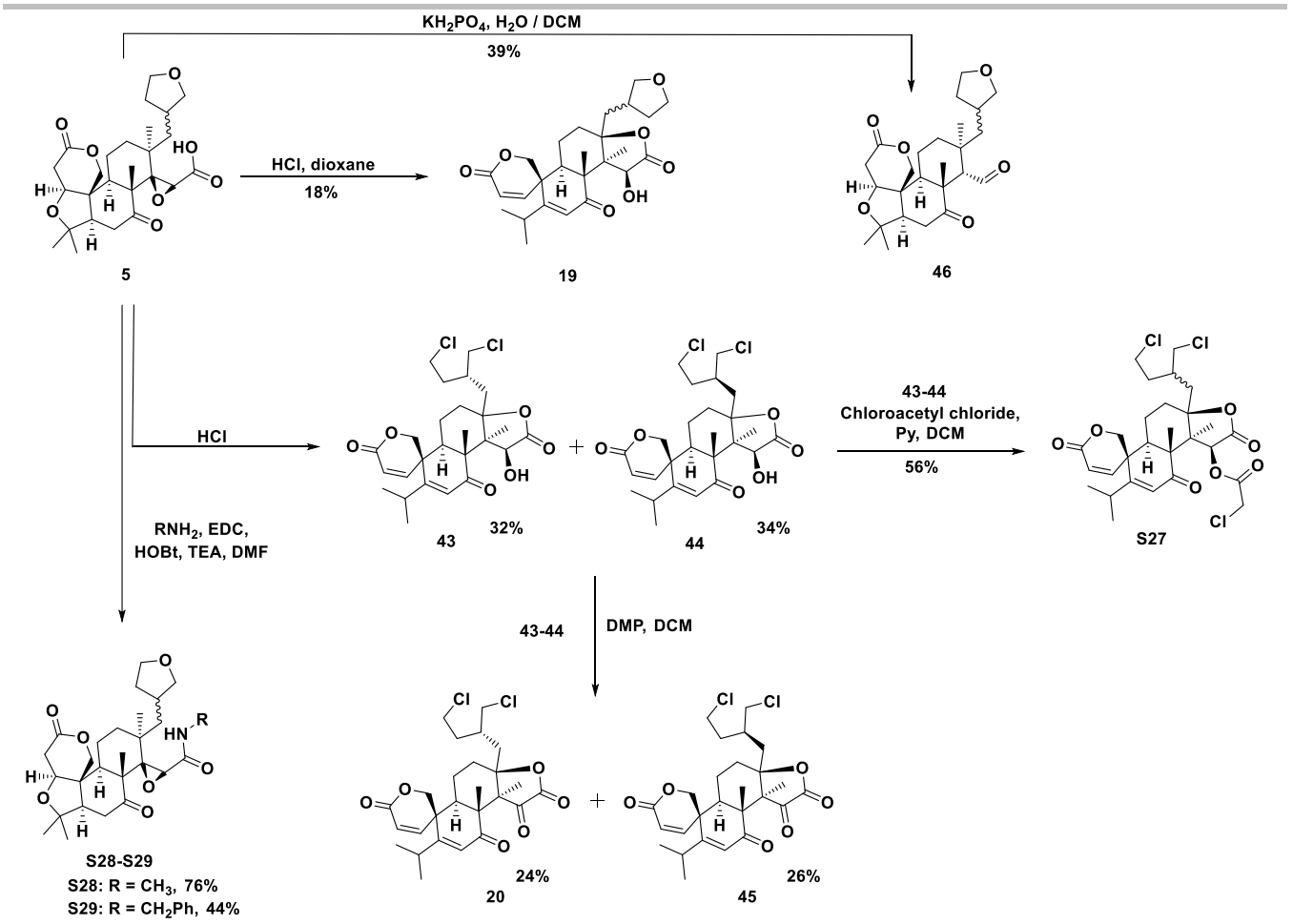
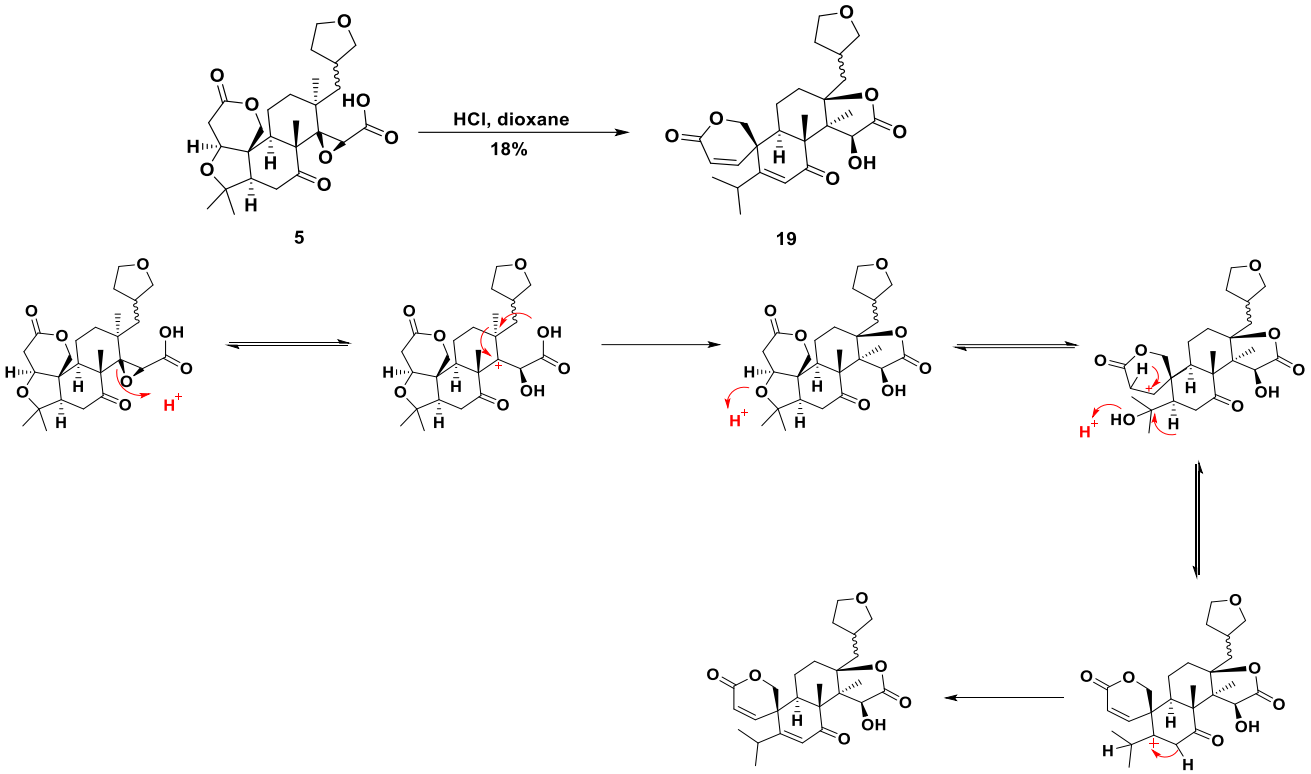


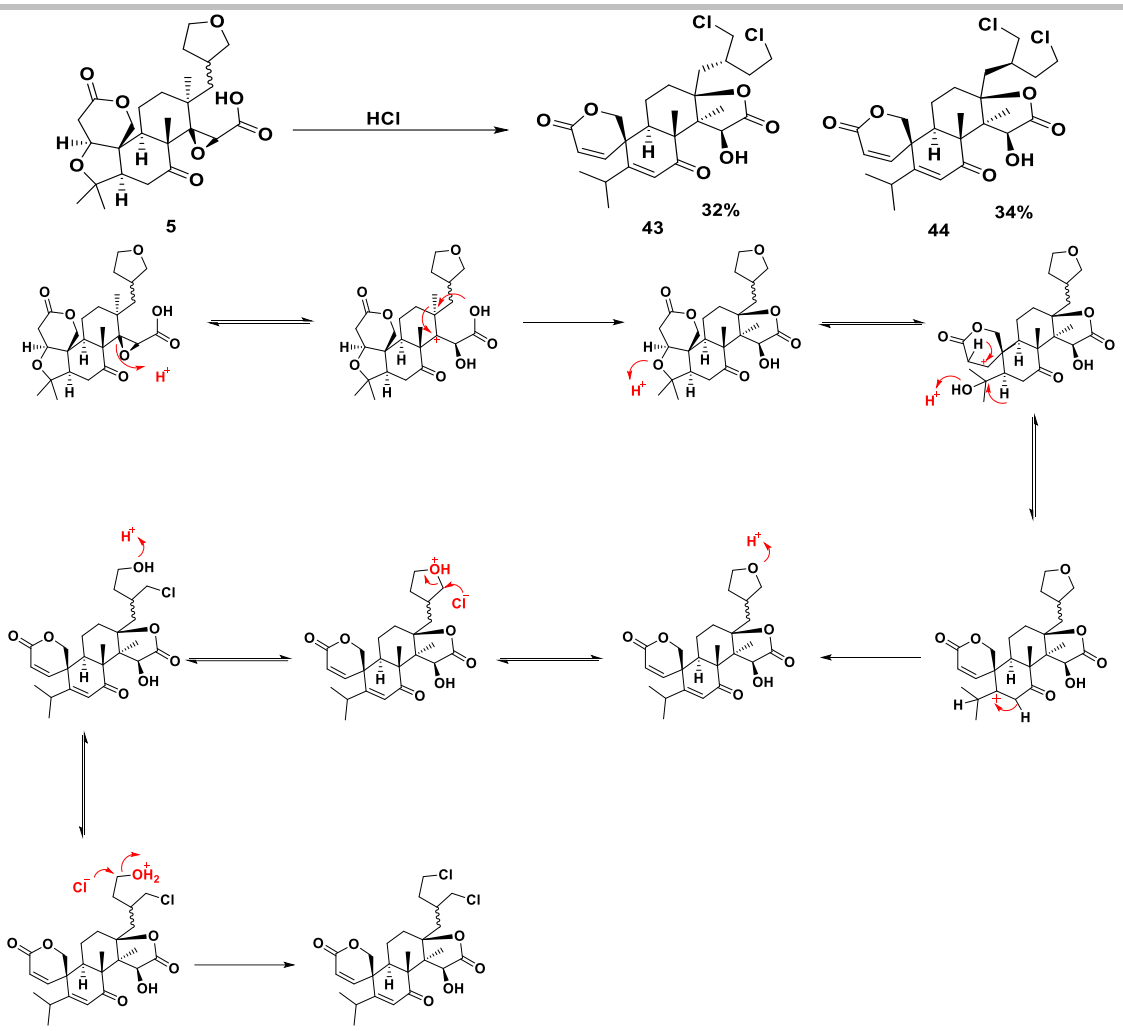
Scheme S11. B-Ring Cleavage and Rearrangement of **4**.



Scheme S12. Ring Manipulation of **5**.



Scheme S13. Proposed mechanism for compound **19** synthesis.



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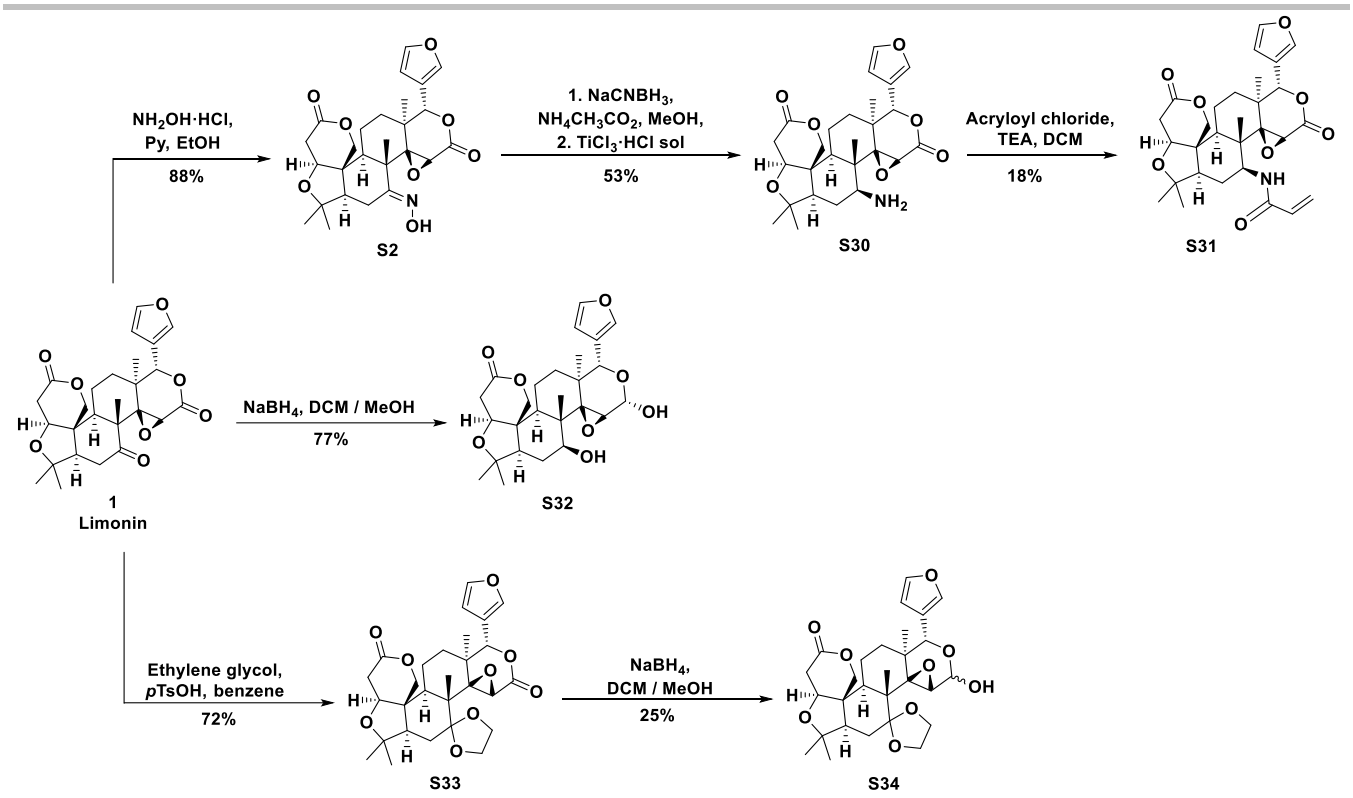
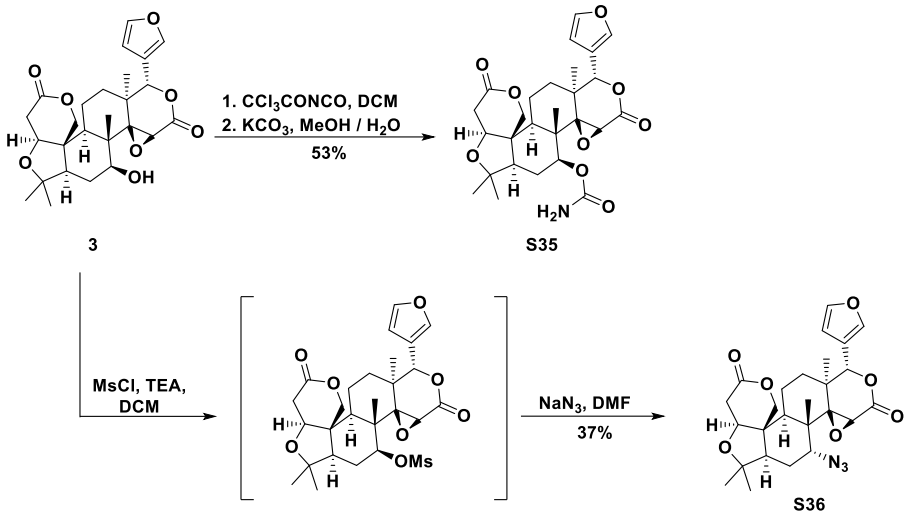
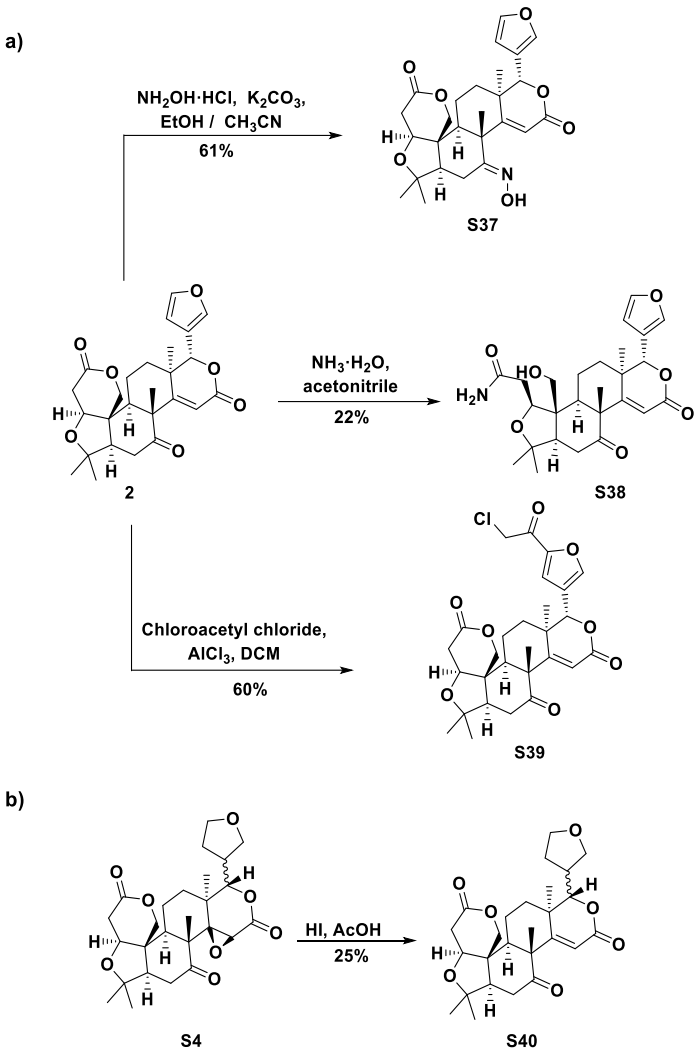


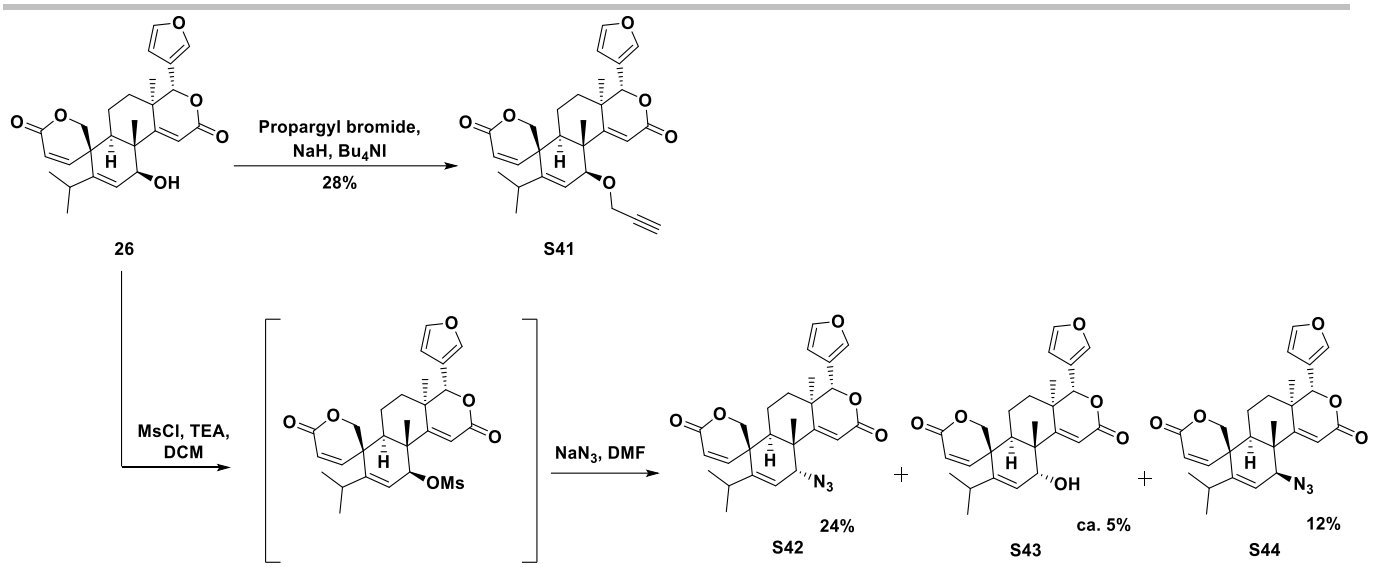
Scheme S15. Limonin B-ring derivatization and fusion.



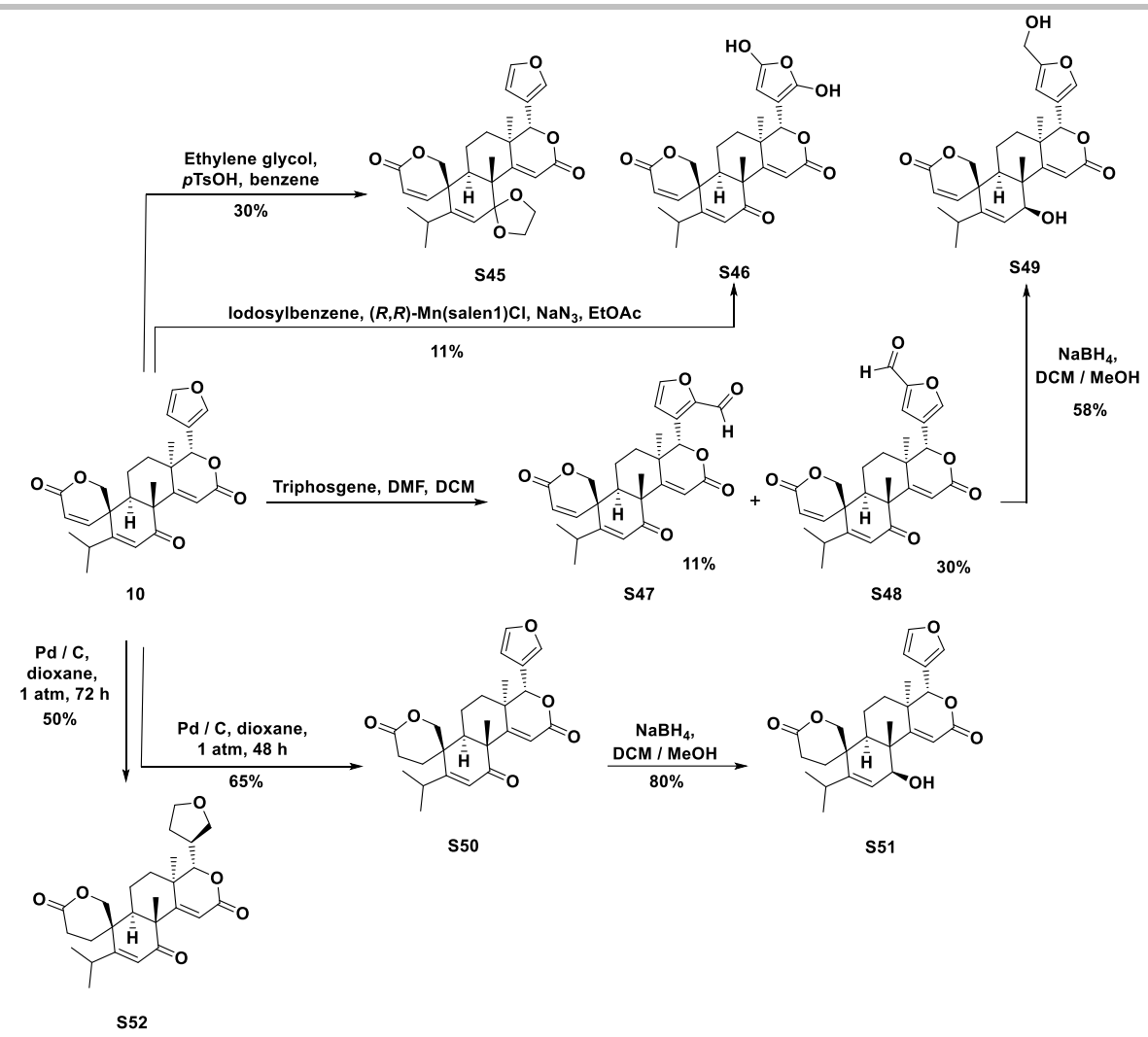
Scheme S16. Derivatization of **3**.



Scheme S17. a) Desoxylimonin derivatization; b) Epoxide cleavage of **S4**.

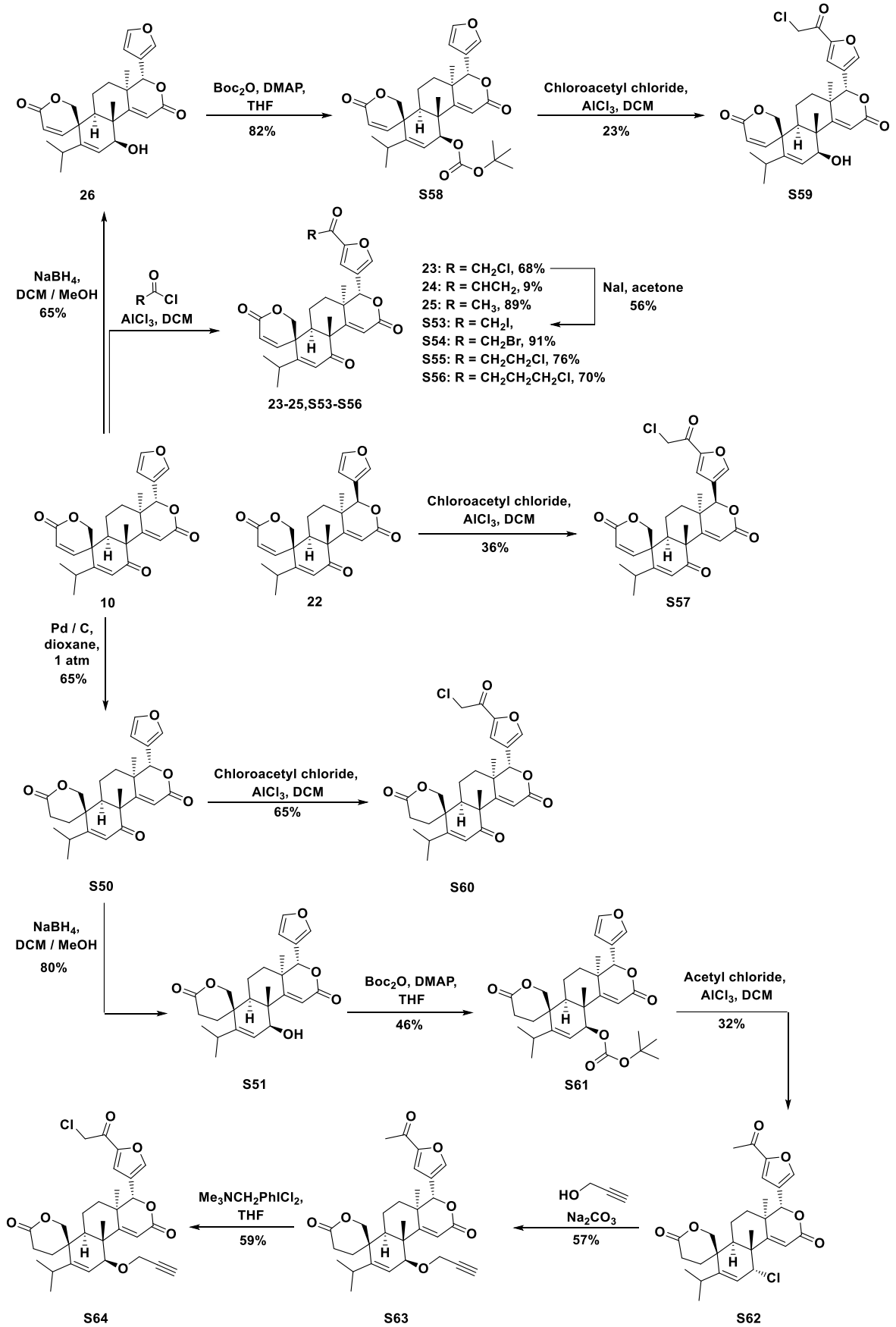


Scheme S18. Derivatization of **26**.

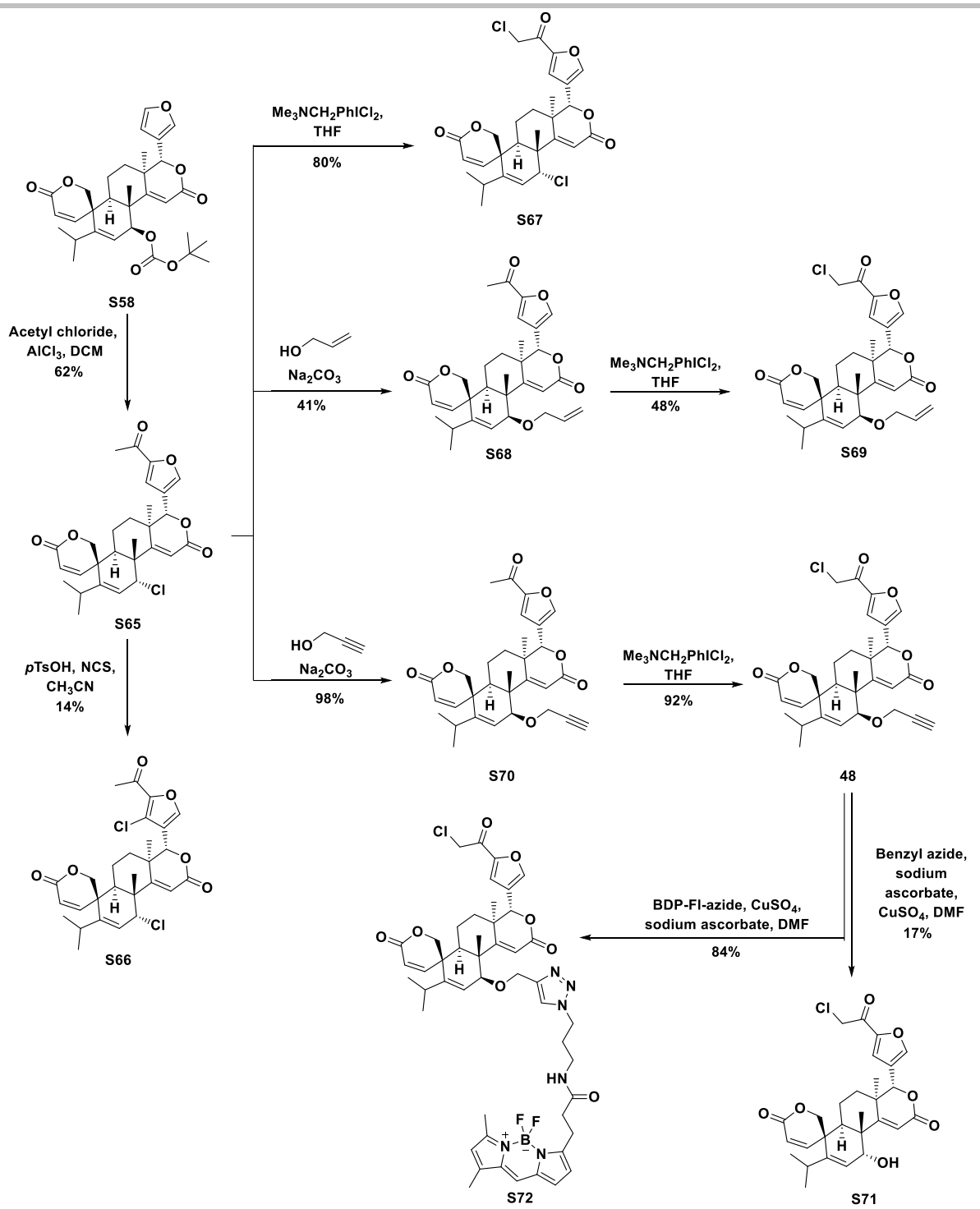


Scheme S19. Derivatization of **10**.

Synthesis of Derivatives for Structure-Activity Relationship Studies



Scheme S20. Structure-activity investigations of compound **23**: functional group manipulations of **10**.



Scheme S21. Structure-activity investigation of compound **23**: functional group manipulations of **S58**.

Supplementary Figures

SUPPORTING INFORMATION

Full Set of CtD Compounds

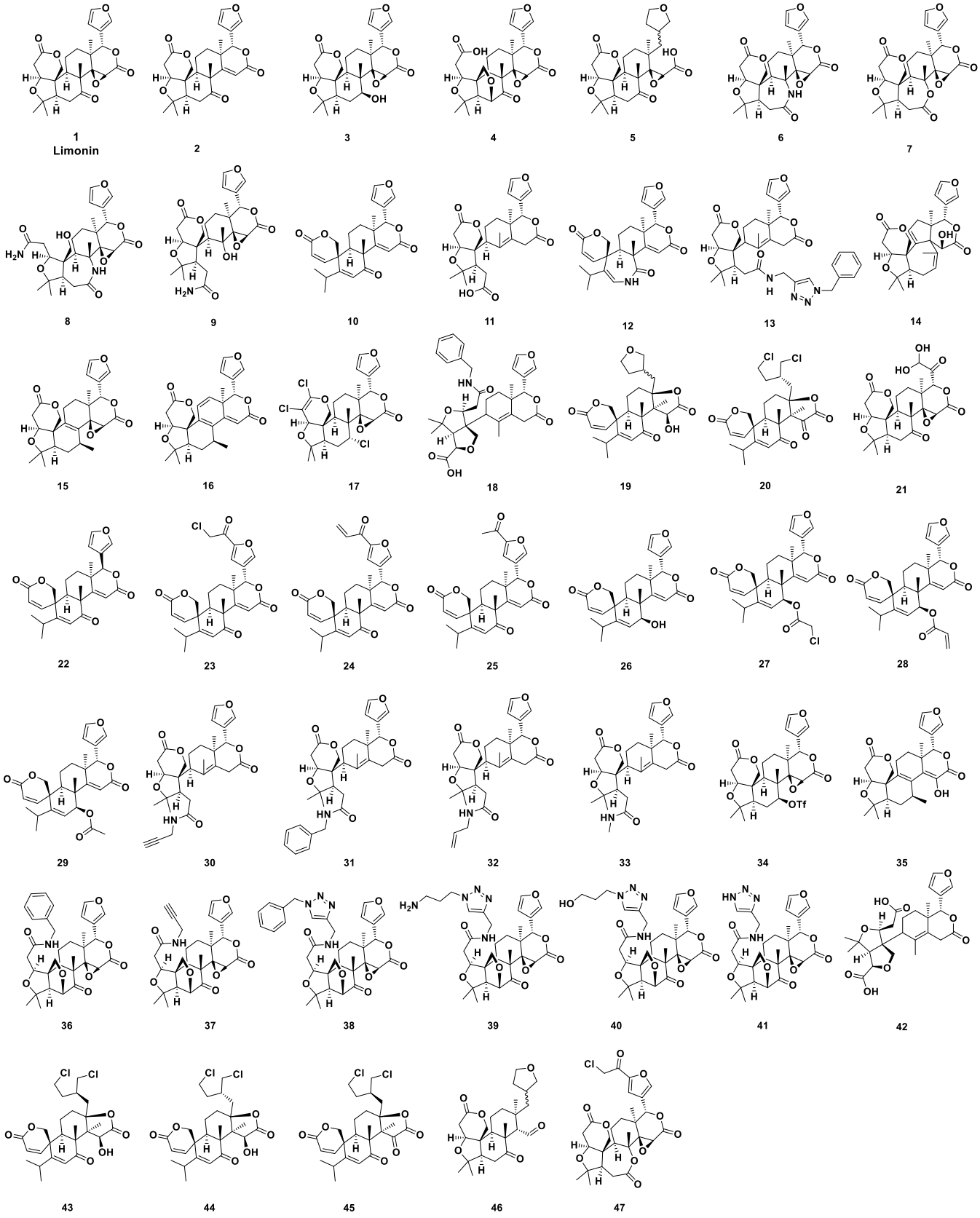


Figure S1. Compounds synthesized by ring distortion of limonin (**1-47**).

SUPPORTING INFORMATION

Full Set of CtD Compounds (continue)

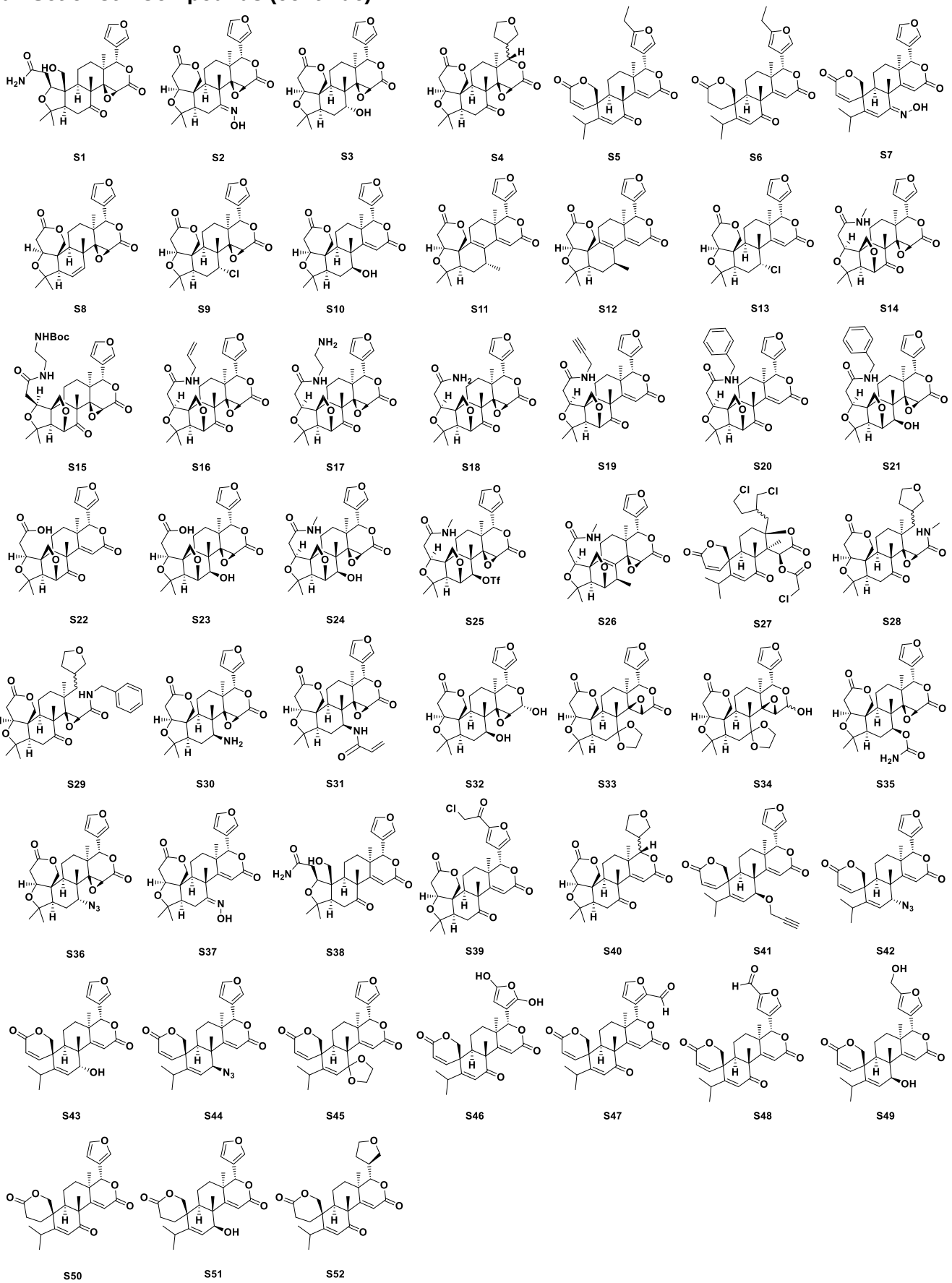


Figure S2. Compounds synthesized by ring distortion of limonin (**S1-S52**).

SUPPORTING INFORMATION

Table S1. Amount of Compounds Synthesized

Compound	Amount Obtained	Compound	Amount Obtained	Compound	Amount Obtained	Compound	Amount Obtained
2	>20 mg	**33**	>20 mg	**S16**	>20 mg	**S47**	>20 mg
3	>20 mg	**34**	>20 mg	**S17**	>20 mg	**S48**	>20 mg
4	>20 mg	**35**	3 mg	**S18**	20 mg	**S49**	>20 mg
5	>20 mg	**36**	>20 mg	**S19**	20 mg	**S50**	>20 mg
6	>20 mg	**37**	>20 mg	**S20**	>20 mg	**S51**	>20 mg
7	>20 mg	**38**	>20 mg	**S21**	>20 mg	**S52**	>20 mg
8	>20 mg	**39**	>20 mg	**S22**	>20 mg	**S53**	14 mg
9	>20 mg	**40**	>20 mg	**S23**	>20 mg	**S54**	>20 mg
10	>20 mg	**41**	>20 mg	**S24**	>20 mg	**S55**	>20 mg
11	>20 mg	**42**	>20 mg	**S25**	>20 mg	**S56**	>20 mg
12	3 mg	**43**	>20 mg	**S26**	>20 mg	**S57**	2 mg
13	>20 mg	**44**	>20 mg	**S27**	>20 mg	**S58**	>20 mg
14	>20 mg	**45**	>20 mg	**S28**	>20 mg	**S59**	3 mg
15	>20 mg	**46**	>20 mg	**S29**	>20 mg	**S60**	>20 mg
16	8 mg	**47**	>20 mg	**S30**	20 mg	**S61**	>20 mg
17	>20 mg	**48**	>20 mg	**S31**	>20 mg	**S62**	>20 mg
18	>20 mg	**S1**	>20 mg	**S32**	>20 mg	**S63**	>20 mg
19	>20 mg	**S2**	>20 mg	**S33**	>20 mg	**S64**	>20 mg
20	>20 mg	**S3**	>20 mg	**S34**	>20 mg	**S65**	>20 mg
21	>20 mg	**S4**	>20 mg	**S35**	>20 mg	**S66**	20 mg
22	6 mg	**S5**	>20 mg	**S36**	>20 mg	**S67**	>20 mg
23	>20 mg	**S6**	18 mg	**S37**	>20 mg	**S68**	>20 mg
24	2.8 mg	**S7**	>20 mg	**S38**	>20 mg	**S69**	16 mg
25	>20 mg	**S8**	>20 mg	**S39**	>20 mg	**S70**	>20 mg
26	>20 mg	**S9**	>20 mg	**S40**	>20 mg	**S71**	2 mg
27	>20 mg	**S10**	>20 mg	**S41**	>20 mg	**S72**	>20 mg
28	>20 mg	**S11**	>20 mg	**S42**	>20 mg		
29	>20 mg	**S12**	12 mg	**S43**	>20 mg		
30	>20 mg	**S13**	>20 mg	**S44**	6 mg		
31	>20 mg	**S14**	>20 mg	**S45**	8 mg		
32	>20 mg	**S15**	>20 mg	**S46**	>20 mg		

Comparison of Complexity Metrics of Limonin Set with Various Small Molecule Compound Libraries

➢ Antibacterial Drugs (O'Shea and Moser Antibacterial)

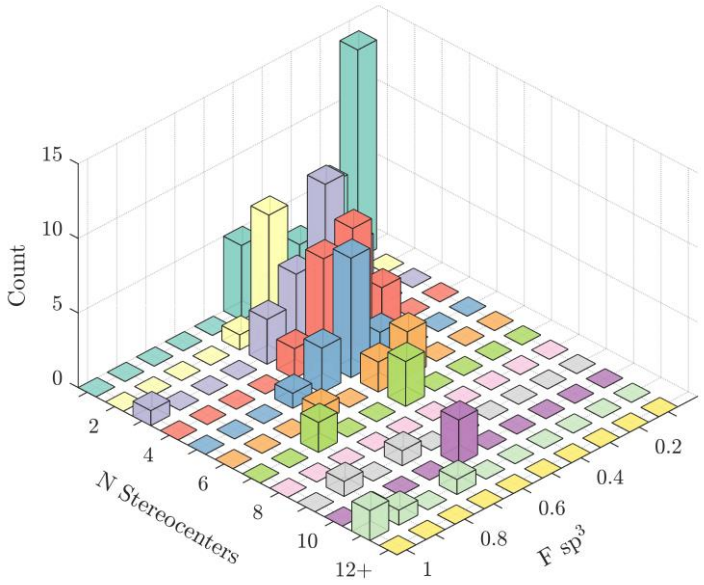


Figure S3. Complexity metrics (Fsp^3 and chiral centers) of Antibacterial Drugs.

➢ Anticancer Drugs (AOD8)

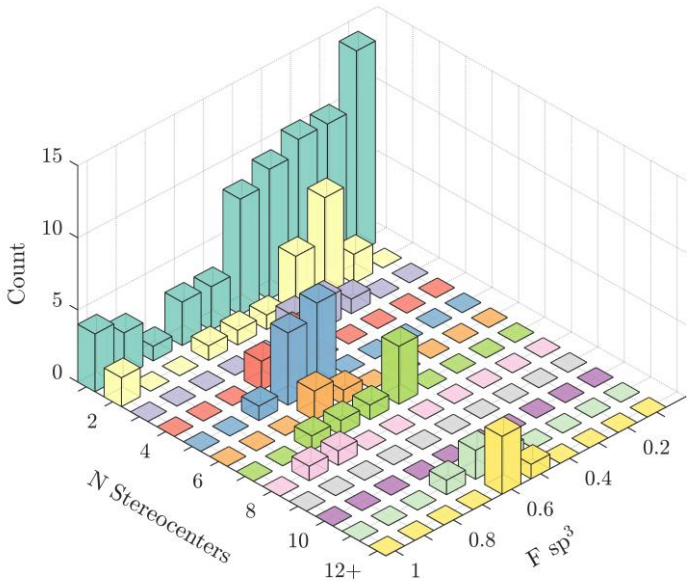


Figure S4. Complexity metrics (Fsp^3 and chiral centers) of Anticancer Drugs.

➢ Chembridge CL

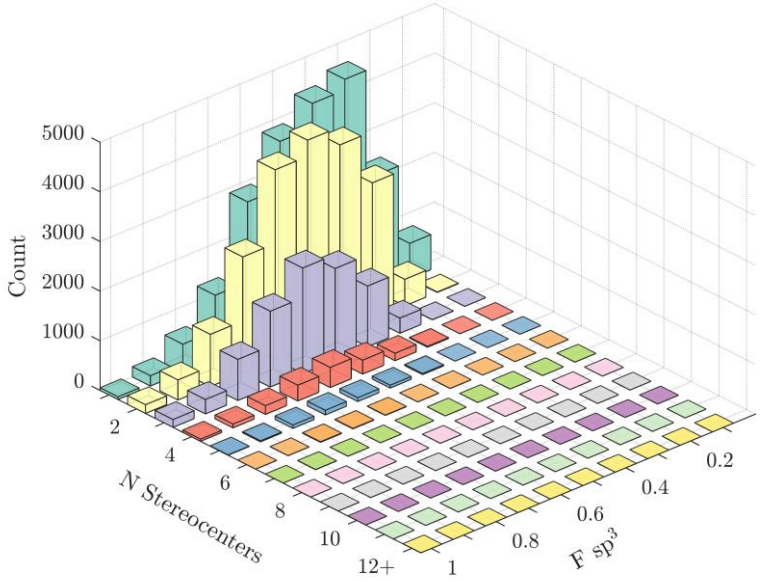


Figure S5. Complexity metrics (Fsp^3 and chiral centers) of Chembridge CL.

➢ Chembridge EXP

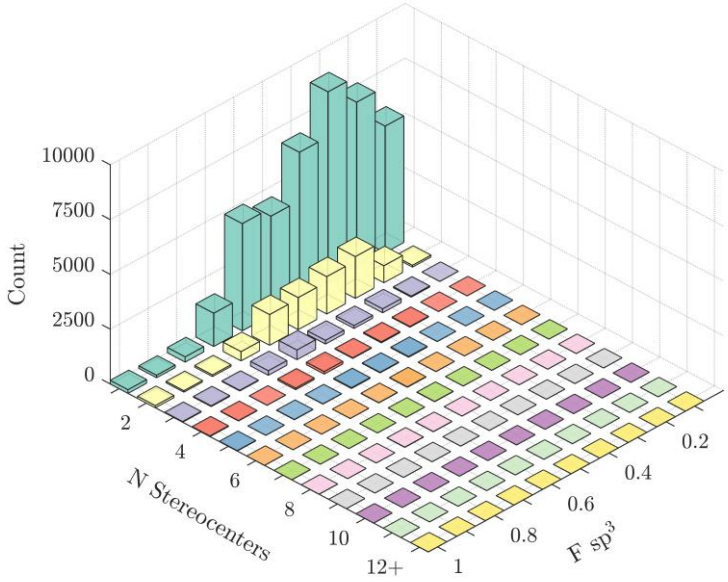


Figure S6. Complexity metrics (Fsp^3 and chiral centers) of Chembridge EXP.

➢ Chembridge Microformat

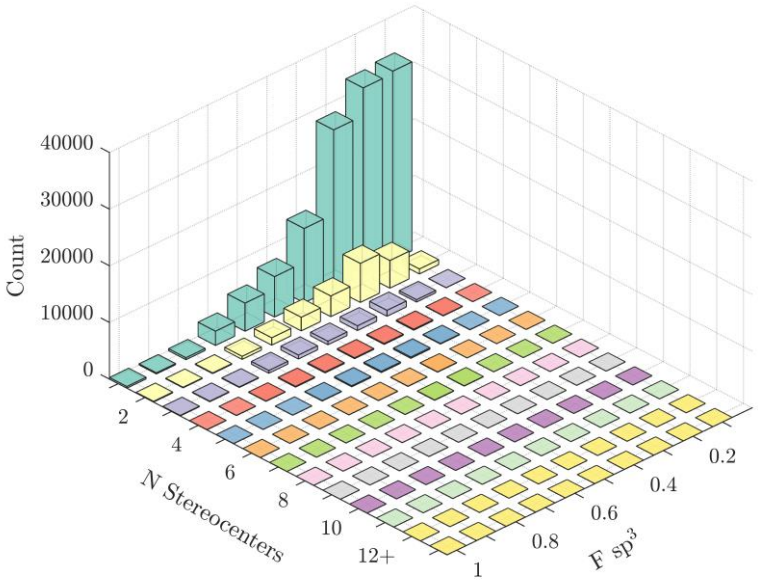


Figure S7. Complexity metrics (Fsp^3 and chiral centers) of Chembridge Microformat.

➢ Drugbank

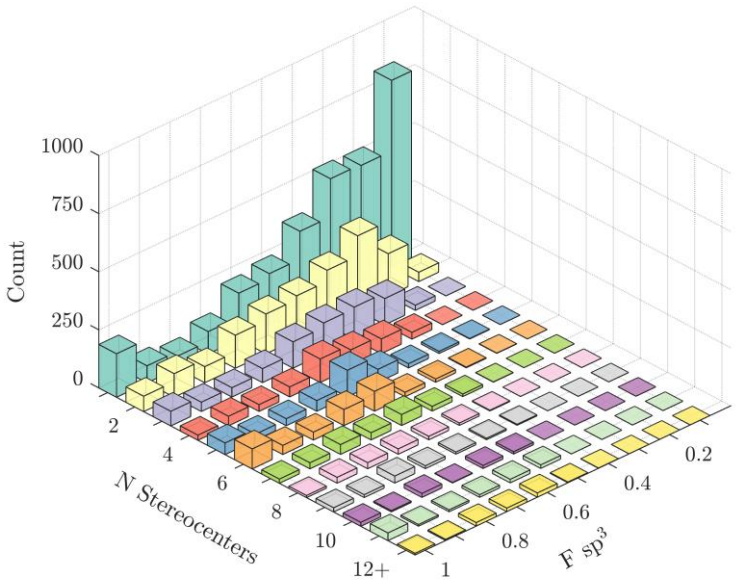


Figure S8. Complexity metrics (Fsp^3 and chiral centers) of Approved drugs (Drugbank library).

➢ NPASS (Natural Products)

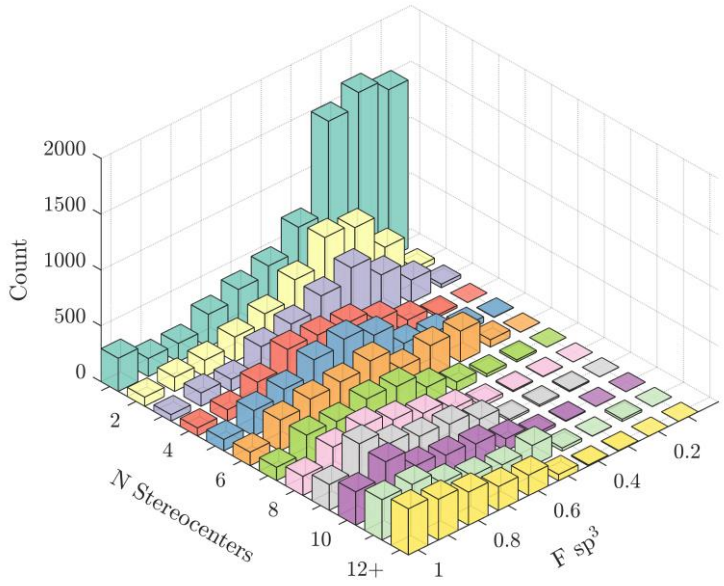


Figure S9. Complexity metrics (Fsp^3 and chiral centers) of Natural Products NPASS.

MLSMR (Natural Products)

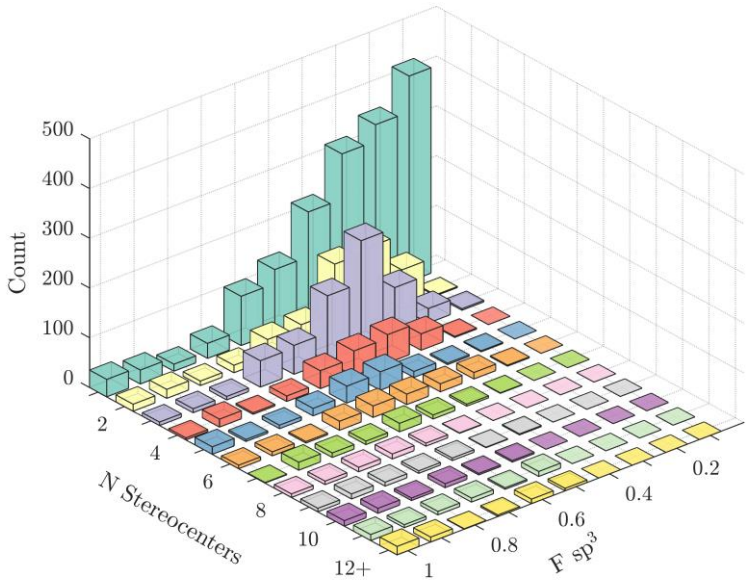


Figure S10. Complexity metrics (Fsp^3 and chiral centers) of Natural Products MLSMR.

➢ CtD Libraries

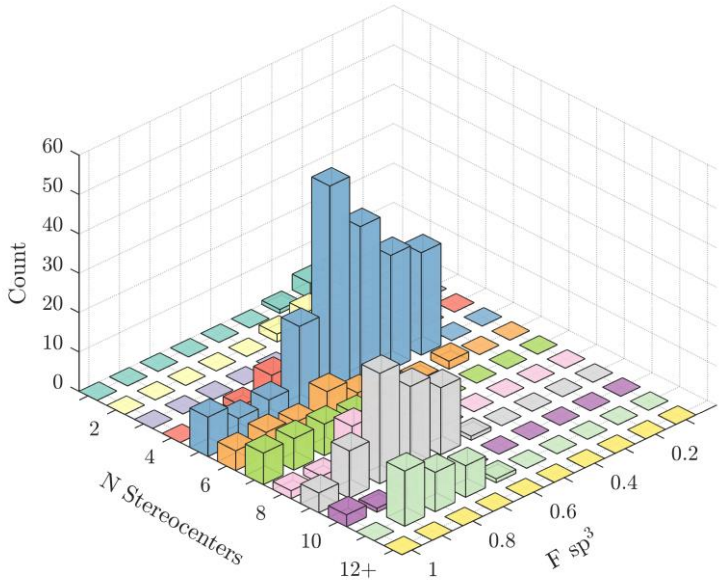


Figure S11. Complexity metrics (Fsp^3 and chiral centers) of Full CtD library.

➢ Limonin CtD Library

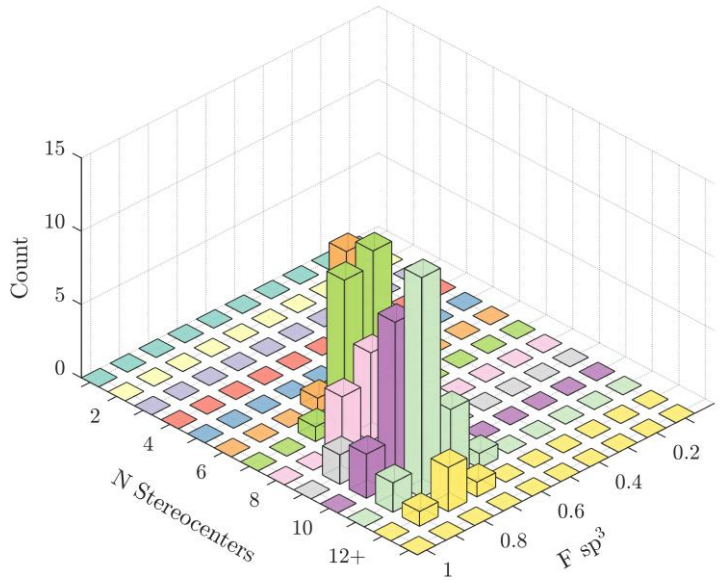


Figure S12. Complexity metrics (Fsp^3 and chiral centers) of Limonin Library.

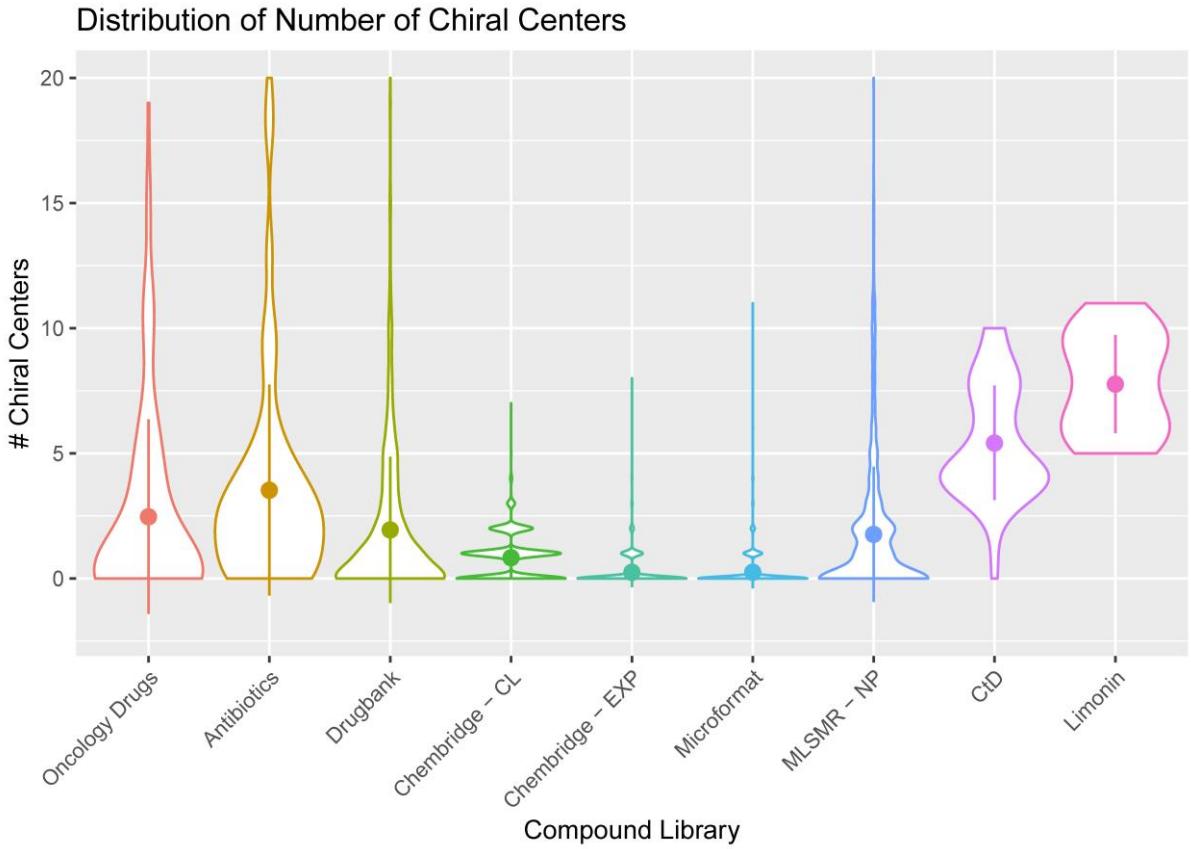


Figure S13. Distribution of Number of Chiral Centers of Limonin CtD library: comparison of number of chiral centers of limonin set with various small molecule compound libraries.

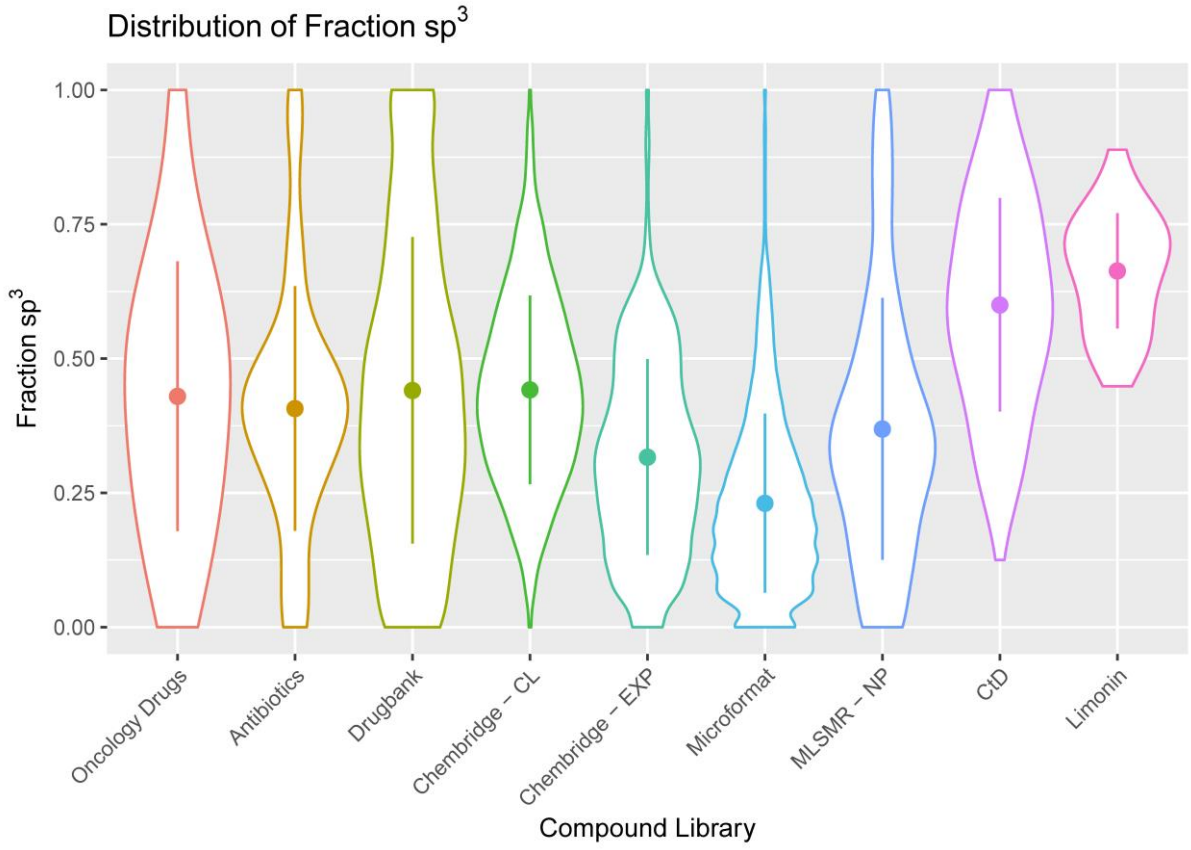


Figure S14. Distribution of Fraction sp^3 of Limonin CtD library: comparison of fraction sp^3 of limonin set with various small molecule compound libraries.

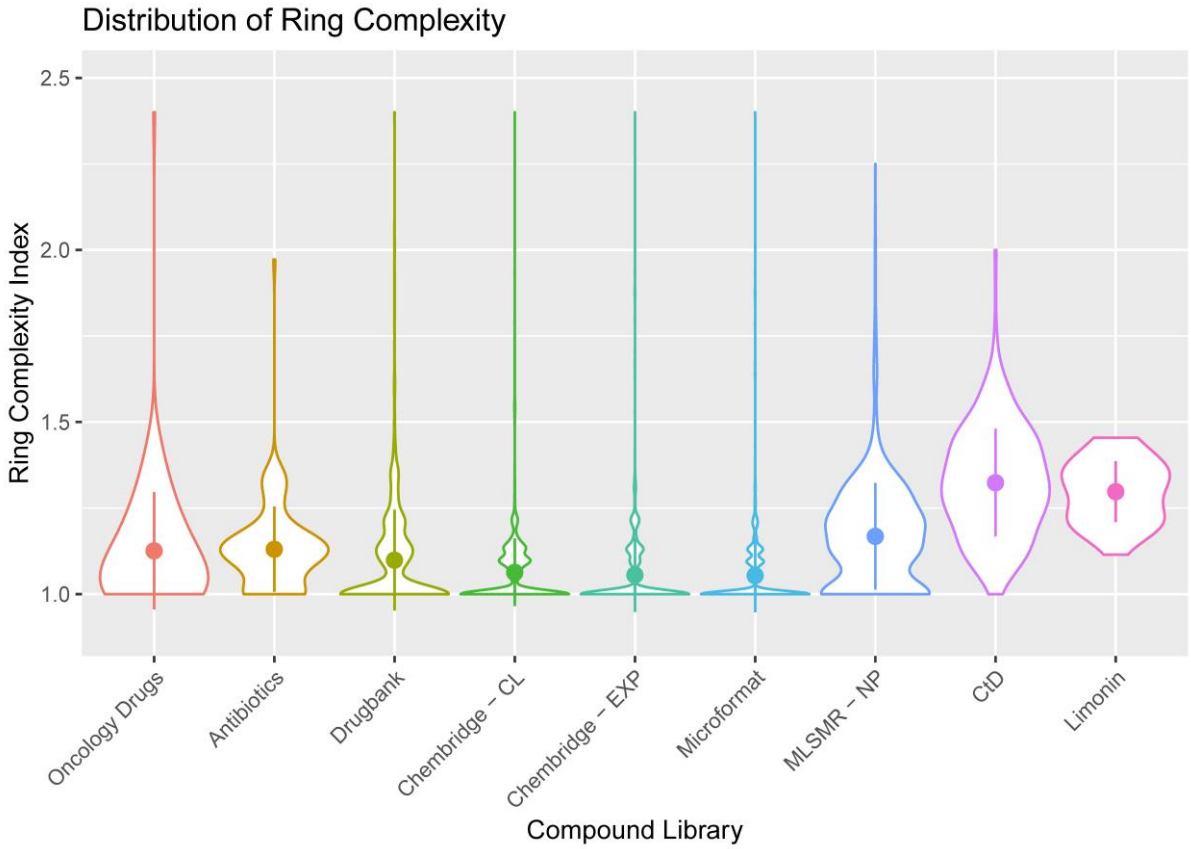


Figure S15. Distribution of Ring Complexity of Limonin CtD library: comparison of Ring Complexity of limonin set with various small molecule compound libraries.

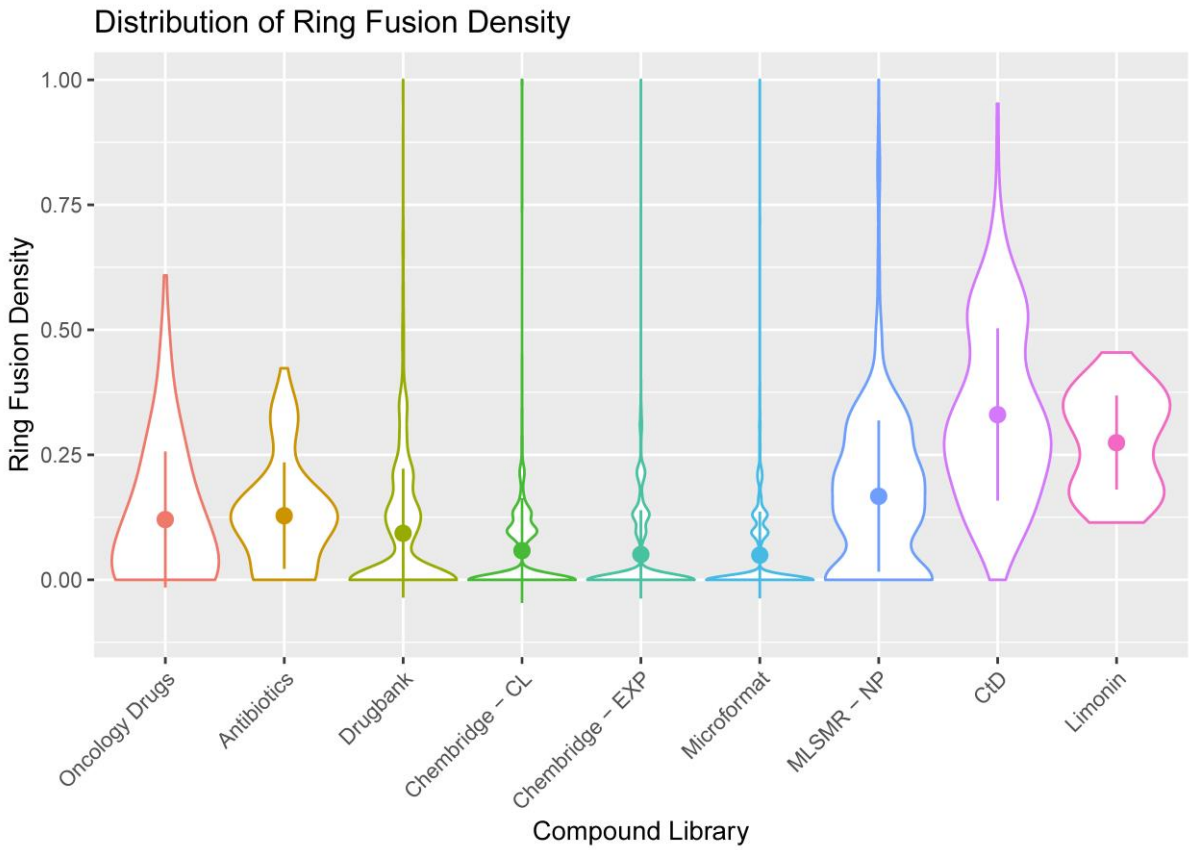


Figure S16. Distribution of Ring Fusion Density of Limonin CtD library: comparison of Ring Fusion Density of limonin set with various small molecule compound libraries.

SUPPORTING INFORMATION

Comparison of Diversity Metrics of Limonin Set with Various Small Molecule Compound Libraries

Table S2. Murcko scaffolds analysis: results of the scaffold diversity analysis of Limonin library

Compound collection	M[a]	N[b]	N/M	N_{sing}[c]	N_{sing}/N	N_{sing}/M
Oncology Drugs	124	98	0.79	82	0.84	0.36
Antibiotics	128	91	0.71	72	0.79	0.56
Drugbank	9377	5266	0.56	4286	0.70	0.36
Chembridge-CL	50000	41954	0.84	38459	0.91	0.77
Chembridge-EXP	49994	12272	0.24	7861	0.64	0.15
Microformat	149799	29295	0.19	17786	0.60	0.12
MLSMR	3357	1098	0.32	617	0.56	0.18
NPASS	2380	1213	0.51	853	0.70	0.36
Lycorine CtD	54	36	0.66	27	0.75	0.50
Pleuromutilin CtD	53	26	0.49	19	0.73	0.35
Limonin CtD	99	52	0.53	36	0.69	0.37

[a] *M* = number of compounds, [b] *N* = number of Murcko frameworks, [c] N_{sing} = number of singleton scaffolds (scaffold that are present in only one examplar molecule).

➢ Antibacterial Drugs (O'Shea and Moser Antibacterial)

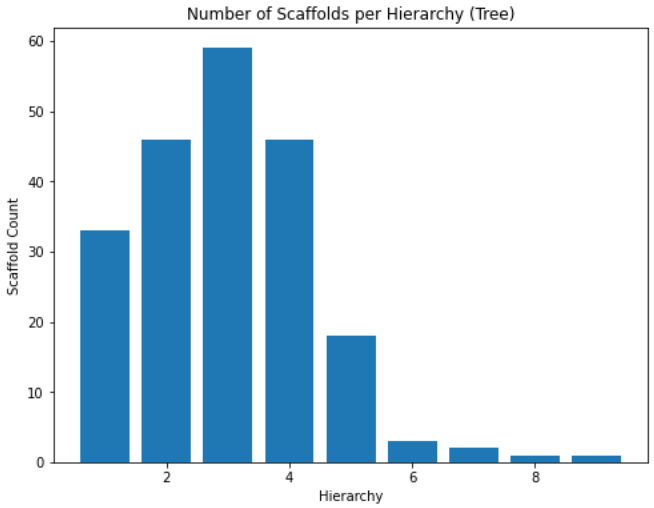


Figure S17. Scaffold tree of antibacterial drugs.

➢ Anticancer Drugs (OAD8)

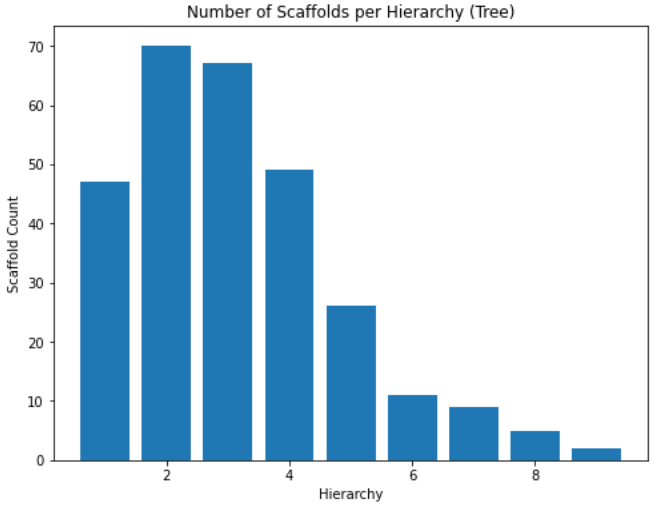


Figure S18. Scaffold tree of anticancer drugs.

➢ Chembridge CL

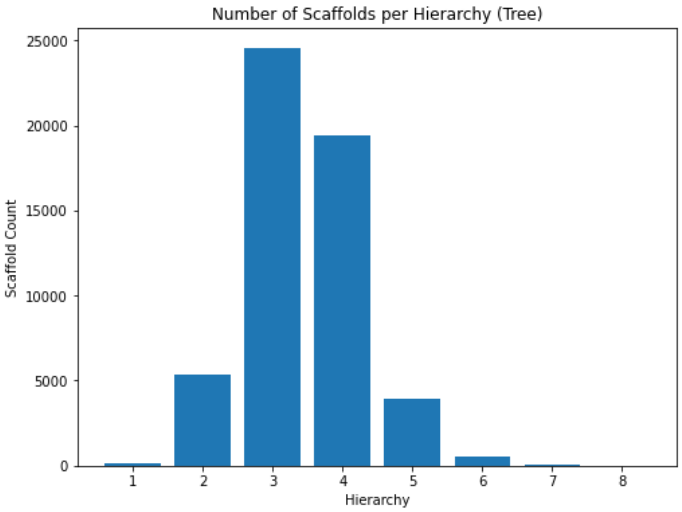


Figure S19. Scaffold tree of Chembridge CL.

➢ Chembridge EXP

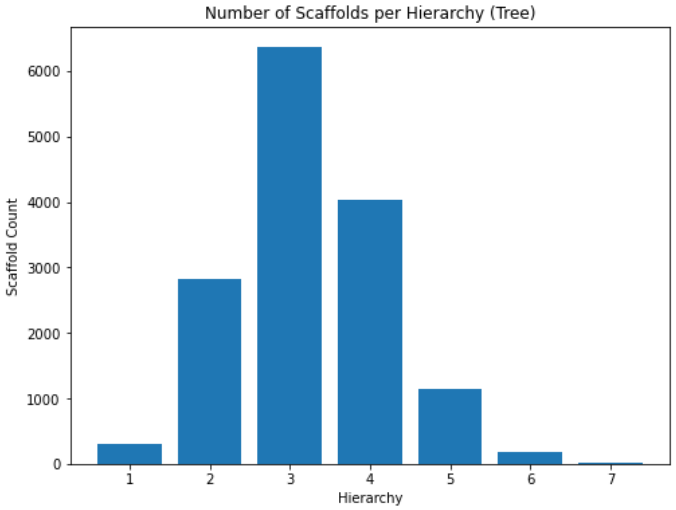


Figure S20. Scaffold tree of Chembridge EXP.

➢ Chembridge Microformat

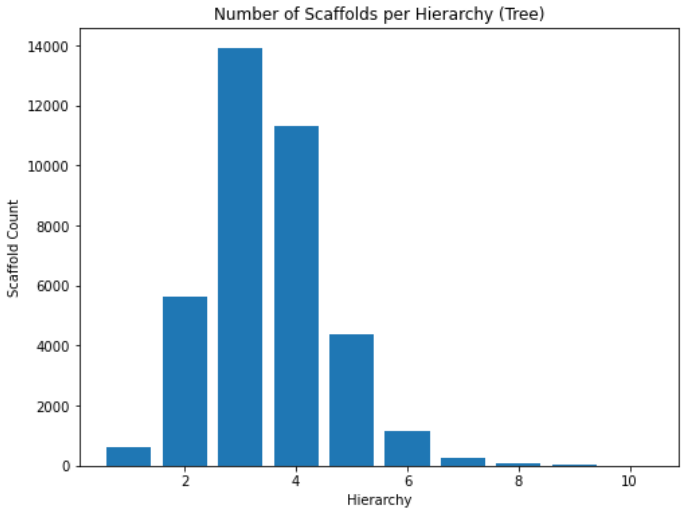


Figure S21. Scaffold tree of Chembridge Microformat.

➢ Drugbank

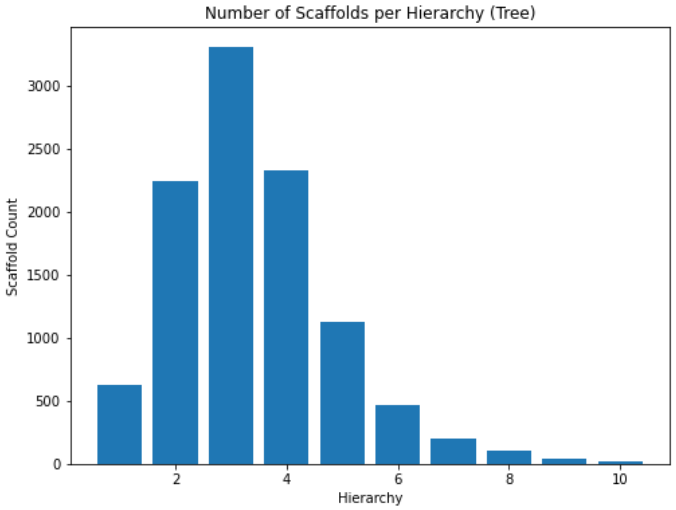


Figure S22. Scaffold tree of approved drugs (Drugbank).

➢ NPASS (Natural Products)

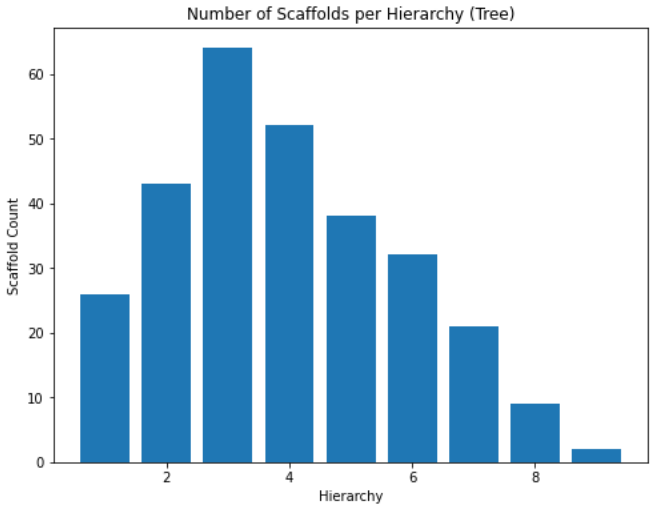


Figure S23. Scaffold tree of natural products NPASS.

➢ MLSMR (Natural Products)

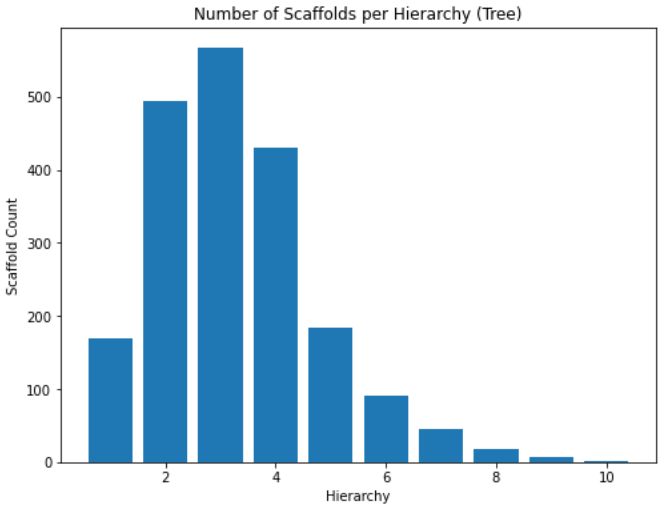


Figure S24. Scaffold tree of natural products MLSMR.

➢ Limonin CtD

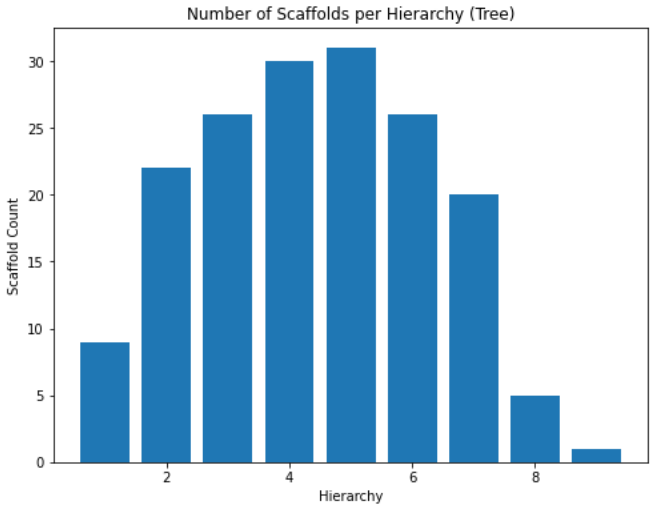


Figure S25. Scaffold tree of limonin CtD library.

➢ Pleuromutilin CtD

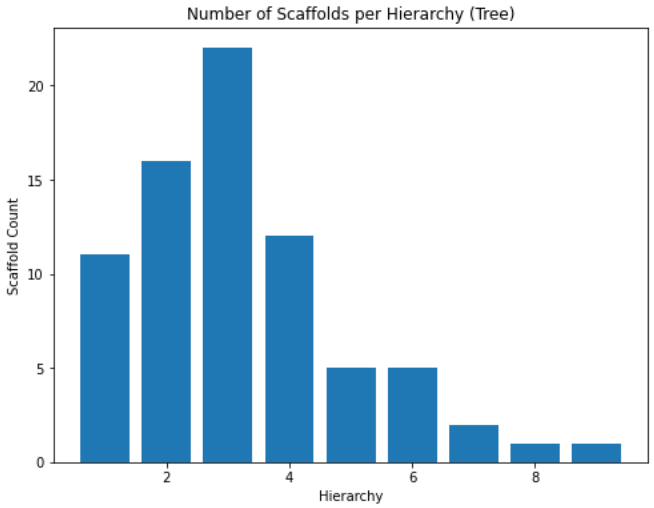


Figure S26. Scaffold tree of pleuromutilin CtD library.

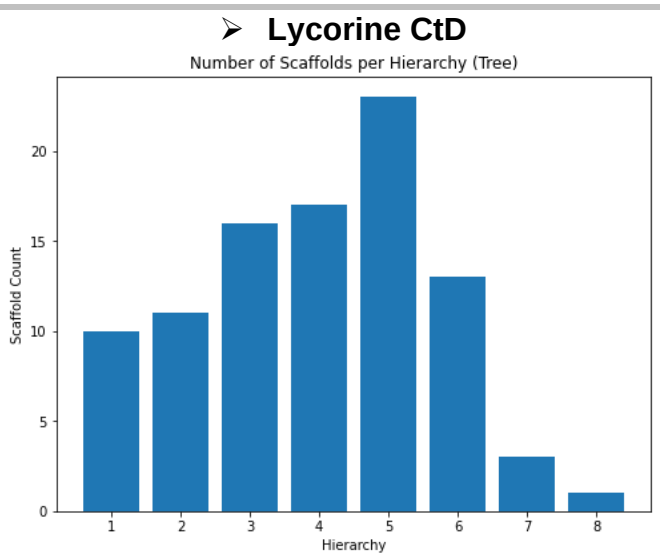


Figure S27. Scaffold tree of lycorine CtD library.

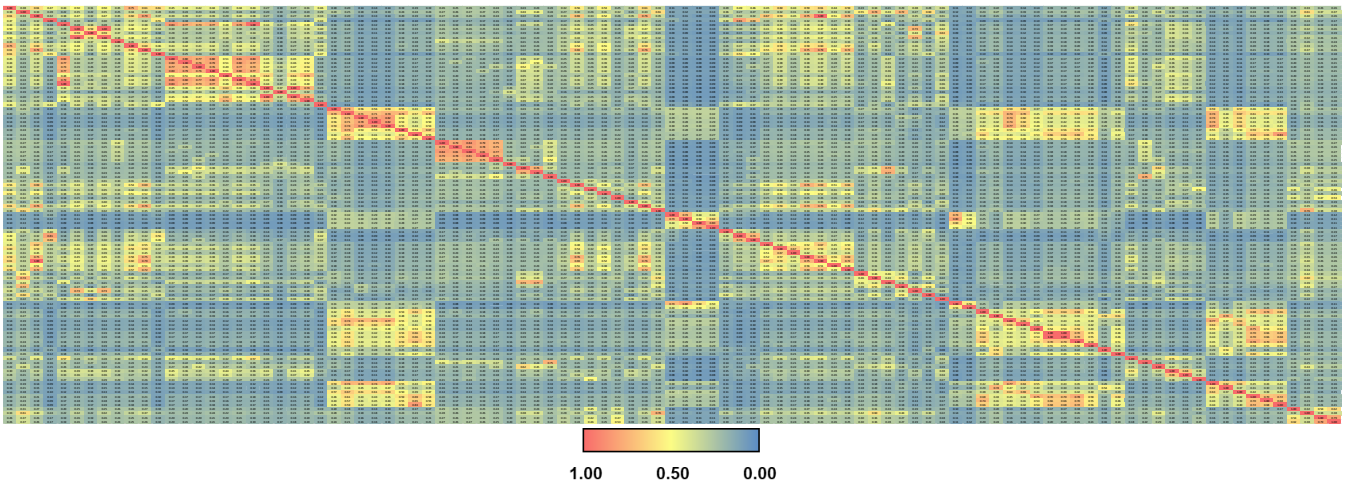


Figure S28. Tanimoto Similarity Matrix for the 99-compound set and limonin: The Tanimoto coefficient was calculated using Canvas (Schrödinger) using ECFP radial molecular fingerprint.

Cell Culture Studies

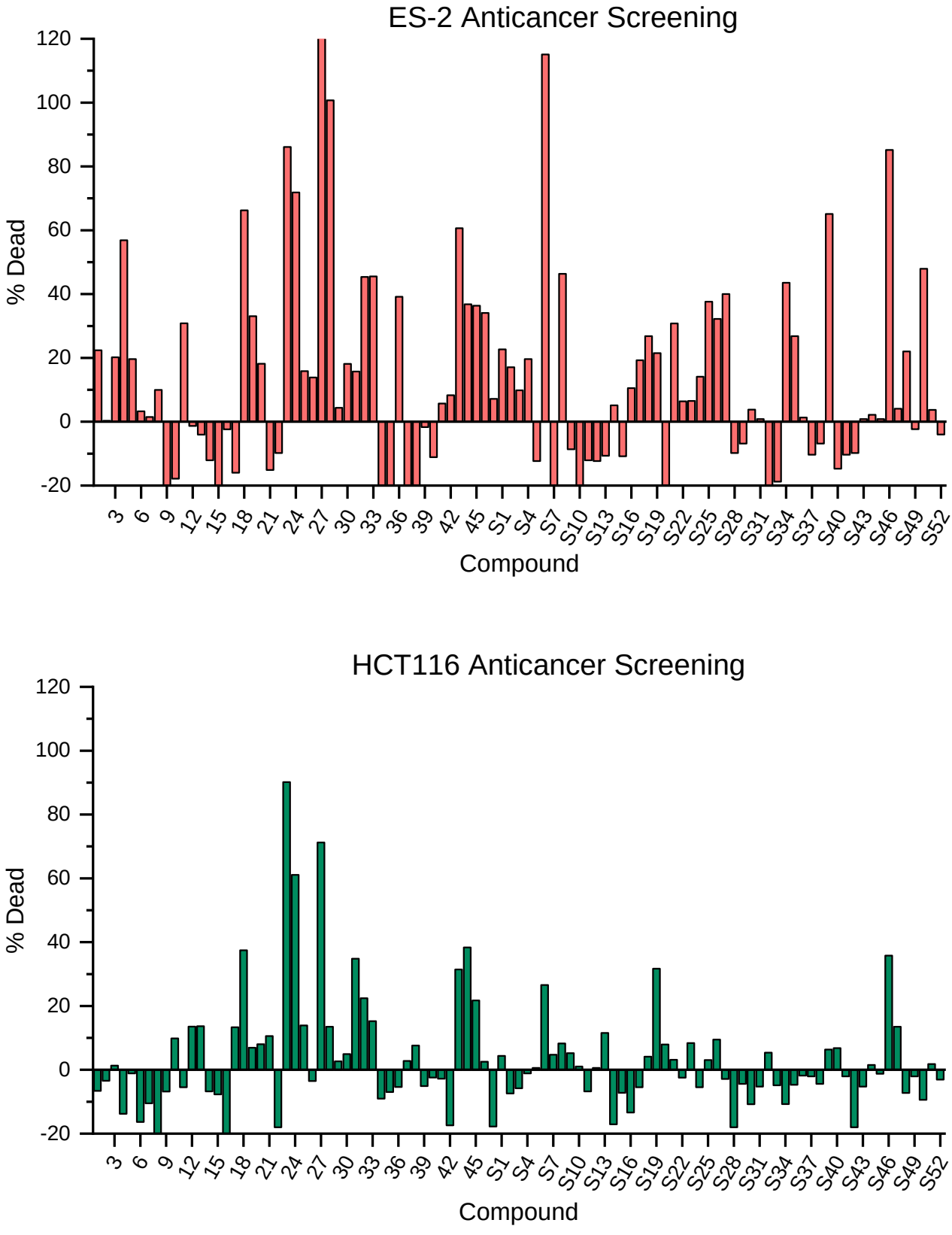


Figure S29. Anticancer screening results. Primary biological screening of limonin CtD library against ES-2 and HCT116 cancer cells. Compounds were tested at 20 µM. Cell viability was measured using Alamar Blue after 72 h.

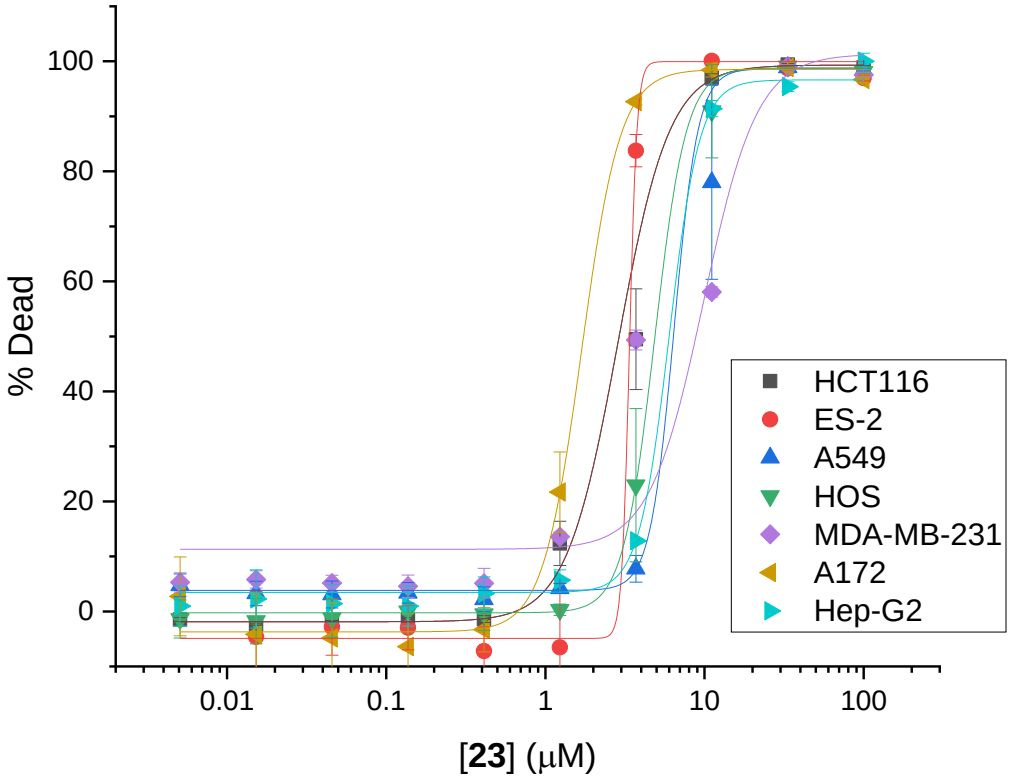
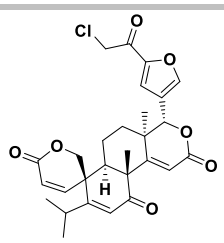
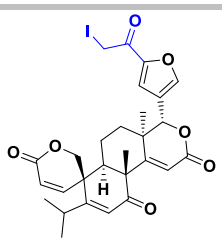


Figure S30. Dose-response curves for **23** against a panel of cancer cells. Bioactivity is expressed as a 72-hour IC_{50} value (in μM) against a panel of cell lines, as measured by Alamar Blue assay. Data represent mean ± SEM., Raptinal (50 μM) was used as dead control, *n* = 3 biological replicates.

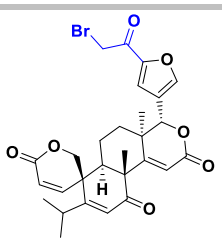
SUPPORTING INFORMATION



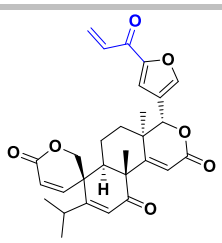
23
3 steps*
HCT116 = 3.28 ± 0.65
ES-2 = 3.65 ± 0.39



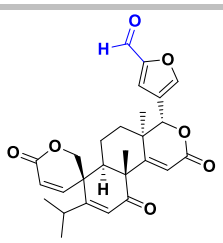
S53
4 steps*
HCT116 = 11.40 ± 0.01
ES-2 = 12.02 ± 3.01



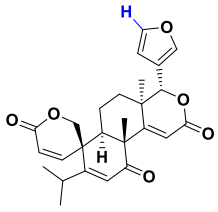
S54
3 steps*
HCT116 = 3.99 ± 0.53
ES-2 = 2.79 ± 0.35



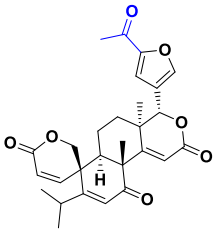
24
3 steps*
HCT116 = 23.04 ± 4.55
ES-2 = 10.81 ± 0.01



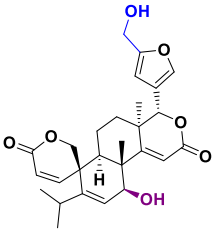
S48
3 steps*
HCT116 = >100
ES-2 = >100



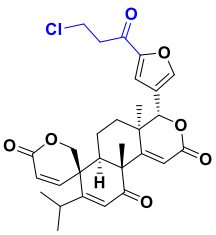
10
2 steps*
HCT116 = >50[a]
ES-2 = >50[a]



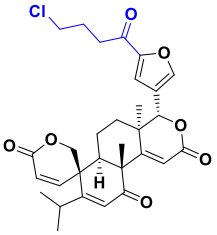
25
3 steps*
HCT116 = >100
ES-2 = >100



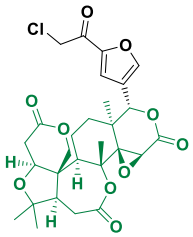
S49
4 steps*
HCT116 = >100
ES-2 = >100



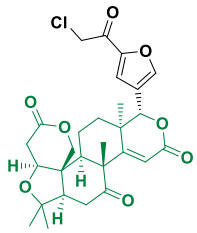
S55
3 steps*
HCT116 = 4.98 ± 0.54
ES-2 = 2.42 ± 0.26



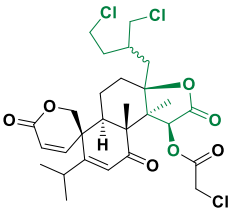
S56
3 steps*
HCT116 = >100
ES-2 = >100



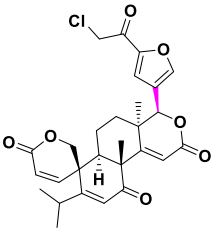
47
2 steps*
HCT116 = >100
ES-2 = >100



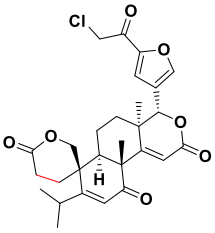
S39
2 steps*
HCT116 = 32.52 ± 3.24
ES-2 = 34.37 ± 0.13



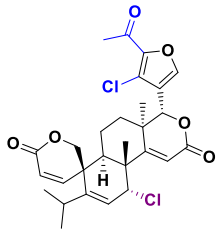
S27
3 steps*
HCT116 = 70.88 ± 7.46
ES-2 = 67.28 ± 2.84



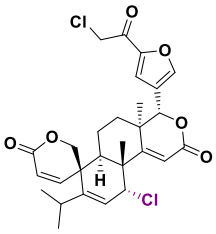
S57
3 steps*
HCT116 = 8.53 ± 1.23
ES-2 = 10.01 ± 0.01



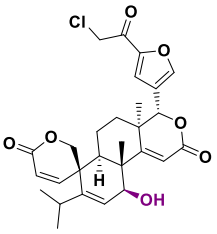
S60
4 steps*
HCT116 = 4.68 ± 0.69
ES-2 = 1.92 ± 0.28



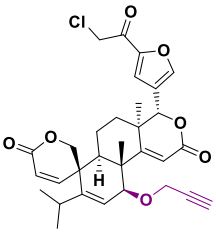
S66
6 steps*
HCT116 = 22.76 ± 2.19
ES-2 = 9.99 ± 1.12



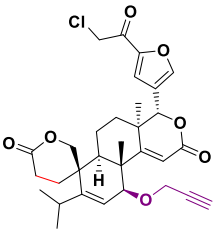
S67
6 steps*
HCT116 = 5.08 ± 0.62
ES-2 = 1.95 ± 0.06



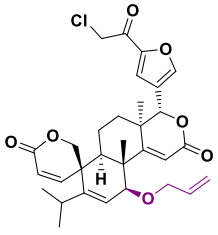
S59
5 steps*
HCT116 = 3.19 ± 1.04
ES-2 = 2.89 ± 0.63



48
7 steps*
HCT116 = 1.60 ± 0.44
ES-2 = 0.58 ± 0.03



S64
8 steps*
HCT116 = 2.45 ± 0.06
ES-2 = 1.27 ± 0.04



S69
7 steps*
HCT116 = 2.56 ± 0.06
ES-2 = 1.38 ± 0.03

Figure S31. Structure-activity relationship of **23** analogs. Bioactivity is expressed as a 72-hour IC_{50} value (in μM) against the HCT116 and ES-2 cell lines (3000 c/w), as measured by Alamar Blue assay. Data represent mean ± SEM. Raptinal (50 μM) was used as dead control, *n* = 3 biological replicates. *number of steps from limonin, [a] not soluble at 100 μM.

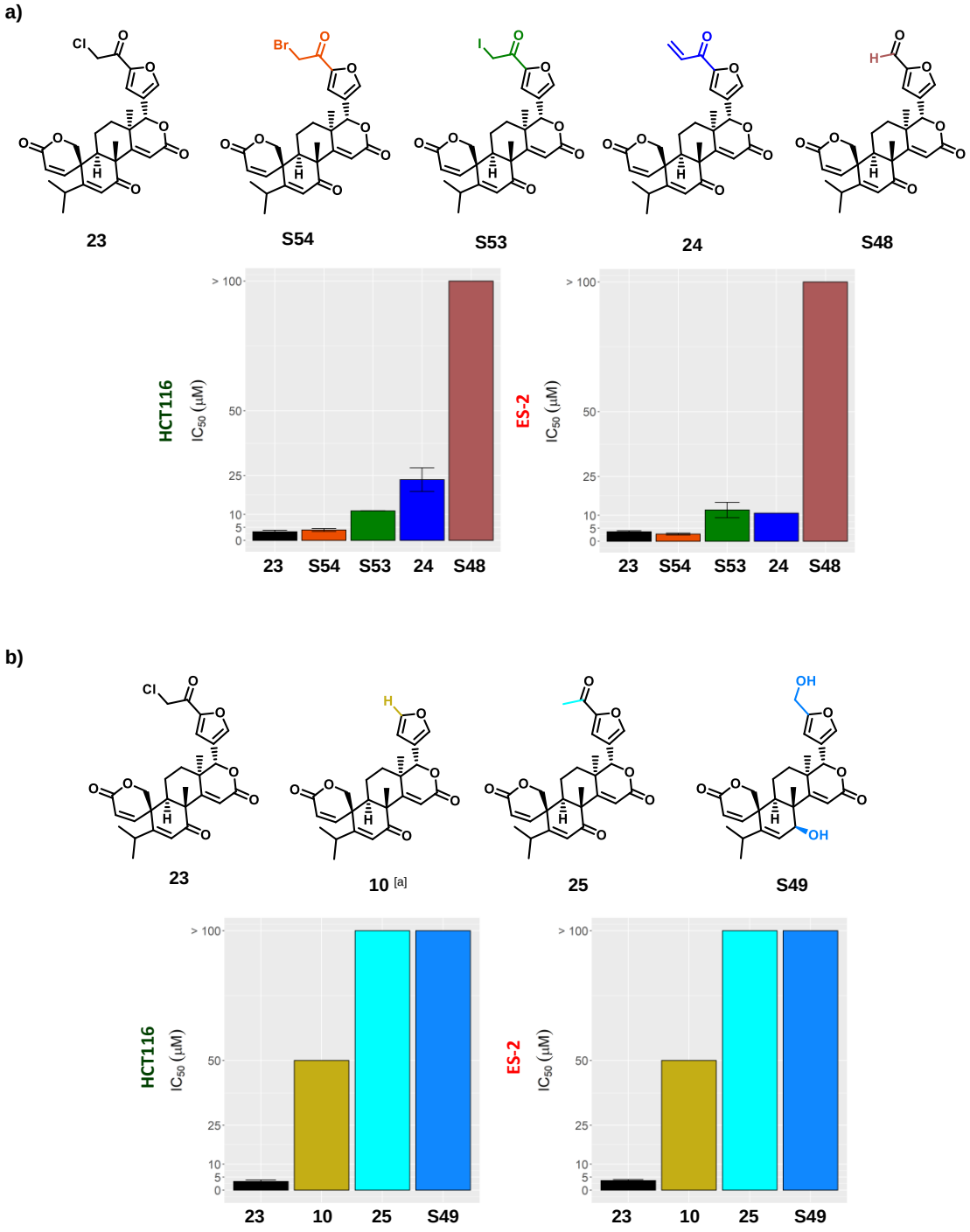


Figure S32. Structure-activity relationship of **23** analogs: effect of the warhead on anticancer activity. a) Electrophile modification; b) Electrophile removal. Bioactivity is expressed as a 72-hour IC_{50} value (in μM) against the HCT116 and ES-2 cell lines (3000 c/w), as measured by Alamar Blue assay. Data represent mean ± SEM. Raptinal (50 μM) was used as dead control, *n* = 3 biological replicates,[a] not soluble at 100 μM.

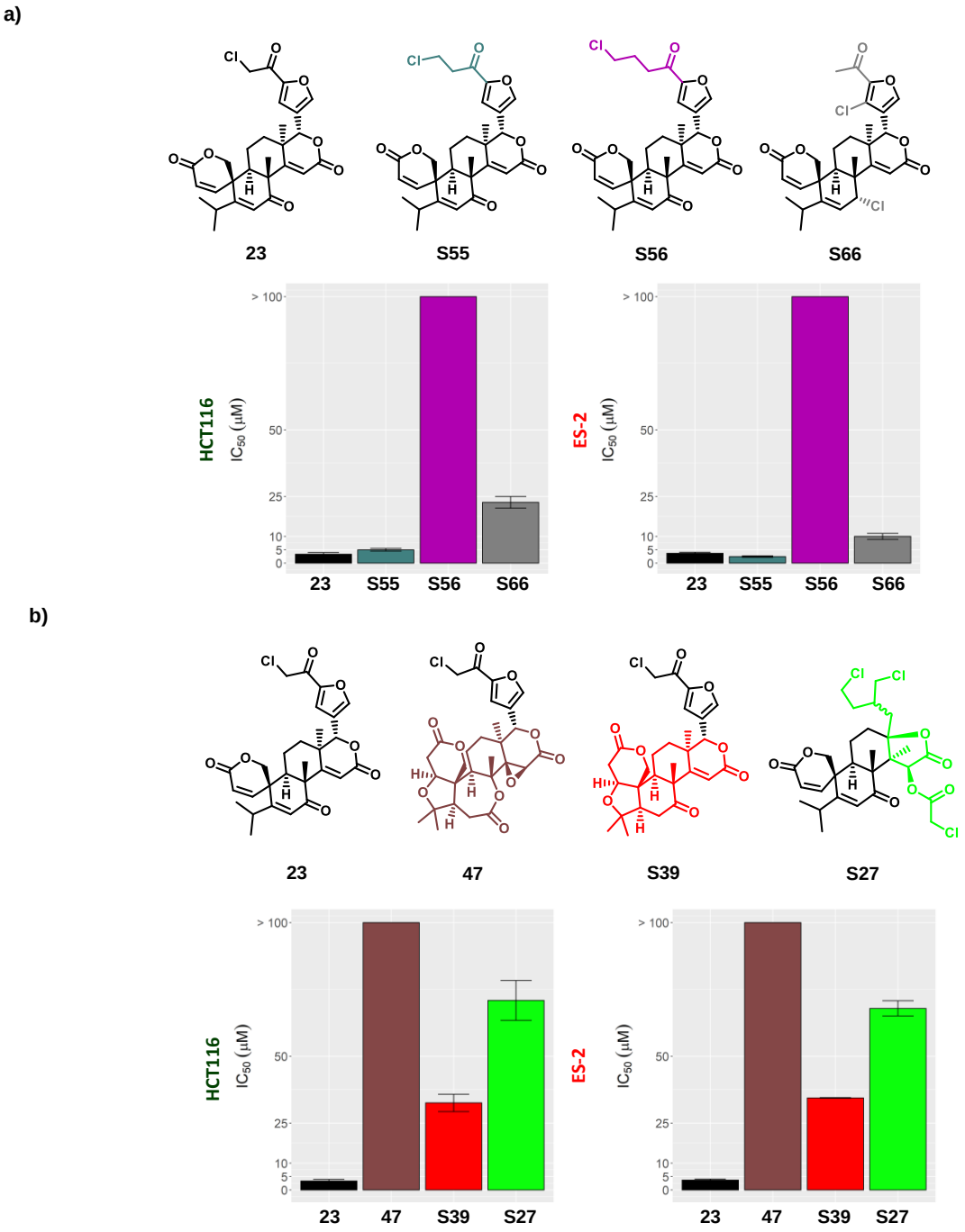


Figure S33. Structure-activity relationship of **23** analogs: effect of warhead and scaffold on anticancer activity. a) Chlorine position modification; b) scaffold replacement. Bioactivity is expressed as a 72-hour IC_{50} value (in μM) against the HCT116 and ES-2 cell lines (3000 c/w), as measured by Alamar Blue assay. Data represent mean ± SEM. Raptinal (50 μM) was used as dead control, *n* = 3 biological replicates.

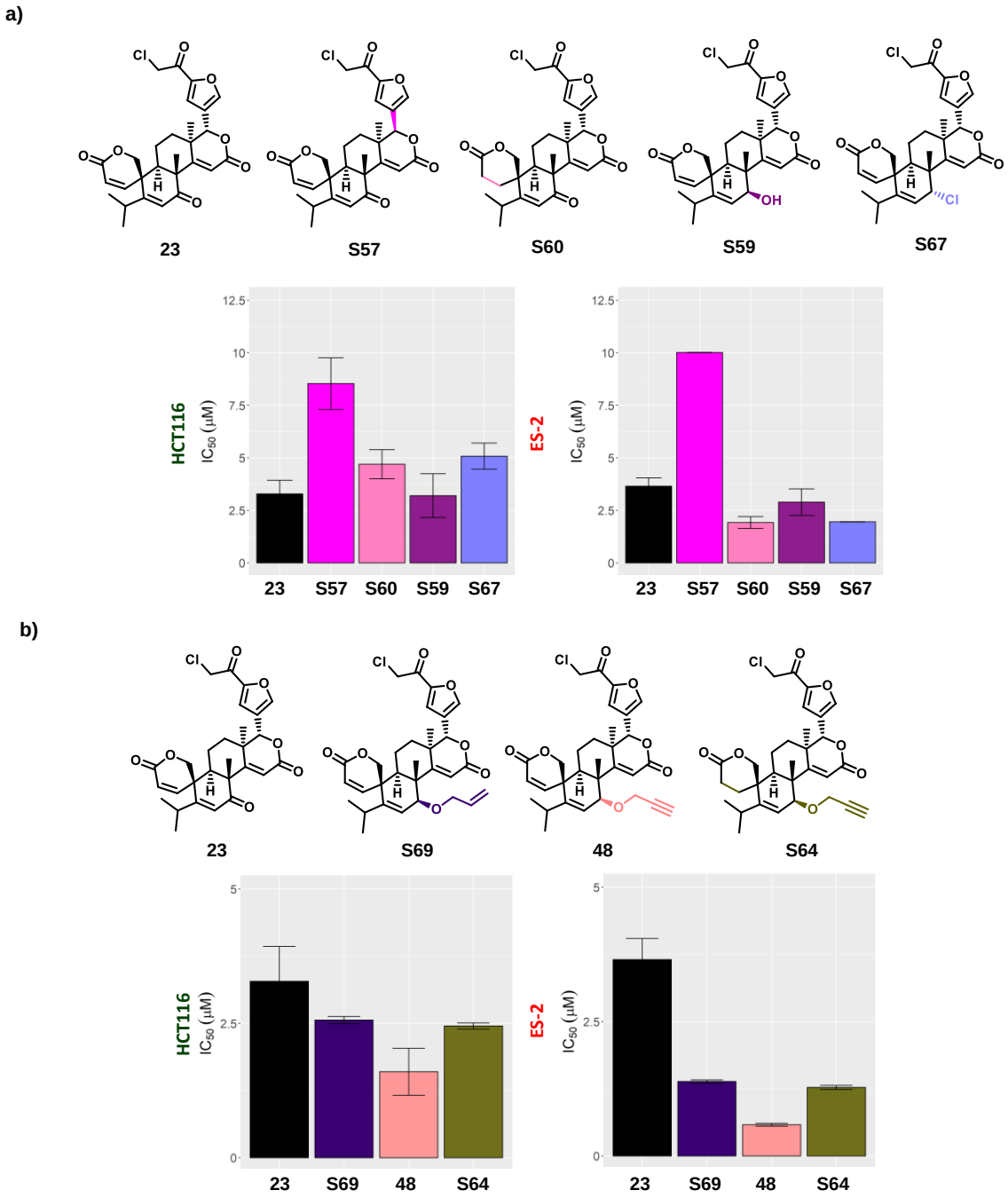


Figure S34. . Structure-activity relationship of **23** analogs: functional group manipulation. a) Effect of furan stereochemistry, A-ring unsaturation, and B ring ketone on the anticancer activity; b) effect of B-ring manipulation. Bioactivity is expressed as a 72-hour IC_{50} value (in μM) against the HCT116 and ES-2 cell lines (3000 c/w), as measured by Alamar Blue assay. Data represent mean ± SEM. Raptinal (50 μM) was used as dead control, *n* = 3 biological replicates.

Full Set SAR derivatives and Intermediates

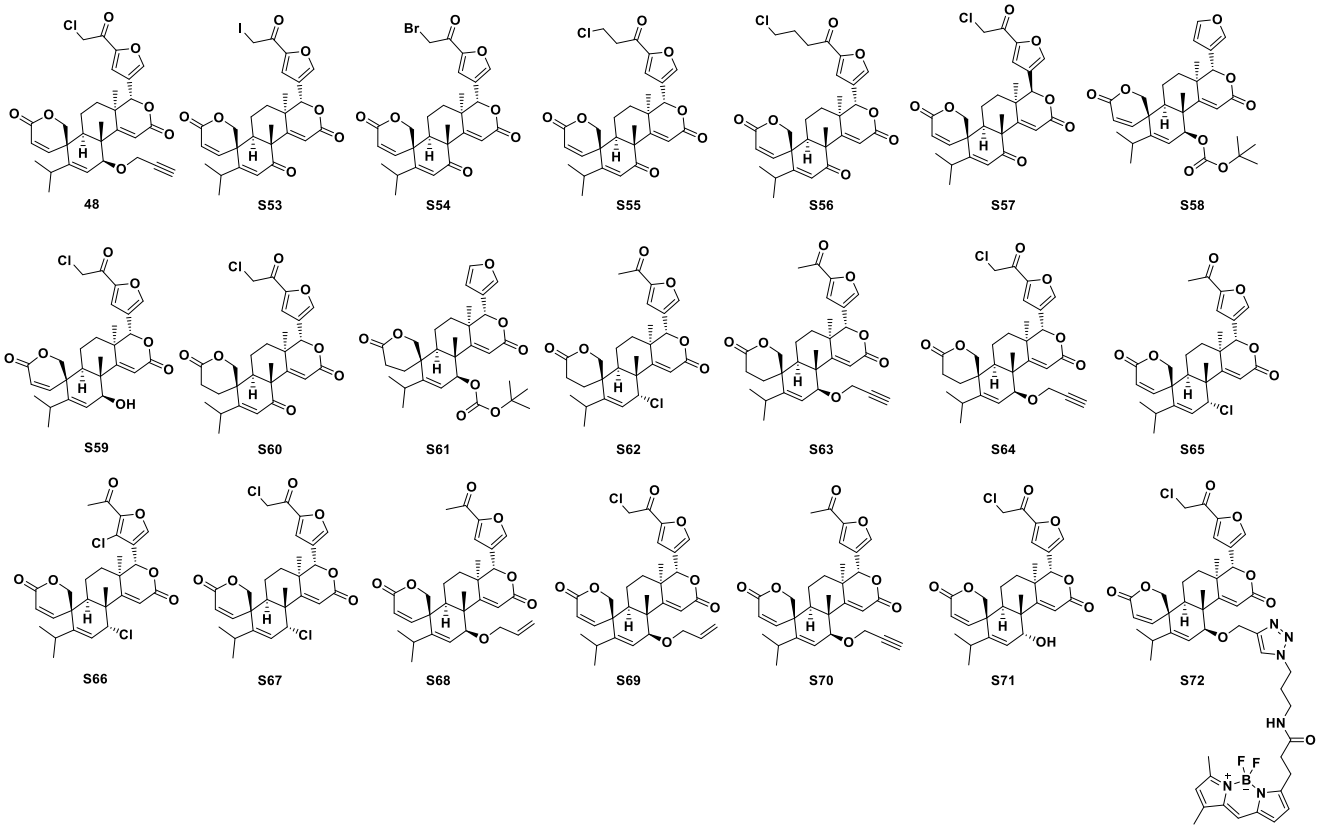


Figure S35. SAR derivatives and Intermediates of **23** (**48**, **S53-S72**).

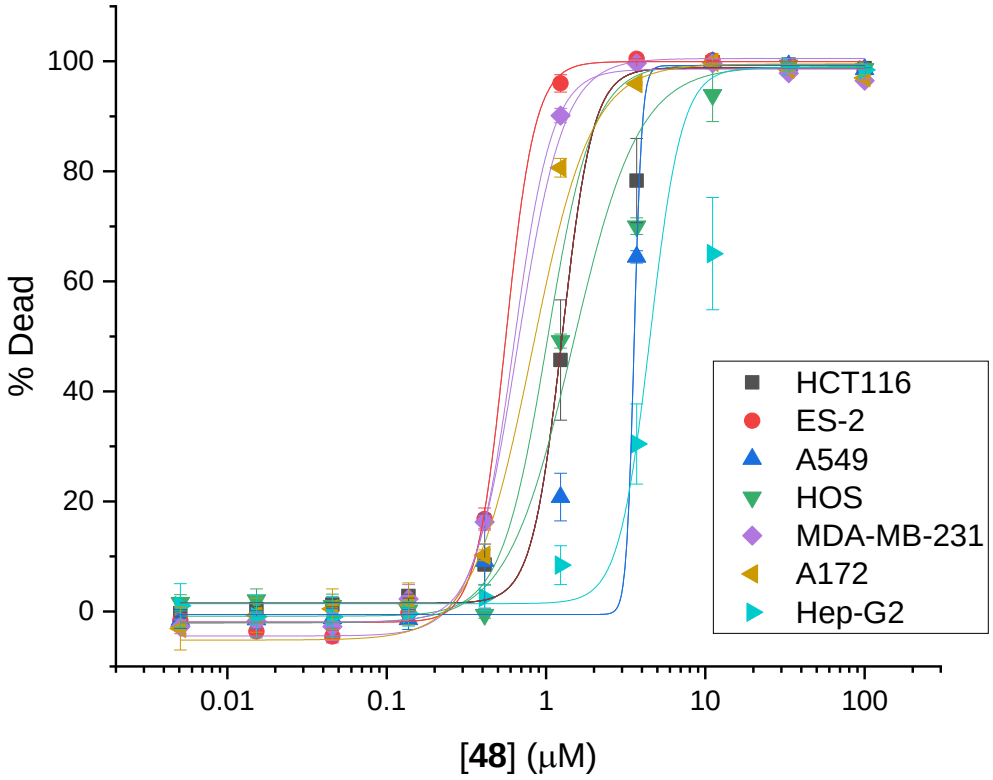


Figure S36. Dose-response curves for **48** against a panel of cancer cells. Bioactivity is expressed as a 72-hour IC_{50} value (in μM) against a panel of cell lines, as measured by Alamar Blue assay Data represent mean ± SEM., Raptinal (50 μM) was used as dead control, *n* = 3 biological replicates.

Mode of Cell Death

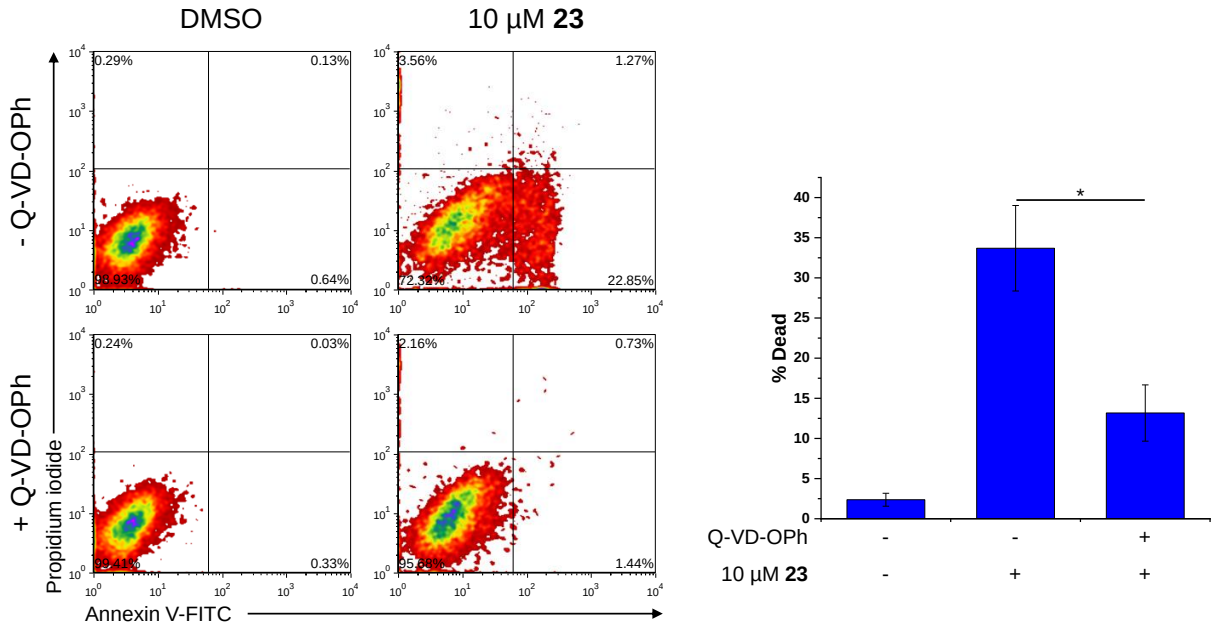


Figure S37. Compound **23** induces apoptotic cell death as assessed by Annexin V and propidium iodide staining. Cells are protected from death induced by **23** by pan-caspase inhibitor, Q-VD-OPh. HCT116 cells were pre-treated with 25 µM Q-VD-OPh and then incubated for 24 h before flow cytometry analysis. n=4, error is SEM, two-tailed t-test, * p<0.05.

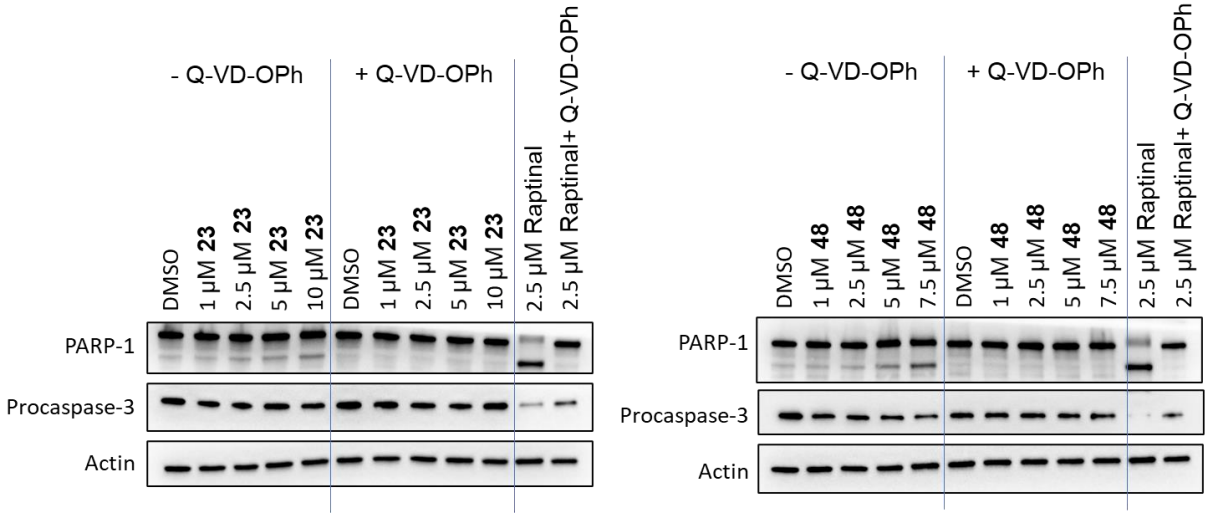


Figure S38. 23 and **48** induce apoptotic cell death after 24 hours. Western blot shows PARP-1 cleavage after 24-hour treatment with **23** and **48** in HCT116 cells. Cells are protected from death induced by **23** and **48** by pan-caspase inhibitor, Q-VD-OPh. 300,000 cells/well, 24 h incubation, 15 µg protein loading, for protection studies, HCT116 cells were pre-treated with 25 µM Q-VD-OPh and then incubated for 24 h, n=2.

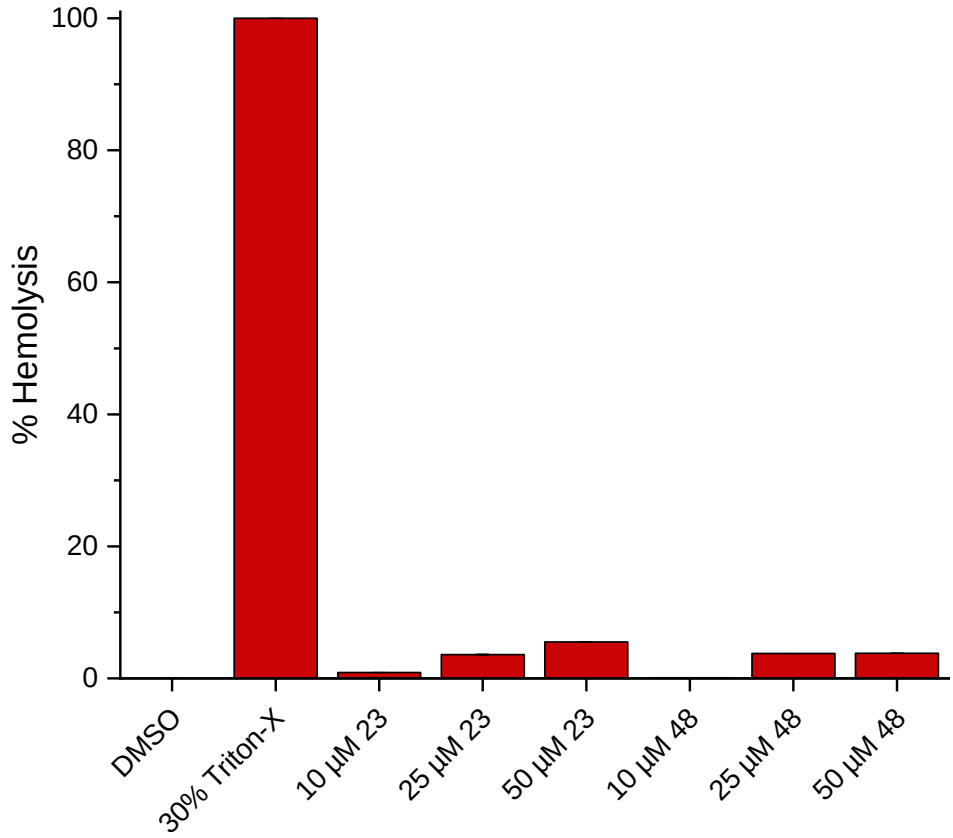


Figure S39. Lack of hemolytic activity of **23** and **48** in red blood cells, upon 2 hours treatment with 10, 25 and 50 µM of each compound; positive control: 30% Triton-X, negative control: DMSO, n=3 independent experiments.

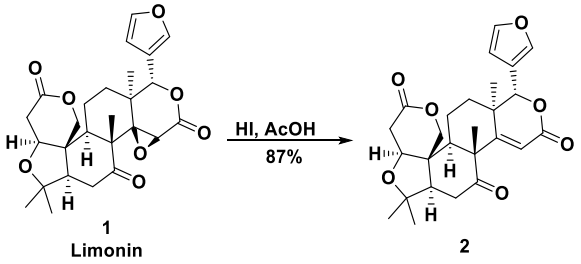
Experimental Procedures

Methods and Characterization

All chemical reagents were purchased from commercial sources and used without further purification. Limonin was purchased from Biopurify Phytochemicals Ltd (98% purity) and was used as received. Anhydrous dichloromethane, tetrahydrofuran, methanol, N,N-dimethylformamide, and acetonitrile used in this study were dried by percolation through columns packed with activated alumina under positive pressure of nitrogen. Reactions were monitored by LC-MS or thin layer chromatography using cerium molybdate and heat or $KMnO_4$ and heat as developing agents. Flash chromatography was performed using silica gel (250-400 mesh). The automated reverse phase purification was performed on a Biotage Isolera using Agela Technologies AQ C18 spherical 20-35 m 100A columns (12 and 40 g cartridges, 12 and 25 mL/min respectively) with gradient elution of H_2O:MeCN containing 0.1% formic acid. Final compounds were dried via lyophilization (Labconco FreeZone 2.5 L) to remove any residual solvents.

NMR spectra (including 2-D) were recorded on Bruker 500 spectrometer at 500 MHz for ^{1}H NMR and 125 MHz for ^{13}C NMR. Chemical shifts (δ scale) are reported in parts per million (ppm) relative to the central peak of the solvent. Coupling constants (J) are given in hertz (Hz). Spectra were obtained in the following solvents (reference peaks included for ^{1}H and ^{13}C NMR): $CDCl_3$ (^{1}H NMR: 7.26 ppm; ^{13}C NMR: 77.23 ppm) and DMSO-*d6* (^{1}H NMR: 2.50 ppm; ^{13}C NMR: 39.52 ppm). NMR experiments were performed at room temperature. Chemical shift values for all ^{1}H NMR and ^{13}C NMR spectra are reported in parts per million (ppm). ^{1}H NMR multiplicities are reported as: s = singlet, d = doublet, t = triplet, q = quartet, hept = heptet, m = multiplet, br = broad. High-resolution mass spectra (HRMS) were acquired using Waters Q-TOF Ultima ESI spectrometer. LCMS spectra were collected using an Agilent 6230 ESI TOF LC/MS spectrometers (10 µL injection) with Agilent eclipse plus C18 columns (1.8 /µm, 2.1 x 50 mm) with a gradient of 2.5-80% acetonitrile in water with 0.1% formic acid (0 min 2.5%, 1 min 2.5%, 7 min 80%, 8 min 80%, 9 min 2.5%, 10 min 2.5%). Melting points (mp) were determined on a Thomas-Hoover capillary melting point apparatus. Optical rotation measurements were performed on a JASCO Model DIP-360 Digital Polarimeter at wavelength 589.

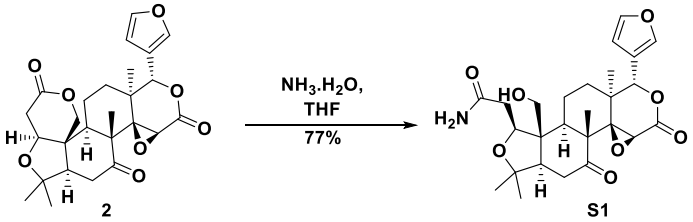
Limonin Derivatives Synthesis and Characterization



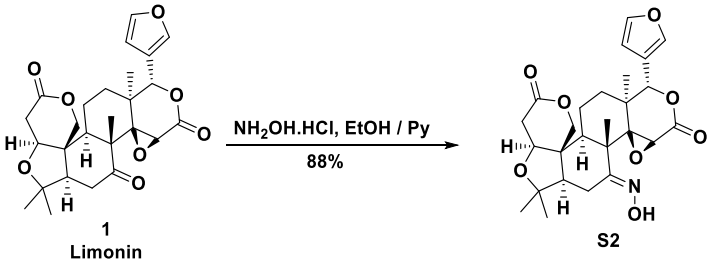
Procedure: A solution of **1** (4 g, 8.5 mmol) in acetic acid (64 mL) and hydriodic acid (64 mL) was heated under reflux for 3 h. The reaction mixture was cooled to room temperature, slowly poured into 400 mL of sodium sulfite saturated solution, and extracted three times with dichloromethane. The organic layers were combined, washed with brine, dried over Na_2SO_4, and concentrated by distillation under reduced pressure. The obtained crude residue was purified by silica gel flash chromatography (hexane-ethyl acetate 4:6) to provide **2** (3.36 g, 87%) as a white solid. Spectral data (^{1}H NMR) was consistent with the literature reported value.[1]

Note: Formation of **10** (150 mg, ca. 5%) was observed by increasing reaction time to 12 h.

^{1}H NMR (DMSO-*d6,* 500 MHz): δ 7.74 (d, *J* = 1.8 Hz, 1H), 7.70 (dd, *J* = 1.8, 1.8 Hz, 1H), 6.63 (s, 1H), 6.54 (d, *J* = 1.8 Hz, 1H), 5.15 (s, 1H), 4.86 (d, *J* = 13.2 Hz, 1H), 4.62 (d, *J* = 13.2 Hz, 1H), 4.13 (d, *J* = 3.8 Hz, 1H), 3.16 (t, *J* = 15.6 Hz, 1H), 2.70 - 2.53 (m, 4H), 2.39 (dd, *J* = 15.6, 3.4 Hz, 1H), 2.15 - 2.08 (m, 1H), 1.73-1.65 (m, 1H), 1.62 - 1.56 (m, 1H), 1.30 (s, 3H), 1.21 - 1.17 (m, 1H), 1.18 (s, 3H), 1.16 (s, 3H), 1.03 (s, 3H).
^{13}C NMR (DMSO-*d6,* 125 MHz): δ 208.13, 170.77, 168. 38, 165.34, 143.78, 142.27, 120.70, 116.84, 110.82, 81.60, 80.25, 78.58, 64.66, 56.47, 50.97, 45.69, 43.10, 38.39, 36.94, 36.11, 30.38, 26.36, 25.70, 21.98, 19.26, 16.60.
HRMS(ESI): m/z calc. for $C_{26}H_{31}O_7$ $[M+H]^+$: 455.2059, found: 455.2061.
mp: >260° C.
Opt. Rot.: $[\alpha]_D^{25}$ = - 43 (c = 0.14, acetone).



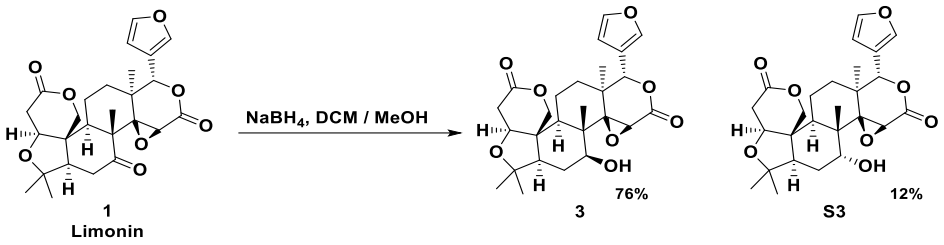
Procedure: Ammonium hydroxide (1 mL) was added dropwise to a solution of **1** (50 mg, 0.106 mmol) in tetrahydrofuran (1.5 mL) and the resulting mixture was stirred at 30° C for 8 h. The reaction mixture was then diluted with water, acidified with 2 M hydrochloric acid, and extracted with dichloromethane. The combined organic layers were washed with brine, dried over Na_2SO_4 and concentrated by distillation under reduced pressure to yield a crude residue that was purified by silica gel flash chromatography (dichloromethane −methanol 97:3) to provide **S1** (40 mg, 77%) as a white solid. Spectral data (^{1}H NMR and ^{13}C NMR) were consistent with literature reported values.[2]



Procedure: Hydroxylamine hydrochloride (600 mg, 8.46 mmol) was added to a solution of **1** (500 mg, 1.06 mmol) in ethanol (25 mL) and pyridine (7.5 mL), and the resulting mixture was heated under reflux for 2.5 h. After completion, the reaction was cooled to room temperature, acidified to pH = 2 by addition of 2 M hydrochloric acid, and extracted three times with dichloromethane. The combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated by distillation under reduced pressure to yield a crude residue that was purified by silica gel flash chromatography (hexane−ethyl acetate 1:1) to provide **S2** (454 mg, 88%) as a white solid. Spectral data were consistent with the literature reported value.[1, 3]

Note: The hydroxy group on the C=N double bond of **S2** adopts the *E* configuration.

^{1}H NMR (DMSO-*d6*, 500 MHz): δ 10.84 (br s, 1H), 7.72 (d, *J* = 1.8 Hz, 1H), 7.66 (dd, *J* = 1.8, 1.8 Hz, 1H), 6.49 (d, *J* = 1.8 Hz, 1H), 5.42 (s, 1H), 4.79 (d, *J* = 13.0 Hz, 1H), 4.35 (d, *J* = 13.0 Hz, 1H), 4.06 (d, *J* = 3.9 Hz, 1H), 3.83 (s, 1H), 3.35 (dd, *J* = 14.6, 3.3 Hz, 1H), 2.79 (d, *J* = 16.5 Hz, 1H), 2.61 (dd, *J* = 16.5, 3.9 Hz, 1H), 2.34 (dd, *J* = 12.0, 2.3 Hz, 1H), 2.15 (t, *J* = 14.6 Hz, 1H), 1.93 (dd, *J* = 14.6, 3.3 Hz, 1H), 1.82 - 1.62 (m, 3H), 1.31 (d, *J* = 13.8 Hz, 1H), 1.18 (s, 3H), 1.15 (s, 3H), 1.04 (s, 3H), 0.88 (s, 3H).
^{13}C NMR (DMSO-*d6*, 125 MHz): δ 170.34, 167.19, 158.84, 143.36, 141.58, 120.30, 110.24, 79.51, 78.52, 77.70, 65.52, 65.25, 58.93, 53.50, 49.02, 45.47, 45.23, 37.22, 35.80, 32.06, 30.08, 21.40, 20.82, 18.57, 18.35, 17.76.
HRMS(ESI): m/z calc. for $C_{26}H_{32}NO_8$ $[M+H]^+$: 486.2130, found: 486.2128.
mp: decomposes upon heating above 230° C.
Opt. Rot.: $[\alpha]_D^{25}$ = - 125 (c = 0.35, acetone).

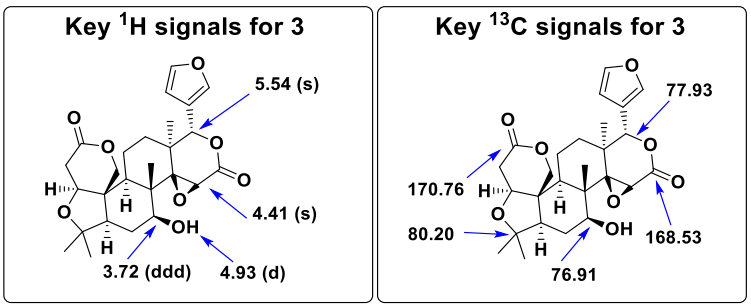


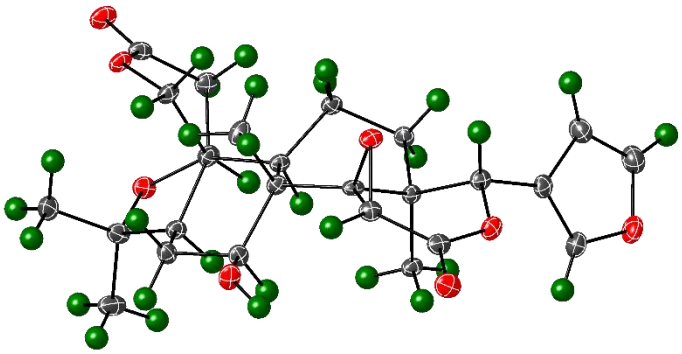
Procedure: A solution of $NaBH_4$ (230 mg, 6.08 mmol) in anhydrous methanol (10 mL) was added to a solution of **1** (500 mg, 1.06 mmol) in dichloromethane (20 mL) at -20° C and the resulting mixture was stirred at -20 °C. After 15 minutes, the reaction was quenched by the addition of a 2 M hydrochloric acid solution and extracted three times with dichloromethane. The organic layers were dried over Na_2SO_4 and concentrated by distillation under reduced pressure to obtained a crude residue that was purified by silica gel flash chromatography (hexane-ethyl acetate 4:6) to provide **3** (380 mg, 76%) and **S3** (60 mg, 12%) as white solids.

Note: Compound **3** is known,[3] however **3** has never been characterized. Compound **3** was crystallized by slow evaporation from dichloromethane and hexane.

3 (380 mg, 76%)

^{1}H NMR (DMSO-*d6*, 500 MHz): δ 7.71 (d, *J* = 1.8 Hz 1H), 7.67 (dd, *J* = 1.8, 1.8 Hz, 1H), 6.50 (d, *J* = 1.8 Hz, 1H), 5.54 (s, 1H), 4.93 (d, *J* = 5.1 Hz, 1H), 4.46 (d, *J* = 2.0 Hz, 2H), 4.41 (s, 1H), 3.99 (d, *J* = 4.0 Hz, 1H), 3.72 (ddd, *J* = 5.0, 10.1, 15.2 Hz, 1H), 2.65 (d, *J* = 16.4 Hz, 1H), 2.56 (dd, *J* = 4.0, 16.4 Hz, 1H), 2.28 (dd, *J* = 12.1, 6.0 Hz, 1H), 2.01 (dd, *J* = 13.2, 2.6 Hz, 1H), 2.00 - 1.99 (m, 1H), 1.67 - 1.51 (m, 4H), 1.19 (s, 3H), 1.23 – 1.19 (m, 1H), 1.17 (s, 3H), 0.97 (s, 3H), 0.83 (s, 3H).
^{13}C NMR (DMSO-*d6*, 125 MHz): δ 170.76, 168.53, 143.82, 142.30, 120.96, 110.76, 80.20, 79.33, 77.94, 76.91, 73.49, 65.76, 55.60, 55.39, 45.64, 45.09, 43.43, 38.94, 36.16, 30.77, 28.41, 25.98, 21.99, 18.71, 17.32, 14.02.
HRMS(ESI): m/z calc. $C_{26}H_{33}O_8$ $[M+H]^+$: 473.2175, found: 473.2173.
mp: 246-247° C.
Opt. Rot.: $[\alpha]_D^{25}$ = - 14 (c = 0.15, acetone).





Crystallography

Experimental Protocol: Intensity data were collected on a Bruker D8 Venture kappa diffractometer equipped with a Photon 100 CMOS detector. An Iμs microfocus Mo source (λ = 0.71073 Å) coupled with a multi-layer mirror monochromator provided the incident beam. The sample was mounted on a 0.3 mm loop with the minimal amount of Paratone-N oil. Data was collected as a series of φ and/or ω scans. Data was collected at 100 K using a cold stream of N_2(g). The collection, cell refinement, and integration of intensity data was carried out with the APEX3 software.[1] A semi-empirical absorption correction was performed with SADABS.[2] The structure was phased with intrinsic methods using SHELXT[3] and refined with the full-matrix least-squares program SHELXL.[4]

CCDC: 2082412

(1) Bruker (2016). APEX3. Bruker AXS, Inc., Madison, Wisconsin, USA.
(2) L. Krause, R. Herbst-Irmer, G. M. Sheldrick, D. Stalke, *J. Appl. Cryst.*, **2015,** *48*, 3–10.
(3) G. M. Sheldrick, *Acta Cryst.* **2015**, A71, 3–8.
(4) G. M. Sheldrick, *Acta Cryst*. **2015**, C71, 3–8.

Table S3. Crystal data and structure refinement for dd43xsa.

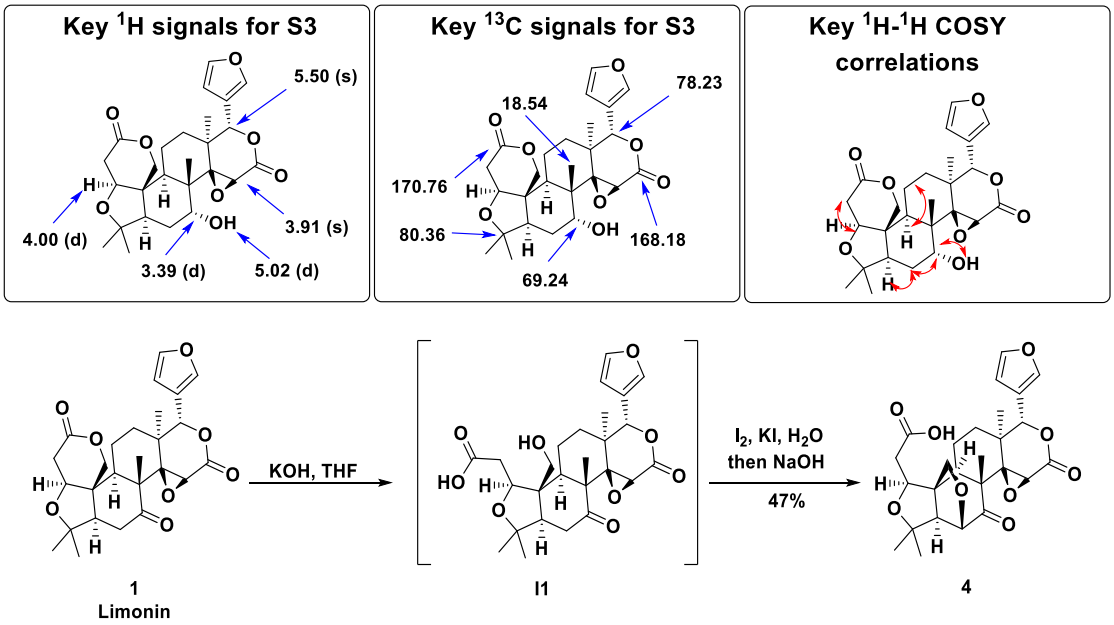
Identification code	dd43xsa
Empirical formula	C27 H34 Cl2 O8
Formula weight	557.44
Temperature	100(2) K
Wavelength	1.54178 Å
Crystal system	Monoclinic
Space group	$P2_1$
Unit cell dimensions	a = 10.0920(3) Åa= 90°.
	b = 11.8505(4) Åb= 109.4079(4)°.
	c = 11.4639(4) Åg = 90°.
Volume	1293.12(7) Å3
Z	2
Density (calculated)	1.432 Mg/m3
Absorption coefficient	2.685 mm-1
F(000)	588
Crystal size	0.583 x 0.374 x 0.13 mm3
Theta range for data collection	4.088 to 72.217°.
Index ranges	-11<=h<=12, -14<=k<=14, -14<=l<=14
Reflections collected	31195
Independent reflections	5081 [R(int) = 0.0348]
Completeness to theta = 67.679°	100.0 %
Absorption correction	Multiscan
Max. and min. transmission	1.0000 and 0.3578
Refinement method	Full-matrix least-squares on F2

Data / restraints / parameters 5081 / 1 / 342
Goodness-of-fit on F2 1.045
Final R indices [I>2sigma(I)]R1 = 0.0265, wR2 = 0.0682
R indices (all data) R1 = 0.0265, wR2 = 0.0682
Absolute structure parameter 0.005(4)
Extinction coefficient 0.0034(5)
Largest diff. peak and hole 0.289 and -0.341 e.Å-3

S3 (60 mg, 12%)

Note: Compound **S3** is known,[3] however **S3** has never been characterized

^{1}H NMR (DMSO-*d6*, 500 MHz): δ 7.70 (d, *J* = 1.8 Hz, 1H), 7.67 (dd, *J* = 1.8, 1.8 Hz, 1H), 6.49 (d, *J* = 1.8 Hz, 1H), 5.50 (s, 1H), 5.02 (d, *J* = 3.5 Hz, 1H), 4.52 (d, *J* = 13.0 Hz, 1H), 4.40 (d, *J* = 13.0 Hz, 1H), 4.00 (d, *J* = 3.75 Hz, 1H), 3.91 (s, 1H), 3.39 (d, *J* = 2.9 Hz, 1H), 2.64 (dd, *J* = 16.5, 1.4 Hz, 1H), 2.59-2.53 (m, 2H), 2.48 (d, *J* = 2.7 Hz, 1H), 1.98 - 1.90 (m, 1H) 1.84 (dt, *J* = 13.7, 2.9 Hz, 1H), 1.70 - 1.56 (m, 2H), 1.50 (ddd, *J* = 2.7, 3.5, 13.7 Hz, 1H), 1.27 - 1 .22 (m, 1H), 1.18 (s, 3H), 1.16 (s, 3H), 0.99 (s, 3H), 0.75 (s, 3H).
^{13}C NMR (DMSO-*d6*, 125 MHz): δ 170.76, 168.18, 143.79, 142.25, 121.11, 110.77, 80.36, 79.88, 78.23, 69.84, 69.24, 66.04, 57.33, 51.91, 45.80, 43.66, 42.00, 37.97, 36.26, 30.82, 26.75, 26.38, 22.13, 18.55, 17.63, 16.72.
HRMS(ESI): m/z calc. for $C_{26}H_{33}O_8$ $[M+H]^+$: 473.2175, found: 473.2161.
mp: 240-242° C.
Opt. Rot.: $[\alpha]_D^{25}$ = - 57 (c = 0.22, acetone).

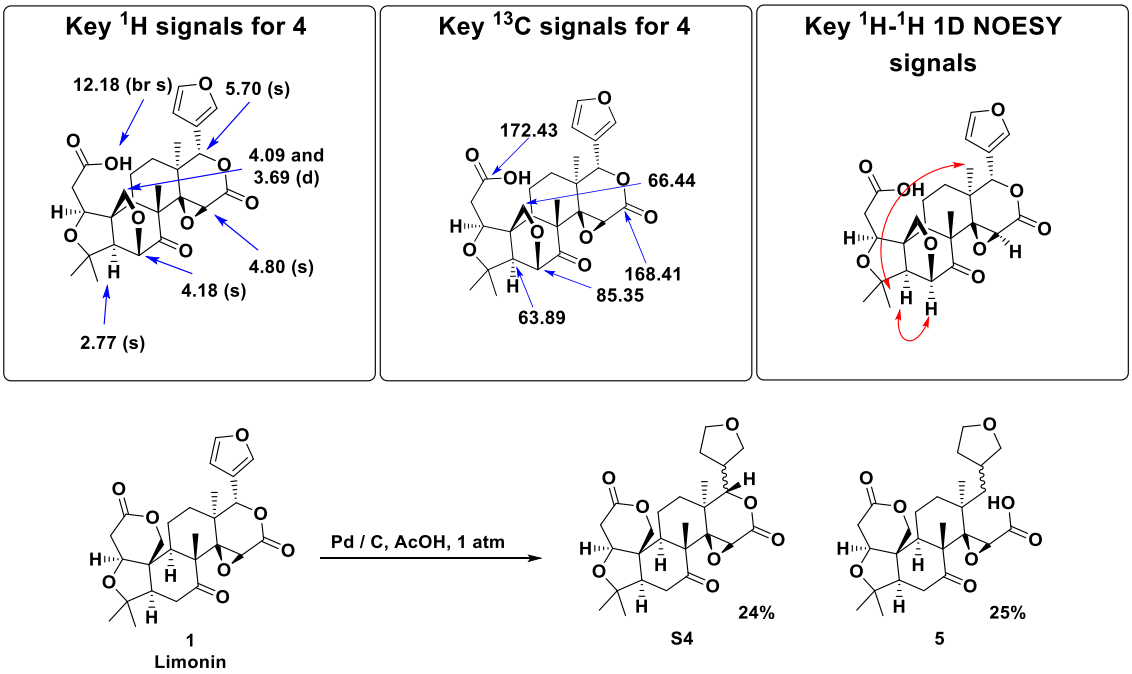


Procedure: 1 (1 g, 2.12 mmol) was dissolved in a solution of KOH (300 mg, 5.34 mmol) in methanol (40 mL), and the resulting solution was heated under reflux for 4 h. The solvent was evaporated under reduced pressure and the residue was taken up in water (20 mL). In a separate flask, Iodine (600 mg, 2.36 mmol) was dissolved in a solution of potassium iodide (600 mg, 3.61 mmol) in water (20 mL) and the resulting solution was added to the reaction mixture and allowed to stir for 5 minutes.
Sodium hydroxide 2M solution was added dropwise to the reaction mixture until the reaction turns yellow, and the resulting yellow solution was allowed to stir for an additional hour. Sodium sulfite (50 mg) was added to the reaction mixture and the resulting solution was acidified with 2M hydrochloric acid to pH 2. After standing a couple of hours, the precipitate was filtered off, dissolved in sodium bicarbonate 5% solution, and washed with dichloromethane (to remove the unreactive **1**). The bicarbonate solution was then acidified to pH 2 and extracted three times with dichloromethane. The organic layers (obtained from the extractions of the acidic solution) were combined, dried over Na_2SO_4, and concentrated by distillation under reduced pressure to afford pure **4** (505 mg, 47%) as a white solid.

Note: Compound **4** synthesis is known,[2] however **4** has never been characterized.

^{1}H NMR (DMSO-*d6*, 500 MHz): δ 12.18 (br s, 1H), 7.71 (d, *J* = 1.8 Hz, 1H), 7.67 (dd, *J* = 1.8, 1.8 Hz, 1H), 6.50 (d, *J* = 1.8 Hz, 1H), 5.70 (s, 1H), 4.80 (s, 1H), 4.23 (dd, *J* = 9.9, 2.1 Hz, 1H), 4.18 (s, 1H), 4.09 (d, *J* = 9.1 Hz, 1H), 3.69 (d, *J* = 9.1 Hz, 1H), 2.81 (dd, *J* = 12.2, 5.9 Hz, 1H), 2.77 (s, 1H), 2.52 (dd, *J* = 15.8, 2.1 Hz, 1H) 2.11 (dd, *J* = 15.8, 9.9 Hz, 1H), 1.91 - 1.65 (m, 3H), 1.53 (s, 3H), 1.27 (s, 3H), 1.22 (s, 3H) , 1.20 - 1.15 (m, 1H), 1.17 (s, 3H).

^{13}C NMR (DMSO-*d6*, 125 MHz): δ 207.23, 172.43, 168.41, 143.86, 142.28, 120.99, 110.67, 85.36, 78.79, 78.01, 76.59, 71.89, 66.45, 63.89, 57.78, 57.37, 47.34, 41.17, 40.60, 37.86, 30.60, 25.74, 25.49, 20.32, 19.84, 17.70.
HRMS(ESI): m/z calc. for $C_{26}H_{31}O_9$ $[M+H]^+$: 487.1968, found: 487.1976.
mp: >260° C.
Opt. Rot.: $[\alpha]_D^{25}$ = - 82 (c = 0.15, acetone).



Procedure: A suspension of **1** (250 mg, 0.53 mmol) in acetic acid (12.5 mL) was hydrogenated in the presence of 10% Pd/C at 1 atm for 48 h. The catalyst was removed by filtration over celite, and the filtrate was evaporated under reduced pressure. The obtained residue was portioned between dichloromethane and a 2% solution of sodium bicarbonate. The aqueous layer was extracted three times with dichloromethane. The organic layers were combined, dried over Na_2SO_4, and concentrated by distillation under reduced pressure to obtained a crude residue that was purified by silica gel flash chromatography (hexane-ethyl acetate 3:7) to provide **S4** (60 mg, 24%) as a white solid.

Note: Compound **S4** synthesis is known,[2] however **S4** has never been fully characterized. **S4** exists as a mixture of two diastereomers.

S4 (60 mg, 24%)

^{1}H NMR (DMSO-*d6*, 500 MHz): δ 4.95 (s, 1H), 4.92 (s, 1H) 4.48-4.43 (m, 2H), 4.33 (d, *J* = 6.4 Hz, 2H), 4.14 (d, *J* = 3.9 Hz, 2H), 3.93 (s, 1H), 3.92 (s, 1H), 3.83 - 3.79 (m, 2H), 3.73 - 3.58 (m, 4H), 3.43 (dd, *J* = 17.5, 8.5 Hz, 1H), 3.28 (dd, *J* = 8.1, 9.2 Hz, 1H), 3.17 - 3.10 (m, 2H), 2.82 (dd, *J* = 16.5, 1.2 Hz, 2H), 2.66 (dd, *J* = 16.5, 3.9 Hz, 2H), 2.58 - 2.54 (m, 2H), 2.49 - 2.43 (m, 2H), 2.37 - 2.32 (m, 2H), 2.26 (dd, *J* = 14.7, 3.5 Hz, 2H), 1.98 - 1.90 (m, 2H), 1.80 - 1.73 (m, 5H), 1.67 - 1.49 (m, 5H), 1.20 (s, 6H), 1.12 (s, 3H), 1.09 (s, 3H), 1.03 (s, 6H), 0.95 (s, 3H), 0.94 (s, 3H).
^{13}C NMR (DMSO-*d6*, 125 MHz): δ 208.49, 170.72, 167.73, 167.62, 84.73, 82.93, 80.00, 79.98, 79.66, 78.93 70.13, 69.76, 67.70, 67.42, 66.84, 66.59, 63.39, 65.37, 58.77, 58.63, 53.45, 53.41, 51.05, 50.96, 47.02, 46.86, 45.78, 45.76, 39.33, 39.20, 38.09, 37.95, 36.68, 36.19, 30.63, 30.18, 29.89, 29.11, 21.91, 20.75, 20.60, 18.32, 17.11, 17.02.
HRMS(ESI): m/z calc. for $C_{26}H_{35}O_8$ $[M+H]^+$: 475.2332, found: 475.2331.
mp: >260° C.
Opt. Rot.: $[\alpha]_D^{25}$ = - 139 (c = 0.18, acetone).

5 was obtained by acidification of the sodium bicarbonate aqueous solution with hydrochloric acid to pH 2. The obtained acidic solution was extracted three times with dichloromethane. The organic layers were combined, dried over Na_2SO_4, and concentration under vacuum. Using this procedure, **5** can be obtained pure (63 mg, 25%) as a white solid.

Note: Compound **5** synthesis is known,[2] however **5** has never been fully characterized. **5** exists as a mixture of two diastereomers.

5 (63 mg, 25%)

^{1}H NMR (DMSO-*d6*, 500 MHz): δ 13.23 (br s, 2H), 4.66 (dd, *J* = 13.1, 3.7 Hz, 2H), 4.54 (d, *J* = 13.1 Hz, 2H), 4.30 (d, *J* = 3.7 Hz, 2H), 3.93 (t, *J* = 7.6 Hz, 1H), 3.85 (t, *J* = 7.6 Hz, 1H), 3.76 - 3.60 (m, 4H), 3.30 (s, 1H), 3.29 (s, 1H), 3.17 (t, *J* = 8.2 Hz, 1H), 3.09 (t, *J* = 8.2

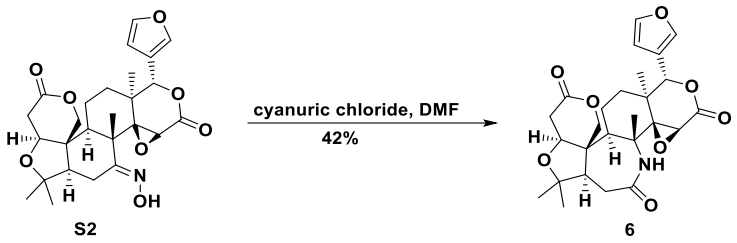
Hz, 1H), 2.91-2.84 (m, 2H), 3.83 - 2.79 (m, 2H), 2.70 (dd, *J* = 16.4 3.5 Hz, 2H), 2.54 - 2.45 (m, 6H), 2.25 - 2.17 (m, 2H), 2.15 - 2.01 (m, 4H), 1.90 - 182 (m, 2H), 1.78 - 1.63 (m, 5H), 1.58 – 1.44 (m, 4H), 1.44 - 1.37 (m, 1H), 1.28 (s, 6H), 1.19 (s, 3H), 1.18 (s, 3H), 1.05 (s, 6H), 1.04 (s, 6H).

^{13}C NMR (DMSO-*d6*, 125 MHz): δ.207.69, 207.59, 170.95, 170.05, 80.32, 78.46, 78.42, 74.40, 74.38, 71.77, 71.71, 67.30, 67.27, 64.19, 64.16, 60.23, 57.94, 57.86, 55.82, 55.39, 51.47, 51.39, 48.07, 47.70, 45.84, 45.82, 43.44, 43.39, 36.82, 36.78, 36.38, 36.14, 36.11, 35.17, 13.98, 34.93, 34.87, 30.78, 27.18, 27.09, 22.19, 20.02, 19.98, 18.43, 18.33.

HRMS(ESI): m/z calc. for $C_{26}H_{37}O_8$ $[M+H]^+$: 477.2488, found: 477.2493.

mp: 162-164° C.

Opt. Rot.: $[\alpha]_D^{25}$ = - 14 (c = 0.13, acetone).



S2 6

Procedure: Cyanuric chloride (38 mg, 0.206 mmol) was added to a dry oven flask and dissolved in DMF (0.5 mL). The resulting solution was stirred until the solution turns yellow, then, **S2** (50 mg, 0.103 mmol) in DMF (0.25 mL) was added. The resulting mixture was stirred at 60° C for 48 h. The solvent was removed under vacuum, and the residue was taken up in water and dichloromethane. The aqueous layer was extracted three times with dichloromethane and the combined organic phases were washed with brine and dried over Na_2SO_4. The solvent was concentrated by distillation under reduced pressure to obtain a crude residue that was purified by silica gel flash chromatography (hexane-ethyl acetate 3:7) to provide **6** (21 mg, 42%) as a white solid.

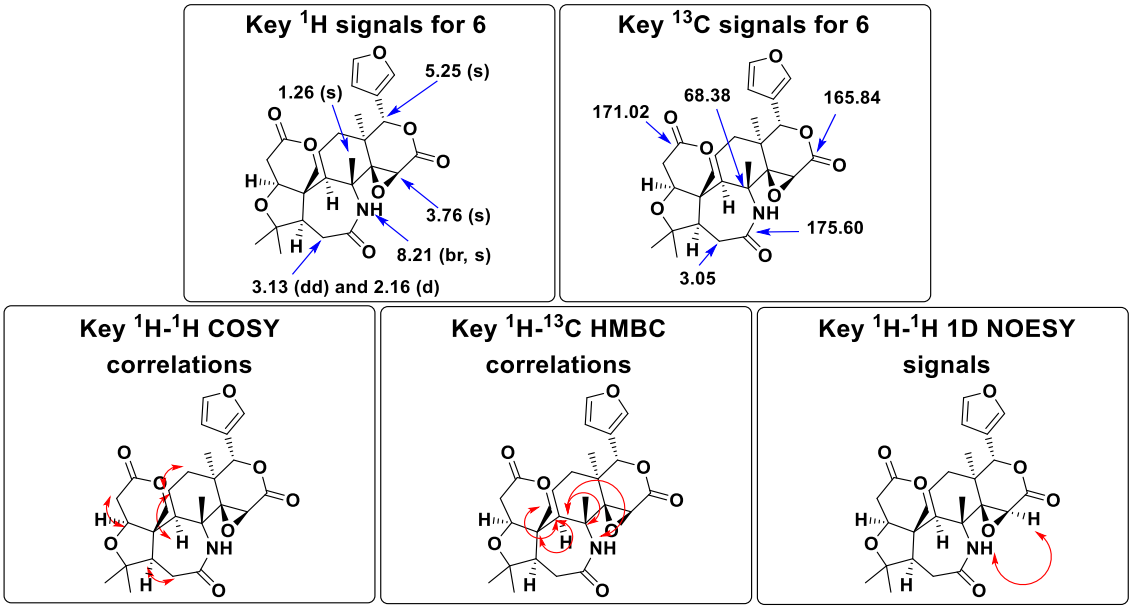
^{1}H NMR (DMSO-*d6*, 500 MHz): δ 8.21 (br s, 1H), 7.73 (d, *J* = 1.7 Hz, 1H), 7.68 (dd, *J* = 1.7, 1.7 Hz, 1H), 6.49 (d, *J* = 1.7 Hz, 1H), 5.25 (s, 1H), 4.83 (d, *J* = 13.0 Hz, 1H), 4.41 (d, *J* = 13.0, 1H), 4.19 (d, *J* = 3.8 Hz, 1H), 3.76 (s, 1H), 3.13 (dd, *J* = 12.5, 16.9 Hz, 1H), 2.91 (d, *J* = 16.0 Hz, 1H), 2.63 (dd, *J* = 16.0, 3.8 Hz, 1H), 2.37 - 2.33 (m, 2H), 2.16 (d, *J* = 16.9 Hz, 1H), 1.78-1.70 (m, 2H), 1.46 - 1.37 (m, 1H), 1.35-1.29 (m, 1H), 1.26 (s, 3H), 1.18 (s, 3H), 0.97 (s, 3H), 0.95 (s, 3H).

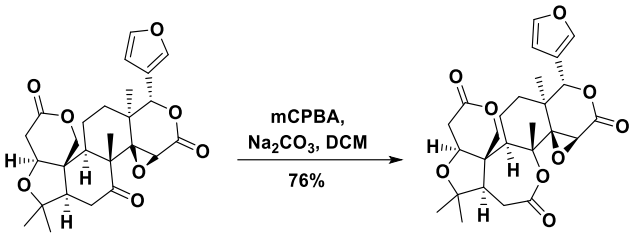
^{13}C NMR (DMSO-*d6*, 125 MHz): δ 175.60, 171.06, 165.86, 143.86, 142.03, 120.50, 110.70, 81.74, 80.31, 77.83, 68.39, 65.58, 59.93, 55.39, 55.12, 54.61, 51.61, 49.02, 37.23, 36.33, 34.06, 33.06, 30.62, 22.21, 20.99, 20.38.

HRMS(ESI): m/z calc. for $C_{26}H_{32}O_8$ $[M+H]^+$: 486.2128, found: 486.2122.

mp: >260° C.

Opt. Rot.: $[\alpha]_D^{25}$ = - 99 (c = 0.13, acetone).



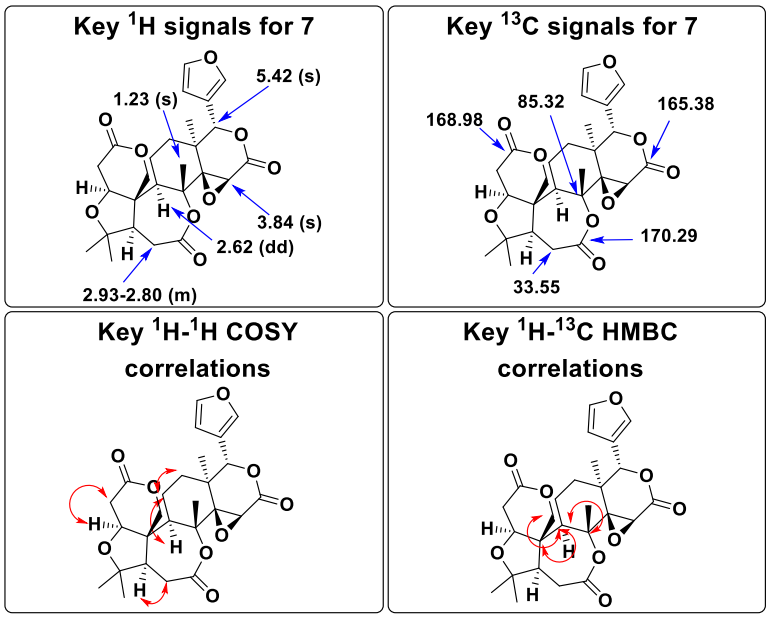


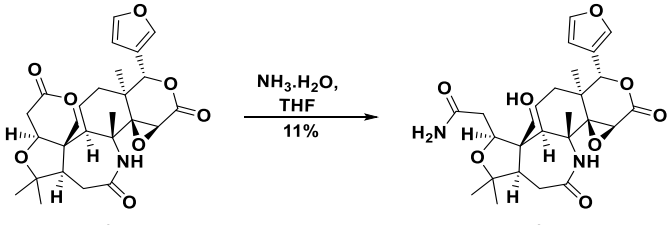
1
Limonin

7

Procedure: Sodium carbonate (63 mg, 0.594 mmol) was added to a solution of **1** (50 mg, 0.106 mmol) in dichloromethane (1.3 mL) and the resulting mixture was stirred for 30 minutes at 0° C. Then, *m*CPBA (69 mg, 0.40 mmol) was added and the reaction was stirred at 30° C for 2 h. The reaction was quenched with water and extracted three times with dichloromethane. The combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated by distillation under reduced pressure to yield a crude residue that was by silica gel flash chromatography (hexane-ethyl acetate 3:7) to provide **7** (39 mg, 76%) as a white solid.

^{1}H NMR (*CDCl*$_3$, 500 MHz): δ 7.45 (d, *J* = 1.7 Hz, 1H), 7.45 (dd, *J* = 1.7, 1.7 Hz, 1H), 6.39 (d, *J* = 1.7 Hz, 1H), 5.42 (s, 1H), 4.69 (d, *J* = 13.1 Hz, 1H), 4.41 (d, *J* = 13.1 Hz, 1H), 4.17 (t, *J* = 2.6 Hz, 1H), 3.94 (s, 1H), 3.52 (dd, *J* = 17.0, 3.5 Hz, 1H), 2.93 - 2.80 (m, 2H), 2.80 (dd, *J* = 17.0, 2.6 Hz, 1H), 2.62 (dd, *J* = 12.6, 1.7 Hz, 1H), 2.39 (dd, *J* = 128, 1.9, 1H), 1.91 - 1.85 (m, 2H), 1.62 - 153 (m, 2H), 1.38 (s, 3H), 1.34 (s, 3H), 1.23 (s, 3H), 1.14 (s, 3H).
^{13}C NMR (*CDCl*$_3$, 125 MHz): δ 170.29, 168.98, 165.38, 143.43, 141.13, 119.45, 109.64, 85.33, 81.88, 80.15, 77.67, 68.66, 64.96, 55.09, 53.73, 52.20, 48.44, 36.73, 36.46, 33.55, 32.24, 30.40, 22.17, 21.23, 20.78, 19.56.
HRMS(ESI): m/z calc. for $C_{26}H_{31}O_9$ $[M+H]^+$: 487.1968, found: 487.1975.
mp: decomposes upon heating above 237° C.
Opt. Rot.: $[\alpha]_D^{25}$ = - 92 (c = 0.11, acetone).





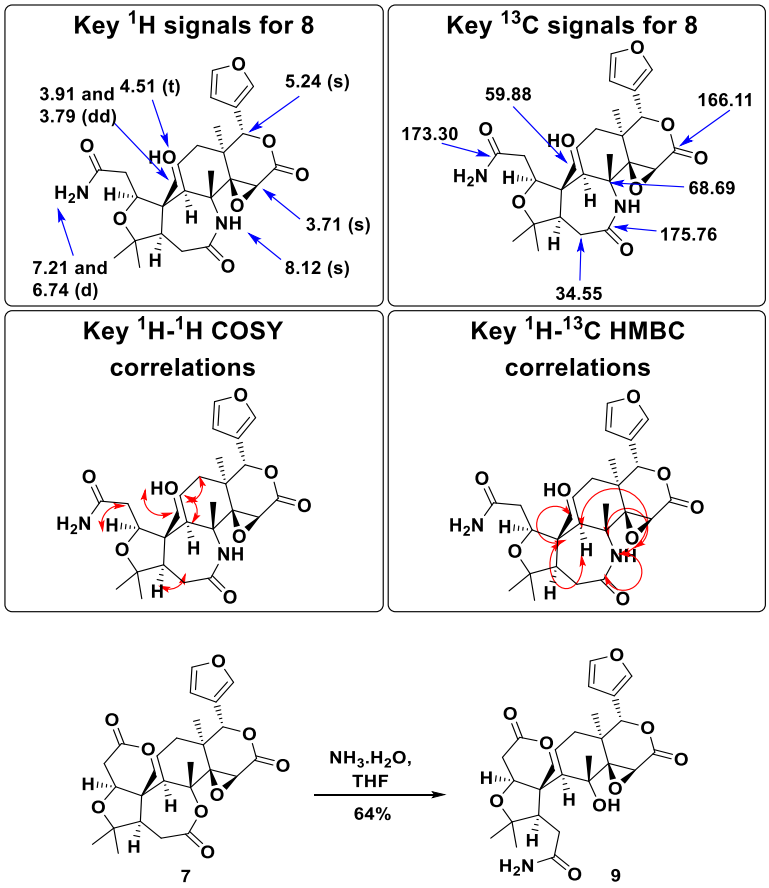
6

8

Procedure: Ammonium hydroxide (4 mL) was added dropwise to a solution of **6** (200 mg, 0.41 mmol) in THF (7 mL) at 0° C and the resulting mixture was stirred at 30° C for 16 h. The reaction mixture was diluted with water, acidified with 2 M hydrochloric acid, and extracted three times with dichloromethane. The combined organic layers were washed with brine, dried over Na_2SO_4, and

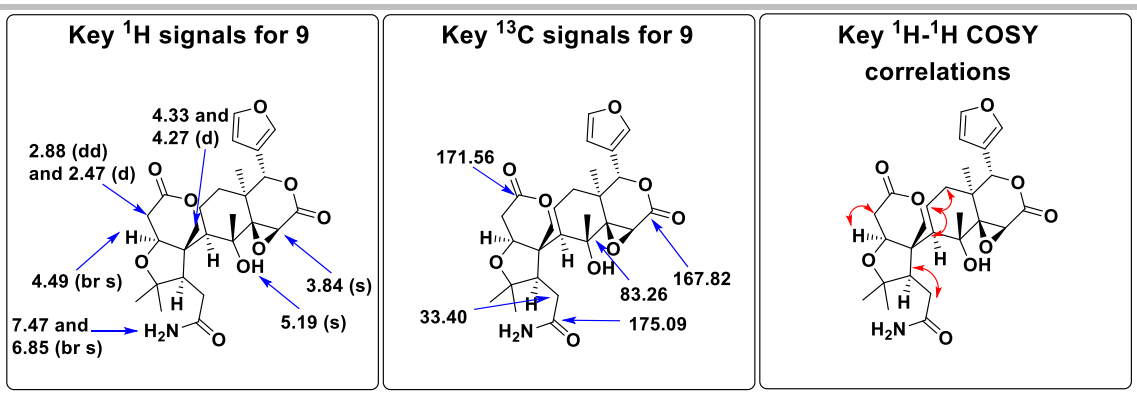
concentrated by distillation under reduced pressure to yield a crude residue that was purified by crystallization using dichloromethane and hexane to provide **8** (22 mg, 11%) as a white solid.

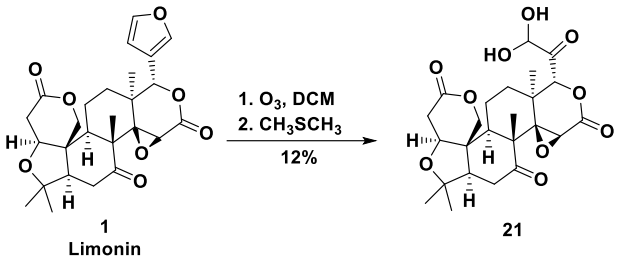
^{1}H NMR (DMSO-*d6*, 500 MHz): δ 8.12 (s, 1H), 7.71 (d, *J* = 1.7 Hz, 1H), 7.67 (dd, *J* = 1.7, 1.7 Hz, 1H), 7.21 (d, *J* = 2.3 Hz, 1H), 6.74 (d, *J* = 2.3 Hz, 1H), 6.48 (d, *J* = 1.7 Hz, 1H), 5.24 (s, 1H), 4.51 (t, *J* = 3.5 Hz, 1H), 3.91 (d, *J* = 8.2 Hz, 1H), 3.91 (dd, *J* = 11.1, 3.5 Hz, 1H), 3.79 (dd, *J* = 11.1, 3.5 Hz, 1H), 3.71 (s, 1H), 2.93 (dd, *J* = 16.9, 12.9 Hz, 1H), 2.84 (dd, *J* = 15.6, 3.2, 1H), 2.35 (dd, *J* = 15.6, 8.2 Hz, 1H), 2.05 - 2.01 (m, 3H), 1.86 (dd, *J* = 14.7, 6.5 Hz, 1H), 1.67 (dd, *J* = 14.7, 6.1 Hz, 1H), 1.60 - 1.51 (m, 1H), 1.29 (s, 3H), 1.26 (s, 3H), 1.16-1.10 (m, 1H), 1.10 (s, 3H), 0.88 (s, 3H).
^{13}C NMR (DMSO-*d6*, 125 MHz): δ 175.76, 173.30, 166.11, 143.81, 141.99, 120.57, 110.73, 83.66, 78.90, 77.91, 68.69, 60.95, 59.88, 55.76, 54.16, 52.62, 51.47, 40.59, 36.54, 34.55, 34.09, 30.10, 24.77, 24.27, 20.65, 19.85.
HRMS(ESI): m/z calc. for $C_{26}H_{35}N_2O_8$ $[M+H]^+$: 503.2393, found: 503.2397.
mp: decomposes upon heating above 223° C.
Opt. Rot.: $[\alpha]_D^{25}$ = - 69 (c = 0.19, acetone).



Procedure: Ammonium hydroxide (2 mL) was added dropwise to a solution of **7** (100 mg, 0.205 mmol) in THF (3.4 mL) at 0° C and the resulting mixture was stirred at 30° C for 16 h. The reaction mixture was diluted with water, acidified with 2M hydrochloric acid, and extracted three times with dichloromethane. The combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated by distillation under reduced pressure to yield a crude residue that was purified by silica gel flash chromatography (dichloromethane−methanol 9:1) to provide **9** (39 mg, 64%) as a white solid.

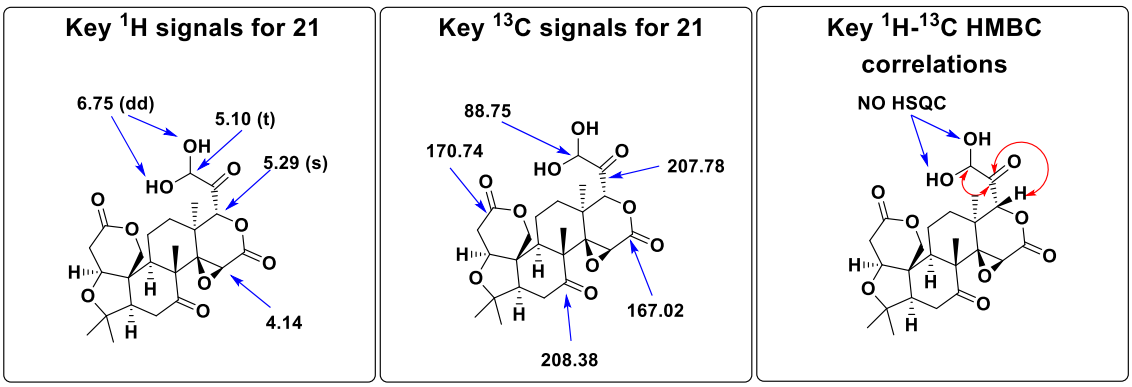
^{1}H NMR (DMSO-*d6*, 500 MHz): δ 7.75 (d, *J* = 1.7 Hz, 1H), 7.68 (dd, *J* = 1.7, 1.7 Hz, 1H), 7.47 (br s, 1H), 6.85 (br s, 1H), 6.53 (d, *J* = 1.7 Hz, 1H), 5.39 (s, 1H), 5.19 (s, 1H), 4.49 (br s, 1H), 4.33 (d, *J* = 12.8, 1H), 4.27 (d, *J* = 12.8 Hz, 1H), 3.84 (s, 1H), 3.18 (br s, 1H), 2.88 (dd, *J* = 16.1, 4.4 Hz, 1H), 2.47 (d, *J* = 16.1 Hz, 1H), 2.30 - 2.25 (m, 3H), 1.83 - 1.79 (m, 1H), 1.76 - 1.72 (m, 1H), 1.38 - 1.25 (m, 2H), 1.22 (s, 3H), 1.20 (s, 3H), 1.04 (s, 3H), 1.02 (s, 3H).
^{13}C NMR ($CDCl_3$+ CD_3OD, 125 MHz): δ 175.09, 171.56, 167.82, 143.17, 141.02, 119.80, 109.90, 83.26, 77.89, 76.48, 70.33, 68.74, 52.61, 51.34, 50.04, 36.91, 36.57, 34.18, 33.40, 31.58, 28.59, 24.86, 22.01, 20.33, 19.66, 14.10
HRMS(ESI): m/z calc. for $C_{26}H_{34}NO_9$ $[M+H]^+$: 504.2234, found: 504.2224.
mp: 202-203° C.
Opt. Rot.: $[\alpha]_D^{25}$ = - 47 (c = 0.14, acetone).

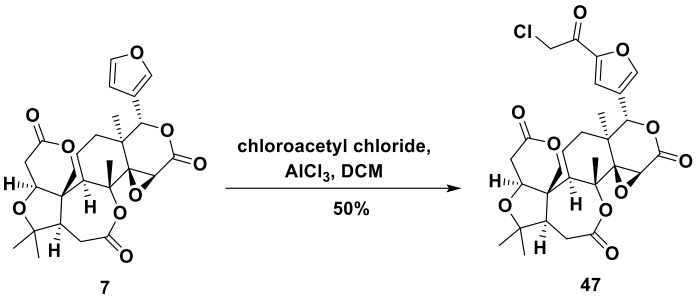




Procedure: Ozone was passed through a solution of **1** (300 mg, 0.64 mmol) in dichloromethane (15 mL) at -78° C until blue color persists. After reaction completion, residual ozone was purged 5 minutes under N_2 and, then, dimethylsulfide (0.1 mL) was added to the mixture. The reaction was allowed to stir at 30° C for additional 12 h before brine was added to the solution. The aqueous layer was extracted three times with dichloromethane. The combined organic layers were dried over Na_2SO_4 and concentrated by distillation under reduced pressure to yield a crude residue that was purified by silica gel flash chromatography (dichloromethane−methanol 9:1) to provide **21** (37 mg, 12%) as a white solid.

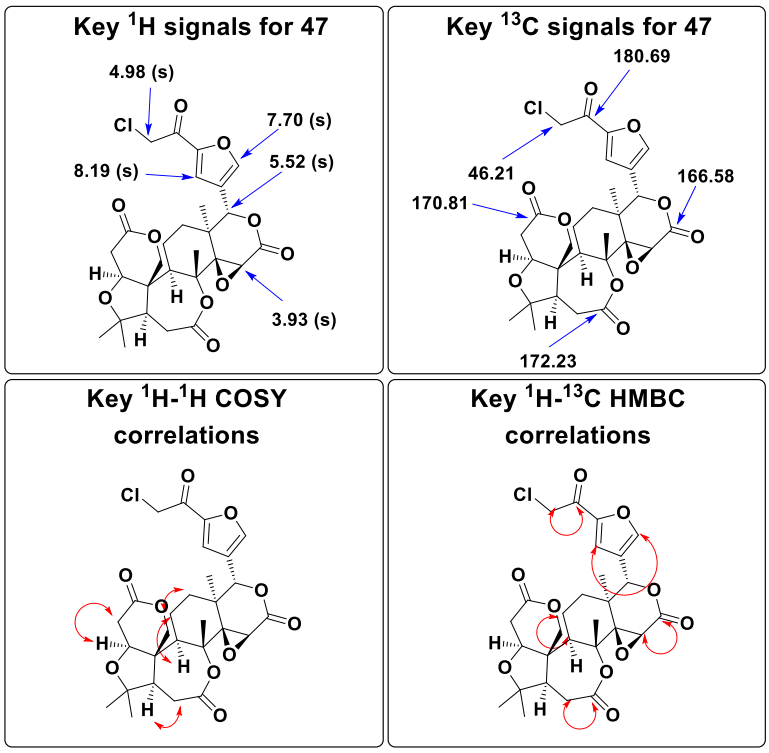
^{1}H NMR (DMSO-*d6,* 500 MHz): δ 6.75 (dd, *J* = 7.7, 6.0 Hz, 2H), 5.29 (s, 1H), 5.10 (t, *J* = 7.7 Hz, 1H), 4.90 (d, *J* = 13.0 Hz, 1H), 4.47 (d, *J* = 13.0 Hz, 1H), 4.10 (d, *J* = 4.1 Hz, 1H), 4.14 (s, 1H), 3.09 (t, *J* = 15.5 Hz, 1H), 2.79 (d, *J* = 16.5 Hz, 1H), 2.63 (dd, *J* = 16.5, 4.1 Hz, 1H), 2.57 (dd, *J* = 12.0, 4.0 Hz, 1H), 2.48 (d, *J* = 3.4 Hz, 1H), 2.26 (dd, *J* = 15.5, 3.4 Hz, 1H), 1.91 - 1.84 (m, 2H), 1.79 - 1,69 (m, 2H), 1.18 (s, 3H), 1.15 (s, 3H), 1.02 (s, 3H), 0.99(s, 3H).
^{13}C NMR ($CDCl_3$+ CD_3OD, 125 MHz): δ 208.41, 202.80, 170.76, 167.04, 88.76, 80.61, 80.02, 78.90, 67.19, 65.21, 58.04, 54.19, 50.50, 46.31, 45.67, 38.47, 36.63, 36.21, 30.24, 28.67, 21.93, 19.93, 17.91, 17.68.
HRMS(ESI): m/z calc. for $C_{24}H_{31}O_{10}$ $[M+H]^+$: 479.1917, found: 479.1933.
mp: decomposes upon heating above 185° C.
Opt. Rot.: $[\alpha]_D^{25}$ = - 111 (c = 0.13, acetone).

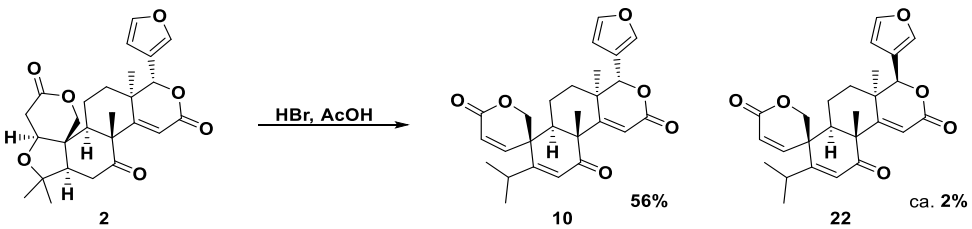




Procedure: $AlCl_3$ (60 mg, 0.45 mmol) was added at 0° C to a cooled solution of **7** (50 mg, 0.10 mmol) in dichloromethane (2 mL). The resulting mixture was stirred 30 minutes, before chloroacetyl chloride (10 µL, 0.12 mmol) was added to the solution. The resulting solution was stirred at 30° C for 12 h. Water was added and the aqueous layer was extracted three times with dichloromethane. The combined organic layers were washed with 2M sodium hydroxide and brine. After drying over Na_2SO_4, the solution was concentrated by distillation at reduced pressure, and the residue was purified by flash chromatography on silica gel (hexane-ethyl acetate 1:1) to obtain **47** (28 mg, 50%) as a white solid.

^{1}H NMR (DMSO-*d6*, 500 MHz): δ 8.19 (s, 1H), 7.70 (s, 1H), 5.52 (s, 1H), 4.93 (s, 2H), 4.91 (d, *J* = 13.0 Hz, 1H), 4.44 (d, *J* = 13.0 Hz, 1H), 4.24 (d, *J* = 3.6 Hz, 1H), 3.99 (s, 1H), 3.45 (dd, *J* = 18.0, 12.9 Hz, 1H), 2.89 (dd, *J* = 16.5, 1.5 Hz, 1H), 2.69 – 2.58 (m, 3H), 2.49 (d, *J* = 12.9 Hz, 1H), 1.87 -1.80 (m, 2H), 1.49 – 1.33 (m, 2H), 1.25 (s, 3H), 1.21 (s, 3H), 1.16 (s, 3H), 0.96 (s, 3H).
^{13}C NMR (DMSO-*d6*, 125 MHz): δ 180.69, 172.23, 170.81, 166.58, 150.09, 147.48, 122.99, 120.11, 85.86, 81.58, 79.96, 77.13, 69.38, 65.13, 53.77, 53.05, 51.70, 48.16, 46.21, 36.97, 36.52, 33.10, 31.37, 30.21, 22.19, 20.44, 20.42, 18.63.
HRMS(ESI): m/z calc. for $C_{28}H_{32}O_{10}Cl$ $[M+H]^+$: 563.1684, found: 563.1686.
mp: decomposes upon heating above 174° C.
Opt. Rot.: $[\alpha]_D^{25}$ = - 59 (c = 0.10, acetone).



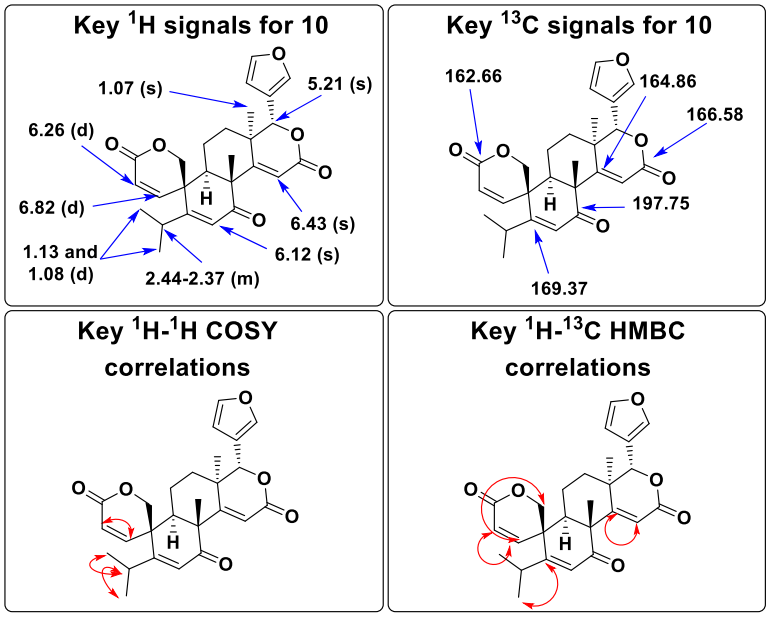


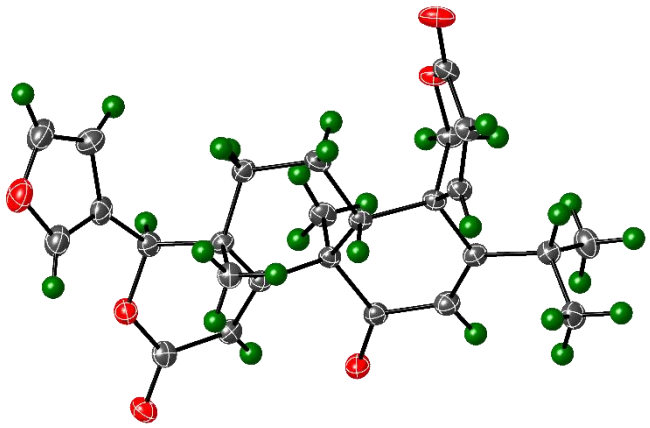
Procedure: Hydrobromic acid (48% in acetic acid, 5 mL) was added to a solution of **2** (500 mg, 0.66 mmol) in glacial acetic acid (2.5 mL) and the resulting solution was heated to 60° C for 2 h. The reaction mixture was then cooled to 0° C and quenched with sodium sulfite saturated solution. The aqueous layer was extracted three times with dichloromethane. The combined organic layers were washed with brine, dried over Na_2SO_4, concentrated by distillation at reduced pressure, and the obtained residue was purified by flash chromatography on silica gel (hexane-ethyl acetate 6:4), giving **10** and **22** as white solids.

10 (163 mg, 56%)

Note: Compound **10** is known,[4] however **10** has never been fully characterized.

^{1}H NMR (DMSO-*d6*, 500 MHz): δ 7.75 (d, *J* = 1.7 Hz, 1H), 7.70 (d, *J* = 1.7, 1.7 Hz, 1H), 6.82 (d, *J* = 9.9 Hz, 1H), 6.56 (d, *J* = 1.7 Hz, 1H), 6.43 (s, 1H), 6.26 (d, *J* = 9.9 Hz, 1H), 6.12 (s, 1H), 5.21 (s, 1H), 4.81 (d, *J* = 12.4 Hz, 1H), 4.63 (d, *J* = 12.4 Hz, 1H), 2.67 (dd, *J* = 12.7, 5.4 Hz, 1H), 2.44 – 2.37 (m, 1H), 1.90 – 1.82 (m, 1H), 1.76 – 1.61 (m, 2H), 1.44 (s, 3H), 1.27 – 1.21 (m, 1H), 1.13 (d, *J* = 6.7 Hz, 3H), 1.08 (d, *J* = 6.7 Hz, 3H), 1.07 (s, 3H).
^{13}C NMR (DMSO-*d6*, 125 MHz): δ 197.75, 169.37, 166.58, 164.86, 162.66, 150.05, 143.82, 142.23, 124.89, 123.03, 120.63, 118.40, 110.83, 81.03, 69.86, 48.30, 45.49, 40.59, 37.77, 30.82, 27.76, 25.31, 24.12, 23.94, 20.94, 17.50.
HRMS(ESI): m/z calc. for $C_{26}H_{29}O_6$ $[M+H]^+$: 473.1964, found: 437.1965.
mp: >260° C.
Opt. Rot.: $[\alpha]_D^{25}$ = - 106 (c = 0.30, acetone).





Crystallography

SUPPORTING INFORMATION

Experimental Protocol: Intensity data were collected on a Bruker D8 Venture kappa diffractometer equipped with a Photon 100 CMOS detector. An Iμs microfocus Mo source (λ = 0.71073 Å) coupled with a multi-layer mirror monochromator provided the incident beam. The sample was mounted on a 0.3 mm loop with the minimal amount of Paratone-N oil. Data was collected as a series of φ and/or ω scans. Data was collected at 100 K using a cold stream of N2(g). The collection, cell refinement, and integration of intensity data was carried out with the APEX3 software.[1] A semi-empirical absorption correction was performed with SADABS.[2] The structure was phased with intrinsic methods using SHELXT[3] and refined with the full-matrix least-squares program SHELXL.[4]

CCDC: 2082413

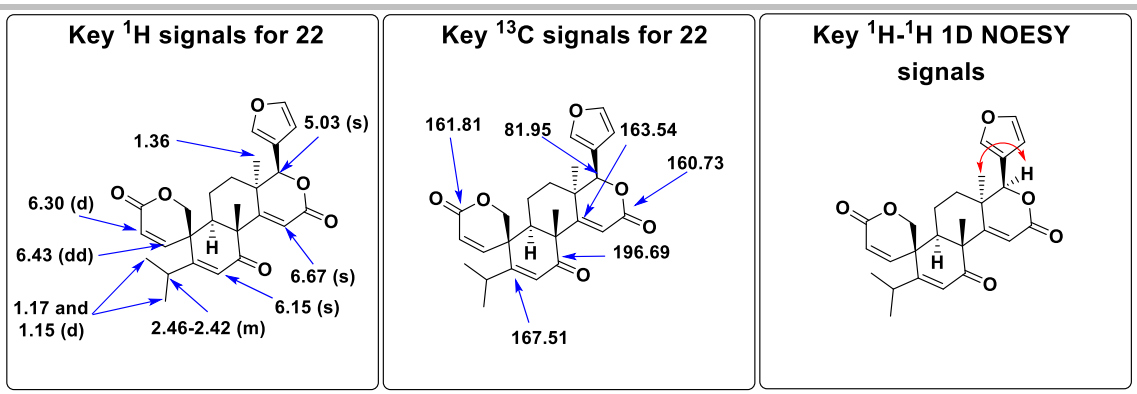
(1) Bruker (2016). APEX3. Bruker AXS, Inc., Madison, Wisconsin, USA.
(2) L. Krause, R. Herbst-Irmer, G. M. Sheldrick, D. Stalke, *J. Appl. Cryst.*, **2015,** *48*, 3–10.
(3) G. M. Sheldrick, *Acta Cryst.* **2015**, A71, 3–8.
(4) G. M. Sheldrick, *Acta Cryst*. **2015**, C71, 3–8.

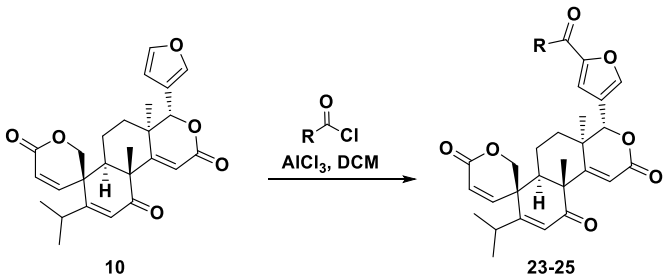
Table S4. Crystal data and structure refinement for dd38ys.

Identification code	dd38ys
Empirical formula	C26 H28 O6
Formula weight	436.48
Temperature	100(2) K
Wavelength	1.54178 Å
Crystal system	Trigonal
Space group	$P3_2$
Unit cell dimensions	a = 29.7882(5) Åa= 90°.
	b = 29.7882(5) Åb= 90°.
	c = 6.30760(10) Å g = 120°.
Volume	4847.11(18) Å3
Z	9
Density (calculated)	1.346 Mg/m3
Absorption coefficient	0.776 mm-1
F(000)	2088
Crystal size	0.351 x 0.307 x 0.177 mm3
Theta range for data collection	2.967 to 74.502°.
Index ranges	-37<=h<=37, -37<=k<=35, -7<=l<=7
Reflections collected	66384
Independent reflections	13091 [R(int) = 0.0358]
Completeness to theta = 67.679°	100.0 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.7538 and 0.6657
Refinement method	Full-matrix least-squares on F2
Data / restraints / parameters	13091 / 169 / 924
Goodness-of-fit on F2	1.044
Final R indices [I>2sigma(I)]	R1 = 0.0253, wR2 = 0.0665
R indices (all data)	R1 = 0.0254, wR2 = 0.0665
Absolute structure parameter	0.01(3)
Extinction coefficient	n/a
Largest diff. peak and hole	0.289 and -0.134 e.Å-3

22 (6 mg, ca. 2%)

^{1}H NMR (DMSO-*d6,* 500 MHz): δ 7.38 (d, *J* = 1.8 Hz 1H), 7.37 (dd, *J* = 1.8, 1.8 Hz, 1H), 6.67 (s, 1H), 6.43 (dd, *J* = 10.0, 1.5 Hz, 1H), 6.30 (d, *J* = 1.8 Hz, 1H), 6.31 (d, *J* = 10.0 Hz, 1H), 6.15 (s, 1H), 5.03 (s, 1H), 4.68 (dd, *J* = 12.3, 1.5 Hz, 1H), 4.49 (d, *J* = 12.3 Hz, 1H) 2.46-2.42 (m, 2H), 1.82- 1.65 (m, 3H), 1.49 (s, 3H), 1.42 – 1.36 (m, 1H), 1.36 (s, 3H), 1.17 (d, *J* = 6.8 Hz, 3H), 1.15 (d, *J* = 6.8 Hz, 3H).
^{13}C NMR ($CDCl_3$, 125 MHz): δ 196.69, 167.51, 163.54, 161.81, 160.73, 148.35, 143.57, 141.73, 125.99, 123.75, 121.54, 119.23, 109.61, 81.95, 69.53, 48.03, 45.59, 41.36, 38.12, 31.05, 30.14, 28.44, 24.39, 24.31, 24.10, 18.33.
HRMS(ESI): m/z calc. for $C_{26}H_{29}O_6$ $[M+H]^+$: 473.1964, found: 437.1963.
mp: >260° C.
Opt. Rot.: $[\alpha]_D^{25}$ = - 67 (c = 0.10, acetone/chloroform).





10

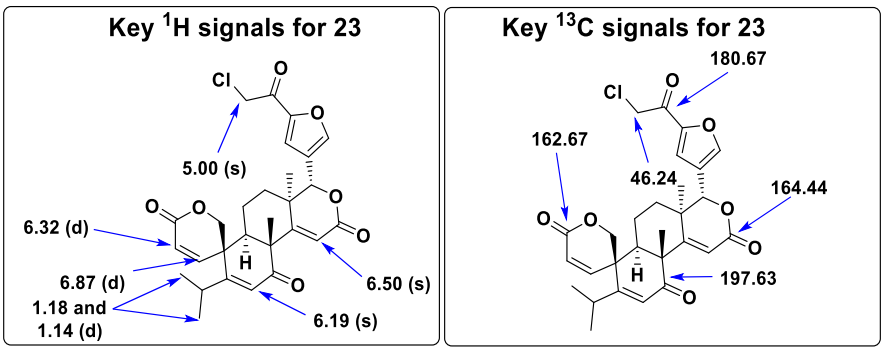
23-25

23; R = CH_2Cl 68%
24; R = $CHCH_2$, 9%
25; R = CH_3 89%

Procedure: $AlCl_3$ (40 mg, 0.30 mmol) was added at 0° C to a cooled solution of **10** (28 mg, 0.065 mmol), in dichloromethane (1.3 mL). The resulting mixture was stirred 30 minutes, before the suitable acyl chloride (0.079 mmol) was added to the solution. The resulting solution was allowed to stir at 30° C for 12 h. Water was added, and the aqueous layer was extracted three times with dichloromethane. The combined organic layers were washed with 2M sodium hydroxide and brine. After drying over Na_2SO_4, the solution was concentrated by distillation at reduced pressure, and the residue was purified by flash chromatography on silica gel (hexane-ethyl acetate 6:4), giving **23-25** (4-89%) as white solids.

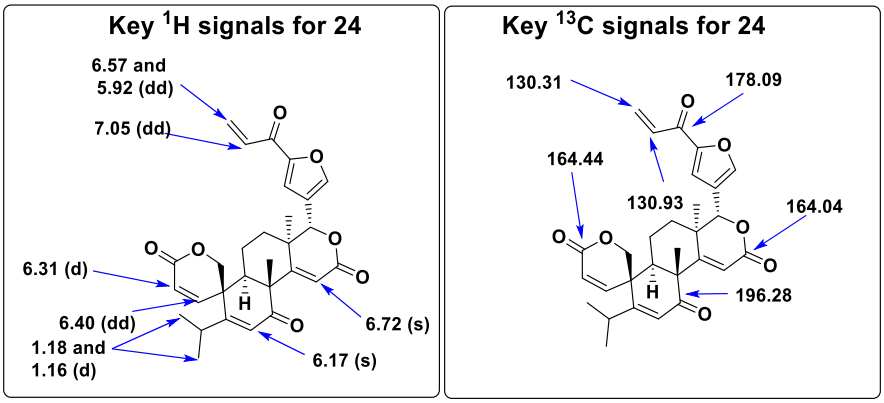
23 (23 mg, 68%)

^{1}H NMR (DMSO-*d6*, 500 MHz): δ 8.22 (s, 1H), 7.74 (s, 1H), 6.87 (d, *J* = 9.9 Hz, 1H), 6.50 (s, 1H), 6.32 (d, *J* = 9.9 Hz, 1H), 6.19 (s, 1H), 5.37 (s, 1H), 5.00 (s, 2H), 4.89 (d, *J* = 12.4, 1H), 4.69 (d, *J* = 12.4 Hz, 1H), 2.73 (dd, *J* = 12.6, 5.4 Hz, 1H), 2.50 – 2.43 (m, 1H), 1.99 – 1.89 (m, 1H), 1.85 - 1.79 (m, 1H), 1.77 - 1.69 (m, 1H), 1.51 (s, 3H), 1.36 – 1.31 (m, 1H), 1.18 (d, *J* = 6.7 Hz, 3H), 1.14 (d, *J* = 6.7 Hz, 3H), 1.12 (s, 3H).
^{13}C NMR (DMSO-*d6*, 125 MHz): δ 197.63, 180.67, 169.34, 166.30, 164.44, 162.67, 149.98, 149.92, 147.52, 124.88, 123.32, 123.05, 120.31, 118.51, 80.19, 69.79, 48.35, 46.24, 45.50, 40.25, 37.59, 30.82, 27.64, 25.27, 24.13, 23.94, 20.88, 17.46.
HRMS(ESI): m/z calc. for $C_{28}H_{30}O_7Cl$ $[M+H]^+$: 513.1693, found: 513.1680.
mp: decomposes upon heating above 140° C.
Opt. Rot.: $[\alpha]_D^{25}$ = - 107 (c = 0.13, acetone).



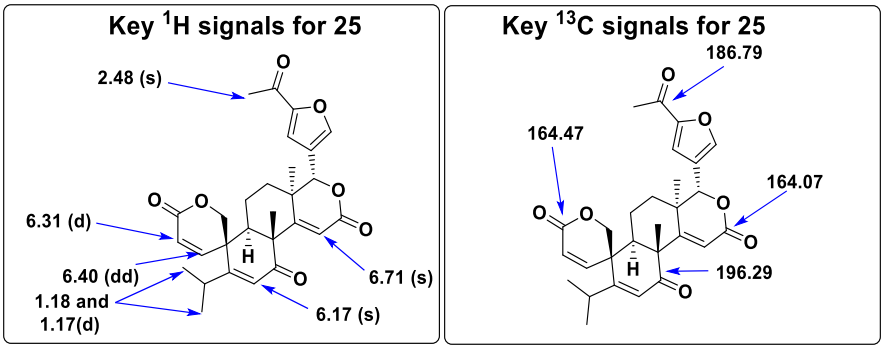
24 (2.8 mg, ca. 9%)

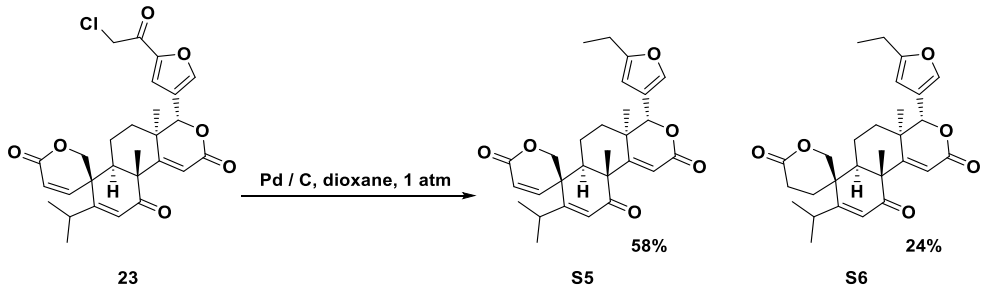
^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.69 (s, 1H), 7.26 (s, 1H), 7.05 (dd, *J* = 17.1, 10.6 Hz, 1H), 6.72 (s, 1H), 6.57 (dd, *J* = 17.1, 1.6 Hz, 1H), 6.40 (dd, *J* = 9.9, 1.6 Hz, 1H), 6.31 (d, *J* = 9.9 Hz, 1H), 6.17 (s, 1H), 5.92 (dd, *J* = 10.6, 1.6 Hz, 1H), 5.09 (s, 1H), 4.78 (dd, *J* = 12.4, 1.6 Hz, 1H), 4.54 (d, *J* = 12.4 Hz, 1H), 2.57 – 2.40 (m, 2H), 2.09 – 1.98 (m, 1H), 1.94 – 1.84 (m, 1H), 1.76 - 169 (m, 1H), 1-54 - 149 (m, 1H), 1.26 (s, 3H), 1.18 (d, *J* = 6.7 Hz, 3H), 1.16 (d, *J* = 6.7 Hz, 3H), 1.12 (s, 3H).
^{13}C NMR ($CDCl_3$,125 MHz): δ 196.28, 178.09, 167.27, 164.44, 164.04, 161.68, 153.11, 148.11, 145.05, 130.93, 130.31, 126.00, 123.79, 122.90, 119.17, 117.27, 81.14, 69.25, 48.13, 45.63, 40.15, 37.82, 31.03, 27.86, 25.50, 24.35, 24.14, 20.96, 17.37.
HRMS(ESI): m/z calc. for $C_{29}H_{31}O_7$ $[M+H]^+$: 491.2070, found: 491.2072.



25 (28 mg, 89%)

^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.63 (s, 1H), 7.17 (s, 1H), 6.71 (s, 1H), 6.40 (dd, *J* = 9.9, 1.6 Hz, 1H), 6.31 (d, *J* = 9.9 Hz, 1H), 6.17 (s, 1H), 5.07 (s, 1H), 4.77 (dd, *J* = 12.4, 1.6 Hz, 1H), 4.54 (d, *J* = 12.4 Hz, 1H), 2.56 – 2.42 (m, 2H), 2.48 (s, 3H), 2.12 – 2.00 (m, 1H), 1.83 - 1.85 (s, 1H), 1.75 – 1.69 (m, 1H), 1.55 – 1.49 (m, 1H), 1.54 (s, 3H), 1.18 (d, *J* = 6.7 Hz, 3H), 1.17 (d, *J* = 6.7 Hz, 3H), 1.12 (s, 3H).
^{13}C NMR ($CDCl_3$, 125 MHz): δ 196.29, 186.79, 167.25, 164.47, 164.07, 161.69, 152.99, 148.13, 144.61, 126.00, 123.77, 122.68, 119.15, 116.30, 81.14, 69.24, 48.12, 45.64, 40.13, 37.80, 31.03, 27.84, 26.05, 25.50, 24.35, 24.14, 20.94, 17.36.
HRMS(ESI): m/z calc. for $C_{28}H_{31}O_7$ $[M+H]^+$: 479.2070, found: 479.2089.
mp: >260° C.
Opt. Rot.: $[\alpha]_D^{25}$ = - 75 (c = 0.05, acetone).

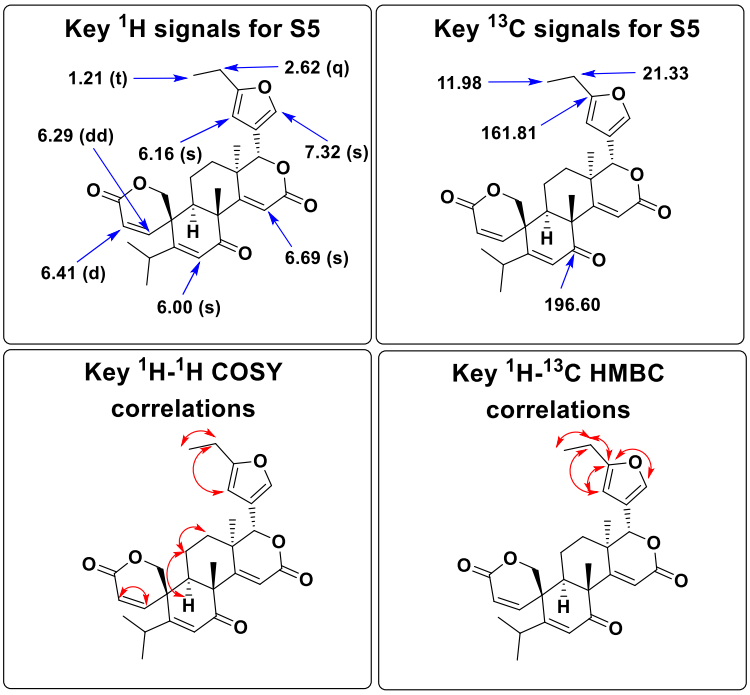




Procedure: A suspension of **23** (80 mg, 0.16 mmol) in dioxane (15 mL) was hydrogenated in the presence of 10% Pd/C at 1 atm for 72 h. The catalyst was removed by filtration over celite, and the filtrate was evaporated under reduced pressure to obtained a crude residue that was purified by silica gel flash chromatography (hexane-ethyl acetate 6:4) to provide **S5** (20 mg, 58%) and **S6** (18 mg, 24%) as white solids.

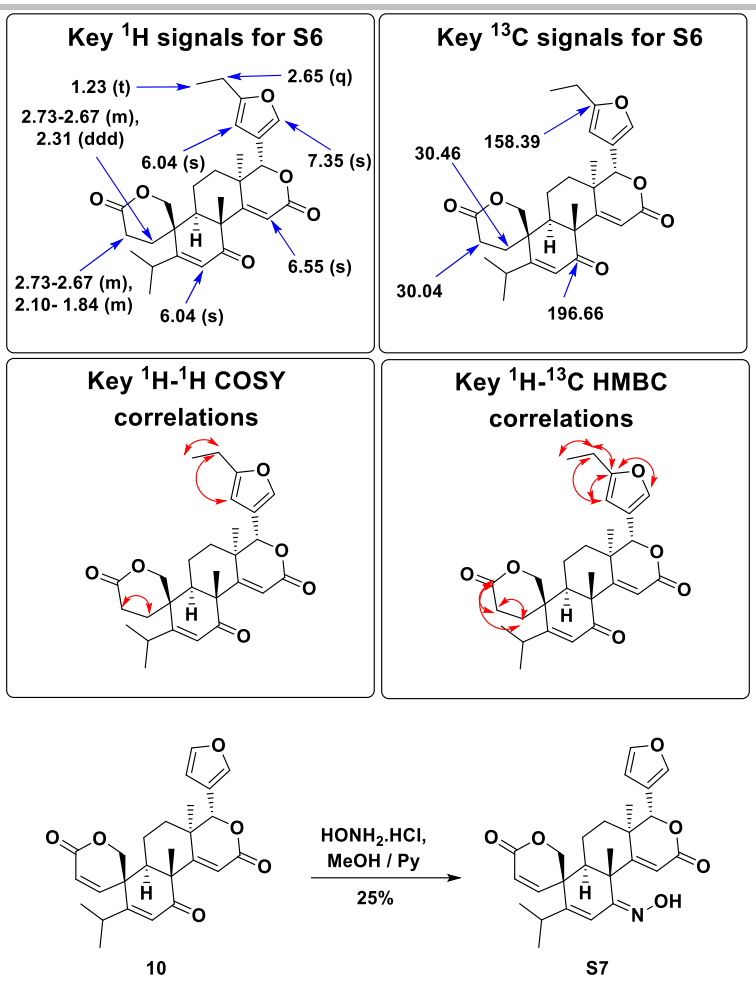
S5 (20 mg, 58%)

^{1}H NMR ($CDCl_3$, 125 MHz): δ 7.32 (s, 1H), 6.69 (s, 1H), 6.41 (dd, *J* = 9.9, 1.4 Hz, 1H), 6.29 (d, *J* = 9.9 Hz, 1H), 6.16 (s, 1H), 6.00 (s, 1H), 4.97 (s, 1H), 4.77 (dd, *J* = 12.4, 1.4 Hz, 1H), 4.53 (d, *J* = 12.4 Hz, 1H), 2.62 (q, *J* = 7.6 Hz, 2H), 2.52 (dd, *J* = 12.9, 5.8 Hz, 1H), 2.46 (hept, *J* = 6.7 Hz, 1H), 2.05 – 1.96 (m, 1H), 1.92 – 1.81 (m, 1H), 1.65 (ddd, *J* = 15.8, 9.7, 6.7 Hz, 1H), 1.54 – 1.52 (m, 1H), 1.52 (s, 3H), 1.21 (t, *J* = 7.6 Hz, 3H), 1.18 (d, *J* = 6.7 Hz, 3H), 1.16 (d, *J* = 6.7 Hz, 3H), 1.14 (s, 3H).
^{13}C NMR ($CDCl_3$, 125 MHz): δ 196.60, 167.11, 164.89, 164.87, 161.81, 158.42, 148.33, 139.47, 126.10, 123.61, 120.32, 118.93, 104.44, 82.13, 69.35, 48.06, 45.64, 40.18, 37.99, 31.01, 27.74, 25.51, 24.34, 24.13, 21.33, 21.00, 17.45, 11.98.
HRMS(ESI): m/z calc. for $C_{28}H_{33}O_6$ $[M+H]^+$: 465.2277, found: 465.2267.
mp: >260° C.
Opt. Rot.: $[\alpha]_D^{25}$ = - 35 (c = 0.05, acetone/chloroform).



S6 (18 mg, 24%)

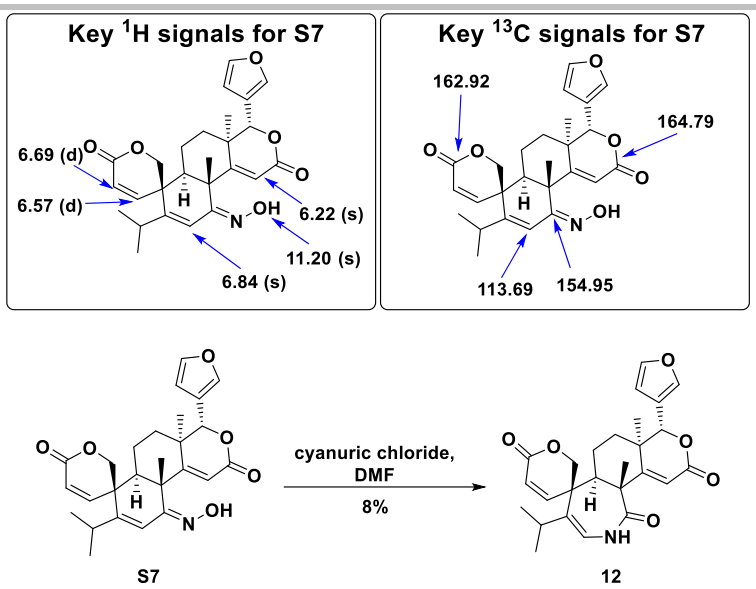
^{1}H NMR ($CDCl_3$, 125 MHz): δ 7.35 (s, 1H), 6.55 (s, 1H), 6.09 (s, 1H), 6.04 (s, 1H), 5.00 (s, 1H), 4.62 (d, *J* = 12.4 Hz, 1H), 4.40 (d, *J* = 12.4 Hz, 1H), 2.73 – 2.67 (m, 2H), 2.65 (q, *J* = 7.6 Hz, 2H), 2.55 (hept, *J* = 6.7 Hz, 1H), 2.44 (dd, *J* = 12.3, 4.8 Hz, 1H), 2.31 (ddd, *J* = 14.5, 14.5, 6.8 Hz, 1H), 2.10 – 1.84 (m, 3H), 1.79 – 1.73 (m, 1H), 1.57 - 1.53 (m, 1H), 1.47 (s, 3H), 1.27 (d, *J* = 6.7 Hz, 3H), 1.26 (s, *J* = 6.7 Hz, 3H), 1.23 (t, *J* = 7.6 Hz, 3H), 1.15 (s, 3H).
^{13}C NMR ($CDCl_3$, 125 MHz): δ 196.66, 171.70, 171.26, 164.82, 164.62, 158.39, 139.45, 124.15, 120.46, 119.93, 104.50, 81.75, 69.15, 49.28, 44.92, 43.09, 37.63, 30.46, 30.43, 30.04, 29.38, 25.02, 24.99, 24.45, 21.91, 21.34, 18.04, 11.99.
HRMS(ESI): m/z calc. for $C_{28}H_{35}O_6$ $[M+H]^+$: 467.2334, found: 467.2419.
mp: >260° C.
Opt. Rot.: $[\alpha]_D^{25}$ = - 19 (c = 0.05, acetone/chloroform).



Procedure: Hydroxylamine hydrochloride (183 mg, 2.64 mmol) was added to a solution of **10** (150 mg, 0.33 mmol) in methanol (7 mL) and pyridine (2.5 mL), and the resulting mixture was heated under reflux for 48 h. The reaction was cooled to room temperature, acidified to pH 2 with 2 M hydrochloric acid, and extracted three times with dichloromethane. The combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated by distillation under reduced pressure to yield a crude residue that was purified by silica gel flash chromatography (hexane−ethyl acetate 1:1) to provide **S7** (37 mg, 25%) as a white solid.

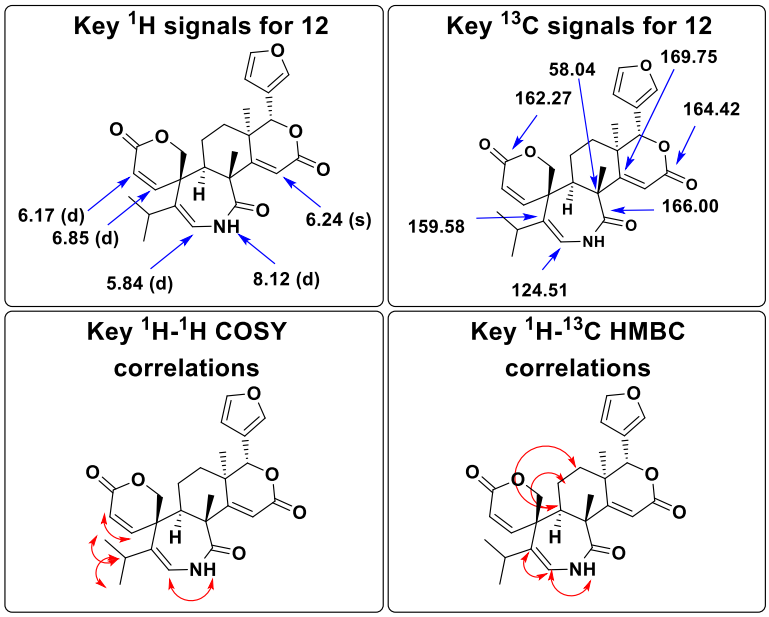
Note: Compound **S7** is known,[2] however **S7** has never been fully characterized. The hydroxy group on the C=N double bond of **S7** adopts the *Z* configuration.

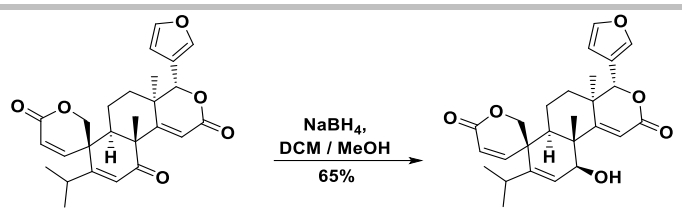
^{1}H NMR (DMSO-*d6*, 500 MHz): δ 11.20 (s, 1H), 7.77 (d, *J* = 1.8 Hz,1H), 7.69 (s, 1H), 6.84 (s, 1H), 6.69 (d, *J* = 9.9 Hz, 1H), 6.57 (d, *J* = 1.8 Hz, 1H), 6.22 (s, 1H), 6.19 (d, *J* = 9.9 Hz, 1H), 5.21 (s, 1H), 4.70 (d, *J* = 12.2 Hz, 1H), 4.57 (d, *J* = 12.2 Hz, 1H), 2.36 (t, *J* = 6.8 Hz,1H), 2.22 (dd, *J* = 12.2, 3.6 Hz, 1H), 1.85 – 1.80 (m, 1H), 1.65 – 1.54 (m, 2H), 1.41 (s, 3H), 1.27 – 1.15 (m, 1H), 1.11 (d, *J* = 6.8 Hz, 3H), 1.07 (d, *J* = 6.8 Hz, 3H), 1.06 (s, 3H).
^{13}C NMR (DMSO-*d6*, 125 MHz): δ 167.46, 164.79, 162.92, 154.97, 154.61, 151.77, 143.79, 142.26, 122.56, 120.78, 120.70, 113.69, 110.91, 80.33, 69.75, 45.37, 43.57, 43.00, 37.82, 30.99, 30.25, 24.96, 24.69, 24.46, 22.73, 19.14.
HRMS(ESI): m/z calc. for $C_{26}H_{30}NO_6I$ $[M+H]^+$: 452.2073, found: 452.2081.
mp: 212-213° C.
Opt. Rot.: $[\alpha]_D^{25}$ = - 54 (c = 0.09, acetone).



Procedure: Cyanuric chloride (59 mg, 0.319 mmol) was added to a dry oven flask and dissolved in DMF (0.8 mL). The resulting solution was stirred until the solution turns yellow, then, **S7** (36 mg, 0.079 mmol) in DMF (0.9 mL) was added. The reaction mixture was stirred at 60° C for 48 h. The reaction was cooled to room temperature, then, water and dichloromethane were added and the aqueous layer was extracted three times with dichloromethane. The combined organic layers were washed with brine and dried over Na_2SO_4. The solvent was concentrated by distillation under reduced pressure to obtain a crude residue of **12** that was purified by silica gel flash chromatography (hexane-ethyl acetate 3:7) to provide **12** (3 mg, 8%) as a white solid.

^{1}H NMR (DMSO-*d6*, 500 MHz): δ 8.12 (d, *J* = 1.9 Hz, 1H), 7.78 (d, *J* = 1.8 Hz, 1H), 7.71 (dd, *J* = 1.8, 1.8 Hz, 1H), 6.85 (d, *J* = 9.9 Hz, 1H), 6.58 (d, *J* = 1.8 Hz, 1H), 6.24 (s, 1H), 6.17 (d, *J* = 9.9 Hz, 1H), 5.84 (d, *J* = 1.9 Hz, 1H), 5.21 (s, 1H), 4.76 (d, *J* = 12.7 Hz, 1H), 4.63 (d, *J* = 12.7 Hz, 1H), 2.65 (dd, *J* = 12.3, 3.0 Hz, 1H), 2.49 (t, *J* = 6.7 Hz, 1H), 1.89 – 1.75 (m, 1H), 1.66 – 1.57 (m, 1H), 1.51 (s, 3H), 1.31 – 1.21 (m, 2H), 1.18 (s, 3H), 1.14 (d, *J* = 6.7 Hz, 3H), 1.05 (d, *J* = 6.7 Hz, 3H).
^{13}C NMR (DMSO-*d6*, 125 MHz): δ 169.75, 166.00, 164.42, 162.27, 159.58, 151.31, 143.86, 142.34, 124.51, 121.11, 120.52, 117.56, 110.90, 80.19, 69.66, 58.04, 49.62, 48.57, 38.47, 31.61, 31.43, 24.96, 24.56, 23.92, 23.00, 22.75.
HRMS(ESI): m/z calc. for $C_{26}H_{30}NO_6$ $[M+H]^+$: 452.2073, found: 452.2070.
mp: >260° C.
Opt. Rot.: $[\alpha]_D^{25}$ = - 155 (c = 0.03, acetone/chloroform).

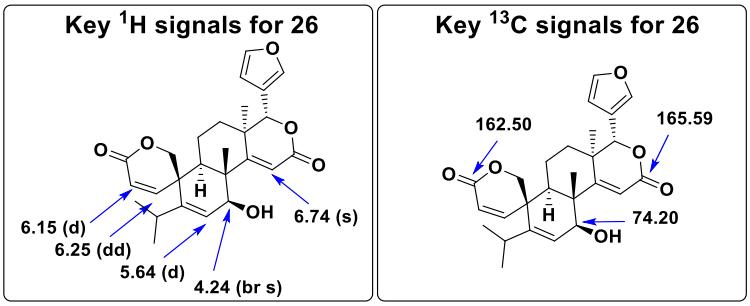


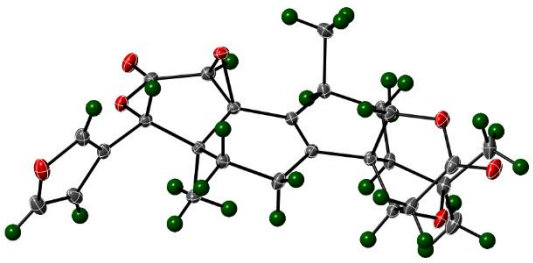


10 26

Procedure: A solution of $NaBH_4$ (23 mg, 0.60 mmol) in anhydrous methanol (1 mL) was added to a solution of **10** (48 mg, 0.11 mmol) in dichloromethane (2 mL) at -20° C and the resulting mixture was stirred at -20 °C. After 15 minutes, the reaction was quenched with a 2 M hydrochloric acid solution and extracted three times with dichloromethane. The organic layers were dried over Na_2SO_4 and concentrated by distillation under reduced pressure to obtained a crude residue that was purified by silica gel flash chromatography (hexane-ethyl acetate 4:6) to provide an amorphous solid that was crystalized with chloroform and hexane to obtain pure **26** (31 mg, 65%).

^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.48 (d, *J* = 1.8 Hz, 1H), 7.42 (dd, *J* = 1.8, 1.8 Hz, 1H), 6.75 (s, 1H), 6.41 (d, *J* = 1.8 Hz, 1H), 6.25 (dd, *J* = 9.9, 1.7 Hz, 1H), 6.15 (d, *J* = 9.9 Hz, 1H), 5.64 (d, *J* = 1.9 Hz, 1H), 5.04 (s, 1H), 4.70 (dd, *J* = 12.5, 1.7 Hz, 1H), 4.49 (d, *J* = 12.5 Hz, 1H), 4.24 (br s, 1H), 2.26 (hept, *J* = 6.8 Hz, 1H), 2.25 (t, 6.7 Hz, 1H), 1.98 – 1.86 (m, 2H), 1.85 – 1.74 (m, 1H), 1.74 – 1.64 (m, 1H), 1.48 (ddd, *J* = 14.6, 10.5, 5.1 Hz, 1H), 1.26 (s, 3H), 1.16 (s, 3H), 1.11 (d, 6.7 Hz, 3H), 1.08 (d, 6.7 Hz, 3H).
^{13}C NMR ($CDCl_3$, 125 MHz): δ 173.33, 165.59, 162.50, 150.79, 145.91, 143.08, 141.35, 128.18, 122.44, 119.97, 117.02, 110.02, 81.69, 74.20, 69.34, 44.88, 42.67, 39.49, 37.75, 29.37, 28.57, 25.21, 25.15, 21.22, 17.65, 17.36.
HRMS(ESI): m/z calc. for $C_{26}H_{31}O_6$ $[M+H]^+$: 439.2121, found: 439.2131.
mp: >260° C.
Opt. Rot.: $[\alpha]_D^{25}$ = - 162 (c = 0.05, acetone).





Crystallography

Experimental Protocol: Intensity data were collected on a Bruker D8 Venture kappa diffractometer equipped with a Photon 100 CMOS detector. An Iμs microfocus Mo source (λ = 0.71073 Å) coupled with a multi-layer mirror monochromator provided the incident beam. The sample was mounted on a 0.3 mm loop with the minimal amount of Paratone-N oil. Data was collected as a series of φ and/or ω scans. Data was collected at 100 K using a cold stream of N2(g). The collection, cell refinement, and integration of intensity data was carried out with the APEX3 software.[1] A semi-empirical absorption correction was performed with SADABS.[2] The structure was phased with intrinsic methods using SHELXT[3] and refined with the full-matrix least-squares program SHELXL.[4]

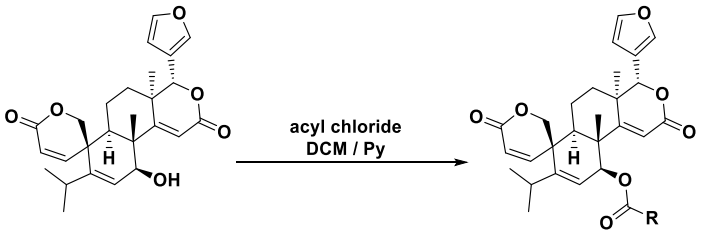
SUPPORTING INFORMATION

CCDC: 2082415

(1) Bruker (2016). APEX3. Bruker AXS, Inc., Madison, Wisconsin, USA.
(2) L. Krause, R. Herbst-Irmer, G. M. Sheldrick, D. Stalke, *J. Appl. Cryst.*, **2015,** *48*, 3–10.
(3) G. M. Sheldrick, *Acta Cryst.* **2015**, A71, 3–8.
(4) G. M. Sheldrick, *Acta Cryst*. **2015**, C71, 3–8.

Table S5. Crystal data and structure refinement for ed19as.

Identification code	ed19as
Empirical formula	C26 H30 O7
Formula weight	454.50
Temperature	100(2) K
Wavelength	1.54178 Å
Crystal system	Monoclinic
Space group	$P2_1$
Unit cell dimensions	a = 9.6959(7) Å a= 90°. b = 11.4093(8) Åb= 98.0088(9)°. c = 10.5779(7) Åg = 90°.
Volume	1158.75(14) Å3
Z	2
Density (calculated)	1.303 Mg/m3
Absorption coefficient	0.774 mm-1
F(000)	484
Crystal size	0.317 x 0.228 x 0.175 mm3
Theta range for data collection	4.221 to 74.392°.
Index ranges	-11<=h<=12, -14<=k<=13, -13<=l<=13
Reflections collected	29849
Independent reflections	4686 [R(int) = 0.0275]
Completeness to theta = 67.679°	100.0 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.7538 and 0.7120
Refinement method	Full-matrix least-squares on F2
Data / restraints / parameters	4686 / 1 / 303
Goodness-of-fit on F2	1.050
Final R indices [I>2sigma(I)]	R1 = 0.0250, wR2 = 0.0674
R indices (all data)	R1 = 0.0250, wR2 = 0.0674
Absolute structure parameter	0.02(3)
Extinction coefficient	0.0038(6)
Largest diff. peak and hole	0.217 and -0.130 e.Å-3



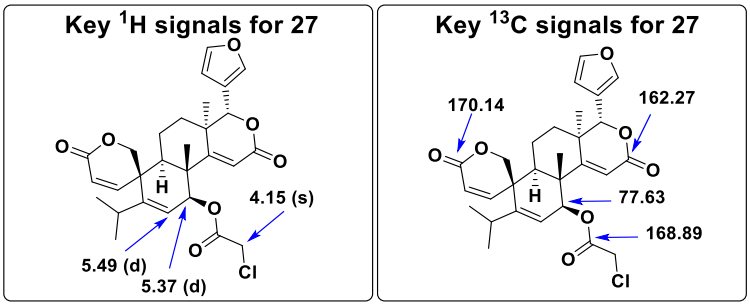
26 **27-29**

27; R = CH_2Cl 92%
28; R = CH_2CHCH_2 14%
29; R = CH_3 81%

Procedure: Pyridine (60 µL, 0.7 mmol) and the suitable acyl chloride (0.8 mmol) were added to a solution of **26** (300 mg, 0.68 mmol) in dichloromethane (10 mL), and the resulting solution was stirred at 30° C for 16 h. Water and dichloromethane were added to the reaction mixture and the aqueous layer was extracted three times with dichloromethane. The combined organic layers were washed with brine and dried over Na_2SO_4. The solvent was concentrated by distillation under reduced pressure and the obtained crude residue was purified by silica gel flash chromatography (hexane-ethyl acetate 1:1) to provide **27-29** (14-92%) as white solids.

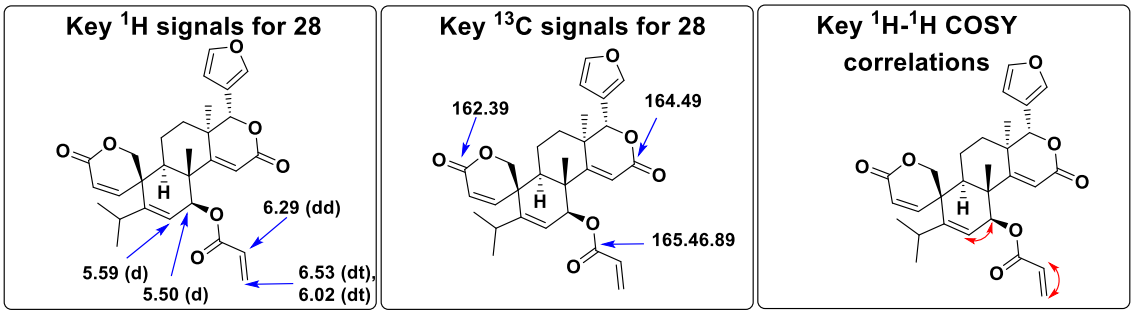
27 (321 mg, 92%)

^{1}H NMR (CDCl$_3$, 500 MHz): δ 7.41 (d, *J* = 1.8 Hz, 1H), 7.35 (dd, *J* = 1.8, 1.8 Hz, 1H), 6.35 (d, *J* = 1.8 Hz, 1H), 6.19 (dd, *J* = 9.9, 1.6 Hz, 1H), 6.13 (d, *J* = 9.9 Hz, 1H), 6.12 (s, 1H), 5.49 (d, *J* = 1.8 Hz, 1H), 5.37 (d, *J* = 1.8 Hz, 1H), 4.96 (s, 1H), 4.64 (dd, *J* = 12.6, 1.6 Hz, 1H), 4.45 (d, *J* = 12.6 Hz, 1H), 4.15 (s, 2H), 2.23 (hept, *J* = 6.8 Hz, 1H), 1.92 (dd, *J* = 11.0, 5.1 Hz, 1H), 1.78 – 1.66 (m, 3H), 1.43 – 1.35 (m, 1H), 1.28 (s, 3H), 1.15 (s, 3H), 1.04 (d, *J* = 6.8 Hz, 3H), 1.02 (d, *J* = 6.8 Hz, 3H).
^{13}C NMR (CDCl$_3$, 125 MHz): δ 170.14, 166.89, 164.45, 162.27, 150.21, 148.34, 143.17, 141.39, 123.59, 122.96, 119.78, 118.11, 110.03, 81.35, 77.63, 68.99, 44.75, 41.72, 40.97, 40.93, 37.82, 30.34, 29.57, 25.07, 24.96, 22.75, 18.18, 17.44.
HRMS(ESI): m/z calc. for $C_{28}H_{32}O_7Cl$ $[M+H]^+$: 515.1837, found: 515.1857.
Opt. Rot.: $[\alpha]_D^{25}$ = - 108 (c = 0.11, acetone).



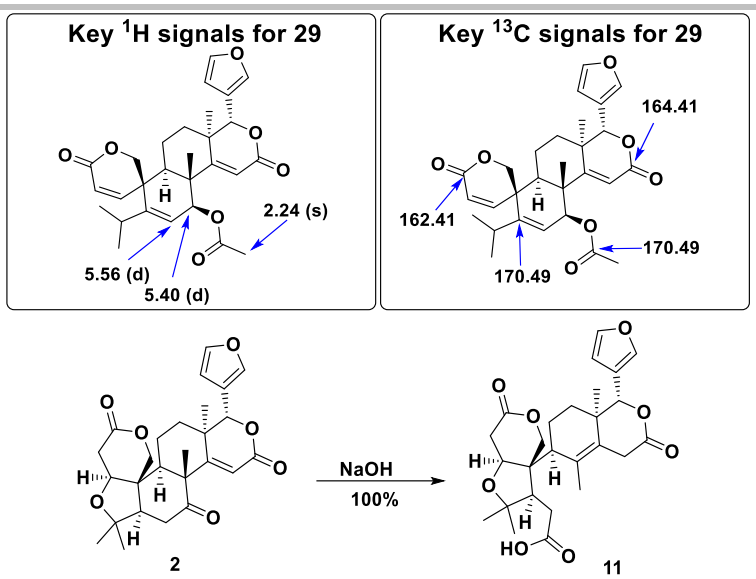
28 (50 mg, 14%)

^{1}H NMR (CDCl$_3$, 500 MHz): δ 7.49 (d, *J* = 1.8 Hz, 1H), 7.44 (dd, *J* = 1.8 Hz, 1H), 6.54 (dt, *J* = 17.3, 0.9 Hz, 1H), 6.44 (d, *J* = 1.8 Hz, 1H), 6.29 (dd, *J* = 17.3, 10.5 Hz, 1H), 6.25 (dd, *J* = 9.9, 1.7 Hz, 1H), 6.21 (d, *J* = 9.9 Hz, 1H), 6.15 (s, 1H), 6.02 (dt, *J* = 10.5, 0.9 Hz, 1H), 5.59 (d, *J* = 1.8 Hz, 1H), 5.50 (d, *J* = 1.8 Hz, 1H), 5.04 (s, 1H), 4.74 (dd, *J* = 12.5, 1.7 Hz, 1H), 4.55 (d, *J* = 12.5 Hz, 1H), 2.31 (hept, *J* = 6.8 Hz, 1H), 2.04 (t, *J* = 8.0 Hz, 1H), 1.86 – 1.74 (m, 3H), 1.52 – 1.46 (m, 1H), 1.38 (s, 3H), 1.24 (s, 3H), 1.12 (d, *J* = 6.8 Hz, 3H), 1.10 (d, *J* = 6.8 Hz, 3H).
^{13}C NMR (CDCl$_3$, 125 MHz): δ 170.65, 165.46, 164.49, 162.39, 150.51, 147.37, 143.11, 141.36, 132.61, 127.79, 124.54, 122.78, 119.89, 117.78, 110.05, 81.36, 75.72, 69.11, 44.78, 41.60, 40.83, 37.77, 30.12, 29.52, 25.08, 24.99, 22.52, 18.06, 17.77.
HRMS(ESI): m/z calc. for $C_{29}H_{33}O_7$ $[M+H]^+$: 493.2226, found: 493.2214.



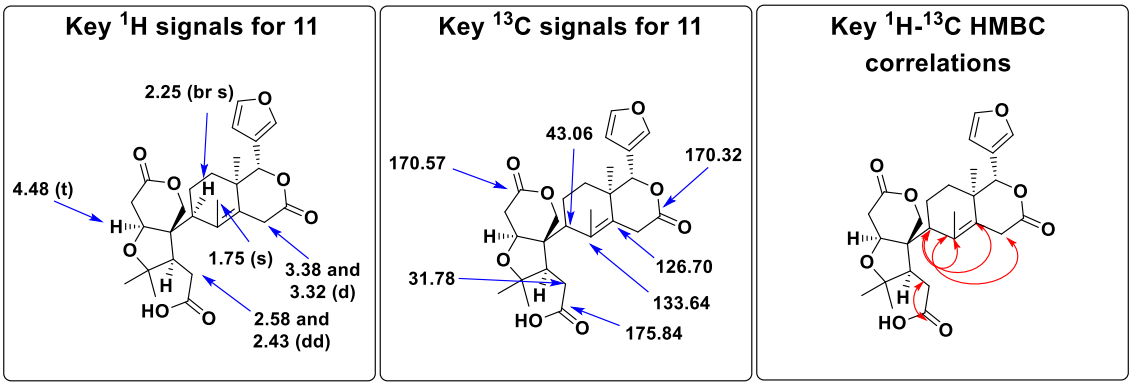
29 (260 mg, 81%)

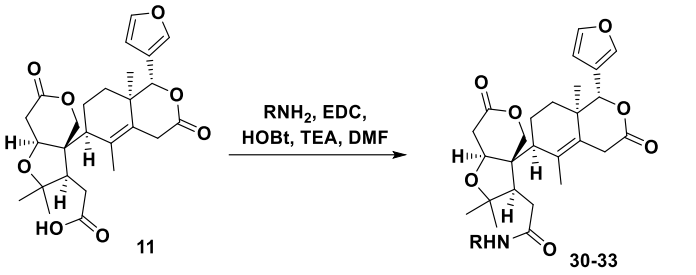
^{1}H NMR (CDCl$_3$, 500 MHz): δ 7.50 (dd, *J* = 1.8, 0.9 Hz, 1H), 7.44 (dd, *J* = 1.8, 1.8 Hz, 1H), 6.44 (dd, *J* = 1.8, 0.9 Hz, 1H), 6.28 (dd, *J* = 9.9, 1.7 Hz, 1H), 6.20 (d, *J* = 9.9 Hz, 1H), 6.19 (s, 1H), 5.56 (d, *J* = 1.8 Hz, 1H), 5.40 (d, *J* = 1.8 Hz, 1H), 5.05 (s, 1H), 4.72 (dd, *J* = 12.4, 1.7 Hz, 1H), 4.54 (d, *J* = 12.4 Hz, 1H), 2.29 (hept, *J* = 6.8 Hz, 1H), 2.24 (s, 3H), 2.00 (dd, *J* = 10.7, 5.0 Hz, 1H), 1.84 – 1.73 (m, 3H), 1.53 – 1.42 (m, 1H), 1.33 (s, 3H), 1.23 (s, 3H), 1.12 (d, *J* = 6.8 Hz, 3H), 1.10 (d, *J* = 6.8 Hz, 3H).
^{13}C NMR (CDCl$_3$, 125 MHz): δ 170.49 (2C), 164.63, 162.41, 150.56, 147.27, 143.13, 141.37, 124.72, 122.77, 119.86, 117.83, 110.05, 81.38, 75.52, 69.08, 44.76, 41.53, 41.05, 37.76, 30.41, 29.47, 25.10, 24.98, 22.74, 21.31, 18.20, 17.43.
HRMS(ESI): m/z calc. for $C_{28}H_{33}O_7$ $[M+H]^+$: 481.2228, found: 481.2226.



Procedure: A suspension of **2** (50 mg, 0.11 mmol) in 2 M sodium hydroxide (1.25 mL), was heated at 110° C for 2 h. The reaction was cooled to room temperature and slowly acidified with concentrated hydrochloric acid to pH 2. The aqueous layer was extracted with dichloromethane, dried over Na_2SO_4, and concentrated by distillation under reduced pressure to yield pure **11** (52 mg, quantitative yield) as a yellow solid.

^{1}H NMR (CDCl$_3$, 500 MHz): δ 7.35 (d, *J* = 1.8 Hz, 1H), 7.31 (dd, *J* = 1.9, 1.8 Hz, 1H), 6.31 (d, *J* = 1.9 Hz, 1H), 5.08 (s, 1H), 4.48 (t, *J* = 3.9 Hz, 1H), 4.21 (d, *J* = 12.2 Hz, 1H), 4.02 (d, *J* = 12.2 Hz, 1H), 3.38 (d, *J* = 21.9, 1H), 3.32 (d, *J* = 21.9, 1H), 2.74 – 2.66 (m, 3H), 2.58 (dd, *J* = 16.9, 12.2 Hz, 1H), 2.43 (dd, *J* = 16.9, 2.3 Hz, 1H), 2.25 (br s, 1H), 1.75 (s, 3H), 1.74 – 1.70 (m, 2H), 1.29 – 1.16 (m, 2H), 1.18 (s, 3H), 1.13 (s, 3H), 0.99 (s, 3H). (31 non-exchangeable protons)
^{13}C NMR (CDCl$_3$, 125 MHz): δ 175.84, 170.57, 170.32, 143.09, 141.26, 133.65, 126.70, 120.39, 109.75, 82.43, 81.21, 75.39, 69.15, 52.28, 48.35, 43.06, 38.00, 34.73, 33.80, 31.78, 29.87, 28.97, 24.99, 22.00, 20.08, 18.11.
HRMS(ESI): m/z calc. for $C_{26}H_{33}O_8$ $[M+H]^+$: 473.2175, found: 473.2182.
mp: 126-128° C.
Opt. Rot.: $[\alpha]_D^{25}$ = - 114 (c = 0.16, acetone).



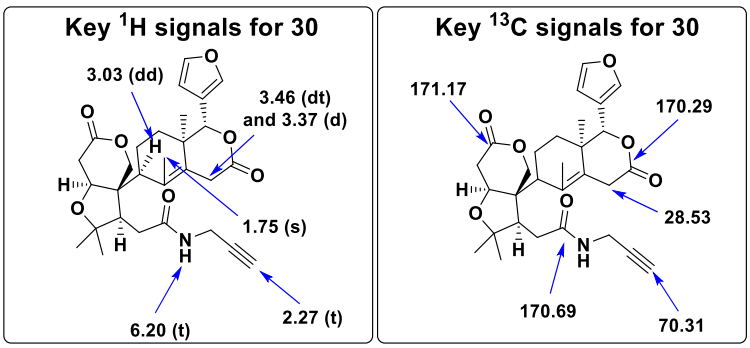


30; R = CH_2CCH 53%
31; R = CH_2Ph 57%
32; R = CH_2CHCH_2 51%
33; R = CH_3 70%

Procedure: HOBt (18 mg, 0.115 mmol), EDC (22 µL, 0.12 mmol), and TEA (29 µL, 0.21 mmol) were added to a solution of **11** (50 mg, 0.11 mmol) in DMF (0.5 ml), and the resulting mixture was stirred 30 minutes at 30° C. The suitable amine (0.12 mmol) was added to the mixture and the reaction was stirred overnight. The reaction was diluted with dichloromethane and washed with water, 5% citric acid, brine, 5% $NaHCO_3$, and Brine. The organic layer was dried over Na_2SO_4, concentrated by distillation at reduced pressure, and the residue was purified by flash chromatography on silica gel (hexane-ethyl acetate 7:3), giving **30-33** (51-70%) as white solids.

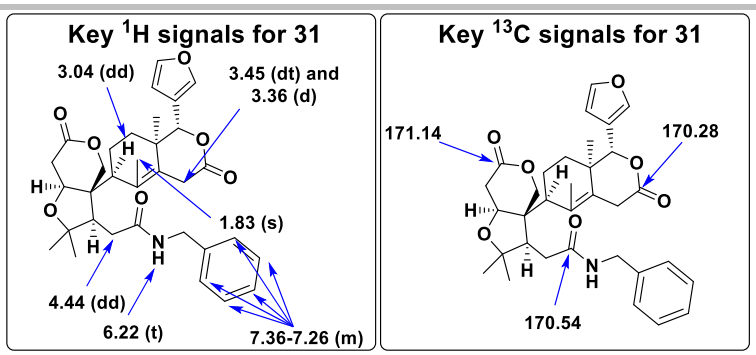
30 (30 mg, 53%)

^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.55 (d, *J* = 1.8 Hz, 1H), 7.37 (dd, *J* = 1.8, 1.8 Hz, 1H), 6.43 (d, *J* = 1.8 Hz, 1H), 6.20 (t, *J* = 5.5 Hz, 1H), 5.41 (s, 1H), 4.63 (t, *J* = 3.8 Hz, 1H), 4.26 (d, *J* = 12.3 Hz, 1H), 4.09 (ddd, *J* = 17.5, 5.5, 2.5 Hz, 1H), 4.04 – 3.94 (m, 2H), 3.46 (dt, *J* = 21.9, 1.9 Hz, 1H), 3.37 (d, *J* = 21.9 Hz, 1H), 3.03 (dd, *J* = 9.7, 4.9 Hz, 1H), 2.75 (t, *J* = 3.8 Hz, 2H), 2.44 – 2.36 (m, 2H), 2.31 (d, *J* = 5.9 Hz, 1H), 2.27 (t, *J* = 2.5 Hz, 1H), 1.84 (s, 3H), 1.80 – 1.72 (m, 1H), 1.70 (d, *J* = 14.5 Hz, 1H), 1.43 (td, *J* = 14.5, 3.4 Hz, 1H), 1.35-1.28 (m, 1H), 1.22 (s, 3H), 1.12 (s, 3H), 1.07 (s, 3H).
^{13}C NMR ($CDCl_3$, 125 MHz): δ 171.17, 170.69, 170.29, 142.80, 142.00, 134.21, 126.45, 120.37, 109.94, 83.03, 80.89, 79.37, 75.85, 71.62, 70.35, 52.26, 47.61, 44.11, 38.06, 34.96, 34.09, 33.96, 29.83, 29.26, 28.53, 24.88, 22.20, 20.14, 18.32.
HRMS(ESI): m/z calc. for $C_{29}H_{36}NO_7$ $[M+H]^+$: 510.2492, found: 510.2494.
mp: 128-129° C.
Opt. Rot.: $[\alpha]_D^{25}$ = - 132 (c = 0.11, acetone).



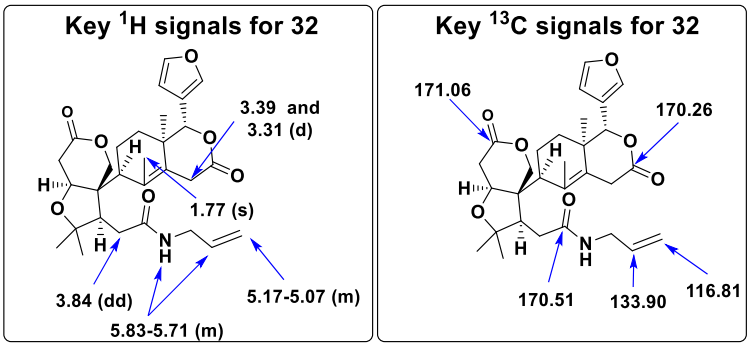
31 (34 mg, 57%)

^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.47 (d, *J* = 1.5 Hz, 1H), 7.36 – 7.26 (m, 6H), 6.40 (d, *J* = 1.9 Hz, 1H), 6.22 (t, *J* = 5.9 Hz, 1H), 5.42 (s, 1H), 4.59 (dd, *J* = 3.8 Hz, 1H), 4.44 (dd, *J* = 6.2, 5.9 Hz, 2H), 4.25 (d, *J* = 12.3 Hz, 1H), 4.01 (d, *J* = 12.3 Hz, 1H), 3.45 (dt, *J* = 21.9, 1.9 Hz, 1H), 3.36 (d, *J* = 21.9 Hz, 1H), 3.04 (dd, *J* = 9.9, 4.8 Hz, 1H), 2.72 (d, *J* = 3.8 Hz, 2H), 2.39 – 2.29 (m, 3H), 1.83 (s, 3H), 1.74 (ddd, *J* = 14.6, 6.0, 3.4 Hz, 1H), 1.72 – 1.64 (m, 1H), 1.46 (td, *J* = 14.3, 3.5 Hz, 1H), 1.22 (s, 3H), 1.11 (s, 3H), 1.10 – 1.07 (m, 1H), 1.06 (s, 3H).
^{13}C NMR ($CDCl_3$, 125 MHz): δ 171.14, 170.54, 170.28, 142.76, 141.87, 138.01, 134.09, 128.81 (2C), 127.87 (2C), 127.67, 126.52, 120.46, 109.96, 83.03, 80.92, 75.84, 70.31, 52.24, 47.71, 44.10, 43.78, 38.07, 34.95, 34.29, 33.95, 29.84, 28.53, 24.93, 22.14, 20.14, 18.28.
HRMS(ESI): m/z calc. for $C_{33}H_{40}NO_{97}$ $[M+H]^+$: 562.2805, found: 562.2806.
mp: 118-120° C.
Opt. Rot.: $[\alpha]_D^{25}$ = - 183 (c = 0.16, acetone).



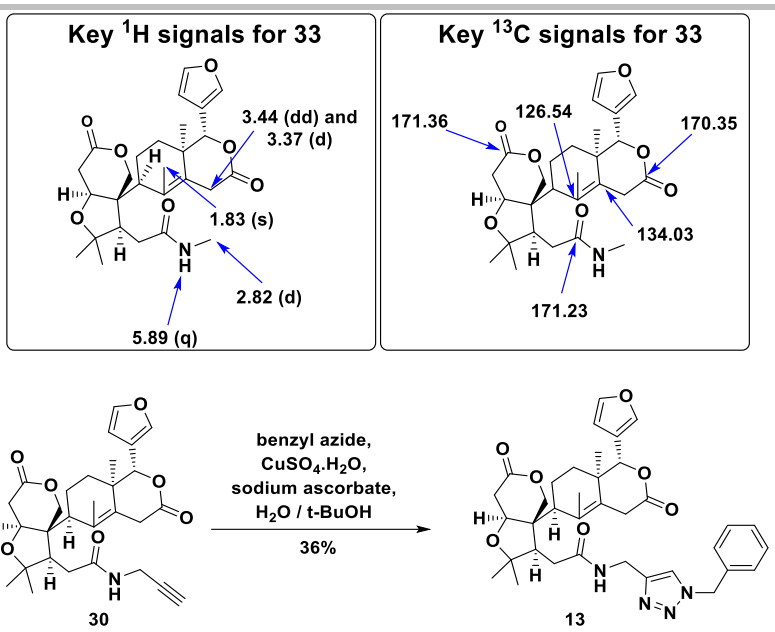
32 (28 mg, 51%)

^{1}H NMR (CDCl$_3$, 500 MHz): δ 7.44 (d, *J* = 1.9 Hz, 1H), 7.30 (dd, *J* = 1.9, 1.9 Hz, 1H), 6.36 (d, *J* = 1.9 Hz, 1H), 5.83 – 5.71 (m, 2H), 5.35 (s, 1H), 5.16 – 5.09 (m, 2H), 4.55 (t, *J* = 3.8 Hz, 1H), 4.21 (d, *J* = 12.2 Hz, 1H), 3.97 (d, *J* = 12.2 Hz, 1H), 3.84 (dd, *J* = 5.7, 5.7 Hz, 2H), 3.39 (d, *J* = 21.8 Hz, 1H), 3.31 (d, *J* = 21.8 Hz, 1H), 2.97 (t, *J* = 7.3 Hz, 1H), 2.69 (d, *J* = 3.8 Hz, 2H), 2.33 (d, *J* = 7.3 Hz, 2H), 2.24 (d, *J* = 5.8 Hz, 1H), 1.77 (s, 3H), 1.69 (ddd, *J* = 14.7, 6.1, 3.3 Hz, 1H), 1.66 – 1.58 (m, 1H), 1.38 (td, *J* = 14.2, 3.5 Hz, 1H), 1.16 (s, 3H), 1.08 (s, 3H), 1.03 – 0.98 (m, 1H), 1.01 (s, 3H).
^{13}C NMR (CDCl$_3$, 125 MHz): δ 171.06, 170.51, 170.26, 142.77, 141.97, 134.20, 133.90, 126.47, 120.44, 116.81, 109.95, 83.01, 80.88, 75.79, 70.25, 52.28, 47.48, 43.97, 42.04, 38.08, 34.99, 34.22, 33.98, 29.89, 28.49, 24.95, 22.20, 20.15, 18.30.
HRMS(ESI): m/z calc. for $C_{29}H_{38}NO_7$ $[M+H]^+$: 512.2648, found: 512.2650.
mp: 110-111° C.
Opt. Rot.: $[\alpha]_D^{25}$ = - 229 (c = 0.13, acetone).



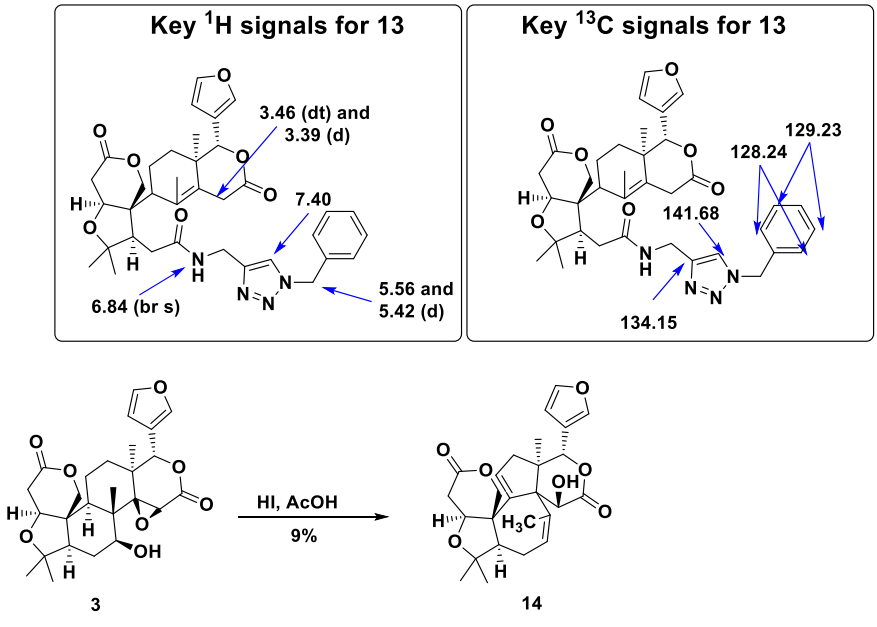
33 (30 mg, 70%)

^{1}H NMR (CDCl$_3$, 500 MHz): δ 7.53 (d, *J* = 1.8 Hz, 1H), 7.37 (dd, *J* = 1.8, 1.8 Hz, 1H), 6.43 (d, *J* = 1.8 Hz, 1H), 5.89 (q, *J* = 4.7 Hz, 1H), 5.42 (s, 1H), 4.60 (t, *J* = 3.9 Hz, 1H), 4.25 (d, *J* = 12.3 Hz, 1H), 4.04 (d, *J* = 12.3 Hz, 1H), 3.44 (dt, *J* = 21.8, 1.8 Hz, 1H), 3.37 (d, *J* = 21.8 Hz, 1H), 3.02 (dd, *J* = 8.3, 6.3 Hz, 1H), 2.82 (d, *J* = 4.7 Hz, 3H), 2.75 (d, *J* = 3.8 Hz, 2H), 2.37 – 2.33 (m, 2H), 2.30 (d, *J* = 5.9 Hz, 1H), 1.83 (s, 3H), 1.74 (ddd, *J* = 14.6, 6.0, 3.3 Hz, 1H), 1.71 – 1.65 (m, 1H), 1.46 (td, *J* = 14.3, 3.6 Hz, 1H), 1.22 (s, 3H), 1.11 (s, 3H), 1.09 – 1.05 (m, 1H), 1.06 (s, 3H).
^{13}C NMR (CDCl$_3$, 125 MHz): δ 171.36, 171.23, 170.35, 142.81, 141.90, 134.03, 126.54, 120.50, 109.92, 82.96, 80.92, 75.69, 70.26, 52.21, 47.72, 44.00, 38.04, 34.97, 34.01, 33.94, 29.82, 28.53, 26.44, 24.83, 22.15, 20.15, 18.30.
HRMS(ESI): m/z calc. for $C_{27}H_{36}NO_7$ $[M+H]^+$: 486.2492, found: 486.24933.
mp: 140-141° C.
Opt. Rot.: $[\alpha]_D^{25}$ = - 214 (c = 0.11, acetone).



Procedure: Copper (II) sulfate (1 mg, 0.004 mmol) and sodium ascorbate (4 mg, 019 mmol) were added to a solution of **30** (100 mg, 0.19 mmol) in H_2O (3 mL) and *t*-BuOH (1.5 mL). Benzyl azide (26 µL, 0,24 mmol) was added to the resulting suspension and the mixture was stirred at 30° C for 48 h. The solvent was then evaporated and the solution was extracted three times with dichloromethane. The combined organic layers were dried over Na_2SO_4 and concentrated by distillation at reduced pressure. The obtained residue was further purified by flash chromatography on silica gel (hexane-ethyl acetate 7:3) to give **13** (43 mg, 36%) as a white solid.

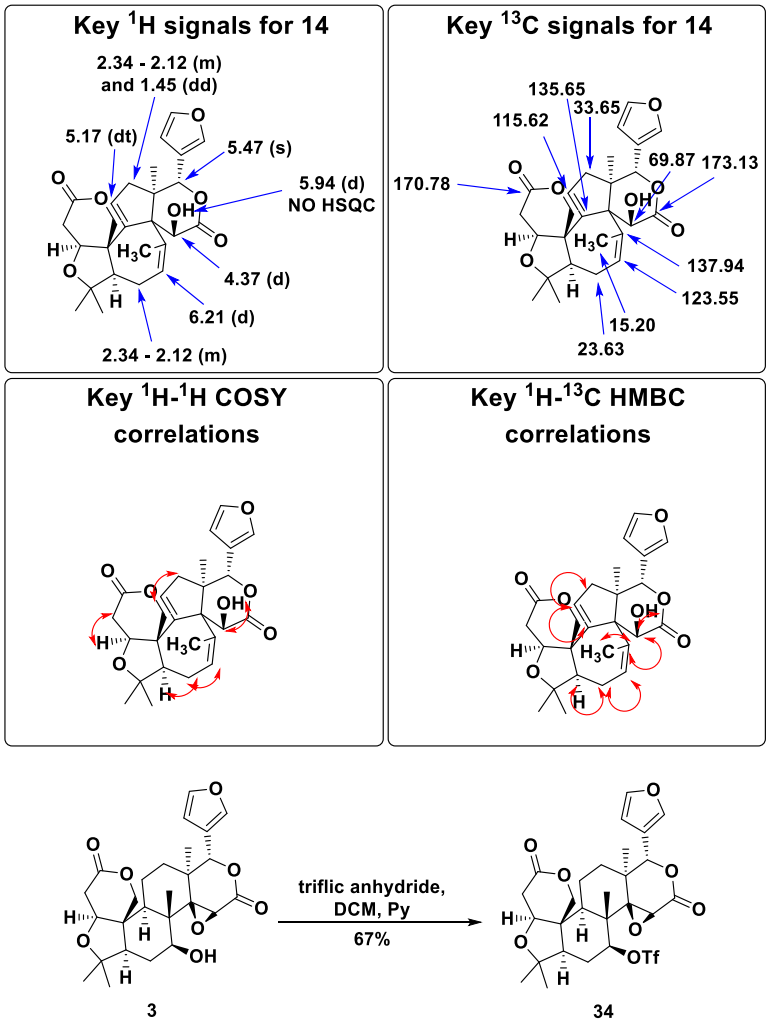
^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.47 (d, *J* = 1.8 Hz, 1H), 7.38 – 7.34 (m, 4H), 7.26 – 7.24 (m, 2H), 6.84 (br s, 1H), 6.38 (d, *J* = 1.9 Hz, 1H), 5.56 (d, *J* = 14.7 Hz, 1H), 5.42 (d, *J* = 14.7 Hz, 1H), 5.35 (s, 1H), 4.57 (t, *J* = 4.1, 1H), 4.55 (dd, 15.5, 5.1 Hz, 1H), 4.44 (dd, 15.5, 5.1 Hz, 1H), 4.26 (d, *J* = 12.2 Hz, 1H), 4.02 (d, *J* = 12.2 Hz, 1H), 3.46 (dt, *J* = 21.8, 1.8 Hz, 1H), 3.39 (d, *J* = 21.9 Hz, 1H), 2.96 (dd, *J* = 11.2, 3.1 Hz, 1H), 2.80 – 2.70 (m, 2H), 2.43 – 2.39 (m, 2H), 2.27 (d, *J* = 5.5 Hz, 1H), 1.82 (s, 3H), 1.74 – 1.66 (m, 2H), 1.41 – 1.34 (m, 1H), 1.26-1.25 (m, 2H), 1.13 (s, 3H), 1.06 (s, 3H), 1.02 (s, 3H).
^{13}C NMR ($CDCl_3$, 125 MHz): δ 170.86, 170.85, 170.24, 142.77, 141.68, 134.15, 133.95, 129.23 (2C), 128.99, 128.24 (2C), 126.63, 120.55, 109.94, 82.95, 80.83, 77.23, 76.77, 75.95, 69.86, 54.48, 52.32, 47.10, 43.47, 37.98, 34.91, 34.79, 33.94, 33.81, 30.01, 28.63, 25.09, 22.23, 20.08, 18.23.
HRMS(ESI): m/z calc. for $C_{36}H_{43}N_4O_7$ $[M+H]^+$: 643.3131, found: 643.3114.



Procedure: A solution of **3** (500 mg, 1.06 mmol) in acetic acid (8.5 mL) and hydriodic acid (8.5 mL) was heated under reflux for 6 h. The reaction mixture was cooled to room temperature and slowly poured into 400 mL of sodium sulfite saturated solution and

extracted three times with dichloromethane. The organic layers were combined, washed with brine, dried over Na_2SO_4, and concentrated by distillation under reduced pressure. The crude residue was purified by silica gel flash chromatography (hexane-ethyl acetate 4:6) to provide **14** (40 mg, 9%) as a white solid.

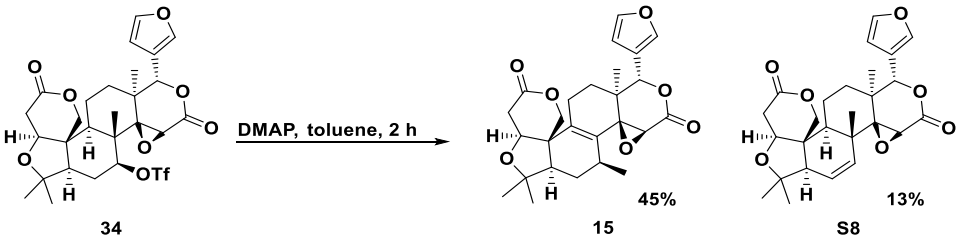
^{1}H NMR (DMSO-*d6*, 500 MHz): δ 7.71 (d, *J* = 1.8 Hz, 1H), 7.68 (dd, *J* = 1.8, 1.8 Hz, 1H), 6.52 (d, *J* = 1.8 Hz, 1H), 6.21 (d, *J* = 4.9 Hz, 1H), 5.94 (d, *J* = 4.9 Hz, 1H), 5.47 (s, 1H), 5.17 (dt, *J* = 4.3, 2.1 Hz, 1H), 4.37 (d, *J* = 11.6 Hz, 1H), 4.37 (d, *J* = 4.9 Hz, 1H), 4.26 (dd, *J* = 4.6, 3.1 Hz, 1H), 3.90 (d, *J* = 11.6 Hz, 1H), 2.98 (dd, *J* = 17.1, 4.6 Hz, 1H), 2.67 (dd, *J* = 17.1, 3.1 Hz, 1H), 2.34 – 2.12 (m, 3H), 2.07 (dd, 12.1, 5.3 Hz, 1H), 1.45 (dd, *J* = 18.5, 5.3 Hz, 1H), 1.18 (s, 3H), 1.09 (s, 3H), 1.09 (s, 3H), 0.86 (s, 3H).
^{13}C NMR (DMSO-*d6*, 125 MHz): δ 173.13, 170.78, 143.26, 141.23, 137.94, 135.65, 123.55, 120.90, 115.62, 110.17, 79.47, 77.46, 74.08, 69.87, 67.03, 53.48, 47.07, 44.40, 38.64, 35.35, 33.65, 30.49, 24.38, 23.63, 15.62, 15.20.
HRMS(ESI): m/z calc. for $C_{26}H_{31}O_7$ $[M+H]^+$: 455.2059, found: 455.20.61.
mp: decomposes upon heating above 130° C.
Opt. Rot.: $[\alpha]_D^{25}$ = - 16 (c = 0.03, acetone/chloroform).



Procedure: Triflic anhydride (81 µL, 0.48 mmol) was added at 0° C to a solution of **3** (115 mg, 0.24 mmol) in dichloromethane (1 mL) and pyridine (77 µL), and the resulting mixture was stirred at 30° C for 1 h. The reaction was quenched with iced water and extracted three times with dichloromethane. The organic layers were combined, washed with brine, dried over Na_2SO_4, and concentrated by distillation under reduced pressure. The crude residue was purified by silica gel flash chromatography (hexane-ethyl acetate 4:6) to provide **34** (97 mg, 67%) as a yellowish solid.

^{1}H NMR (DMSO-*d6*, 500 MHz): δ 7.71 (d, *J* = 1.7 Hz, 1H), 7.69 (dd, *J* = 1.7, 1.7 Hz, 1H), 6.49 (d, *J* = 1.7 Hz, 1H), 5.55 (s, 1H), 4.62 (d, *J* = 13.2 Hz, 1H), 4.50 (d, *J* = 2.1 Hz, 1H), 4.42 (d, *J* = 13.2 Hz, 1H), 4.33 (s, 1H), 4.08 (d, *J* = 3.6 Hz, 1H), 2.68 – 2.56 (m, 3H), 2.26 – 2.14 (m, 3H), 2.04 – 1.90 (m, 1H), 1.75 – 1.69 (m, 1H), 1.65 – 1.59 (m, 1H), 1.30 – 1.23 (m, 1H), 1.27 (s, 3H), 1.19 (s, 3H), 1.04 (s, 3H), 0.83 (s, 3H).
^{13}C NMR (DMSO-*d6*, 125 MHz): δ 170.55, 167.93, 143.96, 142.33, 121.15 (q, *J* = 320 Hz, 1C), 120.68, 110.69, 87.58, 80.44, 79.52, 78.48, 68.82, 65.49, 55.69, 51.50, 45.82, 44.60, 42.17, 38.28, 36.10, 30.61, 26.22, 23.30, 21.99, 18.43, 18.07, 16.47.

^{19}F NMR (DMSO-*d6*, 470 MHz): δ - 77.75.
HRMS(ESI): m/z calc. for $C_{27}H_{32}O_{10}SF_3$ $[M+H]^+$: 605.1668, found: 605.1677.
mp: decomposes upon heating above 100° C.
Opt. Rot.: $[\alpha]_D^{25}$ = + 17 (c = 0.23, acetone).

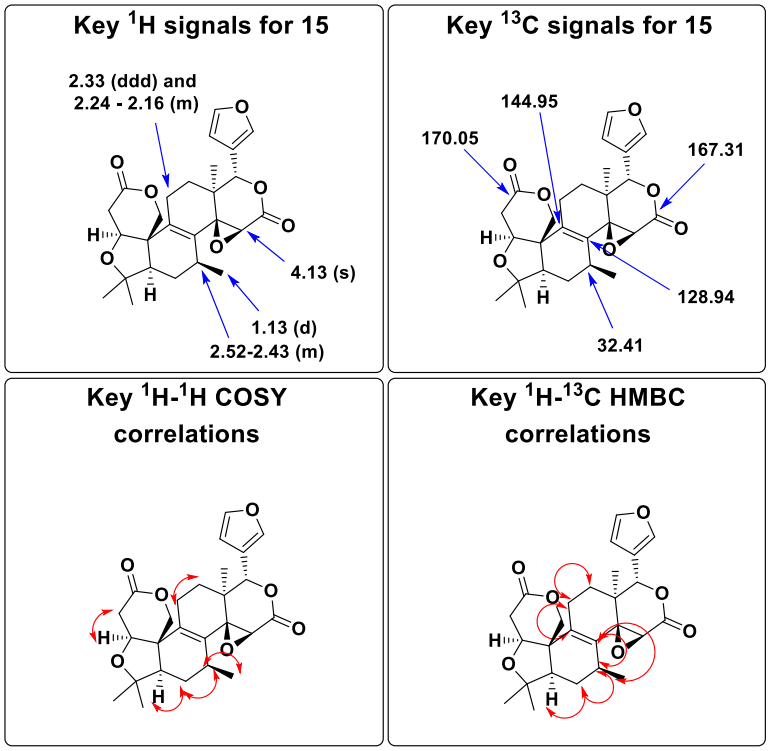


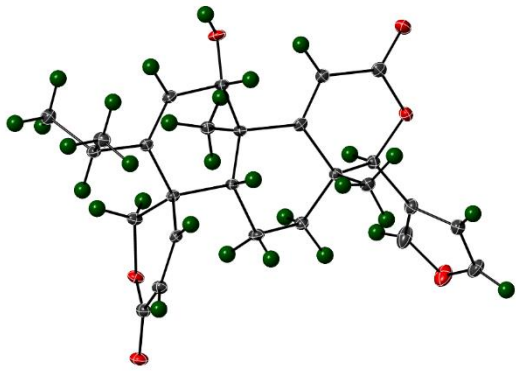
34 15 S8

Procedure: DMAP (220 mg, 1.8 mmol) was added to a solution of **34** (434 mg, 0.7 mmol) in toluene (5 mL) and the resulting solution was heated at 80° C for 2 h. Toluene was evaporated and the residue was partitioned between water and dichloromethane. The aqueous layer was extracted three times with dichloromethane. The organic layers were combined, washed with brine, dried over Na_2SO_4, and concentrated by distillation under reduced pressure. The crude residue was purified by silica gel flash chromatography (hexane-ethyl acetate 1:1) to provide **15** (144 mg, 45%) and **S8** (41 mg, 13%) as white solids.

15 (144 mg, 45%)

^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.42 (dd, *J* = 1.7, 1.7 Hz, 1H), 7.41 (d, *J* = 1.7 Hz, 1H), 6.36 (d, *J* = 1.7 Hz, 1H), 5.48 (s, 1H), 4.51 (d, *J* = 12.6 Hz, 1H), 4.30 (t, *J* = 3.2 Hz, 1H), 4.13 (s, 1H), 4.00 (d, *J* = 12.6 Hz, 1H), 2.94 (dd, *J* = 17.1, 3.2 Hz, 1H), 2.77 (dd, *J* = 17.1, 3.2 Hz, 1H), 2.52 – 2.43 (m, 1H), 2.33 (ddd, *J* = 18.7, 6.4, 1.4 Hz, 1H), 2.24 – 2.16 (m, 1H), 2.15 – 2.05 (m, 2H), 1.68 (ddd, *J* = 18.7, 12.3, 6.4 Hz, 1H), 1.51 (ddd, *J* = 13.0, 6.4, 1.4 Hz, 1H), 1.39 – 1.30 (m, 1H), 1.26 (s, 3H), 1.15 (s, 3H), 1.13 (d, *J* = 6.9 Hz, 3H), 0.94 (s, 3H).
^{13}C NMR ($CDCl_3$, 125 MHz): δ 170.05, 167.31, 144.95, 143.27, 141.22, 128.94, 119.80, 109.90, 80.40, 76.29, 74.26, 67.29, 66.91, 55.47, 54.23, 48.57, 37.74, 36.01, 32.41, 30.43, 27.84, 26.81, 24.11, 23.31, 23.13, 13.28.
HRMS(ESI): m/z calc. for $C_{26}H_{31}O_7$ $[M+H]^+$: 455.2070, found: 455.2074.
mp: 116-118° C.
Opt. Rot.: $[\alpha]_D^{25}$ = + 58 (c = 0.16, acetone).





Crystallography

Experimental Protocol: Intensity data were collected on a Bruker D8 Venture kappa diffractometer equipped with a Photon 100 CMOS detector. An Iμs microfocus Mo source (λ = 0.71073 Å) coupled with a multi-layer mirror monochromator provided the incident beam. The sample was mounted on a 0.3 mm loop with the minimal amount of Paratone-N oil. Data was collected as a series of φ and/or ω scans. Data was collected at 100 K using a cold stream of N2(g). The collection, cell refinement, and integration of intensity data was carried out with the APEX3 software.[1] A semi-empirical absorption correction was performed with SADABS.[2] The structure was phased with intrinsic methods using SHELXT[3] and refined with the full-matrix least-squares program SHELXL.[4]

CCDC: 2082419

(1) Bruker (2016). APEX3. Bruker AXS, Inc., Madison, Wisconsin, USA.
(2) L. Krause, R. Herbst-Irmer, G. M. Sheldrick, D. Stalke, *J. Appl. Cryst.*, **2015,** *48*, 3–10.
(3) G. M. Sheldrick, *Acta Cryst.* **2015**, A71, 3–8.
(4) G. M. Sheldrick, *Acta Cryst*. **2015**, C71, 3–8.

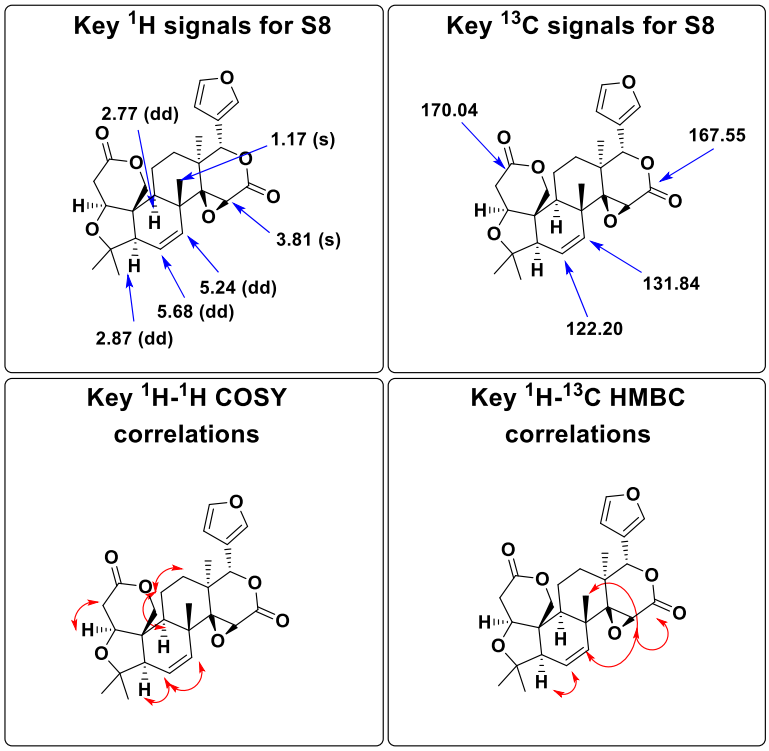
Table S6. Crystal data and structure refinement for ed93as.

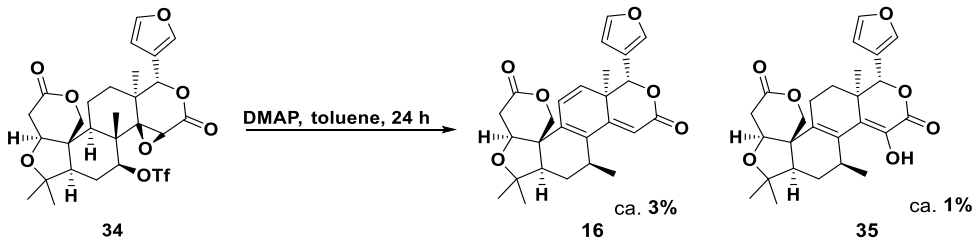
Identification code	ed93as
Empirical formula	C26.50 H30.50 Cl1.50 O6
Formula weight	498.18
Temperature	100(2) K
Wavelength	1.54178 Å
Crystal system	Orthorhombic
Space group	$P2_12_12_1$
Unit cell dimensions	a = 10.3124(5) Åa= 90°.
	b = 17.5945(8) Åb= 90°.
	c = 26.7645(12) Å g = 90°.
Volume	4856.2(4) Å3
Z	8
Density (calculated)	1.363 Mg/m3
Absorption coefficient	2.238 mm-1
F(000)	2104
Crystal size	0.396 x 0.235 x 0.048 mm3
Theta range for data collection	3.006 to 68.261°.
Index ranges	-11<=h<=12, -21<=k<=21, -31<=l<=32
Reflections collected	68728
Independent reflections	8905 [R(int) = 0.0386]
Completeness to theta = 67.679°	100.0 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.7531 and 0.6058
Refinement method	Full-matrix least-squares on F2
Data / restraints / parameters	8905 / 84 / 640
Goodness-of-fit on F2	1.065
Final R indices [I>2sigma(I)]	R1 = 0.0320, wR2 = 0.0869

R indices (all data) R1 = 0.0325, wR2 = 0.0874
Absolute structure parameter -0.003(3)
Extinction coefficient n/a
Largest diff. peak and hole 0.333 and -0.447 e.Å-3

S8 (41 mg, 13%)

^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.38 (d, *J* = 1.7 Hz, 1H), 7.35 (dd, *J* = 1.7, 1.7 Hz, 1H), 6.23 (d, *J* = 1.7 Hz, 1H), 5.68 (dd, *J* = 10.0, 2.4 Hz, 1H), 5.66 (s, 1H), 5.24 (dd, *J* = 10.0, 3.4 Hz, 1H), 4.37 (d, *J* = 12.7 Hz, 1H), 4.31 (d, *J* = 12.7 Hz, 1H). 4.05 (dd, *J* = 3.8, 2.2 Hz, 1H), 3.81 (s, 1H), 2.87 (dd, *J* = 16.6, 3.8 Hz, 1H), 2.77 (dd, *J* = 3.4, 2.4 Hz, 1H), 2.70 (dd, *J* = 13.1, 6.2 Hz, 1H), 2.52 (dd, *J* = 16.6, 2.2 Hz, 1H), 1.95 – 1.87 (m, 1H), 1.78 – 1.72 (m, 1H), 1.69 – 1.65 (m, 1H), 1.52 – 1.43 (m, 1H), 1.27 (s, 3H), 1.20 (s, 3H), 1.17 (s, 3H), 1.14 (s, 3H).
^{13}C NMR ($CDCl_3$, 125 MHz): δ 170.04, 167.55, 143.27, 141.24, 131.84, 122.20, 120.22, 109.53, 80.69, 78.43, 77.23, 73.06, 65.82, 60.59, 58.58, 46.54, 45.14, 41.74, 39.43, 35.66, 31.47, 25.43, 22.23, 21.86, 21.14, 17.60.
HRMS(ESI): m/z calc. for $C_{26}H_{31}O_7$ $[M+H]^+$: 455.2070, found: 455.2074.
Opt. Rot.: $[\alpha]_D^{25}$ = - 84 (c = 0.16, acetone).



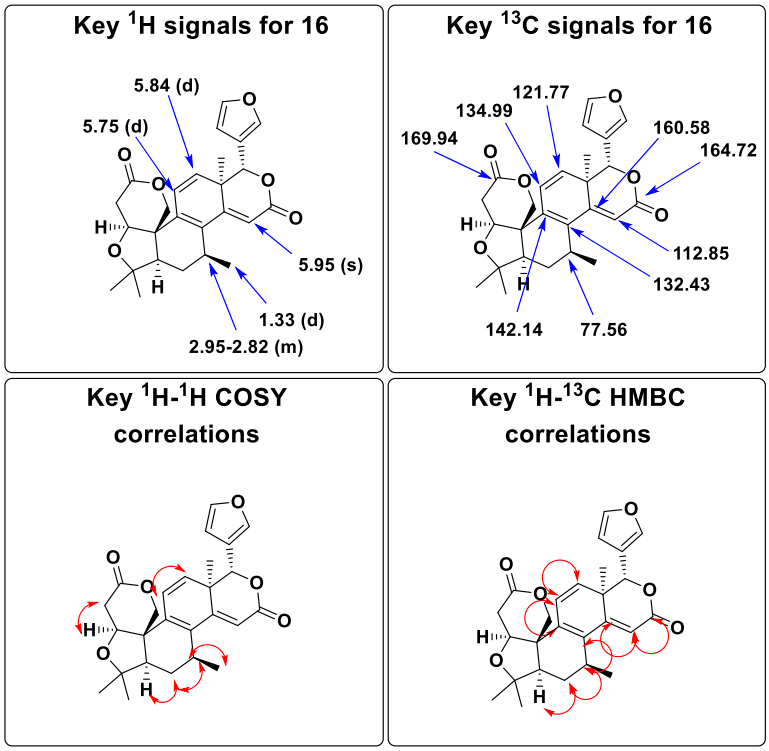


Procedure: DMAP (171 mg, 1.40 mmol) was added to a solution of **34** (340 mg, 0.56 mmol) in toluene (4 mL) and the resulting mixture was heated at 80° C for 24 h. Toluene was evaporated and the residue partitioned between water and dichloromethane. The aqueous layer was extracted three times with dichloromethane. The organic layers were combined, washed with brine, dried over Na_2SO_4, and concentrated by distillation under reduced pressure. The crude residue was purified by silica gel flash chromatography (hexane-ethyl acetate 4:6) to provide **16** (8 mg, ca. 3%) and **35** (3 mg, ca. 1%) as white solids.

Note: Formation of **15** (25 mg, 10%) was observed.

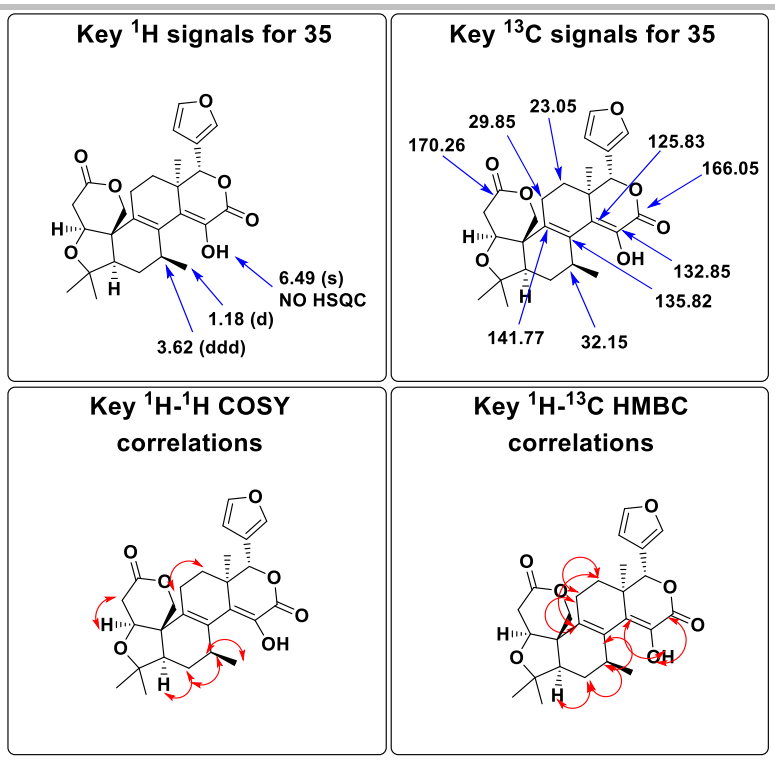
16 (8 mg, ca. 3%)

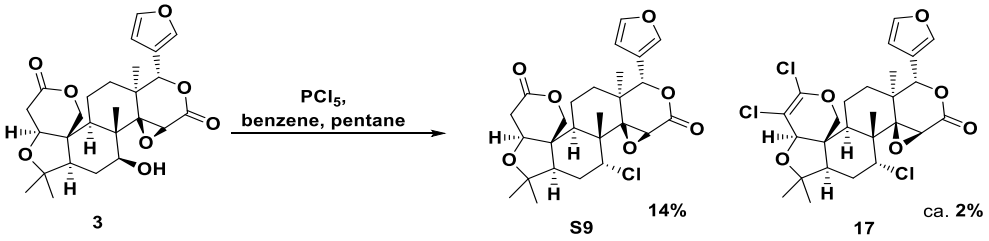
^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.49 (d, *J* = 1.8 Hz, 1H), 7.42 (dd, *J* = 1.8, 1.8 Hz, 1H), 6.43 (dd, *J* = 1.8 Hz, 1H), 5.95 (s, 1H), 5.84 (d, *J* = 9.7 Hz, 1H), 5.75 (d, *J* = 9.7 Hz, 1H), 5.30 (s, 1H), 4.60 (d, *J* = 12.2 Hz, 1H), 4.19 (t, *J* = 3.5 Hz, 1H), 4.07 (d, *J* = 12.2 Hz, 1H), 2.95 – 2.82 (m, 3H), 2.21 (ddd, *J* = 13.4, 9.9, 4.7 Hz, 1H), 2.08 (dd, *J* = 14.9, 4.7 Hz, 1H), 1.40 (ddd, *J* = 14.9, 13.4, 6.2 Hz, 1H), 1.33 (d, *J* = 7.1 Hz, 3H), 1.21 (s, 3H), 1.14 (s, 3H), 1.10 (s, 3H).
^{13}C NMR ($CDCl_3$, 125 MHz): δ 169.94, 164.72, 160.58, 143.49, 142.14, 141.76, 134.99, 132.43, 121.77, 119.47, 112.85, 110.02, 80.38, 77.56, 74.66, 67.38, 54.73, 48.63, 41.75, 36.23, 30.41, 30.21, 27.03, 26.09, 23.60, 22.63.
HRMS(ESI): m/z calc. for $C_{26}H_{29}O_6$ $[M+H]^+$: 437.1964, found: 437.1975.
Opt. Rot.: $[\alpha]_D^{25}$ = + 45 (c = 0.06, acetone).



35 (ca. 3 mg, 1%)

^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.42 (d, *J* = 1.7 Hz, 1H), 7.37 (dd, *J* = 1.7, 1.7 Hz, 1H), 6.49 (s, 1H), 6.35 (d, *J* = 1.7 Hz, 1H), 5.10 (s, 1H), 4.54 (d, *J* = 12.8 Hz, 1H), 4.22 (t, *J* = 3.0 Hz, 1H), 3.95 (d, *J* = 12.8 Hz, 1H), 3.62 (ddd, *J* = 8.0, 6.9, 5.5 Hz, 1H), 2.89 (d, *J* = 17.0, 3.0 Hz, 1H), 2.72 (dd, *J* = 17.0, 3.0 Hz, 1H), 2.22 – 2.11 (m, 3H), 2.03 (ddd, *J* = 13.8, 9.8, 4.2 Hz, 1H), 1.38 – 1.29 (m, 2H), 1.25 – 1.21 (m, 1H), 1.19 (s, 3H), 1.18 (d, *J* = 6.9 Hz, 3H), 1.10 (s, 3H), 0.98 (s, 3H).
^{13}C NMR ($CDCl_3$, 125 MHz): δ 170.26, 166.05, 143.26, 141.77, 141.51, 135.82, 132.85, 125.83, 119.60, 109.91, 80.79, 80.48, 74.99, 67.04, 55.13, 49.11, 38.07, 36.35, 32.15, 30.41, 29.85, 26.61, 26.55, 23.05, 22.91, 17.61.
HRMS(ESI): m/z calc. for $C_{26}H_{31}O_7$ $[M+H]^+$: 455.2070, found: 455.2076.

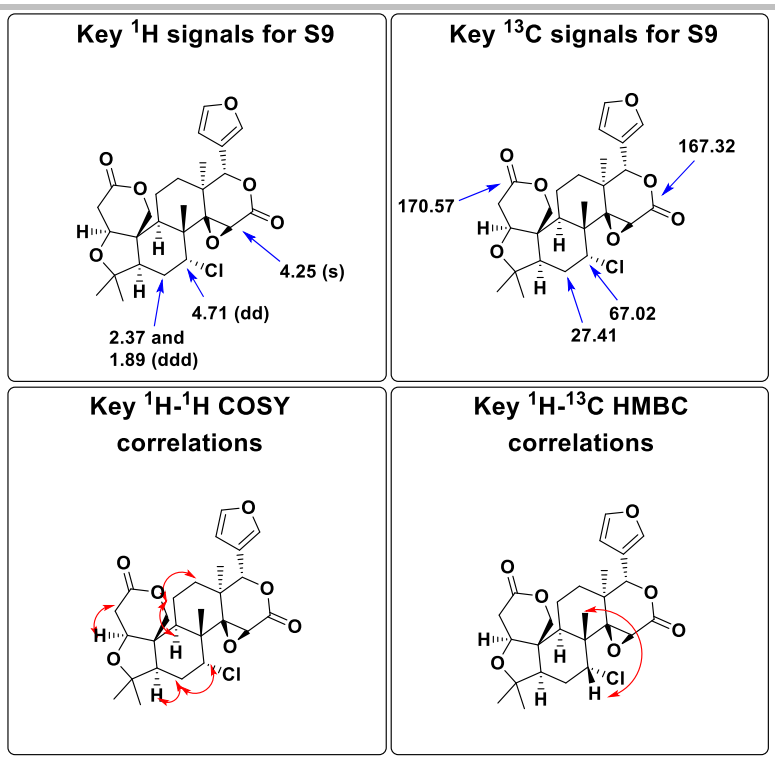




***Procedure*:** PCl_5 (704 mg, 3.36 mmol) was added to a solution of **3** (800 mg, 1.68 mmol) in dry benzene (24 mL) and pentene (24 mL) and the resulting solution was stirred at 30° C for 4 h. Water was added and the aqueous layer was extracted three times with dichloromethane. The organic layers were combined, washed with brine, dried over Na_2SO_4, and concentrated by distillation under reduced pressure. The crude residue was purified by silica gel flash chromatography (hexane-ethyl acetate 1:1) to provide **S9** (120 mg, 14%) and **17** (25 mg, ca. 2%) as white solids.

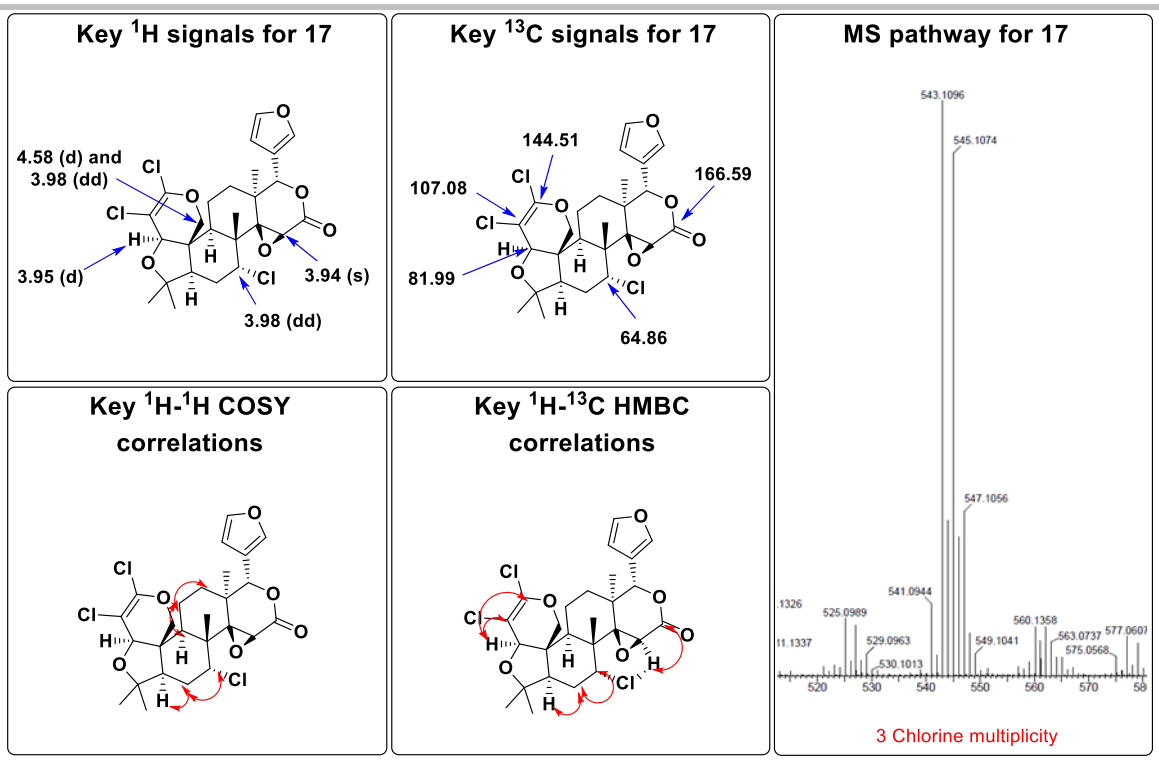
S9 (120 mg, 14%)

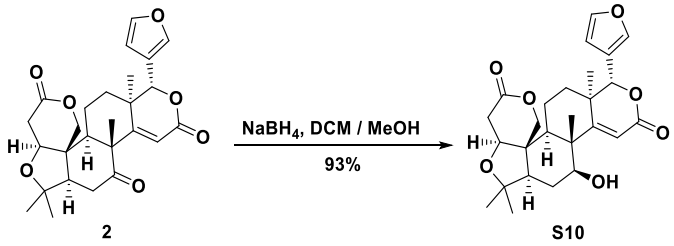
^{1}H NMR (DMSO-d6, 500 MHz): δ 7.75 (d, *J* = 1.7 Hz, 1H), 7.73 (dd, *J* = 1.7, 1.7 Hz, 1H), 6.54 (d, *J* = 1.7 Hz, 1H), 5.60 (s, 1H), 4.69 (d, *J* = 13.1 Hz, 1H), 4.53 (d, *J* = 13.1 Hz, 1H), 4.51 (dd, *J* = 2.8, 2.8 Hz, 1H), 4.25 (s, 1H), 4.18 (d, *J* = 3.7 Hz, 1H), 2.73 – 2.68 (m, 2H), 2.64 (dd, *J* = 16.5, 3.9 Hz, 1H), 2.58 (dd, *J* = 2.5, 13.4 Hz, 1H), 2.37 (ddd, *J* = 14.9, 13.4, 2.8 Hz, 1H), 2.13 – 2.06 (m, 1H), 1.89 (ddd, *J* = 14.9, 2.8, 2.5 Hz, 1H), 1.78 (ddd, *J* = 14.1, 6.7, 2.8 Hz, 1H), 1.71 – 1.63 (m, 1H), 1.35 – 1.29 (m, 1H), 1.25 (s, 3H), 1.25 (s, 3H), 1.07 (s, 3H), 0.99 (s, 3H).
^{13}C NMR (DMSO-d6, 125 MHz): δ 170.57, 167.32, 143.84, 142.29, 120.87, 110.78, 80.15, 79.72, 78.38, 69.89, 67.02, 66.05, 57.81, 53.13, 45.83, 45.63, 41.90, 38.31, 36.09, 30.57, 27.41, 25.60, 22.00, 19.82, 17.42, 16.56.
HRMS(ESI): m/z calc. for $C_{26}H_{32}O_7Cl$ $[M+H]^+$: 491.1837, found: 491.1840.
mp: 181-182° C.
Opt. Rot.: $[\alpha]_D^{25}$ = - 85 (c = 0.12, acetone).



17 (25 mg, ca. 2%)

^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.38 (br s, 2H), 6.31 (s, 1H), 5.56 (s, 1H), 4.65 (dd, *J* = 11.6, 1.7 Hz, 1H), 4.58 (d, *J* = 11.6 Hz, 1H), 3.98 (dd, *J* = 2.9, 2.9 Hz, 1H), 3.94 (s, 1H), 3.93 (d, 1.7 Hz, 1H), 2.78 (dd, *J* = 13.4, 2.8 Hz, 1H), 2.68 (dd, *J* = 13.7, 6.1 Hz, 1H), 2.32- 2.24 (m, 1H), 2.03 (ddd, *J* = 14.0, 13.4, 2.9 Hz, 1H), 1.94 (ddd, *J* = 14.0, 2.9, 2.8 Hz, 1H), 1.90 – 1.81 (m, 1H), 1.63 – 1.45 (m, 2H), 1.34 (s, 3H), 1.32 (s, 3H), 1.29 (s, 3H), 1.20 (s, 3H).
^{13}C NMR ($CDCl_3$, 125 MHz): δ 166.59, 144.51, 143.03, 141.18, 120.34, 109.92, 107.08, 81.99, 79.59, 78.65, 70.55, 69.53, 64.86, 58.28, 52.53, 48.07, 46.45, 40.89, 38.32, 30.50, 27.84, 25.86, 25.27, 20.15, 18.34, 16.04.
HRMS(ESI): m/z calc. for $C_{26}H_{30}O_6Cl_3$ $[M+H]^+$: 543.1108, found: 543.1096.
mp: decomposes upon heating above 160° C.
Opt. Rot.: $[\alpha]_D^{25}$ = - 93 (c = 0.05, acetone/chloroform).

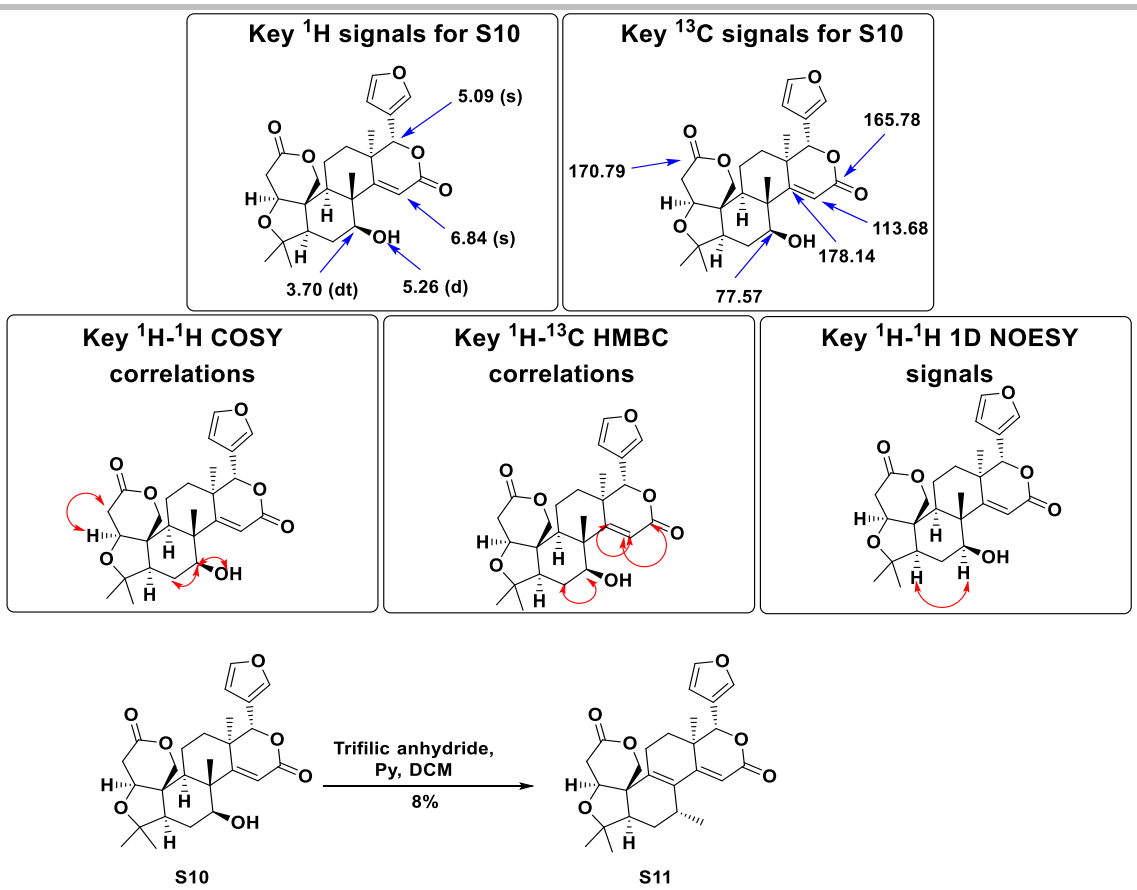




2 S10

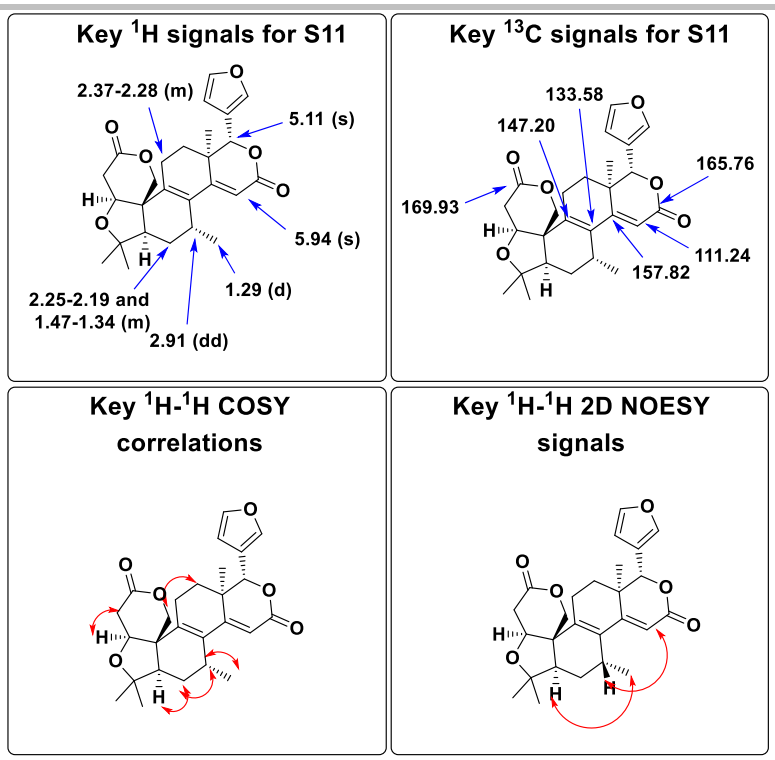
Procedure: $NaBH_4$ (95 mg, 2.5 mmol) in anhydrous methanol (6 mL) was added to a solution of **2** (200 mg, 0.44 mmol) in dichloromethane (8 mL) at -78° C and the resulting mixture was stirred at -78 °C. After 15 minutes, the reaction was quenched by addition of 2 M hydrochloric acid solution and extracted three times with dichloromethane. The organic layers were dried over Na_2SO_4 and concentrated by distillation under reduced pressure to obtained a crude residue that was purified by silica gel flash chromatography (hexane-ethyl acetate 3:7) to provide **S10** (186 mg, 93%) as a white solid.

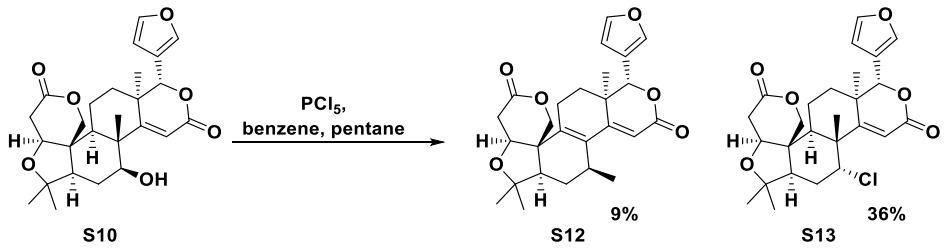
^{1}H NMR (DMSO-d6, 500 MHz): δ 7.73 (d, *J* = 1.7 Hz, 1H), 7.69 (dd, *J* = 1.7, 1.7 Hz, 1H), 6.84 (s, 1H), 6.53 (d, *J* = 1.7 Hz, 1H), 5.26 (d, *J* = 5.1 Hz, 1H), 5.09 (s, 1H), 4.52 (d, *J* = 13.2 Hz, 1H), 4.44 (d, *J* = 13.2 Hz, 1H), 4.01 (d, *J* = 3.8 Hz, 1H), 3.70 (dt, *J* = 10.4, 5.1 Hz, 1H), 2.62 (dd, *J* = 16.5, 1.6 Hz, 1H), 2.56 (dd, *J* = 16.4, 3.8 Hz, 1H), 2.11 – 2.01 (m, 2H), 1.95 (dd, *J* = 13.5, 2.5 Hz, 1H), 1.74 (ddd, *J* = 12.9, 5.3, 2.4 Hz, 1H), 1.69 – 1.54 (m, 3H), 1.19 – 1.16 (m, 1H), 1.17 (s, 3H), 1.14 (s, 3H), 1.04 (s, 3H), 0.98 (s, 3H).
^{13}C NMR (DMSO-d6, 125 MHz): δ 178.14, 170.79, 165.78, 143.74, 142.18, 120.78, 113.68, 110.77, 81.45, 80.20, 78.86, 77.57, 65.41, 56.47, 45.70, 44.78, 42.57, 38.03, 36.08, 30.83, 29.02, 25.30, 22.07, 19.82, 19.60, 17.05.
HRMS(ESI): m/z calc. for $C_{26}H_{33}O_7$ $[M+H]^+$: 457.2226, found: 457.2227.
mp: >260° C.
Opt. Rot.: $[\alpha]_D^{25}$ = + 45 (c = 0.25, acetone).



Procedure: Triflic anhydride (260 µL, 1.5 mmol) was added at 0° C to a solution of **S10** (354 mg, 0.77 mmol) in dichloromethane (4 mL) and pyridine (246 µL) and the resulting mixture was stirred at 30° C for 12 h. The reaction was quenched with iced water and extracted three times with dichloromethane. The organic layers were combined, washed with brine, dried over Na_2SO_4, and concentrated by distillation under reduced pressure. The crude residue was purified by silica gel flash chromatography (hexane-ethyl acetate 4:6) to provide **S11** (28 mg, 8%) as a white solid.

^{1}H NMR* (CDCl$_3$, *500 MHz): δ 7.48 (d, *J* = 1.8 Hz, 1H), 7.44 (dd, *J* = 1.8, 1.8 Hz, 1H), 6.42 (d, *J* = 1.8 Hz, 1H), 5.94 (s, 1H), 5.11 (s, 1H), 4.59 (d, *J* = 12.6 Hz, 1H), 4.31 (t, *J* = 3.2 Hz, 1H), 4.03 (d, *J* = 12.6 Hz, 1H), 2.98 (dd, *J* = 17.1, 3.2 Hz, 1H), 2.91 (dd, *J* = 7.6, 7.0 Hz, 1H), 2.81 (dd, *J* = 17.2, 3.2 Hz, 1H), 2.37 – 2.28 (m, 2H), 2.25 – 2.19 (m, 1H), 2.19 – 2.12 (m, 1H), 1.54 – 1.48 (m, 1H), 1.47 – 1.34 (m, 2H), 1.29 (d, *J* = 7.6 Hz, 3H), 1.27 (s, 3H), 1.18 (s, 3H), 1.02 (s, 3H).
^{13}C NMR* (CDCl$_3$, *125 MHz): δ 169.93, 165.76, 157.82, 147.20, 143.16, 141.27, 133.58, 119.84, 111.24, 109.94, 80.38, 80.25, 74.22, 66.65, 54.75, 49.27, 37.16, 36.15, 30.40 (2C), 28.96, 26.74, 25.44, 23.32, 23.20, 16.46.
***HRMS(ESI)*:** m/z calc. for $C_{26}H_{31}O_6$ $[M+H]^+$: 439.2121, found: 439.2123.
Opt. Rot.: $[\alpha]_D^{25}$ = - 15 (c = 0.03, acetone/chloroform).

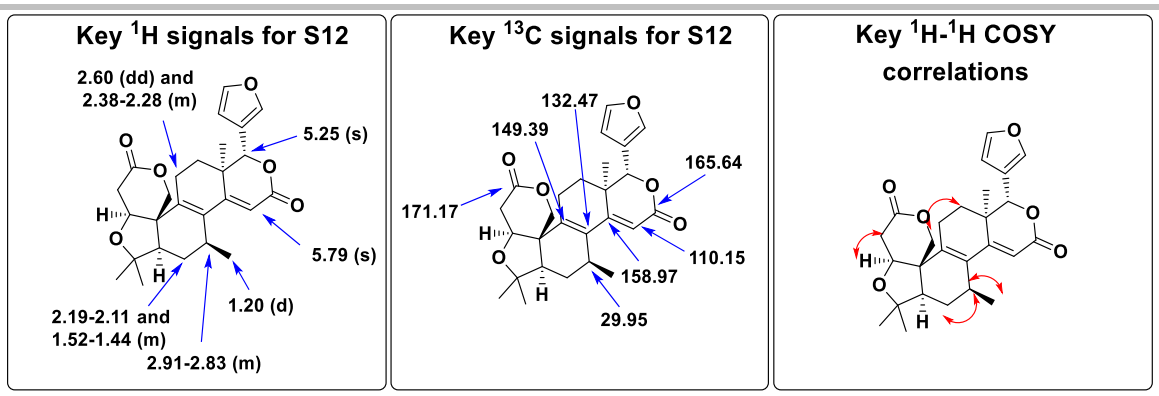




Procedure: PCl_5 (200 mg, 0.96 mmol) was added to a solution of **S10** (220 mg, 0.48 mmol) in dry benzene (8 mL) and pentene (8 mL) and the resulting solution was stirred at 30° C for 24 h. Water was added and the aqueous layer was extracted three times with dichloromethane. The organic layers were combined, washed with brine, dried over Na_2SO_4, and concentrated by distillation under reduced pressure. The crude residue was purified by silica gel flash chromatography (hexane-ethyl acetate 4:6) to provide **S12** (20 mg, 9%) and **S13** (84 mg, 36%) as white solids.

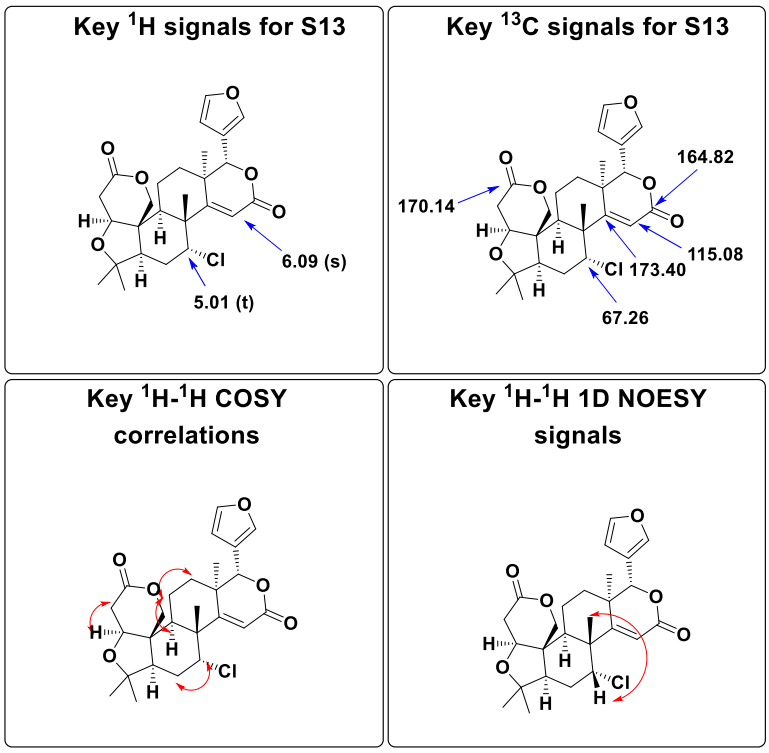
S12 (20 mg, 9%)

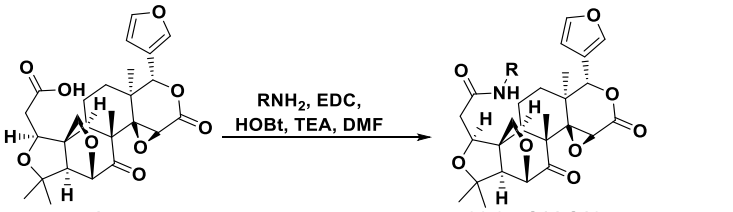
^{1}H NMR (DMSO-d6, 500 MHz): δ 7.76 (d, *J* = 1.8 Hz, 1H), 7.72 (dd, *J* = 1.8, 1.8 Hz, 1H), 6.57 (d, *J* = 1.8 Hz, 1H), 5.79 (s, 1H), 5.25 (s, 1H), 4.41 (d, *J* = 3.4 Hz, 1H), 4.41 (d, *J* = 13.1 Hz, 1H), 4.14 (d, *J* = 13.1 Hz, 1H), 3.04 (dd, *J* = 16.2, 1.6 Hz, 1H), 2.91 – 2.83 (m, 1H), 2.67 (dd, *J* = 16.2, 3.4 Hz, 1H), 2.60 (dd, *J* = 18.0, 5.0 Hz, 1H), 2.38 – 2.28 (m, 1H), 2.19 – 2.11 (m, 2H), 1.52 – 1.44 (m, 1H), 1.35 – 1.28 (m, 1H), 1.27 - 1.21 (m, 1H), 1.20 (d, *J* = 7.0 Hz, 3H), 1.18 (s, 3H), 1.03 (s, 3H), 0.97 (s, 3H).
^{13}C NMR (DMSO-d6, 125 MHz): δ 171.17, 165.64, 158.97, 149.39, 143.90, 142.27, 132.47, 120.55, 110.70, 110.15, 79.89, 79.65, 74.64, 64.64, 53.91, 49.50, 37.03, 36.91, 30.64, 29.95, 29.01, 26.31, 25.68, 23.04, 21.91, 16.84.
HRMS(ESI): m/z calc. for $C_{26}H_{31}O_6$ $[M+H]^+$: 439.2121, found: 439.2123.
Opt. Rot.: $[\alpha]_D^{25}$ = + 43 (c = 0.05, acetone/chloroform).



S13 (84 mg, 36%)

[1]H NMR (DMSO-d6, 500 MHz): *δ* 7.72 (d, *J* = 1.8 Hz, 1H), 7.70 (dd, *J* = 1.8, 1.8 Hz, 1H), 6.53 (d, *J* = 1.8 Hz, 1H), 6.08 (s, 1H), 5.75 (s, 1H), 5.09 (s, 1H), 5.01 (t, *J* = 2.8 Hz, 1H), 4.64 (d, *J* = 13.2 Hz, 1H), 4.51 (d, *J* = 13.2 Hz, 1H), 4.13 (d, *J* = 2.6 Hz, 1H), 2.65 – 2.56 (m, 2H), 2.48 – 2.38 (m, 2H), 2.07 – 1.97 (m, 1H), 1.91 (dt, *J* = 14.4, 2.4 Hz, 1H), 1.78 – 1.66 (m, 1H), 1.53 (dt, *J* = 14.4, 9.9 Hz, 1H), 1.28 – 1.23 (m, 1H), 1.20 (s, 3H), 1.19 (s, 3H), 1.08 (s, 3H), 1.03 (s, 3H).
[13]C NMR (DMSO-d6, 125 MHz): *δ* 173.40, 170.14, 164.82, 143.33, 141.71, 120.17, 115.08, 110.33, 80.92, 79.65, 78.76, 67.26, 65.36, 52.18, 46.72, 45.64, 38.73, 37.27, 35.54, 30.16, 26.77, 26.39, 25.10, 21.59, 16.85, 15.64.
HRMS(ESI): m/z calc. for $C_{26}H_{32}O_6Cl$ $[M+H]^+$: 475.1887, found: 475.1889.
mp: >260° C.
Opt. Rot.: $[\alpha]_D^{25}$ = - 7 (c = 0.14, acetone).





4

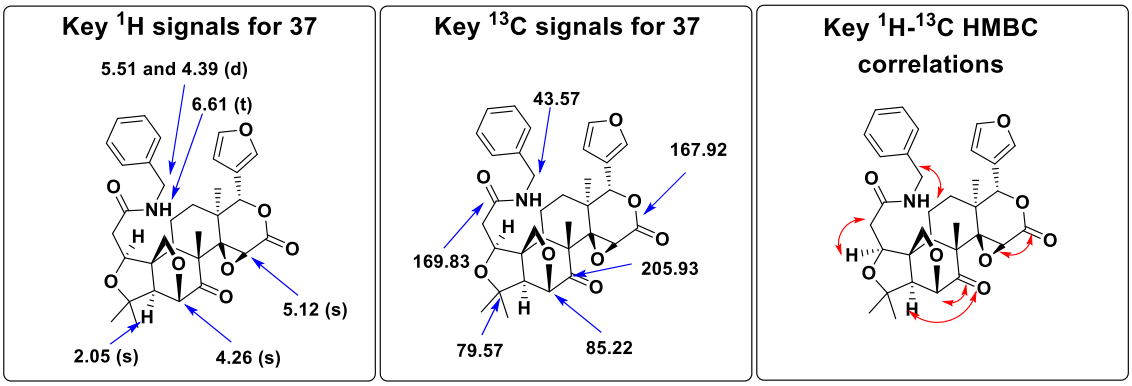
36-37, S14-S16

36; R = CH_2Ph 75%
37; R = CH_2CCH 77%
S14; R = CH_3 78%
S15; R = CH_2CH_2NHBoc 53%
S16; R = CH_2CHCH_2 59%

Procedure: HOBt (75 mg, 0.49 mmol), EDC (95 µL, 0.53 mmol) and TEA (124 µL, 0.89 mmol) were added to a solution of **4** (215 mg, 0.445 mmol) in DMF (1.5 mL), and the resulting mixture was stirred 30 minutes at 30° C. Then, the suitable amine (0.49 mmol) was added to the mixture and the reaction was stirred overnight. The reaction was diluted with dichloromethane and washed with water, 5% citric acid, brine, 5% $NaHCO_3$, and Brine. The organic layer was dried over Na_2SO_4, concentrated by distillation at reduced pressure, and the residue was purified by flash chromatography on silica gel (hexane-ethyl acetate 7:3), giving **36-37,S14-S16** (53-78%) as white solids.

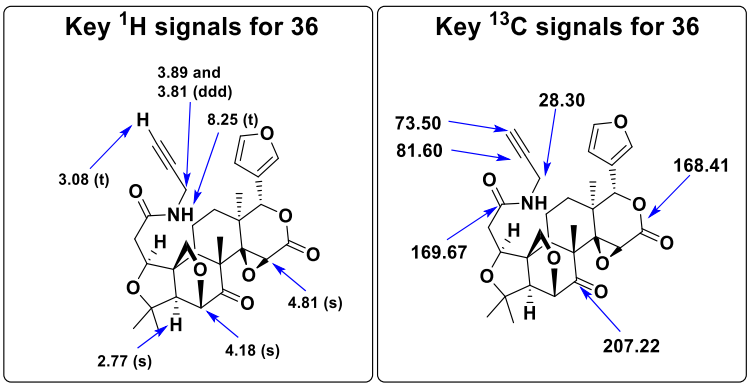
36 (196 mg, 75%)

^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.42 (d, *J* = 1.7 Hz, 1H), 7.41 (dd, *J* = 1.7, 1.7 Hz, 1H), 7.34 - 7.31 (m, 2H), 7.28 - 7.23 (m, 3H), 6.61 (t, *J* = 5.8 Hz, 1H), 6.29 (d, *J* = 1.7 Hz, 1H), 5.73 (s, 1H), 5.12 (s, 1H), 4.51 (dd, *J* = 15.0, 5.8 Hz, 1H), 4.39 (dd, J= 15.0, 5.8 Hz, 1H), 4.26 (s, 1H), 4.22 (dd, *J* = 10.1, 1.7 Hz, 1H), 4.08 (d, *J* = 9.0 Hz 1H), 3.86 (d, *J* = 9.0 Hz, 1H), 2.71 (t, H = 9.5 Hz, 1H), 2.54 (dd, *J* = 14.9, 1.7 Hz, 1H), 2.29 (dd, *J* = 14.9, 10.1 Hz, 1H), 2.05 (s, 1 H), 1.94 - 1.88, (m, 2H), 1.80 - 1.73 (m, 1H), 1.66 (s, 3H), 1.51 - 1.46 (m, 1H), 1.32 (s, 3H), 1.28 (s, 3H), 1.26 (s, 3H).
^{13}C NMR ($CDCl_3$, 125 MHz): δ 205.93, 169.84, 167.92, 143.25, 141.36, 138.09, 128.68 (2C), 127.50, 127.47 (2C), 120.31, 109.63, 85.22, 79.57, 77.80, 77.24, 71.31, 66.78, 66.07, 58.35, 57.04, 47.71, 43.57, 42.92, 40.90, 40.07, 30.65, 25.58, 24.92, 20.81, 19.09, 18.48.
HRMS(ESI): m/z calc. for $C_{33}H_{38}NO_8$ $[M+H]^+$: 576.2597, found: 576.2593.
mp: 111-113° C.
Opt. Rot.: $[\alpha]_D^{25}$ = - 11 (c = 0.18, acetone).



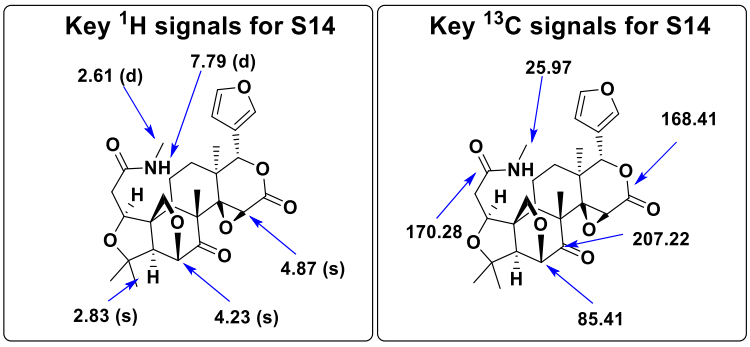
37 (179 mg, 77%)

^{1}H NMR (DMSO-*d6*, 500 MHz): δ 8.25 (t, *J* = 5.5 Hz, 1H), 7.71 (d, *J* = 1.7 Hz, 1H), 7.68 (dd, *J* = 1.7, 1.7 Hz, 1H), 6.51 (d, *J* = 1.7 Hz, 1H), 5.70 (s, 1H), 4.81 (s, 1H), 4.26 (dd, *J* = 9.5, 2.2 Hz, 1H), 4.18 (s, 1H), 4.10 (d, *J* = 9.0 Hz, 1H), 3.89 (ddd, *J* = 17.5, 5.5, 2.5 Hz, 1H), 3.81 (ddd, *J* = 17.5, 5.5, 2.5 Hz, 1H), 3.69 (d, *J* = 9.0 Hz, 1H), 3.08 (t, *J* = 2.5 Hz, 1H), 2.82 (dd, *J* = 12.5, 6.0 Hz, 1H), 2.77 (s, 1H), 2.32 (dd, *J* = 14.7, 2.2 Hz, 1H), 2.11 (dd, *J* = 14.7, 9.5 Hz, 1H), 1.90 – 1.68 (m, 3H), 1.54 (s, 3H), 1.28 (s, 3H), 1.21 (s, 3H), 1.19 – 1.15 (m, 1H), 1.18 (s, 3H).
^{13}C NMR (DMSO-*d6*, 125 MHz): δ 207.22, 169.67, 168.41, 143.87, 142.28, 121.00, 110.67, 85.41, 81.60, 78.65, 78.01, 76.76, 73.50, 71.91, 66.46, 63.90, 57.92, 57.38, 47.35, 41.22, 40.08, 38.83, 30.62, 28.30, 25.75, 25.52, 20.33, 19.88, 17.72.
HRMS(ESI): m/z calc. for $C_{29}H_{34}NO_8$ $[M+H]^+$: 524.2284, found: 524.2276.
mp: 138-139° C.
Opt. Rot.: $[\alpha]_D^{25}$ = - 70 (c = 0.17, acetone).



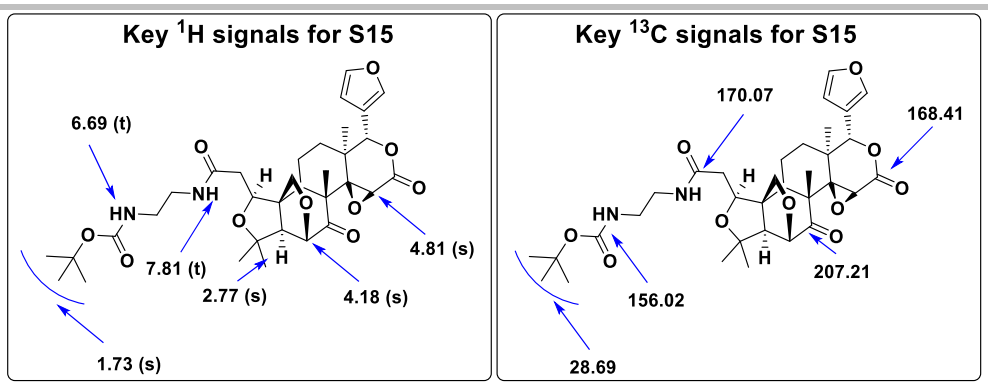
S14 (177 mg, 78%)

^{1}H NMR (DMSO-*d6,* 500 MHz): δ 7.79 (d, *J* = 4.7 Hz, 1H), 7.77 (d, *J* = 1.7 Hz, 1H), 7.73 (dd, *J* = 1.7, 1.7 Hz, 1H), 6.57 (d, *J* = 1.7 Hz, 1H), 5.76 (s, 1H), 4.87 (s, 1H), 4.32 (dd, *J* = 9.7, 2.2 Hz, 1H), 4.23 (s, 1H), 4.16 (d, *J* = 9.0 Hz, 1H), 3.74 (d, *J* = 9.0 Hz, 1H), 2.88 (dd, *J* = 12.6, 6.1 Hz, 1H), 2.83 (s, 1H), 2.61 (d, *J* = 4.7 Hz, 3H), 2.34 (dd, *J* = 14.6, 2.2 Hz, 1H), 2.11 (dd, *J* = 14.6, 9.7 Hz, 1H), 1.97 – 1.75 (m, 3H), 1.59 (s, 3H), 1.34 (s, 3H), 1.27 (s, 3H), 1.25 – 1.20 (m, 1H), 1.23 (s, 3H).
^{13}C NMR (DMSO-*d6,* 125 MHz): δ 207.22, 170.28, 168.41, 143.87, 142.29, 121.00, 110.67, 85.41, 78.61, 78.00, 76.92, 71.89, 66.46, 65.82, 63.93, 57.89, 57.38, 47.35, 41.27, 39.09, 30.65, 25.97, 25.77, 25.54, 20.33, 19.88, 17.73.
HRMS(ESI): m/z calc. for $C_{27}H_{34}NO_8$ $[M+H]^+$: 500.2284, found: 500.2282.
mp: 151-152° C.
Opt. Rot.: $[\alpha]_D^{25}$ = - 88 (c = 0.13, acetone).



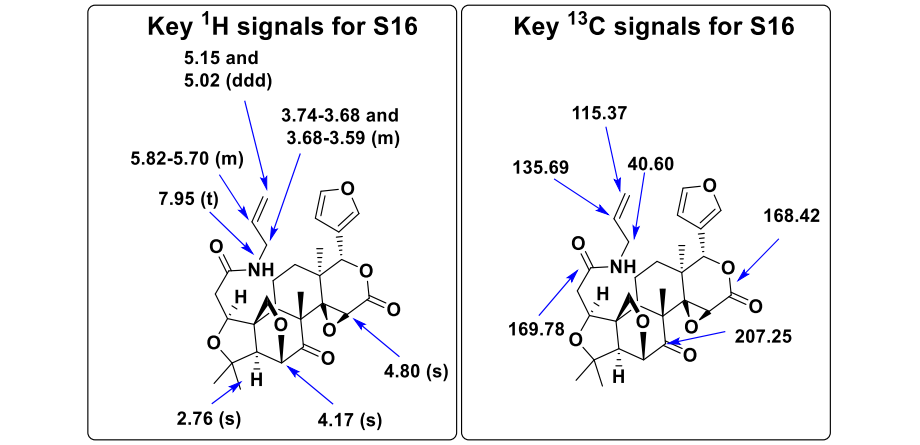
S15 (149 mg, 53%)

^{1}H NMR (DMSO-*d6,* 500 MHz): δ 7.81 (t, *J* = 5.5 Hz, 1H), 7.72 (s, 1H), 7.68 (s, 1H), 6.69 (t, *J* = 5.5 Hz, 1H), 6.51 (s, 1H), 5.71 (s, 1H), 4.81 (s, 1H), 4.26 (d, *J* = 10.1 Hz, 1H), 4.18 (s, 1H), 4.10 (d, *J* = 8.8 Hz, 1H), 3.70 (d, *J* = 8.8 Hz, 1H), 3.09 (p, *J* = 6.2 Hz, 1H), 3.06 – 2.99 (m, 1H), 2.99 – 2.94 (m, 2H), 2.85 -2.79 (m, 1H), 2.77 (br s, 1H), 2.31 (d, *J* = 14.7 Hz, 1H), 2.07 (dd, *J* = 14.7, 10.1 Hz, 1H), 1.87 – 1.79 (m, 2H), 1.77 – 1.70 (m, 1H), 1.54 (s, 3H), 1.37 (s, 9H), 1.29 (s, 3H), 1.22 (s, 3H), 1.20 – 1.58 (m, 1H), 1.18 (s, 3H).
^{13}C NMR (DMSO-*d6,* 125 MHz): δ 207.21, 170.07, 168.41, 156.02, 143.87, 142.29, 120.99, 110.66, 85.42, 78.61, 78.17, 78.00, 76.79, 71.90, 66.46, 63.91, 60.23, 57.93, 57.38, 55.39, 47.35, 41.24, 40.59, 39.17, 30.60, 28.69 (3C), 25.74, 25.51, 20.34, 19.89, 17.75.
HRMS(ESI): m/z calc. for $C_{33}H_{45}N_2O_{10}$ $[M+H]^+$: 629.3074, found: 629.3073.
mp: 139-140° C.
Opt. Rot.: $[\alpha]_D^{25}$ = - 74 (c = 0.21, acetone).



S16 (138 mg, 59%)

^{1}H NMR (DMSO-*d6*, 500 MHz): δ 7.95 (t, *J* = 5.8 Hz, 1H), 7.70 (d, *J* = 1.7 Hz, 1H), 7.67 (dd, *J* = 1.7, 1.7 Hz, 1H), 6.50 (d, *J* = 1.7 Hz, 1H), 5.82 – 5.70 (m, 1H), 5.69 (s, 1H), 5.15 (ddd, *J* = 17.2, 3.5, 1.8 Hz, 1H), 5.02 (ddd, *J* = 10.3, 3.5, 1.7 Hz, 1H), 4.80 (s, 1H), 4.26 (dd, *J* = 9.8, 2.2 Hz, 1H), 4.17 (s, 1H), 4.09 (d, *J* = 8.9 Hz, 1H), 3.74 – 3.68 (m, 1H), 3.70 (d, *J* = 8.9 Hz, 1H), 3.68 – 3.59 (m, 1H), 2.81 (dd, *J* = 12.5, 5.9 Hz, 1H), 2.76 (s, 1H), 2.33 (dd, *J* = 14.5, 2.2 Hz, 1H), 2.12 (dd, *J* = 14.5, 9.8 Hz, 1H), 1.89 – 1.69 (m, 3H), 1.53 (s, 3H), 1.27 (s, 3H), 1.21 (s, 3H), 1.18 – 1.15 (m, 1H), 1.17 (s, 3H).
^{13}C NMR (DMSO-*d6*, 125 MHz): δ 207.25, 169.78, 168.42, 143.87, 142.28, 135.69, 121.00, 115.37, 110.66, 85.42, 78.57, 78.01, 76.93, 71.92, 66.48, 63.93, 57.95, 57.38, 47.36, 41.23, 40.60, 40.56, 39.16, 30.62, 25.75, 25.53, 20.33, 19.88, 17.74.
HRMS(ESI): m/z calc. for $C_{29}H_{36}NO_8$ $[M+H]^+$: 526.2441, found: 526.2453.
mp: 135-136° C.
Opt. Rot.: $[\alpha]_D^{25}$ = - 86 (c = 0.15, acetone).



Procedure: Hydrochloric acid 4M in dioxane (1.5 mL) was added to a solution of **S15** (126 mg, 0.19 mmol) in dioxane (1.5 mL) and the resulting solution was stirred at 30° C for 2 h. The solvent was evaporated and the residue triturated 3 times with hexane and diethyl ether to get a white solid that was further purified by biotage (water-acetonitrile gradient with 1% formic acid) to provide **S17** (27 mg, 27%) as a white solid.

Note: S17 was obtained as a formic acid salt

^{1}H NMR (DMSO-*d6*, 500 MHz): δ 8.28 (s, 1H), 7.94 (t, *J* = 5.6 Hz, 1H), 7.64 (d, *J* = 1.7 Hz, 1H), 7.61 (dd, *J* = 1.7, 1.8 Hz, 1H), 7.30 (s, 1H), 6.44 (d, *J* = 1.8 Hz, 1H), 5.63 (s, 1H), 4.74 (s, 1H), 4.19 (dd, *J* = 9.6, 2.3 Hz, 1H), 4.11 (s, 1H), 4.03 (d, *J* = 8.9 Hz, 1H), 3.63 (d, *J* = 8.9 Hz, 1H), 3.10 (ddd, *J* = 12.3, 6.4, 6.4 Hz, 1H), 3.03 (ddd, *J* = 12.3, 6.4, 6.4 Hz, 1H), 2.75 (dd, *J* = 12.5, 6.0 Hz, 1H), 2.70 (s, 1H),

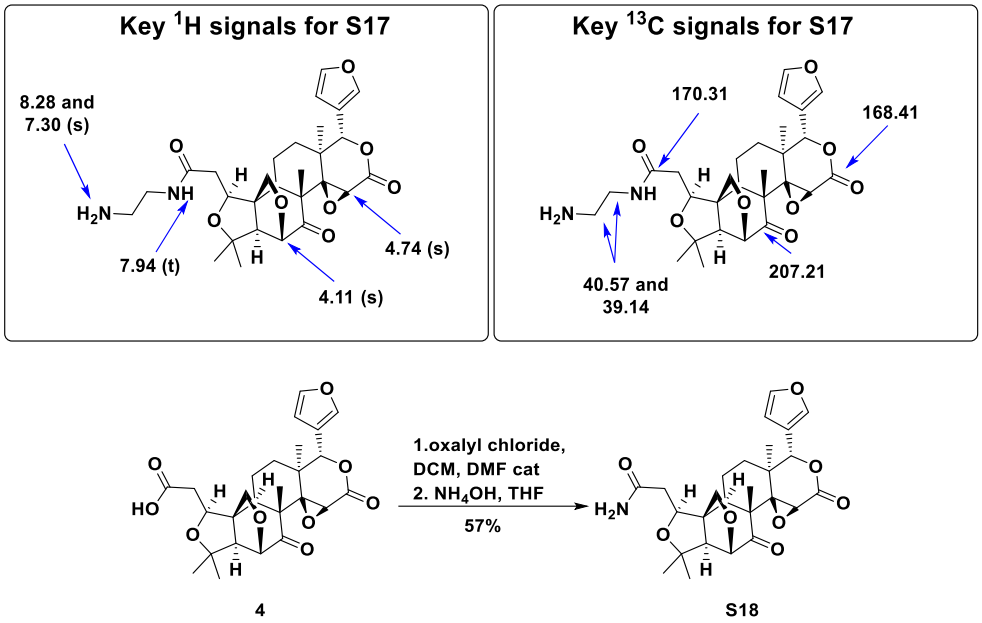
2.60 (t, *J* = 6.4 Hz, 2H), 2.26 (dd, *J* = 14.6, 2.3 Hz, 1H), 2.01 (dd, *J* = 14.6, 9.6 Hz, 1H), 1.83 – 1.64 (m, 3H), 1.47 (s, 3H), 1.21 (s, 3H), 1.14 (s, 3H), 1.10 (s, 3H), 1.10 – 1.08 (m, 1H).

^{13}C NMR (DMSO-*d6*, 125 MHz): δ 207.21, 170.31, 168.41, 165.38 (HCOH), 143.87, 142.29, 128.80, 120.99, 110.66, 85.41, 78.60, 77.99, 76.80, 71.90, 66.47, 63.91, 57.92, 57.38, 47.35, 41.23, 40.59, 40.57, 39.14, 30.61, 25.75, 25.52, 20.33, 19.89, 17.74.

HRMS(ESI): m/z calc. for $C_{28}H_{37}N_2O_8$ $[M+H]^+$: 529.2550, found: 529.2549.

mp: 203-204° C.

Opt. Rot.: $[\alpha]_D^{25}$ = - 160 (c = 0.04, acetone).



Procedure: Oxalyl chloride (10 µL, 0.113 mmol) was added dropwise to a solution of **4** (50 mg, 0.103 mmol) in dichloromethane (1 mL). Then, a drop of DMF was added to the resulting solution and the mixture was stirred at 30° C for 3 h. The solvent was removed under vacuum and the crude residue was taken up in tetrahydrofuran (1 mL) and cooled to 0° C. Ammonium hydroxide (0.2 mL) was added dropwise to the resulting solution and the reaction mixture was stirred at 30° C for additional 12 h. Tetrahydrofuran was evaporated and the aqueous solution was slowly acidified to pH 2 with 0.5 M hydrochloric acid and extracted three times with dichloromethane. The organic layers were combined, washed with brine, dried over Na_2SO_4, and concentrated by distillation under reduced pressure. The crude residue was purified by silica gel flash chromatography (ethyl acetate) to provide **S18** (20 mg, 57%) as a white solid.

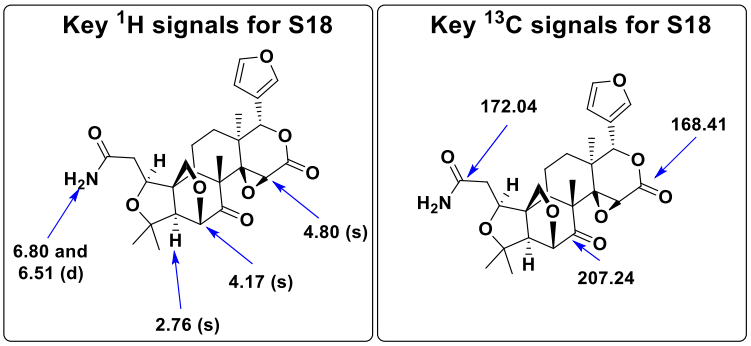
^{1}H NMR (DMSO-*d6*, 500 MHz): δ 7.71 (d, *J* = 1.7 Hz, 1H), 7.67 (dd, *J* = 1.9, 1.7 Hz, 1H), 7.27 (d, *J* = 3.2 Hz, 1H), 6.80 (d, *J* = 3.2 Hz, 1H), 6.51 (d, *J* = 1.9 Hz, 1H), 5.70 (s, 1H), 4.80 (s, 1H), 4.25 (dd, *J* = 9.7, 2.2 Hz, 1H), 4.17 (s, 1H), 4.09 (d, *J* = 9.0 Hz, 1H), 3.69 (d, *J* = 9.0 Hz, 1H), 2.81 (dd, *J* = 12.6, 6.1 Hz, 1H), 2.76 (s, 1H), 2.25 (dd, *J* = 14.7, 2.2 Hz, 1H), 2.04 (dd, *J* = 14.7, 9.7 Hz, 1H), 1.89 – 1.69 (m, 3H), 1.53 (s, 3H), 1.27 (s, 3H), 1.22 (s, 3H), 1.19 – 1.16 (m, 1H), 1.17 (s, 3H).

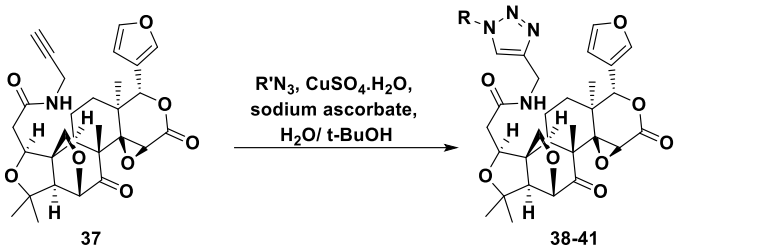
^{13}C NMR (DMSO-*d6*, 125 MHz): δ 207.24, 172.04, 168.41, 143.87, 142.29, 121.00, 110.67, 85.42, 78.53, 78.01, 76.96, 71.91, 66.47, 63.93, 57.90, 57.38, 56.49, 47.35, 41.26, 38.92, 30.64, 25.54, 20.31, 19.88, 19.04, 17.72.

HRMS(ESI): m/z calc. for $C_{26}H_{32}NO_8$ $[M+H]^+$: 486.2128, found: 486.2127.

mp: 170-171° C.

Opt. Rot.: $[\alpha]_D^{25}$ = - 77 (c = 0.15, acetone).





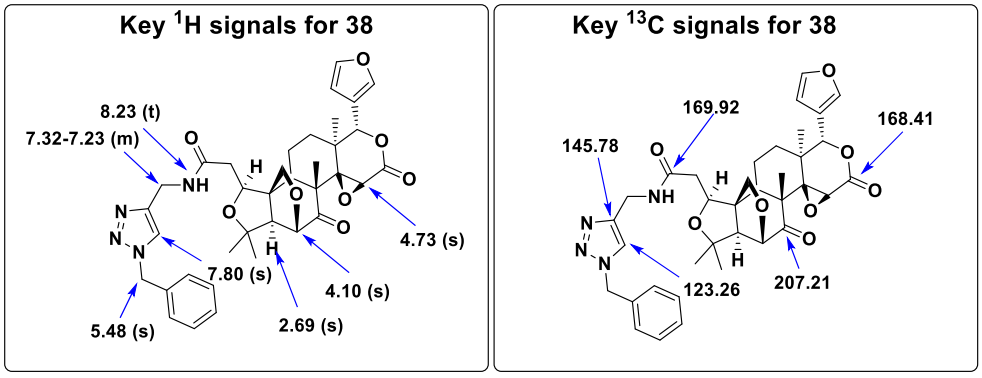
37 38-41

38; R = R' = CH_2Ph 52%
39; R = R' = $CH_2CH_2CH_2NH_2$ 6%
40; R = R' = $CH_2CH_2CH_2OH$ 51%
41; R = H; R' = $Si(CH_3)_3$ 6%

Procedure: Copper (II) sulfate (4 mg, 0.016 mmol) and sodium ascorbate (16 mg, 076 mmol) were added to a solution of **37** (400 mg, 0.76 mmol) in H_2O (3.6 mL) and *t*-BuOH (1.8 mL). To the resulting suspension, the suitable azide (0,96 mmol) was added and the resulting mixture was stirred at 30° C for 48 h. The solvent was evaporated and the solution was extracted three times with dichloromethane. The combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated by distillation at reduced pressure. The obtained residue was purified by flash chromatography on silica gel (hexane-ethyl acetate 7:3), giving **38-41** (6-52%) as white solids.

38 (260 mg, 52%)

^{1}H NMR (DMSO-*d6*, 500 MHz): δ 8.23 (t, *J* = 5.7 Hz, 1H), 7.80 (s, 1H), 7.64 (d, *J* = 1.7 Hz, 1H), 7.61 (dd, *J* = 1.7, 1.7 Hz, 1H), 7.32 – 7.23 (m, 3H), 7.23 – 7.18 (m, 2H), 6.44 (d, *J* = 1.7 Hz, 1H), 5.63 (s, 1H), 5.48 (s, 2H), 4.73 (s, 1H), 4.26 – 4.15 (m, 3H), 4.10 (s, 1H), 4.01 (d, *J* = 8.9 Hz, 1H), 3.61 (d, *J* = 8.9 Hz, 1H), 2.73 (dd, *J* = 12.5, 5.9 Hz, 1H), 2.69 (s, 1H), 2.24 (dd, *J* = 14.5, 2.3 Hz, 1H), 2.03 (dd, *J* = 14.5, 9.8 Hz, 1H), 1.81 – 1.60 (m, 3H), 1.46 (s, 3H), 1.20 (s, 3H), 1.11 (s, 3H), 1.10 – 1.07 (m, 1H), 1.07 (s, 3H).
^{13}C NMR (DMSO-*d6*, 125 MHz): δ 207.21, 169.92, 168.41, 145.78, 143.87, 142.29, 136.54, 129.21 (2C), 128.58, 128.33 (2C), 123.26, 121.00, 110.67, 85.41, 78.60, 78.00, 76.91, 71.90, 66.46, 63.87, 57.93, 57.38, 53.20, 47.34, 41.21, 40.59, 39.02, 34.74, 30.61, 25.72, 25.49, 20.32, 19.88, 17.73.
HRMS(ESI): m/z calc. for $C_{36}H_{41}N_4O_8$ $[M+H]^+$: 657.2924, found: 657.2913.
mp: >260° C.
Opt. Rot.: $[\alpha]_D^{25}$ = - 51 (c = 0.09, acetone).

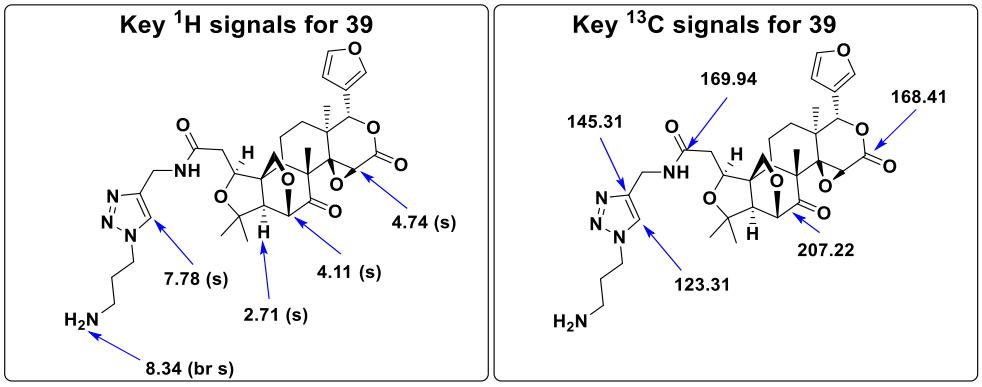


39 (24 mg, 6%)

Note: 39 was purified by biotage (water-acetonitrile gradient with 1% formic acid) and was obtained as a formic acid salt

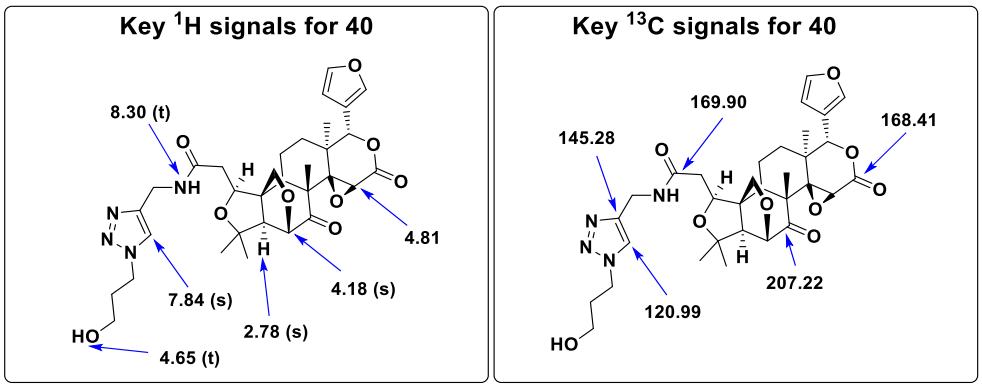
^{1}H NMR (DMSO-*d6*, 500 MHz): δ 8.34 (br s, 2H), 8.24 (t, *J* = 5.7 Hz, 1H), 7.78 (s, 1H), 7.64 (d, *J* = 1.8 Hz, 1H), 7.61 (dd, *J* = 1.8, 1.8 Hz, 1H), 6.44 (d, *J* = 1.8 Hz, 1H), 5.63 (s, 1H), 4.74 (s, 1H), 4.29 (t, *J* = 7.0 Hz, 2H), 4.27 – 4.15 (m, 3H), 4.11 (s, 1H), 4.02 (d, *J* = 8.9 Hz, 1H), 3.62 (d, *J* = 8.9 Hz, 1H), 2.75 (dd, *J* = 12.3, 5.7 Hz, 1H), 2.71 (s, 1H), 2.49 (t, *J* = 6.8 Hz, 1H), 2.45 – 2.43 (m, 1H), 2.26 (dd, *J* = 14.6, 2.3 Hz, 1H), 2.06 (dd, *J* = 14.6, 9.7 Hz, 1H), 1.86 – 1.62 (m, 5H), 1.46 (s, 3H), 1.21 (s, 3H), 1.15 (s, 3H), 1.12 – 1.09 (m, 1H), 1.11 (s, 3H).
^{13}C NMR (DMSO-*d6*, 125 MHz): δ 207.22, 169.94, 168.41, 165.23 (HCOH), 145.31, 143.87, 142.29, 123.31, 120.99, 110.67, 85.42, 79.64, 78.64, 78.00, 76.92, 71.90, 66.48, 63.89, 57.94, 57.37, 47.34, 47.25, 41.23, 39.00, 37.75, 34.73, 31.20, 30.65, 25.73, 25.55, 20.33, 19.88, 17.73.
HRMS(ESI): m/z calc. for $C_{32}H_{42}N_5O_8$ $[M+H]^+$: 624.3033, found: 624.3037.
mp: >260° C.

Opt. Rot.: $[\alpha]_D^{25}$ = - 50 (c = 0.14, acetone).



40 (240 mg, 51%)

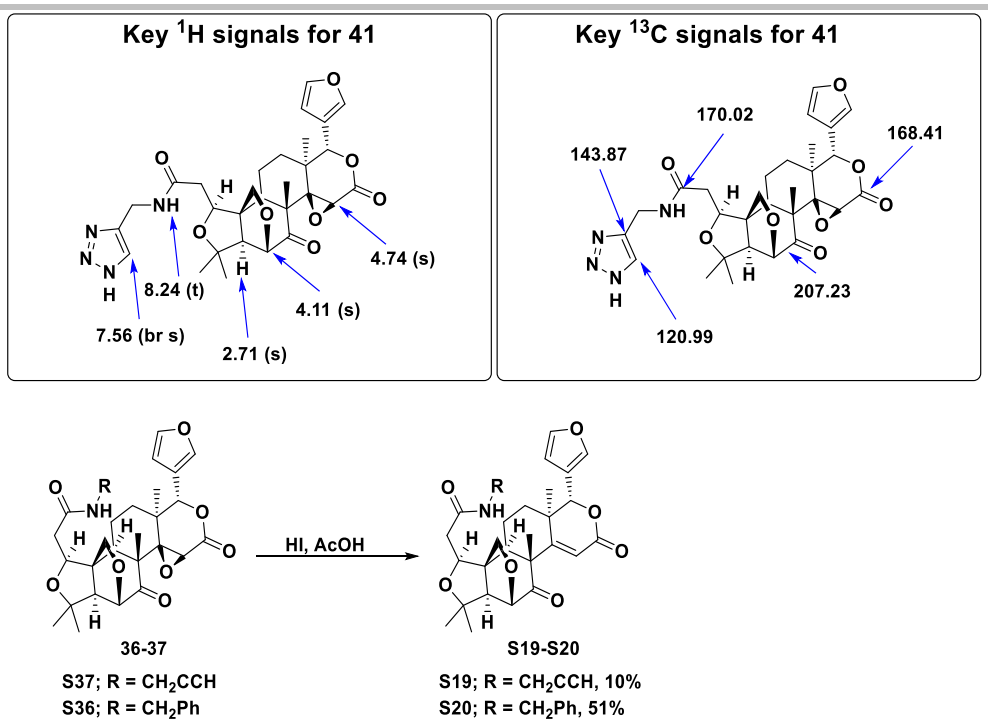
^{1}H NMR (DMSO-*d6*, 500 MHz): δ 8.30 (t, *J* = 5.7 Hz, 1H), 7.84 (s, 1H), 7.71 (d, *J* = 1.8 Hz, 1H), 7.68 (dd, *J* = 1.8, 1.8 Hz, 1H), 6.51 (d, *J* = 1.8 Hz, 1H), 5.70 (s, 1H), 4.81 (s, 1H), 4.65 (t, *J* = 5.0 Hz, 1H), 4.35 (t, *J* = 7.1 Hz, 2H), 4.32 – 4.24 (m, 3H), 4.18 (s, 1H), 4.10 (d, *J* = 8.9 Hz, 1H), 3.70 (d, *J* = 8.9 Hz, 1H), 3.39 (q, *J* = 5.8 Hz, 2H), 2.82 (dd, *J* = 12.3, 6.0 Hz, 1H), 2.78 (s, 1H), 2.33 (dd, *J* = 14.6, 2.3 Hz, 1H), 2.13 (dd, *J* = 14.6, 9.7 Hz, 1H), 1.92 (p, *J* = 6.4 Hz, 2H), 1.88 – 1.70 (m, 3H), 1.54 (s, 3H), 1.28 (s, 3H), 1.23 (s, 3H), 1.18 (s, 3H), 1.18 – 1.16 (m, 1H).
^{13}C NMR (DMSO-*d6*, 125 MHz): δ 207.22, 169.90, 168.41, 145.28, 143.87, 142.29, 123.21, 120.99, 110.67, 85.42, 78.63, 78.00, 76.95, 71.90, 66.48, 63.89, 57.95, 57.87, 57.38, 55.39, 47.35, 46.98, 41.22, 39.03, 34.75, 33.48, 30.64, 25.74, 25.55, 20.34, 19.88, 17.74.
HRMS(ESI): m/z calc. for $C_{32}H_{41}N_4O_9$ $[M+H]^+$: 625.2874, found: 625.2865.
mp: 138-140° C.
Opt. Rot.: $[\alpha]_D^{25}$ = - 51 (c = 0.12, acetone).



41 (32 mg, 6%)

Note: Reaction was performed using trimethylsilyl azide.

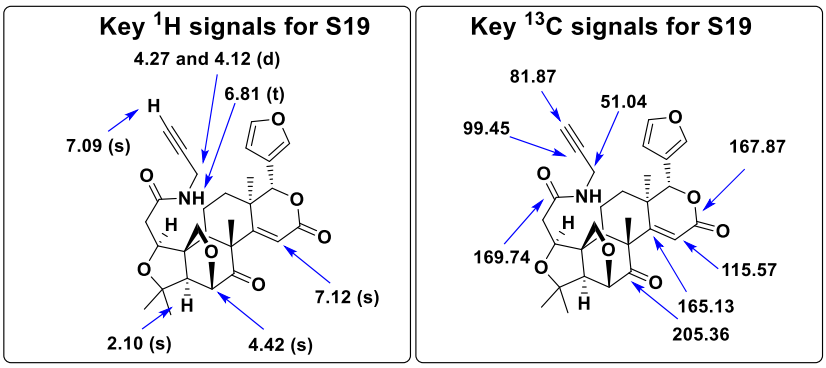
^{1}H NMR (DMSO-*d6*, 500 MHz): δ 14.71 (br s, 1H), 8.24 (t, *J* = 5.7 Hz, 1H), 7.64 (d, *J* = 1.8 Hz, 1H), 7.60 (dd, *J* = 1.8, 1.8 Hz, 1H), 7.56 (br s, 1H), 6.44 (d, *J* = 1.8 Hz, 1H), 5.63 (s, 1H), 4.74 (s, 1H), 4.28 – 4.19 (m, 3H), 4.11 (s, 1H), 4.03 (d, *J* = 8.9 Hz, 1H), 3.63 (d, *J* = 8.9 Hz, 1H), 2.75 (dd, *J* = 12.4, 5.7 Hz, 1H), 2.71 (s, 1H), 2.28 (dd, *J* = 14.5, 2.1 Hz, 1H), 2.06 (dd, *J* = 14.5, 9.9 Hz, 1H), 1.80 – 1.65 (m, 3H), 1.46 (s, 3H), 1.21 (s, 3H), 1.16 (s, 3H), 1.11 (s, 3H), 1.10 – 1.07 (m, 1H).
^{13}C NMR (DMSO-*d6*, 125 MHz): δ 207.23, 170.02, 168.41, 143.87 (2C), 142.28, 120.99 (2C), 110.66, 85.42, 78.63, 78.01, 76.96, 71.91, 66.47, 63.90, 57.95, 57.38, 47.35, 41.21, 40.50, 39.08, 34.32, 30.61, 25.73, 25.53, 20.33, 19.88, 17.74.
HRMS(ESI): m/z calc. for $C_{29}H_{35}N_4O_8$ $[M+H]^+$: 567.2455, found: 567.2459.
mp: 191-193° C.
Opt. Rot.: $[\alpha]_D^{25}$ = - 89 (c = 0.08, acetone).



Procedure: A solution of the suitable amide (0.35 mmol) in acetic acid (2.8 mL) and hydriodic acid (2.8 mL) was heated under reflux for 3 h. The reaction mixture was quenched with a saturated solution of sodium sulfite and extracted three times with dichloromethane. The organic layers were combined, washed with brine, dried over Na_2SO_4, and concentrated by distillation under reduced pressure. The crude residue was purified by silica gel flash chromatography (hexane-ethyl acetate 4:6) to provide **S19-S20** (10-51%) as white solids.

S19 (20 mg, 10%)

^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.49 (s, 1H), 7.43 (d, *J* = 1.9 Hz, 1H), 7.12 (s, 1H), 7.09 (s, 1H), 6.81 (t, *J* = 5.9 Hz, 1H), 6.39 (d, *J* = 1.9 Hz, 1H), 5.01 (s, 1H), 4.42 (s, 1H), 4.27 (dd, *J* = 15.3, 5.9 Hz, 1H), 4.22 (dd, *J* = 10.5, 1.5 Hz, 1H), 4.12 (dd, *J* = 15.3 Hz, 5.9 Hz, 1H), 4.09 (d, *J* = 8.9 Hz, 1H), 3.92 (d, *J* = 8.9 Hz, 1H), 2.56 (dd, *J* = 15.3, 1.5 Hz, 1H), 2.51 (dd, *J* = 13.2, 6.8 Hz, 1H), 2.33 (dd, *J* = 15.3, 10.5 Hz, 1H), 2.10 (s, 1H), 2.06 – 1.85 (m, 2H), 1.73 (s, 3H), 1.68 (dd, *J* = 14.4, 9.7 Hz, 1H), 1.48 (dd, *J* = 14.4, 10.2 Hz, 1H), 1.37 (s, 3H), 1.35 (s, 3H), 1.27 (s, 3H),
^{13}C NMR ($CDCl_3$, 125 MHz): δ 205.36, 169.74, 167.87, 165.13, 143.14, 141.41, 119.91, 115.57, 109.85, 99.45, 85.68, 82.65, 81.87, 79.89, 76.30, 66.39, 65.97, 58.27, 51.04, 48.90, 41.37, 39.98, 39.11, 30.91, 25.99, 25.02, 24.85, 21.10, 18.56.
HRMS(ESI): m/z calc. for $C_{29}H_{34}NO_7$ $[M+H]^+$: 508.2335, found: 508.2358.



S20 (98 mg, 51%)

^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.48 (d, *J* = 1.7 Hz, 1H), 7.42 (dd, *J* = 1.7, 1.7 Hz, 1H), 7.36 - 7.30 (m, 2H), 7.28 - 7.24 (m, 3H), 7.10 (s, 1H), 6.67 (t, *J* = 6.0 Hz, 1H), 6.38 (d, *J* = 1.7 Hz, 1H), 5.00 (s, 1H), 5.51 (dd, *J* = 15.0, 6.0 Hz, 1H), 4.39 (s, 1H), 4.38 (dd, J= 15.0, 6.0 Hz, 1H), 4.22 (dd, *J* = 10.2, 1.7 Hz, 1H), 4.06 (d, *J* = 8.9 Hz 1H), 3.88 (d, *J* = 8.9 Hz, 1H), 2.54 (dd, *J* = 14.9, 1.7 Hz, 1H), 2.71 (dd, H =

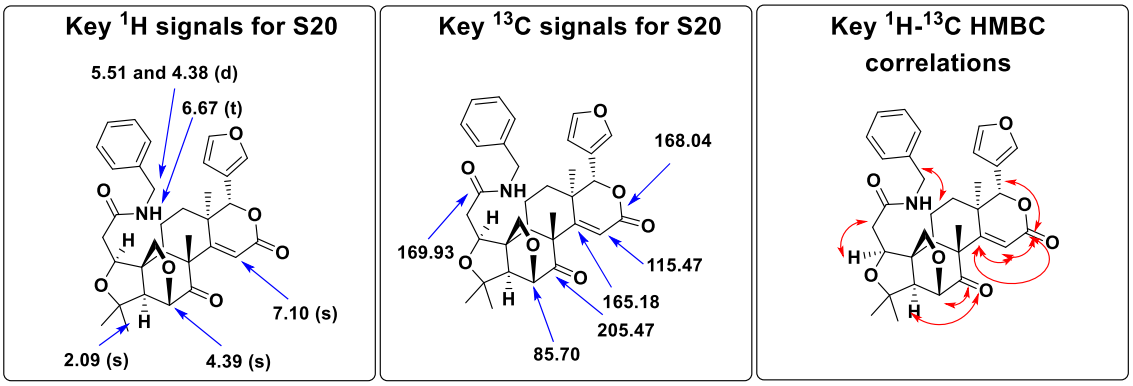
13.1, 6.7 Hz, 1H), 2.29 (dd, *J* = 14.9, 10.2 Hz, 1H), 2.09 (s, 1 H), 2.03 - 1.95 (m, 1H), 1.92 - 1.84 (m, 1H), 1.72 (s, 3H), 1.69 - 1.62 (m, 1H), 1.48 - 1.43 (m, 1H), 1.28 (s, 6H), 1.26 (s, 3H).

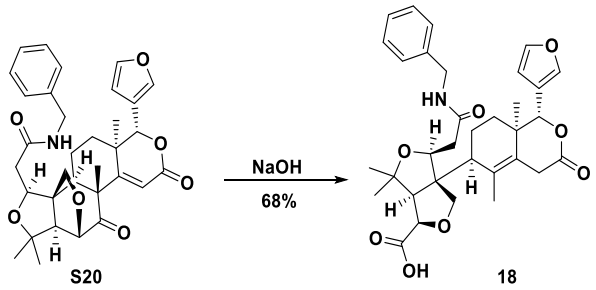
^{13}C NMR (CDCl$_3$, 125 MHz): δ 205.47, 169.93, 168.04, 165.18, 143.12, 141.40, 138.12, 128.66 (2C), 127.47, 127.44 (2C), 119.93, 115.47, 109.88, 85.70, 82.63, 79.50, 76.54, 66.40, 65.99, 58.21, 48.90, 43.54, 41.31, 40.09, 39.10, 30.55, 25.98, 24.94, 24.86, 21.06, 18.50.

HRMS(ESI): m/z calc. for $C_{33}H_{38}NO_7$ $[M+H]^+$: 560.2648, found: 560.2644.

mp: 126-127° C.

Opt. Rot.: $[\alpha]_D^{25}$ = - 62 (c = 0.17, acetone).





Procedure: A suspension of **S20** (100 mg, 0.17 mmol) in 2 M sodium hydroxide (2 mL) and dioxane (2 mL) was heated under reflux for 2 h. The reaction mixture was cooled to room temperature, and the organic solvent was evaporated under vacuum. The aqueous layer was washed with dichloromethane (to remove unreactive starting material) and acidified with 2 M hydrochloric acid. The acid aqueous solution was then extracted three times with dichloromethane. The combined organic layers (obtained by extracting the acidic layer) were washed with brine, dried over Na_2SO_4, and concentrated by distillation under reduced pressure to yield pure **18** (66 mg, 68%) as a white solid.

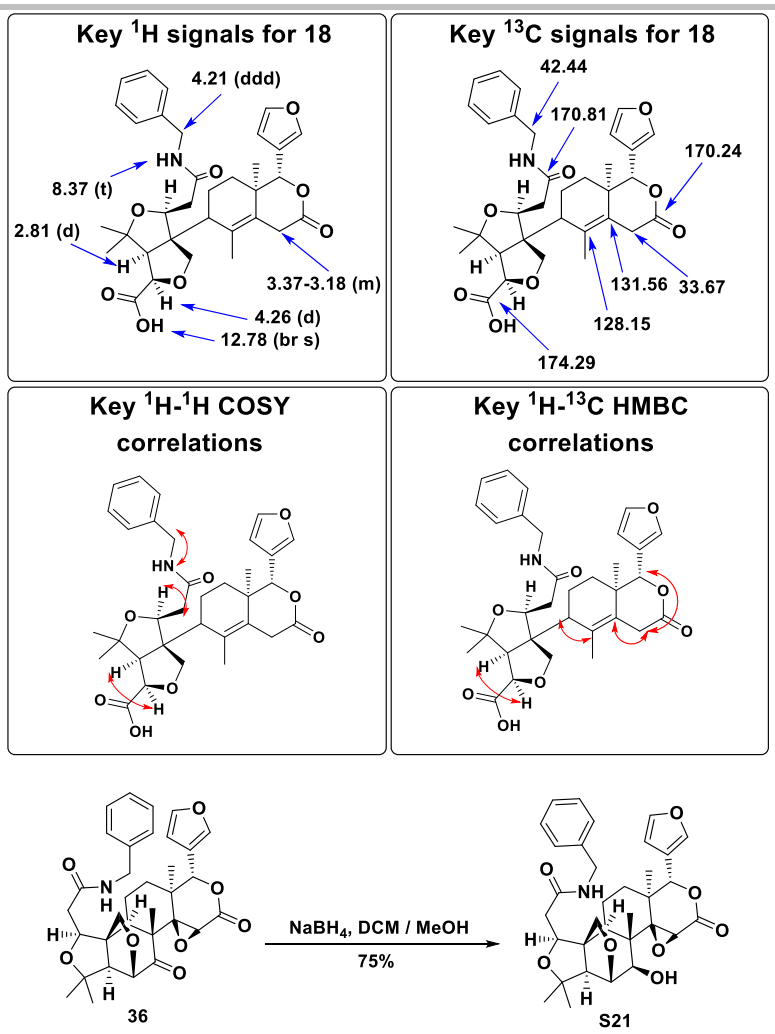
^{1}H NMR (DMSO-*d6*, 500 MHz): δ 12.78 (br s, 1H), 8.37 (t, *J* = 6.0 Hz, 1H), 7.70 (d, *J* = 1.7 Hz, 1H), 7.60 (dd, *J* = 1.7, 1.7 Hz, 1H), 7.26 – 7.11 (m, 5H), 6.50 (d, *J* = 1.7 Hz, 1H), 5.03 (s, 1H), 4.35 (dd, *J* = 9.8, 1.9 Hz, 1H), 4.26 (d, *J* = 4.0 Hz, 1H), 4.21 (ddd, *J* = 15.5, 8.4, 6.0 Hz, 2H), 3.79 (d, *J* = 9.6 Hz, 1H), 3.74 (d, *J* = 9.5 Hz, 1H), 3.37 – 3.18 (m, 2H), 2.81 (d, *J* = 4.0 Hz, 1H), 2.43 – 2.40 (m, 1H), 2.30 (dd, *J* = 14.2, 9.8 Hz, 1H), 2.18 (dd, *J* = 14.2, 1.9 Hz, 1H), 1.77 – 1.67 (m, 1H), 1.61 (s, 3H), 1.61 - 1.56 (m, 1H), 1.22 (s, 6H), 1.22 - 1.15 (m, 1H), 0.85 (s, 3H), 0.85 – 0.82 (m, 1H).

^{13}C NMR (DMSO-*d6*, 125 MHz): δ 174.29, 170.81, 170.24, 143.75, 141.94, 139.94, 131.56, 128.58 (2C), 128.15, 127.56 (2C), 127.09, 121.09, 110.58, 80.77, 80.20, 79.00, 78.08, 72.44, 61.58, 61.51, 44.64, 42.44, 38.72, 37.78, 33.67, 28.99, 27.65, 26.23, 21.55, 21.29, 18.32.

HRMS(ESI): m/z calc. for $C_{33}H_{40}NO_8$ $[M+H]^+$: 578.2754, found: 578.2747.

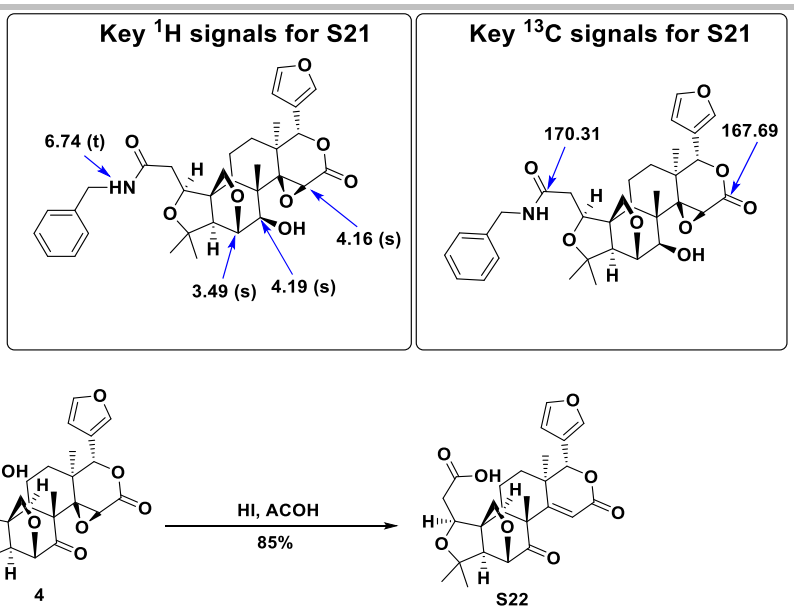
mp: 101-102° C.

Opt. Rot.: $[\alpha]_D^{25}$ = - 91 (c = 0.16, acetone).



Procedure: A solution of $NaBH_4$ (19 mg, 0.5 mmol) in anhydrous methanol (0.85 mL) was added to a solution of **36** (54 mg, 0.09 mmol) in dichloromethane (1.7 mL) at -40° C and the resulting mixture was stirred at -40 °C. After 30 minutes, the reaction was quenched by the addition of a 2 M hydrochloric acid solution and extracted three times with dichloromethane. The organic layers were dried over Na_2SO_4 and concentrated by distillation under reduced pressure to obtained a crude residue that was purified by silica gel flash chromatography (hexane-ethyl acetate 3:7) to provide **S21** (39 mg, 75%) as a white solid.

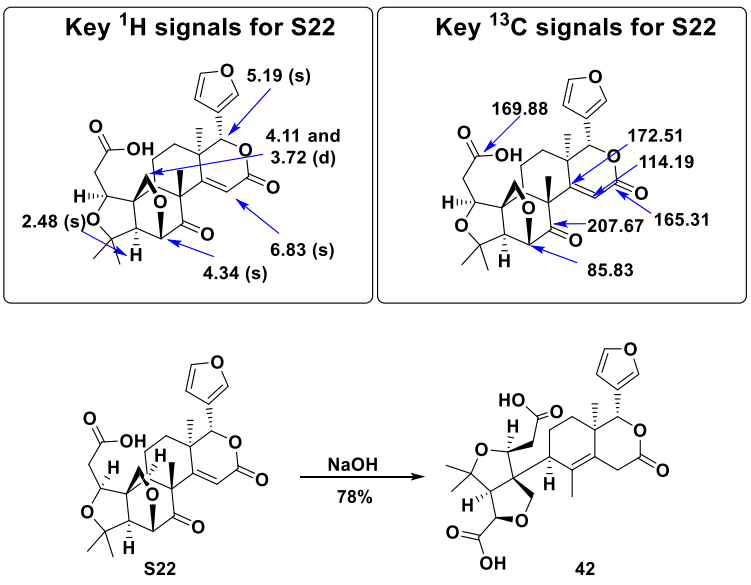
^{1}H NMR ($CDCl_3$, 125 MHz): δ 7.42 (s, 1H), 7.41 (d, *J* = 1.7 Hz, 1H), 7.33 – 7.30 (m, 2H), 7.28 – 7.23 (m, 3H), 6.74 (t, *J* = 5.7 Hz, 1H), 6.29 (d, *J* = 1.7 Hz, 1H), 5.70 (s, 1H), 4.51 (dd, *J* = 15.1, 5.7 Hz, 1H), 4.37 (dd, *J* = 15.1, 5.7 Hz, 1H), 4.19 (s, 1H), 4.16 (s, 1H), 4.14 (dd, *J* = 10.4, 1.5 Hz, 1H), 3.93 (d, *J* = 9.0 Hz, 1H), 3.69 (d, *J* = 9.0 Hz, 1H), 3.49 (s, 1H), 2.53 (dd, *J* = 12.4, 6.8 Hz, 2H), 2.48 (dd, *J* = 15.0, 1.5 Hz, 1H), 2.22 (dd, *J* = 15.0, 10.4 Hz, 1H), 1.89 (s, 1H), 1.87 – 1.79 (m, 1H), 1.79 – 1.68 (m, 1H), 1.54 – 1.47 (m, 1H), 1.47 (s, 3H), 1.28 (s, 3H), 1.27 (s, 3H), 1.23 (s, 3H). (38 non-exchangeable protons)
^{13}C NMR ($CDCl_3$, 125 MHz): δ 170.31, 167.69, 1431.21, 141.25, 138.20, 128.65 (2C), 127.41 (3C), 120.29, 109.62, 82.97, 79.99, 78.47, 78.40, 76.60, 75.30, 66.69, 66.06, 58.29, 58.25, 43.88, 43.48, 42.60, 39.96, 39.88, 31.17, 25.41, 24.76, 20.39, 19.15, 12.68.
HRMS(ESI): m/z calc. for $C_{33}H_{40}NO_8$ $[M+H]^+$: 578.2754, found: 578.2747
Opt. Rot.: $[\alpha]_D^{25}$ = + 46 (c = 0.14, acetone).



Procedure:
A solution of **4** (300 mg, 0.62 mmol) in acetic acid (4 mL) and hydriodic acid (4 mL) was heated under reflux for 3 h. The reaction mixture was cooled to room temperature and slowly poured into 400 mL of sodium sulfite saturated solution and extracted three times with dichloromethane. The organic layers were combined, washed with brine, dried over Na_2SO_4 and concentrated by distillation under reduced pressure. The crude residue was purified by biotage (water-acetonitrile gradient with 1% formic acid) to provide **S22** (110 mg, 85%) as a white solid.

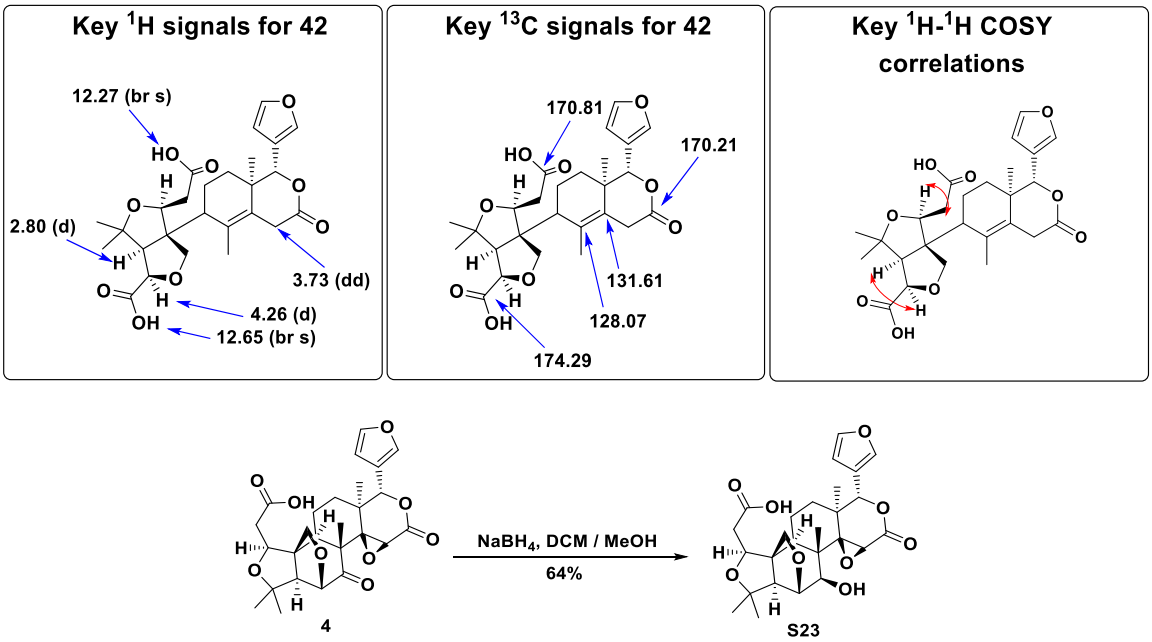
Note: S22 was obtained as a formic acid salt

^{1}H NMR (DMSO-*d6*, 500 MHz): δ 12.21 (br s ,1H), 7.74 (s, 1H), 7.69 (d, *J* = 1.8 Hz, 1H), 6.83 (s, 1H), 6.55 (d, *J* = 1.8 Hz, 1H), 5.19 (s, 1H), 4.34 (s, 1H), 4.30 (dd, *J* = 10.2, 2.0 Hz, 1H), 4.11 (d, *J* = 9.0 Hz, 1H), 3.72 (d, *J* = 9.0 Hz, 1H), 2.69 (dd, *J* = 13.3, 6.2 Hz, 1H), 2.48 (s, 1H), 2.09 (dd, *J* = 15.6, 10.2 Hz, 1H), 1.88 (dd, *J* = 13.3, 3.4 Hz, 1H), 1.78 – 1.72 (m, 2H), 1.63 (s, 3H), 1.34 – 1.26 (m, 1H), 1.24 (s, 3H), 1.21 (s, 3H), 1.18 (s, 3H), 1.16 – 1.12 (m, 1H).
^{13}C NMR (DMSO-*d6*, 125 MHz): δ 207.67, 172.51, 169.88, 165.31, 143.76, 142.25, 120.67, 114.19, 110.79, 85.83, 81.85, 78.70, 76.22, 66.43, 64.59, 57.63, 48.82, 40.58, 38.88, 38.05, 30.50, 25.82, 25.50, 25.04, 20.75, 17.74.
HRMS(ESI): m/z calc. for $C_{26}H_{31}O_8$ $[M+H]^+$: 471.2019, found: 471.2013.
mp: 173-174.
Opt. Rot.: $[\alpha]_D^{25}$ = - 48 (c = 0.12, acetone).



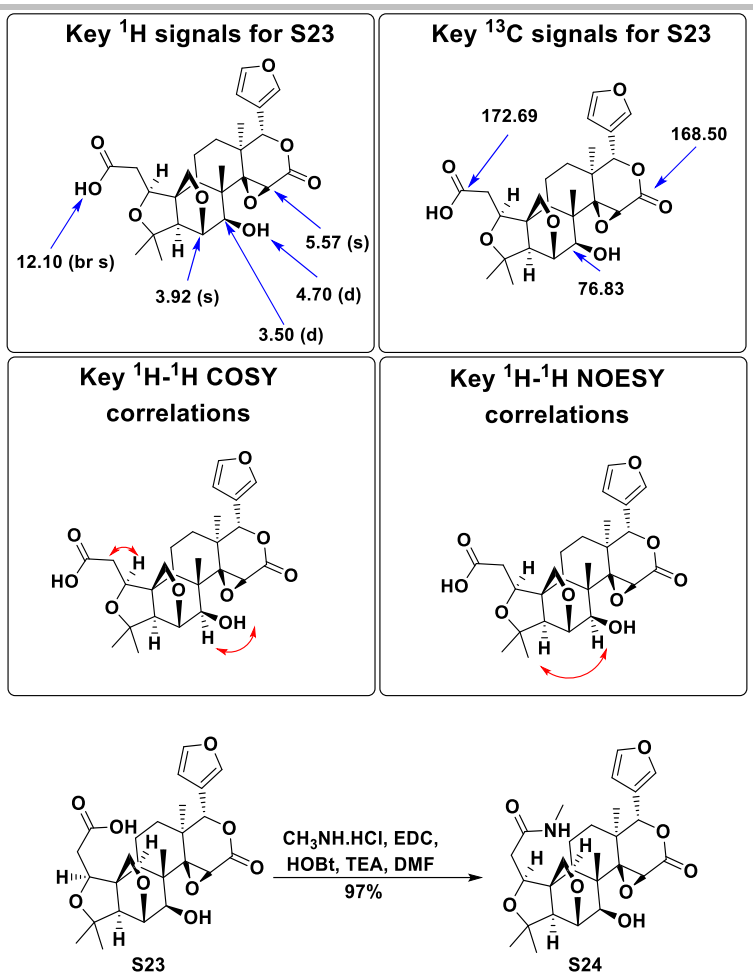
Procedure: A suspension of **S22** (110 mg, 0.23 mmol) in 2 M sodium hydroxide (2.6 mL) was heated under reflux for 2 h. The reaction mixture was cooled to room temperature, and the organic solvent was evaporated under vacuum. The aqueous layer was washed with dichloromethane (to remove unreactive starting material) and acidified with 2 M hydrochloric acid. The acid aqueous solution was then extracted three times with dichloromethane. The combined organic layers (obtained by extracting the acidic layer) were washed with brine, dried over Na_2SO_4, and concentrated by distillation under reduced pressure. The obtained crude residue was purified by biotage (water-acetonitrile gradient with 1% formic acid) to provide **42** (88 mg, 78%) as a white solid.

^{1}H NMR (DMSO-*d6*, 500 MHz,): δ 12.65 (br s, 1H), 12.27 (br s, 1H), 7.70 (d, *J* = 1.8 Hz, 1H), 7.61 (s, 1H), 6.50 (d, *J* = 1.8 Hz, 1H), 4.98 (s, 1H), 4.27 (dd, *J* = 10.2, 1.8 Hz, 1H), 4.26 (d, *J* = 4.1 Hz, 1H), 3.73 (dd, *J* = 12.1, 9.7 Hz, 2H), 3.36 – 3.19 (m, 2H), 2.80 (d, *J* = 4.1 Hz, 1H), 2.43 -2.41 (m, 1H), 2.37 (dd, *J* = 15.3, 1.8 Hz, 1H), 2.20 (dd, *J* = 15.3, 10.2 Hz, 1H), 1.69 – 1.61 (m, 2H), 1.60 (s, 3H), 1.21 (s, 3H), 1.20 (s, 3H), 1.17 – 1.11 (m, 1H), 0.87 – 0.84 (m, 1H), 0.85 (s, 3H).
^{13}C NMR (DMSO-*d6*, 125 MHz): δ 174.24, 173.18, 170.21, 143.78, 141.90, 131.61, 128.07, 121.07, 110.57, 80.79, 80.43, 78.68, 78.00, 72.32, 61.53, 61.42, 44.64, 37.80, 37.50, 33.67, 28.96, 27.54, 26.16, 21.51, 21.37, 18.29.
HRMS(ESI): m/z calc. for $C_{26}H_{33}O_9$ $[M+H]^+$: 489.2125, found: 489.2123.
mp: 153-154° C.
Opt. Rot.: $[\alpha]_D^{25}$ = - 50 (c = 0.07, acetone).



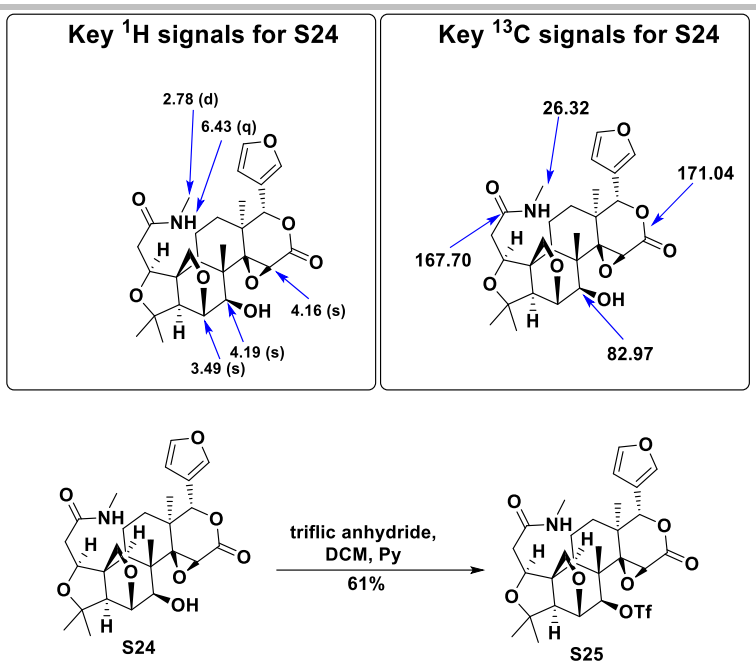
Procedure: A solution of $NaBH_4$ (44 mg, 1.18 mmol) in anhydrous methanol (2 mL) was added to a solution of **4** (100 mg, 0.21 mmol) in dichloromethane (4 mL) at -40° C and the resulting mixture was stirred at -40 °C. After 30 minutes, the reaction was quenched by the addition of a 2 M hydrochloric acid solution and extracted three times with dichloromethane. The organic layers were dried over Na_2SO_4 and concentrated by distillation under reduced pressure to obtained a crude residue that was purified by biotage (water-acetonitrile gradient with 1% formic acid) to provide **S23** (65 mg, 64%) as a white solid.

^{1}H NMR (DMSO-*d6*, 125 MHz): δ 12.10 (br s, 1H), 7.63 (d, *J* = 1.8 Hz, 1H), 7.59 (s, 1H), 6.42 (d, *J* = 1.8 Hz, 1H), 5.57 (s, 1H), 4.70 (d, *J* = 5.7 Hz, 1H), 4.10 (dd, *J* = 10.0, 2.1 Hz, 1H), 3.98 (s, 1H), 3.92 (s, 1H), 3.78 (d, *J* = 8.9 Hz, 1H), 3.50 (d, *J* = 5.7 Hz, 1H), 3.39 (d, *J* = 8.9 Hz, 1H), 2.51 – 2.44 (m, 2H), 2.36 (dd, *J* = 15.6, 2.1 Hz, 1H), 2.17 (s, 1H), 1.93 (dd, *J* = 15.6, 10.0 Hz, 1H), 1.72 – 1.60 (m, 2H), 1.60 – 1.51 (m, 1H), 1.24 (s, 3H), 1.16 (s, 3H), 1.12 (s, 3H), 1.08 (s, 3H).
^{13}C NMR (DMSO-*d6*, 125 MHz): δ 172.69, 168.50, 143.81, 142.16, 121.10, 110.69, 83.89, 79.11, 78.50, 76.83, 76.60, 75.70, 65.89, 64.89, 57.87, 57.80, 43.59, 41.45, 39.71, 37.84, 31.28, 25.70, 25.40, 20.12, 18.49, 13.37.
HRMS(ESI): m/z calc. for $C_{26}H_{33}O_9$ $[M+H]^+$: 489.2125, found: 489.2127
mp: decomposes upon heating above 230° C.
Opt. Rot.: $[\alpha]_D^{25}$ = - 121 (c = 0.06, acetone).



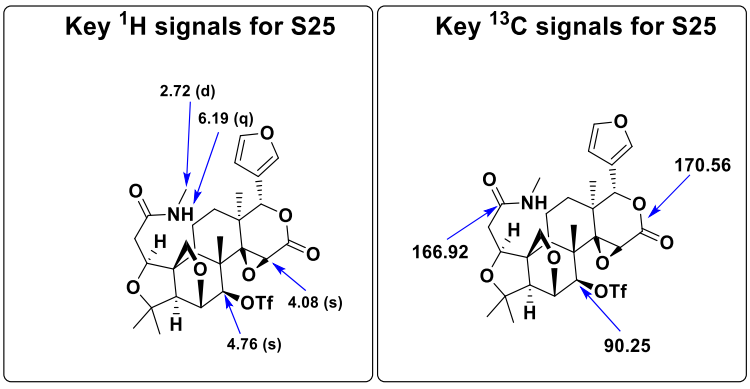
Procedure: HOBt (17 mg, 0.113 mmol), EDC (22 µL, 0.122 mmol) and TEA (28 µL, 0.204 mmol) were added to a solution of **S23** (50 mg, 0.102 mmol) in DMF (1 mL), and the resulting mixture was stirred 30 minutes at 30° C. Then, methylamine hydrochloride (0.49 mmol) was added to the mixture and the reaction was stirred overnight. The reaction was diluted with dichloromethane and washed with water, 5% citric acid, brine, 5% $NaHCO_3$, and Brine. The organic layer was dried over Na_2SO_4, concentrated by distillation at reduced pressure, and the residue was purified by flash chromatography on silica gel (ethyl acetate), giving **S24** (50 mg, 97%) as a white solid.

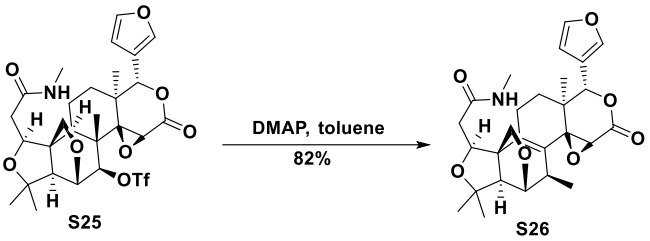
^{1}H NMR (CDCl$_3$, 500 MHz): δ 7.42 (d, *J* = 1.8 Hz, 1H), 7.41 (dd, *J* = 1.8, 1.8 Hz, 1H), 6.43 (q, *J* = 4.8 Hz, 1H), 6.29 (d, *J* = 1.8 Hz, 1H), 5.69 (s, 1H), 4.19 (s, 1H), 4.16 (s, 1H), 4.12 (dd, *J* = 10.6, 1.6 Hz, 1H), 3.92 (d, *J* = 9.0 Hz, 1H), 3.68 (d, *J* = 9.0 Hz, 1H), 3.50 (s, 1H), 2.78 (d, *J* = 4.8 Hz, 2H), 2.52 (dd, *J* = 12.2, 7.0 Hz, 1H), 2.43 (dd, *J* = 15.4, 1.6 Hz, 1H), 2.17 (dd, *J* = 15.4, 10.6 Hz, 1H), 1.89 (s, 1H), 1.86 – 1.80 (m, 2H), 1.77 – 1.67 (m, 1H), 1.53 – 1.48 (m, 1H), 1.47 (s, 3H), 1.32 (s, 3H), 1.30 (s, 3H), 1.26-1.21 (m, 1H), 1.22 (s, 3H). (34 non-exchangeable protons)
^{13}C NMR (CDCl$_3$, 125 MHz): δ 171.04, 167.70, 143.21, 141.23, 120.30, 109.61, 82.97, 80.06, 78.47, 78.41, 76.54, 75.31, 66.69, 66.06, 58.26, 58.23, 43.88, 42.65, 39.95, 39.67, 31.29, 26.32, 25.40, 24.81, 20.35, 19.12, 12.67.
HRMS(ESI): m/z calc. for $C_{27}H_{36}NO_8$ $[M+H]^+$: 502.2441, found: 502.2443.
mp: 158-159° C.
Opt. Rot.: $[\alpha]_D^{25}$ = + 43 (c = 0.15, acetone).



Procedure: Triflic anhydride (80 µL, 0.47 mmol) was added at 0° C to a solution of **S24** (137 mg, 0.24 mmol) in dichloromethane (3 mL) and pyridine (77 µL) and the resulting mixture was stirred at 30° C for 12 h. The reaction was quenched with iced water and extracted three times with dichloromethane. The organic layers were combined, washed with brine, dried over Na_2SO_4, and concentrated by distillation under reduced pressure. The crude residue was purified by silica gel flash chromatography (hexane-ethyl acetate 4:6) to provide **S25** (93 mg, 61%) as a yellowish solid.

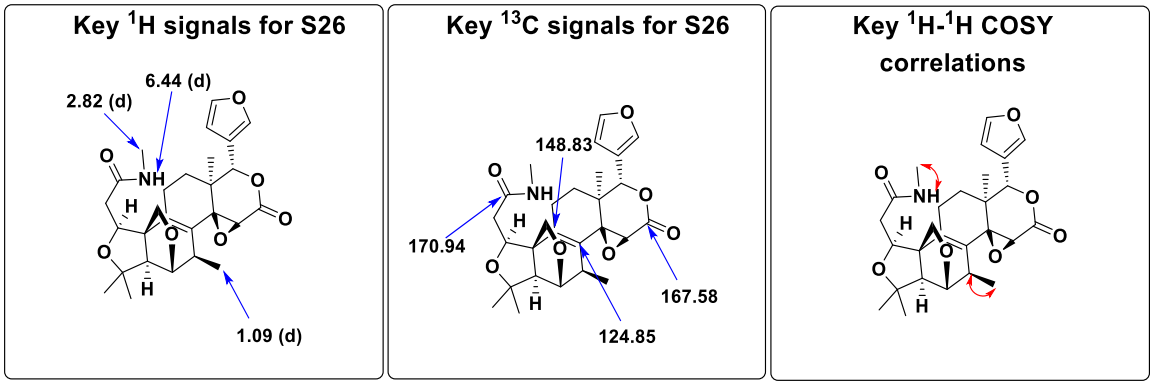
^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.36 (s, 1H), 7.35 (d, *J* = 1.8 Hz, 1H), 6.22 (d, *J* = 1.8 Hz, 1H), 6.19 (q, *J* = 4.8 Hz, 1H), 5.63 (s, 1H), 4.76 (s, 1H), 4.46 (s, 1H), 4.09 (dd, *J* = 10.2, 1.5 Hz, 1H), 4.08 (s, 1H), 3.94 (d, *J* = 9.1 Hz, 1H), 3.69 (d, *J* = 9.1 Hz, 1H), 2.72 (d, *J* = 4.8 Hz, 3H), 2.53 (dd, *J* = 12.4, 6.8 Hz, 1H), 2.37 (dd, *J* = 15.1, 1.5 Hz, 1H), 2.11 (dd, *J* = 15.1, 10.2 Hz, 1H), 1.89 (s, 1H), 1.87 – 1.72 (m, 2H), 1.68 (dd, *J* = 13.7, 8.8 Hz, 1H), 1.53 (s, 3H), 1.42 (dd, *J* = 13.7, 9.4 Hz, 1H), 1.29 (s, 3H), 1.24 (s, 3H), 1.19 (s, 3H).
^{13}C NMR ($CDCl_3$, 125 MHz): δ 170.56, 166.92, 143.34, 141.36, 119.99, 117.98 (q, *J* = 313 Hz, 1C), 109.53, 90.25, 80.13, 79.88, 78.03, 76.38, 74.32, 66.47, 65.81, 58.42, 57.66, 44.04, 43.39, 40.57, 39.67, 31.05, 26.37, 25.19, 24.67, 20.63, 19.29, 13.94..
^{19}F NMR ($CDCl_3$, 470 MHz): δ - 75.22.
HRMS(ESI): m/z calc. for $C_{28}H_{35}NO_{10}SF_3$ $[M+H]^+$: 634.19341, found: 634.1925.
mp: decomposes upon heating above 120° C.
Opt. Rot.: $[\alpha]_D^{25}$ = + 75 (c = 0.08, acetone).

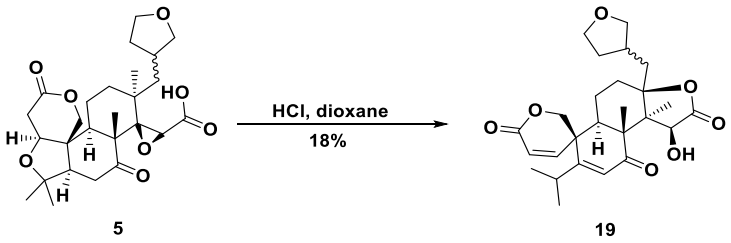




Procedure: DMAP (41 mg, 0.34 mmol) was added to a solution of **S25** (86 mg, 0.13 mmol) in toluene (2 mL) and the resulting solution was heated at 100° C for 12 h. Toluene was evaporated and the residue partitioned between water and dichloromethane. The aqueous layer was extracted three times with dichloromethane. The organic layers were combined, washed with brine, dried over Na_2SO_4, and concentrated by distillation under reduced pressure. The crude residue was purified by silica gel flash chromatography (ethyl acetate) to provide **S26** 87% pure, which was further purified by silica gel flash chromatography (dichloromethane-methanol 95:5) to provide **S26** 90% pure (54 mg, 82%) as a white solid.

^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.45 (d, *J* = 2.0 Hz, 1H), 7.42 (dd, *J* = 2.0, 2.0 Hz 1H), 6.44 (d, *J* = 4.8 Hz, 1H), 6.38 (d, *J* = 2.0 Hz, 1H), 5.53 (s, 1H), 4.35 (dd, *J* = 10.4, 1.6 Hz, 1H), 4.08 (d, *J* = 3.0 Hz, 1H), 4.07 (s, 1H), 3.90 (d, *J* = 7.5 Hz, 1H), 3.76 (d, *J* = 7.5 Hz, 1H), 2.82 (d, *J* = 4.8 Hz, 3H), 2.62 (dd, *J* = 15.2, 1.6 Hz, 1H), 2.40 – 2.29 (m, 3H), 2.16 (s, 1H), 1.71 – 1.58 (m, 2H), 1.56 – 1.47 (m, 1H), 1.34 (s, 3H), 1.33 (s, 3H), 1.09 (d, *J* = 6.7 Hz, 3H), 0.94 (s, 3H).
^{13}C NMR ($CDCl_3$, 125 MHz): δ 170.94, 167.58, 148.83, 143.27, 141.18, 124.85, 119.92, 109.85, 80.51, 79.62, 76.96, 73.74, 73.09, 66.54, 64.68, 58.67, 54.08, 42.51, 40.14, 37.99, 30.86, 26.51, 26.32, 24.67, 23.64, 16.72, 13.45.
HRMS(ESI): m/z calc. for $C_{27}H_{34}NO_7$ $[M+H]^+$: 484.2335, found: 484.2333.
Opt. Rot.: $[\alpha]_D^{25}$ = + 53 (c = 0.15, acetone).



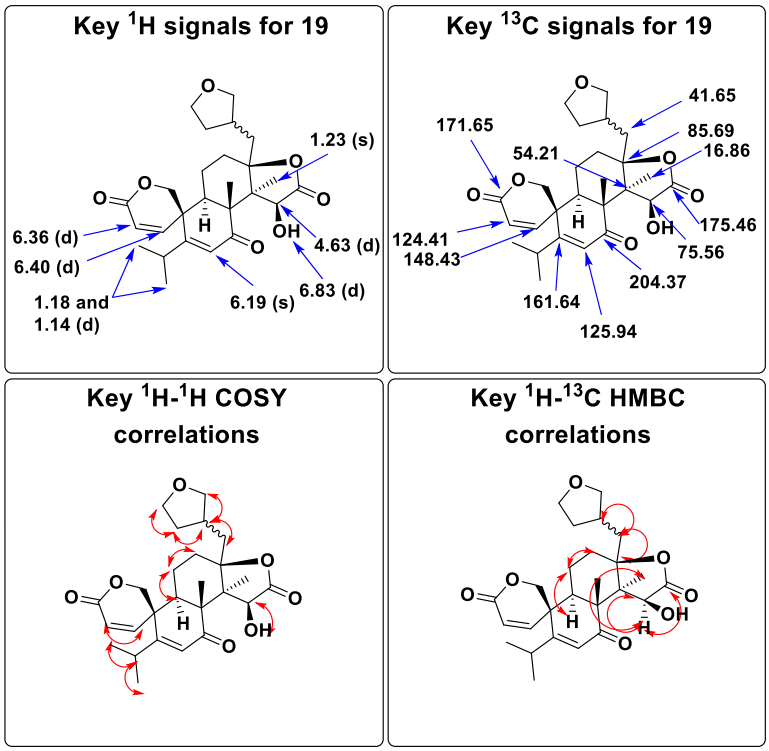


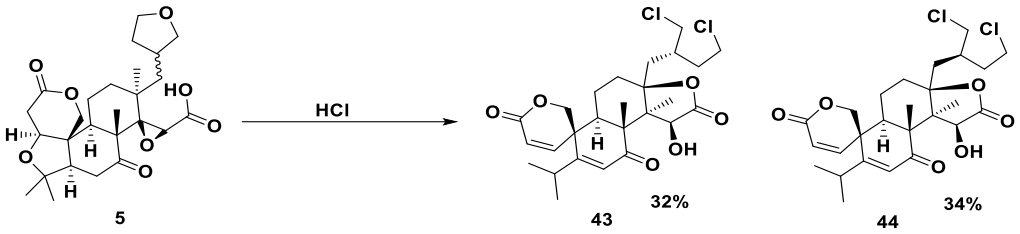
Procedure: Hydrochloric acid (12 M, 3.2 mL) was added to a solution of **5** (200 mg, 0.40 mmol) in dioxane (3.2 mL) and the resulting solution was heated to 100° C for 18 h. After cooling, dioxane was evaporated under vacuum, and the residue was taken up with water (4 mL), and slowly basified to pH 8 with a saturated solution of $NaHCO_3$. The aqueous layer was then extracted three times with dichloromethane. The organic layers were combined, washed with brine, dried over Na_2SO_4, and concentrated by distillation under reduced pressure. The crude residue was purified by silica gel flash chromatography (hexane-ethyl acetate 1:1) to provide **19** (34 mg, 18%) as a white solid.

Note: Compounds **19**, as its starting material, exists as a mixture of two diastereomers (4:3 ratio)

^{1}H NMR ($CDCl_3$, 500 MHz): δ 6.83 (d, *J* = 2.1 Hz, 1H), 6.82 (d, *J* = 2.1 Hz, 1H), 6.40 (d, *J* = 9.9 Hz, 2H), 6.36 (d, *J* = 9.8 Hz, 2H), 6.19 (s, 2H), 4.68 (d, *J* = 12.2 Hz, 2H), 4.63 (d, 2.1 Hz, 1H), 4.61 (d, 2.1 Hz, 1H), 4.47 (d, *J* = 12.2 Hz, 2H), 4.04 (dd, *J* = 8.9, 7.2 Hz, 1H), 3.93 (t, *J* = 7.8 Hz, 1H), 3.87 – 3.61 (m, 6H), 3.23 (t, *J* = 8.3 Hz, 1H), 3.14 (t, *J* = 8.8 Hz, 1H), 2.55 – 2.45 (m, 4H), 2.39 – 2.33 (m, 1H), 2.23 – 2.18 (m, 1H), 2.16 – 2.04 (m, 2H), 2.00 – 1.92 (m, *2*H), 1.87 – 1.71 (m, 4H), 1.67 – 1.58 (m, 4H), 1.50 – 1.43 (m, 2H), 1.48 (s, 3H), 1.47 (s, 3H), 1.24 (s, Hz, 3H), 1.23 (s, 3H), 1.18 (d, *J* = 6.8 Hz, 6H), 1.14 (d, *J* = 6.8 Hz, 6H).

^{13}C NMR (CDCl$_3$, 125 MHz): δ 204.37, 175.46, 175.25, 171.65, 171.63, 161.64, 148.43, 125.94, 124.41, 85.69, 85.64, 75.56, 75.43, 74.06, 73.91, 70.06, 68.23, 67.08, 54.21, 54.12, 52.03, 45.17, 43.97, 42.39, 41.65, 34.94, 34.24, 34.07, 31.86, 31.49, 24.15, 24.00, 18.41, 18.39, 16.95, 16.86.
HRMS(ESI): m/z calc. for $C_{26}H_{35}O_7$ $[M+H]^+$: 459.2383, found: 459.2378.
mp: decomposes upon heating above 240° C.
Opt. Rot.: $[\alpha]_D^{25}$ = - 42 (c = 0.15, acetone).

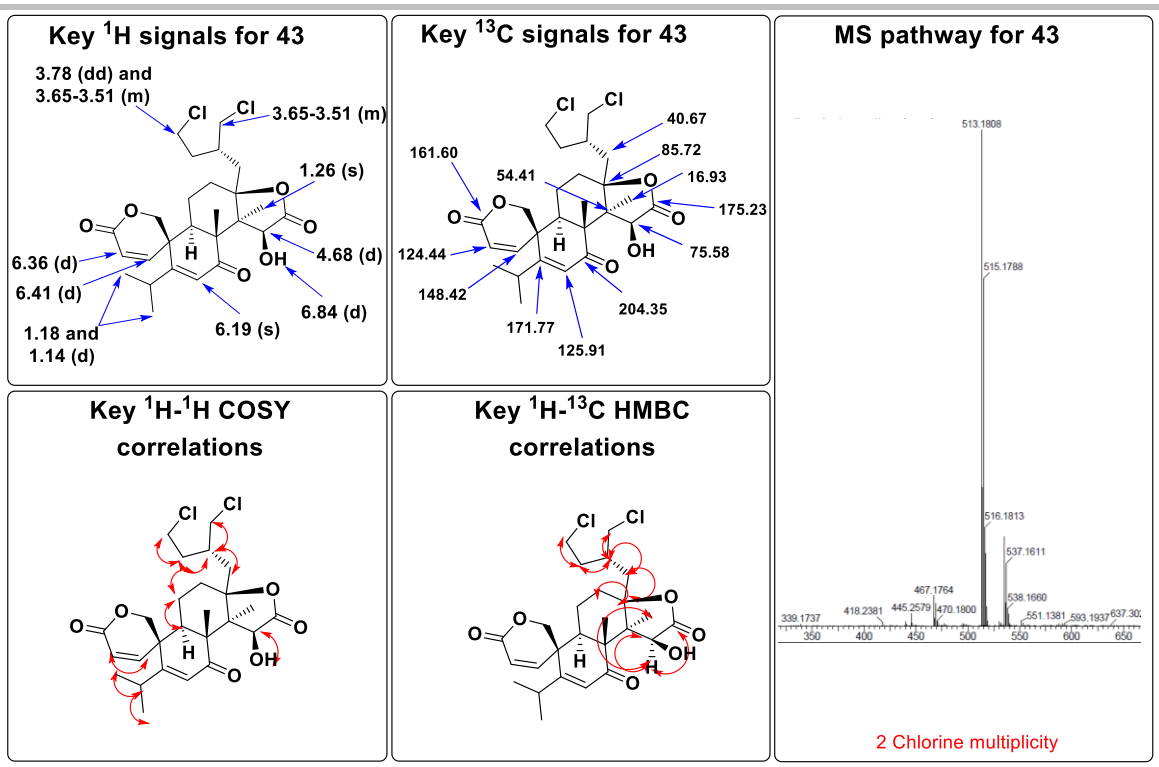




Procedure: A solution of **5** (200 mg, 0.40 mmol) in hydrochloric acid (12 M, 3.2 mL) was refluxed for 18 h. After cooling, the solvent was evaporated and the obtained residue was taken up with water (2 mL), and slowly basified to pH 8 with a saturated solution of $NaHCO_3$. The aqueous layer was then extracted three times with dichloromethane. The organic layers were combined, washed with brine, dried over Na_2SO_4, and concentrated by distillation under reduced pressure. The crude residue was purified by silica gel flash chromatography (hexane-ethyl acetate 1:1) to provide ***43*** (66 mg, 32%) and ***44*** (70 mg, 34%) as a white solid.

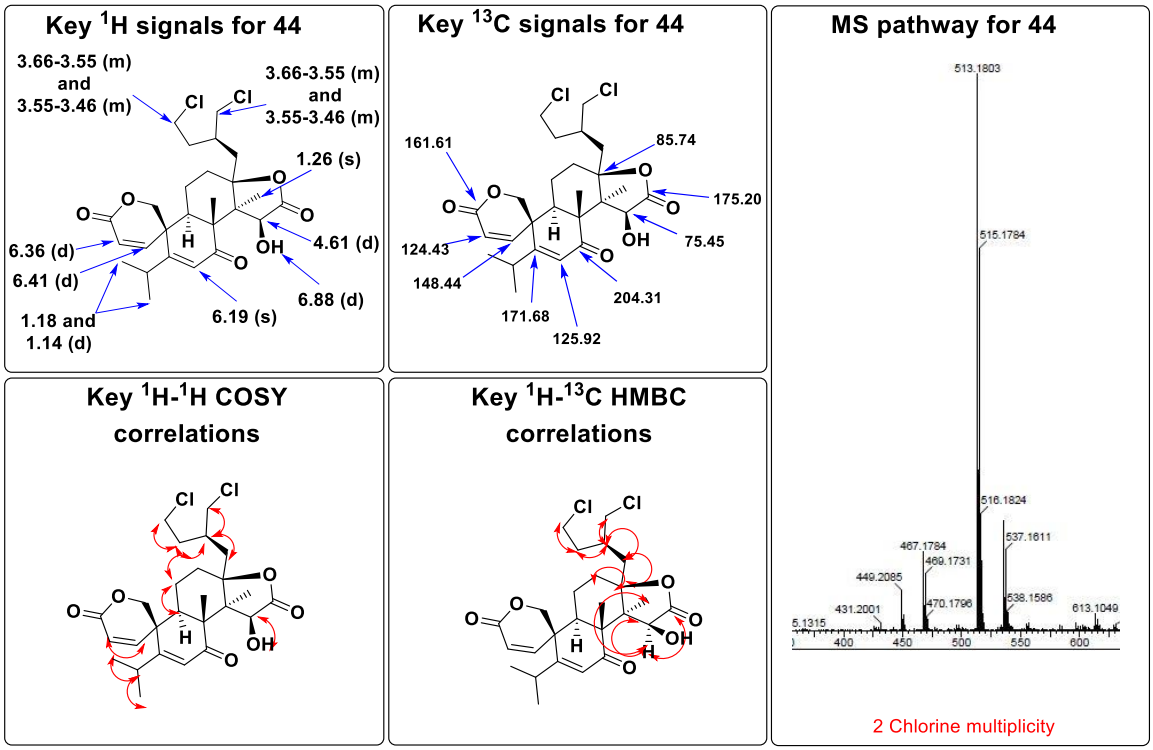
43 *(*66 mg, 32%)

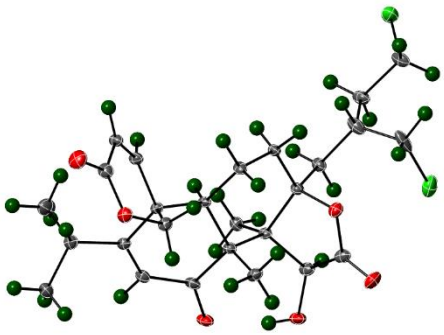
^{1}H NMR (CDCl$_3$, 500 MHz): δ 6.84 (d, *J* = 2.2 Hz, 1H), 6.41 (d, *J* = 9.9 Hz, 1H), 6.36 (d, *J* = 9.9 Hz, 1H), 6.19 (s, 1H), 4.68 (d, *J* = 2.2 Hz, 1H), 4.68 (dd, *J* = 12.2, 1.1 Hz, 1H), 4.47 (d, *J* = 12.2 Hz, 1H), 3.78 (dd, *J* = 11.6, 3.5 Hz, 1H), 3.65 – 3.51 (m, 3H), 2.55 (ddd, *J* = 15.3, 4.2, 2.4 Hz, 1H), 2.49 (p, *J* = 6.7 Hz, 1H), 2.44 – 2.40 (m, 1H), 2.19 (dd, *J* = 14.8, 8.8 Hz, 1H), 2.14 (dd, *J* = 12.8, 2.1 Hz, 1H), 2.04 – 1.93 (m, 2H), 1.78 – 1.71 (m, 1H), 1.66 (ddt, *J* = 13.9, 5.0, 2.2 Hz, 1H), 1.53 – 1.50 (m, 1H), 1.48 (s, 3H), 1.27 – 1.25 (m, 1H), 1.26 (s, 3H), 1.18 (d, *J* = 6.7 Hz, 3H), 1.14 (d, *J* = 6.7 Hz, 3H).
^{13}C NMR (CDCl$_3$, 125 MHz): δ 204.35, 175.23, 171.77, 161.60, 148.42, 125.91, 124.44, 85.72, 75.58, 70.10, 54.41, 52.11, 48.93, 45.16, 44.03, 42.07, 40.67, 35.35, 33.57, 32.02, 31.50, 24.13, 24.00, 18.44, 18.40, 16.93.
HRMS(ESI): m/z calc. for $C_{26}H_{35}O_6Cl_2$ $[M+H]^+$: 513.1811, found: 513.1808.
mp: >260° C.
Opt. Rot.: $[\alpha]_D^{25}$ = - 19 (c = 0.11, acetone).



44 (70 mg, 34%)

H NMR (CDCl₃, 500 MHz): δ 6.88 (d, *J* = 2.2 Hz, 1H), 6.41 (d, *J* = 9.9 Hz, 1H), 6.36 (d, *J* = 9.9 Hz, 1H), 6.19 (s, 1H), 4.67 (dd, *J* = 12.2, 1 Hz, 1H), 4.61 (d, *J* = 2.2 Hz, 1H), 4.47 (d, *J* = 12.2 Hz, 1H), 3.66 – 3.55 (m, 2H), 3.55 – 3.46 (m, 2H), 2.58 – 2.48 (m, 2H), 2.35 – 2.29 (m, 1H), 2.15 (dd, *J* = 12.8, 2.1 Hz, 1H), 2.07 – 1.92 (m, 2H), 1.85 – 1.73 (m, 3H), 1.71 – 1.62 (m, 1H), 1.53 (dd, *J* = 5.5, 1.9 Hz, 1H), 1.48 (s, 3H), 1.26 (s, 3H), 1.18 (d, *J* = 6.8 Hz, 3H), 1.14 (d, *J* = 6.8 Hz, 3H).
^{13}C NMR (CDCl₃, 125 MHz): δ 204.31, 175.20, 171.68, 161.61, 148.44, 125.92, 124.43, 85.74, 75.45, 70.09, 54.50, 52.06, 48.66, 45.18, 44.07, 42.22, 38.61, 36.02, 32.05 (2C), 31.50, 24.13, 24.00, 18.45, 18.40, 16.79.
HRMS(ESI): m/z calc. for $C_{26}H_{35}O_6Cl_2$ $[M+H]^+$: 513.1811, found: 513.1803.
mp: 253-255° C.
Opt. Rot.: $[\alpha]_D^{25}$ = - 38 (c = 0.12, acetone).





Crystallography

Experimental Protocol: Intensity data were collected on a Bruker D8 Venture kappa diffractometer equipped with a Photon 100 CMOS detector. An Iμs microfocus Mo source (λ = 0.71073 Å) coupled with a multi-layer mirror monochromator provided the incident beam. The sample was mounted on a 0.3 mm loop with the minimal amount of Paratone-N oil. Data was collected as a series of φ and/or ω scans. Data was collected at 100 K using a cold stream of N2(g). The collection, cell refinement, and integration of intensity data was carried out with the APEX3 software.[1] A semi-empirical absorption correction was performed with SADABS.[2] The structure was phased with intrinsic methods using SHELXT[3] and refined with the full-matrix least-squares program SHELXL.[4]

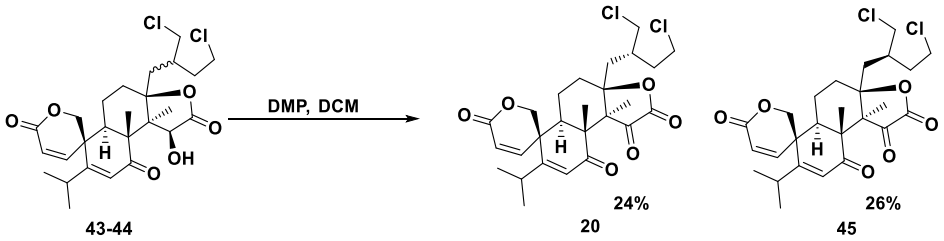
CCDC: 2082416

(1) Bruker (2016). APEX3. Bruker AXS, Inc., Madison, Wisconsin, USA.
(2) L. Krause, R. Herbst-Irmer, G. M. Sheldrick, D. Stalke, *J. Appl. Cryst.*, **2015,** *48*, 3–10.
(3) G. M. Sheldrick, *Acta Cryst.* **2015**, A71, 3–8.
(4) G. M. Sheldrick, *Acta Cryst*. **2015**, C71, 3–8.

Table S7. Crystal data and structure refinement for ed85cs.

Identification code ed85cs

Empirical formula C26 H34 Cl2 O6
Formula weight 513.43
Temperature 100(2) K
Wavelength 0.71073 Å
Crystal system Monoclinic
Space group $P2_1$
Unit cell dimensions a = 8.6271(3) Å a= 90°.
b = 22.9853(8) Åb= 97.1495(10)°.
c = 12.8535(5) Åg = 90°.
Volume 2528.99(16) Å3
Z 4
Density (calculated) 1.348 Mg/m3
Absorption coefficient 0.296 mm-1
F(000) 1088
Crystal size 0.424 x 0.368 x 0.215 mm3
Theta range for data collection 2.379 to 28.303°.
Index ranges -11<=h<=11, -30<=k<=30, -17<=l<=17
Reflections collected 86750
Independent reflections 12497 [R(int) = 0.0472]
Completeness to theta = 25.242° 99.9 %
Absorption correction Semi-empirical from equivalents
Max. and min. transmission 0.7457 and 0.6893
Refinement method Full-matrix least-squares on F2
Data / restraints / parameters 12497 / 83 / 684
Goodness-of-fit on F2 1.097
Final R indices [I>2sigma(I)]R1 = 0.0696, wR2 = 0.1895
R indices (all data) R1 = 0.0707, wR2 = 0.1903
Absolute structure parameter 0.091(14)
Extinction coefficient n/a
Largest diff. peak and hole 1.097 and -0.569 e.Å-3

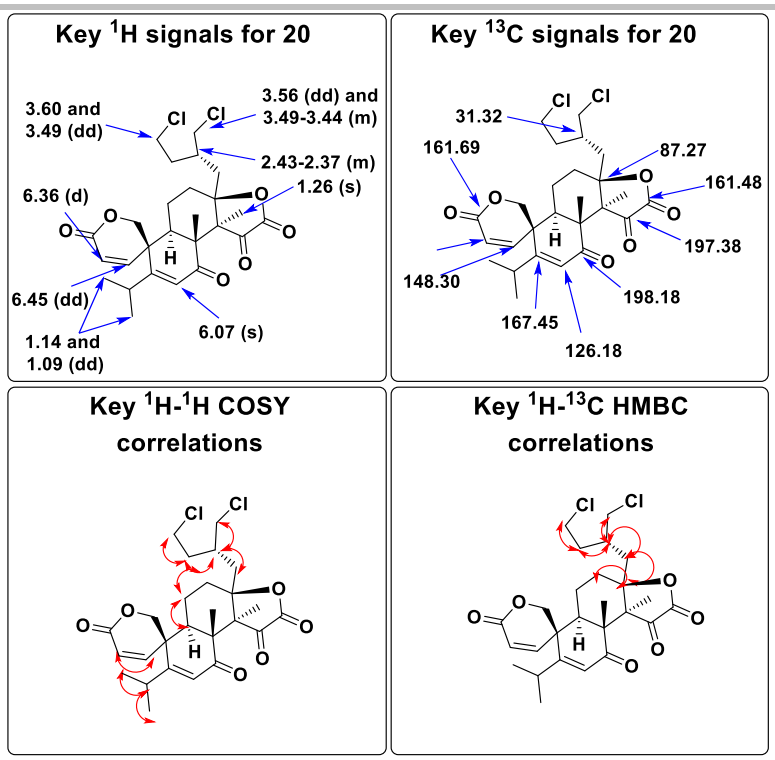


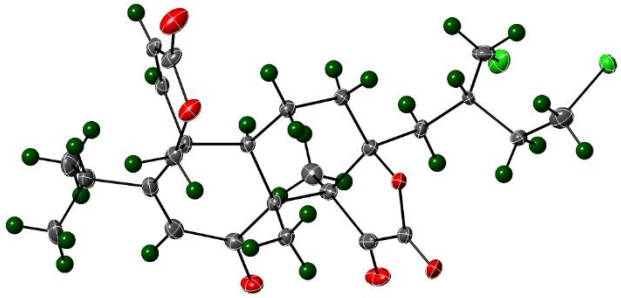
43-44 **20** **45**

Procedure: Dess-Martin periodinane (164 mg, 0.39 mmol) was added to a solution of a mixture of **43** and **44** (100 mg, 0.19 mmol) in dichloromethane (2.4 mL) and the resulting solution was stirred at 30° C for 3 h. A 5% $NaHCO_3$ solution was added to the reaction mixture and the aqueous layer was extracted three times with dichloromethane. The organic layers were combined, washed with brine, dried over Na_2SO_4, and concentrated by distillation under reduced pressure. The crude residue was purified by silica gel flash chromatography (hexane-ethyl acetate 1:1) to provide **20** (23 mg, 24%) and **45** (26 mg, 26%) as white solids.

20 (23 mg, 24%)

^{1}H NMR ($CDCl_3$, 500 MHz): δ 6.45 (dd, *J* = 9.9, 1.5 Hz, 1H), 6.36 (d, *J* = 9.9 Hz, 1H), 6.07 (s, 1H), 4.66 (dd, *J* = 12.3, 1.5 Hz, 1H), 4.46 (d, *J* = 12.3 Hz, 1H), 3.60 (dd, *J* = 11.5, 3.4 Hz, 1H), 3.56 (dd, *J* = 11.4, 5.8 Hz, 1H), 3.49 (dd, *J* = 11.5, 5.8 Hz, 1H), 3.49 – 3.44 (m, 1H), 2.61 (ddd, *J* = 15.3, 4.1, 2.4 Hz, 1H), 2.44 (hept, *J* = 6.7 Hz, 1H), 2.43 – 2.37 (m, 1H), 2.17 – 2.07 (m, 2H), 1.94 (dd, *J* = 13.4, 3.9 Hz, 1H), 1.93 – 1.88 (m, 1H), 1.82 – 1.70 (m, 2H), 1.67 – 1.62 (m, 1H), 1.38 (s, 3H), 1.26 (s, 3H), 1.15 (d, *J* = 6.7, 3H), 1.14 (d, *J* = 6.7, 3H), 1. 09 (dd, *J* = 13.4, 6.5 Hz, 1H).
^{13}C NMR ($CDCl_3$, 125 MHz): δ 198.18, 197.38, 167.45, 161.69, 161.48, 148.30, 126.18, 124.21, 87.27, 69.53, 56.49, 49.92, 48.52, 45.16, 44.07, 42.65, 41.87, 35.24, 32.42, 31.32, 30.80, 24.26, 24.15, 21.06, 18.53, 13.49.
HRMS(ESI): m/z calc. for $C_{26}H_{33}O_6Cl_2$ $[M+H]^+$: 511.1654, found: 511.1668.
mp: 252-253° C.
Opt. Rot.: $[\alpha]_D^{25}$ = - 90 (c = 0.12, acetone).





Crystallography

Experimental Protocol: Intensity data were collected on a Bruker D8 Venture kappa diffractometer equipped with a Photon 100 CMOS detector. An Iμs microfocus Mo source (λ = 0.71073 Å) coupled with a multi-layer mirror monochromator provided the incident beam. The sample was mounted on a 0.3 mm loop with the minimal amount of Paratone-N oil. Data was collected as a series of φ and/or ω scans. Data was collected at 100 K using a cold stream of N2(g). The collection, cell refinement, and integration of intensity data was carried out with the APEX3 software.[1] A semi-empirical absorption correction was performed with SADABS.[2] The structure was phased with intrinsic methods using SHELXT[3] and refined with the full-matrix least-squares program SHELXL.[4]

CCDC: 2082414

(1) Bruker (2016). APEX3. Bruker AXS, Inc., Madison, Wisconsin, USA.
(2) L. Krause, R. Herbst-Irmer, G. M. Sheldrick, D. Stalke, *J. Appl. Cryst.*, **2015,** *48*, 3–10.
(3) G. M. Sheldrick, *Acta Cryst.* **2015**, A71, 3–8.
(4) G. M. Sheldrick, *Acta Cryst*. **2015**, C71, 3–8.

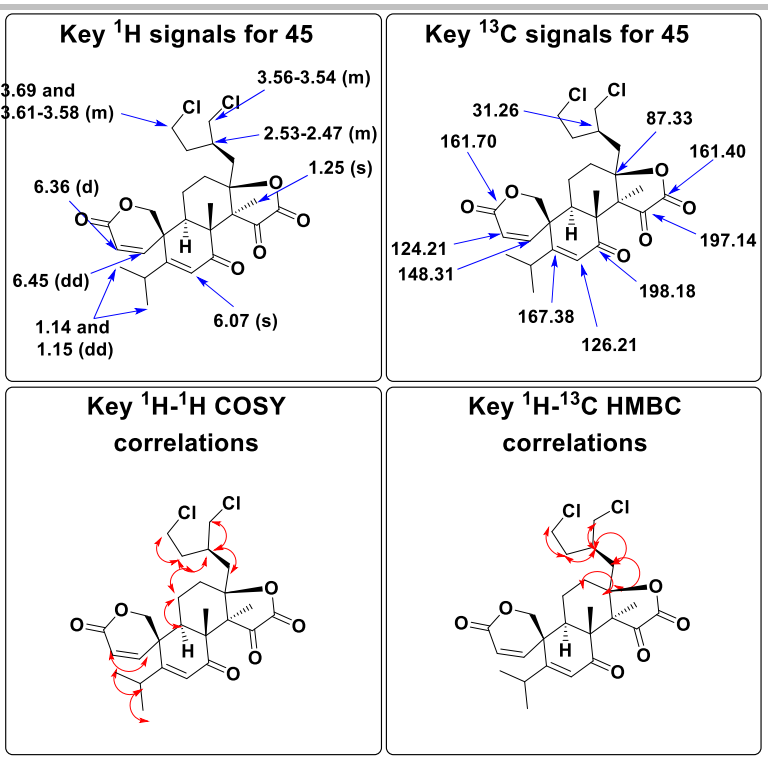
Table S8. Crystal data and structure refinement for ed25ds.

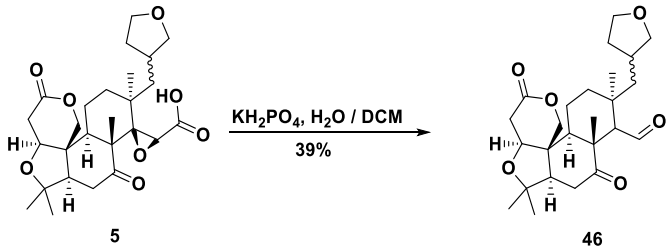
Identification code	ed25ds

Empirical formula C26 H32 Cl2 O6
Formula weight 511.41
Temperature 100(2) K
Wavelength 1.54178 Å
Crystal system Monoclinic
Space group $P2_1$
Unit cell dimensions a = 9.2445(3) Å a= 90°.
b = 11.2142(3) Åb= 109.4239(7)°.
c = 12.7629(4) Åg = 90°.
Volume 1247.82(7) Å3
Z 2
Density (calculated) 1.361 Mg/m3
Absorption coefficient 2.671 mm-1
F(000) 540
Crystal size 0.326 x 0.289 x 0.282 mm3
Theta range for data collection 3.672 to 68.470°.
Index ranges -11<=h<=11, -13<=k<=13, -15<=l<=15
Reflections collected 26142
Independent reflections 4585 [R(int) = 0.0415]
Completeness to theta = 67.679° 100.0 %
Absorption correction Semi-empirical from equivalents
Max. and min. transmission 0.7531 and 0.6555
Refinement method Full-matrix least-squares on F2
Data / restraints / parameters 4585 / 273 / 405
Goodness-of-fit on F2 1.023
Final R indices [I>2sigma(I)]R1 = 0.0334, wR2 = 0.0932
R indices (all data) R1 = 0.0339, wR2 = 0.0938
Absolute structure parameter 0.006(5)
Extinction coefficient n/a
Largest diff. peak and hole 0.471 and -0.230 e.Å-3

45 (26 mg, 26%)

^{1}H NMR ($CDCl_3$, 500 MHz): δ 6.45 (dd, *J* = 9.9, 1.5 Hz, 1H), 6.36 (d, *J* = 9.9 Hz, 1H), 6.07 (s, 1H), 4.66 (dd, *J* = 12.3, 1.5 Hz, 1H), 4.46 (d, *J* = 12.3 Hz, 1H), 3.69 (dd, *J* = 11.7, 3.6 Hz, 1H), 3.61 – 3.58 (m, 1H), 3.56 – 3.54 (m, 2H), 2.63 (dd, *J* = 14.8, 3.4 Hz, 1H), 2.53 – 2.47 (m, 1H), 2.44 (hept, *J* = 6.7, 1H), 2.14 – 2.08 (m, 2H), 2.02 – 1.93 (m, 1H), 1.81 – 1.71 (m, 2H), 1.64 – 1.58 (m, 1H), 1.46 (d, *J* = 6.0 Hz, 2H), 1.38 (s, 3H), 1.25 (s, 3H), 1.15 (d, *J* = 6.7 Hz, 3H), 1.14 (d, *J* = 6.7 Hz, 3H).
^{13}C NMR ($CDCl_3$, 125 MHz): δ 198.18, 197.14, 167.38, 161.70, 161.40, 148.31, 126.21, 124.21, 87.33, 69.51, 56.45, 49.88, 47.72, 45.17, 42.70, 42.39, 42.10, 35.66, 31.32, 31.26, 30.79, 24.27, 24.15, 21.09, 18.51, 13.45.
HRMS(ESI): m/z calc. for $C_{26}H_{33}O_6Cl_2$ $[M+H]^+$: 511.1654, found: 511.1652.
mp: 214-215° C.
Opt. Rot.: $[\alpha]_D^{25}$ = - 118 (c = 0.10, acetone).



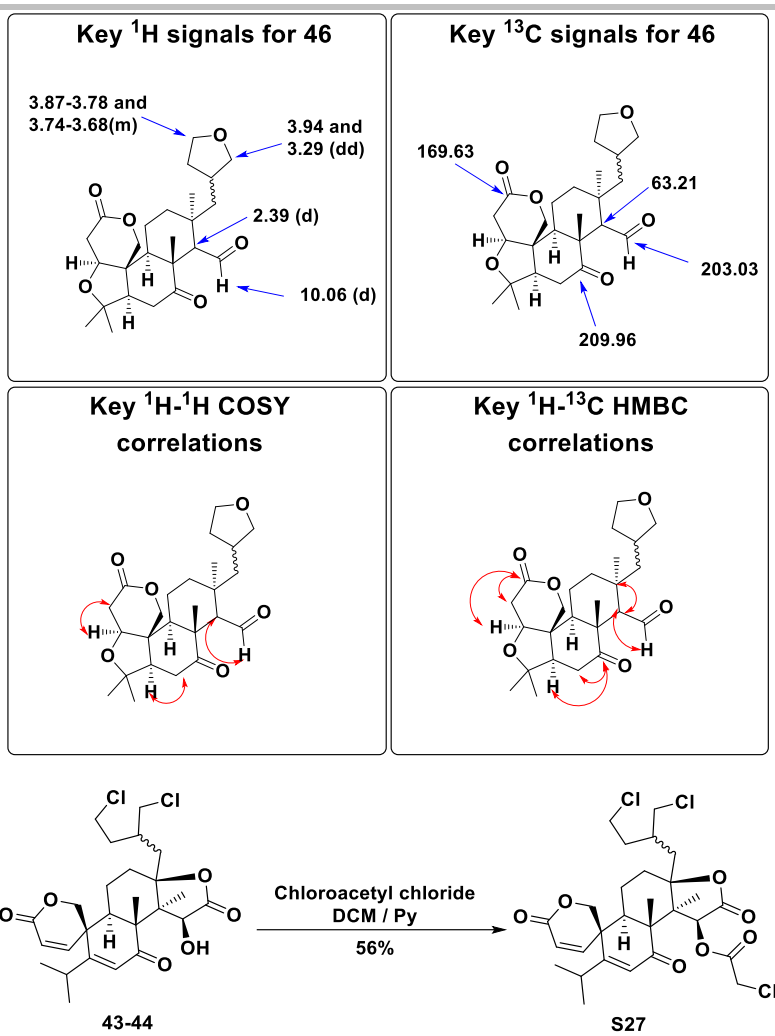


5 46

Procedure: A 0.2 M aqueous solution of potassium phosphate monobasic (1 mL) was added to a solution of **5** (100 mg, 0.20 mmol) in dichloromethane (0.4 mL) and the resulting mixture was heated at 100° C for 24 h. After cooling, water was added to the reaction mixture, and the aqueous layer was extracted three times with dichloromethane. The organic layers were combined, washed with brine, dried over Na_2SO_4, and concentrated by distillation under reduced pressure. The crude residue was purified by silica gel flash chromatography (hexane-ethyl acetate 3:7) to provide **46** (34 mg, 39%) as a white solid.

Note: Compounds **46**, as its starting material, exists as a mixture of two diastereomers (5:4 ratio).

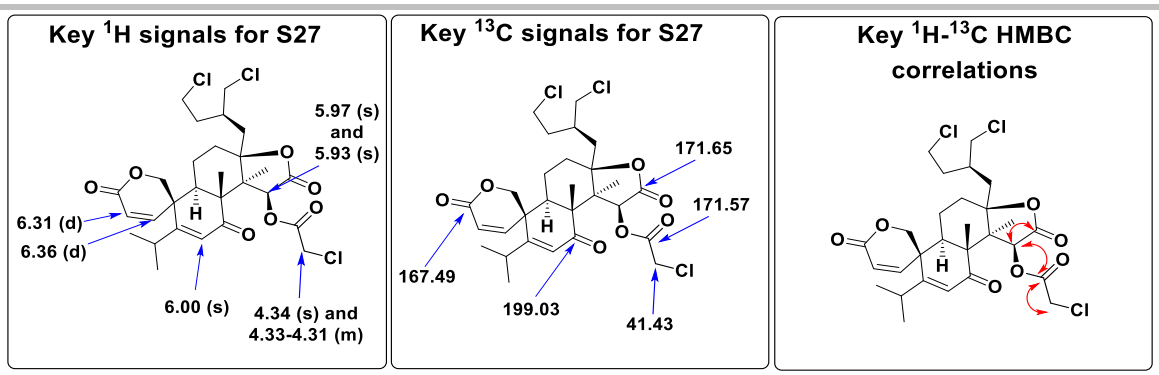
^{1}H NMR ($CDCl_3$, 500 MHz): δ 10.06 (d, *J* = 3.2 Hz, 1H), 10.05 (d, *J* = 3.2 Hz, 1H), 4.73 (d, *J* = 12.7 Hz, 1H), 4.72 (d, *J* = 12.7 Hz, 1H), 4.53 (d, *J* = 12.7 Hz, 1H), 4.51 (d, *J* = 12.7 Hz, 1H), 4.05 (t, *J* = 2.7 Hz, 2H), 3.94 (dd, *J* = 7.6, 7.6 Hz, 1H), 3.90 (dd, *J* = 7.6, 7.6 Hz, 1H), 3.87 – 3.78 (m, 2H), 3.74 – 3.68 (m, 2H), 3.19 – 3.13 (m, *2*H), 2.96 (dd, *J* = 16.9, 3.5 Hz, 2H), 2.89 (dd, *J* = 14.1, 14.1 Hz, 2H), 2.76 (dd, *J* = 16.9, 2.7 Hz, 1H), 2.74 (dd, *J* = 16.9, 2.7 Hz, 1H), 2.39 (d, *J* = 3.2 Hz, 2H), 2.34 (dd, *J* = 14.1, 3.0 Hz, 2H), 2.14 – 2.02 (m, 7H), 1.94 – 1.89 (m, 2H), 1.86 (dd, *J* = 12.8, 3.2 Hz, 1H), 1.80 – 1.71 (m, 2H), 1.71 – 1.64 (m, 4H), 1.59 – 1.55 (m, 3H), 1.54 (s, 3H), 1.52 (s, 3H), 1.52 – 1.42 (m, 3H), 1.25 (s, 6H), 1.17 (s, *6*H), 1.14 (s, 3H), 1.09 (s, 3H).
^{13}C NMR ($CDCl_3$, 125 MHz): δ 209.96, 209.92, 203.02, 202.93, 169.63, 169.55, 80.03, 80.00, 78.50, 78.43, 74.70, 74.36, 67.83, 67.65, 65.44, 65.33, 63.21, 63.17, 60.01, 59.97, 56.17, 56.10, 54.08, 46.26, 46.20, 38.90, 38.88, 38.71, 38.55, 37.12, 37.10, 35.89, 35.86, 35.83, 35.69, 34.90, 34.82, 34.42, 30.28, 30.24, 29.71, 29.00, 21.96, 21.85, 21.03, 20.89, 17.47, 17.44.
HRMS(ESI): m/z calc. for $C_{26}H_{37}O_6$ $[M+H]^+$: 433.2590, found: 433.2591.
mp: 182-183° C.
Opt. Rot.: $[\alpha]_D^{25}$ = - 165 (c = 0.12, acetone).

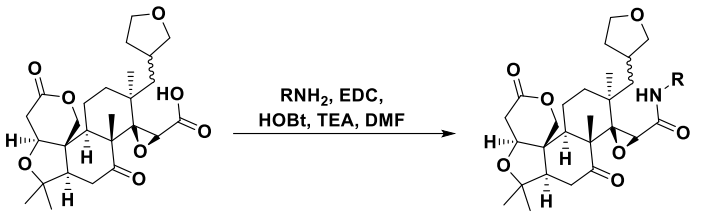


Procedure: Pyridine (12 µL, 0.15 mmol) and chloroacetyl chloride (12 µL, 0.15 mmol) were added to a solution of **43** and **44** (50 mg, 0.10 mmol) in dichloromethane (0.5 mL), and the resulting solution was stirred at 45 °C for 24 h. Water and dichloromethane were added to the mixture and the aqueous layer was extracted three times with dichloromethane. The combined organic layers were washed with brine and dried over Na_2SO_4. The solvent was concentrated by distillation under reduced pressure and the obtained crude residue was purified by silica gel flash chromatography (hexane-ethyl acetate 6:4) to provide **S27** (32 mg, 56%) as a white solid.

Note: Compounds **S27**, as its starting material, exists as a mixture of two diastereomers (1:1 ratio)

H NMR ($CDCl_3$, 500 MHz): δ 6.36 (d, *J* = 9.9 Hz, 2H), 6.31 (d, *J* = 9.9 Hz, 2H), 6.00 (s, 2H), 5.97 (s, 1H), 5.93 (s, 1H), 4.71 (dd, *J* = 12.4, 1.4 Hz, 2H), 4.49 (d, *J* = 12.4 Hz, 2H), 4.34 (s, 2H), 4.33 – 4.31 (m, 2H), 3.80 (dd, *J* = 11.5, 3.4 Hz, 1H), 3.64 – 3.47 (m, 7H), 2.58 – 2.48 (m, 2H), 2.46 – 2.37 (m, 2H), 2.42 (hept, *J* = 6.7 Hz, 2H), 2.33 (dq, *J* = 9.9, 5.4 Hz, 1H), 2.24 (dd, *J* = 14.9, 8.8 Hz, 1H), 2.09 – 1.92 (m, 6H), 1.89 (q, *J* = 3.8, 2.7 Hz, 2H), 1.83 – 1.73 (m, 2H), 1.67 (ddt, *J* = 13.6, 4.8, 2.0 Hz, 2H), 1.62 – 1.48 (m, 2H), 1.43 (s, 3H), 1.43 (s, 3H), 1.31 (s, 6H), 1.15 (d, *J* = 6.8 Hz, 6H), 1.11 (d, *J* = 6.7 Hz, 6H).
^{13}C NMR ($CDCl_3$, 125 MHz): δ 199.03, 171.65, 171.57, 167.49, 167.45, 165.97, 165.92, 161.78, 148.75, 126.63, 126.60, 123.96, 87.23, 76.29, 69.56, 54.75, 54.53, 51.35, 51.33, 48.78, 48.33, 44.99, 44.97, 43.52, 43.48, 42.19, 42.02, 41.43, 41.39, 40.71, 38.46, 35.96, 35.40, 33.43, 31.96, 31.32, 31.27, 30.91, 24.23, 24.19, 18.16, 18.12, 18.07, 17.16, 17.12.
HRMS(ESI): m/z calc. for $C_{28}H_{36}O_7Cl_3$ $[M+H]^+$: 589.1527, found: 589.1527.
mp: decomposes upon heating above 140° C.
Opt. Rot.: $[\alpha]_D^{25}$ = + 43 (c = 0.17, acetone).



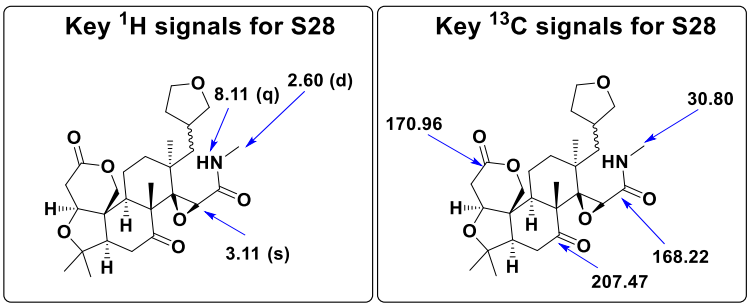


Procedure: HOBt (18 mg, 0.115 mmol), EDC (22 µL, 0.12 mmol) and TEA (29 µL, 0.21 mmol) were added to a solution of **4** (50 mg, 0.10 mmol) in DMF (0.7 ml), and the resulting mixture was stirred 30 minutes at 30° C. The suitable amine (0.11 mmol) was added to the mixture and the reaction was stirred overnight. The reaction was diluted with dichloromethane and washed with water, 5% citric acid, brine, 5% $NaHCO_3$ and Brine. The organic layer was dried over Na_2SO_4, concentrated by distillation at reduced pressure, and the residue was purified by flash chromatography on silica gel (ethyl acetate) giving **S28-S29** (44-76%) as white solids.

S28 (37 mg, 76%)

Note: Compounds **S28**, as its starting material, exists as a mixture of two diastereomers (1:1 ratio)

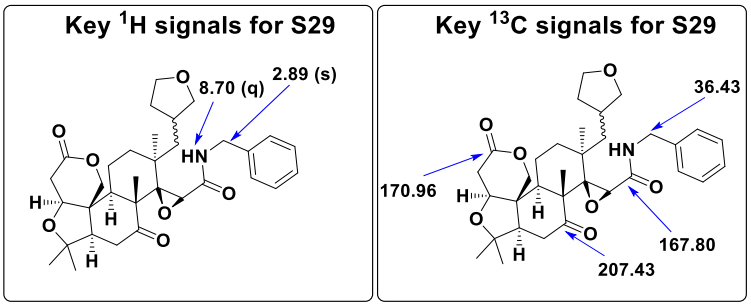
^{1}H NMR (DMSO-*d6*, 500 MHz): δ 8.11 (q, *J* = 4.6 Hz, 2H), 4.62 (d, *J* = 13.1 Hz, 1H), 4.61 (d, *J* = 13.1 Hz, 1H), 4.47 (d, *J* = 13.1 Hz, 2H), 4.22 (d, *J* = 3.7 Hz, 2H), 3.95 (t, *J* = 7.6 Hz, 1H), 3.80 (t, *J* = 7.6 Hz, 1H), 3.68 (ddd, *J* = 17.2, 8.4, 3.8 Hz, 2H), 3.64 – 3.54 (m, 2H), 3.11 (s, 1H), 3.09 (s, 1H), 3.09 (t, *J* = 8.3 Hz, 1H), 3.04 (t, *J* = 8.3 Hz, 1H), 2.85 – 2.74 (m, 4H), 2.66 (ddd, *J* = 17.8, 4.0, 1.6 Hz, 2H), 2.60 (d, *J* = 4.6 Hz, 3H), 2.59 (d, *J* = 4.6 Hz, 3H), 2.48 – 2.36 (m, 6H), 2.23 – 1.95 (m, 6H), 1.82 (dd, *J* = 14.5, 5.2 Hz, 1H), 1.78 – 1.59 (m, 5H), 1.55 (dd, *J* = 14.5, 5.5 Hz, 1H), 1.49 – 1.29 (m, 5H), 1.23 (s, 6H), 1.15 (s, 3H), 1.13 (s, 3H), 0.99 (s, 6H), 0.90 (s, 3H), 0.88 (s, 3H).
^{13}C NMR (DMSO-*d6*, 125 MHz): δ 207.47, 207.31, 170.96, 168.22, 80.34, 78.60, 78.56, 74.34, 71.54, 71.49, 67.46, 67.14, 64.29, 64.26, 59.51, 59.36, 55.70, 55.65, 55.38, 51.95, 51.83, 49.11, 48.58, 45.88, 45.86, 43.77, 43.52, 36.78, 36.72, 36.47, 36.45, 36.20, 36.16, 35.70, 34.92, 34.88, 30.80, 26.73, 26.68, 25.75, 25.73, 22.20, 20.18, 20.12, 18.73, 18.60.
HRMS(ESI): m/z calc. for $C_{27}H_{40}NO_7$ $[M+H]^+$: 490.2805, found: 490.2790.
mp: 134-135° C.
Opt. Rot.: $[\alpha]_D^{25}$ = - 48 (c = 0.25, acetone).

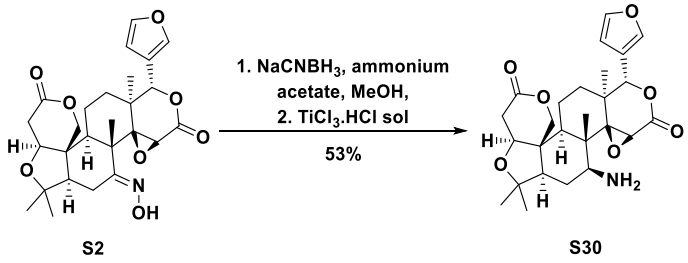


S29 (25 mg, 44%)

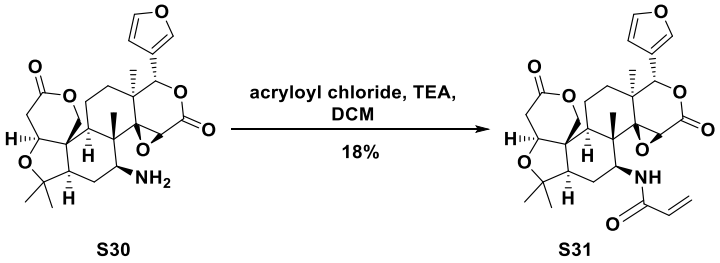
Note: Compounds **S29**, as its starting material, exists as a mixture of two diastereomers (1:1 ratio)

^{1}H NMR (DMSO-*d6,* 500 MHz): δ 8.70 (q, *J* = 5.8 Hz, 2H), 7.33 – 7.26 (m, 8H), 7.25 – 7.22 (m, 2H), 4.60 (d, *J* = 13.1, 1H), 4.59 (d, *J* = 13.1, 1H), 4.46 (d, *J* = 13.1 Hz, 2H), 4.34 (t, *J* = 5.8 Hz, 1H), 4.32 (t, *J* = 5.8 Hz, 1H), 4.24 (d, 4.8 Hz, 2H), 4.20 (d, 4.8 Hz, 2H), 3.91 (t, *J* = 7.6 Hz, 1H), 3.73 (t, *J* = 7.6 Hz, 1H), 3.69 – 3.52 (m, 4H), 3.04 (t, *J* = 8.3 Hz, 1H), 2.97 (t, *J* = 8.3 Hz, 1H), 2.89 (s, 2H), 2.88 – 2.74 (m, 4H), 2.73 (s, 2H), 2.66-2.63 (m, 2H), 2.48 – 2.35 (m, 5H), 2.16 – 2.12 (m, 2H), 2.02 – 1.92 (m, 4H), 1.77 – 1.69 (m, 2H), 1.64 – 1.52 (m, 3H), 1.44 – 1.35 (m, 4H), 1.21 -1.26 (m, 2H), 1.21 (s, 6H), 1.14 (s, 3H), 1.12 (s, 3H), 0.97 (s, 6H), 0.87 (s, 3H), 0.85 (s, 3H).
^{13}C NMR (DMSO-*d6,* 125 MHz): δ 207.43, 170.96, 167.80, 162.79, 139.29, 128.71, 128.27, 127.46, 127.40, 80.34, 78.59, 78.55, 74.29, 74.25, 71.86, 71.82, 67.37, 67.19, 64.27, 59.59, 59.46, 55.71, 55.66, 51.84, 51.72, 48.67, 48.16, 45.87, 45.84, 43.61, 43.45, 42.51, 40.09, 36.84, 36.78, 36.43, 36.26, 36.17, 35.80, 35.34, 34.82, 31.25, 30.84, 27.03, 26.98, 22.19, 20.17, 20.11, 18.61, 18.48.
HRMS(ESI): m/z calc. for $C_{33}H_{44}NO_7$ $[M+H]^+$: 566.3118, found: 566.3101.
mp: 135-136° C.
Opt. Rot.: $[\alpha]_D^{25}$ = - 38 (c = 0.13, acetone).





Procedure: Ammonium acetate (191 mg, 2.74 mmol) and $NaCNBH_3$ (39 mg, 0.62 mmol) were added to a solution of **S2** (100 mg, 0.206 mmol) in methanol (7 mL) at 0° C and the resulting mixture was stirred 0° C for 5 minutes. Hydrochloride solution of $TiCl_3$ (1.5 mL) was added dropwise to the reaction and the resulting mixture was stirred at 30° C for 12 h. The reaction was poured into iced water and washed with dichloromethane. The organic layer was discarded and the aqueous layer adjusted to pH 8.5 with sodium hydroxide. The aqueous layer was then extracted three times with dichloromethane. The combined organic layers were washed with brine, dried over Na_2SO_4 and concentrated by distillation under reduced pressure to yield a crude residue that was purified by silica gel flash chromatography (dichloromethane −methanol 97:3) to provide **S30** (52 mg, 53%) as a white solid. Spectral data (^{1}H NMR and ^{13}C NMR) were consistent with literature reported values.[5]



Procedure: TEA (88 µL, 0.63 mmol) and acryloyl chloride (18 µL, 0.22 mmol) were added to the solution of **S30** (100 mg, 0.21 mmol) in dichloromethane (5 mL) at 0° C, and the resulting solution was stirred at 30° C for 16 h. Water was added and the aqueous layer was extracted three times with dichloromethane. The combined organic layers were washed with brine and dried over Na_2SO_4. The solvent was concentrated by distillation under reduced pressure to obtain a crude residue that was purified by silica gel flash chromatography (hexane-ethyl acetate 4:6) to provide **S31** (20 mg, 18%) as a white solid.

^{1}H NMR (DMSO-*d6,* 500 MHz): δ 7.73 (d, 10.1 Hz, 1 H), 7.71 (d, *J* = 1.8 Hz, 1H), 7.67 (dd, *J* = 1.8, 1.8 Hz, 1H), 6.49 (d, *J* = 1.8 Hz, 1H), 6.39 (dd, *J* = 17.0, 10.2 Hz, 1H), 6.15 (dd, *J* = 17.0, 2.2 Hz, 1H), 5.65 (dd, *J* = 10.2, 2.2 Hz, 1H), 5.47 (s, 1H), 4.50 (d, *J* = 13.1 Hz, 1H), 4.43 (d, *J* = 13.1 Hz, 1H), 4.24 (td, *J* = 10.1, 5.0 Hz, 1H), 4.04 (d, *J* = 3.8 Hz, 1H), 3.80 (s, 1H), 2.69 (d, *J* = 16.5 Hz, 1H), 2.59 (dd,

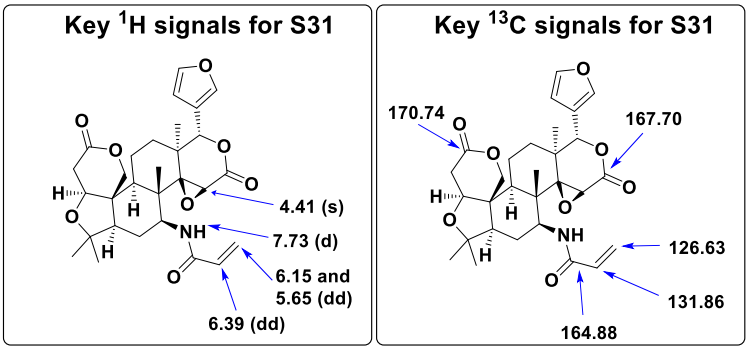
J = 16.5, 3.8 Hz, 1H), 2.43 (dd, *J* = 12.0, 5.1 Hz, 1H), 2.20 (dd, *J* = 13.0, 3.0 Hz, 1H), 1.98 – 1.88 (m, 1H), 1.73 – 1.52 (m, 4H), 1.25 (s, 3H), 1.21 – 1.16 (m, 1H), 1.20 (s, 3H), 0.97 (s, 3H), 0.93 (s, 3H).

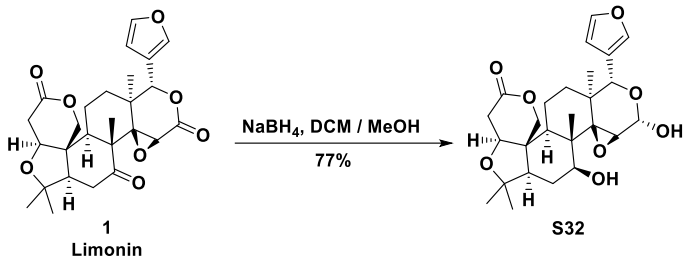
^{13}C NMR (DMSO-*d6*, 125 MHz): δ 170.74, 167.70, 164.88, 143.84, 142.22, 131.86, 126.63, 120.87, 110.73, 80.32, 79.22, 77.81, 72.41, 65.65, 57.43, 55.59, 55.25, 46.35, 45.58, 42.60, 39.11, 36.18, 30.69, 27.44, 26.79, 21.88, 19.30, 18.02, 15.25.

HRMS(ESI): m/z calc. for $C_{29}H_{36}NO^8$ $[M+H]^+$: 526.2441, found: 526.426.

mp: >260° C.

Opt. Rot.: $[\alpha]_D^{25}$ = - 12 (c = 0.13, acetone).





1
Limonin

S32

Procedure: $NaBH_4$ (458 mg, 12.11 mmol) in anhydrous methanol (20 mL) was added to a solution of **1** (1 g, 2.12 mmol) in dichloromethane (40 mL) at -5° C and the resulting mixture was stirred at -5 °C. After 1 hour, the reaction was quenched with 2 M hydrochloric acid and extracted three times with dichloromethane. The organic layers were dried over Na_2SO_4 and concentrated by distillation under reduced pressure to obtained a crude residue that was purified by silica gel flash chromatography (hexane-ethyl acetate 4:6) to provide **S32** (771 mg, 77%) as a white solid.

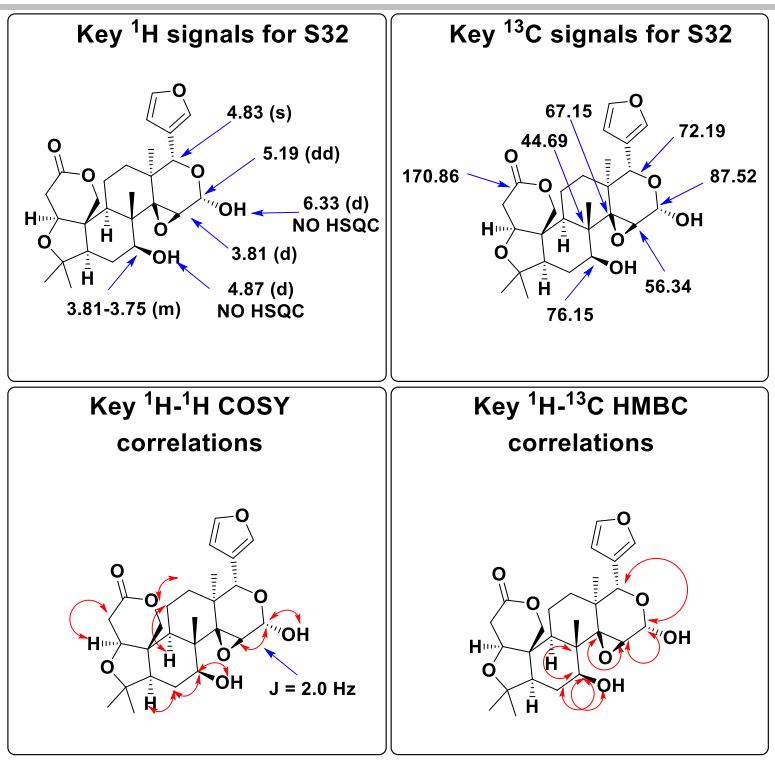
^{1}H NMR (DMSO-*d6*, 500 MHz): δ 7.56 (dd, *J* = 1.7, 1.7 Hz, 1H), 7.48 (d, *J* = 1.7 Hz, 1H), 6.37 (d, *J* = 1.7 Hz, 1H), 6.33 (d, *J* = 6.4 Hz, 1H), 5.19 (dd, *J* = 6.4, 2.0 Hz, 1H), 4.87 (d, *J* = 5.5 Hz, 1H), 4.83 (s, 1H), 4.48 (d, *J* = 13.0 Hz, 1H), 4.31 (d, *J* = 13.0 Hz, 1H), 3.96 (d, *J* = 4.0 Hz, 1H), 3.81 (d, *J* = 2.0 Hz, 1H), 3.81 – 3.75 (m, 1H), 2.73 (d, *J* = 16.4 Hz, 1H), 2.58 (dd, *J* = 16.4, 4.0 Hz, 1H), 2.21 (dd, *J* = 12.4, 3.5 Hz, 1H), 1.89 (dd, *J* = 13.4, 2.8 Hz, 1H), 1.76 – 1.48 (m, 5H), 1.18 (s, 3H), 1.17 (s, 3H), 1.11 – 1.04 (m, 1H), 0.97 (s, 3H), 0.64 (s, 3H).

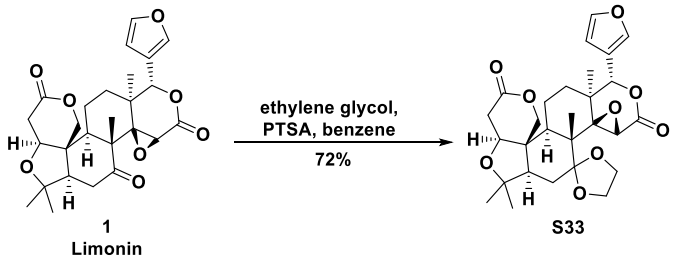
^{13}C NMR (DMSO-*d6*, 125 MHz): δ 170.86, 142.87, 140.82, 123.99, 111.04, 87.52, 79.97, 79.56, 76.15, 72.19, 67.53, 66.11, 58.37, 56.34, 46.57, 45.71, 44.70, 37.11, 36.37, 30.70, 29.61, 28.97, 21.96, 21.45, 18.55, 13.03.

HRMS(ESI): m/z calc. $C_{26}H_{35}O_8$ $[M+H]^+$: 475.2332, found: 475.2318.

mp: 164-165° C.

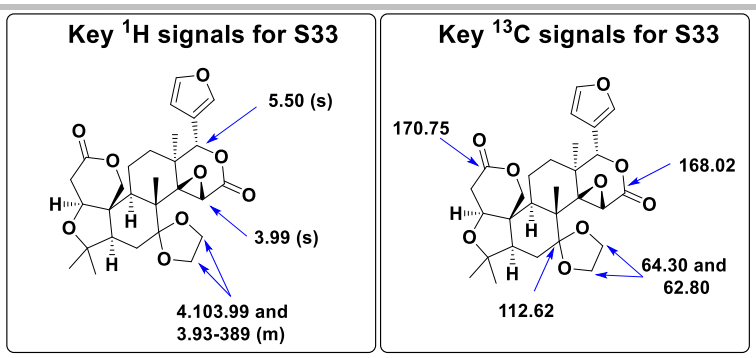
Opt. Rot.: $[\alpha]_D^{25}$ = - 37 (c = 0.25, acetone).

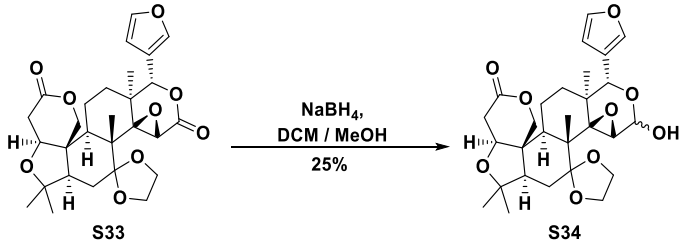




Procedure: PTSA (3 mg, 0.02 mmol) and ethylene glycol (14 µL, 0.25 mmol) were added to a solution of **1** (200 mg, 0.42 mmol) in benzene (10 mL) and the resulting solution was refluxed for 48 h with Dean-Stark apparatus. The solvent was evaporated under vacuum and residue was taken up in dichloromethane and water. The aqueous layer was extracted three times with dichloromethane. The combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated by distillation under reduced pressure to obtained a crude residue that was purified by silica gel flash chromatography (hexane-ethyl acetate 4:6) to provide **S33** (156 mg, 72%) as a white solid.

^{1}H NMR (DMSO-*d6*, 500 MHz): δ 7.71 (d, *J* = 1.8 Hz, 1H), 7.66 (dd, *J* = 1.8, 1.8 Hz, 1H), 6.49 (d, *J* = 1.8, 1H), 5.50 (s, 1H), 4.65 (d, *J* = 13.1 Hz, 1H), 4.39 (d, *J* = 13.1 Hz, 1H), 4.10 – 3.99 (m, 4H), 3.99 (s, 1H), 3.93 – 3.89 (m, 1H), 2.70 (dd, *J* = 16.5, 1.3 Hz, 1H), 2.57 (dd, *J* = 16.5, 4.1 Hz, 1H), 2.47 (d, *J* = 12.5, 4.9 Hz, 1H), 2.13 (dd, *J* = 12.5, 4.0 Hz, 1H), 1.95 – 1.87 (m, 1H), 1.82 – 1.73 (m, 2H), 1.70 – 1.61 (m, 2H), 1.31 – 1.22 (m, 1H), 1.20 (s, 3H), 1.18 (s, 3H), 0.98 (s, 3H), 0.91 (s, 3H).
^{13}C NMR (DMSO-*d6*, 125 MHz): δ 170.75, 168.02, 143.79, 142.29, 120.98, 112.62, 110.80, 79.90, 79.51, 78.10, 68.60, 65.63, 64.30, 62.80, 56.38, 54.14, 46.89, 45.66, 45.53, 38.57, 36.26, 30.68, 27.61, 27.08, 22.07, 18.75, 17.22, 16.94.
HRMS(ESI): m/z calc. $C_{28}H_{35}O_9$ $[M+H]^+$: 515.2281, found: 515.2277.
mp: 255-256° C.
Opt. Rot.: $[\alpha]_D^{25}$ = - 58 (c = 0.21, acetone).



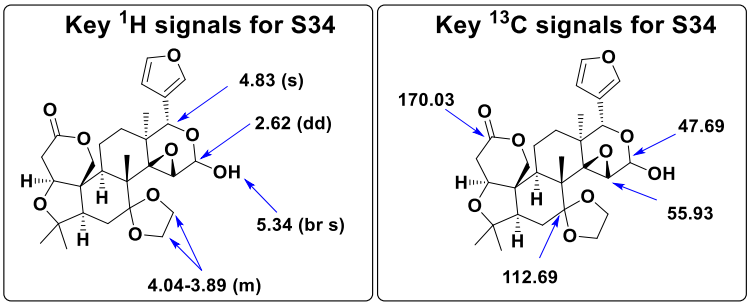


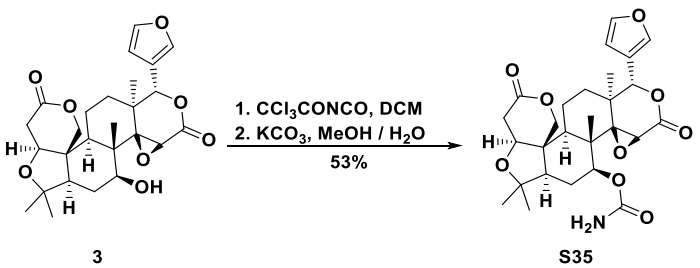
S33 S34

Procedure: $NaBH_4$ (56 mg, 1.52 mmol) in anhydrous methanol (3 mL) was added to a solution of **S33** (140 mg, 0.27 mmol) in dichloromethane (3 mL) at -15° C and the resulting mixture was stirred at -15 °C. After 30 minutes, the reaction was quenched with 2 M hydrochloric acid and extracted three times with dichloromethane. The combined organic layers were dried over Na_2SO_4 and concentrated by distillation under reduced pressure to obtained a crude residue that was purified by silica gel flash chromatography (hexane-ethyl acetate 3:7) to provide **S34** (34 mg, 25%) as a white solid.

Note: Compounds **S34** exists as a mixture of two diastereomers (1:1 ratio).

^{1}H NMR (DMSO-*d6*, 500 MHz): δ 7.27 (d *J* ,= 1.9 Hz, 2H), 7.23 (dd, *J* = 1.9, 1.9 Hz, 2H), 6.24 (d, *J* = 1.9 Hz, 1H), 6.21 (d, *J* = 1.9 Hz, 1H), 5.34 (br s, 1H), 5.19 (br s, 1H), 4.83 (s, 1H), 4.71 (s, 1H), 4.47 (d, *J* = 13.1 Hz, 2H), 4.24 (dd, *J* = 13.1, 1.5 Hz, 2H), 4.06 – 3.89 (m, 10H), 3.78 (d, *J* = 2.2 Hz, 1H), 3.63 (s, 1H), 3.08 (br s, 1H), 2.87 (br s, 1H), 2.85 (dd, *J* = 16.6, 2.8 Hz, 2H), 2.62 (dd, *J* = 5.1, 3.6 Hz, 1H), 2.60 (dd, *J* = 5.1, 3.6 Hz, 1H), 2.56 (d, *J* = 16.6 Hz, 2H), 2.20 (td, *J* = 14.2, 2.9 Hz, 2H), 1.74 – 1.66 (m, 4H), 1.61 -1.52 (m, 6H), 1.37 (s, 3H), 1.35 – 1.26 (m, 2H), 1.24 (s, 3H), 1.20 (s, 6H), 1.04 (s, 6H), 0.84 (s, 3H), 0.82 (s, 3H).
^{13}C NMR (DMSO-*d6*, 125 MHz): δ 170.03, 169.96, 142.41, 142.36, 140.53, 140.50, 122.91, 122.88, 112.69, 112.52, 110.17, 110.14, 89.90, 87.83, 80.28, 80.25, 79.88, 79.85, 72.59, 72.28, 67.23, 66.07, 66.01, 64.91, 64.63, 63.40, 63.31, 56.71, 56.25, 55.93, 47.94, 47.69, 45.62, 45.34, 44.99, 37.88, 36.83, 36.04, 36.02, 30.20, 29.13, 29.02, 28.94, 28.72, 21.51, 21.06, 20.82, 18.26, 18.22, 16.83, 16.74.
HRMS(ESI): m/z calc. $C_{28}H_{37}O_9$ $[M+H]^+$: 517.2438, found: 517.2451.
Opt. Rot.: $[\alpha]_D^{25}$ = - 189 (c = 0.13, acetone).

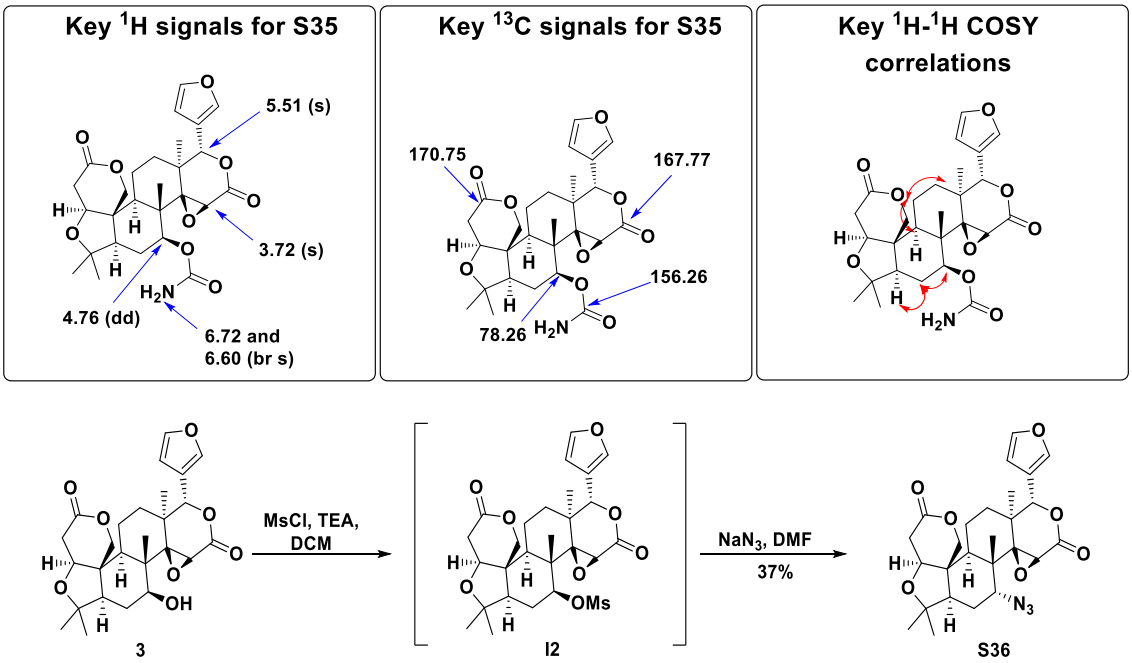




3 S35

Procedure: Trichloro acetyl isocyanate (90 µL, 0.75 mmol) was added at 0° C to a solution of **3** (300 mg, 0.60 mmol) in dichloromethane (3 mL) and the resulting mixture was stirred at 30° C for 2 h. The reaction was concentrated under vacuum and residue taken up in methanol (1.5 mL) and treated with KCO_3 saturated aqueous solution (2 mL). The resulting mixture was stirred at 30° C for an additional 16 h. Methanol was evaporated and the aqueous layer acidified with 0.5 N hydrochloric acid to pH 2 and extracted three times with dichloromethane. The organic layers were combined, washed with brine, dried over Na_2SO_4, and concentrated by distillation under reduced pressure. The crude residue was purified by biotage (water-acetonitrile gradient with 1% of formic acid) to provide **S35** (164.mg, 53%) as a white solid.

^{1}H NMR (DMSO-*d6*, 500 MHz): δ 7.72 (d, *J* = 1.8 Hz, 1H), 7.67 (dd, *J* = 1.8, 1.8 Hz, 1H), 6.72 (br s, 1H), 6.60 (br s, 1H), 6.50 (d, *J* = 1.8 Hz, 1H), 5.51 (s, 1H), 4.76 (dd, *J* = 10.2, 5.0 Hz, 1H), 4.59 (d, *J* = 13.1 Hz, 1H), 4.44 (d, *J* = 13.1 Hz, 1H), 4.01 (d, *J* = 3.9 Hz, 1H), 3.72 (s, 1H), 2.67 (d, *J* = 16.6, 1H), 2.57 (dd, *J* = 16.4, 3.9 Hz, 1H), 2.38 (dd, *J* = 12.0, 4.9 Hz, 1H), 2.14 (dd, *J* = 13.8, 2.5 Hz, 1H), 2.01 – 1.90 (m, 1H), 1.82 (ddd, *J* = 12.7, 5.2, 2.4 Hz, 1H), 1.73 – 1.58 (m, 3H), 1.22 (s, 3H), 1.23 – 1.20 (m, 1H), 1.18 (s, 3H), 0.97 (s, 3H), 0.93 (s, 3H).
^{13}C NMR (DMSO-*d6*, 125 MHz): δ 170.75, 167.77, 156.26, 143.86, 142.33, 120.77, 110.76, 80.13, 79.18, 78.26, 77.88, 72.10, 65.66, 56.32, 55.39, 55.08, 45.59, 45.54, 43.02, 36.14, 30.66, 27.15, 25.11, 21.97, 19.17, 17.64, 14.69.
HRMS(ESI): m/z calc. for $C_{27}H_{34}NO_9$ $[M+H]^+$: 516.2234, found: 516.2242.
mp: 212-213° C.
Opt. Rot.: $[\alpha]_D^{25}$ = + 2 (c = 0.26, acetone).



I2

Procedure: MsCl (151 µL, 1.50 mmol) was added to a solution of **3** (710 mg, 1.50 mmol) in dichloromethane (40 mL) and triethylamine (627 µL, 4.5 mmol) at 0° C and the resulting mixture was stirred at 30° C for 24 h. Water was added and the aqueous layer was extracted three times with dichloromethane. The organic layers were combined, washed with brine, dried over Na_2SO_4, and concentrated by distillation under reduced pressure to provide crude **I2** that was used for next step without further purification.

S36

Procedure: NaN_3 (151 mg, 1.50 mmol) was added to a solution of crude **I2** (1.50 mmol) in DMF (10 mL) and the resulting mixture was stirred at 110° C for 72 h. The reaction was cooled to room temperature, and the solvent removed under vacuum to obtain a crude residue that was taken up with water. Water was extracted three times with dichloromethane and the organic layers were combined, washed with brine, dried over Na_2SO_4 and concentrated by distillation under reduced pressure. The crude residue was purified by silica gel flash chromatography (hexane-ethyl acetate 4:6) to provide **S36** (274 mg, 37%) as a white solid.

^{1}H NMR (DMSO-*d6*, 500 MHz): δ 7.70 (d, *J* = 1.7 Hz, 1H), 7.67 (dd, *J* = 1.7, 1.7 Hz, 1H), 6.49 (d, *J* = 1.7 Hz, 1H), 5.51 (s, 1H), 4.61 (d, *J* = 13.2 Hz, 1H), 4.42 (d, *J* = 13.2 Hz, 1H), 4.18 (s, 1H), 4.08 (d, *J* = 3.7 Hz, 1H), 3.92 (d, *J* = 2.7 Hz, 1H), 2.63 (d, *J* = 16.5 Hz, 1H), 2.57 (dd, *J* = 16.5, 3.7 Hz, 1H), 2.46 (dd, *J* = 12.8, 6.6 Hz, 1H), 2.23 (dd, *J* = 13.6, 2.3 Hz, 1H), 2.09 (ddd, *J* = 14.7, 13.6, 2.7 Hz, 1H),

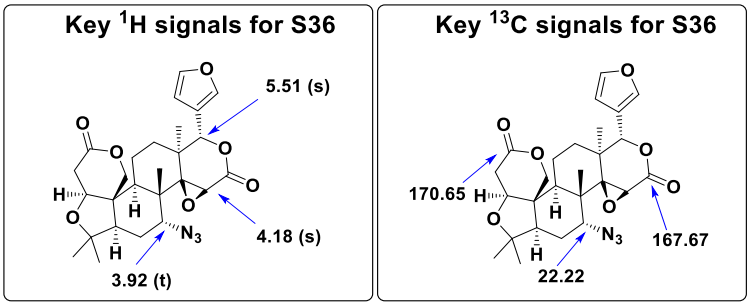
1.99 – 1.91 (m, 1H), 1.82 (ddd, *J* = 14.7, 2.7, 2.3 Hz, 1H), 1.71 – 1.54 (m, 2H), 1.28 – 1.24 (m, 1H), 1.21 (s, 3H), 1.20 (s, 3H), 1.02 (s, 3H), 0.83 (s, 3H).

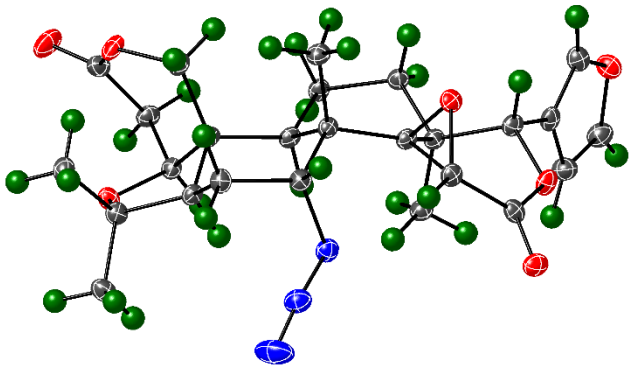
^{13}C NMR (DMSO-*d6*, 125 MHz): δ 170.65, 167.67, 143.84, 142.29, 120.90, 110.77, 80.27, 79.64, 78.25, 69.57, 65.77, 63.55, 56.81, 53.47, 45.82, 43.27, 42.73, 38.14, 36.11, 30.94, 25.99, 22.22, 21.91, 18.77, 17.69, 16.65.

HRMS(ESI): m/z calc. for $C_{26}H_{32}N_3O_7$ $[M+H]^+$: 498.2240, found: 498.2245.

mp: >260° C.

Opt. Rot.: $[\alpha]_D^{25}$ = - 72 (c = 0.19, acetone).





Crystallography

Experimental Protocol: Intensity data were collected on a Bruker D8 Venture kappa diffractometer equipped with a Photon 100 CMOS detector. An Iμs microfocus Mo source (λ = 0.71073 Å) coupled with a multi-layer mirror monochromator provided the incident beam. The sample was mounted on a 0.3 mm loop with the minimal amount of Paratone-N oil. Data was collected as a series of φ and/or ω scans. Data was collected at 100 K using a cold stream of N2(g). The collection, cell refinement, and integration of intensity data was carried out with the APEX3 software.[1] A semi-empirical absorption correction was performed with SADABS.[2] The structure was phased with intrinsic methods using SHELXT[3] and refined with the full-matrix least-squares program SHELXL.[4]

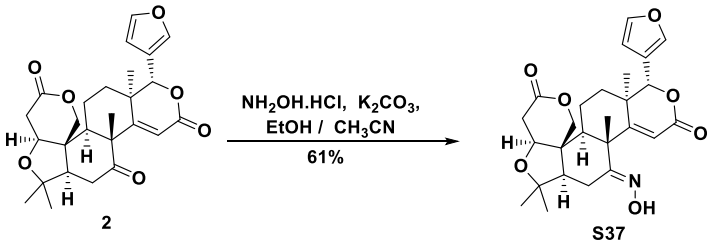
CCDC: 2082417

(1) Bruker (2016). APEX3. Bruker AXS, Inc., Madison, Wisconsin, USA.
(2) L. Krause, R. Herbst-Irmer, G. M. Sheldrick, D. Stalke, *J. Appl. Cryst.*, **2015,** *48*, 3–10.
(3) G. M. Sheldrick, *Acta Cryst.* **2015**, A71, 3–8.
(4) G. M. Sheldrick, *Acta Cryst*. **2015**, C71, 3–8.

Table S9. Crystal data and structure refinement for dd44xs.

Identification code	dd44xs
Empirical formula	C27 H33 Cl2 N3 O7
Formula weight	582.46
Temperature	100(2) K

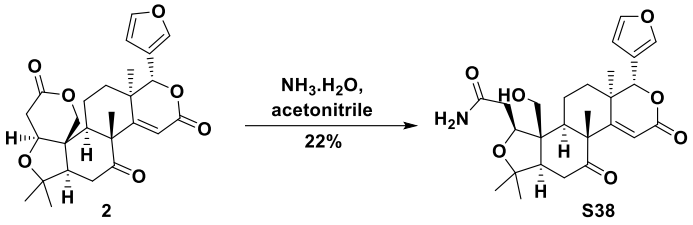
Wavelength 1.54178 Å
Crystal system Monoclinic
Space group $P2_1$
Unit cell dimensions a = 10.1144(6) Åa= 90°.
b = 10.3094(6) Åb= 91.8653(7)°.
c = 12.8229(7) Åg = 90°.
Volume 1336.38(13) Å3
Z 2
Density (calculated) 1.447 Mg/m3
Absorption coefficient 2.630 mm-1
F(000) 612
Crystal size 0.422 x 0.405 x 0.172 mm3
Theta range for data collection 3.448 to 74.801°.
Index ranges -12<=h<=12, -12<=k<=12, -16<=l<=16
Reflections collected 49300
Independent reflections 5410 [R(int) = 0.0288]
Completeness to theta = 67.679° 99.9 %
Absorption correction Semi-empirical from equivalents
Max. and min. transmission 0.7538 and 0.6012
Refinement method Full-matrix least-squares on F2
Data / restraints / parameters 5410 / 1 / 357
Goodness-of-fit on F2 1.029
Final R indices [I>2sigma(I)]R1 = 0.0292, wR2 = 0.0807
R indices (all data) R1 = 0.0292, wR2 = 0.0808
Absolute structure parameter 0.002(3)
Extinction coefficient 0.0017(4)
Largest diff. peak and hole 0.510 and -0.420 e.Å-3



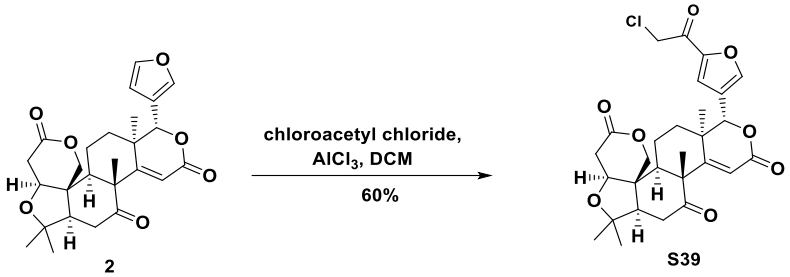
Procedure: Hydroxylamine hydrochloride (34 mg, 0.48 mmol) was added to a solution of **2** (200 mg, 0.44 mmol) and K_2CO_3 (76 mg, 0.55 mmol) in ethanol (4.4 mL) and acetonitrile (4.4 mL), and the resulting mixture was heated under reflux for 4 h. After completion, the reaction was cooled to room temperature, the solid filtered off, and the filtrate concentrate under vacuum. The crude residue was taken up with dichloromethane and washed with brine. The organic layer was dried over Na_2SO_4 and concentrated by distillation under reduced pressure to yield a crude residue that was purified by silica gel flash chromatography (hexane−ethyl acetate 4:6) to provide **S37** (127 mg, 61%) as a white solid. Spectral data (^{1}H NMR) was consistent with literature reported values.[1]

Note: The hydroxy group on the C=N double bond of **S37** adopts the *E* configuration.

^{1}H NMR (DMSO-*d6,* 500 MHz): δ 11.15 (s, 1H), 7.75 (d, *J* = 1.7 Hz, 1H), 7.70 (dd, *J* = 1.7, 1.7 Hz, 1H), 6.63 (s, 1H), 6.56 (d, *J* = 1.7 Hz, 1H), 5.14 (s, 1H), 4.59 (d, *J* = 13.0 Hz, 1H), 4.51 (d, *J* = 13.0 Hz, 1H), 4.12 (d, *J* = 3.7 Hz, 1H), 3.23 (dd, *J* = 16.3, 4.1 Hz, 1H), 2.68 (dd, *J* = 16.3 Hz, 1H), 2.59 (dd, *J* = 16.3, 3.7 Hz, 1H), 2.41 (dd, *J* = 12.6, 6.5 Hz, 1H), 2.31 (dd, *J* = 16.3, 14.9 Hz, 1H), 2.07 – 2.02 (m, 2H), 1.72- 1.66 (m, 2H), 1.34 (s, 3H), 1.21- 1.18 (m, 1H), 1.19 (s, 6H), 1.04 (s, 3H).
^{13}C NMR (DMSO-*d6,* 125 MHz): δ 170.87 165.41, 160.15, 143.76, 142.27, 120.75, 117.18, 110.85, 81.51, 80.55, 78.34, 64.73, 56.80, 46.01, 45.82, 45.29, 40.42, 38.43, 36.21, 30.78, 28.82, 26.35, 22.12, 20.51, 20.30, 17.07.
HRMS(ESI): m/z calc. for $C_{26}H_{32}NO_7$ $[M+H]^+$: 486.2130, found: 486.2128.
mp: >260° C.
Opt. Rot.: $[\alpha]_D^{25}$ = - 41 (c = 0.12, acetone).

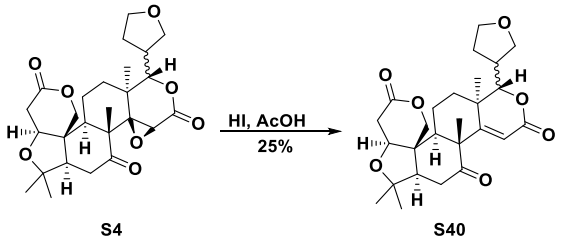


Procedure: Ammonium hydroxide (2 mL) was added dropwise to a solution of **2** (96 mg, 0.21 mmol) in acetonitrile (3 mL) at 0° C and the resulting mixture was stirred at 30° C for 8 h. The reaction mixture was diluted with water, acidified with 2 M hydrochloric acid, and extracted three times with dichloromethane. The combined organic layers were washed with brine, dried over Na_2SO_4 and concentrated by distillation under reduced pressure to yield a crude residue that was purified by silica gel flash chromatography (dichloromethane-methanol 97:3) to provide **S38** (22 mg, 22%) as a white solid. Spectral data (^{1}H NMR and ^{13}C NMR) were consistent with literature reported values.[6]



Procedure: $AlCl_3$ (132 mg, 0.99 mmol) was added at 0° C to a cooled solution of **2** (100 mg, 0.22 mmol) in dichloromethane (4 mL). The resulting mixture was stirred 30 minutes, before chloroacetyl chloride (21 µL, 0.26 mmol) was added to the solution, and the resulting mixture was stirred at 30° C for 15 h. Water was added and the aqueous layer was extracted three times with dichloromethane. The combined organic layers were washed with 2 M sodium hydroxide and brine. After drying over Na_2SO_4, the solution was concentrated by distillation at reduced pressure, and the residue was purified by flash chromatography on silica gel (hexane-ethyl acetate 4:6), giving **S39** (70 mg, 60%) as a white solid. Spectral data (^{1}H NMR) was consistent with literature reported values.[7]

^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.70 (d, *J* = 0.8 Hz, 1H), 7.30 (d, *J* = 0.8 Hz, 1H), 6.87 (s, 1H), 5.03 (s, 1H), 4.68 (d, *J* = 13.1 Hz, 1H), 4.56 (d, *J* = 13.1 Hz, 1H), 4.56 (d, *J* = 2.0 Hz, 2H), 4.10 (t, *J* = 3.6 Hz, 1H), 2.98 (dd, *J* = 16.9, 3.6 Hz, 1H), 2.82 (t, *J* = 15.9 Hz, 1H), 2.63 (dd, *J* = 15.9, 2.2 Hz, 1H), 2.59 (dd, *J* = 16.9, 3.6 Hz, 1H), 2.51 (dd, *J* = 12.6, 7.3 Hz, 1H), 2.28 (dd, *J* = 15.9, 2.2 Hz, 1H), 2.16 – 2.02 (m, 1H), 1.90 – 1.82 (m, 1H), 1.68 – 1.62 (m, 1H), 1.58 – 1.55 (m, 1H), 1.41 (s, 3H), 1.30 (s, 3H), 1.22 (s, 3H), 1.19 (s, 3H).
^{13}C NMR ($CDCl_3$, 125 MHz): δ 205.22, 180.38, 168.95, 165.30, 164.02, 150.73, 145.45, 123.14, 118.04, 117.70, 81.44, 80.61, 78.71, 64.59, 58.30, 50.81, 45.59, 44.94, 44.41, 38.44, 36.58, 35.38, 30.45, 26.70, 25.91, 21.74, 19.89, 17.72.
HRMS(ESI): m/z calc. for $C_{28}H_{32}O_8Cl$ $[M+H]^+$: 531.1786, found: 531.1788.
Opt. Rot.: $[\alpha]_D^{25}$ = - 4 (c = 0.10, acetone).



Procedure: A solution of **S4** (125 mg, 0.27 mmol) in acetic acid (2 mL) and hydriodic acid (2 mL) was heated under reflux for 1.30 h. The reaction mixture was cooled to room temperature and slowly poured into 400 mL of sodium sulfite saturated solution and extracted three times with dichloromethane. The organic layers were combined, washed with brine, dried over Na_2SO_4 and concentrated by distillation under reduced pressure. The crude residue was purified by silica gel flash chromatography (ethyl acetate) to provide **S40** (30 mg, 25%) as a white solid.

Note: Compound **S40** is known,[2] however **S40** has never been fully characterized. **S40**, as its starting material, exists has two diastereoisomers (1:1 ratio).

^{1}H NMR (DMSO-*d6*, 500 MHz): δ 6.58 (s, 2H), 4.91 (d, *J* = 13.1 Hz, 2H), 4.66 (dd, *J* = 13.1, 3.5 Hz, 2H), 4.22 (d, *J* = 3.7 Hz, 2H), 4.17 (d, *J* = 5.9 Hz, 1H), 4.05 (d, *J* = 5.2 Hz, 1H), 3.94 (t, *J* = 8.2, 1H), 3.94 (t, *J* = 8.6, 1H), 3.79 – 3.74 (m 2H), 3.72 – 3.66 (m, 2H), 3.58 (t,

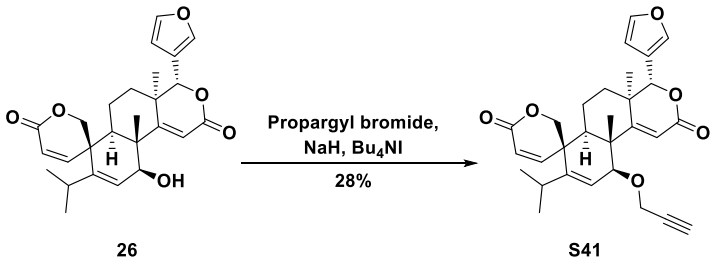
J = 8.6 Hz, 1H), 3.40 (t, *J* = 8.2 Hz, 1H), 3.20 (t, *J* = 15.6 Hz, 2H), 2.78 (d, *J* = 16.3 Hz, 2H), 2.71 (d, *J* = 4.0 Hz, 1H), 2.68 (d, *J* = 4.3 Hz, 1H), 2.66 – 2.60 (m, 4H), 2.44 (dd, *J* = 15.6, 3.4 Hz, 2H), 2.27 – 2.12 (m, 2H), 2.09 – 2.17 (m, 2H), 1.98 – 1.88 (m, 1H), 1.84 – 1.71 (m, 5H), 1.68 – 1.45 (m, 4H), 1.30 (s, 3H), 1.29 (s, 3H), 1.25 (s, 6H), 1.24 (s, 6H), 1.08 (s, 6H).

^{13}C NMR (DMSO-*d6*, 125 MHz): δ 208.14, 208.10, 170.77, 168.29, 168.23, 165.25, 165.13, 116.99, 116.80, 87.74, 86.09, 80.24, 78.58, 70.54, 69.02, 67.85, 67.49, 64.67, 60.23, 56.58, 56.53, 50.99, 50.96, 45.67, 42.78, 42.72, 38.84, 38.76, 38.71, 38.69, 36.93, 36.12, 31.01, 30.37, 28.54, 26.26, 25.67, 25.23, 21.96, 19.87, 19.69, 16.83, 16.80.

HRMS(ESI): m/z calc. for $C_{26}H_{35}O_7$ $[M+H]^+$: 459.2383, found: 459.2389.

mp: >260° C.

Opt. Rot.: $[\alpha]_D^{25}$ = - 95 (c = 0.21, acetone).



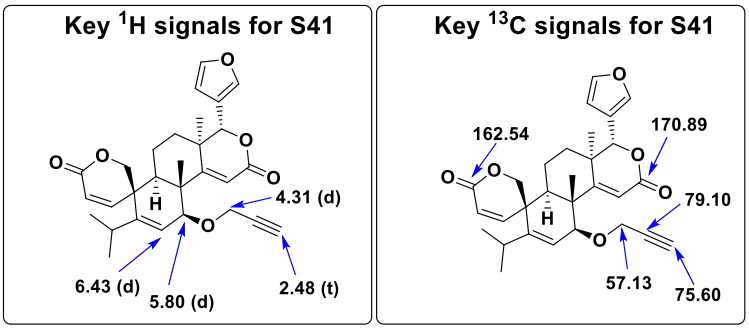
26 **S41**

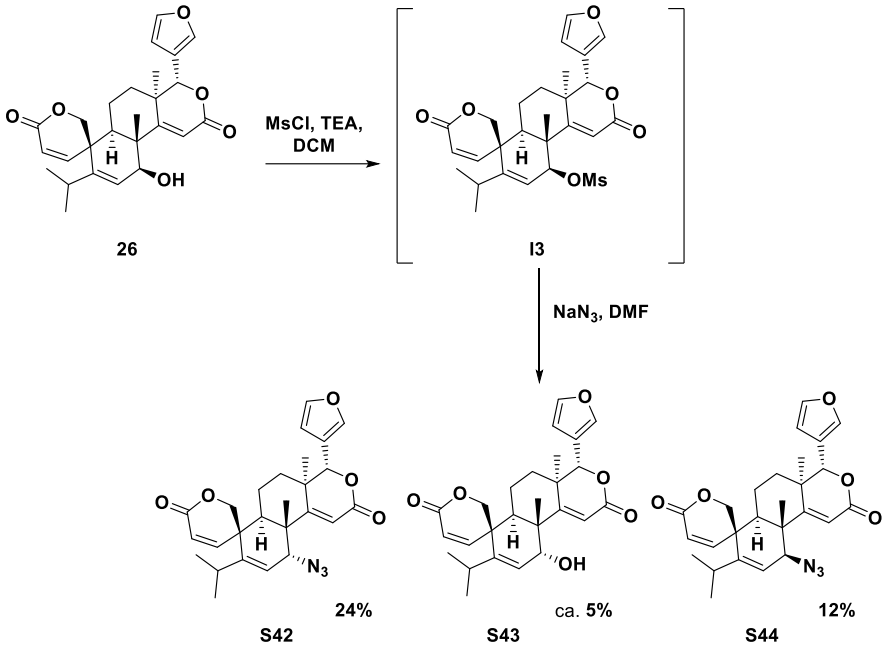
Procedure: NaH (60% dispersion in mineral oil) (10 mg, 0.44 mmol) and propargyl bromide (32 µL, 0.44 mmol) were added at 0°C to a cooled solution of **26** (96 mg, 0.22 mmol) and tetrabutylammonium iodide (48 mg, 0.02 mmol) in THF (2 mL). The resulting solution was stirred at 30° C for 12 h. Sat. aq NH_4Cl solution (20 mL) was added and the aqueous layer was extracted three times with dichloromethane. The combined organic layers were washed with brine. After drying over Na_2SO_4, the solution was concentrated by distillation at reduced pressure, and the residue was purified by flash chromatography on silica gel (hexane-ethyl acetate 6:4) to obtain **S41** (30 mg, 28%) as a white solid.

^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.48 (d, *J* = 1.7 Hz, 1H), 7.42 (dd, *J* = 1.7, 1.7 Hz, 1H), 6.60 (s, 1H), 6.43 (d, *J* = 1.7 Hz, 1H), 6.24 (dd, *J* = 9.9, 1.7 Hz, 1H), 6.16 (d, *J* = 9.9 Hz, 1H), 5.80 (d, *J* = 1.7 Hz, 1H), 5.04 (s, 1H), 4.69 (dd, *J* = 12.6, 1.7 Hz, 1H), 4.50 (d, *J* = 12.6 Hz, 1H), 4.31 (d, *J* = 2.3 Hz, 2H), 4.02 (d, *J* = 1.7 Hz, 1H), 2.48 (t, *J* = 2.3 Hz, 1H), 2.28 (hept, *J* = 6.8 Hz, 1H), 1.91 (dd, *J* = 11.9, 4.6 Hz, 1H), 1.83 – 1.69 (m, 3H), 1.46 (ddd, *J* = 13.7, 9.0, 7.5 Hz, 1H), 1.23 (s, 3H), 1.21 (s, 3H), 1.12 (d, *J* = 6.8 Hz, 3H), 1.09 (d, *J* = 6.8 Hz, 3H).

^{13}C NMR ($CDCl_3$, 125 MHz): δ 170.89, 165.18, 162.54, 150.90, 145.97, 143.02, 141.34, 124.33, 122.55, 120.08, 118.31, 110.07, 81.41, 80.64, 79.10, 75.60, 69.29, 57.13, 44.80, 42.08, 40.46, 37.58, 29.59, 29.39, 25.15, 25.12, 22.20, 17.74, 17.64.

HRMS(ESI): m/z calc. for $C_{29}H_{33}O_6$ $[M+H]^+$: 477.2277, found: 477.2274.





I3

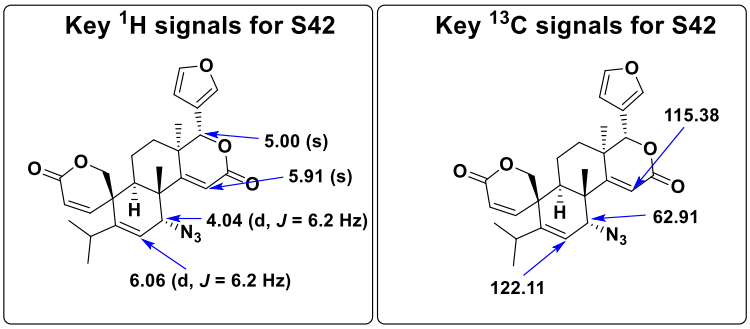
Procedure: MsCl (27 µL, 0.35 mmol) was added to a solution of **26** (116 mg, 0.27 mmol) in dichloromethane (6 mL) and triethylamine (111 µL, 0.80 mmol) at 0° C and the resulting mixture was stirred at 30° C for 2 h. Water was added and the aqueous layer was extracted three times with dichloromethane. The organic layers were combined, washed with brine, dried over Na_2SO_4, and concentrated by distillation under reduced pressure to provide crude **I3** that was used for next step without further purification.

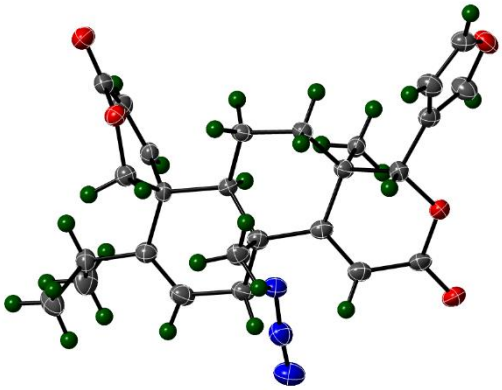
S42-S44

Procedure: NaN_3 (60 mg, 0.27 mmol) was added to a solution of crude **I3** (0.27 mmol) in DMF (2 mL) and the resulting mixture was stirred at 110° C for 12 h. The reaction was cooled to room temperature, and the solvent removed under vacuum to obtain a crude residue that was taken up with water. Water was extracted three times with dichloromethane and the organic layers were combined, washed with brine, dried over Na_2SO_4 and concentrated by distillation under reduced pressure. The crude residue was purified by silica gel flash chromatography (hexane-ethyl acetate 1:1) to provide **S42** (29 mg, 24%) and the epimerization products **S43** (6 mg, ca. 5%) and **S44** (15 mg, 12%), as white solids.

S42 (29 mg, 24%)

^{1}H NMR ($CDCl_3$, 125 MHz): δ 7.47 (d, *J* = 1.8 Hz, 1H), 7.41 (dd, *J* = 1.8, 1.8 Hz, 1H), 6.40 (d, *J* = 1.8 Hz, 1H), 6.32 (dd, *J* = 9.9, 2.1 Hz, 1H), 6.15 (d, *J* = 9.9 Hz, 1H), 6.06 (d, *J* = 6.2 Hz, 1H), 5.91 (s, 1H), 5.00 (s, 1H), 4.64 (dd, *J* = 12.7, 2.1 Hz, 1H), 4.53 (d, *J* = 12.7 Hz, 1H), 4.04 (d, *J* = 6.2 Hz, 1H), 2.36 (hept, *J* = 6.8 Hz, 1H), 2.29 (dd, *J* = 12.5, 7.4 Hz, 1H), 2.08 – 2.00 (m, 1H), 1.91 – 1.79 (m, 1H), 1.61 – 1.54 (m, 2H), 1.27 (s, 3H), 1.16 (s, 3H), 1.15 (d, *J* = 6.8 Hz, 3H), 1.13 (d, *J* = 6.8 Hz, 3H).
^{13}C NMR ($CDCl_3$, 125 MHz): δ 171.89, 164.93, 162.08, 151.37, 149.91, 143.08, 141.27, 122.11, 120.55, 119.93, 115.38, 109.98, 82.20, 68.75, 62.91, 45.26, 42.59, 37.72, 34.19, 30.29, 26.63, 25.92, 24.93, 24.57, 18.35, 15.66.
HRMS(ESI): m/z calc. for $C_{26}H_{30}N_3O_5$ $[M+H]^+$: 464.2179, found: 464.2178.





Crystallography

Experimental Protocol: Intensity data were collected on a Bruker D8 Venture kappa diffractometer equipped with a Photon 100 CMOS detector. An Iμs microfocus Mo source (λ = 0.71073 Å) coupled with a multi-layer mirror monochromator provided the incident beam. The sample was mounted on a 0.3 mm loop with the minimal amount of Paratone-N oil. Data was collected as a series of φ and/or ω scans. Data was collected at 100 K using a cold stream of N2(g). The collection, cell refinement, and integration of intensity data was carried out with the APEX3 software.[1] A semi-empirical absorption correction was performed with SADABS.[2] The structure was phased with intrinsic methods using SHELXT[3] and refined with the full-matrix least-squares program SHELXL.[4]

CCDC: 2082418

(1) Bruker (2016). APEX3. Bruker AXS, Inc., Madison, Wisconsin, USA.
(2) L. Krause, R. Herbst-Irmer, G. M. Sheldrick, D. Stalke, *J. Appl. Cryst.*, **2015,** *48*, 3–10.
(3) G. M. Sheldrick, *Acta Cryst.* **2015**, A71, 3–8.
(4) G. M. Sheldrick, *Acta Cryst*. **2015**, C71, 3–8.

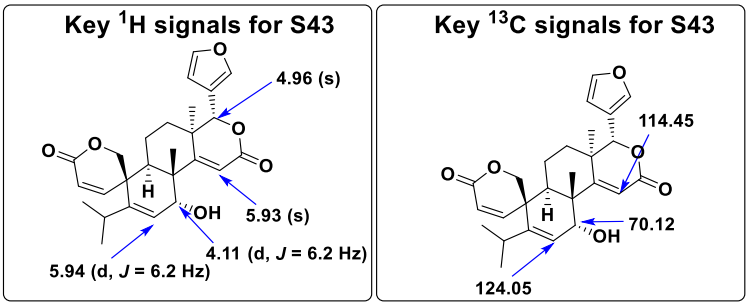
Table S10
Crystal data and structure refinement for ed06es.

Identification code	ed06es
Empirical formula	C26 H29 N3 O5
Formula weight	463.52
Temperature	100(2) K
Wavelength	1.54178 Å
Crystal system	Orthorhombic
Space group	$P2_12_12_1$
Unit cell dimensions	a = 8.3769(6) Å a= 90°.
	b = 9.5428(7) Å b= 90°.
	c = 29.023(2) Å g = 90°.
Volume	2320.1(3) Å3
Z	4
Density (calculated)	1.327 Mg/m3
Absorption coefficient	0.758 mm-1
F(000)	984
Crystal size	0.302 x 0.257 x 0.156 mm3
Theta range for data collection	3.045 to 69.296°.
Index ranges	-10<=h<=10, -11<=k<=11, -34<=l<=35
Reflections collected	45838
Independent reflections	4289 [R(int) = 0.0707]
Completeness to theta = 67.679°	99.9 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.6825 and 0.5643
Refinement method	Full-matrix least-squares on F2
Data / restraints / parameters	4289 / 71 / 339
Goodness-of-fit on F2	1.093

Final R indices [I>2sigma(I)]R1 = 0.0714, wR2 = 0.1708
R indices (all data) R1 = 0.0722, wR2 = 0.1719
Absolute structure parameter -0.2(2)
Extinction coefficient n/a
Largest diff. peak and hole 0.259 and -0.274 e.Å-3

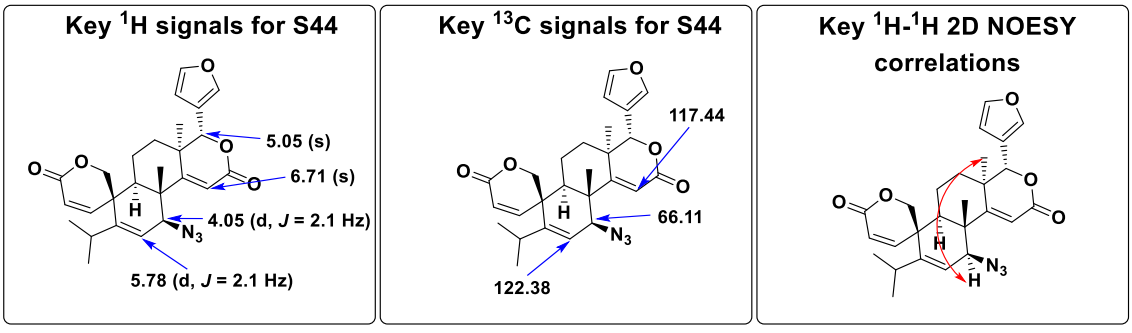
S43 (6 mg, ca. 5%)

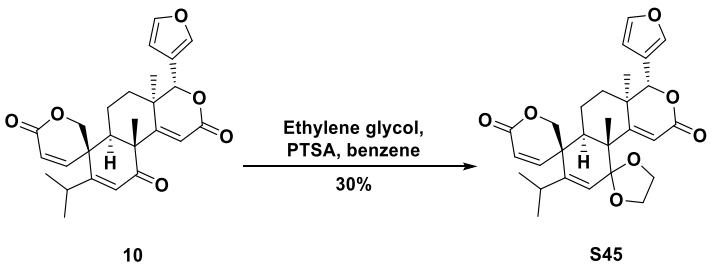
^{1}H NMR ($CDCl_3$, 125 MHz): δ 7.41 (d, *J* = 1.7 Hz, 1H), 7.36 (dd, *J* = 1.7 Hz, 1H), 6.34 (d, *J* = 1.7 Hz, 1H), 6.28 (dd, *J* = 9.9, 2.0 Hz, 1H), 6.06 (d, *J* = 9.9 Hz, 1H), 5.94 (d, *J* = 6.2 Hz, 1H), 5.93 (s, 1H), 4.96 (s, 1H), 4.60 (dd, *J* = 12.6, 2.0 Hz, 1H), 4.46 (d, *J* = 12.6 Hz, 1H), 4.11 (d, *J* = 6.2 Hz, 1H), 2.44 (dd, *J* = 12.4, 7.5 Hz, 1H), 2.27 – 2.18 (m, 1H), 2.02 – 1.95 (m, 1H), 1.87 – 1.73 (m, 1H), 1.53 – 1.47 (m, 2H), 1.16 (s, 3H), 1.08 (s, 3H), 1.06 (d, *J* = 6.6 Hz, 3H), 1.04 (d, *J* = 6.6 Hz, 3H). (29 non-exchangeable protons)
^{13}C NMR ($CDCl_3$, 125 MHz): δ 174.47, 165.33, 162.44, 150.75, 148.43, 143.11, 141.27, 124.05, 121.71, 119.90, 114.45, 109.95, 82.24, 70.12, 69.06, 45.46, 43.69, 37.88, 33.03, 29.77, 26.85, 25.22, 25.02, 24.28, 18.20, 15.67.
HRMS(ESI): m/z calc. for $C_{26}H_{31}O_6$ $[M+H]^+$: 439.2115, found: 439.2121.



S44 (15 mg, 12%)

^{1}H NMR ($CDCl_3$, 125 MHz): δ 7.50 (dd, *J* = 1.6, 0.9 Hz, 1H), 7.44 (dd, *J* = 1.7, 1.6 Hz, 1H), 6.71 (s, 1H), 6.43 (dd, *J* = 1.7, 0.9 Hz, 1H), 6.27 (dd, *J* = 9.9, 1.6 Hz, 1H), 6.21 (d, *J* = 9.9 Hz, 1H), 5.78 (d, *J* = 2.1 Hz, 1H), 5.05 (s, 1H), 4.72 (dd, *J* = 12.7, 1.6 Hz, 1H), 4.53 (d, *J* = 12.7 Hz, 1H), 4.05 (d, *J* = 2.1 Hz, 1H), 2.35 (hept, *J* = 6.8 Hz, 1H), 1.99 – 1.91 (m, 2H), 1.85 – 1.79 (m, 1H), 1.74 – 1.69 (m, 1H), 1.56 – 1.45 (m, 1H), 1.30 (s, 3H), 1.19 (s, 3H), 1.18 (d, *J* = 6.8 Hz, 3H), 1.15 (d, *J* = 6.8 Hz, 3H).
^{13}C NMR ($CDCl_3$, 125 MHz): δ 171.94, 164.95, 162.20, 150.08, 148.79, 143.13, 141.37, 122.84, 122.38, 119.84, 117.44, 109.98, 81.59, 69.06, 66.11, 44.83, 42.33, 40.07, 37.83, 29.92, 28.37, 25.54, 24.92, 21.41, 18.89, 17.50.
HRMS(ESI): m/z calc. for $C_{26}H_{30}N_3O_5$ $[M+H]^+$: 464.2185, found: 464.2178.

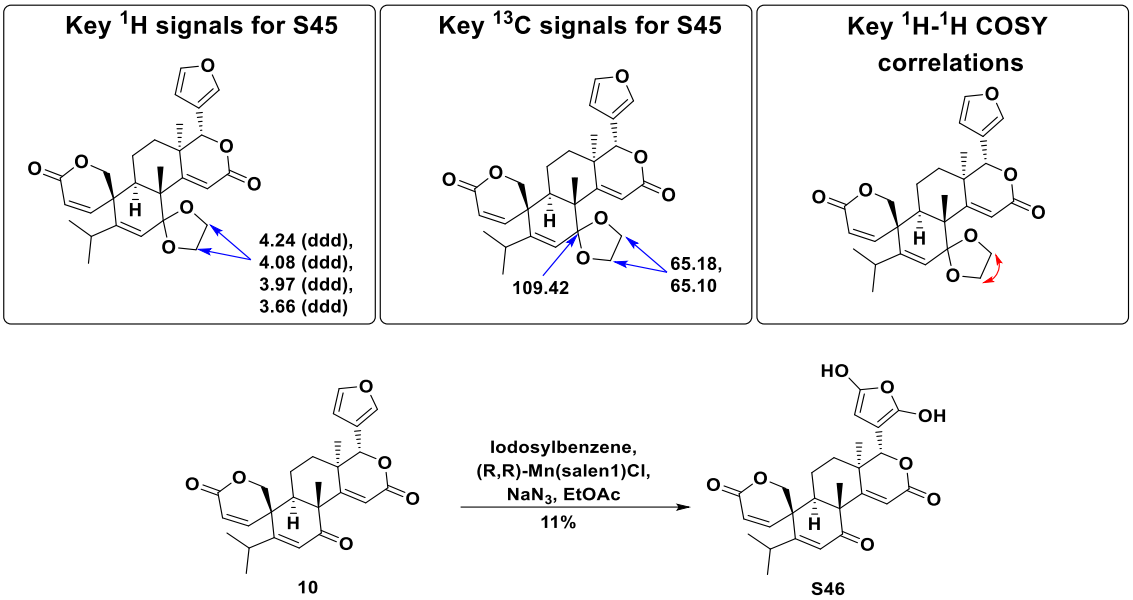




Procedure: PTSA (2 mg, 0.02 mmol) and ethylene glycol (34 µL, 0.56 mmol) were added to a solution of **10** (60 mg, 0.14 mmol) in benzene (6 mL) and the resulting solution was refluxed for 72 h with Dean-Stark apparatus. The solvent was evaporated under vacuum

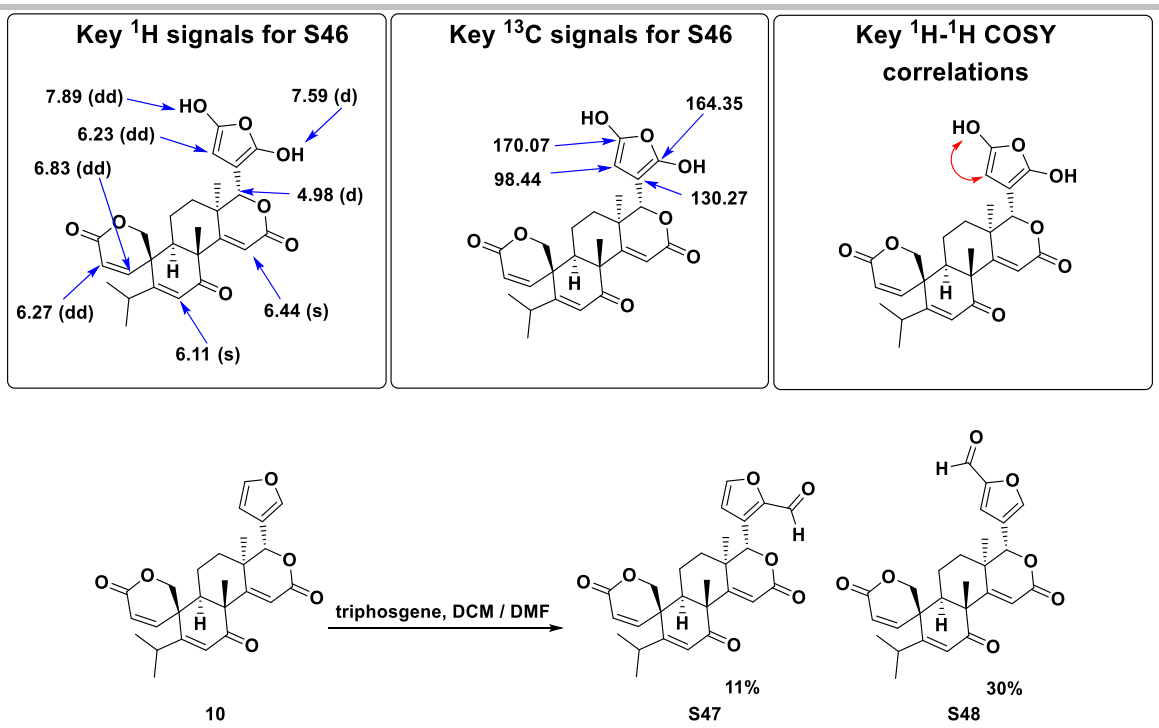
and residue was taken up in dichloromethane and water. The aqueous layer was extracted three times with dichloromethane. The combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated by distillation under reduced pressure to obtained a crude residue that was purified by silica gel flash chromatography (hexane-ethyl acetate 1:1) to provide **S45** (20 mg, 30%) as a white solid.

^{1}H NMR ($CDCl_3$, 125 MHz): δ 7.47 (d, *J* = 1.7 Hz, 1H), 7.41 (dd, *J* = 1.7 Hz, 1H), 6.48 (s, 1H), 6.43 (d, *J* = 1.7 Hz, 1H), 6.32 (dd, *J* = 9.9, 1.6 Hz, 1H), 6.16 (d, *J* = 9.9 Hz, 1H), 5.57 (s, 1H), 5.01 (s, 1H), 4.67 (dd, *J* = 12.5, 1.6 Hz, 1H), 4.49 (d, *J* = 12.5 Hz, 1H), 4.24 (ddd, *J* = 8.2, 6.4, 3.6 Hz, 1H), 4.08 (ddd, *J* = 8.4, 8.2, 6.7 Hz, 1H), 3.97 (ddd, *J* = 7.0, 6.7, 3.6 Hz, 1H), 3.66 (ddd, *J* = 8.4, 7.0, 6.4 Hz, 1H), 2.44 (dd, *J* = 11.9, 5.4 Hz, 1H), 2.27 (hept, *J* = 6.8 Hz, 1H), 1.84 – 1.74 (m, 1H), 1.72 – 1.66 (m, 1H), 1.55 – 1.43 (m, 1H), 1.34 (s, 3H), 1.22 (s, 3H), 1.20 – 1.11 (m, 1H), 1.10 (d, *J* = 6.8 Hz, 3H), 1.09 (d, *J* = 6.8 Hz, 3H).
^{13}C NMR ($CDCl_3$, 125 MHz): δ 169.95, 165.48, 162.53, 150.74, 146.57, 142.96, 141.37, 125.54, 122.35, 120.26, 118.09, 110.21, 109.42, 81.75, 69.21, 65.18, 65.10, 45.98, 44.71, 39.09, 37.88, 29.66, 29.29, 25.01, 24.86, 21.73, 20.36, 17.38.
HRMS(ESI): m/z calc. for $C_{28}H_{33}O_7$ $[M+H]^+$: 481.2226, found: 481.2212.



Procedure: A dried vial was charged with **10** (50 mg, 0.11mmol), iodosylbenzene (20mg, 0.91mmol), and Mn(salen)Cl (2mg, 0.03mmol).Then, 1.5 M sodium azide aqueous solution (0.2 mL) was added followed by ethyl acetate (1 mL) and the resulting mixture was stirred 30° C. After the consumption of solid iodosylbenzene another portion of catalyst (2mg, 0.03mmol), 1.5 M sodium azide aqueous solution (0.2 mL) and), iodosylbenzene (20mg, 0.91mmol) were added sequentially. This step was repeated 4 times before brine was added to the solution. The aqueous layer was extracted 3 times with dichloromethane, dried over Na_2SO_4, the solution was concentrated by distillation at reduced pressure, and the residue was purified by flash chromatography on silica gel (hexane-ethyl acetate 3:7), giving **S46** 90% pure (6 mg, 11%) as a white solid.

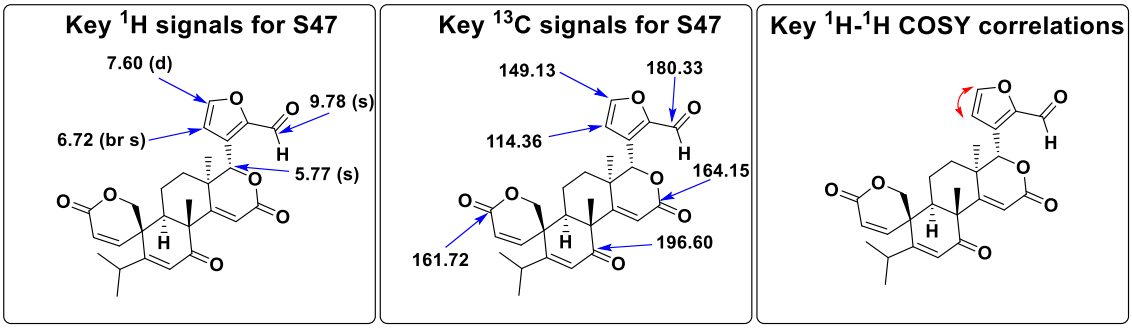
^{1}H NMR (DMSO-*d6*, 500 MHz): δ 7.89 (dd, *J* = 20.6, 17.7 Hz, 1H), 7.59 (d, *J* = 4.0 Hz, 1H), 6.83 (dd, *J* = 10.0, 4.9 Hz, 1H), 6.44 (s, 1H), 6.27 (dd, *J* = 10.0, 2.7 Hz, 1H), 6.23 (dd, *J* = 20.6, 4.0 Hz, 1H), 6.11 (s, 1H), 4.98 (d, *J* = 17.7 Hz, 1H), 4.84 (d, *J* = 12.5 Hz, 1H), 4.62 (dd, *J* = 12.5, 2.7 Hz, 1H), 2.70 (dt, *J* = 12.5, 6.2 Hz, 1H), 2.39 (hept, *J* = 6.8 Hz, 1H), 1.96 – 1.85 (m, 1H), 1.79 – 1.69 (m, 1H), 1.67 – 1.59 (m, 1H), 1.46 – 1.39 (m, 1H), 1.43 (s, 3H), 1.13 (s, 3H), 1.12 (d, *J* = 6.8 Hz, 3H), 1.08 (d, *J* = 6.8 Hz, 3H).
^{13}C NMR (DMSO-*d6*, 125 MHz): δ 197.70, 171.04, 170.07, 169.56, 166.05, 164.35, 162.61, 149.98, 130.51, 124.88, 122.98, 118.22, 98.43, 79.65, 78.88, 70.15, 48.09, 38.15, 38.03, 31.76, 25.51, 24.96, 23.93, 22.56, 20.03, 17.23.
HRMS(ESI): m/z calc. for $C_{26}H_{29}O_8$ $[M+H]^+$: 469.1862, found: 469.1858.



Procedure: A solution of triphosgene (88 mg, 0.30 mmol) in DCM (0.4 mL) was added at at 0 °C dropwise to a cooled solution of **10** (66 mg, 0.15 mmol) in DCM (1 mL) and DMF (24 µL, 0.30 mmol). The resulting solution was stirred at 40 °C for 12 h. Water was added and the aqueous layer was extracted three times with dichloromethane. The combined organic layers were washed with sodium bicarbonate saturated solution and brine. After drying over Na_2SO_4, the solution was concentrated by distillation at reduced pressure, and the residue was purified by flash chromatography on silica gel (hexane-ethyl acetate 1:1) to obtain **S47** (8 mg, 11%) and **S48** (20 mg, 30%) as white solids.

S47 (8 mg, 11%)

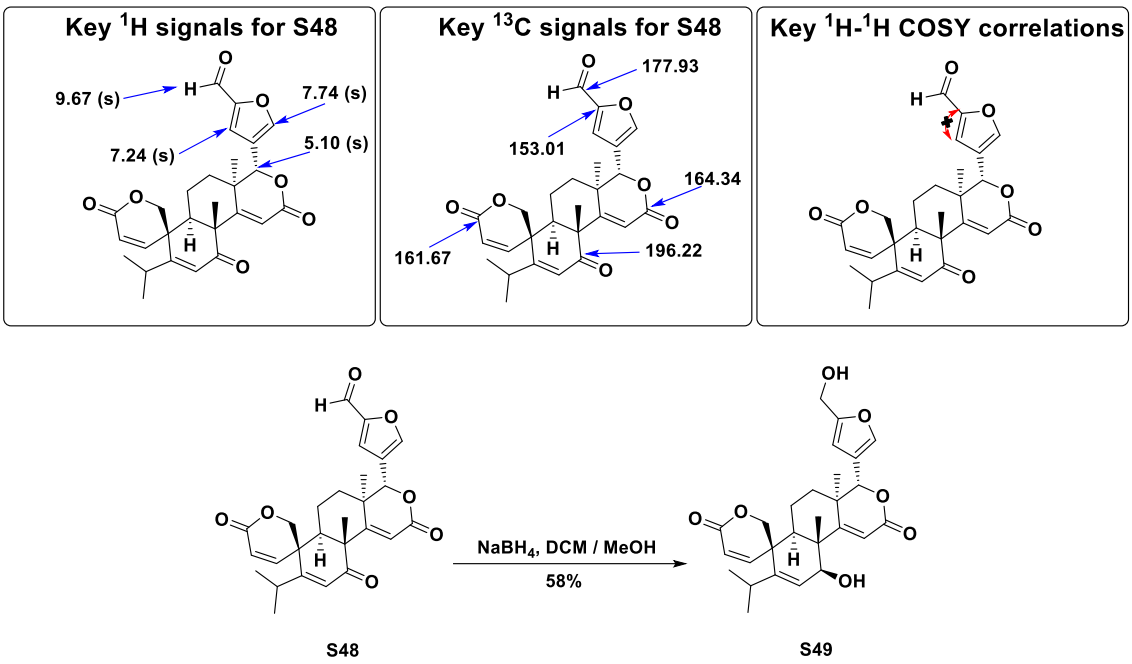
^{1}H NMR ($CDCl_3$, 125 MHz): δ 9.78 (s, 1H), 7.60 (d, *J* = 2.0 Hz, 1H), 6.72 (br s, 1H), 6.68 (s, 1H), 6.31 (d, *J* = 10.0 Hz, 1H), 6.20 (d, *J* = 10.0 Hz, 1H), 6.09 (s, 1H), 5.77 (s, 1H), 4.72 (d, *J* = 12.4 Hz, 1H), 4.47 (d, *J* = 12.4 Hz, 1H), 2.45 – 2.37 (m, 2H), 2.01 – 1.89 (m, 2H), 1.72 (td, *J* = 11.9, 11.0, 5.8 Hz, 1H), 1.51 (s, 3H), 1.21 – 1.15 (m, 1H), 1.12 (s, 3H), 1.11 (d, *J* = 6.8 Hz, 3H), 1.08 (d, *J* = 6.8 Hz, 3H).
^{13}C NMR ($CDCl_3$, 125 MHz): δ 196.60, 180.33, 167.31, 164.65, 164.15, 161.72, 149.13, 148.19, 147.17, 128.66, 125.96, 123.63, 119.04, 114.36, 78.87, 69.41, 48.17, 45.62, 40.32, 39.02, 30.98, 26.14, 25.82, 24.32, 24.13, 21.12, 17.34.
HRMS(ESI): m/z calc. for $C_{27}H_{29}O_7$ $[M+H]^+$: 465.1913, found: 465.1907.
Opt. Rot.: $[\alpha]_D^{25}$ = + 48 (c = 0.04, acetone).



S48 (20 mg, 30%)

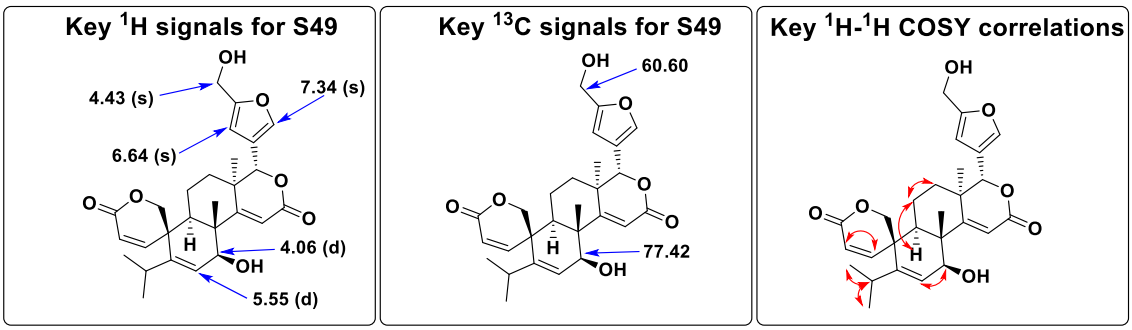
^{1}H NMR ($CDCl_3$, 125 MHz): δ 9.67 (s, 1H), 7.74 (s, 1H), 7.24 (s, 1H), 6.72 (s, 1H), 6.41 (dd, *J* = 9.9, 1.6 Hz, 1H), 6.31 (d, *J* = 9.9 Hz, 1H), 6.17 (s, 1H), 5.10 (s, 1H), 4.78 (dd, *J* = 12.4, 1.6 Hz, 1H), 4.55 (d, *J* = 12.4 Hz, 1H), 2.55 – 2.41 (m, 2H), 2.11 – 2.02 (m, 1H), 1.95 – 1.84 (m, 1H), 1.80 – 1.68 (m, 1H), 1.55 (s, 3H), 1.53 – 1.47 (m, 1H), 1.18 (d, *J* = 6.7 Hz, 3H), 1.17 (d, *J* = 6.7 Hz, 3H), 1.12 (s, 3H).
^{13}C NMR ($CDCl_3$, 125 MHz): δ 196.22, 177.93, 167.22, 164.34, 163.90, 161.67, 153.01, 148.09, 146.18, 126.01, 123.80, 123.07, 119.23, 80.96, 77.22, 69.18, 48.13, 45.65, 40.09, 37.77, 31.03, 27.86, 25.50, 24.36, 24.15, 20.94, 17.33.

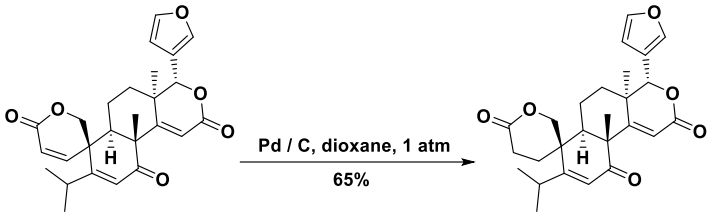
HRMS(ESI): m/z calc. for $C_{27}H_{29}O_7$ $[M+H]^+$: 465.1913, found: 465.1908.



Procedure: A solution of $NaBH_4$ (30 mg, 0.72 mmol) in anhydrous methanol (1.2 mL) was added to a solution of **S48** (60 mg, 0.12 mmol) in dichloromethane (2.4 mL) at -20° C and the resulting mixture was stirred at -78 °C. After 20 minutes, the reaction was quenched by the addition of a 2 M hydrochloric acid solution and extracted three times with dichloromethane. The organic layers were dried over Na_2SO_4 and concentrated by distillation under reduced pressure to obtained a crude residue that was purified by silica gel flash chromatography (hexane-ethyl acetate 3:7) to provide **S49** (32 mg, 58%) as a white solid.

^{1}H NMR ($CDCl_3$/CD_3OD, 125 MHz): δ 7.34 (s, 1H), 6.64 (s, 1H), 6.22 (br s. 1H), 6.21 (dd, *J* = 9.8, 1.6 Hz, 1H), 6.05 (d, *J* = 9.8 Hz, 1H), 5.55 (d, *J* = 1.9 Hz, 1H), 4.92 (s, 1H), 4.64 (dd, *J* = 12.6, 1.6 Hz, 1H), 4.43 (s, 2H), 4.41 (d, *J* = 12.6 Hz, 1H), 4.06 (d, *J* = 1.9 Hz, 1H), 2.15 (hept, *J* = 6.8 Hz, 1H), 1.86 – 1.76 (m, 2H), 1.71 – 1.63 (m, 1H), 1.62 – 1.55 (m, 1H), 1.41 – 1.36 (m, 1H), 1.14 (s, 3H), 1.07 (s, 3H), 1.02 (d, *J* = 6.8 Hz, 3H), 0.98 (d, *J* = 6.8 Hz, 3H). (30 non-exchangeable protons)
^{13}C NMR ($CDCl_3$/CD_3OD, 125 MHz): δ 178.55, 170.68, 167.26, 159.01, 155.61, 148.63, 144.91, 132.95, 125.86, 124.38, 120.34, 111.51, 85.70, 77.42, 73.51, 60.60, 48.74, 46.57, 43.38, 41.61, 33.17, 32.39, 28.91, 28.88, 24.92, 21.50, 21.24.
HRMS(ESI): m/z calc. for $C_{27}H_{33}O_7$ $[M+H]^+$: 469.2226, found: 469.2223.
Opt. Rot.: $[\alpha]_D^{25}$ = + 11 (c = 0.09, acetone).

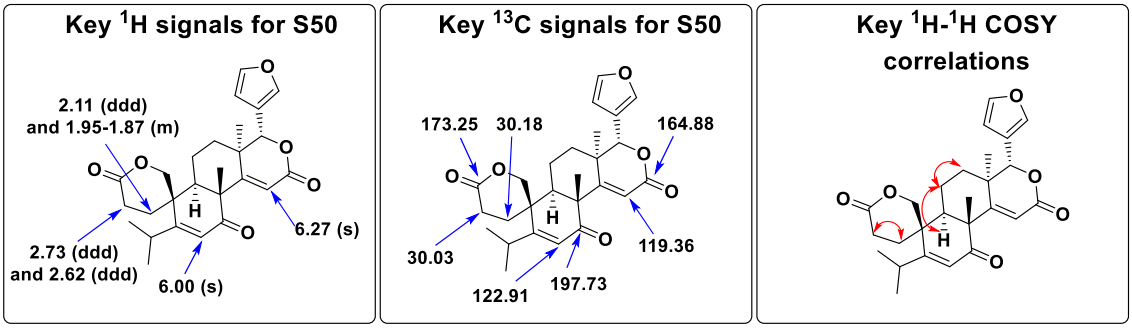


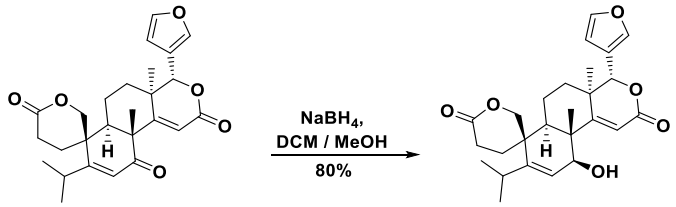


10 S50

Procedure: A suspension of **10** (115 mg, 0.25 mmol) in dioxane (16 mL) was hydrogenated in the presence of 10% Pd/C at 1 atm for 48 h. The catalyst was removed by filtration over celite, and the filtrate was evaporated under reduced pressure to obtained a crude residue that was purified by silica gel flash chromatography (hexane-ethyl acetate dichloromethane 4:5:1) to provide **S50** (71 mg, 65%) as a white solid.

^{1}H NMR (DMSO-*d6*, 125 MHz): δ 7.77 (d, *J* = 1.7 Hz, 1H), 7.70 (dd, *J* = 1.7, 1.7 Hz, 1H), 6.57 (d, *J* = 1.7 Hz, 1H), 6.27 (s, 1H), 6.00 (s, 1H), 5.20 (s, 1H), 4.63 (d, *J* = 12.4 Hz, 1H), 4.47 (d, *J* = 12.4 Hz, 1H), 2.73 (ddd, *J* = 14.7, 8.1, 6.3 Hz, 1H), 2.62 (ddd, *J* = 15.4, 8.1, 6.3 Hz, 1H), 2.57 – 2.52 (m, 1H), 2.36 (dd, *J* = 11.9, 3.9 Hz, 1H), 2.11 (ddd, *J* = 14.7, 8.1, 6.3 Hz, 1H), 1.95 – 1.87 (m, 2H), 1.83 – 1.73 (m, 2H), 1.38 (s, 3H), 1.36 – 1.22 (m, 1H), 1.18 (d, *J* = 6.8 Hz, 3H), 1.13 (d, *J* = 6.8 Hz, 3H), 1.00 (s, 3H).
^{13}C NMR (DMSO-*d6*, 125 MHz): δ 197.73, 174.03, 173.25, 166.31, 164.80, 143.80, 142.23, 122.91, 120.73, 119.36, 110.87, 80.67, 69.18, 49.66, 44.82, 43.19, 37.38, 30.21, 30.18, 30.03, 29.30, 25.00, 24.70, 24.38, 22.00, 17.82.
HRMS(ESI): m/z calc. for $C_{26}H_{31}O_6$ $[M+H]^+$: 439.2121, found: 439.2117.
Opt. Rot.: $[\alpha]_D^{25}$ = - 87 (c = 0.03, acetone).

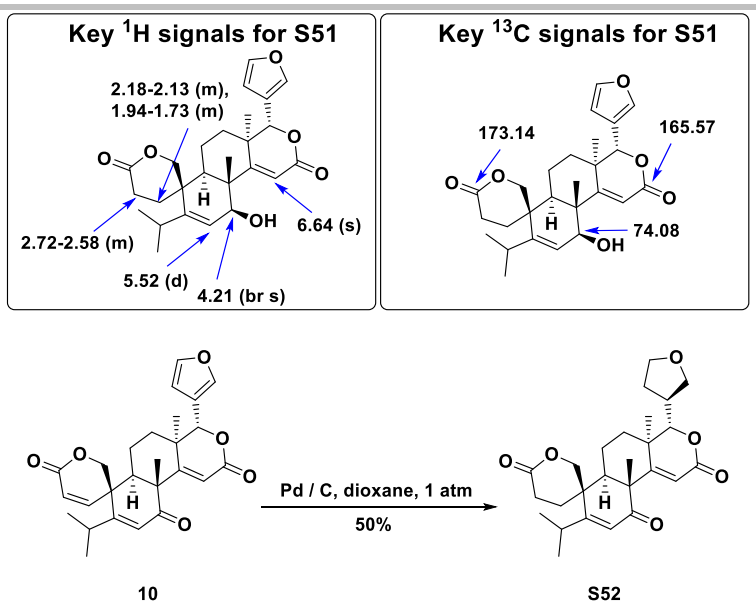




S50 S51

Procedure: A solution of $NaBH_4$ (12 mg, 0. 34 mmol) in anhydrous methanol (1 mL) was added to a solution of **S50** (34 mg, 0.08 mmol) in dichloromethane (2 mL) at -40° C and the resulting mixture was stirred at -20 °C. After 15 minutes, the reaction was quenched with a 2 M hydrochloric acid solution and extracted three times with dichloromethane. The organic layers were dried over Na_2SO_4 and concentrated by distillation under reduced pressure. The obtained crude residue was purified by silica gel flash chromatography (hexane-ethyl acetate 4:6) to provide an amorphous solid that was further purify by crystallization (chloroform/ hexane) to obtain **S51** (34 mg, 80%).

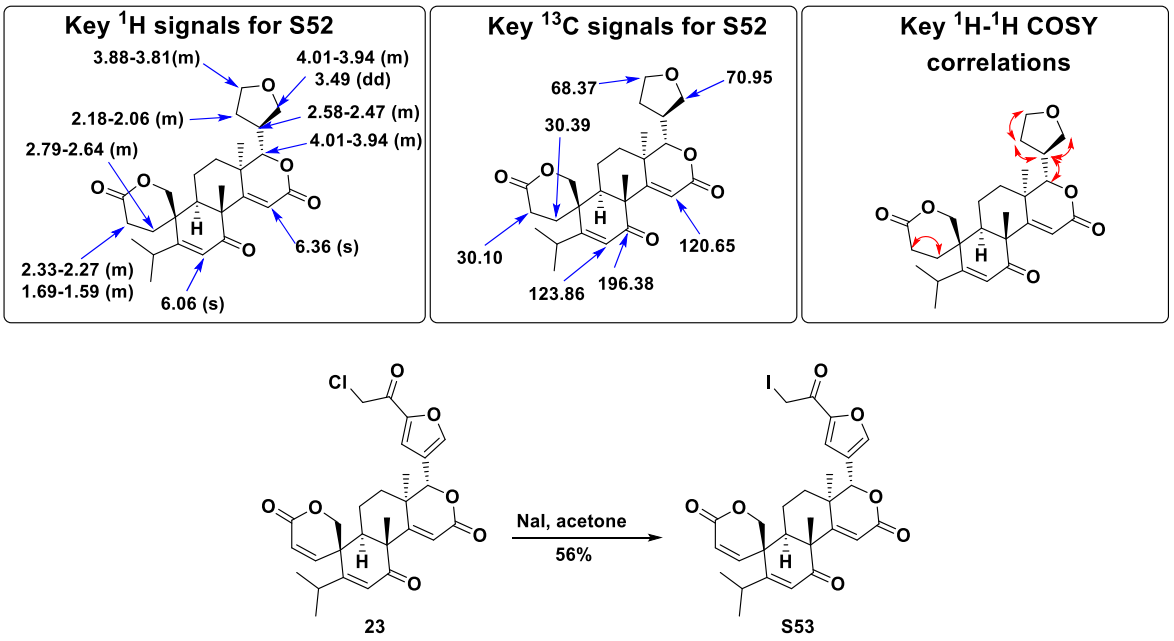
^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.51 (d, *J* = 1.7 Hz, 1H), 7.45 (dd, *J* = 1.7, 1.8 Hz, 1H), 6.64 (s, 1H), 6.46 (d, *J* = 1.8 Hz, 1H), 5.52 (d, *J* = 1.8 Hz, 1H), 5.07 (s, 1H), 4.54 (d, *J* = 12.6 Hz, 1H), 4.31 (d, *J* = 12.6 Hz, 1H), 4.21 (br s, 1H), 2.72 – 2.58 (m, 2H), 2.40 (hept, *J* = 6.7 Hz, 1H), 2.33 – 2.27 (m, 1H), 2.18 – 2.13 (m, 1H), 1.94 – 1.73 (m, 4H), 1.56 – 1.46 (m, 1H), 1.22 (s, 3H), 1.21 (d, *J* = 6.7 Hz, 3H), 1.21 (s, 3H), 1.16 (d, *J* = 6.7 Hz, 3H). (31 non-exchangeable protons)
^{13}C NMR ($CDCl_3$, 125 MHz): δ 173.14, 172.62, 165.57, 149.64, 143.06, 141.36, 125.79, 120.07, 117.38, 110.10, 81.46, 74.08, 69.30, 44.88, 44.29, 41.90, 37.56, 31.72, 30.56, 30.28, 28.85, 25.88, 25.40, 22.35, 18.31, 16.88.
HRMS(ESI): m/z calc. for $C_{26}H_{33}O_6$ $[M+H]^+$: 441.2277, found: 441.2267.



Procedure: A suspension of **10** (50 mg, 0.114 mmol) in dioxane (7 mL) was hydrogenated in the presence of 10% Pd/C at 1 atm for 72 h. The catalyst was removed by filtration over celite, and the filtrate was evaporated under reduced pressure to obtained a crude residue that was purified by silica gel flash chromatography (ethyl acetate-methanol 9:1) to provide **S52** (25 mg, 50%) as a white solid.

Note: Compound **S50** (mono reduced) was also isolated (17 mg, 34%) as a white solid.

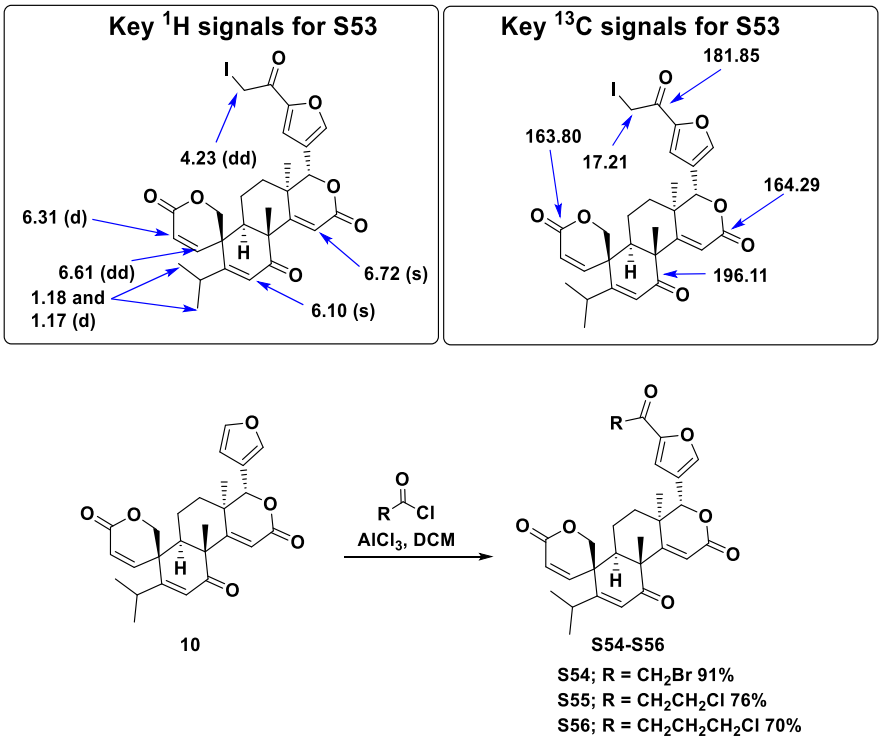
^{1}H NMR (DMSO-*d6*, 125 MHz): δ 6.36 (s, 1H), 6.06 (s, 1H), 4.59 (d, *J* = 12.5 Hz, 1H), 4.38 (d, *J* = 12.5 Hz, 1H), 4.01 – 3.94 (m, 2H), 3.88 – 3.81 (m, 2H), 3.49 (dd, *J* = 9.7, 8.3 Hz, 1H), 2.79 – 2.64 (m, 2H), 2.58 – 2.47 (m, 2H), 2.39 (dd, *J* = 12.9, 3.6 Hz, 1H), 2.33 – 2.27 (m, 1H), 2.18 – 2.06 (m, 2H), 2.05 – 1.98 (m, 1H), 1.96 – 1.82 (m, 2H), 1.69 – 1.59 (m, 2H), 1.40 (s, 3H), 1.26 (d, *J* = 6.8 Hz, 3H), 1.19 (d, *J* = 6.7 Hz, 3H), 1.15 (s, 3H).
^{13}C NMR (DMSO-*d6*, 125 MHz): δ 196.38, 171.71, 171.09, 164.46, 163.72, 123.86, 120.65, 84.86, 70.95, 68.93, 68.37, 49.66, 45.00, 43.10, 38.96, 37.58, 30.76, 30.44, 30.39, 30.10, 28.05, 25.02, 24.50, 24.44, 23.13, 18.48.
HRMS(ESI): m/z calc. for $C_{26}H_{35}O_6$ $[M+H]^+$: 443.2434, found: 443.2417.
mp: >260° C.
Opt. Rot.: $[\alpha]_D^{25}$ = - 249 (c = 0.09, acetone/chloroform).



Procedure: NaI (12 mg, 0.08 mmol) was added to a solution of **23** (20 mg, 0.04 mmol) in acetone (1 mL), and the resulting solution was stirred in the darkness at 40° C for 90 minutes. The solvent was evaporated, and the residue purified by flash chromatography on silica gel (hexane-ethyl acetate 6:4), giving **S53** (14 mg, 56%) as a white solid.

Note: Compound **S53** is not stable in solution.

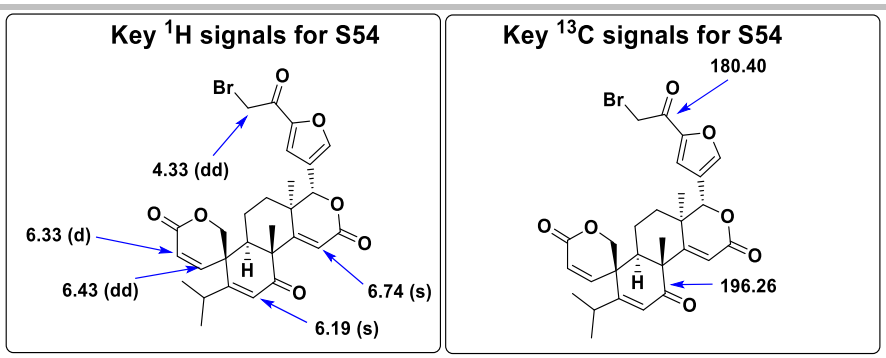
^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.68 (s, 1H), 7.29 (s, 1H), 6.72 (s, 1H), 6.41 (dd, *J* = 9.9, 1.6 Hz, 1H), 6.31 (d, *J* = 9.9 Hz, 1H), 6.17 (s, 1H), 5.09 (s, 1H), 4.78 (dd, *J* = 12.4, 1.6 Hz, 1H), 4.54 (d, *J* = 12.4 Hz, 1H), 4.23 (dd, *J* = 9.7, 15.7 Hz, 2H), 2.53 – 2.44 (m, 2H), 2.09 – 2.01 (m, 1H), 1.94 – 1.87 (m, 1H), 1.76 – 1.70 (m, 1H), 1.57 – 1.50 (m, 1H), 1.54 (s, 3H), 1.18 (d, *J* = 6.7 Hz, 3H), 1.17 (d, *J* = 6.7 Hz, 3H), 1.13 (s, 3H).
^{13}C NMR ($CDCl_3$, 125 MHz): δ 196.11, 181.95, 167.12, 164.29, 163.80, 161.53, 149.89, 147.97, 145.06, 125.86, 123.65, 123.18, 119.04, 117.82, 80.88, 77.11, 69.09, 47.99, 45.50, 39.97, 37.66, 30.90, 27.69, 25.37, 24.22, 24.01, 20.81, 17.21.
HRMS(ESI): m/z calc. for $C_{28}H_{30}O_7I$ $[M+H]^+$: 605.1036, found: 605.1046.



Procedure: $AlCl_3$ (40 mg, 0.30 mmol) was added at 0° C to a cooled solution of **10** (28 mg, 0.065 mmol), in dichloromethane (1.3 mL). The resulting mixture was stirred 30 minutes before the suitable acyl chloride (0.079 mmol) was added to the solution, and the resulting solution was allowed to stir at 30° C for 12 h. Water was added, and the aqueous layer was extracted three times with dichloromethane. The combined organic layers were washed with 2M sodium hydroxide and brine. After drying over Na_2SO_4, the solution was concentrated by distillation at reduced pressure, and the residue was purified by flash chromatography on silica gel (hexane-ethyl acetate 6:4), giving **S54-S56** (70-91%) as white solids.

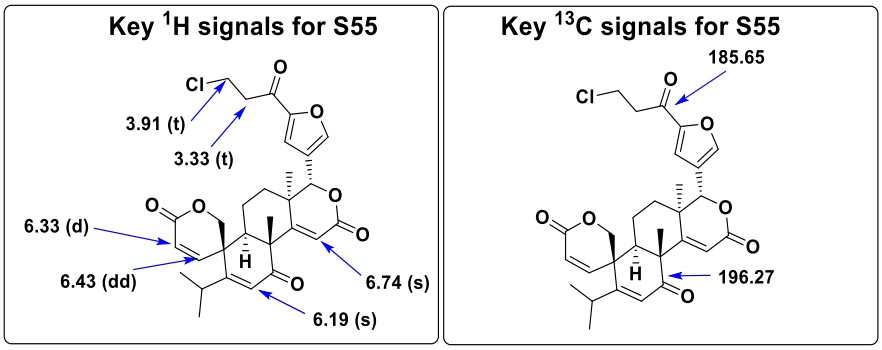
S54 (33 mg, 91%)

^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.72 (s, 1H), 7.34 (s, 1H), 6.74 (s, 1H), 6.43 (dd, *J* = 9.9, 1.5 Hz, 1H), 6.33 (d, *J* = 9.9 Hz, 1H), 6.19 (s, 1H), 5.12 (s, 1H), 4.80 (dd, *J* = 12.4, 1.5 Hz, 1H), 4.57 (d, *J* = 12.4 Hz, 1H), 4.33 (dd, *J* = 15.3, 11.8 Hz, 2H), 2.54 (dd, *J* = 13.0, 5.7 Hz, 1H), 2.49 (hept, *J* = 6.7 Hz, 1H), 2.13 – 2.02 (m, 1H), 1.95 – 1.88 (m, 1H), 1.76 (ddd, *J* = 14.0, 9.7, 6.5 Hz, 1H), 1.56 (s, 3H), 1.57 – 1.51 (m, 1H), 1.20 (d, *J* = 6.7 Hz, 3H), 1.19 (d, *J* = 6.7 Hz, 3H), 1.14 (s, 3H).
^{13}C NMR ($CDCl_3$, 125 MHz): δ 196.26, 180.40, 167.27, 164.46, 163.93, 161.69, 150.45, 148.12, 145.47, 125.99, 123.77, 123.31, 119.15, 118.19, 80.97, 69.21, 48.12, 45.64, 40.08, 37.79, 31.03, 29.71, 27.80, 25.50, 24.35, 24.14, 20.92, 17.32.
HRMS(ESI): m/z calc. for $C_{28}H_{30}O_7Br$ $[M+H]^+$: 557.1175, found: 557.1169.



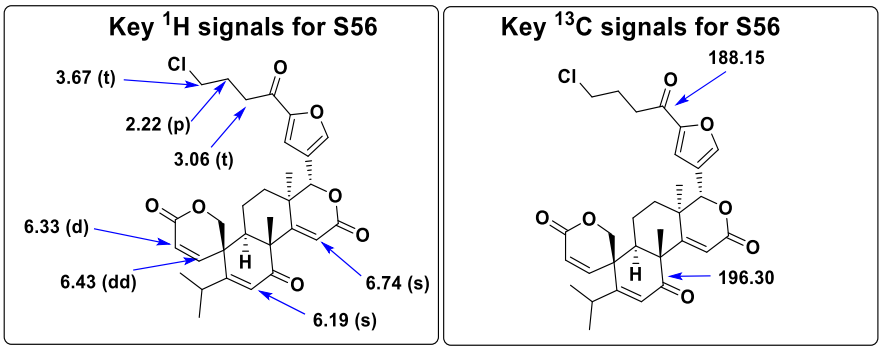
S55 (26 mg, 76%)

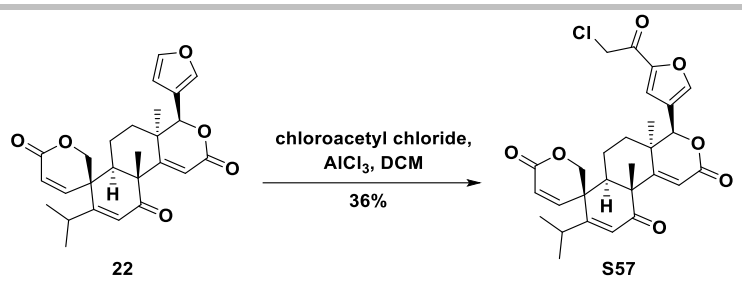
^{1}H NMR (CDCl$_3$, 500 MHz): δ 7.69 (s, 1H), 7.25 (s, 1H), 6.74 (s, 1H), 6.43 (dd, *J* = 9.9, 1.6 Hz, 1H), 6.33 (d, *J* = 9.9 Hz, 1H), 6.19 (s, 1H), 5.11 (s, 1H), 4.80 (dd, *J* = 12.4, 1.6 Hz, 1H), 4.57 (d, *J* = 12.4 Hz, 1H), 3.91 (t, *J* = 6.6 Hz, 2H), 3.33 (t, *J* = 6.6 Hz, 2H), 2.54 (dd, *J* = 13.0, 5.6 Hz, 1H), 2.49 (hept, *J* = 6.7 Hz, 1H), 2.14 – 2.02 (m, 1H), 1.97 – 1.84 (m, 1H), 1.95 – 1.87 (m, 1H), 1.56 (s, 3H), 1.55 – 1.50 (m, 1H), 1.20 (d, *J* = 6.7 Hz, 3H), 1.19 (d, *J* = 6.7 Hz, 3H), 1.14 (s, 3H).
^{13}C NMR (CDCl$_3$, 125 MHz): δ 196.27, 185.65, 167.27, 164.46, 163.99, 161.68, 152.50, 148.12, 144.99, 125.99, 123.77, 122.95, 119.15, 116.75, 81.06, 69.23, 48.12, 45.63, 40.97, 40.11, 38.05, 37.80, 31.03, 27.83, 25.50, 24.35, 24.14, 20.94, 17.34.
HRMS(ESI): m/z calc. for $C_{29}H_{32}O_7Cl$ $[M+H]^+$: 527.1837, found: 527.1820.
mp: decomposes upon heating above 230° C.
Opt. Rot.: $[\alpha]_D^{25}$ = - 110 (c = 0.10, acetone).



S56 (26 mg, 70%)

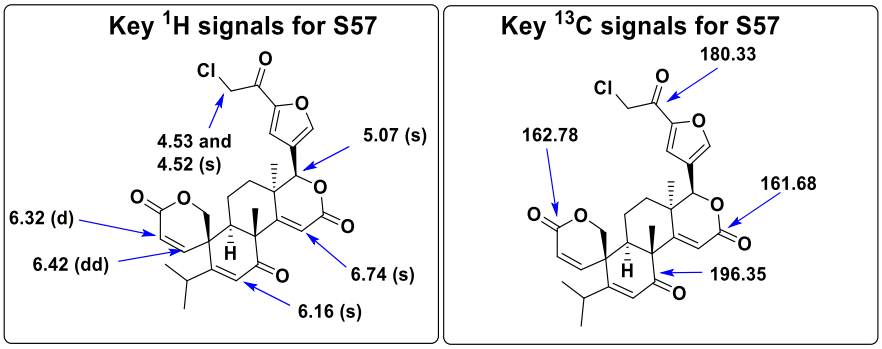
^{1}H NMR (CDCl$_3$, 500 MHz): δ 7.67 (s, 1H), 7.22 (s, 1H), 6.74 (s, 1H), 6.43 (dd, *J* = 9.9, 1.6 Hz, 1H), 6.33 (d, *J* = 9.9 Hz, 1H), 6.19 (s, 1H), 5.10 (s, 1H), 4.80 (dd, *J* = 12.4, 1.6 Hz, 1H), 4.57 (d, *J* = 12.4 Hz, 1H), 3.67 (t, *J* = 6.7 Hz, 2H), 3.06 (t, *J* = 6.7 Hz, 2H), 2.54 (dd, *J* = 13.0, 5.7 Hz, 1H), 2.49 (hept, *J* = 6.7 Hz, 1H), 2.22 (p, *J* = 6.7 Hz, 2H), 2.10 – 2.02 (m, 1H), 1.97 – 1.86 (m, 1H), 1.77 – 1.71 (m, 1H), 1.56 (s, 3H), 1.55 – 1.51 (m, 1H), 1.20 (d, *J* = 6.7 Hz, 3H), 1.19 (d, *J* = 6.7 Hz, 3H), 1.14 (s, 3H).
^{13}C NMR (CDCl$_3$, 125 MHz): δ 196.30, 188.15, 167.26, 164.50, 164.07, 161.71, 152.65, 148.14, 144.67, 126.00, 123.76, 122.70, 119.13, 116.26, 81.13, 69.24, 48.11, 45.63, 44.38, 40.11, 37.81, 35.16, 31.03, 27.82, 26.36, 25.51, 24.35, 24.14, 20.93, 17.34.
HRMS(ESI): m/z calc. for $C_{30}H_{34}O_7Cl$ $[M+H]^+$: 541.1993, found: 541.1980
Opt. Rot.: $[\alpha]_D^{25}$ = - 174 (c = 0.02, acetone).

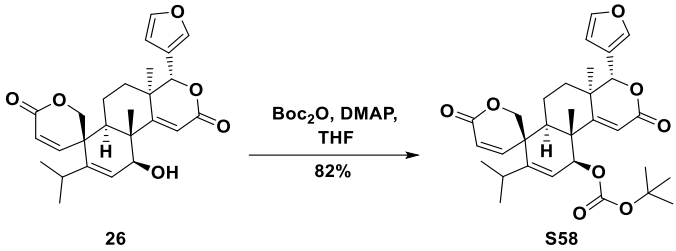




Procedure: $AlCl_3$ (4 mg, 0.03 mmol) was added at 0° C to a cooled solution of **22** (3 mg, 0.006 mmol), in dichloromethane (0.5 mL). The resulting mixture was stirred 30 minutes, before chloroacetyl chloride (1 µL, 0.007 mmol) was added to the solution, and the resulting solution was stirred at 30° C for 12 h. Water was added, and the aqueous layer was extracted three times with dichloromethane. The combined organic layers were washed with 2M sodium hydroxide and brine. After drying over Na_2SO_4, the solution was concentrated by distillation at reduced pressure, and the residue was purified by flash chromatography on silica gel (hexane-ethyl acetate 6:4), giving **S57** (2 mg, 36%) as a white solid.

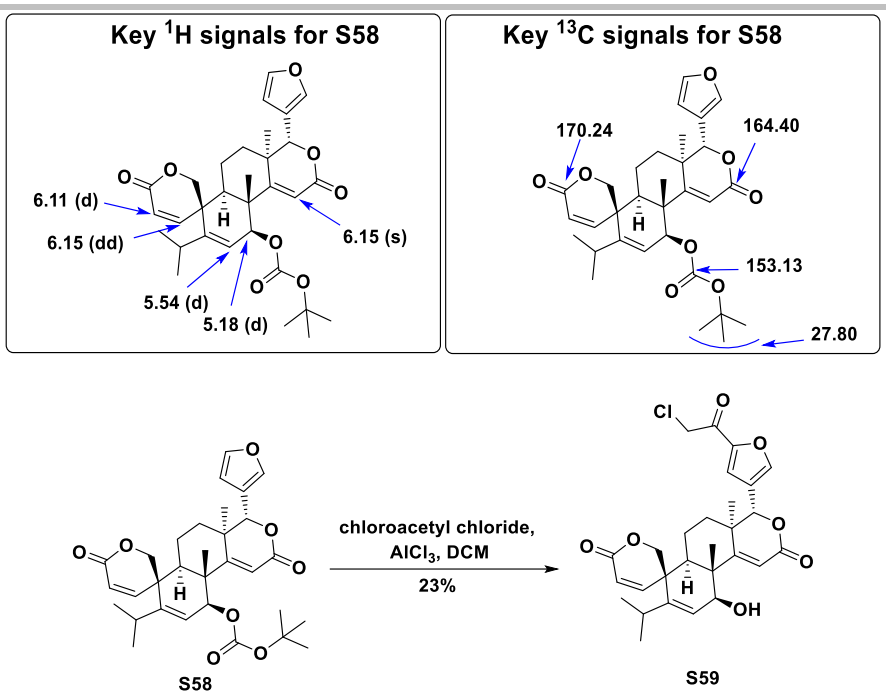
^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.55 (s, *J* = 0.9 Hz, 1H), 7.21 (d, *J* = 0.9 Hz, 1H), 6.74 (s, 1H), 6.42 (dd, *J* = 9.9, 1.4 Hz, 1H), 6.32 (d, *J* = 9.9 Hz, 1H), 6.16 (s, 1H), 5.07 (s, 1H), 4.67 (dd, *J* = 12.4, 1.6 Hz, 1H), 4.53 (s, 1H), 4.52 (s, 1H), 4.49 (d, H = 12.4 Hz, 1H), 2.44 (dt, *J* = 10.4, 6.0 Hz, 2H), 1.89 – 1.79 (m, 1H), 1.79 – 1.71 (m, 1H), 1.67 – 1.59 (m, 1H), 1.52 (s, 3H), 1.48 – 1.43 (m, 1H), 1.35 (s, 3H), 1.17 (d, *J* = 6.7 Hz, 3H), 1.16 (d, *J* = 6.7 Hz, 3H).
^{13}C NMR ($CDCl_3$, 125 MHz): δ196.35, 180.33, 167.64, 162.78, 161.68, 160.87, 150.87, 148.07, 145.33, 125.98, 124.85, 123.89, 119.17, 117.42, 81.03, 69.37, 47.89, 45.59, 44.92, 41.03, 38.14, 31.08, 29.94, 28.24, 24.48, 24.32, 24.11, 18.16.
HRMS(ESI): m/z calc. for $C_{28}H_{30}O_7Cl$ $[M+H]^+$: 513.1680, found: 513.1691.





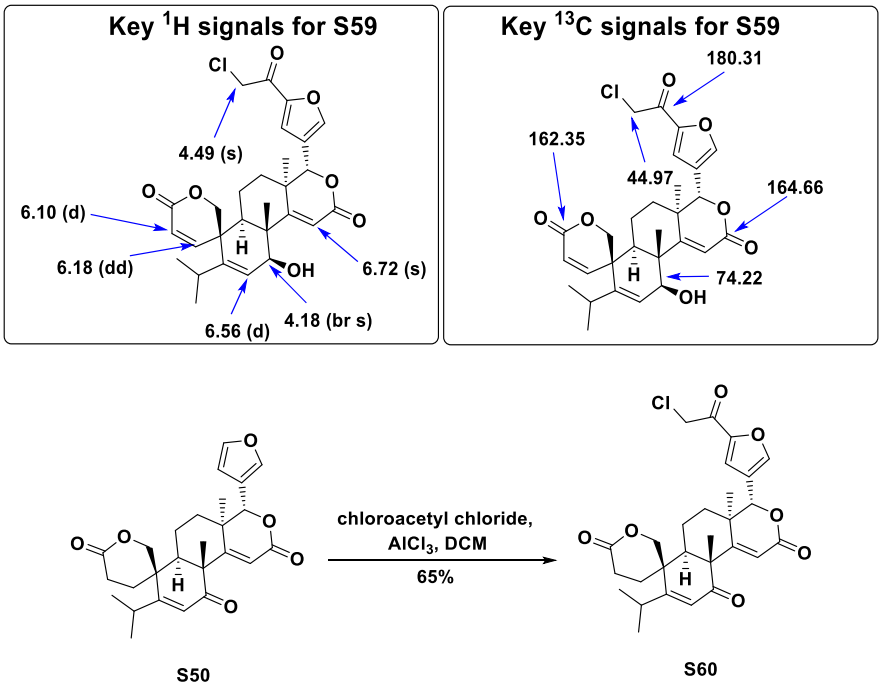
Procedure: DMAP (8 mg, 0.06 mmol) was added to a solution of **26** (20 mg, 0.046 mmol) and di-*tert*-butyl dicarbonate (12 mg, 0.05 mmol) in tetrahydrofuran (1 mL), and the resulting solution was stirred at 30° C for 16 h. The solvent was removed under vacuum and the residue purified by silica gel flash chromatography (hexane-ethyl acetate 4:6) to provide **S58** (20 mg, 82%) as a white solid.

^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.41 (s, 1H), 7.35 (d, *J* = 1.7 Hz, 1H), 6.36 (d, *J* = 1.7 Hz, 1H), 6.18 (dd, *J* = 9.9, 1.5 Hz, 1H), 6.15 (s, 1H), 6.11 (d, *J* = 9.9 Hz, 1H), 5.54 (d, *J* = 1.8 Hz, 1H), 5.18 (d, *J* = 1.8 Hz, 1H), 4.96 (s, 1H), 4.63 (dd, *J* = 12.4, 1.5 Hz, 1H), 4.44 (d, *J* = 12.4 Hz, 1H), 2.20 (hept, *J* = 6.8 Hz, 1H), 1.88 (dd, *J* = 11.5, 4.4 Hz, 1H), 1.75 – 1.65 (m, 3H), 1.47 (s, 9H), 1.43 – 1.33 (m, 1H), 1.23 (s, 3H), 1.17 (s, 3H), 1.03 (d, *J* = 6.8 Hz, 3H), 1.01 (d, *J* = 6.8 Hz, 3H).
^{13}C NMR ($CDCl_3$, 125 MHz): δ 170.24, 164.40, 162.45, 153.13, 150.64, 147.13, 143.08, 141.40, 124.92, 122.76, 119.99, 117.93, 110.11, 83.74, 81.22, 77.57, 69.09, 44.72, 41.90, 41.18, 37.74, 30.63, 29.48, 27.80 (3C), 25.02, 25.00, 22.94, 18.30, 17.39.
HRMS(ESI): m/z calc. for $C_{31}H_{39}O_8$ $[M+H]^+$: 539.2645, found: 539.2667



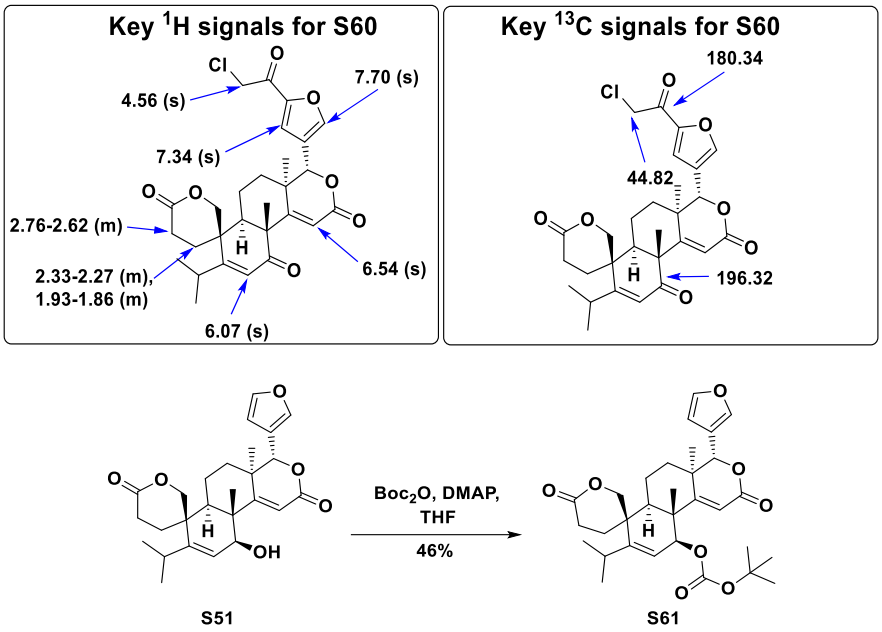
Procedure: $AlCl_3$ (11 mg, 0.08 mmol) was added at 0° C to a cooled solution of **S58** (10 mg, 0.019 mmol), in dichloromethane (0.3 mL). The resulting mixture was stirred 30 minutes, before chloroacetyl chloride (2 µL, 0.022 mmol) was added to the mixture, and the resulting solution was stirred at 30° C for 12 h. Water was added, and the aqueous layer was extracted three times with dichloromethane. The combined organic layers were washed with 2M sodium hydroxide and brine. After drying over Na_2SO_4, the solution was concentrated by distillation at reduced pressure, and the residue was purified by flash chromatography on silica gel (hexane-ethyl acetate 6:4), giving **S59** (3 mg, 23%) as a white solid.

^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.61 (s, 1H), 7.27 (s, 1H), 6.72 (s, 1H), 6.18 (dd, *J* = 9.9, 1.7 Hz, 1H), 6.10 (d, *J* = 9.9 Hz, 1H), 5.56 (d, *J* = 1.9 Hz, 1H), 5.01 (s, 1H), 4.63 (dd, *J* = 12.6, 1.7 Hz, 1H), 4.49 (s, 2H), 4.43 (d, *J* = 12.6 Hz, 1H), 4.18 (br s, 1H), 2.20 (hept, *J* = 6.8 Hz, 1H), 1.93 – 1.82 (m, 2H), 1.81 – 1.71 (m, 1H), 1.66 (ddd, *J* = 14.7, 8.7, 6.1 Hz, 1H), 1.45 1.39 (m, 1H), 1.20 (s, 3H), 1.19 – 1.17 (m, 1H), 1.08 (s, 3H), 1.04 (d, *J* = 6.8 Hz, 3H), 1.02 (d, *J* = 6.8 Hz, 3H).
^{13}C NMR ($CDCl_3$, 125 MHz): δ 180.31, 172.88, 164.66, 162.35, 150.66, 150.53, 146.08, 145.34, 128.00, 123.33, 122.60, 117.98, 117.14, 80.77, 74.22, 69.24, 44.97, 44.86, 42.67, 39.30, 37.56, 29.39, 28.46, 25.21, 25.15, 21.10, 17.75, 17.19.
HRMS(ESI): m/z calc. for $C_{28}H_{32}O_7Cl$ $[M+H]^+$: 515.1837, found: 515.1854.



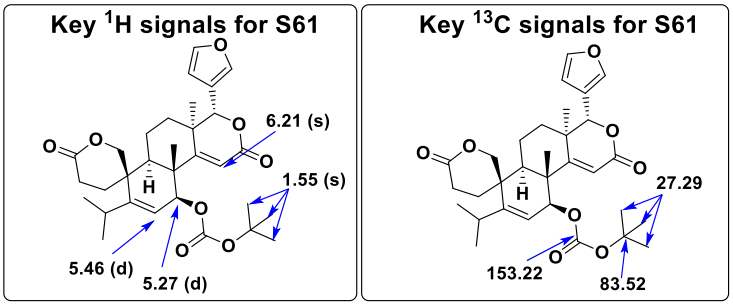
Procedure: $AlCl_3$ (38 mg, 0.28 mmol) was added at 0° C to a cooled solution of **S50** (28 mg, 0.064 mmol), in dichloromethane (1 mL). The resulting mixture was stirred 30 minutes, before chloroacetyl chloride (6 µL, 0.076 mmol) was added to the mixture, and the resulting solution was stirred at 30° C for 12 h. Water was added, and the aqueous layer was extracted three times with dichloromethane. The combined organic layers were washed with 2 M sodium hydroxide and brine. After drying over Na_2SO_4, the solution was concentrated by distillation at reduced pressure, and the residue was purified by flash chromatography on silica gel (hexane-ethyl acetate 6:4), giving **S60** (22 mg, 65%) as a white solid.

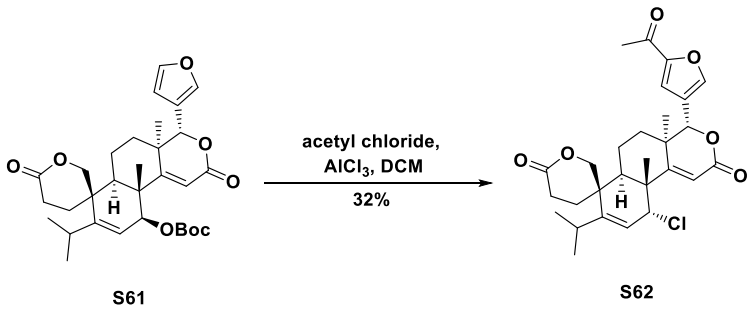
^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.70 (s, 1H), 7.34 (s, 1H), 6.54 (s, 1H), 6.07 (s, 1H), 5.10 (s, 1H), 4.61 (d, *J* = 12.5 Hz, 1H), 4.56 (s, 2H), 4.38 (d, *J* = 12.5 Hz, 1H), 2.76 – 2.62 (m, 2H), 2.53 (hept, *J* = 6.7 Hz, 1H), 2.40 (dd, *J* = 12.0, 5.1 Hz, 1H), 2.33 – 2.27 (m, 1H), 2.07 – 1.92 (m, 2H), 1.93 – 1.86 (m, 1H), 1.84 – 1.77 (m, 1H), 1.64 – 1.47 (m, 1H), 1.47 (s, 3H), 1.26 (d, *J* = 6.7 Hz, 3H), 1.20 (d, *J* = 6.7 Hz, 3H), 1.09 (s, 3H).
^{13}C NMR ($CDCl_3$, 125 MHz): δ 196.32, 180.34, 171.57, 171.42, 164.20, 163.86, 150.65, 145.46, 123.99, 123.44, 120.10, 117.93, 80.63, 68.98, 49.39, 44.99, 44.82, 43.14, 37.42, 30.52, 30.47, 30.01, 29.46, 25.01, 24.93, 24.46, 21.84, 17.95.
HRMS(ESI): m/z calc. for $C_{28}H_{32}O_7Cl$ $[M+H]^+$: 515.1837, found: 515.1840.
Opt. Rot.: $[\alpha]_D^{25}$ = - 37 (c = 0.08, acetone).



Procedure: DMAP (15 mg, 0.12 mmol) was added to a solution of **S51** (42 mg, 0.09 mmol) and di-*tert*-butyl dicarbonate (21mg, 0.102 mmol) in tetrahydrofuran (1.5 mL), and the resulting solution was stirred at 30° C for 16 h. The solvent was removed under vacuum and the residue purified by silica gel flash chromatography (hexane-ethyl acetate 7:3) to provide **S61** (24 mg, 46%) as a white solid.

^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.51 (d, *J* = 1.8 Hz, 1H), 7.44 (dd, *J* = 1.8, 1.8 Hz, 1H), 6.47 (d, *J* = 1.8 Hz, 1H), 6.21 (s, 1H), 5.46 (d, *J* = 1.8 Hz, 1H), 5.27 (d, *J* = 1.8 Hz, 1H), 5.05 (s, 1H), 4.54 (d, *J* = 12.5 Hz, 1H), 4.33 (d, *J* = 12.5 Hz, 1H), 2.74 – 2.58 (m, 2H), 2.40 (hept, *J* = 6.7 Hz, 1H), 2.23 – 2.13 (m, 1H), 1.92 – 1.83 (m, 3H), 1.82 – 1.65 (m, 2H), 1.55 (s, 9H), 1.50 – 1.42 (m, 1H), 1.28 (s, 3H), 1.28 (s, 3H), 1.21 (d, *J* = 6.7 Hz, 3H), 1.14 (d, *J* = 6.7 Hz, 3H).
^{13}C NMR ($CDCl_3$, 125 MHz): δ 172.53, 170.37, 164.45, 153.22, 150.69, 143.05, 141.41, 122.53, 120.11, 118.13, 110.18, 83.52, 81.06, 77.56, 68.91, 46.36, 43.39, 41.85, 37.60, 32.01, 31.94, 30.50, 29.01, 27.79 (3C), 25.61, 25.29, 23.72, 19.12, 16.85.
HRMS(ESI): m/z calc. for $C_{31}H_{41}O_8$ $[M+H]^+$: 541.2801, found: 541.2820.

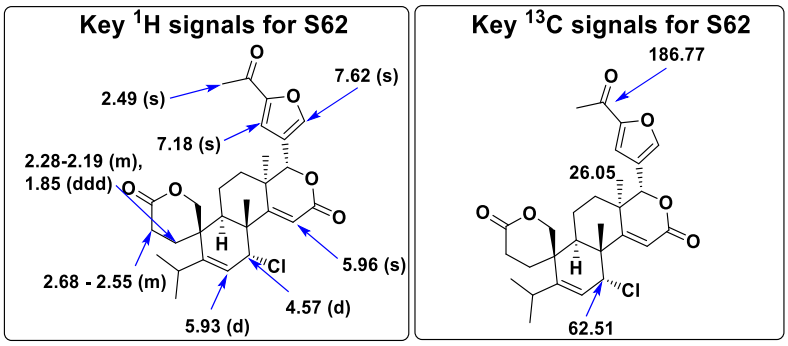


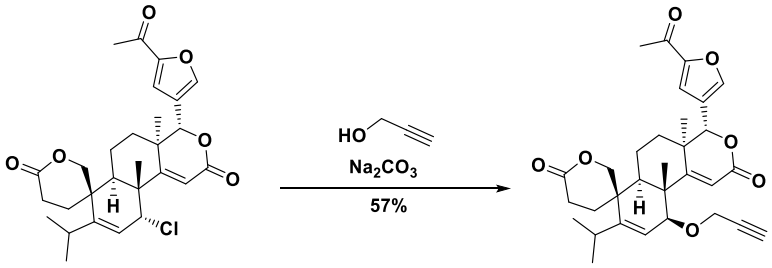


S61 **S62**

Procedure: $AlCl_3$ (290 mg, 2.22 mmol) was added at 0° C to a cooled solution of **S61** (260 mg, 0.50 mmol), in dichloromethane (10 mL). The resulting mixture was stirred 30 minutes before acetyl chloride (60 µL, 0.70 mmol) was added to the mixture, and the resulting solution was stirred at 30° C for 12 h. Water was added, and the aqueous layer was extracted three times with dichloromethane. The combined organic layers were washed with brine. After drying over Na_2SO_4, the solution was concentrated by distillation at reduced pressure, and the residue was purified by flash chromatography on silica gel (hexane-ethyl acetate 4:6), giving **S62** (70 mg, 32%) as a white solid.

^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.62 (s, 1H), 7.18 (s, 1H), 5.96 (s, 1H), 5.93 (d, *J* = 6.2 Hz, 1H), 5.02 (s, 1H), 4.57 (d, *J* = 6.2 Hz, 1H), 4.48 (d, *J* = 12.8 Hz, 1H), 4.30 (d, *J* = 12.8 Hz, 1H), 2.68 – 2.55 (m, 3H), 2.50 – 2.43 (m, 1H), 2.49 (s, 3H), 2.28 – 2.19 (m, 1H), 2.13 – 2.03 (m, 1H), 2.03 – 1.91 (m, 1H), 1.87 (ddd, *J* = 14.9, 12.0, 6.0 Hz, 1H), 1.63 (dd, *J* = 9.2, 2.9 Hz, 1H), 1.62 – 1.55 (m, 1H), 1.33 (s, 3H), 1.24 (d, *J* = 6.7 Hz, 3H), 1.17 (s, 3H), 1.12 (d, *J* = 6.7 Hz, 3H).
^{13}C NMR ($CDCl_3$, 125 MHz): δ 186.77, 172.00, 171.96, 164.49, 152.92, 151.19, 144.53, 122.71, 122.15, 116.47, 115.54, 81.59, 69.01, 62.51, 44.05, 42.65, 37.49, 37.35, 31.79, 30.40, 29.12, 26.79, 26.05, 25.65, 25.19, 25.14, 18.04, 15.84.
HRMS(ESI): m/z calc. for $C_{28}H_{34}O_6Cl$ $[M+H]^+$: 501.2044, found: 501.2050



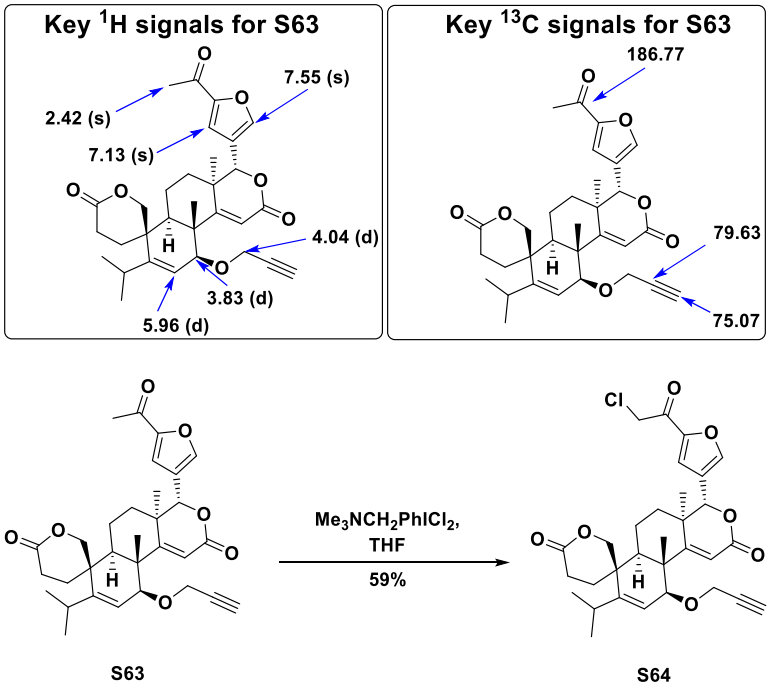


S62 **S63**

Procedure: S62 (70 mg, 0.14 mmol) was added to a suspension of Na_2CO_3 (300 mg, 1.4 mmol) in propargyl alcohol (5 mL) heated at 50° C. The resulting mixture was stirred at 50° C for 16 h. Water was added, and the aqueous layer was extracted three times with dichloromethane. The combined organic layers were washed with brine, dried over Na_2SO_4, the solution was concentrated by distillation at reduced pressure. The obtained residue was purified by preparative thin layer chromatography on silica gel (hexane-ethyl acetate 3:7), giving **S63** (40 mg, 57%) as a white solid.

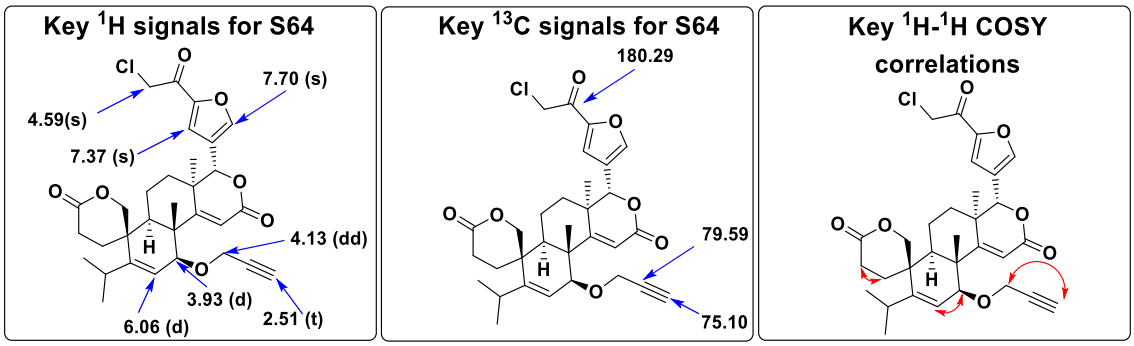
^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.55 (s, 1H), 7.13 (s, 1H), 5.96 (d, *J* = 6.0 Hz, 1H), 5.92 (s, 1H), 4.95 (s, 1H), 4.39 (d, *J* = 12.6 Hz, 1H), 4.22 (d, *J* = 12.6 Hz, 1H), 4.04 (d, *J* = 2.4 Hz, 2H), 3.83 (d, *J* = 6.0 Hz, 1H), 2.65 – 2.49 (m, 2H), 2.42 (s, 3H), 2.42 – 2.31 (m, 3H), 2.16 – 2.06 (ddd, *J* = 15.1, 6.5, 4.7 Hz, 1H), 1.83 – 1.79 (m, 2H), 1.74 (ddd, *J* = 15.1, 11.8, 5.9 Hz, 1H), 1.61 – 1.55 (m, 1H), 1.51 – 1.47 (m, 1H), 1.16 (d, *J* = 6.7 Hz, 3H), 1.11 (s, 3H), 1.08 (s, 3H), 1.07 (d, *J* = 6.7 Hz, 3H).

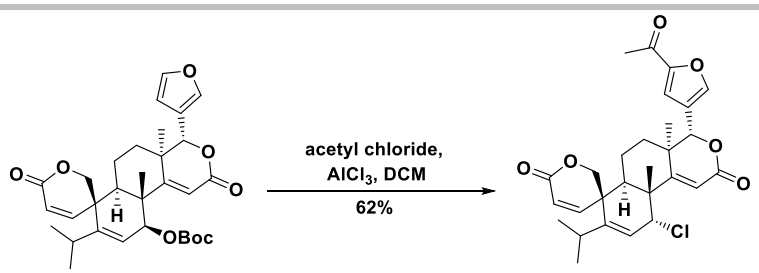
^{13}C NMR ($CDCl_3$, 125 MHz): δ 186.77, 173.74, 172.38, 164.87, 153.49, 152.82, 144.57, 123.09, 120.19, 116.72, 114.79, 81.28, 79.63, 75.07, 69.15, 56.23, 43.59, 42.35, 38.91, 37.24, 31.67, 30.50, 29.71, 29.35, 28.48, 26.04, 25.79, 25.52, 23.53, 19.58, 16.71.
HRMS(ESI): m/z calc. for $C_{31}H_{37}O_7$ $[M+H]^+$: 521.2539, found: 521.2524



Procedure: Benzyltrimethylammonium dichloro iodide (50 mg, 0.15 mmol) was added to a solution of **S63** (40 mg, 0.07 mmol) in THF (5 mL). The resulting mixture was stirred at 40° C for 16 h. Sodium bicarbonate 10% solution was added, and the aqueous layer was extracted three times with dichloromethane. The combined organic layers were washed with sodium thiosulfate saturate solution and brine. After drying over Na_2SO_4, the solution was concentrated by distillation at reduced pressure, and the residue was purified by flash chromatography on silica gel (hexane-ethyl acetate 1:1), giving **S64** (25 mg, 59%) as a white solid.

^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.70 (s, 1H), 7.37 (s, 1H), 6.06 (d, *J* = 6.0 Hz, 1H), 6.02 (s, 1H), 5.06 (s, 1H), 4.59 (s, 2H), 4.48 (d, *J* = 12.6 Hz, 1H), 4.32 (d, *J* = 12.6 Hz, 1H), 4.13 (dd, *J* = 2.4, 1.5 Hz, 2H), 3.93 (d, *J* = 6.0 Hz, 1H), 2.73 – 2.58 (m, 2H), 2.51 (t, *J* = 2.4 Hz, 1H), 2.50 – 2.42 (m, 2H), 2.27 – 2.19 (m, 1H), 1.97 – 1.88 (m, 2H), 1.86 – 1.80 (m, 1H), 1.71 – 1.64 (m, 1H), 1.60 – 1.53 (m 1H), 1.25 (d, *J* = 6.8 Hz, 3H), 1.21 (s, 3H), 1.17 (s, 3H), 1.16 (d, *J* = 6.8 Hz, 3H).
^{13}C NMR ($CDCl_3$, 125 MHz): δ 180.29, 173.67, 172.35, 164.68, 153.52, 150.53, 145.32, 123.70, 120.16, 118.19, 114.81, 81.11, 79.59, 76.84, 75.10, 69.12, 56.20, 45.00, 43.60, 42.36, 38.89, 37.23, 31.67, 30.49, 29.35, 28.49, 25.79, 25.53, 23.52, 19.59, 16.69.
HRMS(ESI): m/z calc. for $C_{31}H_{36}O_7Cl$ $[M+H]^+$: 555.2150, found: 555.2137

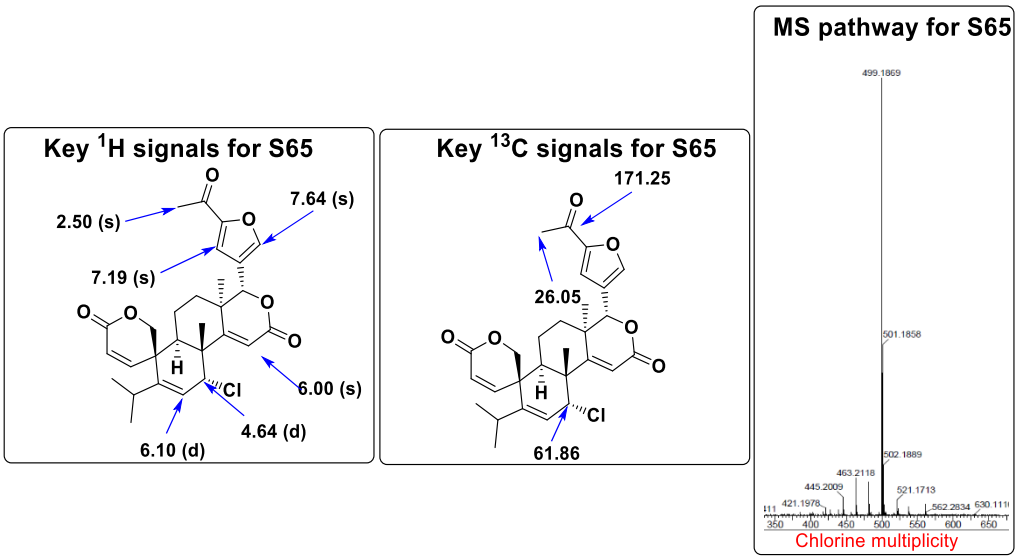


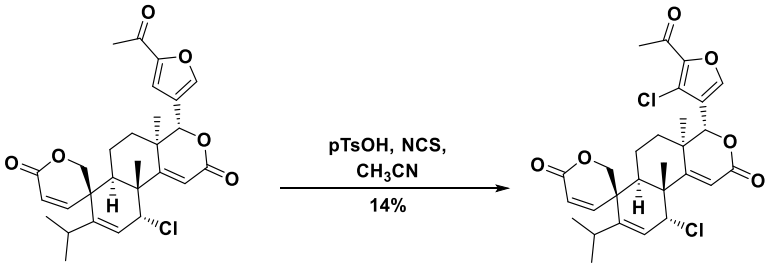


S58 **S65**

Procedure: $AlCl_3$ (72 mg, 0.54 mmol) was added at 0° C to a cooled solution of **S58** (65 mg, 0.12 mmol), in dichloromethane (1.5 mL). The resulting mixture was stirred 30 minutes, before acetyl chloride (10 µL, 0.144 mmol) was added to the mixture, and the resulting solution was stirred at 30° C for 12 h. Water was added, and the aqueous layer was extracted three times with dichloromethane. The combined organic layers were washed with brine. After drying over Na_2SO_4, the solution was concentrated by distillation at reduced pressure, and the residue was purified by flash chromatography on silica gel (hexane-ethyl acetate 1:1), giving **S65** (37 mg, 62%) as a white solid.

^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.64 (s, 1H), 7.19 (s, 1H), 6.39 (dd, *J* = 9.9, 1.9 Hz, 1H), 6.18 (d, *J* = 9.9 Hz, 1H), 6.10 (d, *J* = 6.2 Hz, 1H), 6.00 (s, 1H), 5.06 (s, 1H), 4.69 (dd, *J* = 12.7, 1.9 Hz, 1H), 4.64 (d, *J* = 6.2 Hz, 1H), 4.55 (d, *J* = 12.7 Hz, 1H), 2.65 (dd, *J* = 12.0, 8.0 Hz, 1H), 2.50 (s, 3H), 2.33 (hept, *J* = 6.8 Hz, 1H), 2.21 – 2.08 (m, 1H), 2.01 – 1.89 (m, 1H), 1.64. 1.60 (m, 2H), 1.41 (s, 3H), 1.18 (s, 3H), 1.15 (d, *J* = 6.8 Hz, 3H), 1.13 (d, *J* = 6.8 Hz, 3H).
^{13}C NMR ($CDCl_3$, 125 MHz): δ 186.76, 171.25, 164.33, 161.97, 152.95, 149.56, 147.21, 144.52, 124.39, 122.61, 121.87, 116.36, 115.73, 81.58, 68.81, 61.86, 45.39, 43.37, 37.57, 33.21, 29.81, 26.37, 26.05, 25.46, 24.95, 24.66, 17.67, 15.39.
HRMS(ESI): m/z calc. for $C_{28}H_{32}O_6Cl$ $[M+H]^+$: 499.1887, found: 499.1869.



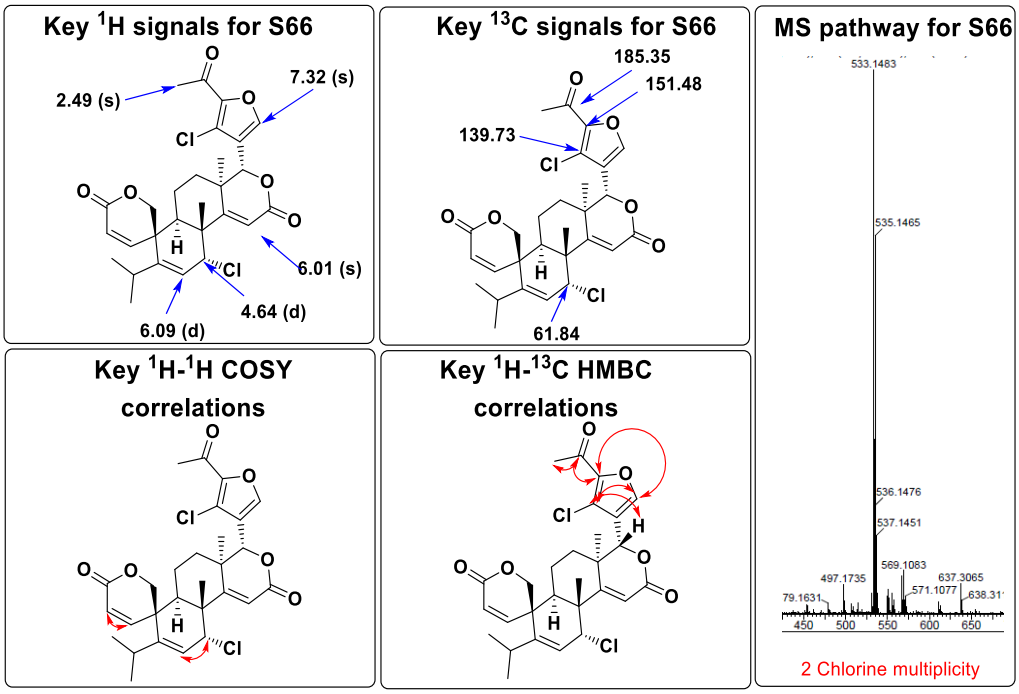


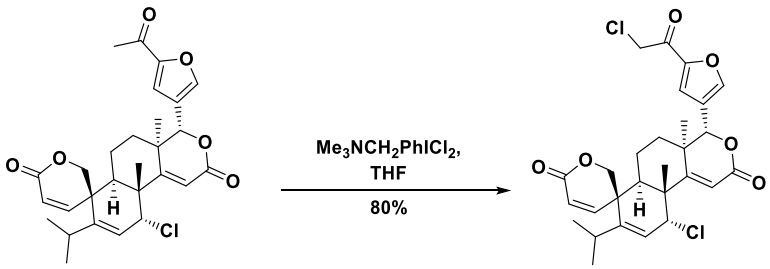
S65 **S66**

Procedure: p-toluenesulfonic acid (80 mg, 0.40 mmol) and N-chlorosuccimide (40 mg, 0.30 mmol) were added to a solution of **S65** (140 mg, 0.30 mmol) in acetonitrile (5 mL). The resulting mixture was stirred at reflux for 12 h. Water was added, and the aqueous layer was extracted three times with dichloromethane. The combined organic layers were washed with brine. After drying over Na_2SO_4,

the solution was concentrated by distillation at reduced pressure, and the residue was purified by preparative thin layer chromatography on silica gel (hexane-ethyl acetate 4:6), giving **S66** (20 mg, 14%) as a white solid.

^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.32 (s, 1H), 6.39 (dd, *J* = 9.9, 1.9 Hz, 1H), 6.18 (d, *J* = 9.9 Hz, 1H), 6.09 (d, *J* = 6.2 Hz, 1H), 6.01 (s, 1H), 5.03 (s, 1H), 4.70 (dd, *J* = 12.8, 1.9 Hz, 1H), 4.64 (d, *J* = 6.2 Hz, 1H), 4.56 (d, *J* = 12.8 Hz, 1H), 2.66 (dd, *J* = 11.9, 8.3 Hz, 1H), 2.49 (s, 3H), 2.34 (hept, *J* = 6.6 Hz, 1H), 2.24 – 2.12 (m, 1H), 1.98 – 1.88 (m, 1H), 1.70 – 1.62 (m, 1H), 1.52 – 1.44 (m, 1H), 1.43 (s, 3H), 1.27 (s, 3H), 1.15 (d, *J* = 6.6 Hz, 3H), 1.13 (d, *J* = 6.6 Hz, 3H).
^{13}C NMR ($CDCl_3$, 125 MHz): δ 185.35, 170.91, 164.06, 161.96, 151.48, 149.56, 147.33, 139.73, 124.33, 121.88, 118.62, 117.95, 115.74, 79.99, 68.85, 61.84, 45.45, 43.45, 38.86, 33.15, 29.82, 26.22, 25.79, 25.69, 24.96, 24.66, 17.77, 15.36.
HRMS(ESI): m/z calc. for $C_{28}H_{31}O_6Cl_2$ $[M+H]^+$: 533.1498, found: 533.1483.

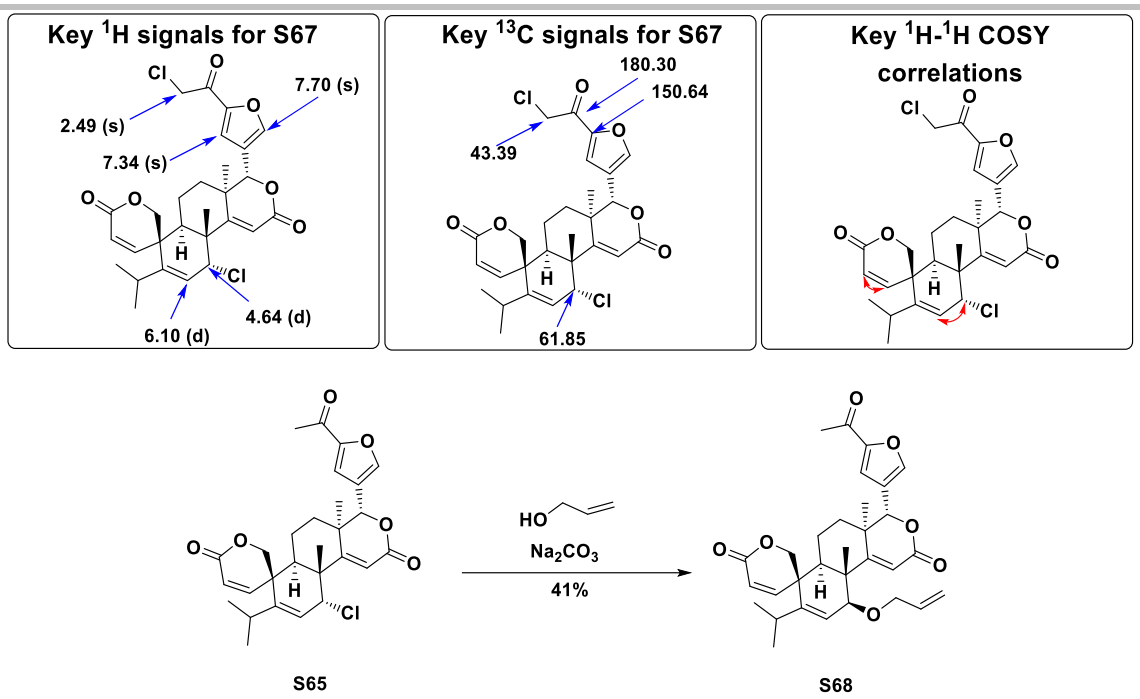




S65 S67

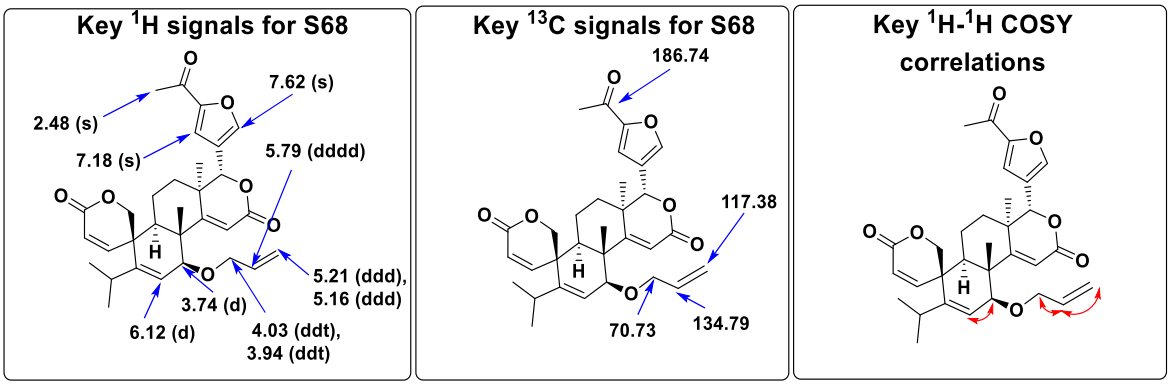
Procedure: Benzyltrimethylammonium dichloro iodide (50 mg, 0.15 mmol) was added to a solution of **S65** (35 mg, 0.07 mmol) in THF (2.5 mL). The resulting mixture was stirred at 30° C for 12 h. 10% sodium bicarbonate solution was added, and the aqueous layer was extracted three times with dichloromethane. The combined organic layers were washed with sodium thiosulfate saturate solution and brine. After drying over Na_2SO_4, the solution was concentrated by distillation at reduced pressure, and the residue was purified by flash chromatography on silica gel (hexane-ethyl acetate 1:1), giving **S67** (30 mg, 80%) as a white solid.

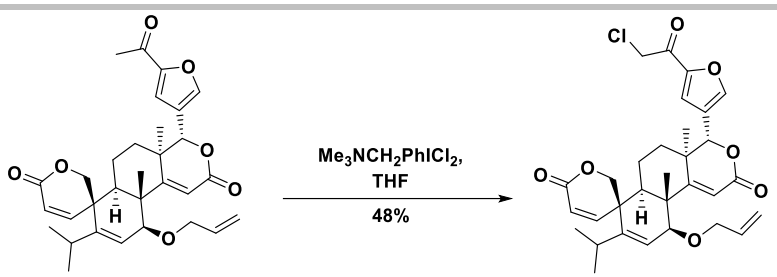
^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.70 (s, 1H), 7.34 (s, 1H), 6.39 (dd, *J* = 9.9, 2.0 Hz, 1H), 6.18 (d, *J* = 9.9 Hz, 1H), 6.10 (d, *J* = 6.2 Hz, 1H), 6.00 (s, 1H), 5.07 (s, 1H), 4.69 (4.69 (dd, *J* = 12.8, 2.0 Hz, 1H), 4.64 (d, *J* = 6.2 Hz, 1H), 4.58 (s, 2H), 4.55 (d, *J* = 12.8 Hz, 1H), 2.65 (dd, *J* = 12.1, 1.9 Hz, 1H), 2.33 (hept, *J* = 6.8 Hz, 1H), 2.21 – 2.13 (m, 1H), 1.99 – 1.91 (m, 1H), 1.65 – 1.59 (m, 2H), 1.41 (s, 3H), 1.18 (s, 3H), 1.14 (d, *J* = 6.8 Hz, 3H), 1.12 (d, *J* = 6.8 Hz, 3H).
^{13}C NMR ($CDCl_3$, 125 MHz): δ 180.30, 171.20, 164.15, 161.96, 150.64, 149.54, 147.23, 145.28, 124.37, 123.20, 121.90, 117.91, 115.76, 81.41, 68.80, 61.85, 45.38, 44.98, 43.39, 37.57, 33.20, 29.82, 26.38, 25.46, 24.96, 24.66, 17.69, 15.37.
HRMS(ESI): m/z calc. for $C_{28}H_{31}O_6Cl_2$ $[M+H]^+$: 533.1498, found: 533.1490.



Procedure: S65 (80 mg, 0.16 mmol) was added to a suspension of Na_2CO_3 (350 mg, 1.6 mmol) in allylic alcohol (6 mL) heated at 50° C. The resulting mixture was stirred at 85° C for 48 h. Water was added, and the aqueous layer was extracted three times with dichloromethane. The combined organic layers were washed with brine, dried over Na_2SO_4, the solution was concentrated by distillation at reduced pressure, and the residue was purified by flash chromatography on silica gel (hexane-ethyl acetate 3:1), giving **S68** (34 mg, 41%) as a white solid.

^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.62 (s, 1H), 7.18 (s, 1H), 6.35 (dd, *J* = 9.9, 1.8 Hz, 1H), 6.13 (d, *J* = 9.9 Hz, 1H), 6.12 (d, *J* = 5.8 Hz, 1H), 5.94 (s, 1H), 5.79 (dddd, *J* = 17.2, 10.3, 5.9, 5.7 Hz, 1H), 5.21 (ddd, *J* = 17.2, 1.6, 1.5 Hz, 1H), 5.16 (ddd, *J* = 10.3, 1.6, 1.4 Hz, 1H), 5.02 (s, 1H), 4.63 (dd, *J* = 12.6, 1.8 Hz, 1H), 4.51 (d, *J* = 12.6 Hz, 1H), 4.03 (ddt, *J* = 12.5, 5.7, 1.4 Hz, 1H), 3.94 (ddt, *J* = 12.5, 5.9, 1.5, 1.5 Hz, 1H), 3.74 (d, *J* = 5.8 Hz, 1H), 2.54 (dd, *J* = 12.8, 6.8 Hz, 1H), 2.48 (s, 3H), 2.32 (hept, *J* = 6.8 Hz, 1H), 2.04 – 1.91 (m, 1H), 1.89 – 1.77 (m, 1H), 1.66 – 1.48 (m, 2H), 1.20 (s, 3H), 1.13 (s, 3H), 1.12 (d, *J* = 6.8 Hz, 3H), 1.10 (d, *J* = 6.8 Hz, 3H).
^{13}C NMR ($CDCl_3$, 125 MHz): δ 186.74, 173.58, 164.91, 162.44, 152.85, 150.67, 148.54, 144.53, 134.79, 123.40, 122.94, 121.67, 117.38, 116.61, 114.28, 81.42, 77.22, 70.73, 69.05, 53.44, 42.95, 37.61, 34.06, 29.89, 27.53, 26.03, 25.22, 25.14, 23.88, 18.65, 15.87.
HRMS(ESI): m/z calc. for $C_{31}H_{37}O_7$ $[M+H]^+$: 521.2539, found: 521.2551.

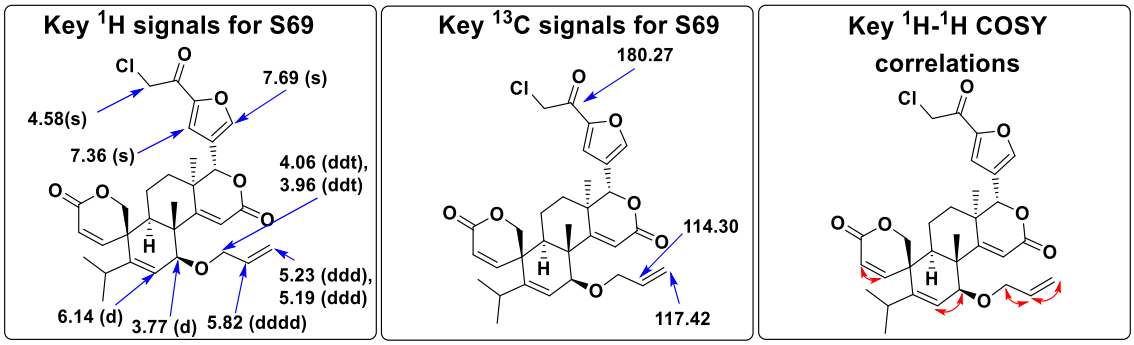


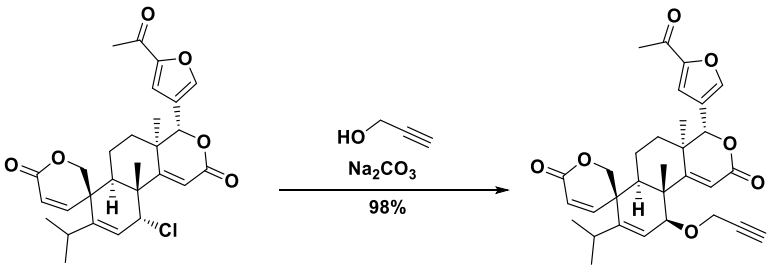


S68 **S69**

Procedure: Benzyltrimethylammonium dichloro iodide (50 mg, 0.12 mmol) was added to a solution of **S68** (30 mg, 0.06 mmol) in THF (3 mL). The resulting mixture was stirred at 40° C for 16 h. Sodium bicarbonate 10% solution was added, and the aqueous layer was extracted three times with dichloromethane. The combined organic layers were washed with sodium thiosulfate saturate solution and brine. After drying over Na_2SO_4, the solution was concentrated by distillation at reduced pressure, and the residue was purified by flash chromatography on silica gel (hexane-ethyl acetate 6:4), giving **S69** (16 mg, 48%) as a white solid.

^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.69 (s, 1H), 7.36 (s, 1H), 6.37 (dd, *J* = 9.9, 1.8 Hz, 1H), 6.15 (d, *J* = 9.9 Hz, 1H), 6.14 (d, *J* = 5.8 Hz, 1H), 5.97 (s, 1H), 5.82 (dddd, *J* = 17.2, 10.4, 5.7 Hz, 1H), 5.23 (ddd, *J* = 17.2, 1.6, 1.4 Hz, 1H), 5.19 (ddd, *J* = 10.4, 1.6, 1.4 Hz, 1H), 5.06 (s, 1H), 4.66 (dd, *J* = 12.6, 1.8 Hz, 1H), 4.58 (s, 2H), 4.54 (d, *J* = 12.6 Hz, 1H), 4.06 (ddt, *J* = 12.5, 5.7, 1.4 Hz, 1H), 3.96 (ddt, *J* = 12.5, 5.7, 1.4 Hz, 1H), 3.77 (d, *J* = 5.8 Hz, 1H), 2.57 (dd, *J* = 12.8, 6.8 Hz, 1H), 2.34 (hept, *J* = 6.7 Hz, 1H), 2.10 – 1.94 (m, 1H), 1.89 – 1.81 (m, 1H), 1.70 – 1.58 (m, 2H), 1.23 (s, 3H), 1.15 (s, 3H), 1.14 (d, *J* = 6.7 Hz, 3H), 1.13 (d, *J* = 6.7 Hz, 3H).
^{13}C NMR ($CDCl_3$, 125 MHz): δ 180.27, 173.52, 164.72, 162.42, 150.63, 150.56, 148.57, 145.27, 134.76, 123.54, 123.38, 121.70, 118.09, 117.42, 114.30, 81.23, 77.22, 70.72, 69.03, 45.25, 44.98, 42.97, 37.60, 34.04, 29.90, 27.54, 25.22, 25.14, 23.87, 18.67, 15.85.
HRMS(ESI): m/z calc. for $C_{31}H_{36}O_7Cl$ $[M+H]^+$: 555.2150, found:. 555.2156



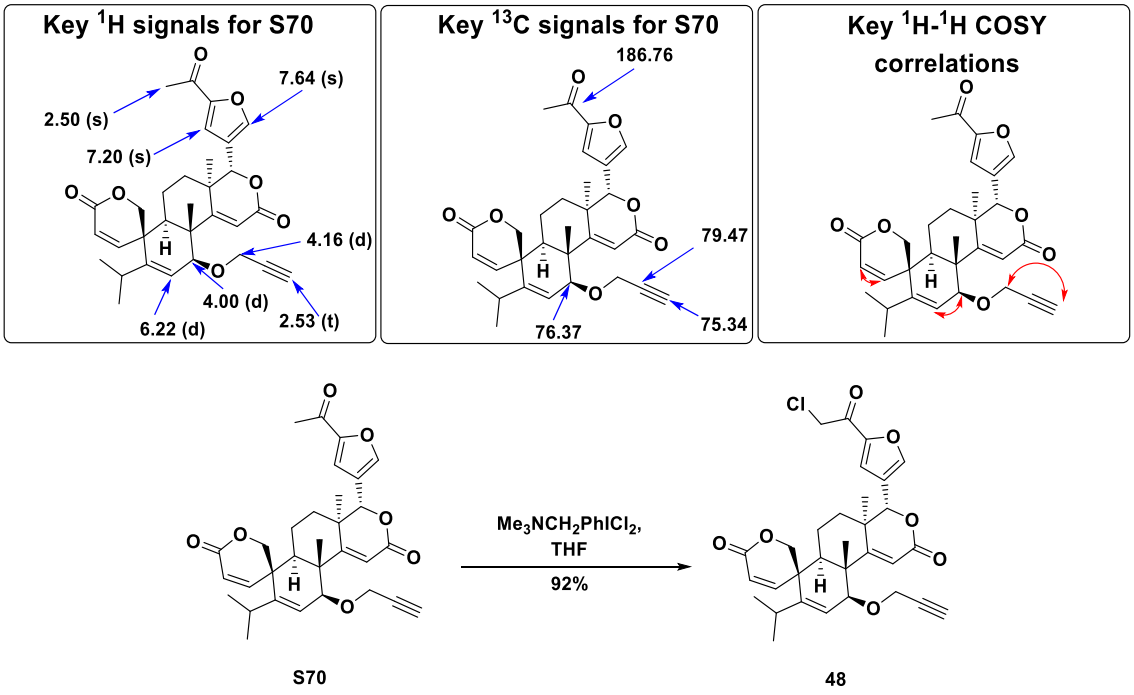


S65 **S70**

Procedure: S65 (67 mg, 0.13 mmol) was added to a suspension of Na_2CO_3 (136 mg, 1.30 mmol) in propargyl alcohol (2.3 mL) heated at 50° C. The resulting mixture was stirred at 50° C for 16 h. Water was added, and the aqueous layer was extracted three times with dichloromethane. The combined organic layers were washed with brine and dried over Na_2SO_4, The solution was concentrated by distillation at reduced pressure, and the residue was purified by flash chromatography on silica gel (hexane-ethyl acetate 4:6), giving **S70** (66 mg, 98%) as a white solid.

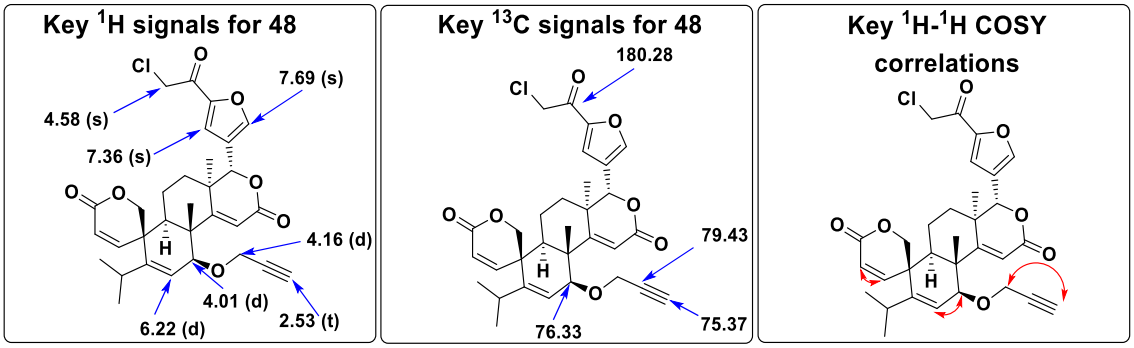
^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.64 (s, 1H), 7.20 (s, 1H), 6.37 (dd, *J* = 9.9, 1.8 Hz, 1H), 6.22 (d, *J* = 5.9 Hz, 1H), 6.15 (d, *J* = 9.9 Hz, 1H), 6.03 (s, 1H), 5.05 (s, 1H), 4.66 (dd, *J* = 12.6, 1.9 Hz, 1H), 4.54 (d, *J* = 12.6 Hz, 1H), 4.16 (d, *J* = 2.3 Hz, 2H), 4.00 (d, *J* = 5.9 Hz, 1H), 2.53 (t, *J* = 2.3 Hz, 1H), 2.50 (s, 3H), 2.35 (hept, *J* = 6.8 Hz, 1H), 2.05 – 1.93 (m, 1H), 1.91 – 1.79 (m, 1H), 1.69 – 1.51 (m, 3H), 1.25 (s, 3H), 1.15 (s, 3H), 1.14 (d, *J* = 6.8 Hz, 3H), 1.13 (d, *J* = 6.8 Hz, 3H).

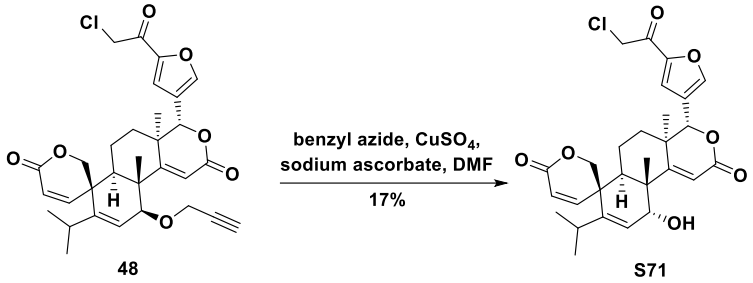
^{13}C NMR ($CDCl_3$, 125 MHz): δ 186.76, 172.90, 164.76, 162.38, 152.85, 150.48, 149.51, 144.55, 122.96, 122.69, 121.76, 116.61, 114.76, 81.36, 79.47, 76.37, 75.34, 69.00, 56.36, 45.26, 42.75, 37.47, 34.14, 29.99, 27.66, 26.03, 25.14 (2C), 23.89, 18.82, 15.93.
HRMS(ESI): m/z calc. for $C_{31}H_{35}O_7$ $[M+H]^+$: 519.2383, found: 519.2382.



Procedure: Benzyltrimethylammonium dichloro iodide (70 mg, 0.20 mmol) was added to a solution of **S70** (52 mg, 0.10 mmol) in THF (4.3 mL). The resulting mixture was stirred at 40° C for 16 h. 10% sodium bicarbonate solution was added, and the aqueous layer was extracted three times with dichloromethane. The combined organic layers were washed with sodium thiosulfate saturate solution and brine. After drying over Na_2SO_4, the solution was concentrated by distillation at reduced pressure, and the residue was purified by flash chromatography on silica gel (hexane-ethyl acetate 1:1), giving **48** (51 mg, 92%) as a white solid.

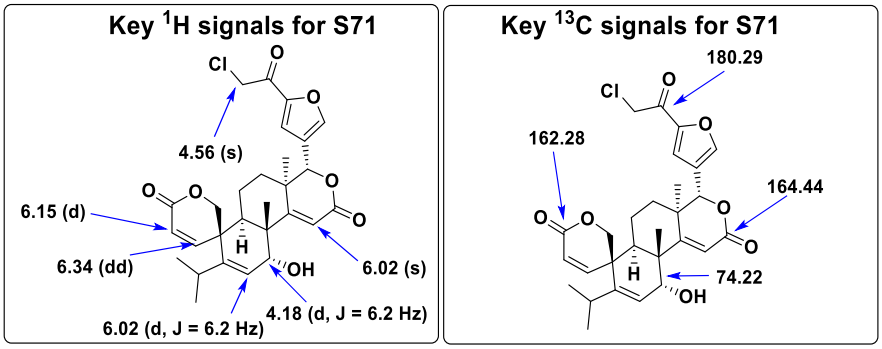
^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.69 (s, 1H), 7.36 (s, 1H), 6.36 (dd, *J* = 9.9, 1.8 Hz, 1H), 6.22 (d, *J* = 5.8 Hz, 1H), 6.16 (d, *J* = 9.9 Hz, 1H), 6.03 (s, 1H), 5.07 (s, 1H), 4.66 (dd, *J* = 12.6, 1.8 Hz, 1H), 4.58 (s, 2H), 4.55 (d, *J* = 12.6 Hz, 1H), 4.16 (d, *J* = 2.4 Hz, 2H), 4.01 (d, *J* = 5.8 Hz, 1H), 2.53 (t, *J* = 2.4 Hz, 1H), 2.54 – 2.52 (m, 1H), 2.35 (hept, *J* = 6.8 Hz, 1H), 2.05 – 1.96 (m, 1H), 1.89 – 181 (m, 1H), 1.68 – 1.62 (m, 1H), 1.60 – 1.53 (m, 1H), 1.25 (s, 3H), 1.15 (s, 3H), 1.14 (d, *J* = 6.8 Hz, 3H), 1.13 (d, *J* = 6.8 Hz, 3H)
^{13}C NMR ($CDCl_3$, 125 MHz): δ 180.28, 172.83, 164.58, 162.36, 150.56, 150.44, 149.55, 145.29, 123.56, 122.65, 121.79, 118.10, 114.79, 81.18, 79.43, 76.33, 75.37, 68.98, 56.33, 45.26, 44.99, 42.77, 37.45, 34.11, 29.99, 27.66, 25.15, 25.13, 23.88, 18.84, 15.91.
HRMS(ESI): m/z calc. for $C_{31}H_{34}O_7Cl$ $[M+H]^+$: 553.1993, found: 553.1986.
mp: 110-111° C.
Opt. Rot.: $[\alpha]_D^{25}$ = - 57 (c = 0.10, acetone).

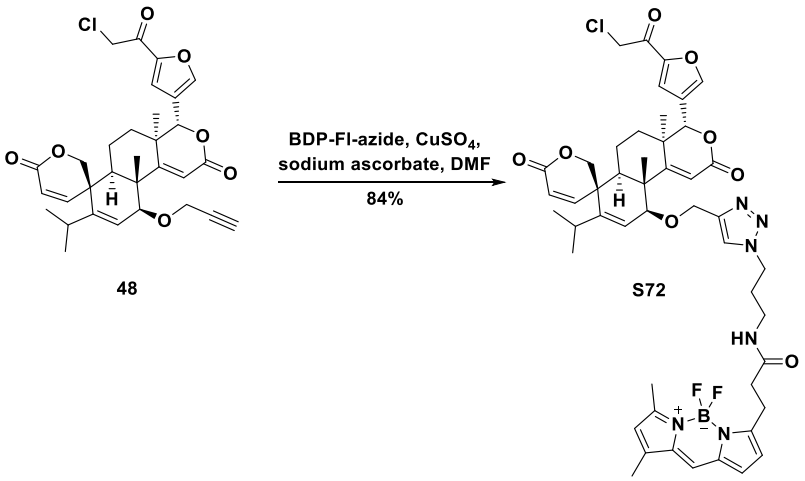




Procedure: Copper (II) sulfate (4 mg, 0.018 mmol) and sodium ascorbate (3 mg, 018 mmol) were added to a solution of **48** (10 mg, 0.018 mmol), benzyl azide (3 mg, 0.20 mmol) in DMF (0.5 mL) and the resulting mixture was stirred at 30° C for 16 h. Water was added, and the aqueous layer was extracted three times with dichloromethane. The combined organic layers were washed with two times with brine. After drying over Na_2SO_4, the solution was concentrated by distillation at reduced pressure, and the residue was purified by flash chromatography on silica gel (hexane-ethyl acetate 1:1), giving **S71** (2 mg, 17%) as a white solid.

^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.68 (s, 1H), 7.33 (s, 1H), 6.34 (dd, *J* = 9.9, 1.9 Hz, 1H), 6.15 (d, *J* = 9.9 Hz, 1H), 6.02 (s, 1H), 6.02 (d, *J* = 6.2 Hz, 1H), 5.07 (s, 1H), 4.66 (dd, *J* = 12.6, 1.9 Hz, 1H), 4.56 (s, 2H), 4.53 (d, *J* = 12.6 Hz, 1H), 4.18 (d, *J* = 6.2 Hz, 1H), 2.50 (dd, *J* = 12.5, 7.4 Hz, 1H), 2.31 (hept, *J* = 6.8 Hz, 1H), 2.12 – 2.03 (m, 1H), 1.92 – 1.84 (m, 1H), 1.68 – 1.56 (m, 2H), 1.24 (s, 3H), 1.14 (s, 3H), 1.12 (d, *J* = 6.7 Hz, 3H), 1.10 (s, *J* = 6.7 Hz, 3H). (30 non-exchangeable protons)
^{13}C NMR ($CDCl_3$, 125 MHz): δ 180.29, 173.99, 164.44, 162.28, 150.67, 150.48, 148.63, 145.23, 123.99, 123.24, 121.91, 117.89, 114.55, 81.28, 70.14, 68.96, 45.43, 44.98, 43.68, 37.70, 33.04, 29.78, 26.96, 25.21, 25.03, 24.26, 18.27, 15.60.
HRMS(ESI): m/z calc. for $C_{28}H_{32}O_7Cl$ $[M+H]^+$: 515.1837, found: 515.1854.





Procedure: Copper (II) sulfate (9 mg, 0.036 mmol) and sodium ascorbate (7 mg, 036 mmol) were added to a solution of **48** (20 mg, 0.36 mmol), BDP-Fl-azide (14 mg, 0.36 mmol) in DMF (0.8 mL) and the resulting mixture was stirred at 30° C for 3 h. Water was added, and the aqueous layer was extracted three times with dichloromethane. The combined organic layers were washed with two times with brine. After drying over Na_2SO_4, the solution was concentrated by distillation at reduced pressure, and the residue was purified by flash chromatography on silica gel (ethyl acetate - methanol 99:1), giving **72** (28 mg, 84%) as an orange solid.

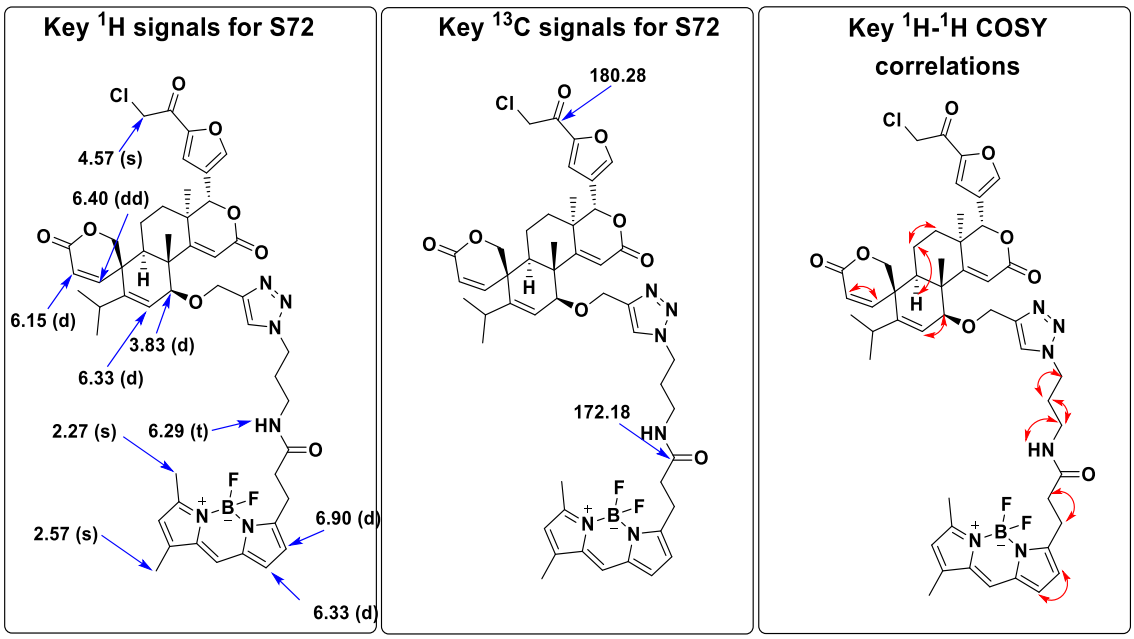
SUPPORTING INFORMATION

^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.65 (s, 1H), 7.58 (s, 1H), 7.32 (s, 1H), 7.11 (s, 1H), 6.90 (d, *J* = 4.0 Hz, 1H), 6.40 (dd, *J* = 9.9, 1.7 Hz, 1H), 6.33 (d, *J* = 5.7 Hz, 1H), 6.33 (d, *J* = 4.0 Hz, 1H), 6.29 (t, *J* = 6.2 Hz, 1H), 6.16 (s, 1H), 6.15 (d, *J* = 9.9 1H), 5.50 (s, 1H), 5.00 (s, 1H), 4.70 – 4.59 (m, 3H), 4.57 (s, 2H), 4.54 (d, *J* = 12.5 Hz, 1H), 4.39 (t, *J* = 6.6 Hz, 2H), 3.83 (d, *J* = 5.7 Hz, 1H), 3.35 3.38 (m, 3H), 3.19 (dq, *J* = 12.9, 6.2 Hz, 1H), 2.72 – 2.64 (m, 2H), 2.57 (s, 3H), 2.56 – 2.50 (m, 1H), 2.41 – 2.31 (m, 1H), 2.27 (s, 3H), 2.19 – 2.12 (m, 2H), 2.05 – 1.97 (m, 1H), 1.86 – 1.81 (m, 1H), 1.63 – 1.50 (m, 2H), 1.17 (s, 3H), 1.16 (d, *J* = 6.7 Hz, 3H), 1.14 (d, *J* = 6.7 Hz, 3H), 1.08 (s, 3H).

^{13}C NMR ($CDCl_3$, 125 MHz): δ 180.28, 173.97, 172.18, 165.15, 162.41, 160.27, 157.38, 150.57, 149.60, 145.25, 144.07 (2C), 135.15, 133.33, 128.29 (2C), 123.94, 123.87, 123.32, 122.64, 121.72, 120.47, 118.03, 117.29, 114.18, 81.17, 74.72, 69.00, 60.92, 47.61, 45.39, 44.99, 42.70, 37.66, 36.20, 35.68, 33.81, 30.09, 29.74, 27.19, 25.38, 25.06, 24.80, 23.76, 18.29, 15.68, 14.97, 11.35.

HRMS(ESI): m/z calc. for $C_{48}H_{55}N_6O_8ClF_2B$ $[M+H]^+$: 927.3831, found: 927.3802.

Opt. Rot.: $[\alpha]_D^{25}$ = - 74 (c = 0.04, acetone).



SUPPORTING INFORMATION

Computational Analyses

Library data for Chembridge Diverset™-CL, Diverset™-EXP, and Microformat libraries were obtained from ChemBridge website (https://www.chembridge.com/). Library data for approved antibacterials was obtained from the O'Shea and Moser.[8] Library data for approved cancer drugs was obtained from NCI as Approved Oncology Drugs Set VII (https://wiki.nci.nih.gov/display/NCIDTPdata?Compound+Sets). The Drugbank library and the Molecular Libraries Small Molecule Repository (MLSMR-NP) were obtained respectively from Drugbank website (https://www.drugbank.ca/) and PubChem website (https://pubchem.ncbi.nlm.nih.gov/). Natural product NPASS Compound Collection (NPASS) was obtained from Natural Product Activity and Species Source Database website (http://bidd2.nus.edu.sg/NPASS/). Lycorine and Pleuromutilin libraries are available at the following site https://github.com/HergenrotherLab. Limonin library is described herein. All the parameters were calculated using a Python program that implements RDKit. Source code can be found at the following site https://github.com/HergenrotherLab

Murcko Scaffolds Analysis

For Murcko scaffolds, compound structures were converted in .sdf library format in ChemDraw (Cambridgesoft, Cambridge, MA). Murcko scaffolds were generated using ScaffoldGraph.[9]

The program using the Python Spyder editor with the following syntax:

```
"""
@author: lucia
"""

import scaffoldgraph as sg

import networkx as nx

import matplotlib.pyplot as plt

import numpy as np

from rdkit.Chem import Draw
from rdkit import Chem
import rdkit
import random
import os
from collections import Counter

#%%
sdf_file = ('fullset-limonin.sdf') # Example SDF file (Limonin CtD library)
supplier = Chem.SDMolSupplier(sdf_file)
network = sg.ScaffoldNetwork.from_sdf(sdf_file, progress=True)

# We can access the number of molecule nodes and scaffold nodes in the graph
n_scaffolds_net = network.num_scaffold_nodes
n_molecules_net = network.num_molecule_nodes

print('\nGenerated scaffold network from [4] molecules with {} scaffolds\n'.format(n_molecules_net, n_scaffolds_net))

molecules = list(network.get_molecule_nodes())

# Calculate number of scaffolds and singletons
frag_to_save = []
for i in range(len(molecules)):
    mol_id = i
    pubchem_id = molecules[mol_id]
    smiles_iter = network.nodes[pubchem_id]['smiles']
    frags_iter = sg.get_all_murcko_fragments(Chem.MolFromSmiles(smiles_iter))
    num_rings = []
    for mol in frags_iter:
        num_rings.append(rdkit.Chem.rdMolDescriptors.CalcNumRings(mol))
    m = max(num_rings)
    position_max = [i for i, J in enumerate(num_rings) if J == m]
    frag_to_save.append(frags_iter[position_max[0]])
list_smiles = []
for frag_saved in frag_to_save:
    list_smiles.append(Chem.MolToSmiles(frag_saved))

smiles_no_duplicate = set(list_smiles)

count_unique_smiles = Counter(list_smiles)
number_of_unique_smiles= []
```

```
for key_count in count_unique_smiles.keys():
    if count_unique_smiles[key_count]==1:
        number_of_unique_smiles.append(count_unique_smiles[key_count])
# Number of scaffold
N = len(smiles_no_duplicate)
Nsing = sum(number_of_unique_smiles)

print("Number of scaffolds is",N)
print("Number of singletons is",Nsing)
```

Scaffold Tree Analysis

For scaffold tree analysis, compound structures were converted in .sdf library format in ChemDraw (Cambridgesoft, Cambridge, MA). For each dataset, all duplicated fragments were removed and the numbers of unique fragments were counted. Scaffold Trees were generated using ScaffoldGraph.[9]

Tanimoto Similarity matrix

For the Tanimoto Similarity analysis (**Figure S28**), compound structures were converted in .sdf library format in ChemDraw (Cambridgesoft, Cambridge, MA). Tanimoto similarity coefficients were calculated using Canvas 2018 (Schrödinger, New York, NY), using the Similarity/Distance Matrix application with radial fingerprints (ECFP). The obtained values were exported to Excel (Microsoft, Redmond, WA) where a heatmap was generated using a three color scale set to 0.0 (blue), 0.5 (yellow), and 1.0 (red).

SUPPORTING INFORMATION

Biological Studies

Methods

Cell culture: Cells were grown at 37 °C under a humified 5% CO_2 atmosphere in a culture media consisting of high-glucose (Life Technology) DMEM media for A172 (glioblastoma) cells and HepG2 (hepatocellular carcinoma), or EMEM media for HOS (osteosarcoma) cells, or RPMI 1640 for A549 (lung carcinoma), ES-2 (ovarian carcinoma), HCT116 (colorectal carcinoma), and MDA-MB-231 (triple-negative breast cancer) cells. All media were supplemented with 10% FBS (Gemini) and 1% penicillin/streptomycin. All cell lines were authenticated by the University of Arizona Genetics Core using an autosomal STR profile.

Anticancer screen: For each cell line, 40 µL of the appropriate media were added to two 384-well plates. At the UIUC High-throughput Screening Facility, a Thermo Scientific Matrix PlateMate Plus was used to transfer 100 nL of 10 mM compound stocks in DMSO to one plate for each cell line. 100 nL DMSO was added to the other plate for each cell line. Plates were kept at room temperature until seeding. Cells were harvested and put on ice for at least 5 minutes before seeding 10 µL of the appropriate concentration of cells (1000 cells/well) in one plate with compound and one with DMSO. 1 µL of 2.5 mM Raptinal was added as a dead control. Plates were sealed with gas-permeable seals and left at room temperature for 45 minutes before being put in the incubator. Plates were incubated for 72 hours and then 5 µL of Alamar blue was added to each well, and allowed to incubate for 3-4 h, until a visible color change occurred. Fluorescence was measured in a Molecular Devices SpectraMax M3 (excitation wavelength: 555 nm; emission wavelength: 585 nm; cutoff 570 nm; autogain). The percent cell death calculated for the plates treated with DMSO was subtracted from the compound treated plates.

Cell viability assay: Cells were seeded according to **Table S11** below in a 96-well plate and allowed to attach overnight. To each well, 1 µL of the investigation compound in DMSO was added (1% final concentration). On each plate, at least 3 technical replicates per compound were performed. DMSO was used as a negative control and Raptinal (final concentration 50 µM) as a positive control. Plates were incubated at 37 °C for 72 hours. At that time, 10 µL of Alamar blue was added to each well and allowed to incubate for 3-4 h, until a visible color change occurred. Fluorescence was measured as described above. Wells were normalized to DMSO- and Raptinal-treated cells. IC_{50} values were calculated using OriginPro 2019 (OriginLab). IC_{50} values are reported as the average of three separate experiments along with SEM values.

Table S11. Cell line seeding densities for cell viability assay

Cell line	Cell/well	Cell line	Cell/well
HCT116	3000	HOS	2500
ES2	3000	MDA-MB-231	3000
A172	3000	Hep-G2	8000
A549	3000		

Cell viability via Flow cytometry

HCT116 cells (300,000 cells/well) were plated overnight in 6-well plates, prior to addition of compounds. For protection studies, samples were pre-treated with 25 µM Q-VD-PPh for two hours before compound addition. Cells were incubated for 24 h and harvested in flow tubes along with media and debris. Tubes were centrifuged at 1000 RCF for 3 minutes. Cells were washed with PBS and then resuspended in 450 µl of Annexin V binding buffer (10 mM HEPES, 2.5 mM $CaCl_2$, 150 mM NaCl, pH 7.4) with Annexin V-FITC (Southern Biotech 10040-02) (2.8 µl per sample) and propidium iodide (Sigma Aldrich) (0.25 µl of 1 mg/mL solution per sample). Samples were protected from light and kept on ice until testing. Samples were analyzed on a BD LSR II Flow Cytometry Analyzer. Ten thousand events were recorded per sample using FCS Express Version 5. Percent death was calculated by subtracting the lower left quadrant from 100.

Western blot

HCT116 cells were pre-treated with 25 µM Q-VD-OPh for 2 h. Then compound was added and cells were incubated for 24 h. Cells were harvested by centrifugation (3 min, 1000 RCF), washed with PBS and resuspended in RIPA lysis buffer (10 mM Tris base, 1 mM EDTA, 0.5 mM EGTA, 1% Triton-X-100, 0.1% sodium deoxycholate, 0.1% SDS, 140 mM NaCl with a 1:100 dilution of Protease Inhibitor Cocktail Set III (Calbiochem)). Protein concentration was assessed using a BCA protein assay (Pierce). Samples were resolved in a 4-20% gradient SDS-PAGE gel (Bio-Rad) at 160 V for 40 minutes, and then transferred to an activated PVDF membrane (Millipore) in Towbin transfer buffer (192 mM glycine, 25 mM Tris- HCl, 20% methanol, pH = 8.3) for 2 h at 45 V. Membranes were blocked for 1 h at 4˚C in bovine serum albumin [BSA] and then incubated with primary antibodies overnight at 4 ºC. (Cell Signaling Technology, procaspase-3 9662, PARP-1 9542, β-actin 4970). Blots were washed with TBST and incubated with secondary antibody for 1 h. Blots were imaged in SuperSignal West Pico Solution (Pierce) using a BioRad ChemiDoc Touch with Image Lab software.

SUPPORTING INFORMATION

Hemolysis assay

100 µl of whole blood was combined with 500 µl of saline and centrifuged for 5 min at 4 °C at 300 xg. The supernatant was aspirated and cells were resuspended in 500 µl saline and the process was repeated three times to wash cells. Cells were then resuspended in 800 µl red blood cell buffer (10 mM Na_2HPO_4 (pH7.4), 150 mM NaCl, 1 mM $MgCl_2$ in water). 19 µl of red blood cell buffer was added to PCR tubes followed by 1 µl of DMSO solution of compounds. 30% triton X-100 in water was used as a positive control. Tubes were centrifuged to combine everything. Then, 10 µl of washed red blood cells were added to each tube. Tubes were incubated at 37 °C for 2 h and then centrifuged for 5 min, 300 xg at 4 °C. 20 µl of the supernatant was transferred to wells of a clear bottom 384-well plate and absorbance read at 540nm. The percent lysis was normalized to the positive control at 100%. All samples were done in triplicate. Compounds were tested at three concentrations (10 µM, 25 µM and 50 µM).

Abbreviations

BDP-Fl-azide: *N*-(3-azidopropyl)-3-(5,5-difluoro-7,9-dimethyl-5*H*-5l4,6l4-dipyrrolo[1,2-c:2',1'-f][1,3,2]diazaborinin-3-yl)propanamide

DCM: dichloromethane

DMAP: 4-Dimethylaminopyridine

DMF: dimethylformamide

DMP: Dess–Martin periodinane

EDC: 1-Ethyl-3-(3-dimethylaminopropyl)carbodiimide

EtOAc: ethyl acetate

ESI: electrospray ionization

HOBt: Hydroxybenzotriazole

HRMS: high-resolution mass spectra

LCMS: liquid chromatography–mass spectrometry

***m*CPBA**: *meta*-Chloroperoxybenzoic acid

mp: melting point

MS: mass spectra

NCS: *N*-Chlorosuccinimide

NMR: nuclear magnetic resonance

Py: pyridine

***p*TsOH**: *para*-Toluenesulfonic acid

(*R*,*R*)-Mn(salen1)Cl: (*R,R*)-(−)-*N,N'*-Bis(3,5-di-*tert*-butylsalicylidene)-1,2-cyclohexanediaminomanganese(III) chloride

SEM: Standard error of the mean

TEA: triethylamine

THF: tetrahydrofuran

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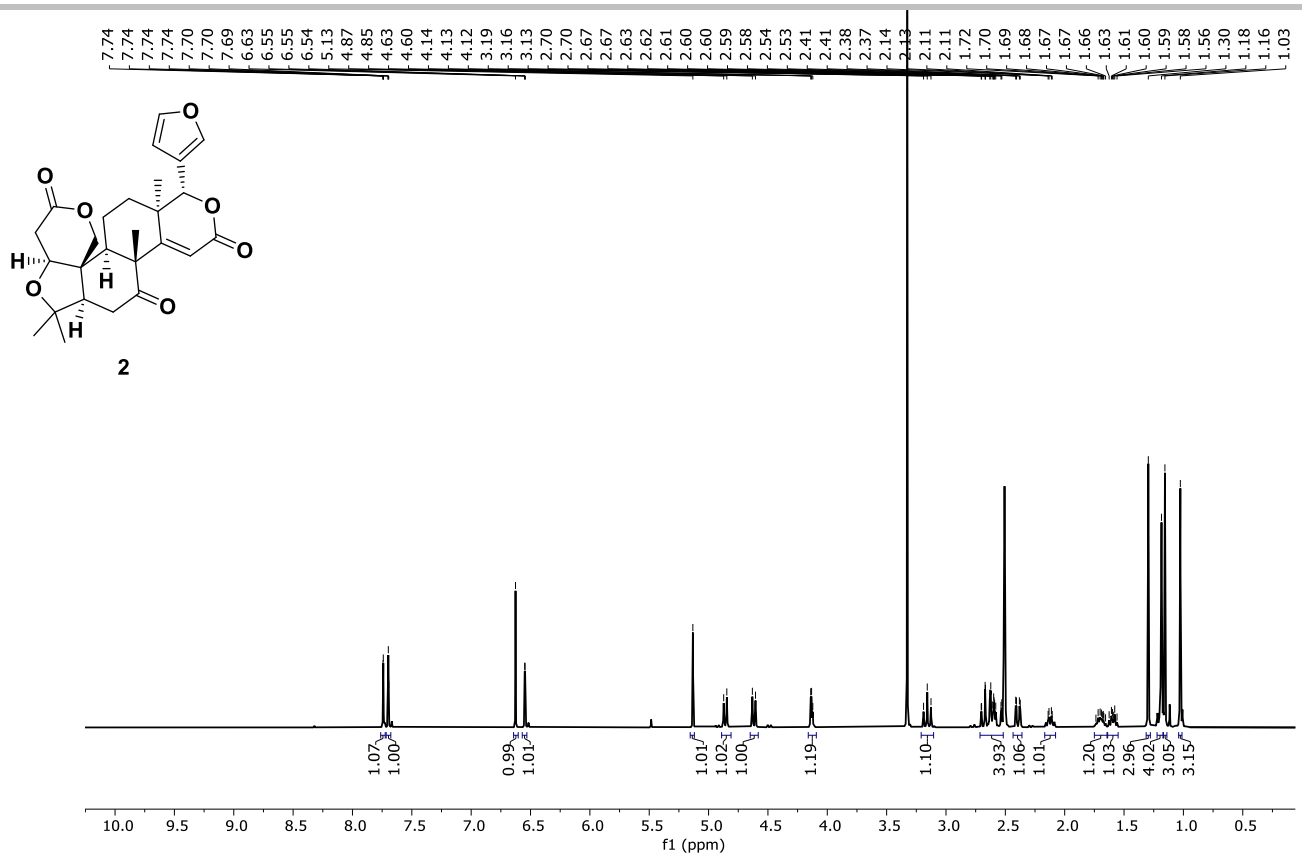
SUPPORTING INFORMATION

Spectral Data



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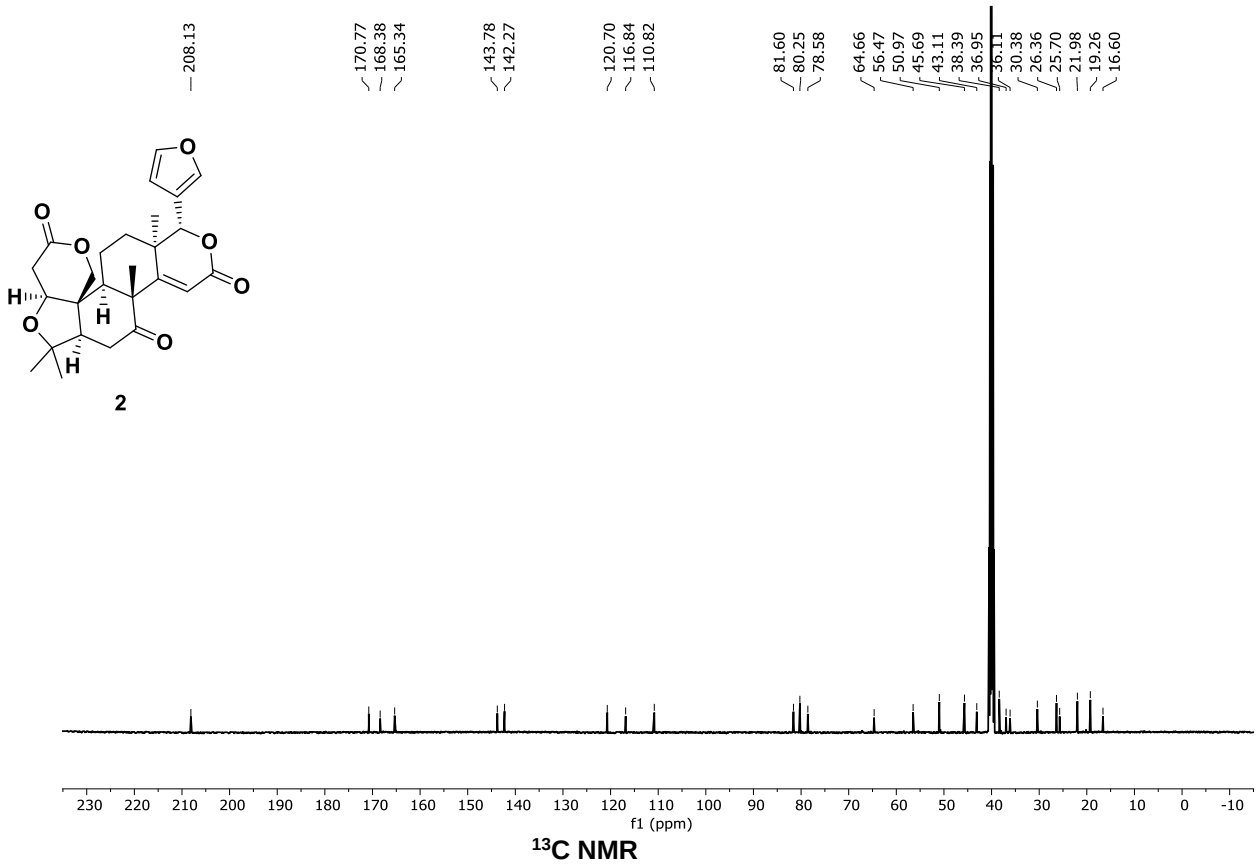

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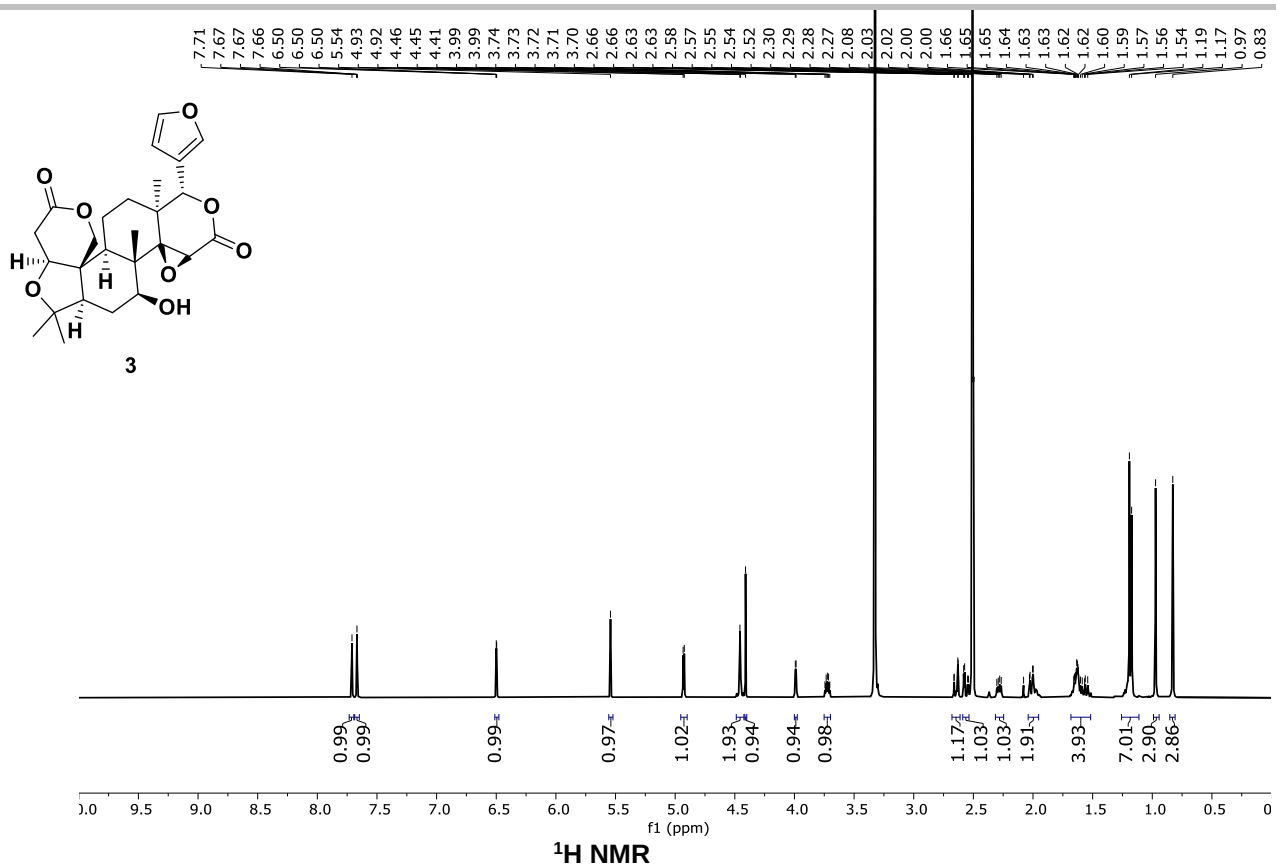

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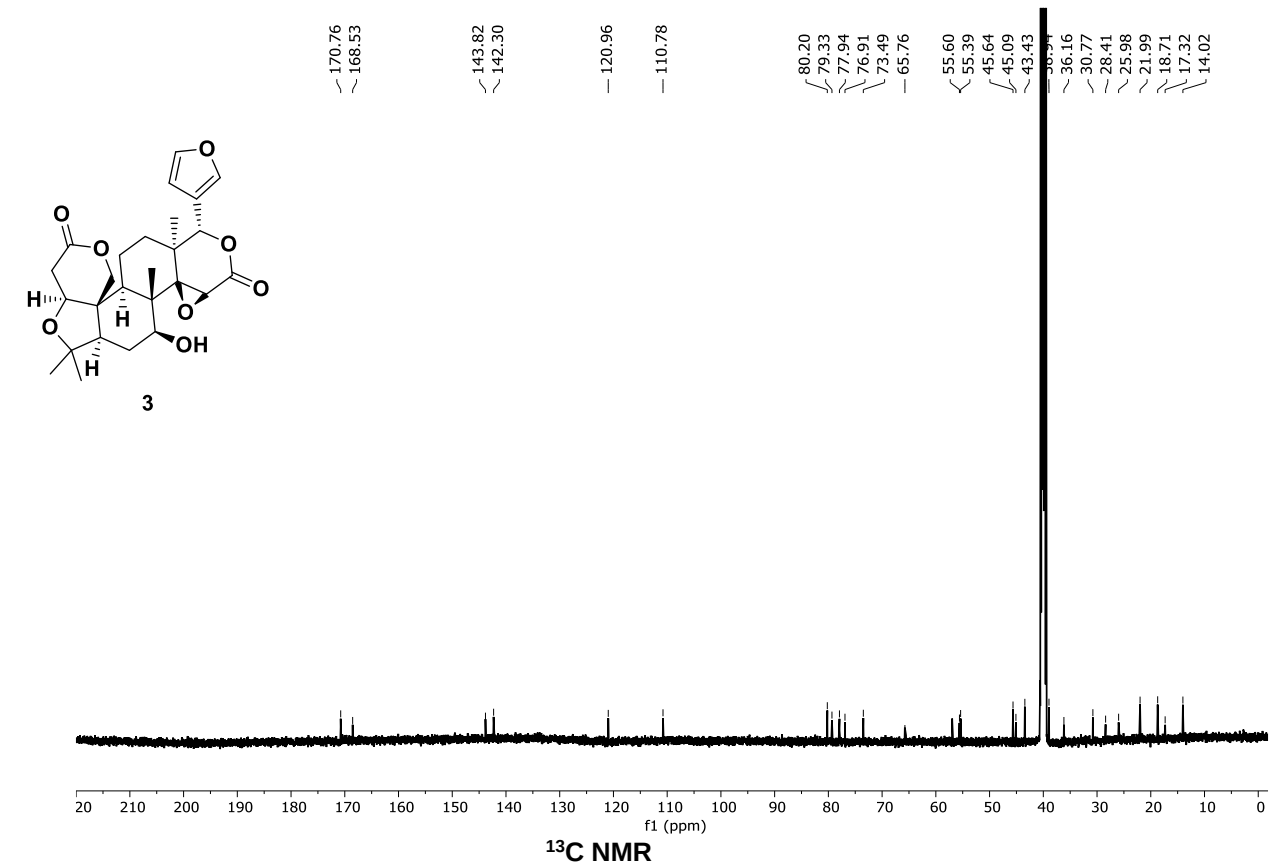

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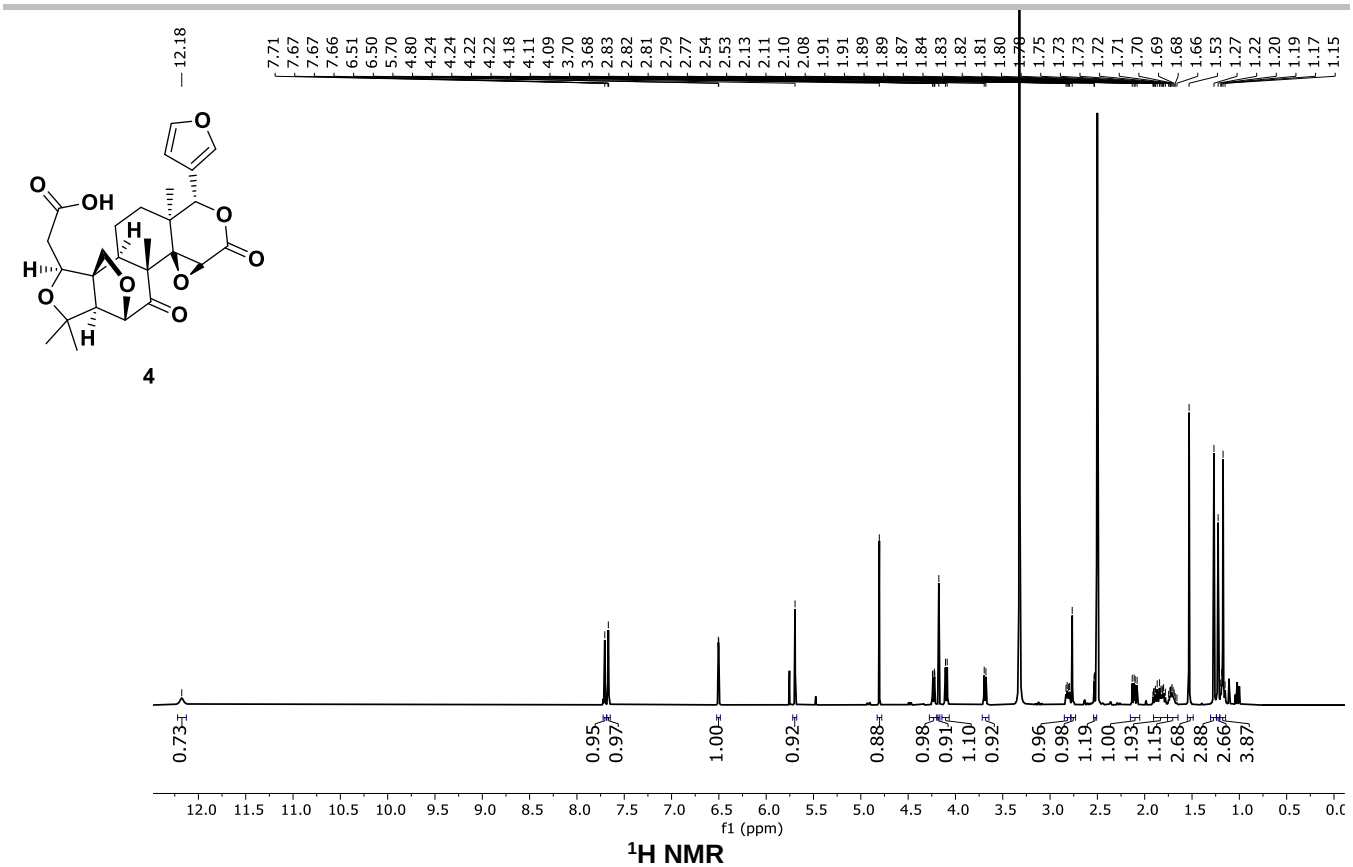

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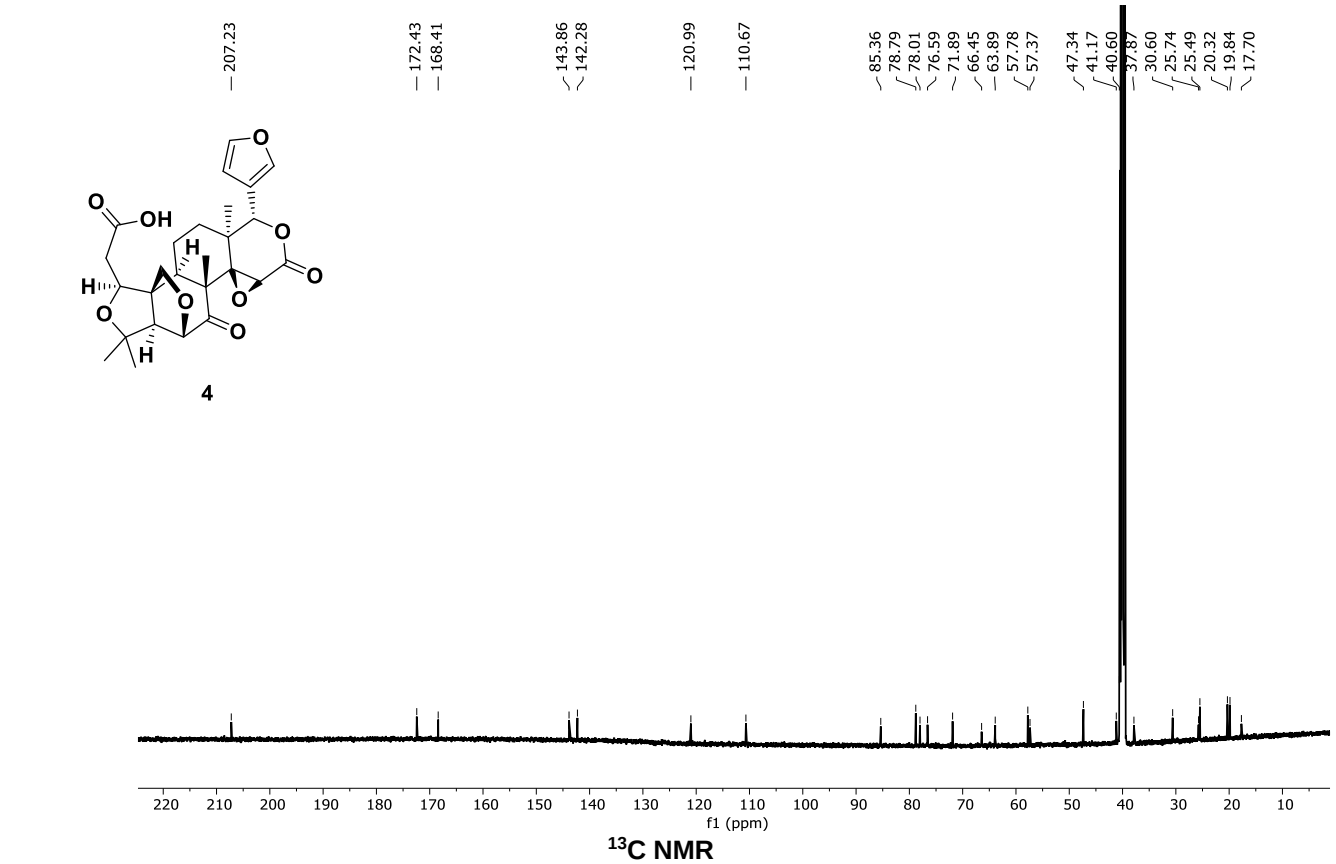

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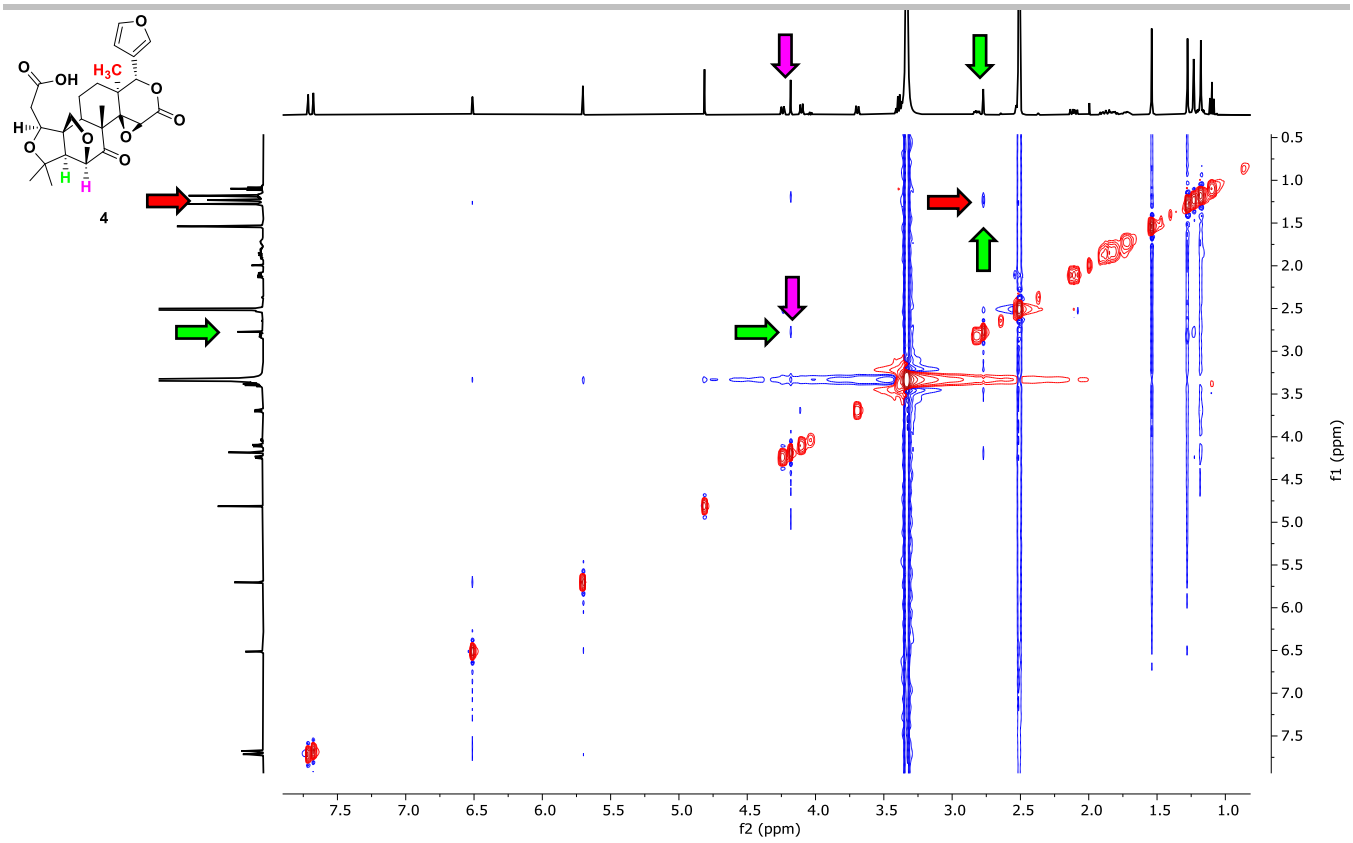

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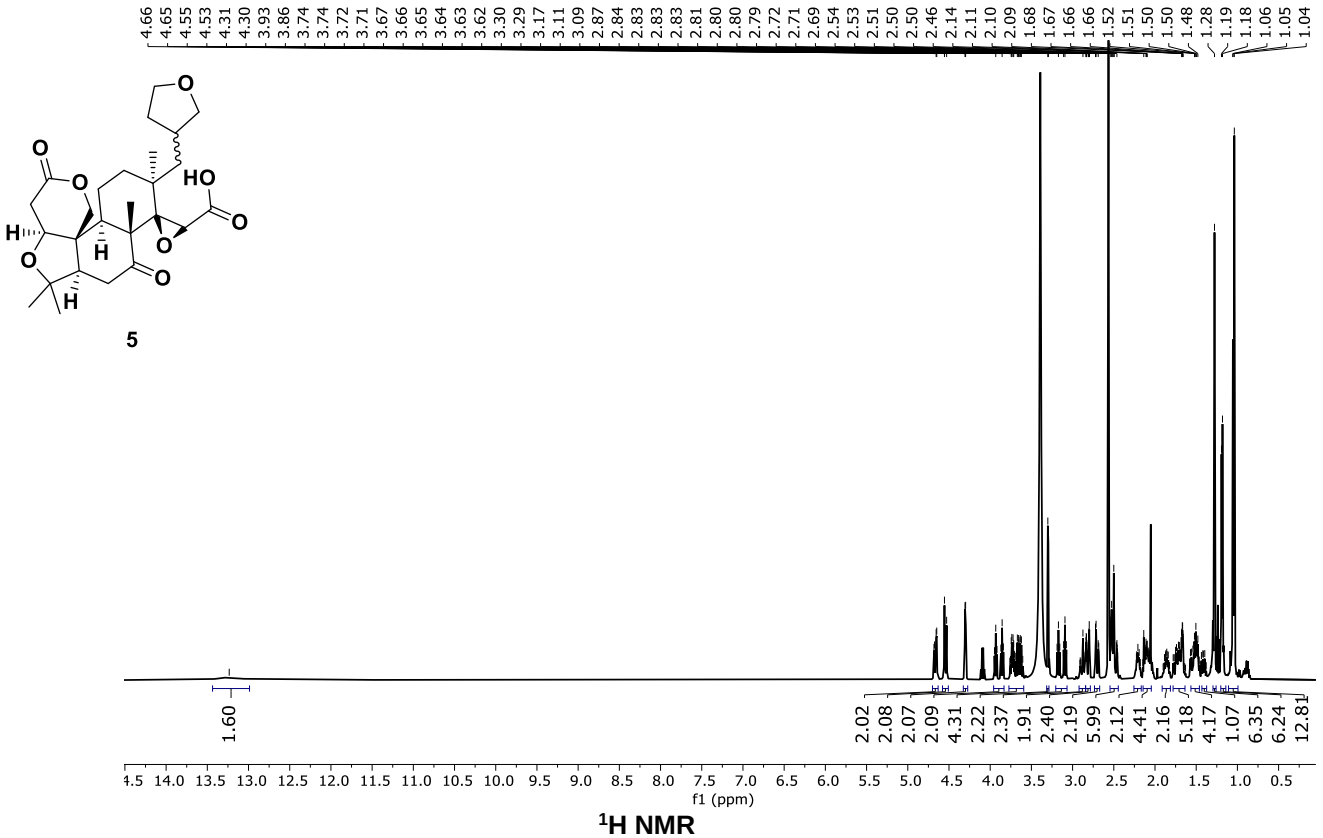

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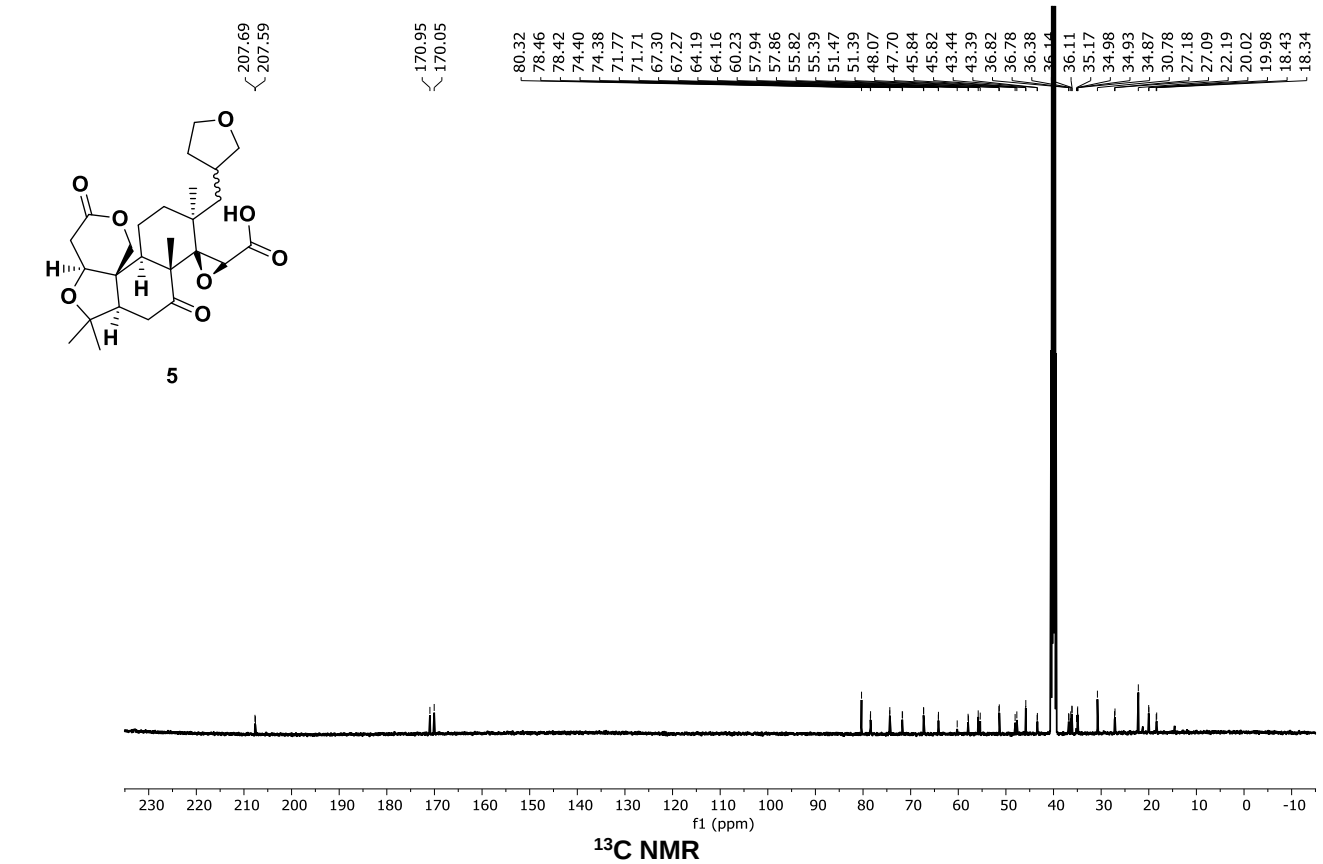

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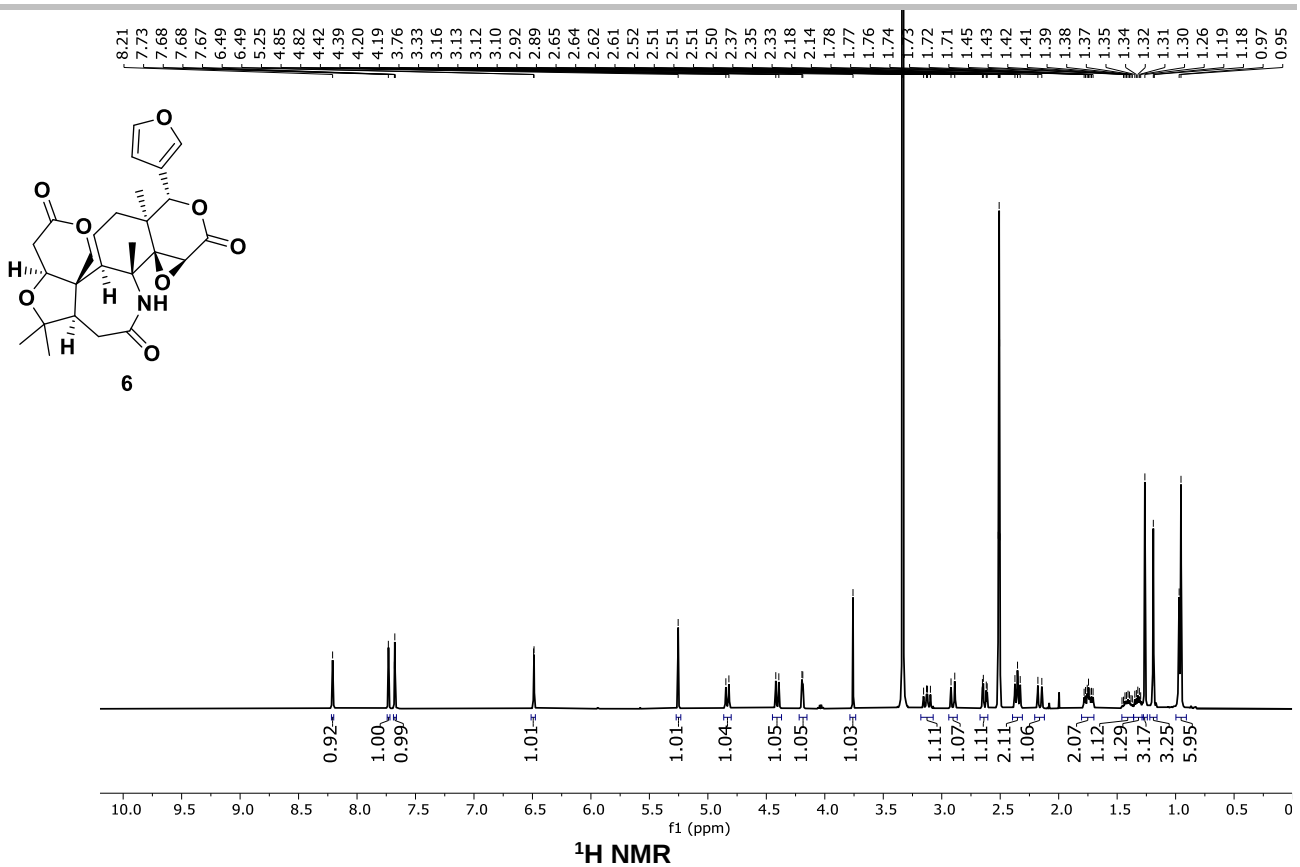

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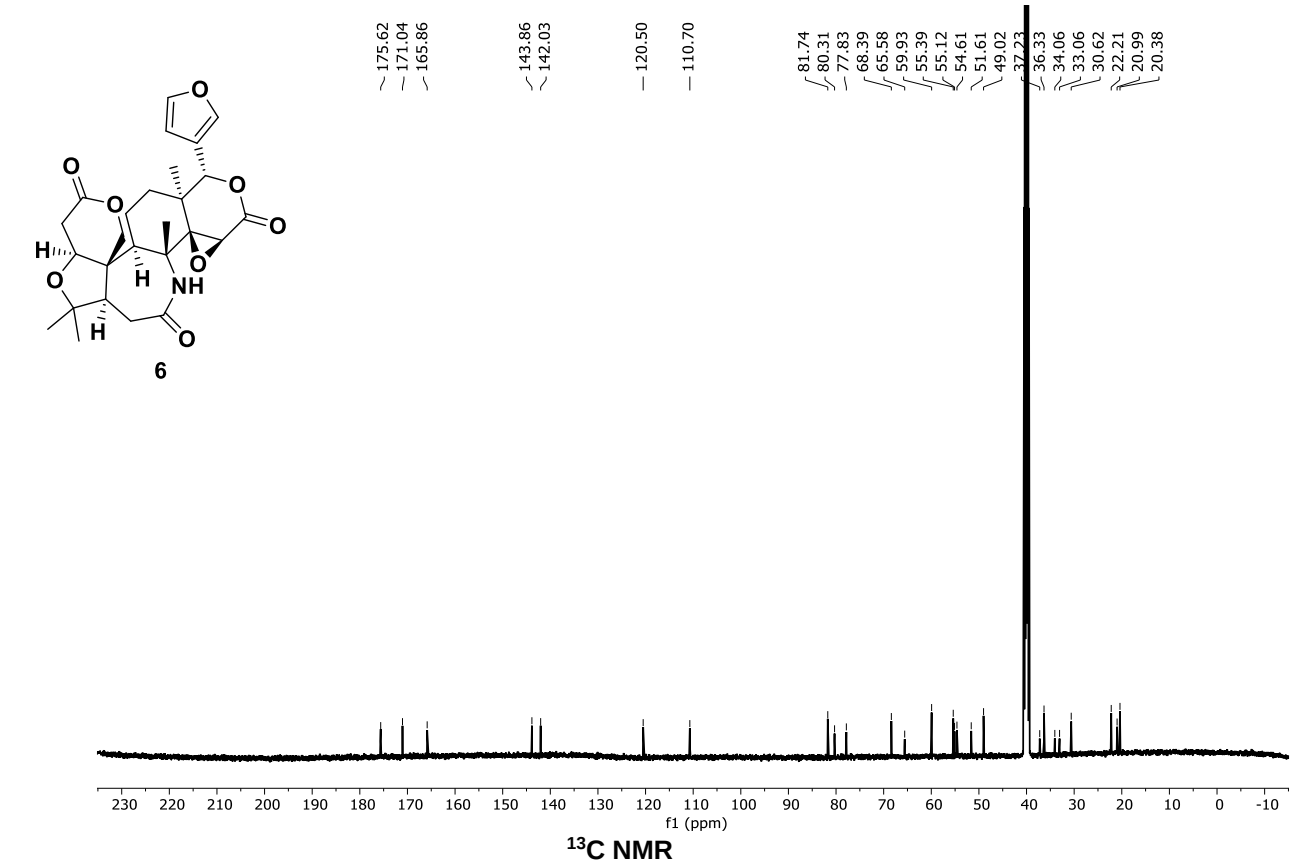

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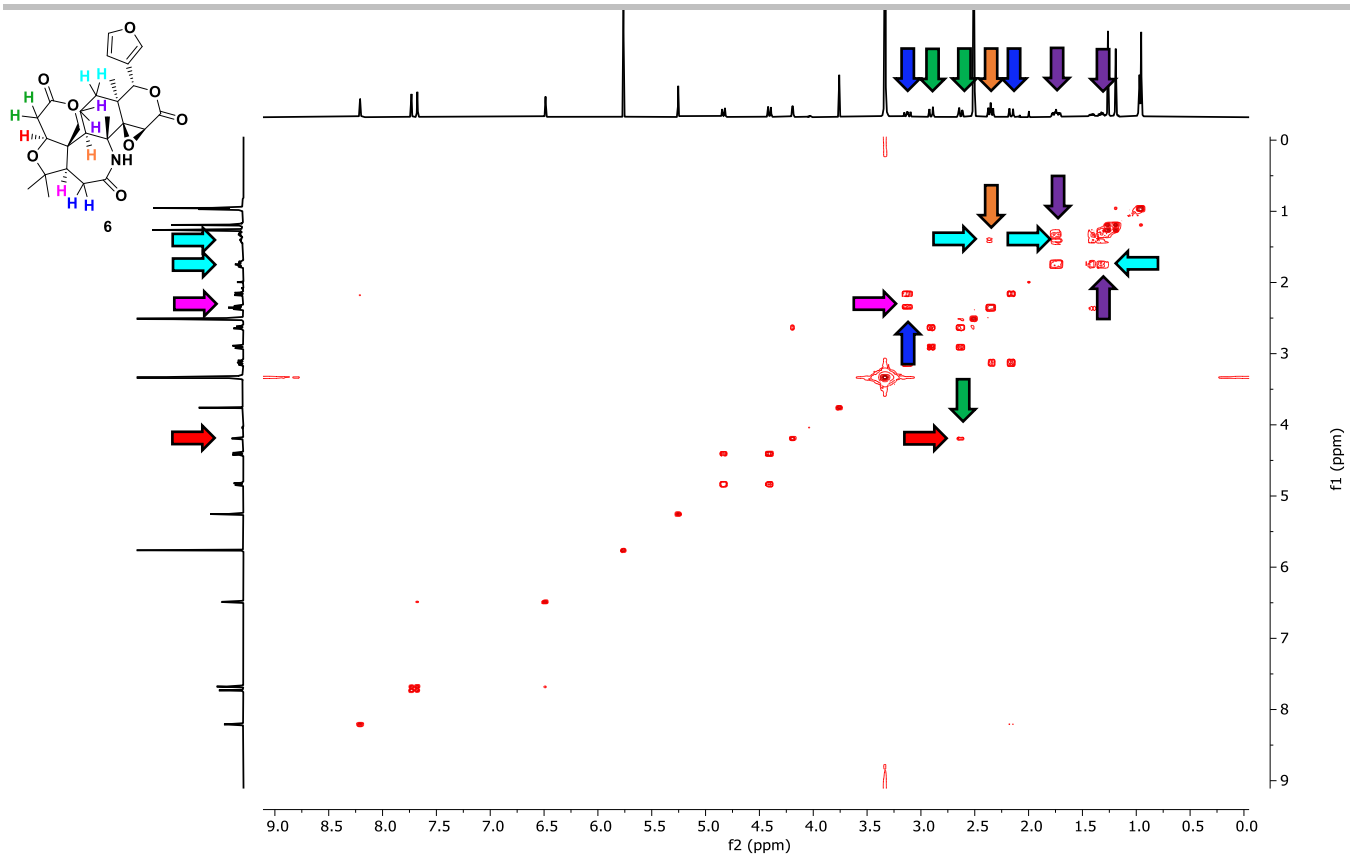

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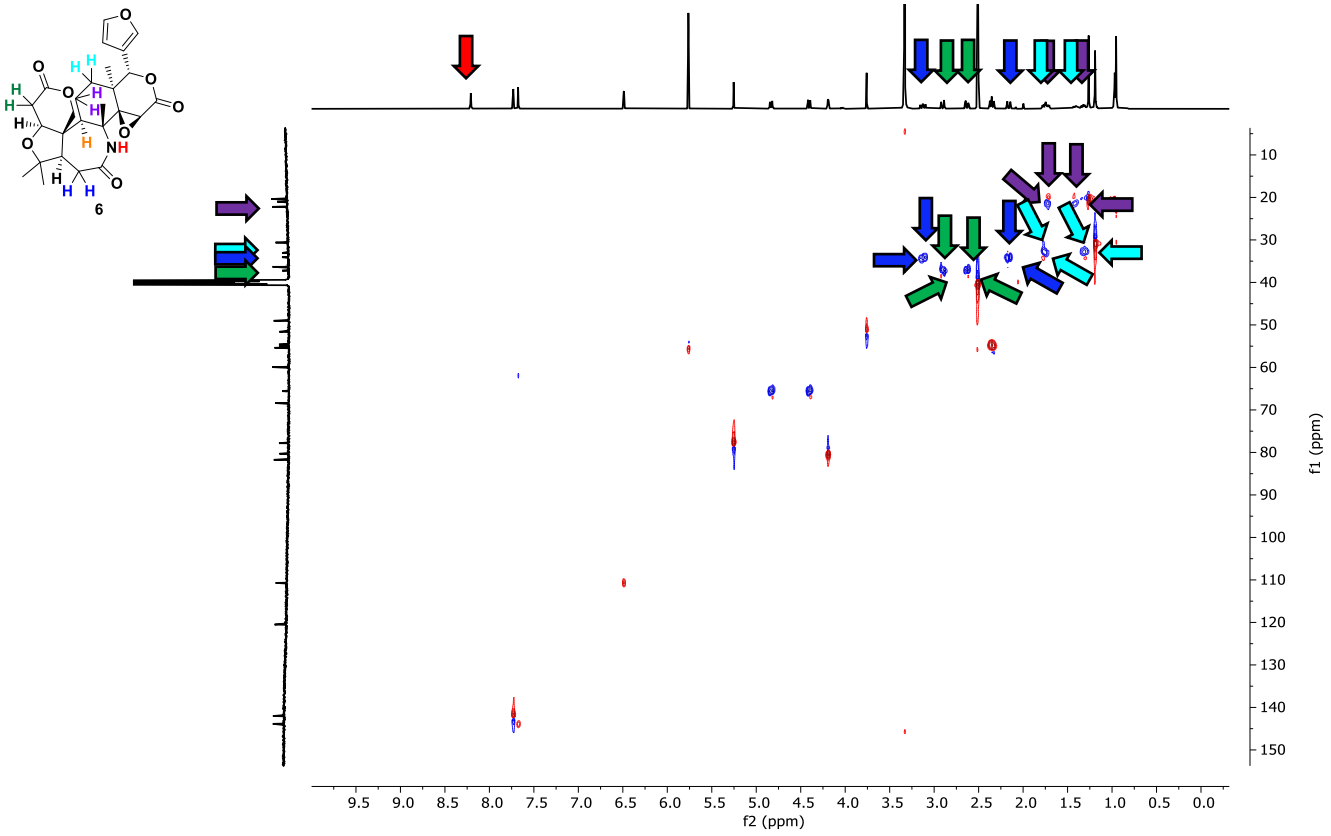

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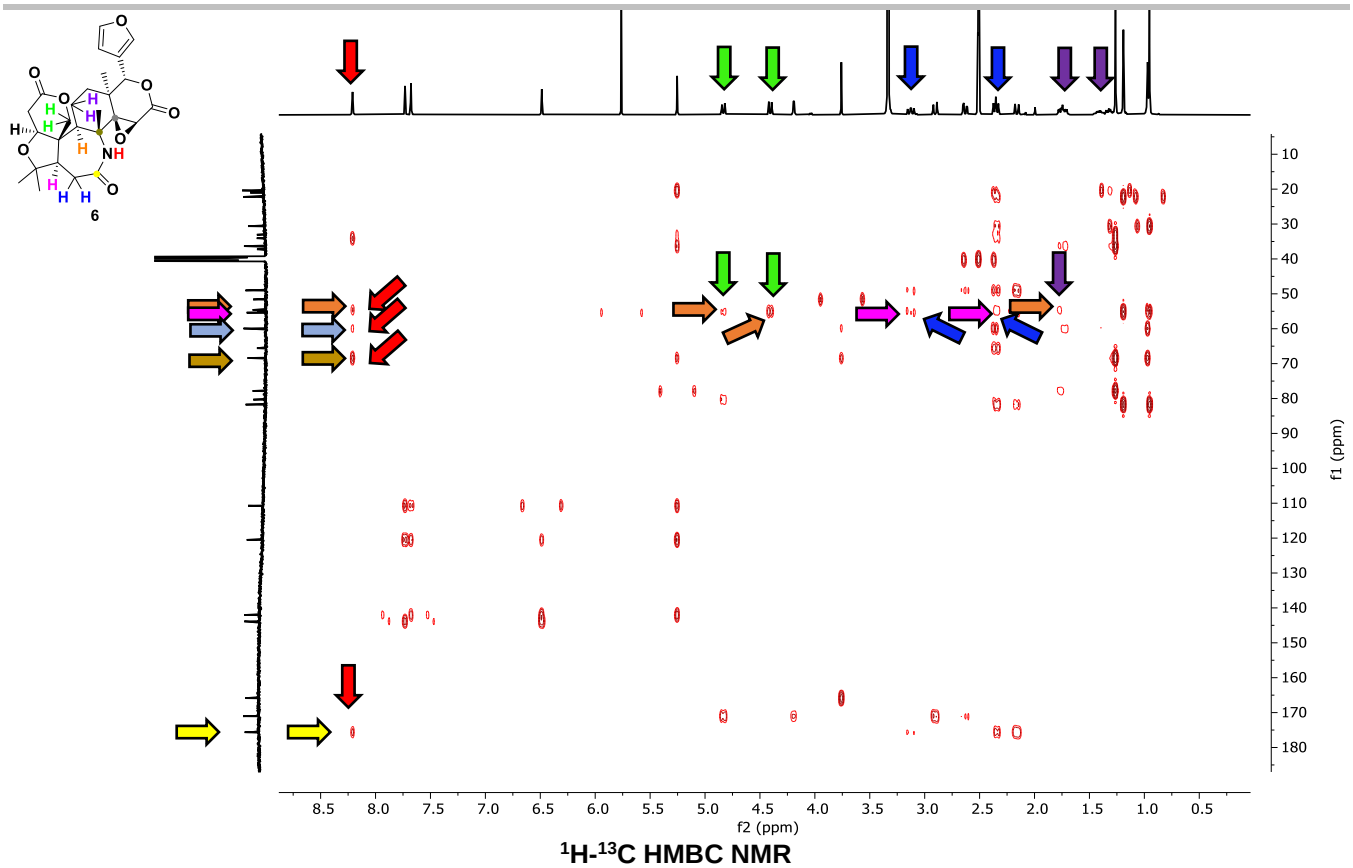

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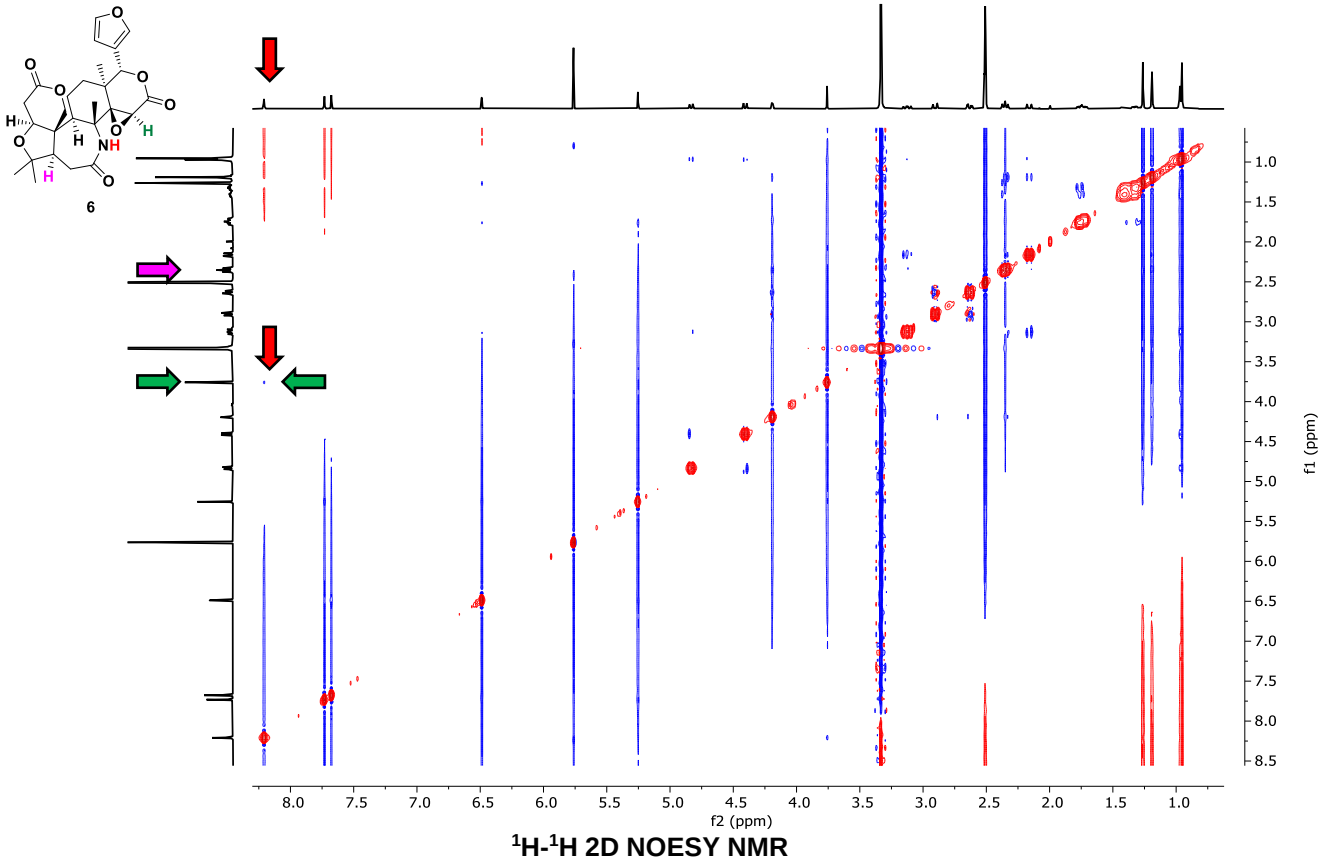

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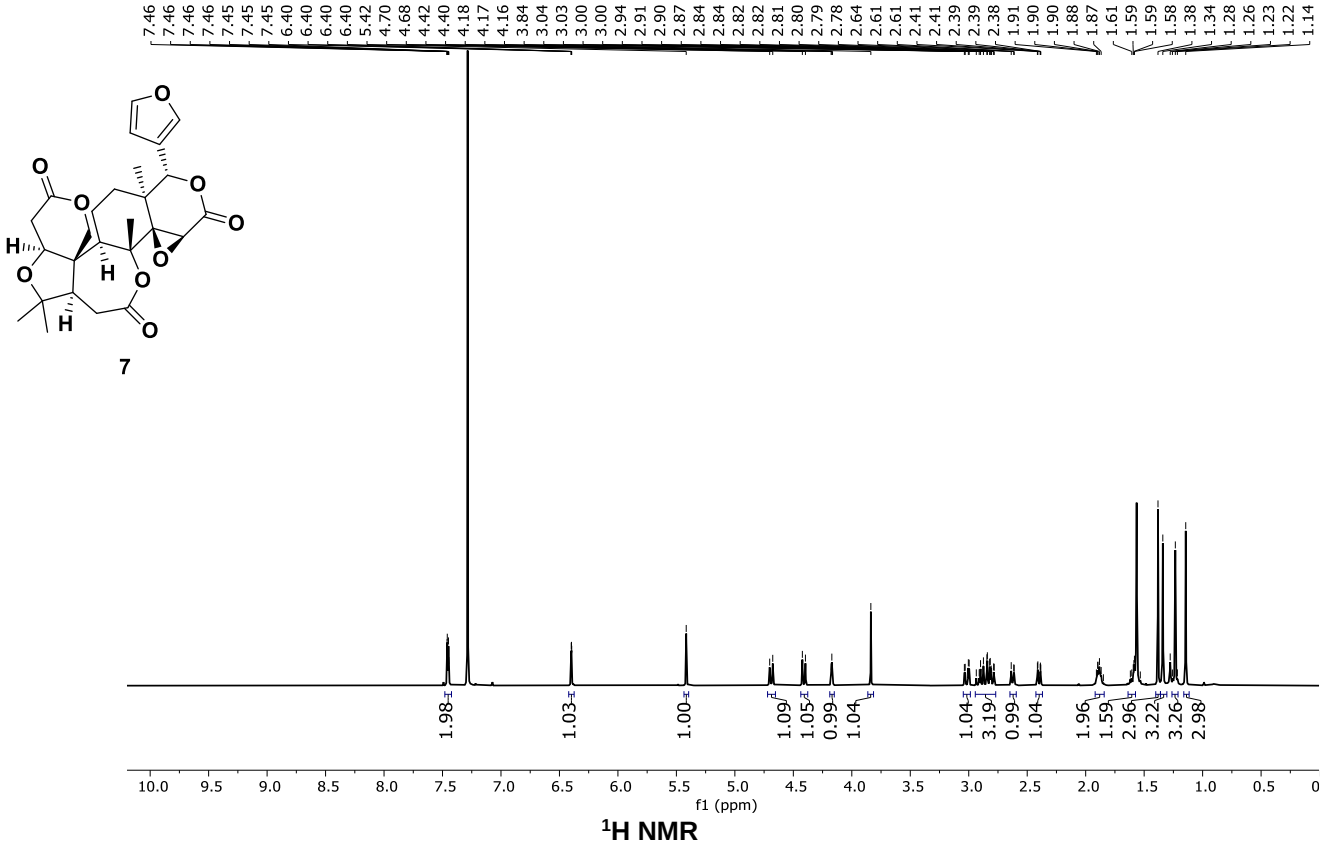

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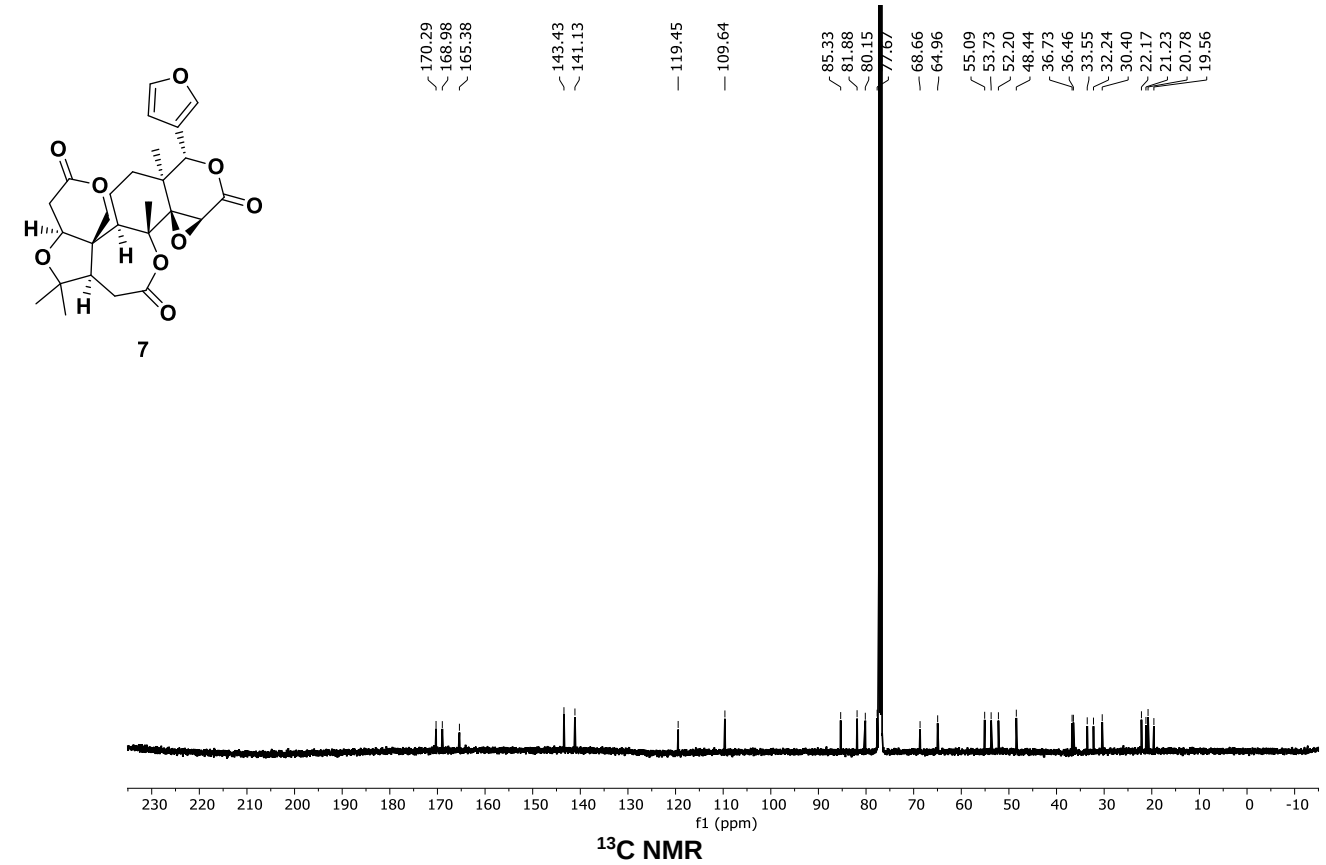

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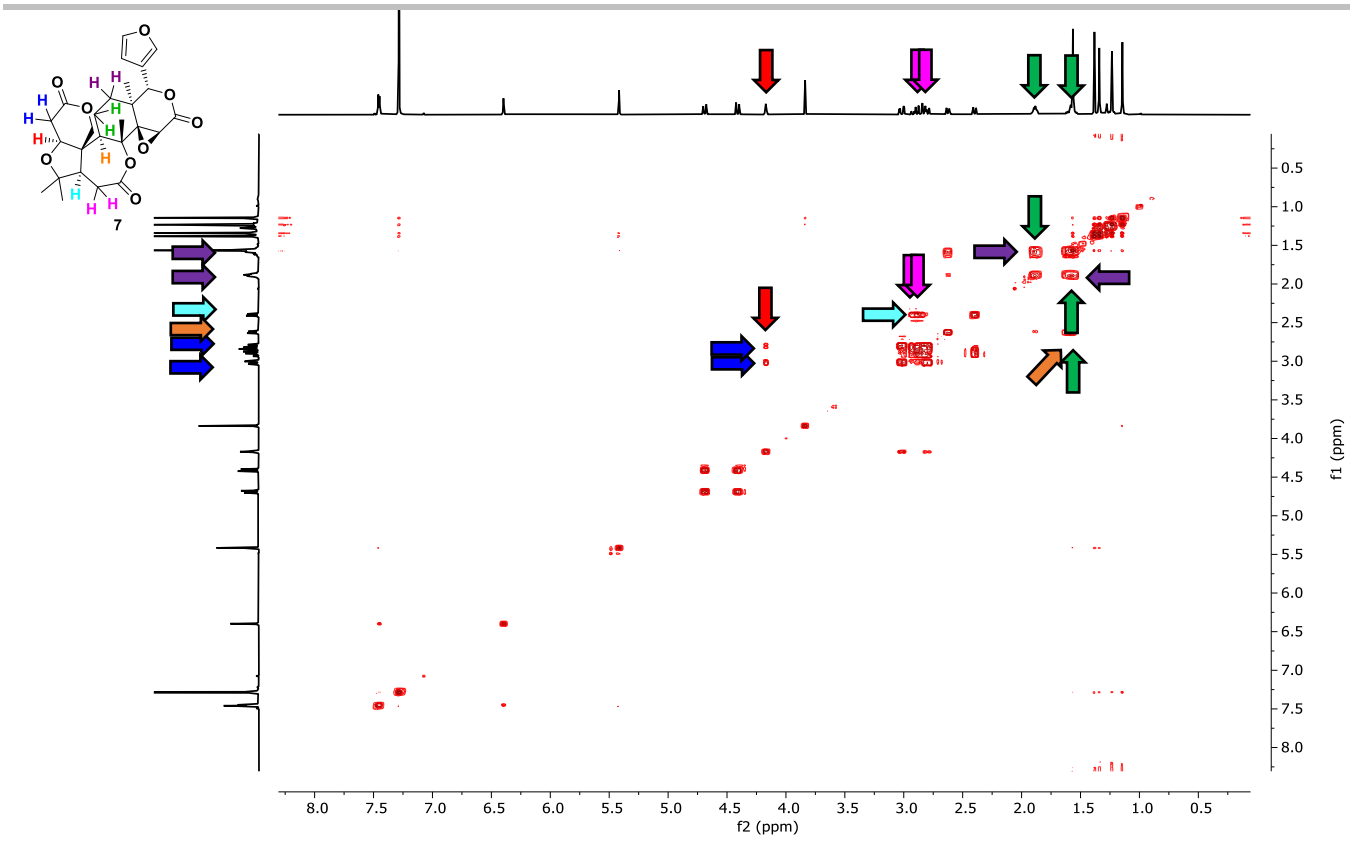

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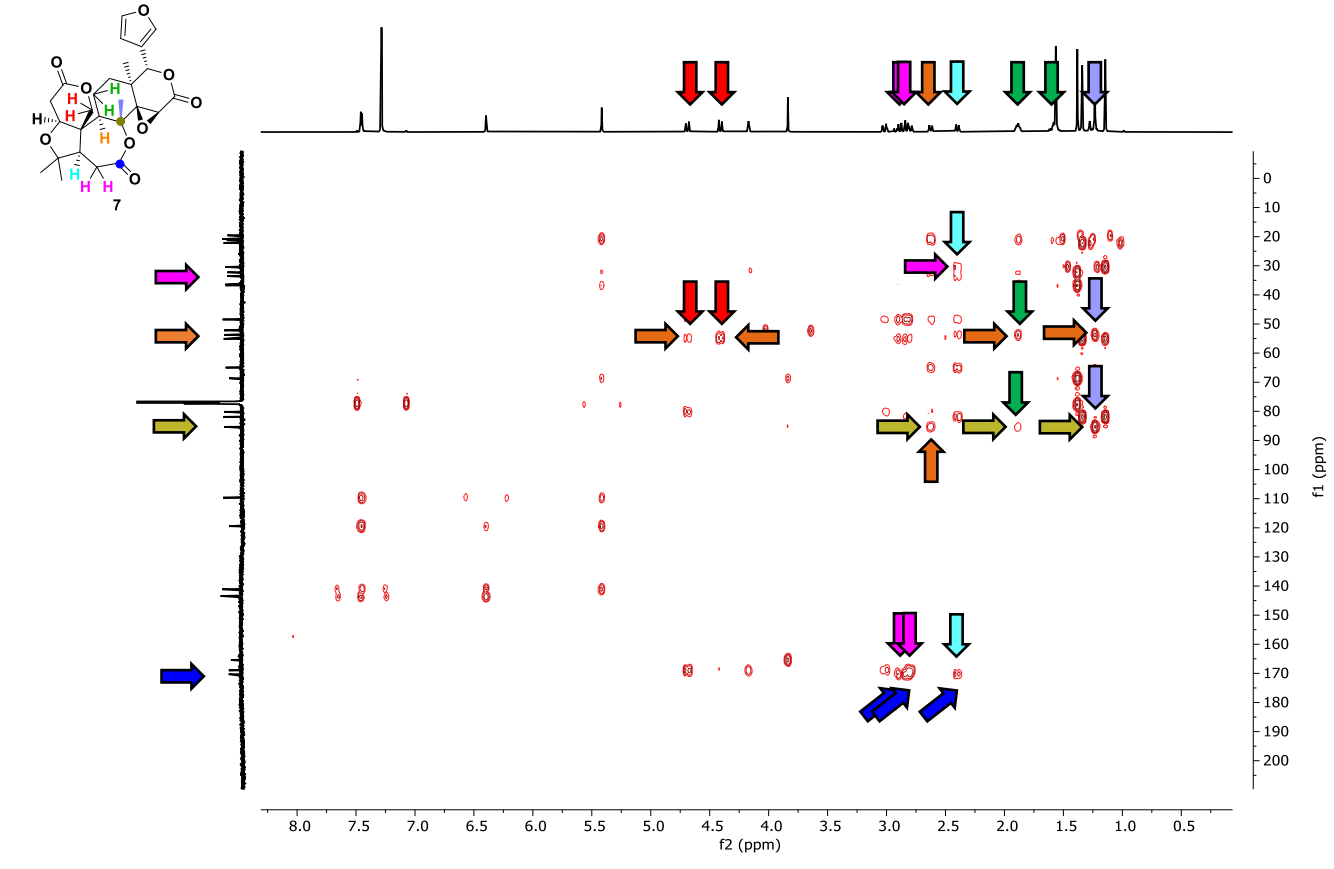

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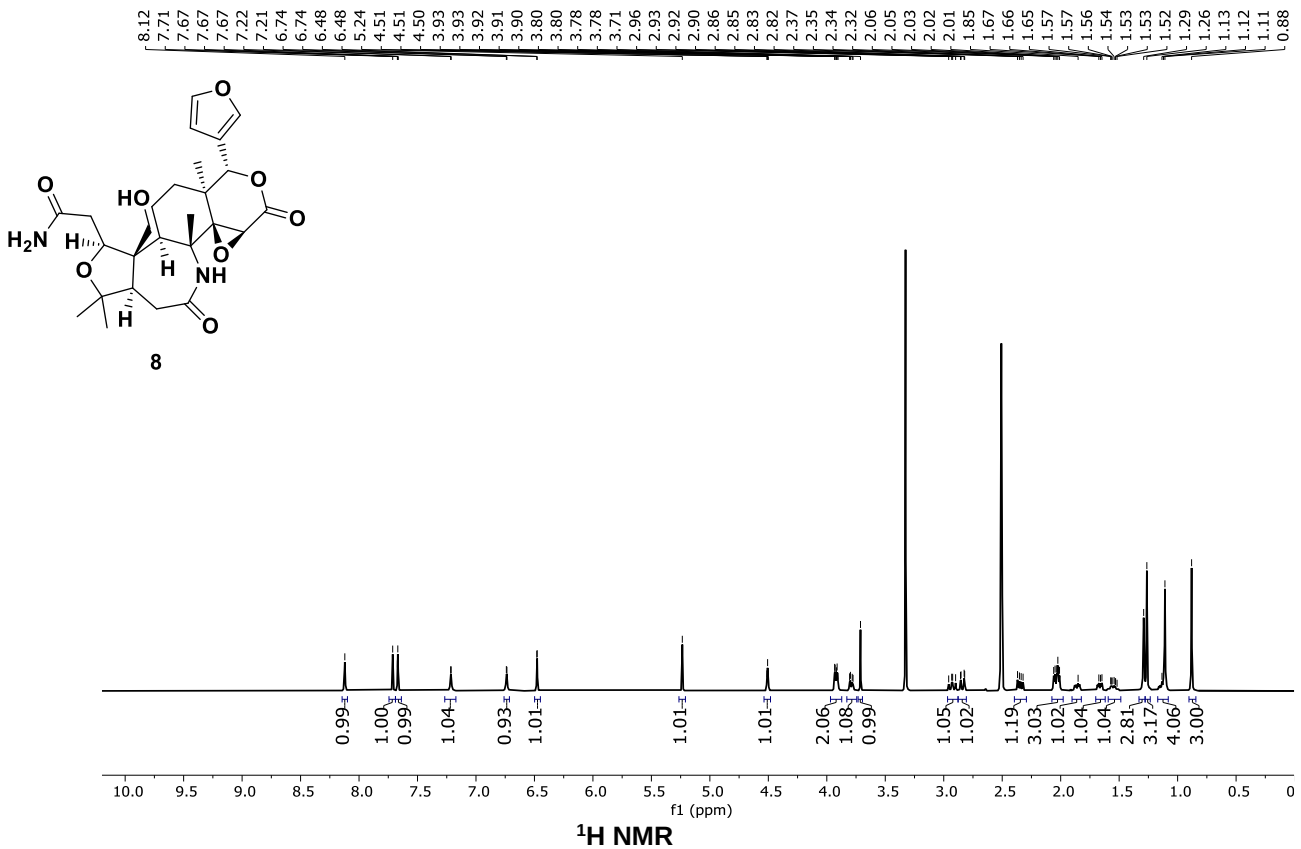

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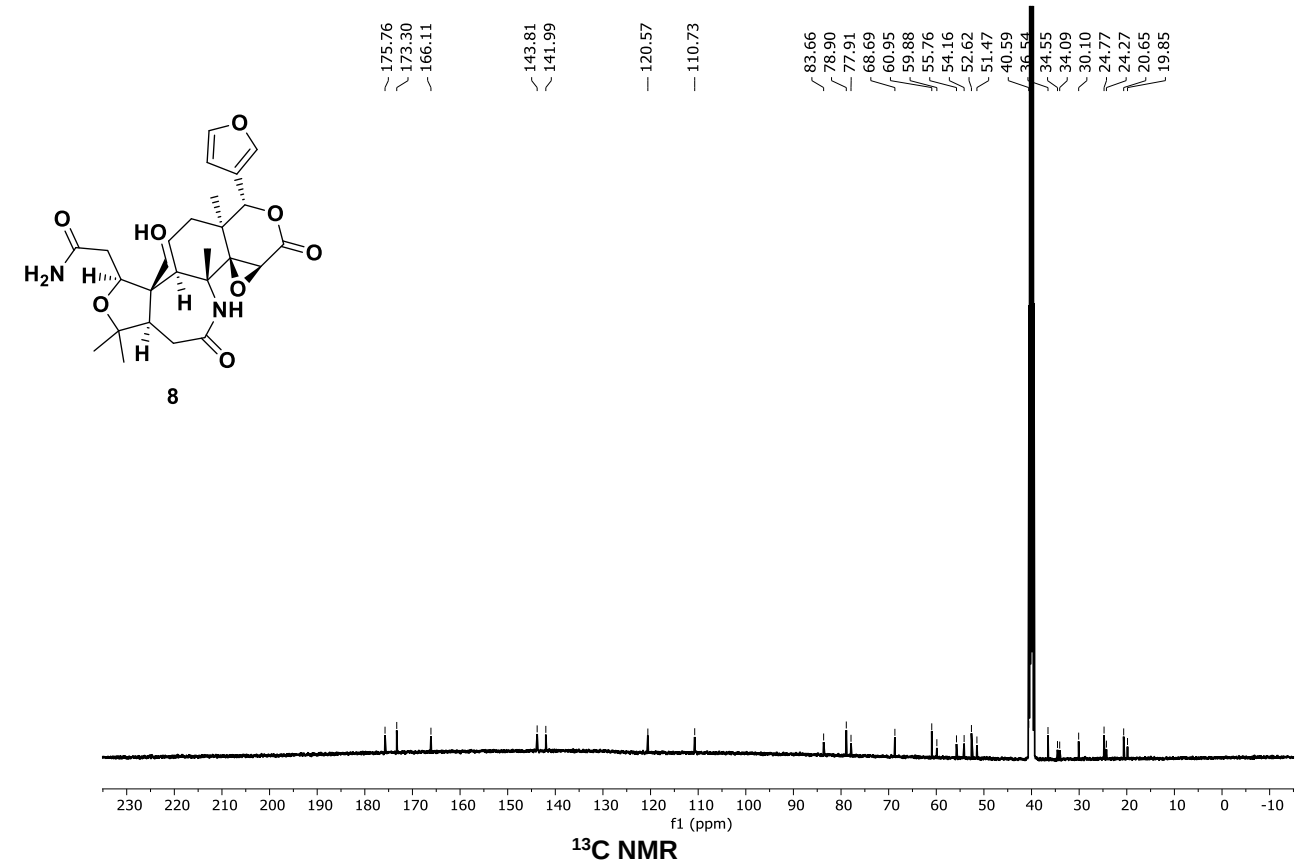

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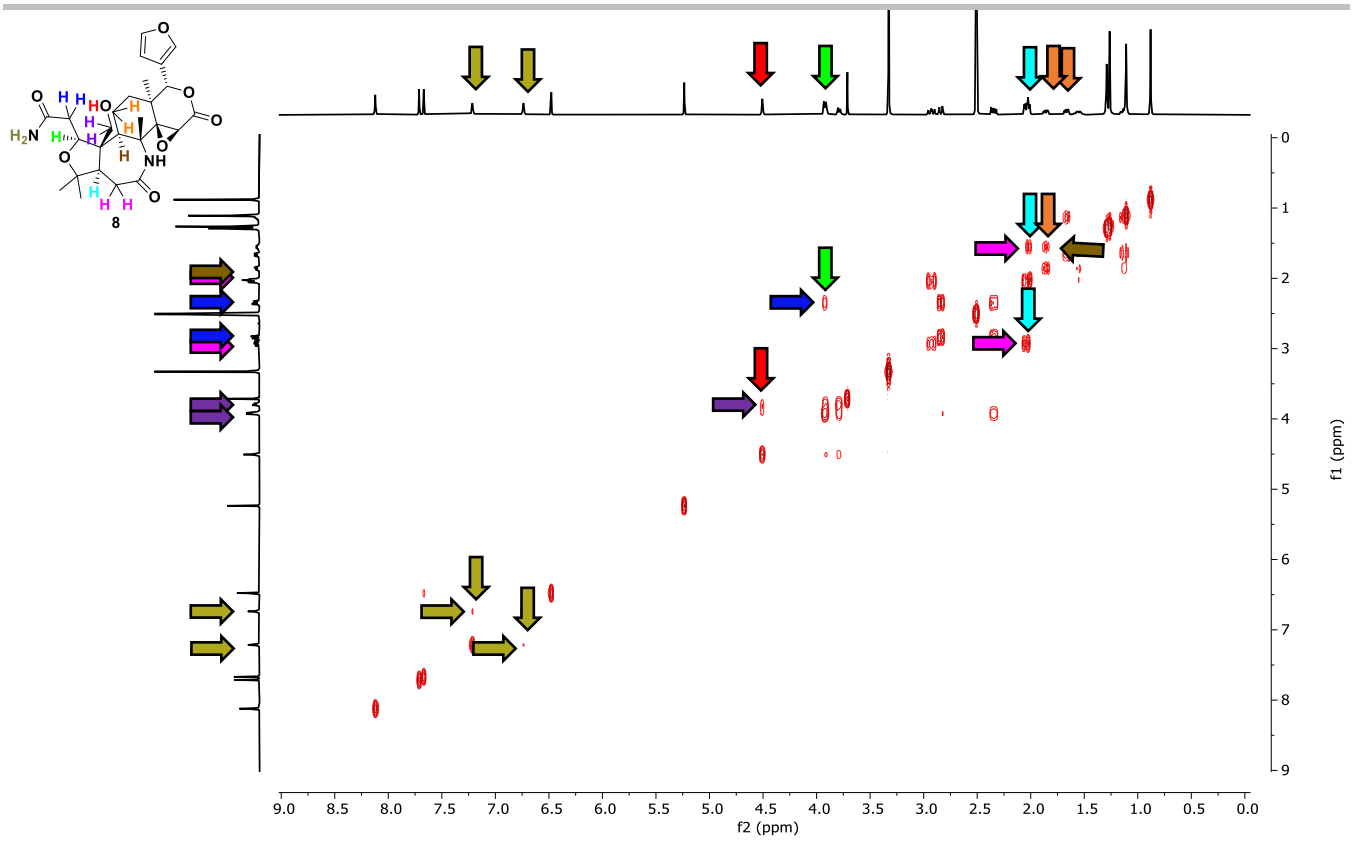

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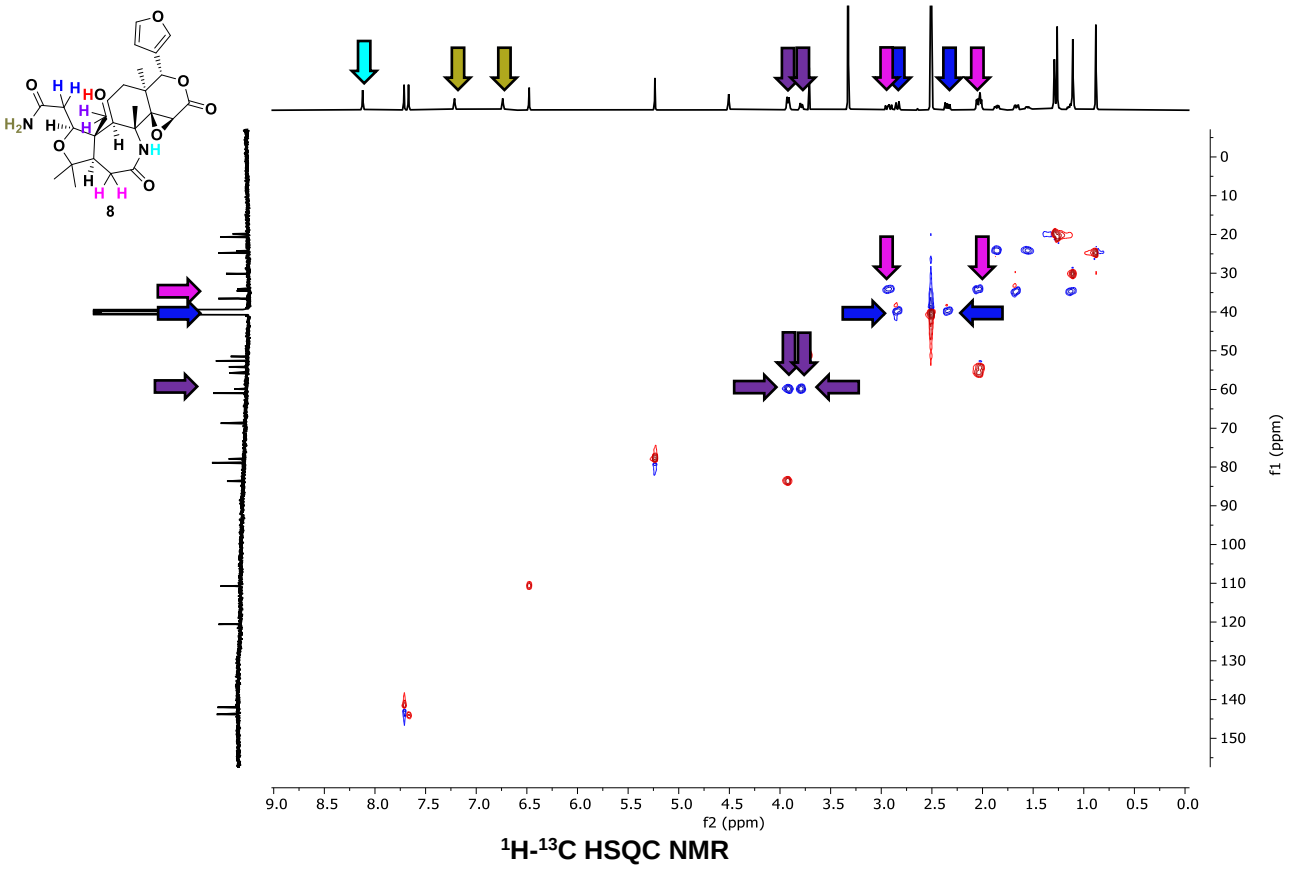

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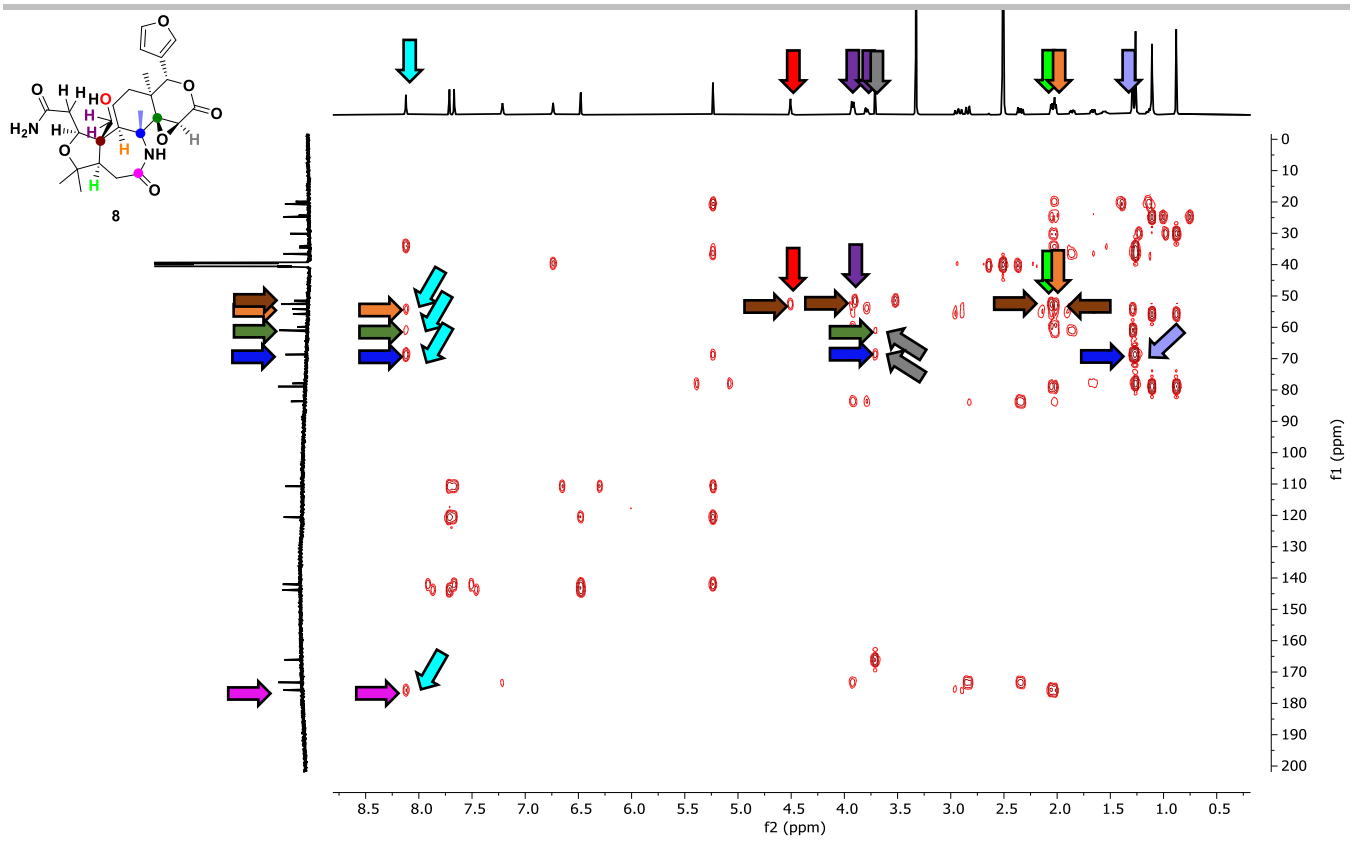

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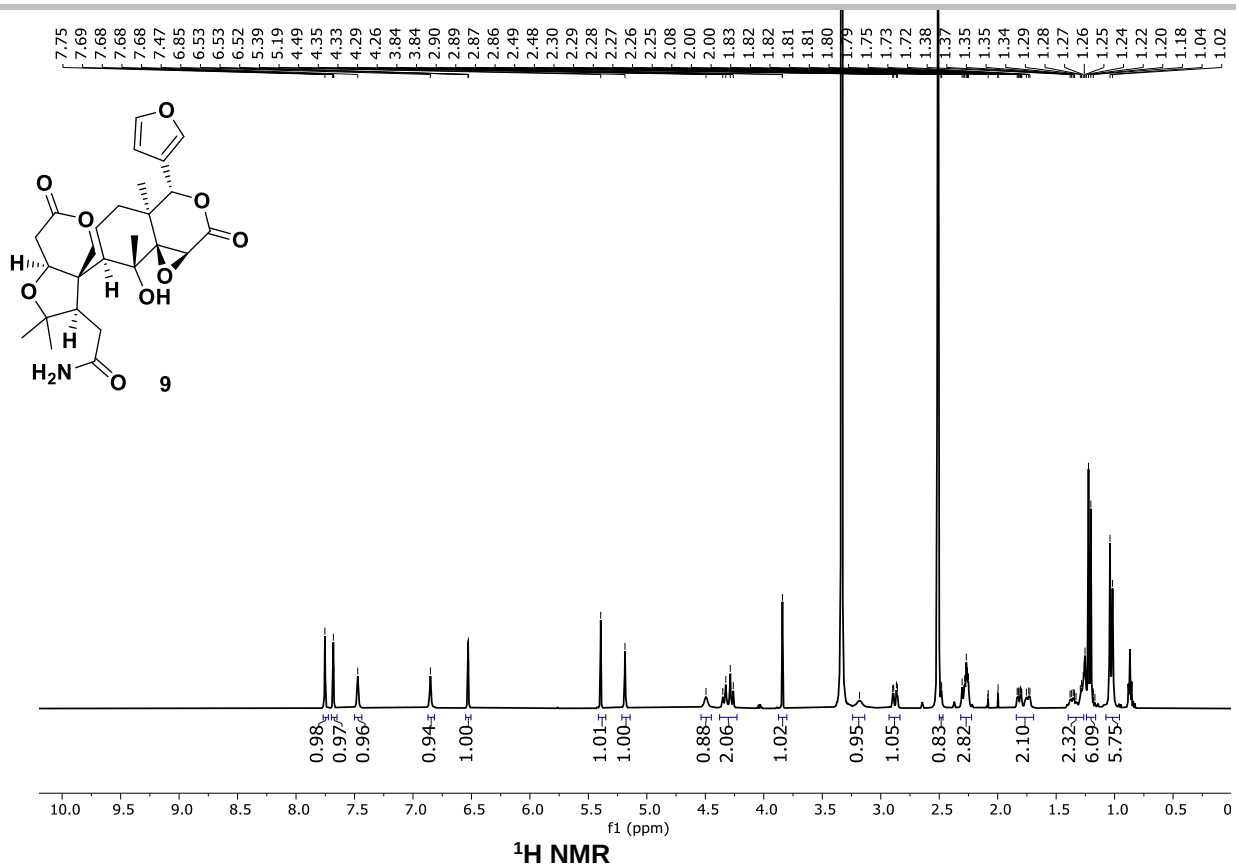

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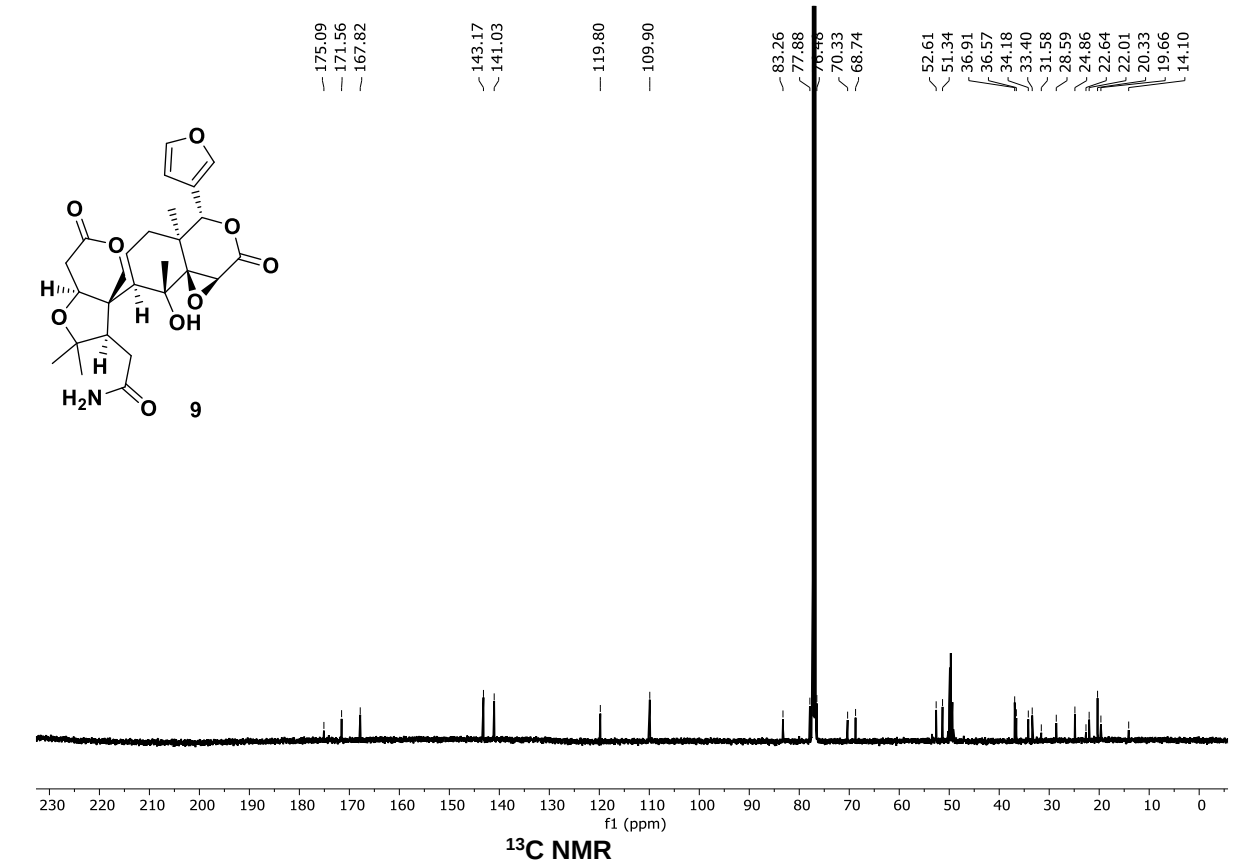

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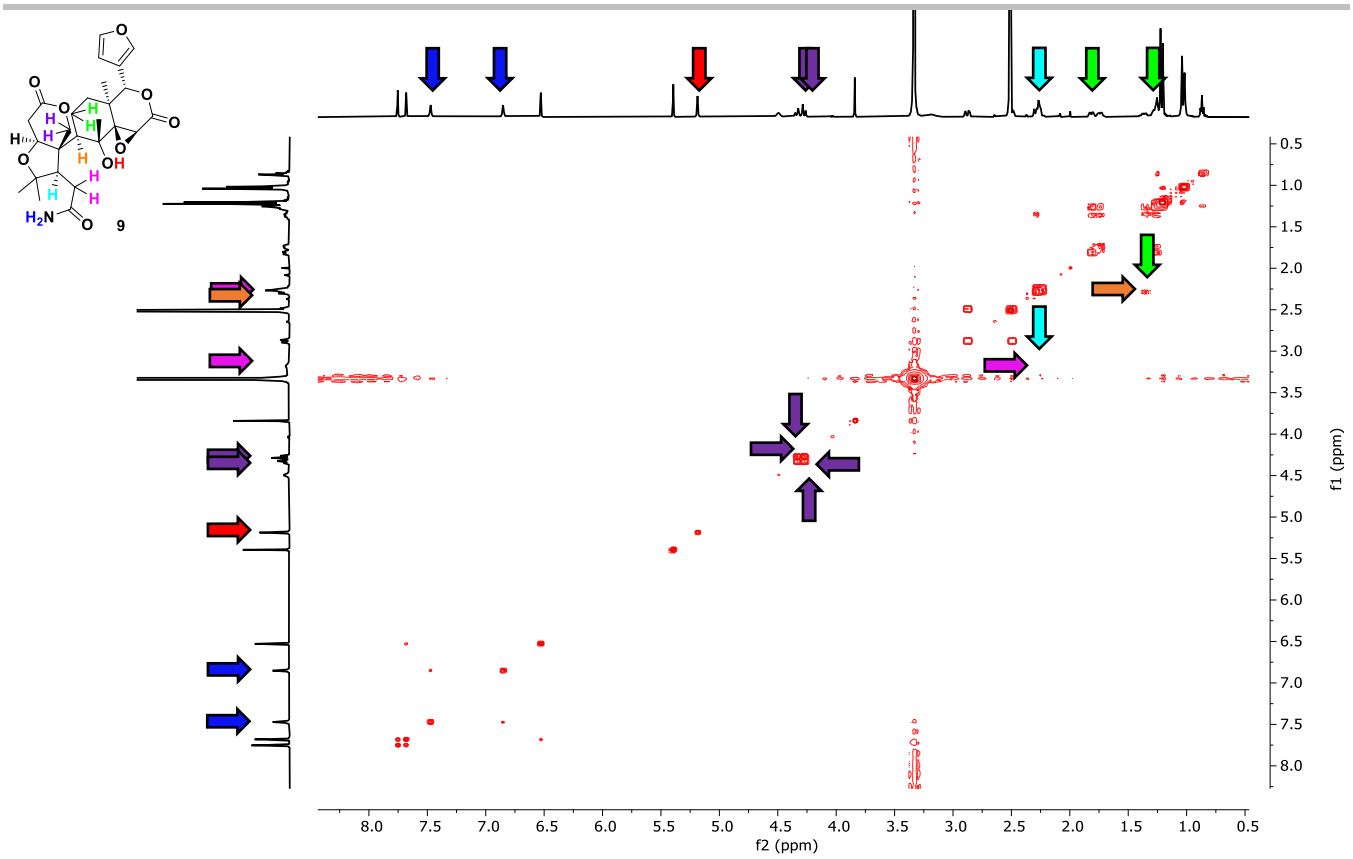

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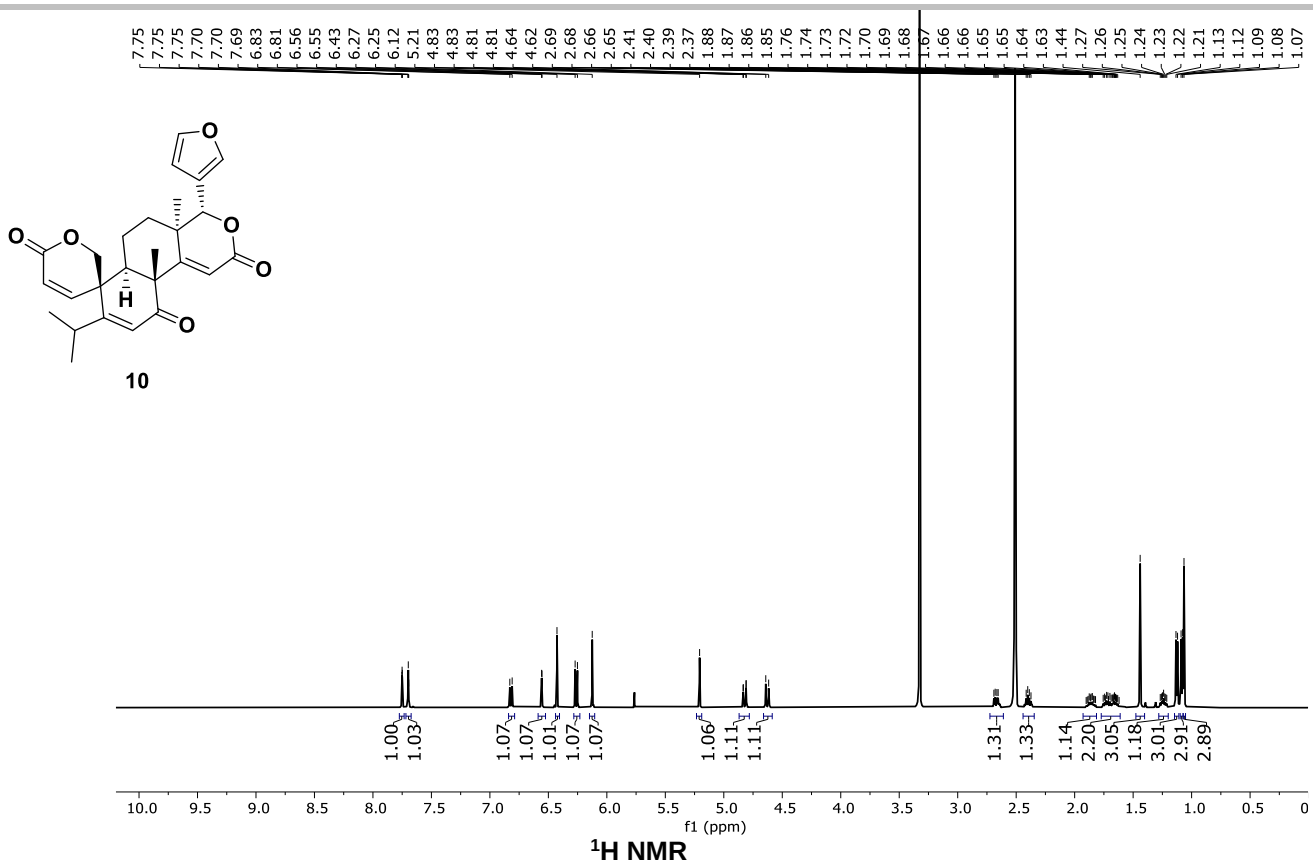

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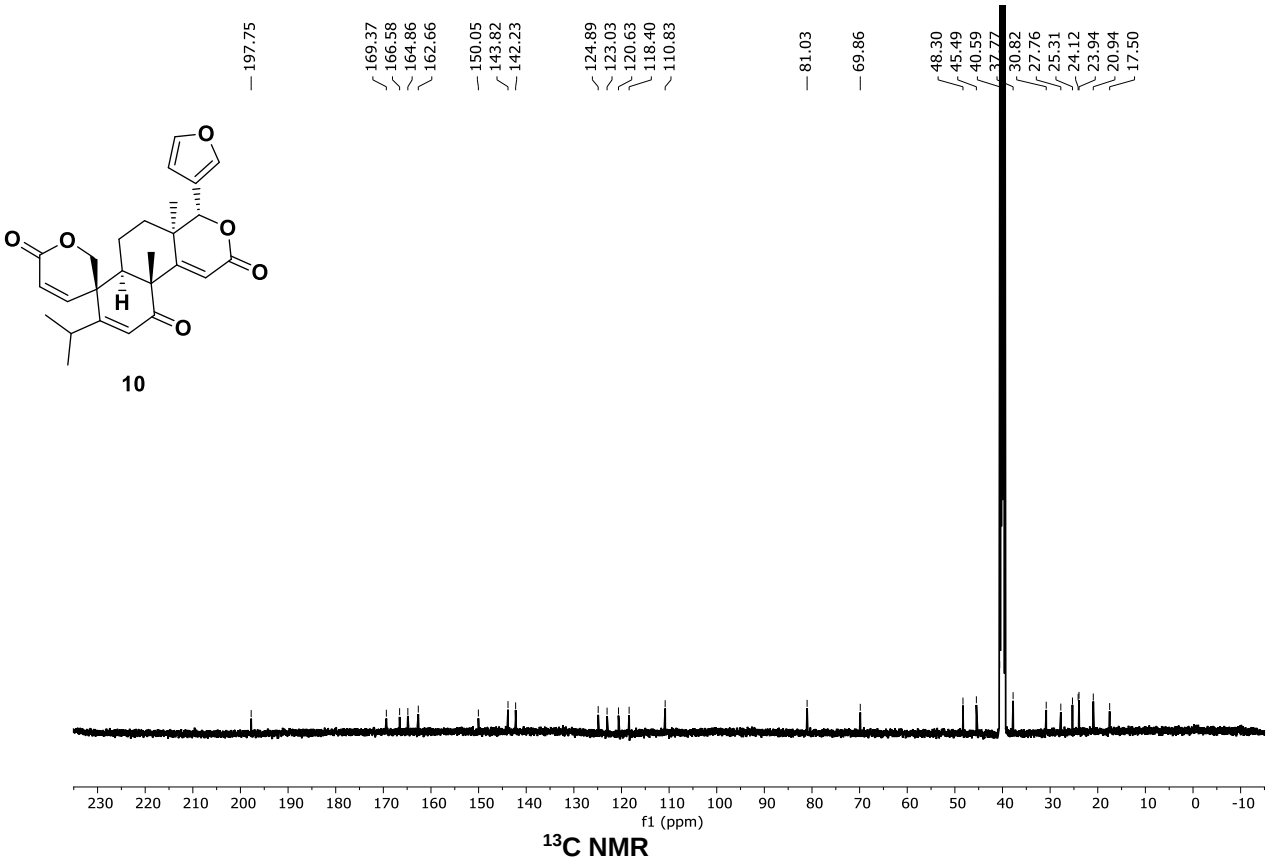

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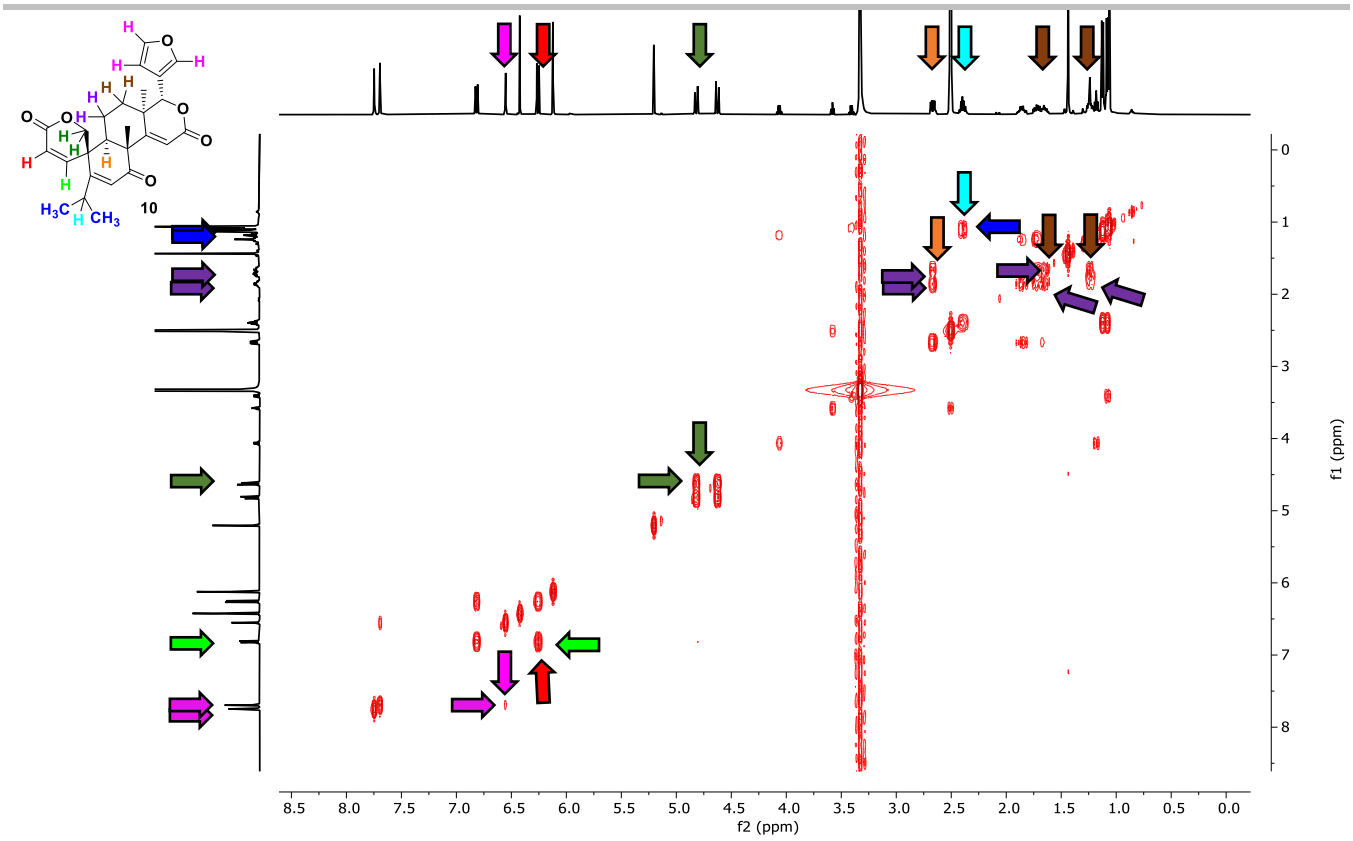

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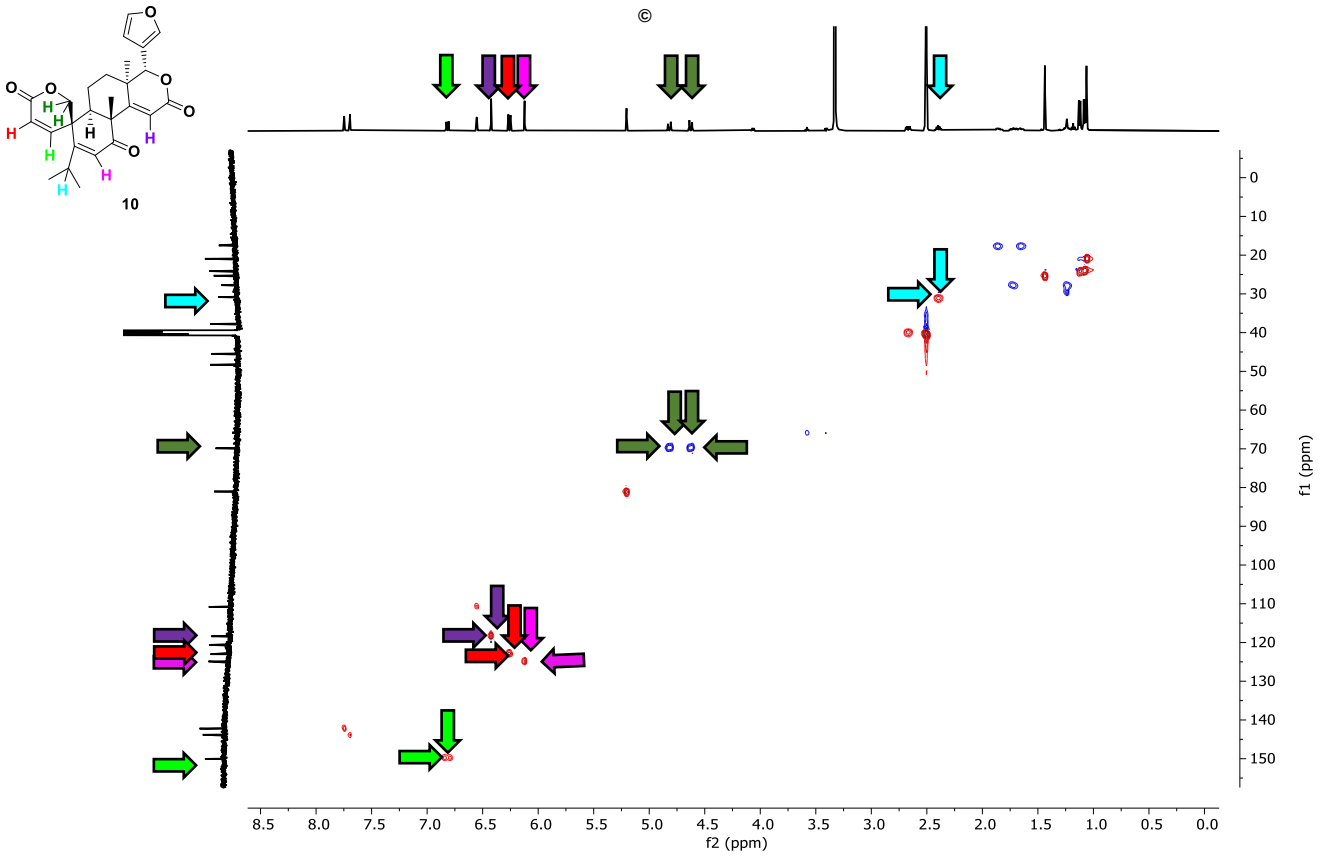

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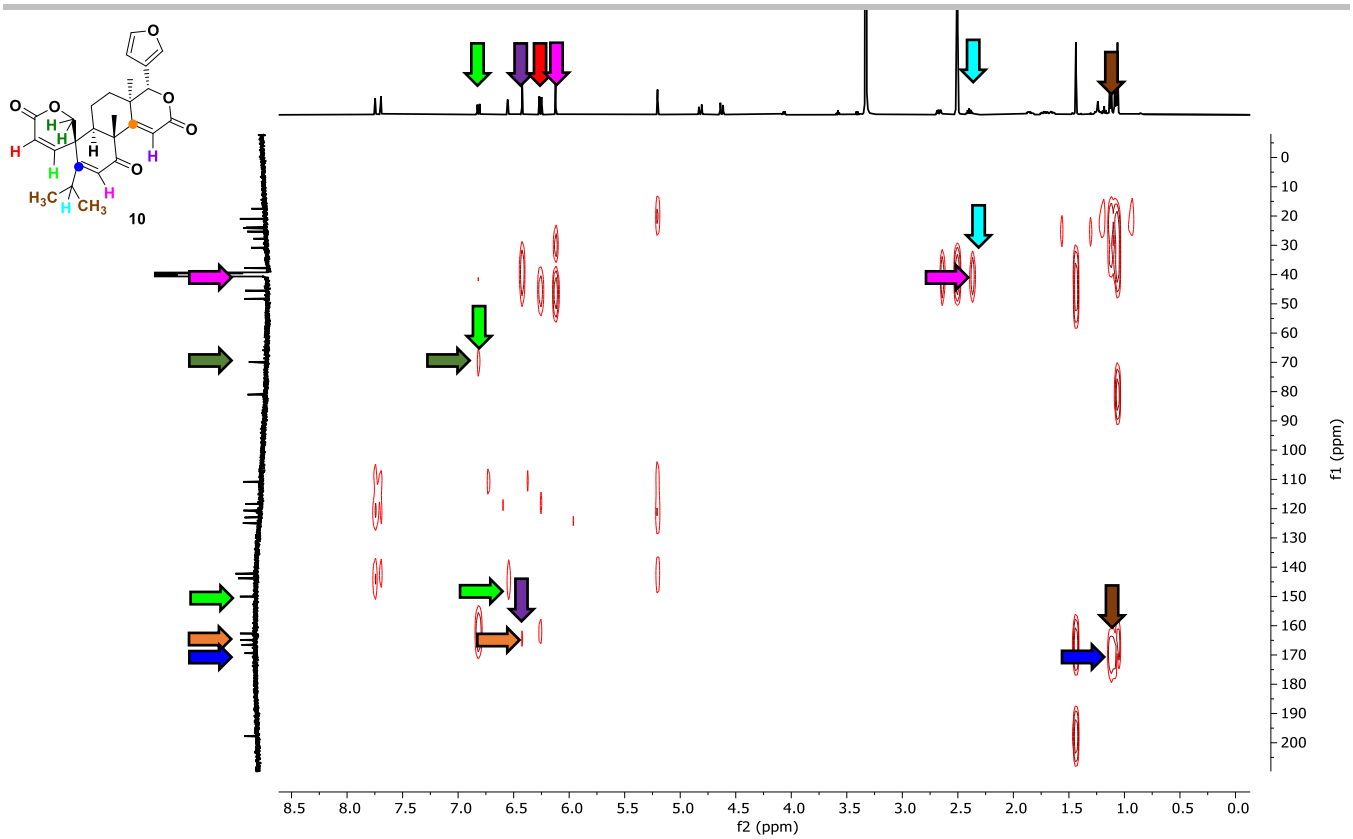
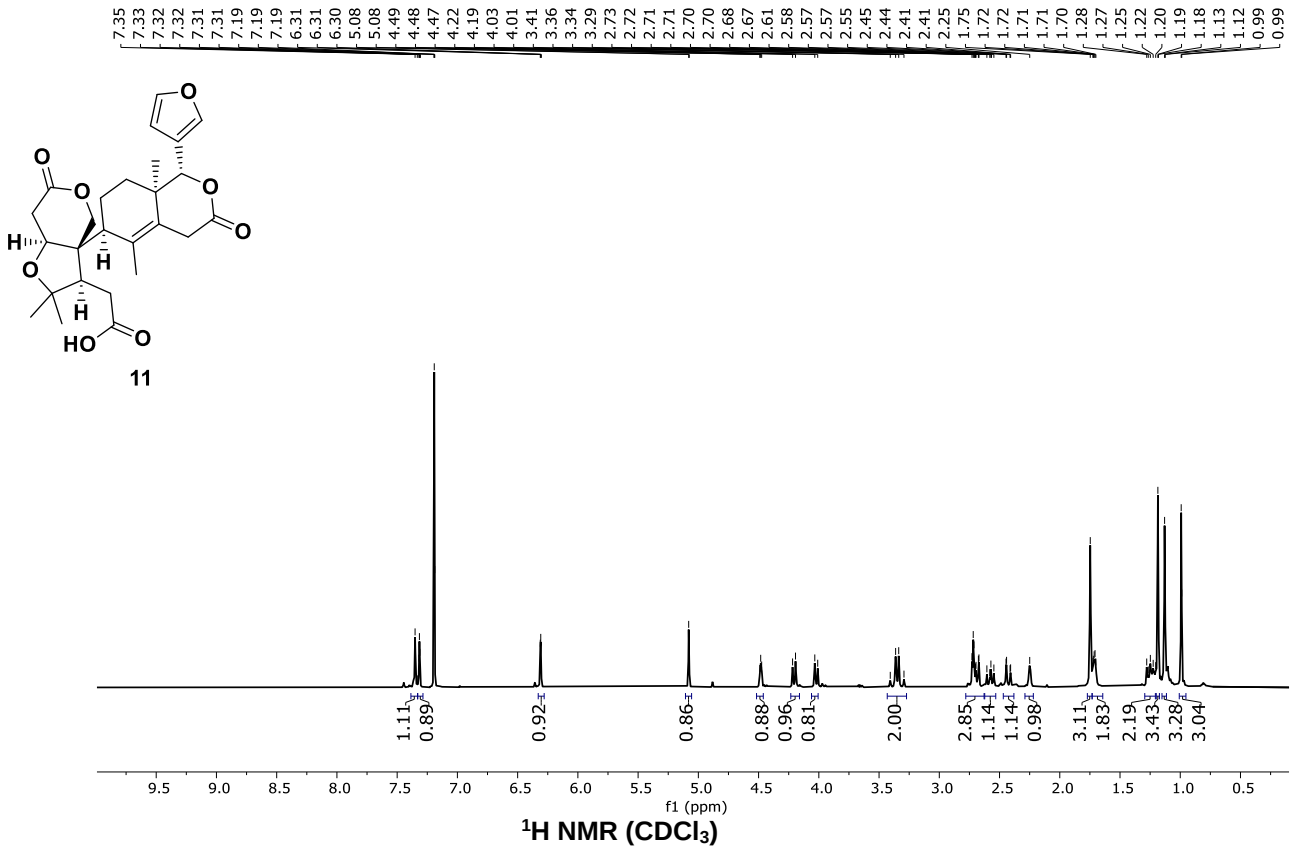
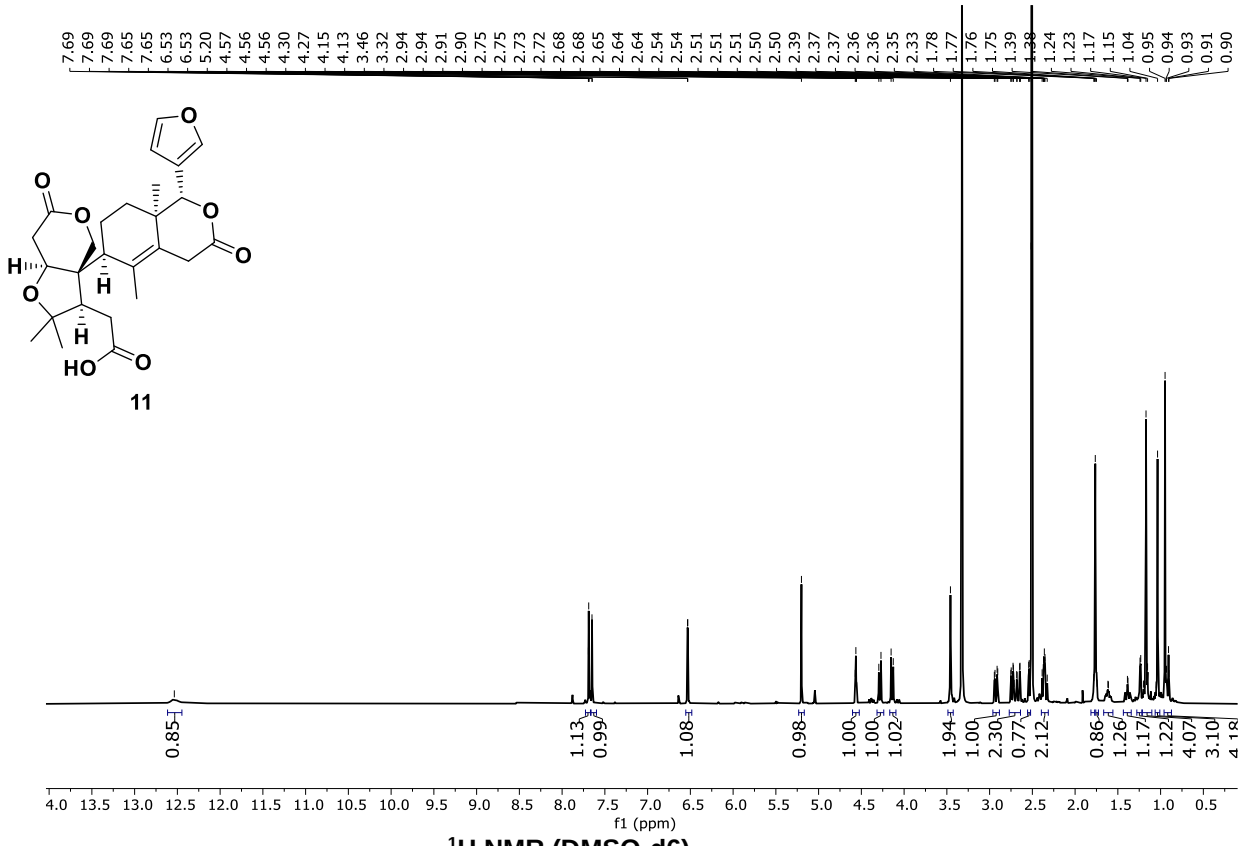


^{1}H-^{13}C HMBC NMR



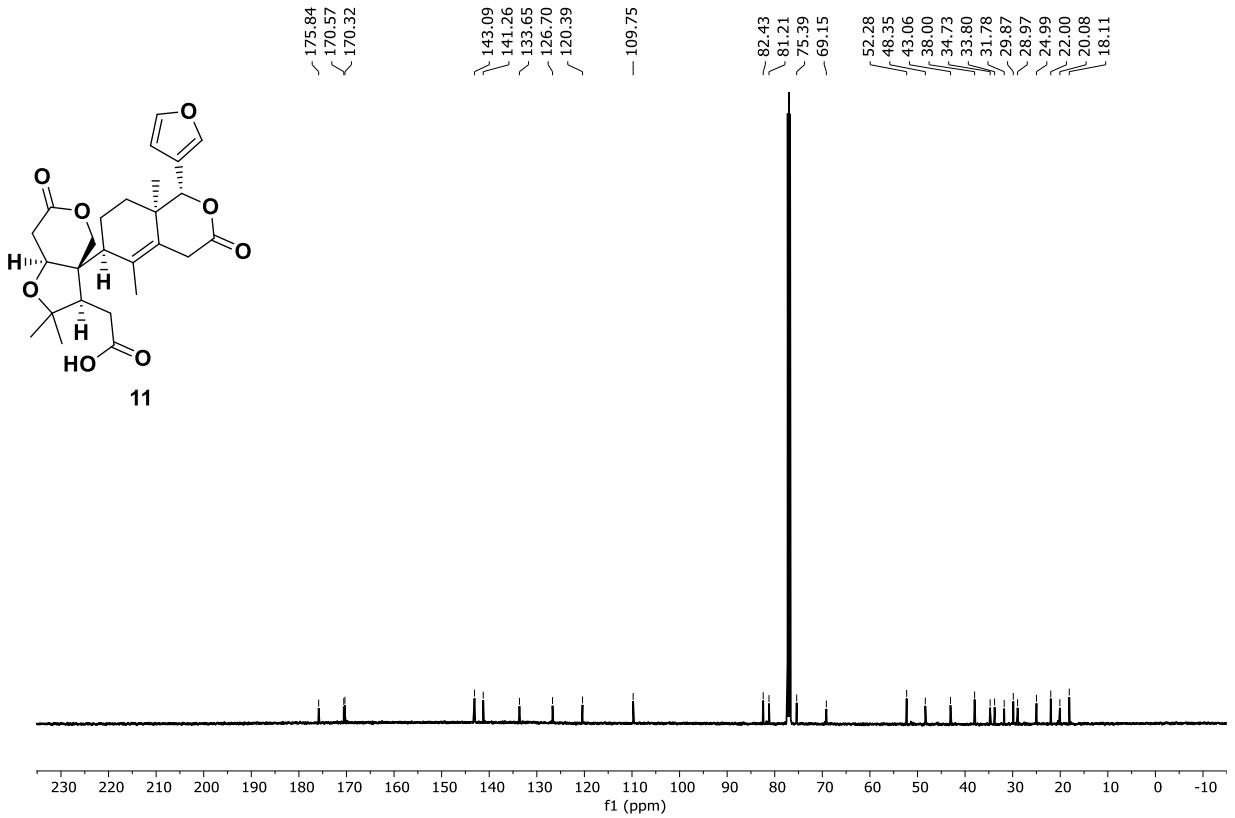
11

^{1}H NMR ($CDCl_3$)

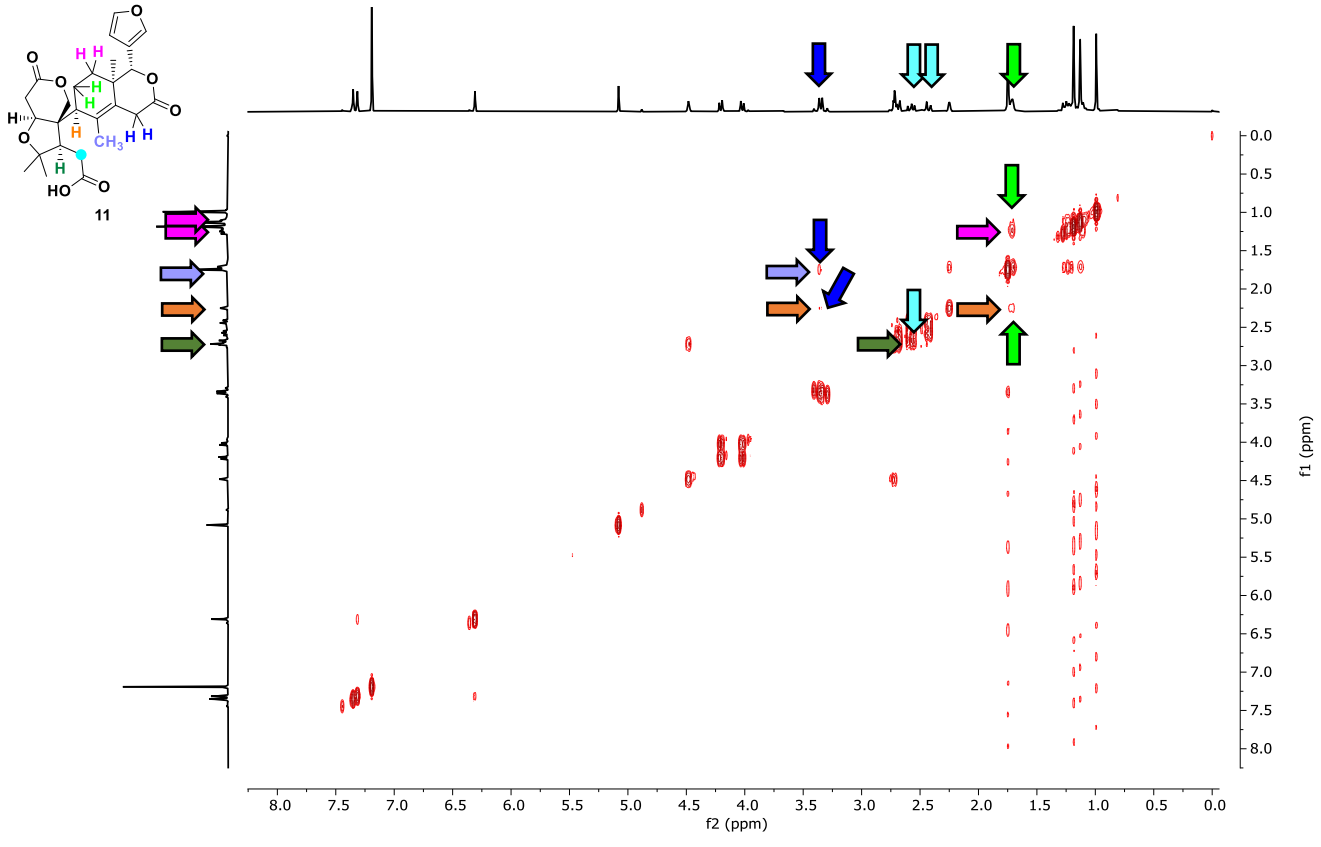


11

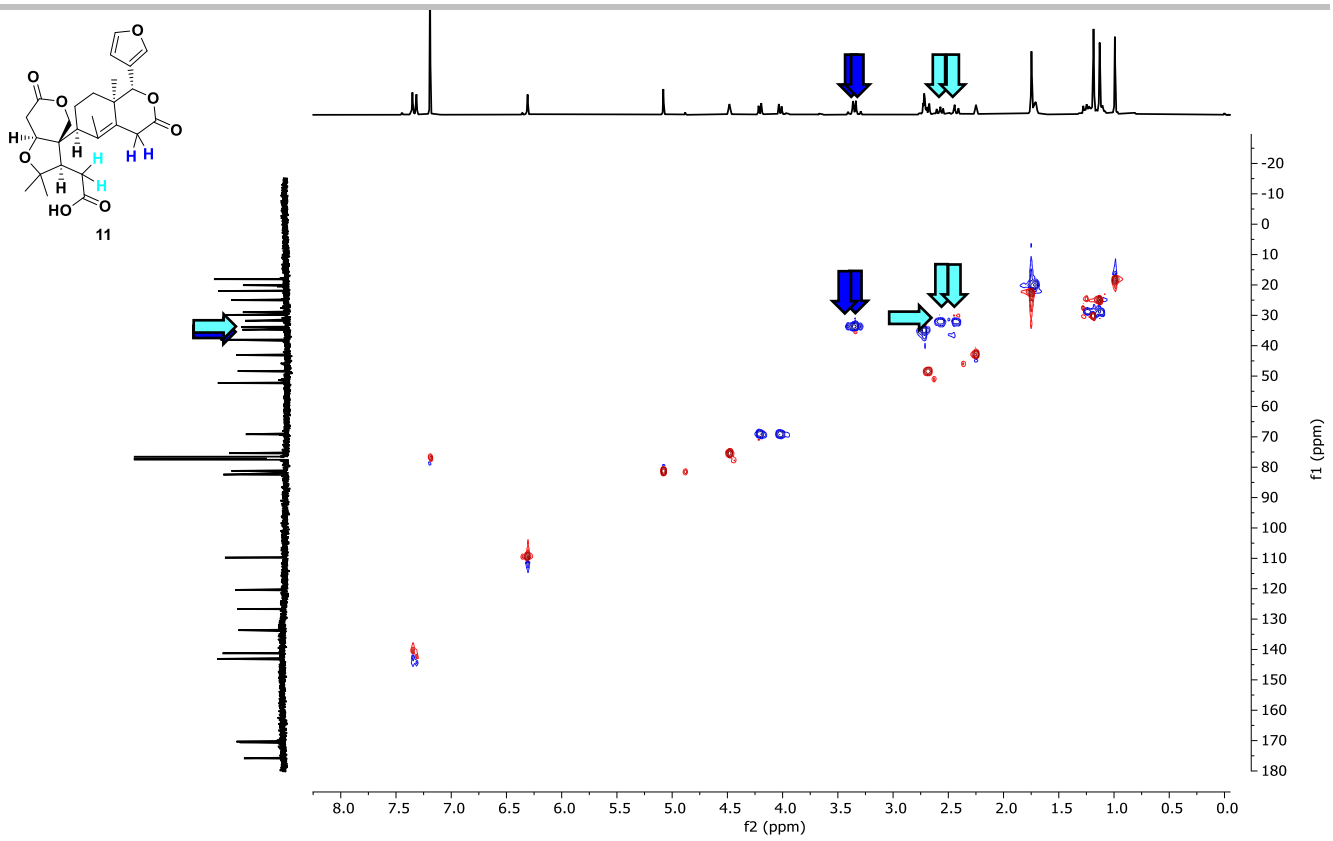
^{1}H NMR (DMSO-d6)



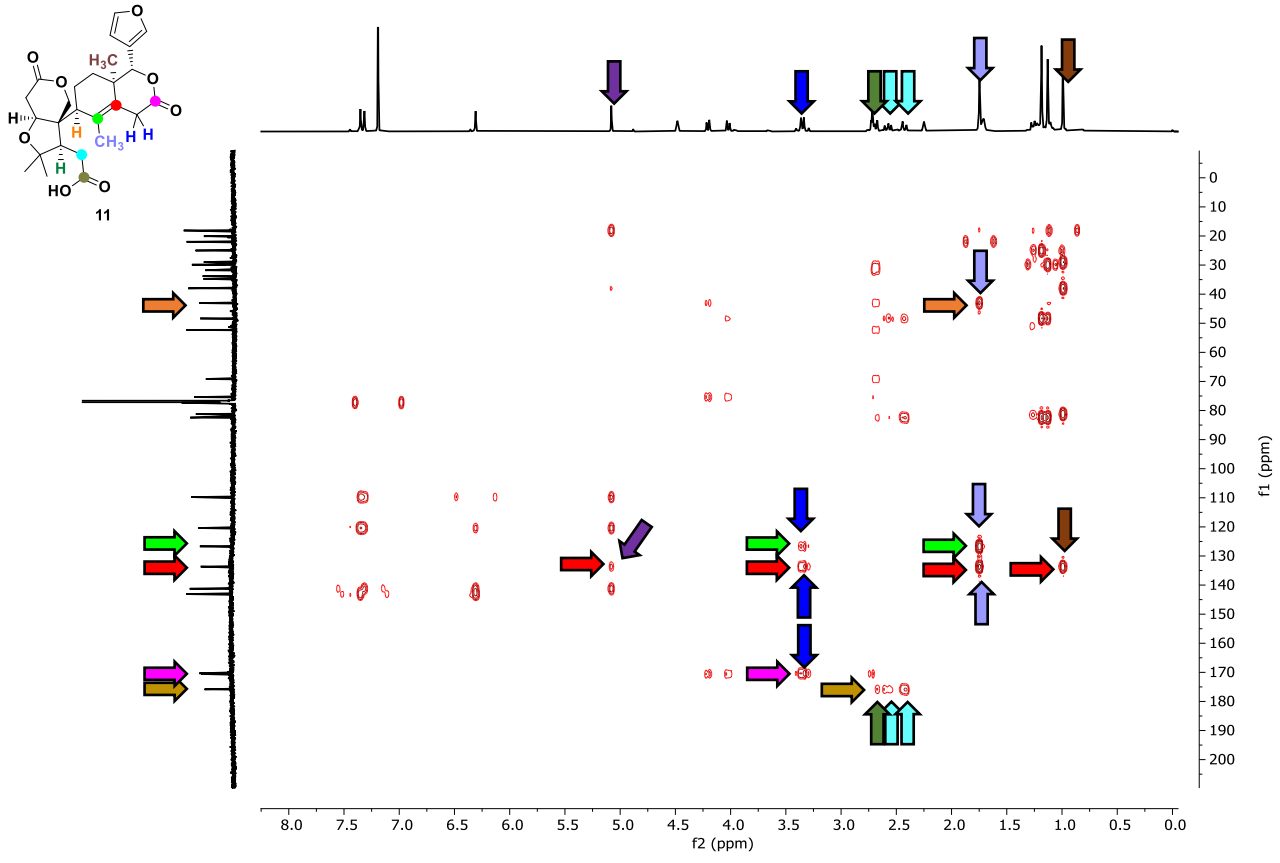
^{13}C NMR ($CDCl_3$)



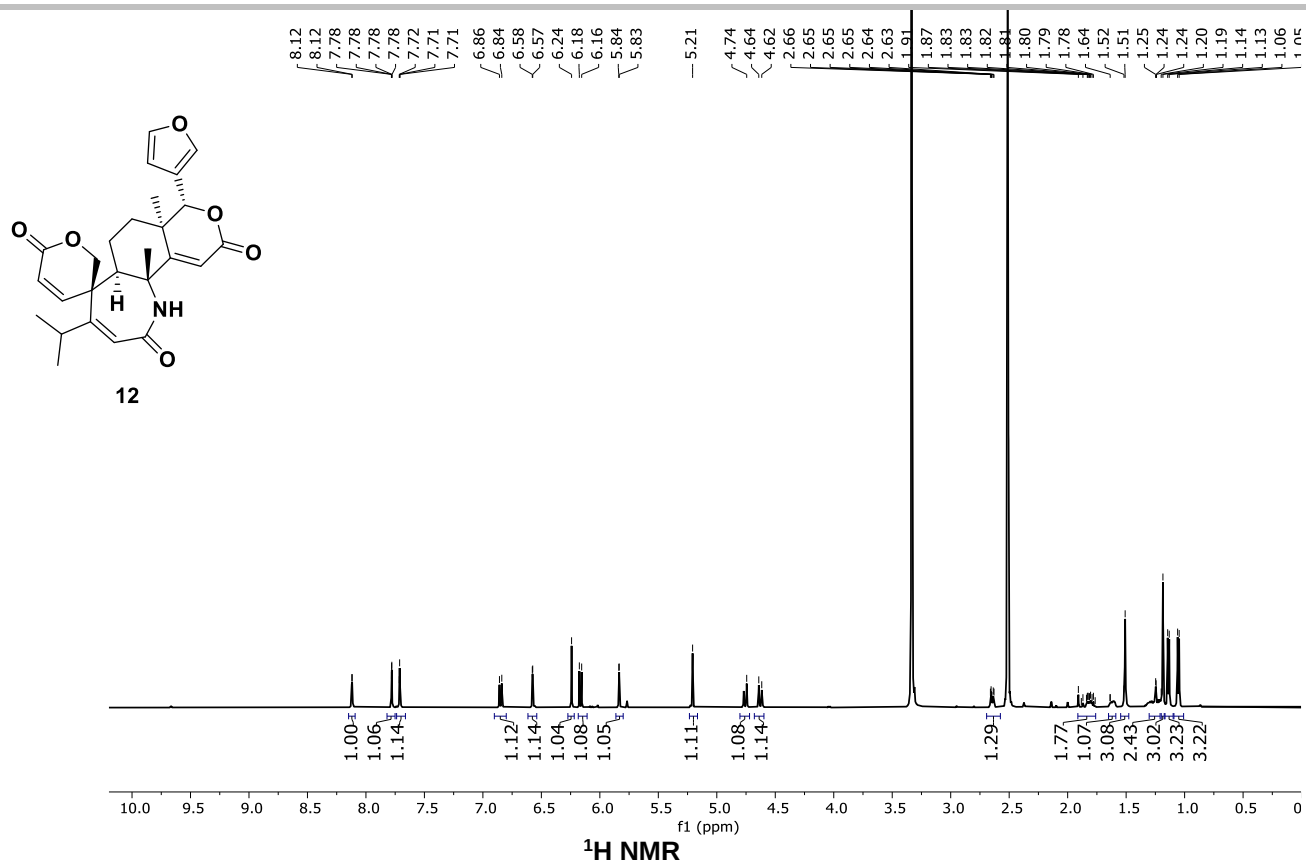
^{1}H-^{1}H COSY NMR



^{1}H-^{13}C HSQC NMR

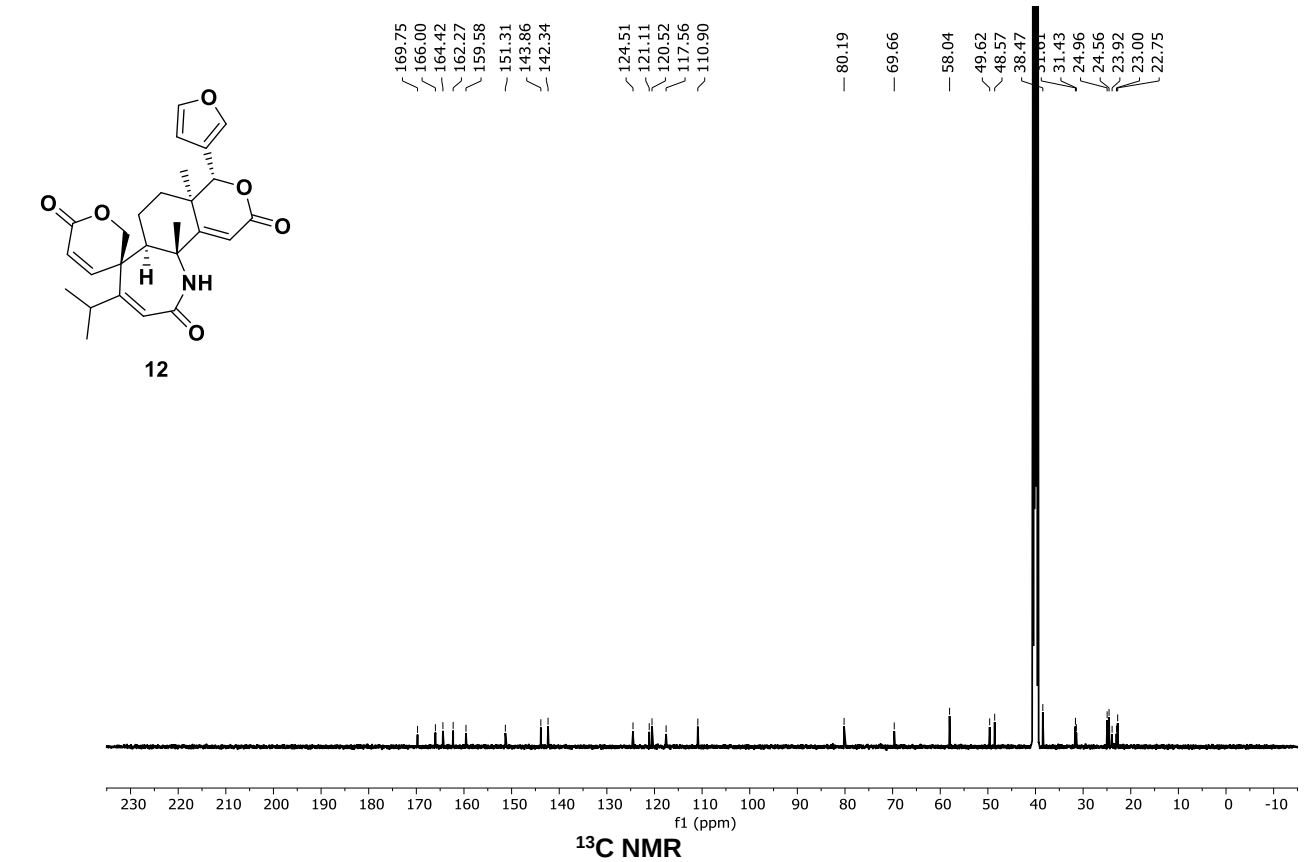


^{1}H-^{13}C HMBC NMR



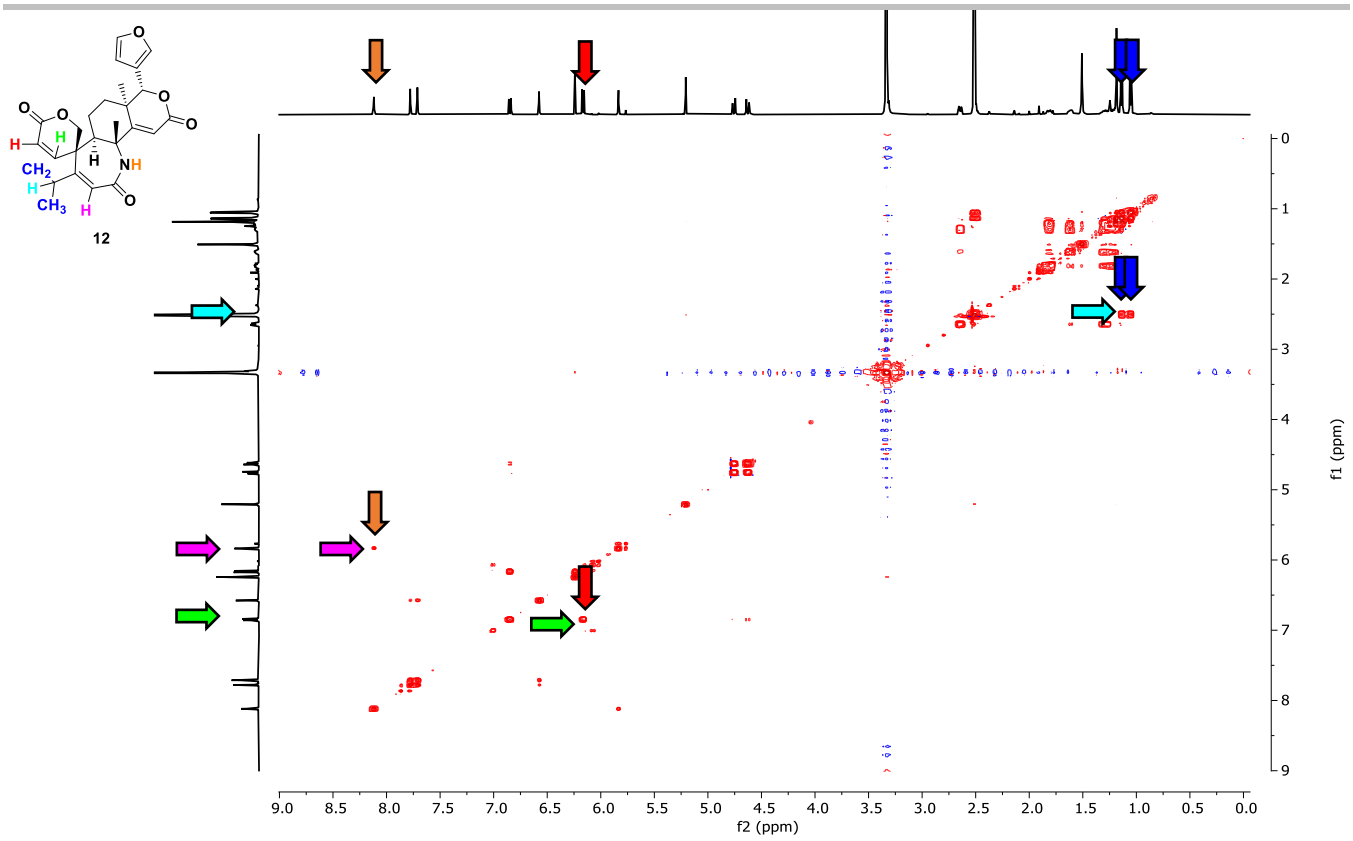
12

^{1}H NMR

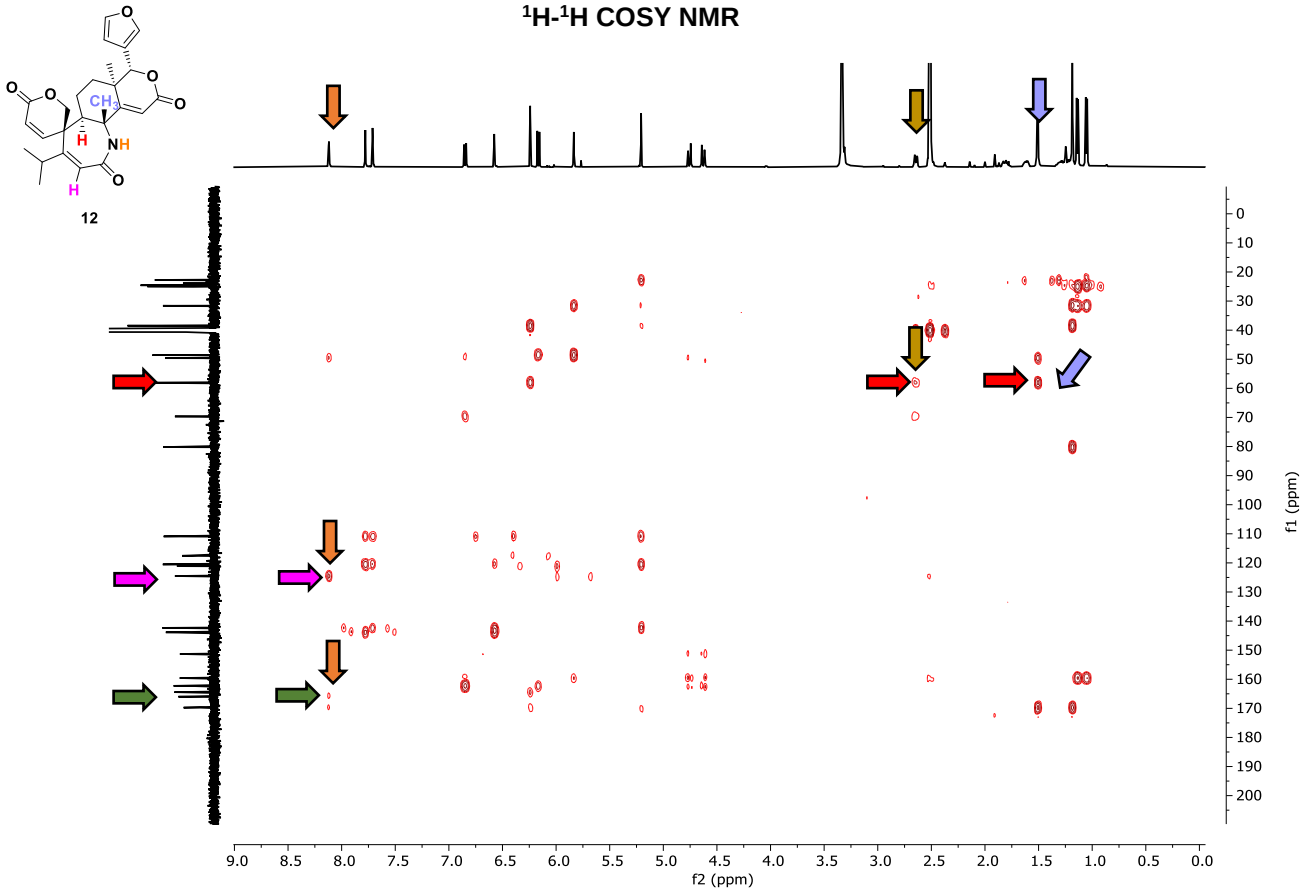


12

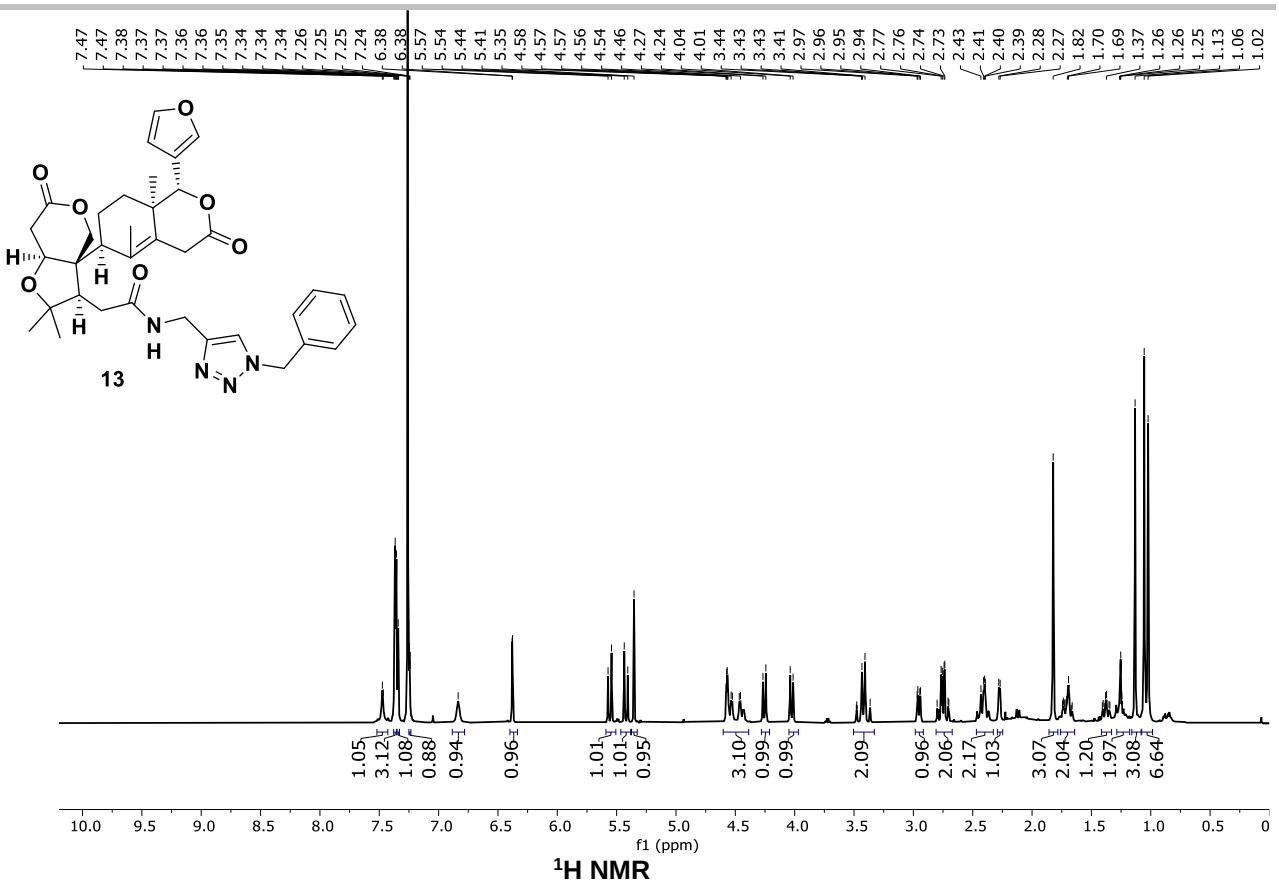
^{13}C NMR



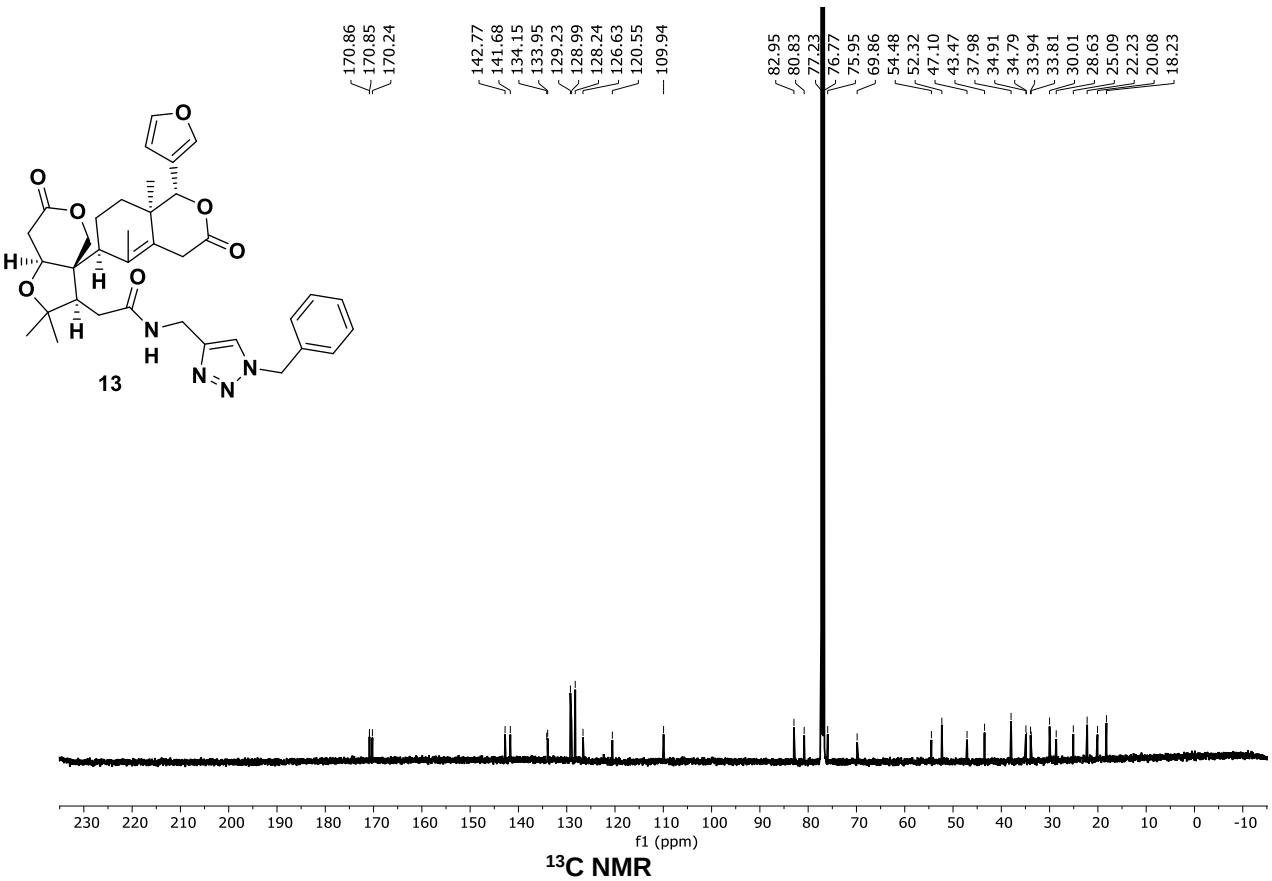
^{1}H-^{1}H COSY NMR



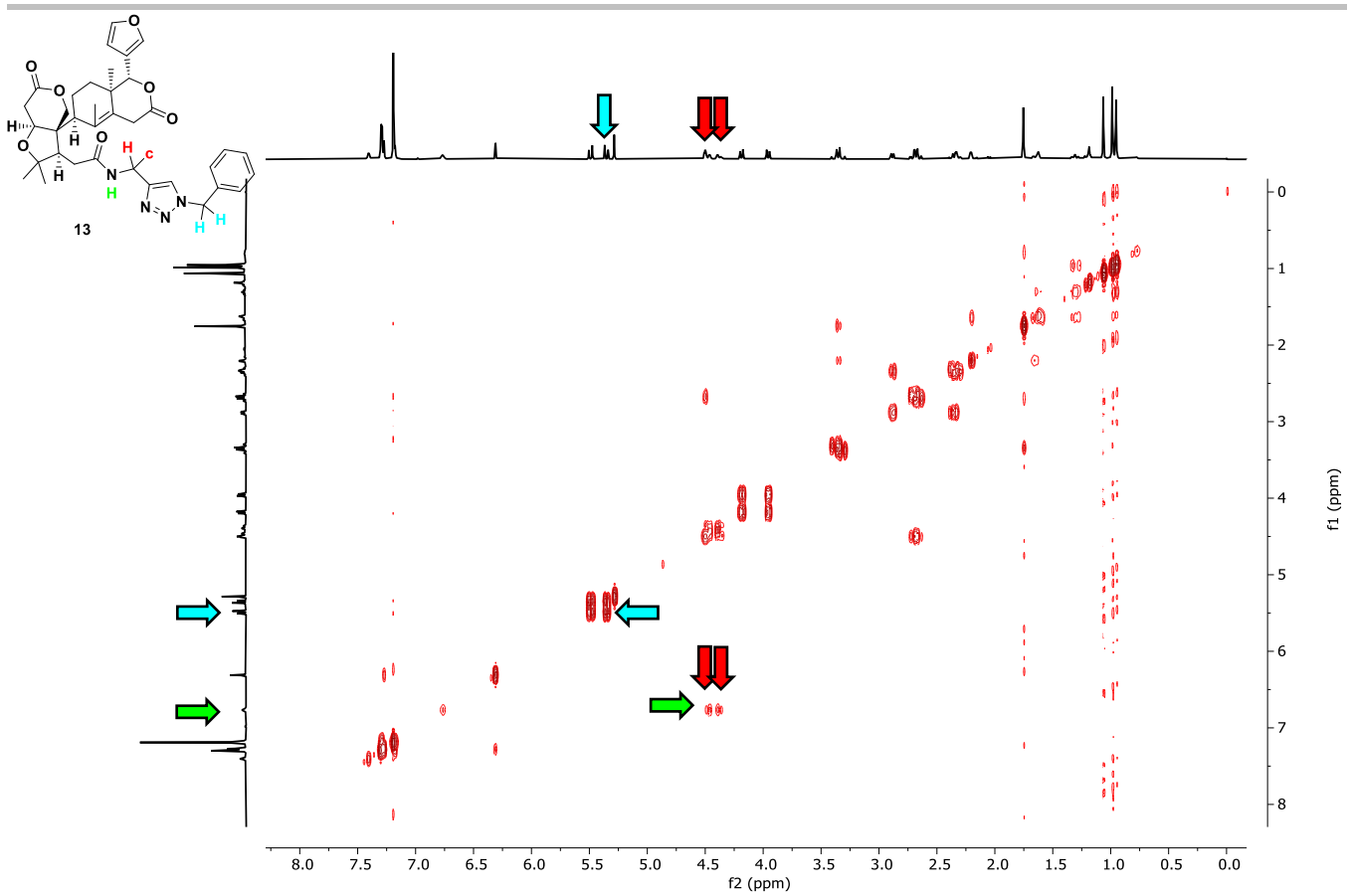
^{1}H-^{13}C HMBC NMR



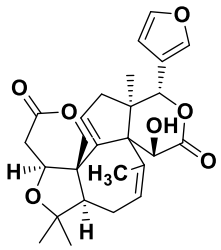
^{1}H NMR



^{13}C NMR

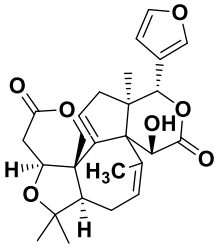


^{1}H-^{1}H COSY NMR



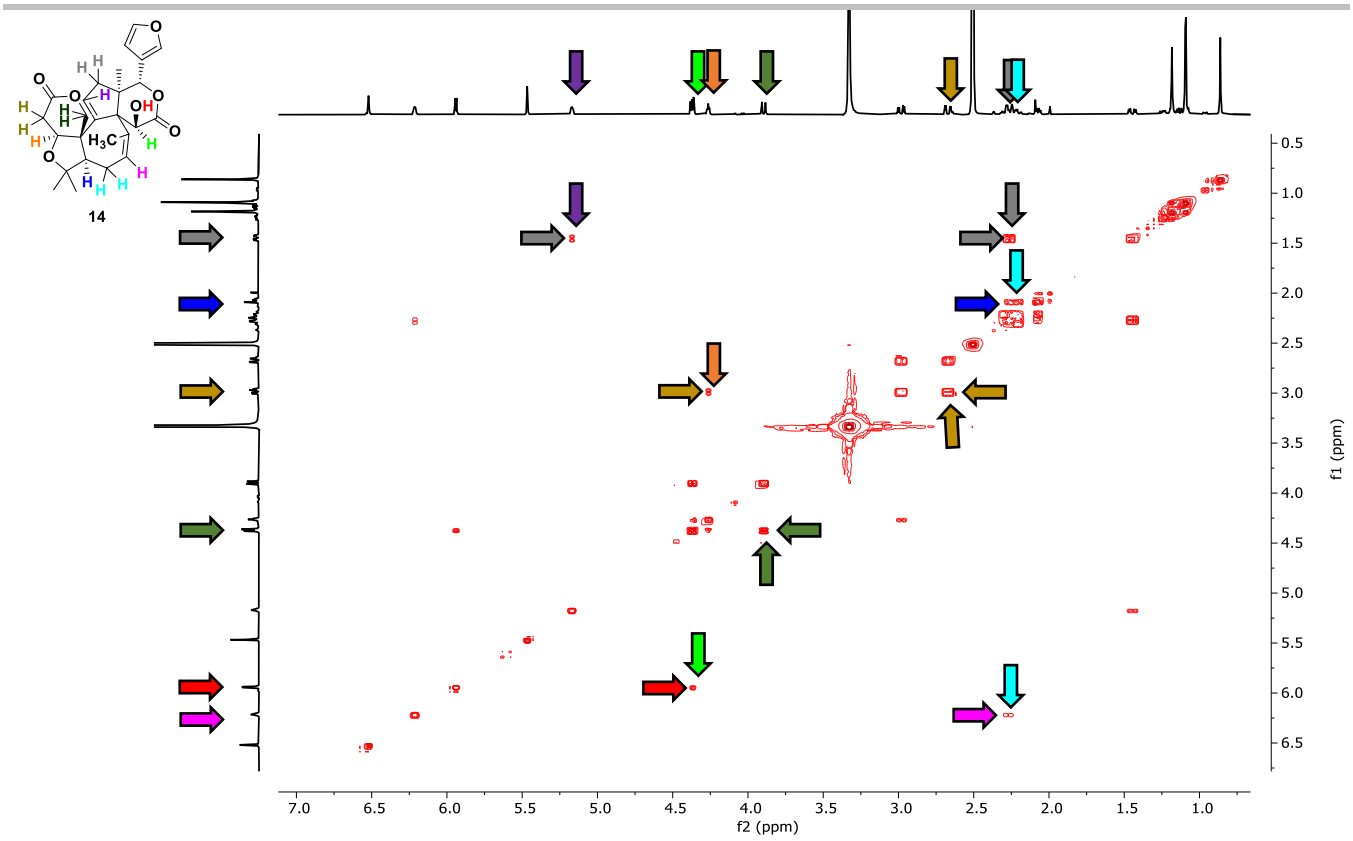
14

^{1}H NMR

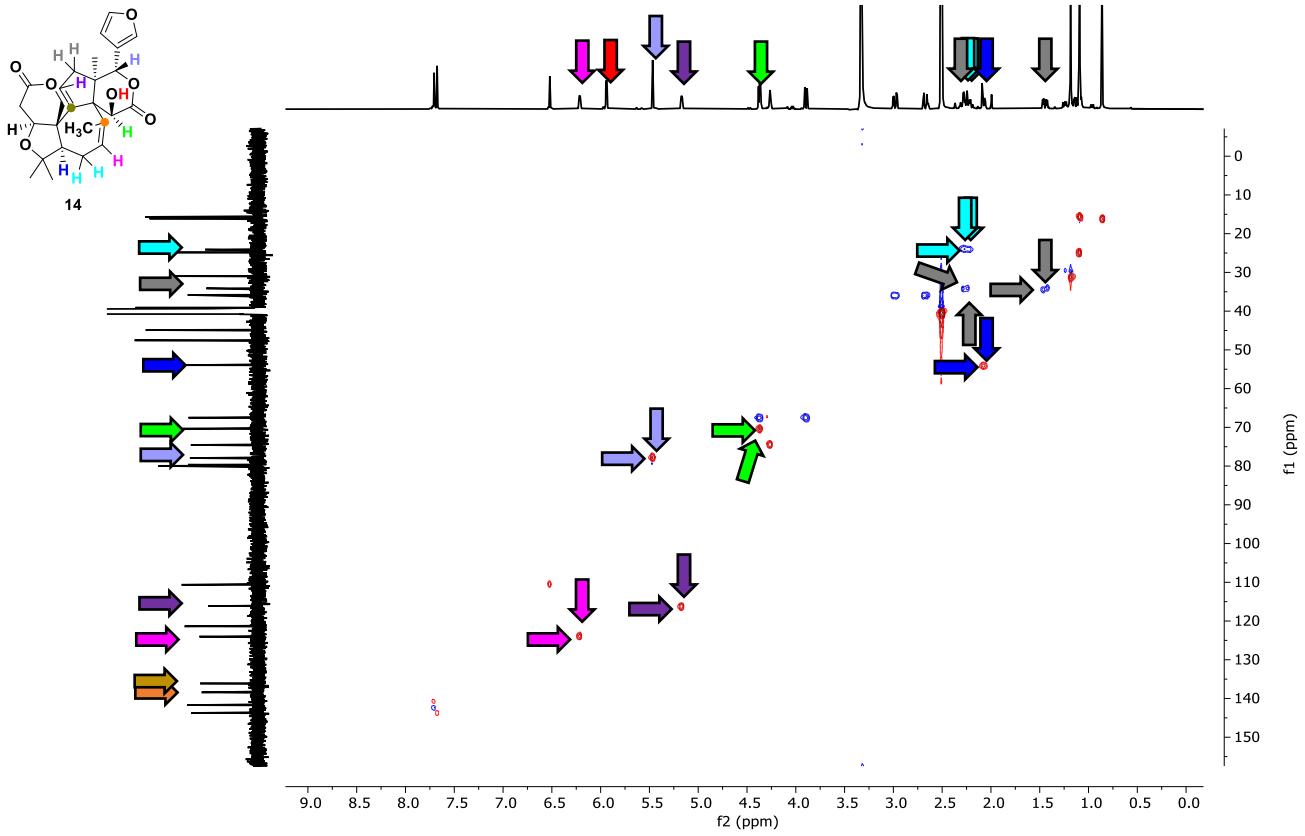


14

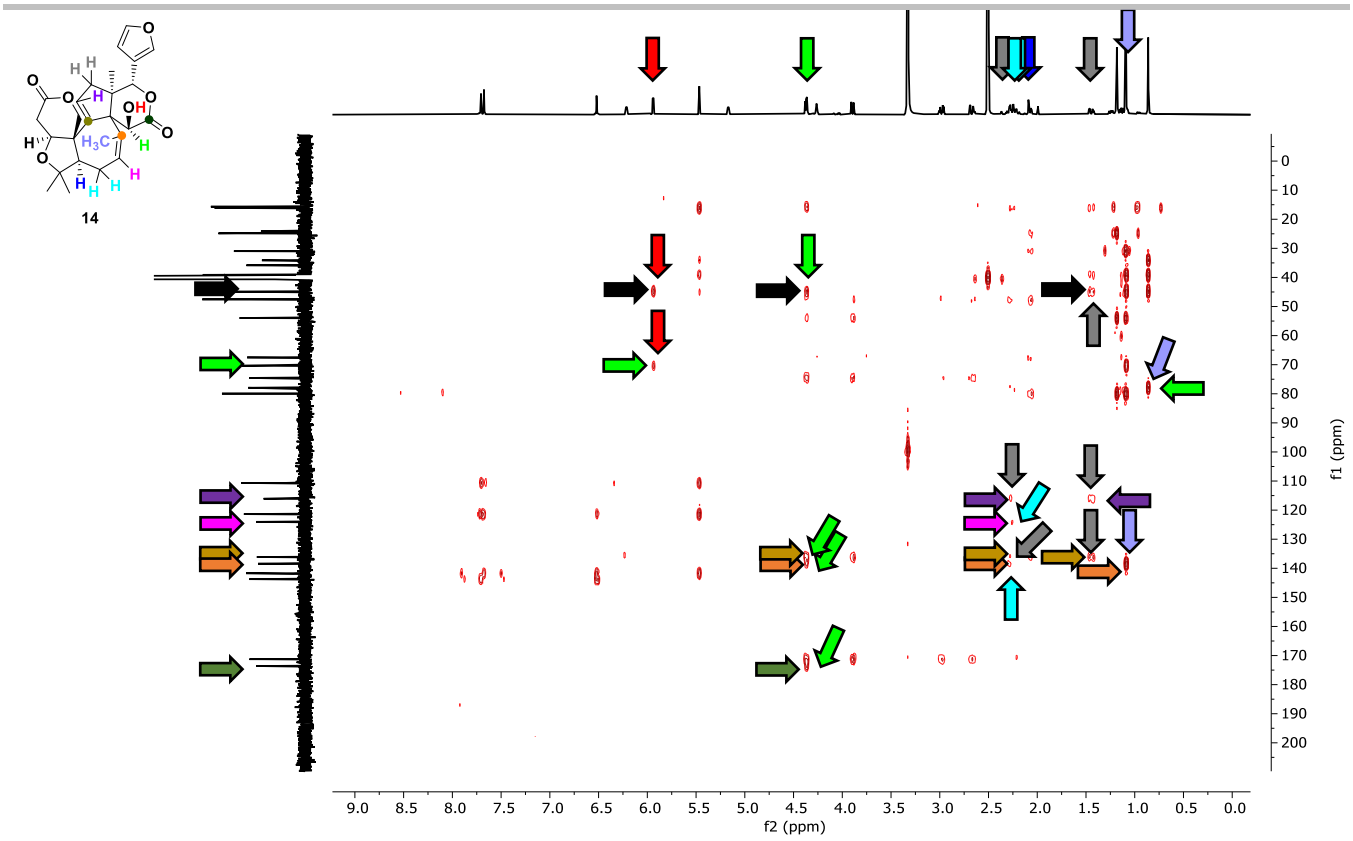
^{13}C NMR



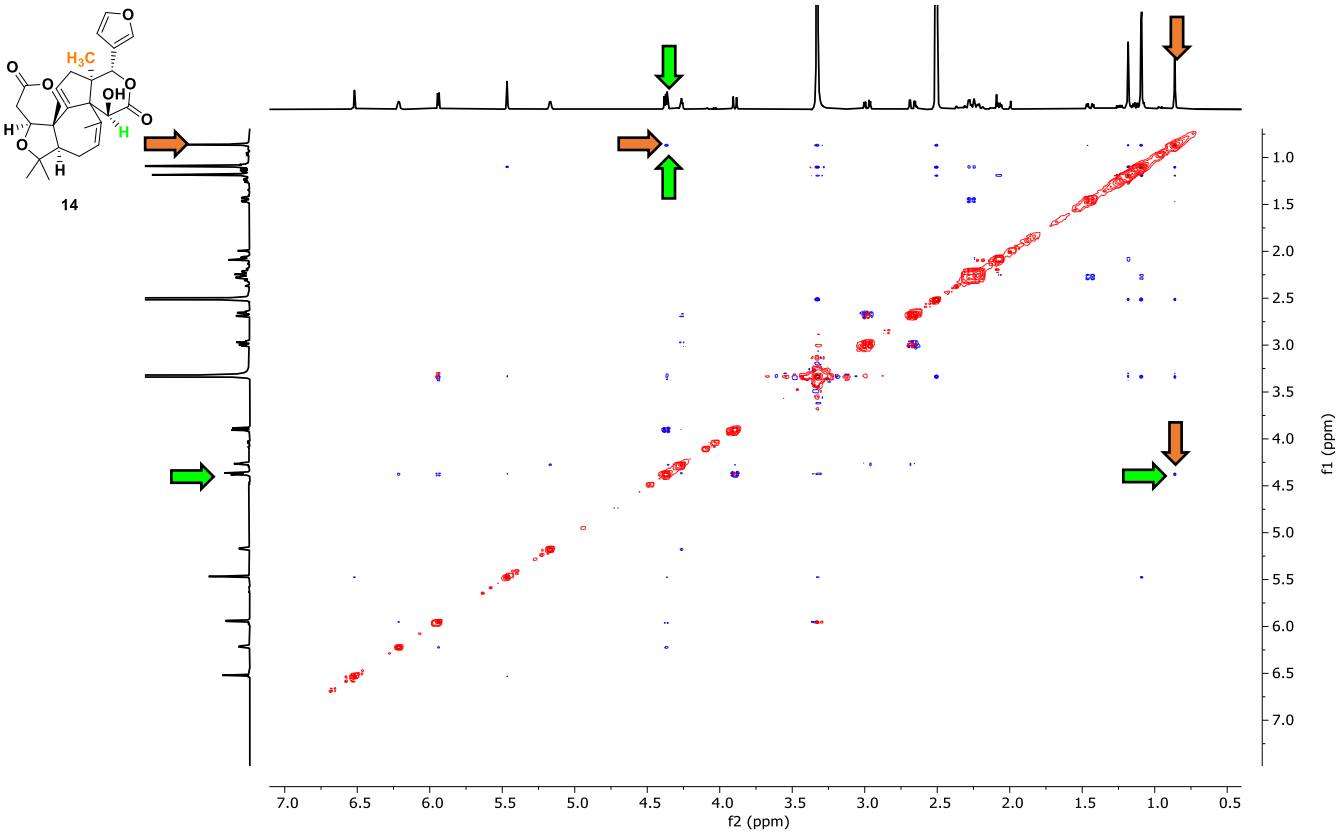
^{1}H-^{1}H COSY NMR



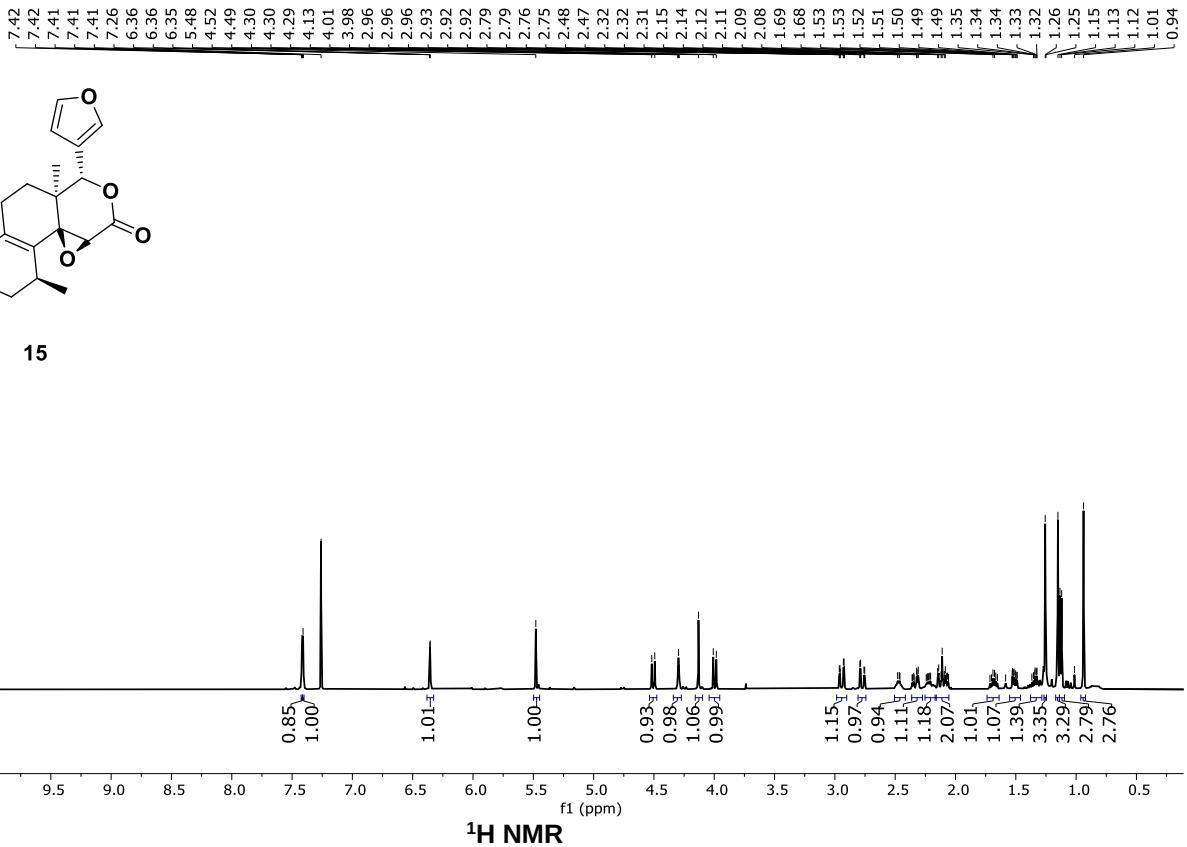
^{1}H-^{13}C HSQC NMR



^{1}H-^{13}C HMBC NMR

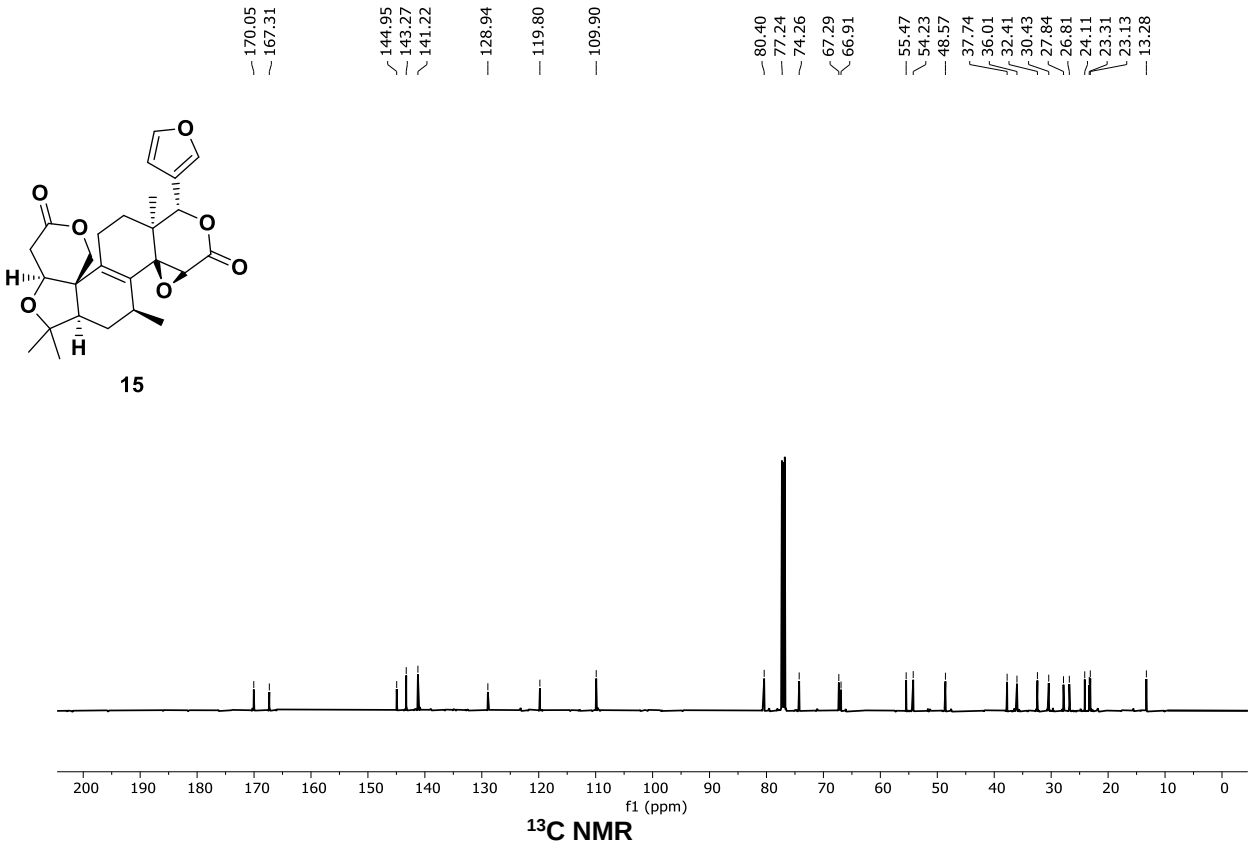


^{1}H-^{1}H NOESY NMR



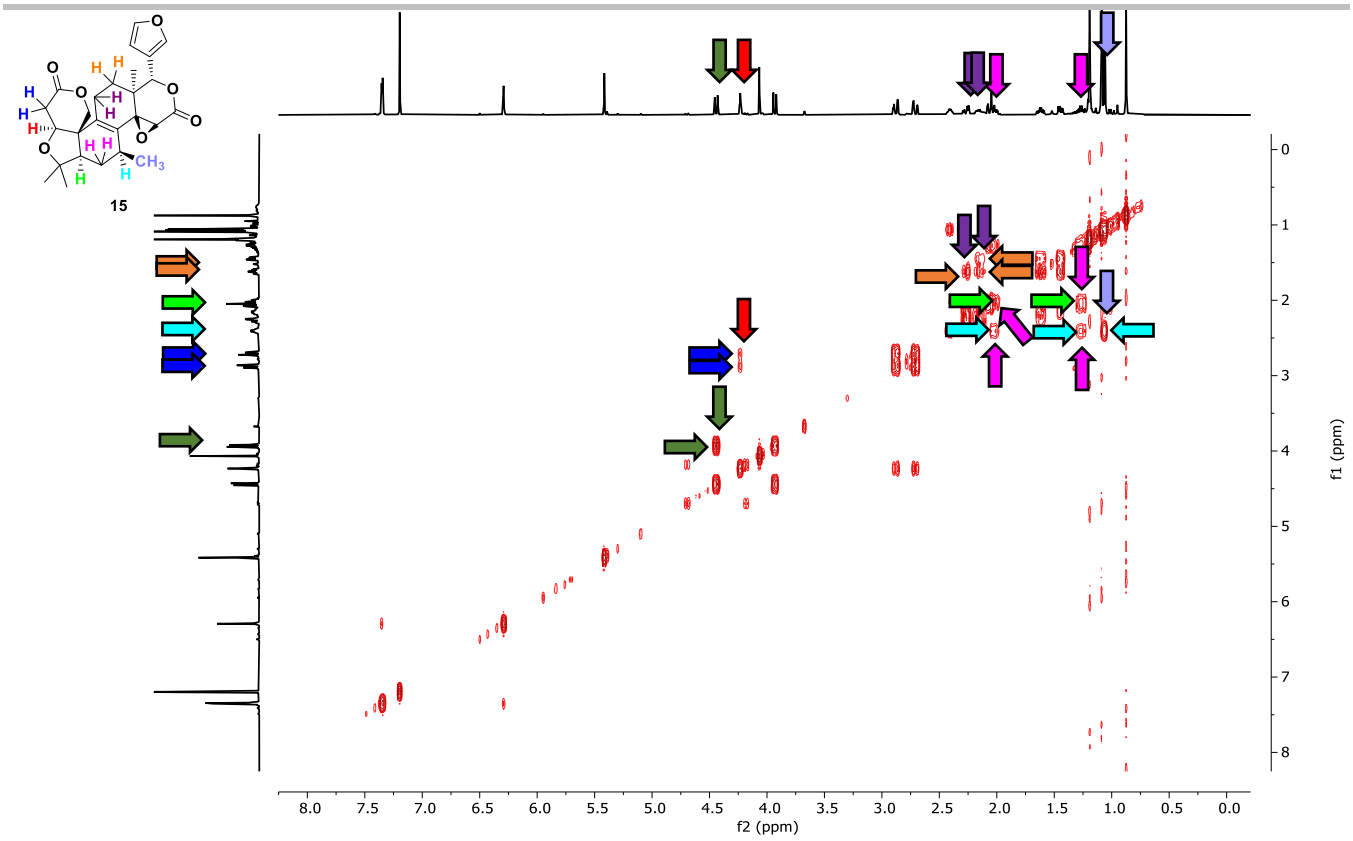
15

^{1}H NMR

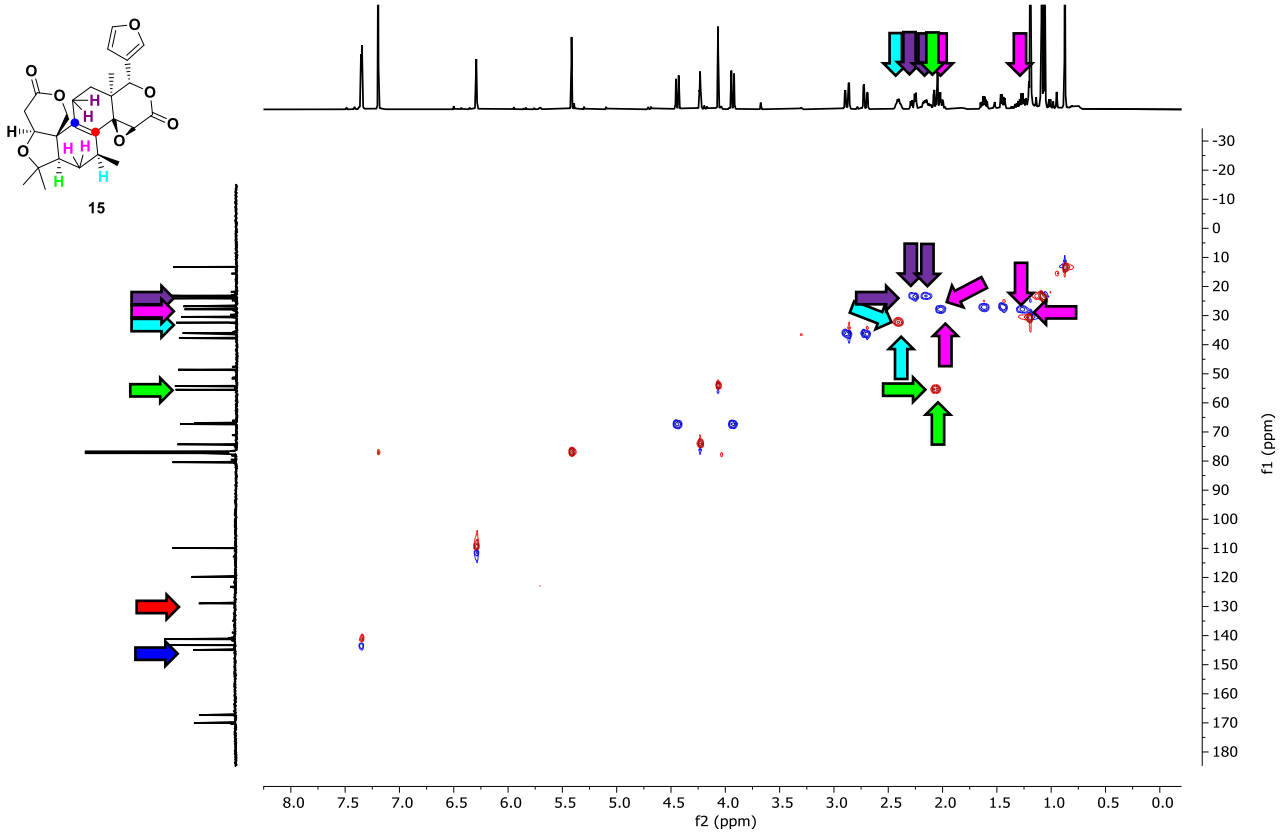


15

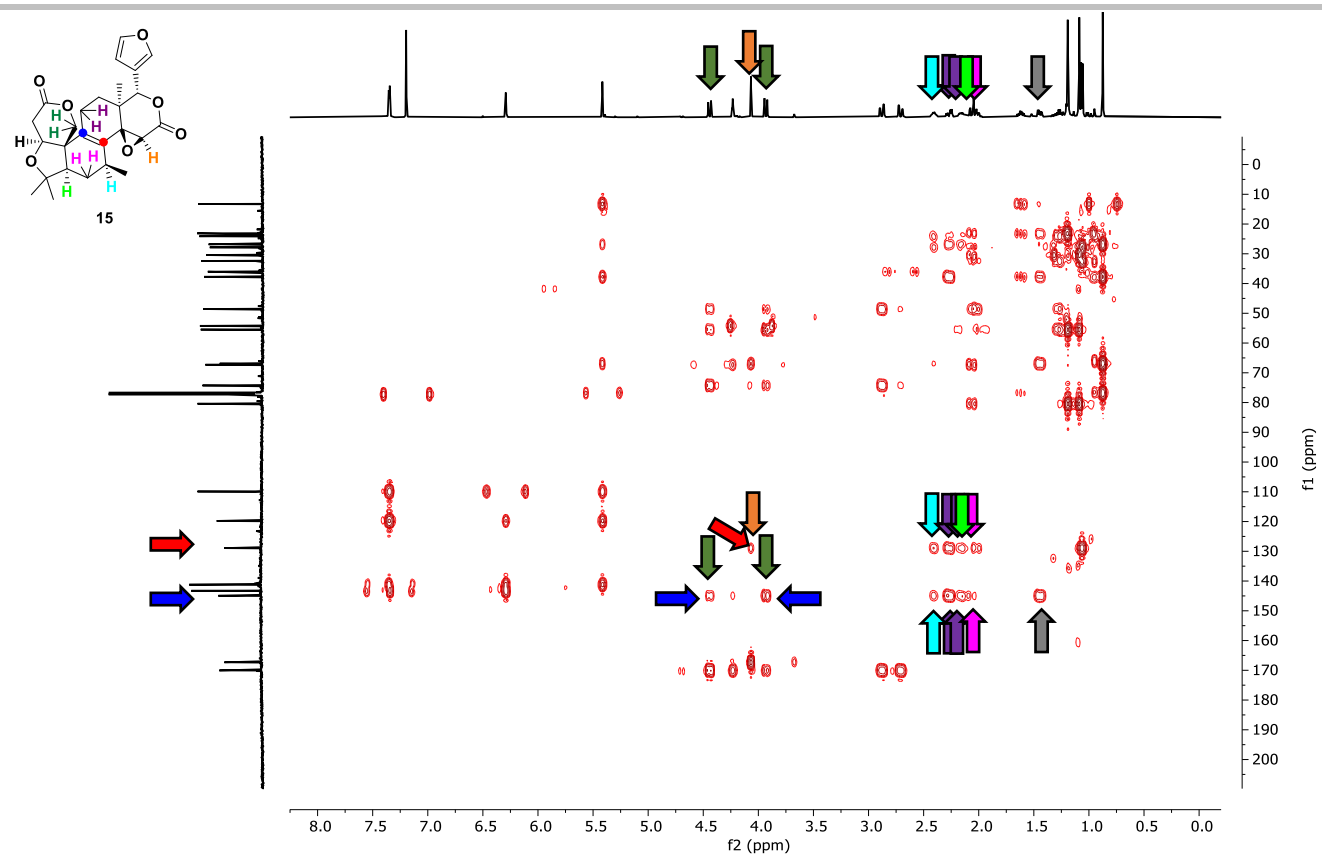
^{13}C NMR



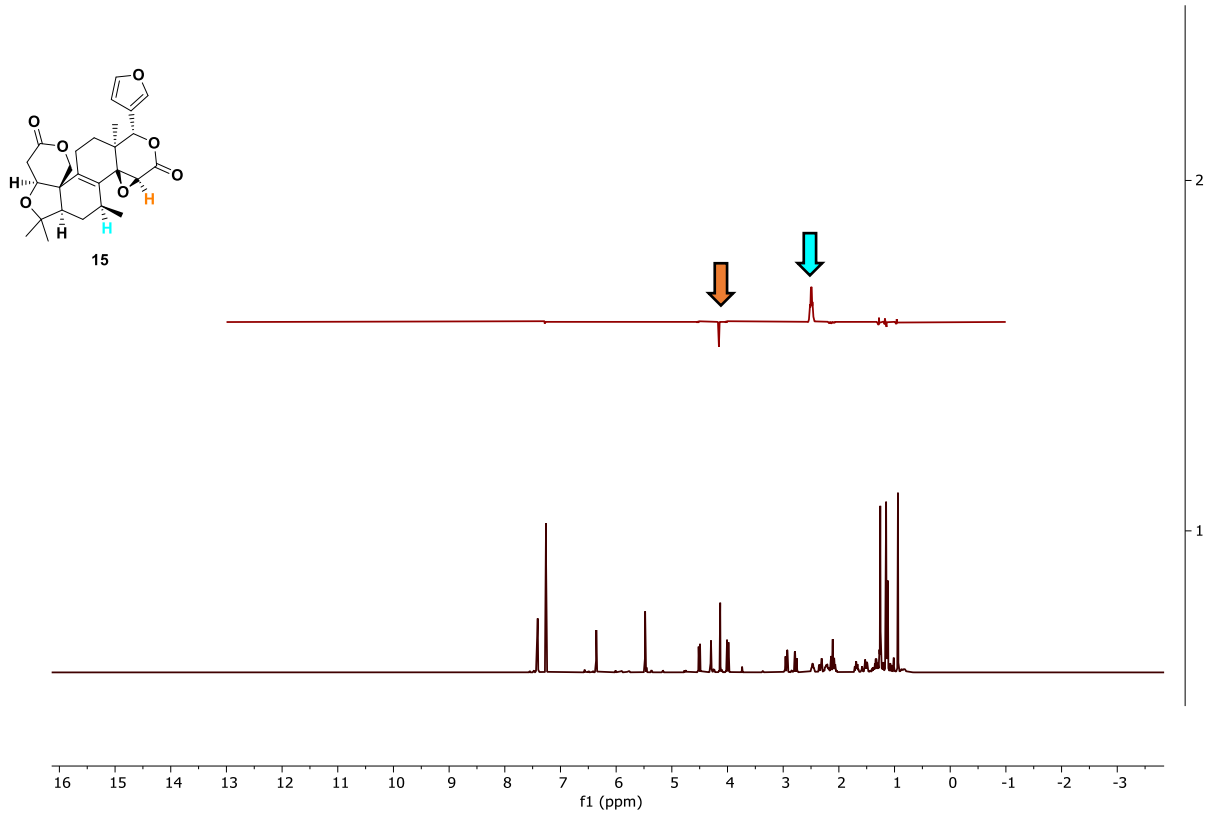
^{1}H-^{1}H COSY NMR



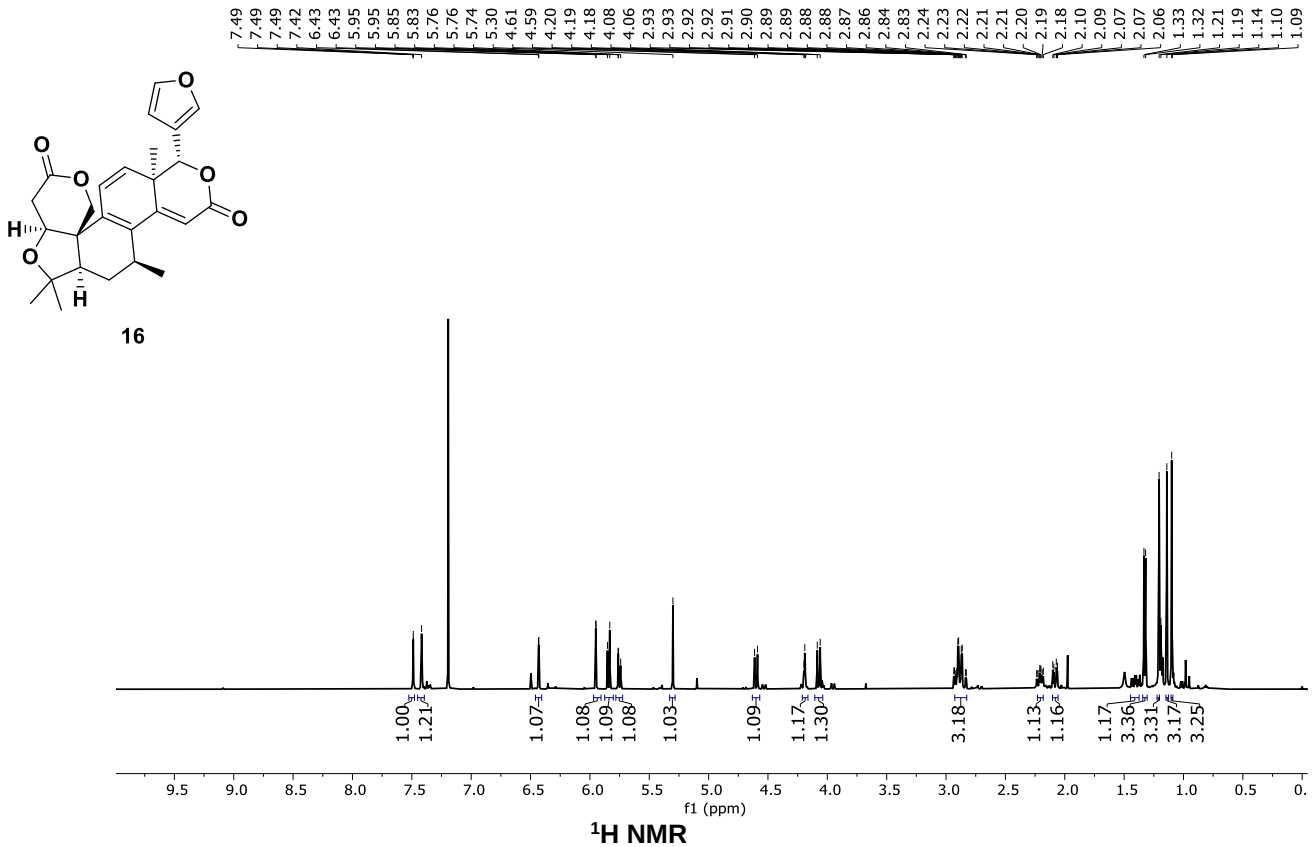
^{1}H-^{1}H HSQC NMR



^{1}H-^{13}C HMBC NMR

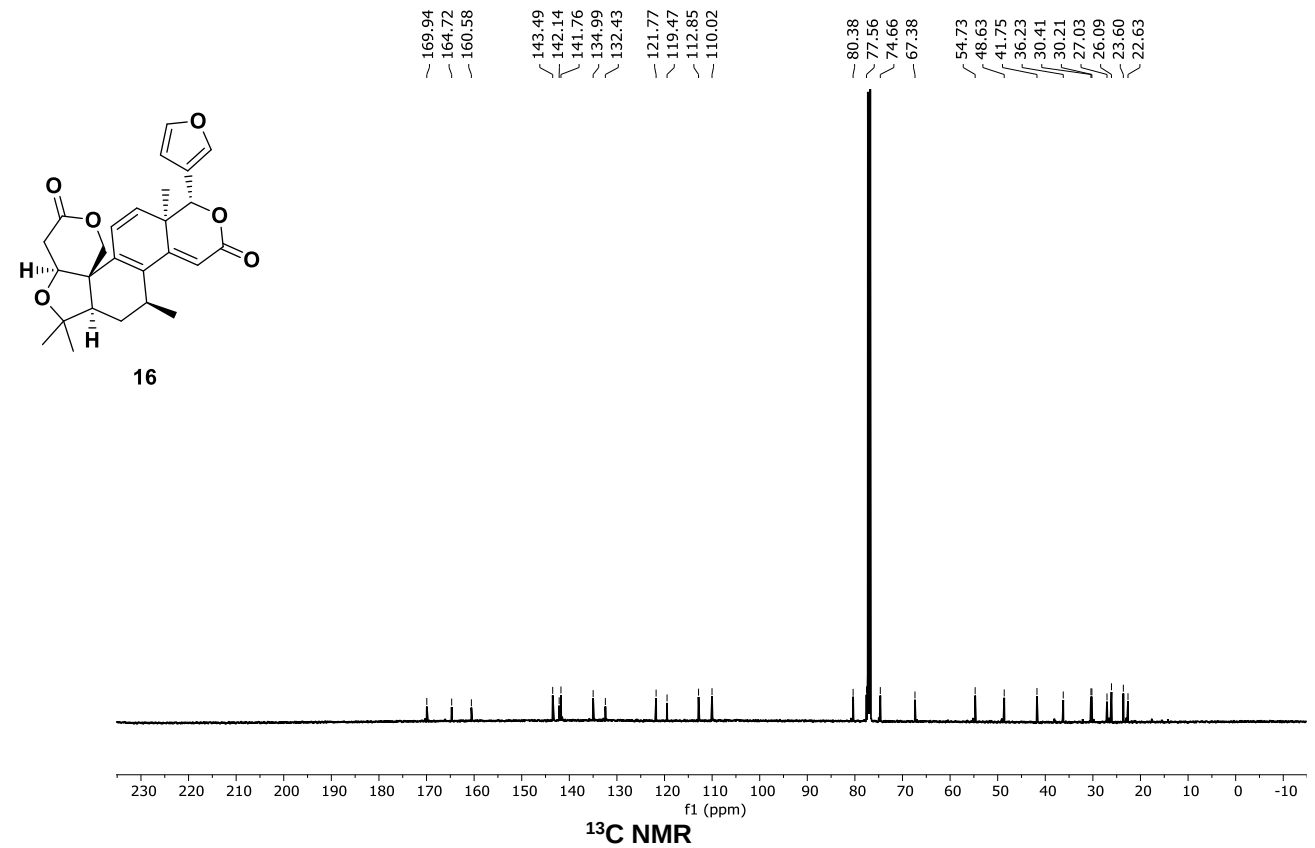


^{1}H-^{1}H NOESY 1D NMR



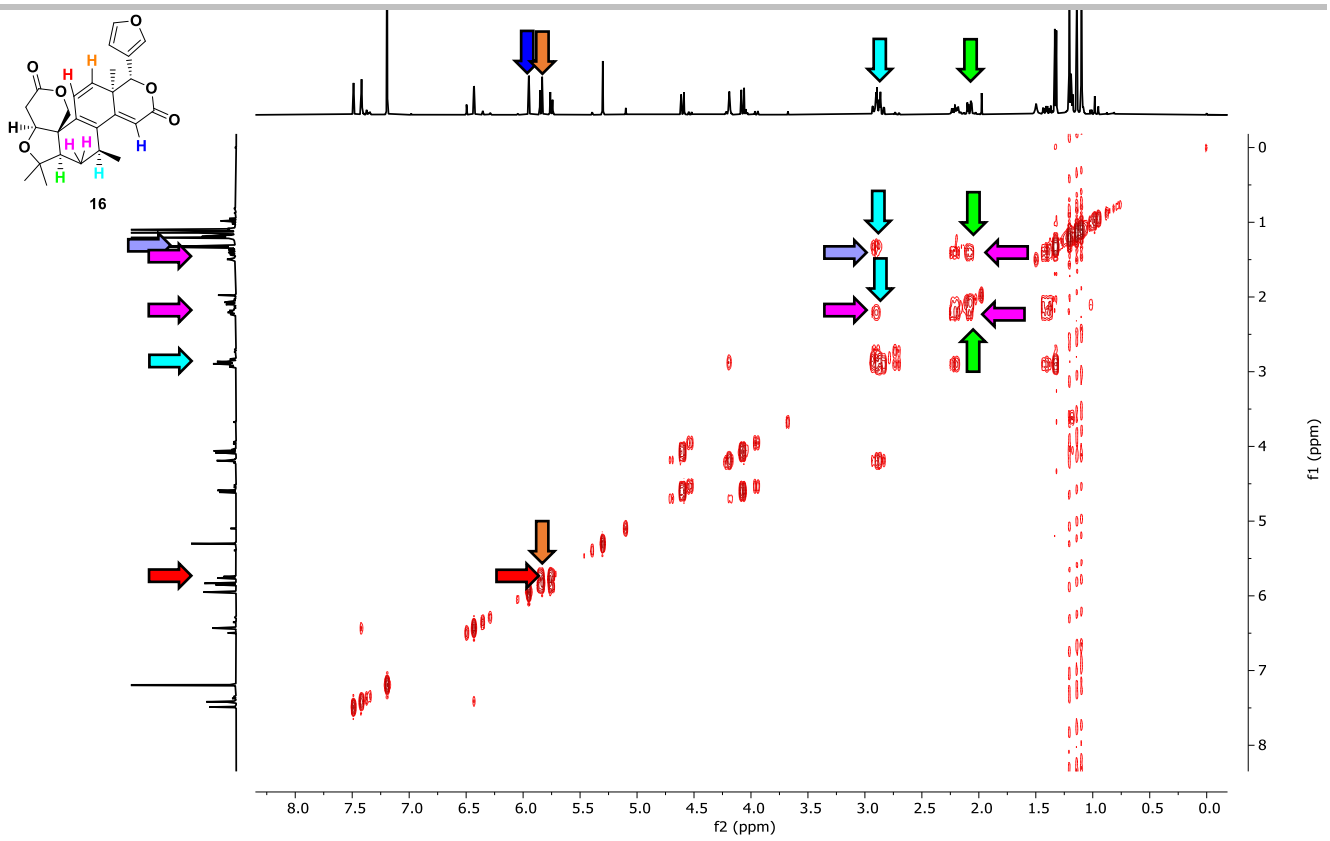
16

^{1}H NMR

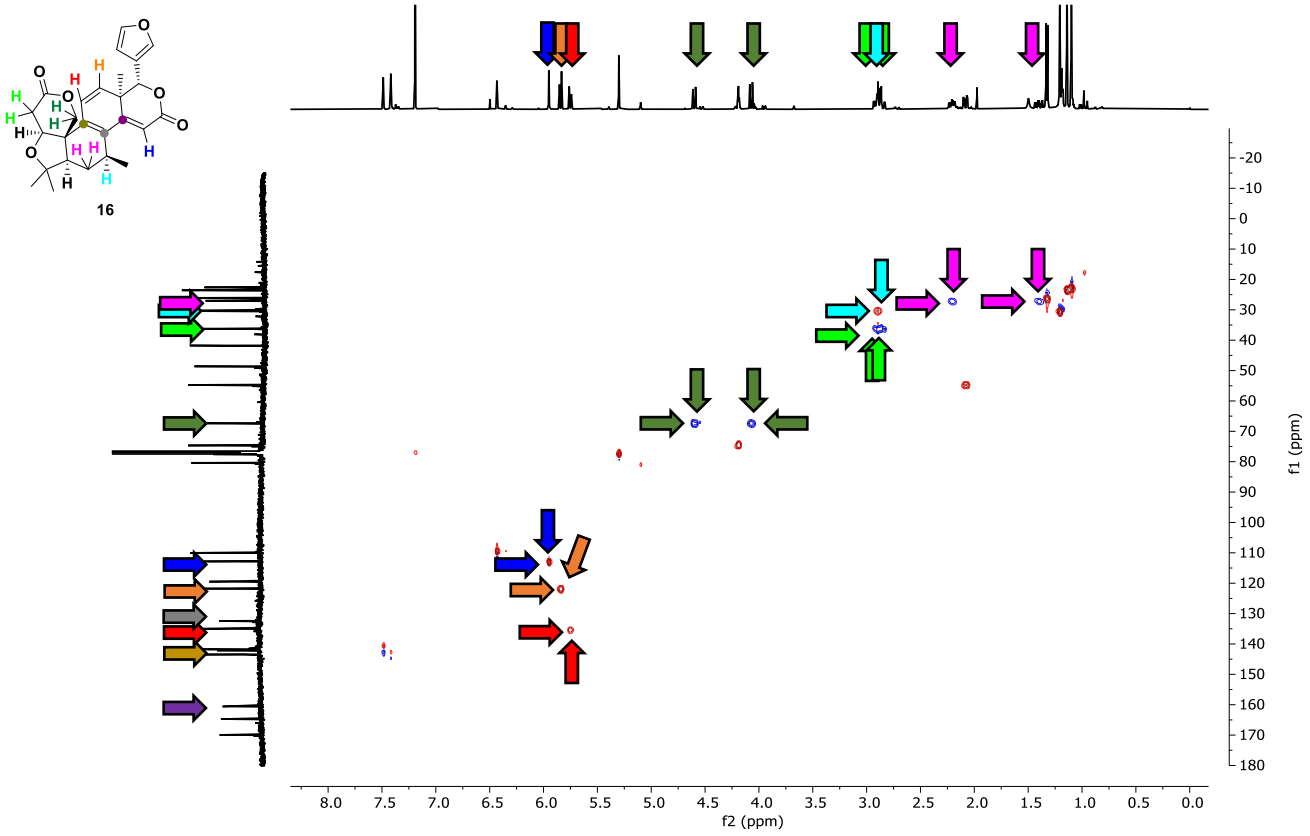


16

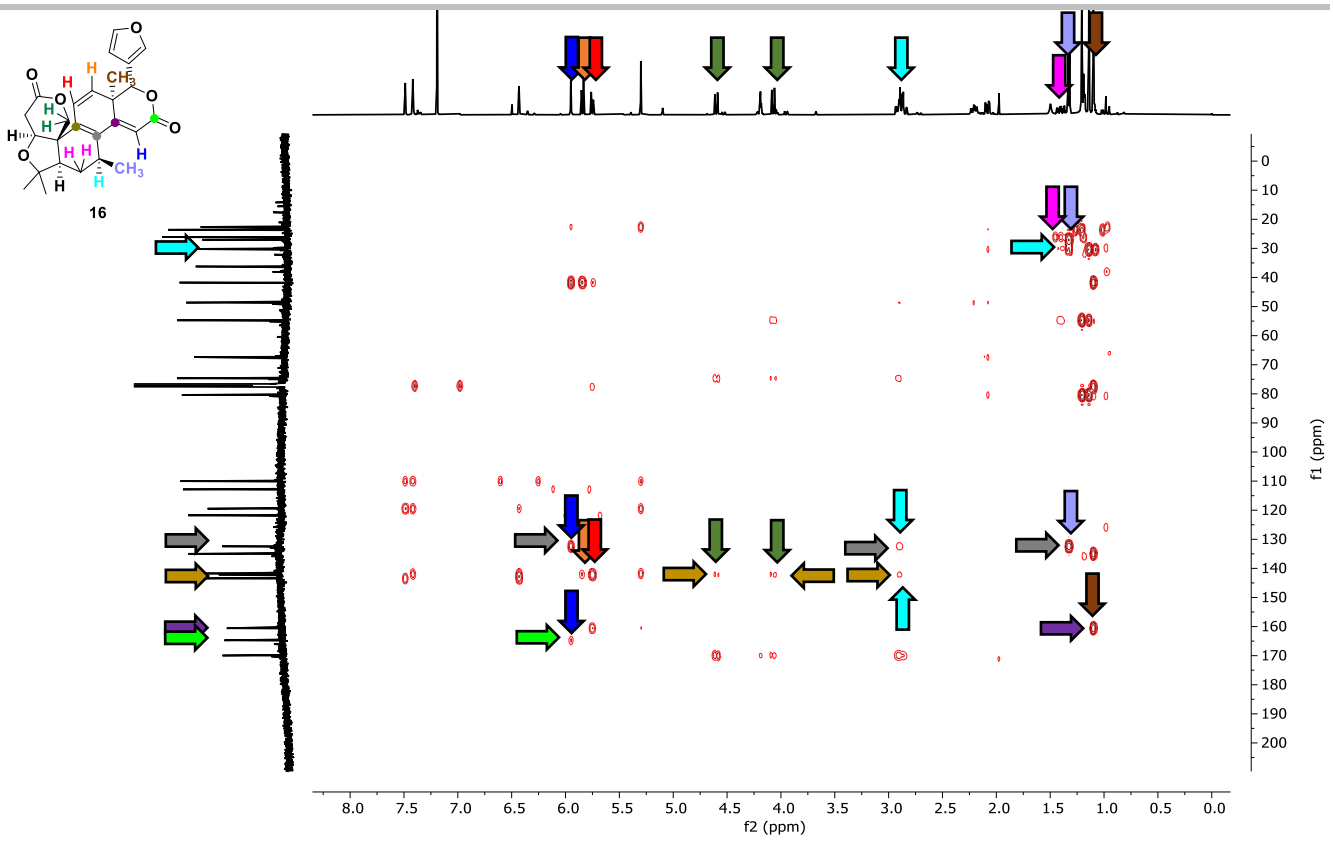
^{13}C NMR



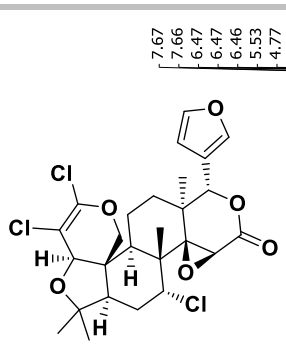
^{1}H-^{1}H COSY NMR



^{1}H-^{13}C HSQC NMR

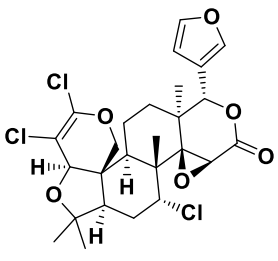


^{1}H-^{13}C HMBC NMR



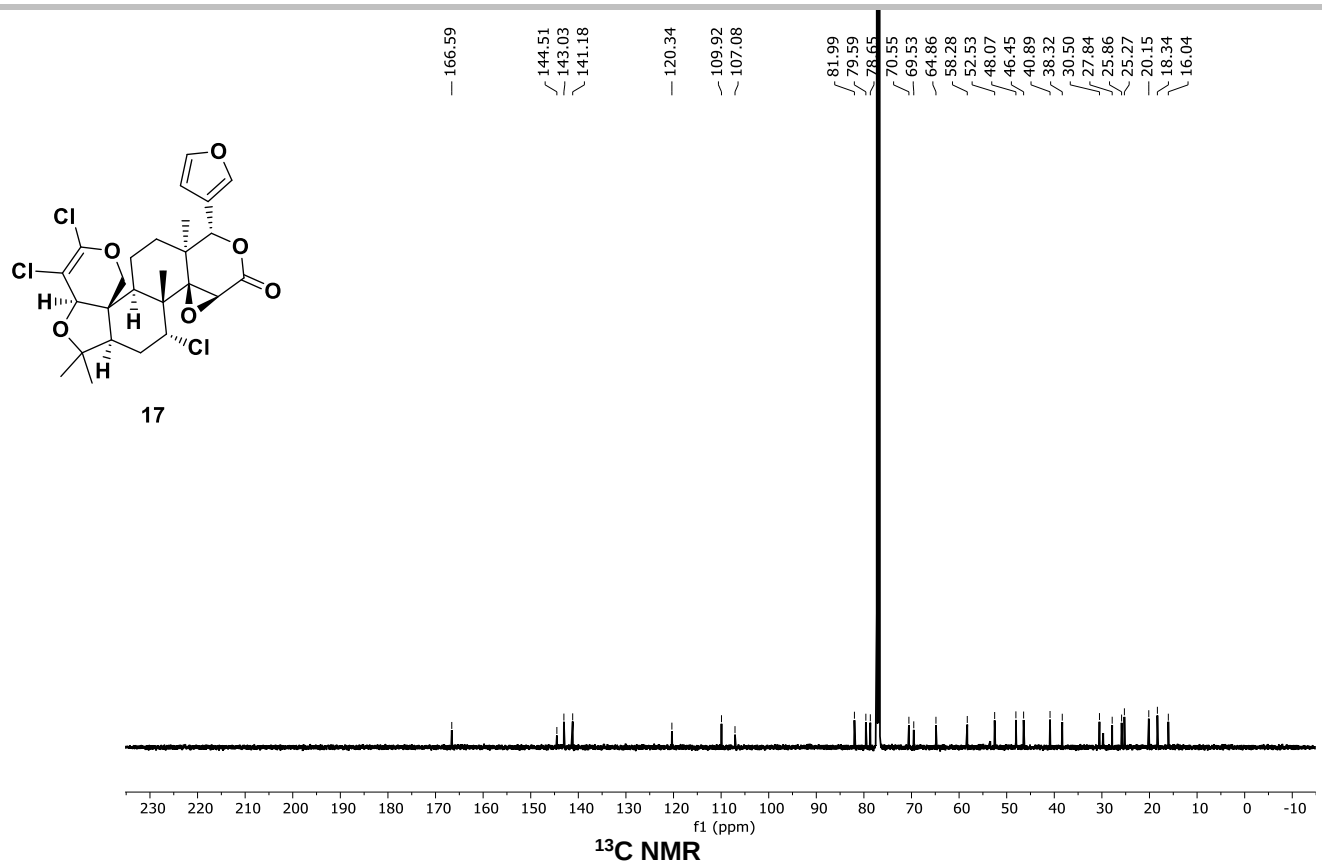
17

^{1}H NMR (DMSO-d6)



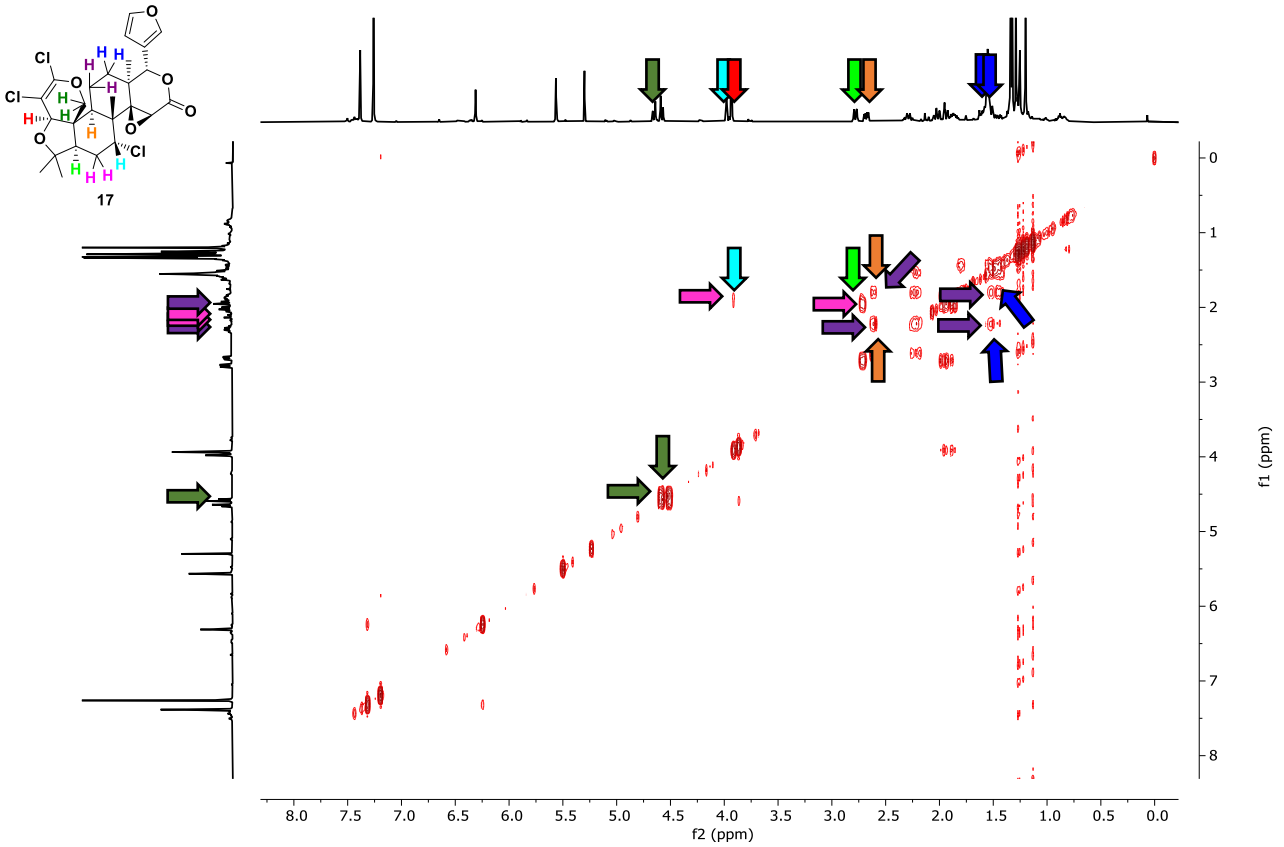
17

^{1}H NMR ($CDCl_3$)



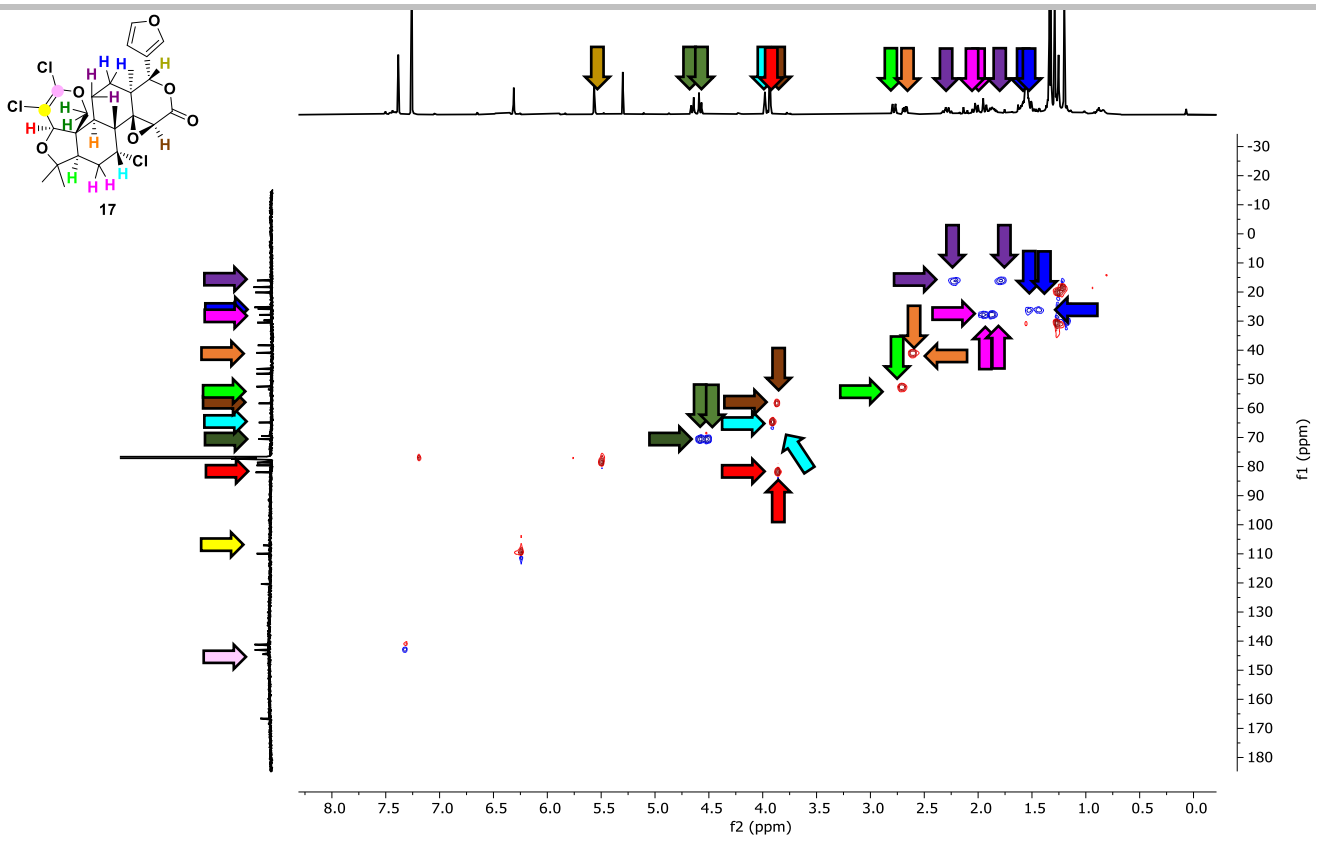
17

^{13}C NMR

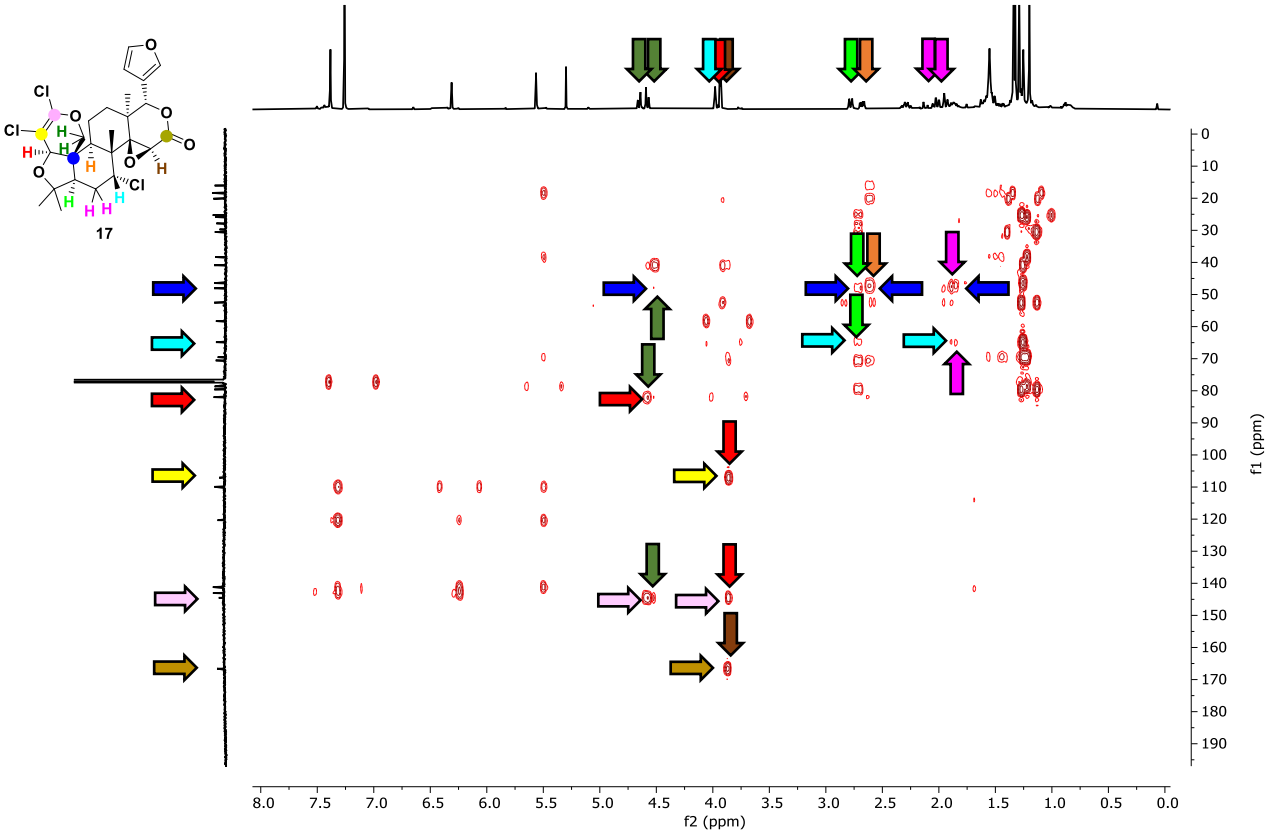


17

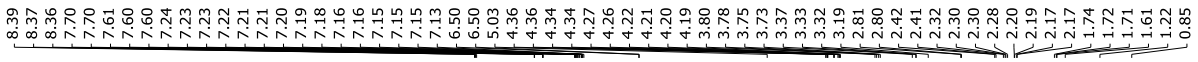
^{1}H-^{1}H COSY NMR

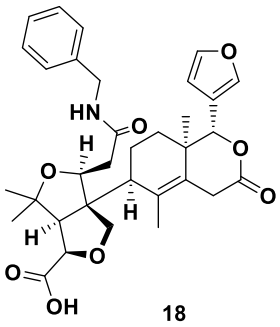


^{1}H-^{13}C HSQC NMR

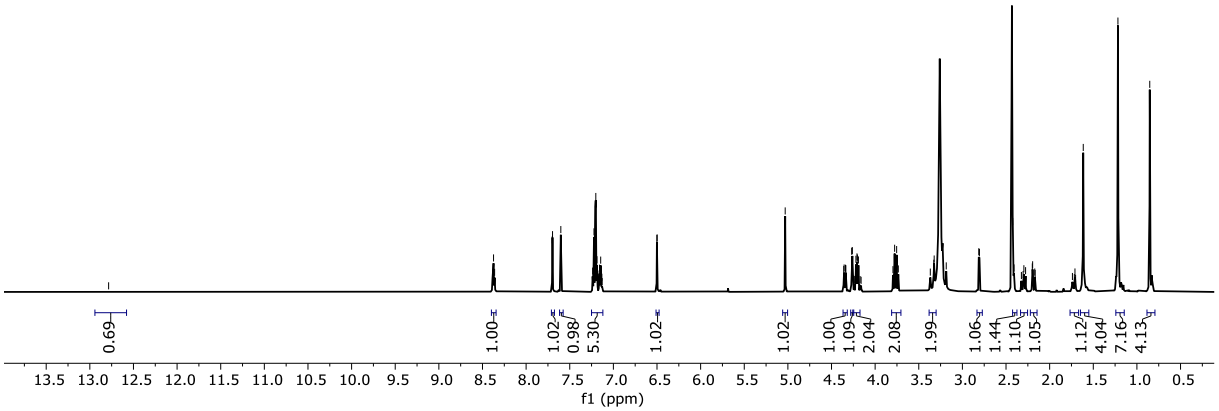


^{1}H-^{13}C HMBC NMR

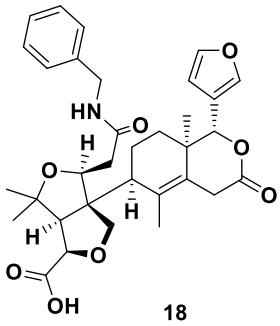




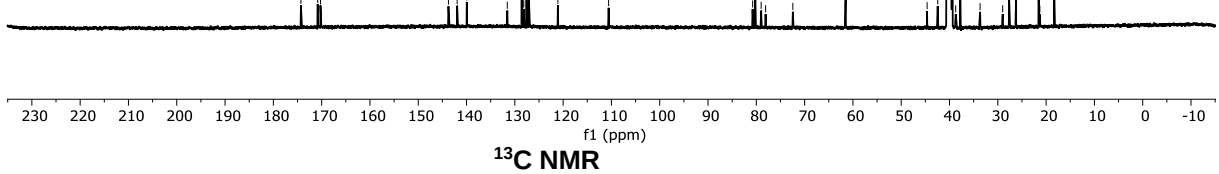
18



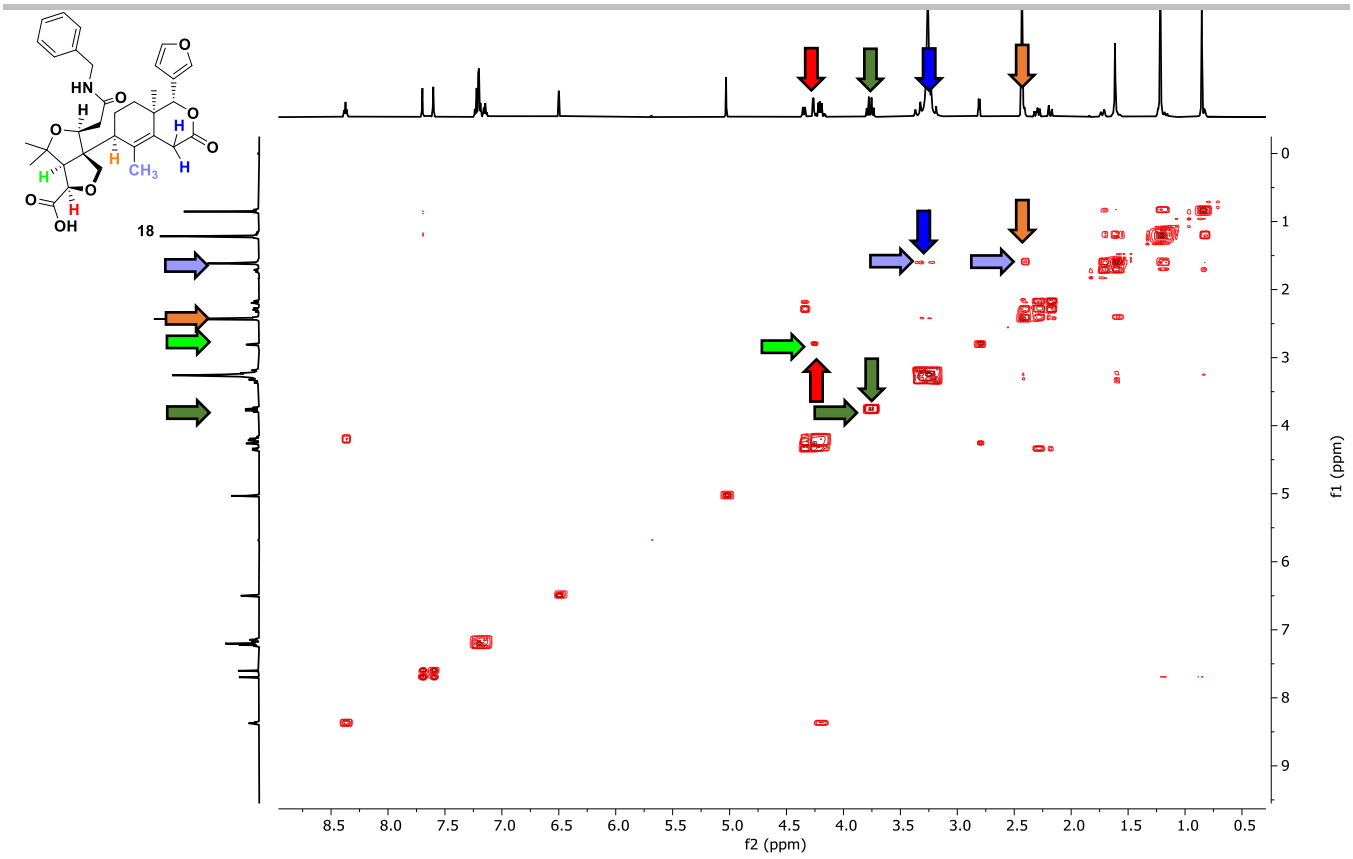
^{1}H NMR



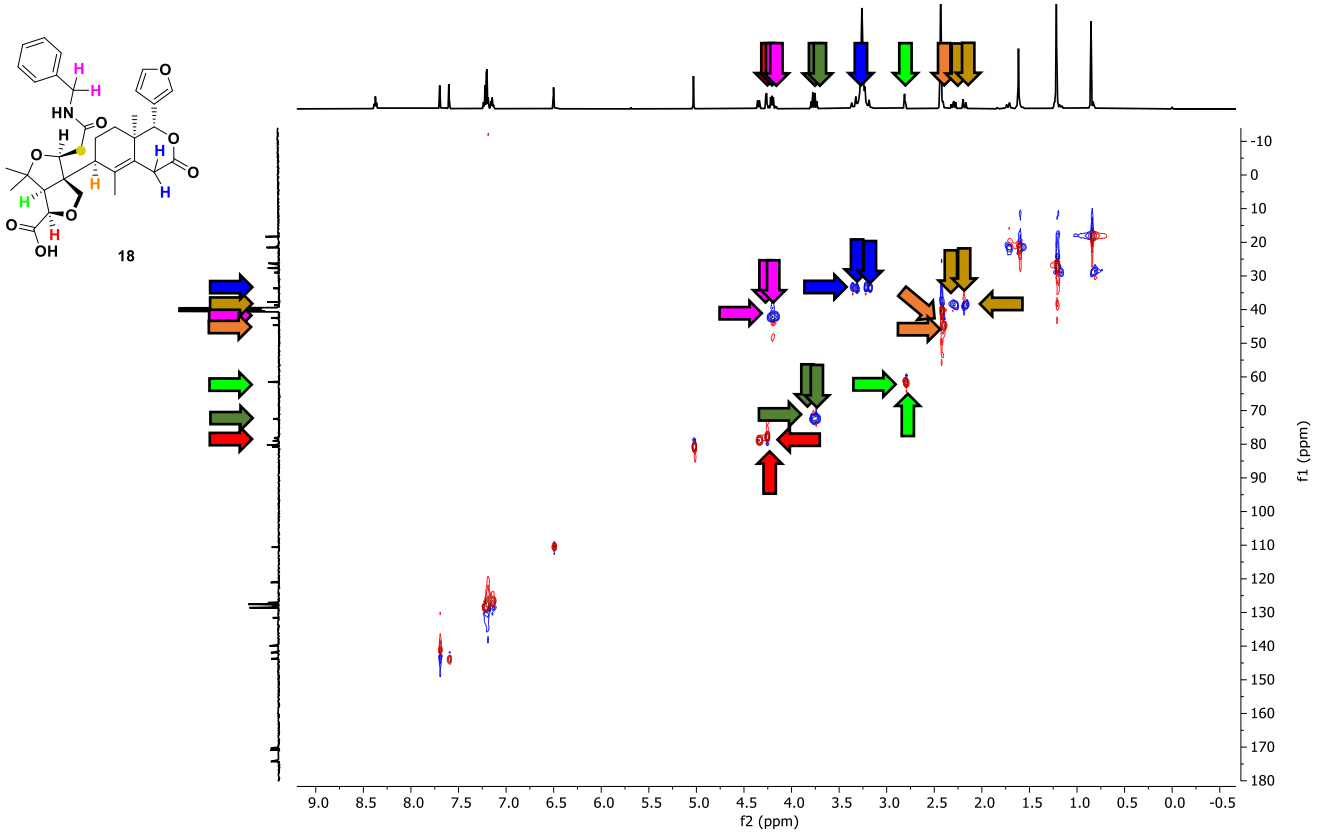
18



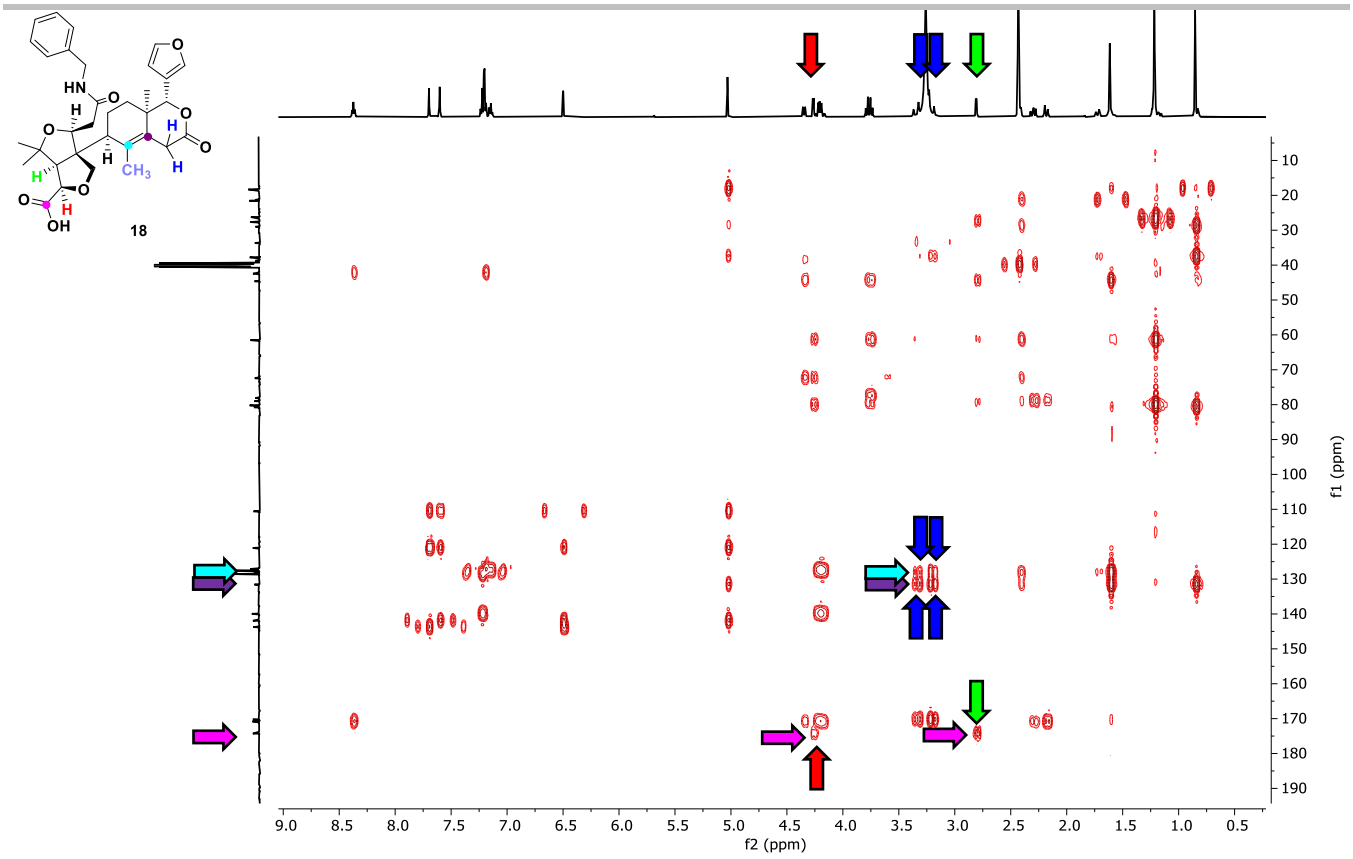
^{13}C NMR



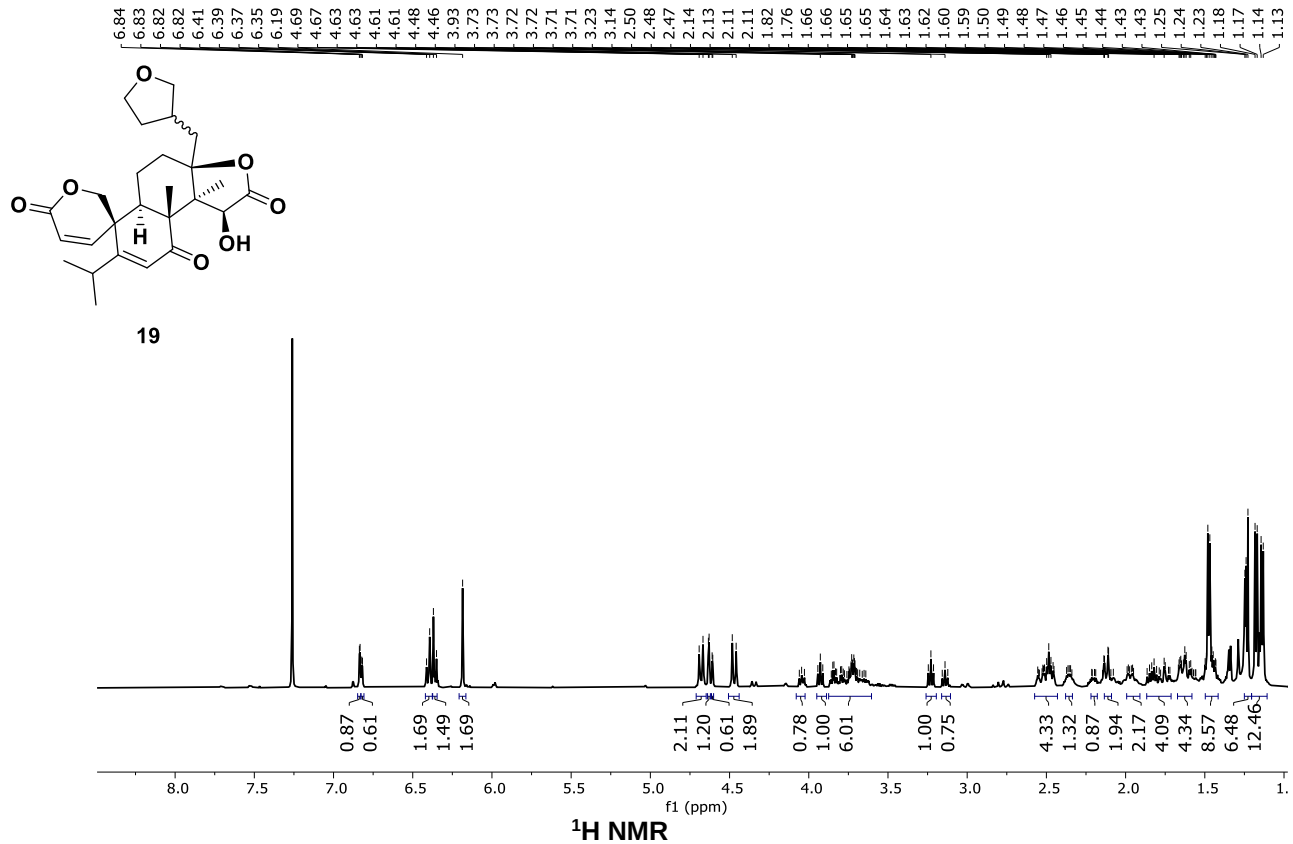
^{1}H-^{1}H COSY NMR



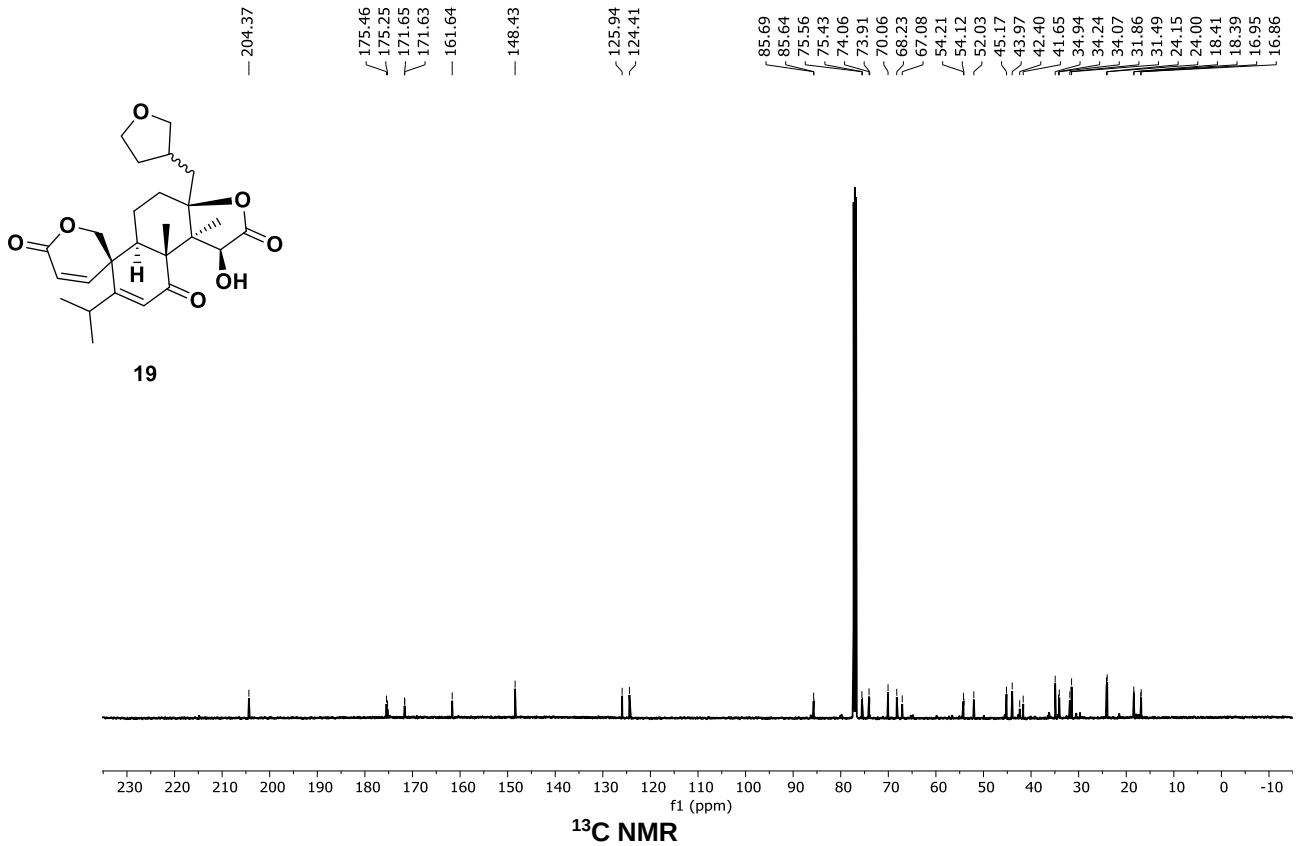
^{1}H-^{13}C HSQC NMR



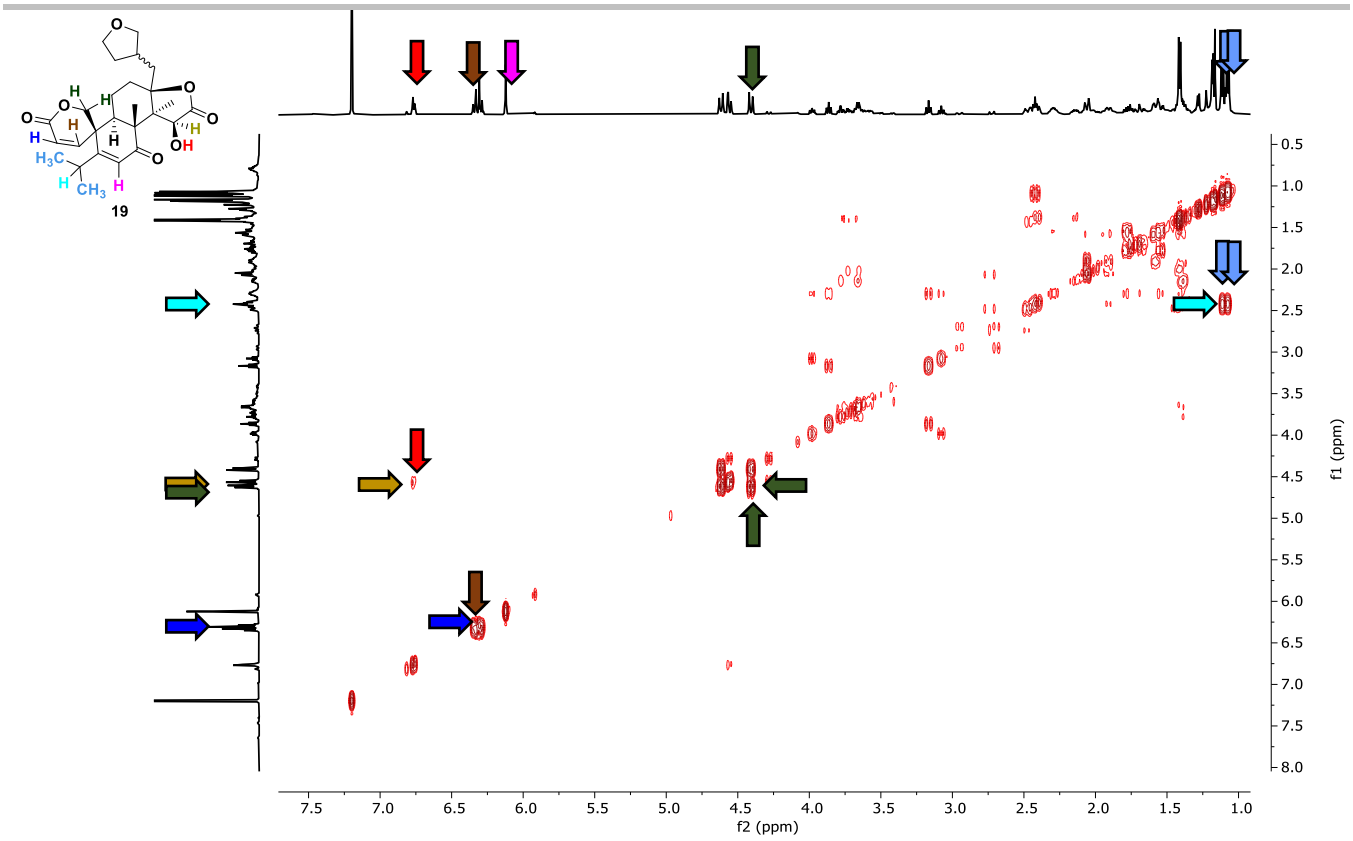
^{1}H-^{13}C HMBC NMR



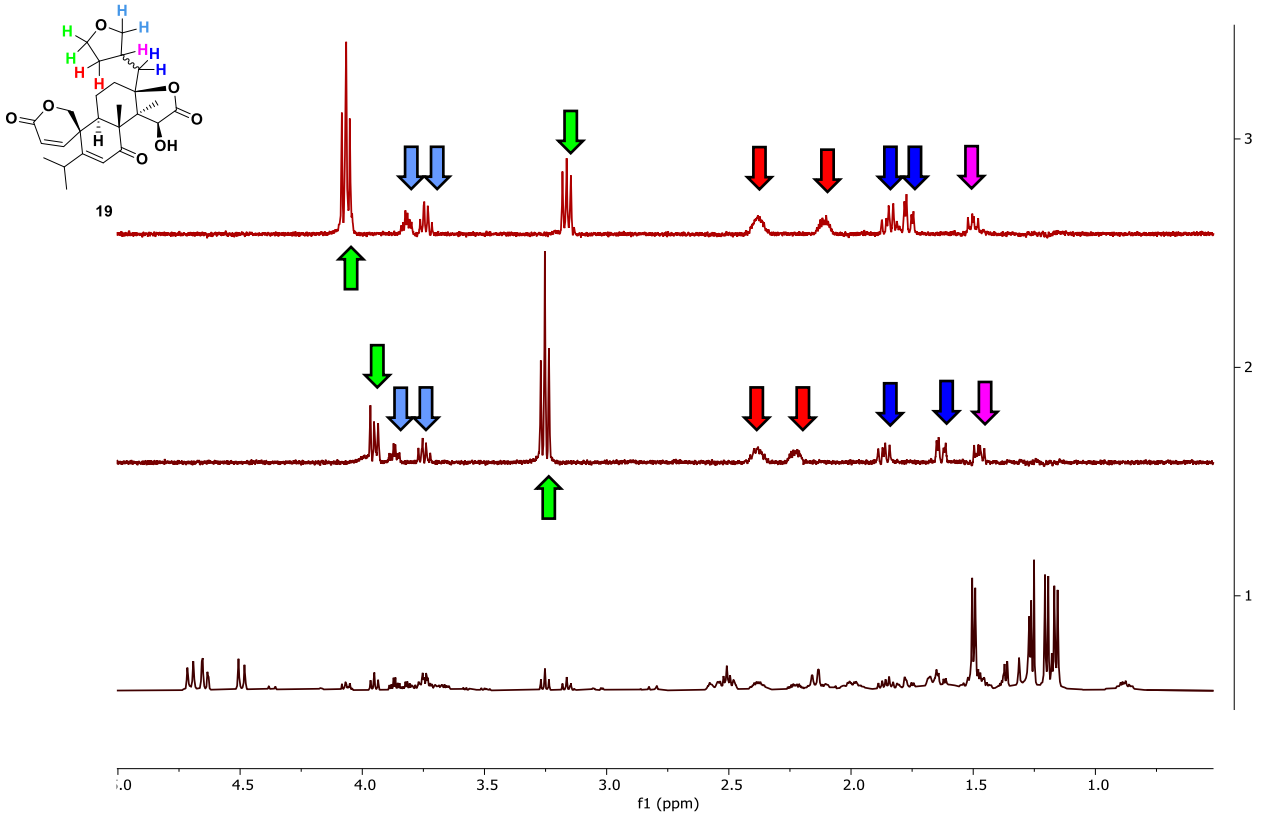
^{1}H NMR



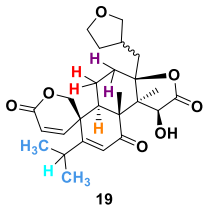
^{13}C NMR

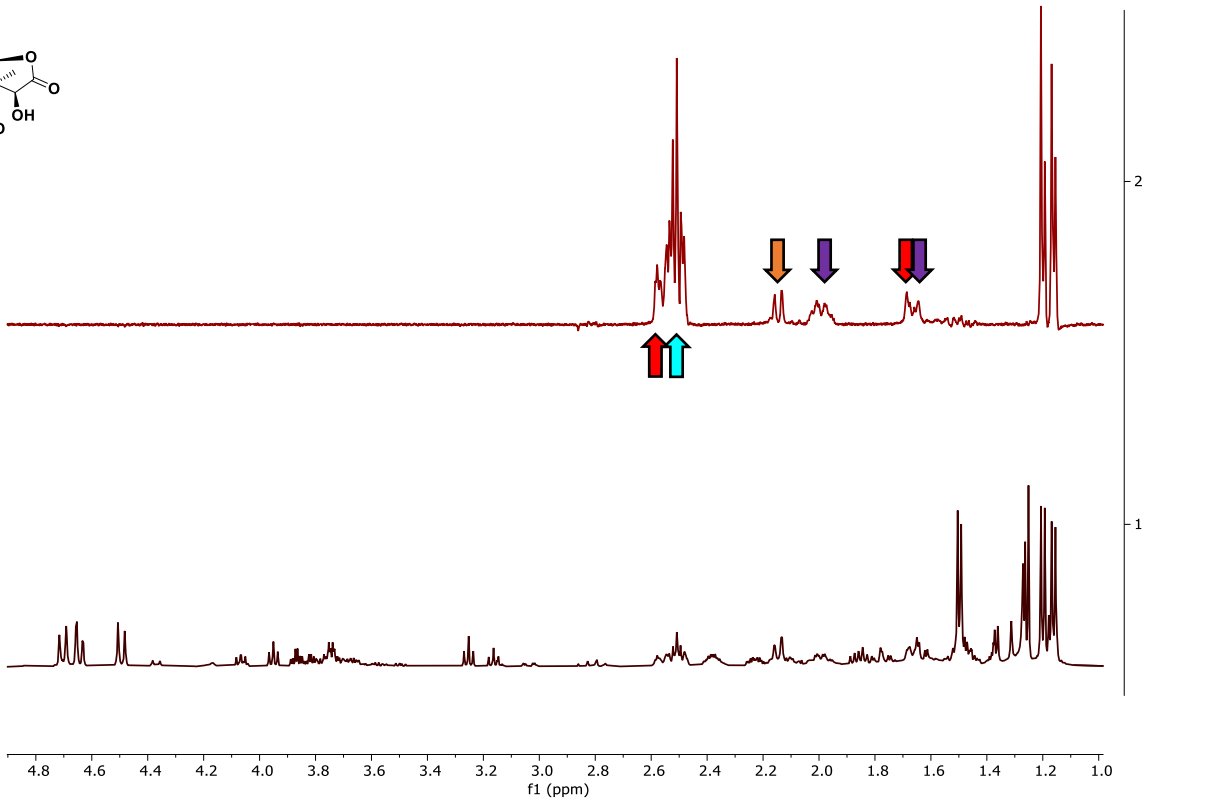


^{1}H-^{1}H COSY NMR

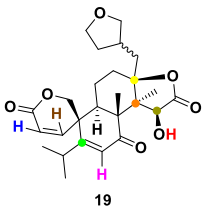


^{1}H-^{1}H 1D TOCSY NMR (two diastereoisomers)

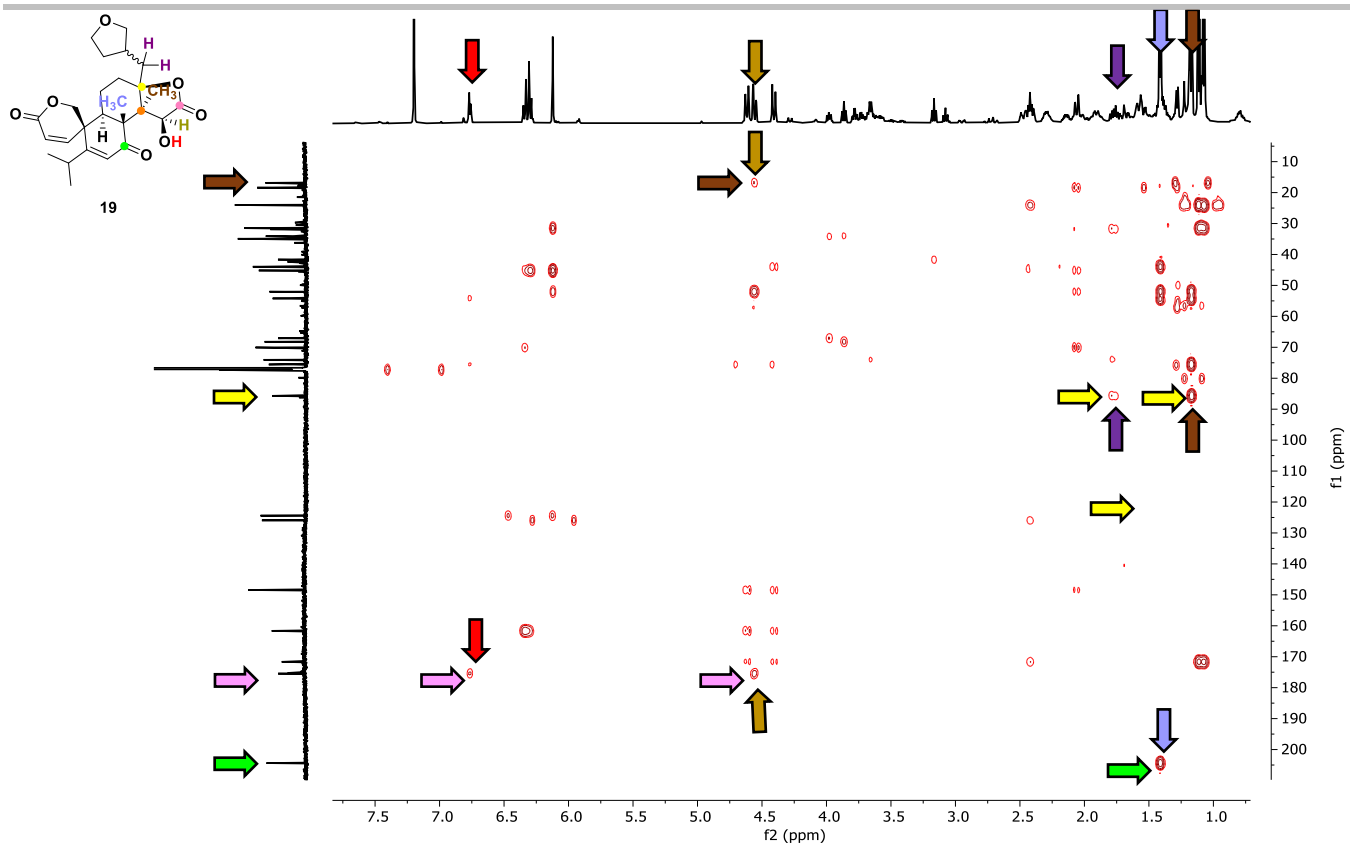




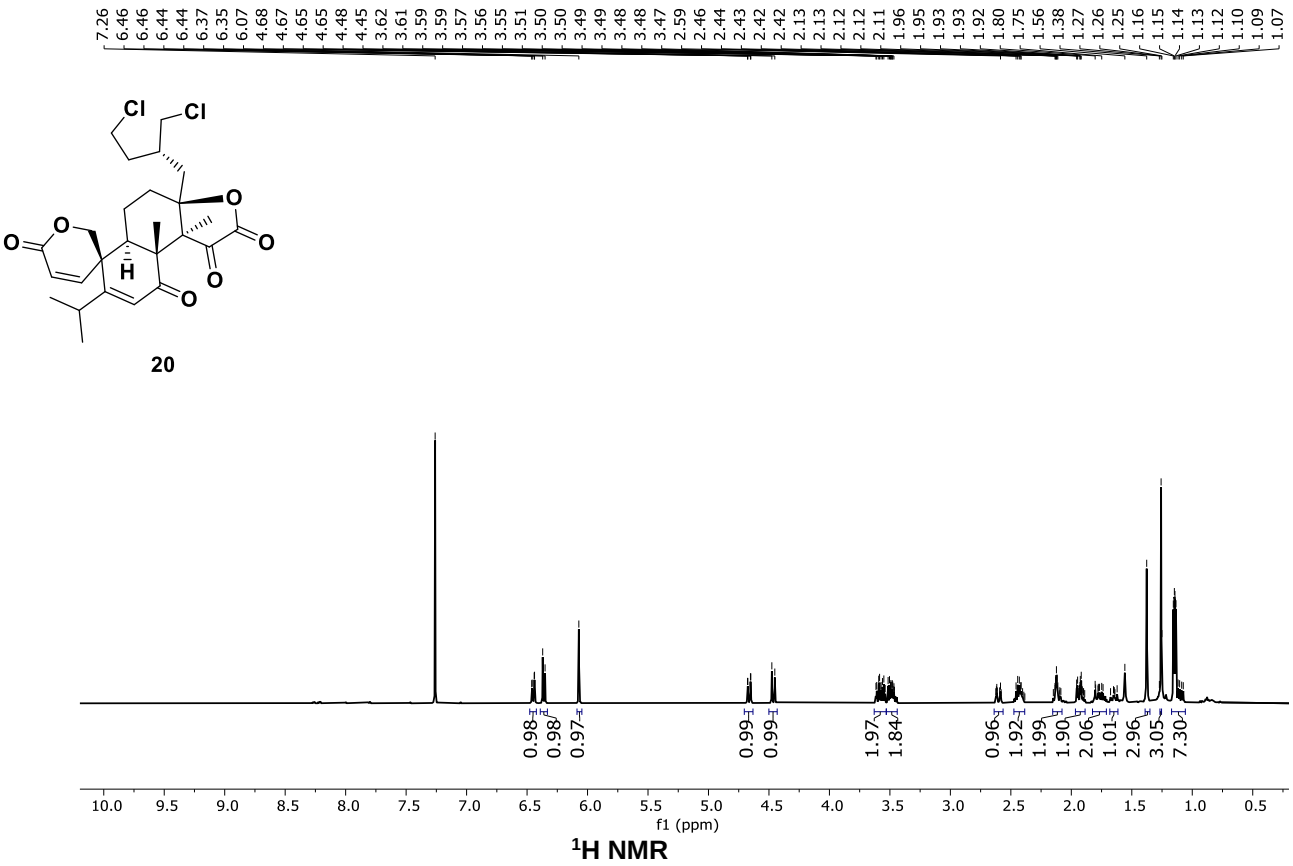
^{1}H-^{1}H 1D TOCSY NMR (one of the two diastereoisomers)



^{1}H-^{13}C HSQC NMR



^{1}H-^{13}C HMBC NMR



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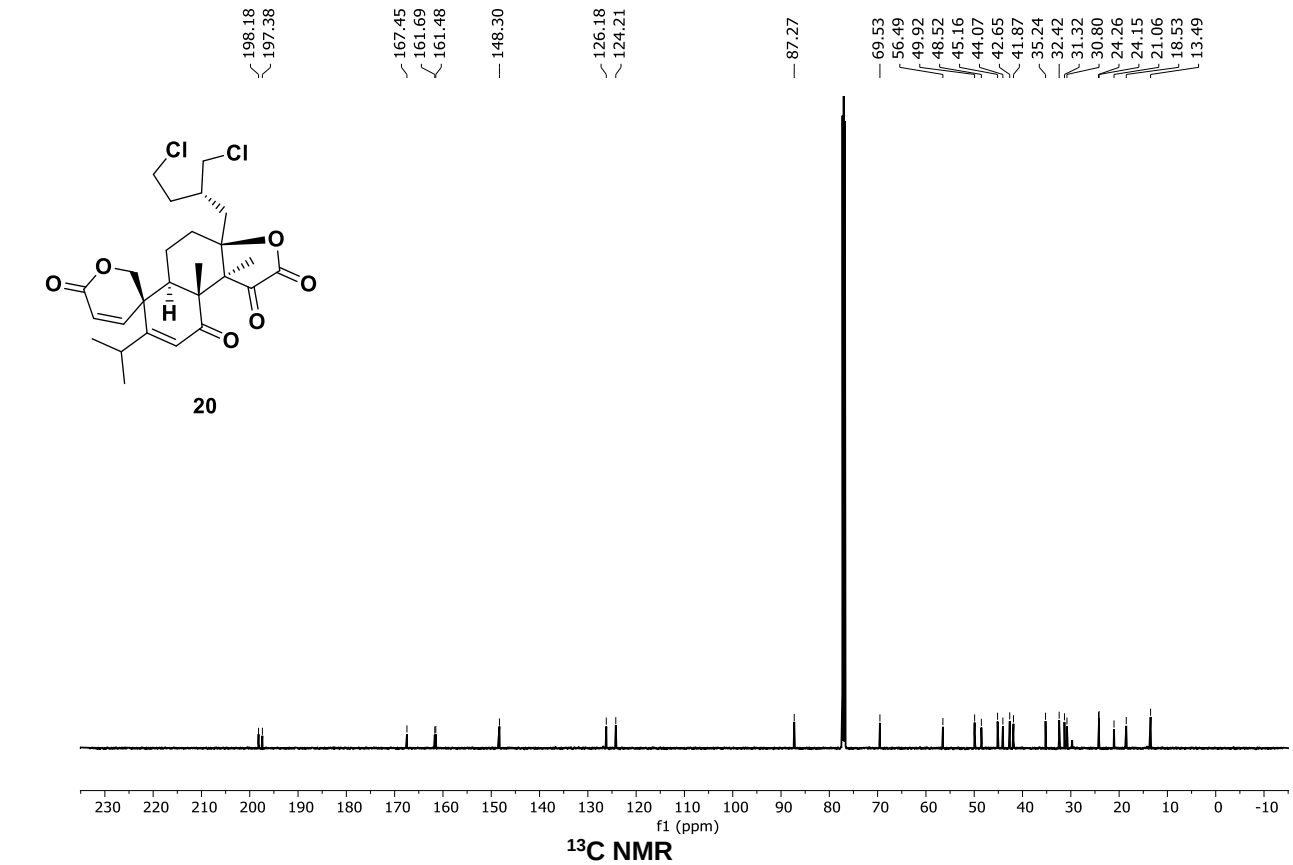
^{1}H NMR



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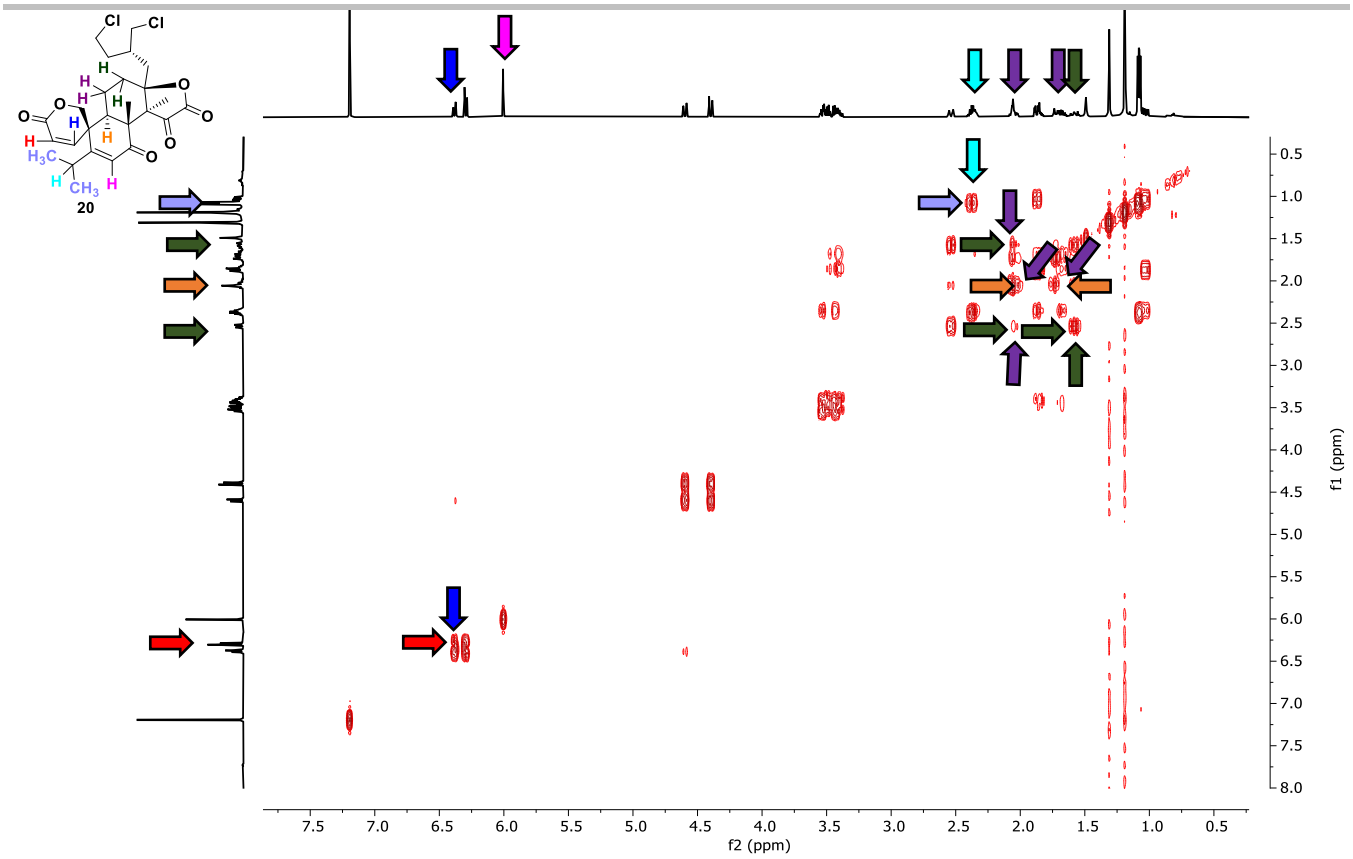
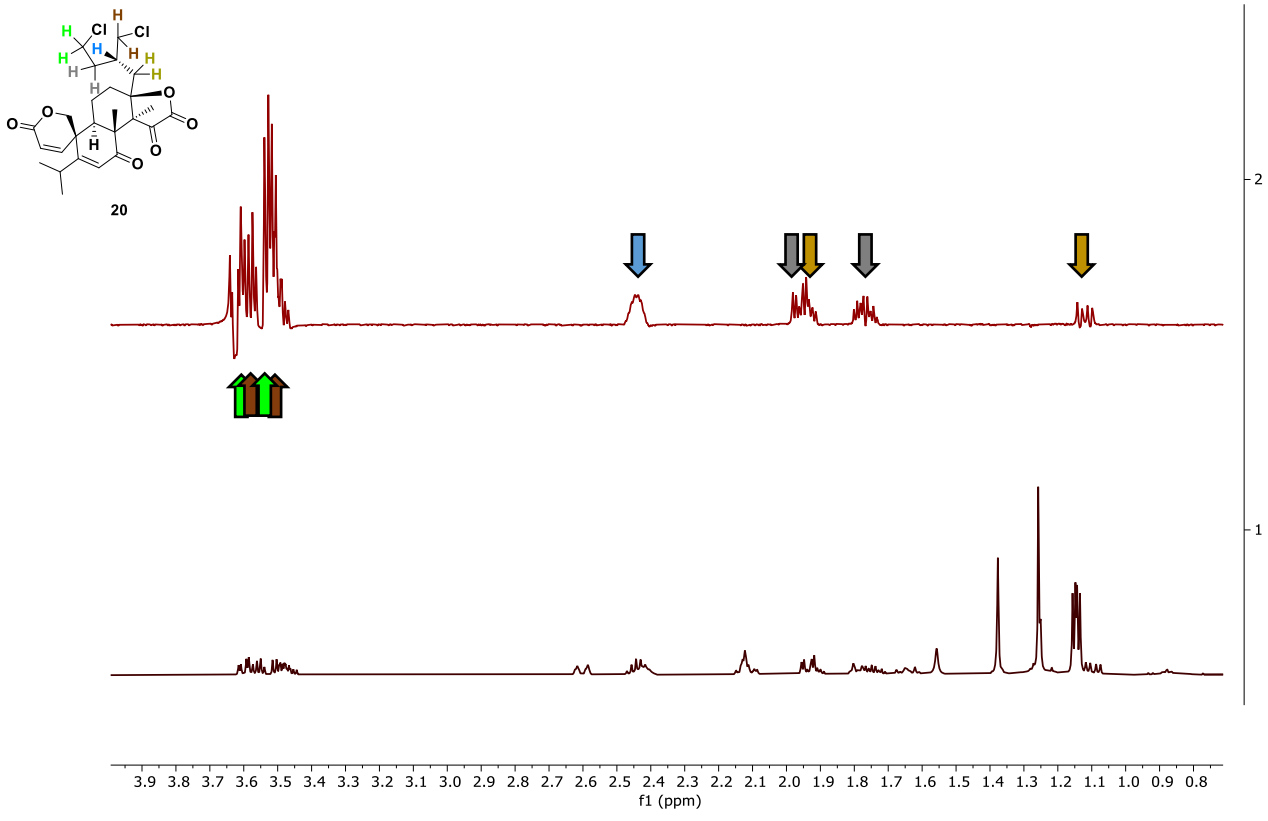
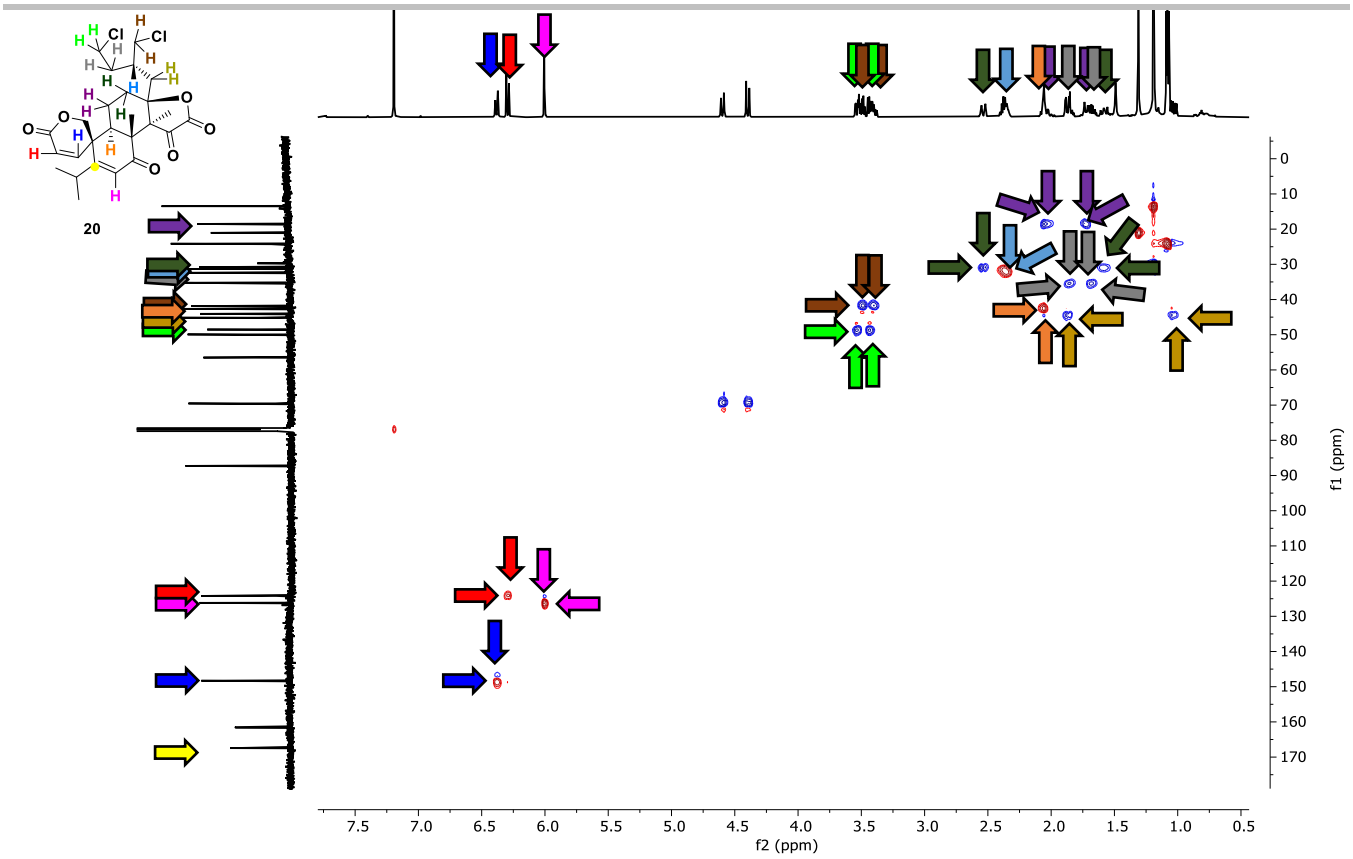


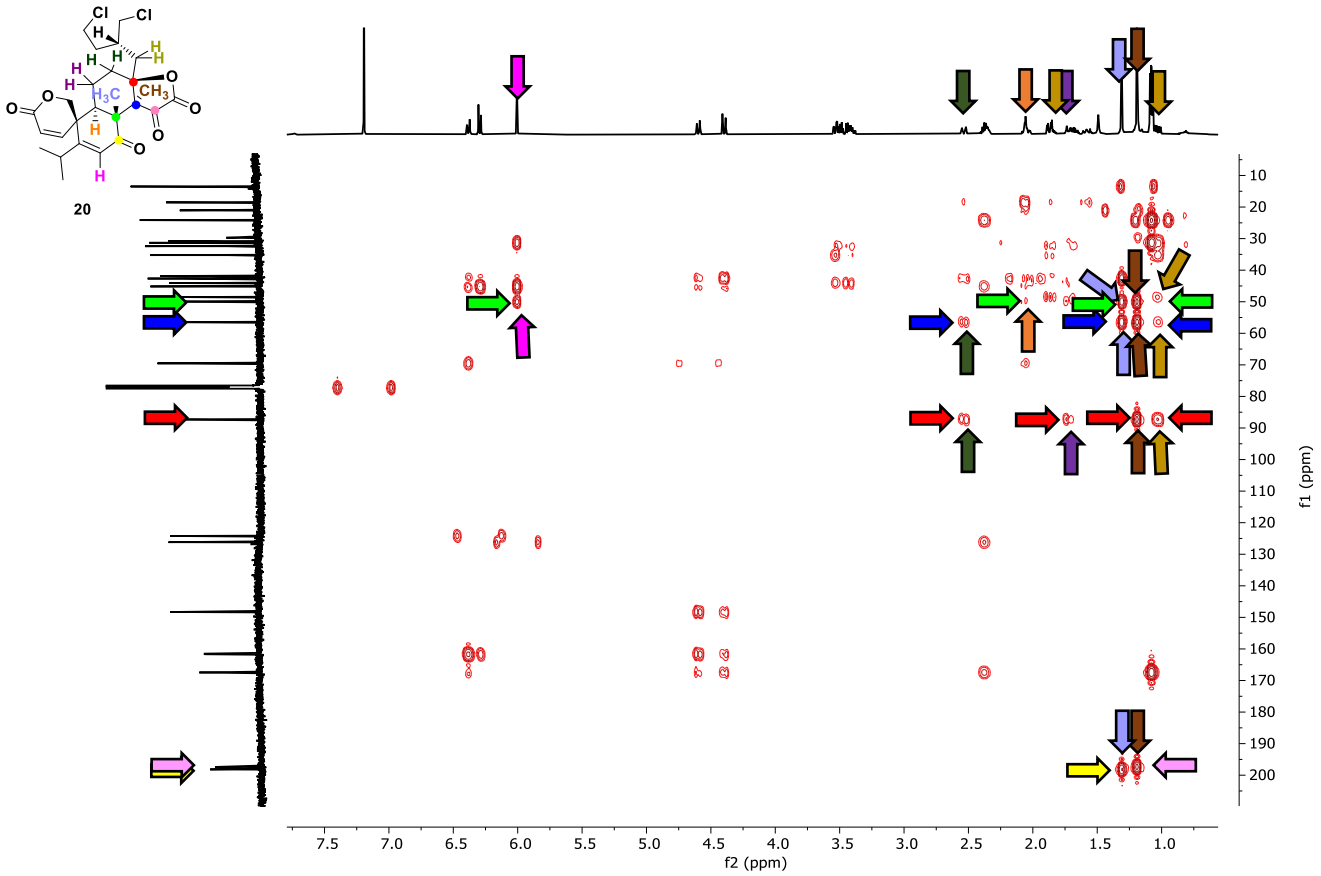
^{1}H-^{1}H COSY NMR



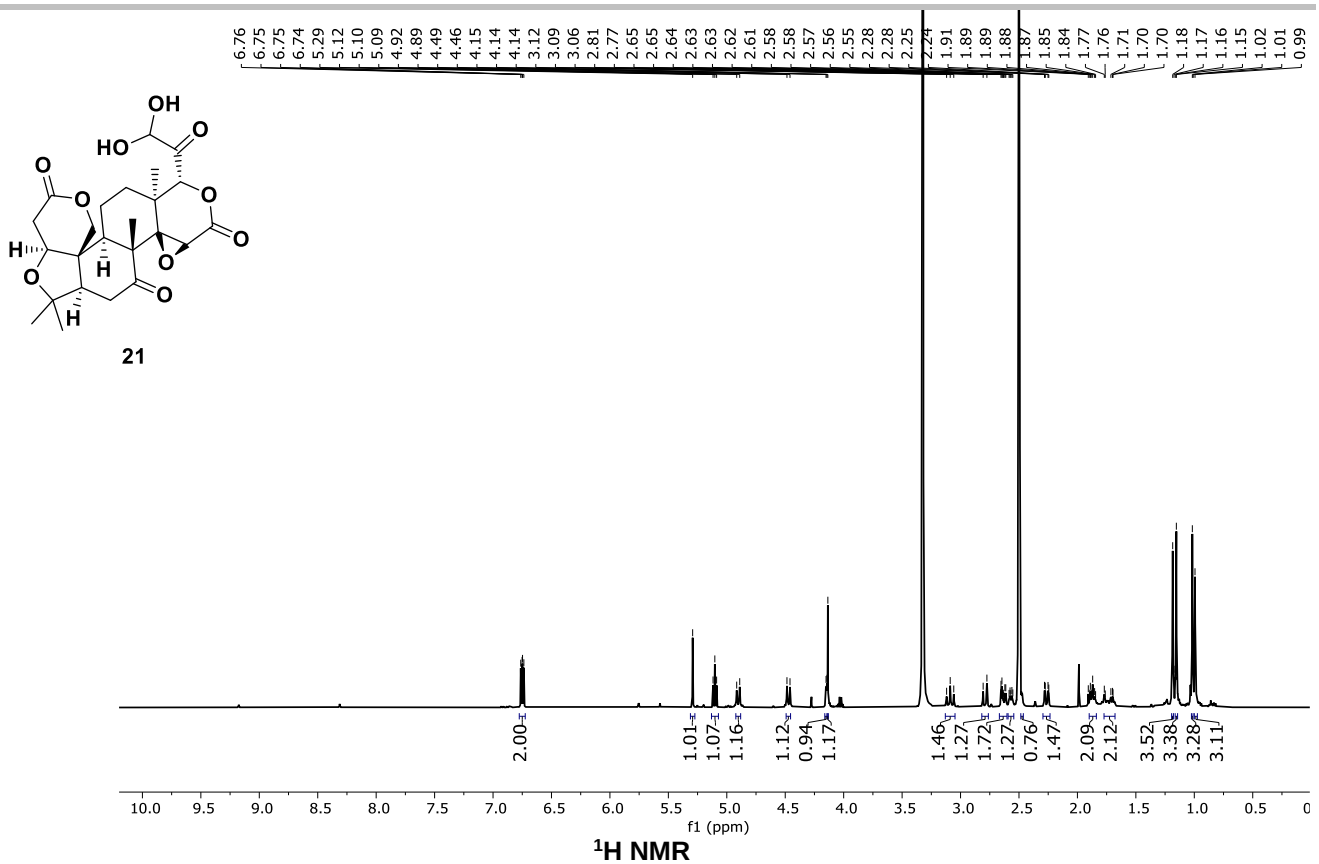
^{1}H-^{1}H 1D TOCSY NMR



^{1}H-^{13}C HSQC NMR

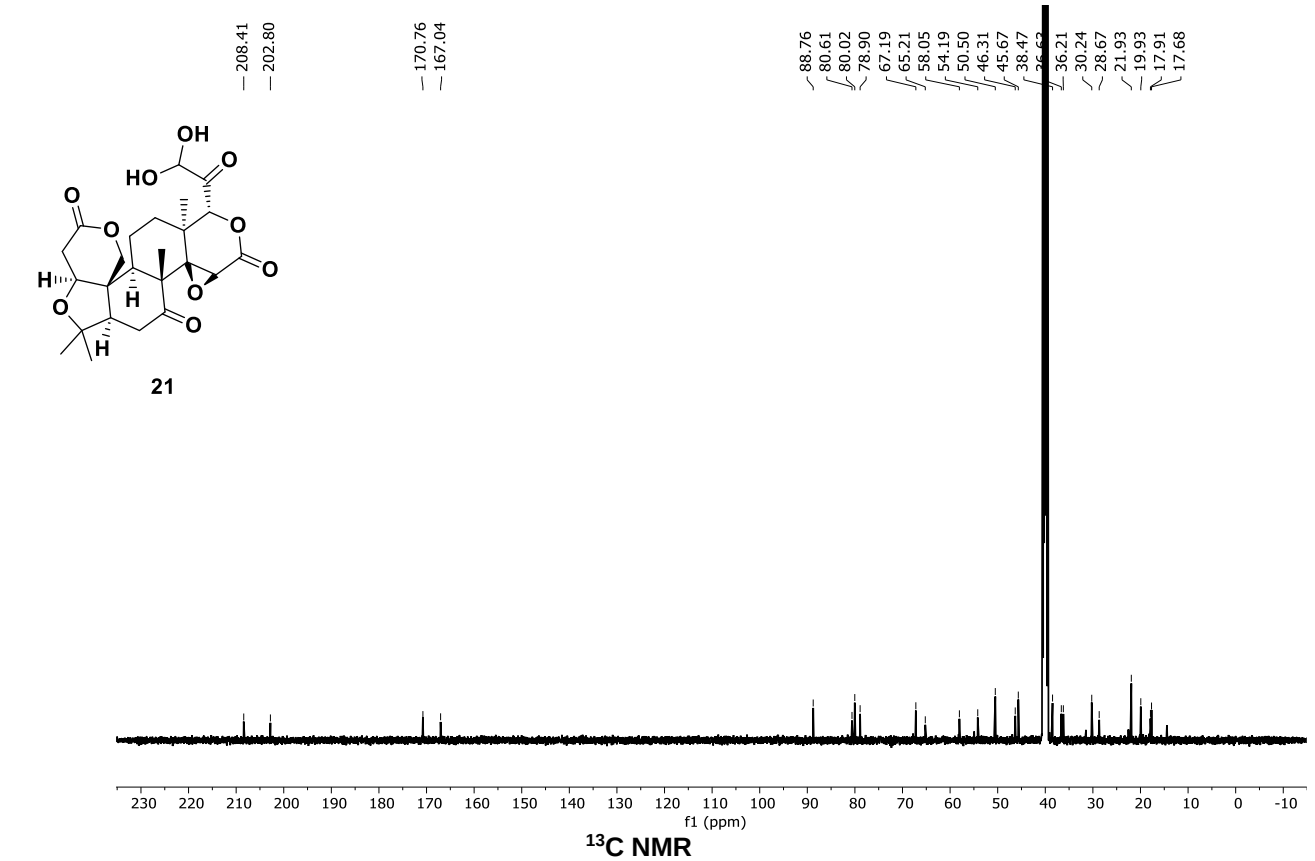


^{1}H-^{13}C HMBC NMR



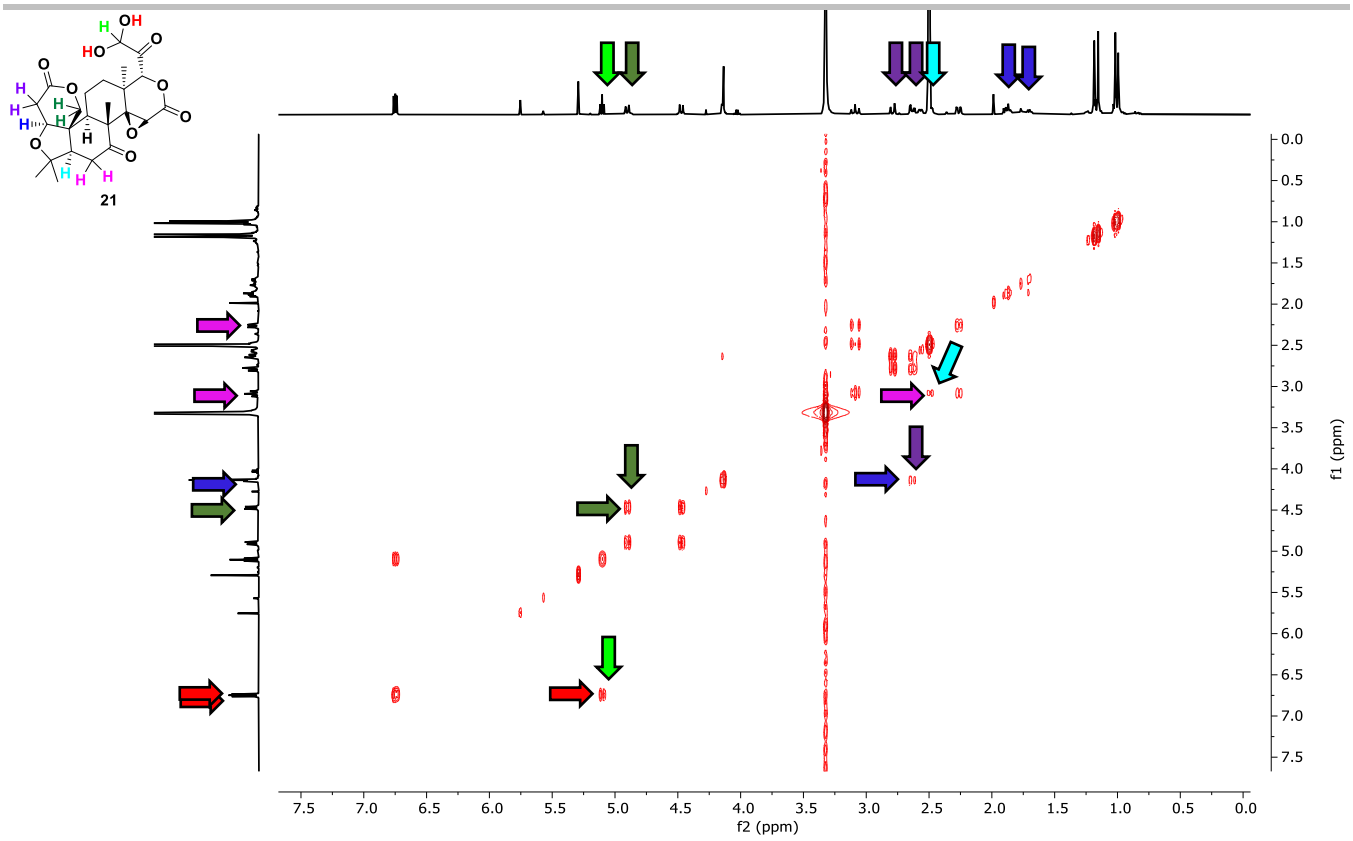
21

^{1}H NMR

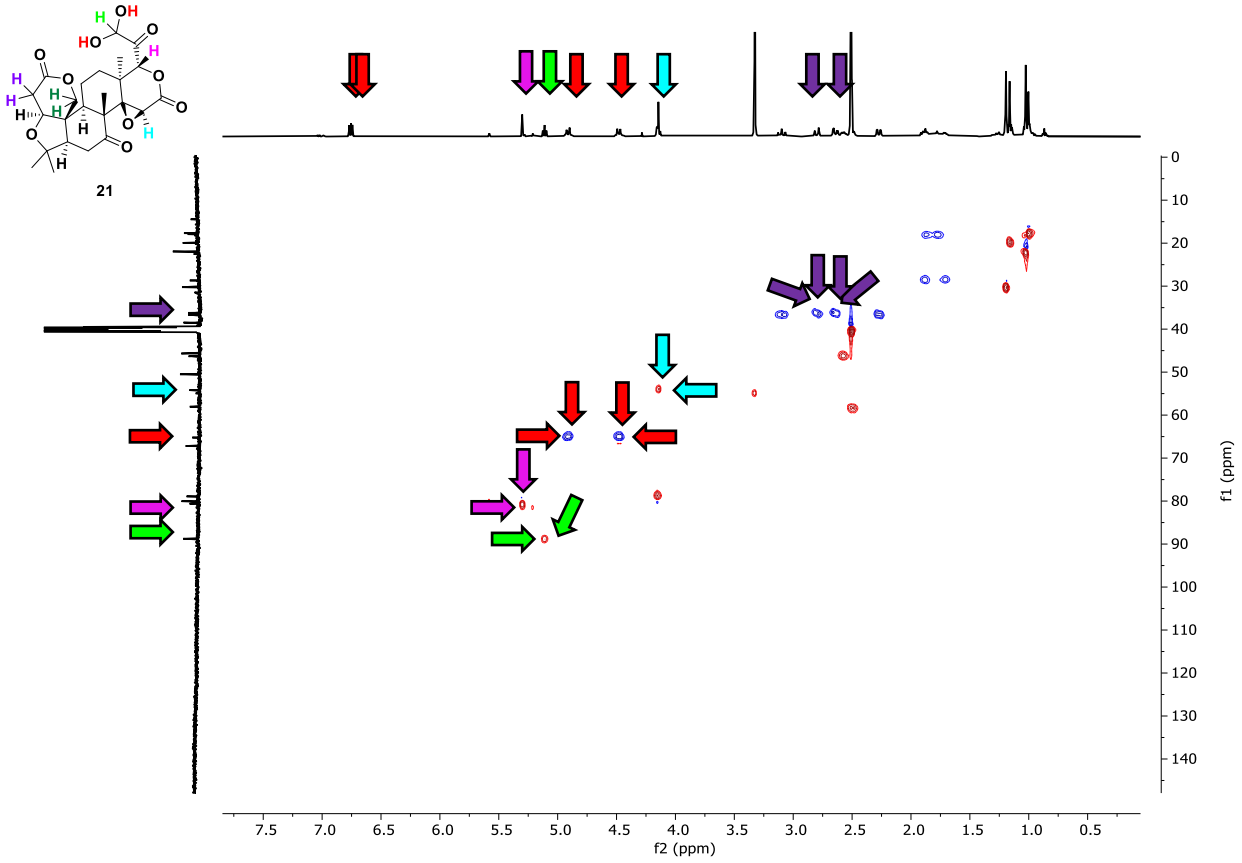


21

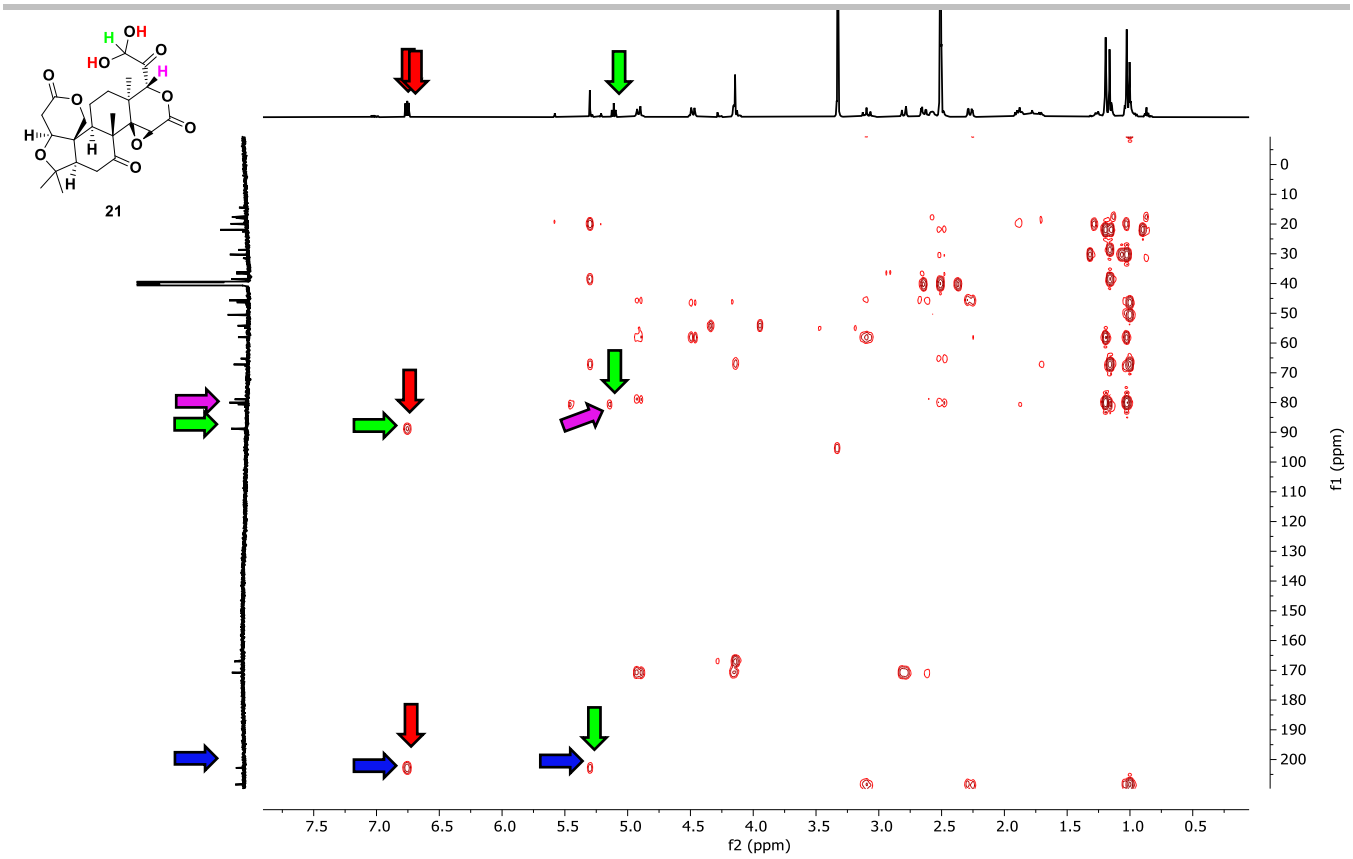
^{13}C NMR



^{1}H-^{1}H COSY NMR



^{1}H-^{13}C HSQC NMR



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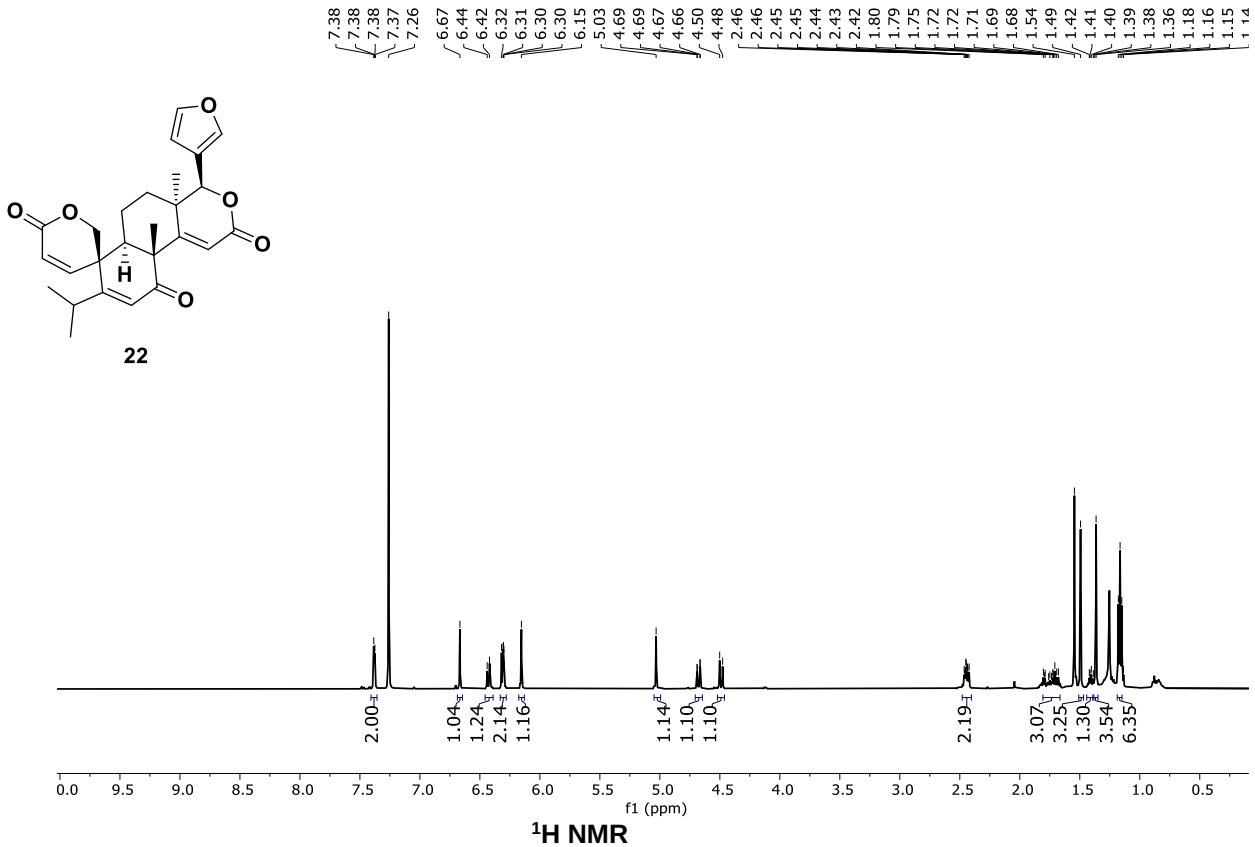

22

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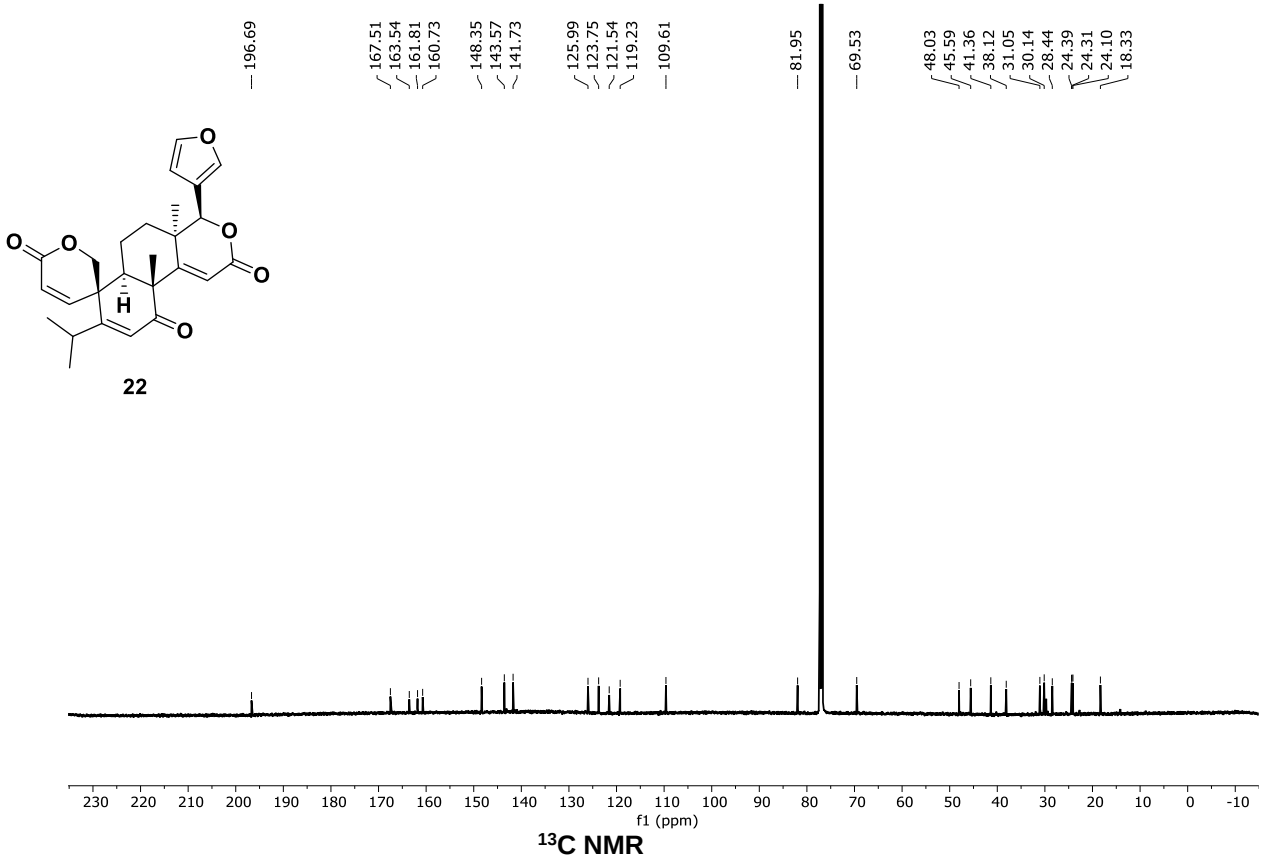

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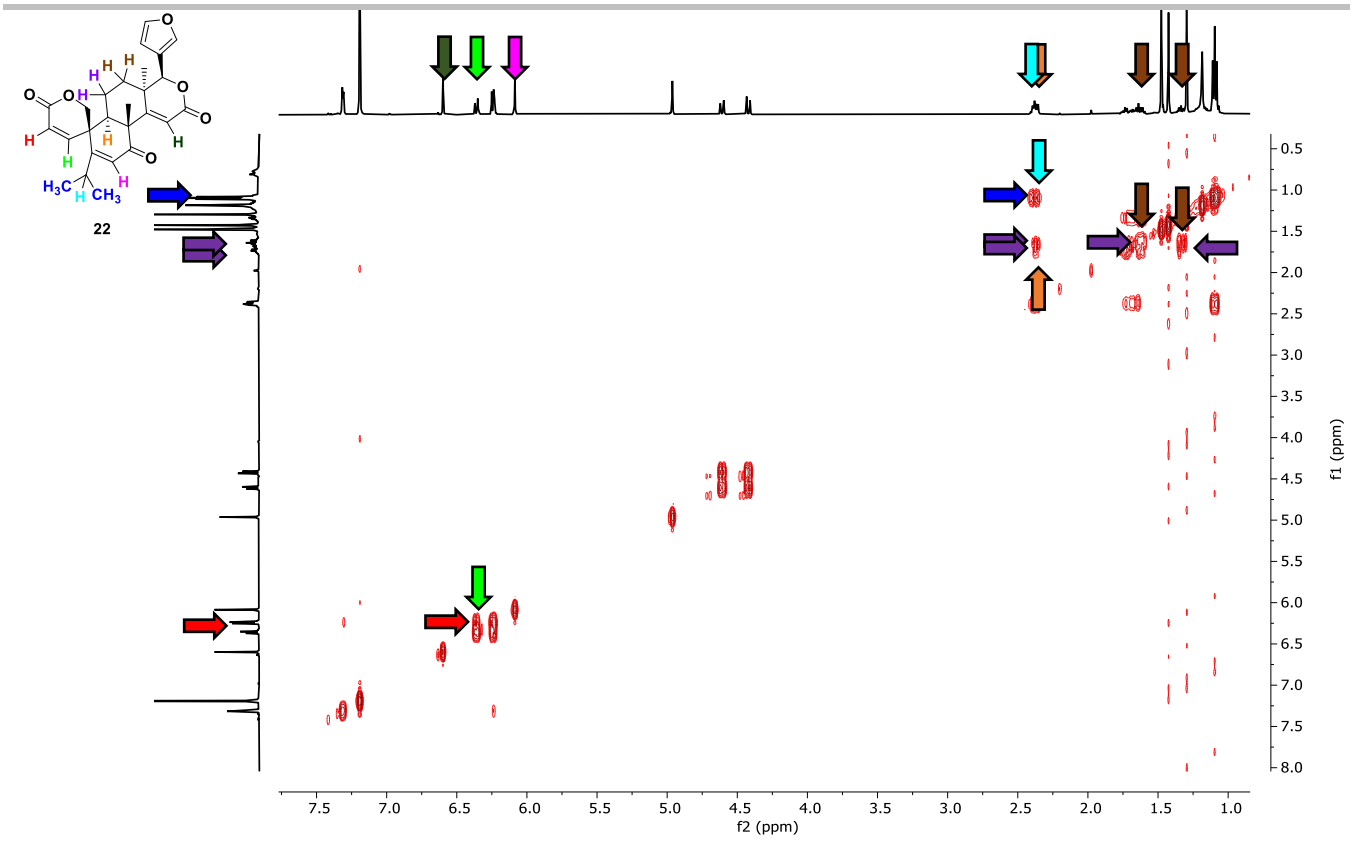
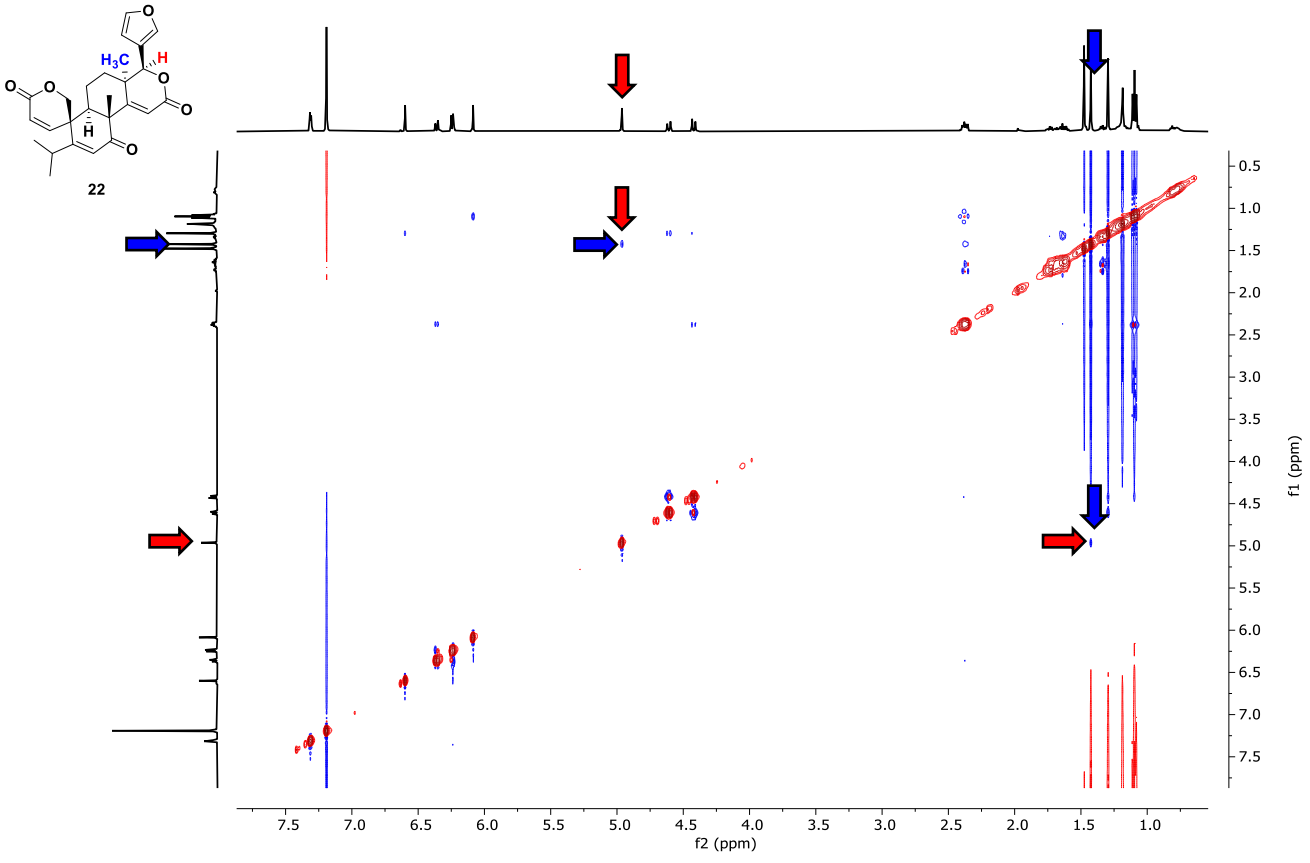


^{1}H-^{1}H COSY NMR



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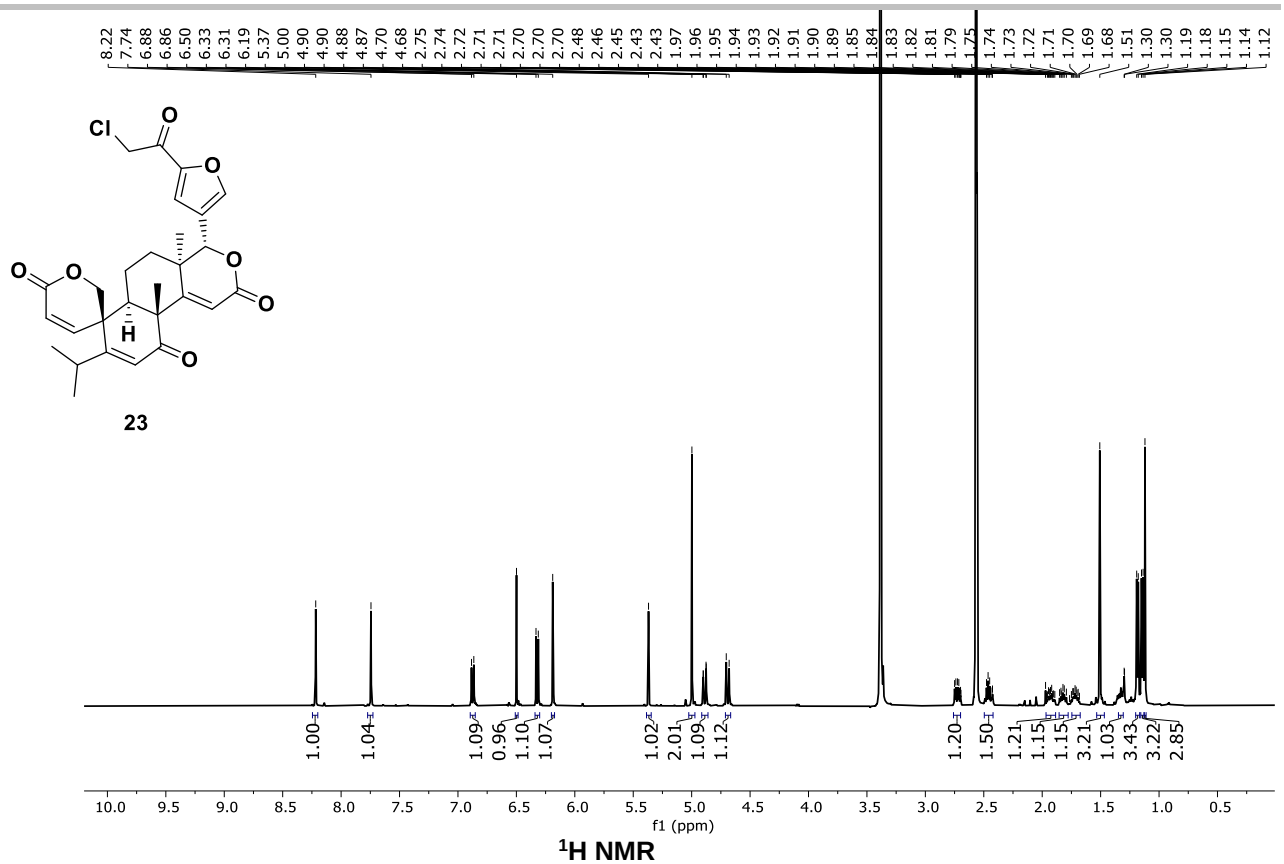
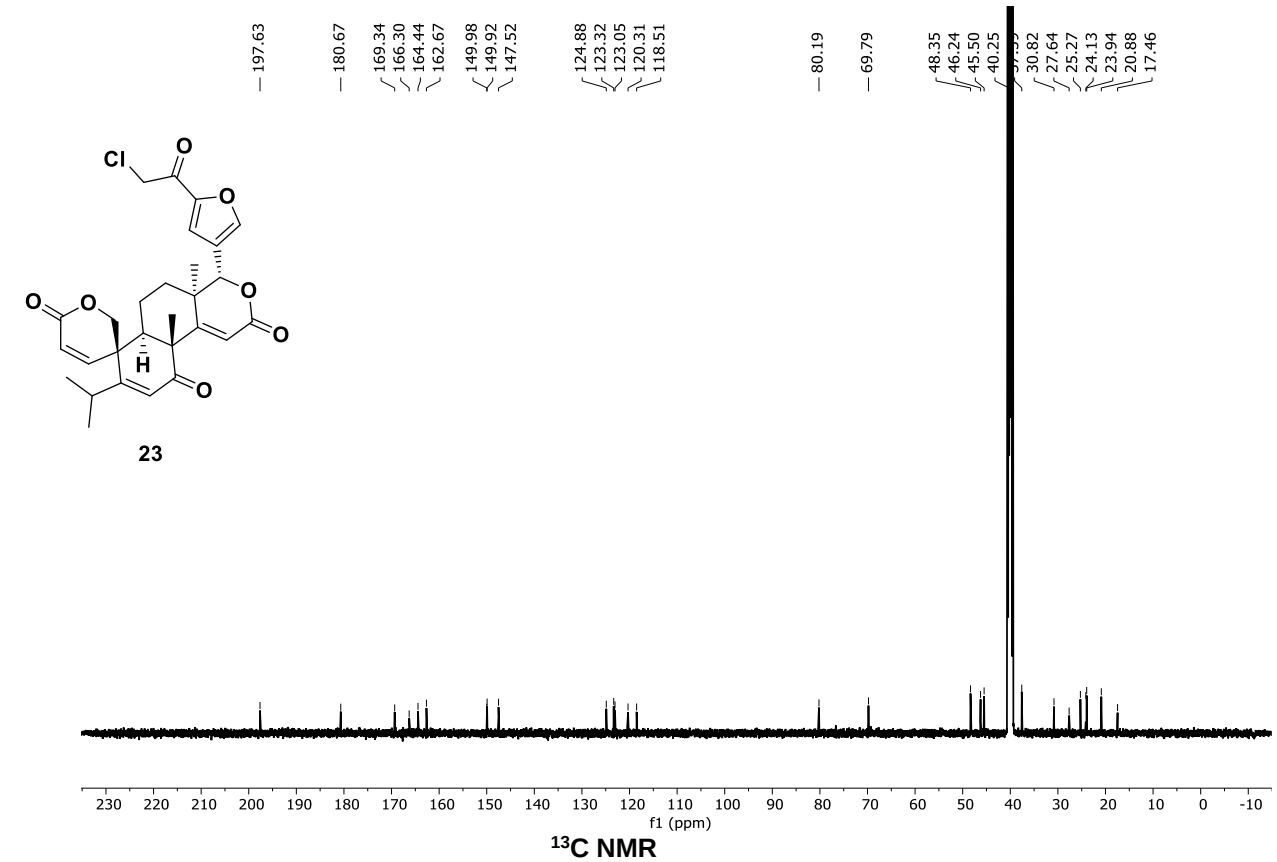
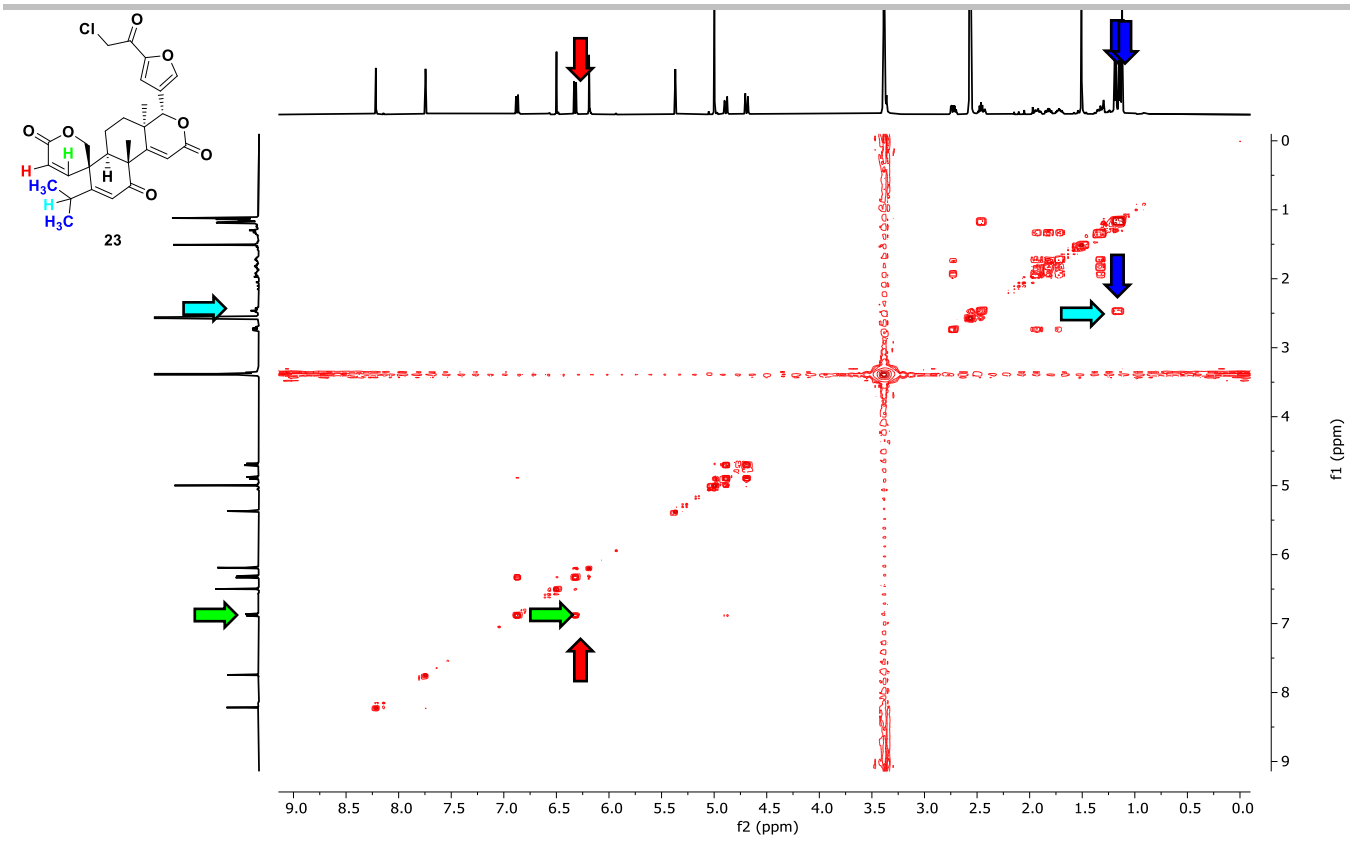


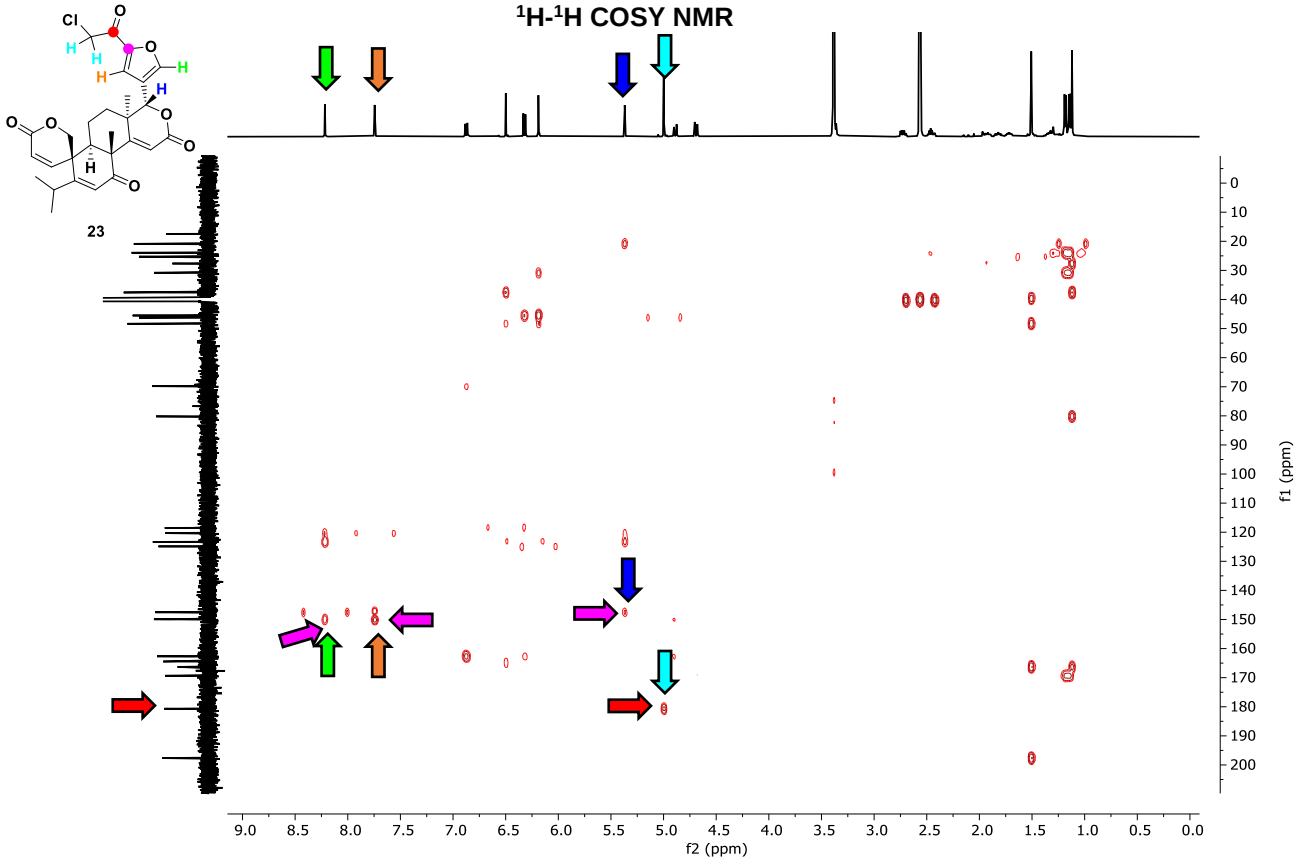
^{1}H NMR



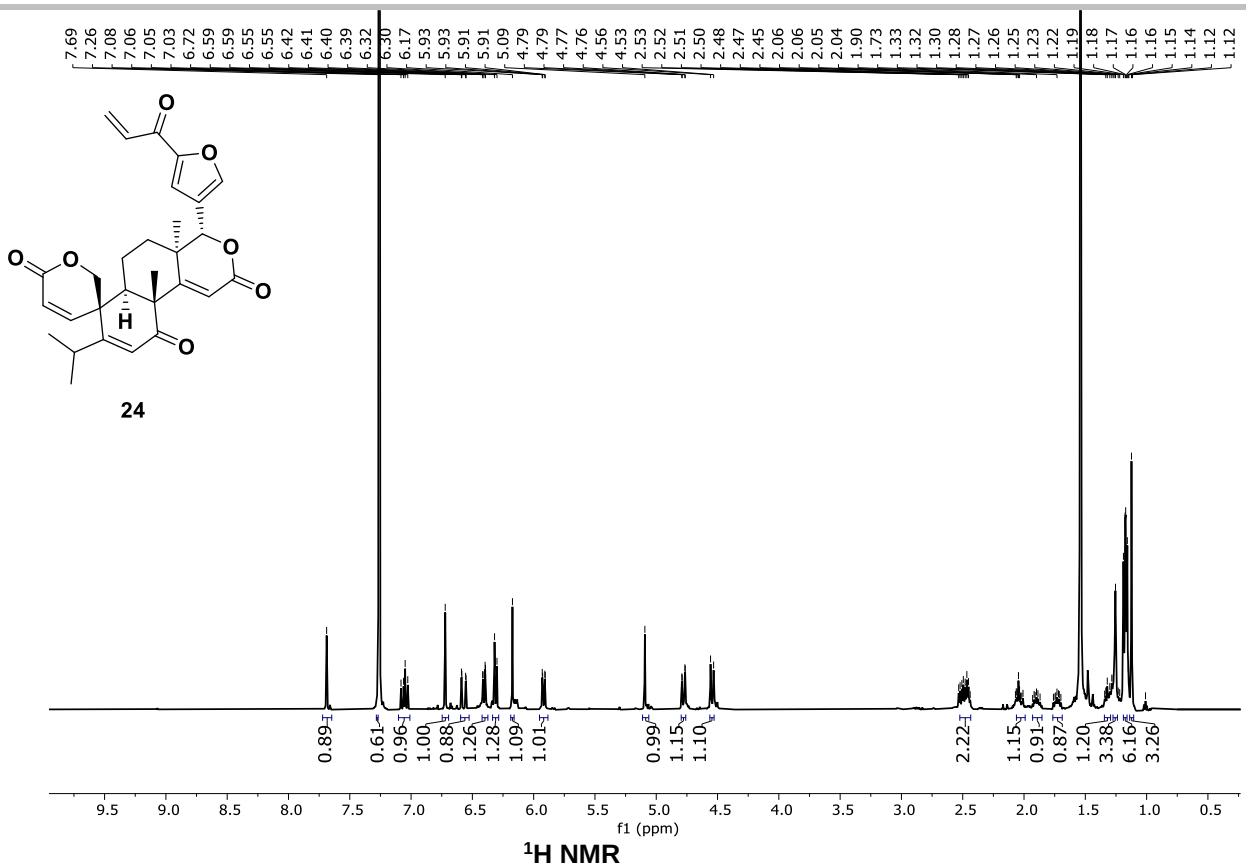
^{13}C NMR



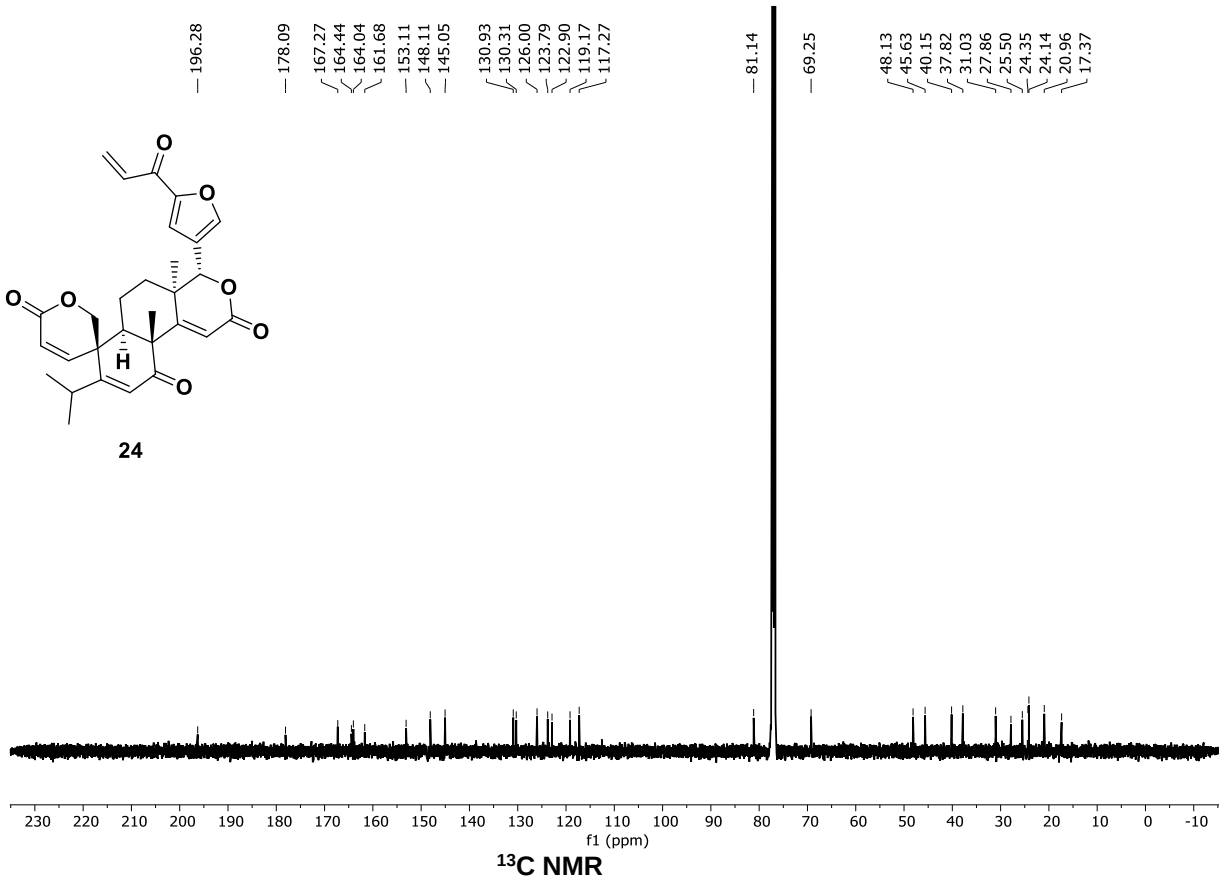
^{1}H-^{1}H COSY NMR



^{1}H-^{13}C HMBC NMR



^{1}H NMR



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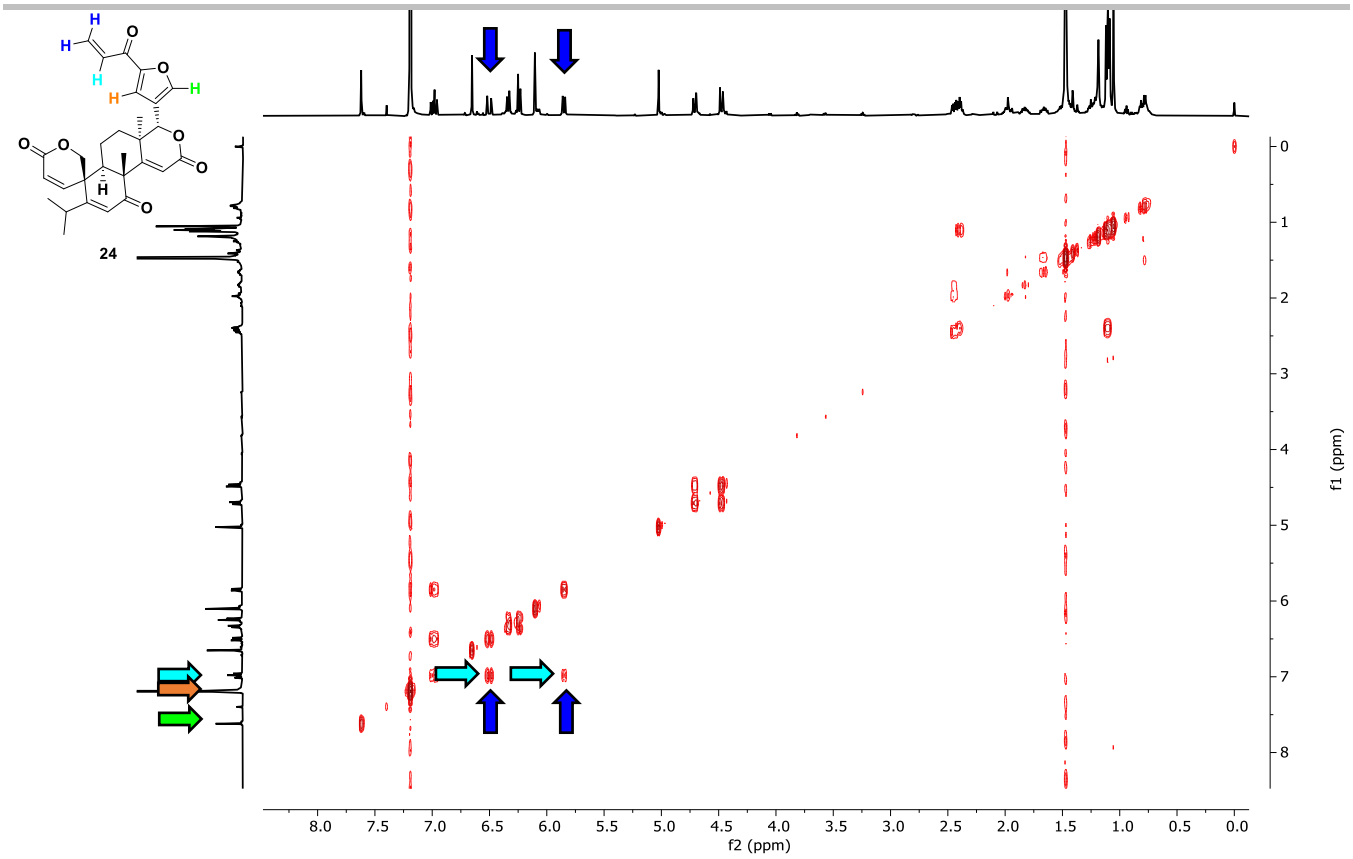
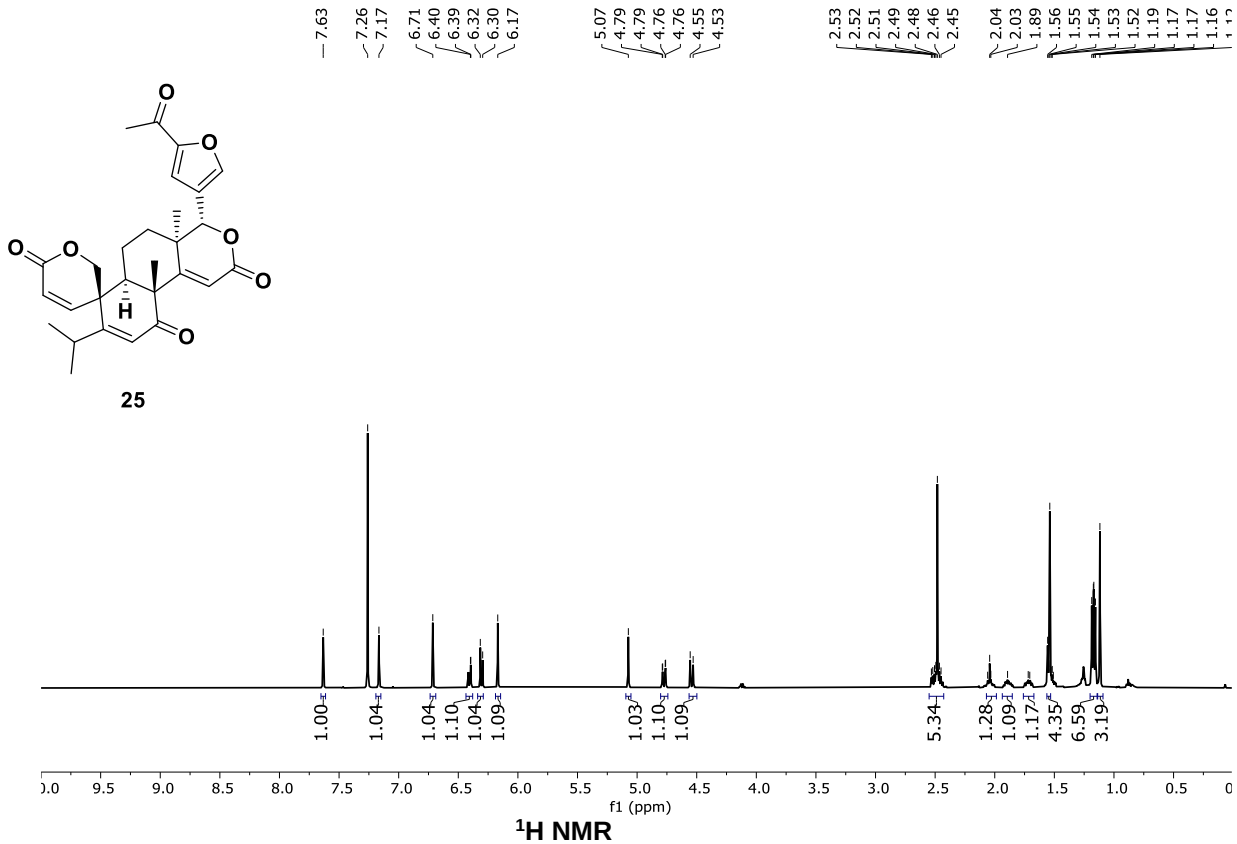
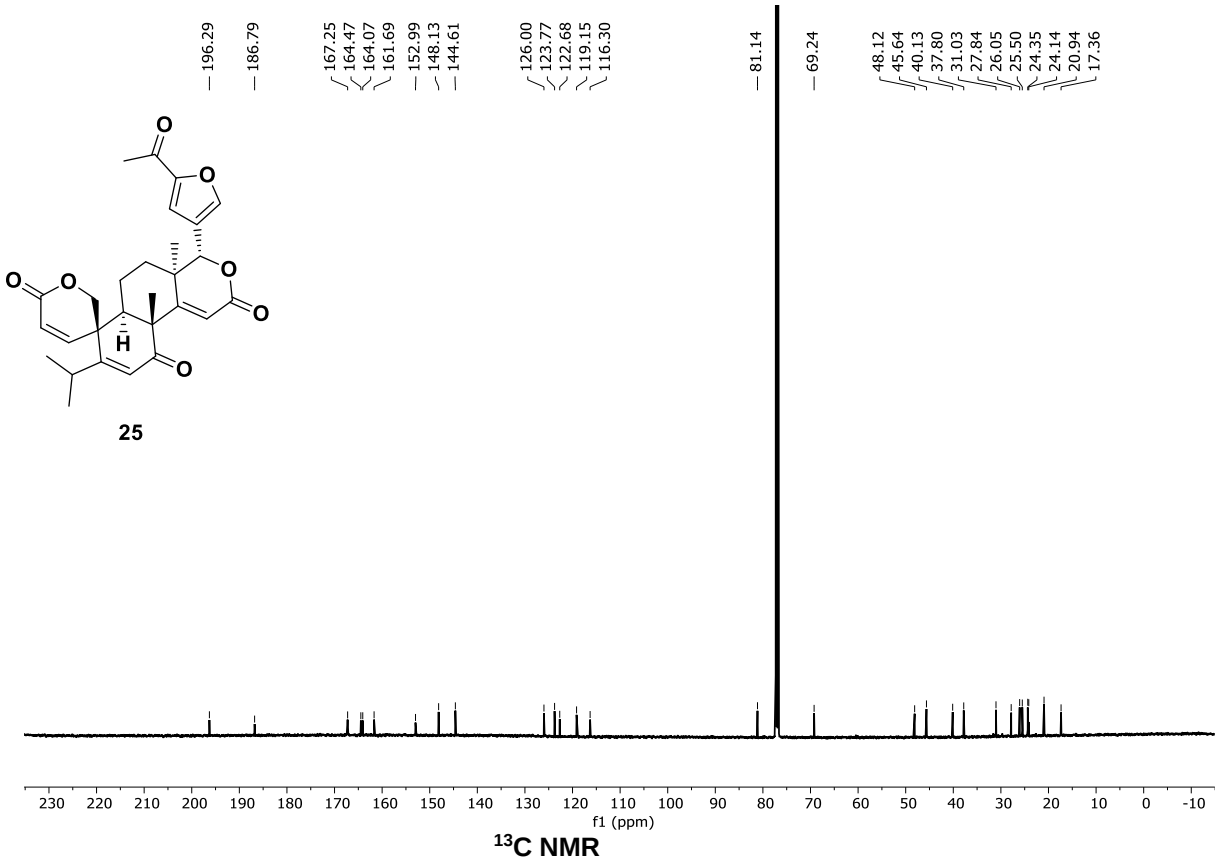


^{1}H-^{1}H COSY NMR



25

^{1}H NMR



25

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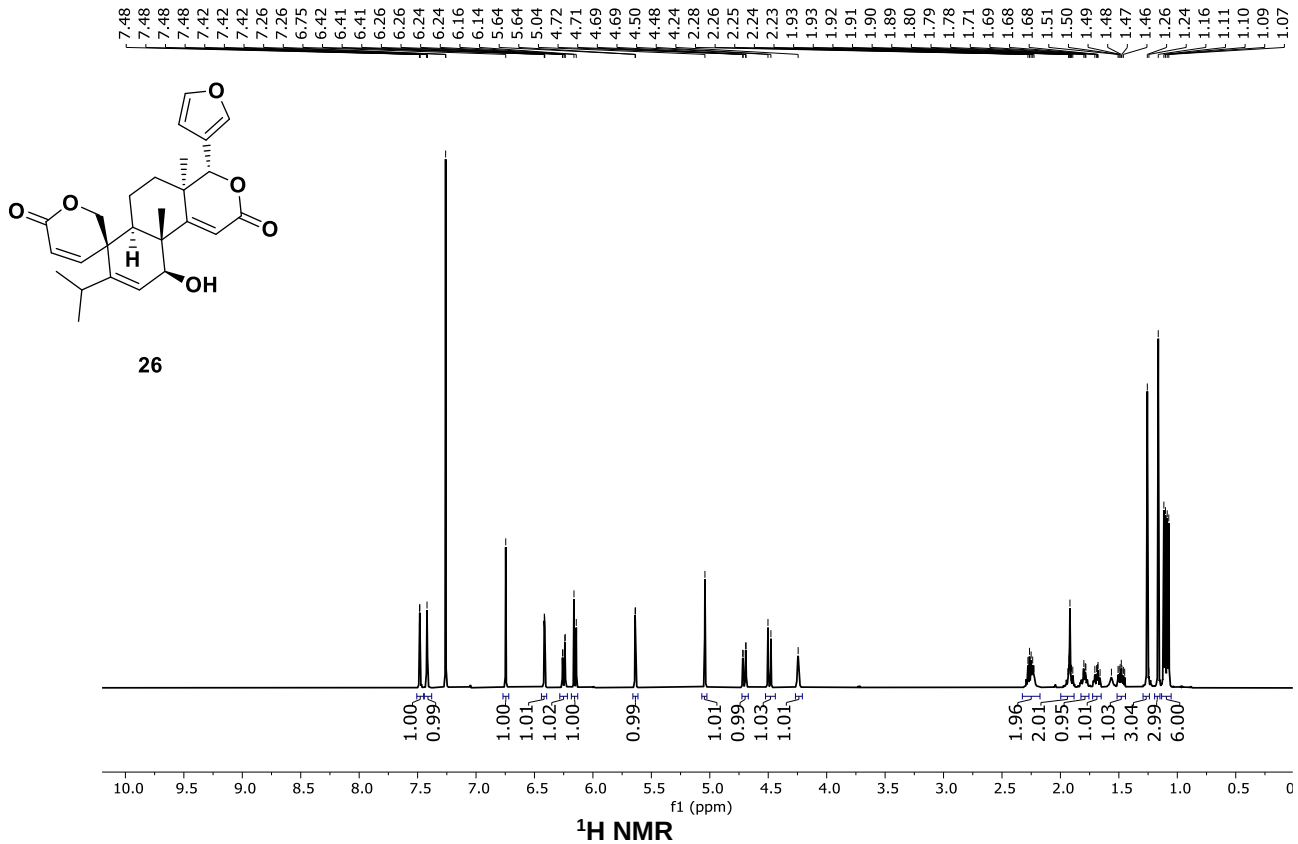
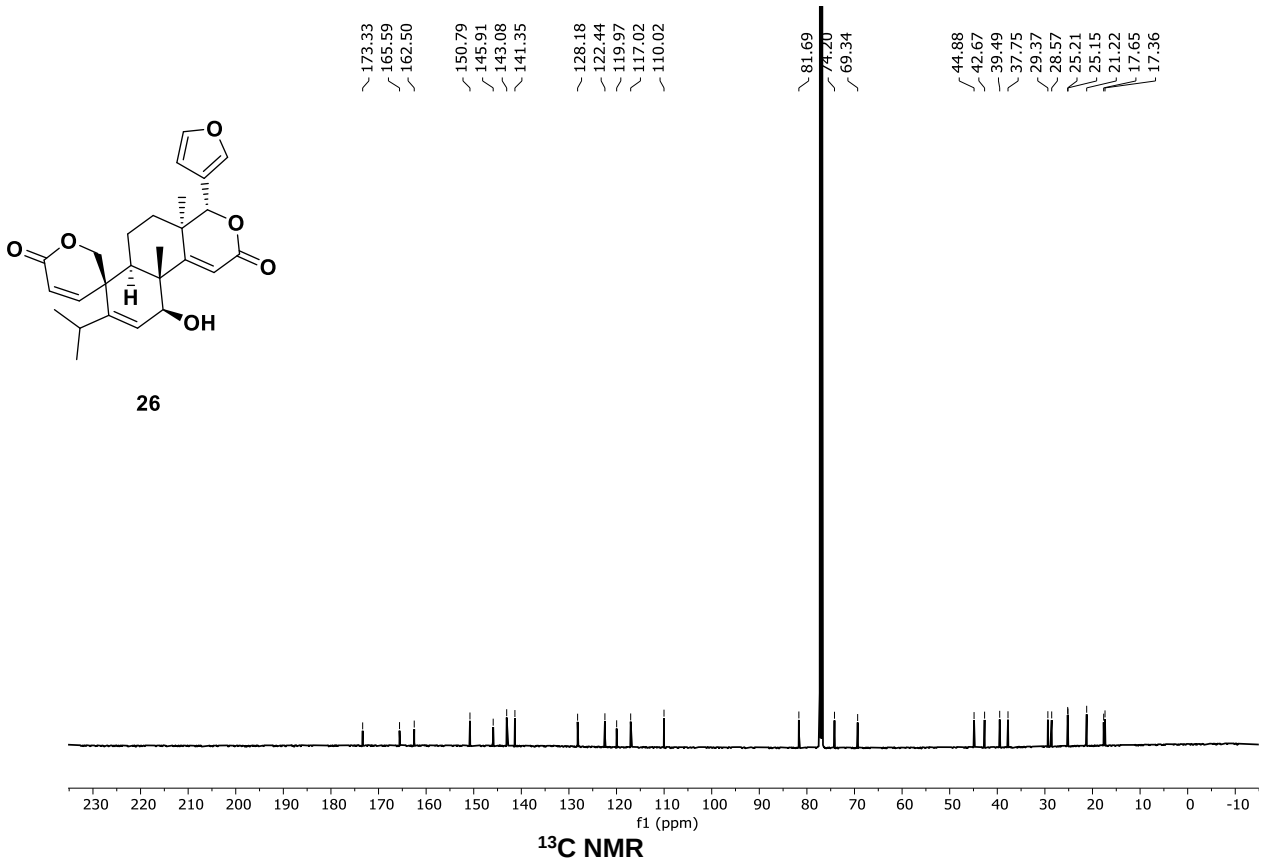


26

^{1}H NMR



26

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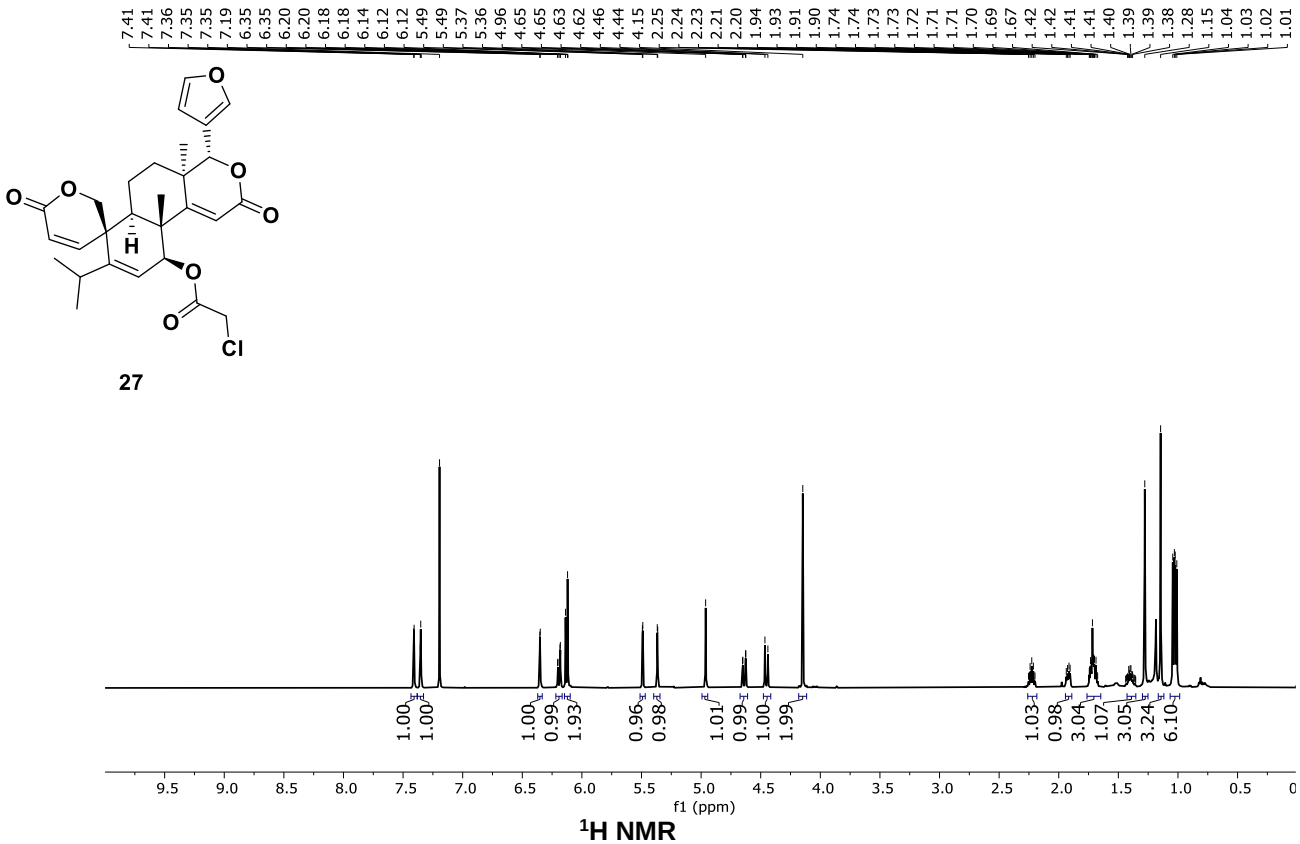
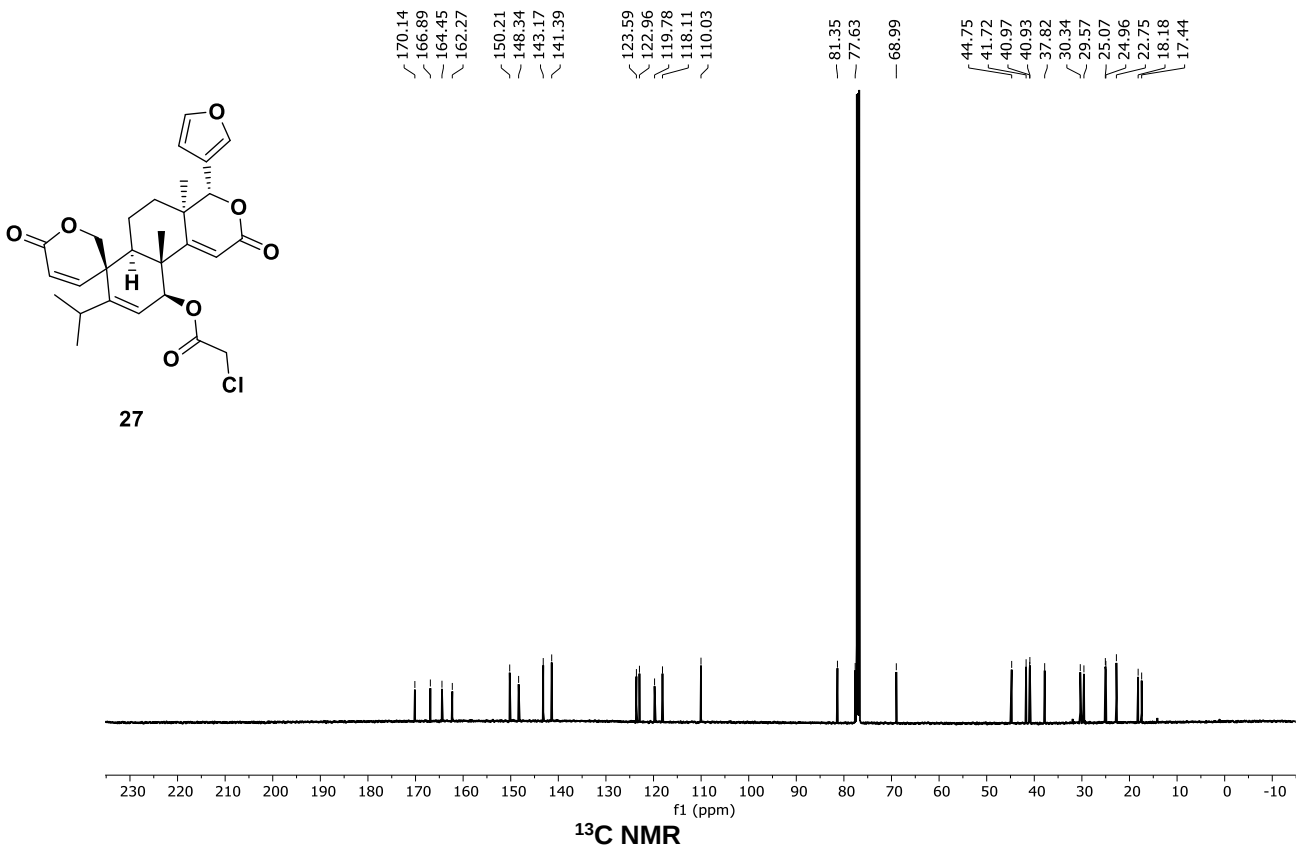


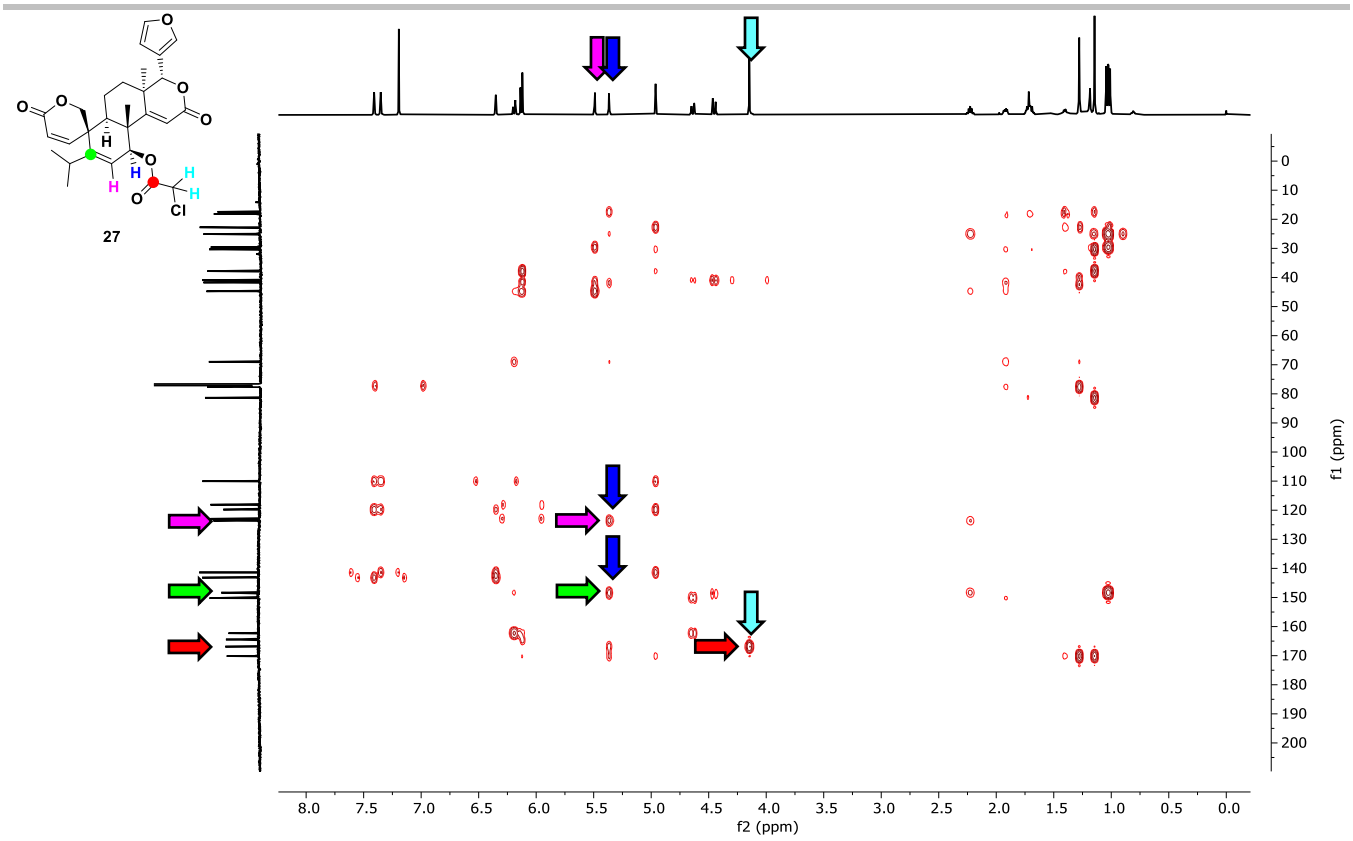
27

^{1}H NMR

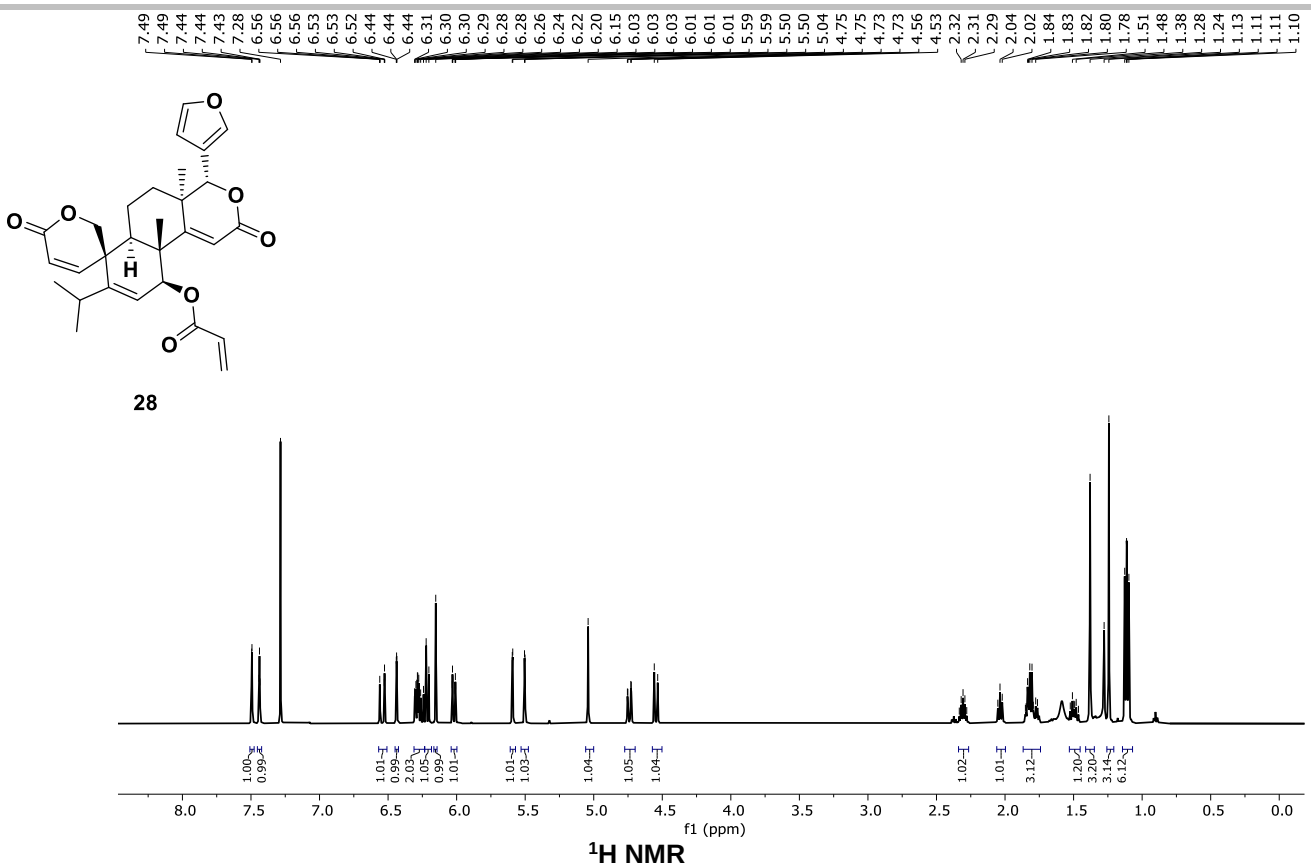


27

^{13}C NMR

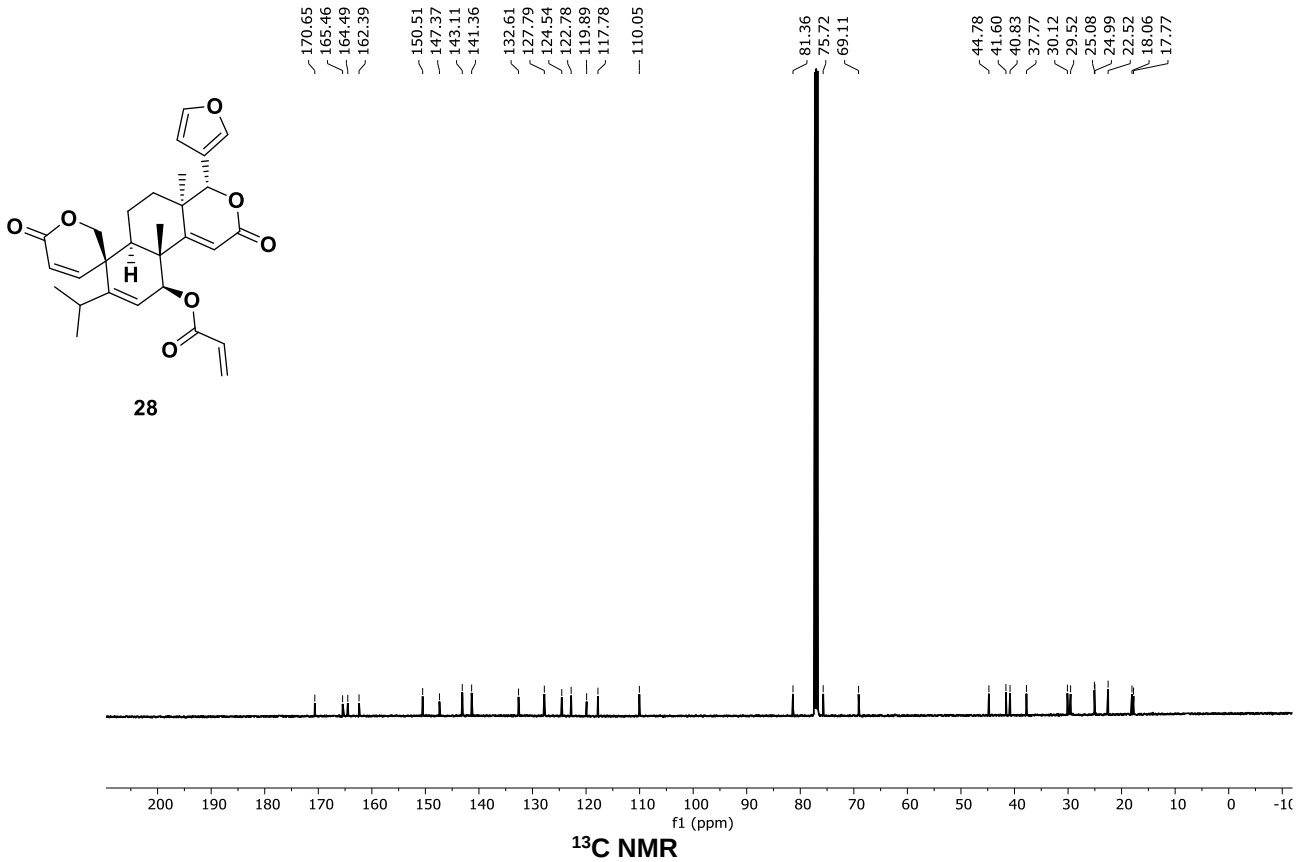


^{1}H-^{13}C HMBC NMR



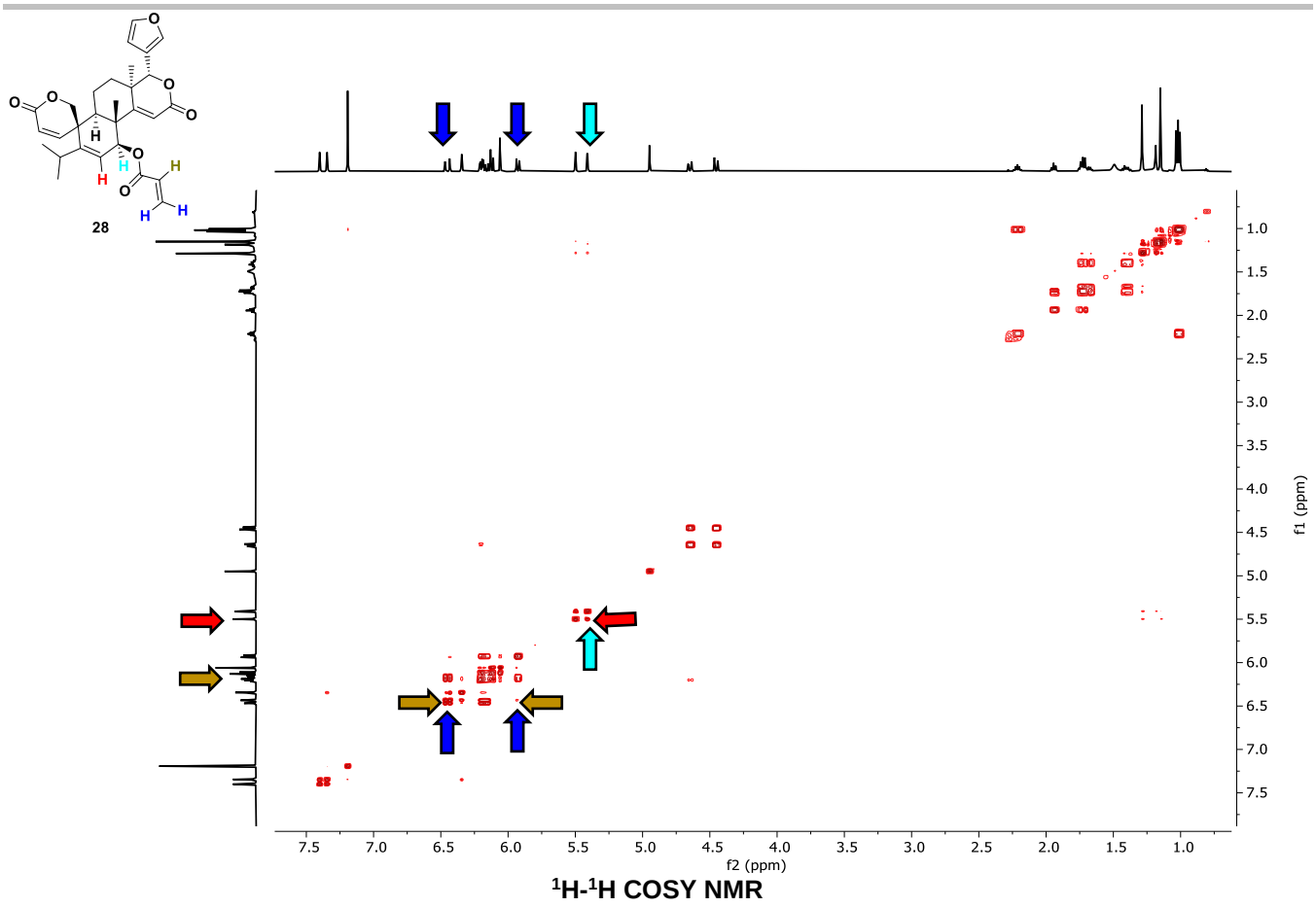
28

^{1}H NMR

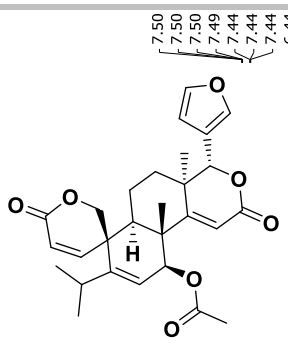


28

^{13}C NMR

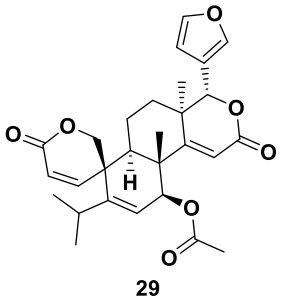


^{1}H-^{1}H COSY NMR



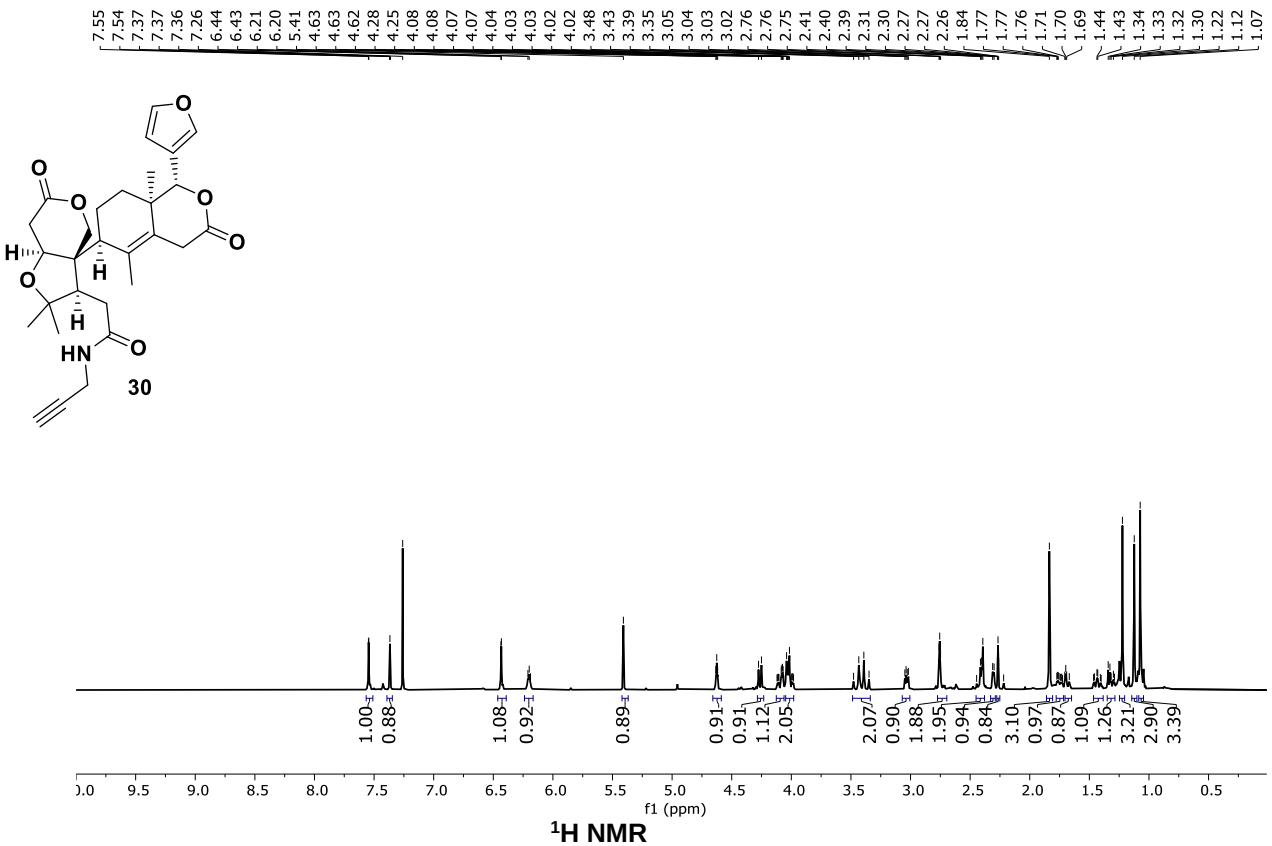
29

^{1}H NMR

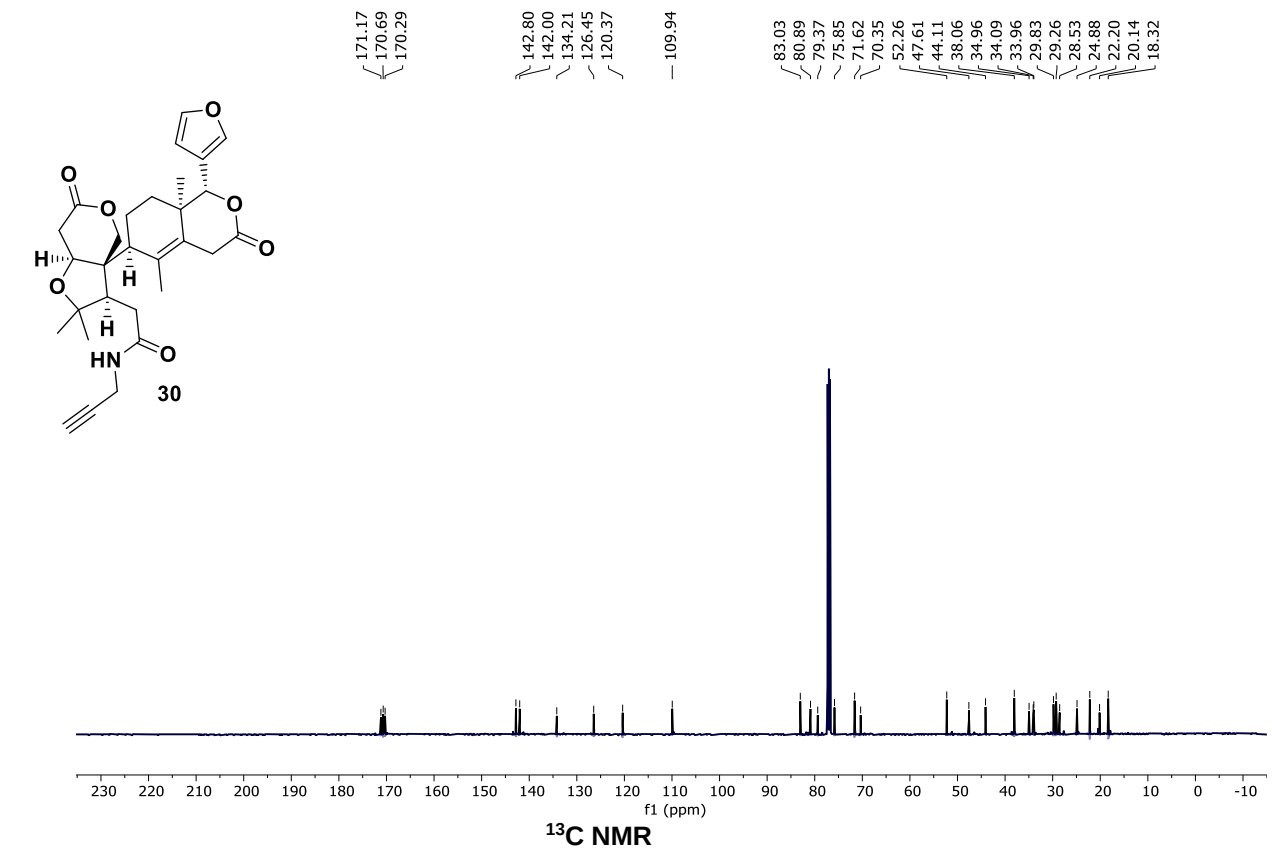


29

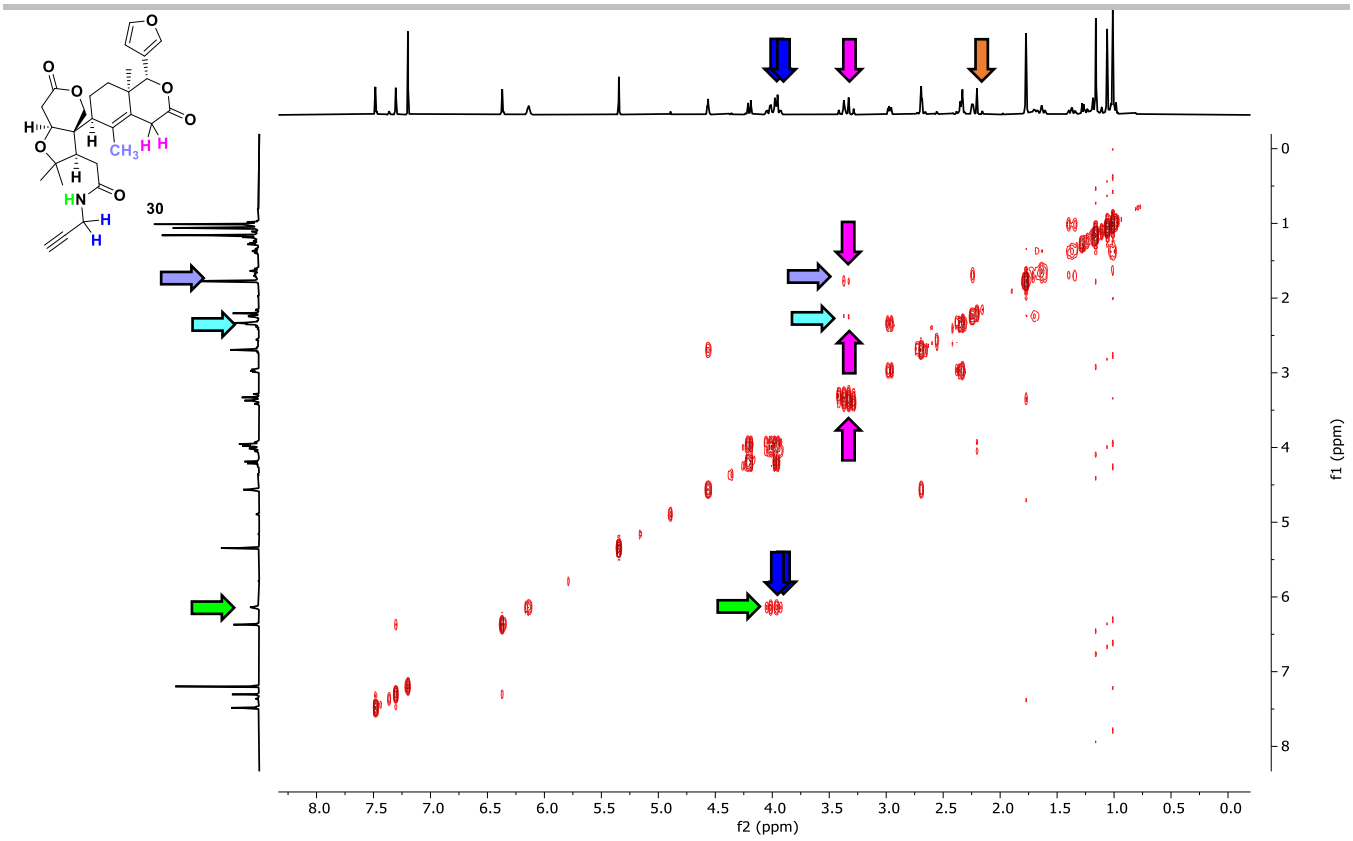
^{13}C NMR



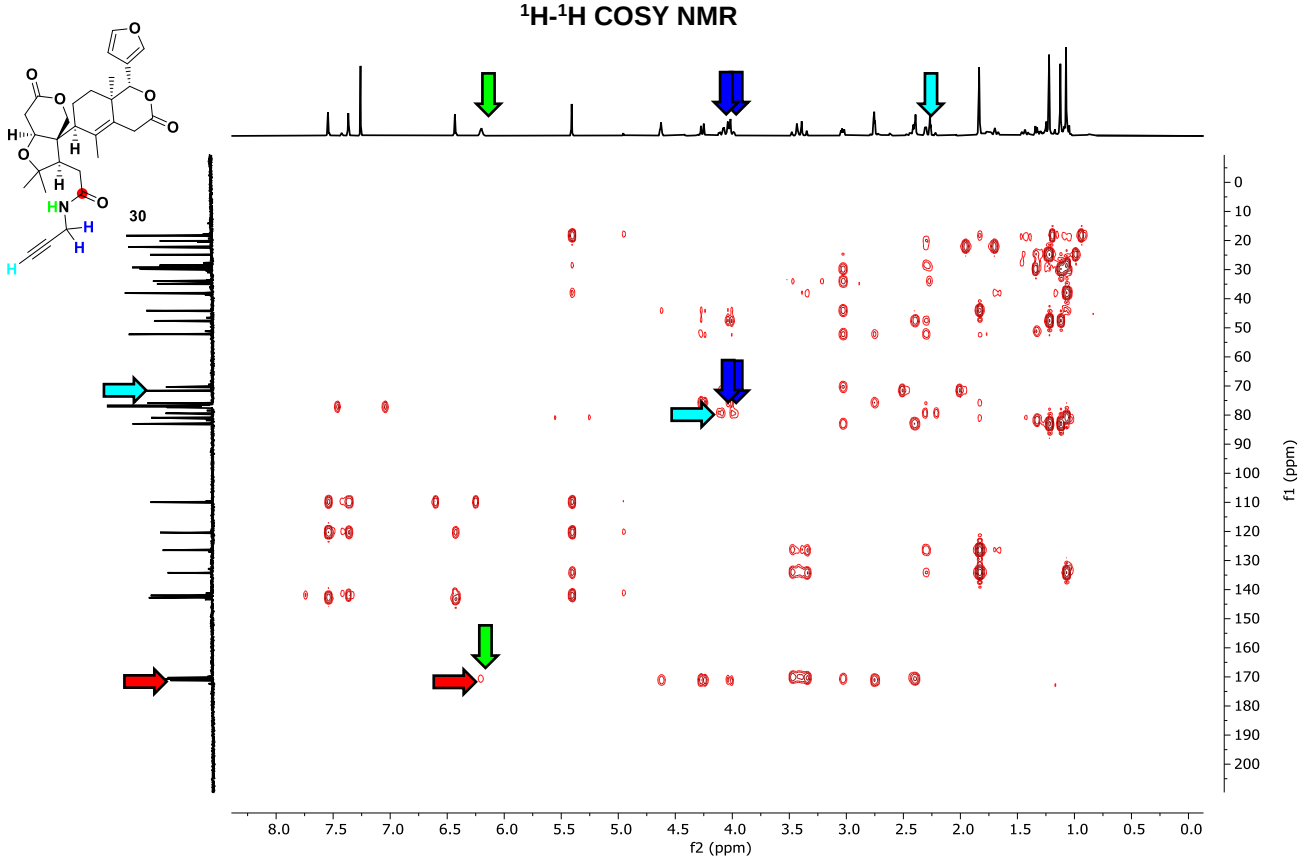
^{1}H NMR



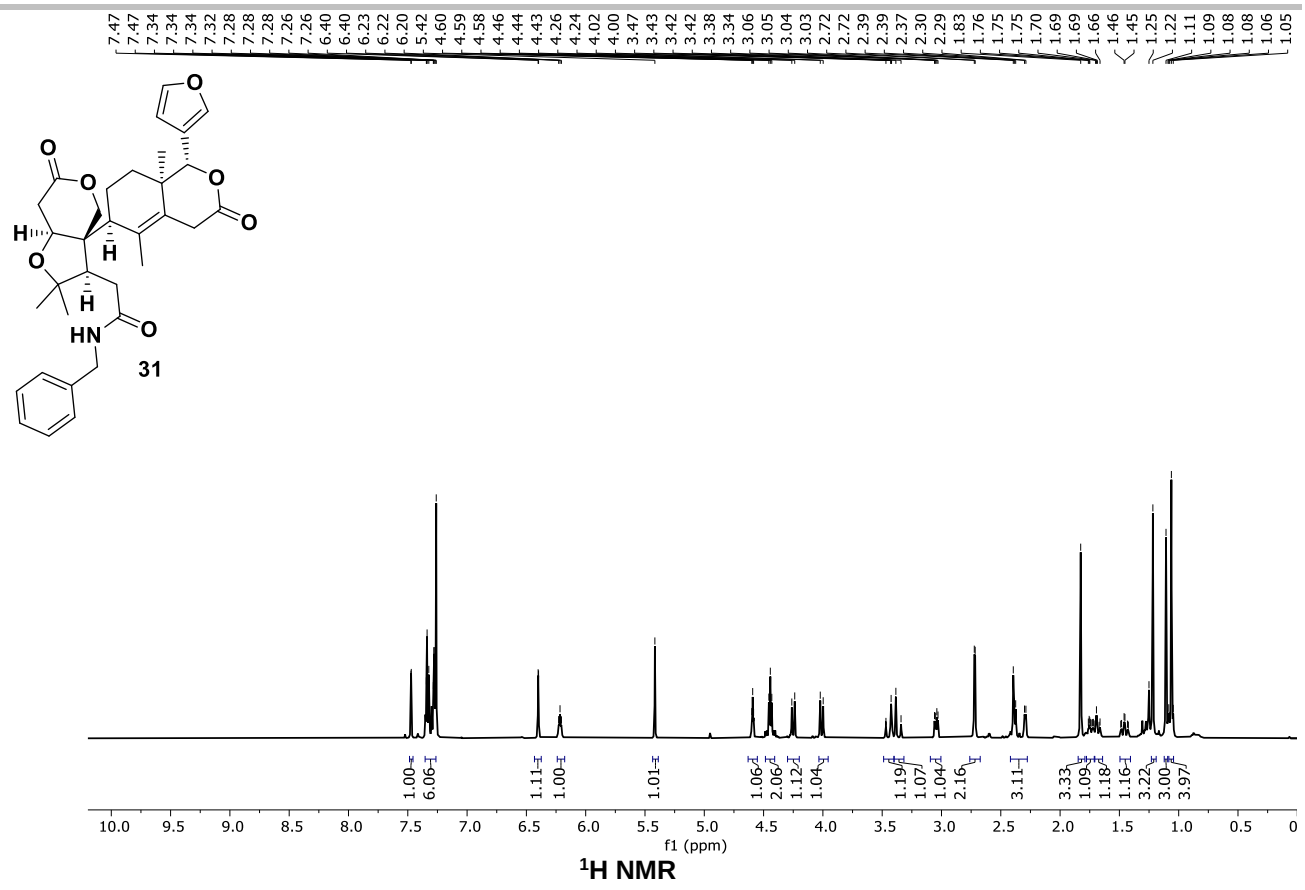
^{13}C NMR



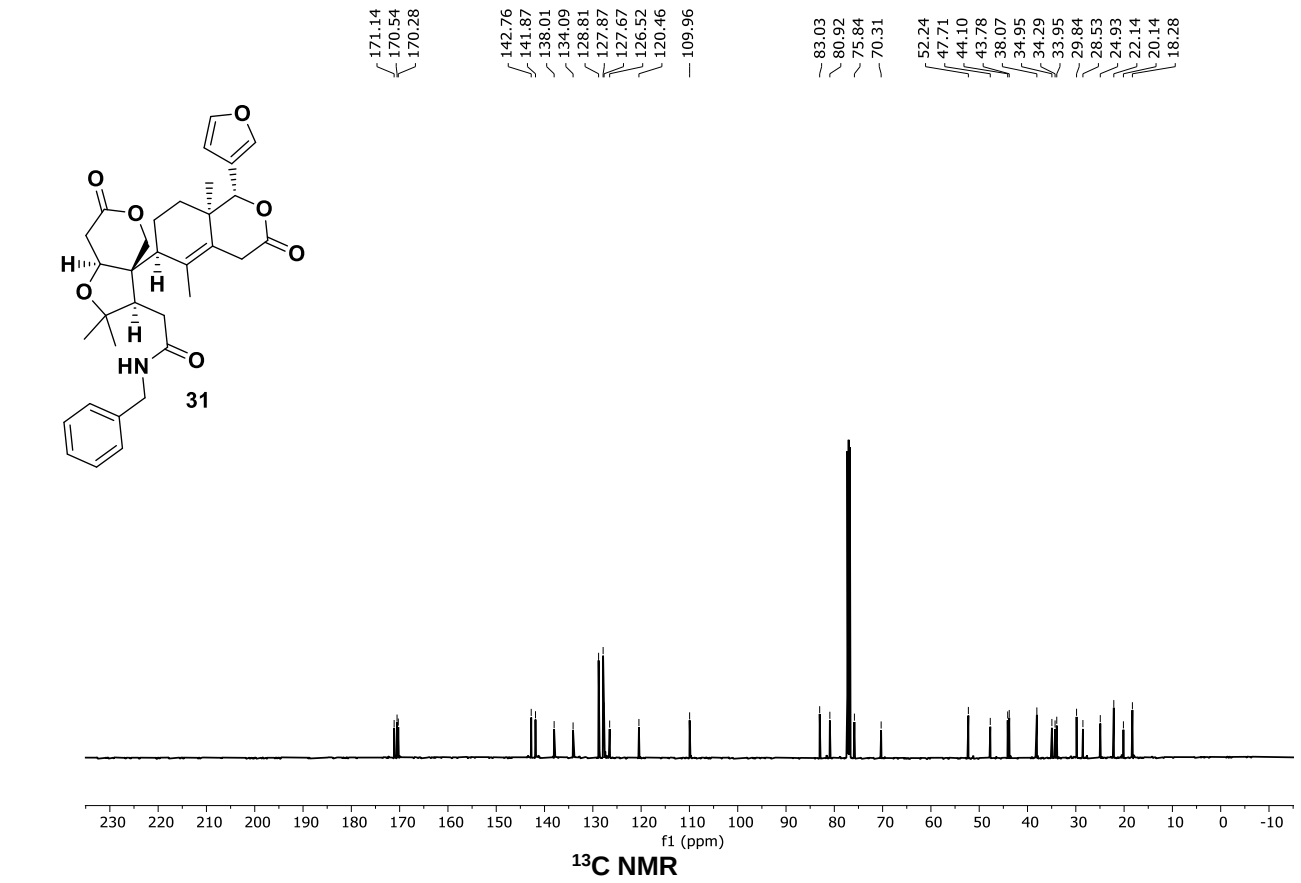
^{1}H-^{1}H COSY NMR



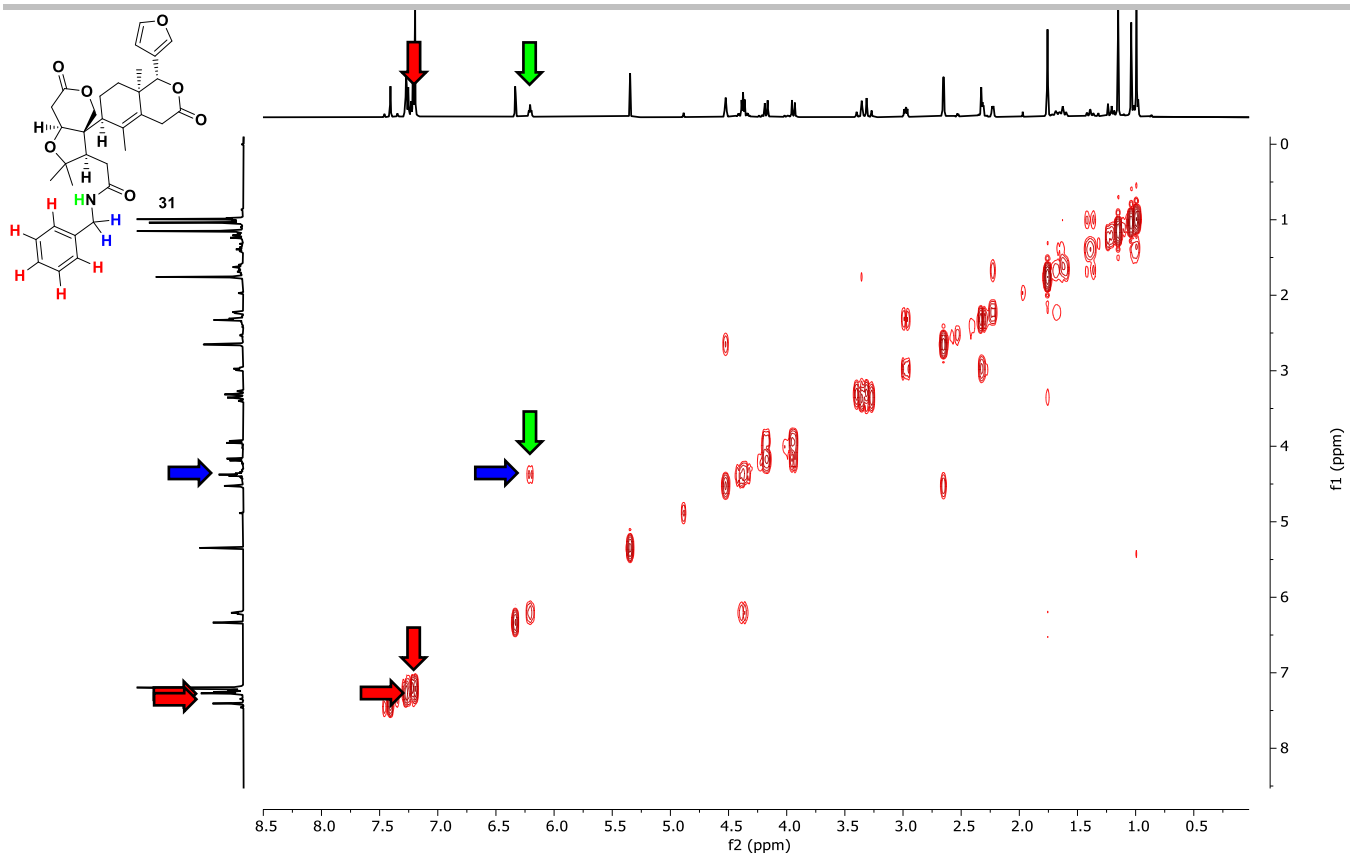
^{1}H-^{13}C HMBC NMR



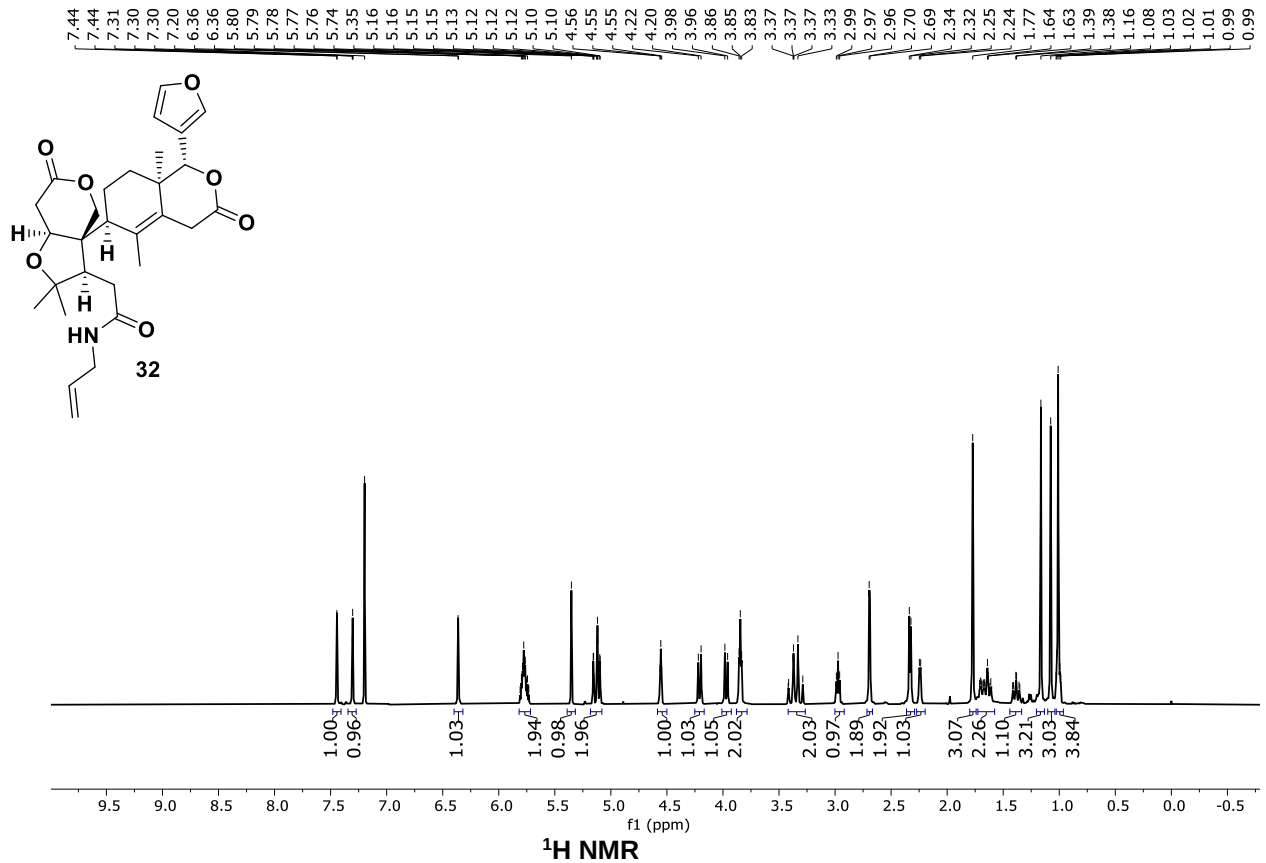
^{1}H NMR



^{13}C NMR

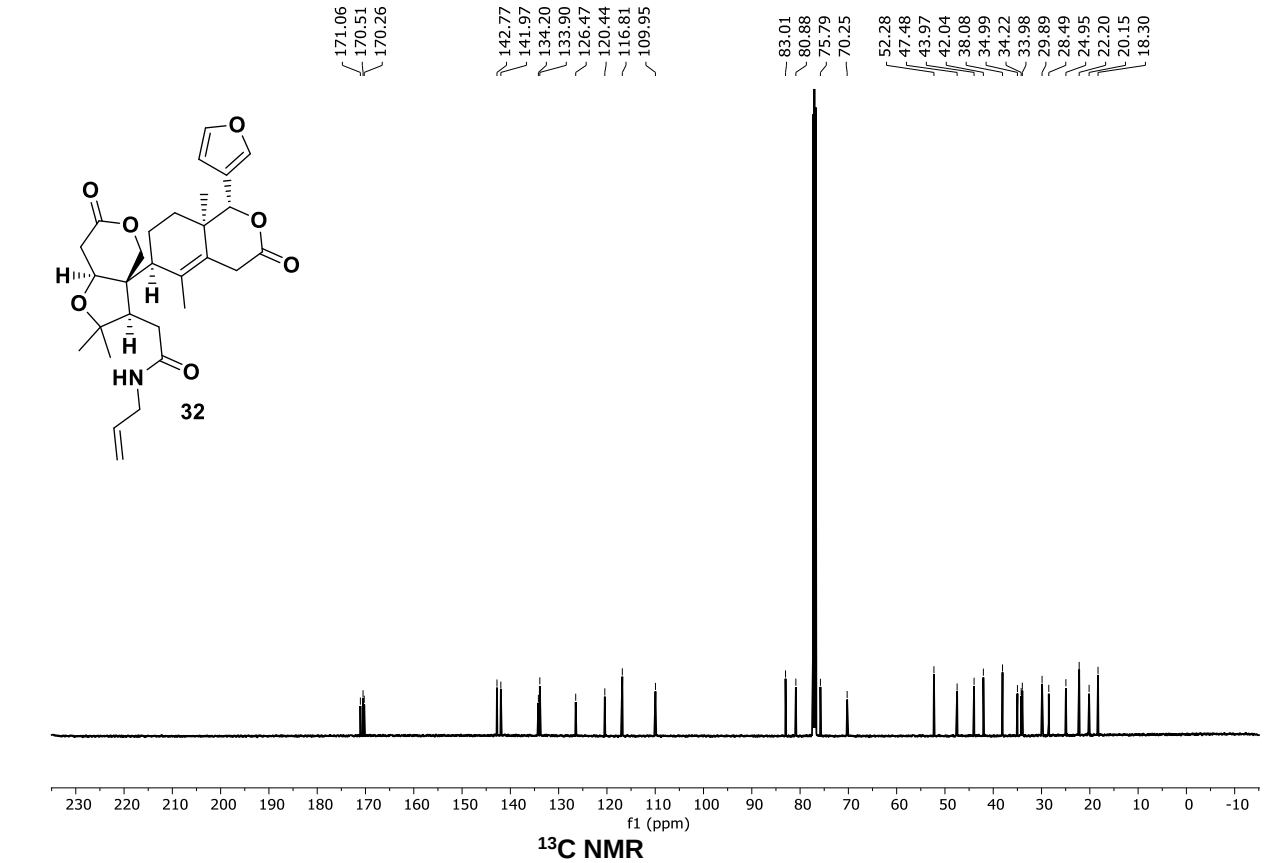


^{1}H-^{1}H COSY NMR



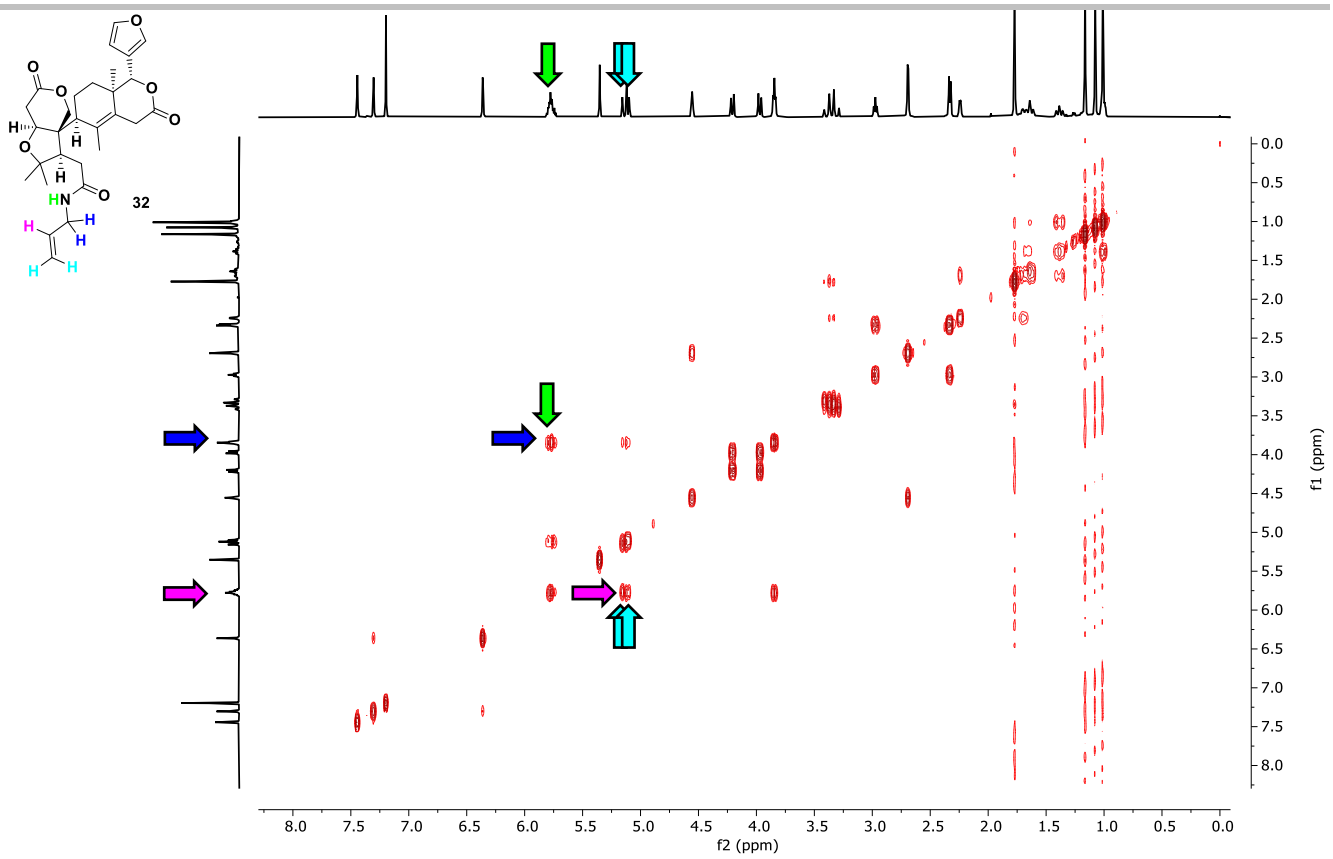
32

^{1}H NMR

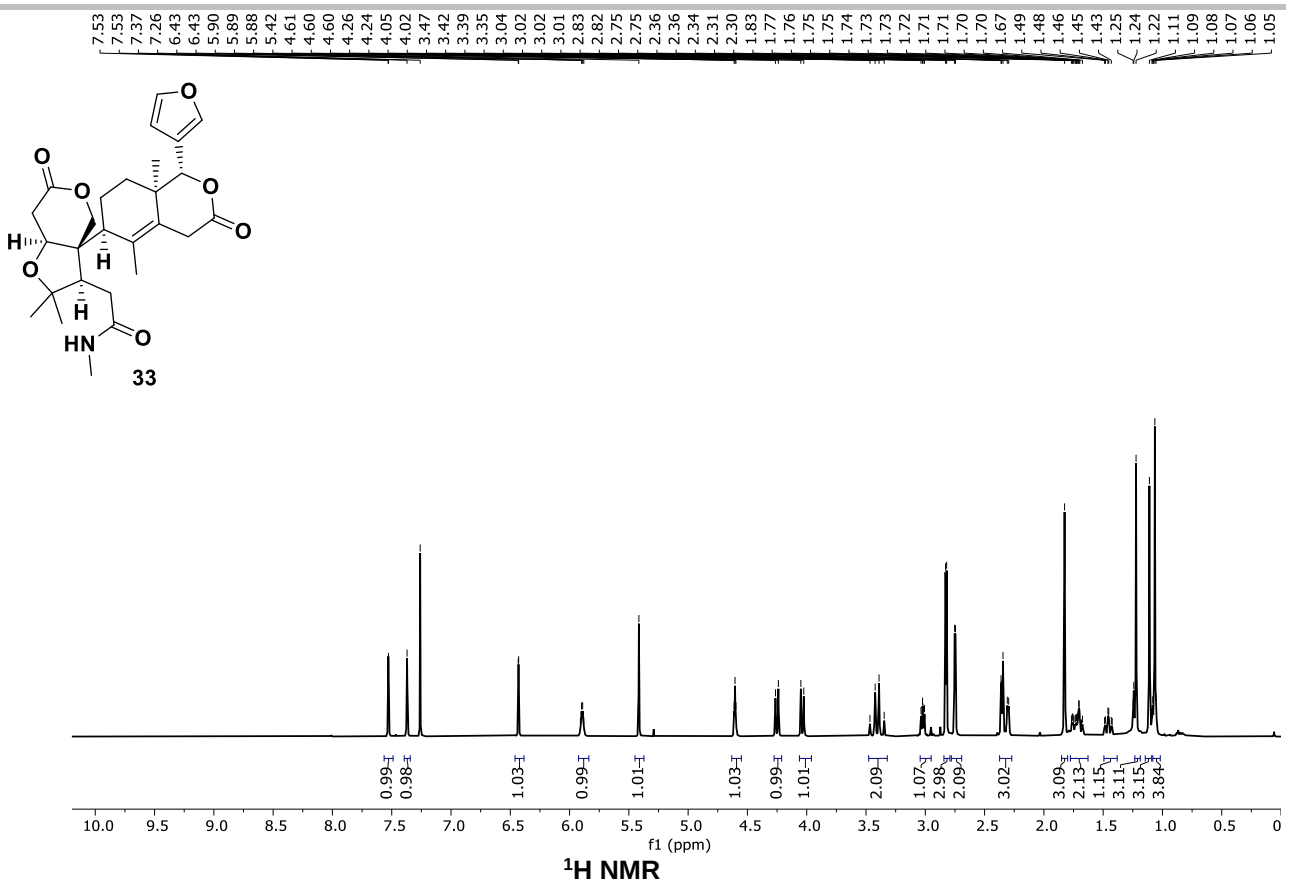


32

^{13}C NMR

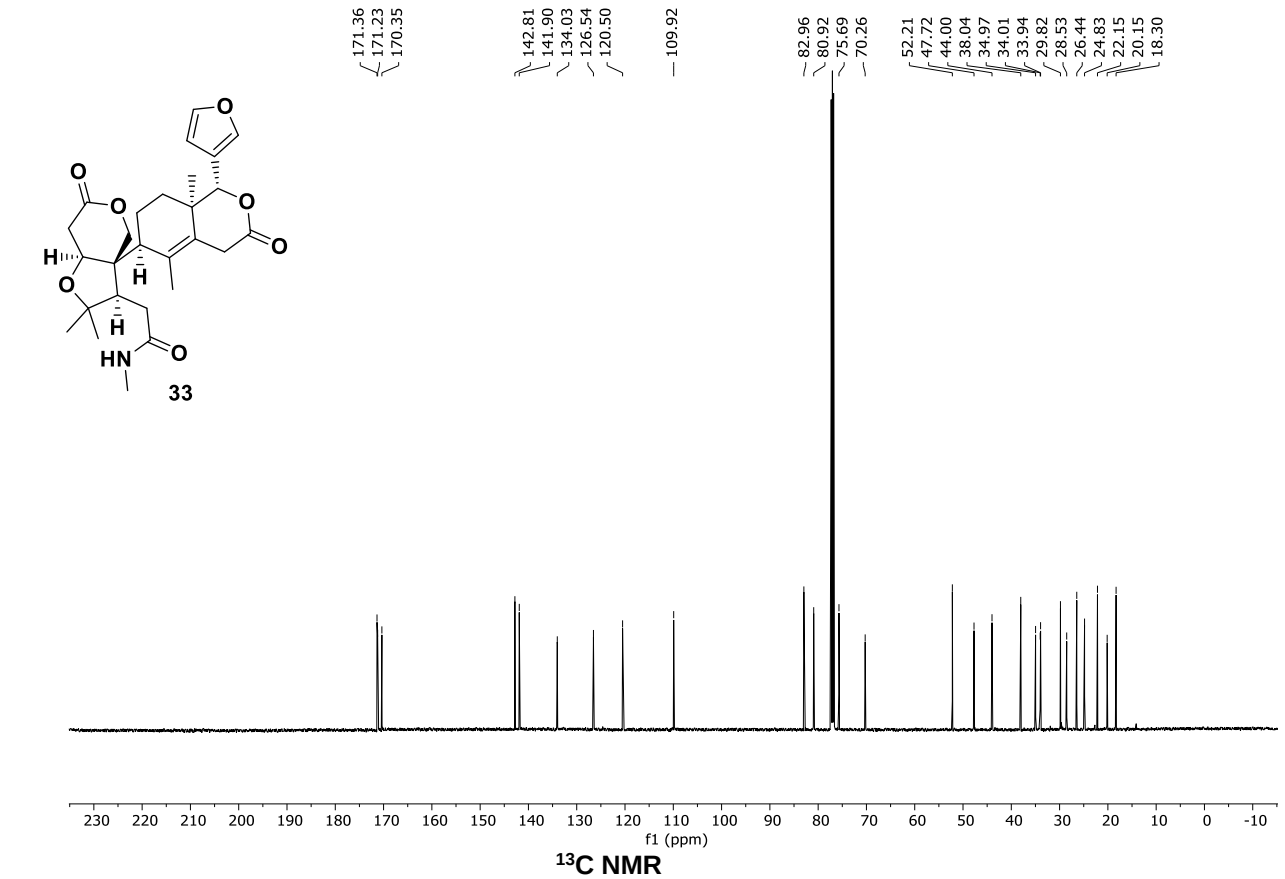


^{1}H-^{1}H COSY NMR



33

^{1}H NMR



33

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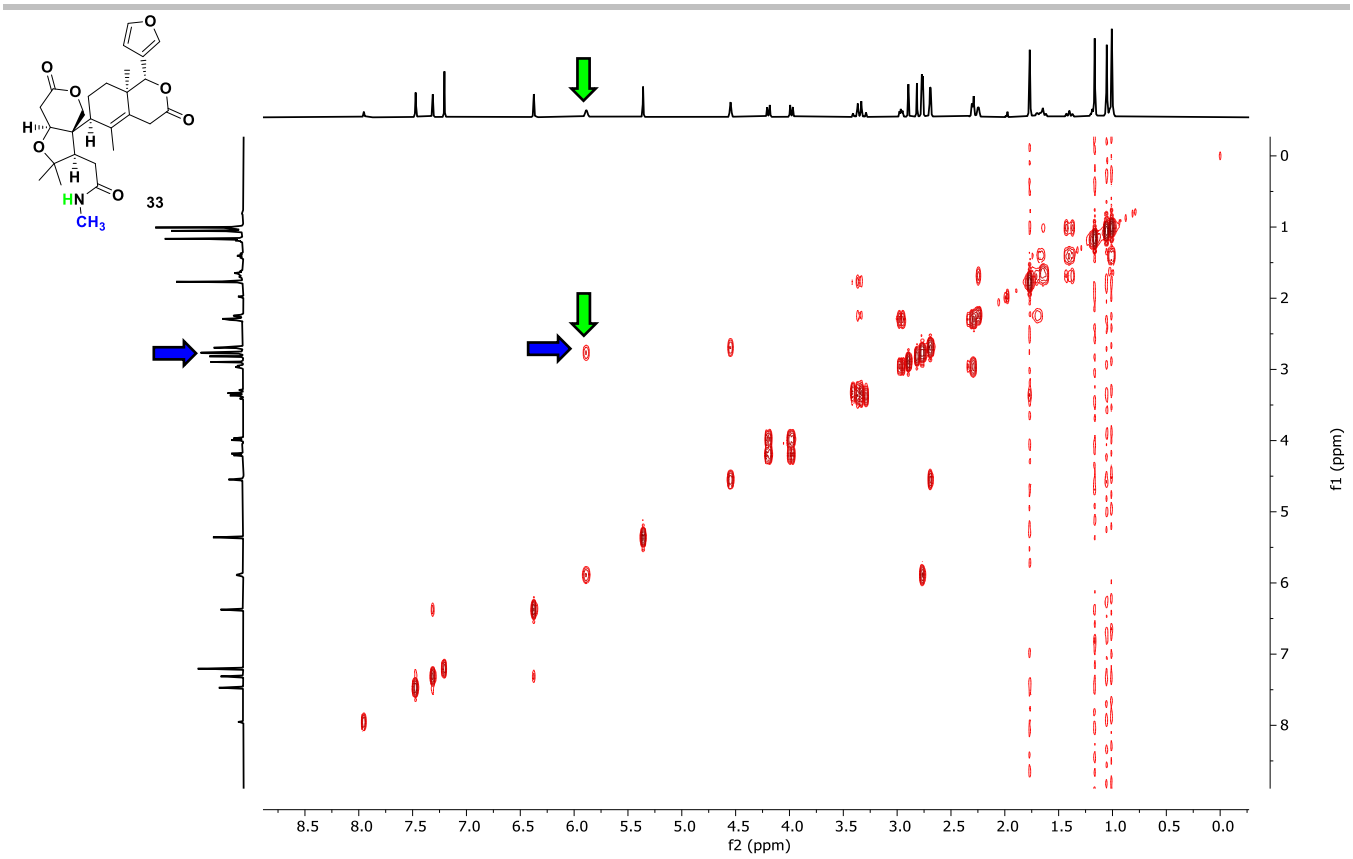
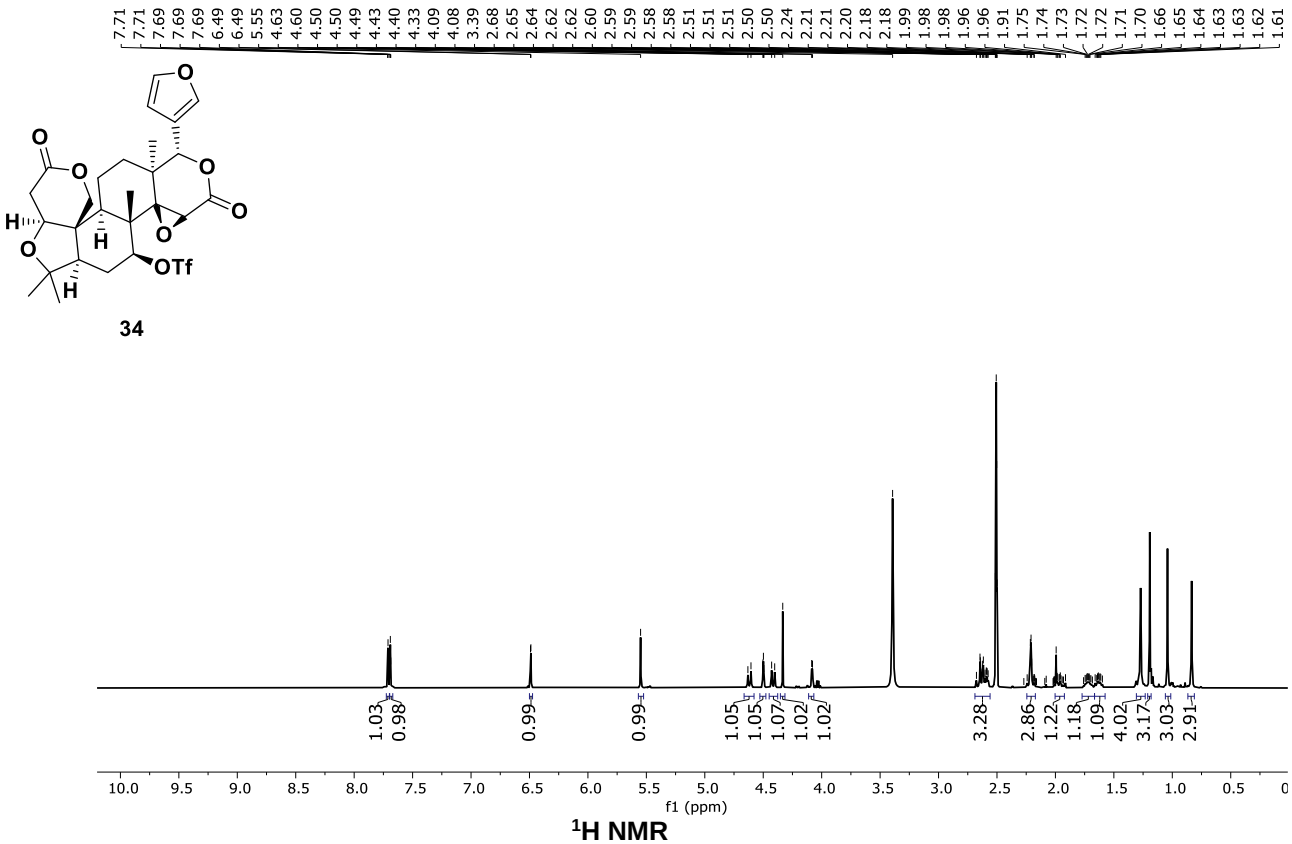
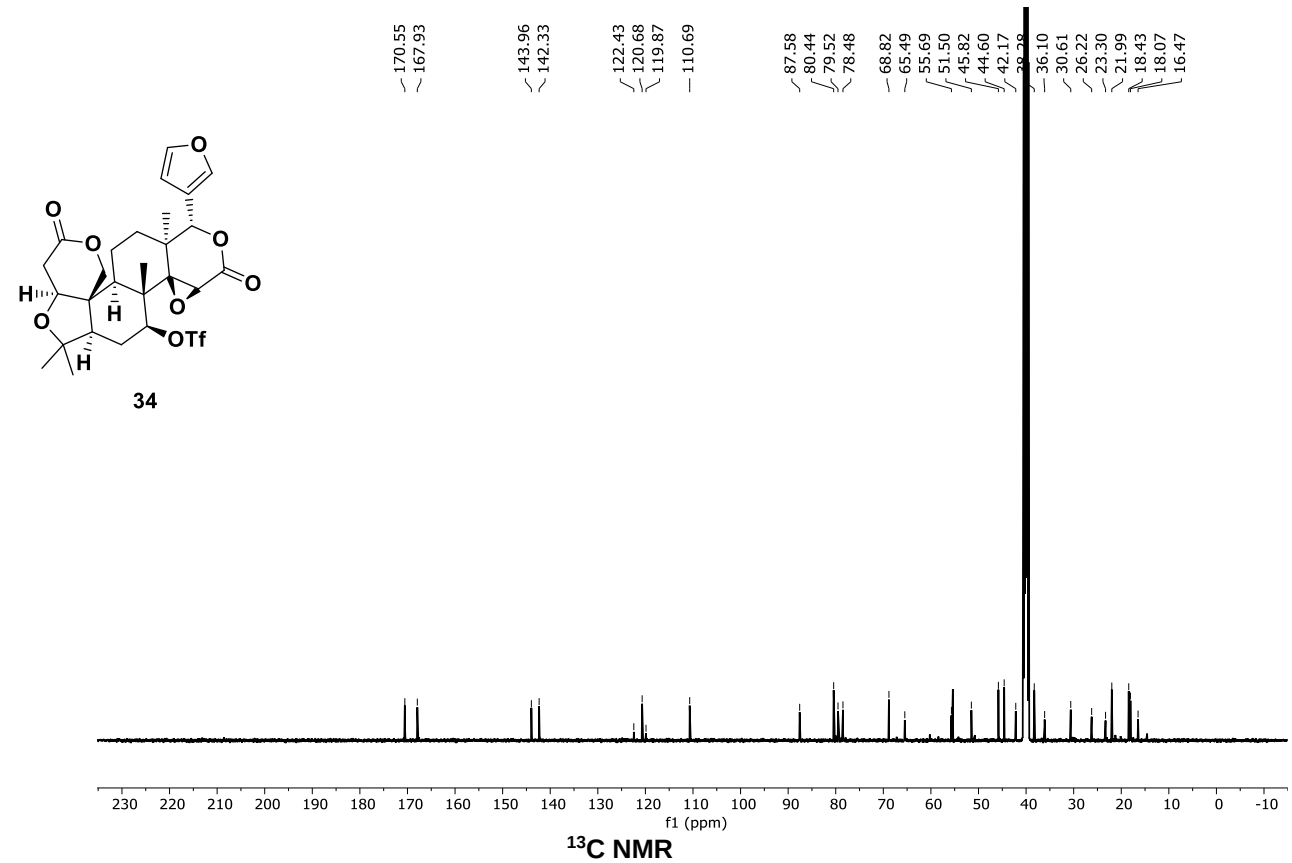


^{1}H-^{1}H COSY NMR



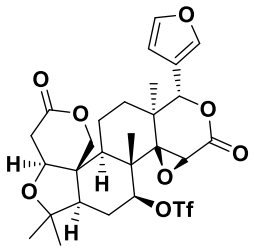
34

^{1}H NMR



34

^{13}C NMR


O
O
O
O
O
H
O
H
OTf
H

34

-77.7474
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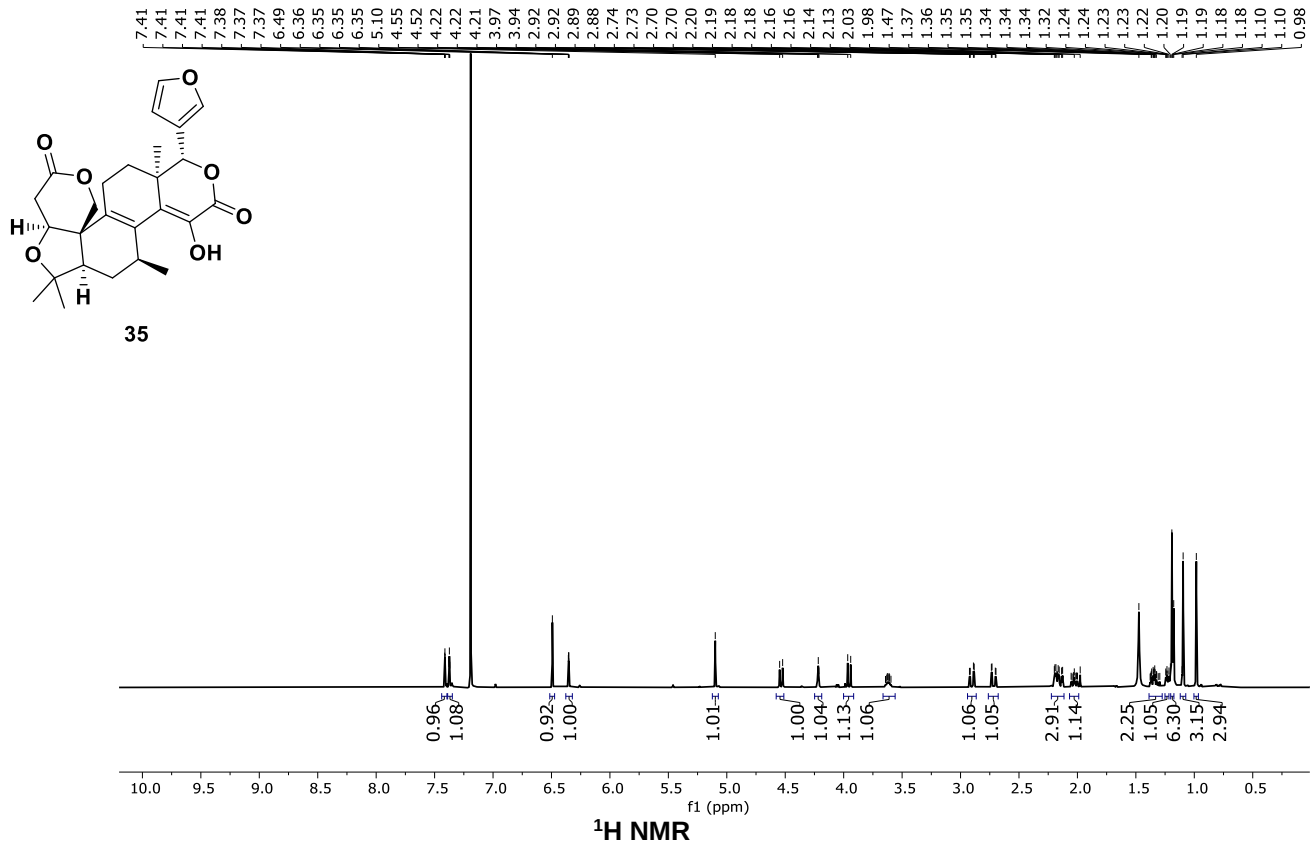
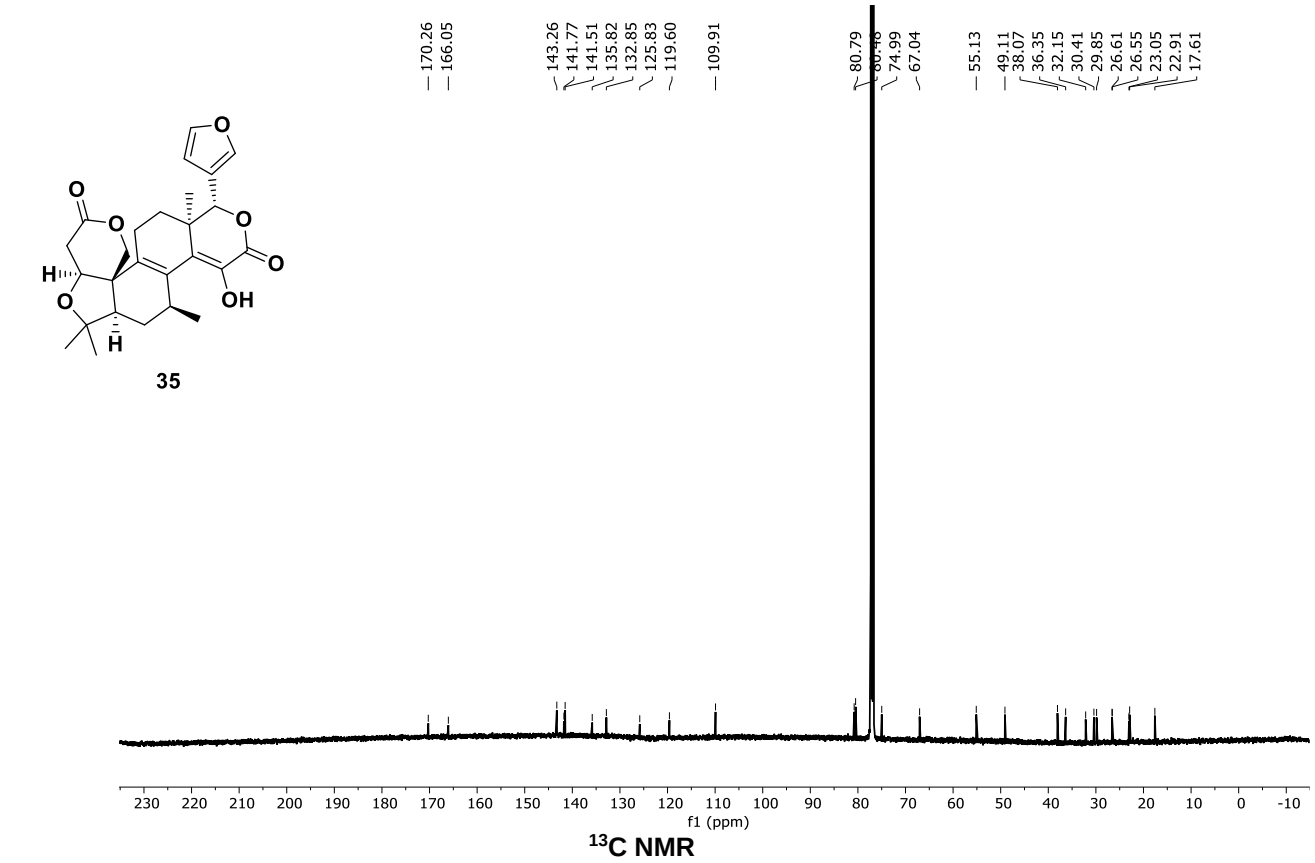
f1 (ppm)

^{19}F NMR



35

^{1}H NMR



35

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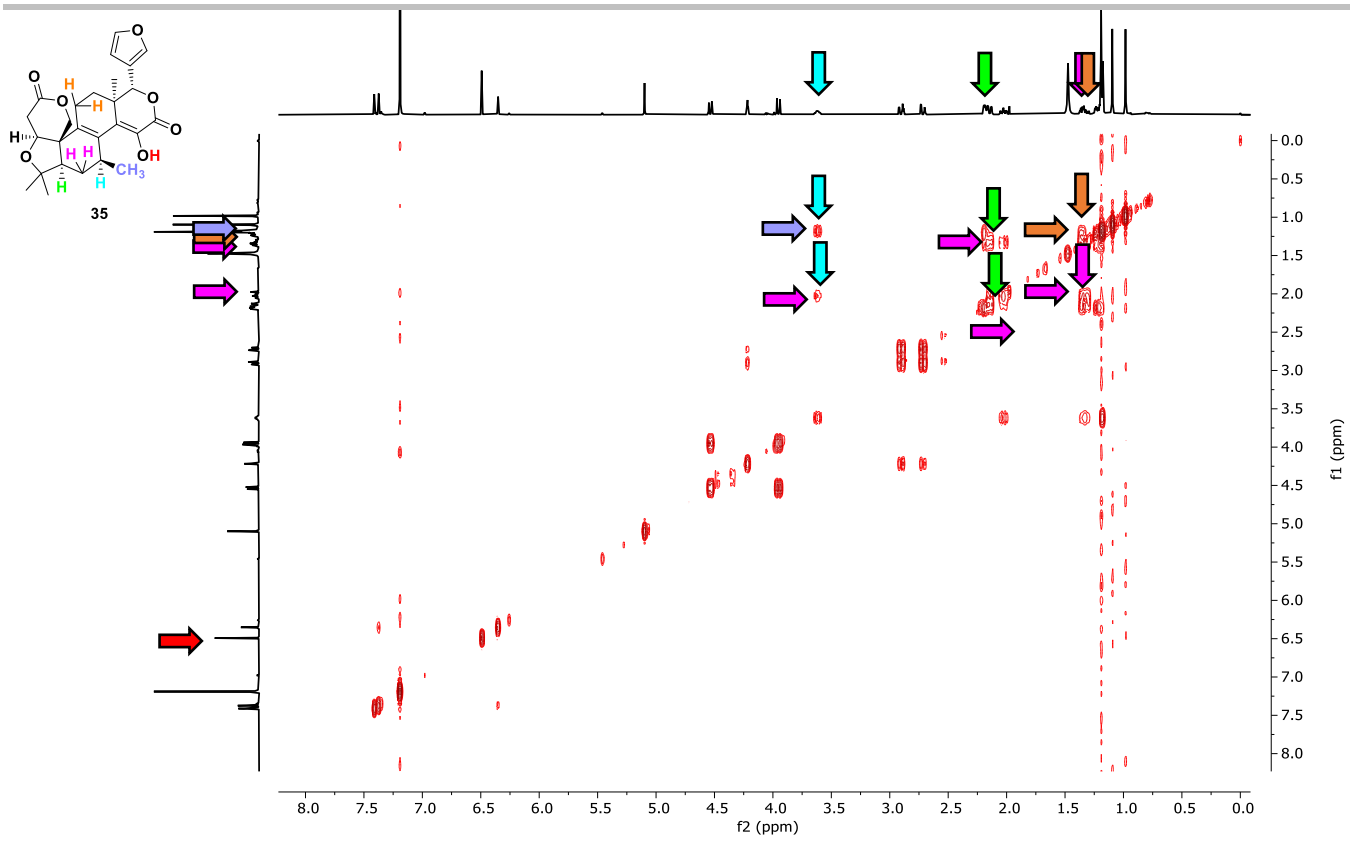
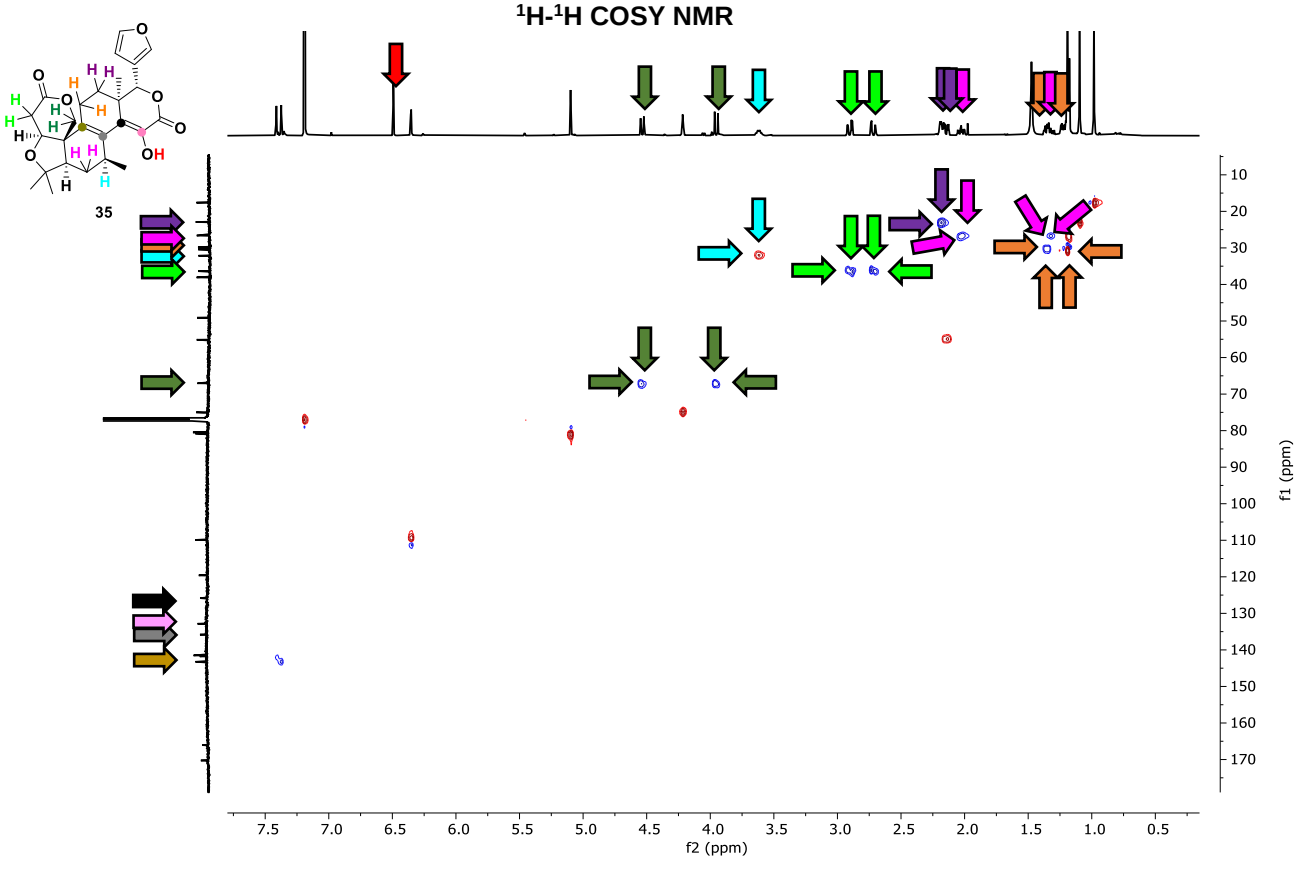


^{1}H-^{1}H COSY NMR



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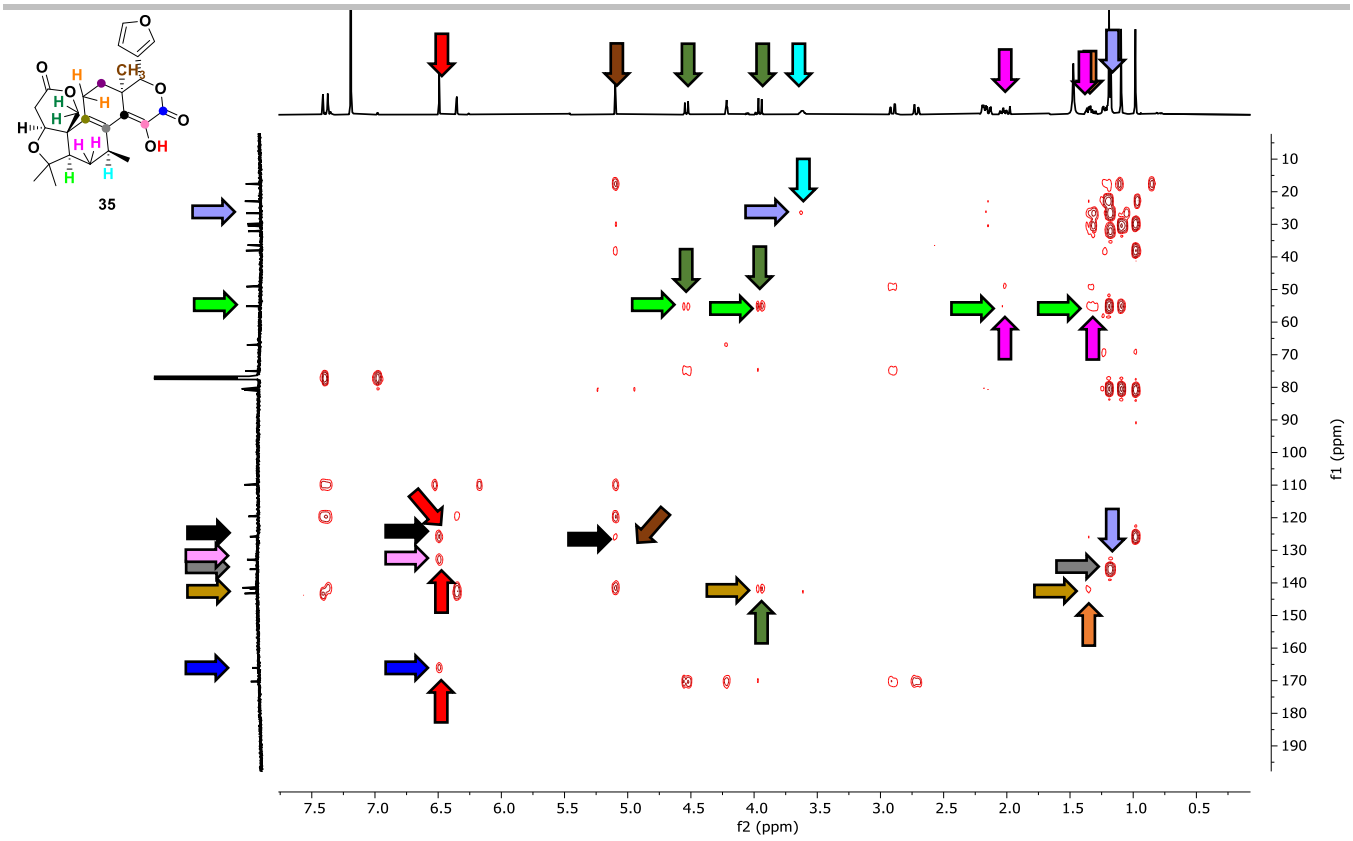
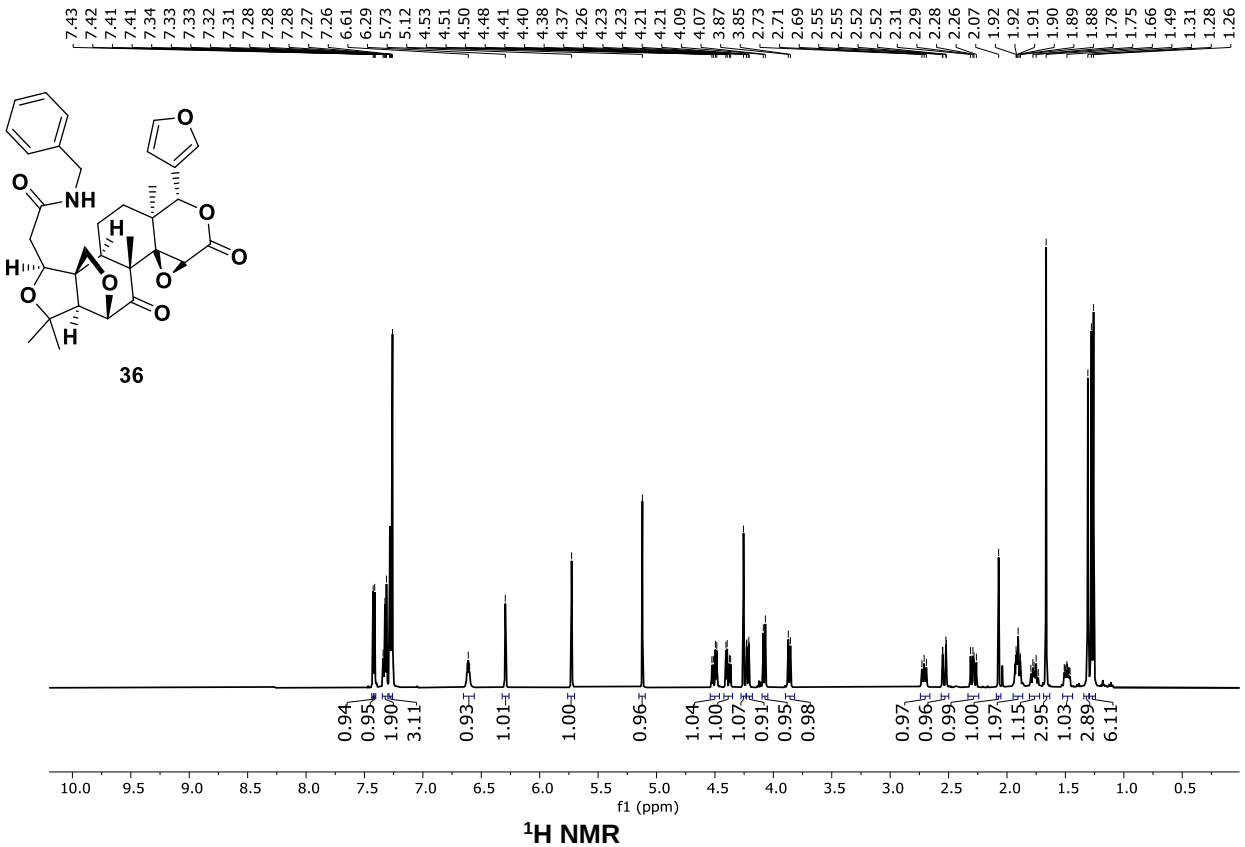
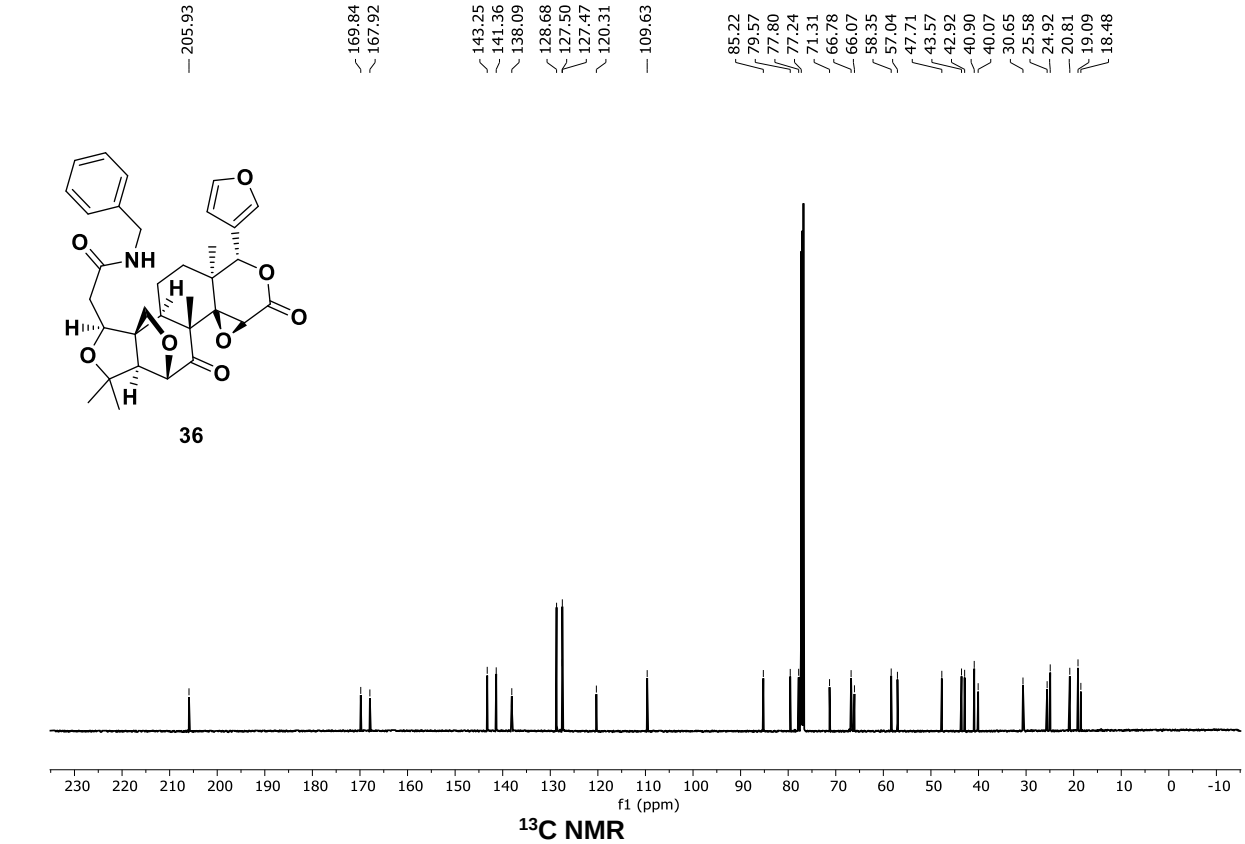


^{1}H-^{13}C HMBC NMR



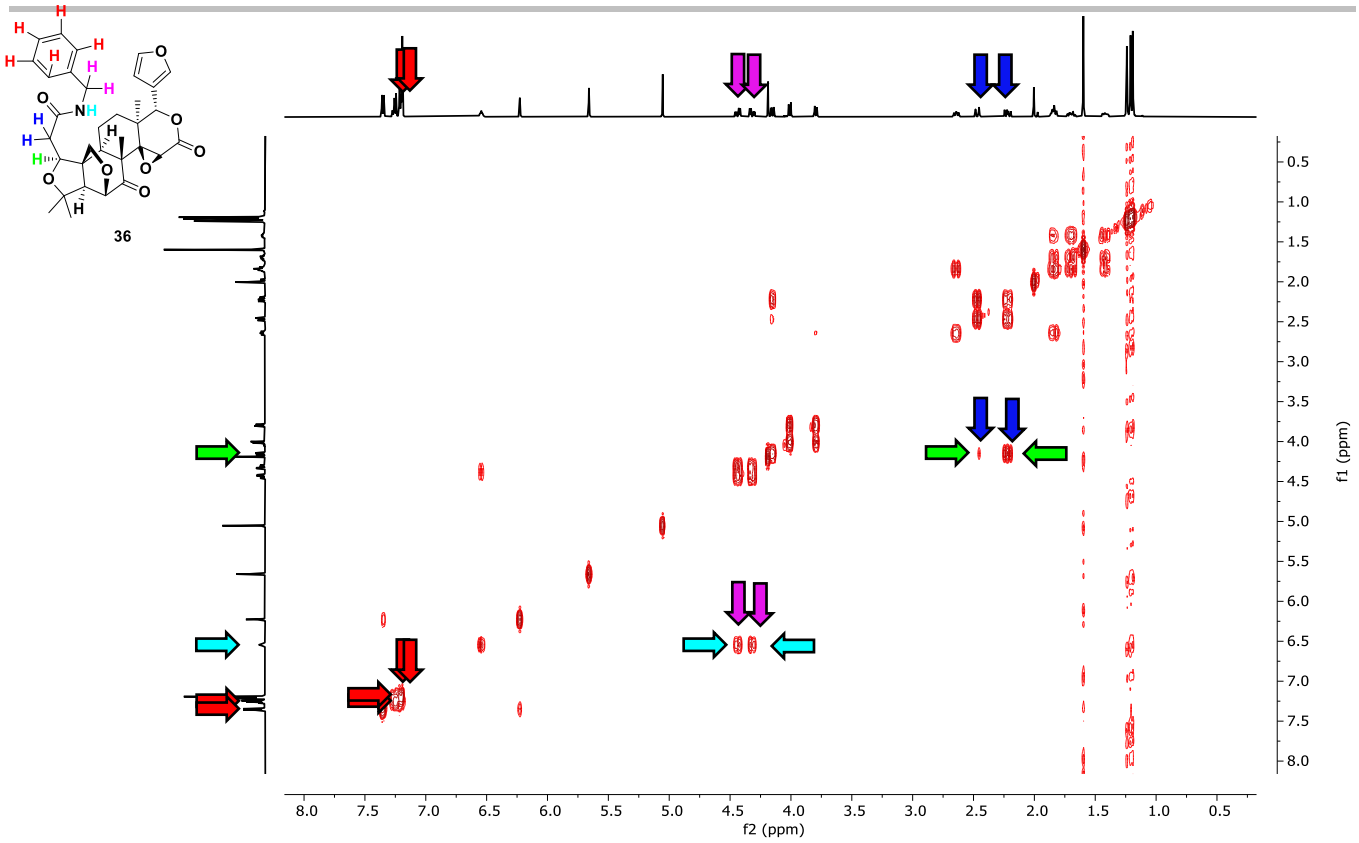
36

^{1}H NMR

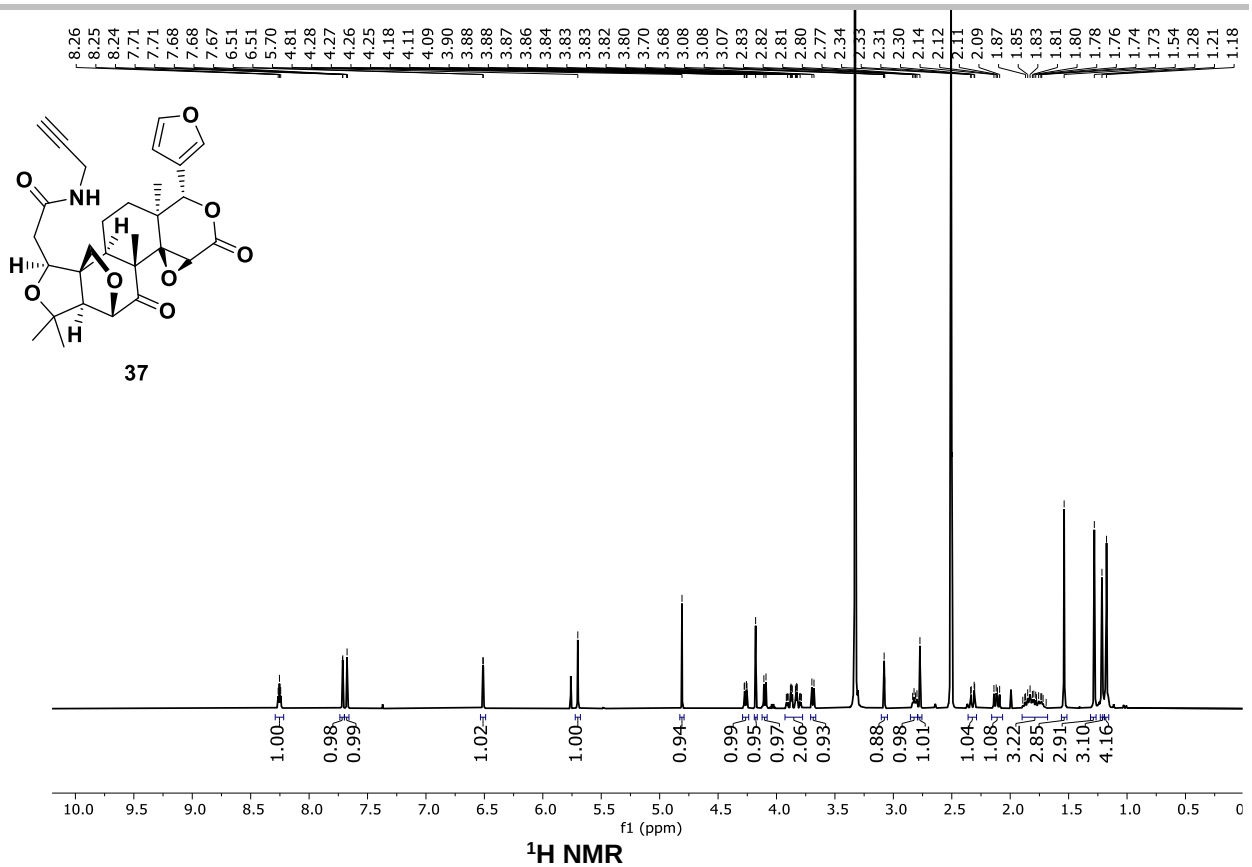


36

^{13}C NMR

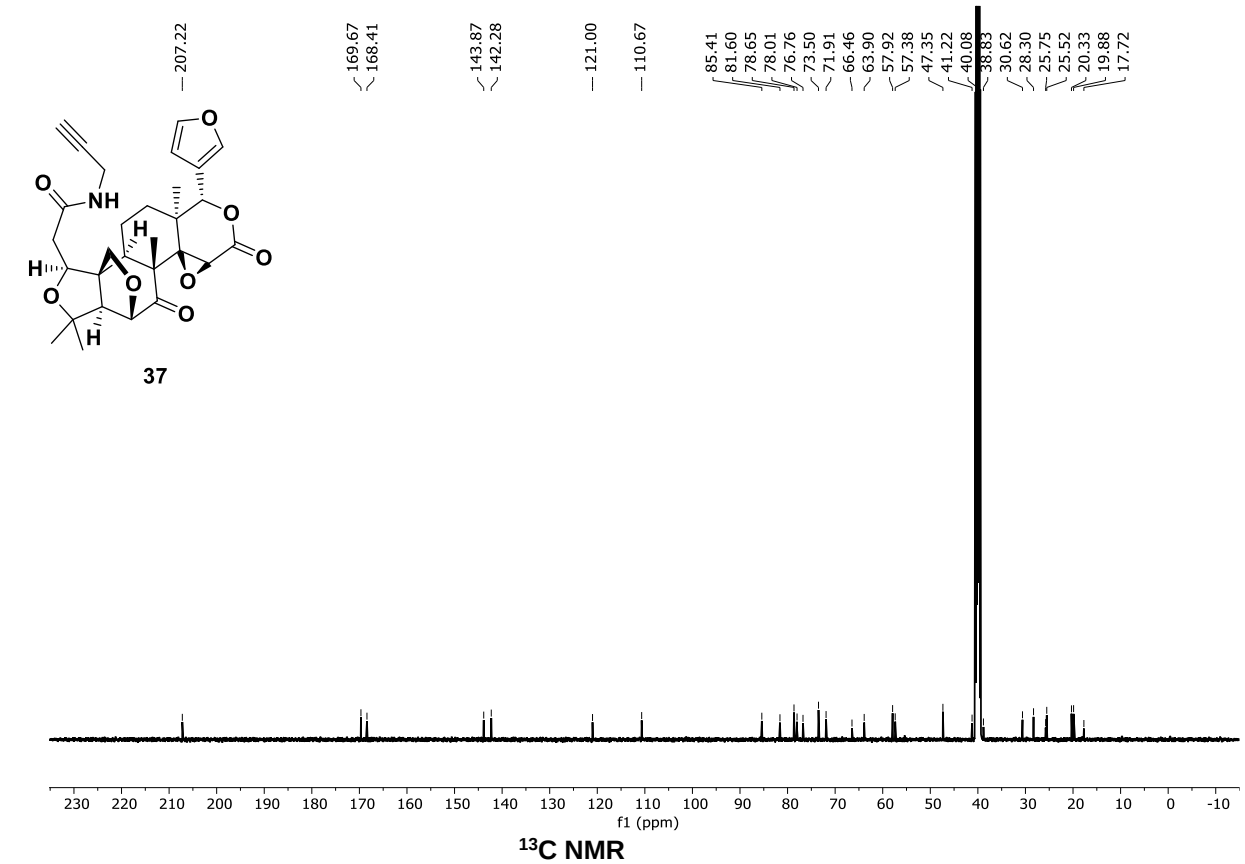


^{1}H-^{1}H COSY NMR



37

^{1}H NMR



37

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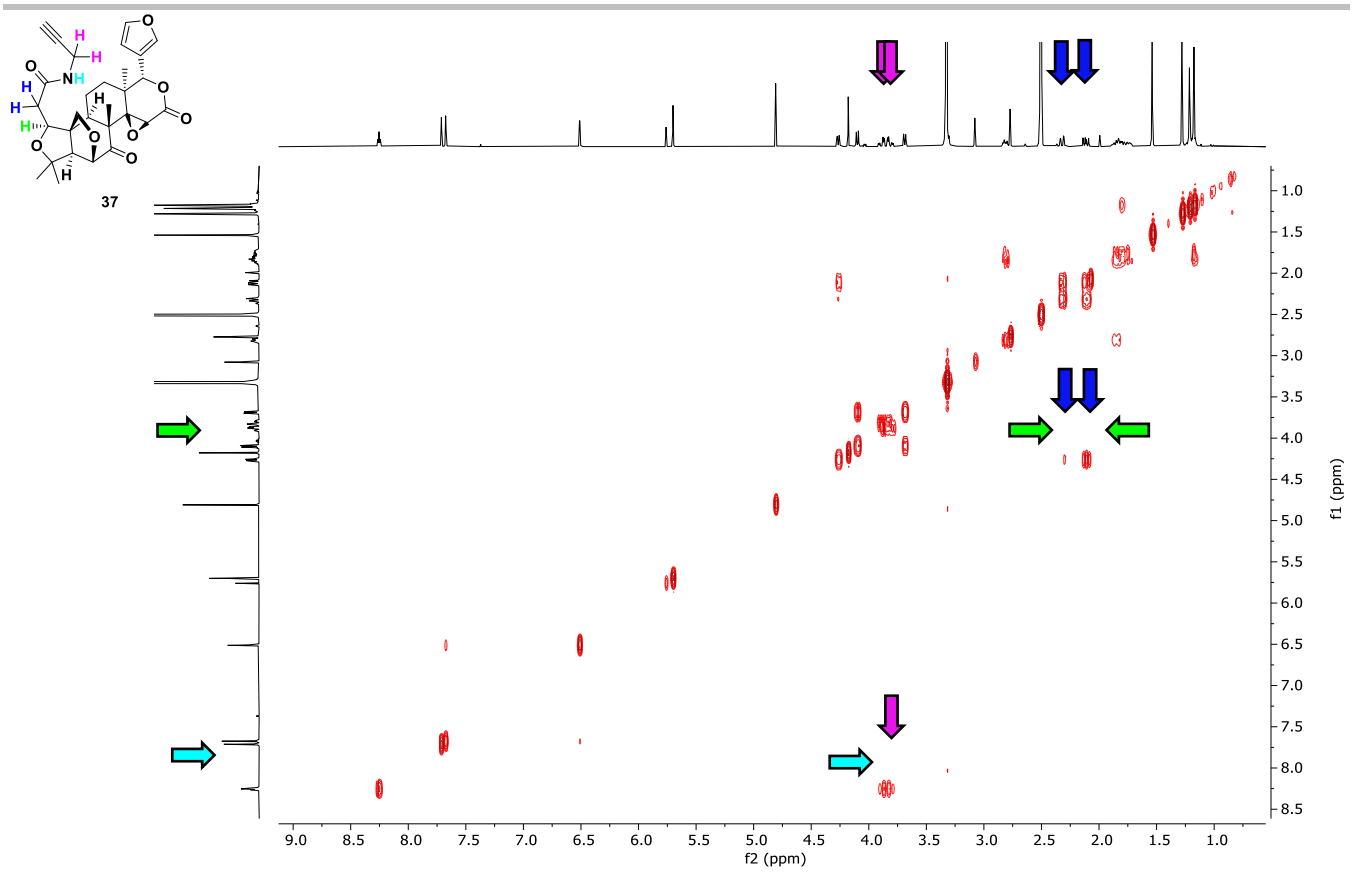
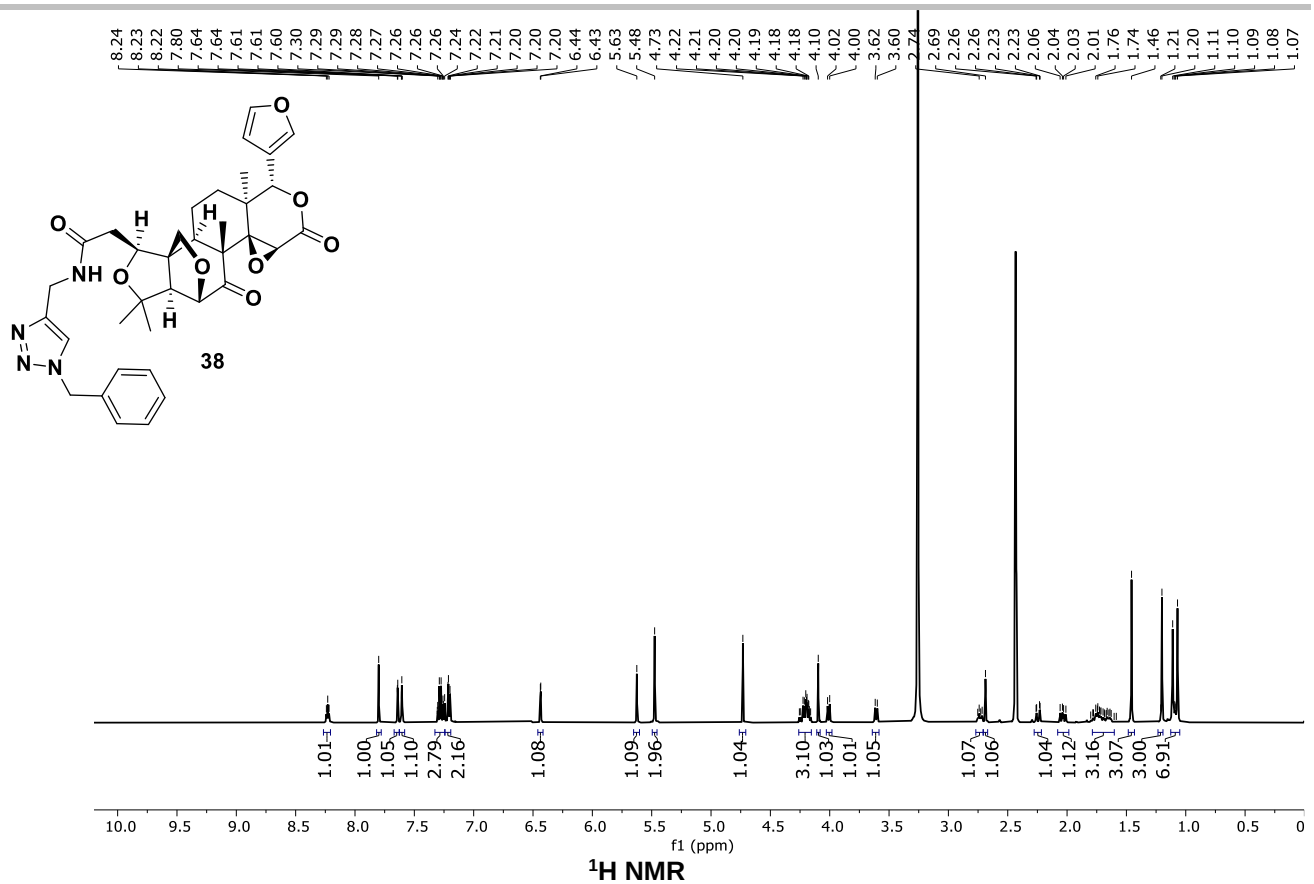
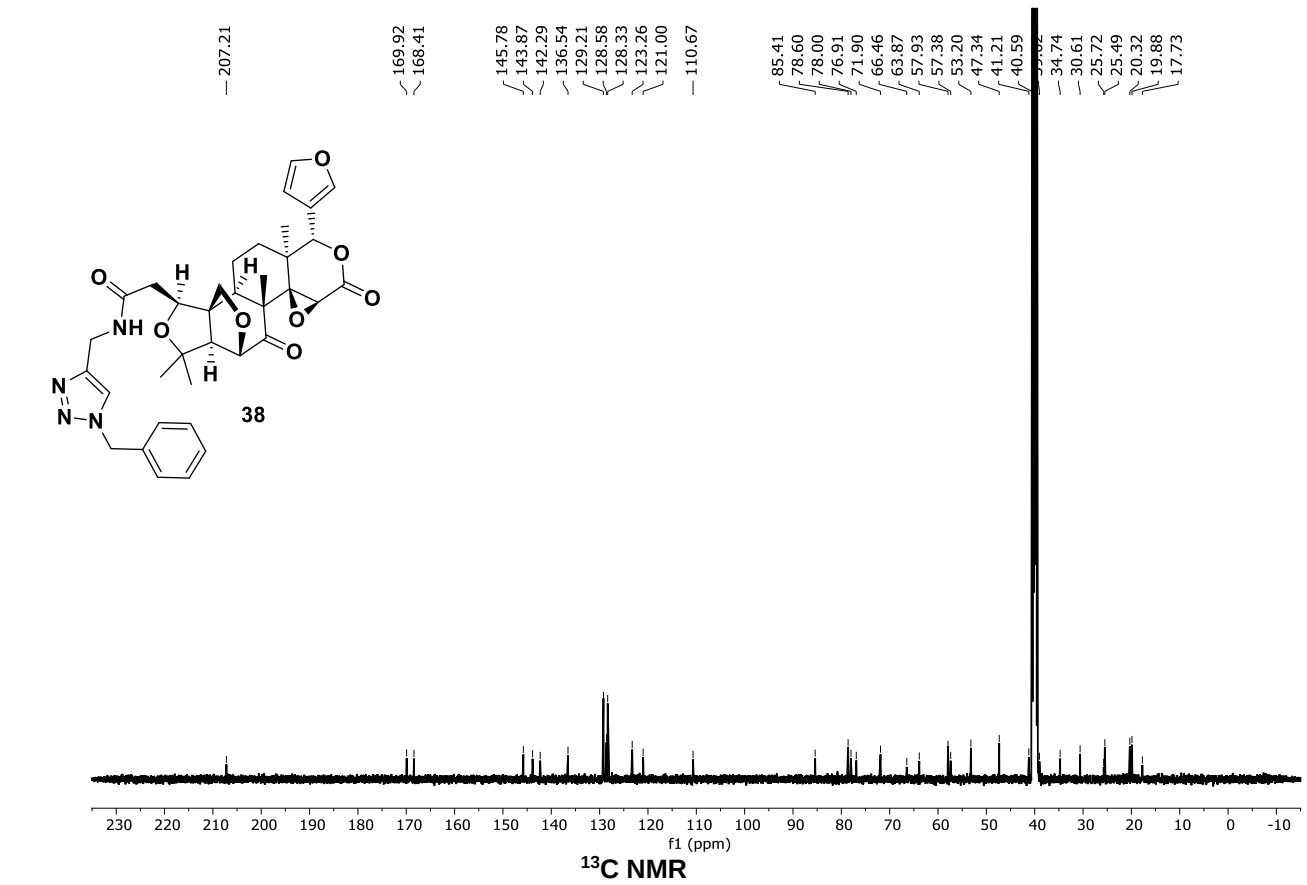


^{1}H-^{1}H COSY NMR



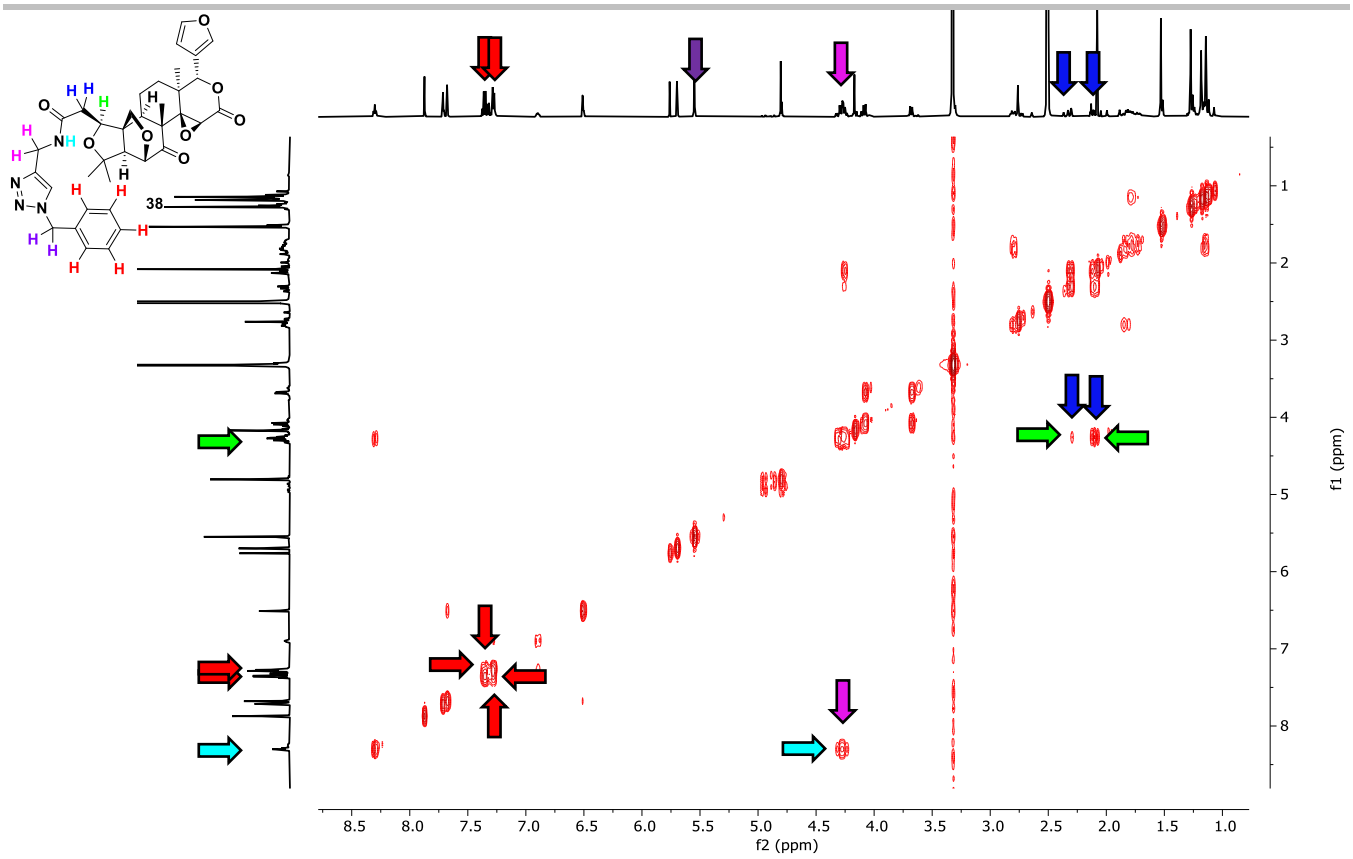
38

^{1}H NMR

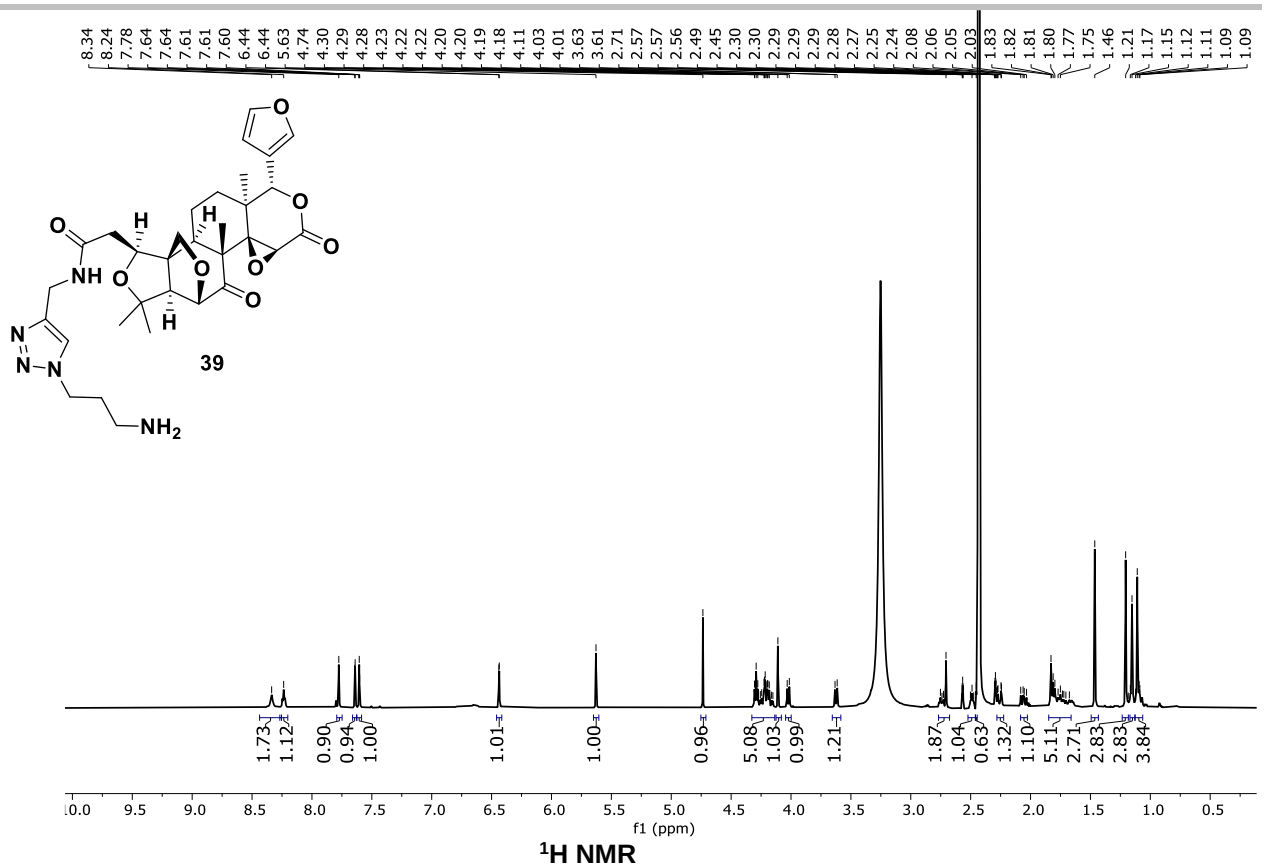


38

^{13}C NMR



^{1}H-^{1}H COSY NMR



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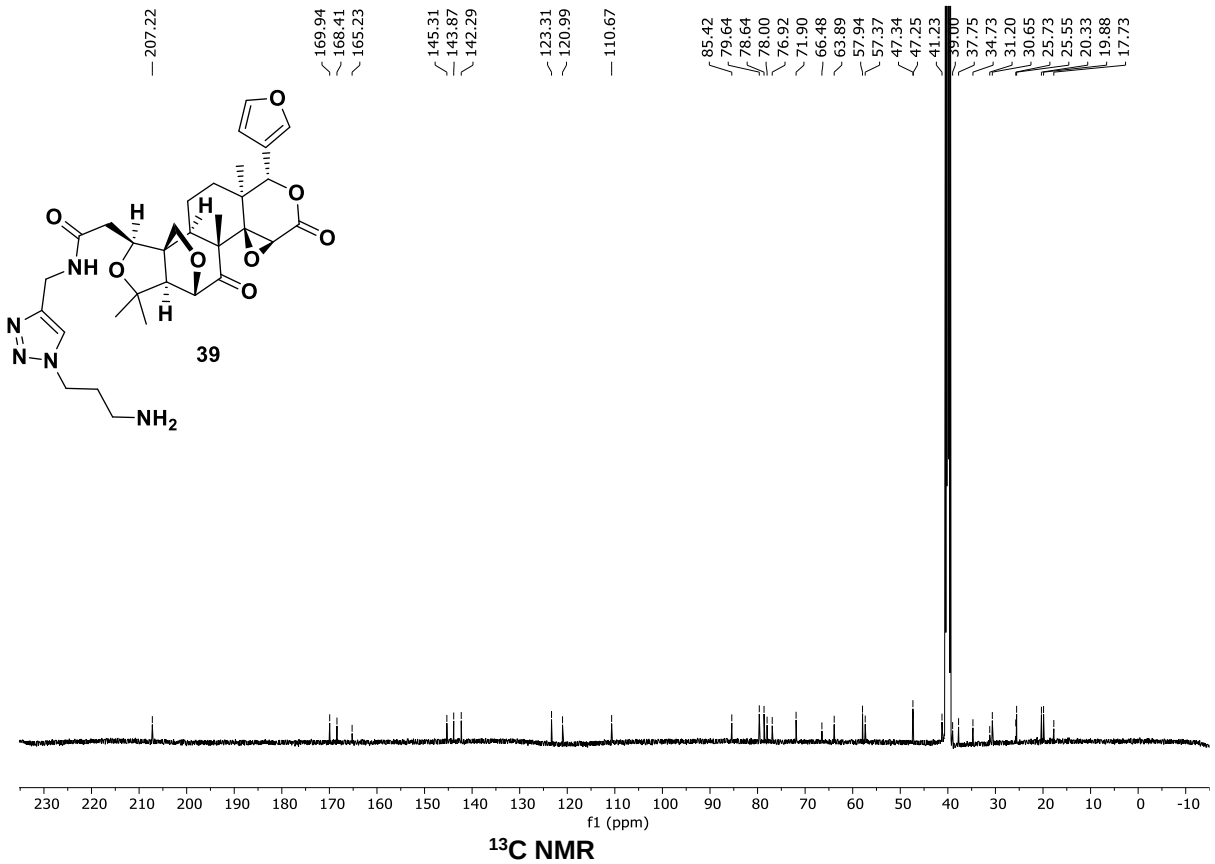
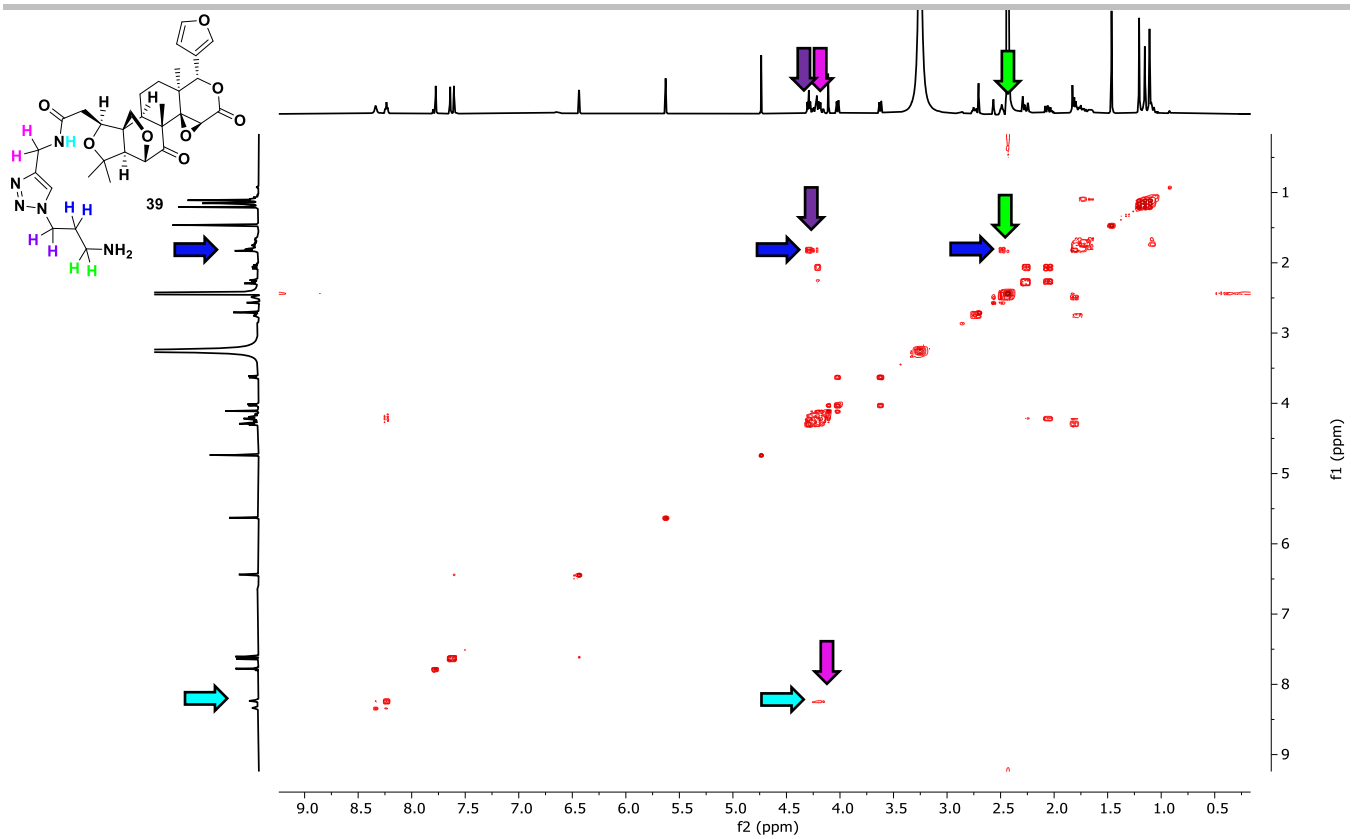


^{13}C NMR



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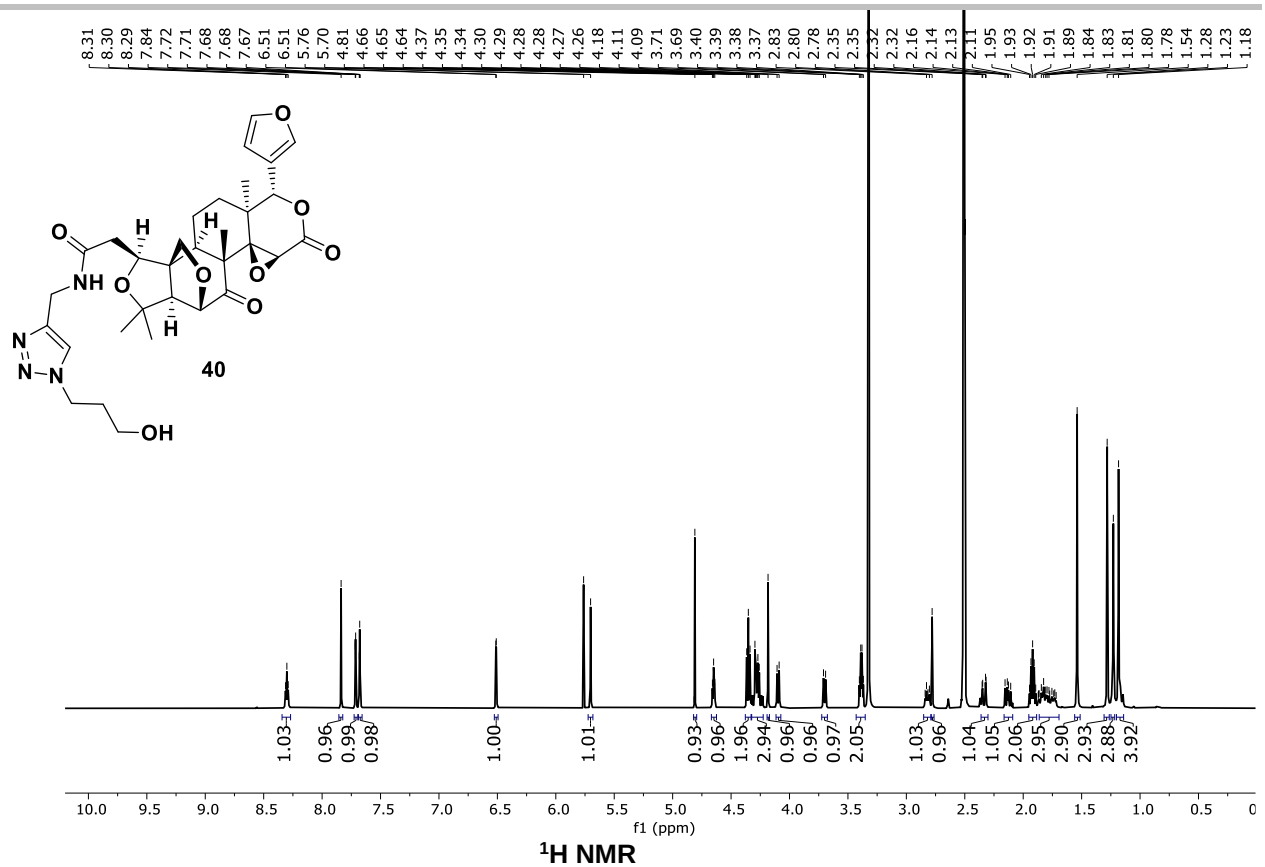
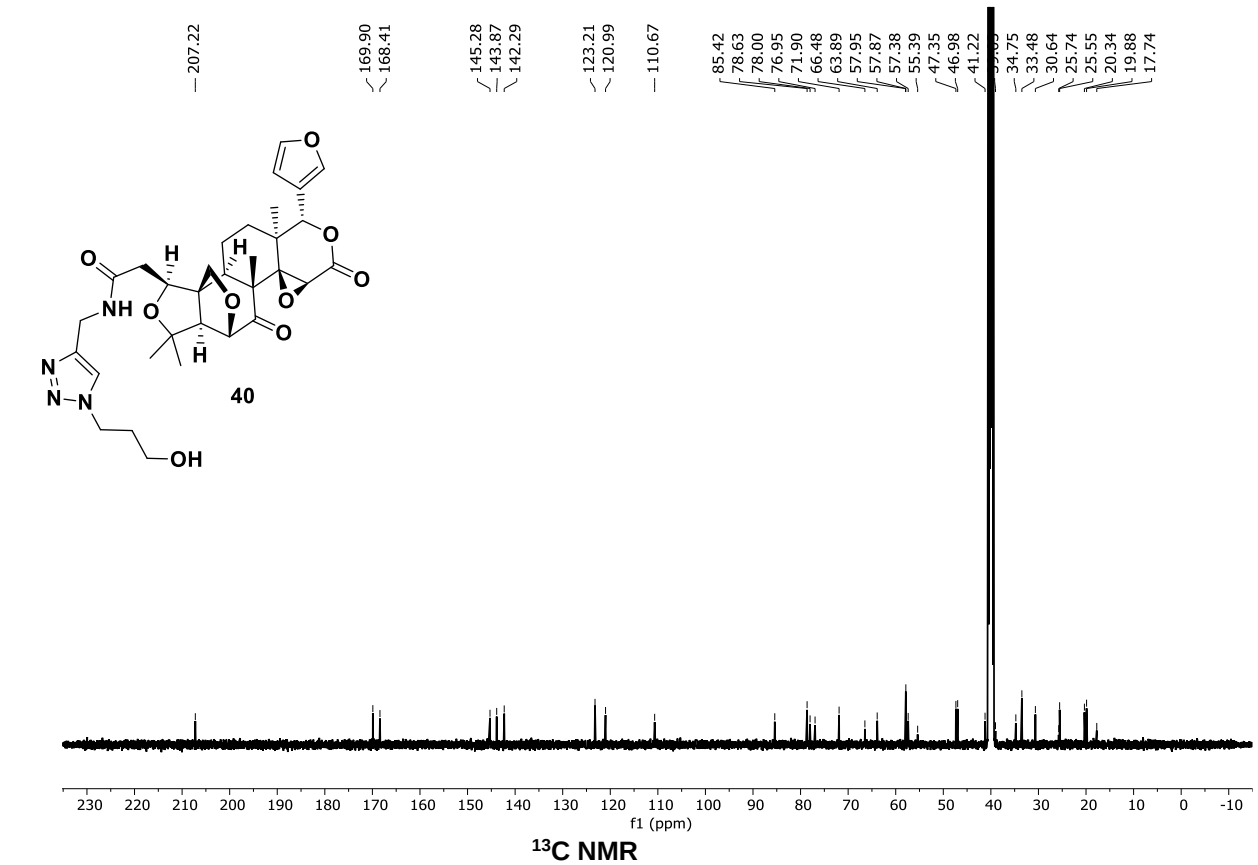


40

^{1}H NMR



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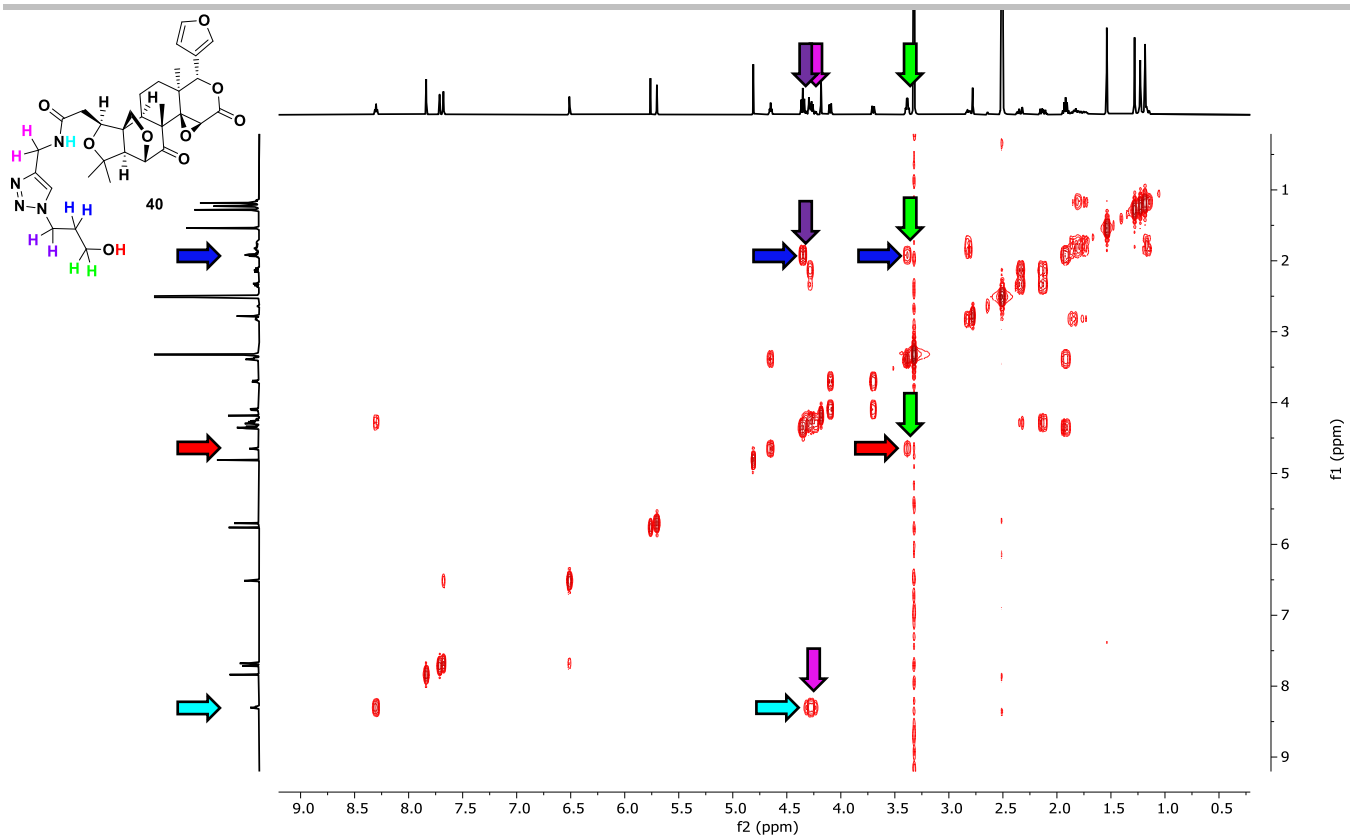
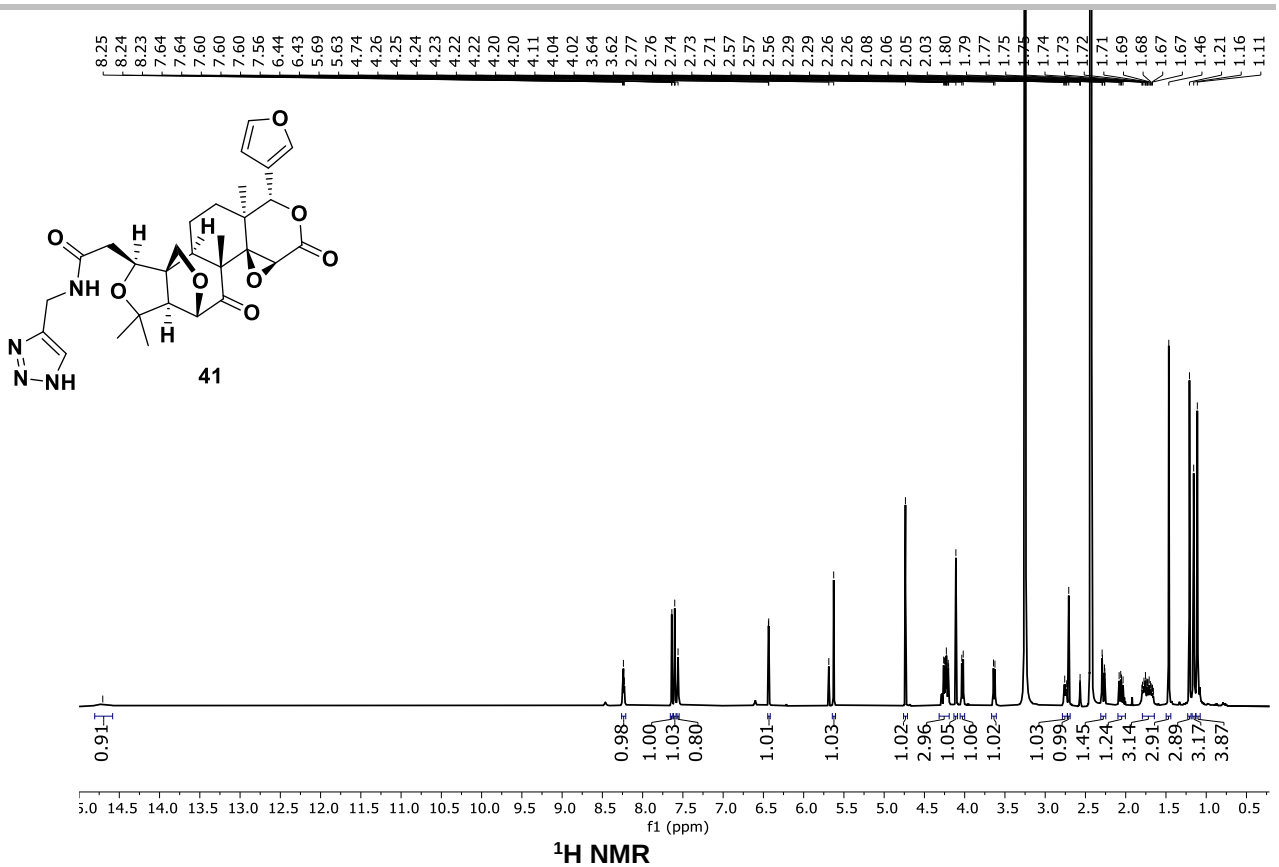
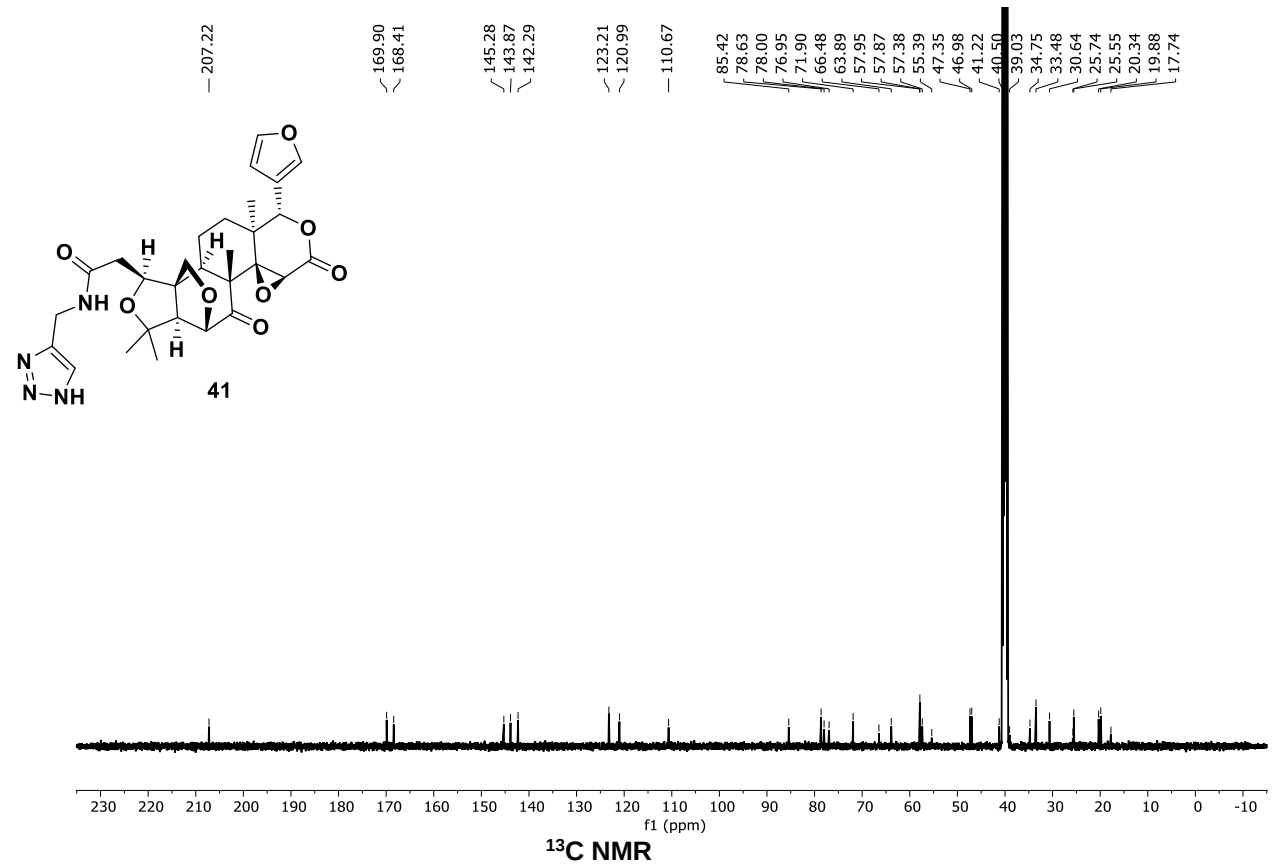


^{1}H-^{1}H COSY NMR



41

^{1}H NMR



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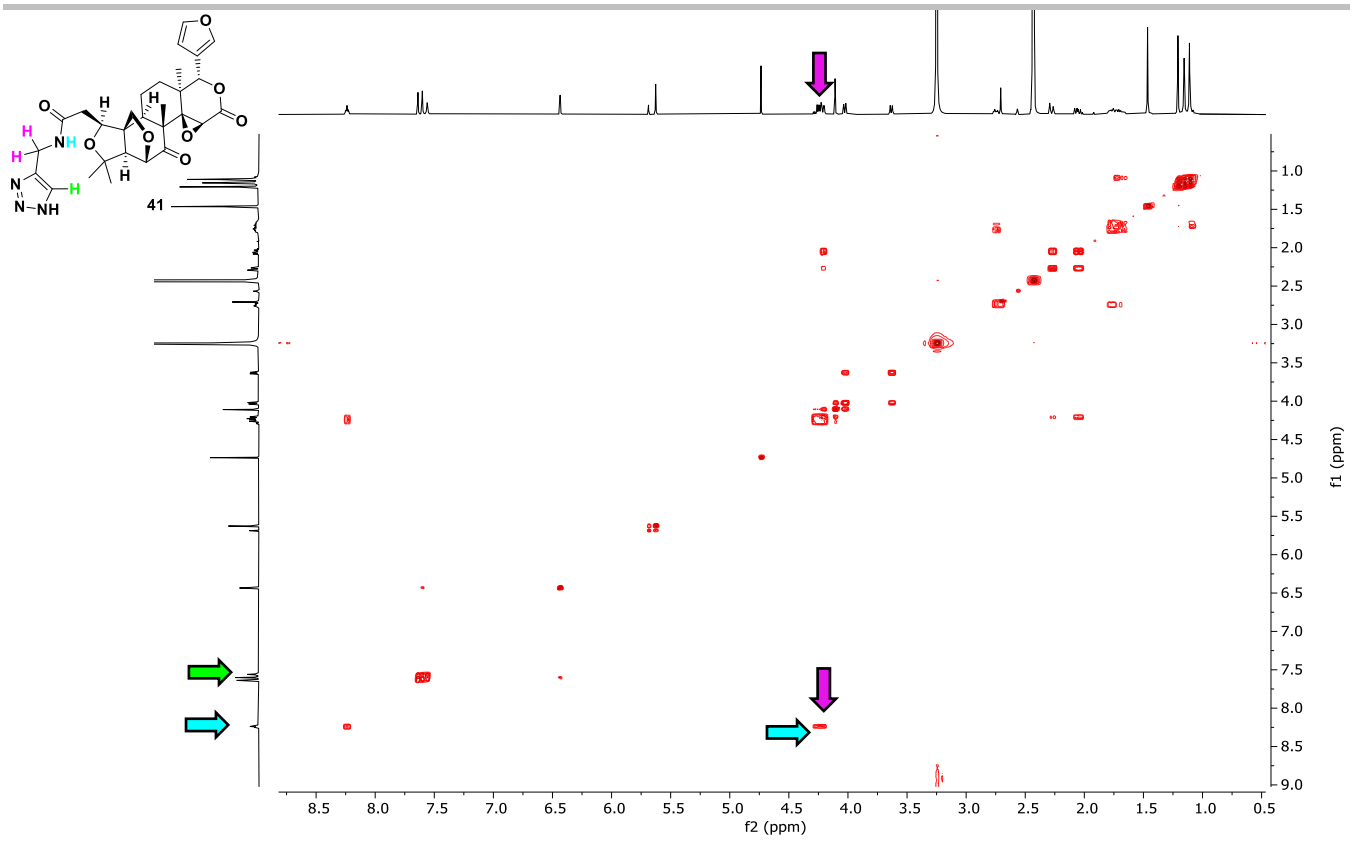

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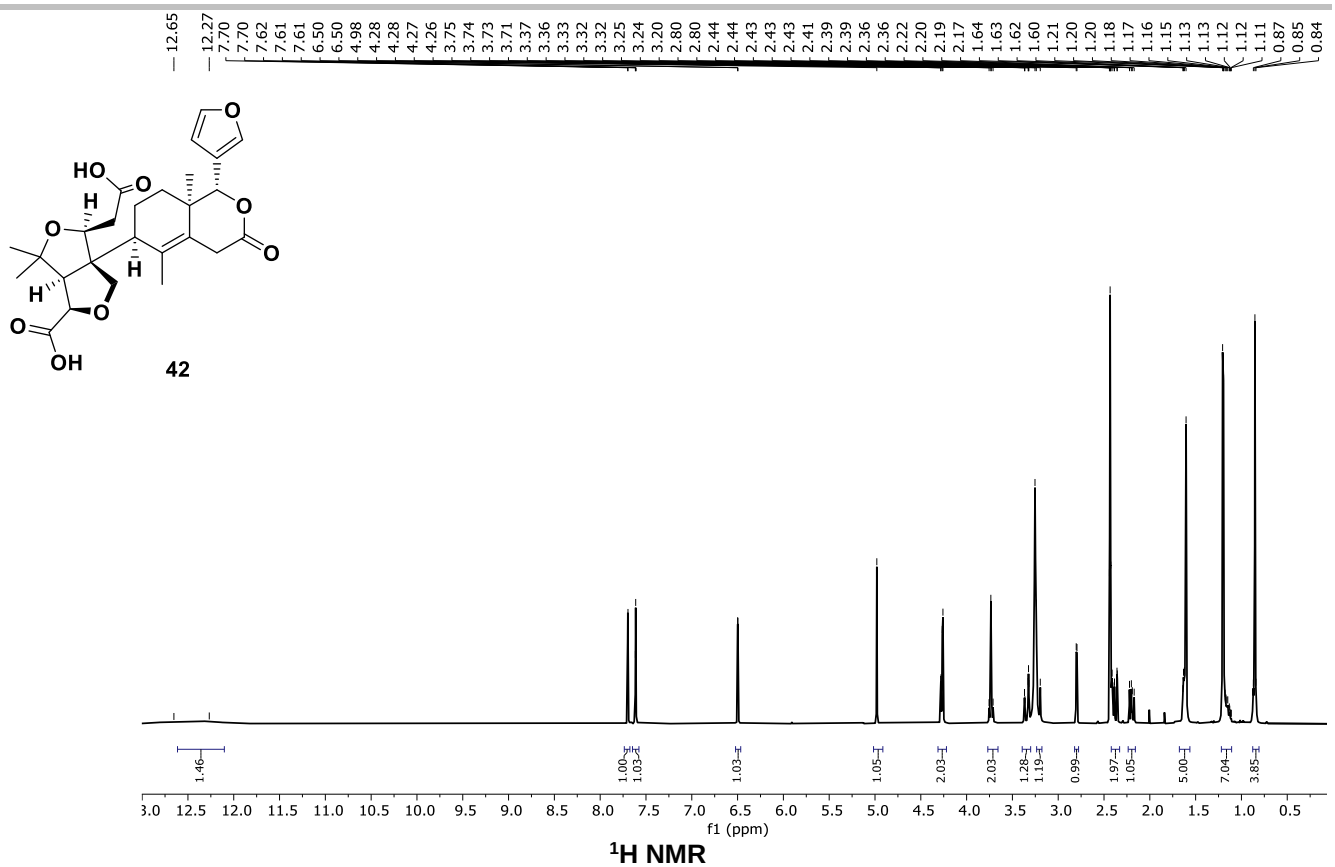

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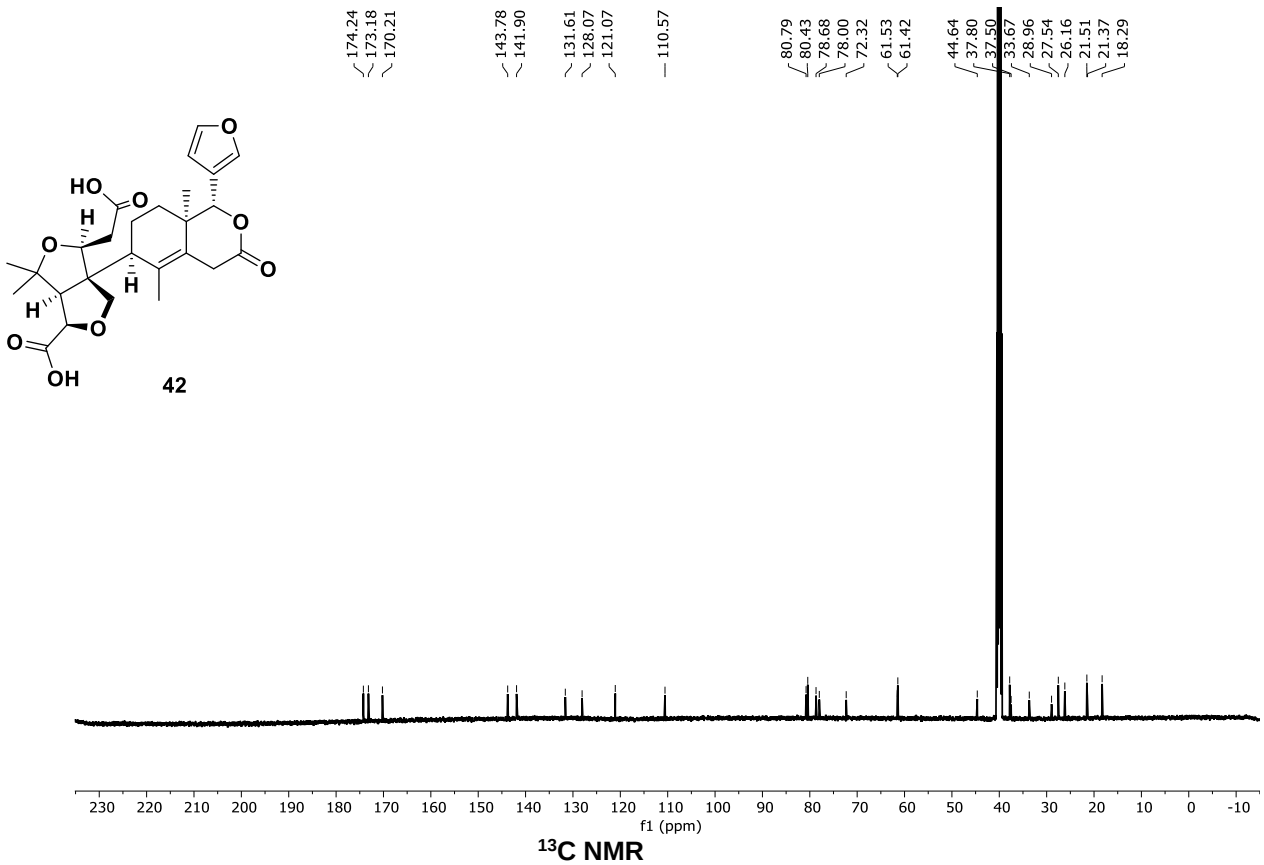
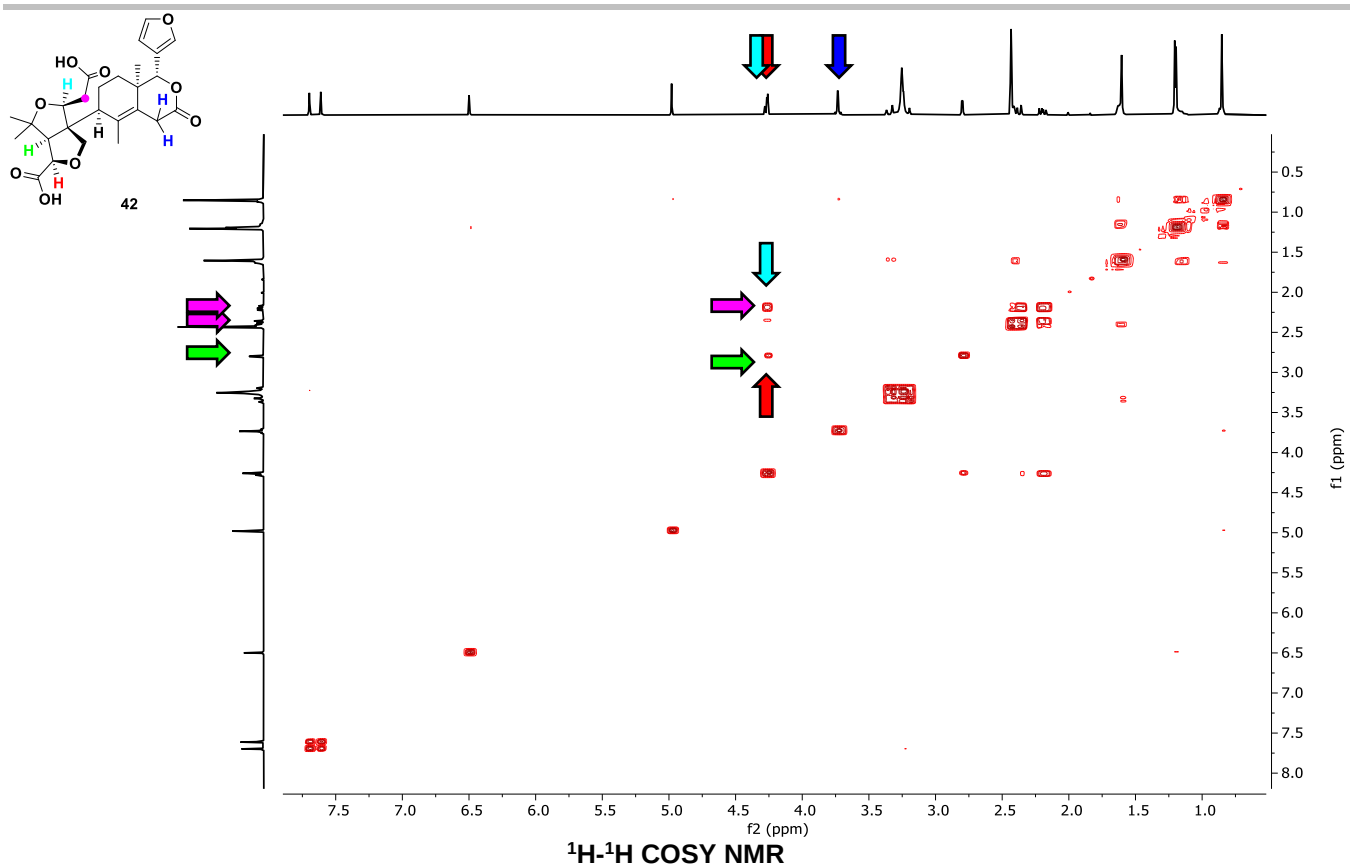
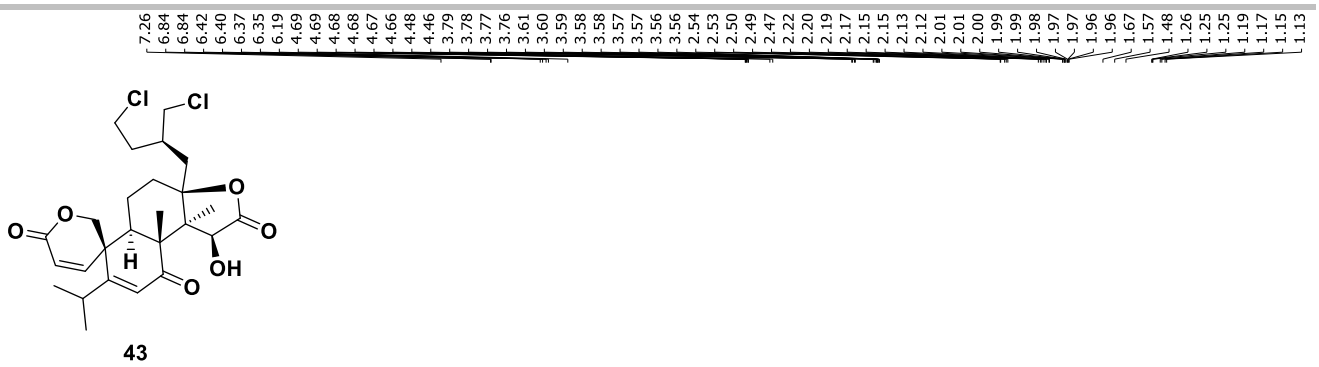


^{13}C NMR



^{1}H-^{1}H COSY NMR



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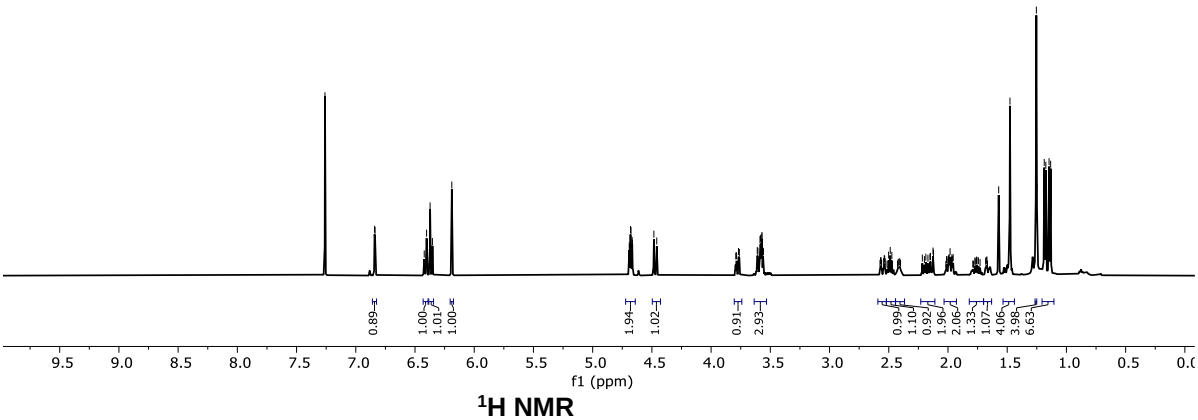
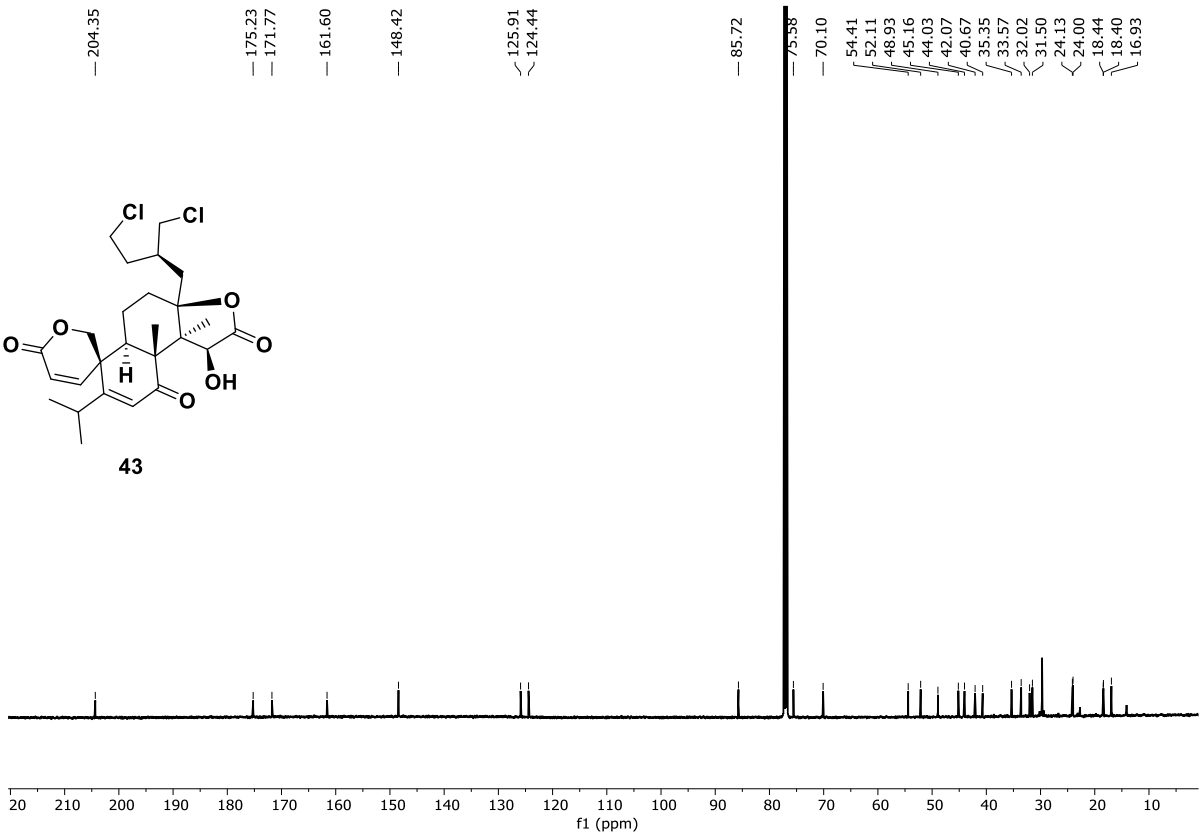


^{1}H NMR



43

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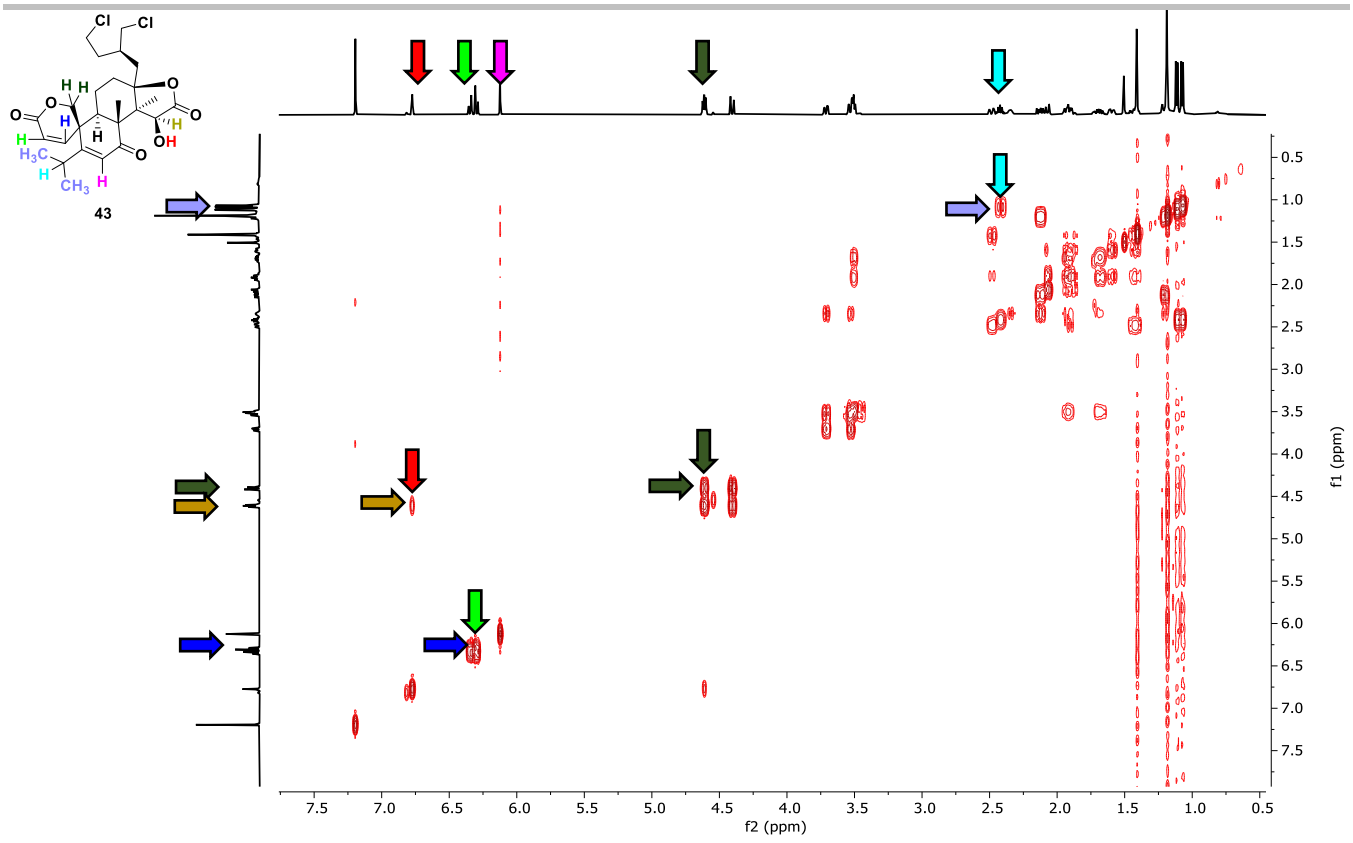
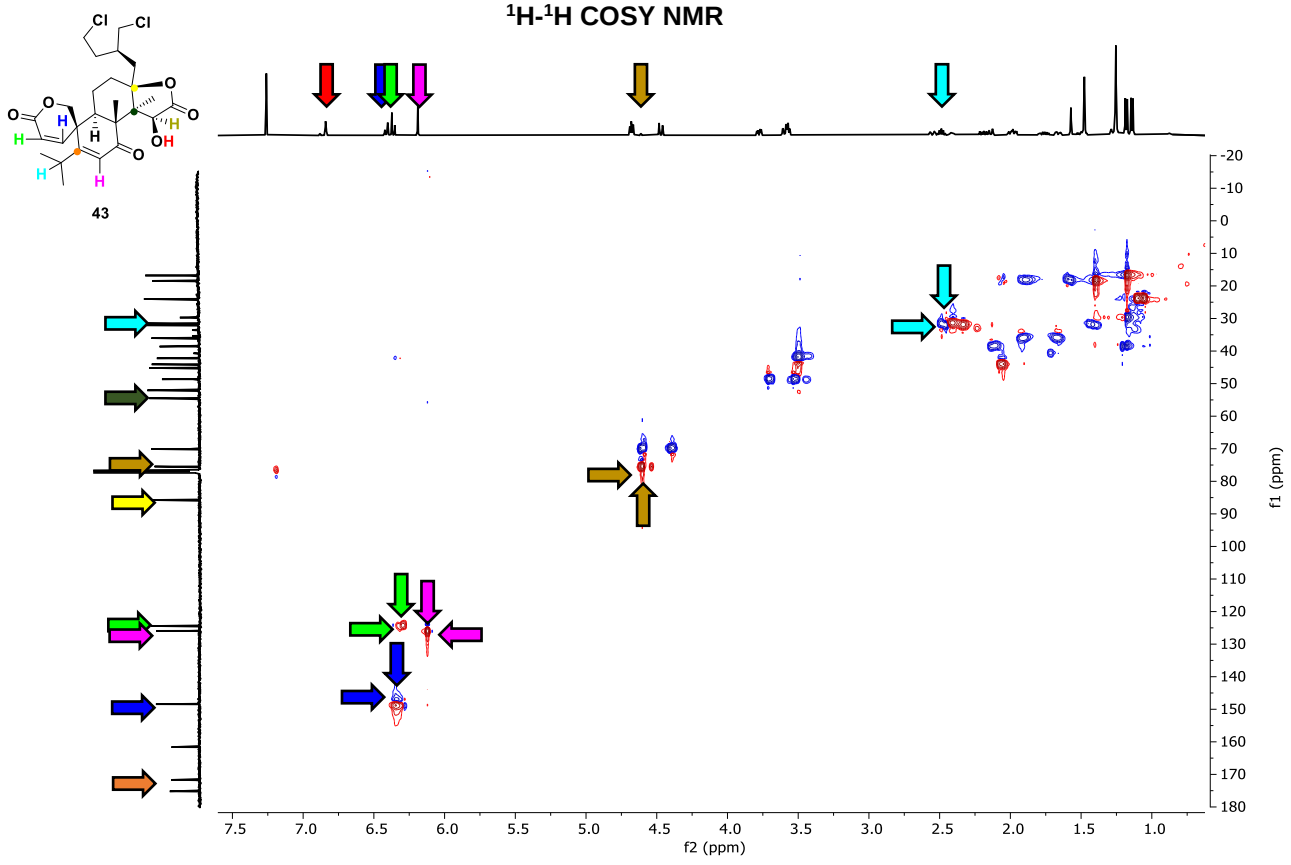


^{1}H-^{1}H COSY NMR



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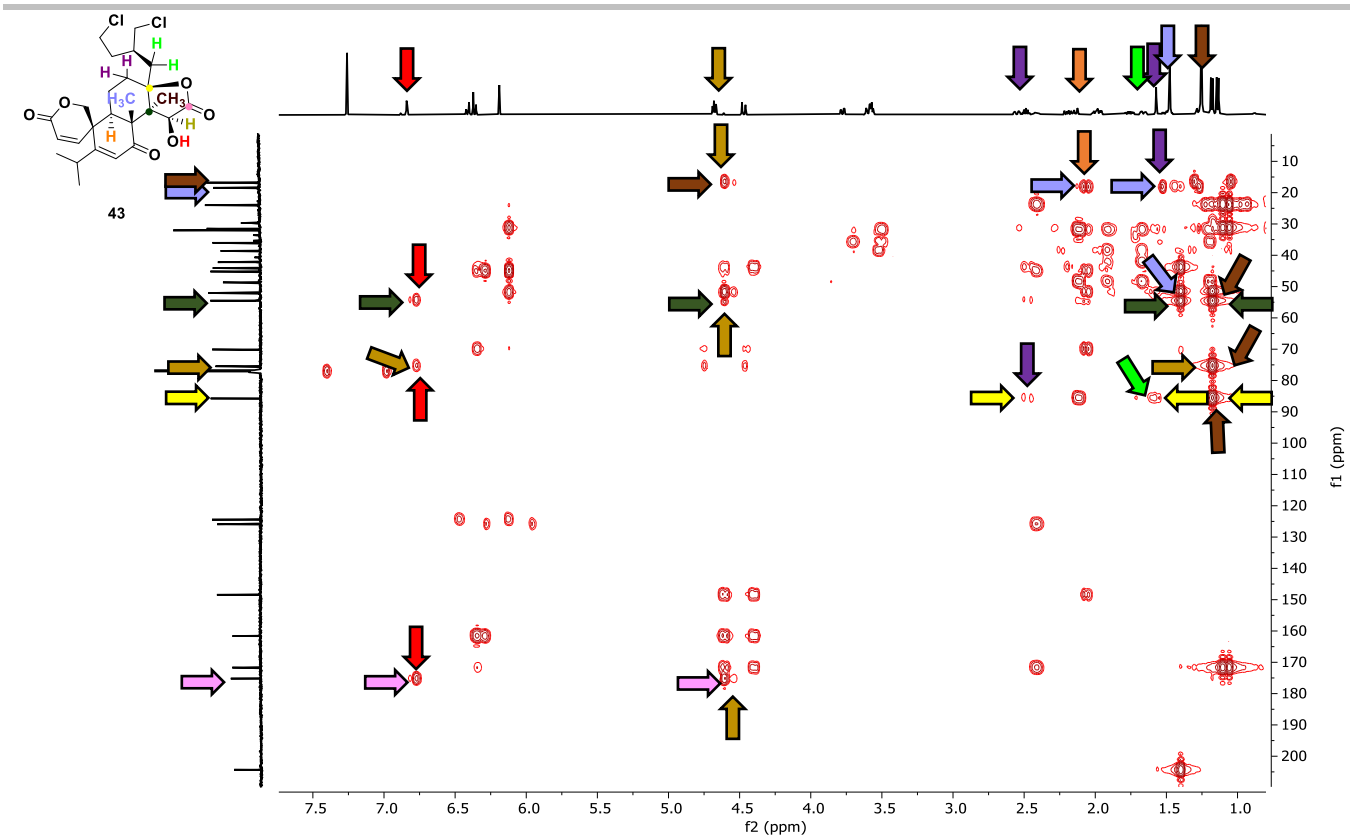

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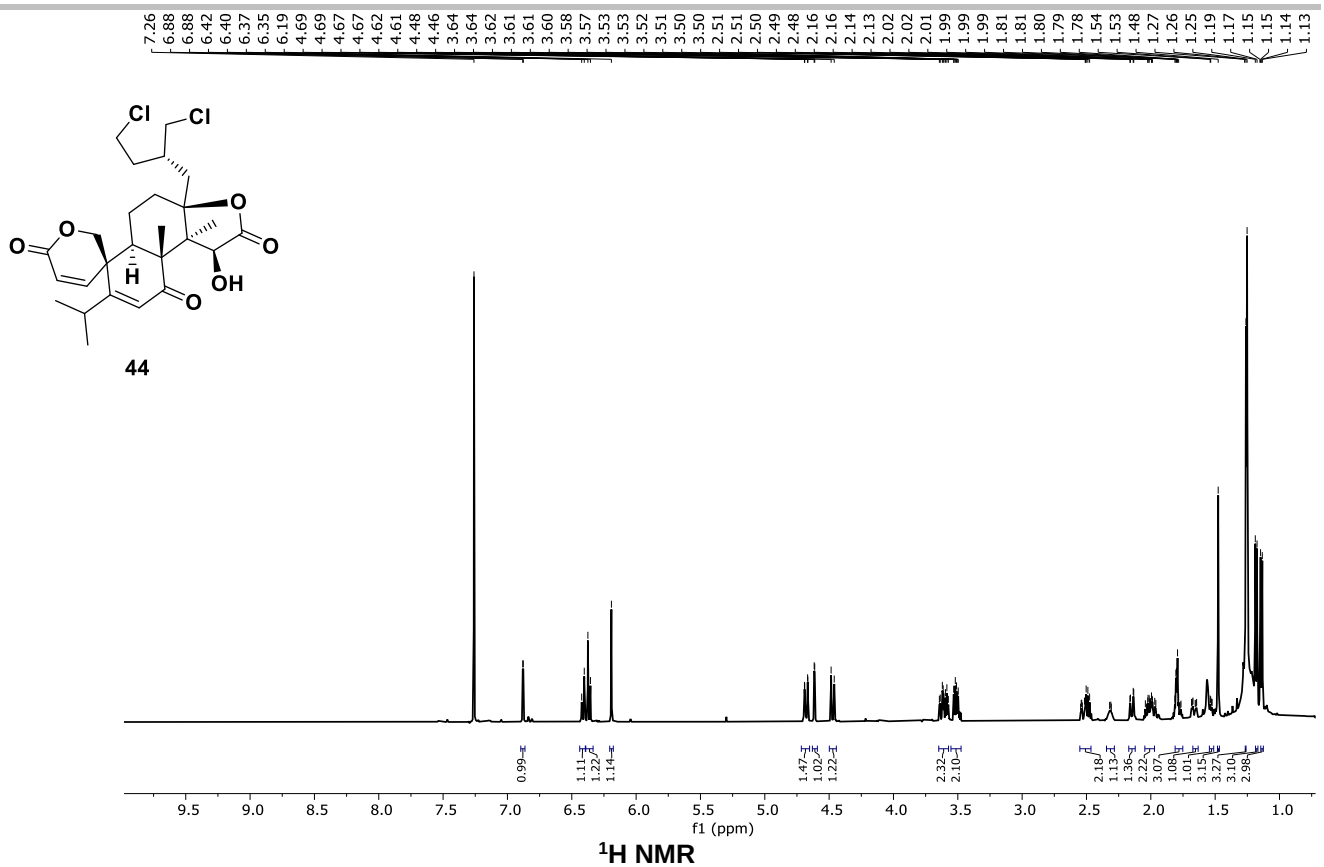

44

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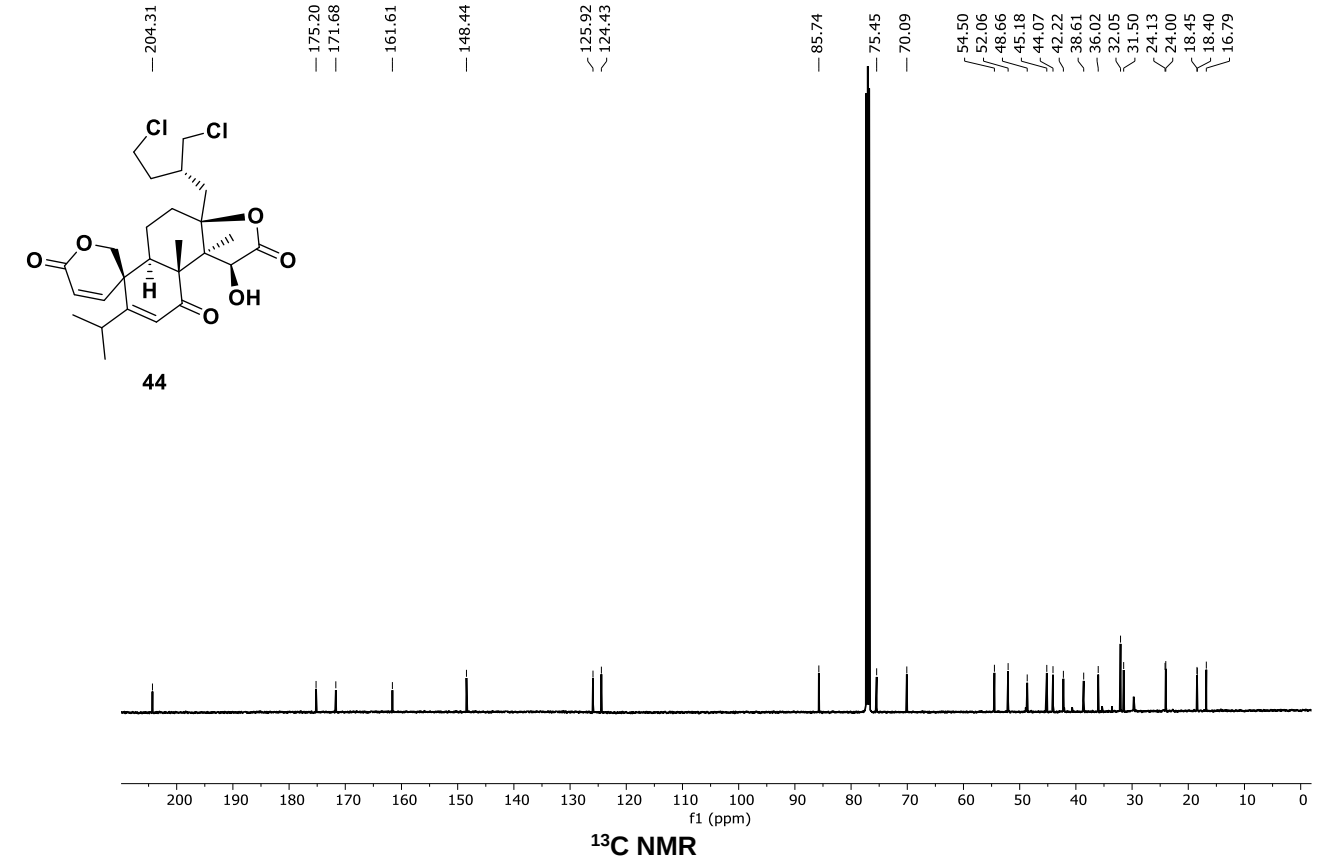

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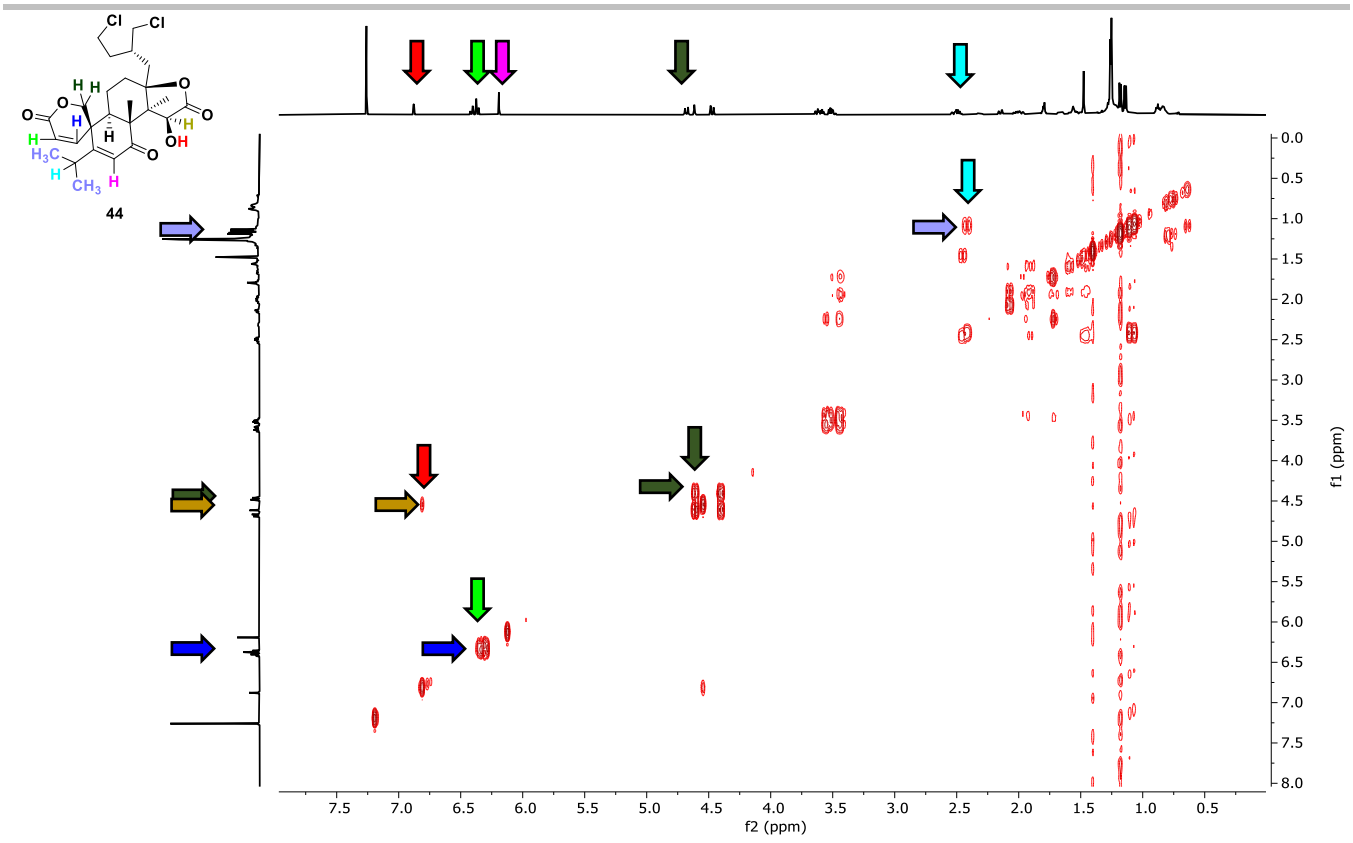

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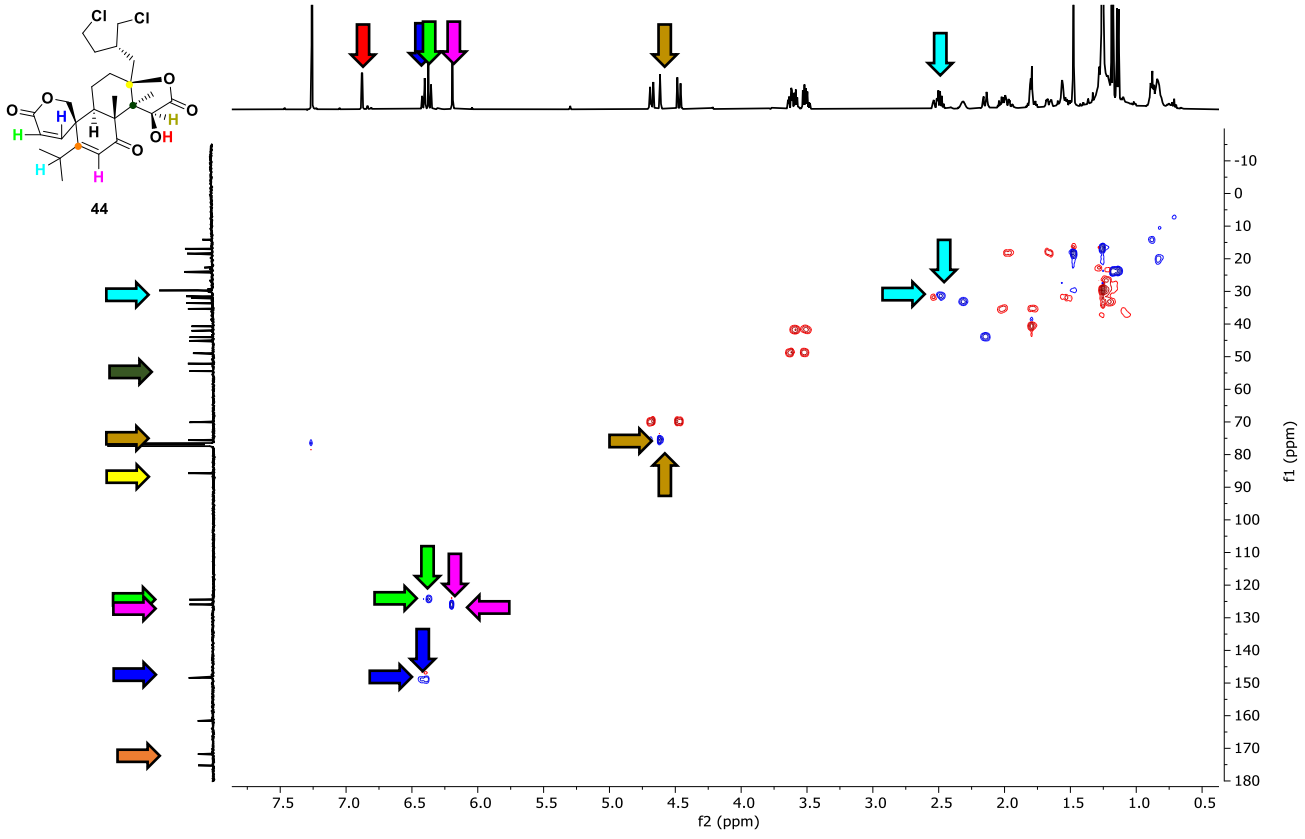

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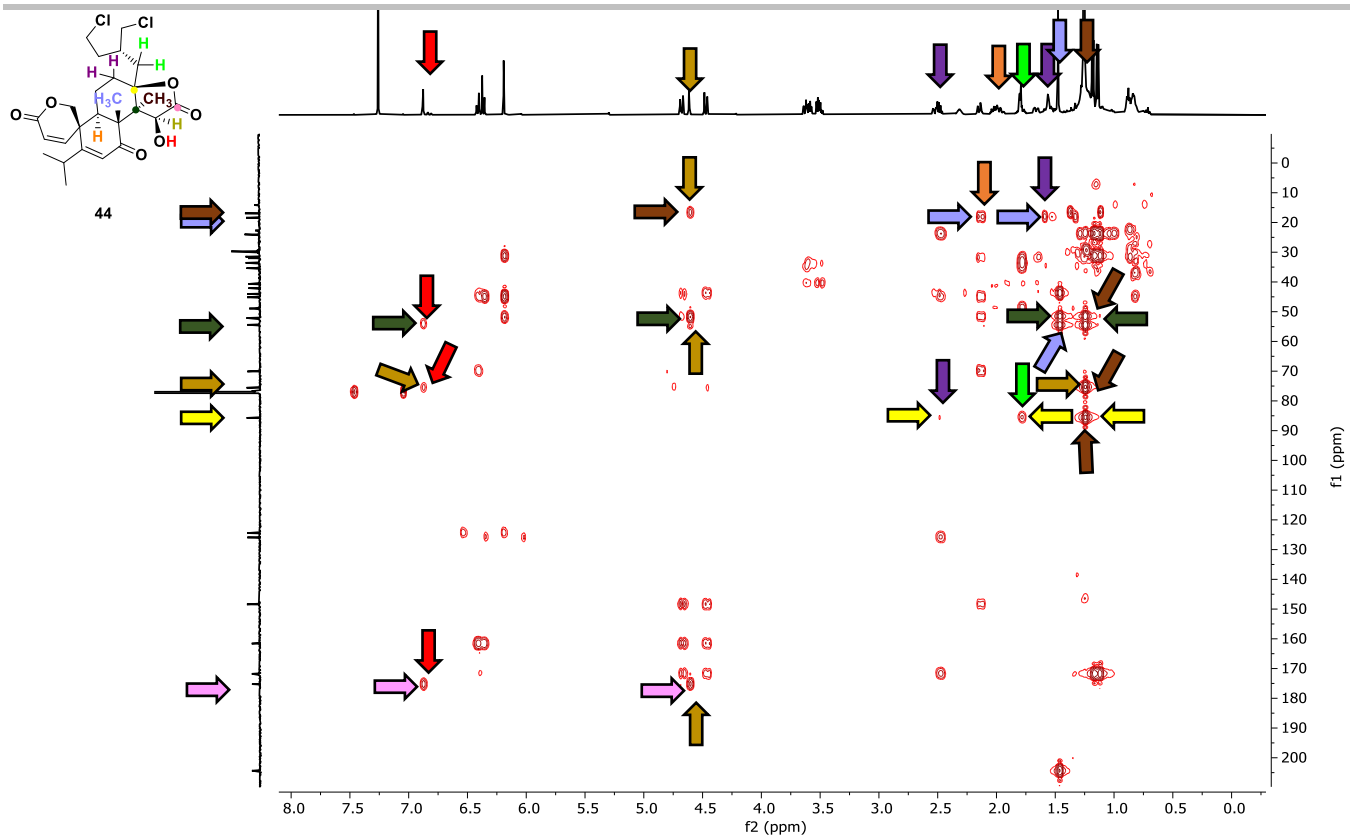

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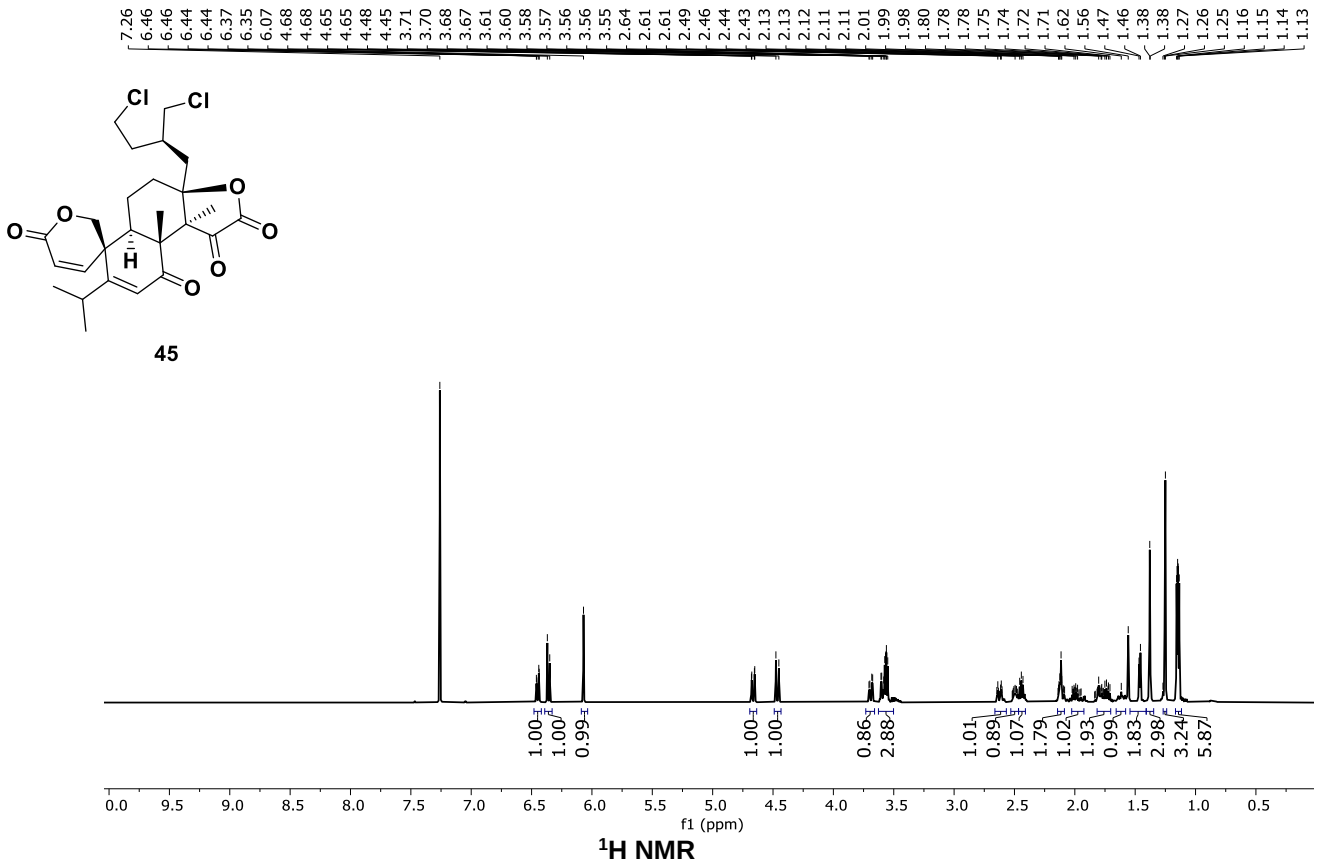

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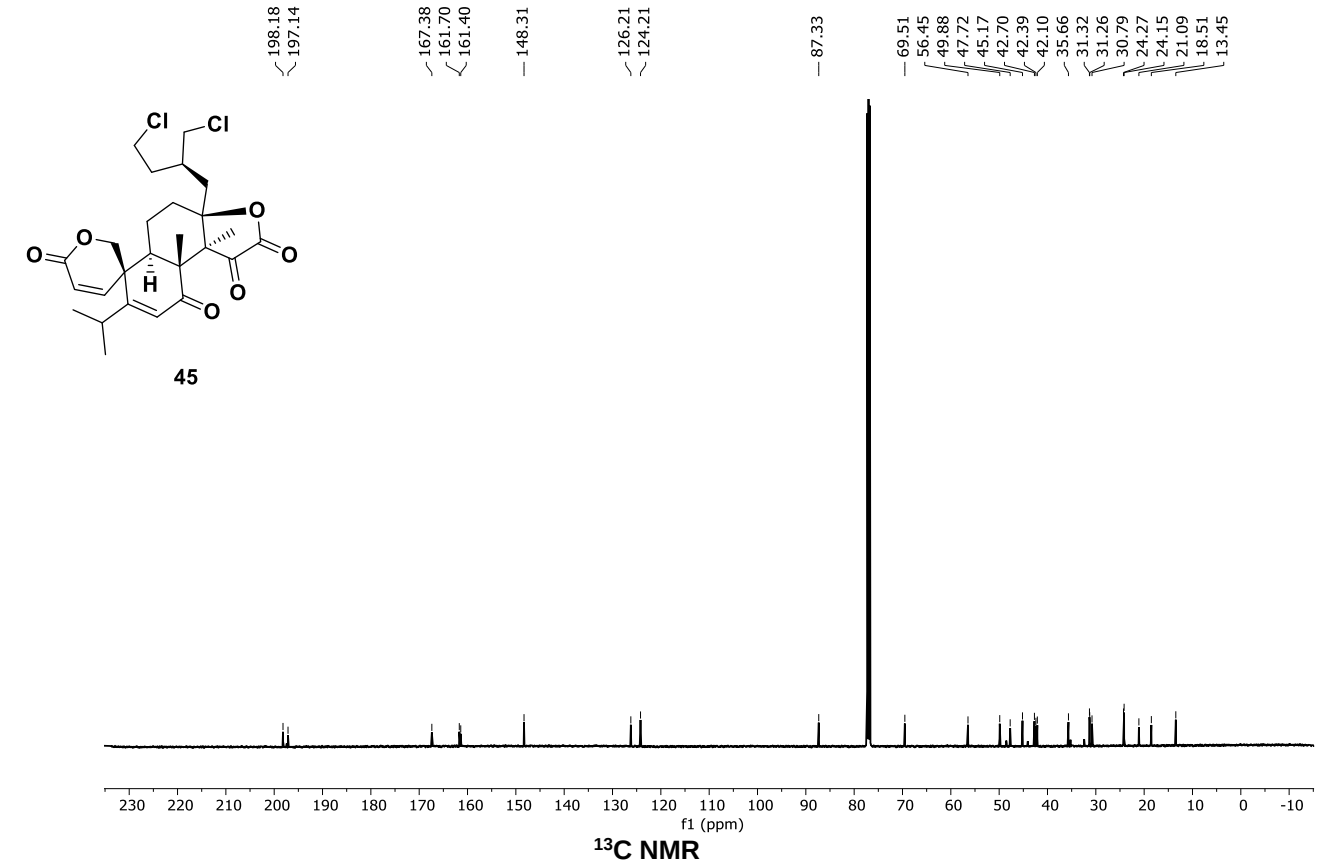

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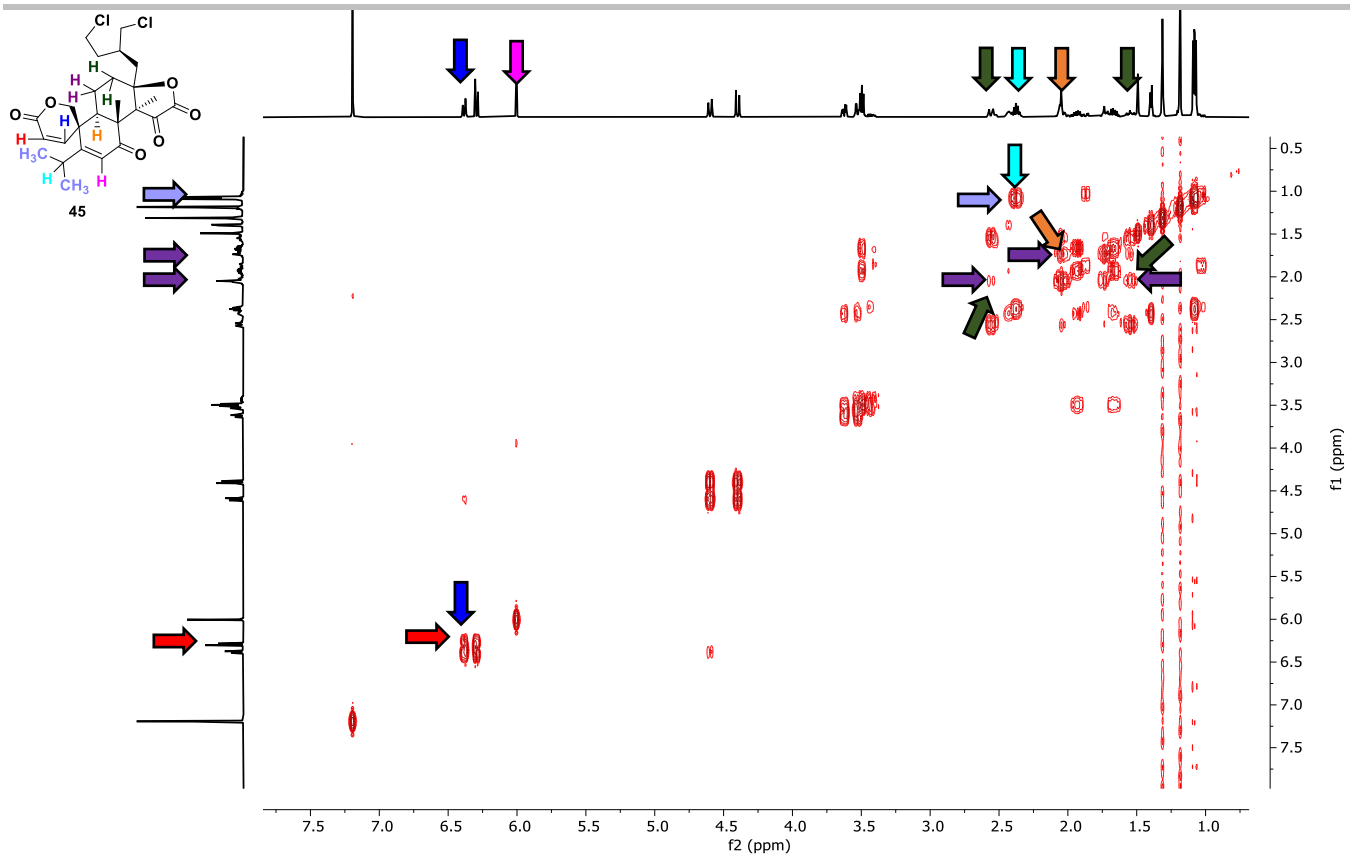
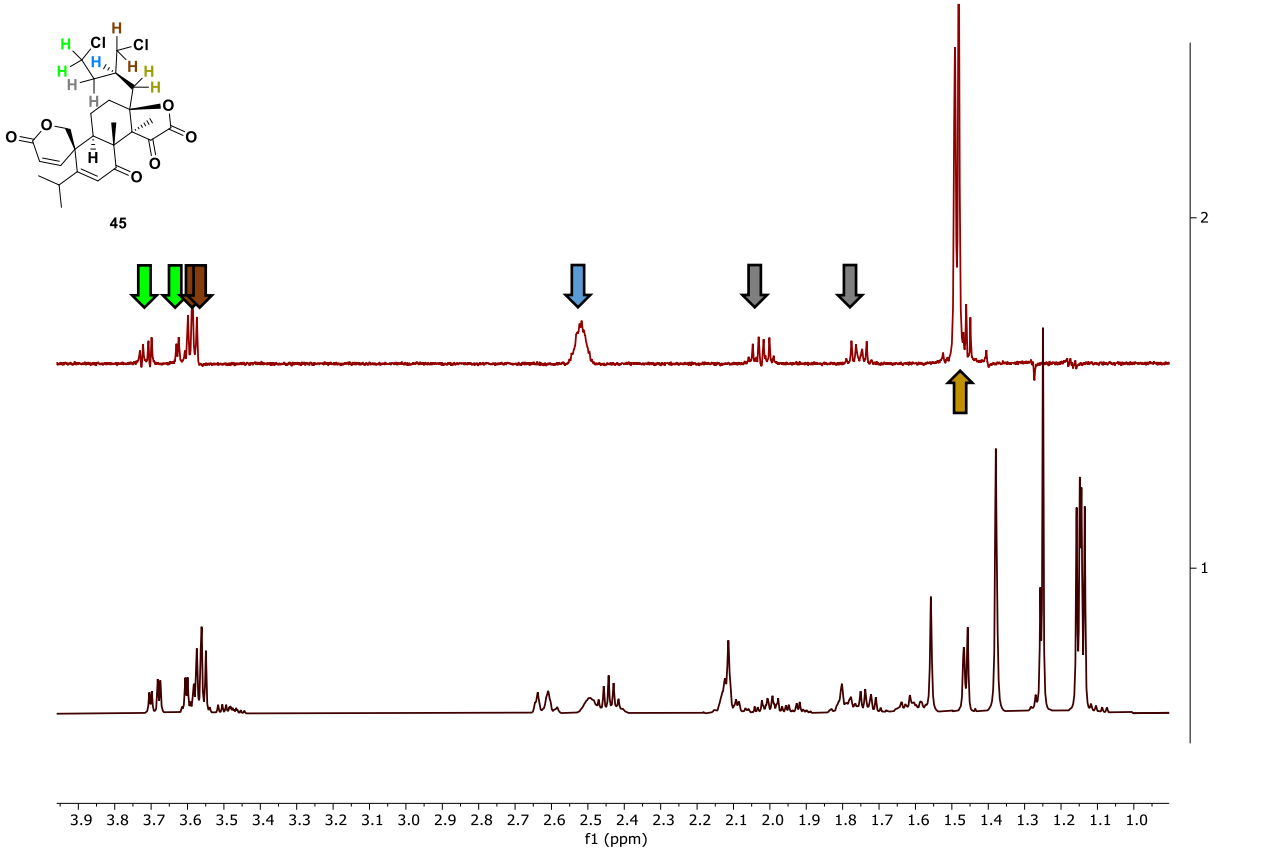
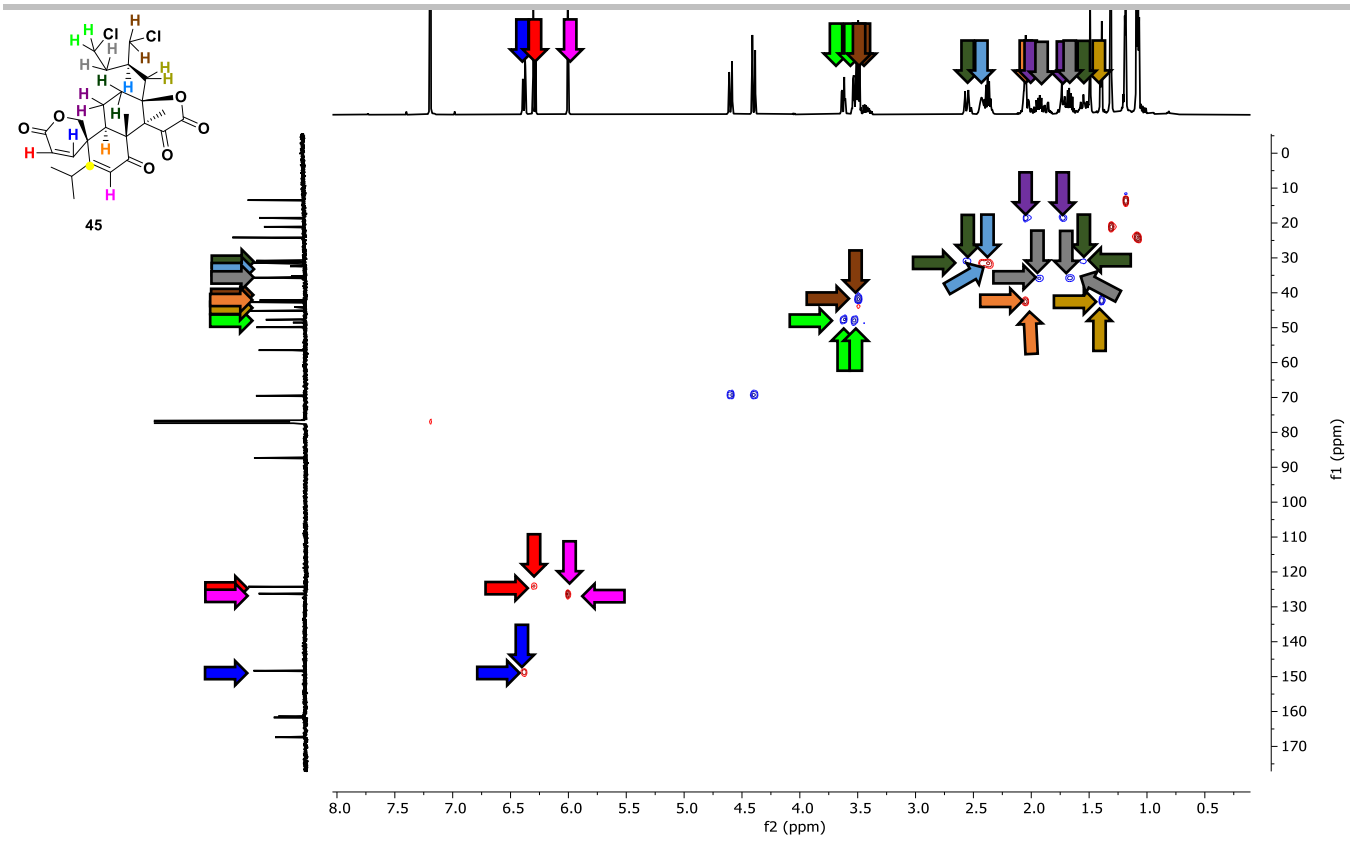


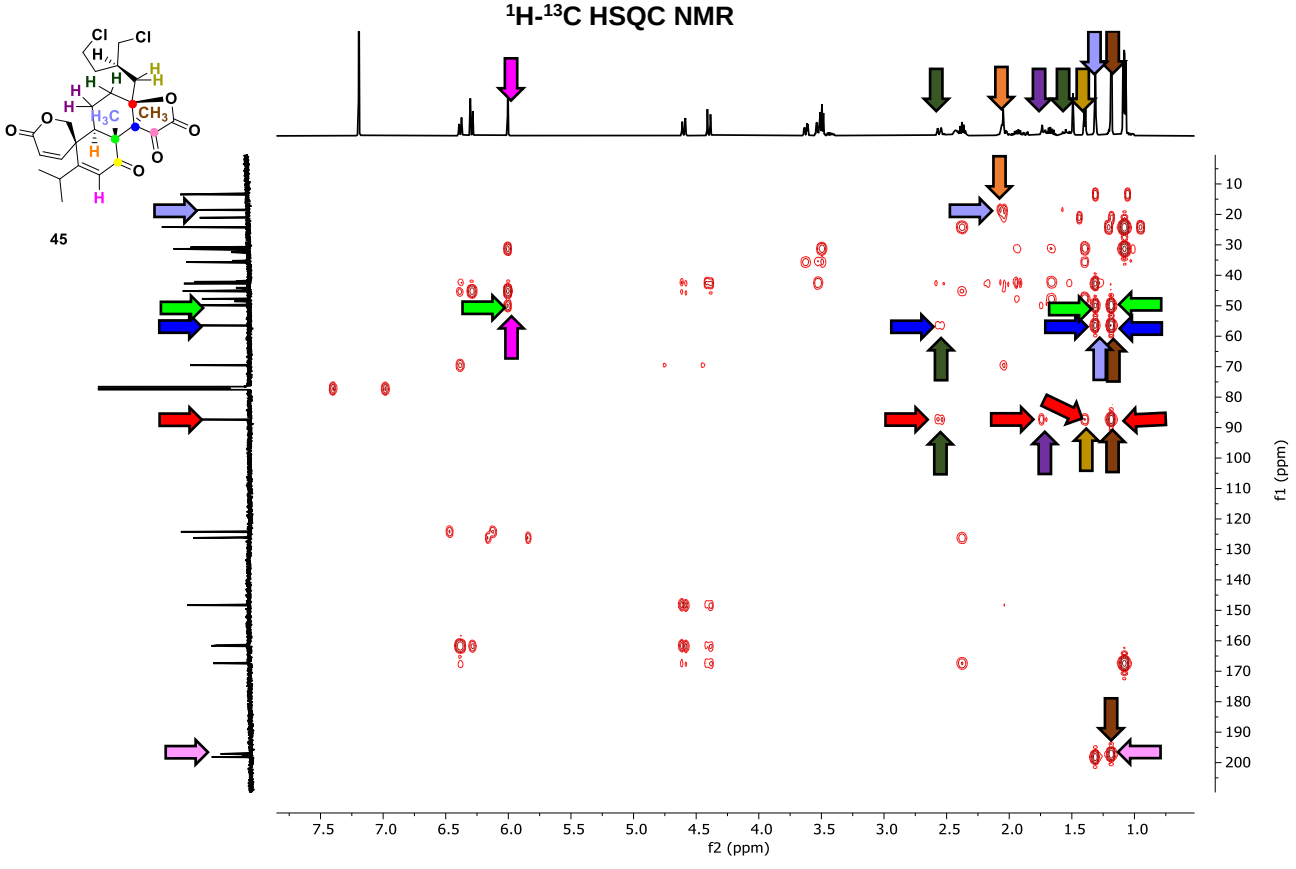
^{1}H-^{1}H COSY NMR



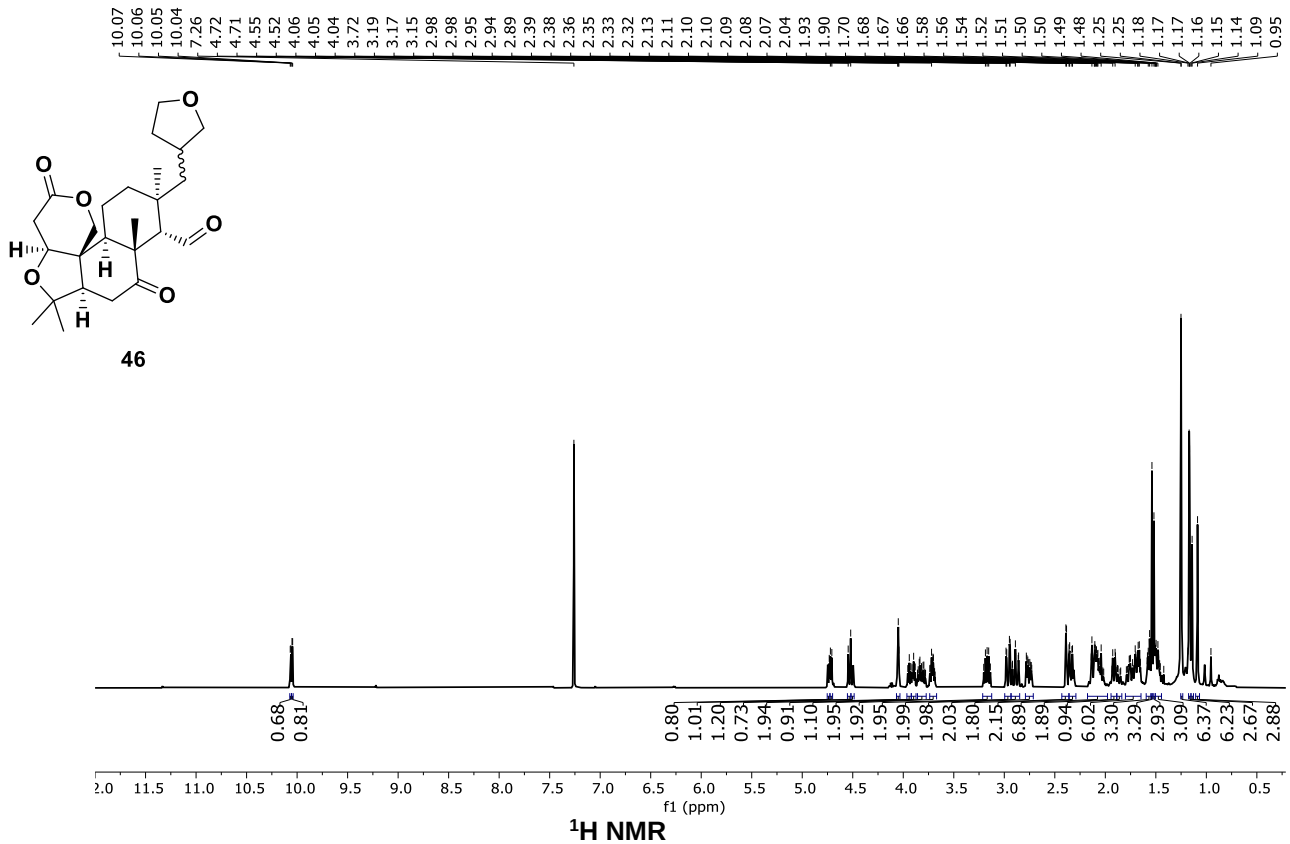
^{1}H-^{1}H 1D TOCSY NMR



^{1}H-^{13}C HSQC NMR

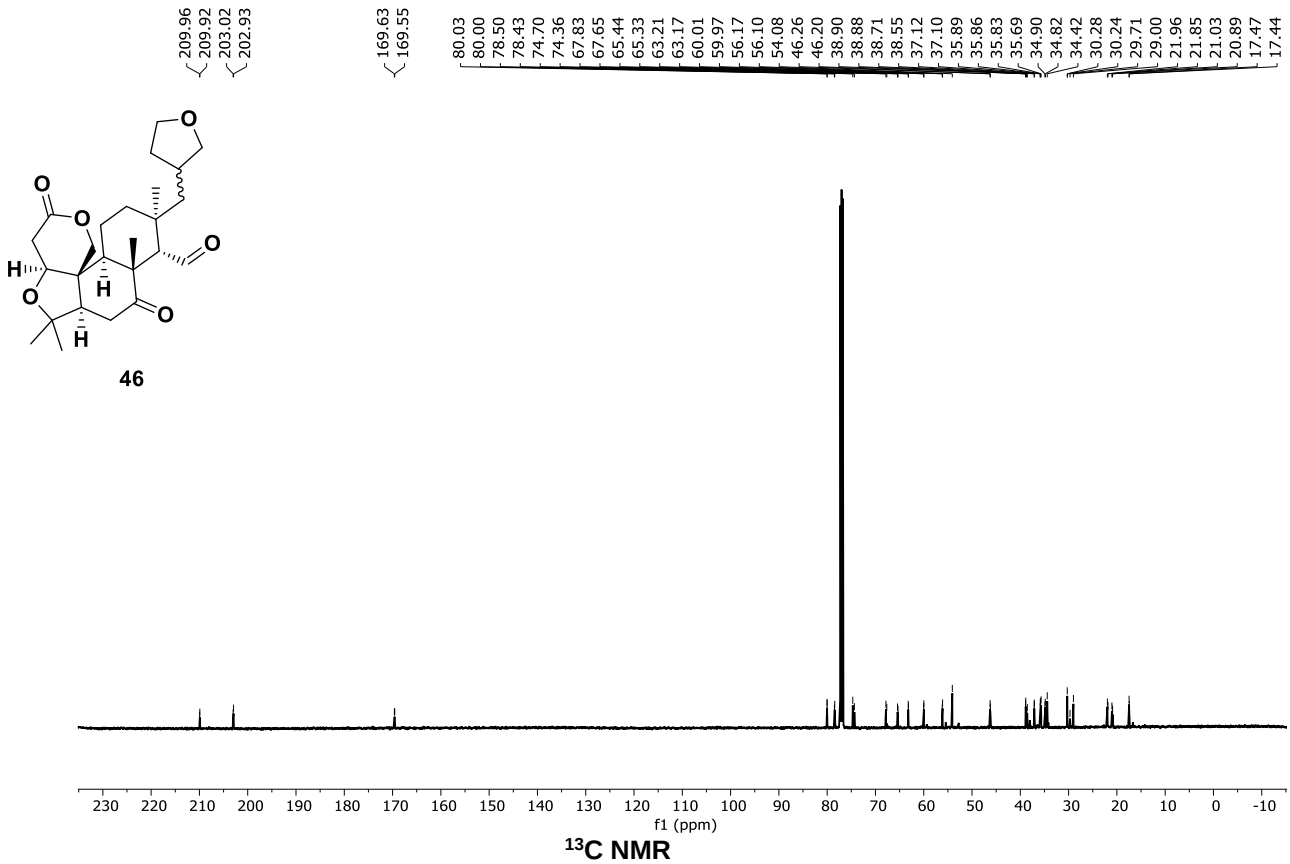


^{1}H-^{13}C HMBC NMR



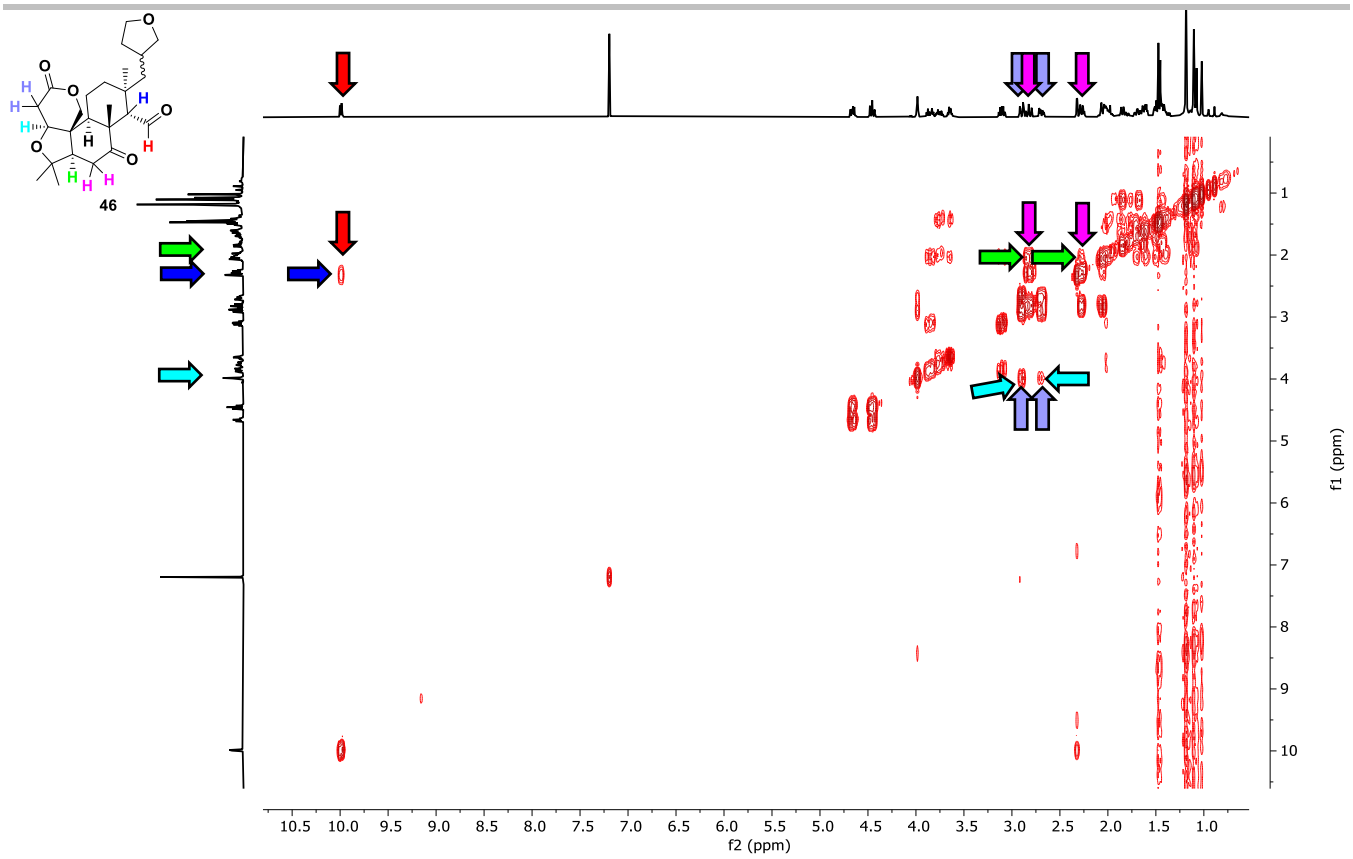
46

^{1}H NMR

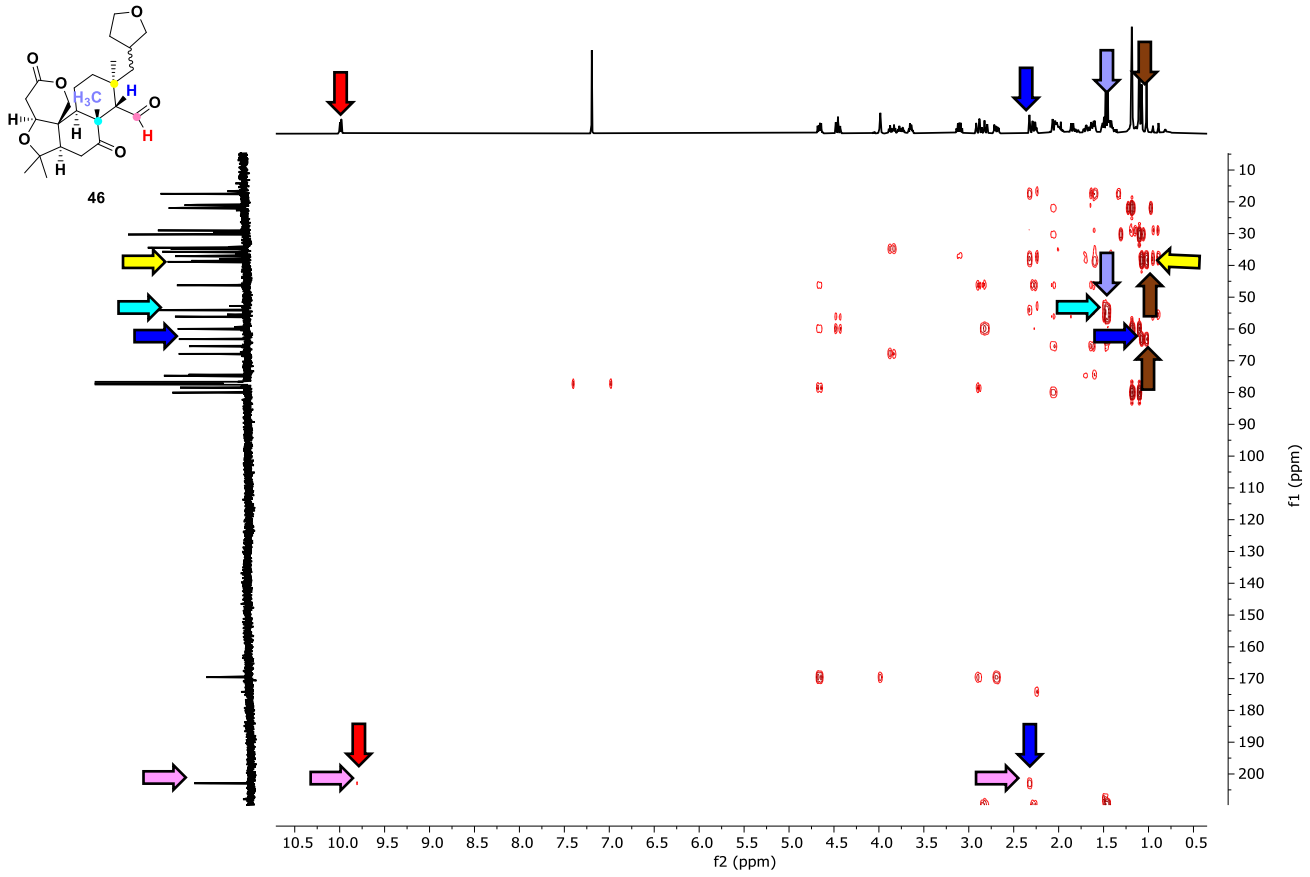


46

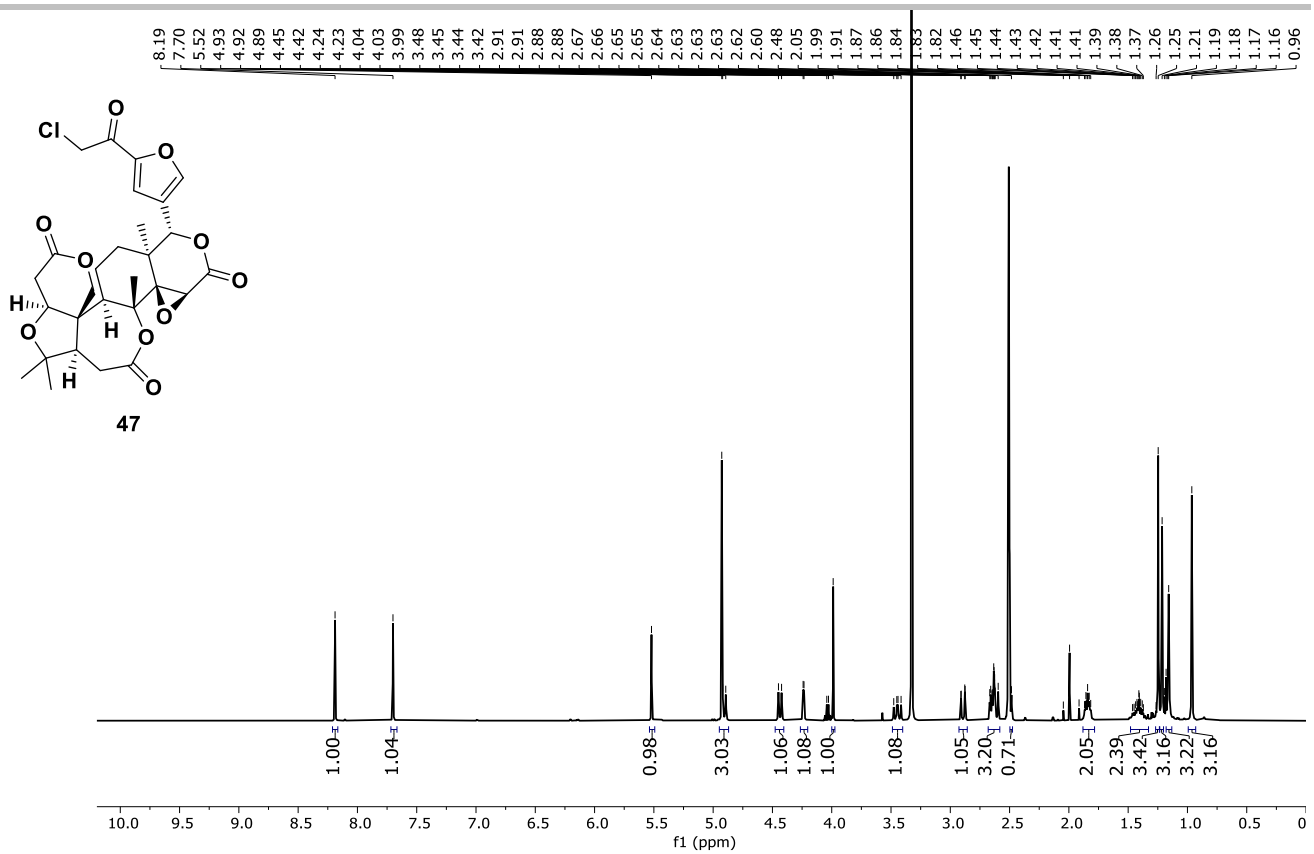
^{13}C NMR



^{1}H-^{1}H COSY NMR

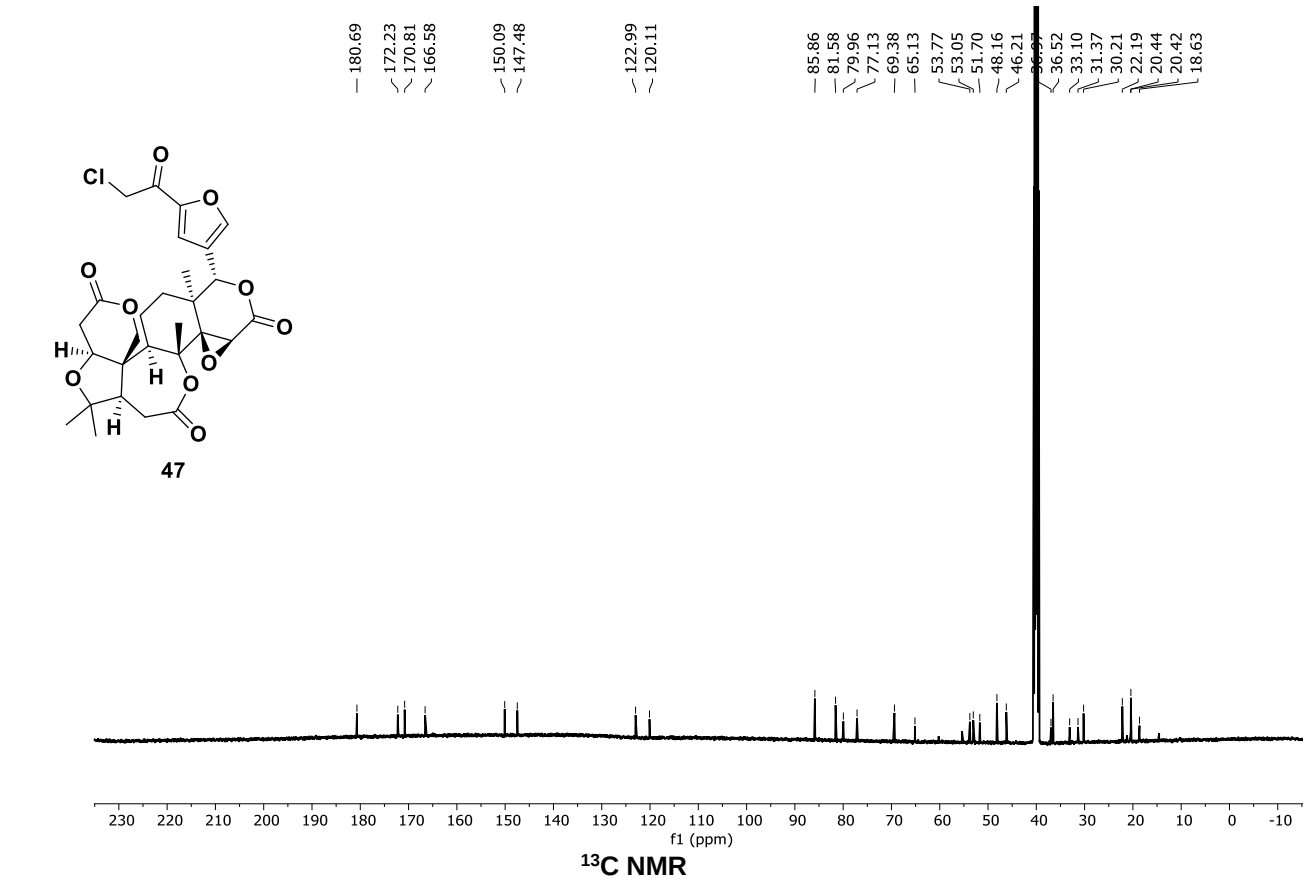


^{1}H-^{13}C HMBC NMR



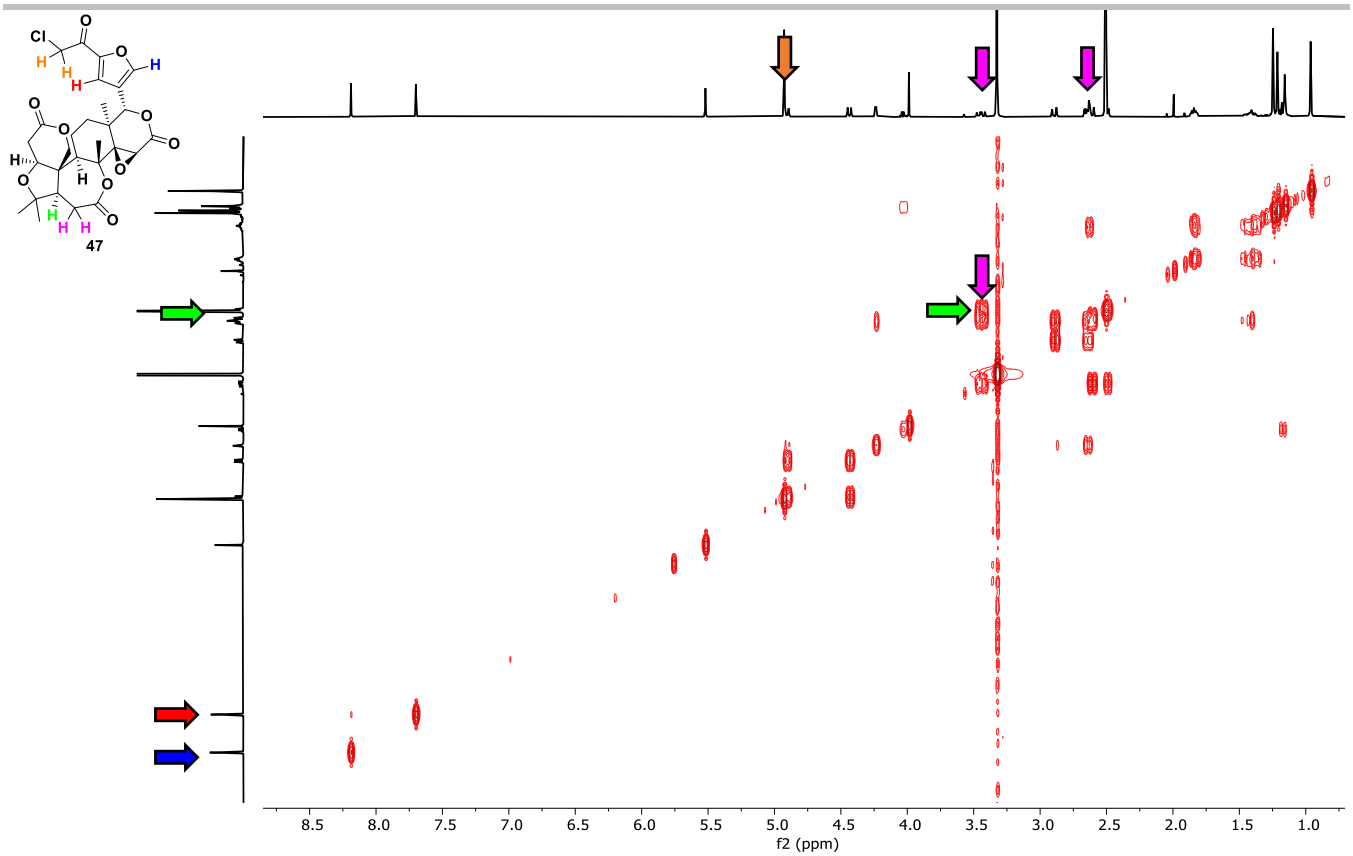
47

^{1}H NMR

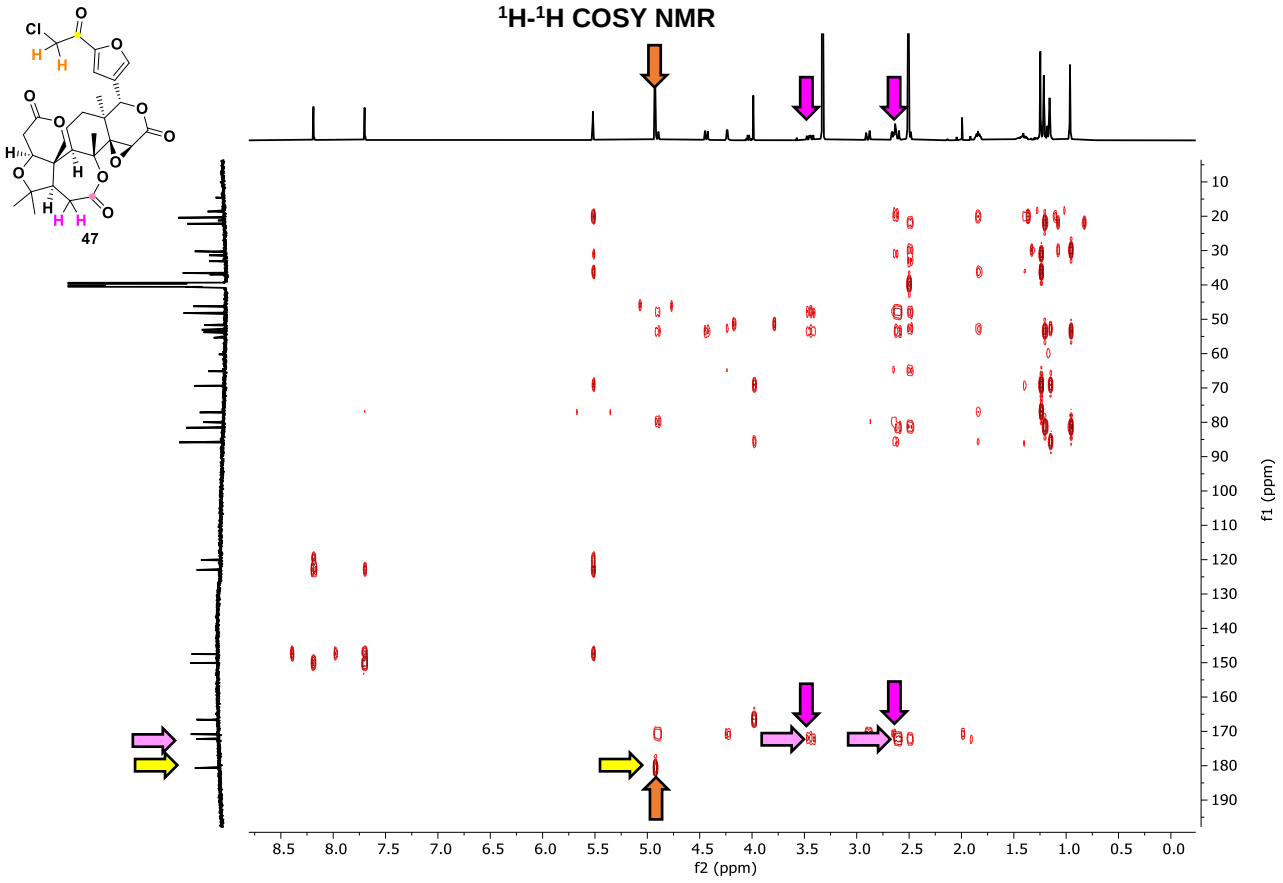


47

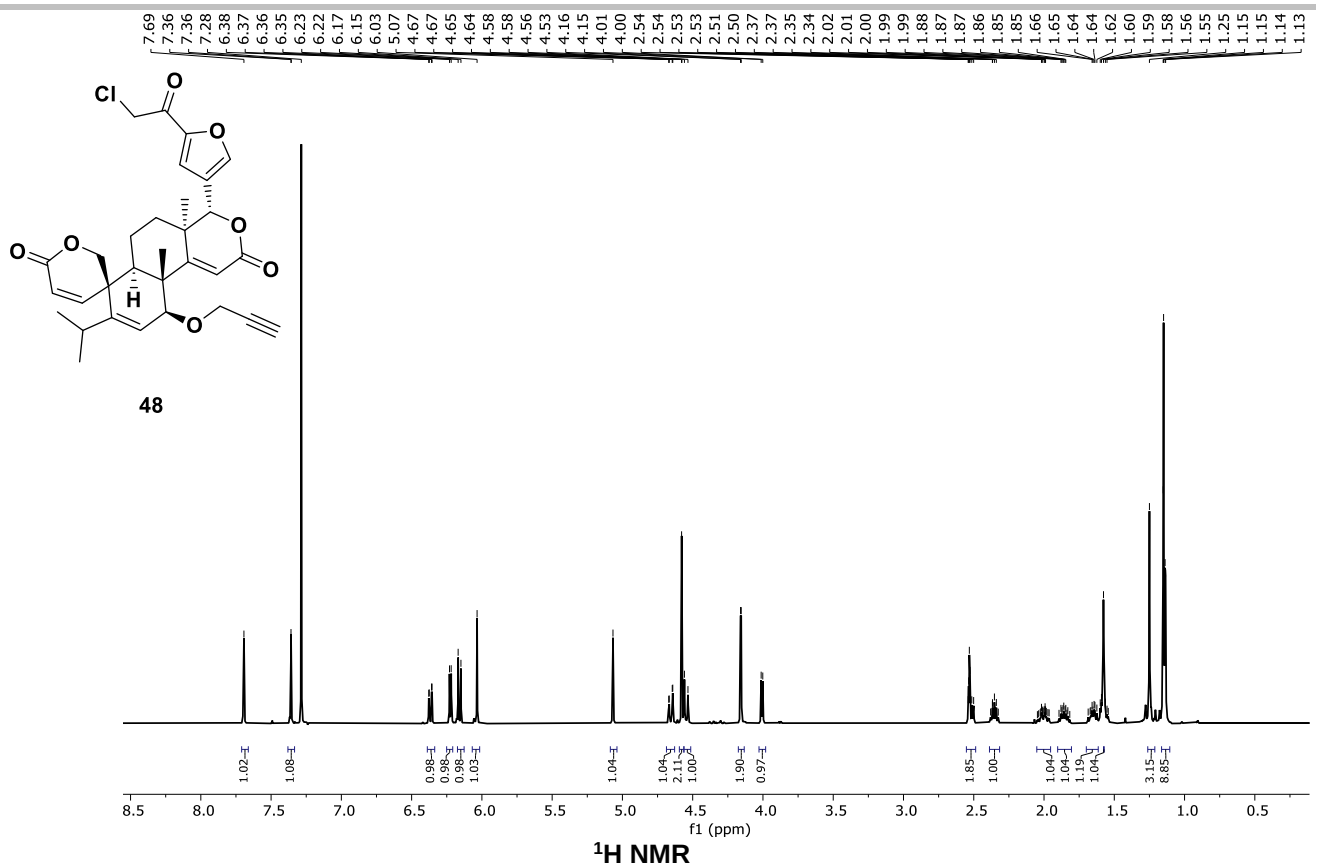
^{13}C NMR



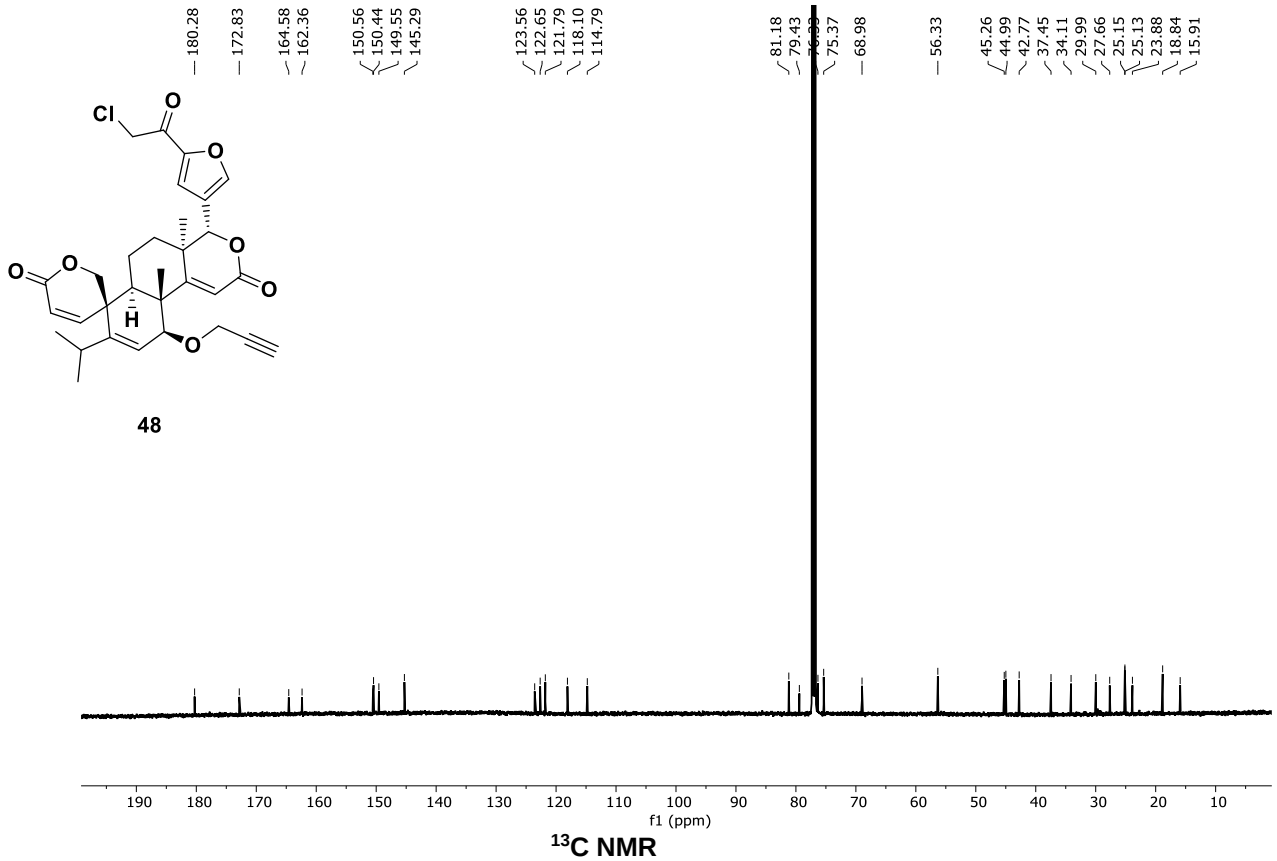
^{1}H-^{1}H COSY NMR



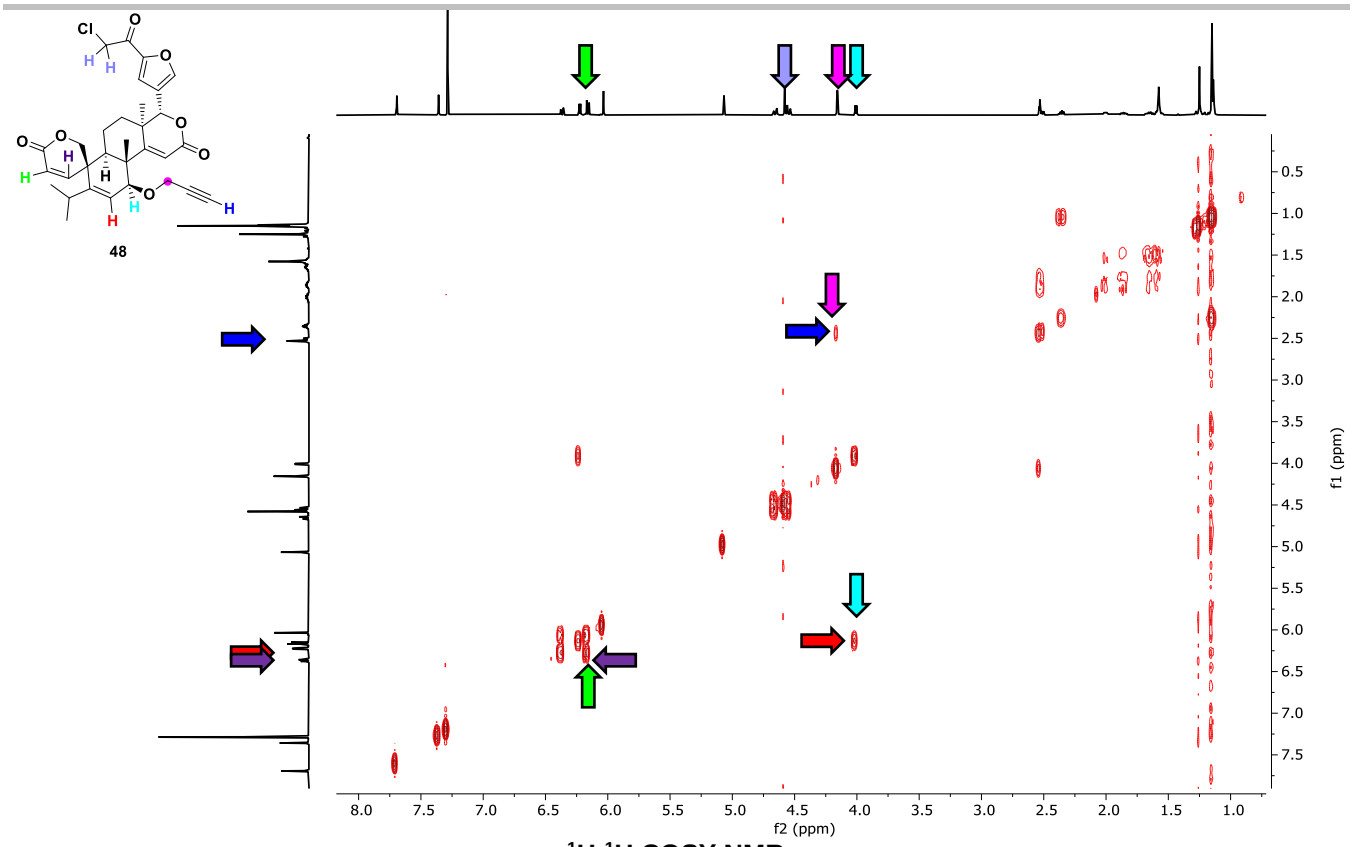
^{1}H-^{13}C HMBC NMR



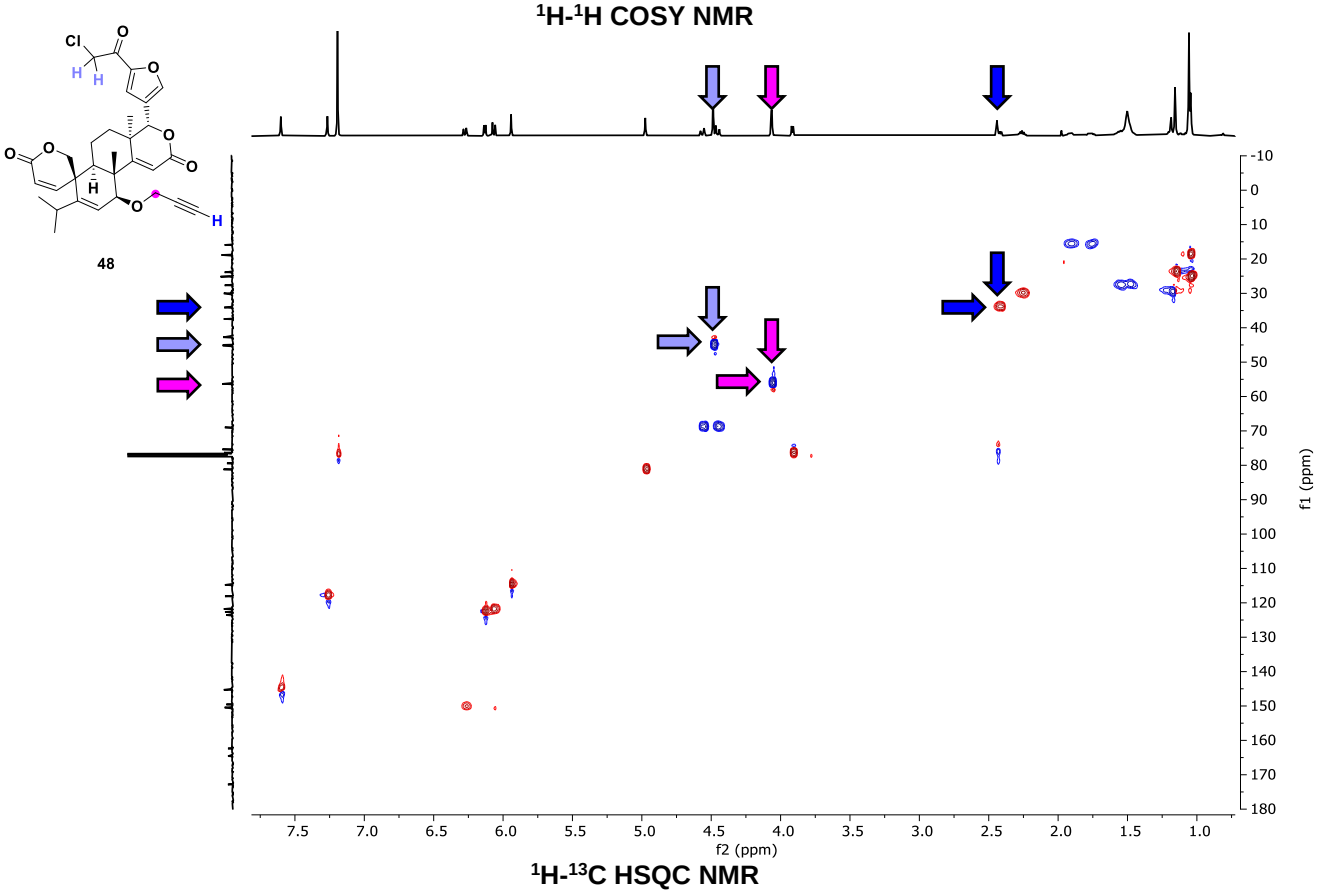
^{1}H NMR



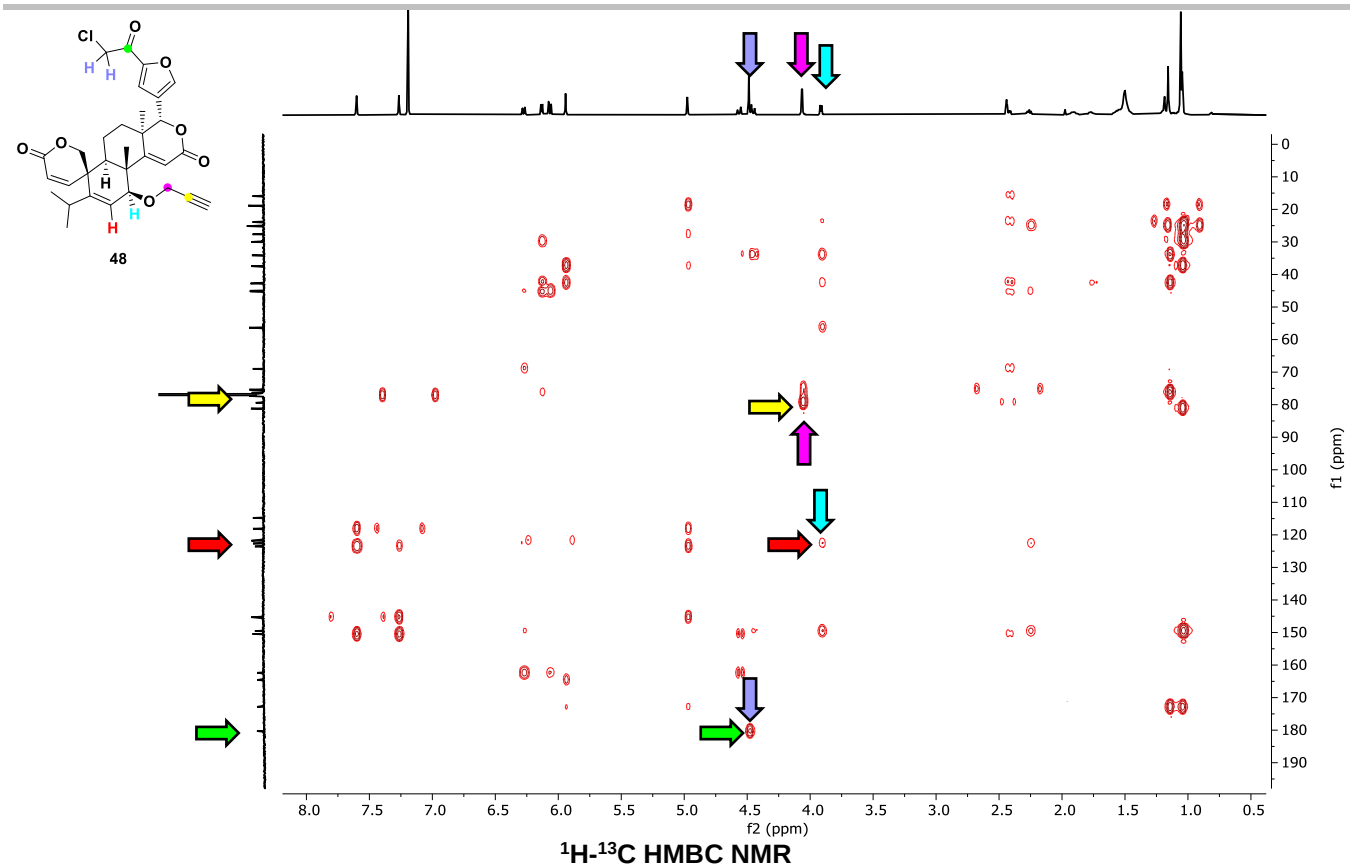
^{13}C NMR



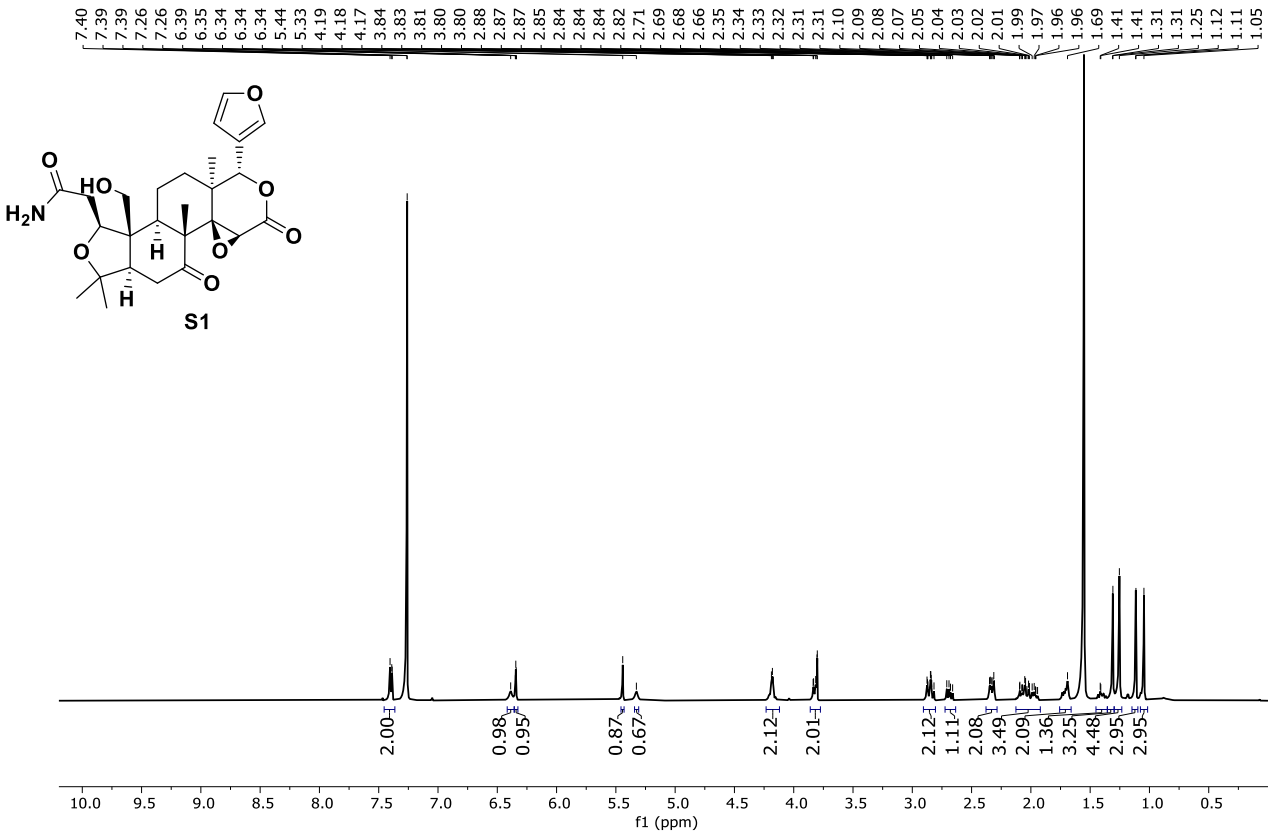
^{1}H-^{1}H COSY NMR



^{1}H-^{13}C HSQC NMR

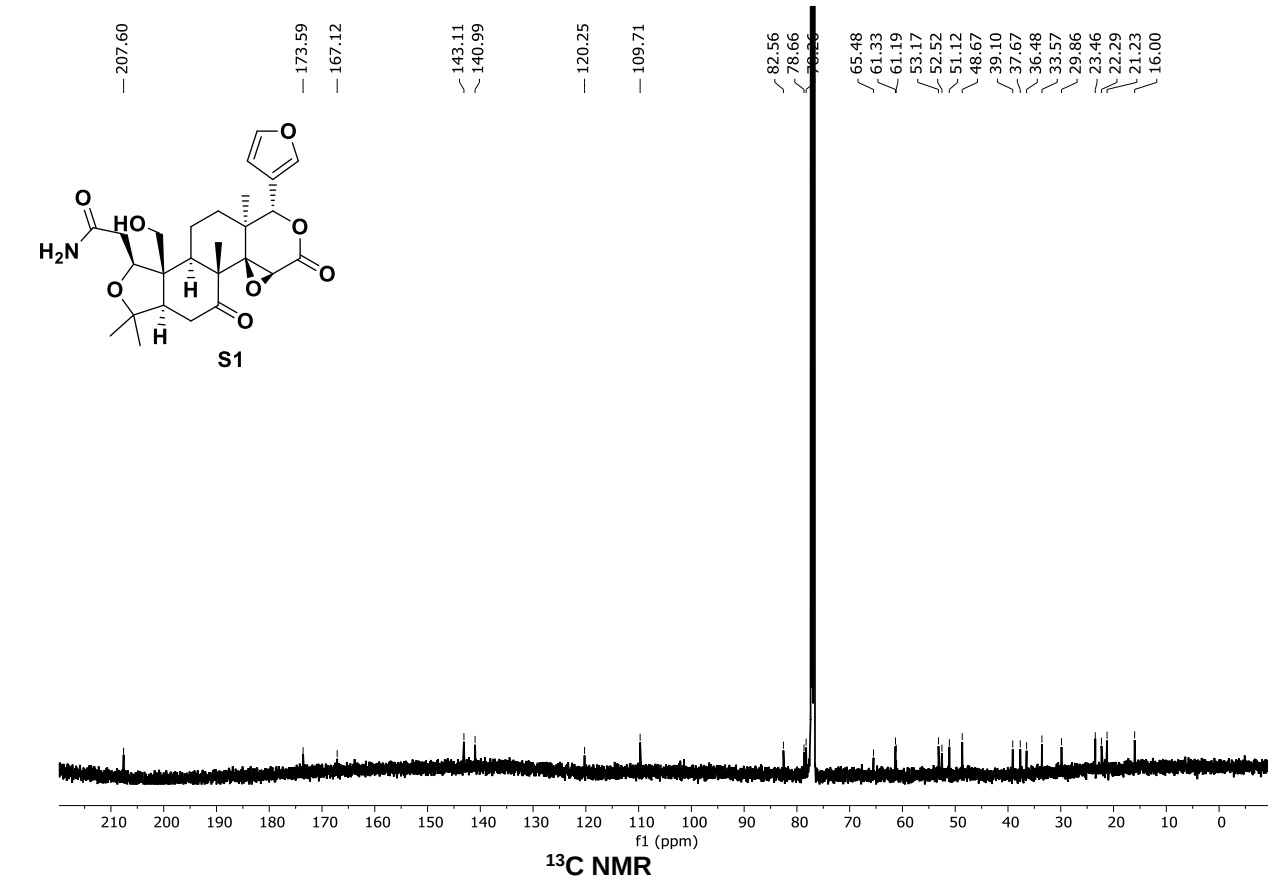


^{1}H-^{13}C HMBC NMR



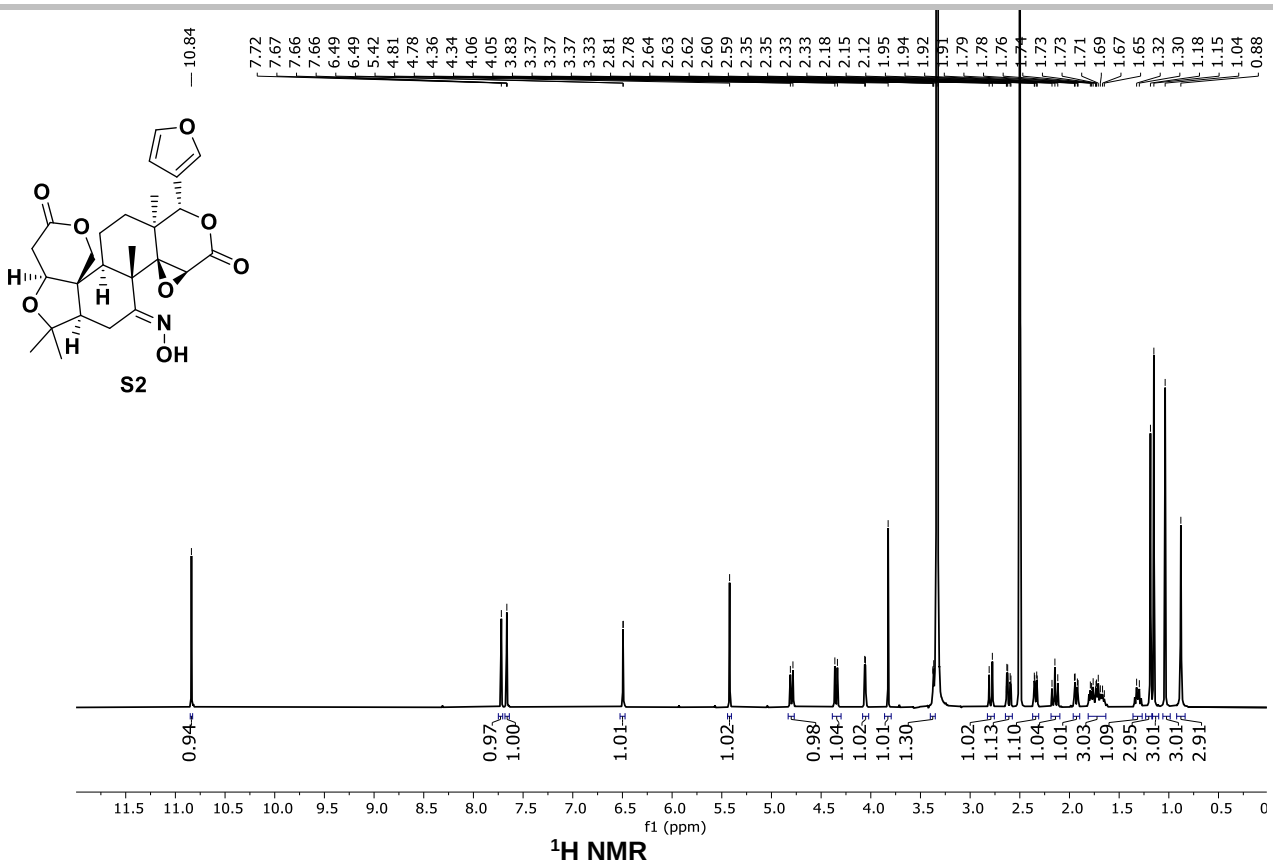
S1

^{1}H NMR



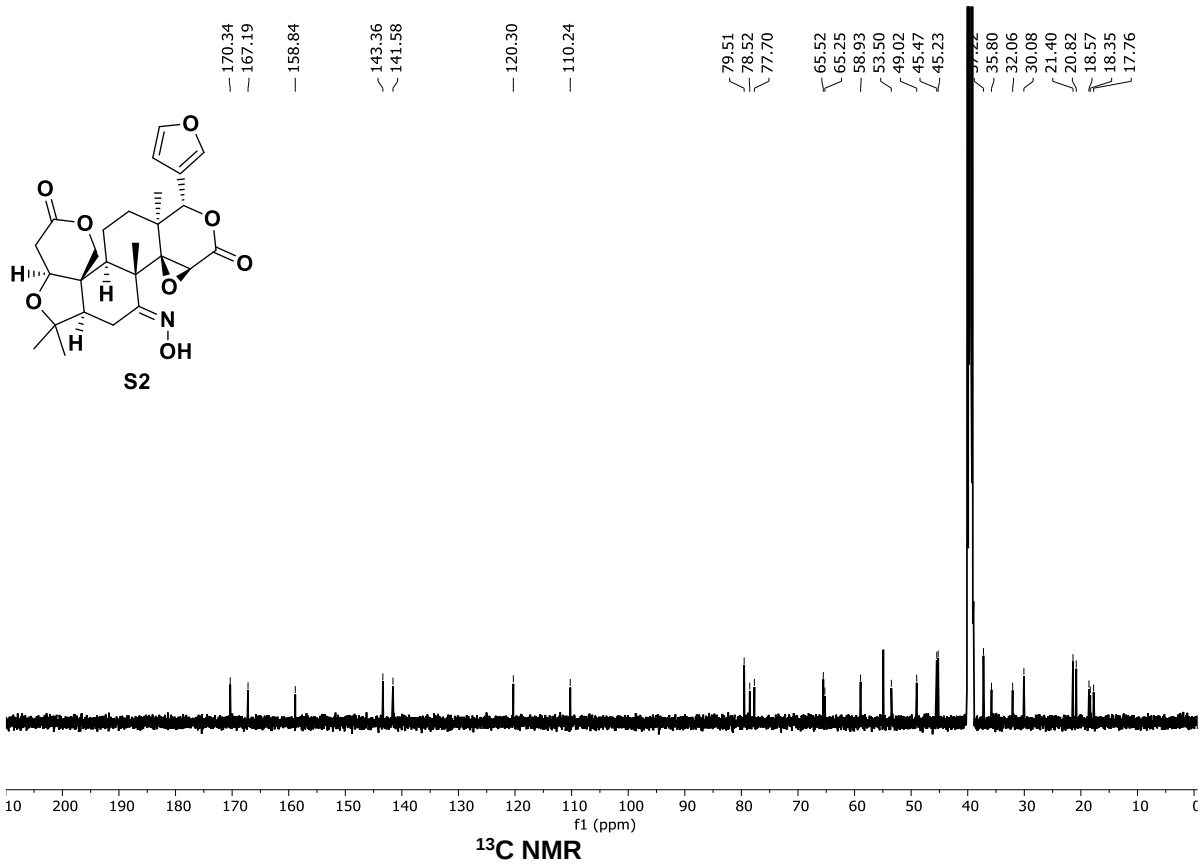
S1

^{13}C NMR



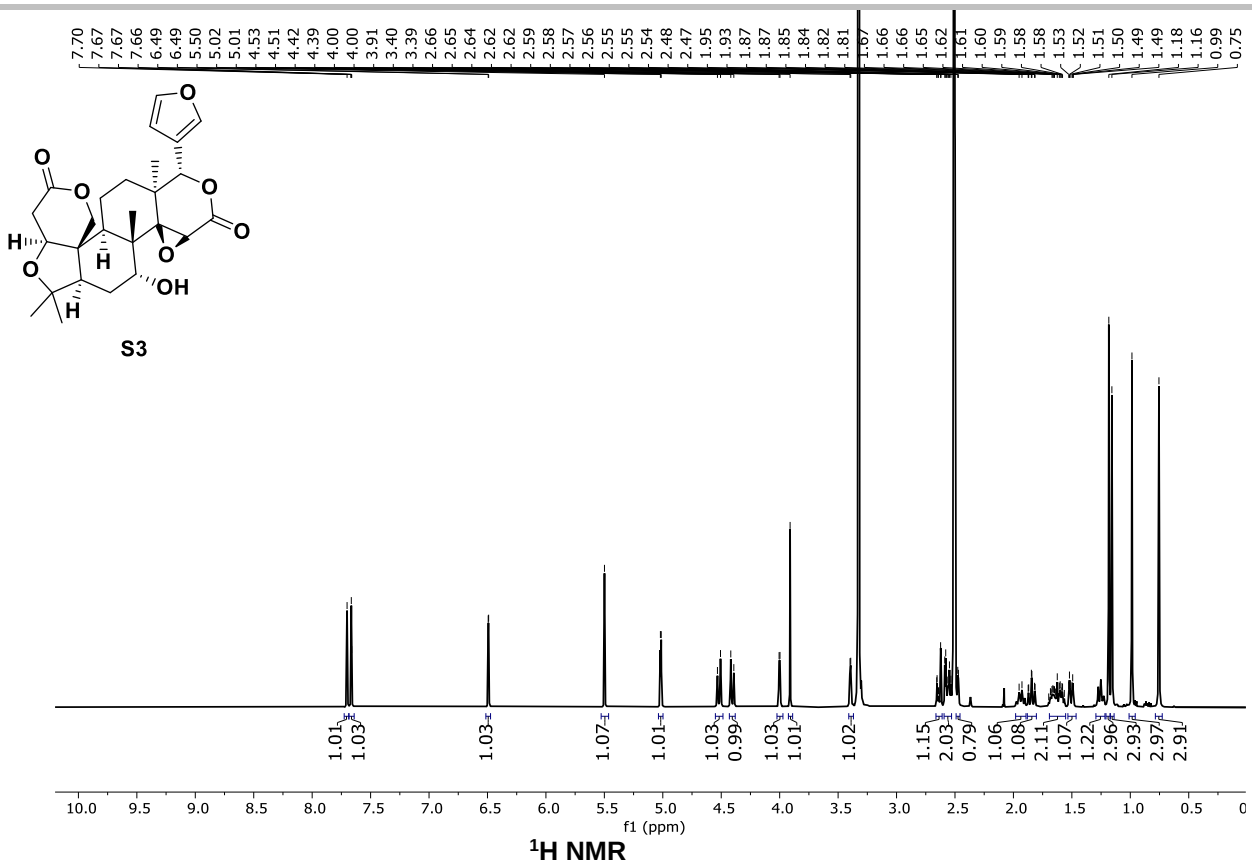
S2

^{1}H NMR



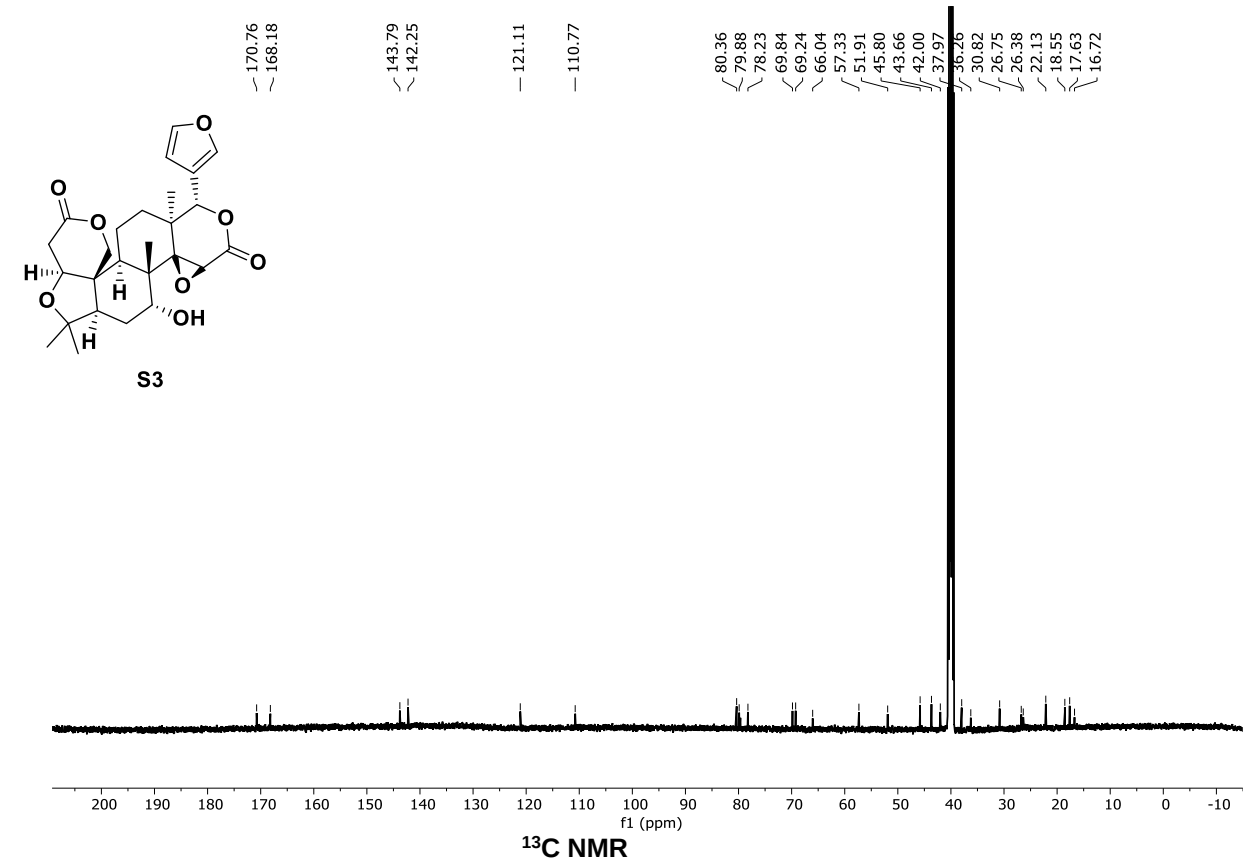
S2

^{13}C NMR



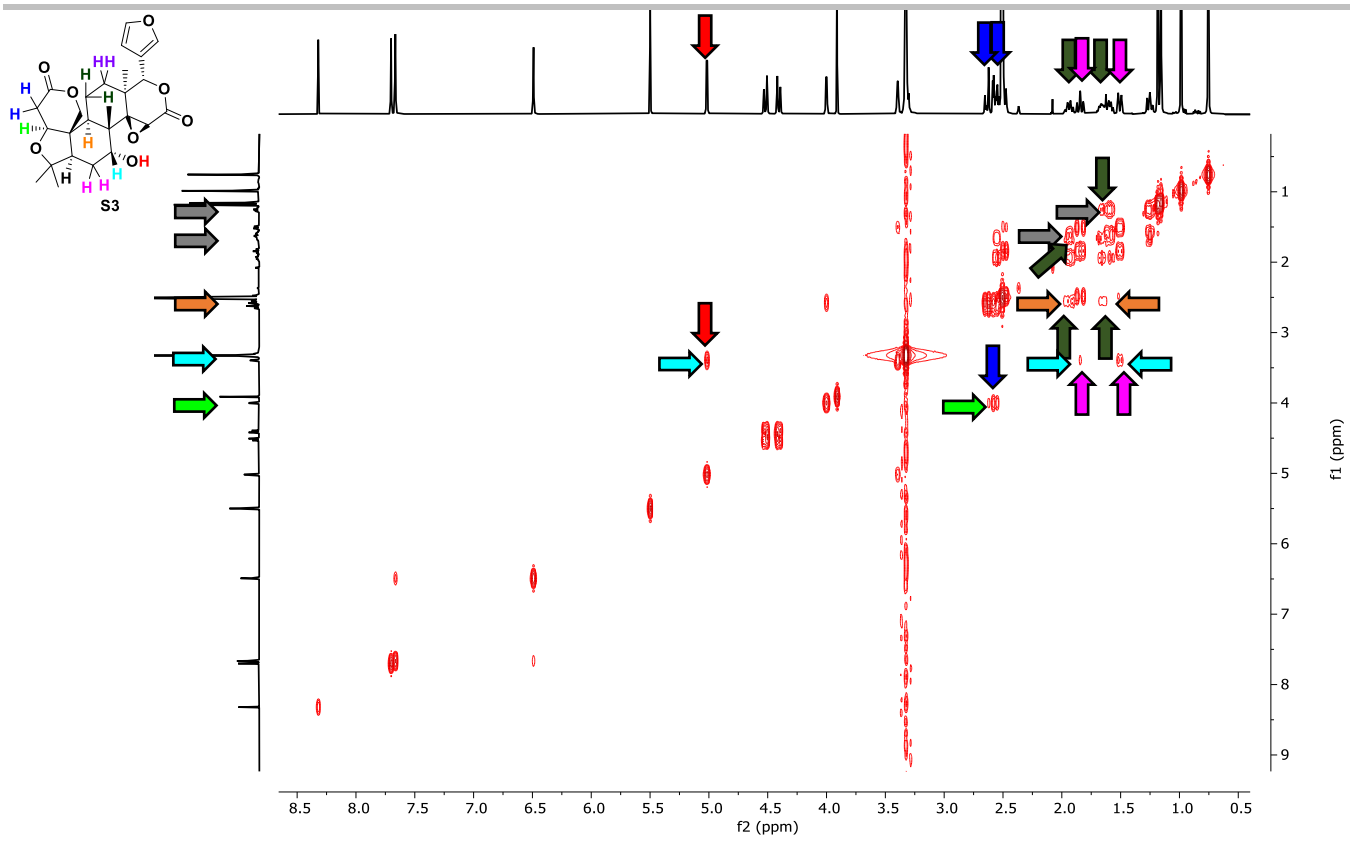
S3

^{1}H NMR

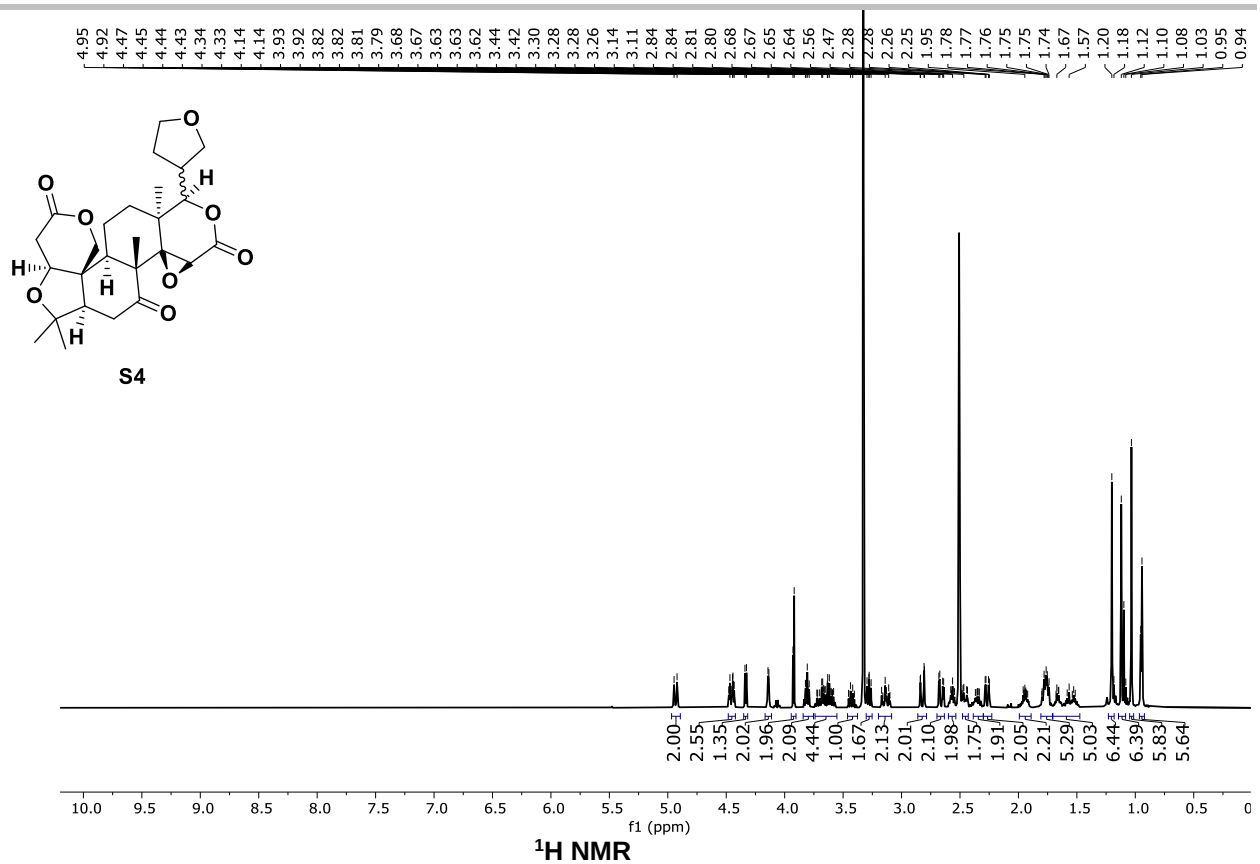


S3

^{13}C NMR

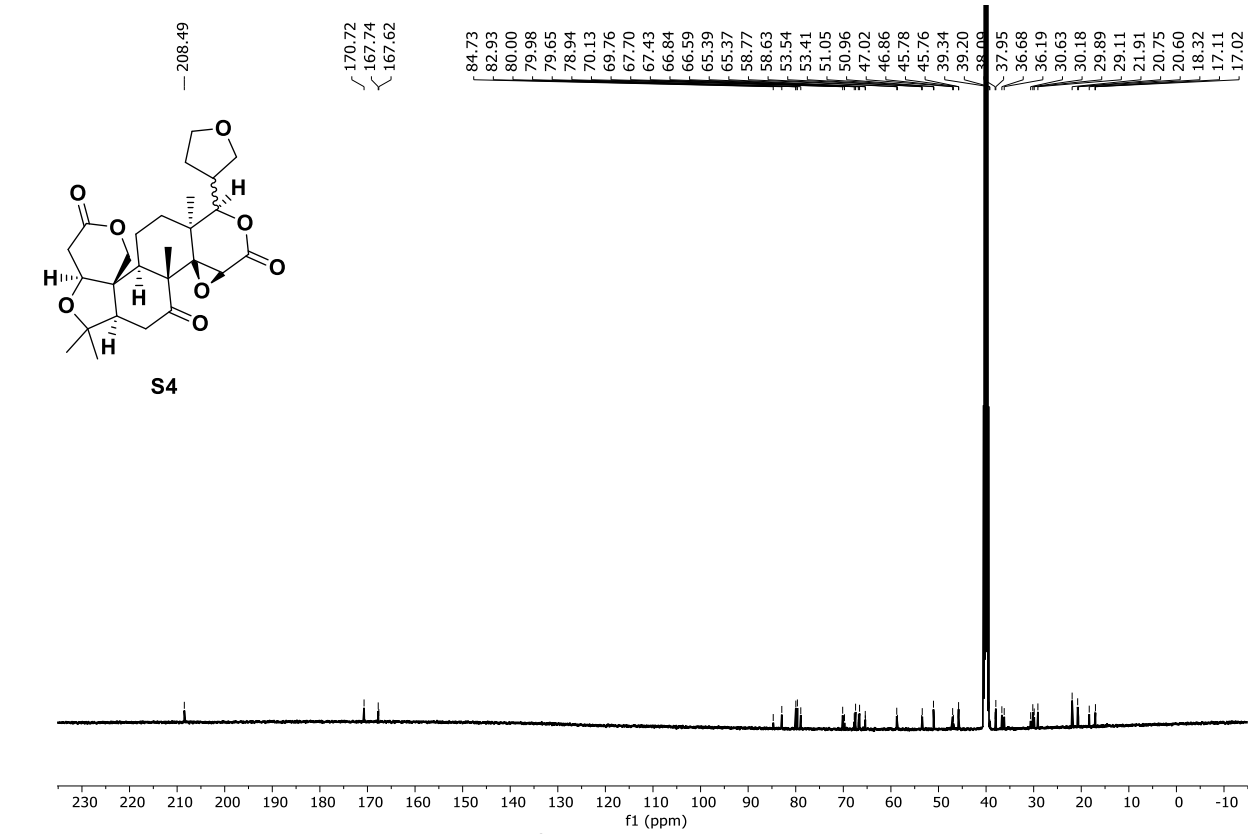


^{1}H-^{1}H COSY NMR



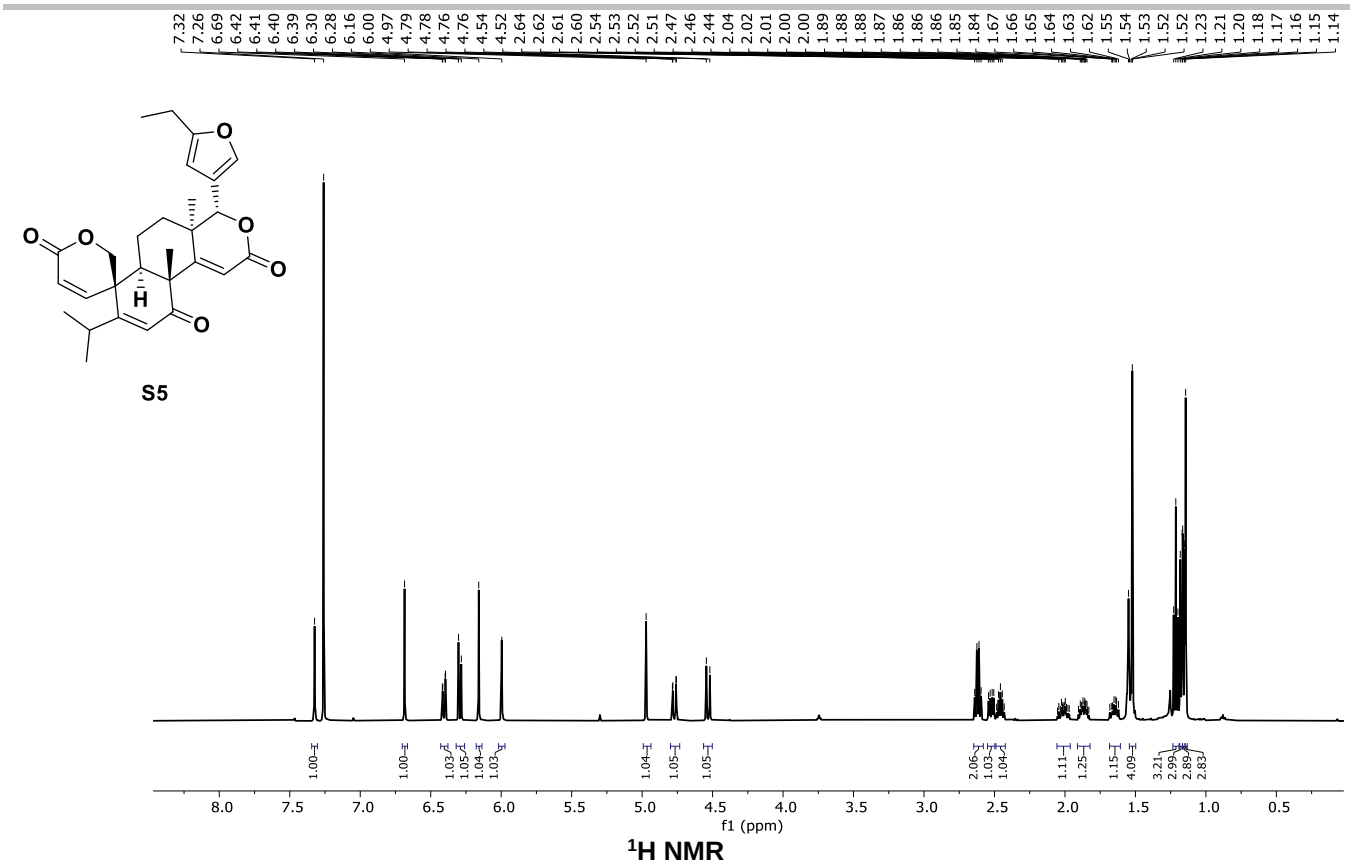
S4

^{1}H NMR

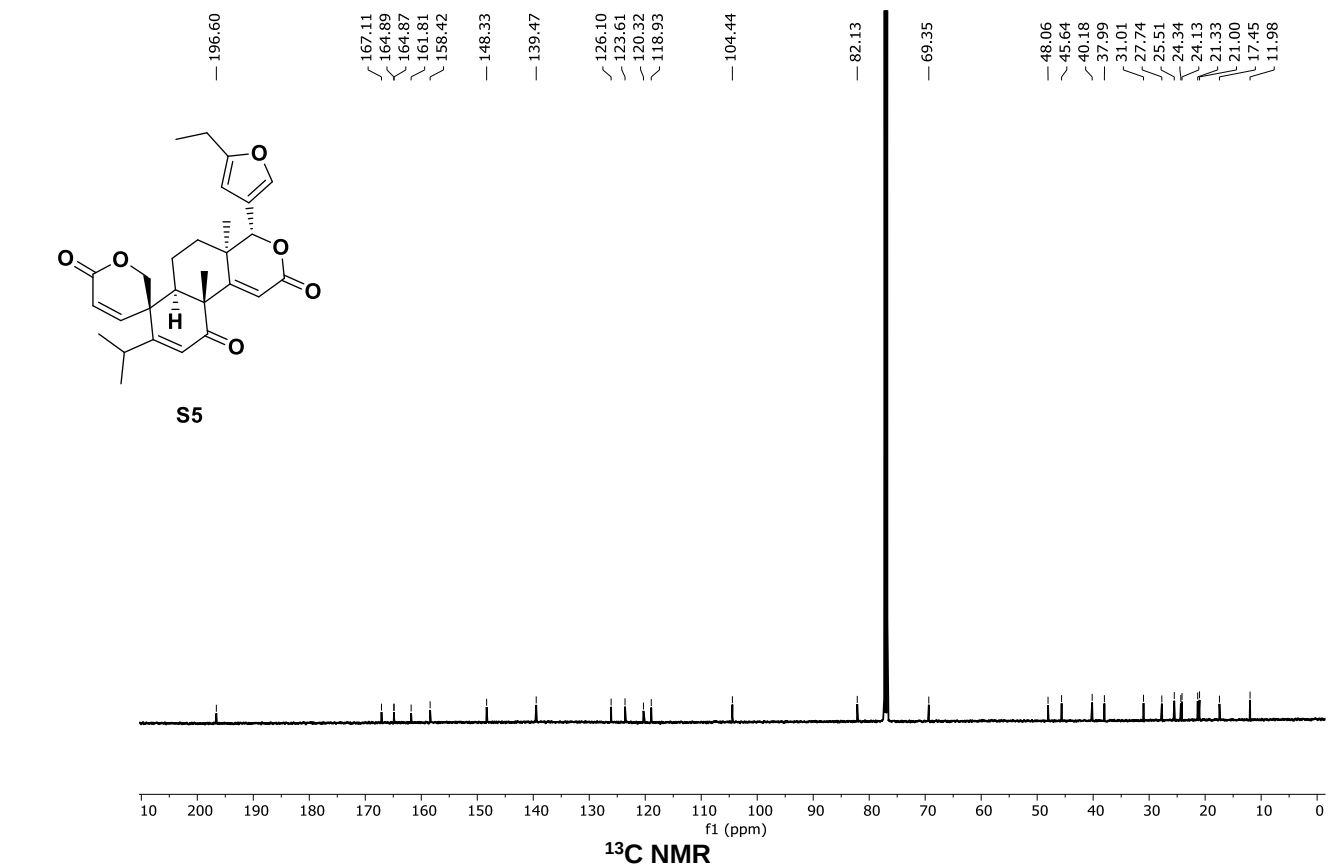


S4

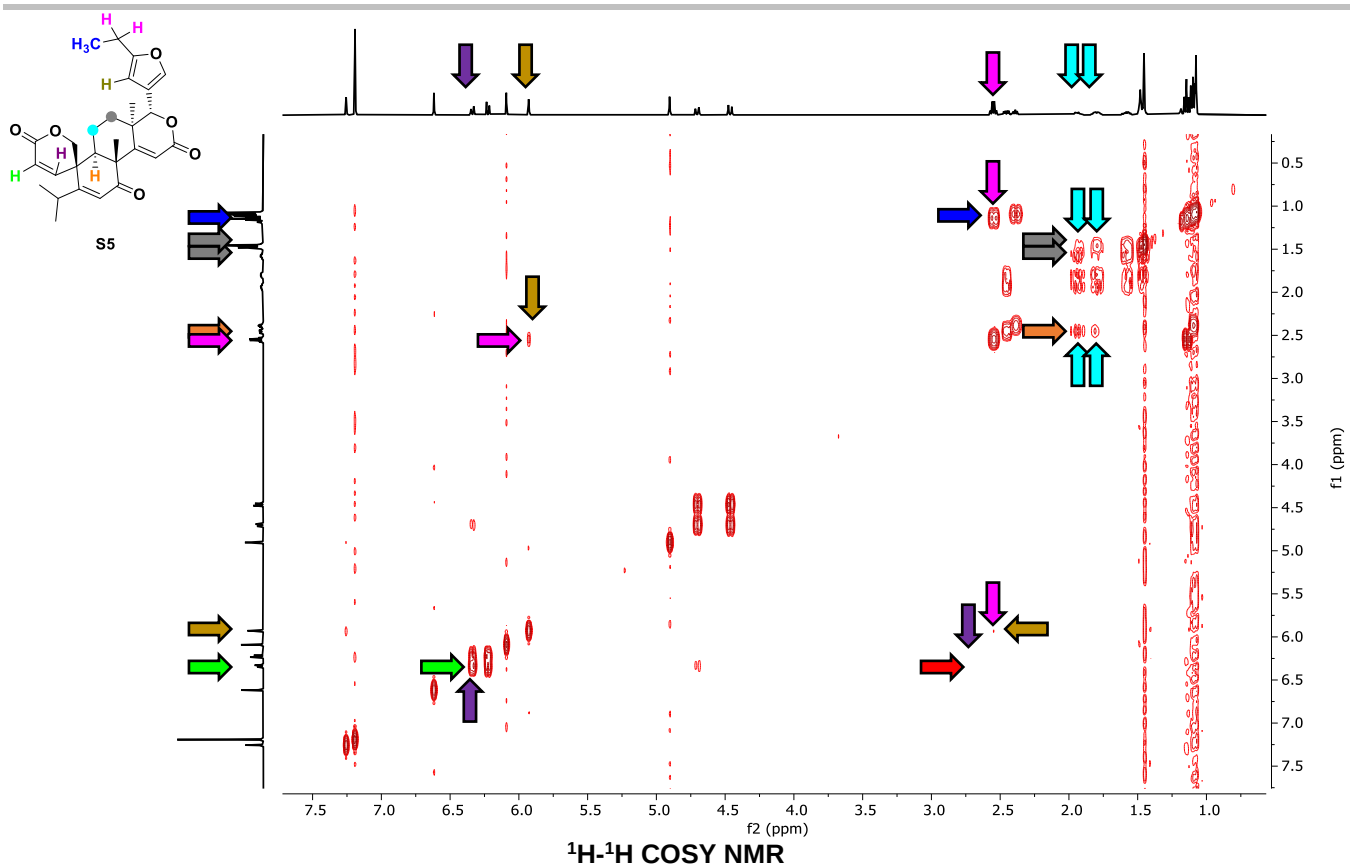
^{13}C NMR



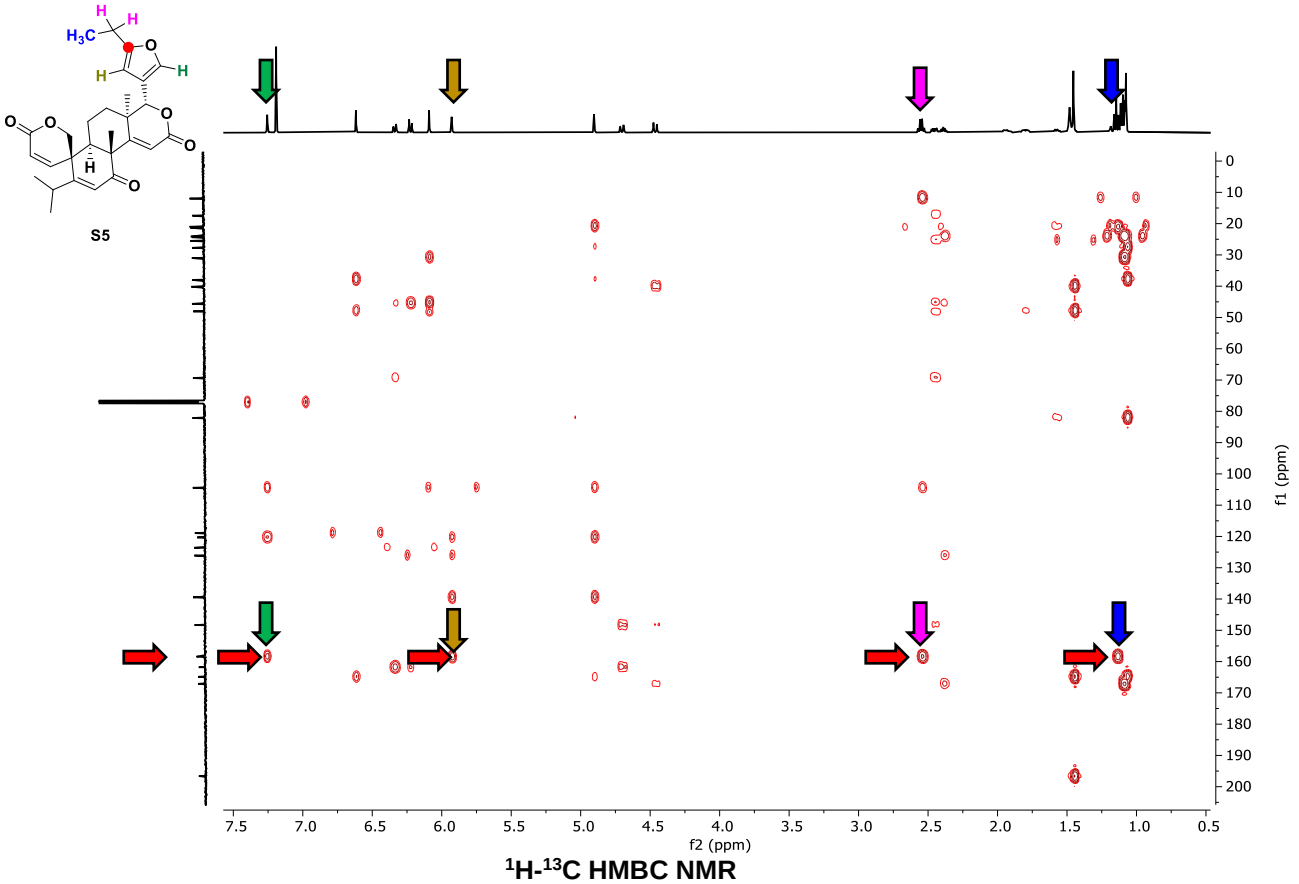
^{1}H NMR



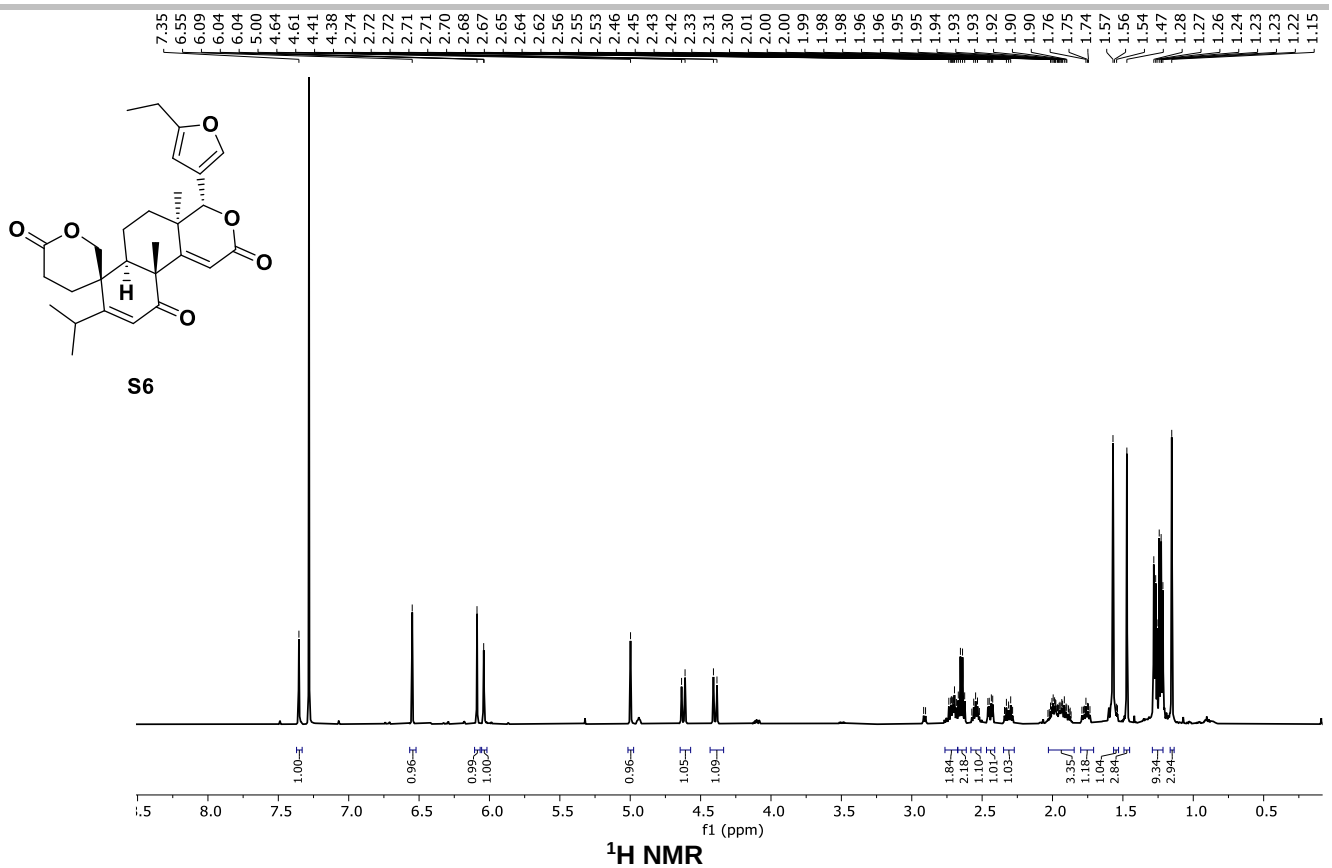
^{13}C NMR



^{1}H-^{1}H COSY NMR

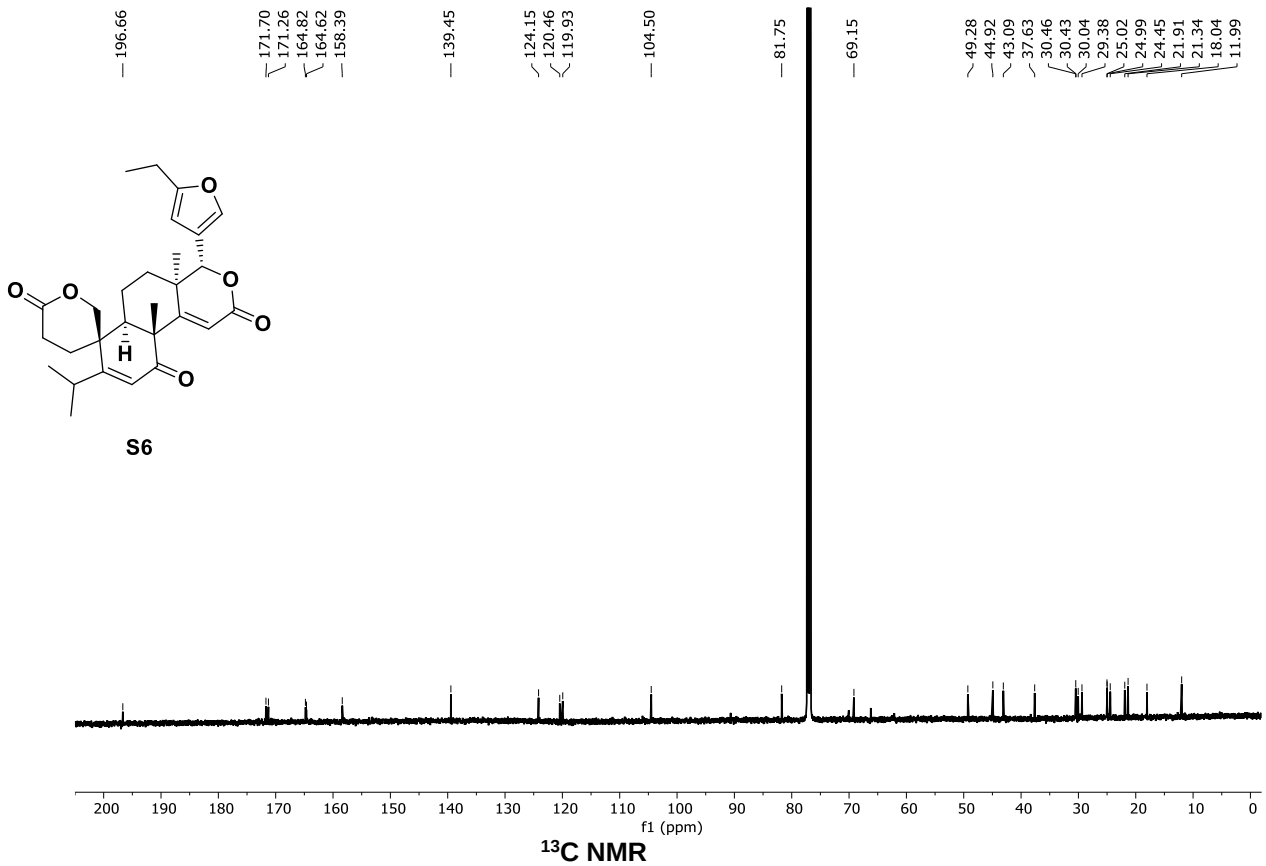


^{1}H-^{13}C HMBC NMR



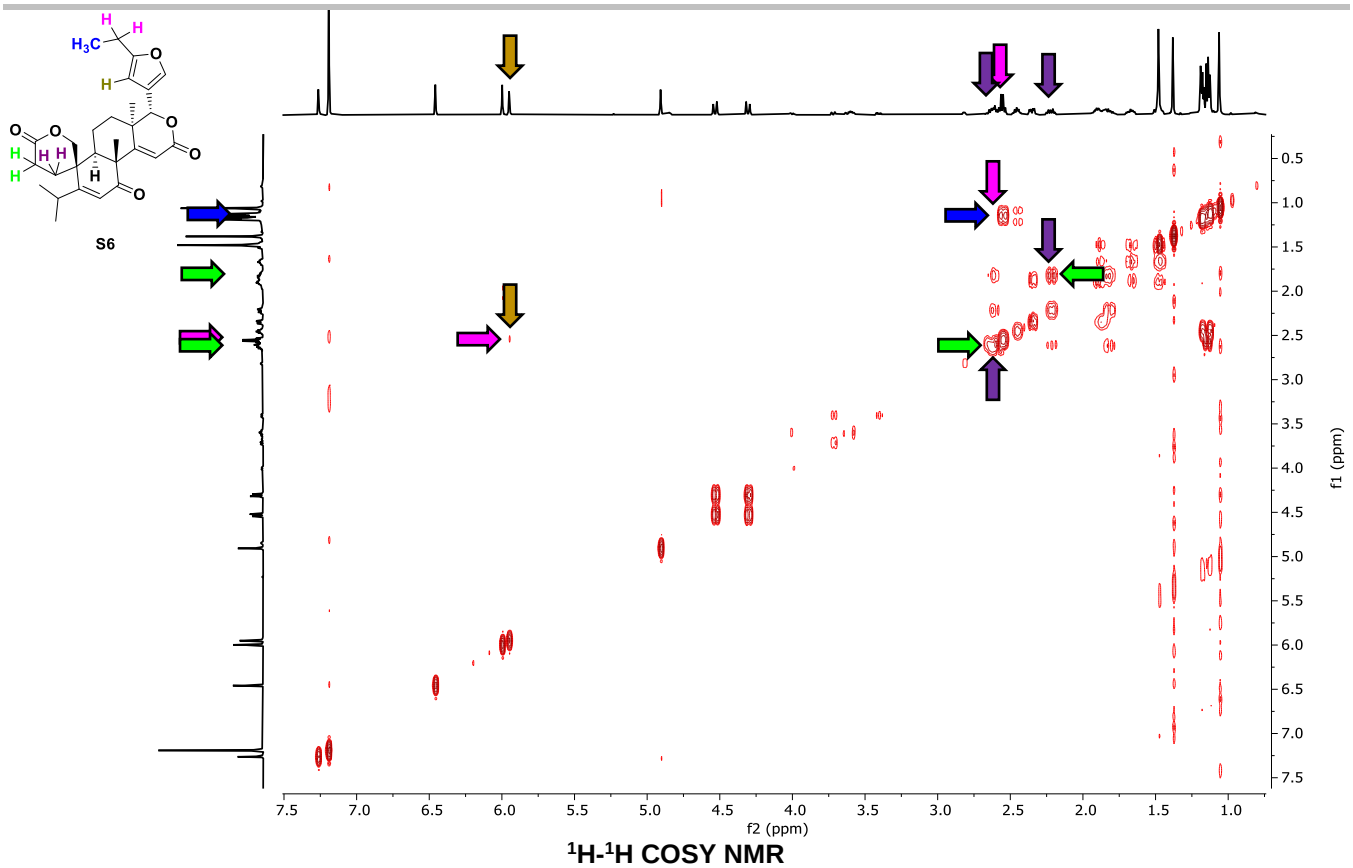
S6

^{1}H NMR

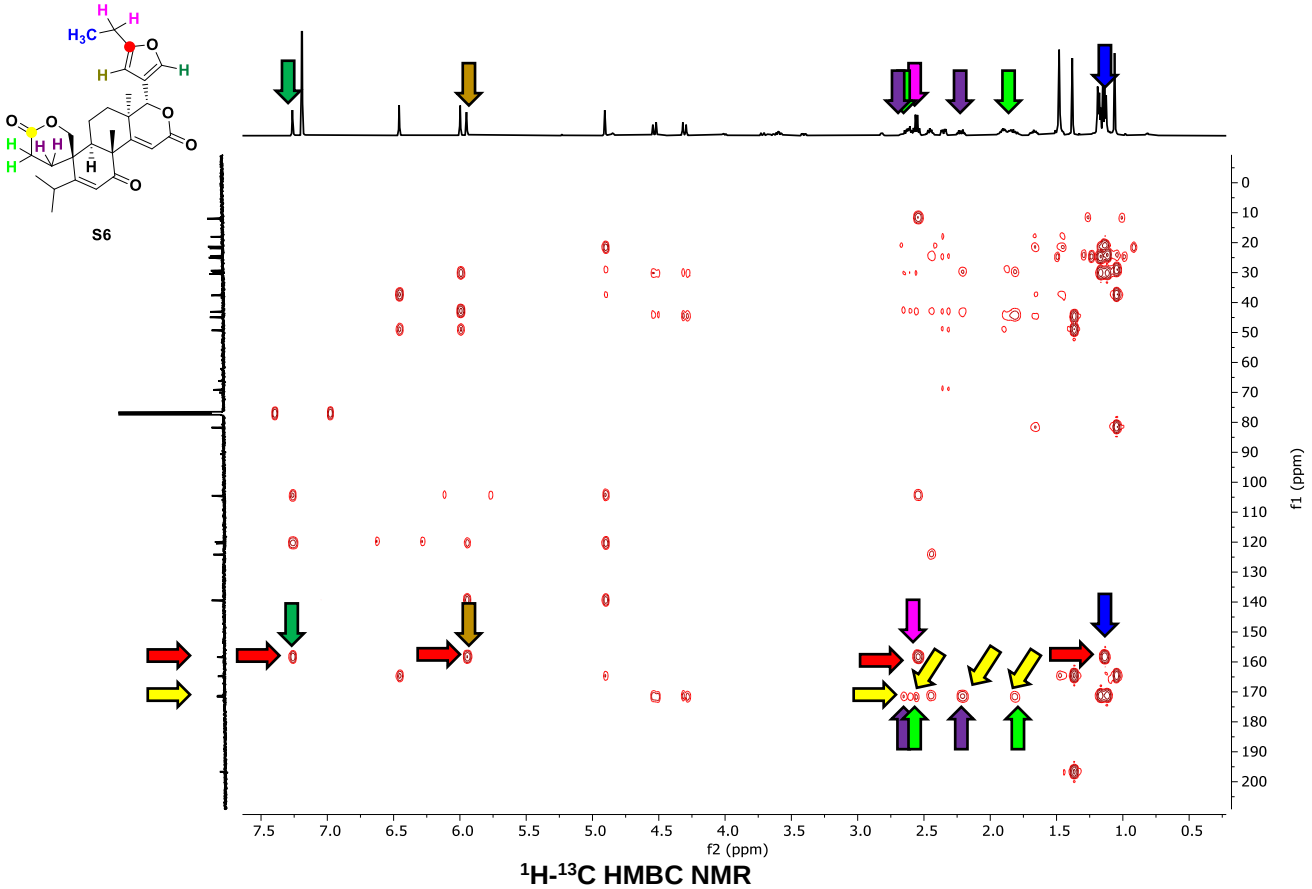


S6

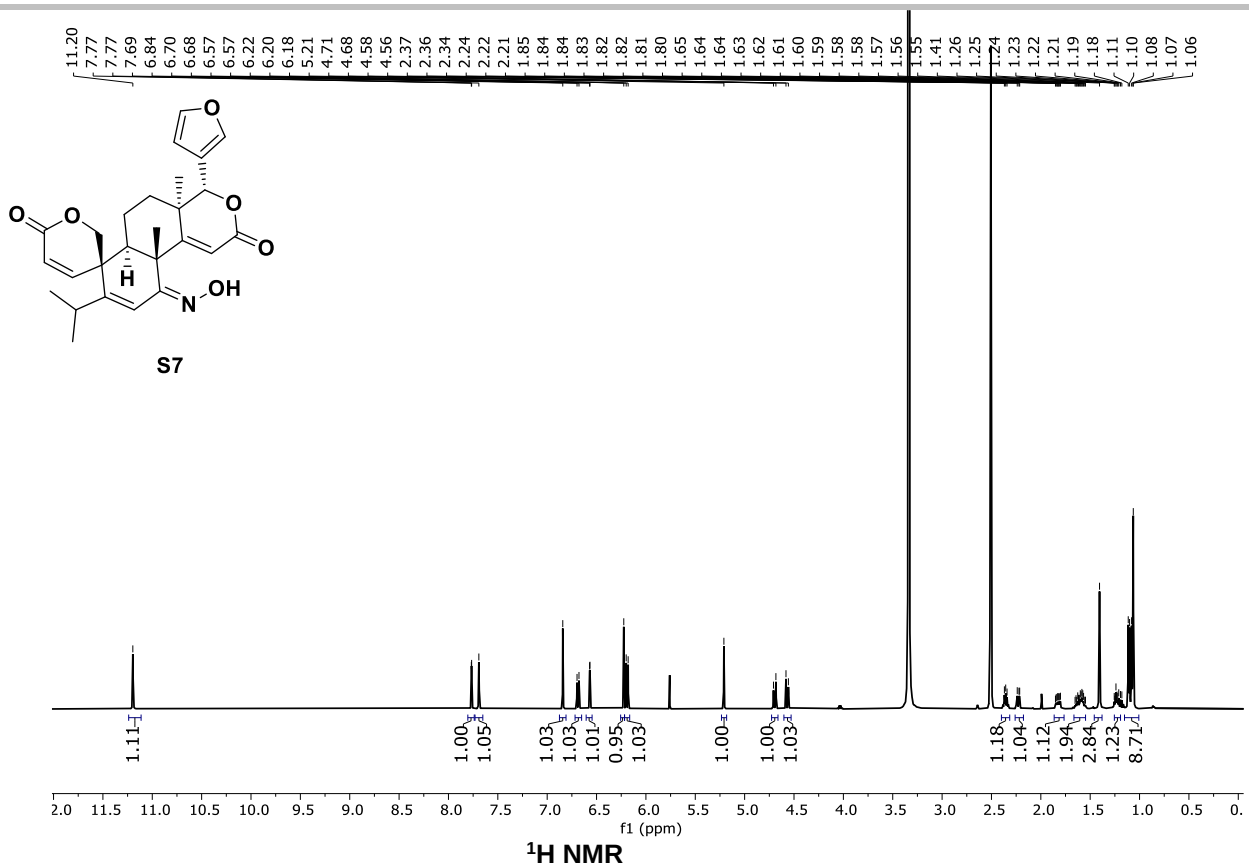
^{13}C NMR



^{1}H-^{1}H COSY NMR

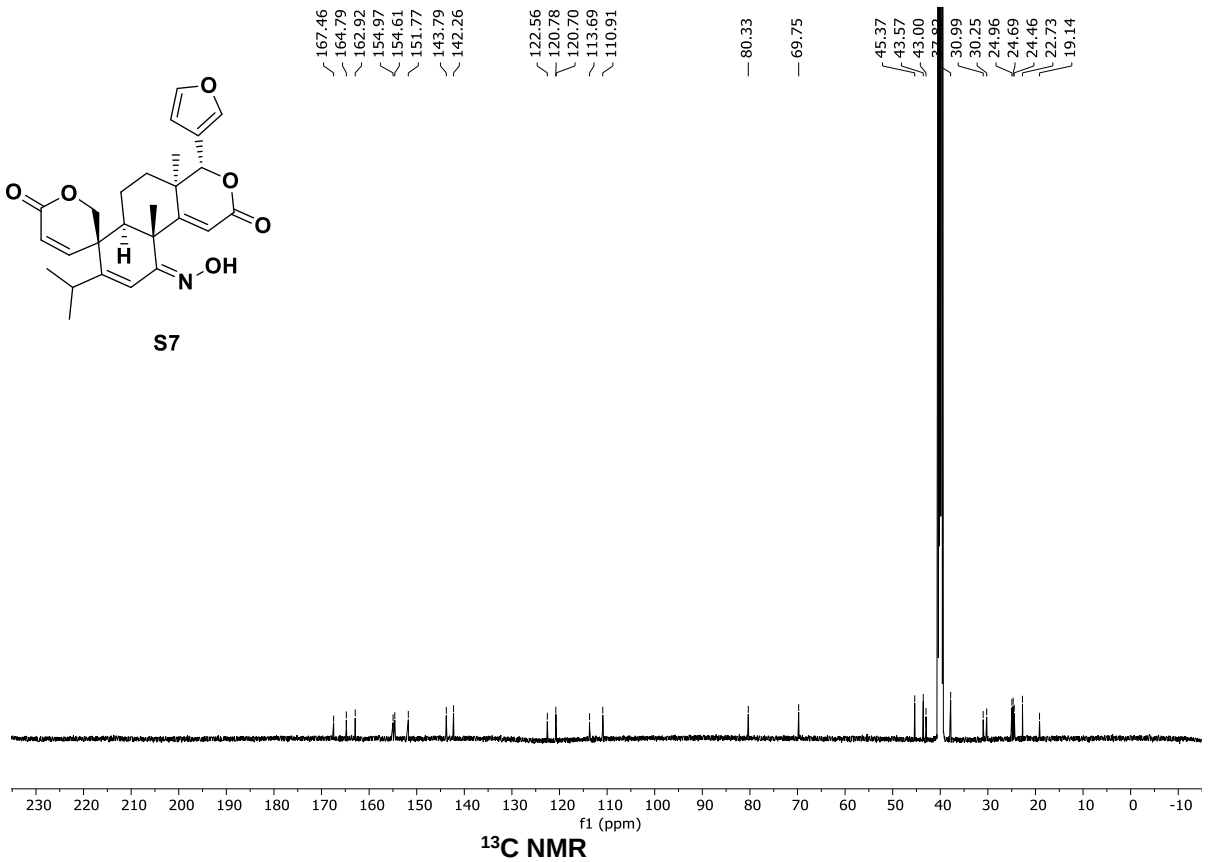


^{1}H-^{13}C HMBC NMR



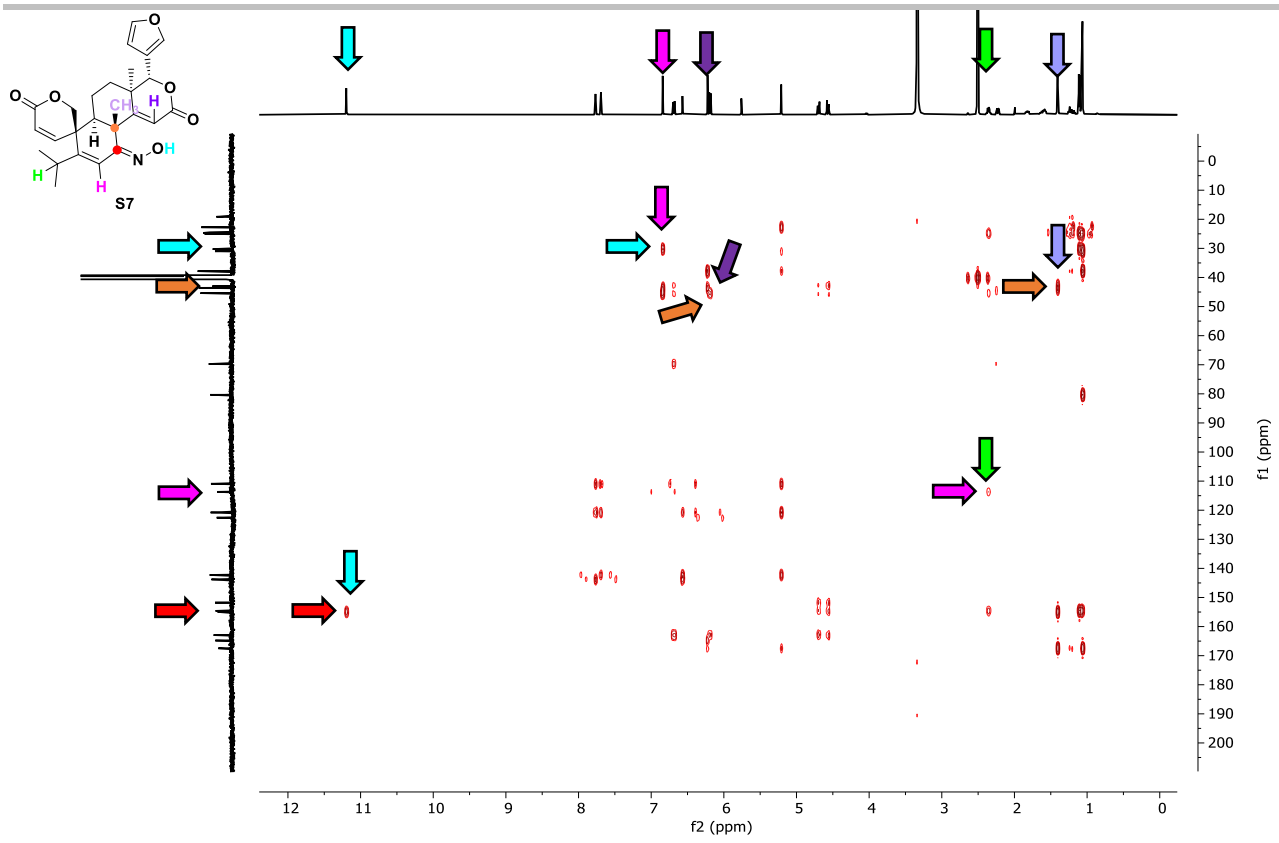
S7

^{1}H NMR

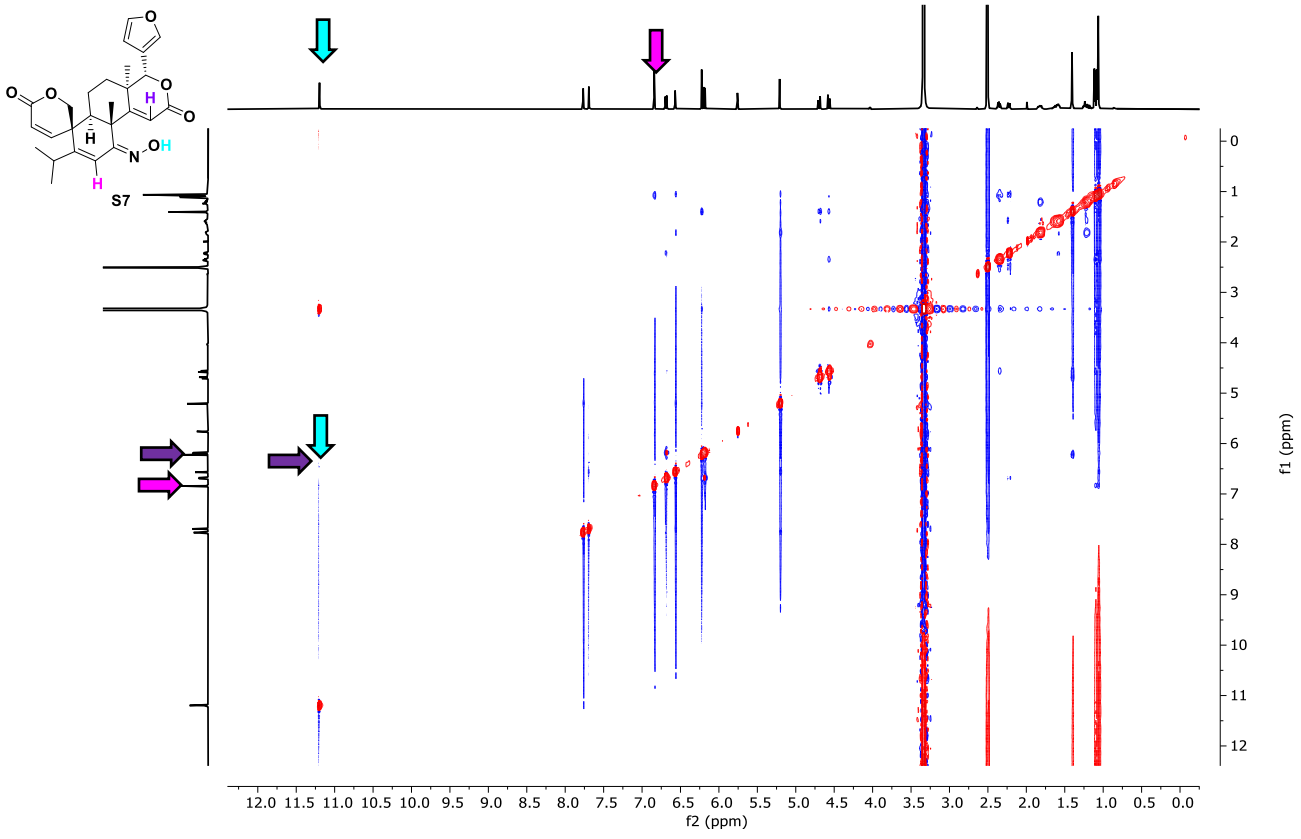


S7

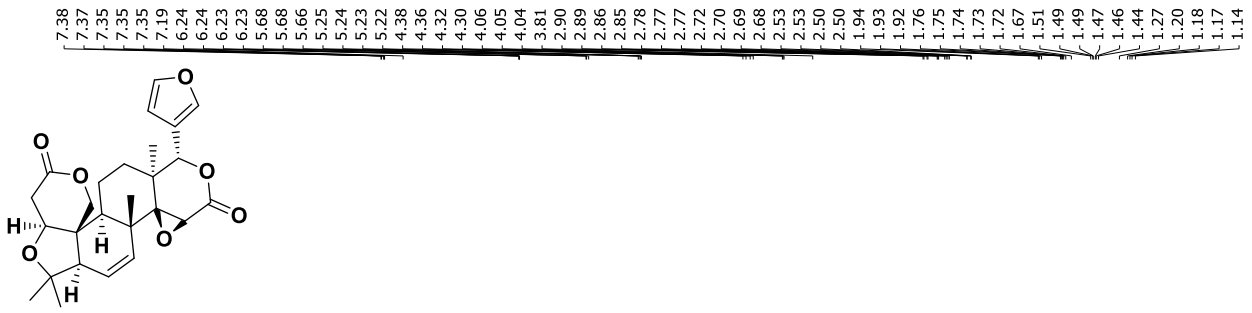
^{13}C NMR



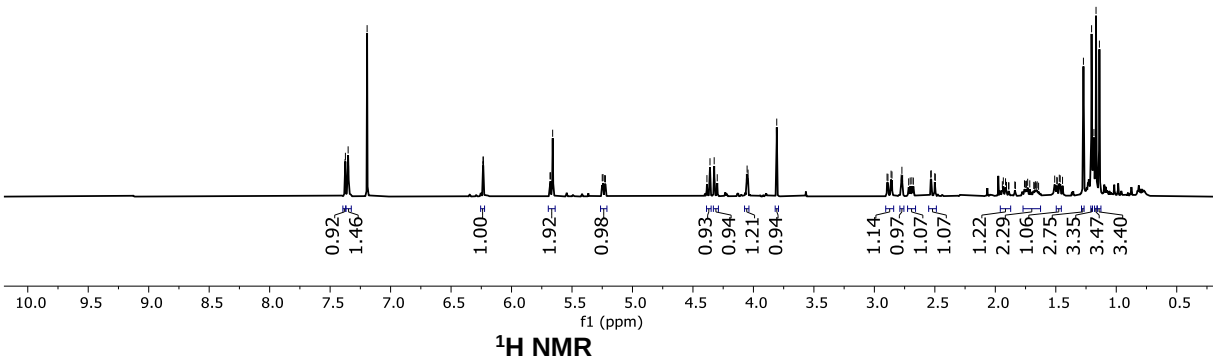
^{1}H-^{13}C HMBC NMR



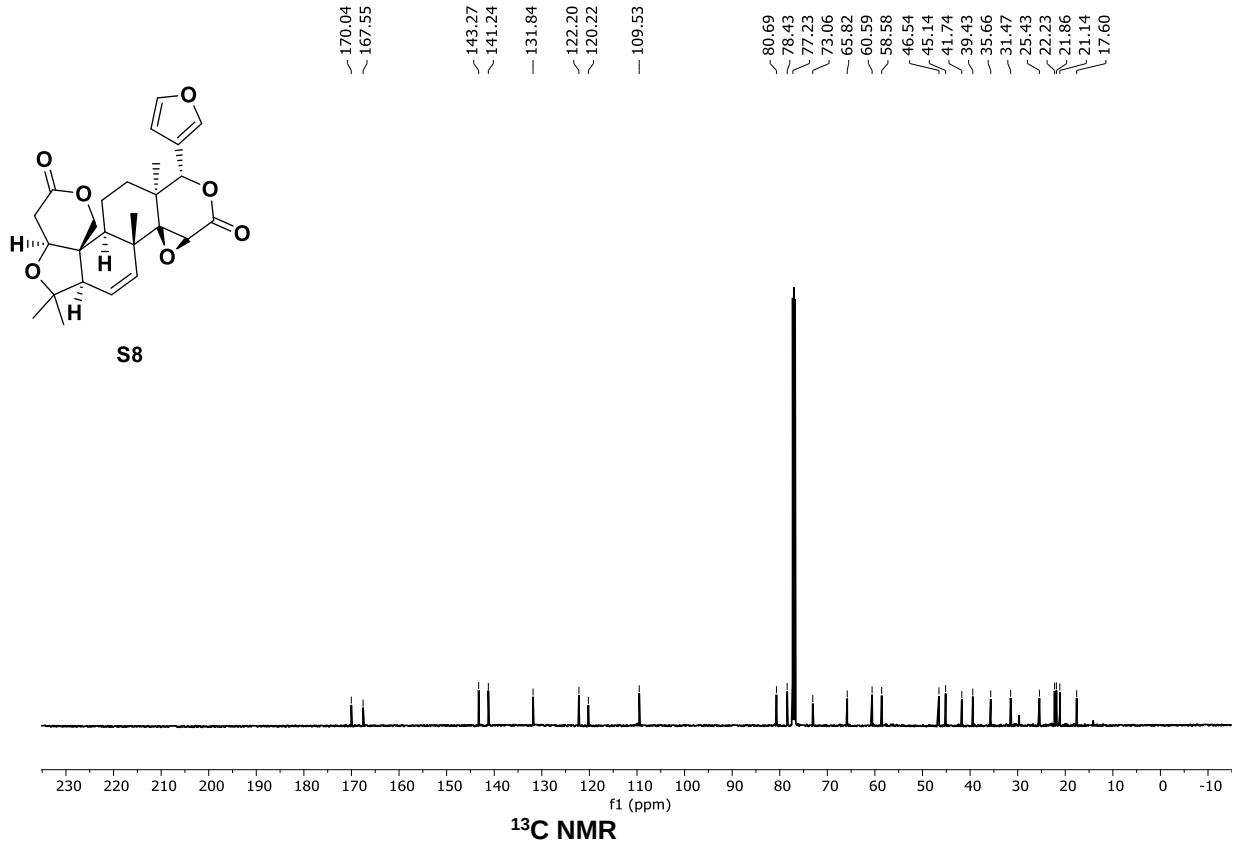
^{1}H-^{1}H NOESY NMR



S8

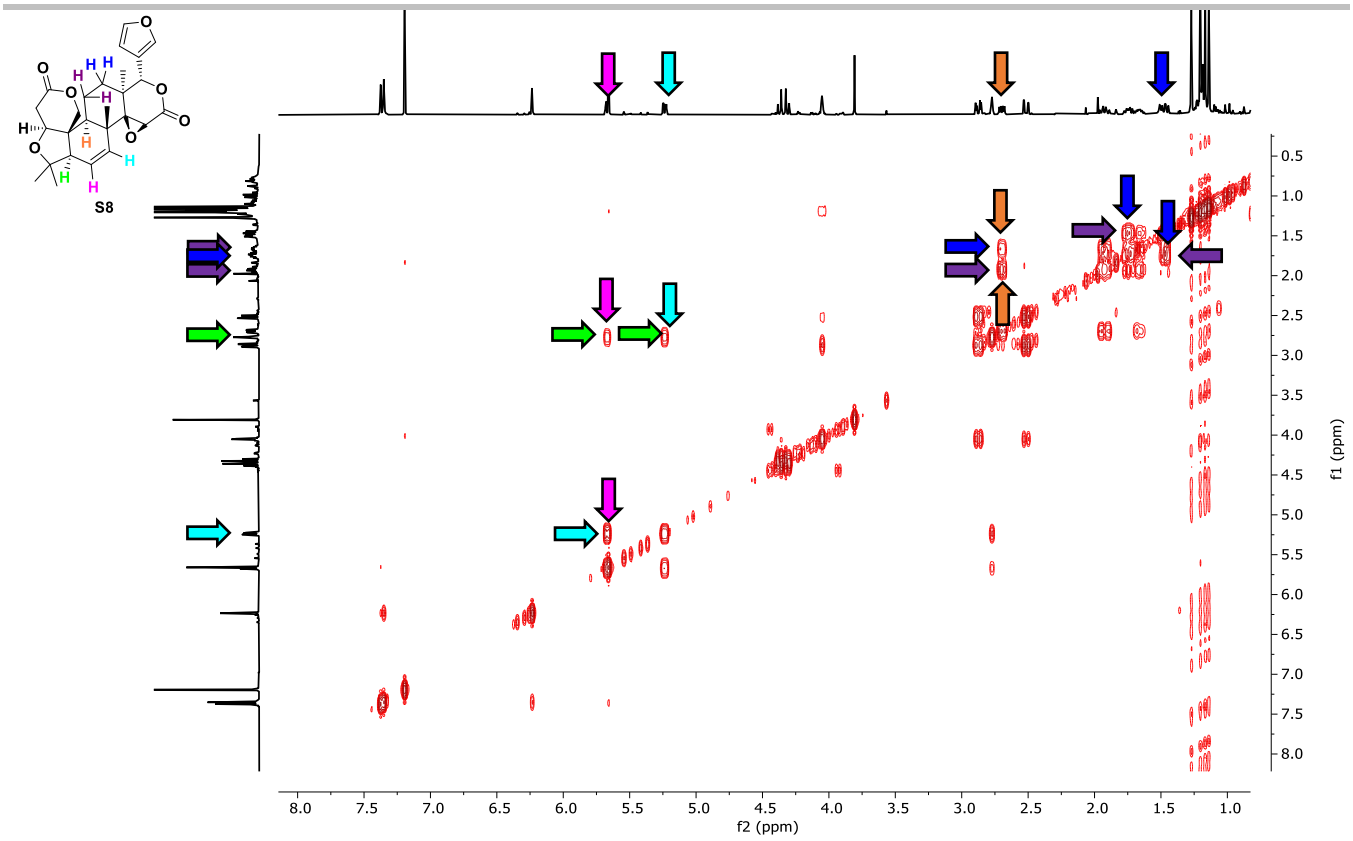


^{1}H NMR

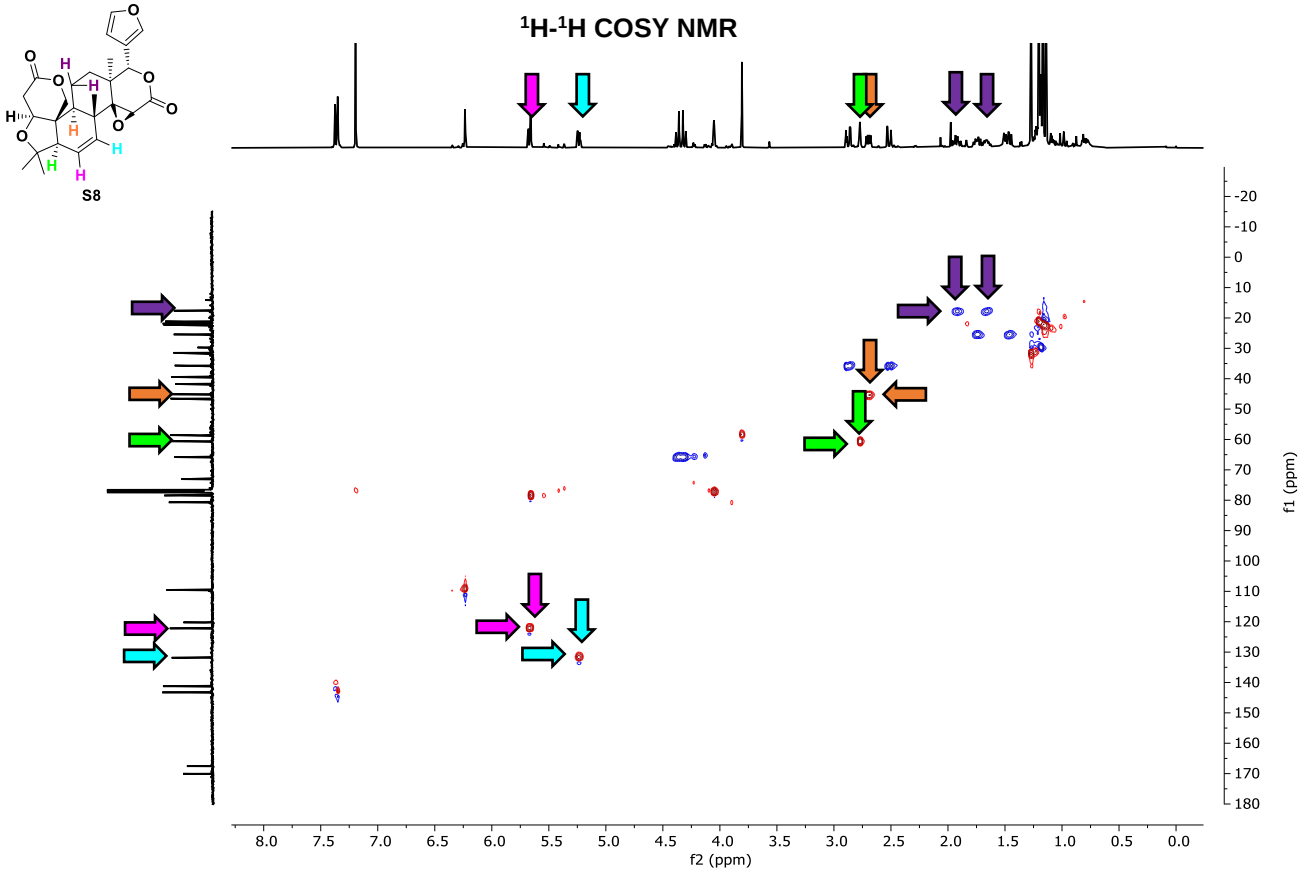


S8

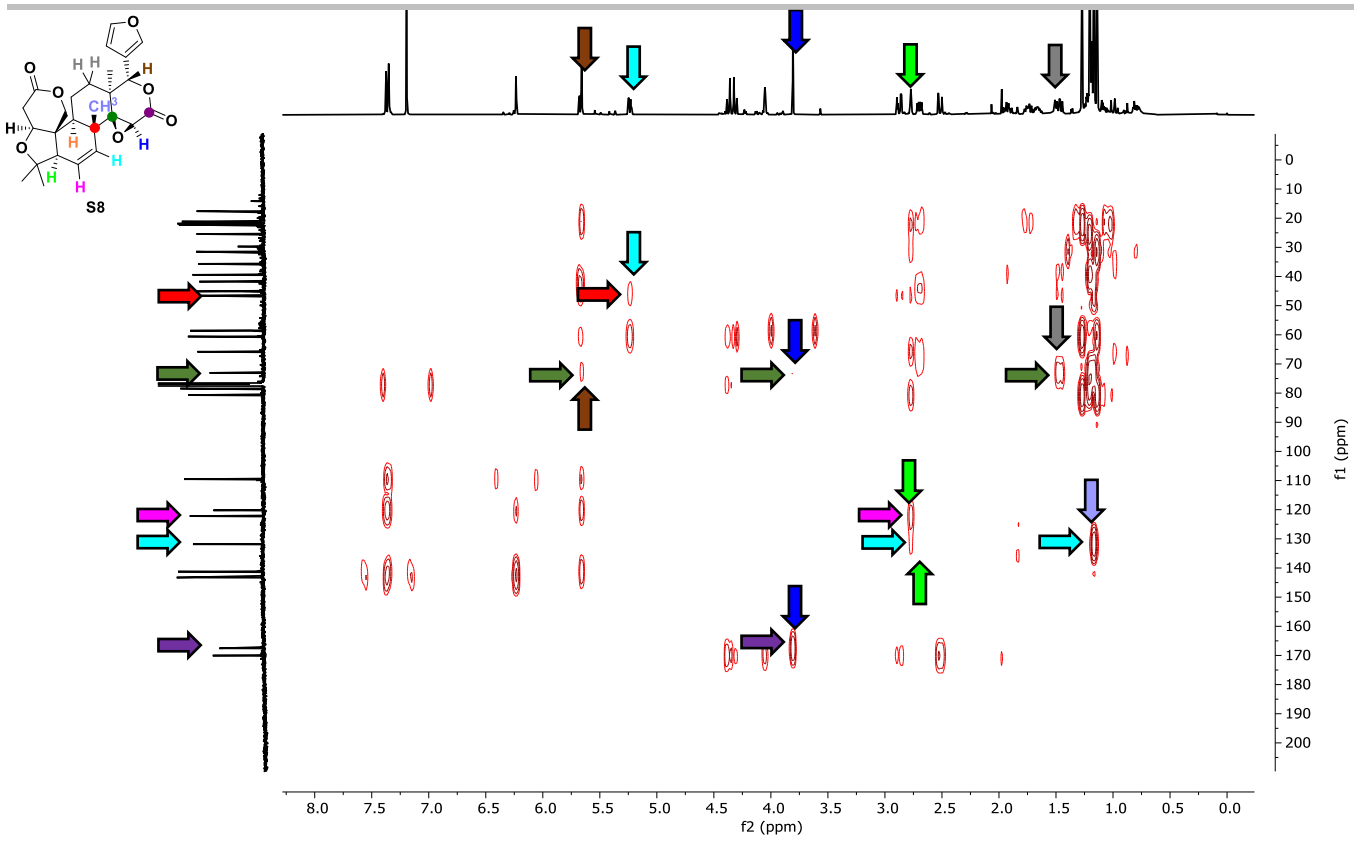
^{13}C NMR



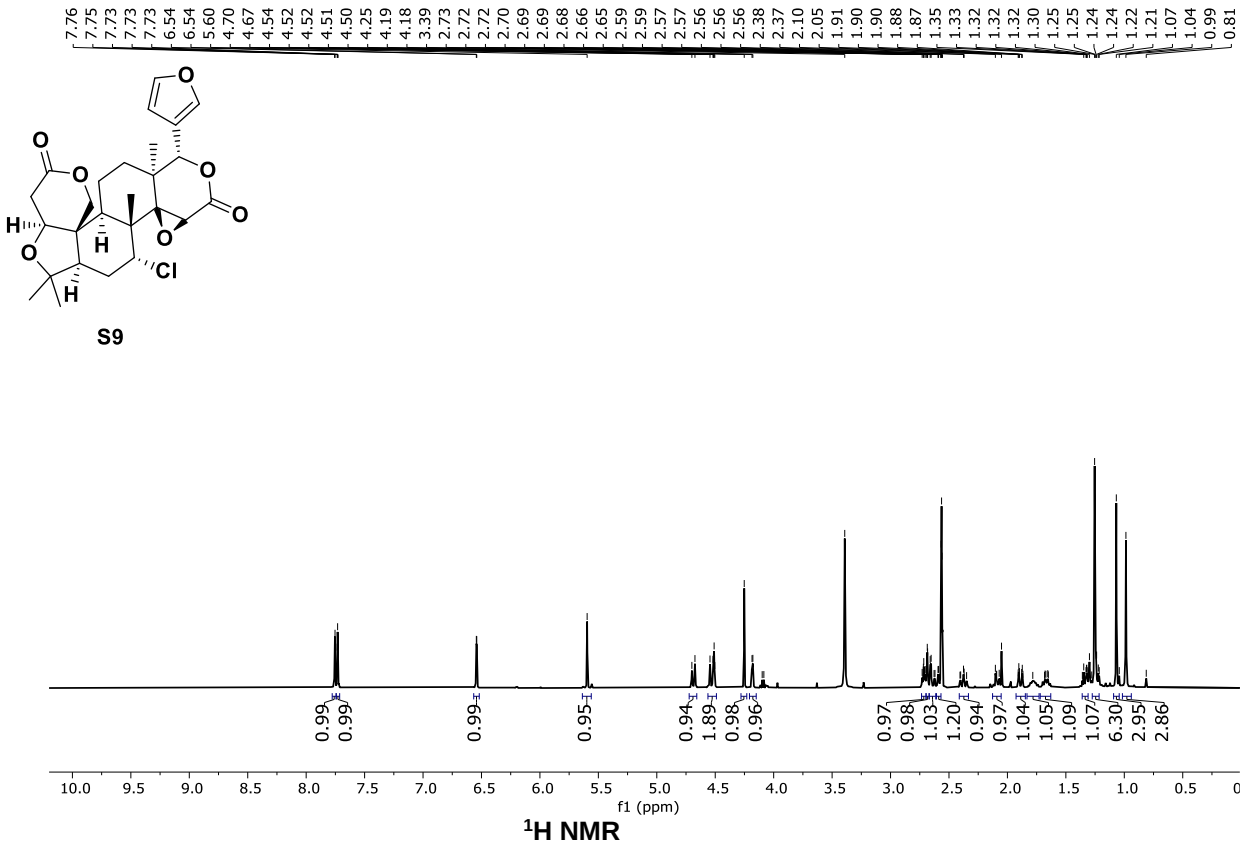
^{1}H-^{1}H COSY NMR



^{1}H-^{13}C HSQC NMR

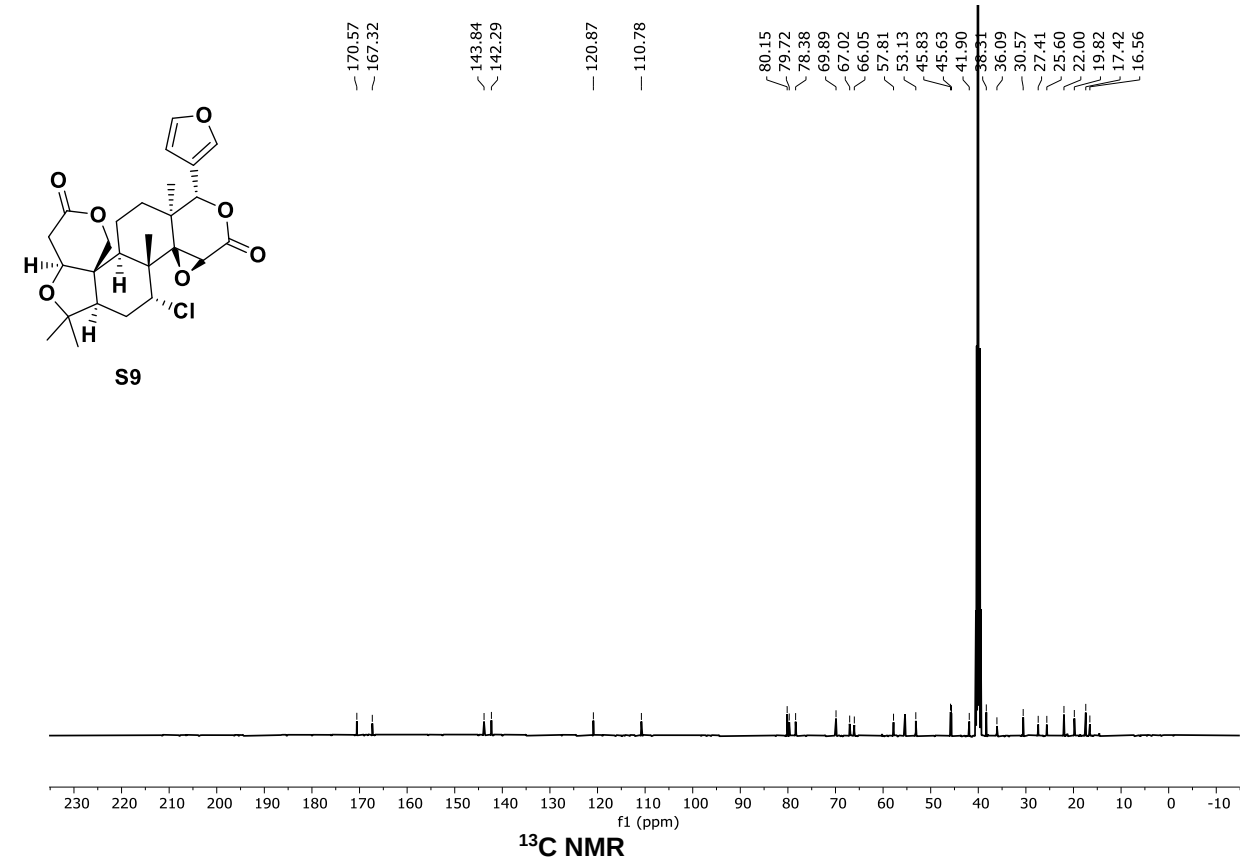


^{1}H-^{13}C HMBC NMR



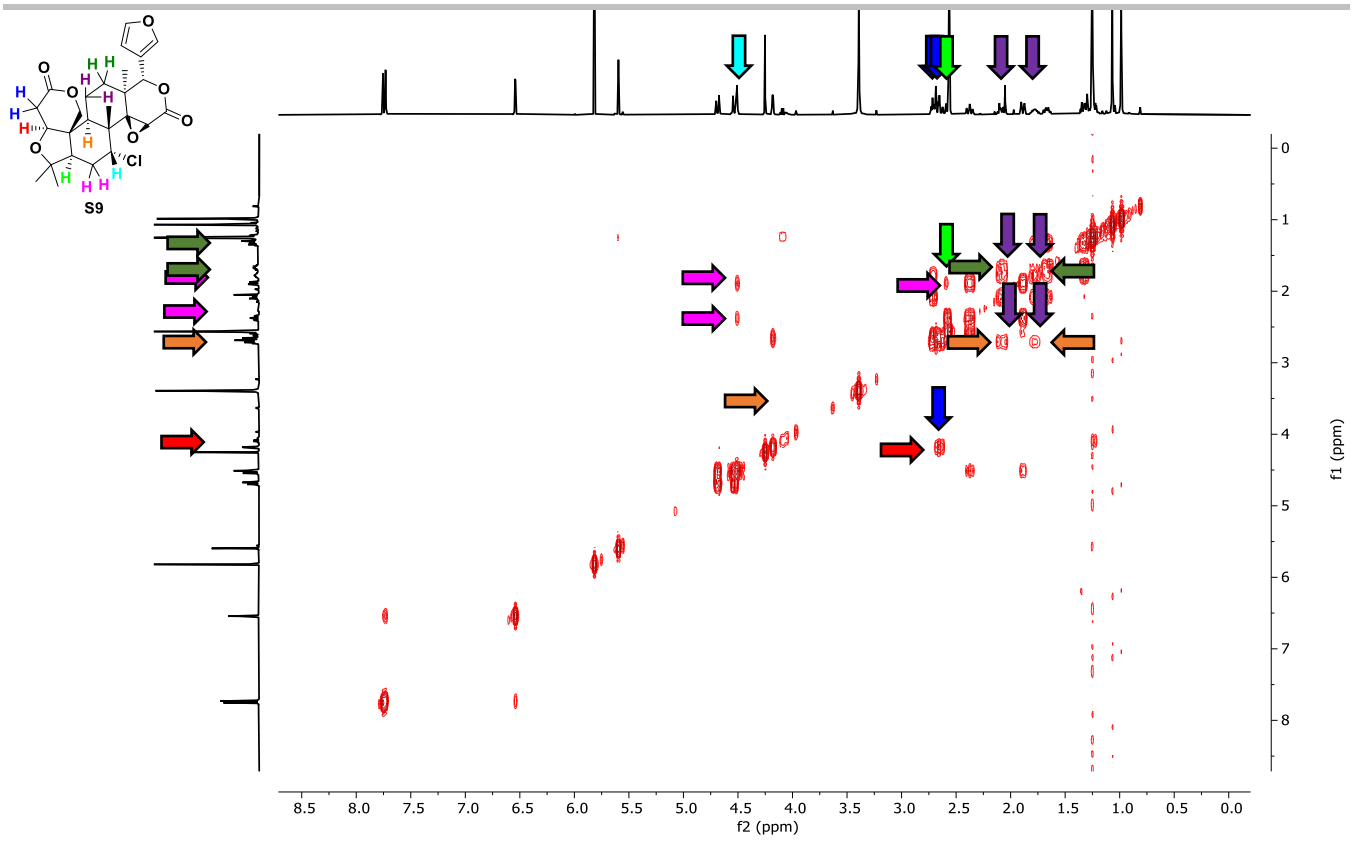
S9

^{1}H NMR

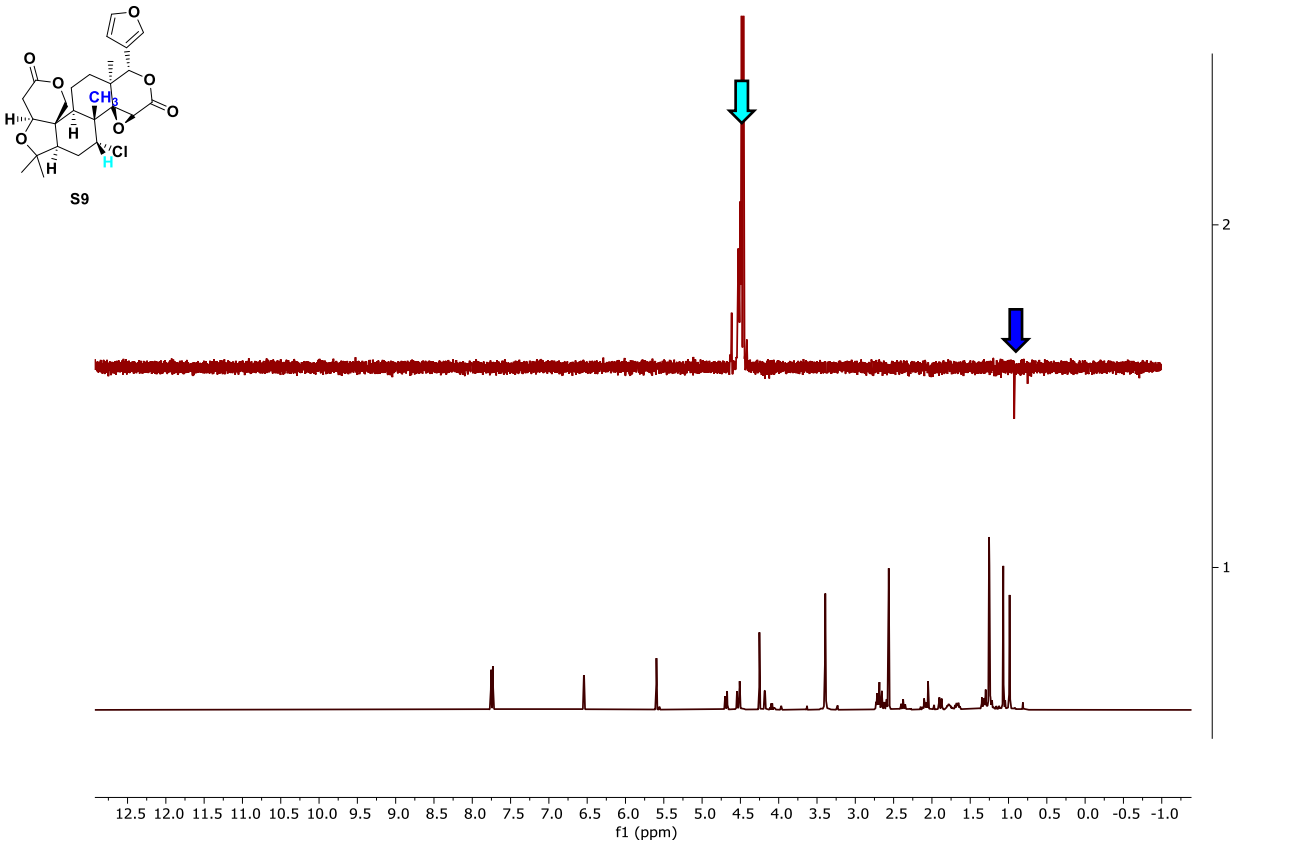


S9

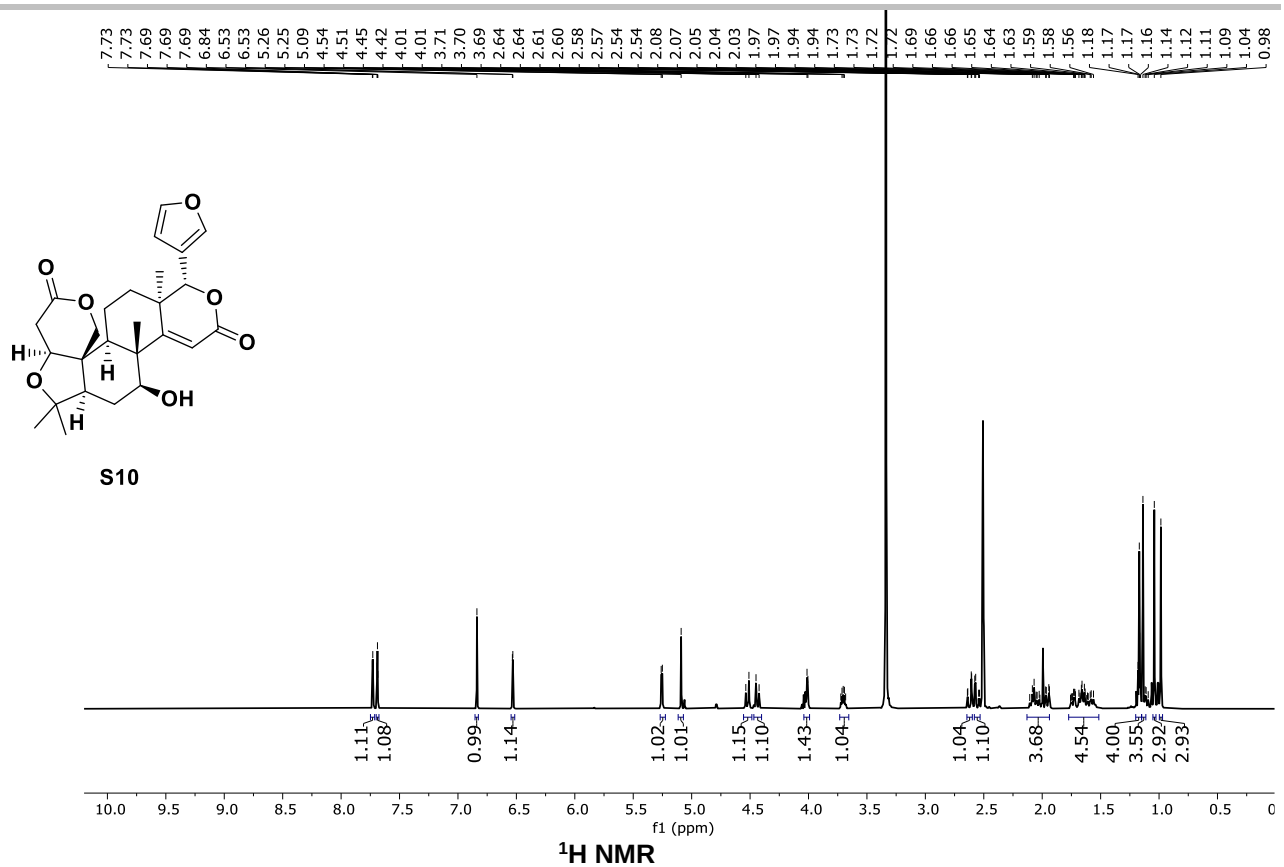
^{13}C NMR



^{1}H-^{1}H COSY NMR

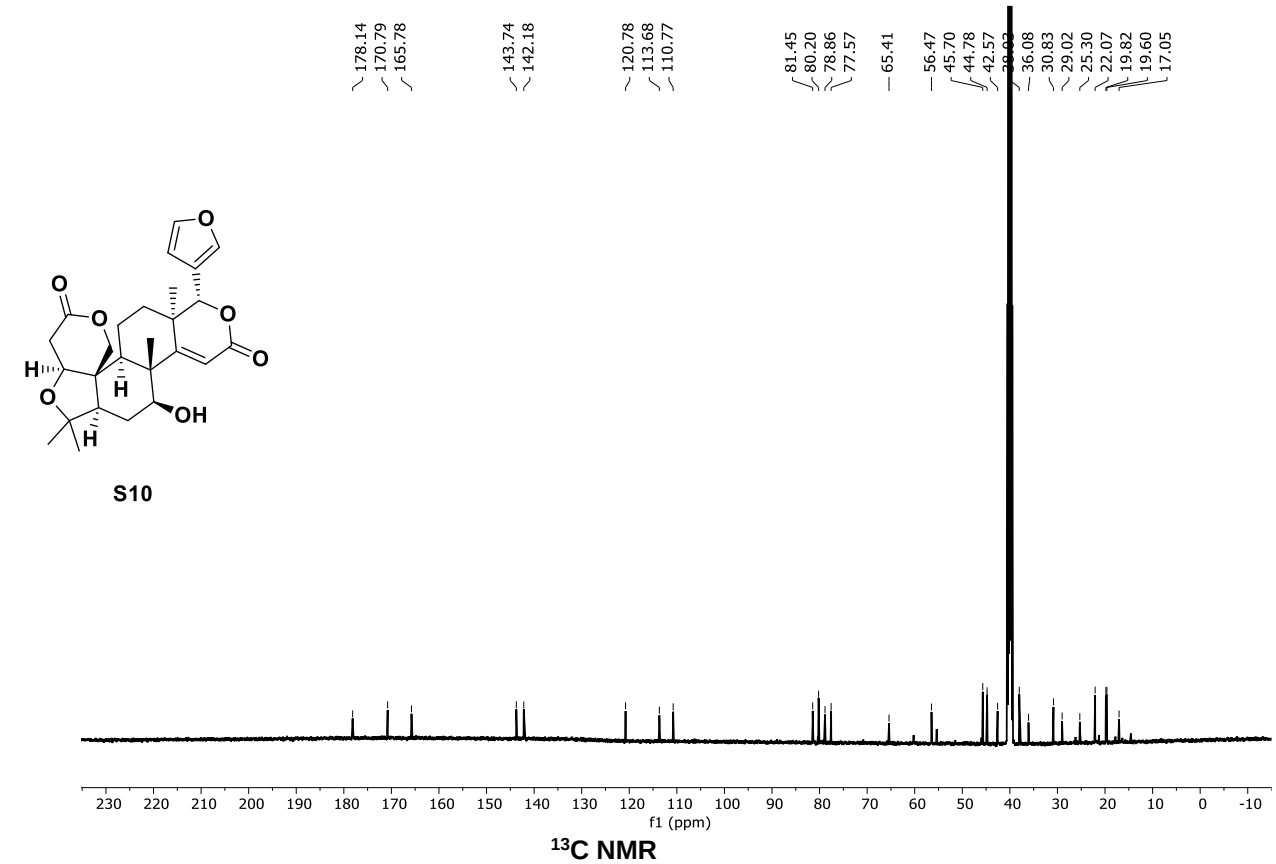


^{1}H-^{1}H 1D NOESY NMR



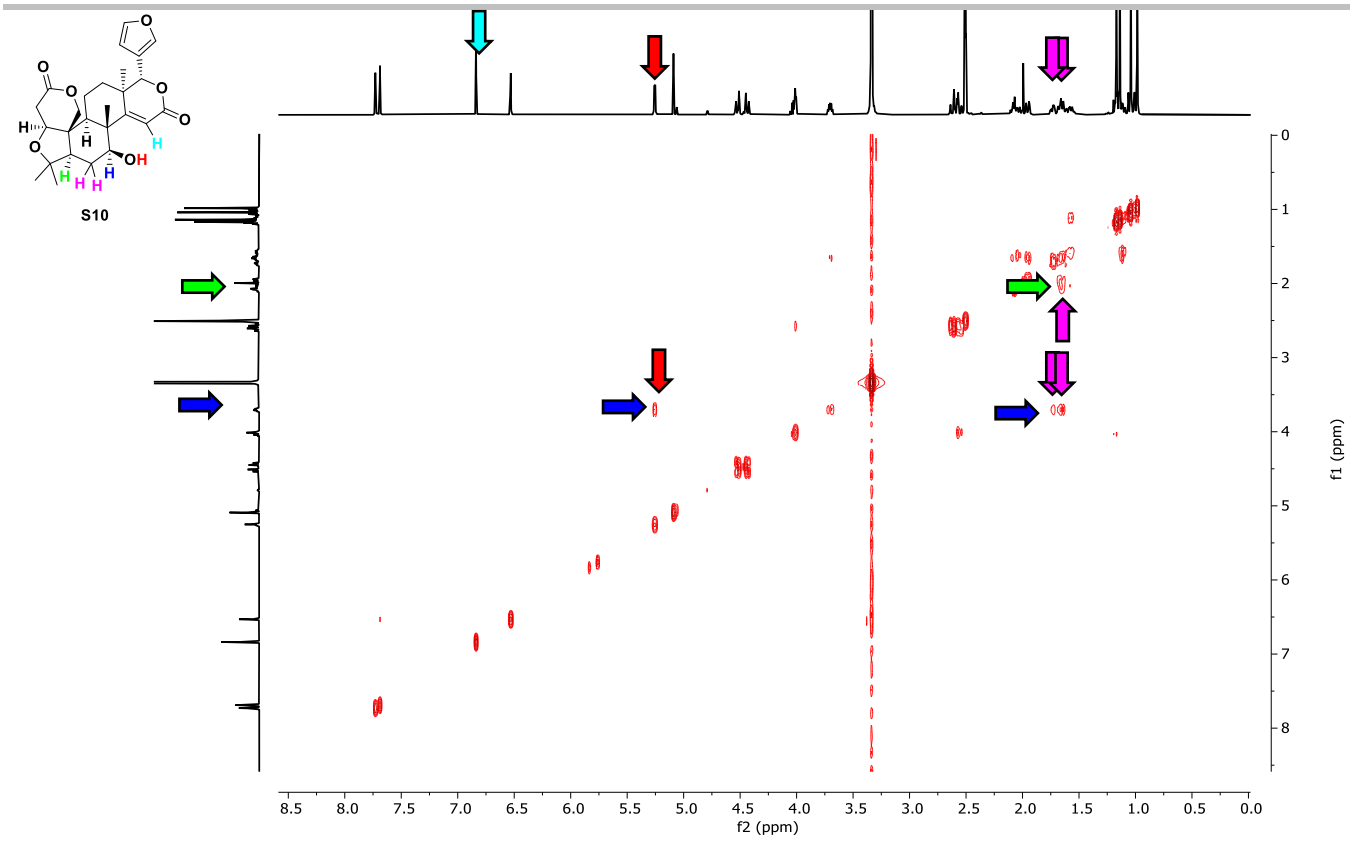
S10

^{1}H NMR

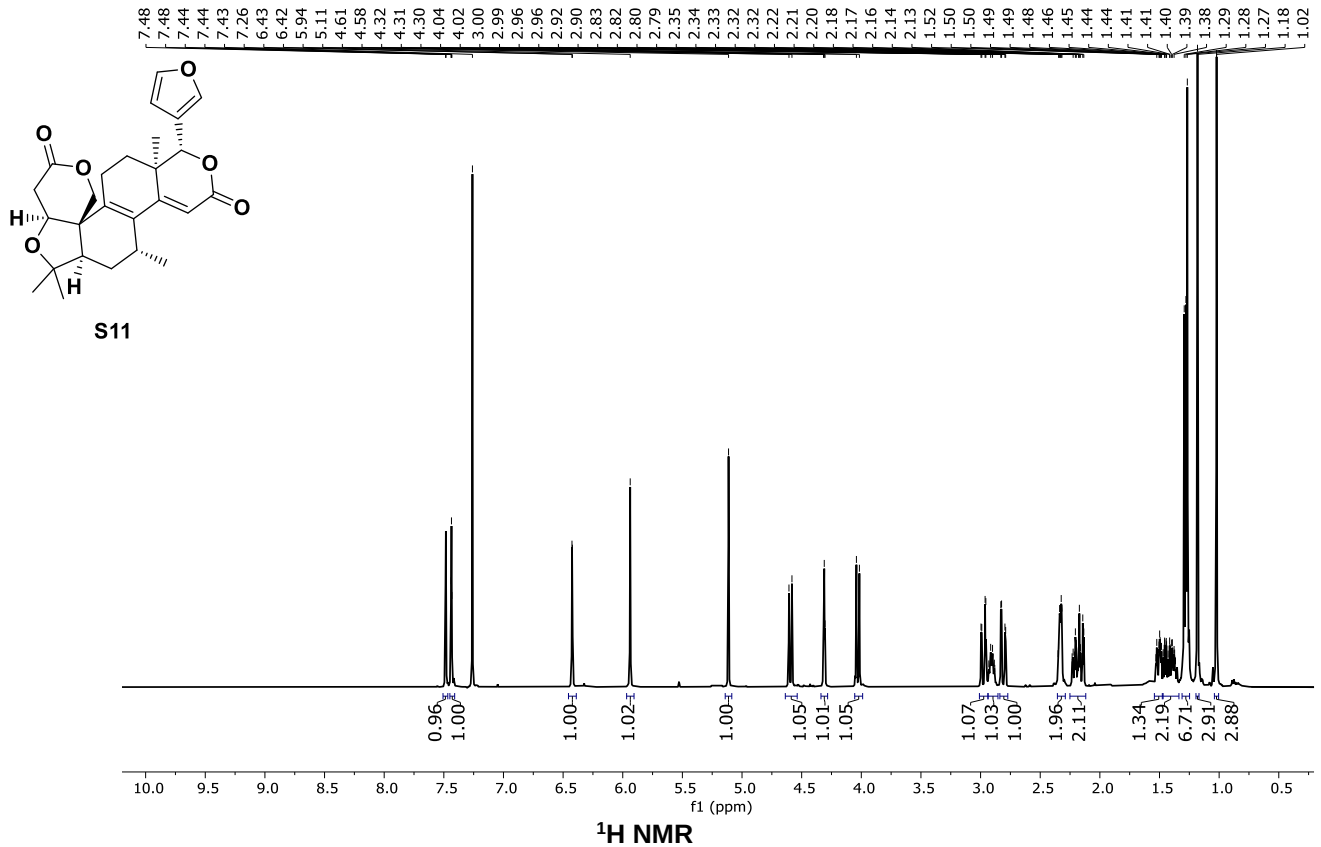


S10

^{13}C NMR

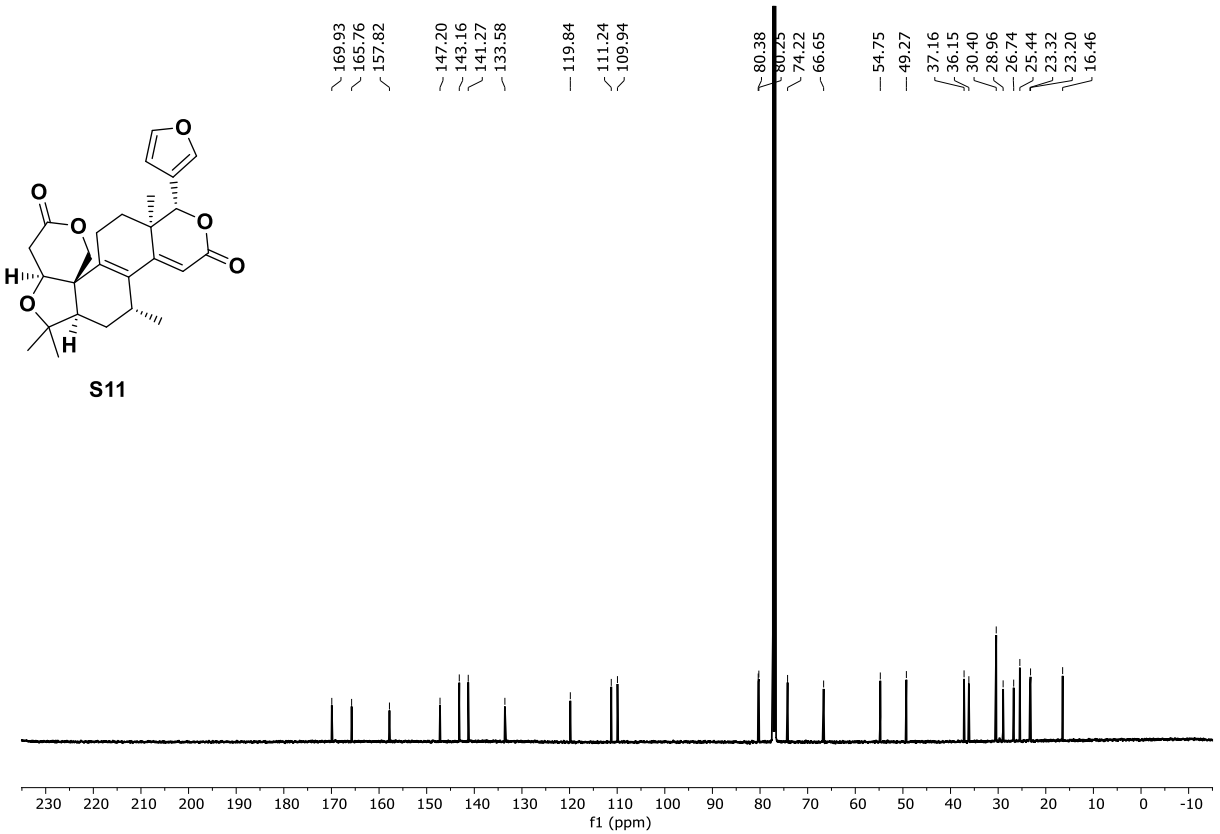


^{1}H-^{1}H COSY NMR



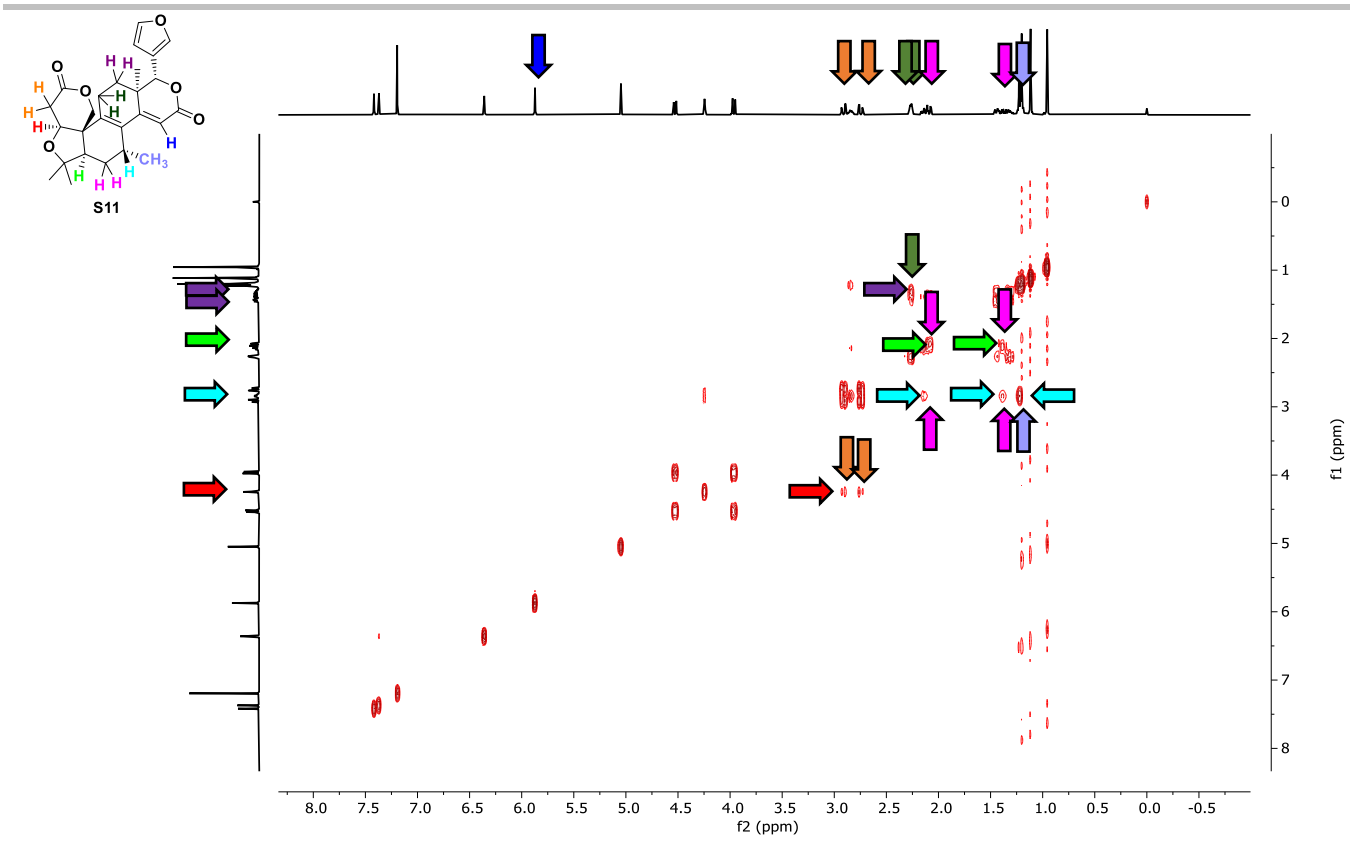
S11

^{1}H NMR

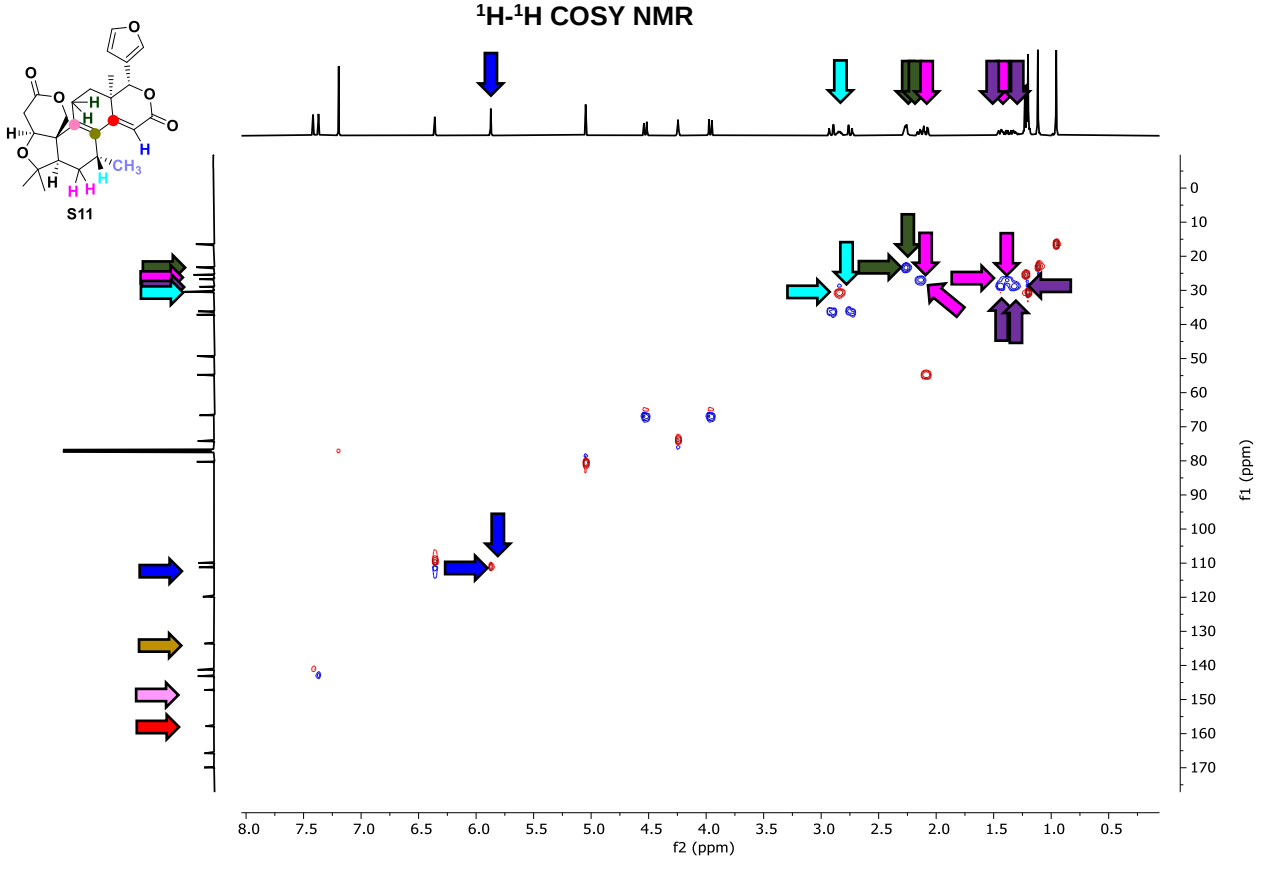


S11

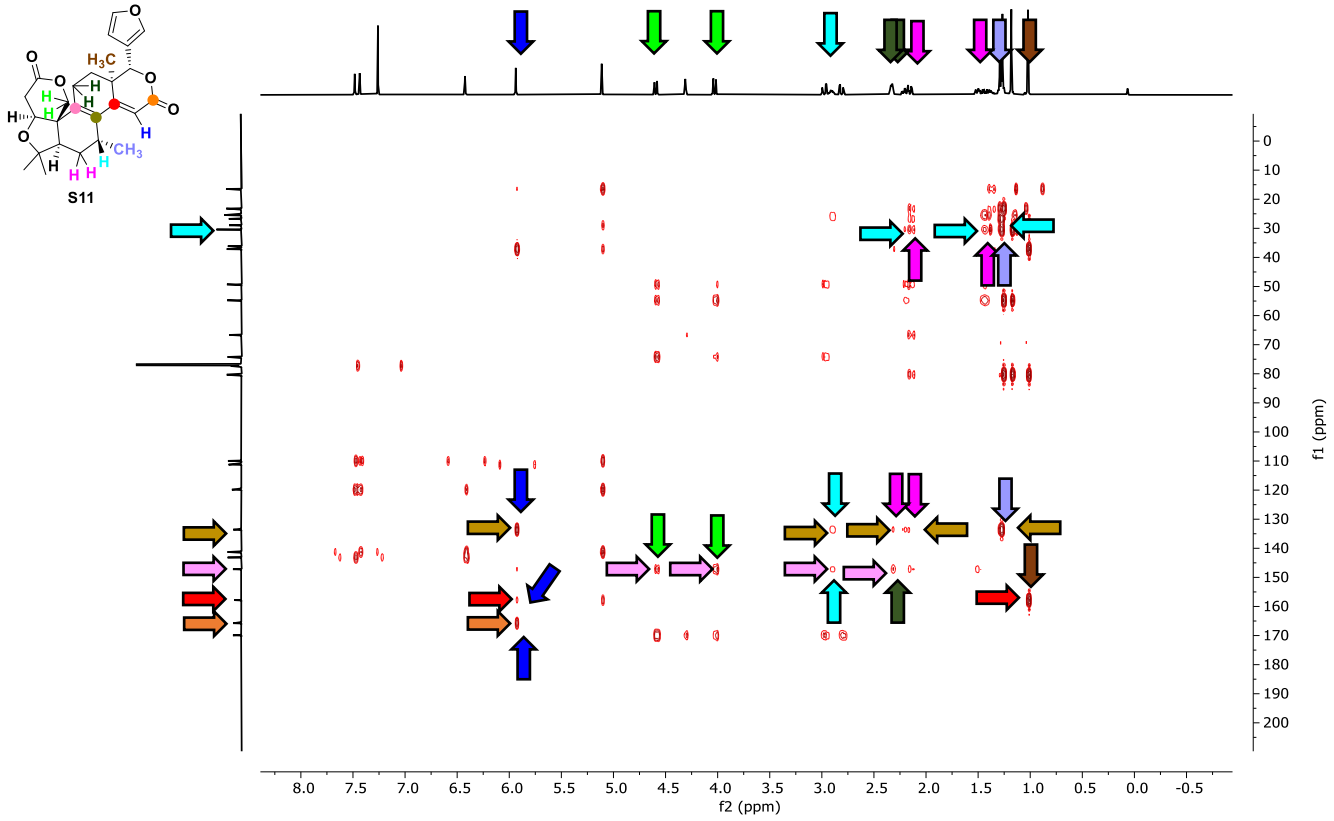
^{13}C NMR



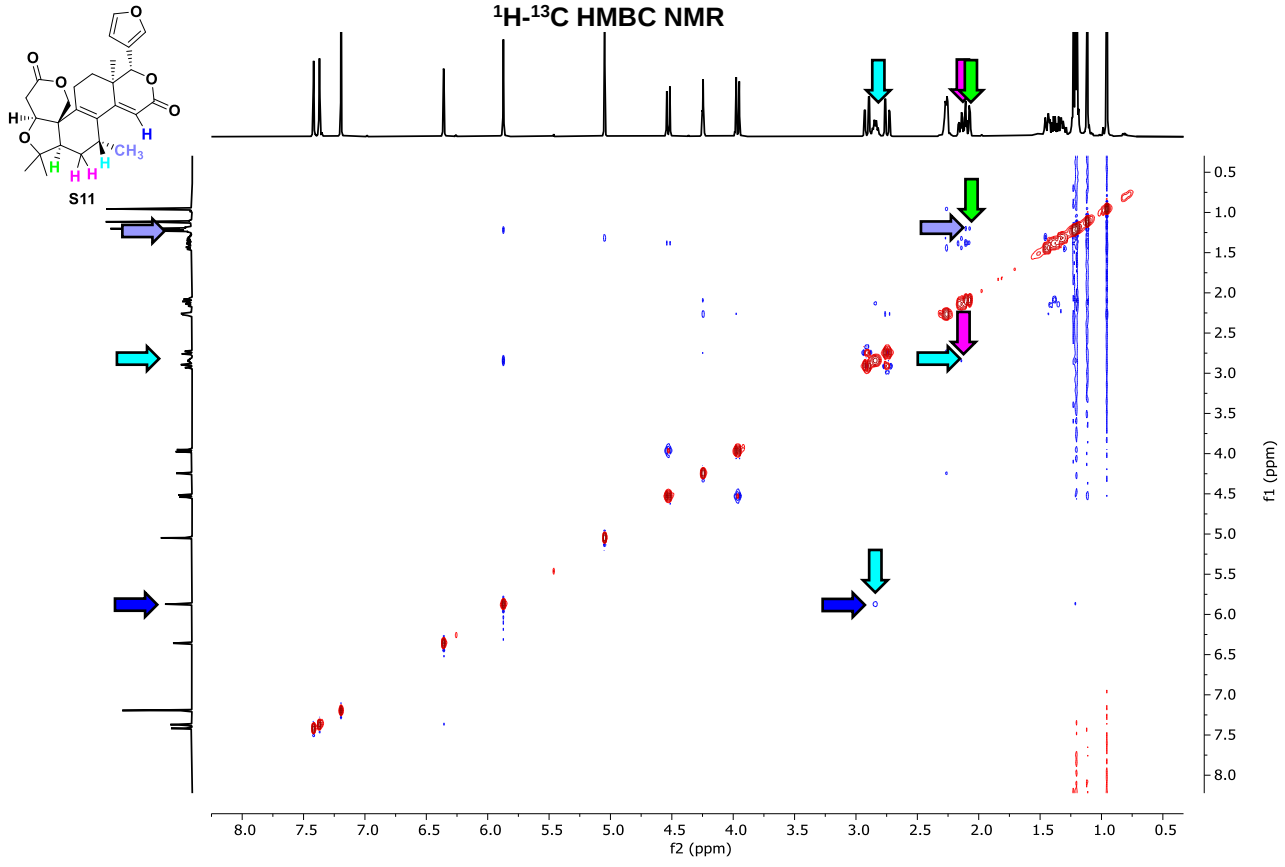
^{1}H-^{1}H COSY NMR



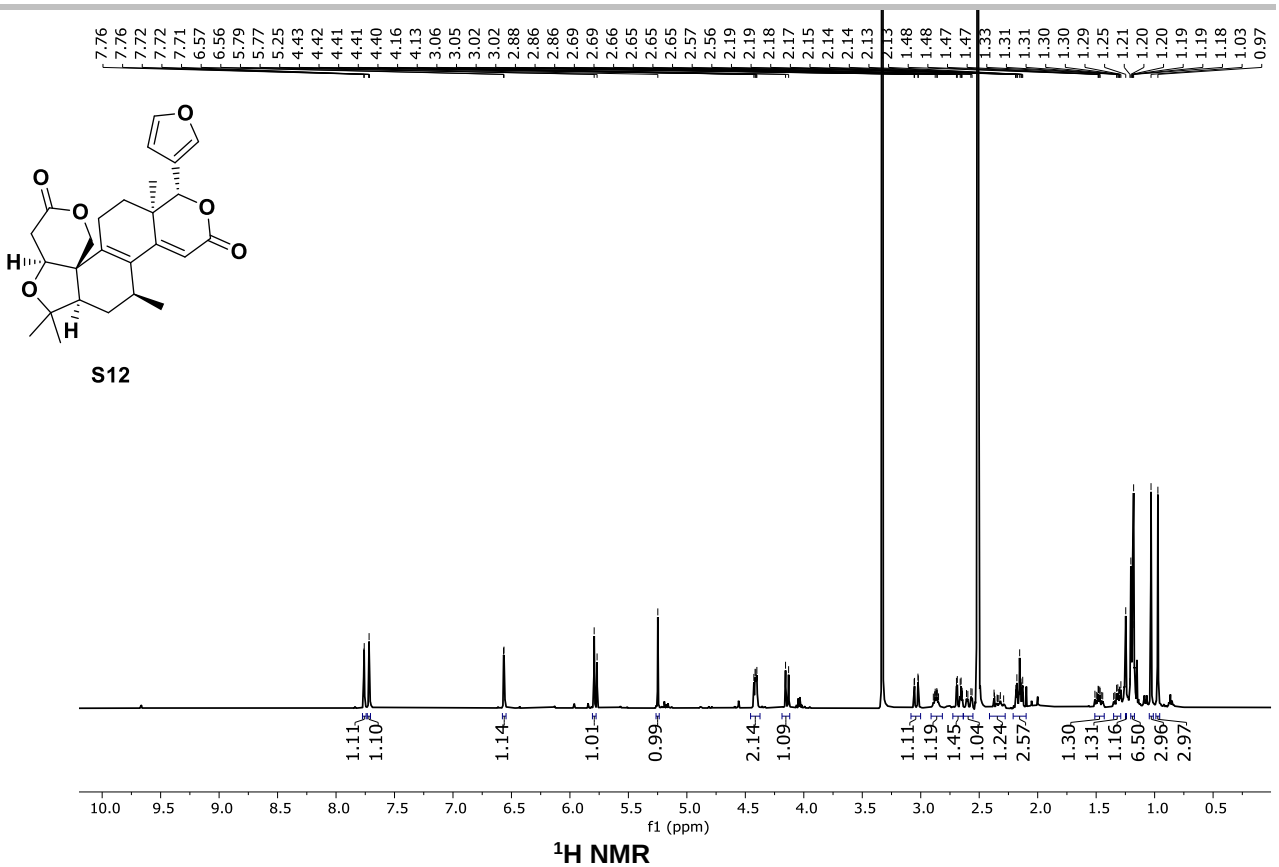
^{1}H-^{13}C HSQC NMR



^{1}H-^{13}C HMBC NMR

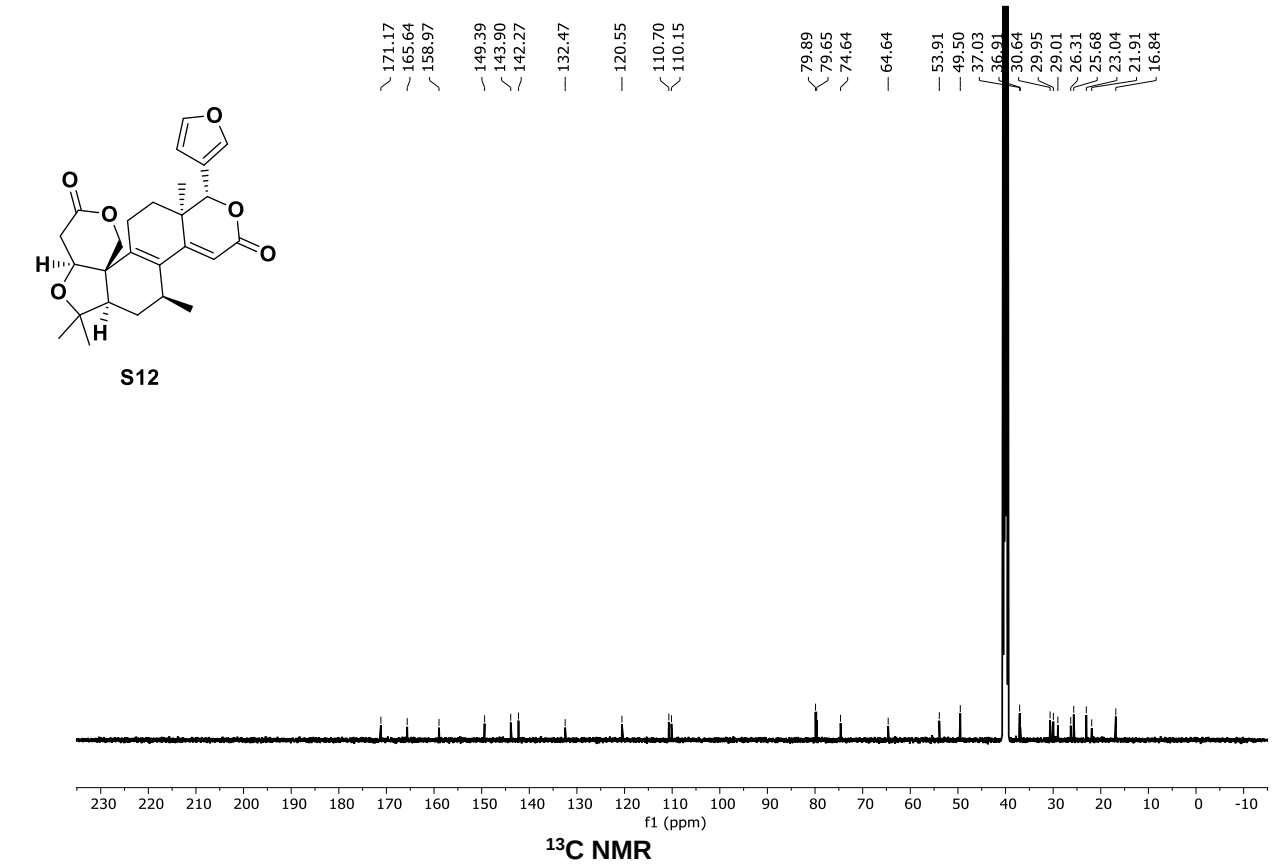


^{1}H-^{1}H NOESY NMR



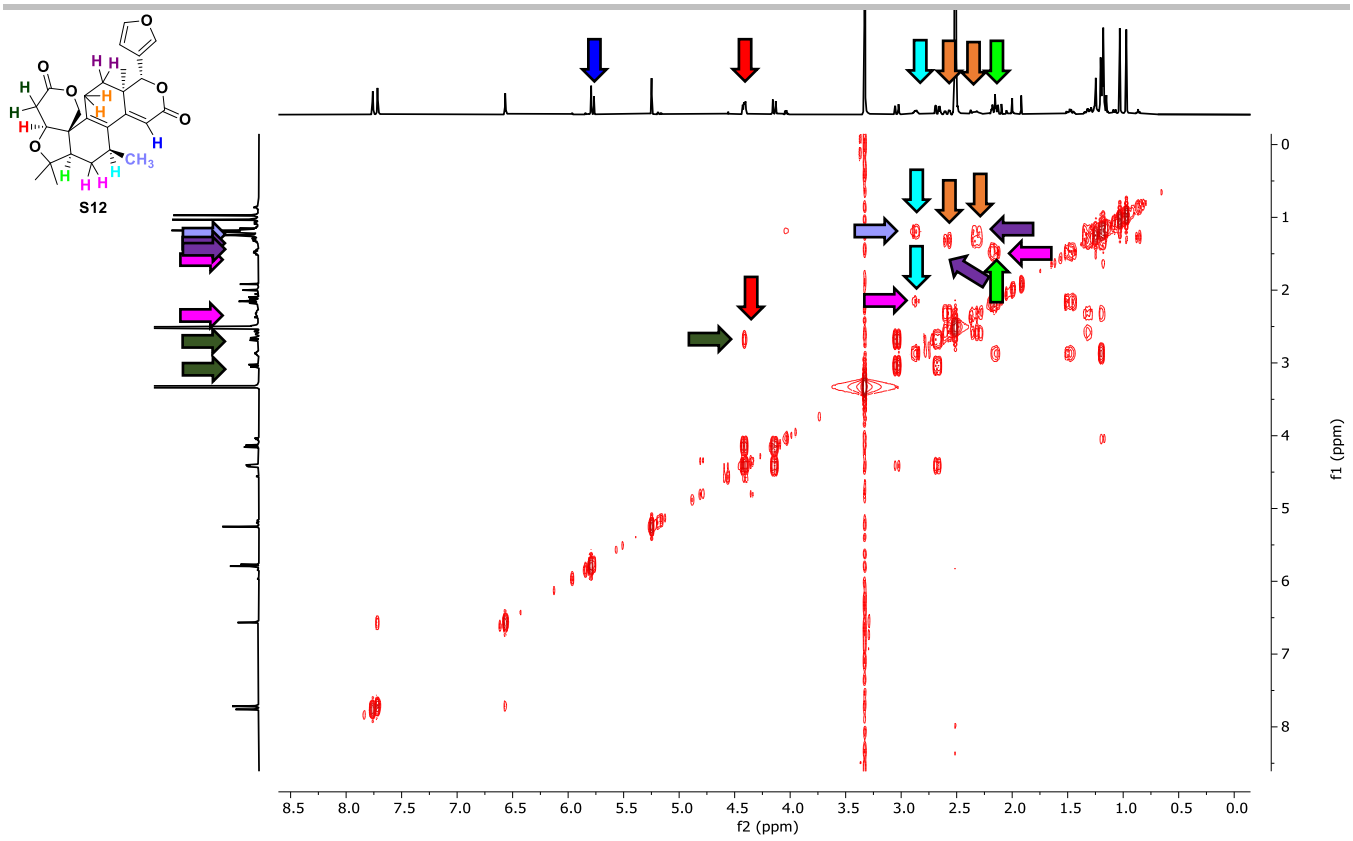
S12

^{1}H NMR

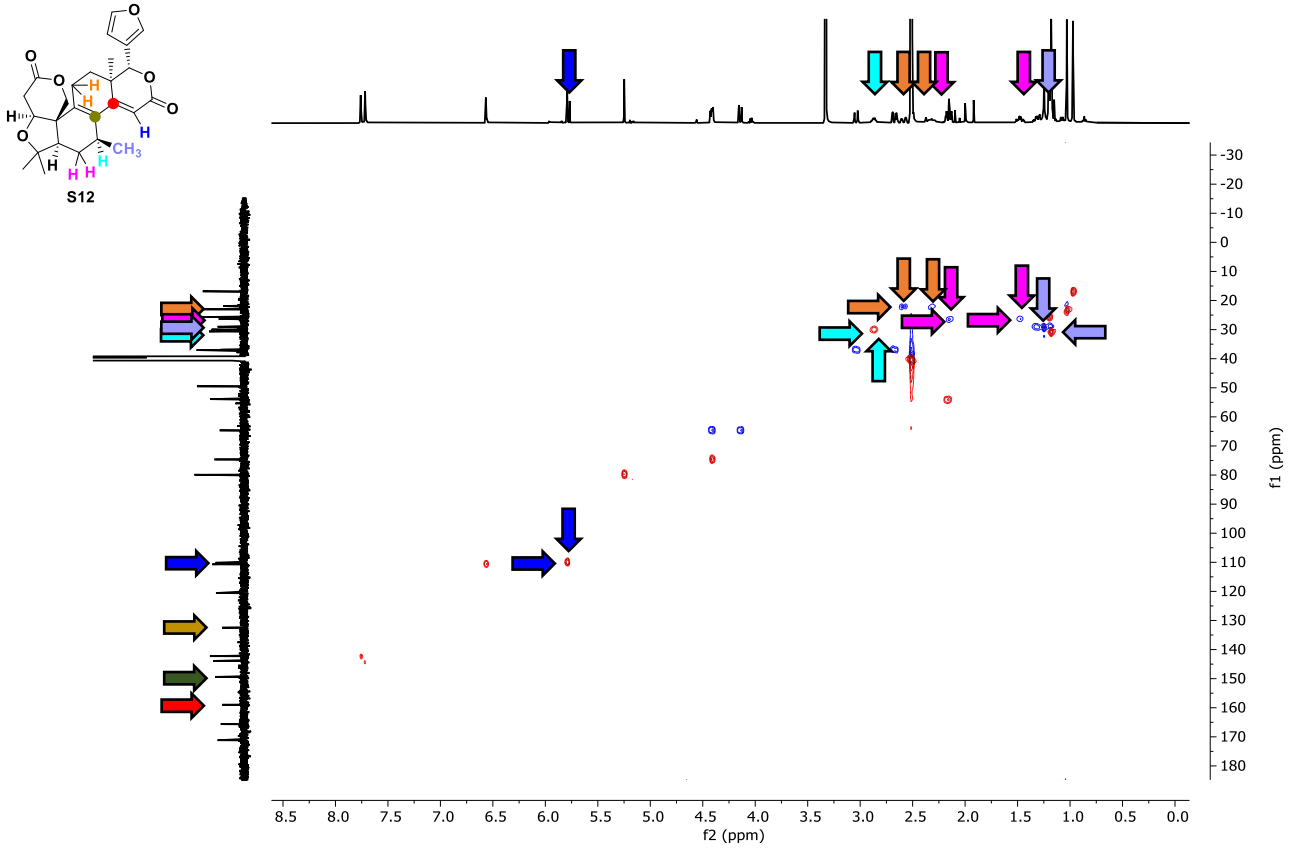


S12

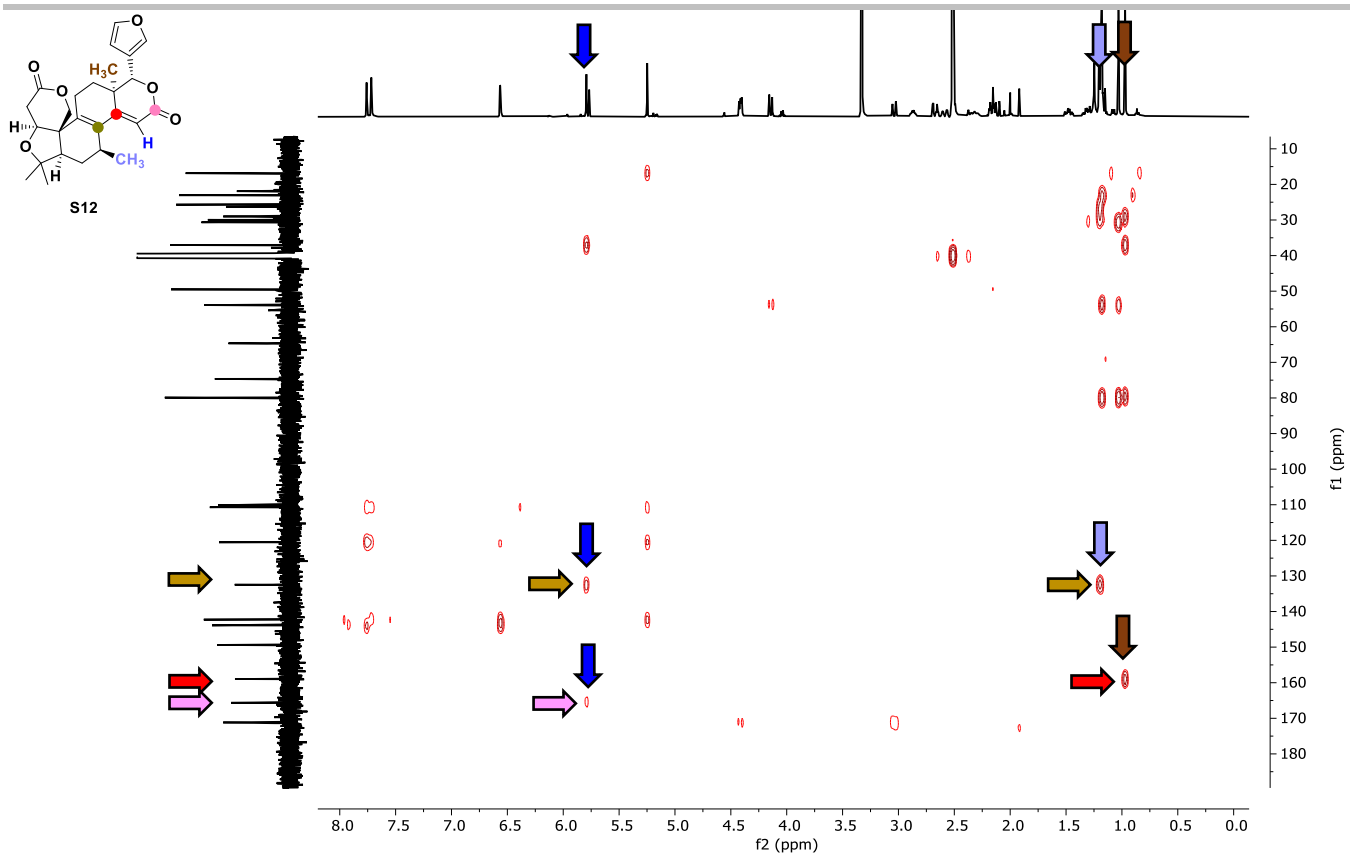
^{13}C NMR



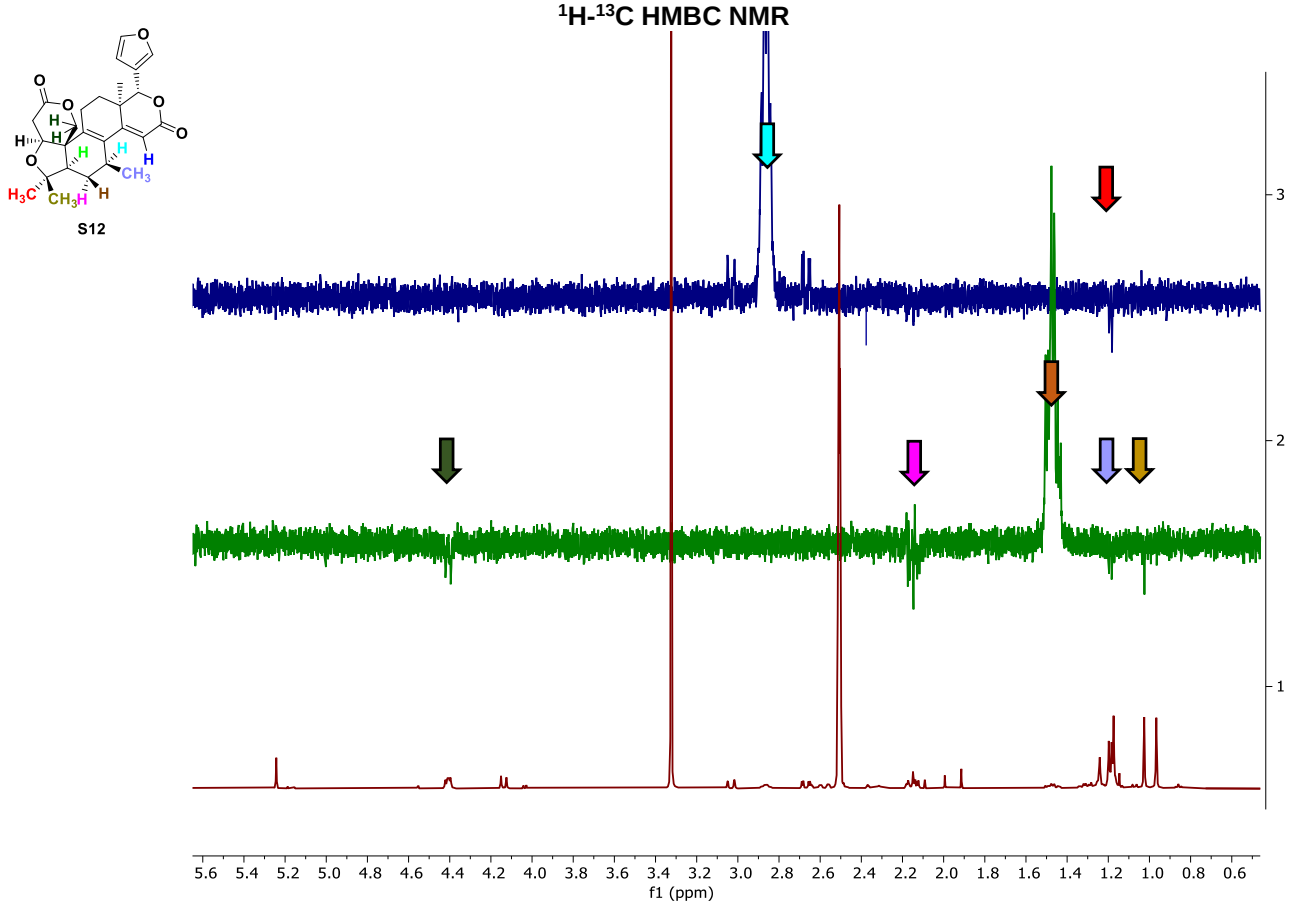
^{1}H-^{1}H COSY NMR



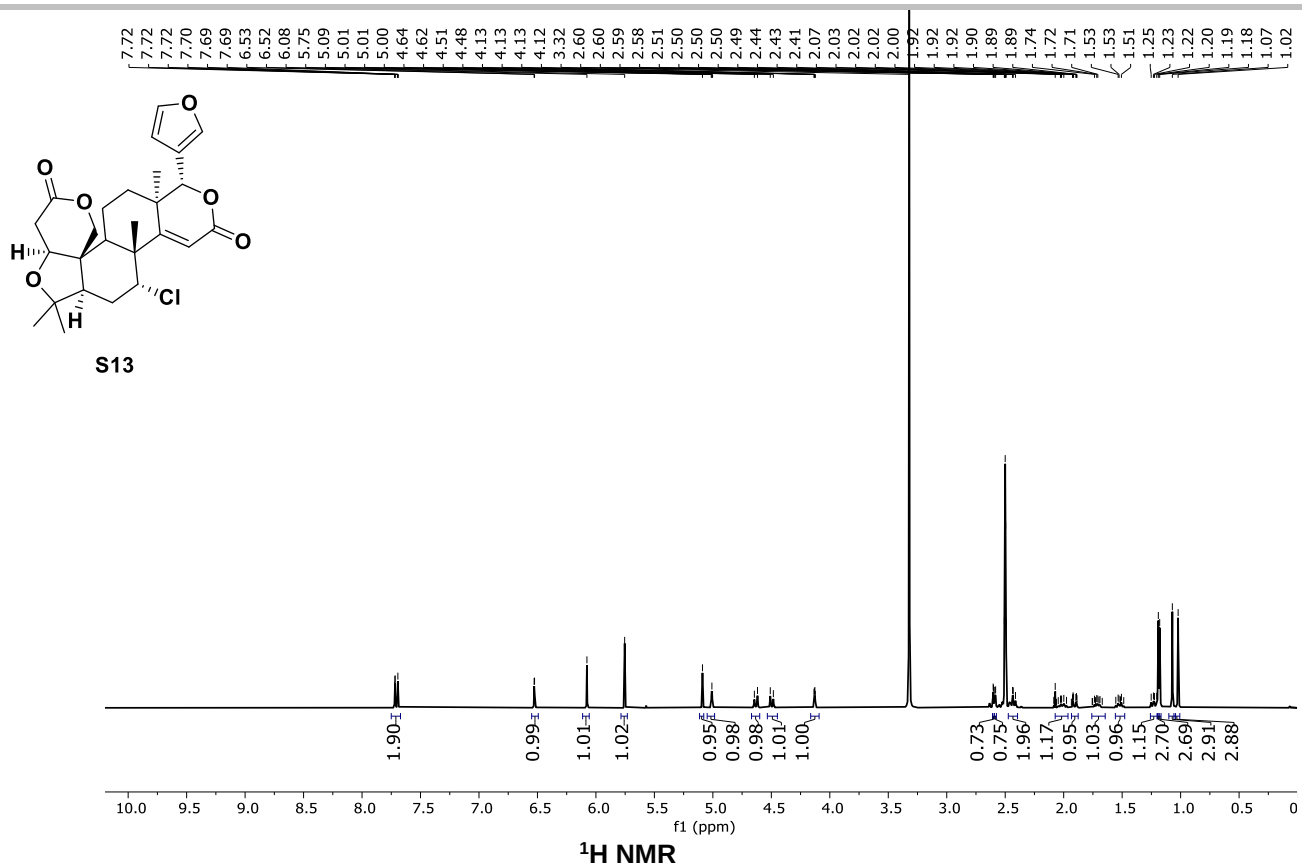
^{1}H-^{13}C HSQC NMR



^{1}H-^{13}C HMBC NMR

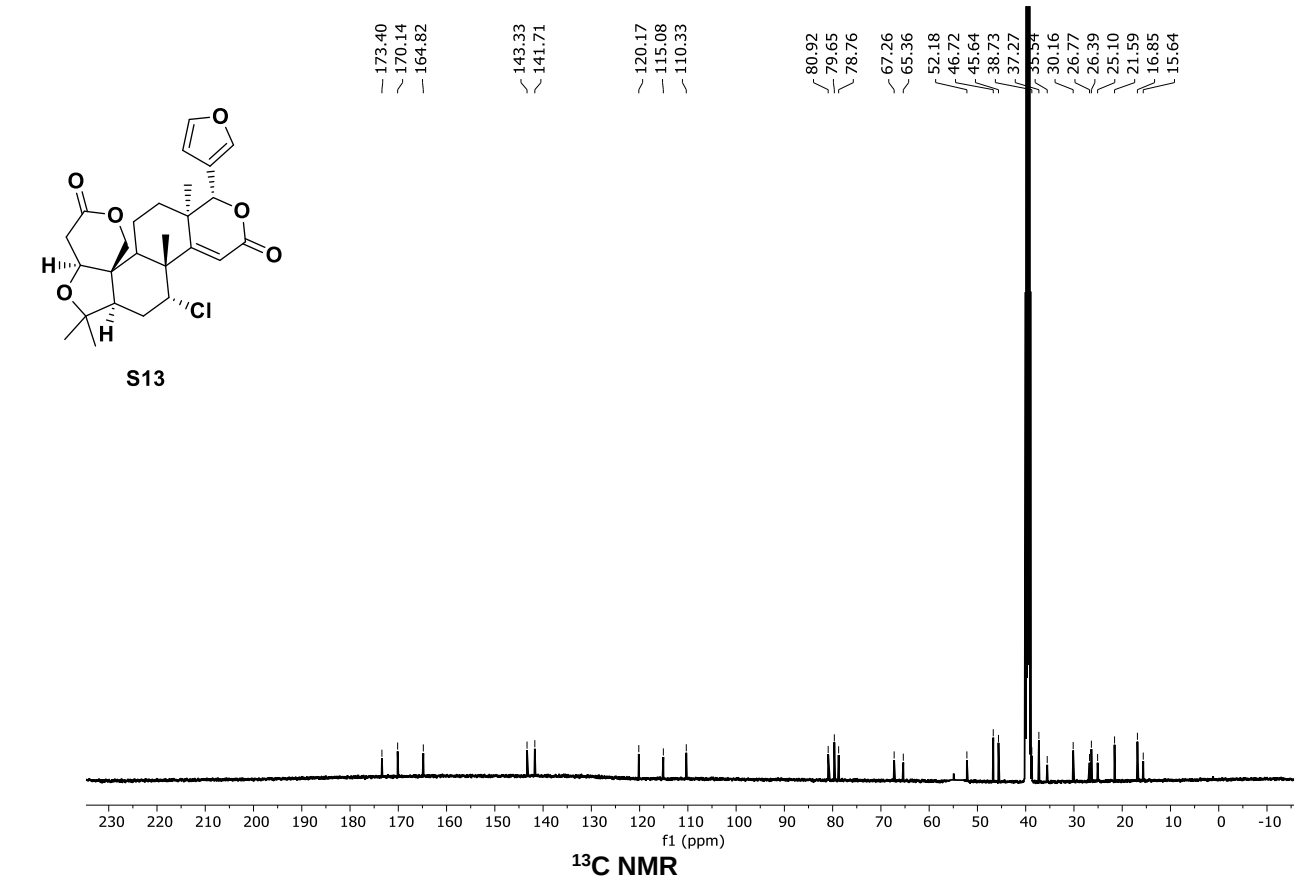


^{1}H-^{1}H 1D NOESY NMR



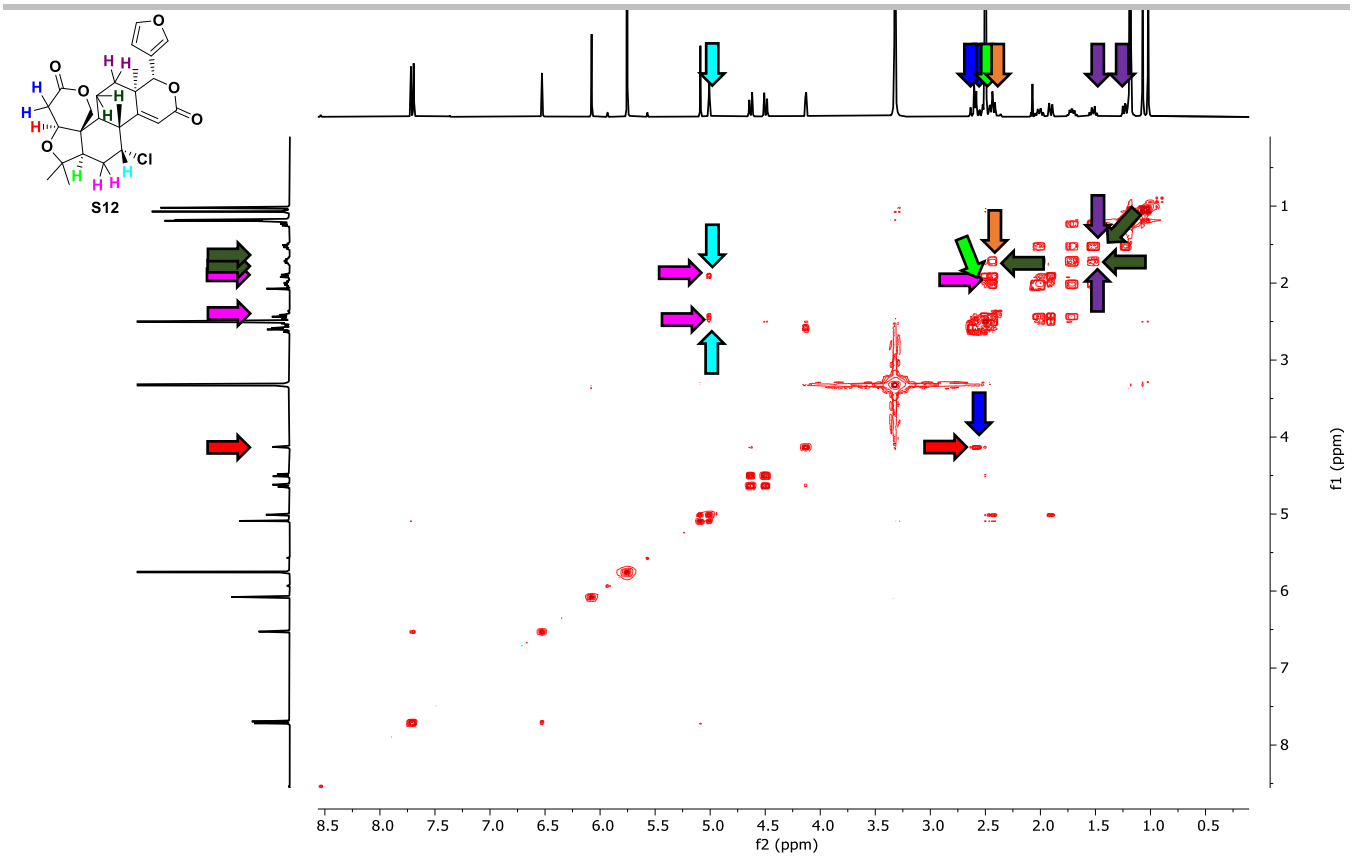
S13

^{1}H NMR

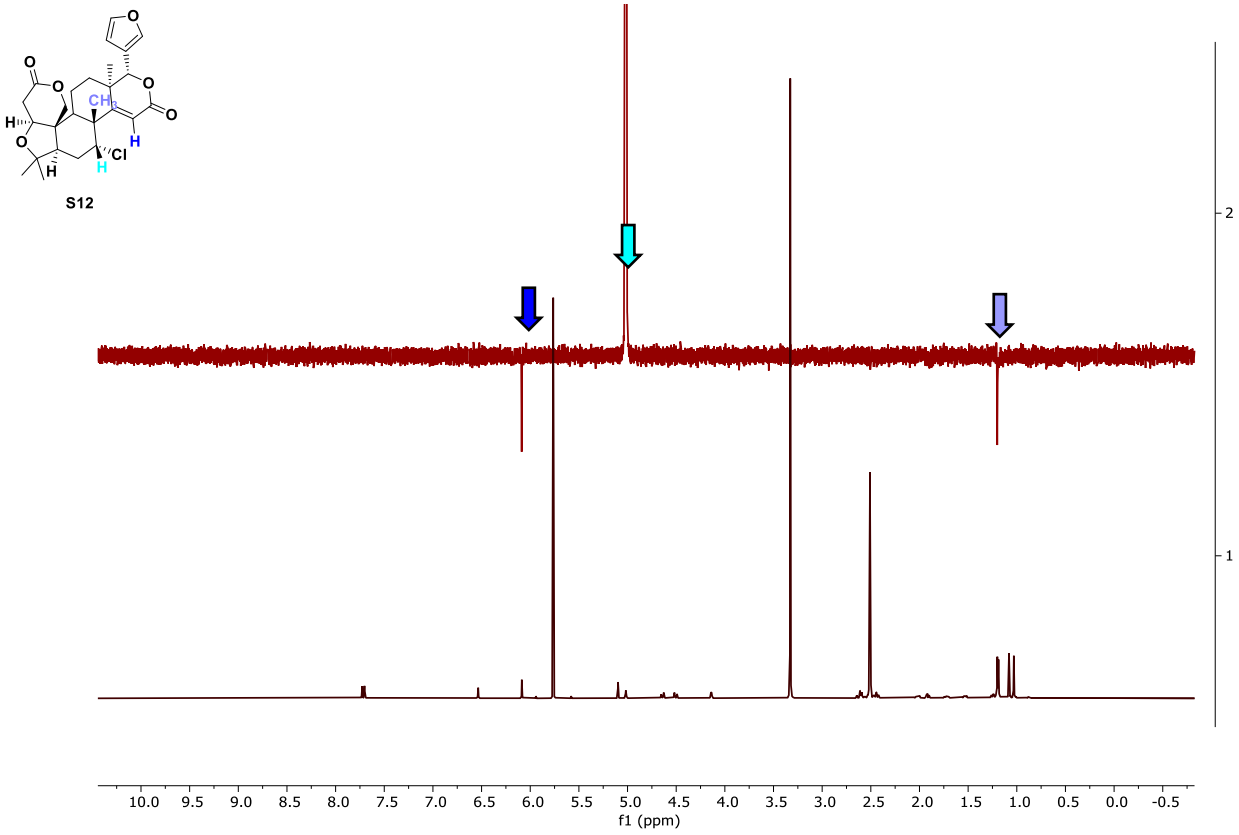


S13

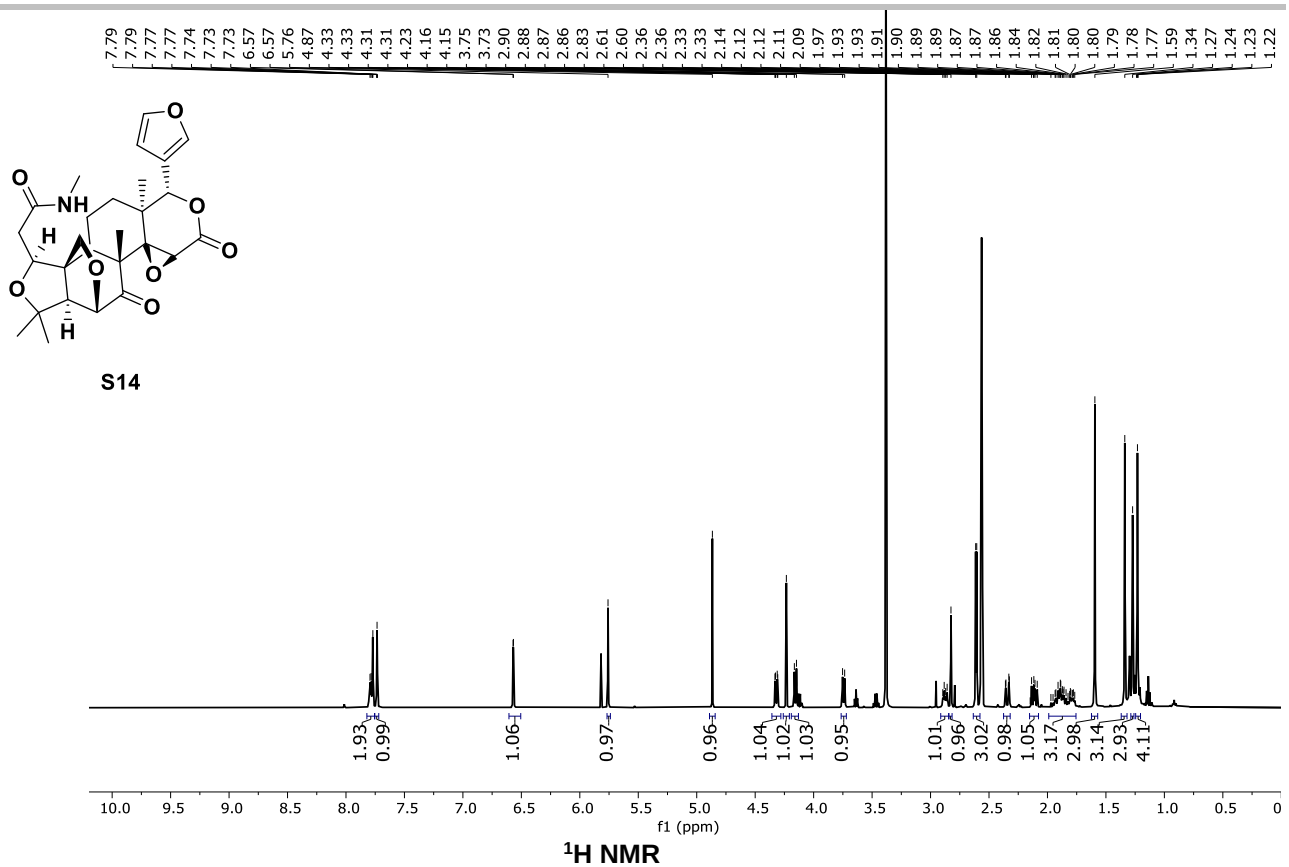
^{13}C NMR



^{1}H-^{1}H COSY NMR

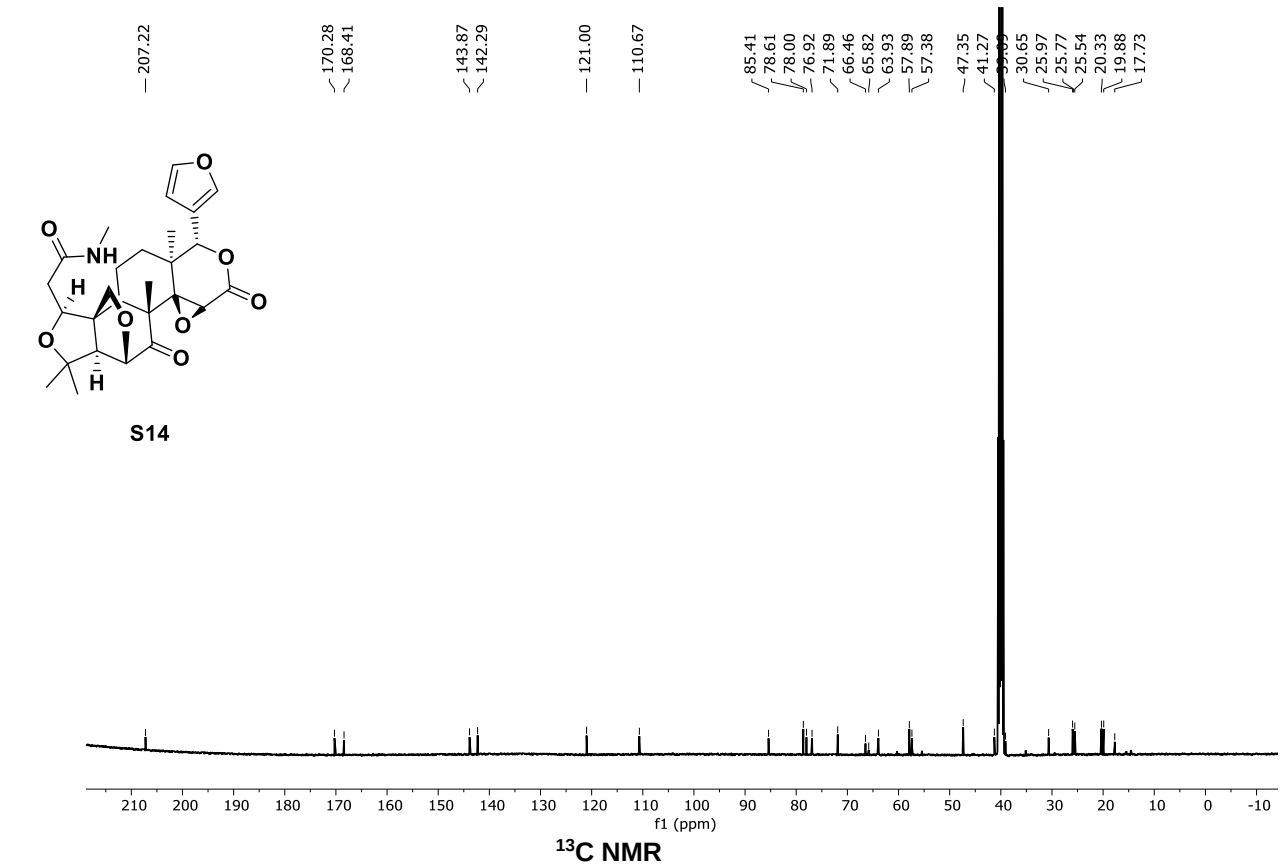


^{1}H-^{1}H 1D NOESY NMR



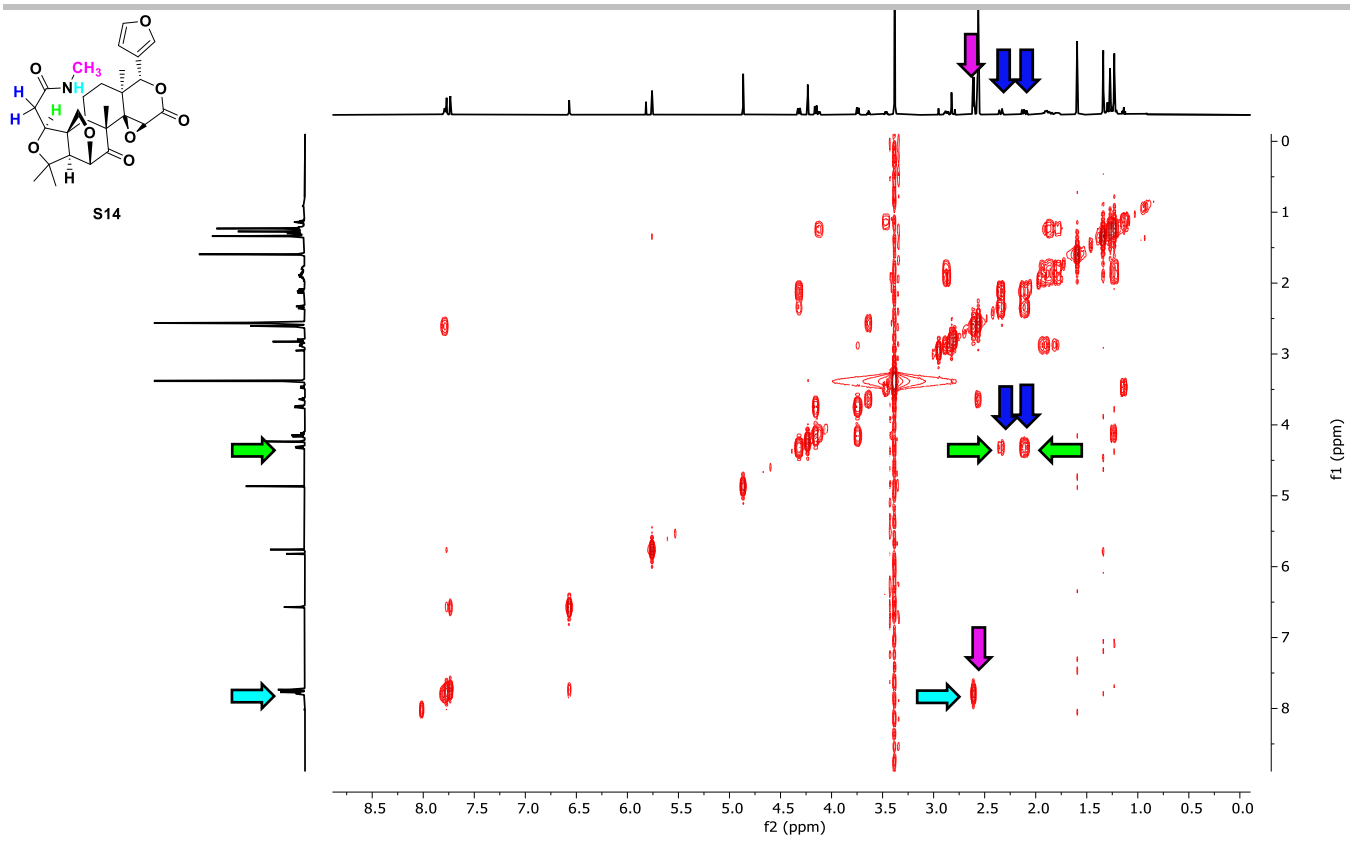
S14

^{1}H NMR

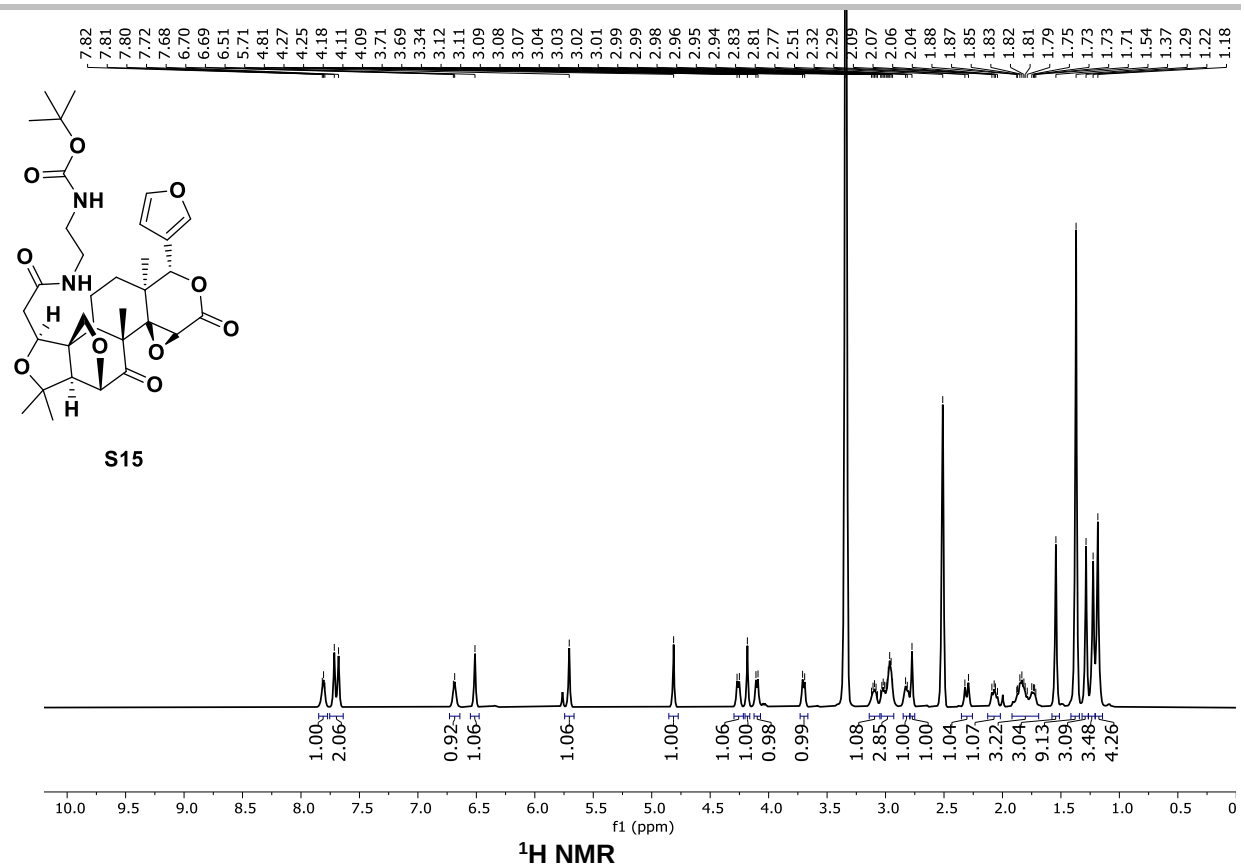


S14

^{13}C NMR

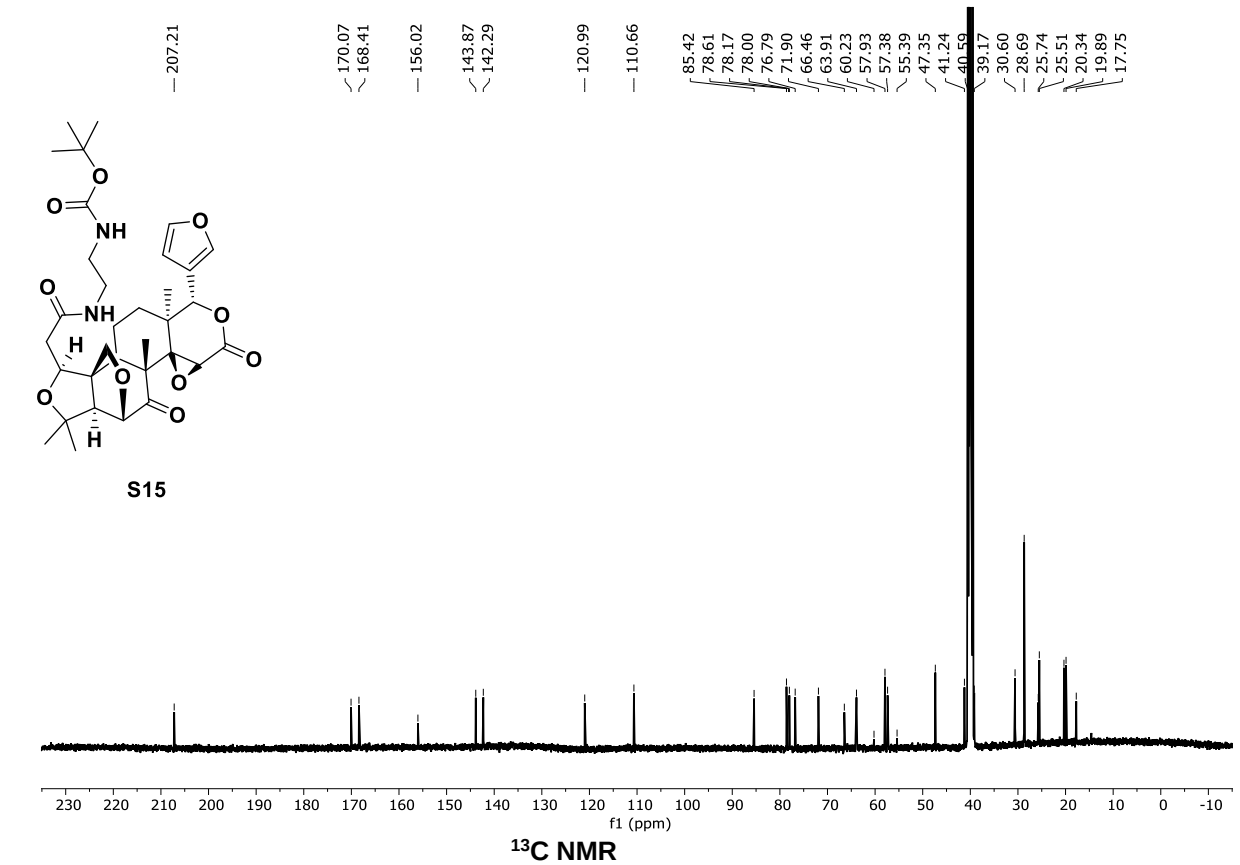


^{1}H-^{1}H COSY NMR



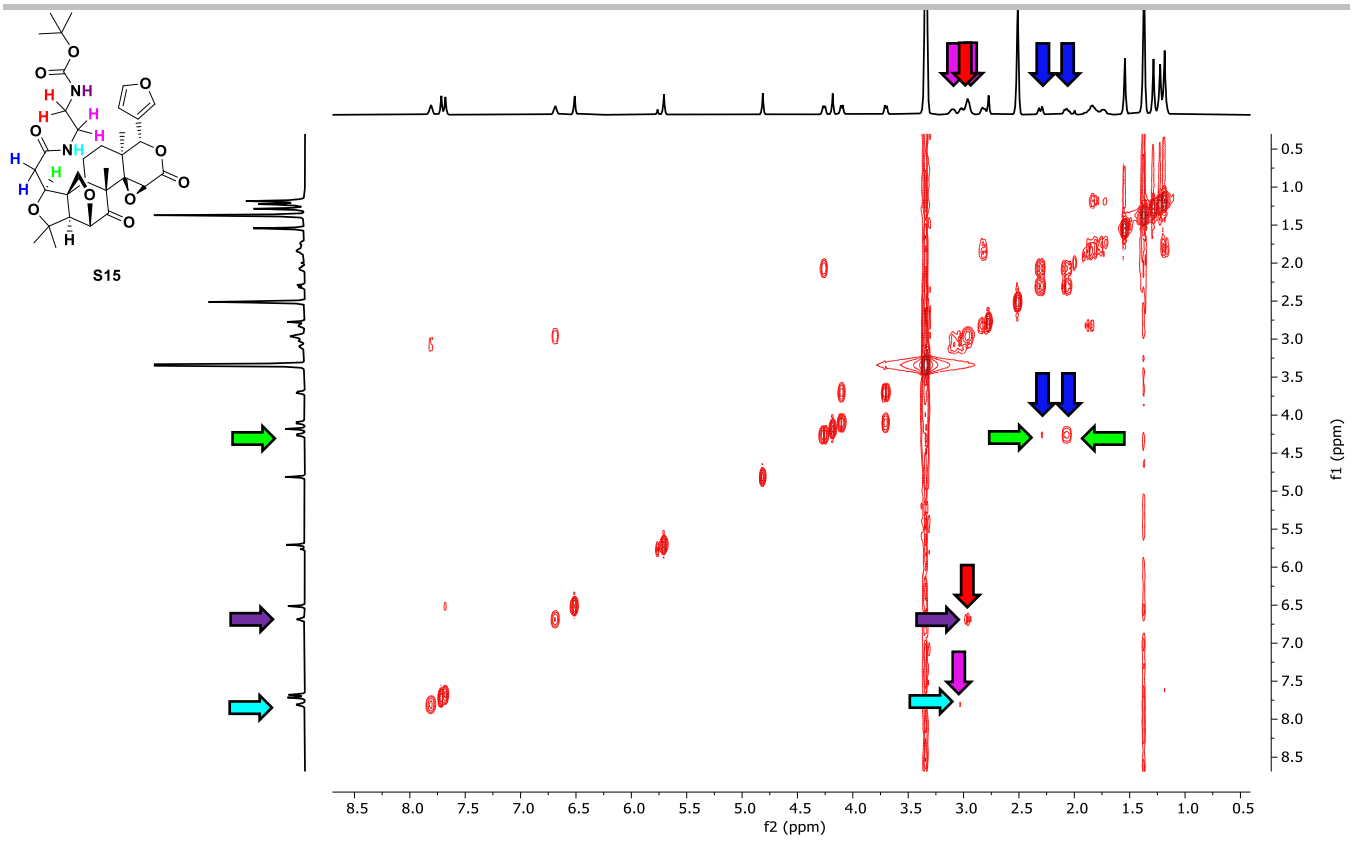
S15

^{1}H NMR

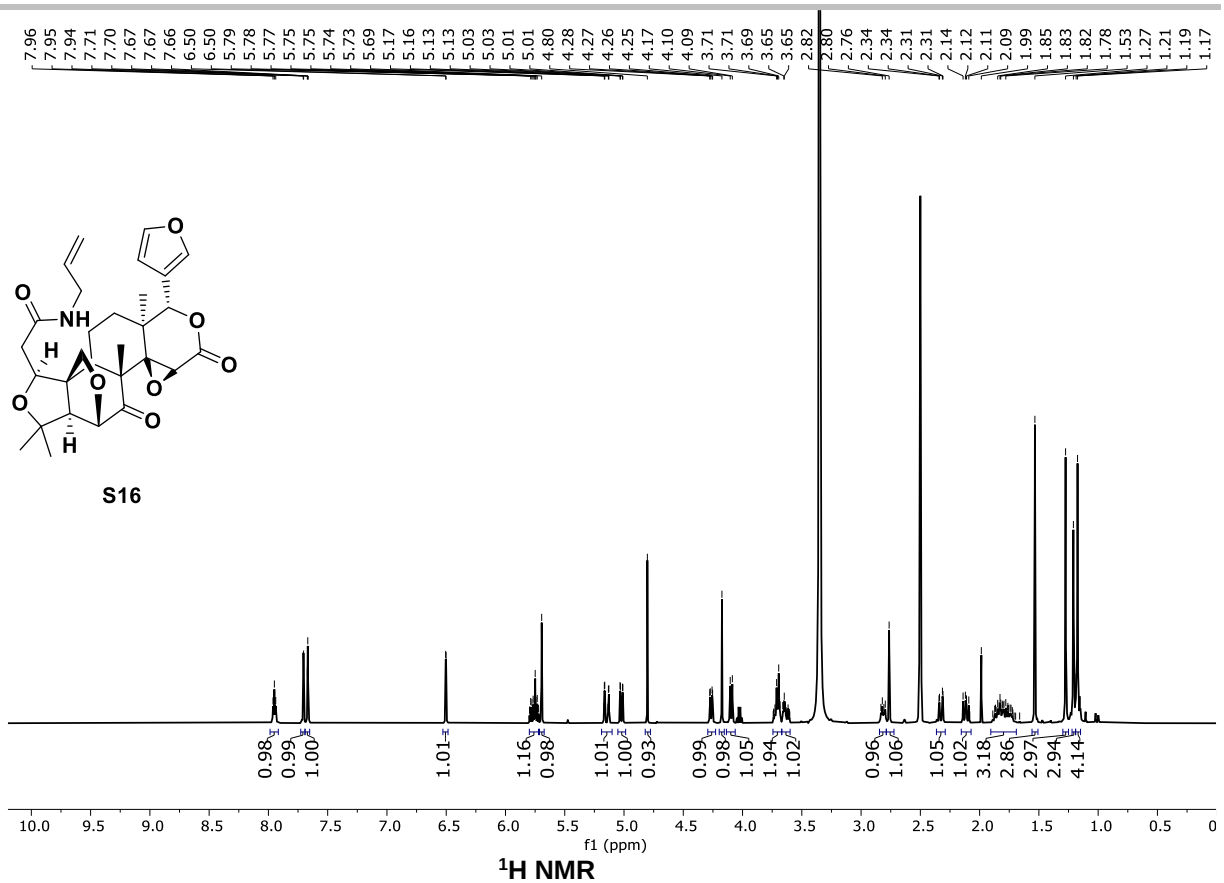


S15

^{13}C NMR

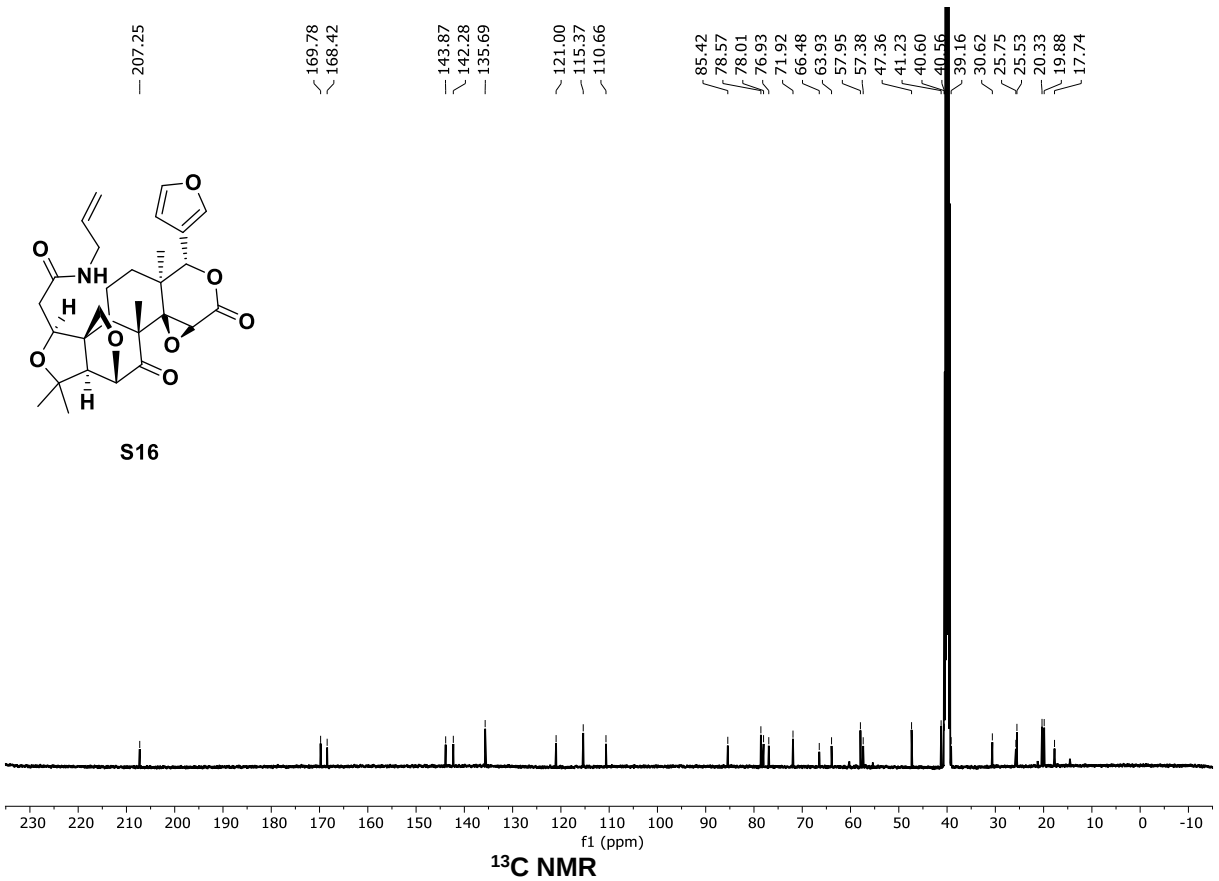


^{1}H-^{1}H COSY NMR



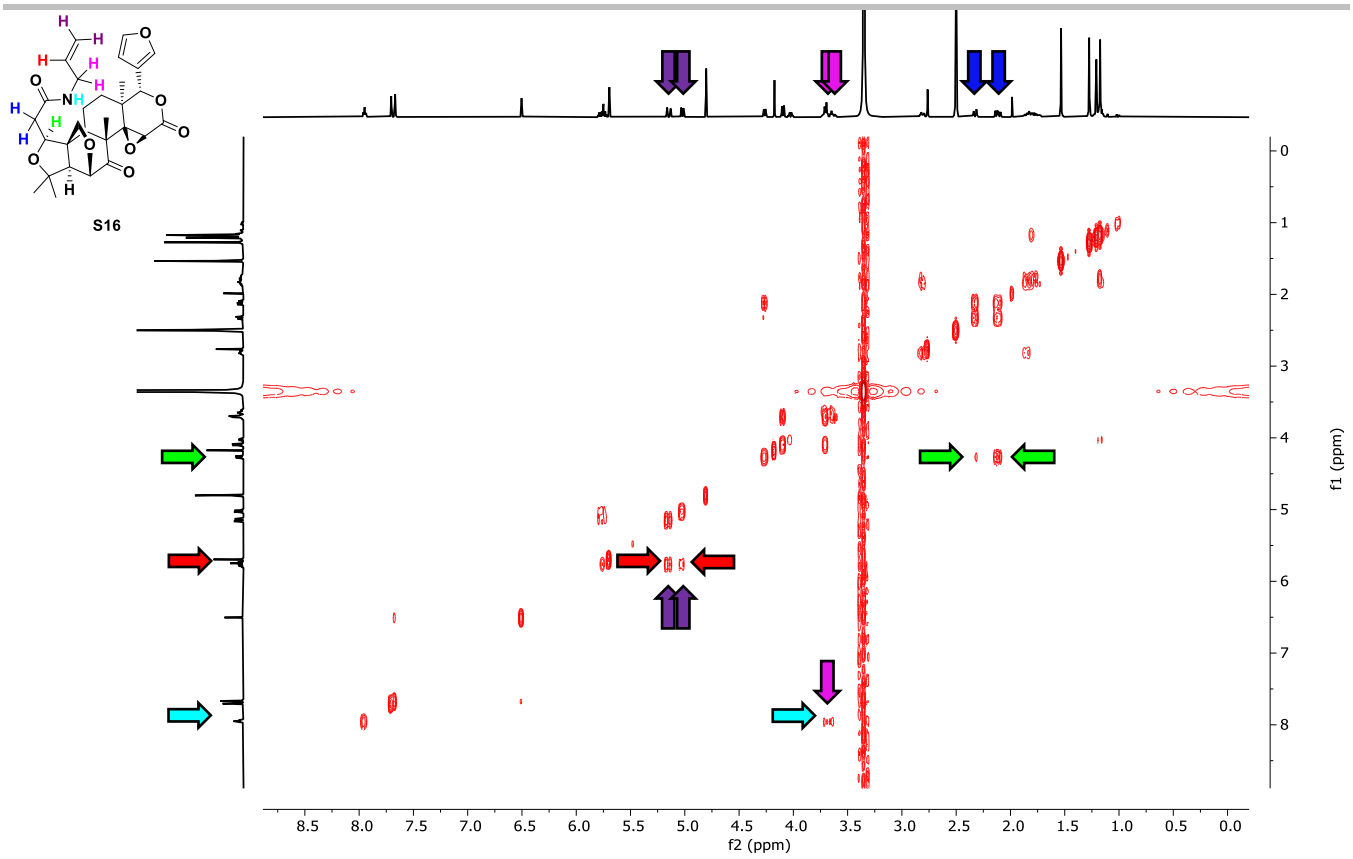
S16

^{1}H NMR

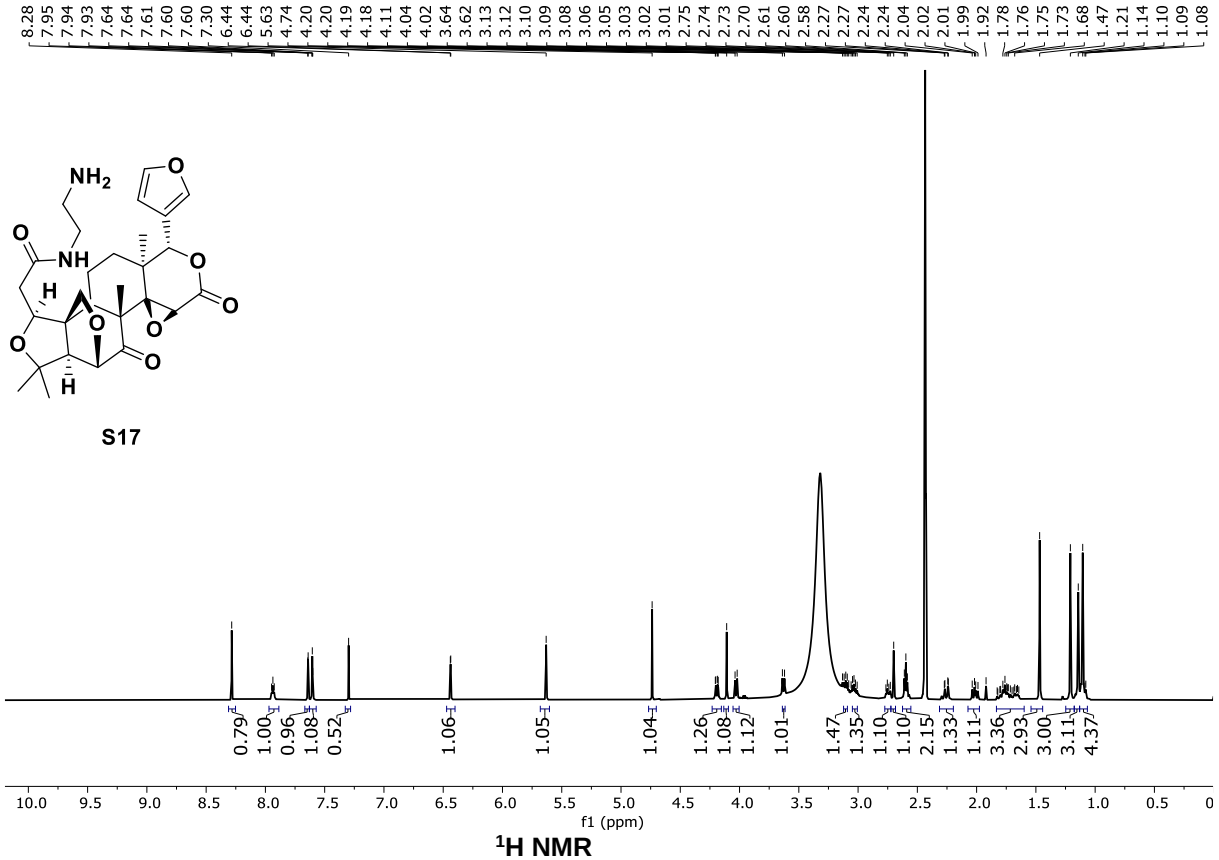


S16

^{13}C NMR

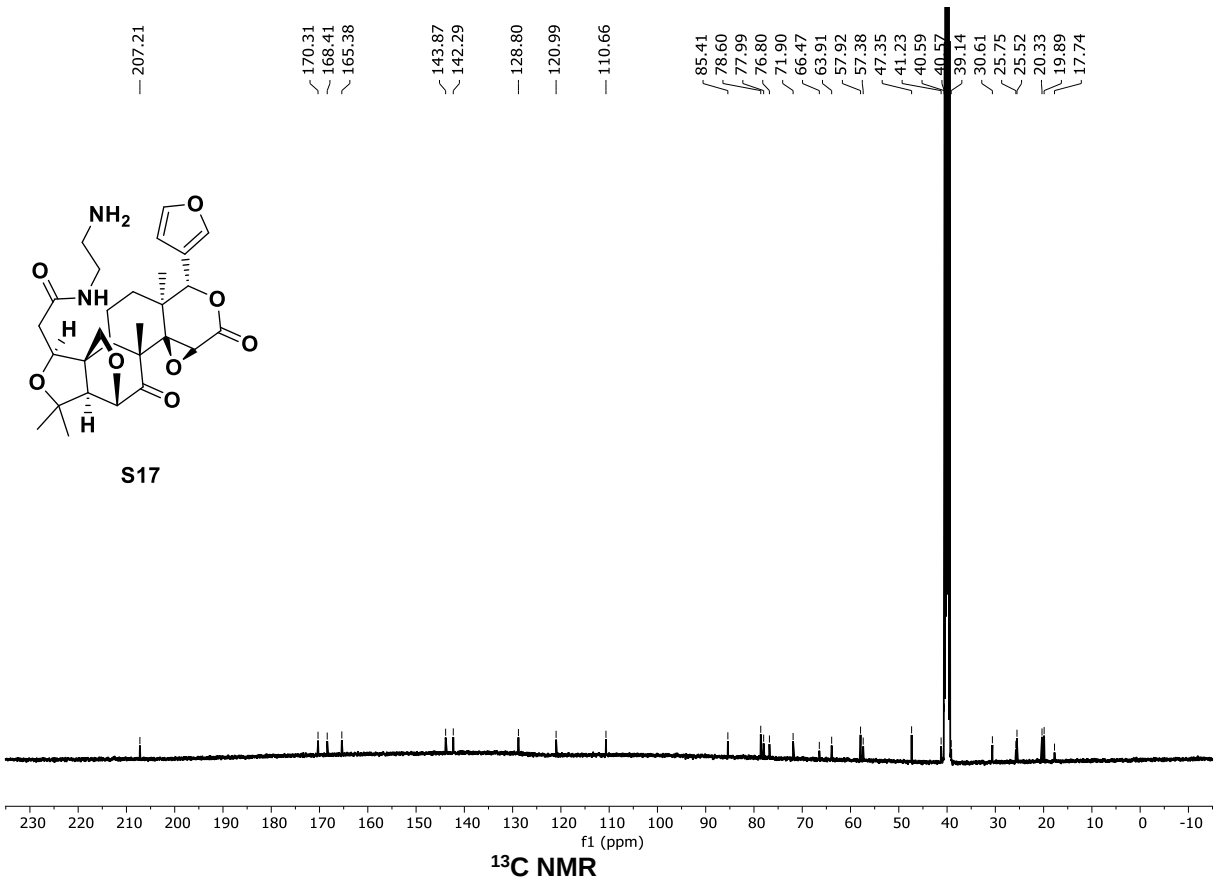


^{1}H-^{1}H COSY NMR



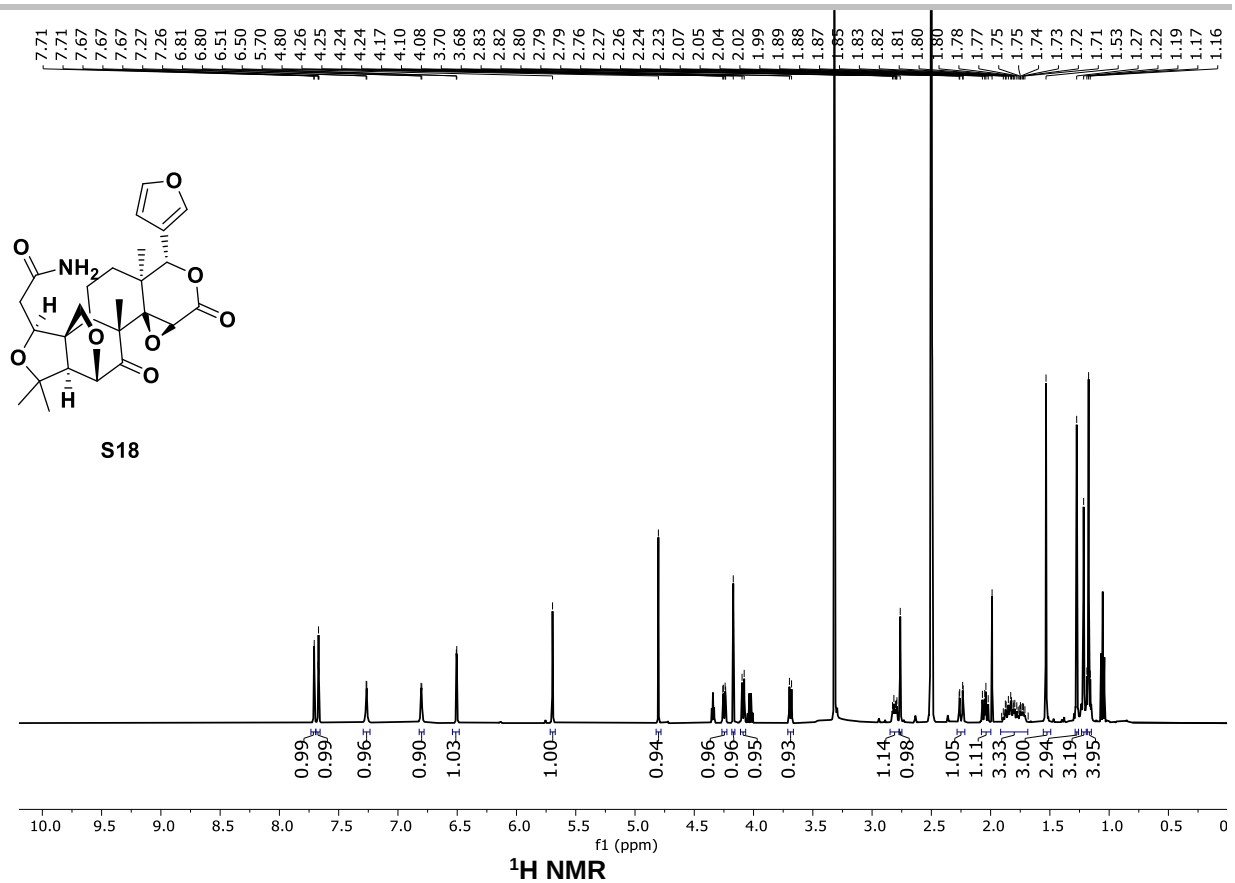
S17

^{1}H NMR



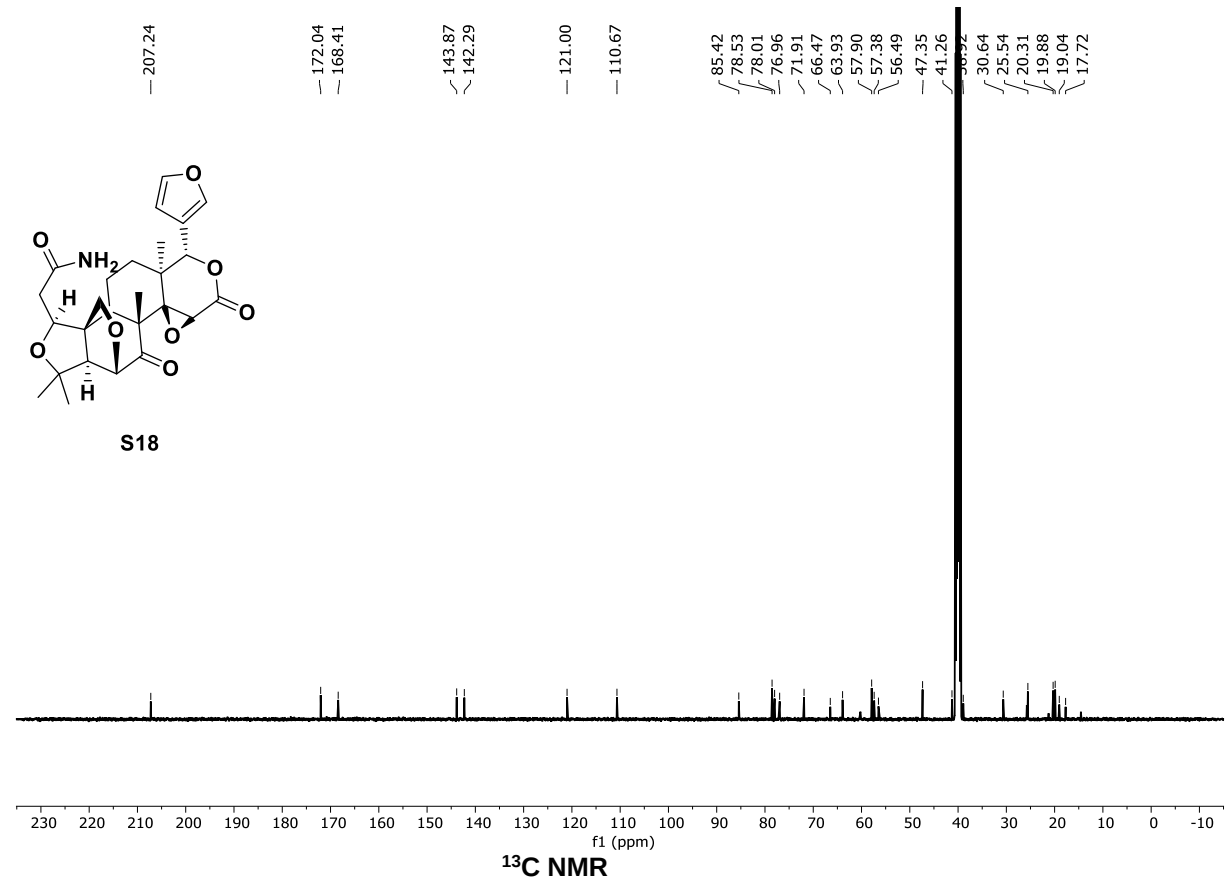
S17

^{13}C NMR



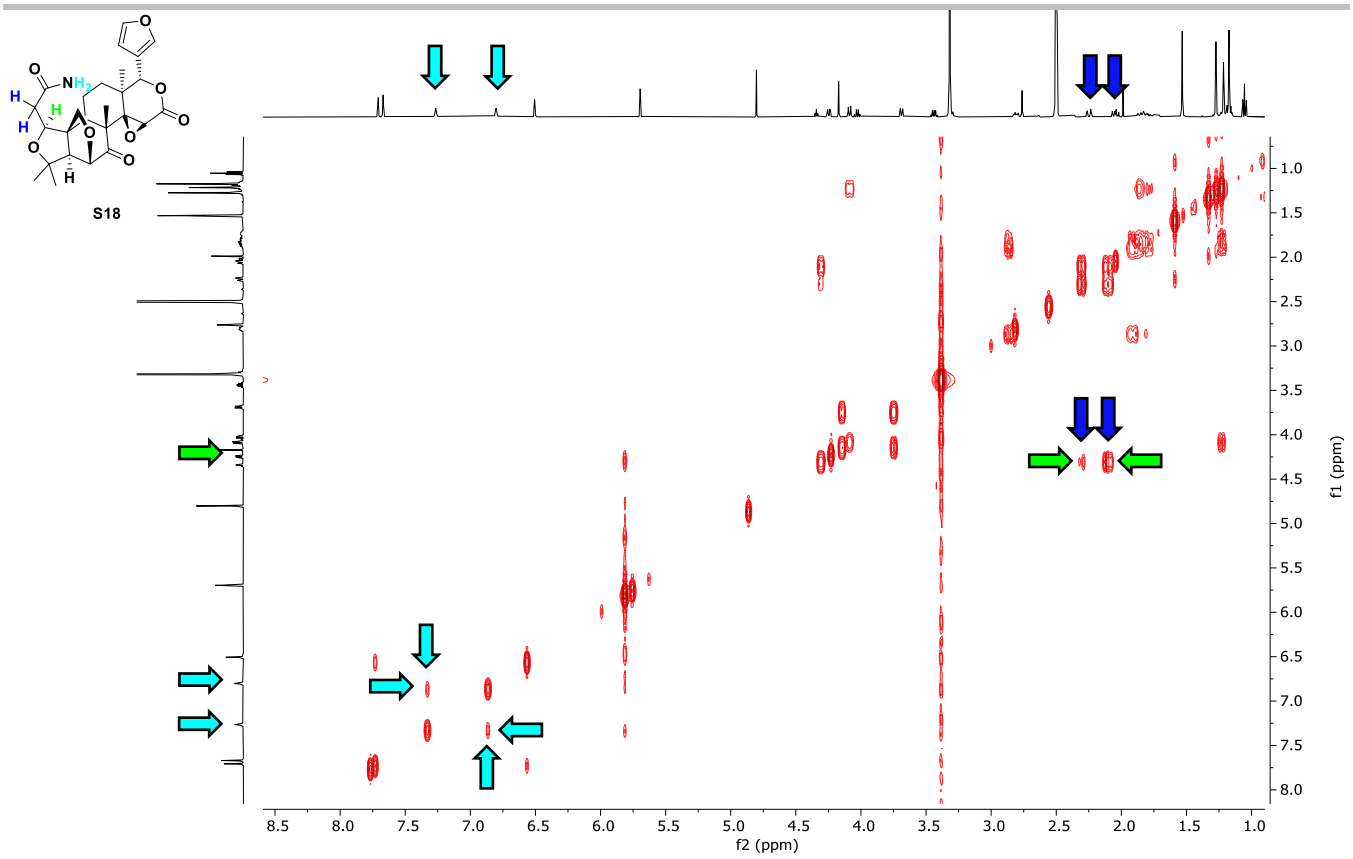
S18

^{1}H NMR

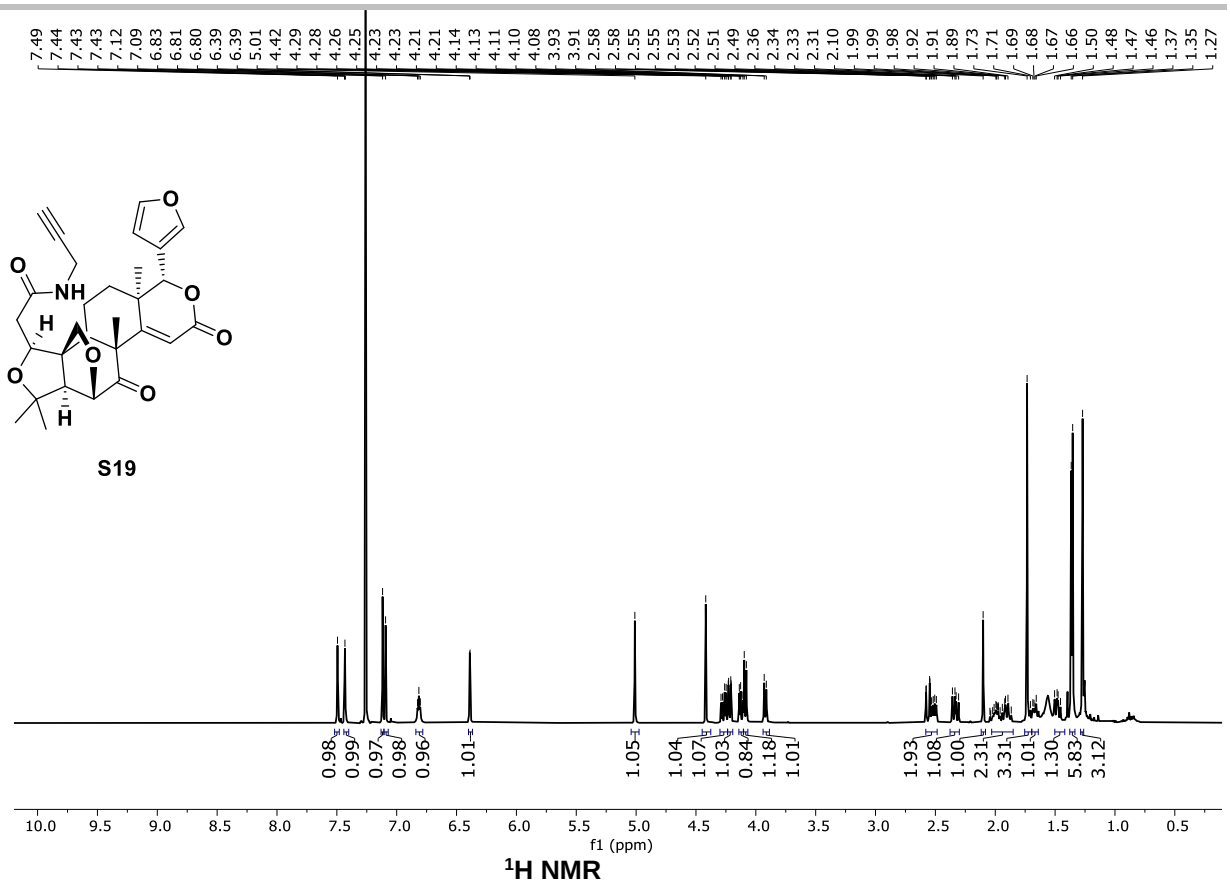


S18

^{13}C NMR

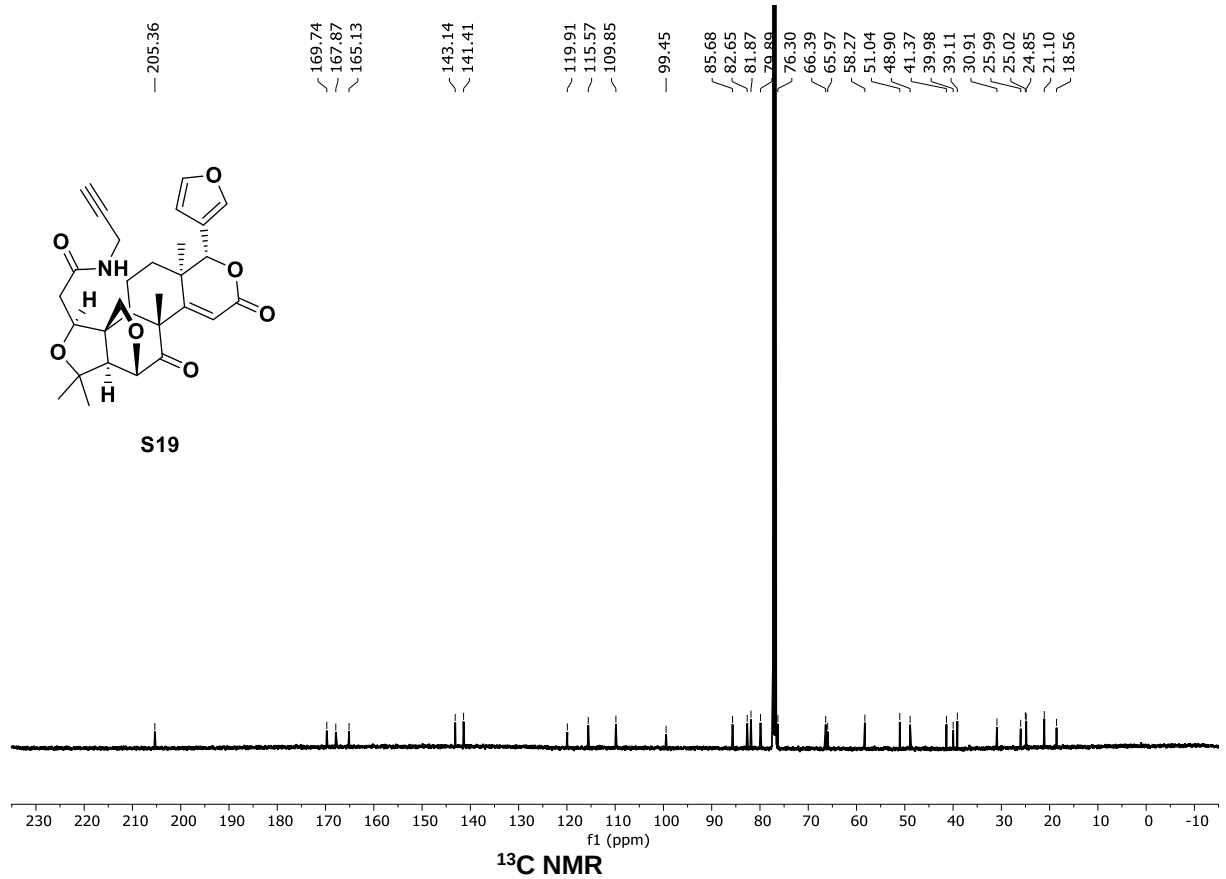


^{1}H-^{1}H COSY NMR



S19

^{1}H NMR



S19

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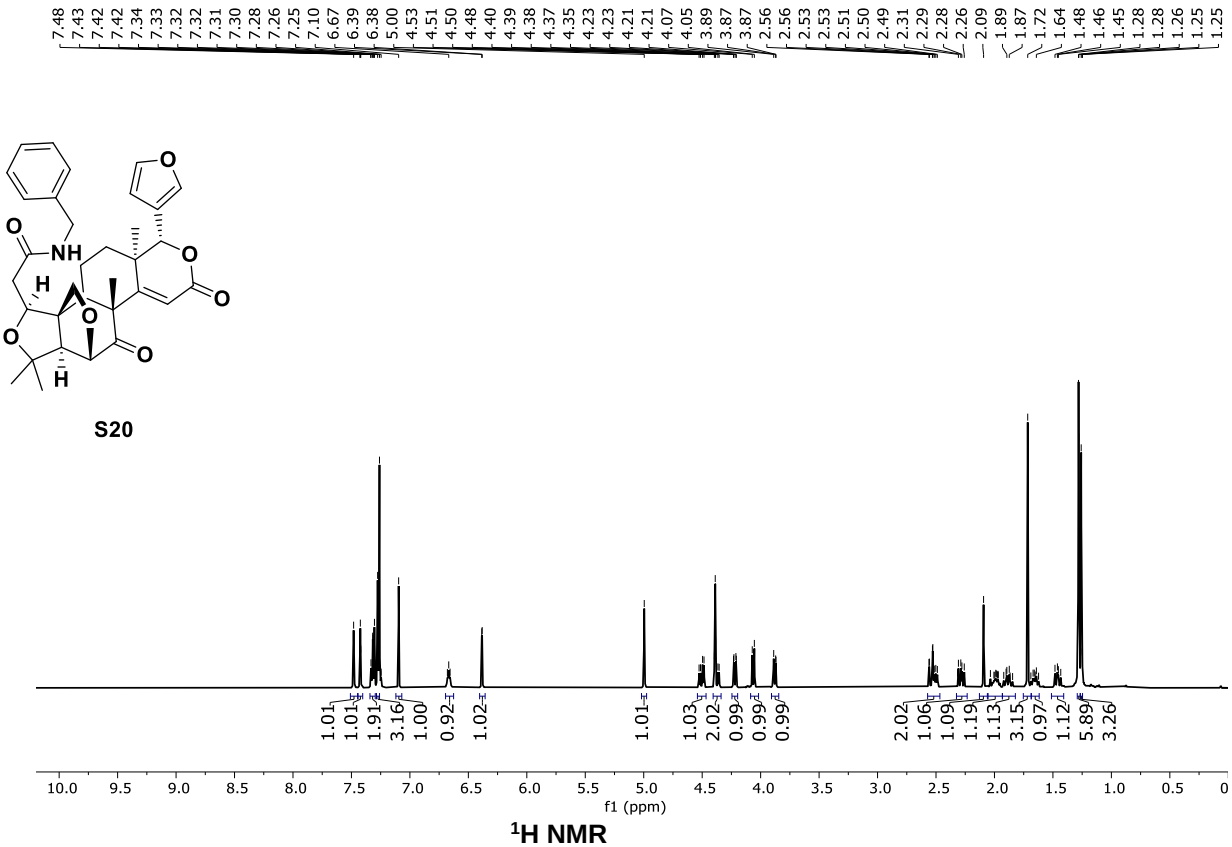
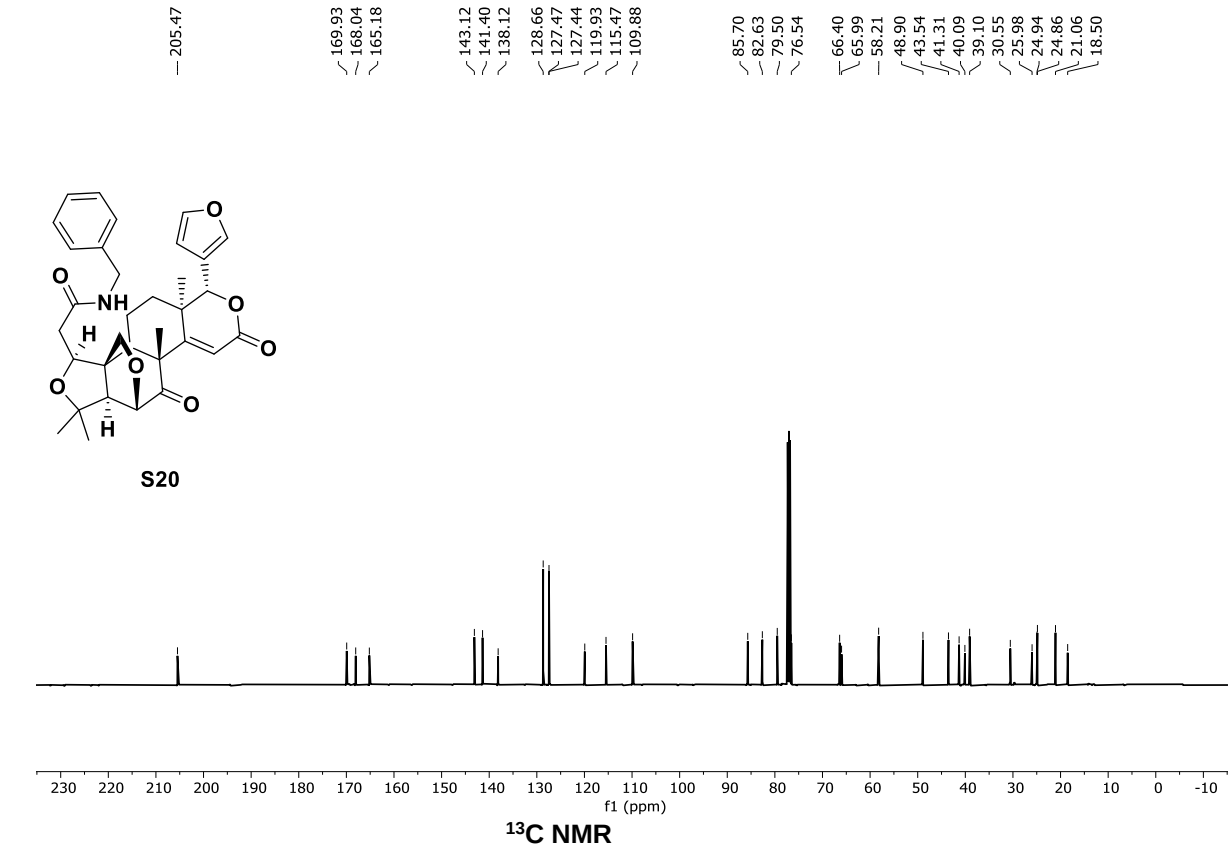
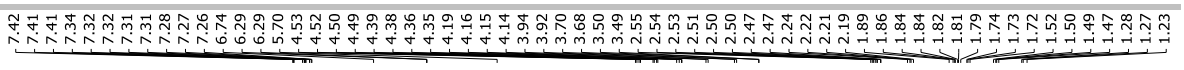
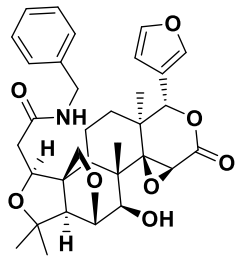


^{1}H NMR

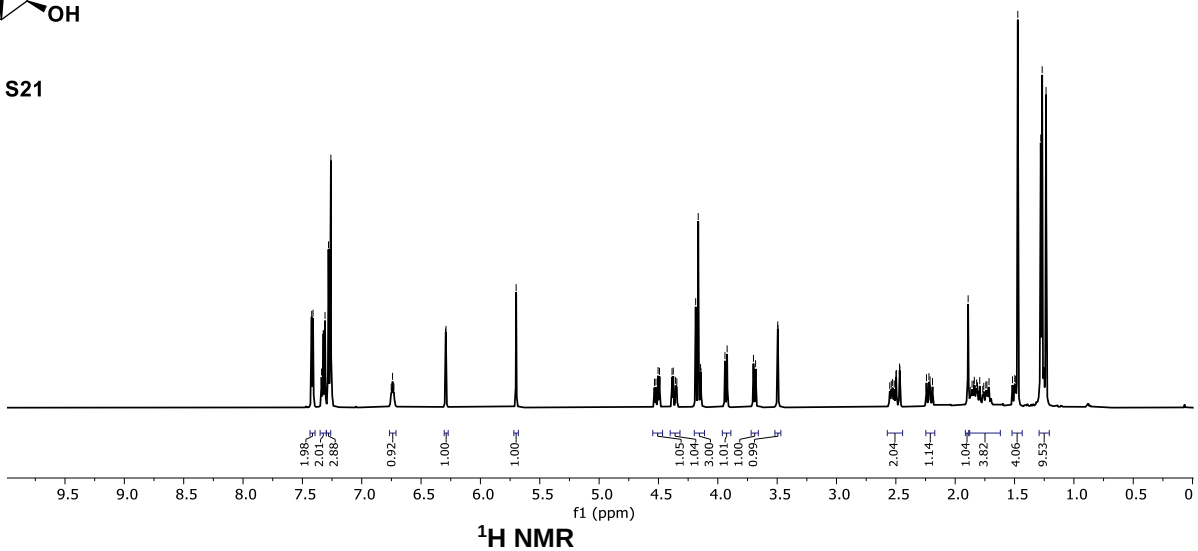


^{13}C NMR

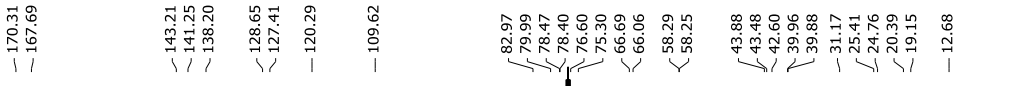


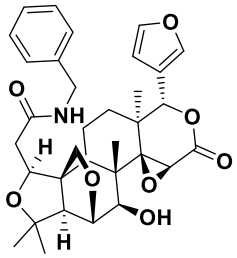


S21

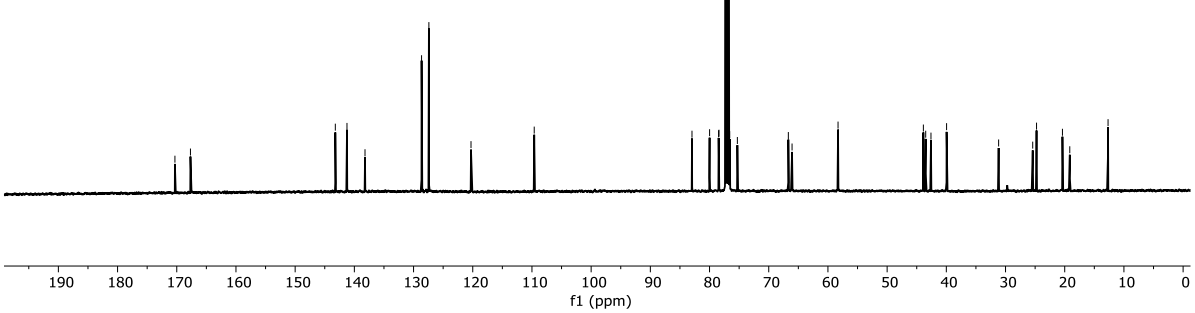


^{1}H NMR

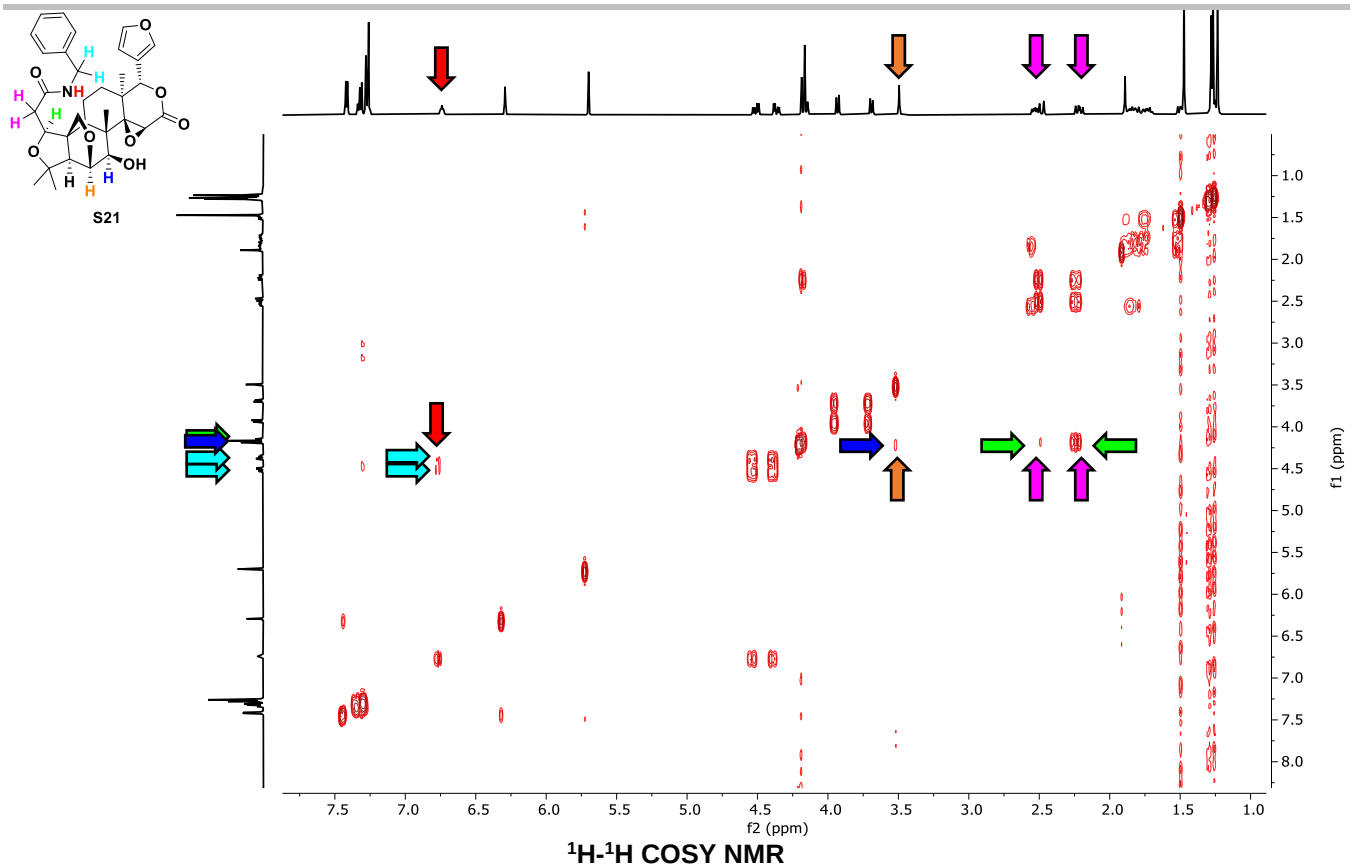




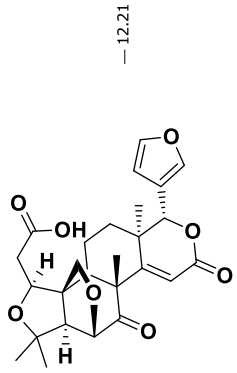
S21



^{13}C NMR

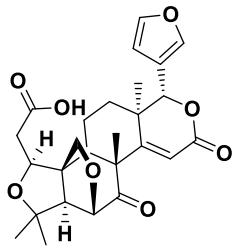


^{1}H-^{1}H COSY NMR



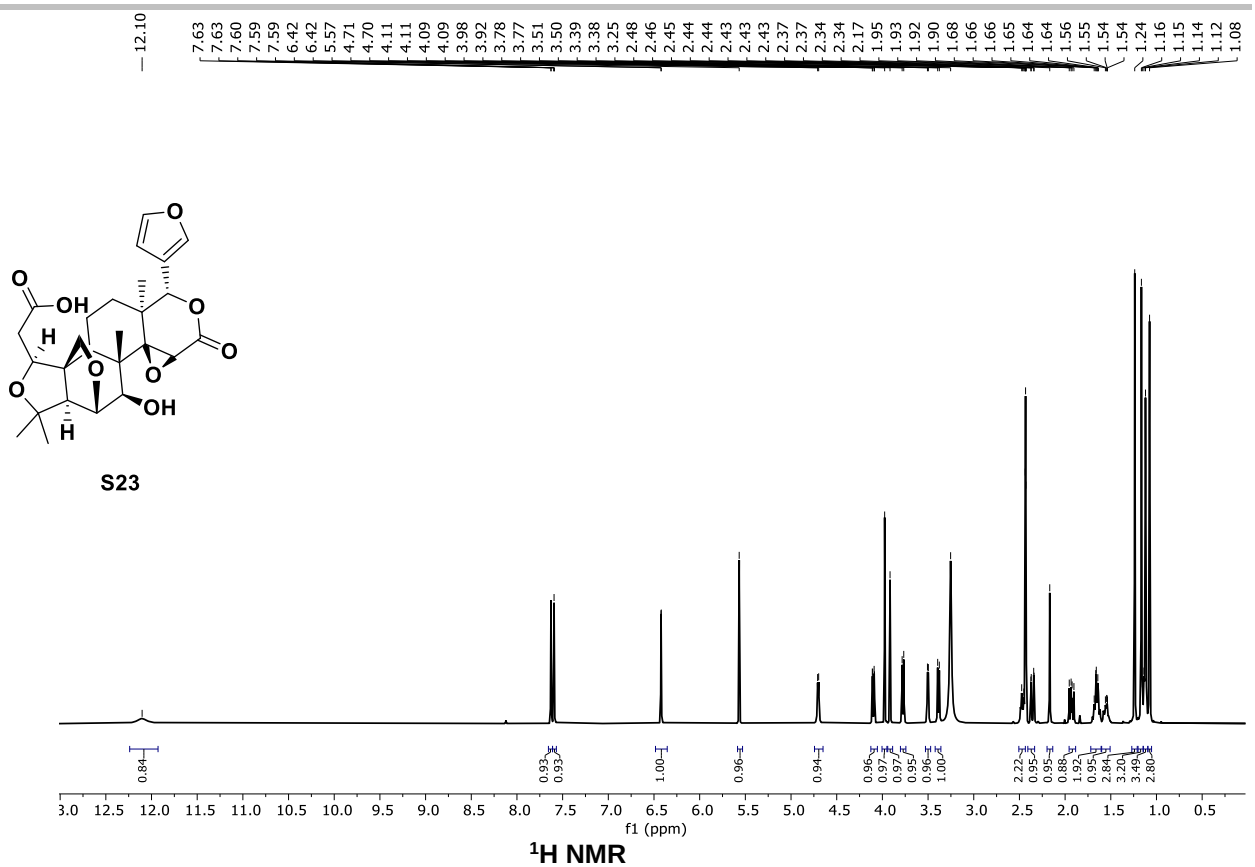
S22

^{1}H NMR



S22

^{13}C NMR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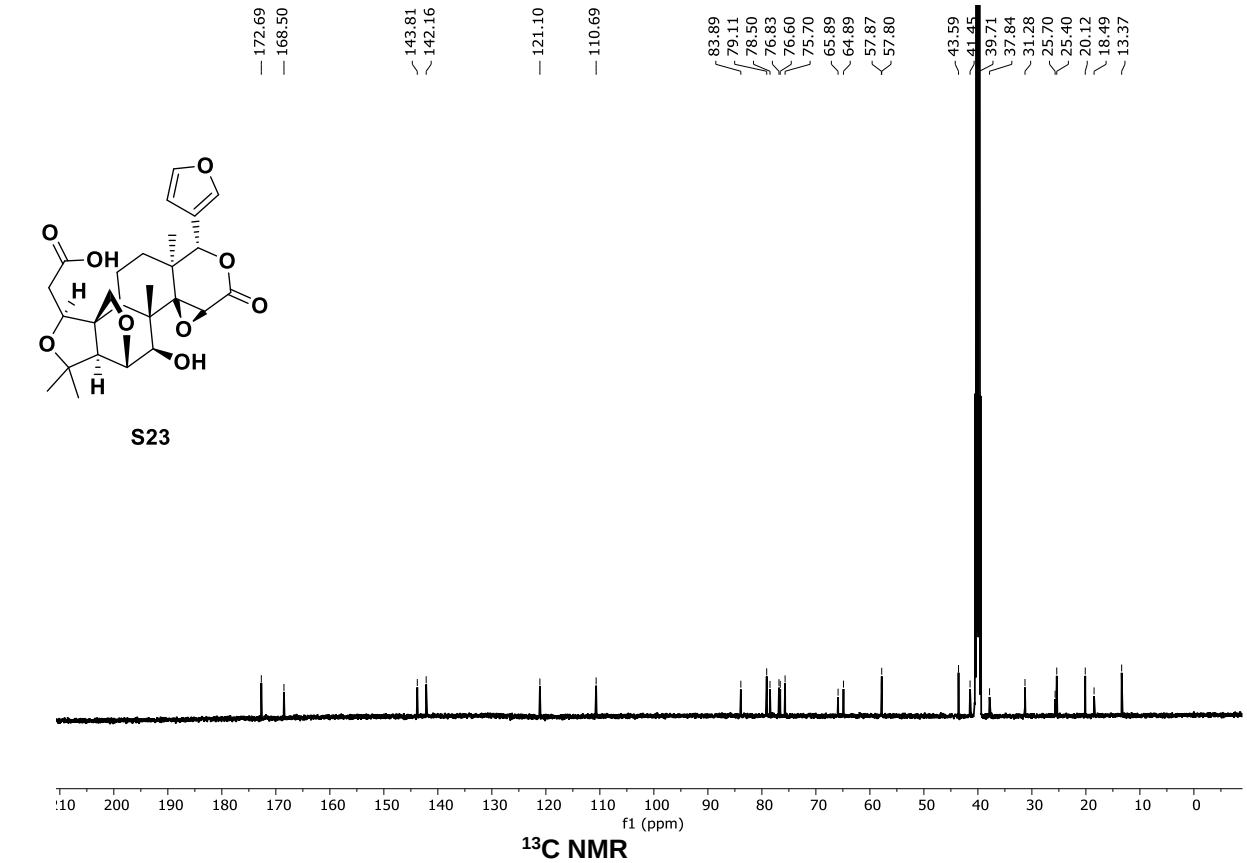
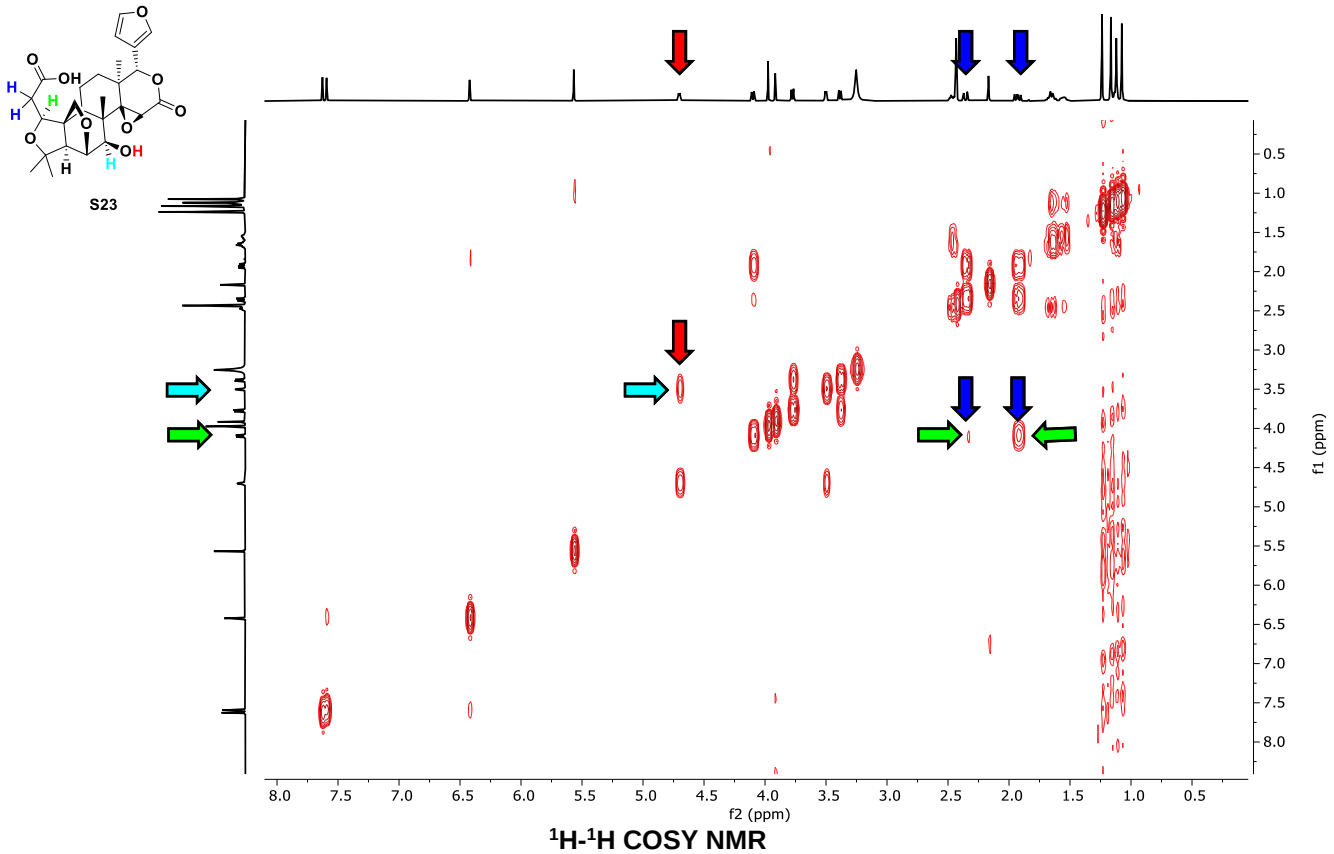
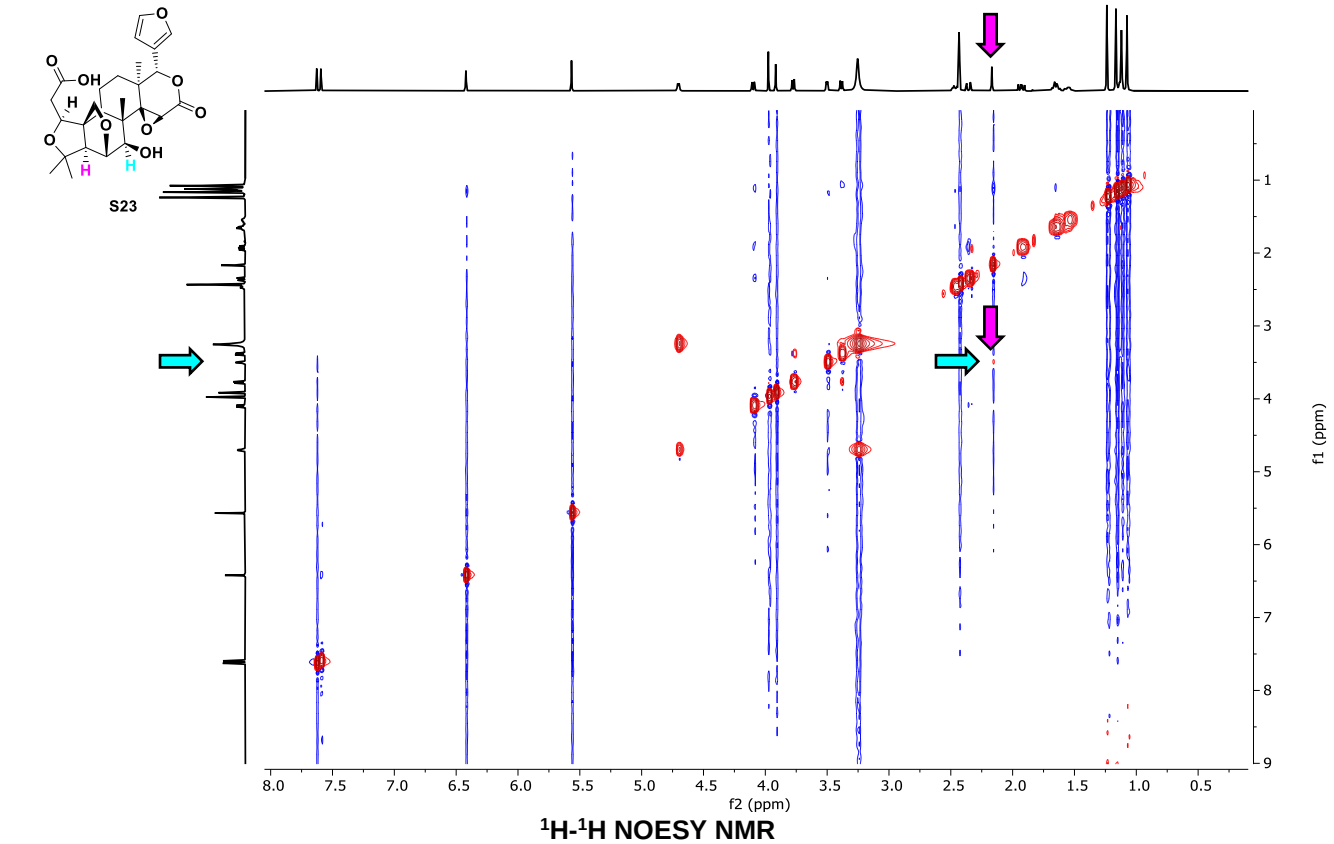
2.34
2.17
1.95
1.93
1.92
1.90
1.68
1.66
1.66
1.65
1.64
1.64
1.56
1.55
1.54
1.54
1.24
1.16
1.15
1.14
1.12
1.08
O
O
OH
H
O
O
O
O
O
OH
H
S23
0.84
0.93
0.93
1.00
0.96
0.94
0.96
0.97
0.97
0.95
0.96
1.00
2.22
0.95
0.88
1.92
0.95
2.84
3.20
3.49
2.80
f1 (ppm)
1H NMR

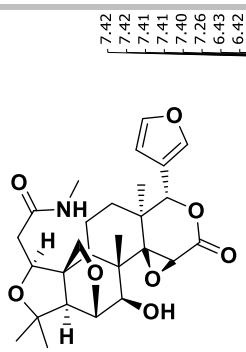

172.69
168.50
143.81
142.16
121.10
110.69
83.89
79.11
78.50
76.83
76.60
75.70
65.89
64.89
57.87
57.80
43.59
41.45
39.71
37.84
31.28
25.70
25.40
20.12
18.49
13.37
O
O
OH
H
O
O
O
O
O
OH
H
S23
f1 (ppm)
13C NMR



^{1}H-^{1}H COSY NMR

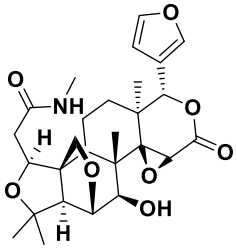


^{1}H-^{1}H NOESY NMR



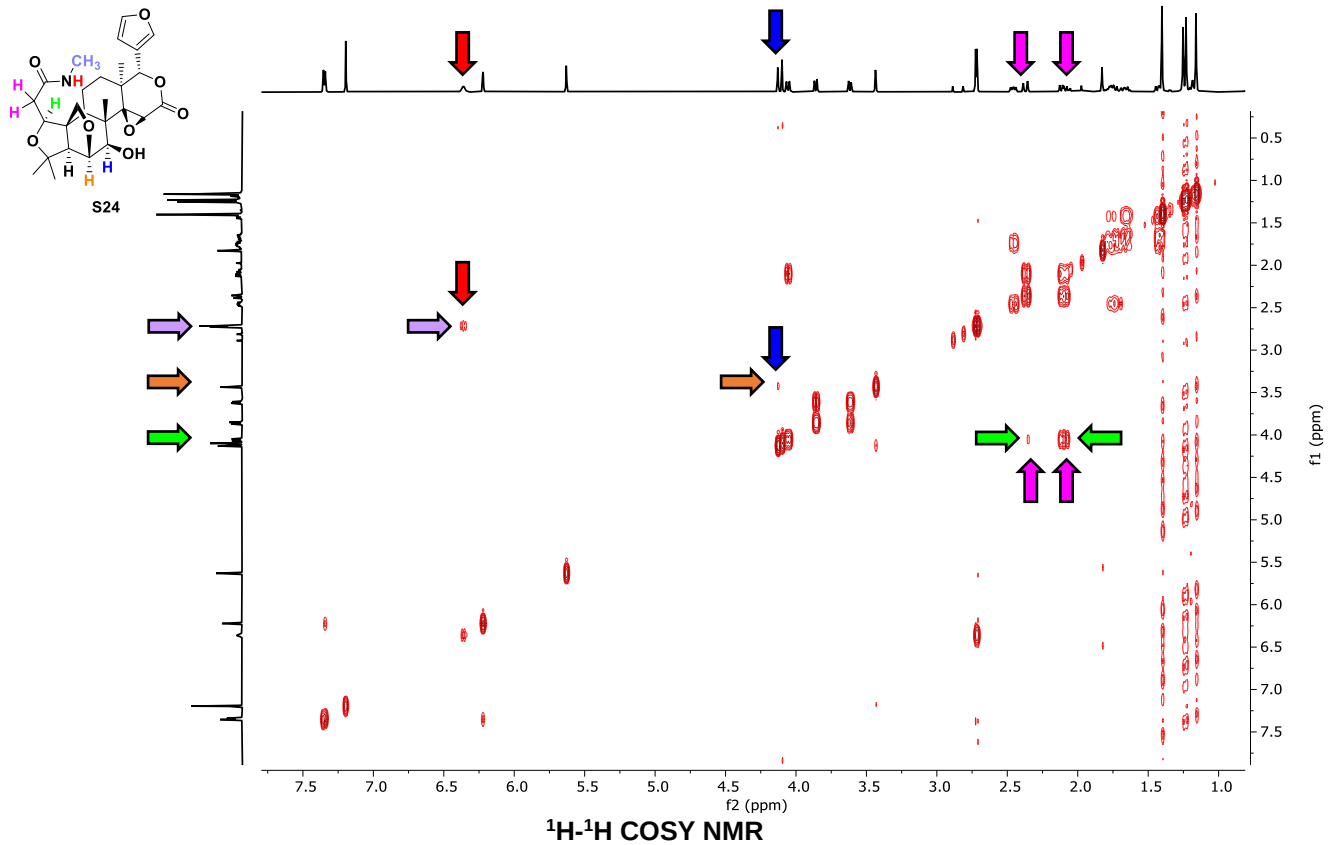
S24

^{1}H NMR

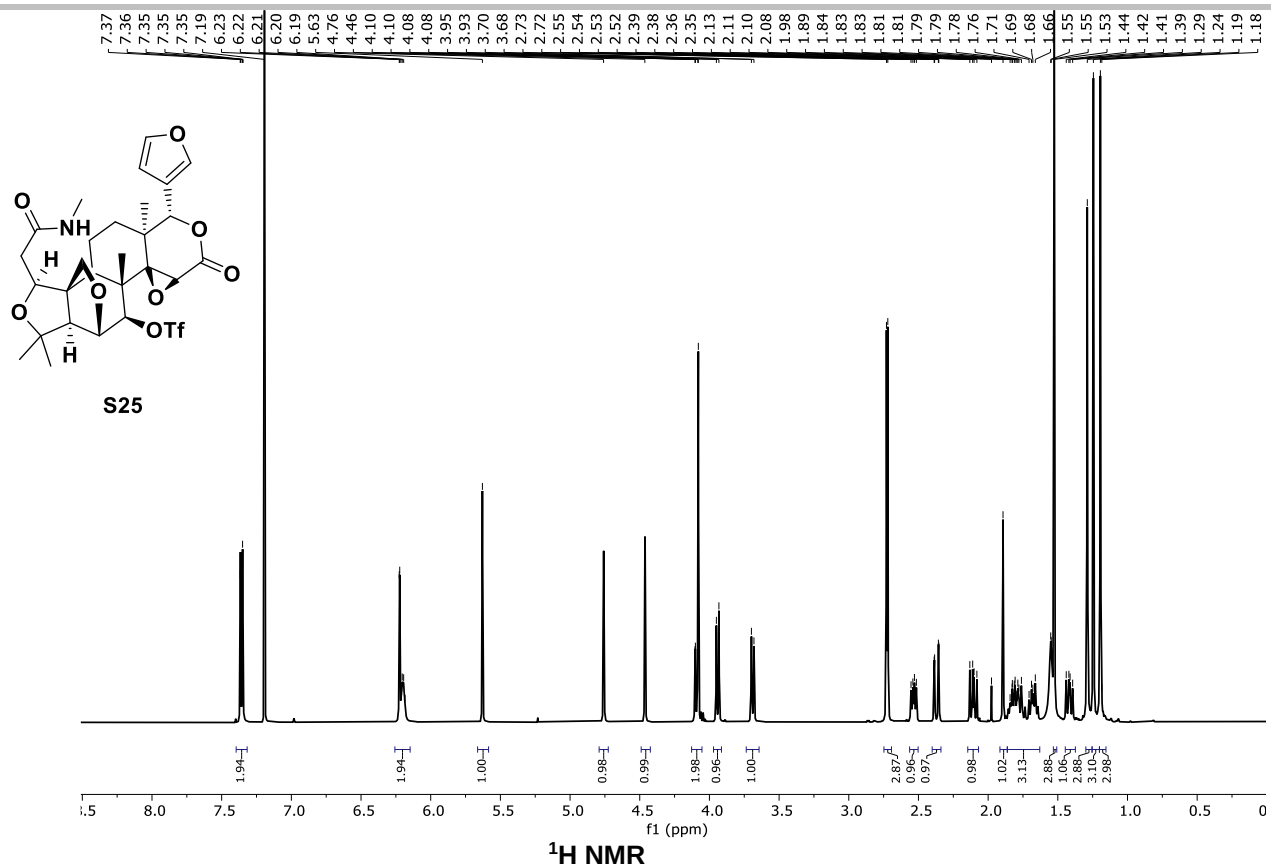


S24

^{13}C NMR

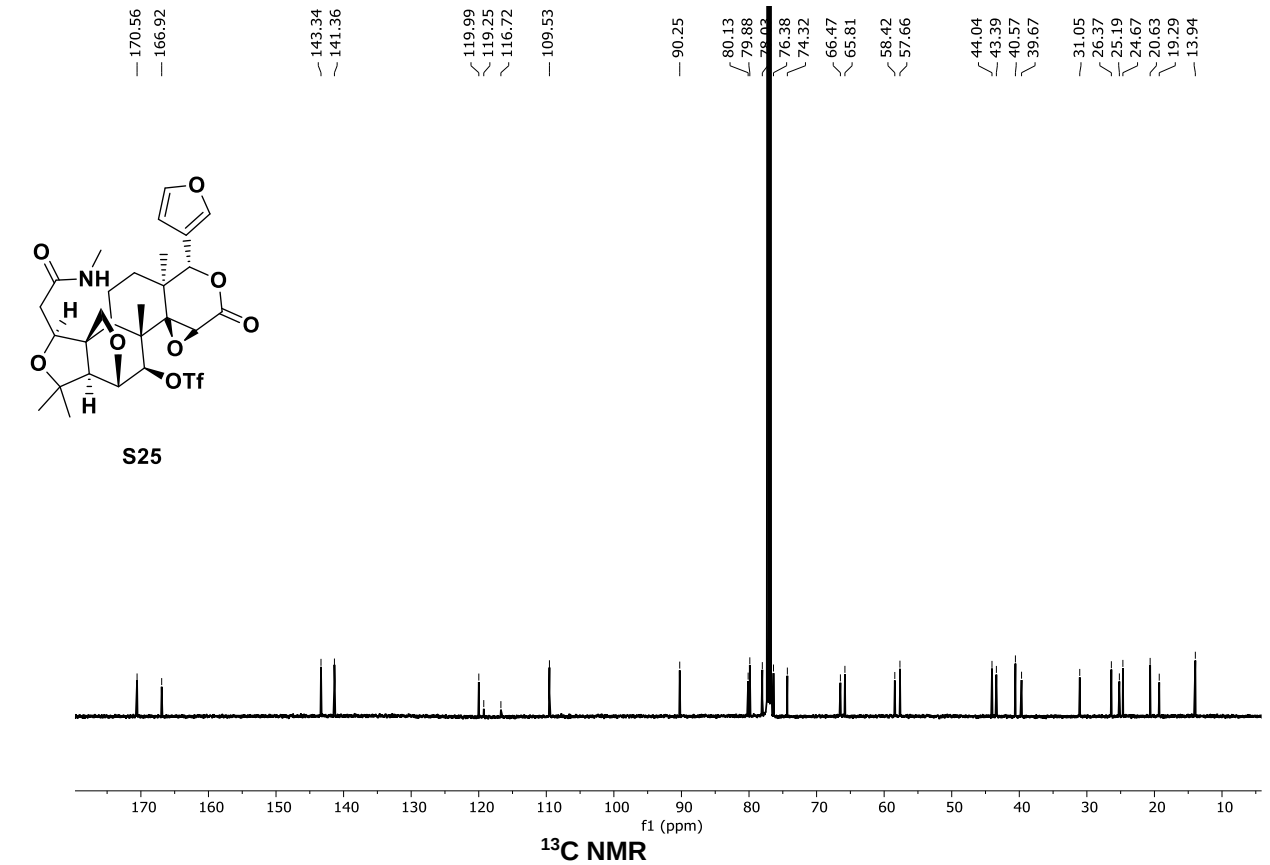


^{1}H-^{1}H COSY NMR



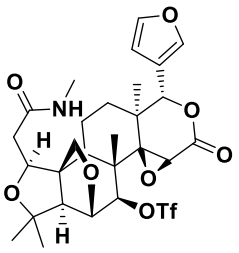
S25

^{1}H NMR



S25

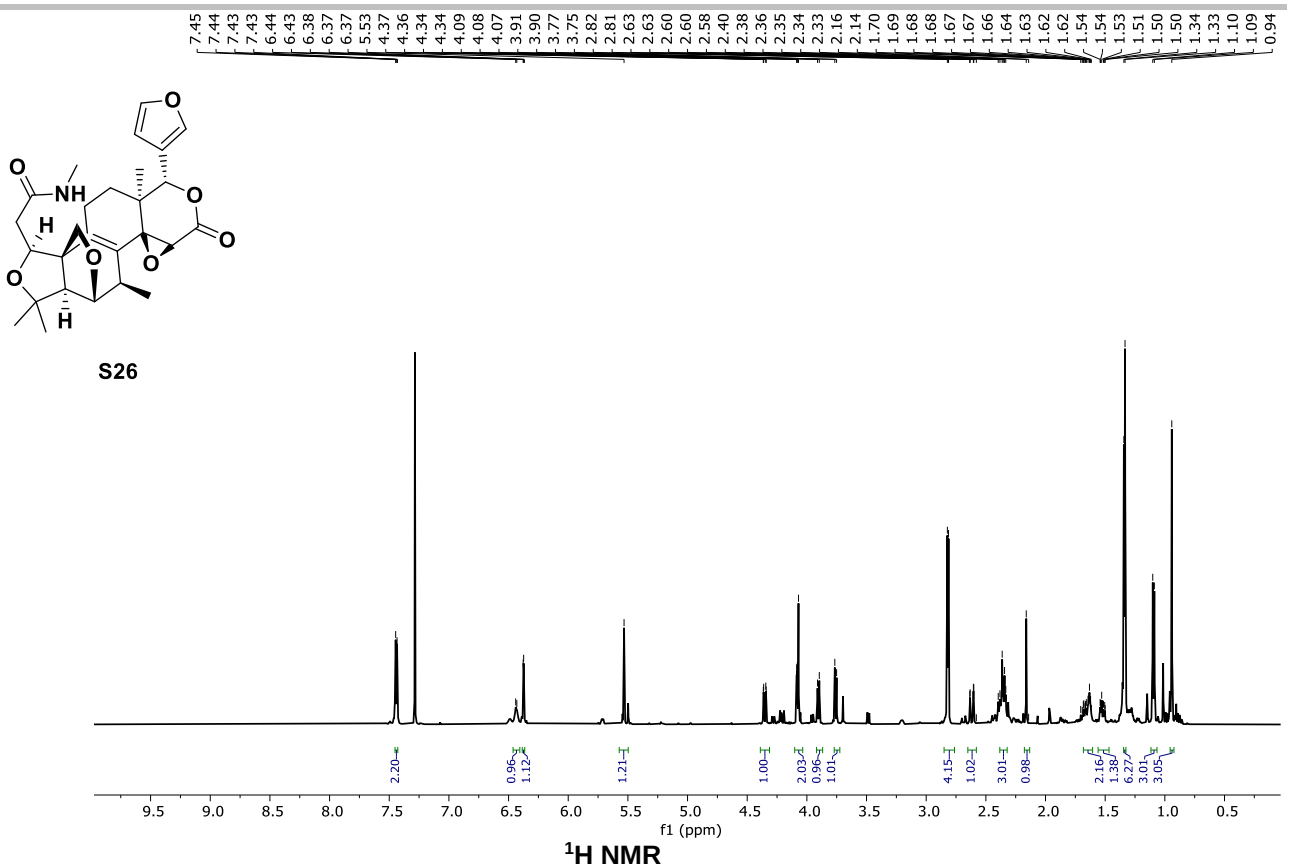
^{13}C NMR


O
O
NH
H
O
O
O
O
O
OTf
H

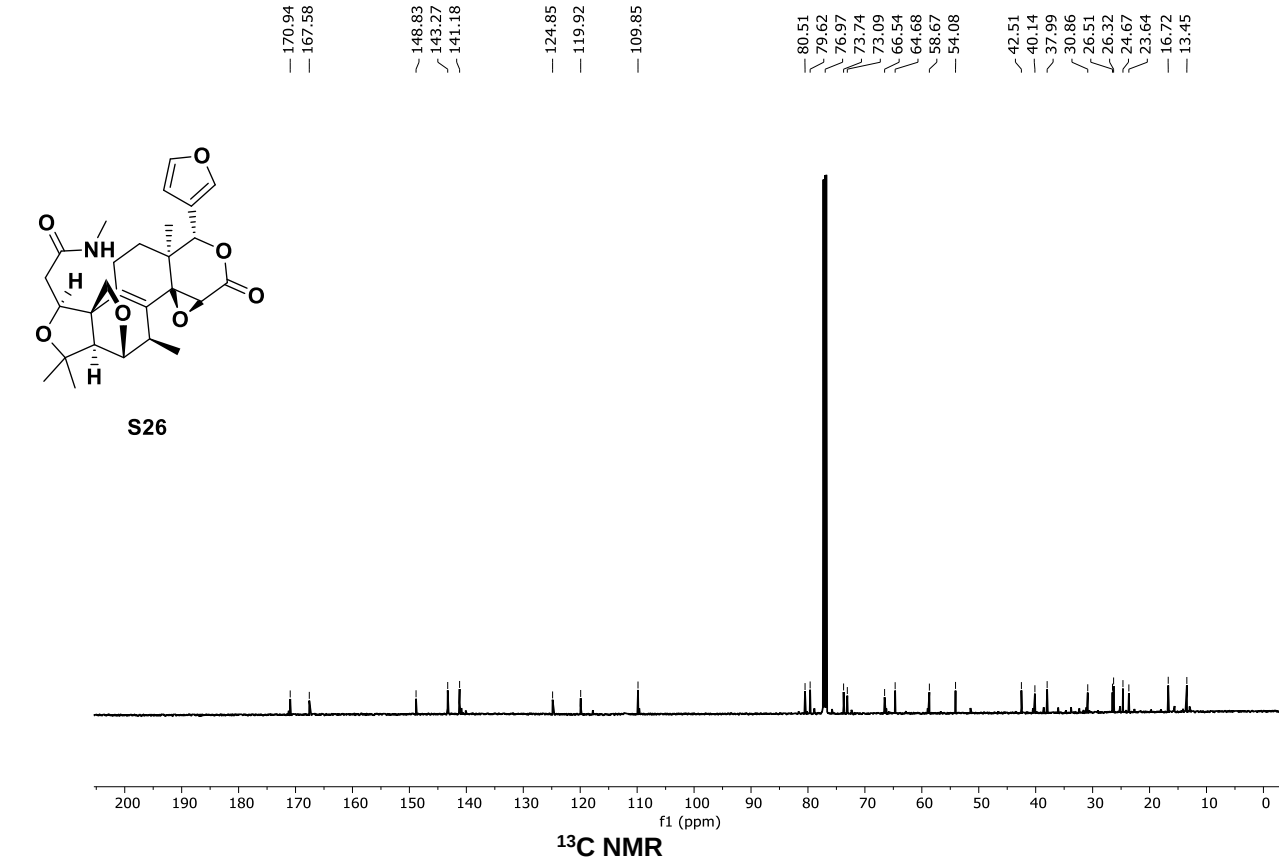
S25

-75.22
20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210 -2
f1 (ppm)

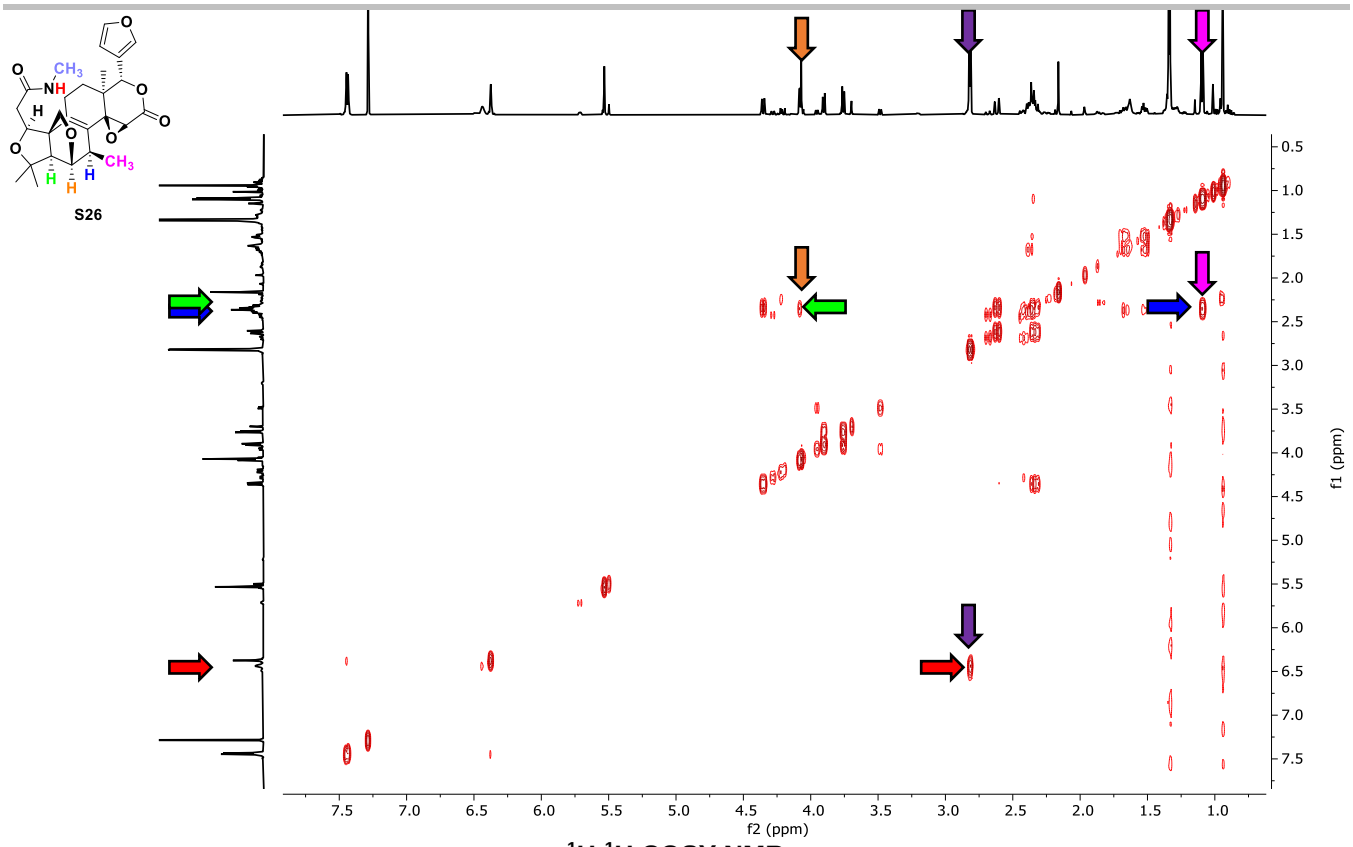
^{19}F NMR



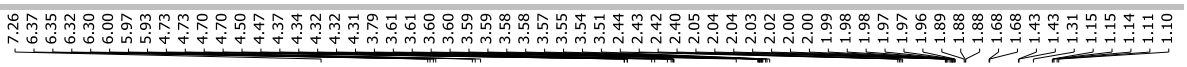
^{1}H NMR

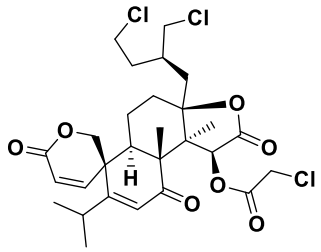


^{13}C NMR

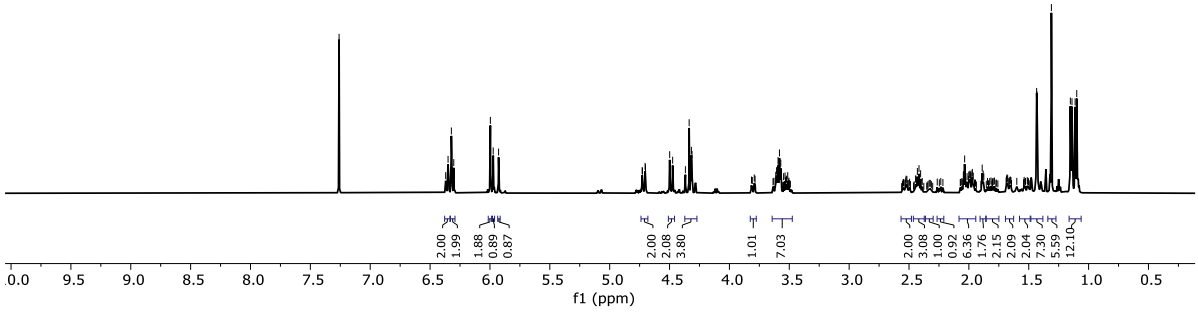


^{1}H-^{1}H COSY NMR

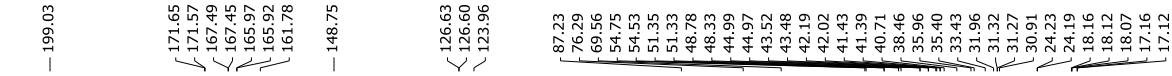


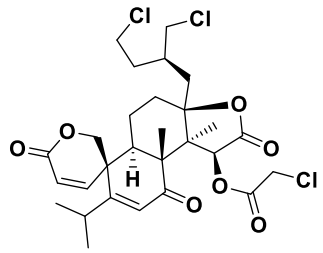


S27



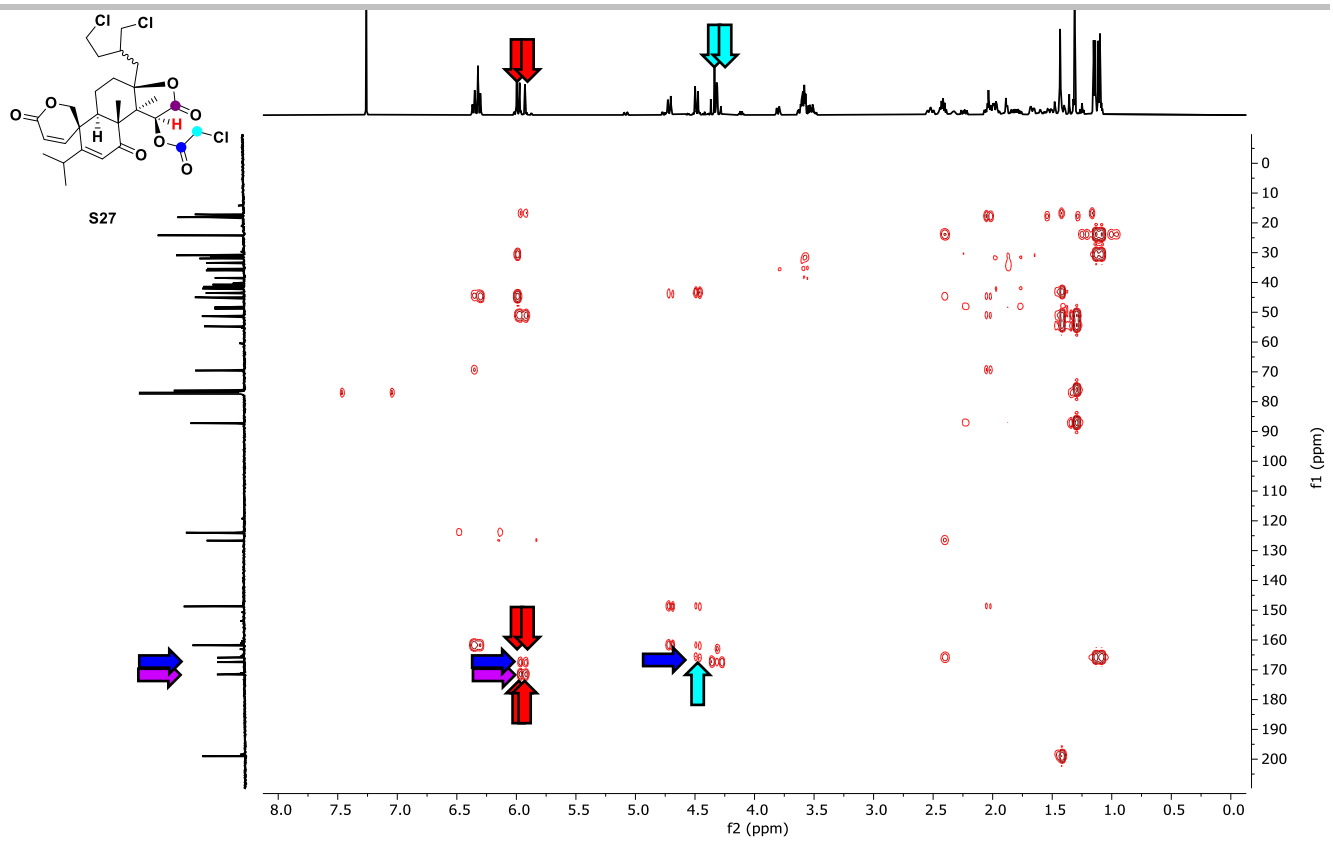
^{1}H NMR



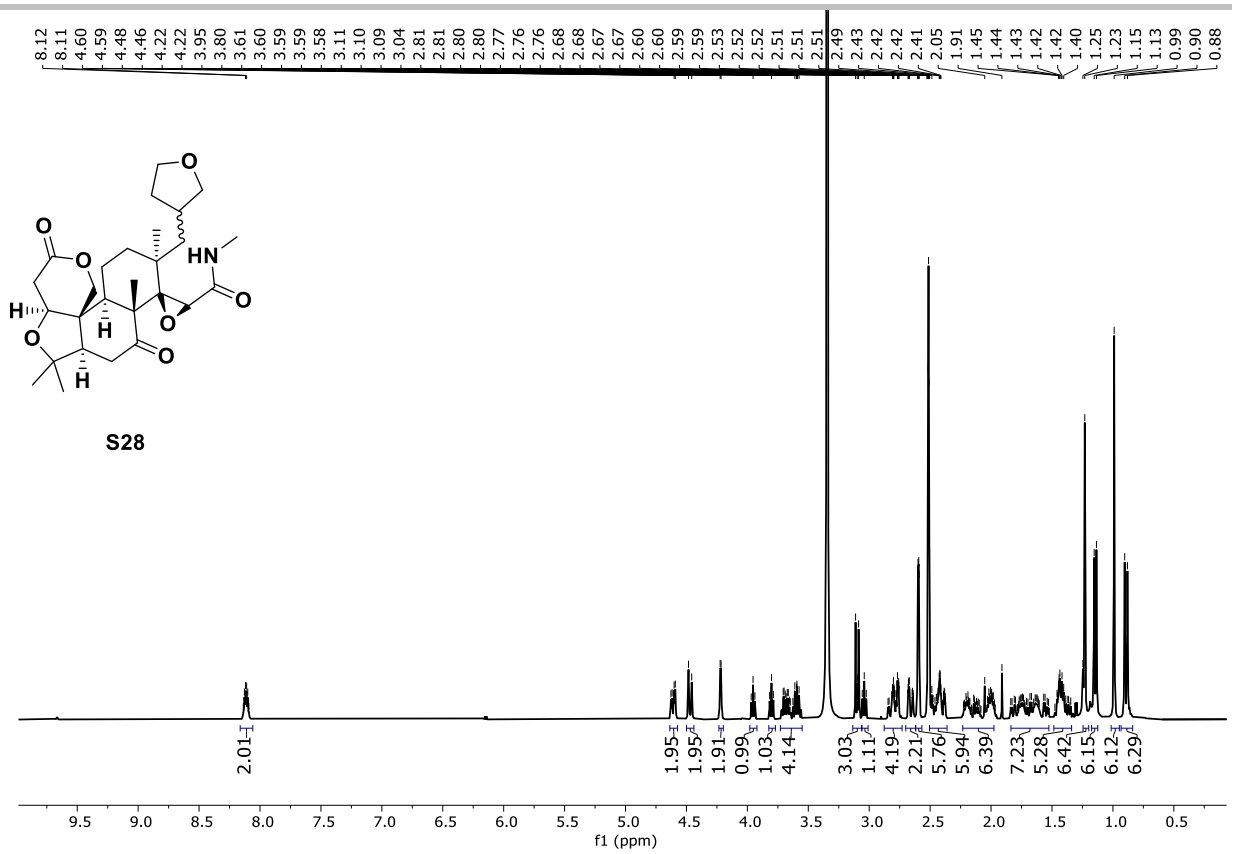


S27

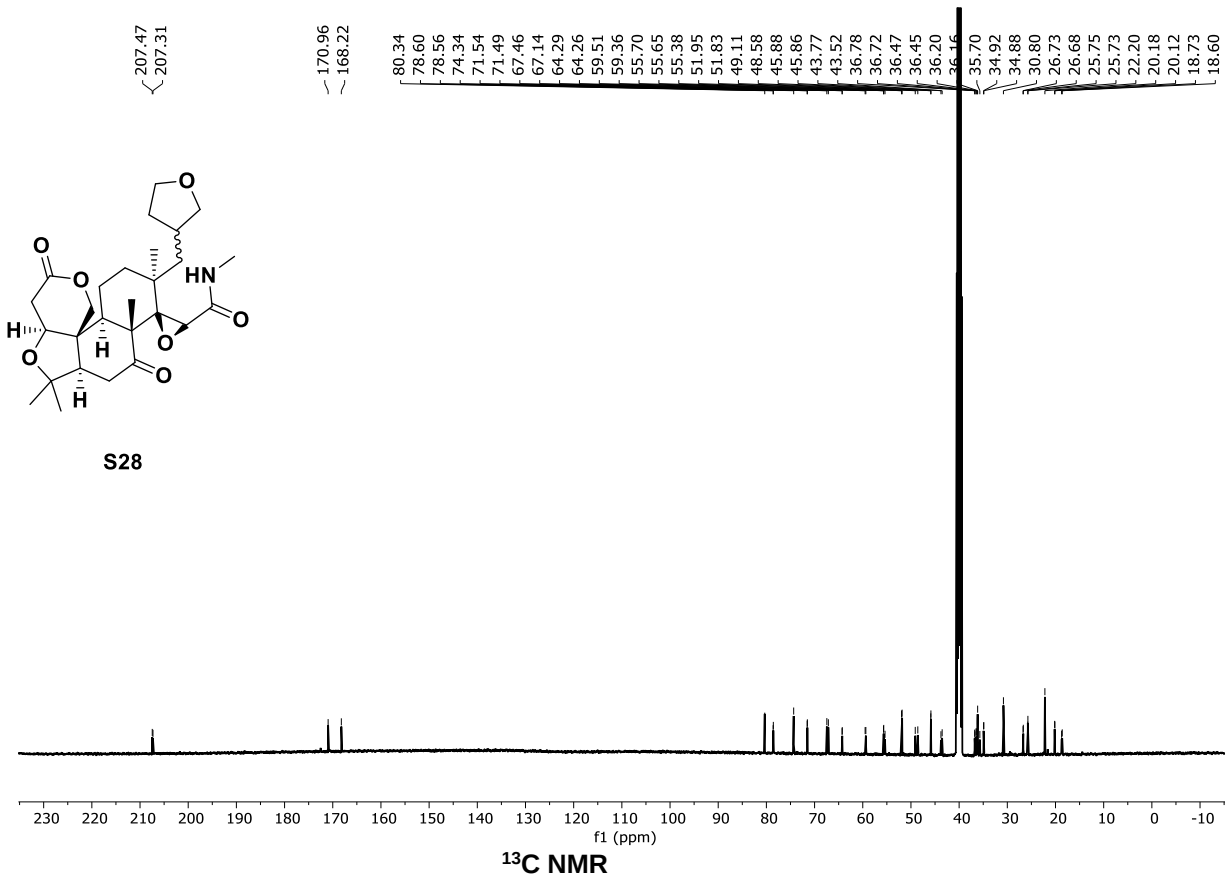
^{13}C NMR



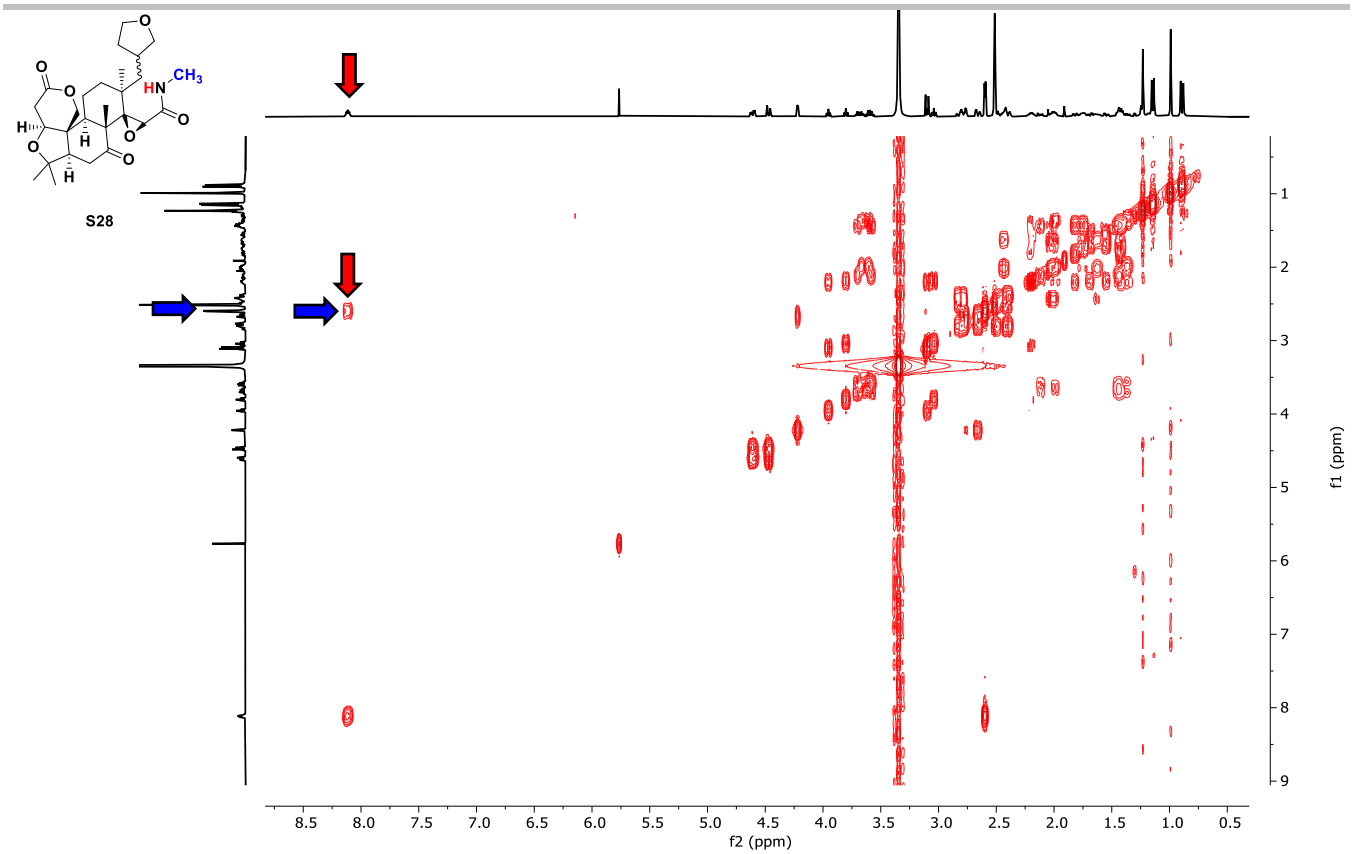
^{1}H-^{13}C HMBC NMR



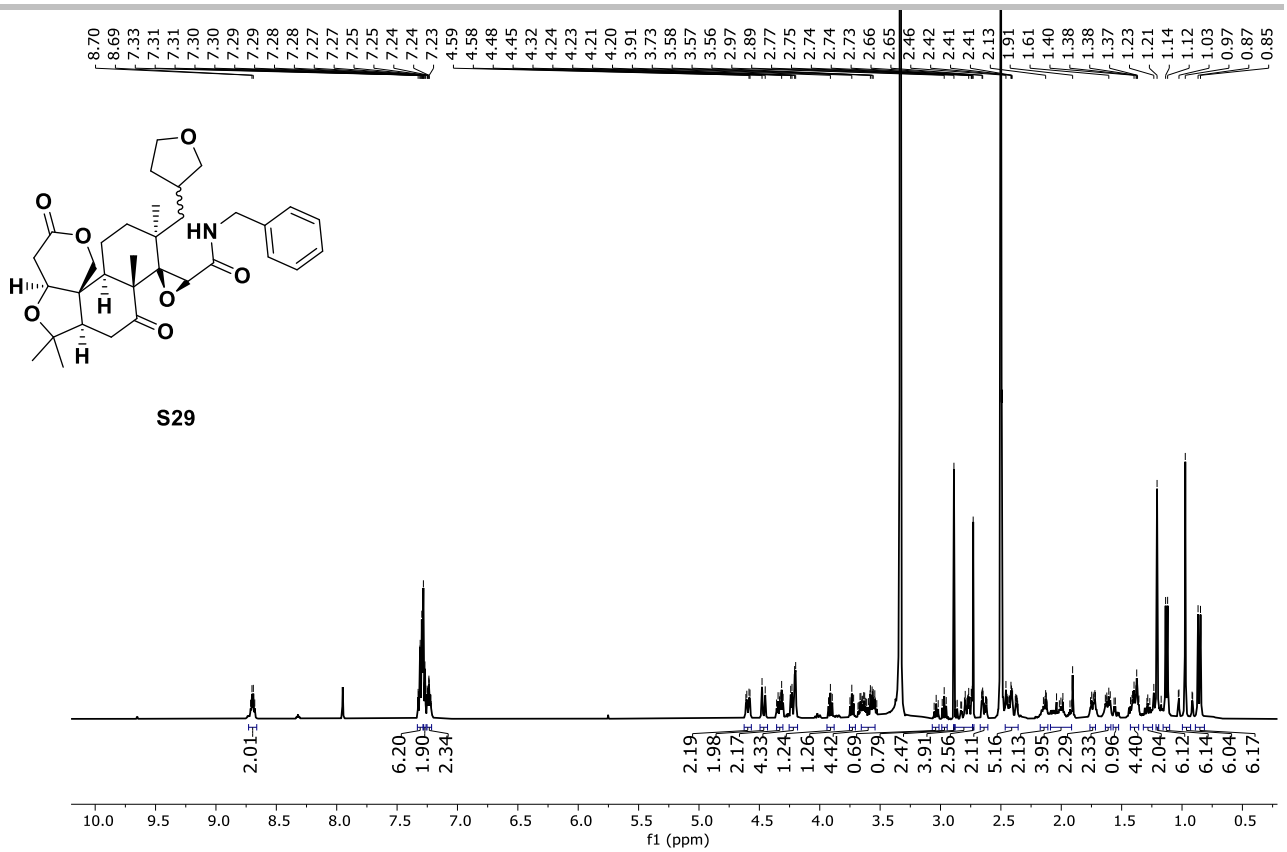
^{1}H NMR



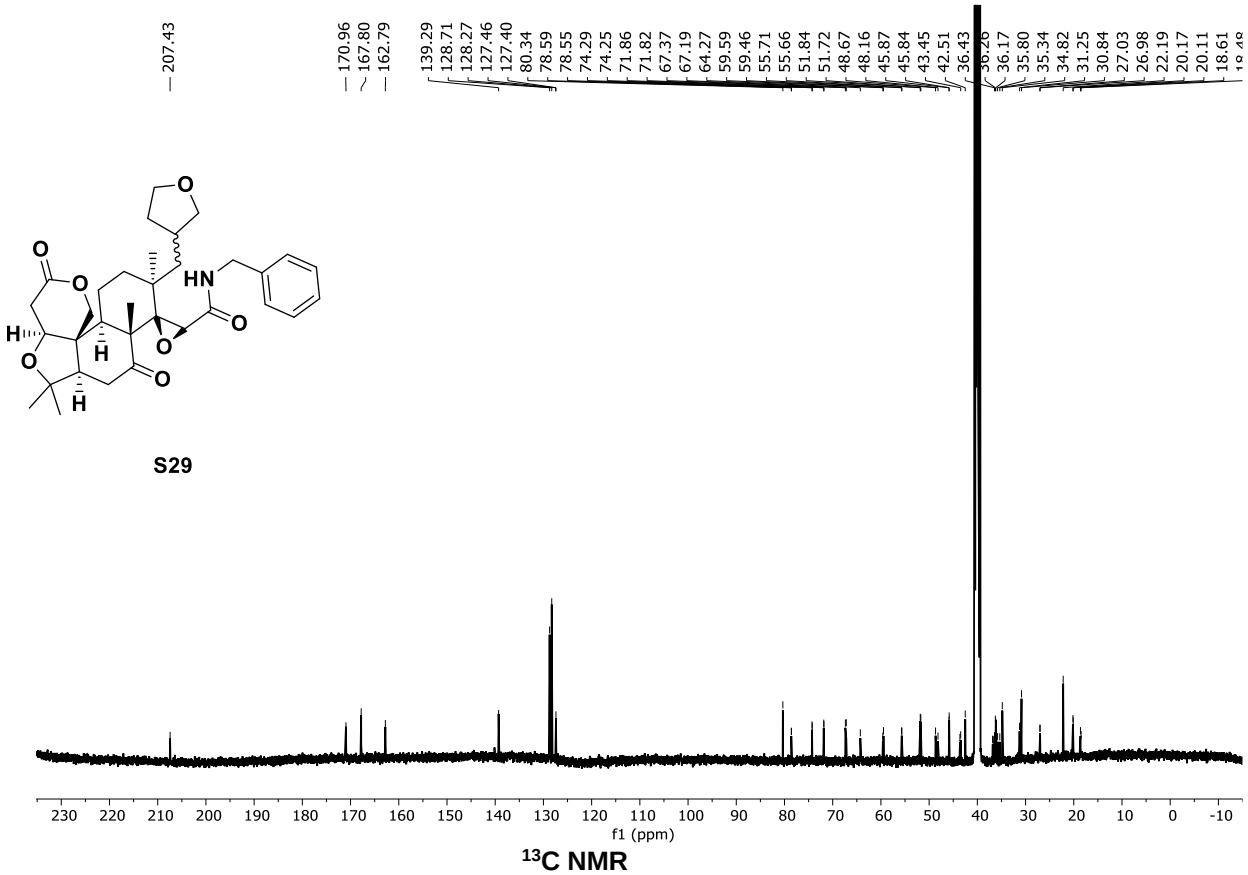
^{13}C NMR



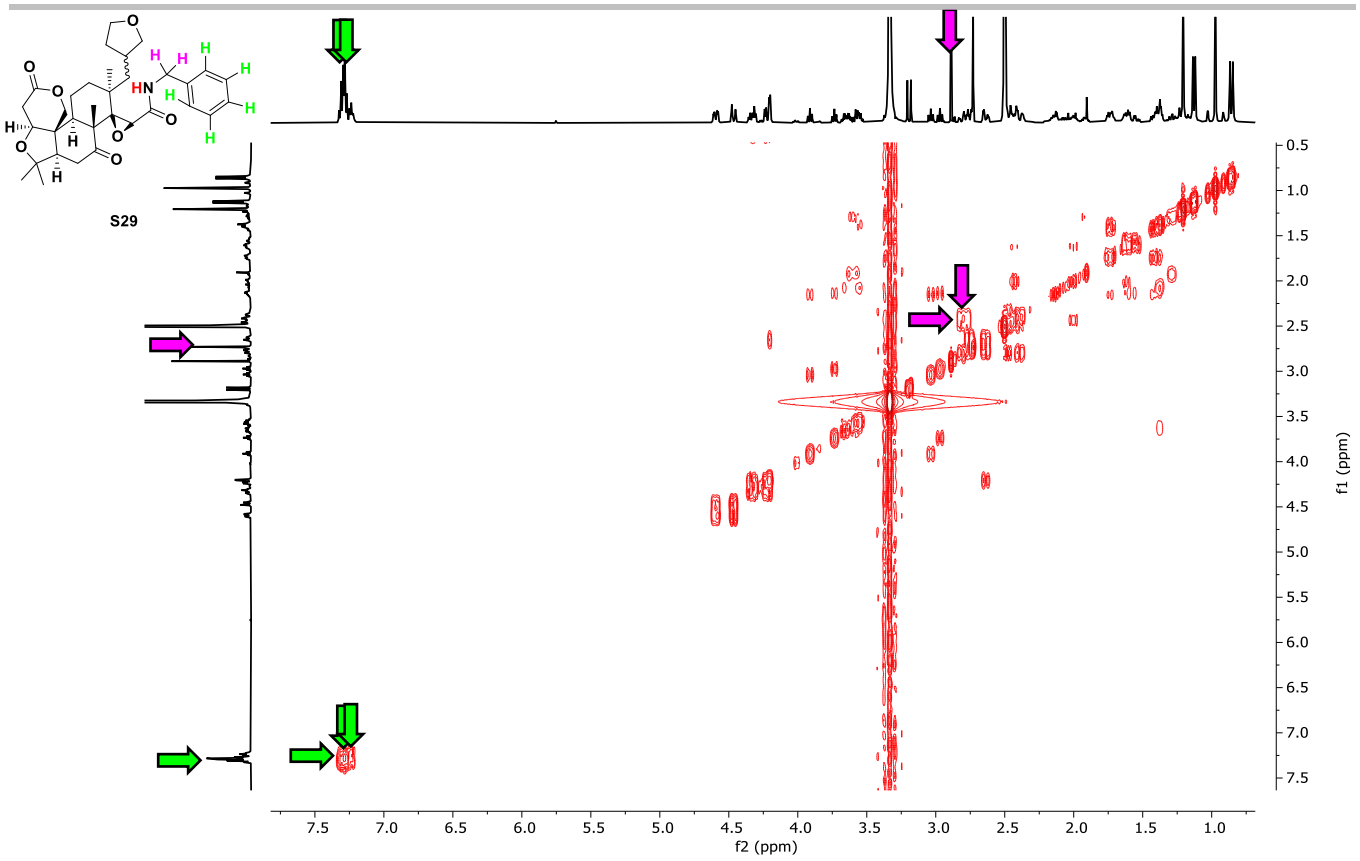
^{1}H-^{1}H COSY NMR



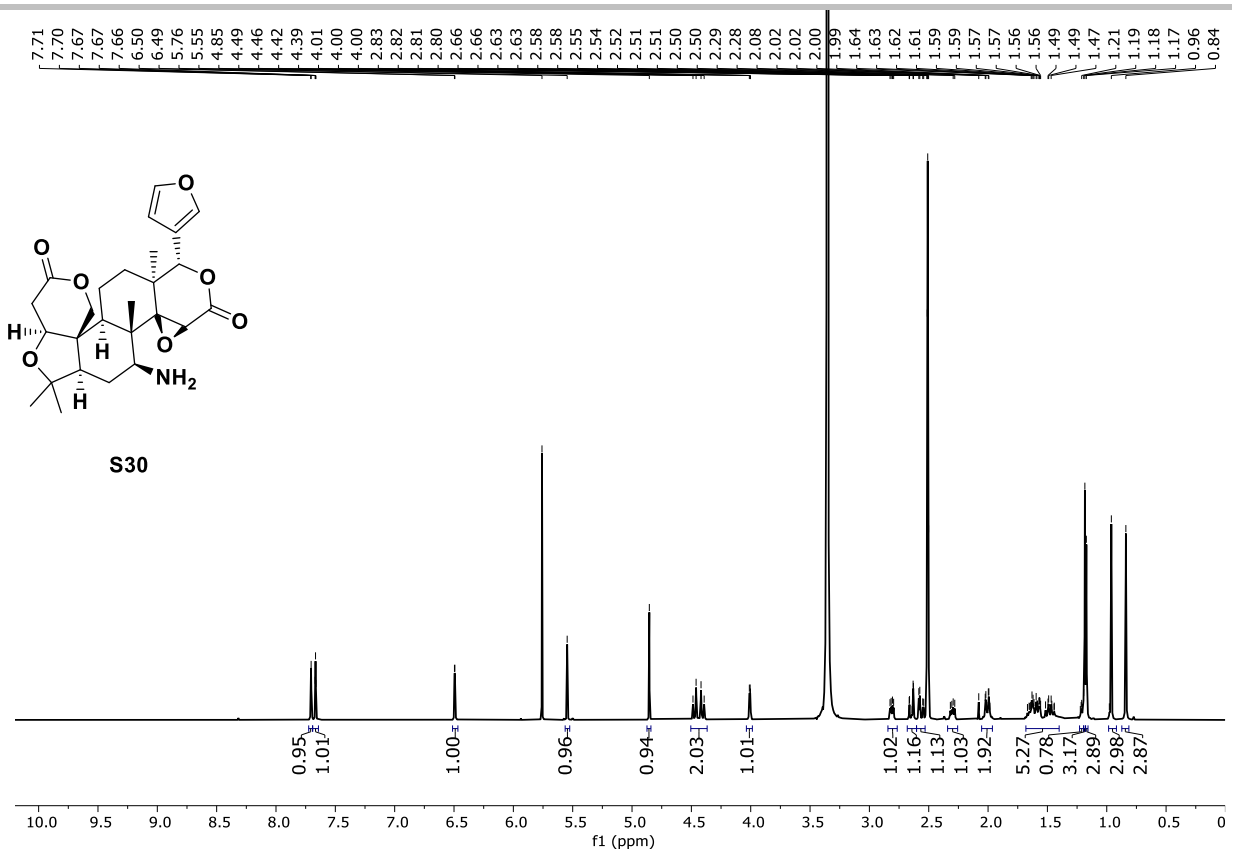
^{1}H NMR



^{13}C NMR

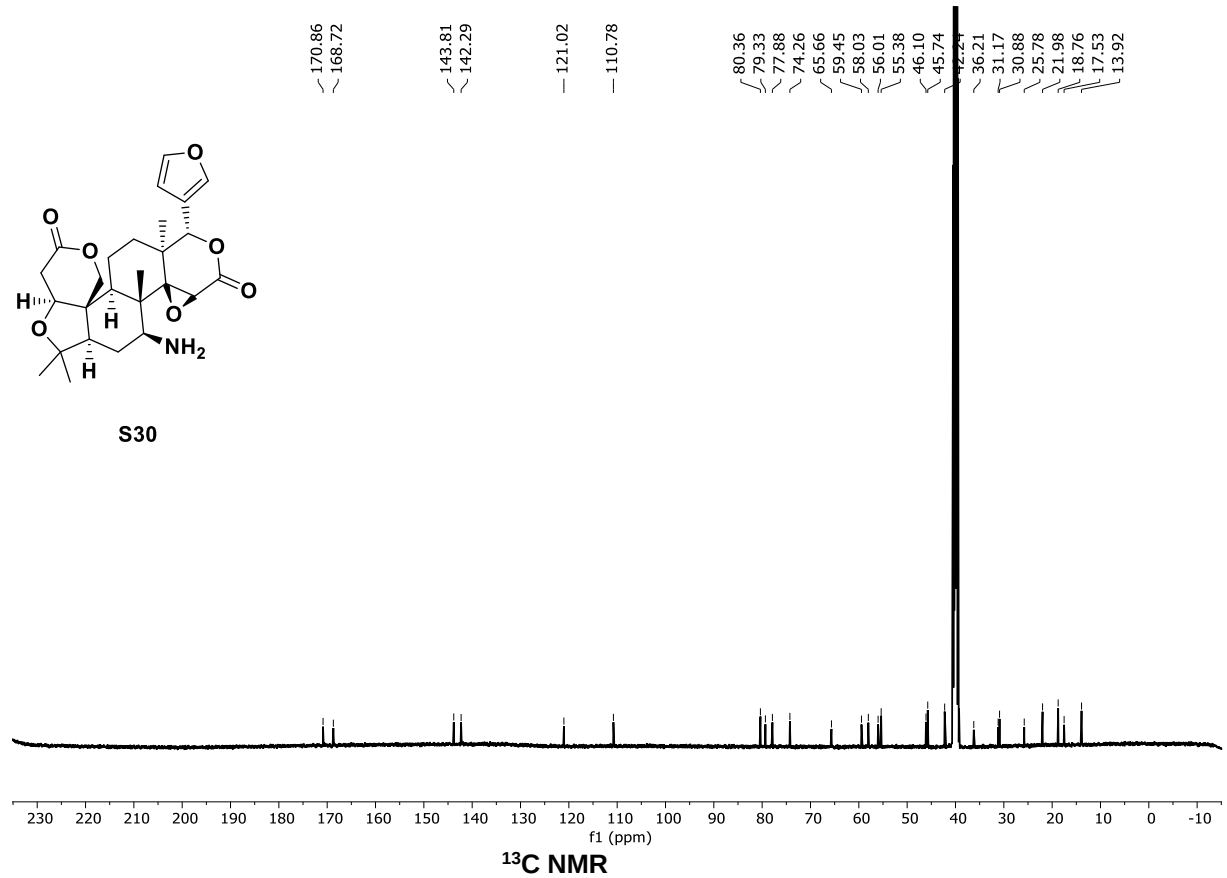


^{1}H-^{1}H COSY NMR



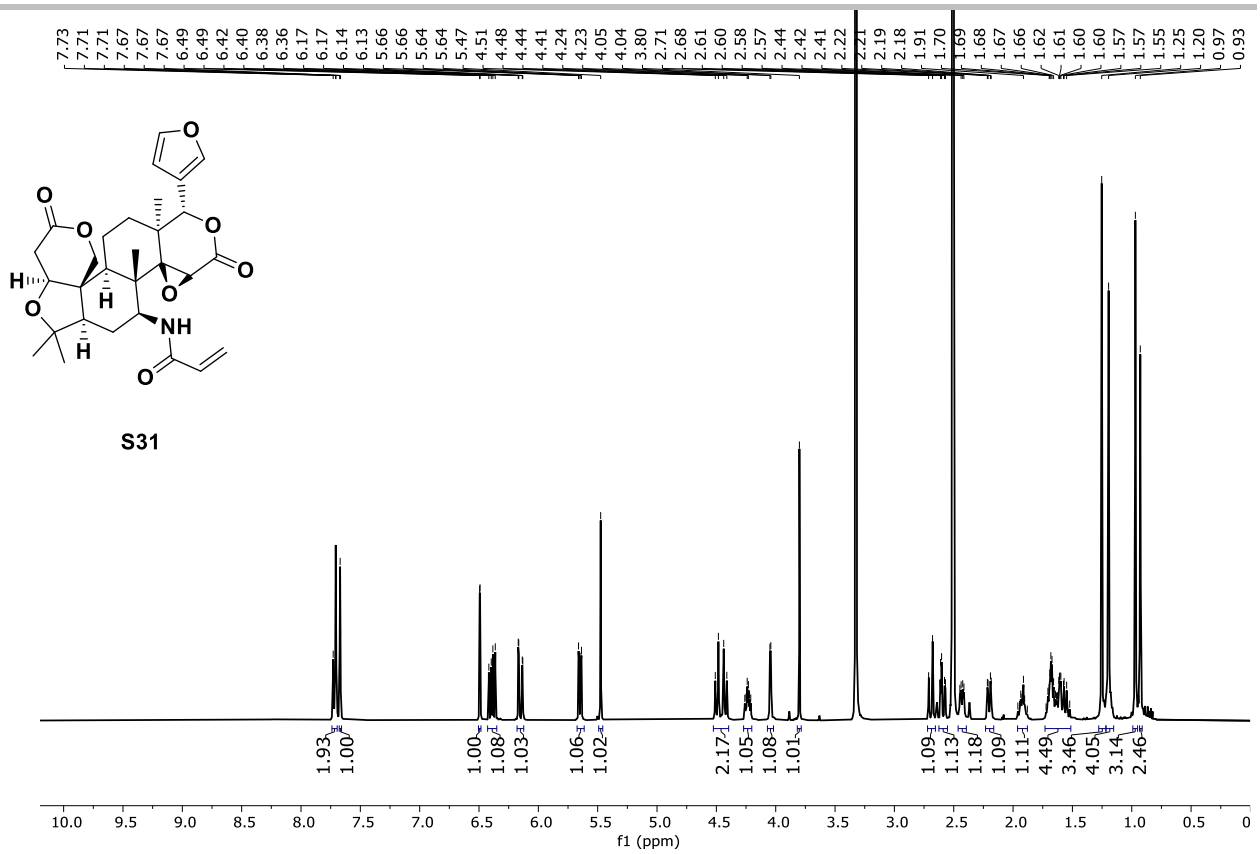
S30

^{1}H NMR



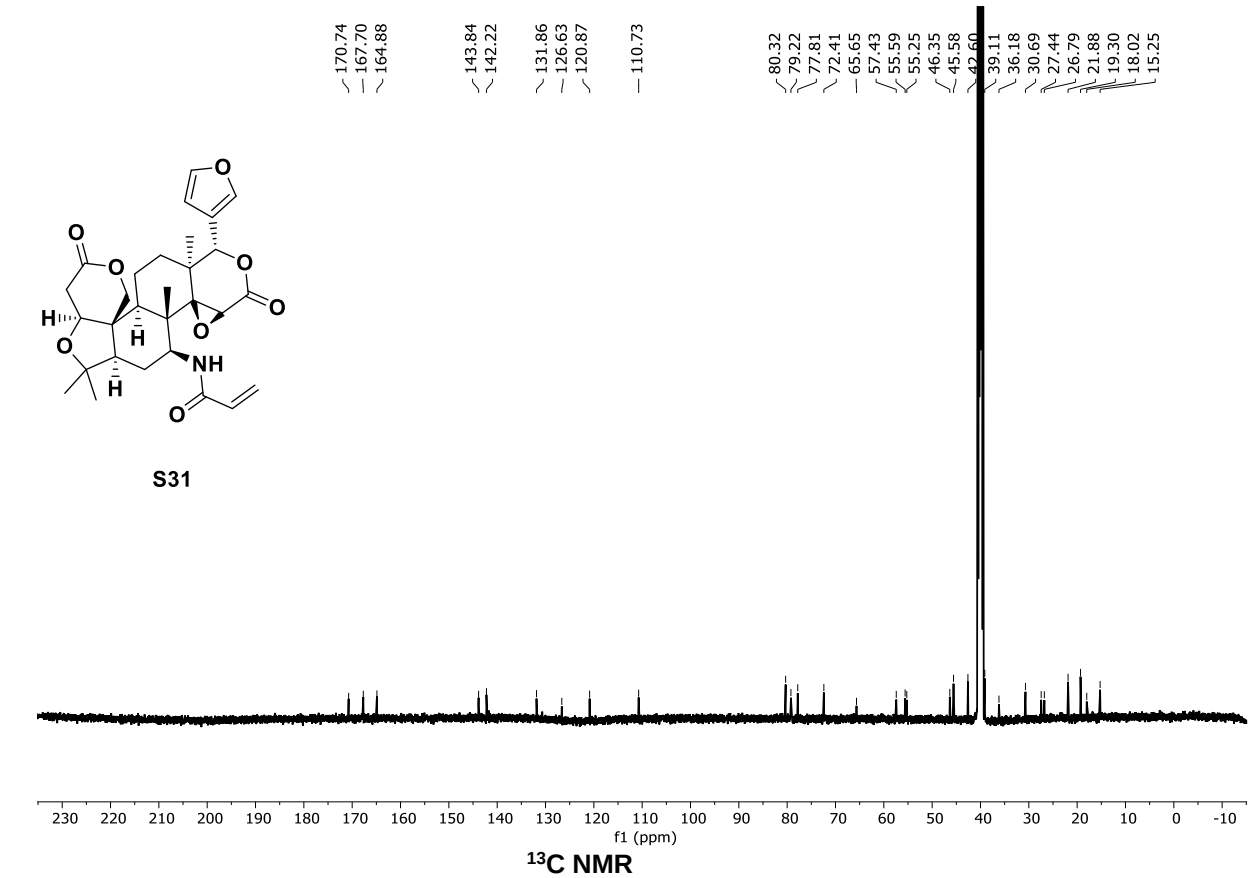
S30

^{13}C NMR



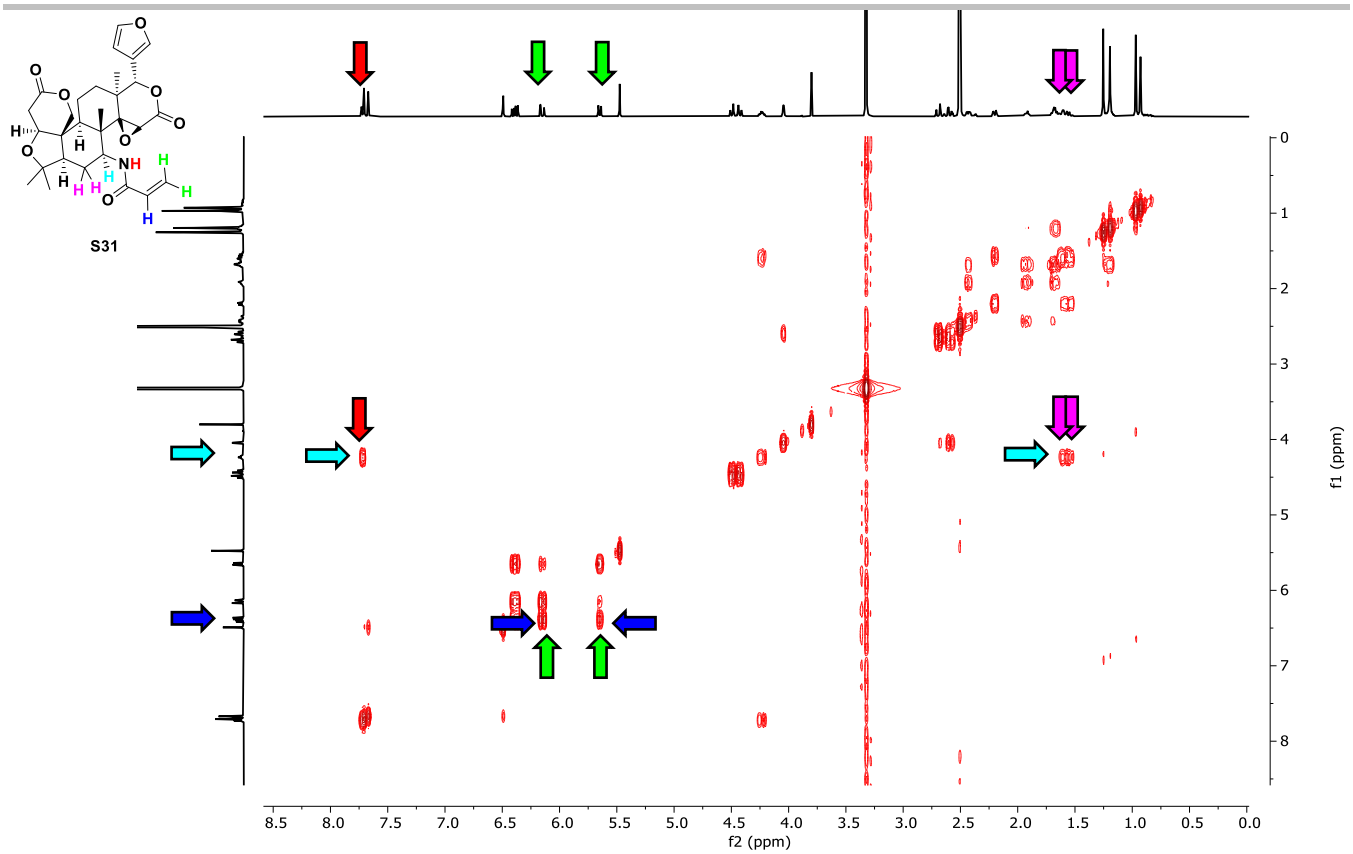
S31

^{1}H NMR

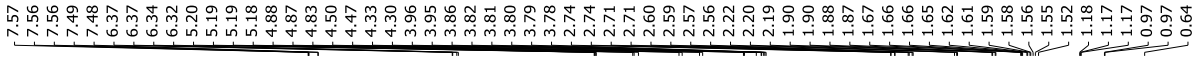


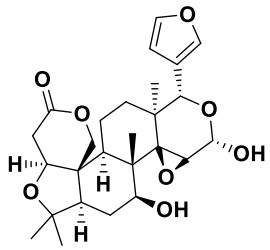
S31

^{13}C NMR

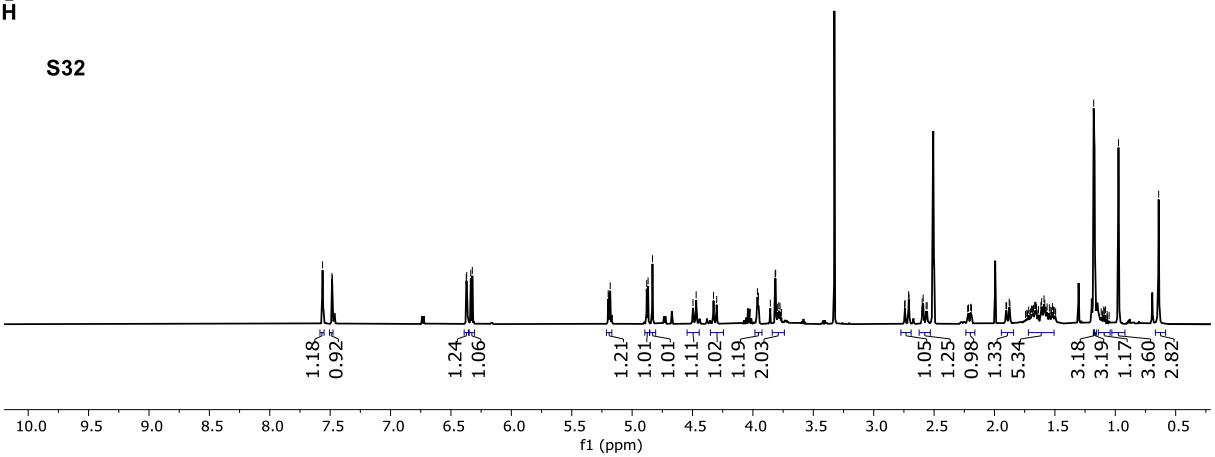


^{1}H-^{1}H COSY NMR

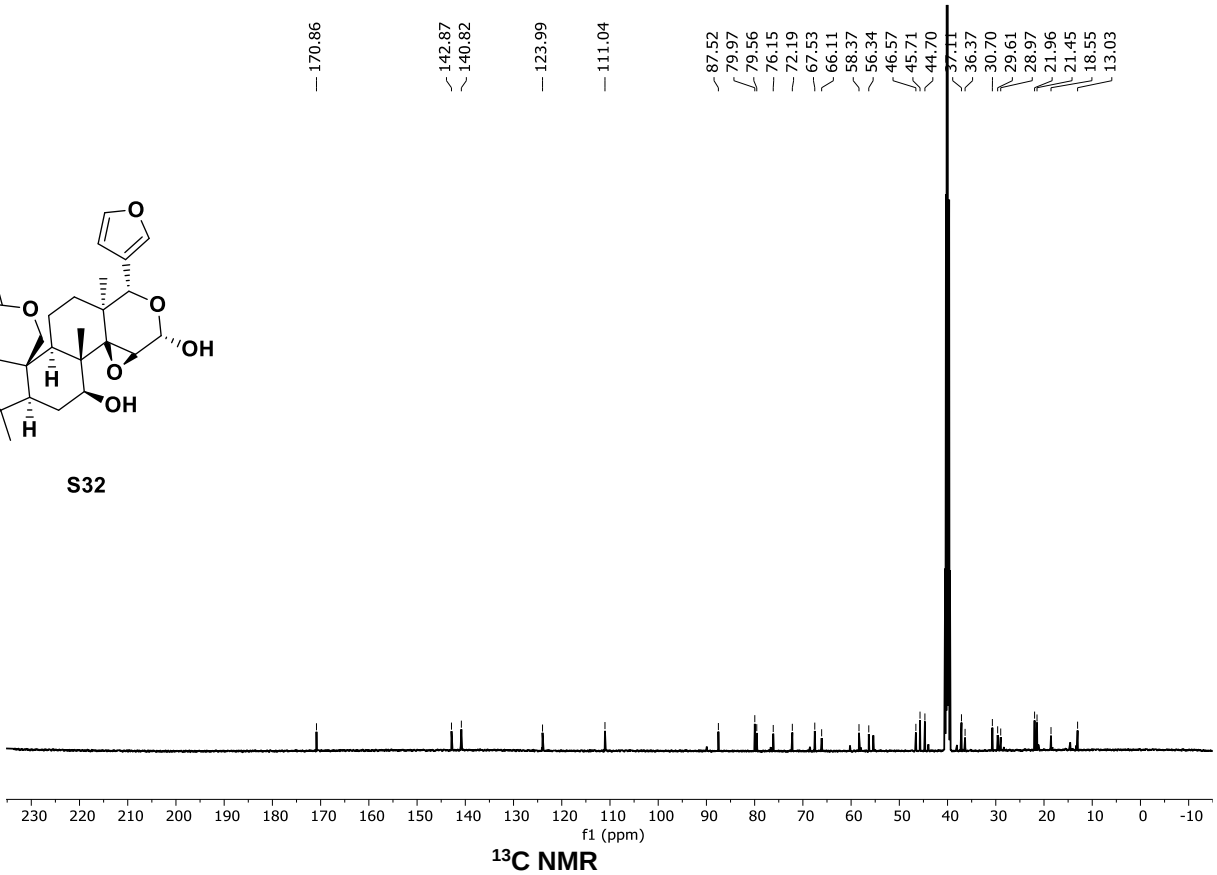




S32

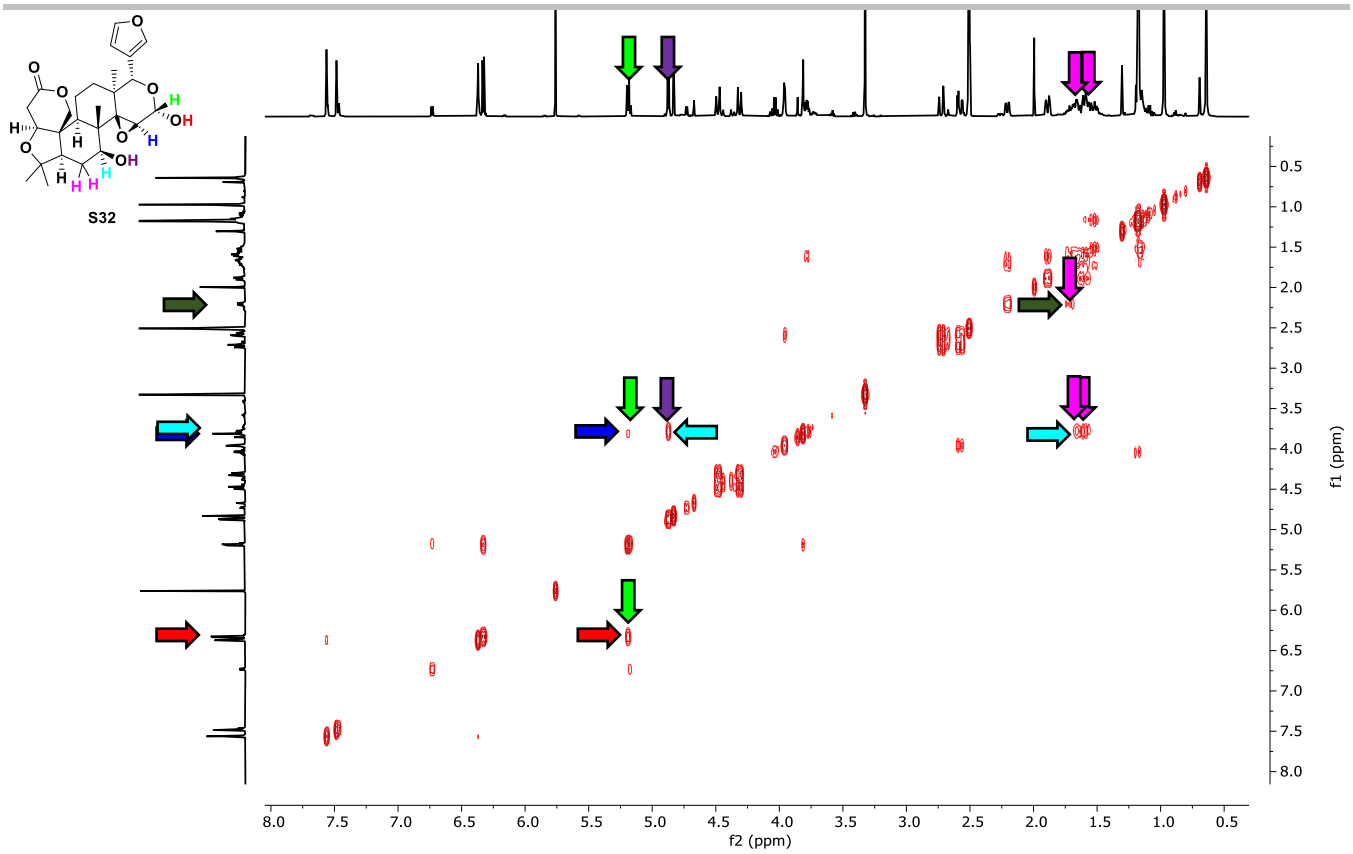


^{1}H NMR

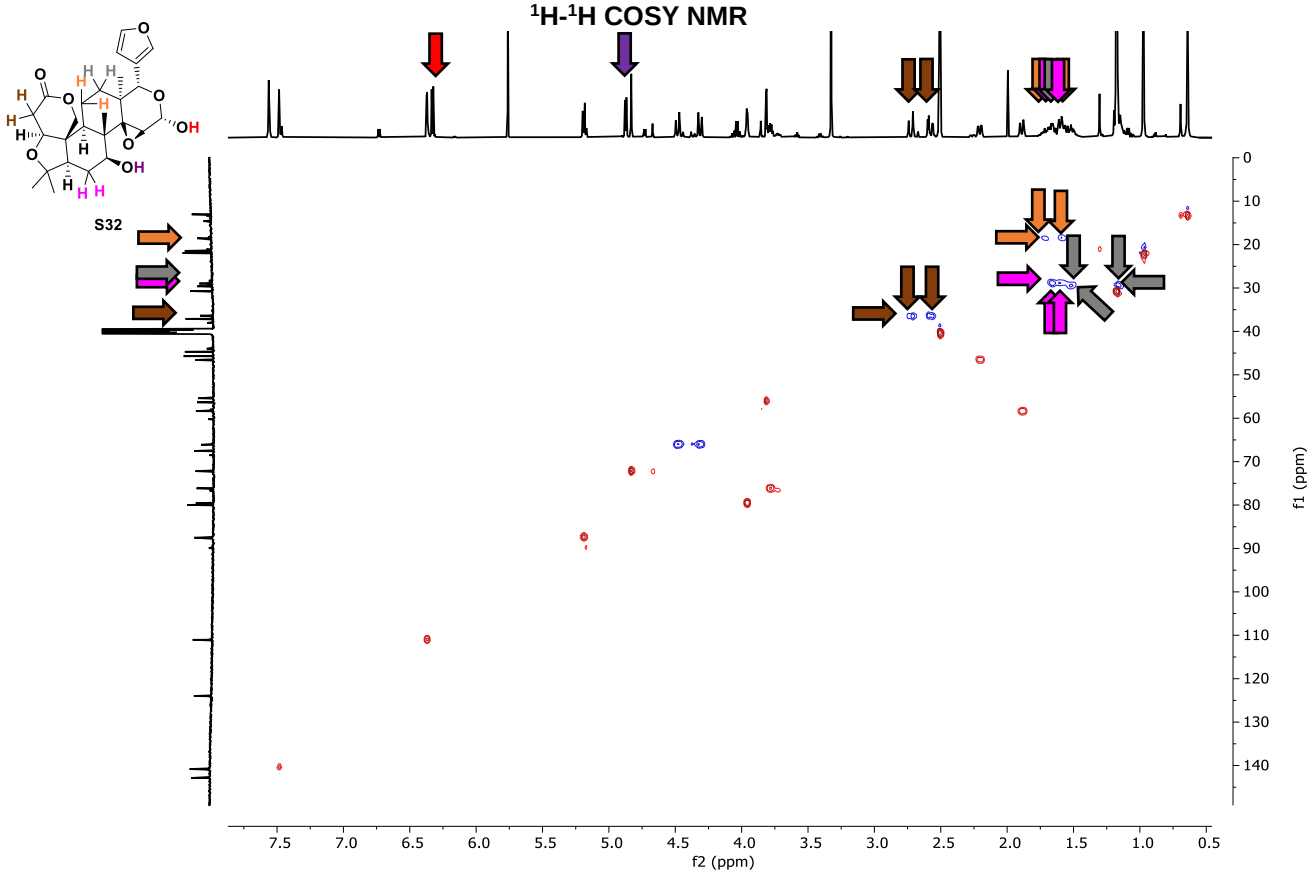


^{13}C NMR

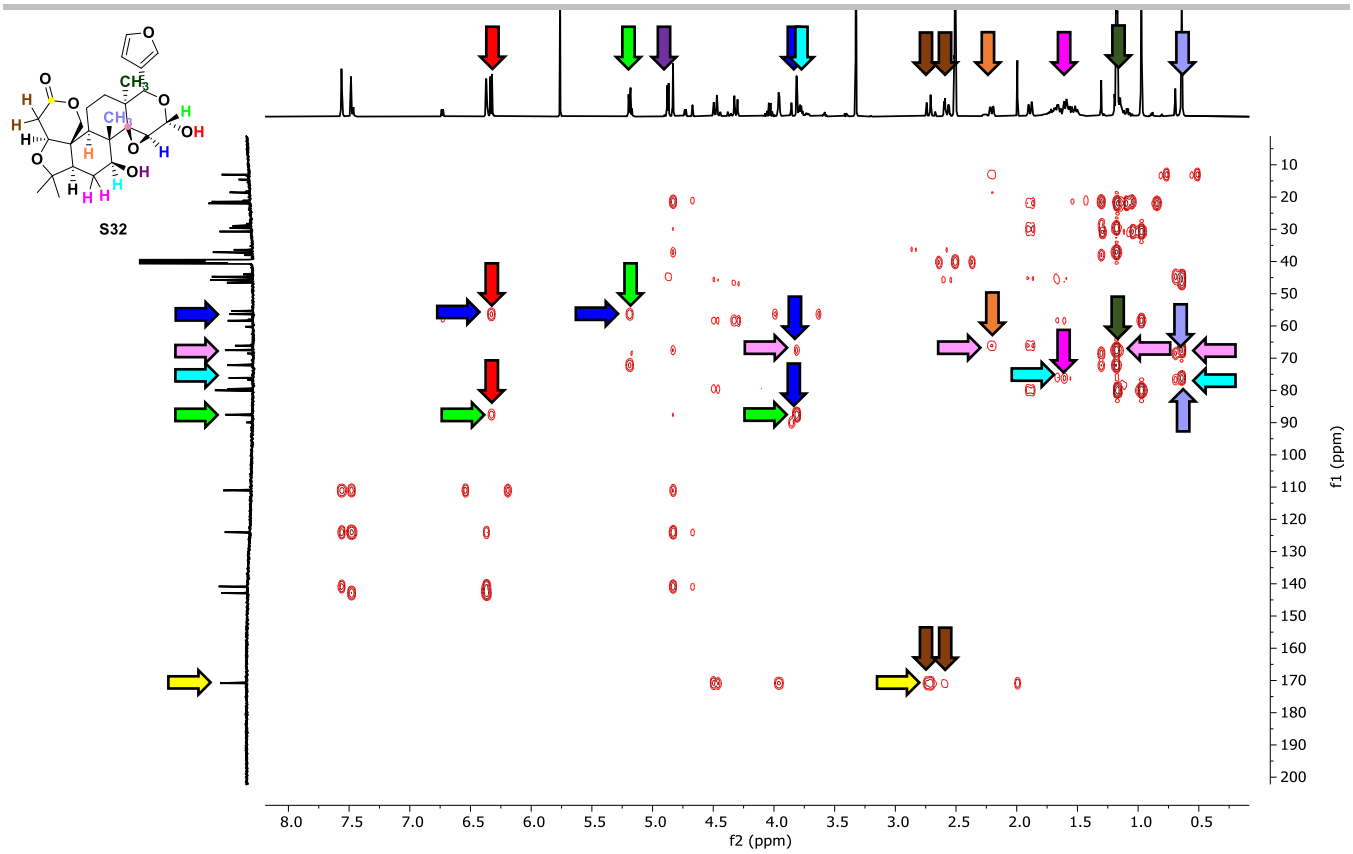
S32



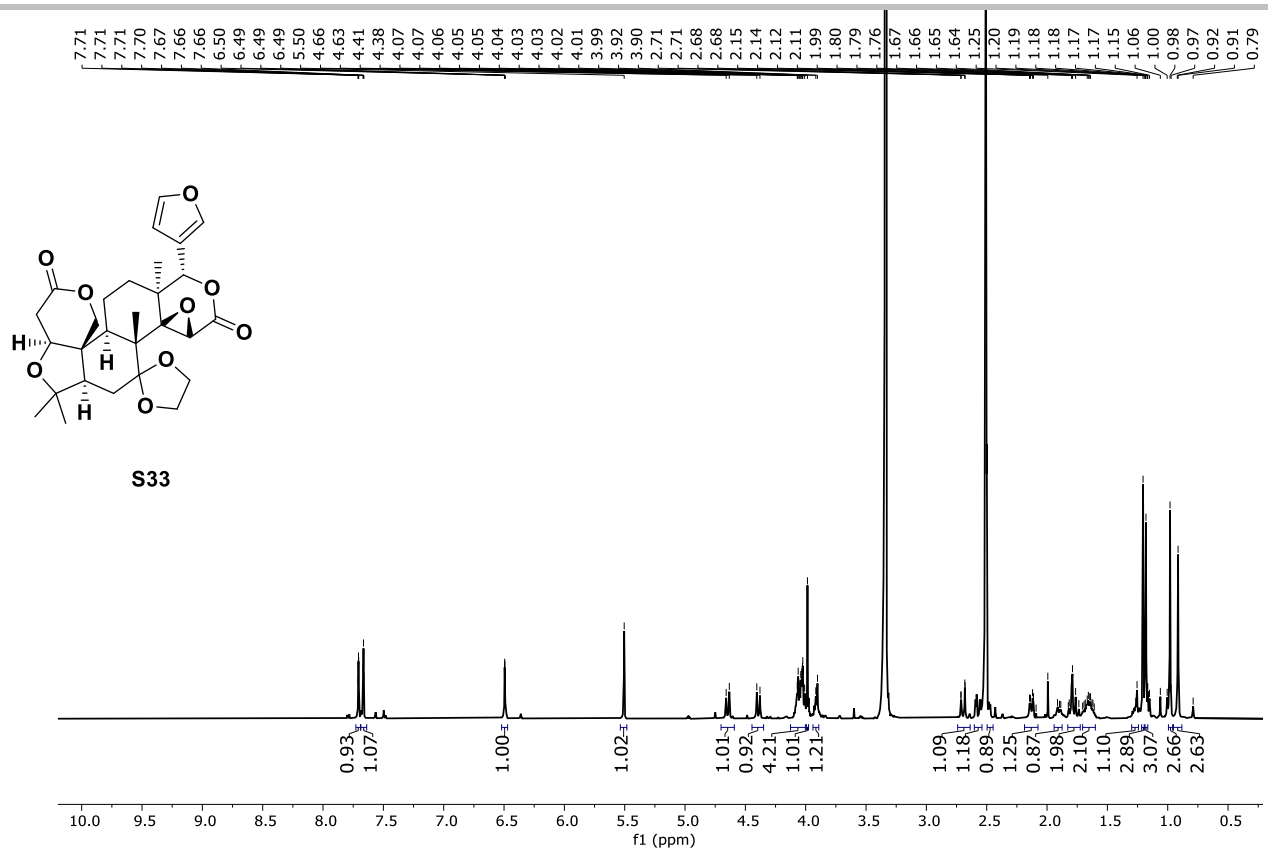
^{1}H-^{1}H COSY NMR



^{1}H-^{13}C HSQC NMR

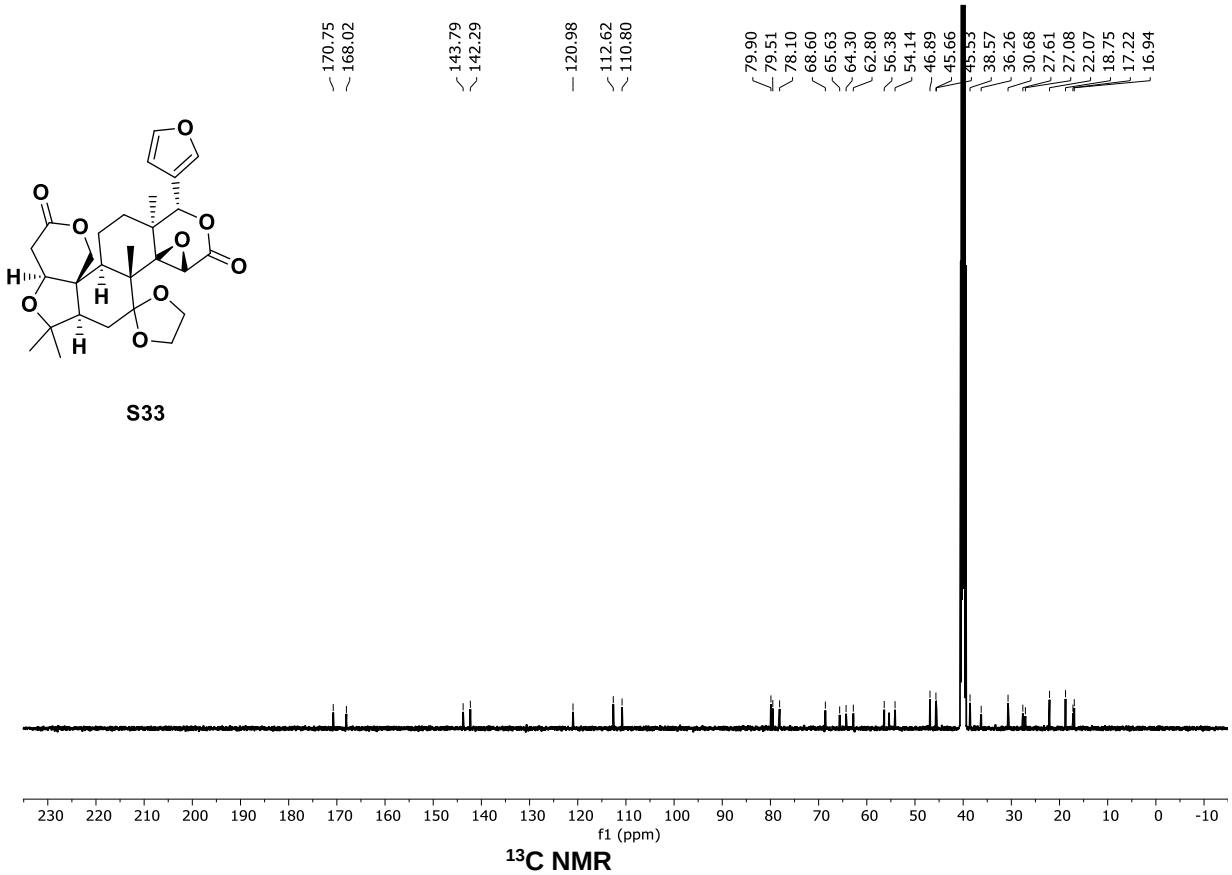


^{1}H-^{13}C HMBC NMR



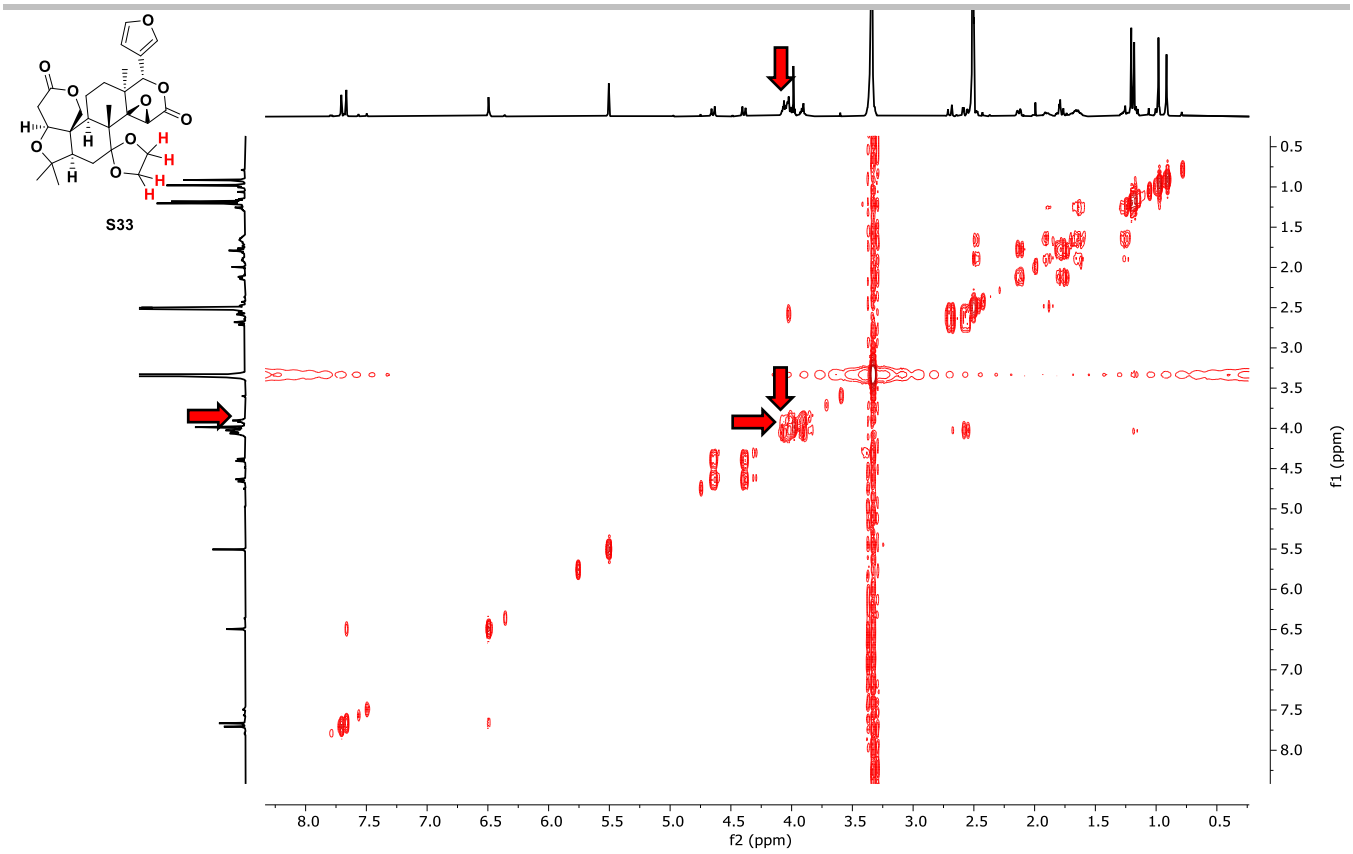
S33

^{1}H NMR

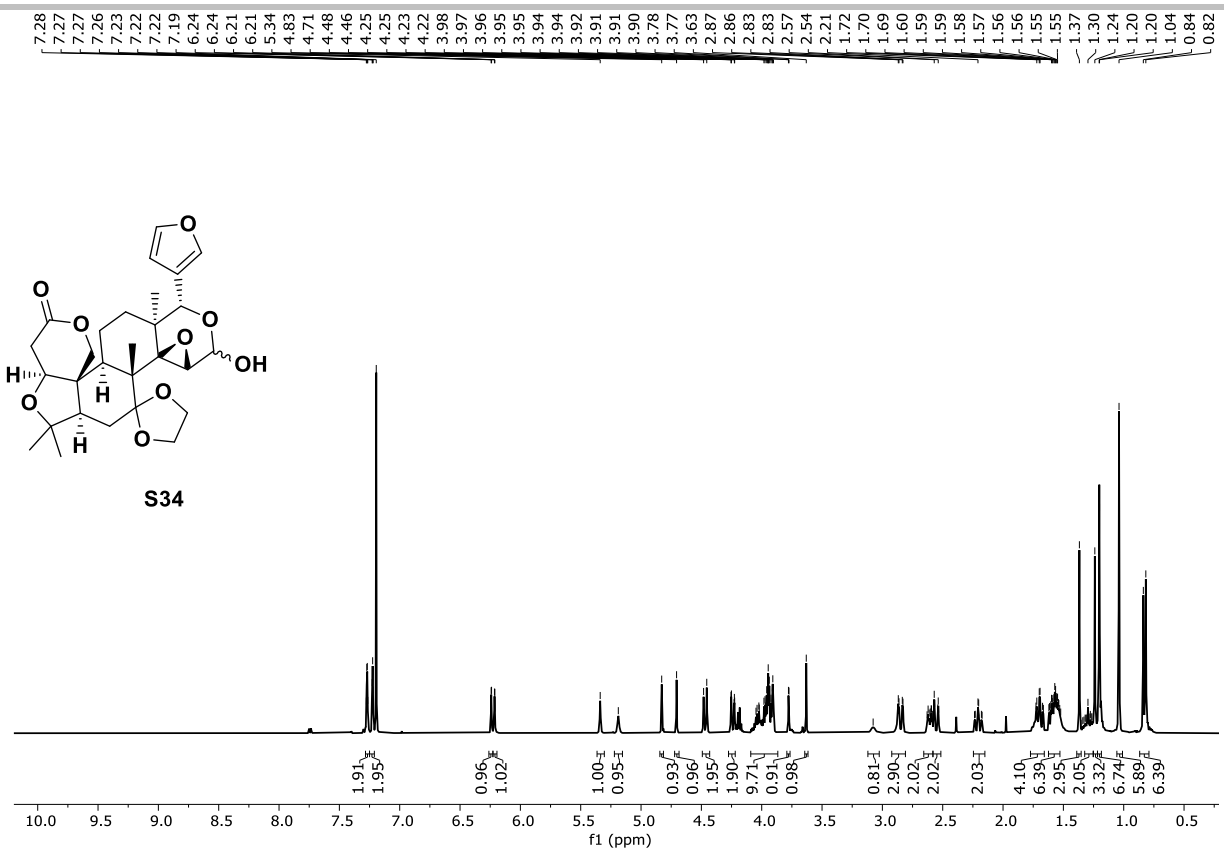


S33

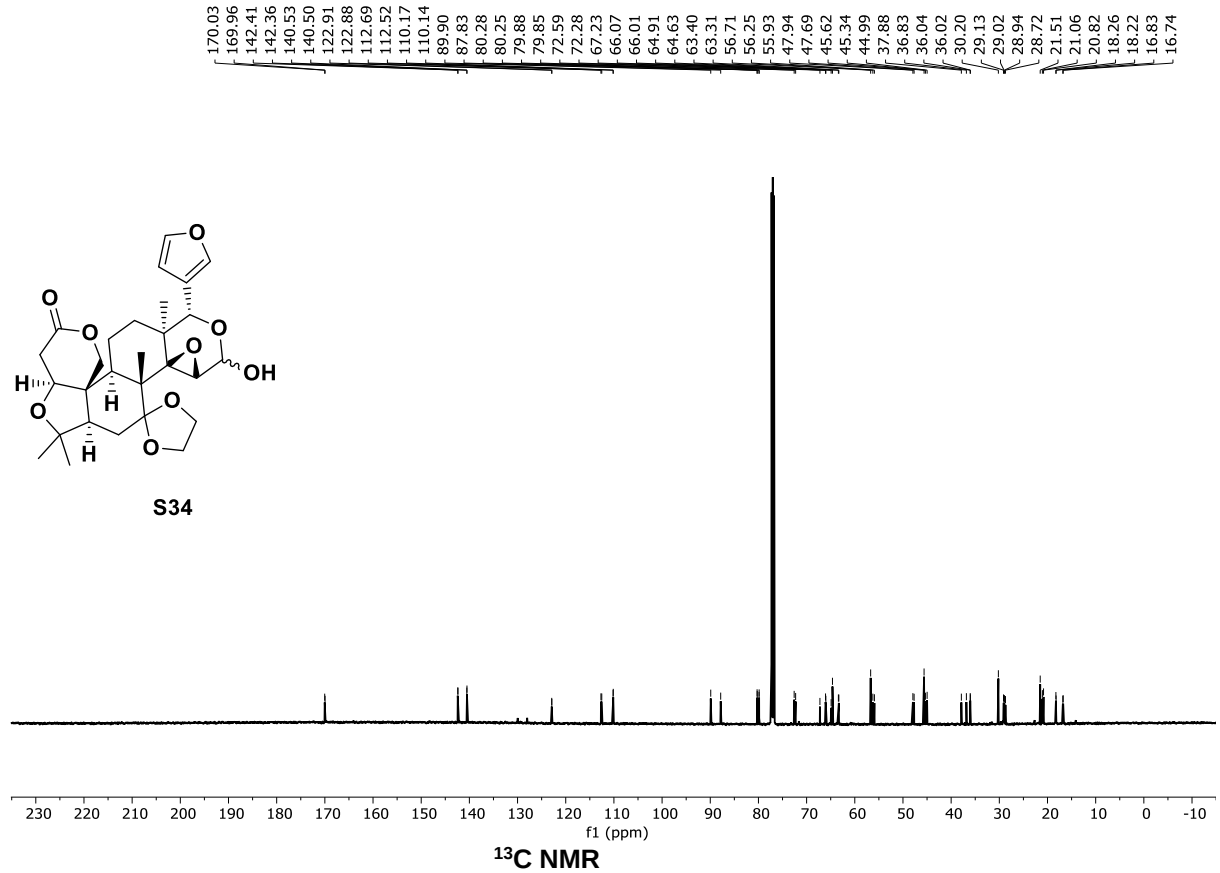
^{13}C NMR



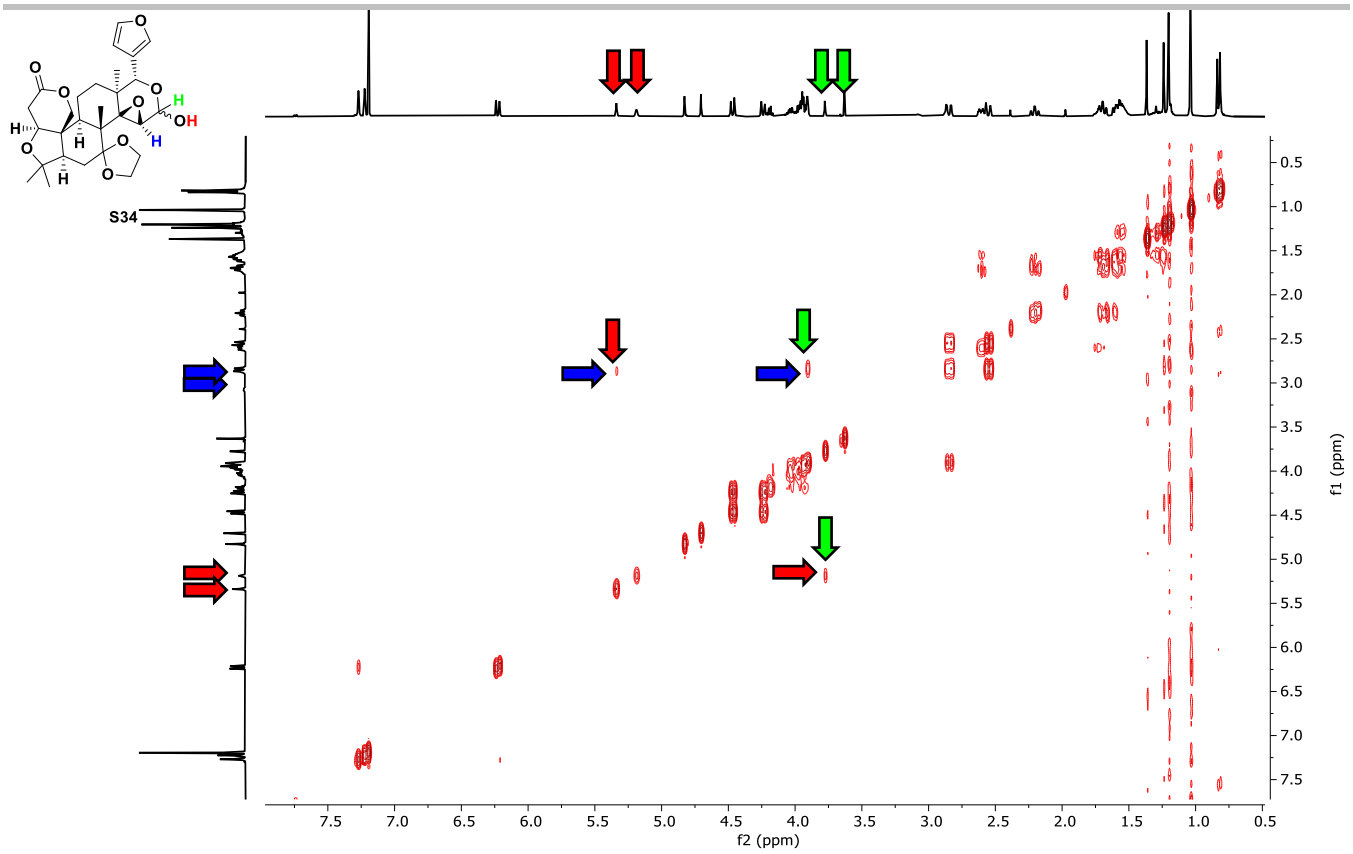
^{1}H-^{1}H COSY NMR



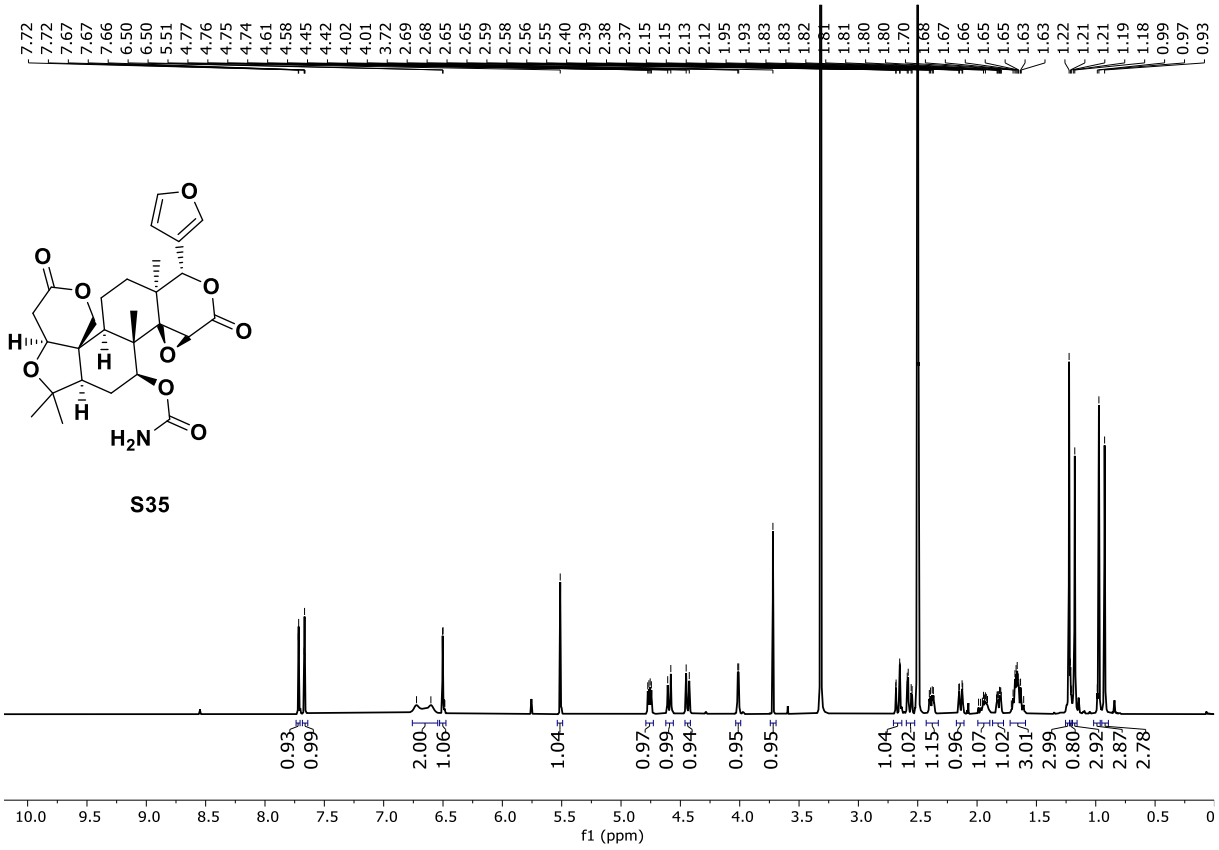
^{1}H NMR



^{13}C NMR

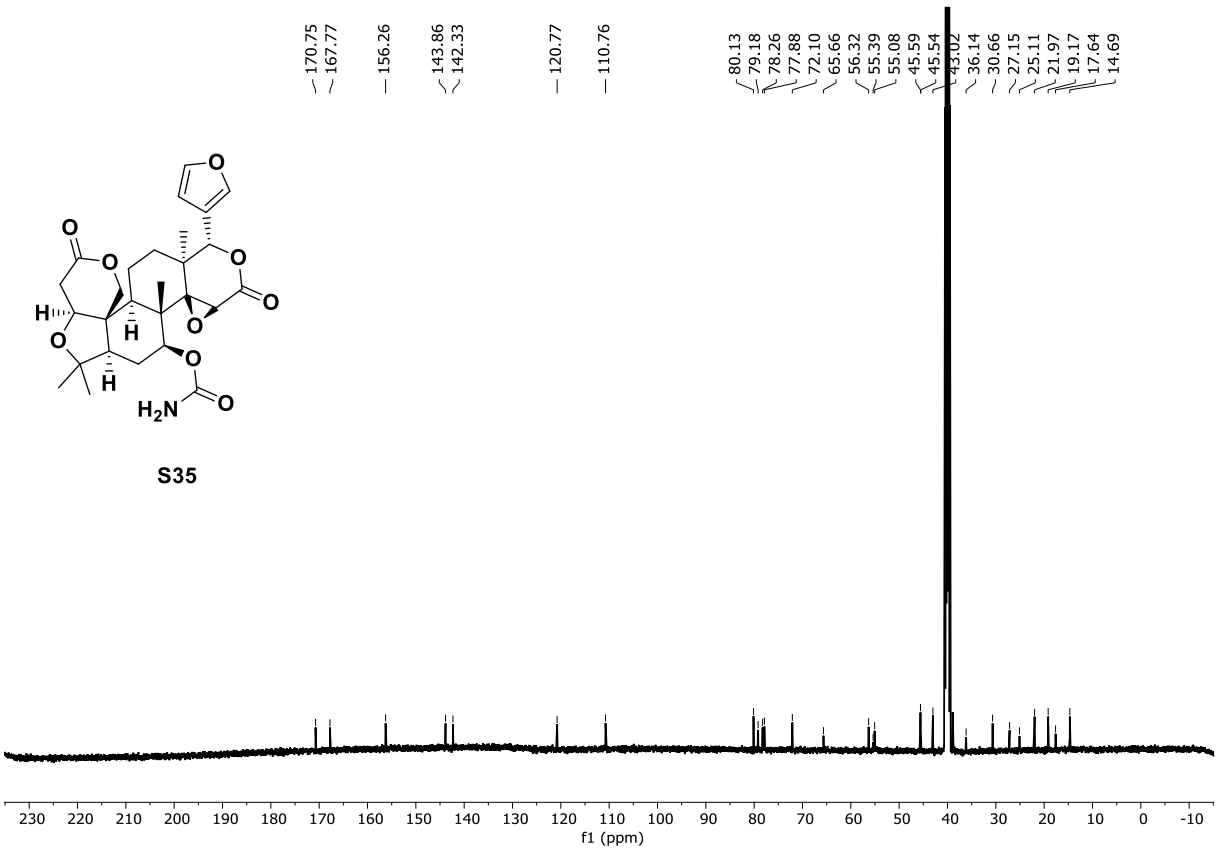


^{1}H-^{1}H COSY NMR



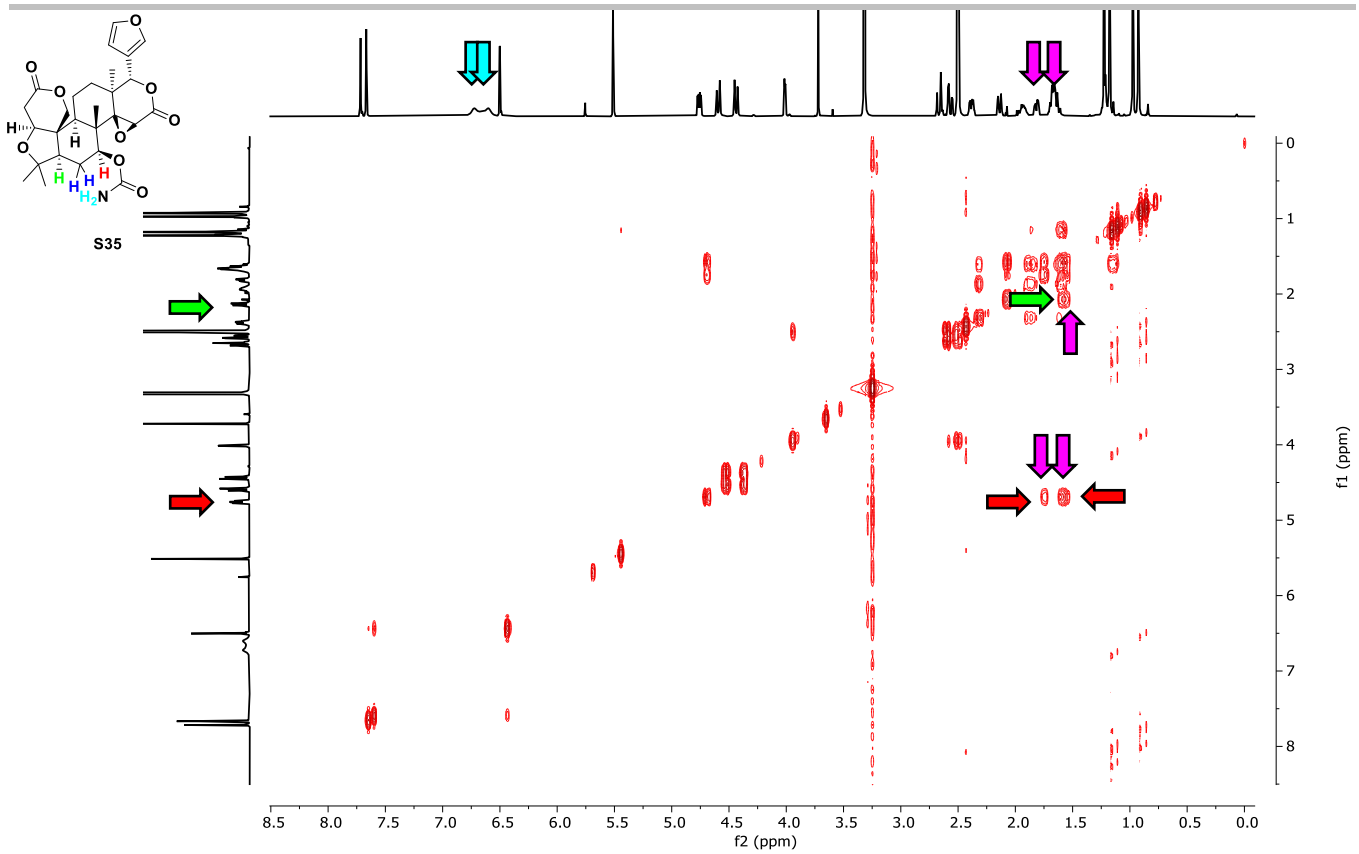
S35

^{1}H NMR

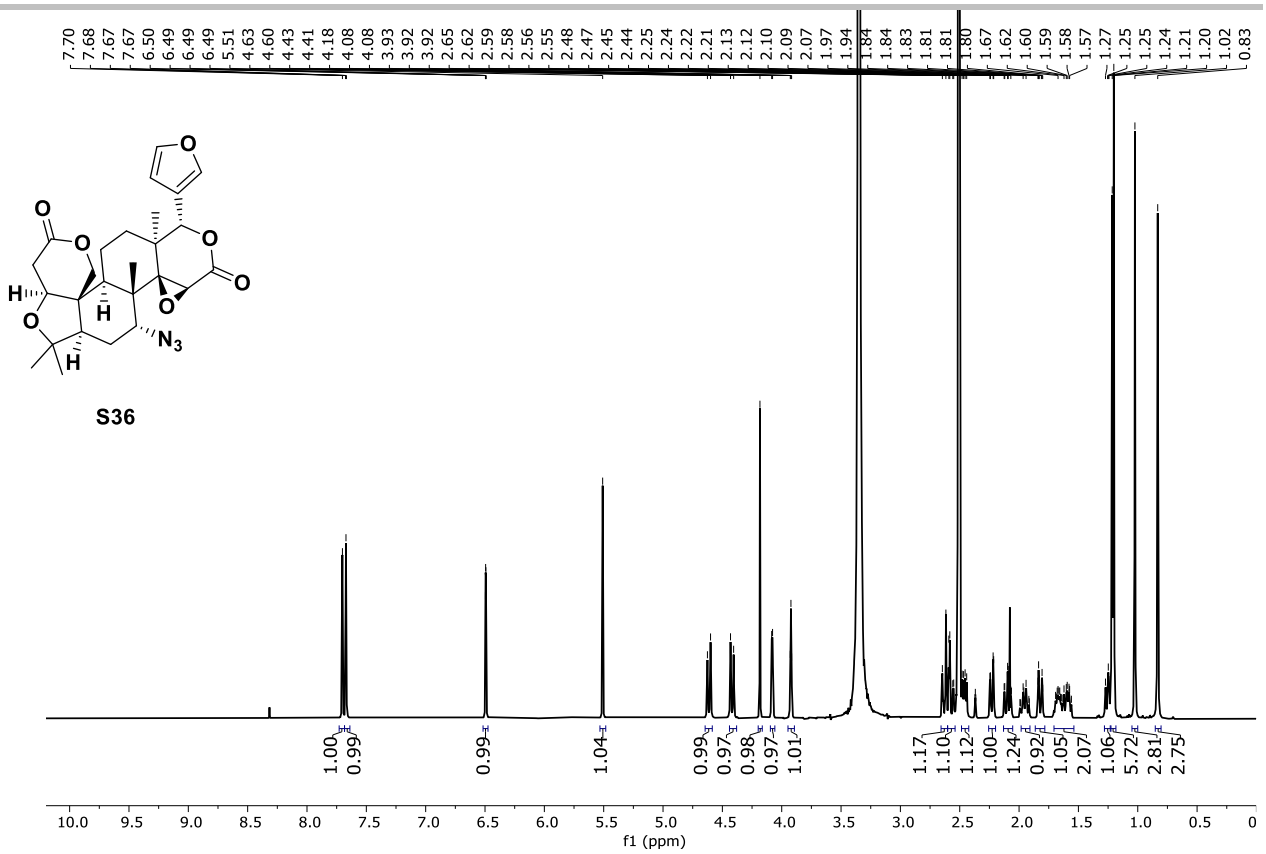


S35

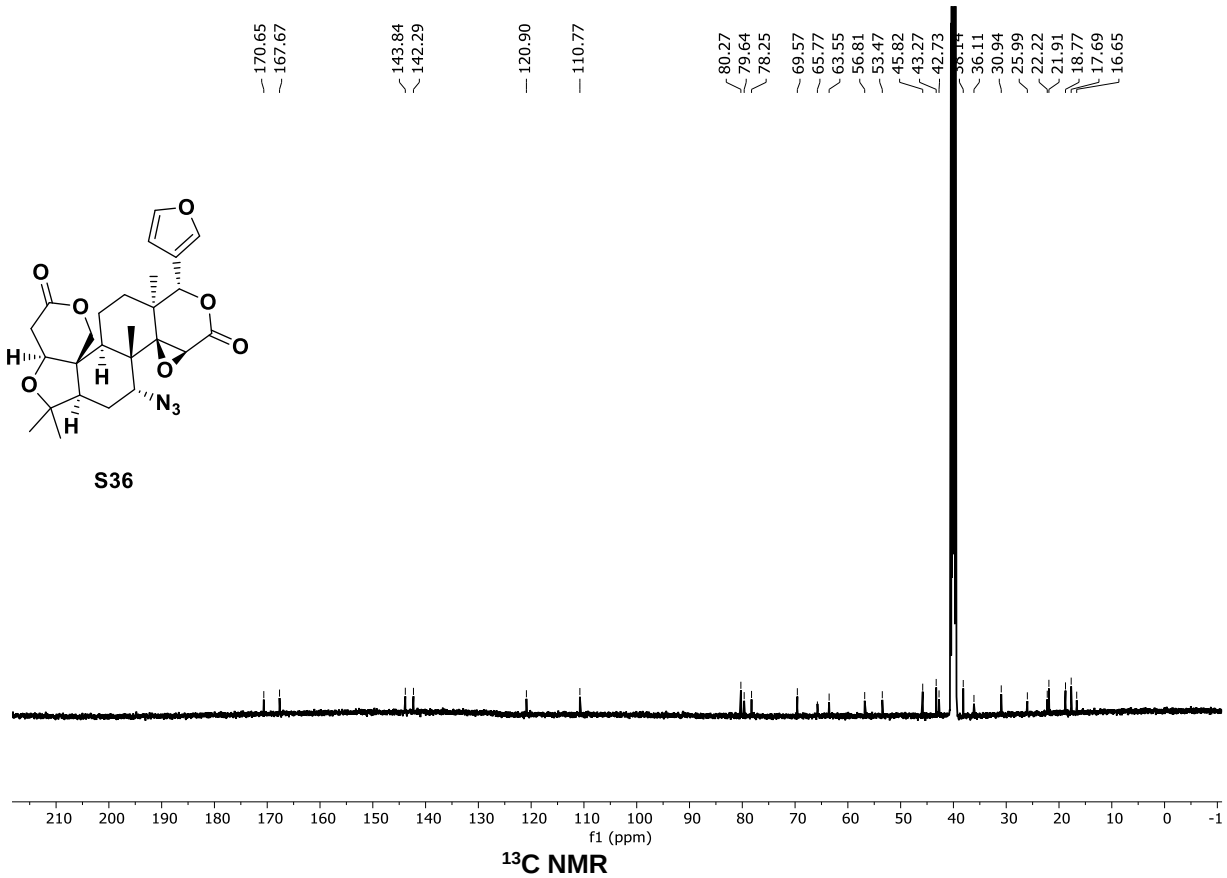
^{13}C NMR



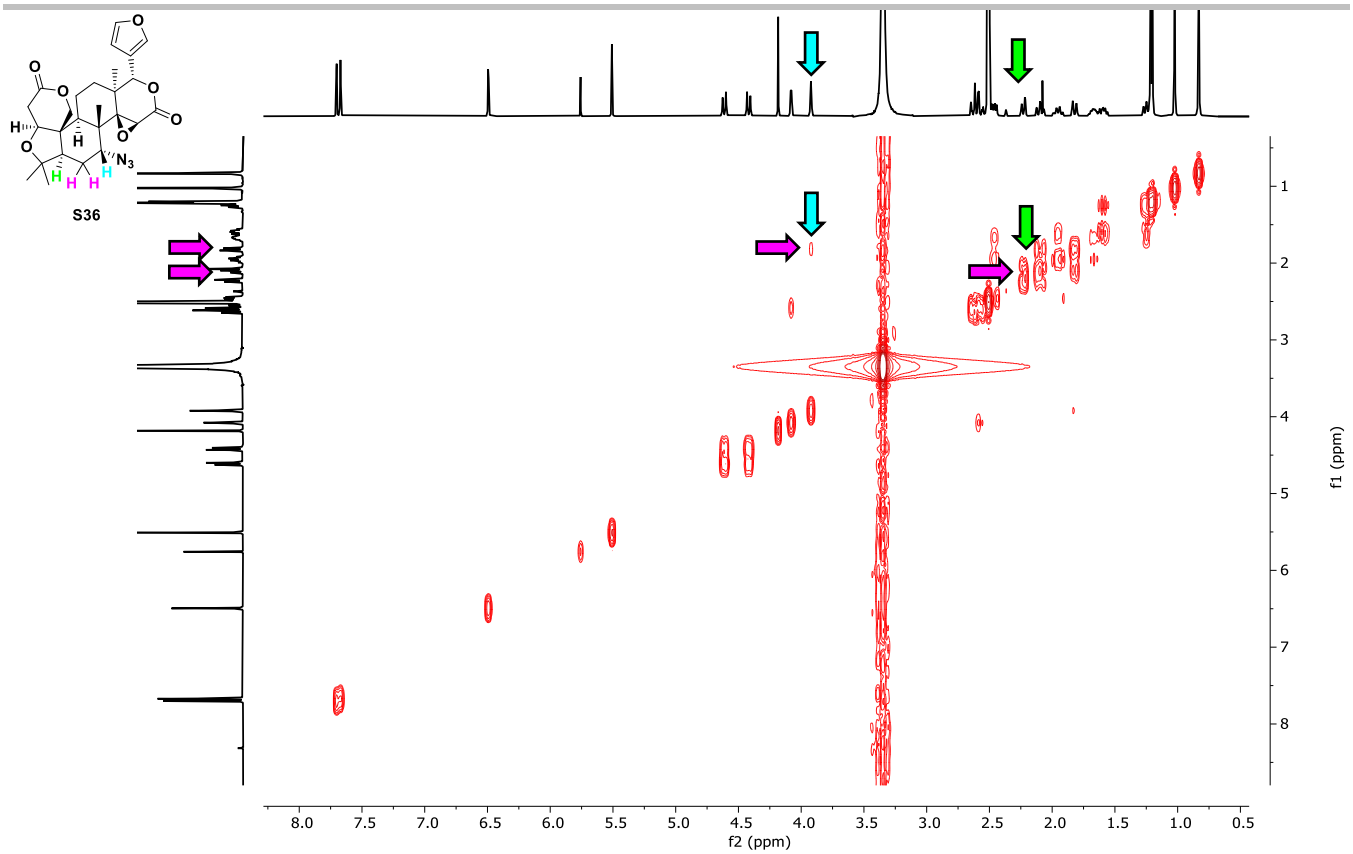
^{1}H-^{1}H COSY NMR



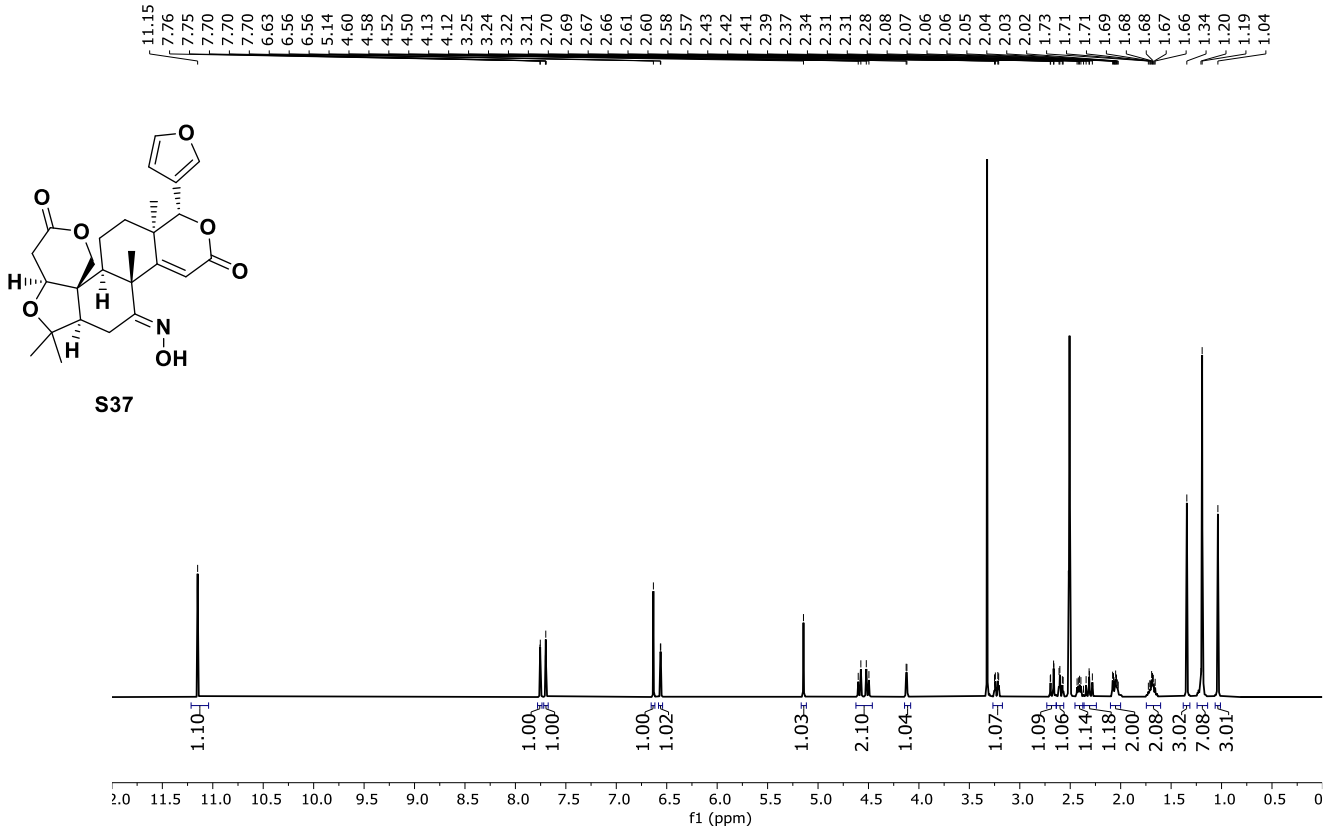
^{1}H NMR



^{13}C NMR

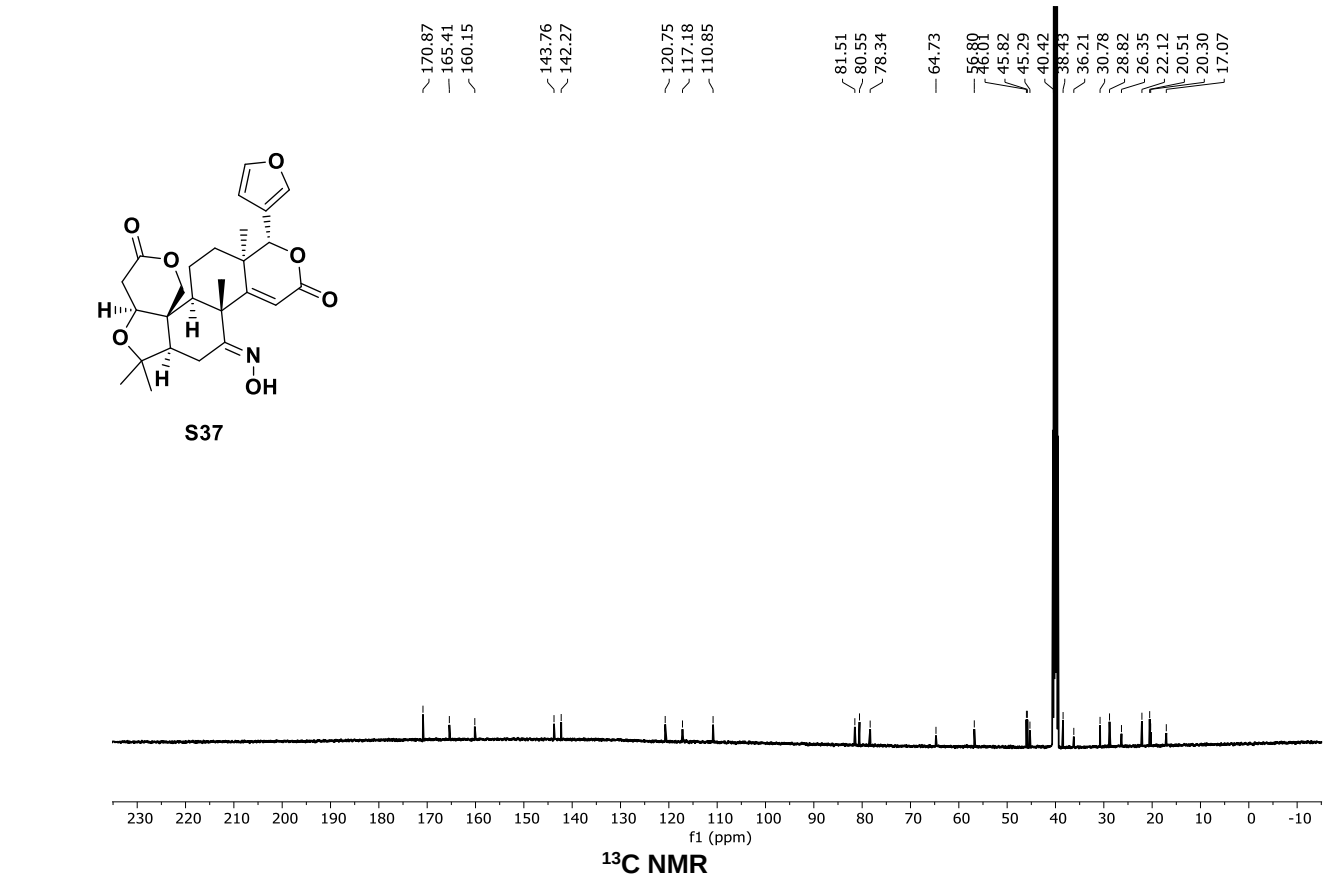


^{1}H-^{1}H COSY NMR



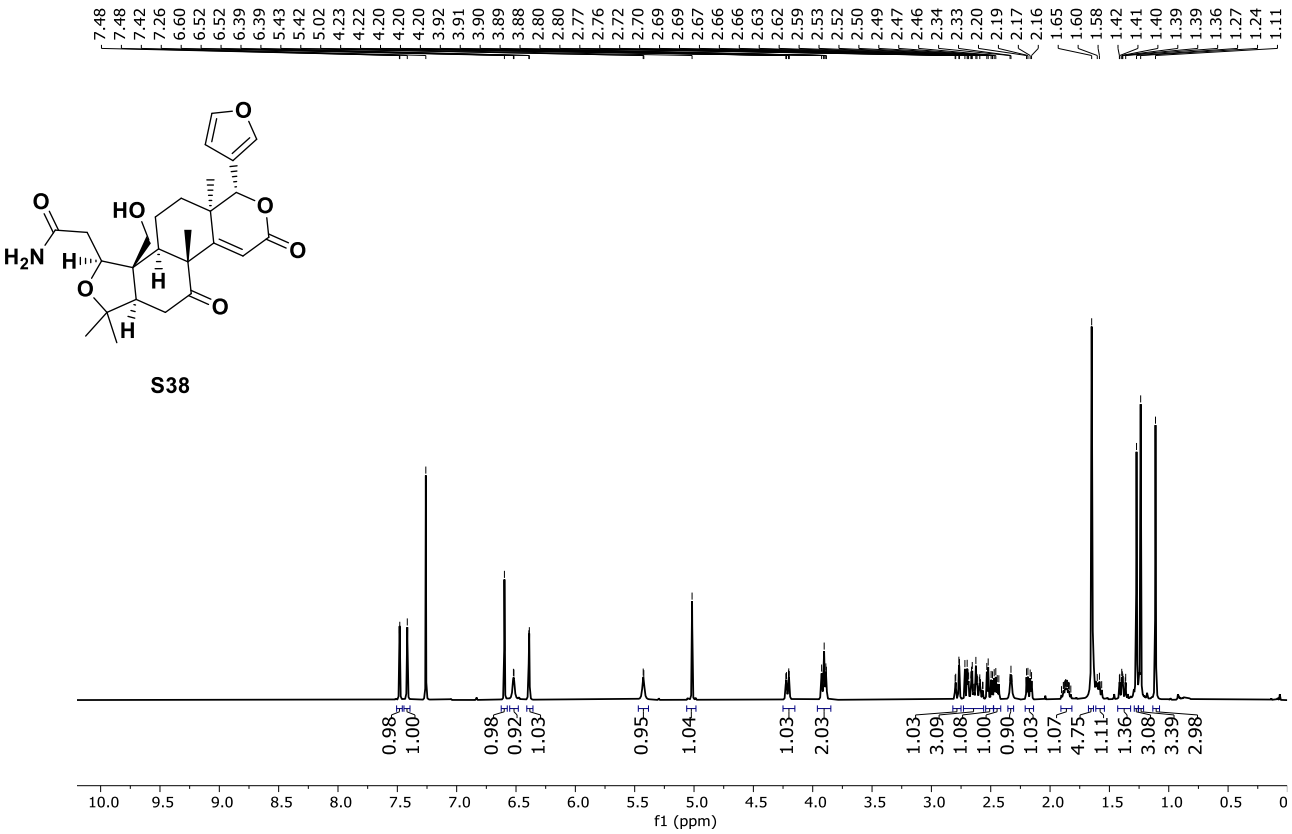
S37

^{1}H NMR

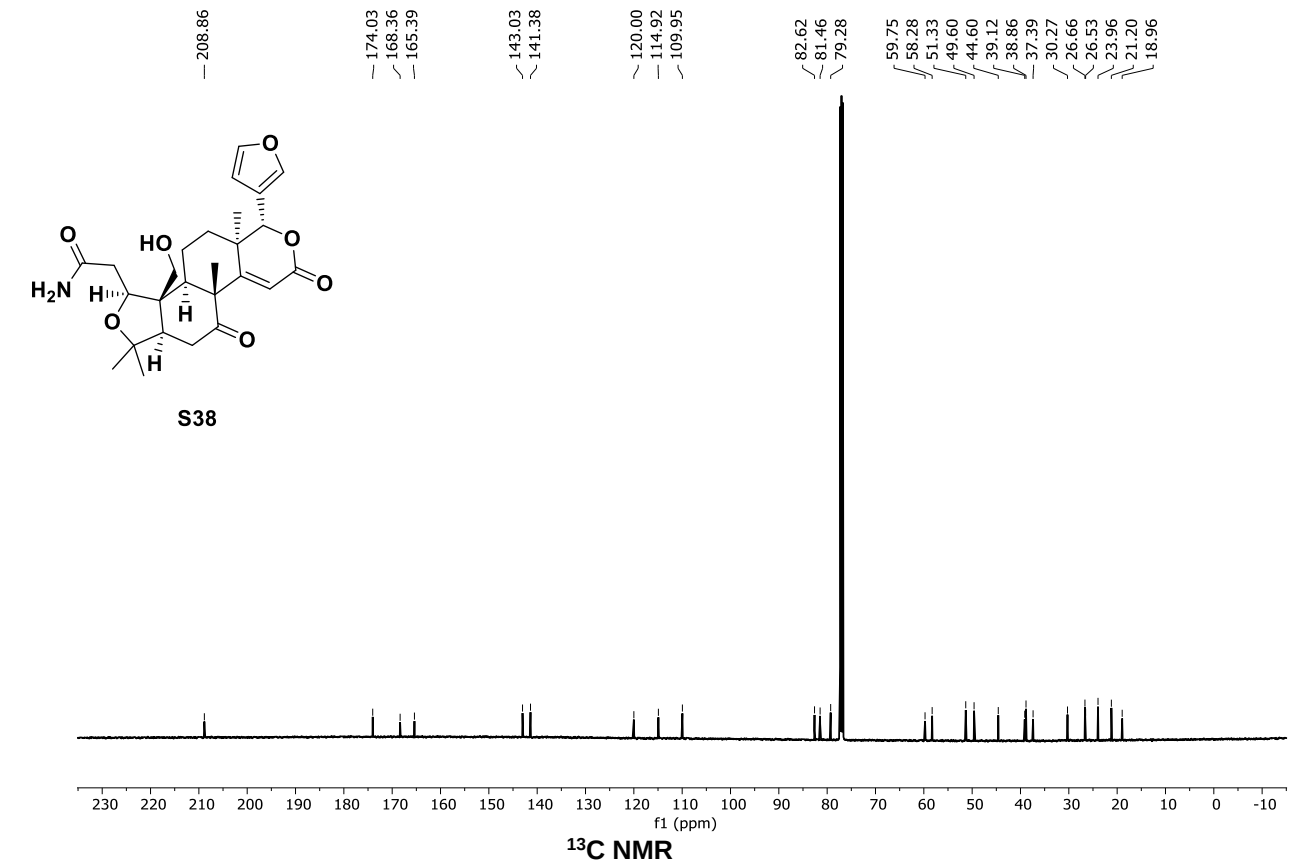


S37

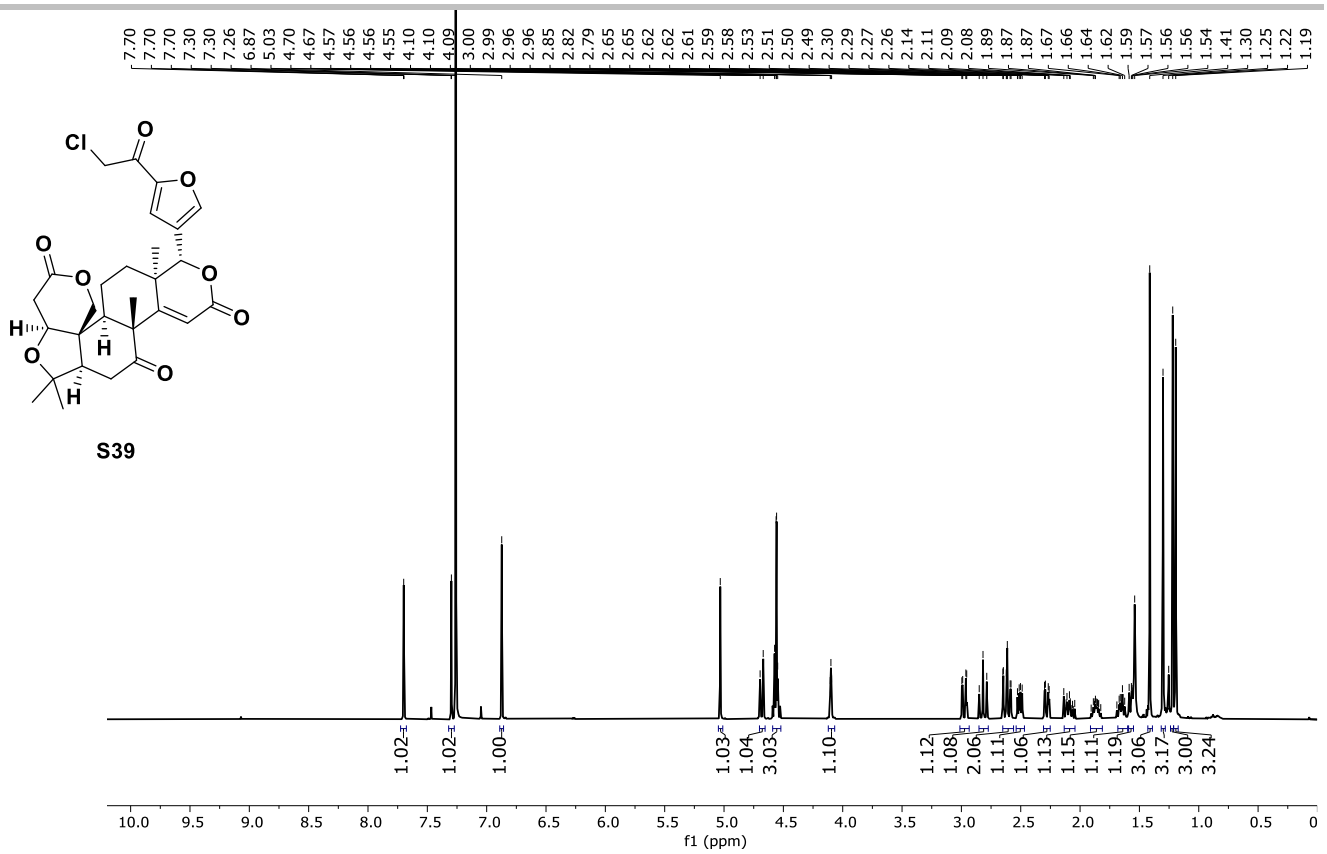
^{13}C NMR



^{1}H NMR

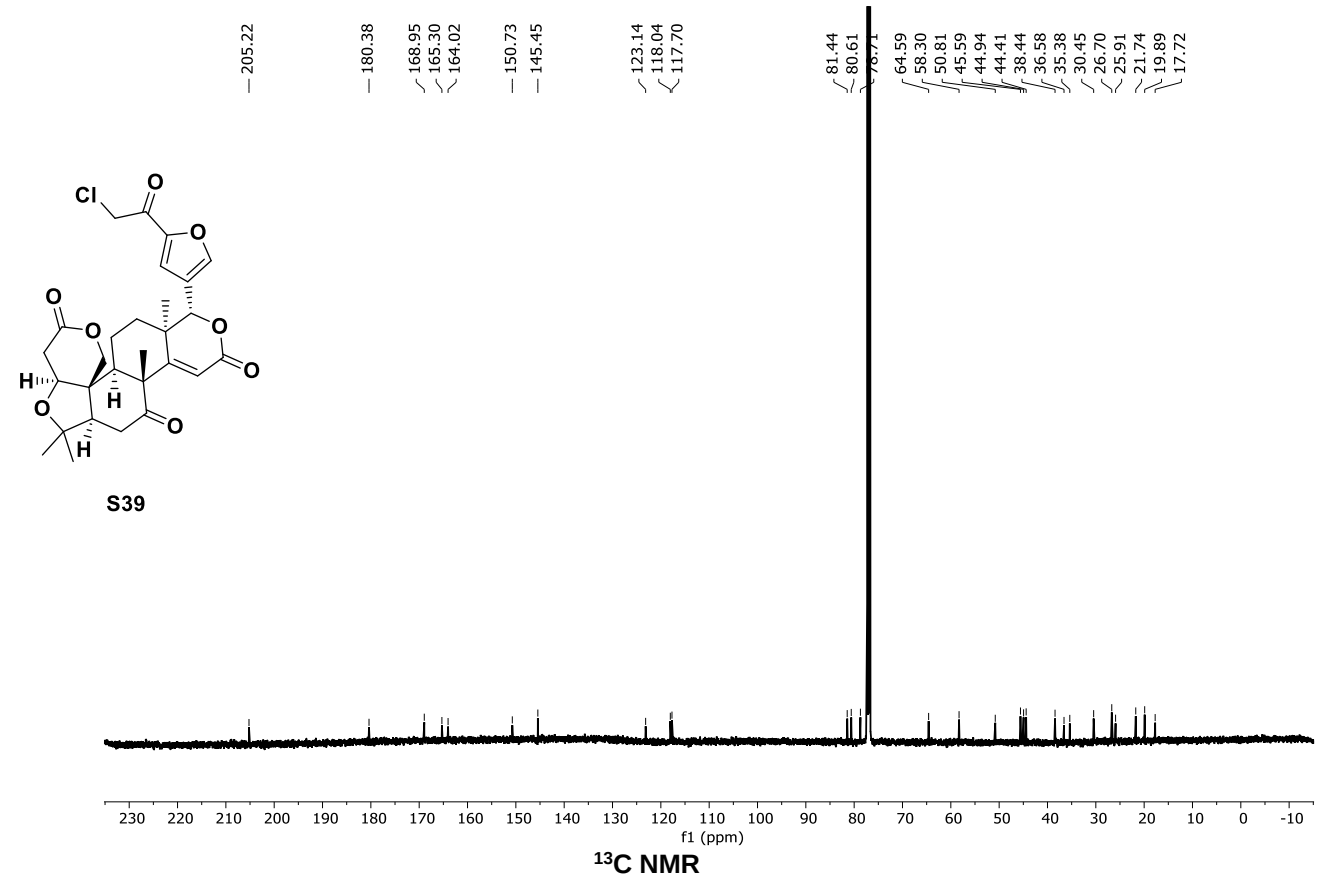


^{13}C NMR



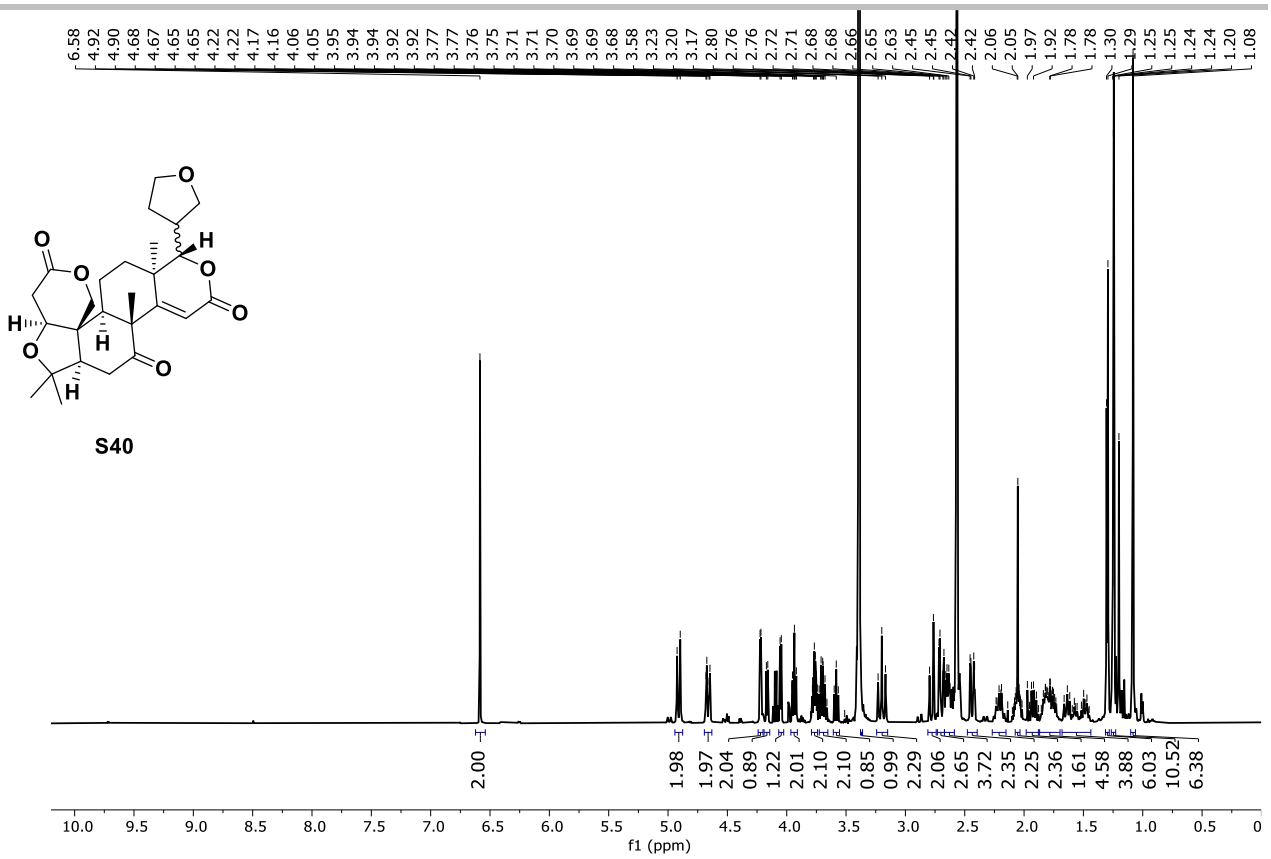
S39

^{1}H NMR



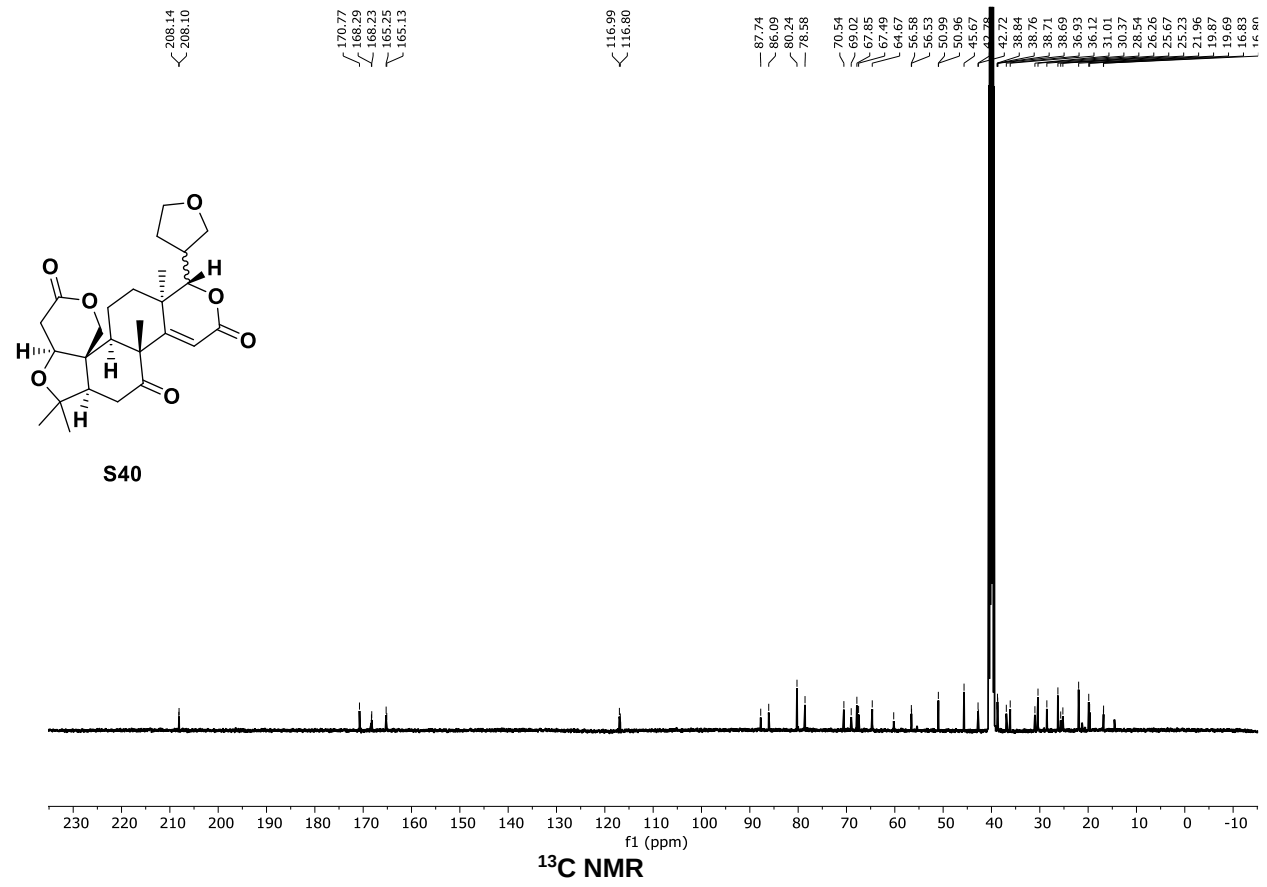
S39

^{13}C NMR



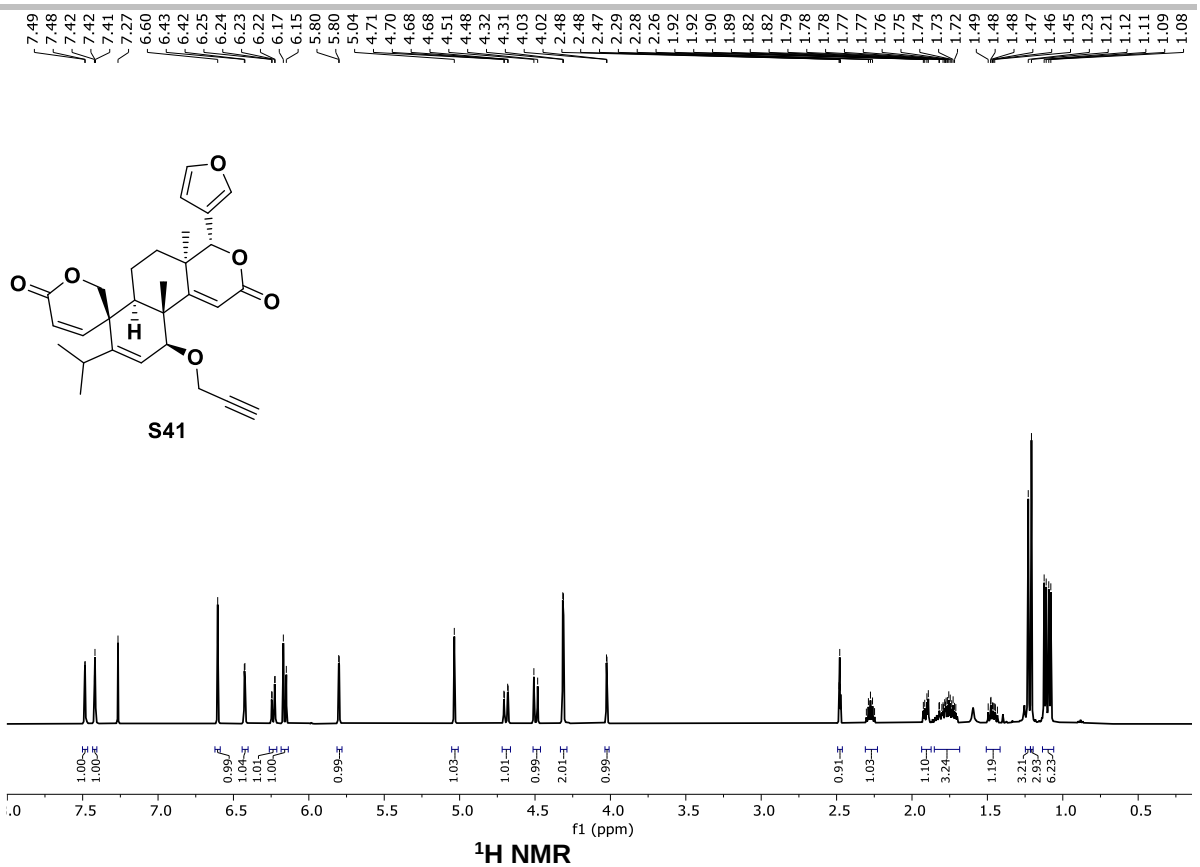
S40

^{1}H NMR

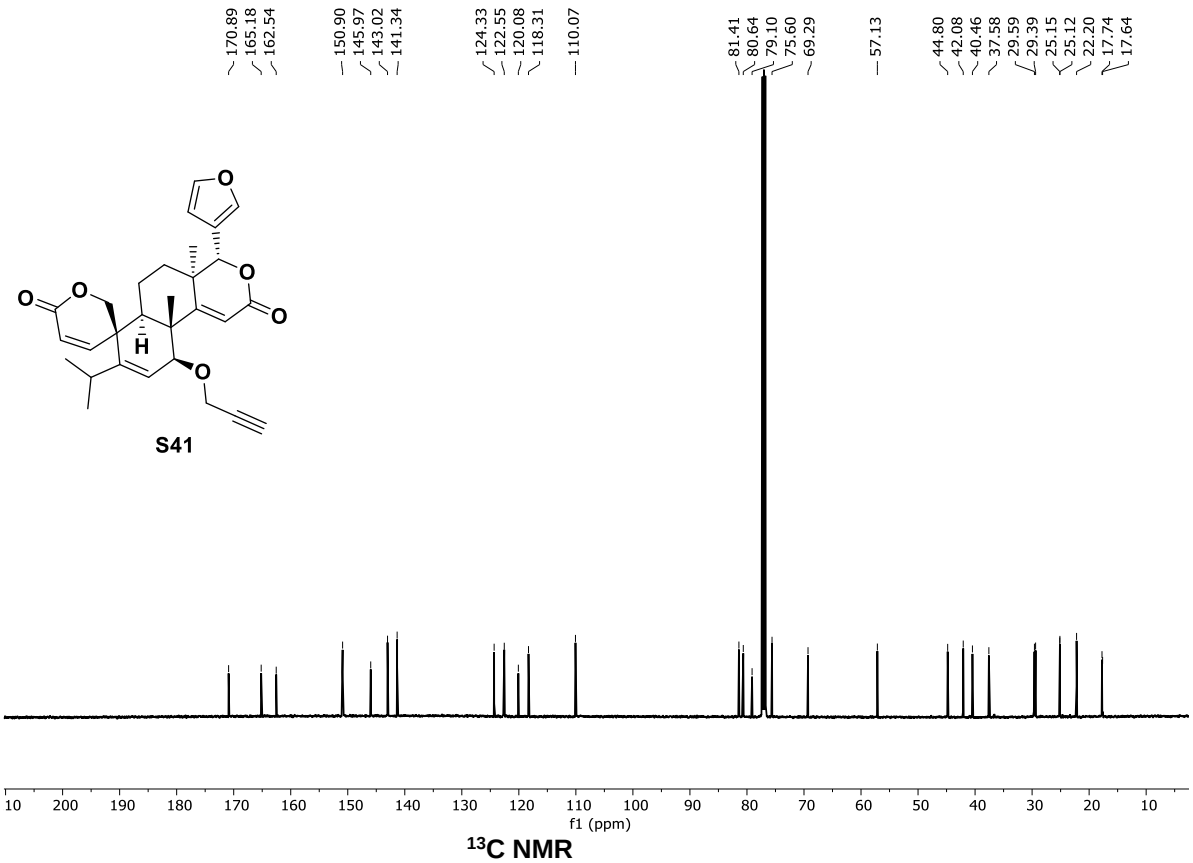


S40

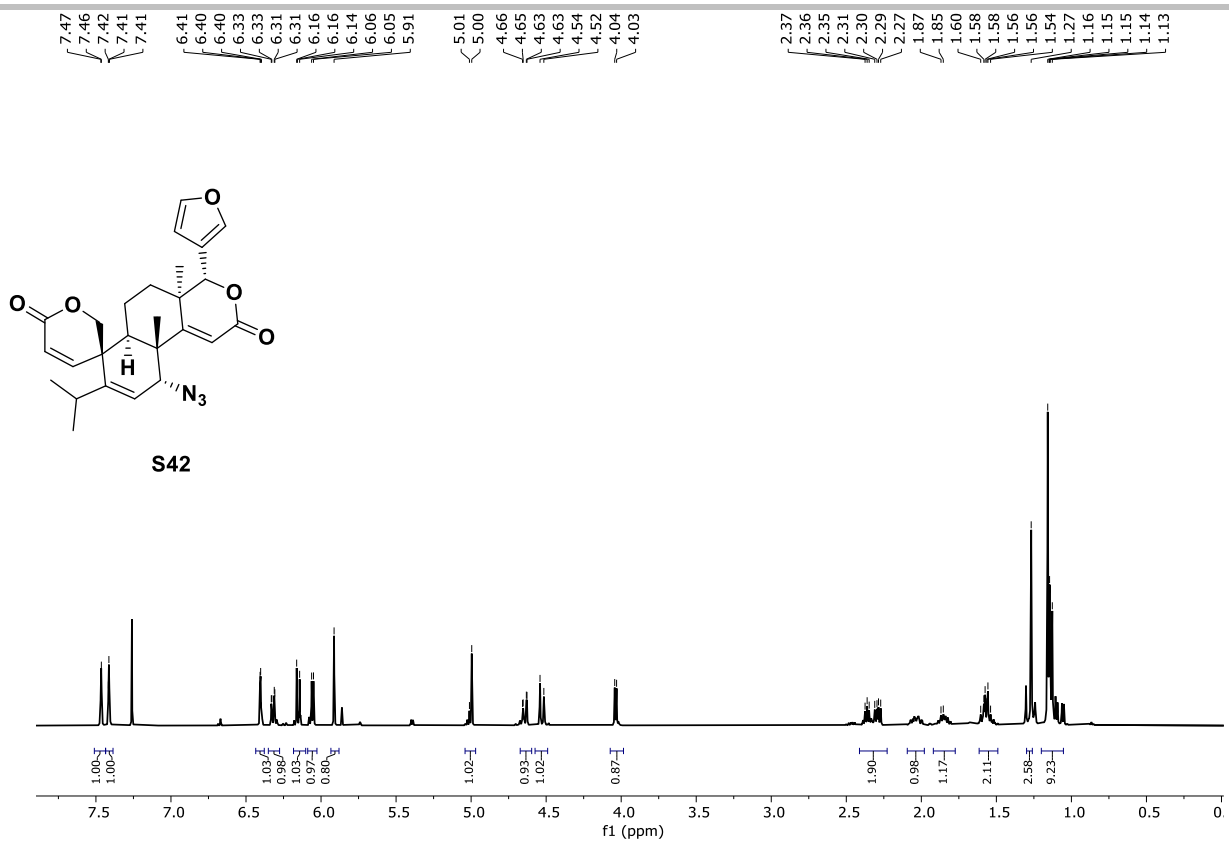
^{13}C NMR



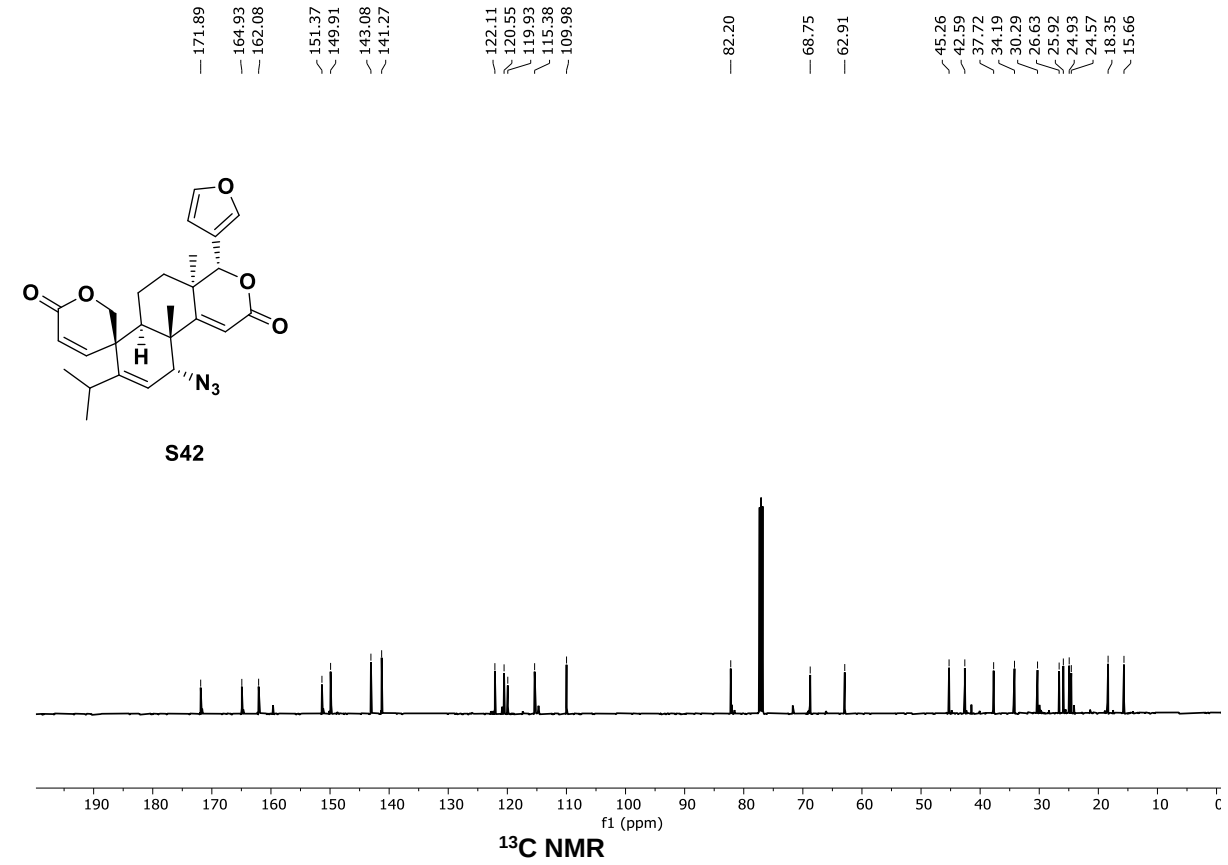
^{1}H NMR



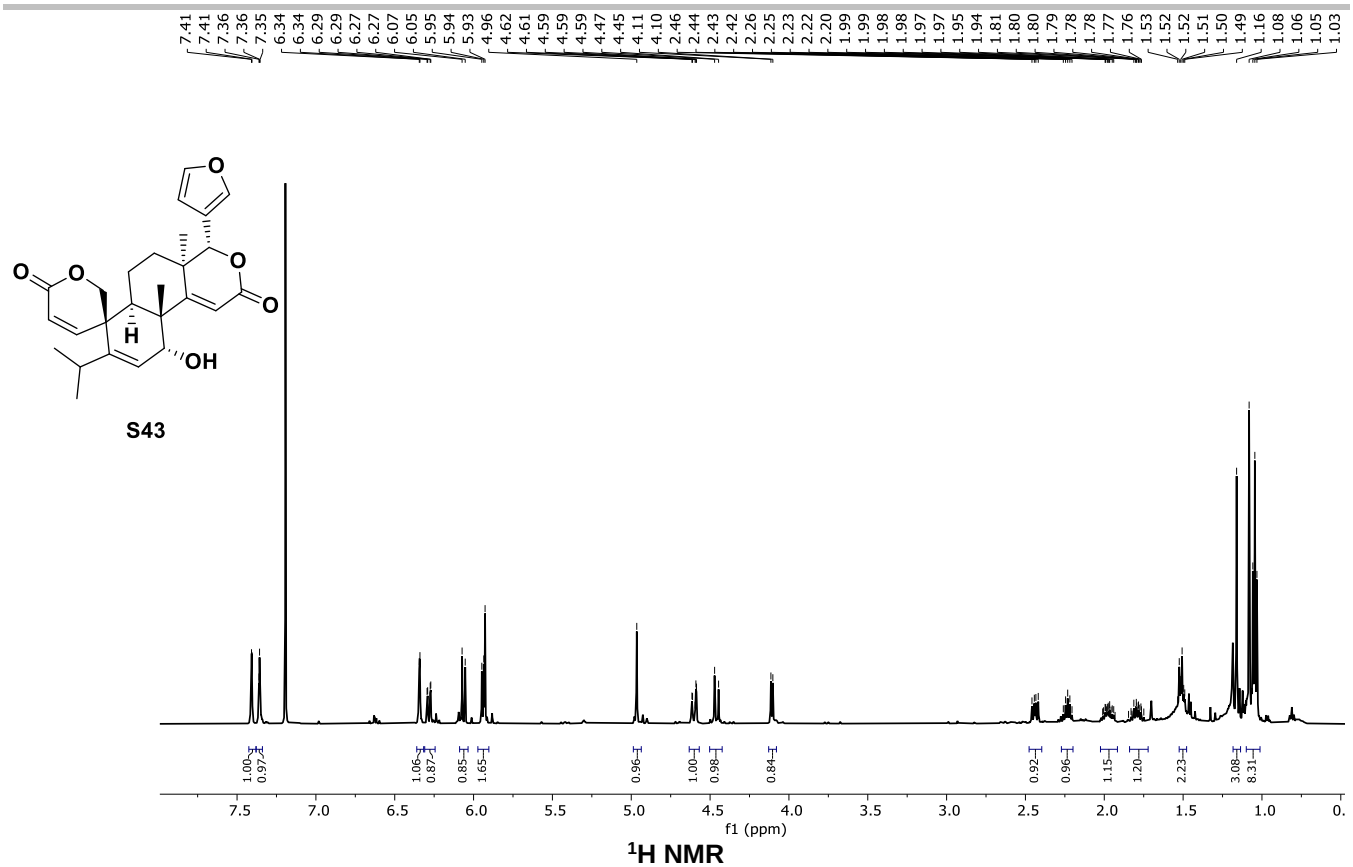
^{13}C NMR



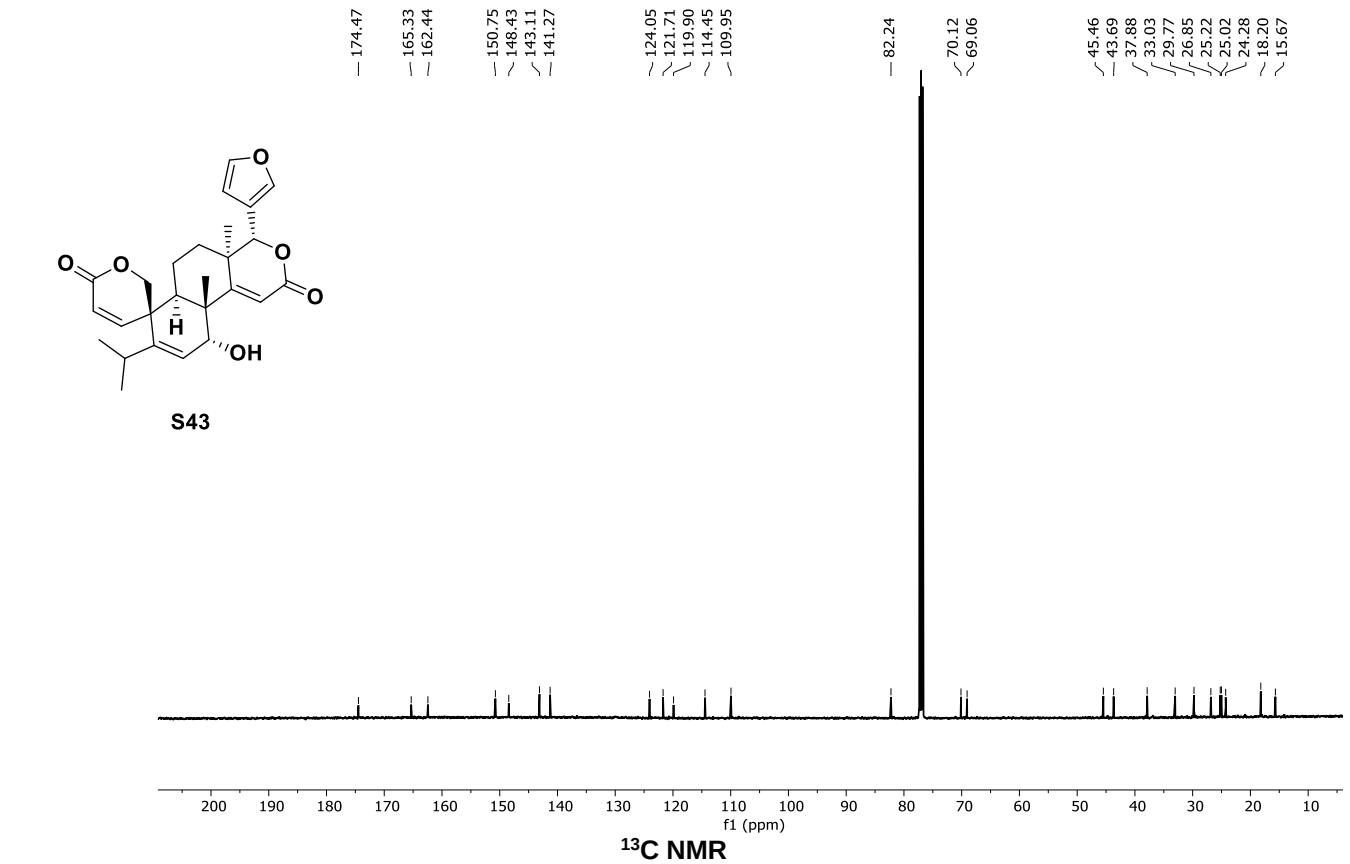
^{1}H NMR



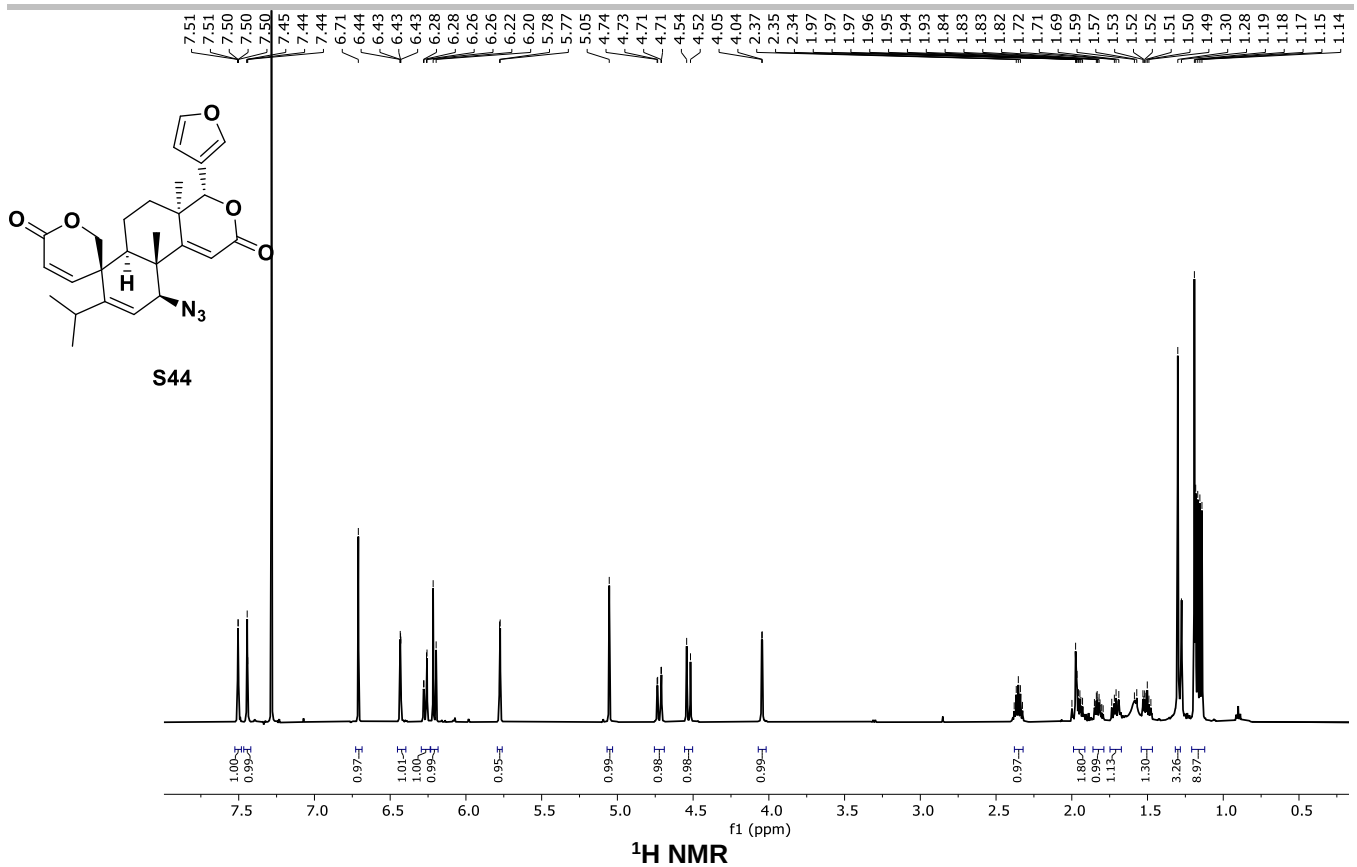
^{13}C NMR



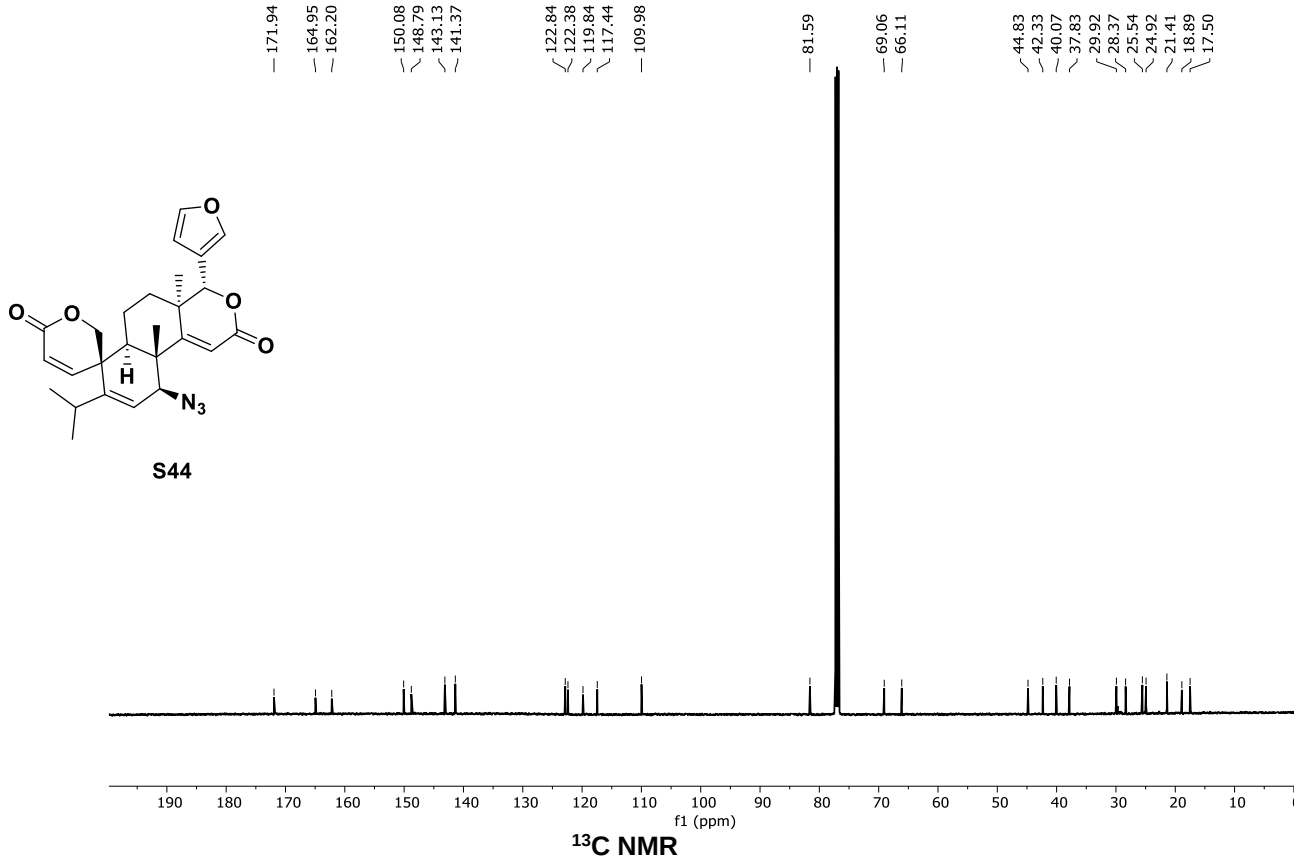
^{1}H NMR



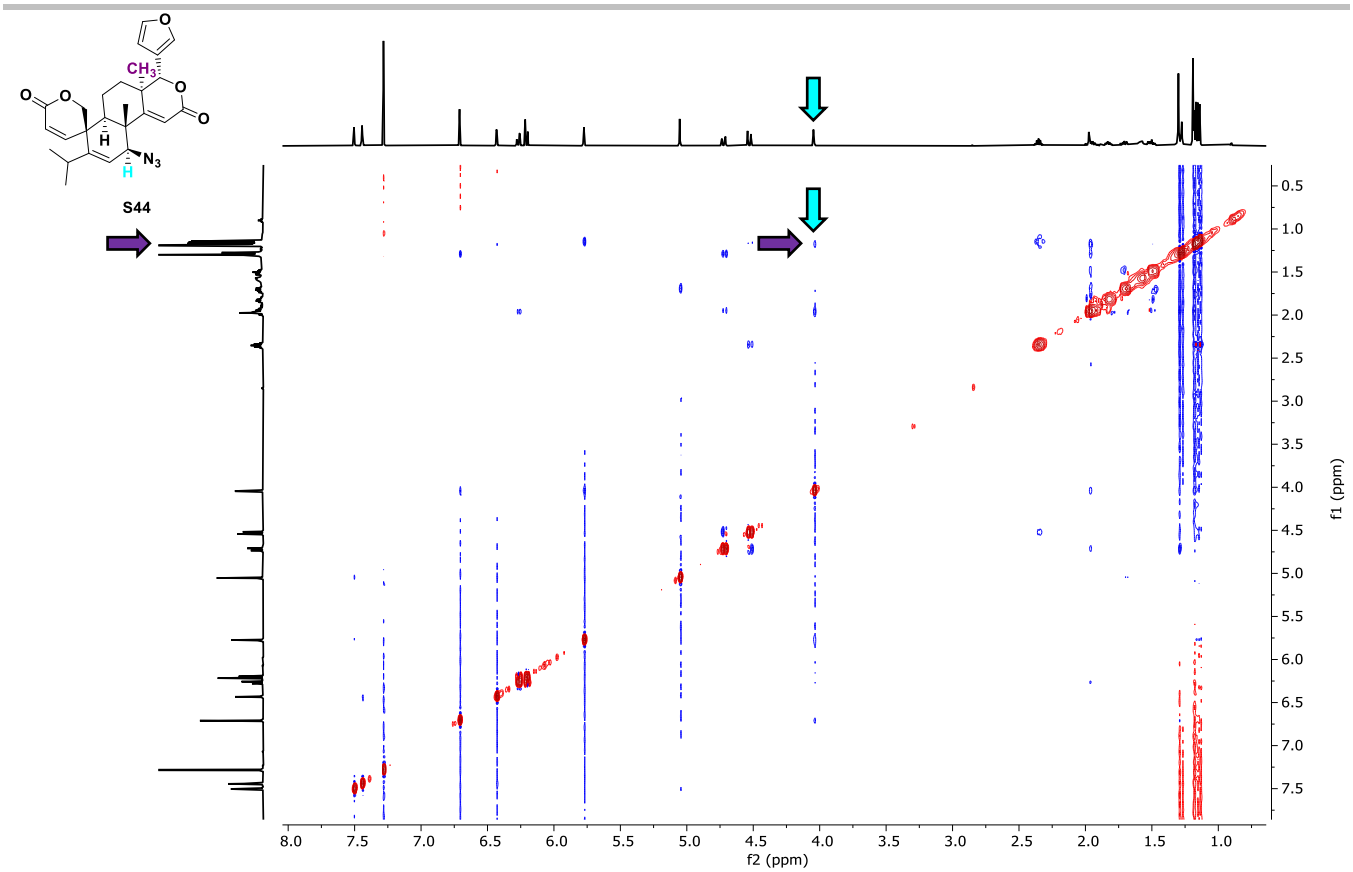
^{13}C NMR



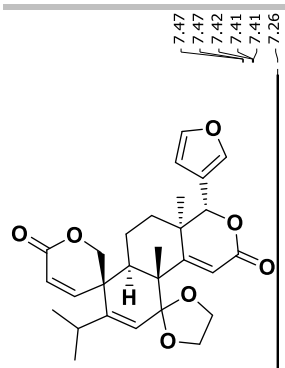
^{1}H NMR



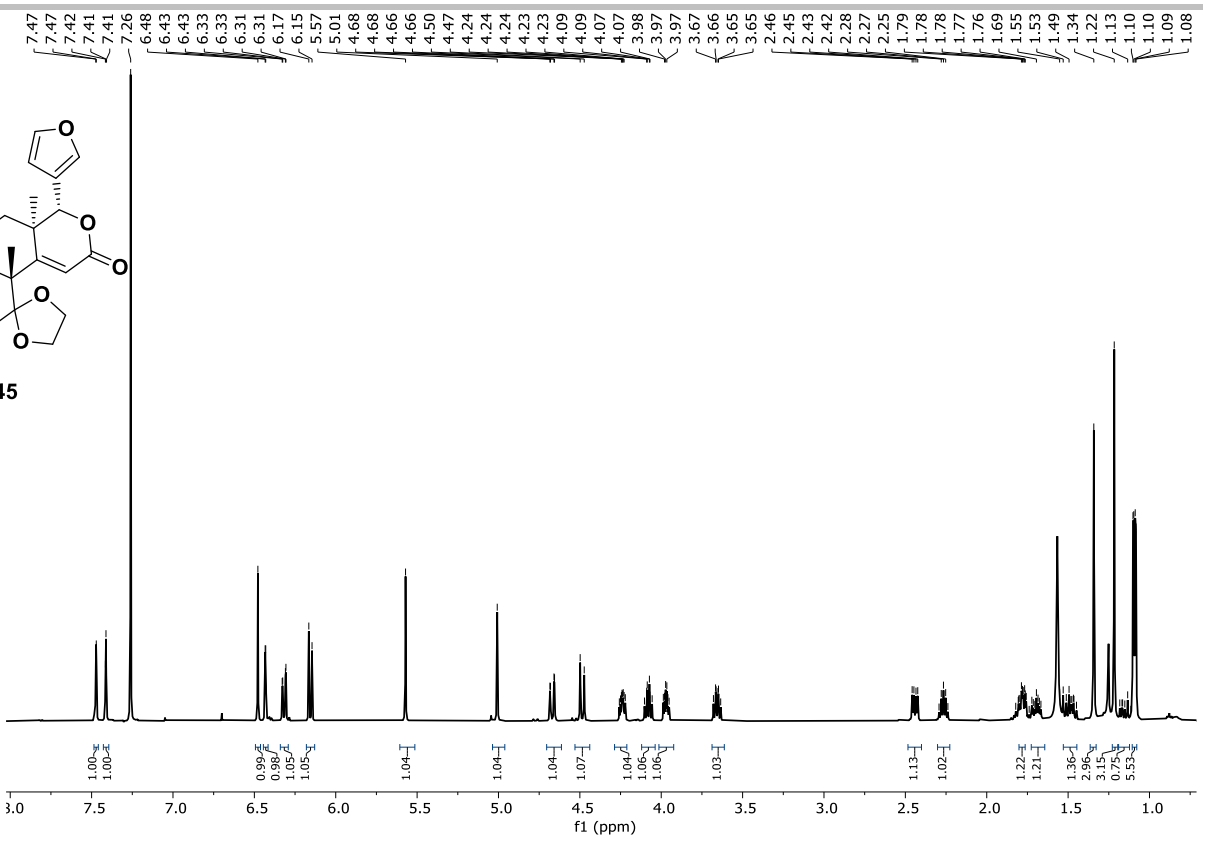
^{13}C NMR



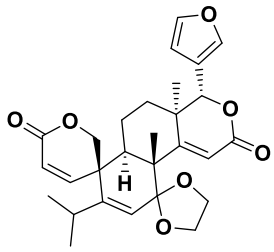
^{1}H-^{1}H 2D NOESY NMR



S45

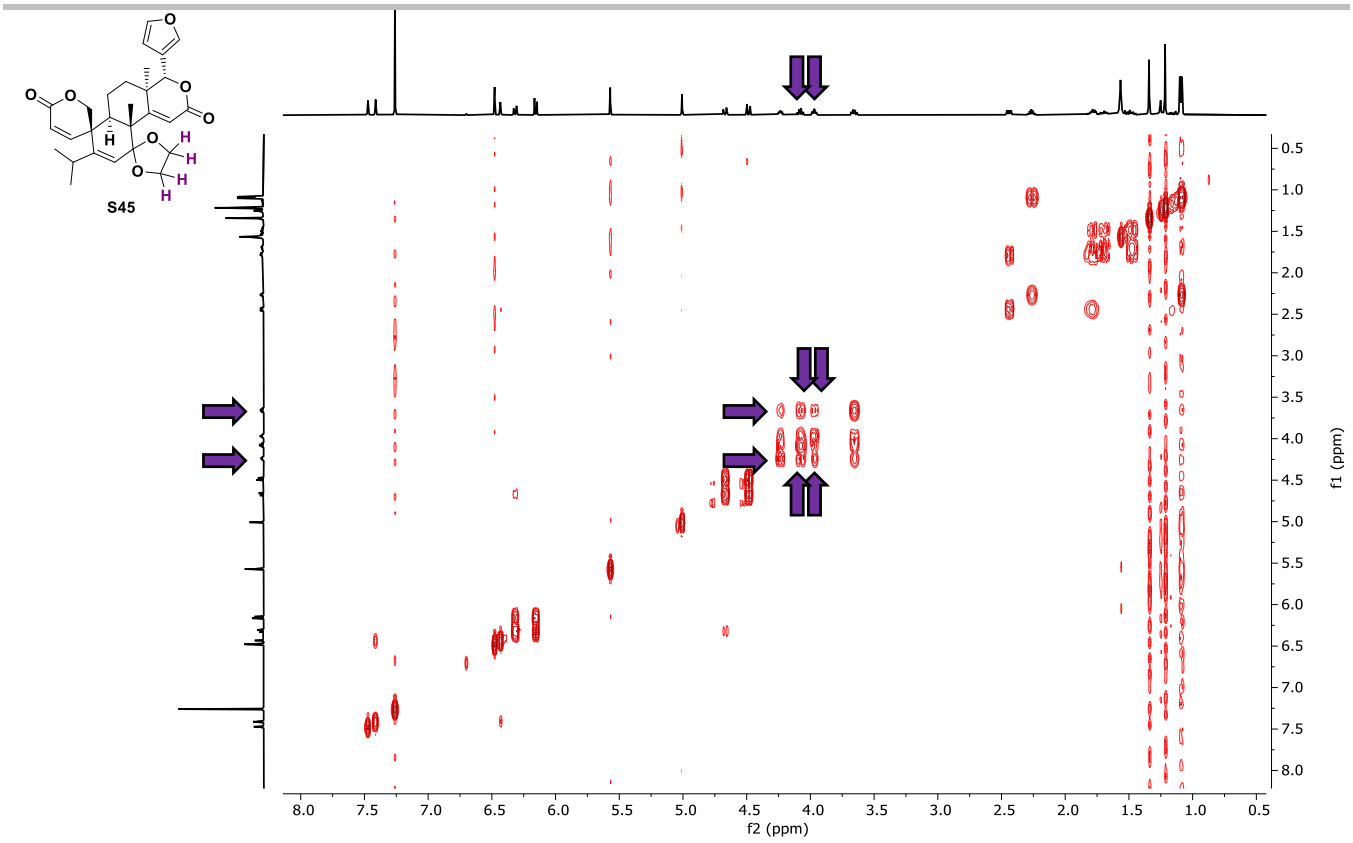


^{1}H NMR

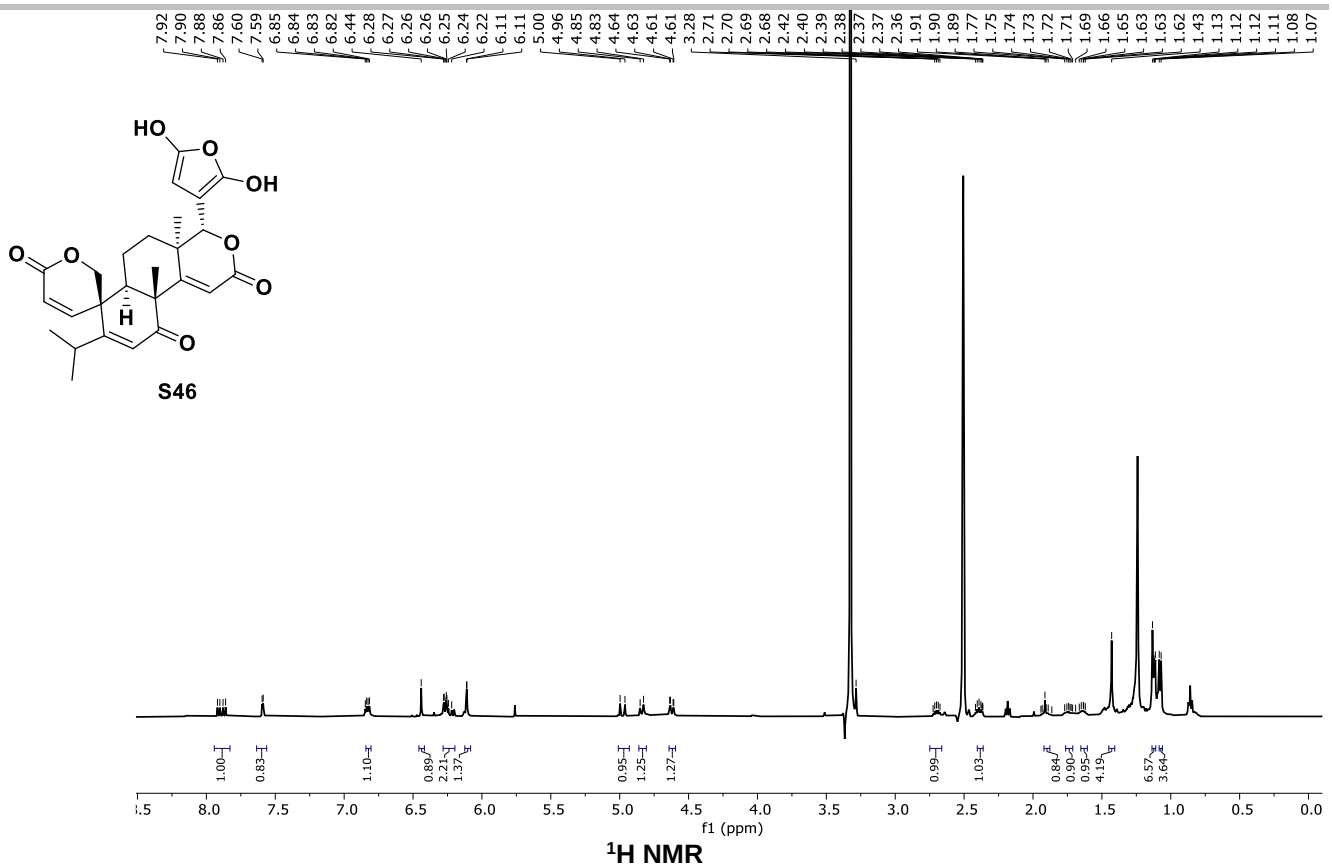


S45

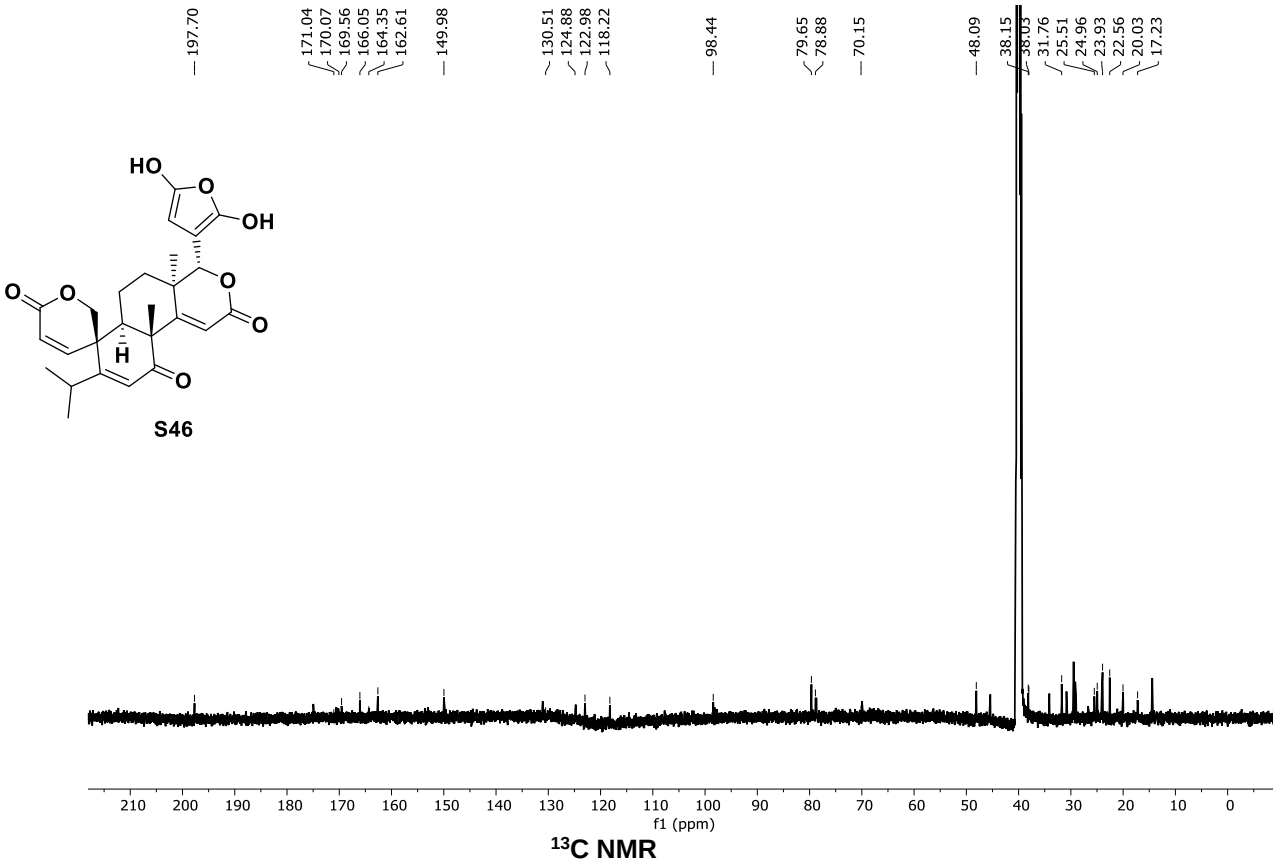
^{13}C NMR



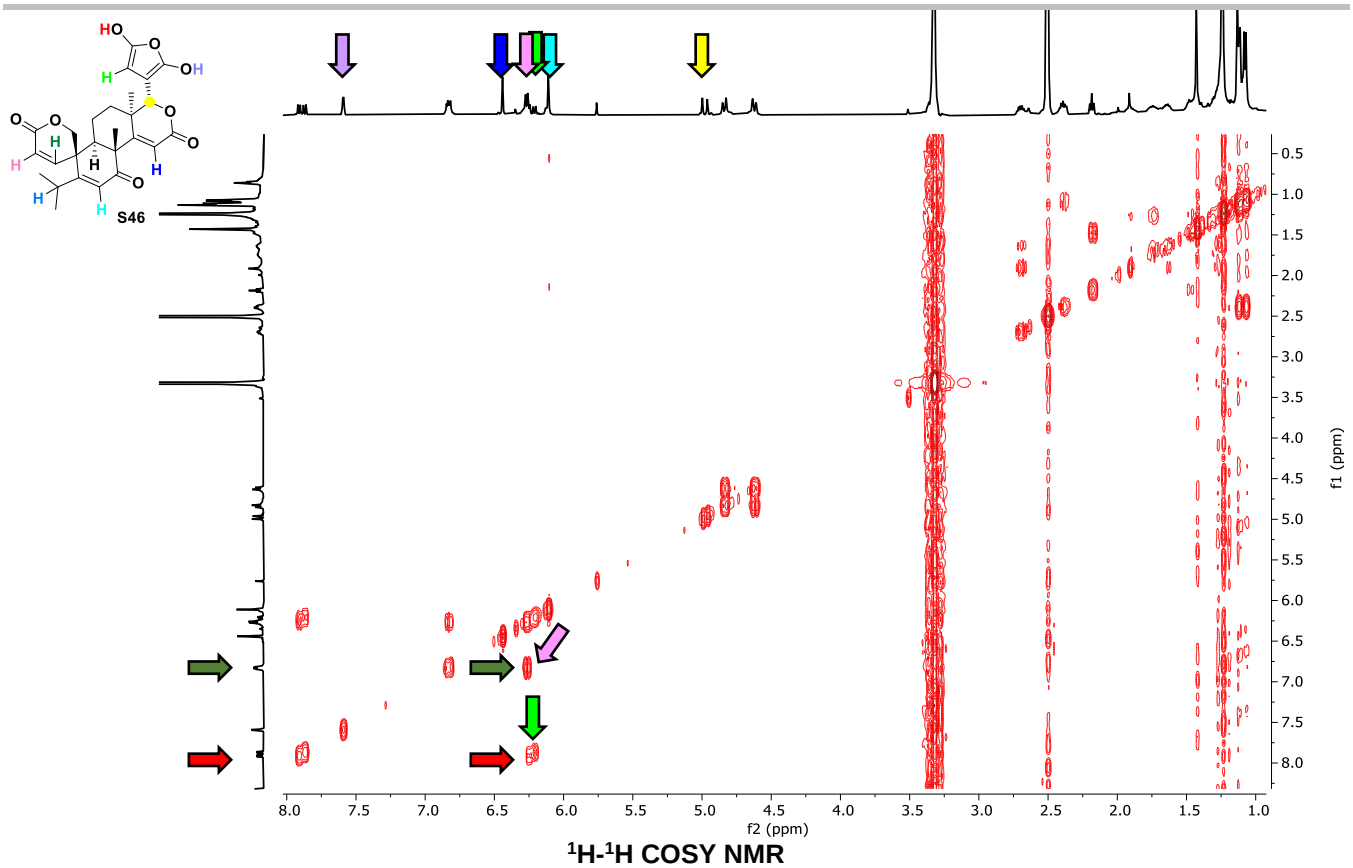
^{1}H-^{1}H COSY NMR



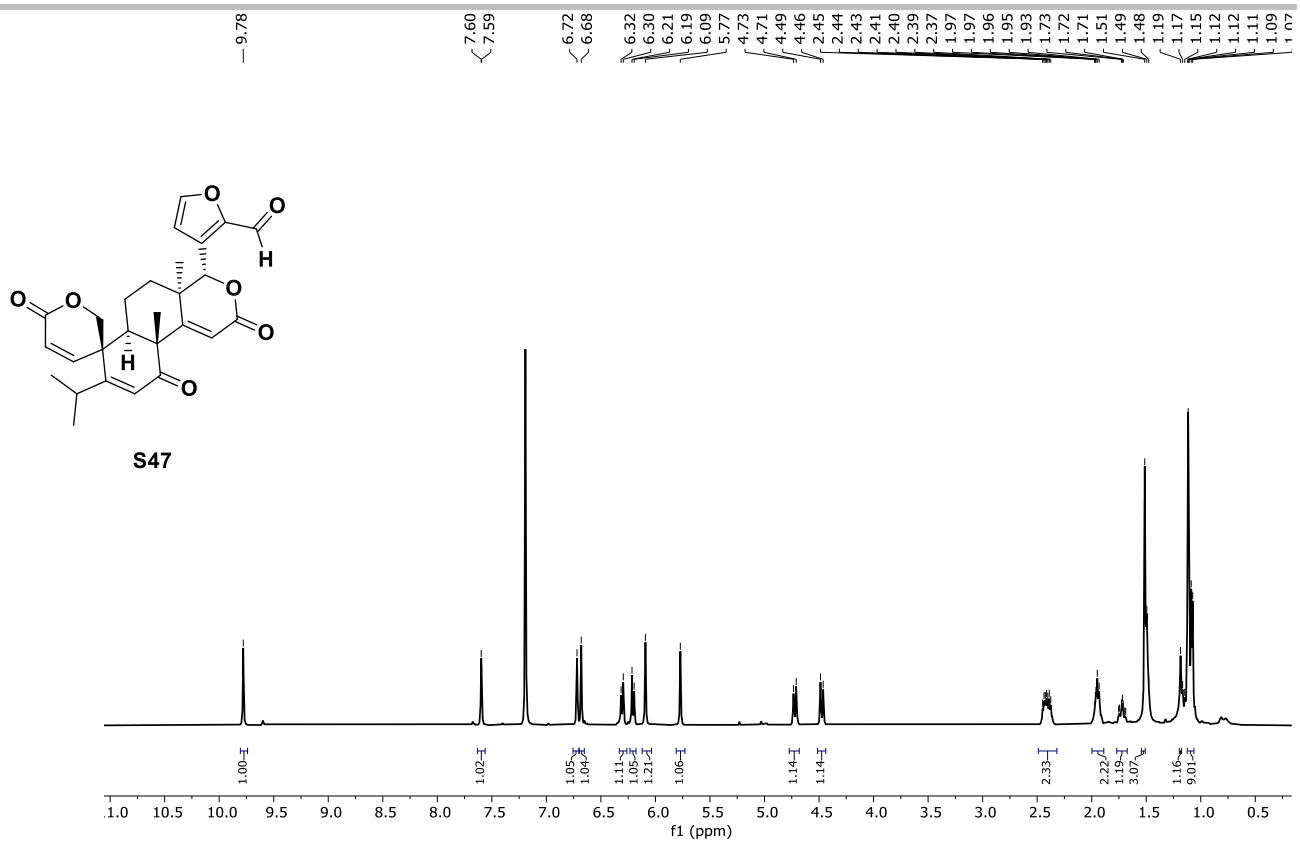
^{1}H NMR



^{13}C NMR

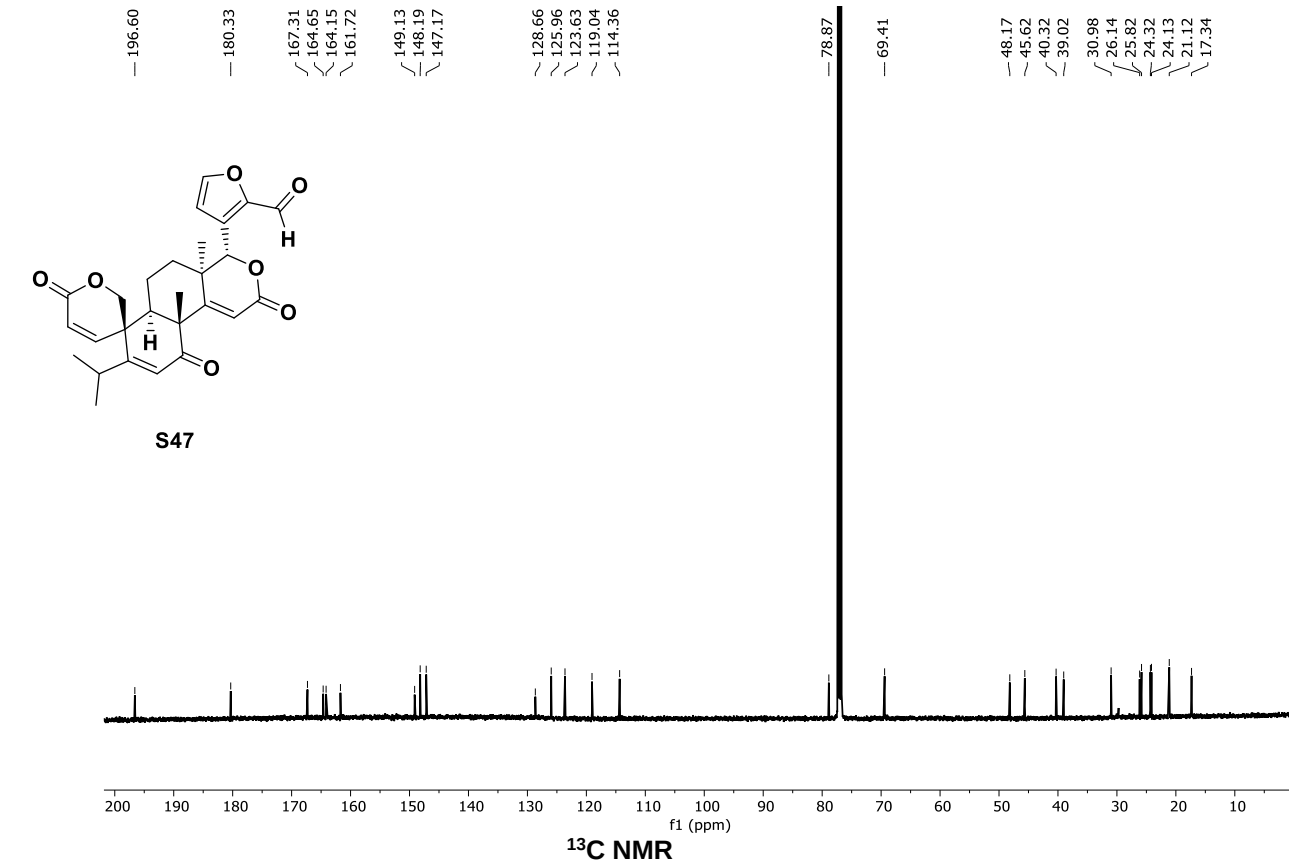


^{1}H-^{1}H COSY NMR



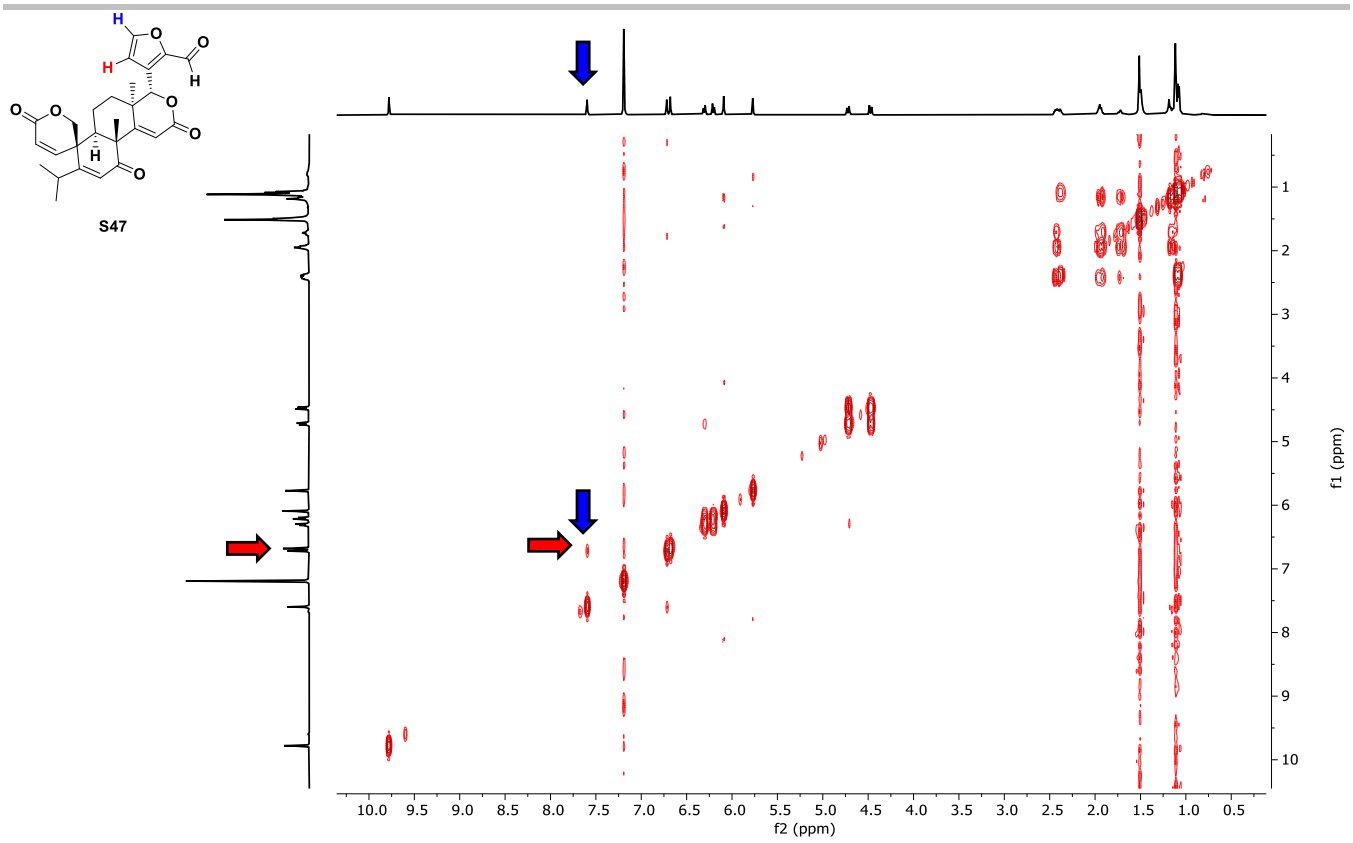
S47

^{1}H NMR

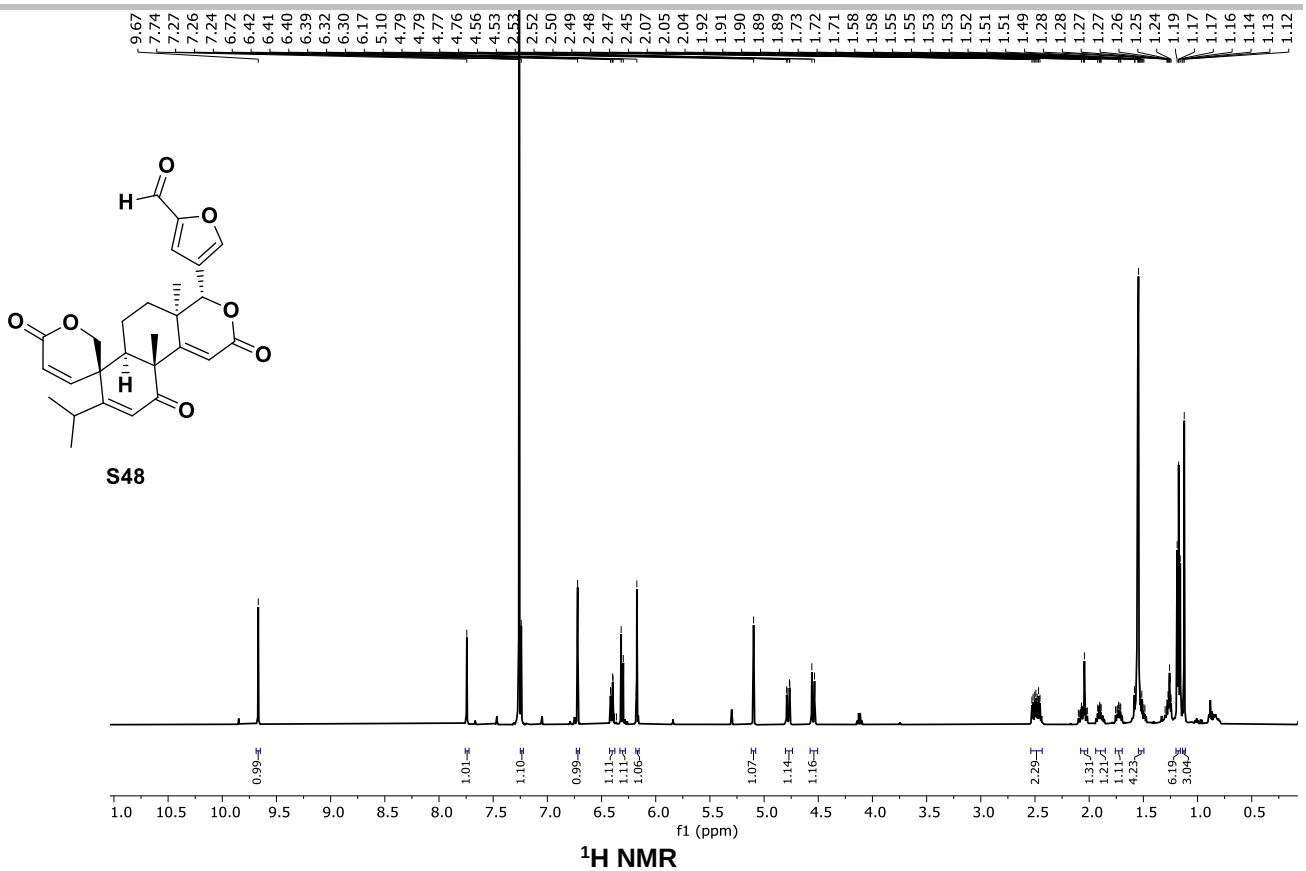


S47

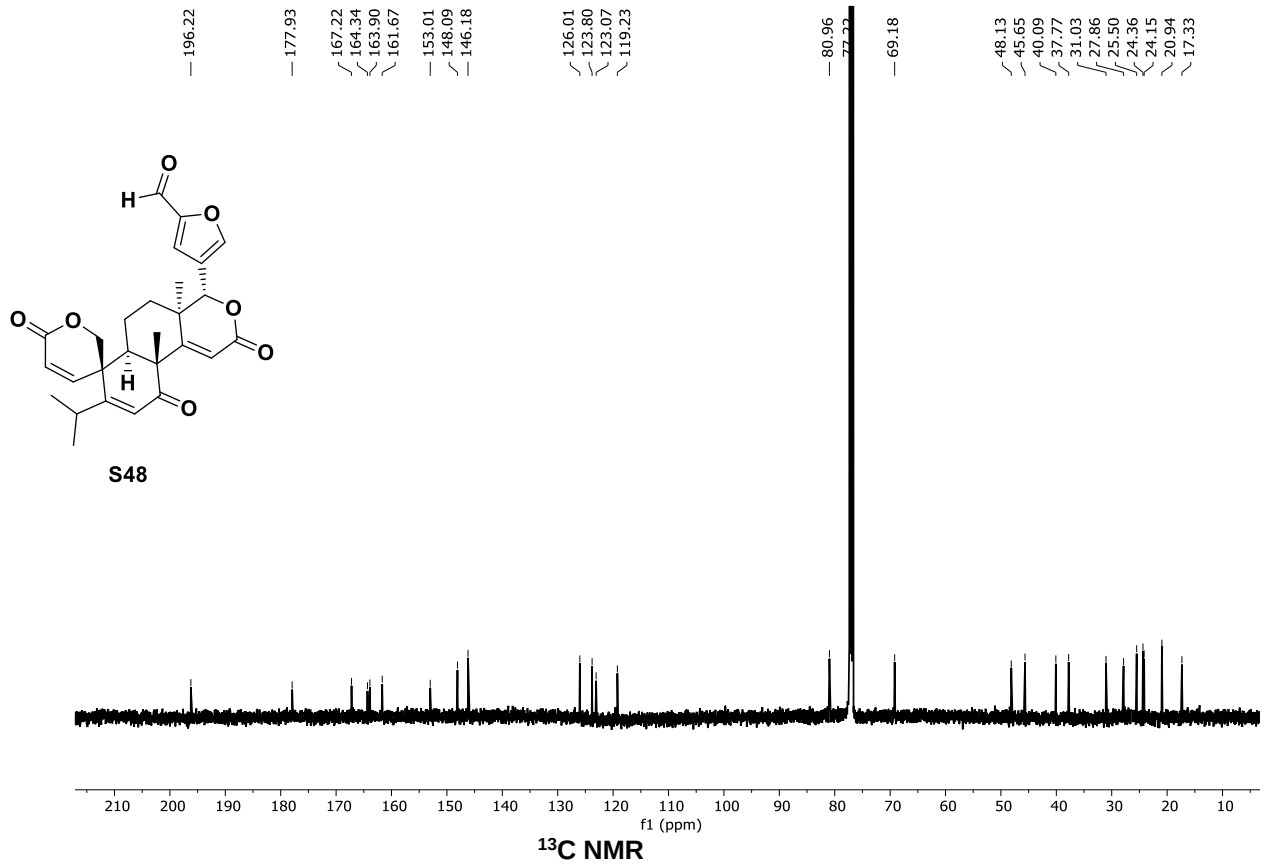
^{13}C NMR



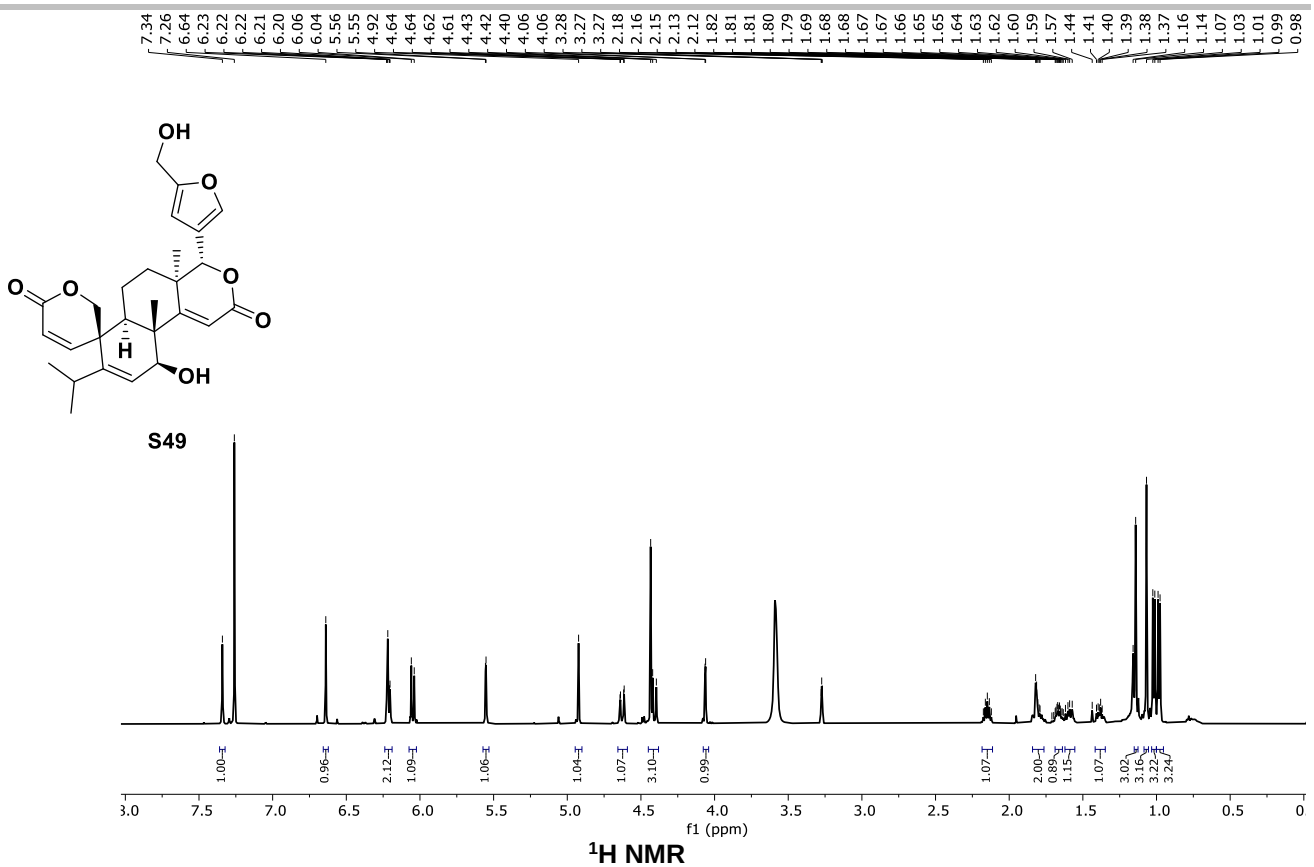
^{1}H-^{1}H COSY NMR



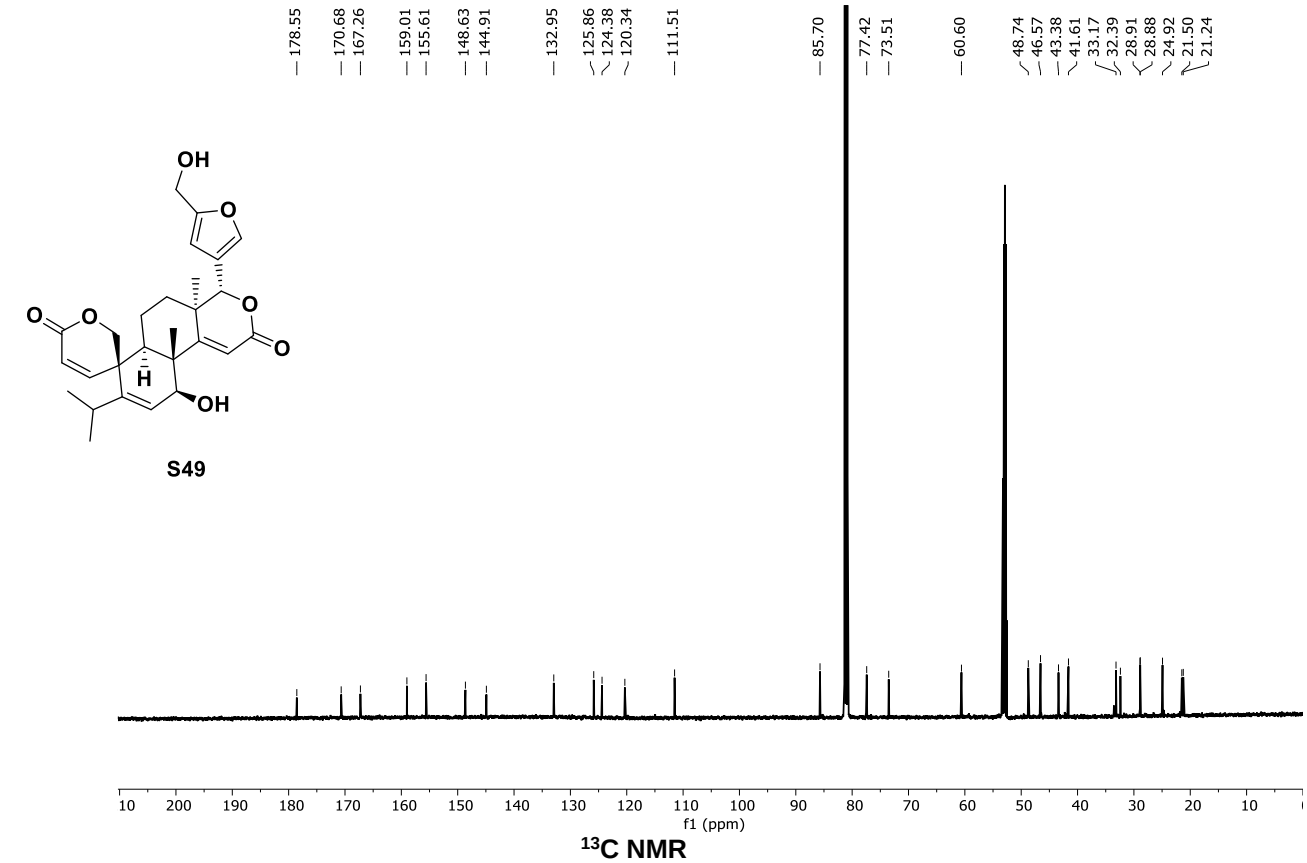
^{1}H NMR



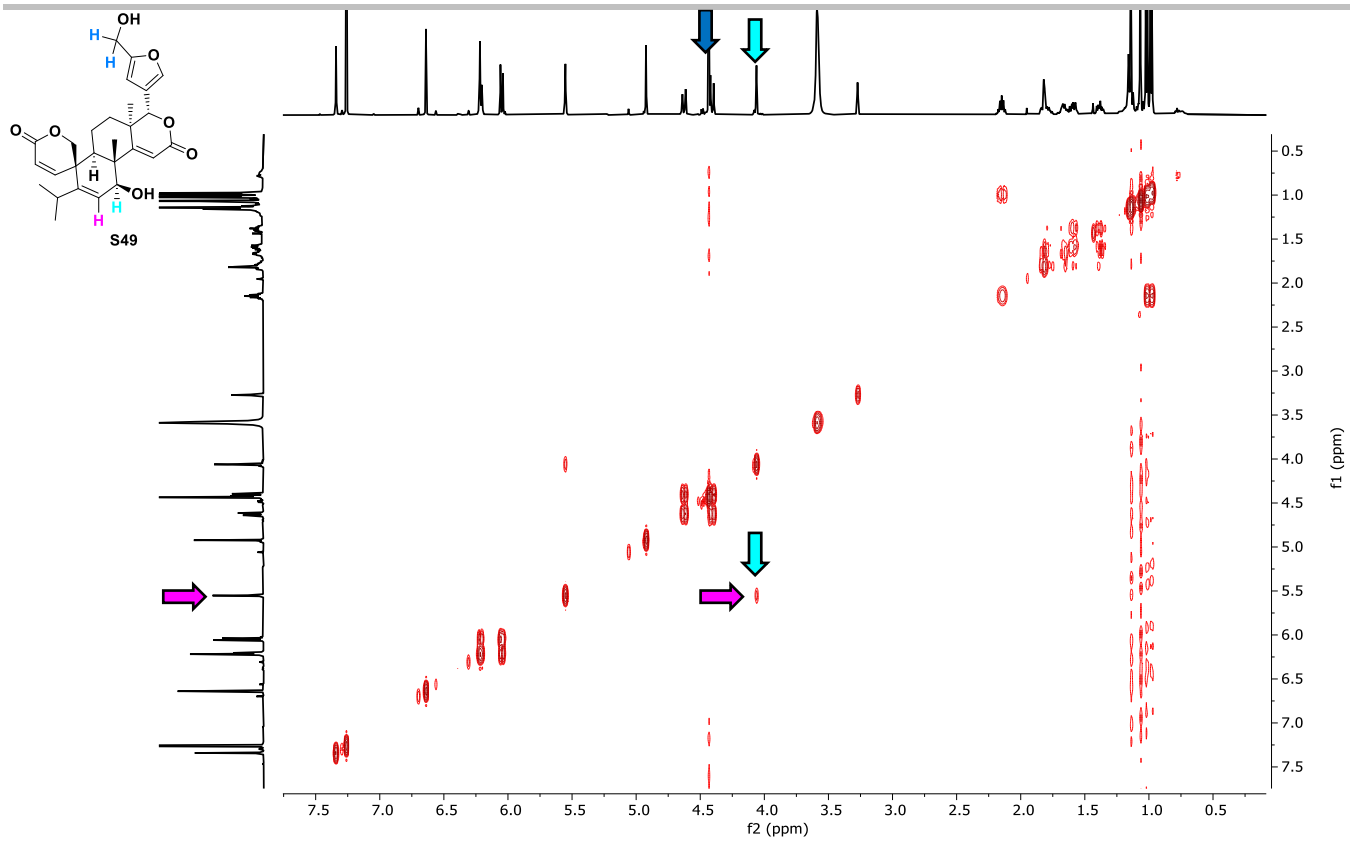
^{13}C NMR



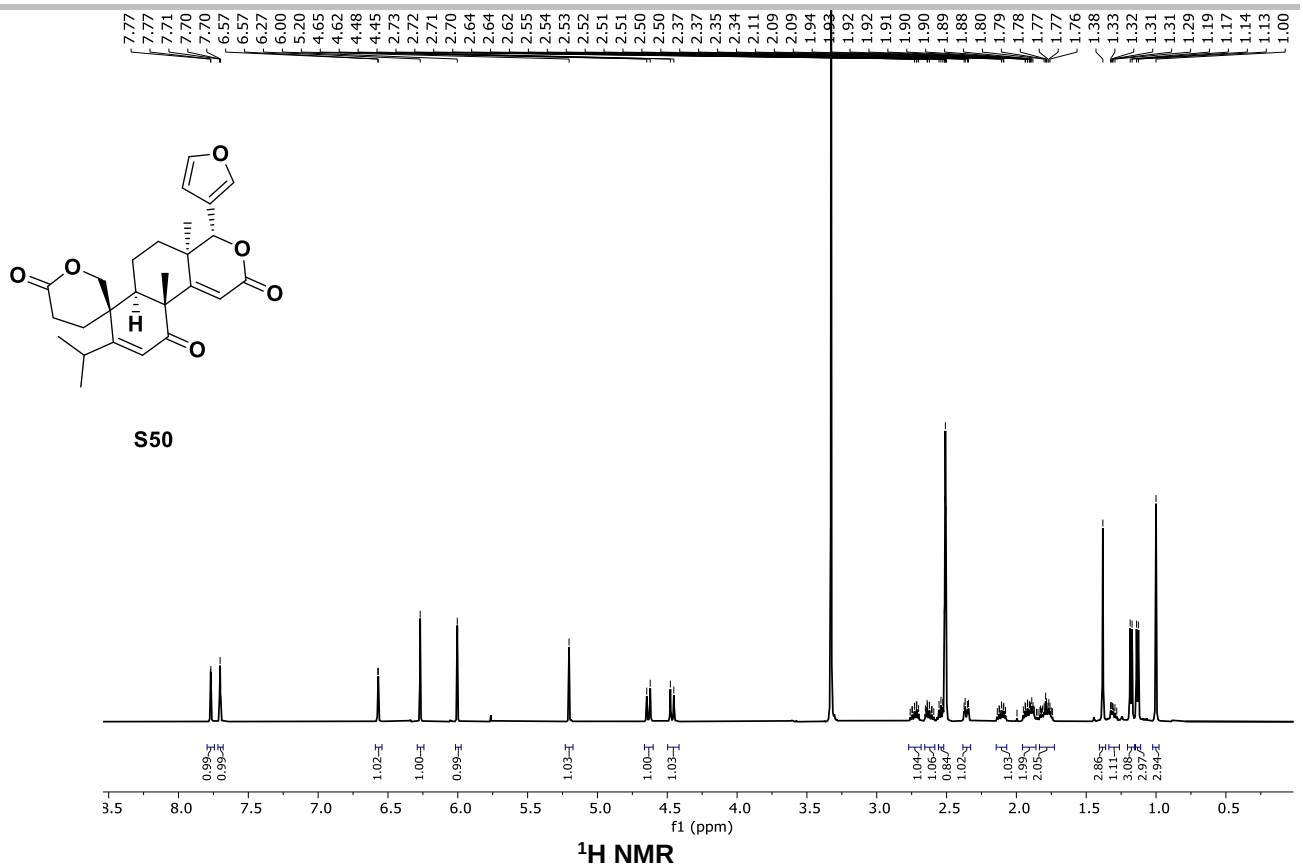
^{1}H NMR



^{13}C NMR

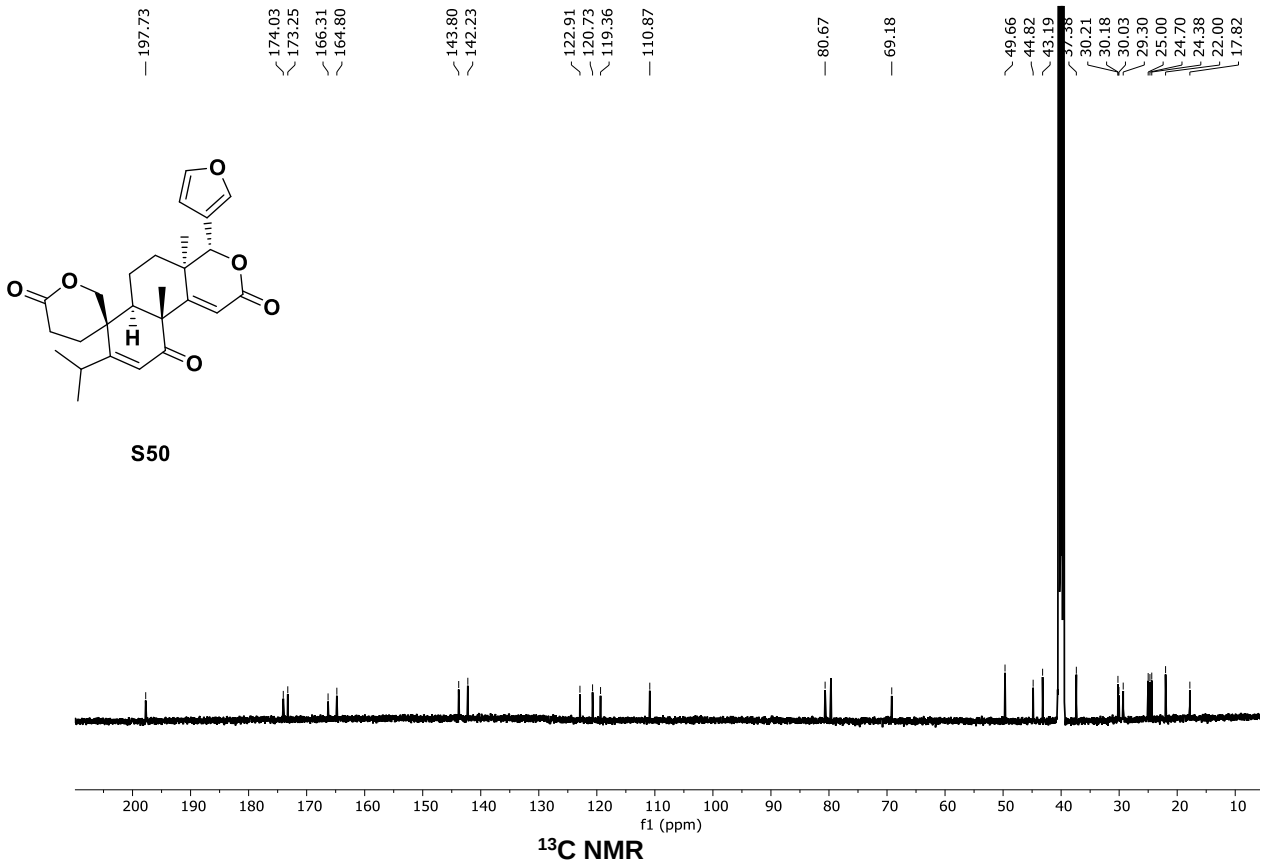


^{1}H-^{1}H COSY NMR



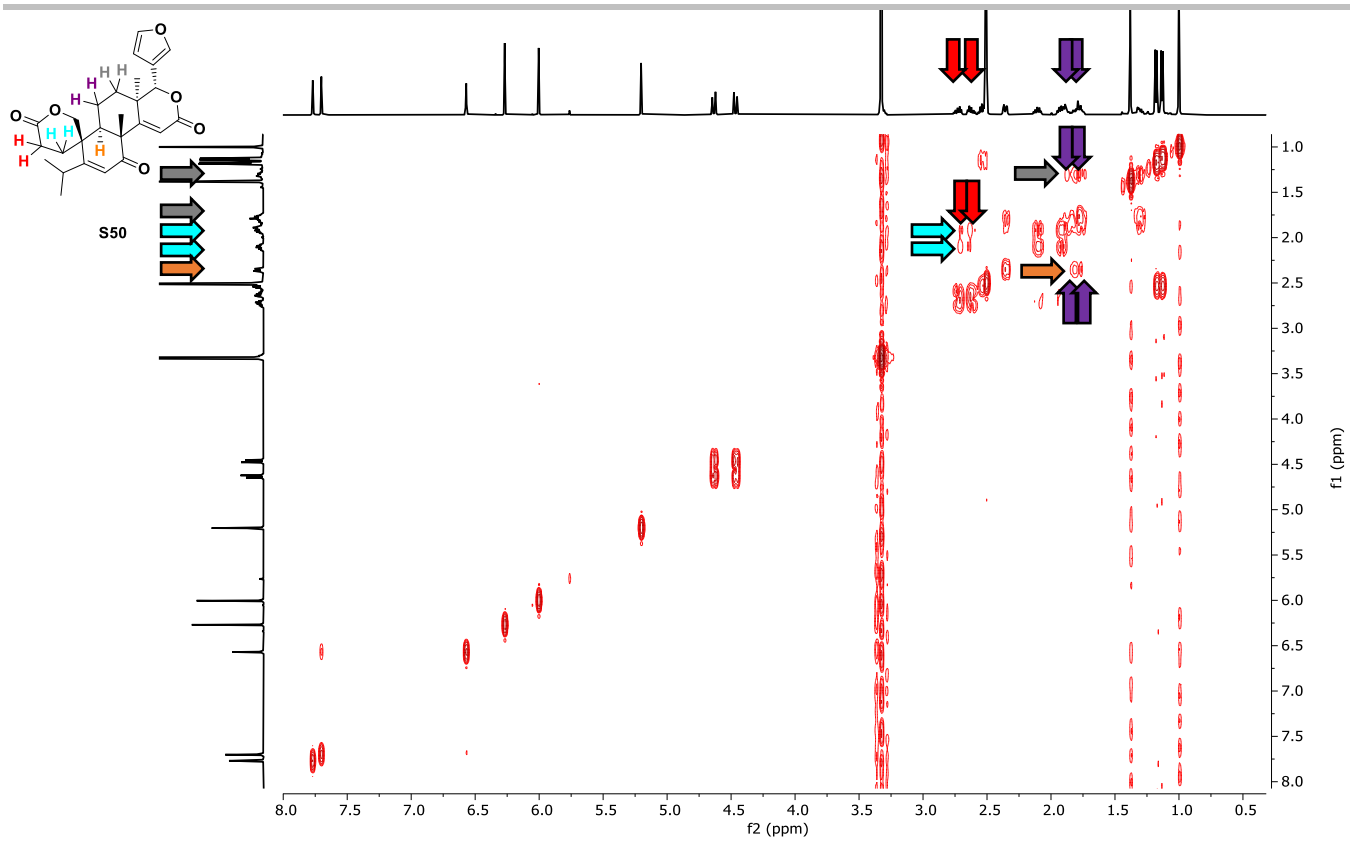
S50

^{1}H NMR

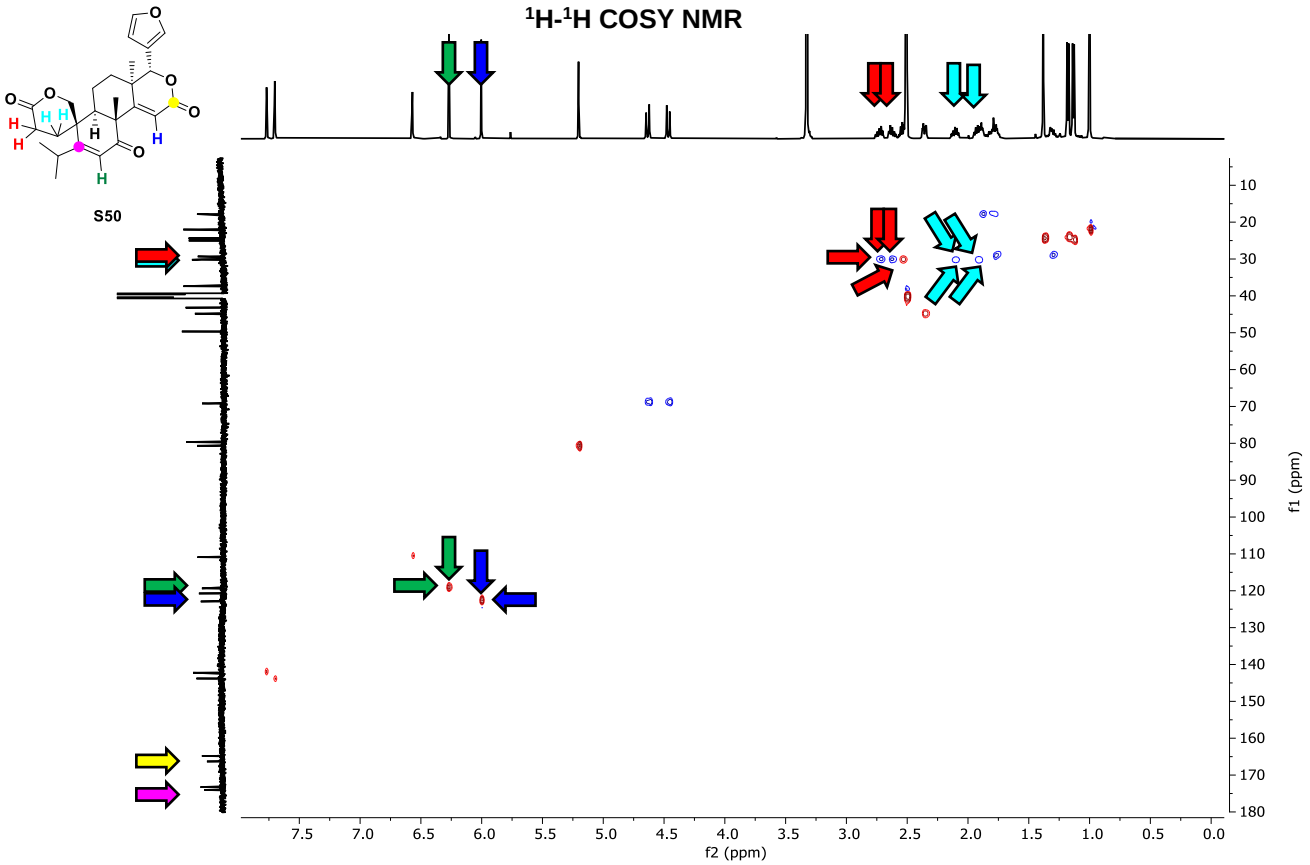


S50

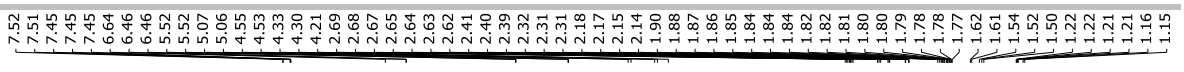
^{13}C NMR

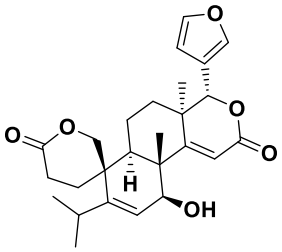


^{1}H-^{1}H COSY NMR

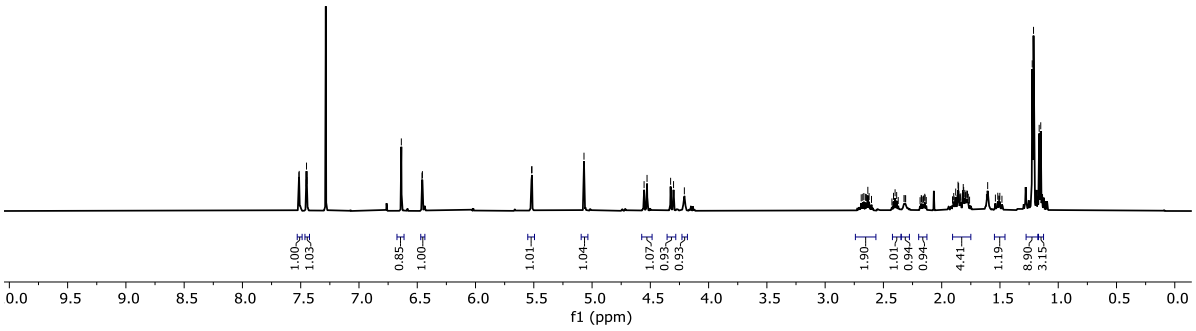


^{1}H-^{13}C HSQC NMR

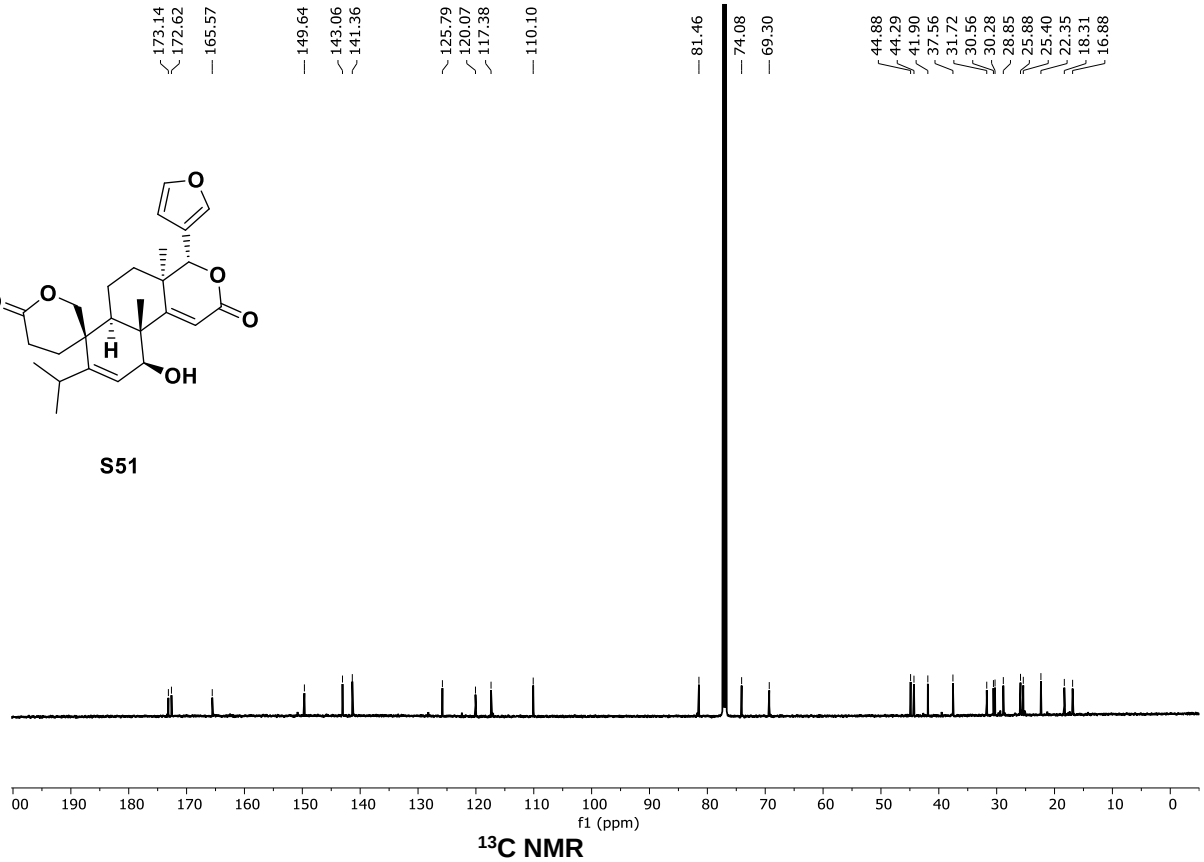




S51

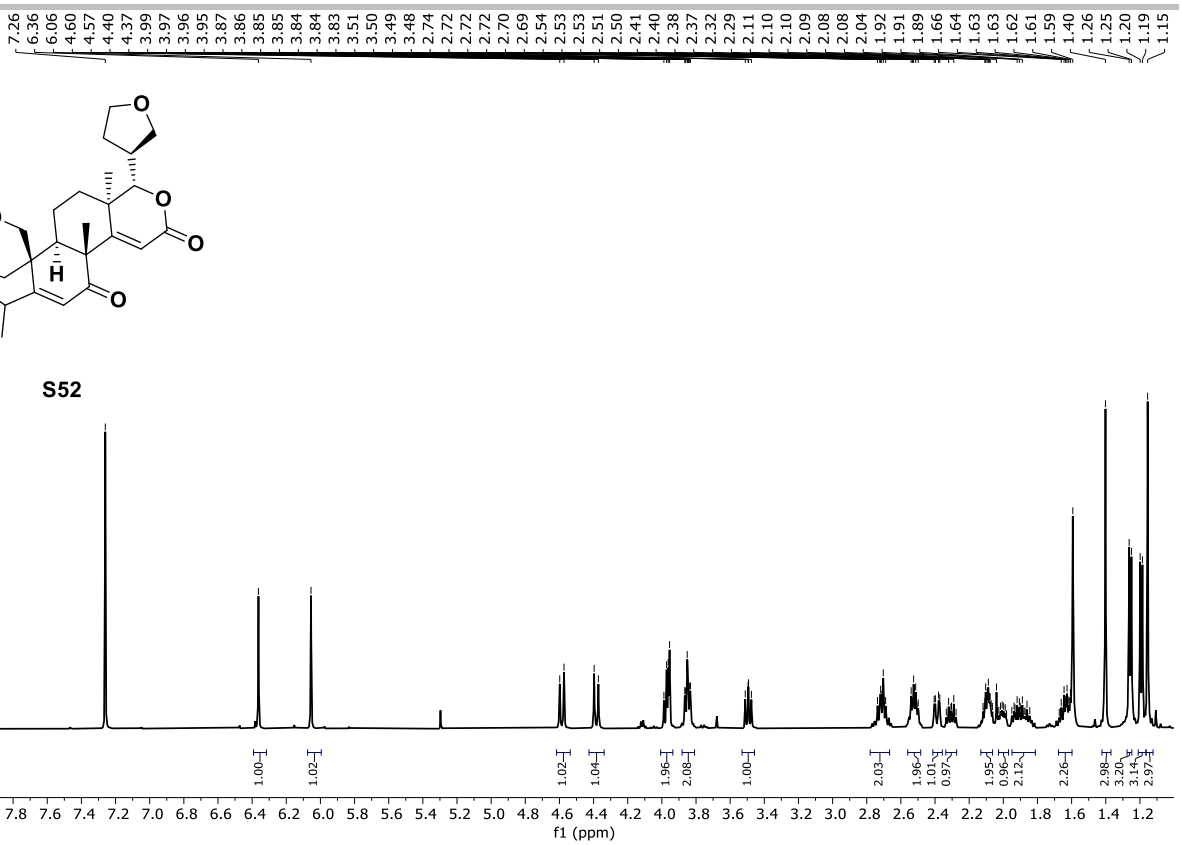


^{1}H NMR



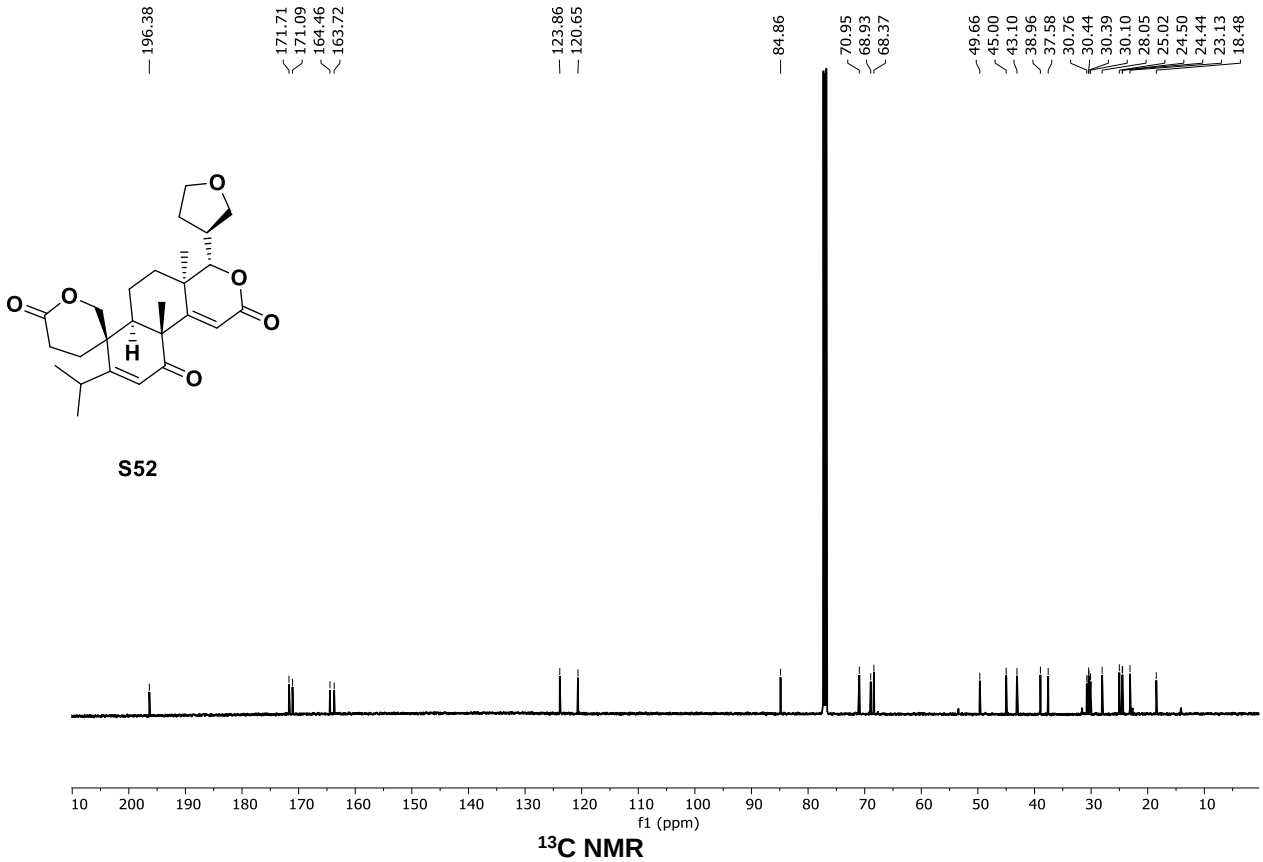
S51

^{13}C NMR



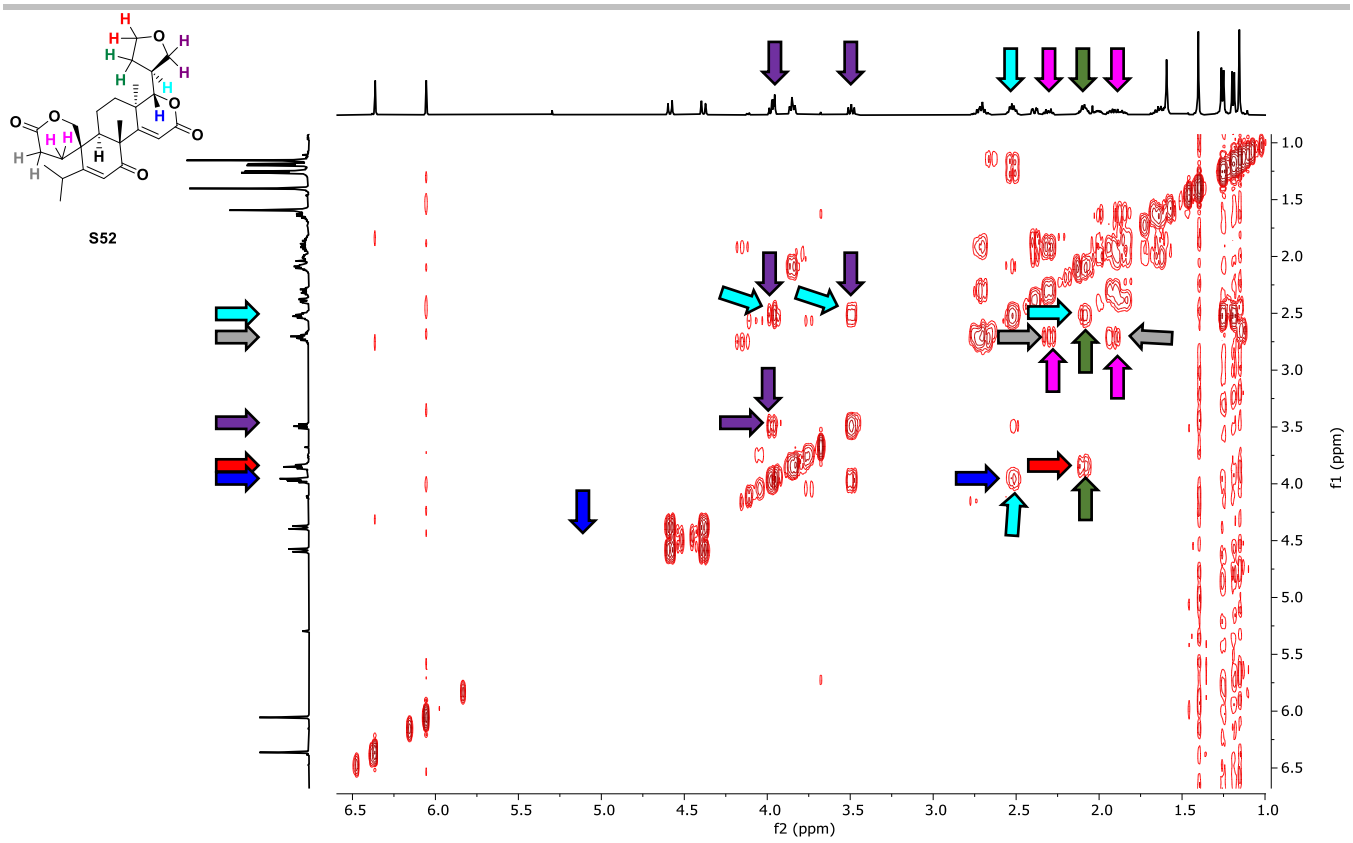
S52

^{1}H NMR

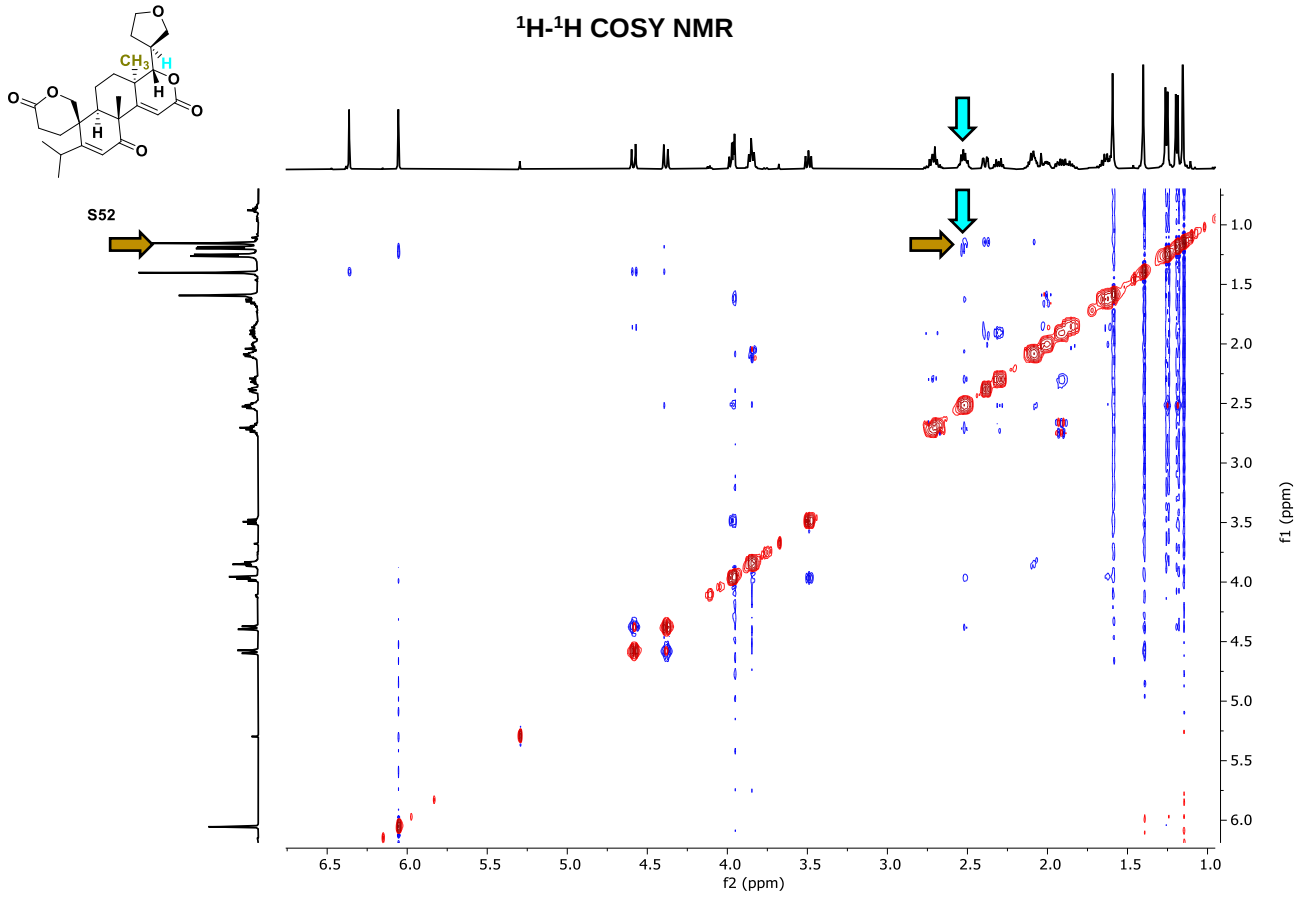


S52

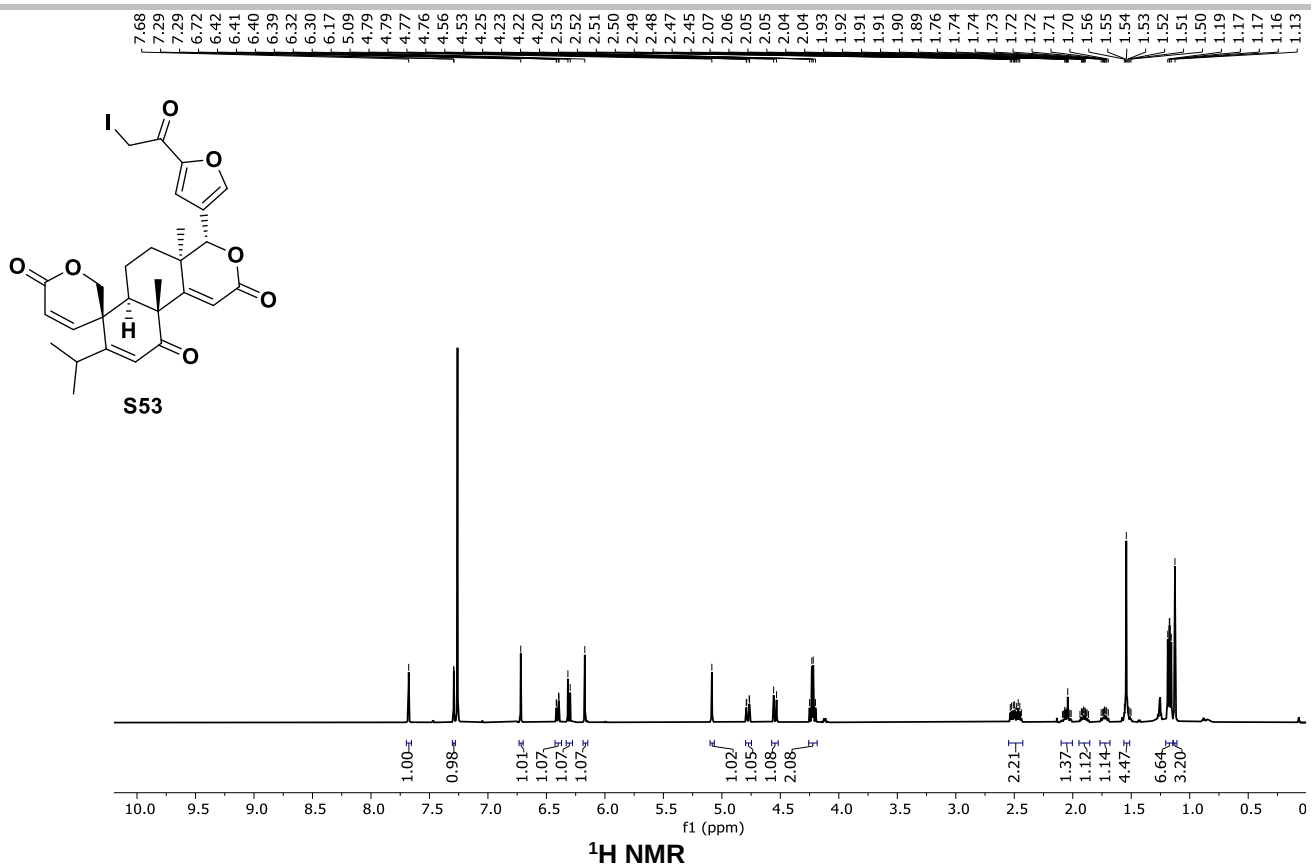
^{13}C NMR



^{1}H-^{1}H COSY NMR

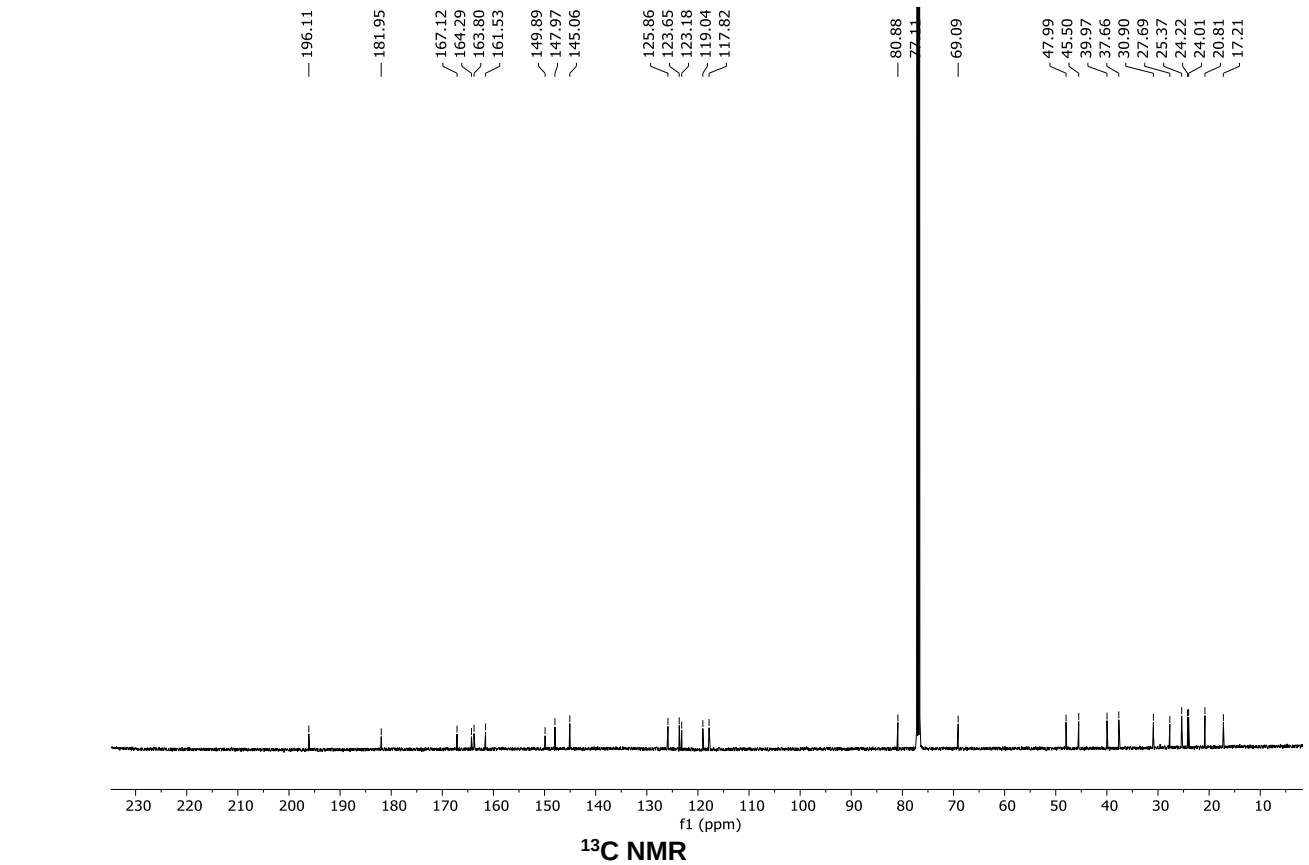


^{1}H-^{1}H 2D NOESY NMR

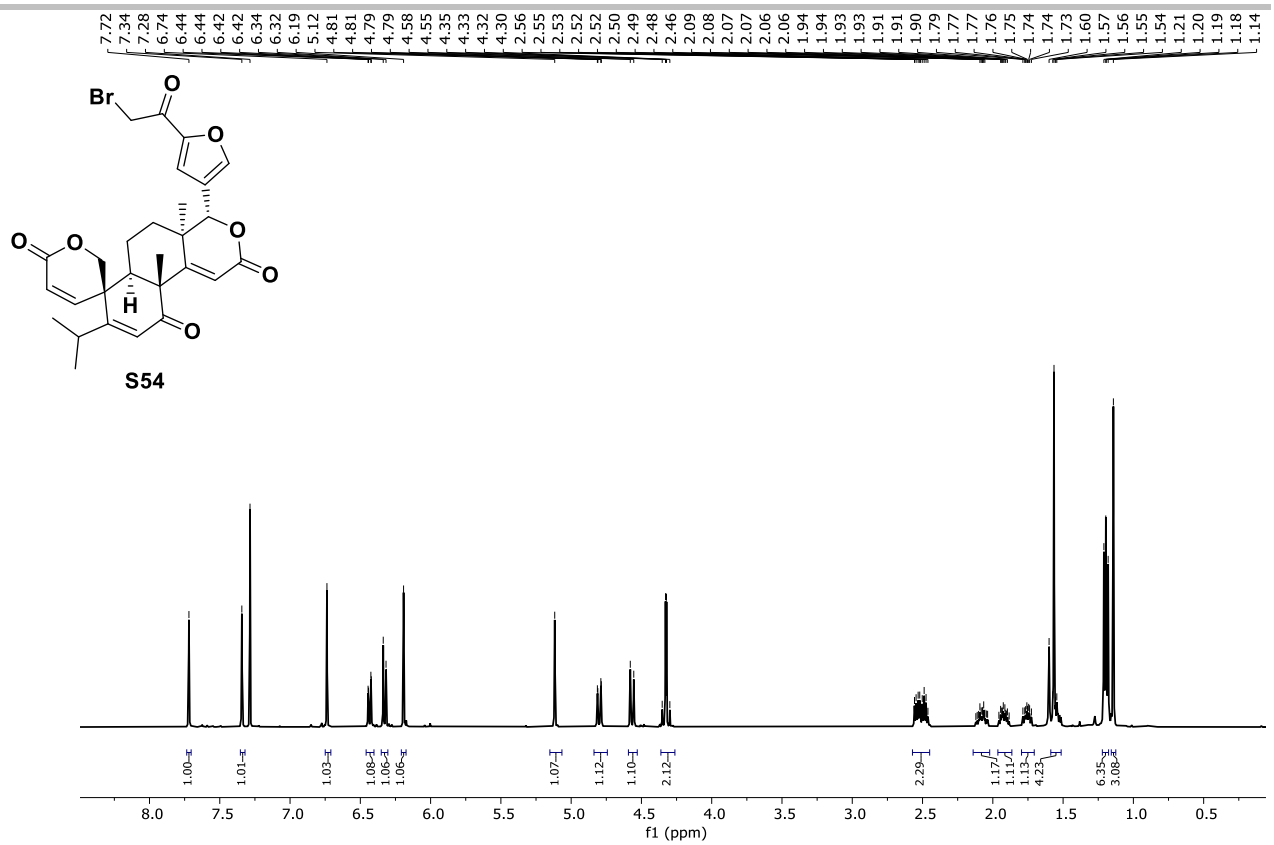


S53

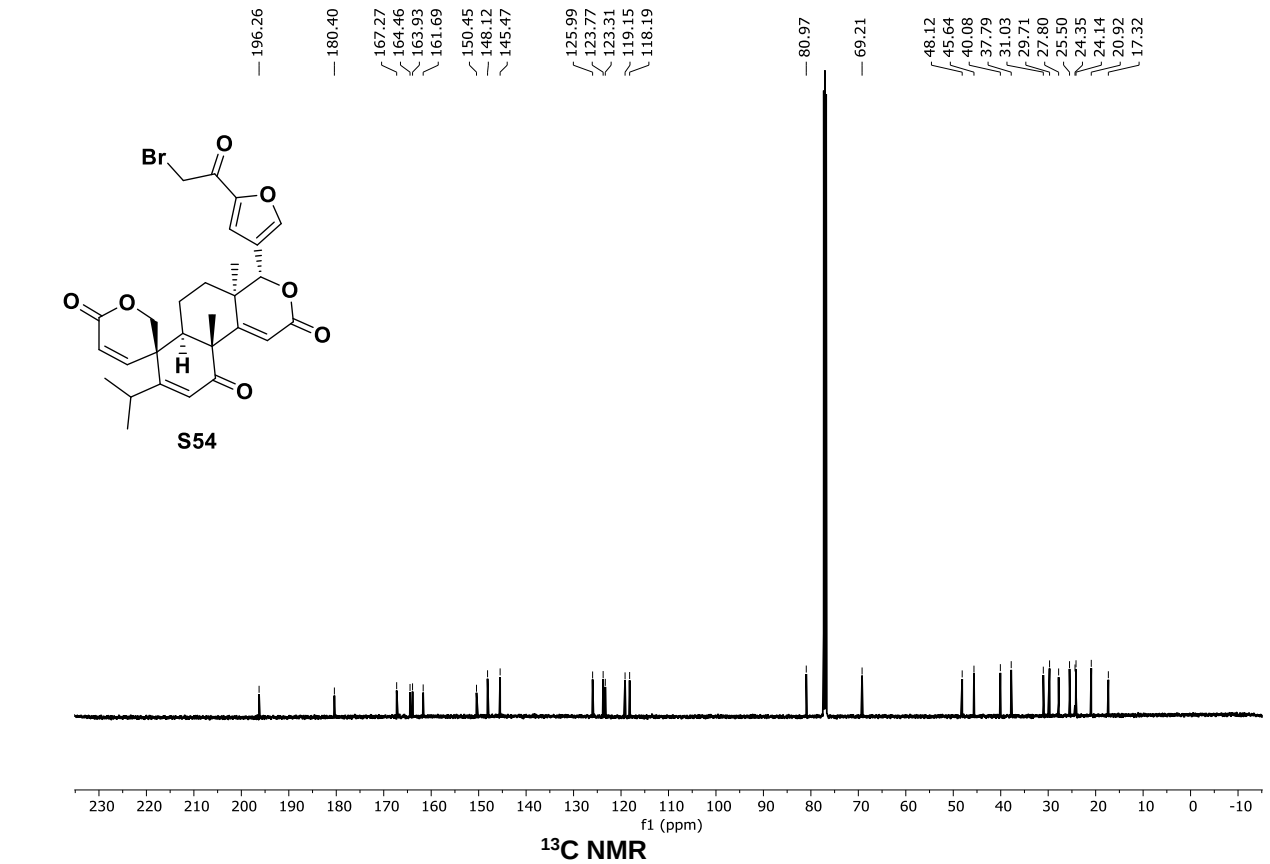
^{1}H NMR



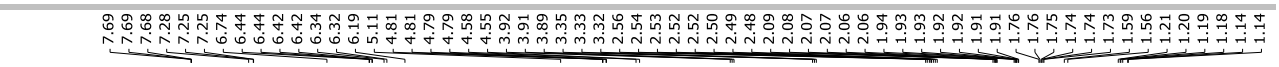
^{13}C NMR

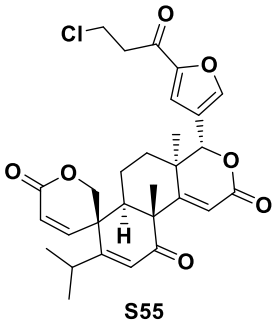


^{1}H NMR

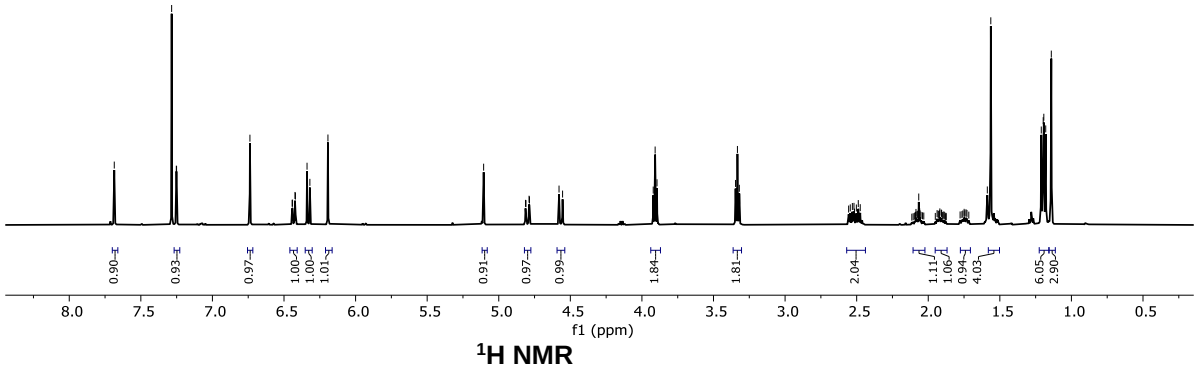


^{13}C NMR

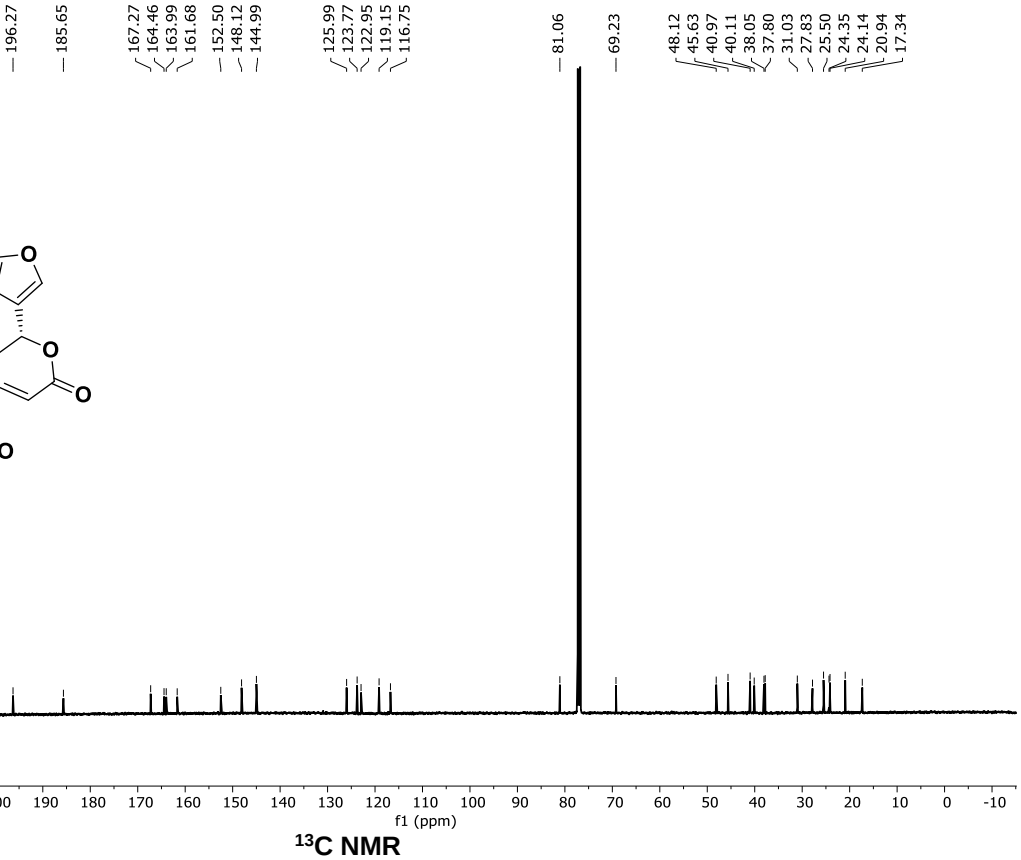


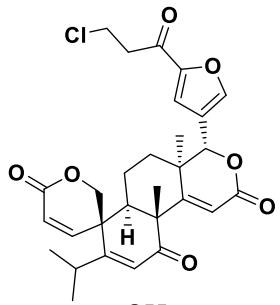


S55



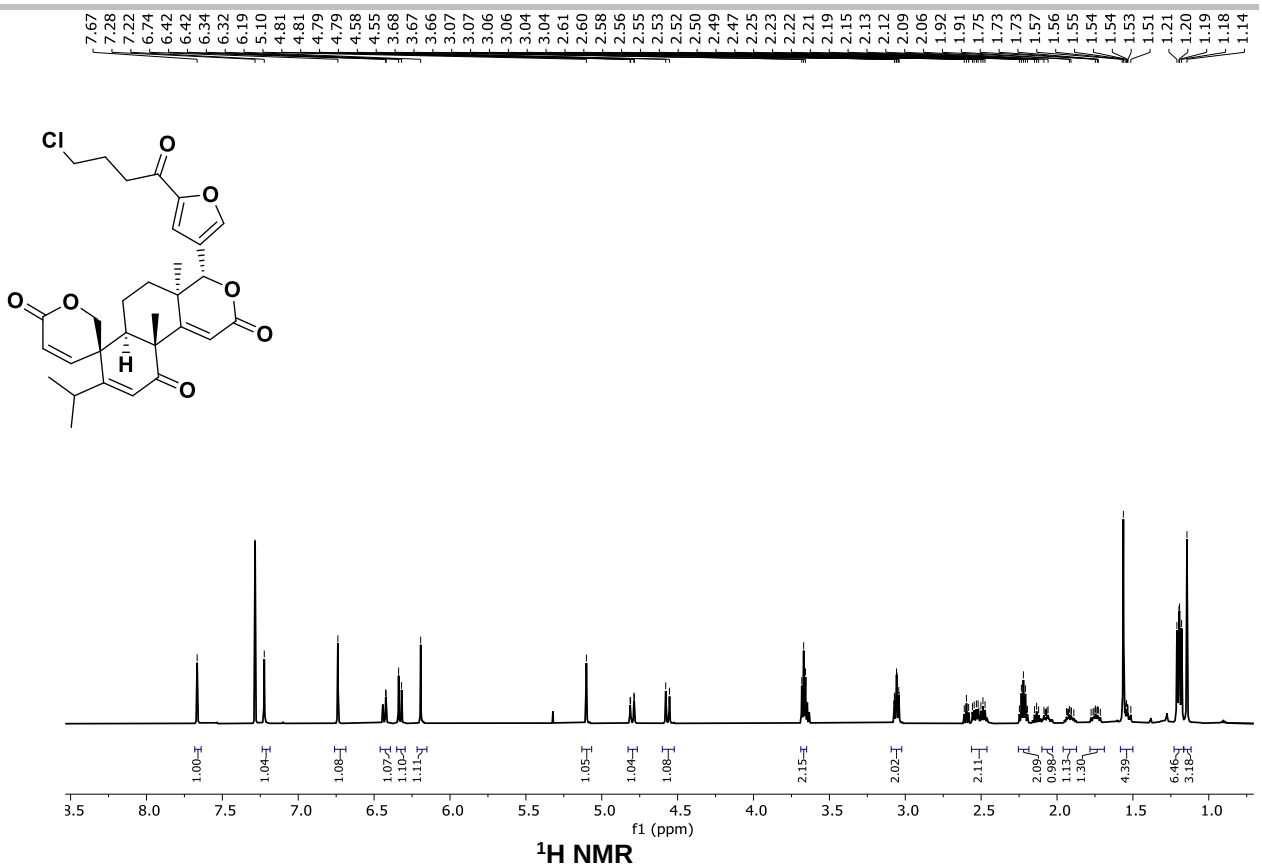
^{1}H NMR



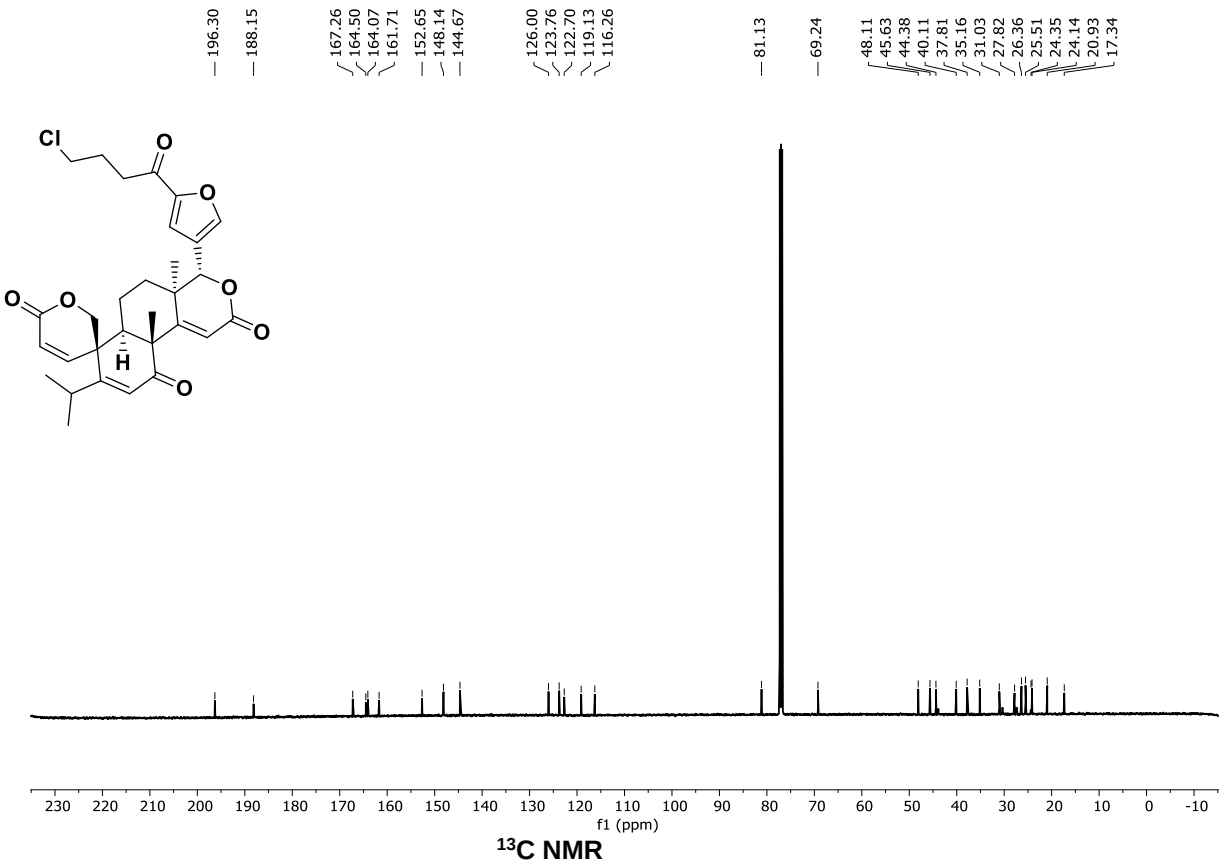


S55

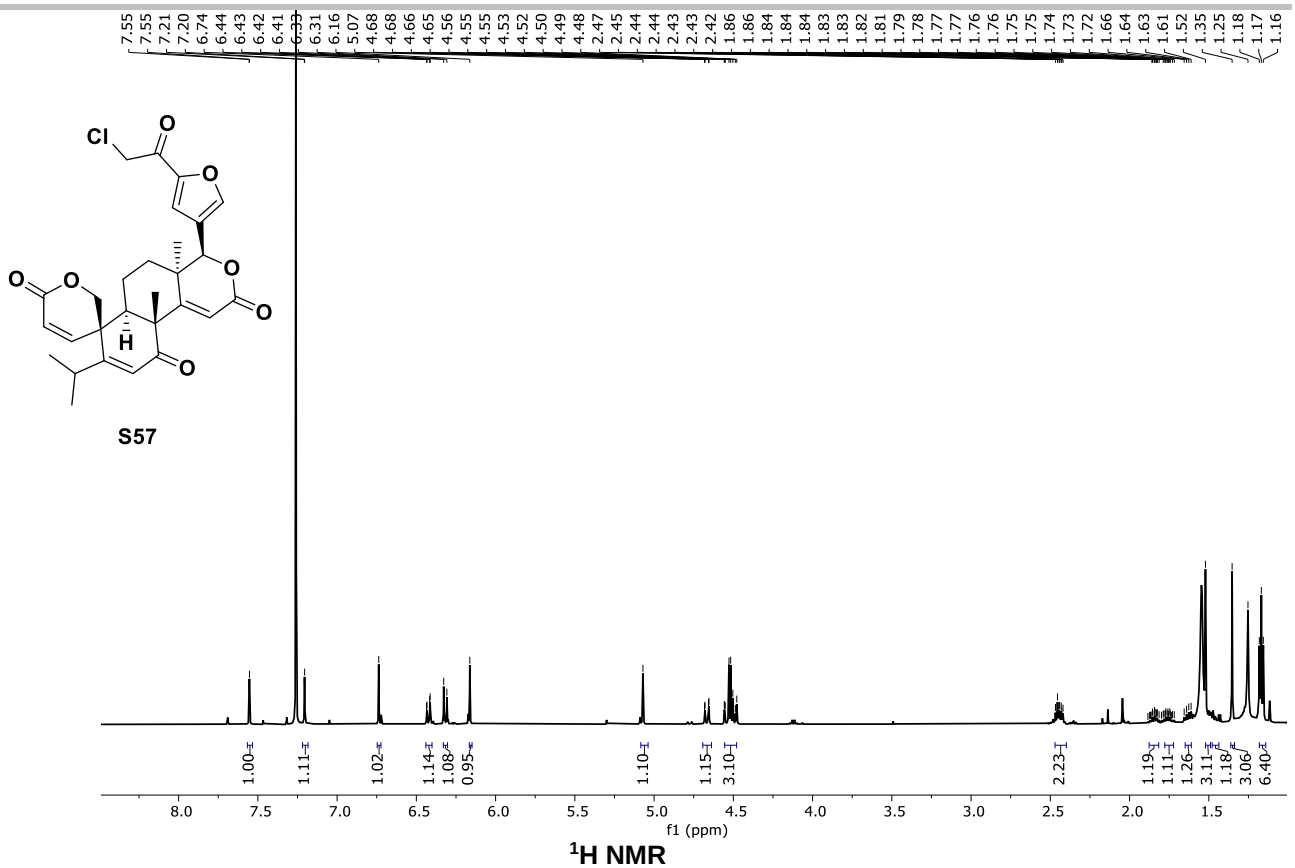
^{13}C NMR



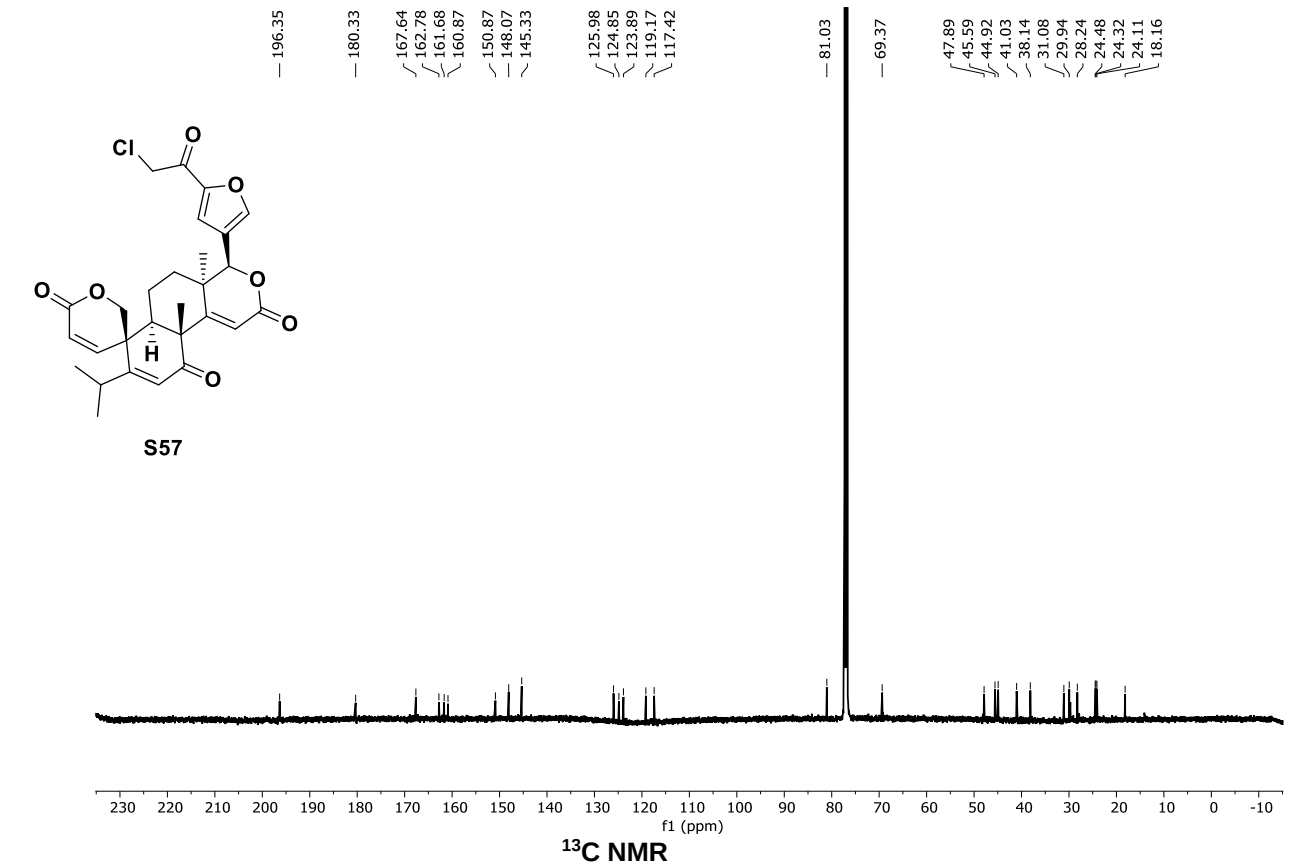
^{1}H NMR



^{13}C NMR



^{1}H NMR



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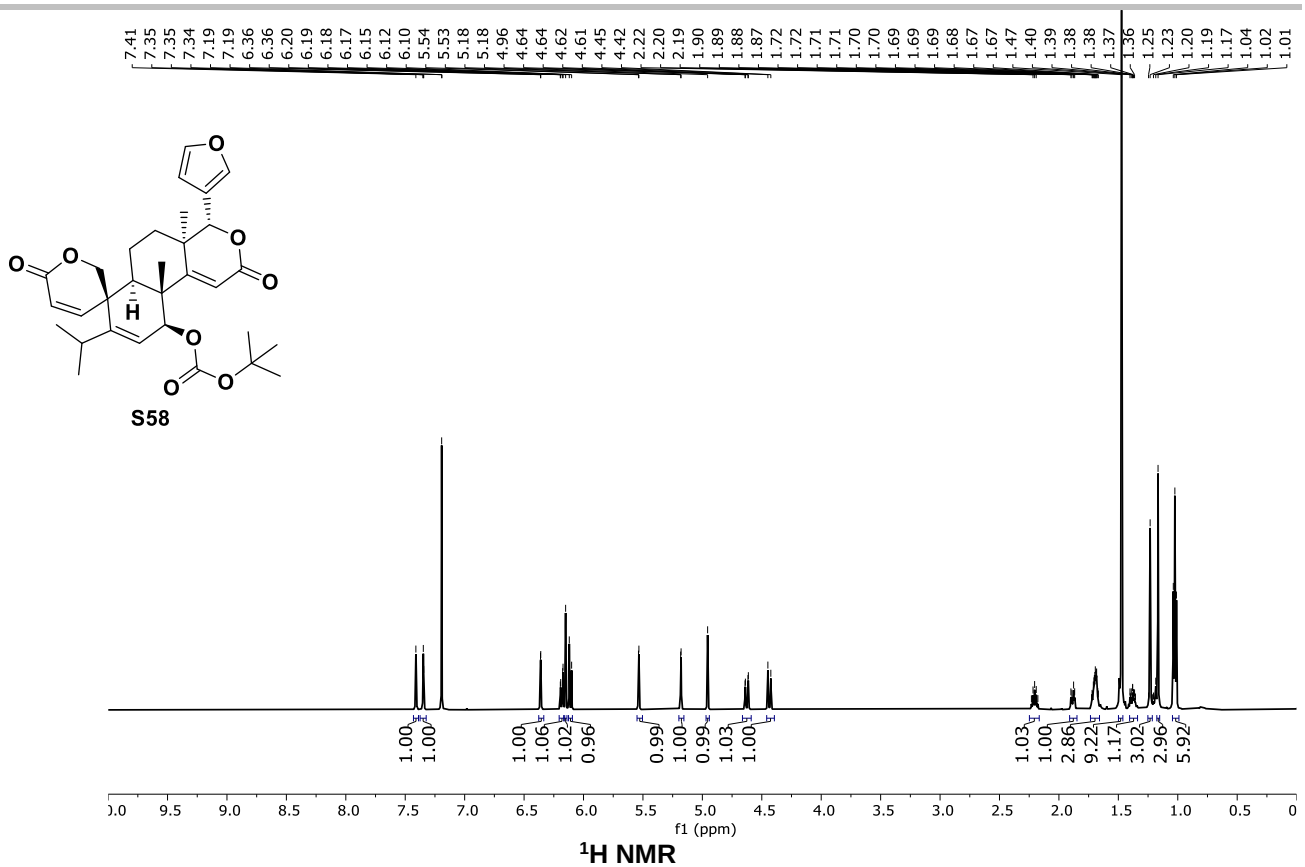
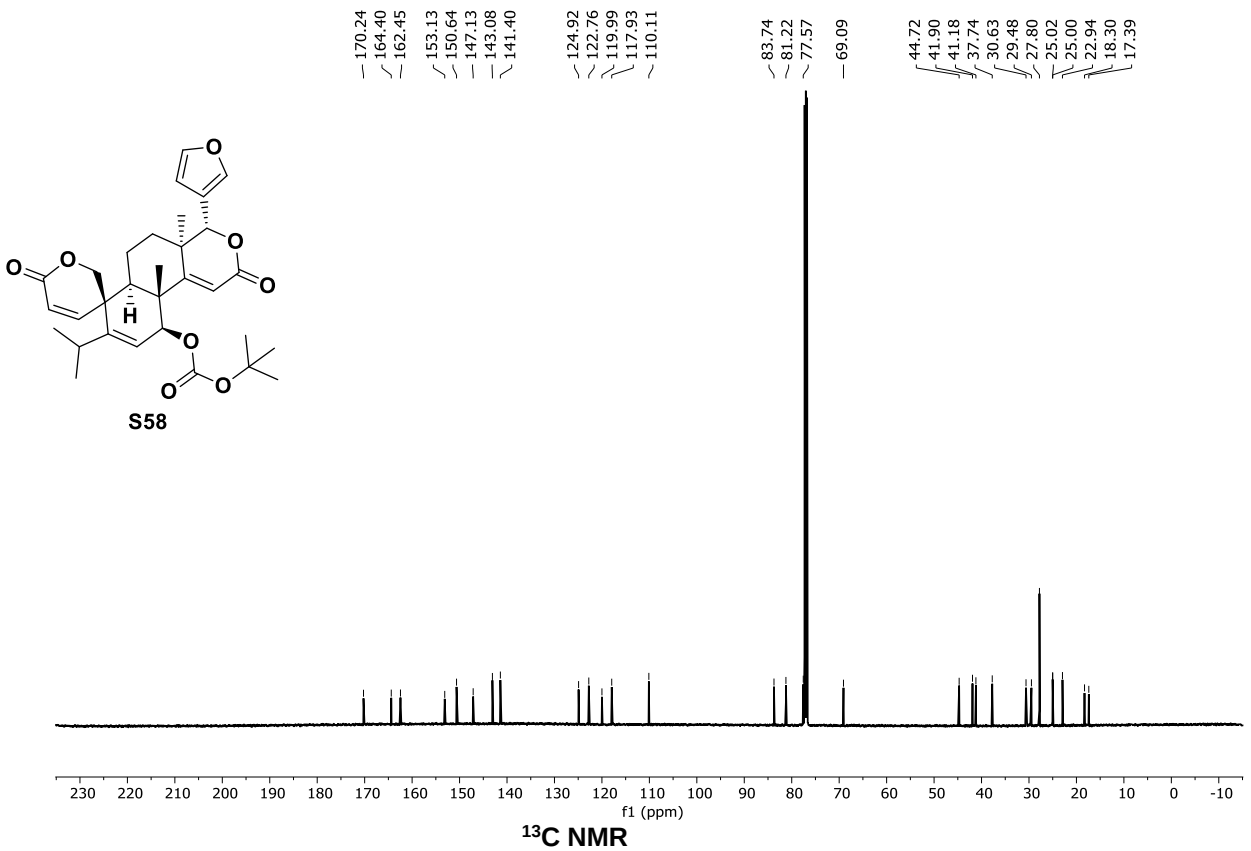
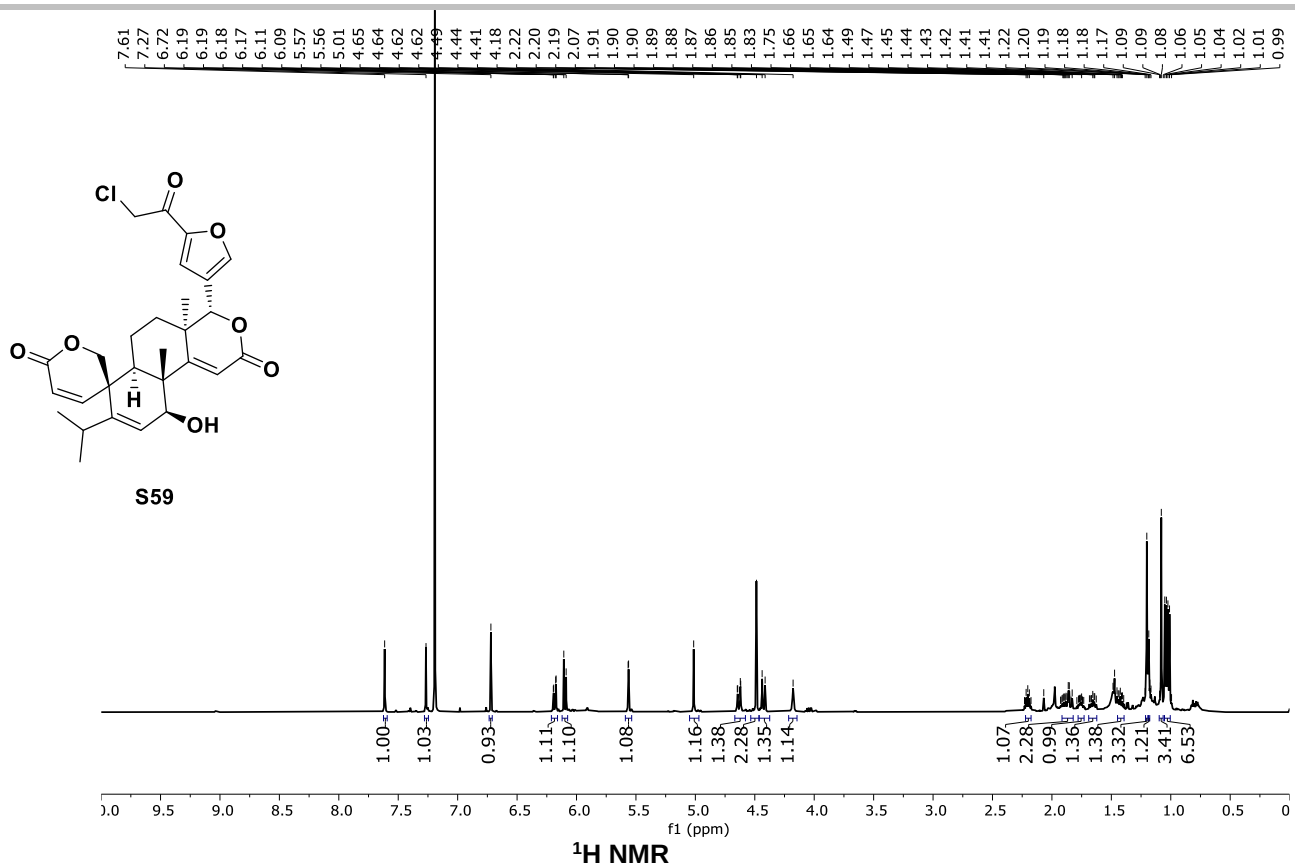


^{1}H NMR

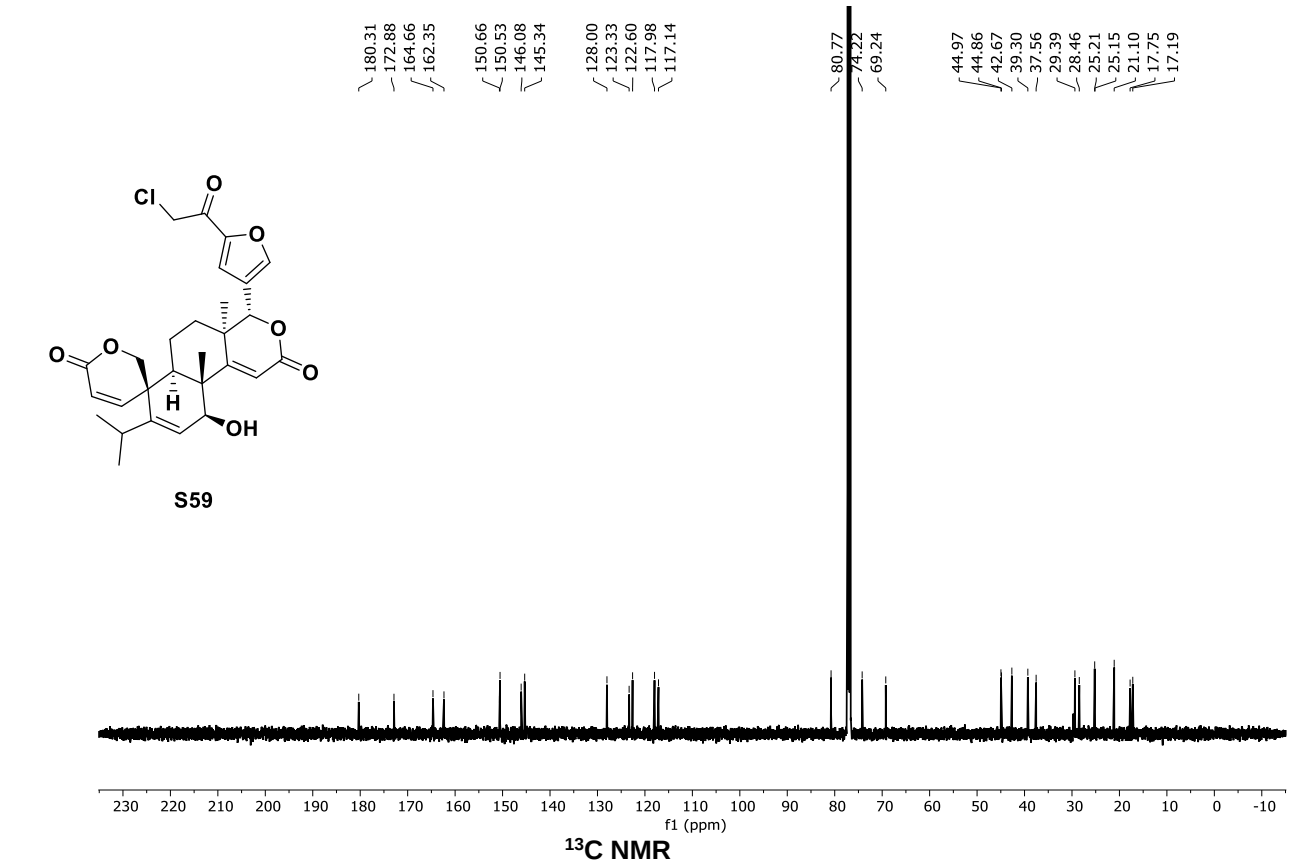


^{13}C NMR



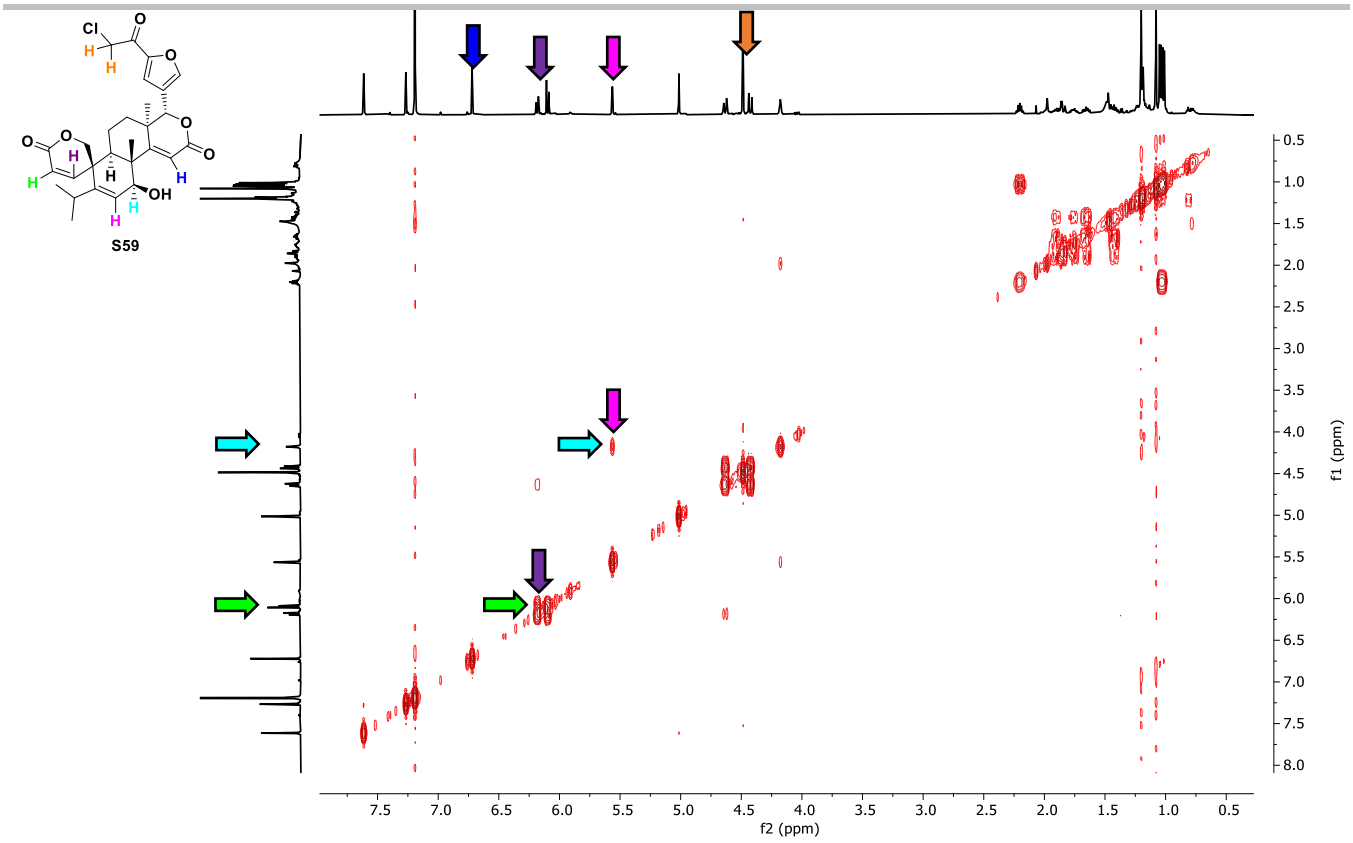
S59

^{1}H NMR

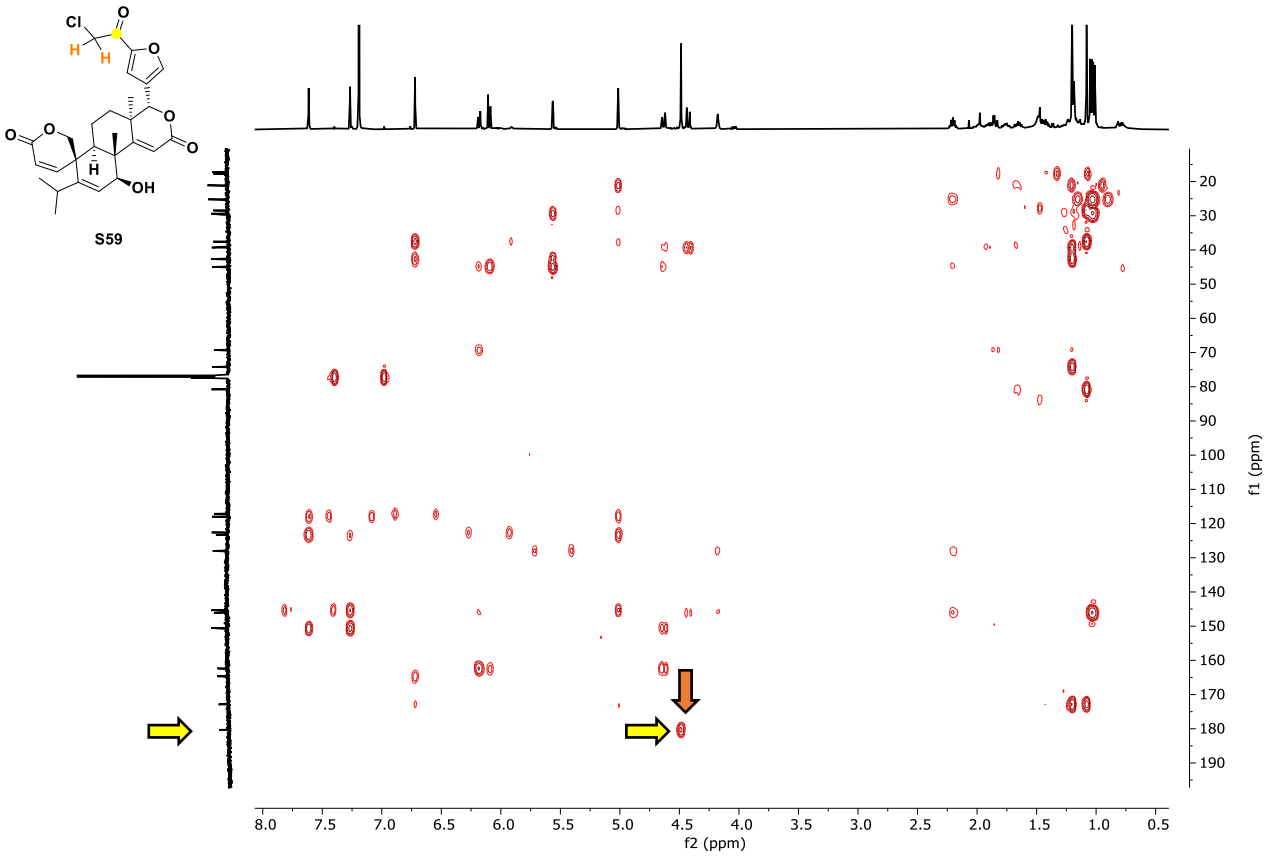


S59

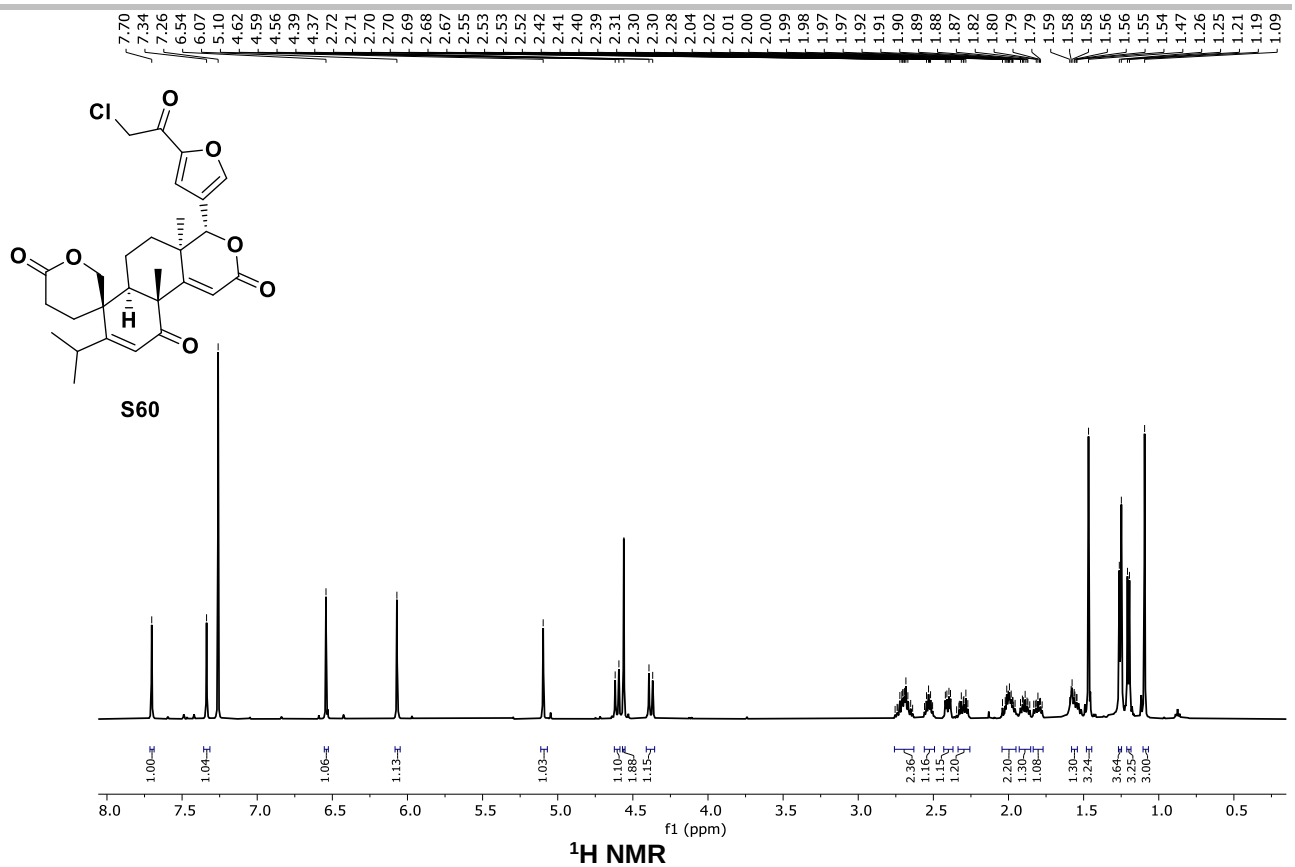
^{13}C NMR



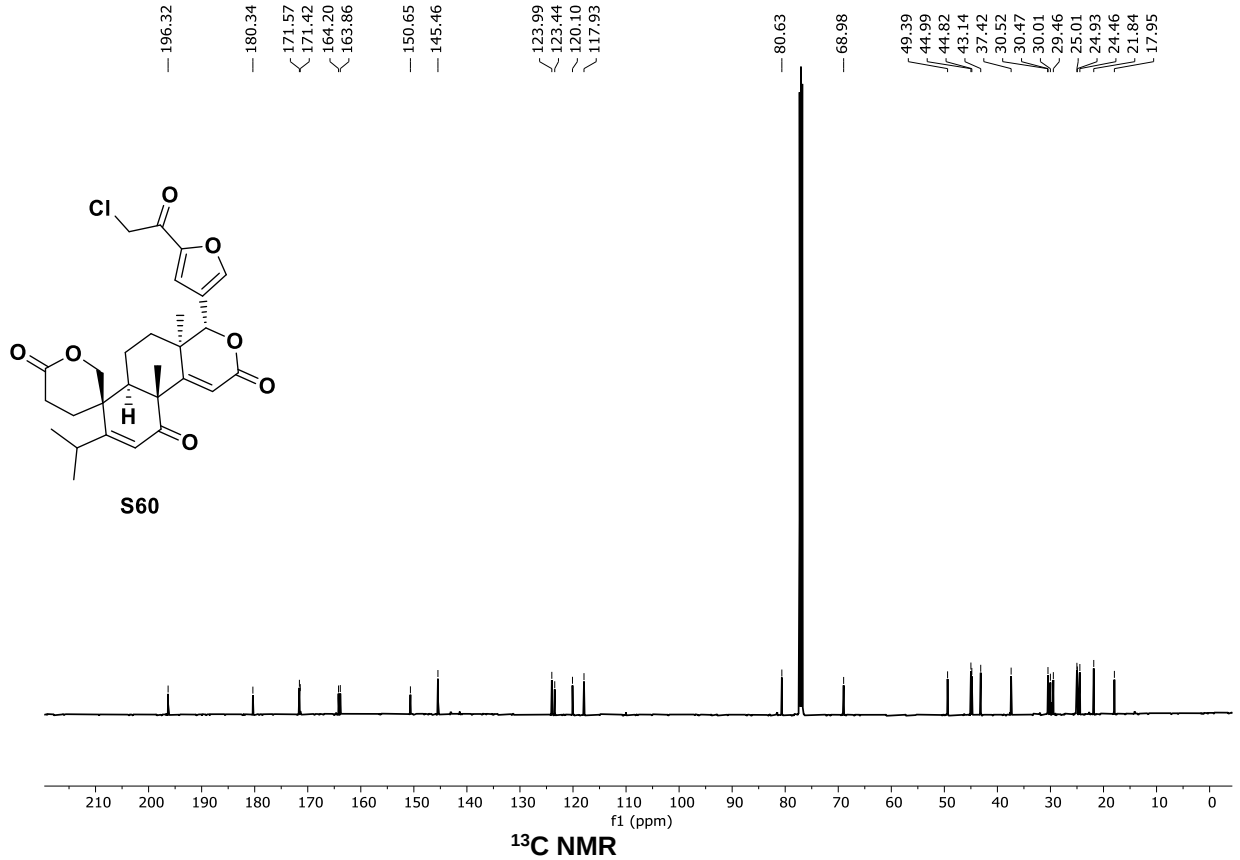
^{1}H-^{1}H COSY NMR



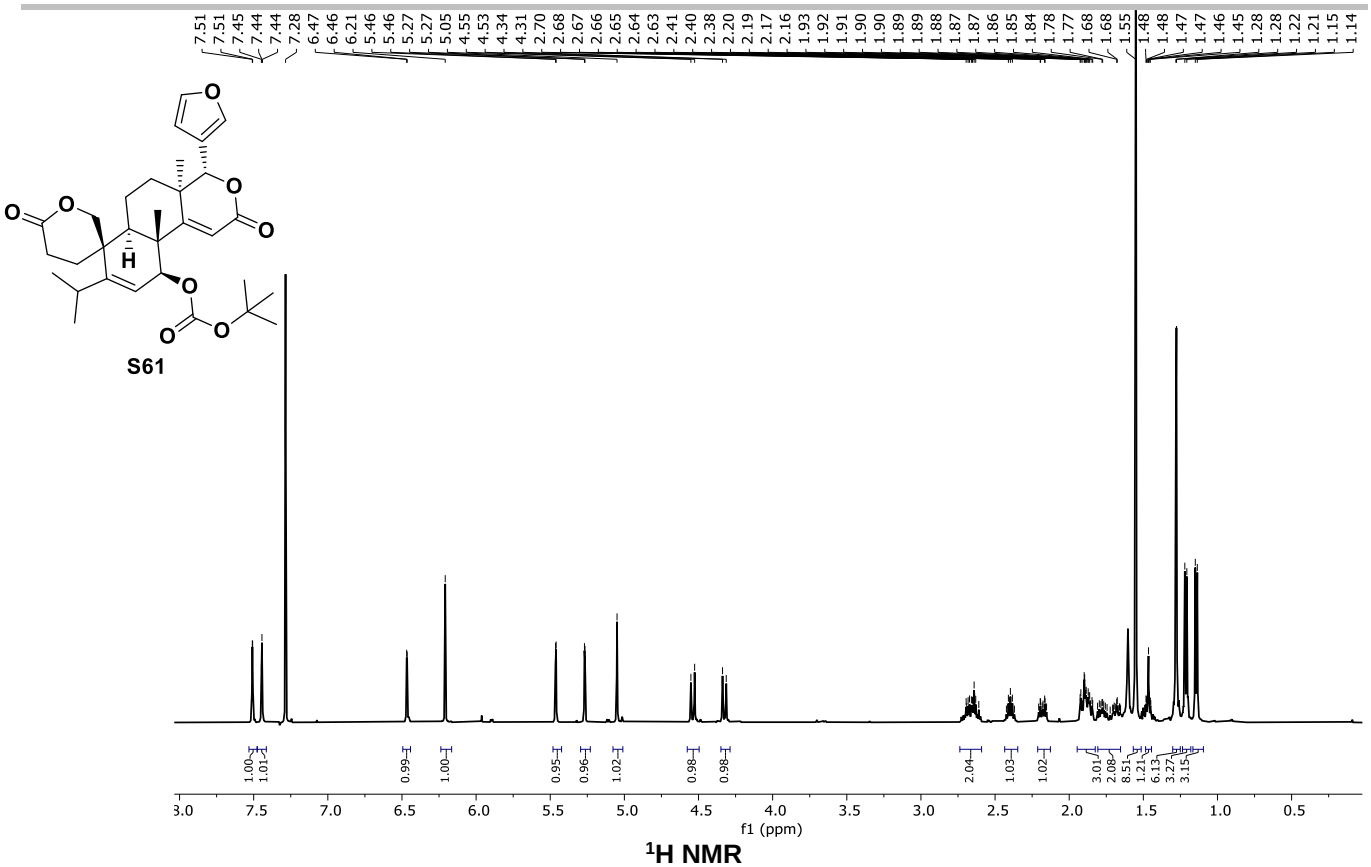
^{1}H-^{13}C HMBC NMR



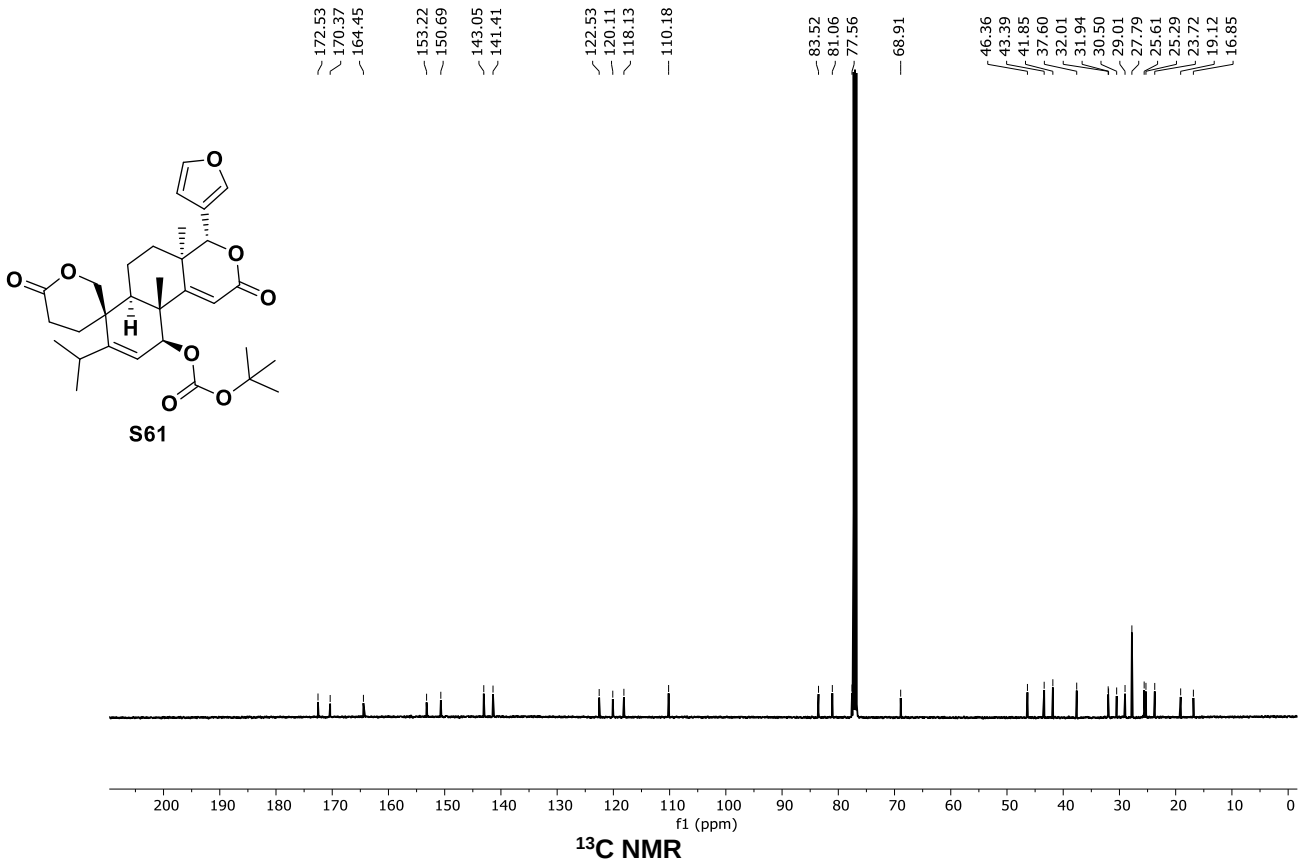
^{1}H NMR



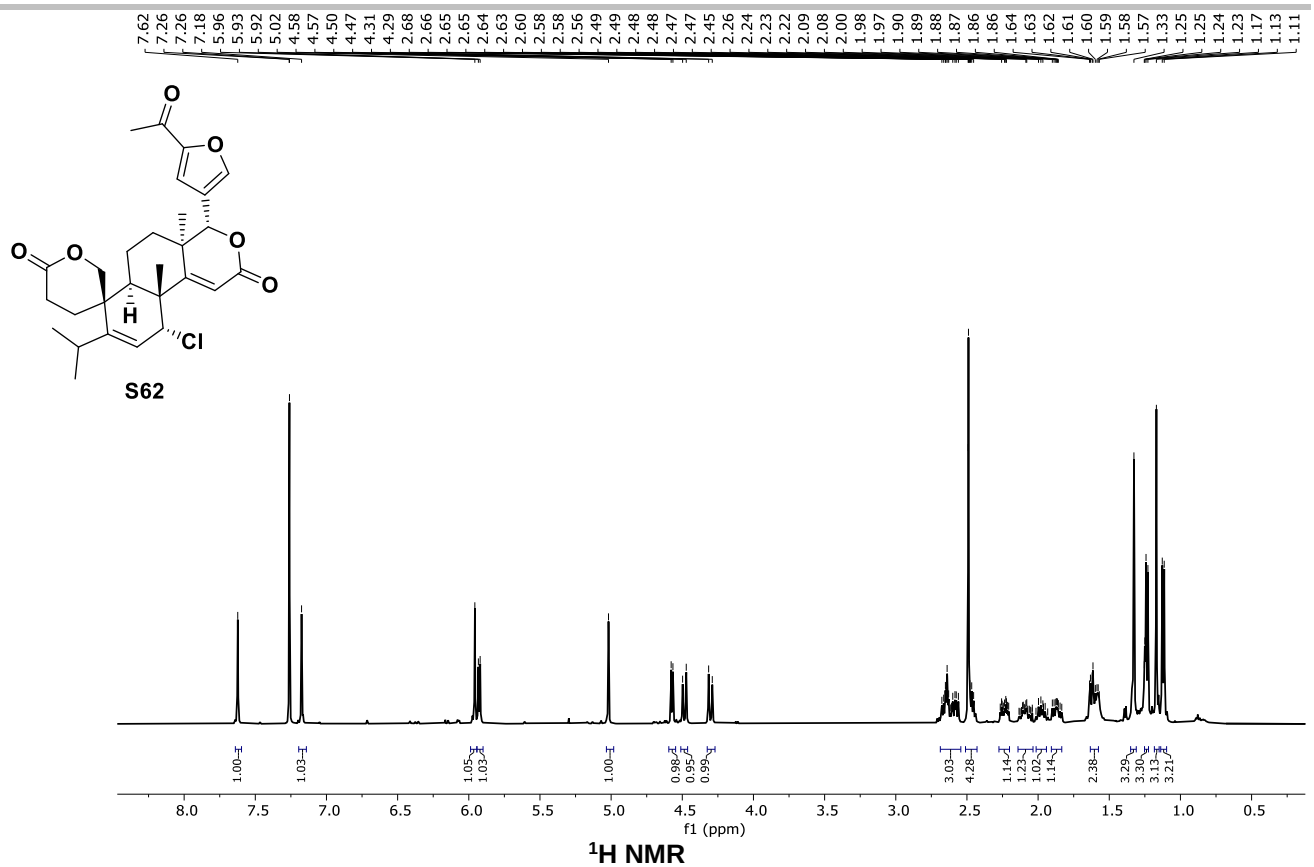
^{13}C NMR



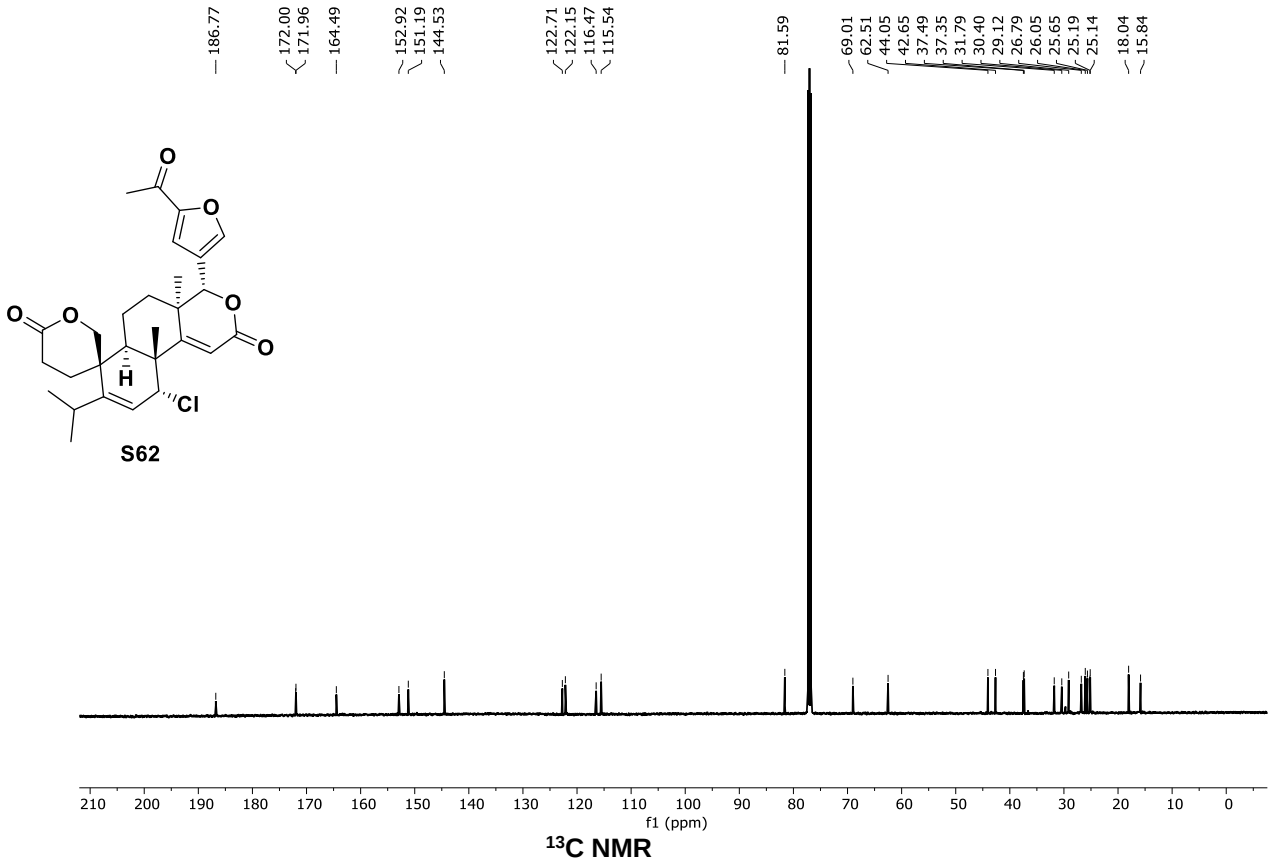
^{1}H NMR



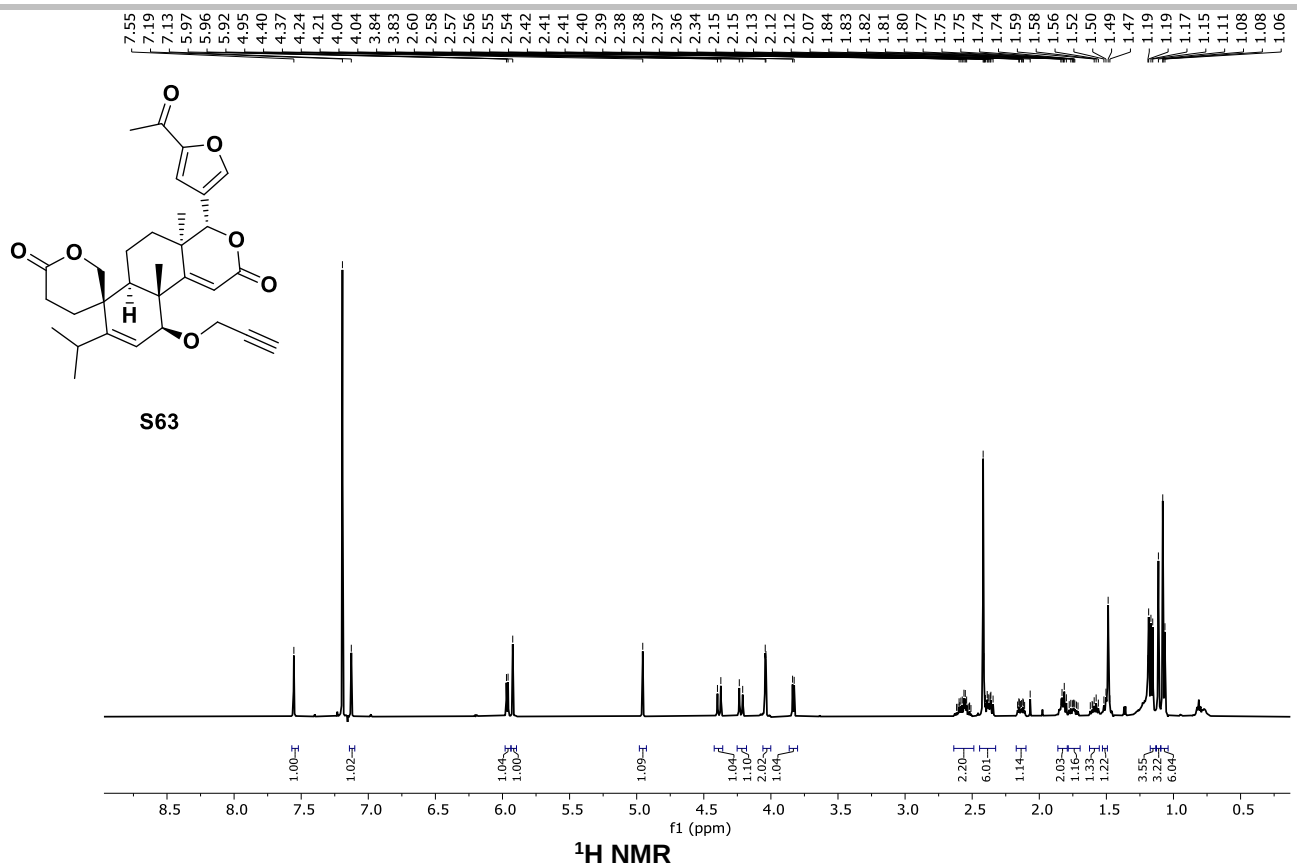
^{13}C NMR



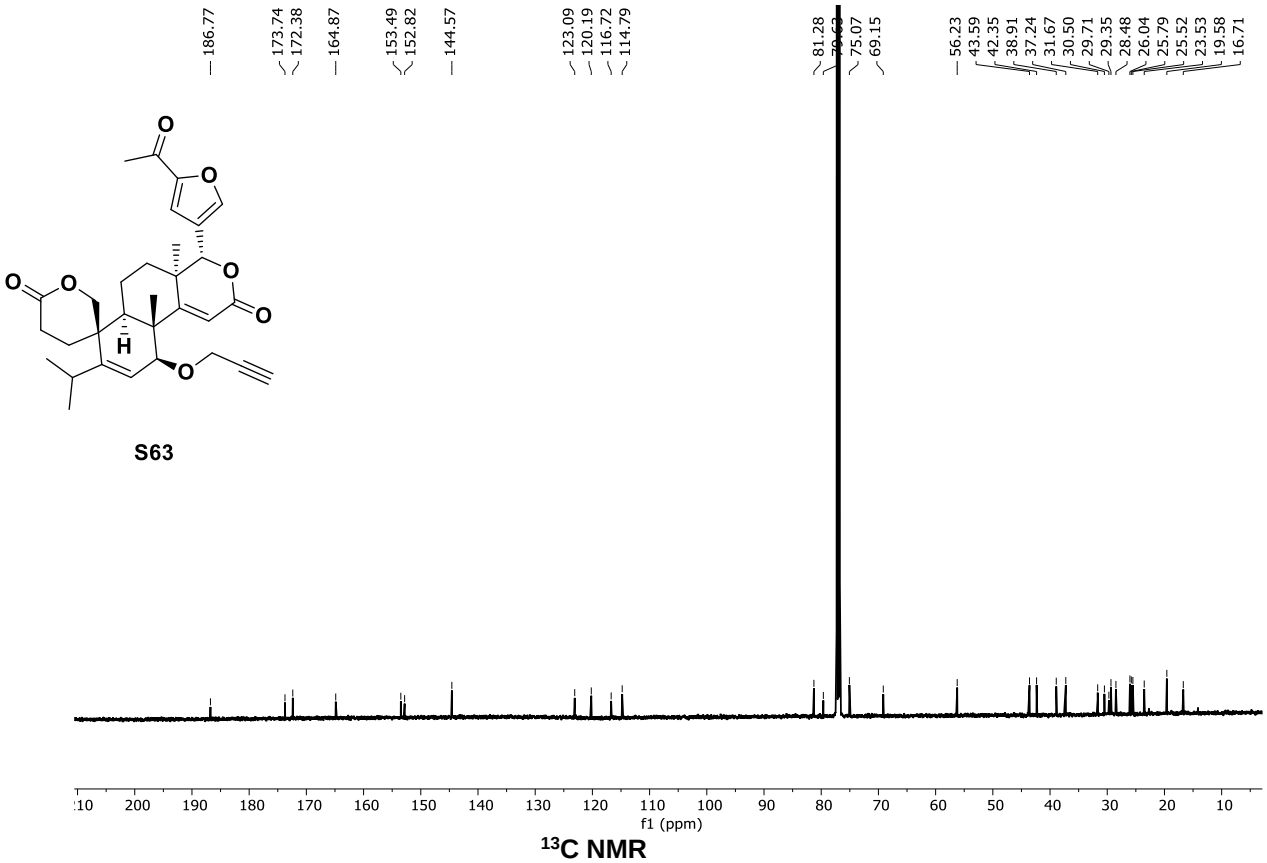
^{1}H NMR



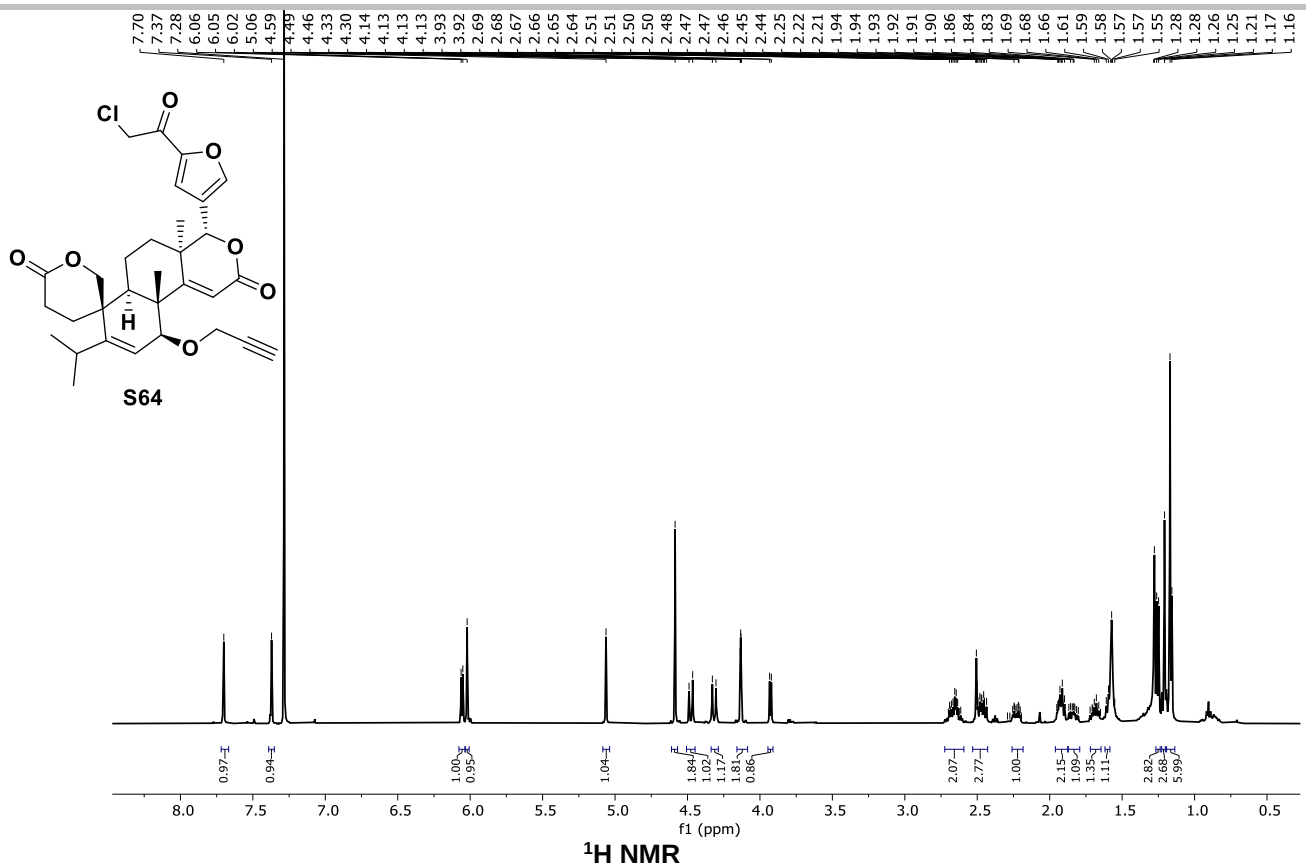
^{13}C NMR



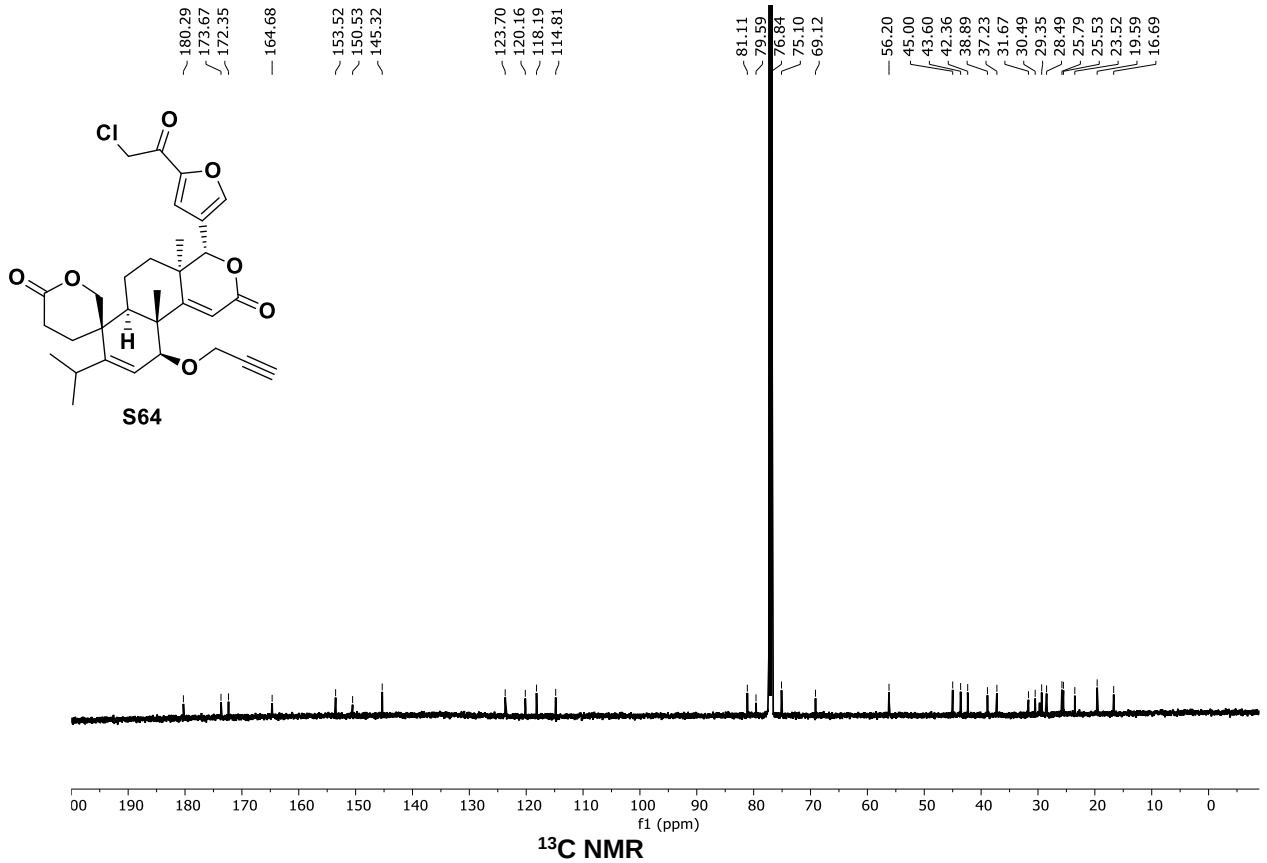
^{1}H NMR



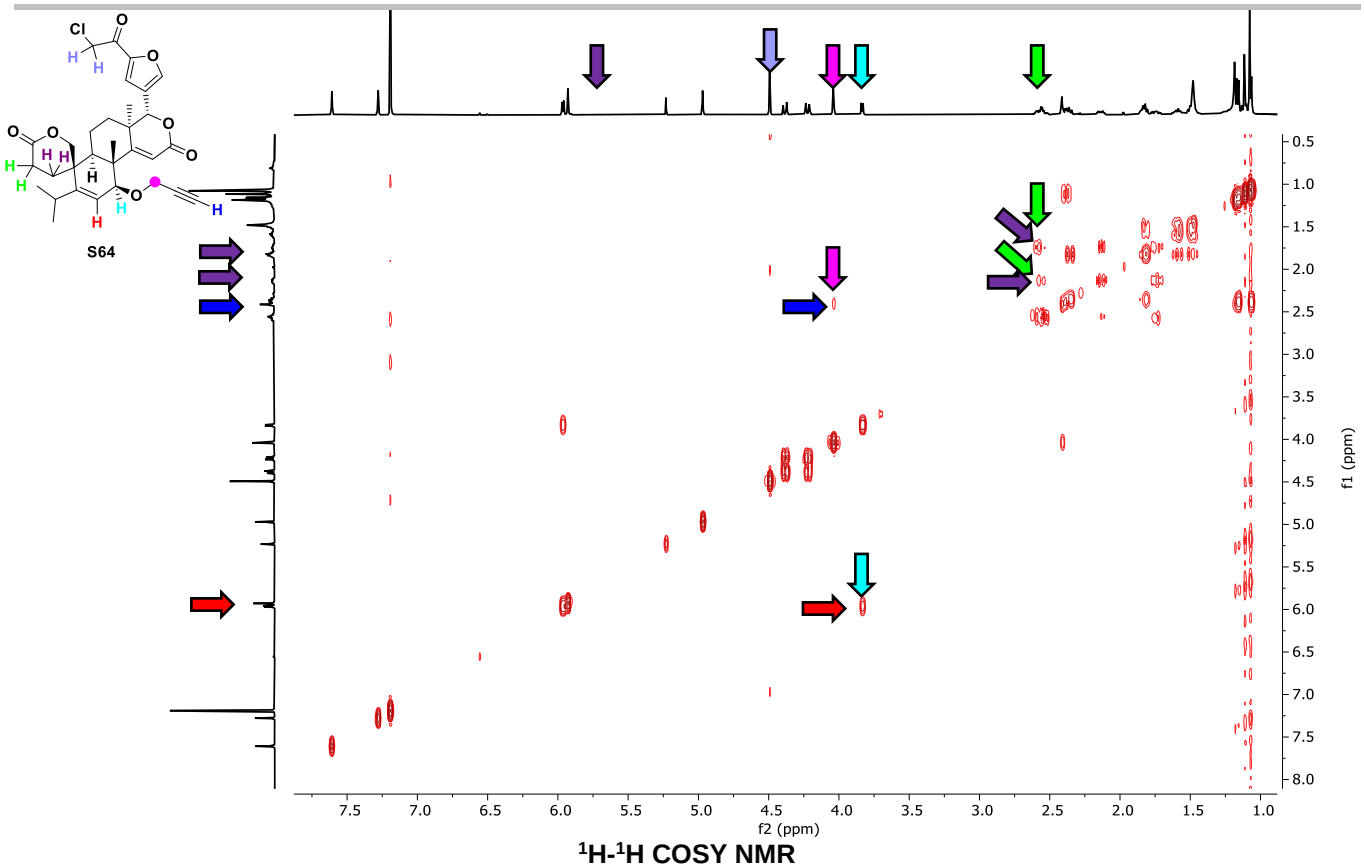
^{13}C NMR



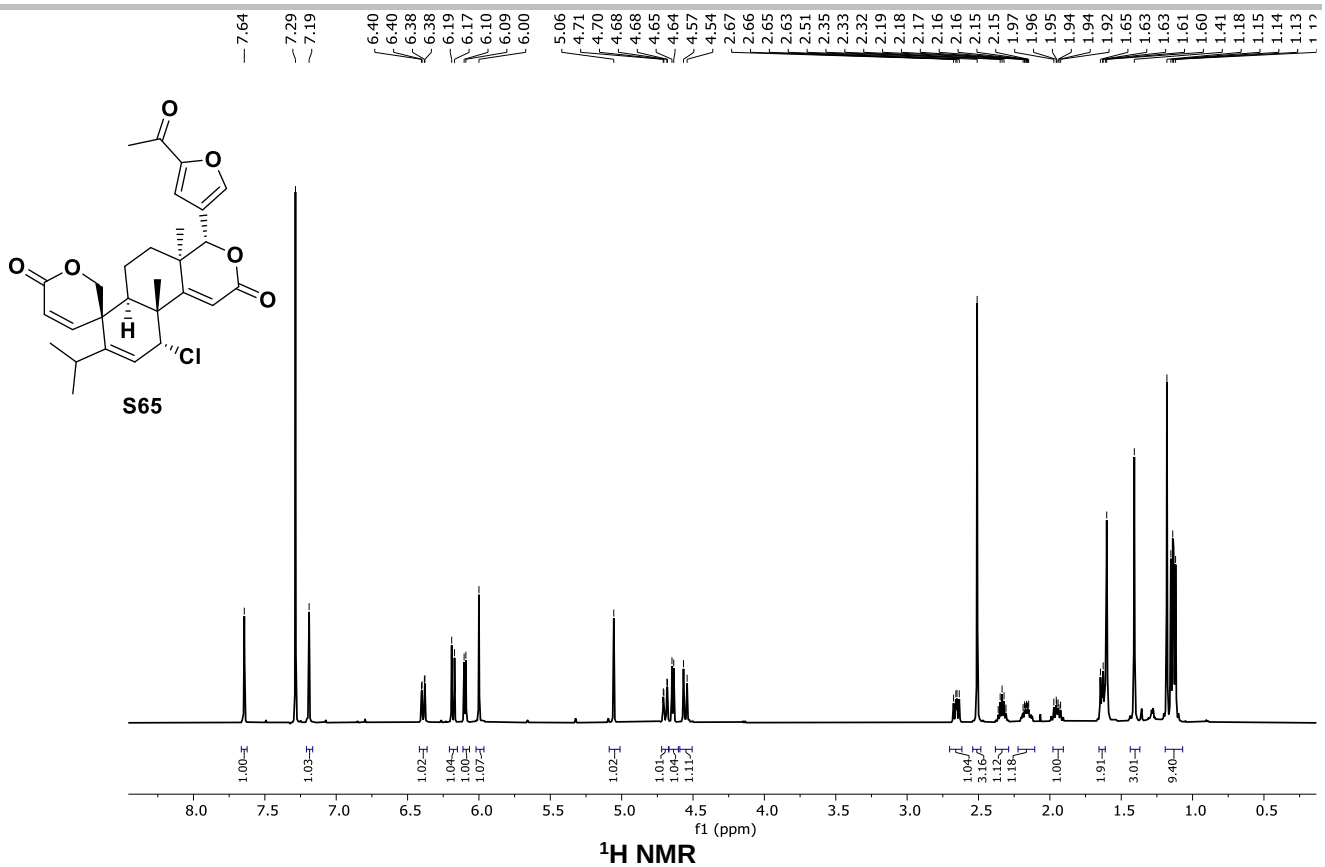
^{1}H NMR



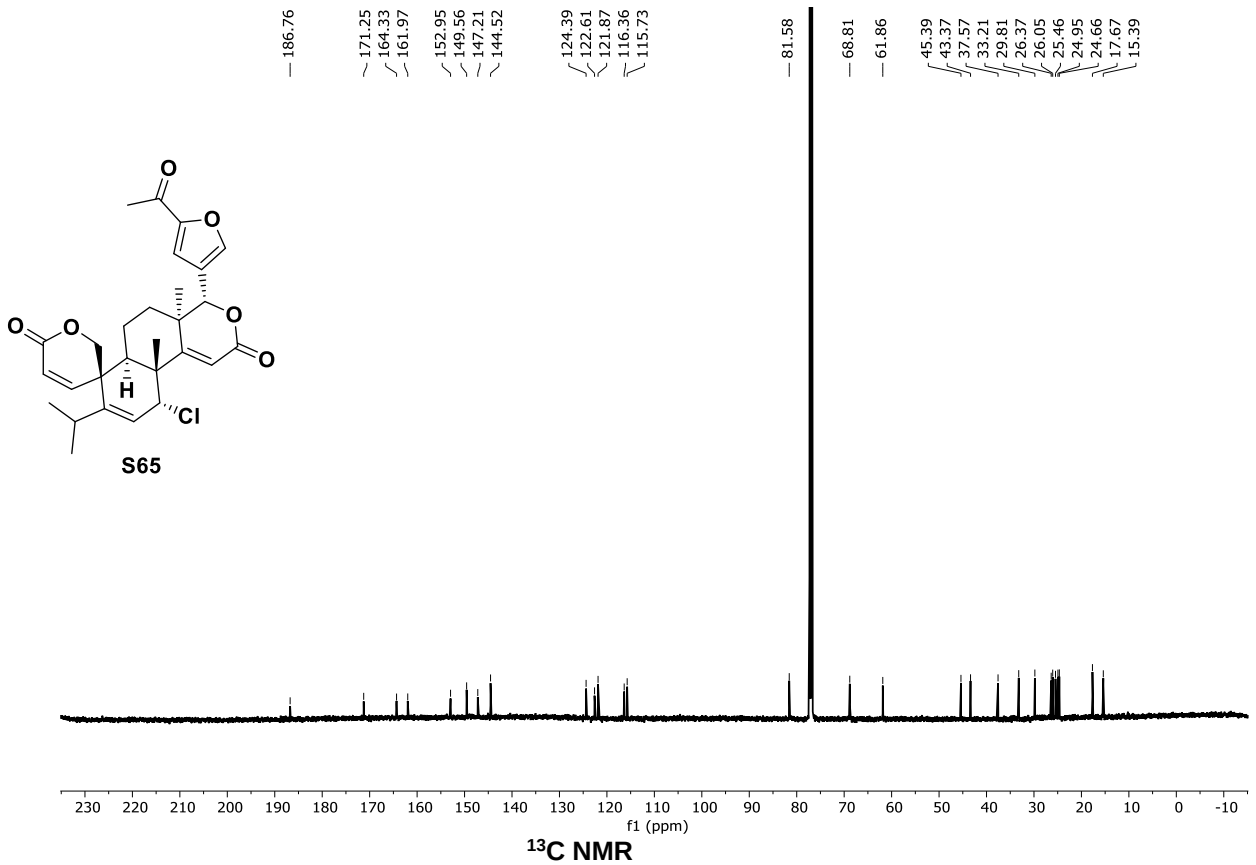
^{13}C NMR



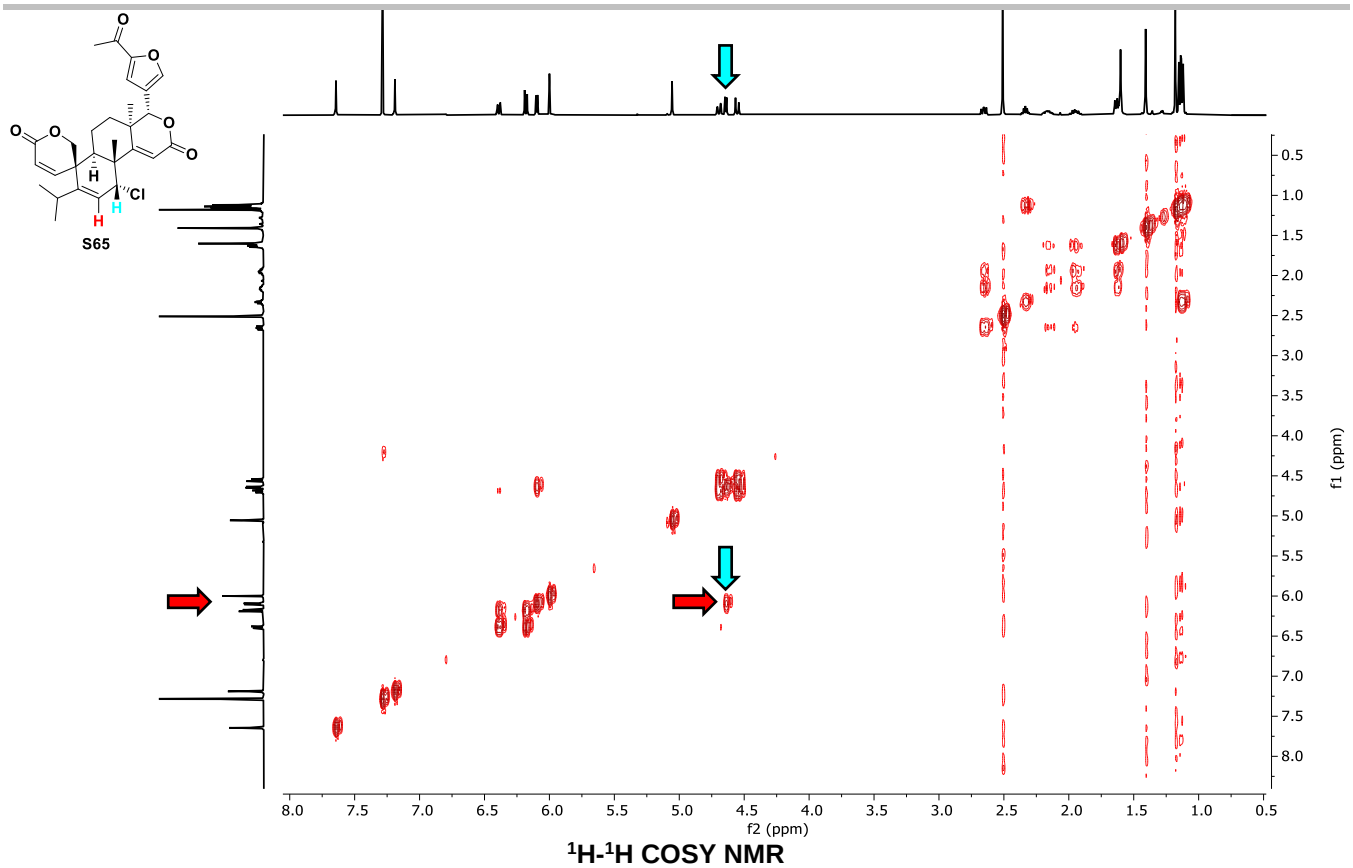
^{1}H-^{1}H COSY NMR



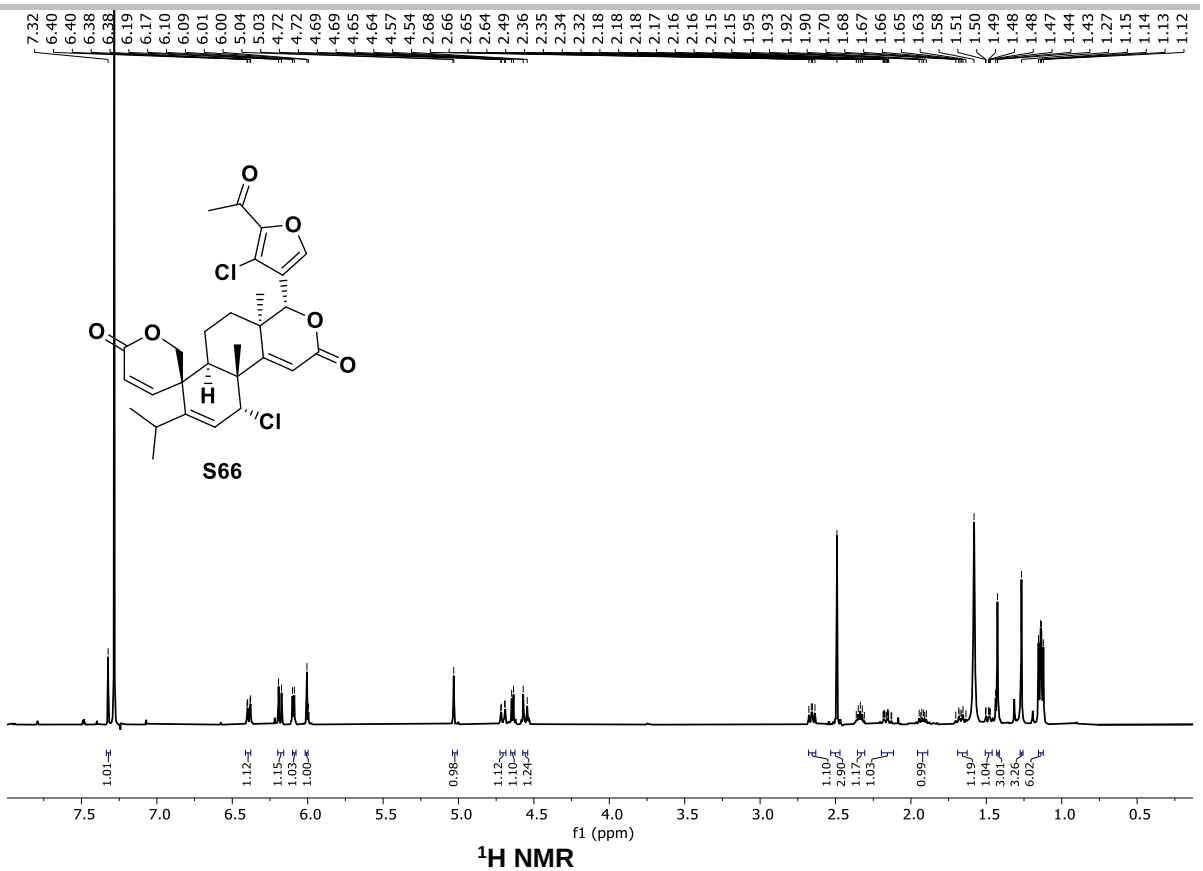
^{1}H NMR



^{13}C NMR

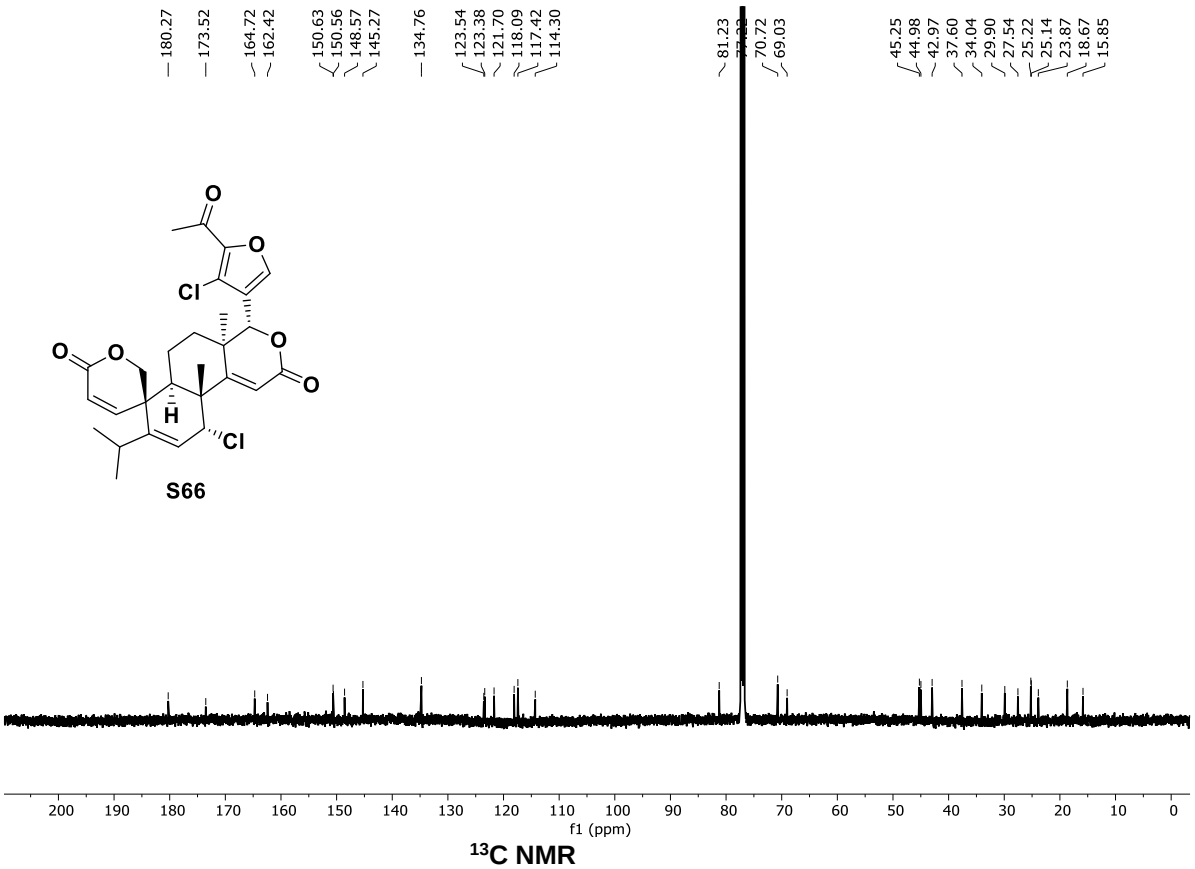


^{1}H-^{1}H COSY NMR



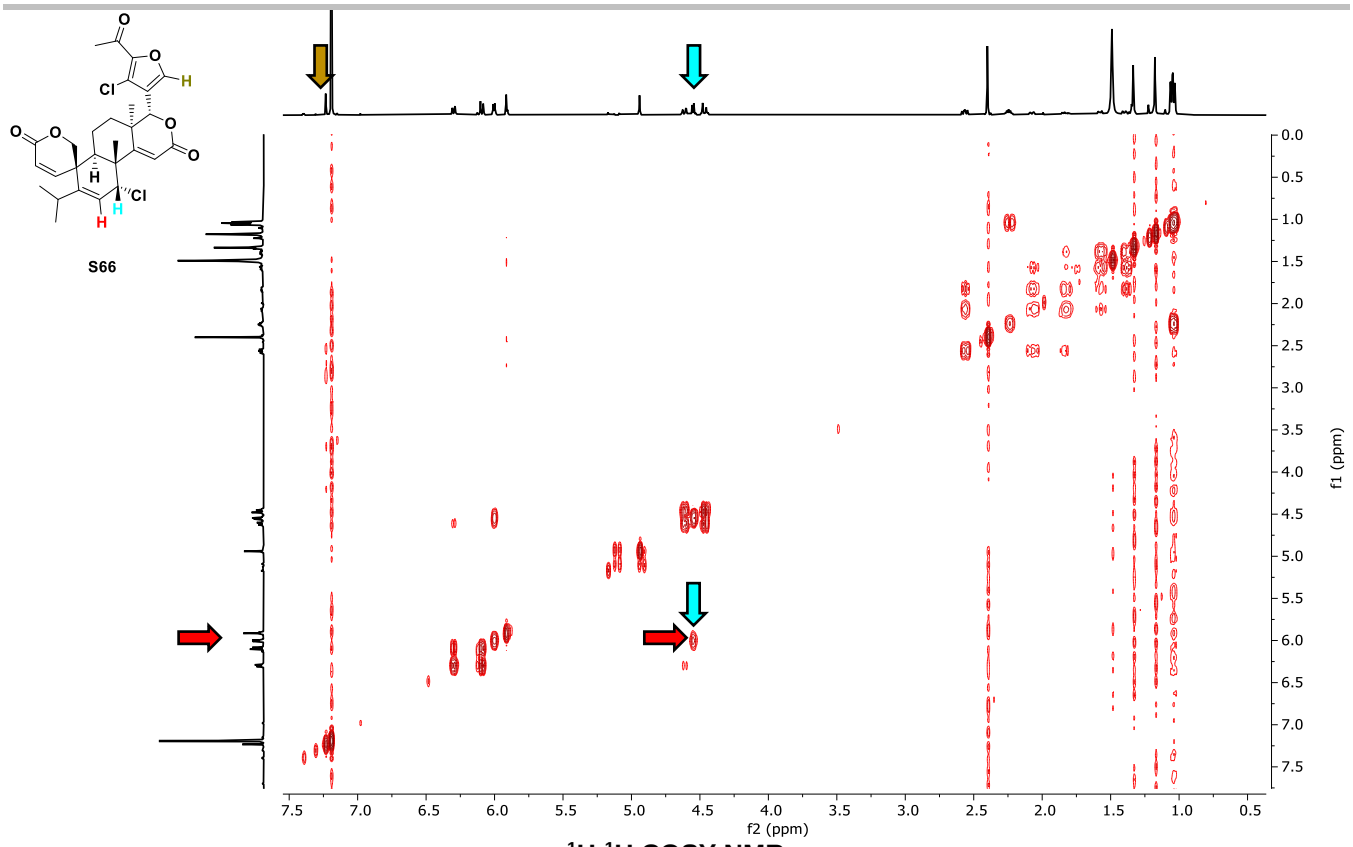
S66

^{1}H NMR

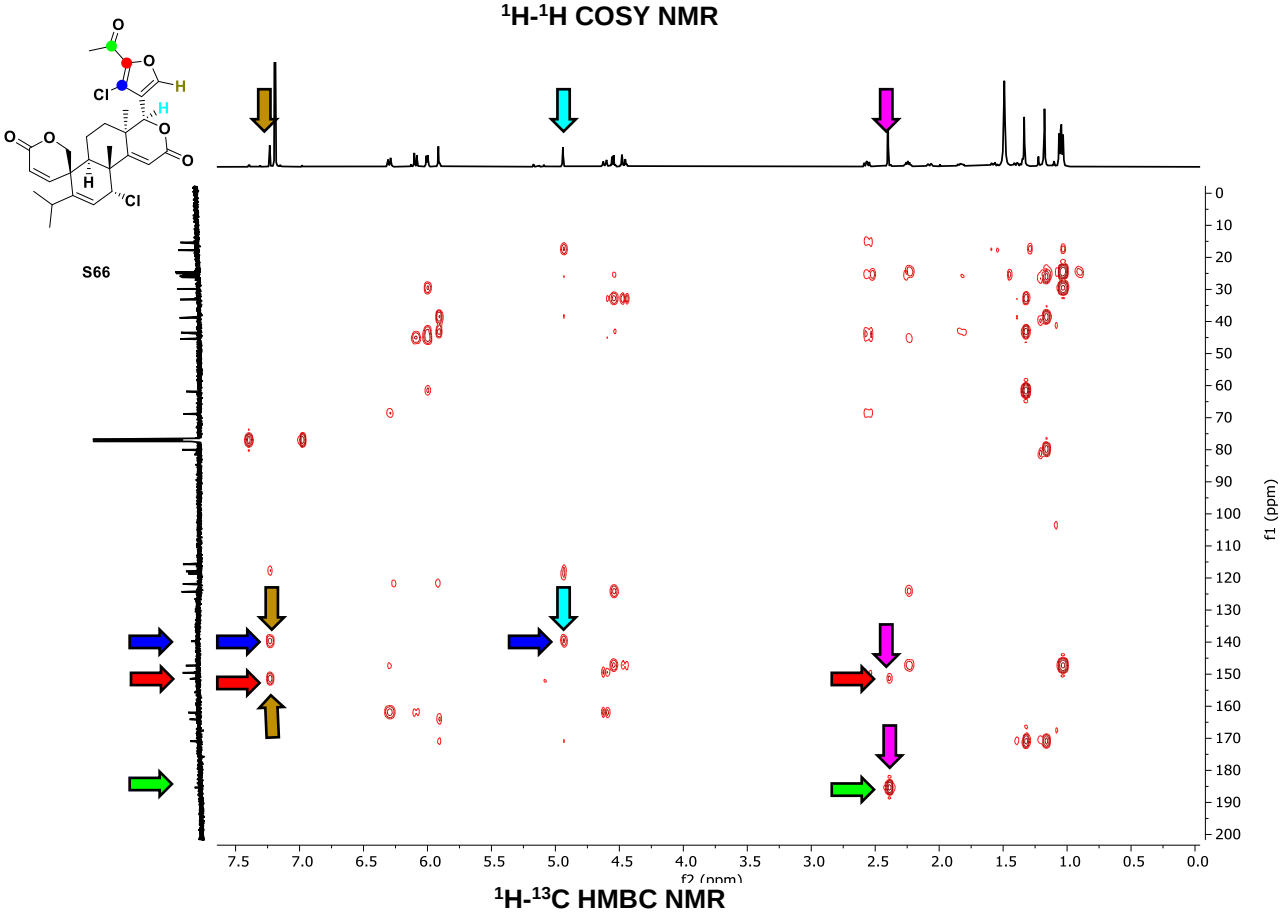


S66

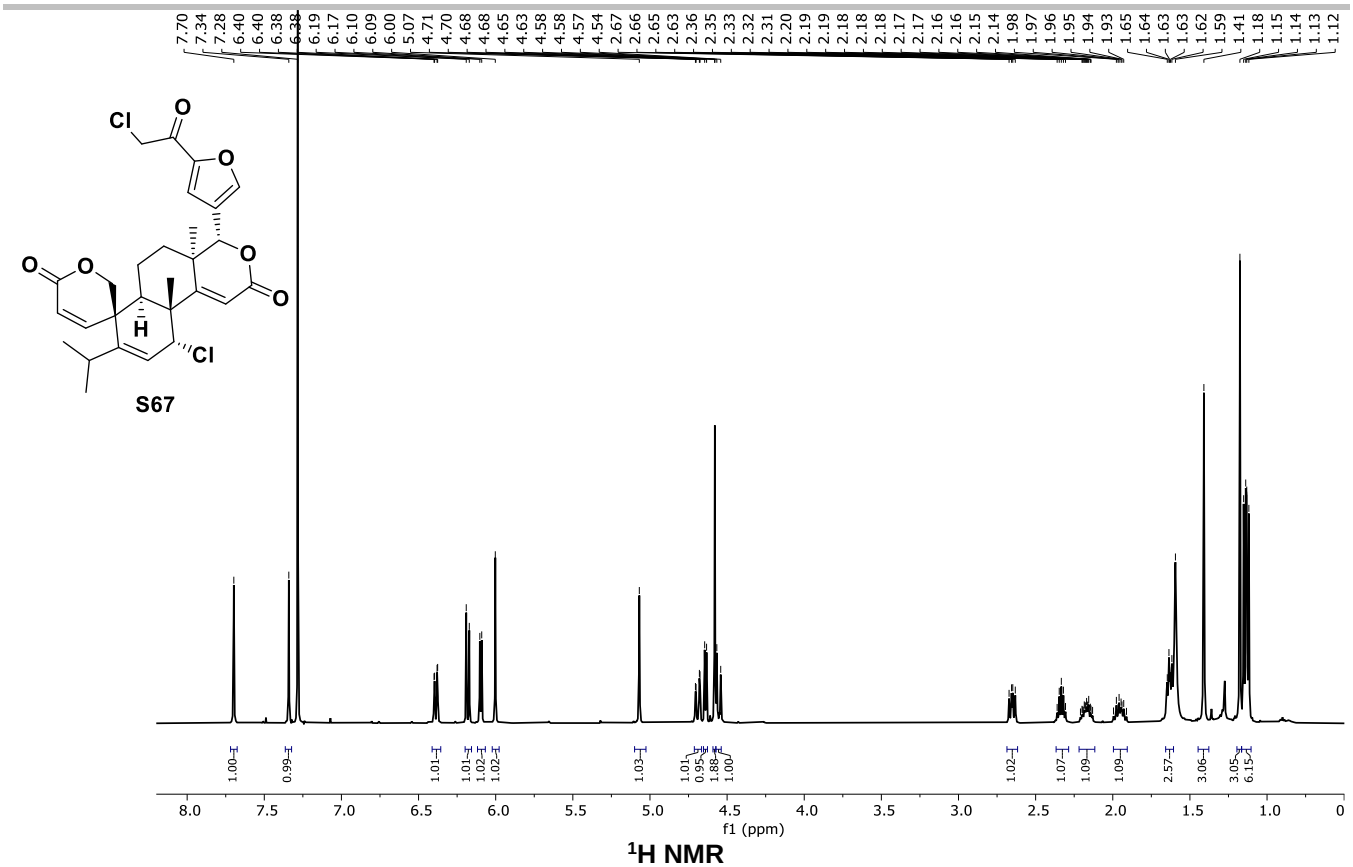
^{13}C NMR



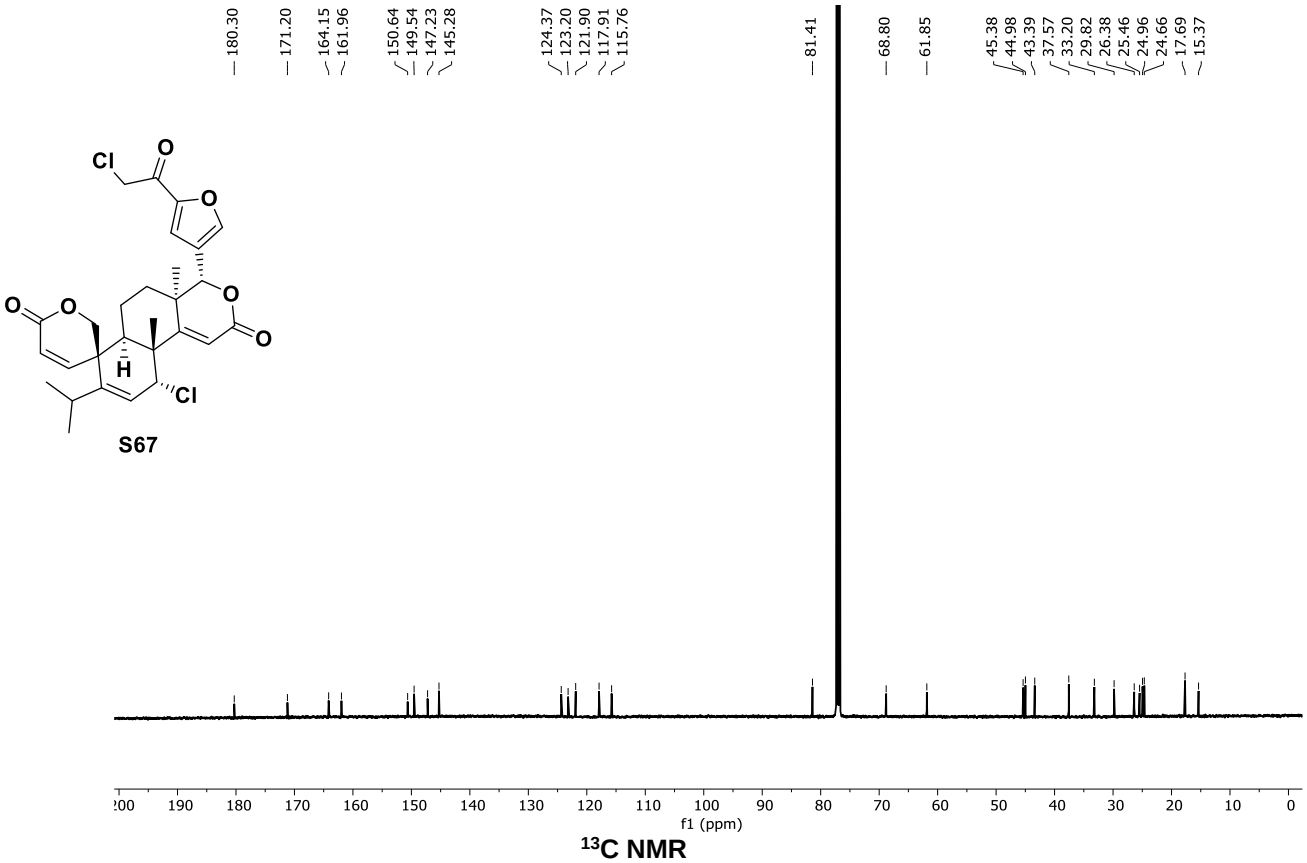
^{1}H-^{1}H COSY NMR



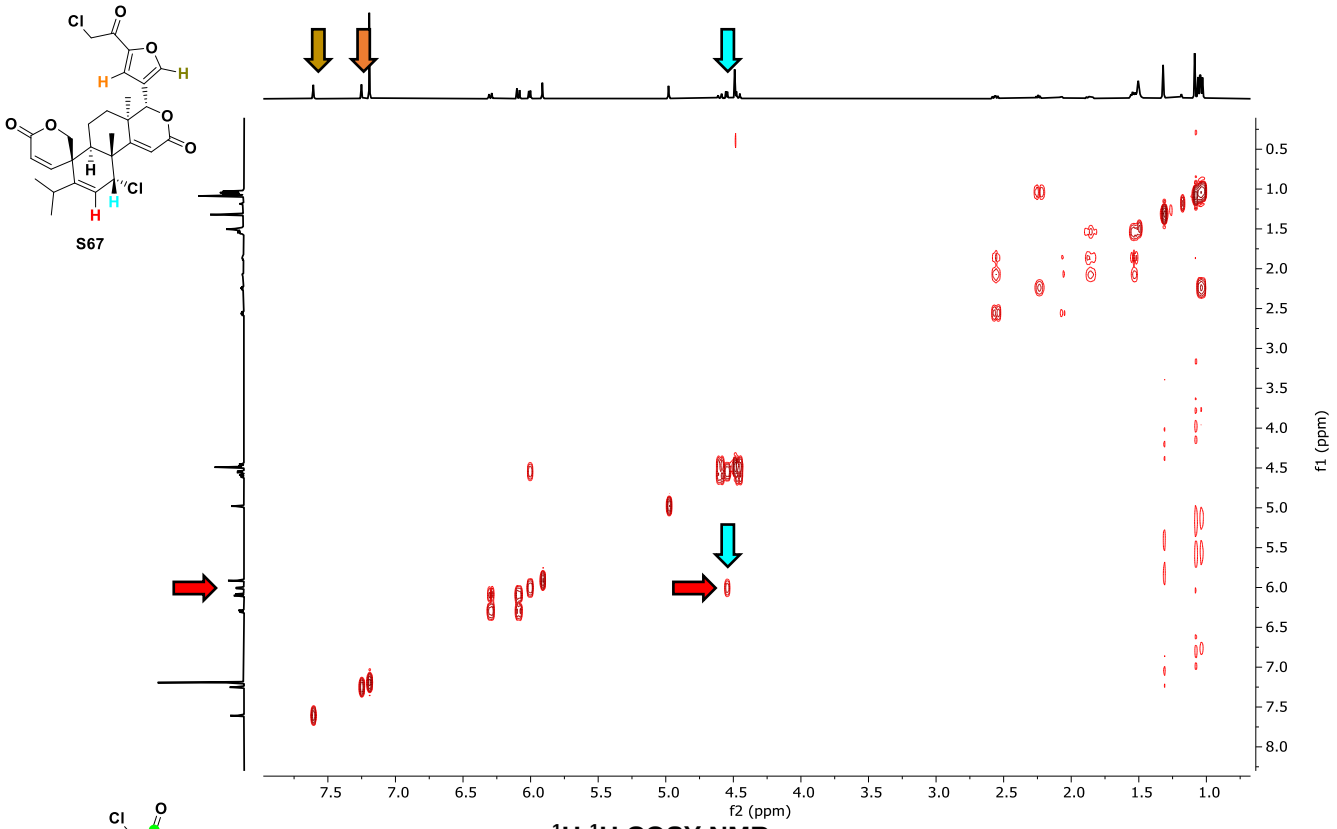
^{1}H-^{13}C HMBC NMR



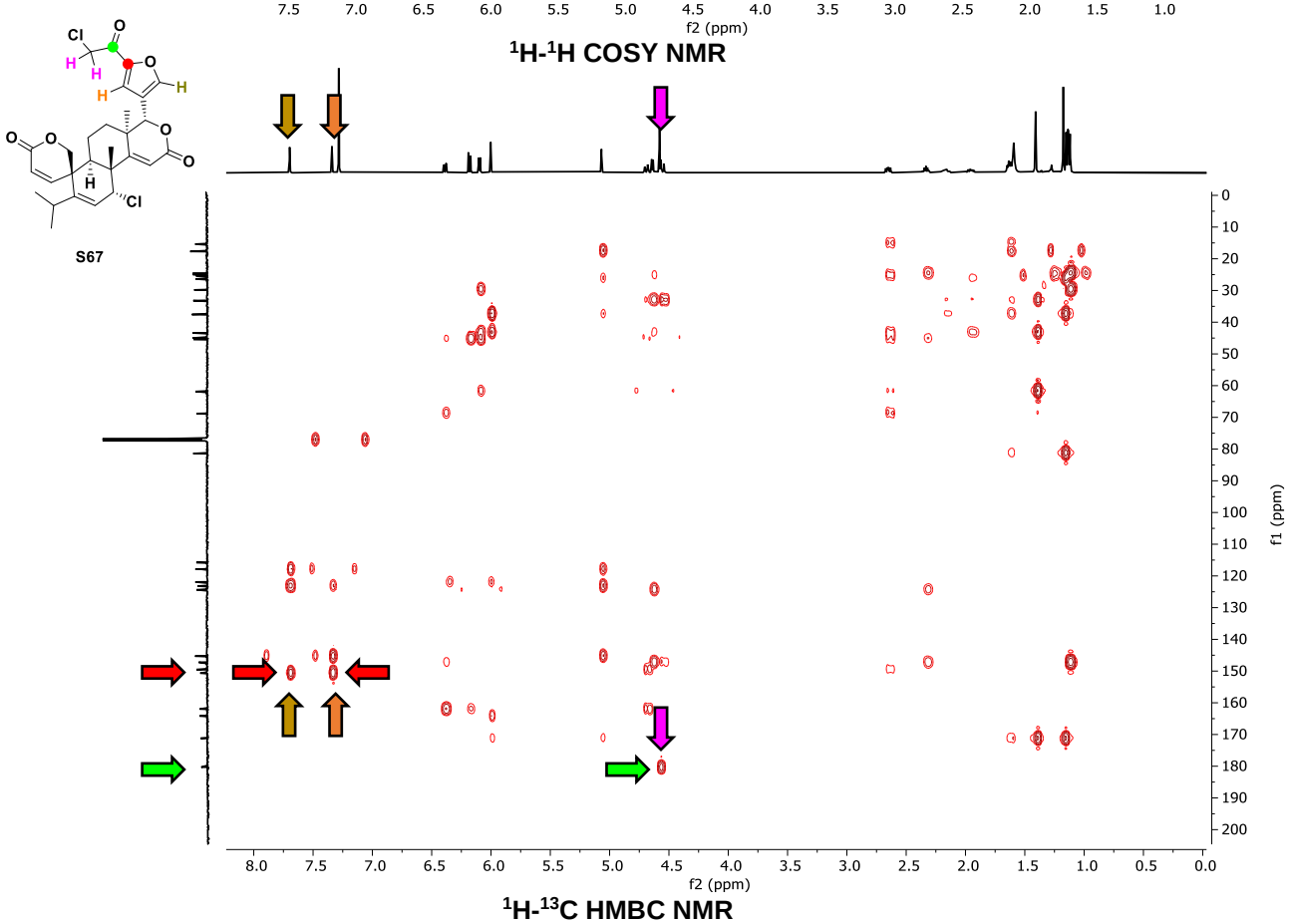
^{1}H NMR



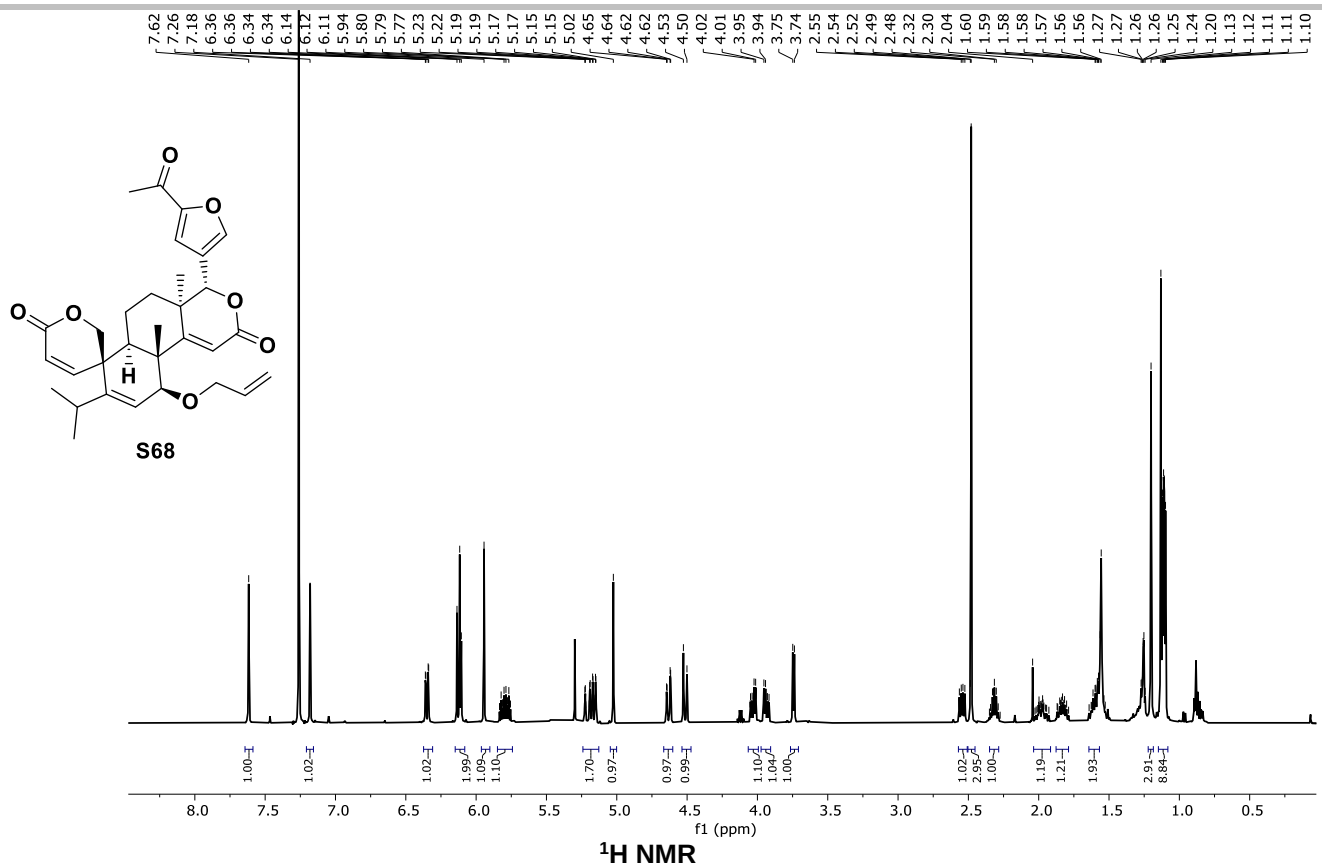
^{13}C NMR



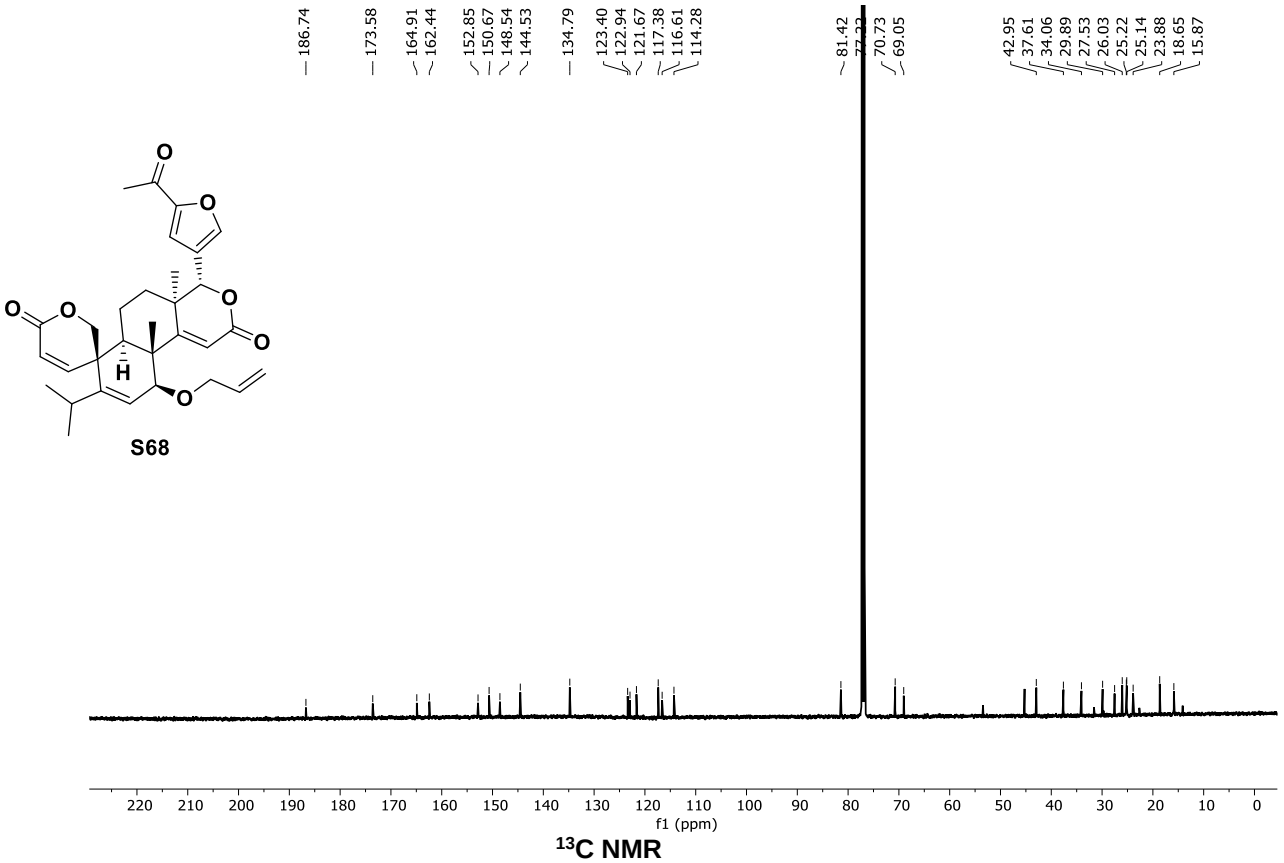
^{1}H-^{1}H COSY NMR



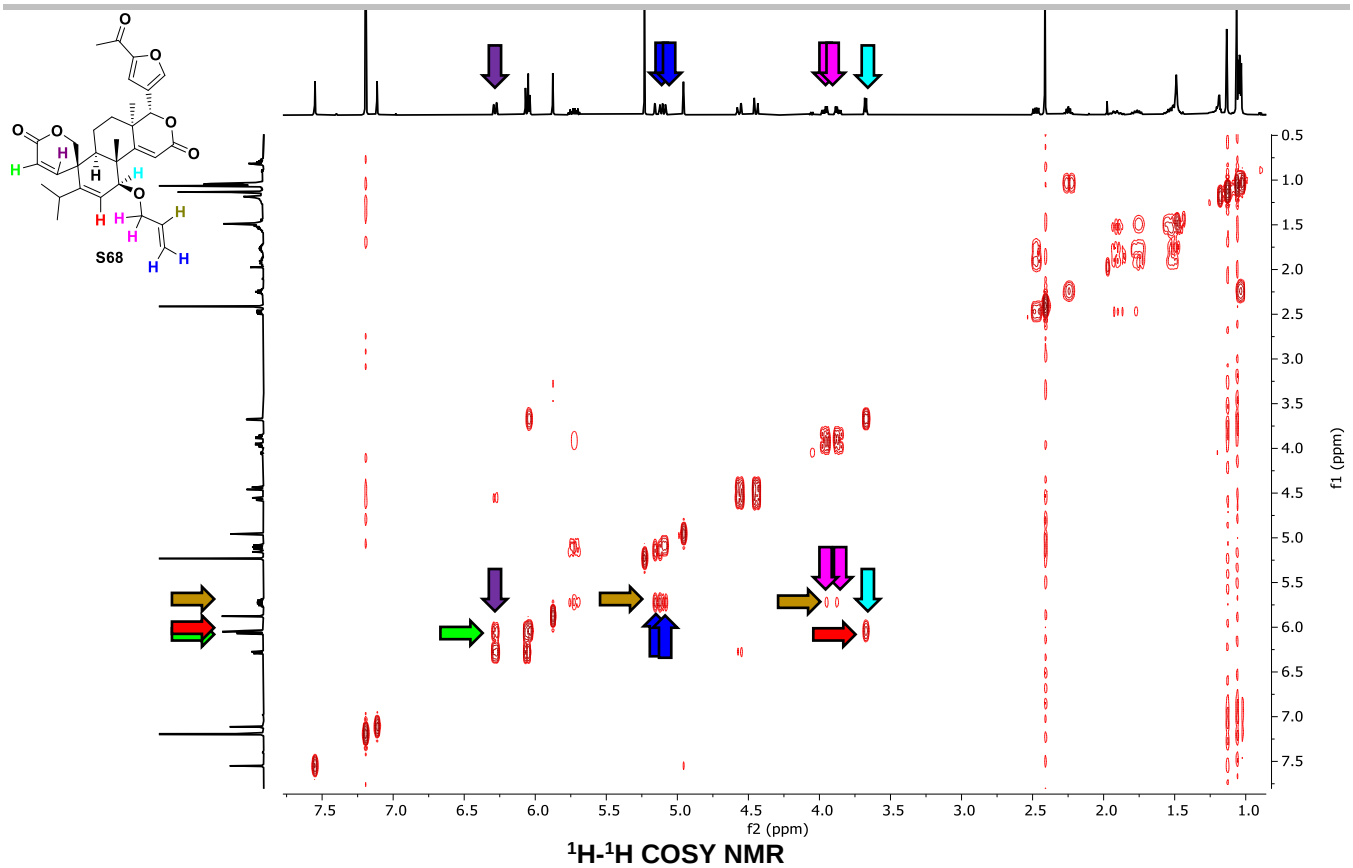
^{1}H-^{13}C HMBC NMR



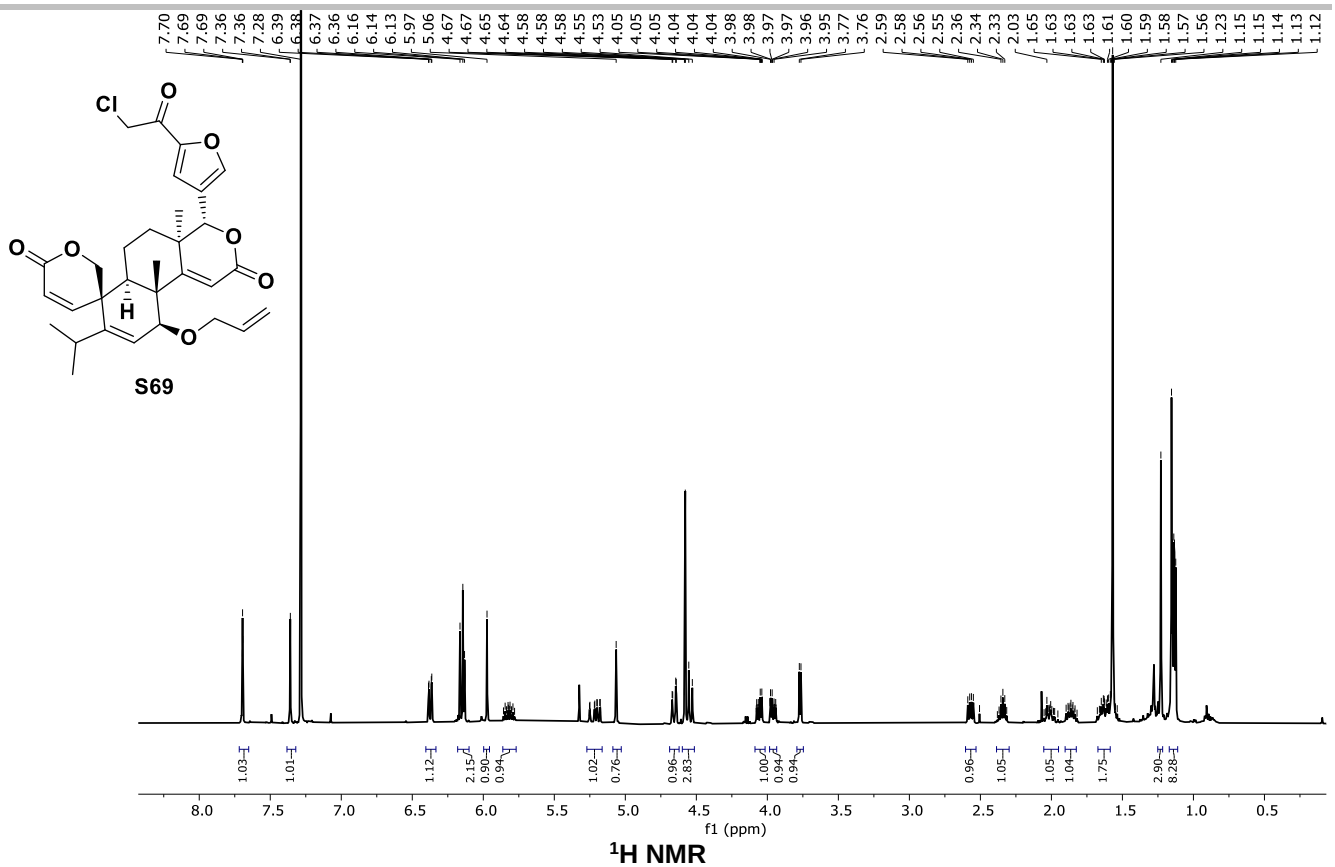
^{1}H NMR



^{13}C NMR

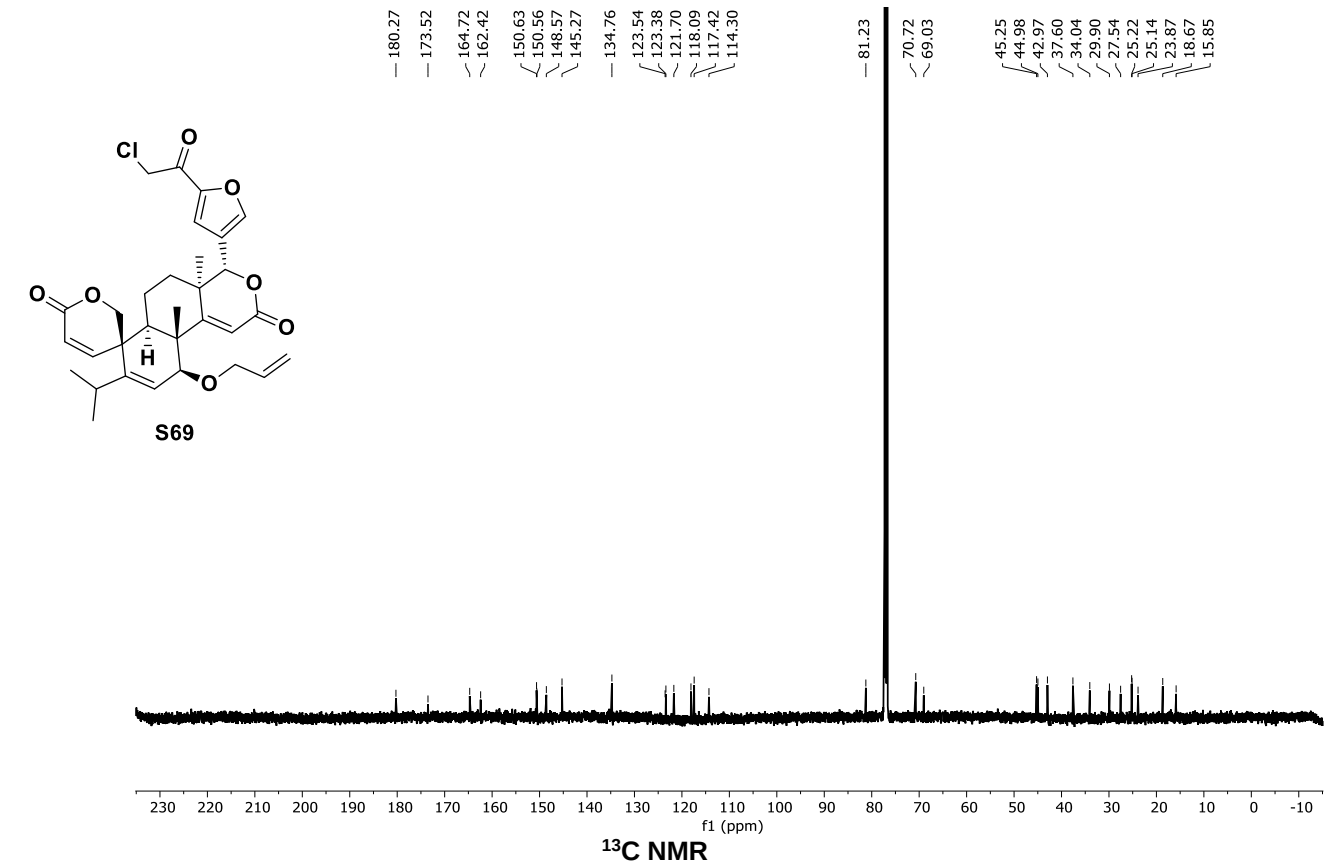


^{1}H-^{1}H COSY NMR



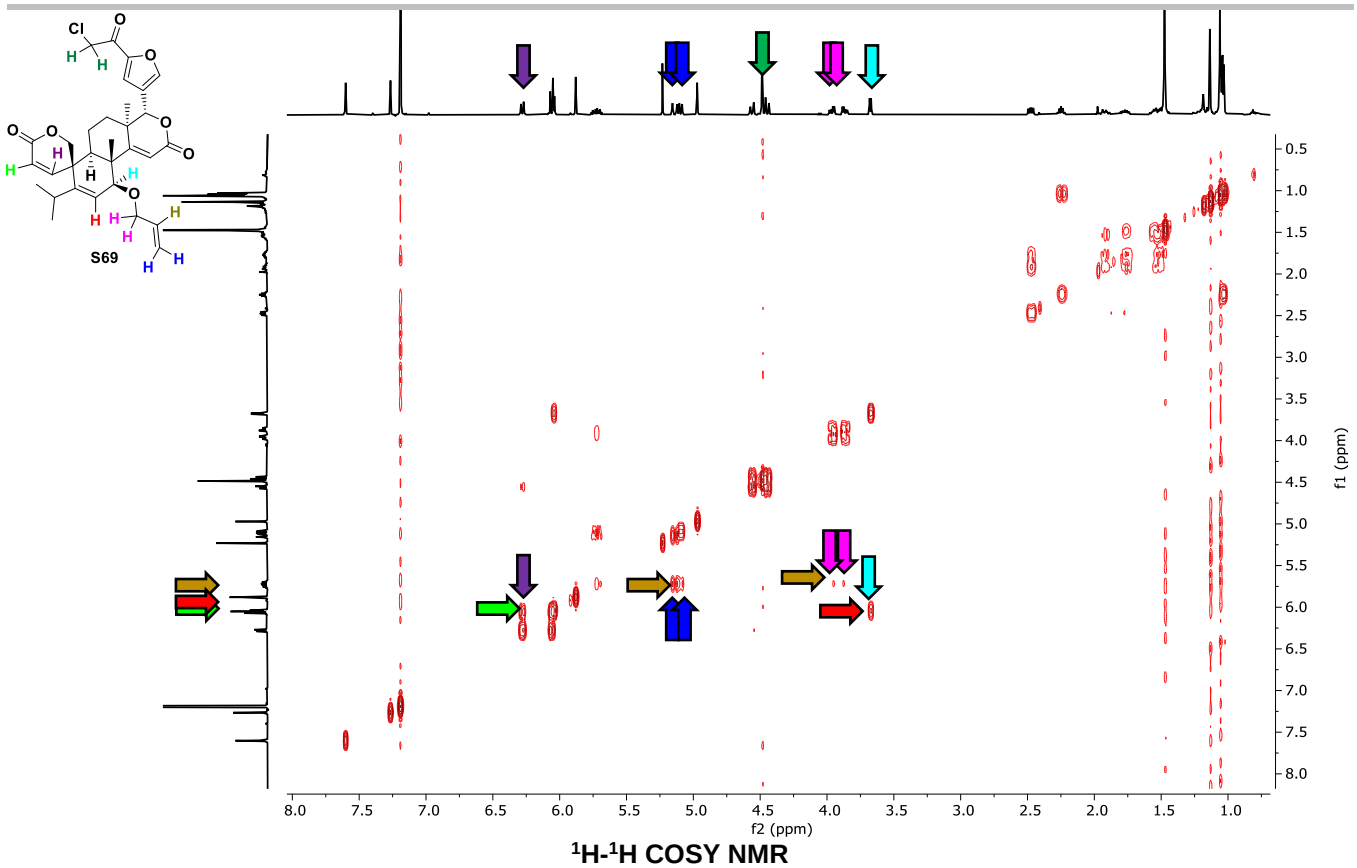
S69

^{1}H NMR

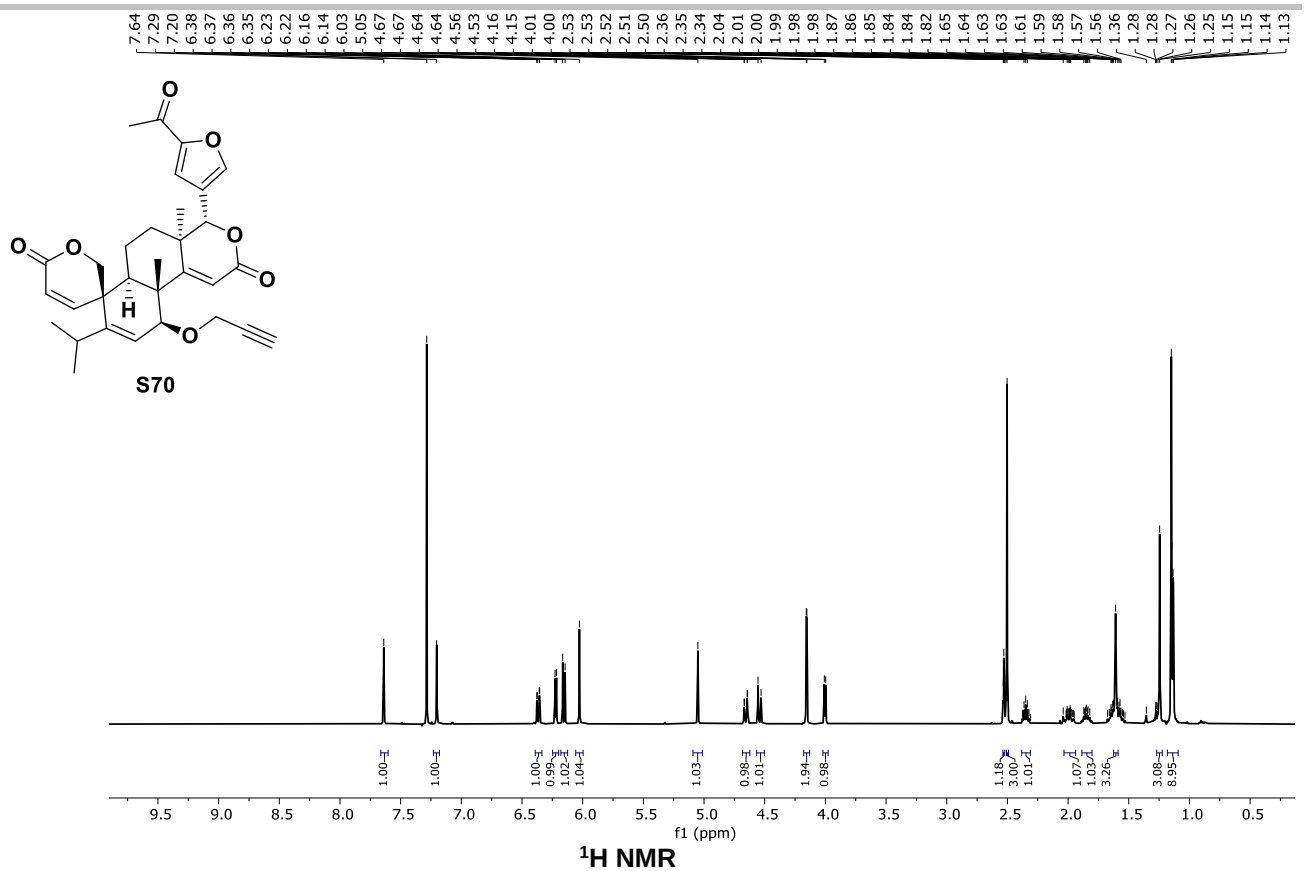


S69

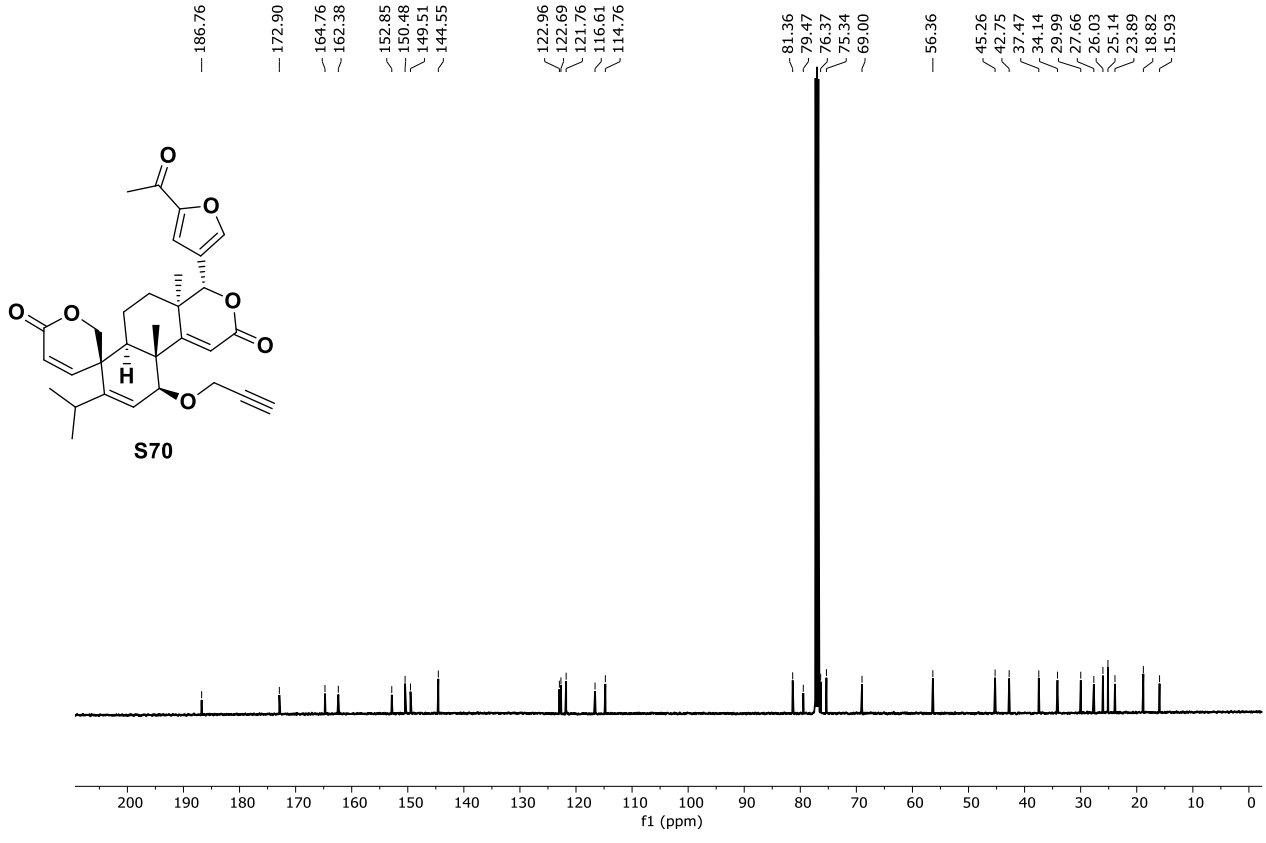
^{13}C NMR



^{1}H-^{1}H COSY NMR



^{1}H NMR



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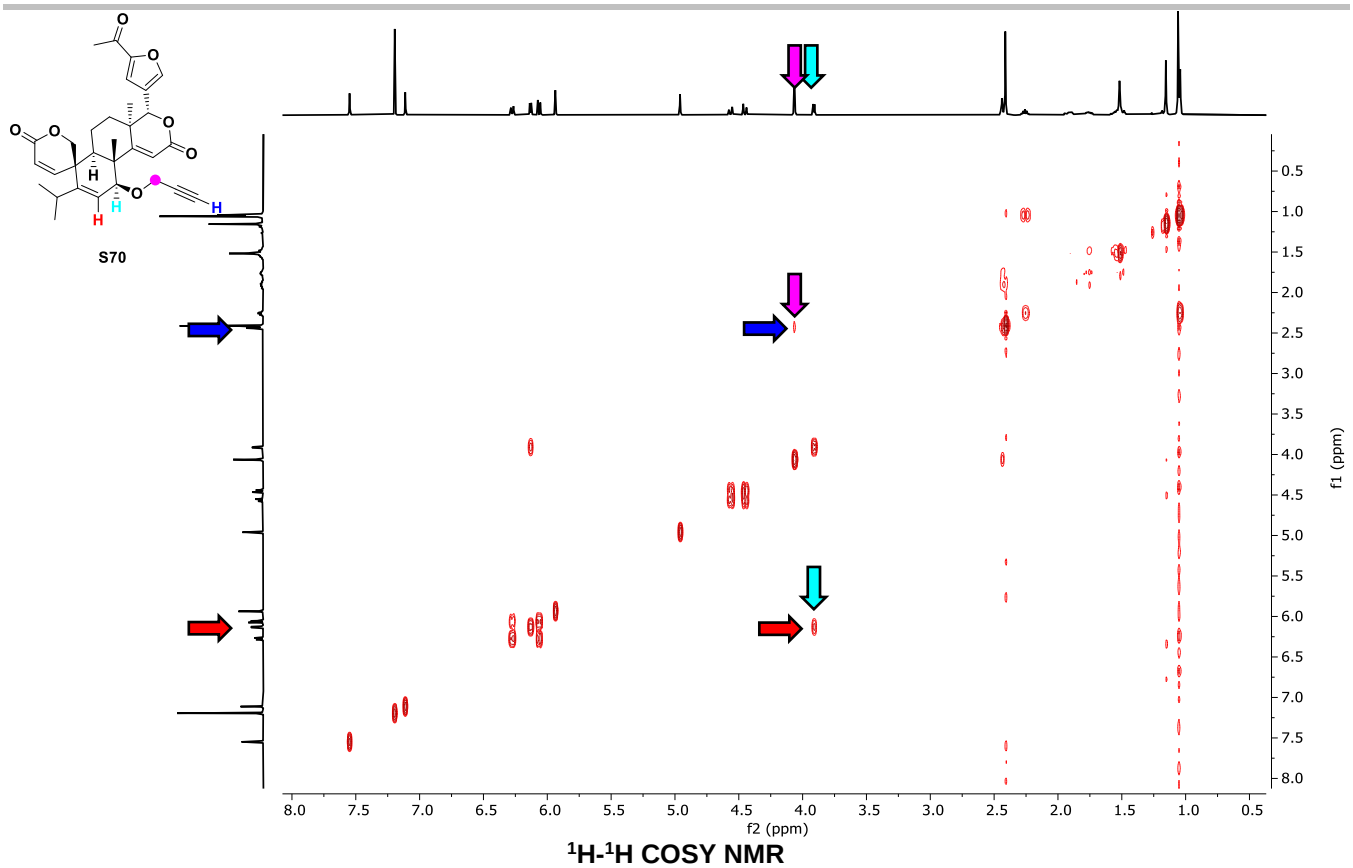
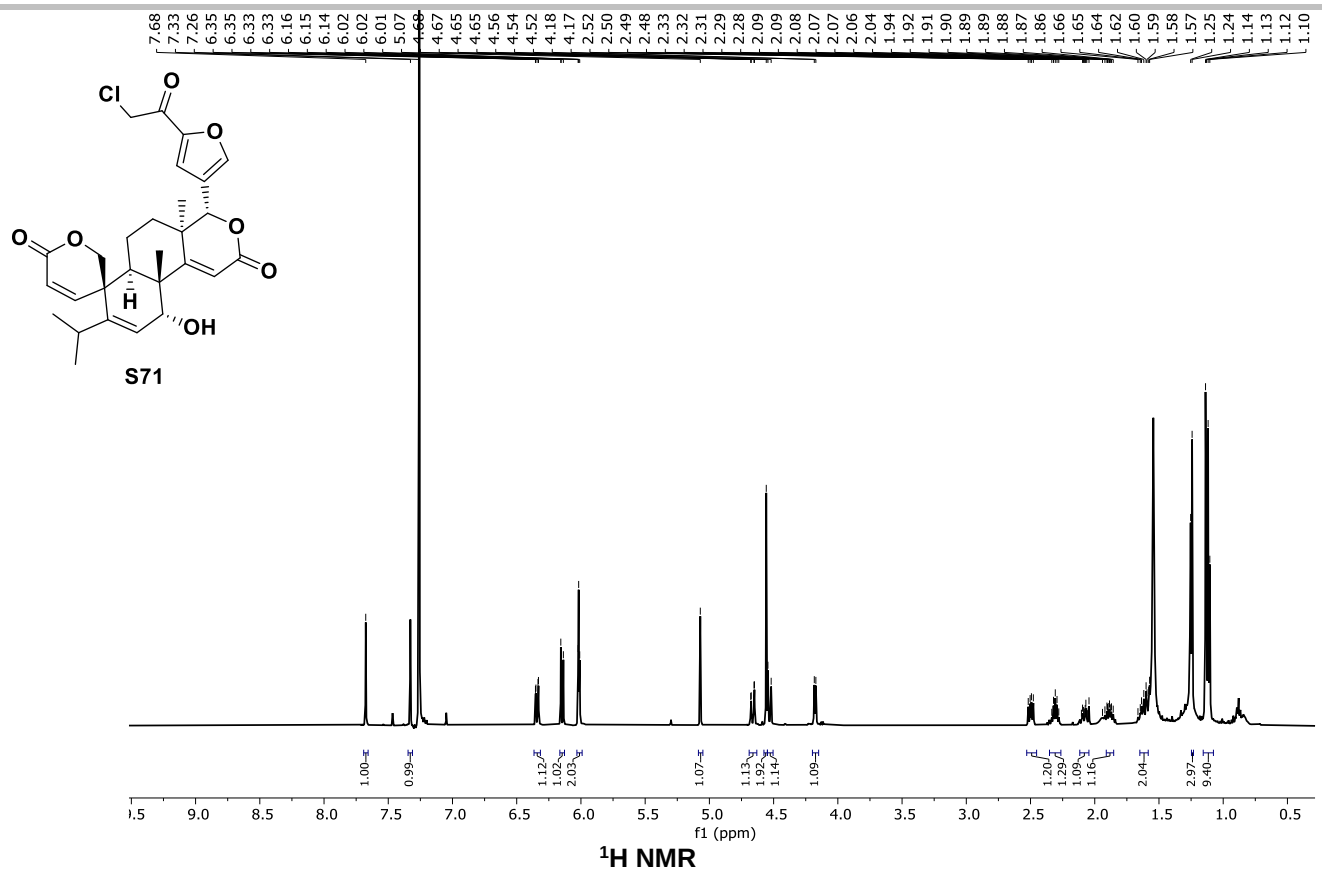
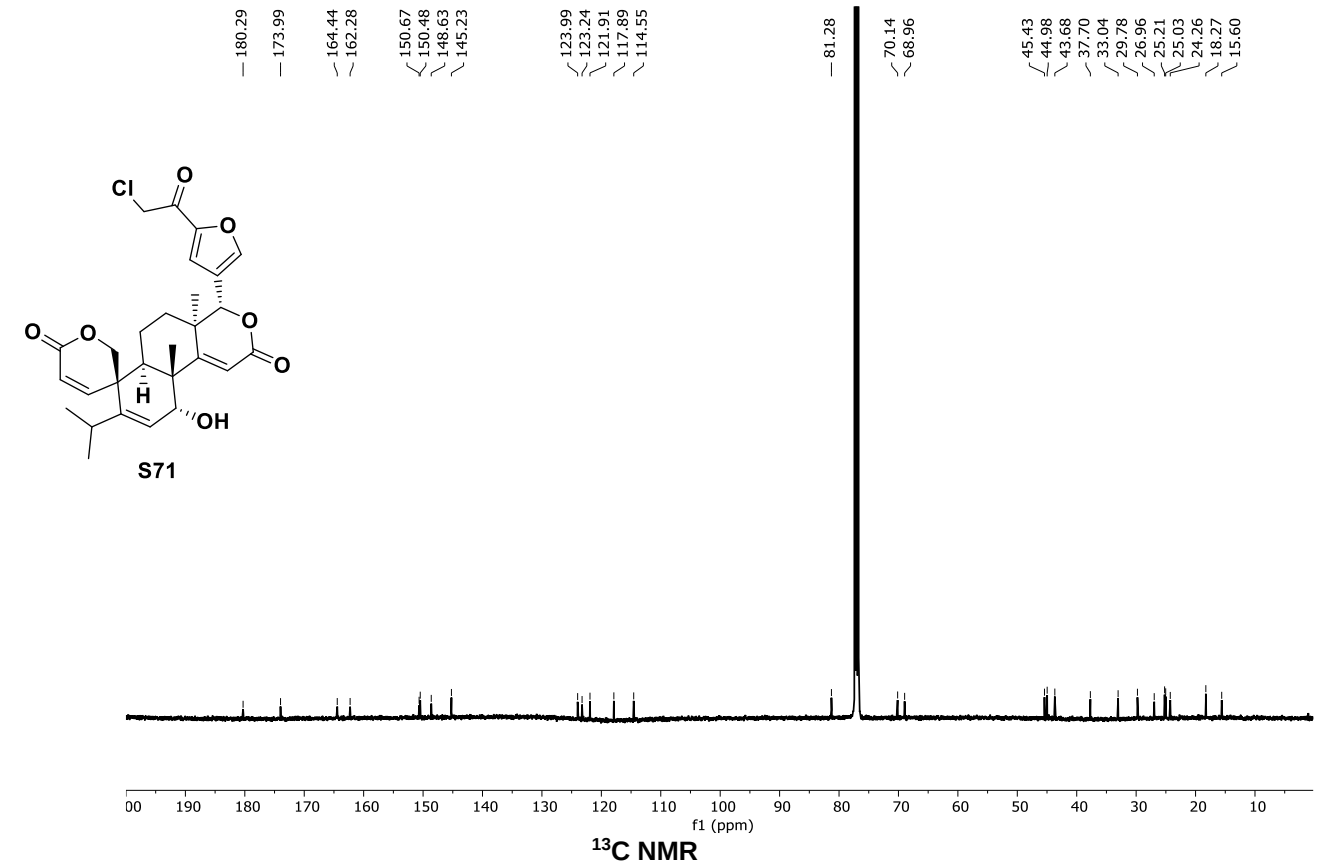


^{1}H-^{1}H COSY NMR



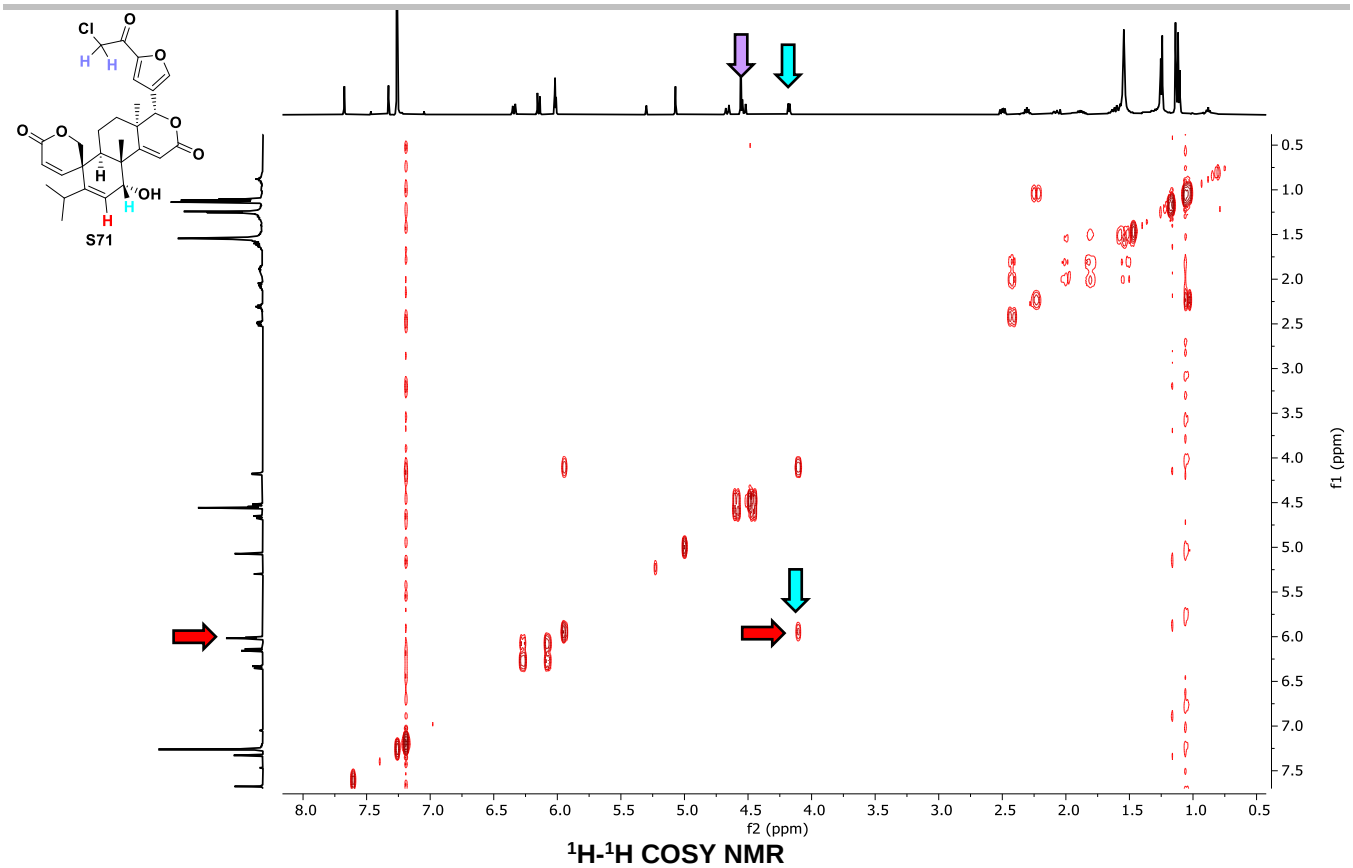
S71

^{1}H NMR

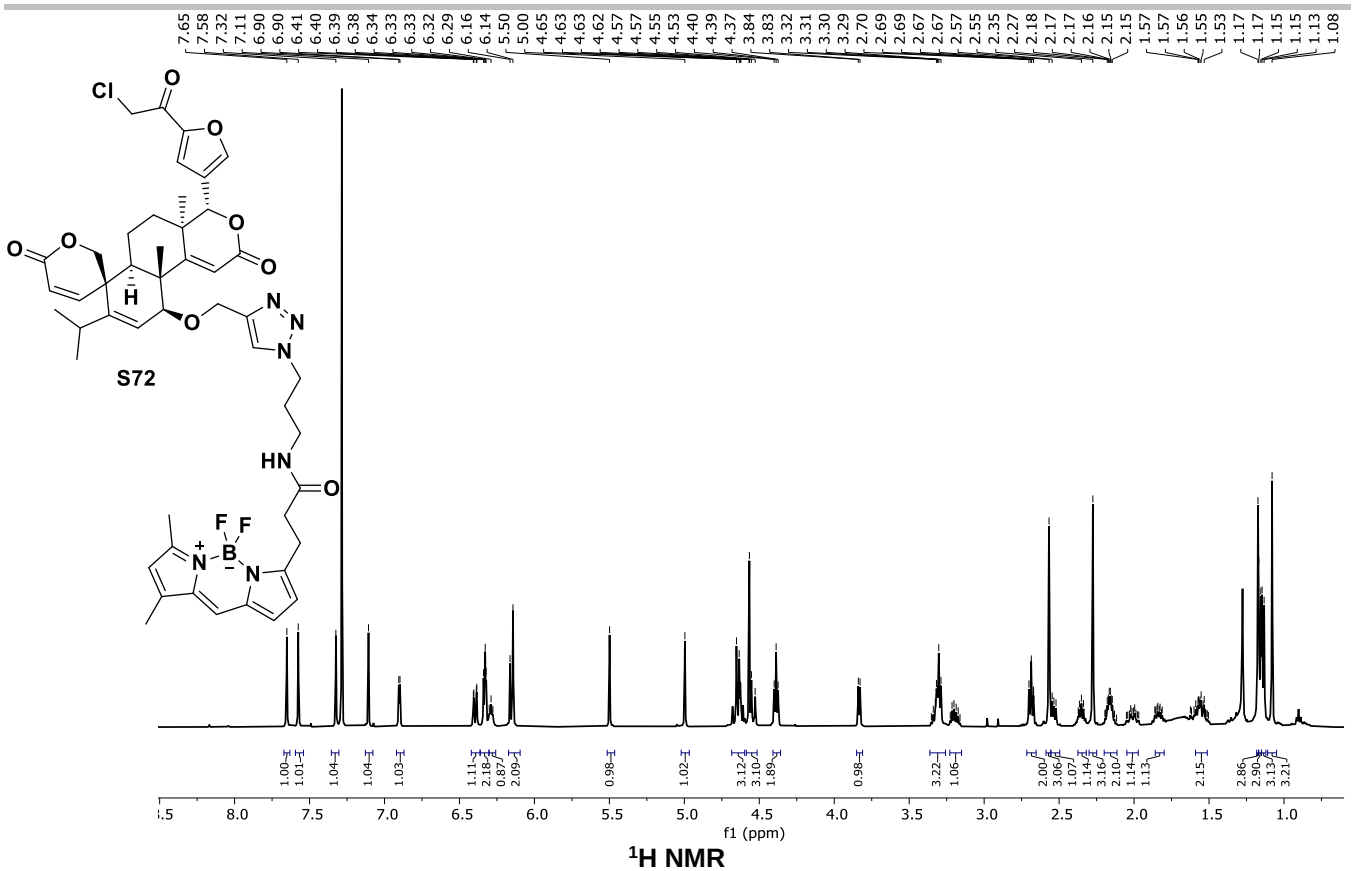


S71

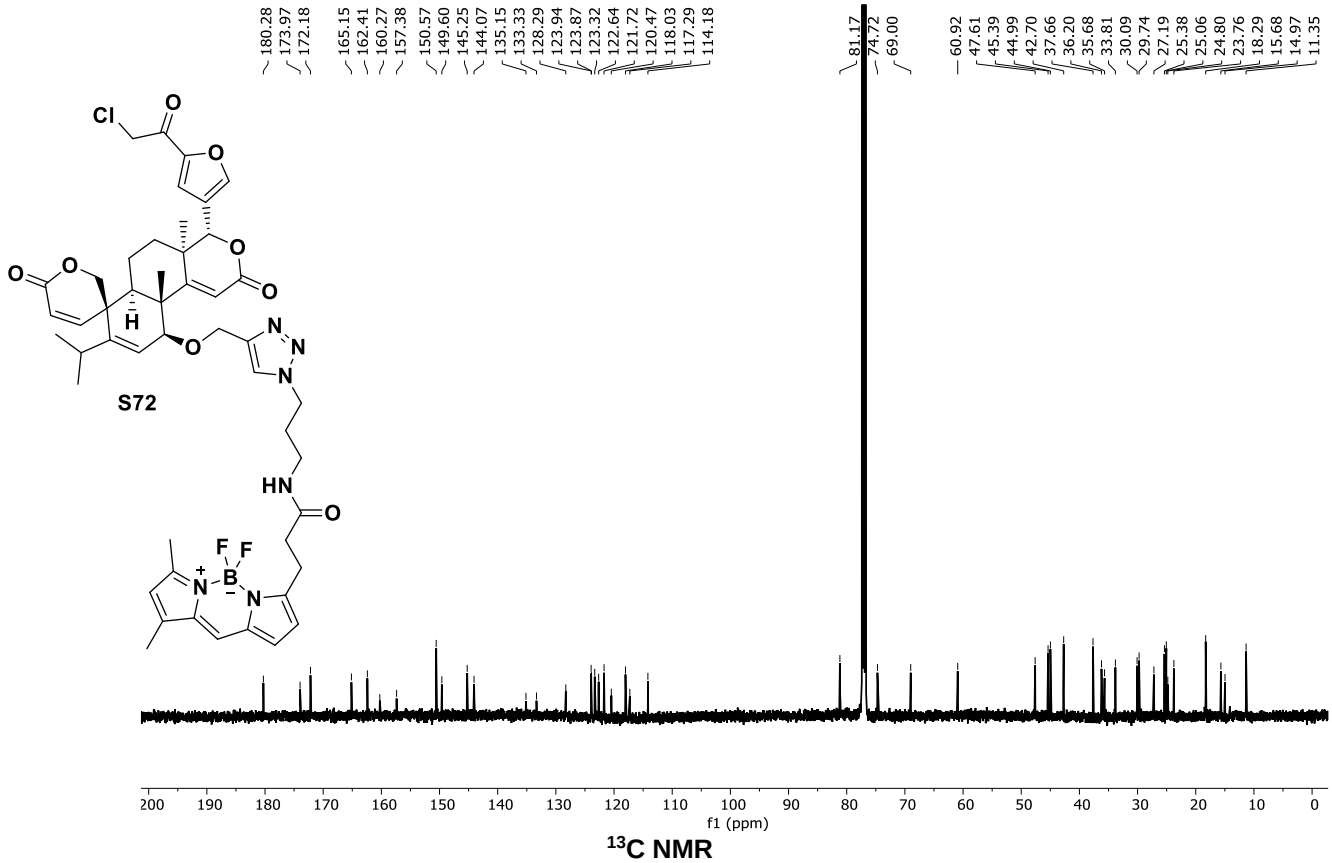
^{13}C NMR



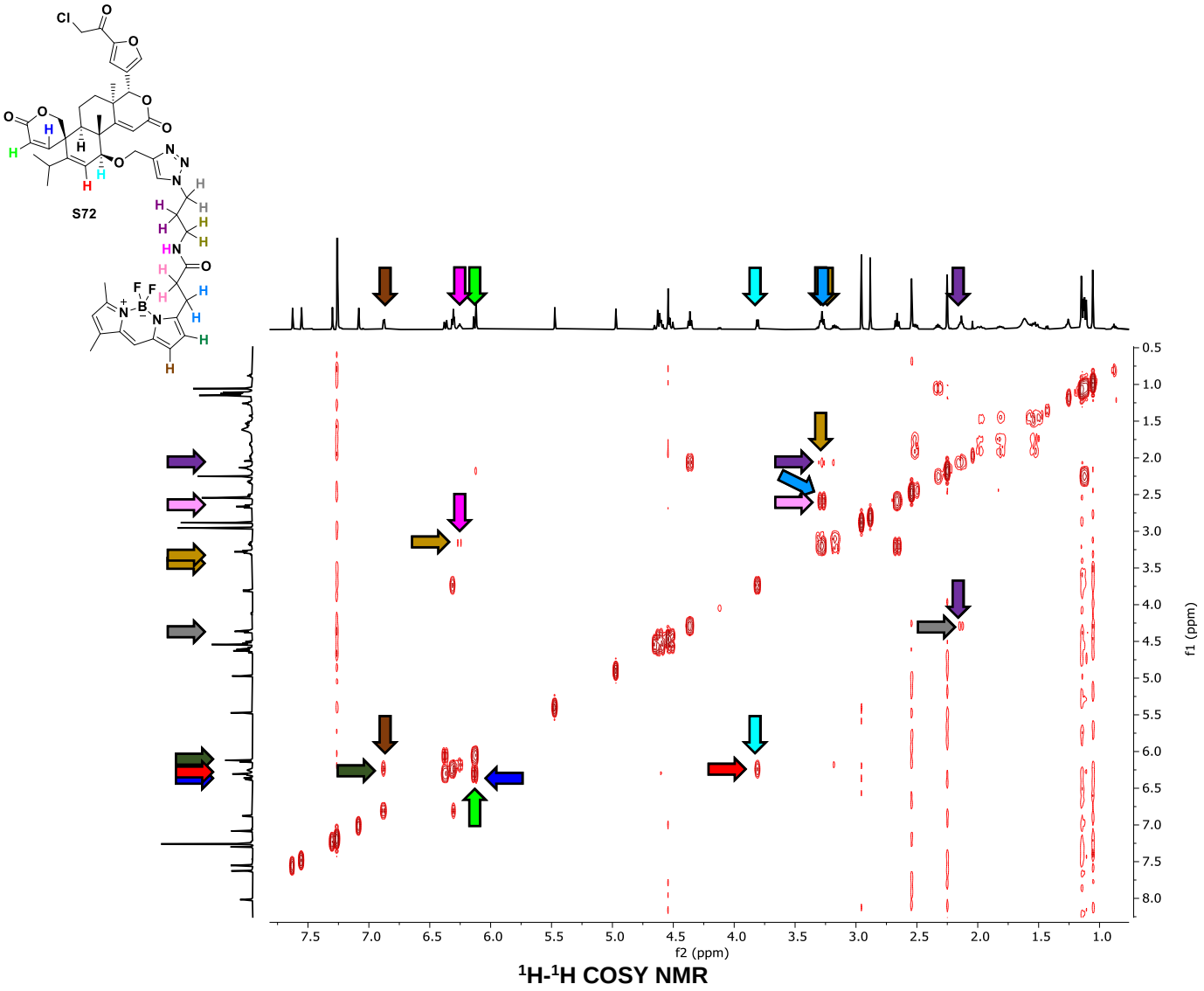
^{1}H-^{1}H COSY NMR



^{1}H NMR



^{13}C NMR



^{1}H-^{1}H COSY NMR