

Supplementary Information

Cytotoxic Indolocarbazoles from *Actinomadura mellioura* ATCC 39691

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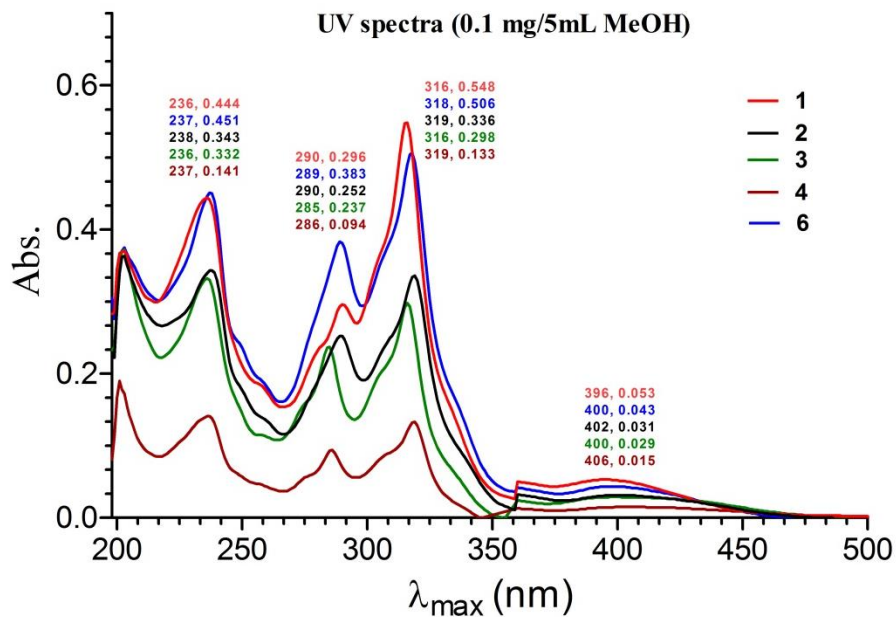


Figure S1. UV (MeOH) spectra of AT2433-A1 (**6**), A3, A4, A5 and B3 (**1-4**).

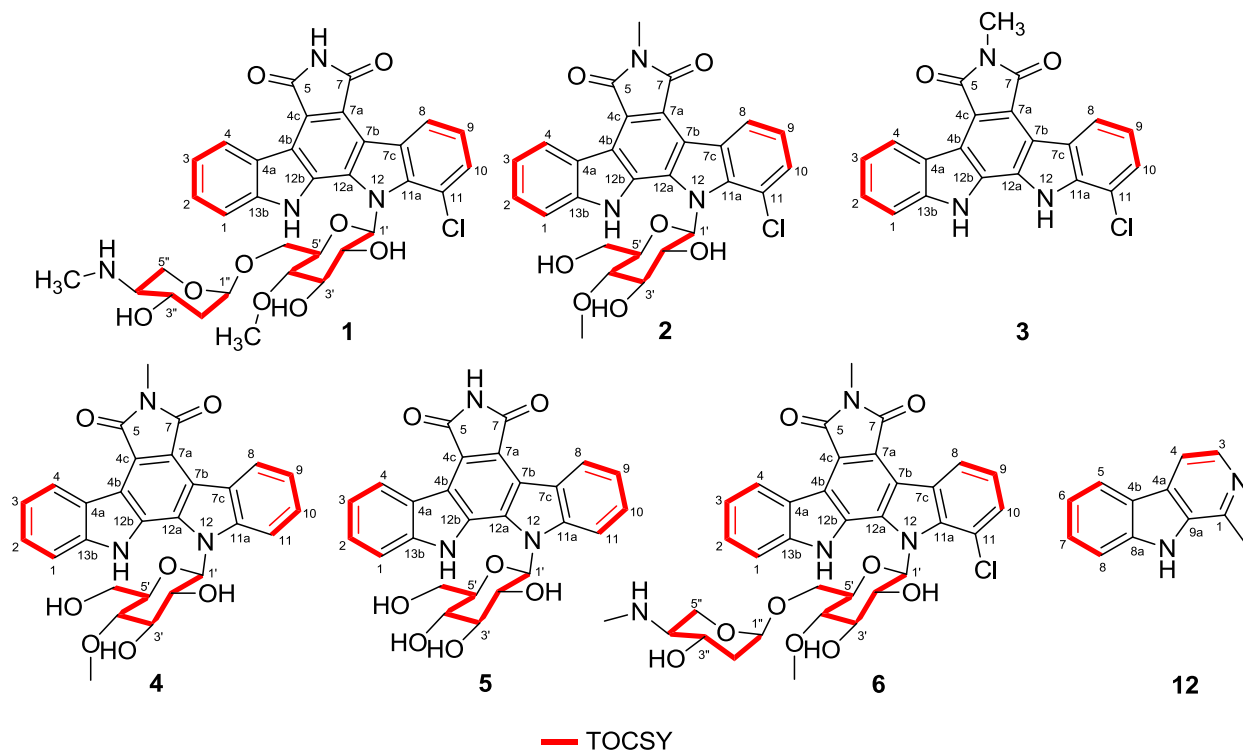


Figure S2. TOCSY (—) correlations in AT2433-A1 (**6**), A3, A4, A5, B3 (**1-4**), BMY-41219 (**5**) and harman (1-methyl- β -carboline, **12**).



Figure S3. *Actinomadura mellioura* ATCC 39691 culture broth after inoculation and cultivation on A-medium at 28 °C, and 200 rpm for 6 days

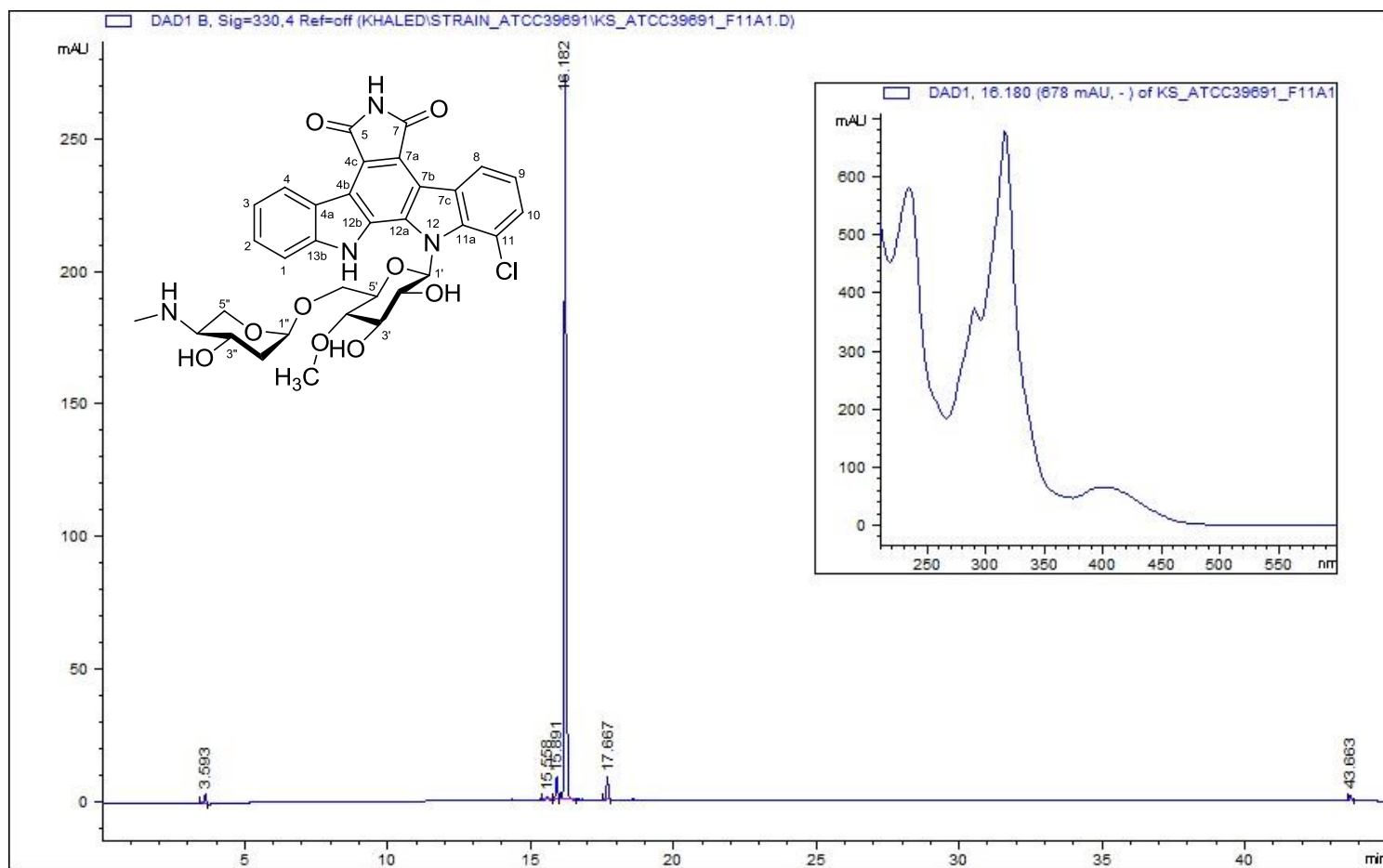


Figure S4. HPLC of AT2433-A3 (**1**). HPLC-conditions: Detection wavelength 254 nm; **solvent A:** H₂O/0.1% TFA; **solvent B:** CH₃CN; flow rate: 1.0 mL min⁻¹; 0-35 min, 5%-100% B; 35-40 min, 100% B; 40-41 min, 100%-5% B; 41-45 min, 5% B). UV-vis inset of full wavelength 190-600 nm.

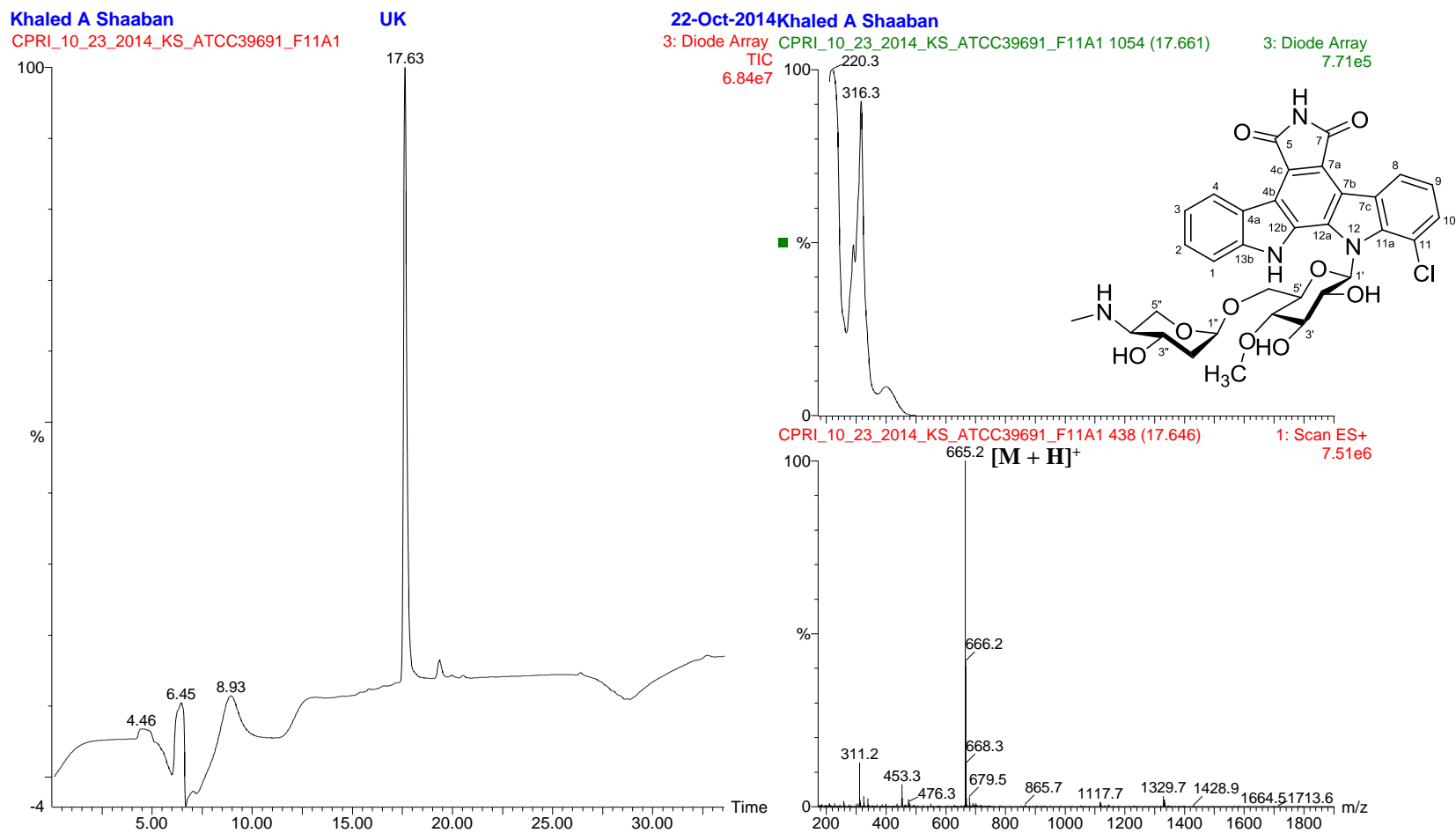


Figure S5. HPLC/UV/MS analyses of the purified AT2433-A3 (1). Detection wavelength: 210-500; **solvent A:** H₂O/0.1% Formic acid, **solvent B:** CH₃CN/0.1% Formic acid; flow rate: 0.5 mL min⁻¹; 0-4 min, 10% B; 4-22 min, 10-100% B; 22-27 min, 100% B; 27-29 min, 100%-10% B; 29-35 min, 10 % B.

14-0527 #64-67 RT: 1.68-1.76 AV: 4 NL: 1.79E8
T: FTMS + p ESI Full ms [300.00-1000.00]

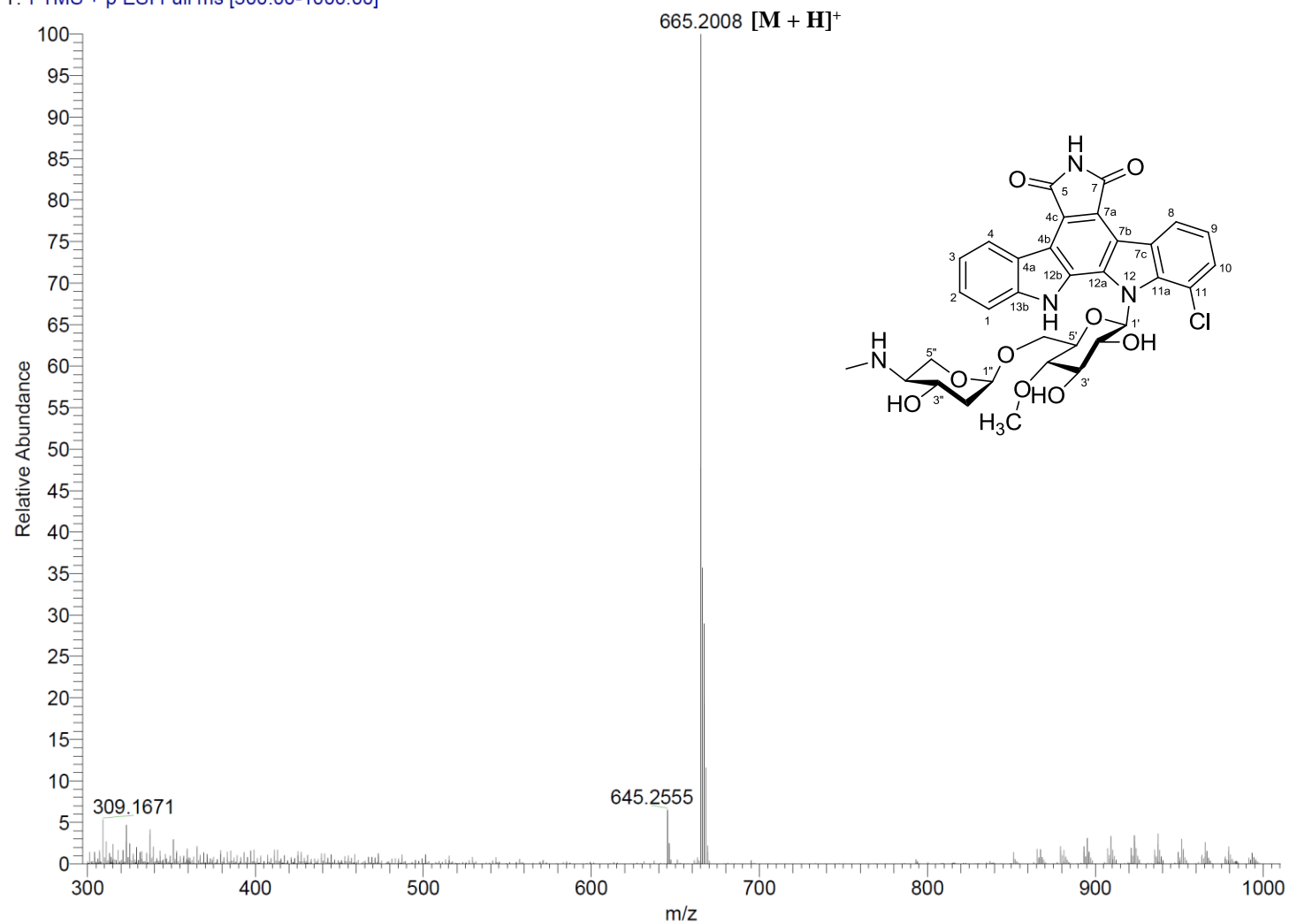


Figure S6. (+)-HRESI-MS spectrum of AT2433-A3 (**1**)

14-0527 #50-57 RT: 1.31-1.50 AV: 8 NL: 4.72E5
T: FTMS - p ESI Full ms [300.00-1000.00]

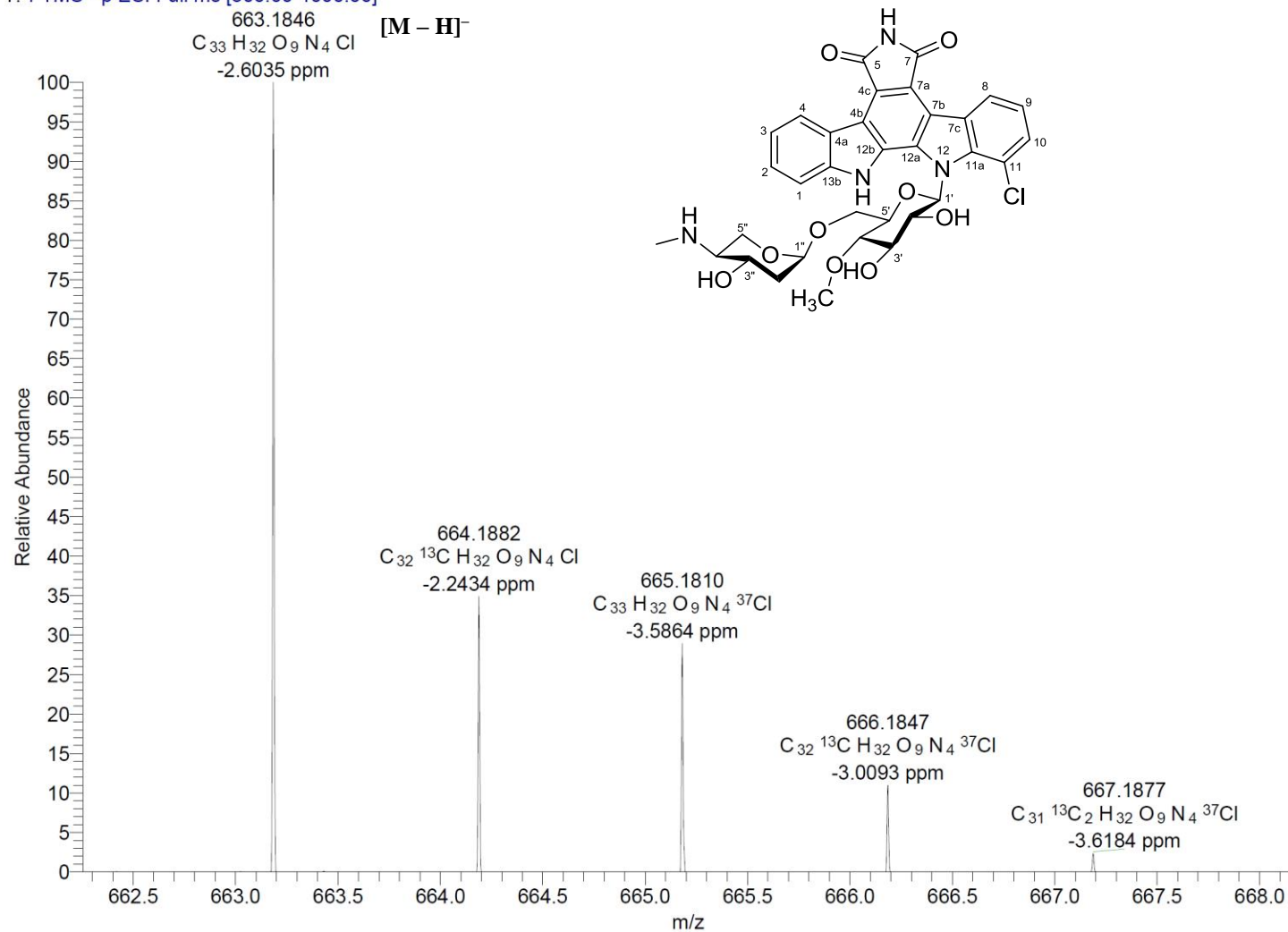


Figure S7. (-)-HRESI-MS spectrum of AT2433-A3 (1)

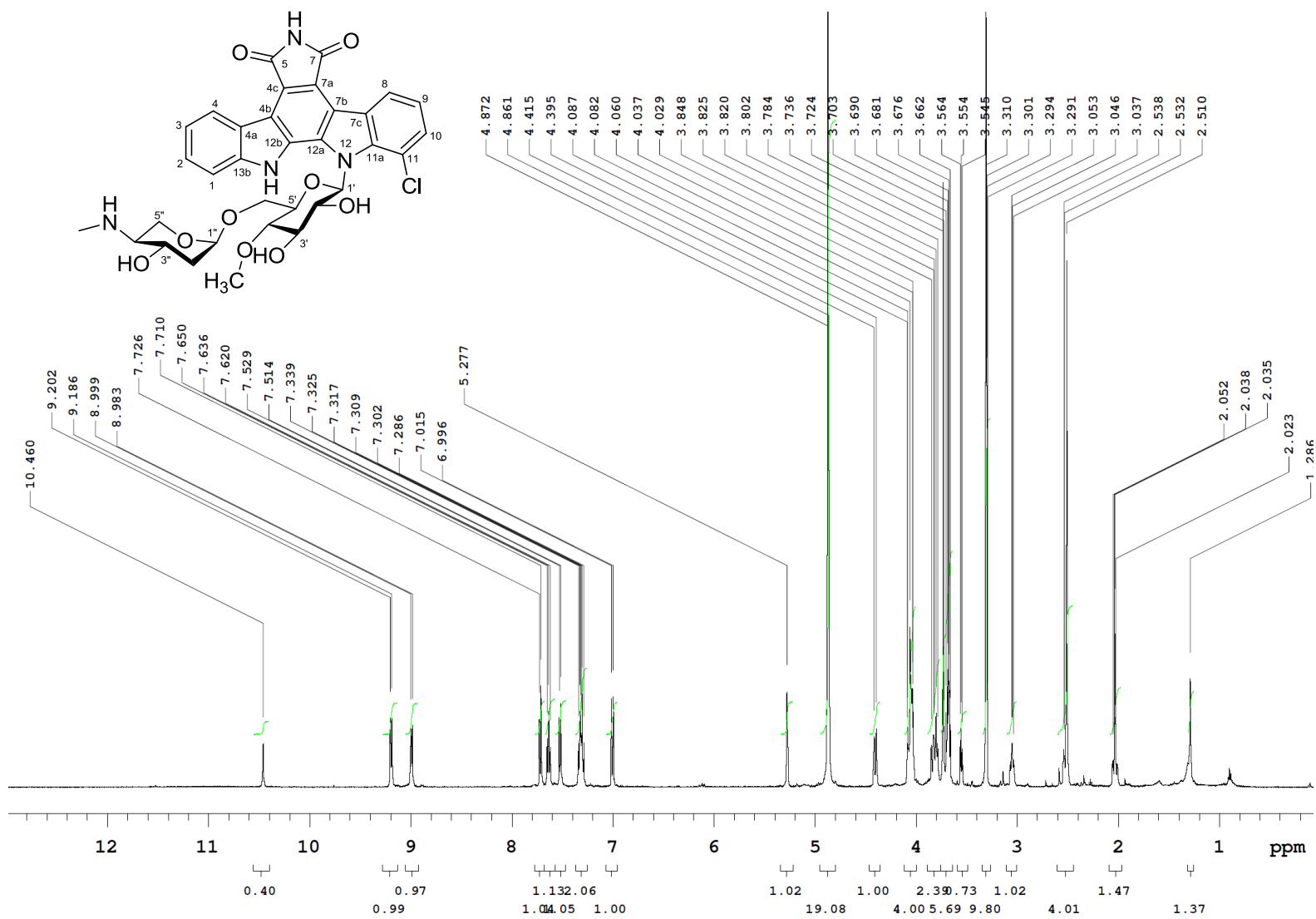


Figure S8. ¹H NMR spectrum (CD₃OD, 500 MHz) of AT2433-A3 (**1**)

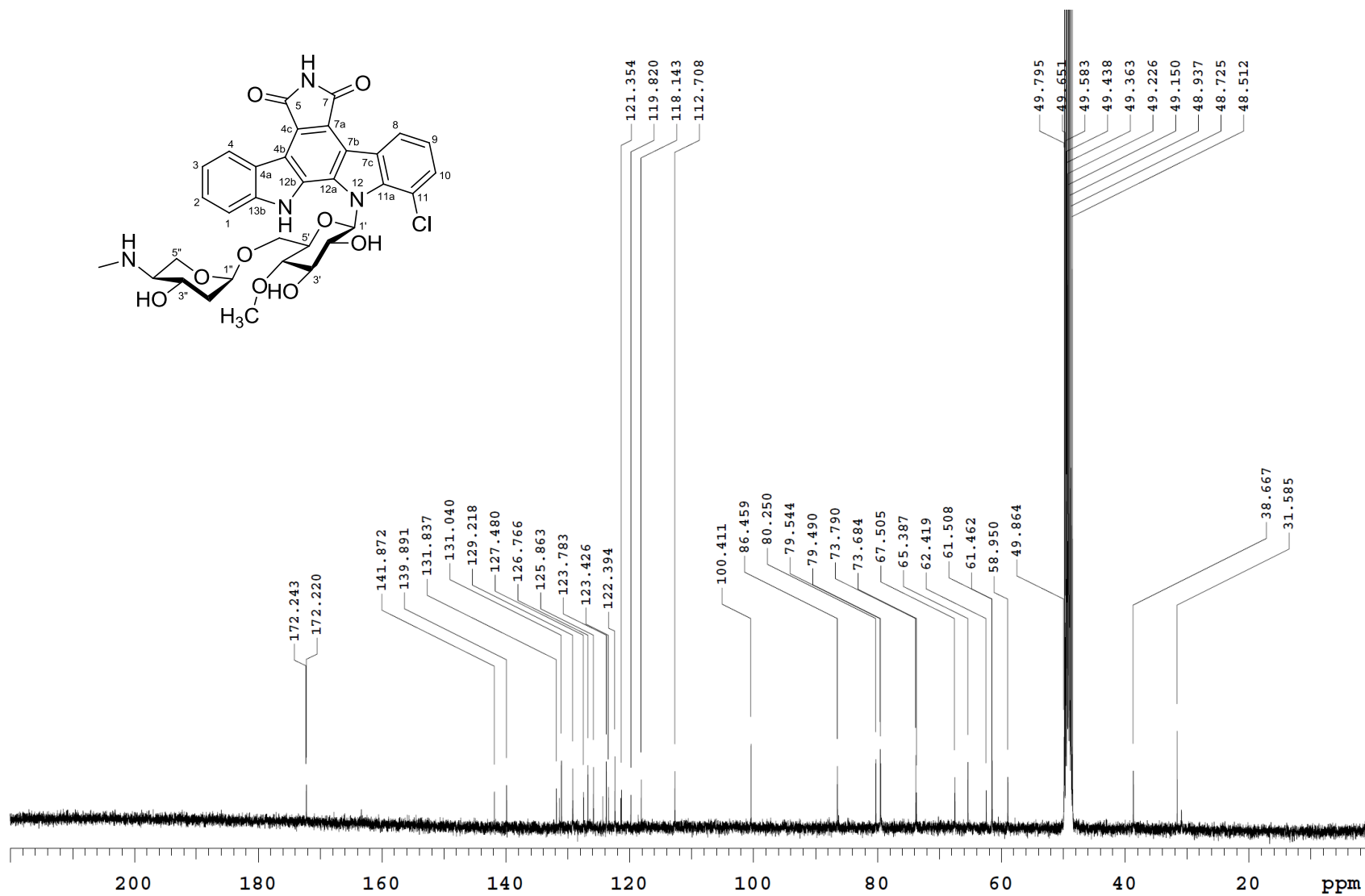


Figure S9. ¹³C NMR spectrum (CD₃OD, 100 MHz) of AT2433-A3 (**1**)

500 MHz, CD3OD, 80 min
Khaled A. Shaaban

Sample: Khaled_A_Shaaban
File: xp

Pulse Sequence: gCOSY

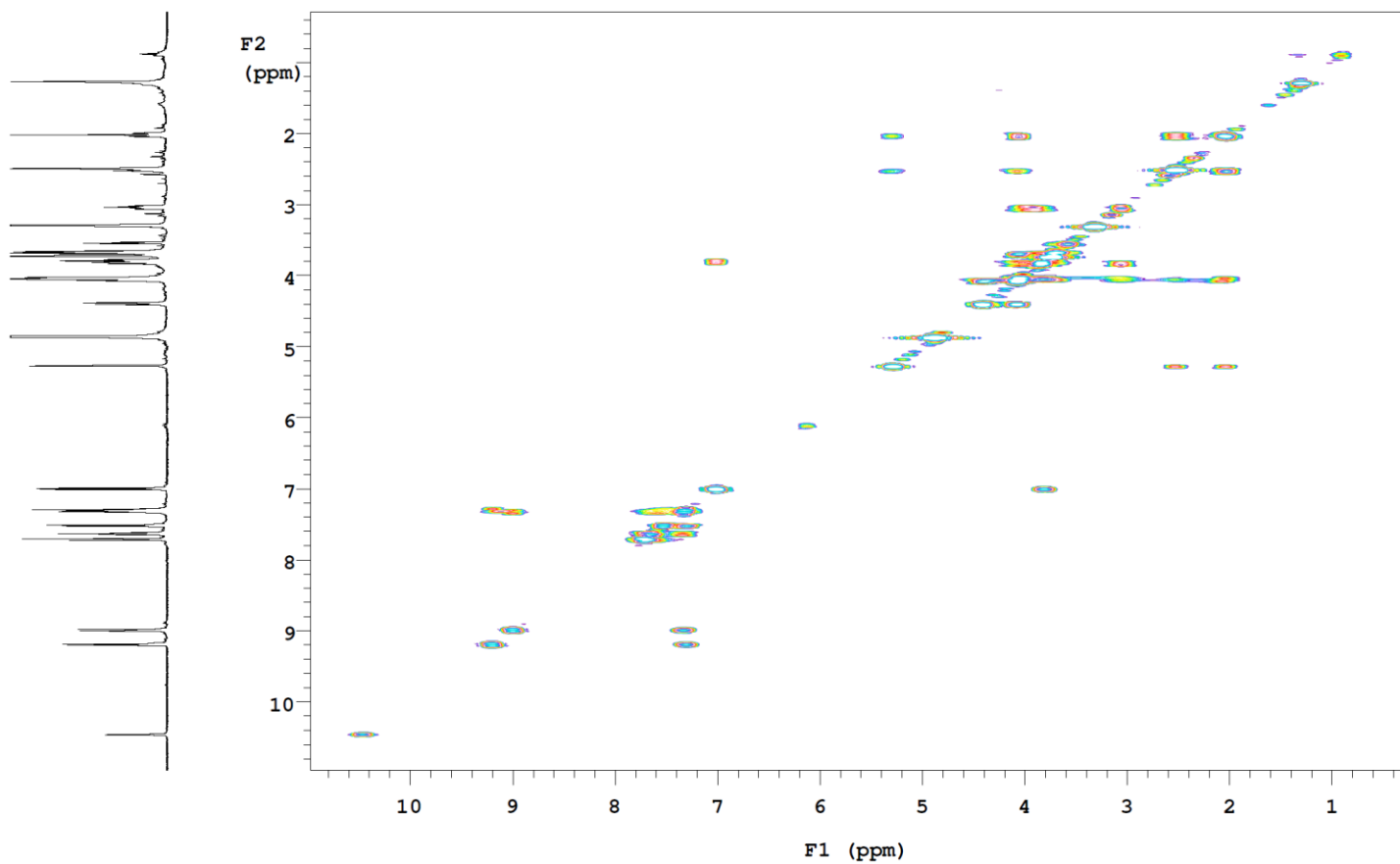
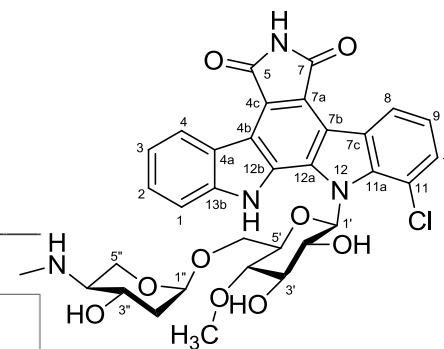
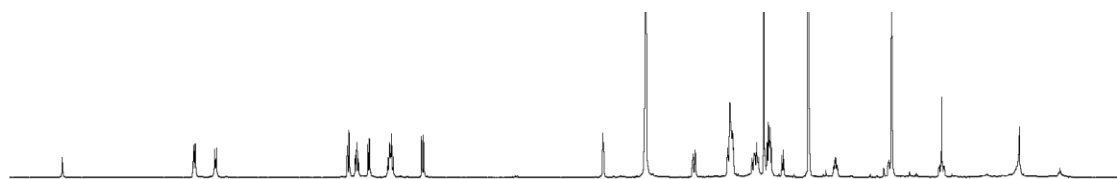


Figure S10. ^1H - ^1H COSY spectrum (CD₃OD, 500 MHz) of AT2433-A3 (**1**)

500 MHz, CD₃OD, 4 hrs
Khaled A. Shaaban

Sample: Khaled_A_Shaaban
File: xp

Pulse Sequence: gHSQC

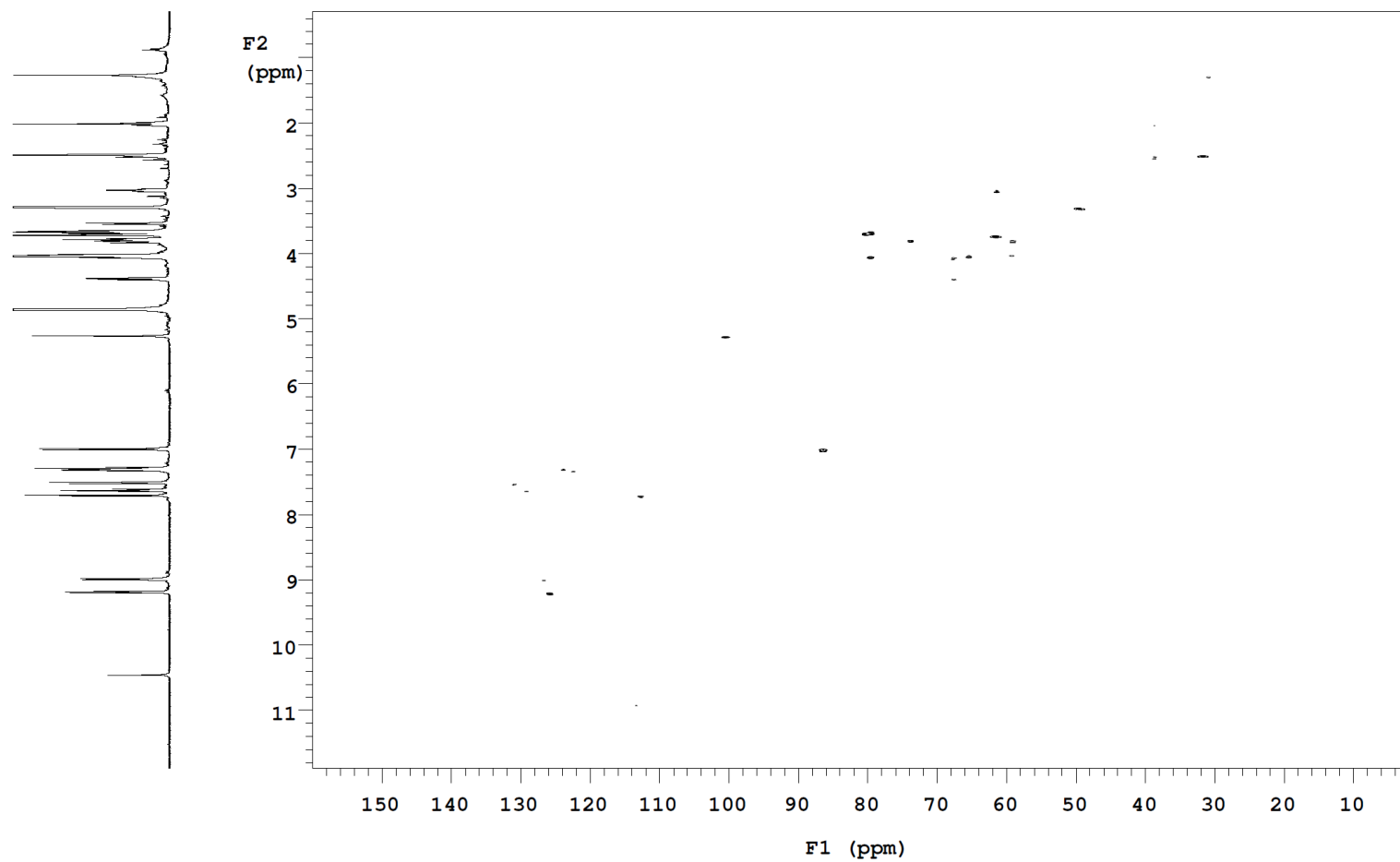
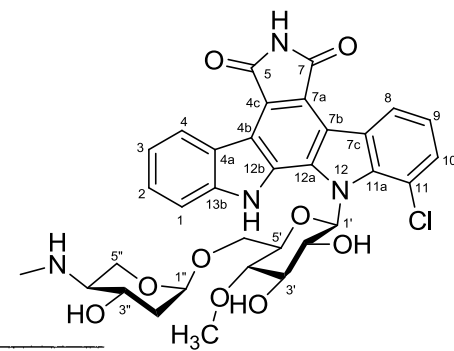


Figure S11. HSQC spectrum (CD₃OD, 500 MHz) of AT2433-A3 (**1**)

500 MHz, CD3OD, 45 hrs
Khaled A. Shaaban

Sample: Khaled_A_Shaaban
File: xp

Pulse Sequence: gHMBC

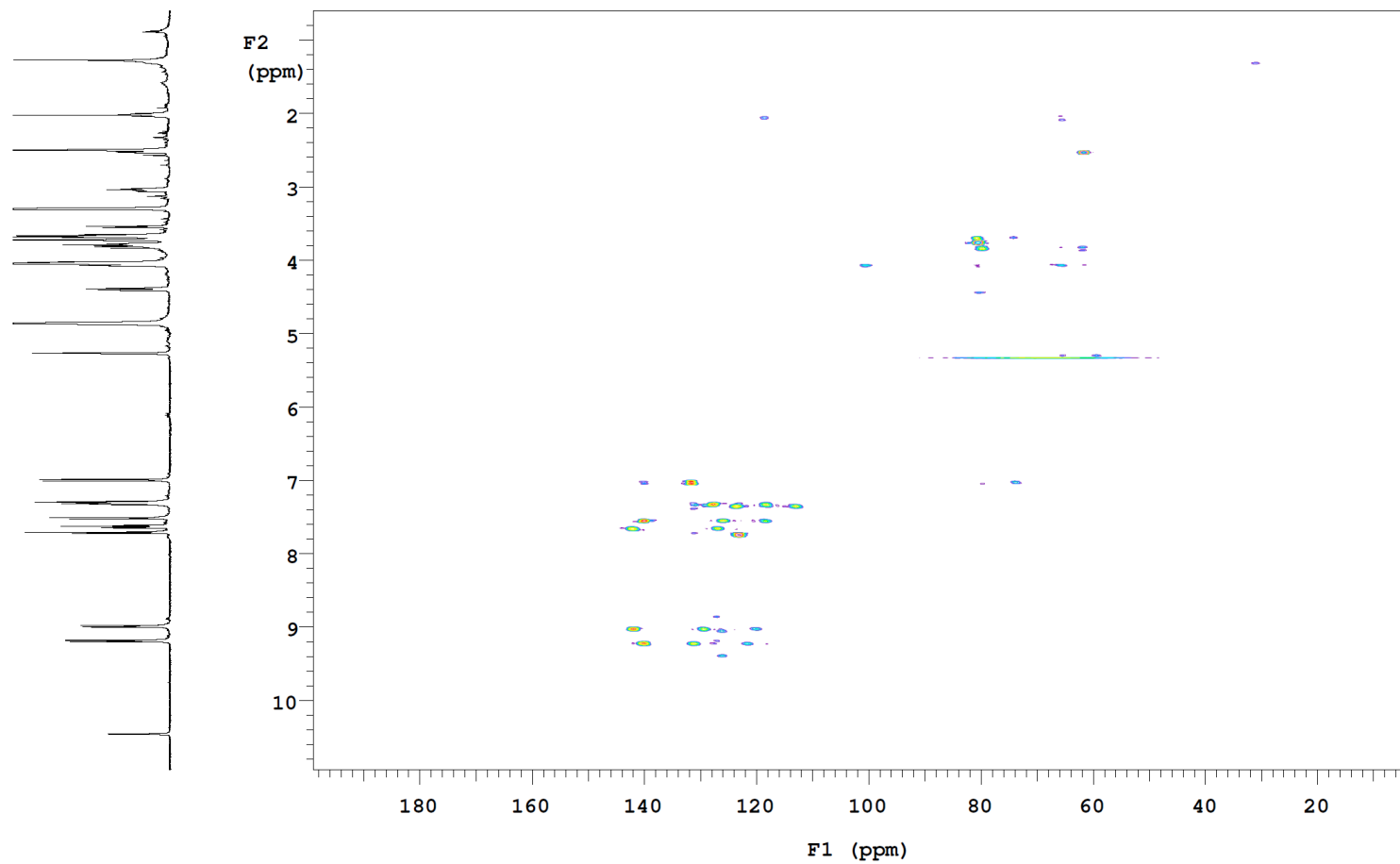
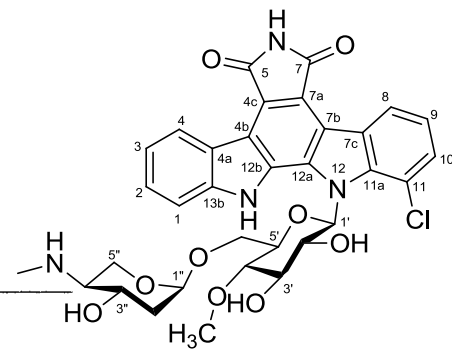


Figure S12. HMBC spectrum (CD₃OD, 500 MHz) of AT2433-A3 (**1**)

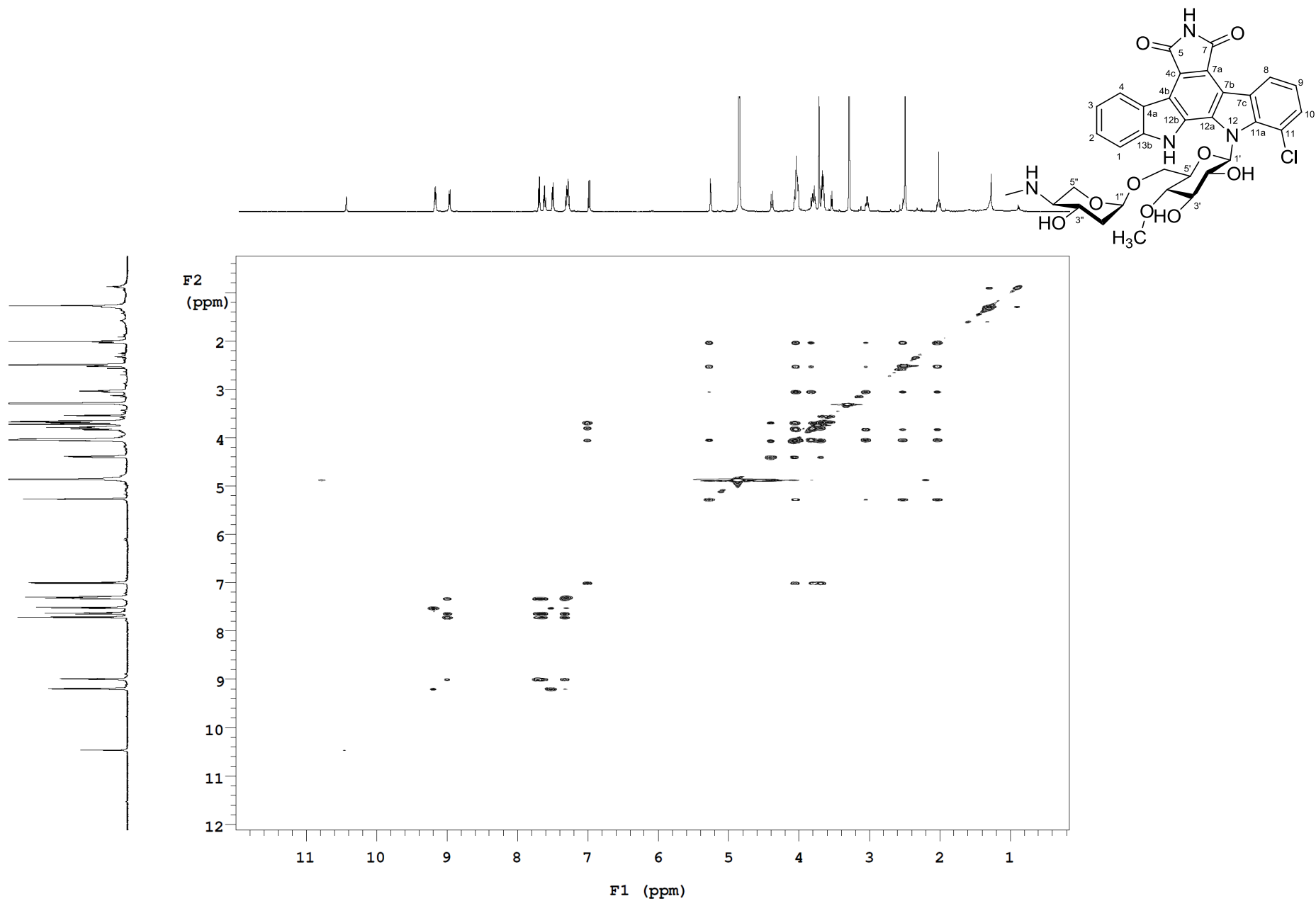


Figure S13. TOCSY spectrum (CD₃OD, 500 MHz) of AT2433-A3 (**1**)

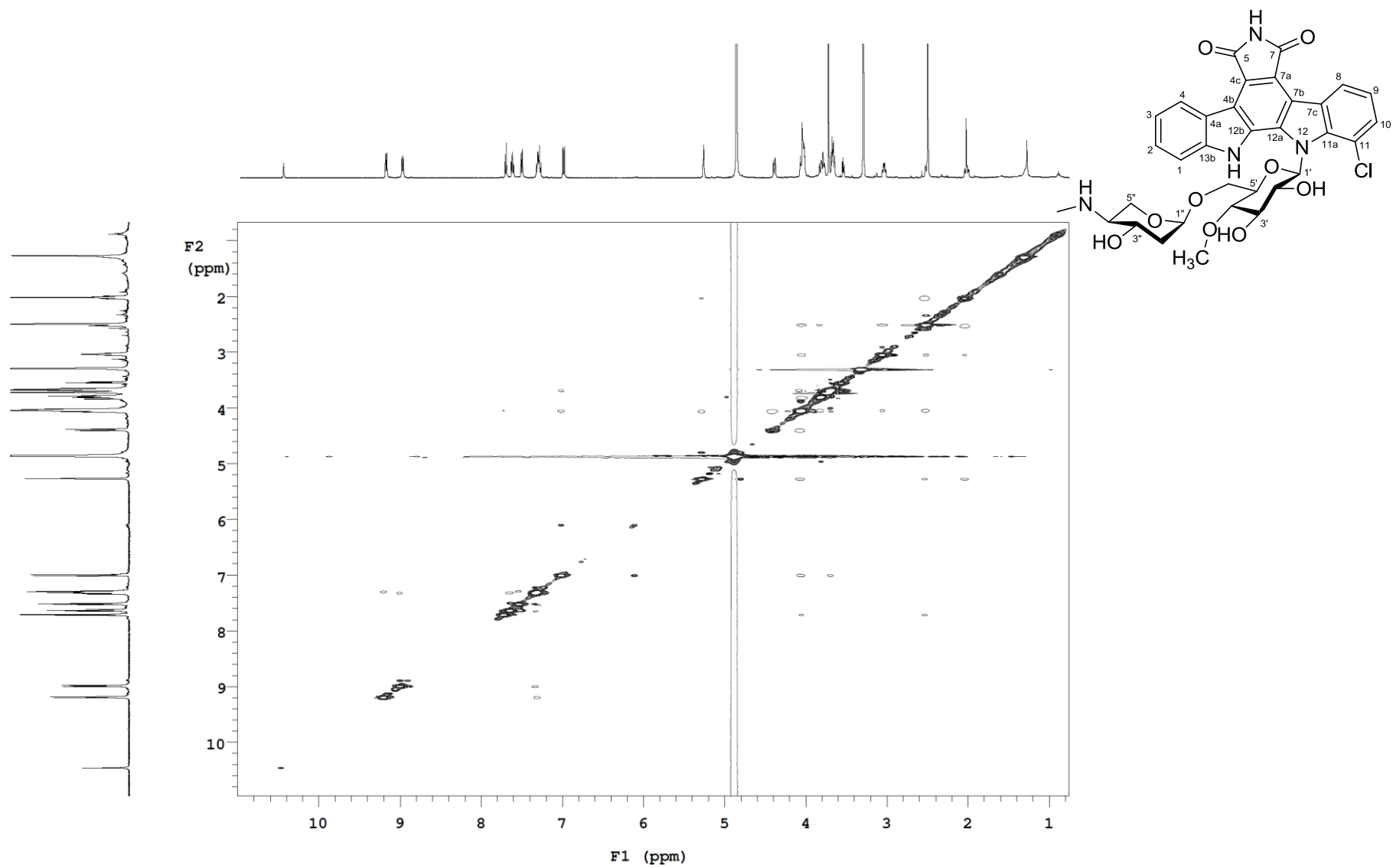


Figure S14. NOESY spectrum (CD₃OD, 500 MHz) of AT2433-A3 (**1**)

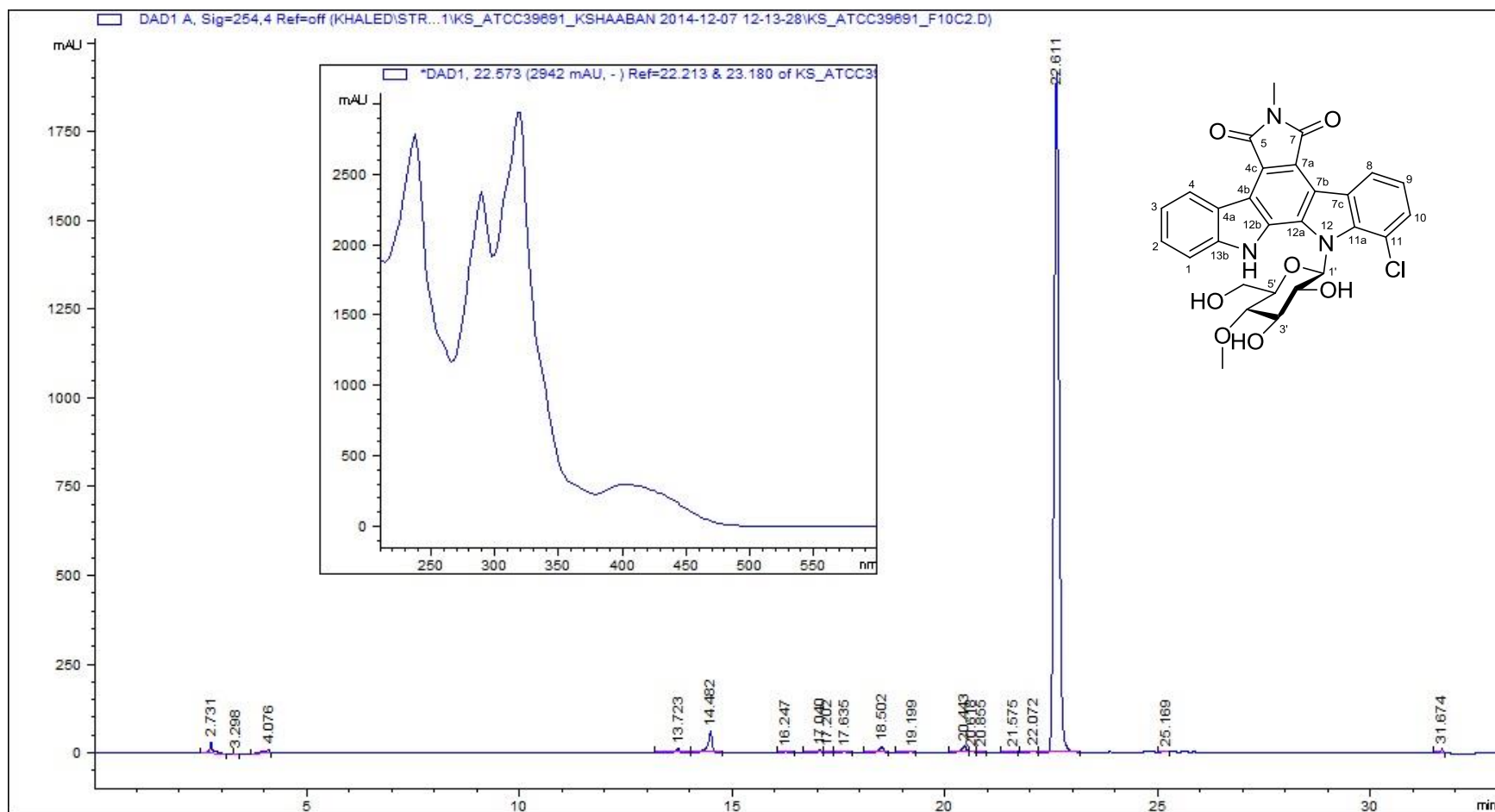


Figure S15. HPLC of AT2433-A4 (2). HPLC-conditions: Detection wavelength 254 nm; **solvent A:** H₂O/0.1% TFA; **solvent B:** CH₃CN; flow rate: 0.5 mL min⁻¹; 0-4 min, 10% B; 4-22 min, 10-100% B; 22-27 min, 100% B; 27-29 min, 100%-10% B; 29-35 min, 10 % B. UV-vis inset of full wavelength 190-600 nm.

14-0575 #19-38 RT: 0.50-0.99 AV: 20 NL: 3.06E6
T: FTMS - p ESI Full ms [200.00-1000.00]

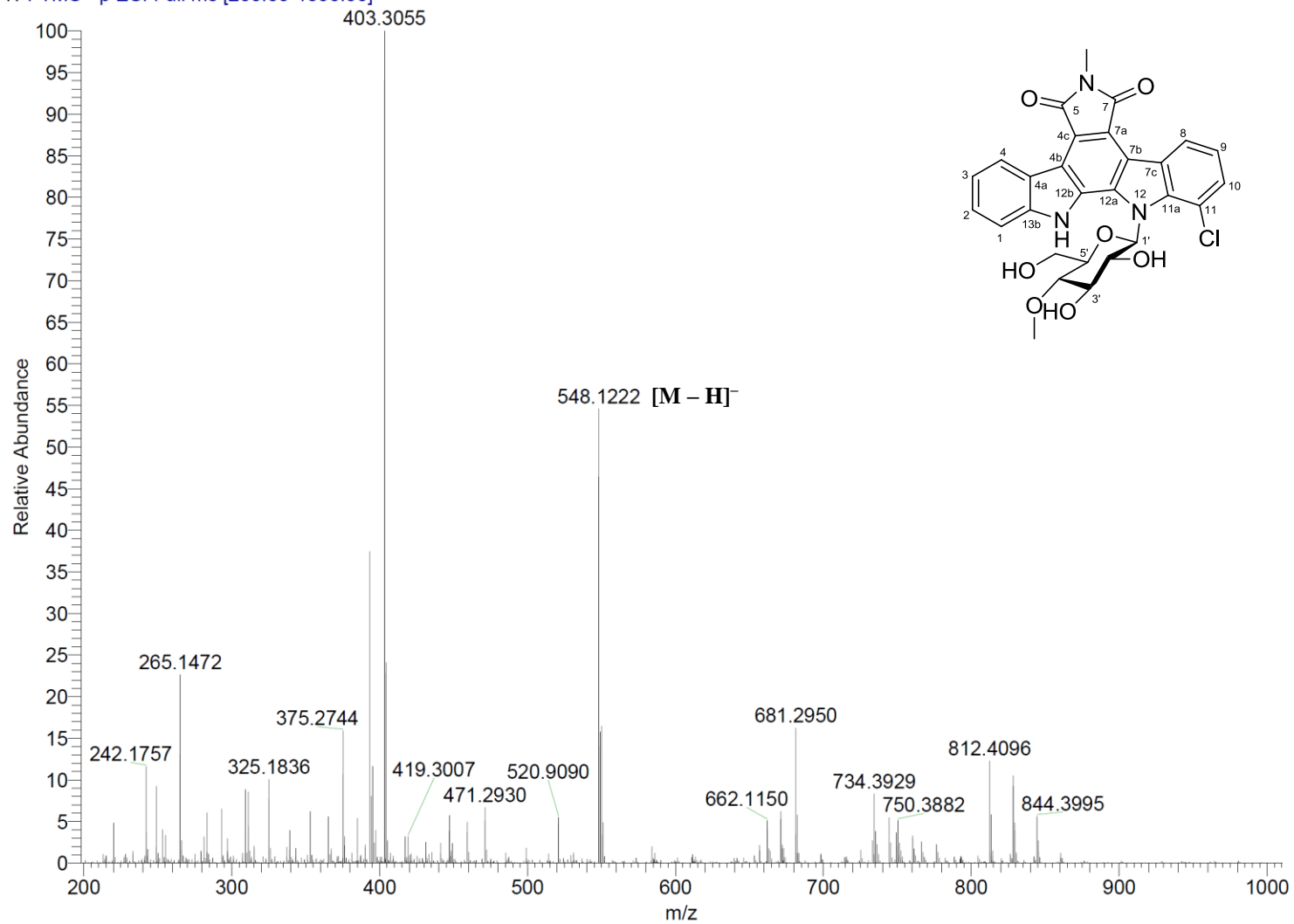


Figure S16: (-)-HRESI-MS spectrum of AT2433-A4 (**2**)

14-0575 #116-125 RT: 3.08-3.28 AV: 8 NL: 3.57E5
T: FTMS + p ESI Full lock ms [200.00-1000.00]

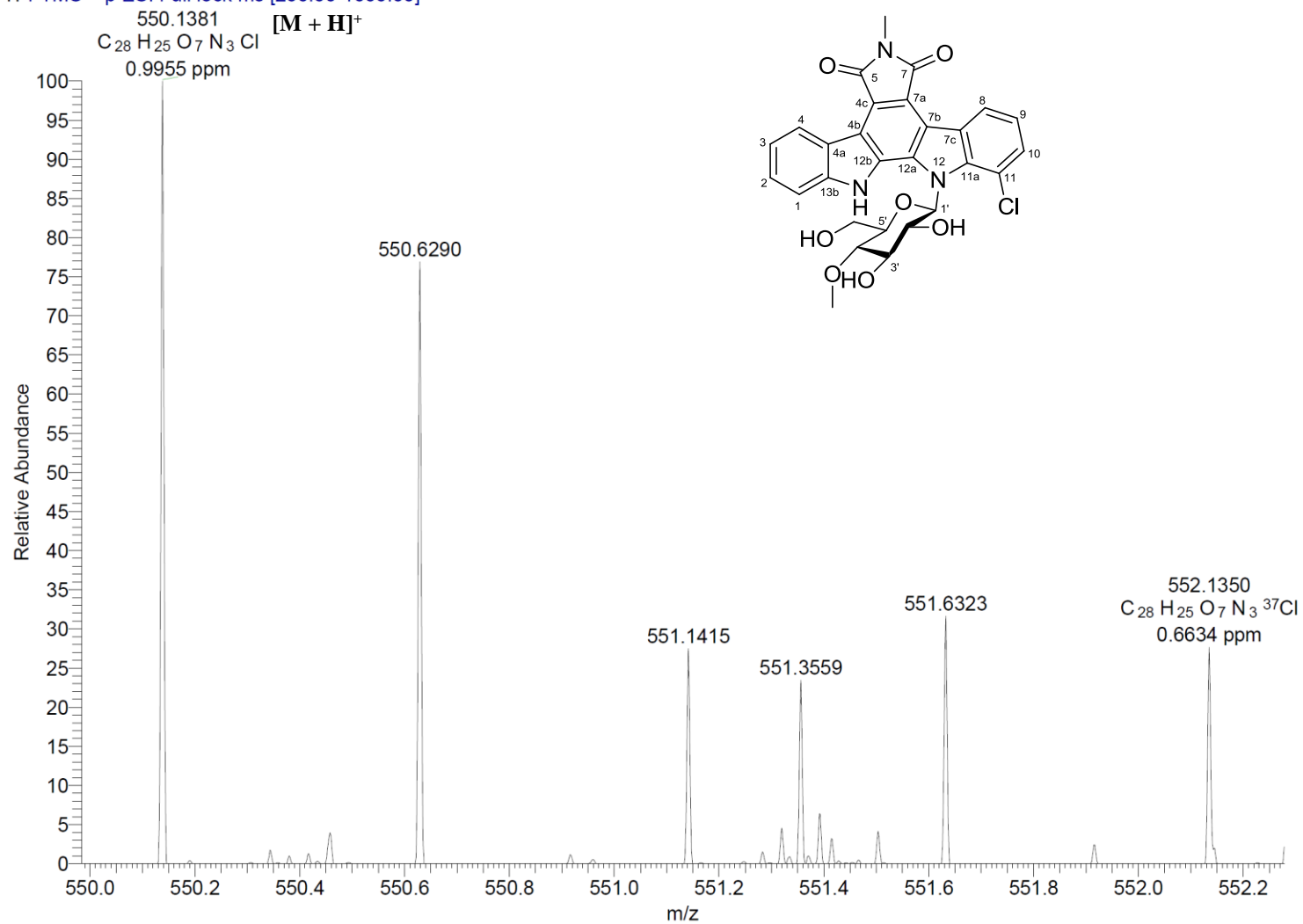


Figure S17: (+)-HRESI-MS spectrum of AT2433-A4 (2)

500 MHz, DMSO-d₆, nt=256
Khaled A. Shaaban

Sample: khaled_A_Shaaban
File: xp

Pulse Sequence: s2pul

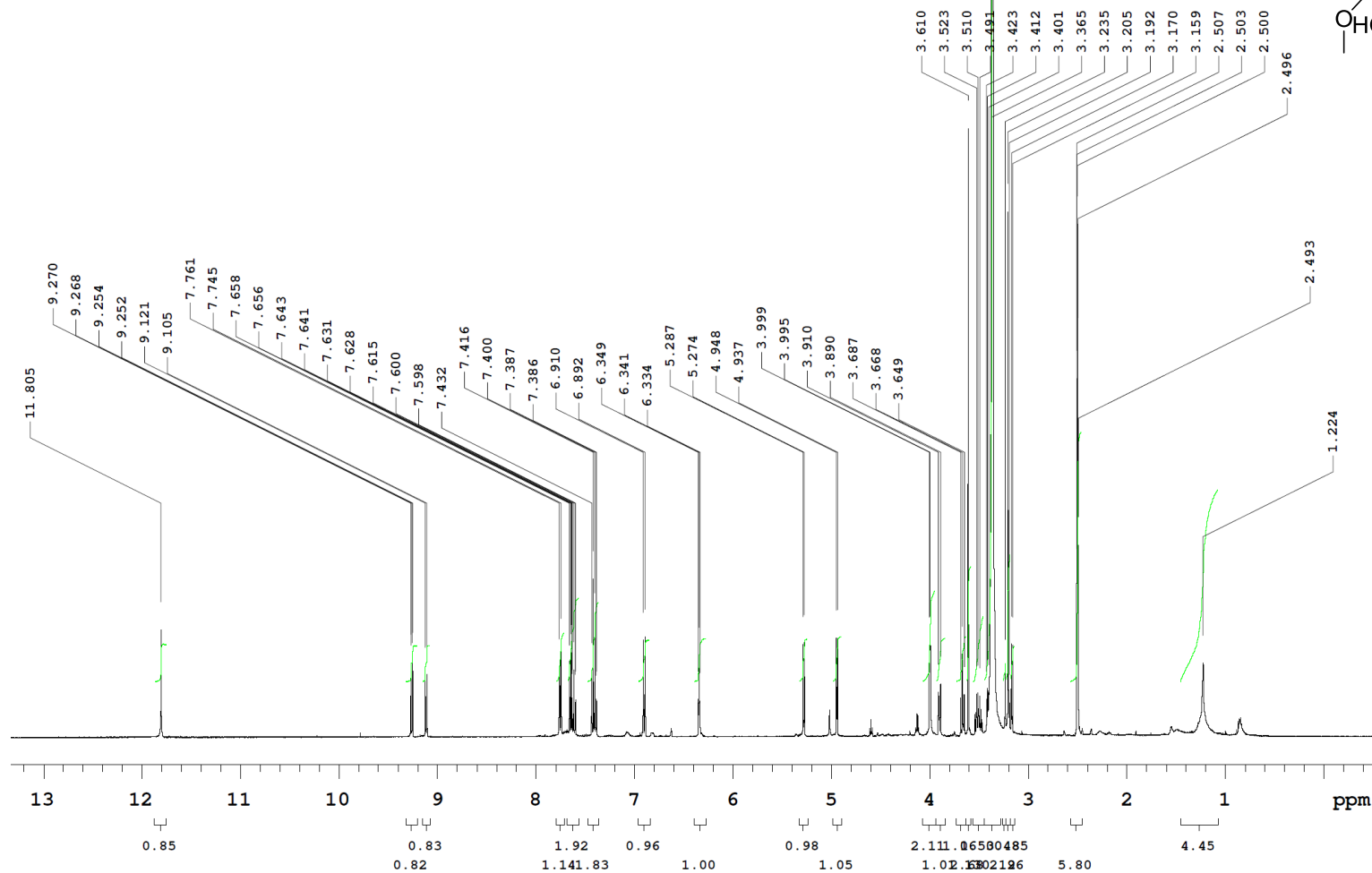


Figure S18: ¹H NMR spectrum (DMSO-d₆, 500 MHz) of AT2433-A4 (2)

Khaled A. Shaaban, F10C2

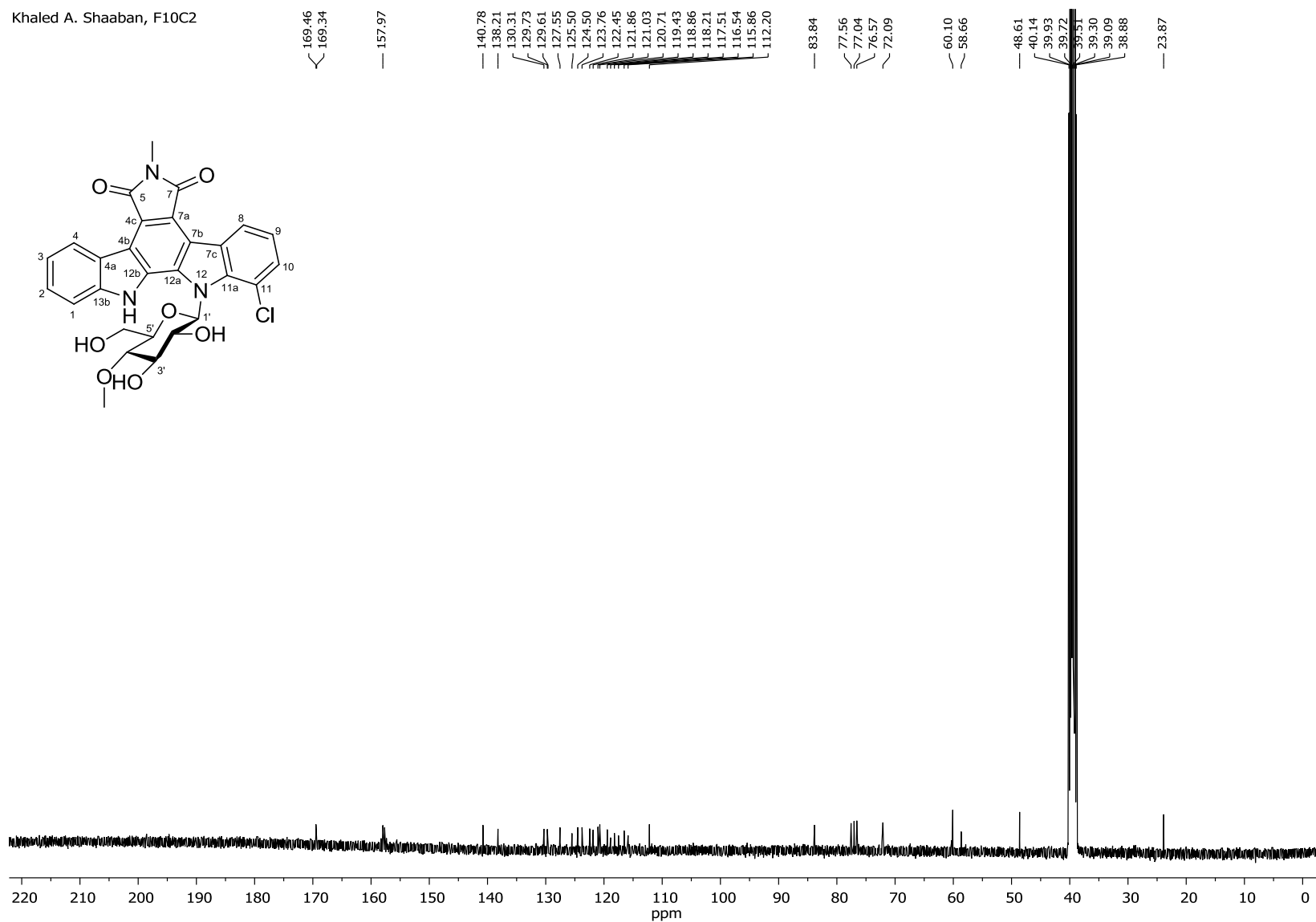


Figure S19: ^{13}C NMR spectrum (DMSO- d_6 , 100 MHz) of AT2433-A4 (2)

500 MHz, DMSO-d₆, 80 min
Khaled A. Shaaban

Sample: khaled_A_Shaaban
File: xp

Pulse Sequence: gCOSY

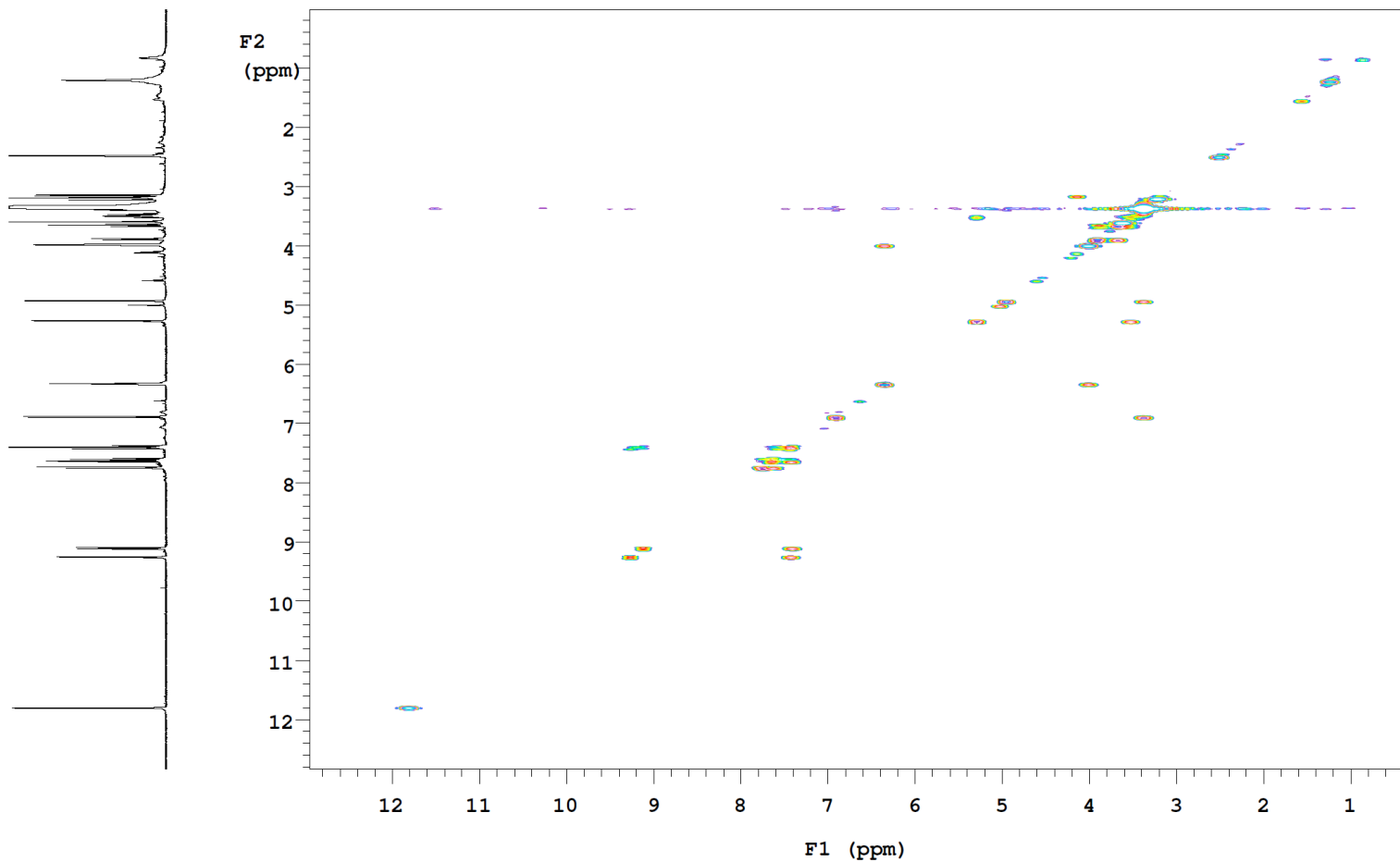
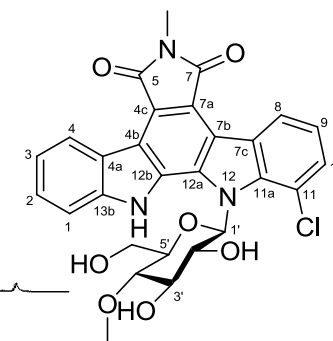


Figure S20: ^1H - ^1H COSY spectrum (DMSO- d_6 , 500 MHz) of AT2433-A4 (2)

500 MHz, DMSO-d₆, 5 hrs
Khaled A. Shaaban

Sample: khaled_A_Shaaban
File: xp

Pulse Sequence: gHSQC

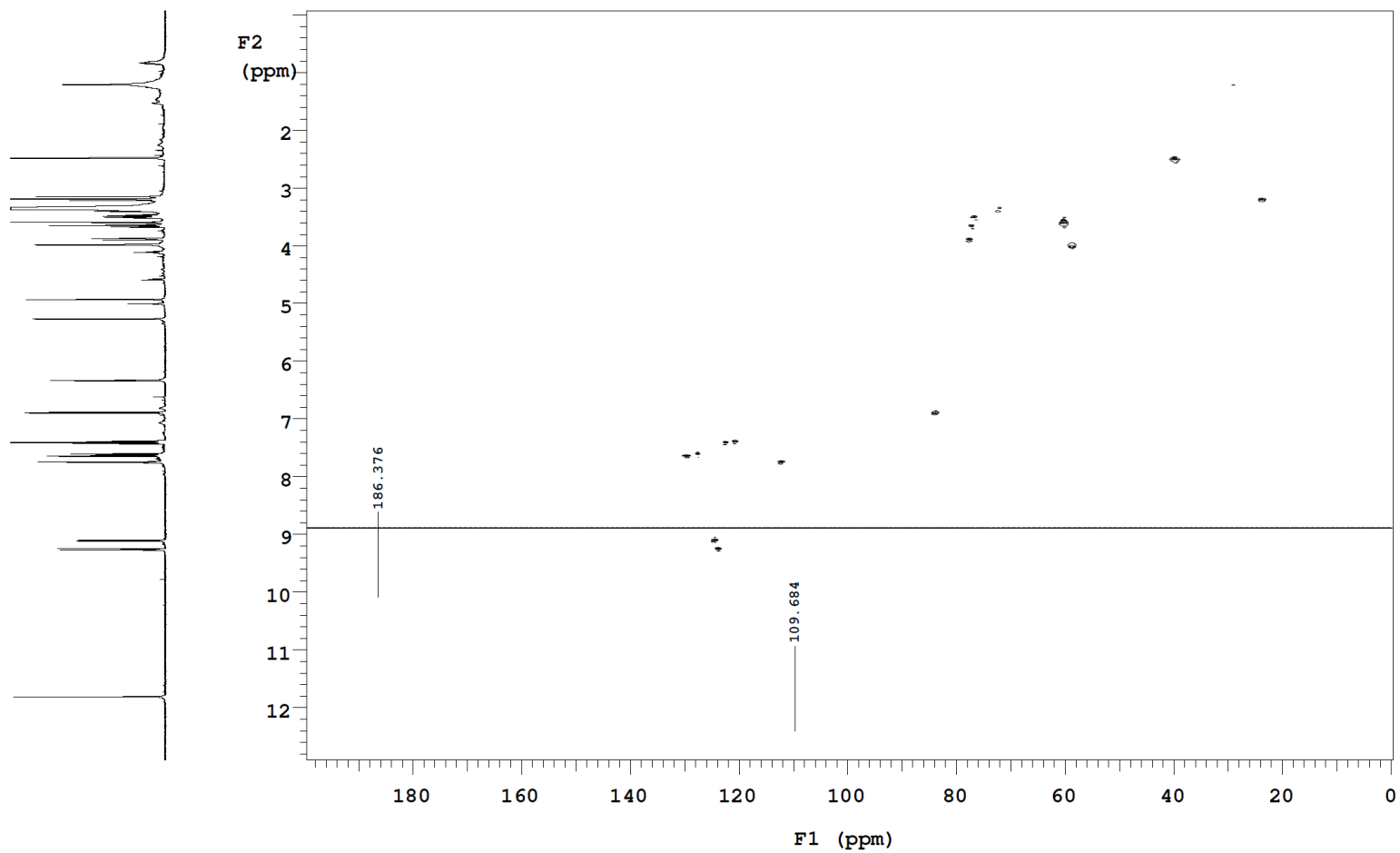
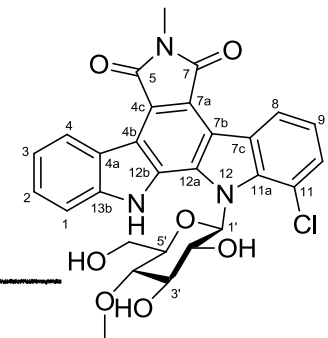


Figure S21: HSQC spectrum (DMSO-*d*₆, 500 MHz) of AT2433-A4 (2)

500 MHz, DMSO-d₆, 24 hrs
Khaled A. Shaaban

Sample: khaled_A_Shaaban
File: xp

Pulse Sequence: gHMBC

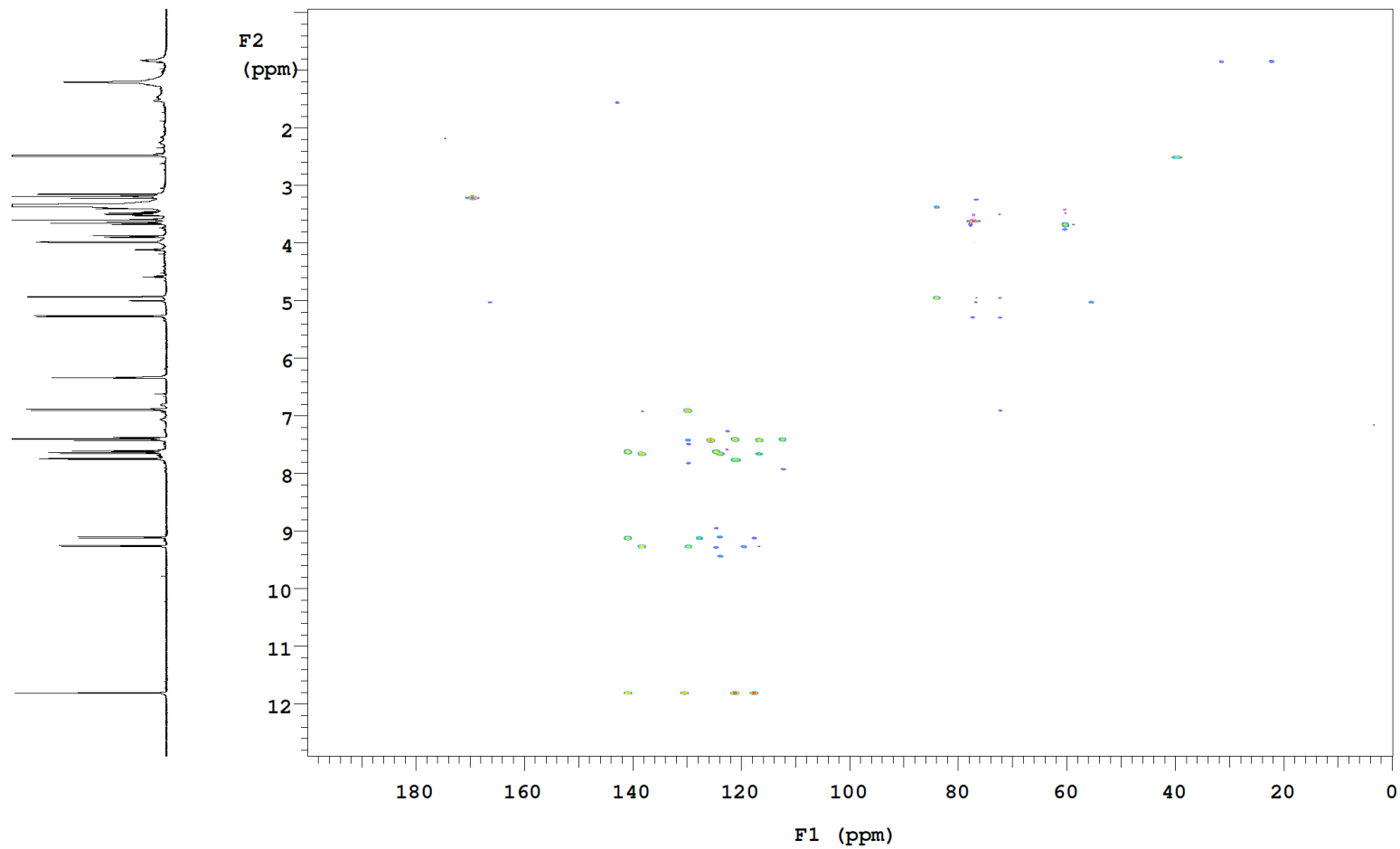
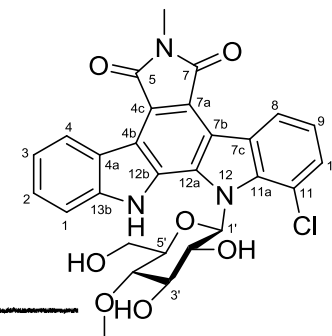


Figure S22: HMBC spectrum (DMSO-d₆, 500 MHz) of AT2433-A4 (2)

500 MHz, DMSO-d₆, 5 hrs
Khaled A. Shaaban

Sample: khaled_A_Shaaban
File: xp

Pulse Sequence: TOCSY

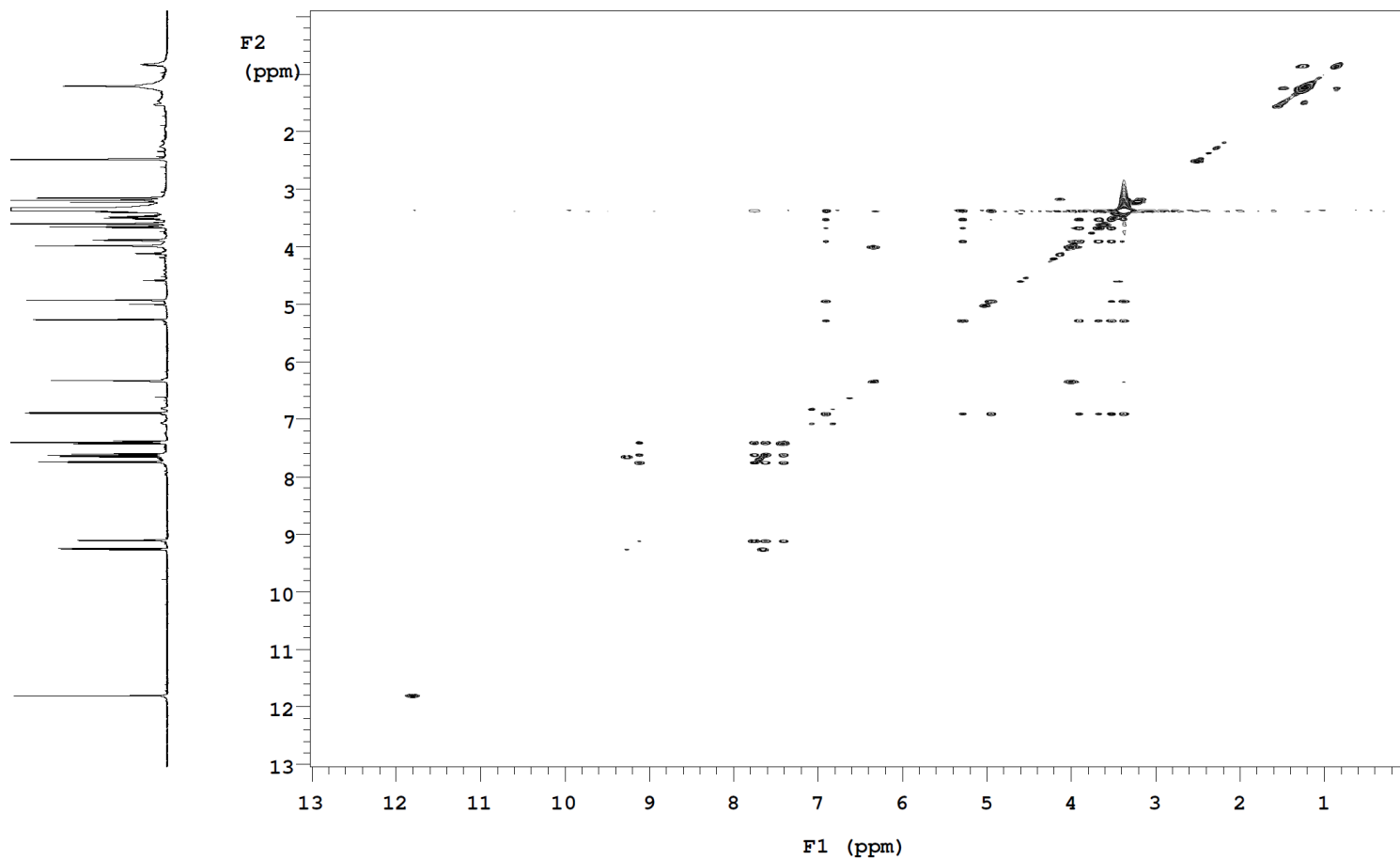
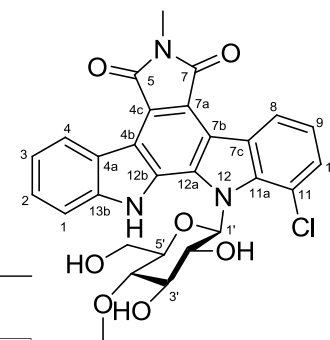
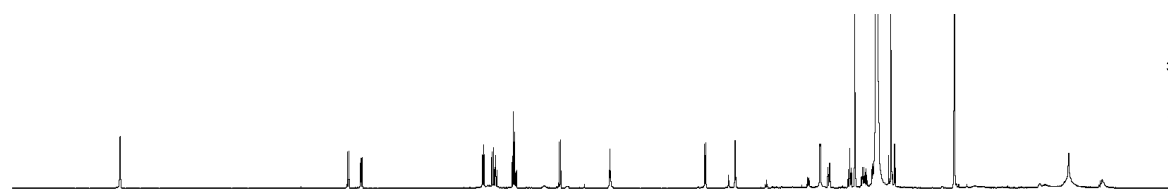


Figure S23: TOCSY spectrum (DMSO-*d*₆, 500 MHz) of AT2433-A4 (2)

500 MHz, DMSO-d₆, 15 hrs
Khaled A. Shaaban

Sample: khaled_A_Shaaban
File: xp

Pulse Sequence: NOESY

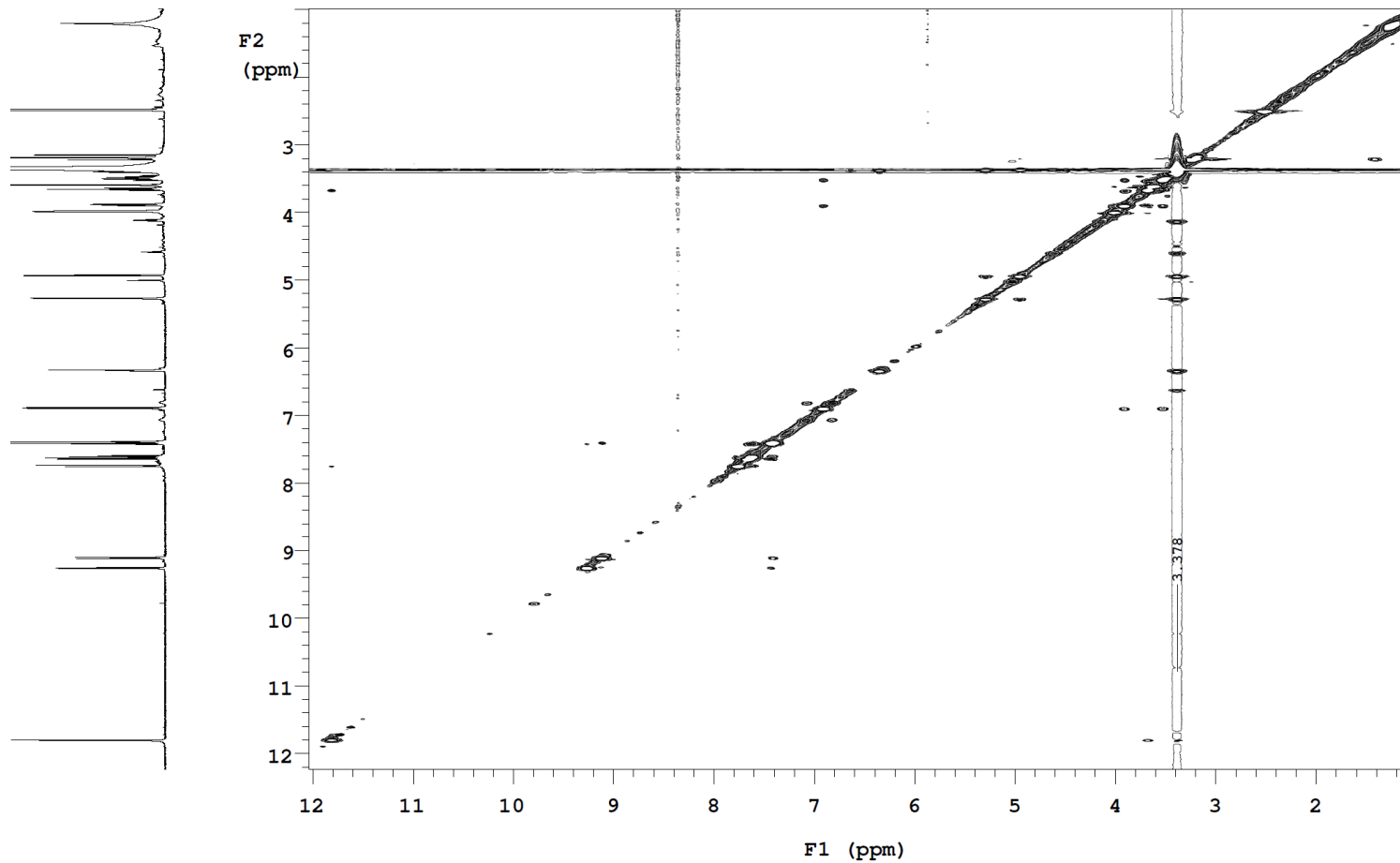
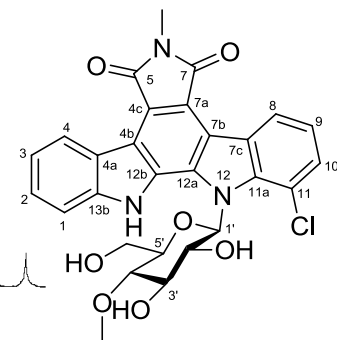


Figure S24: NOESY spectrum (DMSO-*d*₆, 500 MHz) of AT2433-A4 (**2**)

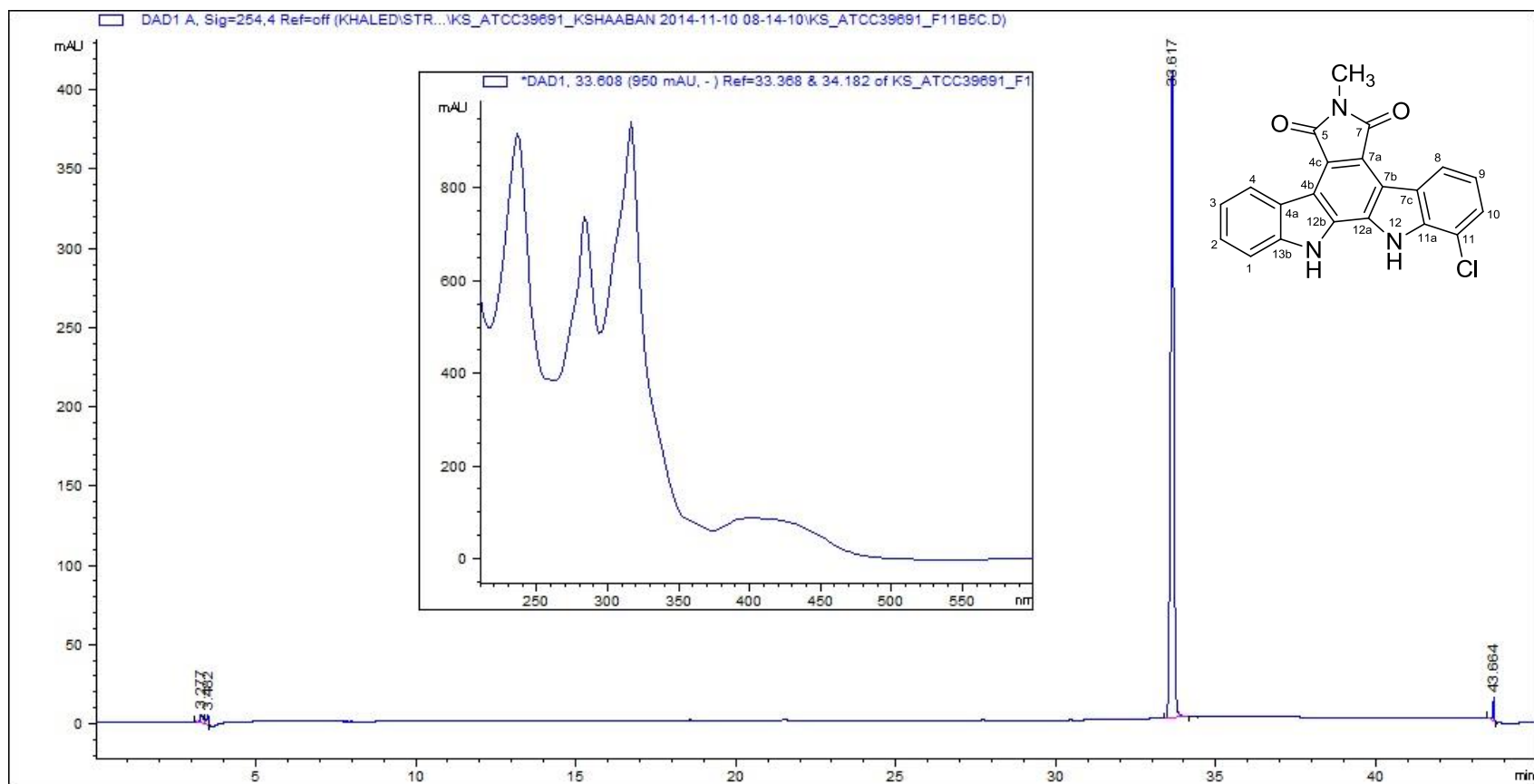


Figure S25: HPLC of AT2433-A5 (**3**). HPLC-conditions: Detection wavelength 254 nm; **solvent A:** H₂O/0.1% TFA; **solvent B:** CH₃CN; flow rate: 1.0 mL min⁻¹; 0-35 min, 5%-100% B; 35-40 min, 100% B; 40-41 min, 100%-5% B; 41-45 min, 5% B). UV-vis inset of full wavelength 190-600 nm.

14-0567a #1-36 RT: 0.03-0.96 AV: 36 NL: 2.78E7
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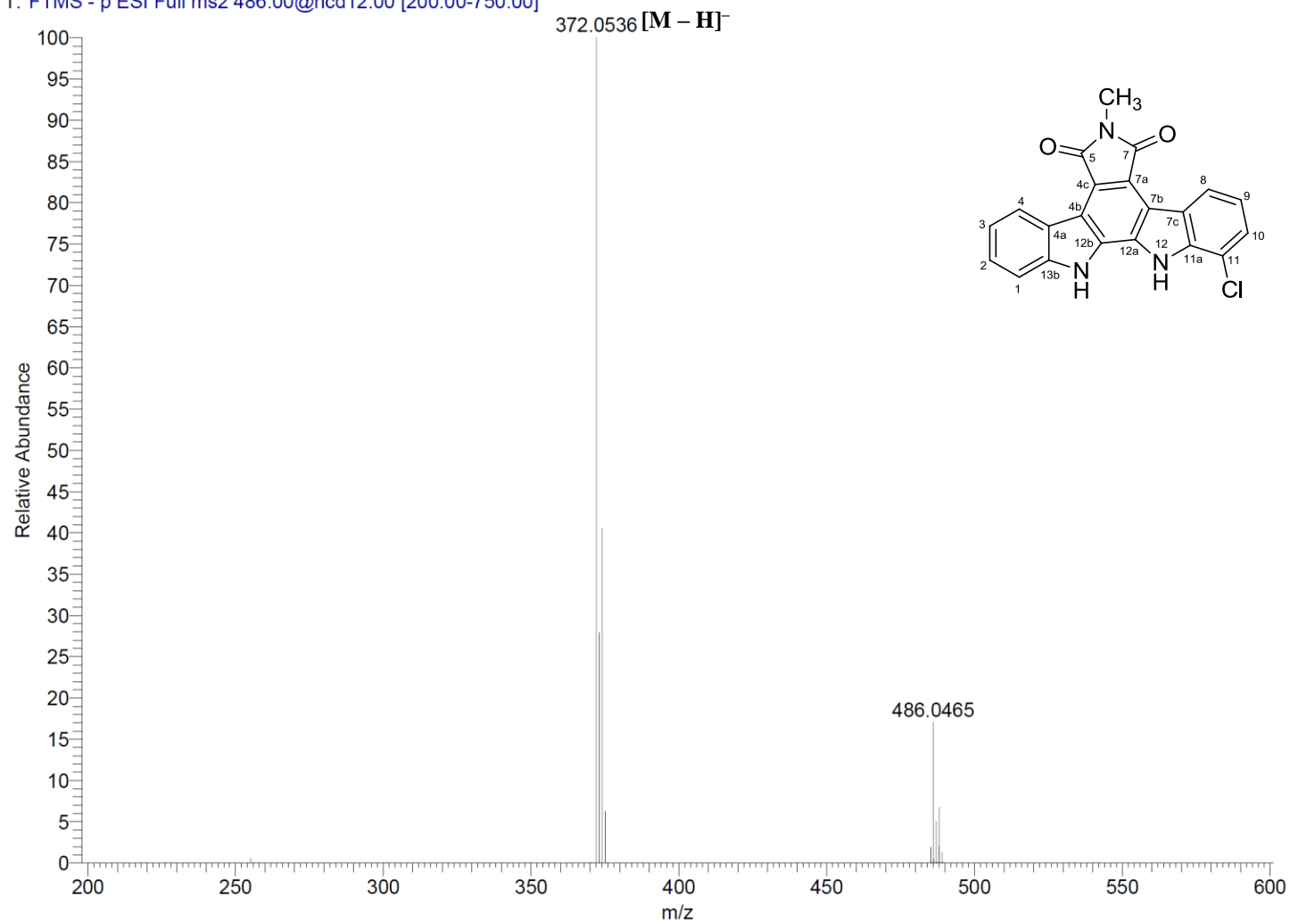


Figure S26: (-)-HRESI-MS spectrum of AT2433-A5 (3)

500 MHz, DMSO-d₆, nt=265
Khaled A. Shaaban

Sample: khaled_A_Shaaban
File: xp

Pulse Sequence: s2pul

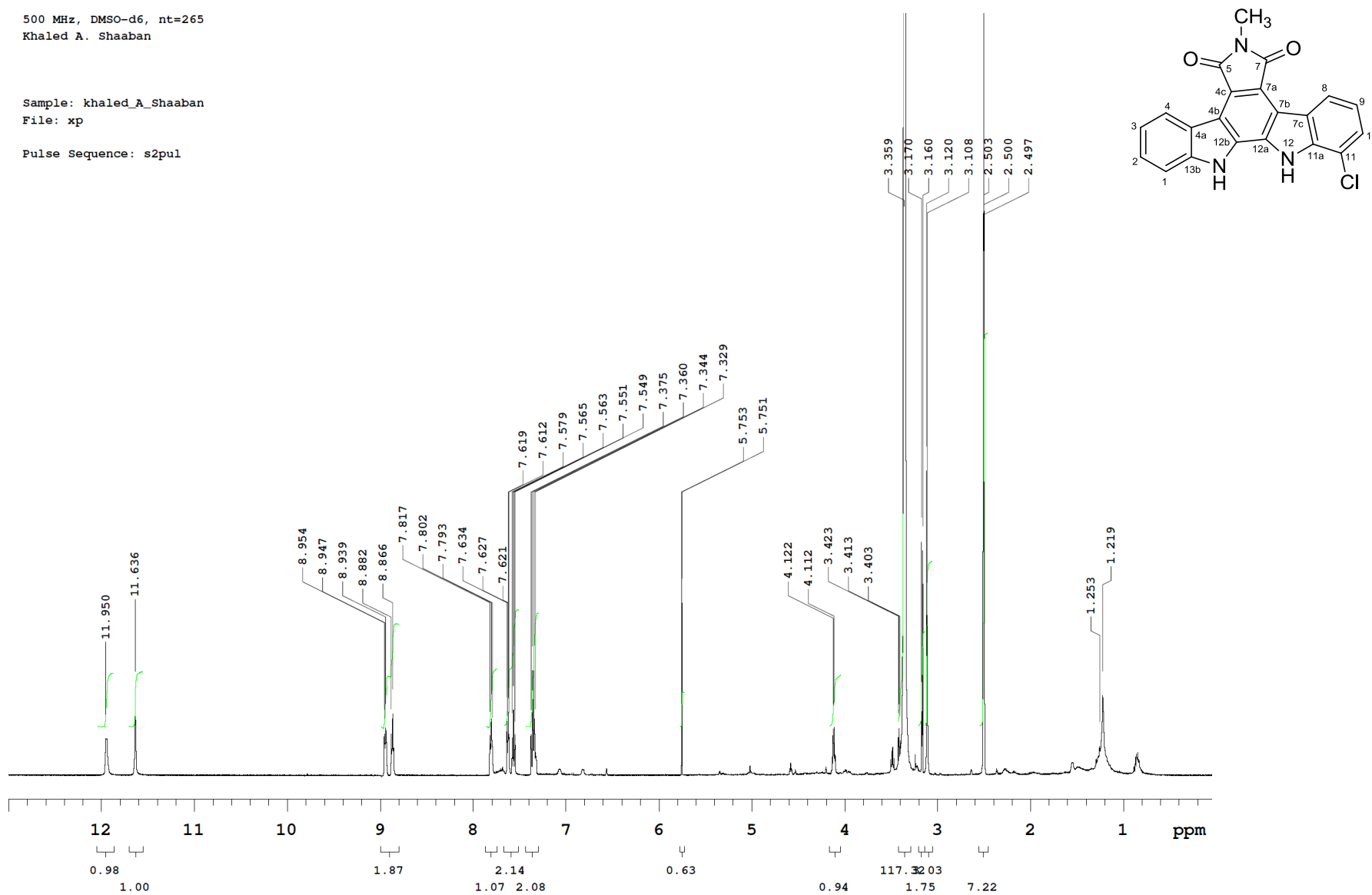


Figure S27: ¹H NMR spectrum (DMSO-d₆, 500 MHz) of AT2433-A5 (3)

Khaled A. Shaaban, F11B5C

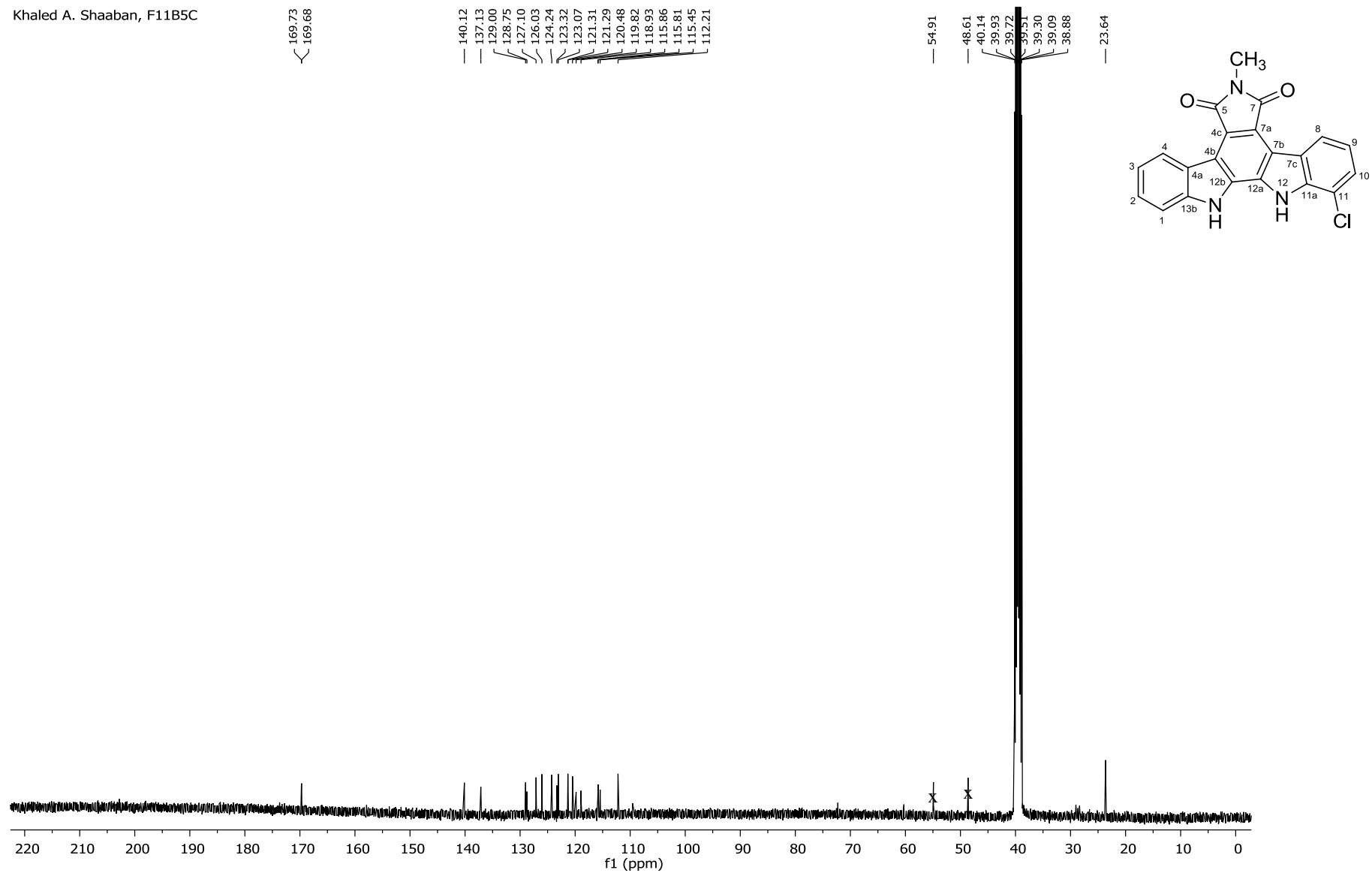


Figure S28: ¹³C NMR spectrum (DMSO-*d*₆, 100 MHz) of AT2433-A5 (**3**)

500 MHz, DMSO-d6, 2 hrs
Khaled A. Shaaban

Sample: khaled_A_Shaaban
File: xp

Pulse Sequence: gCOSY

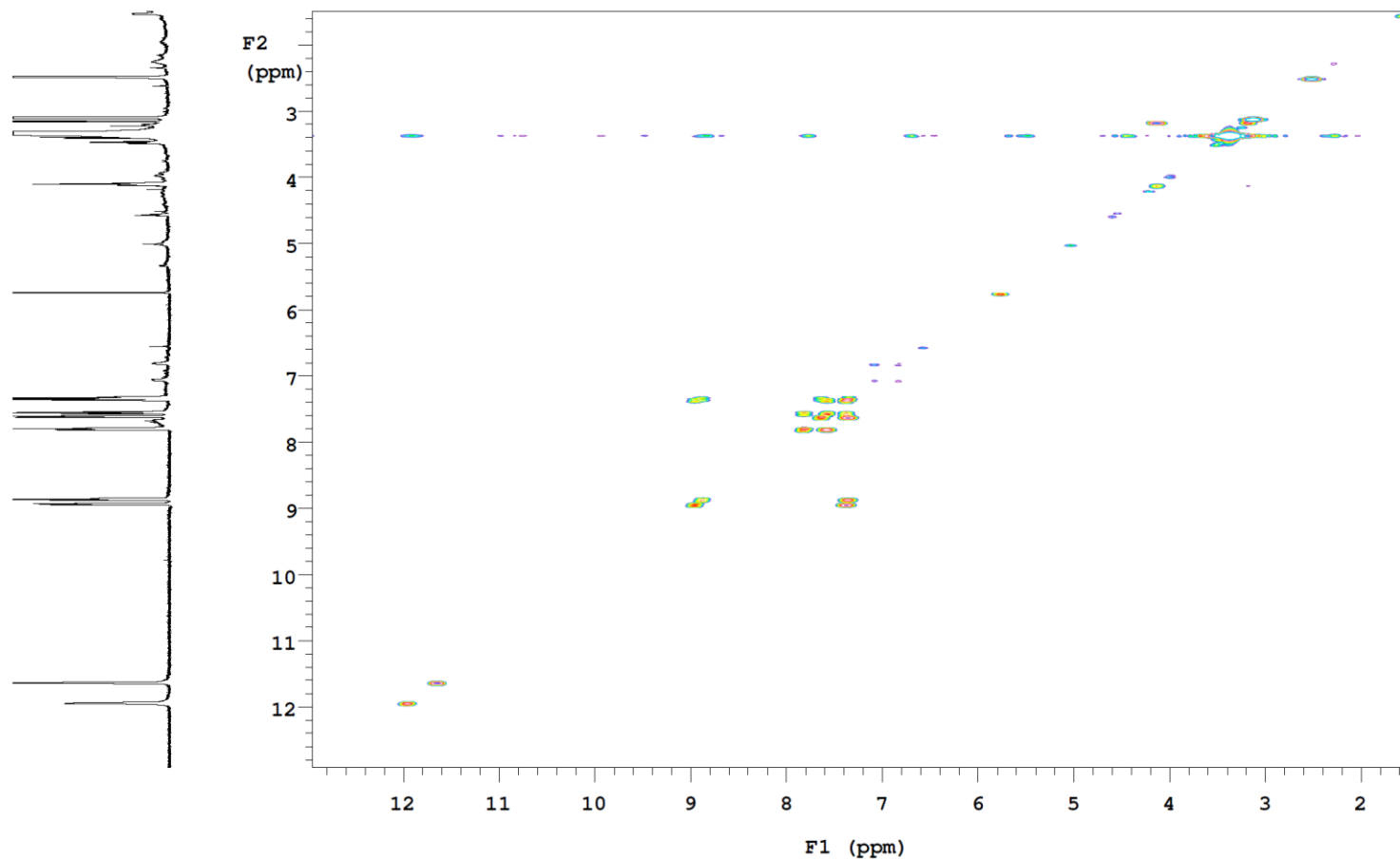
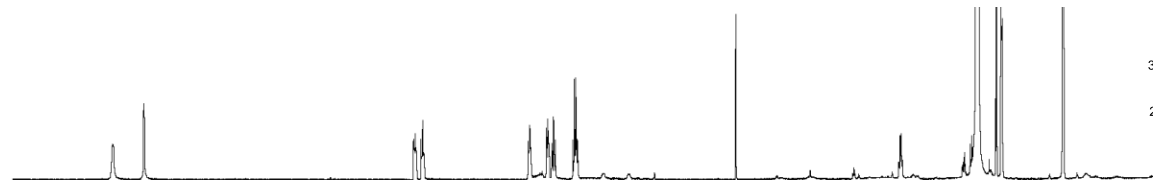
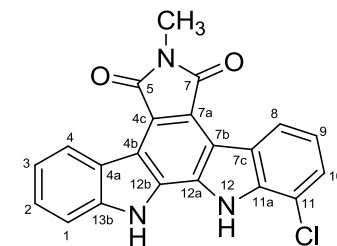


Figure S29: ¹H-¹H COSY spectrum (CD₃OD, 500 MHz) of AT2433-A5 (**3**)

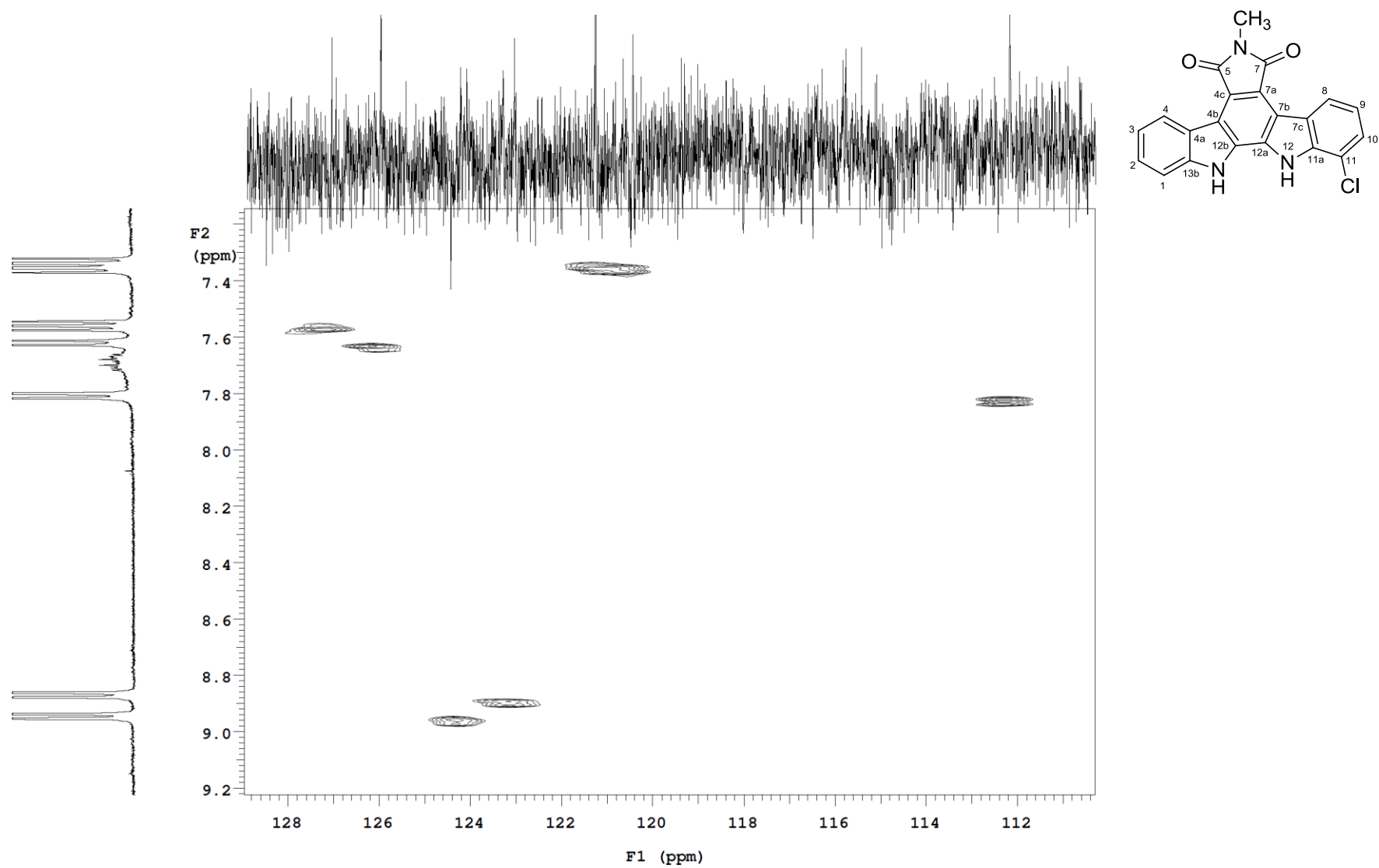


Figure S30: Enlarged HSQC spectrum (DMSO-*d*₆, 500 MHz) of AT2433-A5 (**3**)

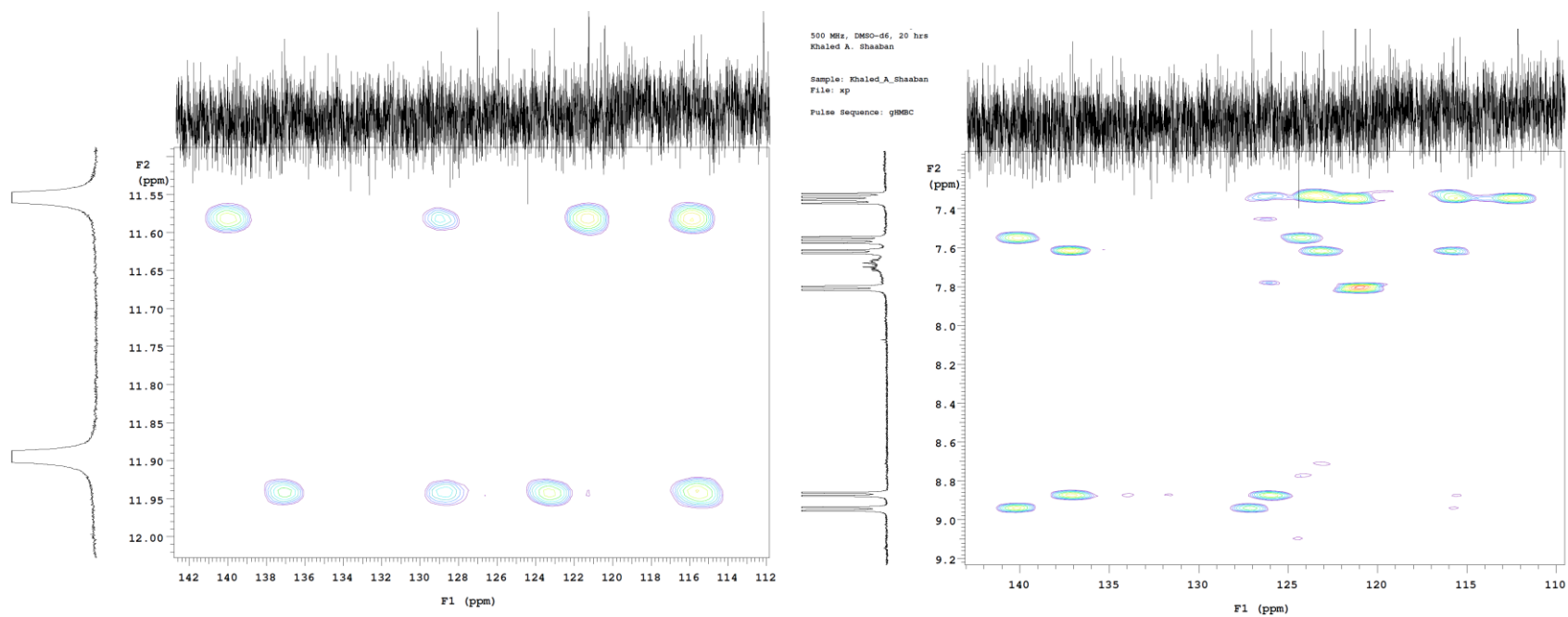
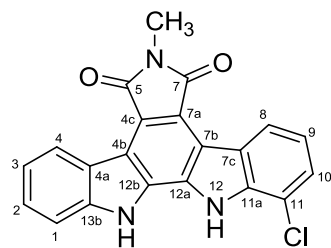


Figure S31: Enlarged HMBC spectrum (DMSO-*d*₆, 500 MHz) of AT2433-A5 (3)

500 MHz, DMSO-d₆, 3 hrs
Khaled A. Shaaban

Sample: Khaled_A_Shaaban
File: xp

Pulse Sequence: TOCSY

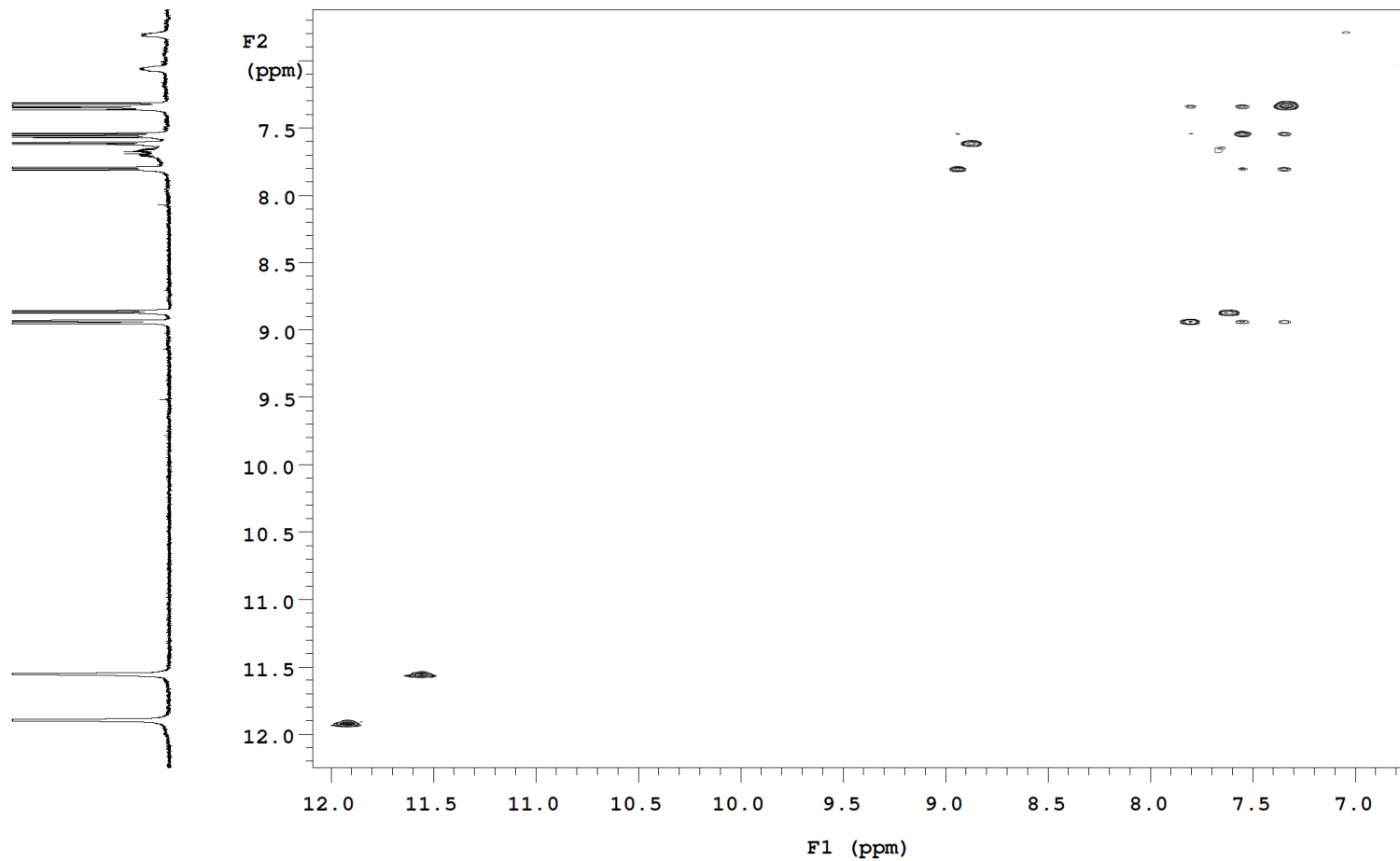
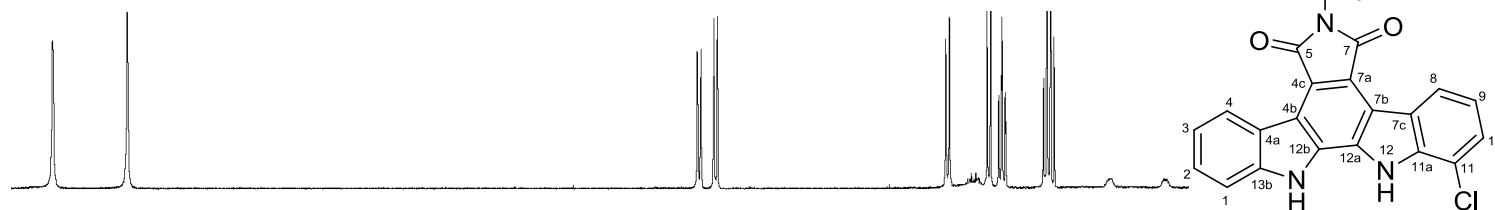


Figure S32: Enlarged TOCSY spectrum (DMSO-*d*₆, 500 MHz) of AT2433-A5 (**3**)

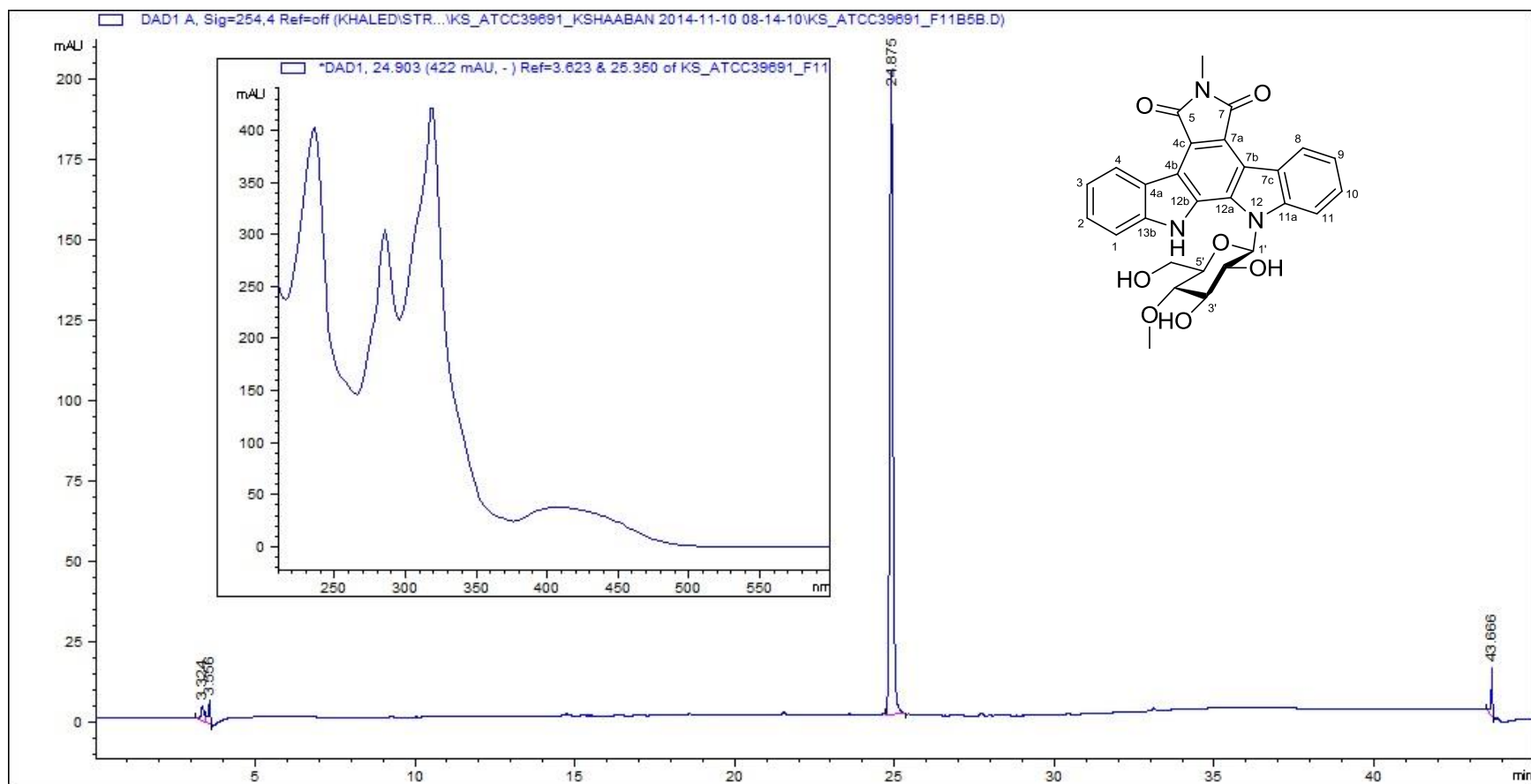


Figure S33: HPLC of AT2433-B3 (**4**). HPLC-conditions: Detection wavelength 254 nm; **solvent A:** H₂O/0.1% TFA; **solvent B:** CH₃CN; flow rate: 1.0 mL min⁻¹; 0-35 min, 5%-100% B; 35-40 min, 100% B; 40-41 min, 100%-5% B; 41-45 min, 5% B). UV-vis inset of full wavelength 190-600 nm.

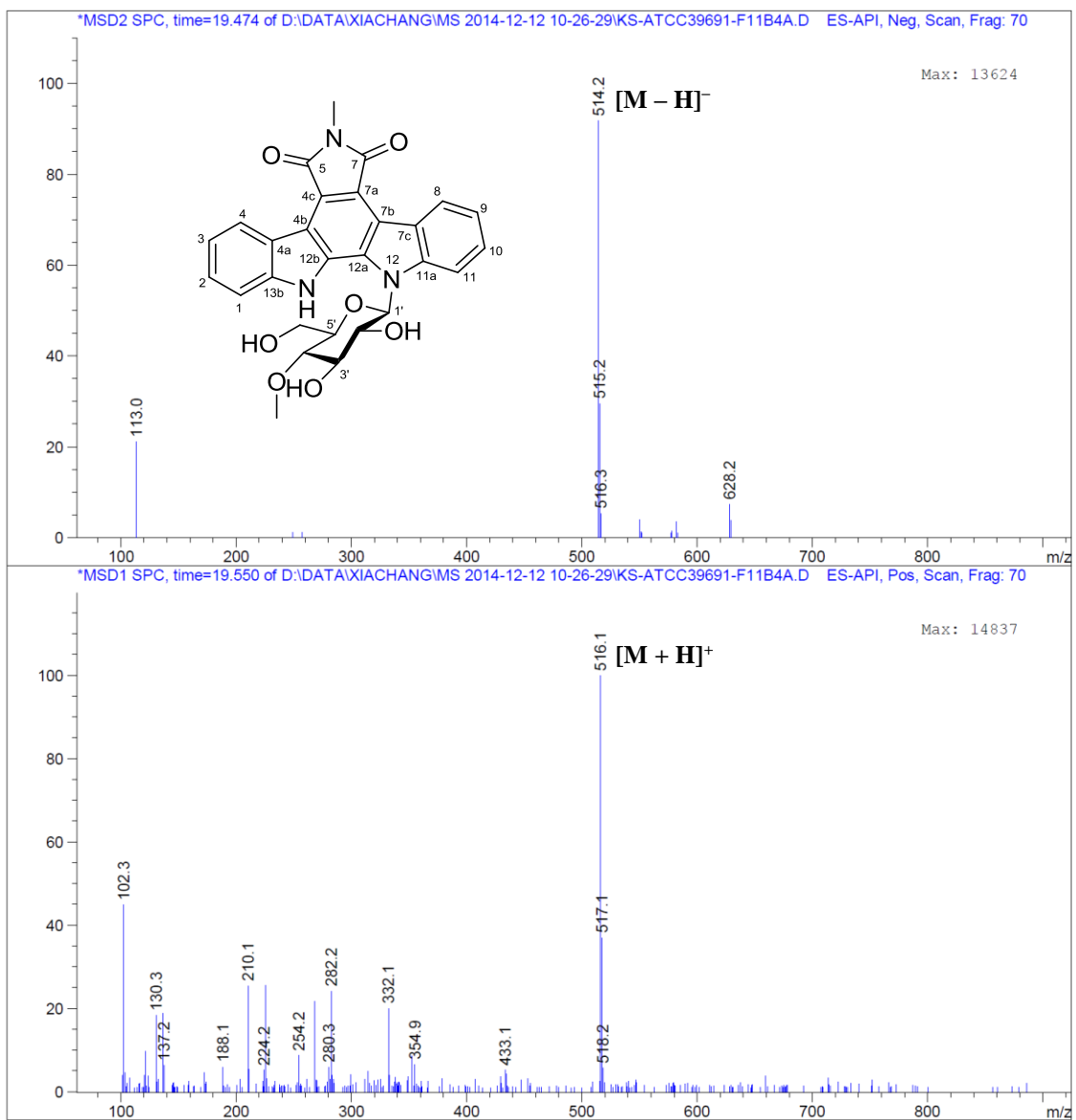


Figure S34: (+) and (-)-APCI-MS spectra of AT2433-B3 (4)

14-0554 #4-32 RT: 0.10-0.84 AV: 29 NL: 9.89E5
T: FTMS - p ESI Full ms [300.00-1000.00]

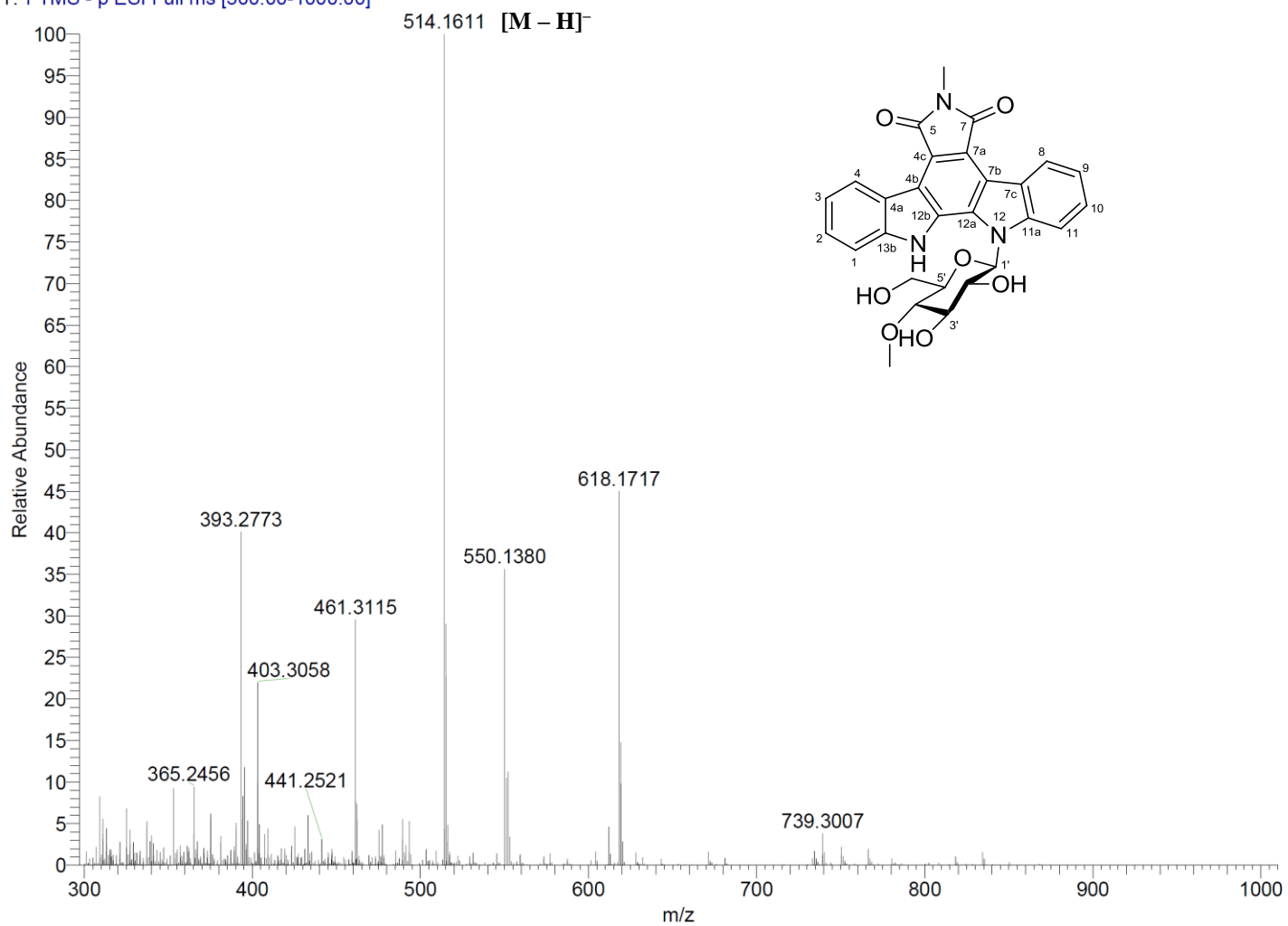


Figure S35: (-)-HRESI-MS spectrum of AT2433-B3 (4)

14-0554 #93-109 RT: 2.44-2.86 AV: 17 NL: 4.64E5
T: FTMS + p ESI Full lock ms [350.00-650.00]

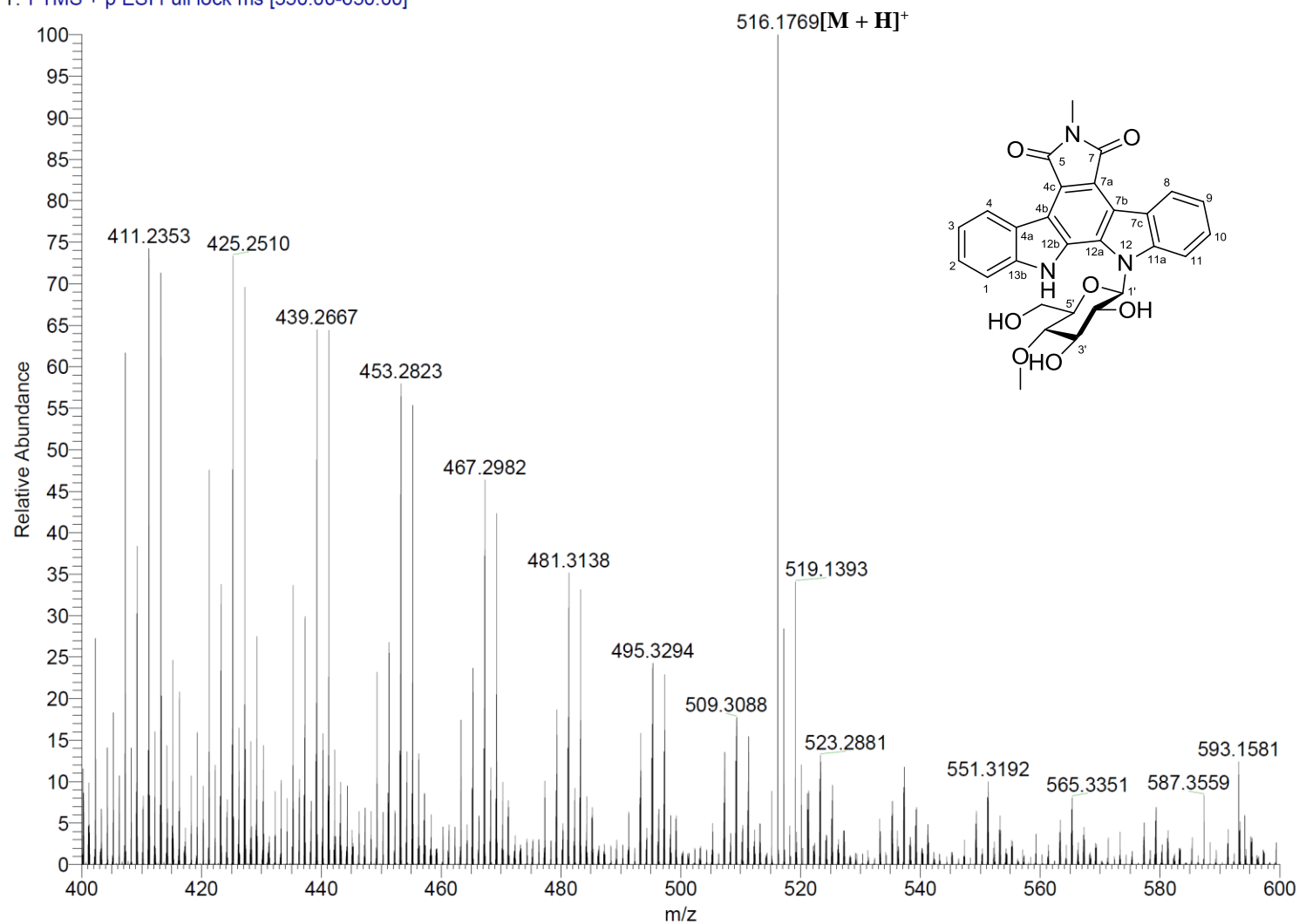


Figure S36: (+)-HRESI-MS spectrum of AT2433-B3 (4)

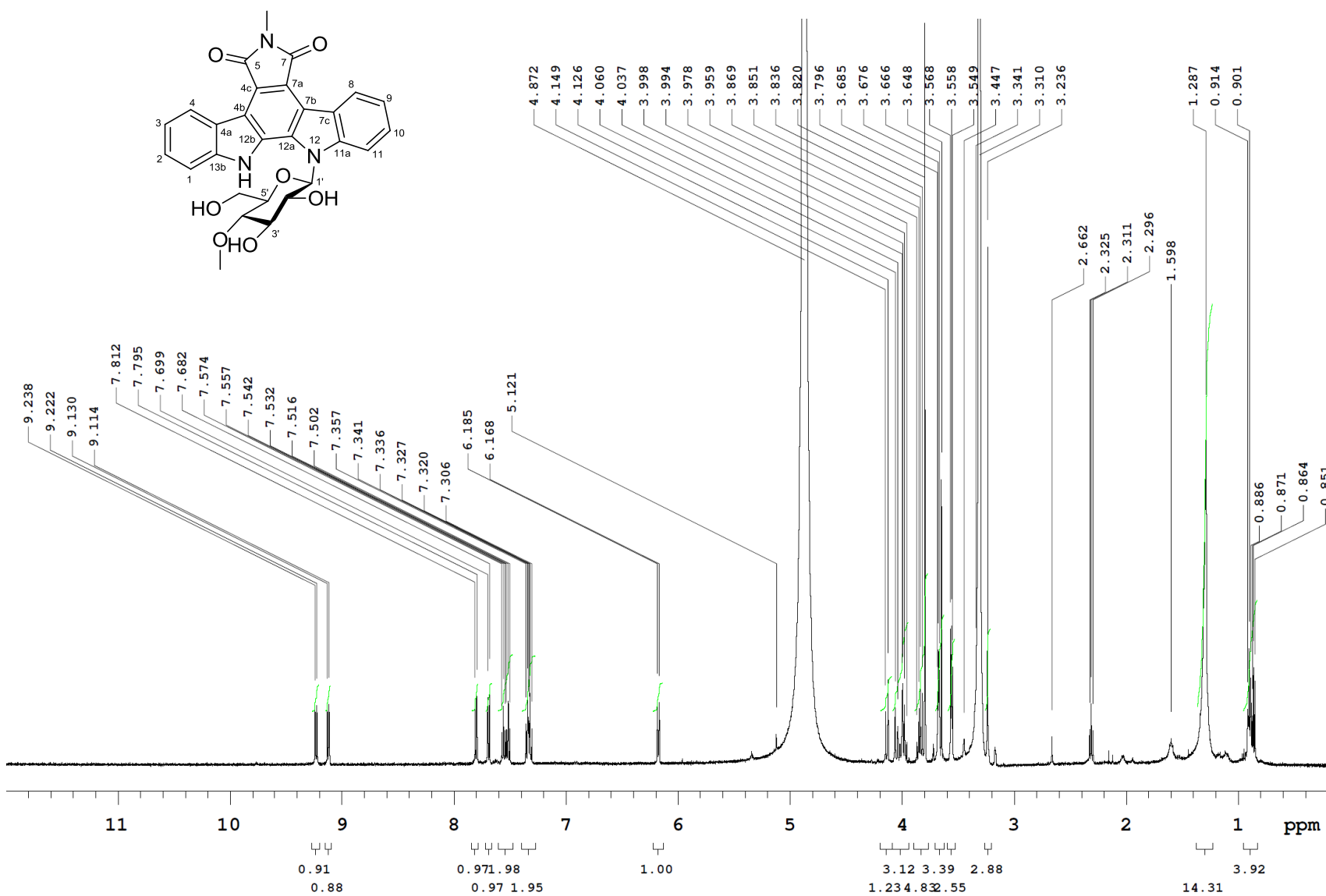


Figure S37: ¹H NMR spectrum (CD₃OD, 500 MHz) of AT2433-B3 (4)

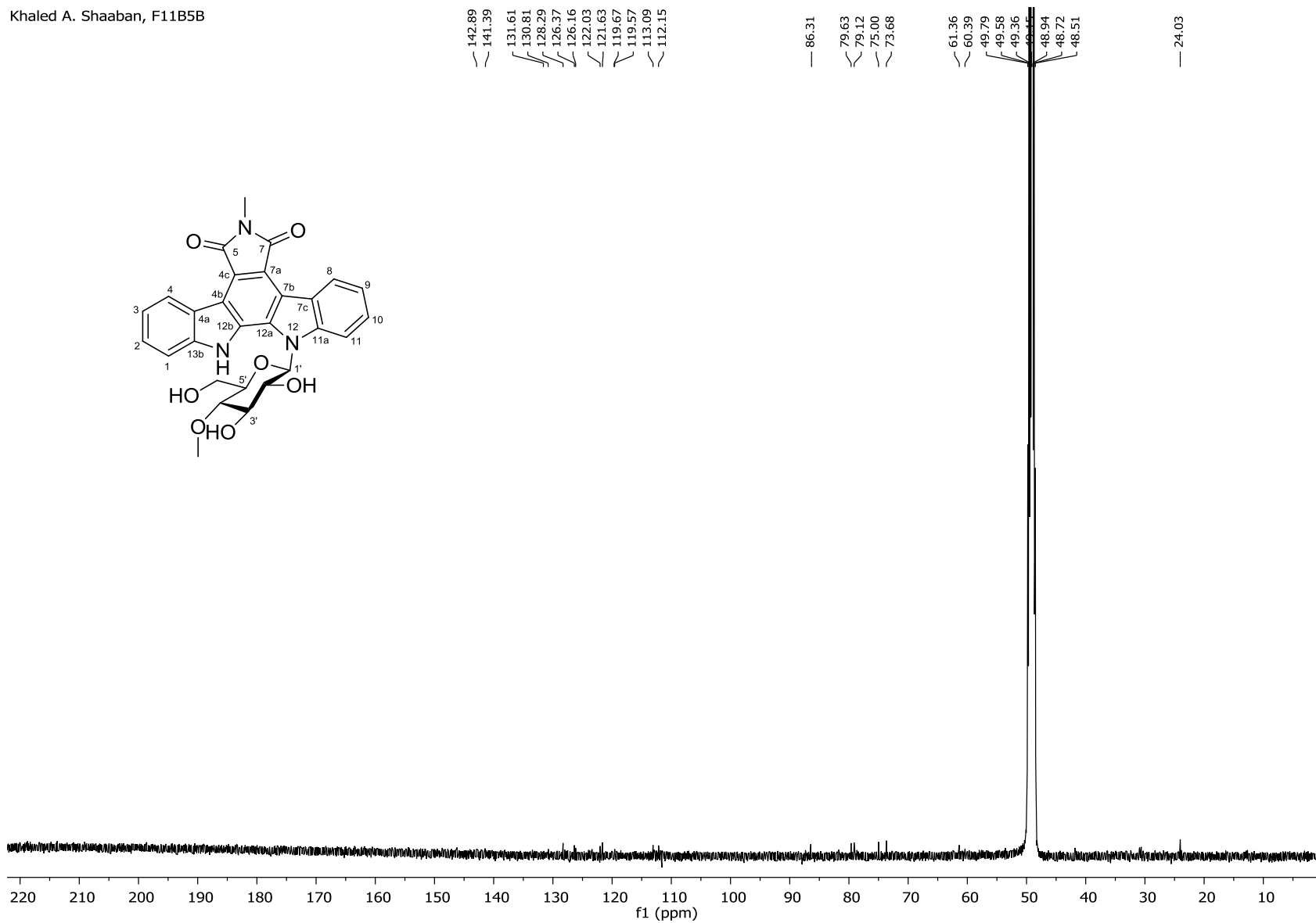


Figure S38: ¹³C NMR spectrum (CD₃OD, 100 MHz) of AT2433-B3 (4)

500 MHz, CD3OD, 80 min
Khaled A. Shaaban

Sample: Khaled_A_Shaaban
File: xp

Pulse Sequence: gCOSY

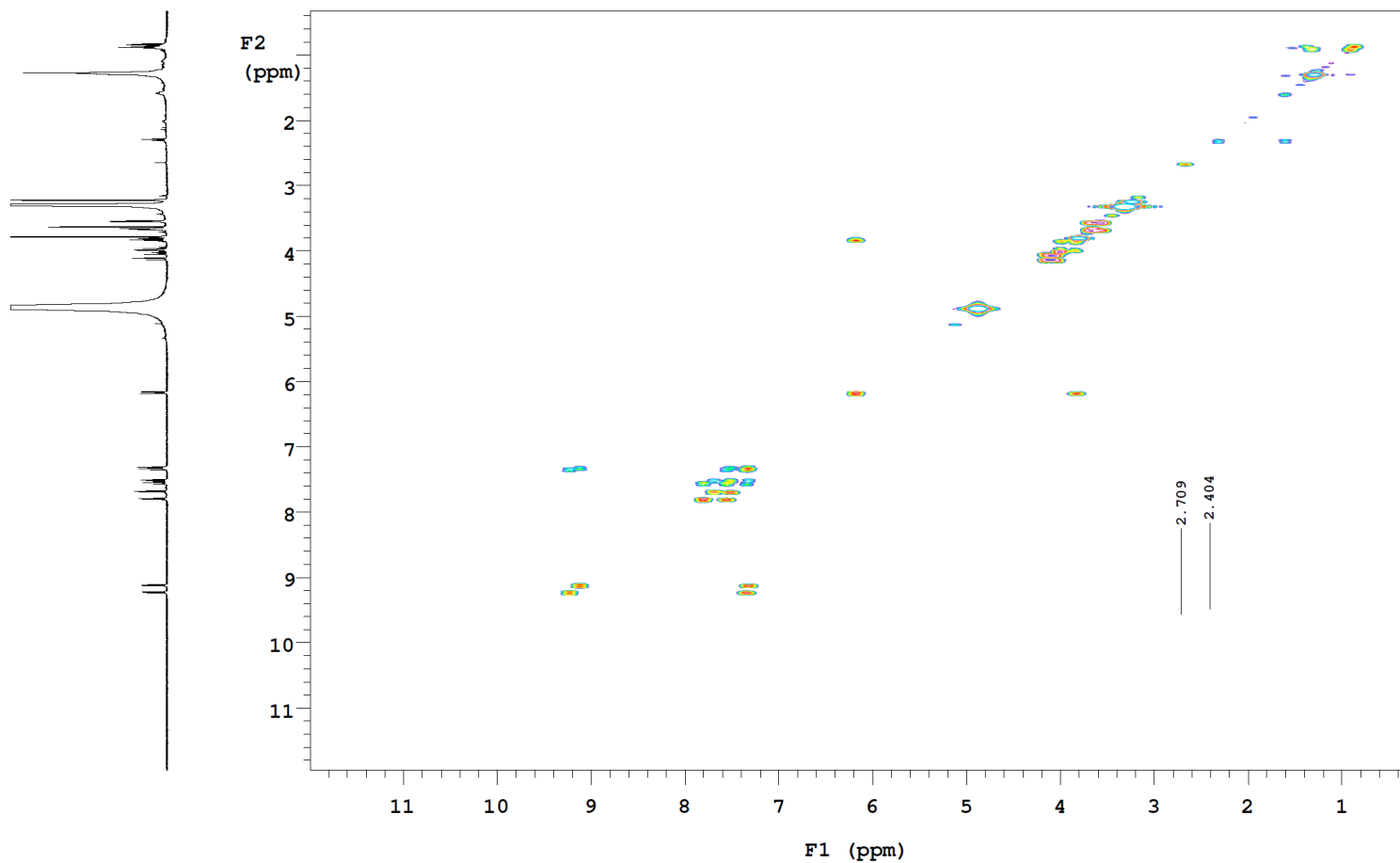
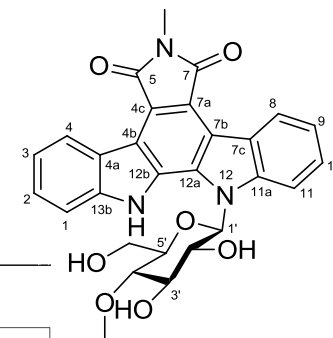


Figure S39: ^1H - ^1H COSY spectrum (CD_3OD , 500 MHz) of AT2433-B3 (**4**)

500 MHz, CD₃OD, 5 hrs
Khaled A. Shaaban

Sample: Khaled_A_Shaaban
File: xp

Pulse Sequence: gHSQC

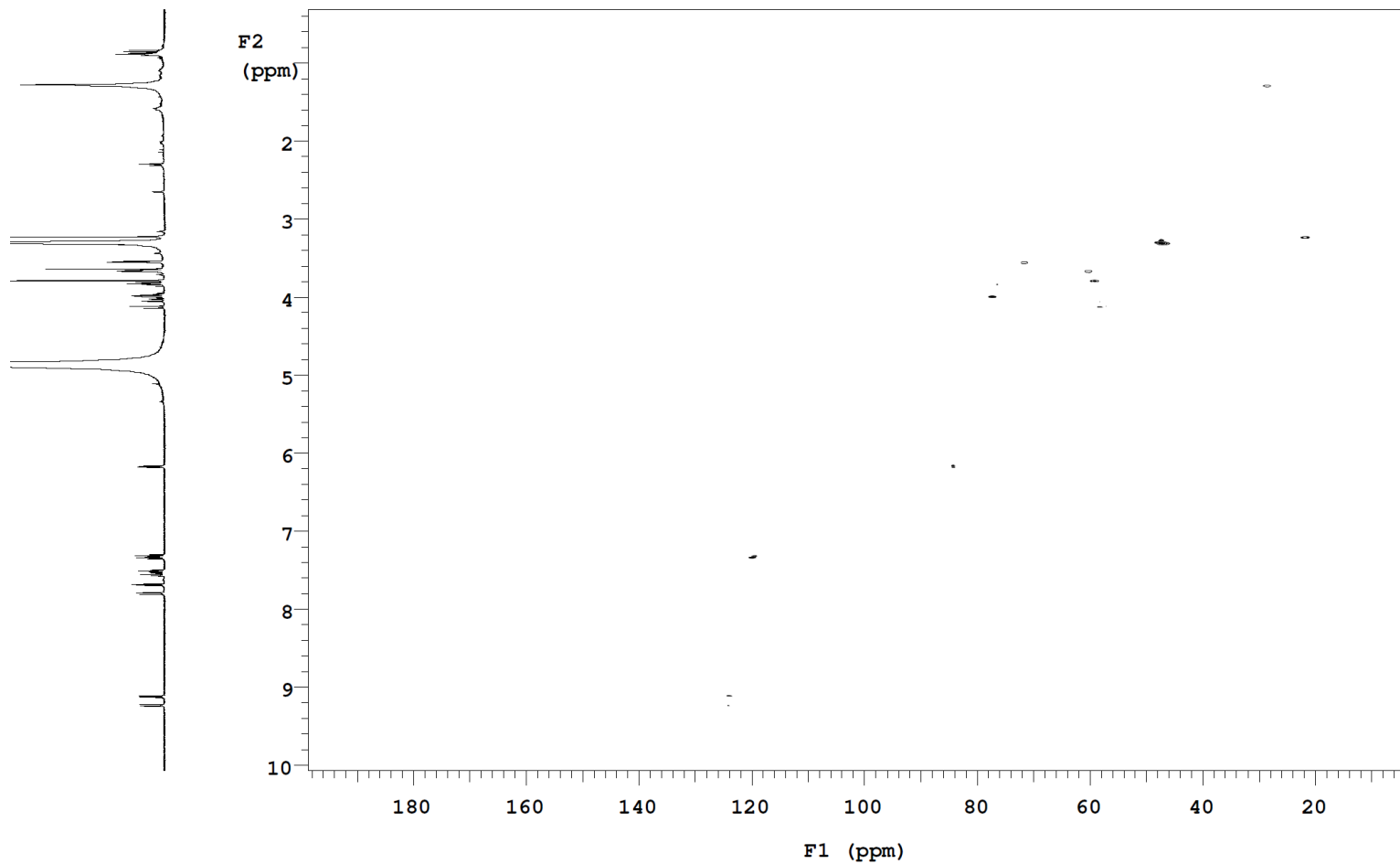
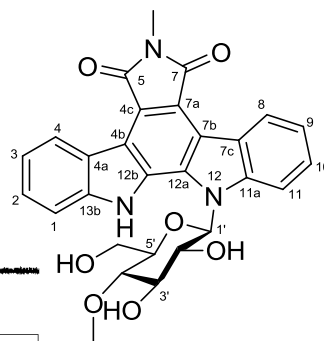


Figure S40: HSQC spectrum (CD₃OD, 500 MHz) of AT2433-B3 (**4**)

500 MHz, CD₃OD, 20 hrs
Khaled A. Shaaban

Sample: Khaled_A_Shaaban
File: xp

Pulse Sequence: gHMBC

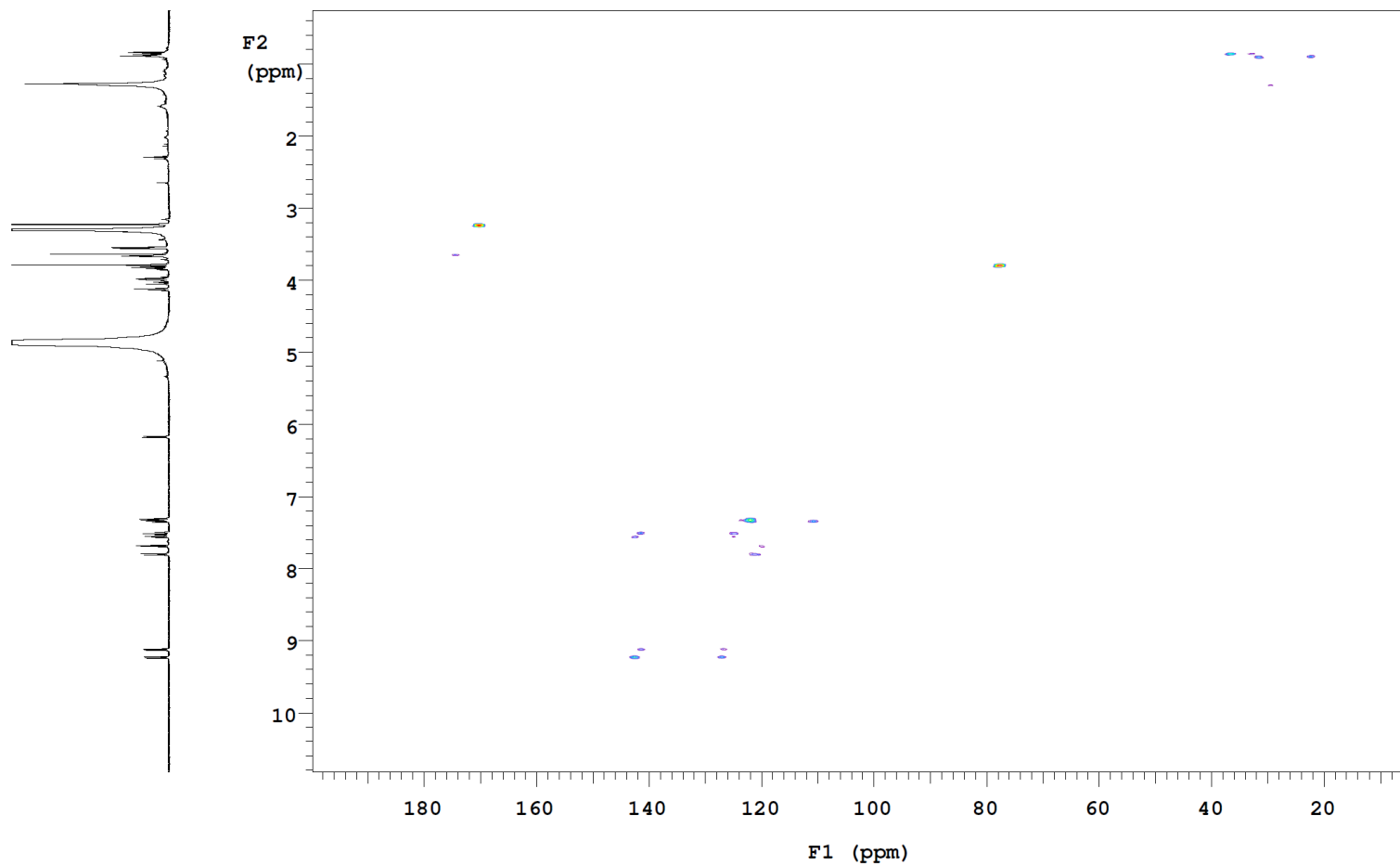
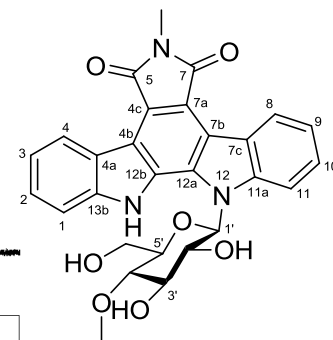


Figure S41: HMBC spectrum (CD₃OD, 500 MHz) of AT2433-B3 (4)

500 MHz, CD₃OD, 5 hrs
Khaled A. Shaaban

Sample: Khaled_A_Shaaban
File: xp

Pulse Sequence: TOCSY

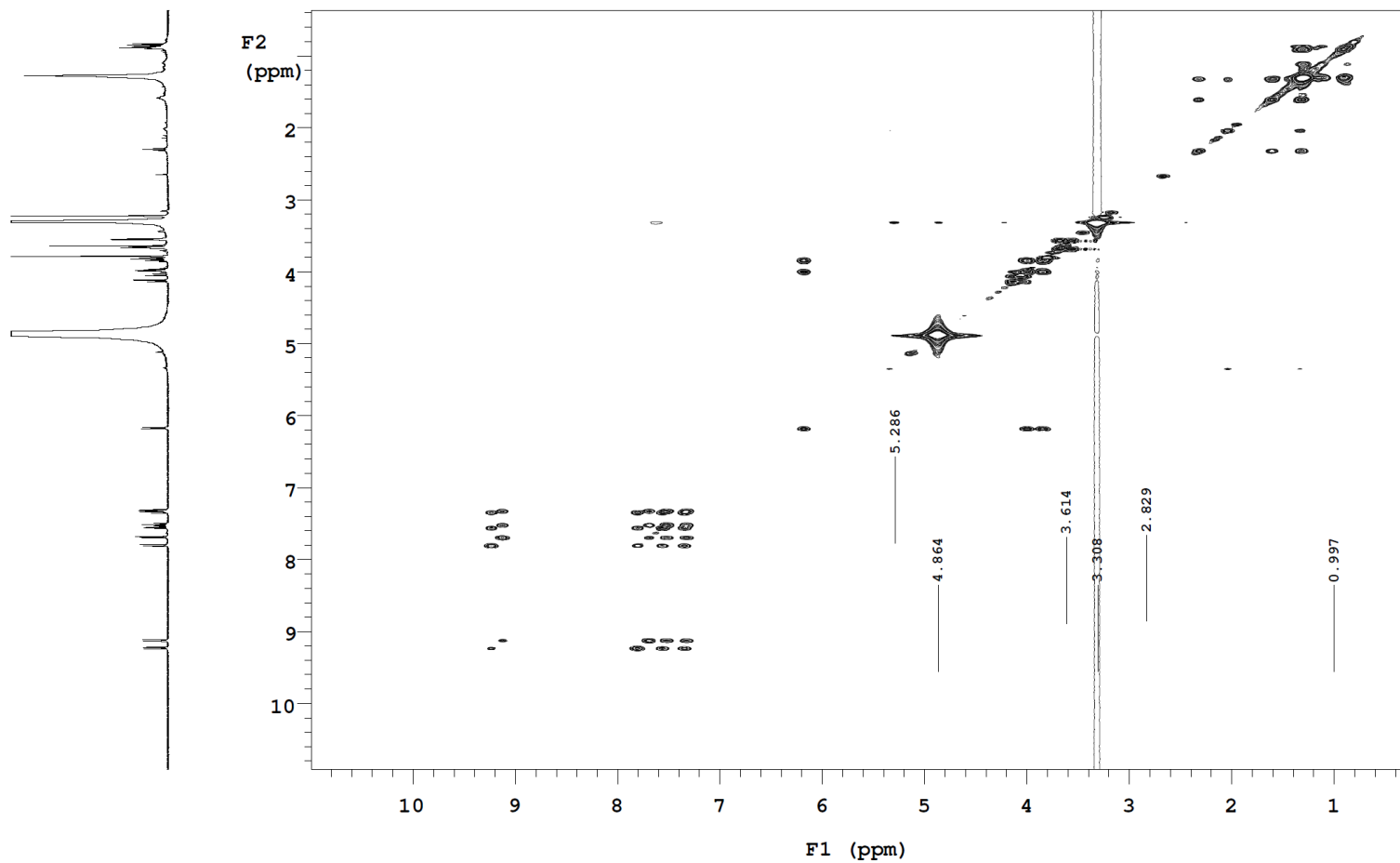
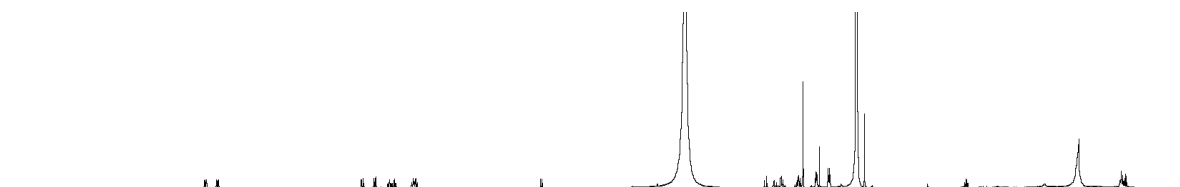
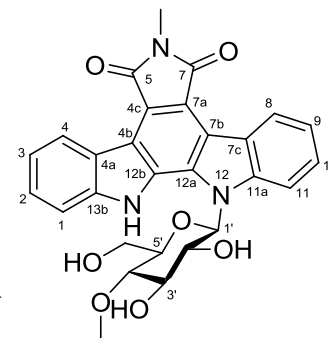


Figure S42: TOCSY spectrum (CD₃OD, 500 MHz) of AT2433-B3 (**4**)

500 MHz, CD₃OD, 9 hrs
Khaled A. Shaaban

Sample: Khaled_A_Shaaban
File: xp

Pulse Sequence: NOESY

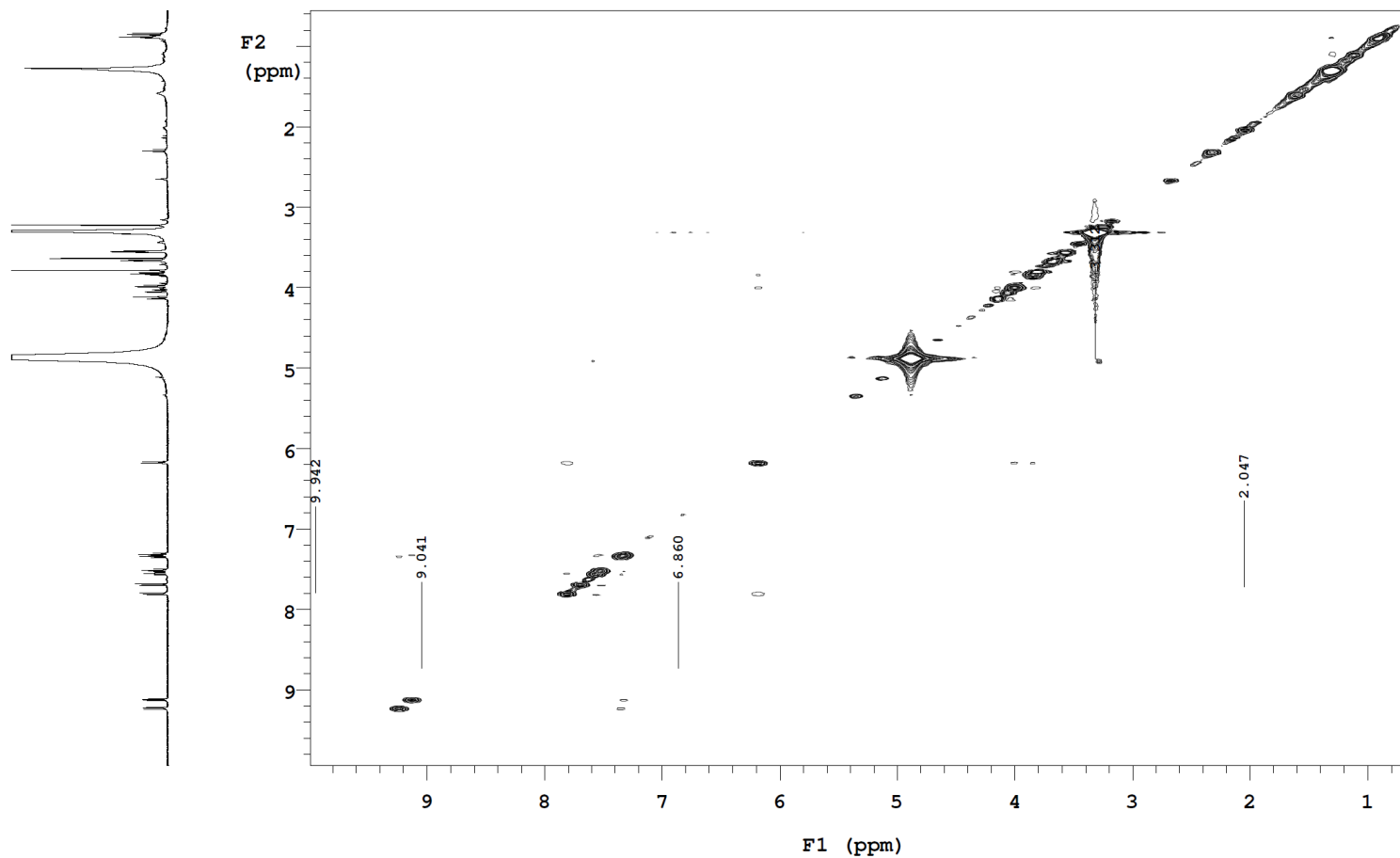
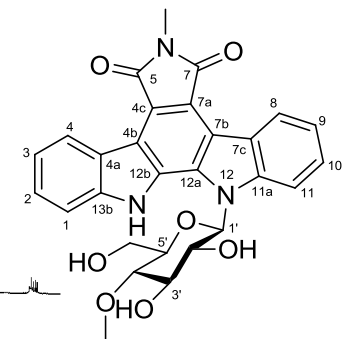
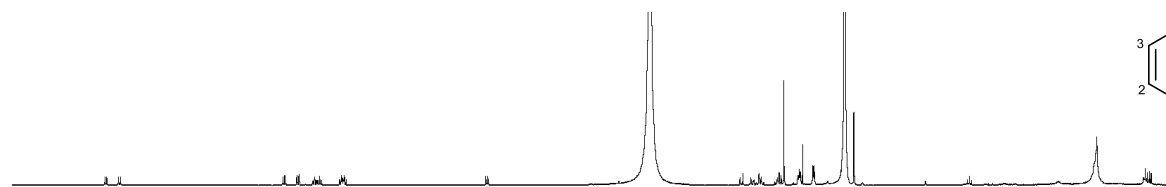
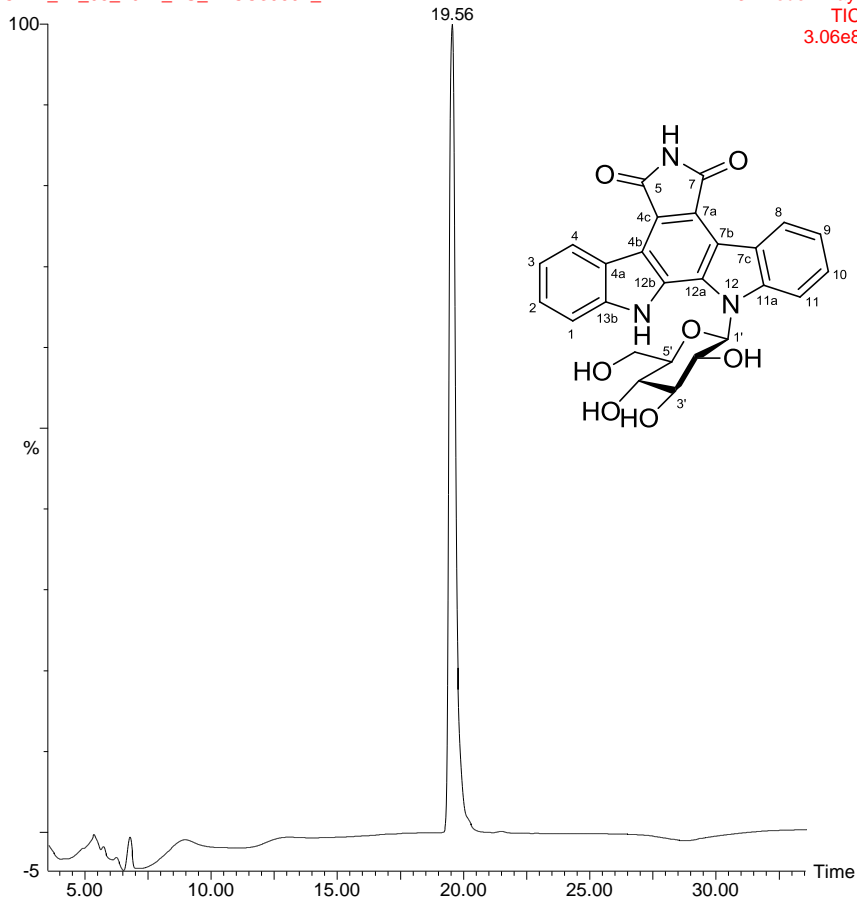


Figure S43: NOESY spectrum (CD₃OD, 500 MHz) of AT2433-B3 (4)

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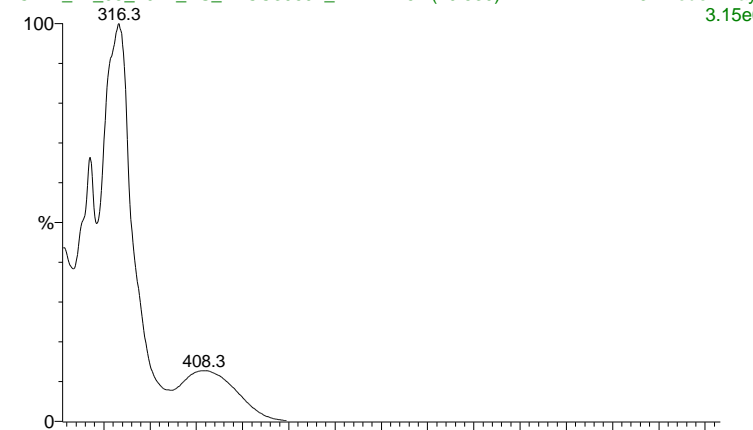
05-Nov-2014
3: Diode Array
TIC
3.06e8



Khaled A Shaaban

CPRI_11_05_2014_KS_ATCC39691_F7A1 1167 (19.539)

3: Diode Array
3.15e6



CPRI_11_05_2014_KS_ATCC39691_F7A1 485 (19.542)

1: Scan ES+
1.20e6

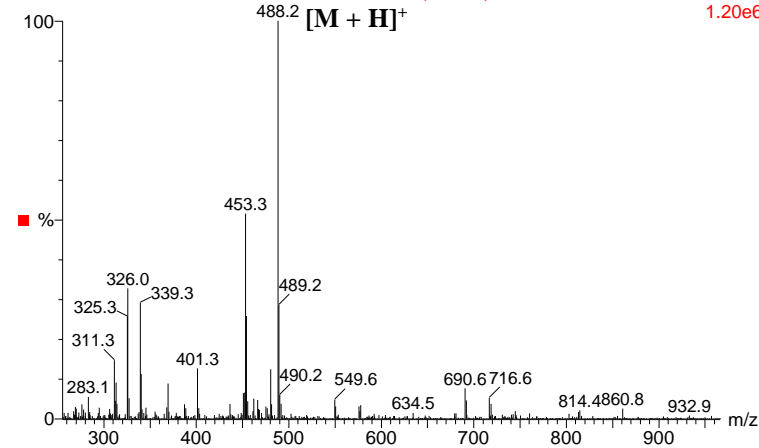
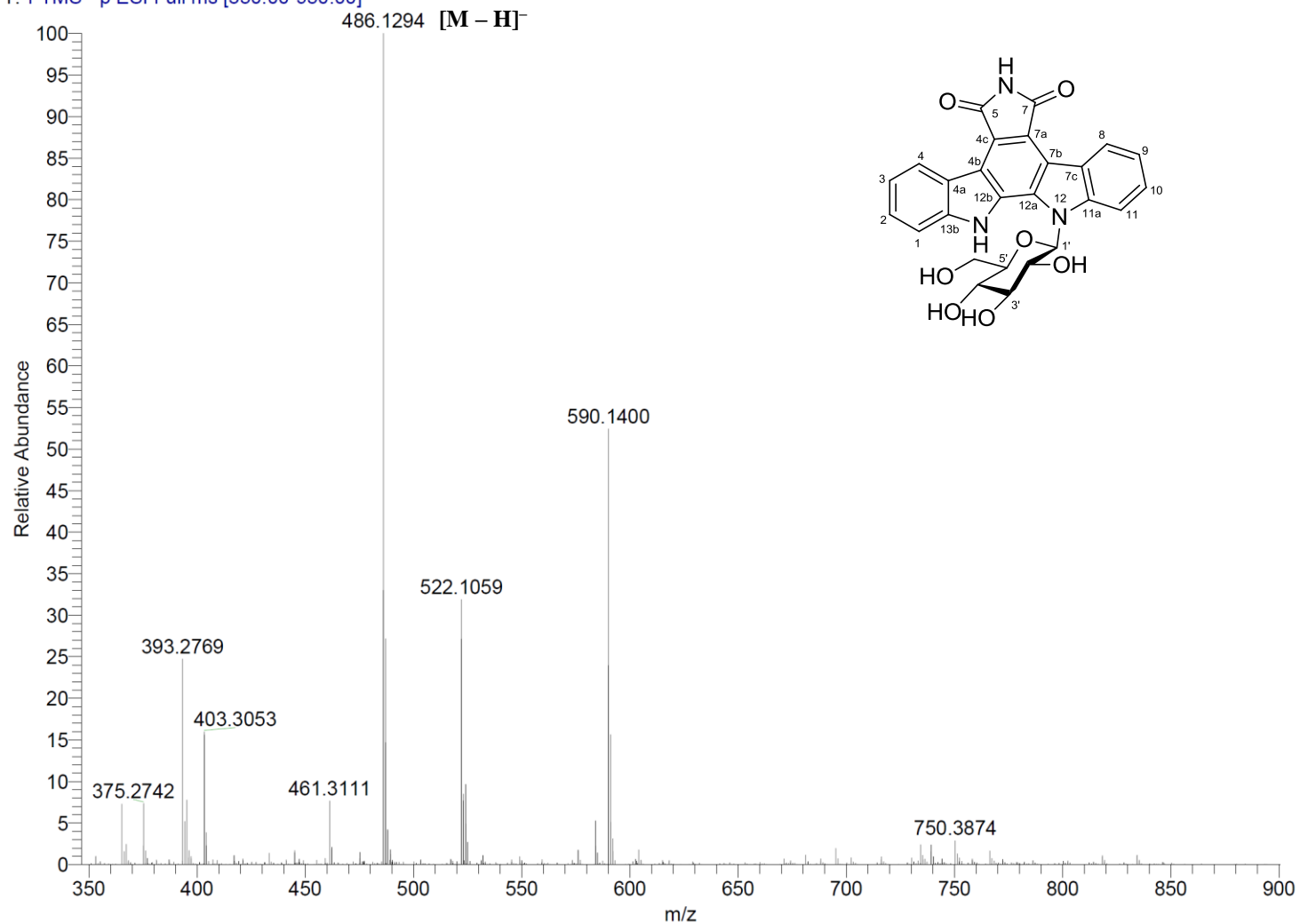


Figure S44: HPLC/UV/MS analyses of the purified BMY-41219 (**5**). Detection wavelength: 210-500; **solvent A:** H₂O/0.1% Formic acid, **solvent B:** CH₃CN/0.1% Formic acid; flow rate: 0.5 mL min⁻¹; 0-4 min, 10% B; 4-22 min, 10-100% B; 22-27 min, 100% B; 27-29 min, 100%-10% B; 29-35 min, 10 % B.

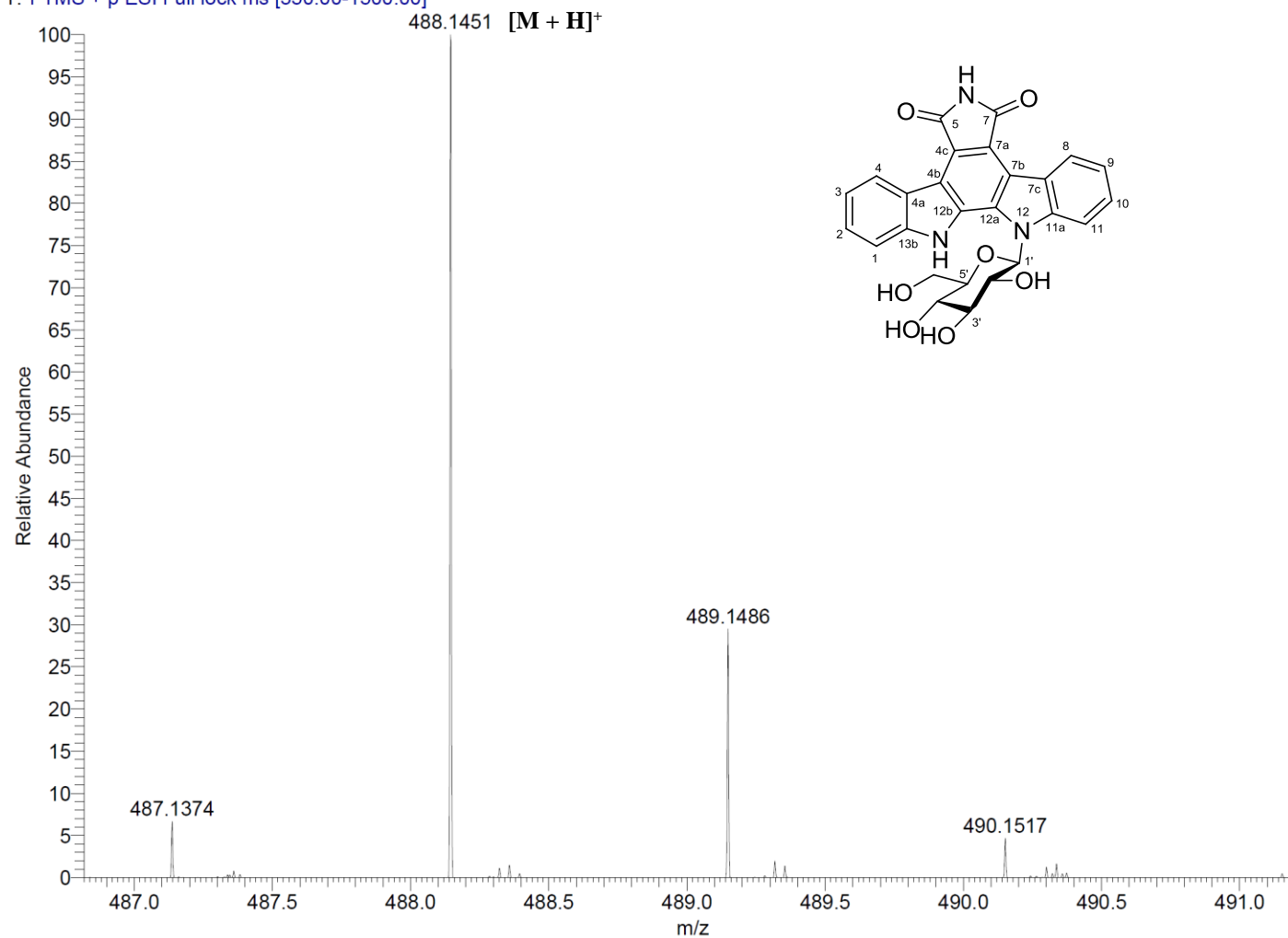
14-0528 #59-88 RT: 1.55-2.31 AV: 30 NL: 8.92E6

T: FTMS - p ESI Full ms [350.00-950.00]

**Figure S45:** (-)-HRESI-MS spectrum of BMY-41219 (5)

14-0528 #121-133 RT: 3.18-3.49 AV: 13 NL: 1.03E7

T: FTMS + p ESI Full lock ms [350.00-1500.00]

**Figure S46:** (+)-HRESI-MS spectrum of BMY-41219 (5)

500 MHz, CD3OD, nt=32
Khaled A. Shaaban

Sample: Khaled_A_Shaaban
File: xp

Pulse Sequence: s2pul

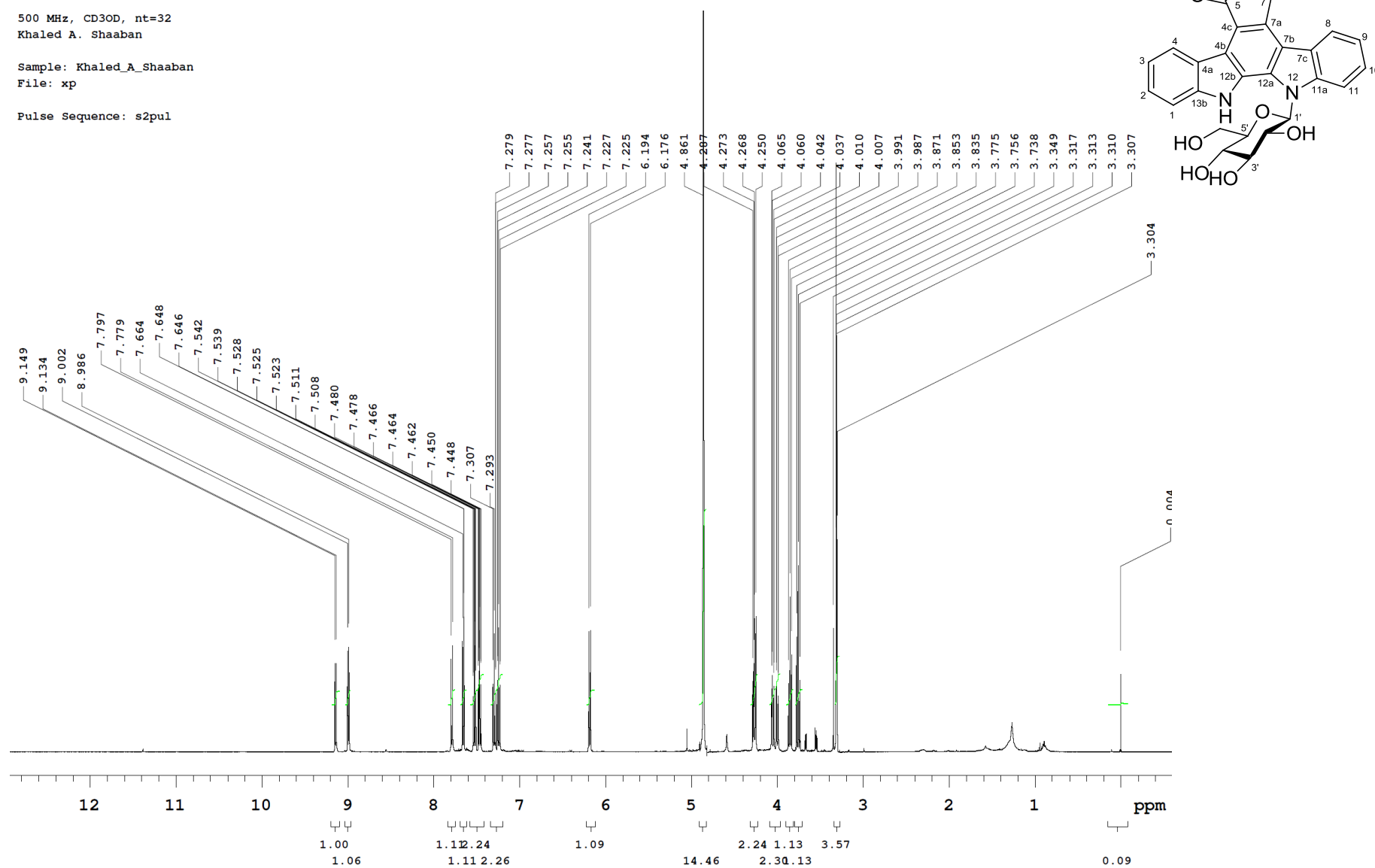


Figure S47: ¹H NMR spectrum (CD₃OD, 500 MHz) of BMY-41219 (5)

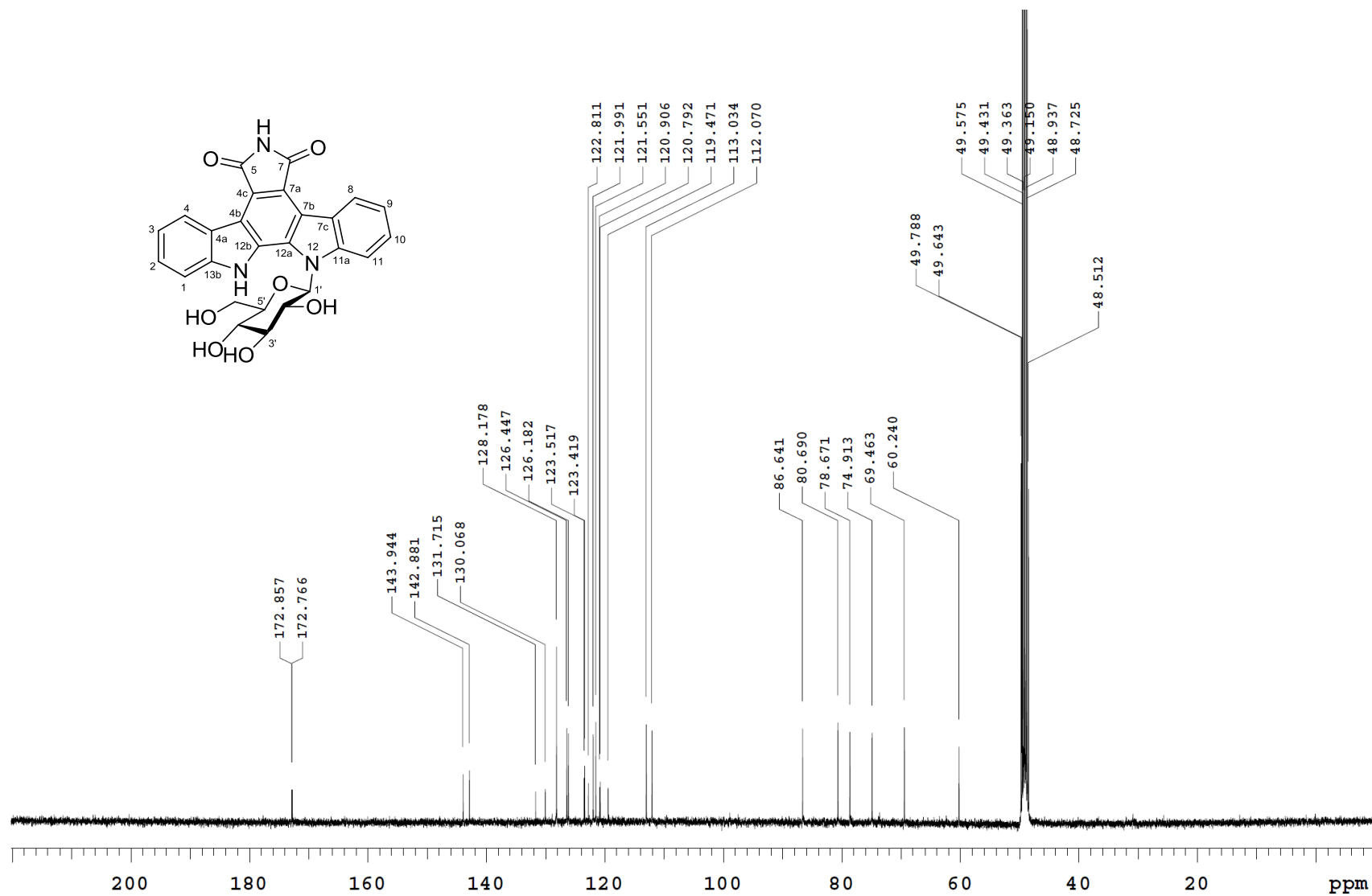


Figure S48: ¹³C NMR spectrum (CD₃OD, 100 MHz) of BMY-41219 (5)

KS_ATCC39691_F7A1_gCOSY_11_05_2014
500 MHz, CD3OD, 80 min
Khaled A. Shaaban

Sample: Khaled_A_Shaaban
File: xp

Pulse Sequence: gCOSY

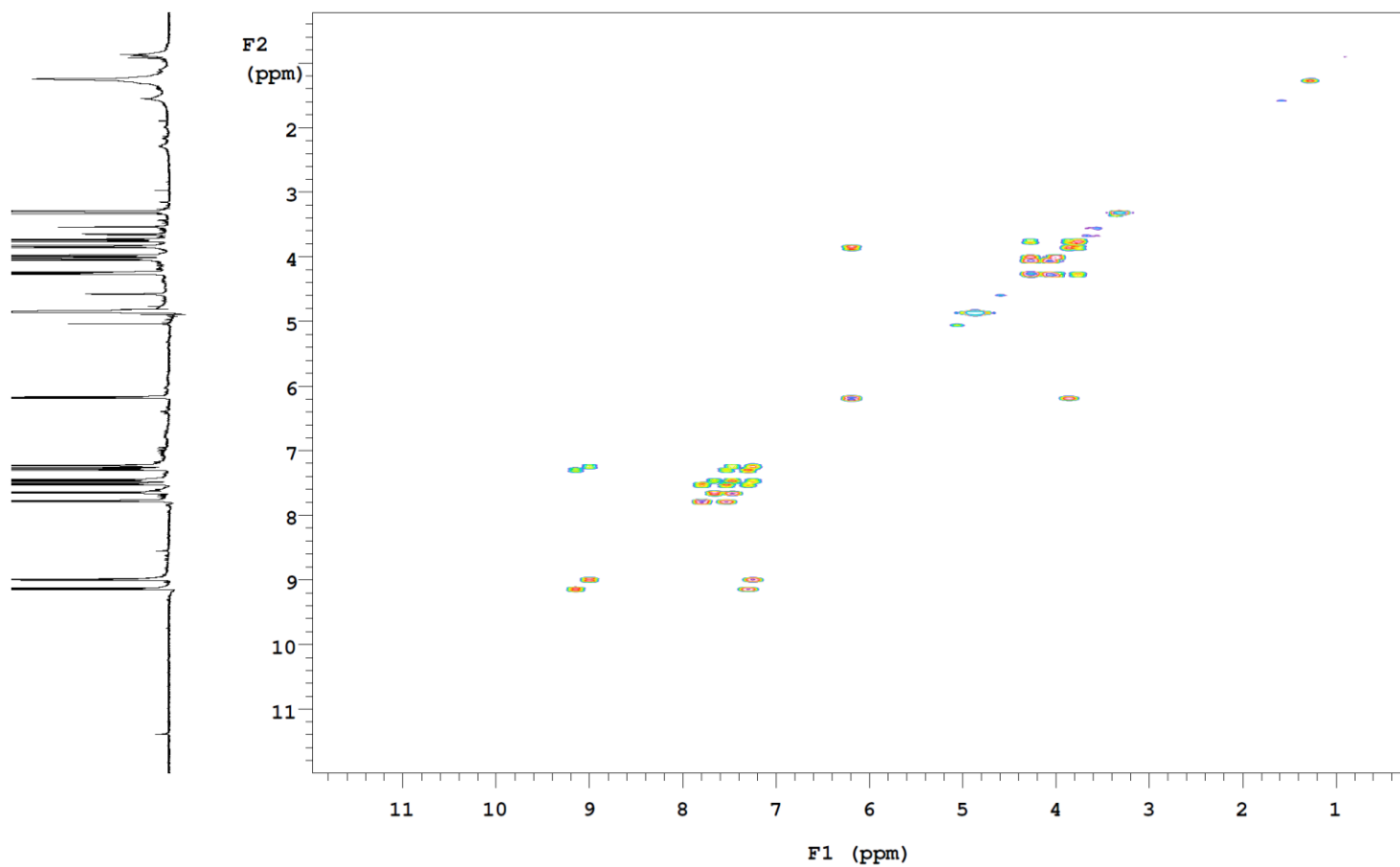
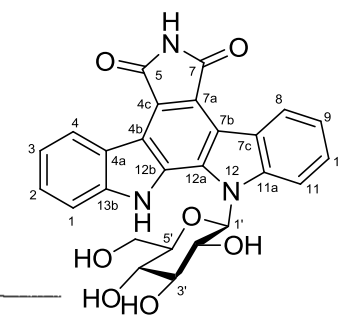
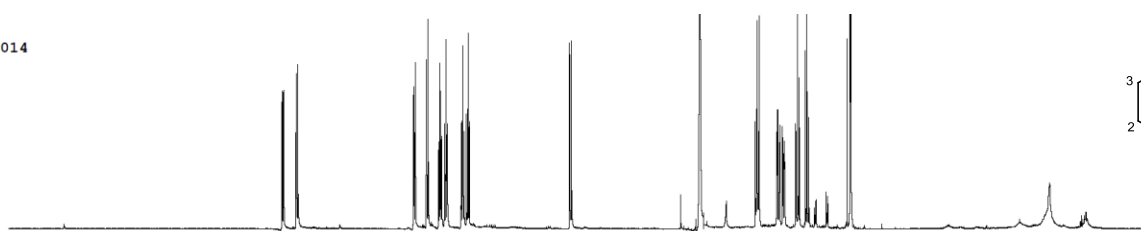


Figure S49: ^1H - ^1H COSY spectrum (CD_3OD , 500 MHz) of BMY-41219 (**5**)

KS_ATCC39691_F7A1_gHSQC_11_06_2014
500 MHz, CD3OD, 3 hrs
Khaled A. Shaaban

Sample: Khaled_A_Shaaban
File: xp

Pulse Sequence: gHSQC

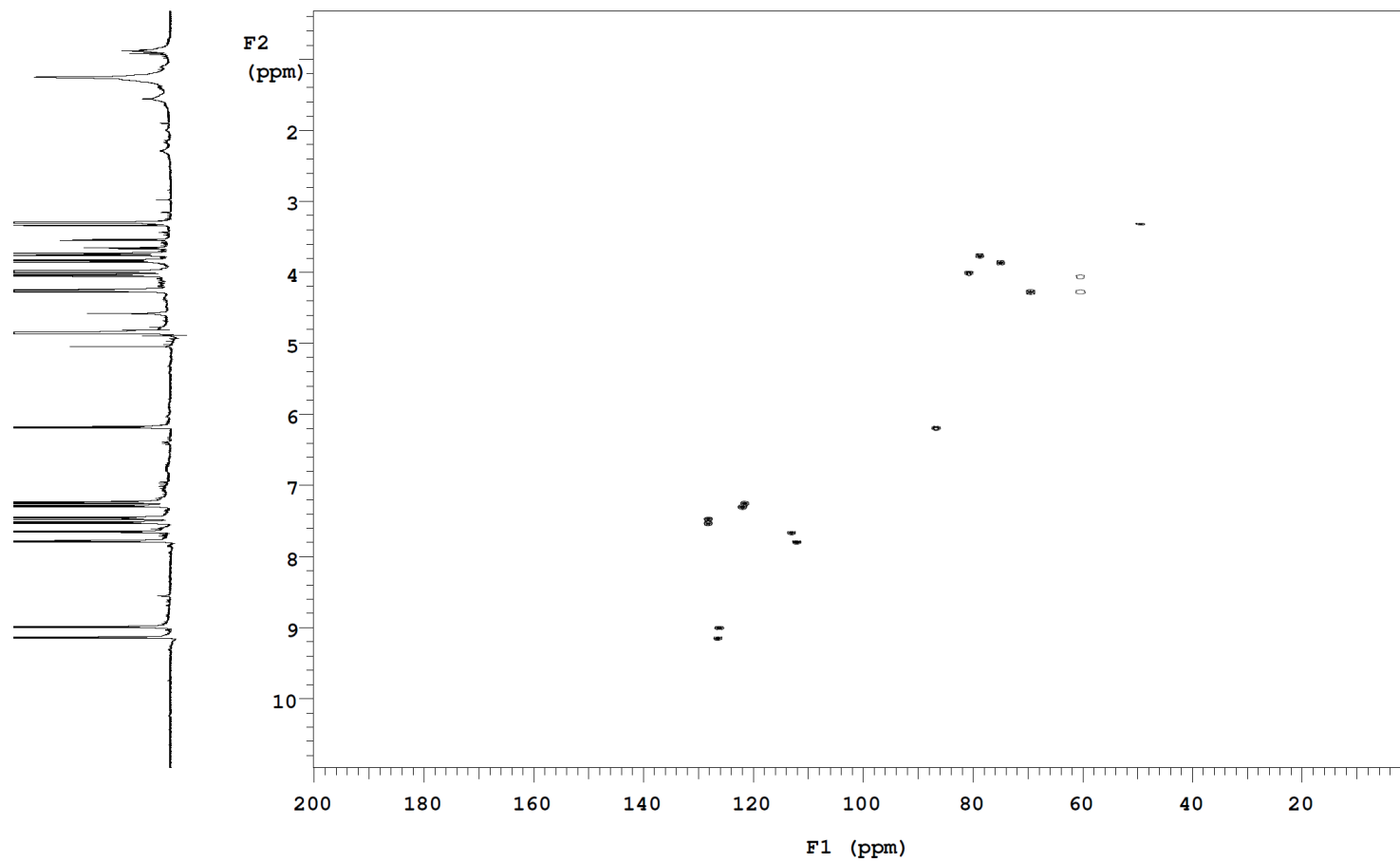
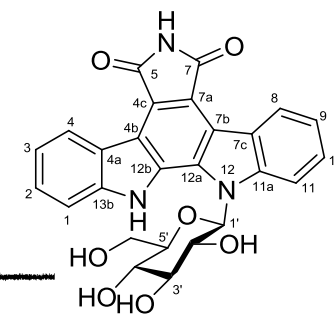


Figure S50: HSQC spectrum (CD₃OD, 100 MHz) of BMY-41219 (5)

KS_ATCC39691_F7A1_gHMBC_11_06_2014
500 MHz, CD3OD, 11 hrs
Khaled A. Shaaban

Sample: Khaled_A_Shaaban
File: xp

Pulse Sequence: gHMBC

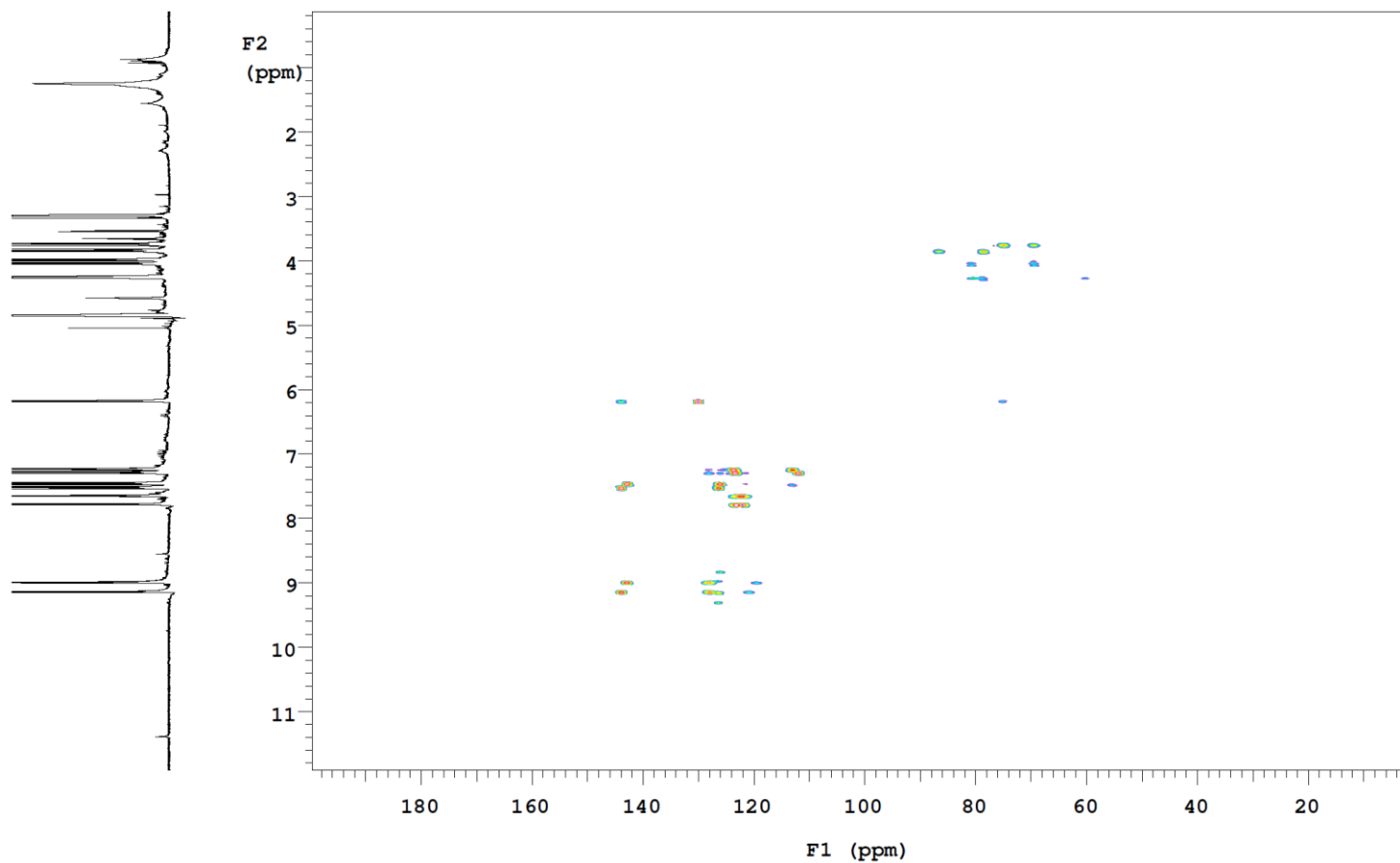
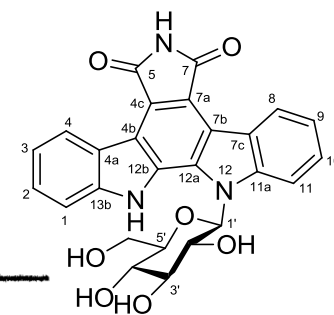


Figure S51: HMBC spectrum (CD₃OD, 100 MHz) of BMY-41219 (5)

KS_ATCC39691_F7A1_TOCSY_11_06_2014
500 MHz, CD3OD, 3 hrs
Khaled A. Shaaban

Sample: Khaled_A_Shaaban
File: xp

Pulse Sequence: TOCSY

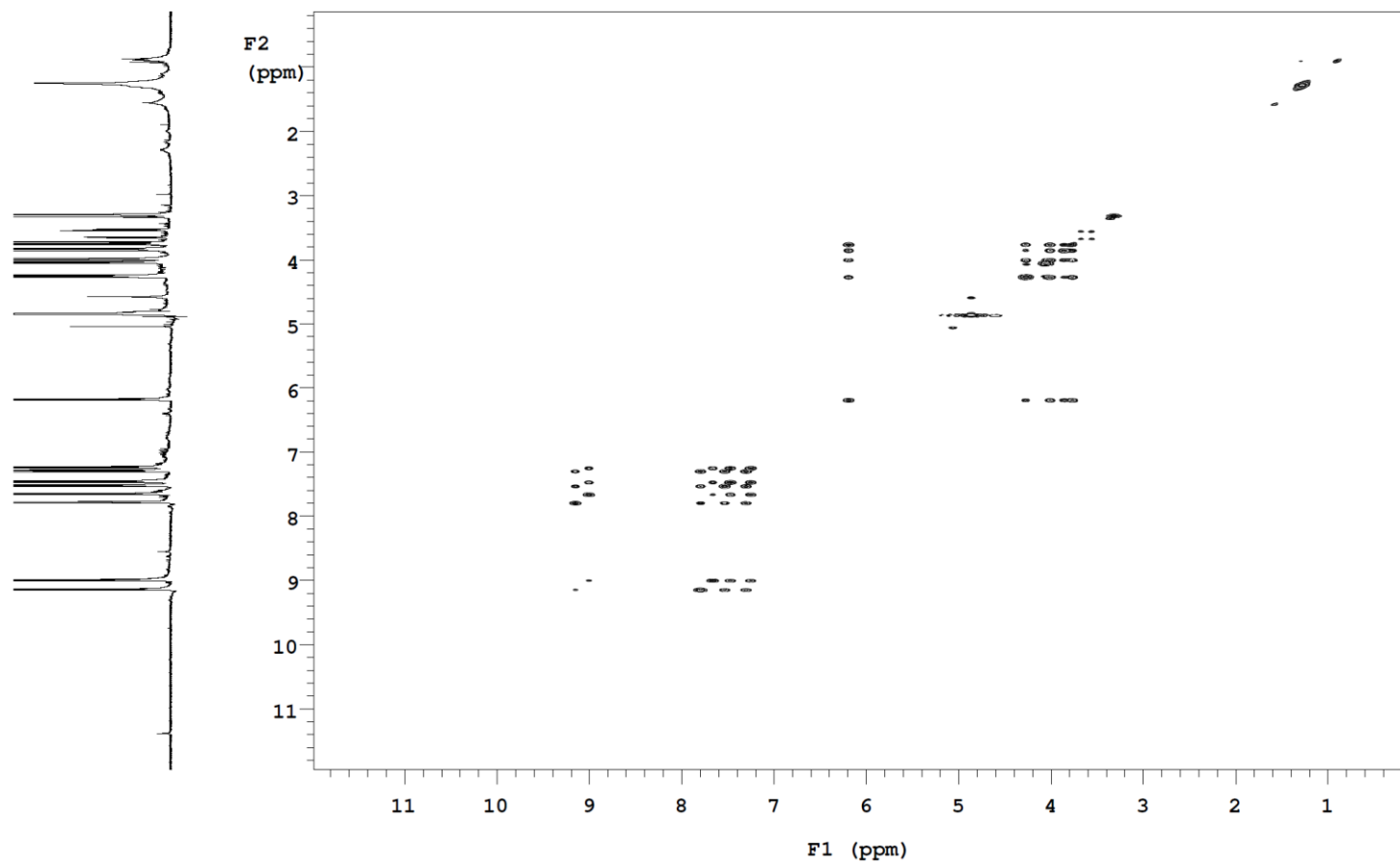
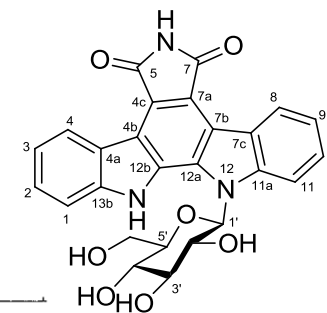
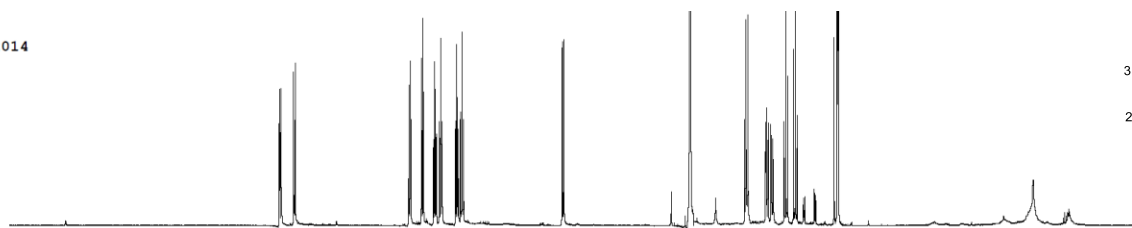


Figure S52: TOCSY spectrum (CD₃OD, 100 MHz) of BMY-41219 (5)

KS_ATCC39691_F7A1_NOESY_11_08_2014
500 MHz, CD3OD, 18 hrs
Khaled A. Shaaban

Sample: Khaled_A_Shaaban
File: xp

Pulse Sequence: NOESY

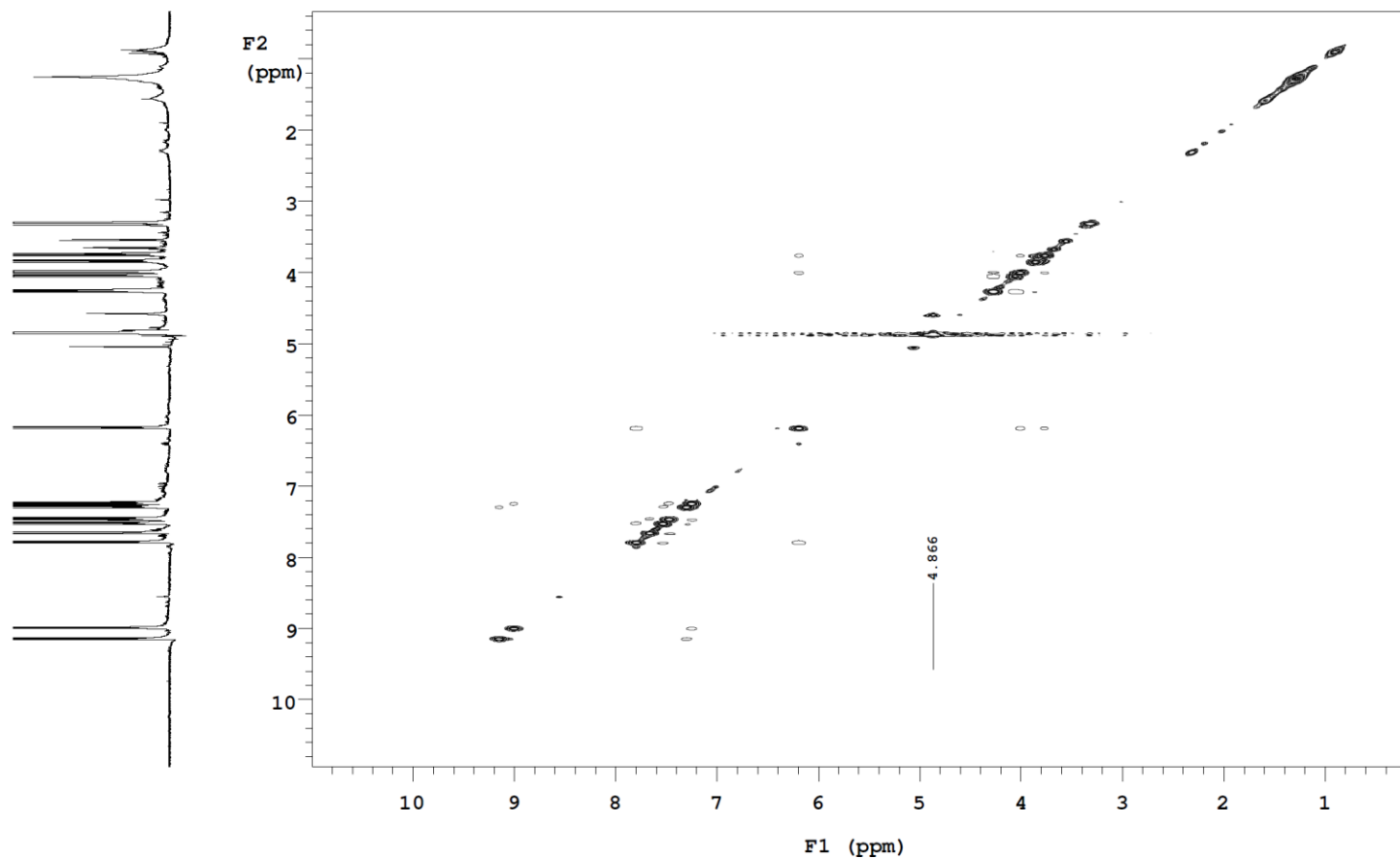
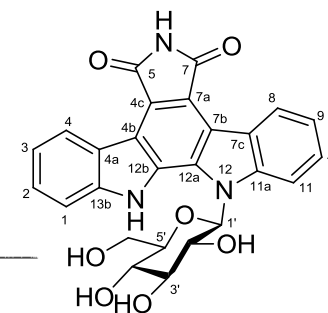
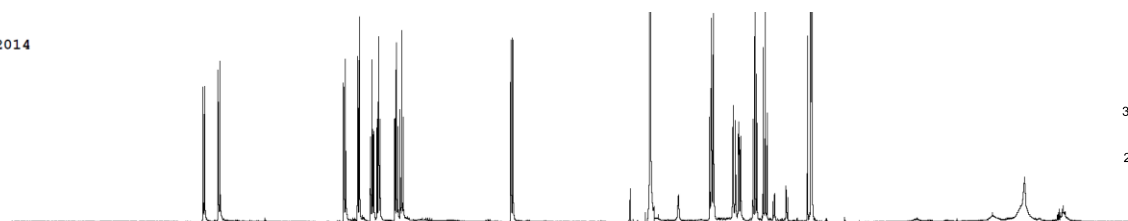


Figure S53: NOESY spectrum (CD₃OD, 100 MHz) of BMY-41219 (**5**)

Khaled A Shaaban
CPRI_10_23_2014_KS_ATCC39691_F11H

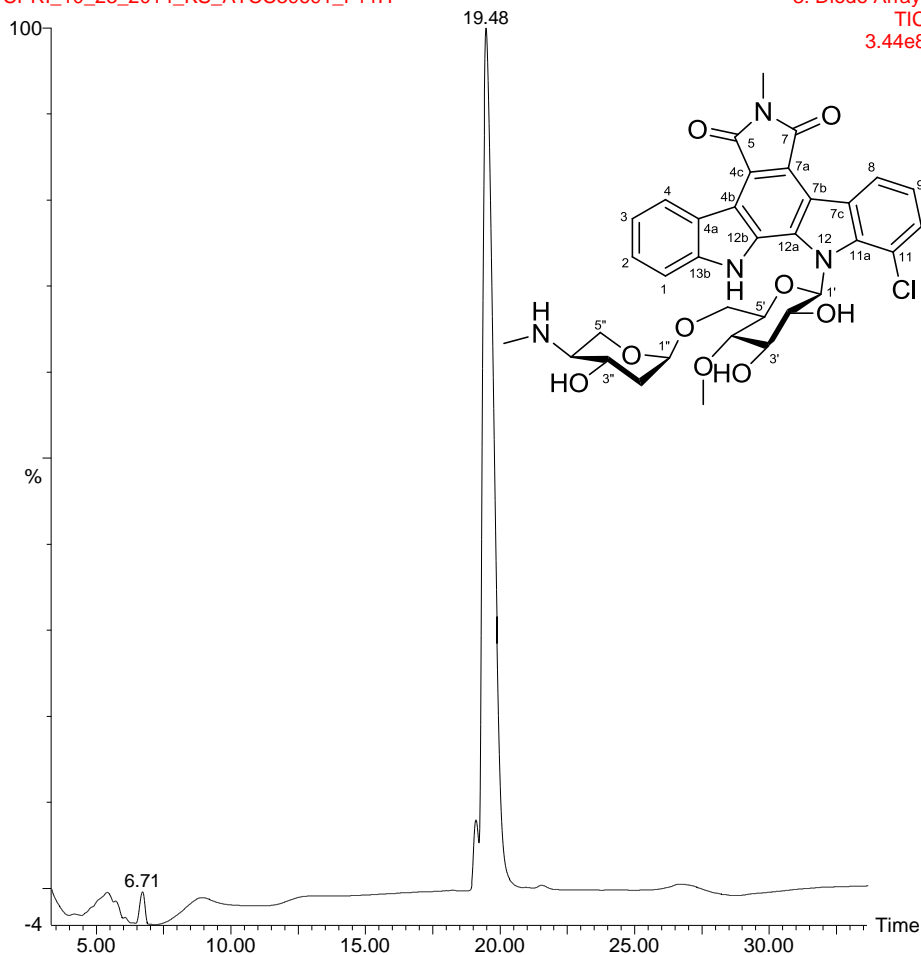
UK

22-Oct-2014
3: Diode Array
TIC
3.44e8

Khaled A Shaaban

CPRI_10_23_2014_KS_ATCC39691_F11H 1166 (19.525)

3: Diode Array
3.18e6



CPRI_10_23_2014_KS_ATCC39691_F11H 485 (19.542) 1: Scan ES+
2.49e7

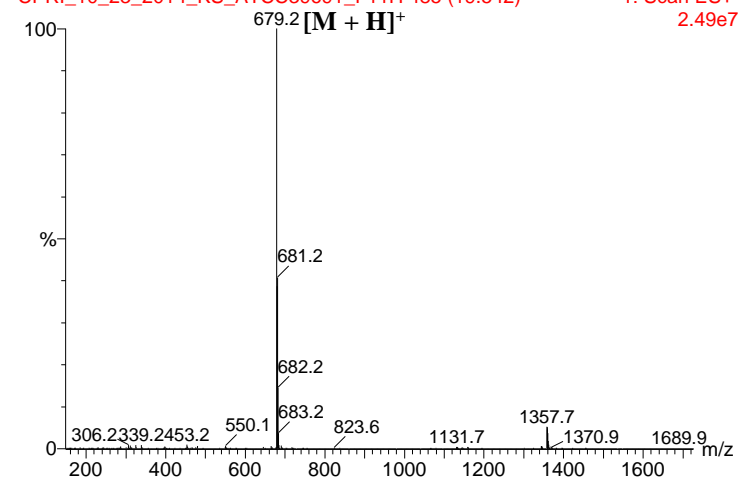


Figure S54: HPLC/UV/MS analyses of AT2433-A1 (**6**). Detection wavelength: 210-500; **solvent A:** H₂O/0.1% Formic acid, **solvent B:** CH₃CN/0.1% Formic acid; flow rate: 0.5 mL min⁻¹; 0-4 min, 10% B; 4-22 min, 10-100% B; 22-27 min, 100% B; 27-29 min, 100%-10% B; 29-35 min, 10 % B.

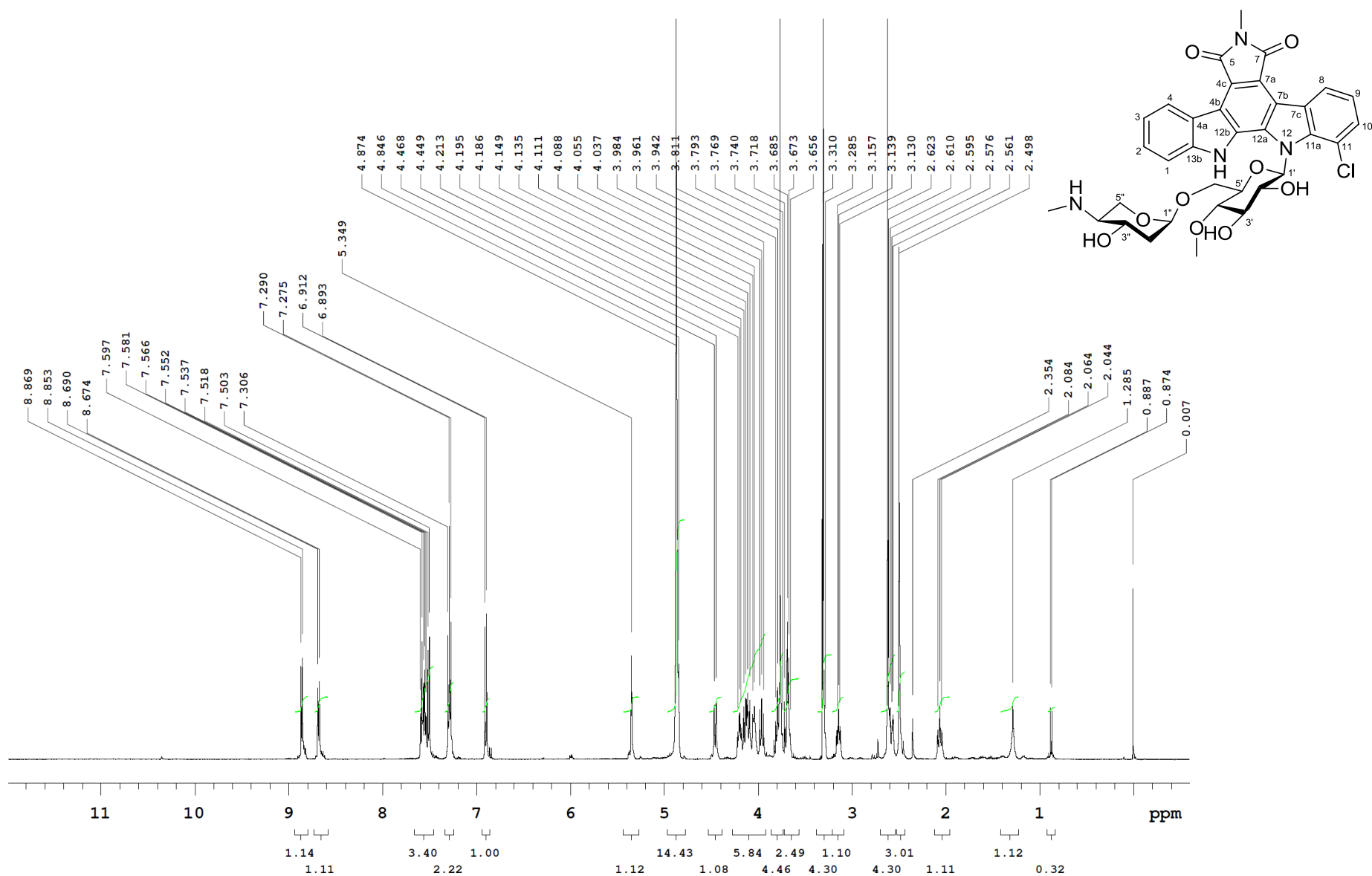


Figure S55: ¹H NMR spectrum (CD₃OD, 500 MHz) of AT2433-A1 (6)

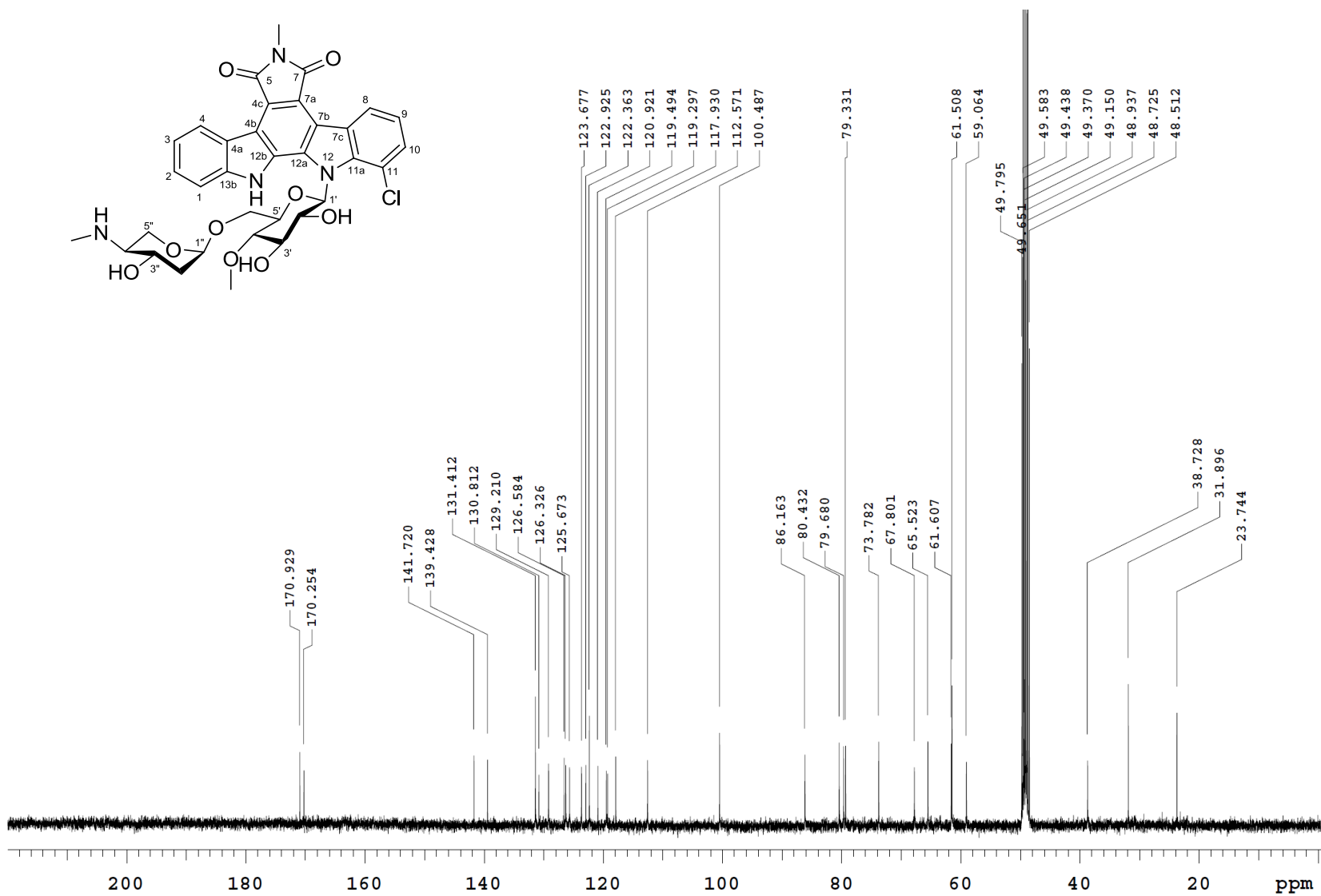


Figure S56: ¹³C NMR spectrum (CD₃OD, 100 MHz) of AT2433-A1 (6)

500 MHz, CD₃OD, 80 min
Khaled A. Shaaban

Sample: Khaled_A_Shaaban
File: xp

Pulse Sequence: gCOSY

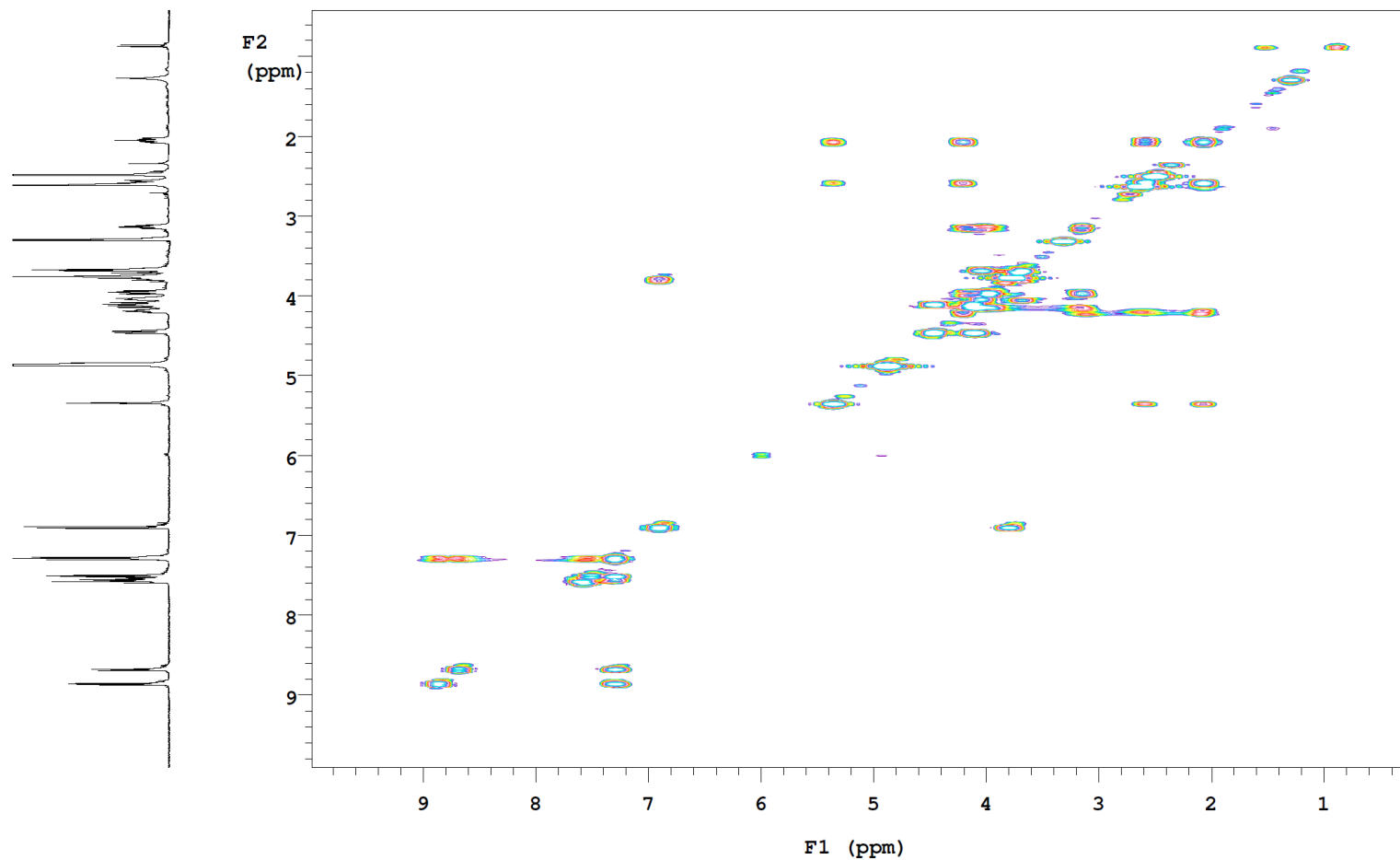
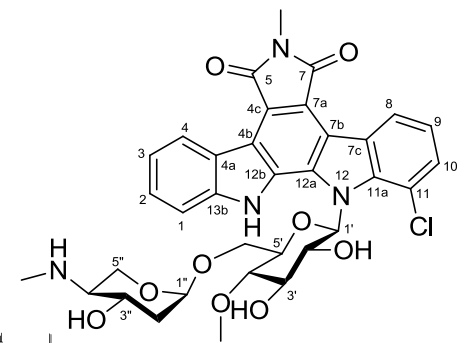
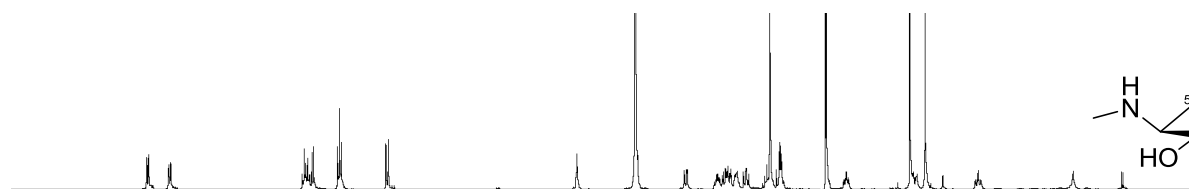


Figure S57: ¹H-¹H COSY spectrum (CD₃OD, 500 MHz) of AT2433-A1 (**6**)

500 MHz, CD₃OD, 2 hrs
Khaled A. Shaaban

Sample: Khaled_A_Shaaban
File: xp

Pulse Sequence: gHSQC

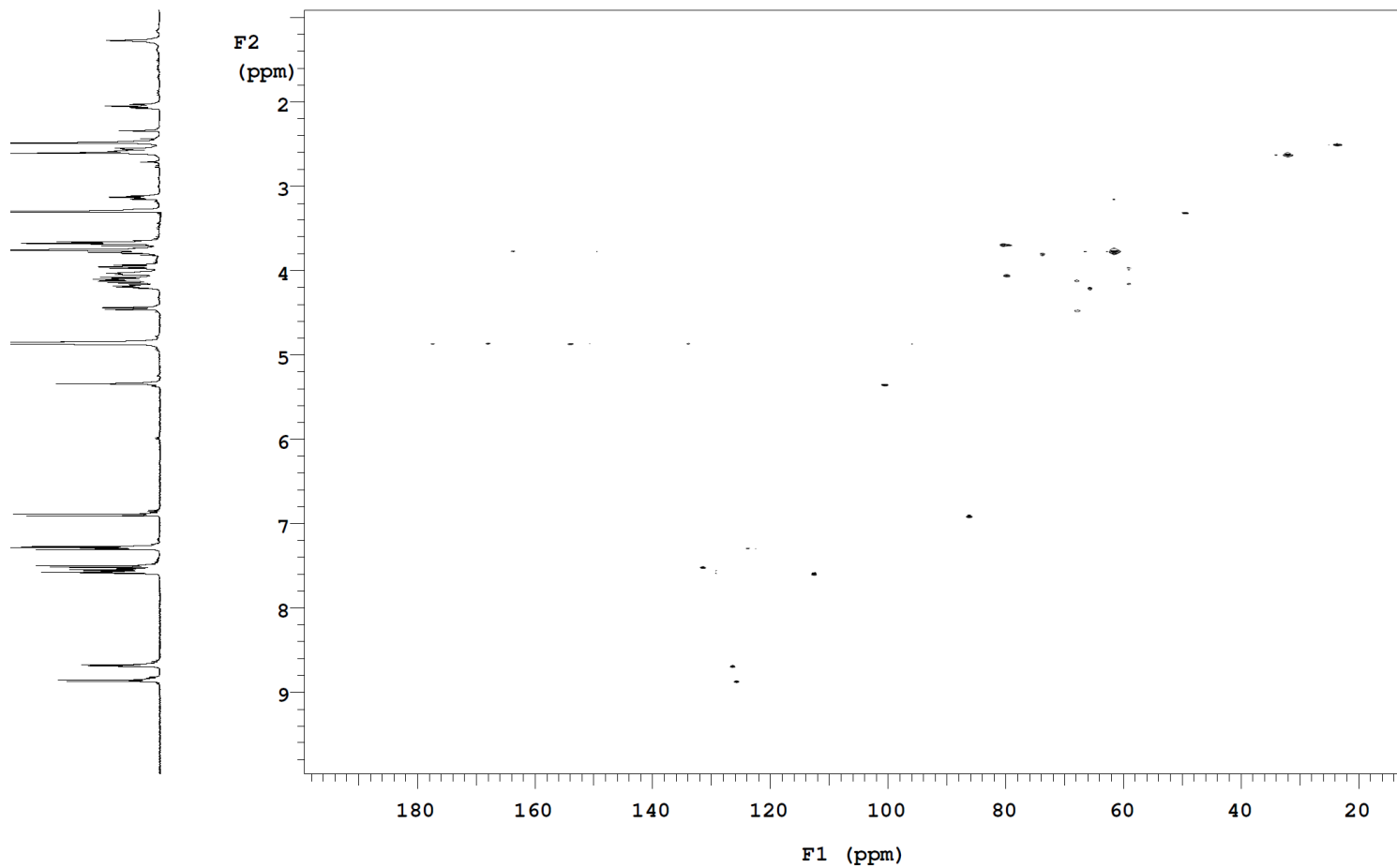
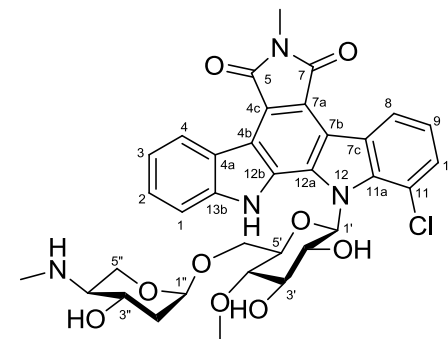


Figure S58: HSQC spectrum (CD₃OD, 500 MHz) of AT2433-A1 (**6**)

500 MHz, CD3OD, 12 hrs
Khaled A. Shaaban

Sample: Khaled_A_Shaaban
File: xp

Pulse Sequence: gHMBC

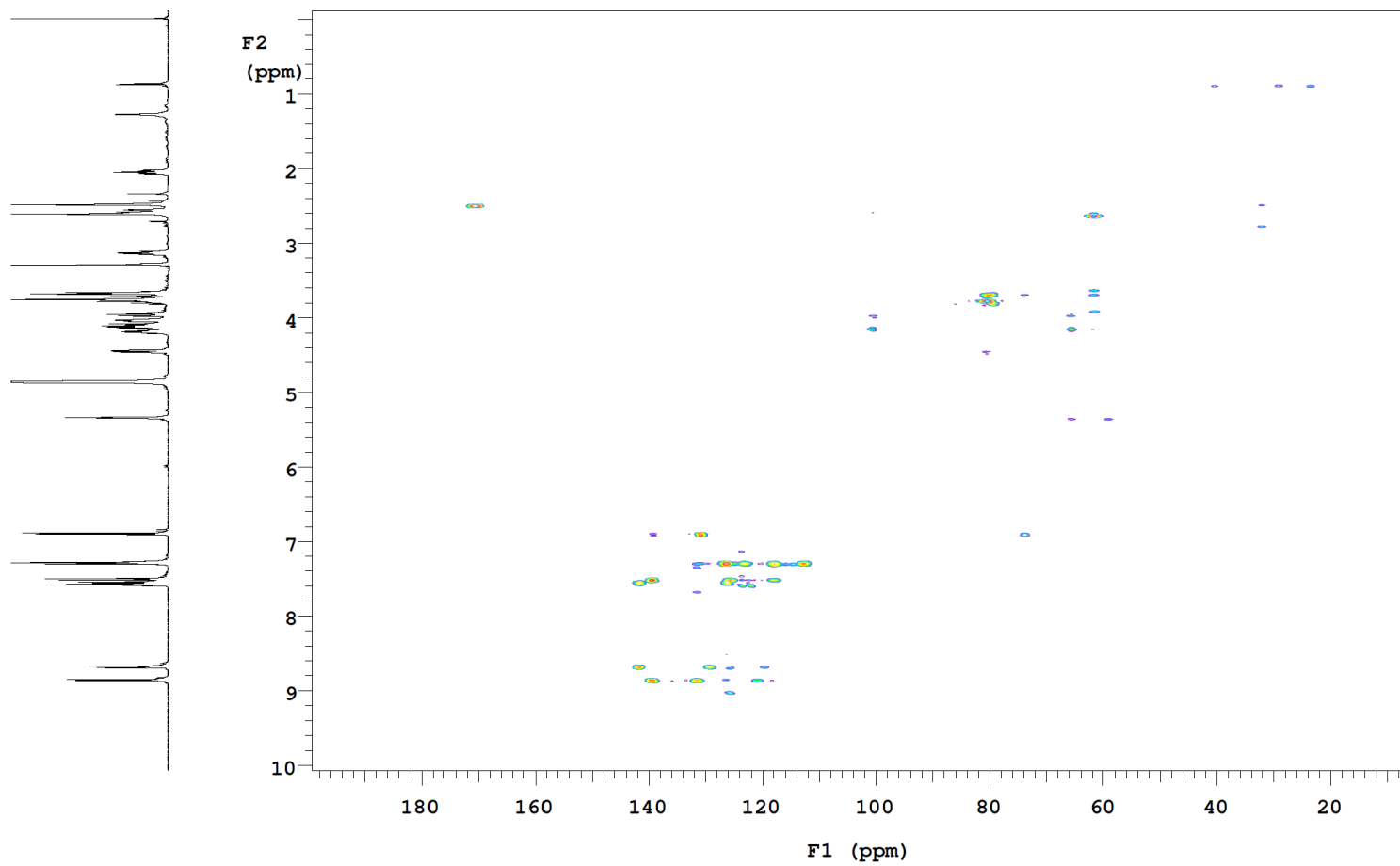
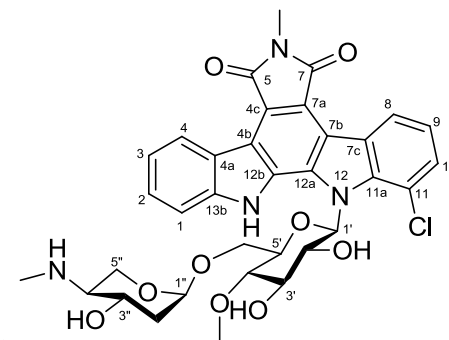


Figure S59: HMBC spectrum (CD₃OD, 500 MHz) of AT2433-A1 (**6**)

500 MHz, CD₃OD, 5 hrs
Khaled A. Shaaban

Sample: Khaled_A_Shaaban
File: xp

Pulse Sequence: TOCSY

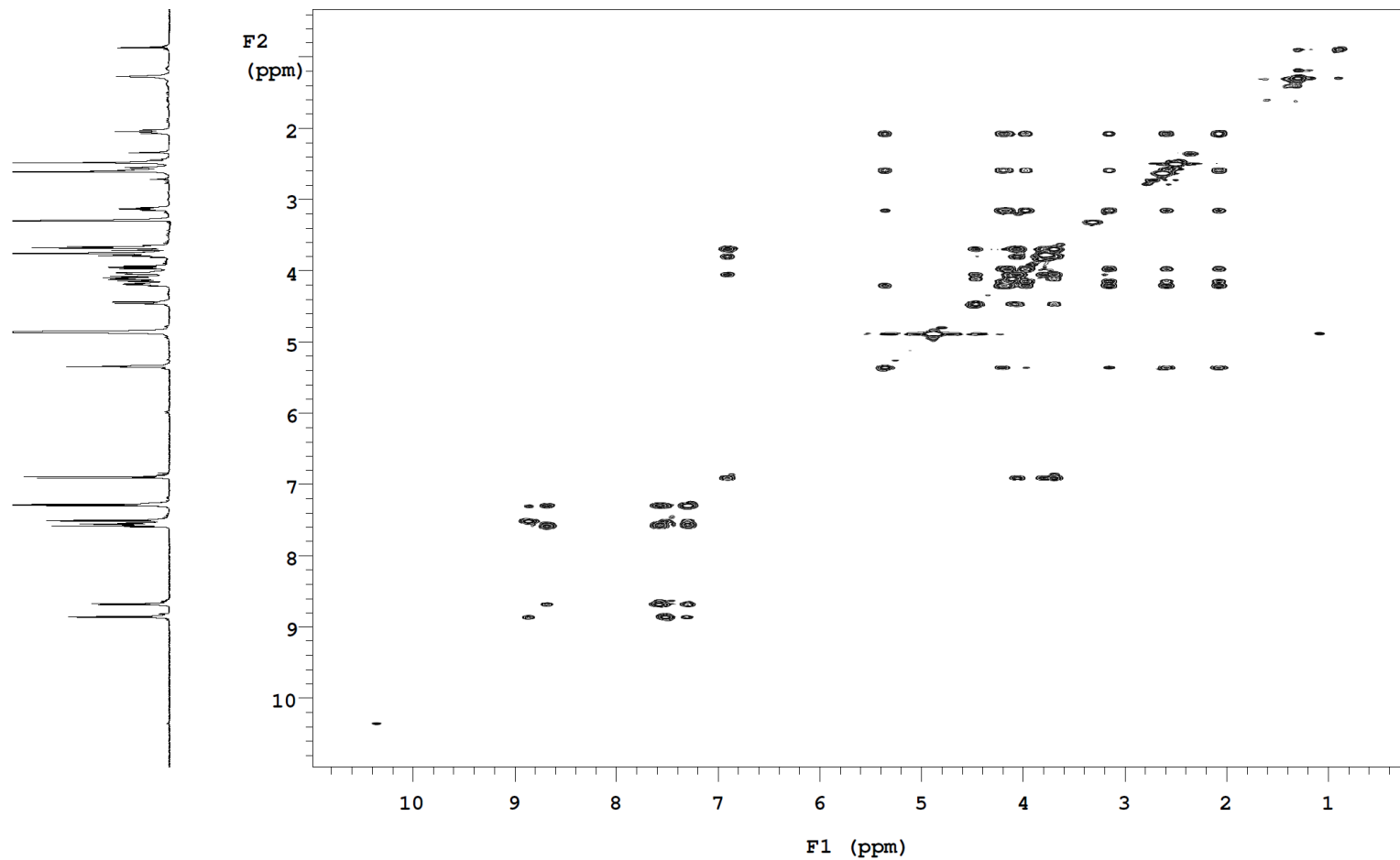
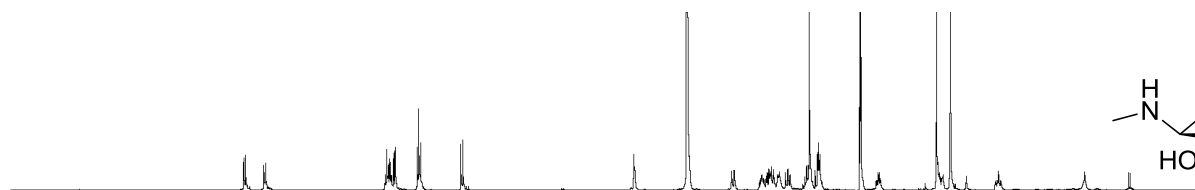
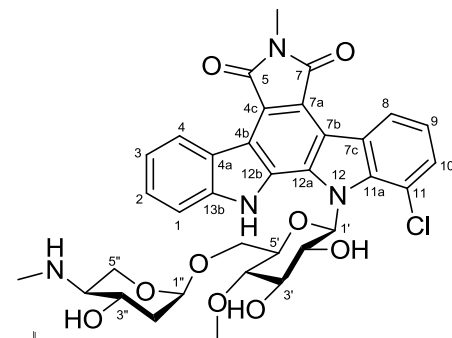


Figure S60: TOCSY spectrum (CD₃OD, 500 MHz) of AT2433-A1 (6)

500 MHz, CD₃OD, 9 hrs
Khaled A. Shaaban

Sample: Khaled_A_Shaaban
File: xp

Pulse Sequence: NOESY

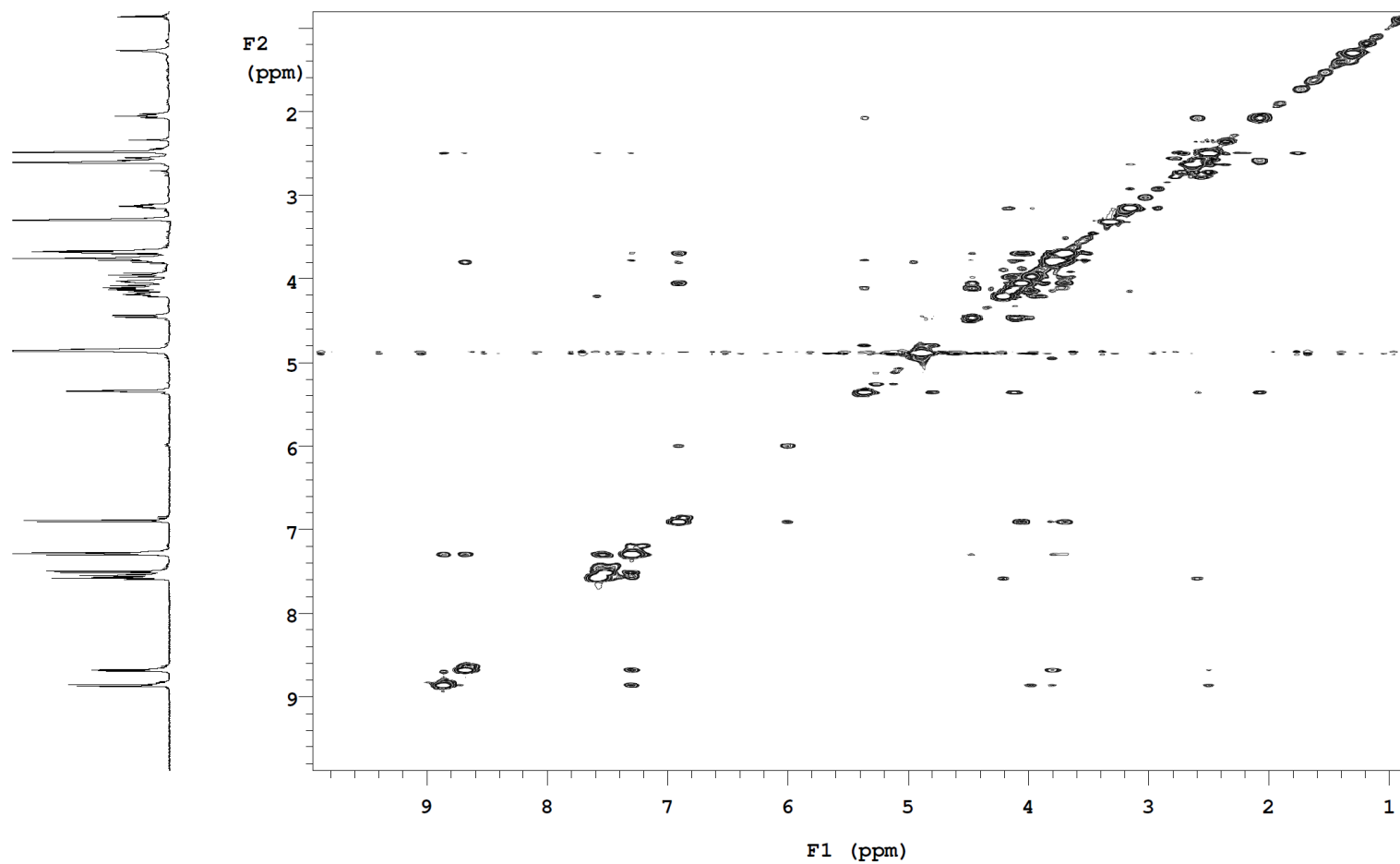
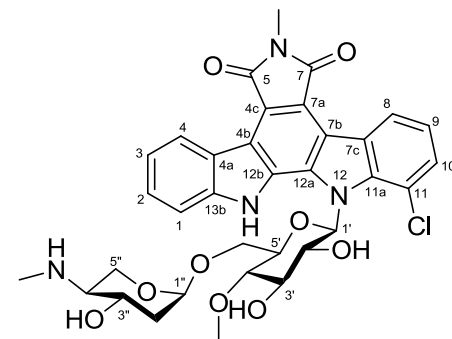


Figure S61: NOESY spectrum (CD₃OD, 500 MHz) of AT2433-A1 (6)

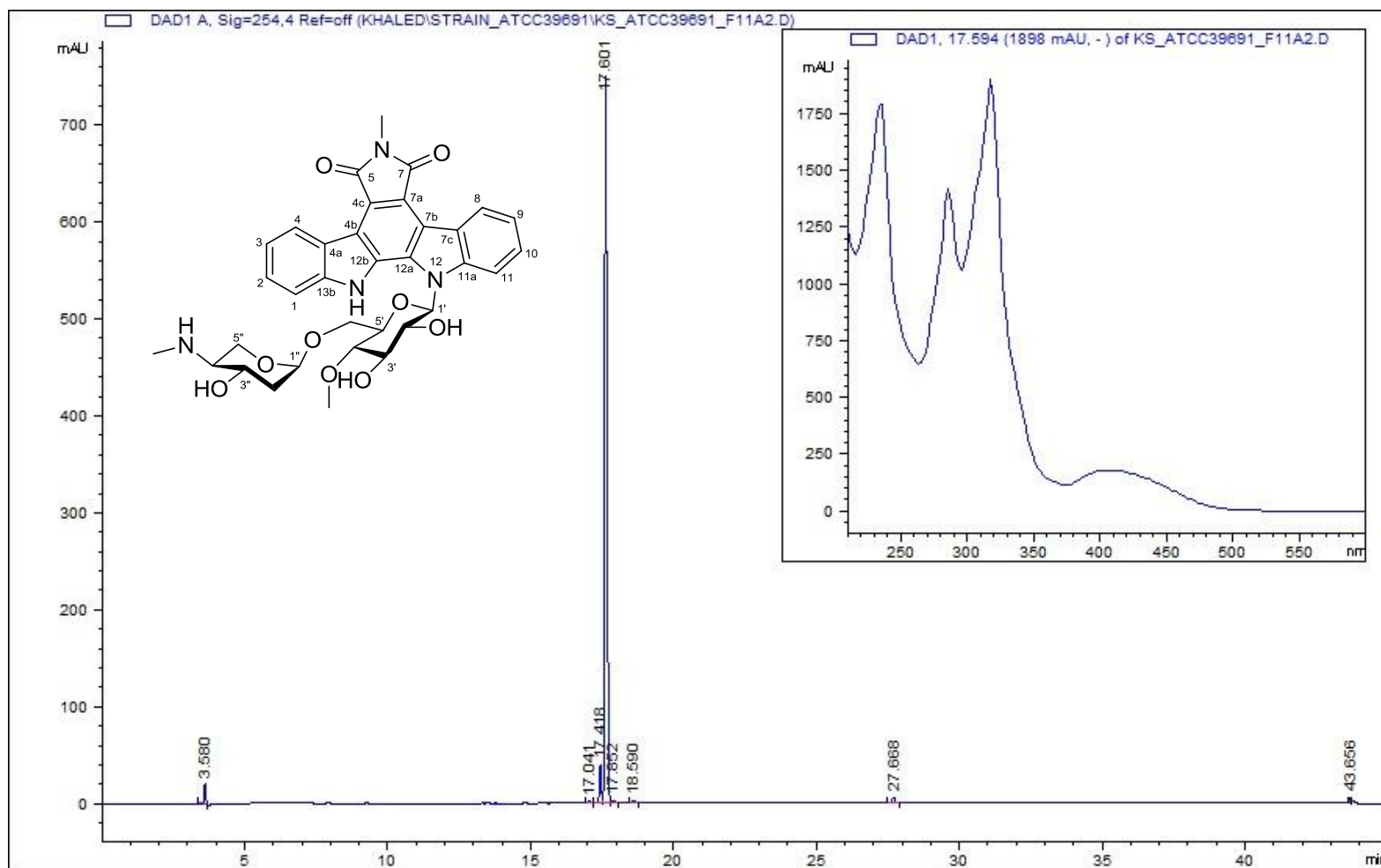


Figure S62: HPLC of AT2433-B1 (7). HPLC-conditions: Detection wavelength 254 nm; **solvent A:** H₂O/0.1% TFA; **solvent B:** CH₃CN; flow rate: 1.0 mL min⁻¹; 0-35 min, 5%-100% B; 35-40 min, 100% B; 40-41 min, 100%-5% B; 41-45 min, 5% B). UV-vis inset of full wavelength 190-600 nm.

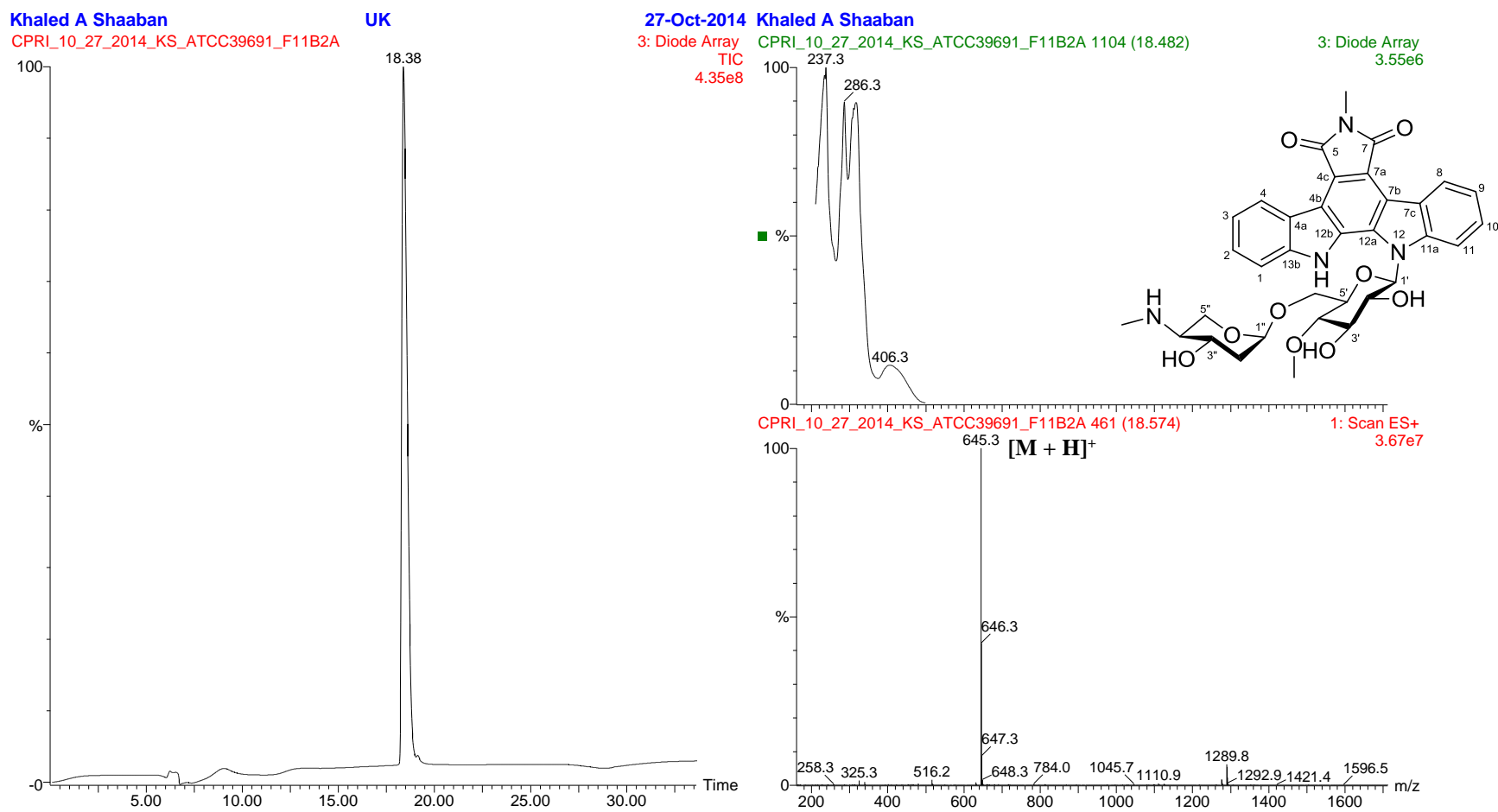


Figure S63: HPLC/UV/MS analyses of AT2433-B1 (**7**). Detection wavelength: 210-500; **solvent A:** H₂O/0.1% Formic acid; **solvent B:** CH₃CN/0.1% Formic acid; flow rate: 0.5 mL min⁻¹; 0-4 min, 10% B; 4-22 min, 10-100% B; 22-27 min, 100% B; 27-29 min, 100%-10% B; 29-35 min, 10% B.

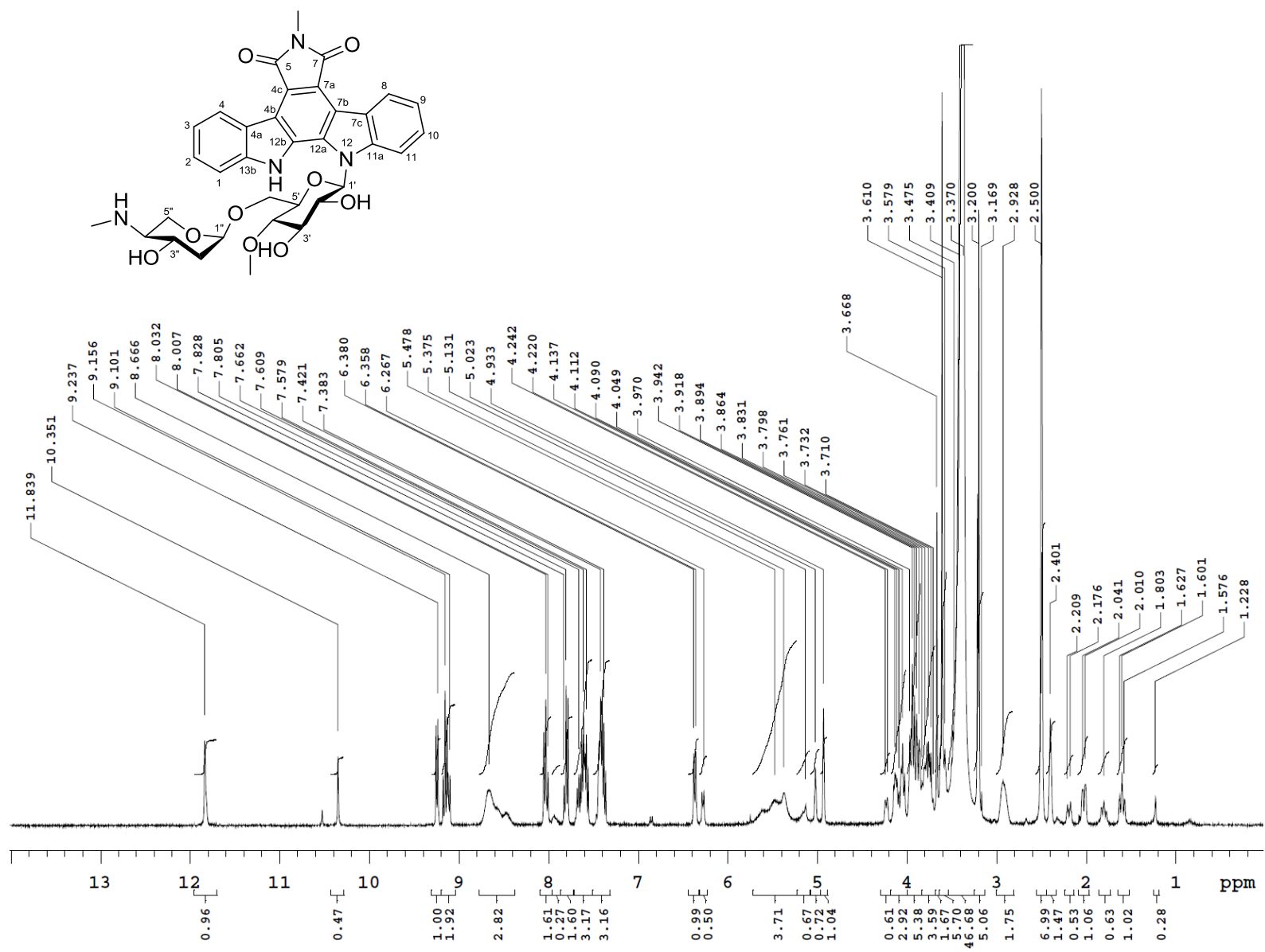


Figure S64: ¹H NMR spectrum (DMSO-d₆, 400 MHz) of AT2433-B1 (7)

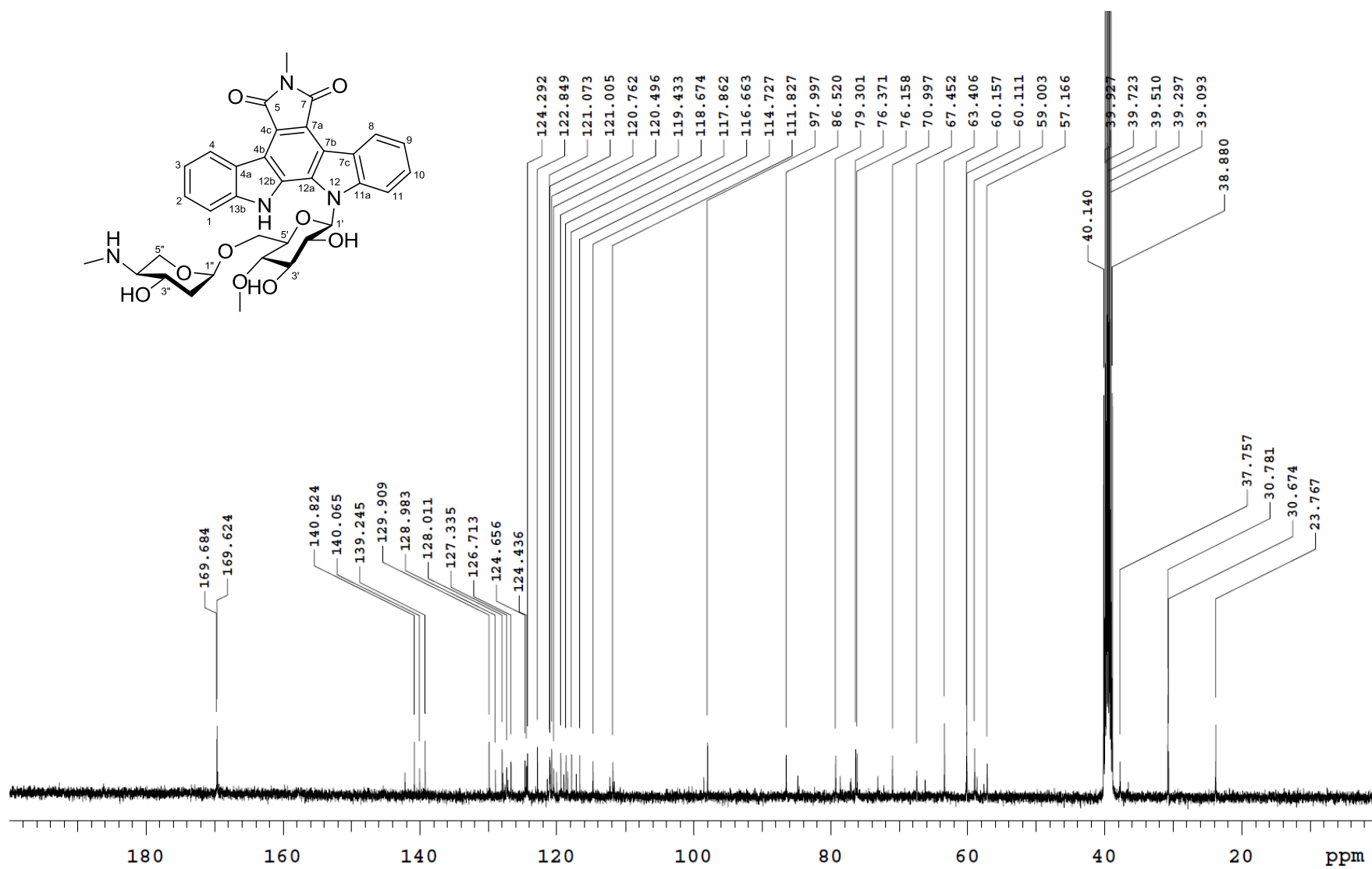


Figure S65: ¹³C NMR spectrum (DMSO-*d*₆, 100 MHz) of AT2433-B1 (7)

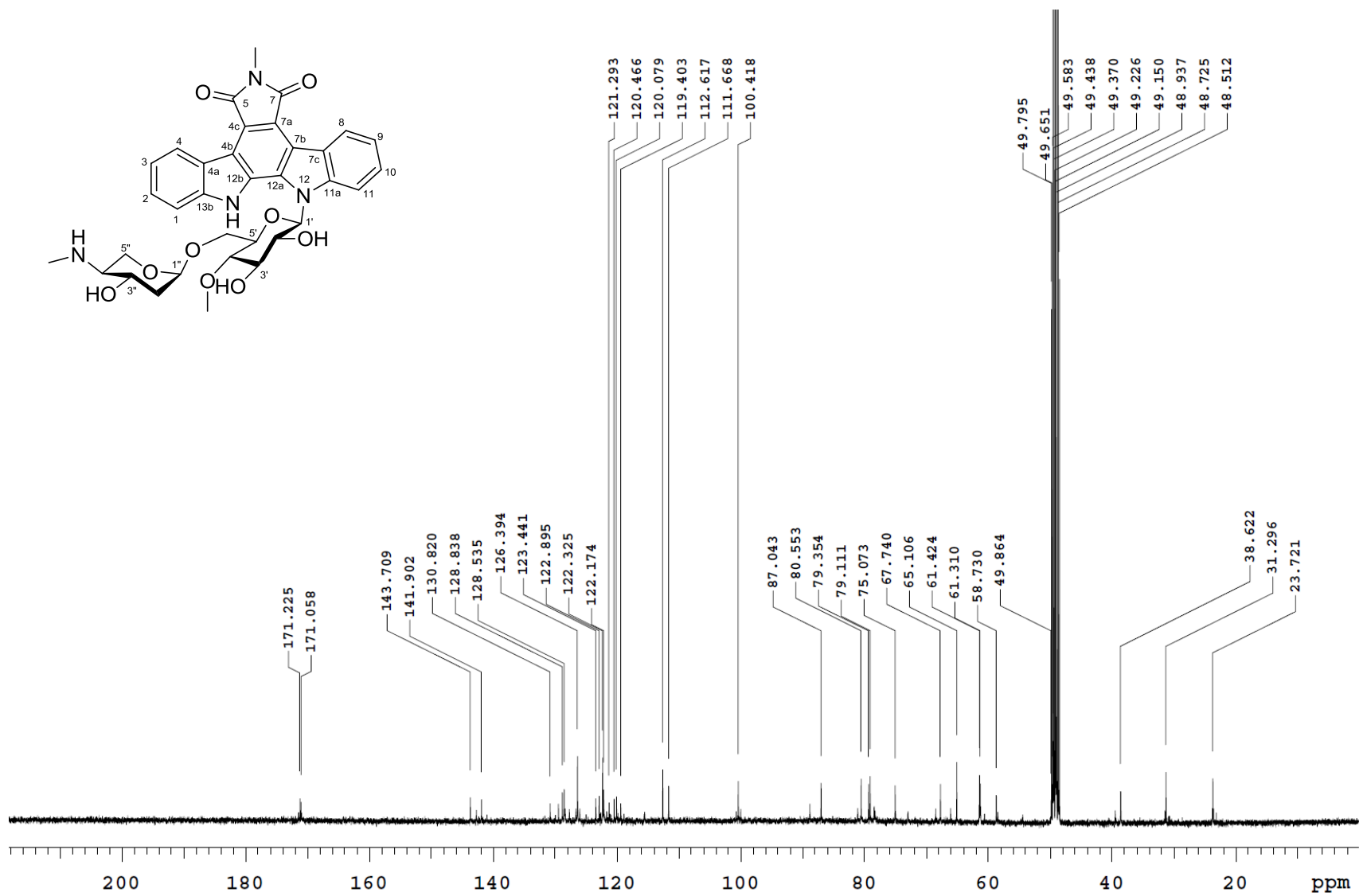


Figure S66: ¹³C NMR spectrum (CD₃OD, 100 MHz) of AT2433-B1 (7)

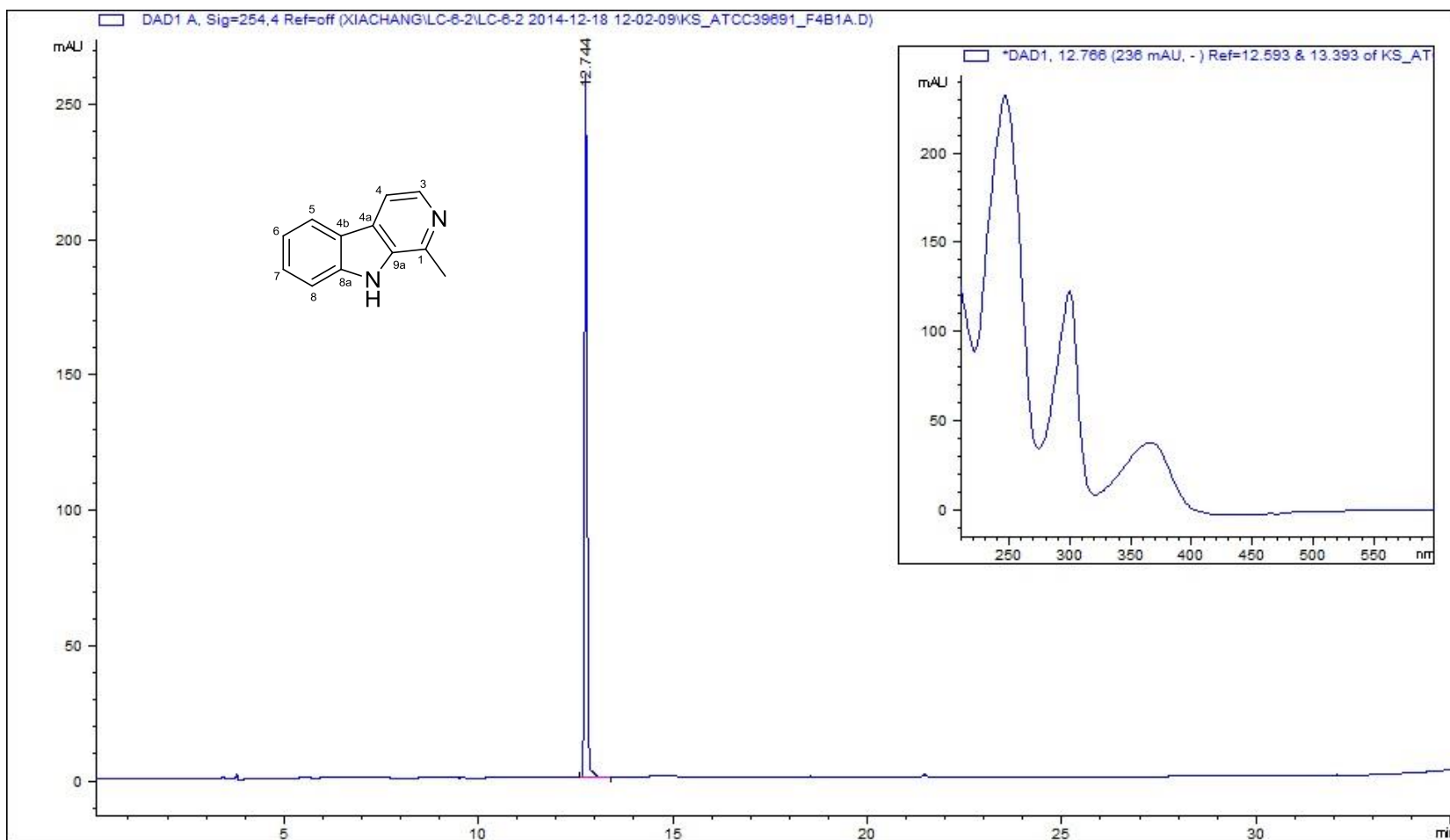


Figure S67: HPLC of harman “1-methyl- β -carboline” (**12**). HPLC-conditions: Detection wavelength 254 nm; **solvent A:** H₂O/0.1% TFA; **solvent B:** CH₃CN; flow rate: 0.5 mL min⁻¹; 0-4 min, 10% B; 4-22 min, 10-100% B; 22-27 min, 100% B; 27-29 min, 100%-10% B; 29-35 min, 10% B. UV-vis inset of full wavelength 190-600 nm.

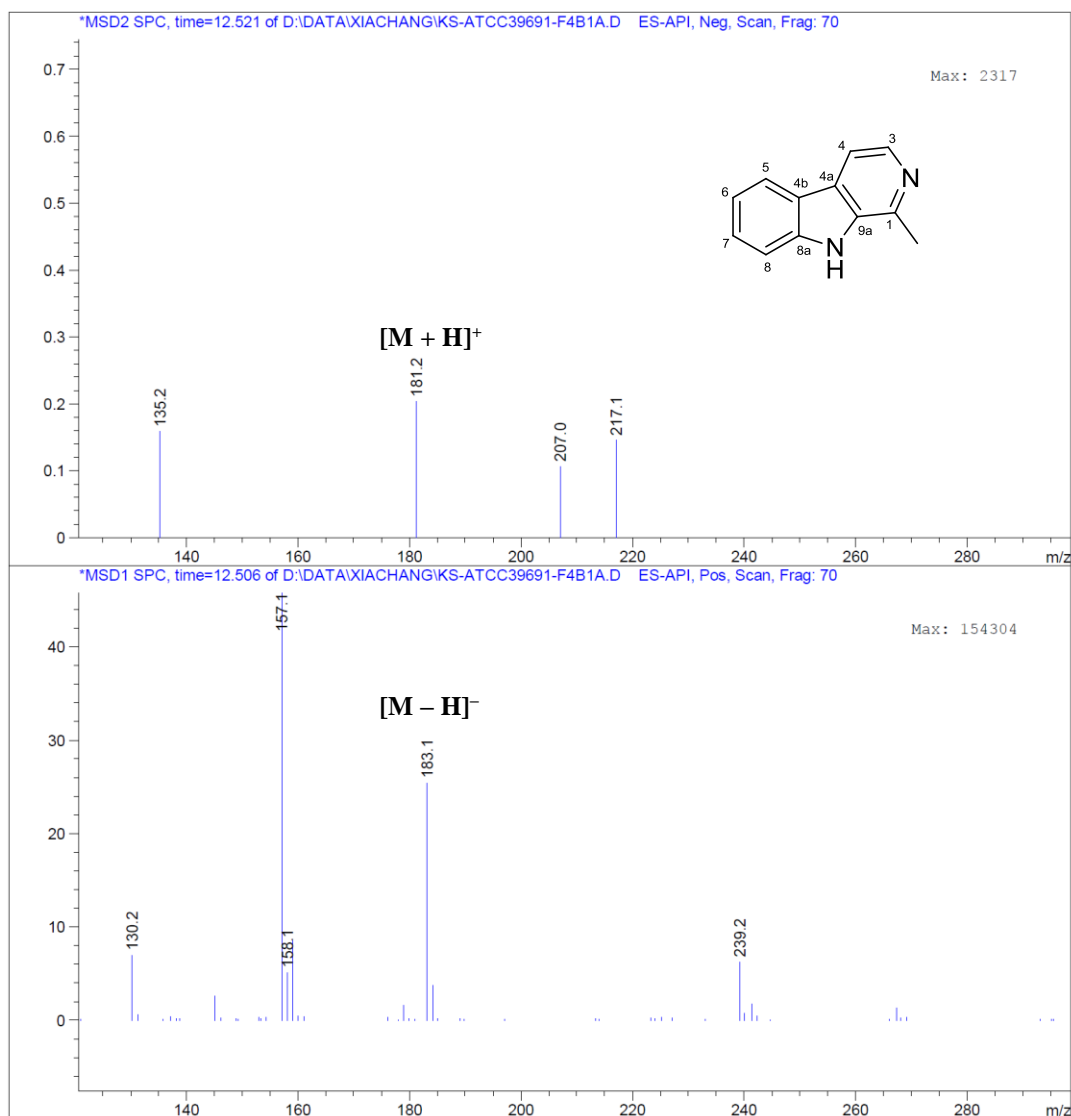


Figure S68: (+) and (-)-APCI-MS spectra of harman "1-methyl- β -carboline" (**12**)

14-0616 #55-81 RT: 1.44-2.12 AV: 27 NL: 2.46E8
T: FTMS + p ESI Full lock ms [100.00-1000.00]

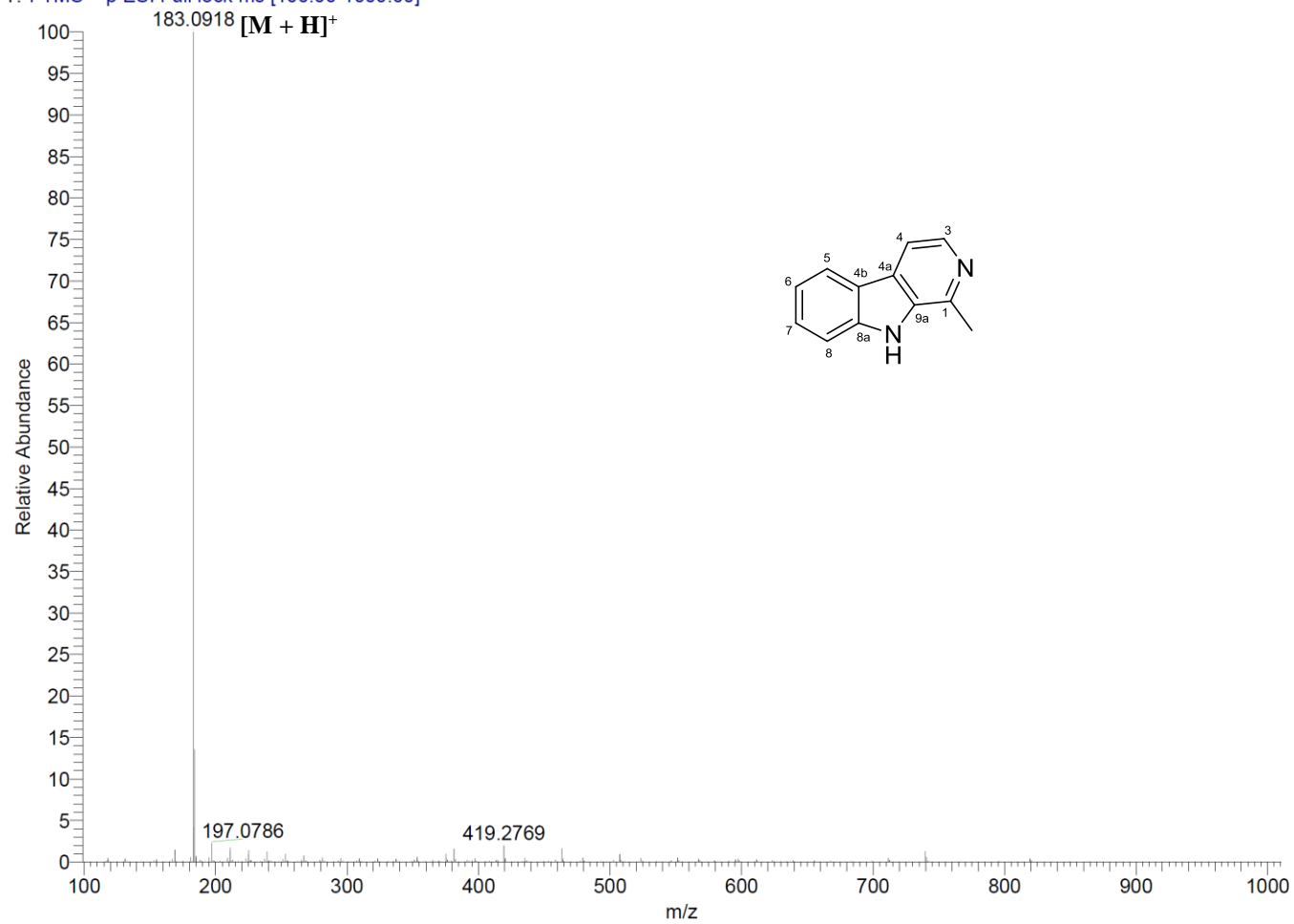


Figure S69: (+)-HRESI-MS spectrum of harman “1-methyl-β-carboline” (12)

500 MHz, DMSO-d₆, nt=256
Khaled A. Shaaban

Sample: khaled_A_Shaaban
File: xp

Pulse Sequence: s2pul

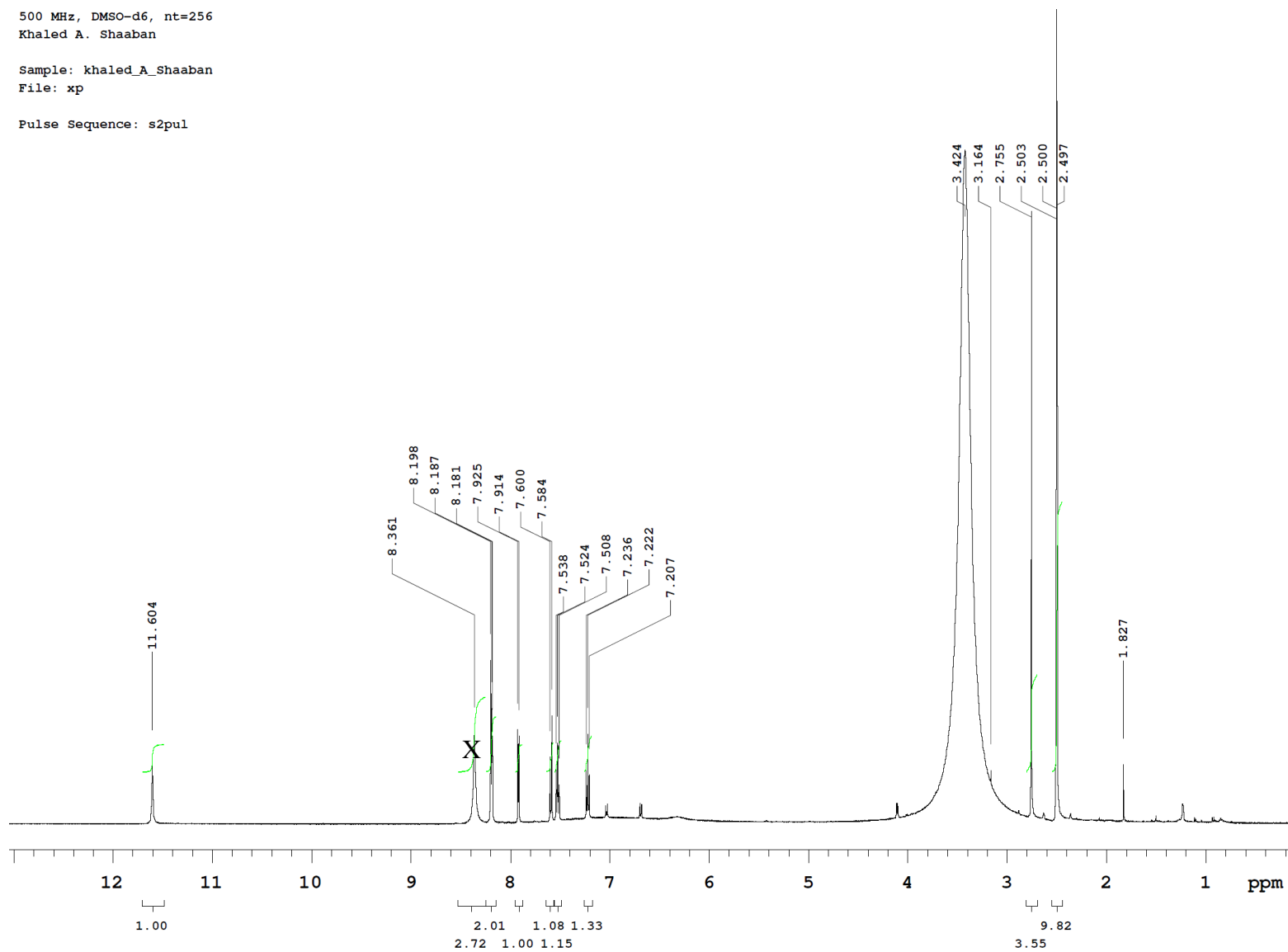


Figure S70: ¹H NMR spectrum (DMSO-d₆, 500 MHz) of harman "1-methyl-β-carboline" (12)

125 MHz, DMSO-d₆, 40 hrs
Khaled A. Shaaban

Sample: khaled_A_Shaaban
File: xp

Pulse Sequence: s2pul

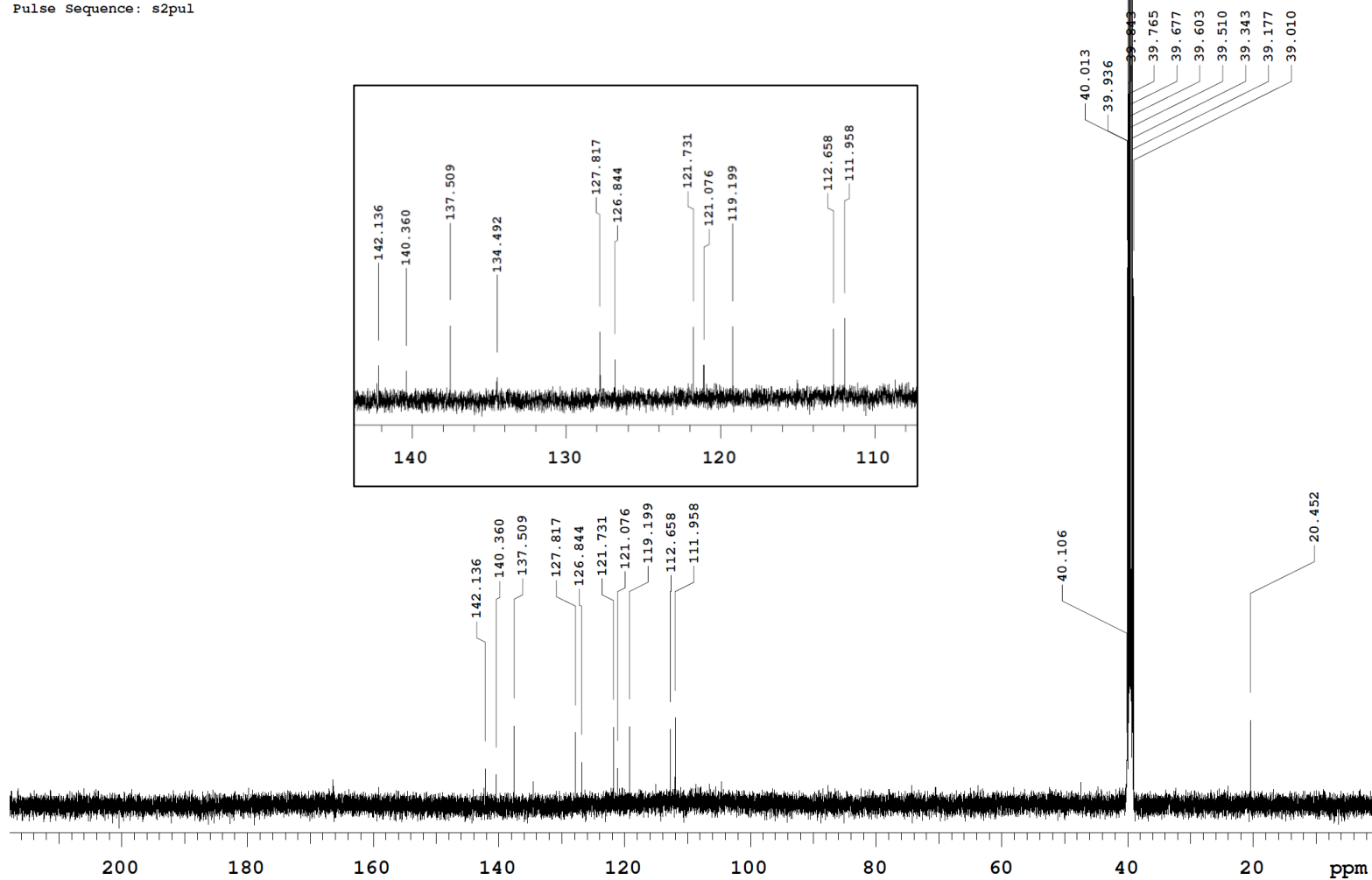
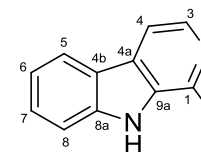


Figure S71: ^{13}C NMR spectrum (DMSO- d_6 , 125 MHz) of harman “1-methyl- β -carboline” (12)

500 MHz, DMSO-d₆, 2 hrs
Khaled A. Shaaban

Sample: khaled_A_Shaaban
File: xp

Pulse Sequence: gCOSY

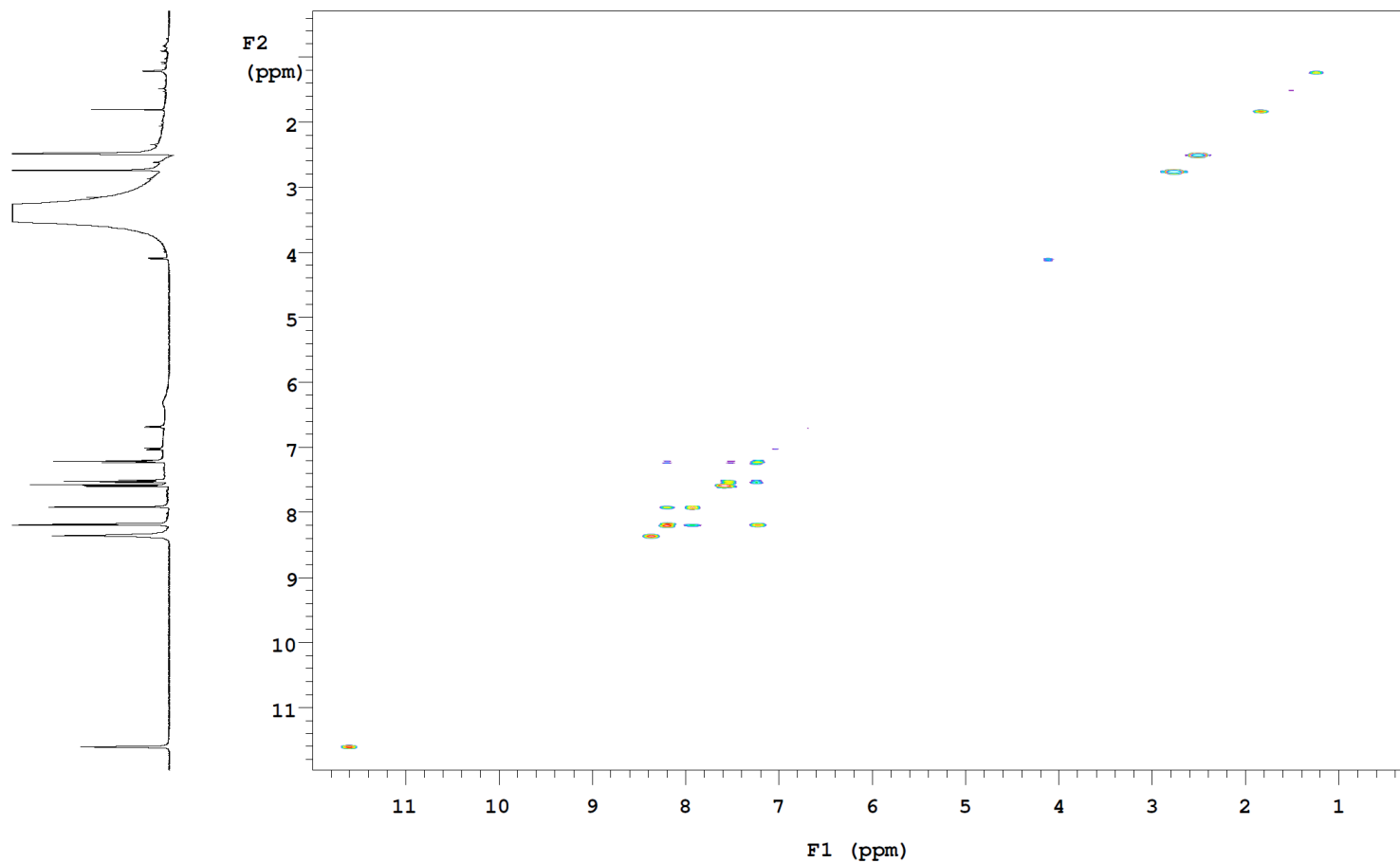
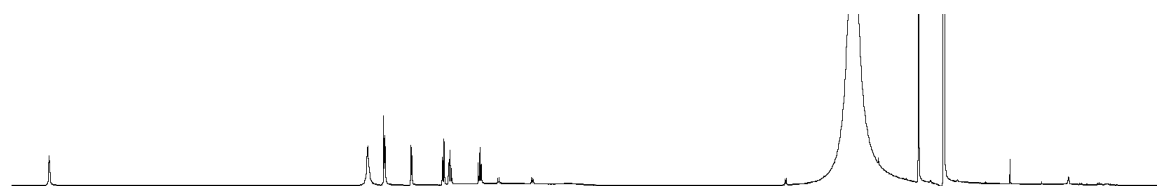
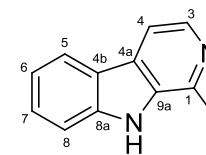


Figure S72: ¹H-¹H COSY spectrum (DMSO-*d*₆, 500 MHz) of harman “1-methyl-β-carboline” (**12**)

Sample: khaled_A_Shaaban
File: xp
Pulse Sequence: gHSQC

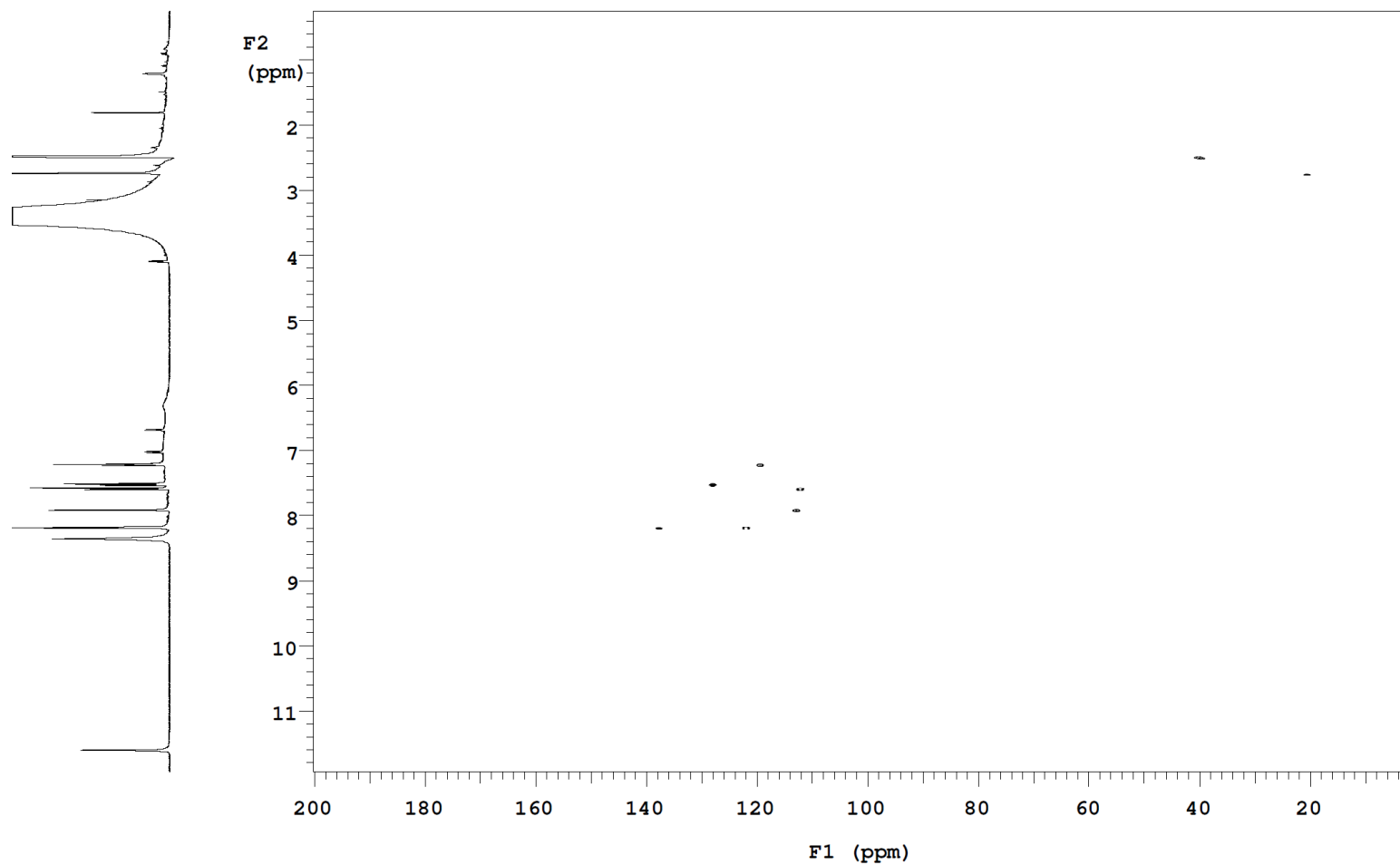
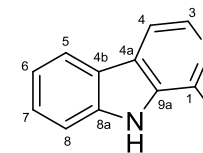


Figure S73: HSQC spectrum (DMSO-*d*₆, 500 MHz) of harman “1-methyl- β -carboline” (**12**)

KS_ATCC39691_F4B1A_gHMBC_12_23_2014
500 MHz, DMSO-d₆, 22 hrs
Khaled A. Shaaban

Sample: khaled_A_Shaaban
File: xp

Pulse Sequence: gHMBC

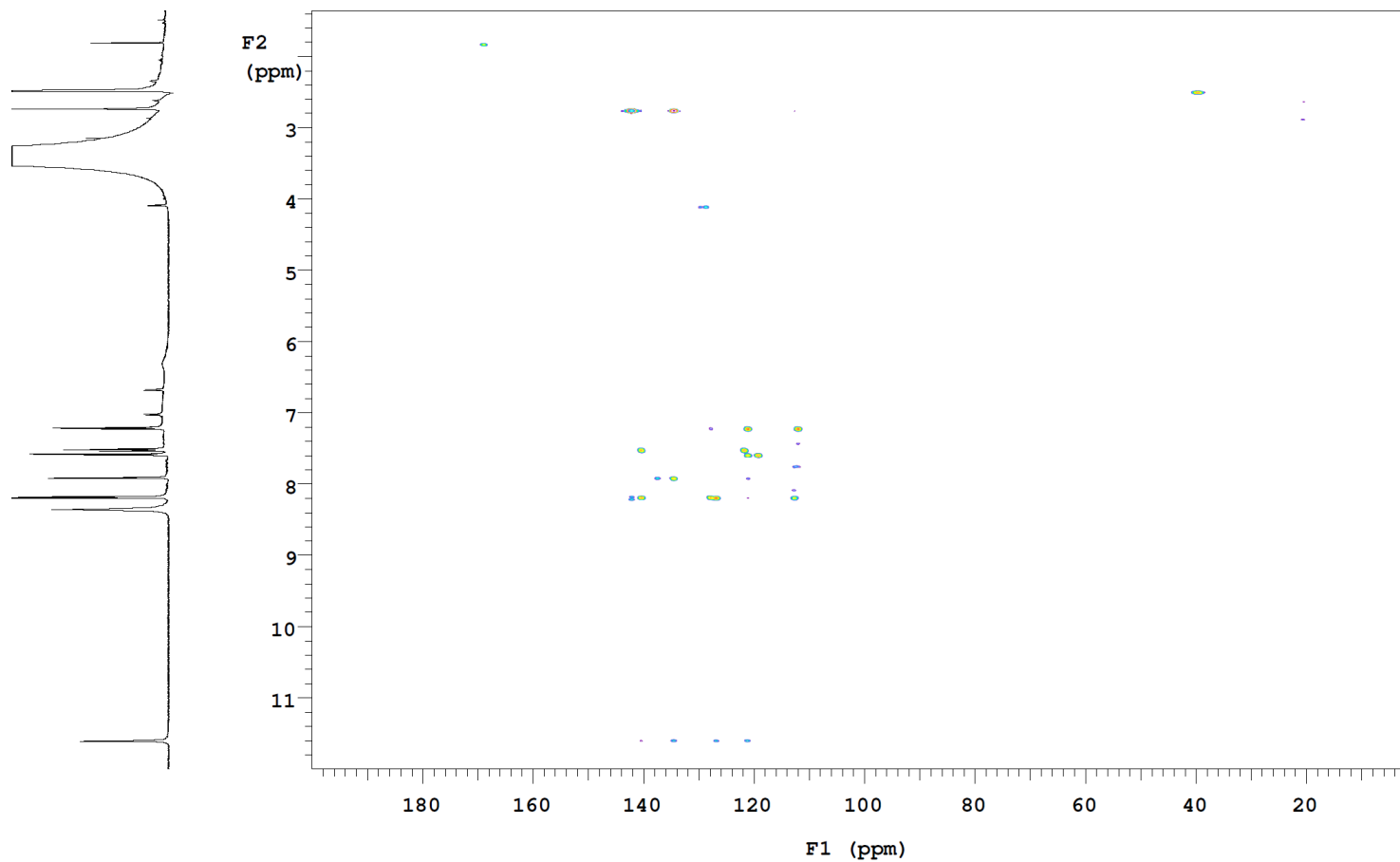
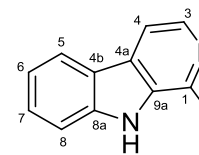


Figure S74: HMBC spectrum (DMSO-*d*₆, 500 MHz) of harman “1-methyl- β -carboline” (**12**)

KS_ATCC39691_F4B1A_TOCSY_12_26_2014
500 MHz, DMSO-d6, 5 hrs
Khaled A. Shaaban

Sample: khaled_A_Shaaban
File: xp

Pulse Sequence: TOCSY

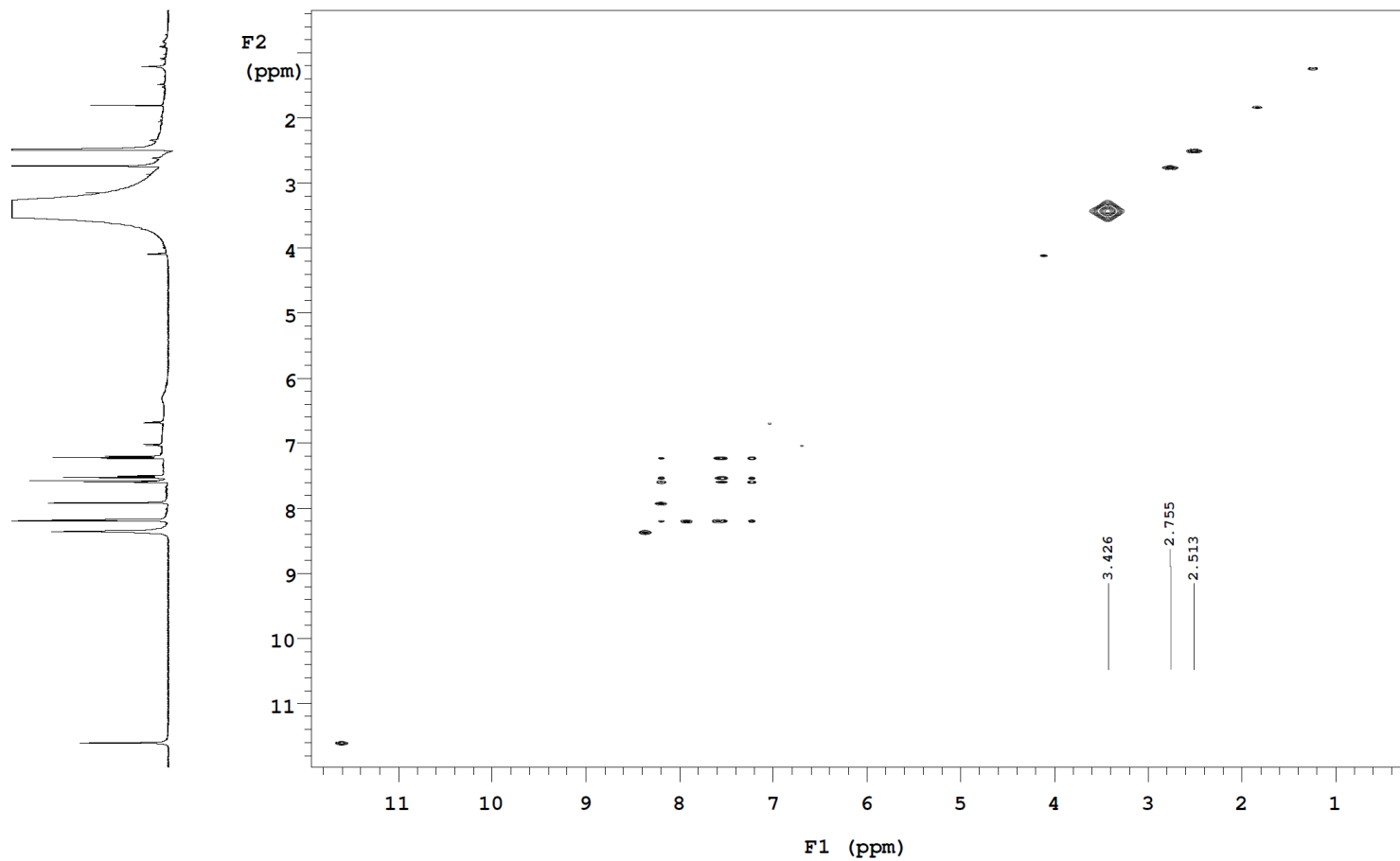
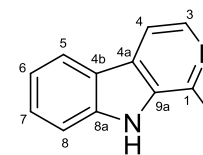


Figure S75: TOCSY spectrum (DMSO-*d*₆, 500 MHz) of harman “1-methyl- β -carboline” (**12**)

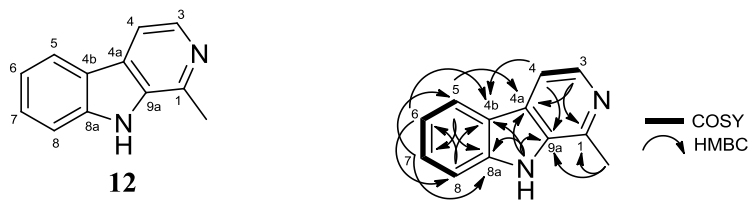


Figure S77. Chemical structure, ^1H - ^1H -COSY and selected HMBC correlations in harman (**12**)

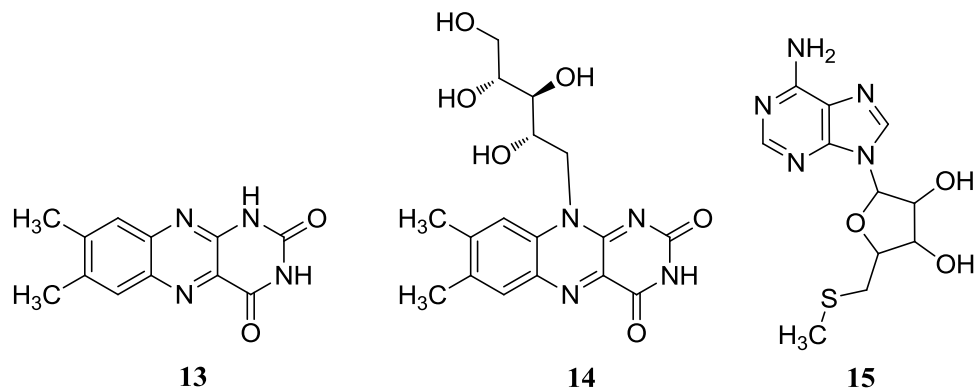


Figure S78: Chemical structures of lumichrome (**13**), riboflavin (**14**) and 5'-methylthioadenosine (**15**)

Table S1. Cytotoxic activities of compounds **1-7** at 10 μ M (average of three independent replicates); see Figure 4.

Compounds	PC3		A549		U118	
	Mean	SD	Mean	SD	Mean	SD
Veh. Control	100.0	10.3	100.0	23.6	100.0	23.7
1	39.0	0.6	19.9	1.4	31.3	1.6
2	69.0	5.6	47.4	4.6	40.5	0.7
3	154.9	13.7	164.0	27.3	186.1	9.6
4	98.3	5.2	96.6	11.3	61.0	8.4
5	47.7	1.2	32.6	3.5	53.6	5.9
6	27.0	0.8	10.5	0.5	20.8	0.7
7	36.4	1.3	16.6	0.7	29.4	1.2

SD= Standard deviation, Vehicle control= 1% DMSO and media

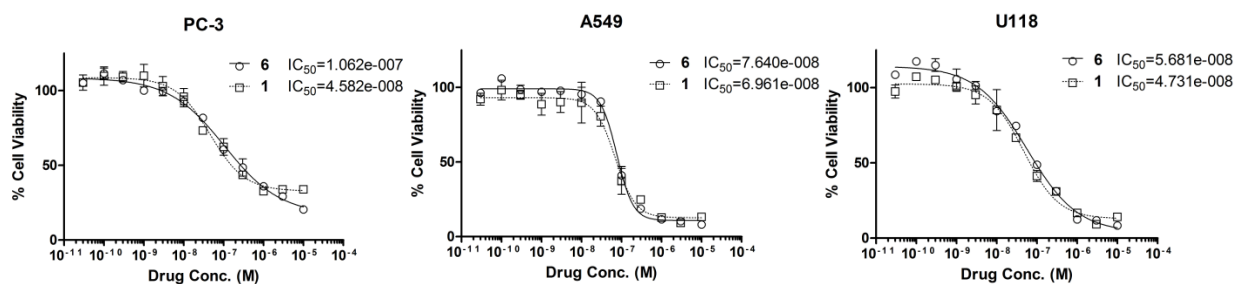


Figure S79. Dose–response curve of AT2433-A3 (**1**) and AT2433-A1 (**6**) in PC3 (Prostate), A549 (lung) and U118 (brain) human cancer cell lines at 72h; see Table 3.

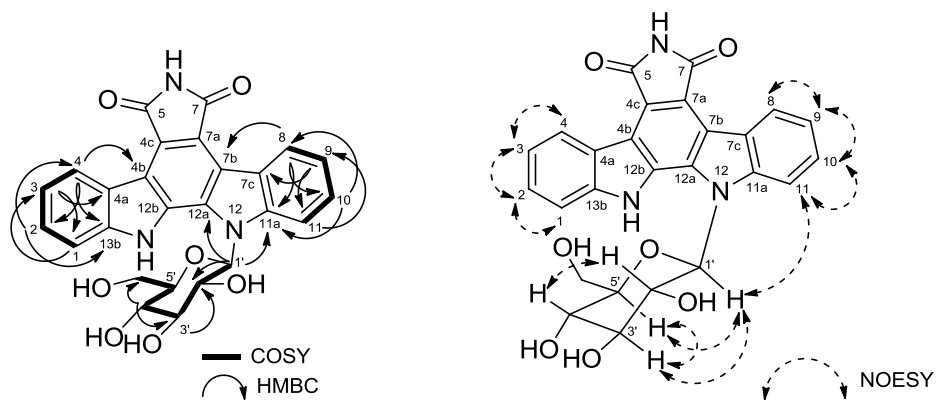


Figure S80. Selected ^1H - ^1H -COSY, HMBC and NOESY correlations in BMY-41219 (**5**)

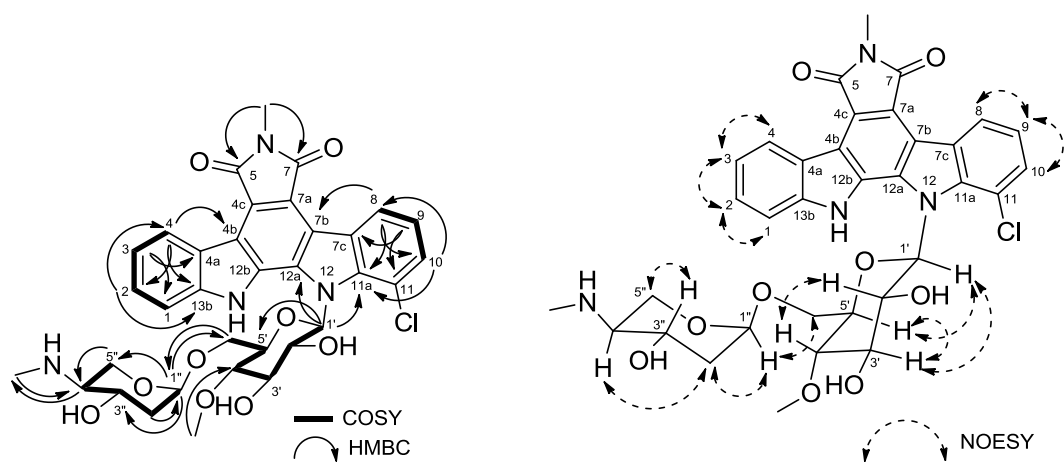


Figure S81. Selected ^1H - ^1H -COSY, HMBC and NOESY correlations in AT2433-A1 (**6**)

Table S2. ^{13}C (100 MHz) and ^1H NMR data of compounds **5-7**

Position	BMY-41219 (5) ^{a,b)}		AT2433-A1 (6) ^{a,b)}		AT2433-B1 (7) ^{a)}		
	δ_{C} , type	$\delta_{\text{H}}^{\text{c)}$, m (<i>J</i> in Hz)	δ_{C} , type	$\delta_{\text{H}}^{\text{c)}$, m (<i>J</i> in Hz)	δ_{C} , type ^{d)}	δ_{C} , type ^{b)}	$\delta_{\text{H}}^{\text{d,e)}$, m (<i>J</i> in Hz)
1	113.0, CH	7.66, dd (8.0, 1.0)	112.6, CH	7.58, d (8.0)	112.3, CH	112.6, CH	7.81, d (8.4)
2	128.2, CH	7.47, td (7.0, 1.0)	129.2, CH	7.55, td (7.0, 1.5)	127.9, CH	128.5, CH	7.67, t (7.6)
3	121.5, CH	7.24, td (7.0, 1.0)	122.4, CH	7.29, t (8.0)	121.4, CH	121.3, CH	7.42, t (7.6)
4	126.2, CH	9.00, dd (7.0, 1.0)	126.3, CH	8.68, d (8.0)	126.7, CH	126.4, CH	9.25, d (8.4)
4a	123.5, C	-	122.9, C	-	122.8, C	122.9, C	-
4b	119.5, C	-	119.5, C	-	119.4, C	119.1, C	-
4c	120.8, C	-	119.3, C	-	119.0, C	120.1, C	-
5	172.7, C	-	170.3, C	-	169.6, C	171.1, C	-
6- CH_3	-	-	23.7, CH_3	2.50, s	23.8, CH_3	23.7, CH_3	3.20, s
7	172.8, C	-	170.9, C	-	169.7, C	171.2, C	-
7a	122.8, C	-	122.4, C	-	120.8, C	120.5, C	-
7b	120.8, C	-	120.9, C	-	120.8, C	119.4, C	-
7c	123.4, C	-	126.6, C	-	124.7, C	123.4, C	-
8	126.4, CH	9.13, dd (7.5, 0.5)	125.7, CH	8.87, dd (8.0, 1.0)	124.4, CH	126.4, CH	9.16, d (8.8)
9	122.0, CH	7.29, td (8.0, 1.0)	123.7, CH	7.29, t (7.5)	124.3, CH	122.3, CH	7.42, t (7.6)
10	128.2, CH	7.52, td (7.0, 1.5)	131.4, CH	7.51, dd (7.5, 1.0)	128.0, CH	128.8, CH	7.67, t (7.6)
11	112.0, C	7.78, d (9.0)	117.9, C	-	111.8, CH	111.7, CH	8.05, d (8.8)
11a	143.9, C	-	139.4, C	-	139.2, C	143.7, C	-
12	-	-	-	-	-	-	-
12a	130.0, C	-	130.8, C	-	129.0, C	129.5, C	-
12b	131.7, C	-	131.4, C	-	129.9, C	130.8, C	-
13	-	-	-	-	-	-	11.83, brs
13a	142.9, C	-	141.7, C	-	140.8, C	141.9, C	-
1'	86.6, CH	6.19, d (9.0)	86.2, CH	6.90, d (9.5)	86.5, CH	87.0, CH	6.38, d (8.8)
2'	74.9, CH	3.85, t (9.0)	73.8, CH	3.79, m	71.0, CH	75.1, CH	3.41, m
2'-OH	-	-	-	-	-	-	5.47-5.37, brs
3'	78.7, CH	3.76, t (9.5)	79.3, CH	3.69, m	76.2, CH	79.1, CH	3.50, m
3'-OH	-	-	-	-	-	-	5.28, d (6.5)
4'	69.5, CH	4.27, t (9.5)	80.4, CH	3.69, m	79.3, CH	80.6, CH	3.67, m
4'- OCH_3	-	-	61.5, CH_3	3.77, s	59.0, CH_3	61.4, CH_3	3.63, s
5'	80.7, CH	4.00, dd (9.5, 2.0)	79.7, CH	4.05, m	76.4, CH	79.4, CH	3.94, m
6'	60.2, CH_2	4.26, d (9.0), 4.06, dd (11.5, 2.5)	67.8, CH_2	4.46, dd (11.5, 2.0), 4.12, dd (11.5, 3.5)	67.5, CH_2	67.7, CH_2	3.97, m
6'-OH	-	-	-	-	-	-	-
1''	-	-	100.4, CH	5.35, t (3.0)	100.0, CH	100.4, CH	4.93, brs
2''	-	-	38.7, CH_2	2.60 - 2.56, m	37.8, CH_2	38.6, CH_2	2.04, m
				2.06, m			1.60, m
3''	-	-	65.5, CH	4.20, m	63.4, CH	65.1, CH	4.15, m
4''	-	-	61.6, CH	3.13, m	60.2, CH	61.3, CH	2.93, m
4''- NHCH_3	-	-	31.9, CH_3	2.62, s	30.8, CH_3	31.3, CH_3	2.22, s
5''	-	-	59.1, CH_2	4.14, dd (11.0, 4.0) 3.96, dd (11.5, 9.5)	57.2, CH_2	58.7, CH_2	4.06, m 3.92, m

Assignments supported by 2D HSQC and HMBC experiments

^{a)} See supporting information for the NMR spectra; ^{b)} CD_3OD ; ^{c)} 500 MHz; ^{d)} $\text{DMSO}-d_6$; ^{e)} 400 MHz

Physico-chemical properties of compounds 5-7 and harman (12)

BMY-41219 (**5**): yellow solid; UV/vis (MeOH) λ_{\max} 227, 285, 316, 408 nm; ^1H NMR (CD_3OD , 500 MHz) and ^{13}C NMR (CD_3OD , 100 MHz), see Table S2; (+)-APCI-MS: m/z 488 $[\text{M} + \text{H}]^+$; (+)-HR-ESI-MS: m/z 488.1451 $[\text{M} + \text{H}]^+$ (calcd for $\text{C}_{26}\text{H}_{22}\text{N}_3\text{O}_7$, 488.1452); (-)-HR-ESI-MS: m/z 486.1294 $[\text{M} - \text{H}]^-$ (calcd for $\text{C}_{26}\text{H}_{20}\text{N}_3\text{O}_7$, 486.1295).

AT2433-A1 (**6**): yellow solid; UV/vis (MeOH) λ_{\max} ($\log \epsilon$) 237 (4.18), 289 (4.11), 318 (4.23), 400 (3.16) nm; ^1H NMR (CD_3OD , 500 MHz) and ^{13}C NMR (CD_3OD , 100 MHz), see Table S2; (+)-APCI-MS: m/z 679 $[\text{M} + \text{H}]^+$.

AT2433-B1 (**7**): yellow solid; UV/vis (MeOH) λ_{\max} 237, 286, 319, 406 nm; ^1H NMR ($\text{DMSO}-d_6$, 400 MHz) and ^{13}C NMR ($\text{DMSO}-d_6$, 100 MHz), (CD_3OD , 100 MHz), see Table S2; (+)-APCI-MS: m/z 645 $[\text{M} + \text{H}]^+$.

Harman (*1-Methyl- β -carboline*, **12**): white powder; blue UV-absorbing (254 nm), fluorescence (365 nm); pale-yellow with anisaldehyde/ H_2SO_4 spraying reagent; R_f 0.38 (silica gel, 10% MeOH- CH_2Cl_2); UV λ_{\max} 238, 295, 368 nm; ^1H NMR ($\text{DMSO}-d_6$, 500 MHz): δ 11.60 (brs, 1H, NH), 8.20 (d, $J = 5.5$ Hz, 1H, H-3), 8.19 (d, $J = 8.5$ Hz, 1H, H-5), 7.92 (d, $J = 5.5$ Hz, 1H, H-4), 7.59 (d, $J = 8.0$ Hz, 1H, H-8), 7.52 (t, $J = 7.0$ Hz, 1H, H-7), 7.22 (t, $J = 7.0$ Hz, 1H, H-6), 2.76 (s, 3H, 1- CH_3); ^{13}C NMR ($\text{DMSO}-d_6$, 125 MHz): δ 142.1 (Cq-1), 140.4 (Cq-8a), 137.5 (CH-3), 134.5 (Cq-9a), 127.8 (CH-7), 126.8 (Cq-4a), 121.7 (CH-5), 121.1 (Cq-4b), 119.2 (CH-6), 112.7 (CH-4), 112.0 (CH-8), 20.5 (1- CH_3); (+)-APCI-MS: m/z 183 $[\text{M} + \text{H}]^+$; (-)-APCI-MS: m/z 181 $[\text{M} - \text{H}]^-$; (+)-HR-ESI-MS: m/z 183.0918 $[\text{M} + \text{H}]^+$ (calcd for $\text{C}_{12}\text{H}_{11}\text{N}_2$, 183.0917); (-)-HR-ESI-MS: m/z 181.0771 $[\text{M} - \text{H}]^-$ (calcd for $\text{C}_{12}\text{H}_9\text{N}_2$, 181.0771). See figure S77, for COSY and HMBC correlations.