

Supplementary Data

Indole- and Pyrazole-Glycyrrhetic Acid Derivatives as PTP1B Inhibitors: Synthesis, In Vitro and In Silico Studies

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Table with ¹H and ¹³C NMR chemical shifts (δ) of compounds **4f** and **5f**. ¹H NMR and ¹³C NMR spectra of final compounds. Spectra resulting from different NMR experiments (NOESY, COSY, HSQC and HMBC) of compounds **4f** and **5f**. UPLC-ESI-MS data of final compounds are available.

Table S1. ^1H and ^{13}C NMR chemical shifts (δ) of compounds **4f** and **5f**

a						
H/C number ^a	V	¹ H NMR δ(ppm) ^a	¹³ C NMR δ(ppm) ^a	H/C number ^b	¹ H NMR δ(ppm) ^b	¹³ C NMR δ(ppm) ^b
1	a	2.3 and 4.0	37.5	1	2.17 and 3.55	37.03
2	l	-	108.4	2	-	114.40
3	u	-	142.07	3	-	145.79
4	e	-	34.2	4	-	34.45
5	s	1.44	53.1	5	1.32	53.58
6	d	1.39 and 1.72	18.68	6	1.52 and 1.68	18.05
7	e	1.55 and 1.80	32.2	7	1.42 and 1.70	31.80
8	t	-	45.5	8	-	44.71
9	e	-	60.5	9	2.57	59.76
10	r	-	38.1	10	-	37.75
11	m	-	199.8	11	-	198.85
12	i	-	129.01	12	5.47	127.46
13	n	5.80	169.30	13	-	170.36
14	e	-	44.01	14	-	44.84
15	d	-	27.74	15	1.35 and 1.80	26.40
16	f	1.28 and 2.08	26.63	16	0.99 and 2.10	26.04
17	o	1.07 and 2.06	31.10	17	-	31.46
18	r	-	48.3	18	2.06	48.25
19	c	1.69 and 2.02	41.10	19	1.69 and 2.11	41.02
20	o	-	43.5	20	-	43.31
21	m	1.55 and 1.79	32.06	21	1.33 and 1.83	30.59
22	p	1.37 and 1.44	37.92	22	1.25 and 1.36	37.70
23	o	1.27	23.51	23	0.97	29.54
24	u	1.33	31.14	24	0.94	22.74
25	n	1.18	16.16	25	1.04	15.63
26	d	1.24	28.73	26	1.08	18.12
27	4	1.23	18.50	27	1.08	28.03
28	f	0.87	28.57	28	0.75	28.18
29	b	1.42	23.59	29	1.35	23.07
30	V	-	182.06	30	-	177.76
3a'	a	-	137.75	1'	-	145.95
4'	l	7.79	116.39	2'	7.86	126.12
5'	u	-	121.58	3'	7.61	130.19
6'	e	7.34	118.00	4'	7.86	126.15
7'	s	7.34	110.38	5'	7.61	129.74
7a'	d	-	127.86	6'	-	126.08
CF ₃	e	-	126.10	CF ₃	-	122.75
NH	t	7.91	-	Pyrazole-CH	7.36	138.69
	e					

rmixed for compound **5f**

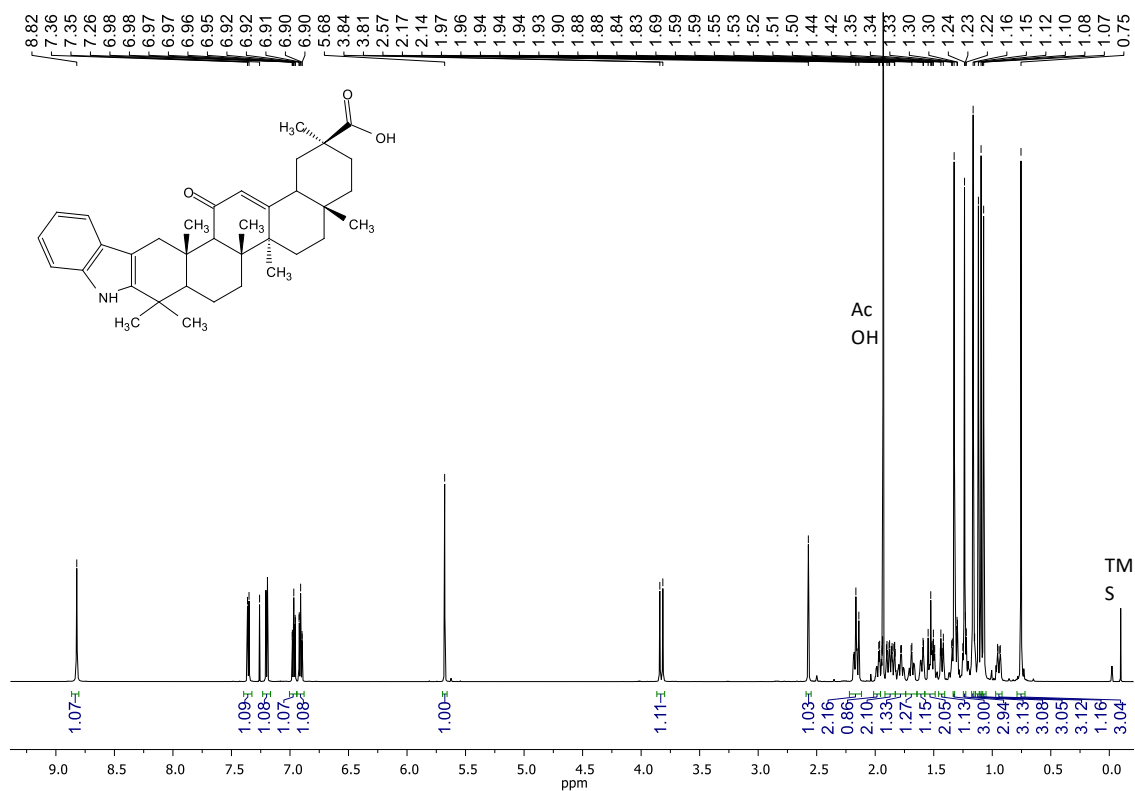


Figure S1. ¹H NMR (600 MHz) spectrum of compound **4a** in CDCl₃

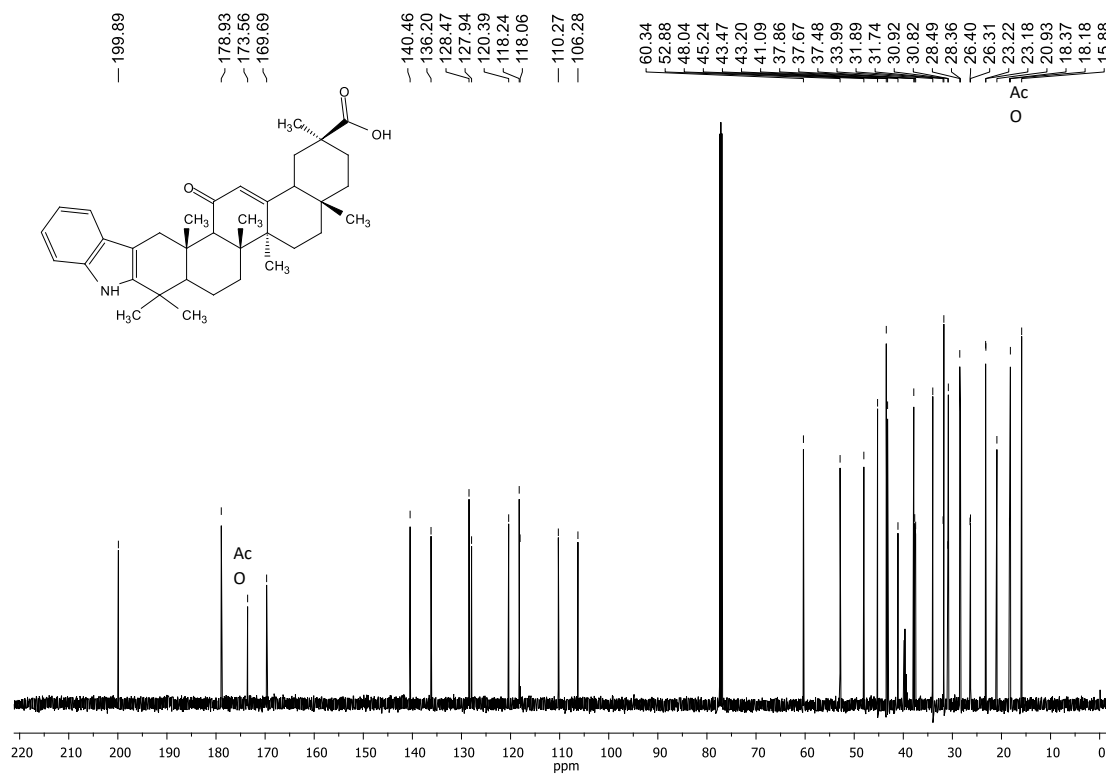


Figure S2. ¹³C NMR (151 MHz) spectrum of compound **4a** in CDCl₃

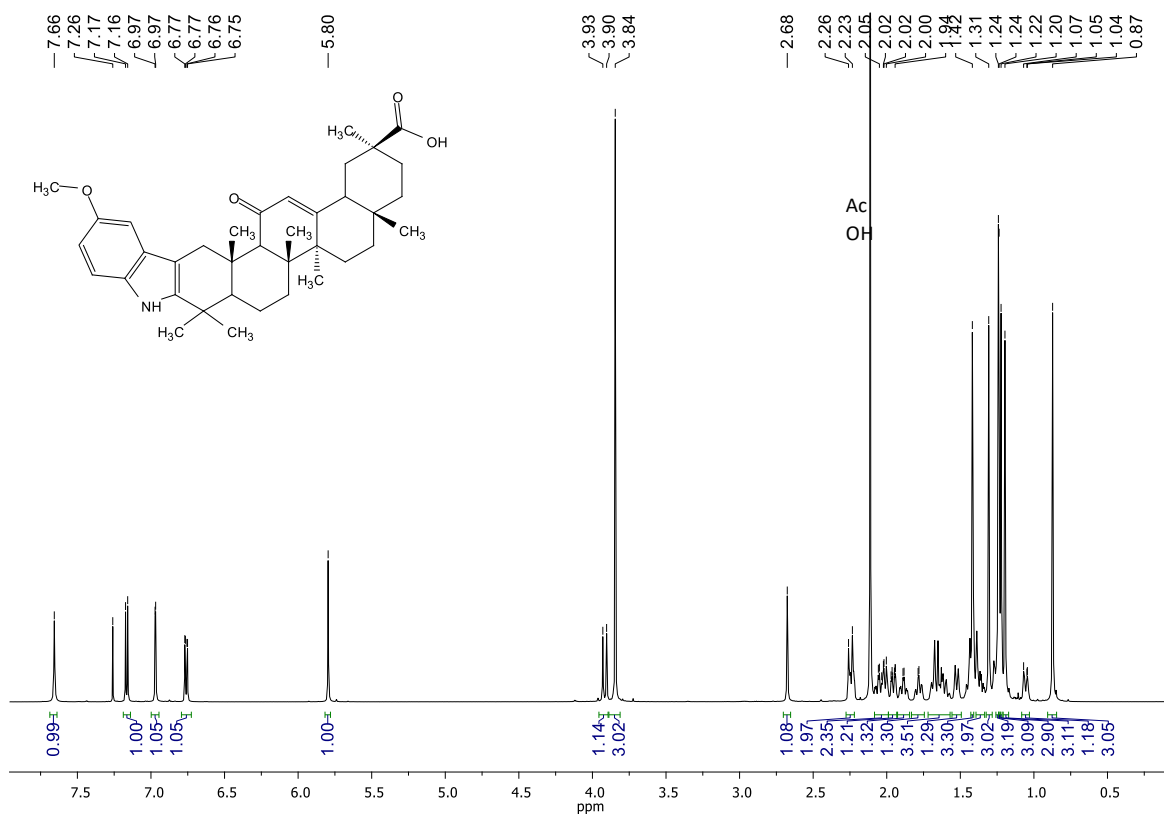


Figure S3. ^1H NMR (600 MHz) spectrum of compound **4b** in CDCl_3

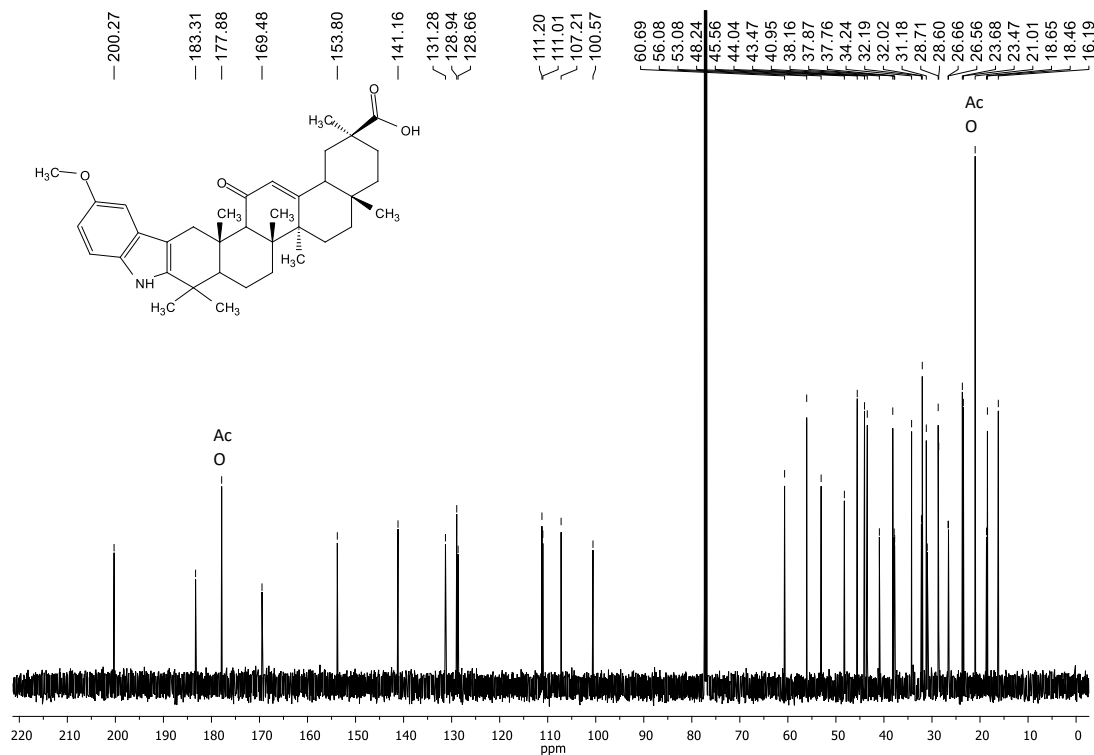


Figure S4. ^{13}C NMR (151 MHz) spectrum of compound **4b** in CDCl_3

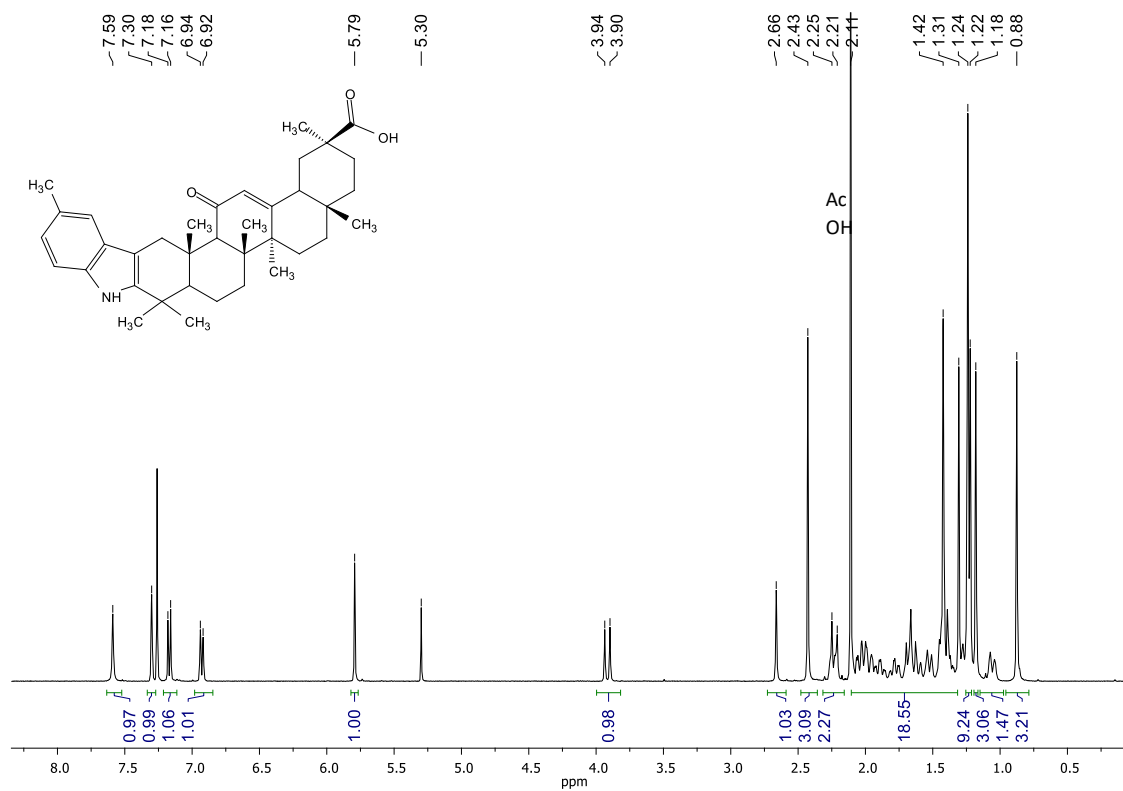


Figure S5. ^1H NMR (600 MHz) spectrum of compound **4c** in CDCl_3

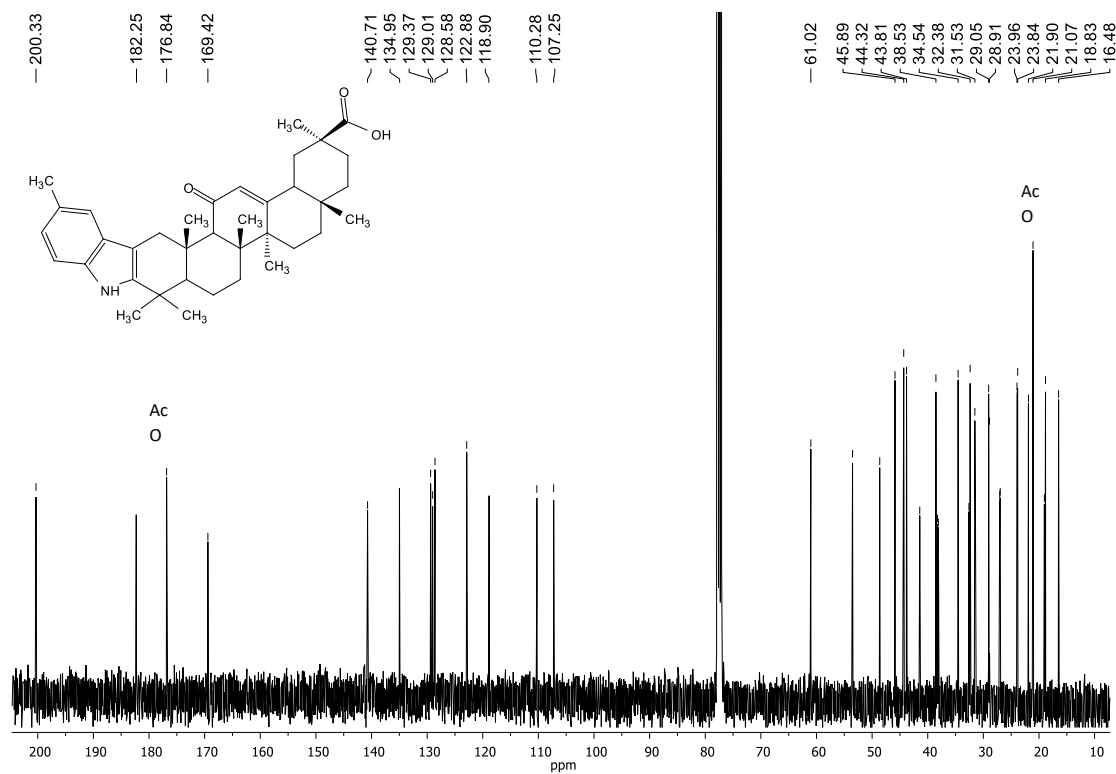


Figure S6. ^{13}C NMR (151 MHz) spectrum of compound **4c** in CDCl_3

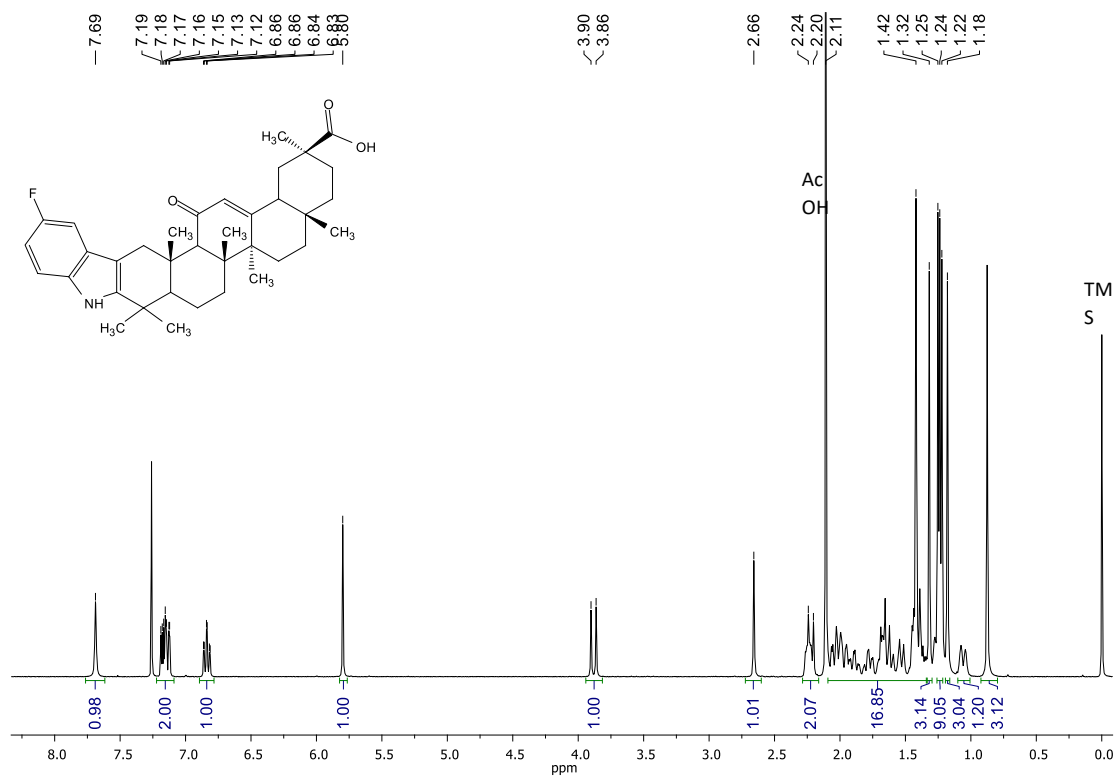


Figure S7. ^1H NMR (600 MHz) spectrum of compound **4d** in CDCl_3

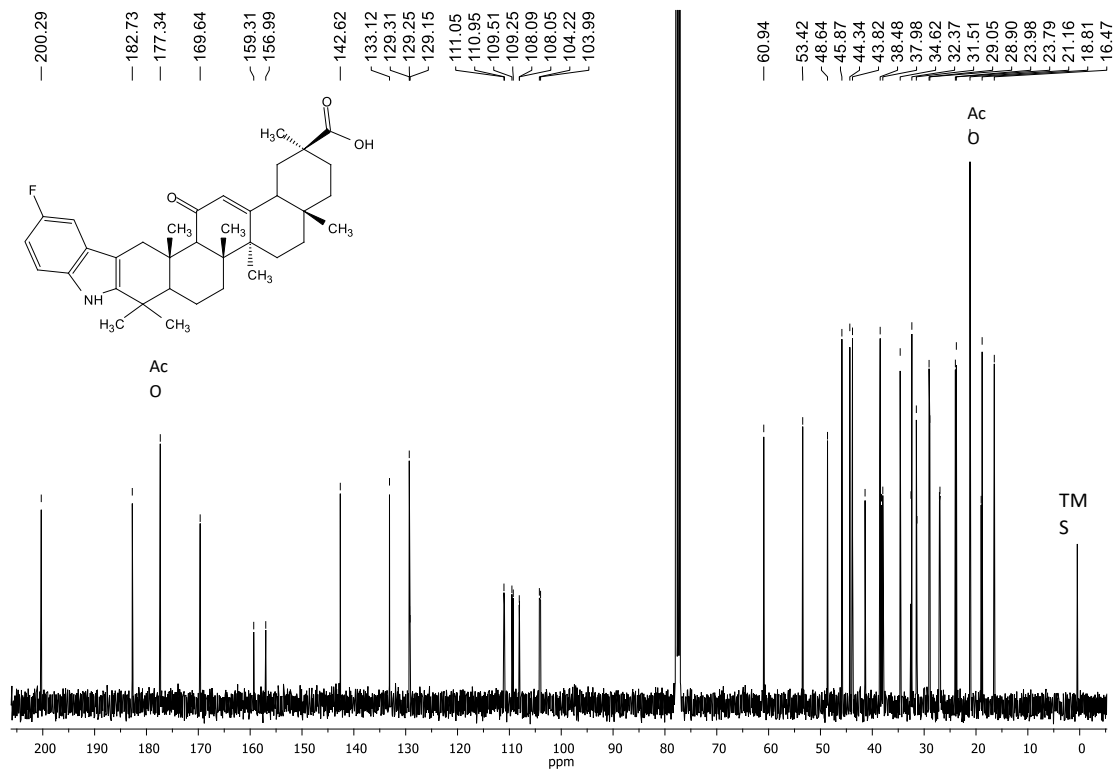


Figure S8. ^{13}C NMR (151 MHz) spectrum of compound **4d** in CDCl_3

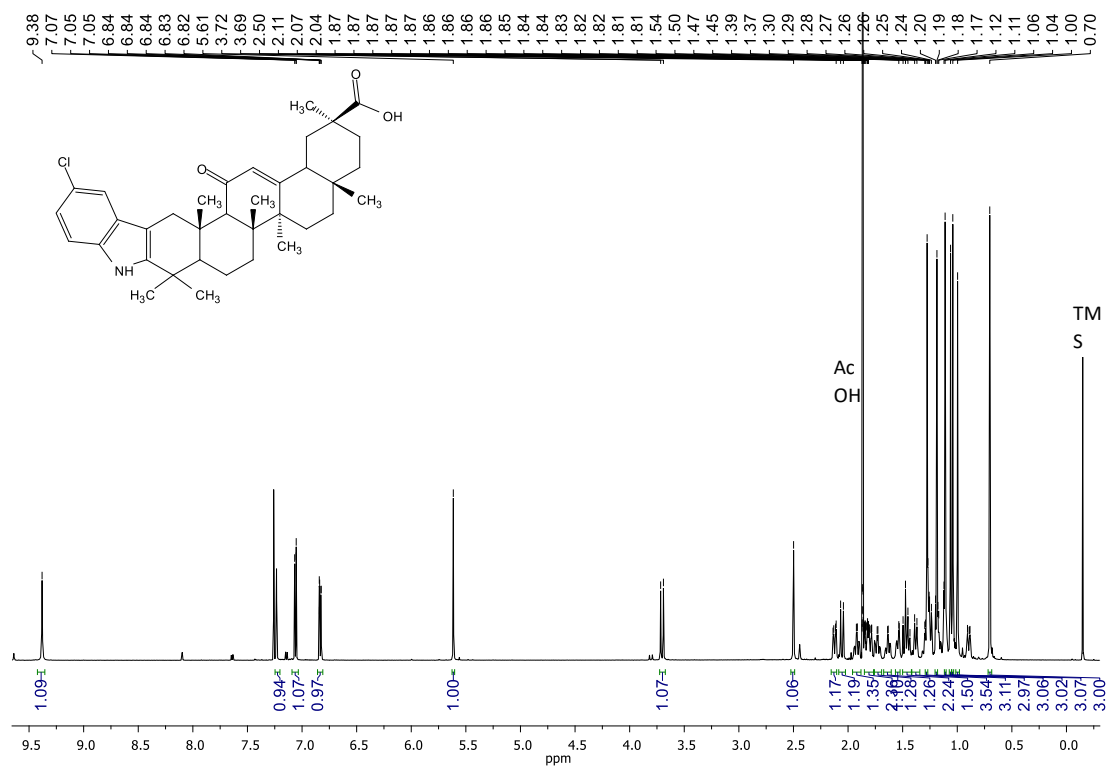


Figure S9. ¹H NMR (600 MHz) spectrum of compound **4e** in CDCl₃

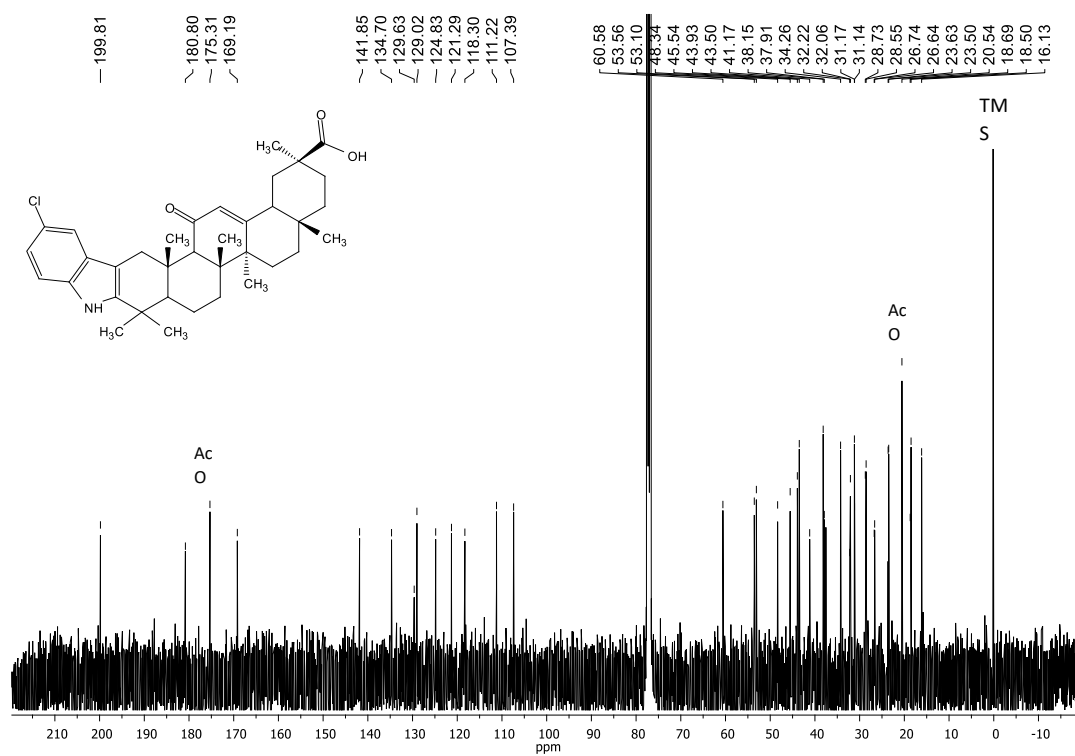


Figure S10. ¹³C NMR (151 MHz) spectrum of compound **4e** in CDCl₃

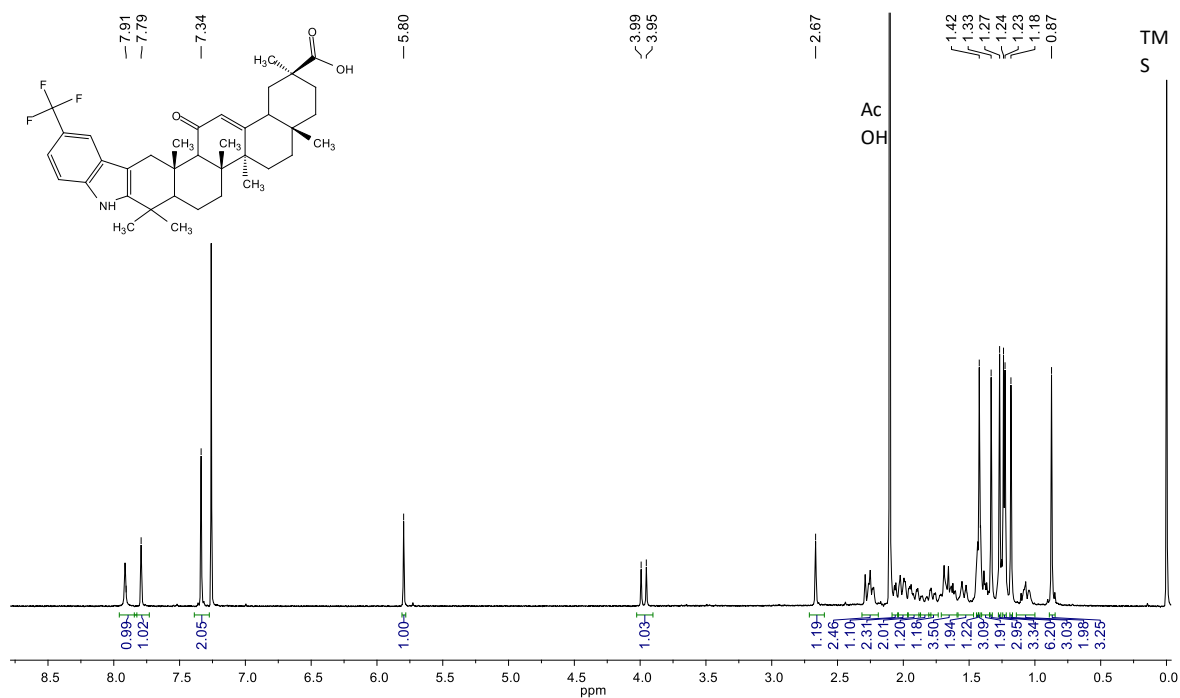


Figure S11. ^1H NMR (400 MHz) spectrum of compound **4f** in CDCl_3

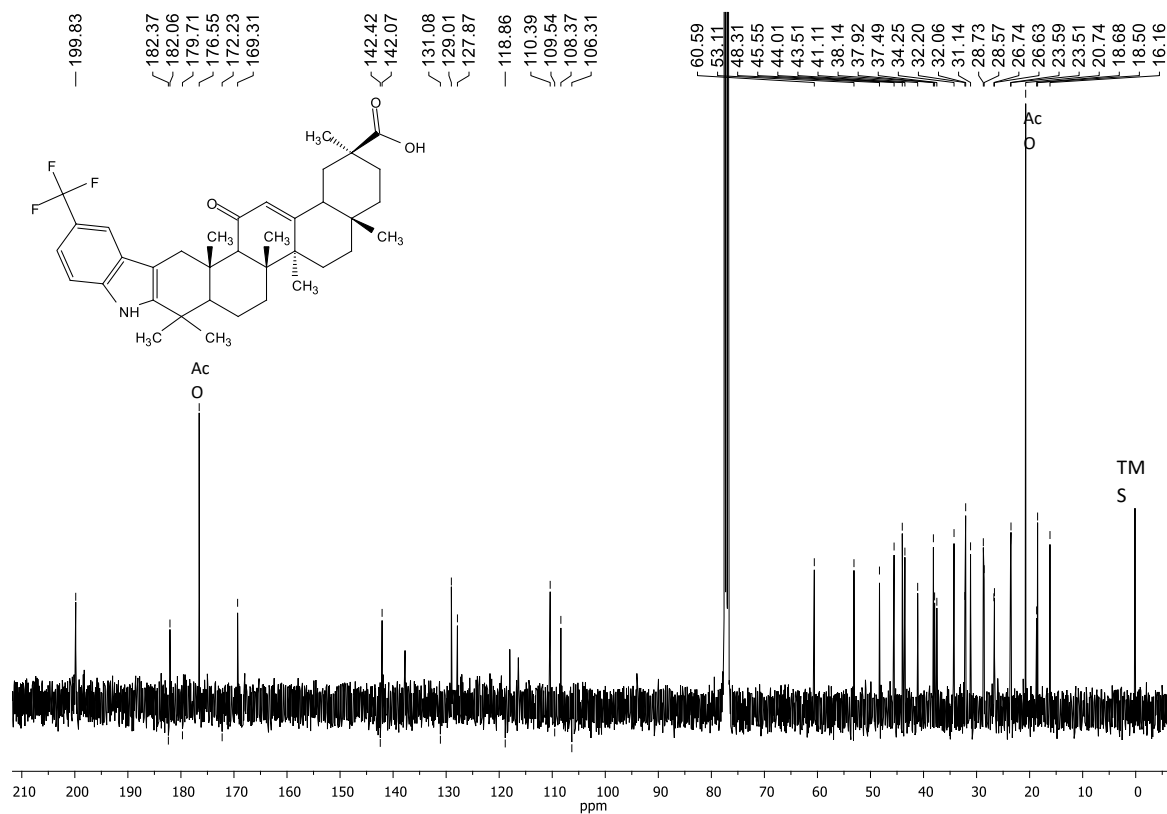


Figure S12. ^{13}C NMR (151 MHz) spectrum of compound **4f** in CDCl_3

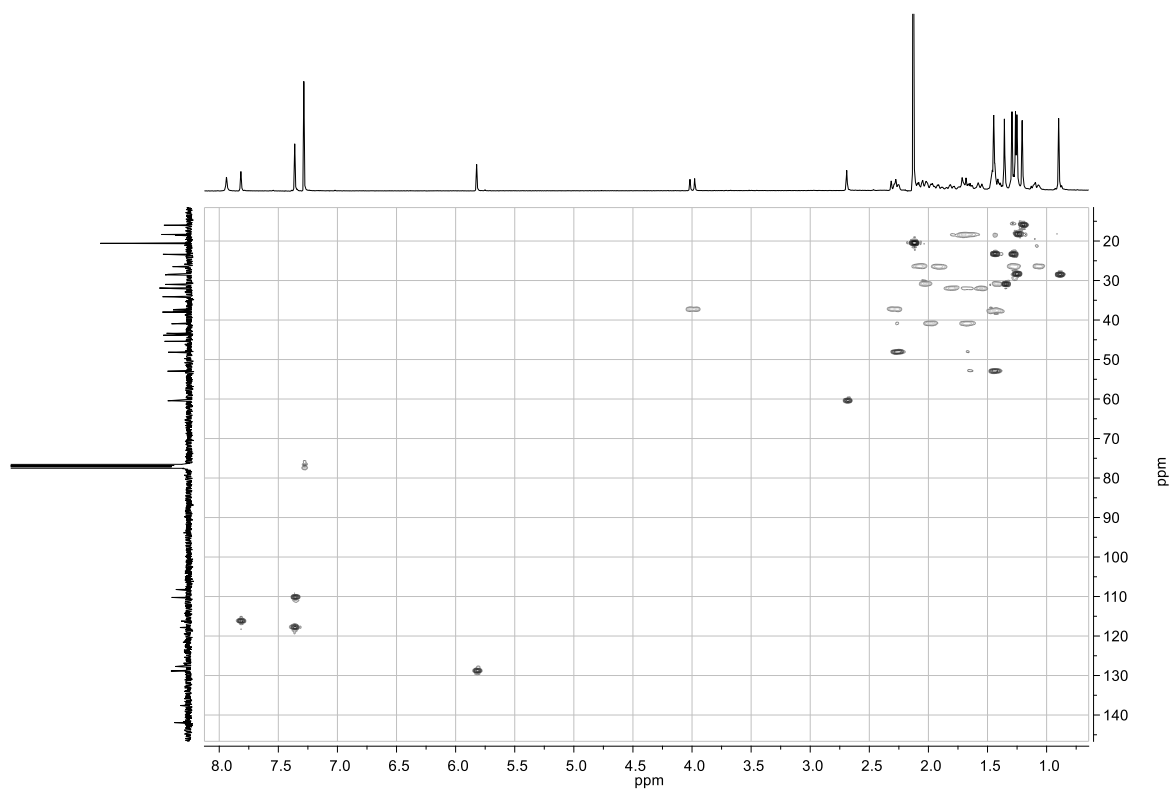


Figure S13. HSQC spectrum of compound **4f** in CDCl₃

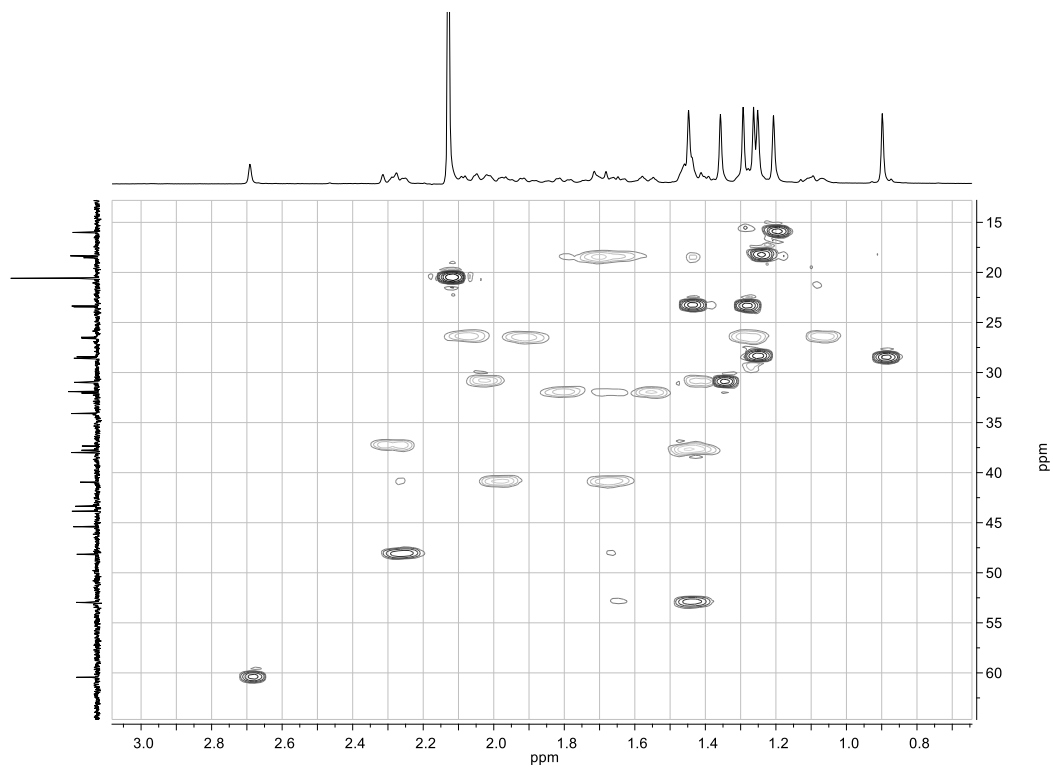


Figure S14. HSQC spectrum (0 – 3.0 ppm) of compound **4f** in CDCl₃

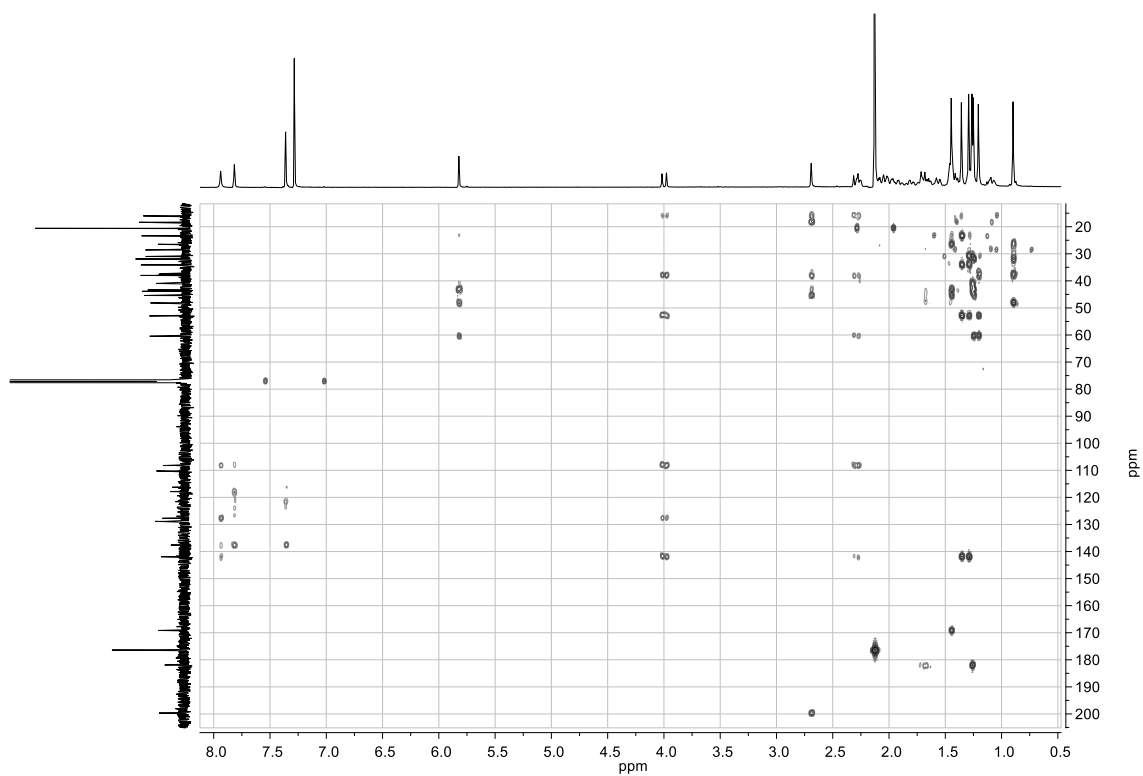


Figure S15. HMBC spectrum of compound **4f** in CDCl_3

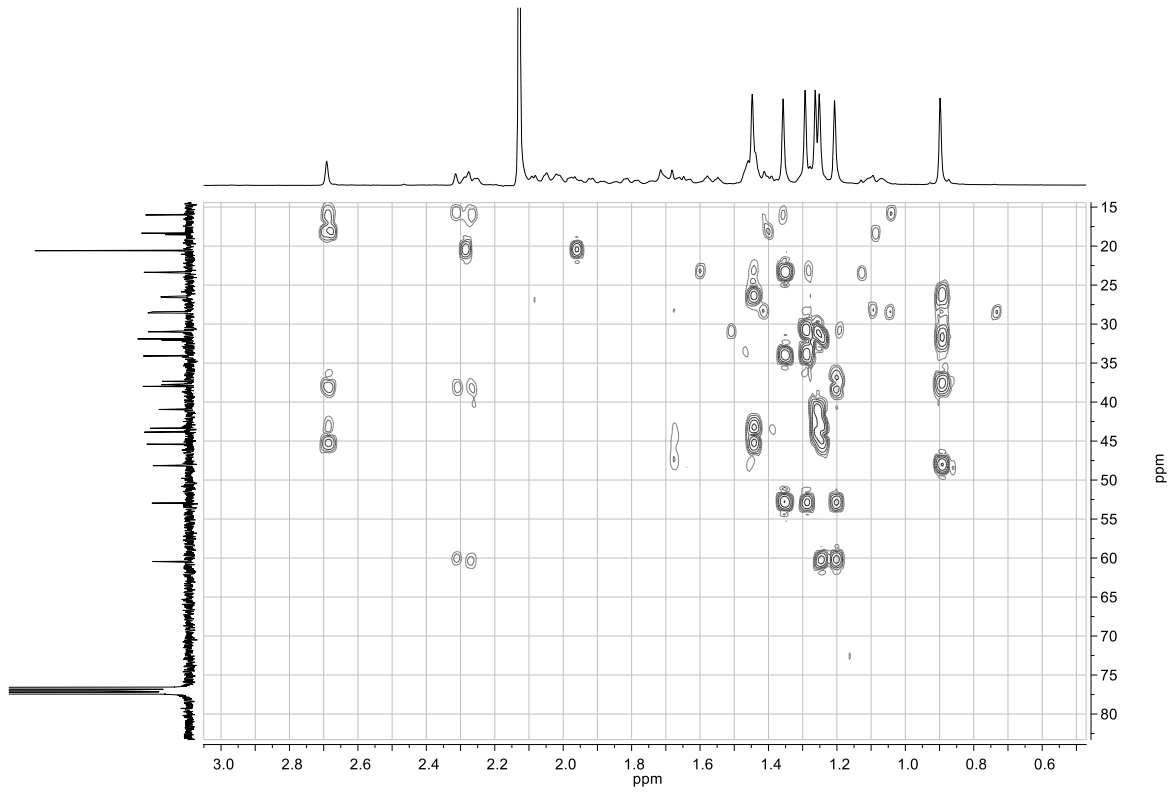


Figure S16. HMBC spectrum (0 – 3.0 ppm) of compound **4f** in CDCl_3

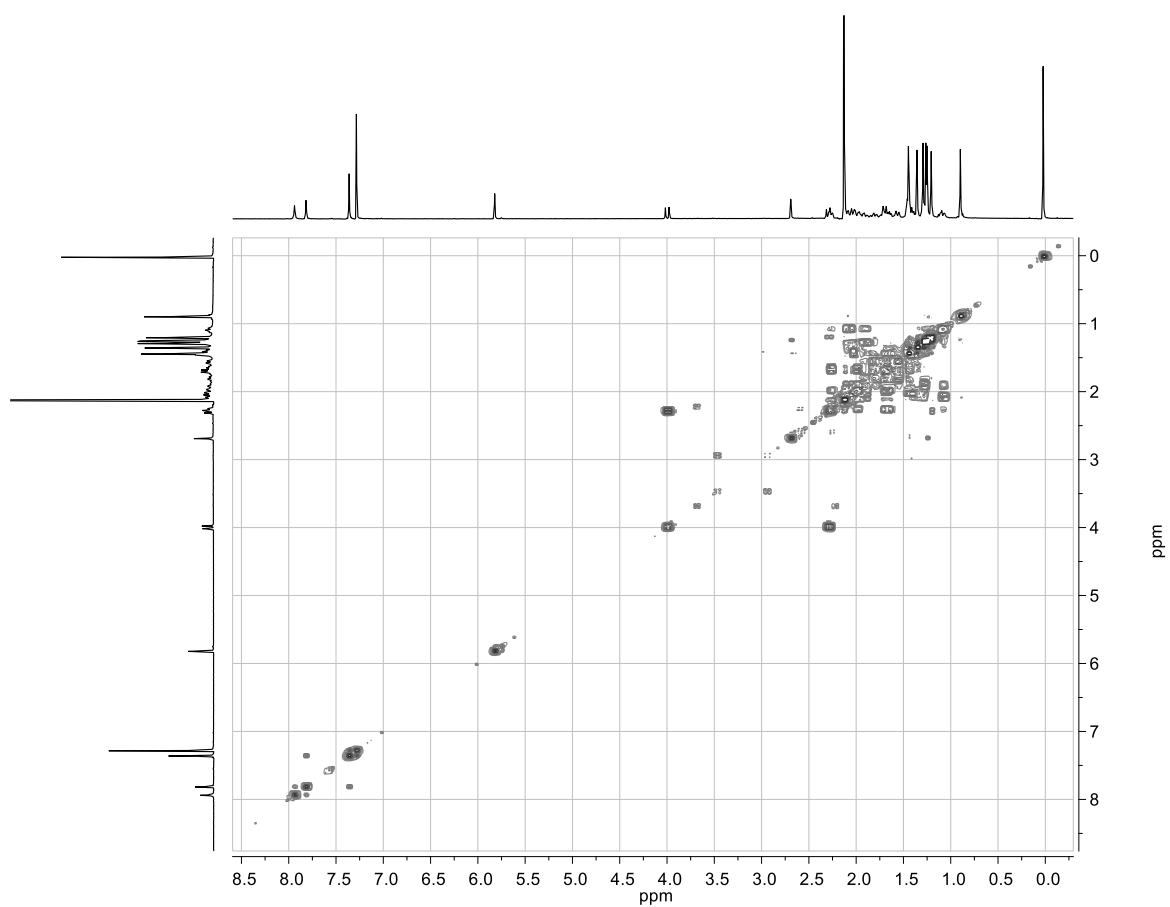


Figure S17. COSY spectrum of compound **4f** in CDCl_3

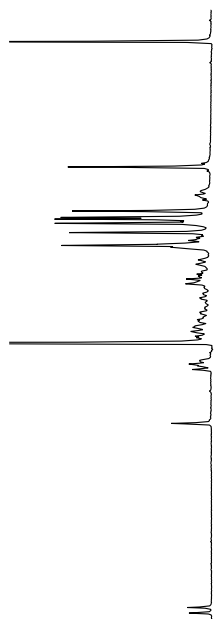


Figure S18. COSY spectrum (0 – 3.0 ppm) of compound **4f** in CDCl₃

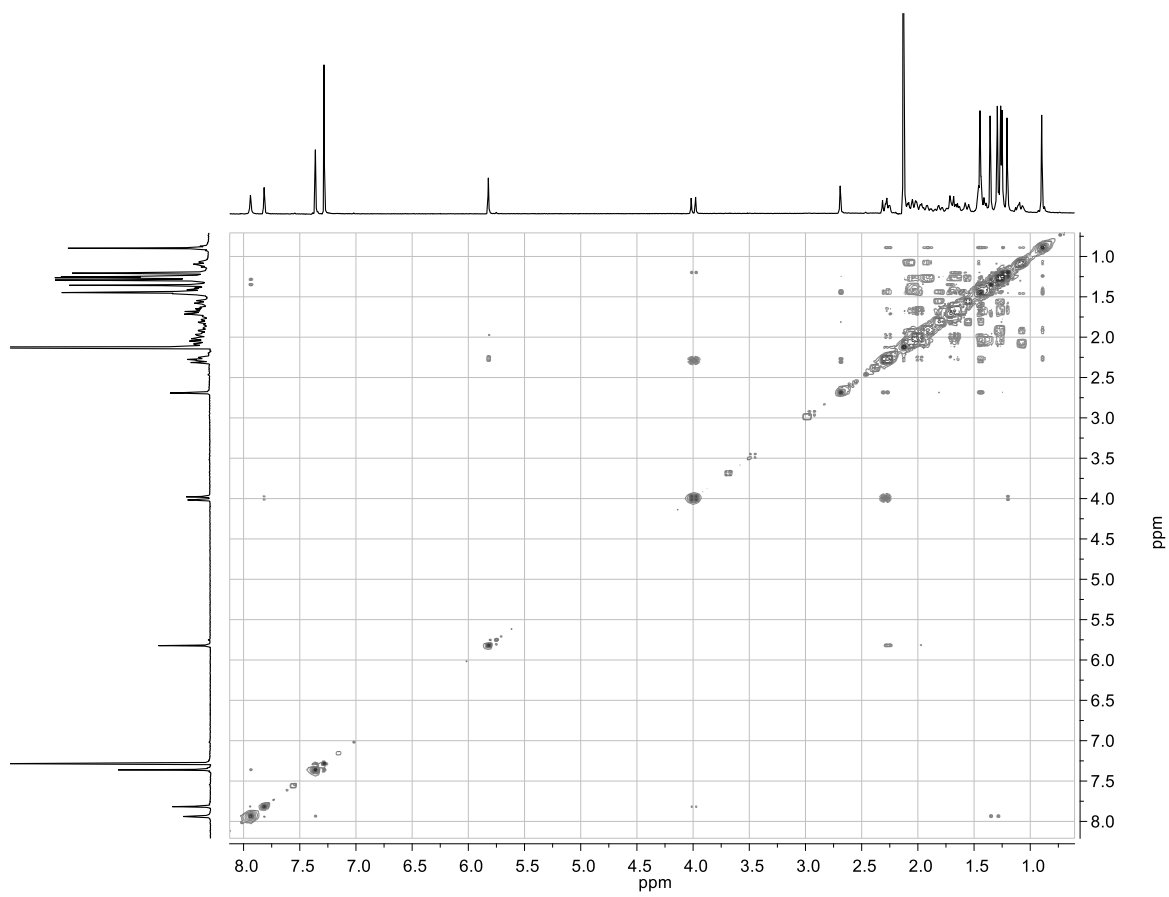


Figure S19. NOESY spectrum of compound **4f** in CDCl₃

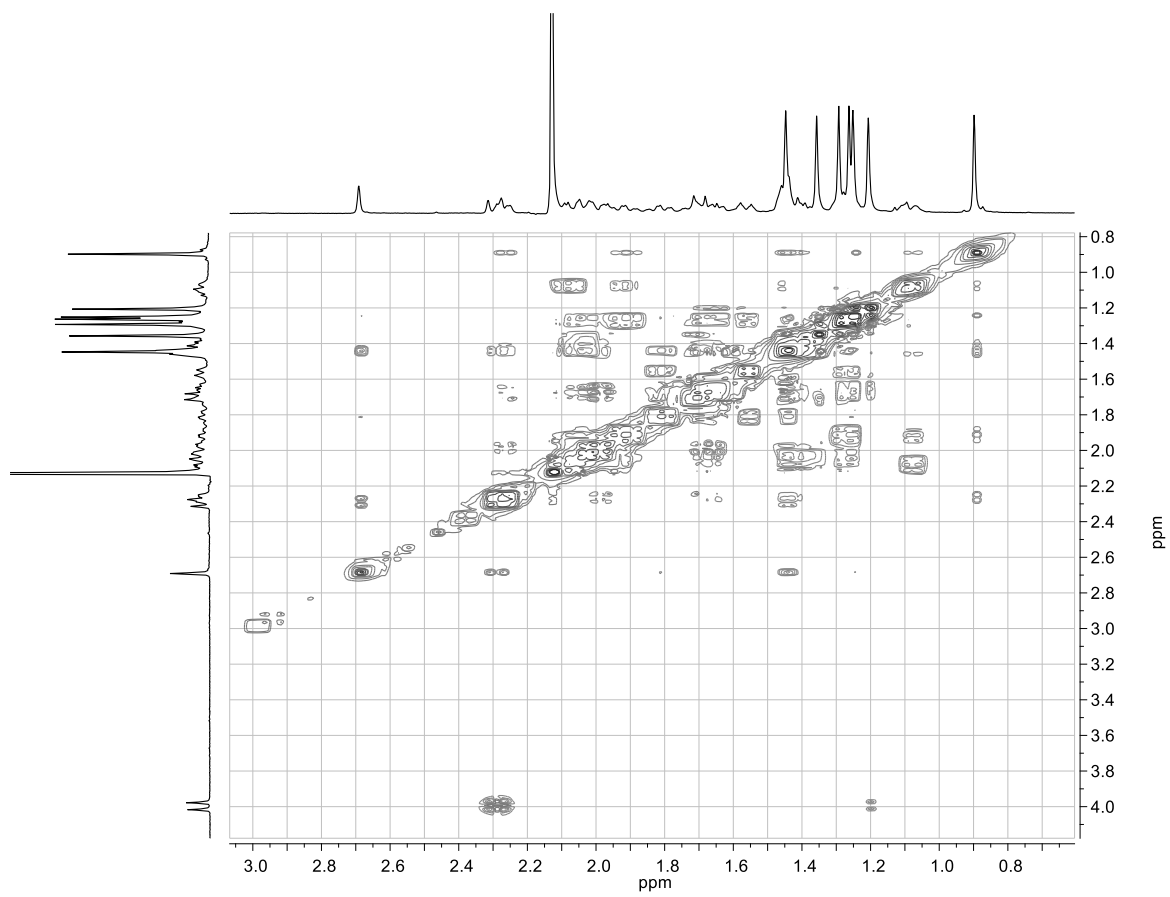


Figure S20. NOESY spectrum (0 – 3.0 ppm) of compound **4f** in CDCl₃

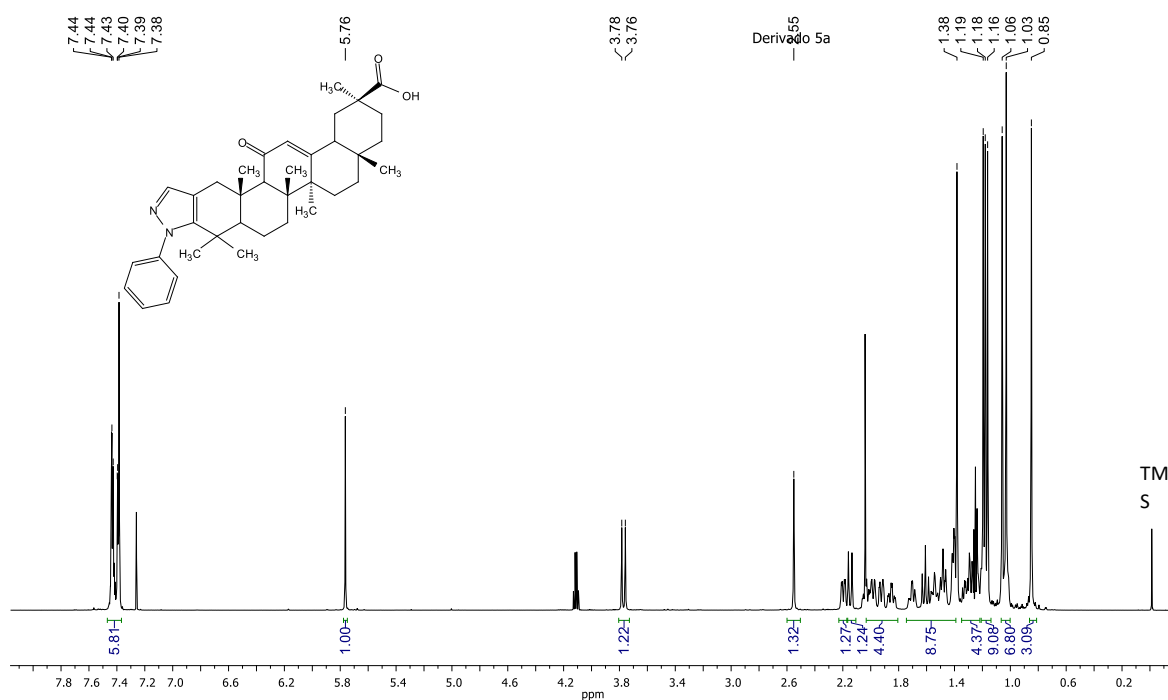


Figure S21. ^1H NMR (600 MHz) spectrum of compound 5a in CDCl_3

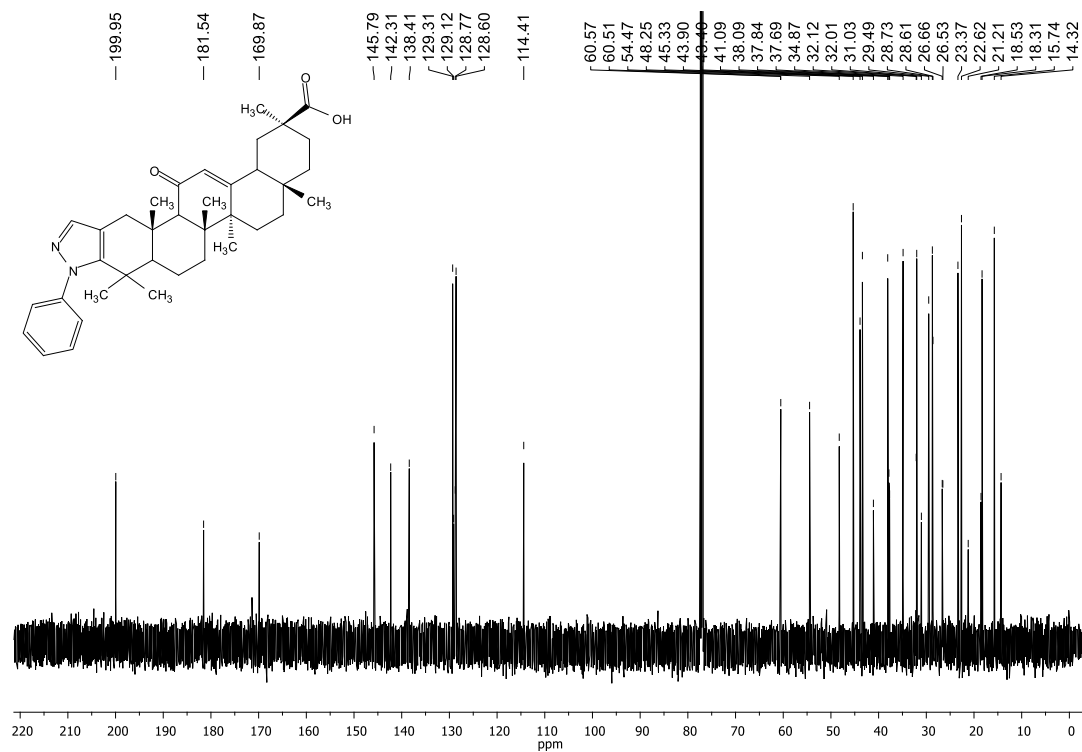


Figure S22. ^{13}C NMR (151 MHz) spectrum of compound 5a in CDCl_3

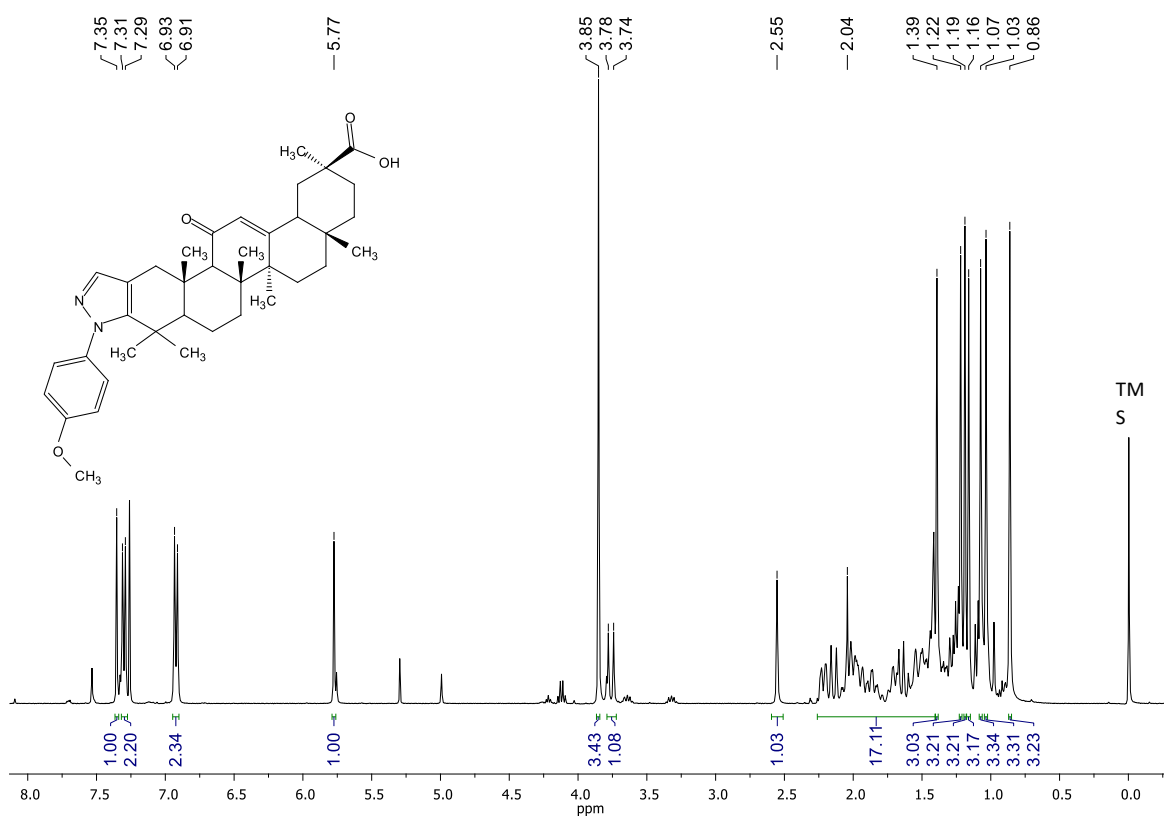


Figure S23. ¹H NMR (400 MHz) spectrum of compound **5b** in CDCl₃

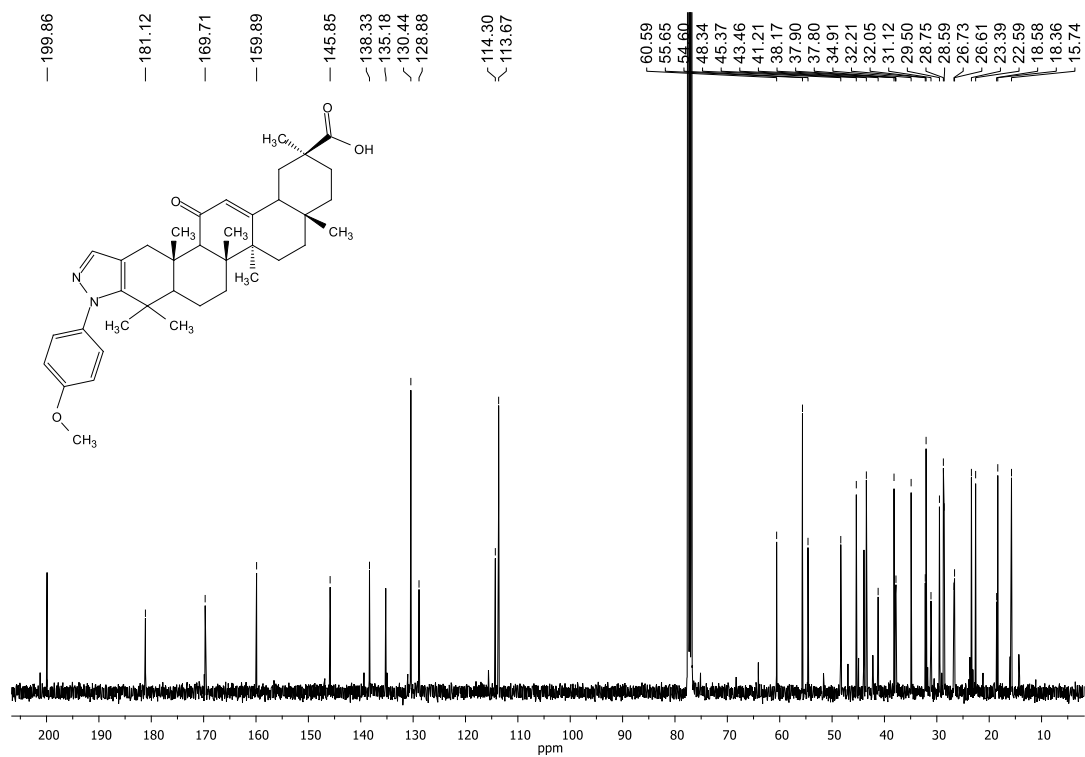


Figure S24. ¹³C NMR (151 MHz) spectrum of compound **5b** in CDCl₃

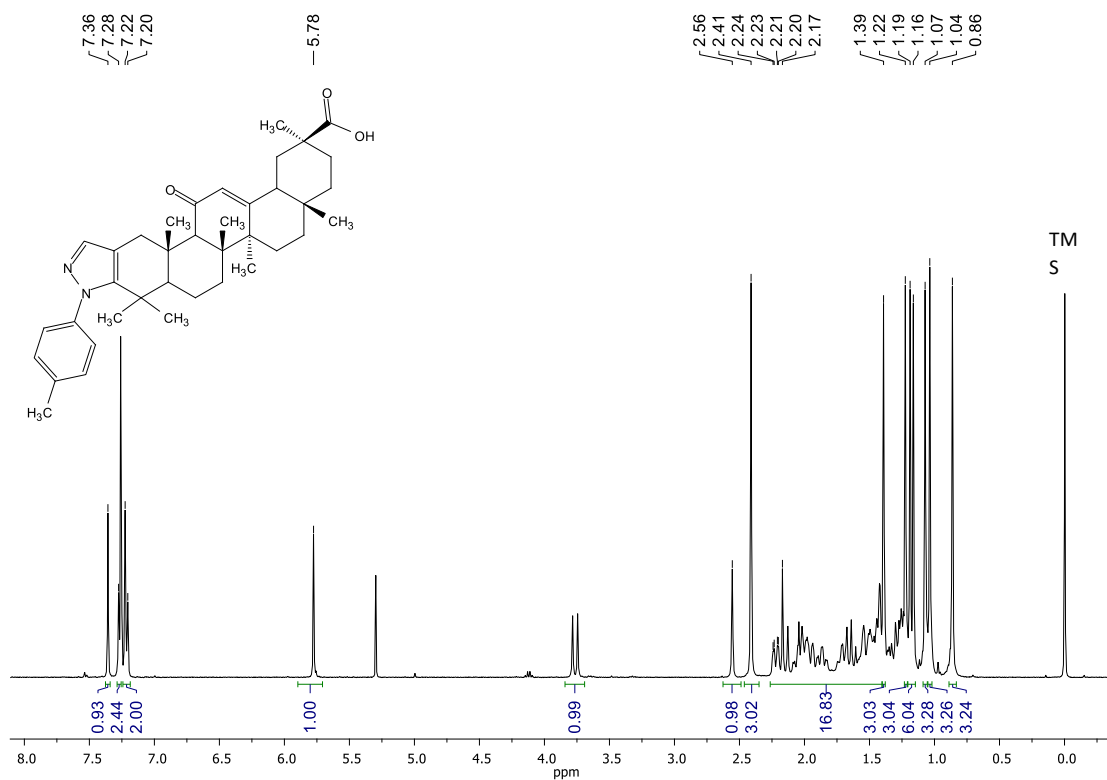


Figure S25. ¹H NMR (400 MHz) spectrum of compound **5c** in CDCl₃

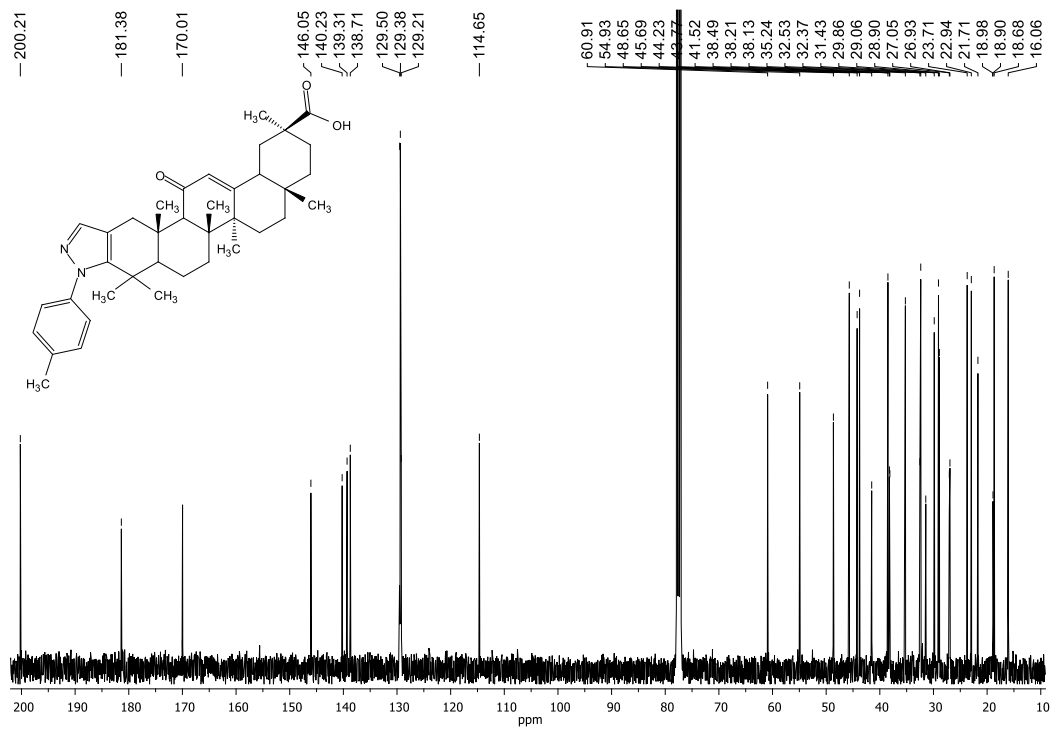


Figure S26. ¹³C NMR (151 MHz) spectrum of compound **5c** in CDCl₃

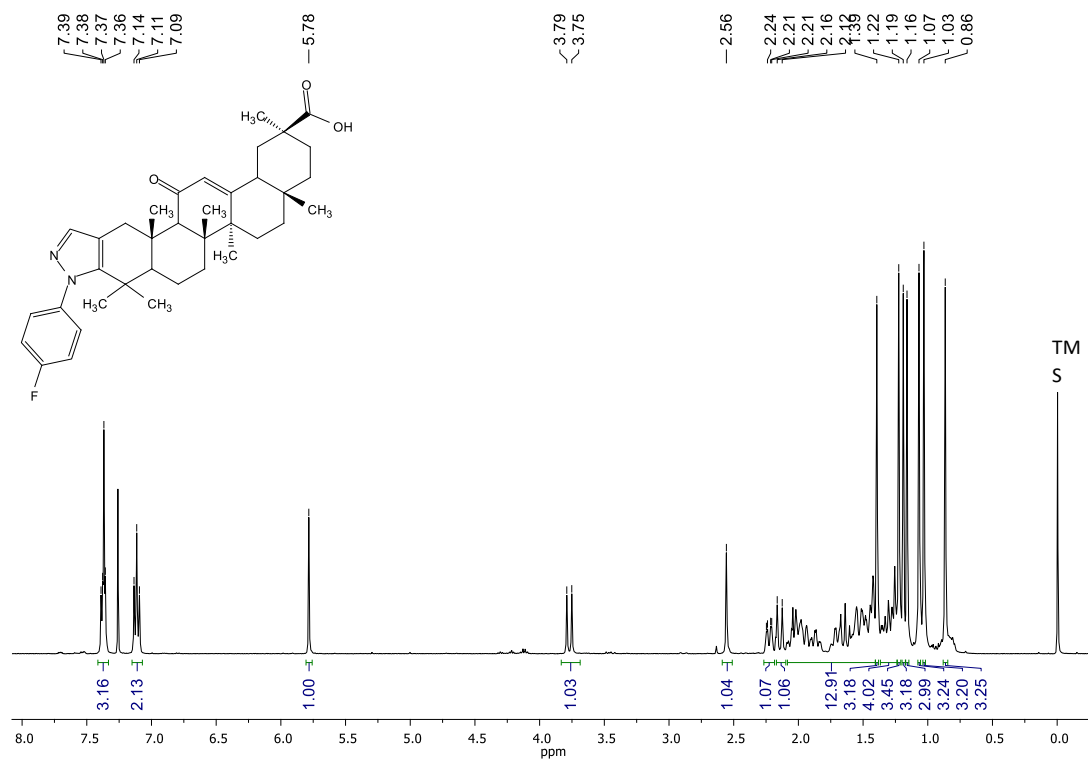


Figure S27. ^1H NMR (400 MHz) spectrum of compound **5d** in CDCl_3

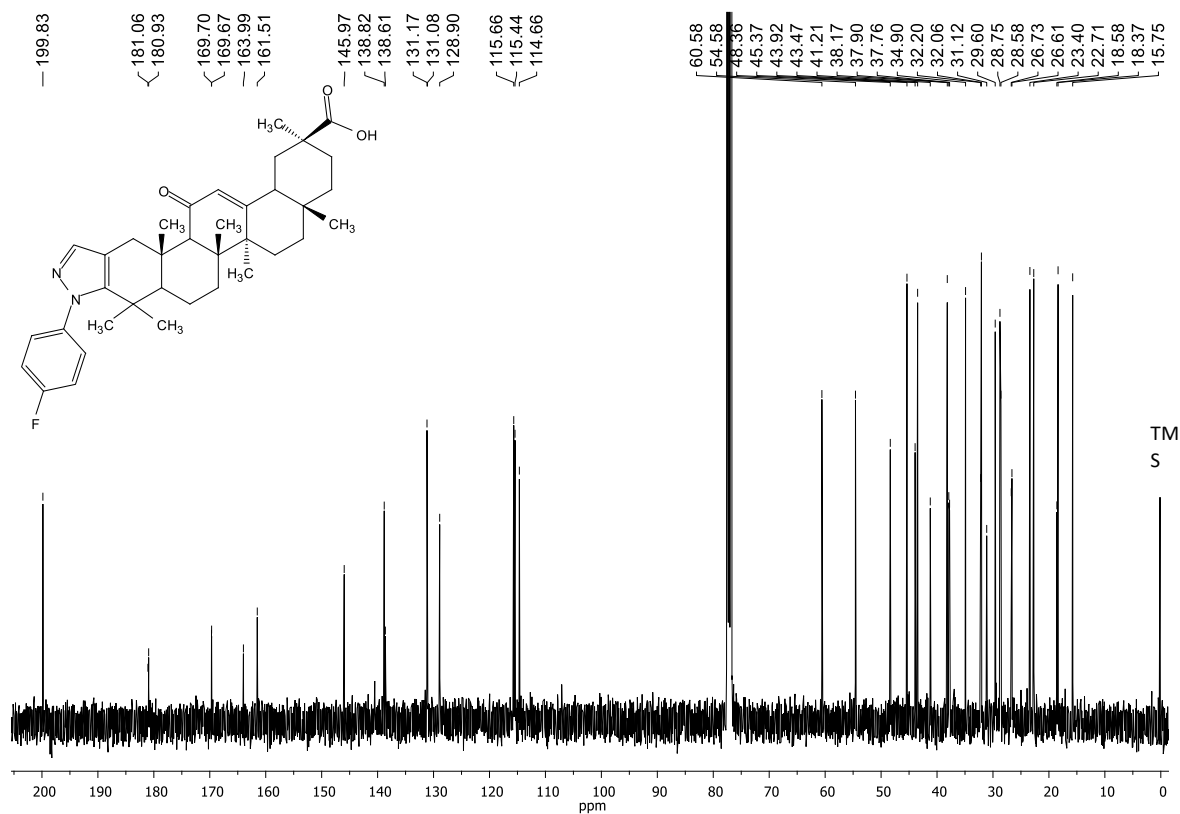


Figure S28. ^{13}C NMR (151 MHz) spectrum of compound **5d** in CDCl_3

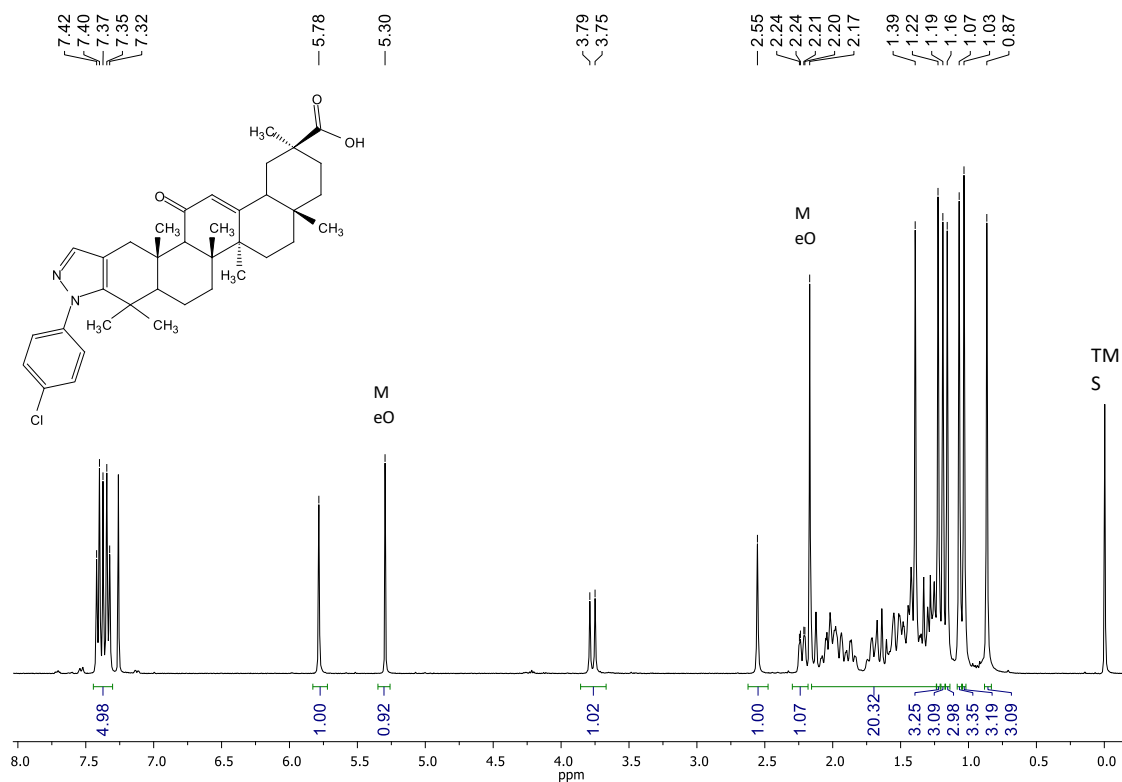


Figure S29. ¹H NMR (400 MHz) spectrum of compound **5f** in CDCl₃

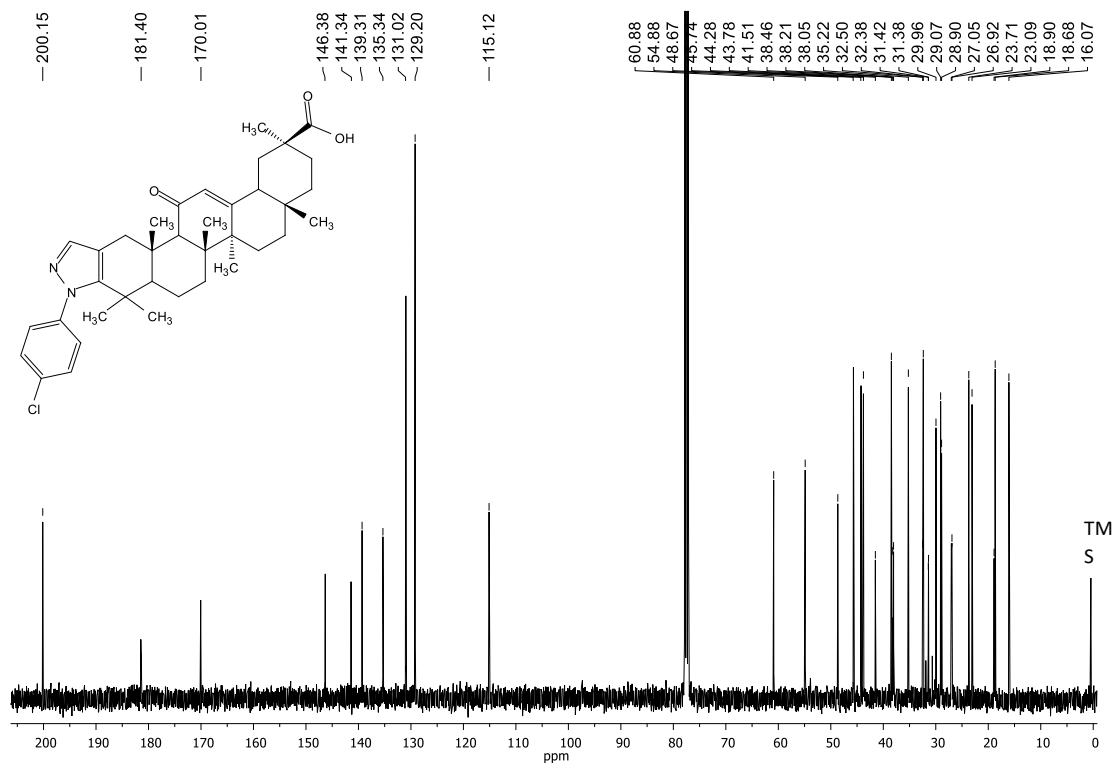


Figure S30. ¹³C NMR (151 MHz) spectrum of compound **5f** in CDCl₃

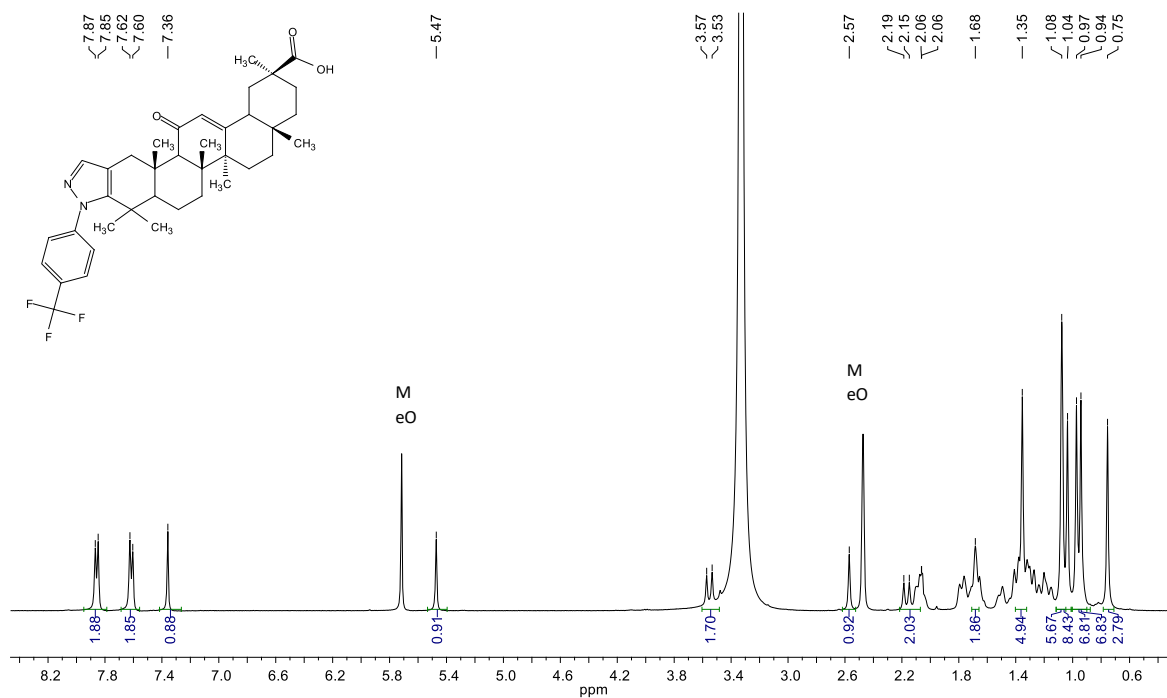


Figure S31. ¹H NMR (400 MHz) spectrum of compound **5f** in DMSO-d₆

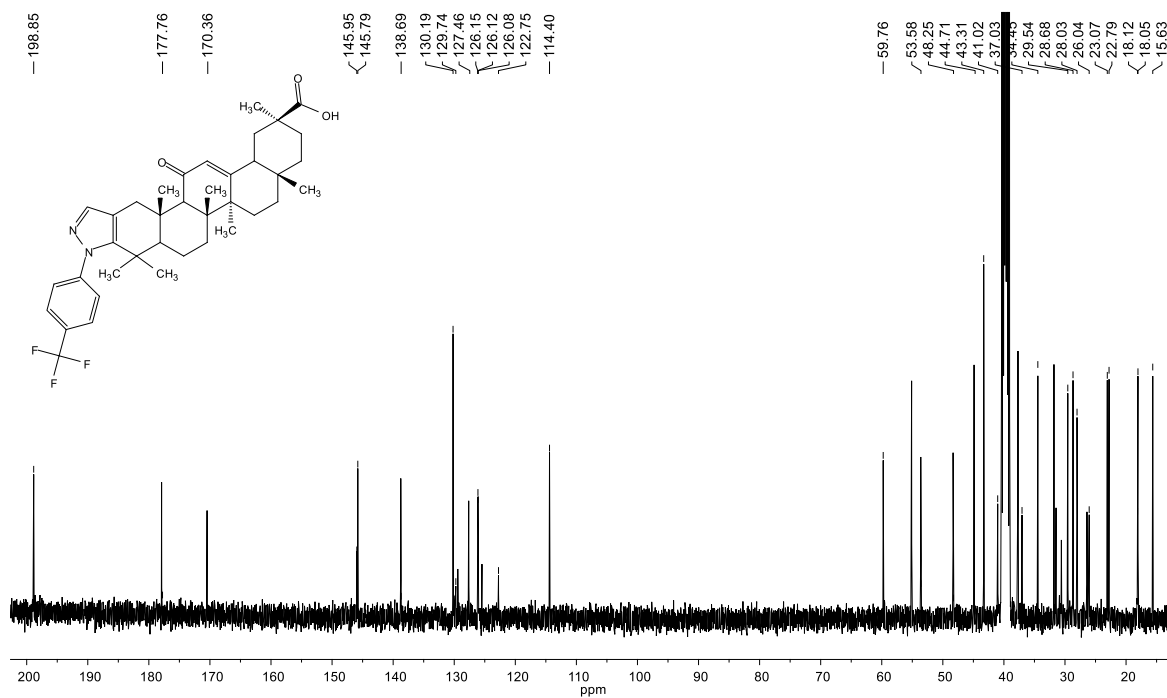


Figure S32. ¹³C NMR (151 MHz) spectrum of compound **5f** in DMSO-d₆

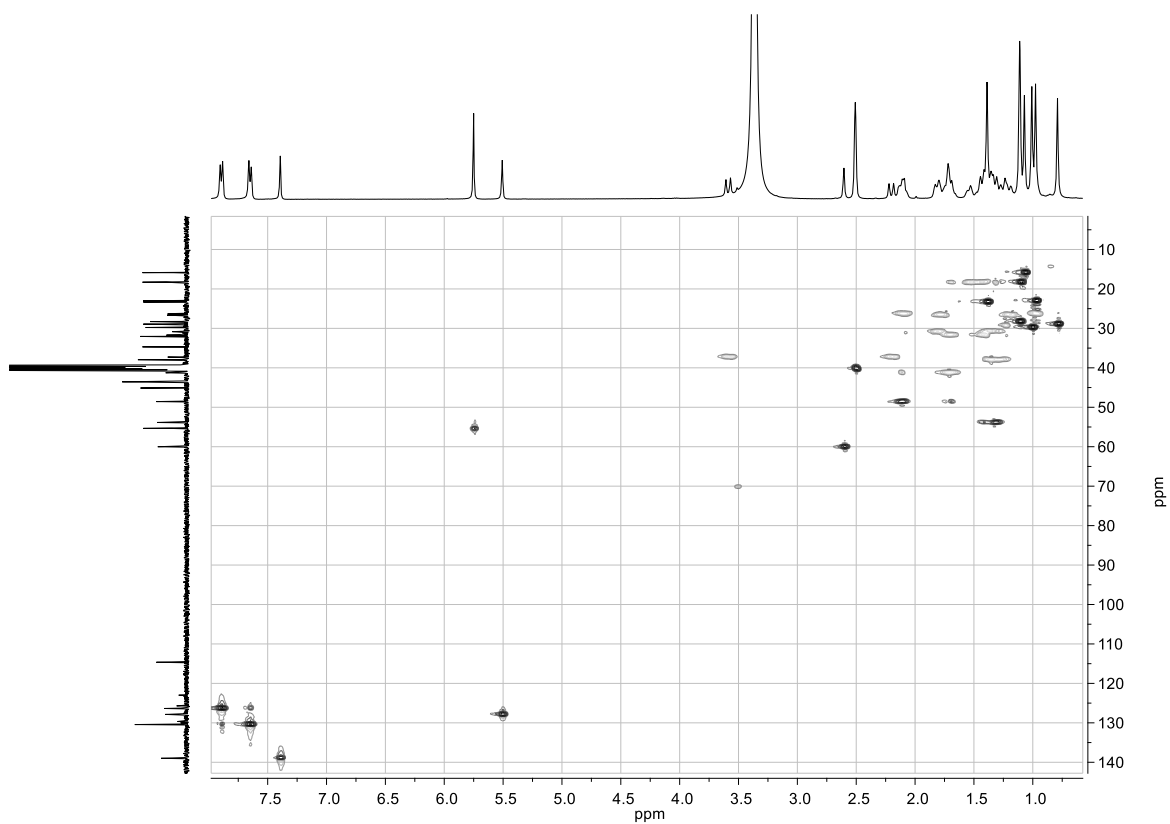


Figure S33. HSQC spectrum of compound **5f** in DMSO-d₆

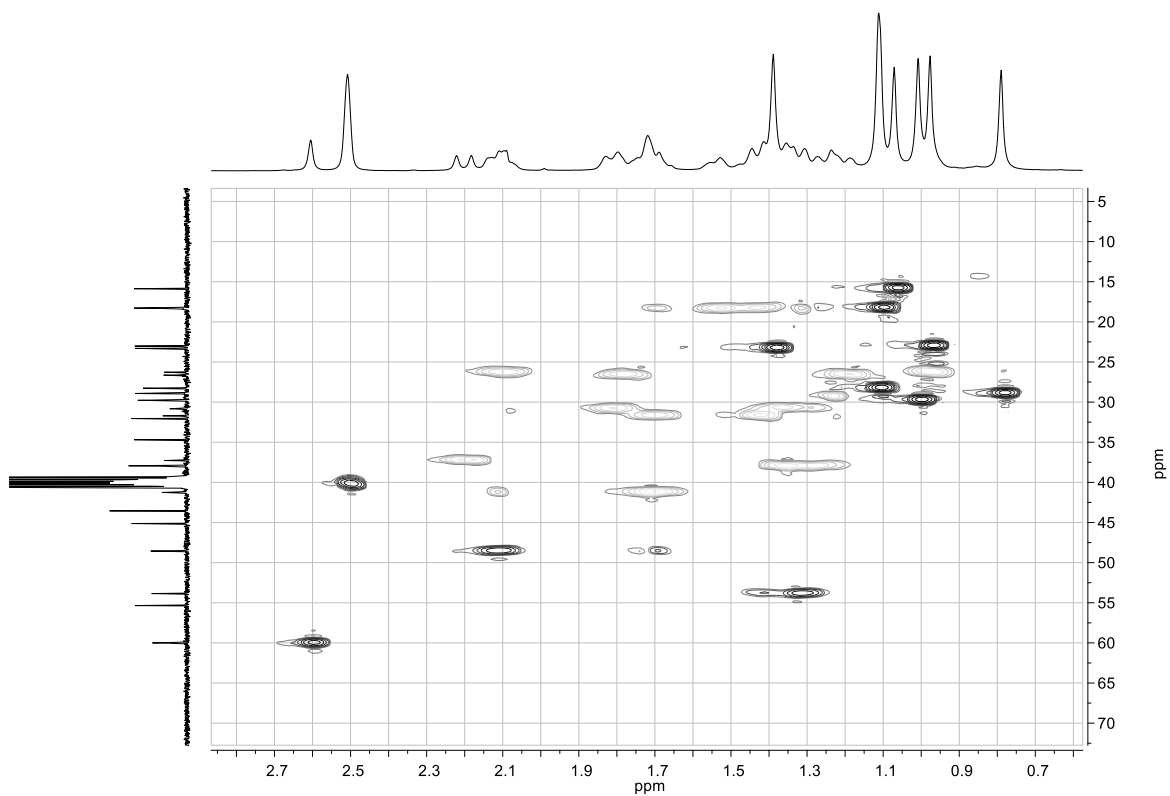


Figure S34. HSQC spectrum (0 – 2.7 ppm) of compound 5f in DMSO-d₆

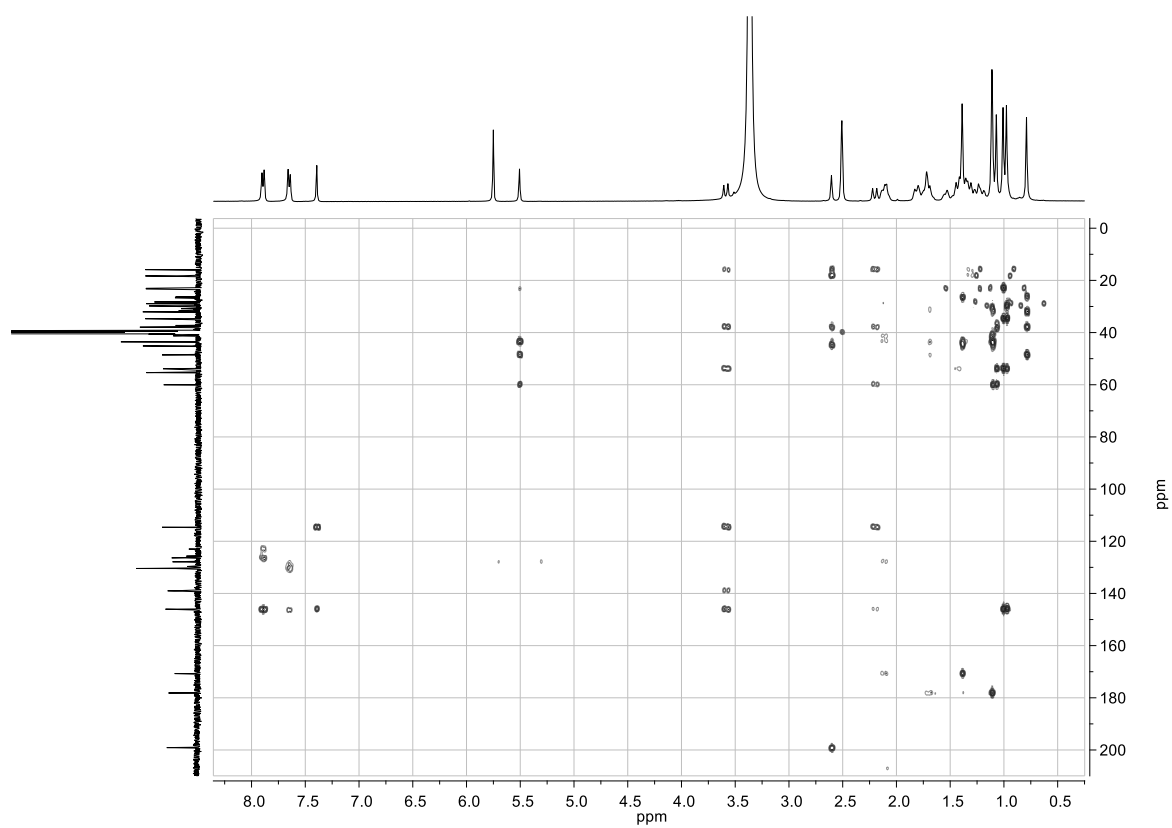


Figure S35. HMBC spectrum of compound **5f** in DMSO-d₆

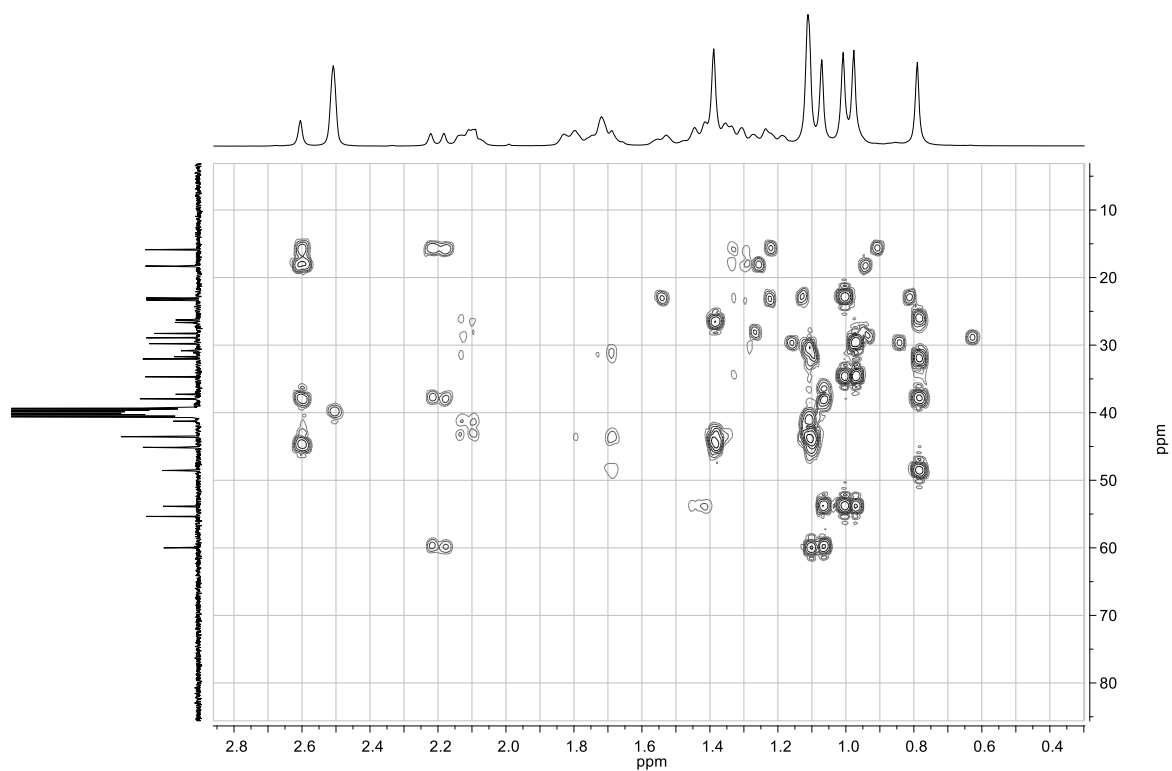


Figure S36. HMBC spectrum (0 – 2.8 ppm) of compound **5f** in DMSO-d₆

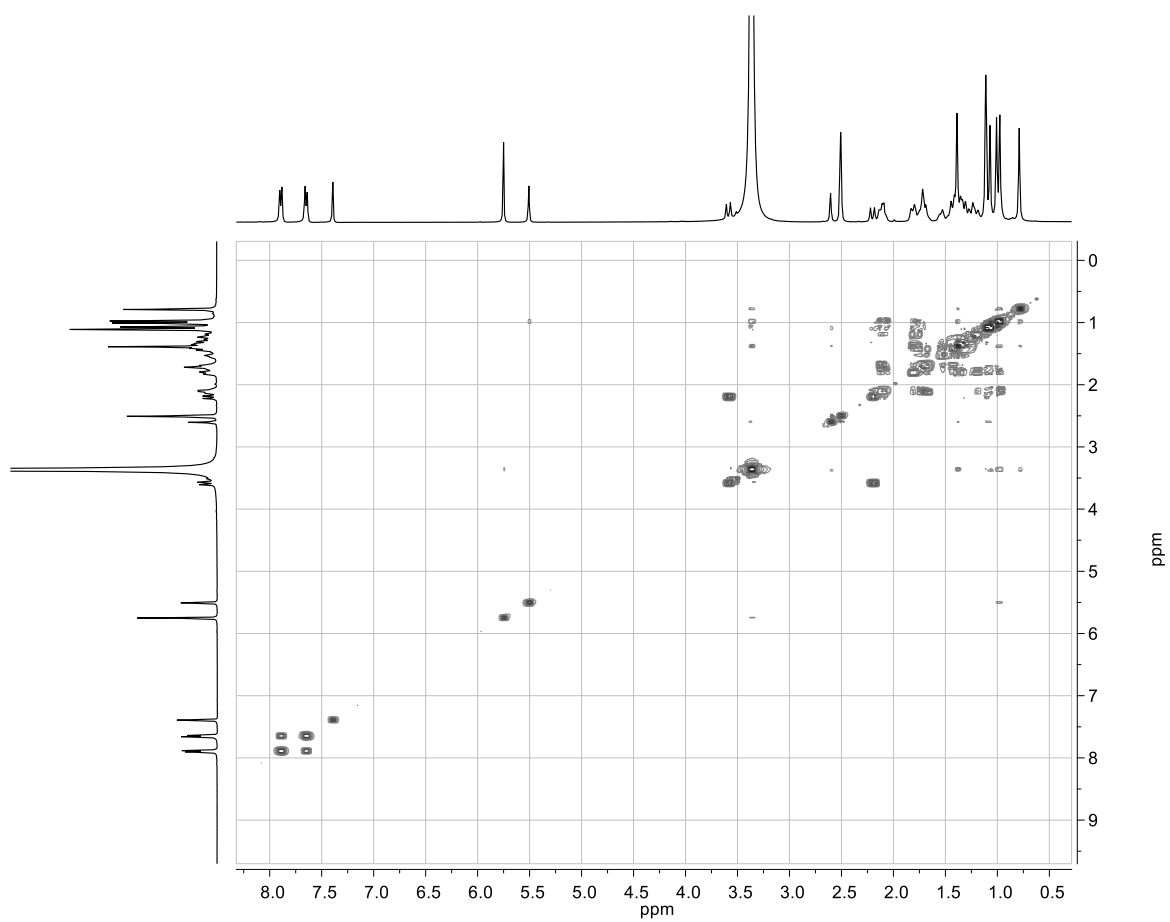


Figure S37. COSY spectrum of compound **5f** in DMSO-d₆

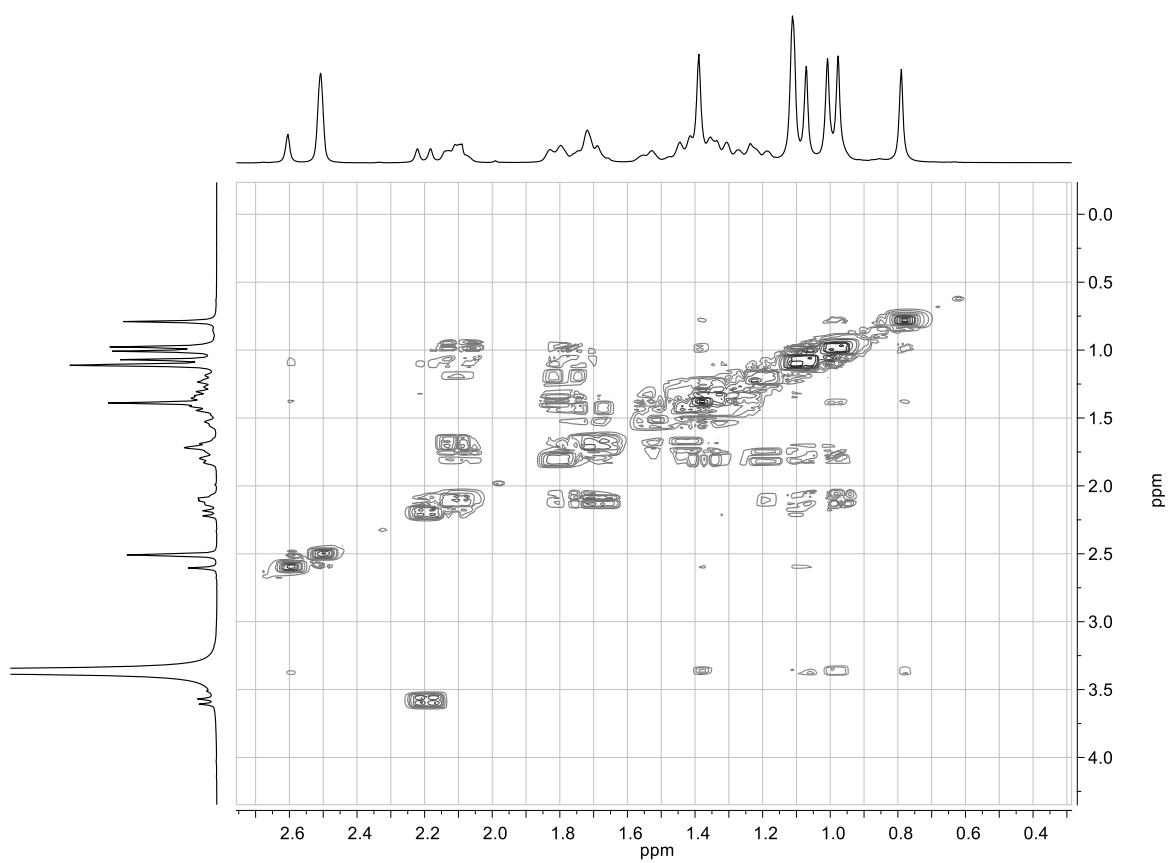


Figure S38. COSY spectrum (0 – 3.0 ppm) of compound **5f** in DMSO-d₆

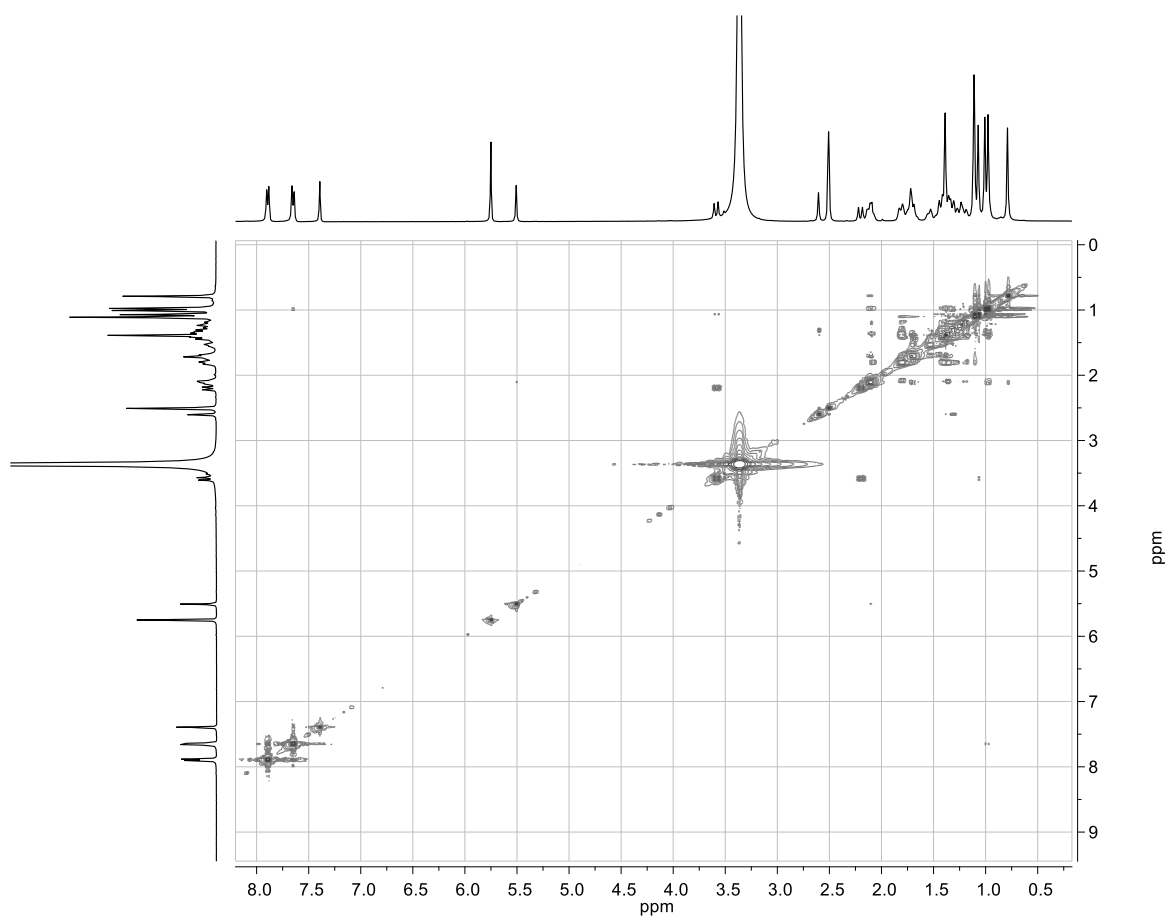


Figure S39. NOESY spectrum of compound **5f** in DMSO-d₆

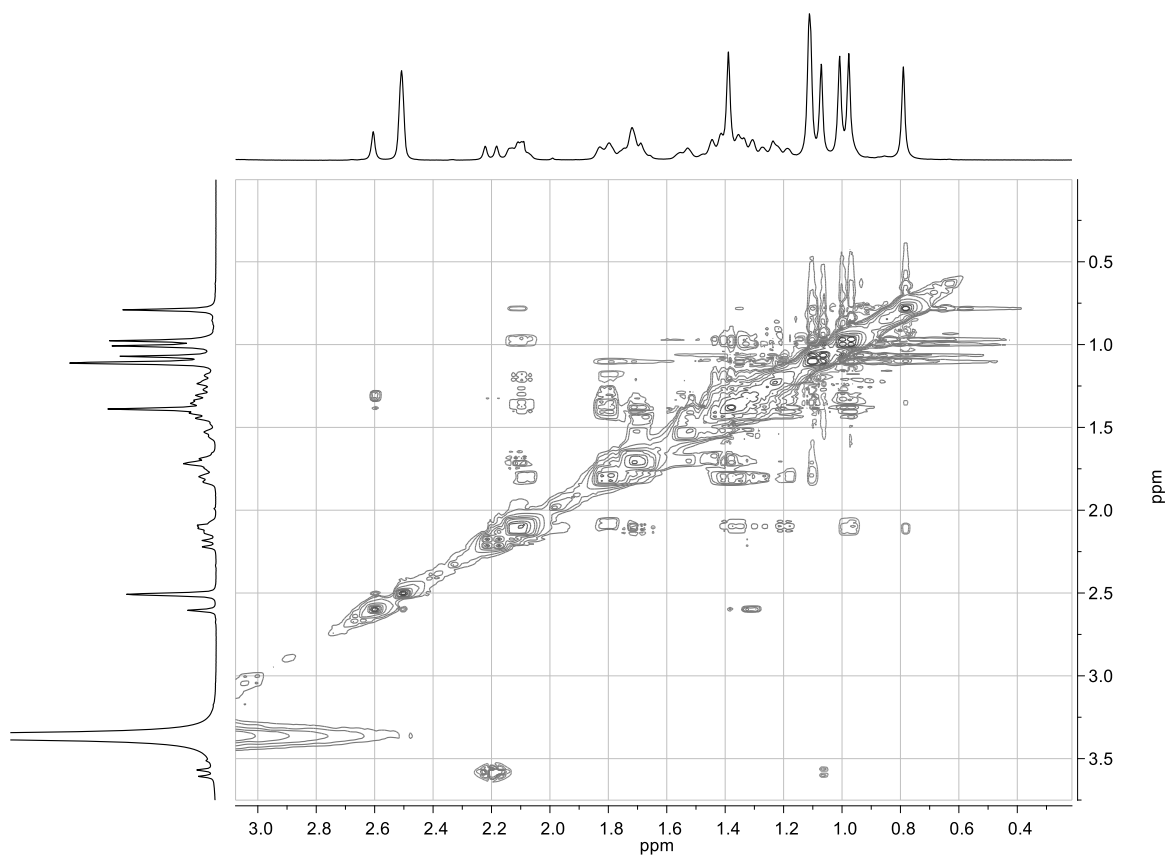


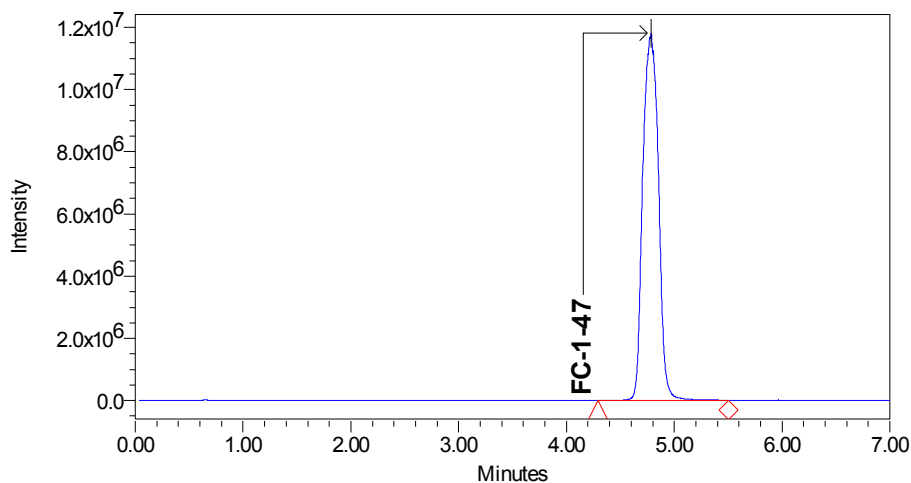
Figure S40. NOESY spectrum (0 – 3.0 ppm) of compound **5f** in DMSO-d₆

For the synthesis of indole-GA series, it is important to mention that we did not use *meta*-phenylhydrazines because we will obtain isomeric mixtures of these compounds which are difficult to purify.

SAMPLE INFORMATION

Sample Name:	FC-1-47	Acquired By:	
Sample Type:	Unknown	Sample Set Name	001 Prueba 17 FC 1 47 dil
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Injection #:	1	Injection Volume:	10.00 ul
Run Time:	7.0 Minutes	Date Acquired:	6/2/2021 11:41:27 AM CDT
Column Name:	ACQUITY UPLC HSS T3 1.8um 3.0 x 100 mm		

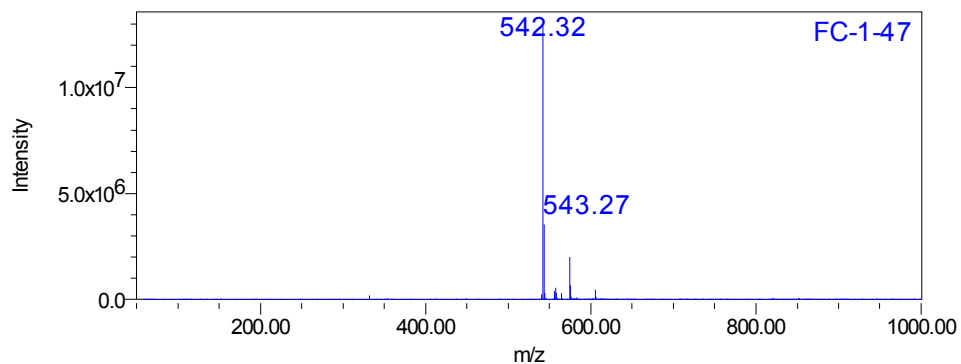
Auto-Scaled Chromatogram



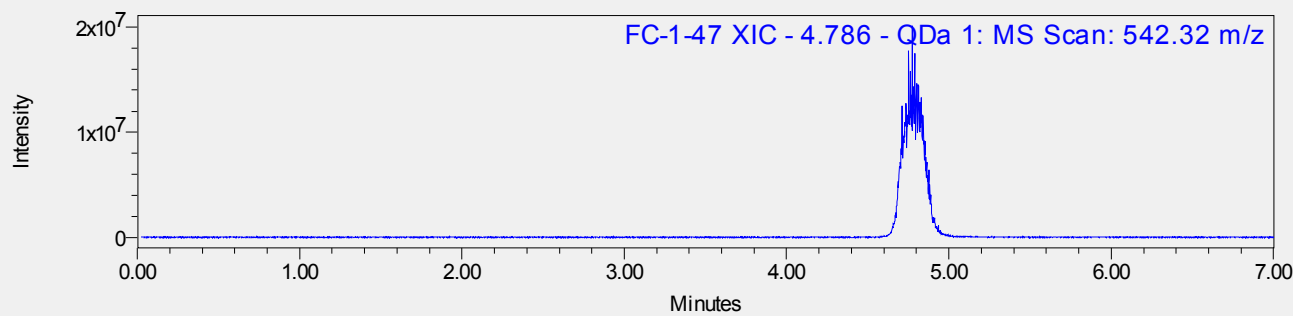
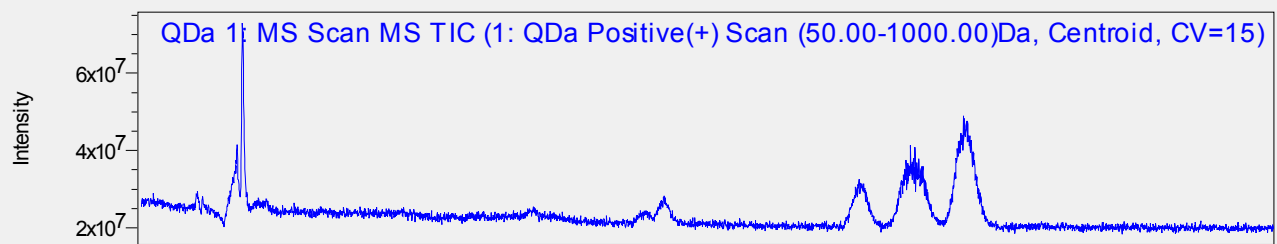
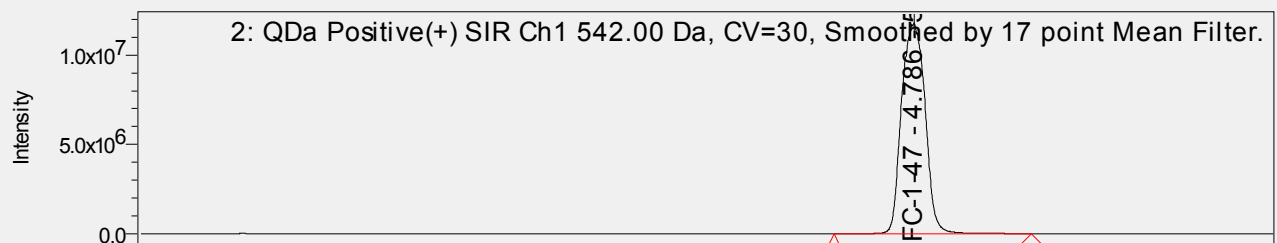
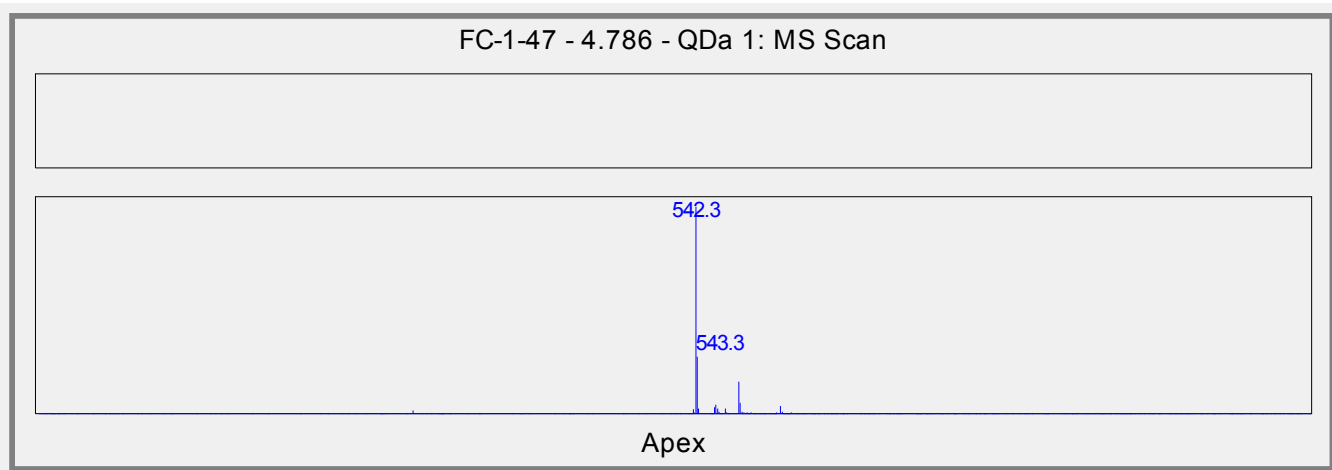
Peak Results

	Name	RT	Area	Height	MS 3D Channel Name
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Match Plot



UPLC-ESI-MS data of compound 4a

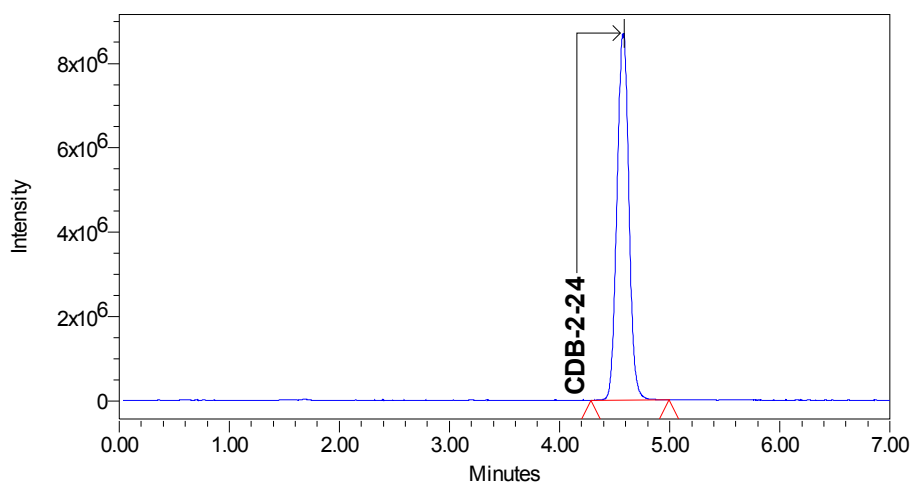


UPLC-ESI-MS data of compound 4a

SAMPLE INFORMATION

Sample Name:	CDB-2-24	Acquired By:	
Sample Type:	Unknown	Sample Set Name	001 Prueba 2 CDB 2 24 Dil
Vial:	2:B,3	Acq. Method Set:	ID 002 QPDA
Injection #:	1	Injection Volume:	10.00 ul
Run Time:	7.0 Minutes	Date Acquired:	6/2/2021 2:33:20 PM CDT
Column Name:	ACQUITY UPLC HSS T3 1.8um 3.0 x 100 mm		

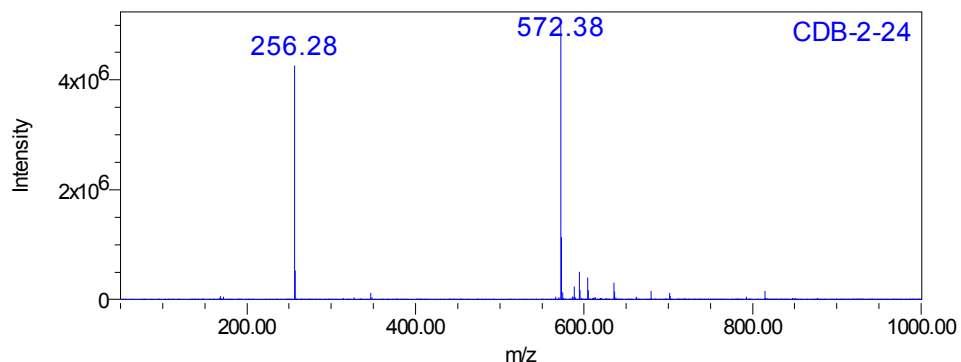
Auto-Scaled Chromatogram



Peak Results

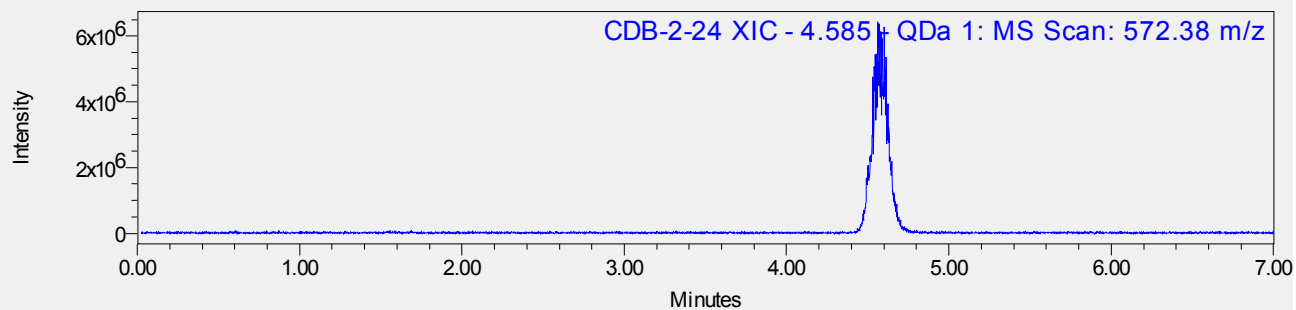
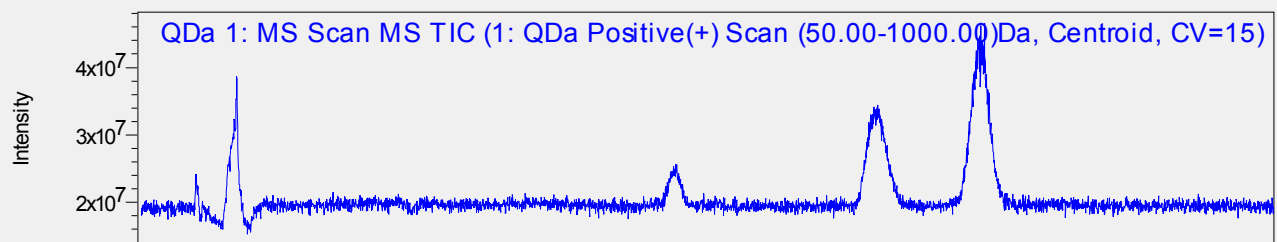
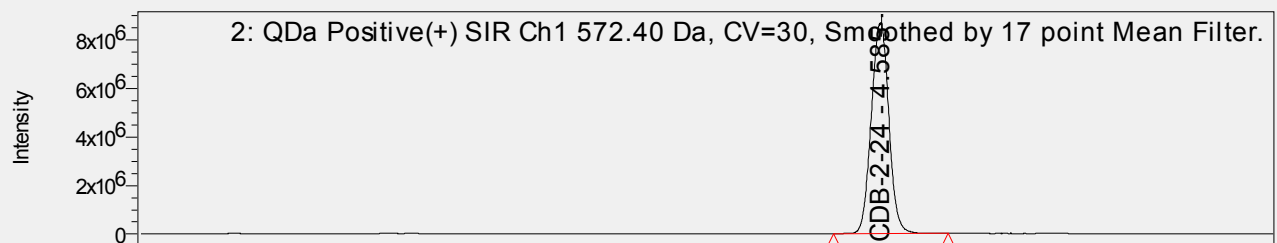
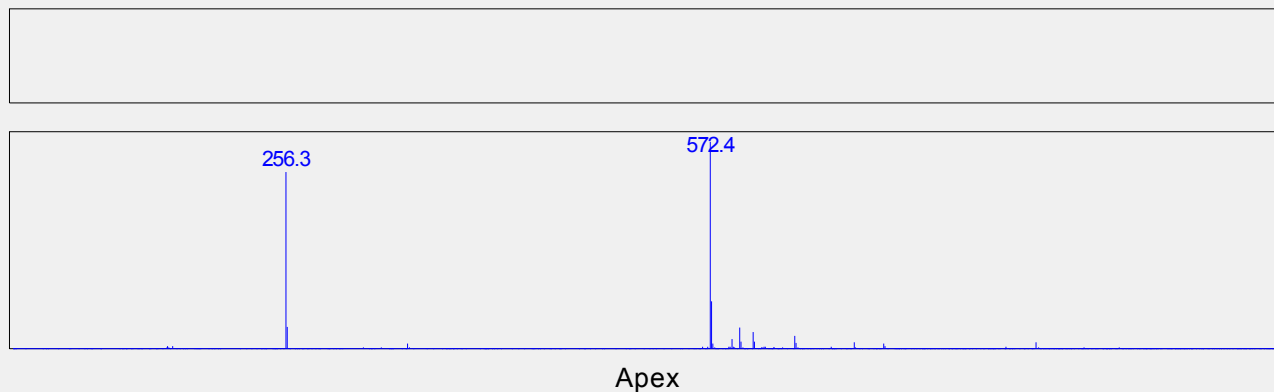
	Name	RT	Area	Height	MS 3D Channel Name
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Match Plot



UPLC-ESI-MS data of compound 4b

CDB-2-24 - 4.585 - QDa 1: MS Scan

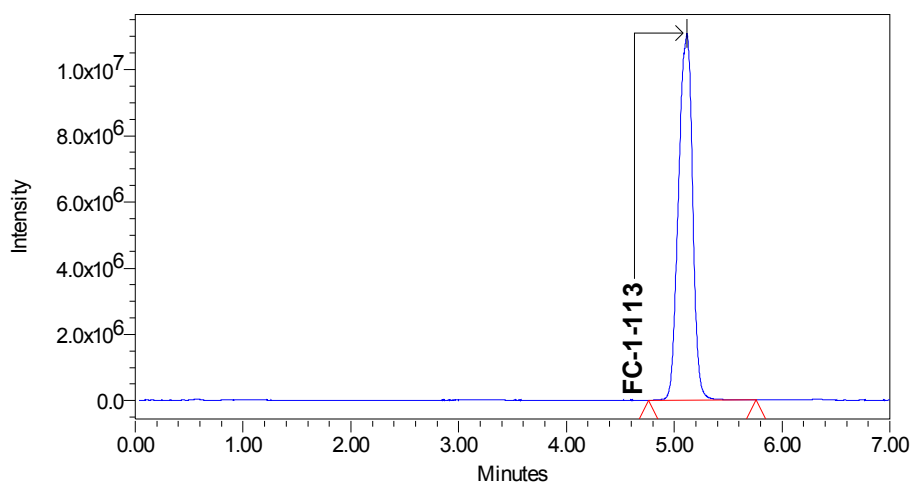


UPLC-ESI-MS data of compound 4b

SAMPLE INFORMATION

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Sample Type:	Unknown	Sample Set Name	001 Prueba 2 FC 1 113 Dil
Vial:	2:C,2	Acq. Method Set:	ID 004 QPDA
Injection #:	1	Injection Volume:	10.00 ul
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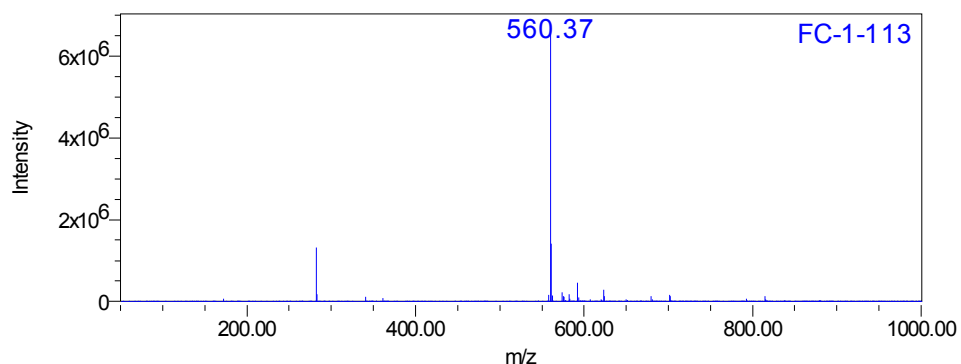
Auto-Scaled Chromatogram



Peak Results

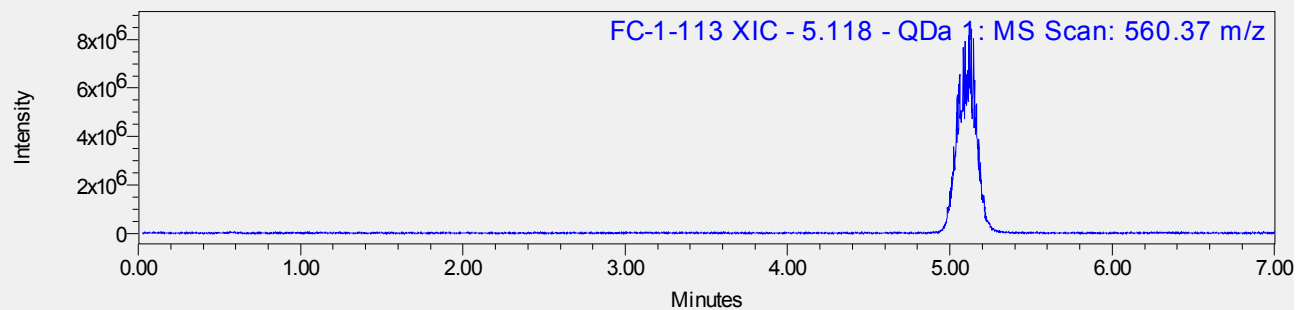
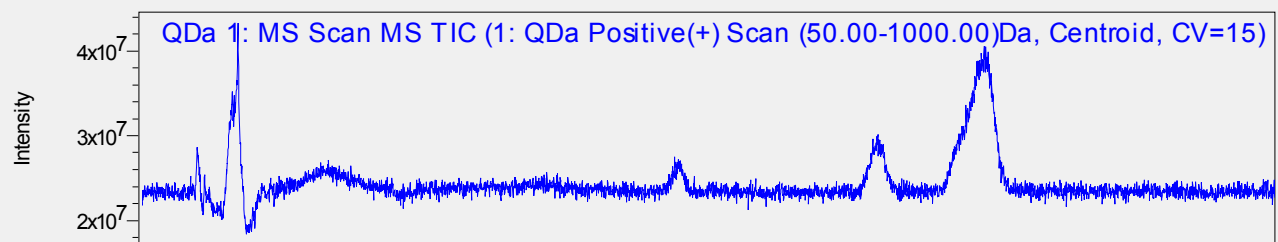
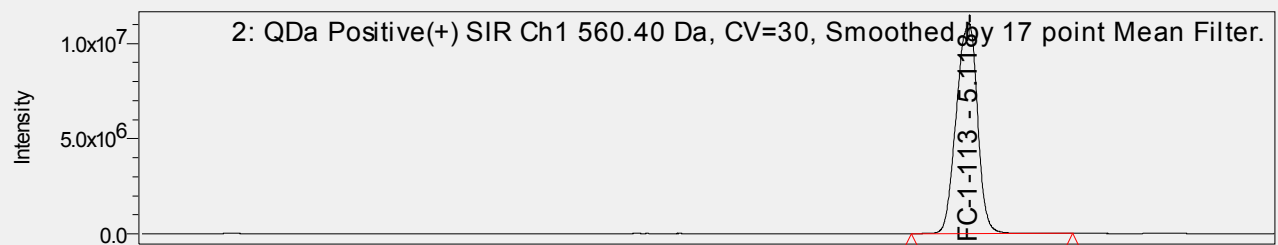
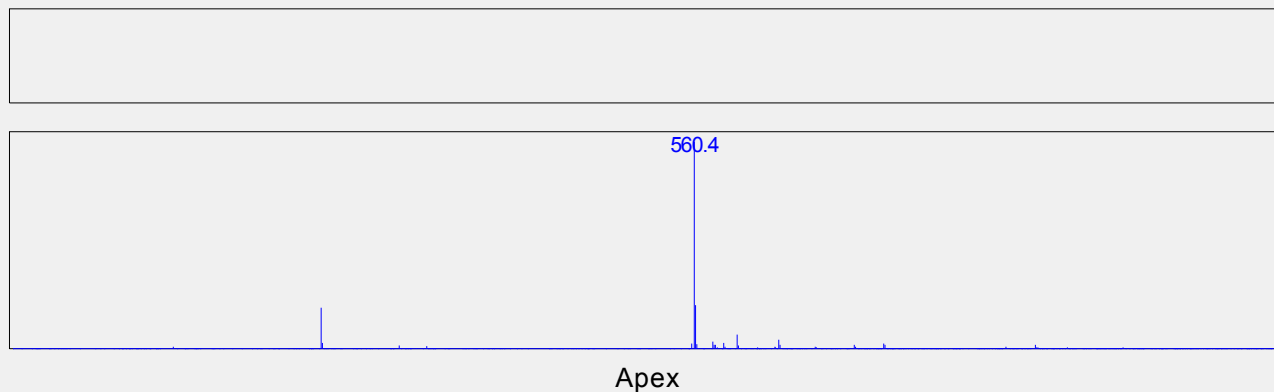
	Name	RT	Area	Height	MS 3D Channel Name
1	FC-1-113	5.118	100670643	11069832	QDa 1: MS Scan

Match Plot



UPLC-ESI-MS data of compound 4c

FC-1-113 - 5.118 - QDa 1: MS Scan

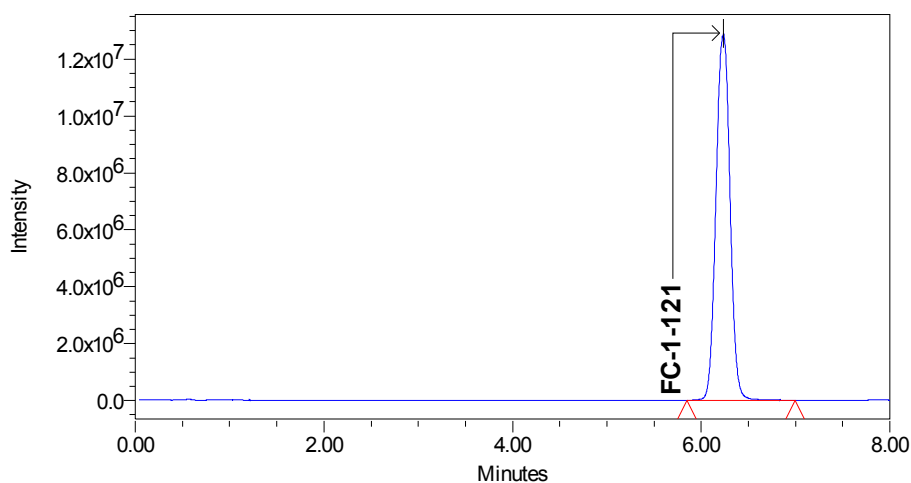


UPLC-ESI-MS data of compound 4c

SAMPLE INFORMATION

Sample Name:	FC-1-121	Acquired By:	
Sample Type:	Unknown	Sample Set Name	001 Prueba 2 FC 1 121
Vial:	2:E,2	Acq. Method Set:	ID 006 QPDA
Injection #:	1	Injection Volume:	10.00 ul
Run Time:	8.0 Minutes	Date Acquired:	6/4/2021 11:03:52 AM CDT
Column Name:	ACQUITY UPLC HSS T3 1.8um 3.0 x 100 mm		

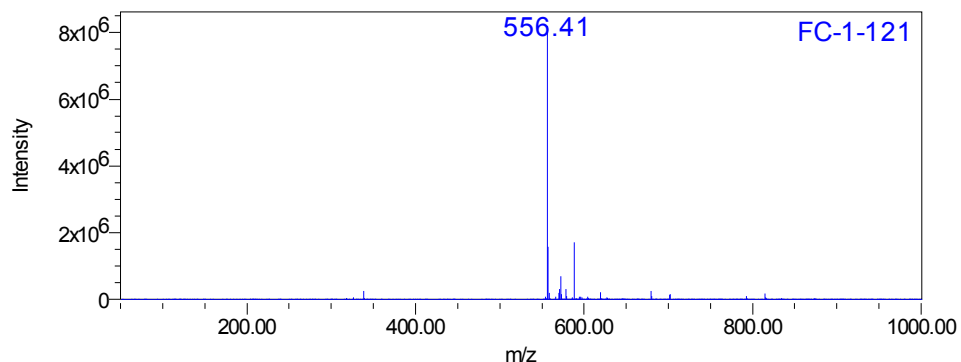
Auto-Scaled Chromatogram



Peak Results

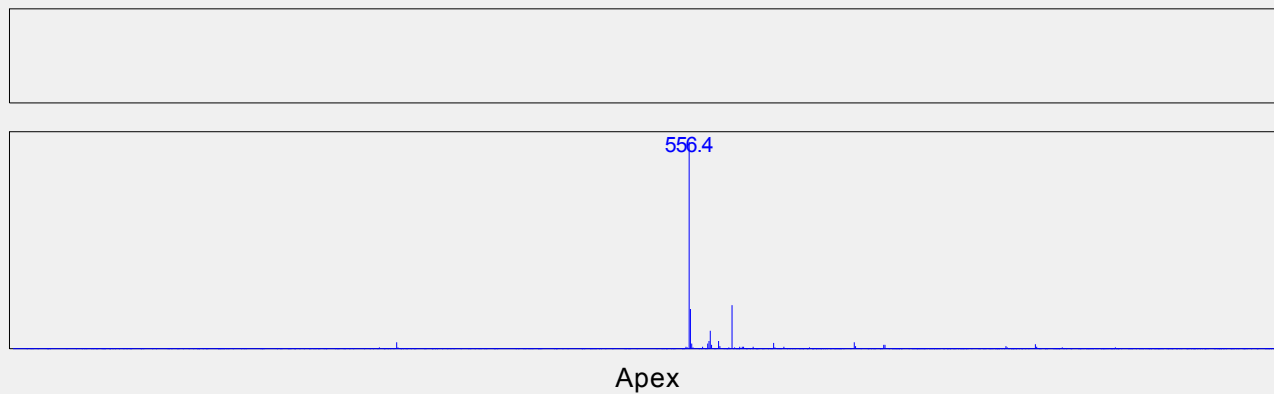
	Name	RT	Area	Height	MS 3D Channel Name
1	FC-1-121	6.235	132861055	12900302	QDa 1: MS Scan

Match Plot

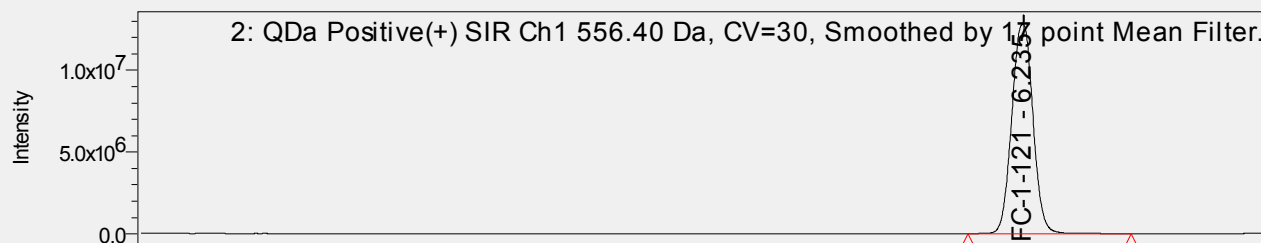


UPLC-ESI-MS data of compound 4d

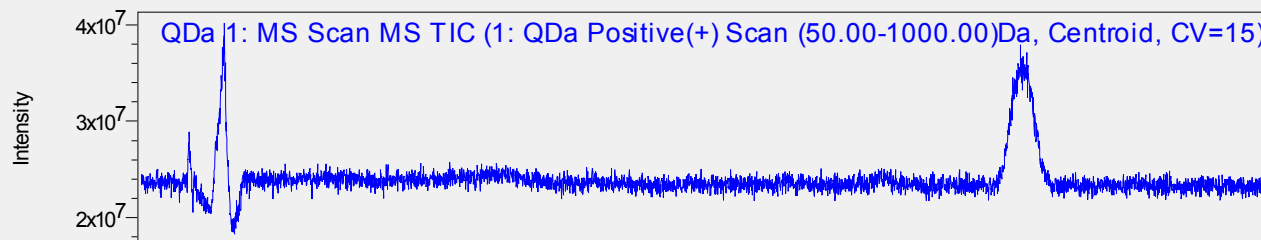
FC-1-121 - 6.235 - QDa 1: MS Scan



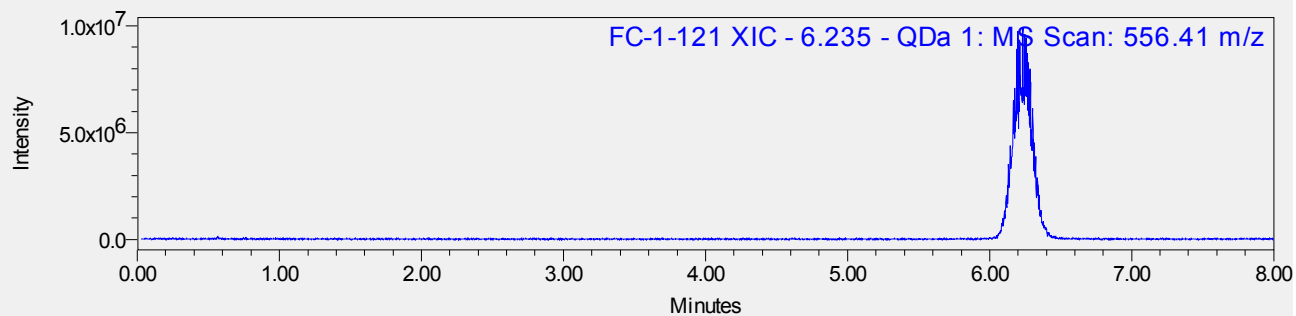
2: QDa Positive(+) SIR Ch1 556.40 Da, CV=30, Smoothed by 17 point Mean Filter.



QDa 1: MS Scan MS TIC (1: QDa Positive(+) Scan (50.00-1000.00)Da, Centroid, CV=15)



FC-1-121 XIC - 6.235 - QDa 1: MS Scan: 556.41 m/z

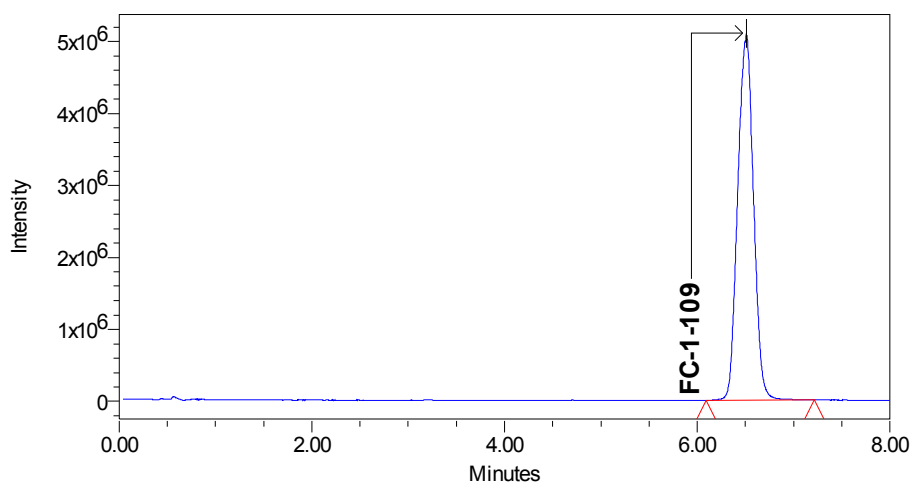


UPLC-ESI-MS data of compound 4d

SAMPLE INFORMATION

Sample Name:	FC-1-109	Acquired By:	
Sample Type:	Unknown	Sample Set Name	001 Prueba 2 FC 1 109 Dil
Vial:	2:D,2	Acq. Method Set:	ID 005 QPDA
Injection #:	1	Injection Volume:	10.00 ul
Run Time:	8.0 Minutes	Date Acquired:	6/4/2021 10:32:00 AM CDT
Column Name:	ACQUITY UPLC HSS T3 1.8um 3.0 x 100 mm		

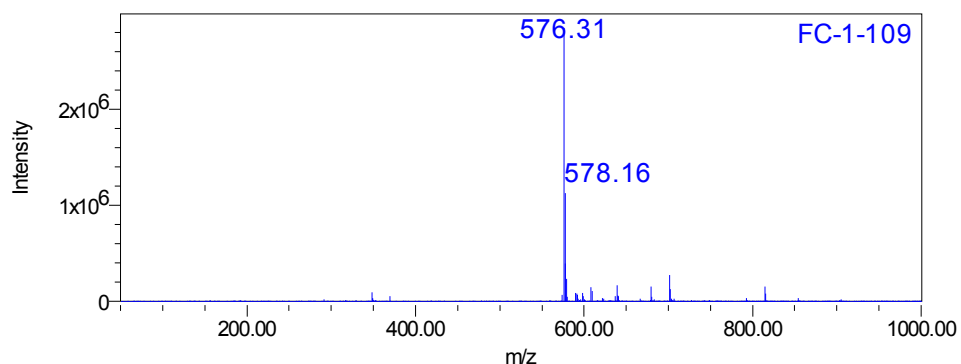
Auto-Scaled Chromatogram



Peak Results

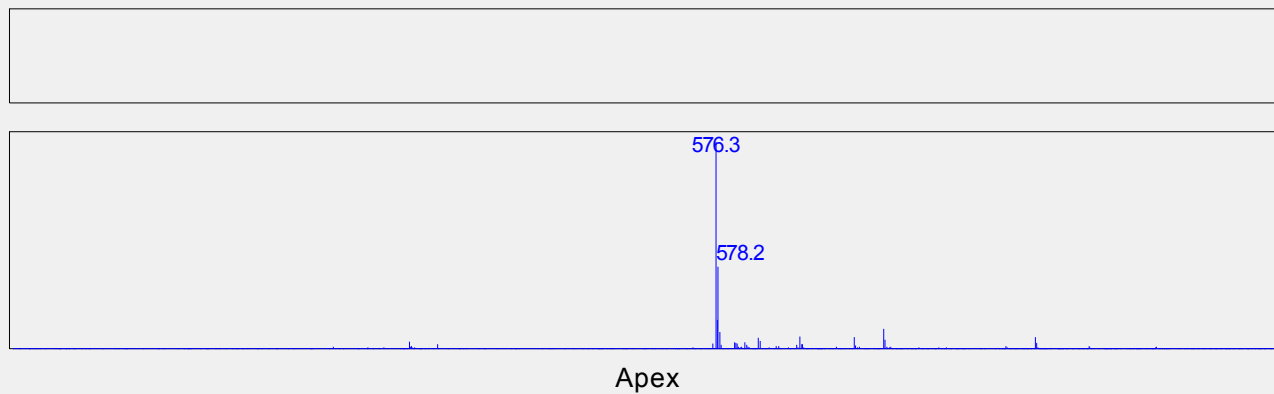
	Name	RT	Area	Height	MS 3D Channel Name
1	FC-1-109	6.510	57968220	5089974	QDa 1: MS Scan

Match Plot

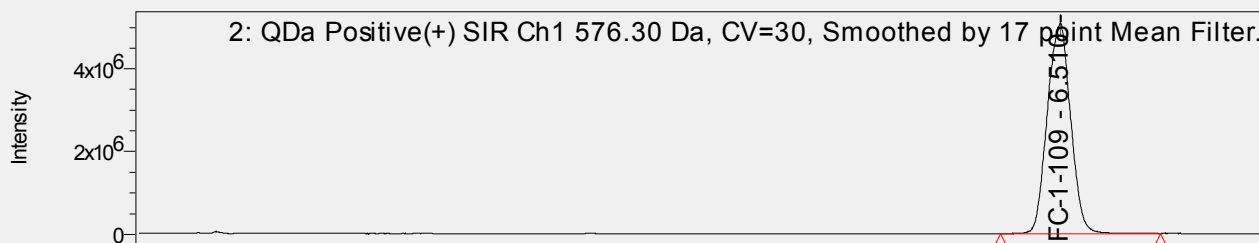


UPLC-ESI-MS data of compound 4e

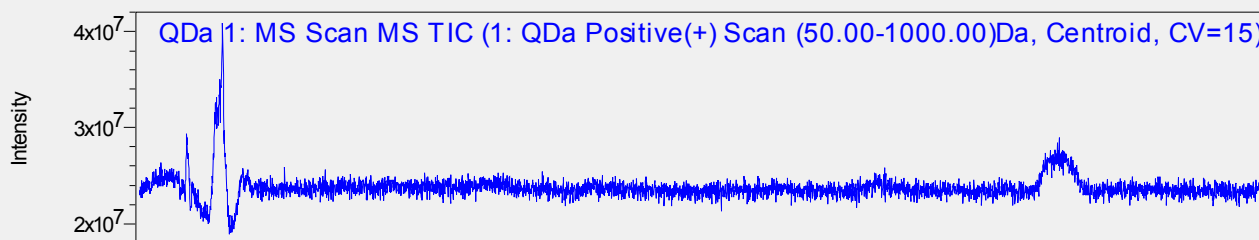
FC-1-109 - 6.510 - QDa 1: MS Scan



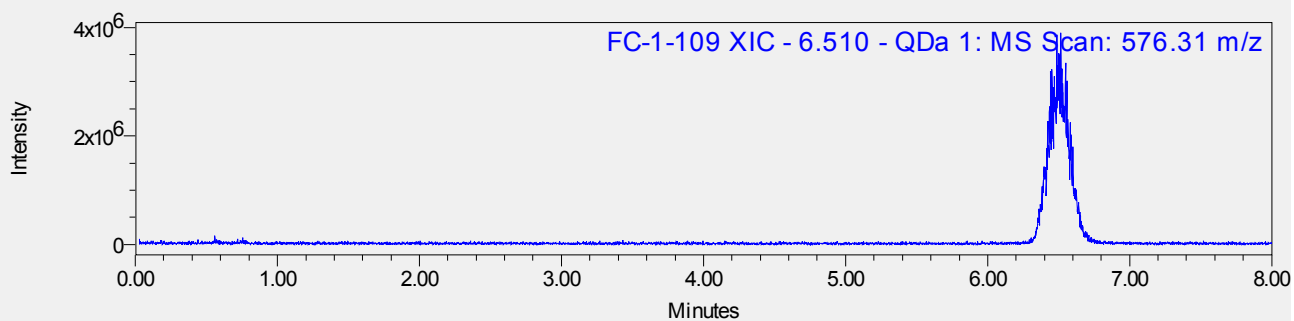
2: QDa Positive(+) SIR Ch1 576.30 Da, CV=30, Smoothed by 17 point Mean Filter.



QDa 1: MS Scan MS TIC (1: QDa Positive(+) Scan (50.00-1000.00)Da, Centroid, CV=15)



FC-1-109 XIC - 6.510 - QDa 1: MS Scan: 576.31 m/z

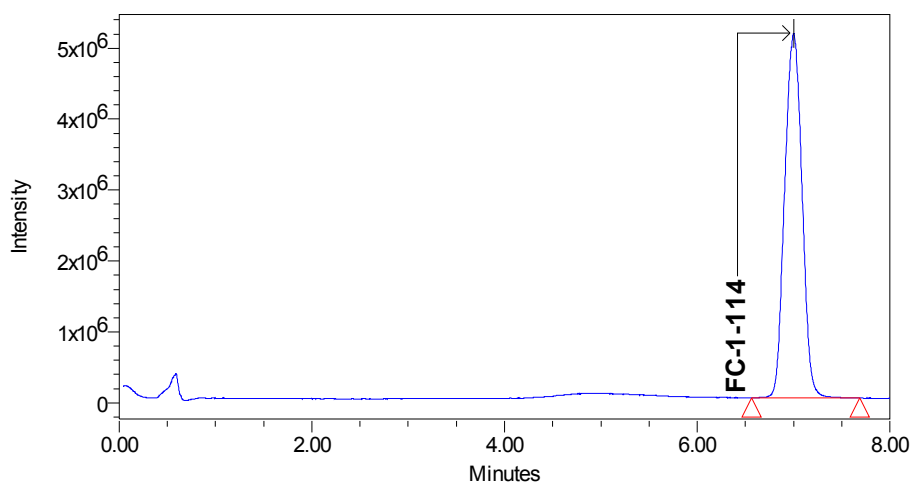


UPLC-ESI-MS data of compound 4e

SAMPLE INFORMATION

Sample Name:	FC-1-114	Acquired By:	
Sample Type:	Unknown	Sample Set Name	001 Prueba 2 FC 1 114 Dil
Vial:	2:F,2	Acq. Method Set:	ID 007 QPDA
Injection #:	1	Injection Volume:	10.00 ul
Run Time:	8.0 Minutes	Date Acquired:	6/4/2021 11:34:13 AM CDT
Column Name:	ACQUITY UPLC HSS T3 1.8um 3.0 x 100 mm		

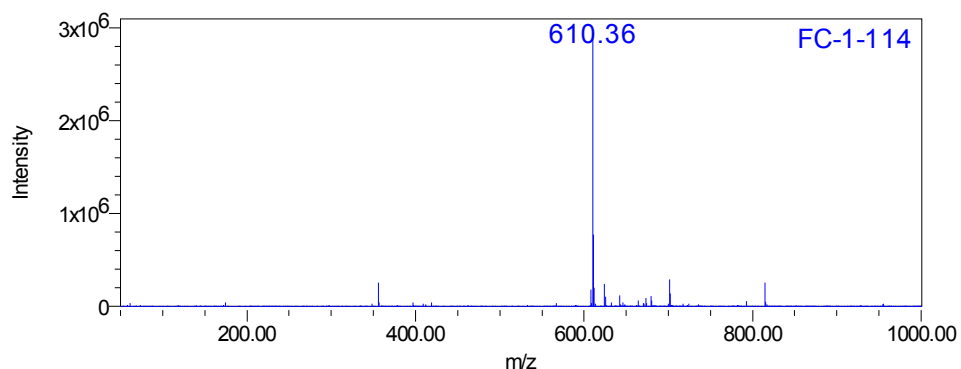
Auto-Scaled Chromatogram



Peak Results

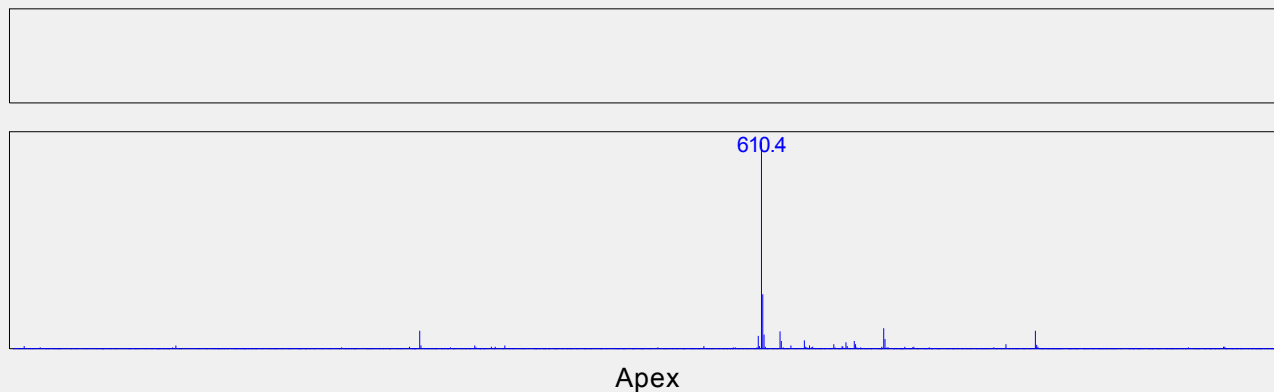
	Name	RT	Area	Height	MS 3D Channel Name
1	FC-1-114	7.001	64379463	5143460	QDa 1: MS Scan

Match Plot

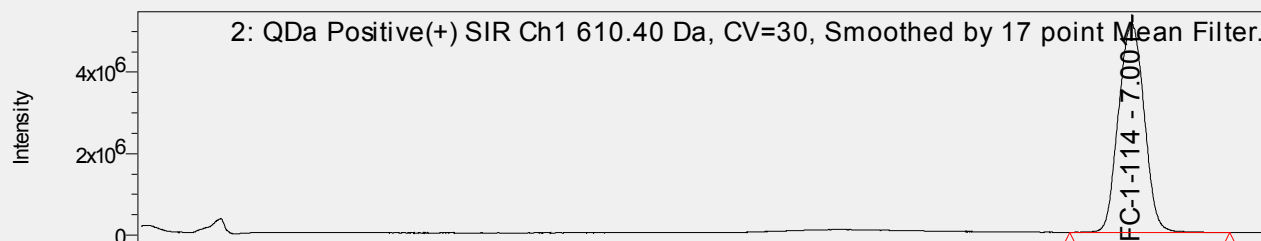


UPLC-ESI-MS data of compound 4f

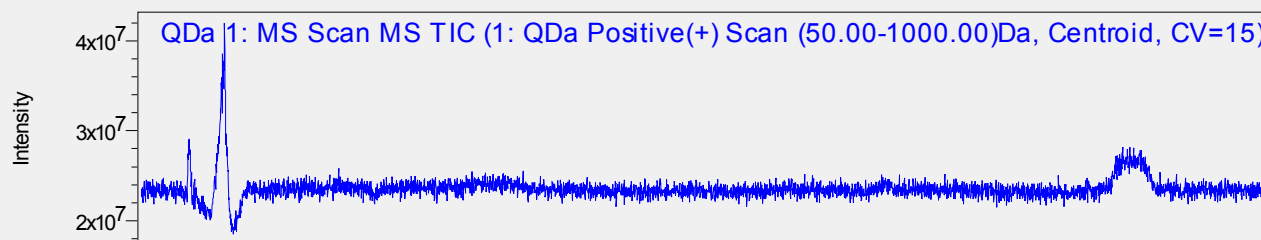
FC-1-114 - 7.001 - QDa 1: MS Scan



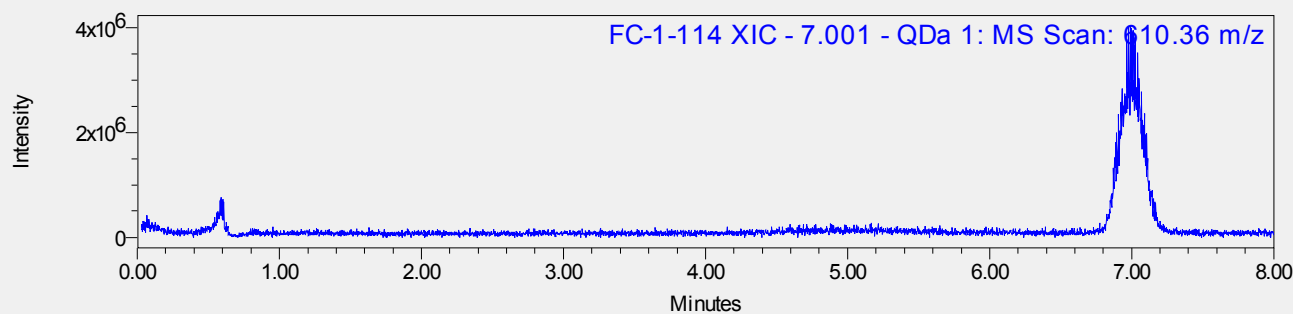
2: QDa Positive(+) SIR Ch1 610.40 Da, CV=30, Smoothed by 17 point Mean Filter.



QDa 1: MS Scan MS TIC (1: QDa Positive(+) Scan (50.00-1000.00)Da, Centroid, CV=15)



FC-1-114 XIC - 7.001 - QDa 1: MS Scan: 610.36 m/z

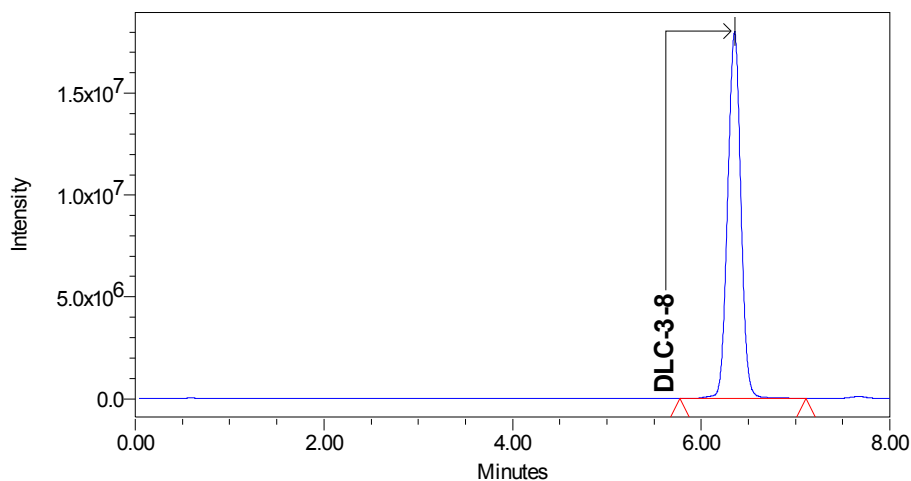


UPLC-ESI-MS data of compound 4f

SAMPLE INFORMATION

Sample Name:	DLC-3-8	Acquired By:	
Sample Type:	Unknown	Sample Set Name	001 Prueba 2 DLC 3 8
Vial:	2:A,3	Acq. Method Set:	ID 008 QPDA
Injection #:	1	Injection Volume:	10.00 μ l
Run Time:	8.0 Minutes	Date Acquired:	6/4/2021 12:26:06 PM CDT
Column Name:	ACQUITY UPLC HSS T3 1.8 μ m 3.0 x 100 mm		

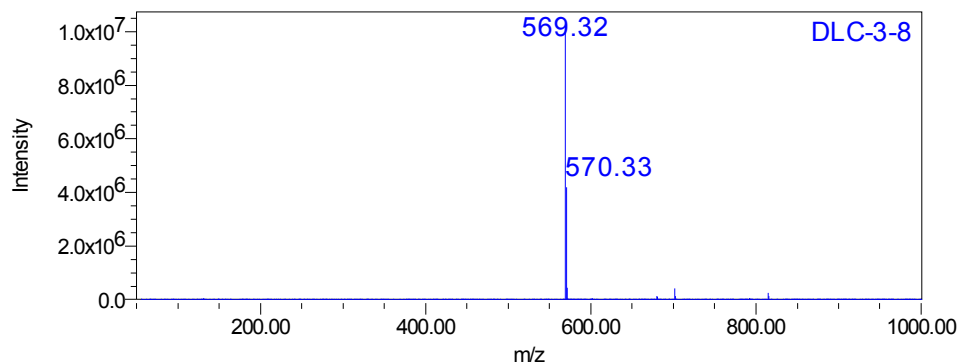
Auto-Scaled Chromatogram



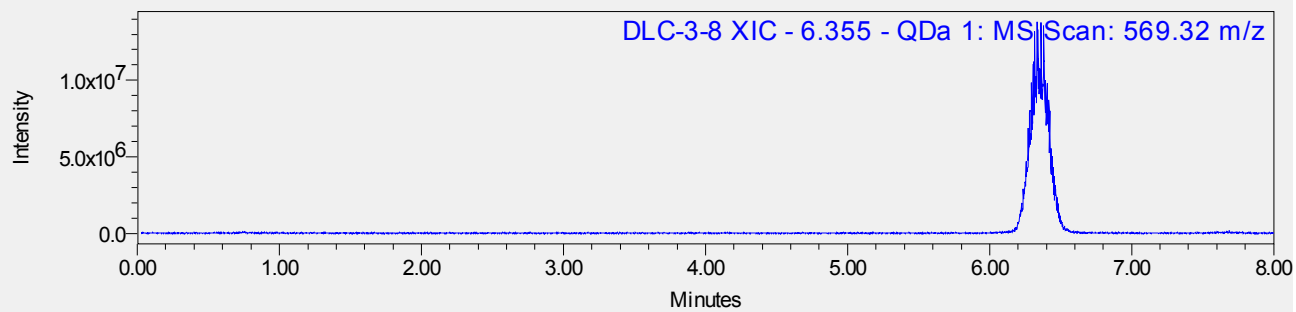
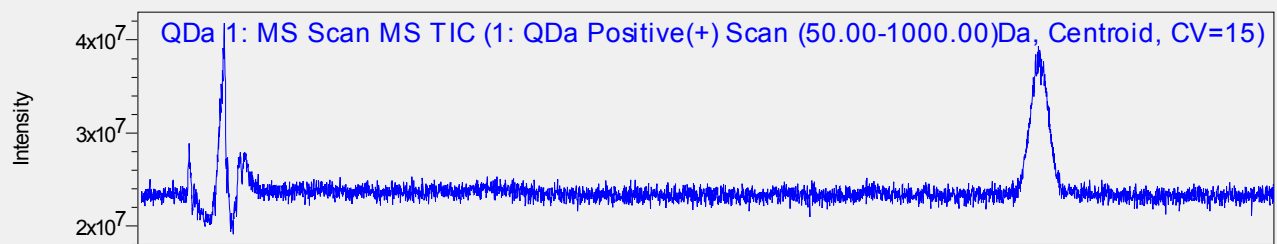
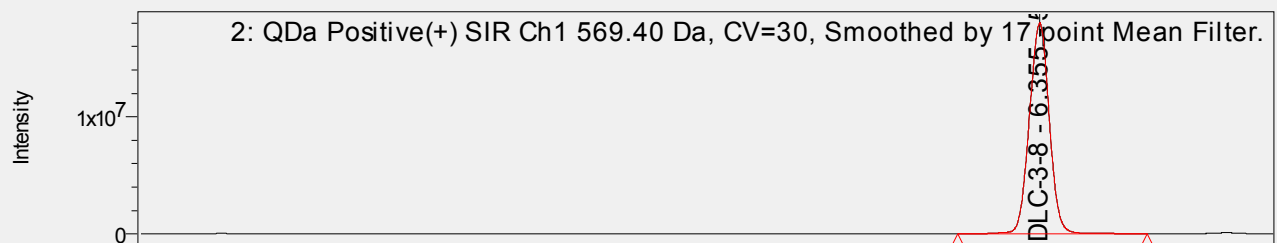
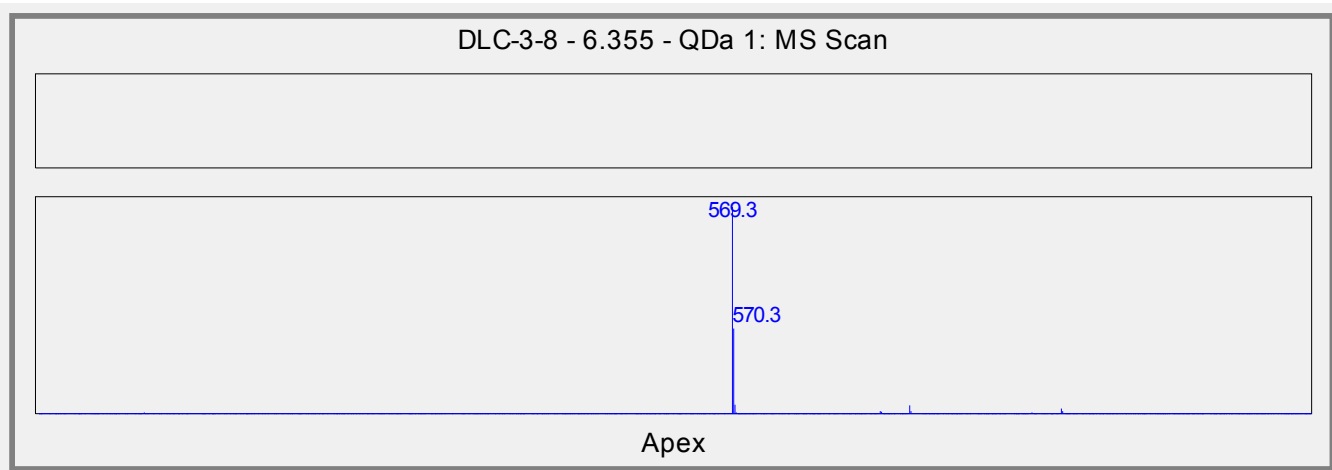
Peak Results

	Name	RT	Area	Height	MS 3D Channel Name
1	DLC-3-8	6.355	175052351	18027727	QDa 1: MS Scan

Match Plot



UPLC-ESI-MS data of compound 5a

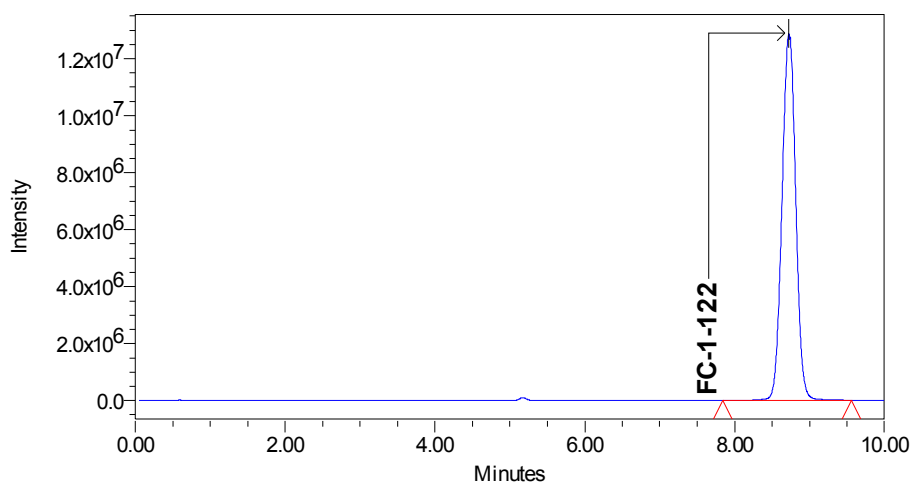


UPLC-ESI-MS data of compound 5b

SAMPLE INFORMATION

Sample Name:	FC-1-122	Acquired By:	
Sample Type:	Unknown	Sample Set Name	001 Prueba 2 FC 1 122
Vial:	2:B,3	Acq. Method Set:	ID 013 QPDA
Injection #:	1	Injection Volume:	10.00 μ l
Run Time:	10.0 Minutes	Date Acquired:	6/21/2021 1:19:33 PM CDT
Column Name:	ACQUITY UPLC HSS T3 1.8 μ m 3.0 x 100 mm		

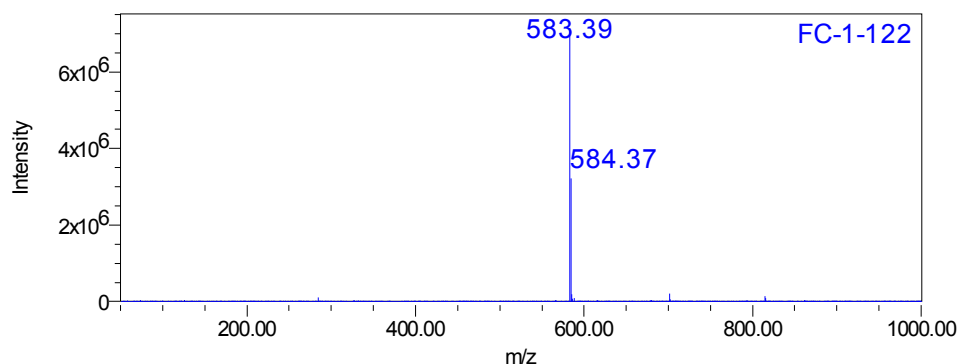
Auto-Scaled Chromatogram



Peak Results

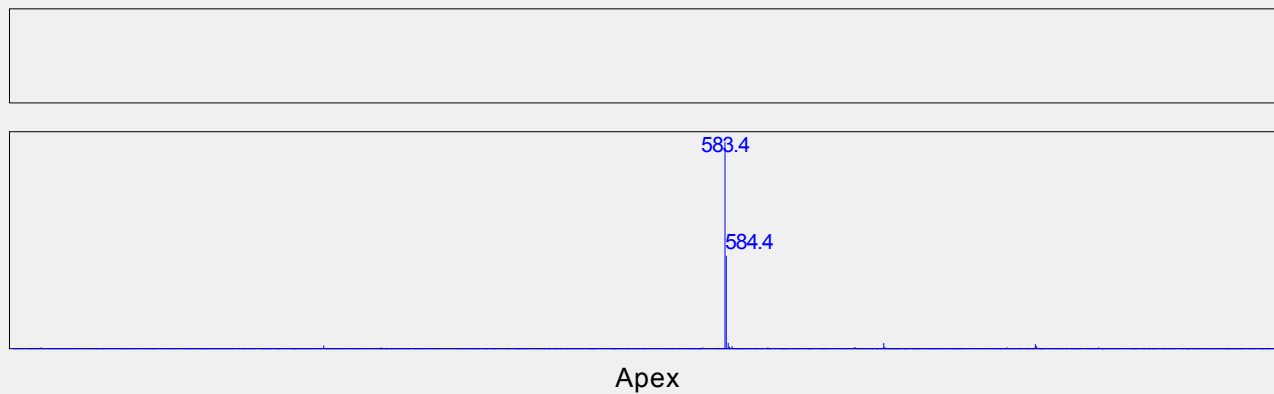
	Name	RT	Area	Height	MS 3D Channel Name
1	FC-1-122	8.721	163186315	12882045	QDa 1: MS Scan

Match Plot

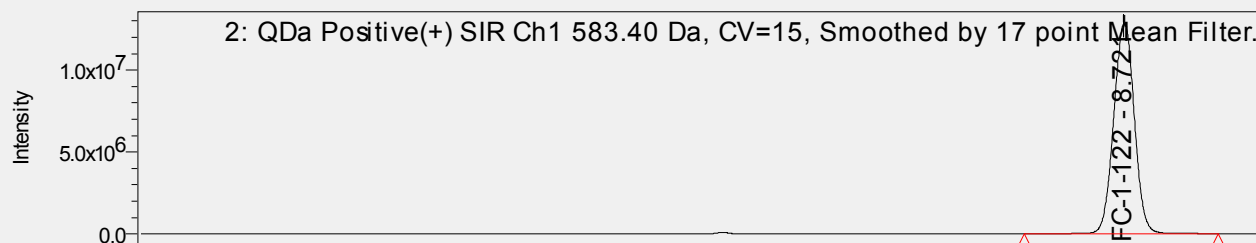


UPLC-ESI-MS data of compound 5c

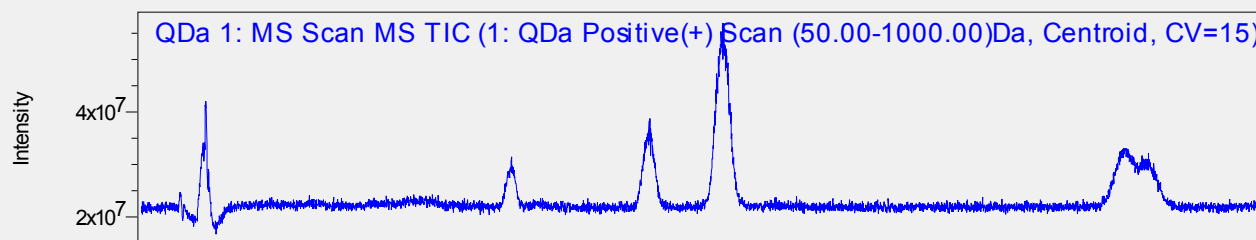
FC-1-122 - 8.721 - QDa 1: MS Scan



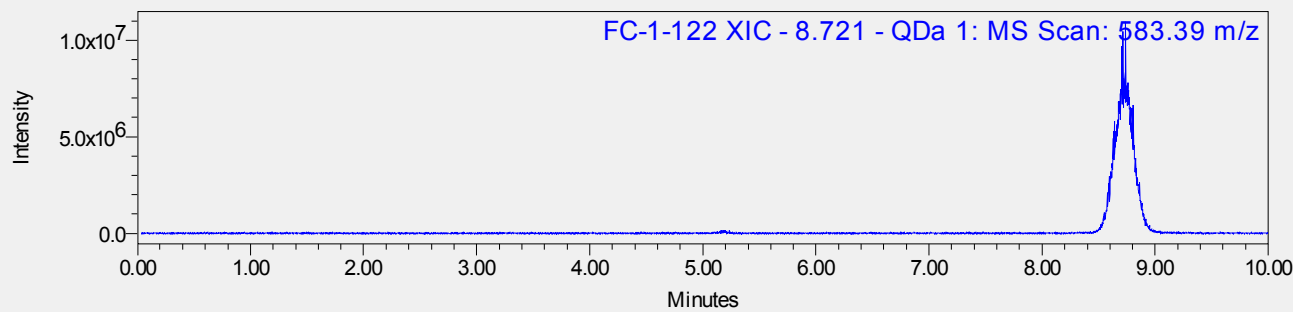
2: QDa Positive(+) SIR Ch1 583.40 Da, CV=15, Smoothed by 17 point Mean Filter.



QDa 1: MS Scan MS TIC (1: QDa Positive(+) Scan (50.00-1000.00)Da, Centroid, CV=15)



FC-1-122 XIC - 8.721 - QDa 1: MS Scan: 583.39 m/z

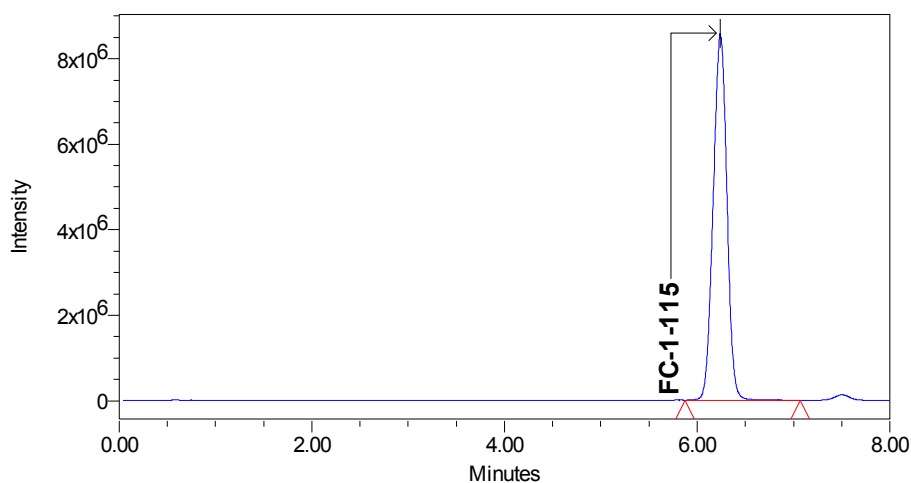


UPLC-ESI-MS data of compound 5c

SAMPLE INFORMATION

Sample Name:	FC-1-115	Acquired By:	
Sample Type:	Unknown	Sample Set Name	001 Prueba 2 FC 1 115
Vial:	2:B,2	Acq. Method Set:	ID 011 QPDA
Injection #:	1	Injection Volume:	10.00 ul
Run Time:	10.0 Minutes	Date Acquired:	6/21/2021 1:08:41 PM CDT
Column Name:	ACQUITY UPLC HSS T3 1.8um 3.0 x 100 mm		

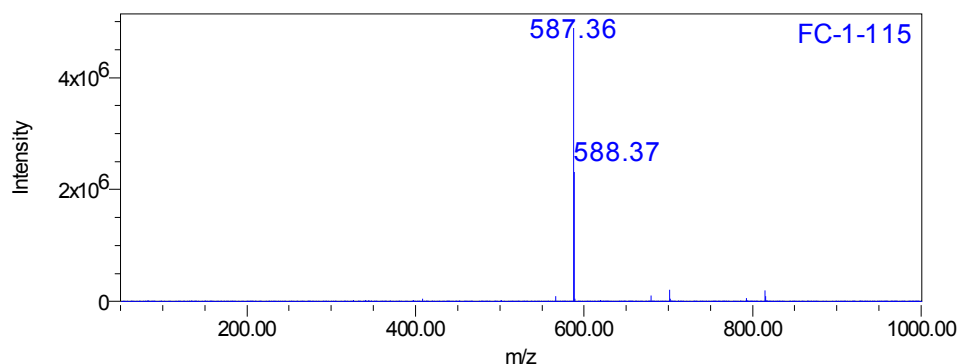
Auto-Scaled Chromatogram



Peak Results

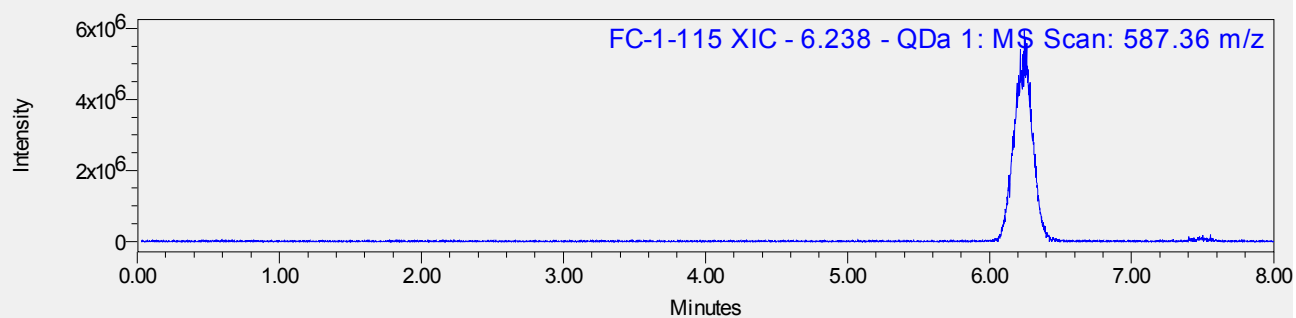
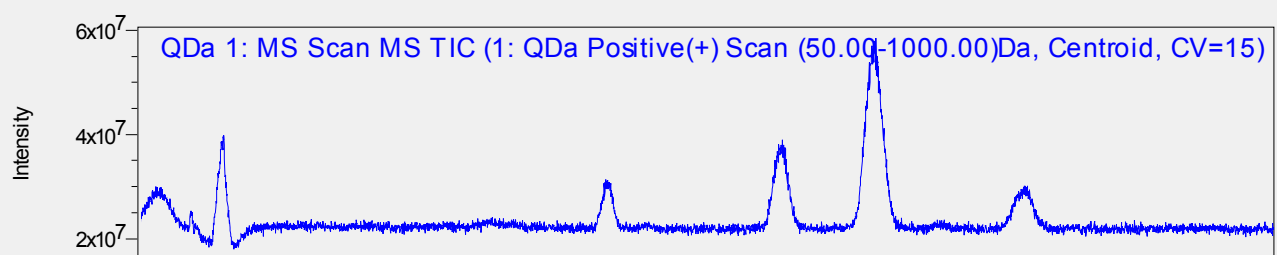
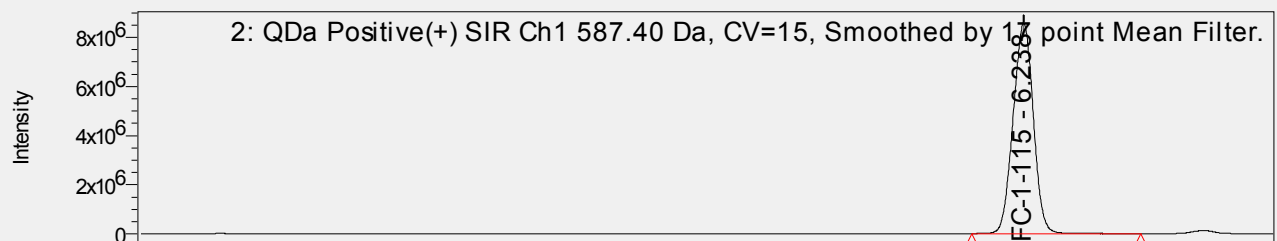
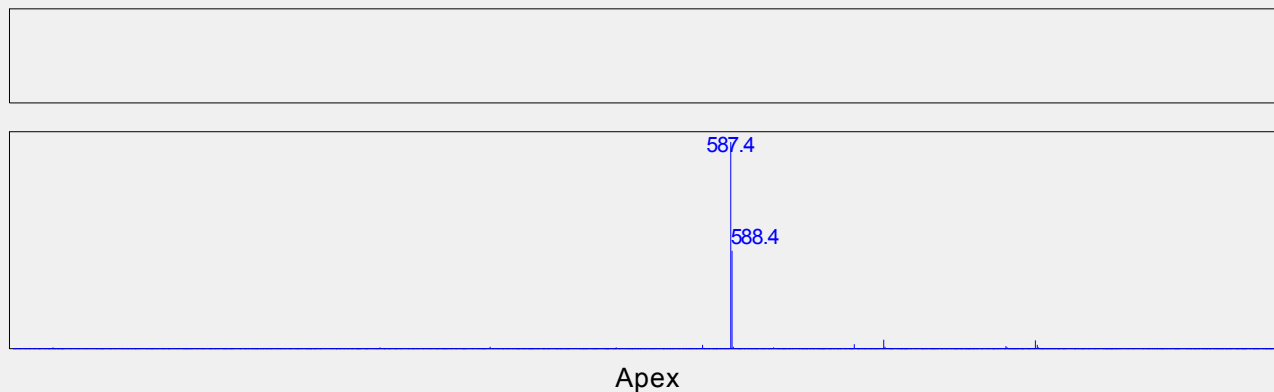
	Name	RT	Area	Height	MS 3D Channel Name
1	FC-1-115	6.238	84701456	8589486	QDa 1: MS Scan

Match Plot



UPLC-ESI-MS data of compound 5d

FC-1-115 - 6.238 - QDa 1: MS Scan

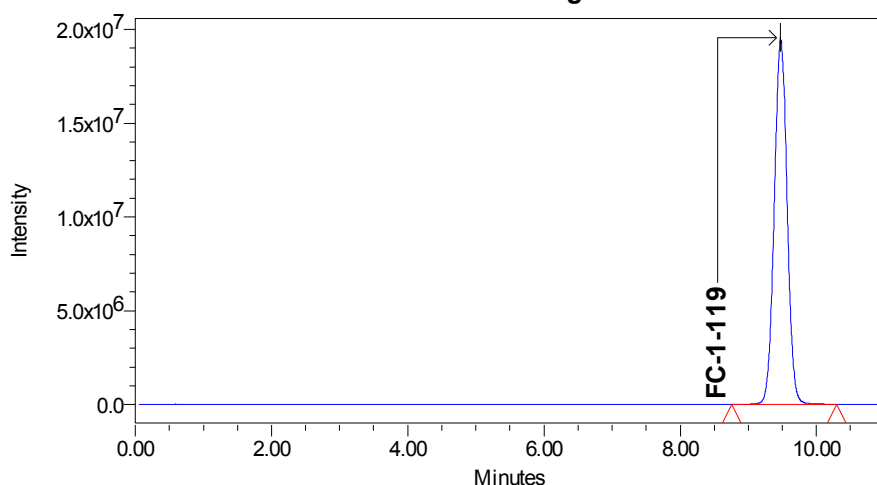


UPLC-ESI-MS data of compound 5d

SAMPLE INFORMATION

Sample Name:	FC-1-119	Acquired By:	
Sample Type:	Unknown	Sample Set Name	001 Prueba 1 FC 1 119
Vial:	2:A,4	Acq. Method Set:	ID 012 QPDA
Injection #:	1	Injection Volume:	10.00 ul
Run Time:	11.0 Minutes	Date Acquired:	6/21/2021 12:37:11 PM CDT
Column Name:	ACQUITY UPLC HSS T3 1.8um 3.0 x 100 mm		

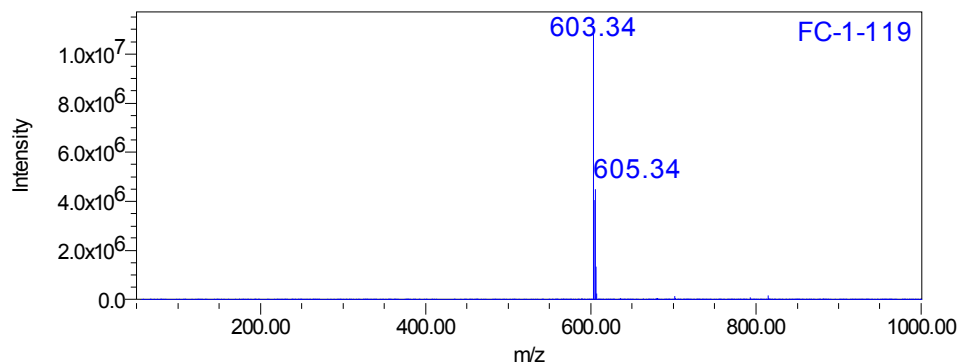
Auto-Scaled Chromatogram



Peak Results

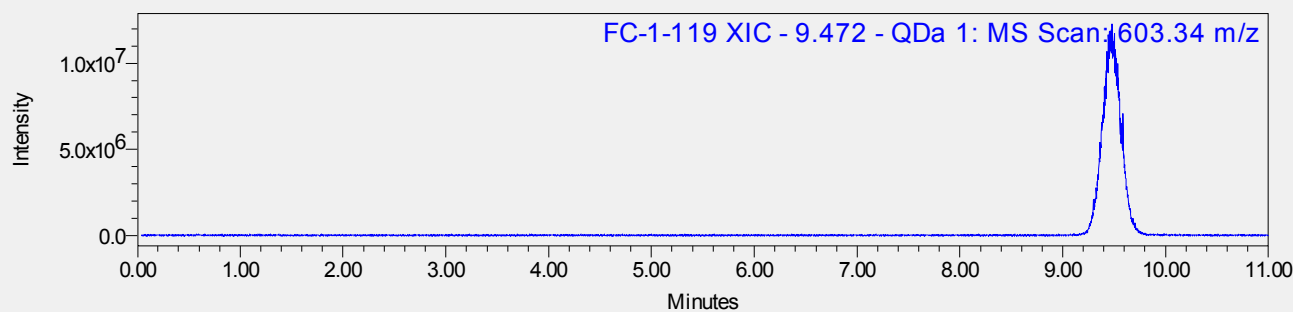
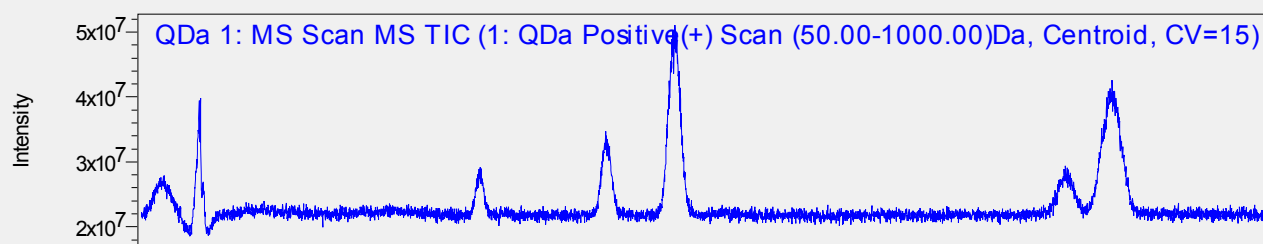
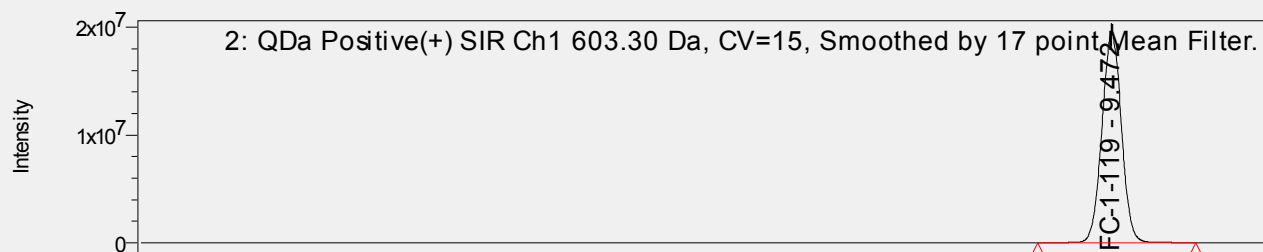
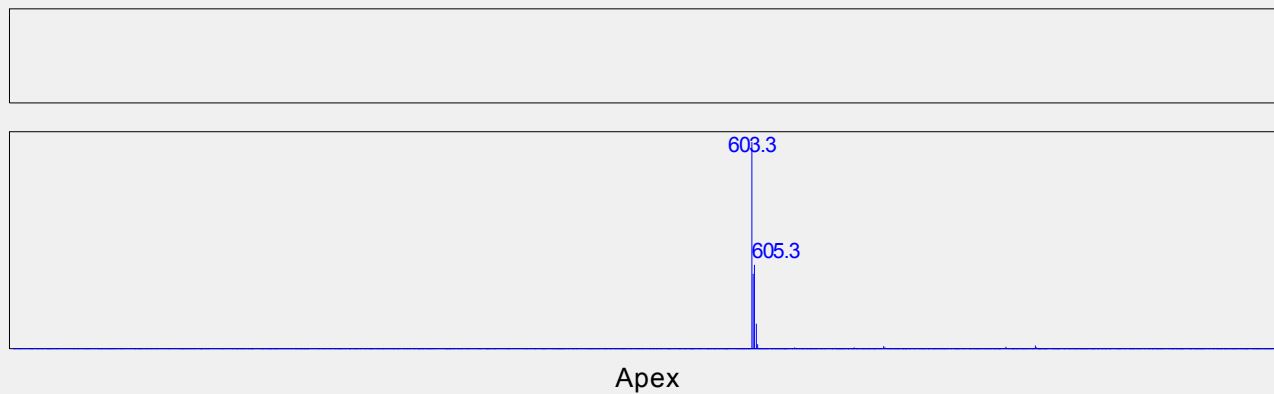
	Name	RT	Area	Height	MS 3D Channel Name
1	FC-1-119	9.472	256951373	19564042	QDa 1: MS Scan

Match Plot



UPLC-ESI-MS data of compound 5e

FC-1-119 - 9.472 - QDa 1: MS Scan

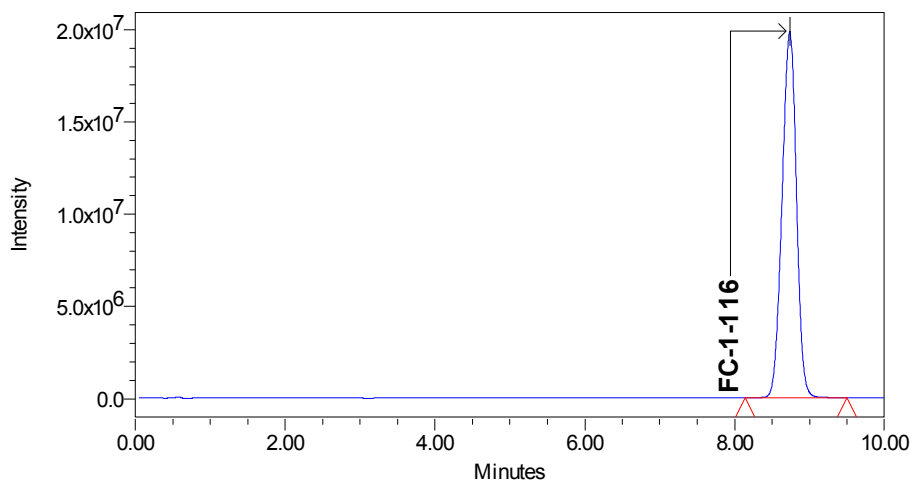


UPLC-ESI-MS data of compound 5e

SAMPLE INFORMATION

Sample Name:	FC-1-116	Acquired By:	
Sample Type:	Unknown	Sample Set Name	001 Prueba 1 FC 1 116
Vial:	2:A,6	Acq. Method Set:	ID 014 QPDA
Injection #:	1	Injection Volume:	10.00 ul
Run Time:	10.0 Minutes	Date Acquired:	6/21/2021 12:49:01 PM CDT
Column Name:	ACQUITY UPLC HSS T3 1.8um 3.0 x 100 mm		

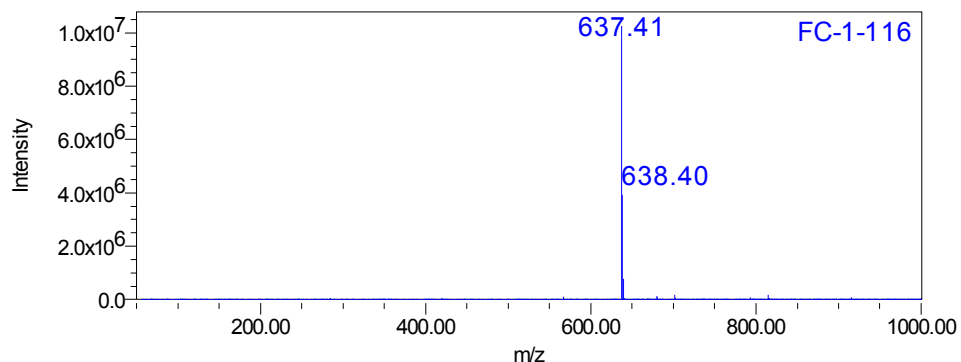
Auto-Scaled Chromatogram



Peak Results

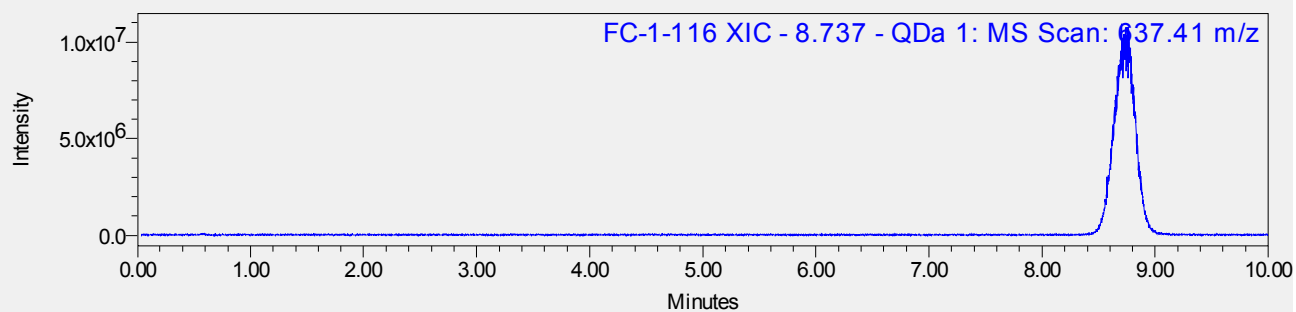
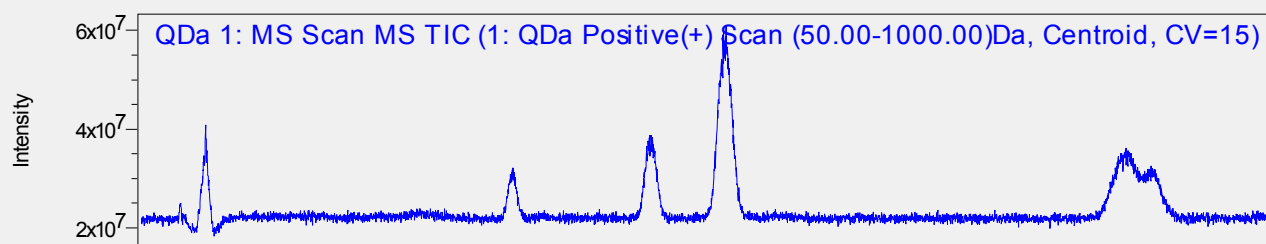
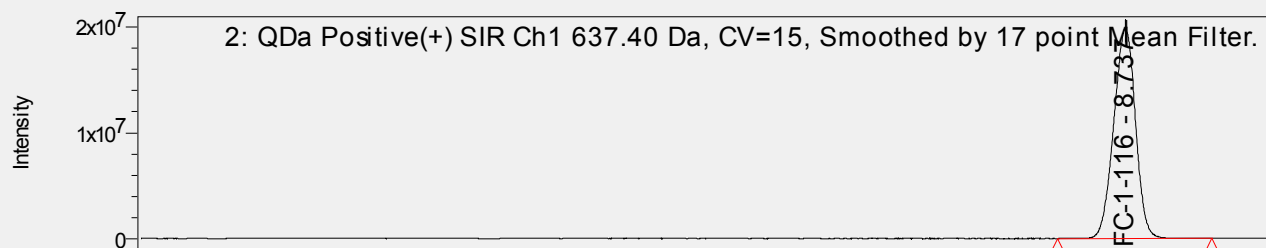
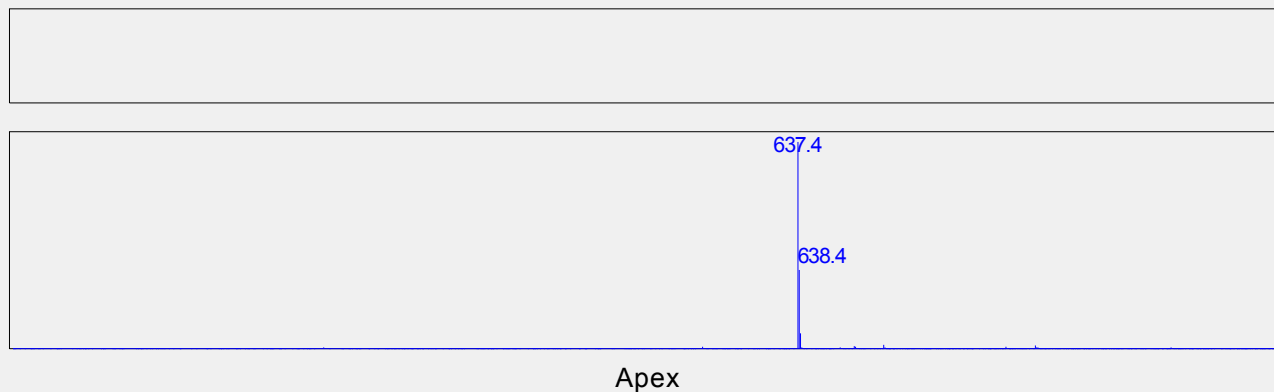
	Name	RT	Area	Height	MS 3D Channel Name
1	FC-1-116	8.737	264967548	19878952	QDa 1: MS Scan

Match Plot



UPLC-ESI-MS data of compound 5f

FC-1-116 - 8.737 - QDa 1: MS Scan



UPLC-ESI-MS data of compound 5f