Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry.

Synthesis and Characterization of Photoaffinity Labelling reagents Towards the Hsp90 C-terminal Domain

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Synthesis of photoaffinity labelling (PAL) reagents 1-5

1. 4-(4-(3-(trifluoromethyl)-3*H*-diazirin-3-yl)phenyl)methanyl-novobiocin (1)

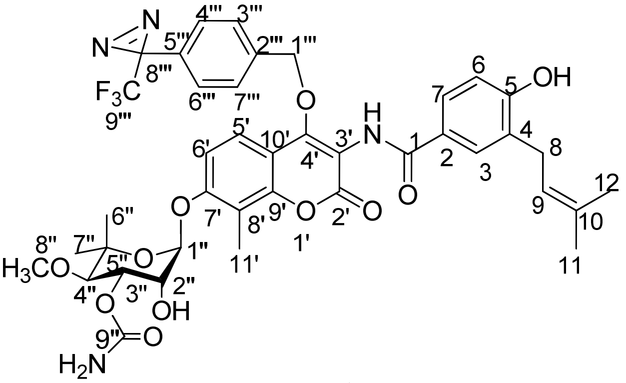
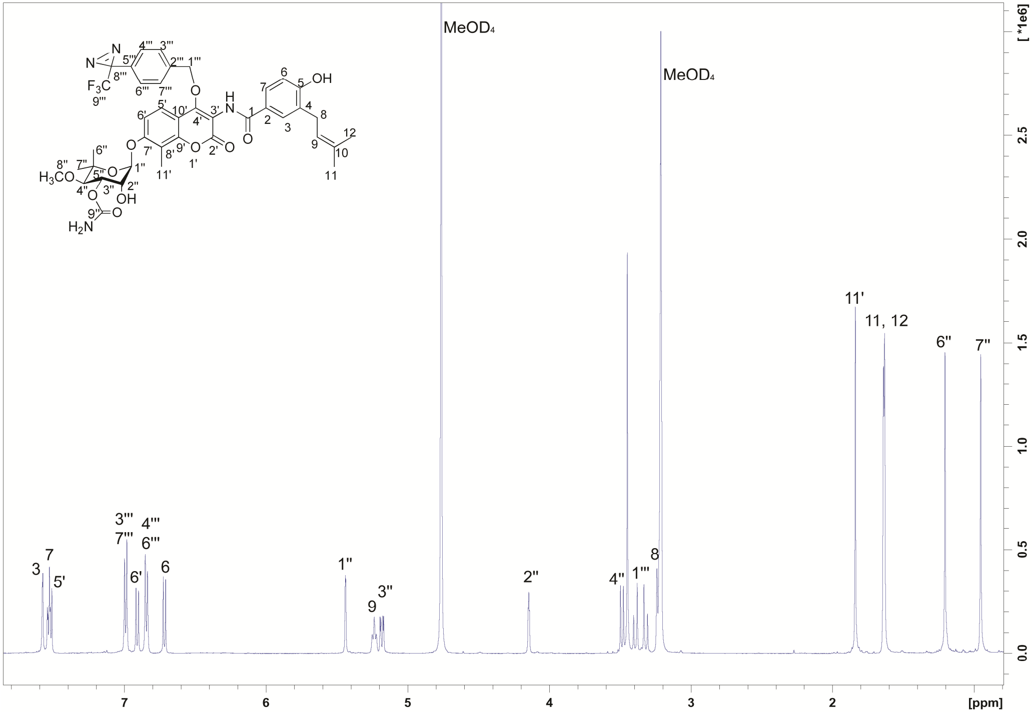
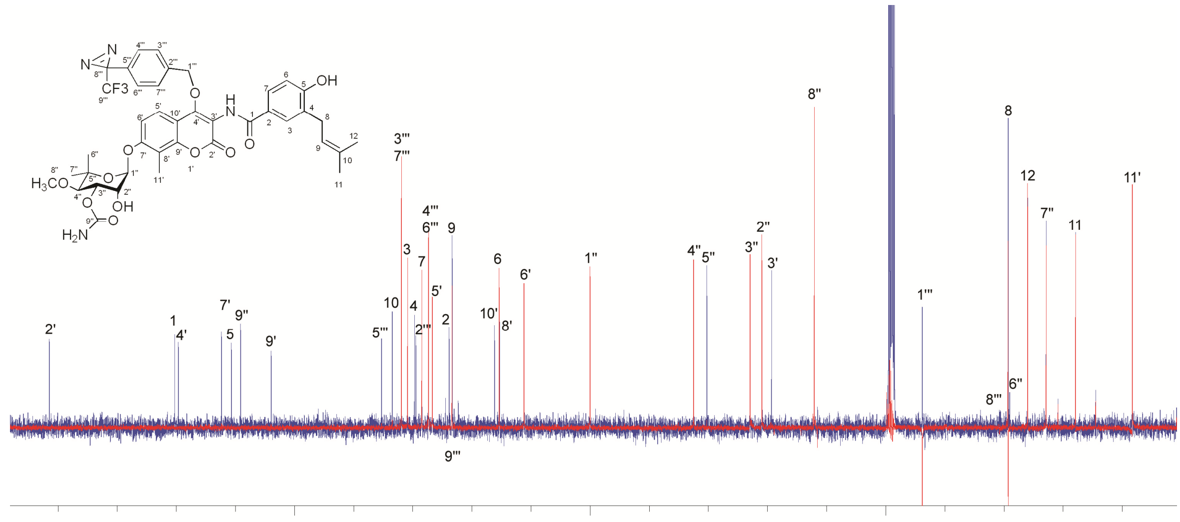


Figure S1. NMR assignment of compound **1**. a) ^{1}H-NMR with individual proton assigned to each peak. b) Combined ^{13}C (black) and DEPT135 (red) NMR with individual carbon assignment. c) HMBC assignment for compound 1. Long range coupling between H1''' and C4'. It also shows the coupling between C4'''/C6''' and C8'''. d) ^{13}CNMR of 3-(4-(bromomethyl) phenyl) -3-(trifluoromethyl)-3H-diazirine. e) HMBC of 3-(4-(bromomethyl) phenyl)-3-(trifluoromethyl)-3H-diazirine. Coupling between H4/6 and C8 can be observed. Solvent peaks are not fully labelled.



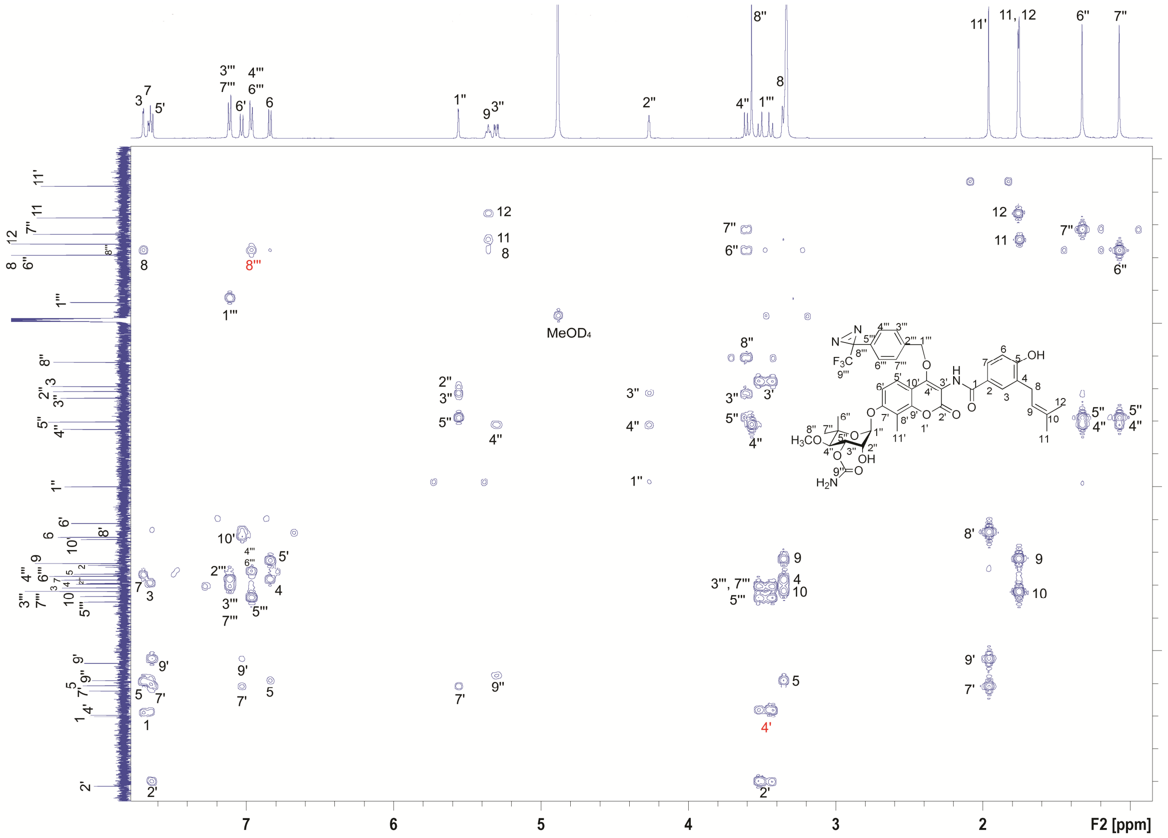
a)



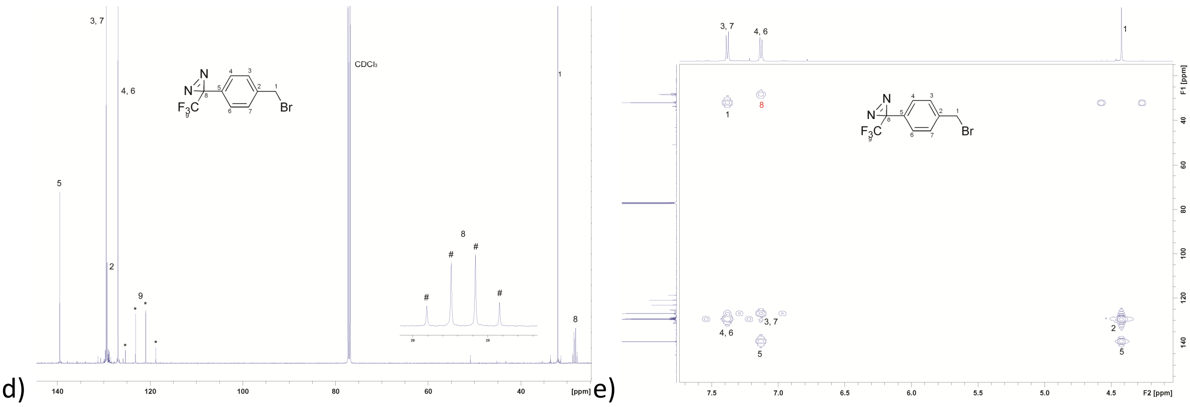
H3CO
OH
H2N
CF3
N
2'
1
4'
7'
5
9''
9'
5'''
10
3
3'''
7'''
7
4
2'''
4'''
6'''
5'
9
2
10'
6
8'
6'
1''
4''
5''
3''
2''
3'
8''
1'''
8'''
8
6''
12
7''
11
11'
9'''
150
100
50
[ppm]

b)

c)



3
7
5'
3'''
7'''
6'
4'''
6'''
6
1''
9
3''
2''
4''
1'''
8''
8
11'
11, 12
6''
7''
8'''
1'''
MeOD4
2''
3''
5''
4''
1''
10'
2'''
5'''
5'
4
3''', 7'''
5'''
10
9'
7'
5
9''
2'
4'
8'
F1 [ppm]
F2 [ppm]
50
100
150
7
6
5
4
3
2



The multiplicities in the C8''' and C9''' (Fig S1) resonance due to the J coupling to 3 × ^{19}F were apparent, which are normally difficult to be observed in ^{13}C NMR spectra, since the signal is spread over multiple lines and can be buried in the noise. This peak can be clearly identified in the NMR spectrum of the starting material (compound **6**, Fig S1d) and HMBC shows consistent coupling between H4'''/6''' and C8''' (Fig. 2, Fig. S1e).

Table S1. ^1H & ^{13}CNMR individual peak assignment of compound **1**

Site	^{13}C /ppm	^{1}H /ppm	Multi-plicity	$J_{(H,H)}$ (Hz)
1	169.70			
2	123.89			
3	130.91	7.55	s	
4	129.71			
5	160.6			
6	115.43	6.69	d	8.9
7	128.51	7.51	d	8.4
8	29.33	3.21	m	
9	123.40	5.20	t	7.4
10	133.50			
11	26.10	1.60	s	
12	17.93	1.60	s	
1'	-			
2'	191.50			
3'	69.34			
4'	170.30			
5'	126.69	7.50	d	7.4
6'	111.25	6.88	d	8.4
7'	162.50			
8'	115.33			
9'	154.10			
10'	116.21			
11'	8.30	1.81	s	
1''	100.07	5.41	s	
2''	71.01	4.12	s	
3''	72.96	5.15	d	10.8
4''	82.55	3.46	d	10.8
5''	80.34			

6''	29.34	1.18	s	
7''	22.92	0.93	s	
8''	62.08	3.42	s	
9''	159.17			
1'''	43.90	3.33	dd	11.8, 36.9
2'''	127.34			
3'''	131.94	6.96	d	7.9
4'''	129.72	6.81	d	7.9
5'''	135.31			
6'''	127.34	6.81	d	7.9
7'''	131.94	6.96	d	7.9
8'''	29.10			
9'''	123.20			

2. 3-amino-4,7-dihydroxy-8-methyl-2H-chromen-2-one (7)

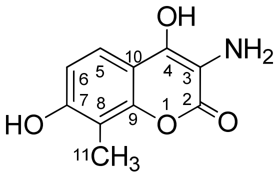


Table S2. NMR assignment of compound **7**

Site*	^{13}C /ppm	^{1}H /ppm	Multi-plicity	$J_{(H,H)}$ (Hz)
1	-			
2	164.2			
3	96.2			
4	161.7			
5	122.6	7.77	d	8.03
6	113.7	6.95	d	8.56
7	162.3			
8	113.5			
9	153.6			
10	108.1			
11	9.2	2.28	s	

3. 4-acetoxy-3-(3-methylbut-2-en-1-yl)benzoic acid (8)

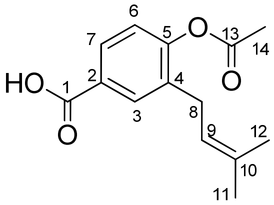


Table S3. NMR assignment of compound **8**

Site*	^{13}C /ppm	^{1}H /ppm	Multi-plicity	$J_{(H,H)}$ (Hz)
1	171.8			
2	127.1			
3	132.2	8.03	s	
4	129.3			
5	163.4			
6	123.6	7.17	d	8.3
7	129.5	8.01	d	8.3
8	29.3	3.31	d	7.4
9	121.0	5.28	t	7.1
10	134.1			
11	26.3	1.79	s	
12	17.7	1.75	s	
13	168.9			
14	21.0	2.34	s	

4. 4-((4,7-dihydroxy-8-methyl-2-oxo-2H-chromen-3-yl)carbamoyl)-2-(3-methylbut-2-en-1-yl)phenyl acetate (9)

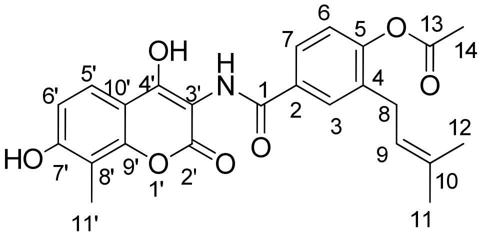
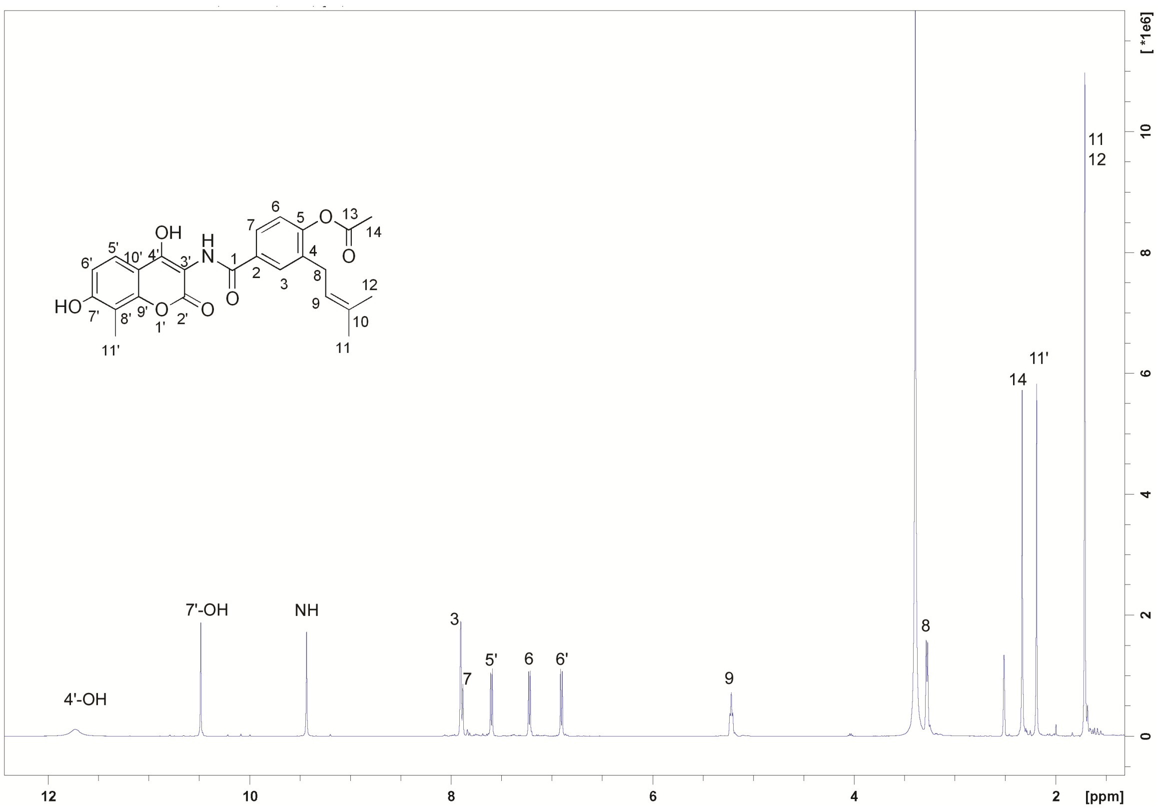


Figure S2. NMR assignment of compound **9**. a) ^{1}HNMR. b) ^{13}CNMR. c) HMBC. 7'-OH couples to C7', C8' and C9'; NH couples to C4' and C1 indicating the formation of amide bond. Solvent peaks are not fully labelled.



[*1e6]
10
8
6
4
2
0
11
12
14
11'
8
9
3
7
5'
6
6'
NH
7'-OH
4'-OH
12
10
8
6
4
2
[ppm]
OH
NH
HO
O
4'
3'
10'
5'
6'
7'
8'
9'
1'
2'
11'
1
2
3
4
5
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8
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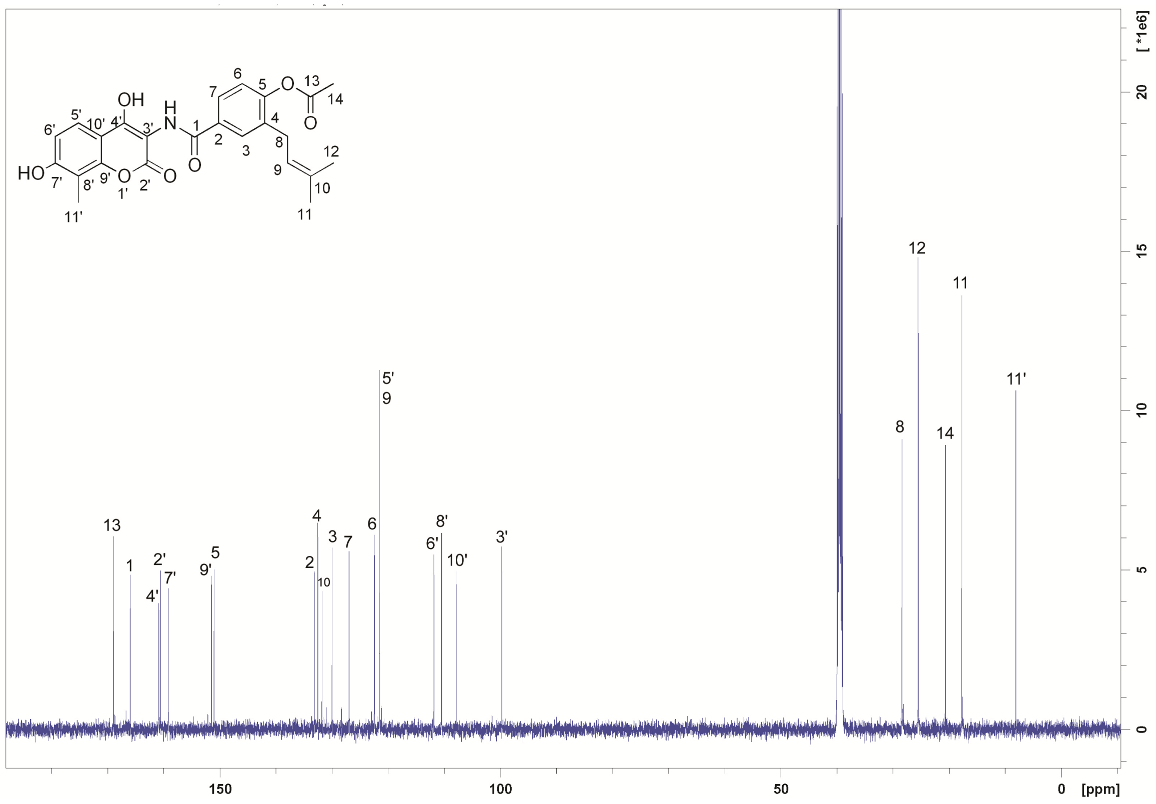
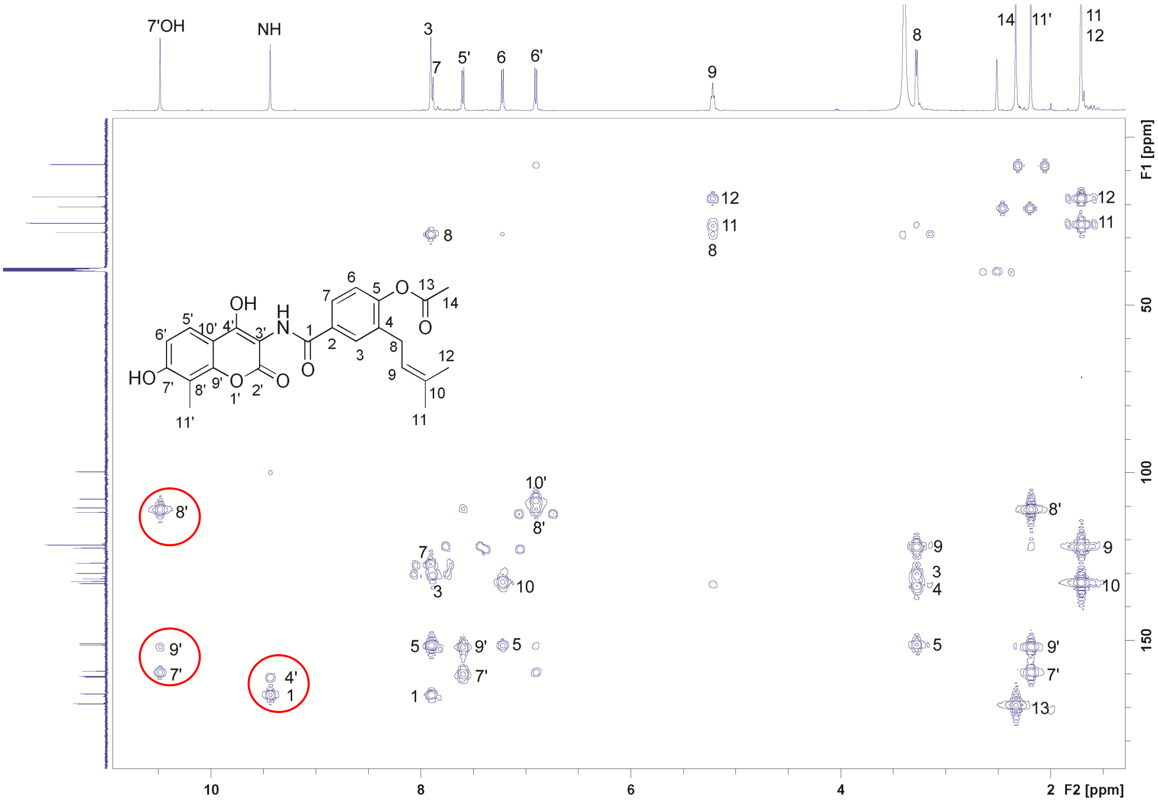
10
11
12
13
14

a)



[*1e6]
20
15
10
5
0
13
1
2'
4'
7'
9'
5
2
4
10
3
7
6
5'
9
6'
8'
10'
3'
8
12
14
11
11'
150
100
50
0
[ppm]

b)



c)

Table S4. NMR assignment of compound **9**

Site	^{13}C /ppm	^{1}H /ppm	Multiplicity	$J_{(H,H)}$ (Hz)
1	165.94			
2	133.13			
3	129.96	7.90	s	
4	132.50			
5	150.99			
6	122.44	7.22	d	8.1
7	126.94	7.89	d	8.5
8	28.99	3.28	d	7.1
9	121.55	5.22	t	6.8
10	131.75			
11	26.36	1.71	s	
12	18.51	1.71	s	
13	168.89			
14	21.16	2.33	s	
1'	-			
2'	160.57			
3'	99.72			
4'	160.85			
5'	121.52	7.61	d	8.1
6'	111.83	6.90	d	8.1
7'	159.10			
8'	110.43			
9'	151.47			

10'	108.07			
11'	8.88	2.19	s	
4'-OH		11.73	br	
7'-OH		10.52	s	
NH		9.44	s	

5. 4-((7-hydroxy-8-methyl-2-oxo-4-((4-(3-(trifluoromethyl)-3H-diazirin-3-yl)benzyl)oxy)-2H-chromen-3-yl)carbamoyl)-2-(3-methylbut-2-en-1-yl)phenyl acetate (10)

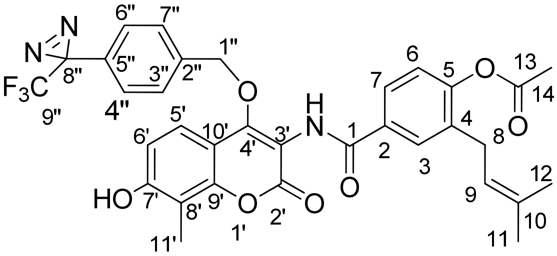
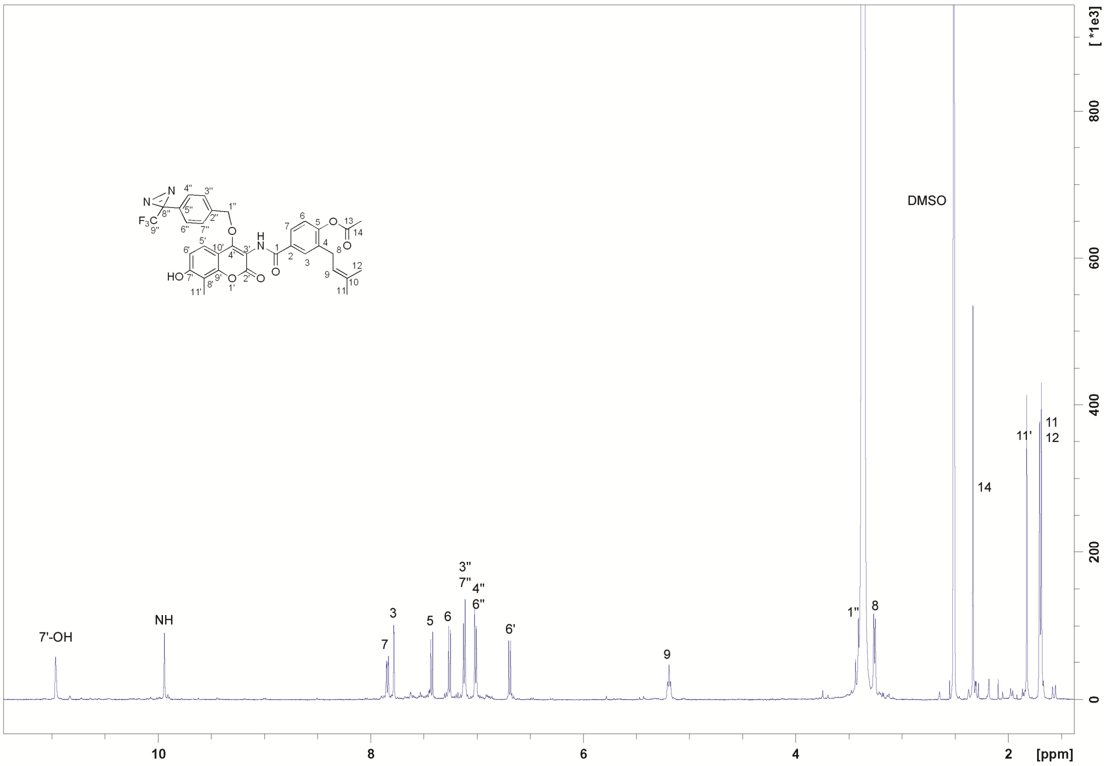
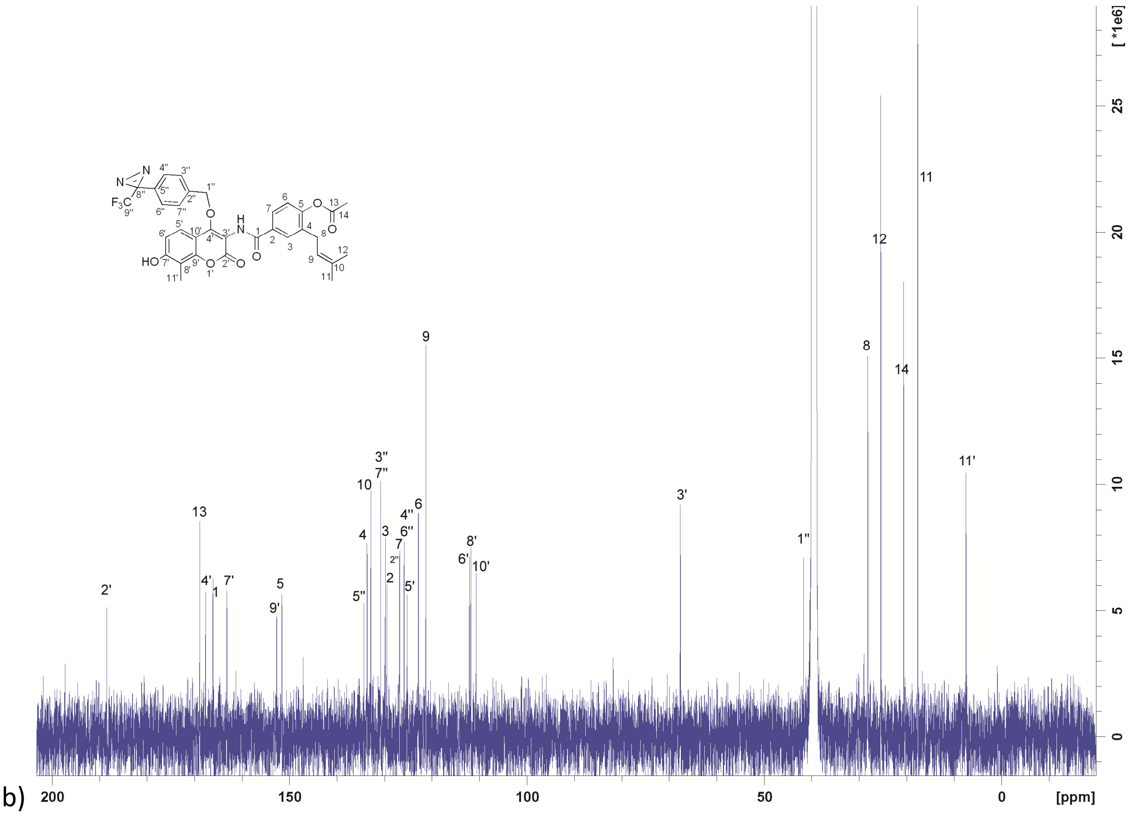
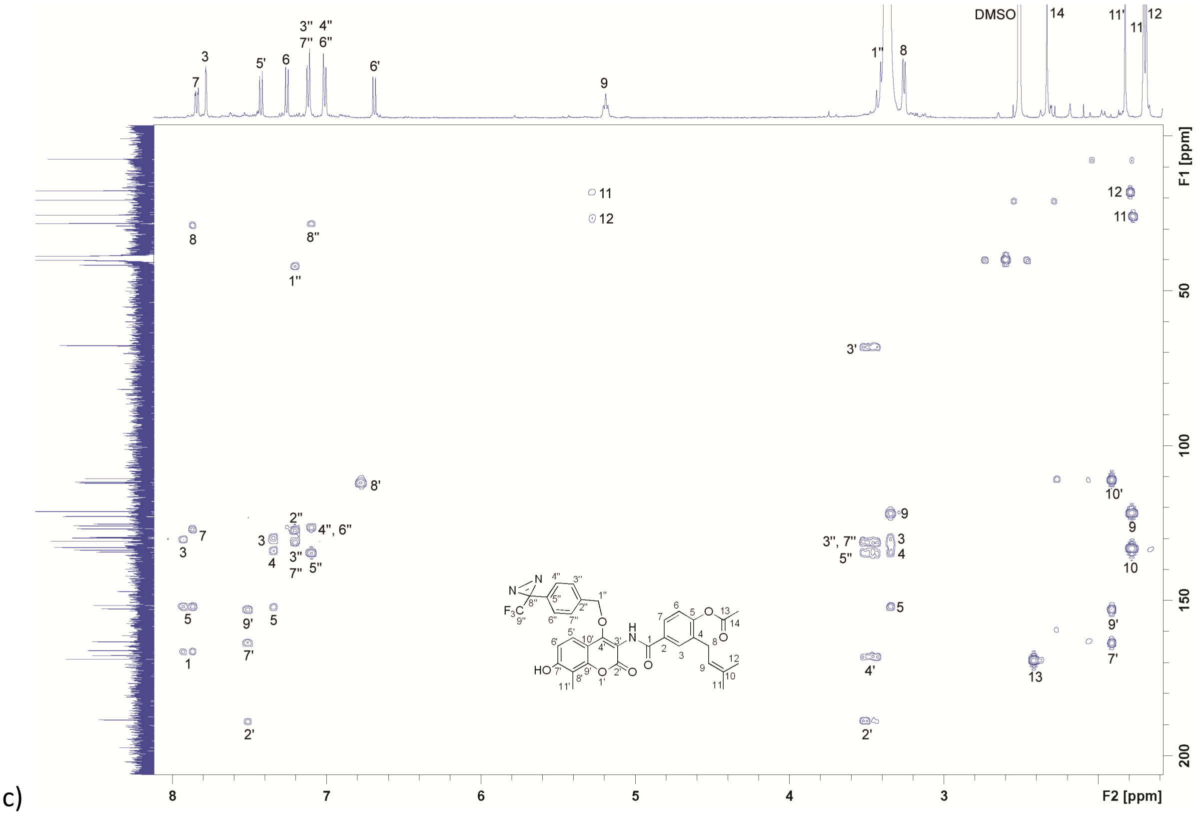


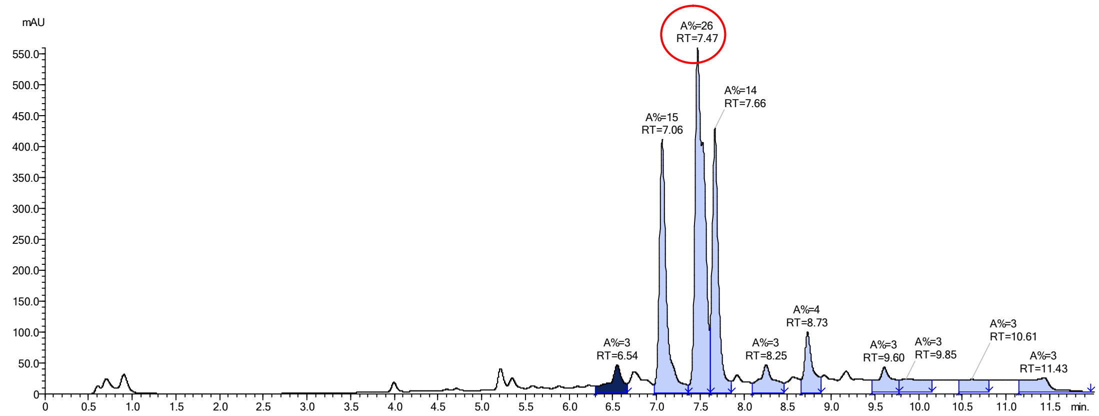
Figure S3. NMR assignment of compound **10**. a) ^{1}HNMR. 7'-OH and NH signals can be seen but no 4'-OH signal b) ^{13}CNMR. c) HMBC. H1" couples to C4' proves the linkage. Solvent peaks are not fully labelled. d) Analytical LC shows the formation of 2 products in the present of starting material. e) MS shows the formation of product at 7.47 min (636, $[M+H^+]^+$; 1293, $[2M+Na^+]^+$; 1928, $[2M+Na^+]^+$). f) Analytical LC show the purity of compound 10 after preparative HPLC.



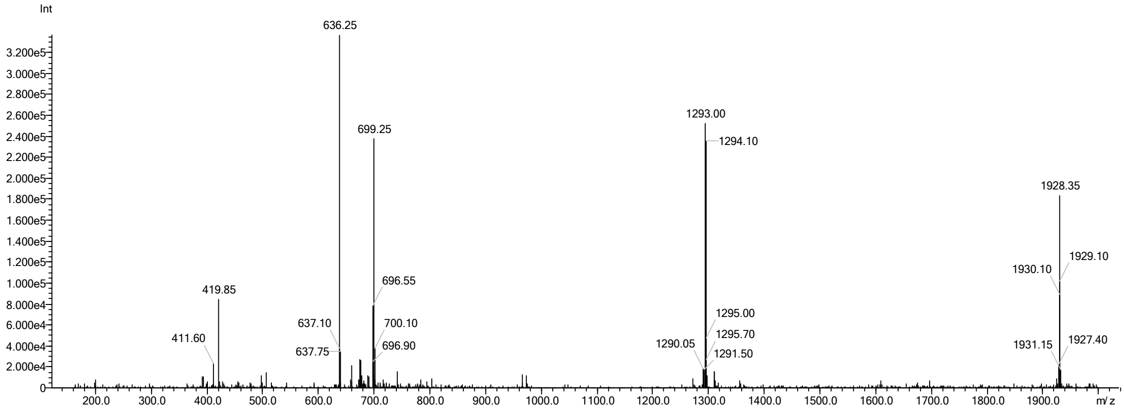
a)


b)
[*1e6]
2'
13
4'
1
7'
5
9'
5''
4
10
3''
7''
3
2
2''
7
4''
6''
6
5'
9
8'
6'
10'
3'
1''
8
12
14
11
11'
200
150
100
50
0
[ppm]
25
20
15
10
5
0

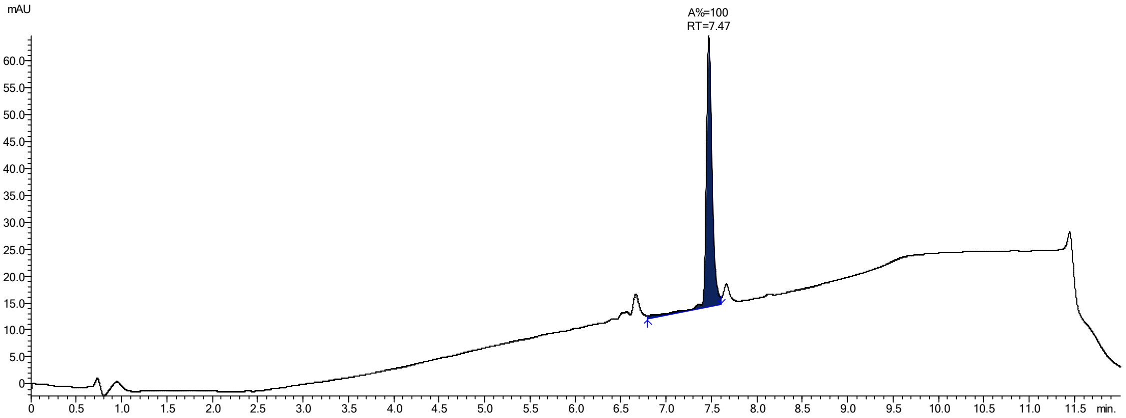

c)
DMSO
14
11'
11
12
7
3
5'
6
3''
7''
4''
6''
6'
9
1''
8
F1 [ppm]
F2 [ppm]
8
8''
1''
11
12
3'
8'
2''
4'', 6''
3
4
3''
7''
5''
7
3
5
9'
5
1
7'
2'
9
3'', 7''
5''
3
4
5
4'
2'
10'
9
10
9'
7'
13
50
100
150
200
8
7
6
5
4
3



d)



e)



f)

Table S5. NMR assignment of compound **10**

Site	^{13}C /ppm	^{1}H /ppm	Multi-plicity	$J_{(H,H)}$ (Hz)
1	166.05			
2	129.46			
3	129.82	7.86	s	
4	133.61			
5	151.56			
6	122.84	7.34	d	8.2
7	126.72	7.92	d	8.8
8	28.92	3.34	d	7.6
9	121.24	5.28	t	7.1

10	132.80			
11	18.45	1.79	s	
12	26.06	1.77	s	
13	169.90			
14	8.19	2.42	s	
1'	-			
2'	188.40			
3'	67.69			
4'	167.57			
5'	125.24	7.51	d	9.5
6'	112.05	6.77	d	8.9
7'	163.17			
8'	111.78			
9'	152.69			
10'	110.68			
11'	7.49	1.90	m	
1''	42.4	3.4	d	
2''	126.84			
3''	130.78	7.21	d	7.6
4''	125.87	7.09	d	7.6
5''	134.30			
6''	125.87	7.09	d	7.6
7''	130.78	7.21	d	7.6
8''	28.43			
9''	123.76			
7'-OH		10.96	s	
NH		9.93	s	

6. 4-((7-hydroxy-8-methyl-4-oxo-2-((4-(3-(trifluoromethyl)-3H-diazirin-3-yl)benzyl)oxy)-4H-chromen-3-yl)carbamoyl)-2-(3-methylbut-2-en-1-yl)phenyl acetate (11)

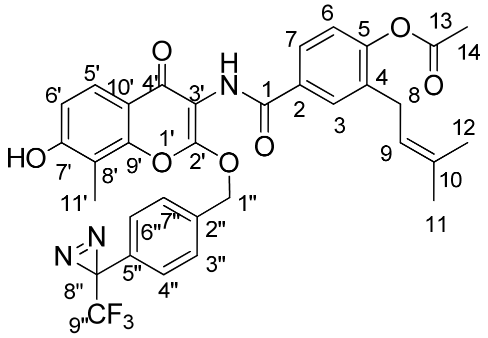
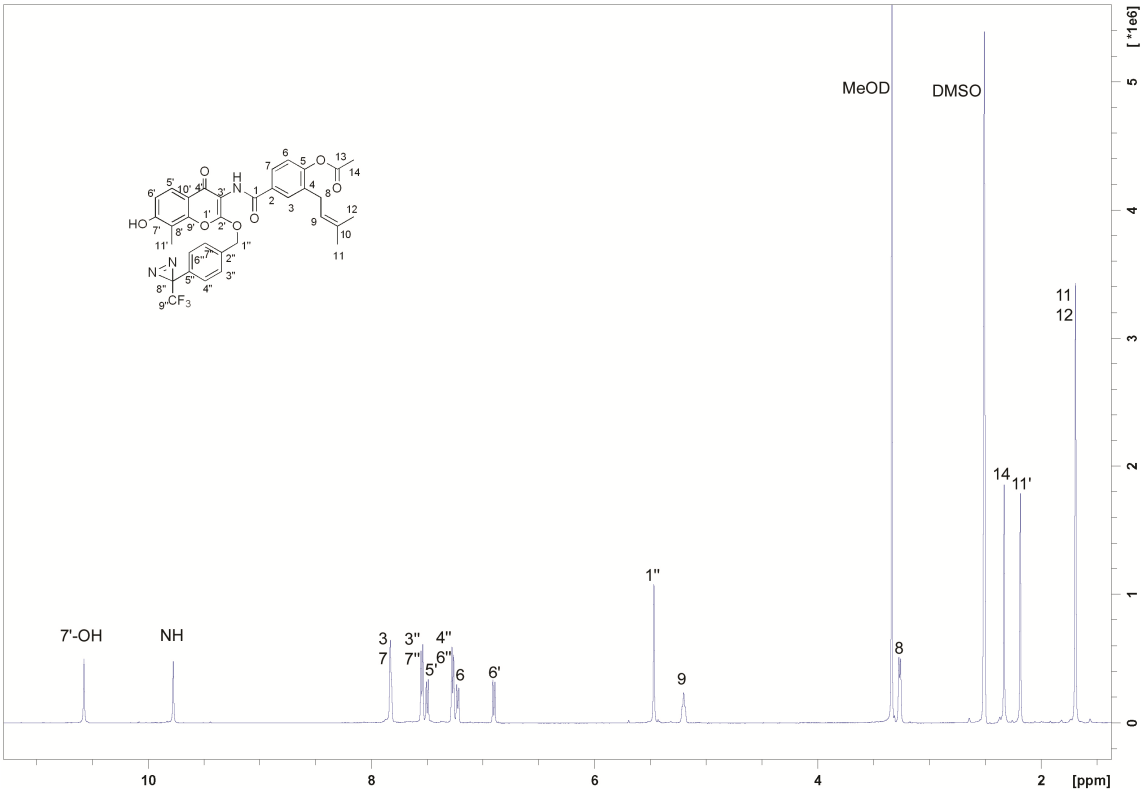
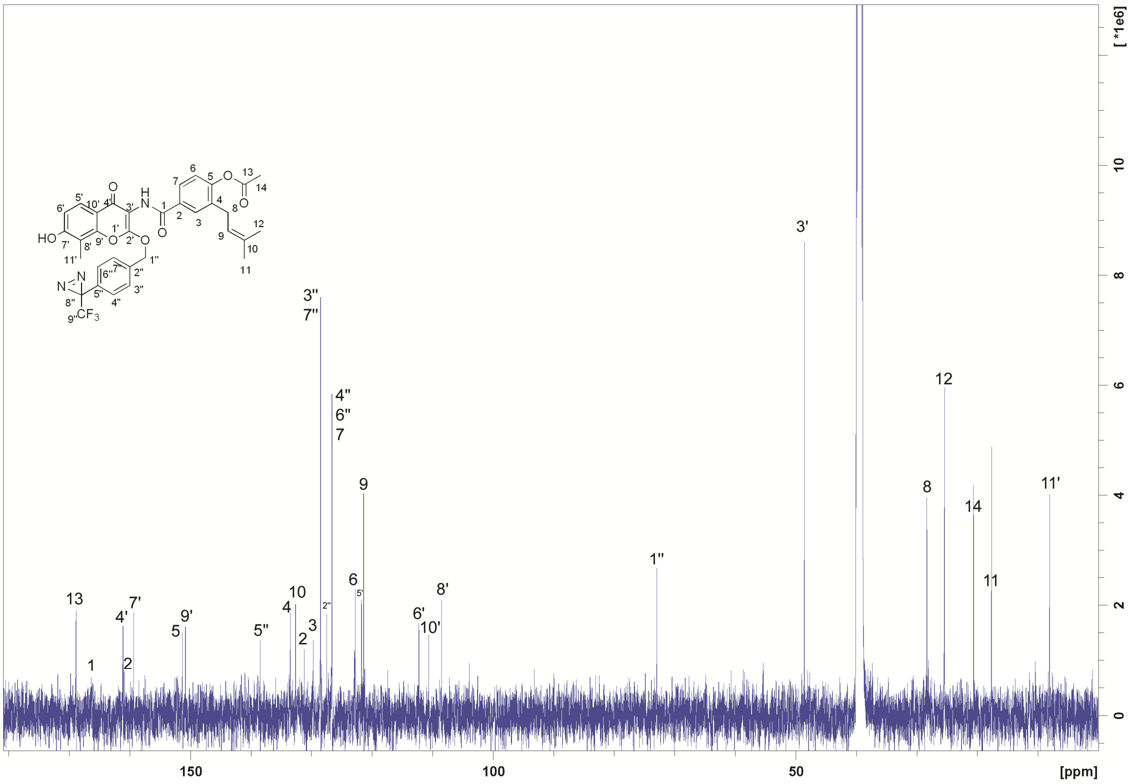


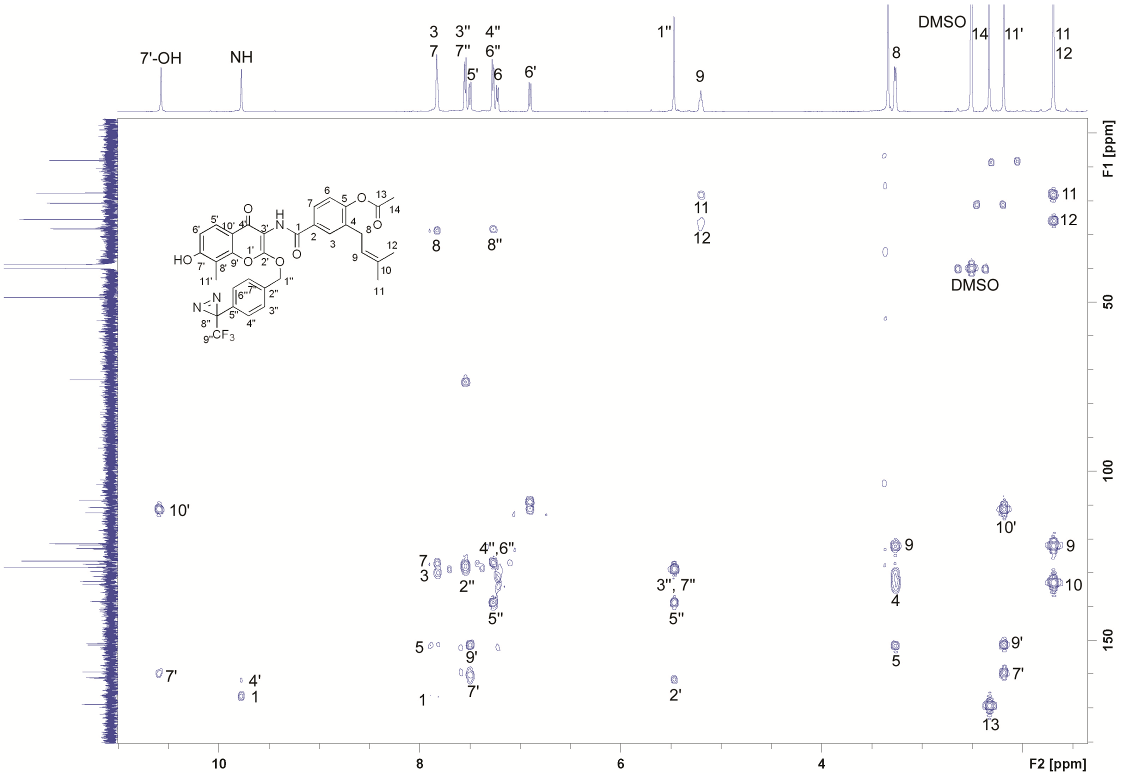
Figure S4. NMR assignment of compound **11**. a) ^{1}HNMR. 7'-OH and NH signals can be seen but no 4'-OH signal b) ^{13}CNMR. c) HMBC. H1'' couples to C2'. d) Zoom in spectrum to show the difference between C2' & C4'. Solvent peaks are not fully labelled. e) Analytical LC show the formation of the product at 7.66 min. f). MS shows the formation of product (636, [M+H^{+}]$^{+}$; 1293, [2M+Na^{+}]$^{+}$; 1928, [2M+Na^{+}]$^{+}$). g) Analytical LC shows the purity of compound **11** after preparative HPLC.


[*1e6]
MeOD
DMSO
7'-OH
NH
3
7
3''
7''
5'
4''
6''
6
6'
1''
9
8
14
11'
11
12
10
8
6
4
2
[ppm]
0
1
2
3
4
5

a)

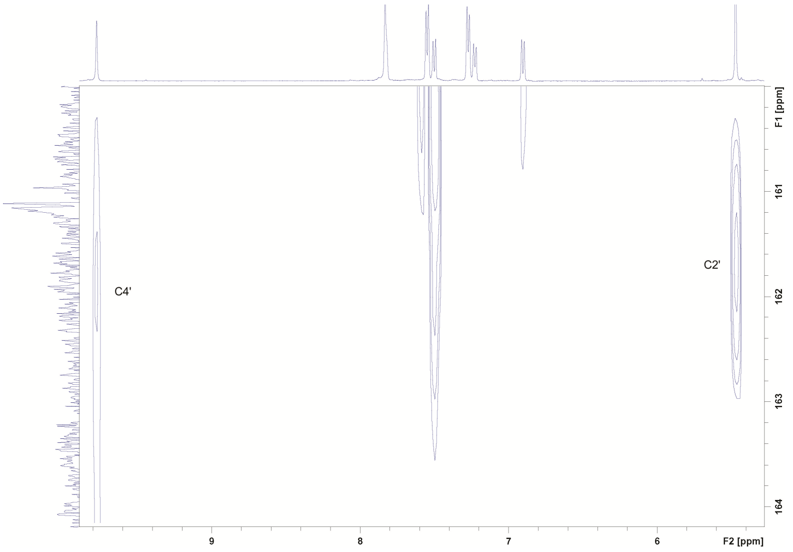

[*1e6]
13
1
4'
2
7'
5
9'
5''
4
10
2
3
2''
3''
7''
4''
6''
7
6
5'
9
6'
10'
8'
1''
3'
8
12
14
11
11'
150
100
50
[ppm]
0
2
4
6
8
10

b)



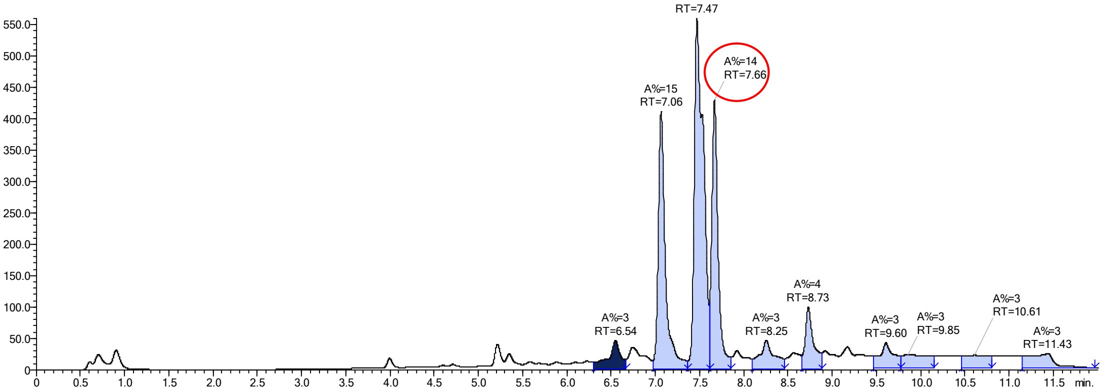
7'-OH
NH
3
7
3''
7''
5'
4''
6''
6
6'
1''
9
8
DMSO
14
11'
11
12
F1 [ppm]
50
100
150
F2 [ppm]
10
8
6
4
2
10'
4''
7'
4'
1
5
9'
1
2''
5''
3'',7''
2'
4
13
HO
N
CF$_3$

c)



C4'
C2'
F1 [ppm]
161
162
163
164
9
8
7
6
F2 [ppm]

d)



mAU
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500.0
450.0
400.0
350.0
300.0
250.0
200.0
150.0
100.0
50.0
0
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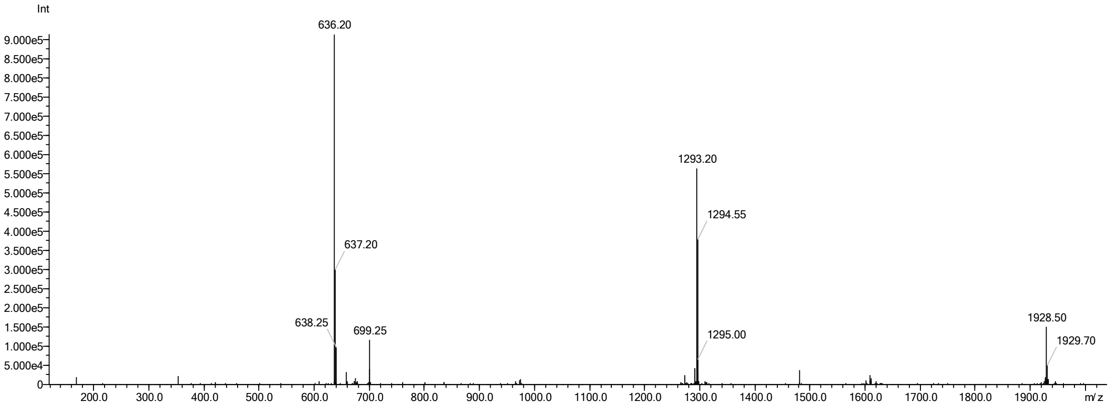
RT=7.47
A%=14
RT=7.66
A%=15
RT=7.06
A%=4
RT=8.73
A%=3
RT=6.54
A%=3
RT=8.25
A%=3
RT=9.60
A%=3
RT=9.85
A%=3
RT=10.61
A%=3
RT=11.43
0
0.5
1.0
1.5
2.0
2.5
3.0
3.5
4.0
4.5
5.0
5.5
6.0
6.5
7.0
7.5
8.0
8.5
9.0
9.5
10.0
10.5
11.0
11.5
min.

e)



f)

g)

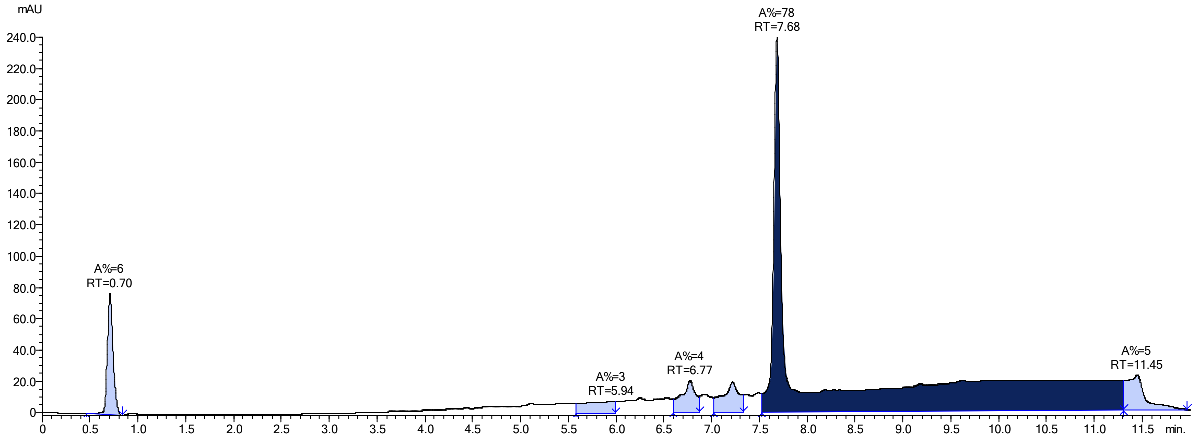


Table S6. NMR assignment of compound **11**.

Site	^{13}C /ppm	^{1}H /ppm	Multi-plicity	$J_{(H,H)}$ (Hz)
1	166.23			
2	131.17			
3	129.70	7.83	s	
4	133.49			
5	151.38			
6	122.76	7.22	d	8.8
7	126.62	7.82	d	5.8
8	28.39	3.27	d	7.4
9	121.34	5.20	t	5.7
10	132.63			
11	17.59	1.69	s	
12	25.36	1.69	s	
13	168.90			
14	20.81	2.33	s	
1'	-			
2'	160.97			
3'	48.71			
4'	161.16			
5'	121.75	7.50	d	8.9

6'	112.27	6.90	d	8.8
7'	159.37			
8'	108.52			
9'	150.83			
10'	110.66			
11'	8.12	2.19	s	
1''	73.10	5.46	s	
2''	127.50			
3''	128.52	7.55	d	7.5
4''	126.62	7.27	d	8.1
5''	138.46			
6''	126.62	7.27	d	8.1
7''	128.52	7.55	d	7.5
8''	28.56			
9''	124.0			

7. (2S,3R,5R,6R)-2-((3-(4-acetoxy-3-(3-methylbut-2-en-1-yl)benzamido)-8-methyl-4-oxo-2-((4-(3-(trifluoromethyl)-3H-diazirin-3-yl)benzyl)oxy)-4H-chromen-7-yl)oxy)-6-(acetoxymethyl)tetrahydro-2H-pyran-3,4,5-triyl triacetate (12)

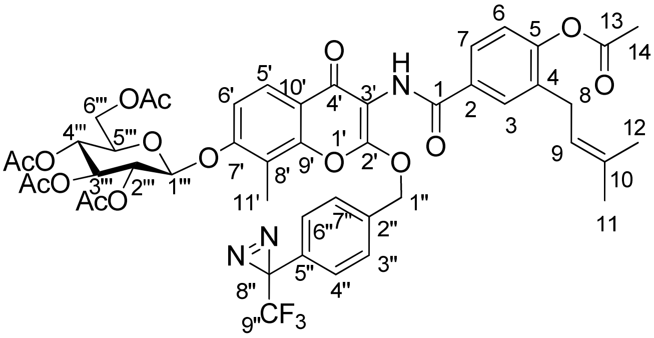
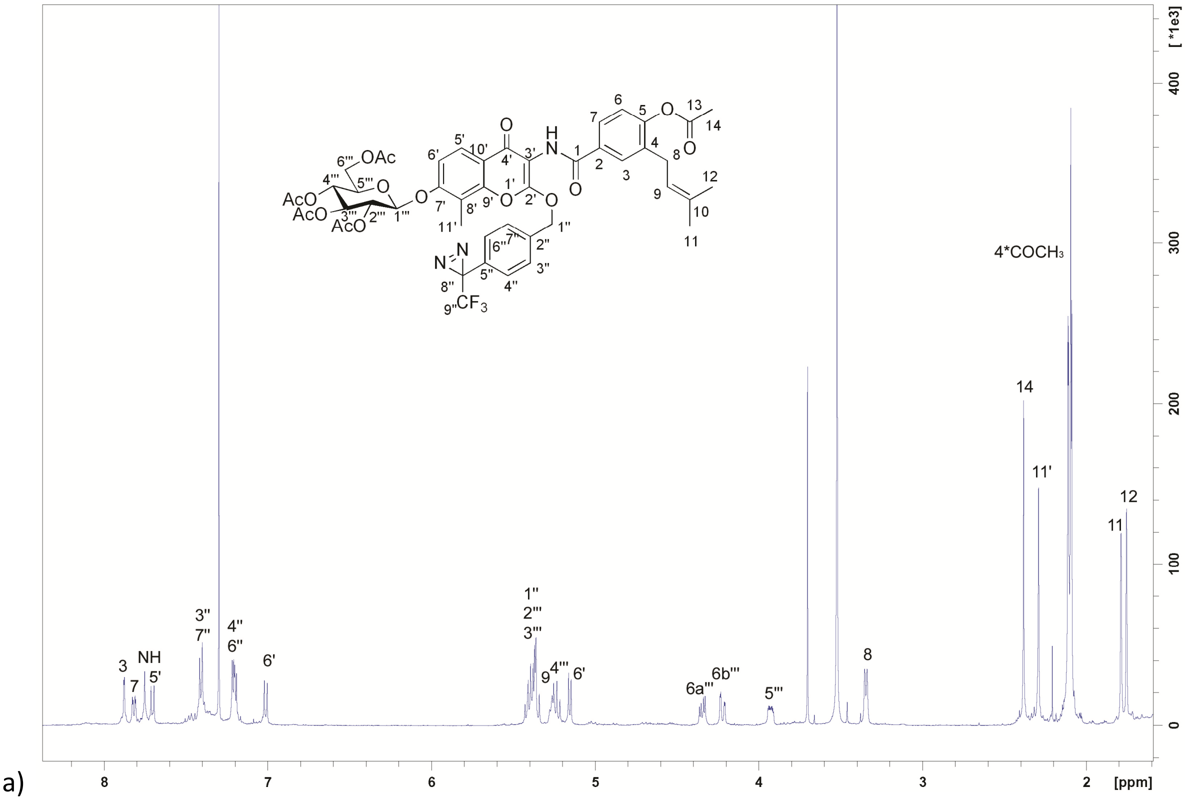
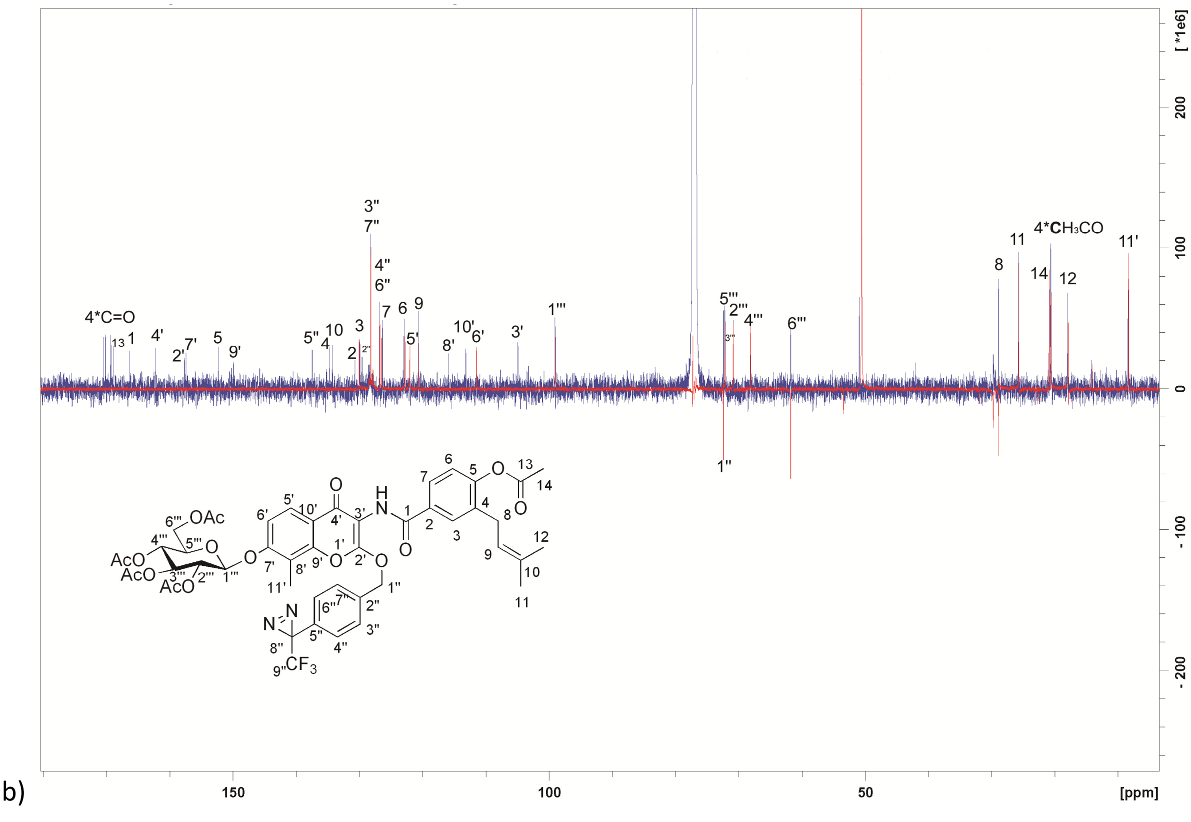
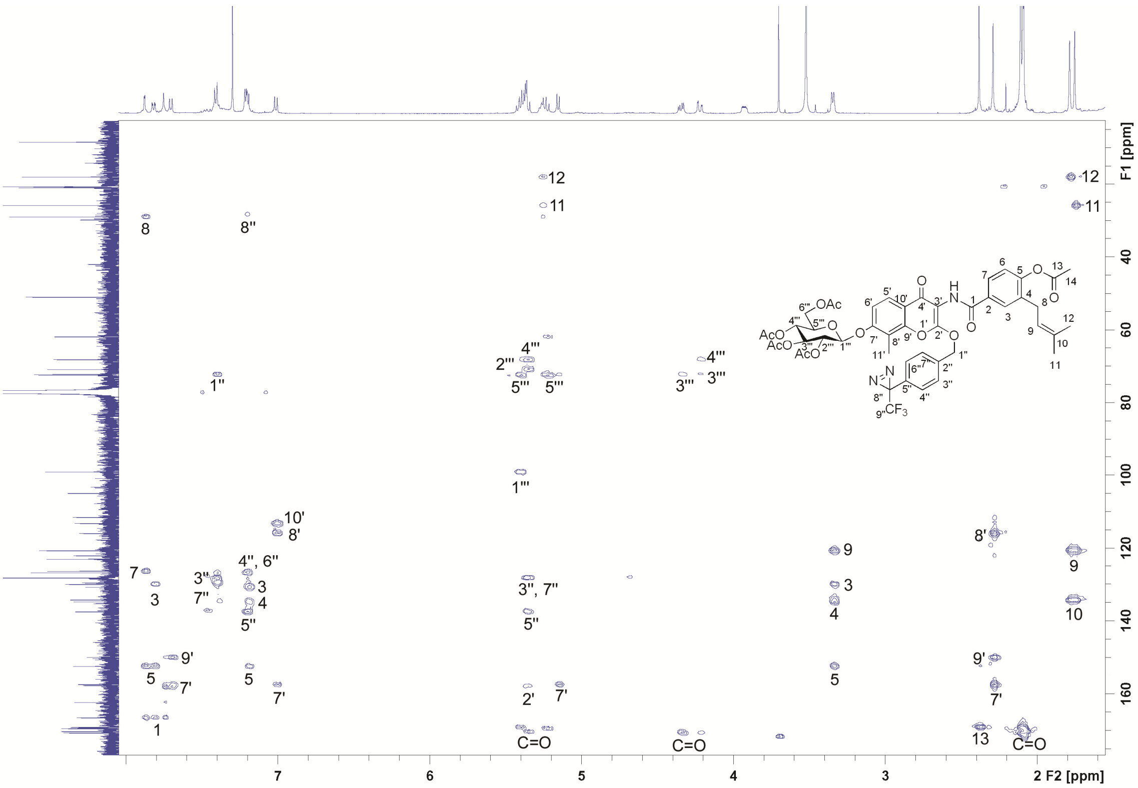


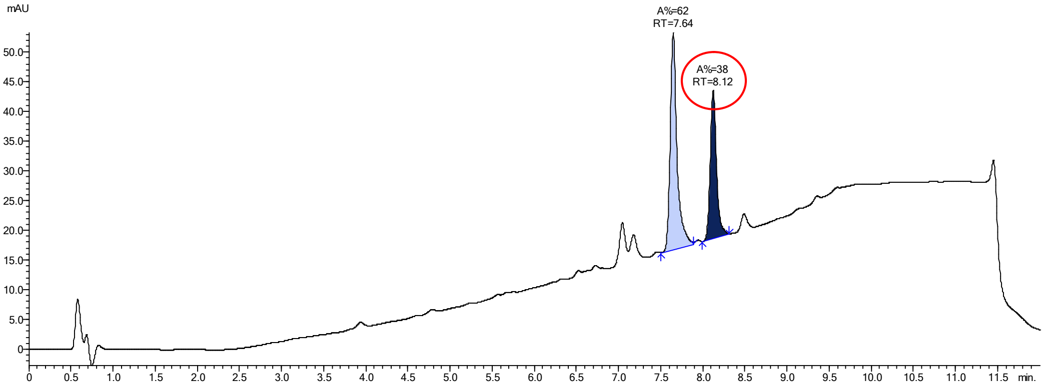
Figure S5. NMR assignment of compound **12**. a) ^{1}H-NMR. b) Combined ^{13}C (black) and DEPT135 (red) NMR. c) HMBC. Long range coupling between H1''' and C7'; H1'' and C2'. Solvent peaks are not fully labelled. d) Analytical LC shows the formation of product in the present of starting material. e) MS shows the formation of product (966, [M+H^{+}]$^{+}$, 988, [2M+Na^{+}]$^{+}$, 1953, [3M+Na^{+}]$^{+}$). f) Analytical LC shows the purity of compound **12** after preparative HPLC.


a)
[*1e3]
400
300
200
100
0
4*COCH₃
14
11'
12
11
3
7
NH
5'
3''
7''
4''
6''
6'
1''
2'''
3'''
9
4'''
6'
6a'''
6b'''
5'''
8
8
7
6
5
4
3
2
[ppm]

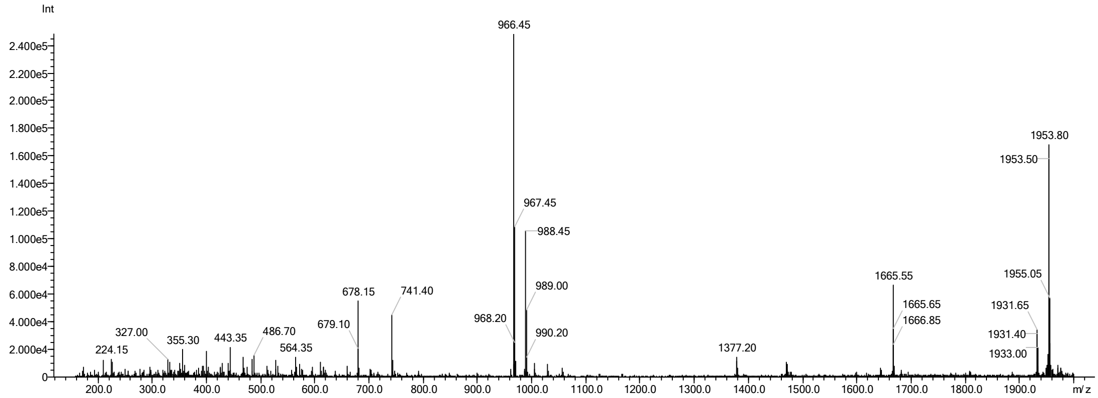

b)
[*1e6]
200
100
0
- 100
- 200
4*C=O
13
1
4'
2'
7'
5
9'
5''
10
4
3
2
2''
3''
7''
4''
6''
7
6
5'
9
8'
10'
6'
3'
1'''
5'''
2'''
3'''
4'''
6'''
1''
8
11
14
4*CH₃CO
12
11'
150
100
50
[ppm]


F1 [ppm]
20
40
60
80
100
120
140
160
F2 [ppm]
7
6
5
4
3
2
12
11
8
8''
1''
4'''
2'''
5'''
5'''
4'''
3'''
3'''
1'''
10'
8'
4'', 6''
7
3''
7''
3
4
5''
3
3'', 7''
5''
9
3
4
8'
9
10
9'
5
7'
5
7'
2'
7'
5
9'
7'
1
C=O
C=O
13
C=O
AcO
AcO
AcO
OAc
N
N
CF3
O
H
N

c)


mAU
50.0
45.0
40.0
35.0
30.0
25.0
20.0
15.0
10.0
5.0
0
A%=62
RT=7.64
A%=38
RT=8.12
0 0.5 1.0 1.5 2.0 2.5 3.0 3.5 4.0 4.5 5.0 5.5 6.0 6.5 7.0 7.5 8.0 8.5 9.0 9.5 10.0 10.5 11.0 11.5 min.

d)


Int
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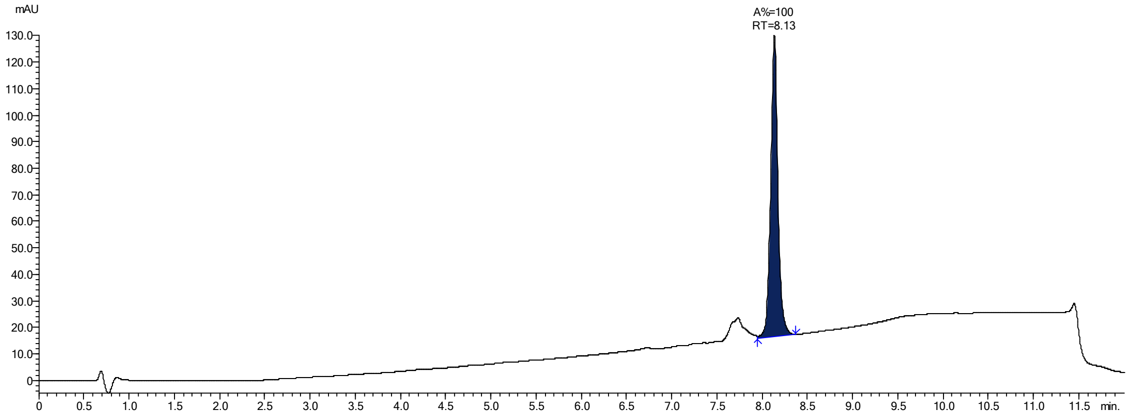
2.200e5
2.000e5
1.800e5
1.600e5
1.400e5
1.200e5
1.000e5
8.000e4
6.000e4
4.000e4
2.000e4
0
966.45
967.45
988.45
989.00
968.20
990.20
678.15
741.40
679.10
327.00
355.30
443.35
486.70
564.35
224.15
1377.20
1665.55
1665.65
1666.85
1953.80
1953.50
1955.05
1931.65
1931.40
1933.00
200.0 300.0 400.0 500.0 600.0 700.0 800.0 900.0 1000.0 1100.0 1200.0 1300.0 1400.0 1500.0 1600.0 1700.0 1800.0 1900.0 m/z

e)



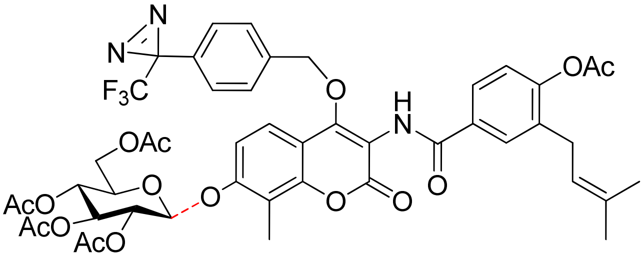
f)

Table S7. NMR assignment of compound **12**

Site	^{13}C /ppm	^{1}H /ppm	Multi-plicity	$J_{(H,H)}$ (Hz)
1	166.62			
2	130.82			
3	129.97	7.88	d	2.33
4	134.78			
5	152.50			
6	123.11	7.20	d	8.33
7	126.38	7.82	dd	2.46, 8.49
8	28.92	3.34	d	7.02
9	120.78	5.25	m	
10	134.27			
11	25.71	1.79	s	
12	17.90	1.75	s	
13	168.98			
14	20.82	2.38	s	
1'	-			
2'	157.78			
3'	104.95			
4'	162.43			
5'	122.03	7.70	d	9.02
6'	111.62	7.01	d	9.07
7'	157.33			
8'	116.11			
9'	150.00			
10'	113.19			
11'	8.4	2.29	s	
1''	72.49	5.38	m	
2''	129.64			
3''	128.26	7.50	d	8.60
4''	126.82	7.21	d	8.21
5''	137.73			
6''	126.82	7.21	d	8.21
7''	128.26	7.50	d	8.60
8''	28.19			
9''	126			

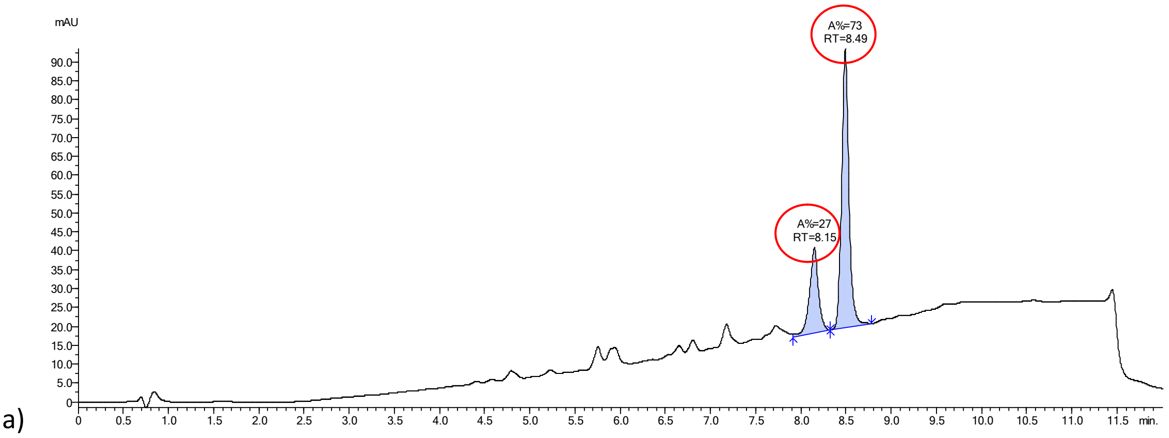
1'''	99.22	5.15	d	7.68
2'''	70.89	5.39	m	
3'''	72.18	5.36	m	
4'''	68.22	5.24	m	
5'''	72.23	3.93	m	
6a'''	62.01	4.34	dd	4.66, 12.41
6b'''	62.01	4.22	dd	3.10, 12.40
COCH3 *4		2.11-2.09	s	
COCH3 *4	20.69			
COCH3	170.51, 170.22, 169.41, 169.21			
NH		7.75	s	

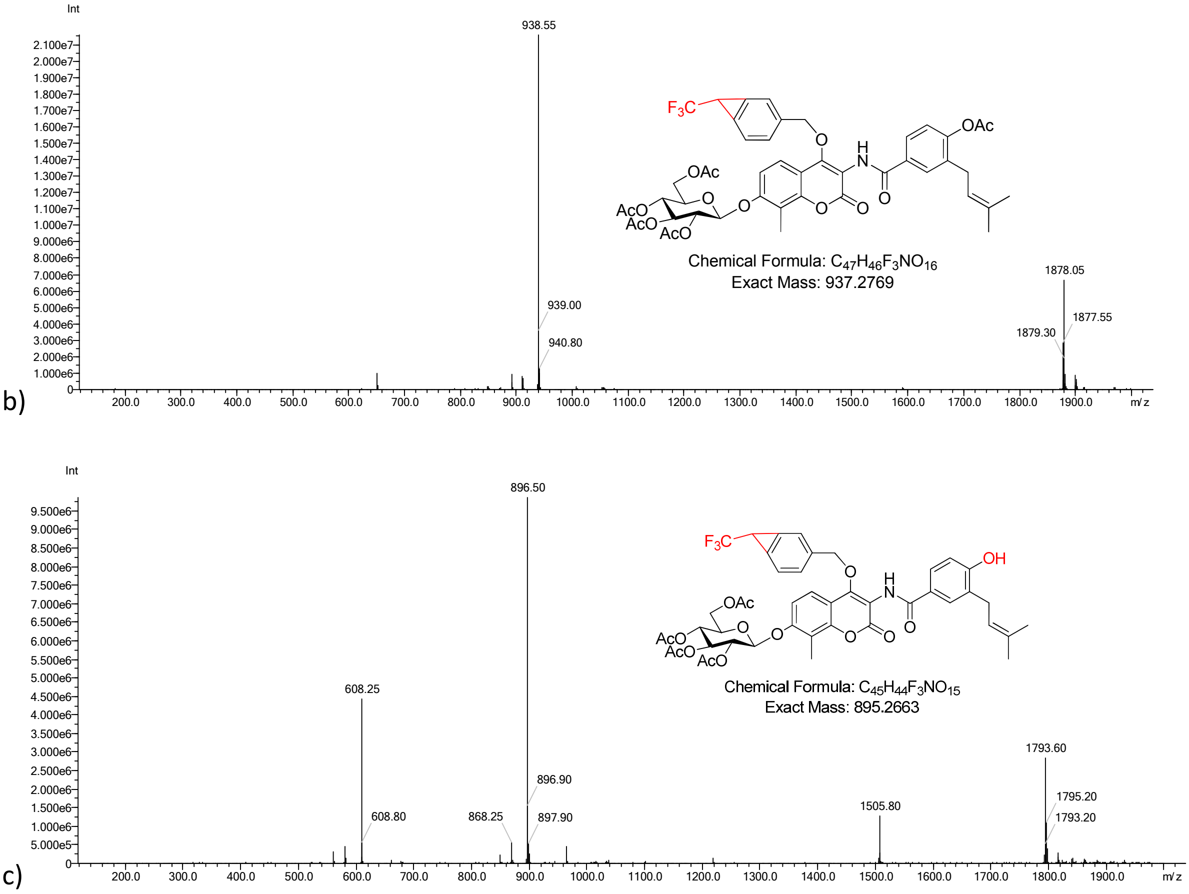
8. Glycosylation of compound 10



The same procedure was followed in the synthesis of compound **12**. However, no desired glycosylation product formed but new reactions with N_2 removal and possible insert reactions were discovered by LCMS (Fig. S5). Structures were proposed according to their masses.

Figure S6. Analytical LC/MS result of the glycosylation of compound **10**. a) Analytical LC indicates the formation of 2 products. b) MS of peak at 8.49 min and possible structure. c) MS of peak at 8.15 min and possible structure.





9. Synthesis of (2S,3R,5R,6R)-2-((3-(4-acetoxy-3-(3-methylbut-2-en-1-yl)benzamido)-7-hydroxy-8-methyl-2-oxo-2H-chromen-4-yl)oxy)-6-(acetoxymethyl)tetrahydro-2H-pyran-3,4,5-triyl triacetate (14)

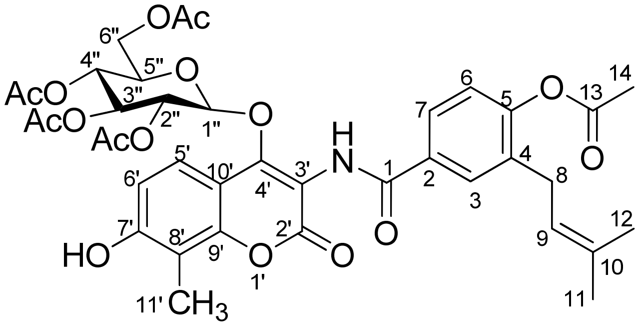
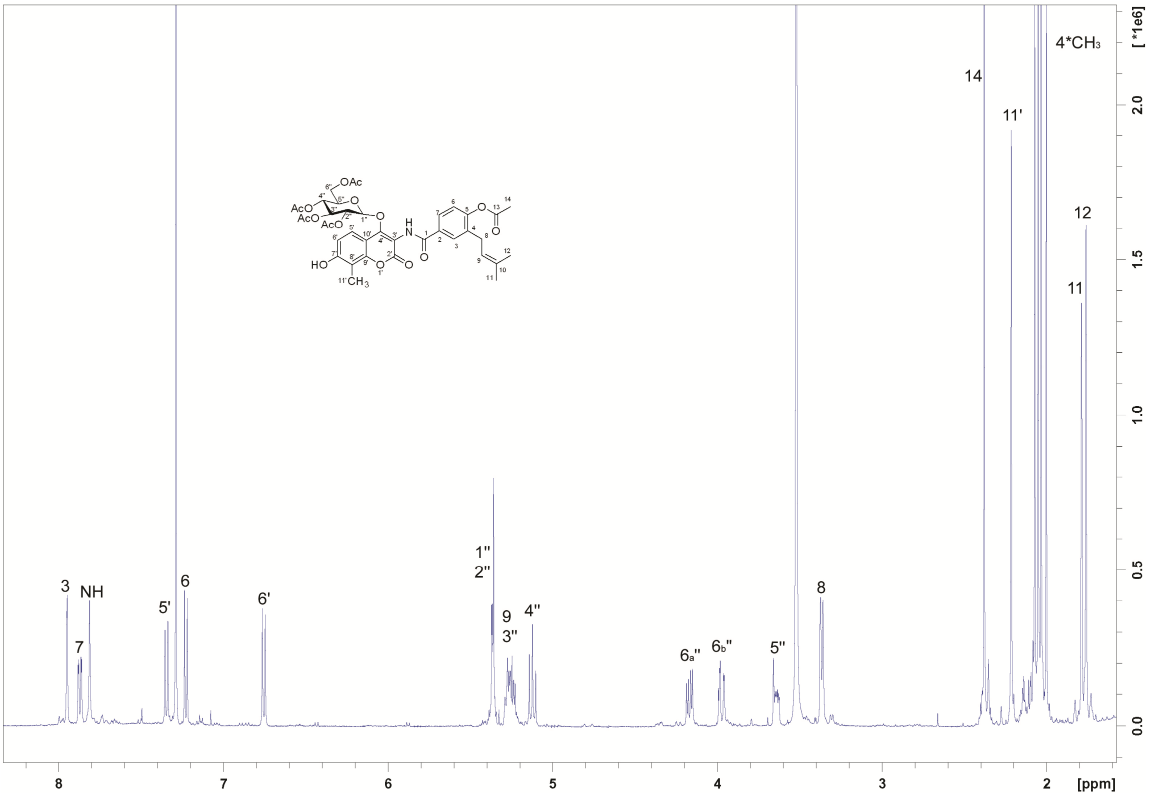
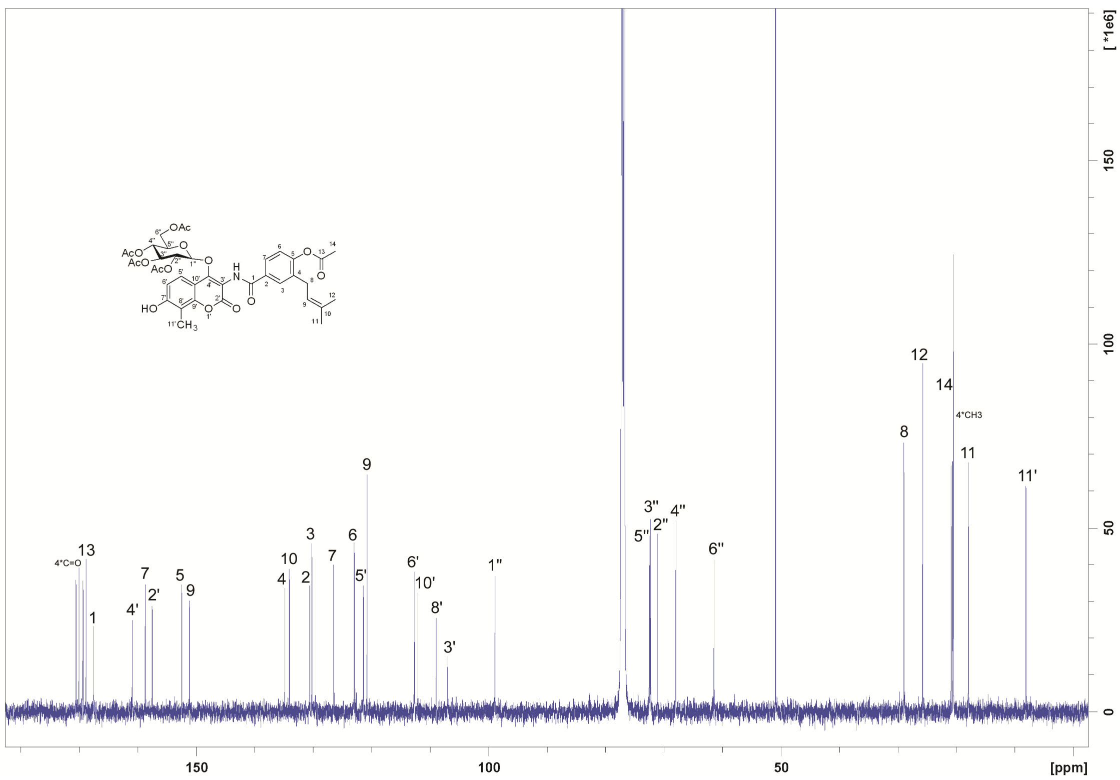


Figure S7. NMR assignment of compound **14**. a) ^{1}H-NMR. b) ^{13}C-NMR. c) HMBC. Long range coupling between H1" and C4' is not strong enough to be visible but could be found in the next product. d) Analytical LC shows the formation of products in the present of starting material. e) MS shows the formation of product (7.07 min) (766, $[M\text{-}H^+]^-$, 1533, $[2M\text{-}H^+]^-$). f) Analytical LC shows the purity of compound **14** after preparative HPLC.



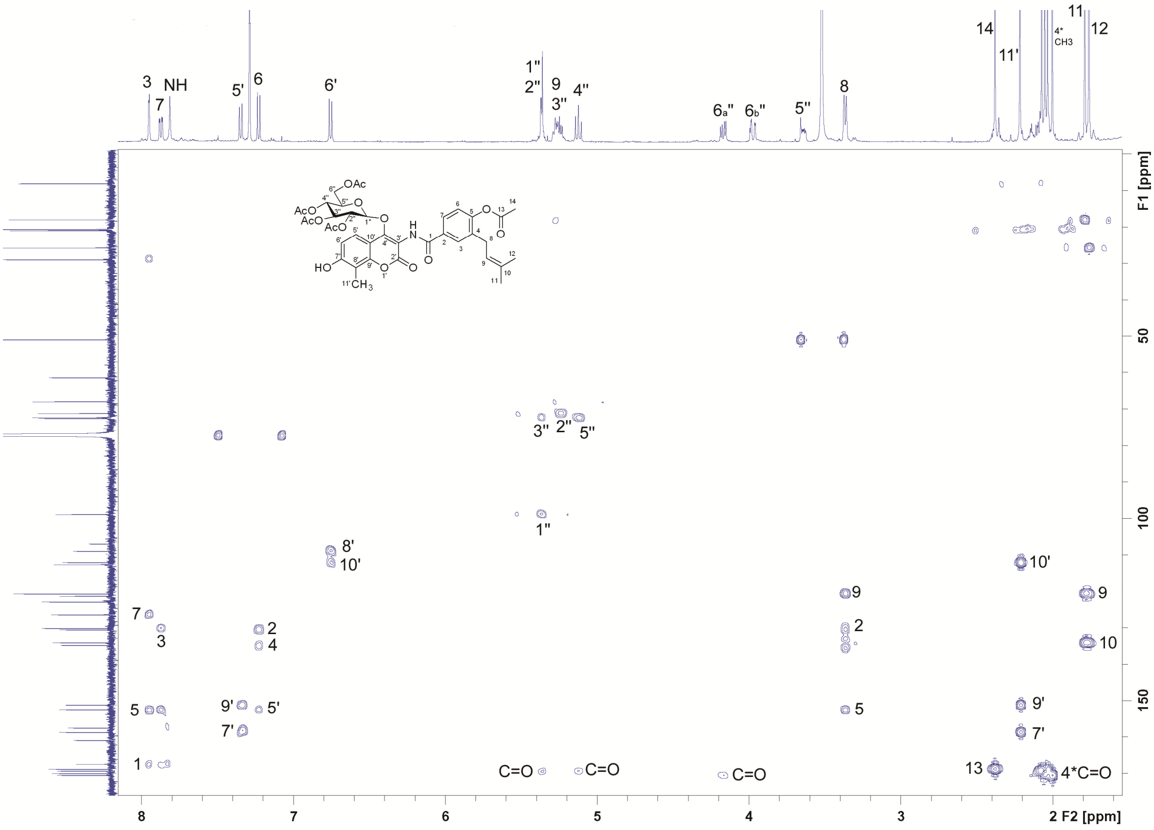
3
NH
7
5'
6
6'
1''
2''
9
3''
4''
6a''
6b''
5''
8
14
11'
4*CH3
12
11
[*1e6]
2.0
1.5
1.0
0.5
0.0
8
7
6
5
4
3
2
[ppm]

a)



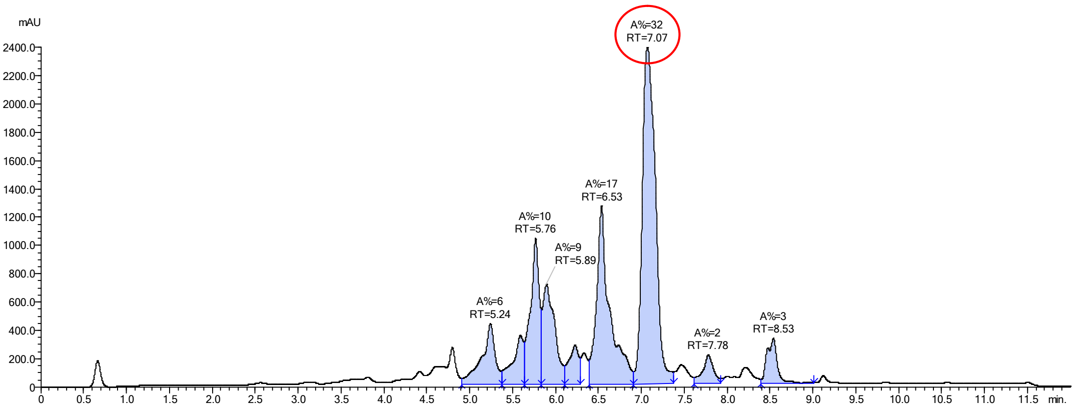
4*C=O
13
1
7
2'
4'
5
9
10
4
3
2
7
6
5'
9
6'
10'
8'
3'
1''
3''
5''
2''
4''
6''
8
12
14
4*CH3
11
11'
[*1e6]
150
100
50
0
150
100
50
[ppm]

b)



3
NH
7
5'
6
6'
1''
2''
9
3''
4''
6a''
6b''
5''
8
14
11'
4*
CH3
11
12
F1 [ppm]
50
100
150
3'' 2'' 5''
1''
8'
10'
10'
9
9
7
3
2
4
2
10
5
9'
5'
5
9'
7'
7'
1
C=O
C=O
C=O
13
4*C=O
8
7
6
5
4
3
2 F2 [ppm]
OAc
AcO
AcO
AcO
HO
CH3
O
H
N

c)



mAU
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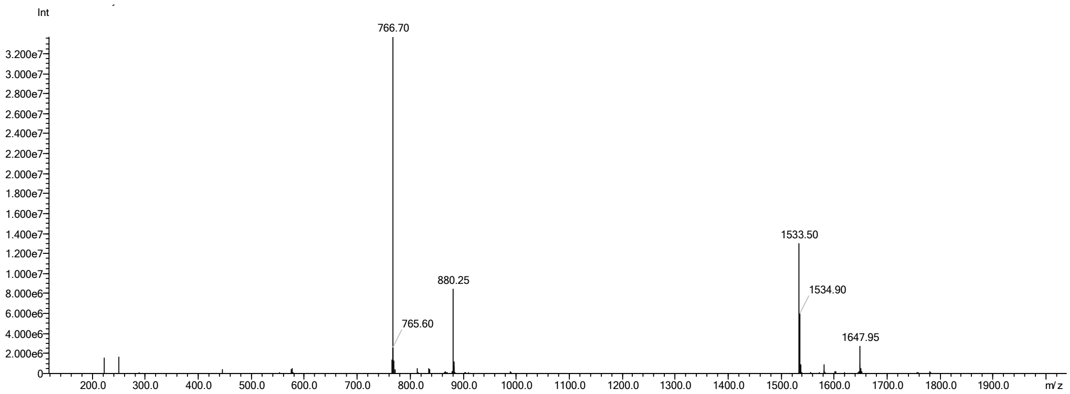
A%=17
RT=6.53
A%=10
RT=5.76
A%=9
RT=5.89
A%=6
RT=5.24
A%=2
RT=7.78
A%=3
RT=8.53
2400.0
2200.0
2000.0
1800.0
1600.0
1400.0
1200.0
1000.0
800.0
600.0
400.0
200.0
0
0
0.5
1.0
1.5
2.0
2.5
3.0
3.5
4.0
4.5
5.0
5.5
6.0
6.5
7.0
7.5
8.0
8.5
9.0
9.5
10.0
10.5
11.0
11.5
min.

d)



Int
766.70
765.60
880.25
1533.50
1534.90
1647.95
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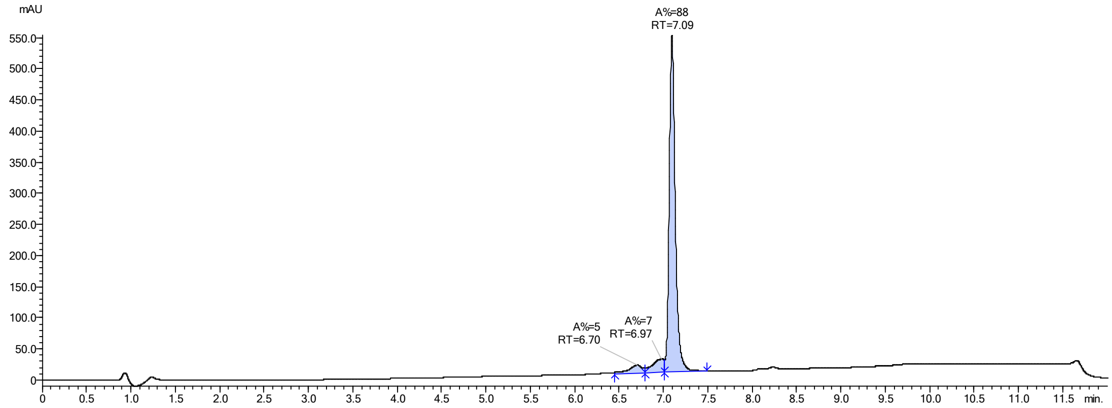
3.000e7
2.800e7
2.600e7
2.400e7
2.200e7
2.000e7
1.800e7
1.600e7
1.400e7
1.200e7
1.000e7
8.000e6
6.000e6
4.000e6
2.000e6
0
200.0
300.0
400.0
500.0
600.0
700.0
800.0
900.0
1000.0
1100.0
1200.0
1300.0
1400.0
1500.0
1600.0
1700.0
1800.0
1900.0
m/z

e)



f)

Table S8. NMR assignment of compound **14**

Site	^{13}C /ppm	^{1}H /ppm	Multi-plicity	$J_{(H,H)}$ (Hz)
1	167.51			
2	130.57			
3	130.19	7.95	s	
4	134.87			
5	152.49			
6	123.00	7.23	d	9.15
7	126.49	7.87	d	8.56
8	29.05	3.37	d	7.85
9	120.79	5.27	m	
10	134.06			
11	25.76	1.79	s	
12	17.96	1.76	S	
13	168.85			
14	20.55	2.38	s	
NH		7.81	s	
1'	-			
2'	157.55			
3'	107.02			
4'	160.98			
5'	121.41	7.35	d	9.18
6'	112.64	6.75	d	9.21
7'	158.71			
8'	109.01			
9'	151.16			
10'	112.10			
11'	8.08	2.21	s	
1''	98.95	5.36	m	
2''	71.20	5.36	m	
3''	72.35	5.24	m	
4''	67.98	5.12	t	9.39
5''	72.57	3.64	m	
6a''	61.49	4.17	dd	6.15, 12.31
6b''	61.49	4.24	dd	2.53, 12.03
$\underline{CH_3}CO$	20.54-20.63	2.07, 2.05, 2.03, 2.00	s	

CH3<u>CO</u>	170.56, 170.05, 169.39, 169.33			

10. (3R,5R,6R)-2-((3-(4-acetoxy-3-(3-methylbut-2-en-1-yl)benzamido)-8-methyl-2-oxo-7-((4-(3-(trifluoromethyl)-3H-diazirin-3-yl)benzyl)oxy)-2H-chromen-4-yl)oxy)-6-(acetoxymethyl)tetrahydro-2H-pyran-3,4,5-triyl triacetate (15)

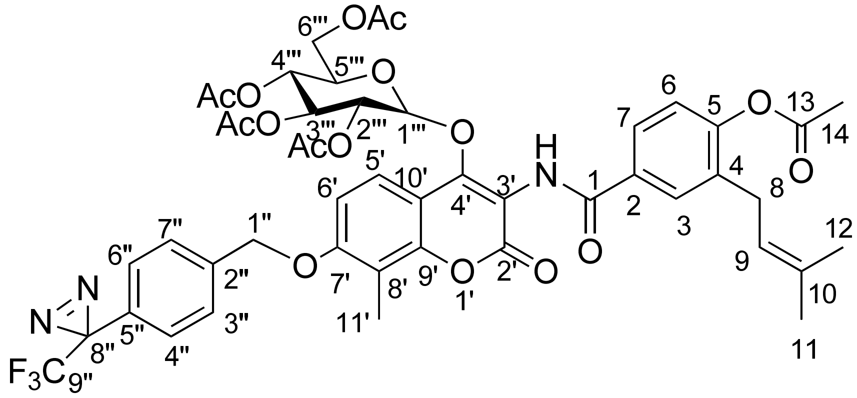
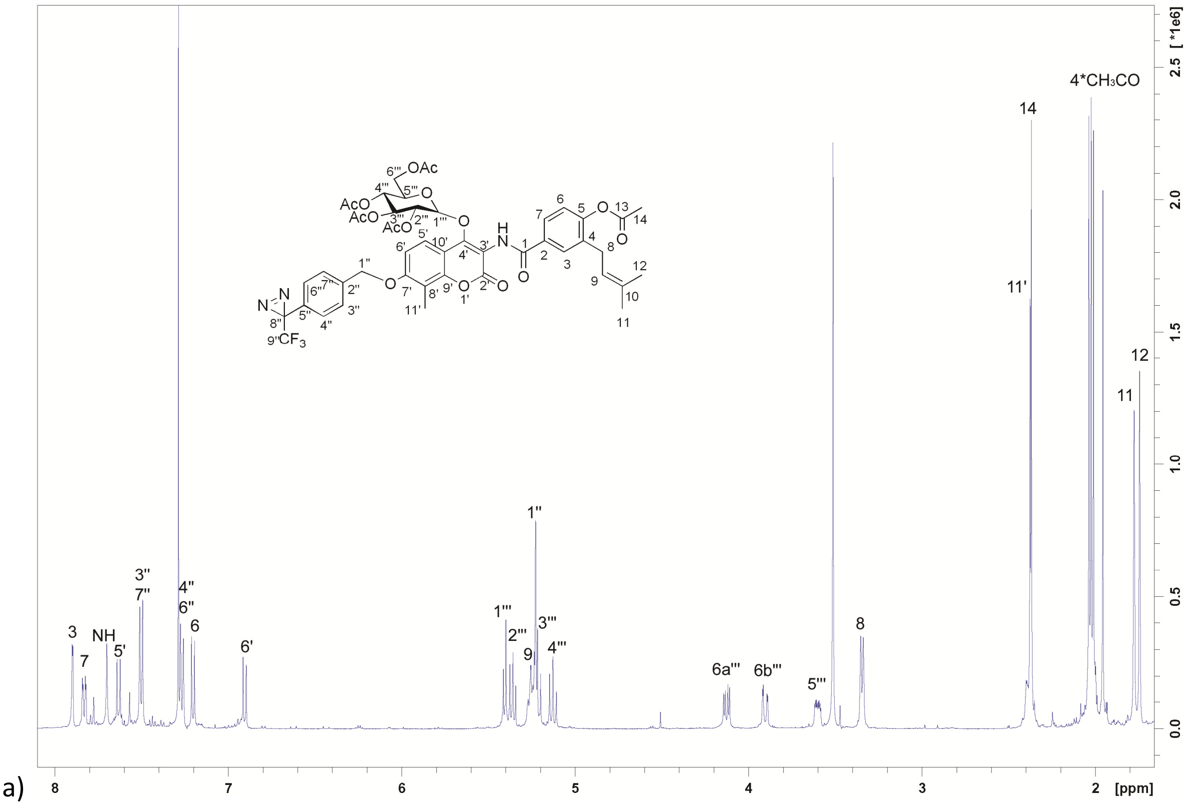
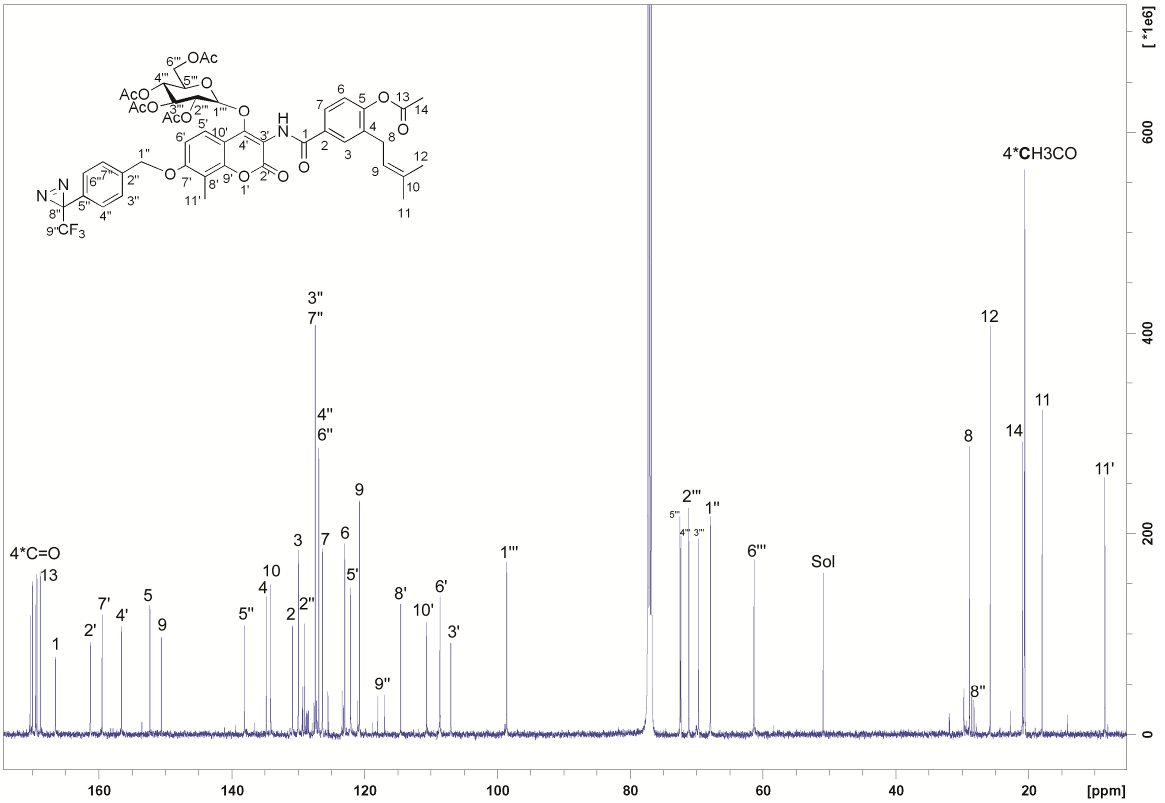
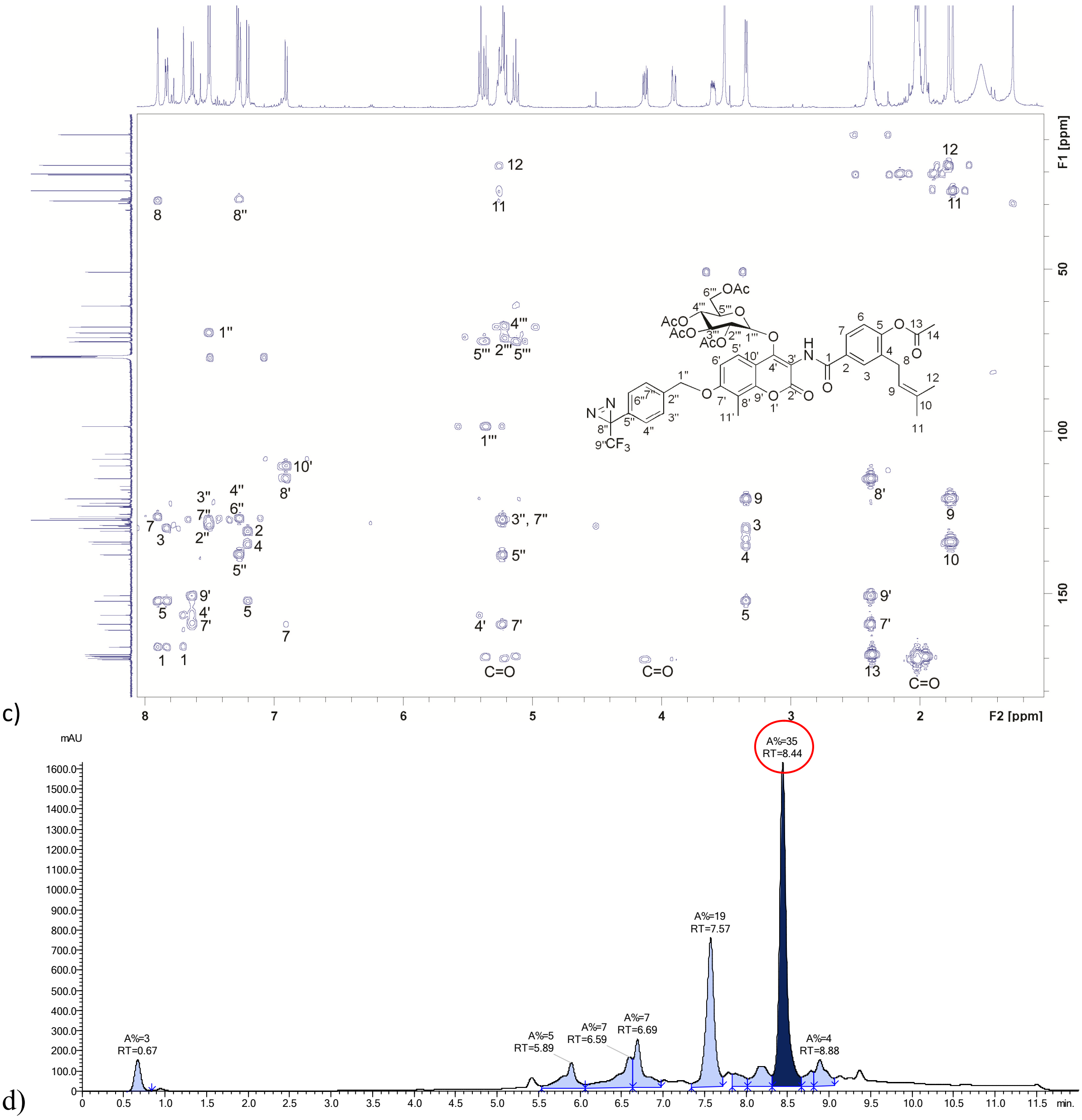


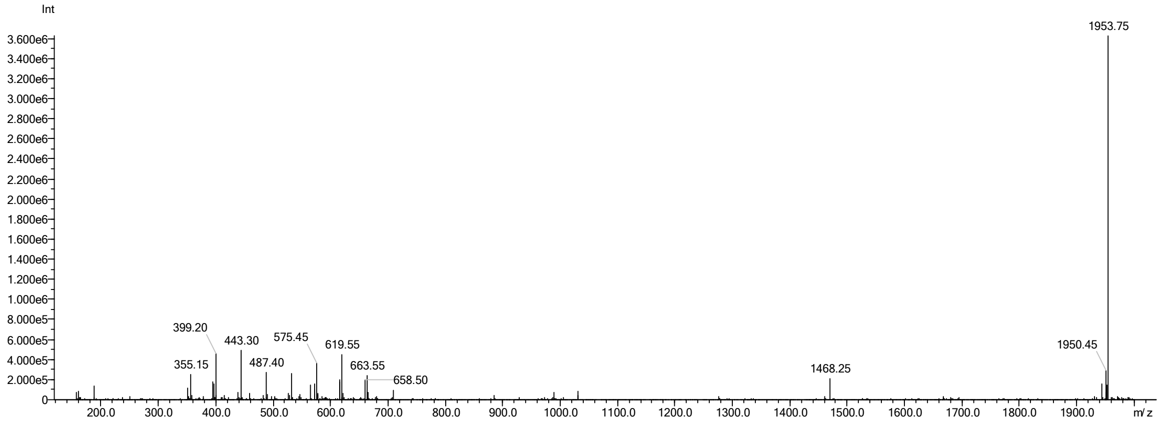
Figure S8. NMR assignment of compound **15**. a) ^{1}H-NMR. b) ^{13}C-NMR. c) HMBC. Long range coupling between H1''' and C4', H1" and C7' can be seen proves the structure of compound **14**. d) Analytical LC shows the formation of products in the present of starting material. e) MS shows the formation of product (8.44 min) (1953, [2M+Na^{+}]$^{+}$). f) Analytical LC shows the purity of compound **15** after preparative HPLC.



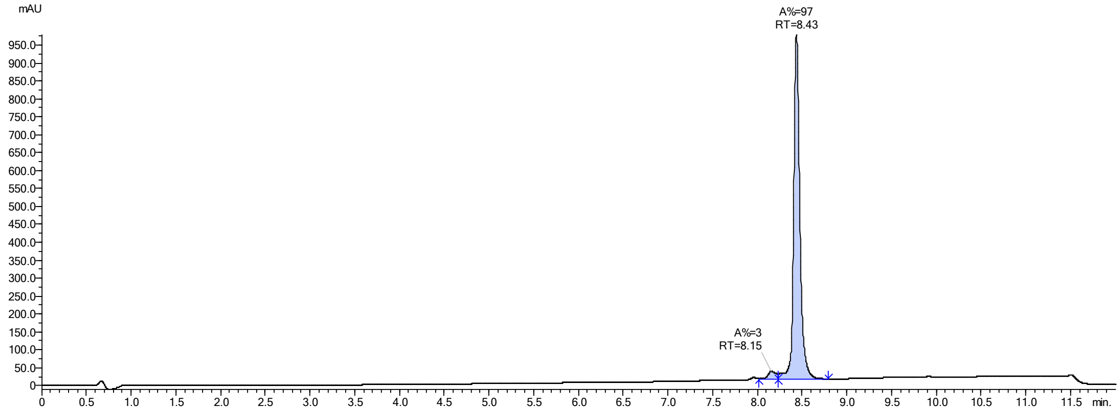

4*C=O
13
1
2'
7'
4'
5
9
5''
4
10
2
3
2''
3''
7''
4''
6''
7
6
5'
9
9''
8'
10'
6'
3'
1'''
5'''
4'''
3'''
2'''
1''
6'''
Sol
8
8''
12
14
4*CH3CO
11
11'
[*1e6]
600
400
200
0
160
140
120
100
80
60
40
20
[ppm]
OAc
AcO
AcO
AcO
NH
CF3

b)


c)
F1 [ppm]
F2 [ppm]
8
7
6
5
4
3
2
50
100
150
12
11
8
8''
1''
4'''
5'''
2'''
5'''
1'''
10'
8'
3''
7''
2''
4''
6''
7
3
2
4
5''
3'', 7''
5''
9
3
4
8'
9
10
9'
4'
7'
5
5
7
4'
7'
5
9'
7'
1
1
C=O
C=O
13
C=O
OAc
AcO
AcO
AcO
O
NH
N=N
CF3
d)
mAU
1600.0
1500.0
1400.0
1300.0
1200.0
1100.0
1000.0
900.0
800.0
700.0
600.0
500.0
400.0
300.0
200.0
100.0
0
A%=3
RT=0.67
A%=5
RT=5.89
A%=7
RT=6.59
A%=7
RT=6.69
A%=19
RT=7.57
A%=35
RT=8.44
A%=4
RT=8.88
0
0.5
1.0
1.5
2.0
2.5
3.0
3.5
4.0
4.5
5.0
5.5
6.0
6.5
7.0
7.5
8.0
8.5
9.0
9.5
10.0
10.5
11.0
11.5
min.



e)



f)

Table S9. NMR assignment of compound **15**

Site	^{13}C /ppm	^{1}H /ppm	Multi-plicity	$J_{(H,H)}$ (Hz)
1	166.50			
2	130.84			
3	129.95	7.89	s	
4	134.77			
5	152.29			
6	122.98	7.20	d	8.42
7	126.32	7.83	d	8.91
8	28.93			
9	120.77	5.26	m	
10	134.12			
11	25.75	1.78	s	
12	18.00	1.75	S	
13	168.84			
14	20.89	2.37	s	
1'	-			
2'	161.29			
3'	106.98			
4'	156.61			
5'	122.08	7.63	d	9.22
6'	108.63	6.90	d	8.76
7'	159.49			
8'	114.54			

9'	150.58			
10'	110.65			
11'	8.48	2.34	s	
1''	69.67	5.23	s	
2''	129.03			
3''	127.42	7.50	d	8.64
4''	126.89	7.26	d	8.21
5''	138.08			
6''	126.89	7.26	d	8.21
7''	127.42	7.50	d	8.64
8''	28.56			
9''	117.37			
1'''	98.57	5.40	d	8.63
2'''	71.15	5.36	t	7.90
3'''	72.34	5.22	m	
4'''	67.86	5.13	t	8.77
5'''	72.46	3.64	m	
6a'''	61.34	4.13	dd	5.69, 12.8
6b'''	61.34	3.90	dd	2.13, 12.09
NH		7.70	s	
CH3CO		2.03, 2.03, 2.01, 1.96	s	
$\underline{C}$H3CO	20.62, 20.55, 20.55, 20.53			
CH3$\underline{C}$O	170.34, 169.98, 169.52, 169.33			

11. 4-hydroxy-N-(8-methyl-2-oxo-7-((4-(3-(trifluoromethyl)-3H-diazirin-3-yl)benzyl)oxy)-4-(((3R,5S,6R)-3,4,5-trihydroxy-6-(hydroxymethyl)tetrahydro-2H-pyran-2-yl)oxy)-2H-chromen-3-yl)-3-(3-methylbut-2-en-1-yl)benzamide (2) and 4-hydroxy-N-(4-hydroxy-8-methyl-2-oxo-7-((4-(3-(trifluoromethyl)-3H-diazirin-3-yl)benzyl)oxy)-2H-chromen-3-yl)-3-(3-methylbut-2-en-1-yl)benzamide (3)

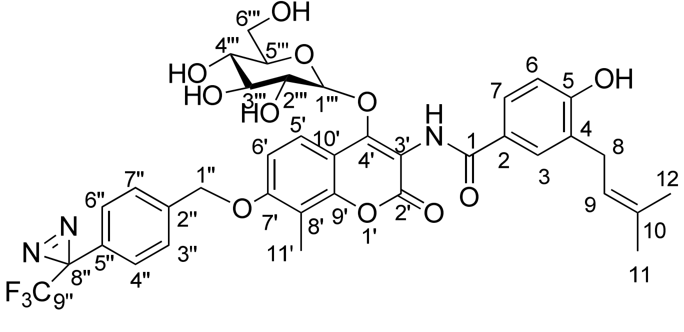
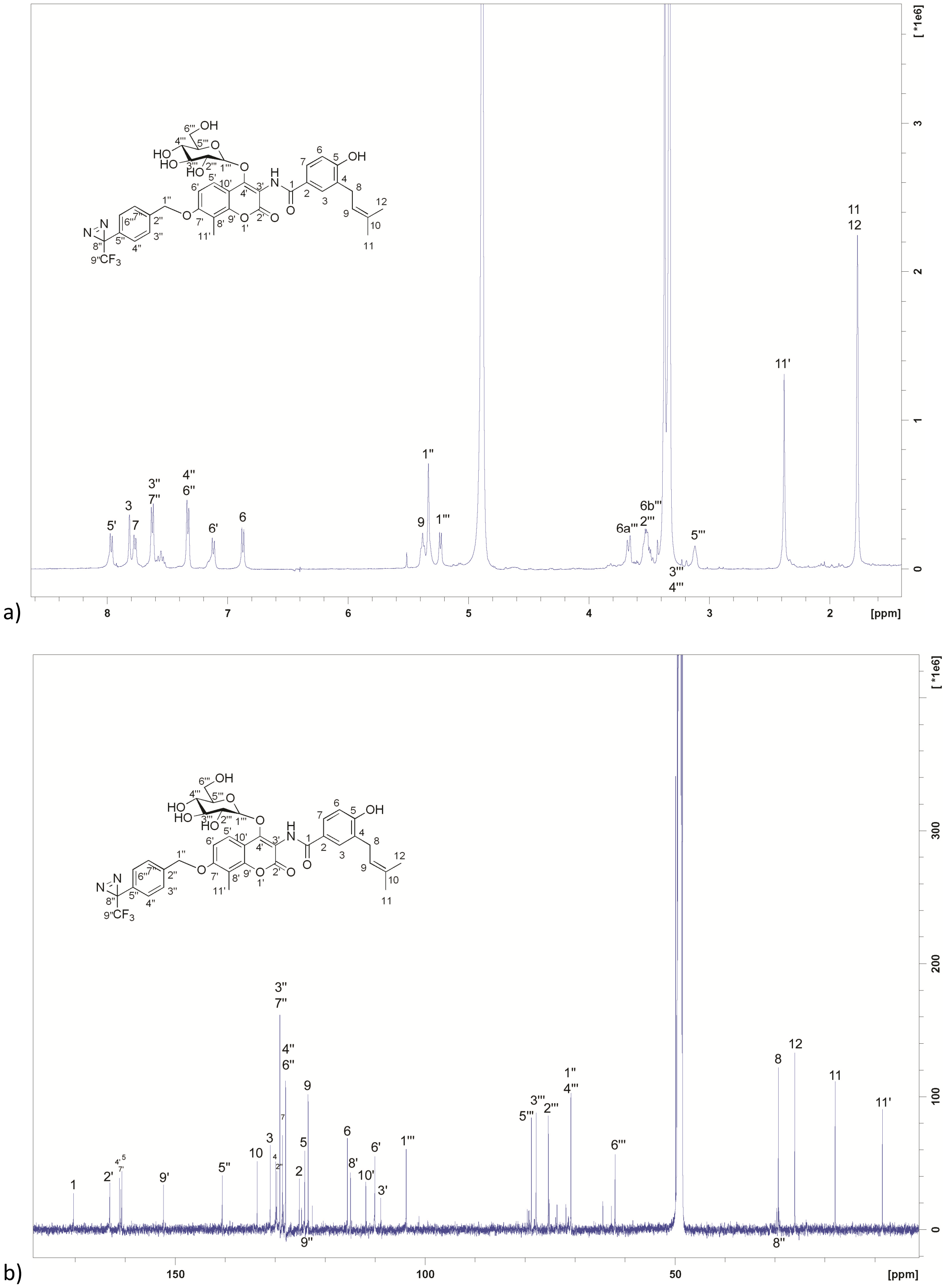
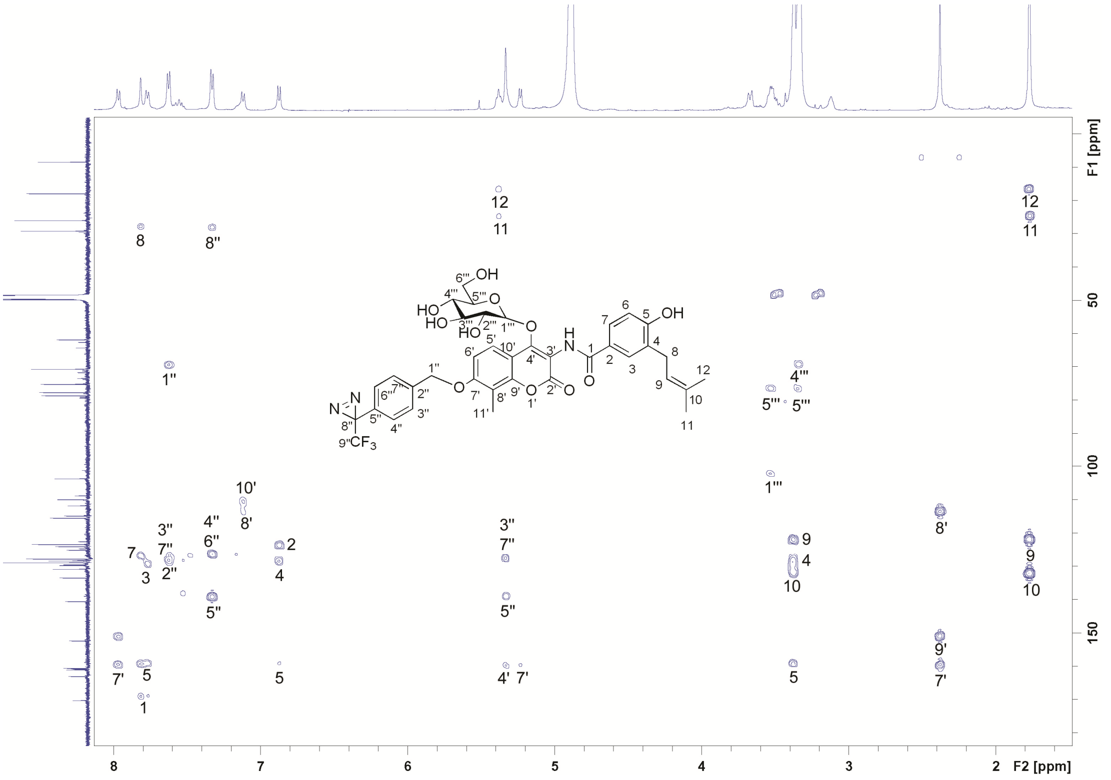


Figure S9. NMR assignment of compound **2**. a) ^{1}H-NMR. b) ^{13}C-NMR. c) HMBC. Long range coupling between H1''' and C4', H1'' and C7' can be seen. d) Analytical LC shows the formation of products in the present of starting material. e) MS shows the formation of product (6.85 min, 754 [M-H$^+$]$^-$). f), MS of product with one acetyal group remaining (7.20 min, 754 [M-H$^+$]$^-$)) g), MS of product with four acetyal groups remaining (8.10 min, 922 [M-H$^+$]$^-$)). h), MS of product with glucose moiety removal (compound 5, 9.23 min, 592 [M-H$^+$]$^-$)). i) HPLC shows the purity of compound **2** after preparative HPLC.

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150
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7
6
5
4
3
2
12
11
8
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1''
10'
8'
4''
6''
3''
7''
2''
7
3
2
4
5''
7'
5
1
3''
7''
5''
4'
7'
4'''
5'''
5'''
1'''
9
4
10
8'
9'
7'
9
10
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4'''
5'''
HO
HO
3'''
2'''
HO
1'''
O
5'
10'
6'
4'
3'
NH
1
O
6
7
5
OH
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3
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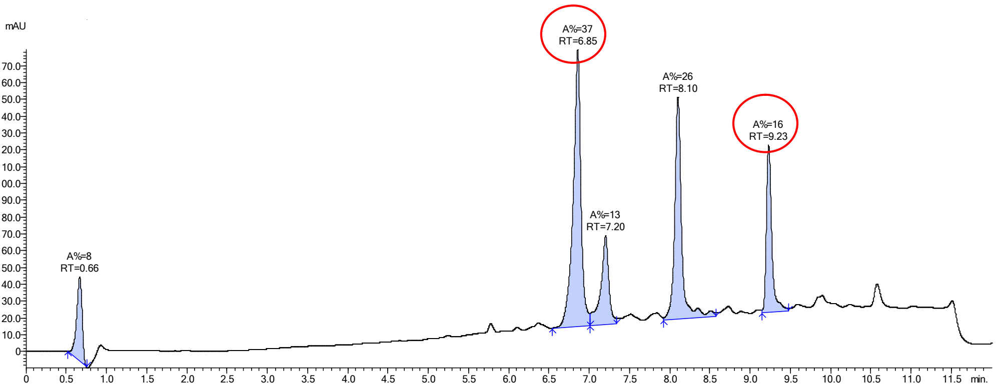
10
11
1''
2''
O
7'
8'
9'
O
1'
2'
O
11'
6''
7''
3''
4''
5''
N
N
8''
9''CF$_3$

c)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50.0
40.0
30.0
20.0
10.0
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RT=6.85
A%=13
RT=7.20
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RT=8.10
A%=16
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1.0
1.5
2.0
2.5
3.0
3.5
4.0
4.5
5.0
5.5
6.0
6.5
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8.0
8.5
9.0
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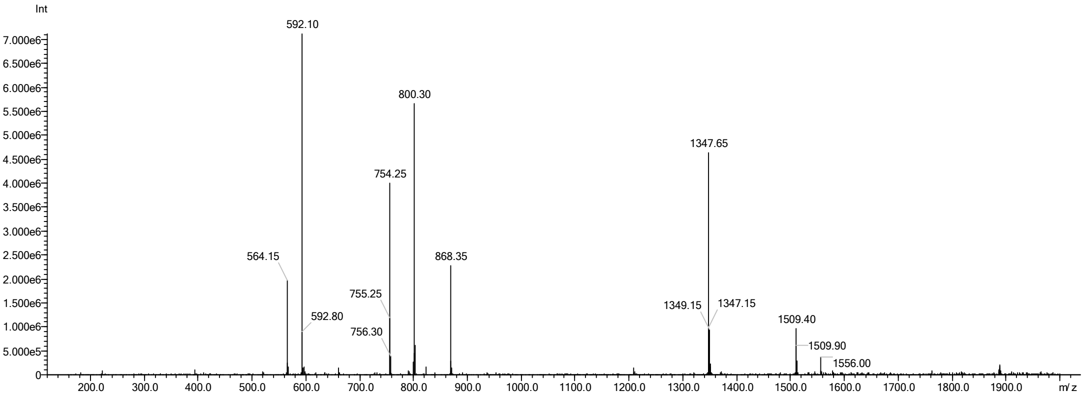
10.5
11.0
11.5
min.

d)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2.000e6
1.500e6
1.000e6
5.000e5
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800.30
1347.65
754.25
564.15
868.35
755.25
592.80
756.30
1349.15
1347.15
1509.40
1509.90
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1800.0
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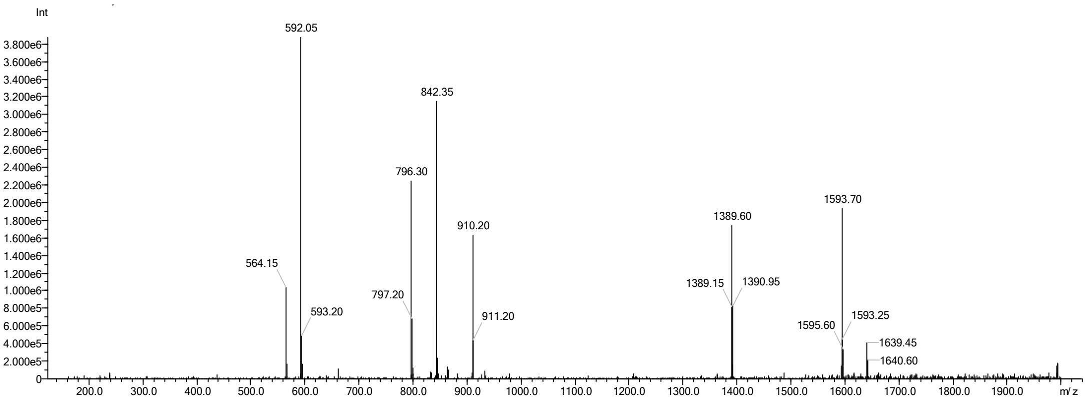
m/z

e)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1.200e6
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4.000e5
2.000e5
0
592.05
842.35
796.30
910.20
1389.60
1593.70
564.15
797.20
593.20
911.20
1389.15
1390.95
1595.60
1593.25
1639.45
1640.60
200.0
300.0
400.0
500.0
600.0
700.0
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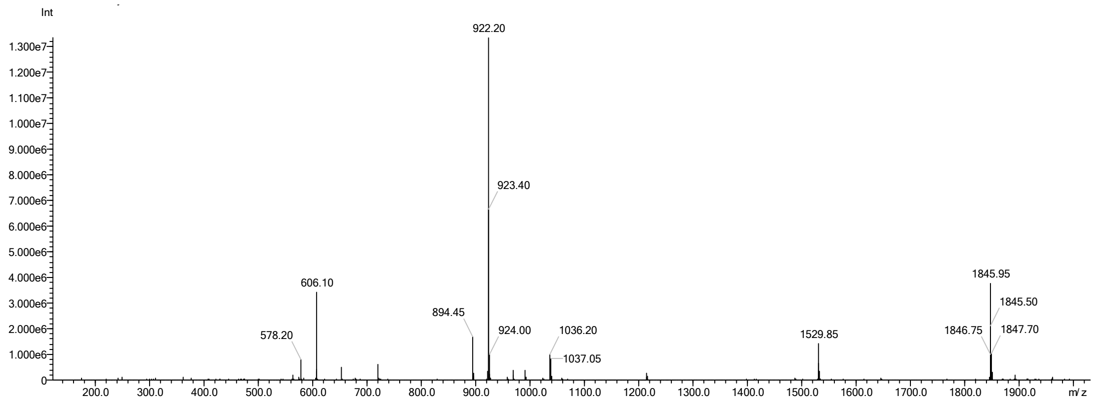
1800.0
1900.0
m/z

f)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894.45
924.00
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1037.05
1529.85
1845.95
1845.50
1846.75
1847.70
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700.0
800.0
900.0
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1400.0
1500.0
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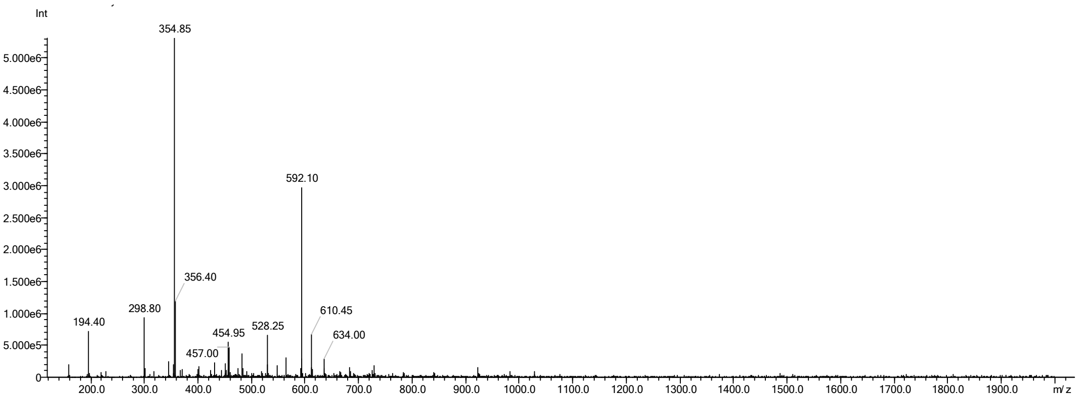
1800.0
1900.0
m/z

g)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356.40
194.40
298.80
454.95
528.25
610.45
457.00
634.00
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400.0
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700.0
800.0
900.0
1000.0
1100.0
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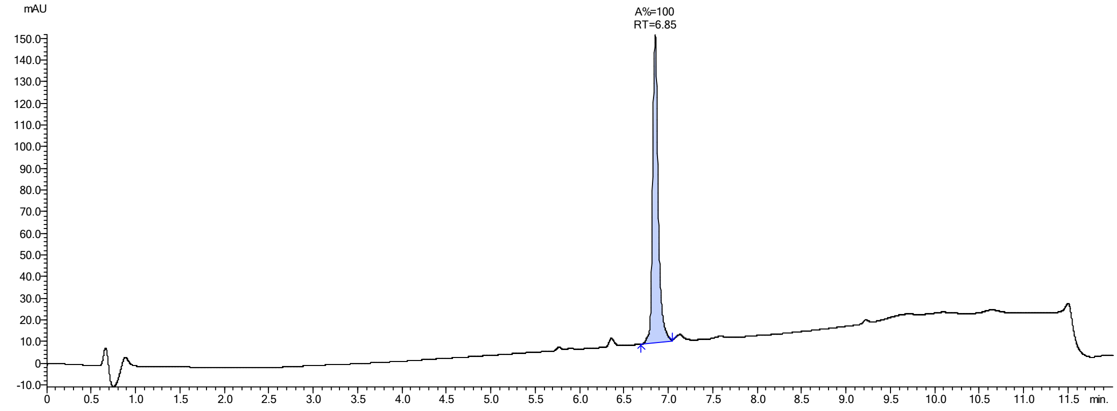
1300.0
1400.0
1500.0
1600.0
1700.0
1800.0
1900.0
m/z

h)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30.0
20.0
10.0
0
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0
0.5
1.0
1.5
2.0
2.5
3.0
3.5
4.0
4.5
5.0
5.5
6.0
6.5
7.0
7.5
8.0
8.5
9.0
9.5
10.0
10.5
11.0
11.5
min.

i)

Table S10. NMR assignment of compound **2**

Site	^{13}C /ppm	^{1}H /ppm	Multi-plicity	$J_{(H,H)}$ (Hz)
1	170.34			
2	125.26			
3	130.98	7.82	s	
4	129.96			
5	160.66			
6	115.53	6.87	d	8.63
7	128.52	7.77	d	8.61
8	29.33	3.42	m	
9	123.41	5.38	m	
10	133.57			
11	26.1	1.77	s	
12	18.0	1.77	s	
1'	-			
2'	163.09			
3'	108.87			
4'	161.14			
5'	124.12	7.97	d	8.61
6'	110.06	7.12	d	7.75
7'	160.88			
8'	114.92			
9'	152.38			
10'	111.92			
11'	8.4	2.38	s	
1''	70.82	5.33	s	
2''	129.71			
3''	129.04	7.63	d	7.75
4''	127.92	7.33	d	8.62
5''	140.59			
6''	127.92	7.33	d	8.62
7''	129.04	7.63	d	7.75
8''	29.41			
9''	123.75			
1'''	103.76	5.22	d	8.82
2'''	75.35	3.49	m	
3'''	77.74	3.30	m	
4'''	70.82	3.36	m	
5'''	78.76	3.12	m	
6a'''	61.96	3.68	d	11.80
6b'''	61.96	3.52	m	

Note: H6 and H6' chemical shit changed.

H1'' coupled to C7'; H1''' coupled to C4'

C9'' and C8'' visible in CNMR

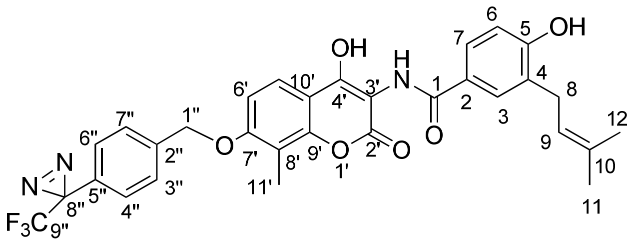
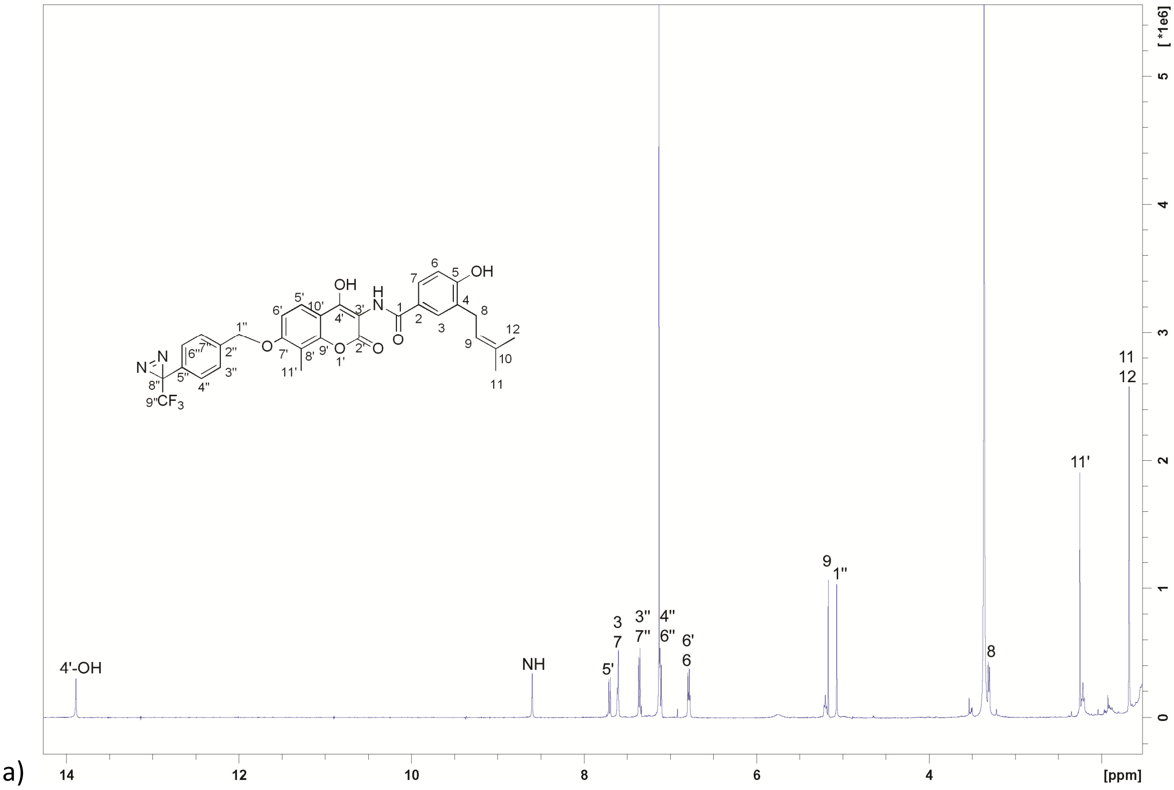
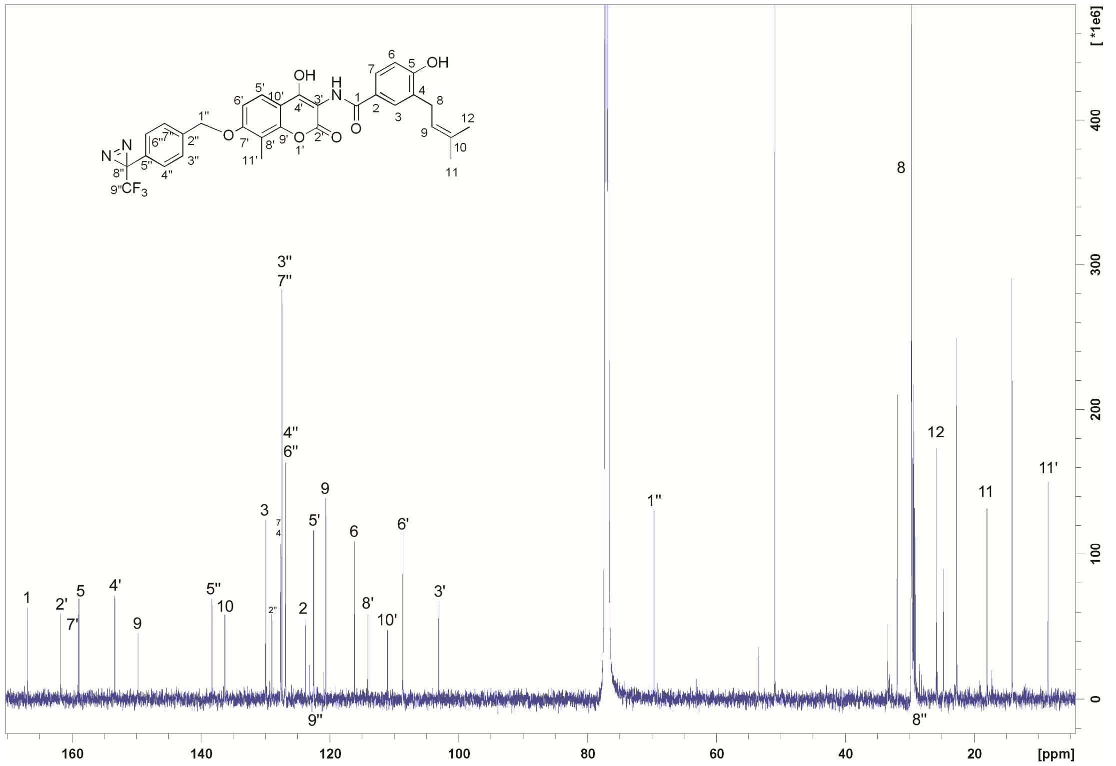


Figure S10. NMR assignment of compound **3**. a) ^{1}H-NMR, 4'-OH 13.89 ppm. b) ^{13}C-NMR. c) HMBC. Long range coupling between 4'-OH and C4', H1" and C7' can be seen. d) Analytical LC shows the purity of compound **3** after preparative HPLC (Analytical LC/MS data refer to Fig. S8).

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120
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80
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7'
5
4'
9
5''
10
3
2''
7
4
3''
7''
4''
6''
2
5'
9
6
8'
10'
6'
3'
9''
1''
8
8''
12
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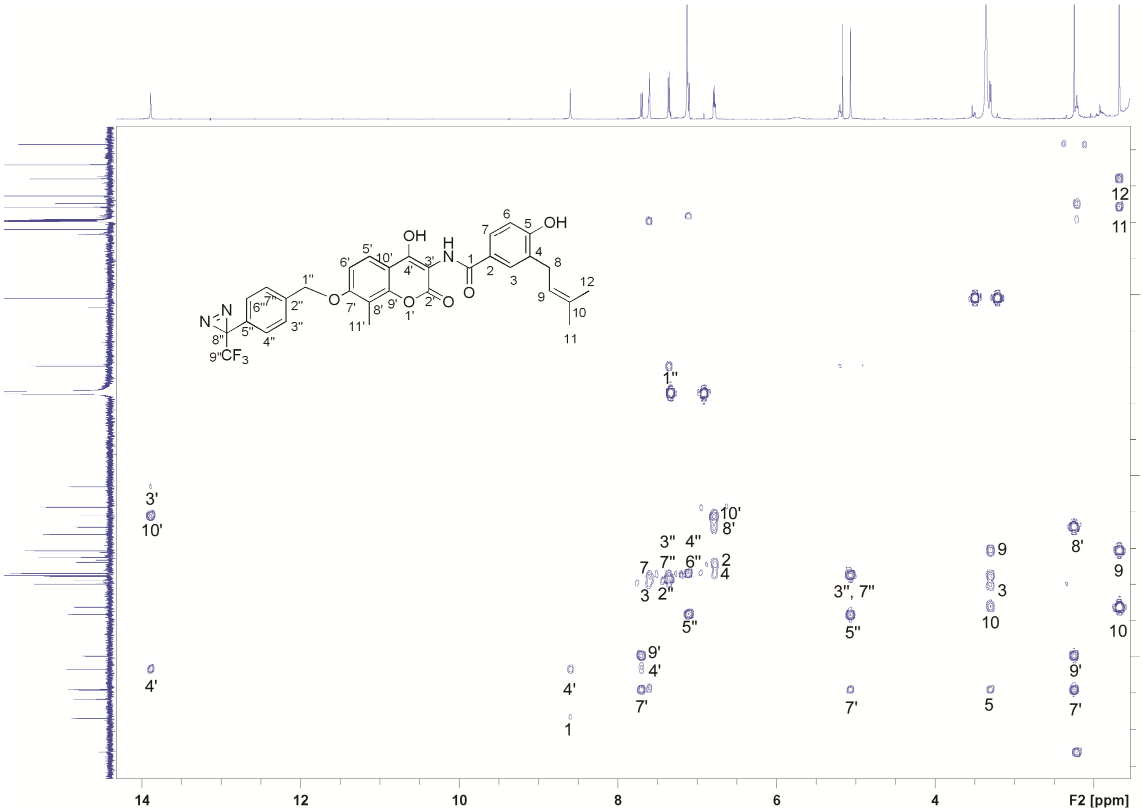
11'
OH
NH
OH
O
O
O
N
N
CF3

b)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4
2
F2 [ppm]
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3'
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9
10
9'
4'
4'
7'
4'
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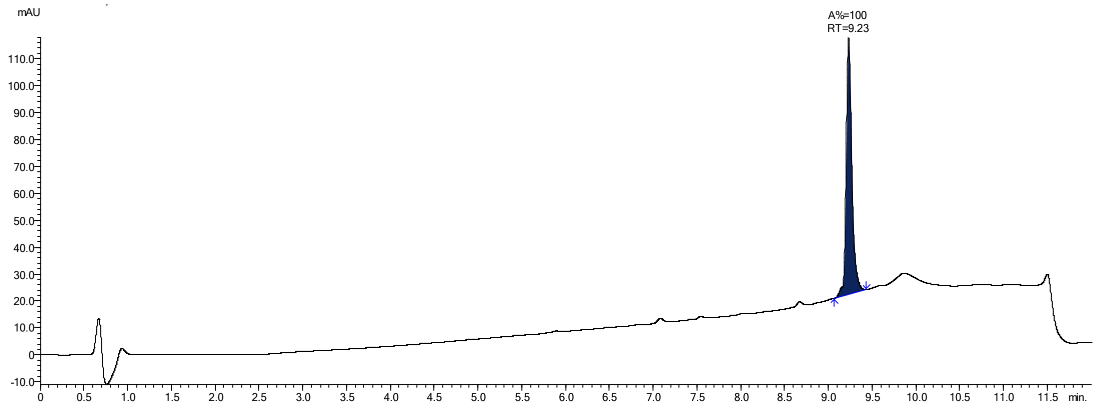
7'
5
9'
7'
OH
NH
OH
O
O
O
N
N
CF3

c)



d)

Table S11. NMR assignment of compound **3**

Site	^{13}C /ppm	^{1}H /ppm	Multi-plicity	$J_{(H,H)}$ (Hz)
1	166.95			
2	123.81			
3	129.92	7.61	s	
4	127.58			
5	158.97			
6	116.22	6.78	d	8.99
7	127.64	7.61	m	
8	29.77	3.30	d	7.64
9	120.59	5.17	s	
10	136.27			
11	25.82	1.68	s	
12	18.11	1.68	s	
1'	-			
2'	161.76			
3'	103.06			
4'	153.40			
5'	122.57	7.70	d	9.13
6'	108.67	6.79	d	8.67
7'	159.12			
8'	114.15			
9'	149.81			
10'	111.07			
11'	8.50	2.25	s	
1''	69.91	5.07	s	
2''	129.02			
3''	127.41	7.36	d	9.18
4''	126.85	7.11	d	9.18
5''	138.29			
6''	126.85	7.11	d	9.18
7''	127.41	7.36	d	9.18
8''	28.70			
9''	122.10			
4'-OH		13.89	s	
NH		8.60	s	

HMBC H1'' couple to C7'; 4-OH couple to C4'

4-OH 13.89ppm

12. 4-hydroxy-N-(8-methyl-4-oxo-2-((4-(3-(trifluoromethyl)-3H-diazirin-3-yl)benzyl)oxy)-7-(((2S,3R,5S,6R)-3,4,5-trihydroxy-6-(hydroxymethyl)tetrahydro-2H-pyran-2-yl)oxy)-4H-chromen-3-yl)-3-(3-methylbut-2-en-1-yl)benzamide (4)

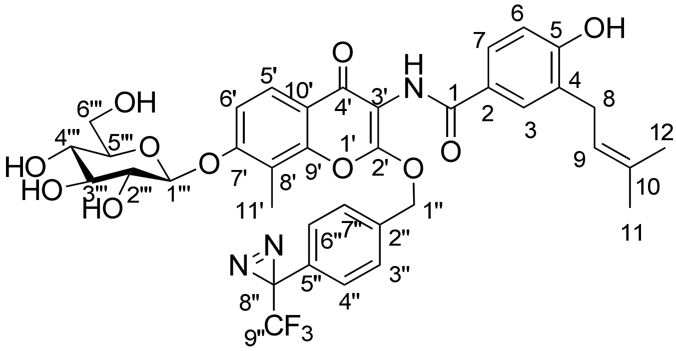
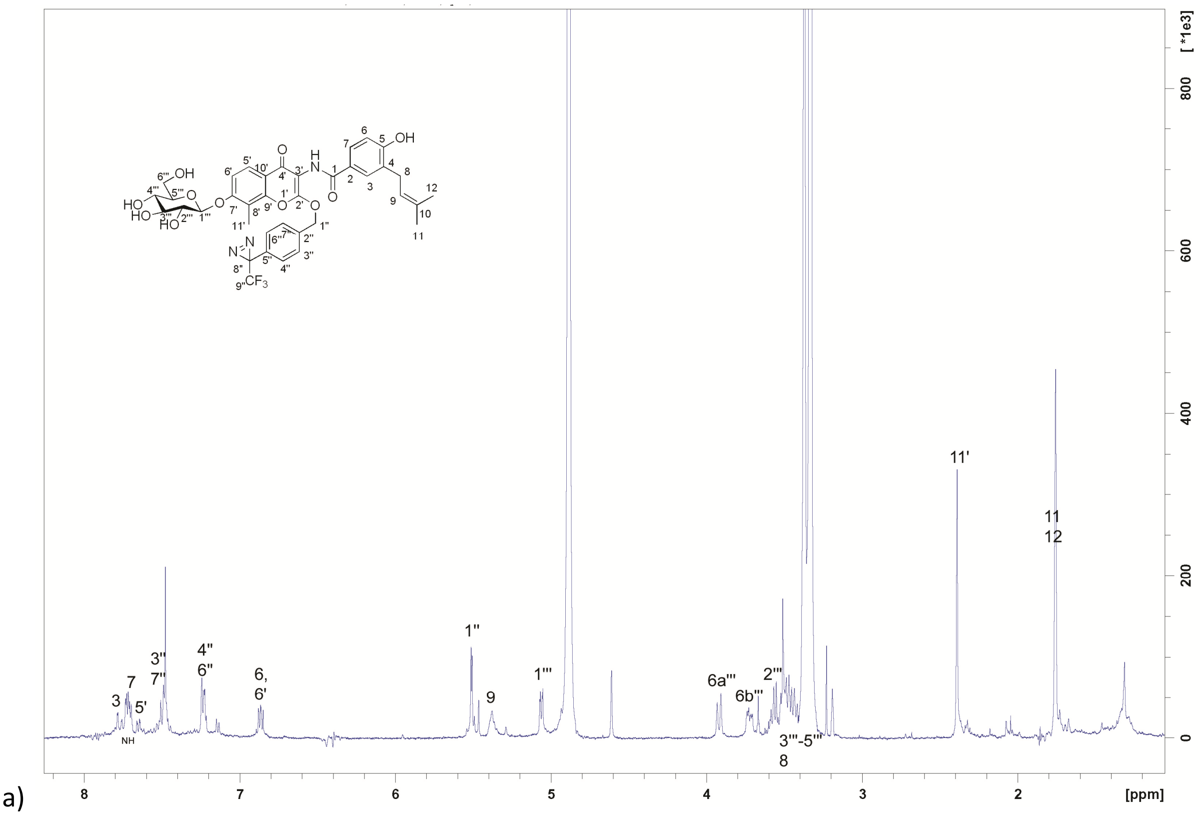
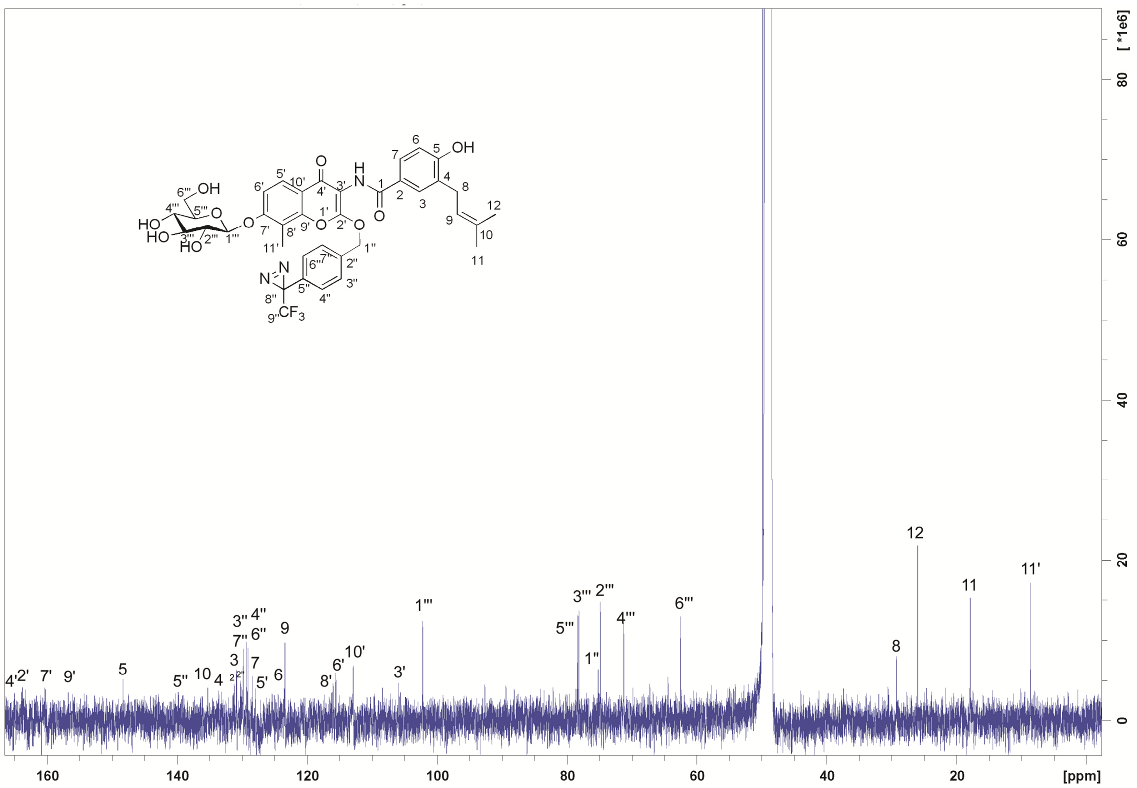


Figure S11. NMR assignment of compound **4**. a) ^{1}H-NMR. b) ^{13}C-NMR. c) HMBC. Long range coupling between H1''' and C7', H1'' and 47' can be seen. d) Analytical LC shows the formation of products in the present of starting material. e) MS shows the formation of product (6.25 min) (755, [M-H$^+$]$^-$). f) Analytical LC show the purity of compound **4** after preparative HPLC.

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40
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2'
7'
9'
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10
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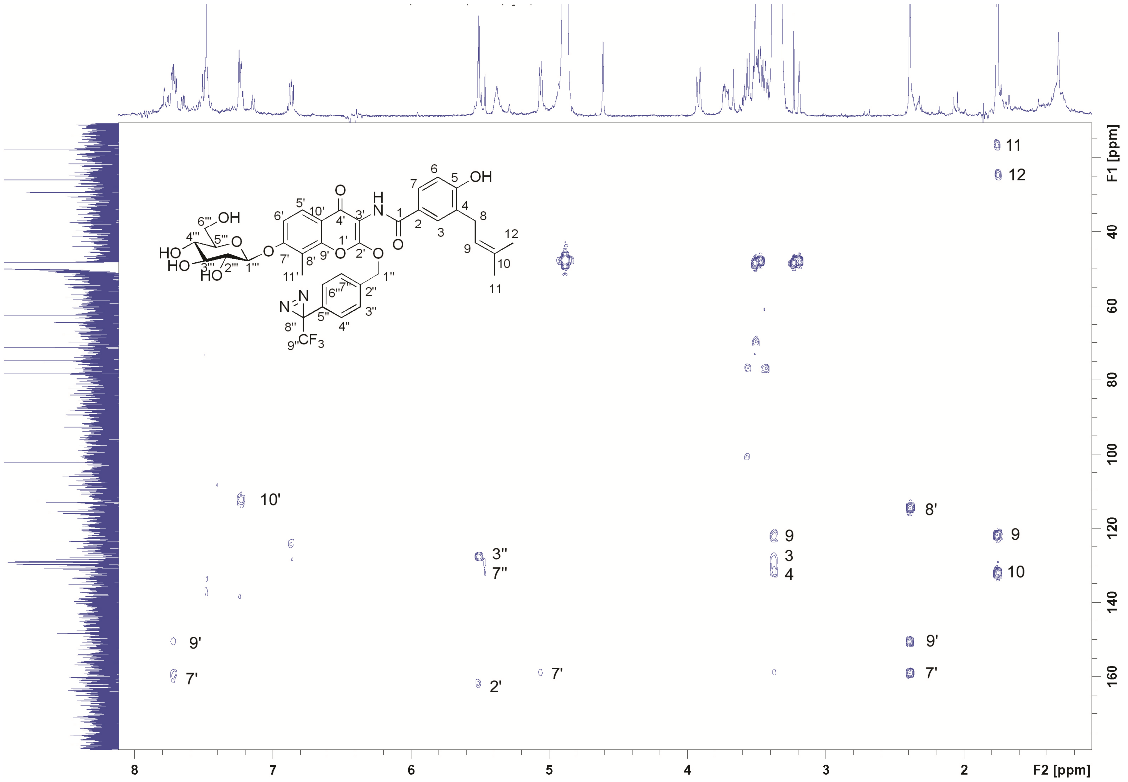
2''
3''
7''
4''
6''
7
5'
6
9
8'
6'
10'
3'
1'''
5'''
3'''
2'''
1''
4'''
6'''
8
12
11
11'
160
140
120
100
80
60
40
20
[ppm]
OH
O
NH
HO
N
CF3

b)


11
12
10'
8'
9
3
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9
10
3''
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9'
7'
7'
2'
7'
F1 [ppm]
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60
80
100
120
140
160
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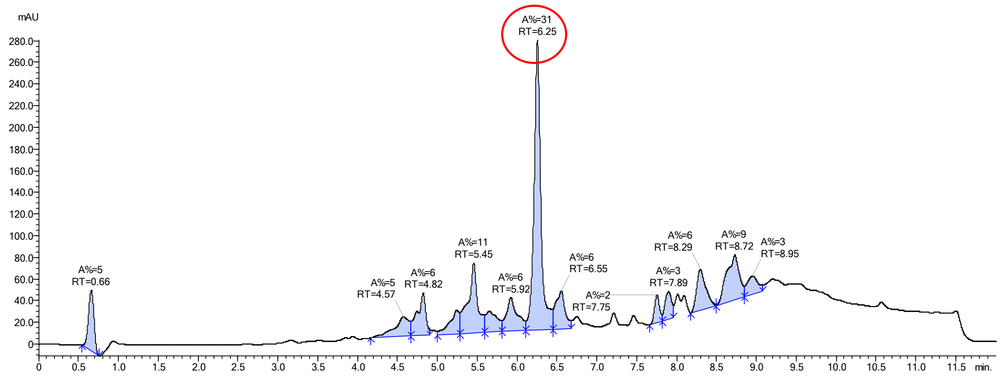
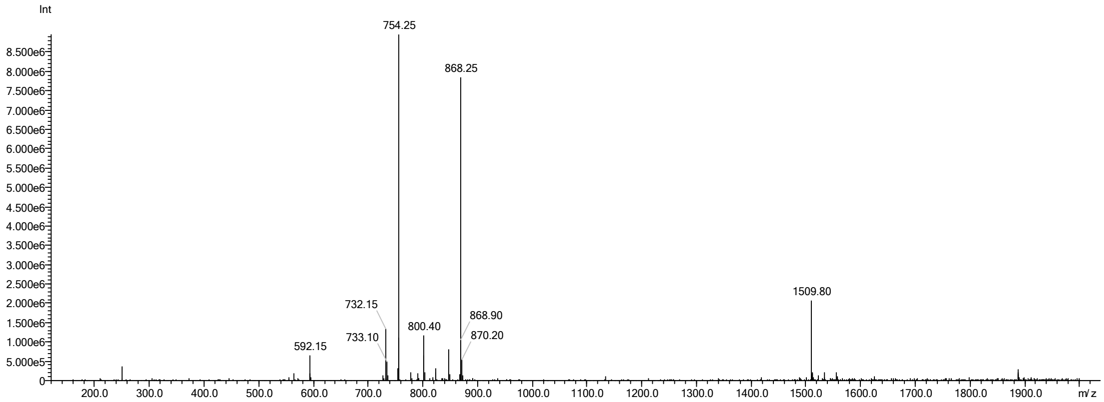
7
6
5
4
3
2
F2 [ppm]

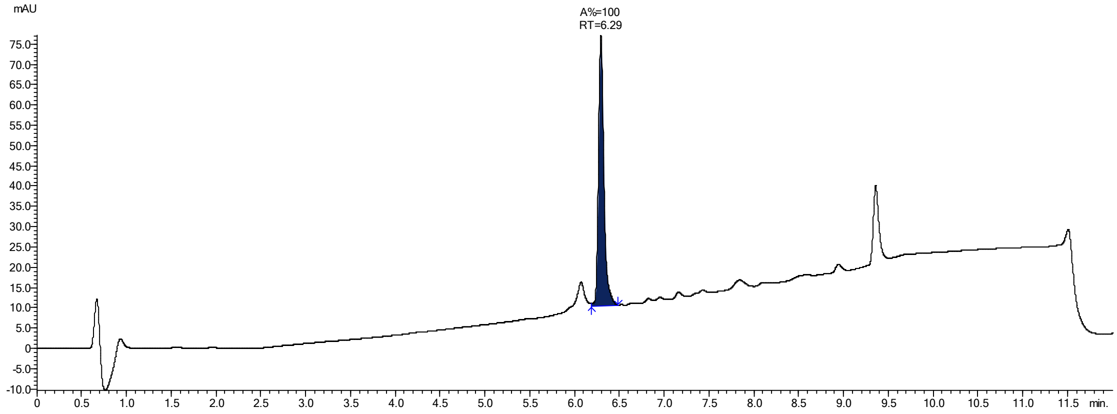
c)



d)



e)



f)

Table S12. NMR assignment of compound **4**

Site	^{13}C /ppm	^{1}H /ppm	Multi-plicity	$J_{(H,H)}$ (Hz)
1	164.0			
2	131.2			
3	131.0	7.79	s	
4	133.7			
5	148.6			
6	123.40	6.87	d	6.4
7	128.47	7.70	m	
8	29.32	3.4	m	
9	123.39	5.38	m	
10	135.5			
11	26.00	1.76	s	

12	17.96	1.76	s	
1'	-			
2'	163.81			
3'	105.9			
4'	164.2			
5'	127.99			
6'	115.53	6.85	d	6.3
7'	160.53			
8'	116.3			
9'	154.4			
10'	112.9			
11'	8.63	2.39	s	
1''	75.20	5.51	d	3.3
2''	130.4			
3''	129.33	7.48	m	
4''	112.97	7.23	m	
5''	139.8			
6''	112.97	7.23	m	
7''	129.33	7.48	m	
8''	28.19			
9''	126			
1'''	102.21	5.06	d	7.9
2'''	74.86	3.56	m	
3'''	78.17	3.49	m	
4'''	71.26	3.46	m	
5'''	78.39	3.41	m	
6a'''	62.52	3.92	d	12.15
6b'''	62.52	3.72	dd	5.5, 12.15
NH		7.71	s	

HMBC 1'' coupled to 2'; 1''' coupled to 7'

13. 4-hydroxy-N-(7-hydroxy-8-methyl-2-oxo-4-((4-(3-(trifluoromethyl)-3H-diazirin-3-yl)benzyl)oxy)-2H-chromen-3-yl)-3-(3-methylbut-2-en-1-yl)benzamide (5)

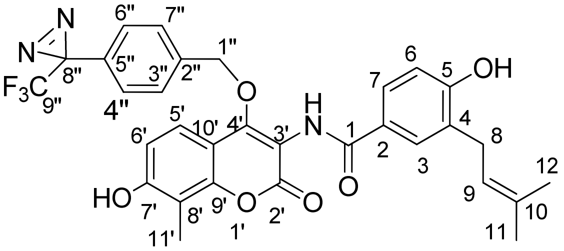
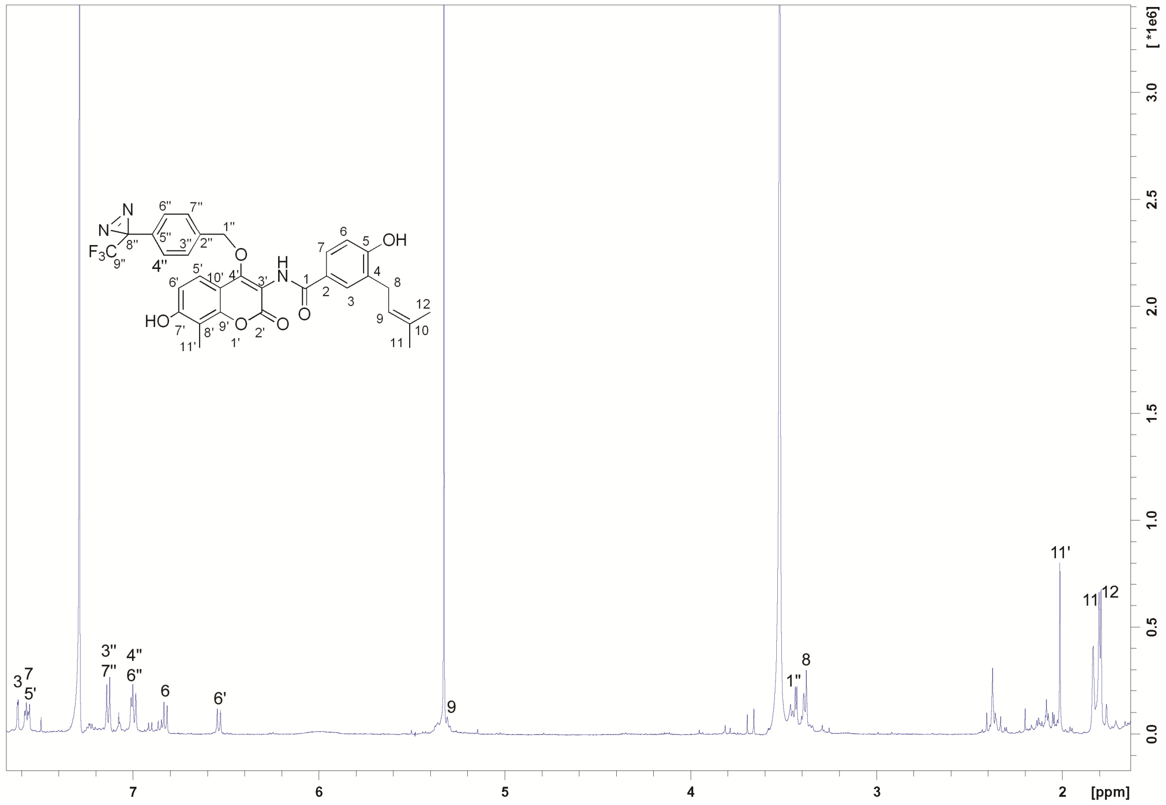


Figure S12. NMR assignment of compound **5**. a) ^{1}H-NMR. b) ^{13}C-NMR. c) HMBC. d) Analytical LC shows the formation of products in the present of starting material. e) MS shows the formation of product (7.12 min) (594, $[M+H^{+}]^{+}$). f) Analytical LC show the purity of compound **5** after preparative HPLC.



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F3C
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9''
6''
7''
5''
3''
2''
1''
4''
O
5'
10'
4'
3'
NH
1
O
7
6
5
OH
4
2
3
8
9
12
10
11
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HO
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6''
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9
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8
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11
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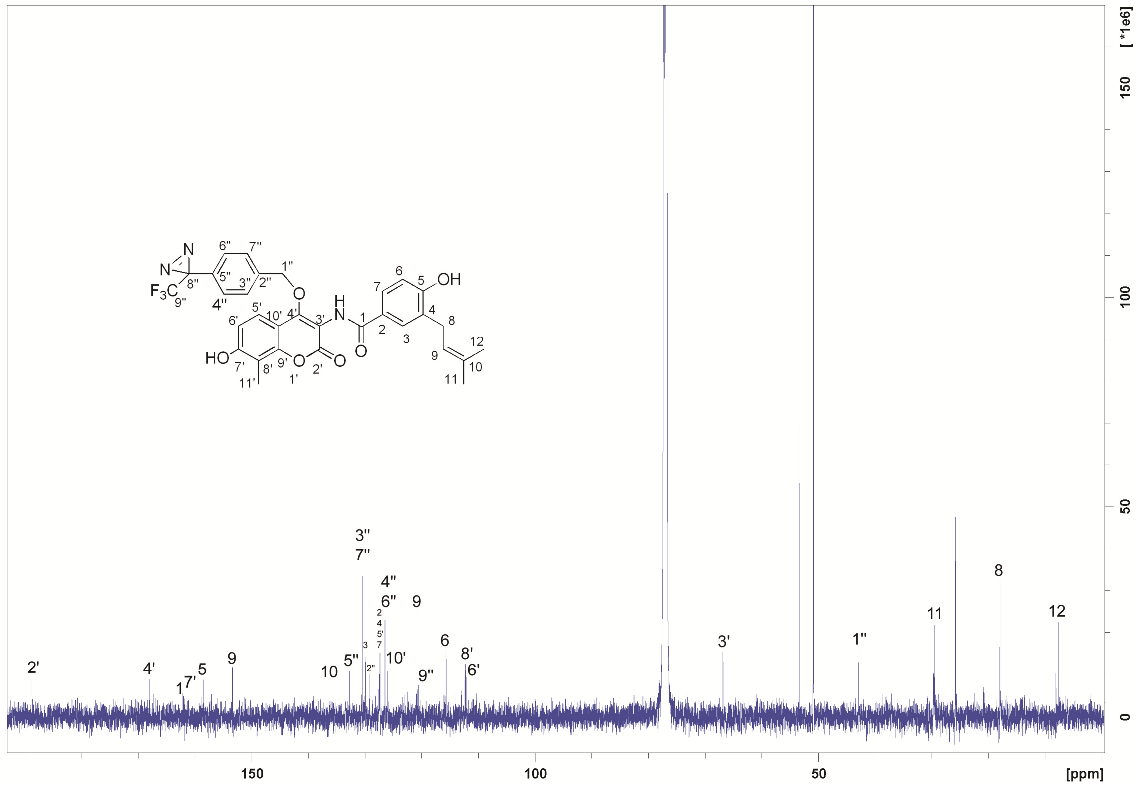
a)



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F3C
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9''
6''
7''
5''
3''
2''
1''
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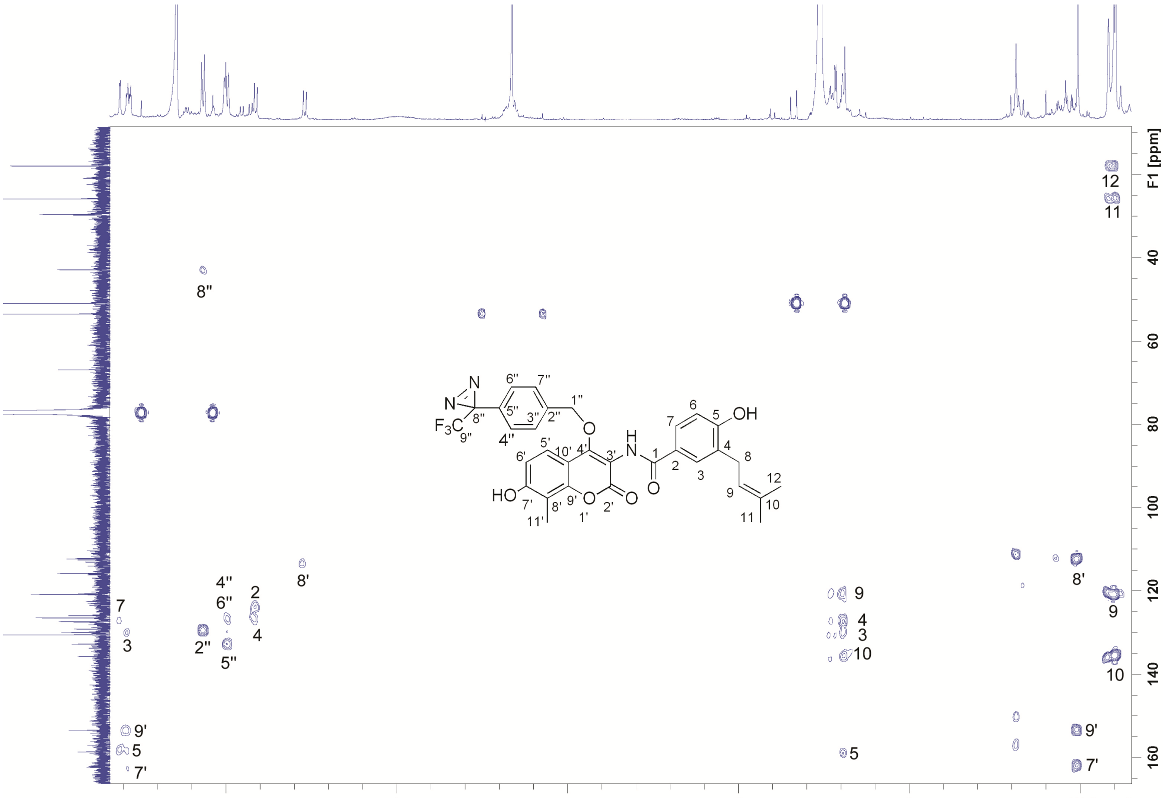
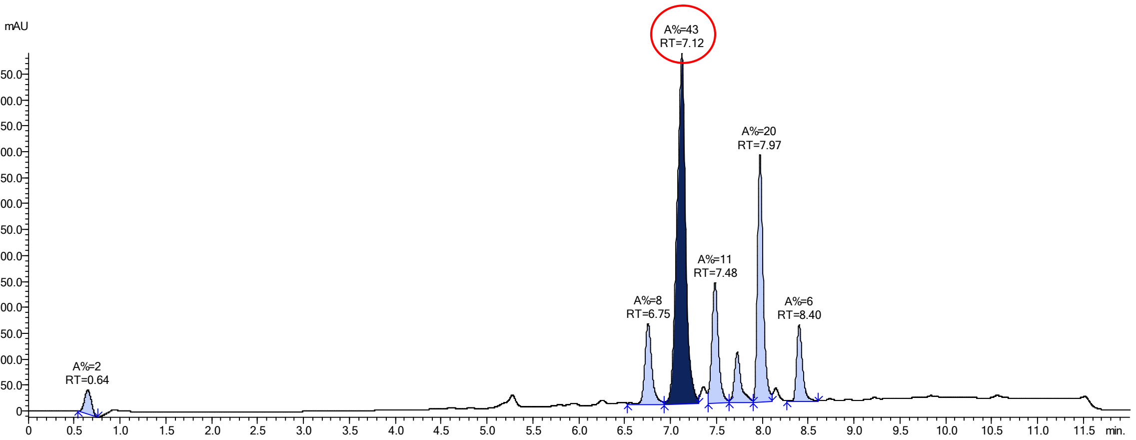
O
5'
10'
4'
3'
NH
1
O
7
6
5
OH
4
2
3
8
9
12
10
11
6'
HO
7'
8'
9'
O
2'
O
11'
1'
2'
4'
1
7'
5
9
10
5''
3
2''
3''
7''
2
4
5'
7
4''
6''
10'
9
9''
6
8'
6'
3'
1''
11
8
12
150
100
50
[ppm]
0
50
100
150
[*1e6]

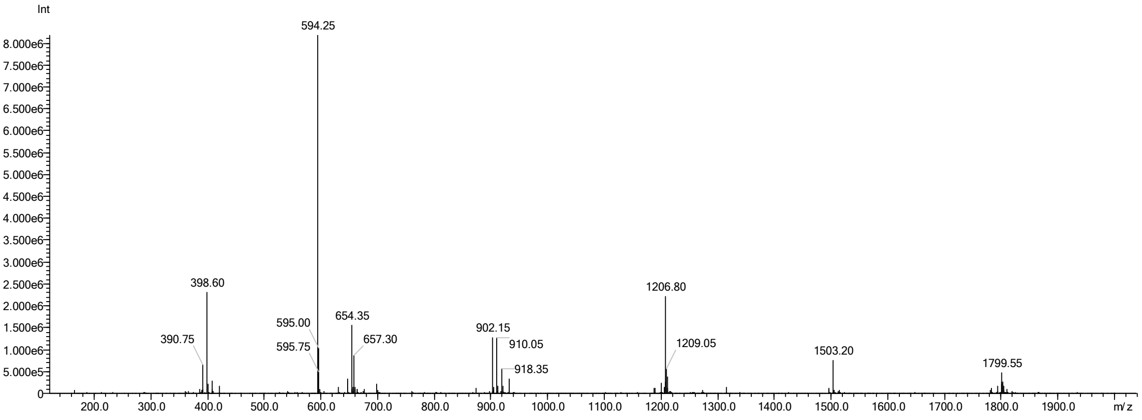
b)


F1 [ppm]
F2 [ppm]
7
6
5
4
3
40
60
80
100
120
140
160
12
11
8''
7
3
4''
6''
2
4
2''
5''
8'
9
4
3
10
8'
9
10
9'
5
7'
5
9'
7'
N
N
F3C
9''
8''
5''
4''
6''
7''
3''
2''
1''
O
H
N
1
O
2
3
4
8
7
6
5
OH
9
12
10
11
4'
3'
10'
5'
6'
HO
7'
8'
11'
9'
O
1'
2'
O

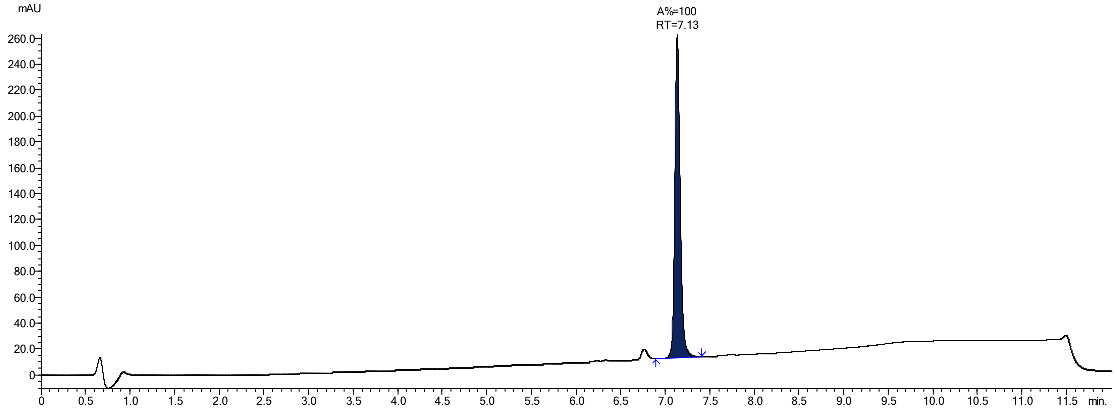
c)


mAU
650.0
600.0
550.0
500.0
450.0
400.0
350.0
300.0
250.0
200.0
150.0
100.0
50.0
0
A%=2
RT=0.64
A%=8
RT=6.75
A%=43
RT=7.12
A%=11
RT=7.48
A%=20
RT=7.97
A%=6
RT=8.40
0
0.5
1.0
1.5
2.0
2.5
3.0
3.5
4.0
4.5
5.0
5.5
6.0
6.5
7.0
7.5
8.0
8.5
9.0
9.5
10.0
10.5
11.0
11.5
min.

d)


Int
8.000e6
7.500e6
7.000e6
6.500e6
6.000e6
5.500e6
5.000e6
4.500e6
4.000e6
3.500e6
3.000e6
2.500e6
2.000e6
1.500e6
1.000e6
5.000e5
0
594.25
398.60
390.75
595.00
595.75
654.35
657.30
902.15
910.05
918.35
1206.80
1209.05
1503.20
1799.55
200.0
300.0
400.0
500.0
600.0
700.0
800.0
900.0
1000.0
1100.0
1200.0
1300.0
1400.0
1500.0
1600.0
1700.0
1800.0
1900.0
m/z

e)



f)

Table S13. NMR assignment of compound **5**

Site	^{13}C /ppm	^{1}H /ppm	Multi-plicity	$J_{(H,H)}$ (Hz)
1	162.3			
2	127.5			
3	130.0	7.63	d	2.01
4	127.5			
5	158.4			
6	115.7	6.83	d	8.01
7	127.4	7.57	m	
8	25.8	3.38	d	7.51
9	120.9	5.31	m	
10	135.7			
11	29.5	1.80	s	
12	18.1	1.79	s	
1'	-			
2'	188.9			
3'	67.4			
4'	168.0			
5'	127.5	7.57	m	
6'	112.1	6.53	d	8.61
7'	162.1			
8'	112.3			
9'	153.4			
10'	126.0			
11'	8.0	2.01	s	
1''	43.3	3.44	m	
2''	129.2			
3''	130.5	7.13	d	8.03
4''	126.5	7.00	d	8.03
5''	132.8			
6''	126.5	7.00	d	8.03
7''	130.5	7.13	d	8.03
8''	43.0			
9''	120.6			