Supporting Information

Synthesis of Hupehenols A, B, and E from Protopanaxadiol

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[c] *Shanghai Institute of Materia Medica, Chinese Academy of Sciences, Shanghai 201203, China*

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Supporting Information

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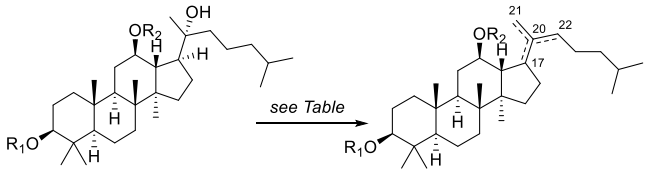
Table S1. Attempts to Prepare $\Delta^{(17,20)}$ Olefin



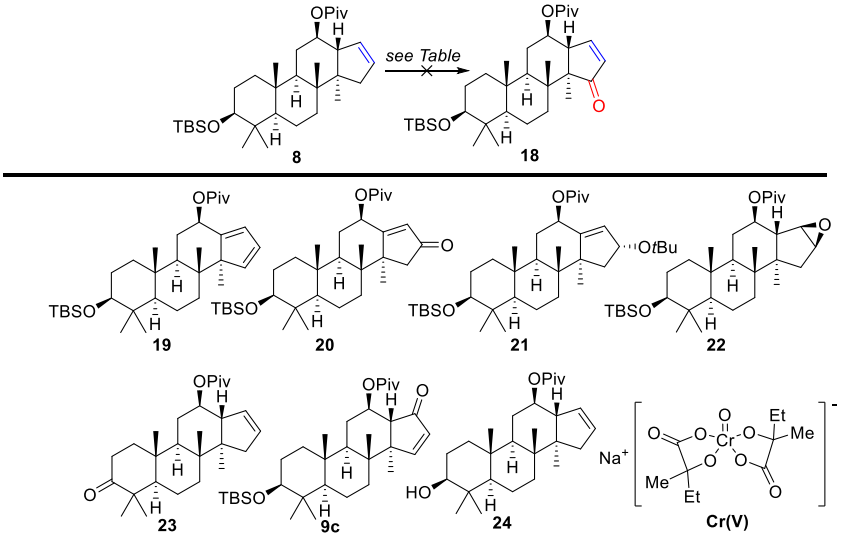
14a $R_1 = R_2 = Ac$
14b $R_1 = R_2 = MOM$
14c $R_1 = TBS$, $R_2 = Piv$

15a $R_1 = R_2 = Ac$
15b $R_1 = R_2 = MOM$
15c $R_1 = TBS$, $R_2 = Piv$

entry	substrate	conditions	yield% ($\Delta^{17(20)}$:$\Delta^{20(22)}$:$\Delta^{20(21)}$)[a]
1	**14a**	*p*TSA(cat.), toluene, reflux, 3 h	70 (0:2.5:1)
2	**14a**	$SOCl_2$, pyr., 0 °C-rt, 0.5 h	70 (0:2.5:1)
3	**14a**	$POCl_3$, pyr., 40 °C, 6 h	**85 (0:4.7:1)**
4	**14a**	MsCl, DBU, benzene, 0-80 °C,12 h	NR
5	**14a**	MsCl, TEA, DCM, 0 °C-rt, 3 h	70 (0:3:1)
6	**14a**	Burgess' reagent, toluene, reflux, 2 h	80 (0:1.5:1)
7	**14a**	$BF_3 \cdot Et_2O$, DCM, 0 °C, 0.5 h	65 (0:3.5:1)
8	**14a**	DEAD, PPh_3, THF, 0-50 °C, 4 h	77 (0:3:1)
9	**14b**	$POCl_3$, pyr., 40 °C, 8 h	**80 (0:3:1)**
10	**14c**	$POCl_3$, pyr., 40 °C, 12 h	**82 (0:4:1)**

[a]The ratios were determined by the isolated yields of compounds **16** and **10** after ozonolysis of olefins.

Table S2. Attempts to Achieve Allylic Oxidation of Olefin **8**



entry	conditions	products (yield%)[a]
1	SeO_2, 1,4-dioxane, rt, 24 h	no reaction
2	SeO_2, 1,4-dioxane/benzene (1:1), rt, 24 h	no reaction
3	SeO_2, 1,4-dioxane/benzene (1:1), 80 °C, 2 h	**19** (90)
4[b]	SeO_2, TBHP, benzene, rt-60 °C, 72 h	**20** (30), **21** (35)
5[b]	CrO_3, 3,5-dimethylpyrazole, DCM, -20 °C, 24 h	no reaction
6[b]	CrO_3, 3,5-dimethylpyrazole, DCM, rt, 12 h	**22** (42)
7	CrO_3, TBHP (70% aq.), DCM, rt, 8 h	**23** (70)
8[b]	CuCl, TBHP, benzene, 60 °C, 72 h	**20** (23), **22** (12), **9c** (10)
9[b]	$Mn(OAc)_3$, TBHP, ethyl acetate, 3 Å MS, rt, 5 d	**20** (8), **22** (5), **9c** (<5)
10[b]	Pd/C, TBHP, K_2CO_3, DCM, rt, 48 h	**20** (<5), **22** (<5)
11[b]	PDC, TBHP (70% aq.), benzene, rt, 48 h	**20** (41), **22** (<5), **9c** (38)
12[b]	Cr(V), MnO_2, 15-crown-5, trifluorotoluene, 80 °C, 72 h	**20** (<5), **9c** (<5)
13	DDQ, DMF, H_2O (10 equiv.), 80 °C, 3 h	**24** (quant.)

[a]Isolated yields.

[b]Recovery of starting materials.

Table 1. 11β-HSD1 Inhibition of Synthetic Compounds

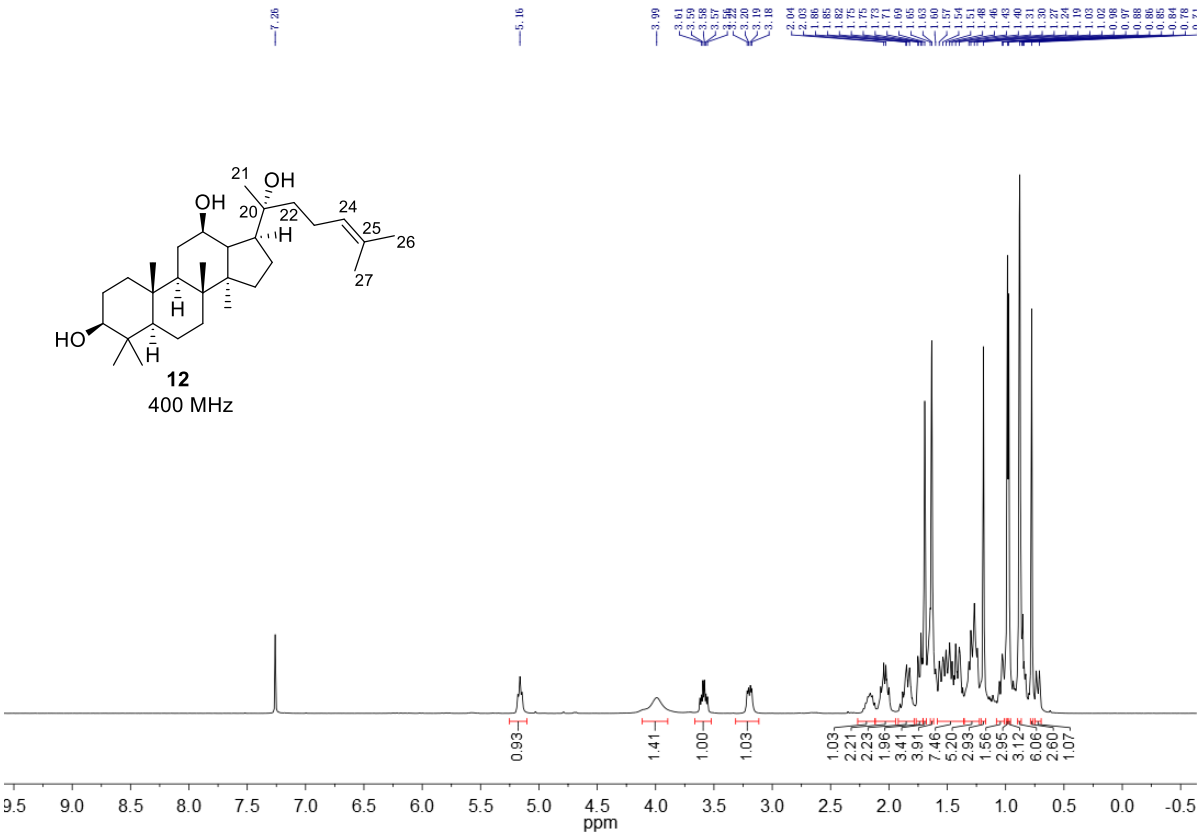
entry	1 μM inhibitory ratio		IC_{50}	
	human 11β-HSD1	mouse 11β-HSD1	human 11β-HSD1	mouse 11β-HSD1
12	16.13%	12.35%	ND[b]	ND
14a	13.24%	7.55%	ND	ND
14b	7.90%	7.75%	ND	ND
16a	81.12%	10.77%	0.1 μM	ND
10a	69.36%	40.91%	0.2 μM	ND
10b	15.43%	11.48%	ND	ND
11a	12.21%	12.53%	ND	ND
17	32.77%	17.43%	ND	ND
8	0.96%	8.74%	ND	ND
19	12.50%	10.04%	ND	ND
[a]	28.86%	10.84%	ND	ND
20	32.37%	7.22%	ND	ND
21	28.29%	35.17%	ND	ND
22	2.85%	10.55%	ND	ND
23	2.61%	7.91%	ND	ND
24	33.33%	9.44%	ND	ND
27	35.64%	7.98%	ND	ND
30	88.42%	76.48%	44.0 nM[d]	0.4 μM
hupehenol B	94.43%	27.08%	26.0 nM	3.3 μM
GA[c]	96.20%	94.91%	7.4 nM	12.1 nM

[a] 3-OTBS-removed product of compound **19**.

[b] ND: The IC_{50} value was not determined if the inhibitory ratio was less than 50%.

[c] Glycyrrhetinic acid (GA) was used as a positive control.

[d] $P > 0.05$ vs hupehenol B.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3.61
3.59
3.58
3.57
3.56
3.22
3.20
3.19
3.18
2.04
2.03
1.86
1.85
1.82
1.75
1.73
1.71
1.69
1.65
1.63
1.60
1.57
1.54
1.51
1.48
1.46
1.43
1.40
1.31
1.30
1.27
1.24
1.19
1.03
1.02
0.98
0.97
0.88
0.86
0.85
0.84
0.78
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OH
20
22
H
24
25
26
27
H
HO
H
12
400 MHz
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1.41
1.00
1.03
1.03
2.21
2.23
1.96
3.41
3.91
7.46
5.20
2.93
1.56
2.95
3.12
6.06
2.60
1.07
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
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0.0
-0.5
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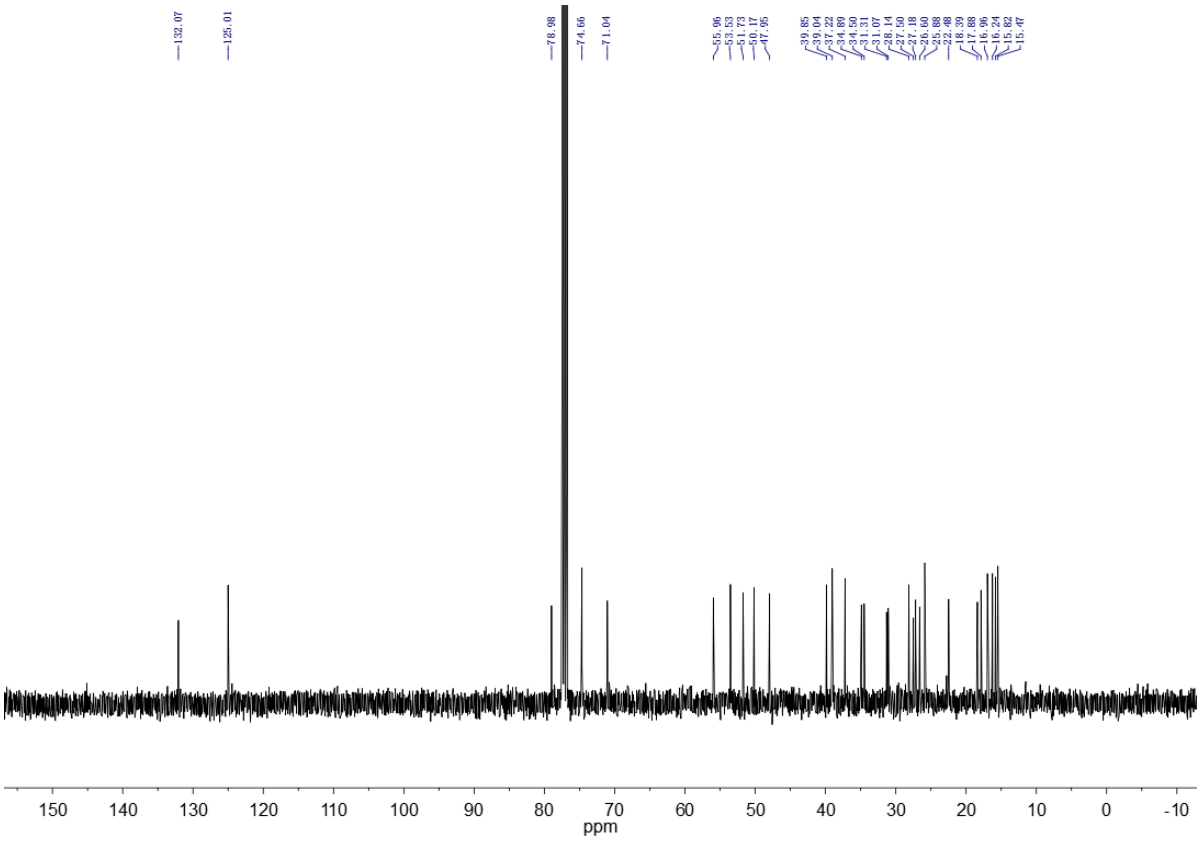
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71.04
55.96
53.53
51.73
50.17
47.95
39.85
39.04
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34.88
34.50
31.31
31.07
28.14
27.50
27.18
26.40
25.88
22.48
18.39
17.88
16.96
16.34
15.82
15.47
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110
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90
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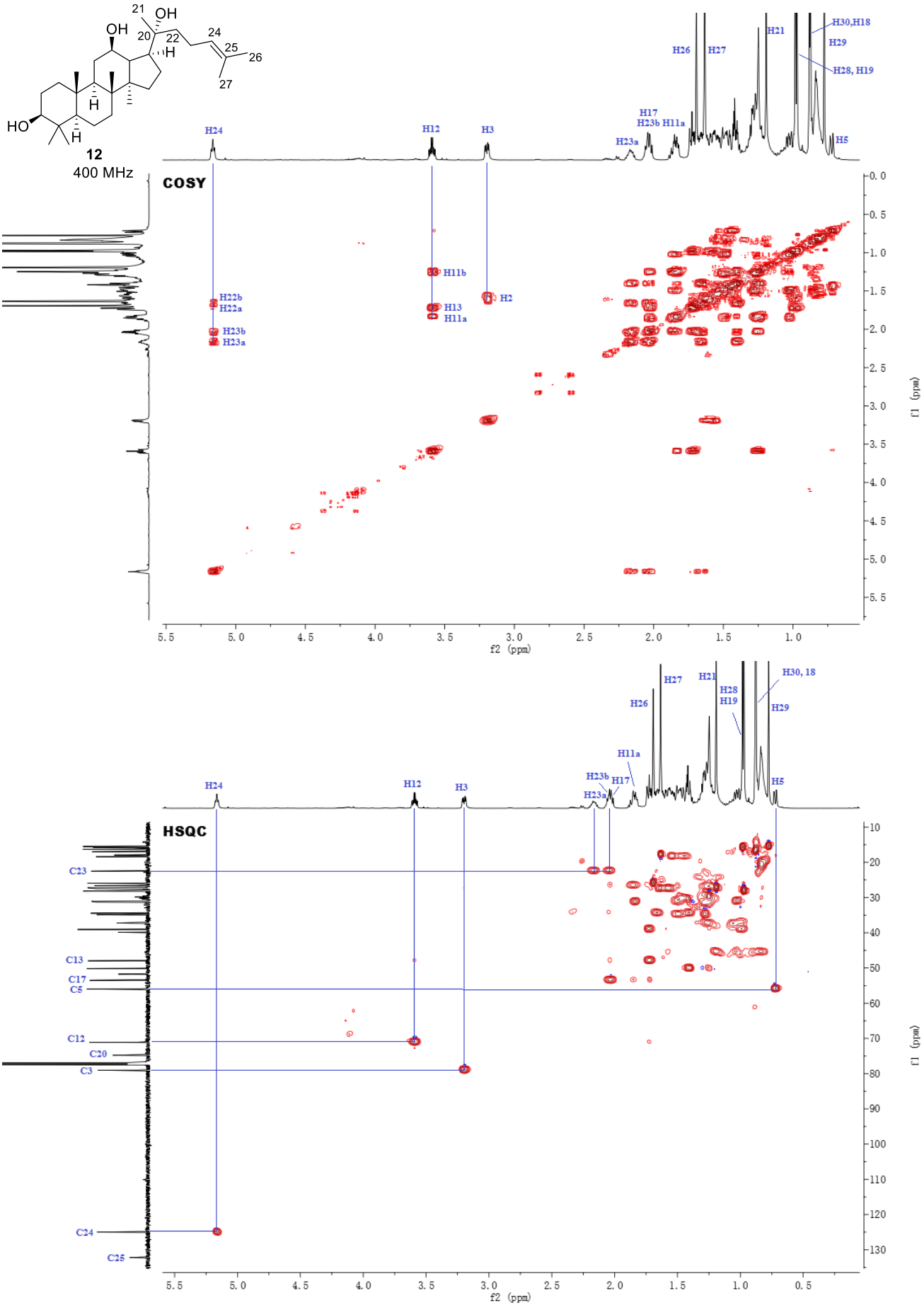
70
60
50
40
30
20
10
0
-10
ppm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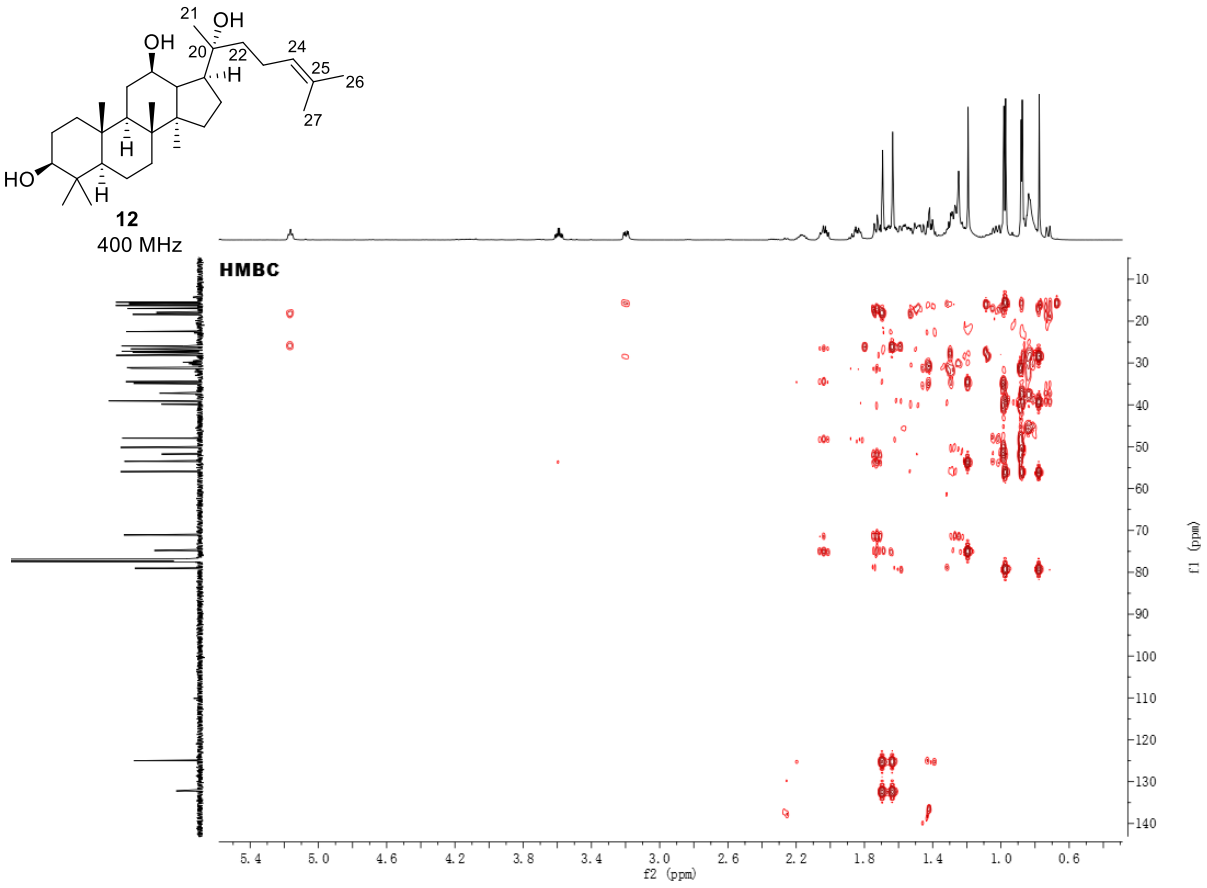
HSQC
f2 (ppm)
f1 (ppm)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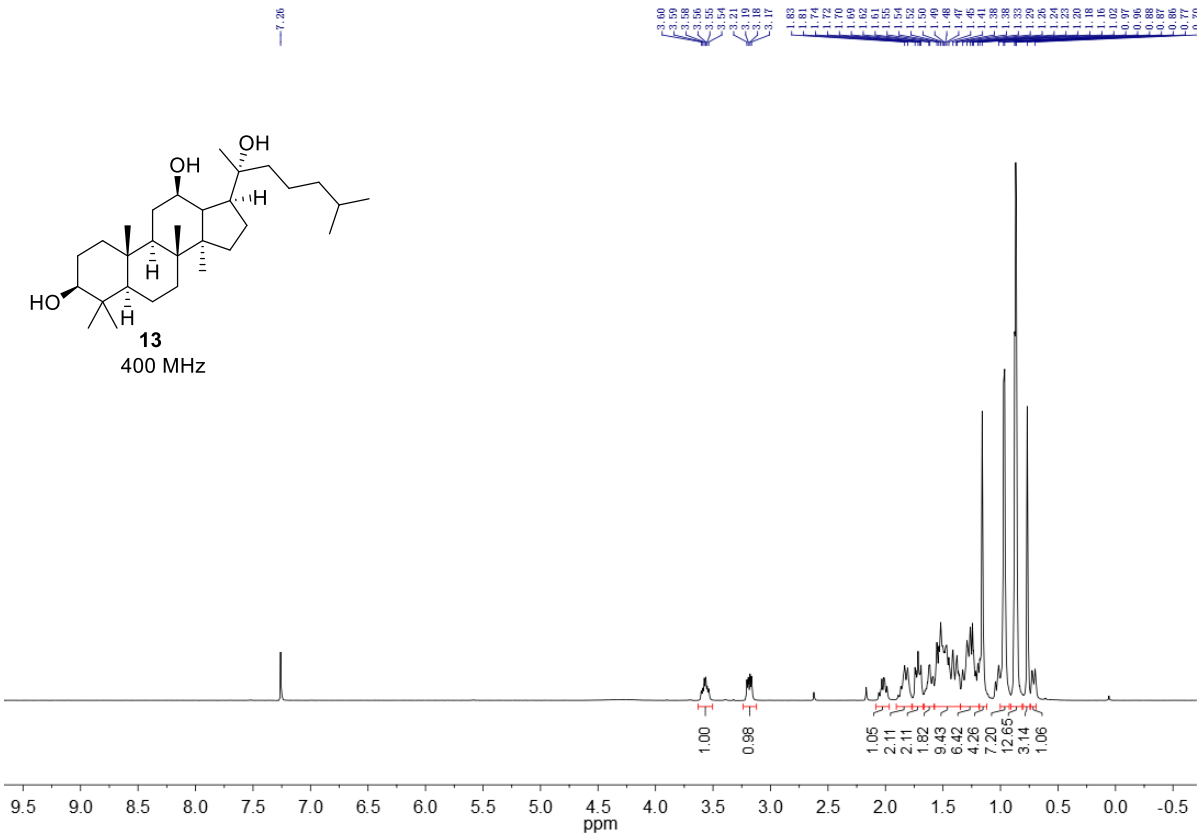
OH
OH
20
22
H
24
25
26
27
HO
H
H
12
400 MHz
HMBC
f2 (ppm)
f1 (ppm)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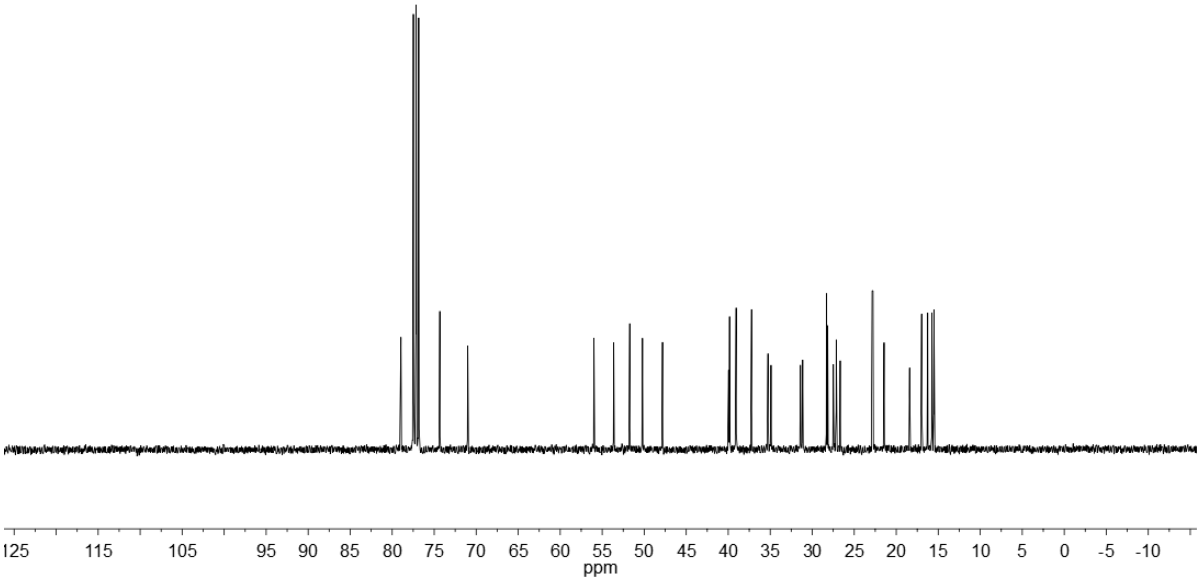
H
HO
H
H
13
400 MHz
ppm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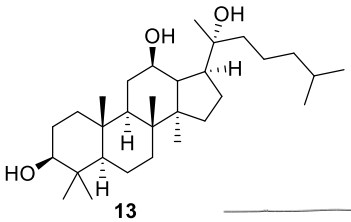
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OH
H
HO
H
H

13

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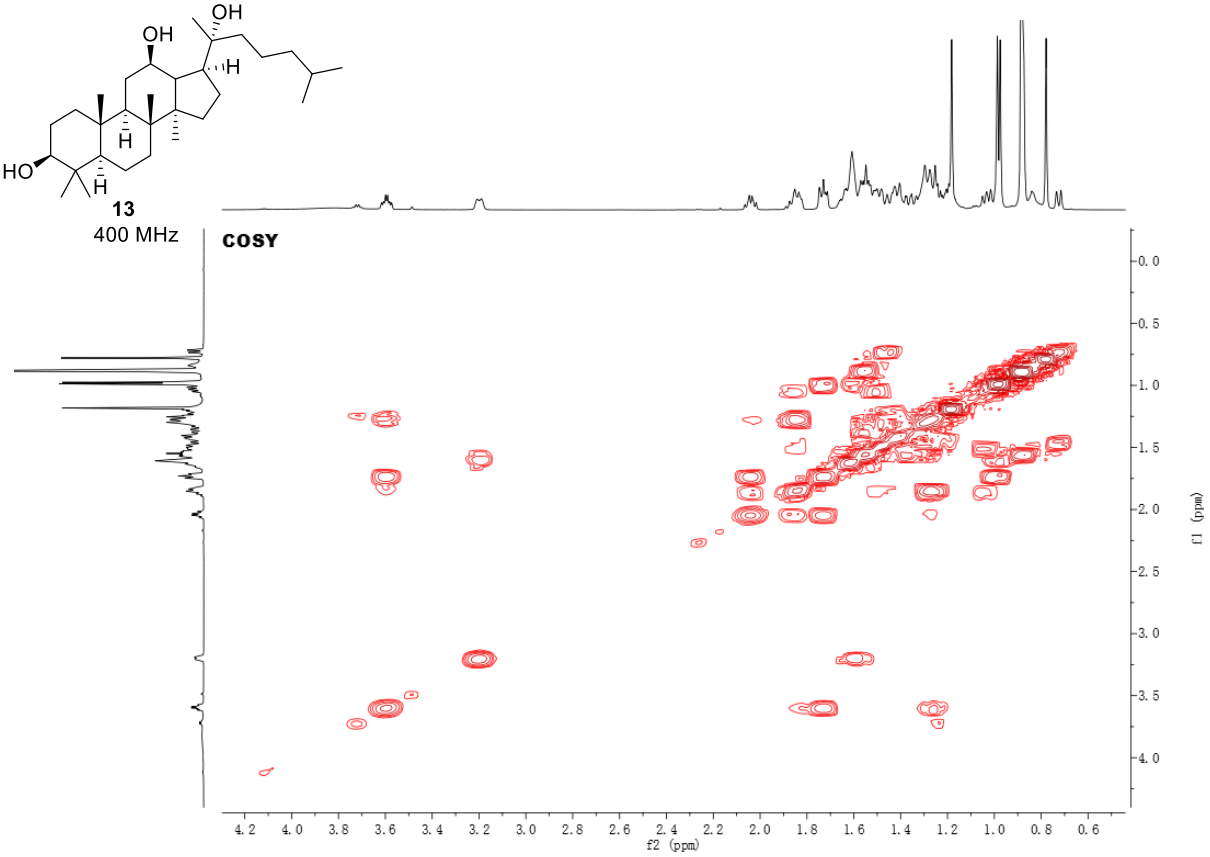
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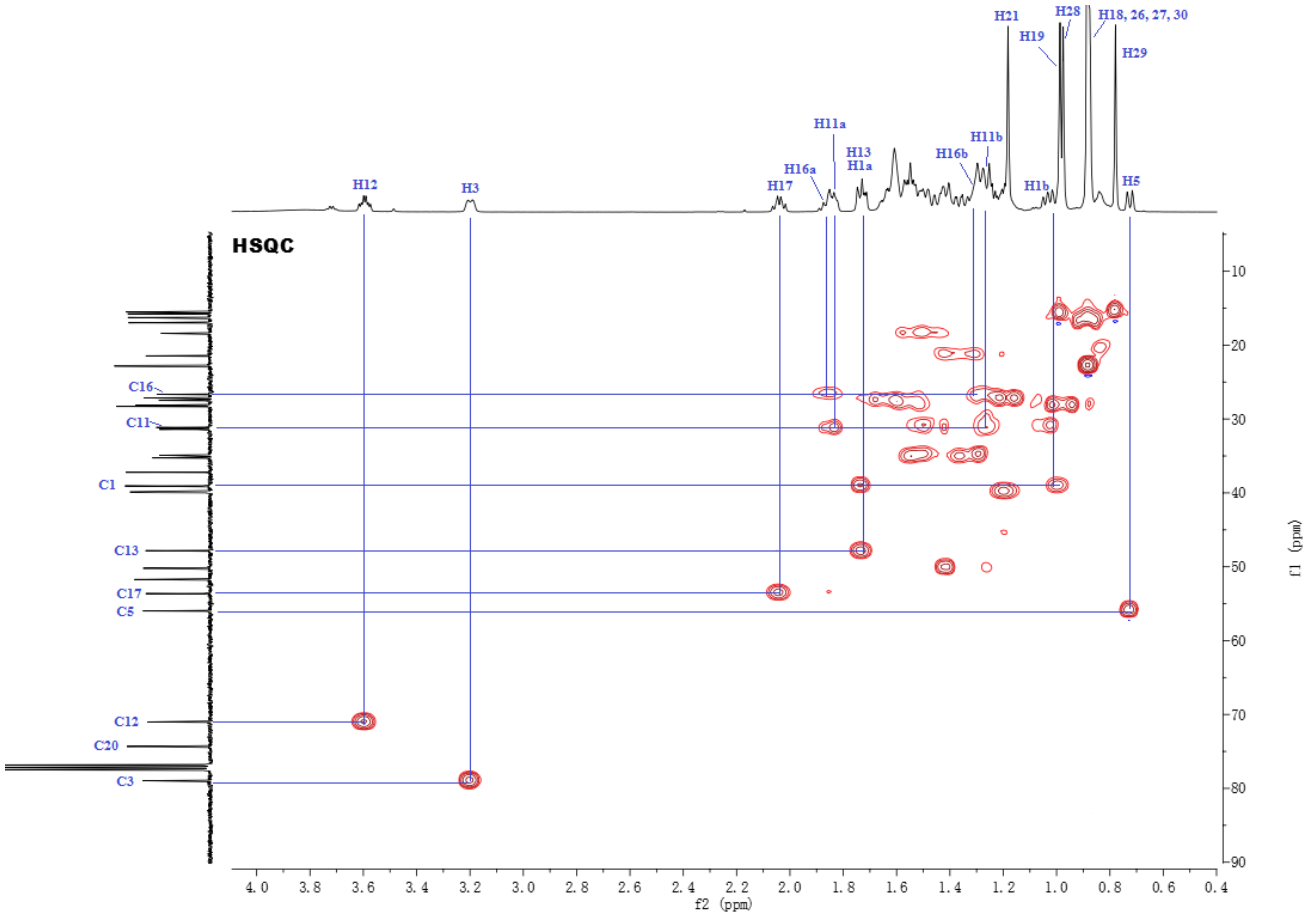
H21
H19
H28
H18, 26, 27, 30
H29
H11a
H13
H1a
H16a
H16b
H11b
H12
H3
H17
H1b
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C11
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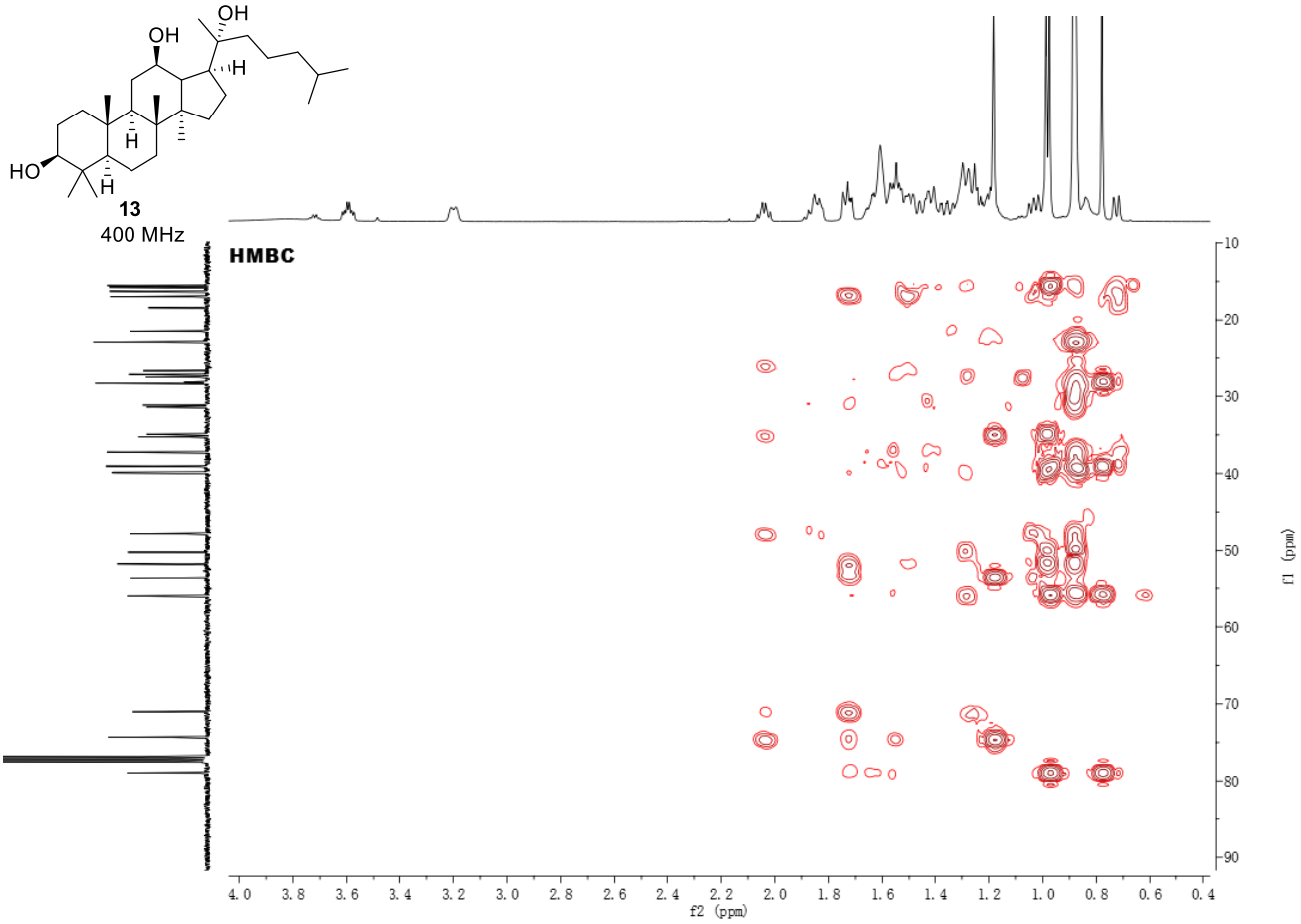
C5
C12
C20
C3
f2 (ppm)
f1 (ppm)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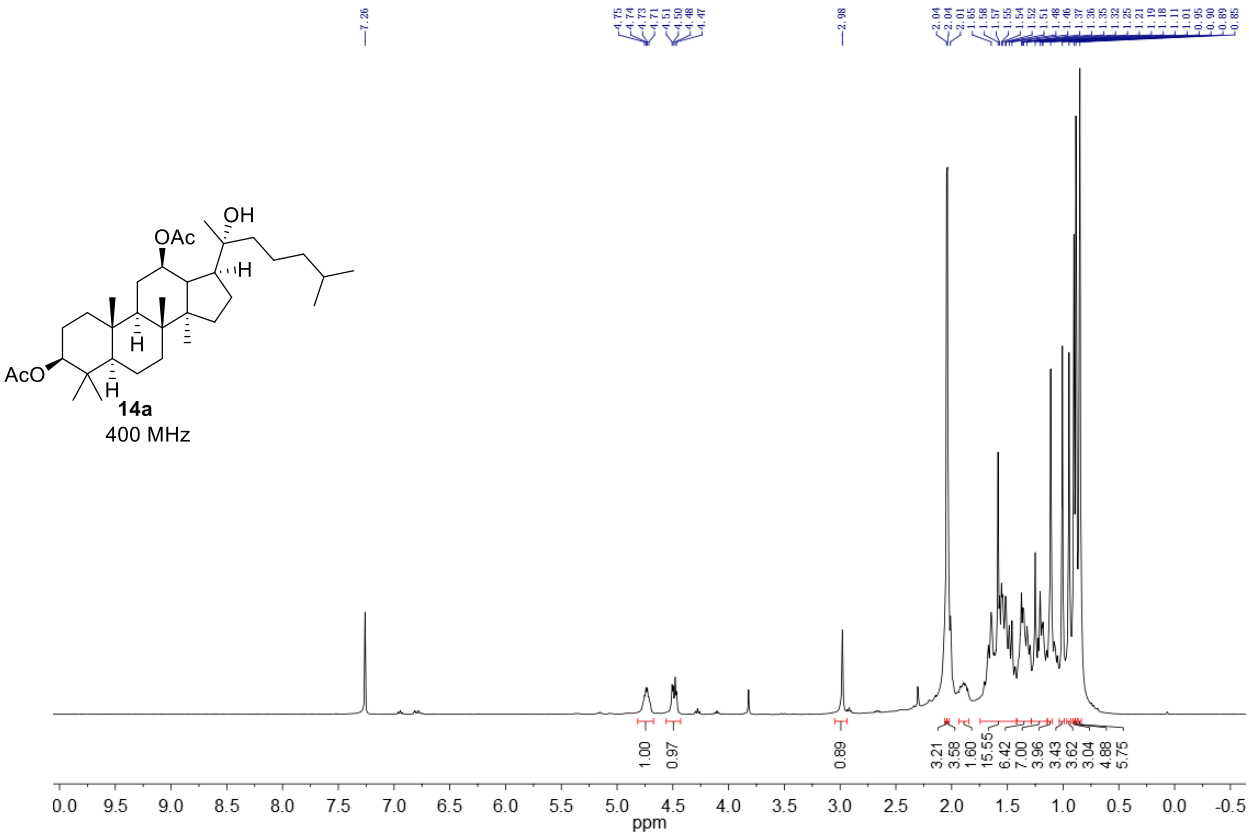
H
HO
H
H
13
400 MHz
HMBC
f2 (ppm)
f1 (ppm)


OH
OAc
H
H
AcO
H
14a
400 MHz
7.26
4.75
4.74
4.73
4.71
4.51
4.50
4.48
4.47
2.98
2.04
2.04
2.01
1.65
1.58
1.57
1.55
1.54
1.52
1.51
1.48
1.46
1.37
1.36
1.35
1.32
1.25
1.21
1.19
1.18
1.11
1.01
0.95
0.90
0.89
0.85
1.00
0.97
0.89
3.21
3.58
1.60
15.55
6.42
7.00
3.96
3.43
3.62
3.04
4.88
5.75
0.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
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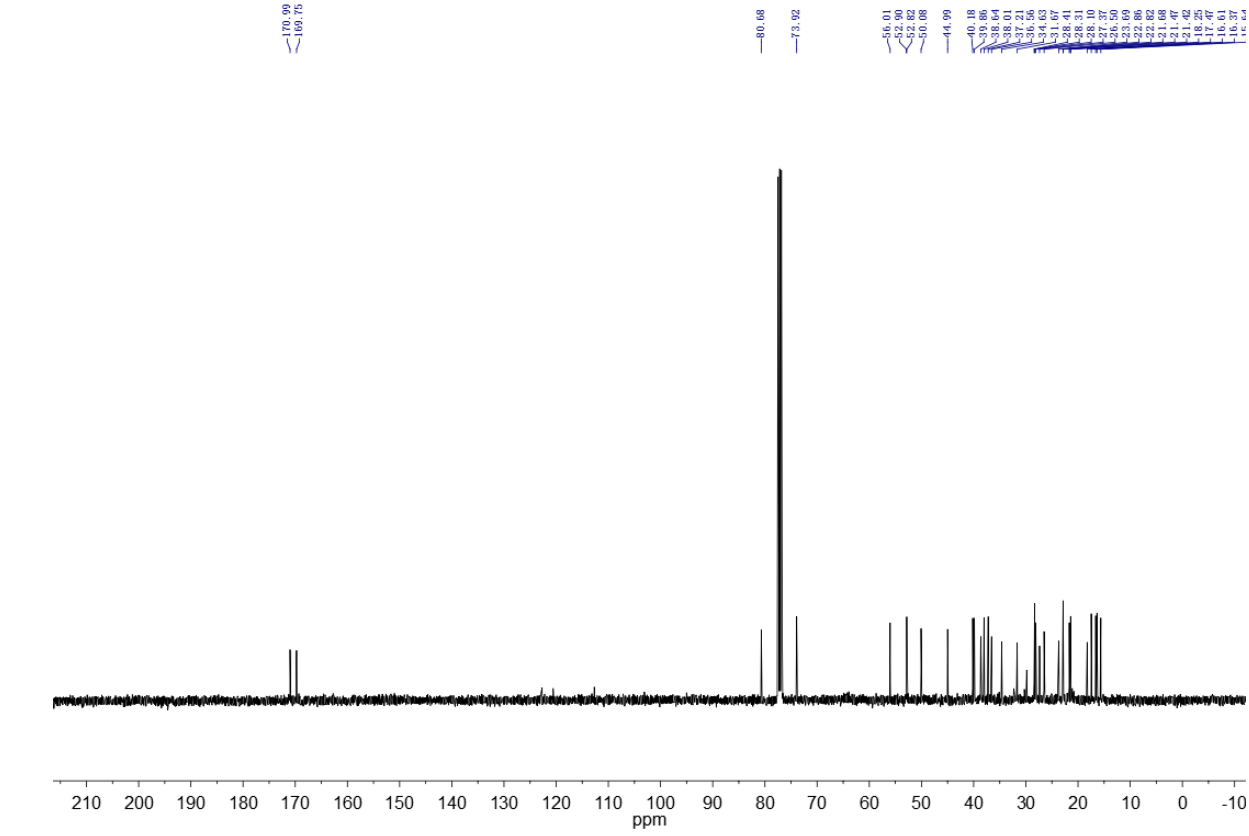
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52.82
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38.01
37.21
36.56
34.63
31.67
28.41
28.31
28.10
27.37
27.30
23.69
22.86
22.82
21.68
21.47
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18.25
17.47
16.61
16.37
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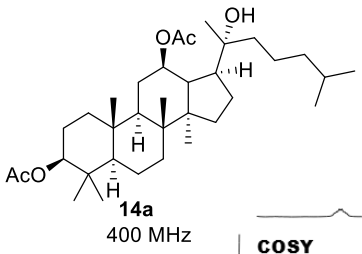
ppm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H
H
AcO
H
14a
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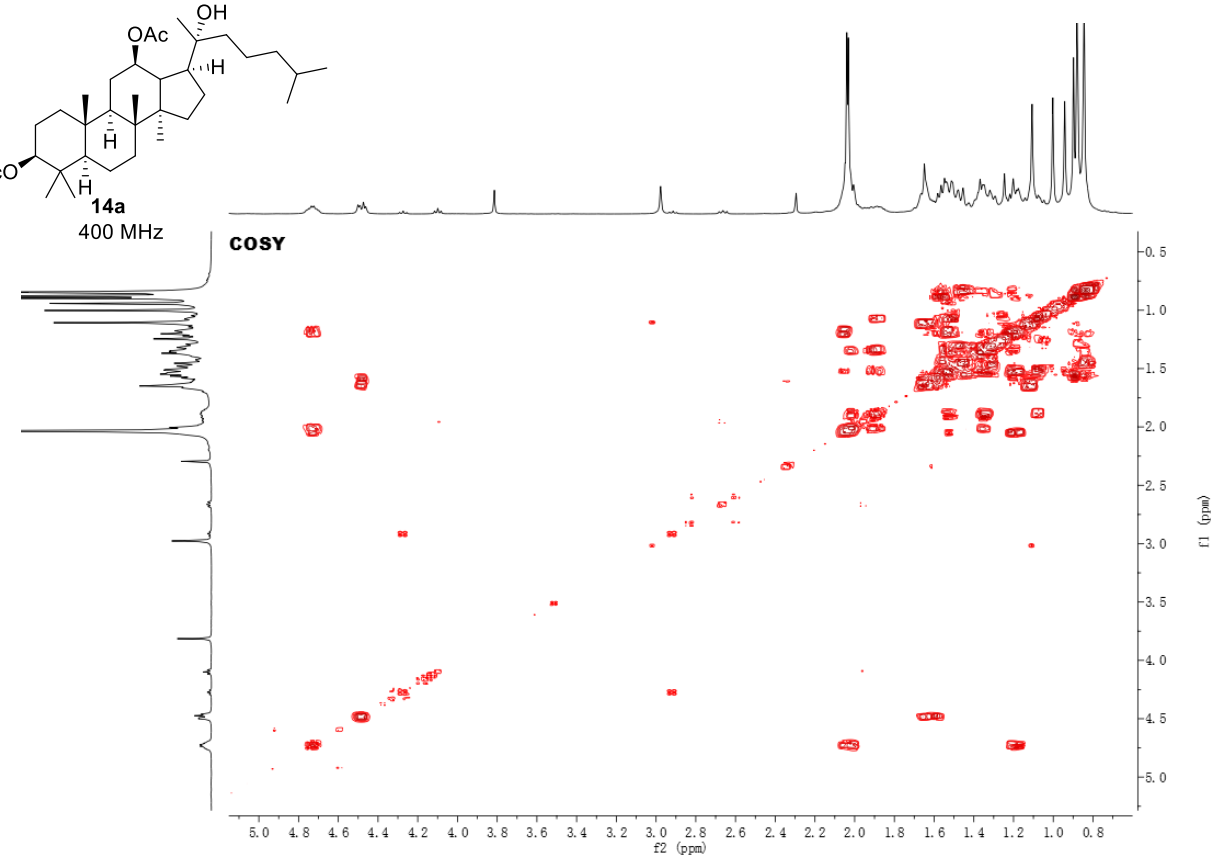
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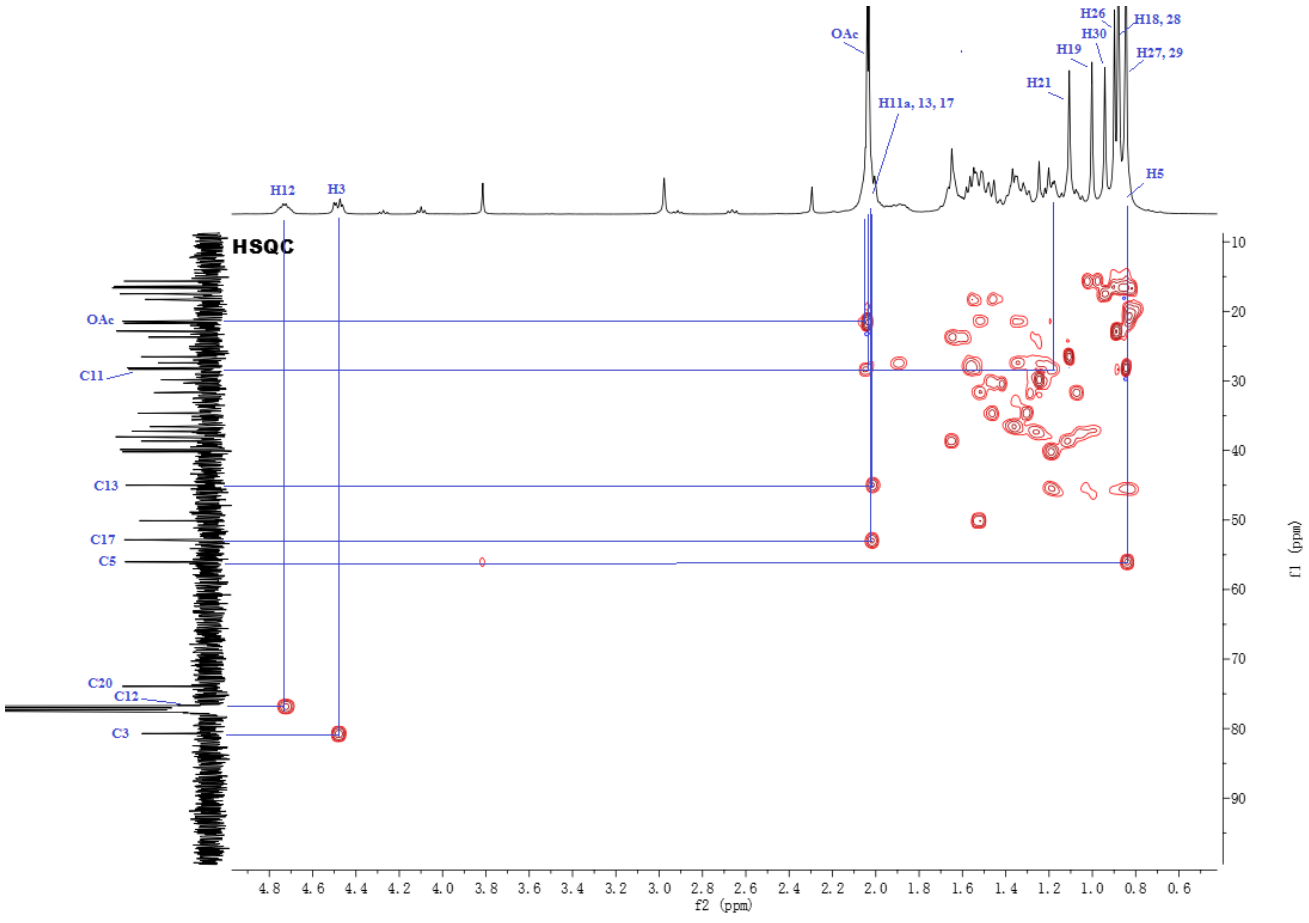
f1 (ppm)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H26
H30
H19
H18, 28
H27, 29
H21
H5
H12
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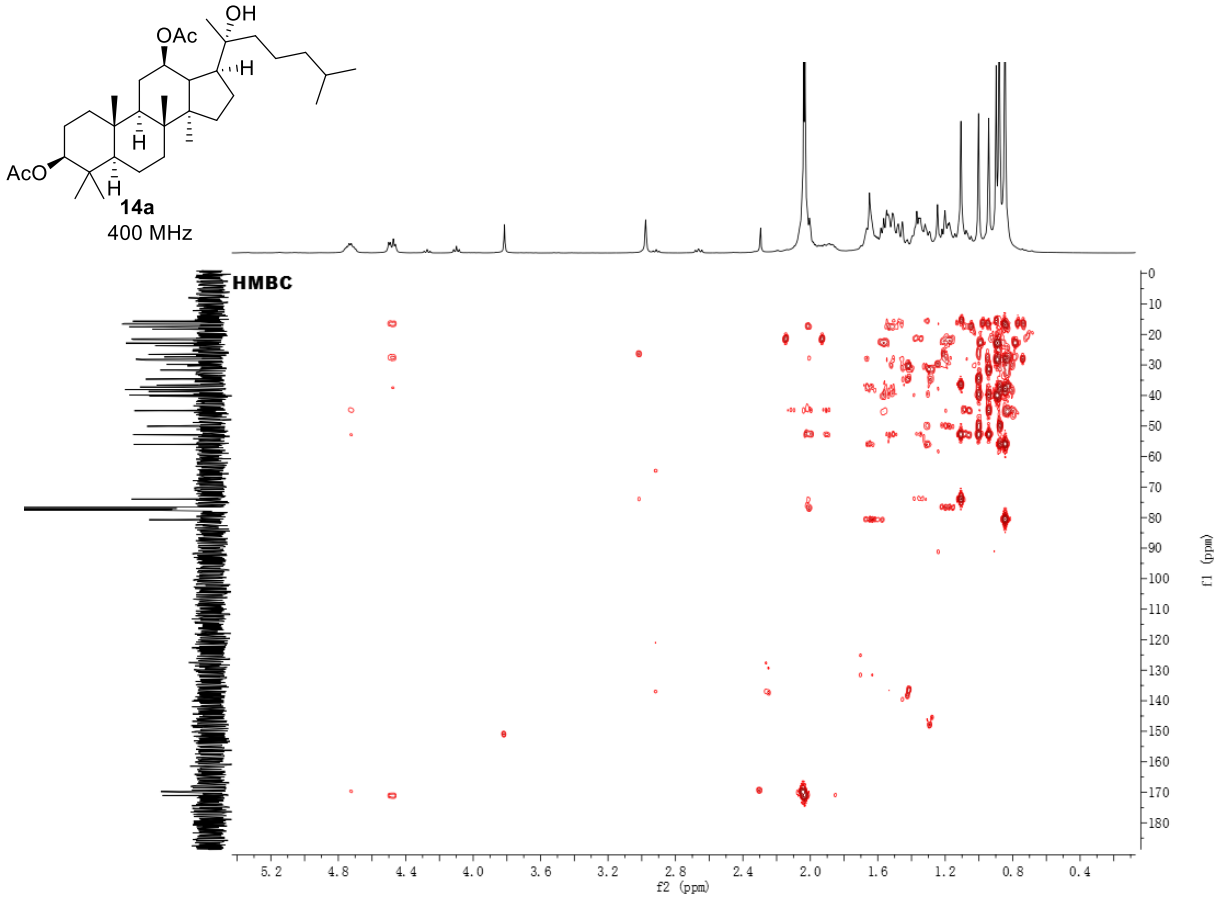
HSQC
OAc
C11
C13
C17
C5
C20
C12
C3
f2 (ppm)
f1 (ppm)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H
AcO
H
14a
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HMBC
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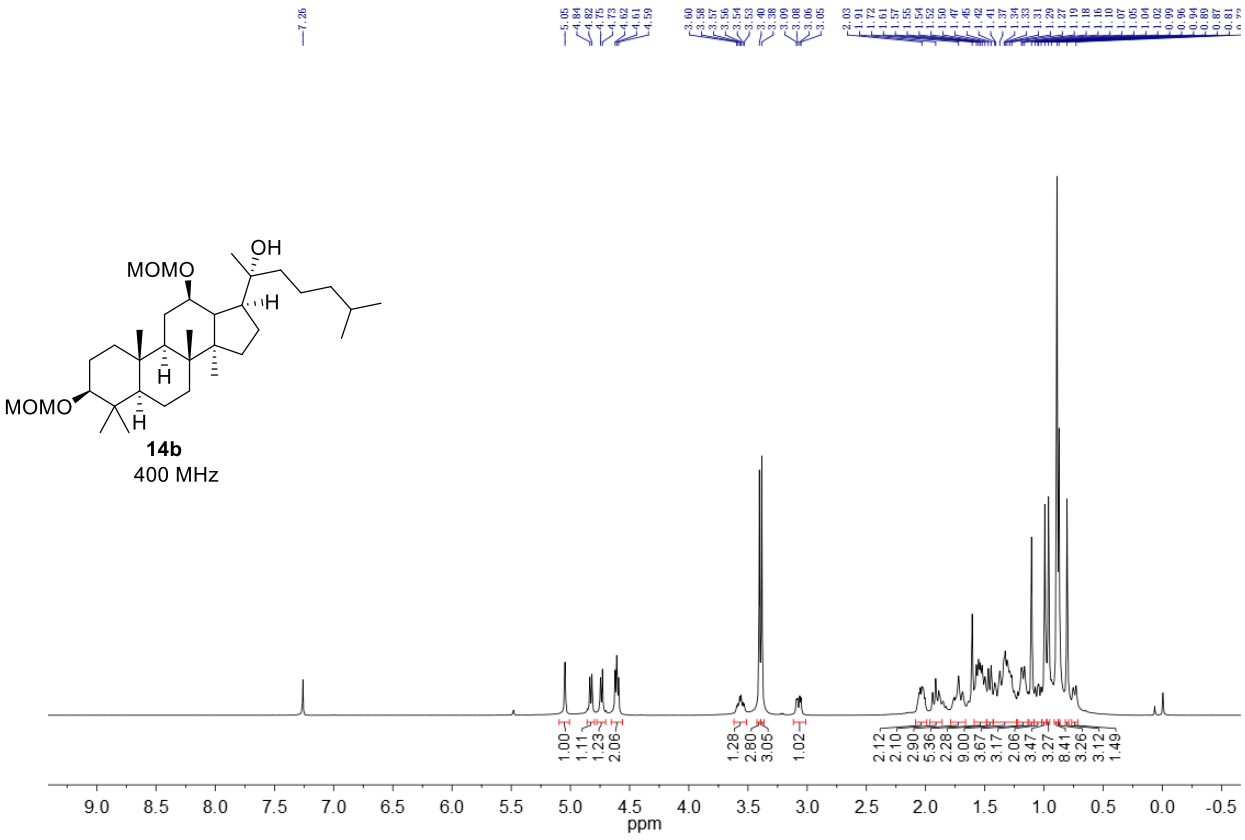
f1 (ppm)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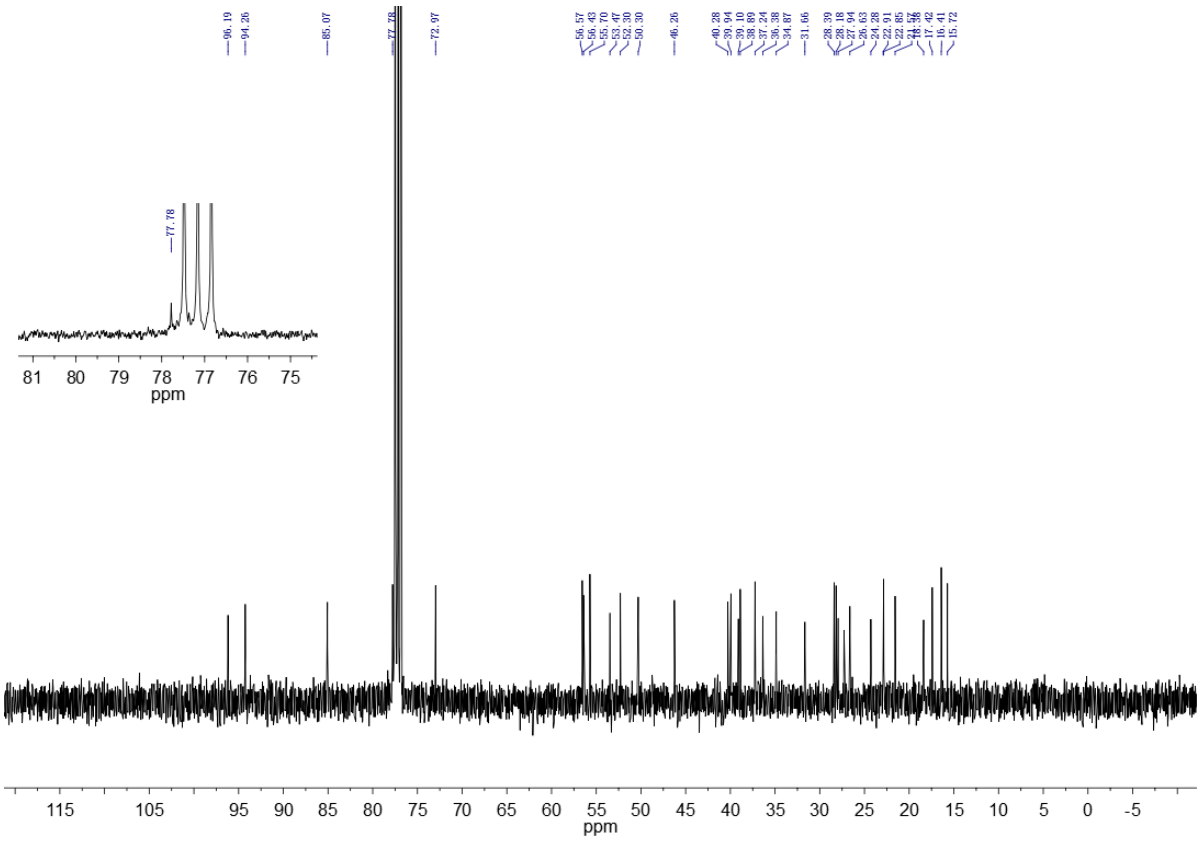
H
H
MOMO
H
14b
400 MHz
ppm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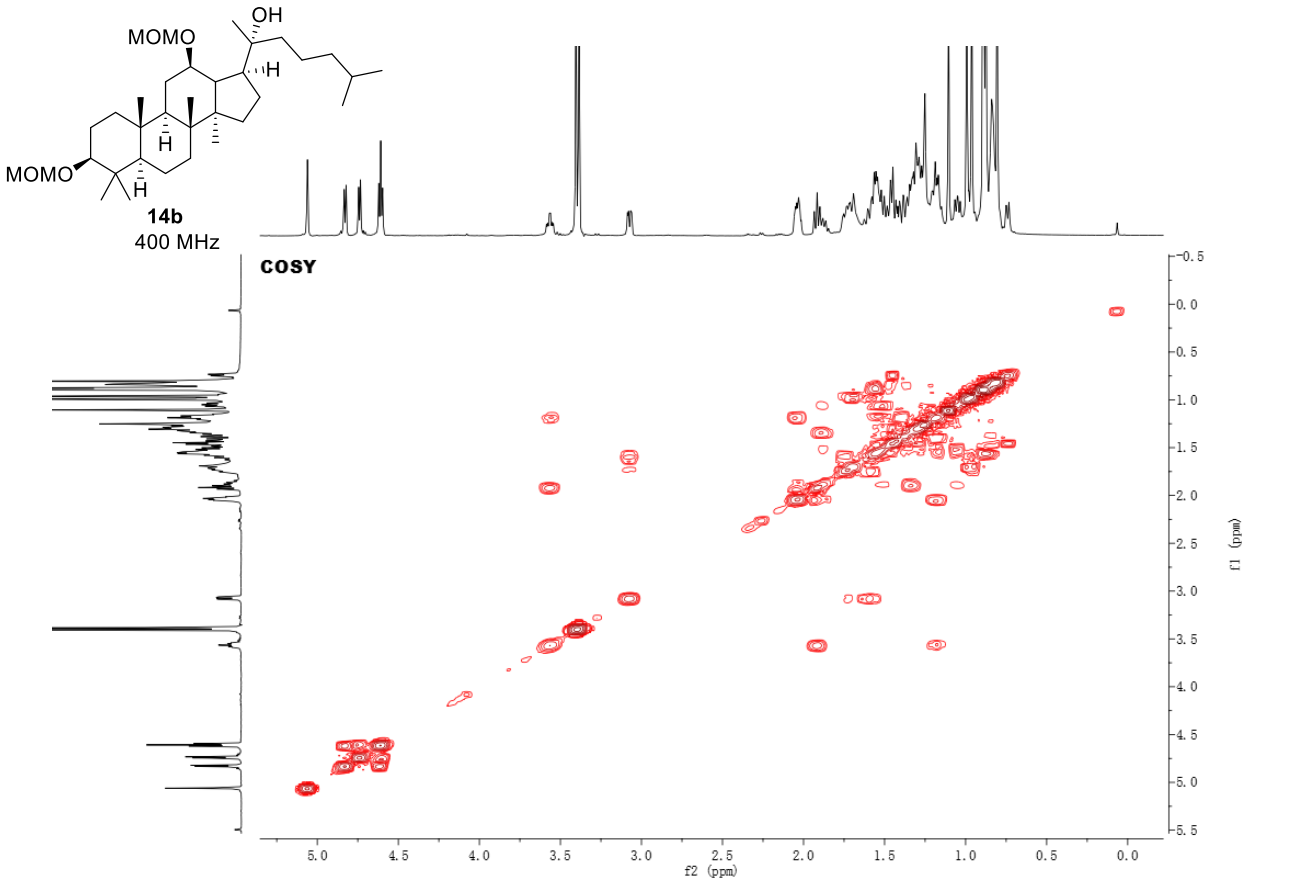
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H
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14b
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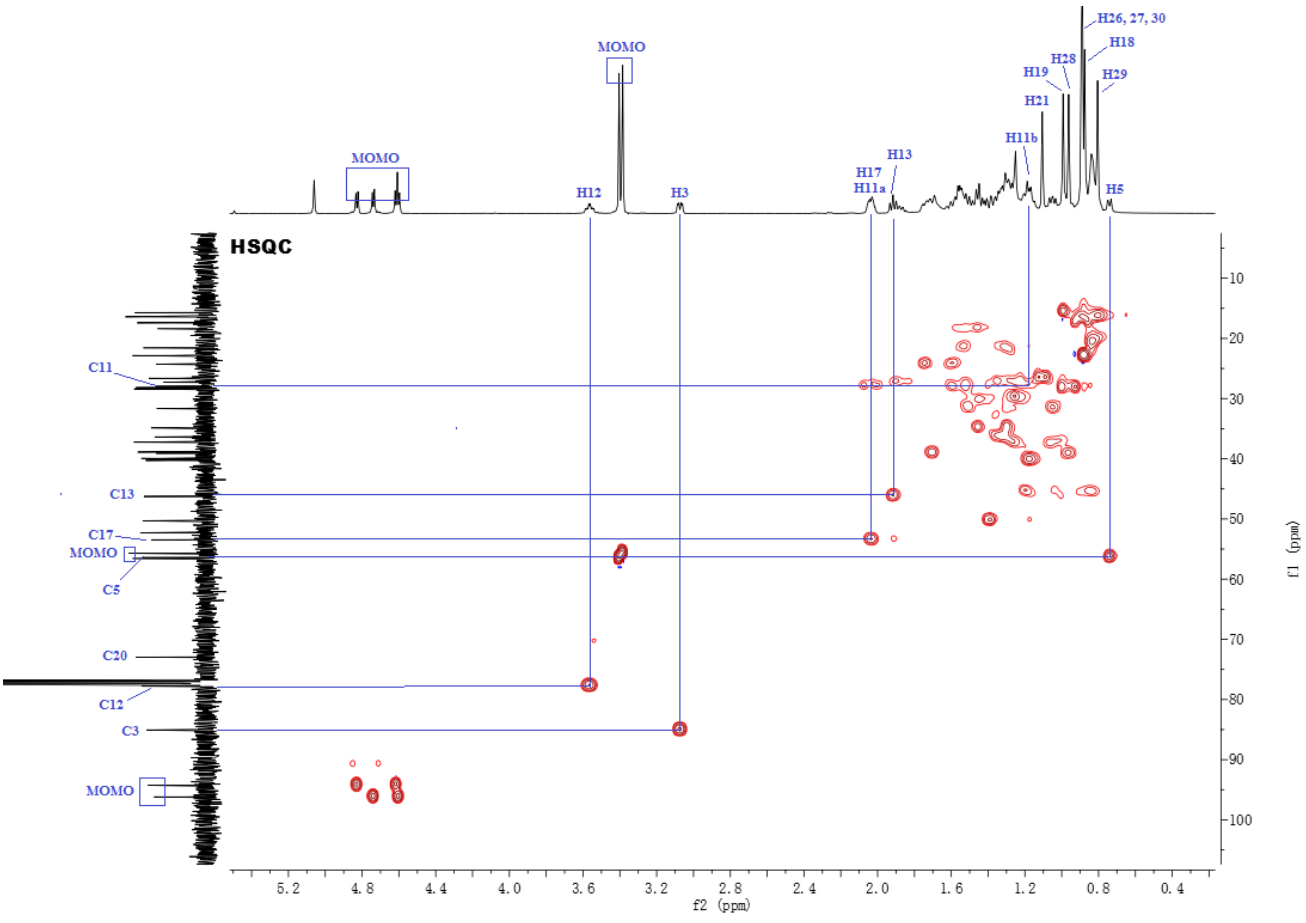
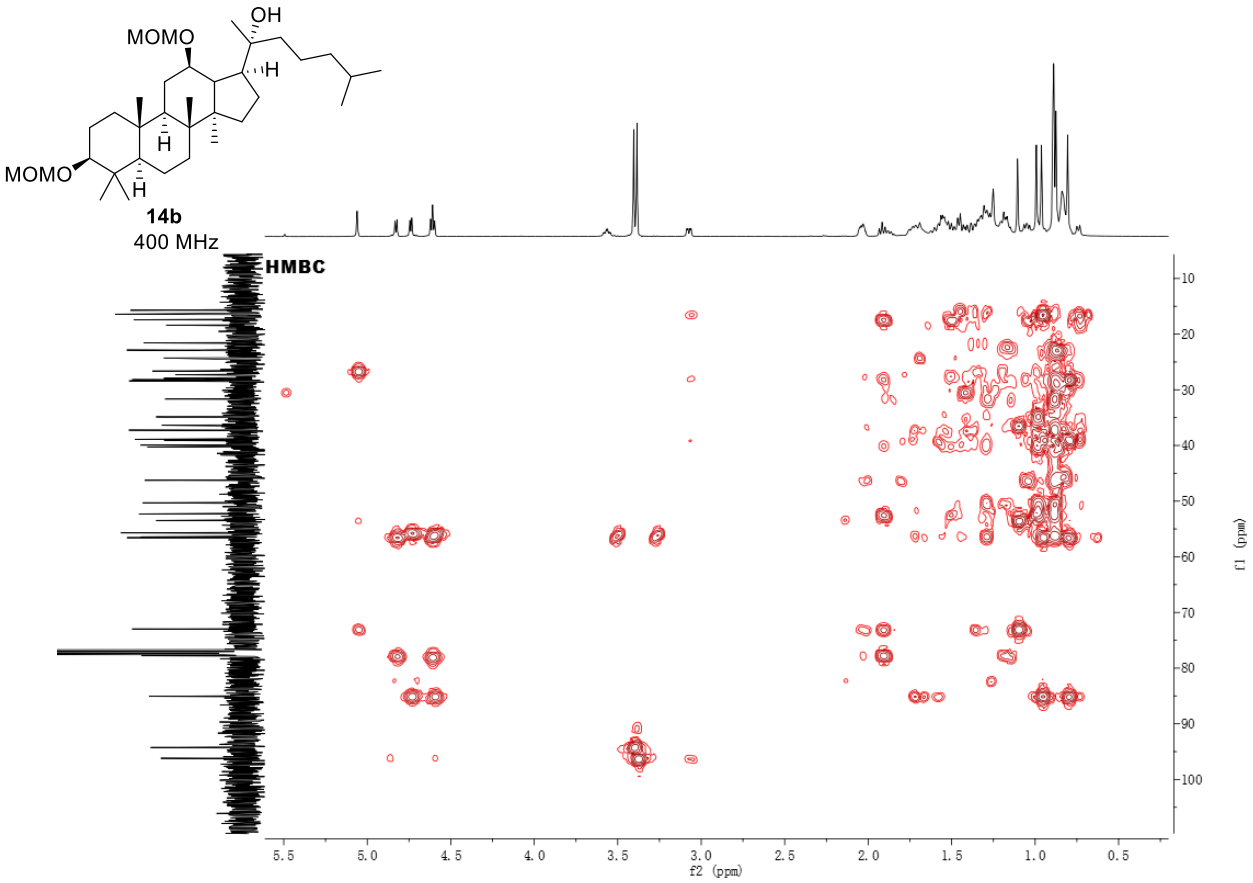
f1 (ppm)


MOMO
MOMO
H12
H3
H17
H11a
H13
H11b
H21
H19
H28
H26, 27, 30
H18
H29
H5
HSQC
C11
C13
C17
MOMO
C5
C20
C12
C3
MOMO
f2 (ppm)
f1 (ppm)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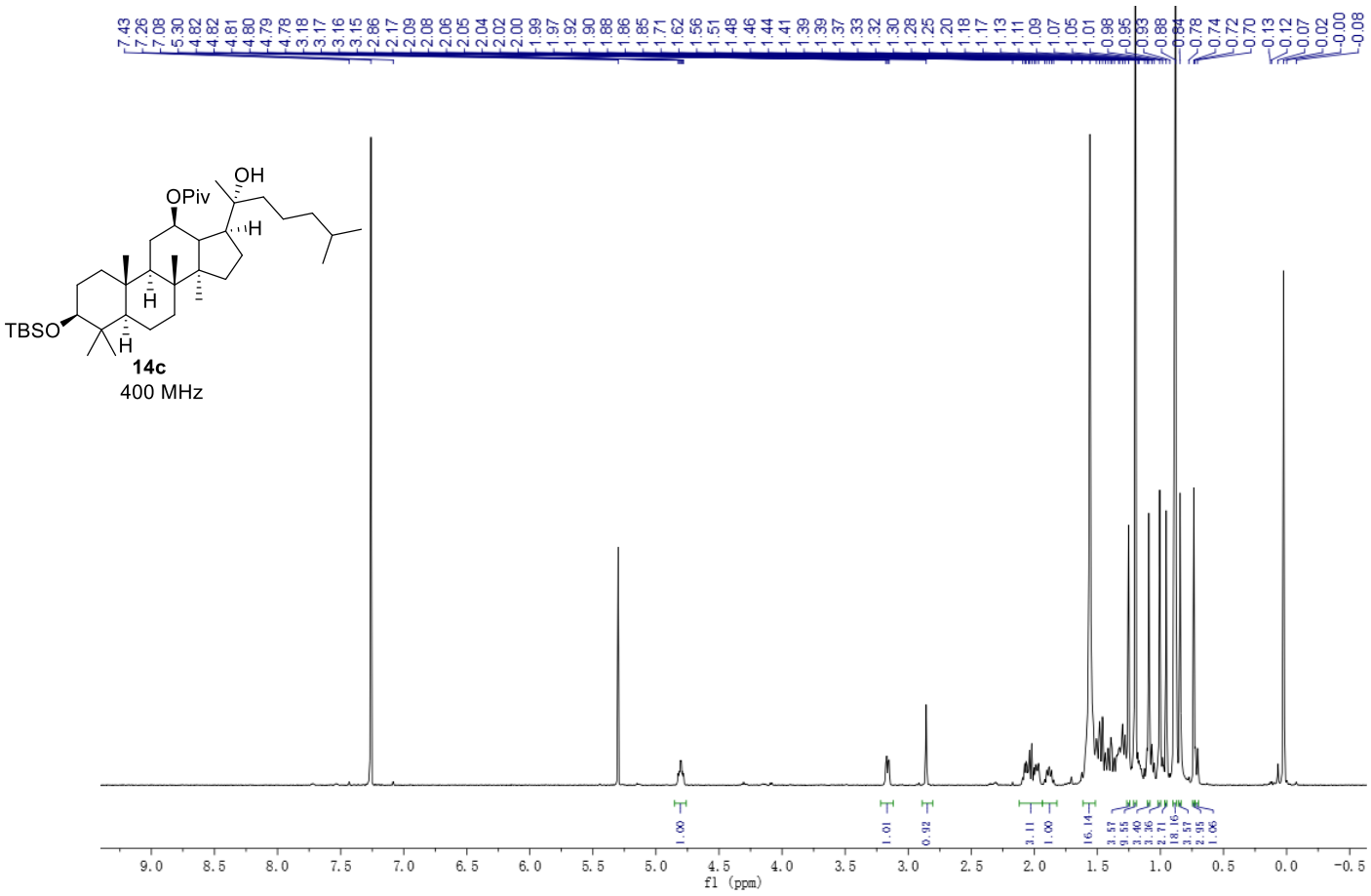
OH
H
H
MOMO
H
14b
400 MHz
HMBC
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f2 (ppm)
10
20
30
40
50
60
70
80
90
100
f1 (ppm)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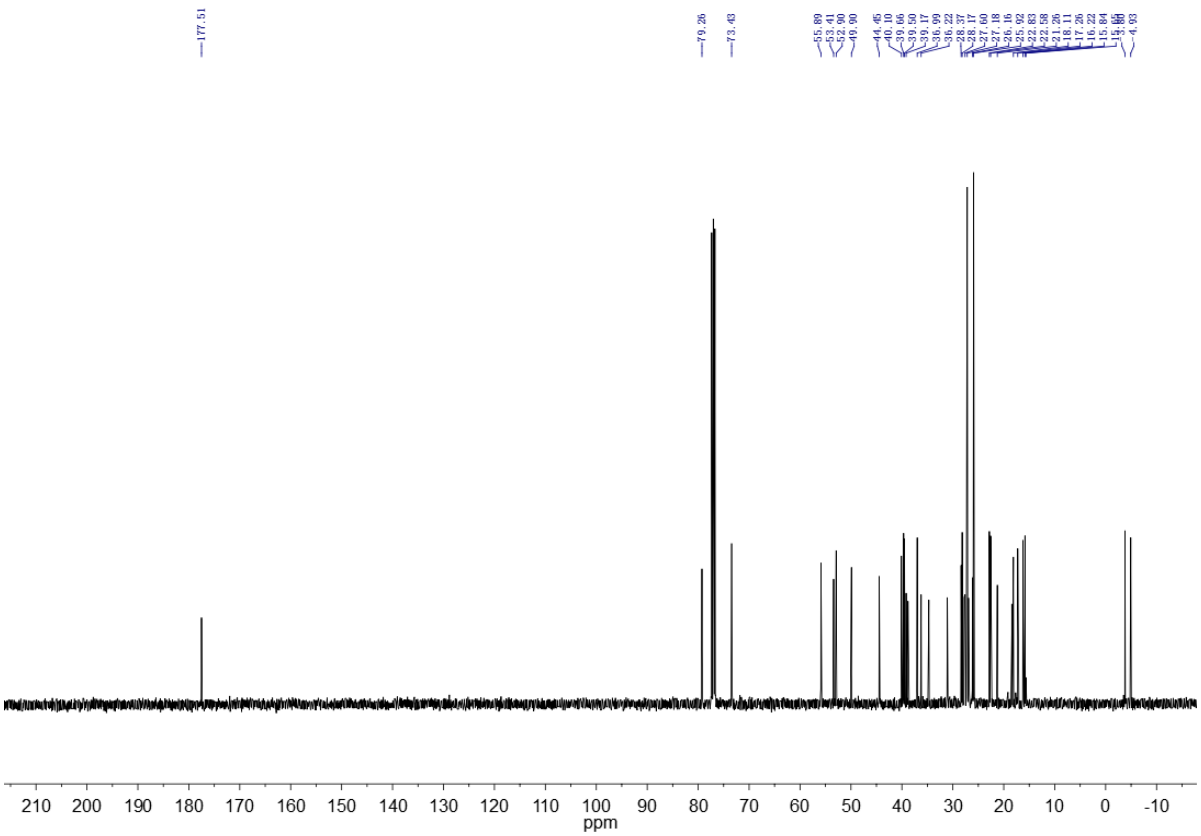
OPiv
H
H
TBSO
H
14c
400 MHz
f1 (ppm)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28.37
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27.18
26.16
25.92
22.83
22.58
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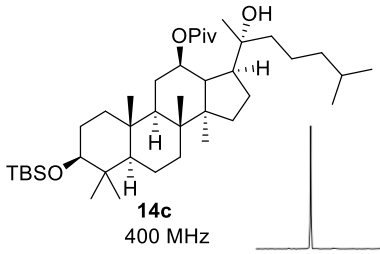
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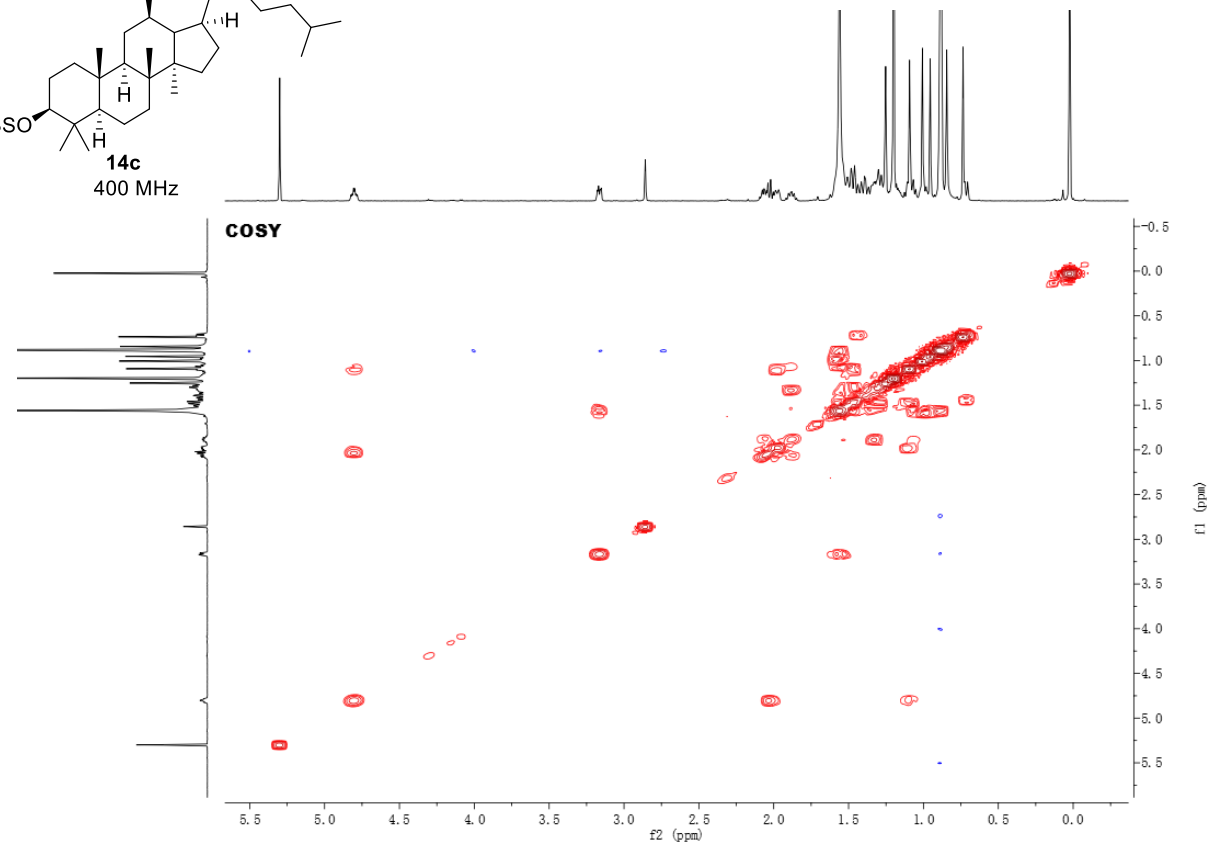
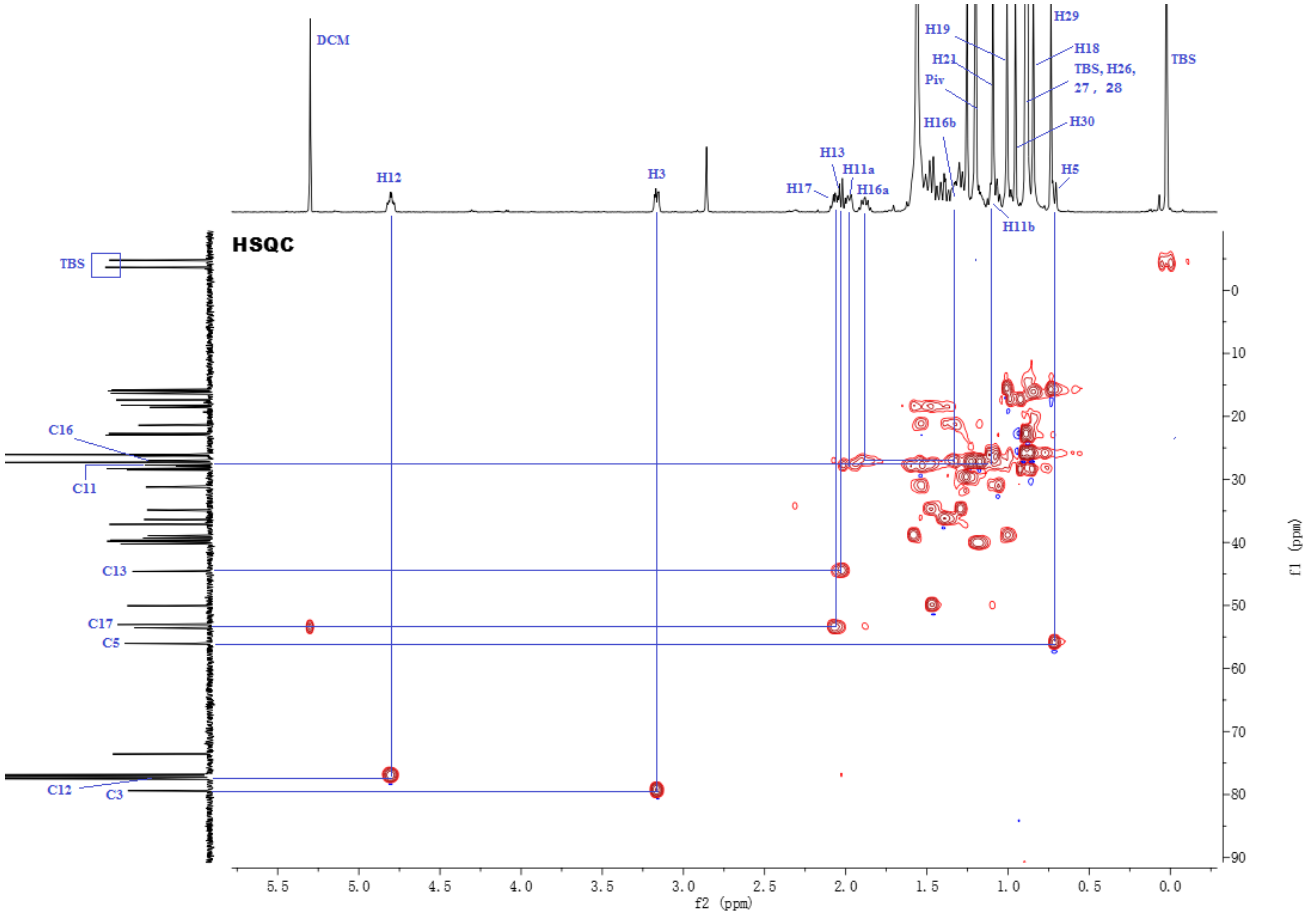
H
H
TBSO
H

14c
400 MHz


COSY
f2 (ppm)
f1 (ppm)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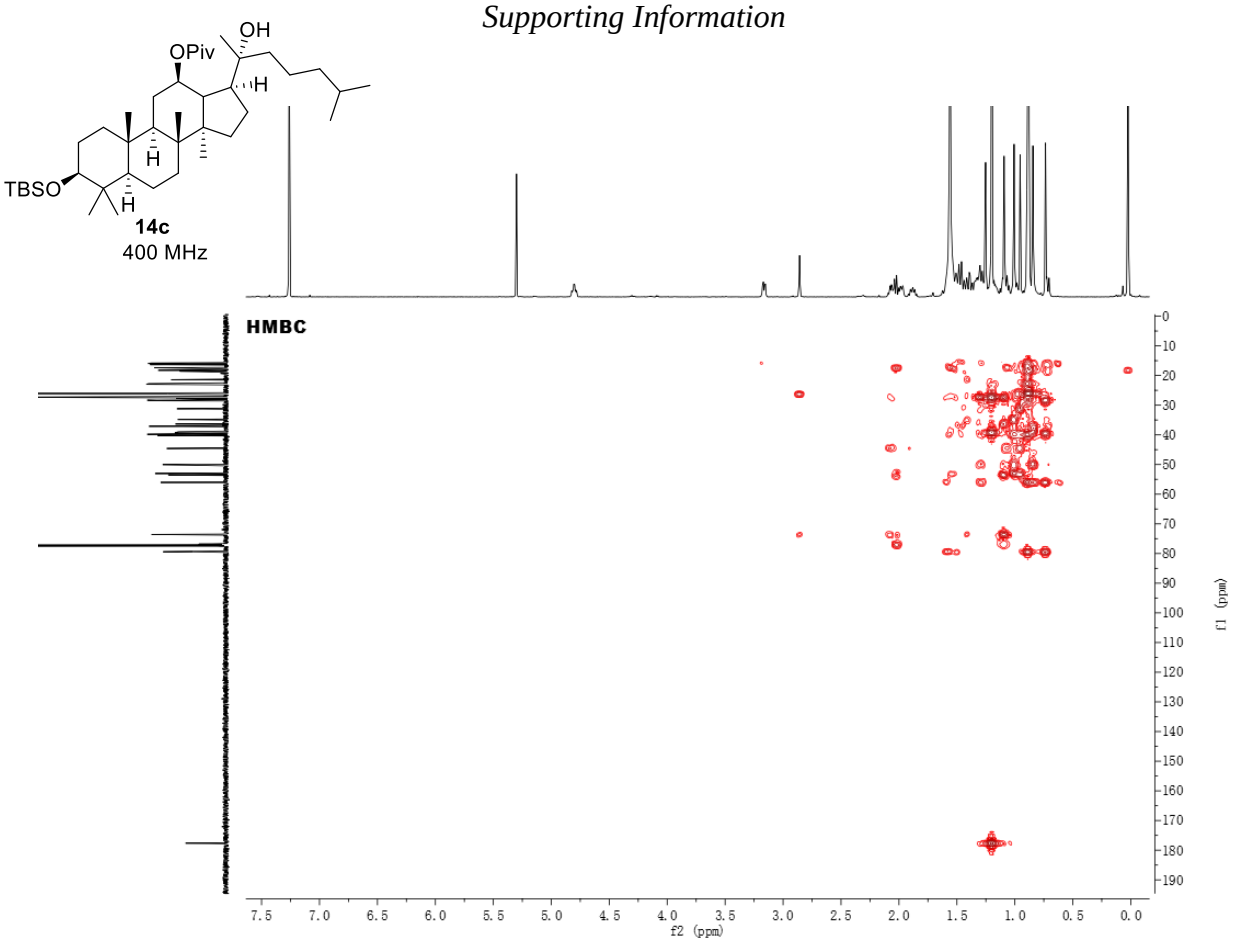
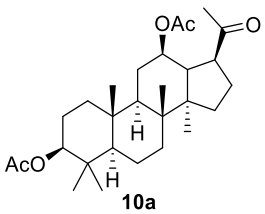
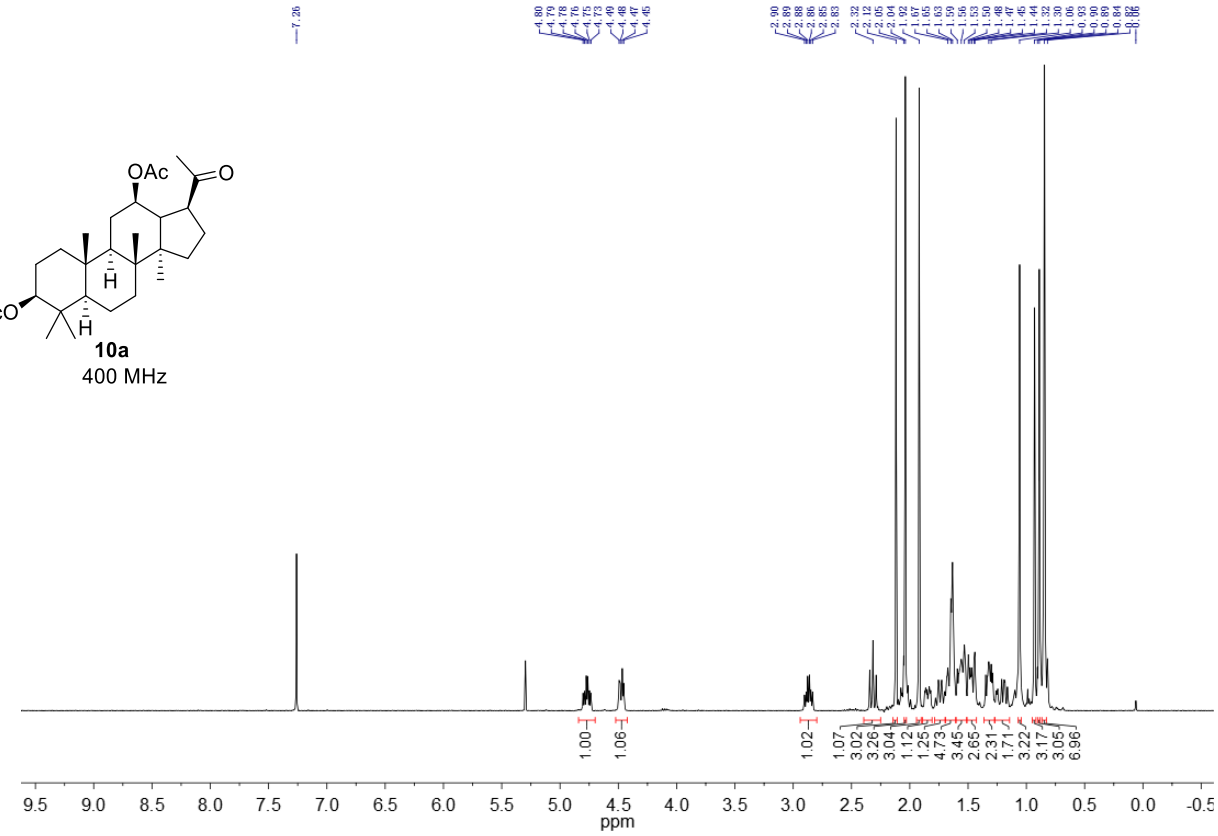
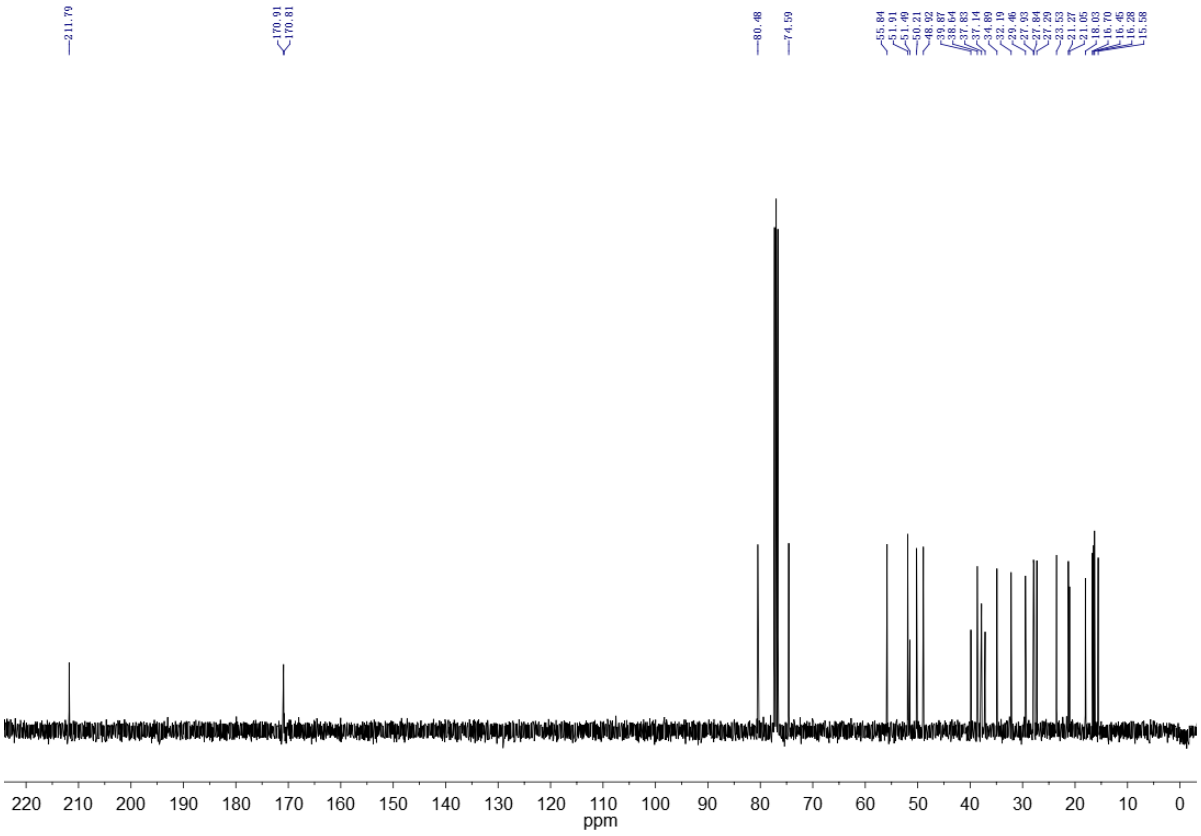
H12
H3
H17
H13
H11a
H16a
H19
H21
Piv
H16b
H11b
H29
H18
TBS, H26, 27, 28
H30
H5
TBS
HSQC
TBS
C16
C11
C13
C17
C5
C12
C3
f2 (ppm)
f1 (ppm)

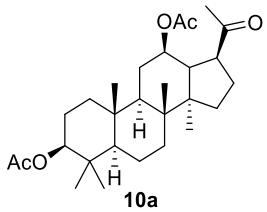

OPiv
OH
H
H
H
TBSO
14c
400 MHz
HMBC
f2 (ppm)
f1 (ppm)



10a
400 MHz

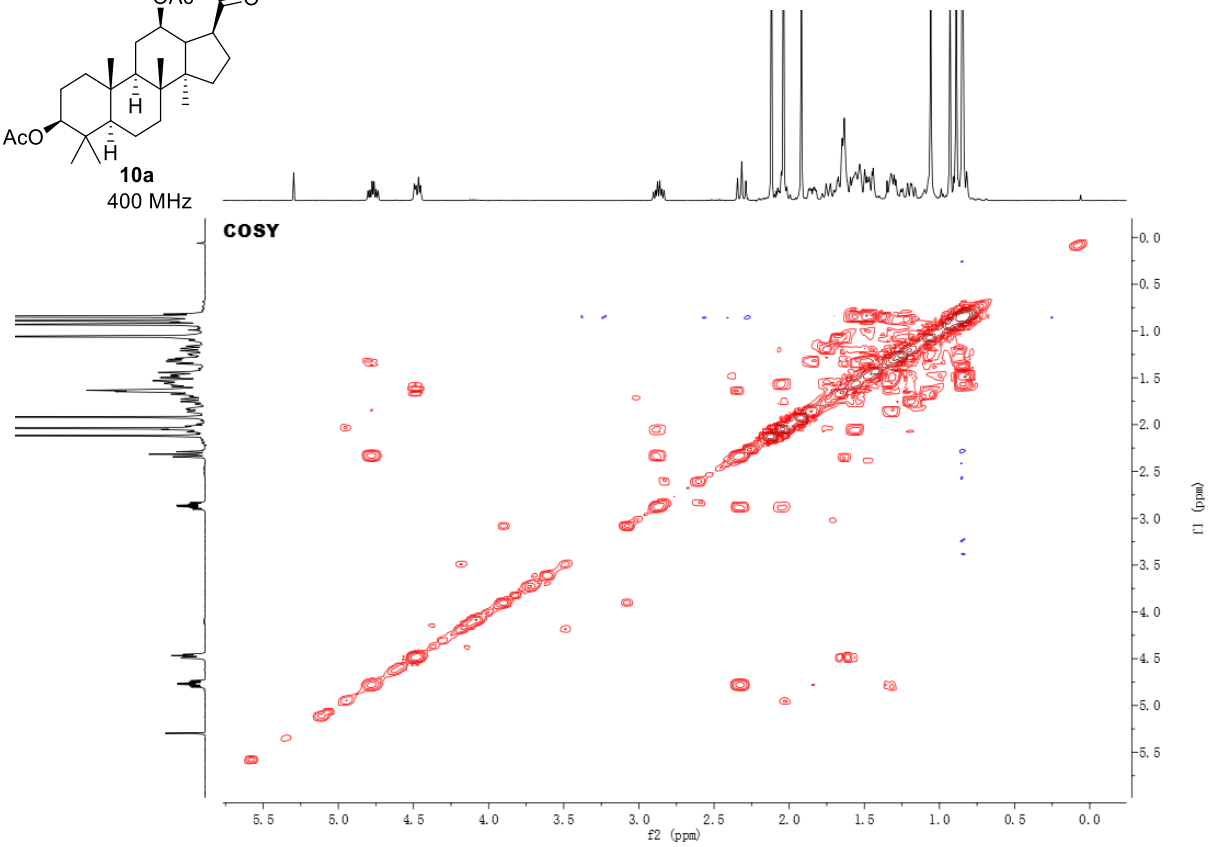


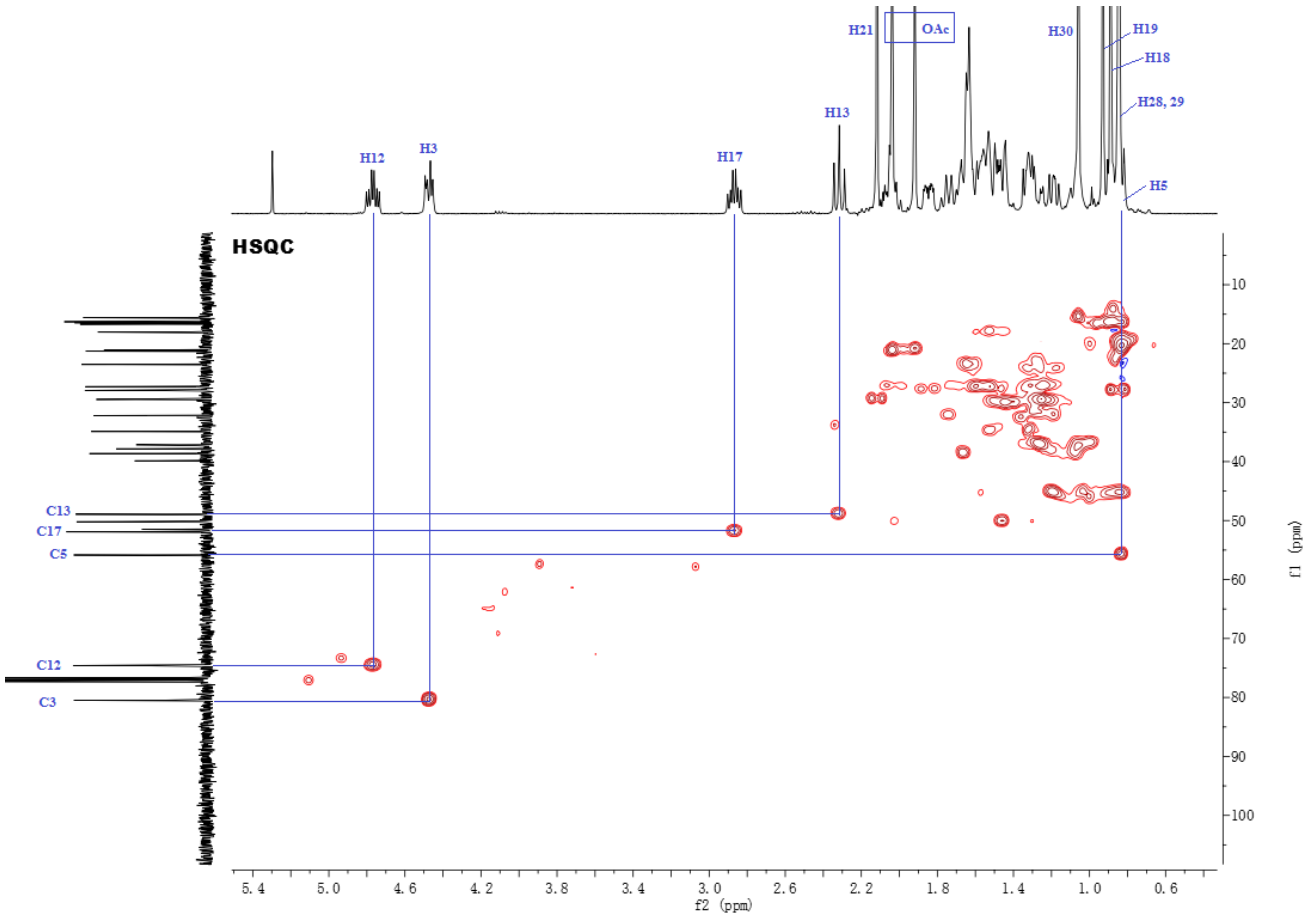


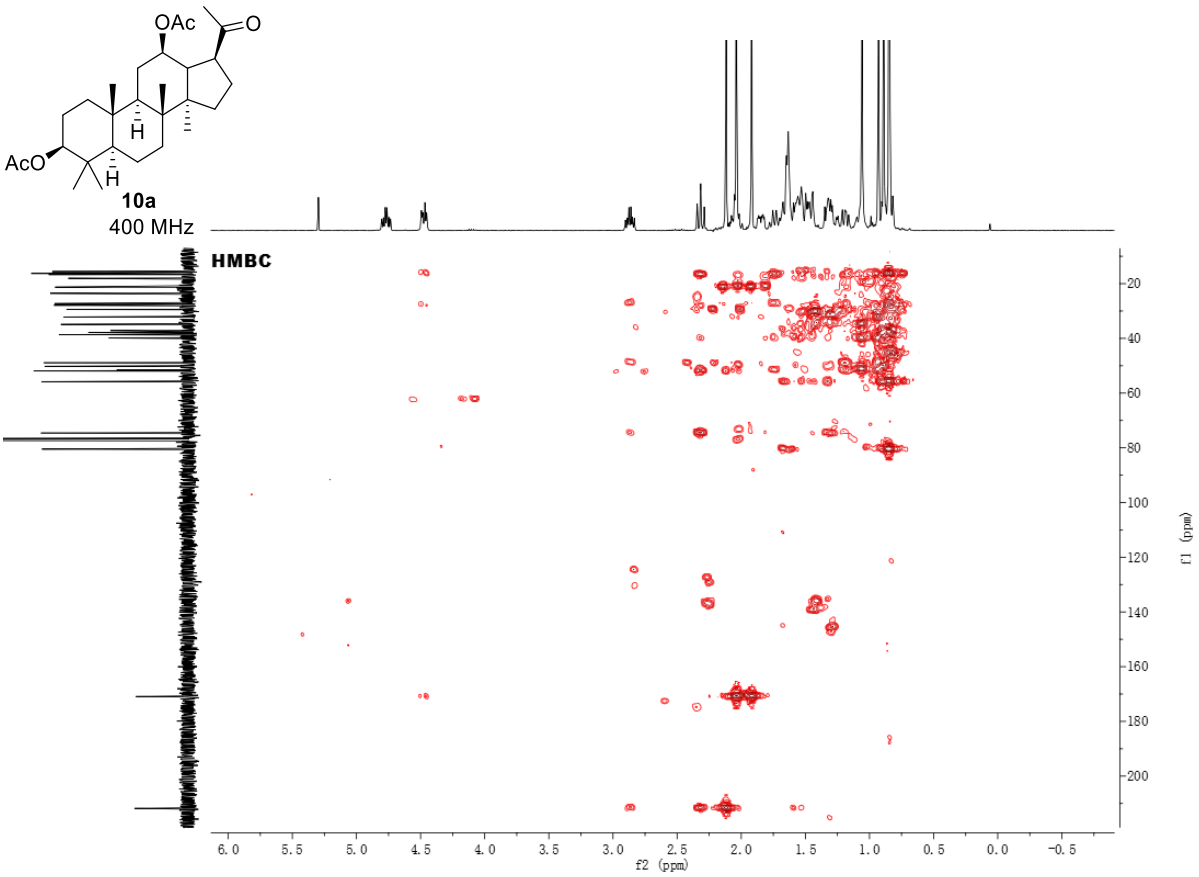

OAc
O
AcO
H
H

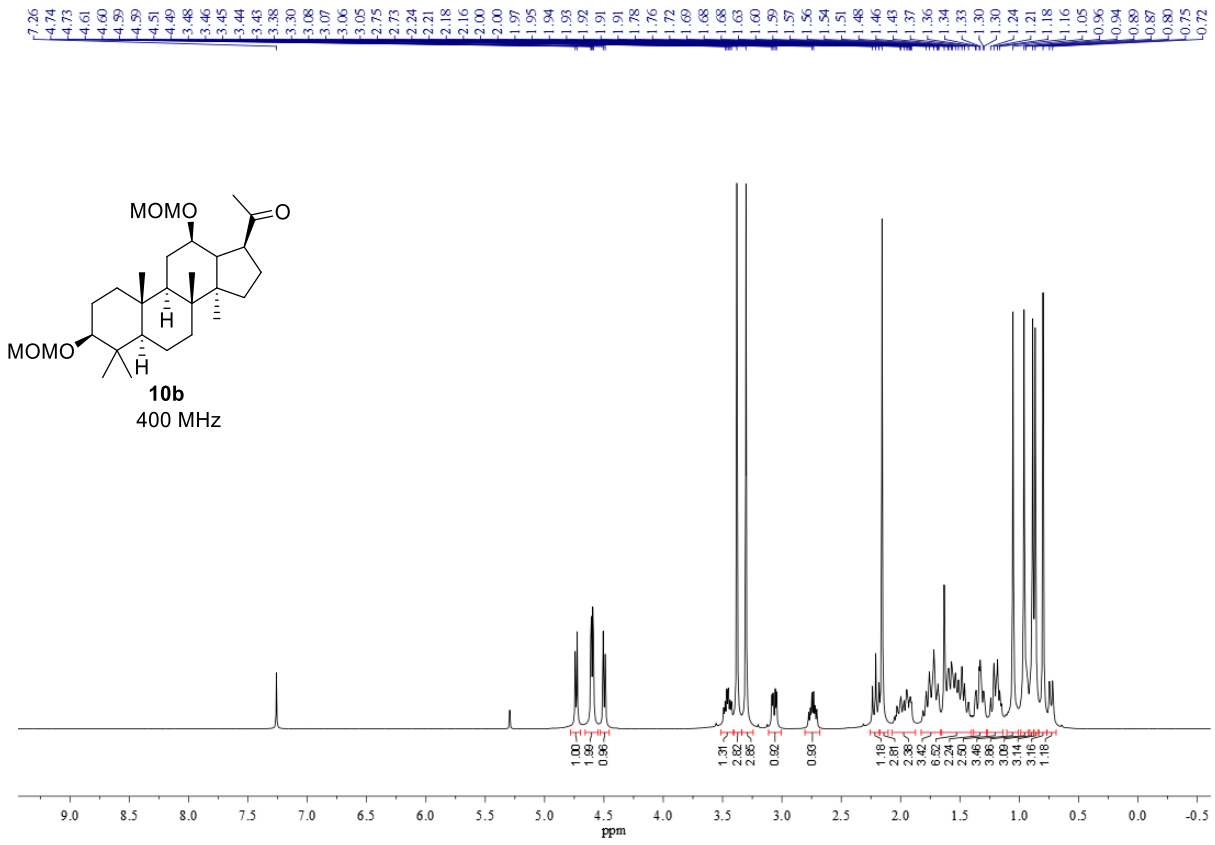
10a

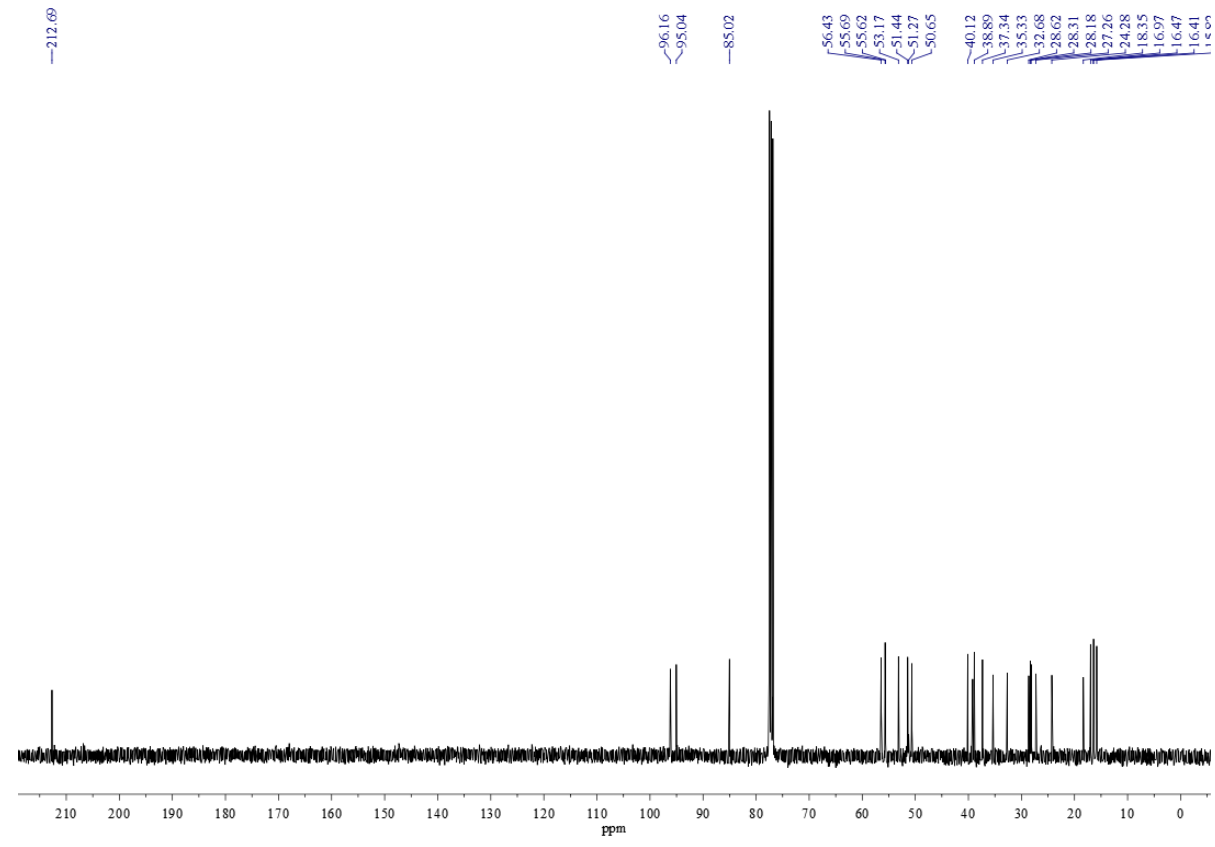
400 MHz

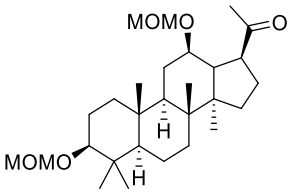

COSY
f2 (ppm)
f1 (ppm)


H21
OAc
H30
H19
H18
H28, 29
H13
H12
H3
H17
H5
HSQC
C13
C17
C5
C12
C3
f2 (ppm)
f1 (ppm)

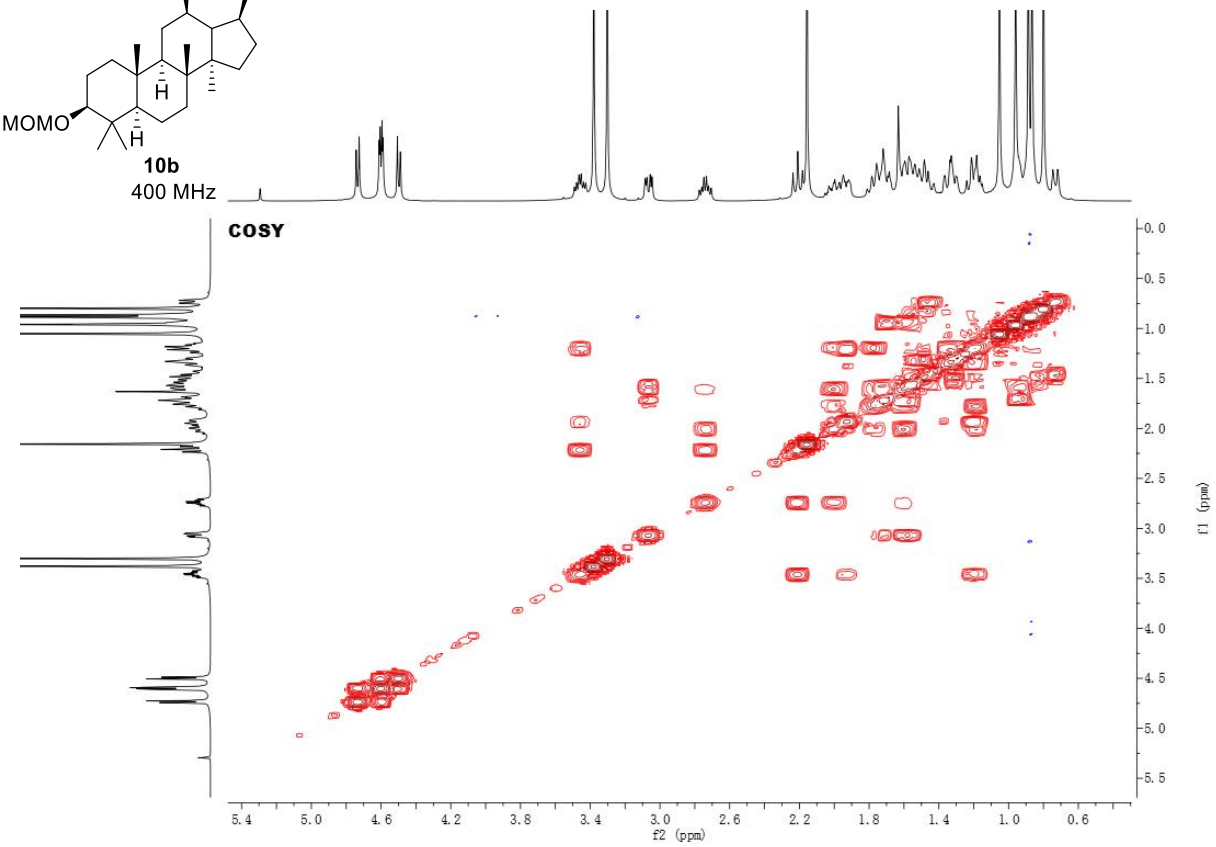

OAc
O
AcO
H
H
10a
400 MHz
HMBC
f2 (ppm)
f1 (ppm)

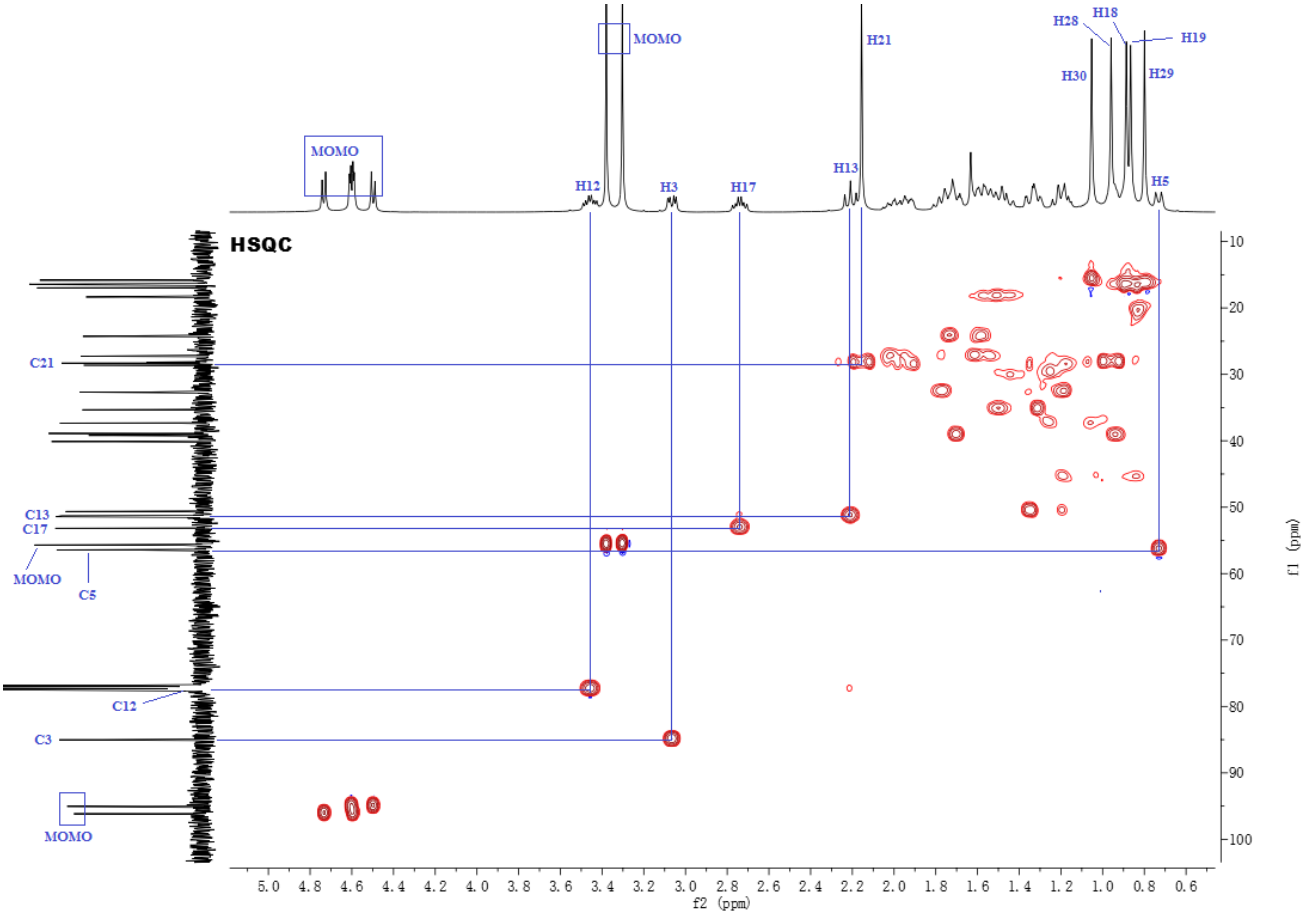

MOMO
O
MOMO
H
H
10b
400 MHz
ppm

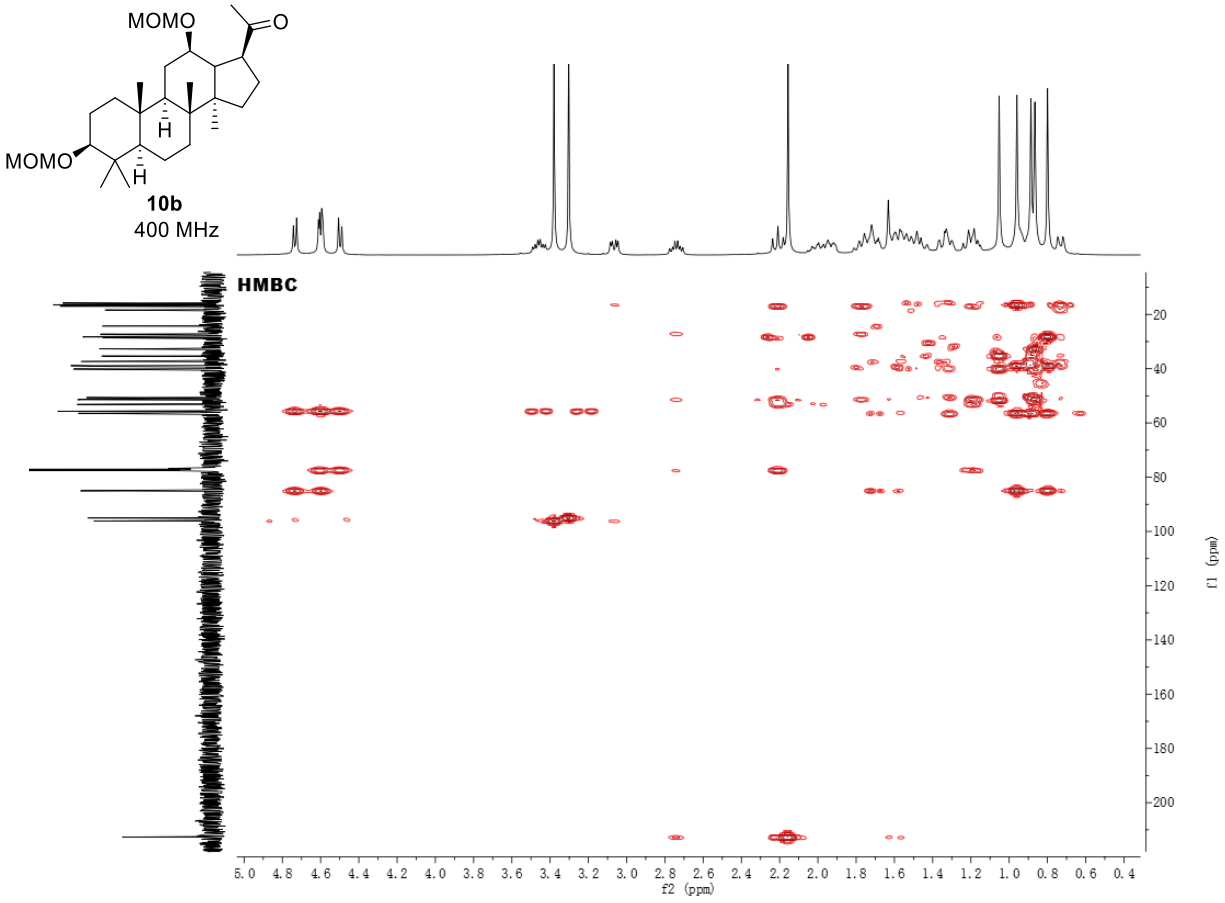

ppm

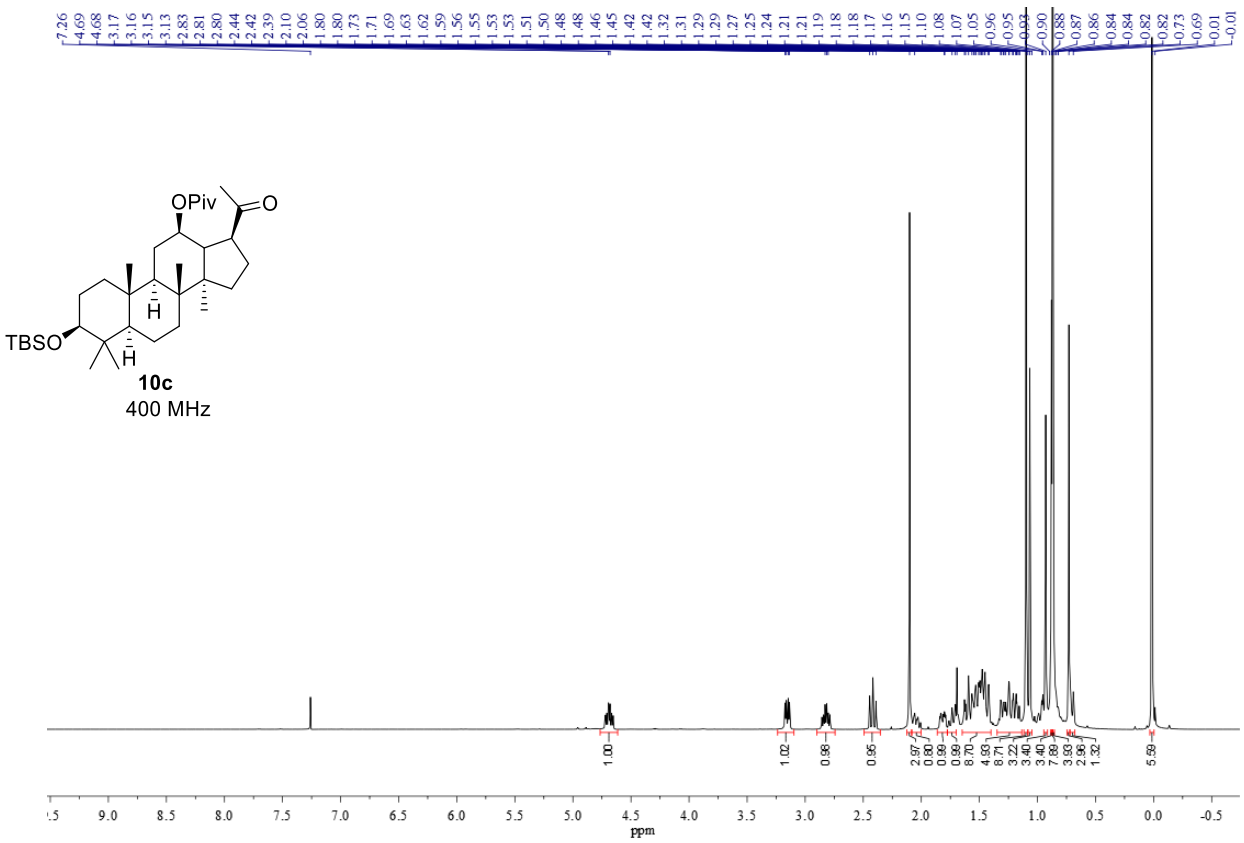

MOMO
O
H
MOMO
H

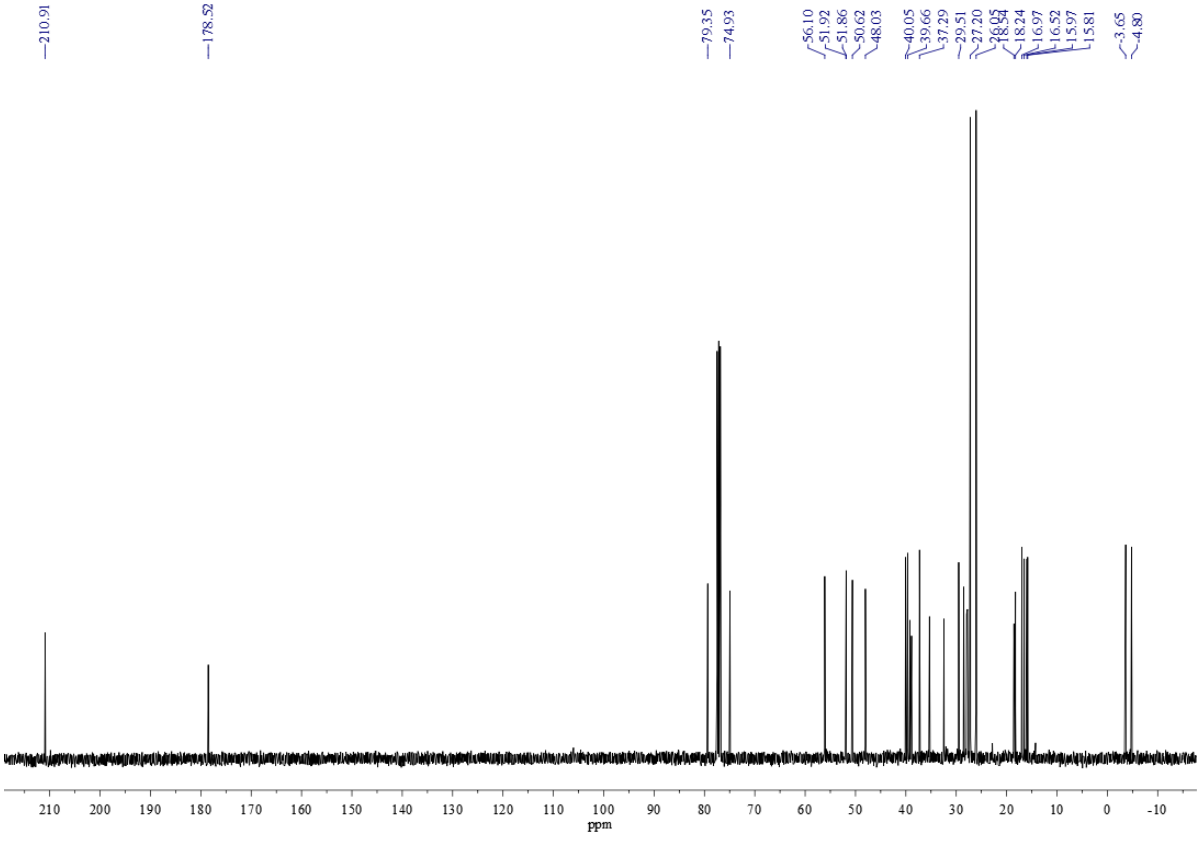
10b
400 MHz

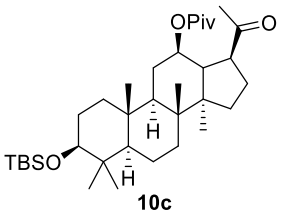

COSY
5.4
5.0
4.6
4.2
3.8
3.4
3.0
2.6
2.2
1.8
1.4
1.0
0.6
f2 (ppm)
0.0
0.5
1.0
1.5
2.0
2.5
3.0
3.5
4.0
4.5
5.0
5.5
f1 (ppm)


MOMO
MOMO
H12
H3
H17
H13
H21
H28
H18
H19
H30
H29
H5
HSQC
C21
C13
C17
MOMO
C5
C12
C3
MOMO
5.0
4.8
4.6
4.4
4.2
4.0
3.8
3.6
3.4
3.2
3.0
2.8
2.6
2.4
2.2
2.0
1.8
1.6
1.4
1.2
1.0
0.8
0.6
f2 (ppm)
10
20
30
40
50
60
70
80
90
100
f1 (ppm)

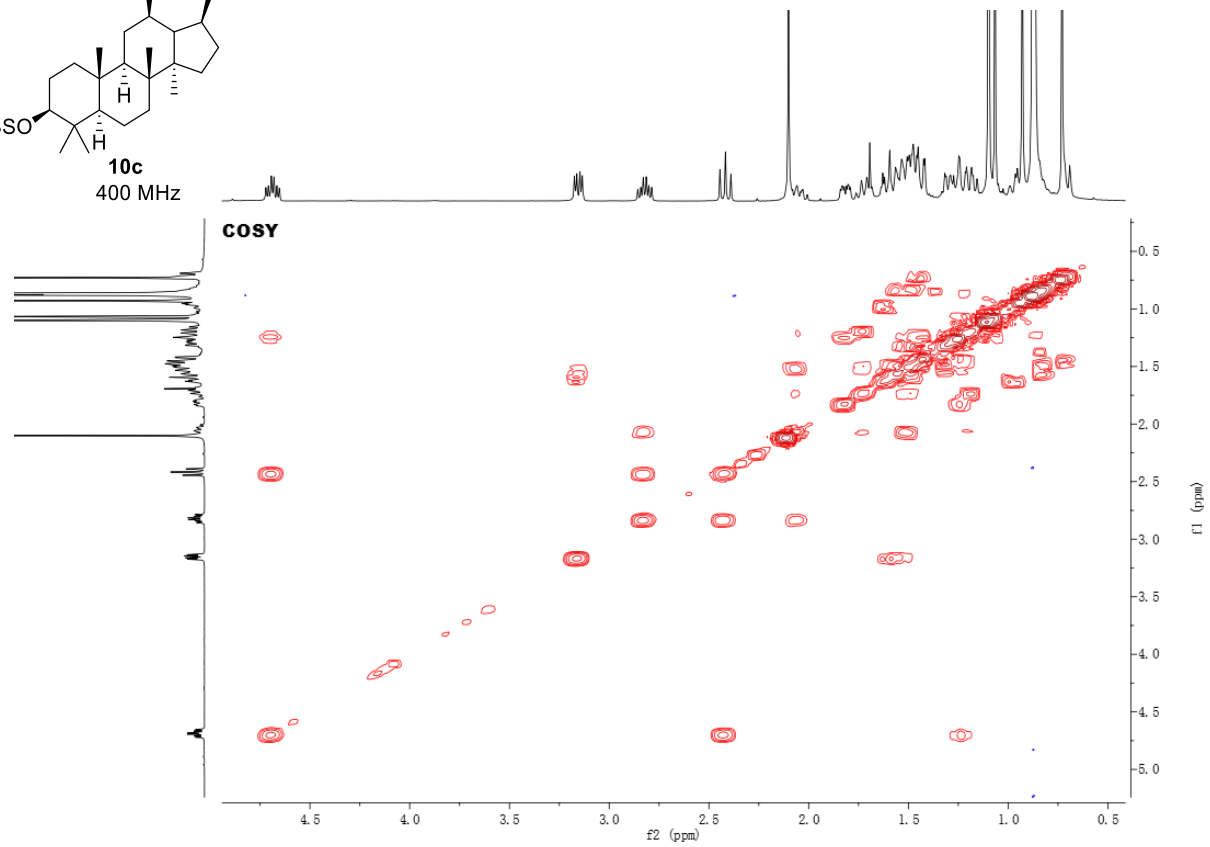

MOMO
O
MOMO
H
H
10b
400 MHz
HMBC
f2 (ppm)
f1 (ppm)

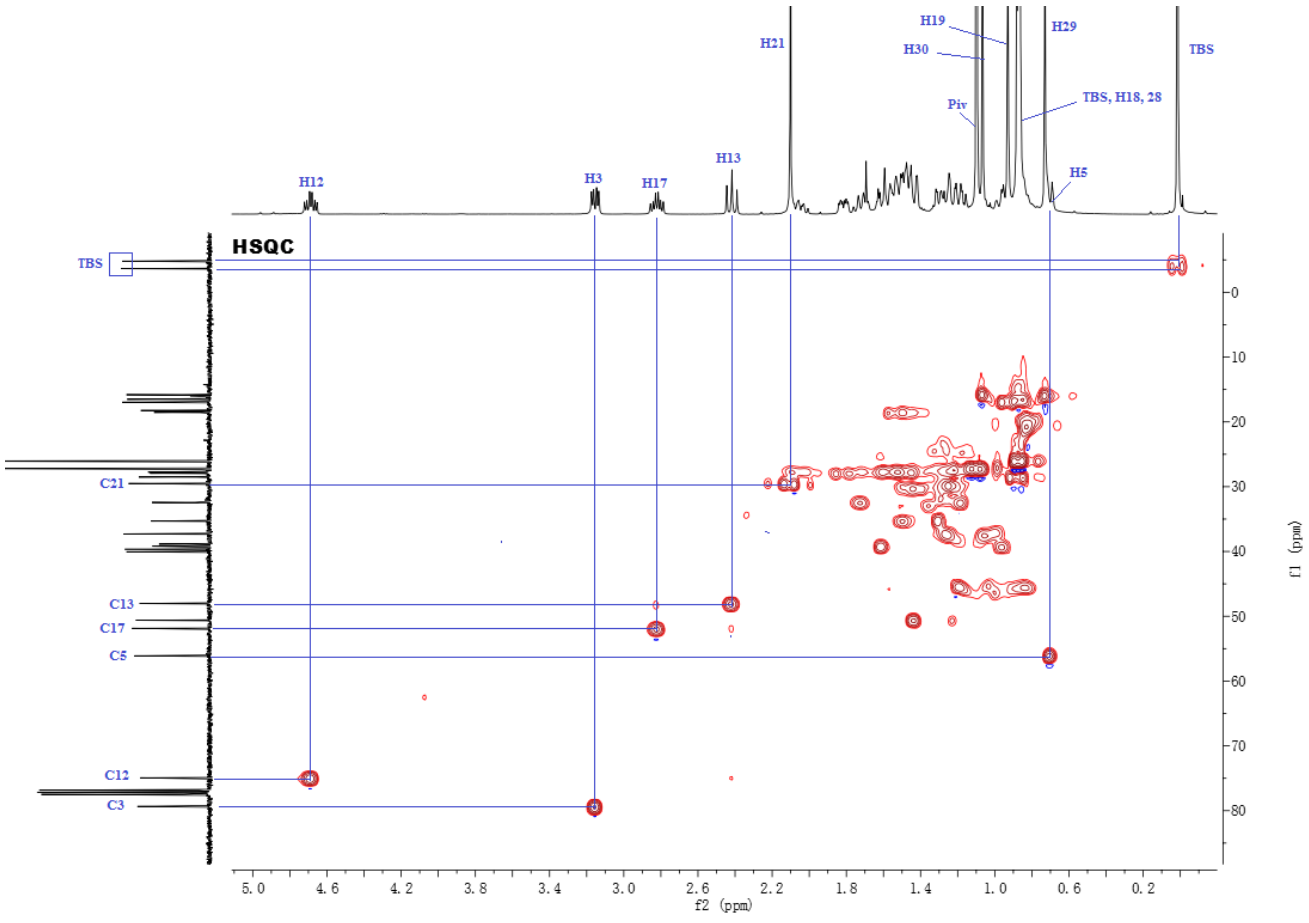

OPiv
O
TBSO
H
H
10c
400 MHz
ppm

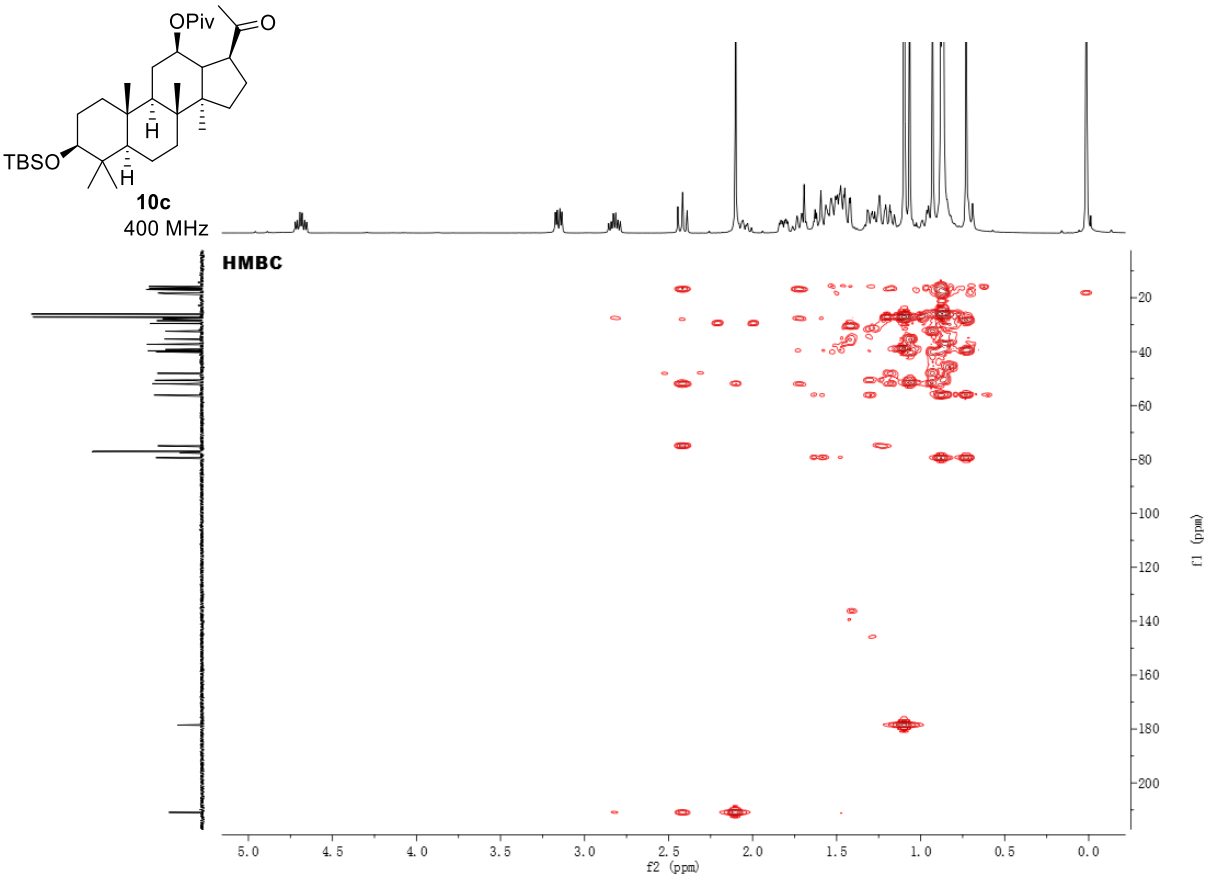

ppm

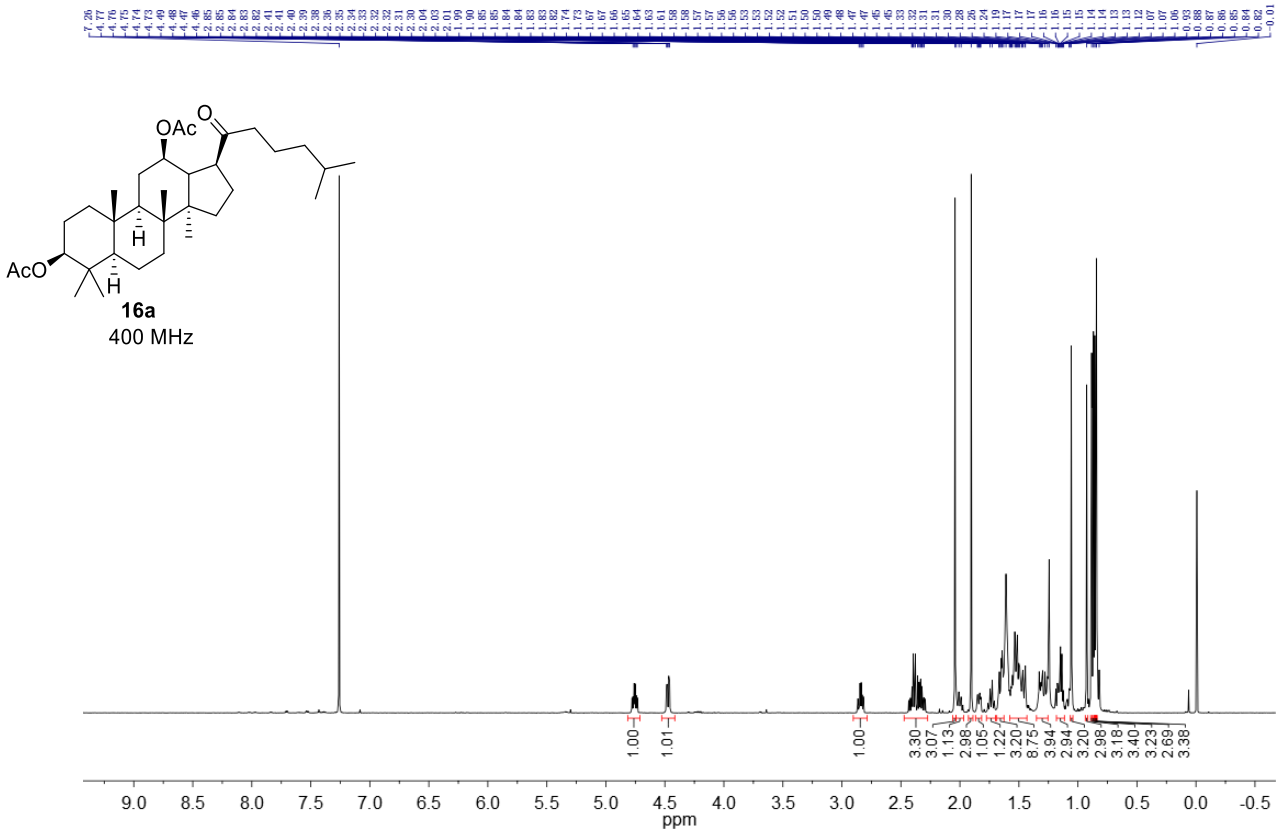

OPiv
O
TBSO
H
H

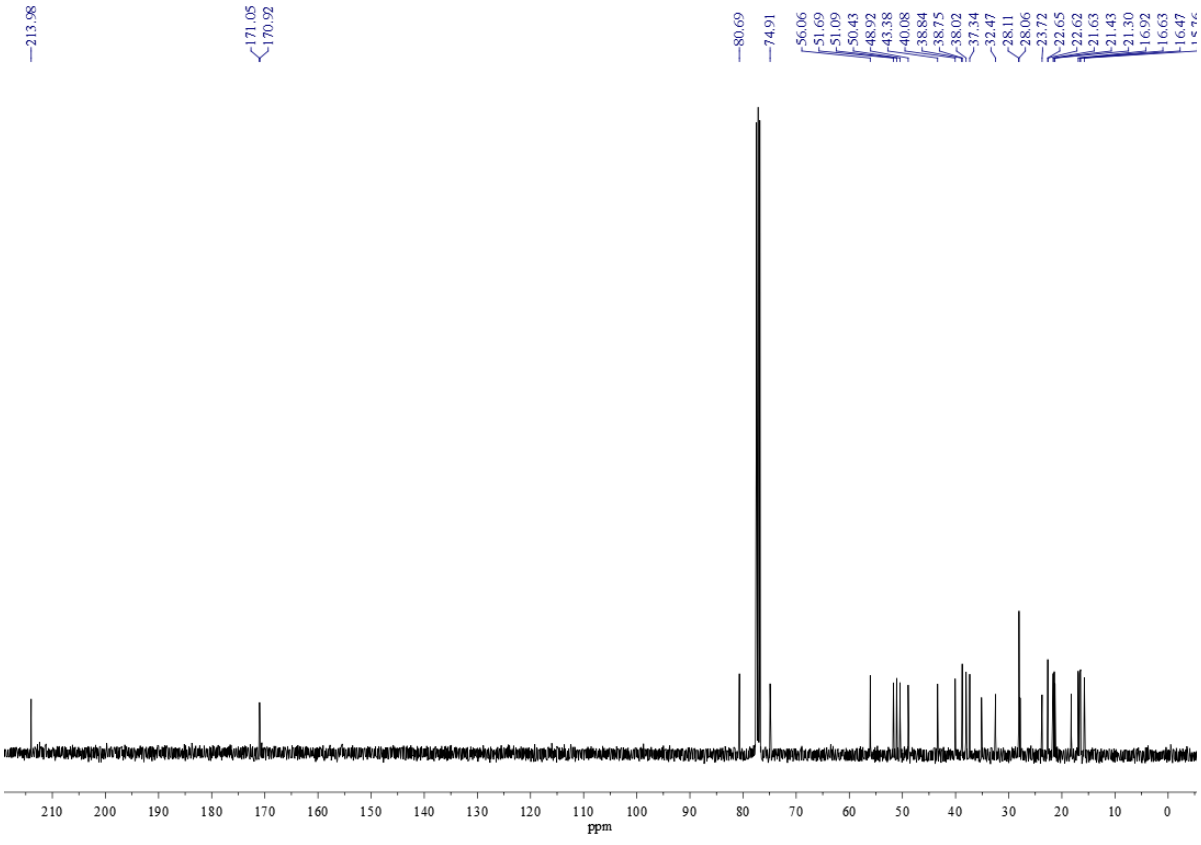
10c
400 MHz

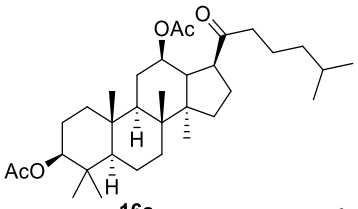

COSY
f2 (ppm)
f1 (ppm)


H21
H19
H30
H29
TBS
Piv
TBS, H18, 28
H12
H3
H17
H13
H5
HSQC
TBS
C21
C13
C17
C5
C12
C3
f2 (ppm)
f1 (ppm)

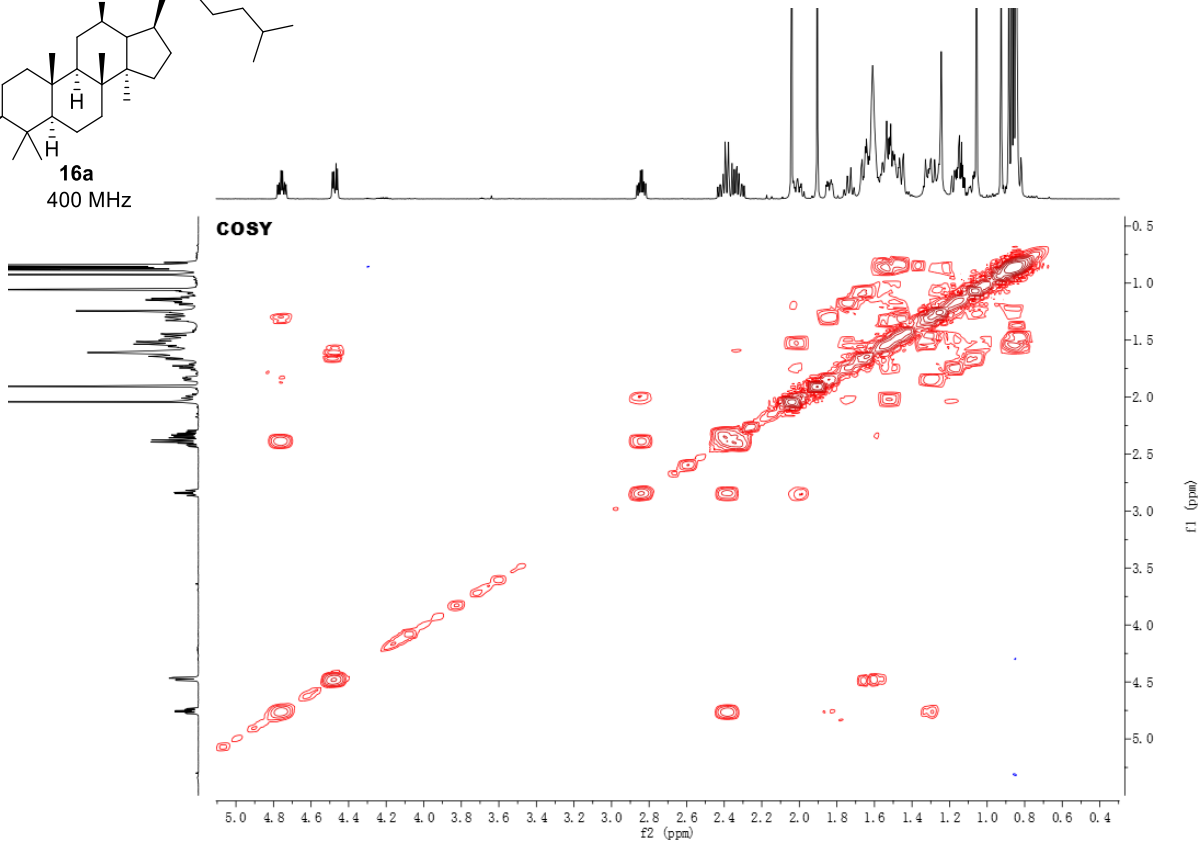

OPiv
O
H
TBSO
H
10c
400 MHz
HMBC
20
40
60
80
100
120
140
160
180
200
f1 (ppm)
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f2 (ppm)

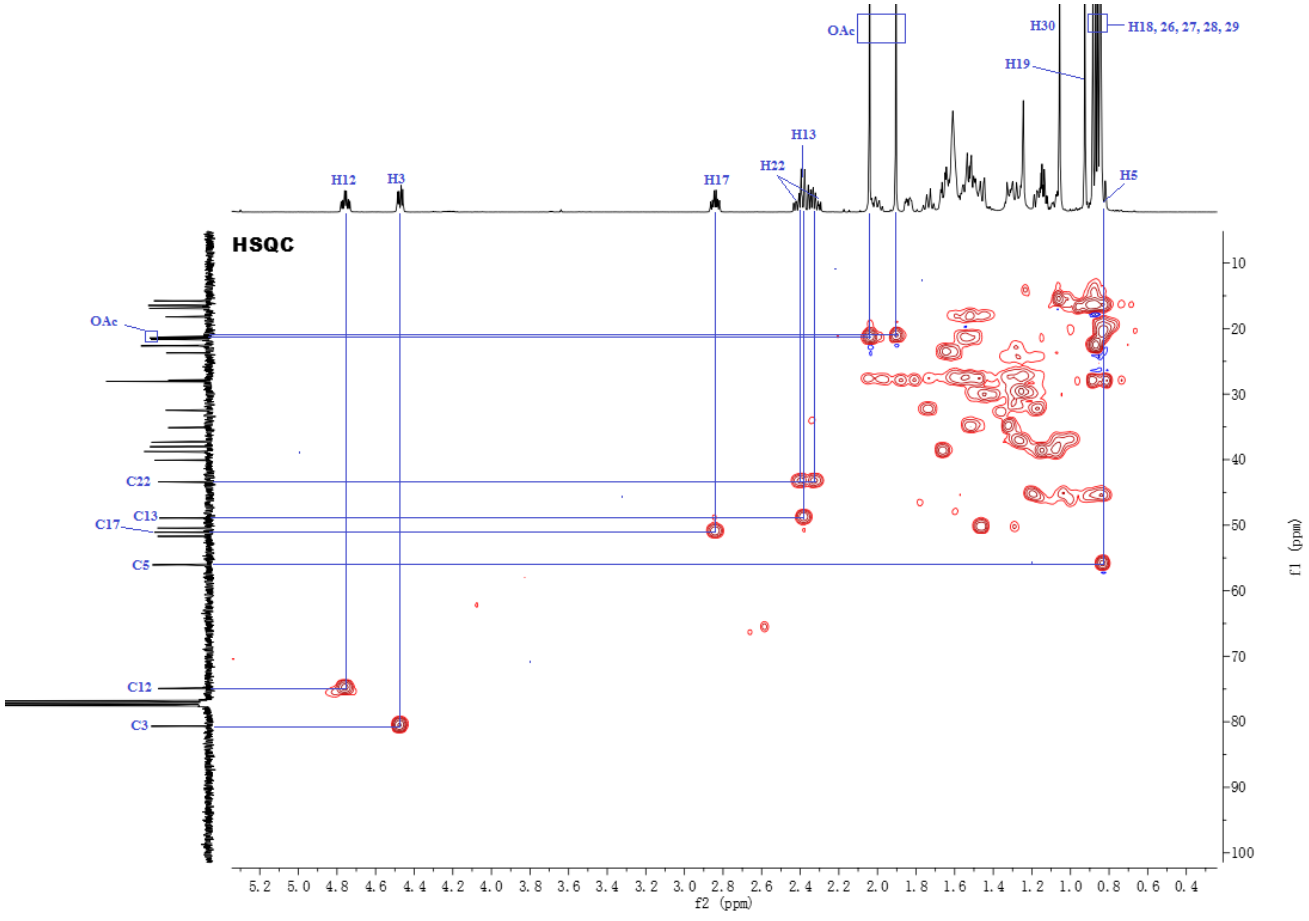

OAc
O
H
AcO
H
16a
400 MHz
ppm

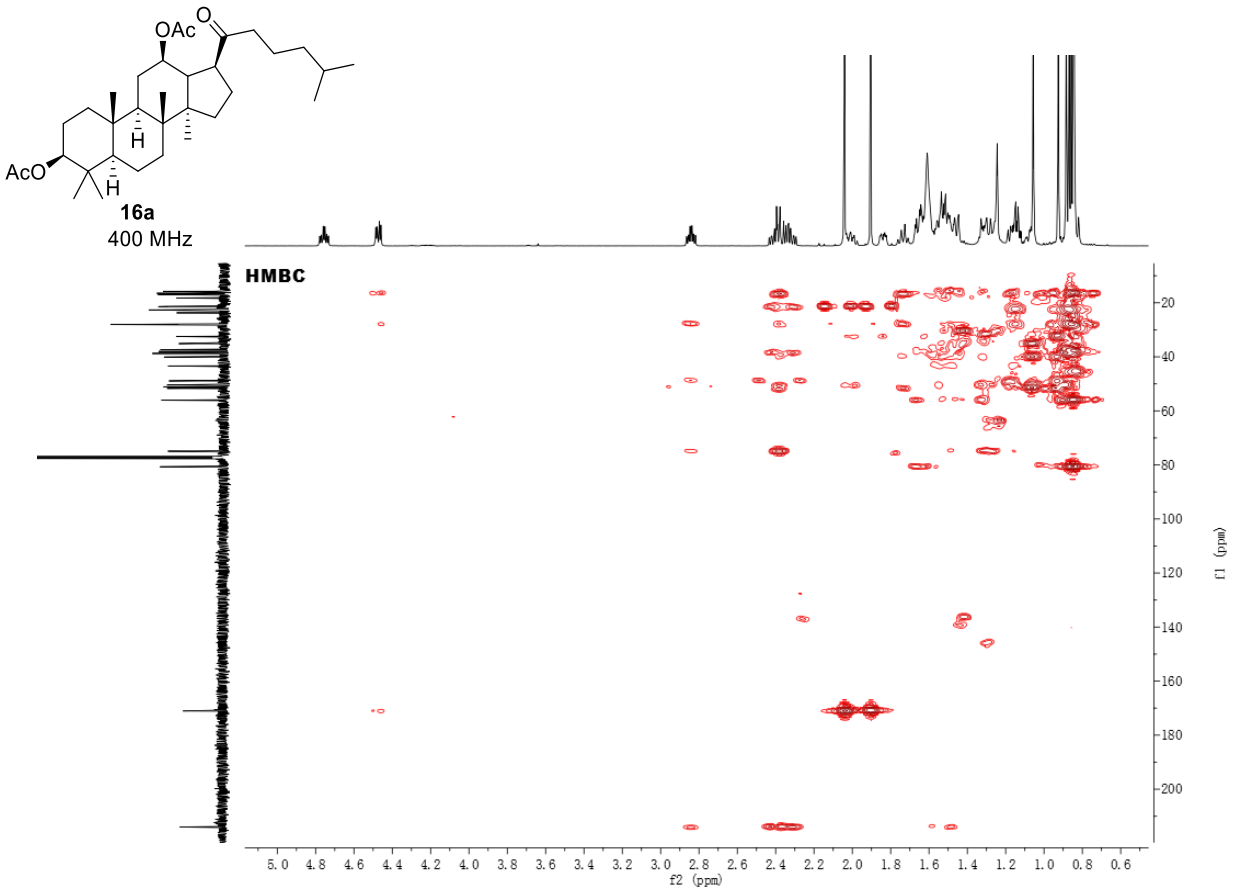

ppm

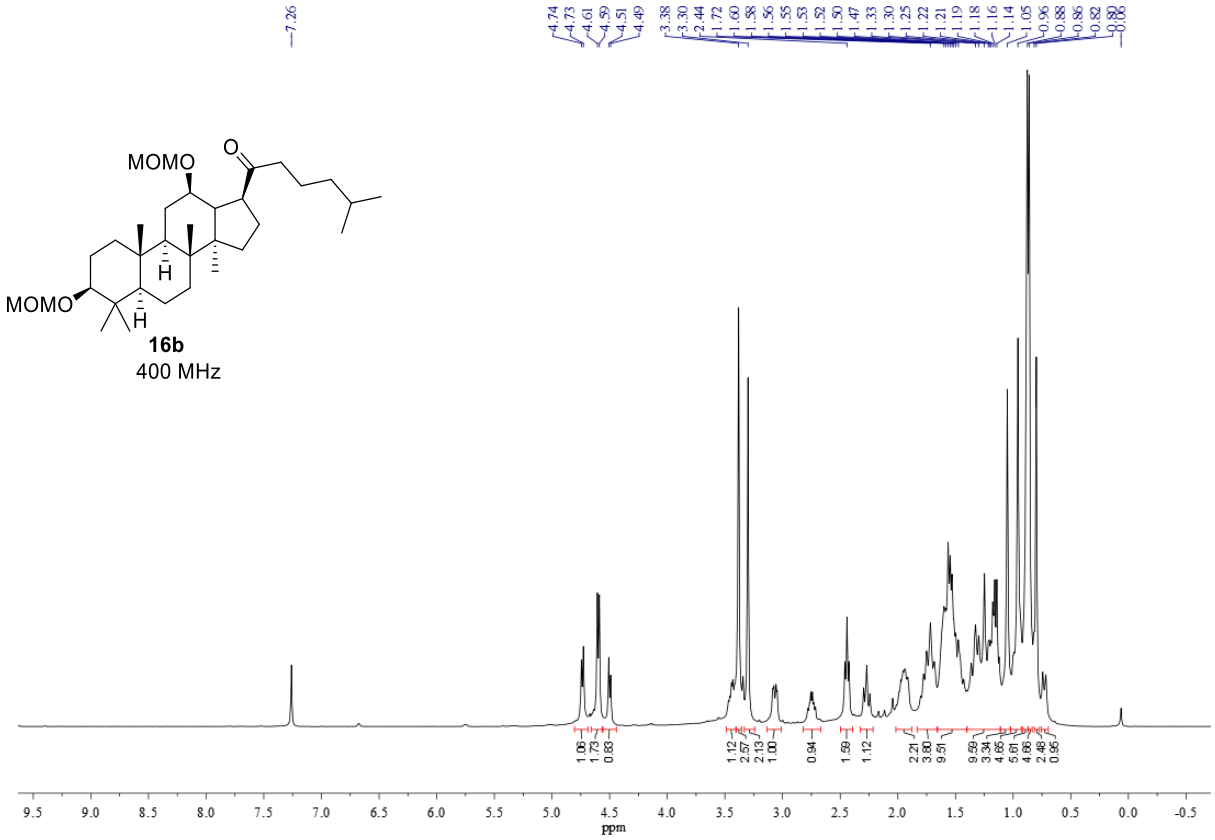

OAc
O
AcO
H
H

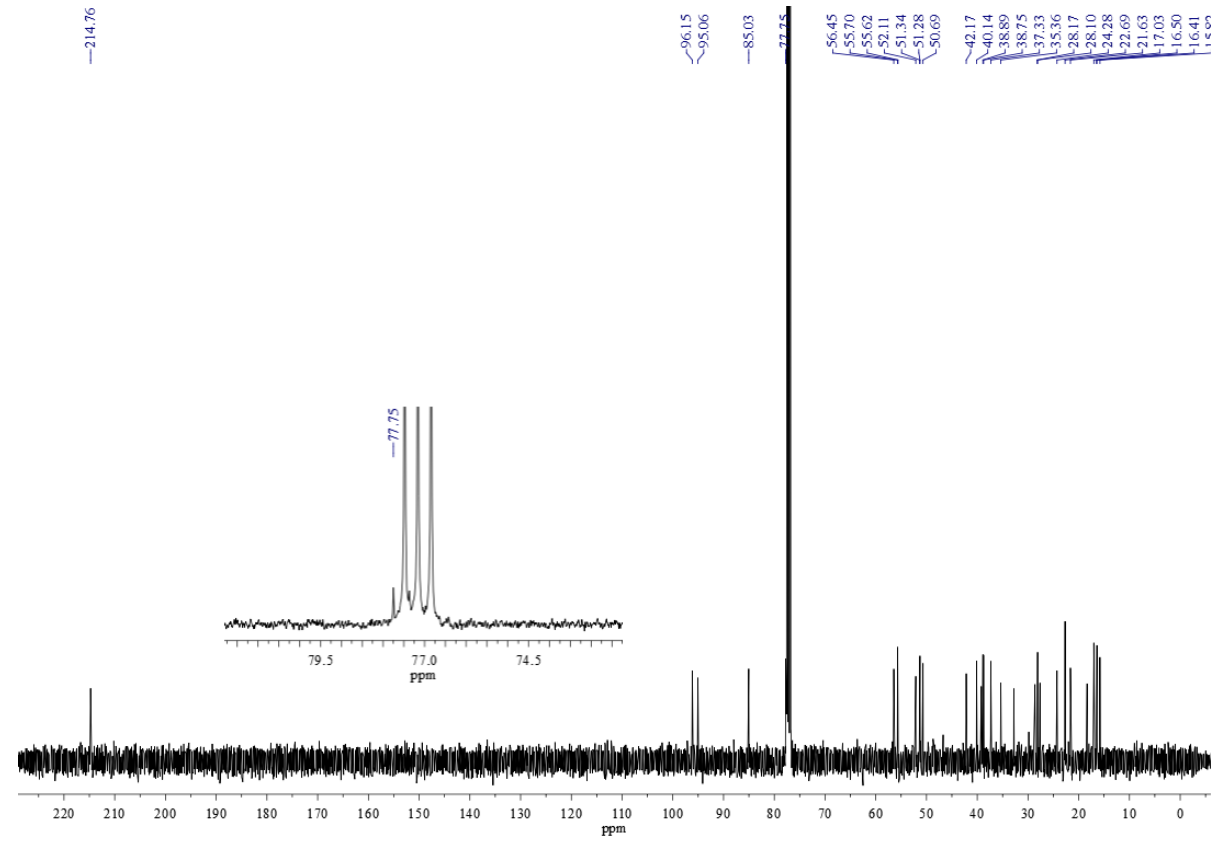
16a
400 MHz

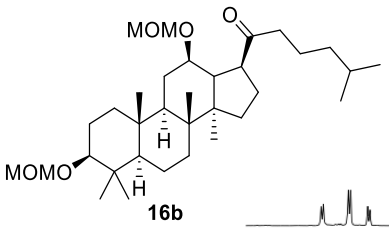

COSY
f2 (ppm)
f1 (ppm)


HSQC
OAc
H30
H18, 26, 27, 28, 29
H19
H13
H22
H12
H3
H17
H5
C22
C13
C17
C5
C12
C3
f2 (ppm)
f1 (ppm)


OAc
O
AcO
H
H
16a
400 MHz
HMBC
f2 (ppm)
f1 (ppm)

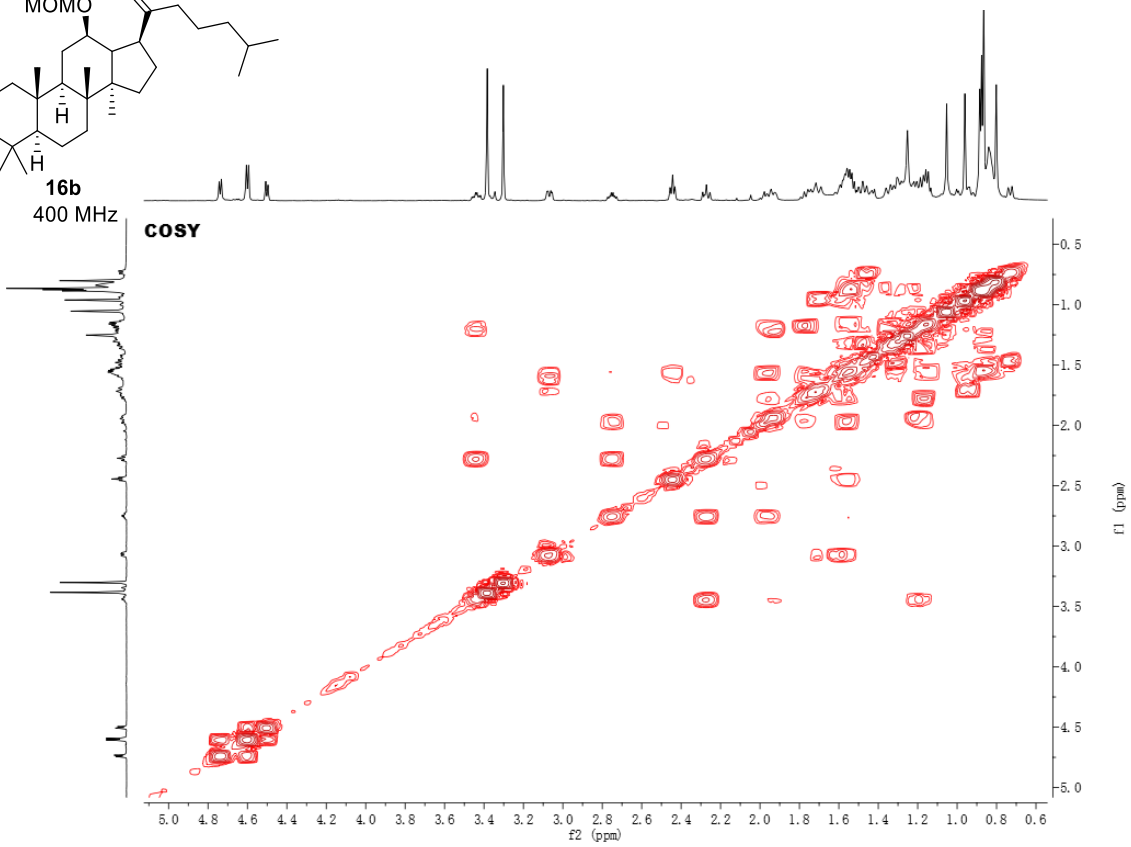

MOMO
O
MOMO
H
H
16b
400 MHz
ppm

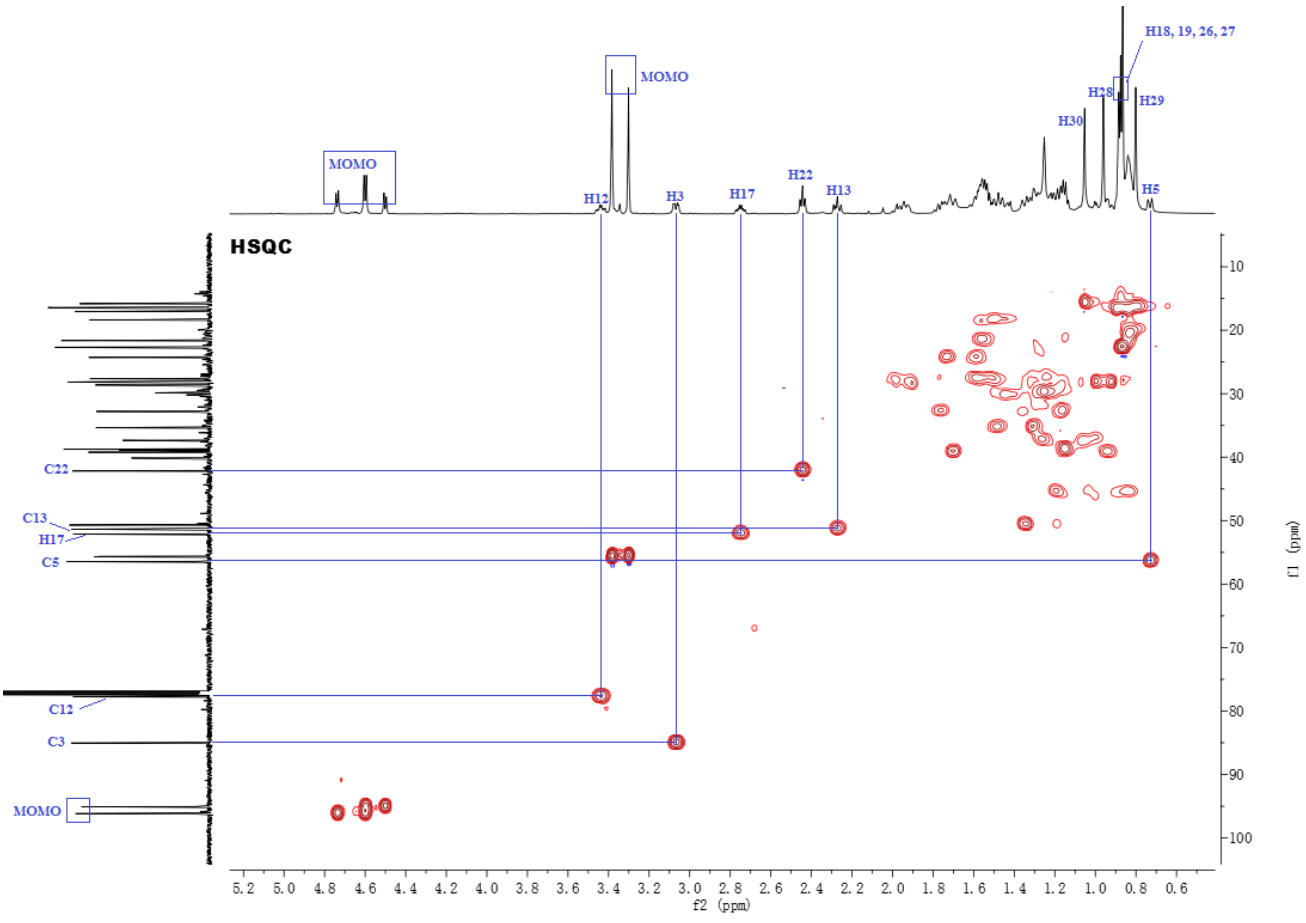

ppm

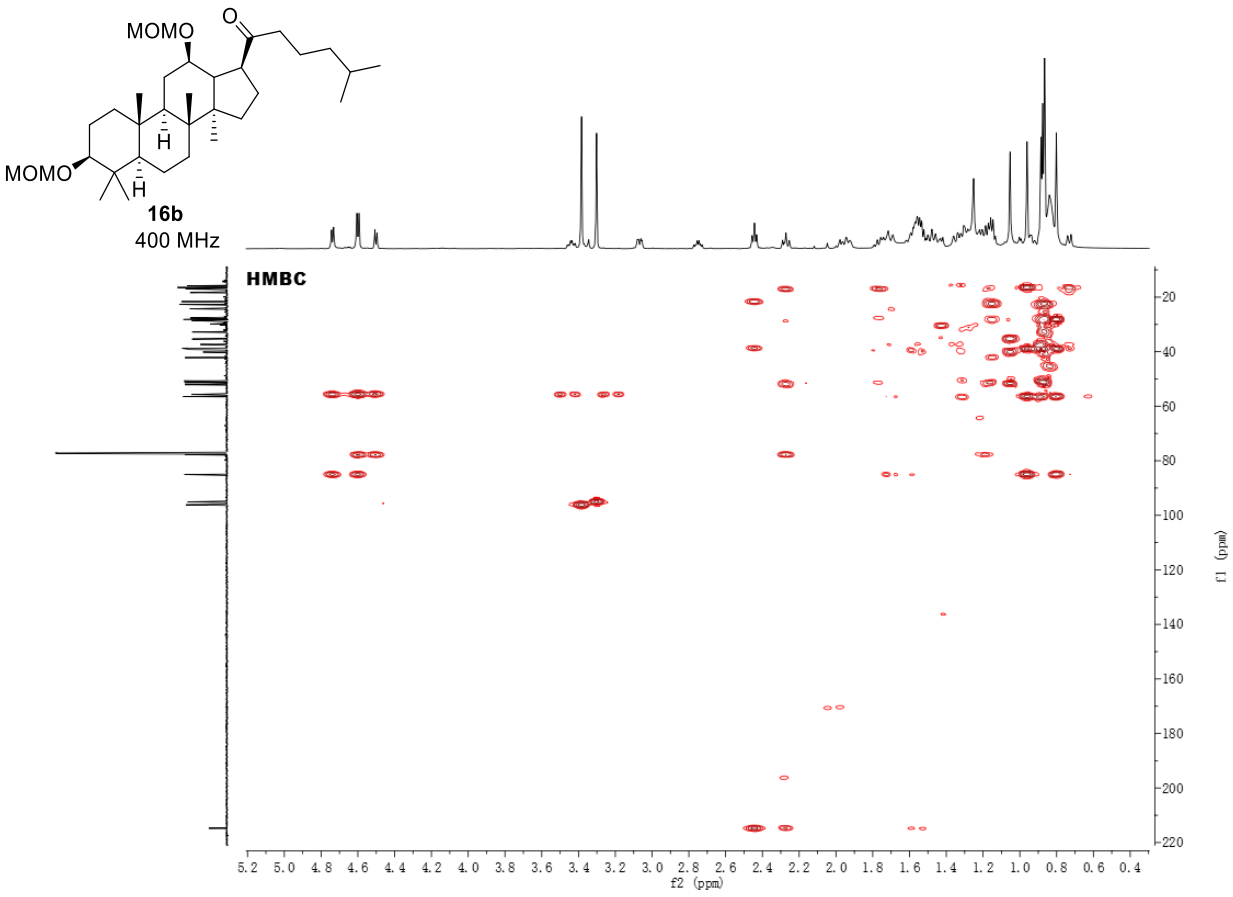

MOMO
O
H
MOMO
H

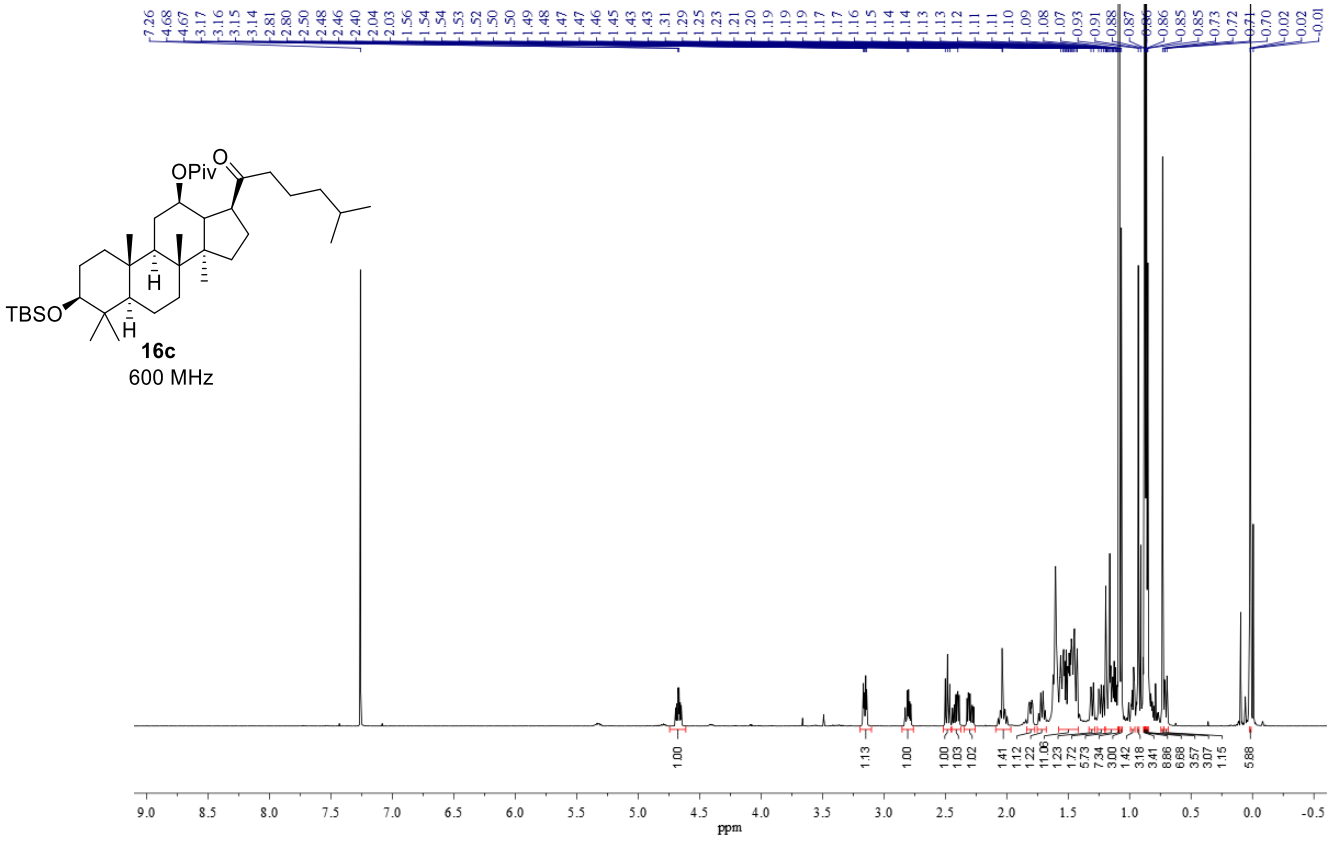
16b

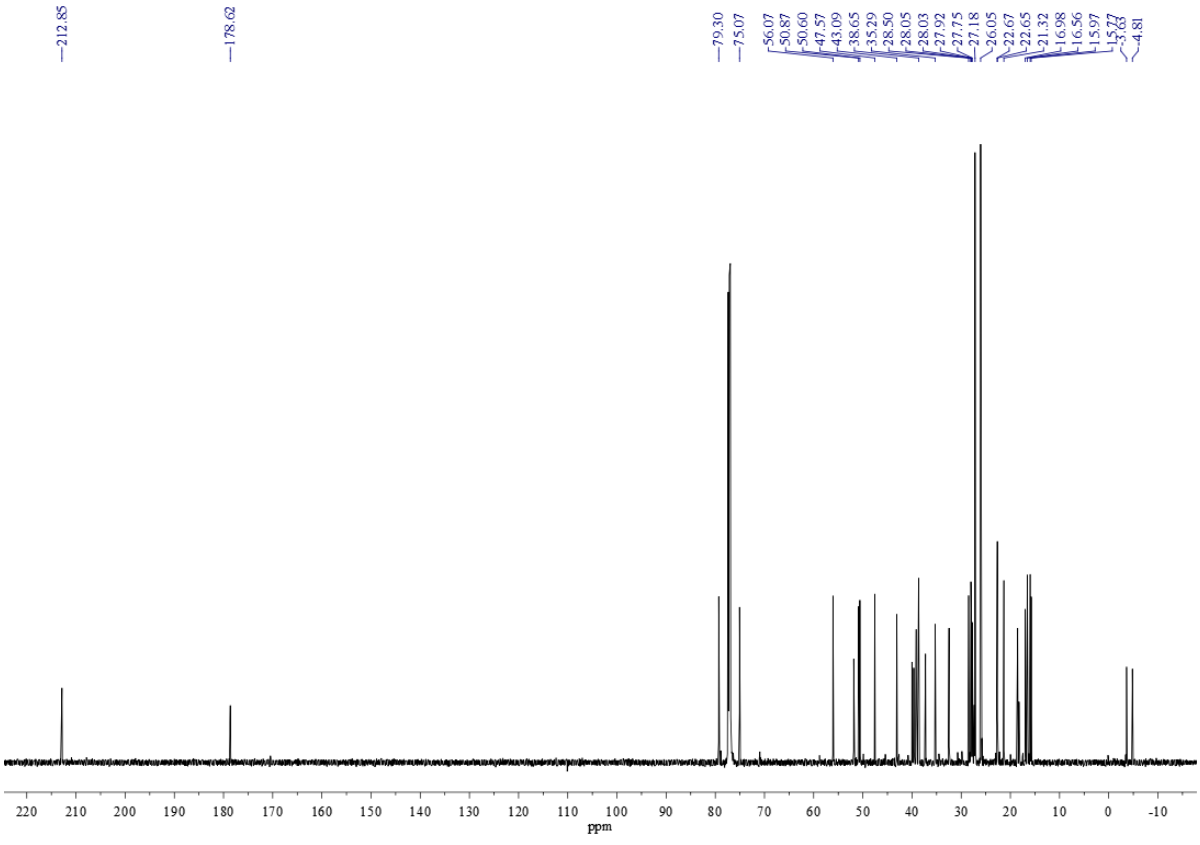
400 MHz

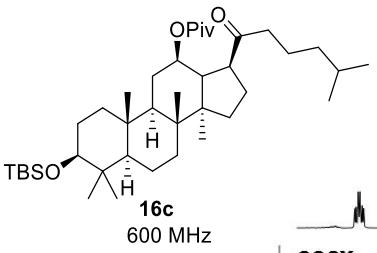

COSY
f2 (ppm)
f1 (ppm)


HSQC
MOMO
MOMO
H18, 19, 26, 27
H28
H29
H30
H12
H3
H17
H22
H13
H5
C22
C13
H17
C5
C12
C3
MOMO
f2 (ppm)
f1 (ppm)

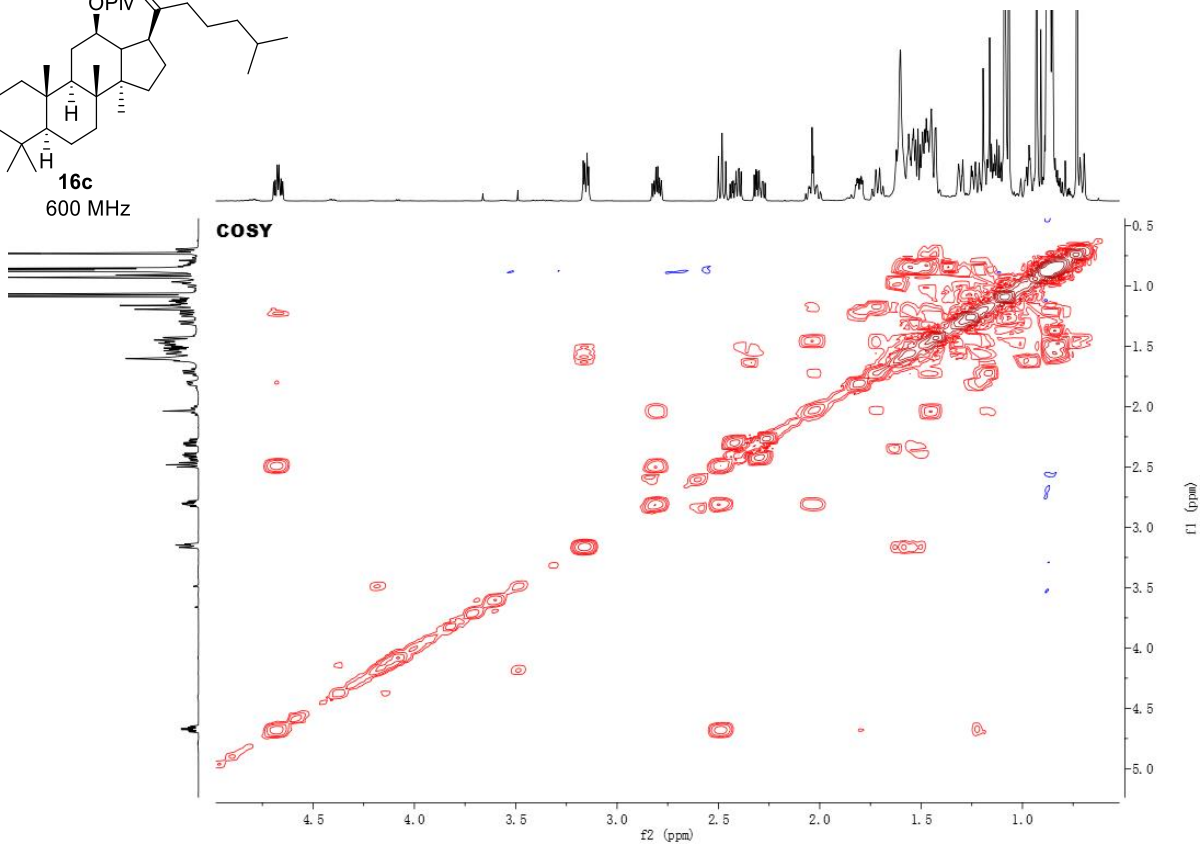

MOMO
O
MOMO
H
H
16b
400 MHz
HMBC
f2 (ppm)
f1 (ppm)

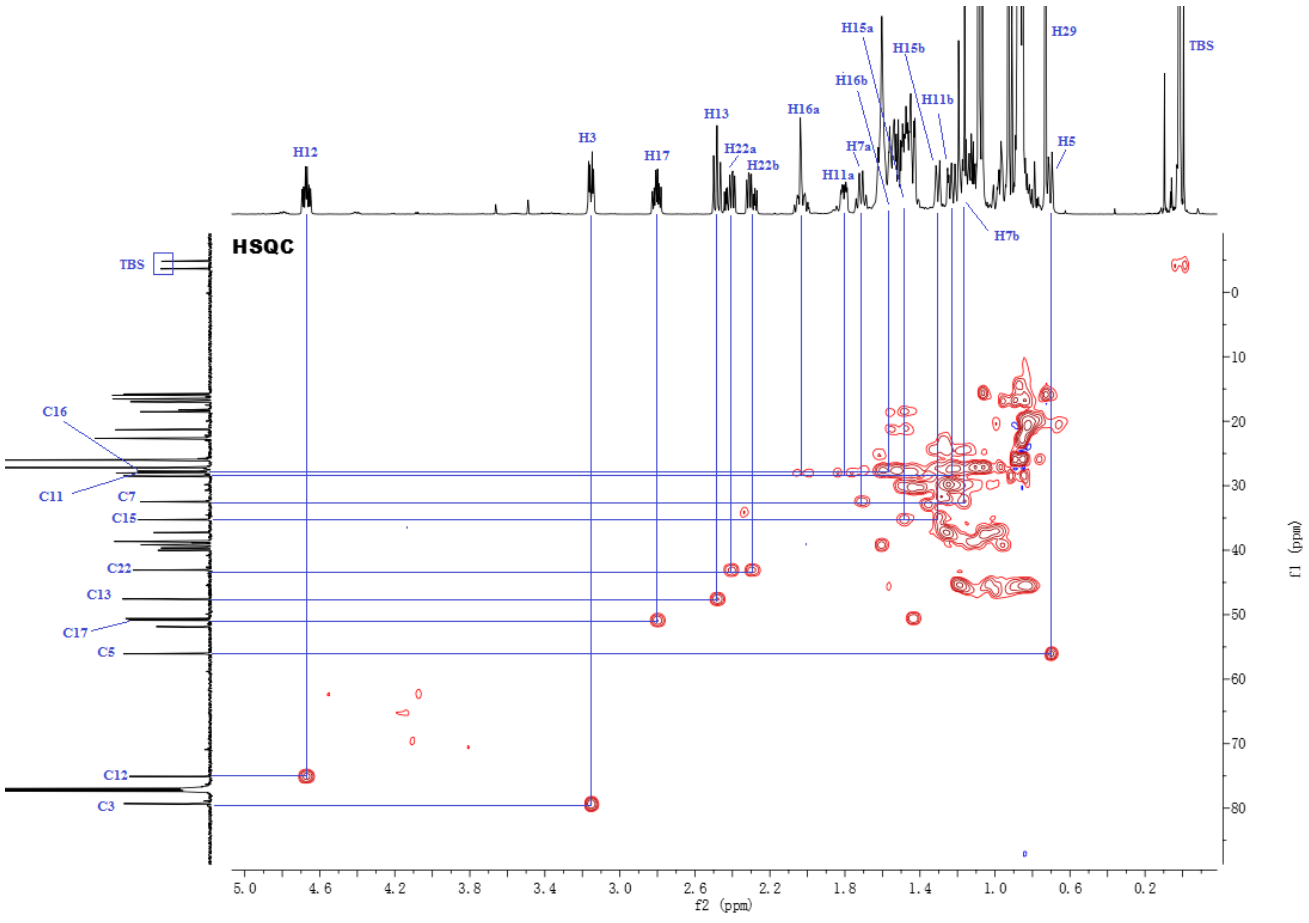

OPiv
O
H
TBSO
H
16c
600 MHz
ppm

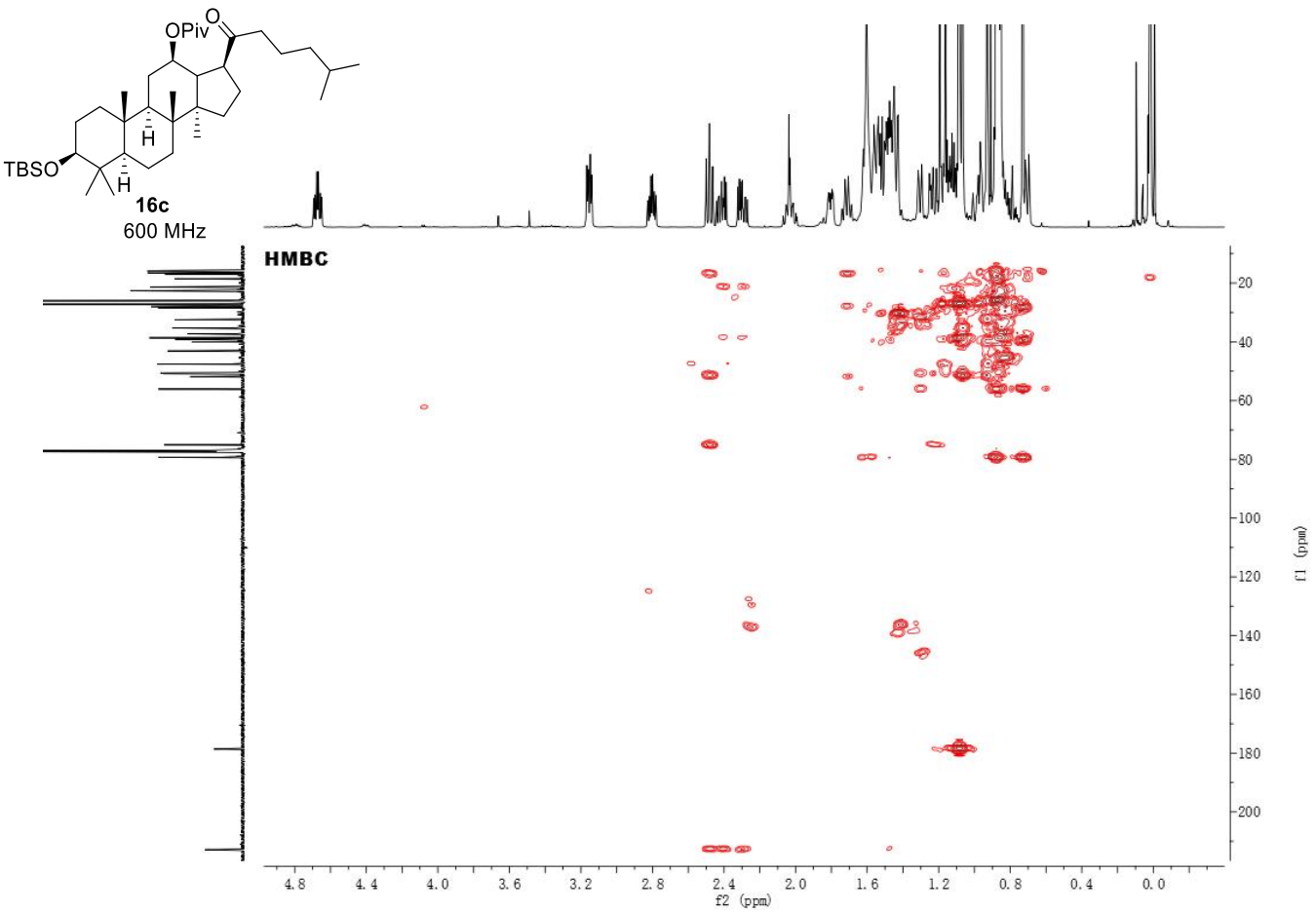

212.85
178.62
79.30
75.07
ppm

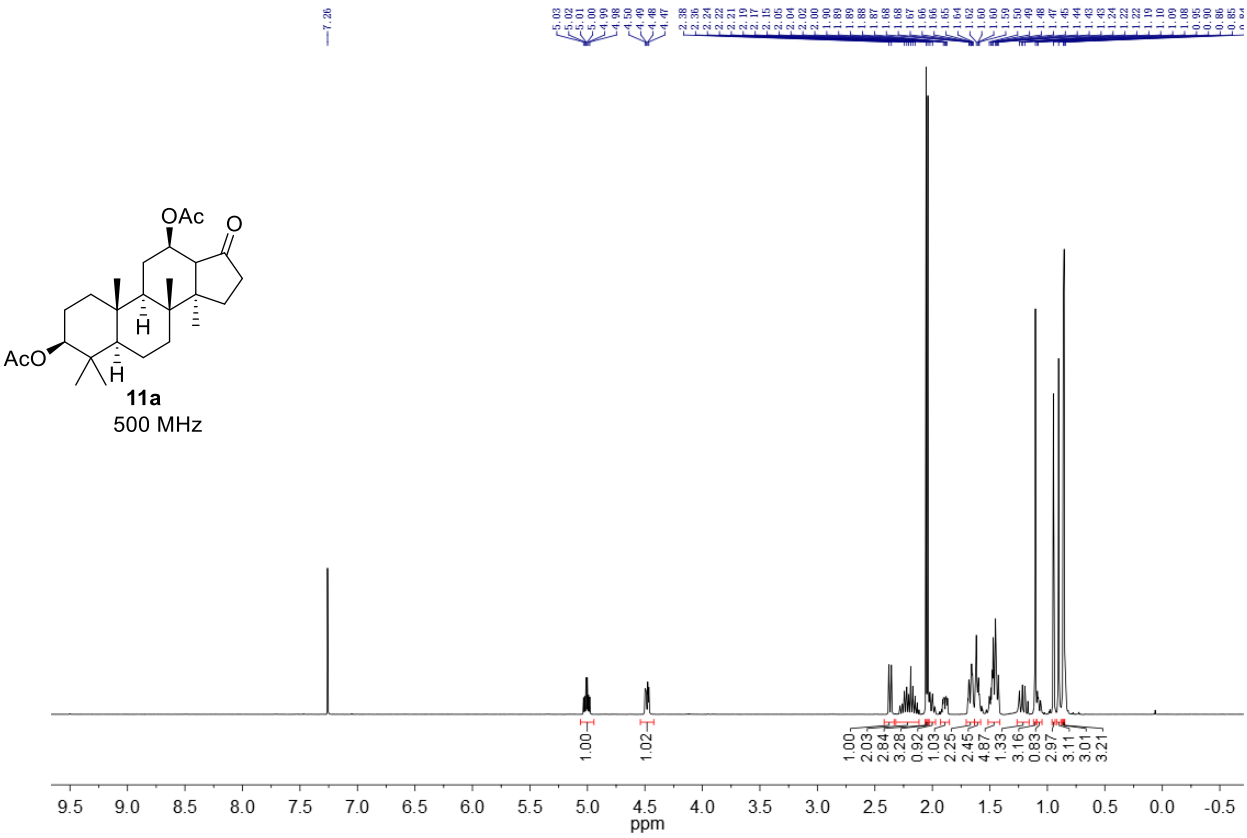

OPiv
O
TBSO
H
H

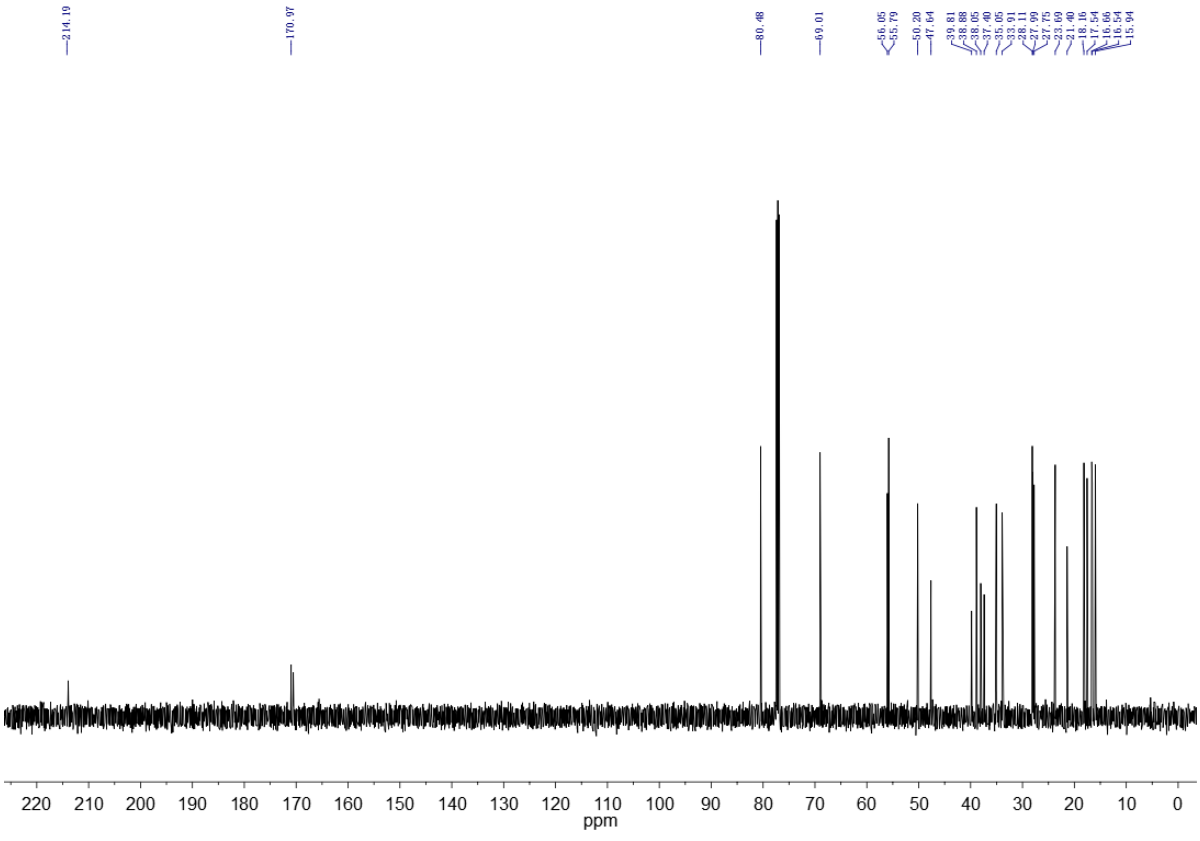
16c
600 MHz

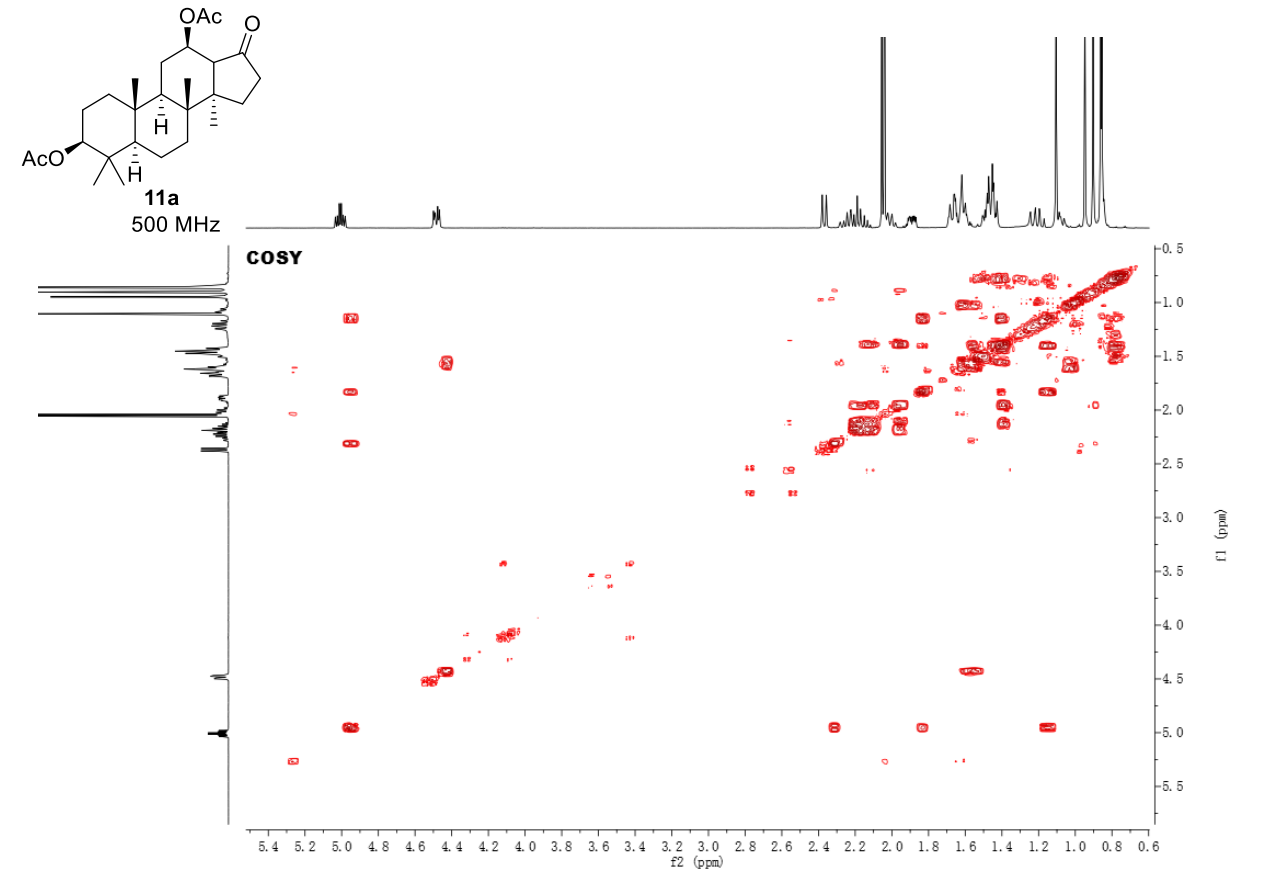

COSY
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
f2 (ppm)
0.5
1.0
1.5
2.0
2.5
3.0
3.5
4.0
4.5
5.0
f1 (ppm)

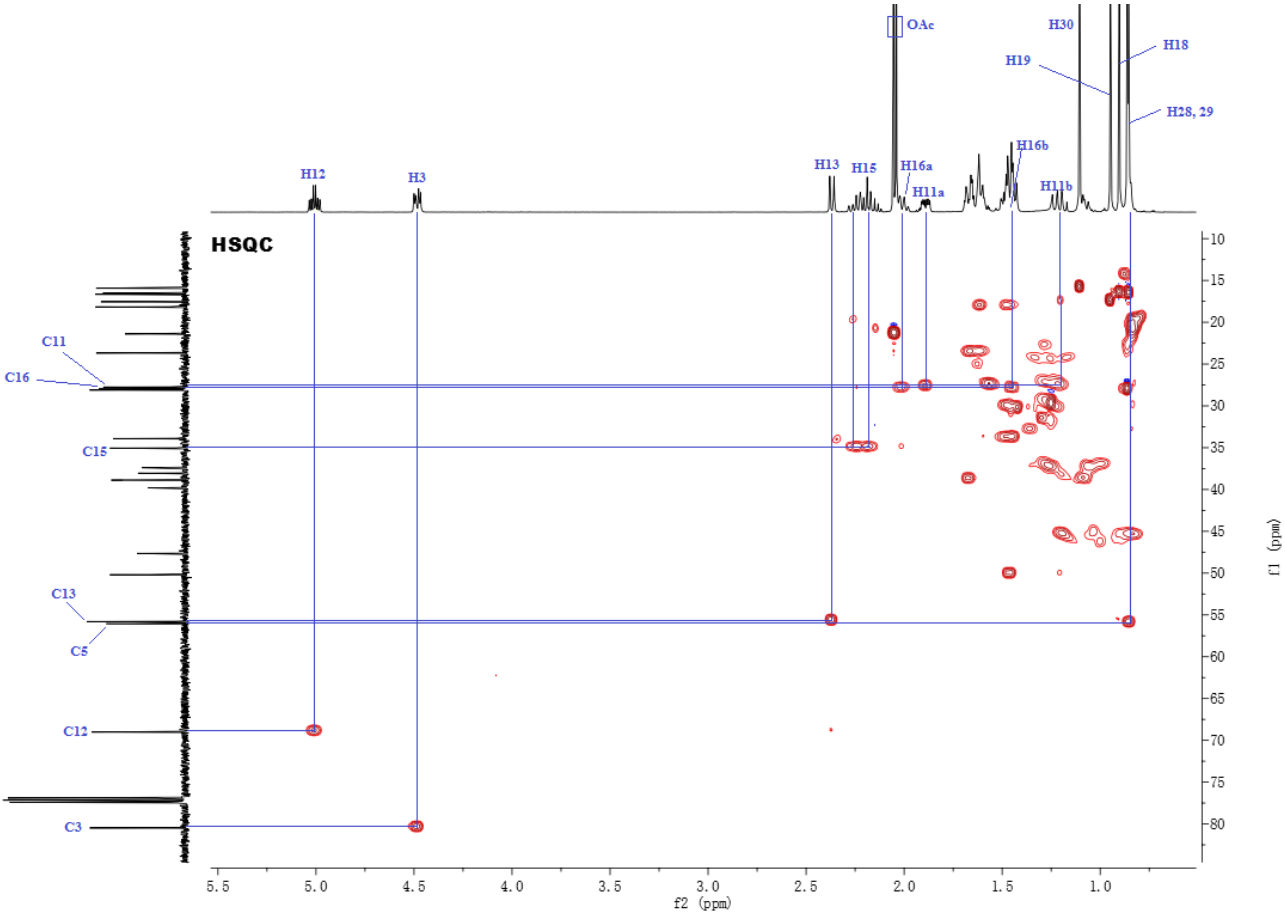

H12
H3
H17
H13
H22a
H22b
H16a
H15a
H15b
H16b
H11b
H7a
H11a
H29
H5
TBS
H7b
HSQC
TBS
C16
C11
C7
C15
C22
C13
C17
C5
C12
C3
5.0
4.6
4.2
3.8
3.4
3.0
2.6
2.2
1.8
1.4
1.0
0.6
0.2
f2 (ppm)
0
10
20
30
40
50
60
70
80
f1 (ppm)

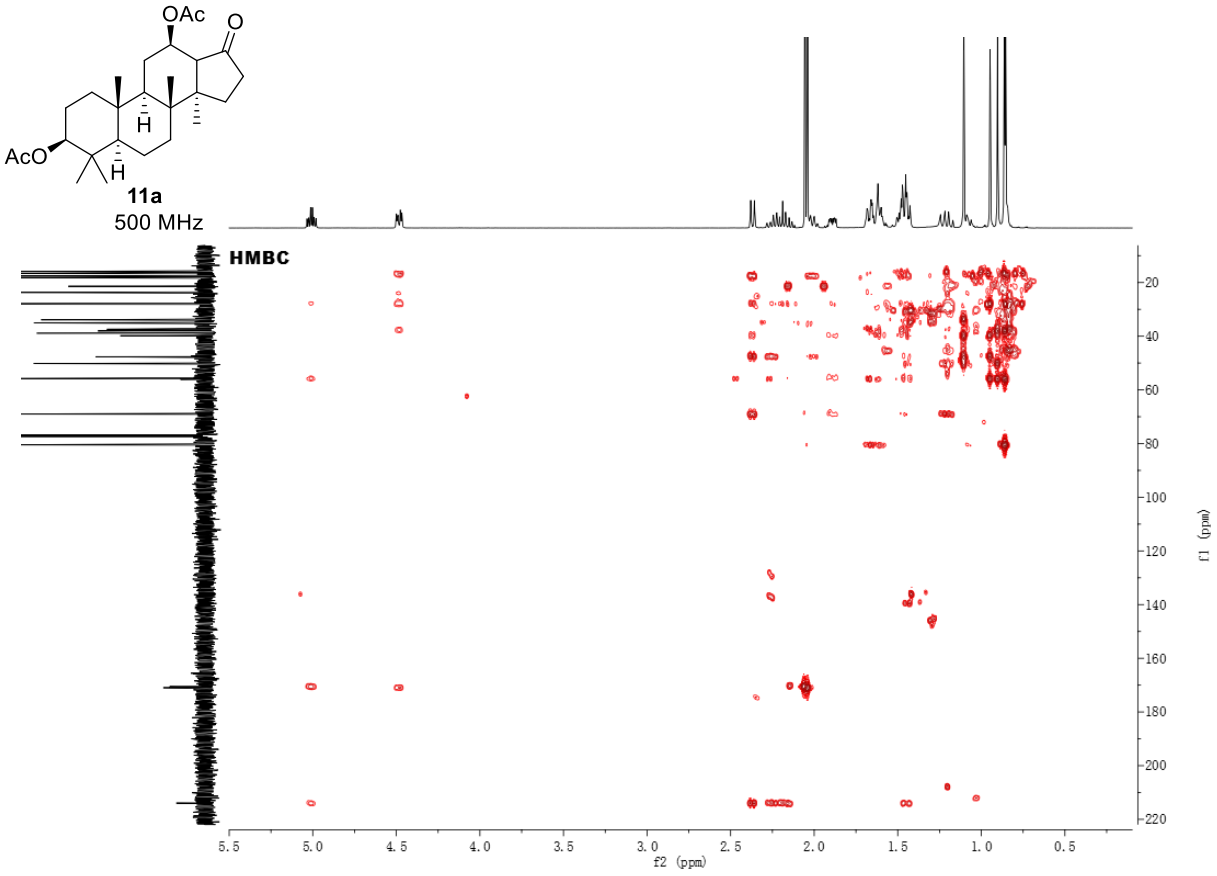

OPiv
O
H
TBSO
H
16c
600 MHz
HMBC
20
40
60
80
100
120
140
160
180
200
f1 (ppm)
4.8
4.4
4.0
3.6
3.2
2.8
2.4
2.0
1.6
1.2
0.8
0.4
0.0
f2 (ppm)

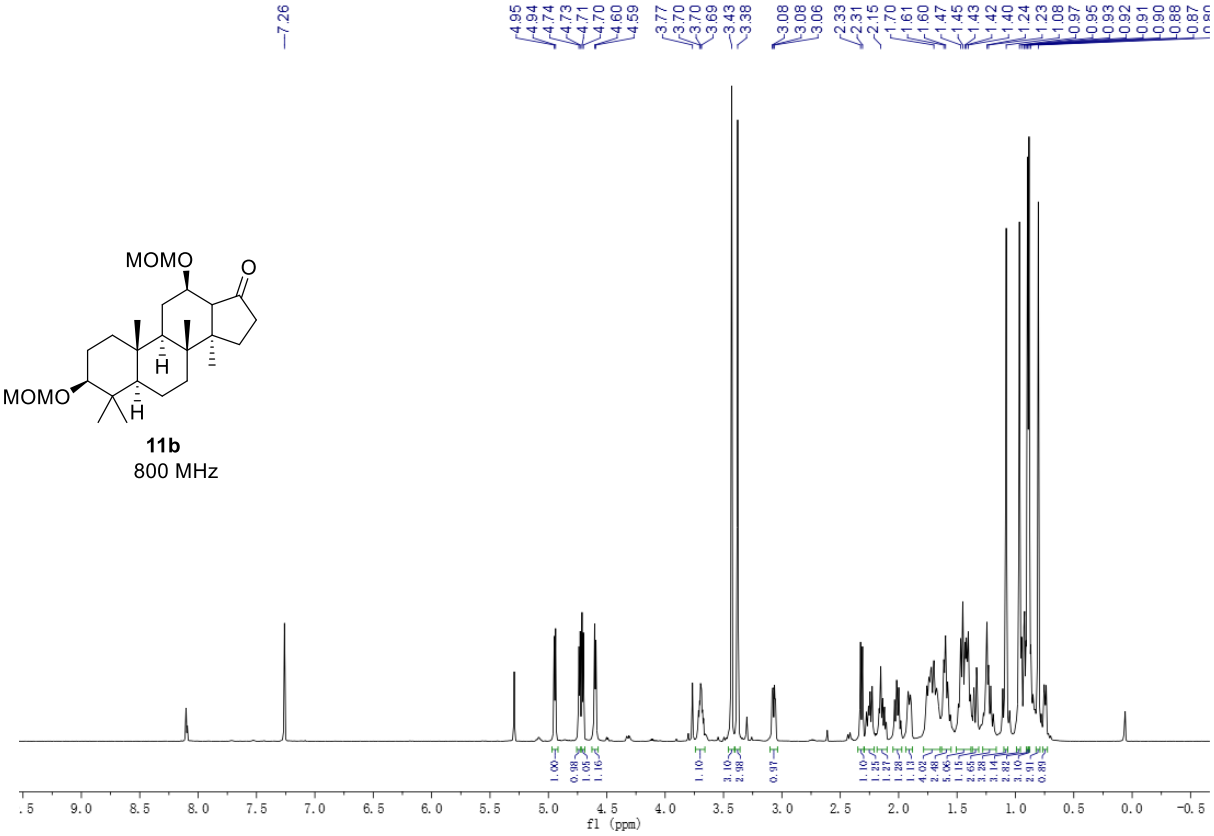

OAc
O
AcO
H
H
11a
500 MHz
ppm

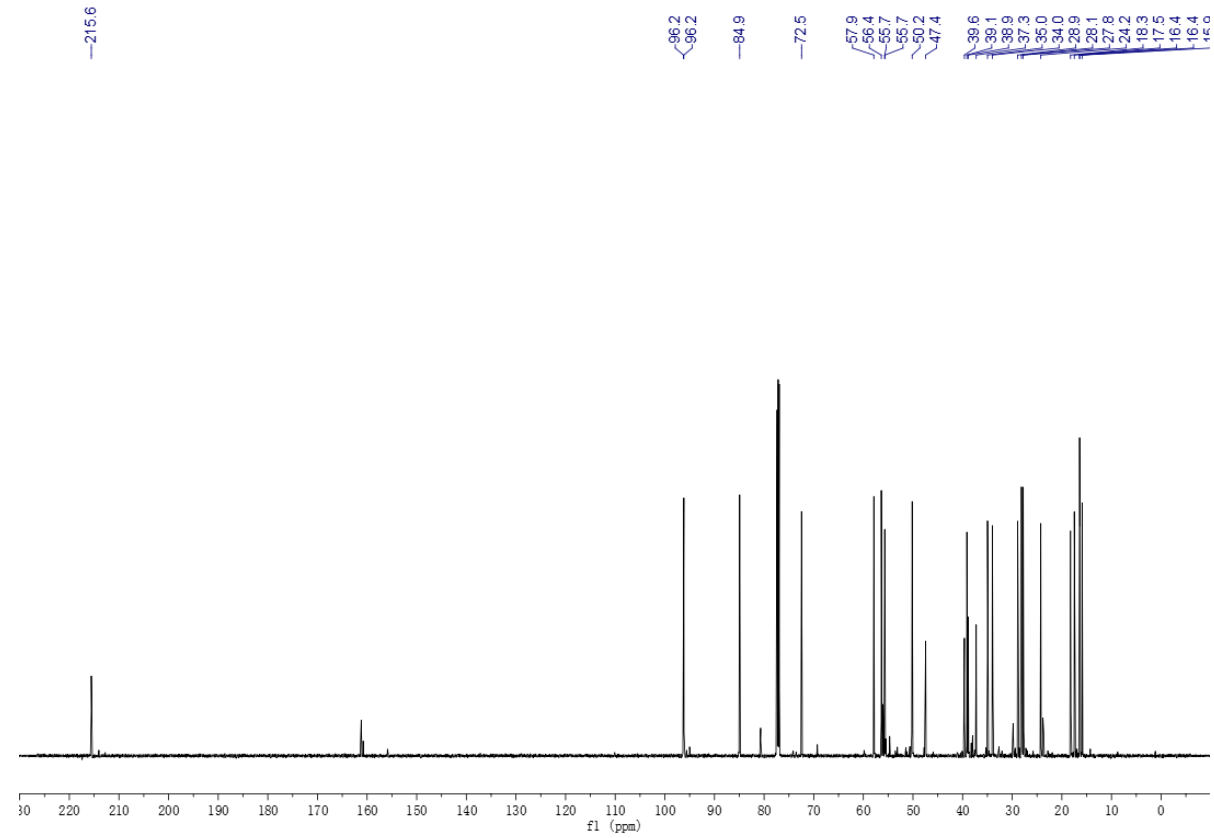

ppm

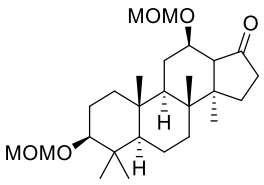

OAc
O
AcO
H
H
11a
500 MHz
COSY
f2 (ppm)
f1 (ppm)


OAc
H30
H18
H19
H28, 29
H16b
H12
H3
H13
H15
H16a
H11a
H11b
HSQC
C11
C16
C15
C13
C5
C12
C3
f2 (ppm)
f1 (ppm)

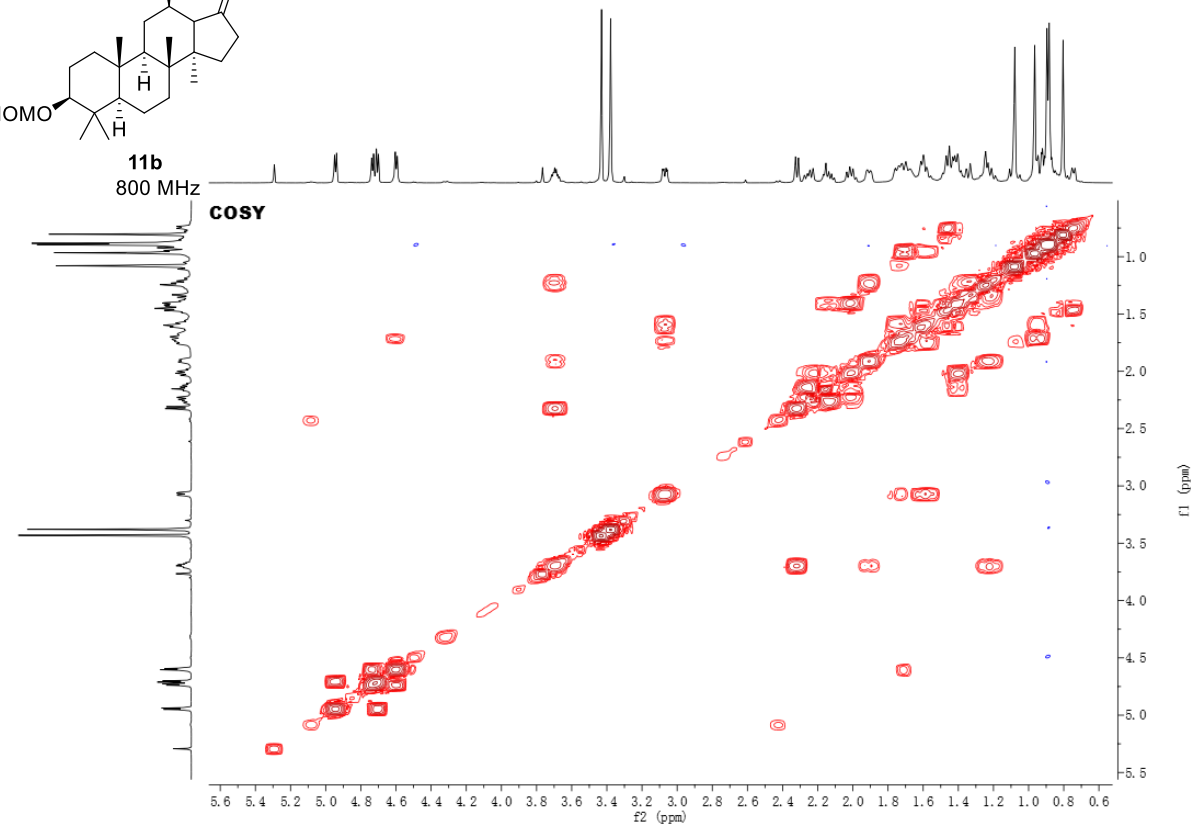

OAc
O
AcO
H
H
11a
500 MHz
HMBC
f2 (ppm)
f1 (ppm)

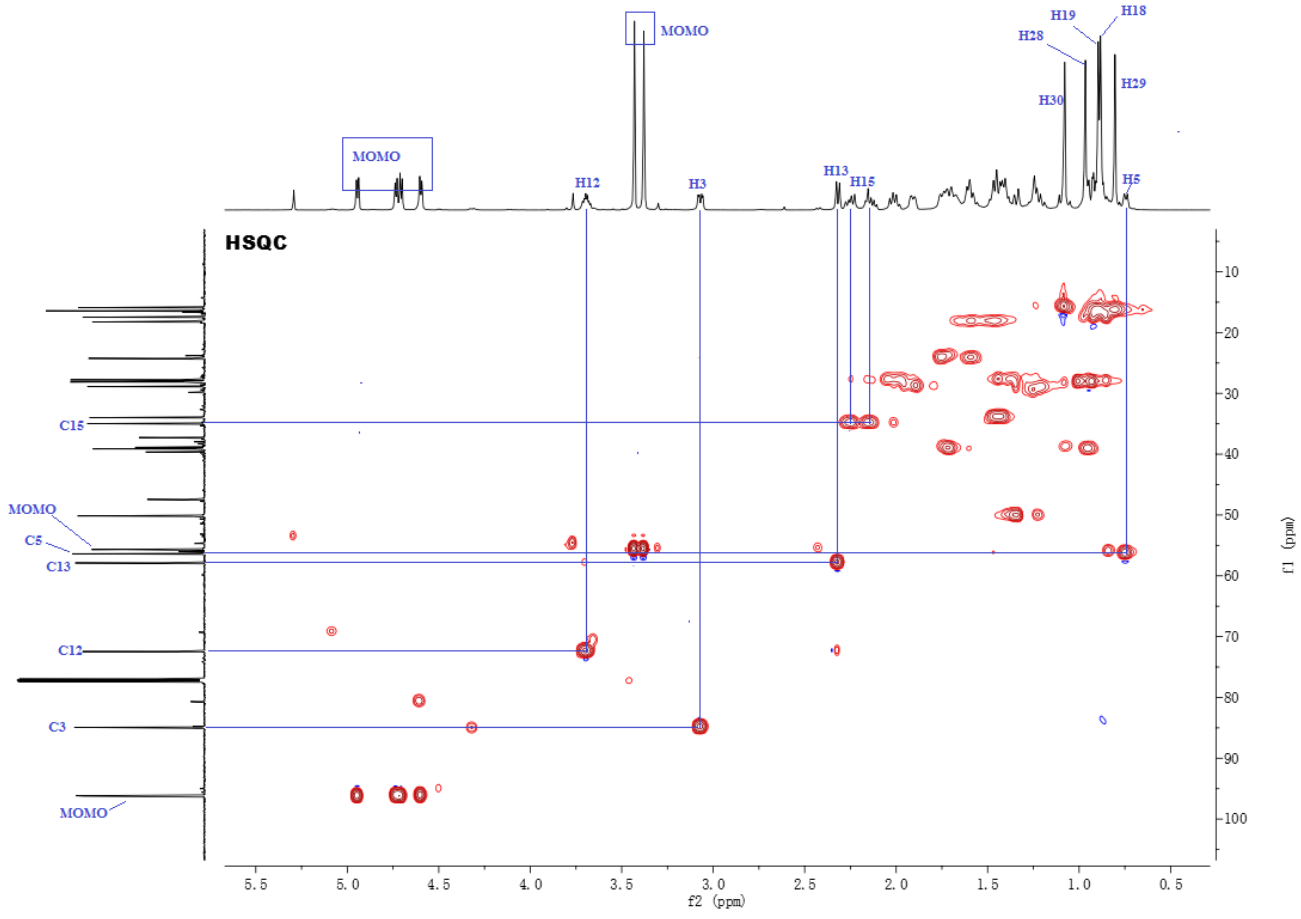

MOMO
O
H
MOMO
H
11b
800 MHz
f1 (ppm)

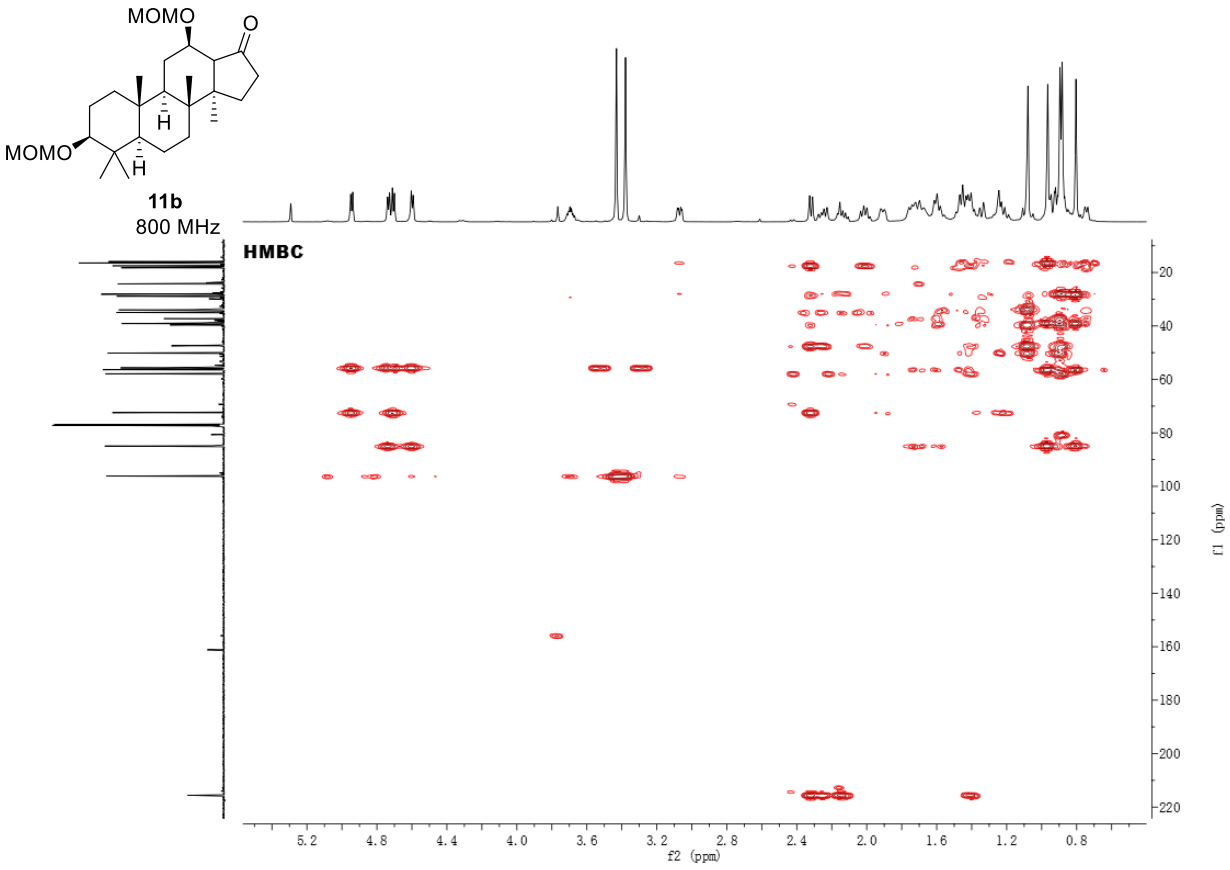

f1 (ppm)

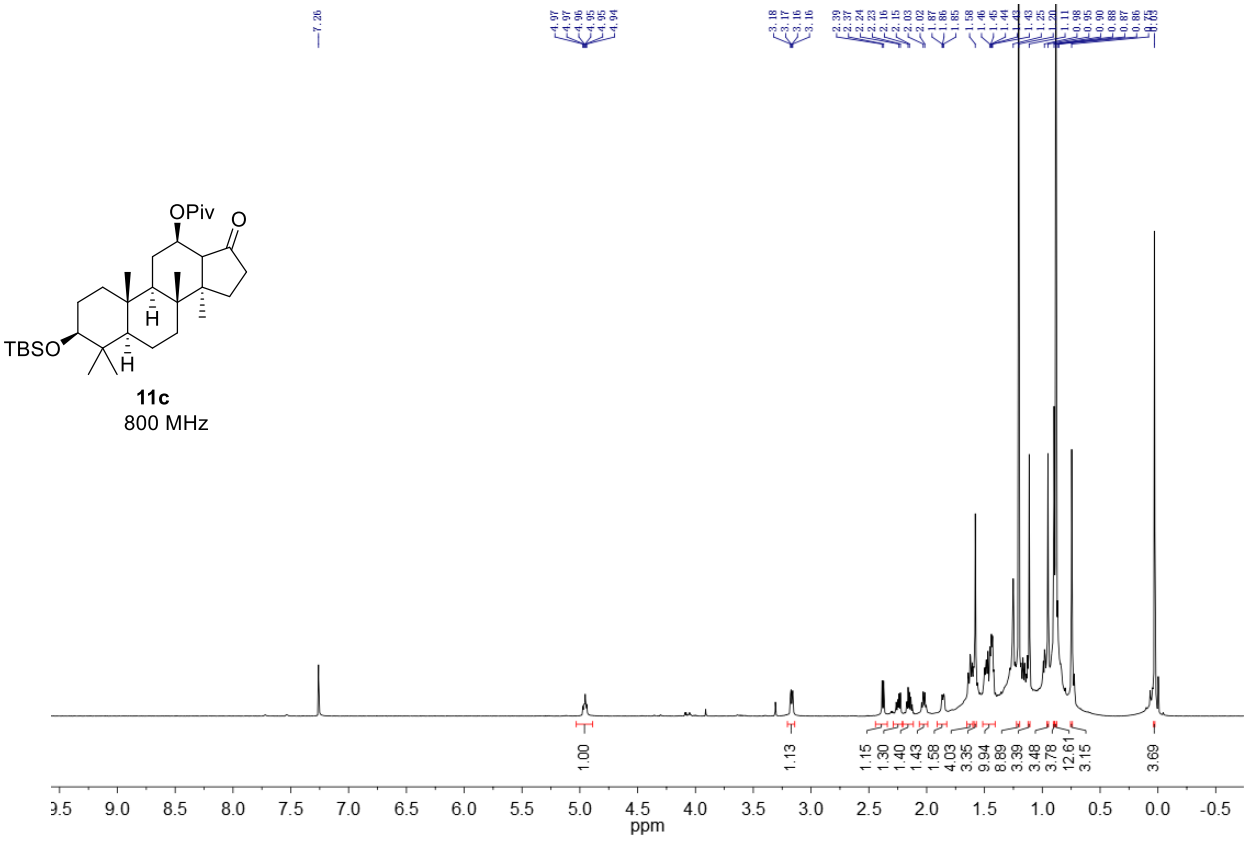

MOMO
O
H
MOMO
H

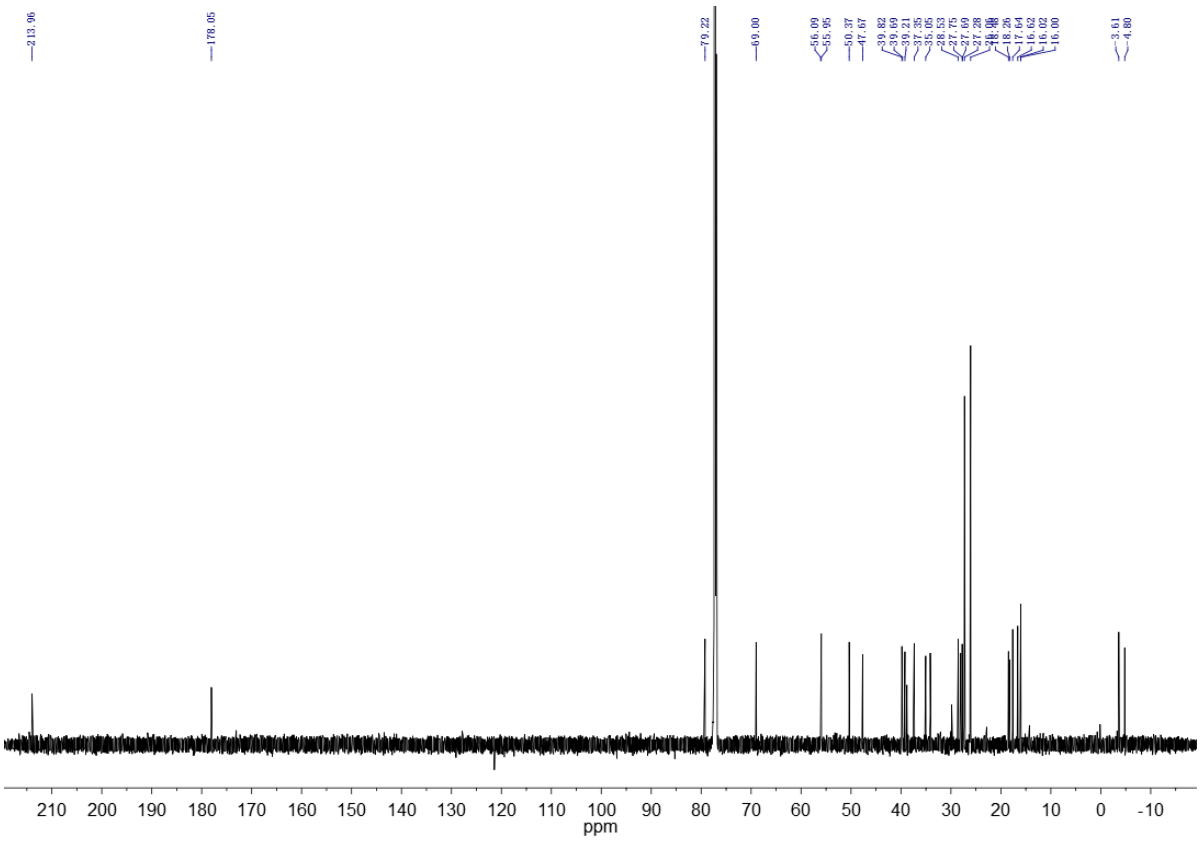
11b
800 MHz

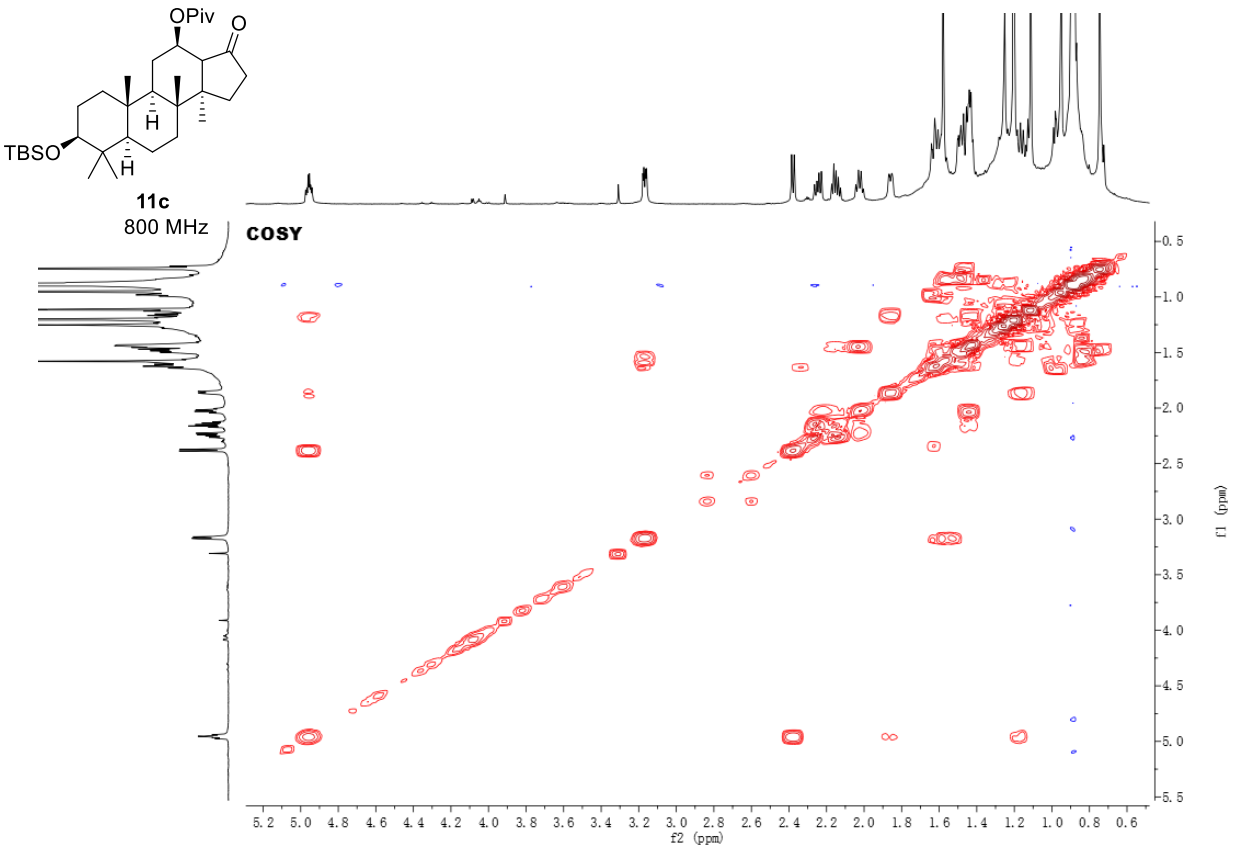

COSY
f2 (ppm)
f1 (ppm)

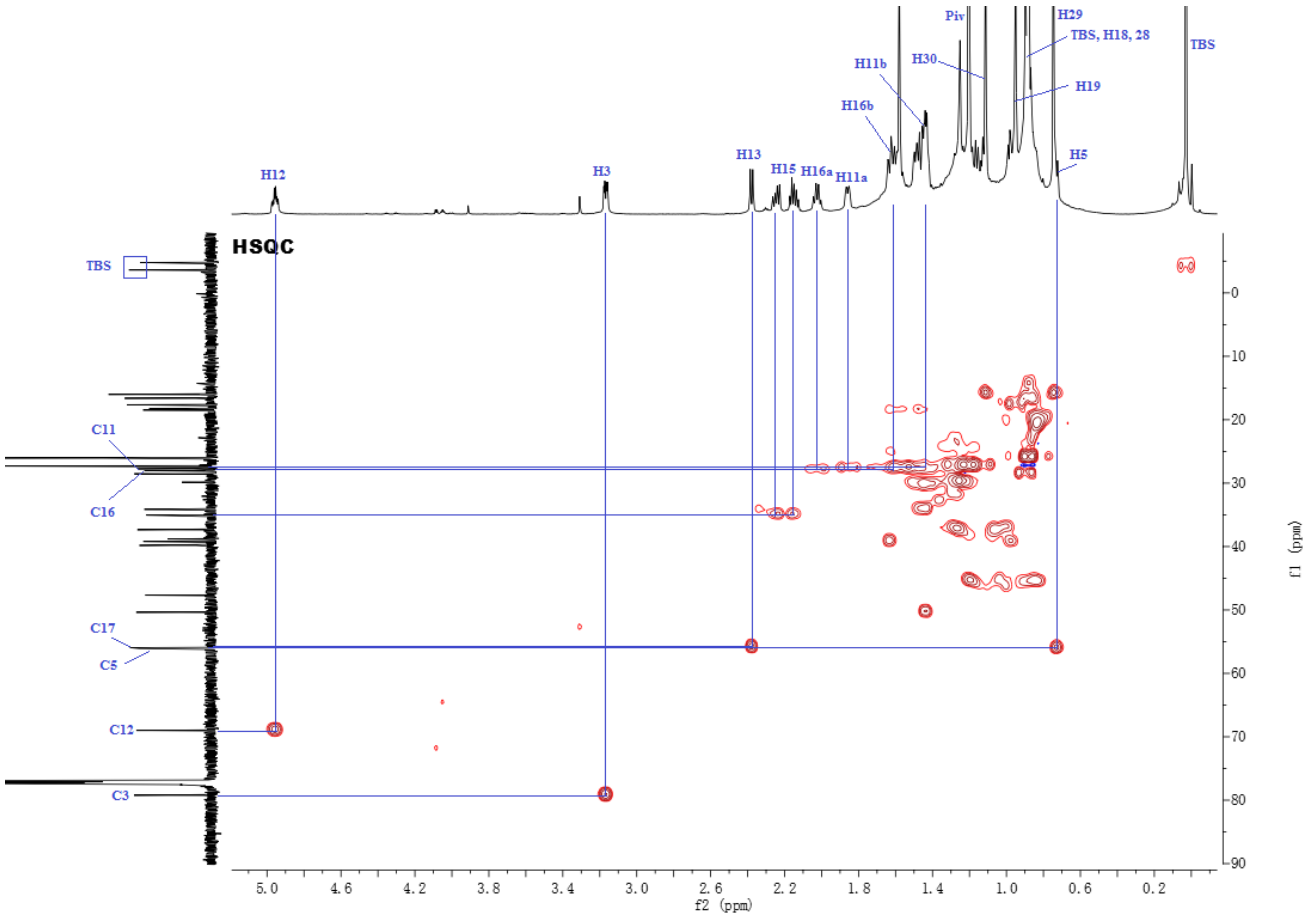

MOMO
MOMO
H12
H3
H13
H15
H19
H18
H28
H29
H30
H5
HSQC
C15
MOMO
C5
C13
C12
C3
MOMO
f2 (ppm)
f1 (ppm)

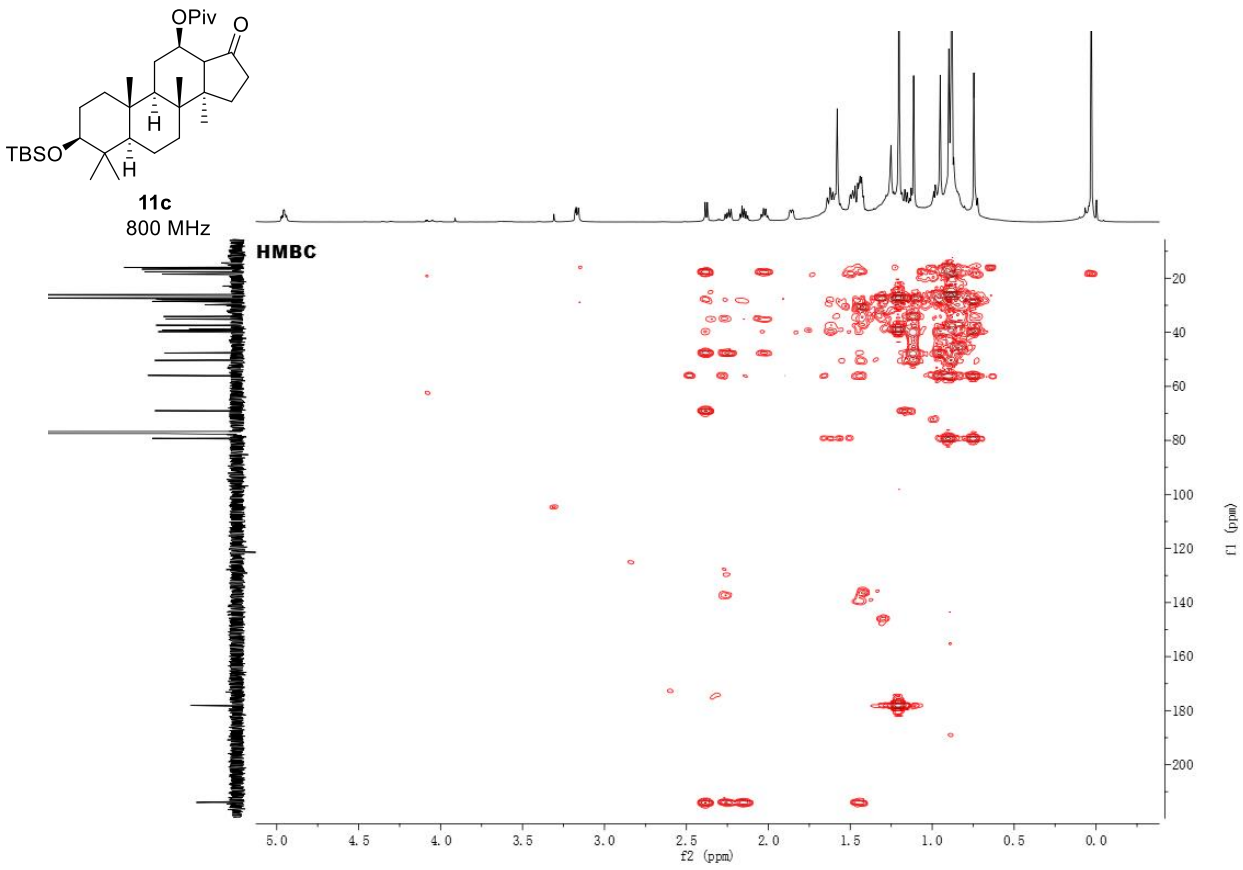

MOMO
O
MOMO
H
H
11b
800 MHz
HMBC
f2 (ppm)
f1 (ppm)

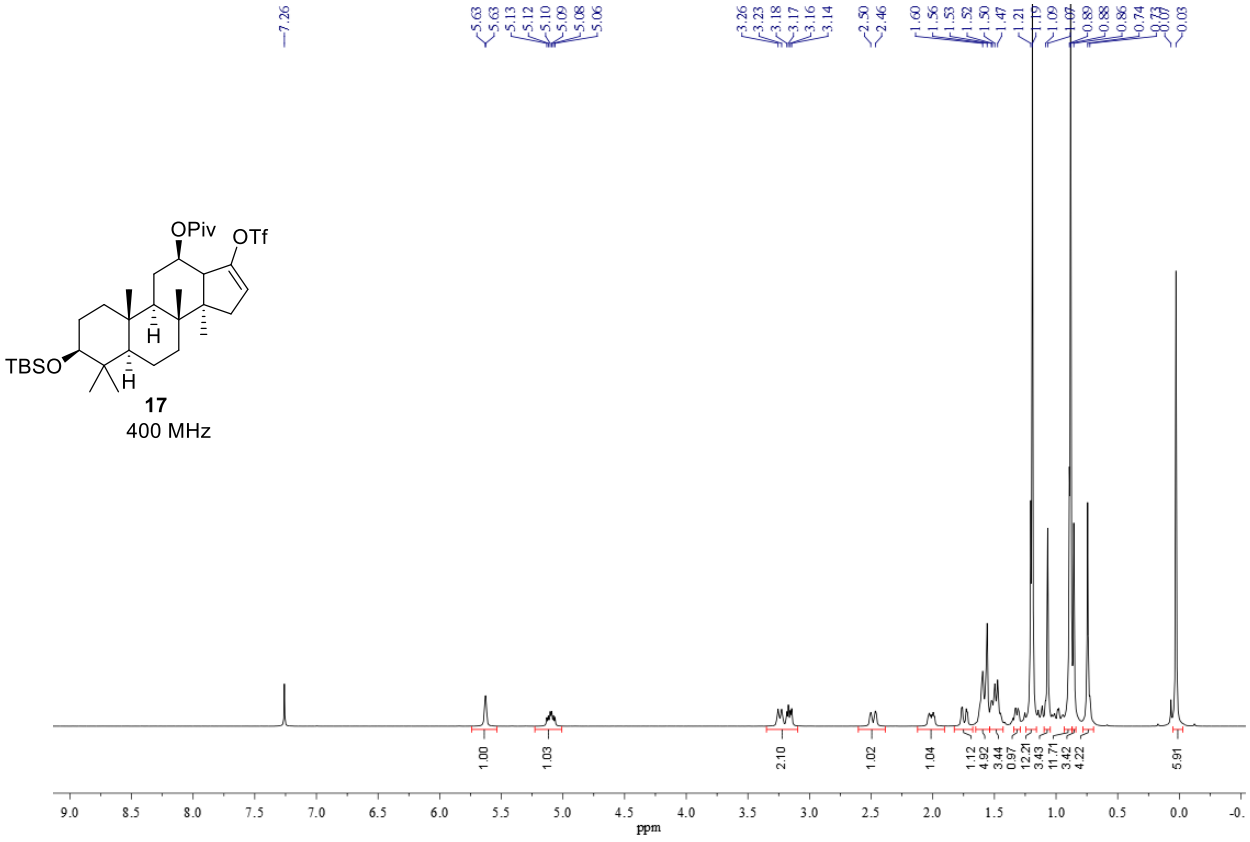

OPiv
O
TBSO
H
H
11c
800 MHz
ppm

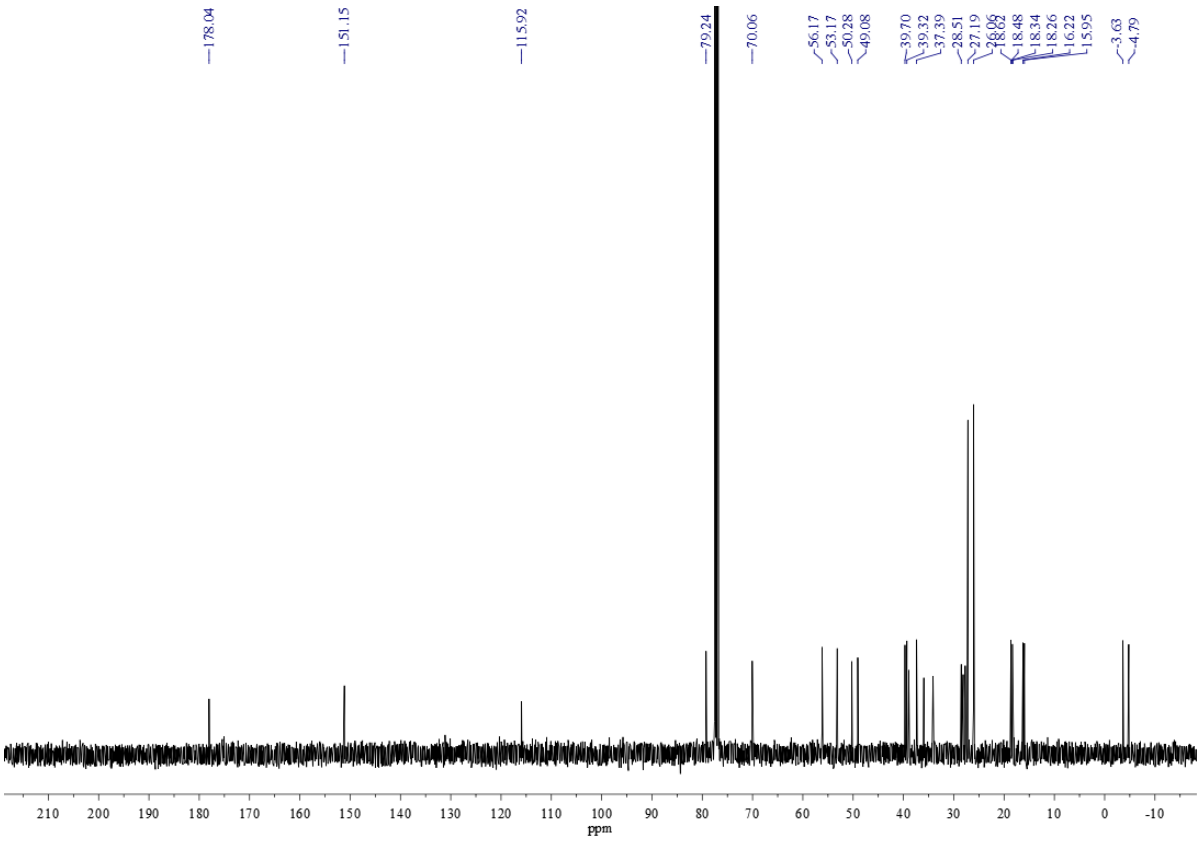

ppm

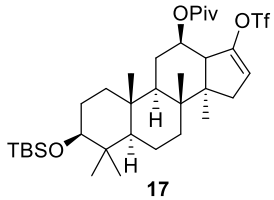

OPiv
O
TBSO
H
H
11c
800 MHz
COSY
f2 (ppm)
f1 (ppm)


Piv
H29
TBS, H18, 28
TBS
H11b
H30
H19
H16b
H5
H13
H15
H16a
H11a
H12
H3
HSQC
TBS
C11
C16
C17
C5
C12
C3
f2 (ppm)
f1 (ppm)

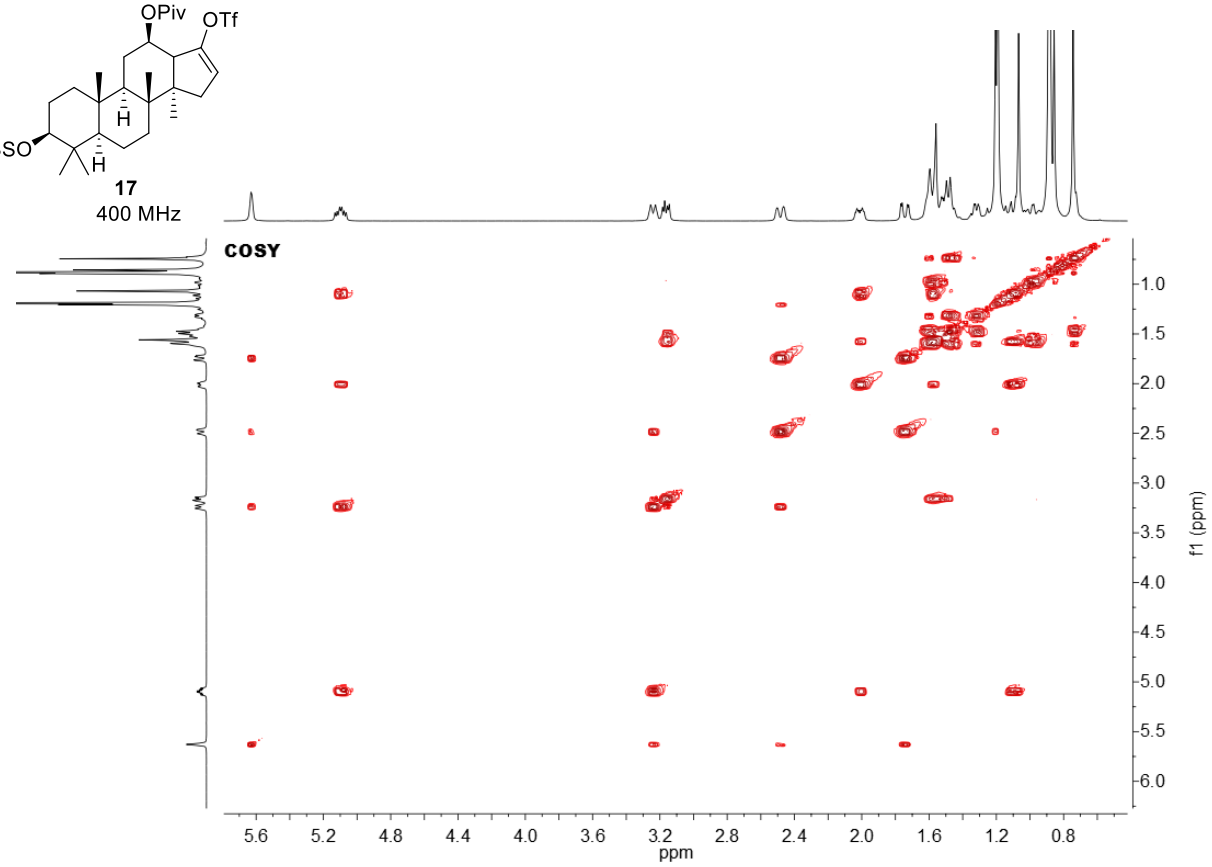

OPiv
O
TBSO
H
H
11c
800 MHz
HMBC
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f2 (ppm)
20
40
60
80
100
120
140
160
180
200
f1 (ppm)

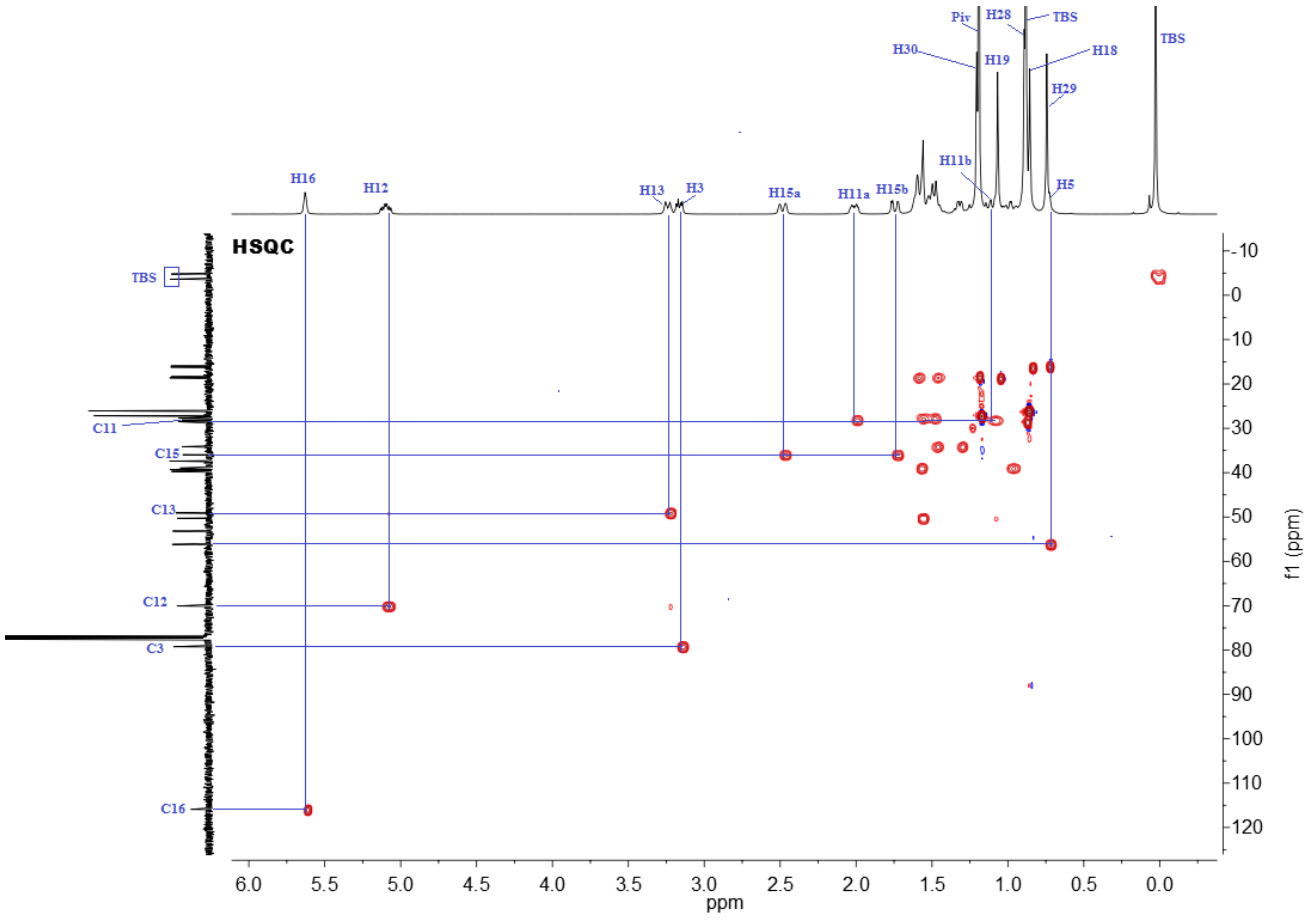

OPiv
OTf
TBSO
H
H
17
400 MHz
7.26
5.63
5.63
5.13
5.12
5.10
5.09
5.08
5.06
3.26
3.23
3.18
3.17
3.16
3.14
2.50
2.46
1.60
1.56
1.53
1.52
1.50
1.47
1.21
1.19
1.09
1.07
0.89
0.88
0.86
0.74
0.07
0.03
1.00
1.03
2.10
1.02
1.04
1.12
4.92
3.44
0.97
12.21
3.43
11.71
3.42
4.22
5.91
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm

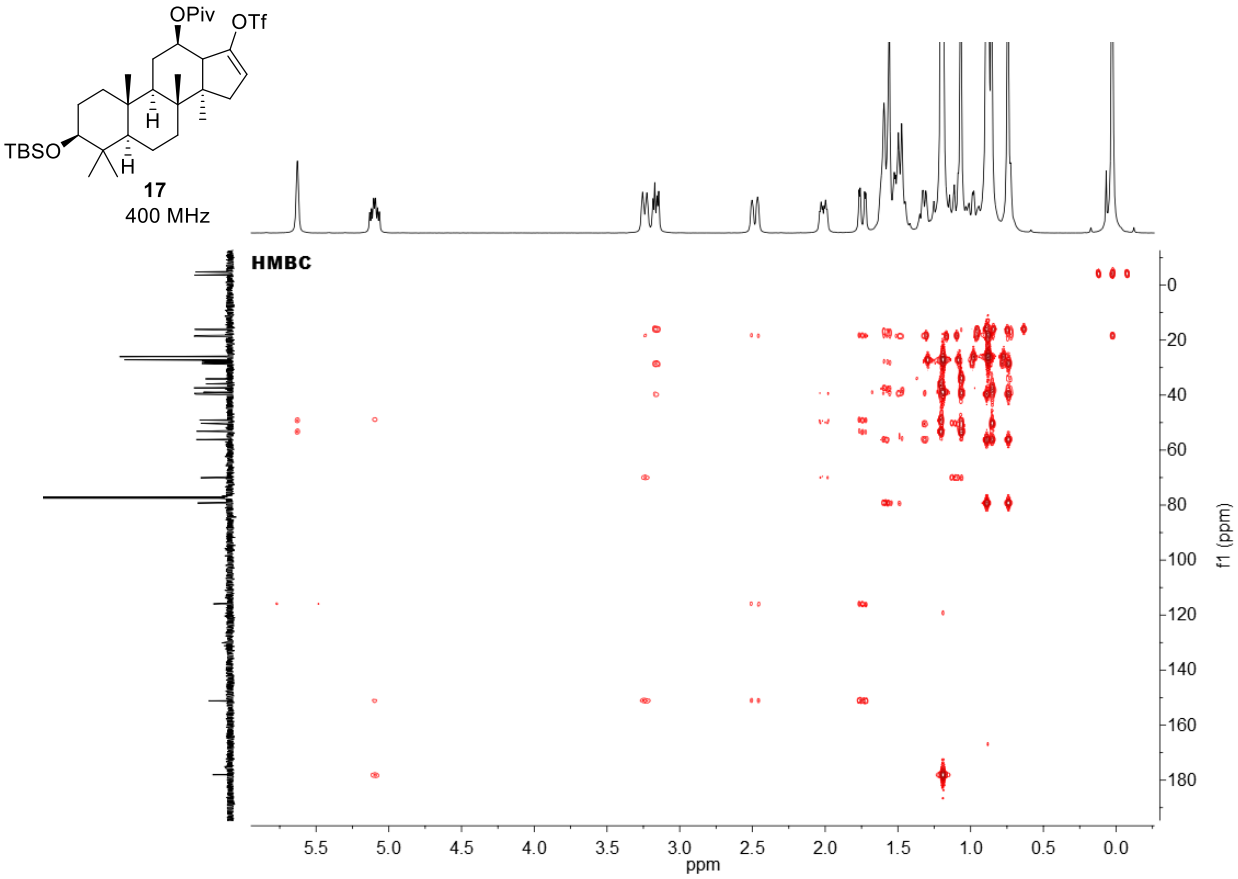

178.04
151.15
115.92
79.24
70.06
56.17
53.17
50.28
49.08
39.70
39.32
37.39
28.51
27.19
26.06
18.62
18.48
18.34
18.26
16.22
15.95
-3.63
-4.79
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
ppm

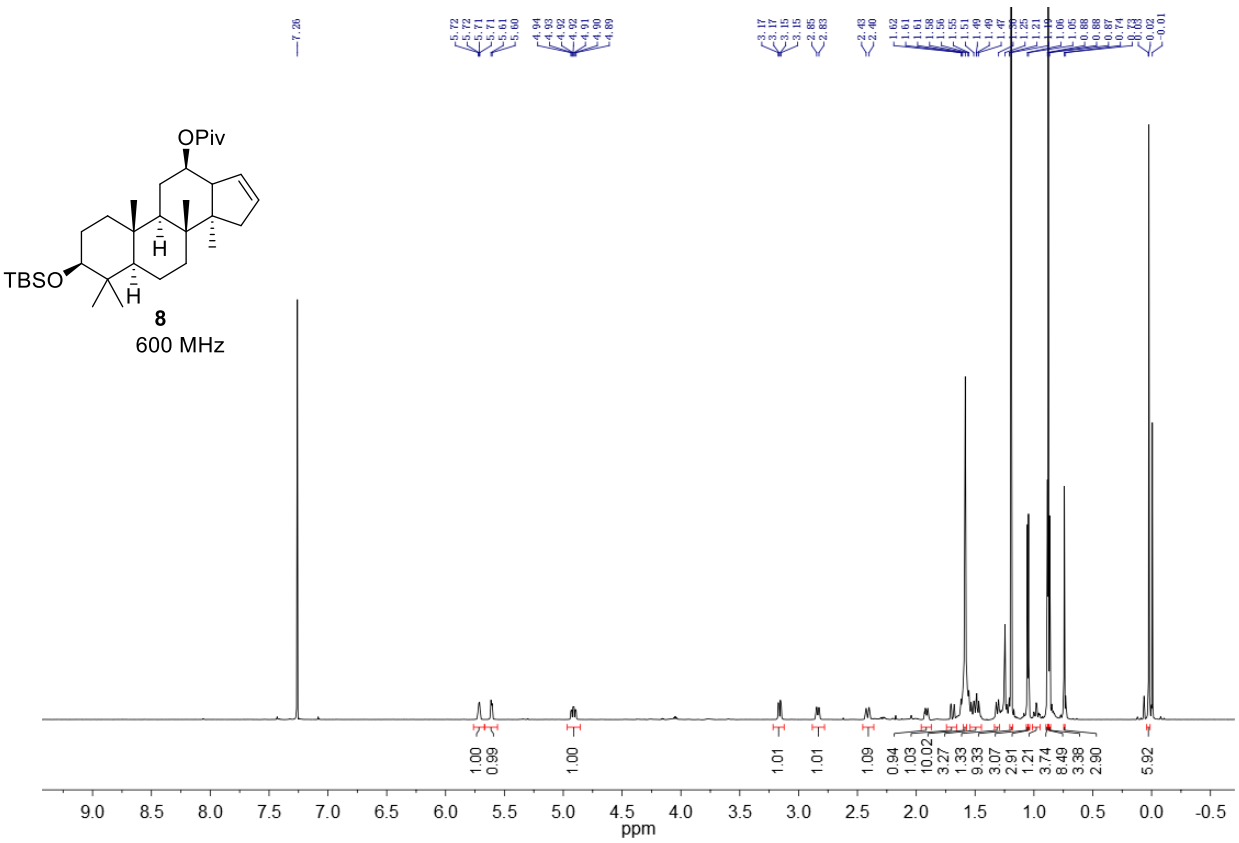

OPiv
OTf
TBSO
H
H

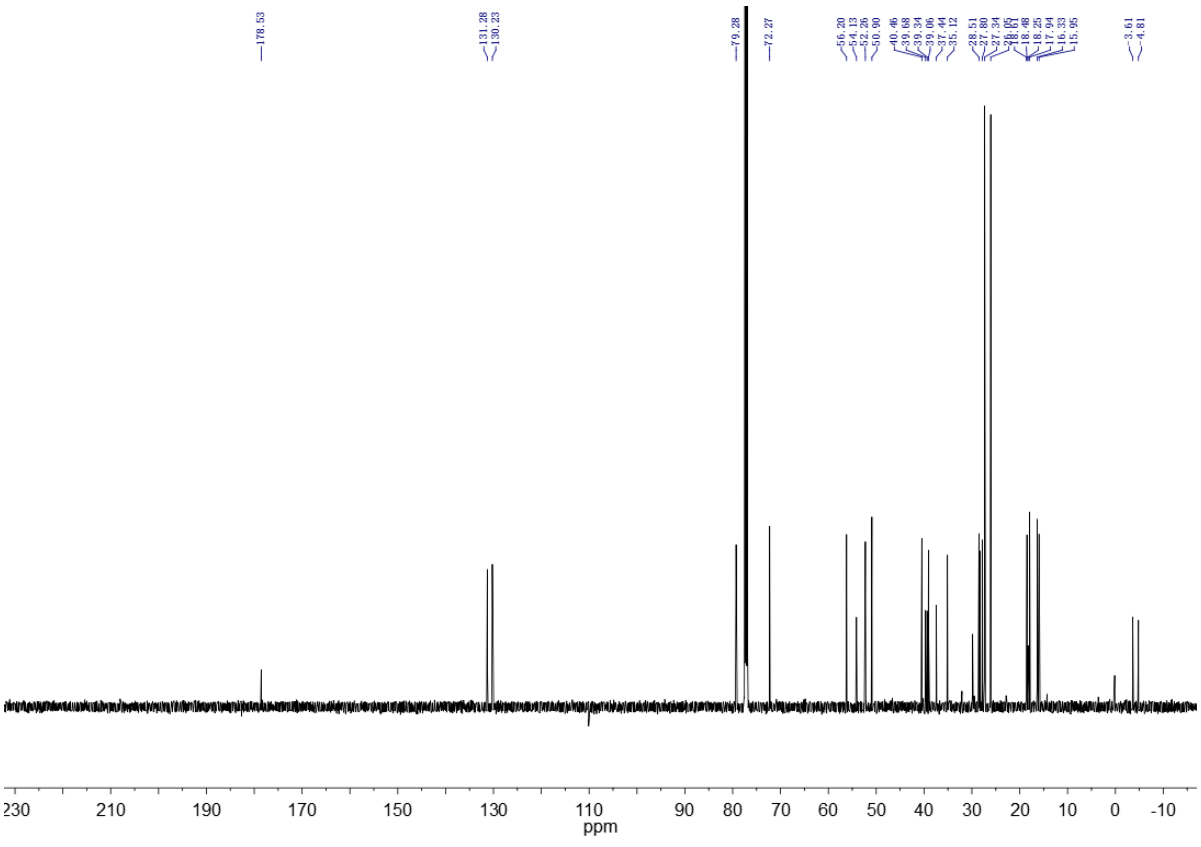
17
400 MHz

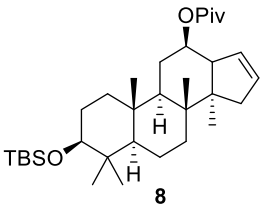

COSY
5.6
5.2
4.8
4.4
4.0
3.6
3.2
2.8
2.4
2.0
1.6
1.2
0.8
ppm
1.0
1.5
2.0
2.5
3.0
3.5
4.0
4.5
5.0
5.5
6.0
f1 (ppm)


HSQC
Piv
H28
TBS
H30
H19
H18
TBS
H29
H11b
H16
H12
H13
H3
H15a
H11a
H15b
H5
TBS
C11
C15
C13
C12
C3
C16
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
-10
0
10
20
30
40
50
60
70
80
90
100
110
120
f1 (ppm)


OPiv
OTf
TBSO
H
H
17
400 MHz
HMBC
0
20
40
60
80
100
120
140
160
180
f1 (ppm)
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm

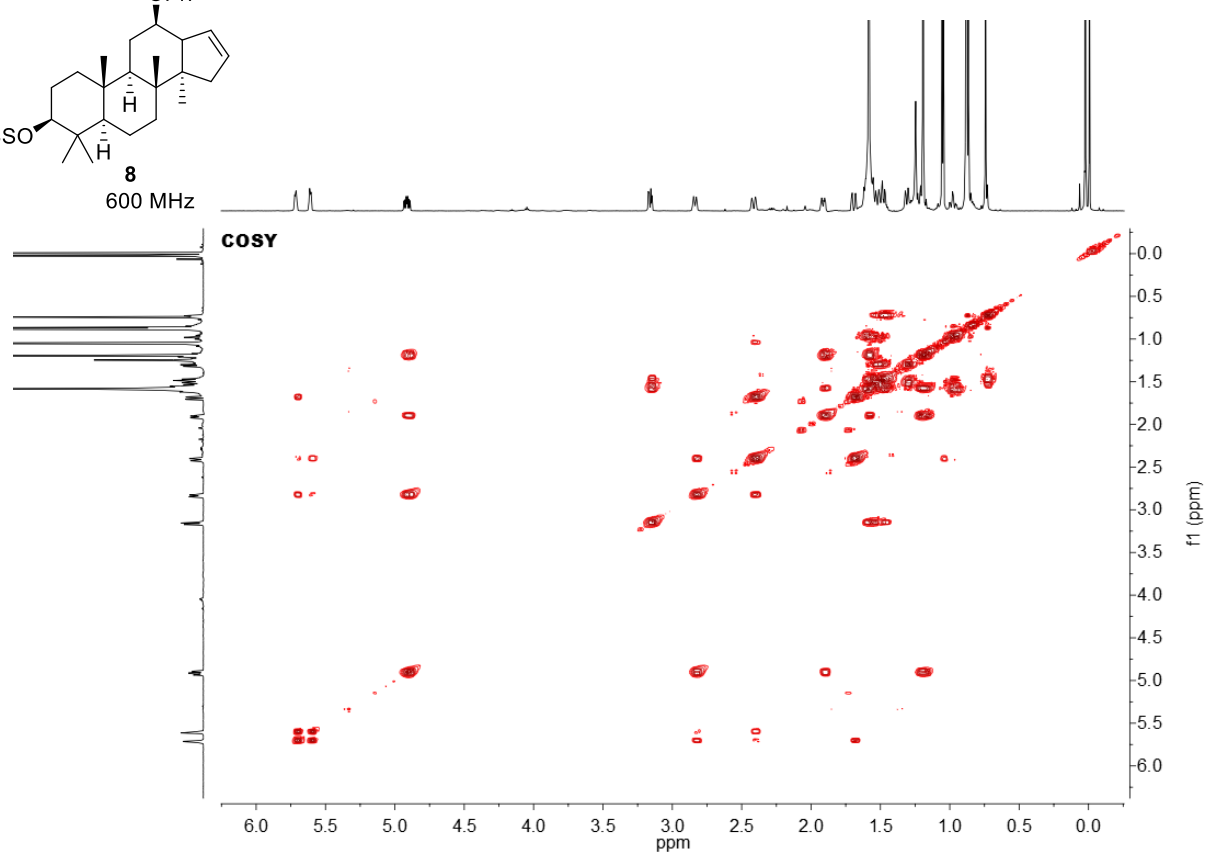

OPiv
TBSO
H
H
8
600 MHz
ppm

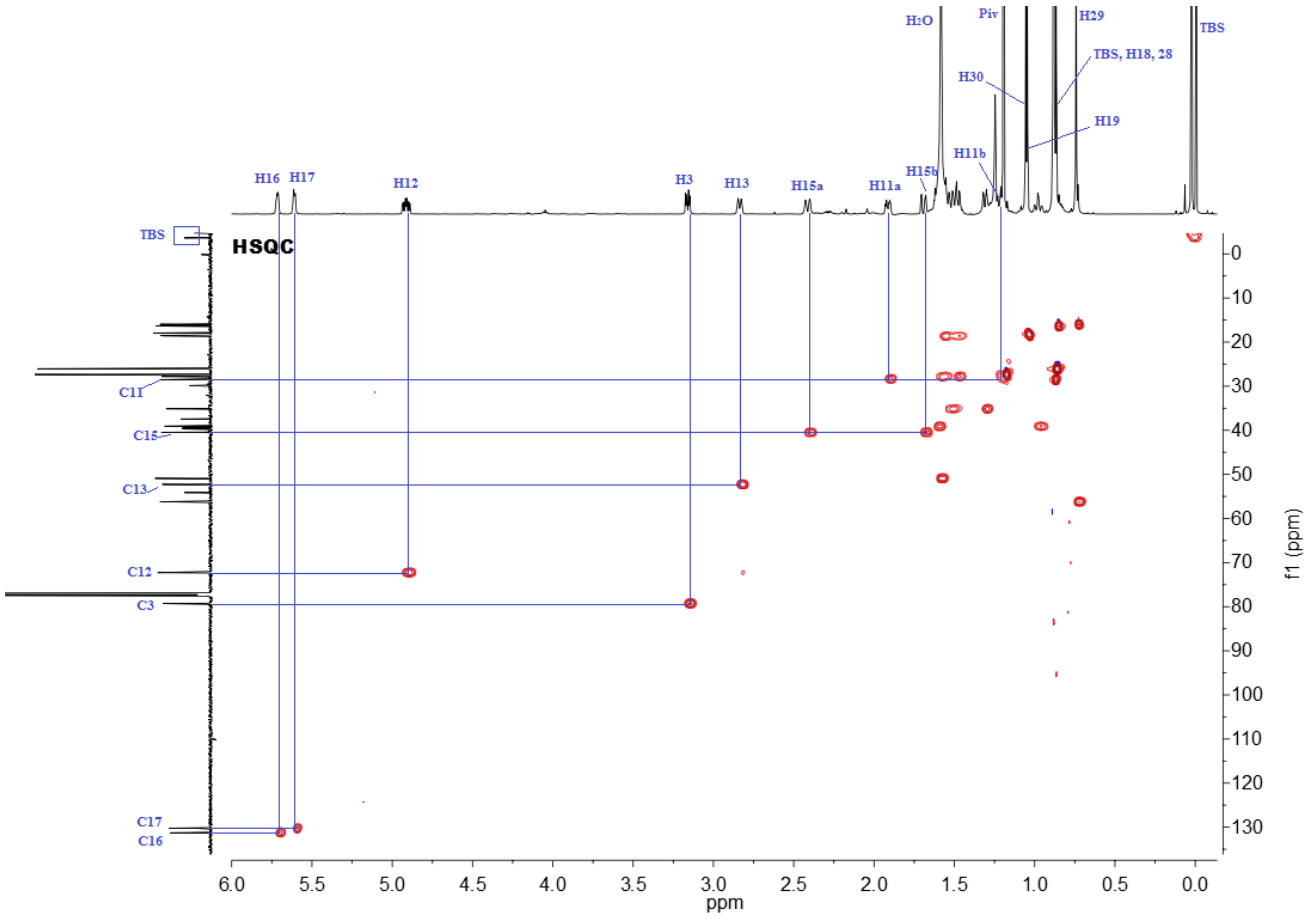

ppm

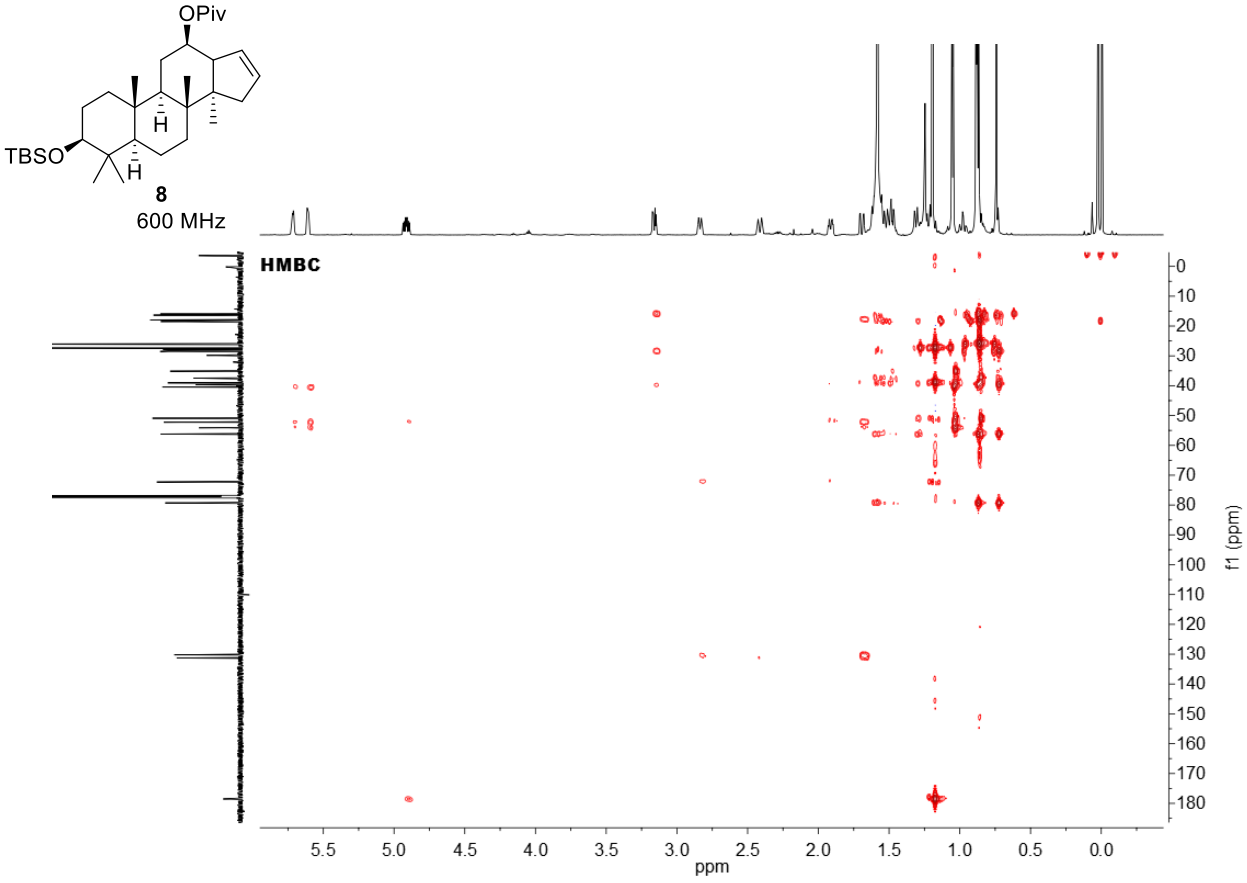

OPiv
TBSO
H
H

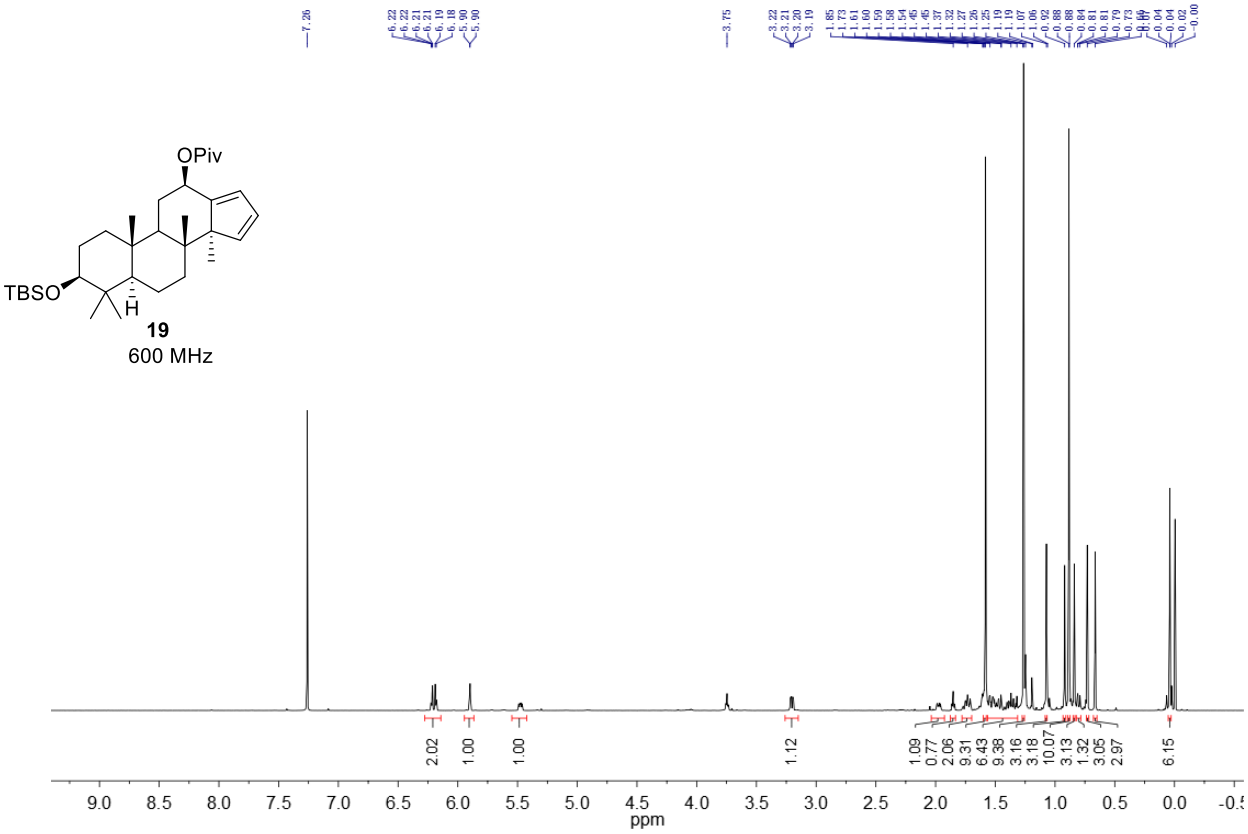
8

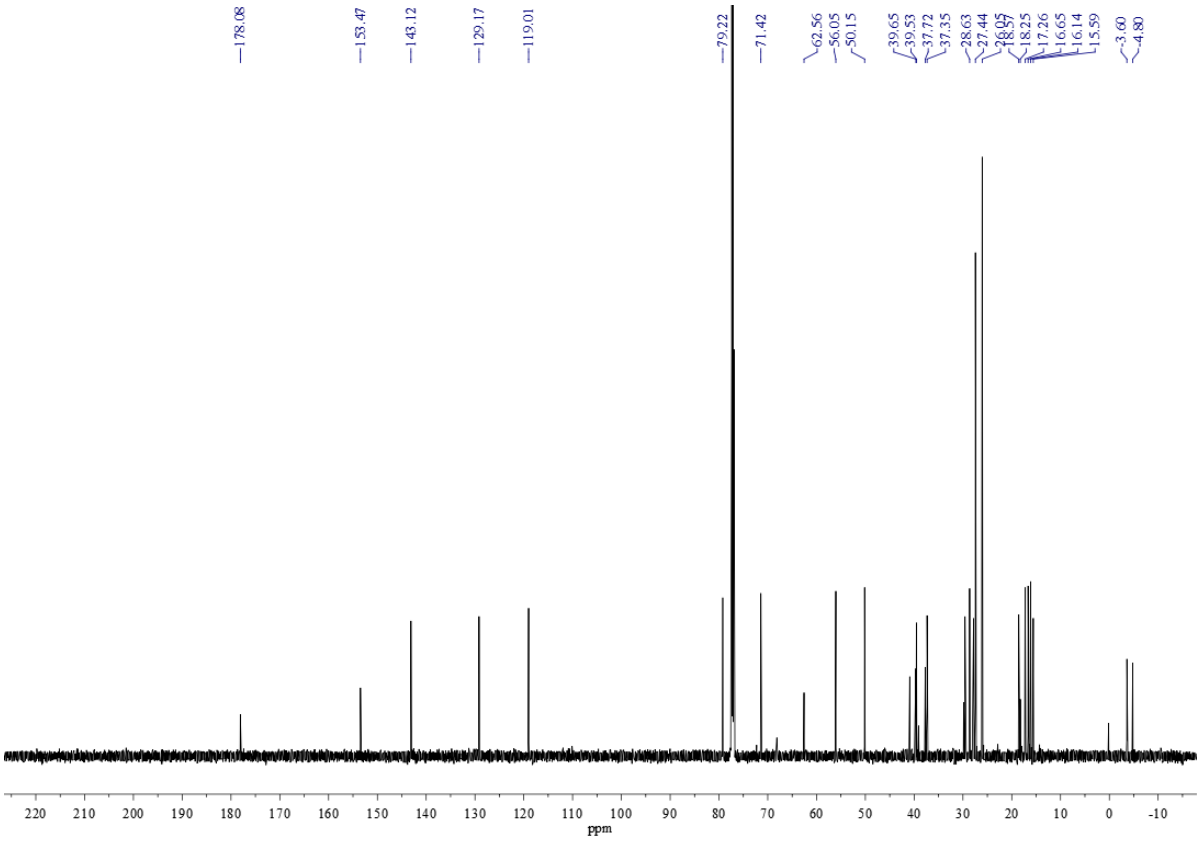
600 MHz

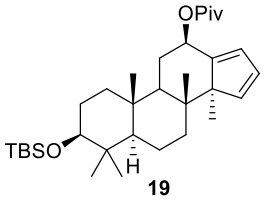

COSY
ppm
f1 (ppm)

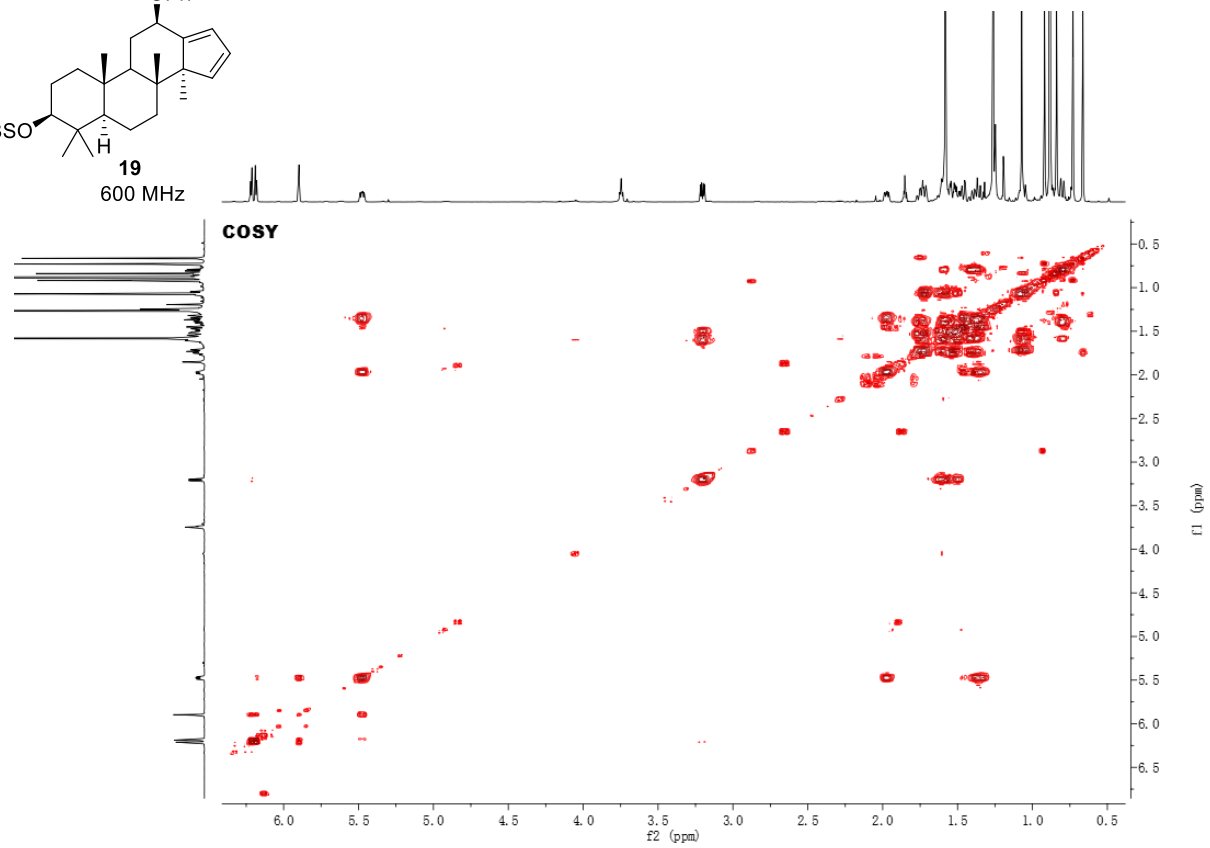

H2O
Piv
H29
TBS
TBS, H18, 28
H30
H19
H11b
H15b
H16
H17
H12
H3
H13
H15a
H11a
TBS
HSQC
C11
C15
C13
C12
C3
C17
C16
ppm
f1 (ppm)

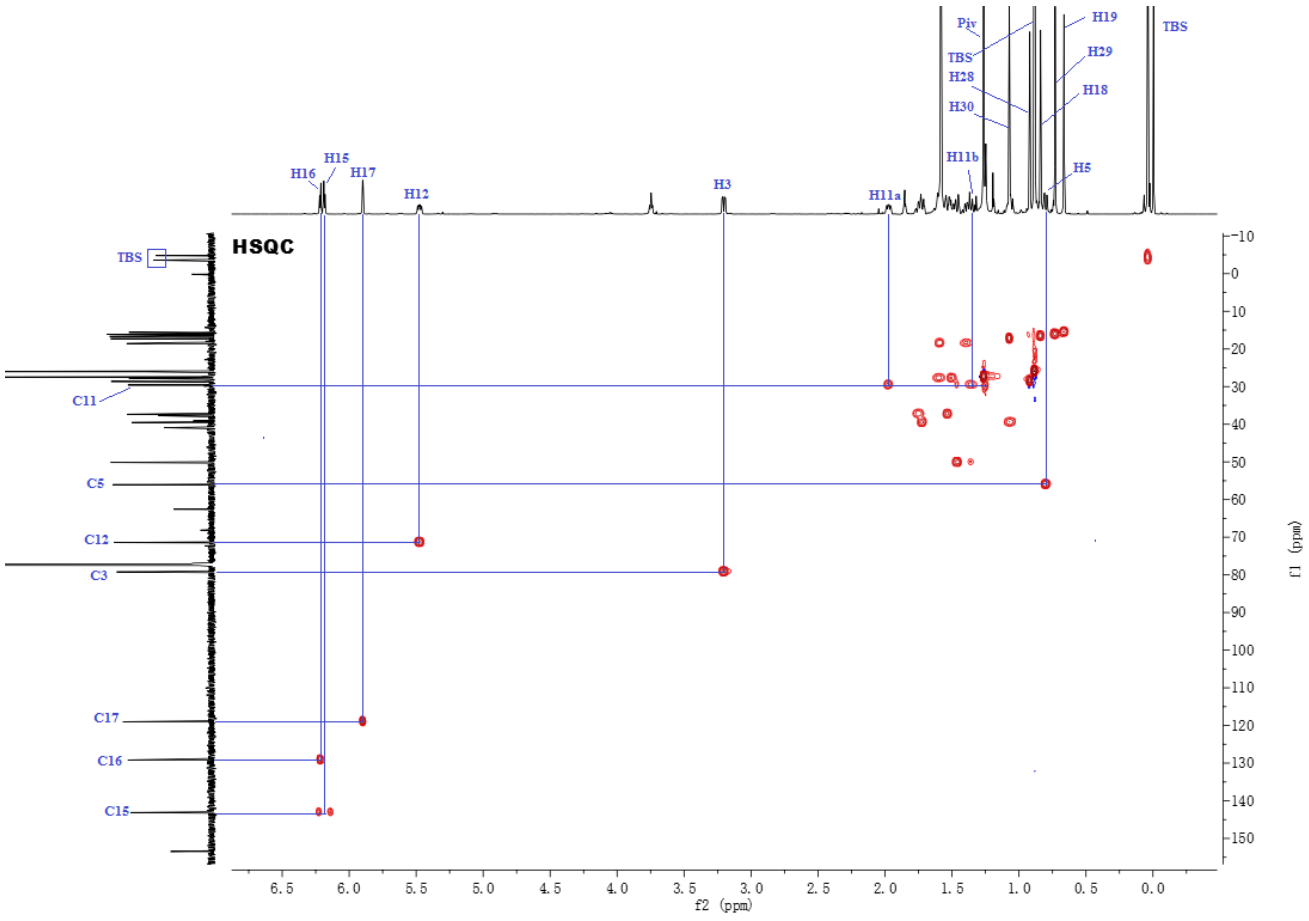

OPiv
TBSO
H
H
8
600 MHz
HMBC
ppm
f1 (ppm)

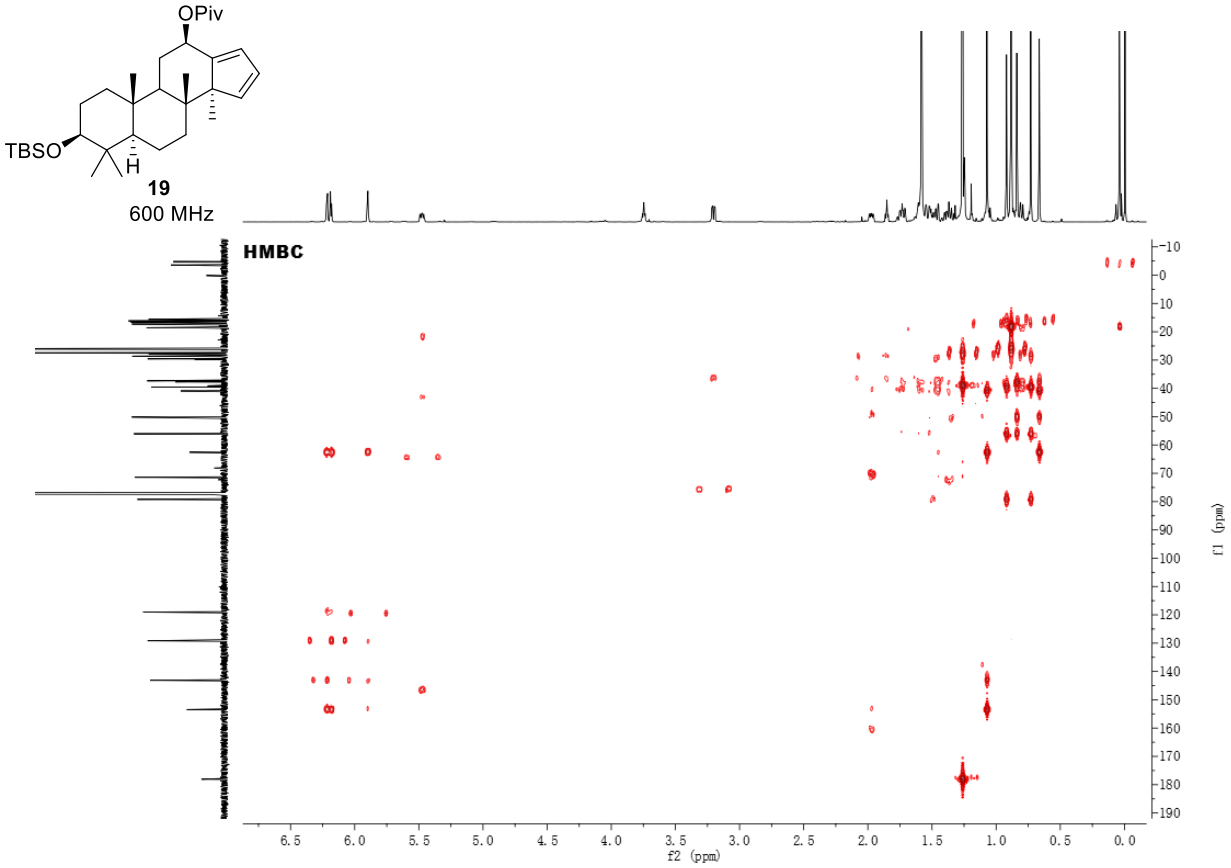

OPiv
TBSO
H
19
600 MHz
ppm

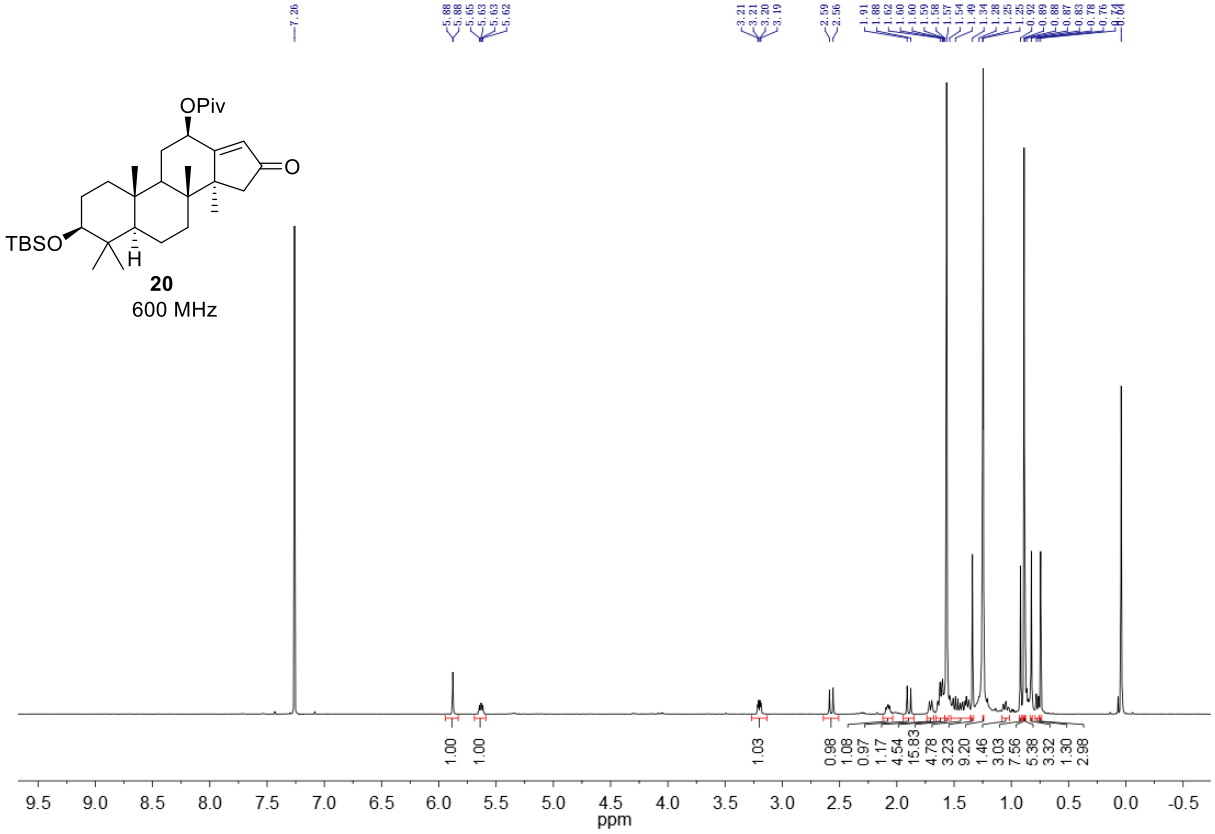

ppm

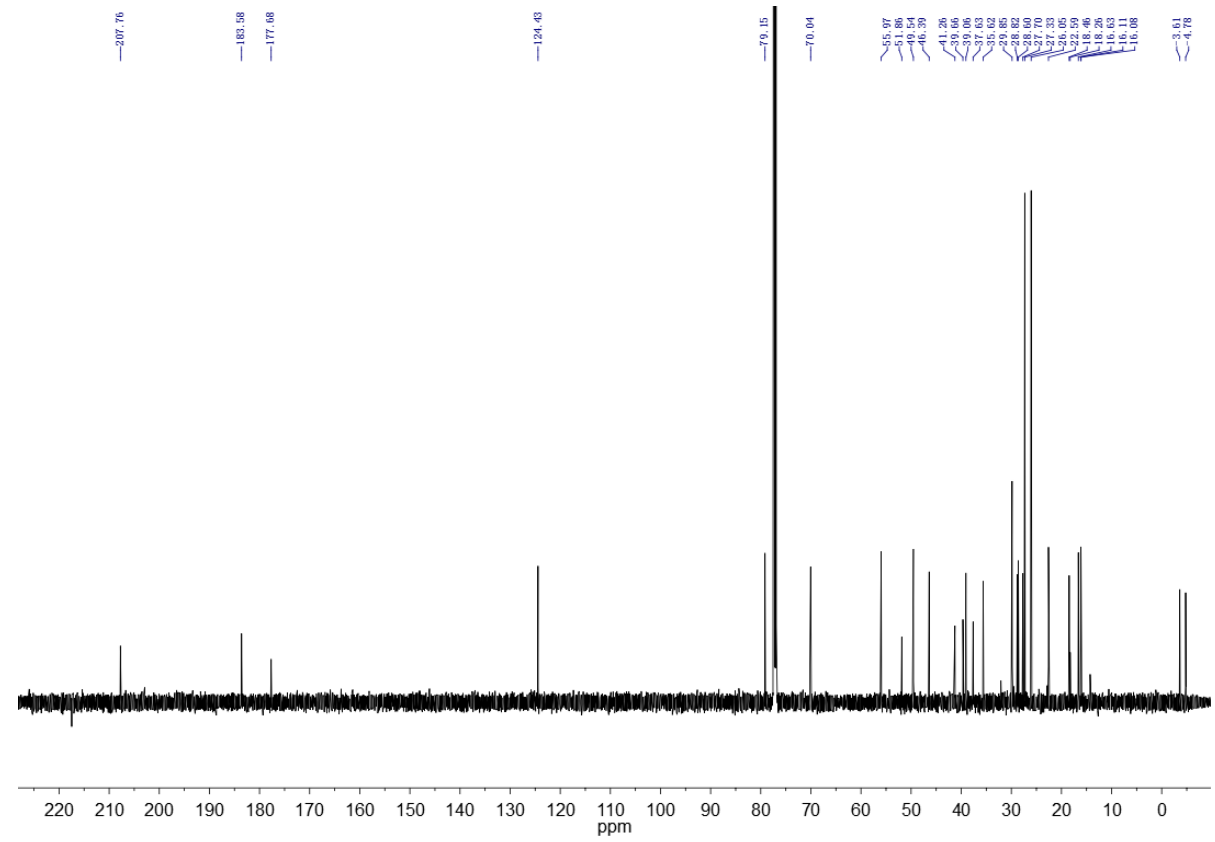

OPiv
TBSO
H
19
600 MHz

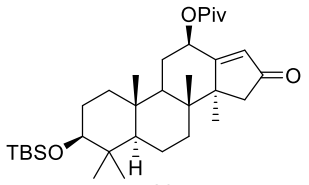

COSY
f2 (ppm)
f1 (ppm)


HSQC
Piv
TBS
H28
H30
H11b
H19
TBS
H29
H18
H5
H16
H15
H17
H12
H3
H11a
TBS
C11
C5
C12
C3
C17
C16
C15
f2 (ppm)
f1 (ppm)

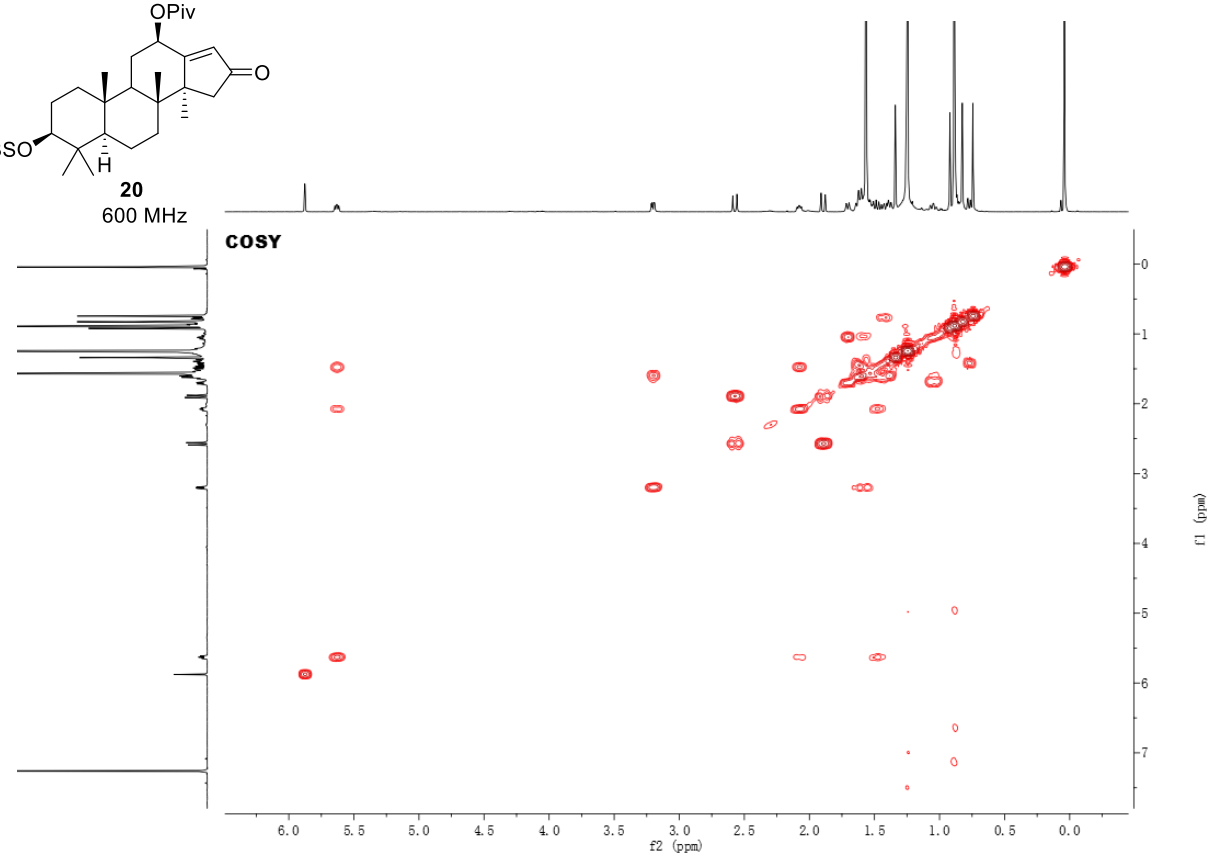

OPiv
TBSO
H
19
600 MHz
HMBC
f2 (ppm)
f1 (ppm)

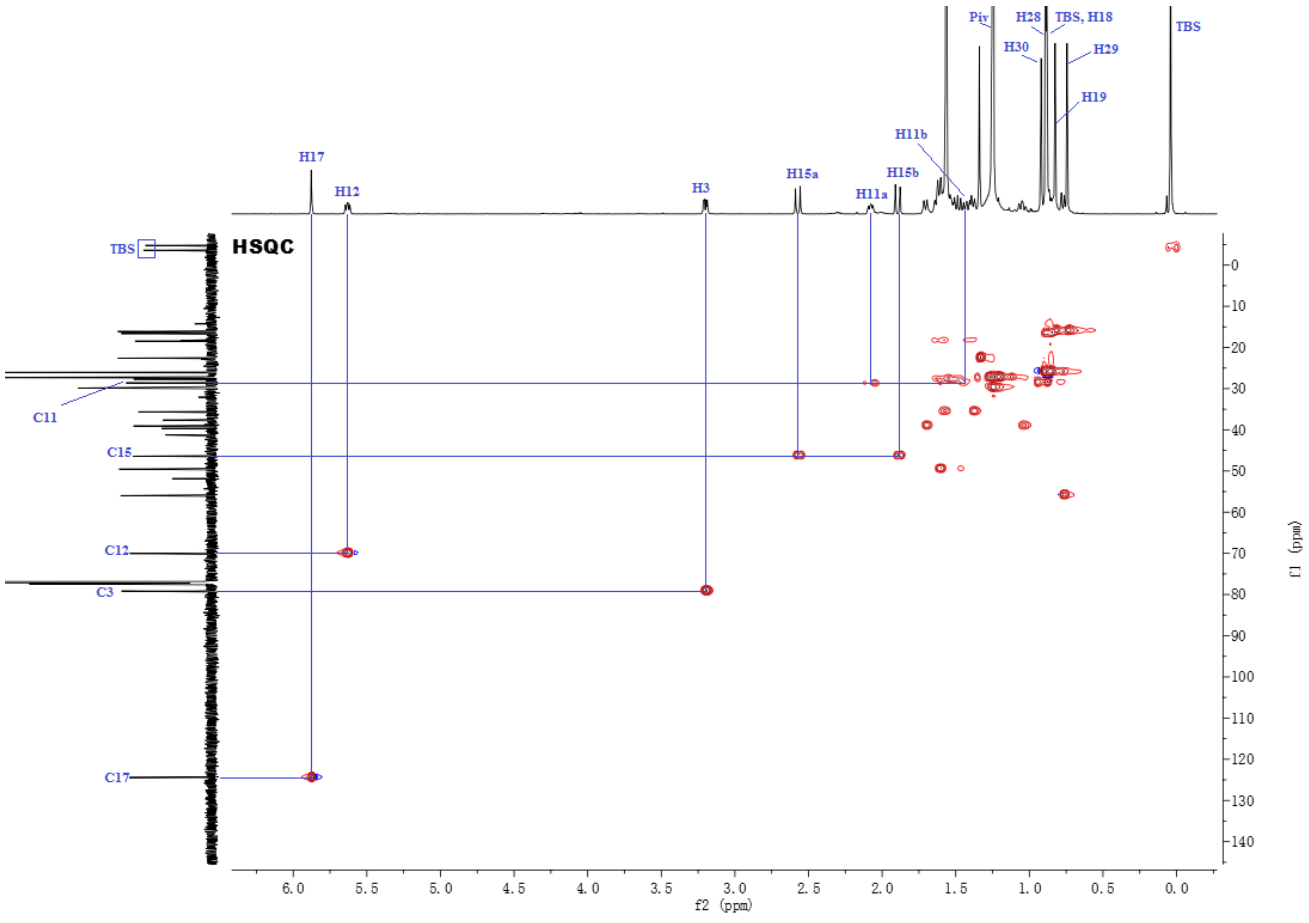

OPiv
O
TBSO
H
20
600 MHz
ppm

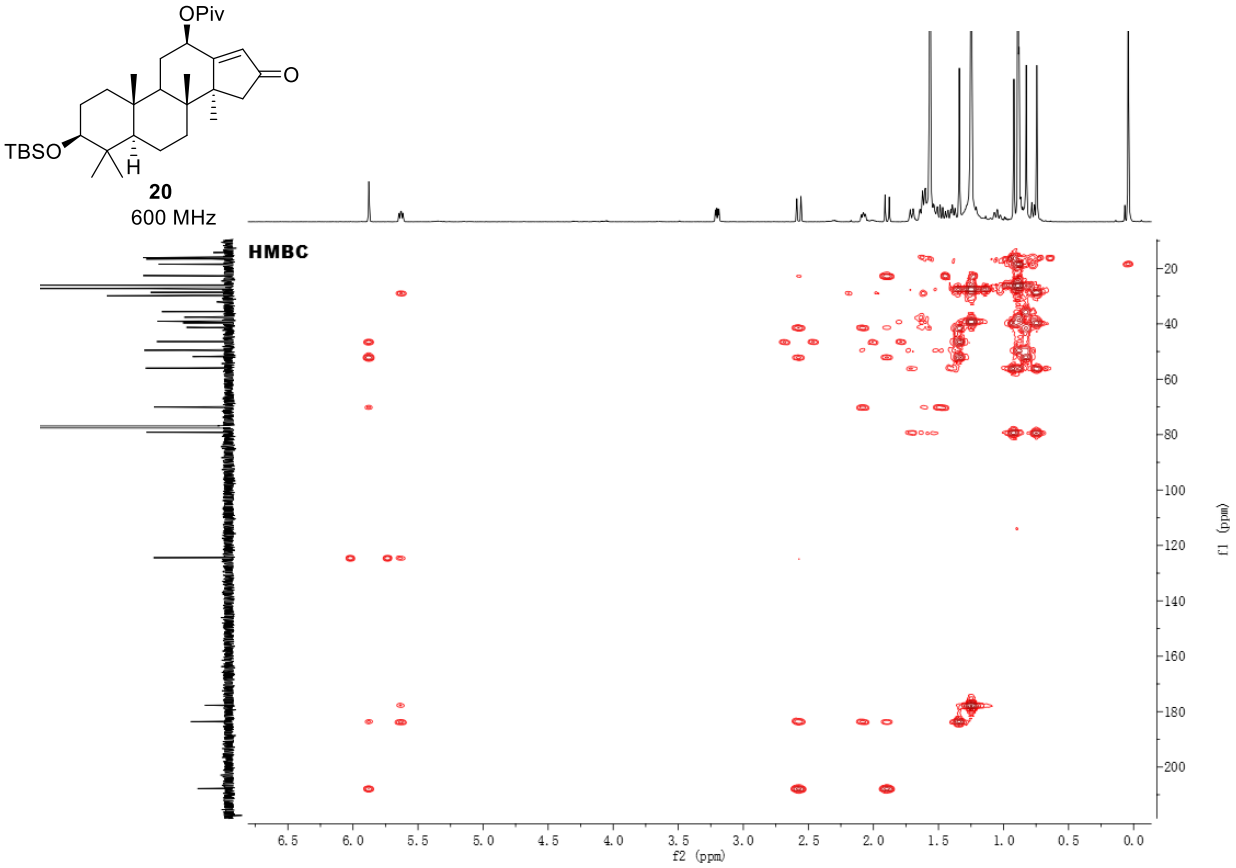

ppm

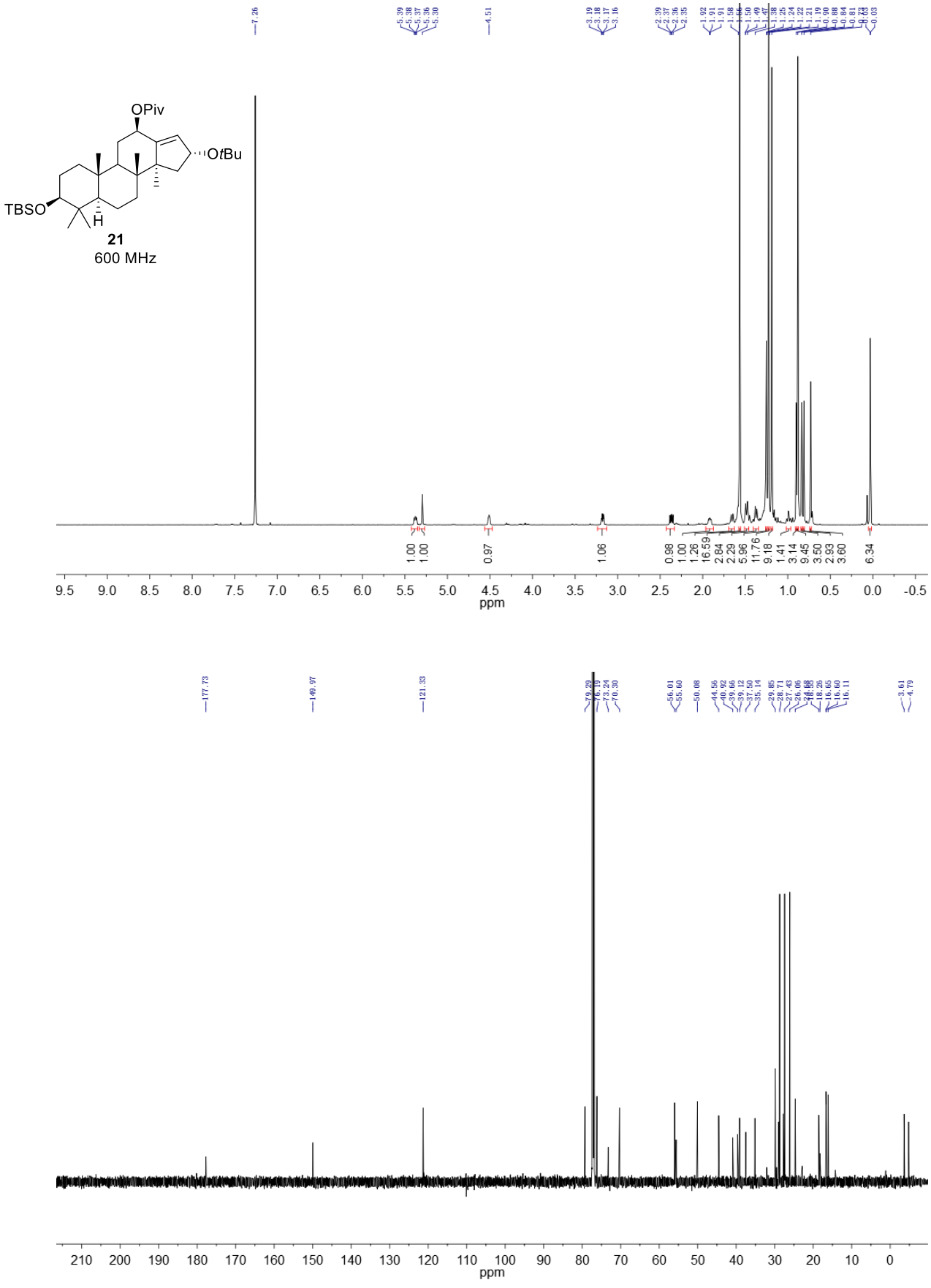

OPiv
O
TBSO
H

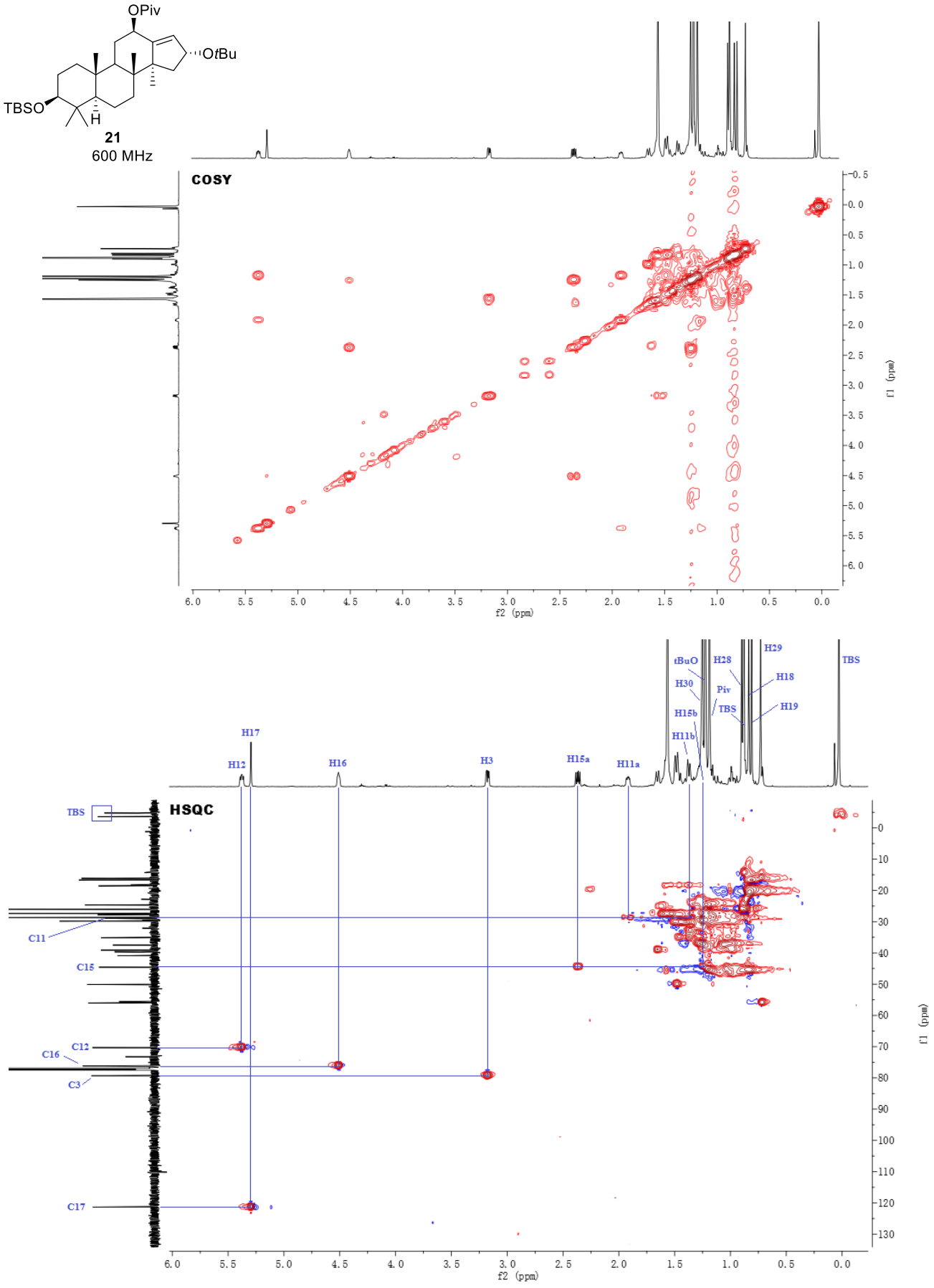
20
600 MHz

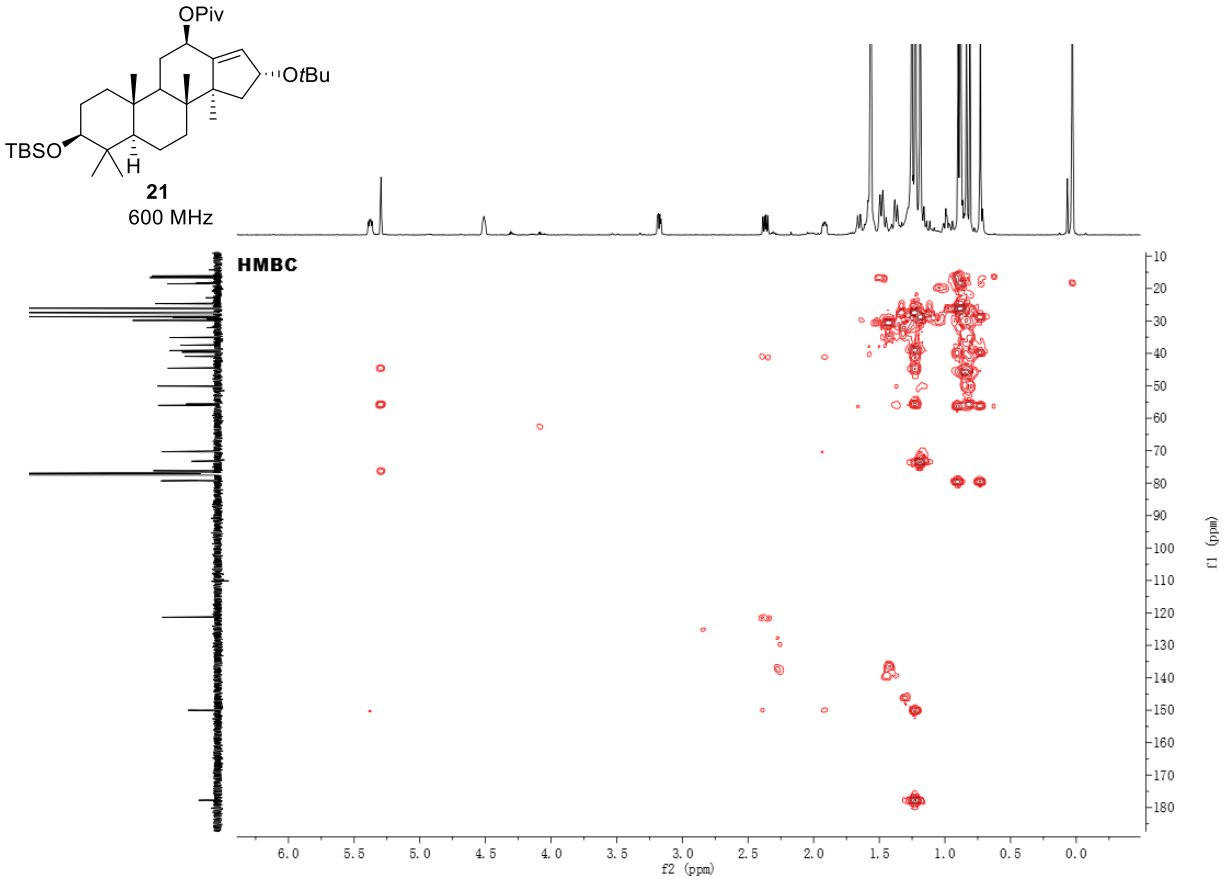

COSY
f2 (ppm)
f1 (ppm)

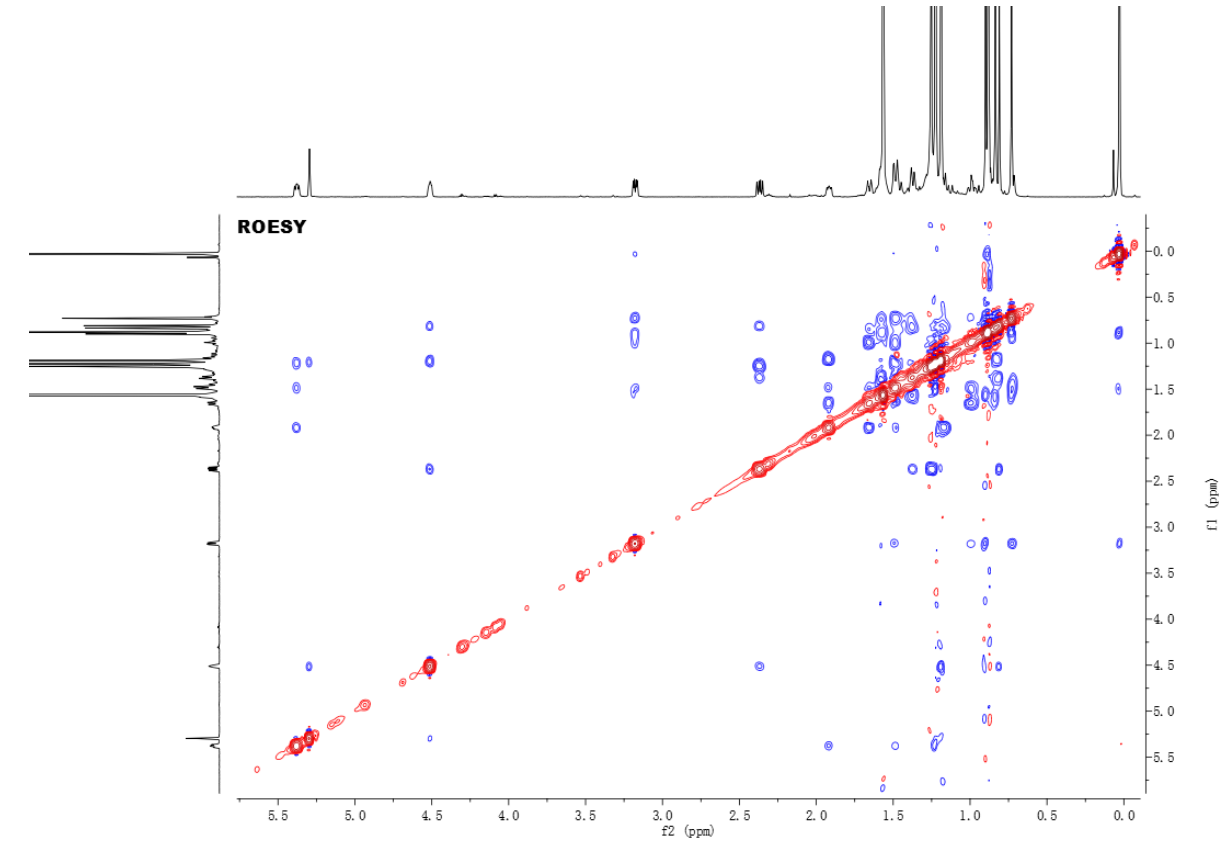

HSQC
Piv
H28
TBS, H18
TBS
H30
H29
H19
H11b
H17
H12
H3
H15a
H15b
H11a
TBS
C11
C15
C12
C3
C17
f2 (ppm)
f1 (ppm)

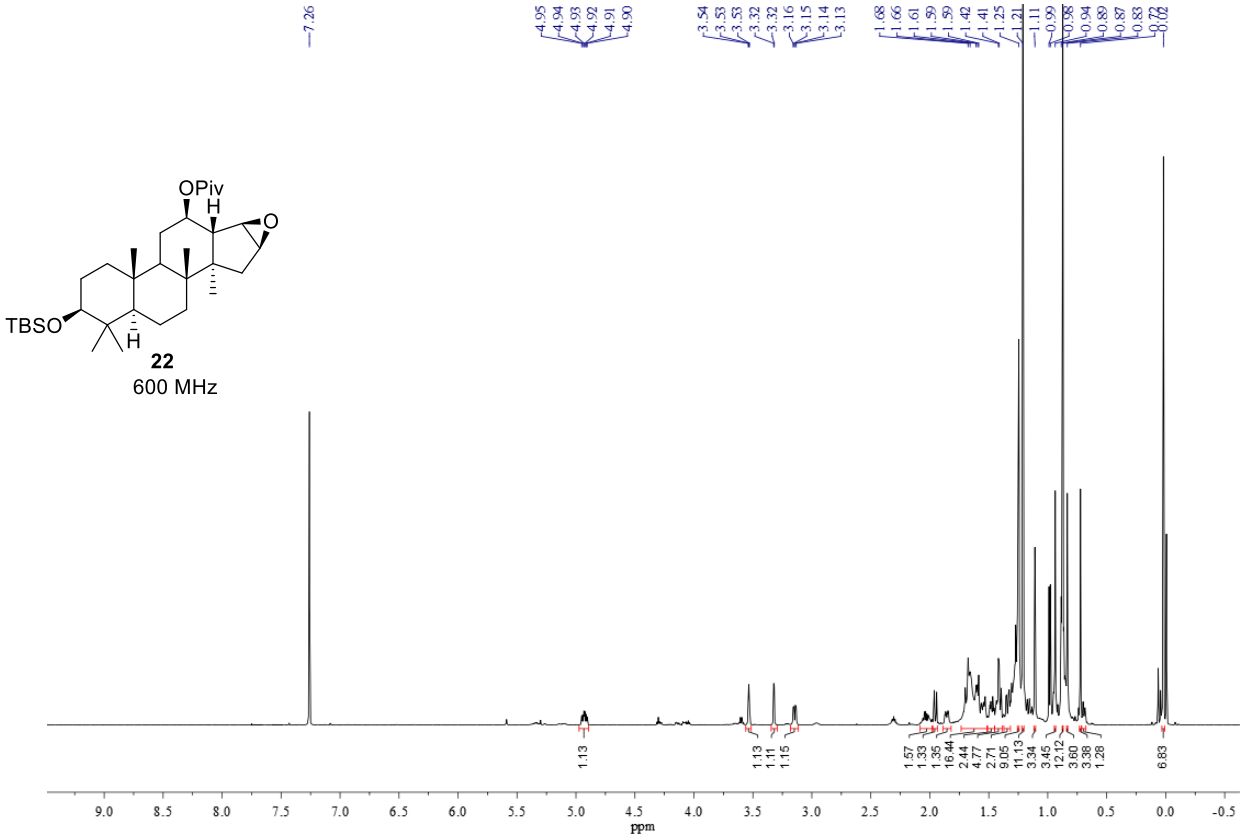

OPiv
O
TBSO
H
20
600 MHz
HMBC
f2 (ppm)
f1 (ppm)

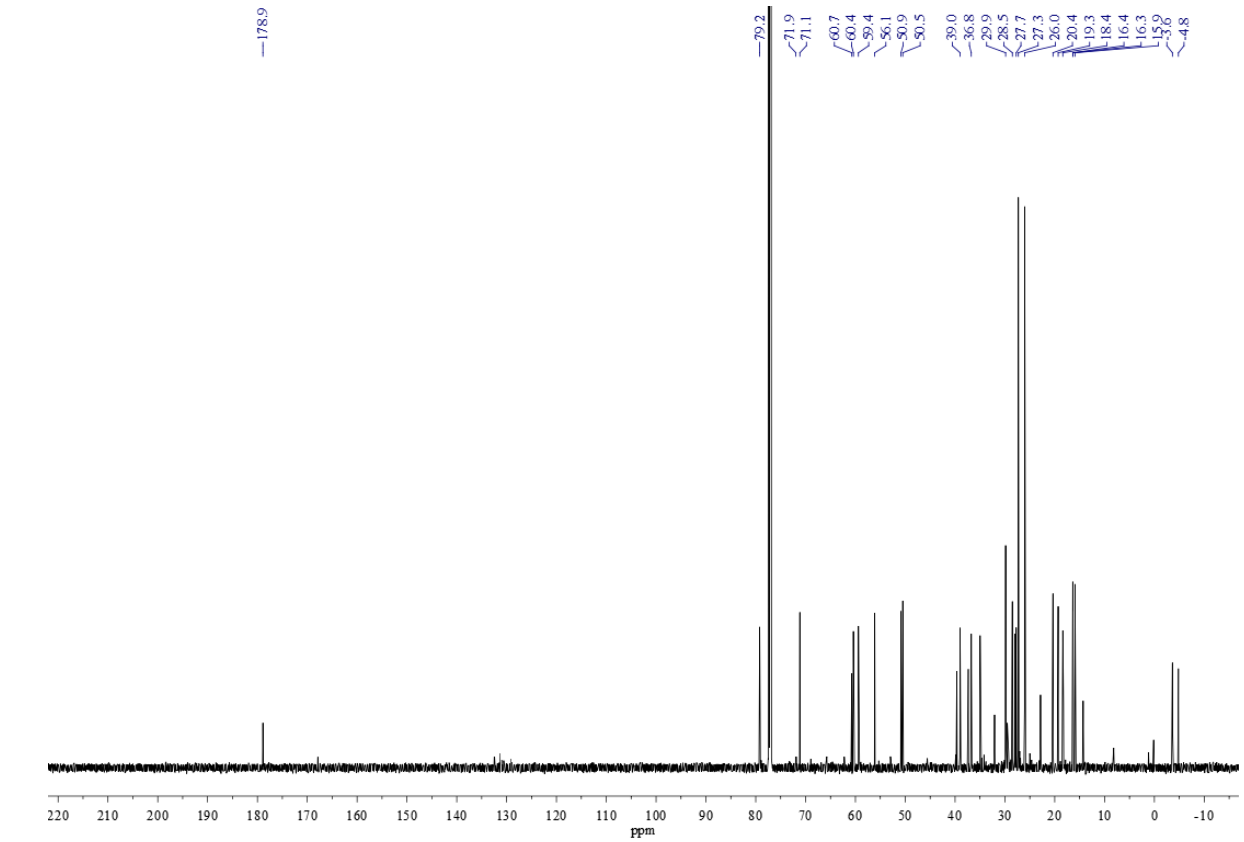

OPiv
OtBu
TBSO
H
21
600 MHz
ppm
ppm

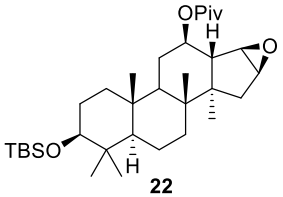

OPiv
OtBu
TBSO
H
21
600 MHz
COSY
f2 (ppm)
f1 (ppm)
HSQC
tBuO
H28
H29
TBS
H30
Piv
H18
H15b
TBS
H19
H11b
H17
H12
H16
H3
H15a
H11a
TBS
C11
C15
C12
C16
C3
C17


OPiv
OtBu
TBSO
H
21
600 MHz
HMBC
f2 (ppm)
f1 (ppm)


ROESY
f2 (ppm)
f1 (ppm)

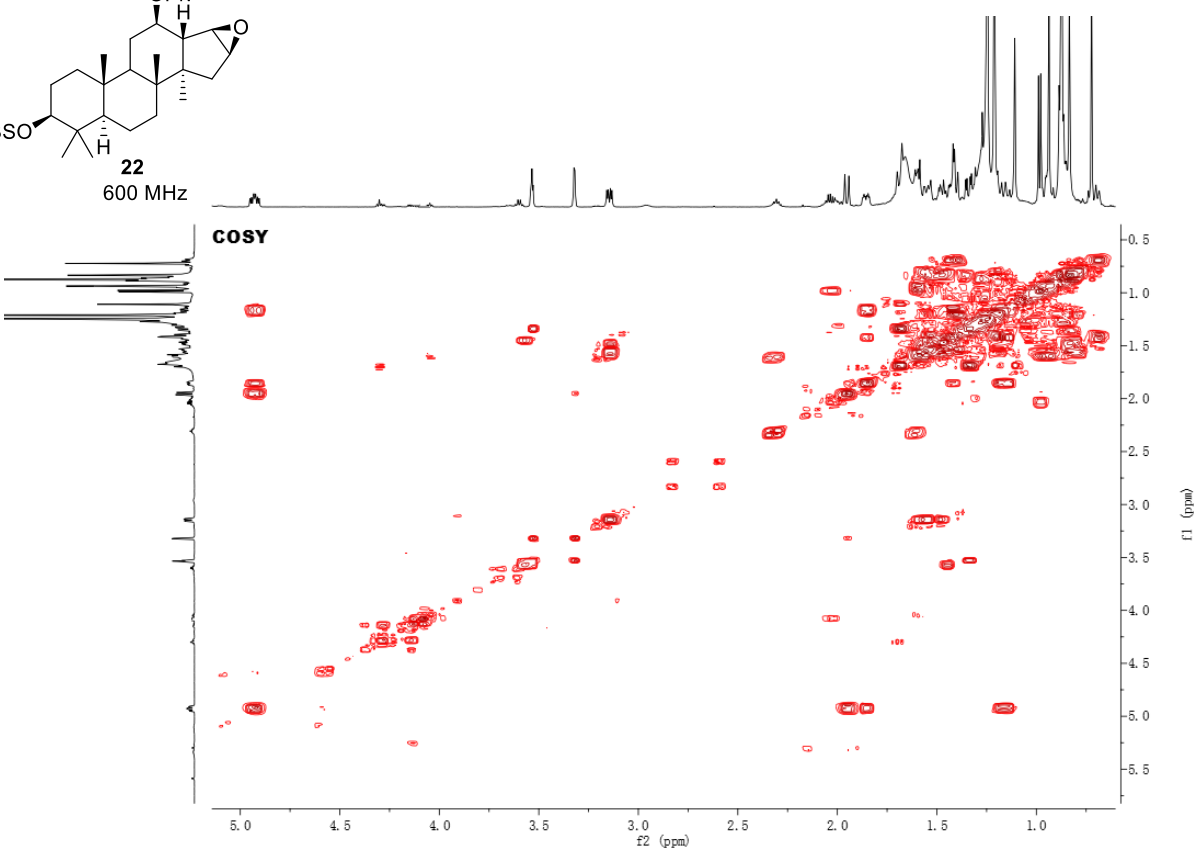

OPiv
H
O
TBSO
H
22
600 MHz
7.26
4.95
4.94
4.93
4.92
4.91
4.90
3.54
3.53
3.53
3.32
3.32
3.16
3.15
3.14
3.13
1.68
1.66
1.61
1.59
1.59
1.42
1.41
1.25
1.21
1.11
0.99
0.98
0.94
0.89
0.87
0.83
0.02
0.02
1.13
1.13
1.11
1.15
1.57
1.33
1.35
16.44
2.44
4.77
2.71
9.05
11.13
3.34
3.45
12.12
3.60
3.38
1.28
6.83
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
ppm

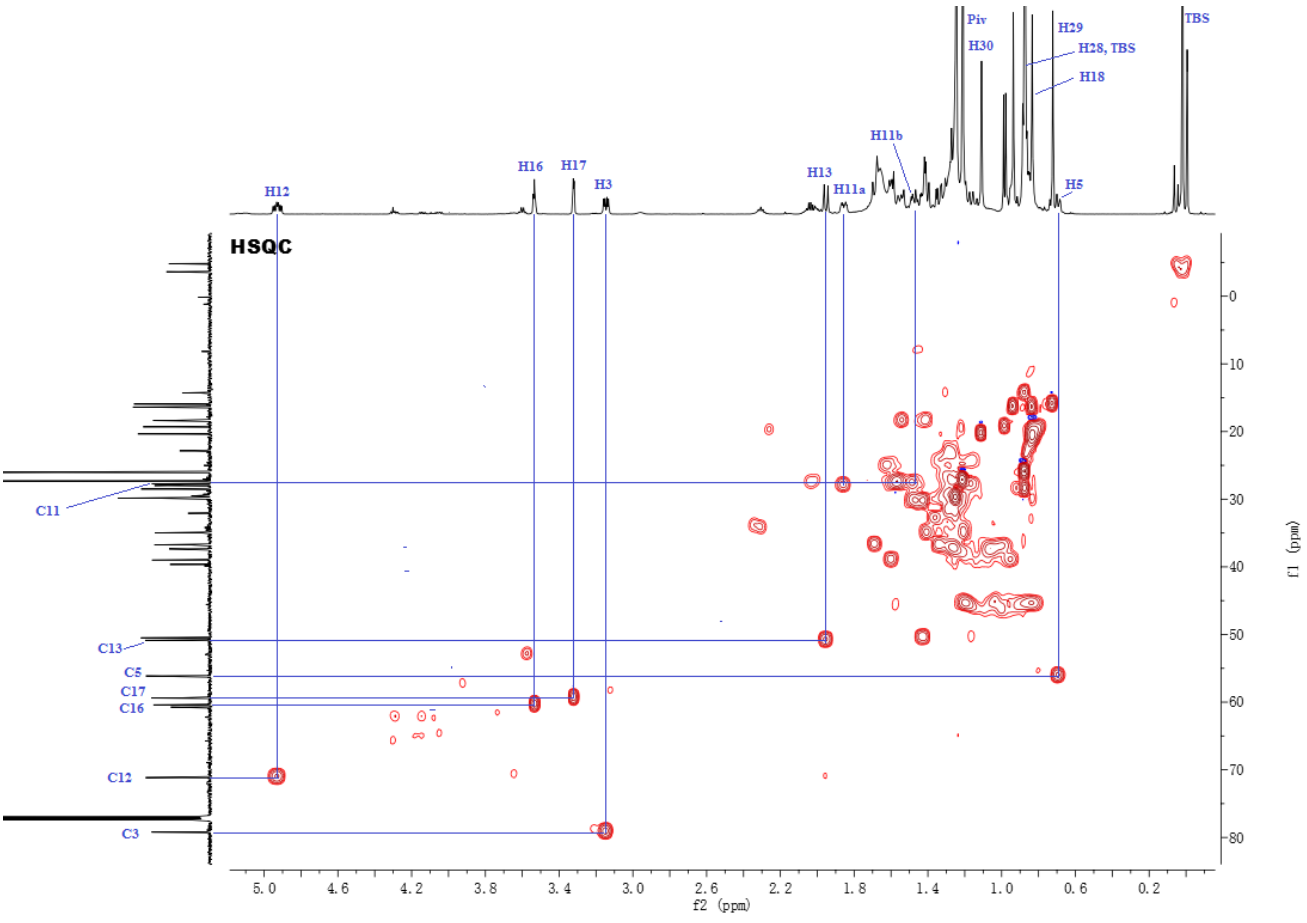

178.9
79.2
71.9
71.1
60.7
60.4
59.4
56.1
50.9
50.5
39.0
36.8
29.9
28.5
27.7
27.3
26.0
20.4
19.3
18.4
16.4
16.3
15.9
-3.6
-4.8
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
ppm

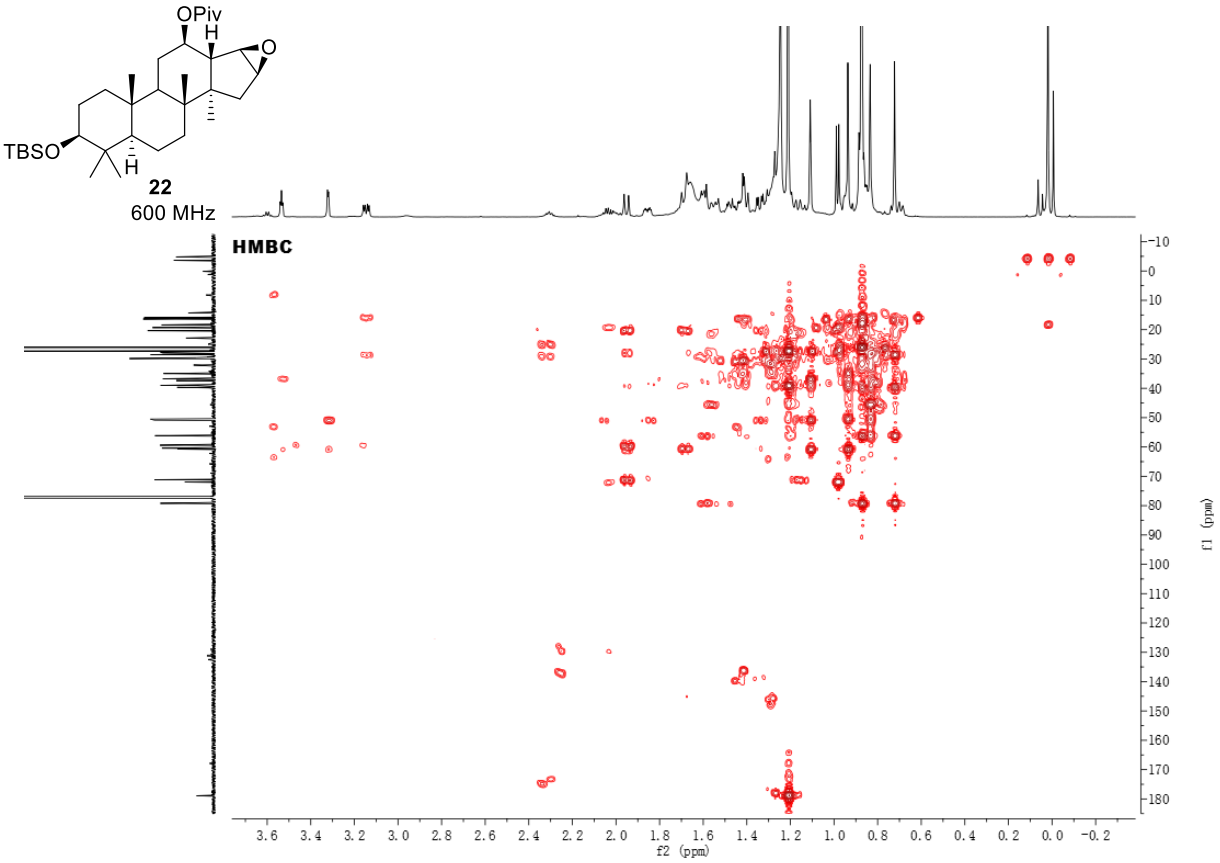

OPiv
H
O
TBSO
H

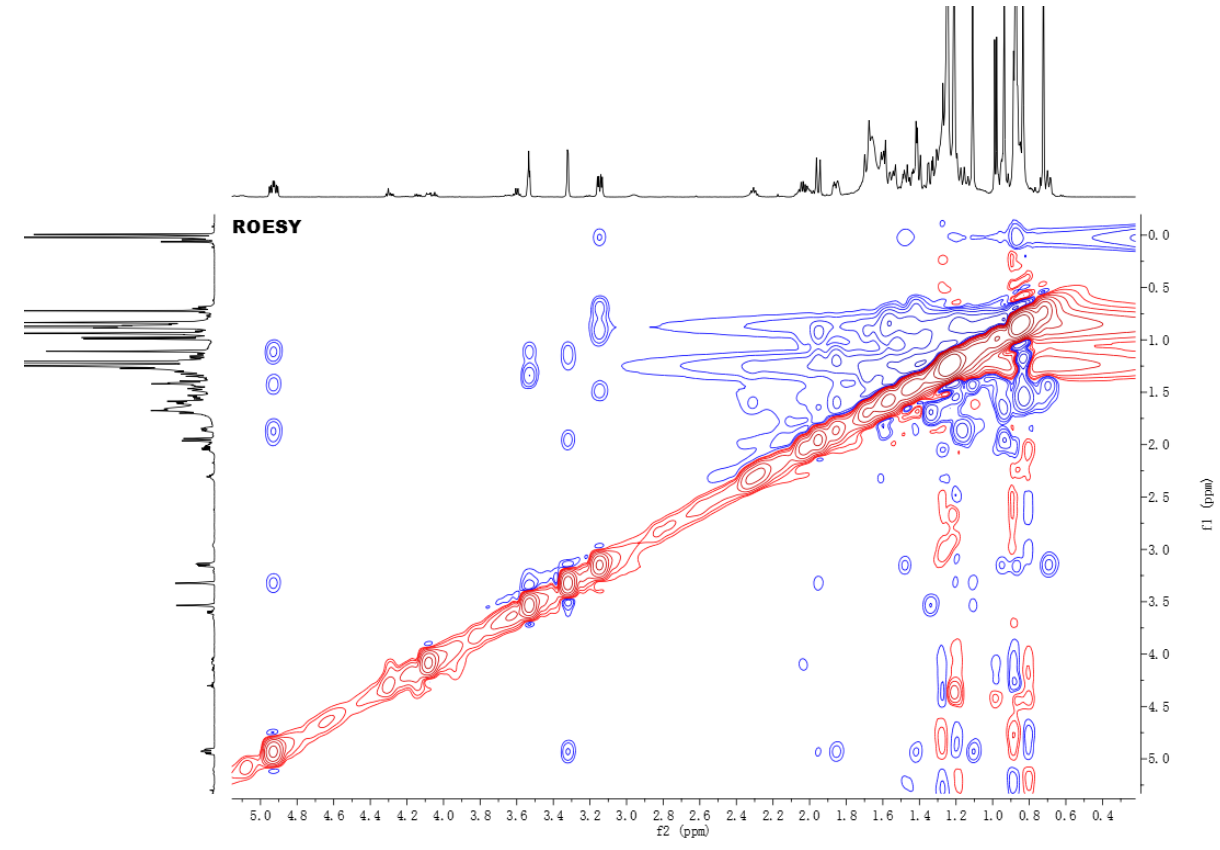
22

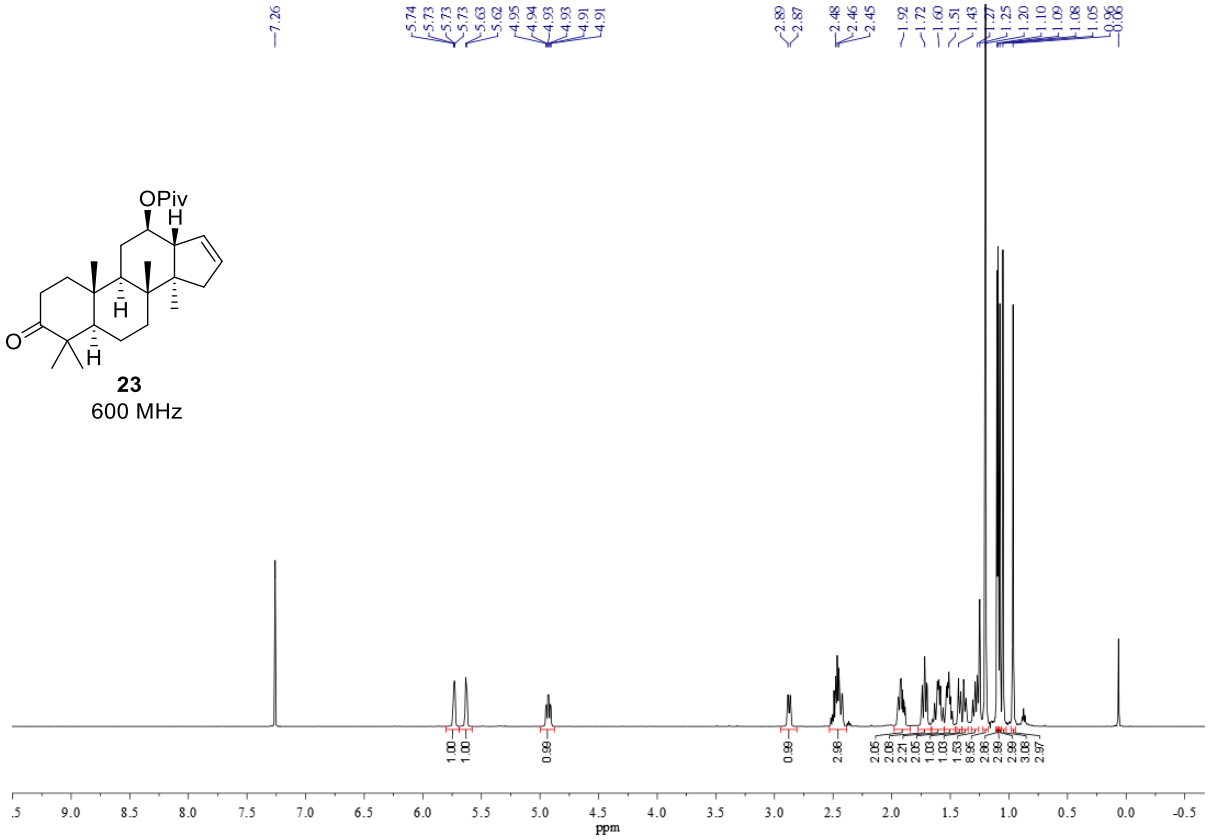
600 MHz

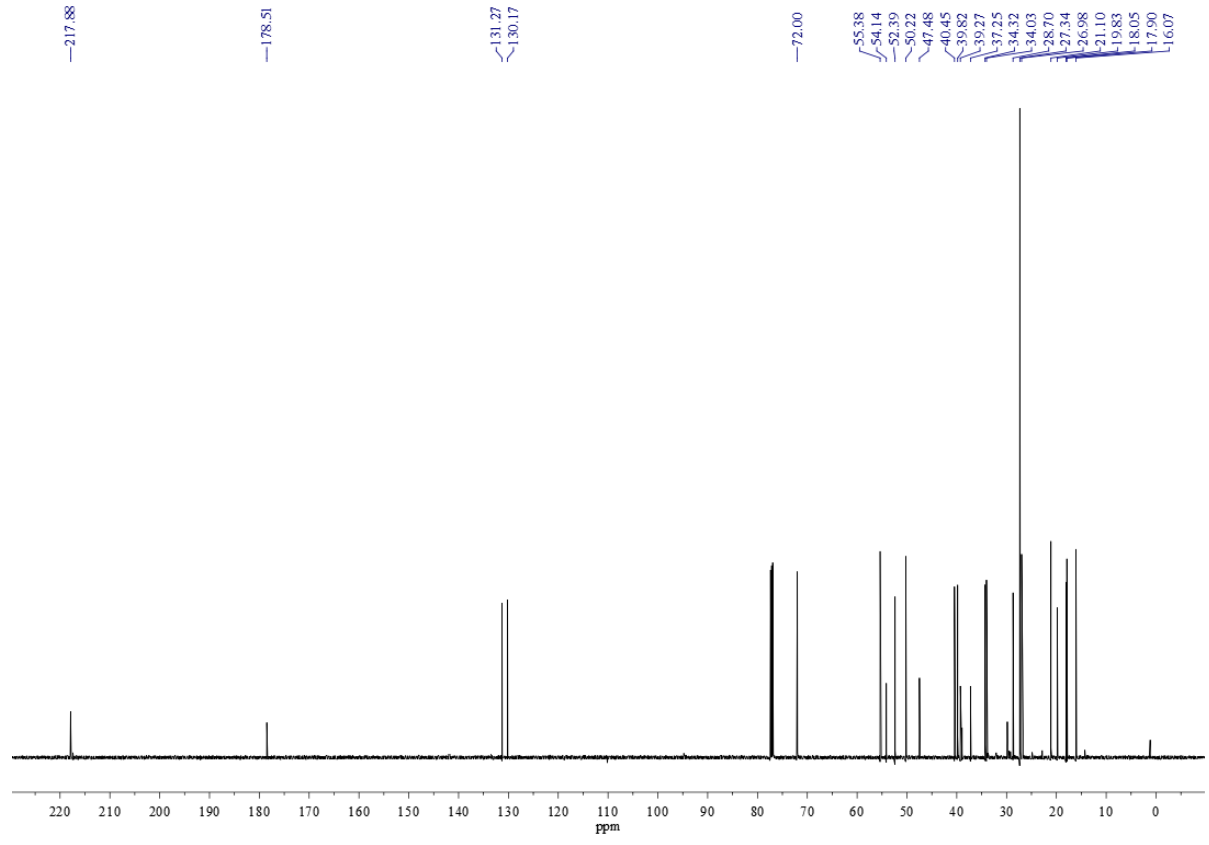

COSY
f2 (ppm)
f1 (ppm)

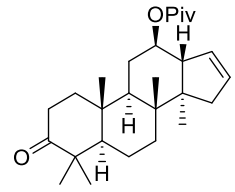

Piv
H30
H29
H28, TBS
H18
TBS
H11b
H16
H17
H12
H3
H13
H11a
H5
HSQC
C11
C13
C5
C17
C16
C12
C3
f2 (ppm)
f1 (ppm)


OPiv
H
O
TBSO
H
22
600 MHz
HMBC
f2 (ppm)
f1 (ppm)


ROESY
f2 (ppm)
f1 (ppm)

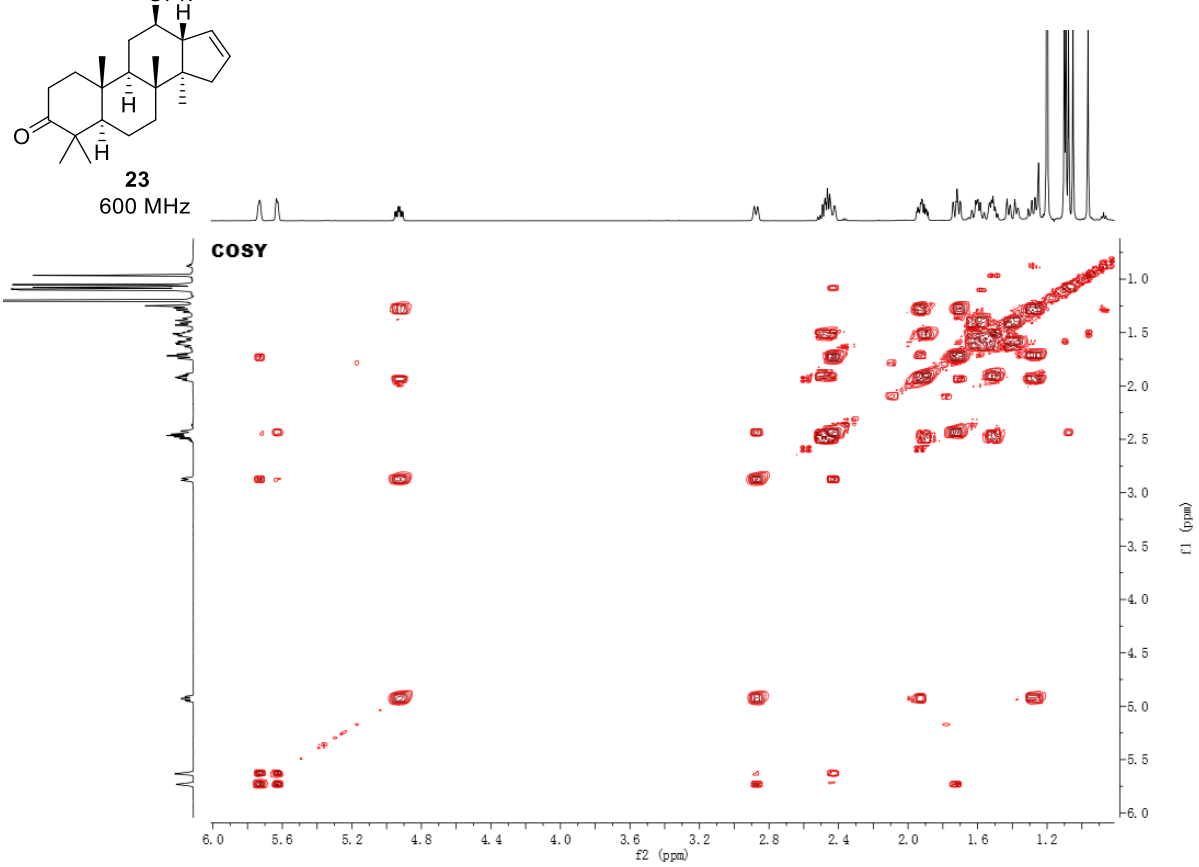

OPiv
H
H
H
O
23
600 MHz
ppm

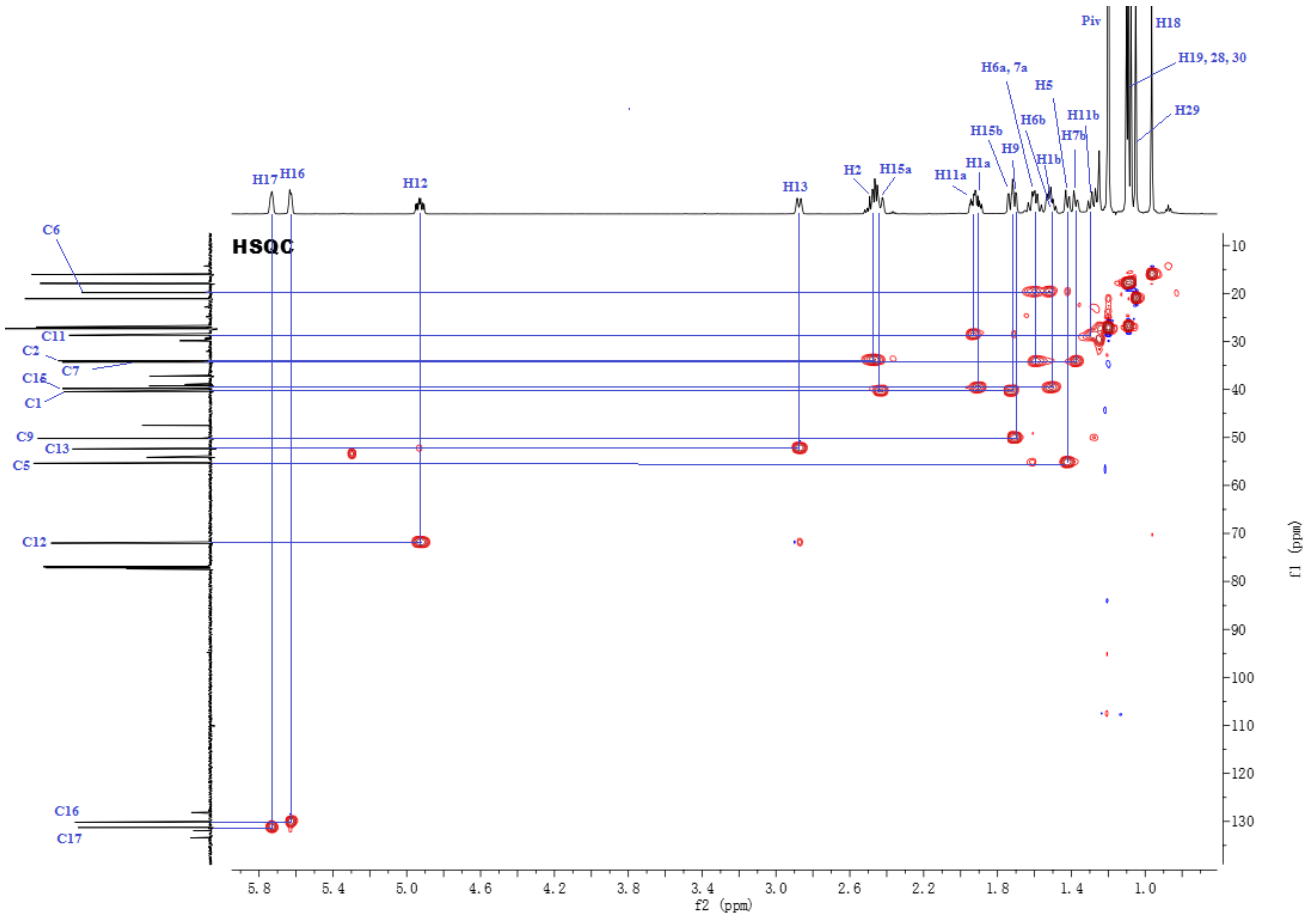

ppm

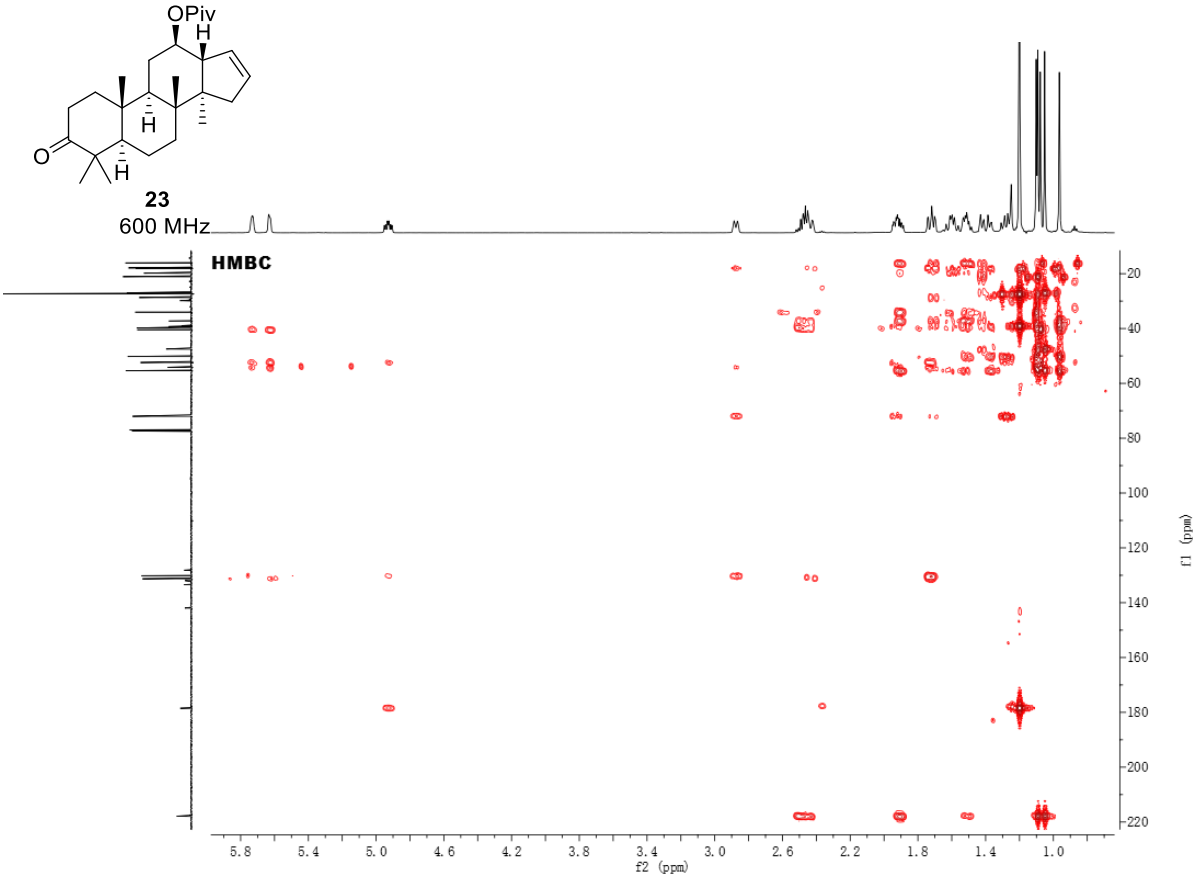

OPiv
H
H
O
H

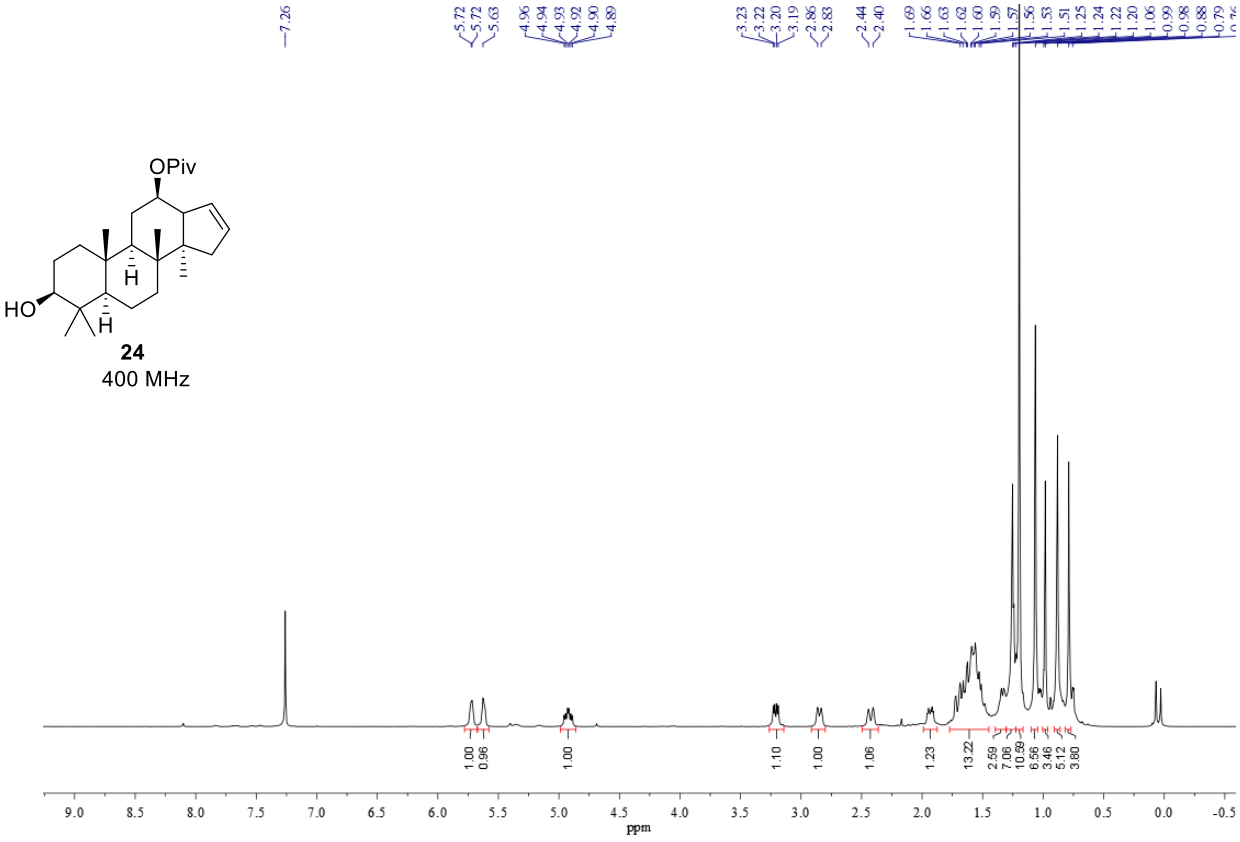
23

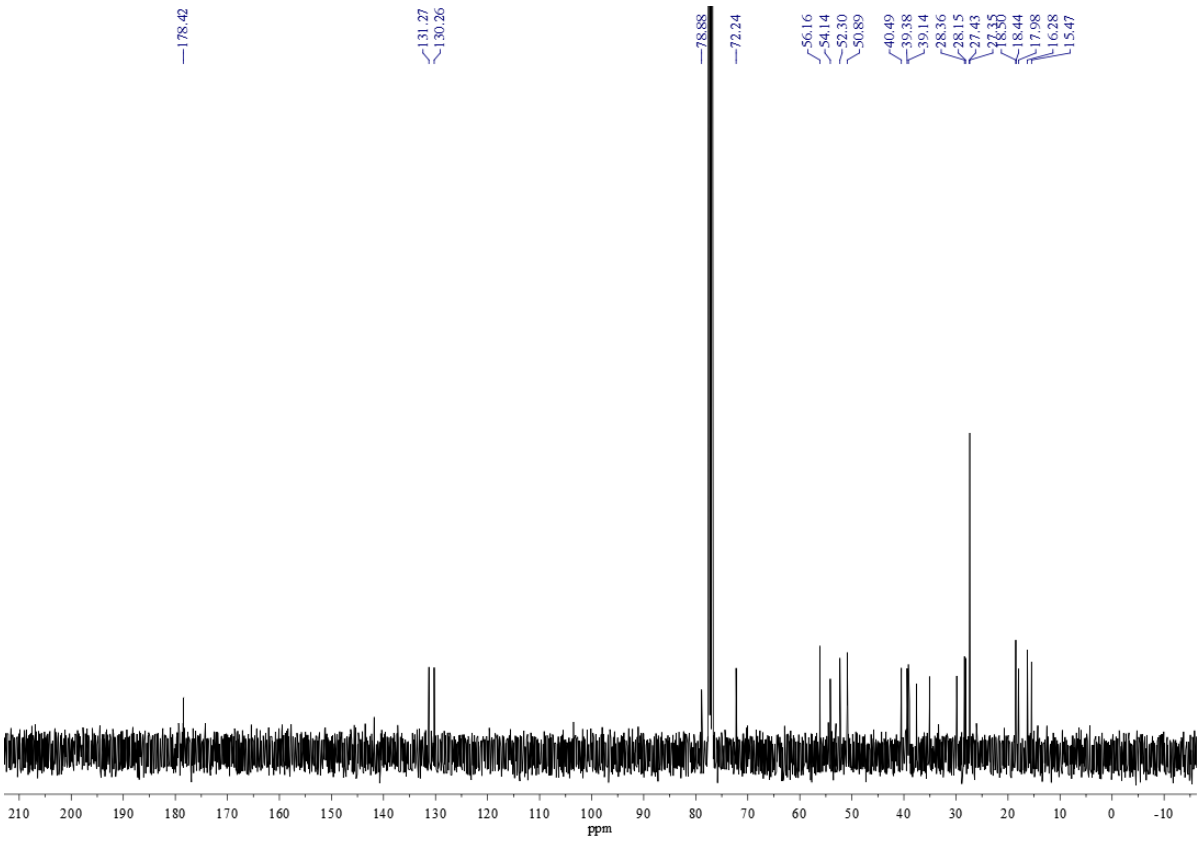
600 MHz

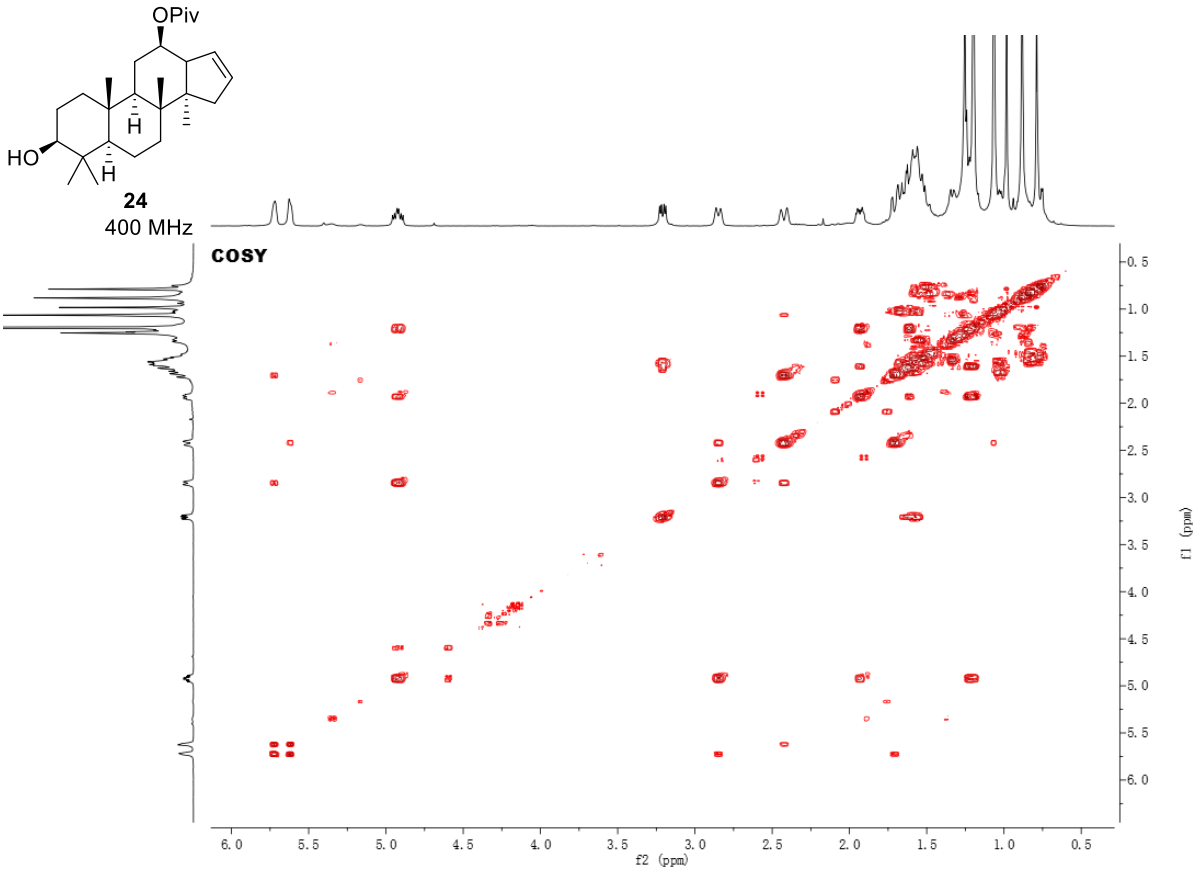

COSY
f2 (ppm)
f1 (ppm)

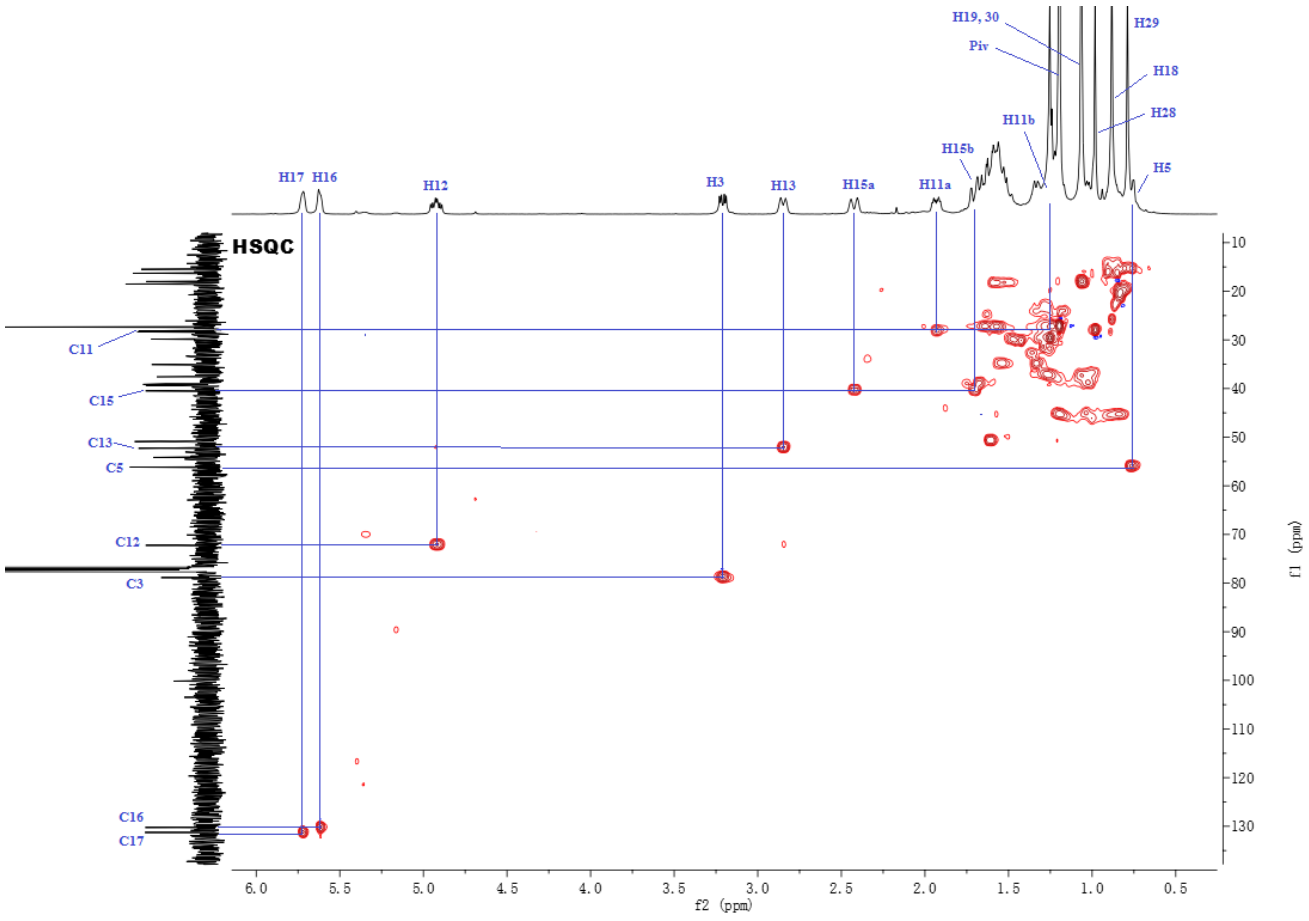

HSQC
Piv
H18
H19, 28, 30
H29
H6a, 7a
H5
H6b
H11b
H15b
H7b
H9
H1b
H1a
H11a
H2
H15a
H13
H12
H17
H16
C6
C11
C2
C7
C15
C1
C9
C13
C5
C12
C16
C17
f2 (ppm)
f1 (ppm)

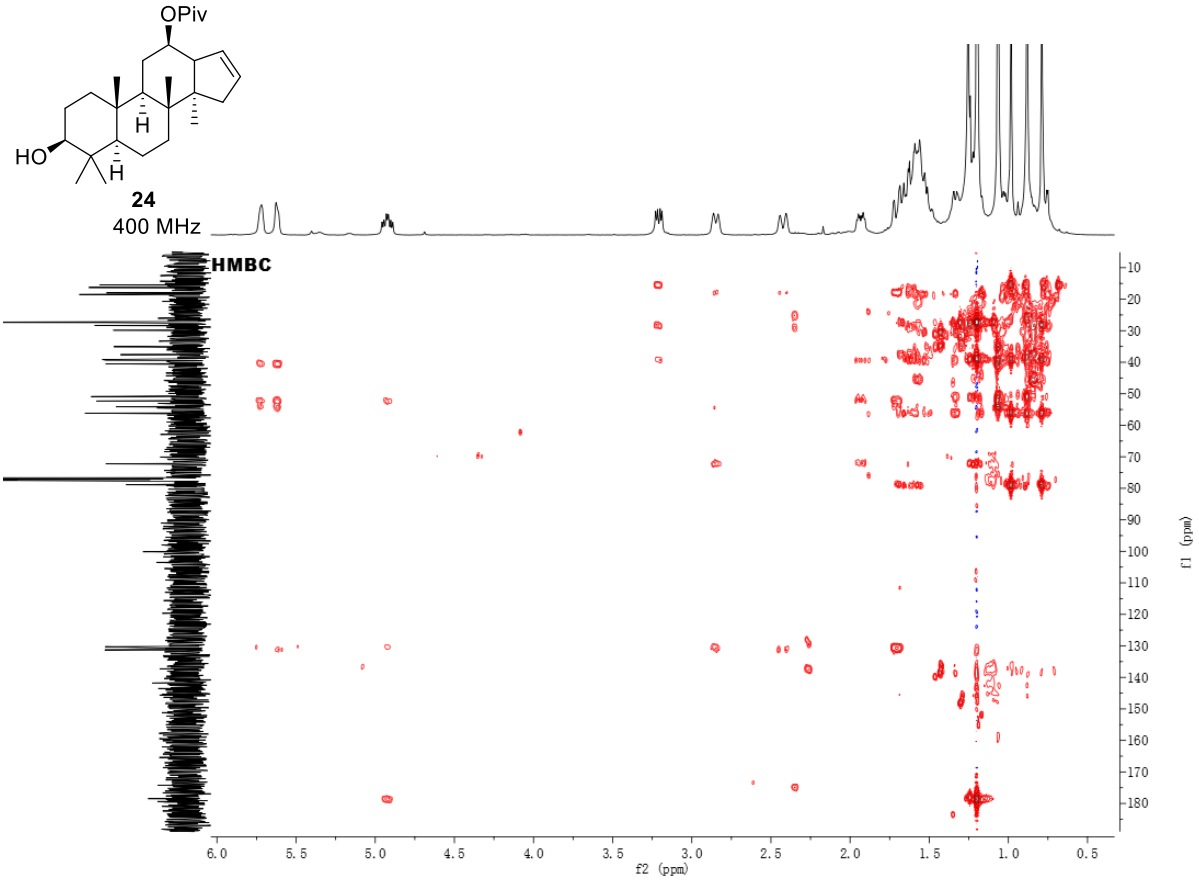

OPiv
H
H
O
H
23
600 MHz
HMBC
20
40
60
80
100
120
140
160
180
200
220
f1 (ppm)
5.8
5.4
5.0
4.6
4.2
3.8
3.4
3.0
2.6
2.2
1.8
1.4
1.0
f2 (ppm)

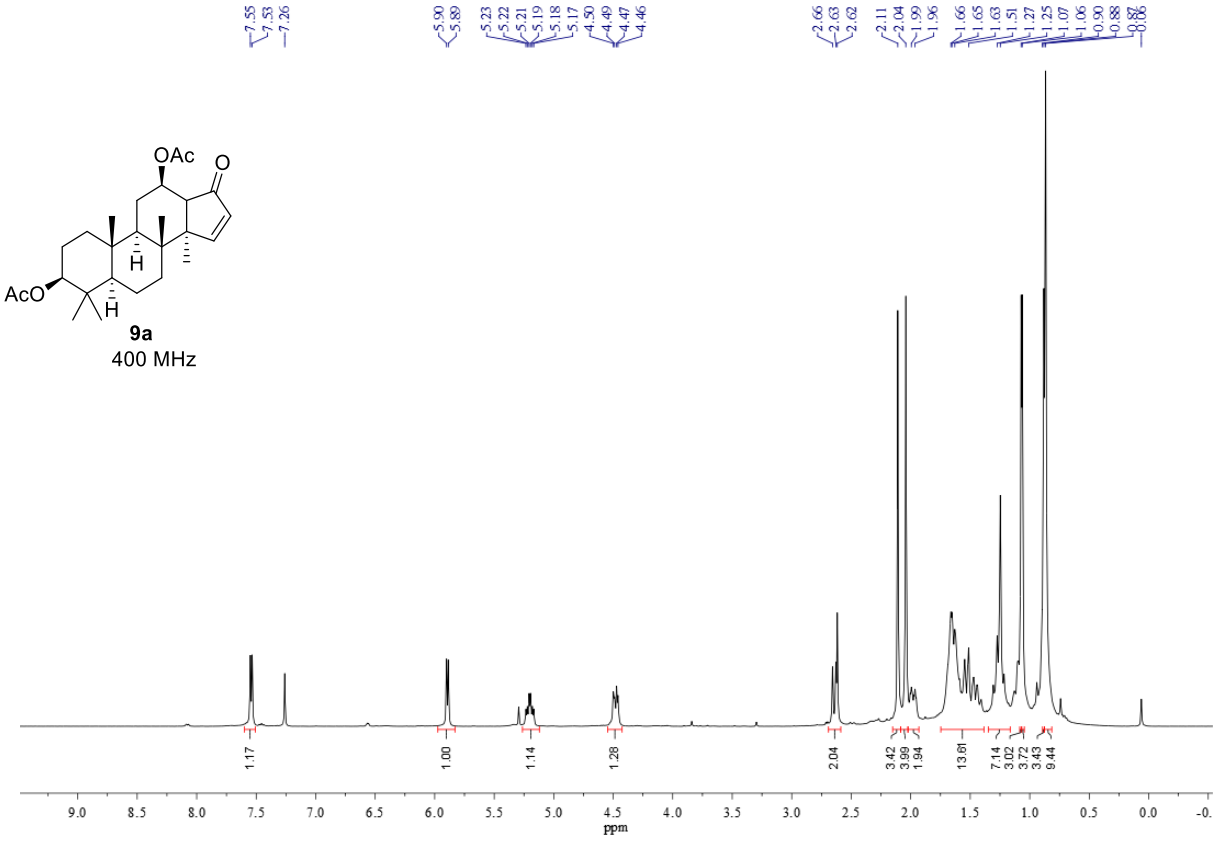

OPiv
HO
H
H
24
400 MHz
ppm

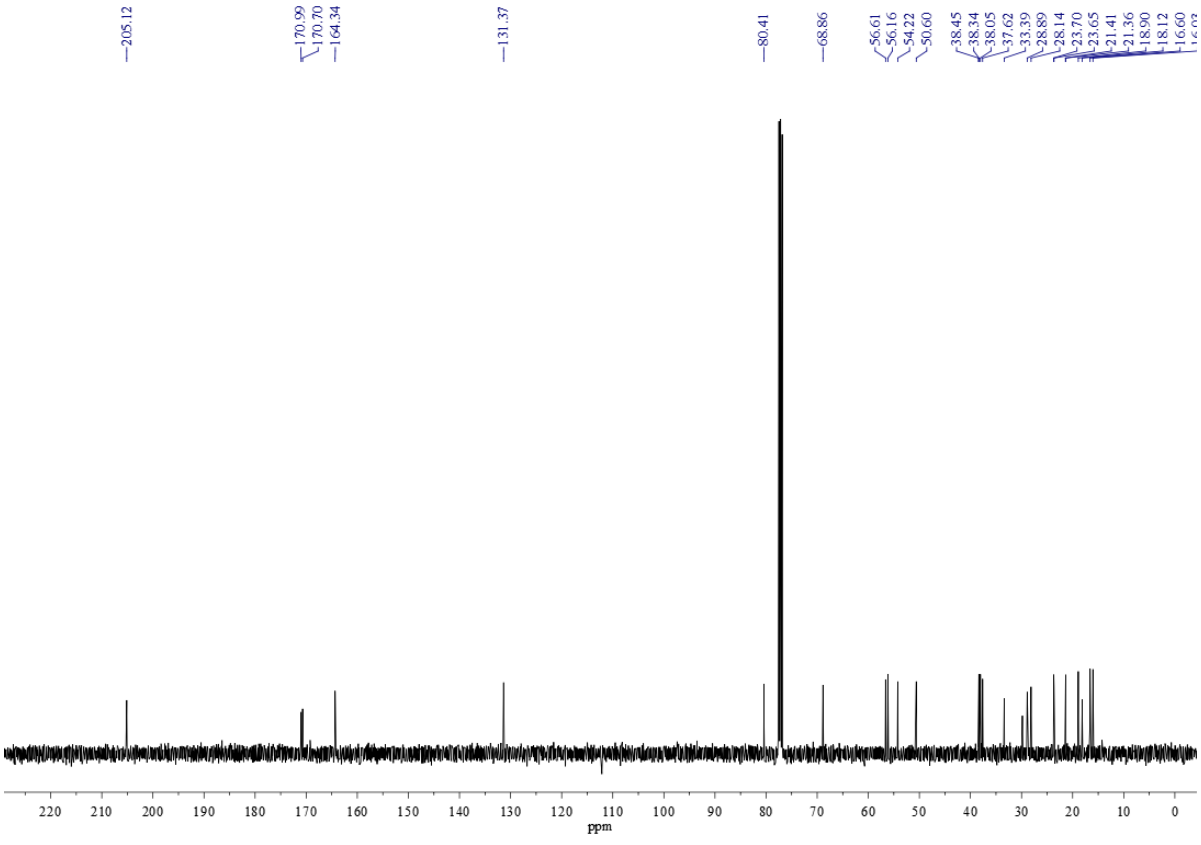

ppm

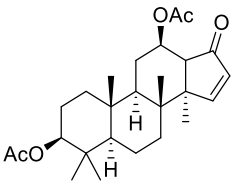

OPiv
HO
H
H
24
400 MHz
COSY
f2 (ppm)
f1 (ppm)


H19, 30
Piv
H29
H18
H28
H11b
H15b
H5
H17
H16
H12
H3
H13
H15a
H11a
HSQC
C11
C15
C13
C5
C12
C3
C16
C17
f2 (ppm)
f1 (ppm)


OPiv
HO
H
H
24
400 MHz
HMBC
f2 (ppm)
f1 (ppm)

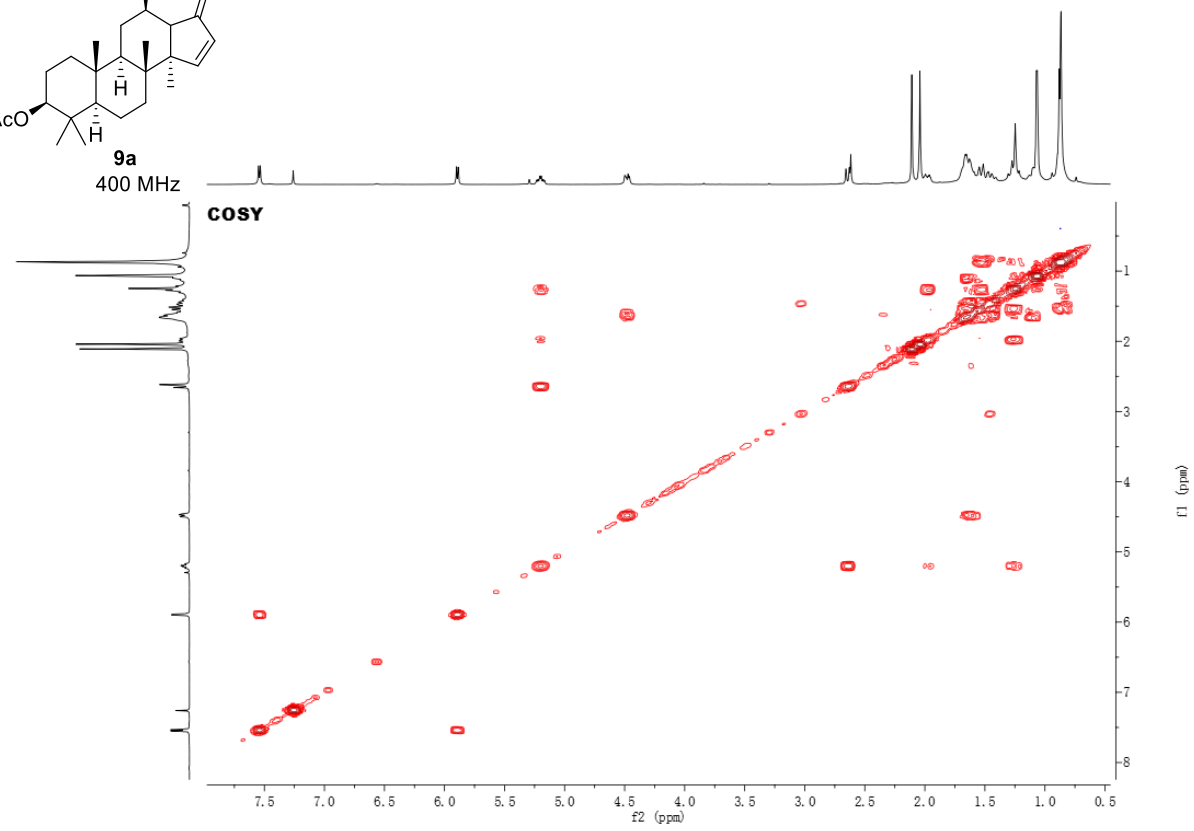

OAc
O
AcO
H
H
9a
400 MHz
7.55
7.53
7.26
5.90
5.89
5.23
5.22
5.21
5.19
5.18
5.17
4.50
4.49
4.47
4.46
2.66
2.63
2.62
2.11
2.04
1.99
1.96
1.66
1.65
1.63
1.51
1.27
1.25
1.07
1.06
0.90
0.88
0.87
0.08
1.17
1.00
1.14
1.28
2.04
3.42
3.99
1.94
13.61
7.14
3.02
3.72
3.43
9.44
ppm

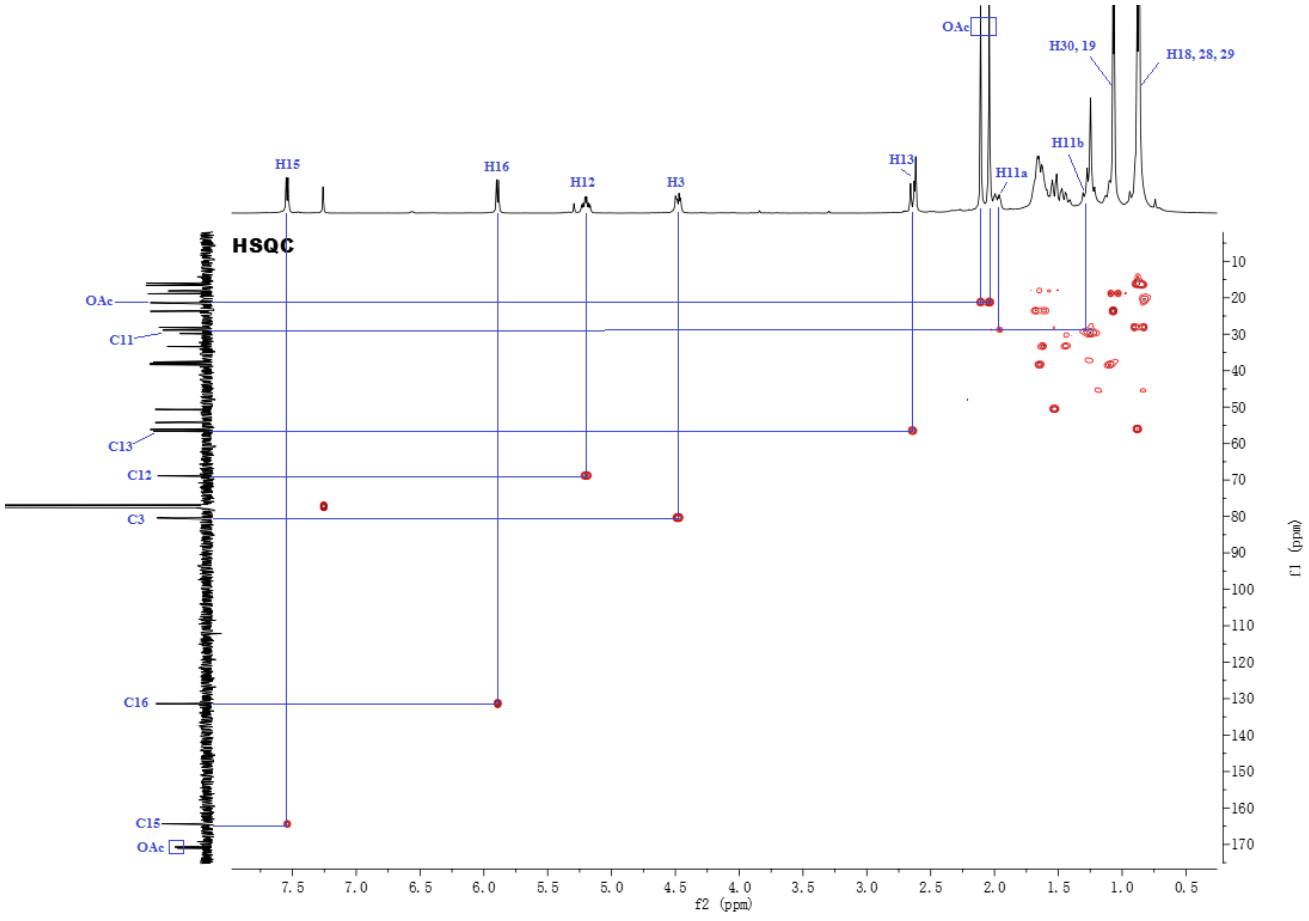

205.12
170.99
170.70
164.34
131.37
80.41
68.86
56.61
56.16
54.22
50.60
38.45
38.34
38.05
37.62
33.39
28.89
28.14
23.70
23.65
21.41
21.36
18.90
18.12
16.60
ppm

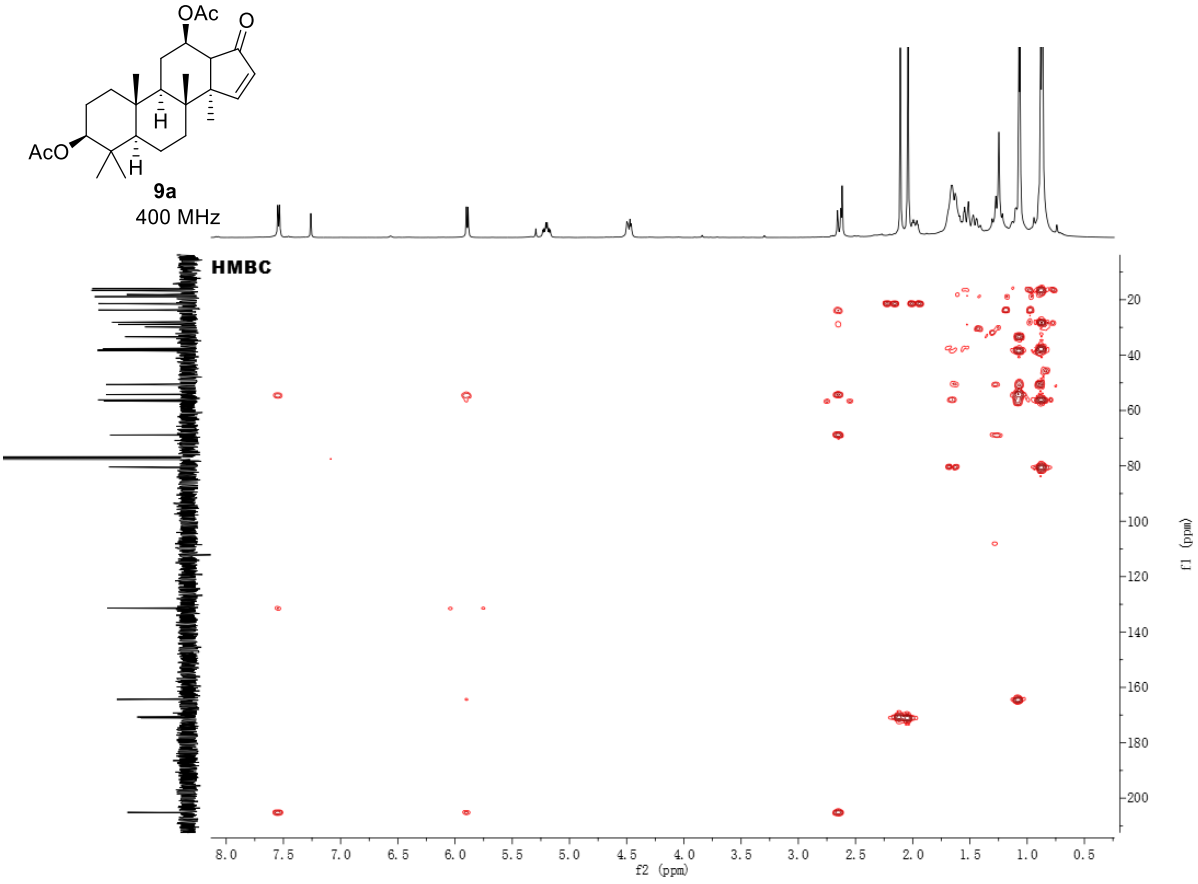

OAc
O
AcO
H
H

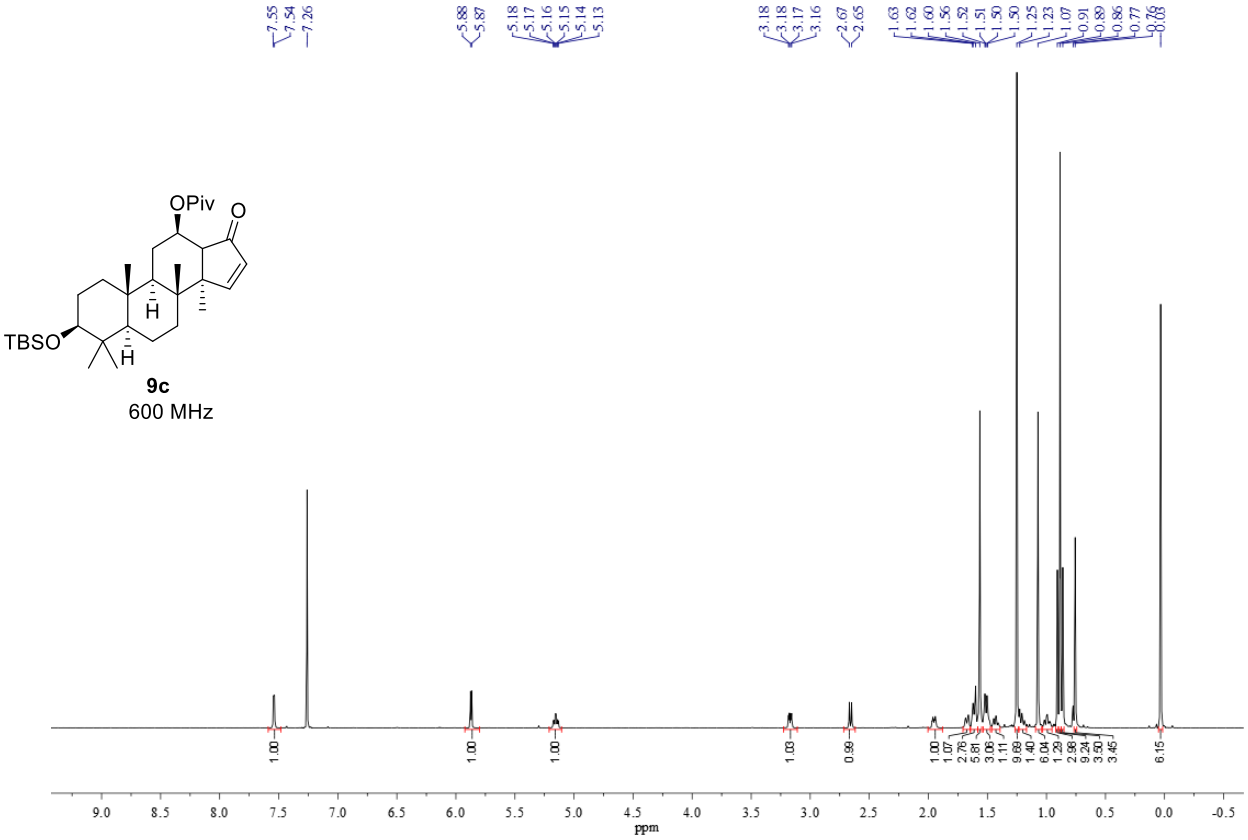
9a

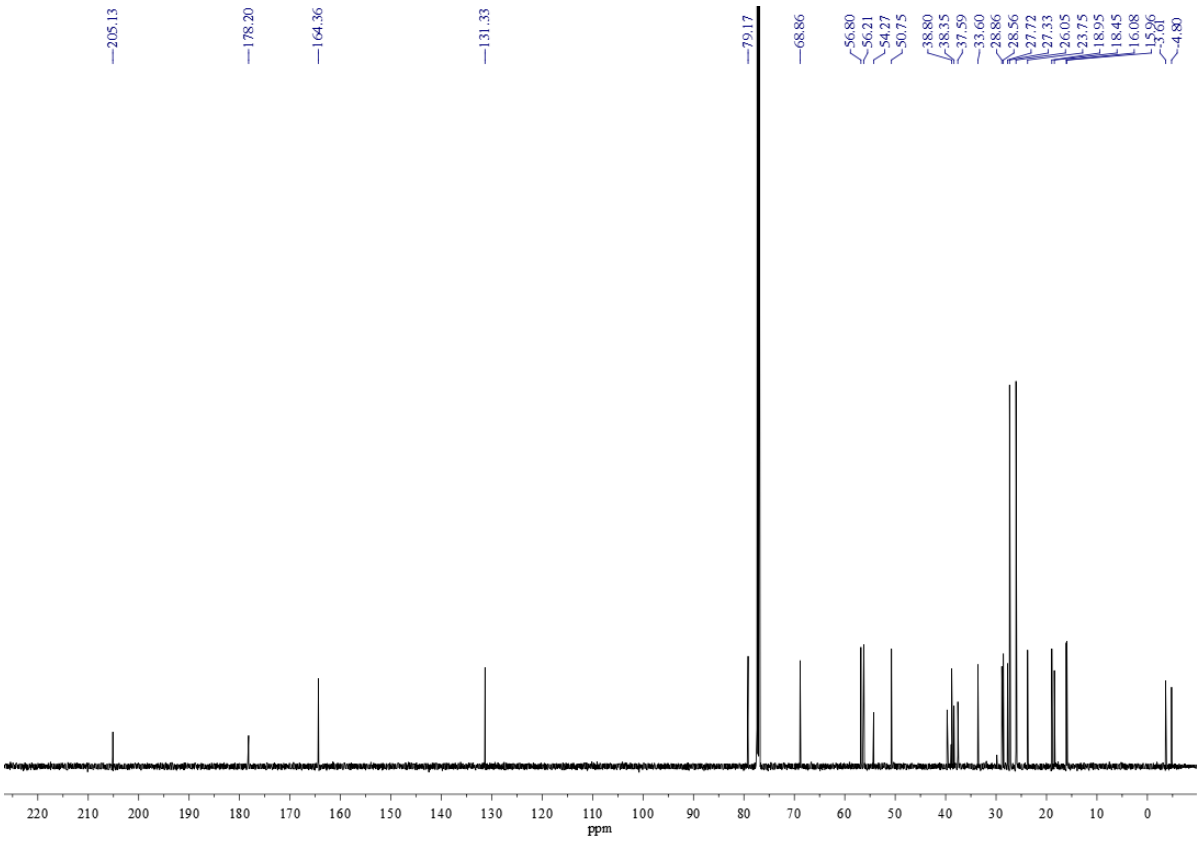
400 MHz

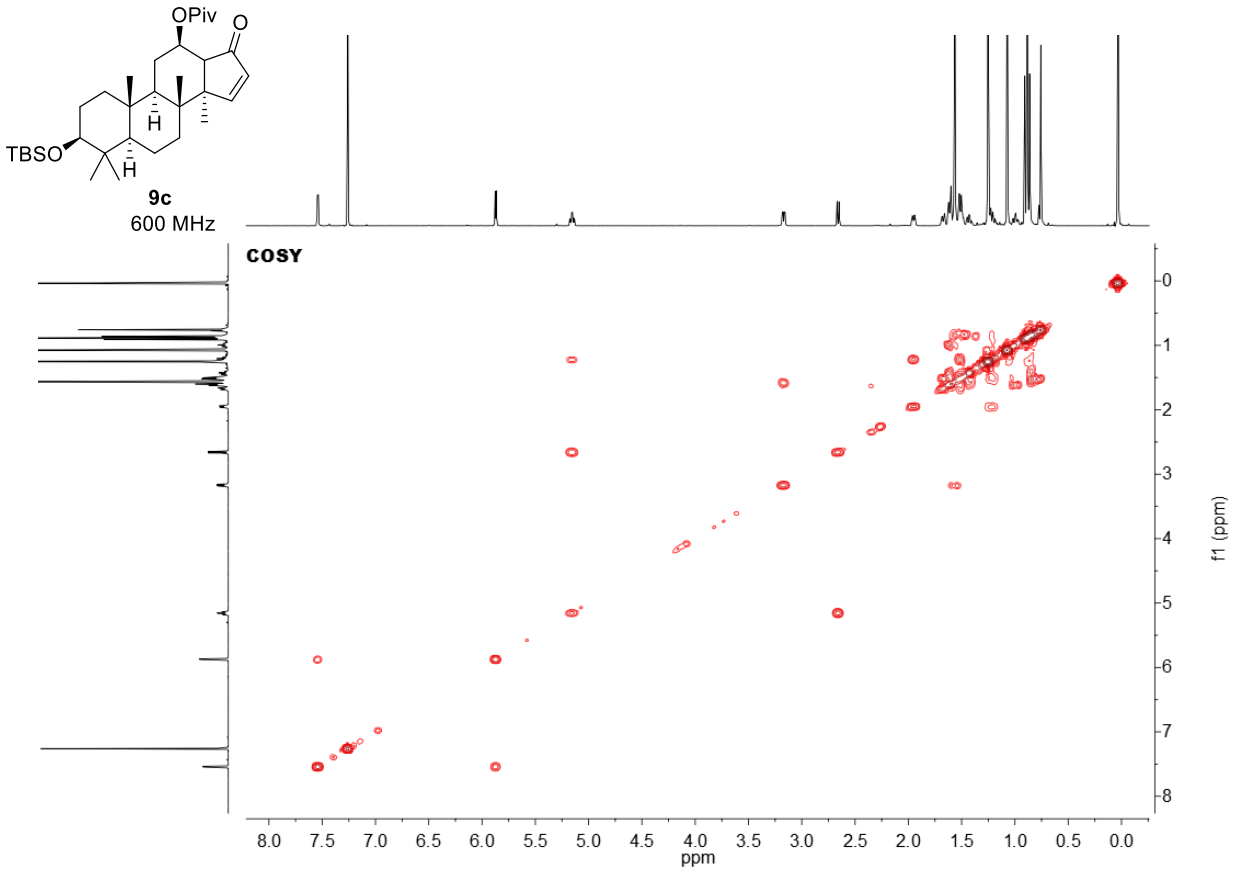

COSY
f2 (ppm)
f1 (ppm)

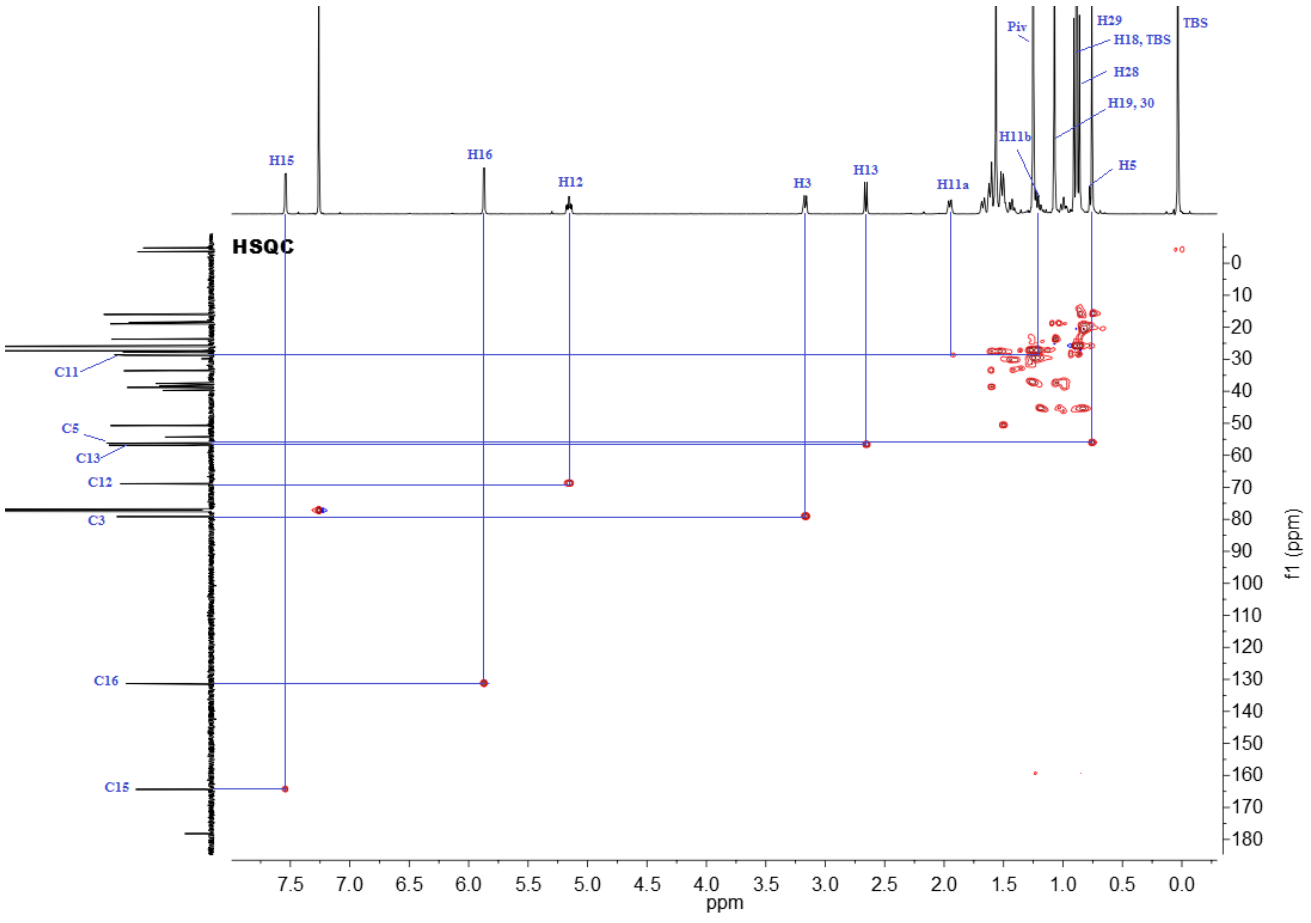

OAc
H30, 19
H18, 28, 29
H15
H16
H12
H3
H13
H11a
H11b
HSQC
OAc
C11
C13
C12
C3
C16
C15
OAc
f2 (ppm)
f1 (ppm)

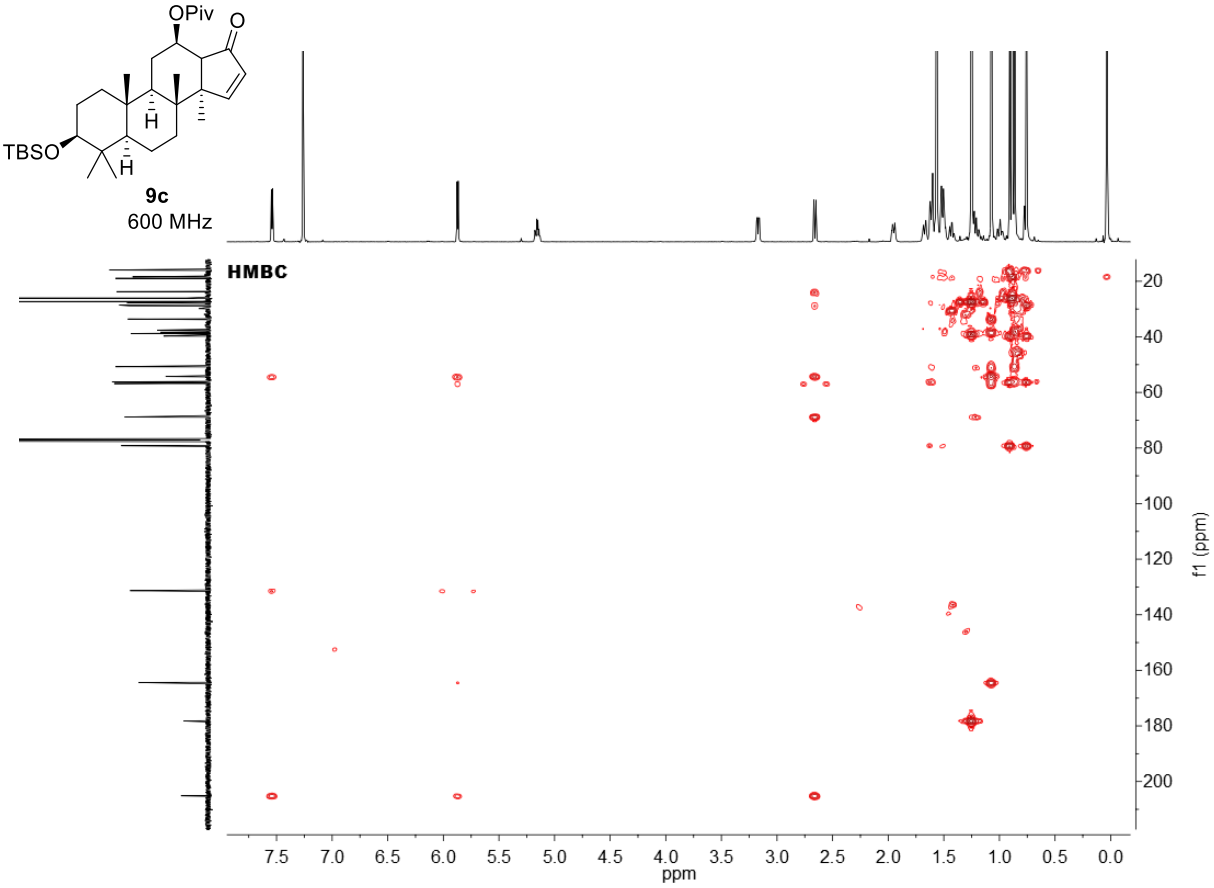

OAc
O
AcO
H
H
9a
400 MHz
HMBC
f2 (ppm)
f1 (ppm)

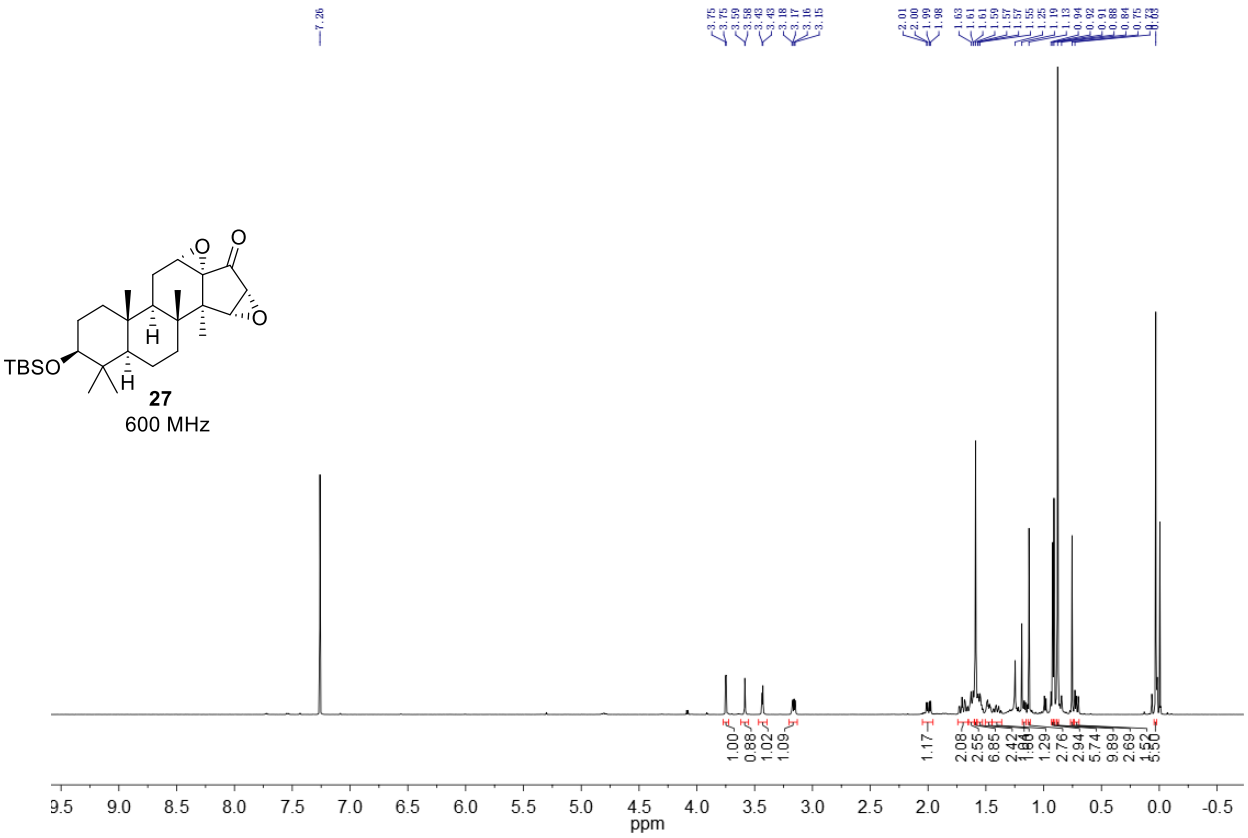

OPiv
O
TBSO
H
H
9c
600 MHz
ppm

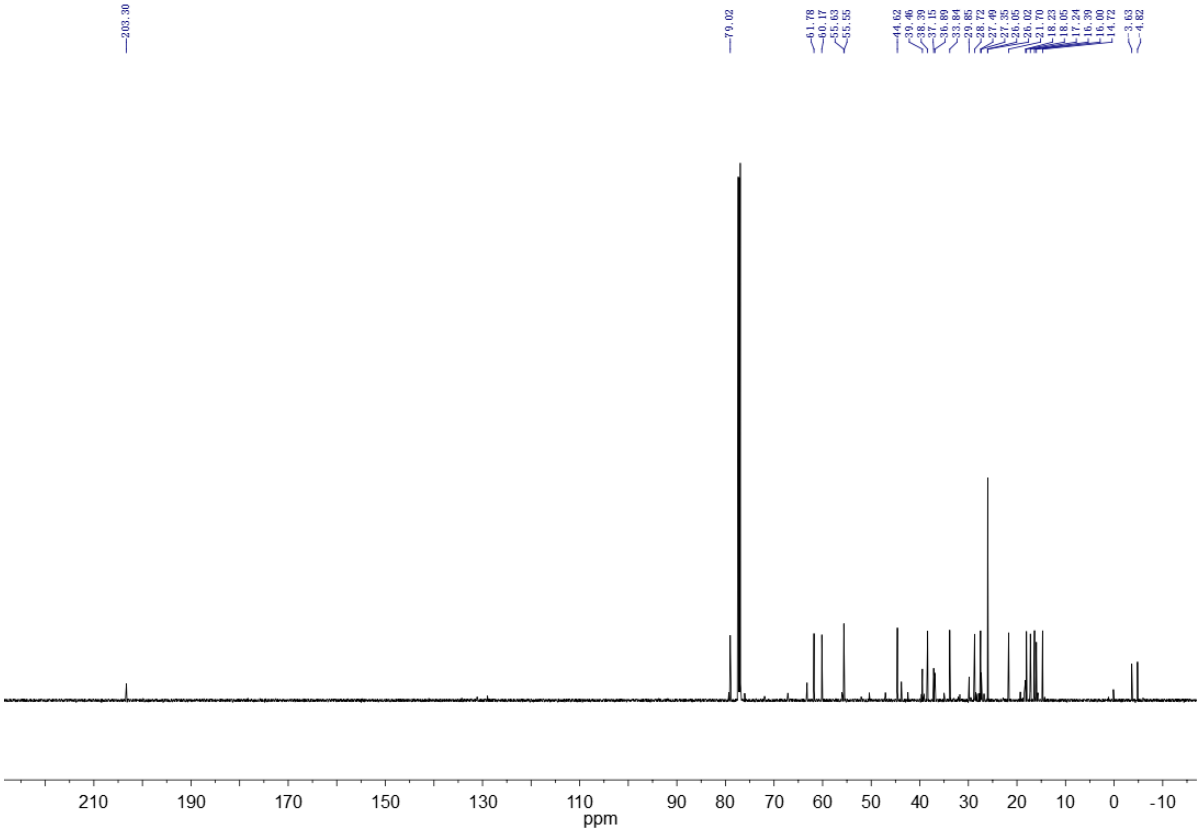

ppm

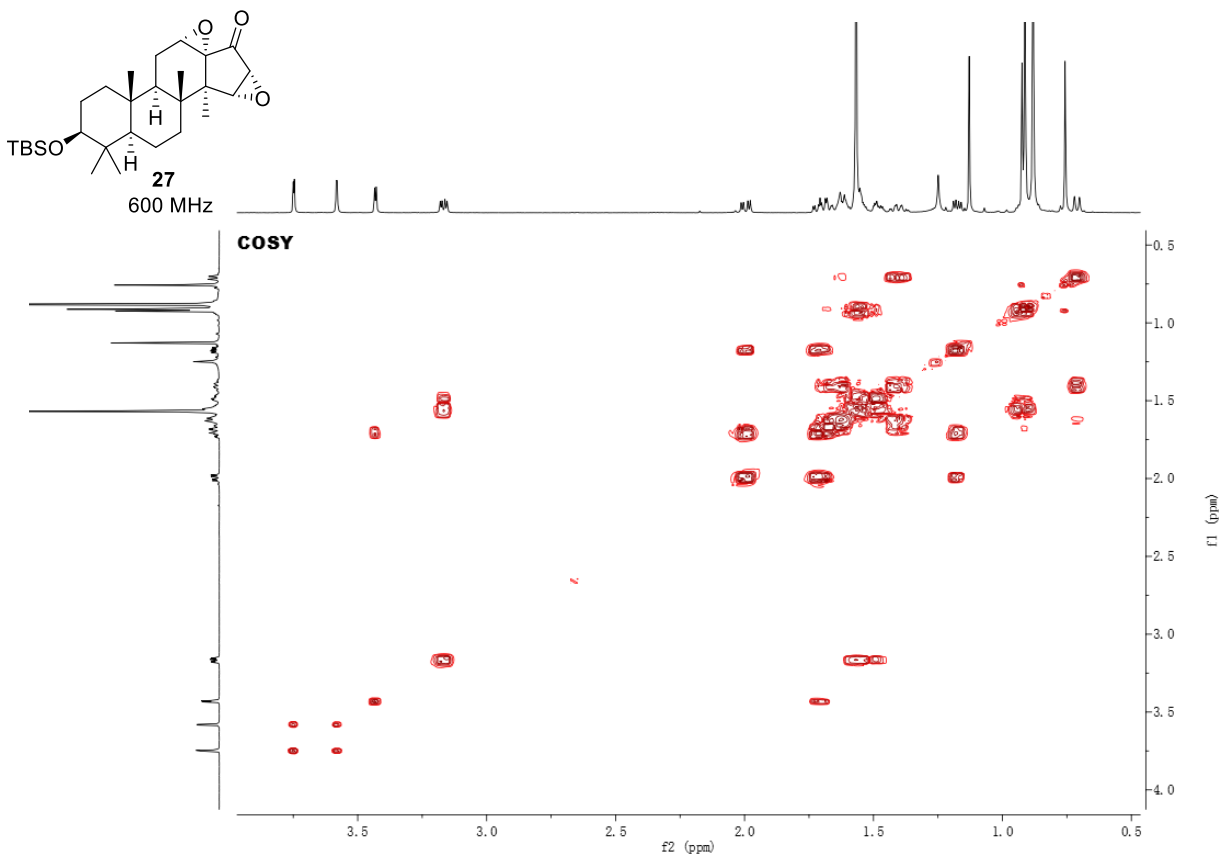

OPiv
O
TBSO
H
H
9c
600 MHz
COSY
f1 (ppm)
ppm

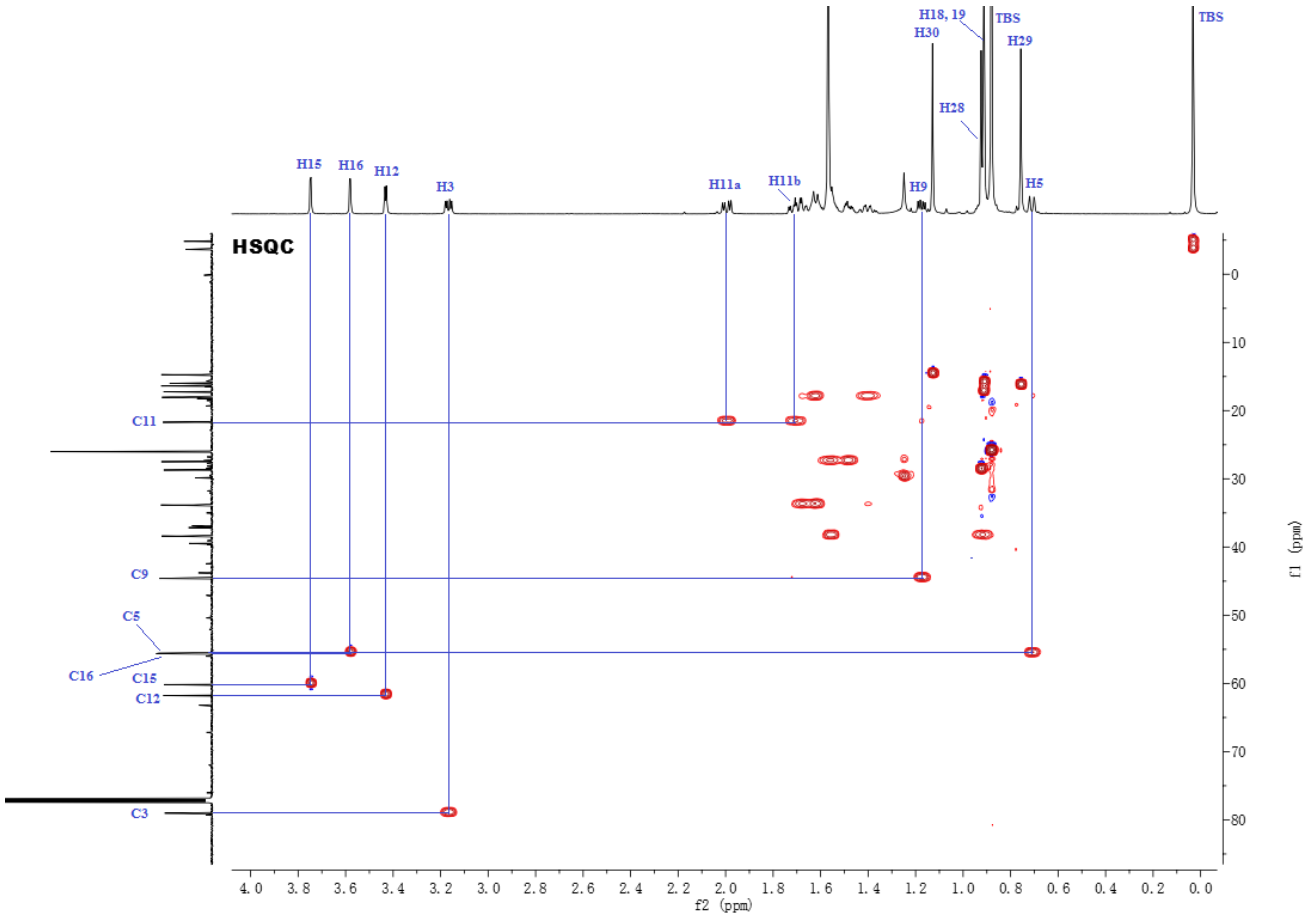

H15
H16
H12
H3
H13
H11a
H11b
Piv
H29
H18, TBS
H28
H19, 30
H5
TBS
HSQC
C11
C5
C13
C12
C3
C16
C15
f1 (ppm)
ppm

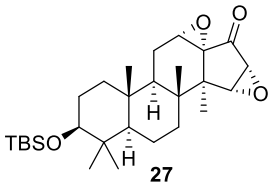

OPiv
O
TBSO
H
H
9c
600 MHz
HMBC
20
40
60
80
100
120
140
160
180
200
f1 (ppm)
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm


TBSO
O
O
O
H
H
27
600 MHz
ppm


ppm

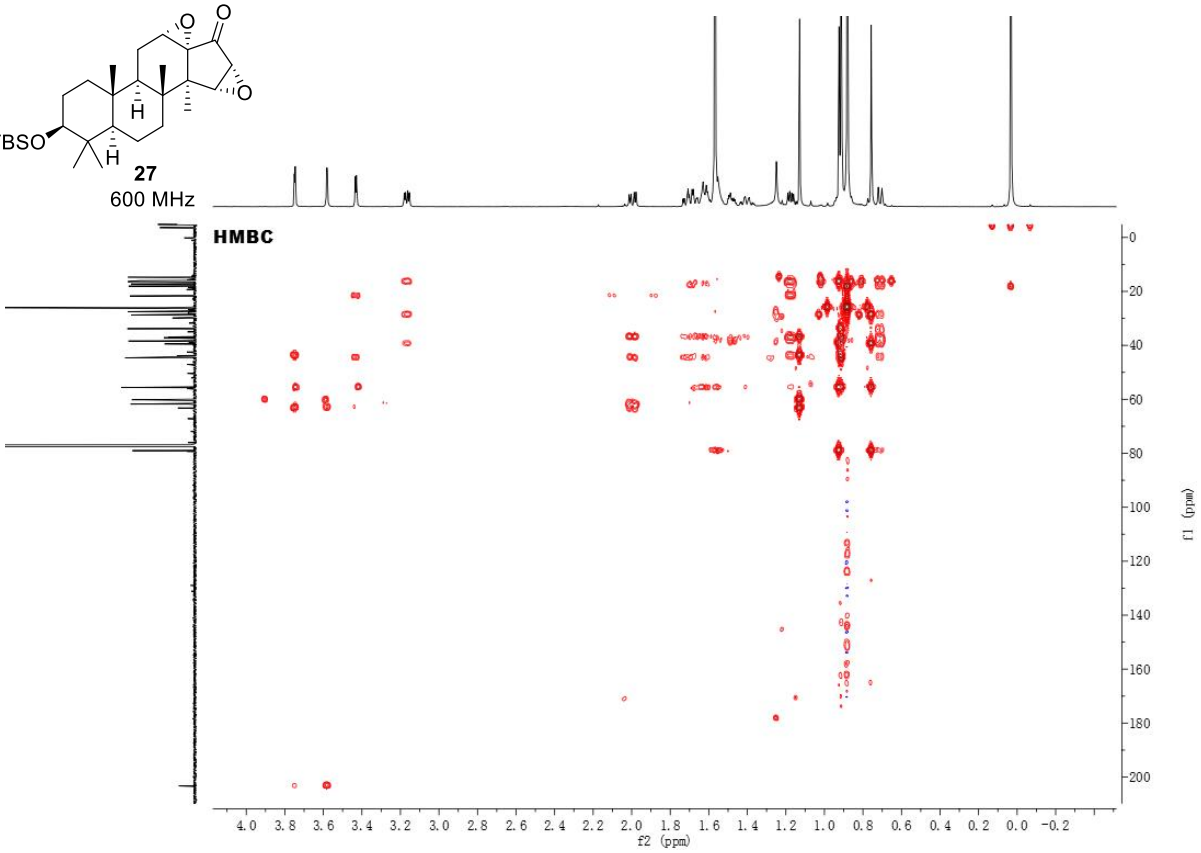

TBSO
O
O
O
H
H
27
600 MHz
COSY
f2 (ppm)
f1 (ppm)

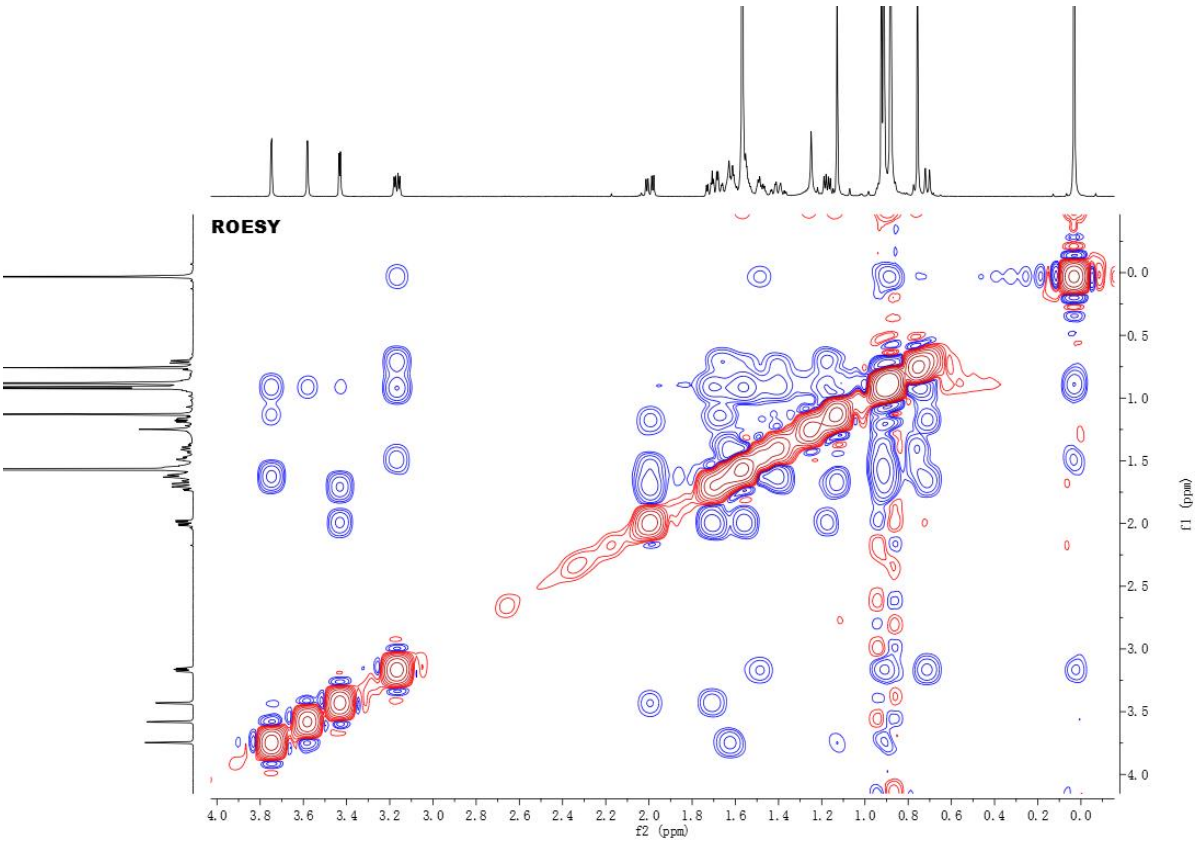

H18, 19
H30
TBS
H29
TBS
H28
H15
H16
H12
H3
H11a
H11b
H9
H5
HSQC
C11
C9
C5
C16
C15
C12
C3
f2 (ppm)
f1 (ppm)

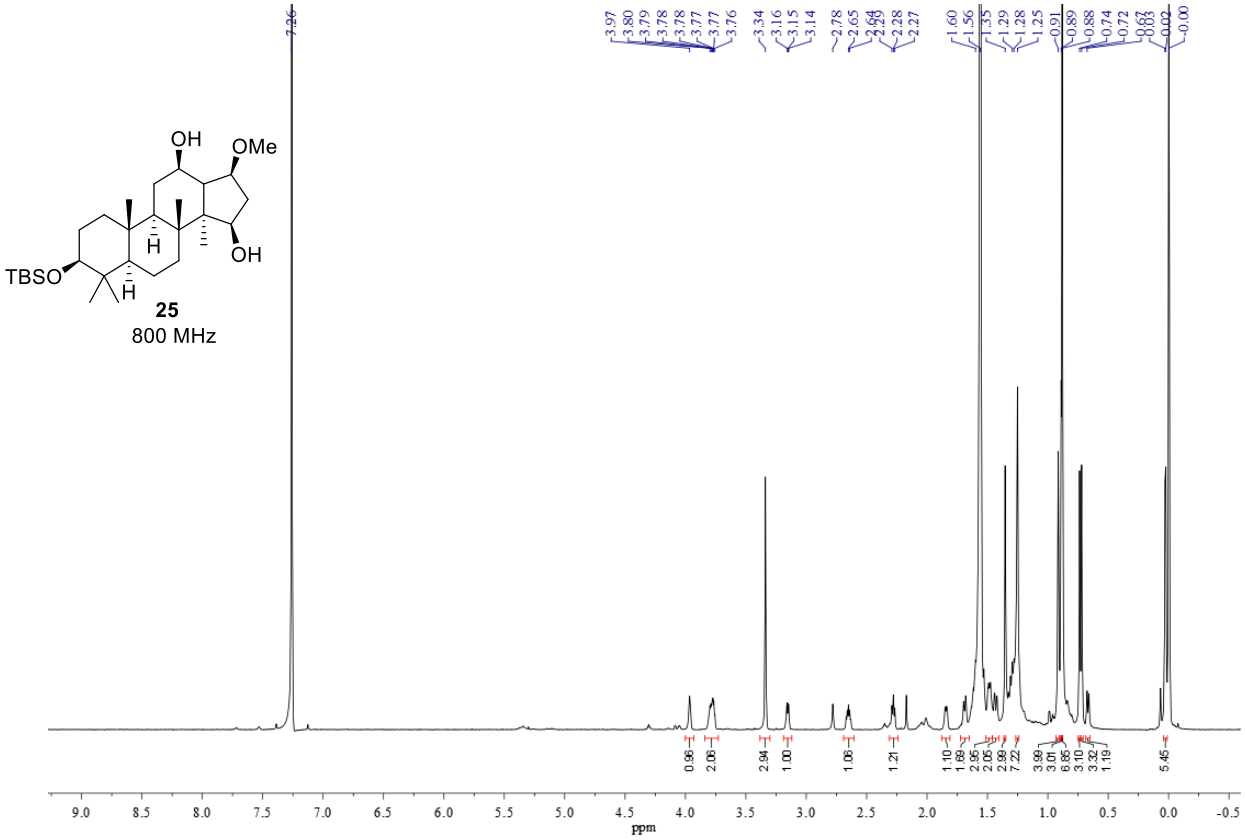


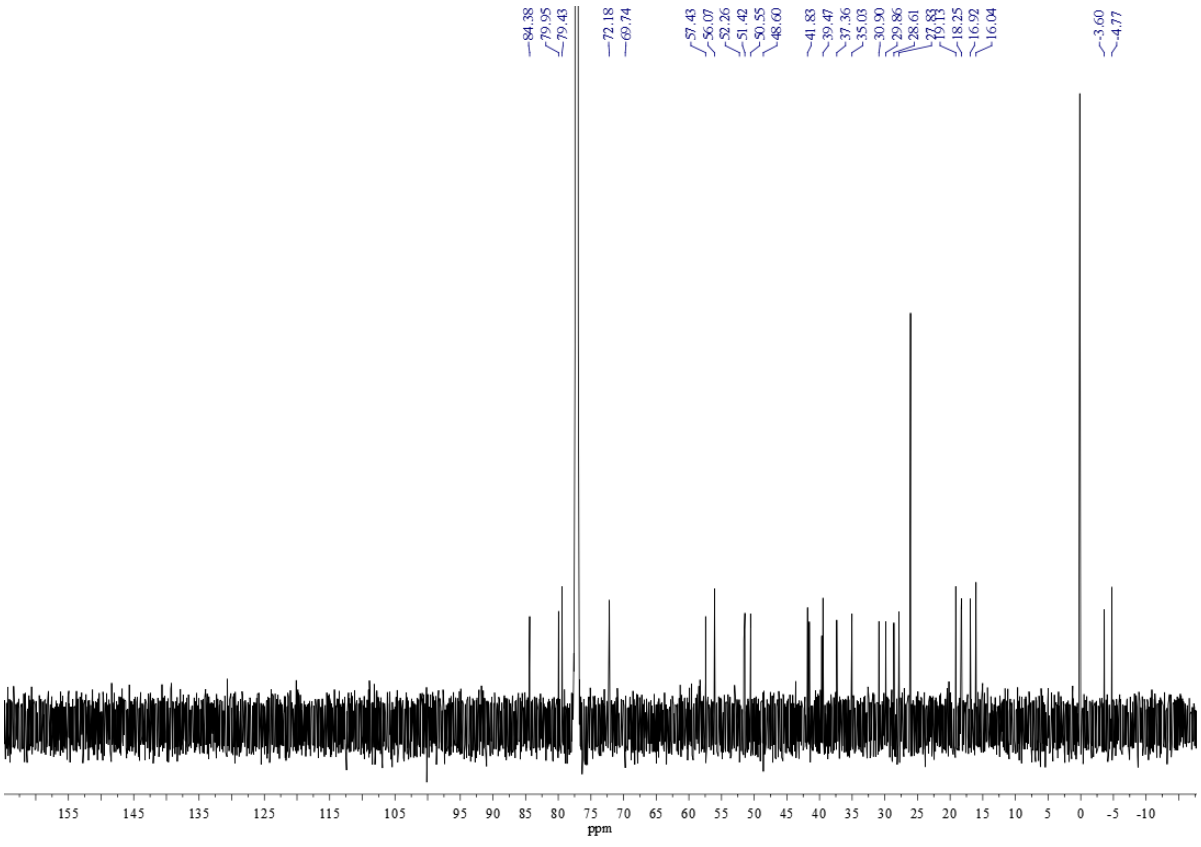
27

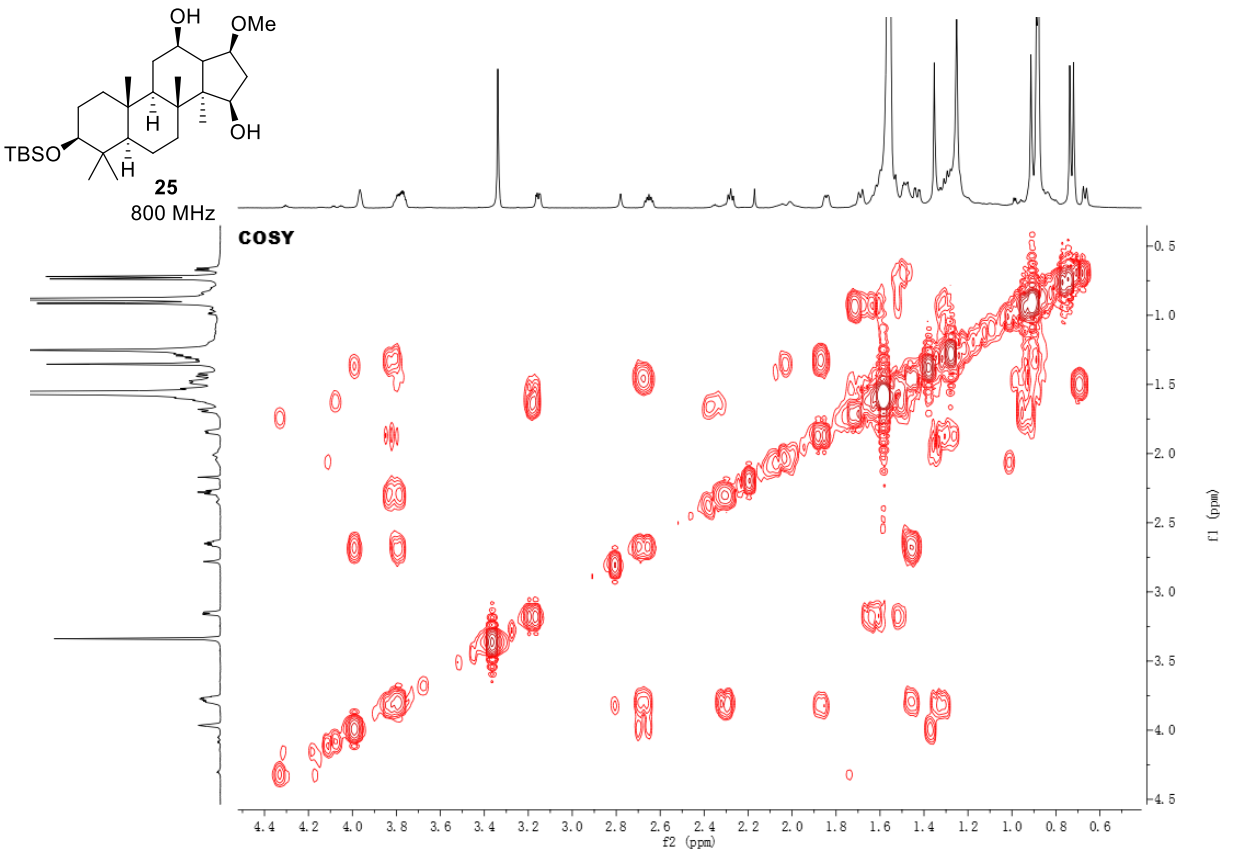
600 MHz

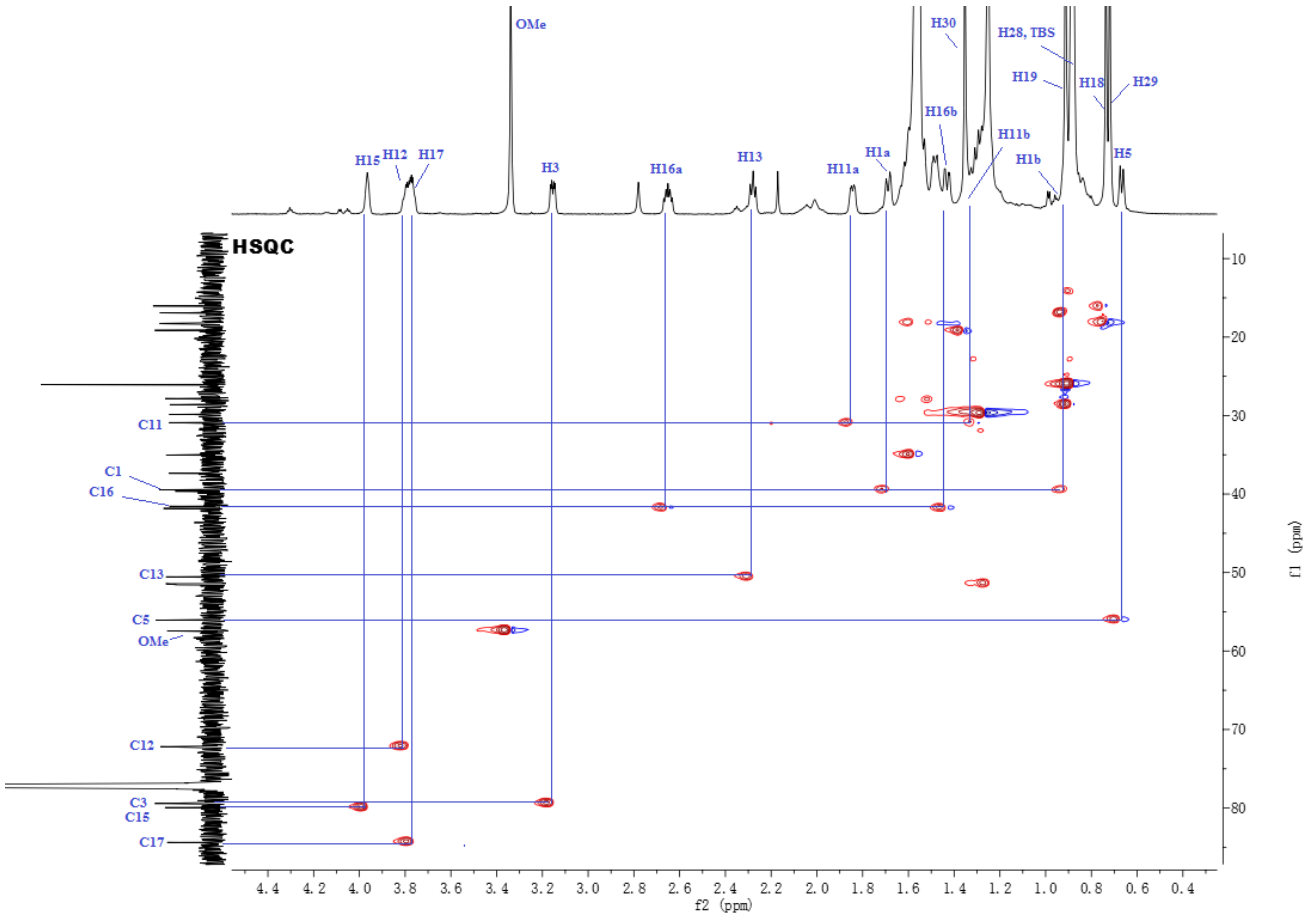


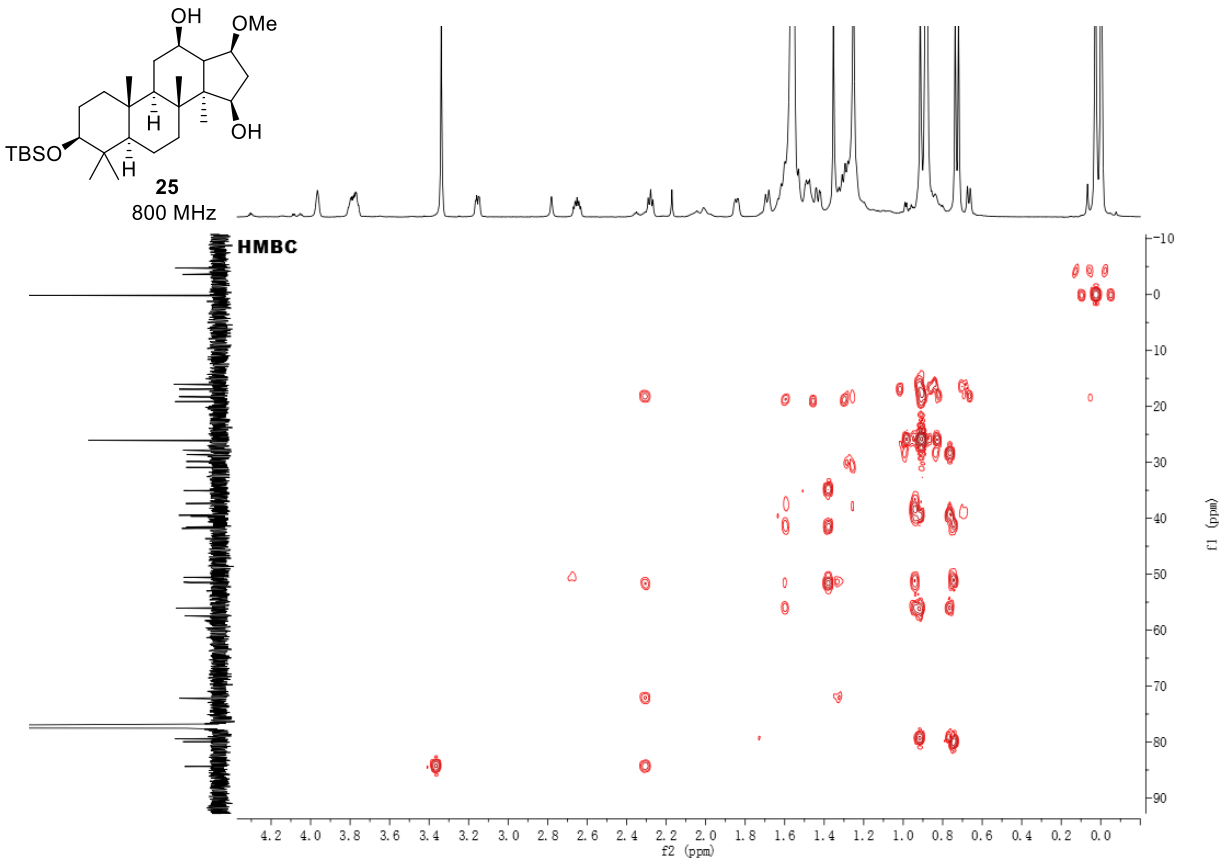


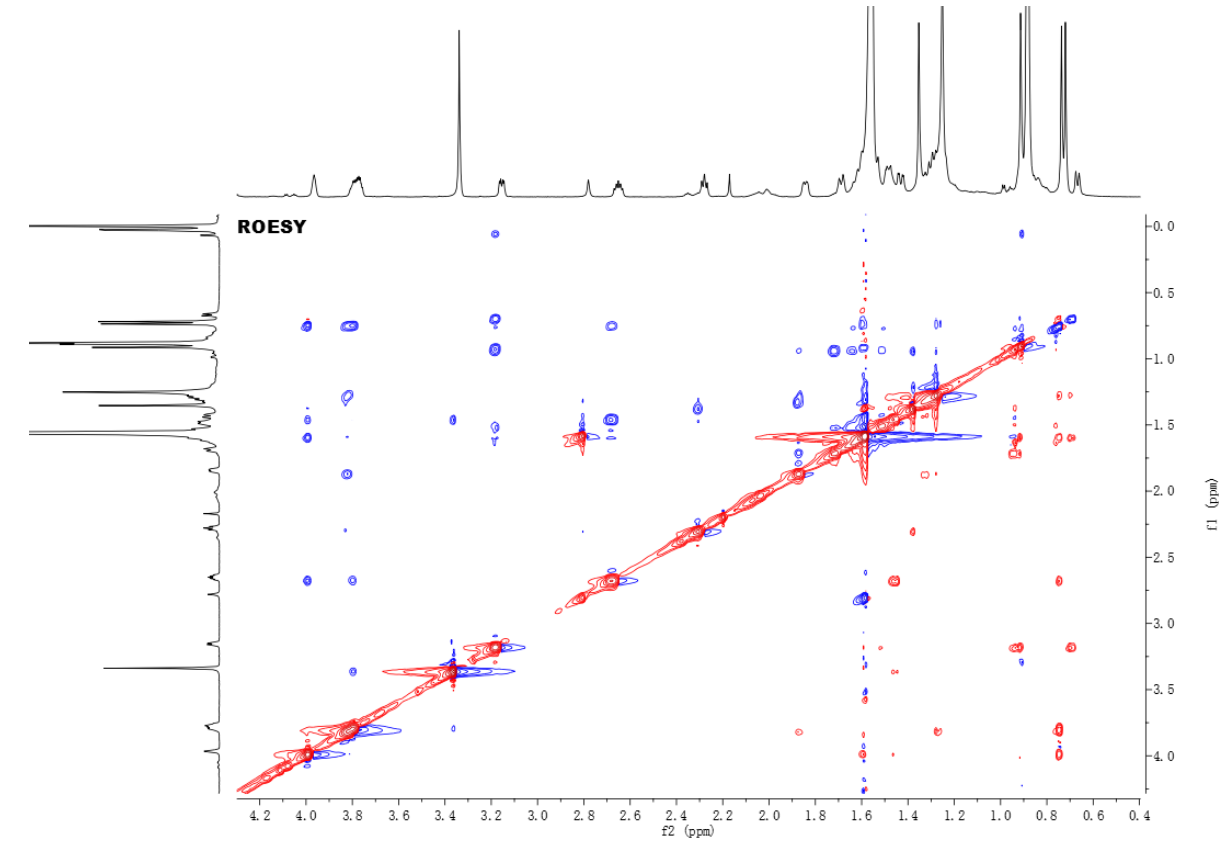

OH
OMe
OH
TBSO
H
H
25
800 MHz
ppm

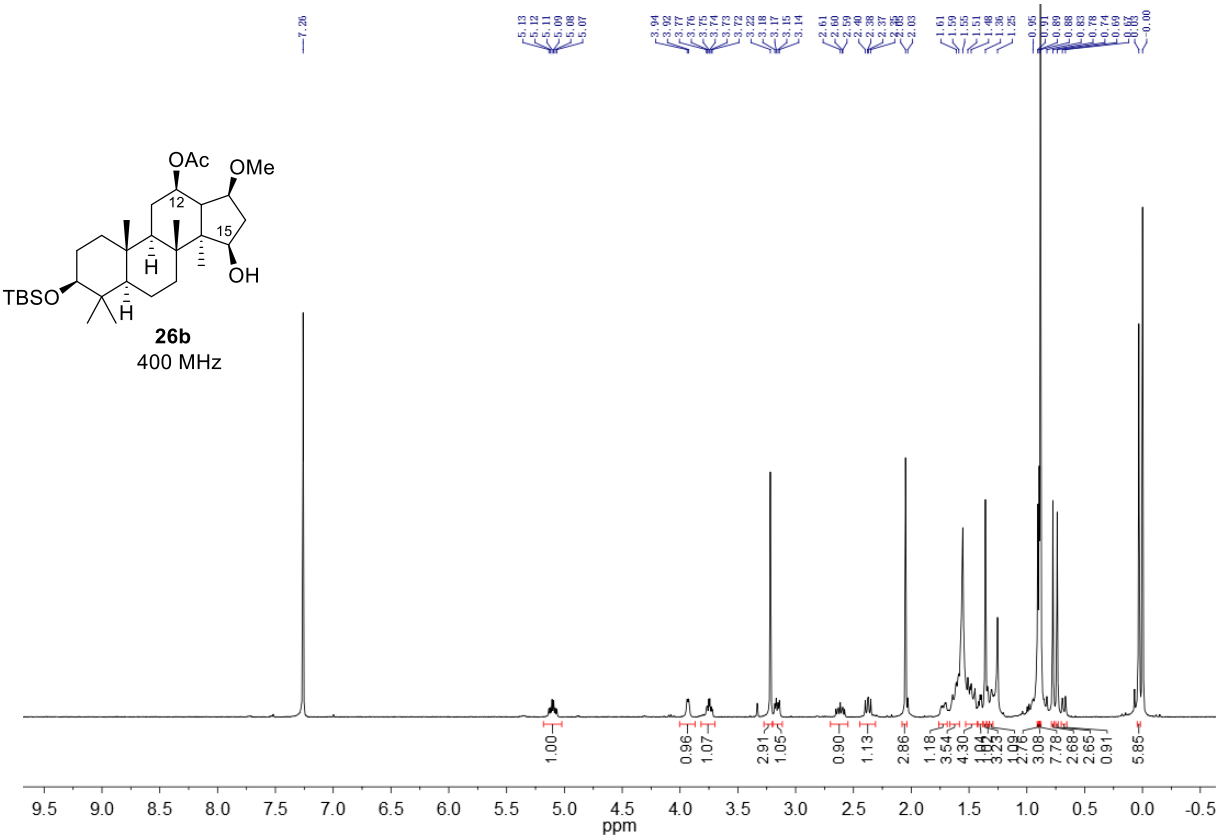

ppm

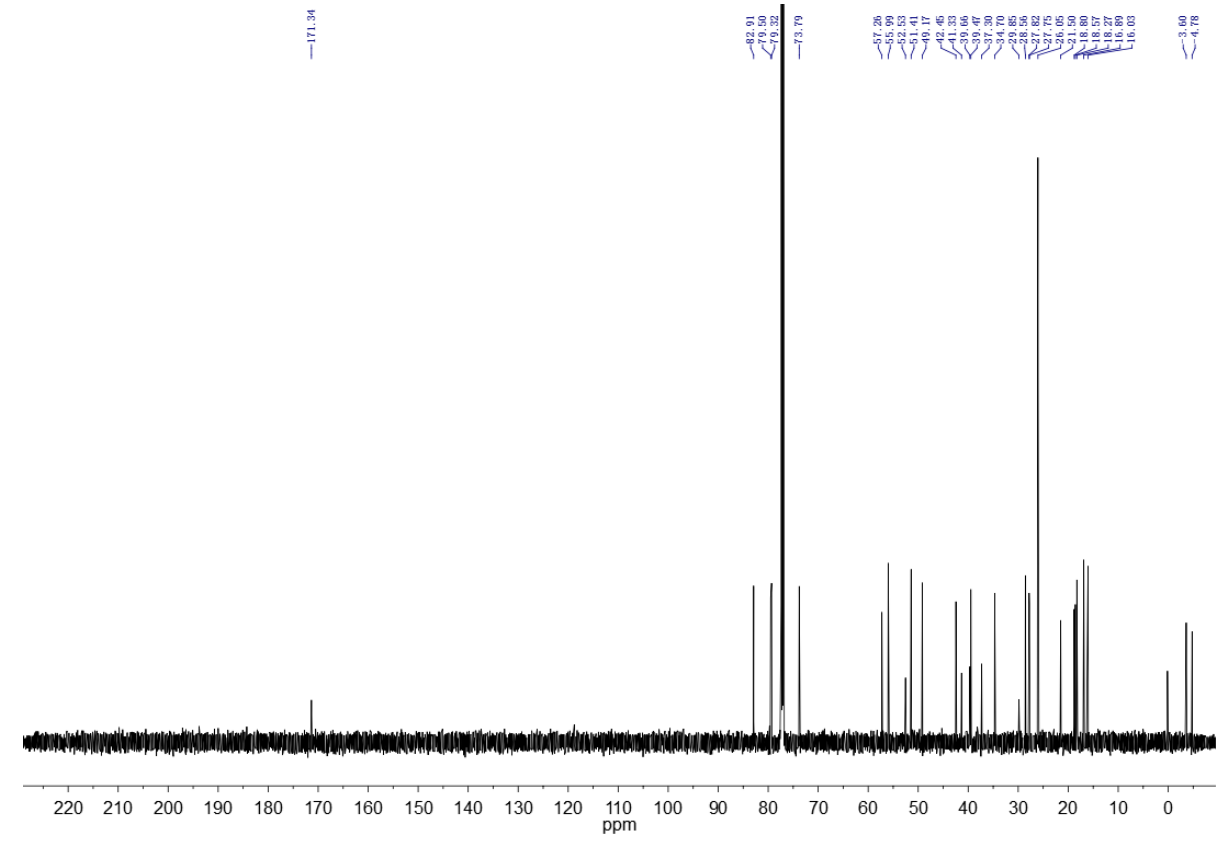

OH
OMe
H
OH
TBSO
H
25
800 MHz
COSY
f2 (ppm)
f1 (ppm)

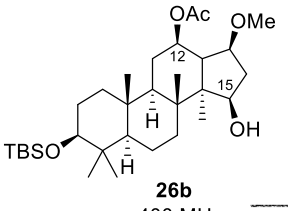

OMe
H30
H28, TBS
H19
H18
H29
H16b
H11b
H15
H12
H17
H3
H16a
H13
H11a
H1a
H1b
H5
HSQC
C11
C1
C16
C13
C5
OMe
C12
C3
C15
C17
f2 (ppm)
f1 (ppm)


OH
OMe
OH
TBSO
H
H
25
800 MHz
HMBC
f2 (ppm)
f1 (ppm)

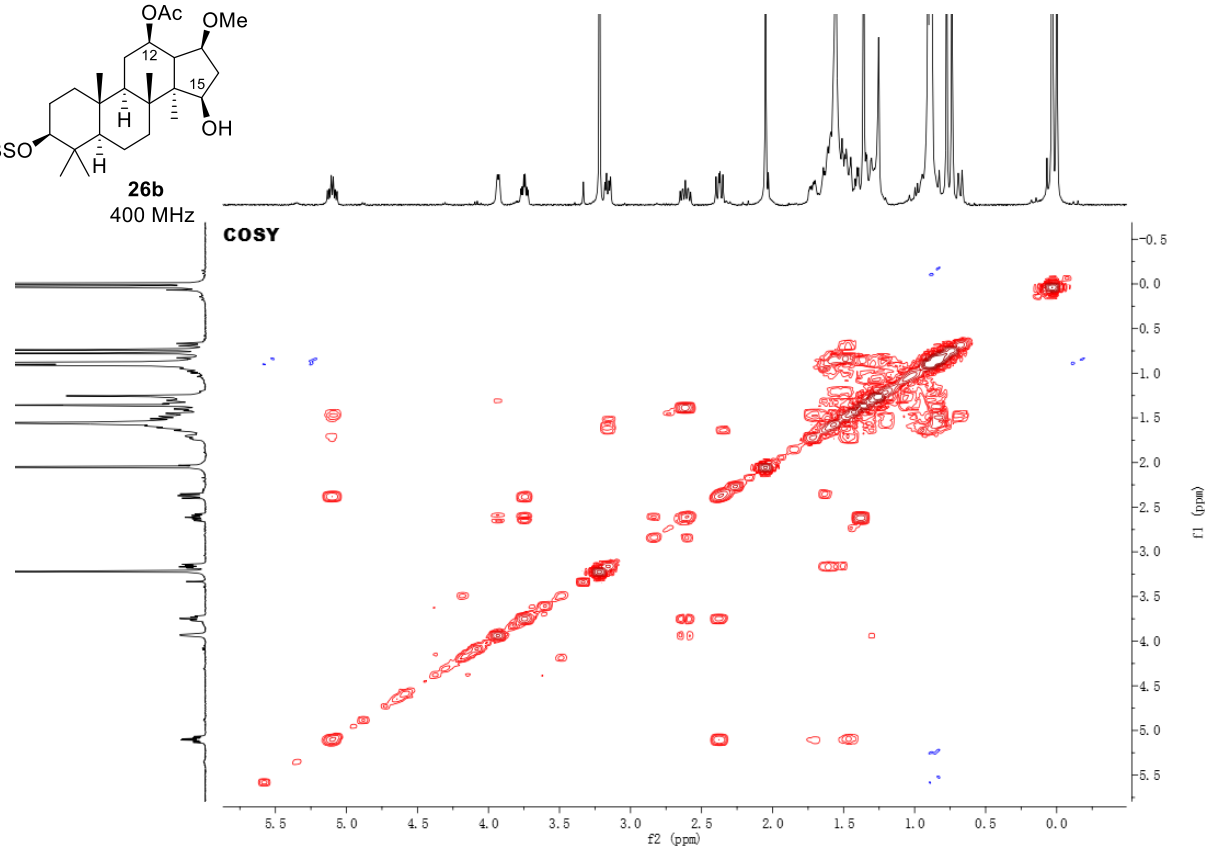

ROESY
f2 (ppm)
f1 (ppm)

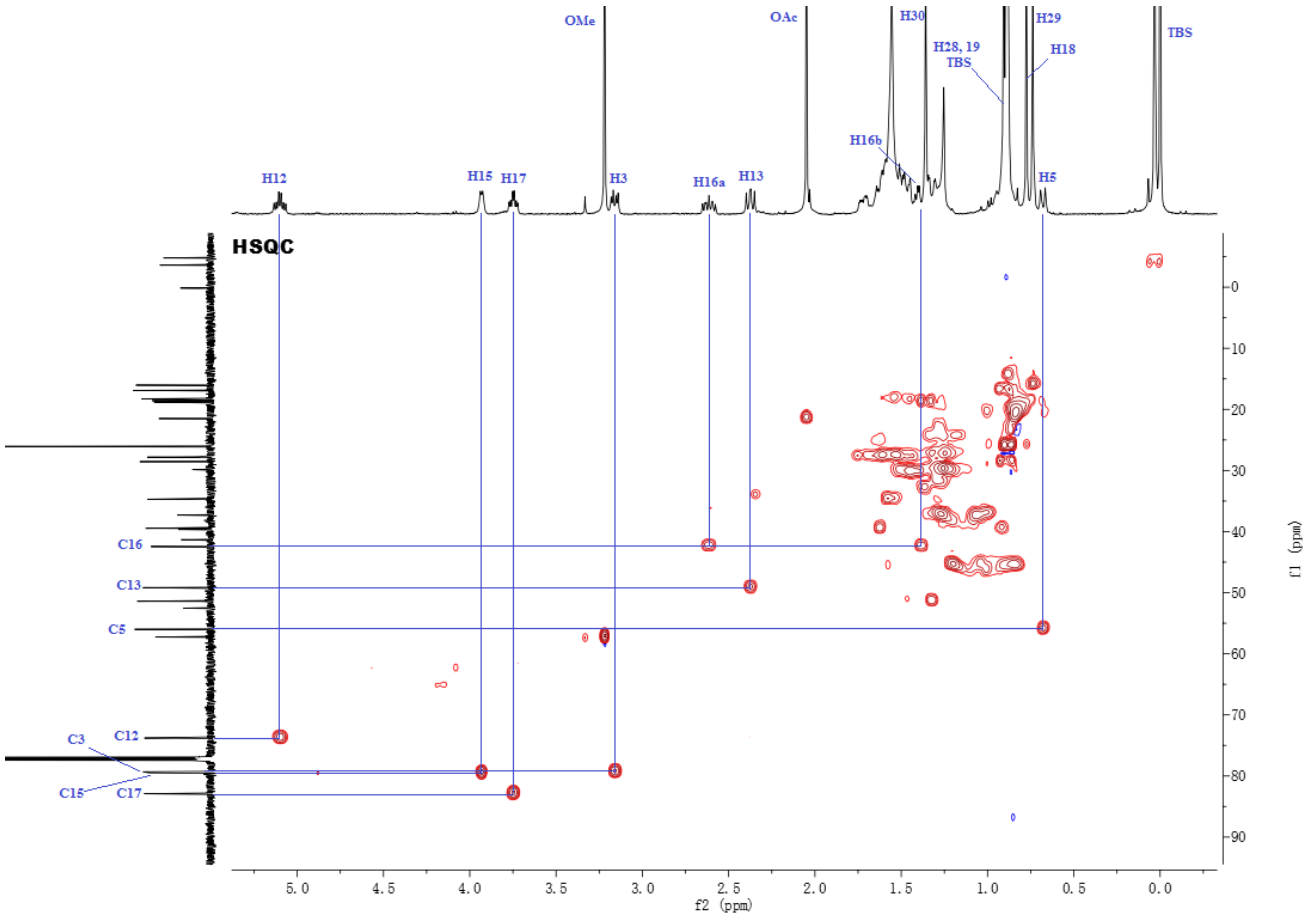

OAc
OMe
12
15
H
OH
TBSO
H
26b
400 MHz
ppm

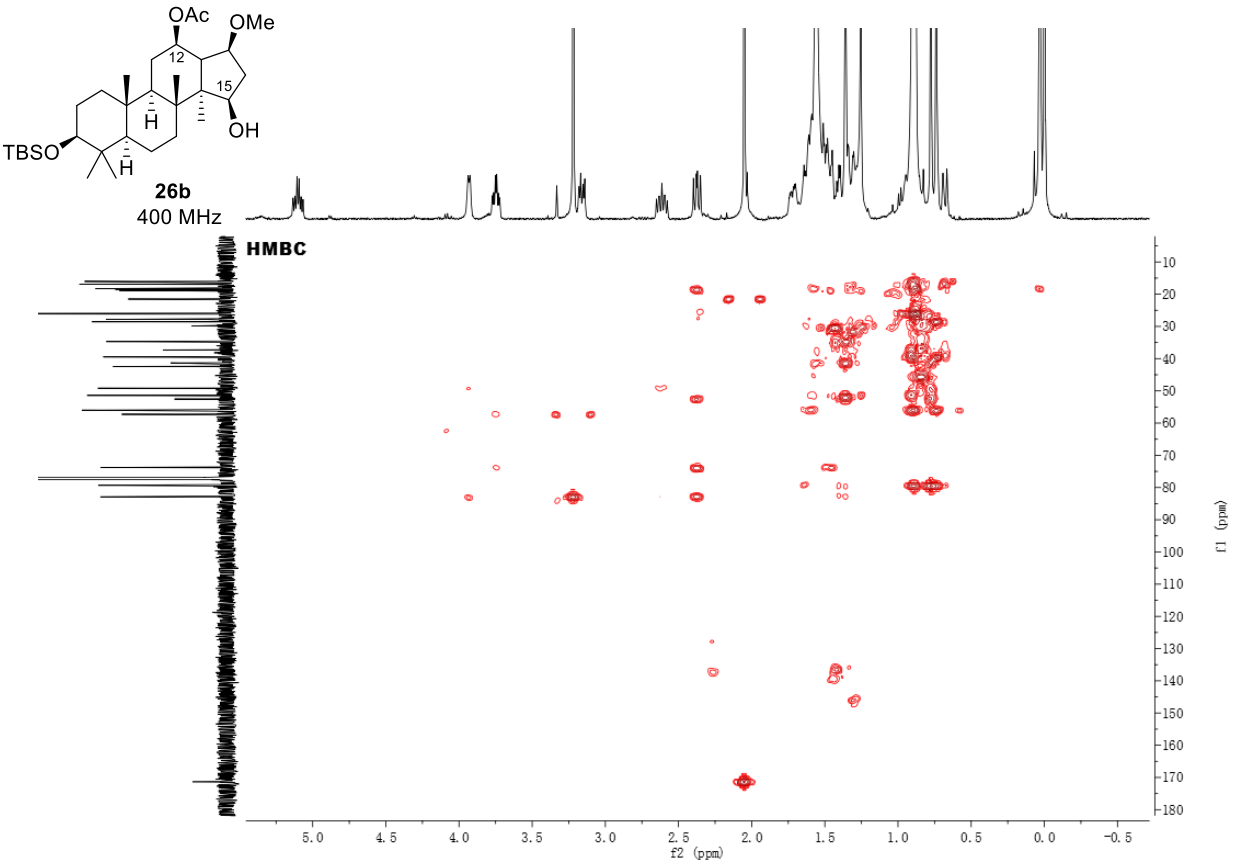

ppm

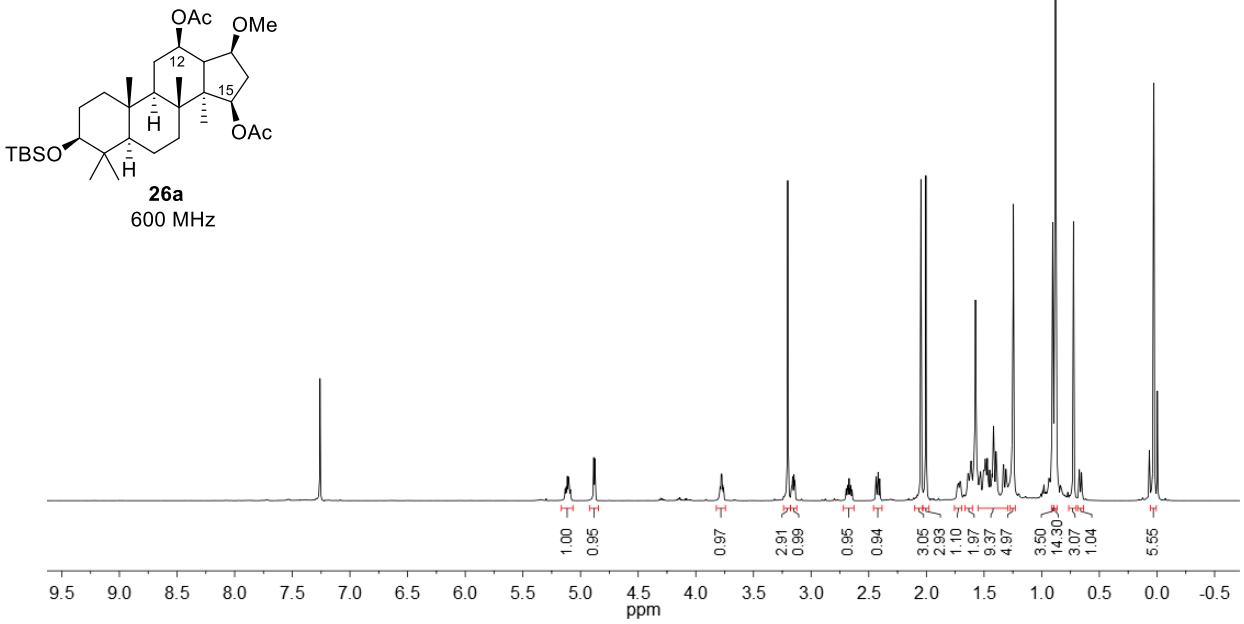

OAc
OMe
12
15
H
OH
TBSO
H

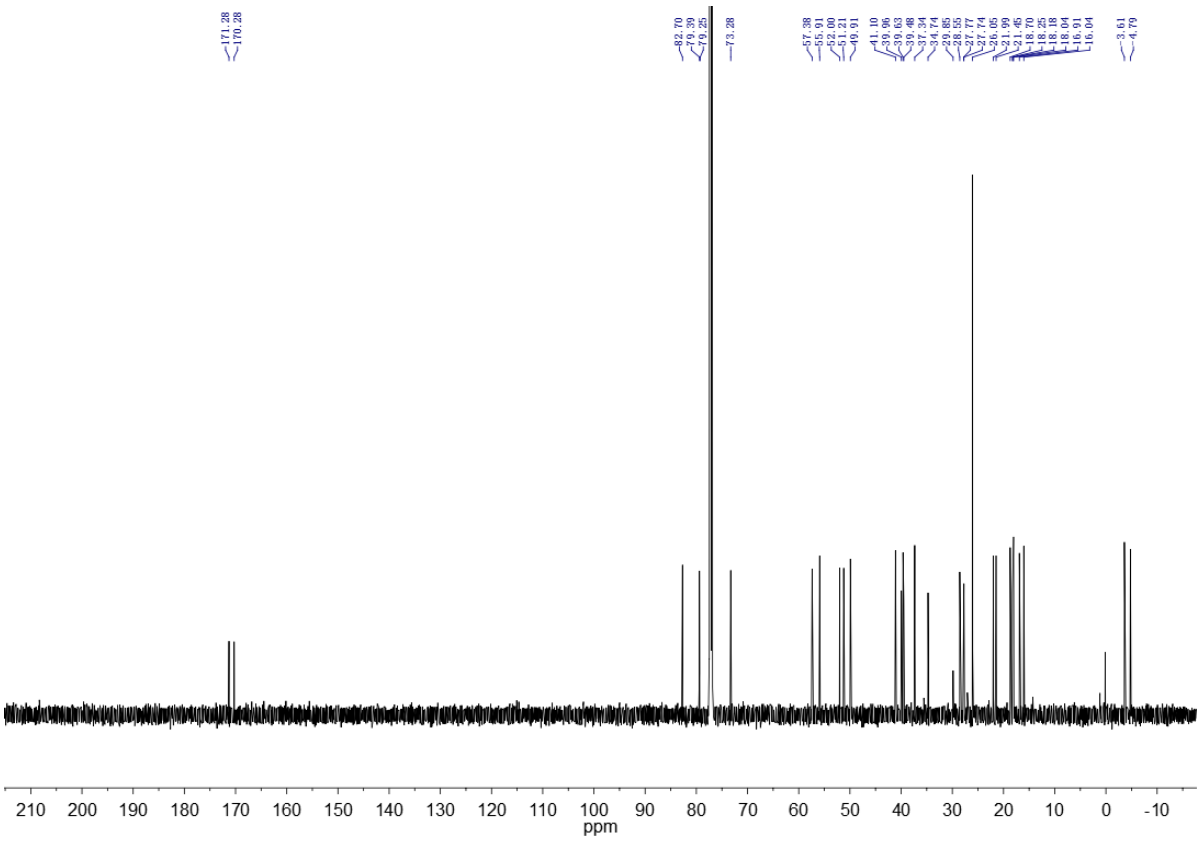
26b
400 MHz

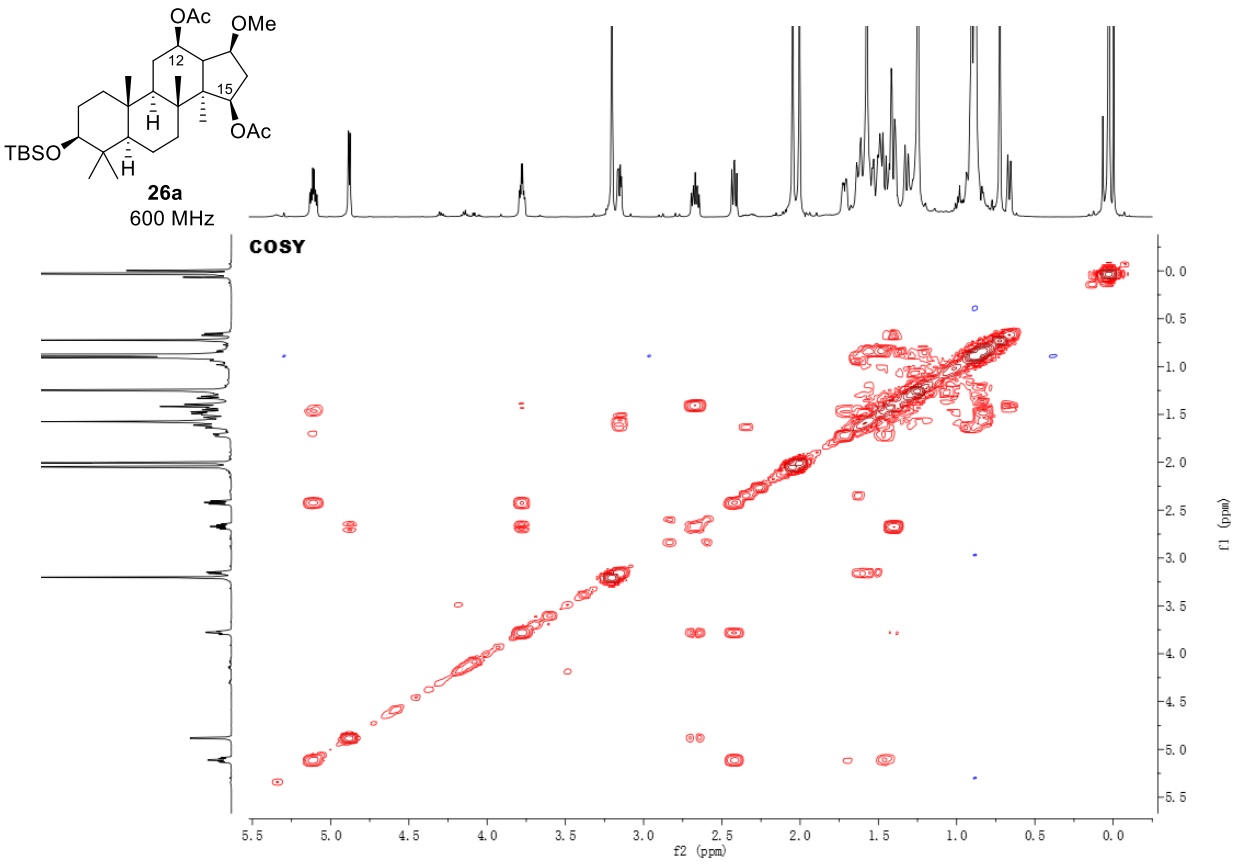

COSY
f2 (ppm)
f1 (ppm)

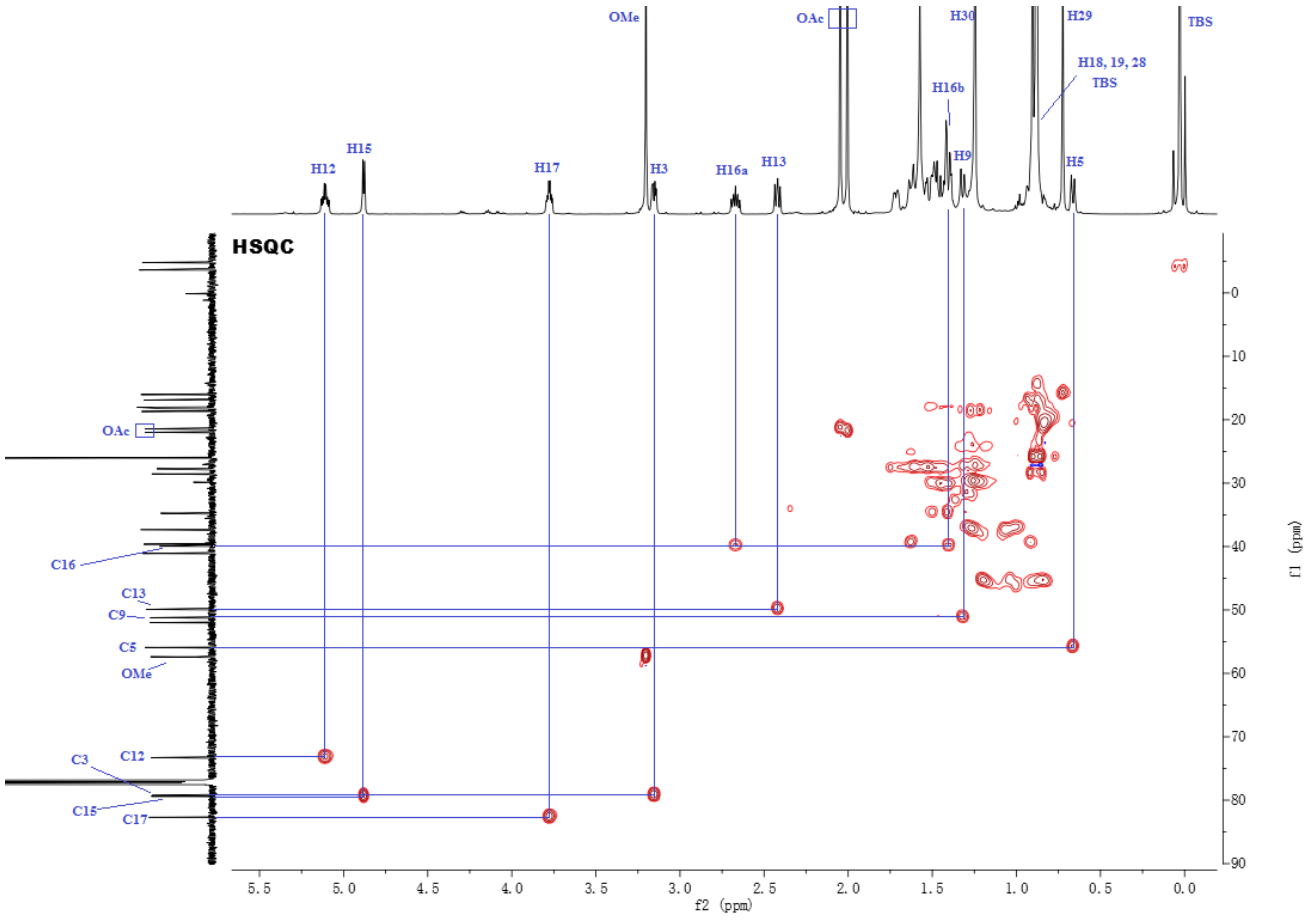

HSQC
OMe
OAc
H30
H29
TBS
H28, 19 TBS
H18
H16b
H12
H15
H17
H3
H16a
H13
H5
C16
C13
C5
C3
C12
C15
C17
f2 (ppm)
f1 (ppm)

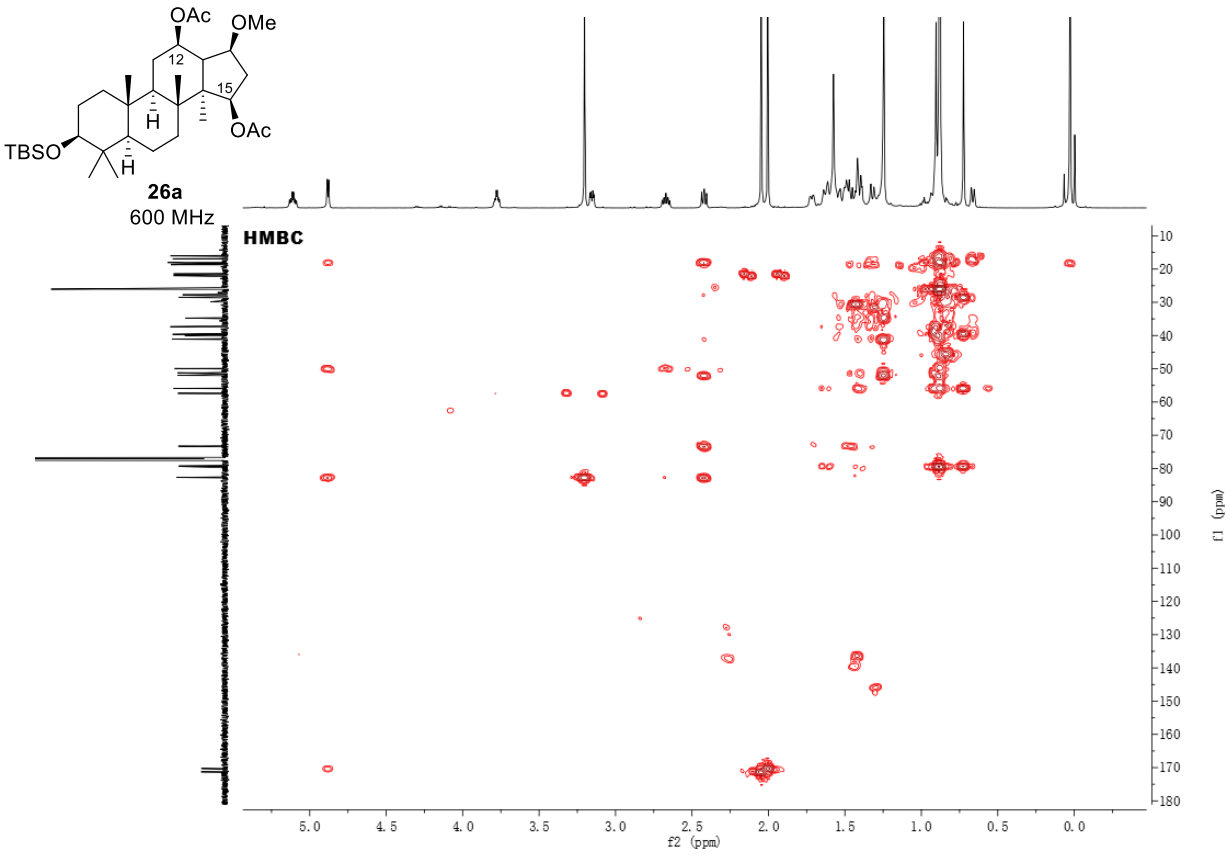

OAc
OMe
12
15
H
OH
TBSO
H
26b
400 MHz
HMBC
f2 (ppm)
f1 (ppm)

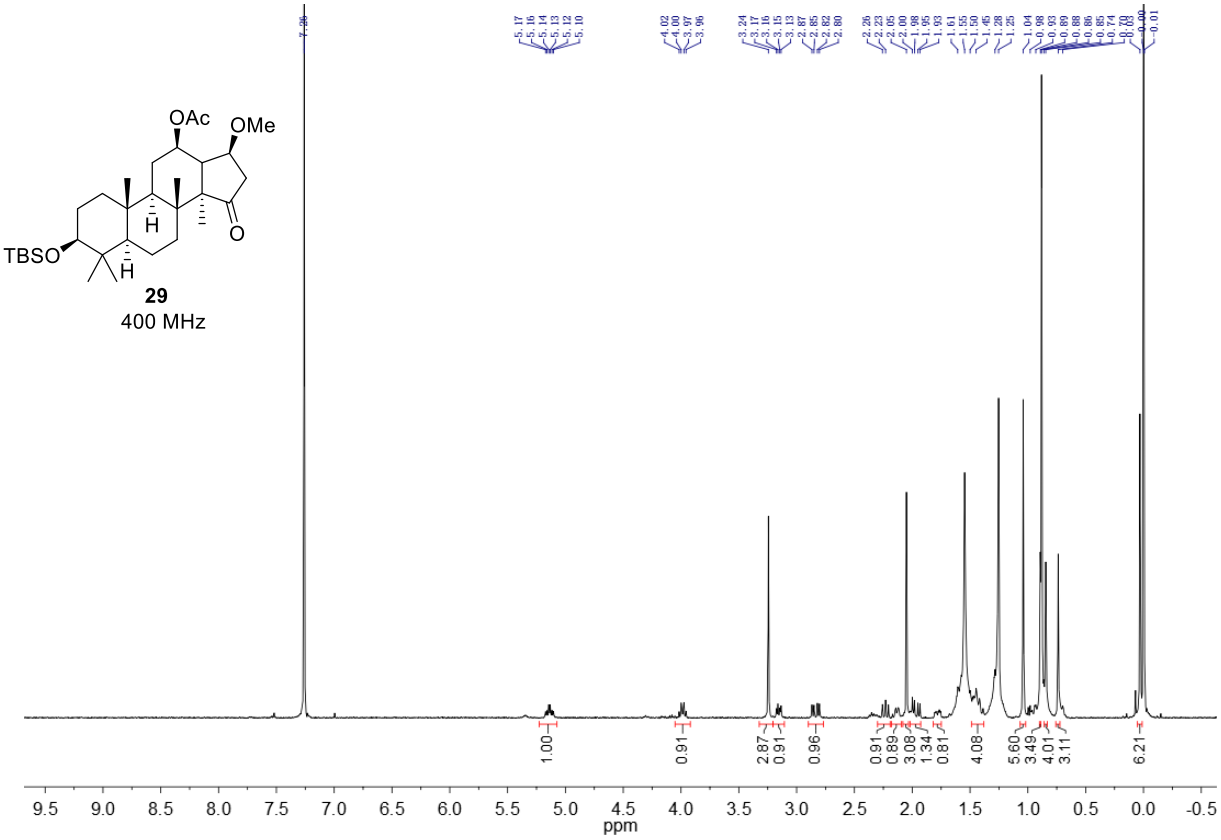

OAc
OMe
12
15
H
TBSO
H
OAc
26a
600 MHz
ppm

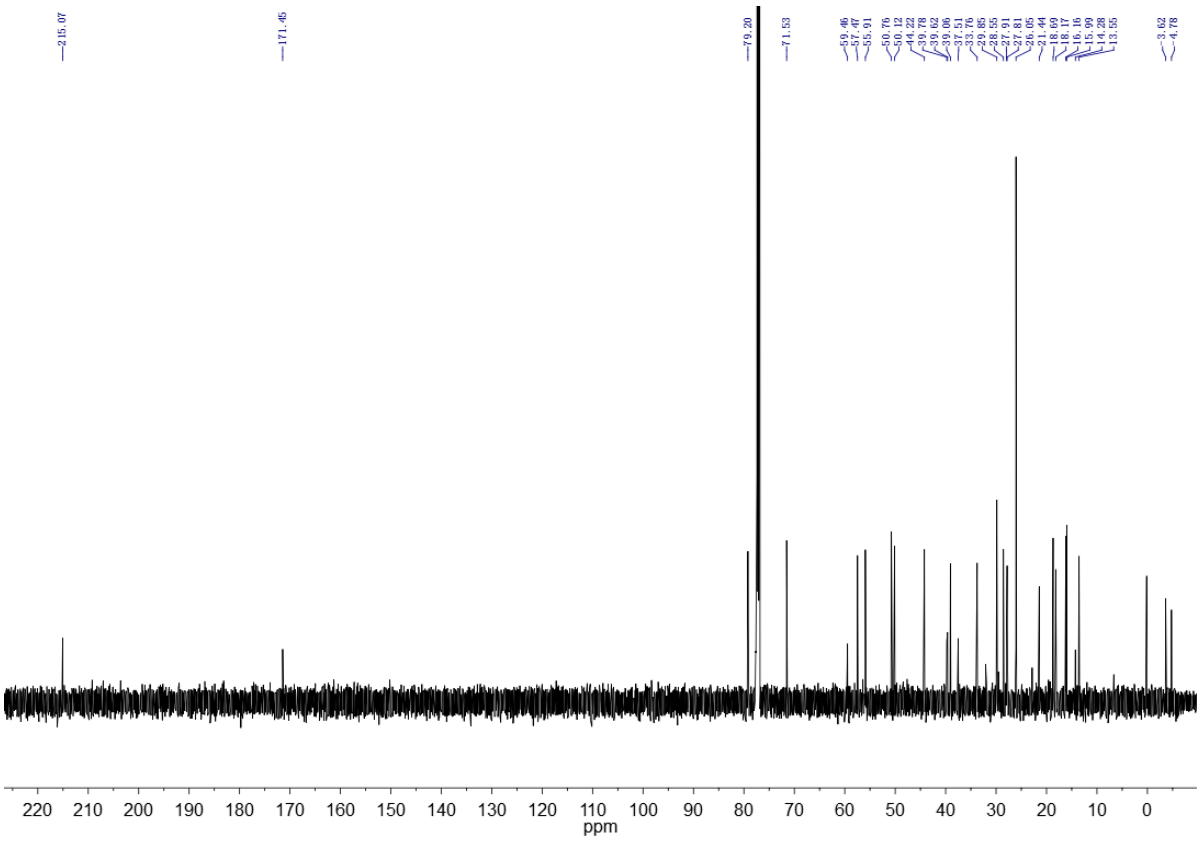

ppm

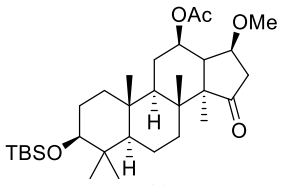

OAc
OMe
12
15
H
OAc
TBSO
H
26a
600 MHz
COSY
f2 (ppm)
f1 (ppm)


OMe
OAc
H30
H29
TBS
H18, 19, 28
TBS
H16b
H15
H12
H17
H3
H16a
H13
H9
H5
HSQC
OAc
C16
C13
C9
C5
OMe
C3
C12
C15
C17
f2 (ppm)
f1 (ppm)


OAc
OMe
12
15
H
OAc
TBSO
H
26a
600 MHz
HMBC
f2 (ppm)
f1 (ppm)

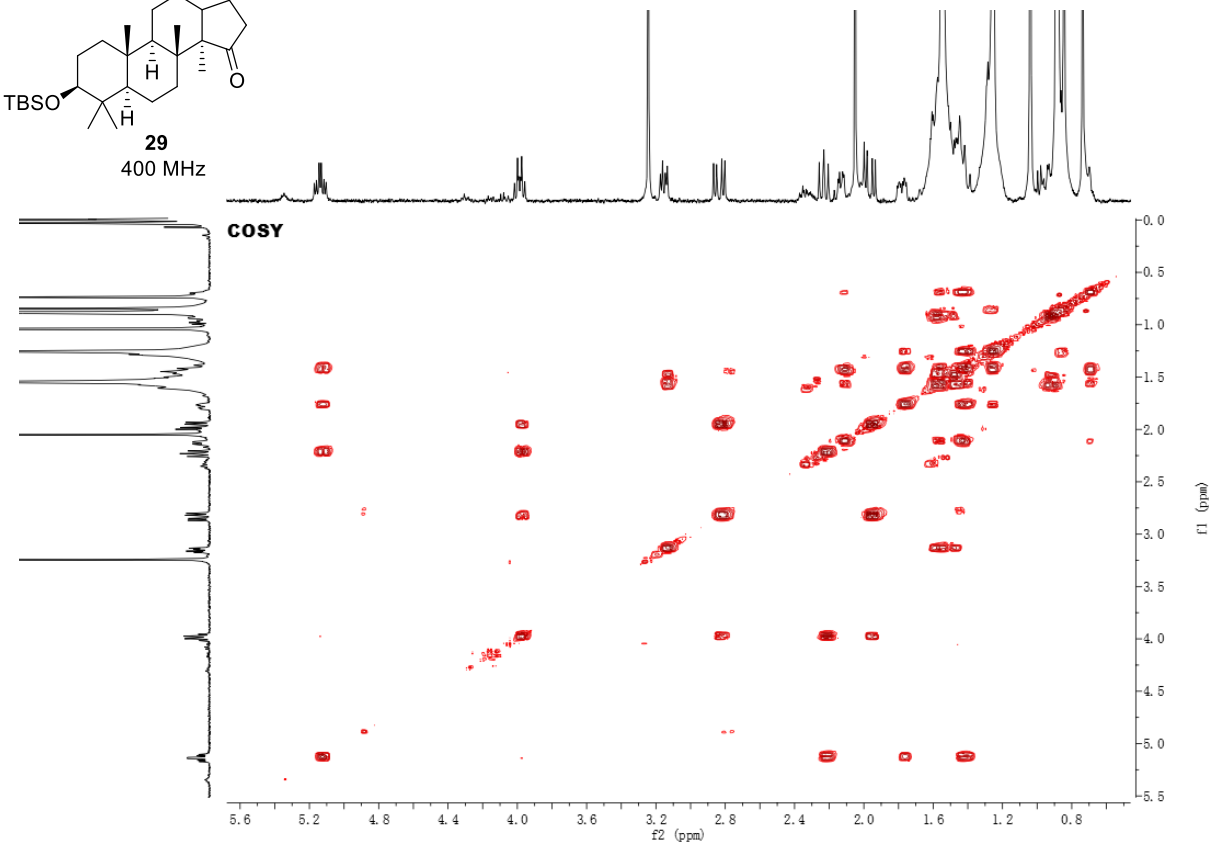

OAc
OMe
TBSO
H
H
O
29
400 MHz
ppm

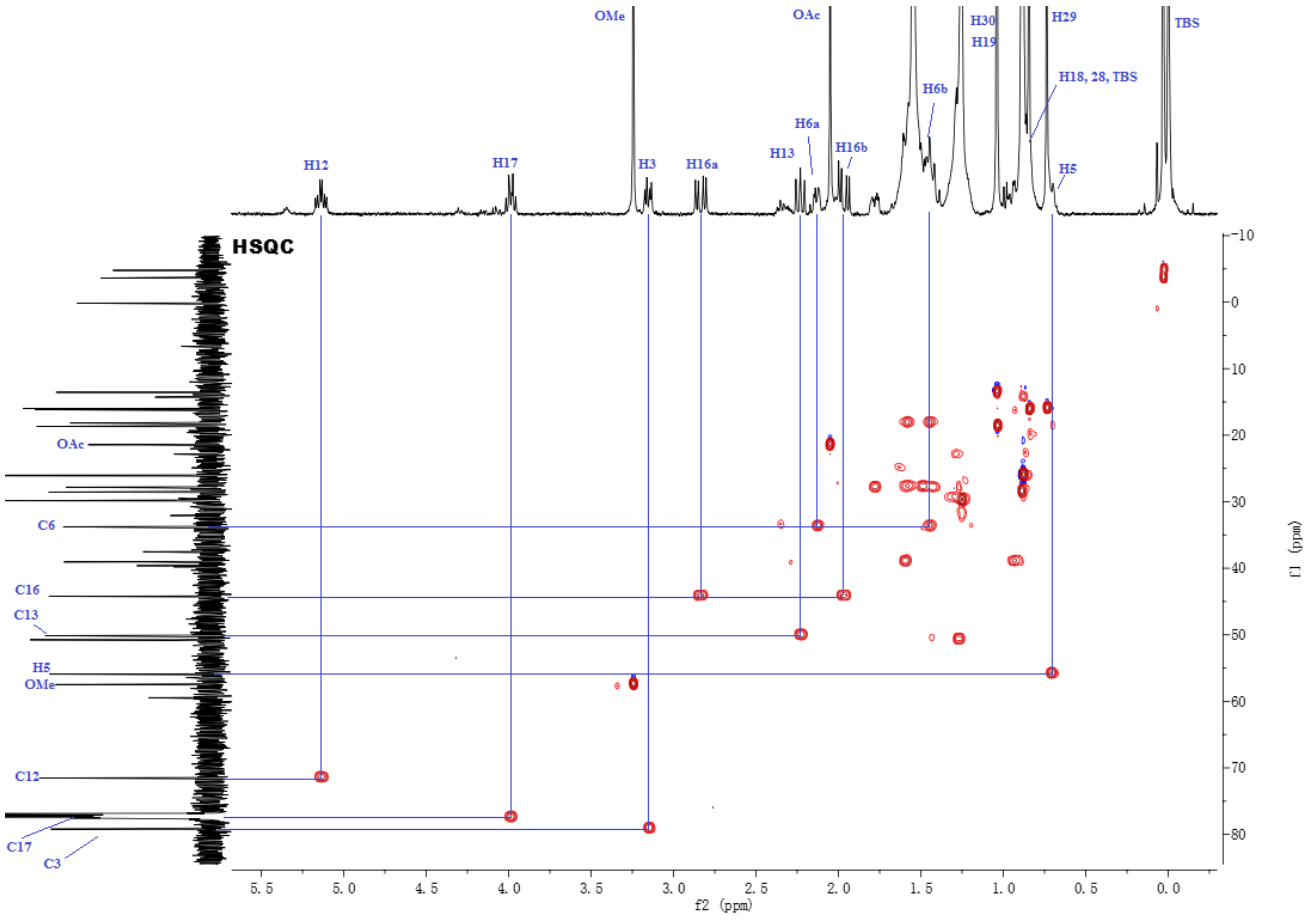

ppm

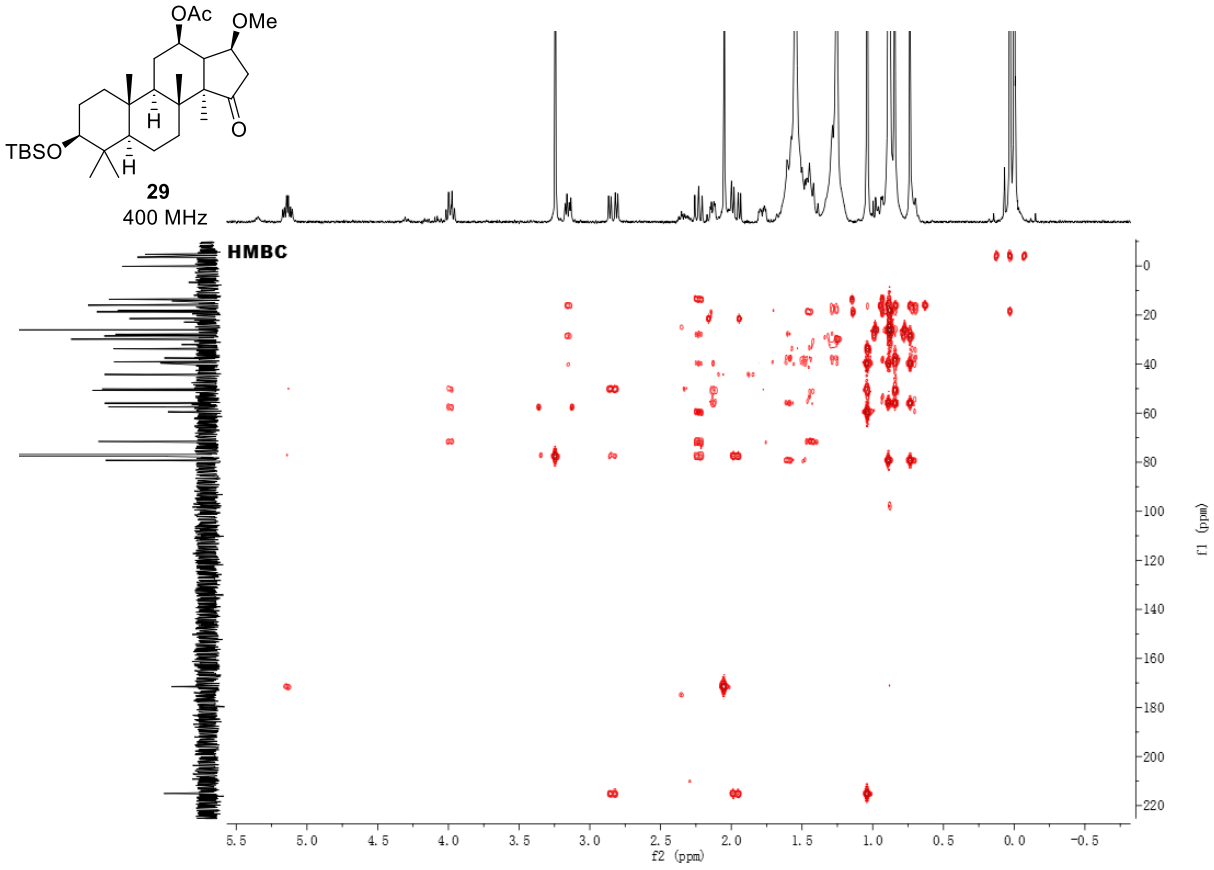

OAc
OMe
TBSO
H
H
O

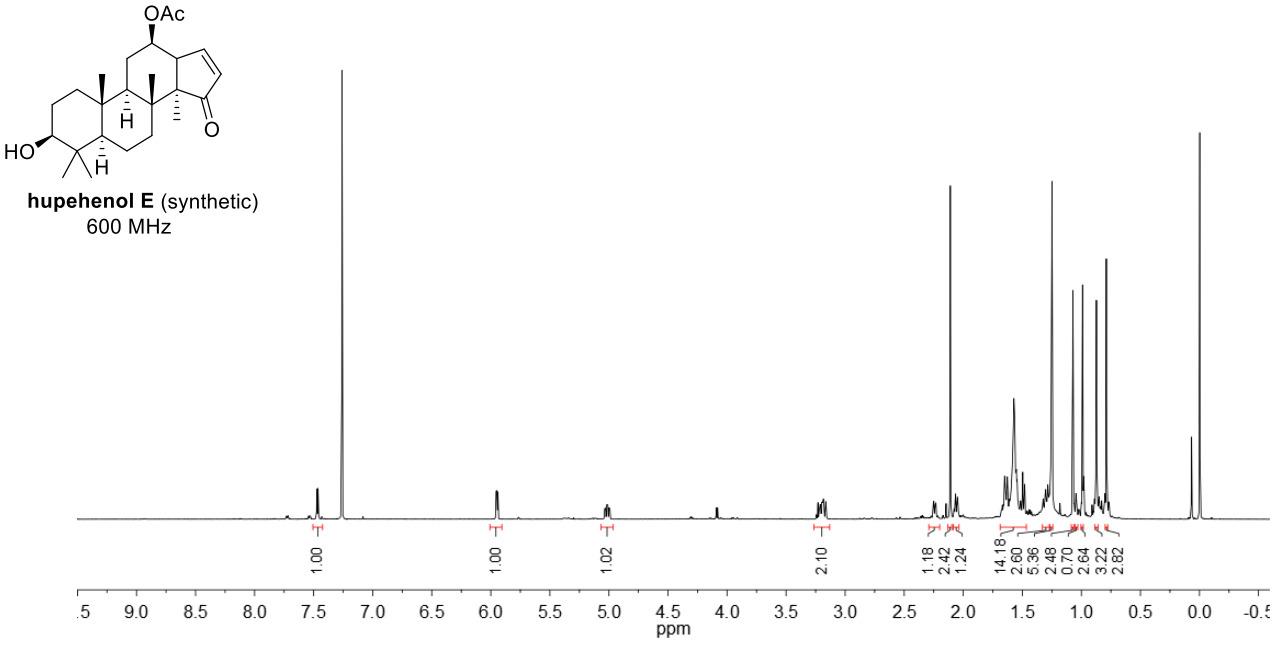
29

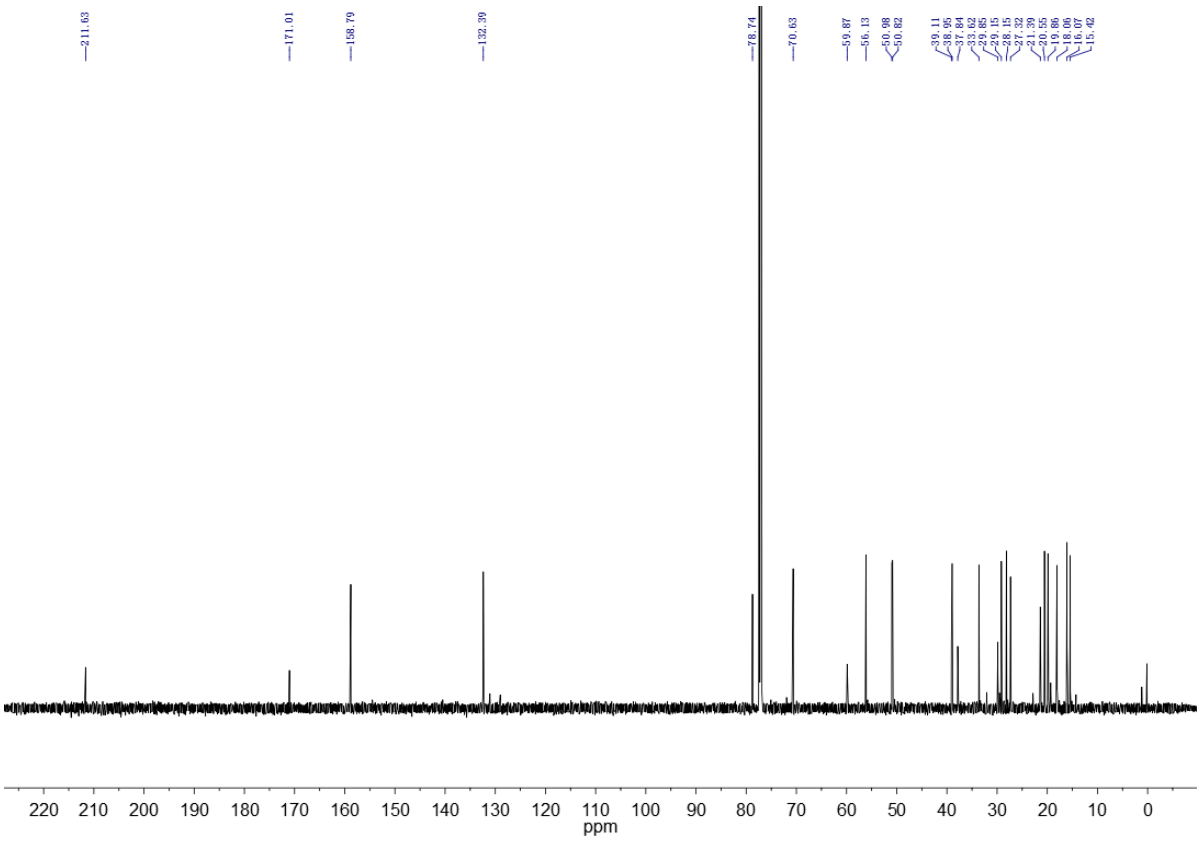
400 MHz

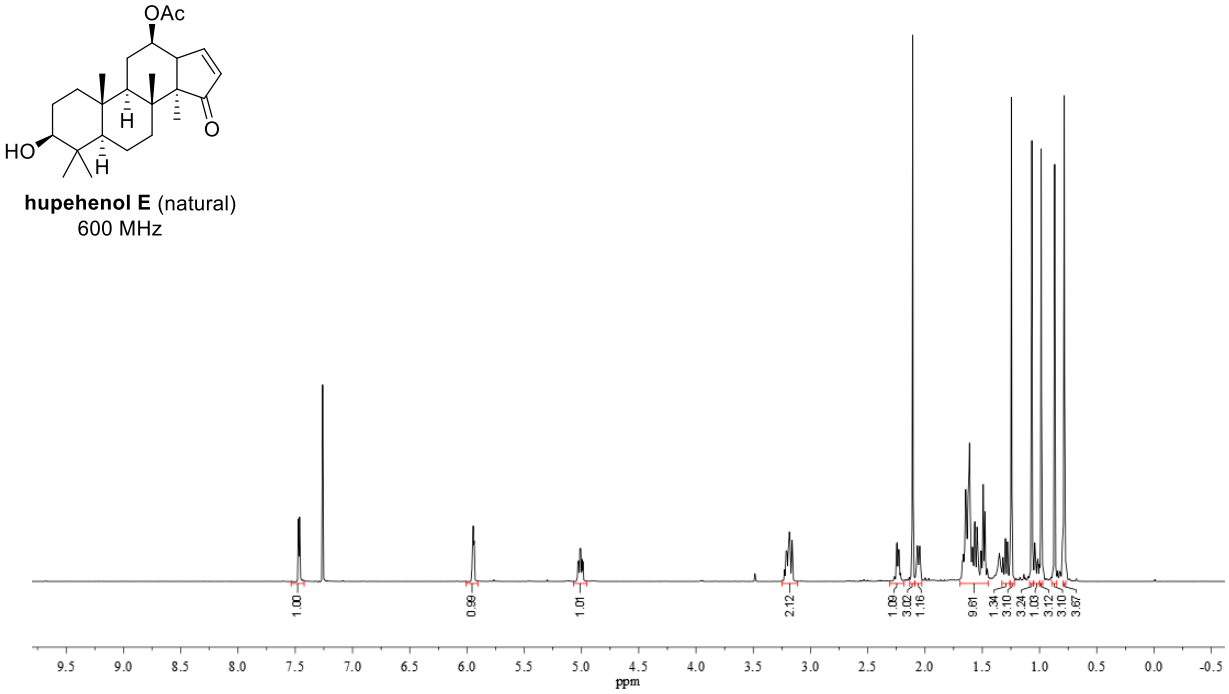

COSY
f2 (ppm)
f1 (ppm)

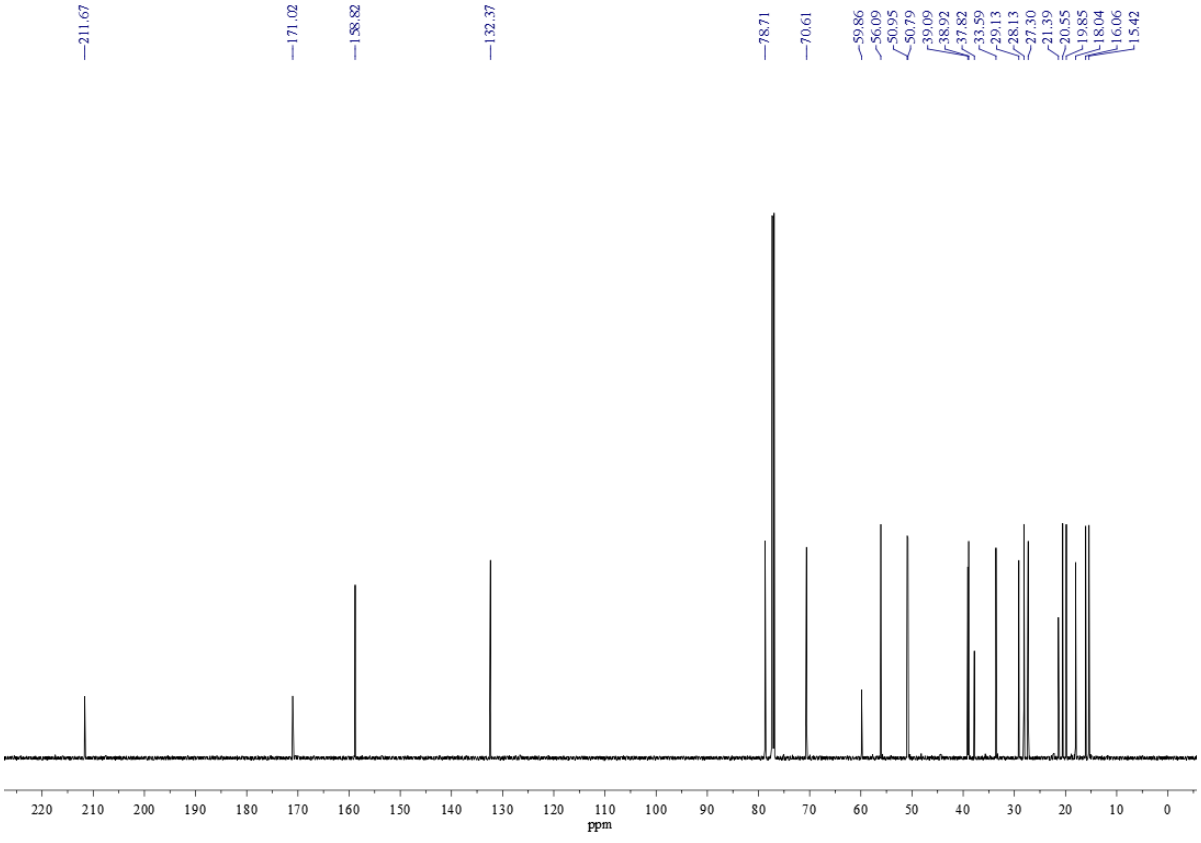

HSQC
OMe
OAc
H30
H19
H29
TBS
H18, 28, TBS
H6b
H6a
H16b
H13
H12
H17
H3
H16a
H5
OAc
C6
C16
C13
H5
OMe
C12
C17
C3
f2 (ppm)
f1 (ppm)

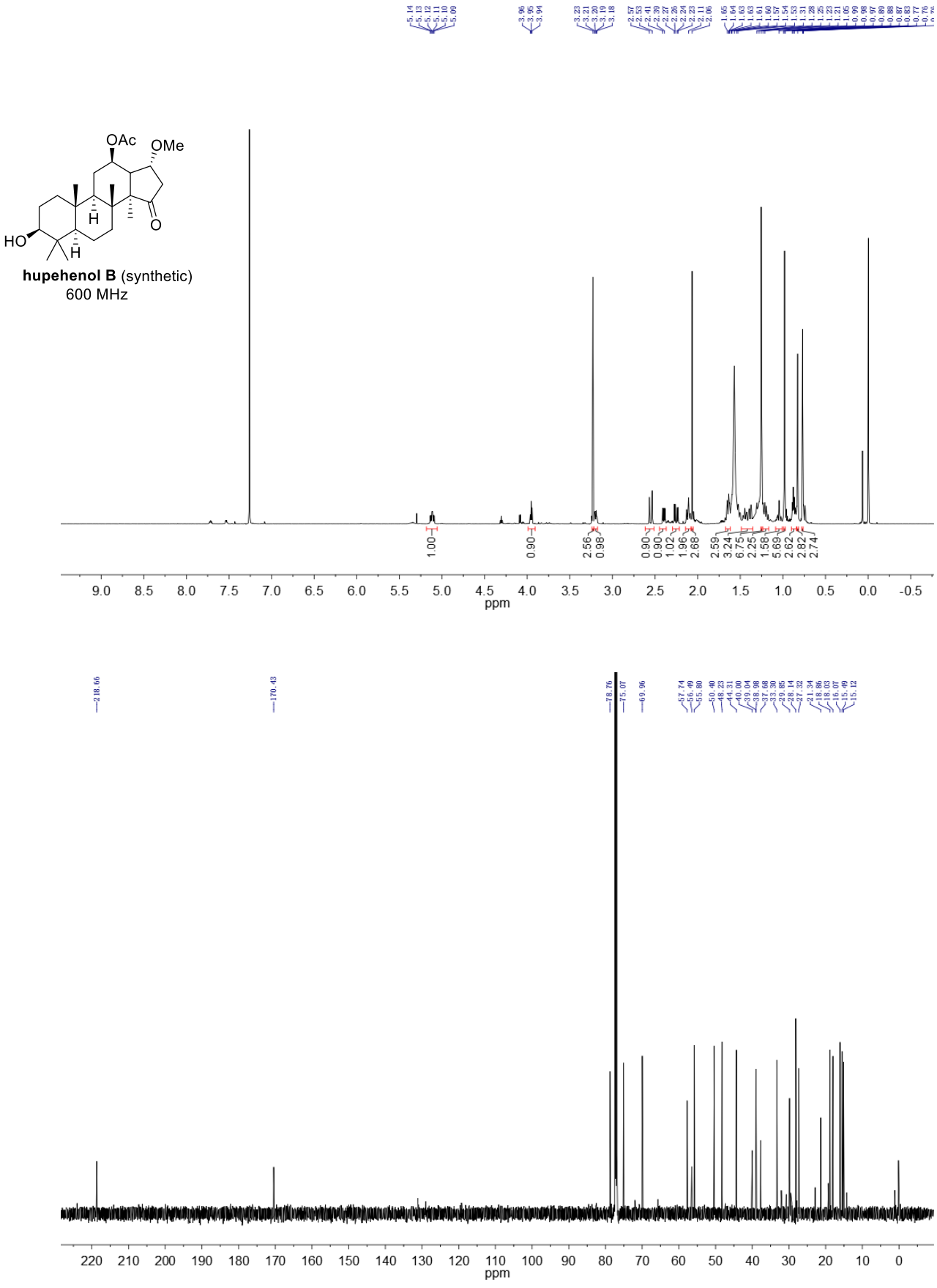

OAc
OMe
H
O
TBSO
H
29
400 MHz
HMBC
f2 (ppm)
f1 (ppm)

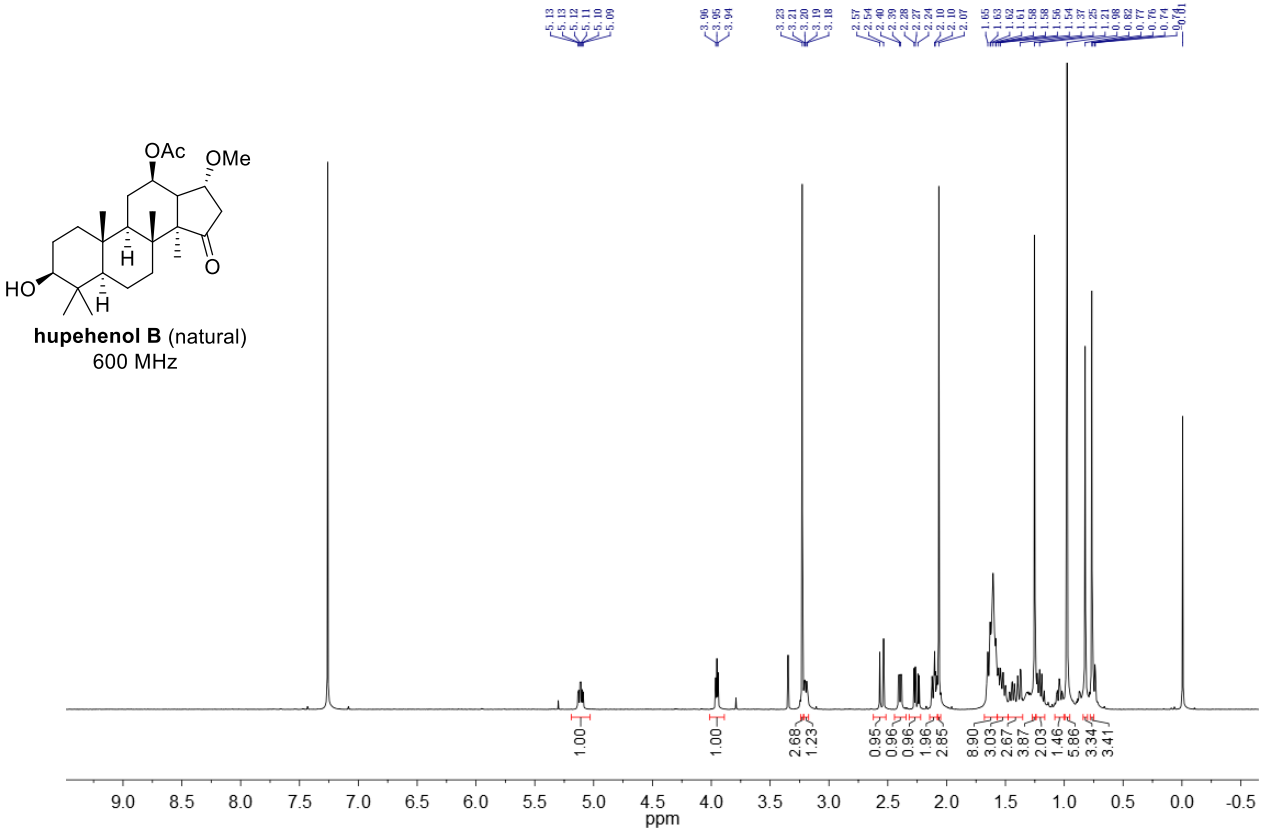

OAc
HO
H
H
O
hupehenol E (synthetic)
600 MHz
ppm

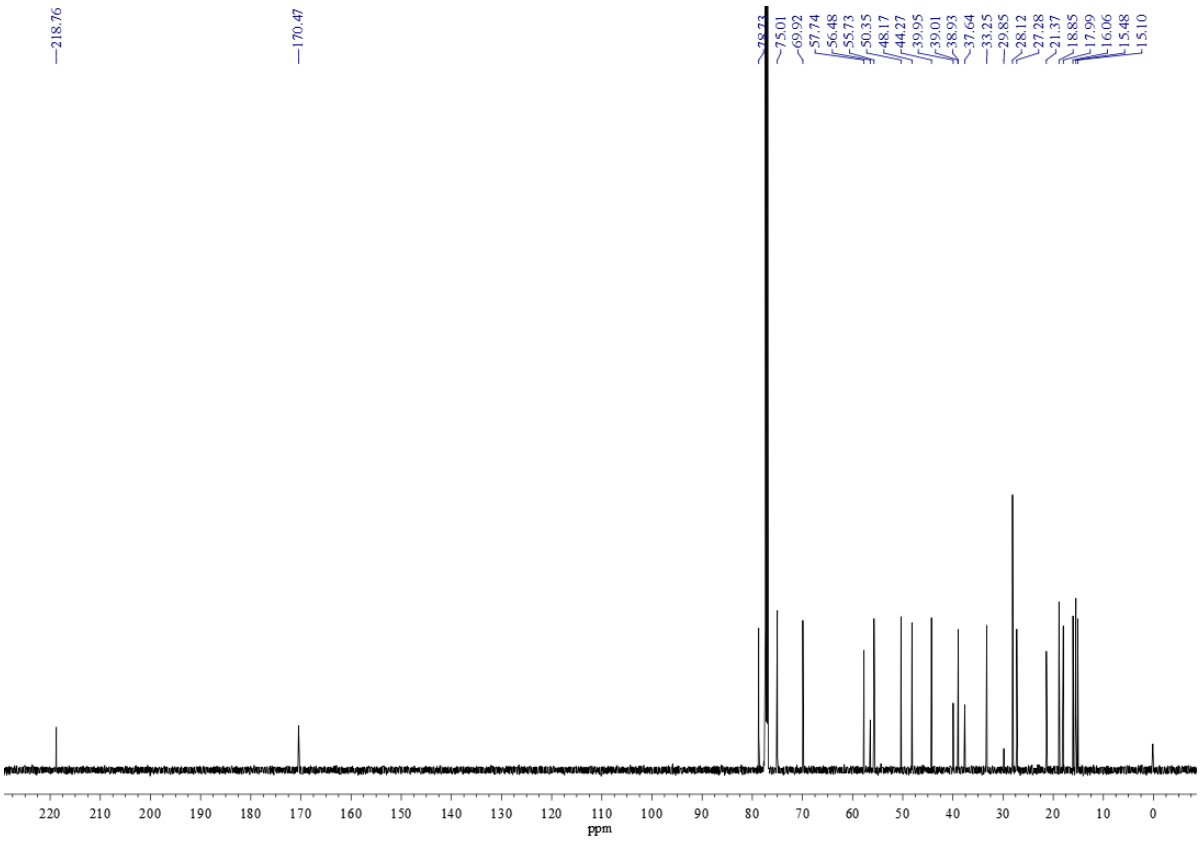

ppm

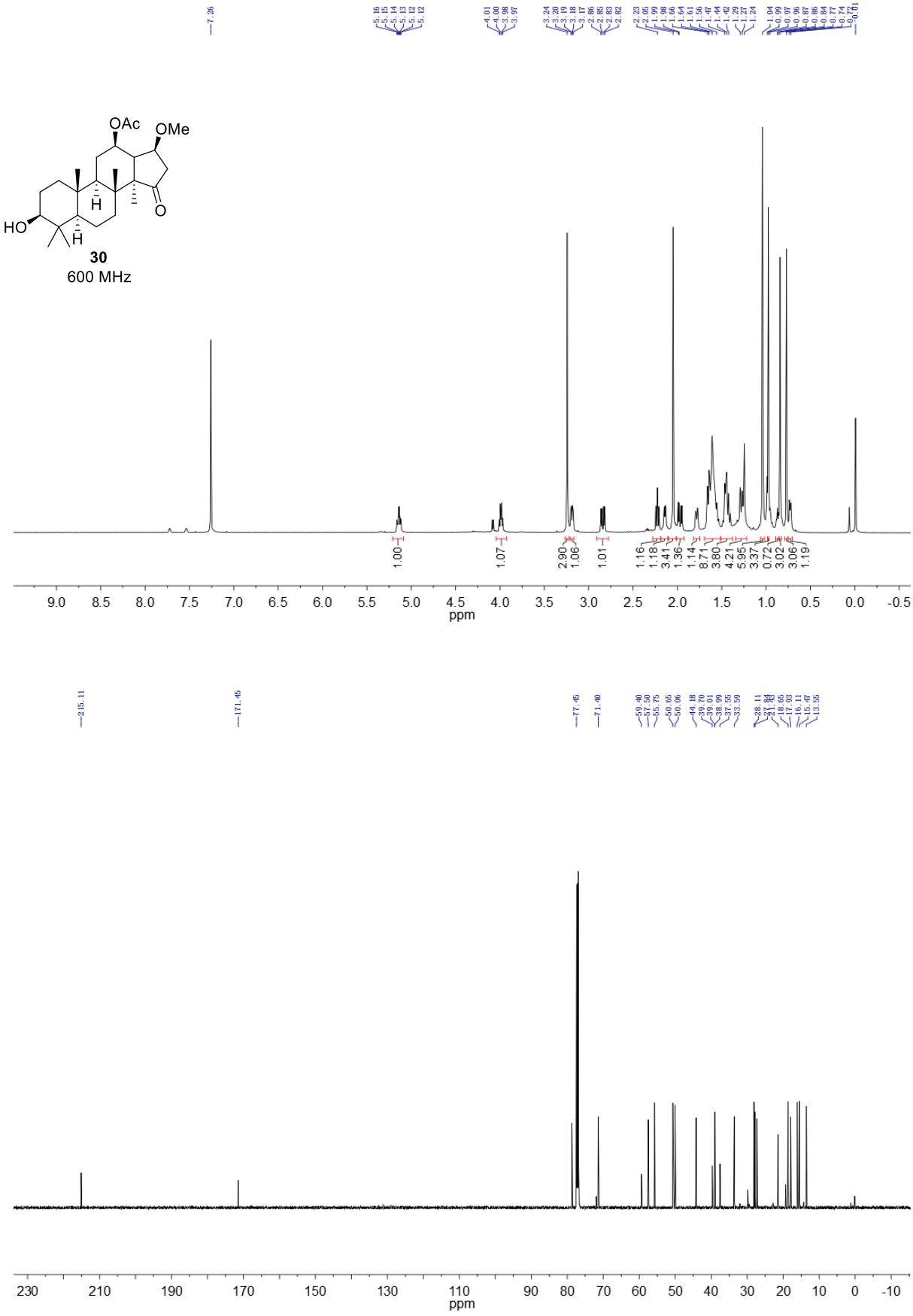

OAc
HO
H
H
O
hupehenol E (natural)
600 MHz
ppm

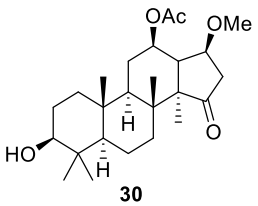

ppm


OAc
OMe
HO
H
H
O
hupehenol B (synthetic)
600 MHz
ppm
ppm


OAc
OMe
HO
H
H
O
hupehenol B (natural)
600 MHz
ppm

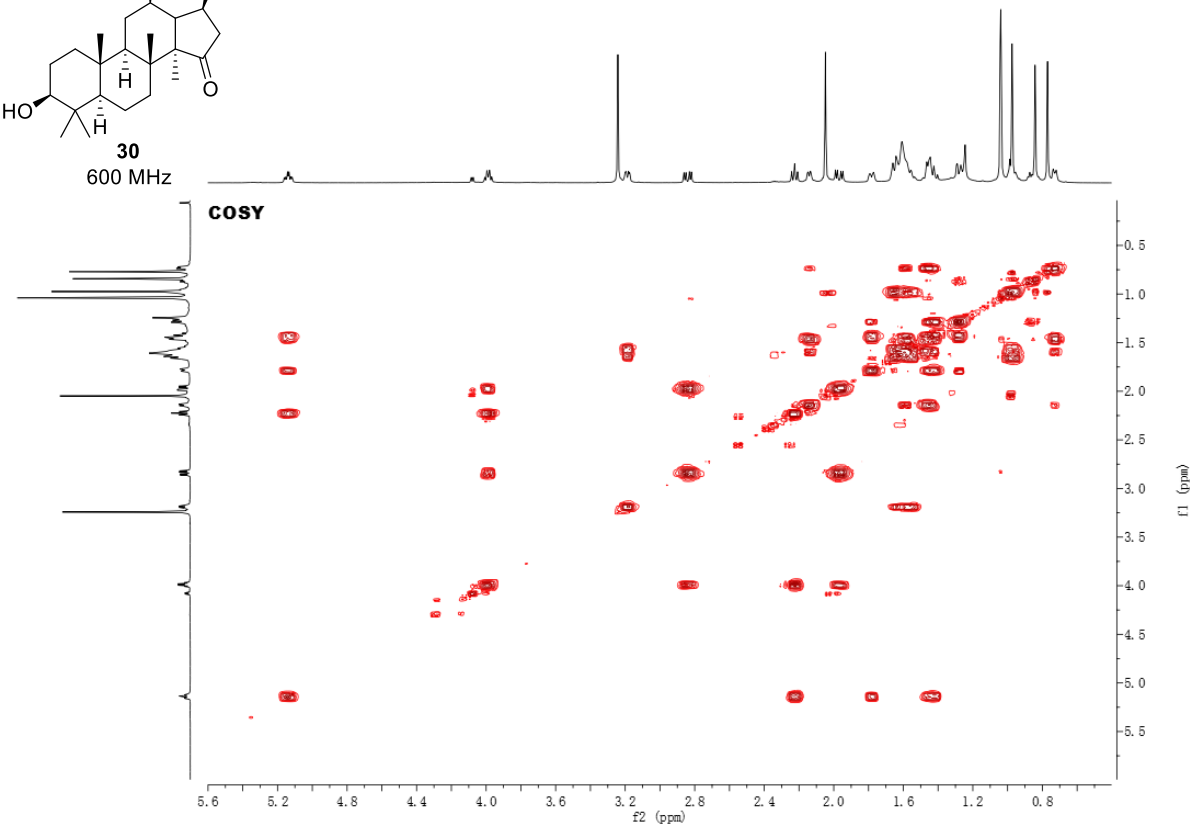

218.76
170.47
ppm

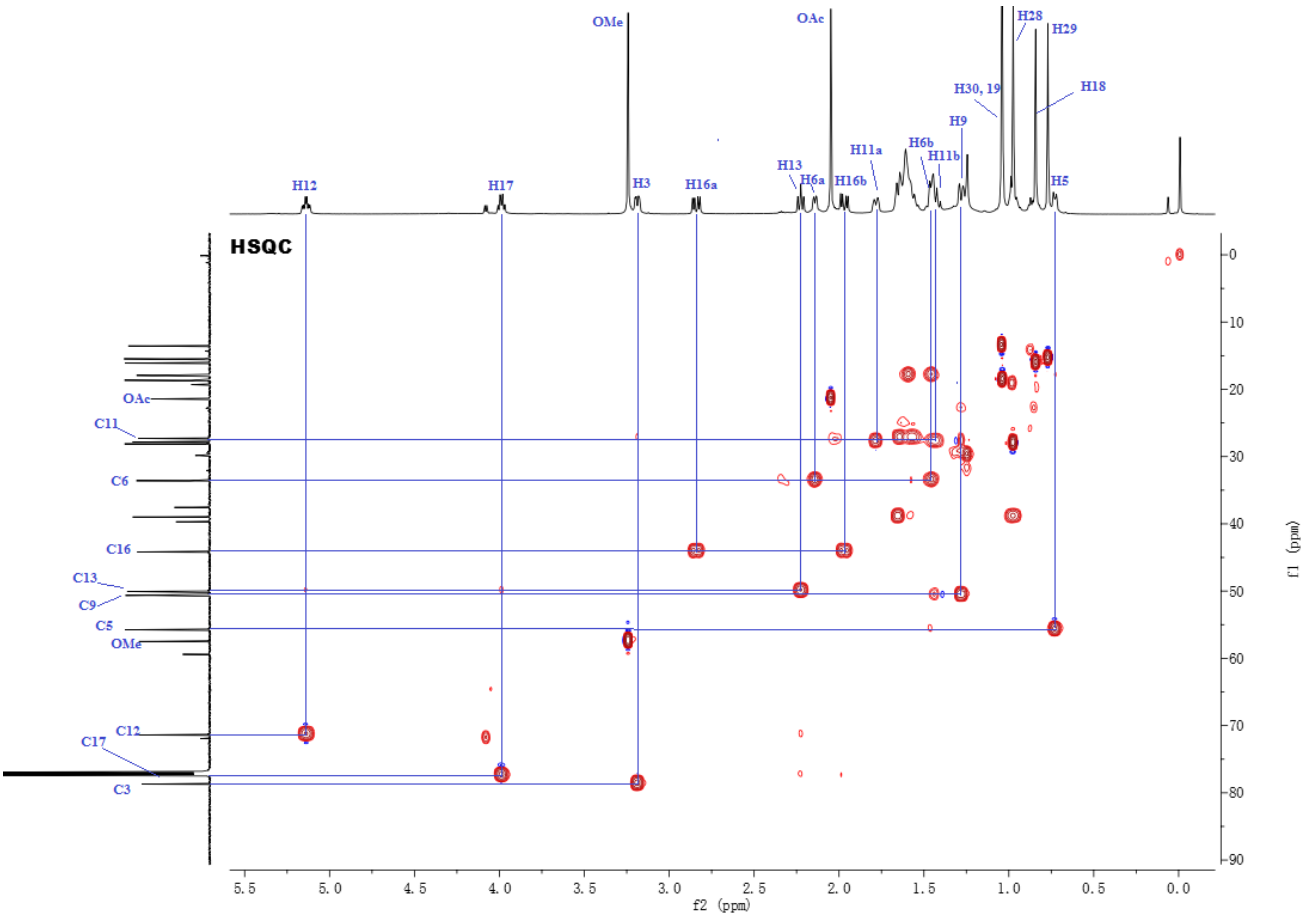

OAc
OMe
HO
H
H
O
30
600 MHz
ppm
ppm

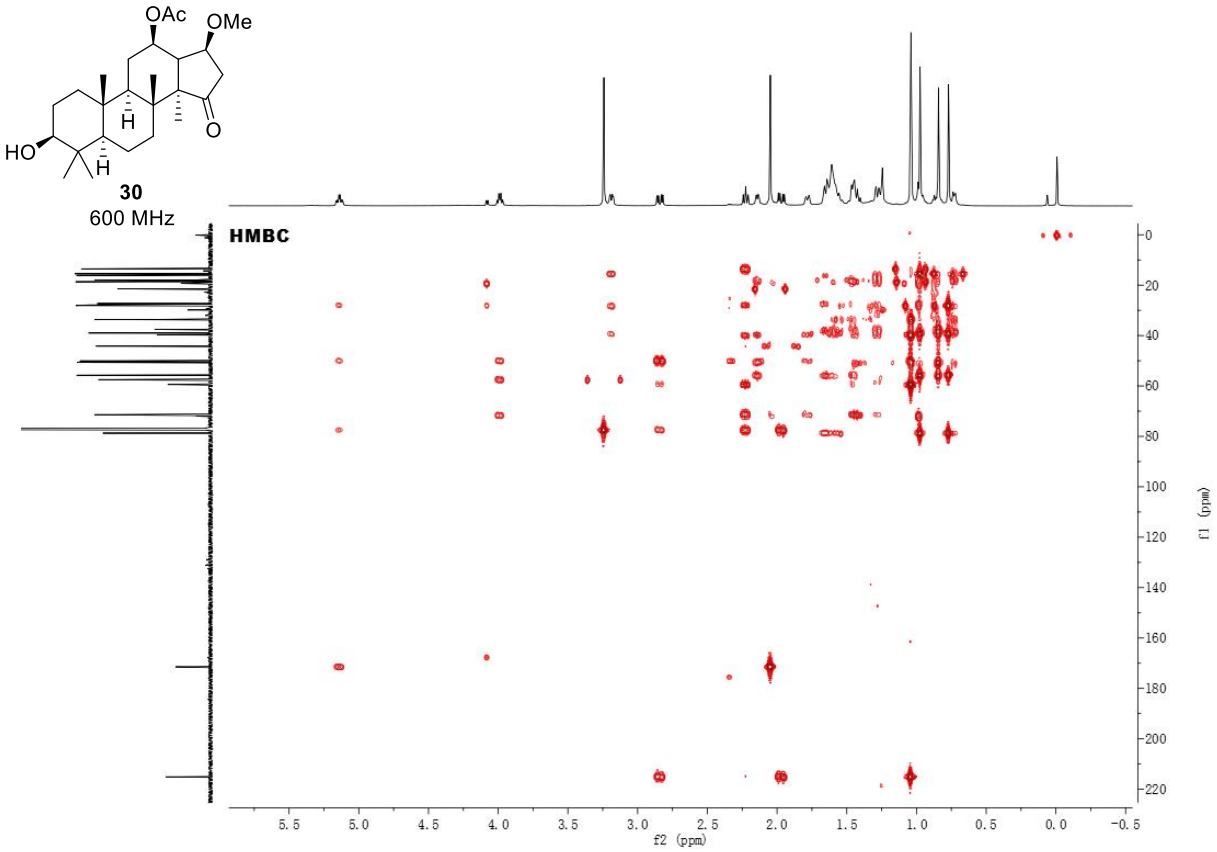

OAc
OMe
HO
H
H
O

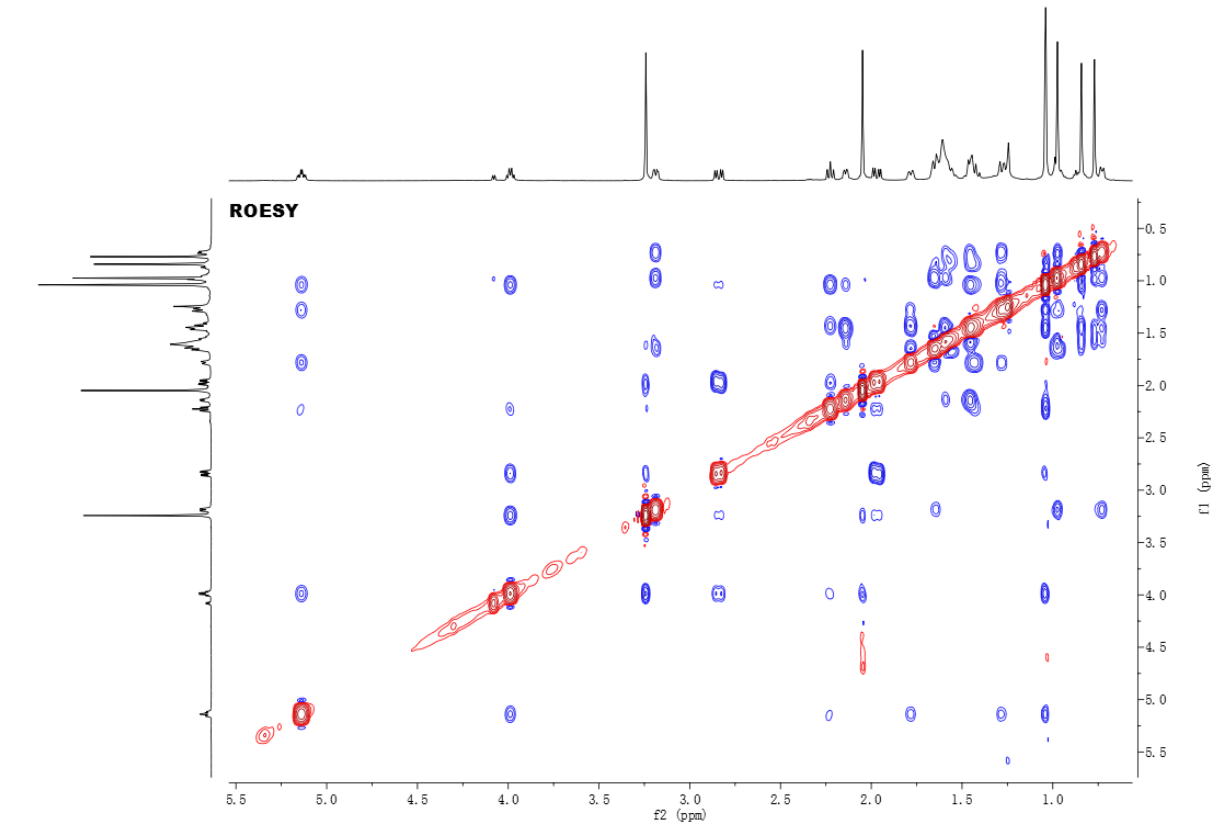
30

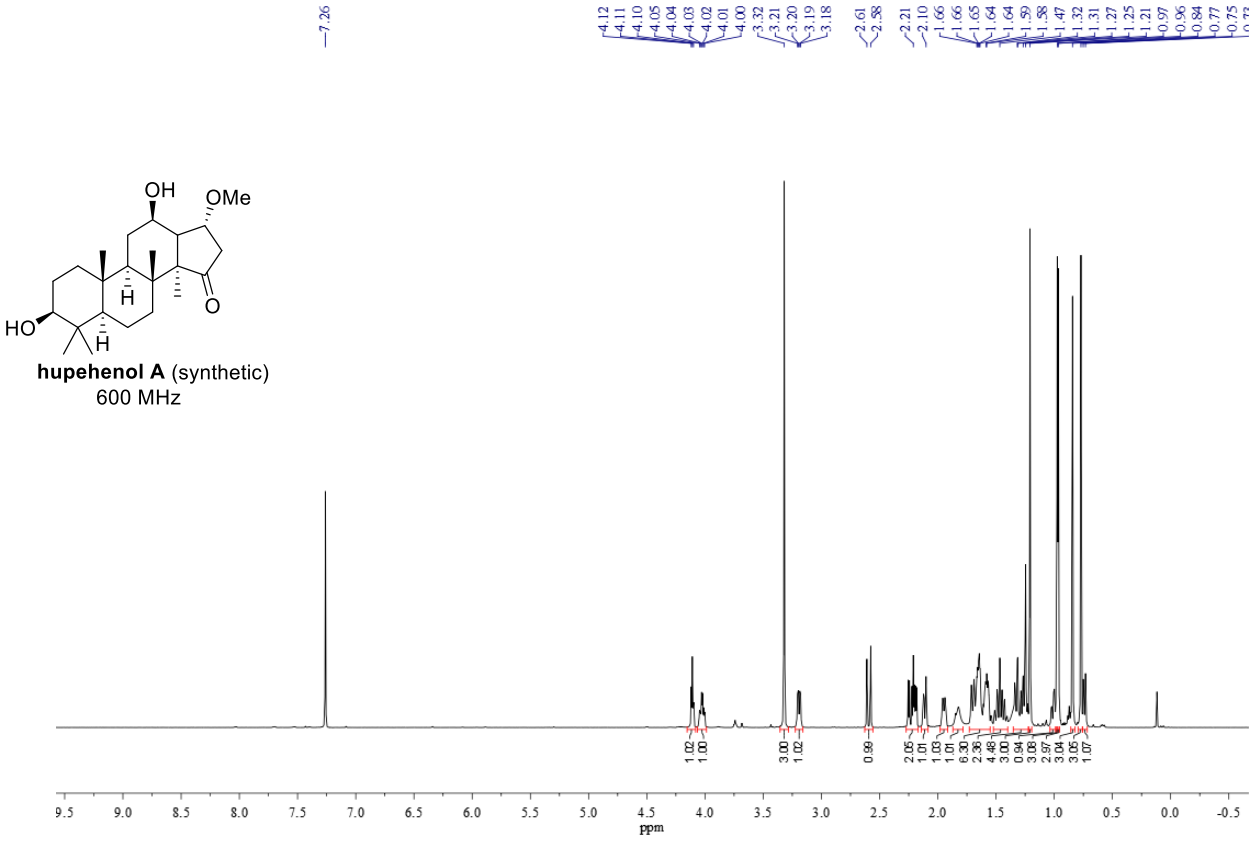
600 MHz

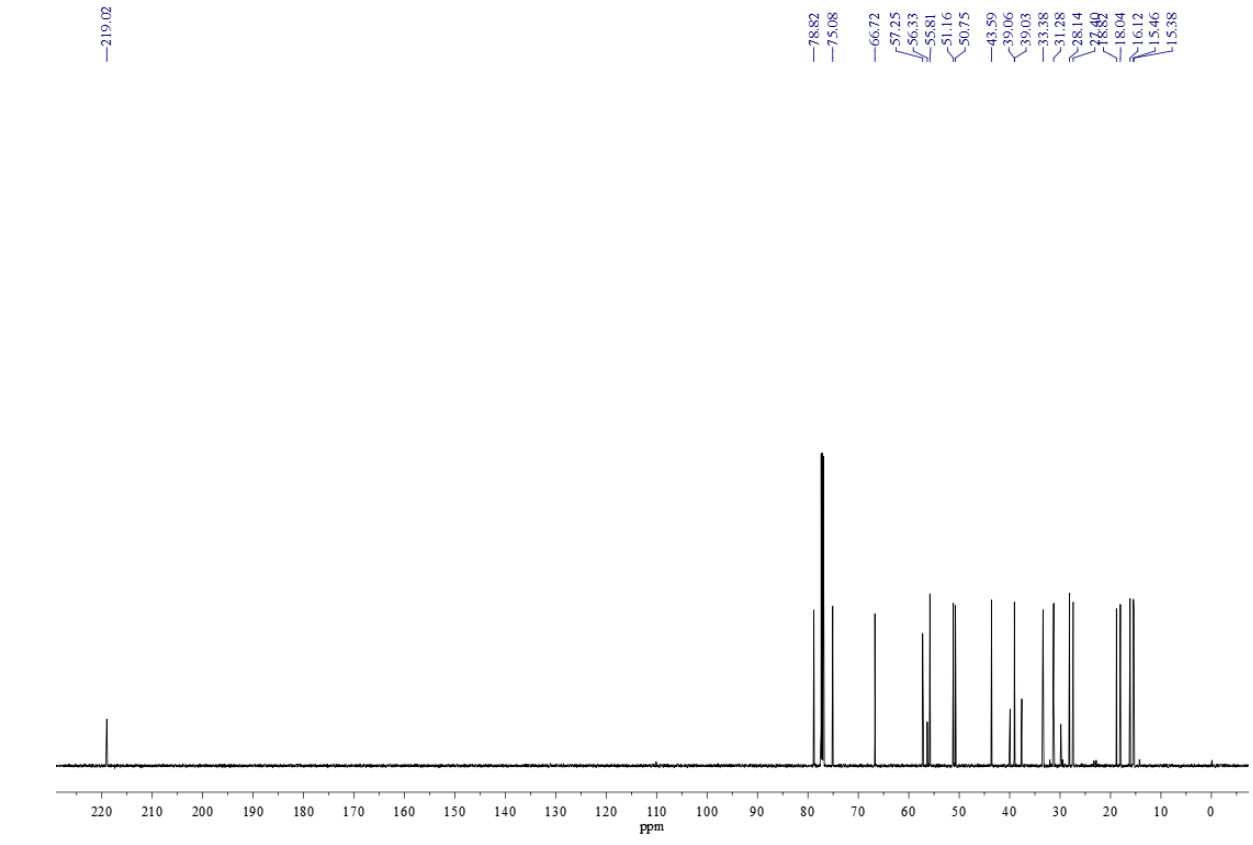

COSY
f2 (ppm)
f1 (ppm)

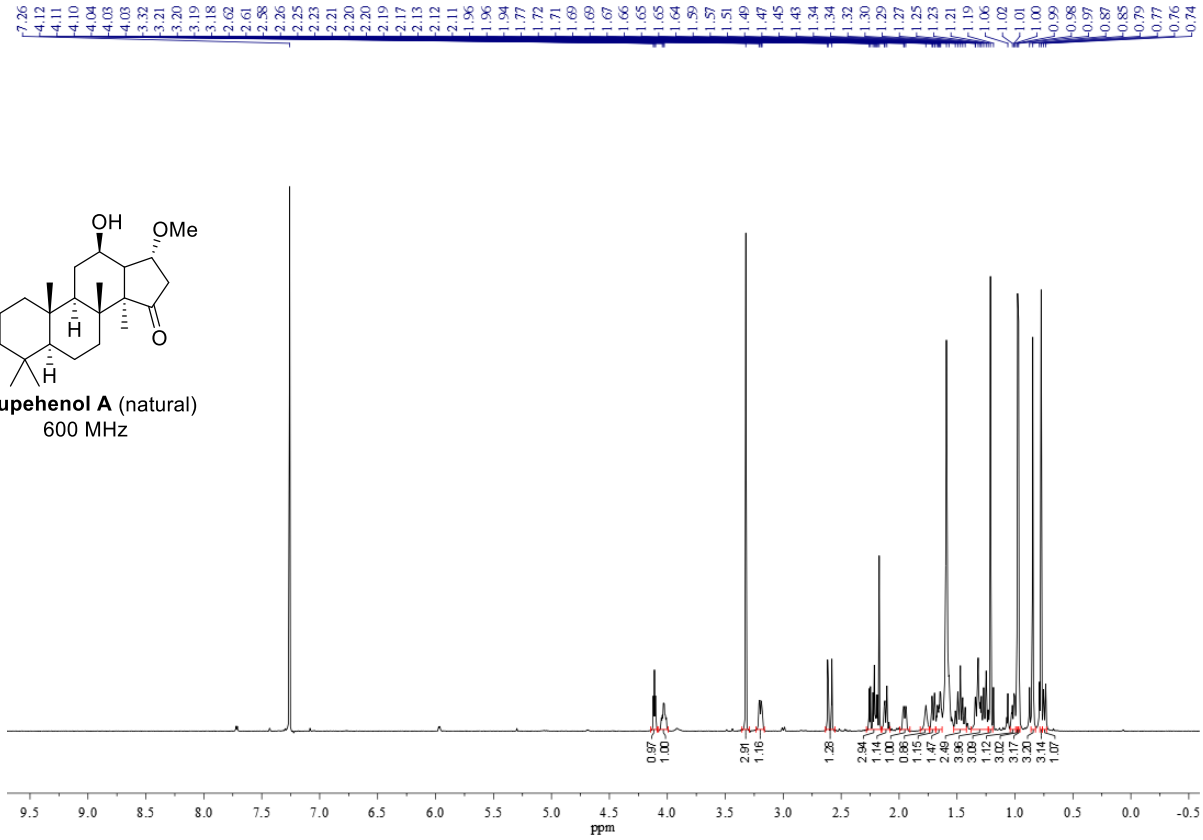

HSQC
OMe
OAc
H28
H29
H30, 19
H18
H9
H11a
H6b
H11b
H13
H6a
H16b
H12
H17
H3
H16a
H5
OAc
C11
C6
C16
C13
C9
C5
OMe
C12
C17
C3
f2 (ppm)
f1 (ppm)

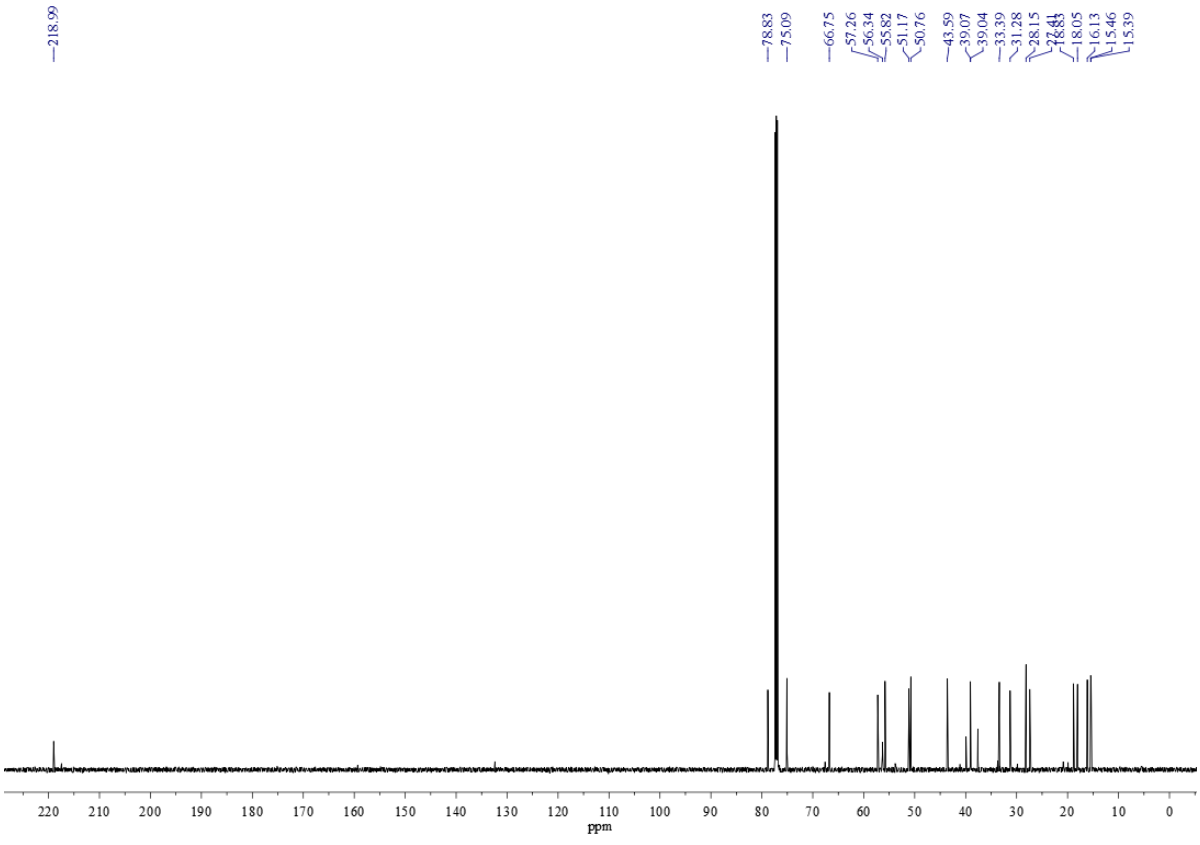

OAc
OMe
HO
H
H
O
30
600 MHz
HMBC
f2 (ppm)
f1 (ppm)

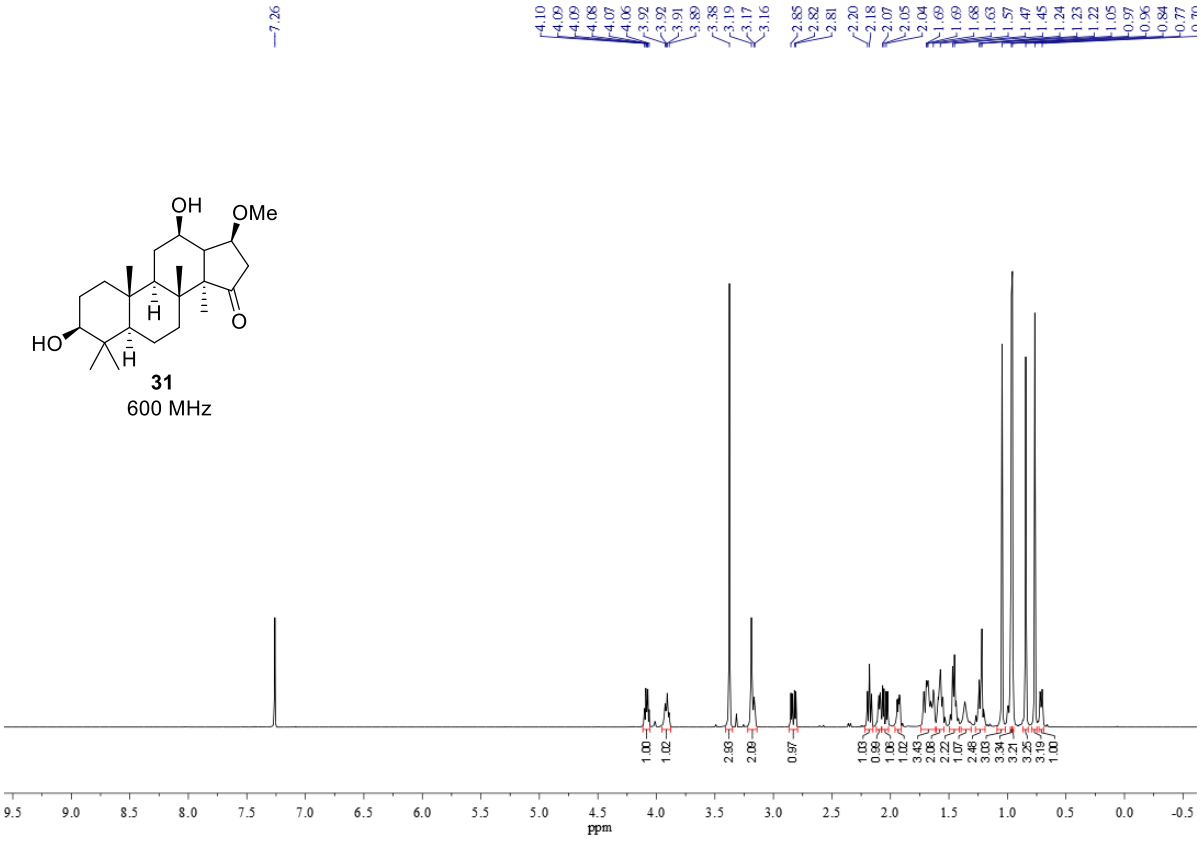

ROESY
f2 (ppm)
f1 (ppm)

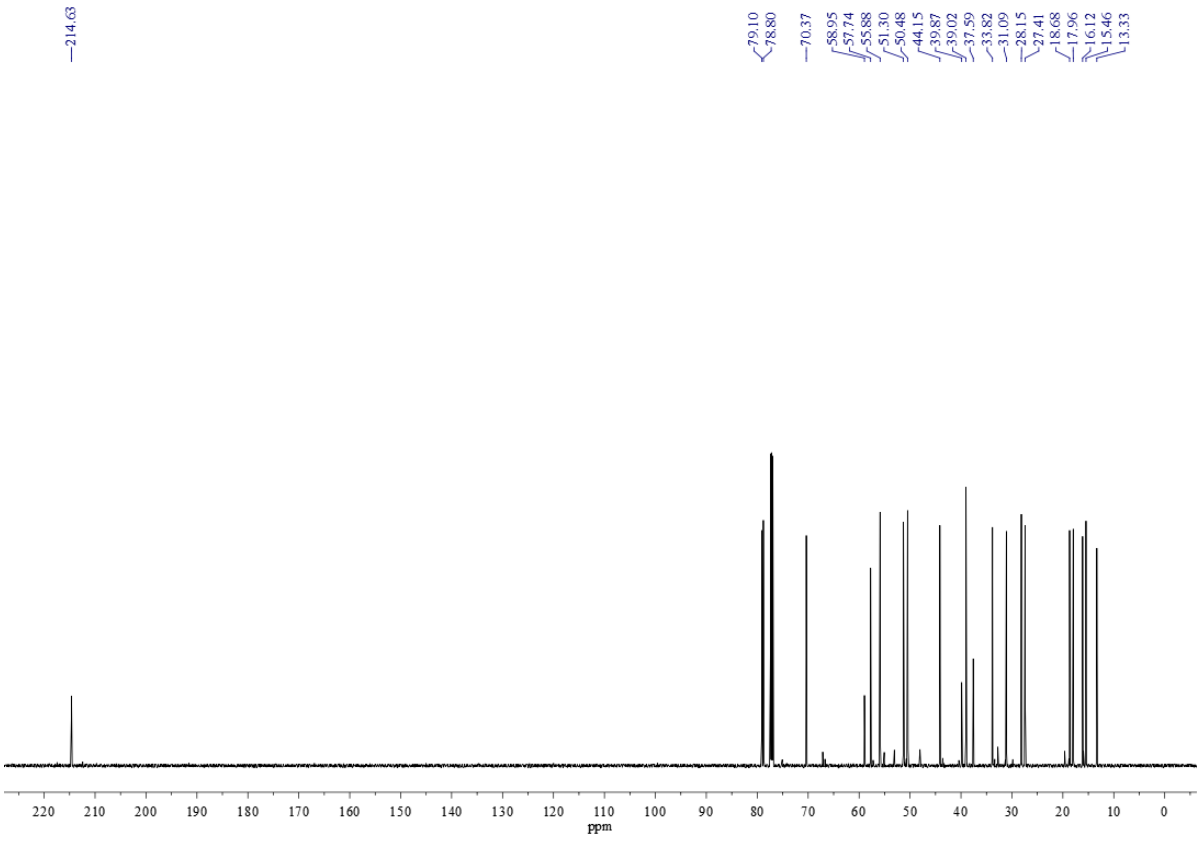

OH
OMe
H
O
HO
H
hupehenol A (synthetic)
600 MHz
ppm

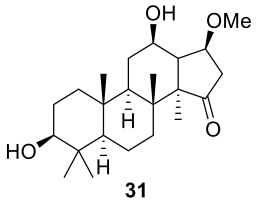

ppm


OH
OMe
H
O
HO
H
hupehenol A (natural)
600 MHz
ppm

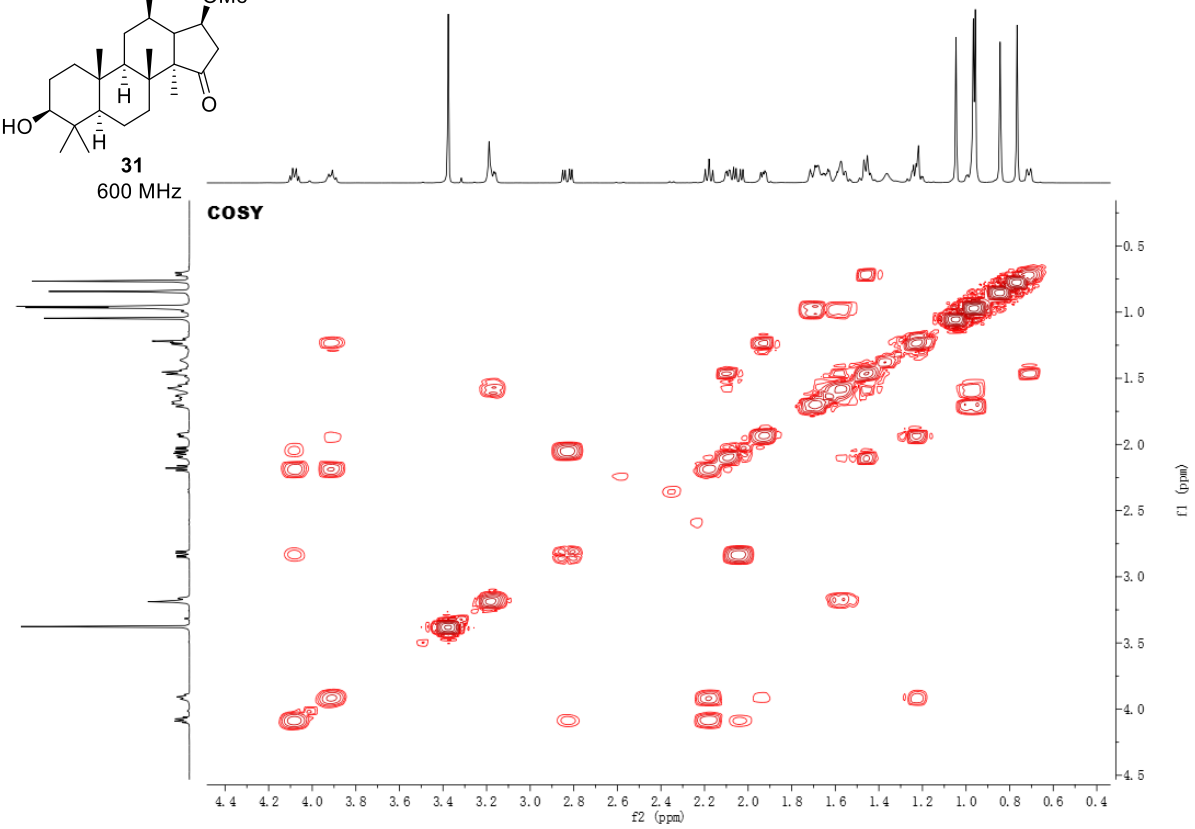

ppm

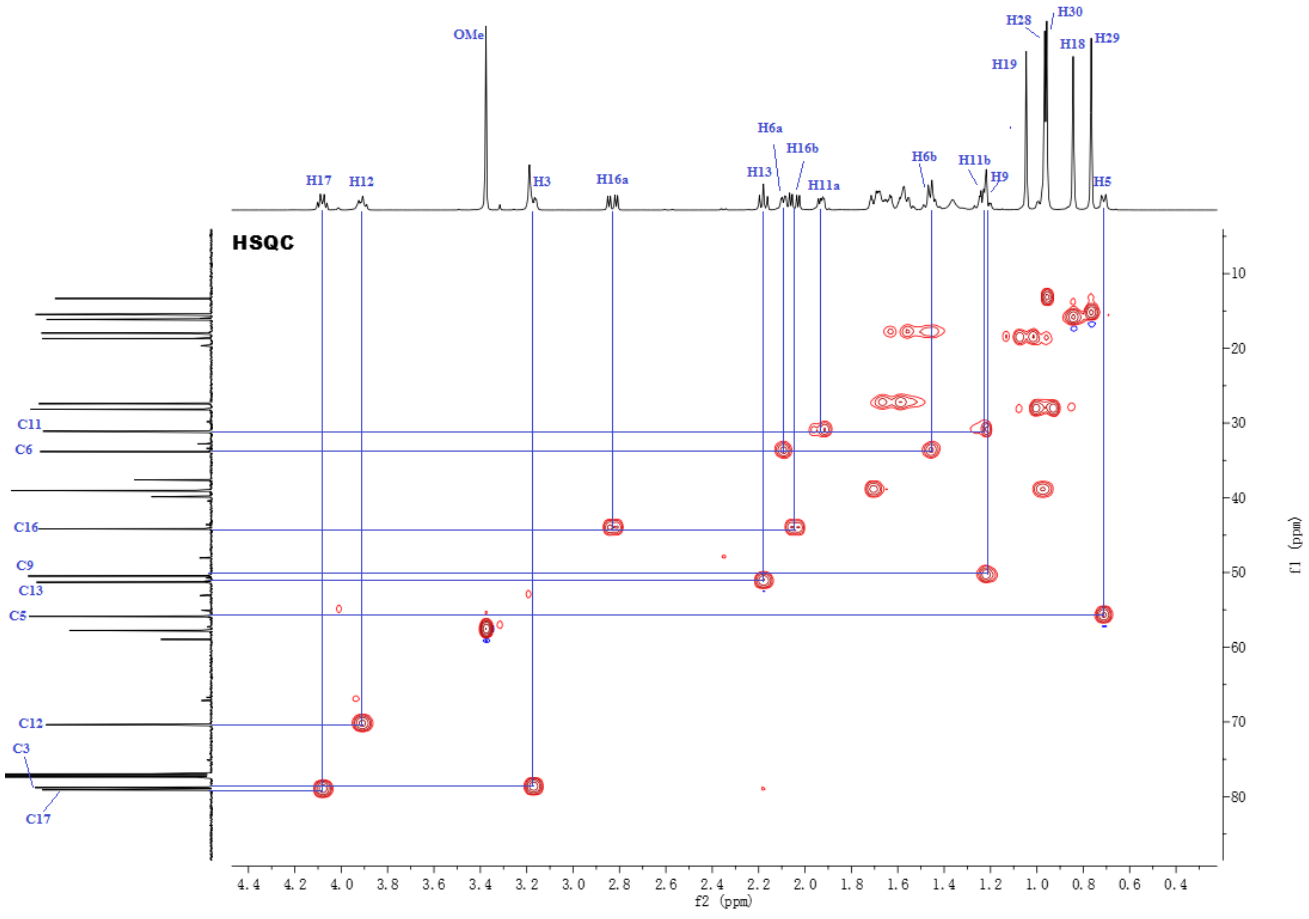

OH
OMe
H
HO
H
O
31
600 MHz
7.26
4.10
4.09
4.09
4.08
4.07
4.06
3.92
3.92
3.91
3.89
3.38
3.19
3.17
3.16
2.85
2.82
2.81
2.20
2.18
2.07
2.05
2.04
1.69
1.69
1.68
1.63
1.57
1.47
1.45
1.24
1.23
1.22
1.05
0.97
0.96
0.84
0.77
1.00
1.02
2.89
2.09
0.97
1.03
0.99
1.00
1.02
3.43
2.08
2.22
1.07
2.48
3.03
3.34
3.21
3.25
3.19
1.00
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
ppm

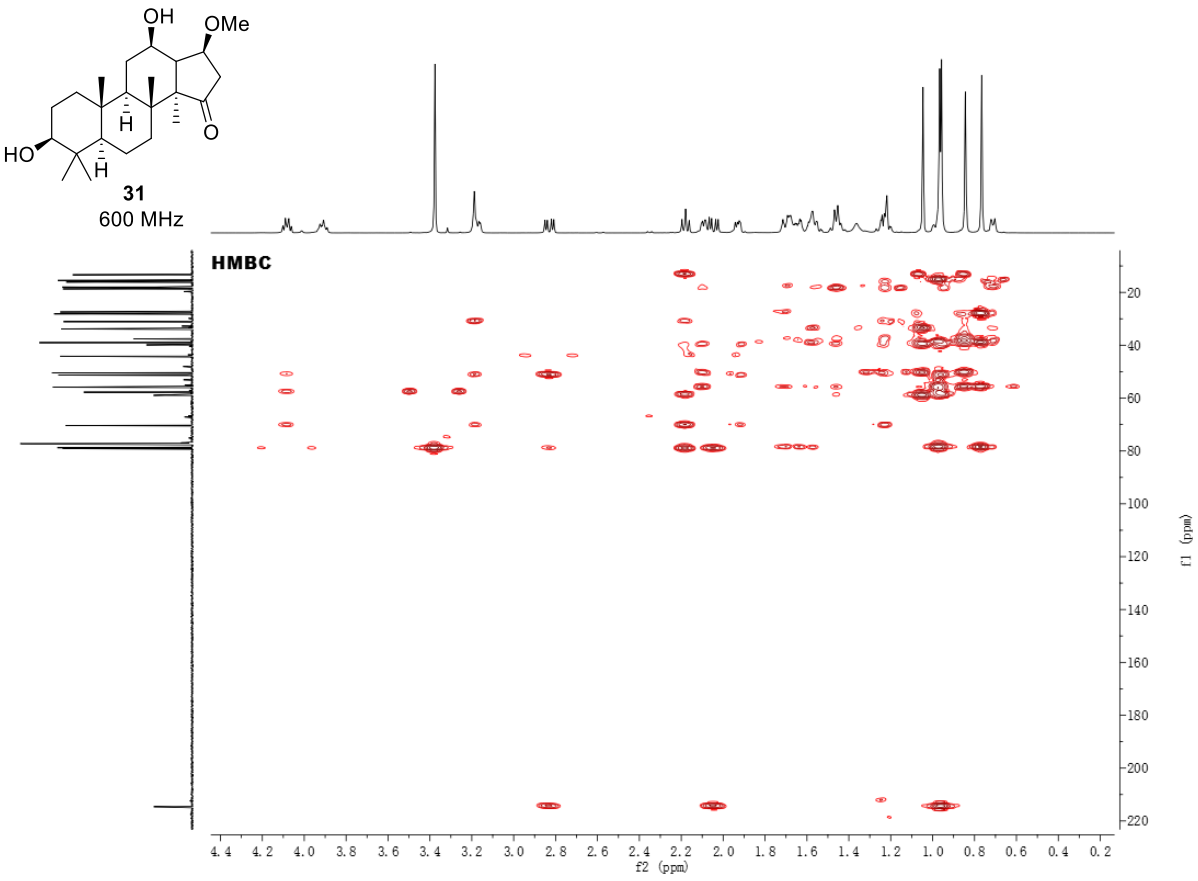

214.63
79.10
78.80
70.37
58.95
57.74
55.88
51.30
50.48
44.15
39.87
39.02
37.59
33.82
31.09
28.15
27.41
18.68
17.96
16.12
15.46
13.33
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm


OH
OMe
H
HO
H
O

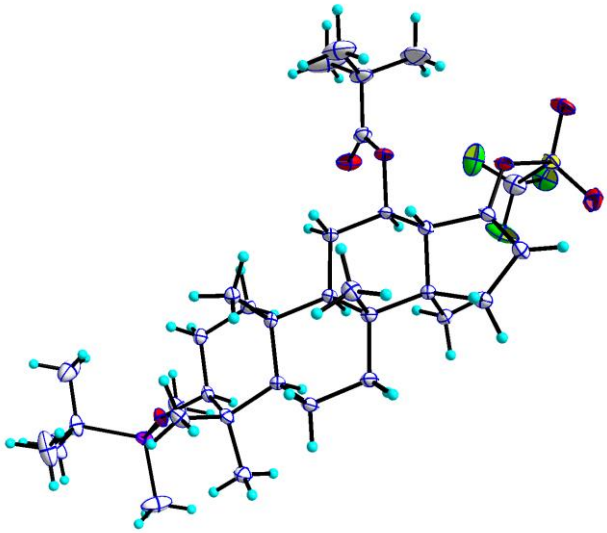
31
600 MHz


COSY
f2 (ppm)
f1 (ppm)


HSQC
OMe
H17
H12
H3
H16a
H6a
H16b
H13
H11a
H6b
H11b
H9
H19
H28
H30
H18
H29
H5
C11
C6
C16
C9
C13
C5
C12
C3
C17
f2 (ppm)
f1 (ppm)

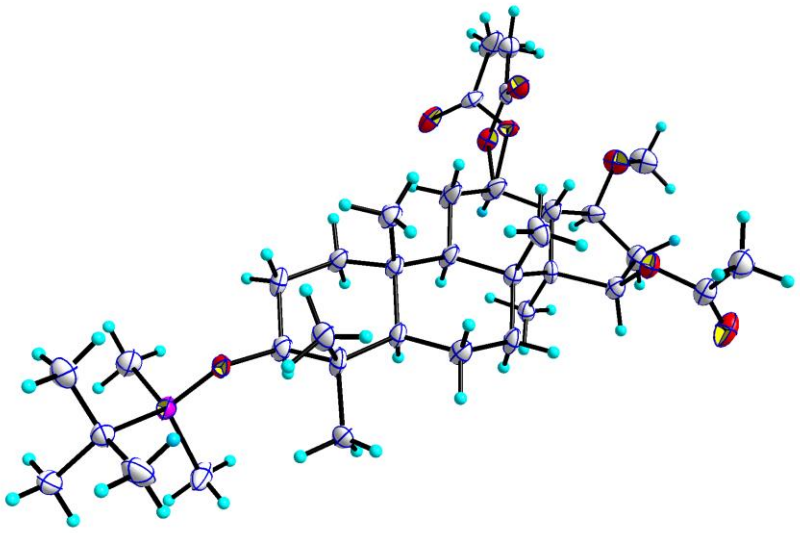

OH
OMe
HO
H
H
O
31
600 MHz
HMBC
f2 (ppm)
f1 (ppm)

Crystal data for compound **17**: $C_{34}H_{57}F_3O_6SSi$, M = 678.95, orthorhombic, a = 9.526(2) Å, b = 15.182(3) Å, c = 25.702(5) Å, α = 90.00 °, β = 90.00 °, γ = 90.00 °, V = 3717.2(13) Å^3, T = 100(2) K, space group $P212121$, Z = 4, μ(MoKα) = 0.174 mm^{-1}, 36539 reflections measured, 9281 independent reflections (R_{int} = 0.0567). The final R_1 values were 0.0449 ($I > 2\sigma(I)$). The final $wR(F^2)$ values were 0.1104 ($I > 2\sigma(I)$). The final R_1 values were 0.0546 (all data). The final $wR(F^2)$ values were 0.1154 (all data). The goodness of fit on F^2 was 1.050. Flack parameter = -0.02(6). (**CCDC 1405681**)



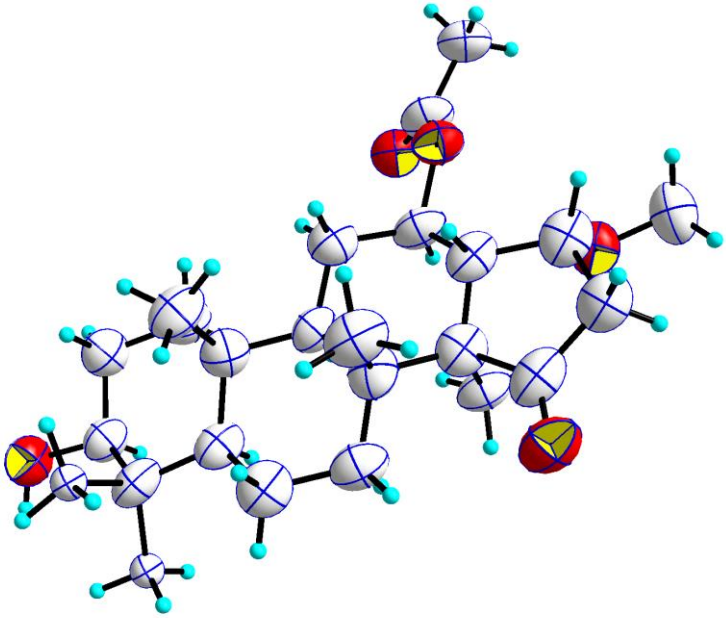
Displacement ellipsoids are drawn at the 50% probability level.

Crystal data for compound **26a**: $C_{33}H_{58}O_6Si$, M = 578.88, monoclinic, a = 11.1824(8) Å, b = 12.1736(10) Å, c = 12.1396(9) Å, α = 90.00 °, β = 100.485(3) °, γ = 90.00 °, V = 1625.0(2) Å^3, T = 100(2) K, space group $P21$, Z = 2, μ(CuKα) = 0.960 mm^{-1}, 12191 reflections measured, 4693 independent reflections (R_{int} = 0.0555). The final R_1 values were 0.0771 ($I > 2\sigma(I)$). The final $wR(F^2)$ values were 0.2346 ($I > 2\sigma(I)$). The final R_1 values were 0.0793 (all data). The final $wR(F^2)$ values were 0.2370 (all data). The goodness of fit on F^2 was 1.163. Flack parameter = 0.11(6). The Hooft parameter is 0.127(18) for 1812 Bijvoet pairs. (**CCDC 1405682**)



Displacement ellipsoids are drawn at the 50% probability level.

Crystal data for compound **4**: $C_{25}H_{40}O_5$, M = 420.57, orthorhombic, a = 7.3472(5) Å, b = 11.4681(8) Å, c = 26.6223(19) Å, α = 90.00 °, β = 90.00 °, γ = 90.00 °, V = 2243.2(3) Å^3, T = 100(2) K, space group $P212121$, Z = 4, μ(CuKα) = 0.676 mm^{-1}, 11376 reflections measured, 3830 independent reflections (R_{int} = 0.0912). The final R_1 values were 0.1555 ($I > 2\sigma(I)$). The final $wR(F^2)$ values were 0.3719 ($I > 2\sigma(I)$). The final R_1 values were 0.2829 (all data). The final $wR(F^2)$ values were 0.4569 (all data). The goodness of fit on F^2 was 1.582. Flack parameter = 0.3(9). (**CCDC 1405683**)



Displacement ellipsoids are drawn at the 50% probability level.