

Supplementary Data

First synthesis and characterization of new impurities in obeticholic acid

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²*Department of Pharmaceutical Engineering, China Pharmaceutical University, 24 Tongjiaxiang, Nanjing 210009, P. R. of China*

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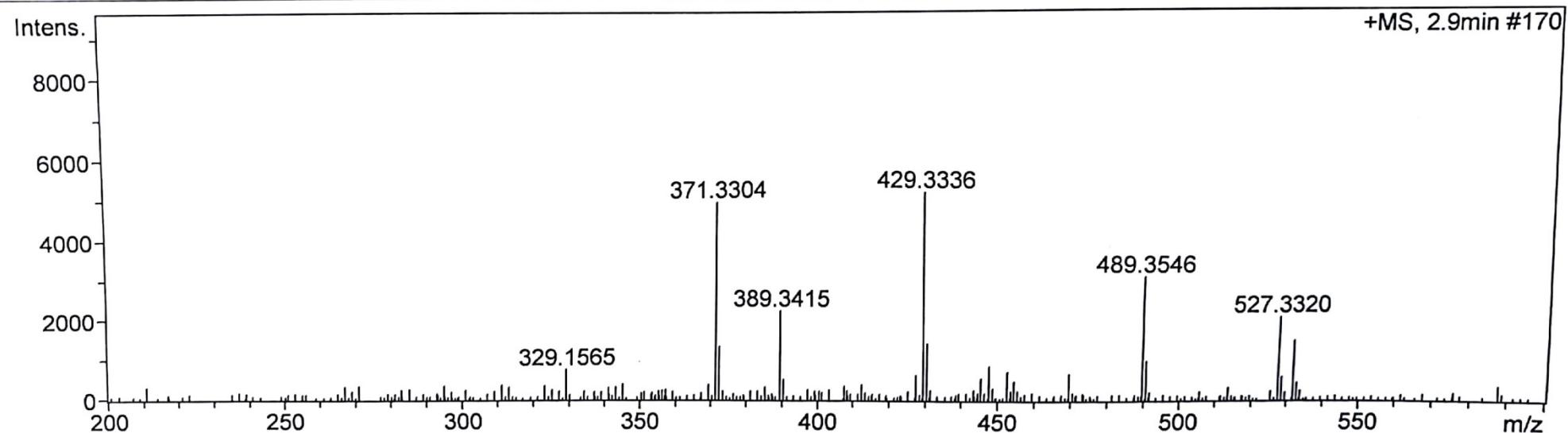
Figure S44. HMBC spectrum of impurity **2**.

Mass Spectrum SmartFormula Report

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Sample Name	14238-06-1	Instrument / Ser#	maXis 4G 21240
Comment			

Acquisition Parameter

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Figure S1. HRMS spectrum of compound 8.

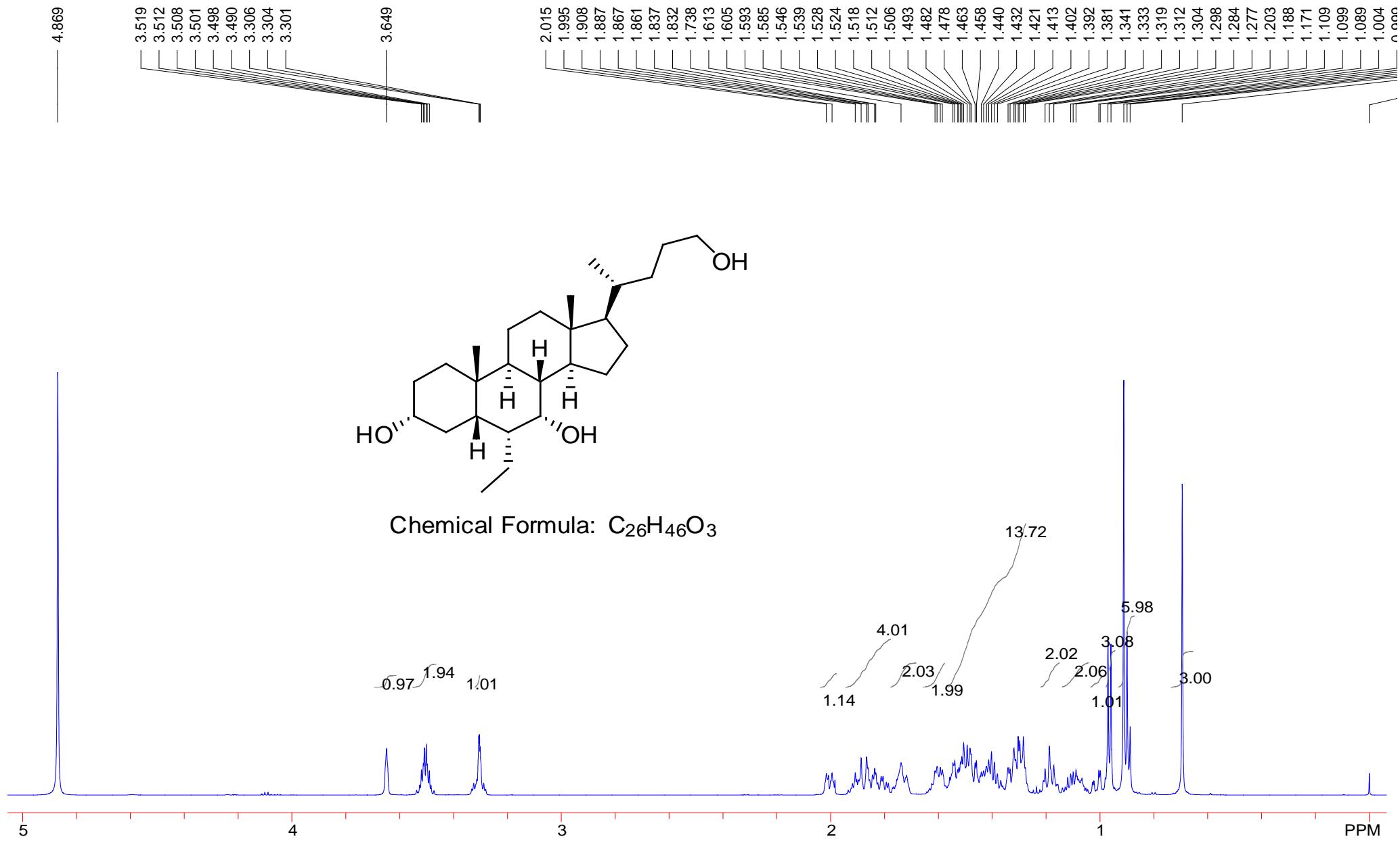


Figure S2. ^1H NMR spectrum of compound 8.

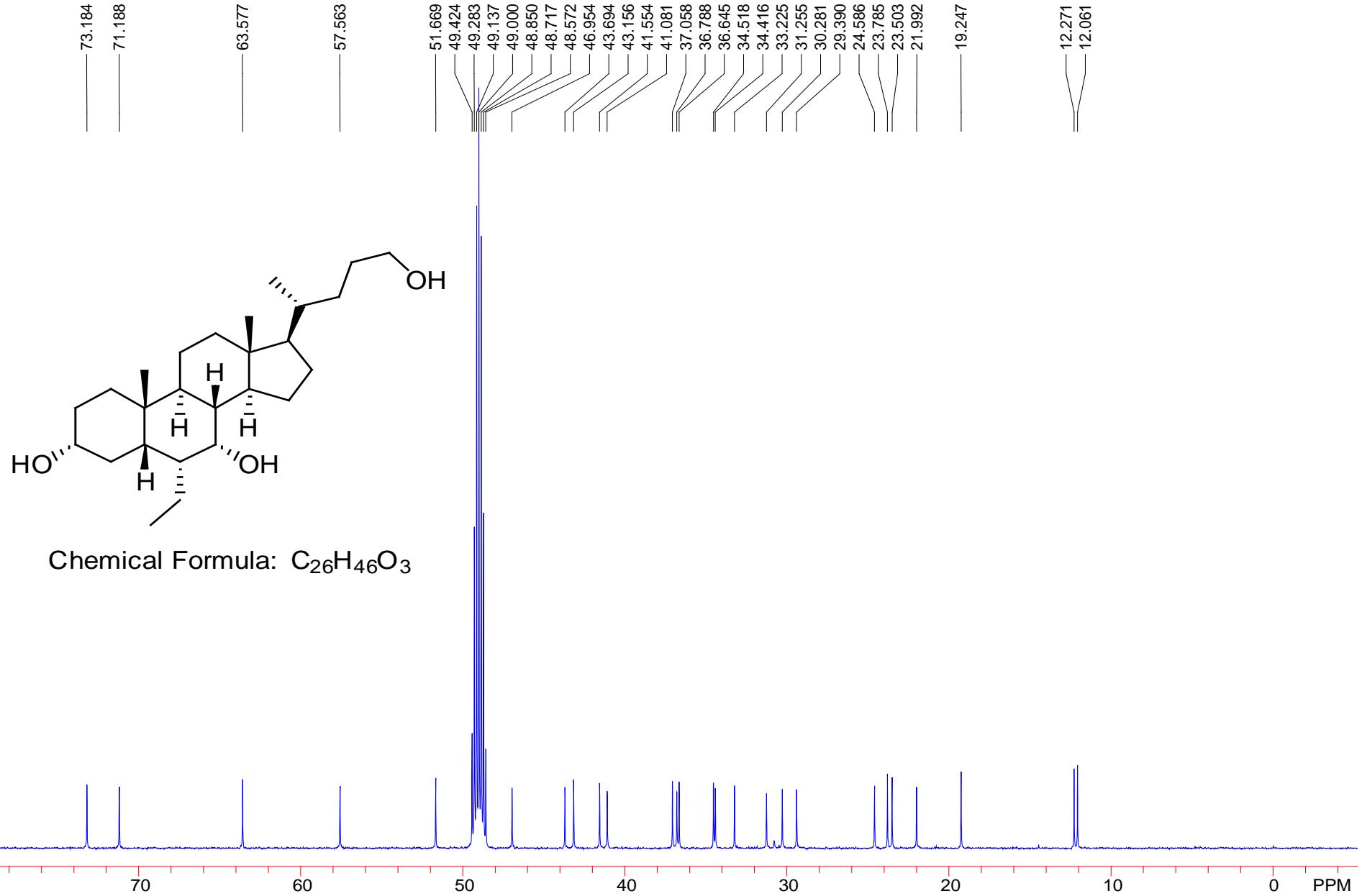
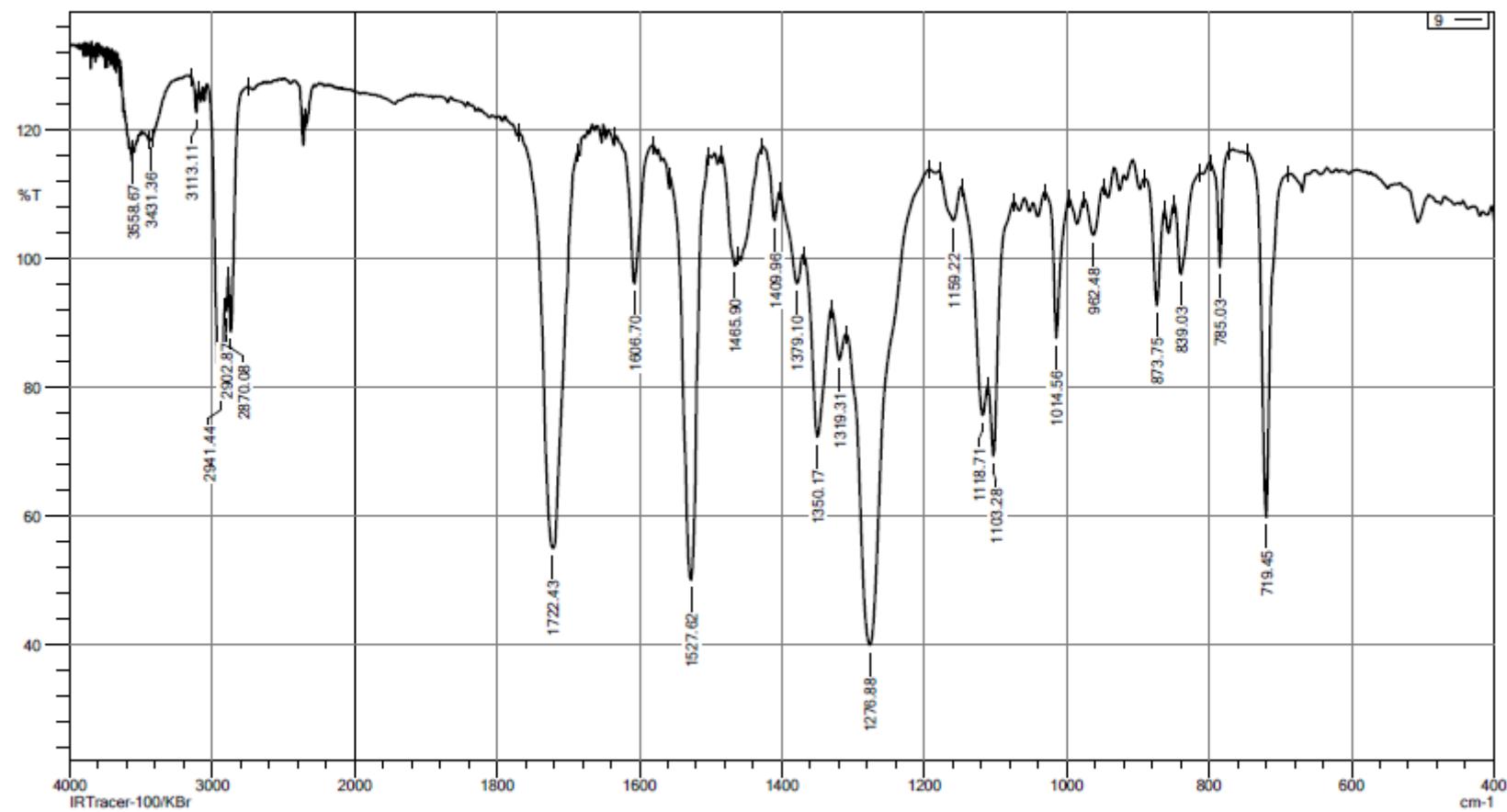


Figure S3. ^{13}C NMR spectrum of compound 8.



1/1

Figure S4. FT-IR spectrum of compound **9**.

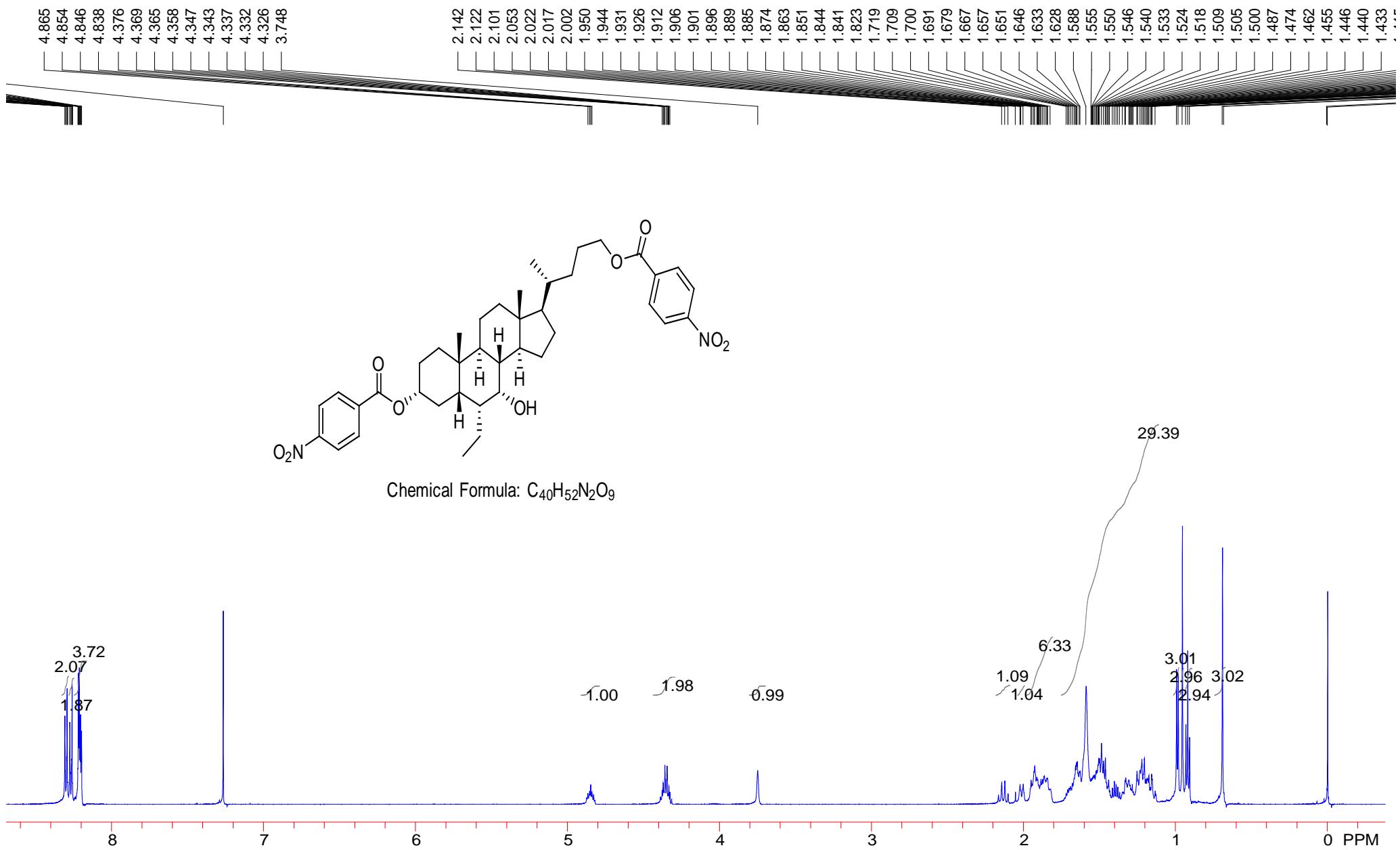


Figure S5. ^1H NMR spectrum of compound 9.

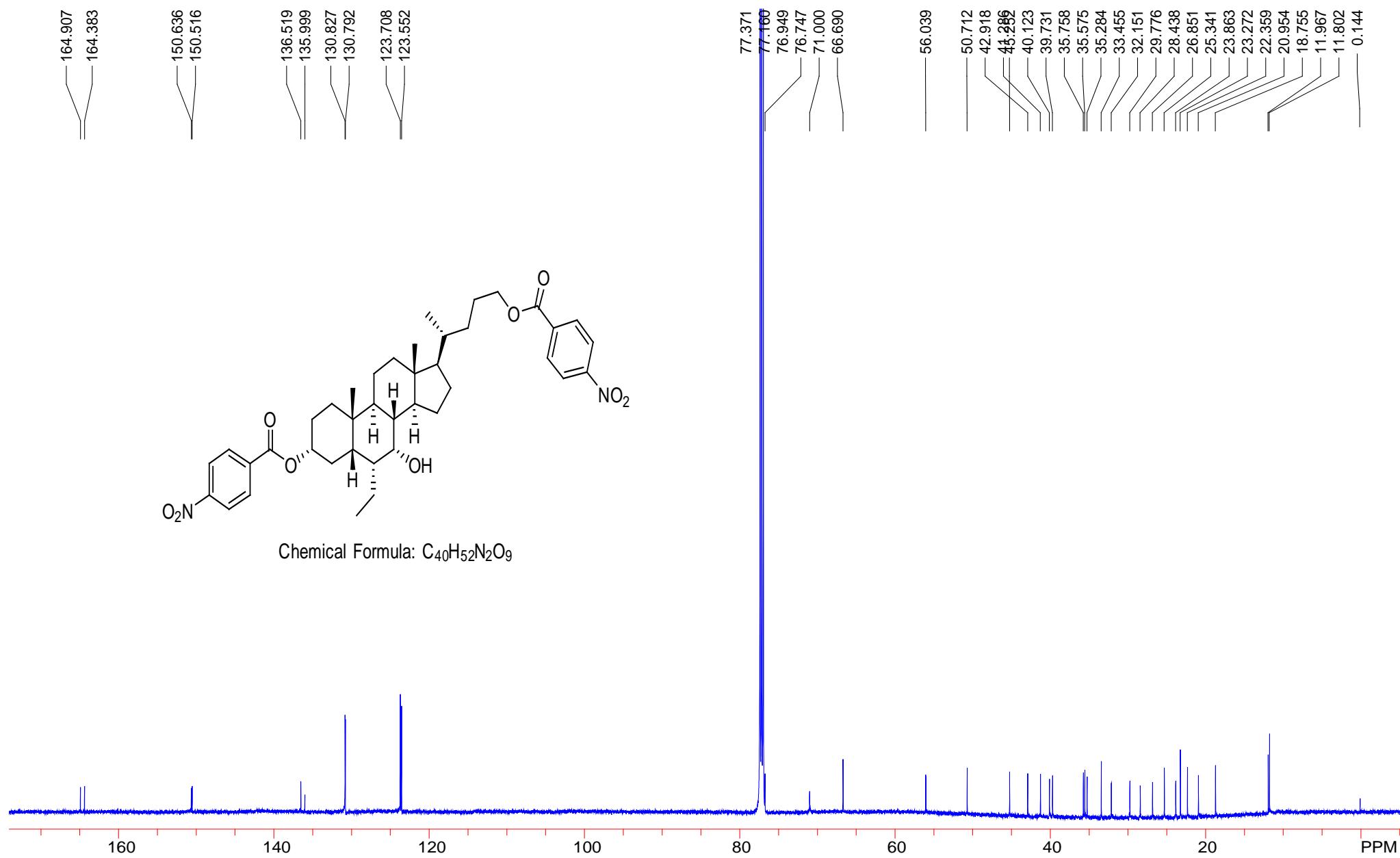
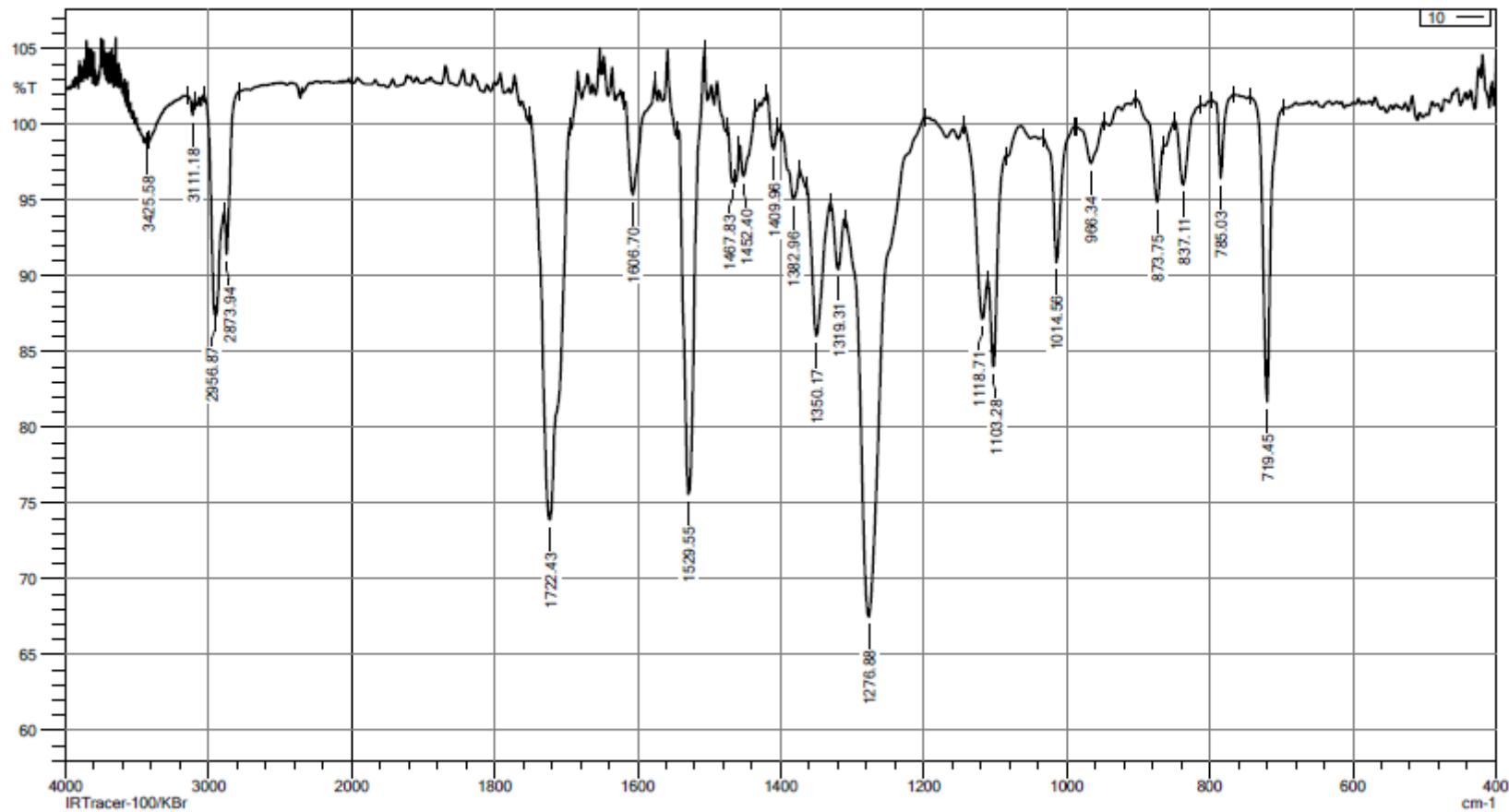


Figure S6. ^{13}C NMR spectrum of compound 9.



1/1

Figure S7. FT-IR spectrum of compound **10**.

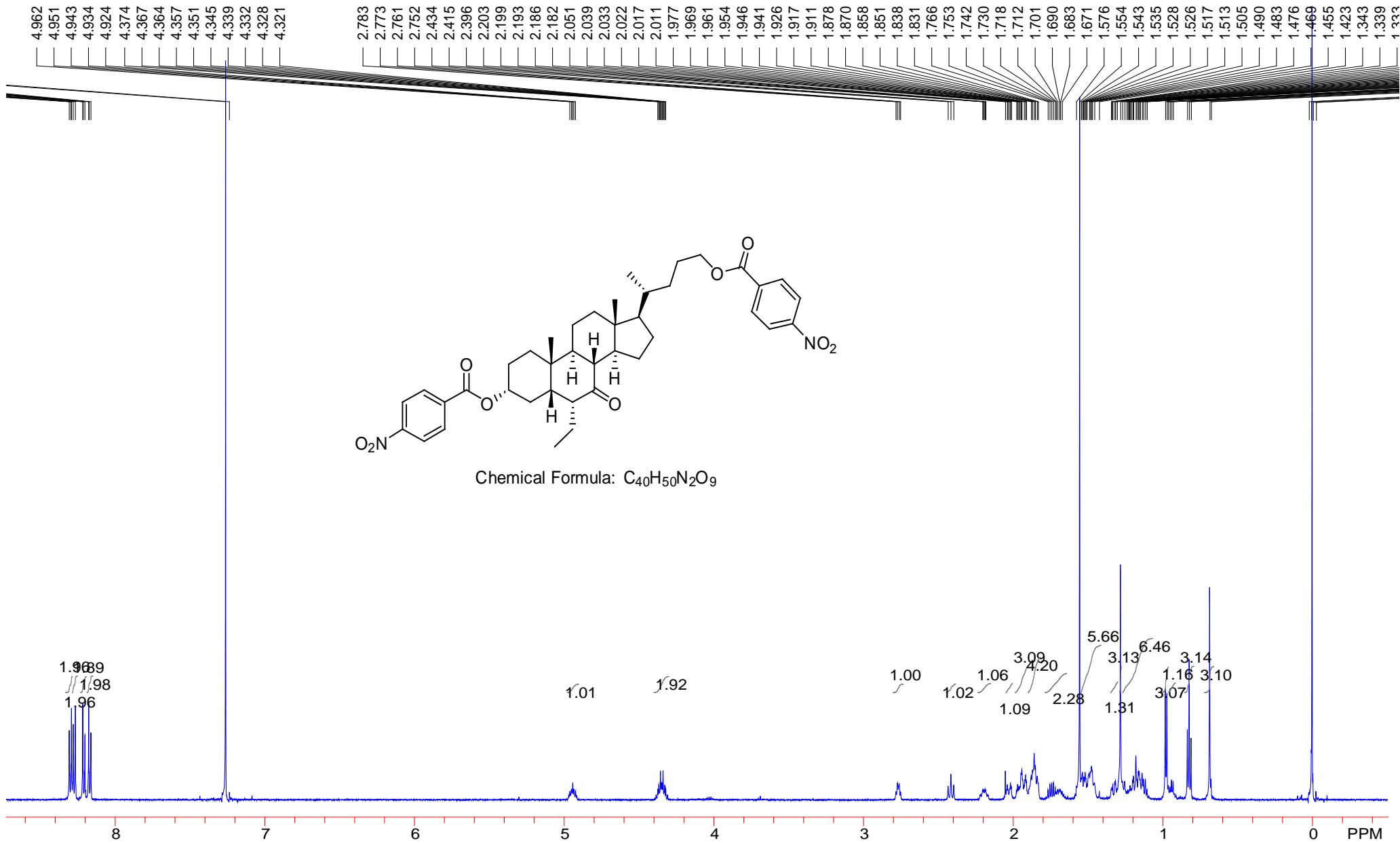


Figure S8. ^1H NMR spectrum of compound **10**.

212.826

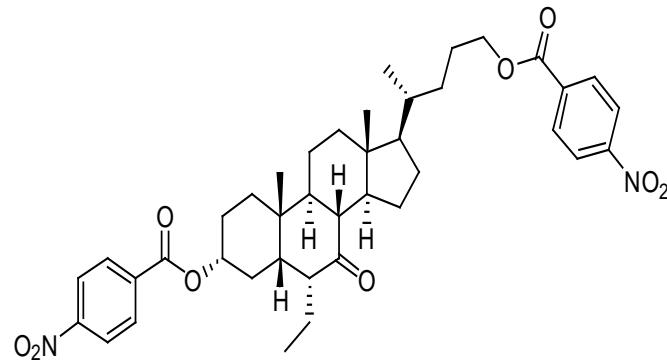
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164.067

150.496

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135.853
130.689
130.653
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66.511

52.054
50.629
54.940
50.013
48.998
43.921
42.660
38.980
35.775
35.289
33.836
32.045
28.441
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26.079
25.213
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Chemical Formula: $C_{40}H_{50}N_2O_9$

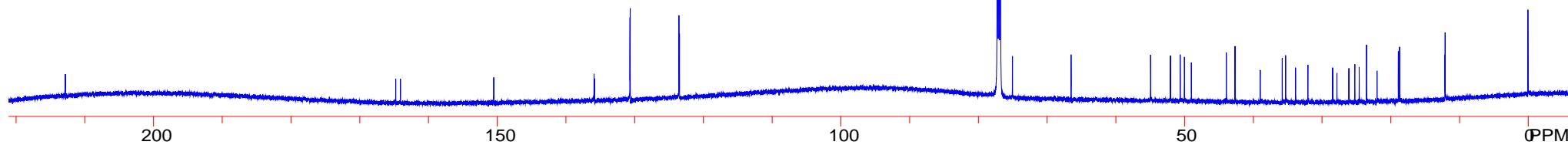
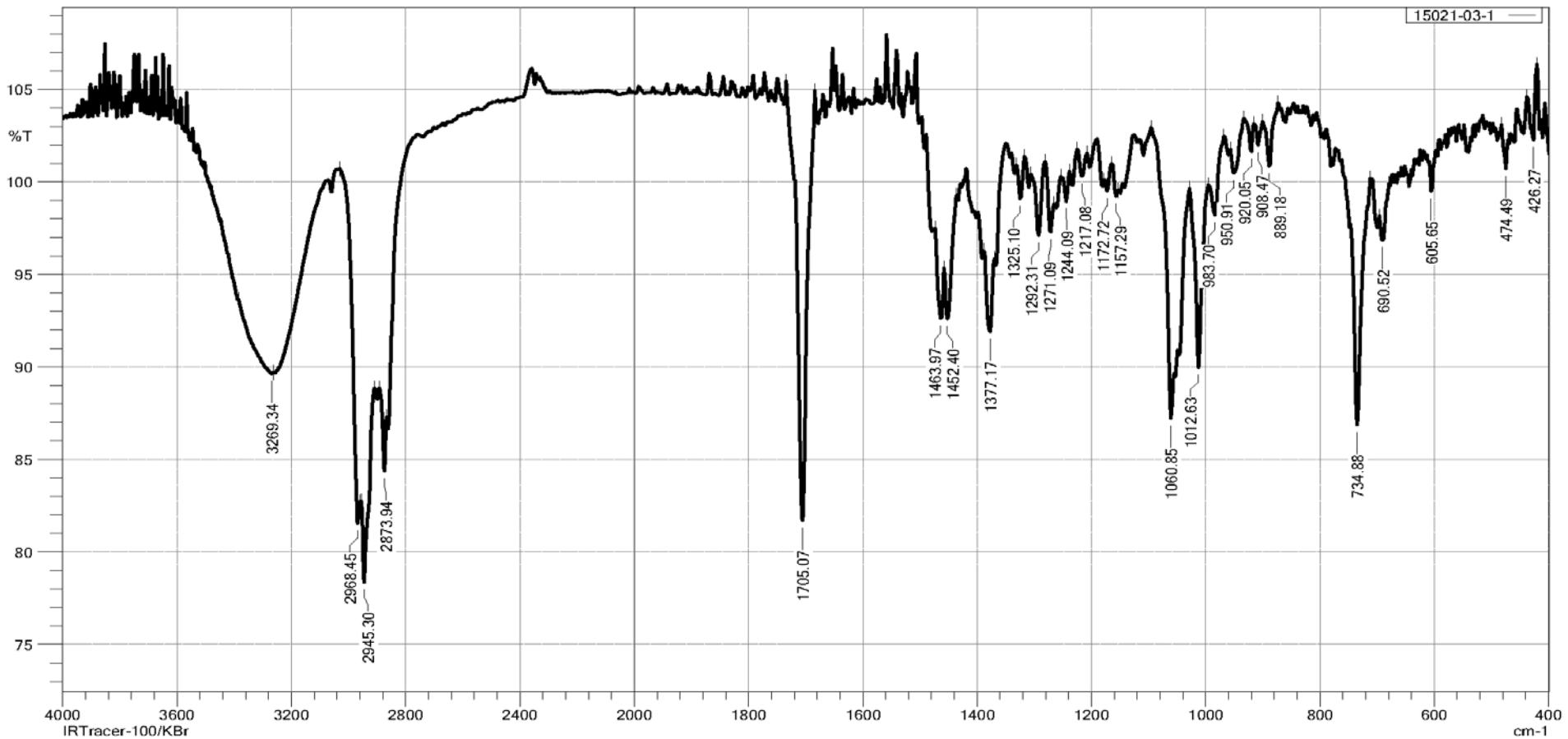


Figure S9. ^{13}C NMR spectrum of compound **10**.

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**Figure S10.** FT-IR spectrum of impurity 1.

Mass Spectrum SmartFormula Report

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Comment

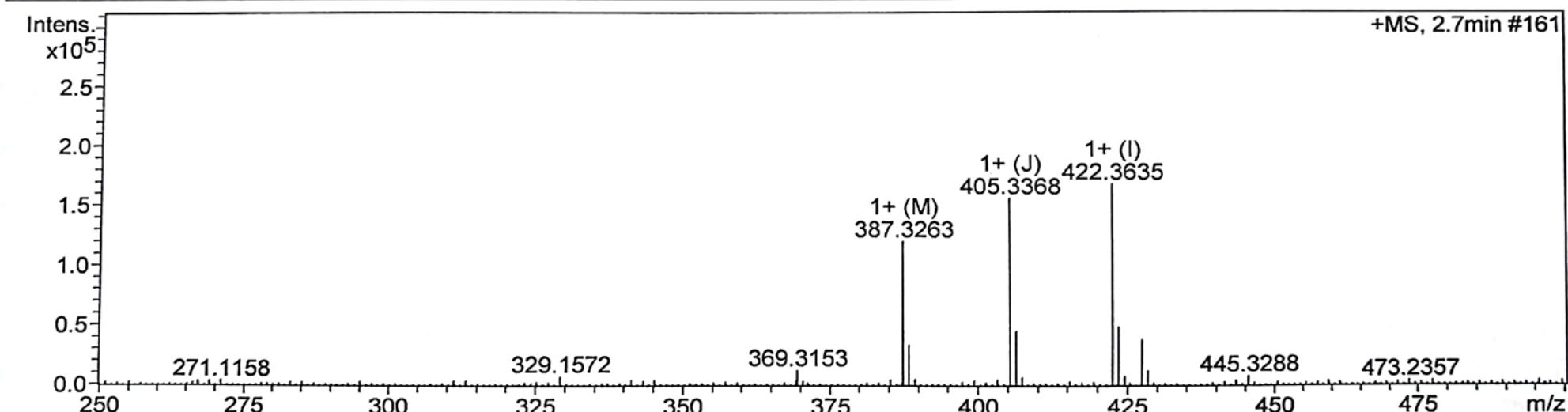
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Operator BDAL@DE

Instrument / Ser# maXis 4G 21240

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Scan End	1500 m/z	Set Collision Cell RF	600.0 Vpp	Set Divert Valve	Waste



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422.3635	1	C 26 H 48 N O 3	100.00	422.3629	-1.5	-1.2	0.8	3.5	even	ok
427.3184	1	C 26 H 44 Na O 3	100.00	427.3183	-0.3	-0.3	25.5	4.5	even	ok

Figure S11. HRMS spectrum of impurity 1.

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2.141
2.136
2.130
2.124
2.120
2.108
2.103
2.054
2.050
2.044
2.033
2.028
2.023
1.936
1.931
1.921
1.915
1.909
1.899
1.893
1.882
1.874
1.867
1.859
1.852
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1.700
1.689
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1.663
1.653
1.638
1.632
1.624
1.615
1.604
1.593
1.585
1.547
1.526
1.520
1.505
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1.466
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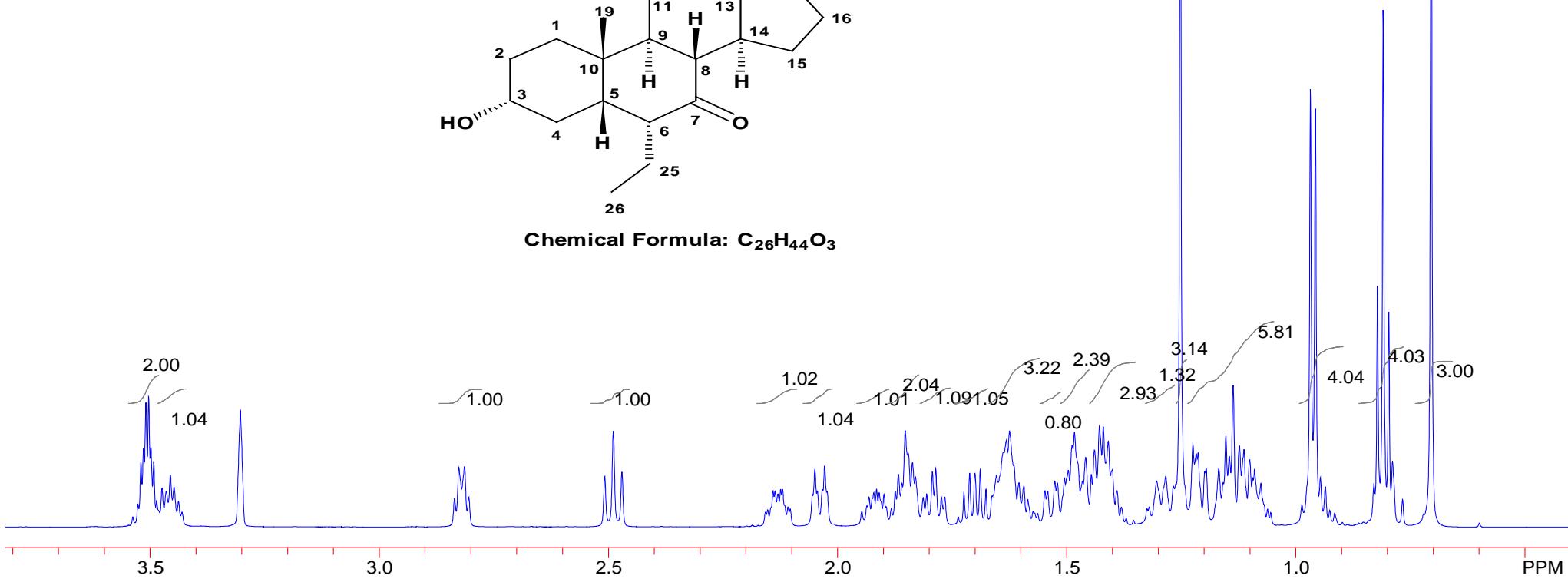
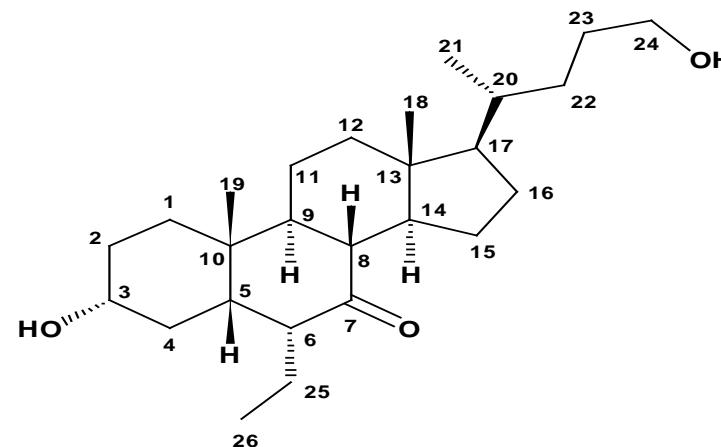


Figure S12. 1H NMR spectrum of impurity 1.

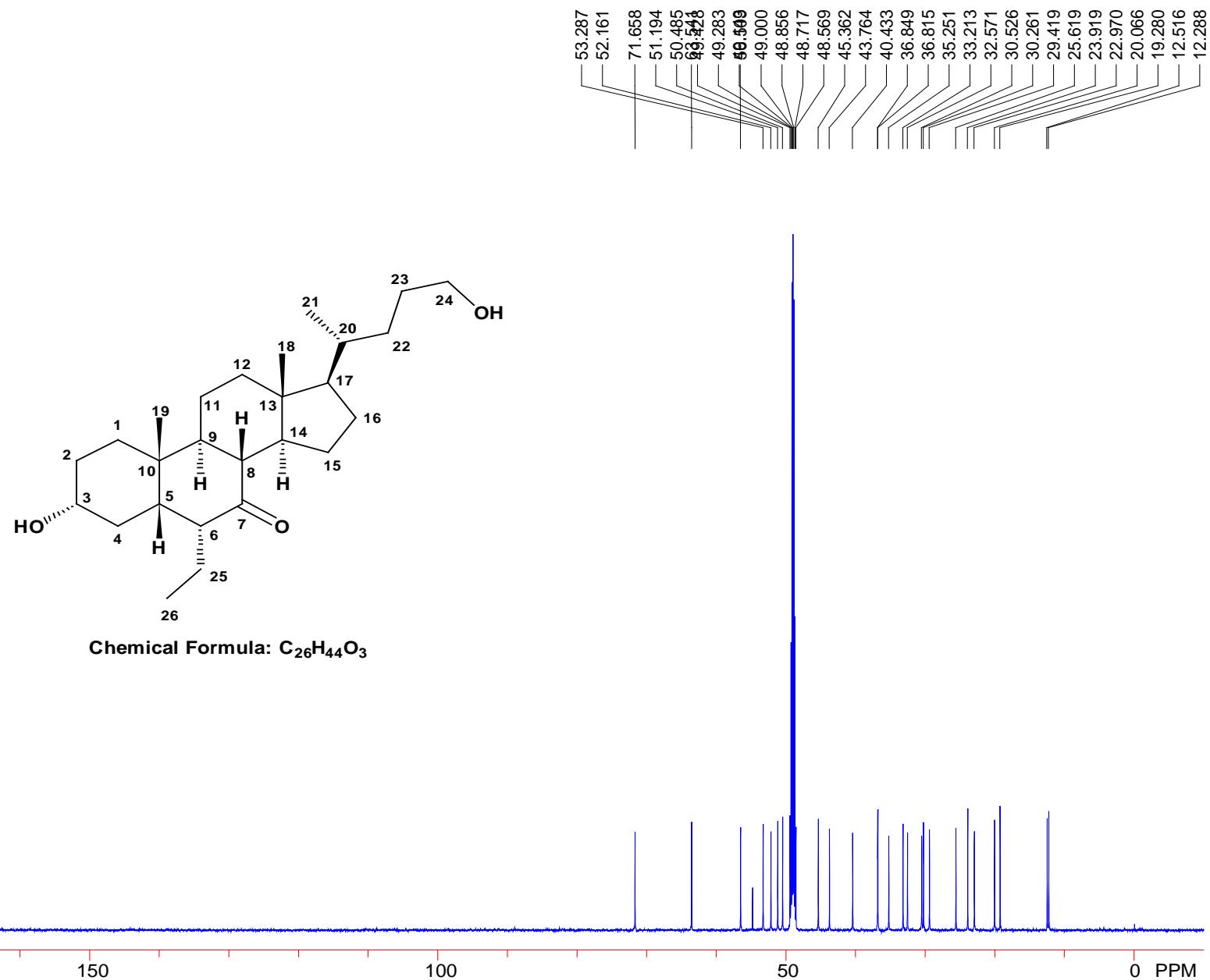


Figure S13. ^{13}C NMR spectrum of impurity 1.

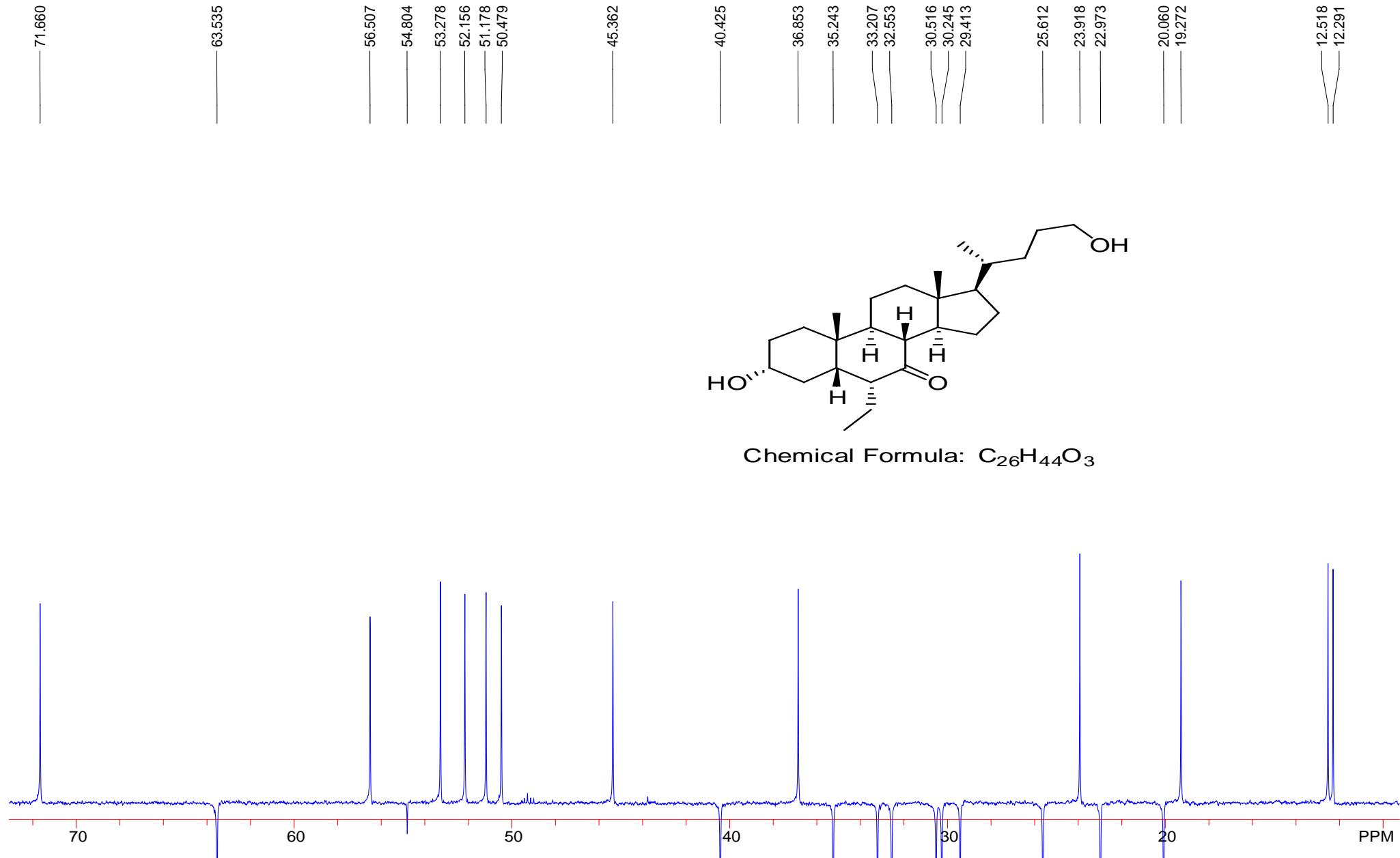


Figure S14. DEPT 135 spectrum of impurity 1.

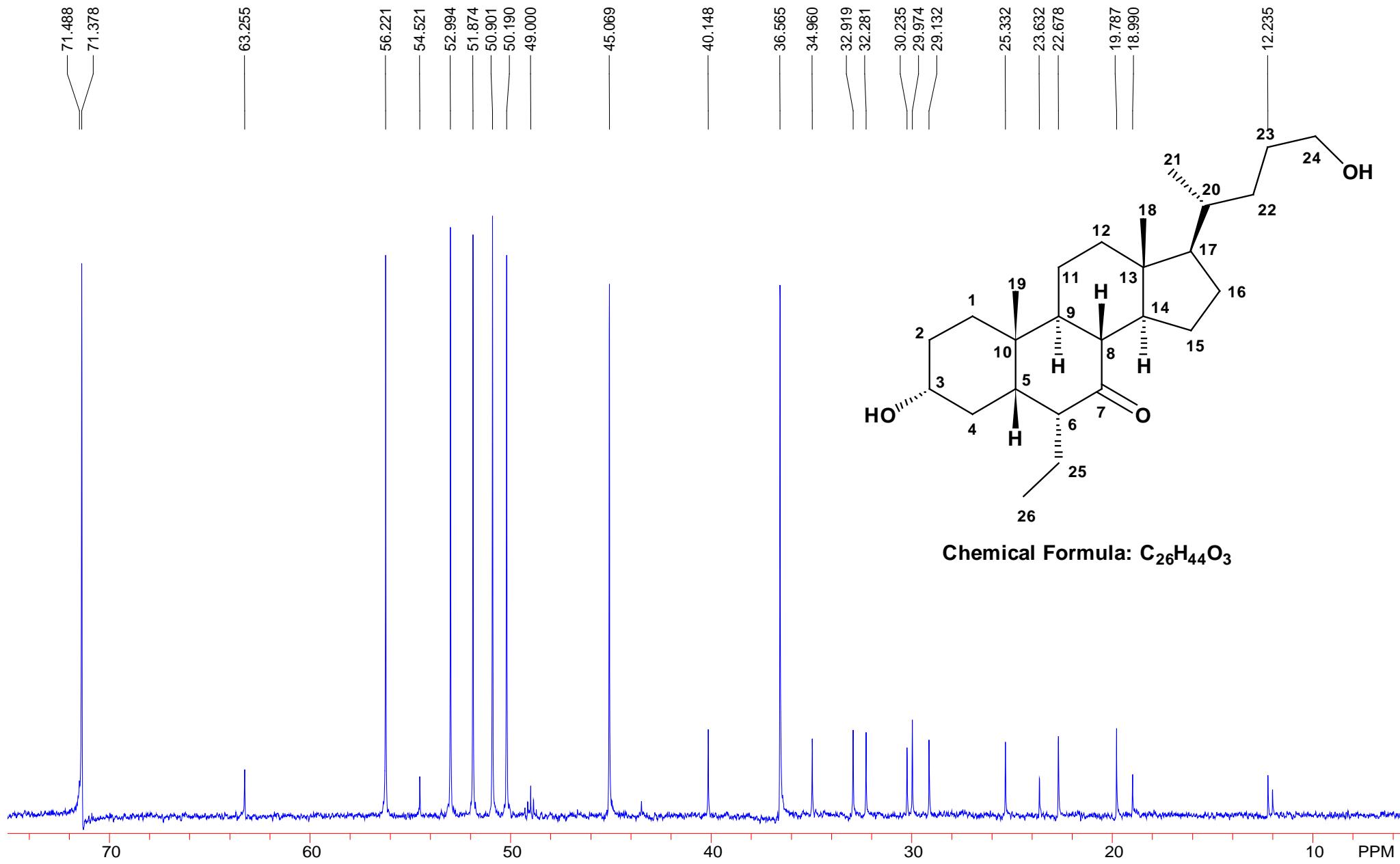


Figure S15. DEPT 90 spectrum of impurity 1.

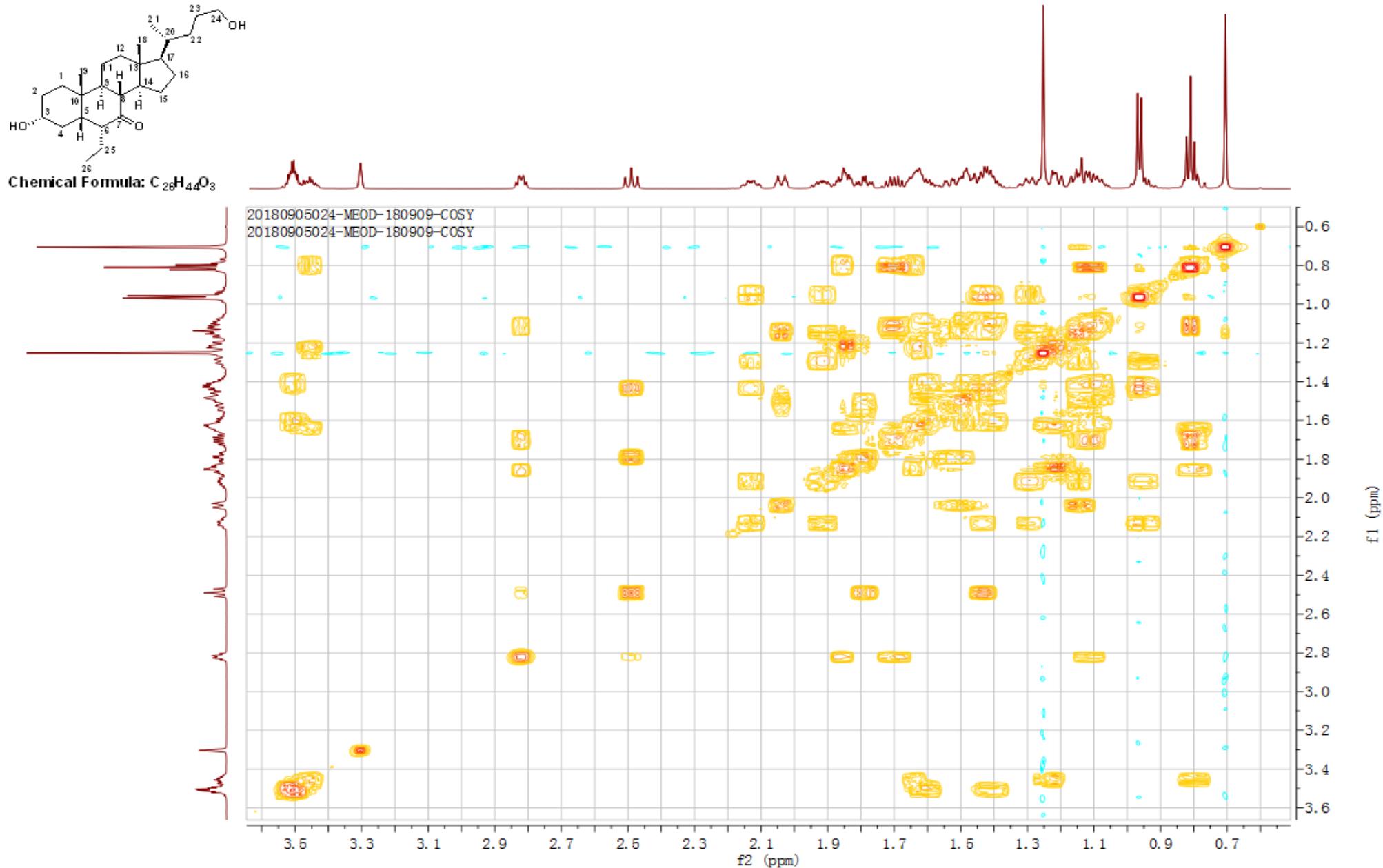


Figure S16. H-H COSY spectrum of impurity 1.

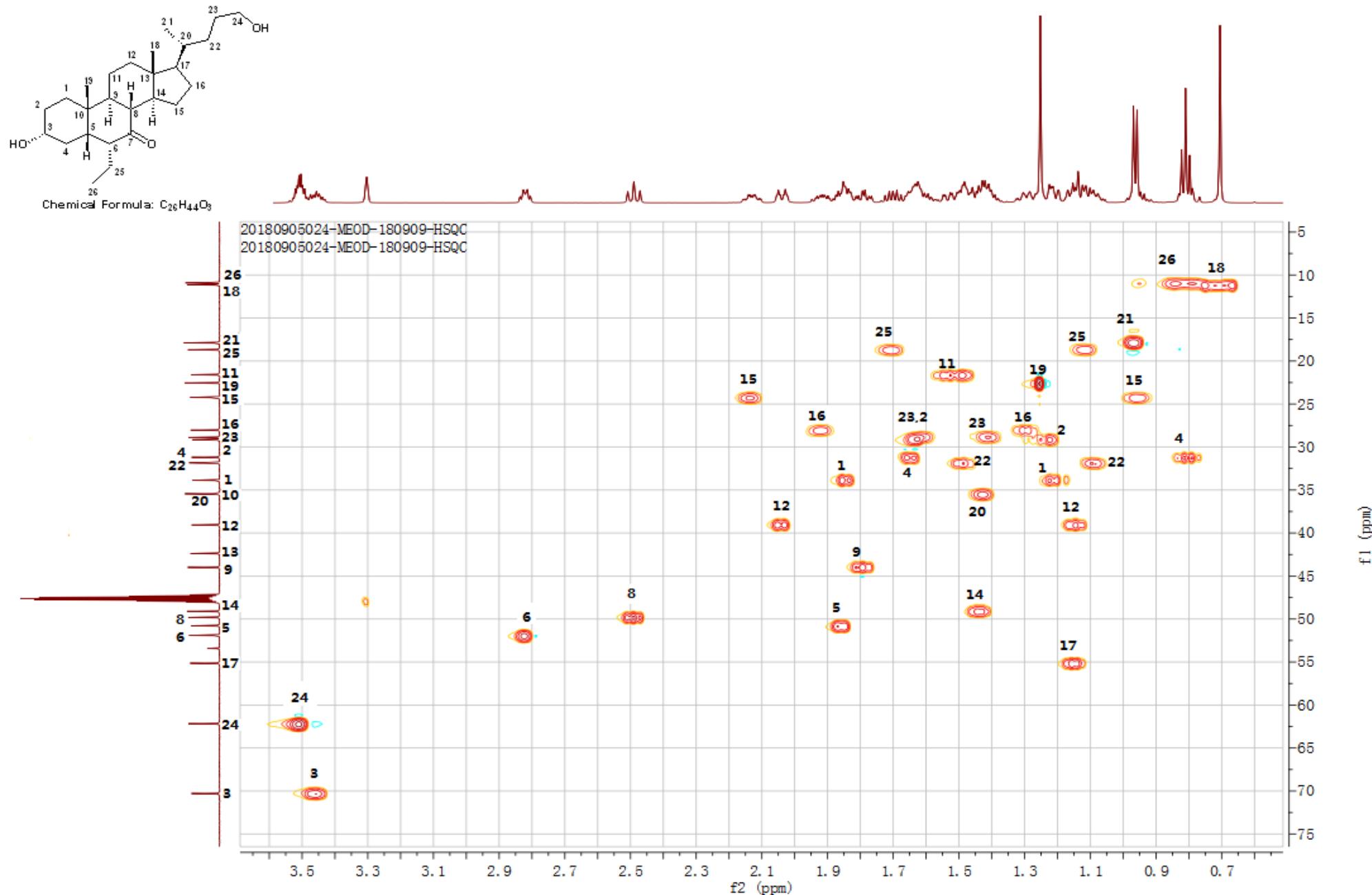


Figure S17. HSQC spectrum of impurity 1.

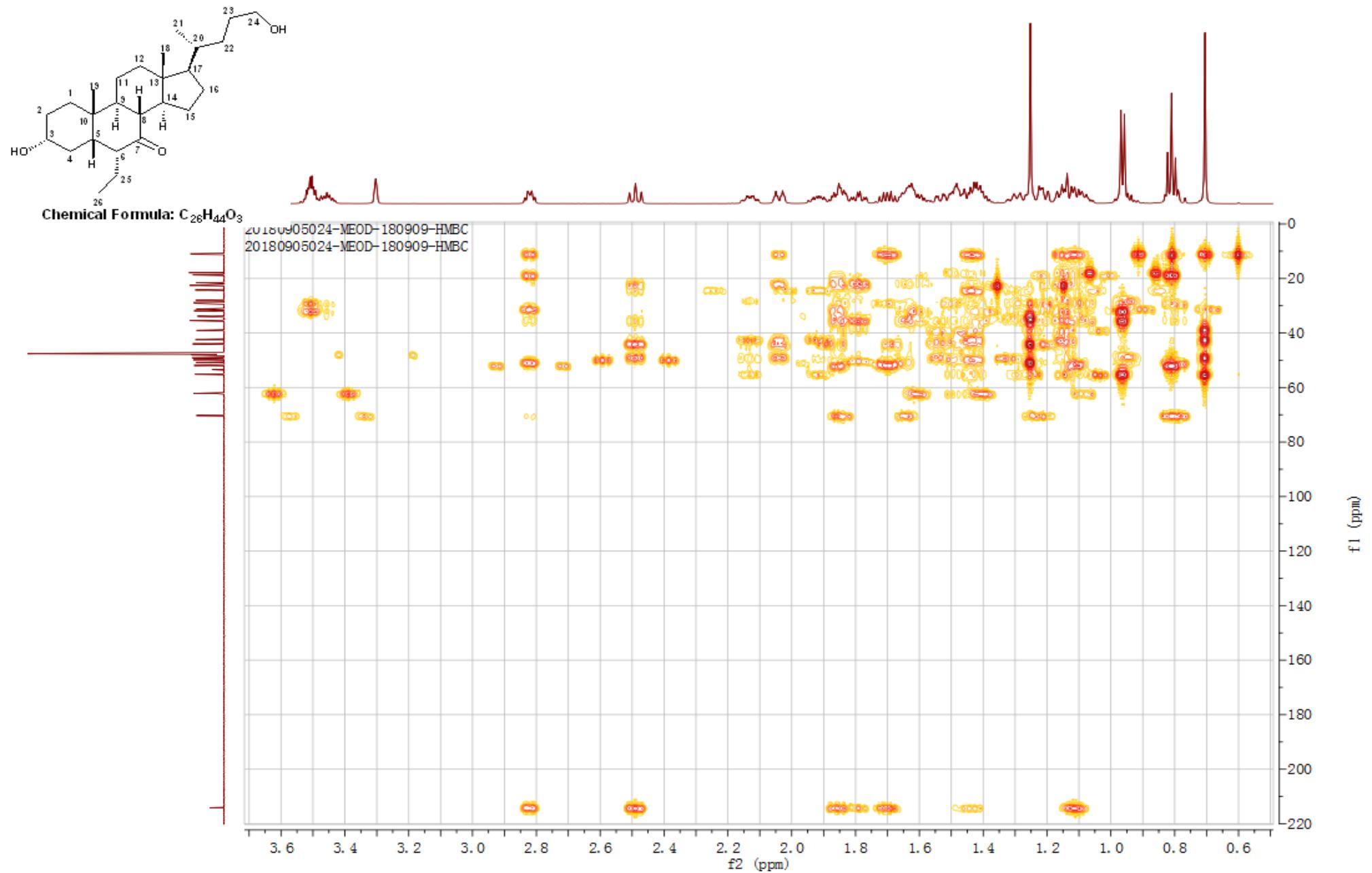


Figure S18. HMBC spectrum of impurity 1.

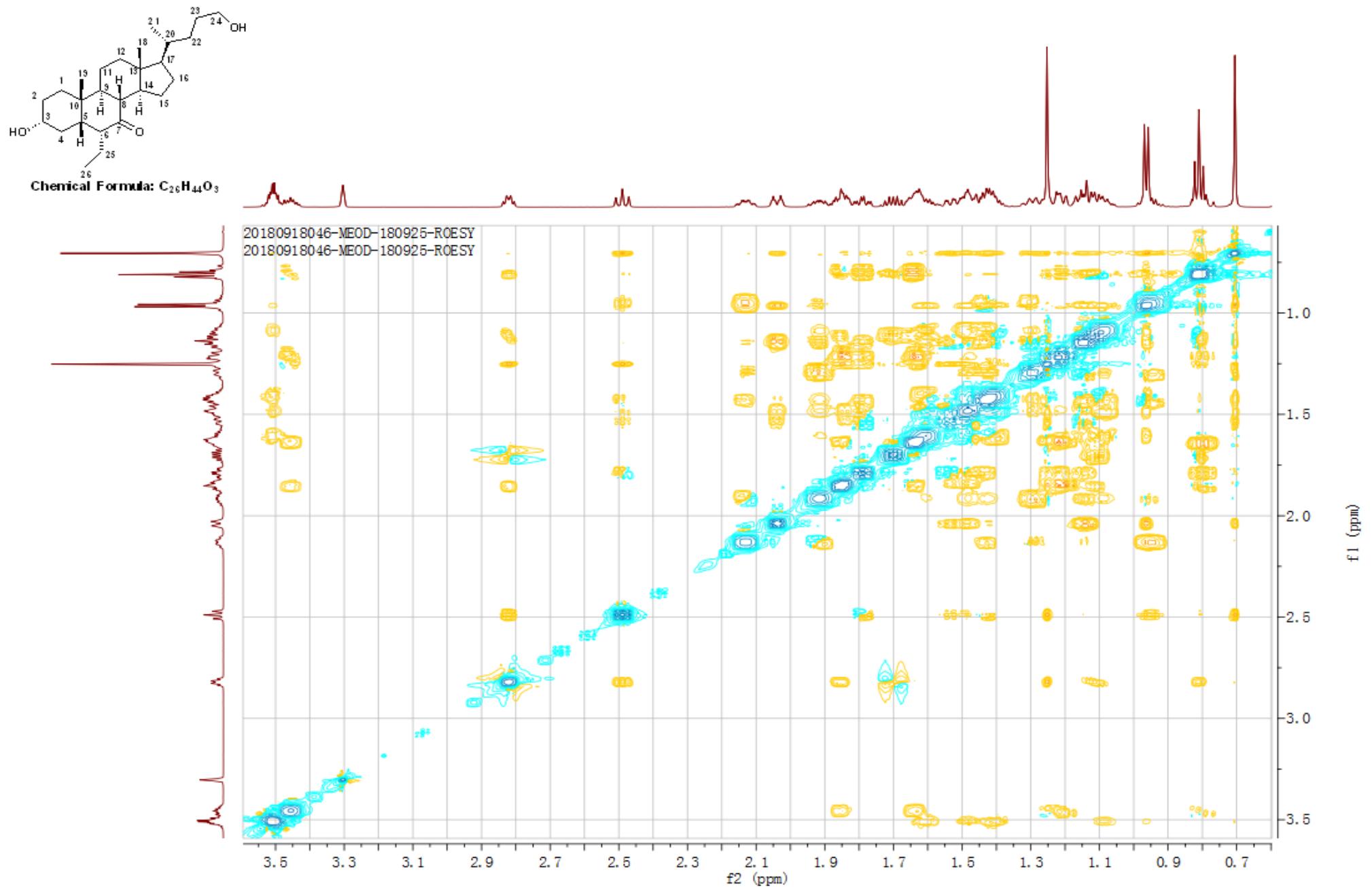


Figure S19. ROESY spectrum of impurity 1.

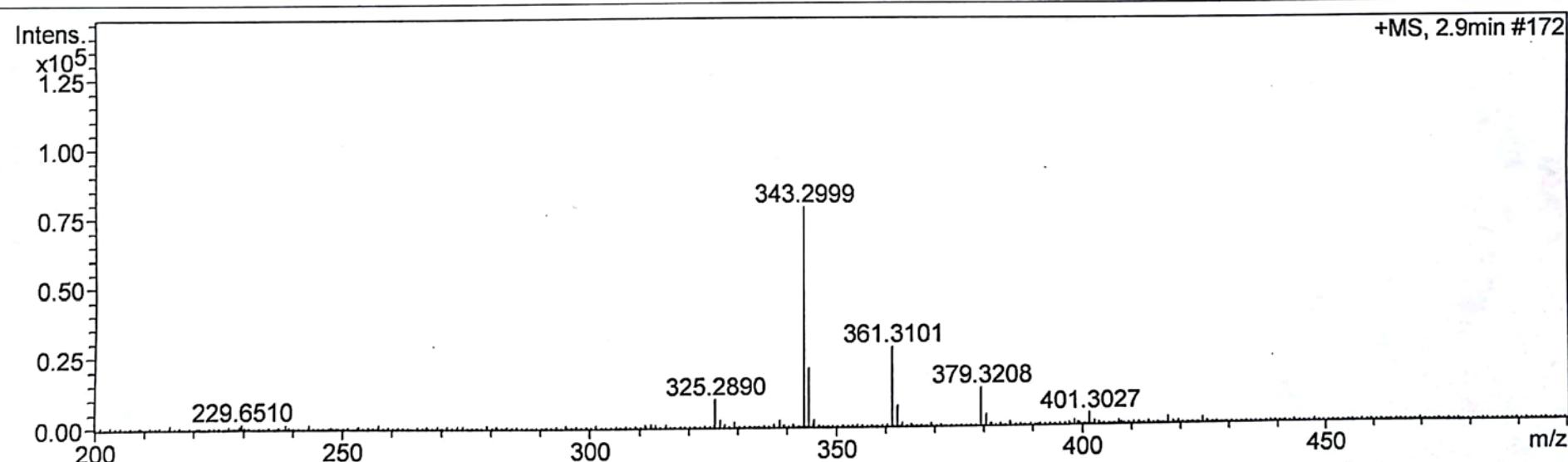
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Method 20150915.m Operator BDAL@DE
Sample Name 14237-91-1 Instrument / Ser# maXis 4G 21240
Comment

Acquisition Parameter

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Scan End	1500 m/z	Set Collision Cell RF	600.0 Vpp	Set Divert Valve	Waste



Meas. m/z	#	Formula	Score	m/z	err [ppm]	Mean err [ppm]	mSigma	rdb	e ⁻ Conf	N-Rule
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Figure S20. HRMS spectrum of compound 11.

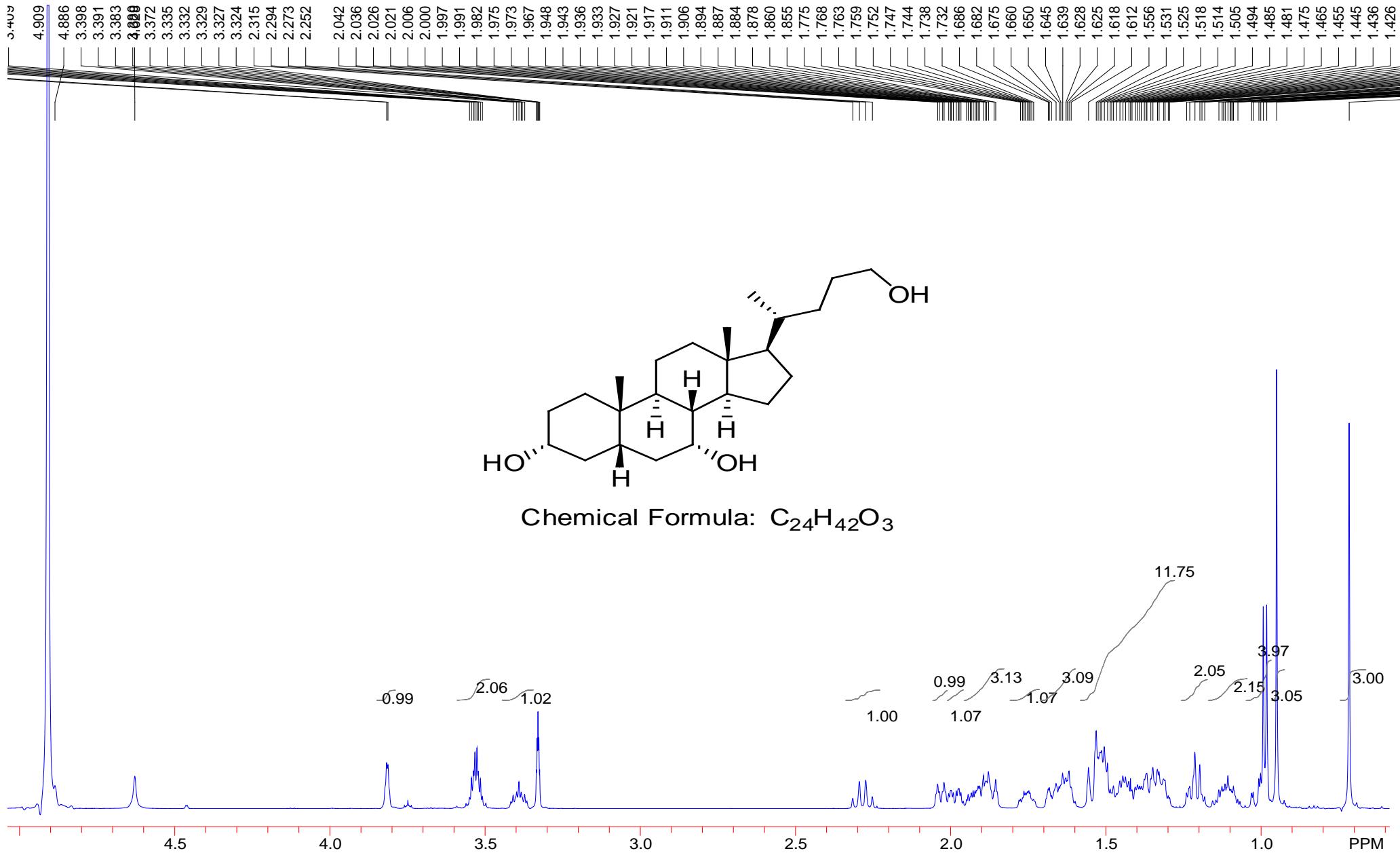


Figure S21. ^1H NMR spectrum of compound 11.

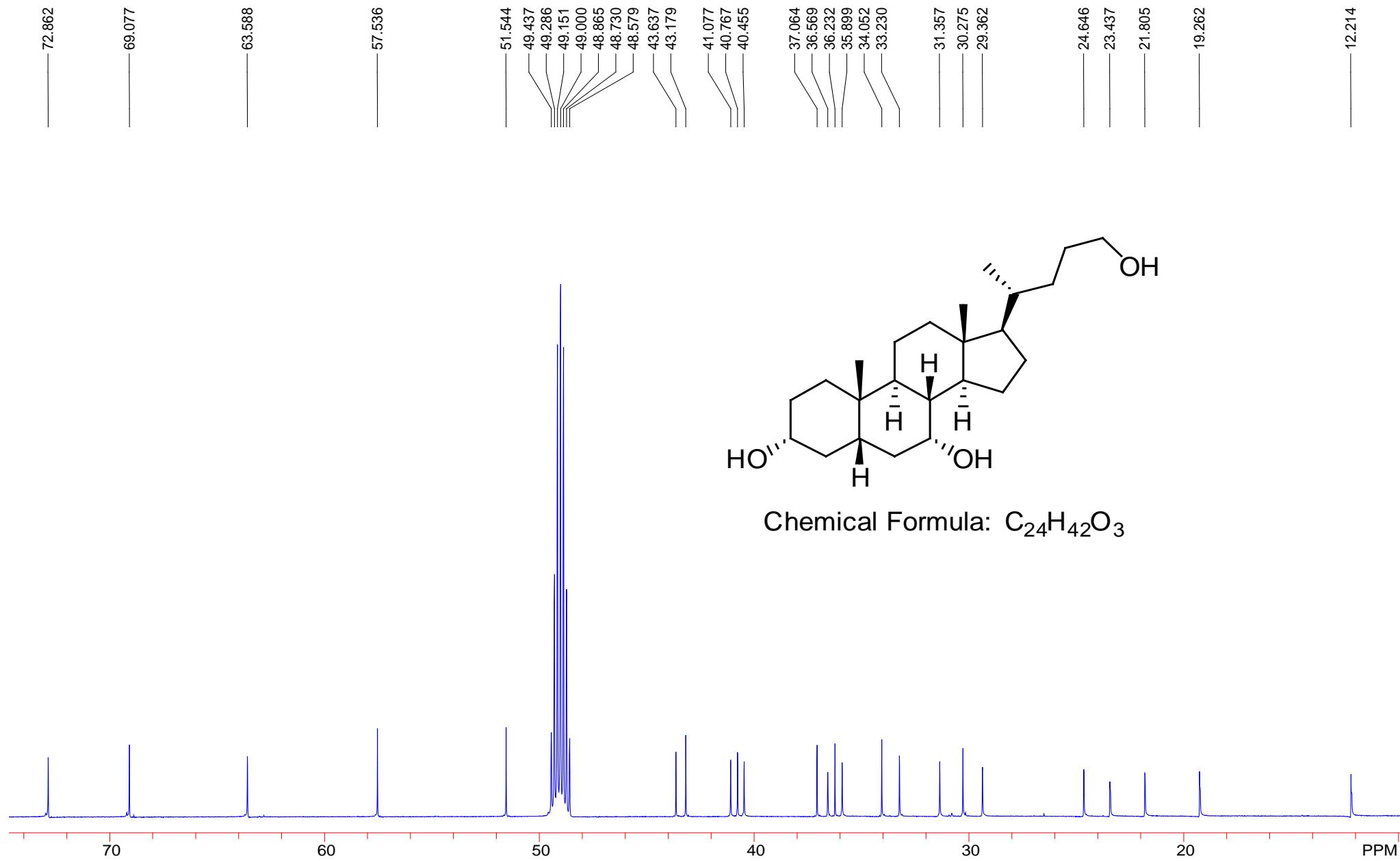
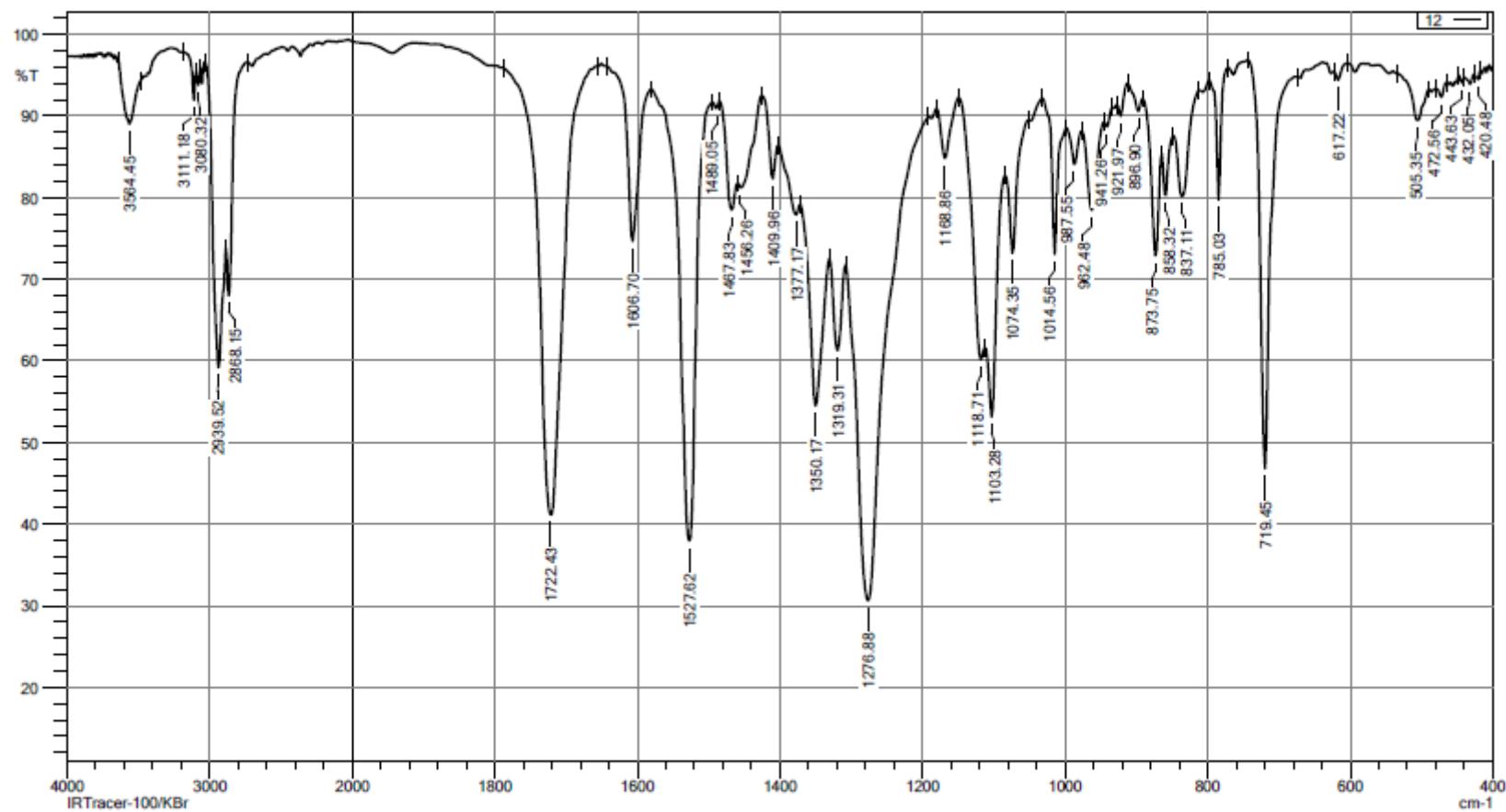


Figure S22. ^{13}C NMR spectrum of compound **11**.



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Figure S23. FT-IR spectrum of compound **11**.

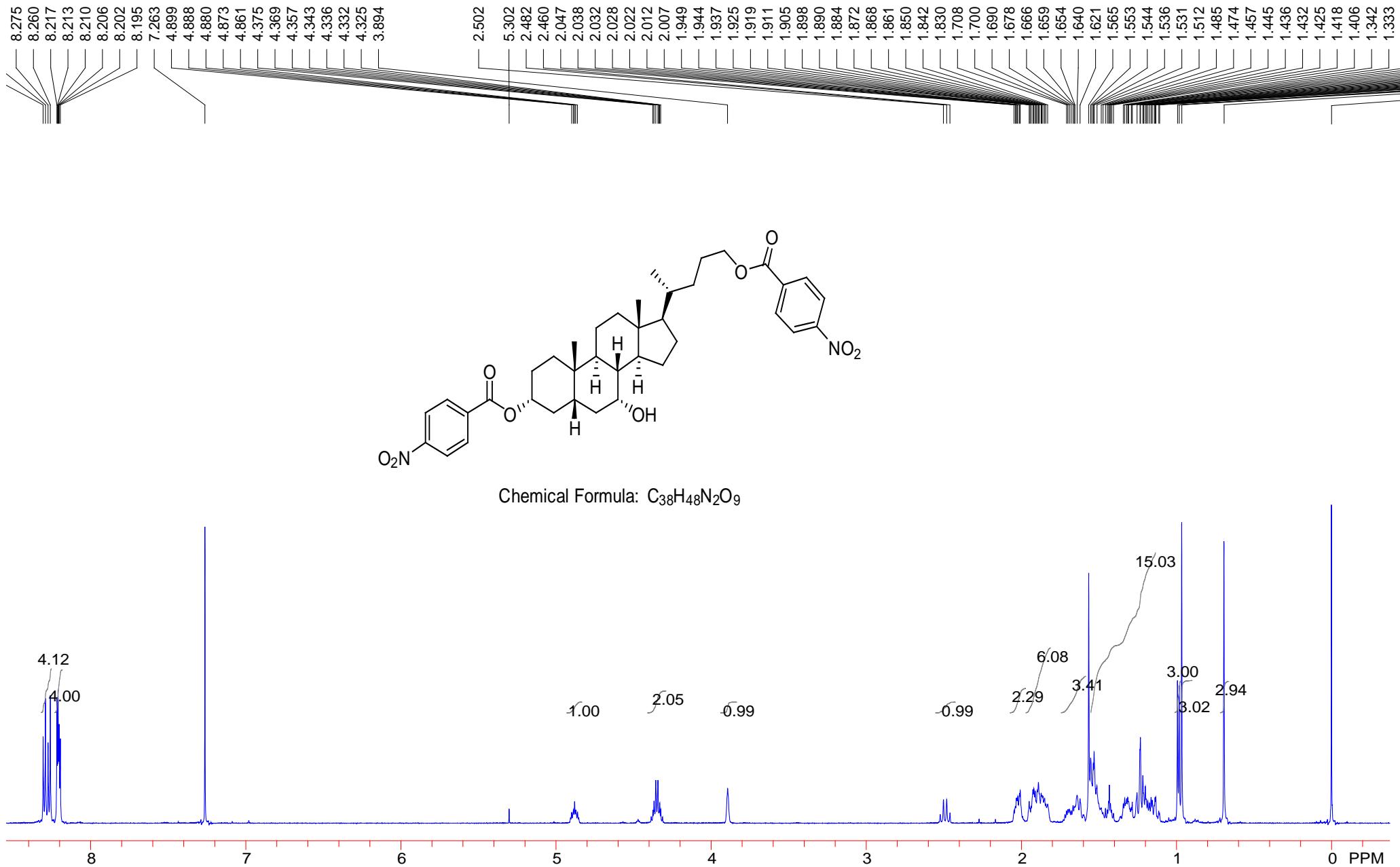


Figure S24. ^1H NMR spectrum of compound 12.

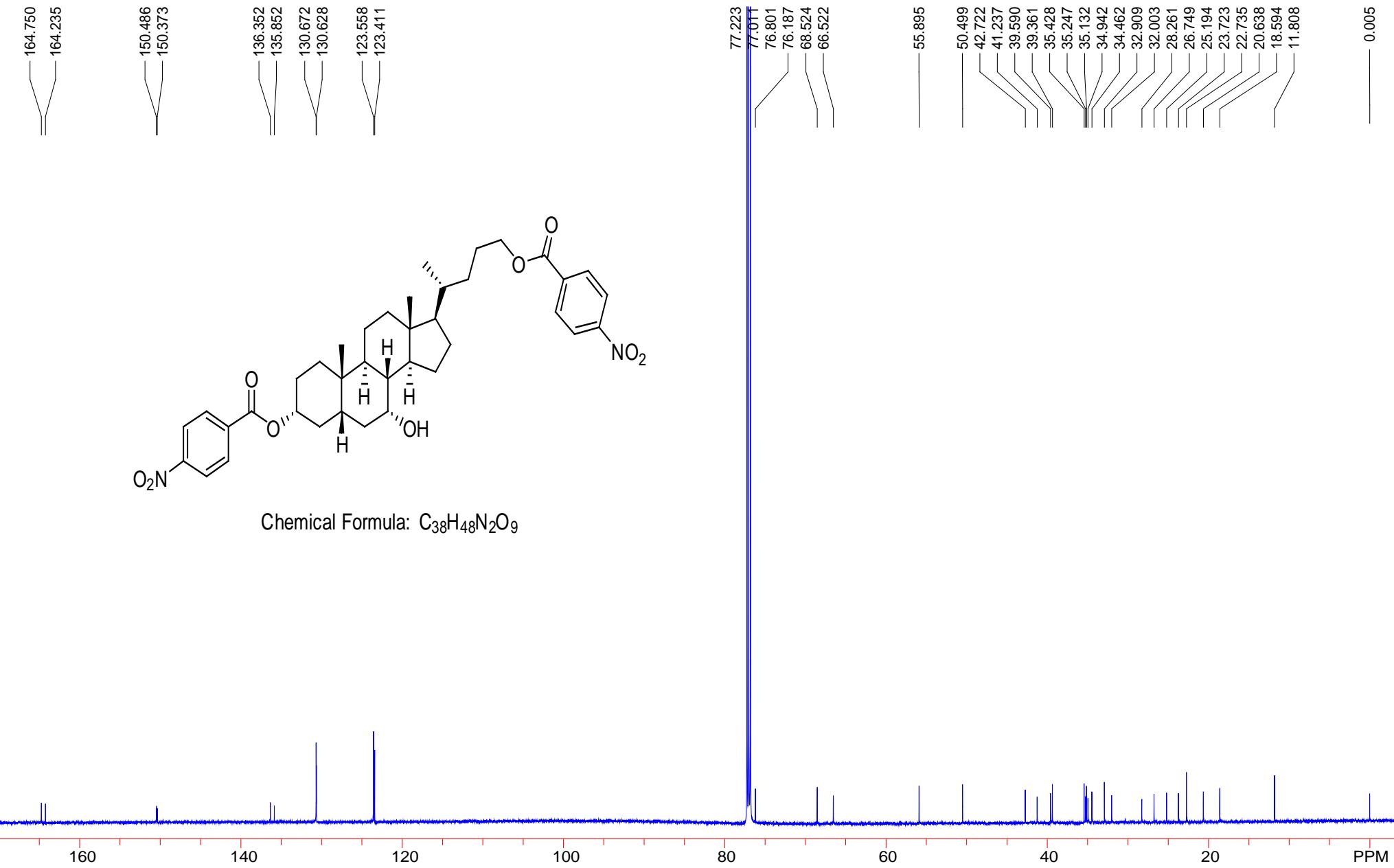


Figure S25. ^{13}C NMR spectrum of compound 12.

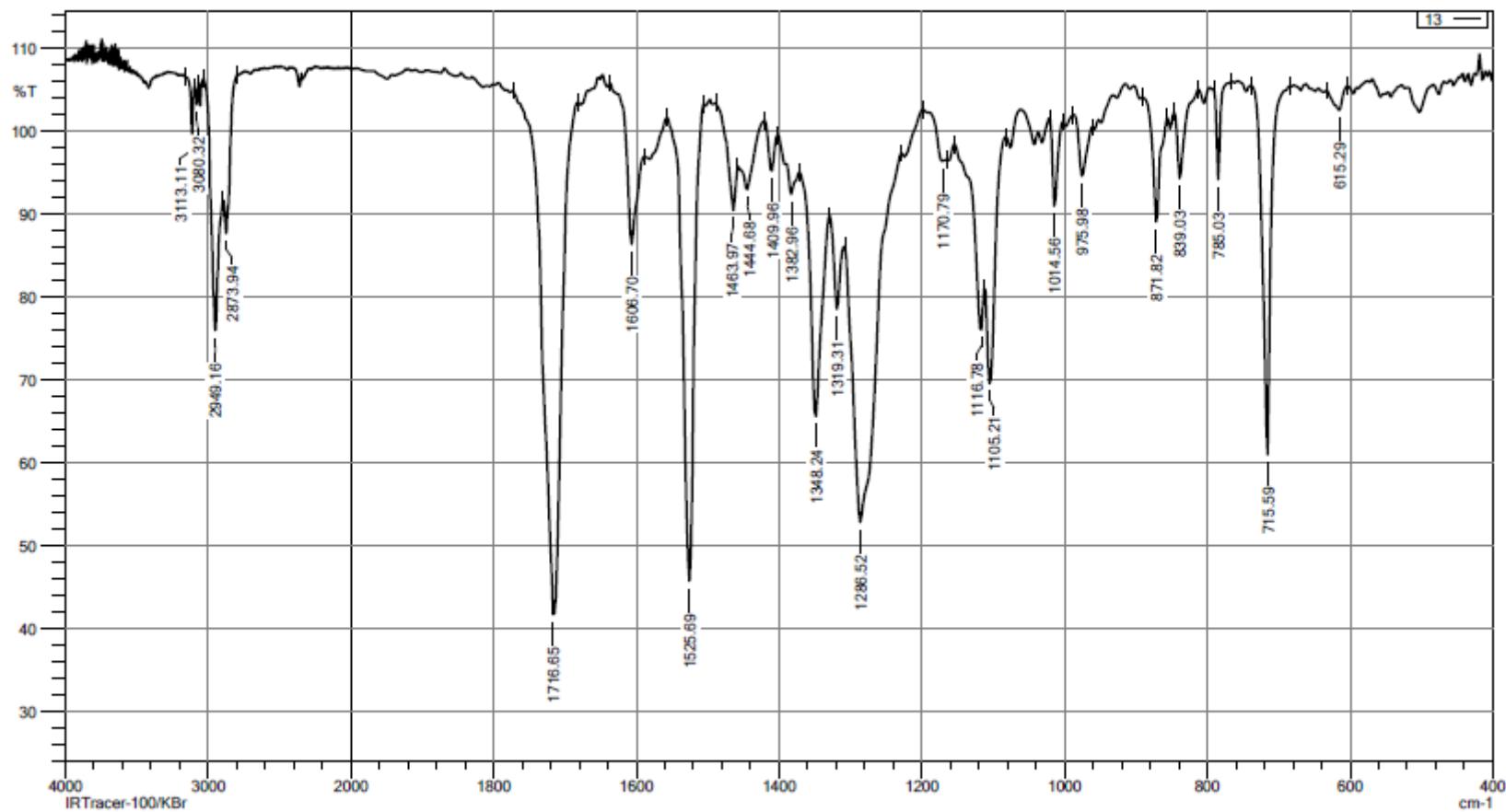


Figure S26. FT-IR spectrum of compound **13**.

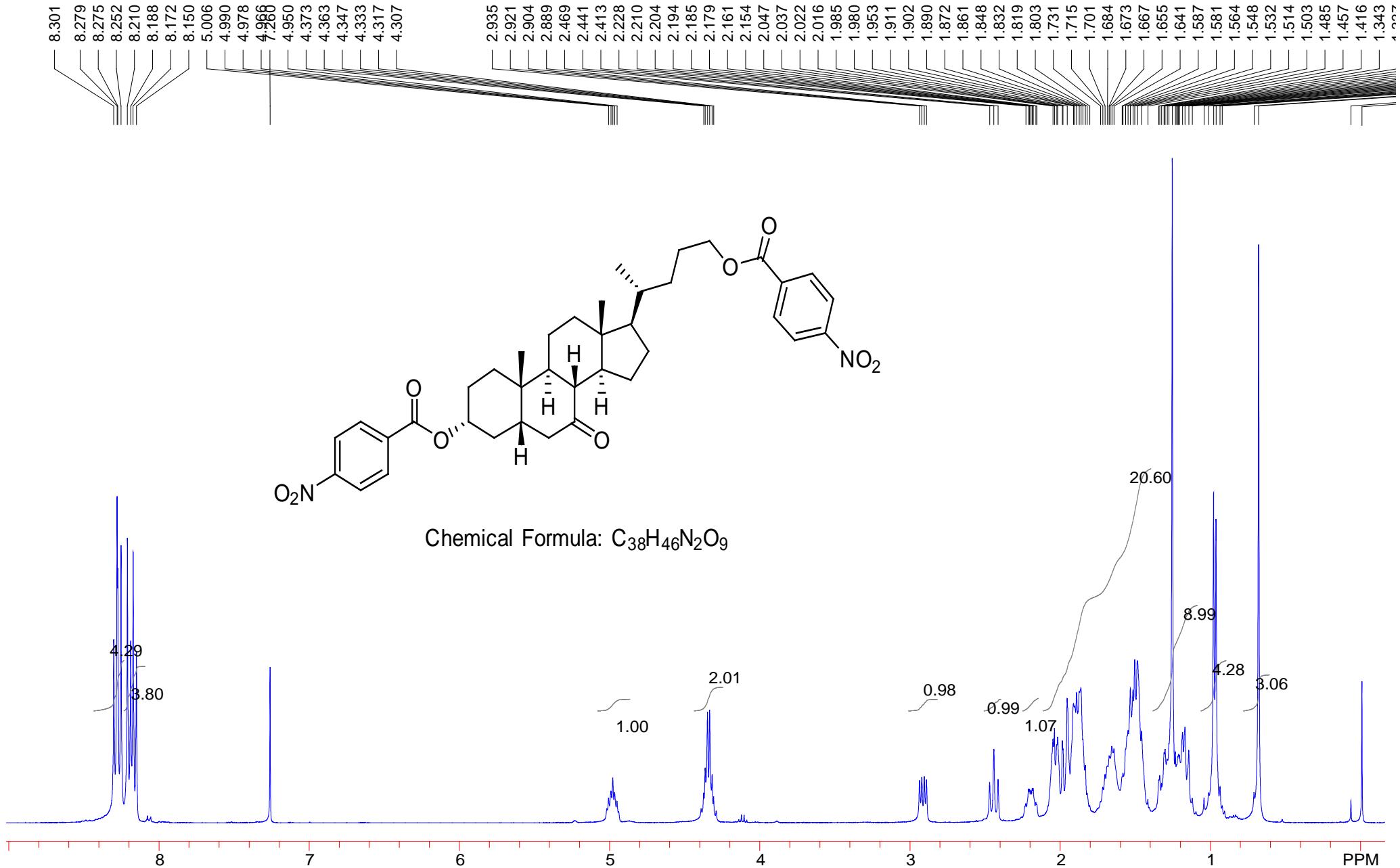
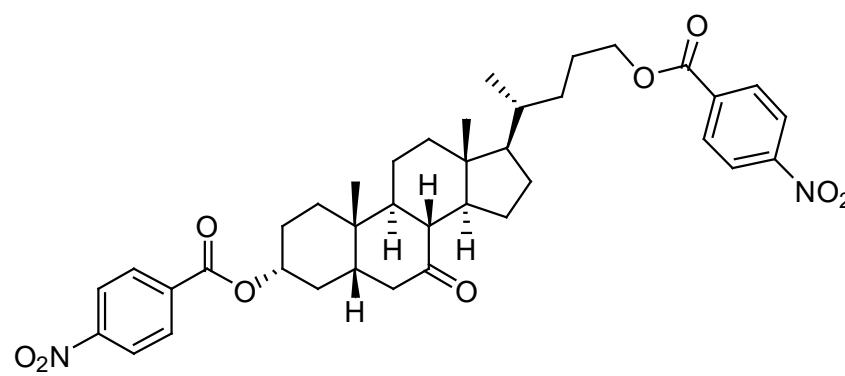
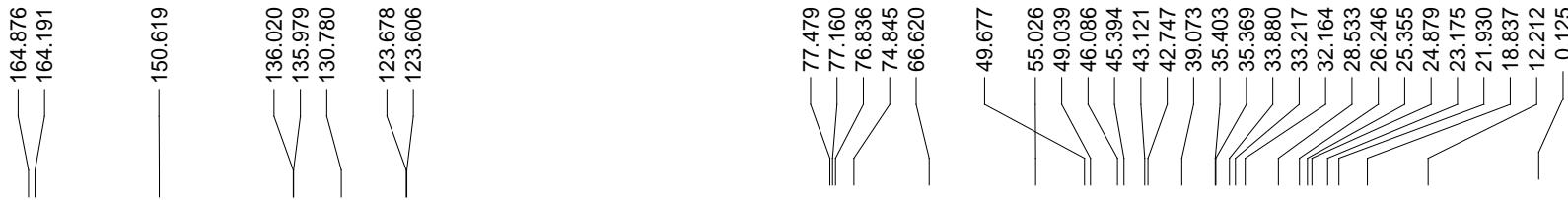


Figure S27. ^1H NMR spectrum of compound **13**.

212.042



Chemical Formula: $\text{C}_{38}\text{H}_{46}\text{N}_2\text{O}_9$

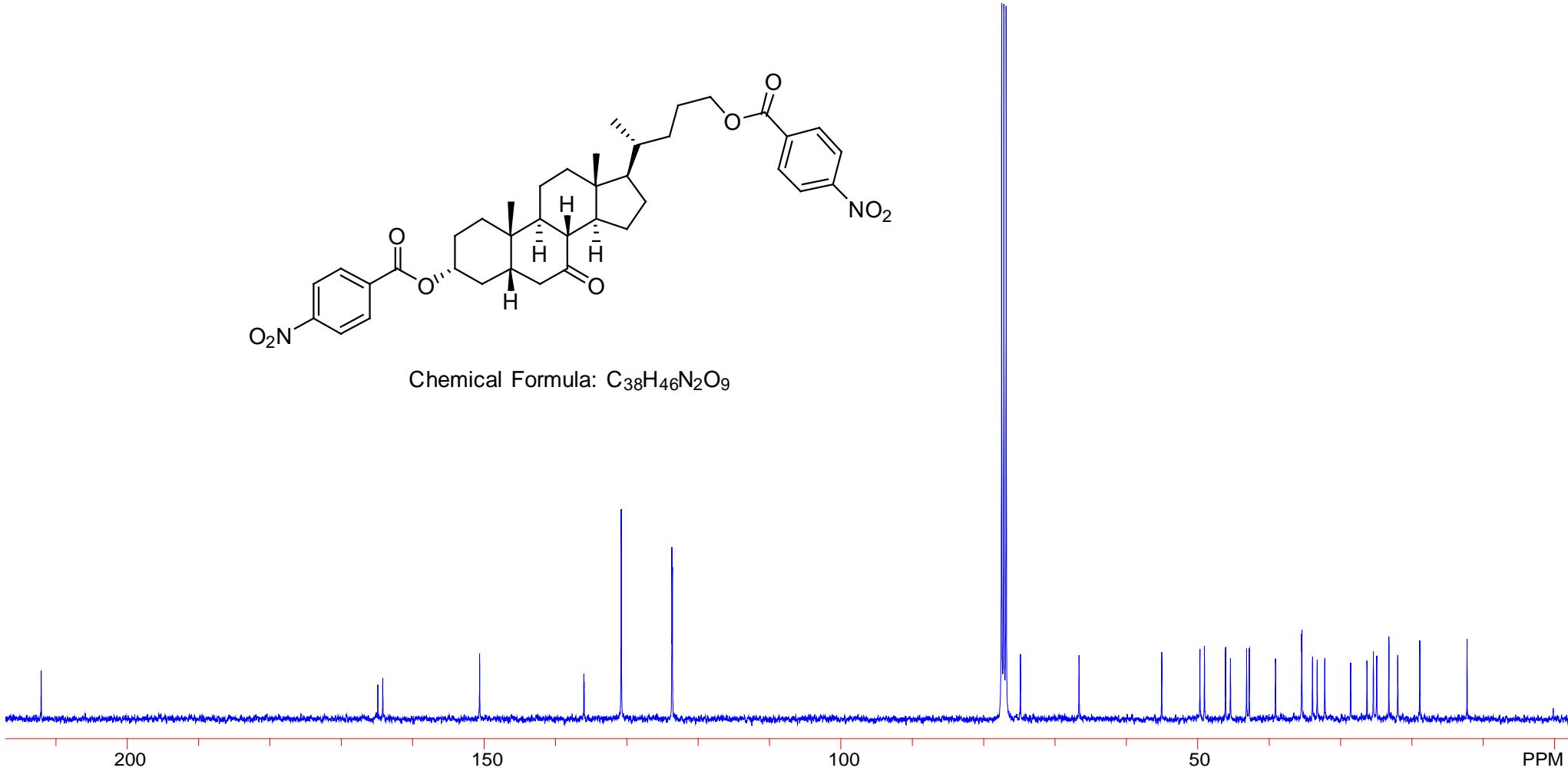


Figure S28. ^{13}C NMR spectrum of compound 13.

Mass Spectrum SmartFormula Report

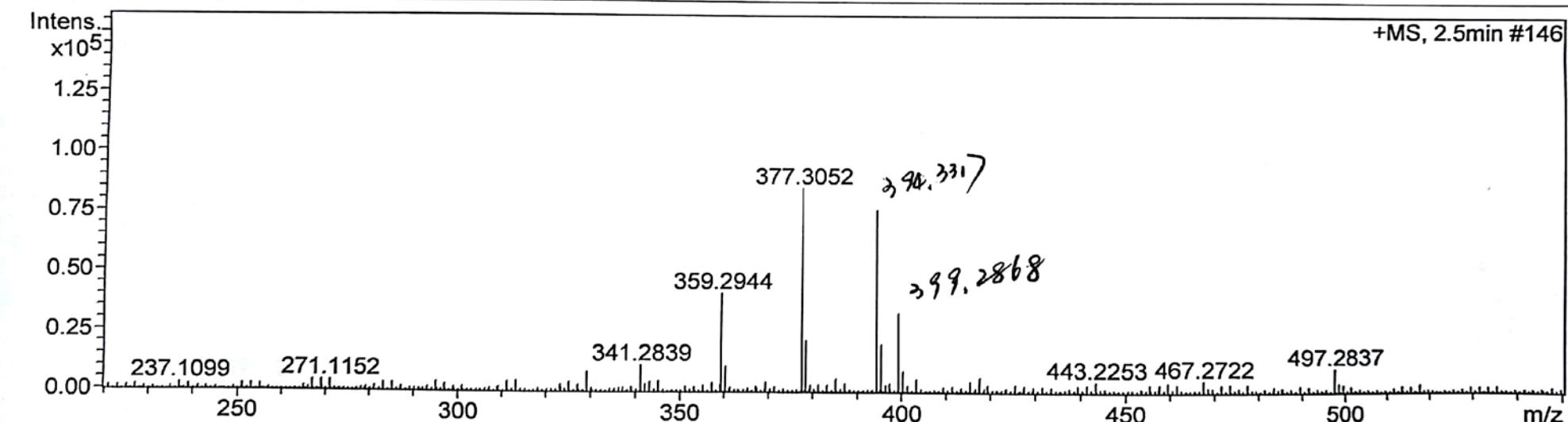
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Instrument / Ser# maXis 4G 21240

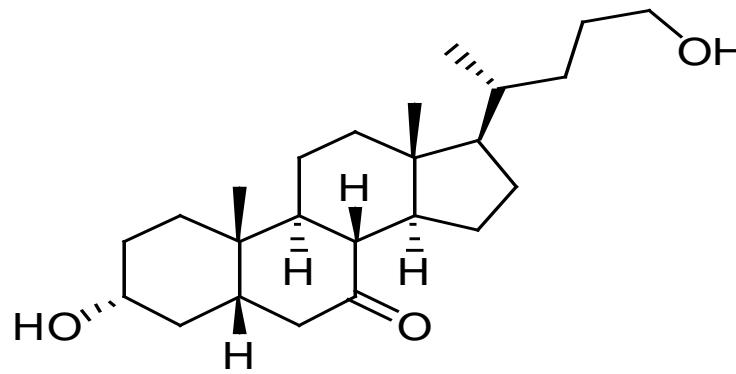
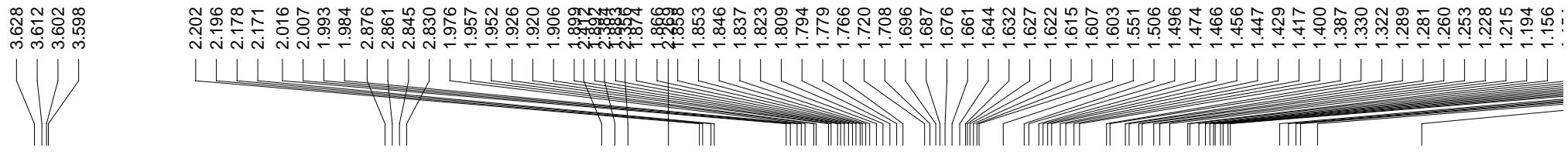
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Scan End	1500 m/z	Set Collision Cell RF	600.0 Vpp	Set Divert Valve	Waste



Meas. m/z	#	Formula	Score	m/z	err [ppm]	Mean err [ppm]	mSigma	rdb	e⁻ Conf	N-Rule
377.3052	1	C 24 H 41 O 3	100.00	377.3050	-0.5	-0.4	8.4	4.5	even	ok
394.3317	1	C 24 H 44 N O 3	100.00	394.3316	-0.3	-0.2	5.6	3.5	even	ok
399.2868	1	C 24 H 40 Na O 3	100.00	399.2870	0.4	0.4	4.5	4.5	even	ok

Figure S29. HRMS spectrum of compound 14.



Chemical Formula: $\text{C}_{24}\text{H}_{40}\text{O}_3$

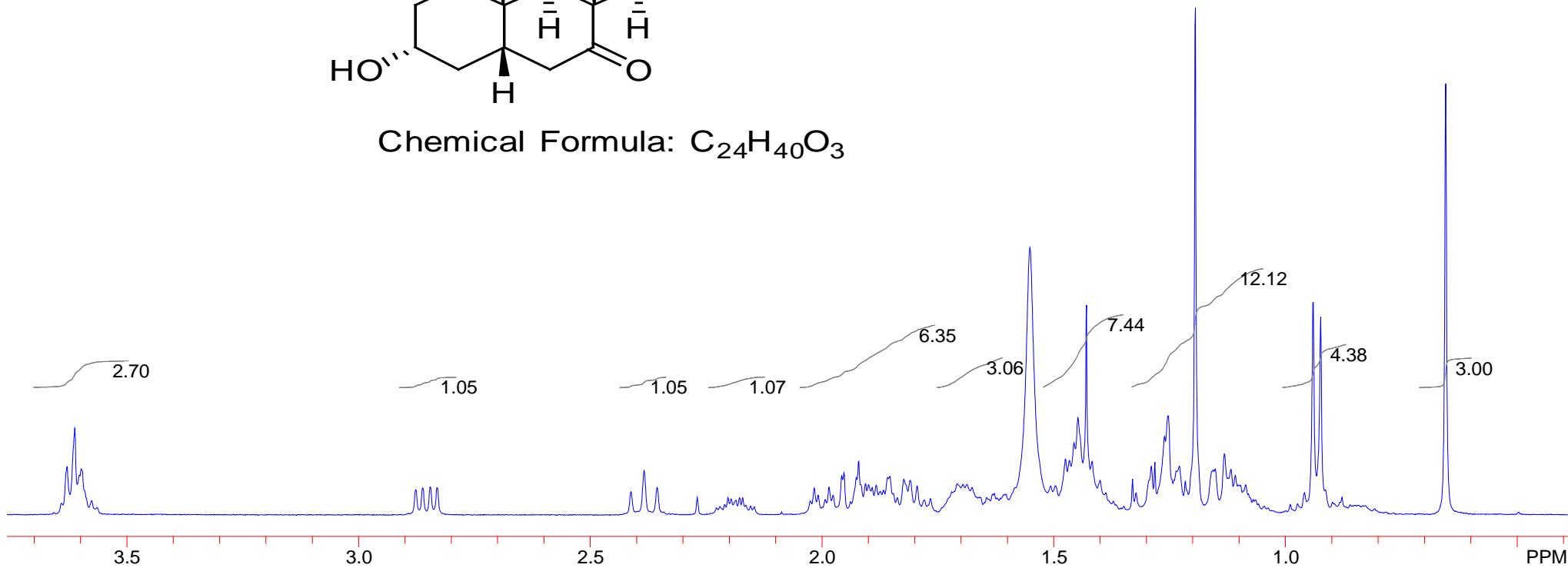
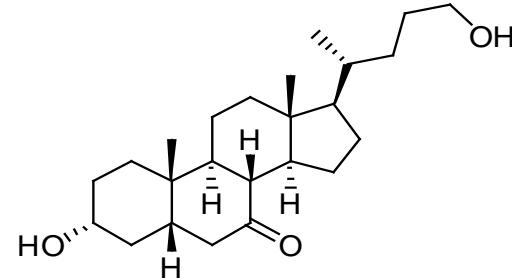


Figure S30. ^1H NMR spectrum of compound **14**.

212.156



Chemical Formula: $C_{24}H_{40}O_3$

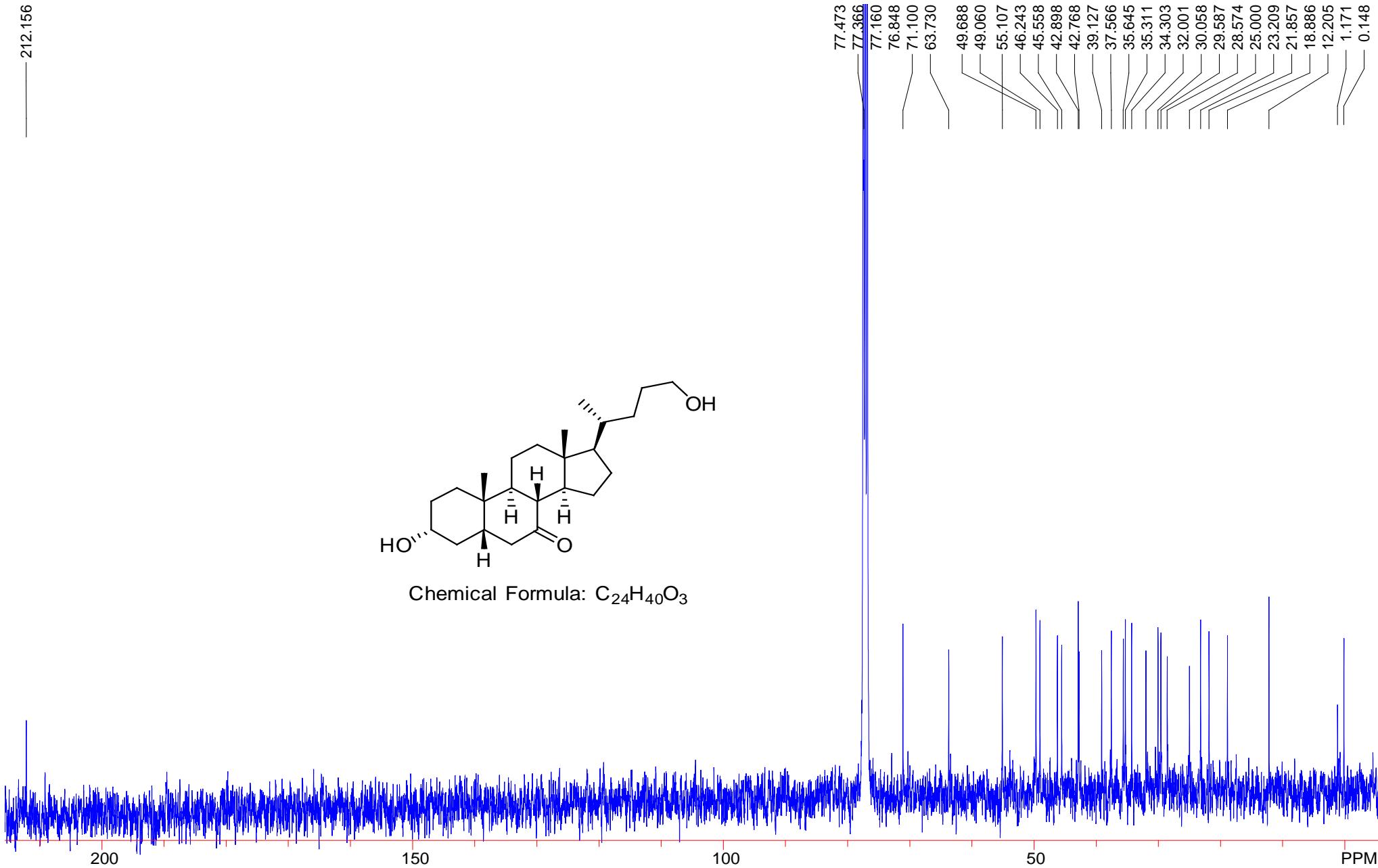


Figure S31. ^{13}C NMR spectrum of compound 14.

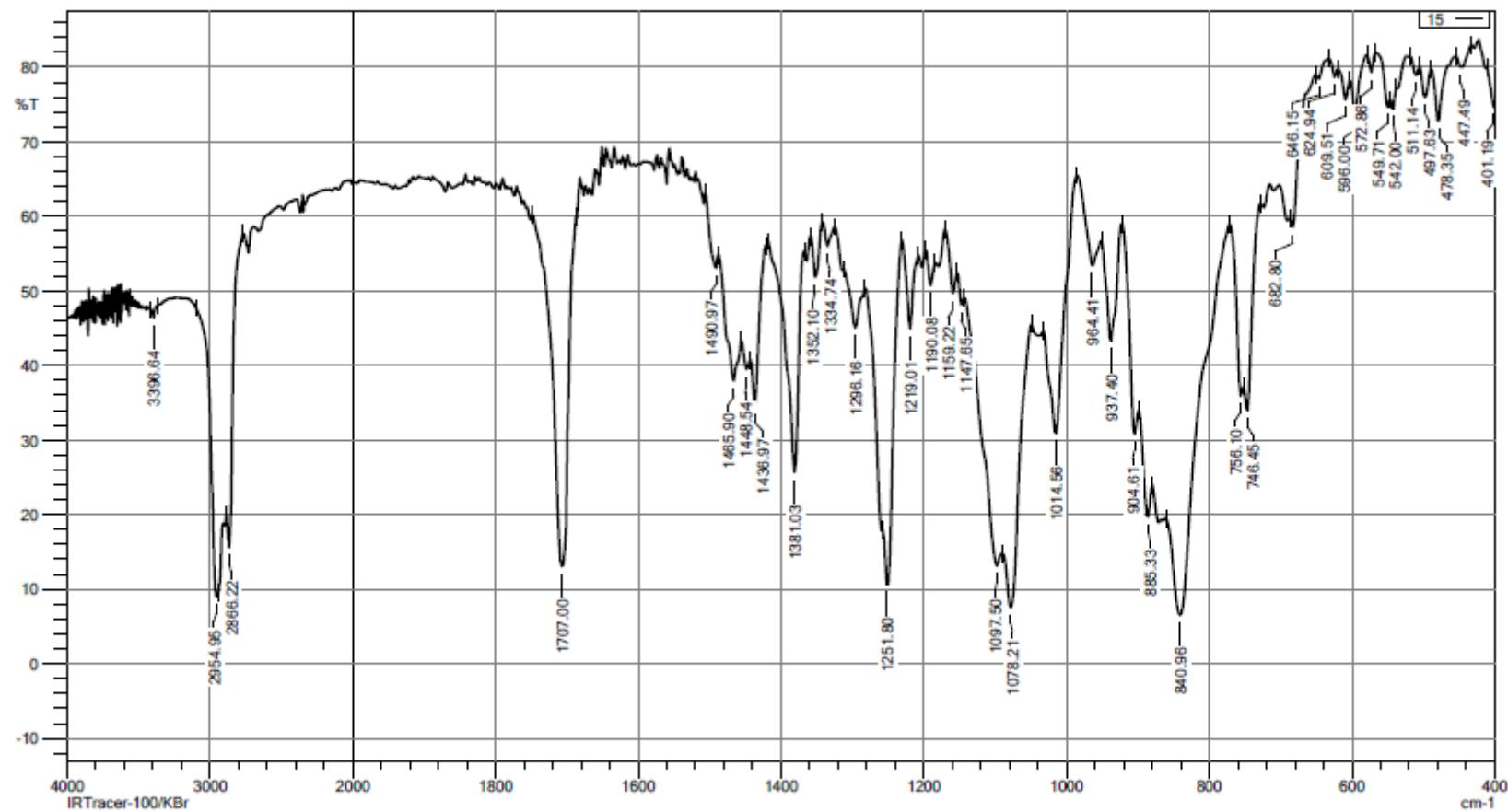


Figure S32. FT-IR spectrum of compound **15**.

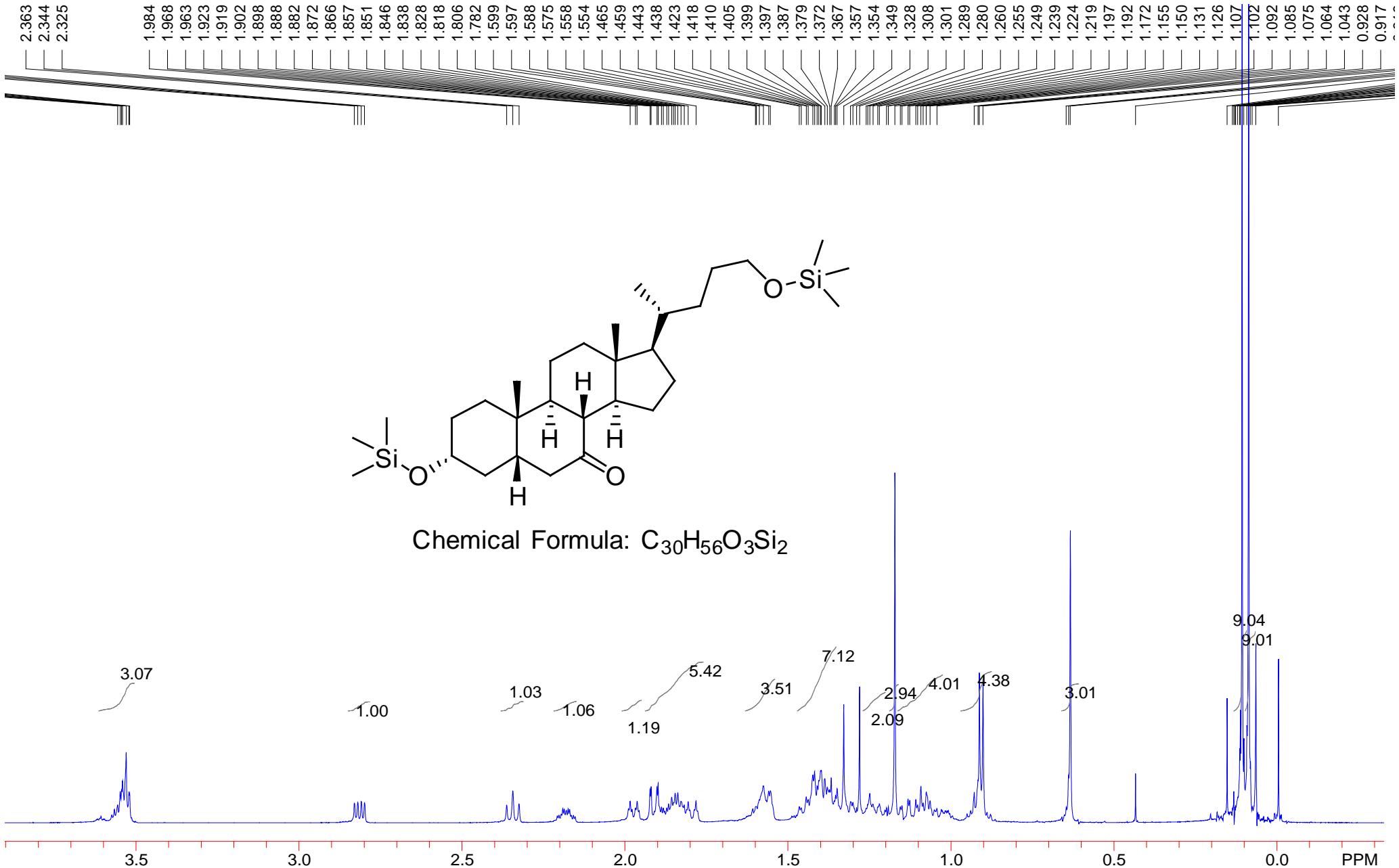
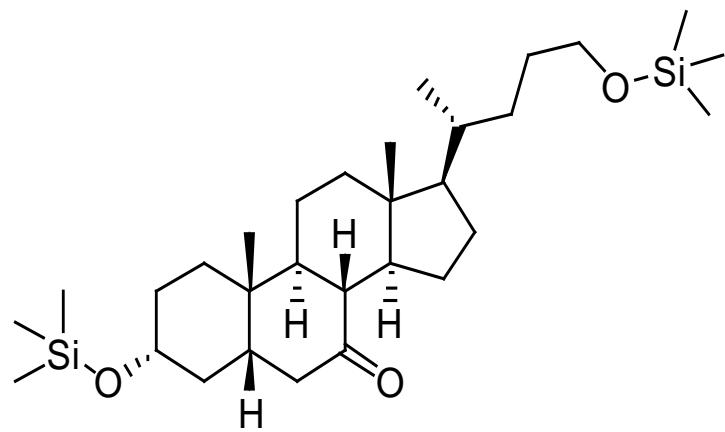


Figure S33. ^1H NMR spectrum of compound **15**.

211.920



Chemical Formula: $C_{30}H_{56}O_3Si_2$

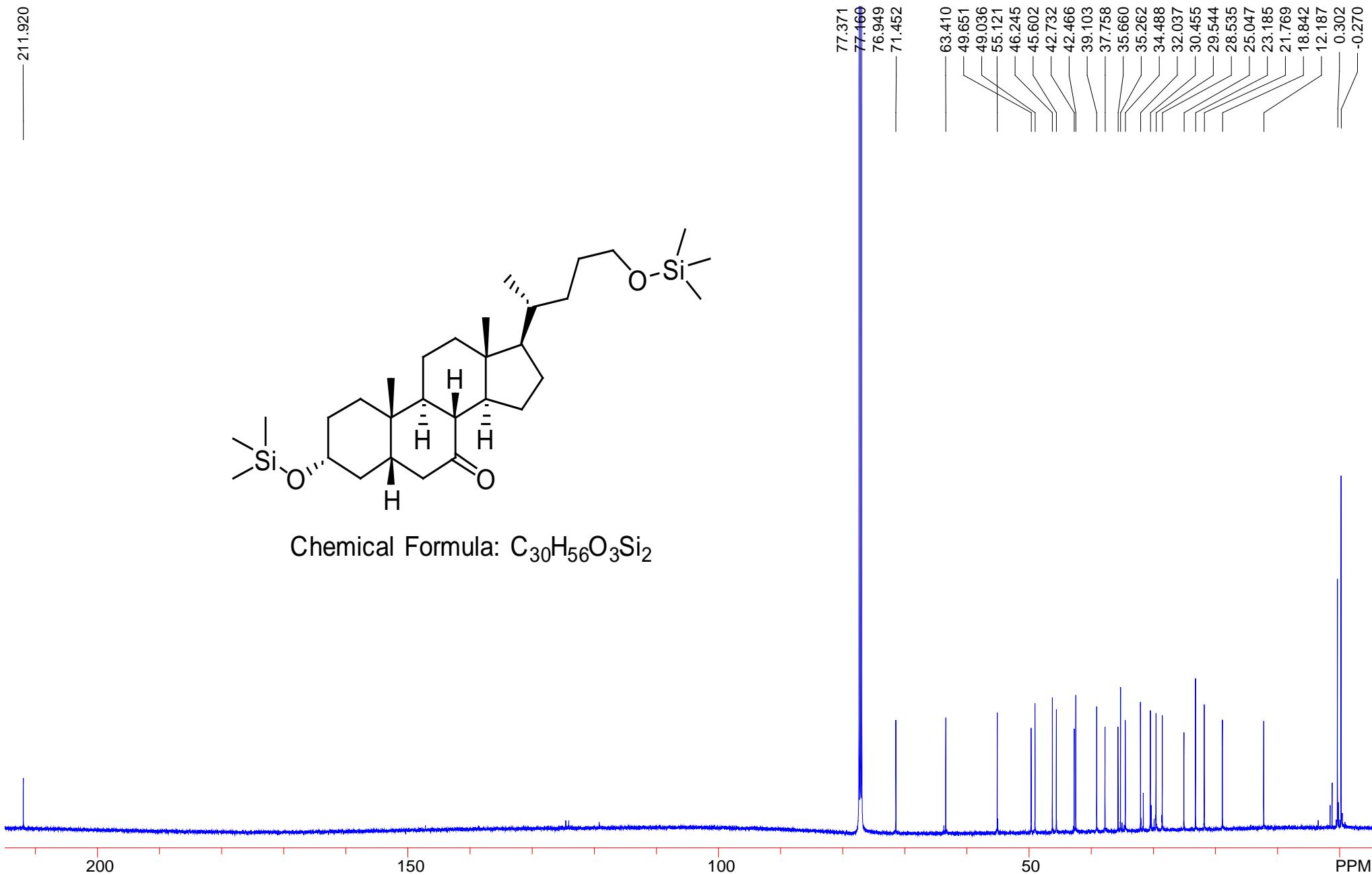
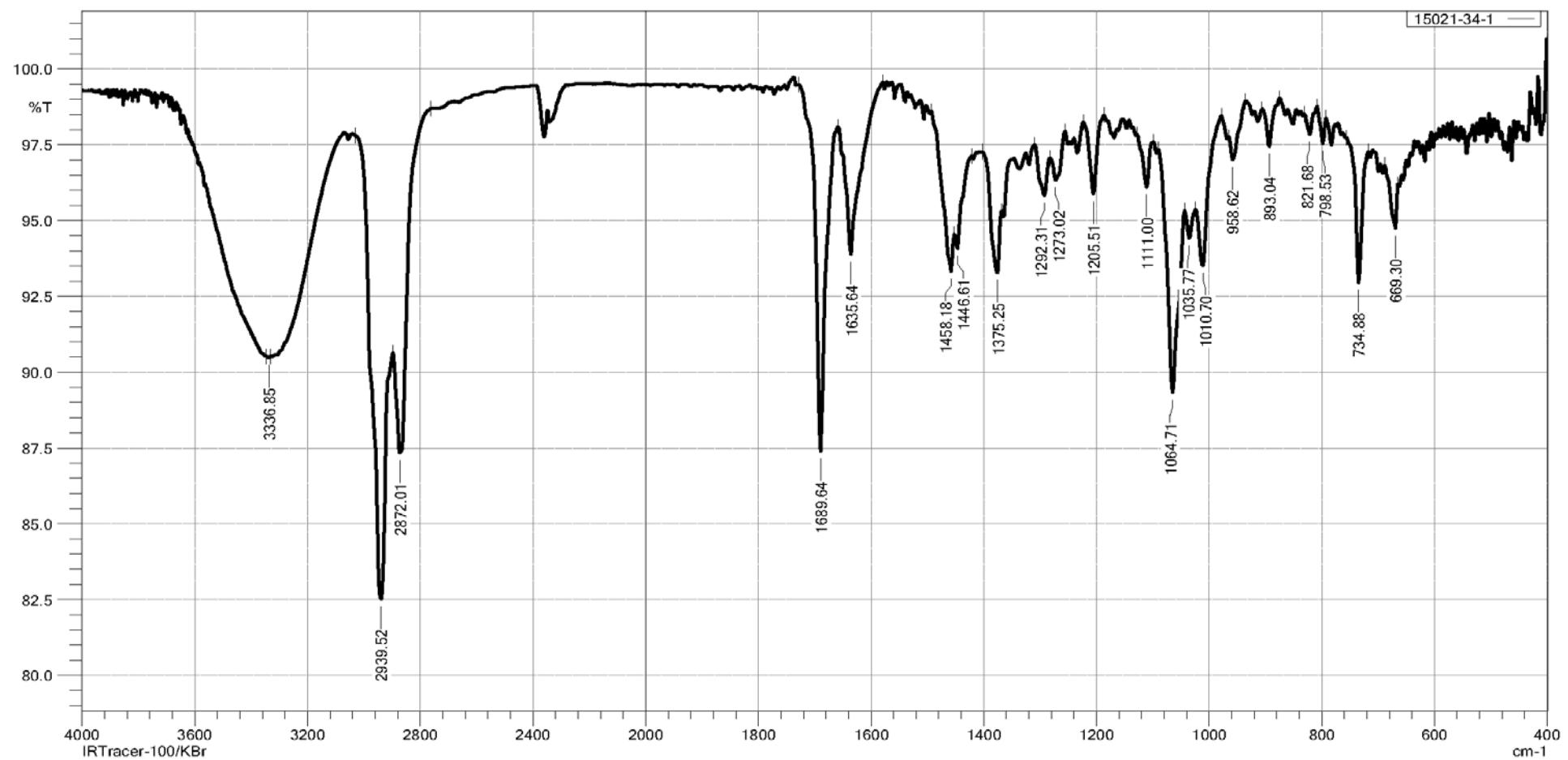


Figure S34. ^{13}C NMR spectrum of compound 15.

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9/28/2018 2:33:14 PM

**Figure S35.** FT-IR spectrum of impurity 2.

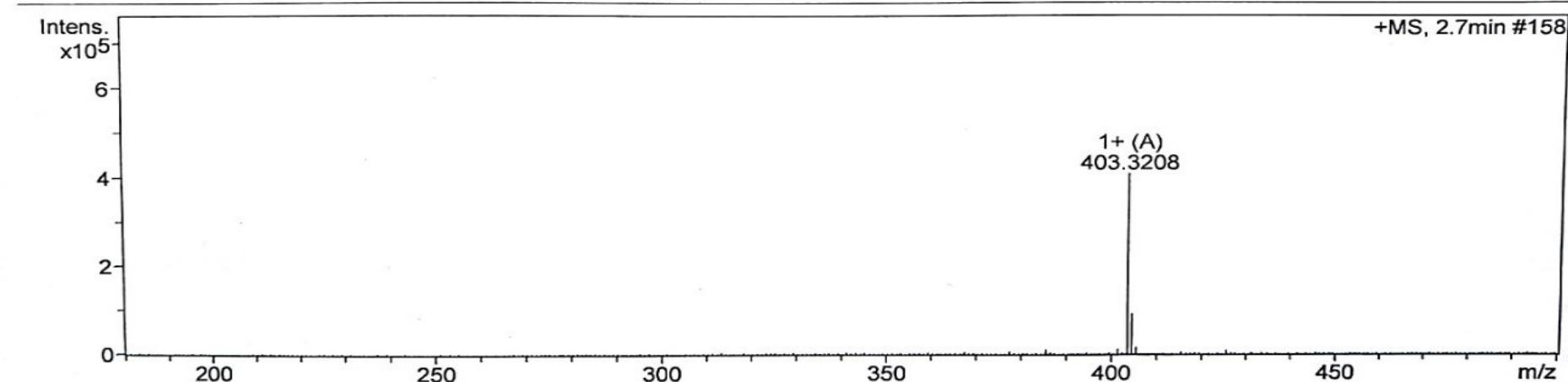
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Method 20150915.m Operator BDAL@DE
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Comment

Acquisition Parameter

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Scan End	1500 m/z	Set Collision Cell RF	600.0 Vpp	Set Divert Valve	Waste



Meas. m/z	#	Formula	Score	m/z	err [ppm]	Mean err [ppm]	mSig ma	rdb	e ⁻ Conf	N-R rule
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Figure S36. HRMS spectrum of impurity 2.

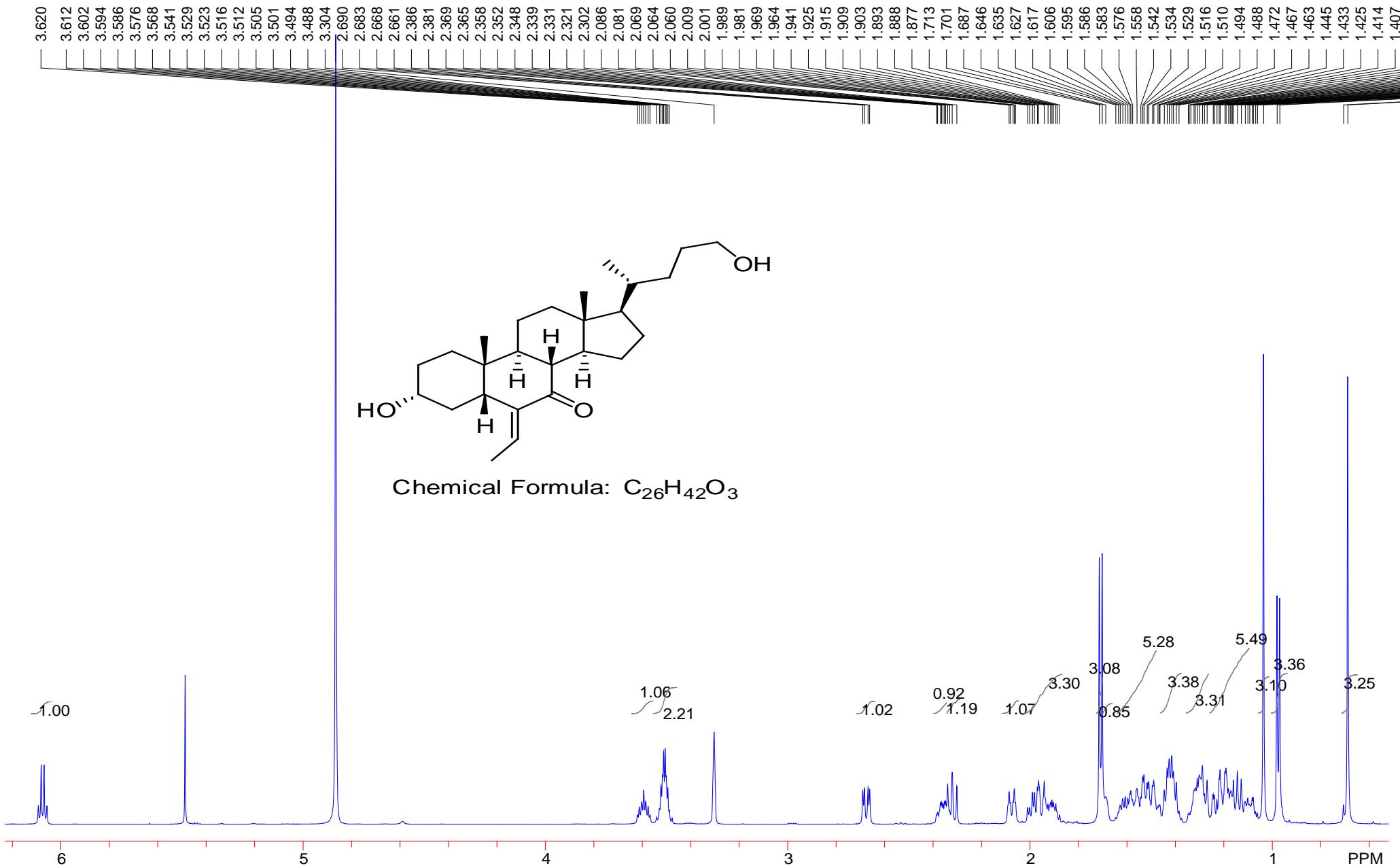
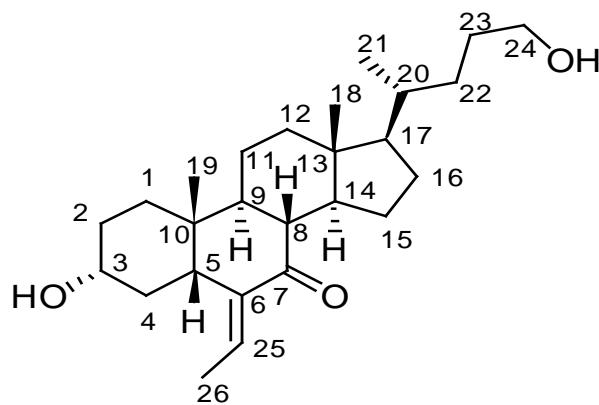
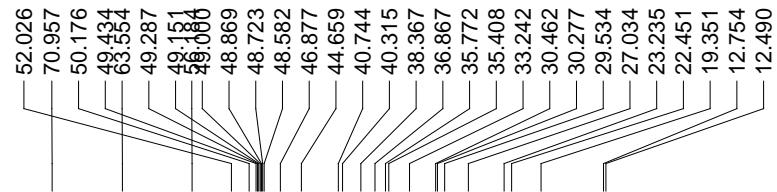


Figure S37. ^1H NMR spectrum of impurity 2.

207.644

145.376

130.336



Chemical Formula: $C_{26}H_{42}O_3$

200

150

100

50

PPM

Figure S38. ^{13}C NMR spectrum of impurity 2.

130.336

70.945

63.552

56.176

52.021

50.173

46.867

40.738

40.314

38.364

36.870

35.402

33.229

30.451

30.268

29.537

27.022

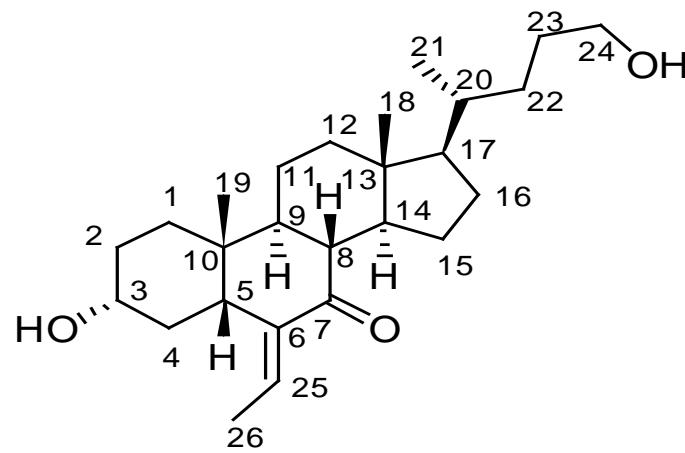
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12.496



Chemical Formula: $C_{26}H_{42}O_3$

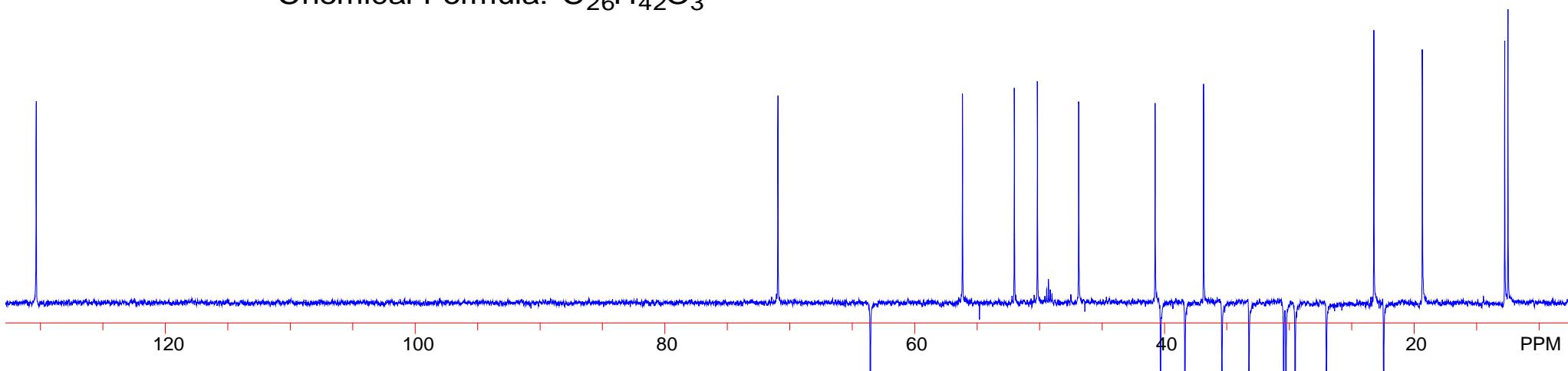


Figure S39. DEPT 135 spectrum of impurity 2.

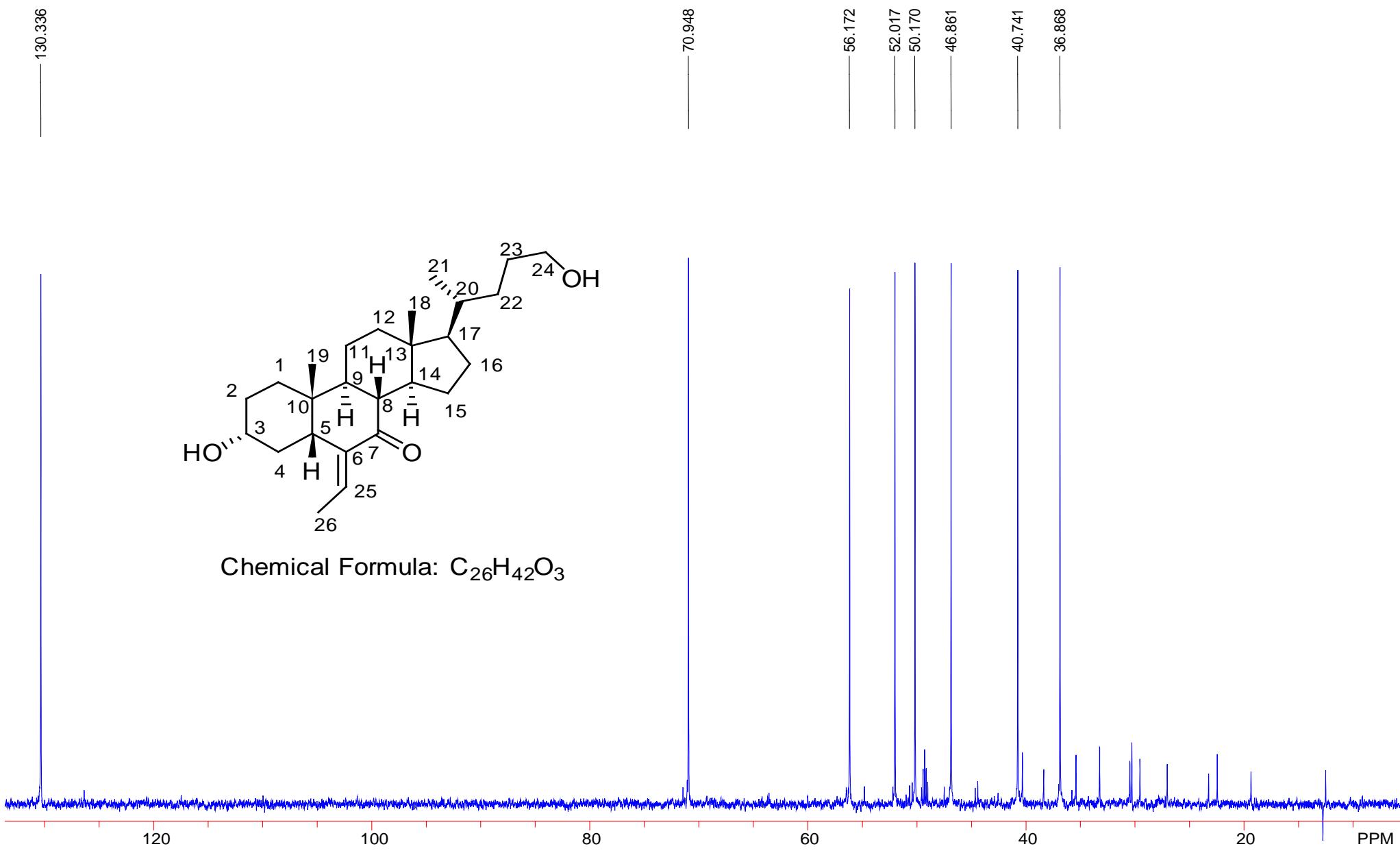


Figure S40. DEPT 90 spectrum of impurity 2.

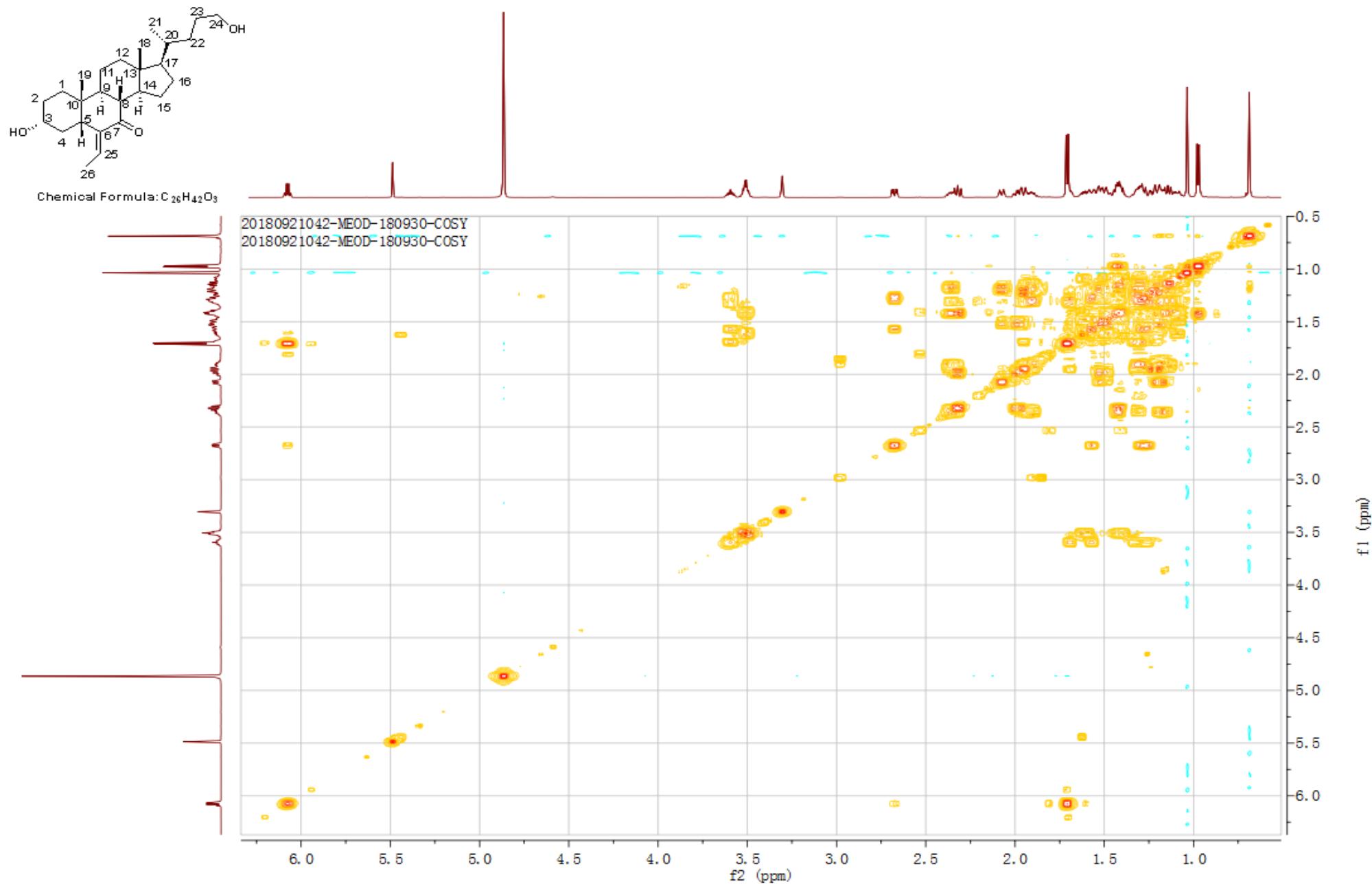


Figure S41. H-H COSY spectrum of impurity 2.

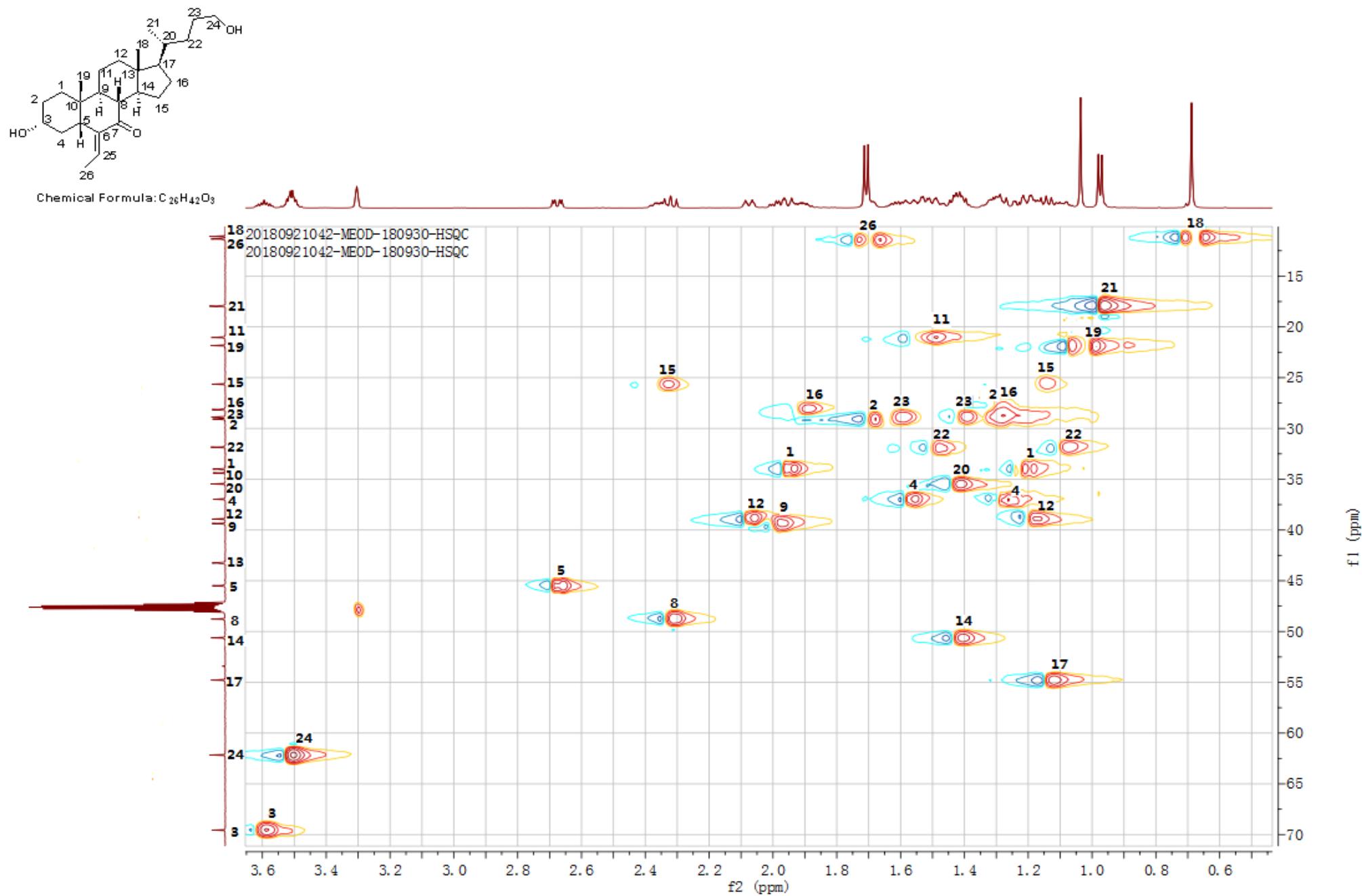


Figure S42. HSQC-1 spectrum of impurity 2.

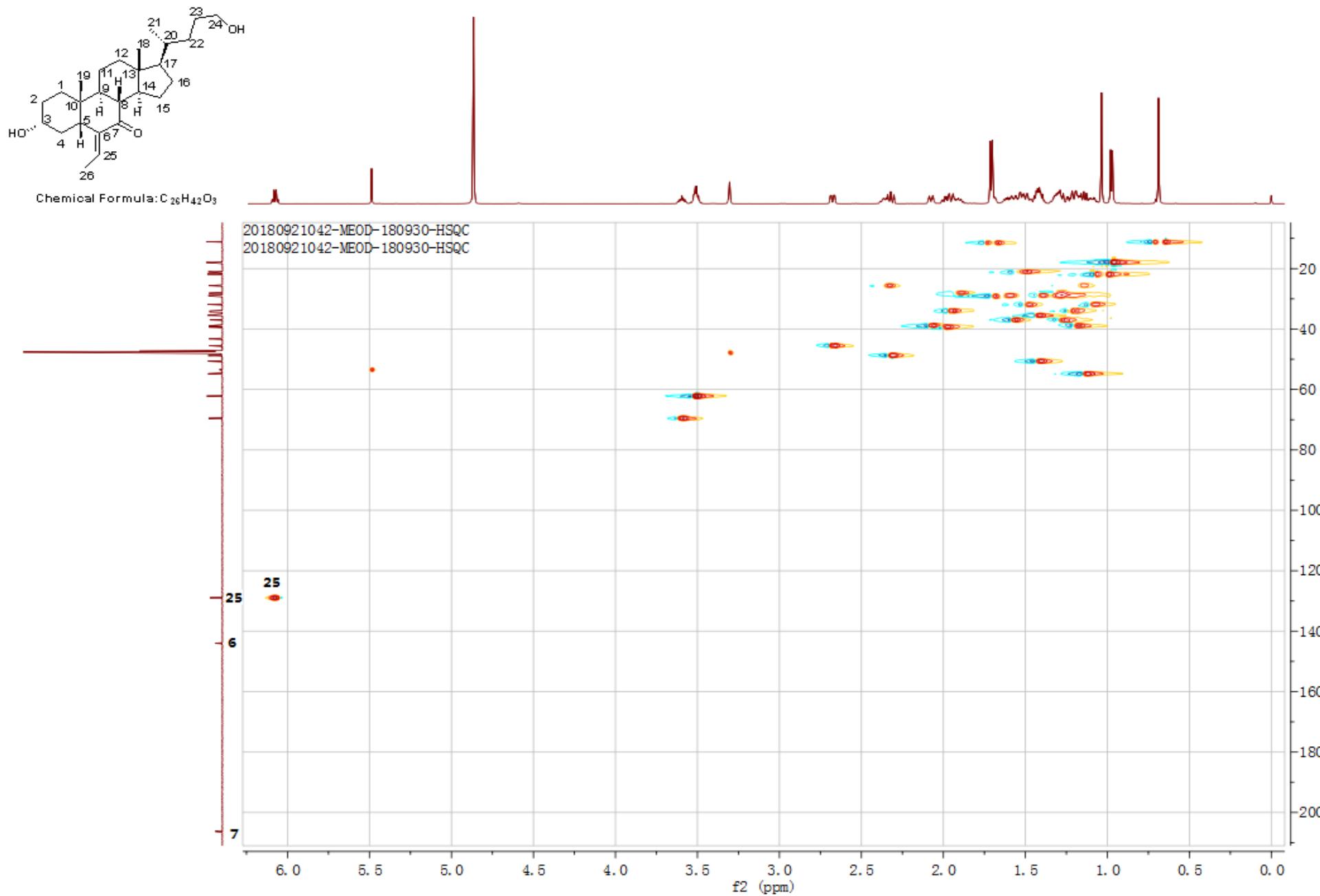


Figure S43. HSQC-2 spectrum of impurity 2.

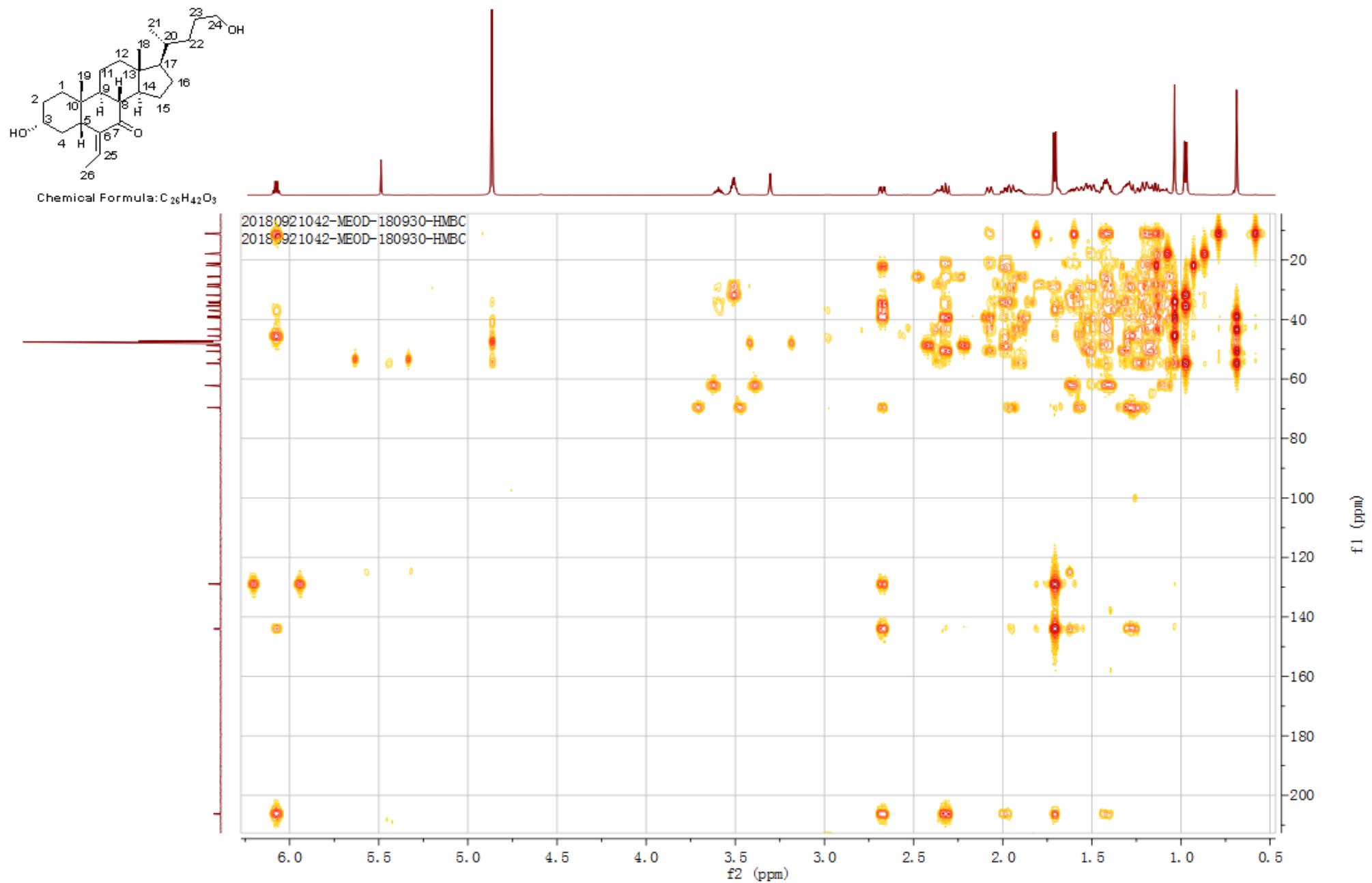


Figure S44. HMBC spectrum of impurity 2.