Supporting information

Total Synthesis and Stereochemical Revision of Xiamenmycin A

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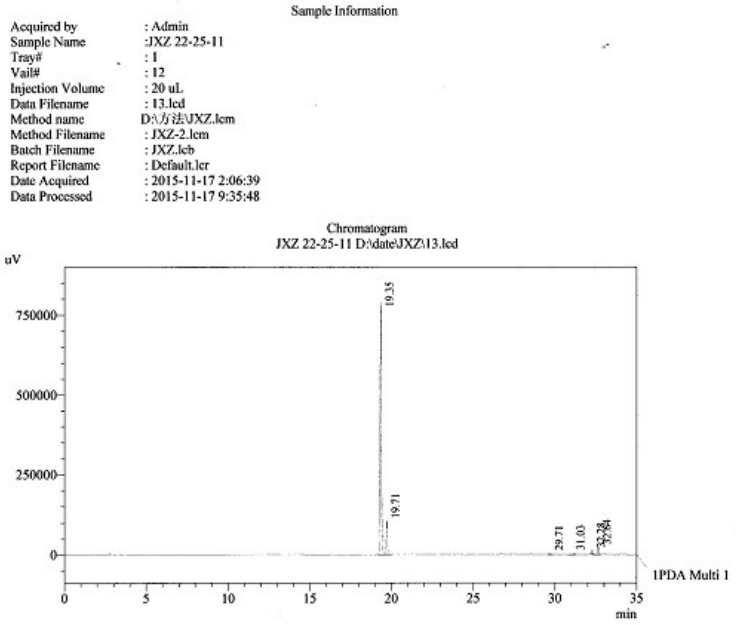
Contents

General Information

Solvents were dried according to standard procedures where needed. All reagents and solvents were purchased from commercial suppliers. Column chromatography was carried out on silica gel (160–200 mesh). Melting points were measured on microscope melting point apparatus**.** IR spectra were recorded on a Thermo Nicolet 5700 FT-IR microscope Centaur μ s spectrophotometer. NMR spectra were recorded on 400 or 600 MHz NMR spectrometer. Chemical shifts are referenced to the residual solvent peak and reported in ppm (δ scale) and all coupling constant (*J*) values are given in Hz. The following multiplicity abbreviations are used: (s) singlet, (d) doublet, (t) triplet, (q) quartet, (m) multiplet, and (br) broad. ESI-HRMS data were measured on orbitrap mass spectrometer.

HPLC analysis: Column: Pinnade II C18 Column size: 0.46 cm I.D. x 25 cm L x 5 μ m; column temperature: 35℃; injection volume: 20μL; mobile phase: CH_3CN/H_2O/0.1%HCOOH; flow rate: 1.0mL/min Wavelength : 272nm; a gradient program was used as follows:

Time(min)	CH_3CN(%)	H_2O(%)
0	5	95
5	5	95
35	90	10
40	90	10
50	5	95
55	5	95



PeakTable

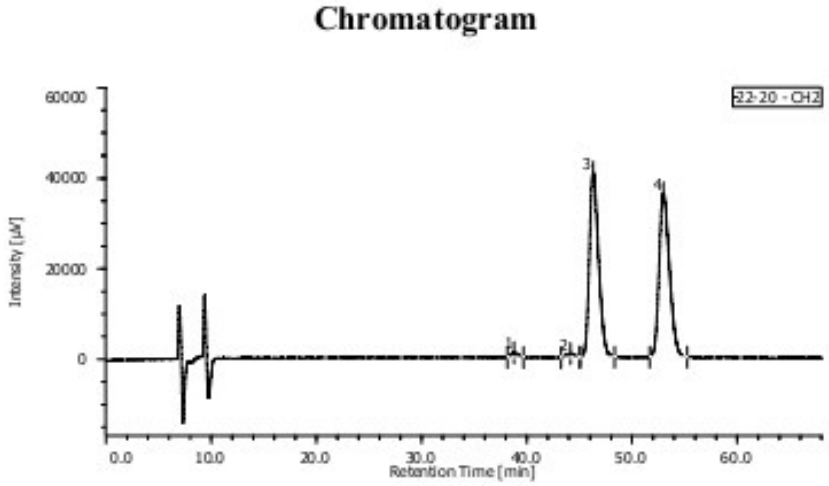
PDA Ch1 272nm 4nm

Peak#	Ret. Time	Area	Height	Area %
1	19.34	4080229	789568	82.389
2	19.70	554239	106634	11.191
3	29.71	23795	4479	0.480
4	31.03	39953	5912	0.807
5	32.28	74034	13252	1.495
6	32.64	138968	23930	2.806
7	36.98	41176	7852	0.831
Total		4952395	951628	100.000

HPLC spectra of compound 7 and 7′ (entry 11 in Table 1)

HPLC ANALYSIS

Determination of the enantiomeric excess of compound **6** and **16.** column**:** CHIRALPAK OJ-H 0.46 cm I.D. x 25 cm L x 5 μ m; column temperature: 25℃; injection volume: 10μL; mobile phase: hexane/*i*-PrOH (9/1); flow rate: 0.3mL/min Wavelength: 272 nm



Chromatogram Information

User Name	Administrator
Date Modified	2015-10-29 16:24:52
Description	
HPLC System Name	HPLC
Injection Date	2015-10-29 15:12:14
Volume	10.00 [μL]
Sample Number	1
Project Name	chiral drugs-sep
Acquisition Time	68.0 [min] + 10.0 [min]
Acquisition Sequence	IXZ-22-20-OJ-IPA10(0.5-70-272)
Control Method	IXZ-OJ-IPA10(0.5-70-272)
Peak ID Table	
Calibration Method	
Additional Information	

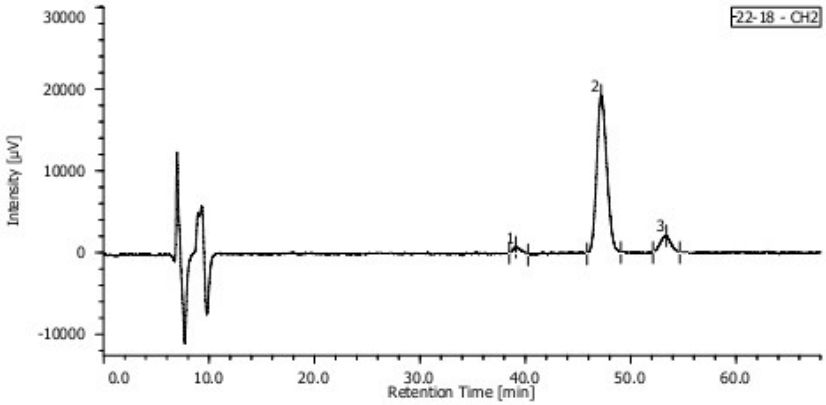
Channel & Peak Information Table

Chromatogram Name	22-20-CH2
Sample Name	
Channel Name	CH2
Sampling Interval	500 [msec]
Peak Method	pxz-oj-peak
Formula	
Decision	

#	Peak Name	CH	tR [min]	Area [μV*sec]	Height [μV]	Area%	Height%	Resolution	Symmetry Factor	Capacity Factor
1	Unknown	2	38.767	51475	1064	1.018	1.346	3.855	1.195	N/A
2	Unknown	2	44.150	52509	933	1.040	1.180	1.396	N/A	N/A
3	Unknown	2	46.292	2480269	40840	49.056	51.663	3.948	1.290	N/A
4	Unknown	2	52.967	2471606	36215	48.885	45.811	N/A	1.277	N/A

HPLC spectra of rac-6

Chromatogram



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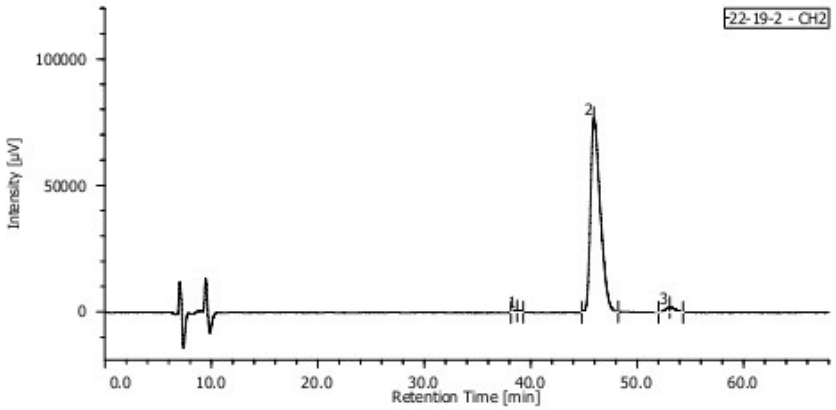
Description	
HPLC System Name	HPLC
Injection Date	2015-10-29 18:45:31
Volume	20.00 [μL]
Sample Number	3
Project Name	chiral drugs-sep
Acquisition Time	68.0 [min]
Acquisition Sequence	JXZ-22-18-OJ-IPA10(0.5-70-272)
Control Method	JXZ-OJ-IPA10(0.5-70-272)
Peak ID Table	
Calibration Method	
Additional Information	

Channel & Peak Information Table	
Chromatogram Name	22-18-CH2
Sample Name	
Channel Name	CH2
Sampling Interval	500 [msec]
Peak Method	jxz-oj-peak
Formula	
Decision	

#	Peak Name	CH	tR [min]	Area [μV sec]	Height [μV]	Area%	Height%	Resolution	Symmetry Factor	Capacity Factor
1	Unknown	2	39.083	45208	793	3.025	3.566	4.902	1.447	N/A
2	Unknown	2	47.192	1301437	19365	87.069	87.079	3.358	1.161	N/A
3	Unknown	2	53.350	149112	2080	9.969	9.355	N/A	1.029	N/A

HPLC spectra of 6

Chromatogram



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Description	
HPLC System Name	HPLC
Injection Date	2015-10-29 16:28:09
Volume	10.00 [μL]
Sample Number	2
Project Name	chiral drugs-sep
Acquisition Time	68.0 [min]
Acquisition Sequence	JXZ-22-19-2-OJ-IPA10(0.5-70-272)
Control Method	JXZ-OJ-IPA10(0.5-70-272)
Peak ID Table	
Calibration Method	
Additional Information	

Channel & Peak Information Table	
Chromatogram Name	22-19-2-CH2
Sample Name	
Channel Name	CH2
Sampling Interval	500 [msec]
Peak Method	jxz-oj-peak
Formula	
Decision	

#	Peak Name	CH	tR [min]	Area [μV sec]	Height [μV]	Area%	Height%	Resolution	Symmetry Factor	Capacity Factor
1	Unknown	2	38.708	18950	508	0.376	0.640	5.325	1.002	N/A
2	Unknown	2	45.933	4895067	76838	97.074	96.849	4.172	1.543	N/A
3	Unknown	2	53.058	128607	1992	2.550	2.510	N/A	1.084	N/A

HPLC spectra of 6（After recrystallization）

Data File E:\DATA\ZYH\201508180000003.D
Sample Name: 21-6

Acq. Operator : □ □ Seq. Line : 1
Acq. Instrument : Agilent 1260 Location : Vial 1
Injection Date : 8/18/2015 12:07:38 AM Inj : 3
Inj Volume : 10 µl

Acq. Method : C:\Chem32\1\DATA\ZYH\20150727 2015-08-18 12-24-45\20150818.M
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Analysis Method : C:\CHEM32\2\METHODS\150818.M
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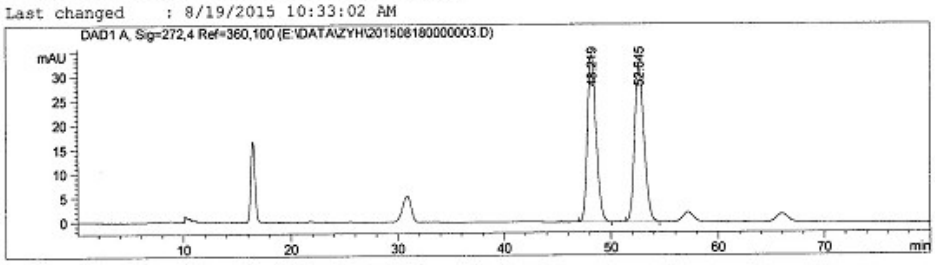

Area Percent Report

Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: DAD1 A, Sig=272,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	48.219	BB	0.8650	1948.58386	34.39162	50.0452
2	52.645	BB	0.9428	1945.06433	31.56852	49.9548
Totals :				3893.64819	65.96015	

*** End of Report ***

HPLC spectra of rac-16

Data File E:\DATA\ZYH\201508180000006.D
Sample Name: 22-9-BL

Acq. Operator	: □ □	Seq. Line	: 3
Acq. Instrument	: Agilent 1260	Location	: Vial 3
Injection Date	: 8/18/2015 4:10:35 AM	Inj	: 1
		Inj Volume	: 10 µl
Acq. Method	: C:\Chem32\1\DATA\ZYH\20150727 2015-08-18 12-24-45\20150818.M		
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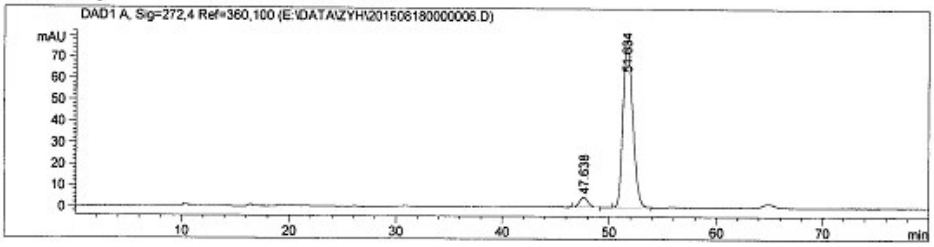
Analysis Method	: C:\CHEM32\2\METHODS\150818.M		
Last changed	: 8/19/2015 10:34:01 AM		



Area Percent Report

Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: DAD1 A, Sig=272,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	47.638	BB	0.6618	244.94620	4.49463	4.7715
2	51.634	BB	0.9497	4888.58838	78.16419	95.2285
Totals :				5133.53458	82.65883	

*** End of Report ***

HPLC spectra of 16

HPLC analysis for compound **1**, **24** and natural xiamenmycin A: CHIRALPAK OZ-H; Column size: 0.46 cm I.D. x 25 cm L x 5 μm; column temperature: 35℃; injection volume: 5 μL; mobile phase: n-Hexane/EtOH/TFA =80/20/0.1 (V/V/V); flow rate: 1.0 mL/min Wavelength: 254 nm

A) Mixture of synthetic samples

Column	:	CHIRALCEL® OZ-H
Column size	:	0.46 cm I.D. ×25 cm L×5 μm
Injection	:	25 μl
Mobile phase	:	烷烃和醇类
Flow rate	:	
Wave length	:	
Temperature	:	
Sample solution	:	取 19-9 和 40-3 各 100UL 用 EtOH Hexane 稀释到 1ML
HPLC equipment	:	Shimadzu LC 20 with UV detector SPD-20A

Sample structure A150106X 19-9+40-3

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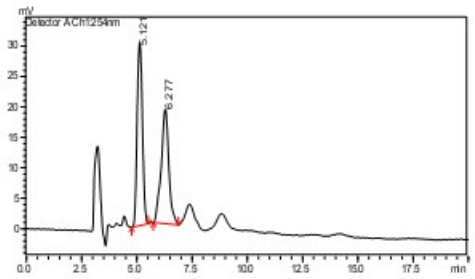

<Column Performance Report>

Peak No.	Time	Area	Area %	Plate number	Tailing	Resolution
1	5.121	501812	52.6832	2002.330	1.123	--
2	6.277	450697	47.3168	1692.447	1.034	2.164

B) Compound 1 (synthetic sample)

Column	:	CHIRALCEL® OZ-H
Column size	:	0.46 cm I.D. ×25 cm L×5 μm
Injection	:	5 μl
Mobile phase	:	
Flow rate	:	
Wave length	:	
Temperature	:	
Sample solution	:	送样已配
HPLC equipment	:	Shimadzu LC 20 with UV detector SPD-20A

Sample structure A150106X 19-9

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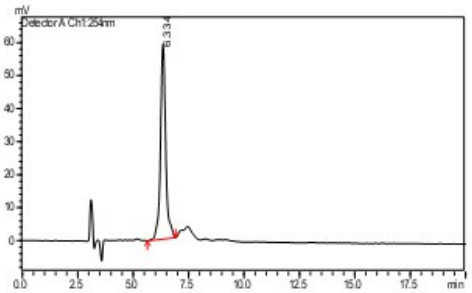

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Peak No.	Time	Area	Area %	Plate number	Tailing	Resolution
1	6.334	971074	100.0000	3647.273	1.156	--

C) Compound 24 (synthetic sample)

Column	:	CHIRALCEL® OZ-H
Column size	:	0.46 cm I.D. ×25 cm L×5 µm
Injection	:	5 µl
Mobile phase	:	
Flow rate	:	
Wave length	:	
Temperature	:	
Sample solution	:	送样已配
HPLC equipment	:	Shimadzu LC 20 with UV detector SPD-20A

Sample structure A150106X 40-3

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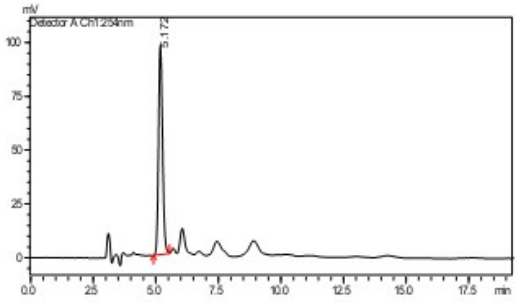

<Column Performance Report>

Peak No.	Time	Area	Area %	Plate number	Tailing	Resolution
1	5.172	1092709	100.0000	4120.876	1.227	--

D) Xiamenmycin sample (natural product)

Column	:	CHIRALCEL® OZ-H
Column size	:	0.46 cm I.D. ×25 cm L×5 µm
Injection	:	5 µl
Mobile phase	:	
Flow rate	:	
Wave length	:	
Temperature	:	
Sample solution	:	送样已配
HPLC equipment	:	Shimadzu LC 20 with UV detector SPD-20A

Sample structure A150106X XiaA

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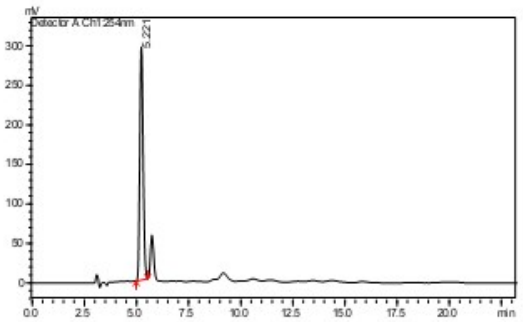
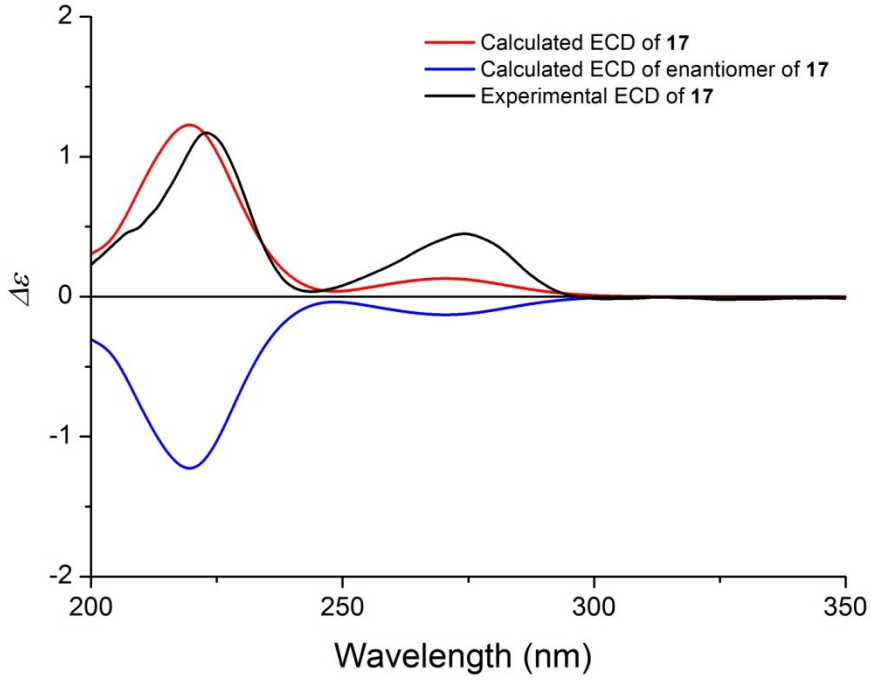
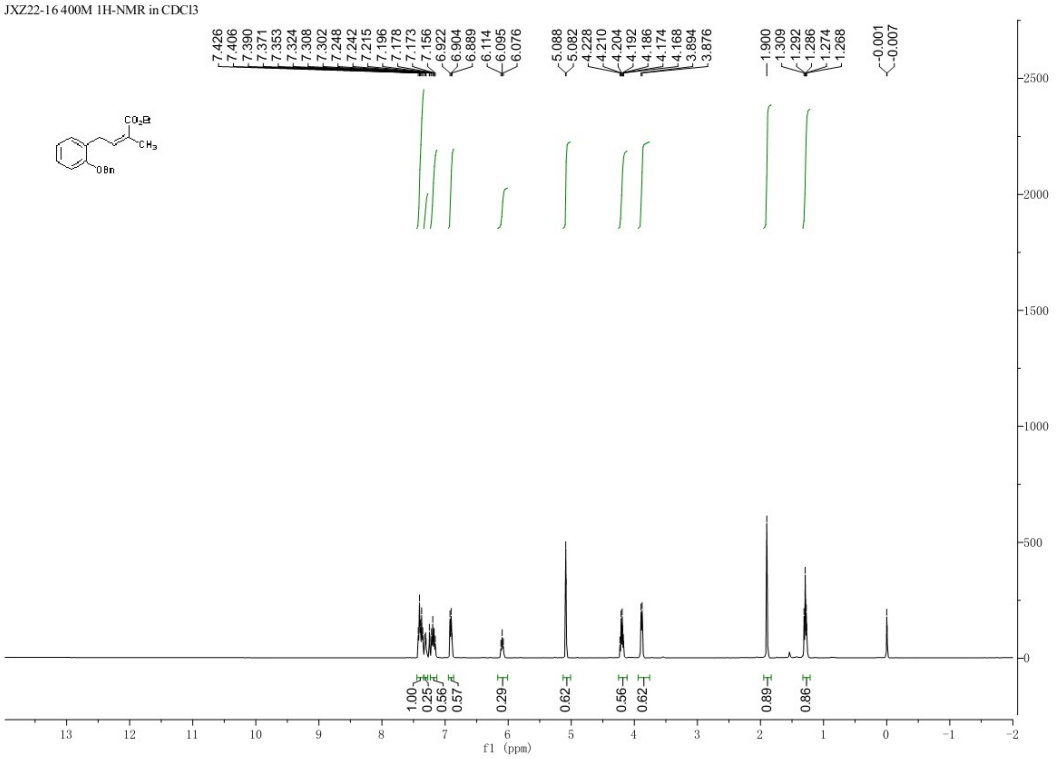


<Column Performance Report>

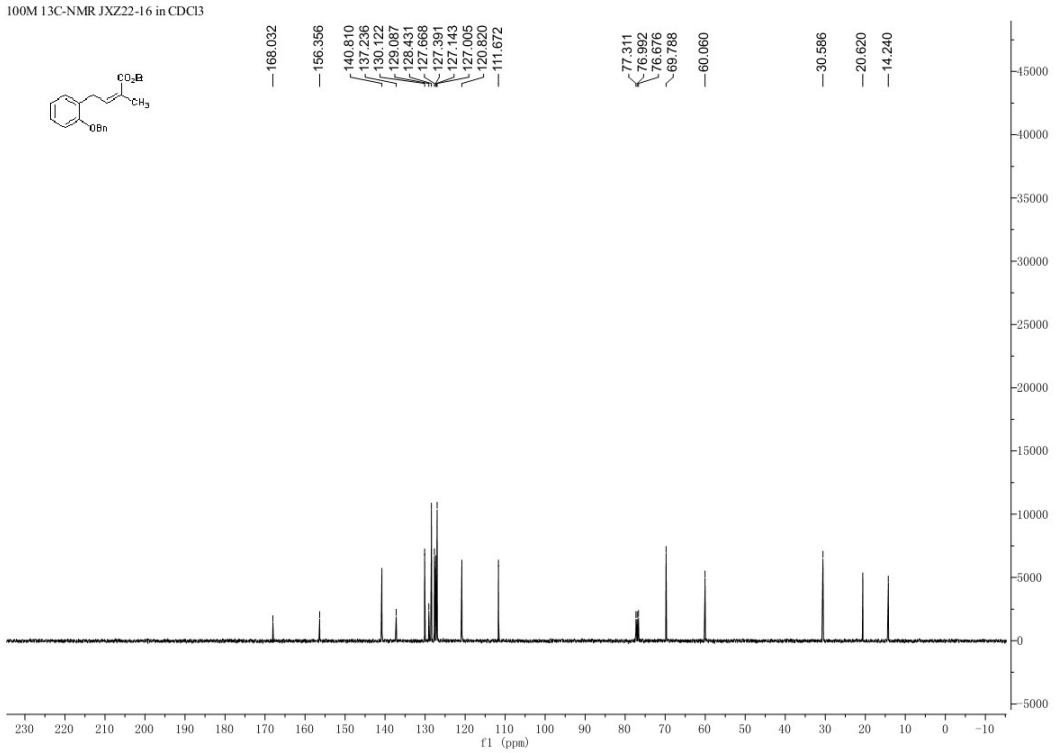
Peak No.	Time	Area	Area %	Plate number	Tailing	Resolution
1	5.221	3311420	100.0000	4150.407	1.208	--



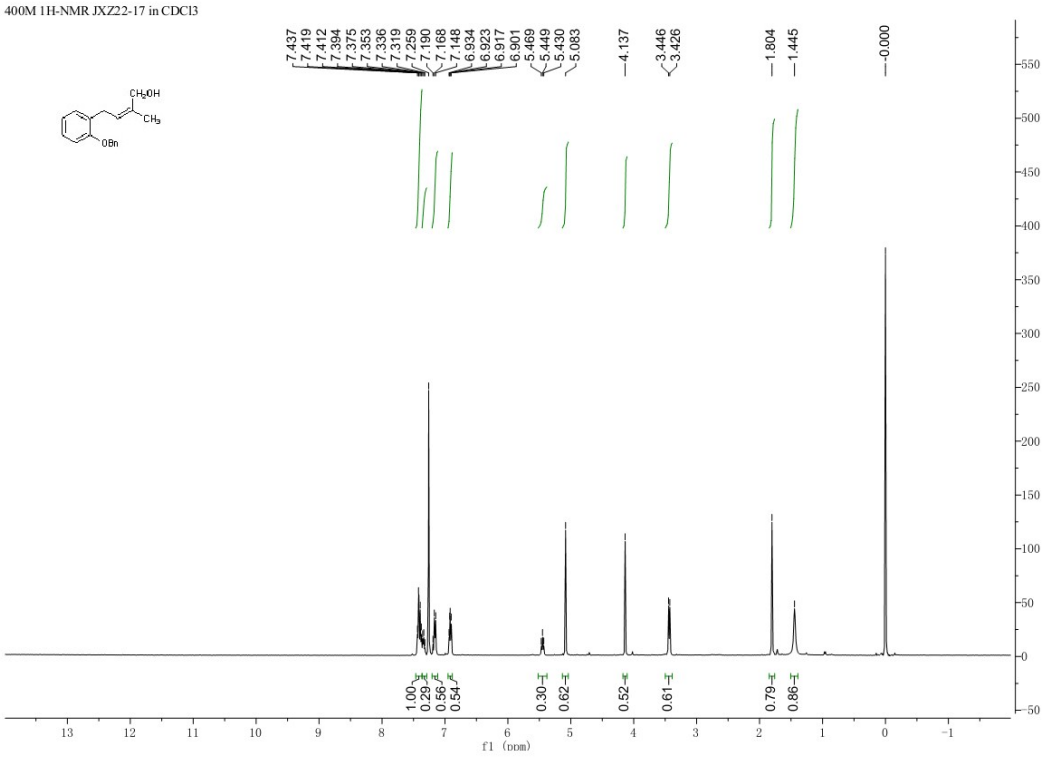
The theoretical CD spectrum and experimental CD spectrum of **17**



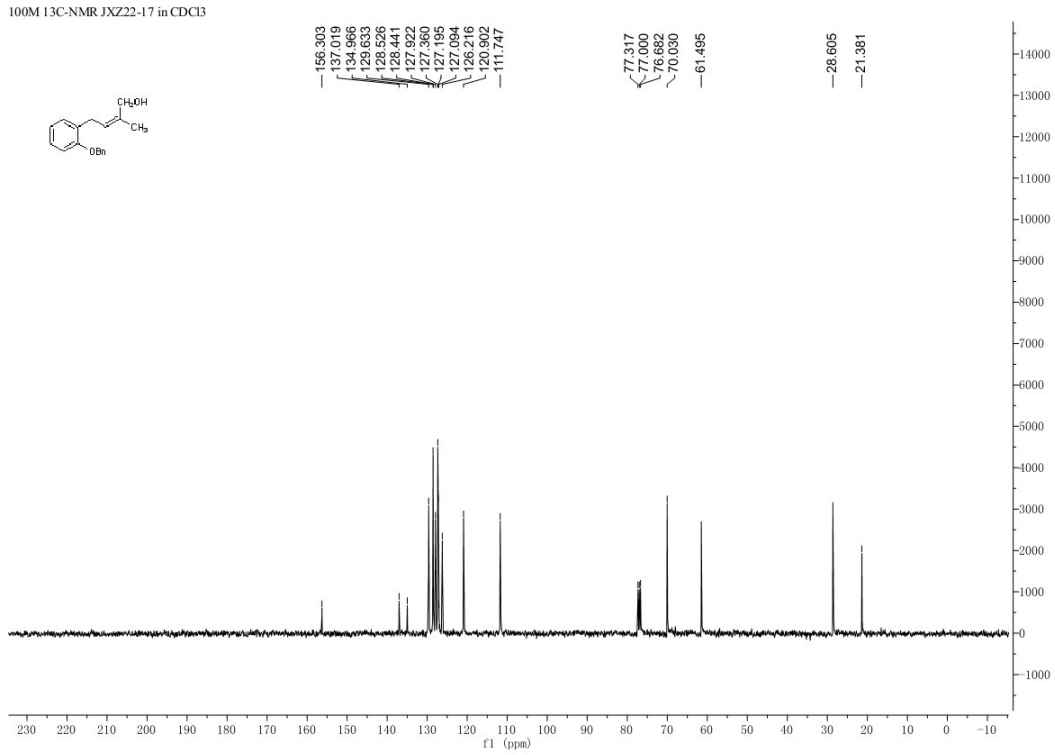
^{1}H NMR spectra of compound **4**



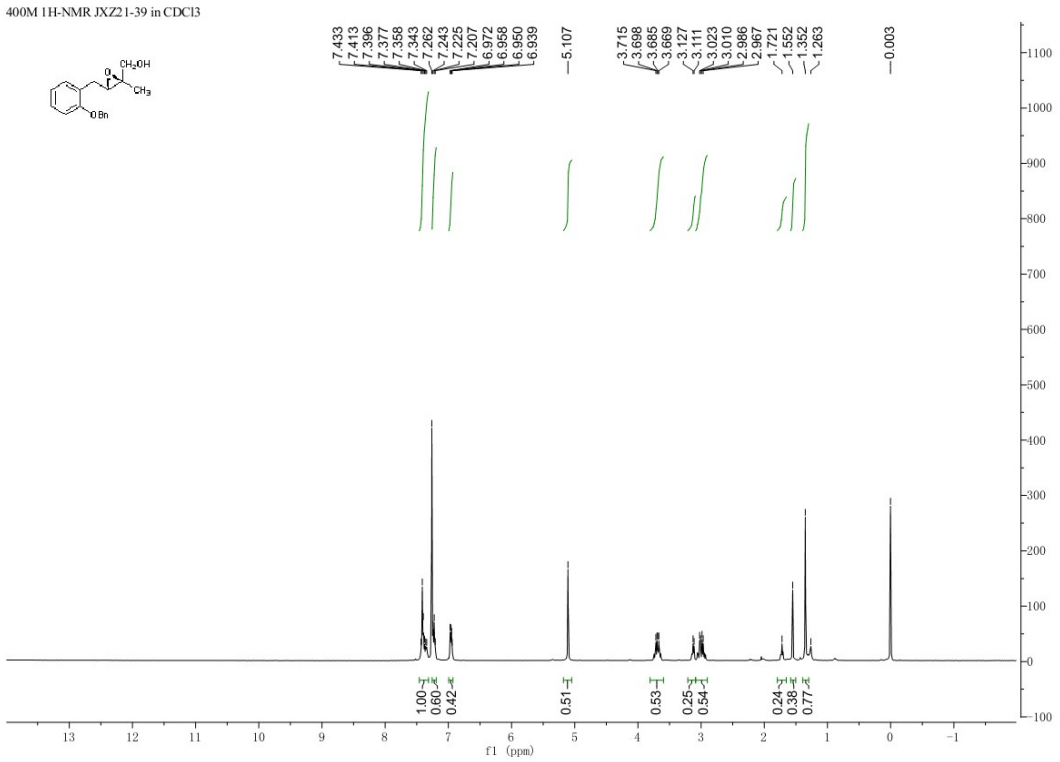
^{13}C NMR spectra of compound **4**



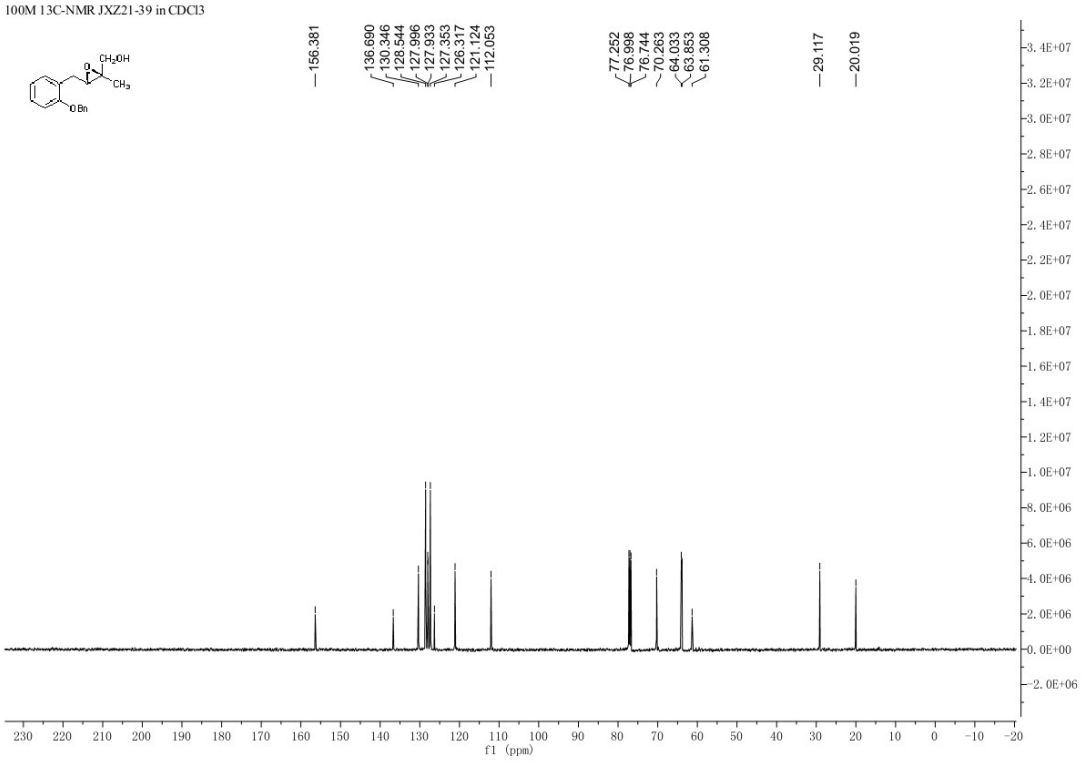
^{1}H NMR spectra of compound **5**



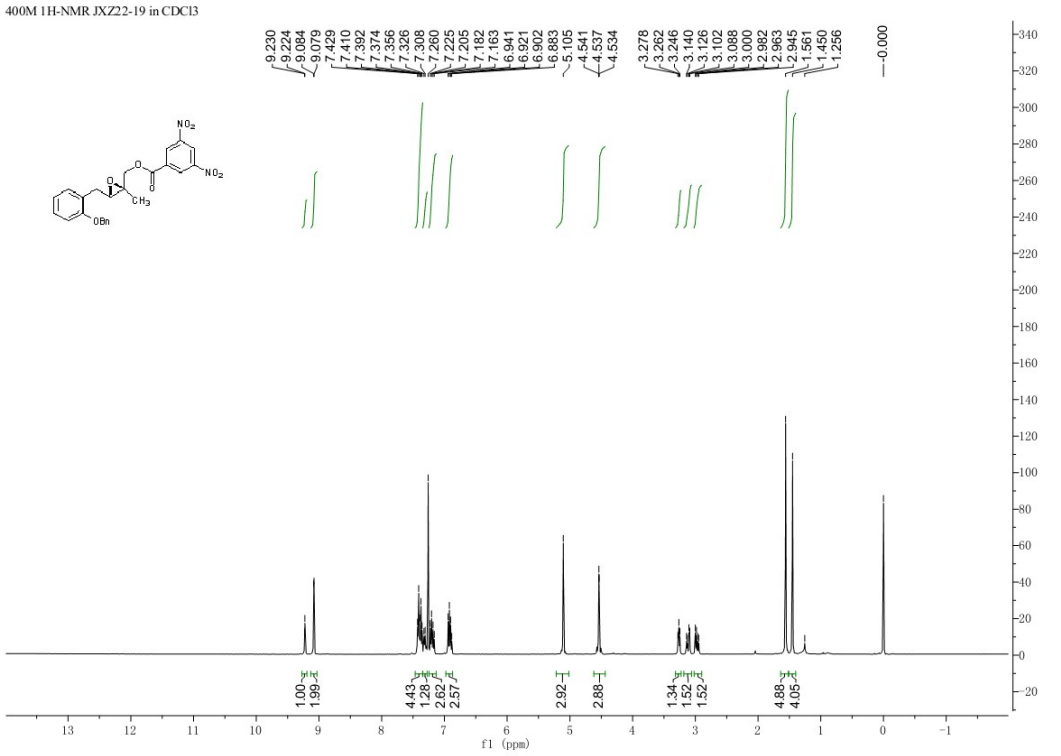
^{13}C NMR spectra of compound **5**



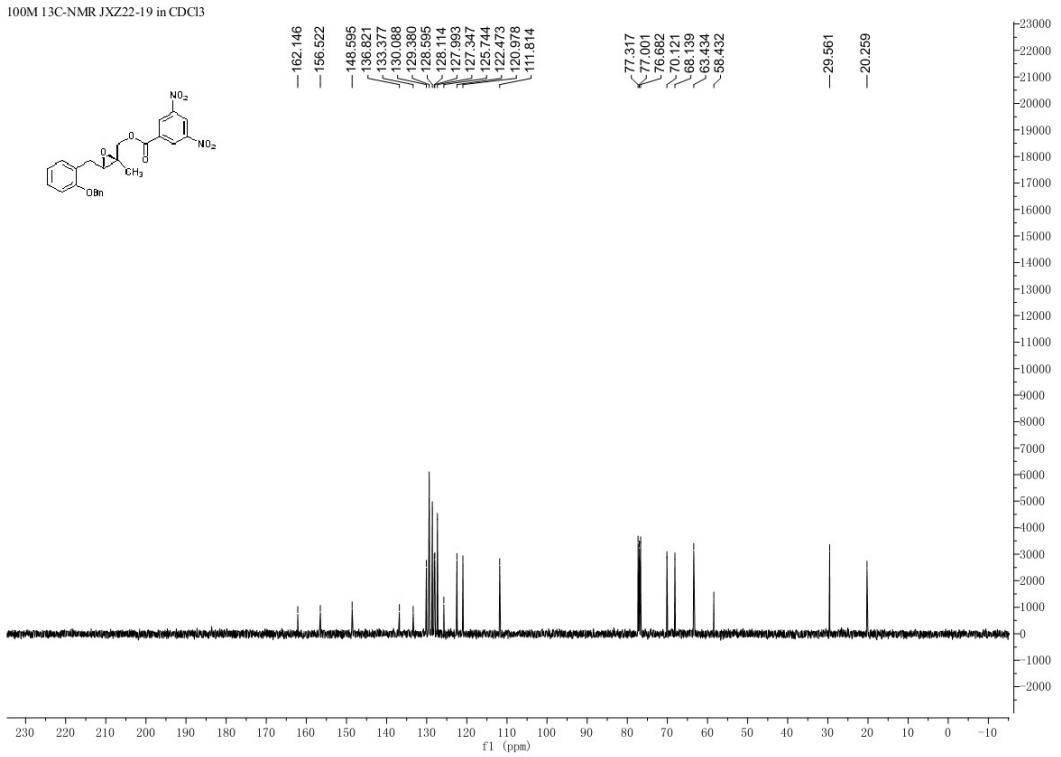
^{1}H NMR spectra of compound **6**



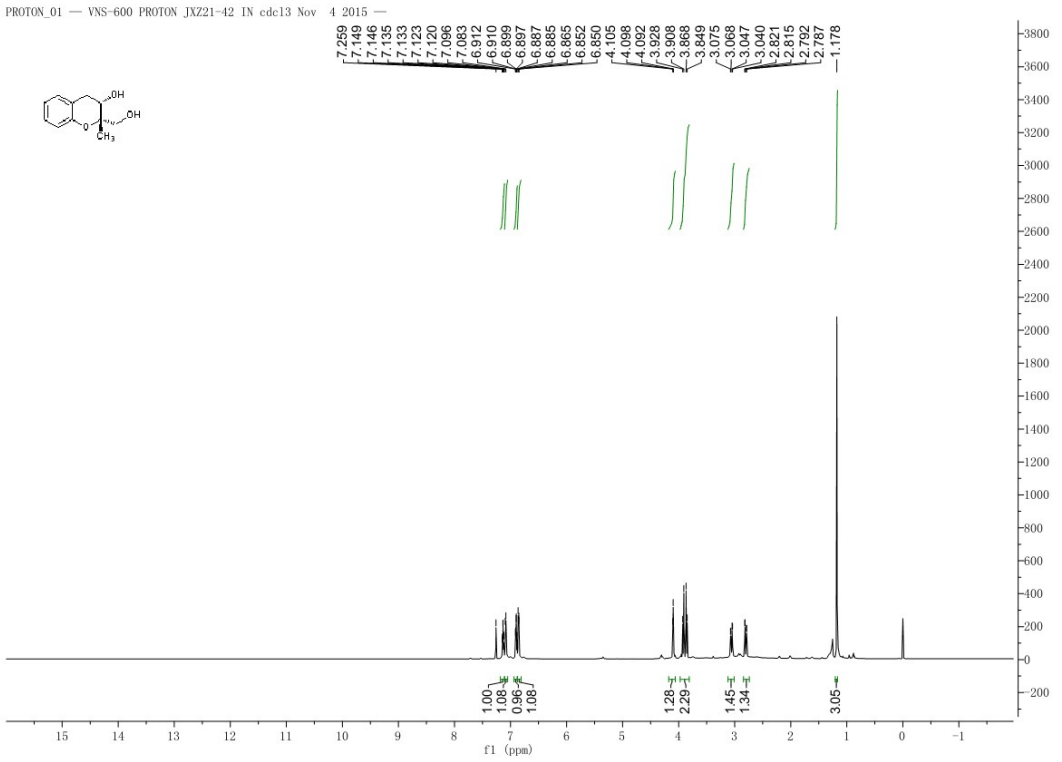
^{13}C NMR spectra of compound **6**



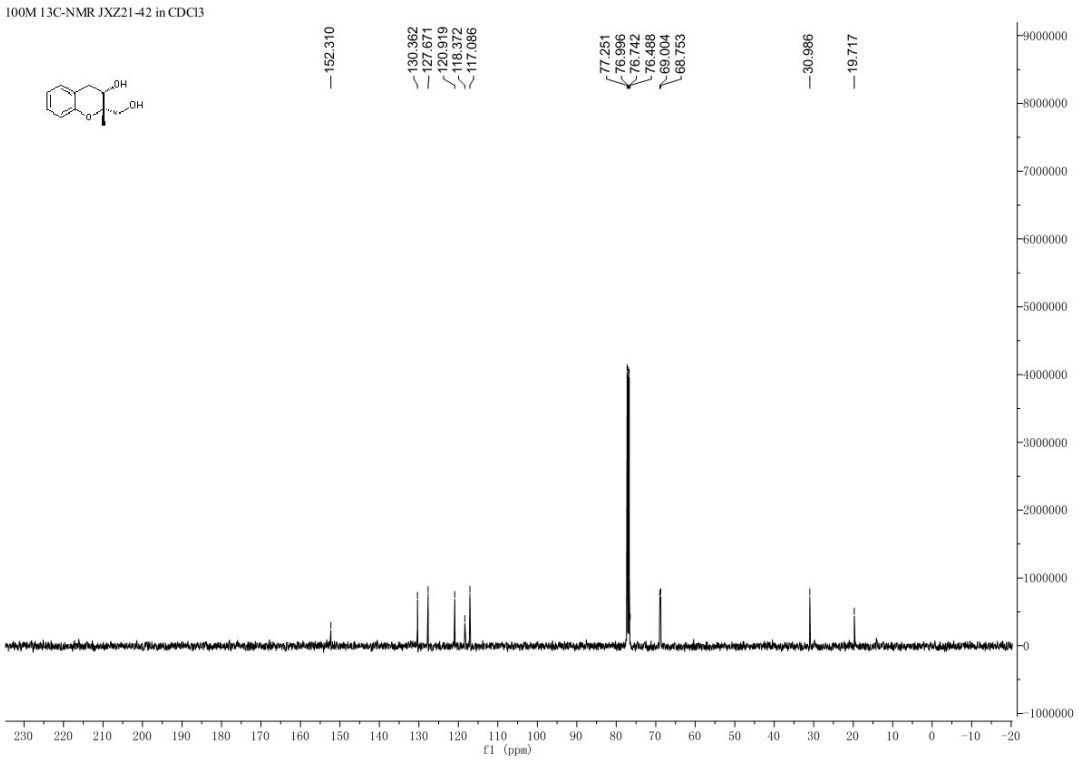
^{1}H NMR spectra of compound **6b**



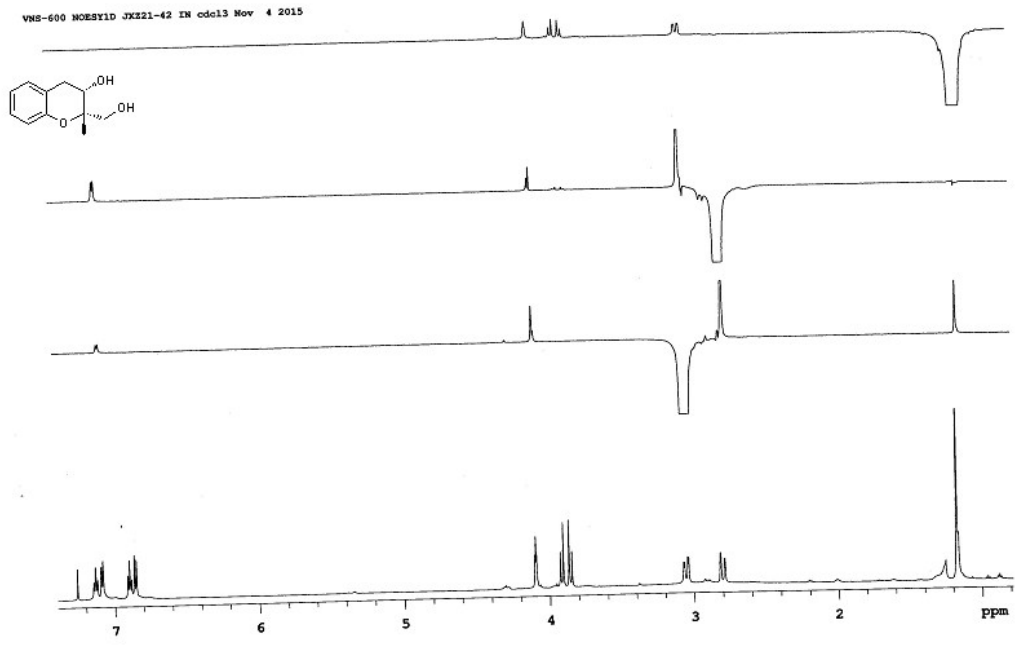
^{13}C NMR spectra of compound **6b**



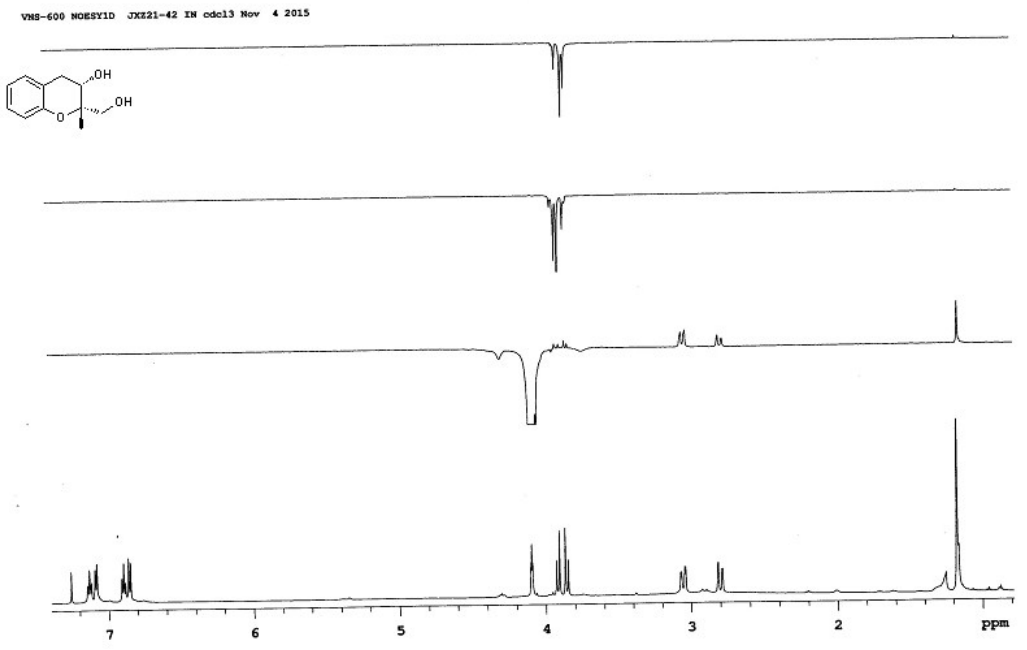
^{1}H NMR spectra of compound **7**



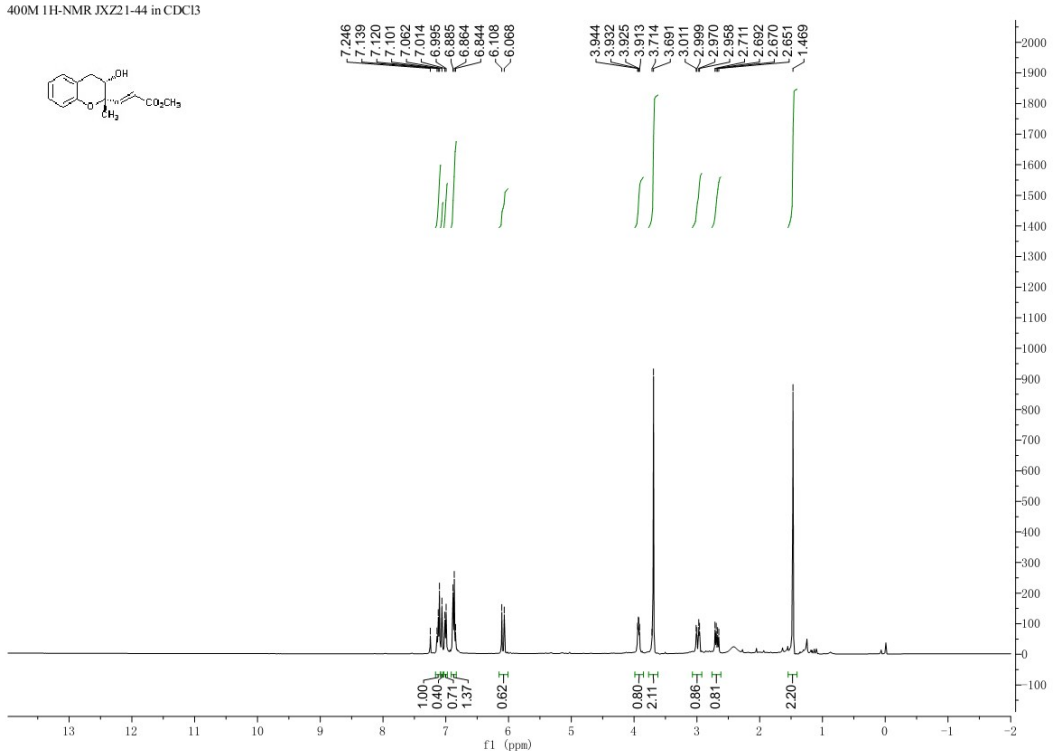
^{13}C NMR spectra of compound **7**



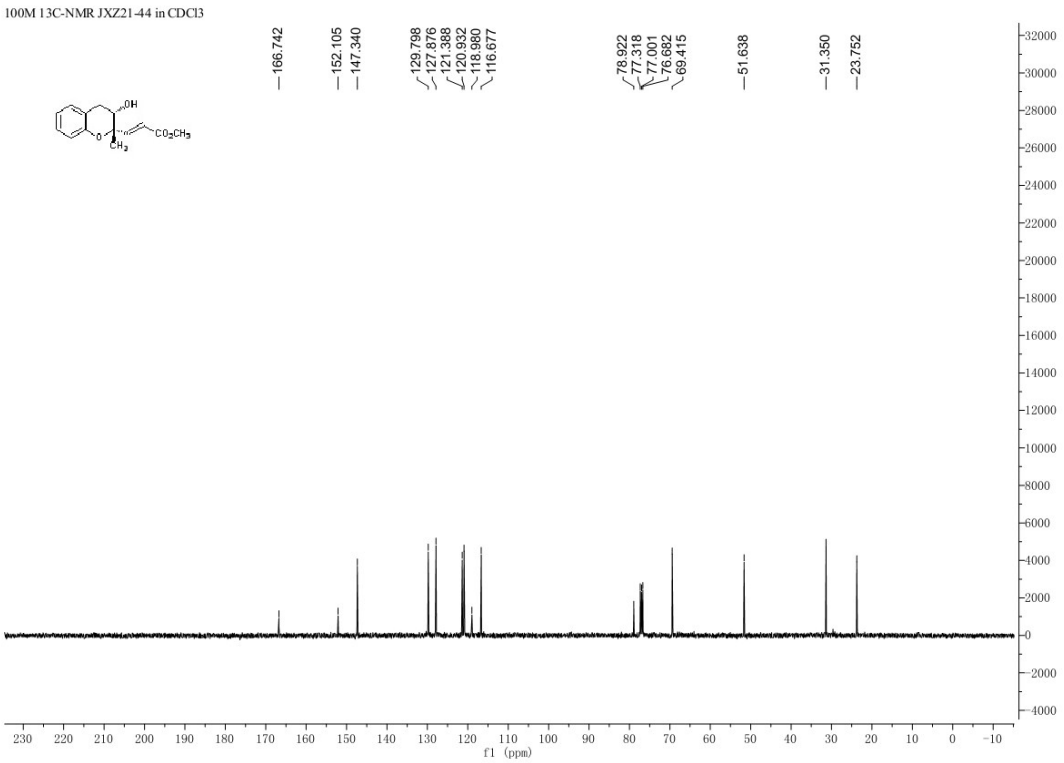
NOE spectra of compound **7**



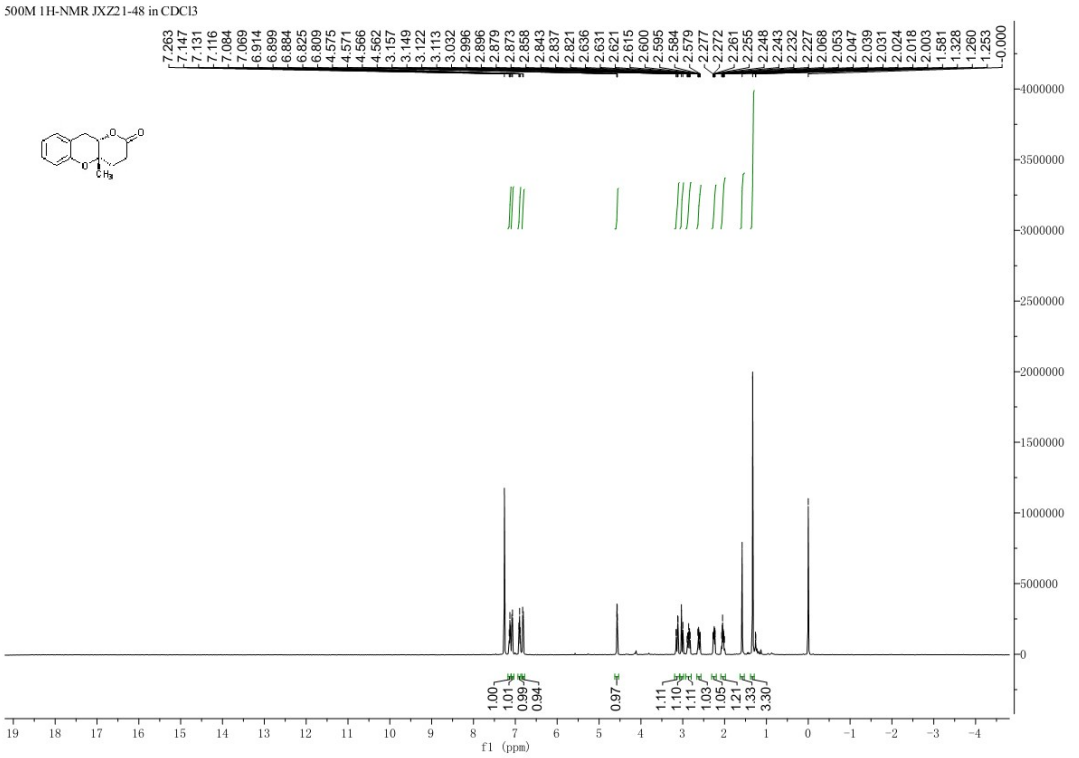
NOE spectra of compound **7**



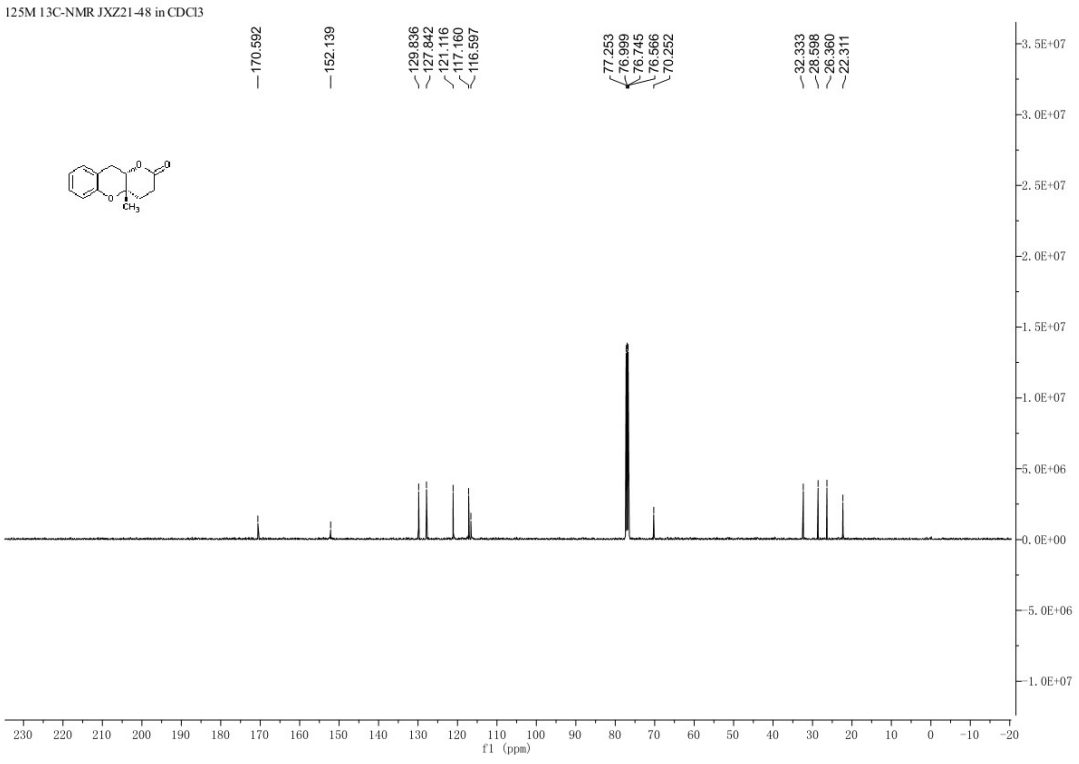
^{1}H NMR spectra of compound **8**



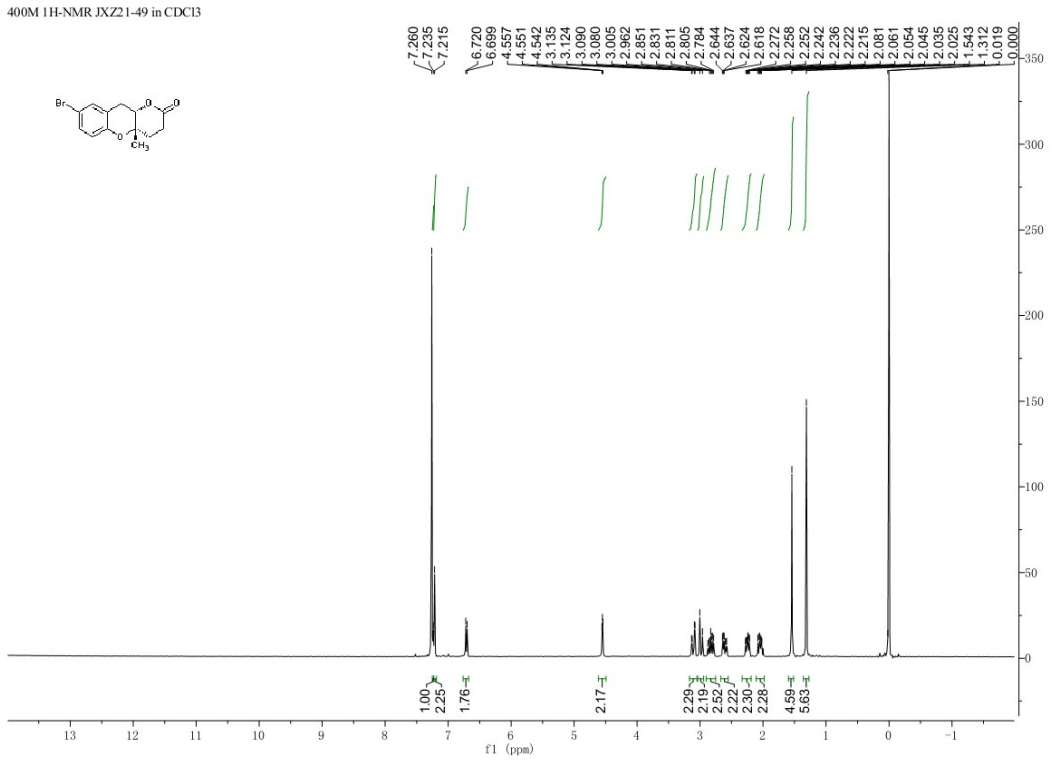
^{13}C NMR spectra of compound **8**



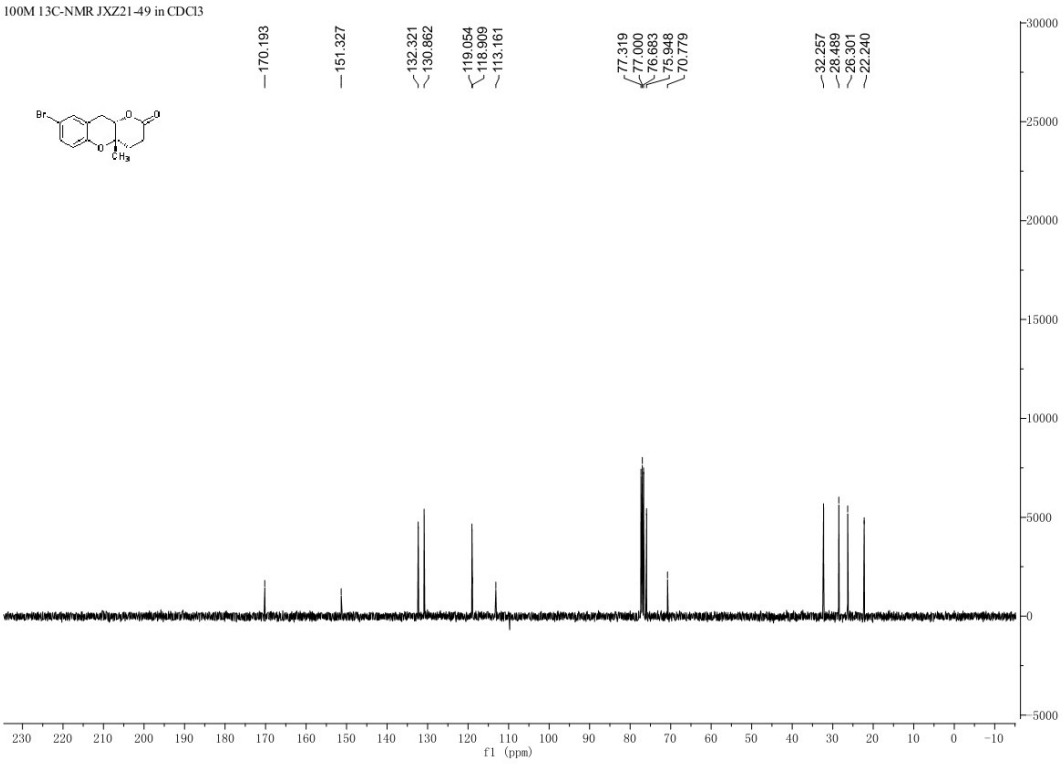
^{1}H NMR spectra of compound **9**



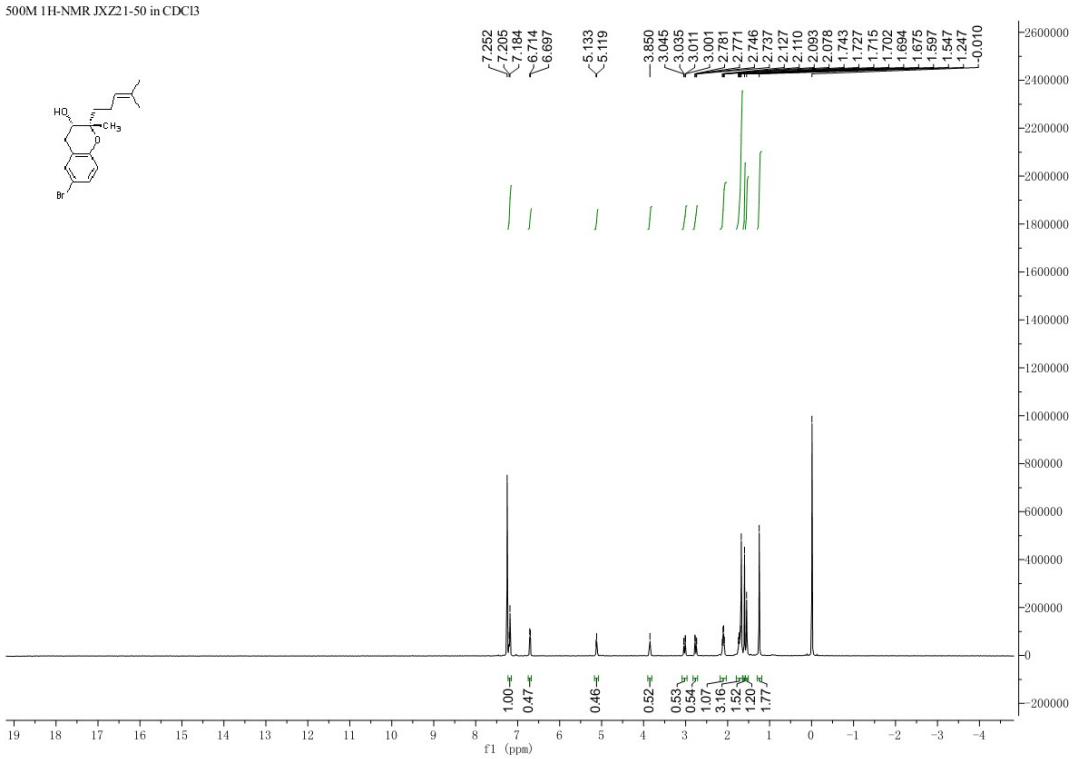
^{13}C NMR spectra of compound **9**



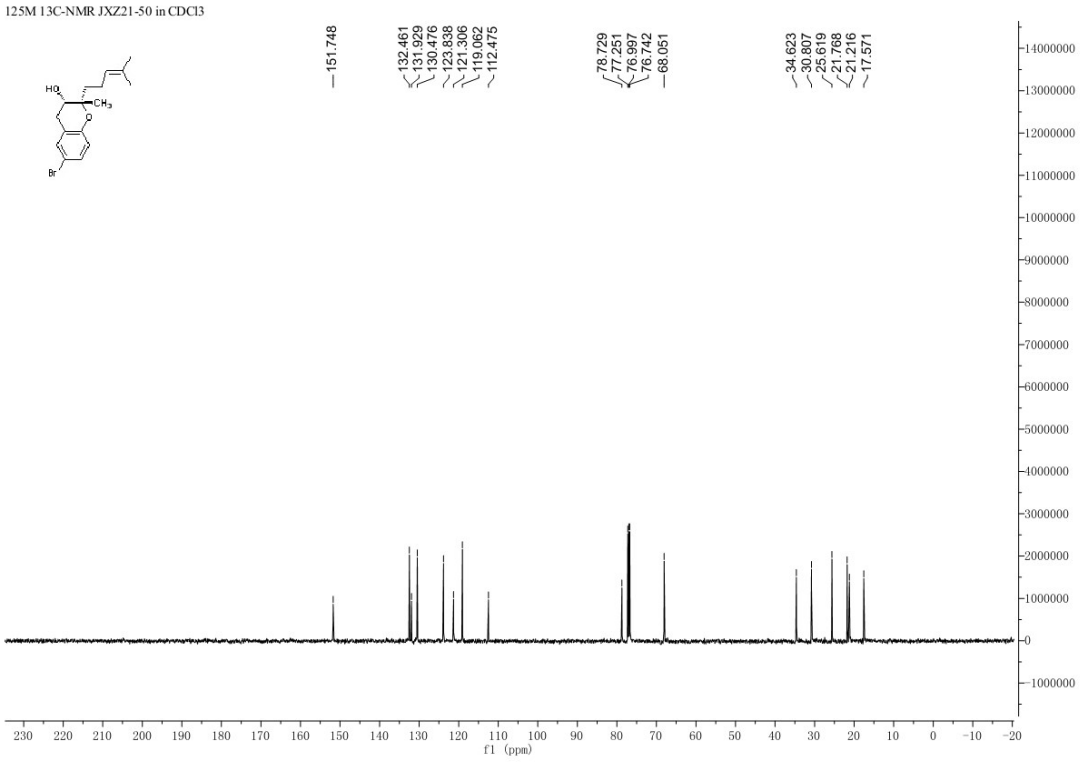
^{1}H NMR spectra of compound **10**



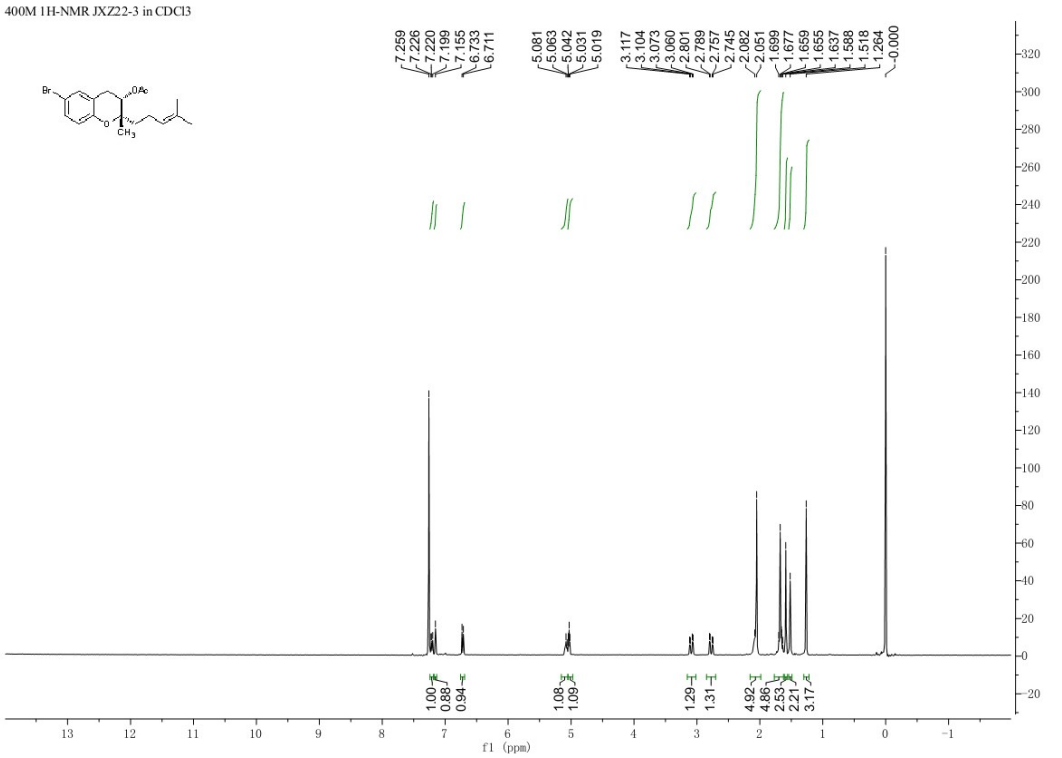
^{13}C NMR spectra of compound **10**



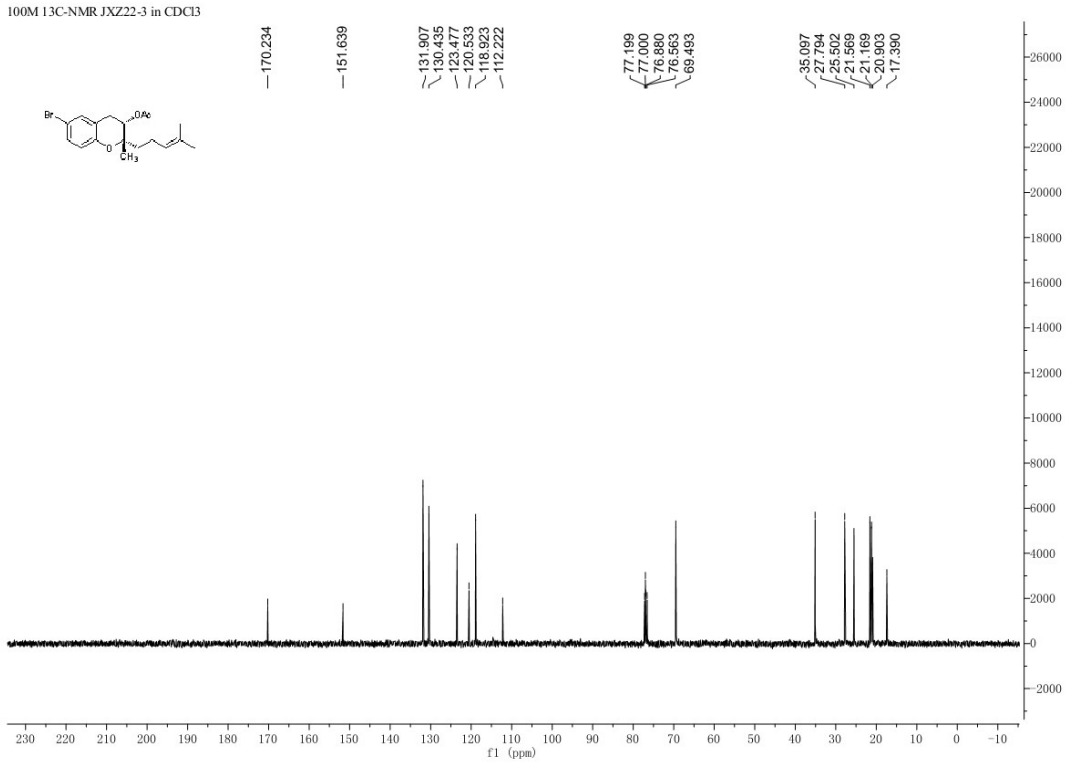
^{1}H NMR spectra of compound **11**



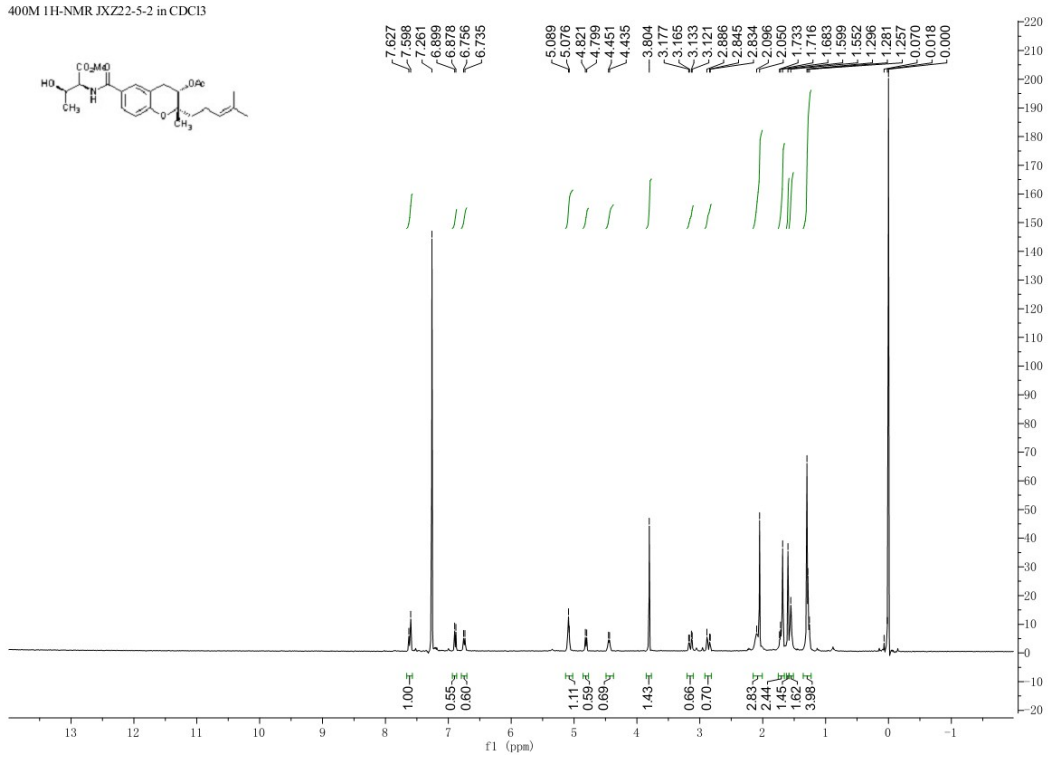
^{13}C NMR spectra of compound **11**



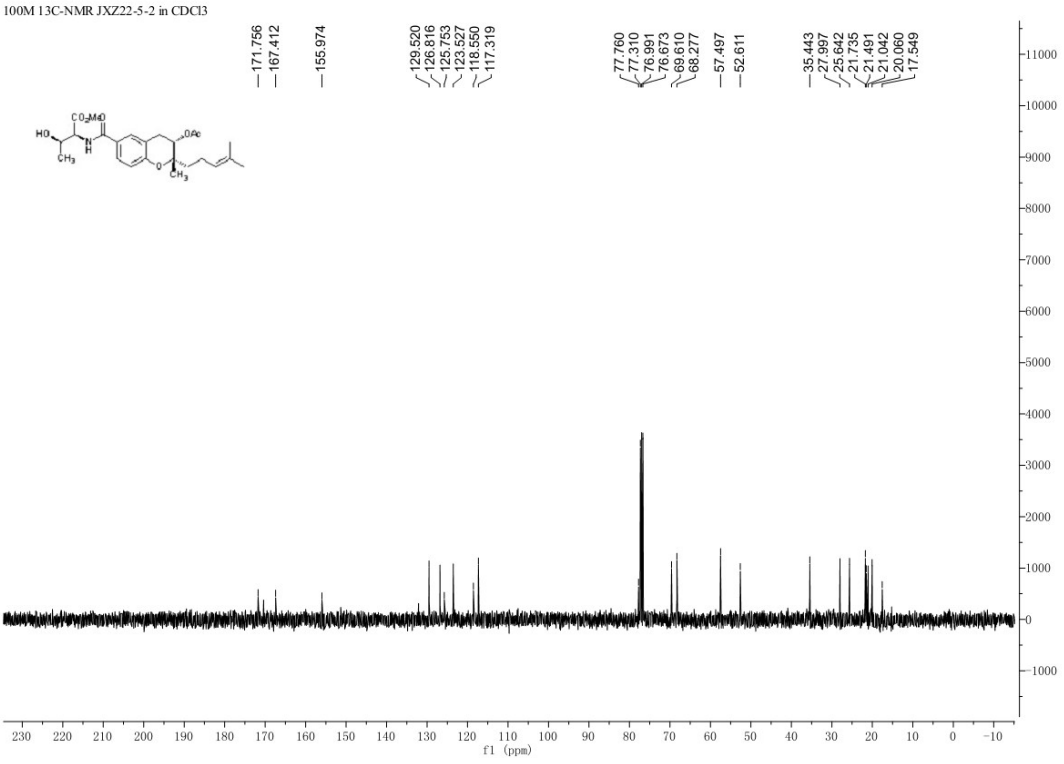
^{1}H NMR spectra of compound **12**



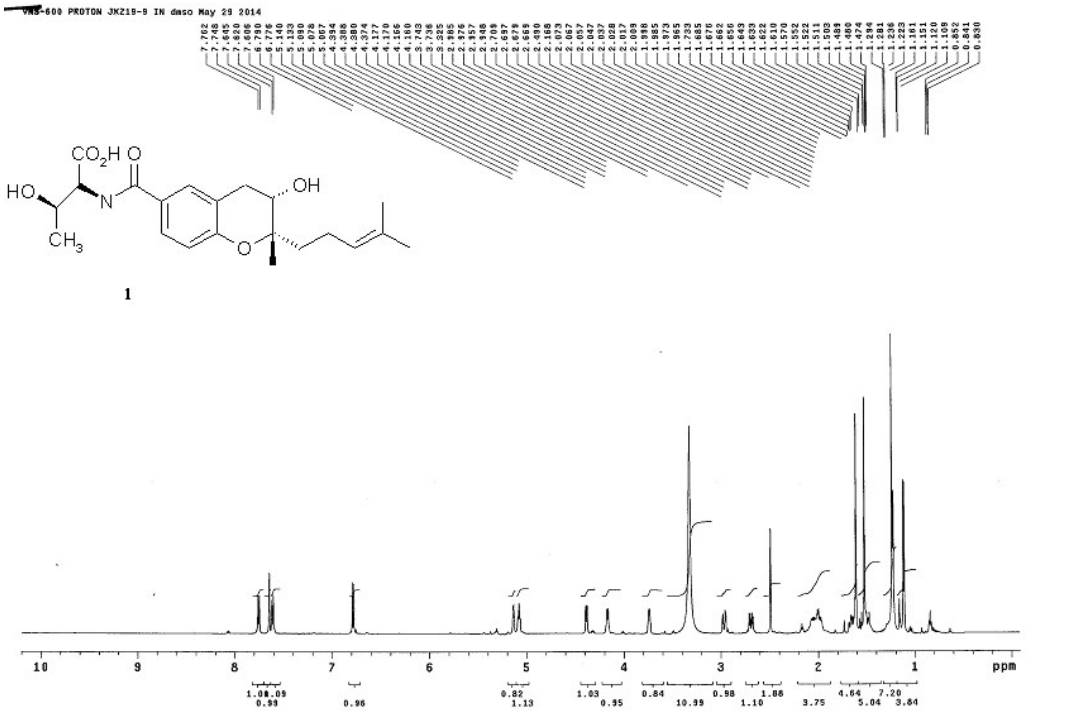
^{13}C NMR spectra of compound **12**



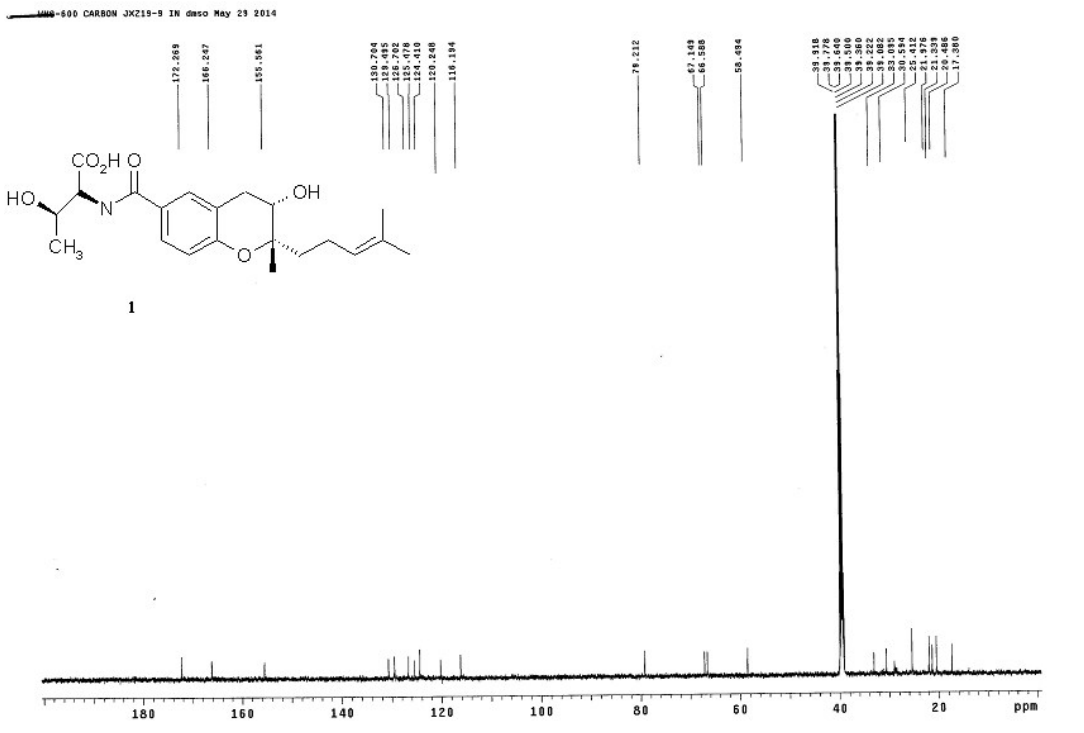
^{1}H NMR spectra of compound **13**



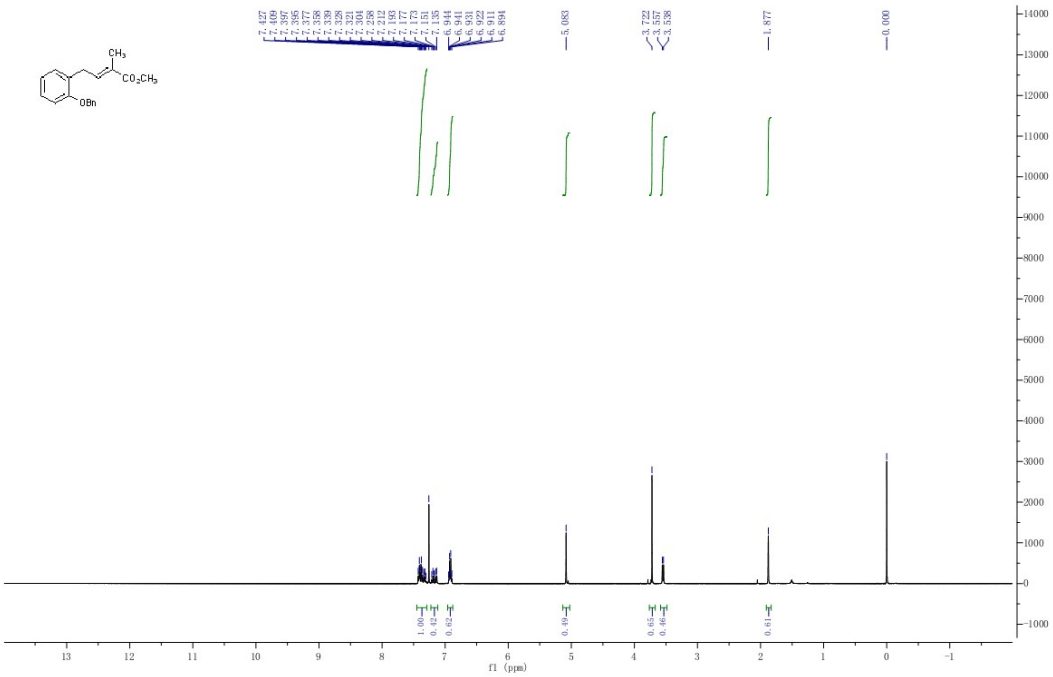
^{13}C NMR spectra of compound **13**



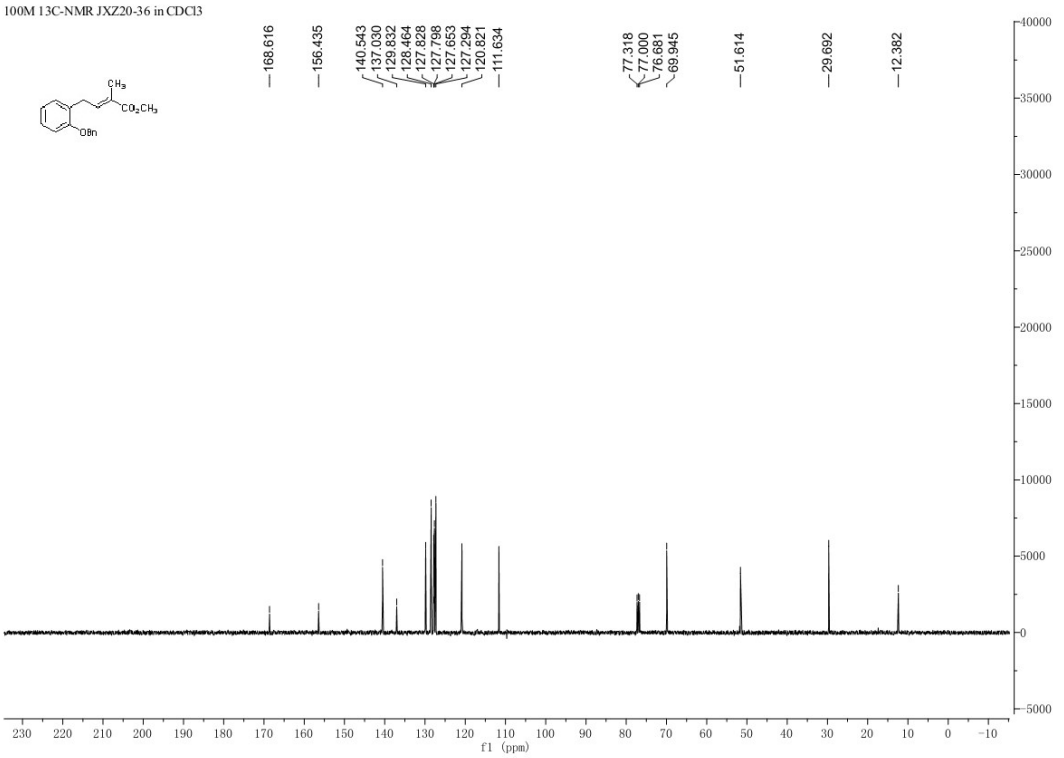
^{1}H NMR spectra of compound **1**



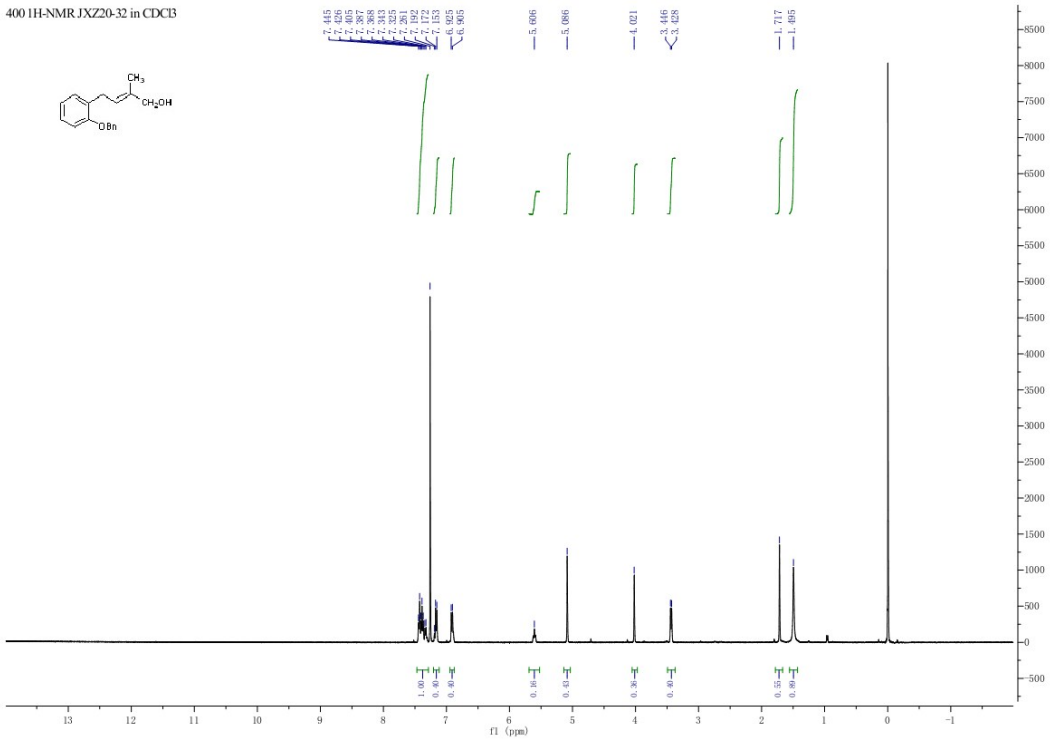
^{13}C NMR spectra of compound **1**



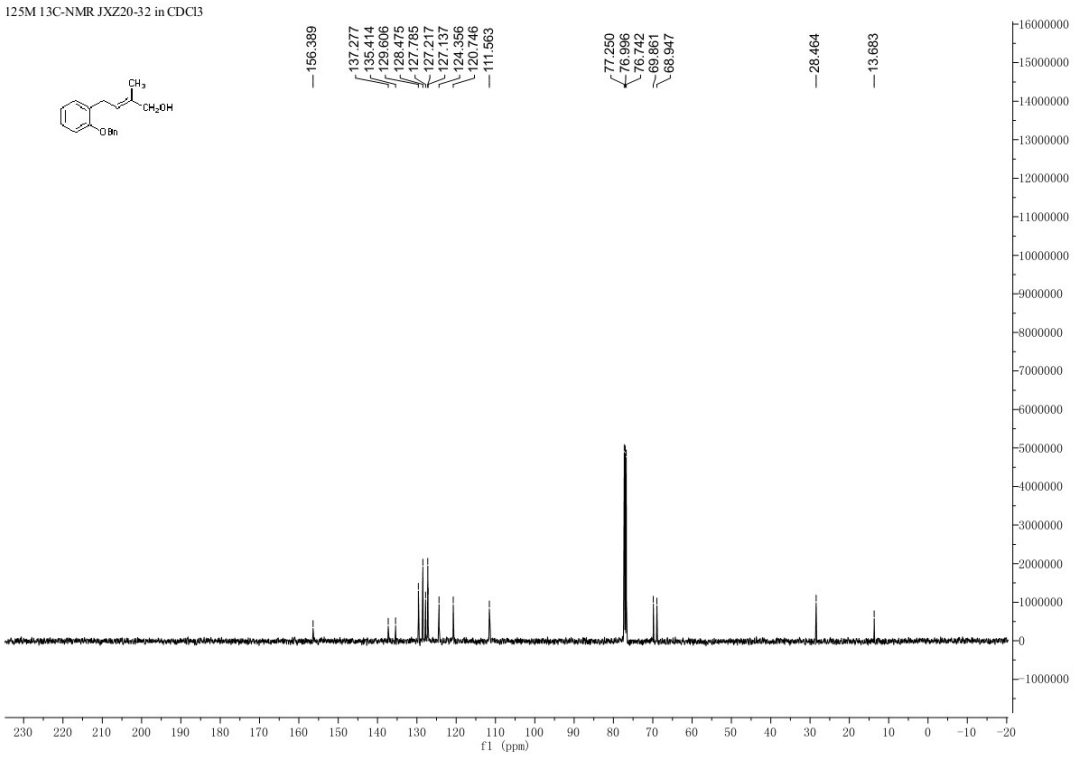
^{1}H NMR spectra of compound **14**



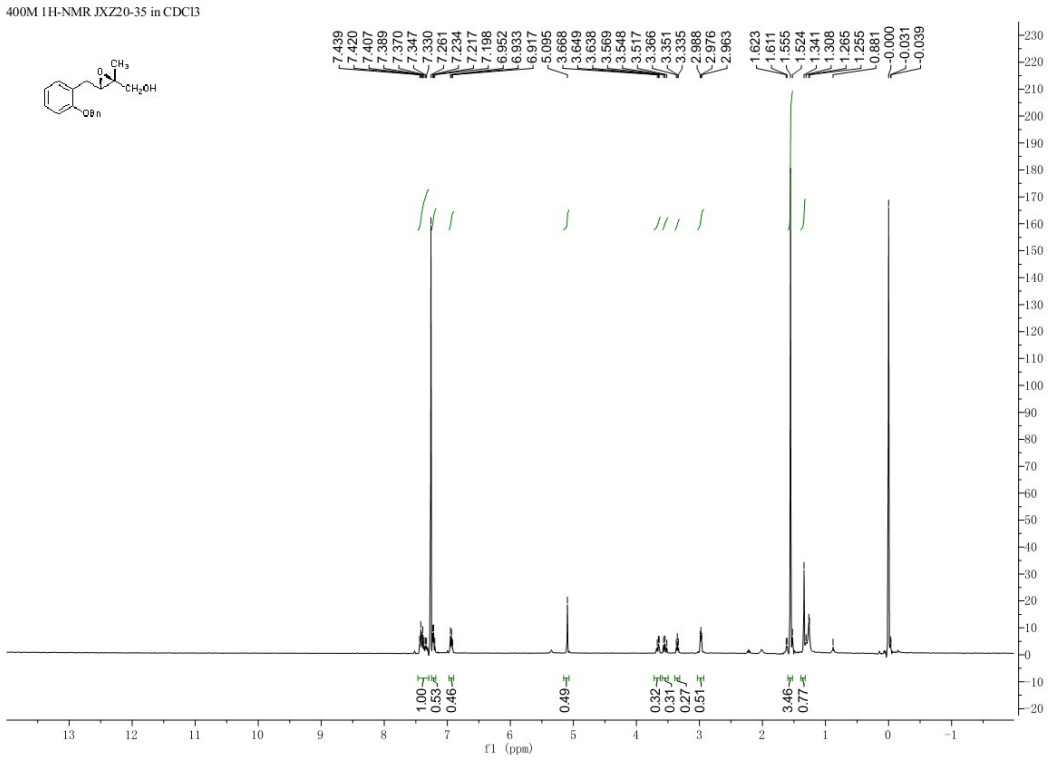
^{13}C NMR spectra of compound **14**



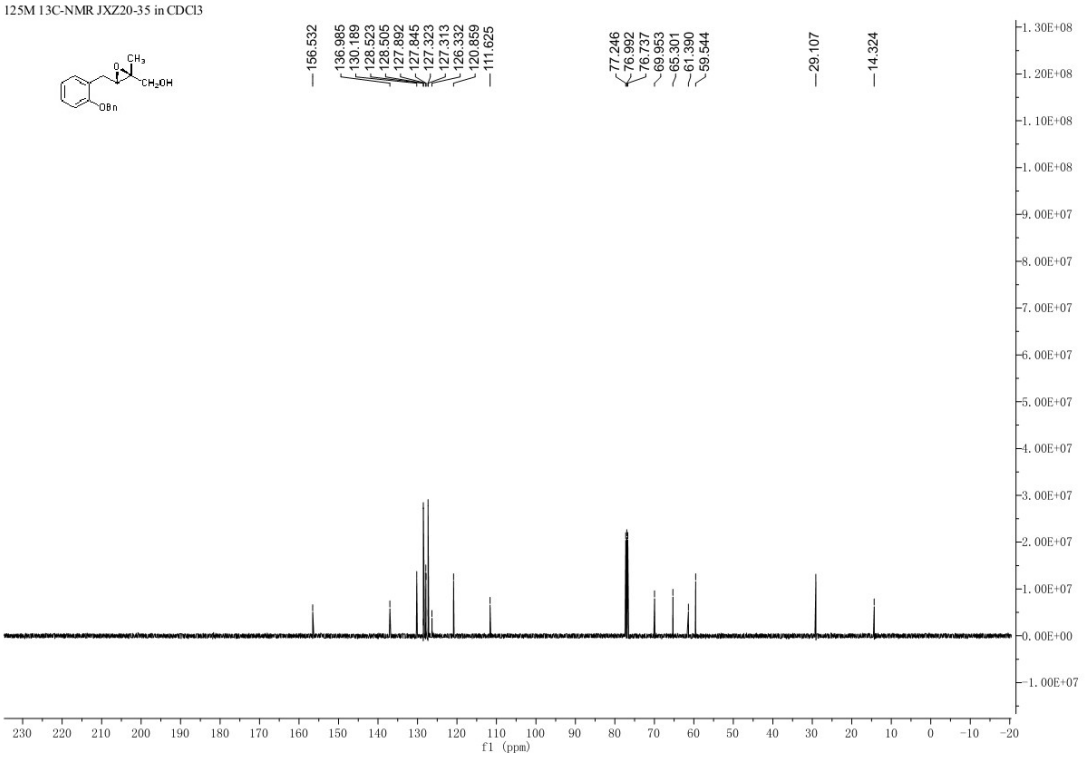
^{1}H NMR spectra of compound **15**



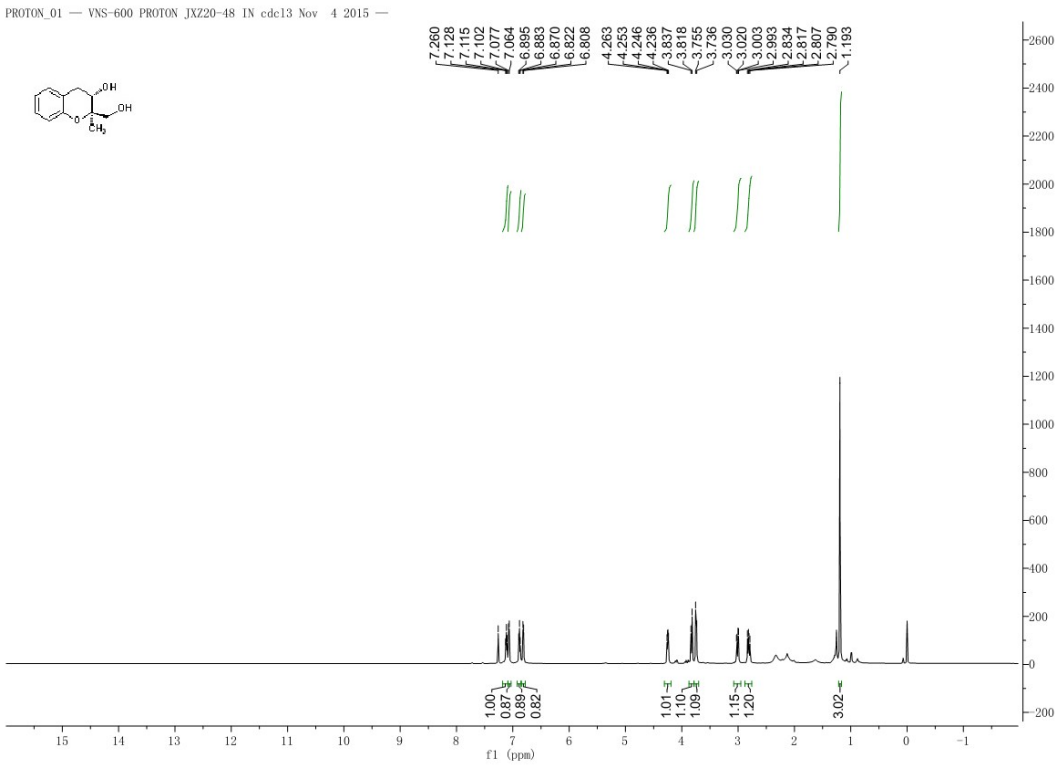
^{13}C NMR spectra of compound **15**



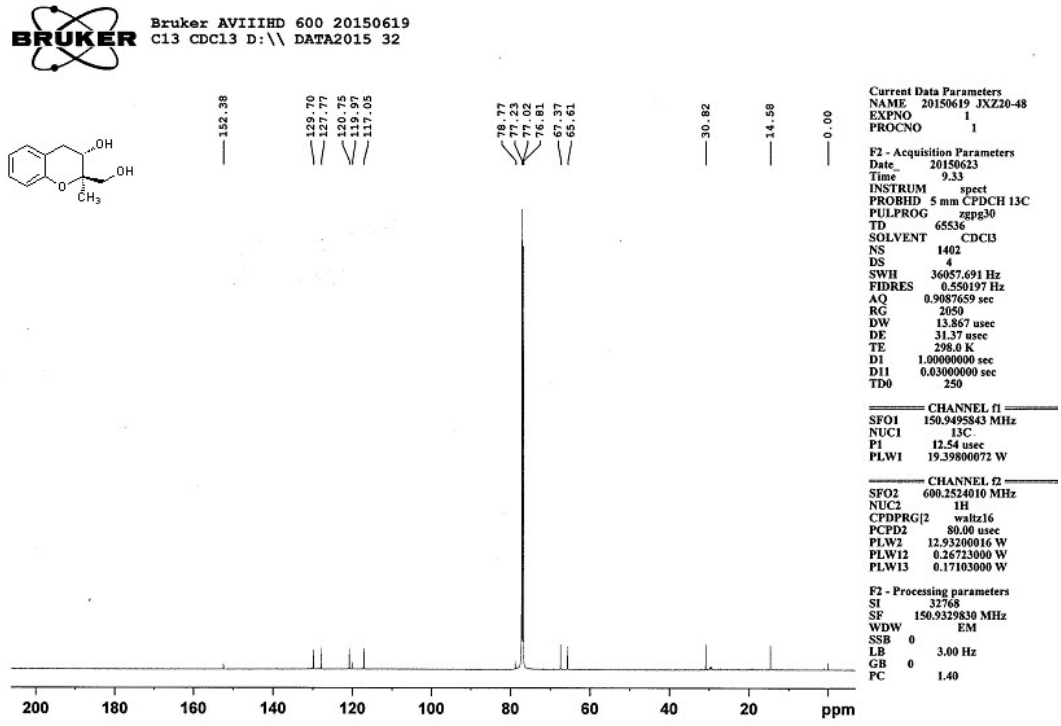
^{1}H NMR spectra of compound **16**



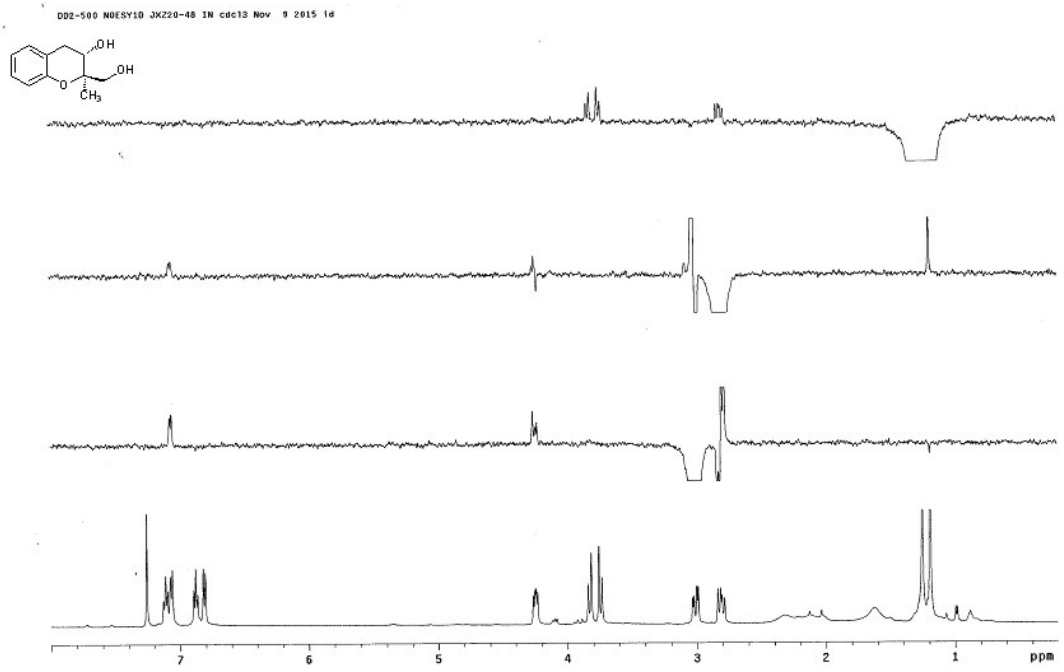
^{13}C NMR spectra of compound **16**



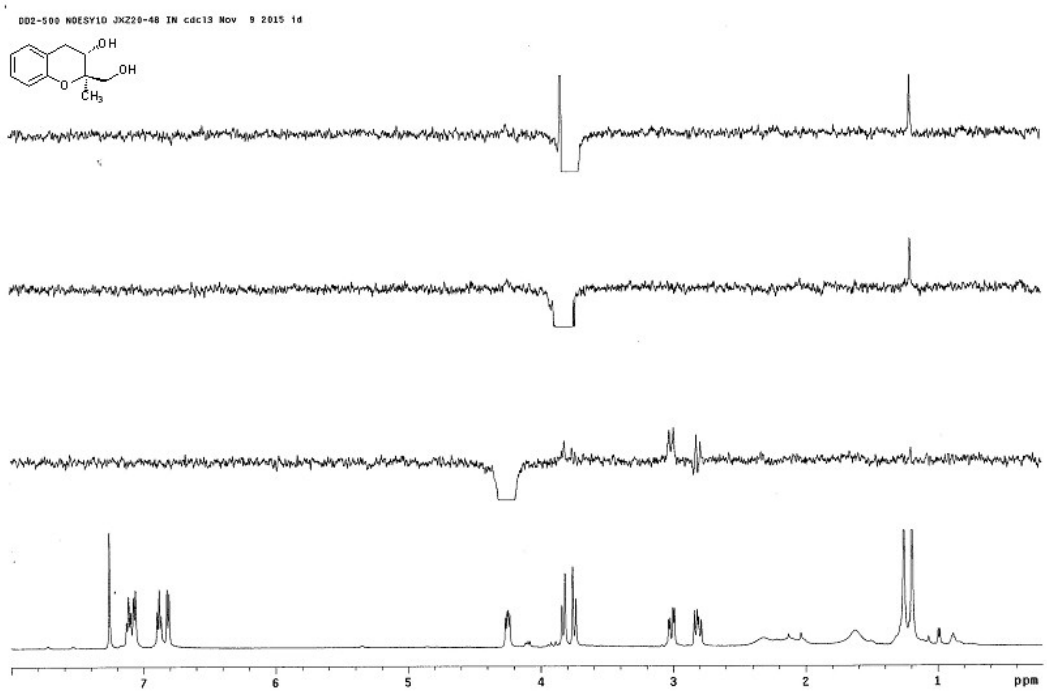
^{1}H NMR spectra of compound **17**



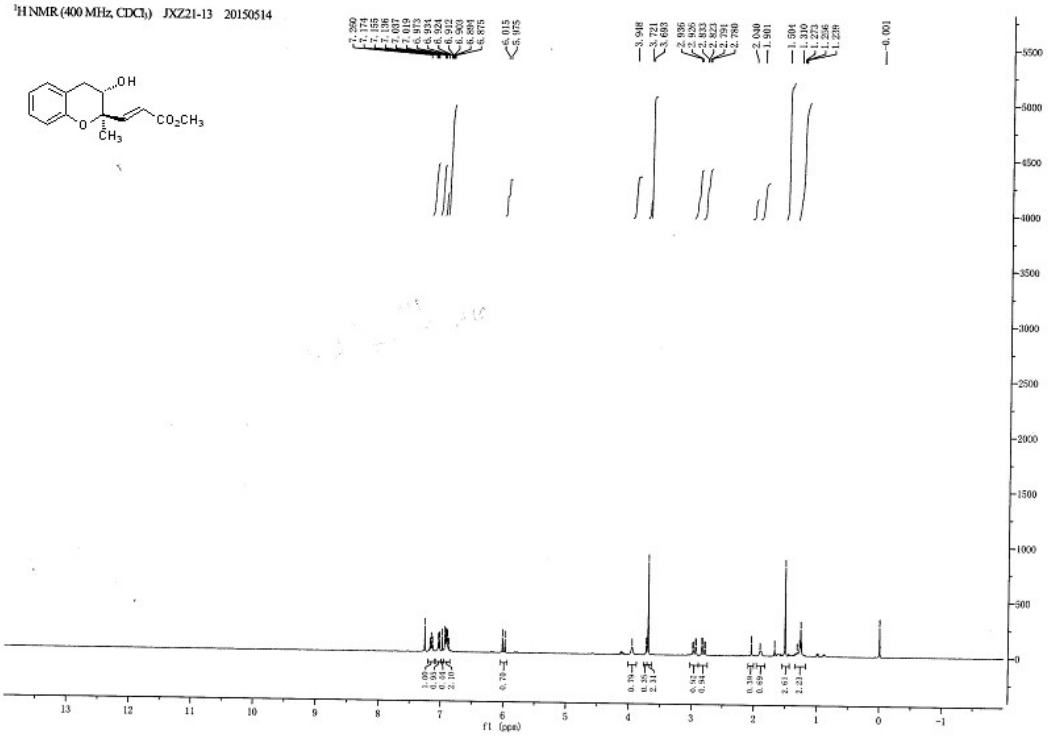
^{13}C NMR spectra of compound **17**



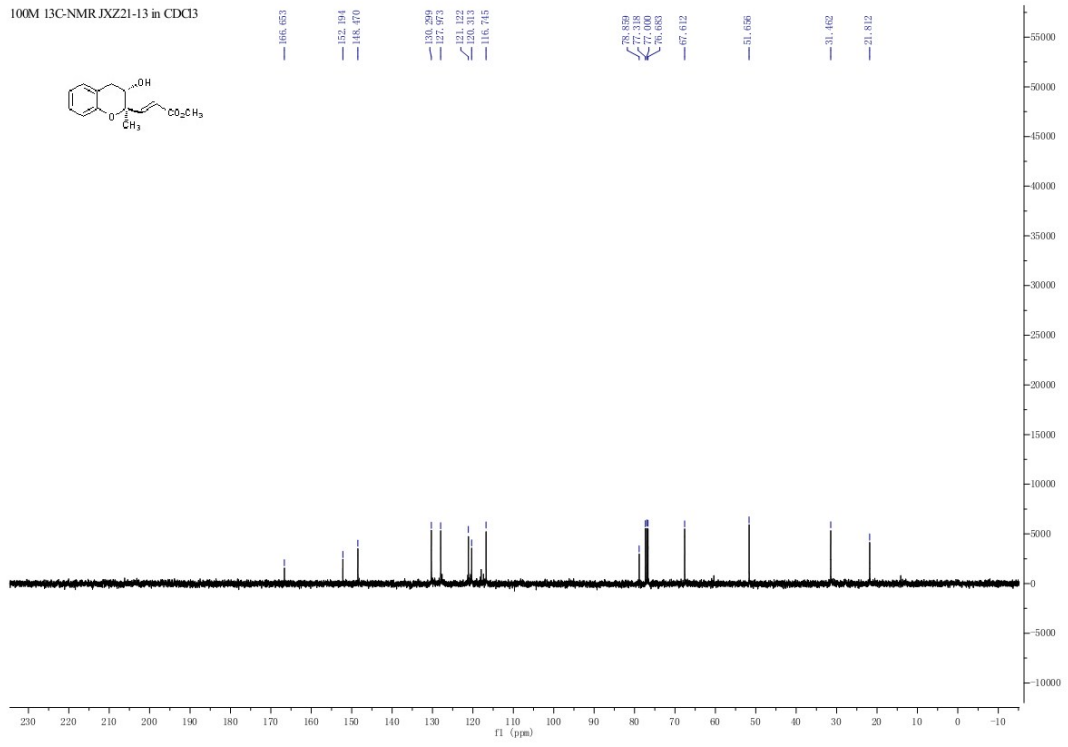
NOE spectra of compound **17**



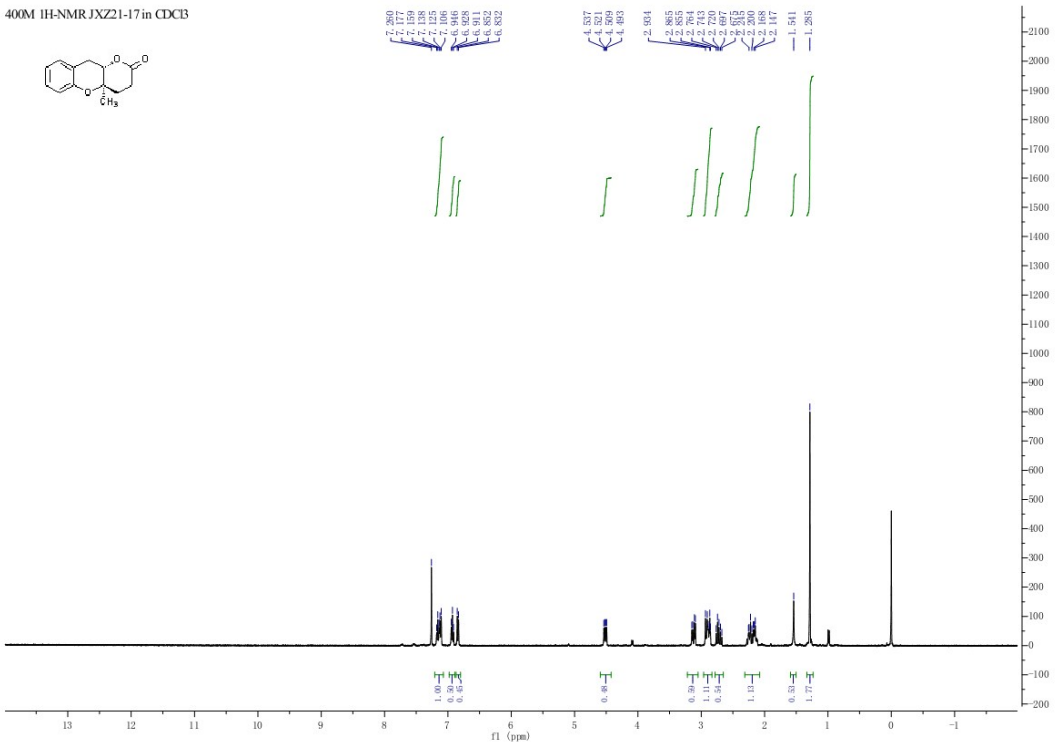
NOE spectra of compound **17**



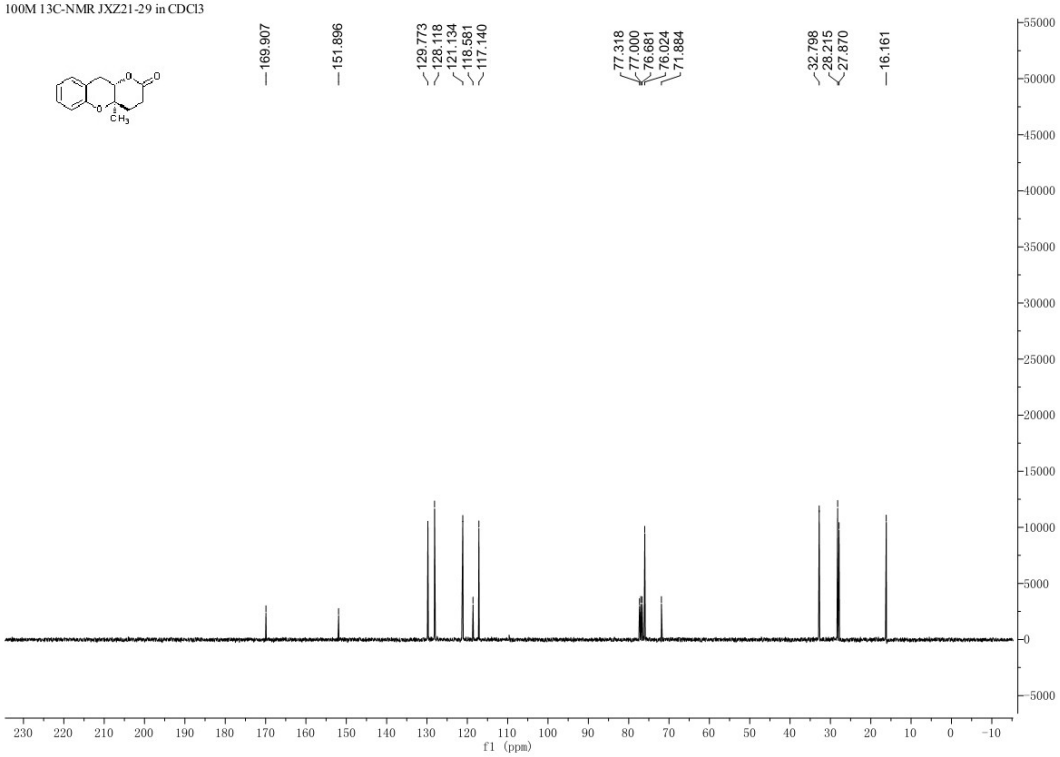
^{1}H NMR spectra of compound **18**



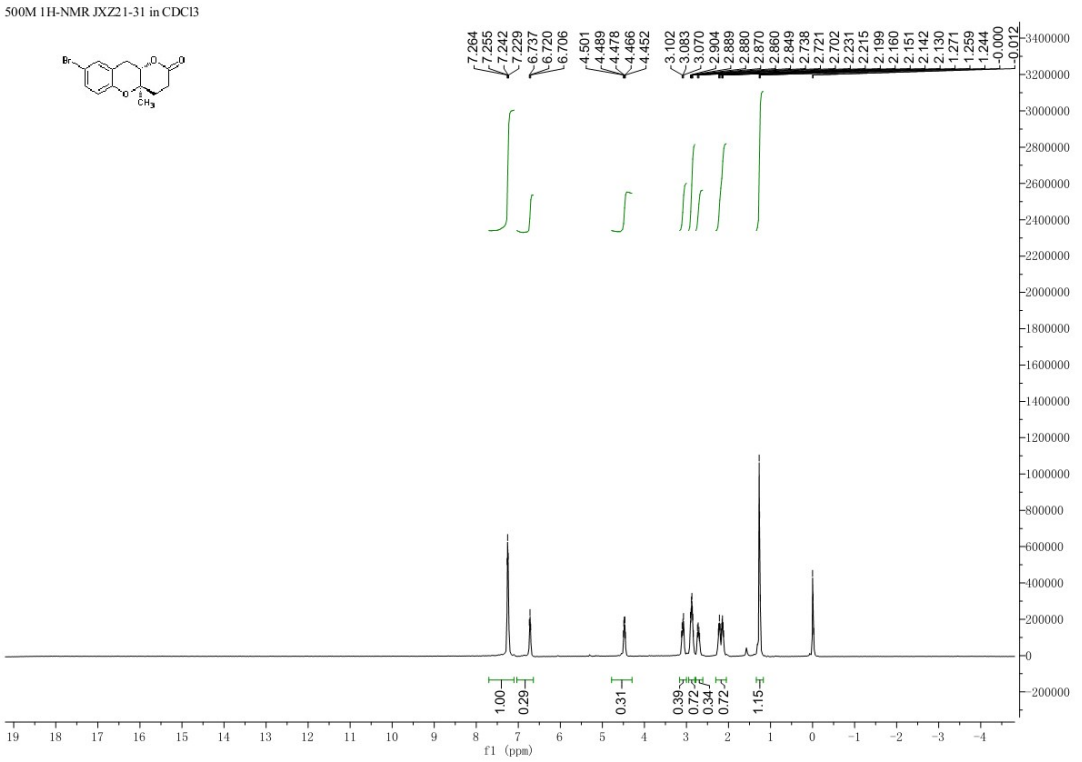
^{13}C NMR spectra of compound **18**



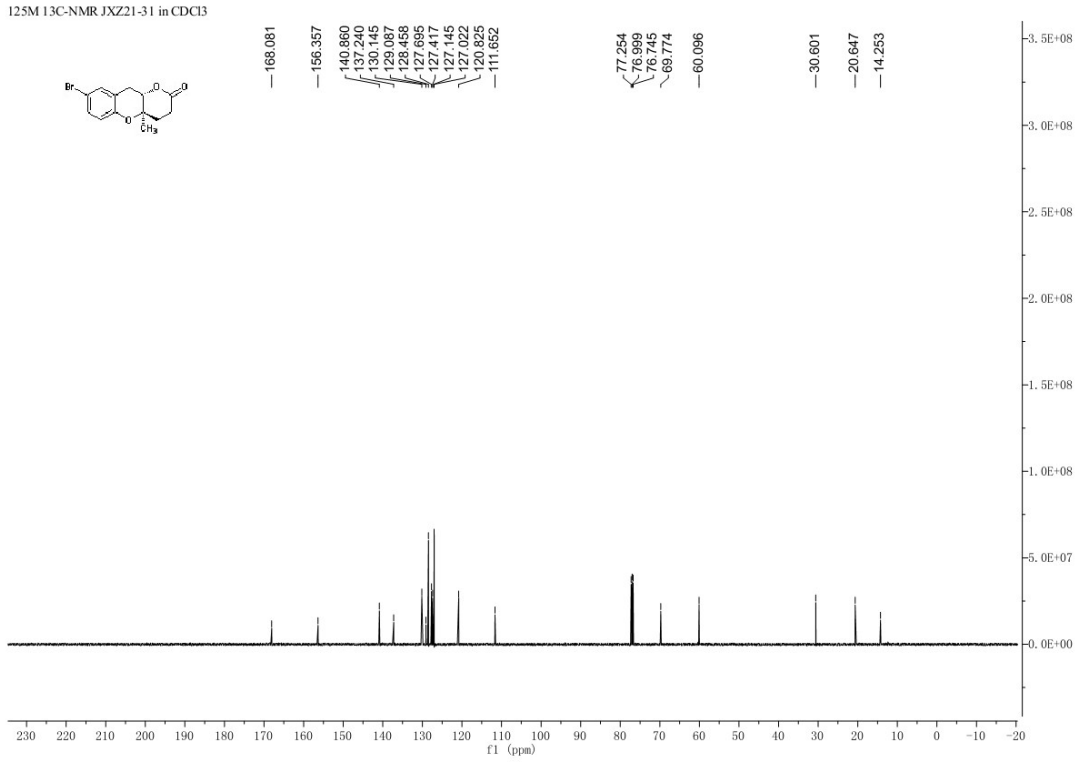
^{1}H NMR spectra of compound **19**



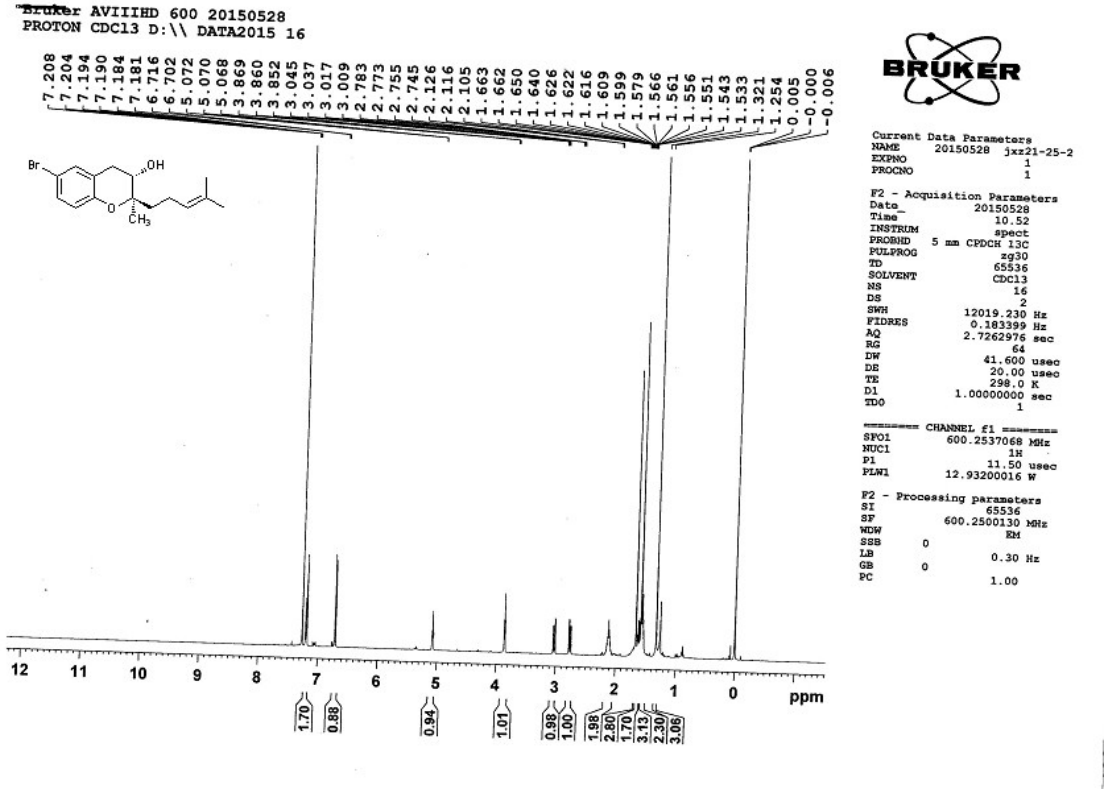
^{13}C NMR spectra of compound **19**



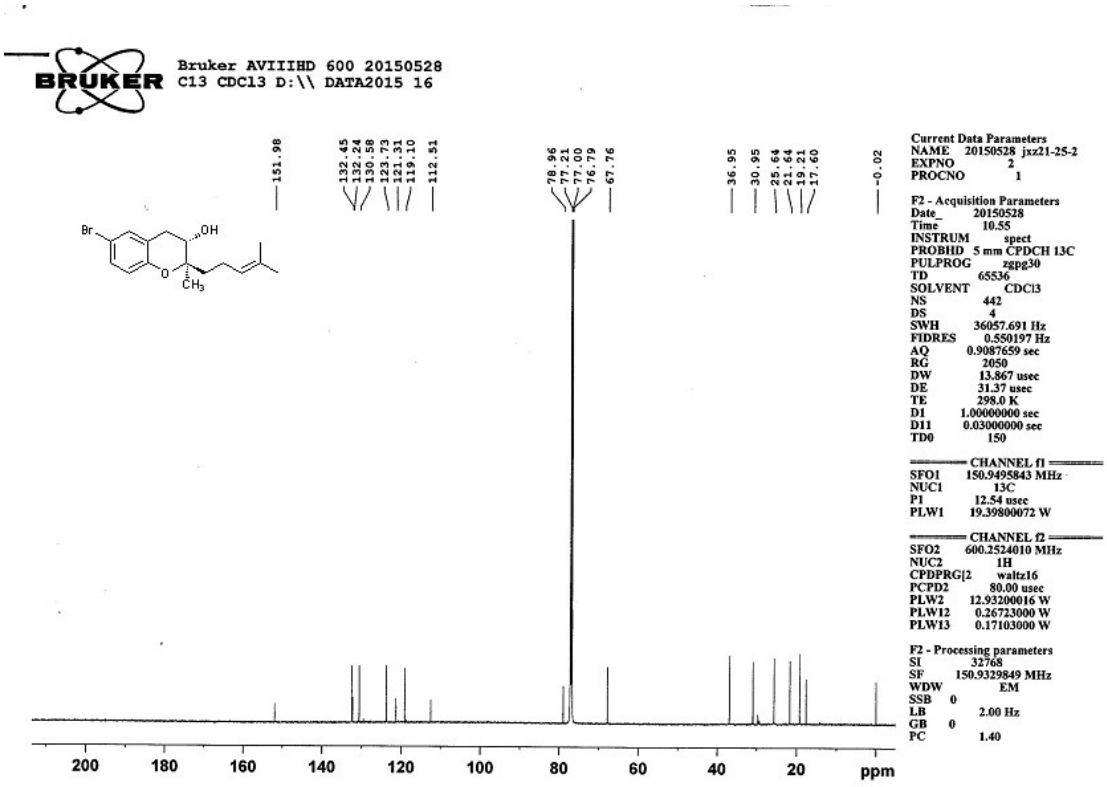
^{1}H NMR spectra of compound **20**



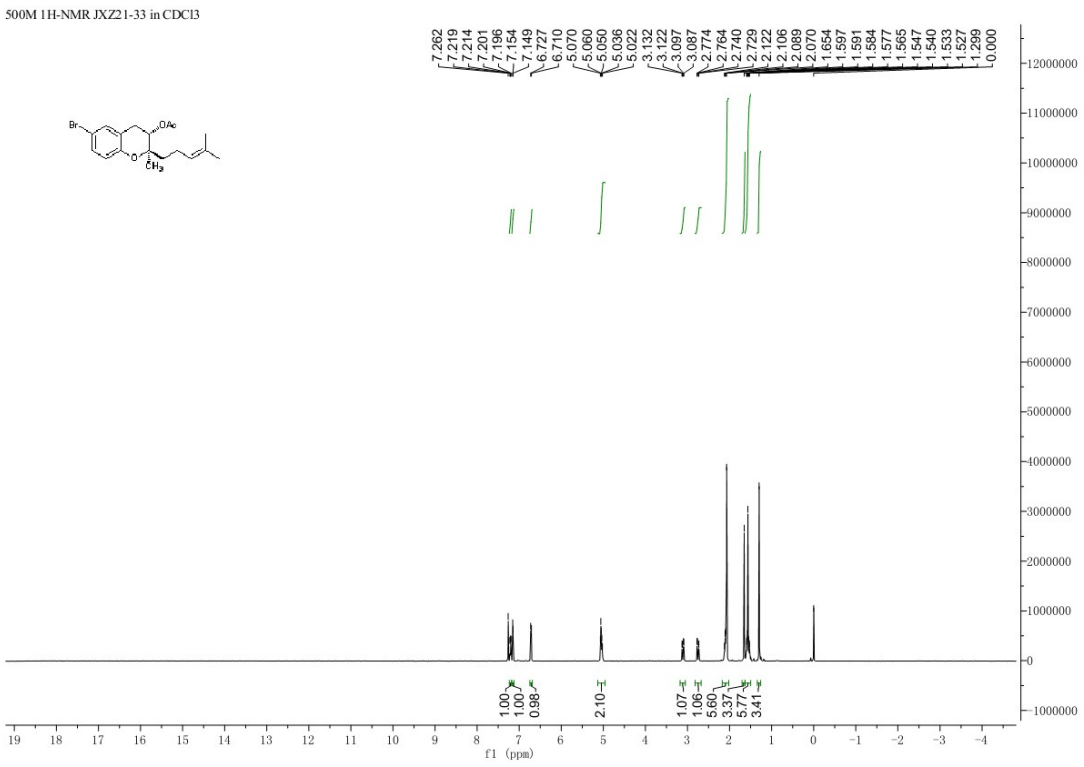
^{13}C NMR spectra of compound **20**



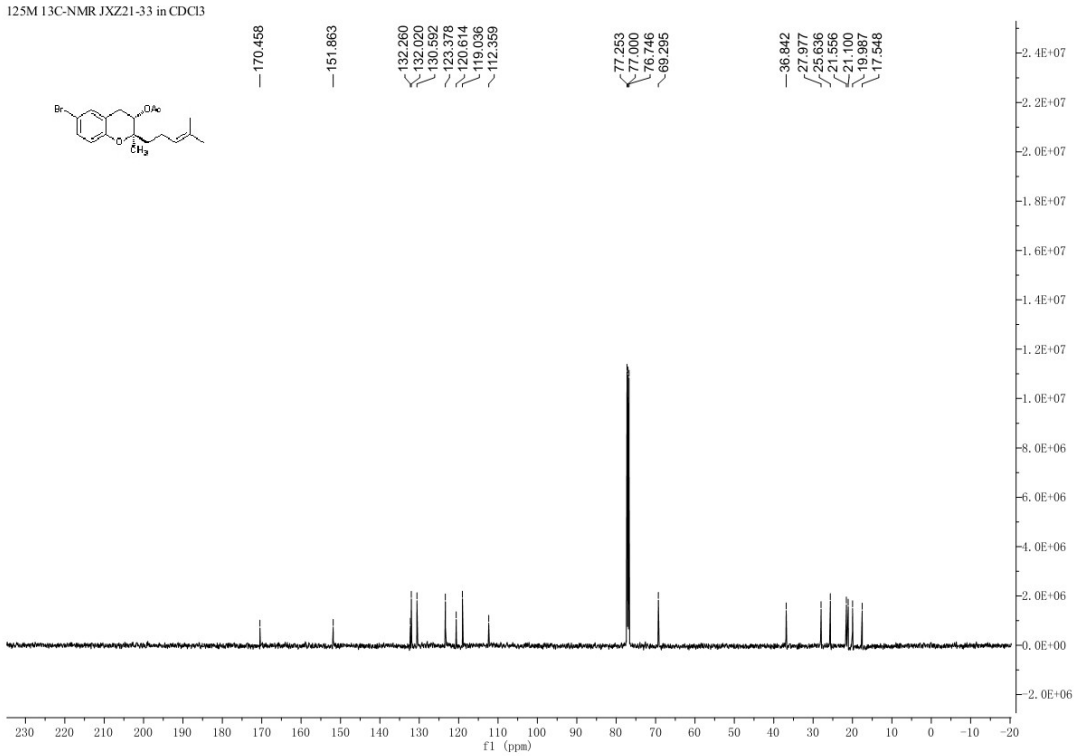
^{1}H NMR spectra of compound **21**



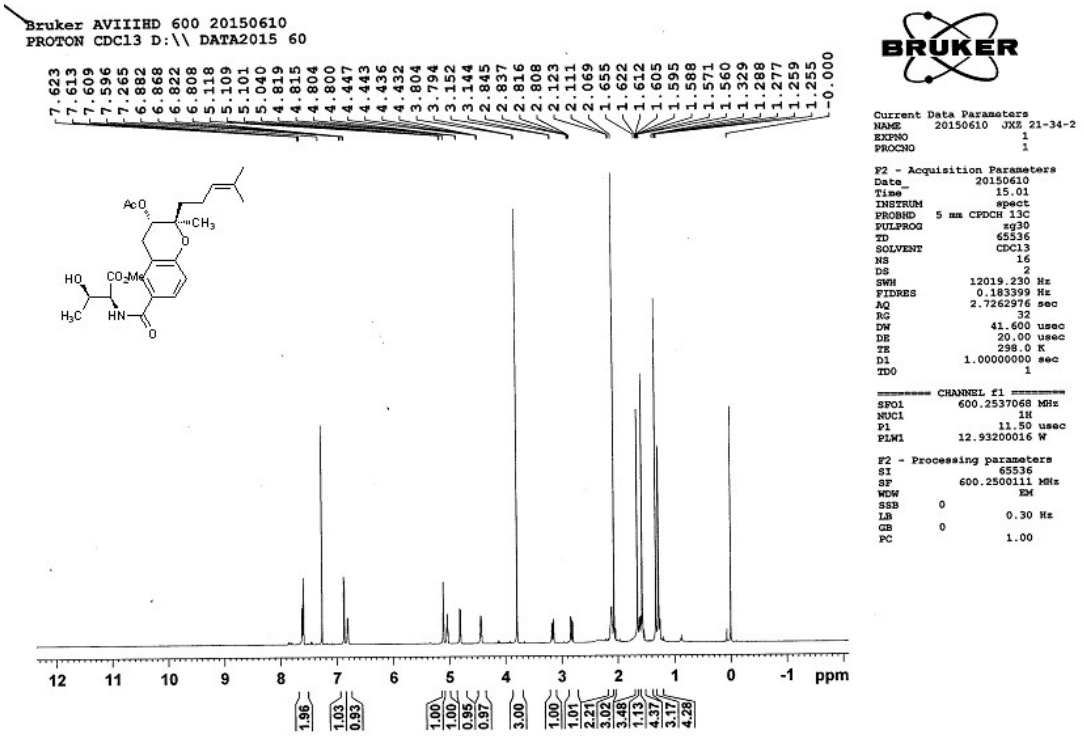
^{13}C NMR spectra of compound **21**



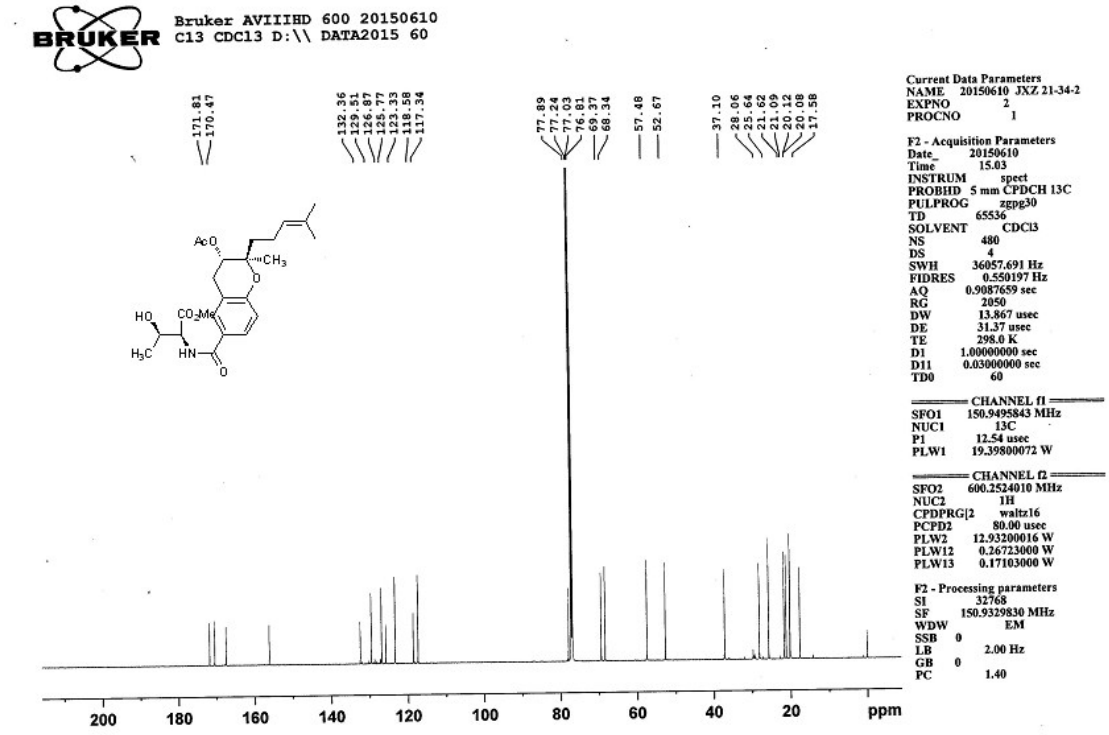
^{1}H NMR spectra of compound **22**



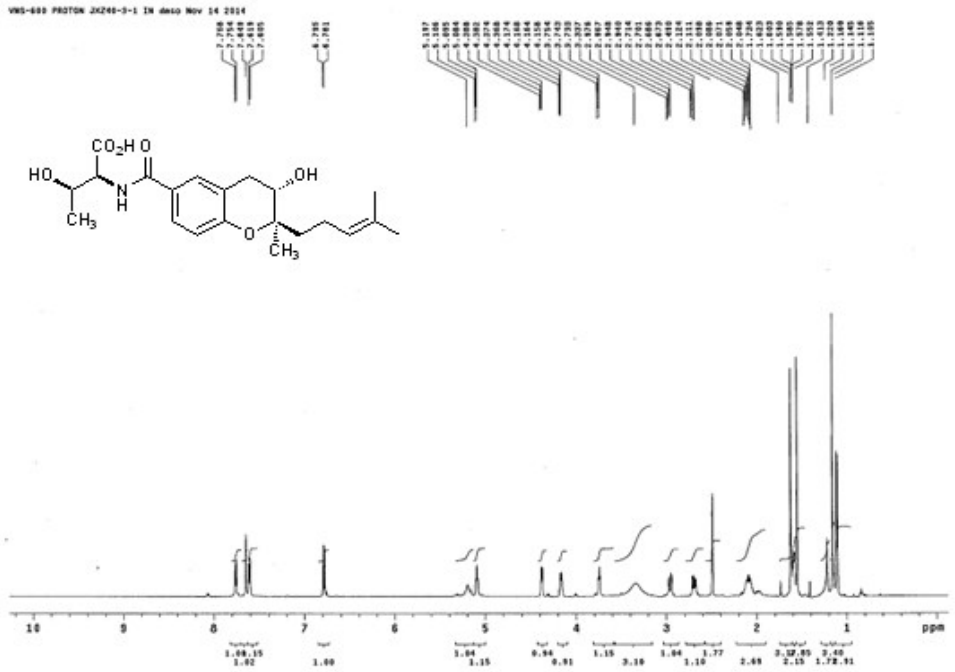
^{13}C NMR spectra of compound **22**



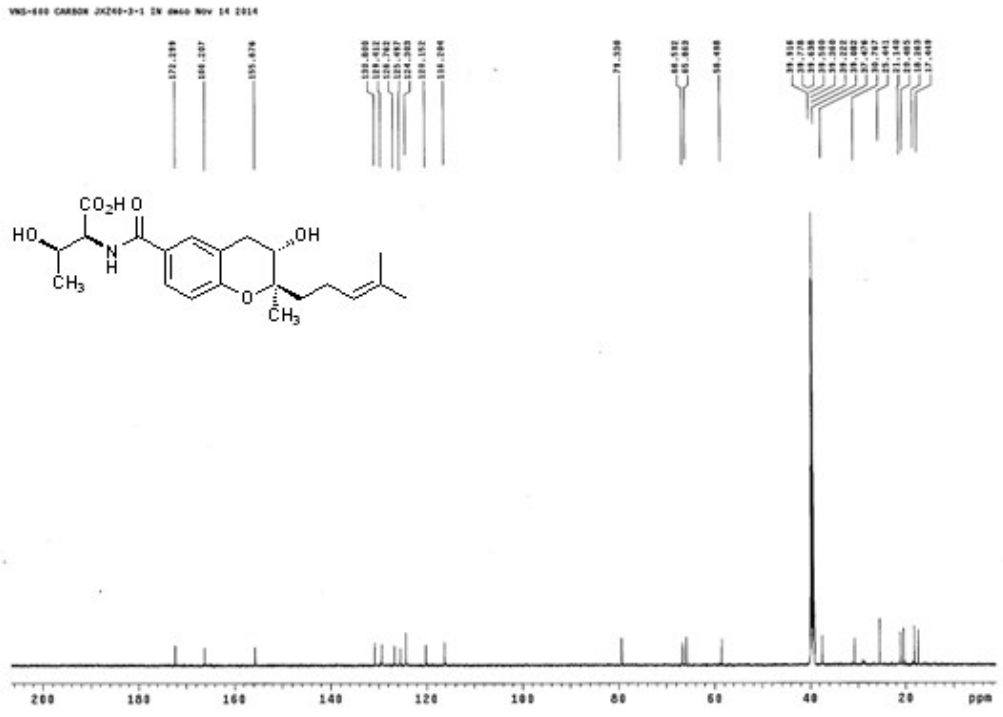
^{1}H NMR spectra of compound **23**



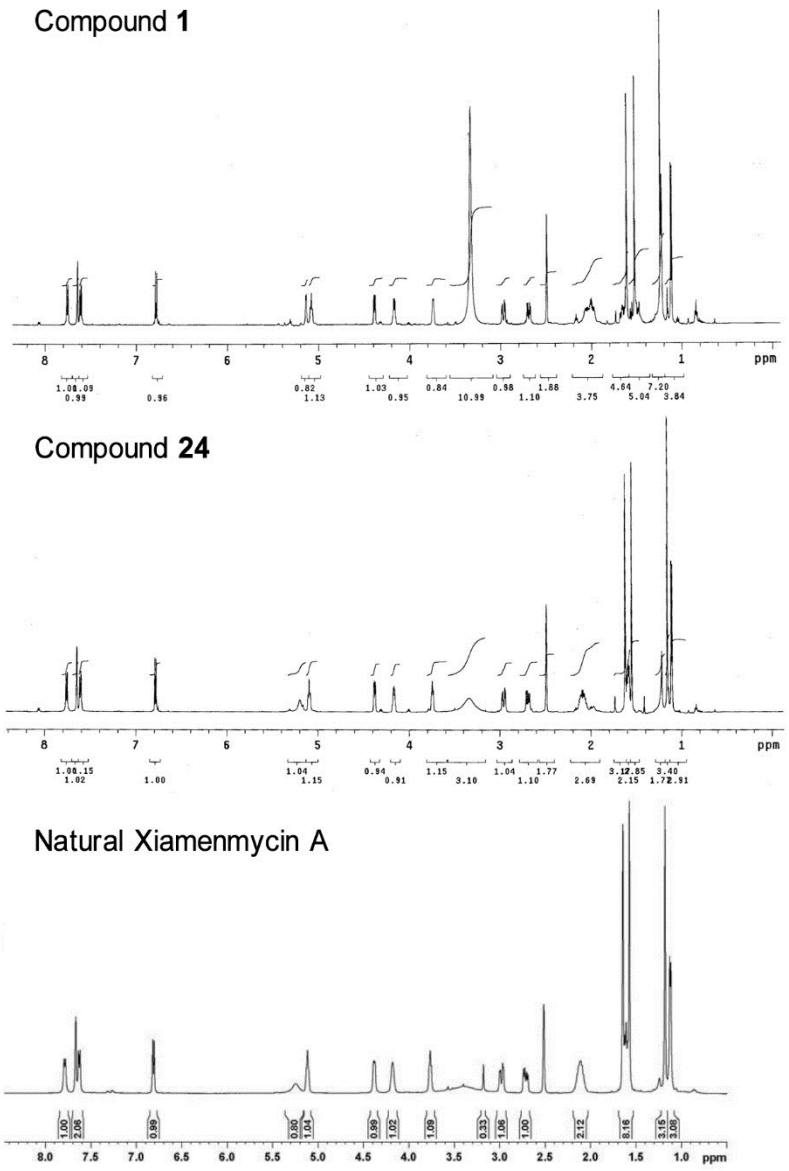
^{13}C NMR spectra of compound **23**



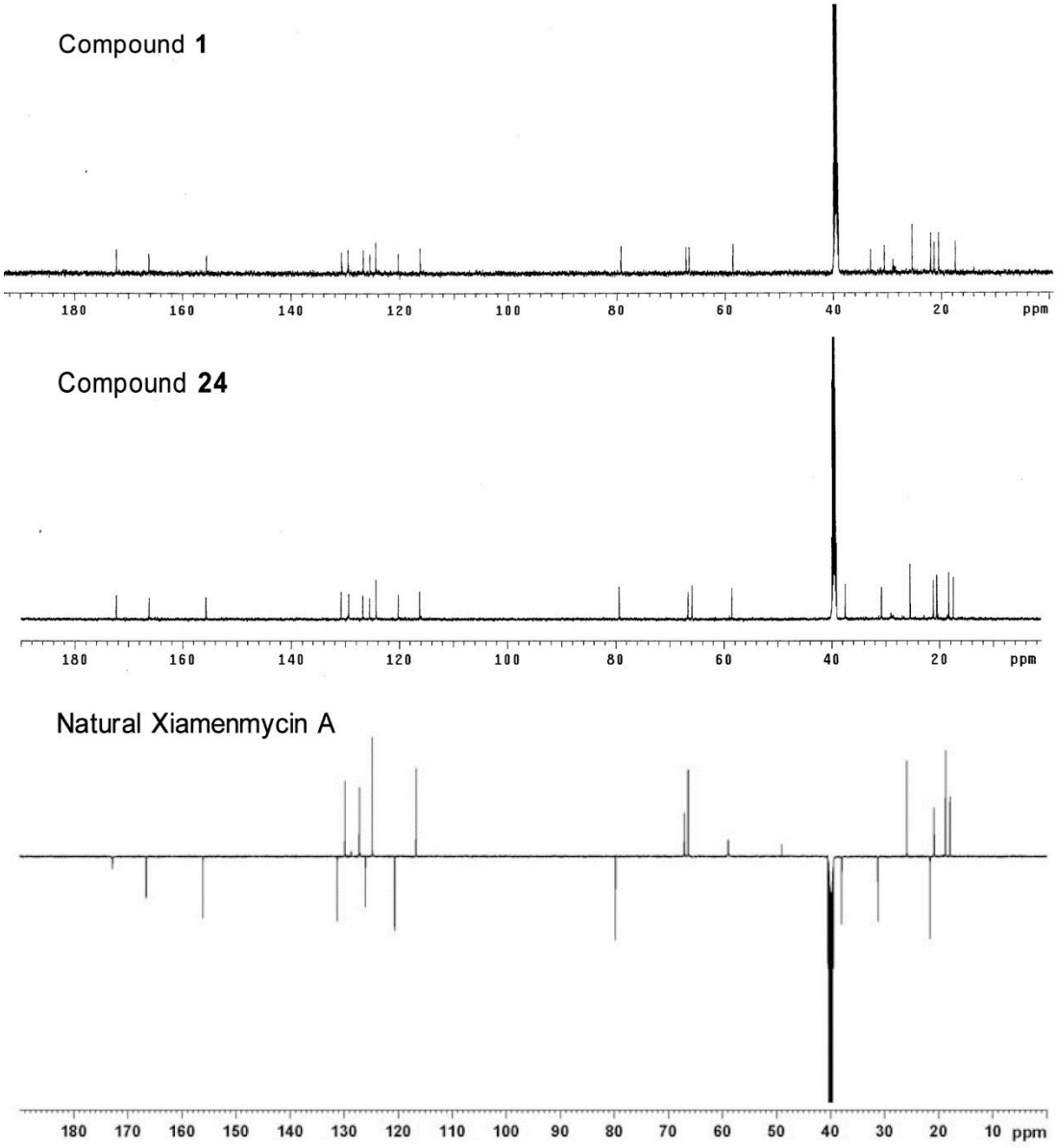
^{1}H NMR spectra of compound **24**



^{13}C NMR spectra of compound **24**



^{1}H NMR comparison of **1**, **24** and natural xiamenmycin A



^{13}C NMR comparison of **1**, **24** and natural xiamenmycin A

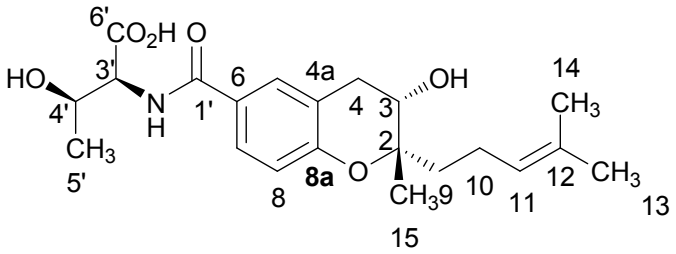


Table the comparison of 1H and 13CNMR data of compound 1, 24 and reported natural xiamenmycin A

Position	δ_H(*J* in Hz)			δ_C		
	Natural Xiamenmycin A[1]	Compound **24**	Compound **1**	Natural Xiamenmycin A[1]	Compound **24**	Compound **1**
1	--	--	--	--	--	--
2	--	--	--	79.8	79.3	79.2
3	3.77, t	3.74,t(5.4)	3.74, br.	66.3	65.9	66.6
4	2.71,dd (17.3, 7.4)	2.69,dd (16.8,7.8)	2.69, dd (16.8, 7.2)	31.2	30.8	30.6
	2.98, dd (17.3, 5.2)	2.96,dd (16.8, 5.4)	2.96, dd (16.8, 5.4)			
4a	--	--	--	120.6	120.2	120.3
5	7.67, s	7.65, s	7.65, s	129.8	129.4	129.5
6	--	--	--	126.0	125.5	125.5
7	7.63, d (8.4)	7.61,d (8.4)	7.61, d (8.4)	127.2	126.8	126.7
8	6.81, d (8.4)	6.79, d (8.4)	6.78, d (8.4)	116.7	116.2	116.2
8a	--	--	--	156.1	155.7	155.6
9	1.60, m	1.59, m	1.69-1.61	38.0	37.5	33.1
10	2.10, m	2.09, m	2.05, m	21.6	21.1	21.3
11	5.12, dd(7.1,1.3)	5.10, t(6.6)	5.08,t (7.2)	124.8	124.3	124.4
12	--	--	--	131.3	130.8	130.7
13	1.57, s	1.55, s	1.52, s	17.9	17.4	17.4
14	1.65,s	1.62, s	1.62, s	25.9	25.4	25.4
15	1.18, s	1.16, s	1.23, s	18.7	18.3	22.0
1’	--	--	--	166.6	166.2	166.3
2’	7.78, d (7.8)	7.77,d (8.4)	7.75,d (8.4)	--	--	--
3’	4.38, brd	4.38,dd(3.6,8.4)	4.38,dd(3.6,8.4)	58.9	58.5	58.5
4’	4.18, brs	4.17,m	4.17, m	67.1	66.6	67.2
5’	1.12, d (6.0)	1.11,d(6.6)	1.11, d (6.6)	20.9	20.5	20.5
6’	--		--	172.8	172.3	172.3

1. M. J. Xu, X. J. Liu, Y. L. Zhao, D. Liu, Z. H. Xu, X. M. Lang, P. Ao, W. H. Lin, S. L. Yang, Z. G. Zhang and J. Xu, *Marine drugs*, 2012, **10**, 639-654.