Isochromophilones A−F, Cytotoxic Chloroazaphilones from the Marine Mangrove Endophytic Fungus *Diaporthe* sp. SCSIO 41011

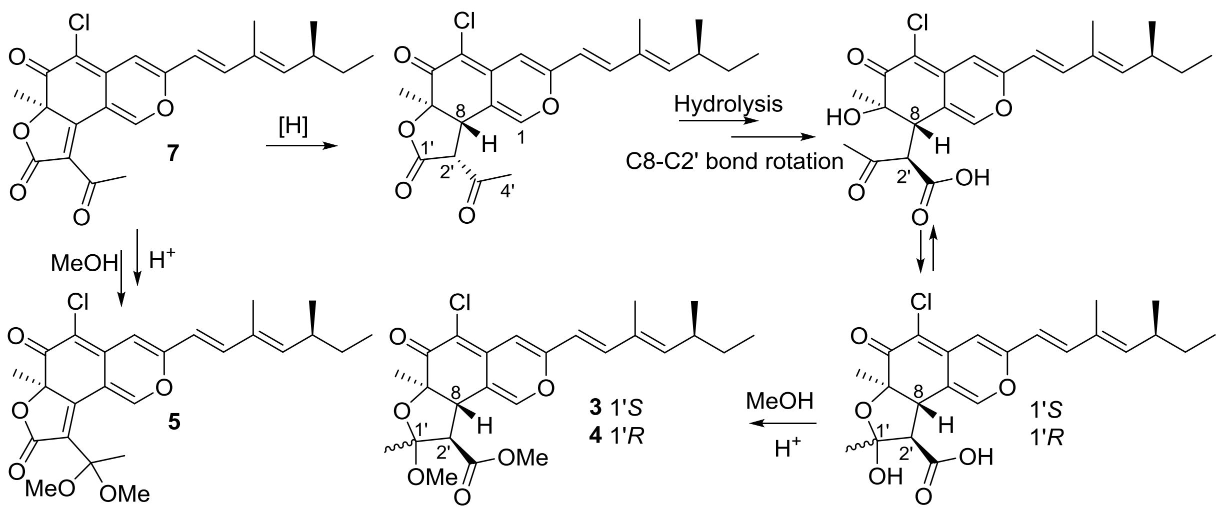
Xiaowei Luo,[†,‡] Xiuping Lin,[†] Huaming Tao,[§] Junfeng Wang,[†] Jiayi Li,[†,§] Bin Yang,[†] Xuefeng Zhou,[*,†] and Yonghong Liu[*,†,‡]

[†]CAS Key Laboratory of Tropical Marine Bio-resources and Ecology, Guangdong Key Laboratory of Marine Materia Medica, South China Sea Institute of Oceanology, Chinese Academy of Sciences, Guangzhou 510301, China

[‡]University of Chinese Academy of Sciences, Beijing 100049, China

[§]School of Traditional Chinese Medicine, Southern Medical University, Guangzhou 510515, China

Contents of Supporting Information



Scheme S1. Proposed chemical formations of **3**−**5**.

Table S1. ^{1}H (700 MHz) and ^{13}C NMR (175 MHz) Data for Compounds 1−2, 5−6 (δ in ppm, J in Hz)

	1[a]		**2**[a]		**5**[b]		**6**[c]	
pos.	δ_H	δ_C, type	δ_H	δ_C, type	δ_H	δ_C, type	δ_H	δ_C, type
1	6.65, s	139.7, CH	6.66, s	139.9, CH	7.98, s	150.3, CH	6.05, s	96.4, CH
3		154.5, C		154.7, C		157.6, C		157.2, C
4	6.15, s	104.3, CH	6.14, s	104.2, CH	6.62, s	105.8, CH	6.36, s	102.0, CH
4a		127.6, C		127.7, C		140.6, C		143.9, C
5		113.0, C		111.3, C		108.7, C		122.5, C
6	4.23, s	76.2, CH	3.93, s	85.7, CH		184.0, C		186.3, C
7		84.4, C		84.7, C		86.8, C		86.1, C
8	3.64, overlapped	38.7, CH	3.62, overlapped	39.3, CH		155.8, C		72.5, C
8a		114.4, C		114.2, C		110.5, C		65.1, C
9	6.08, d (16.1)	119.2, CH	6.06, d (16.1)	119.1, CH	6.12, d (16.1)	116.1, CH	6.42, d (16.1)	119.6, CH
10	6.78, d (16.1)	138.4, CH	6.78, d (16.1)	138.6, CH	7.11, d (16.1)	142.9, CH	7.09, d (16.1)	142.5, CH
11		133.5, C		133.4, C		132.1, C		134.0, C
12	5.48, d (10.0)	145.0, CH	5.49, d (10.0)	145.0, CH	5.72, d (10.0)	148.8, CH	5.79, d (10.0)	147.9, CH
13	2.46, m	35.9, CH	2.48, m	35.9, CH	2.48, m	35.3, CH	2.48, m	34.9, CH
14	1.27−1.43, m	31.3, CH_2	1.29−1.43, m	31.3, CH_2	1.30−1.43, m	30.2, CH_2	1.27−1.43, m	30.0, CH_2
15	0.86, t (7.7)	12.3, CH_3	0.87, t (7.7)	12.2, CH_3	0.88, t (7.7)	12.1, CH_3	0.83, t (7.7)	12.3, CH_3
16	1.00, d (7.0)	20.8, CH_3	1.00, d (7.0)	20.9, CH_3	1.00, d (7.0)	20.4, CH_3	0.97, d (7.0)	20.6, CH_3
17	1.81, s	12.6, CH_3	1.82, s	12.6, CH_3	1.86, s	12.6, CH_3	1.81, s	12.7, CH_3
18	1.19, s	18.4, CH_3	1.21, s	18.8, CH_3	1.63, s	25.9, CH_3	1.58, s	18.7, CH_3
19			3.62, s	61.1, CH_3				
1′		173.0, C		172.7, C		168.0, C		167.1, C
2′	3.60, overlapped	54.4, CH	3.62, overlapped	54.1, CH		125.7, C		103.6, C
3′		202.9, C		202.7, C		100.7, C		161.4, C
4′	2.50, s	30.1, CH_3	2.51, s	30.1, CH_3	1.64, s	22.1, CH_3	2.08, s	15.8, CH_3
5′					3.23, s	49.3, CH_3		
6′					3.19, s	48.6, CH_3		

[a]In CD_3OD. [b]In $CDCl_3$. [c]In DMSO-d_6

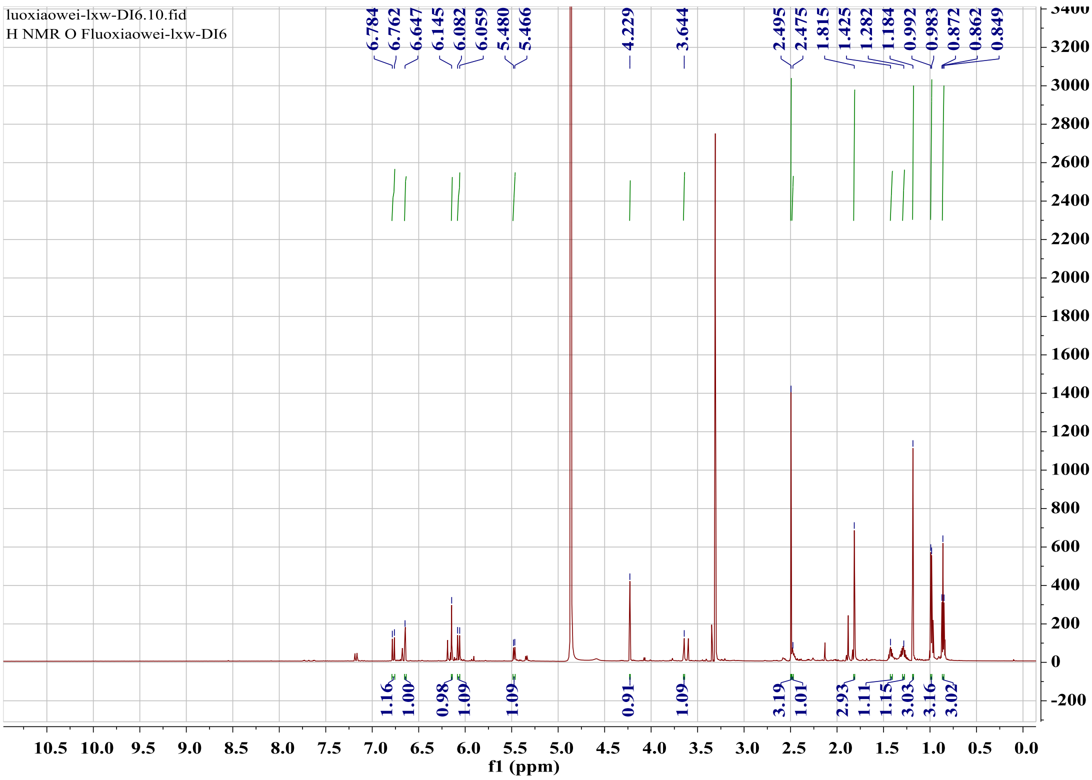
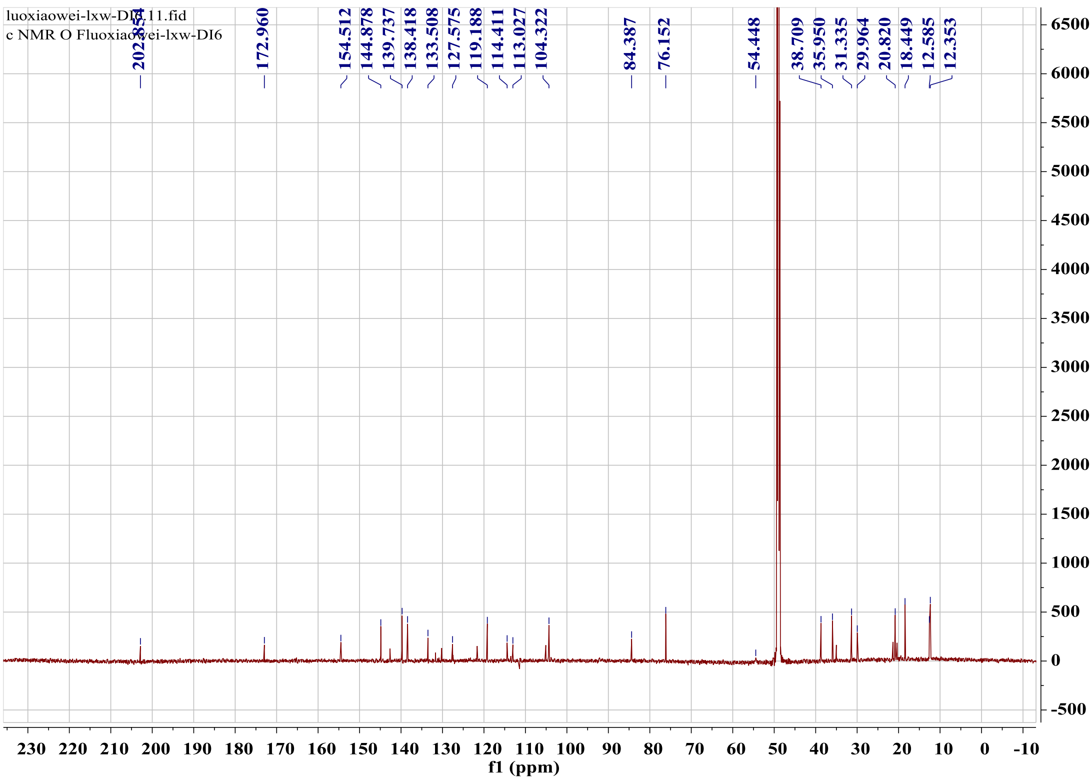


Figure S1. [1]H NMR spectrum of isochromophilone A (**1**) (CD_3OD, 700 MHz)



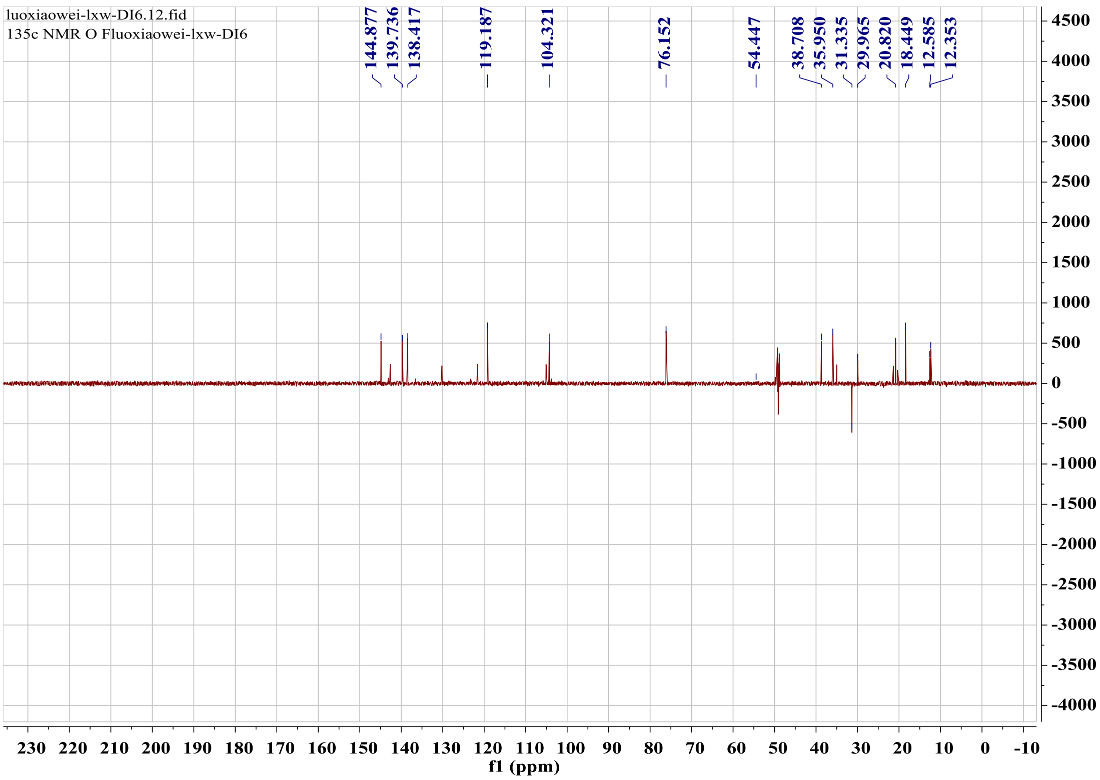


Figure S2. ^{13}C NMR and DEPT spectra of isochromophilone A (**1**) (CD_3OD, 175 MHz)

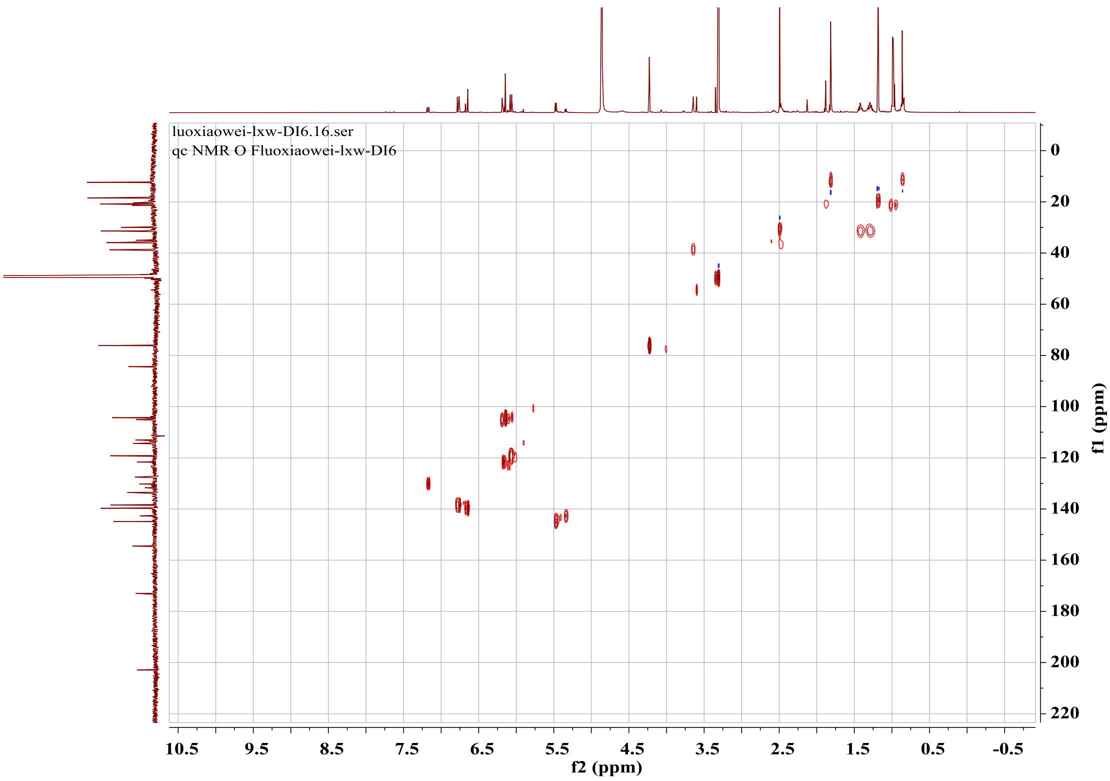


Figure S3. HSQC spectrum of isochromophilone A (**1**) (CD_3OD)

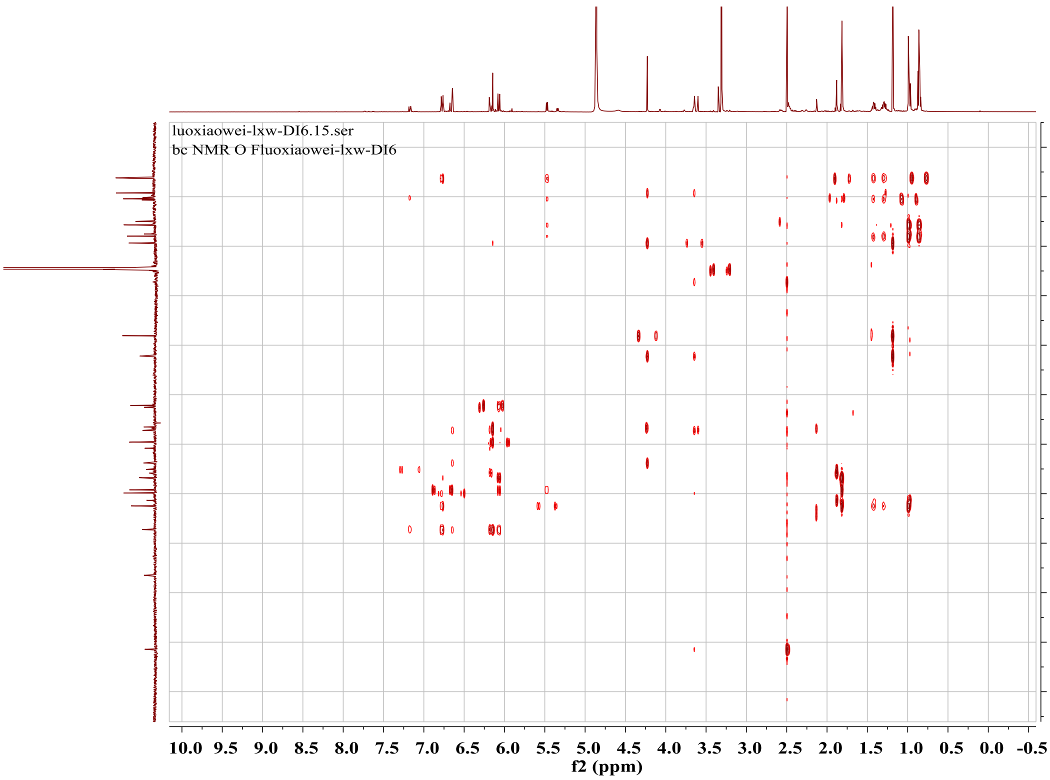


Figure S4. HMBC spectrum of isochromophilone A (**1**) (CD_3OD)

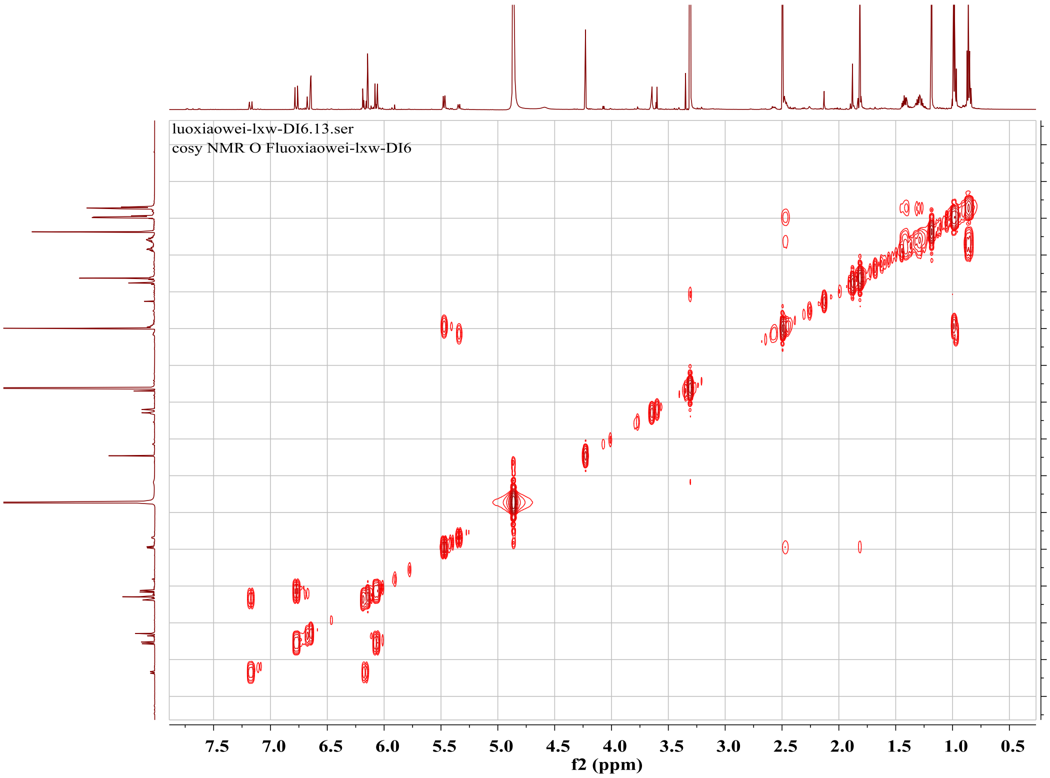
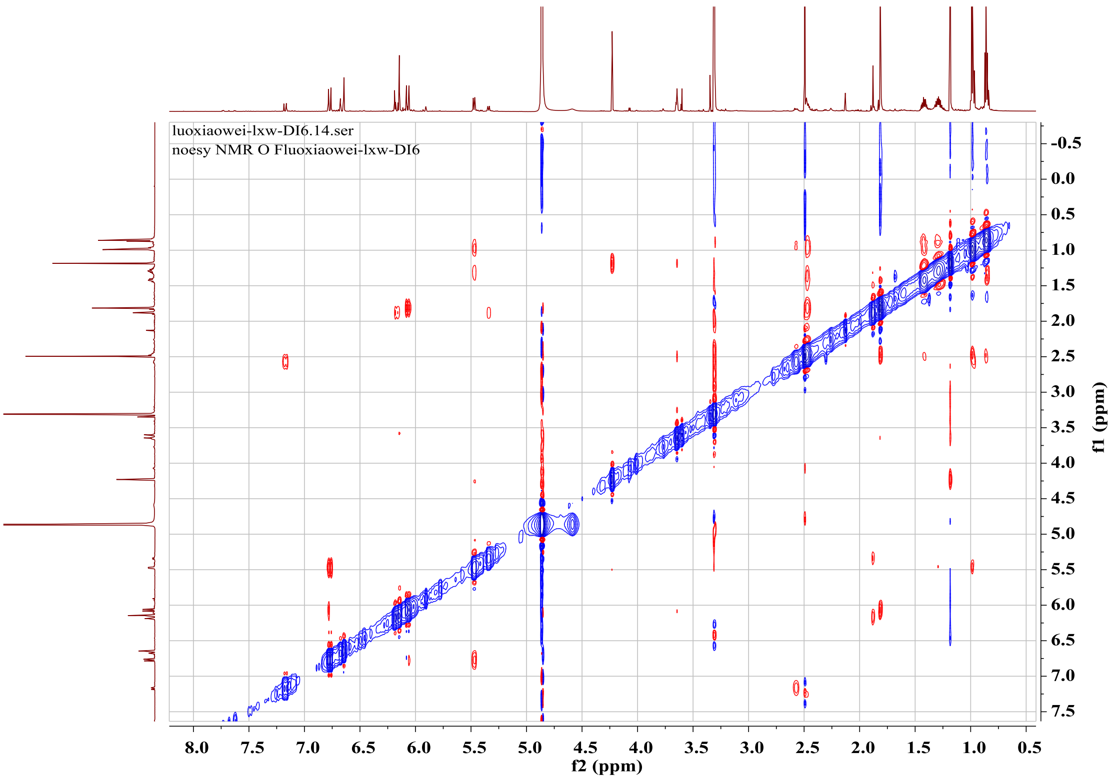


Figure S5. ^1H-^1H COSY spectrum of isochromophilone A (**1**) (CD_3OD)



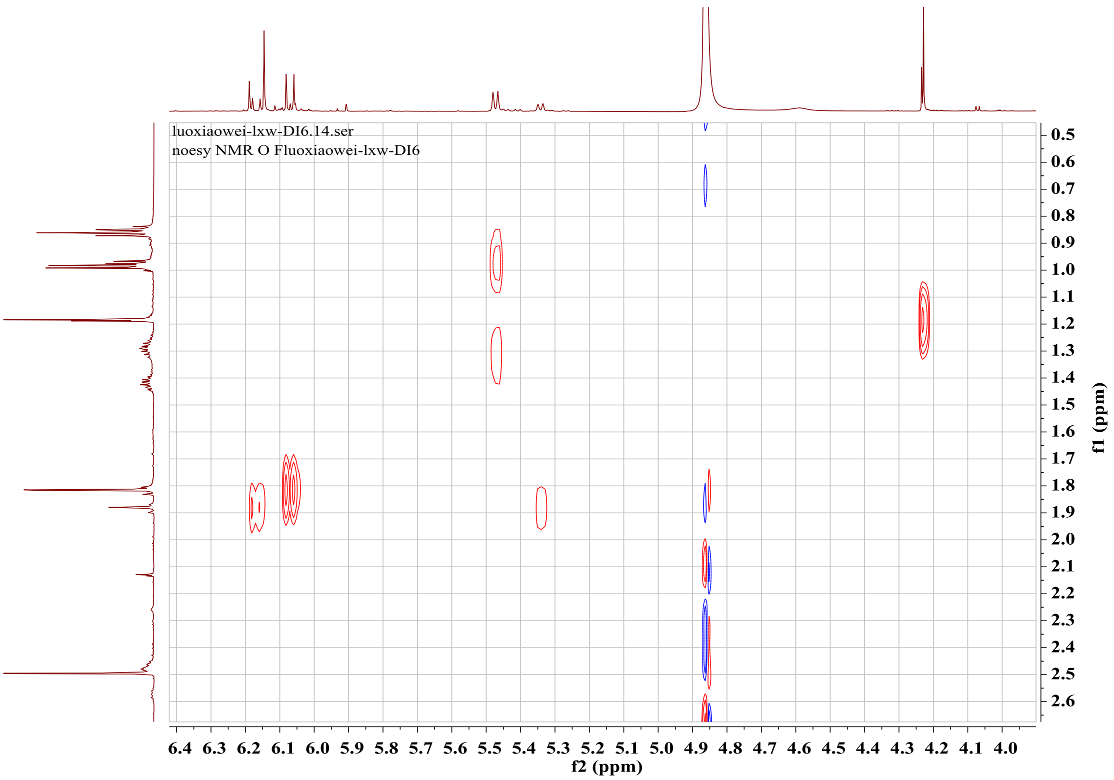
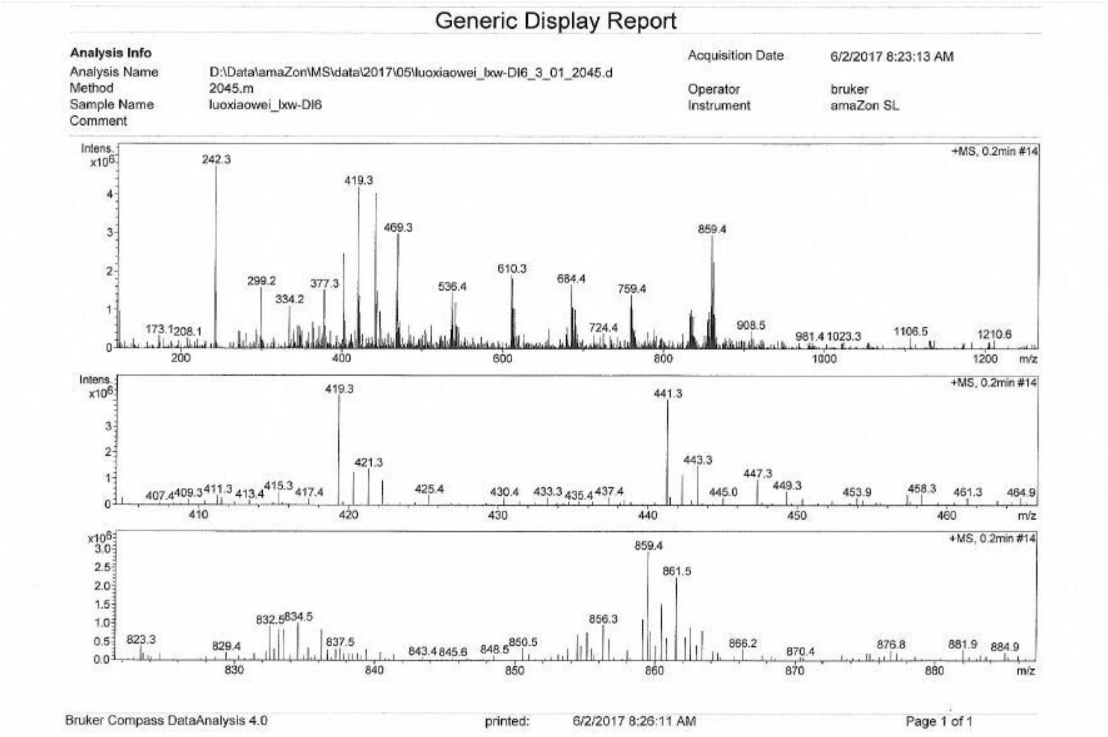


Figure S6. NOESY spectrum of isochromophilone A (**1**) (CD_3OD)



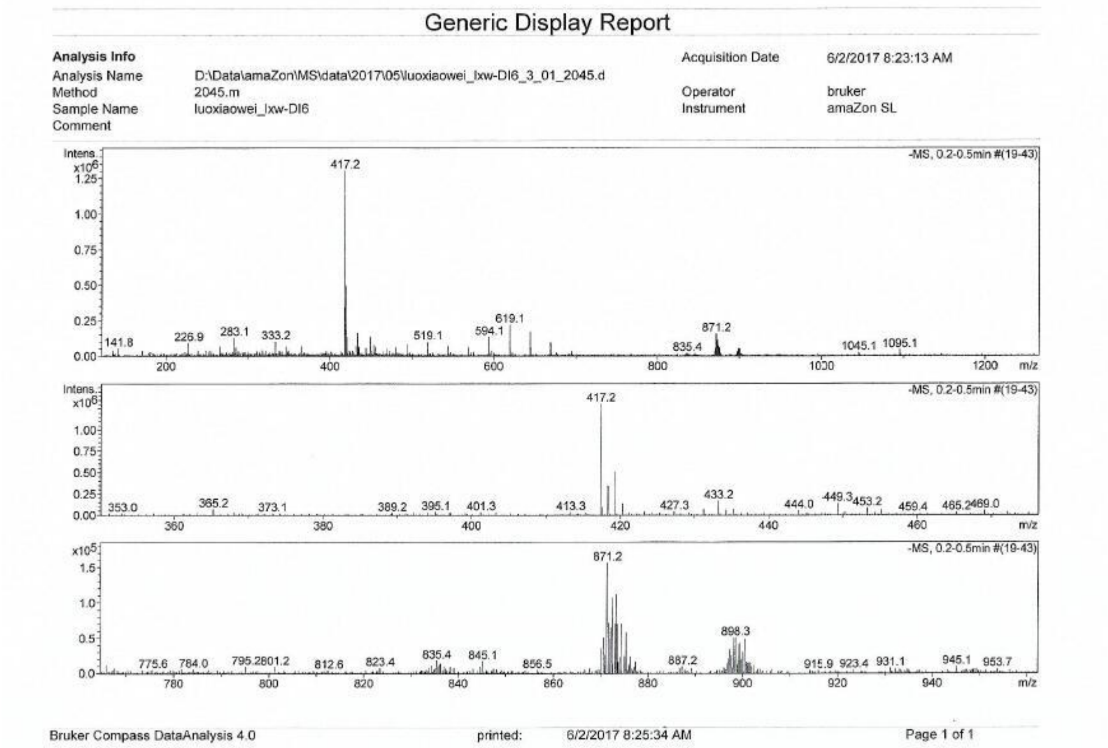
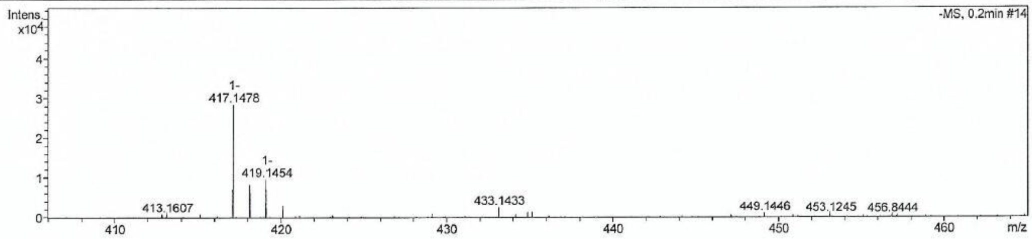


Figure S7. Positive and negative LR-ESI-MS spectra of isochromophilone A (**1**)

Mass Spectrum SmartFormula Report

Analysis Info		Acquisition Date	6/8/2017 9:46:59 AM
Analysis Name	D:\Data\MS\data\201706\luoxiaowei_lxw-DI6_neg_11_01_3100.d		
Method	LC_Direct Infusion_neg_100-1000mz.m	Operator	SCSIO
Sample Name	luoxiaowei_lxw-DI6_neg	Instrument	maXis 255552.00029
Comment			

Acquisition Parameter					
Source Type	ESI	Ion Polarity	Negative	Set Nebulizer	0.4 Bar
Focus	Active	Set Capillary	4000 V	Set Dry Heater	180 °C
Scan Begin	100 m/z	Set End Plate Offset	-500 V	Set Dry Gas	4.0 l/min
Scan End	2000 m/z	Set Charging Voltage	0 V	Set Divert Valve	Waste
		Set Corona	0 nA	Set APCI Heater	0 °C



Meas. m/z	#	Ion Formula	Score	m/z	err [ppm]	err [mDa]	mSigma	rdb	e⁻ Conf	N-Rule
417.147848	1	C23H26ClO5	100.00	417.147425	-1.0	-0.4	21.4	10.5	even	ok
453.124488	1	C23H27Cl2O5	100.00	453.124103	0.9	0.4	71.6	9.5	even	ok
835.301714	1	C46H53Cl2O10	100.00	835.302127	0.5	0.4	36.8	19.5	even	ok

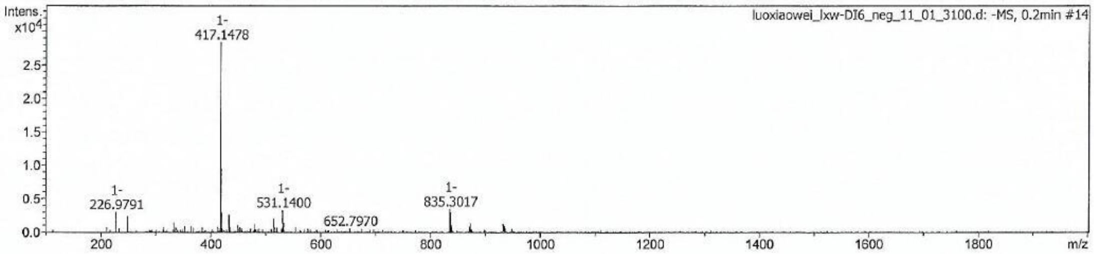
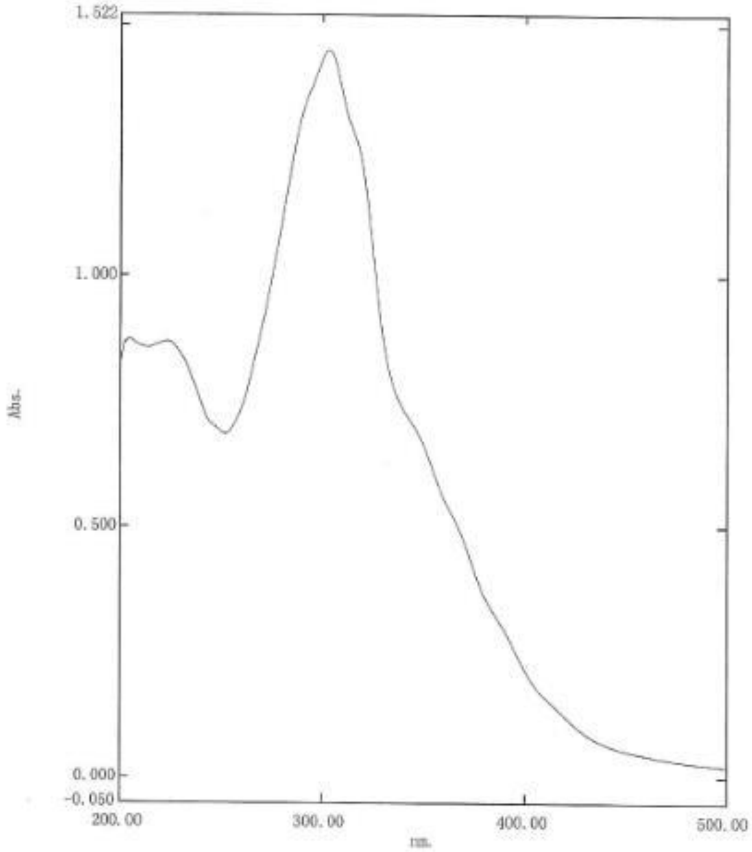


Figure S8. Negative HR-ESI-MS spectrum of isochromophilone A (**1**)



[测定属性]
波长范围 (nm.): 200.00 到 500.00
扫描速度: 中速
采样间隔: 0.2
自动采样间隔: 启用
扫描模式: 单个

[仪器属性]
仪器类型: UV-2600 系列
测定方式: 吸收值
狭缝宽: 2.0
积分时间: 0.1 秒.
光源转换波长: 323.0 nm
检测器单元: 直接
S/R 转换: 标准
阶梯校正: OFF

[附件属性]
附件: 无

[数据处理参数]
阈值: 0.0100000
点: 4
内插: 停用
平均: 停用

[样品准备属性]
重量:
体积:
稀释:
光程长:
附加信息:

418.1 40μg/ml

No.	P/V	波长(nm)	吸收值	描述
1	↑	302.60	1.451	4.181
2	↑	223.60	0.869	3.958
3	↑	204.80	0.874	3.959

Figure S9. UV spectrum of isochromophilone A (**1**)

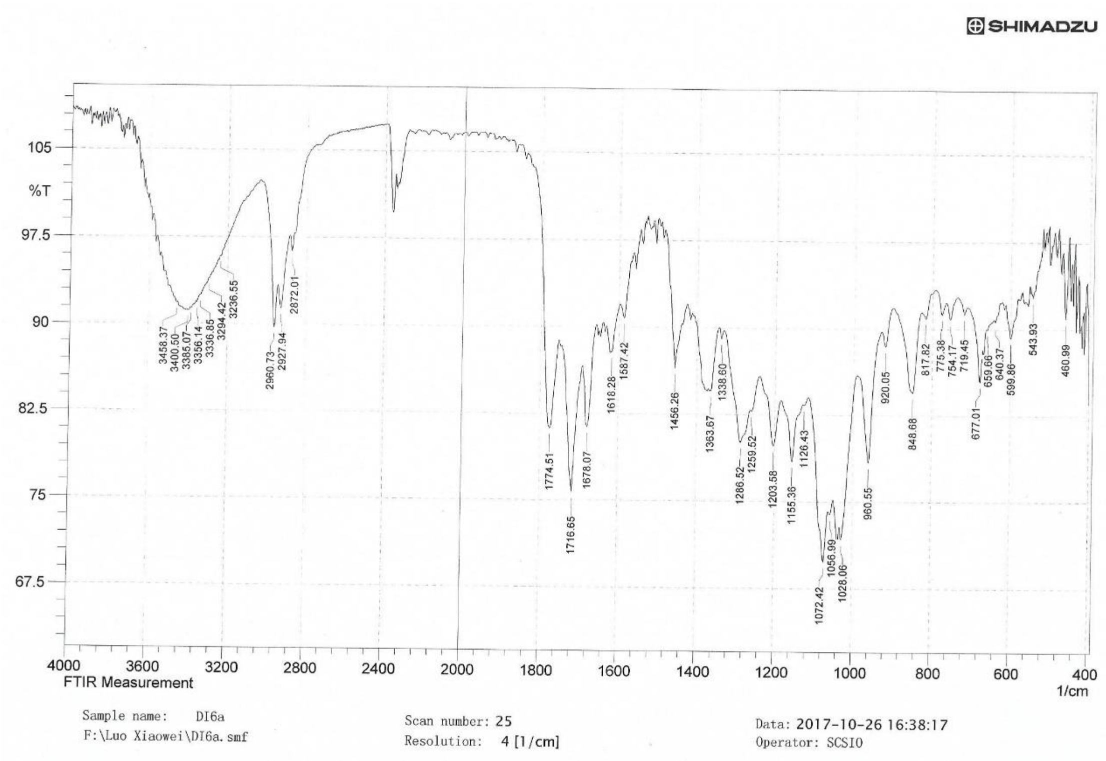


Figure S10. IR spectrum of isochromophilone A (**1**)

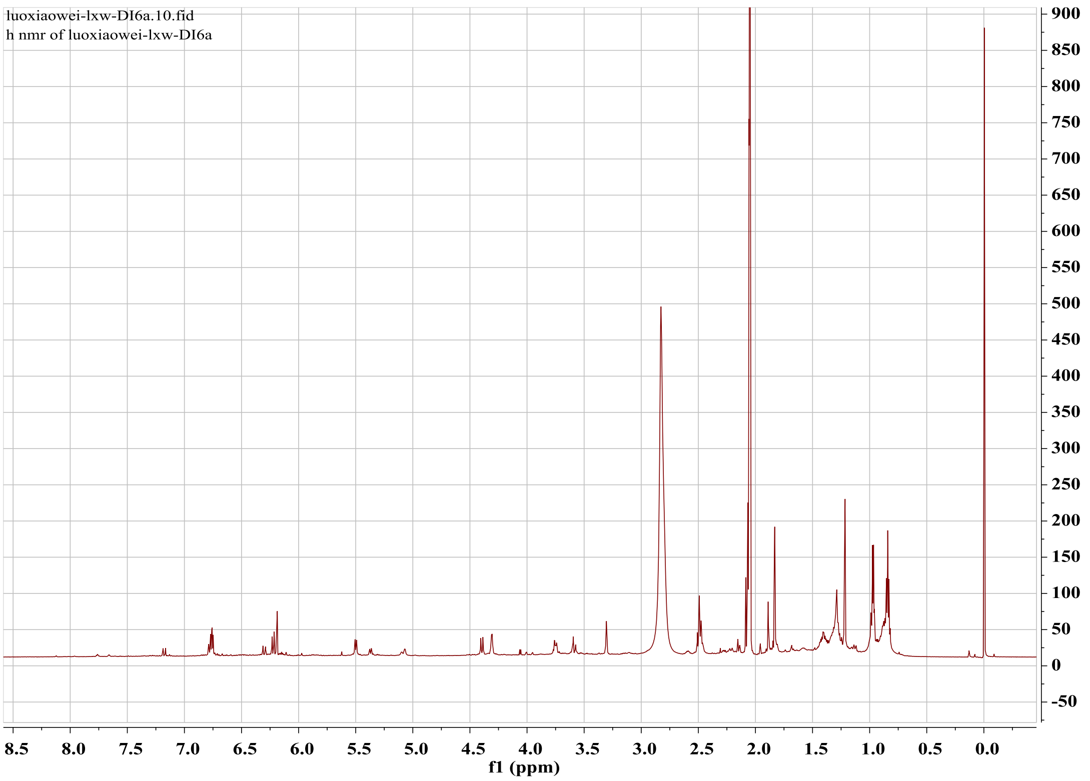


Figure S11. ^{1}H NMR spectrum of isochromophilone A (**1**) (acetone-d_6, 700 MHz)

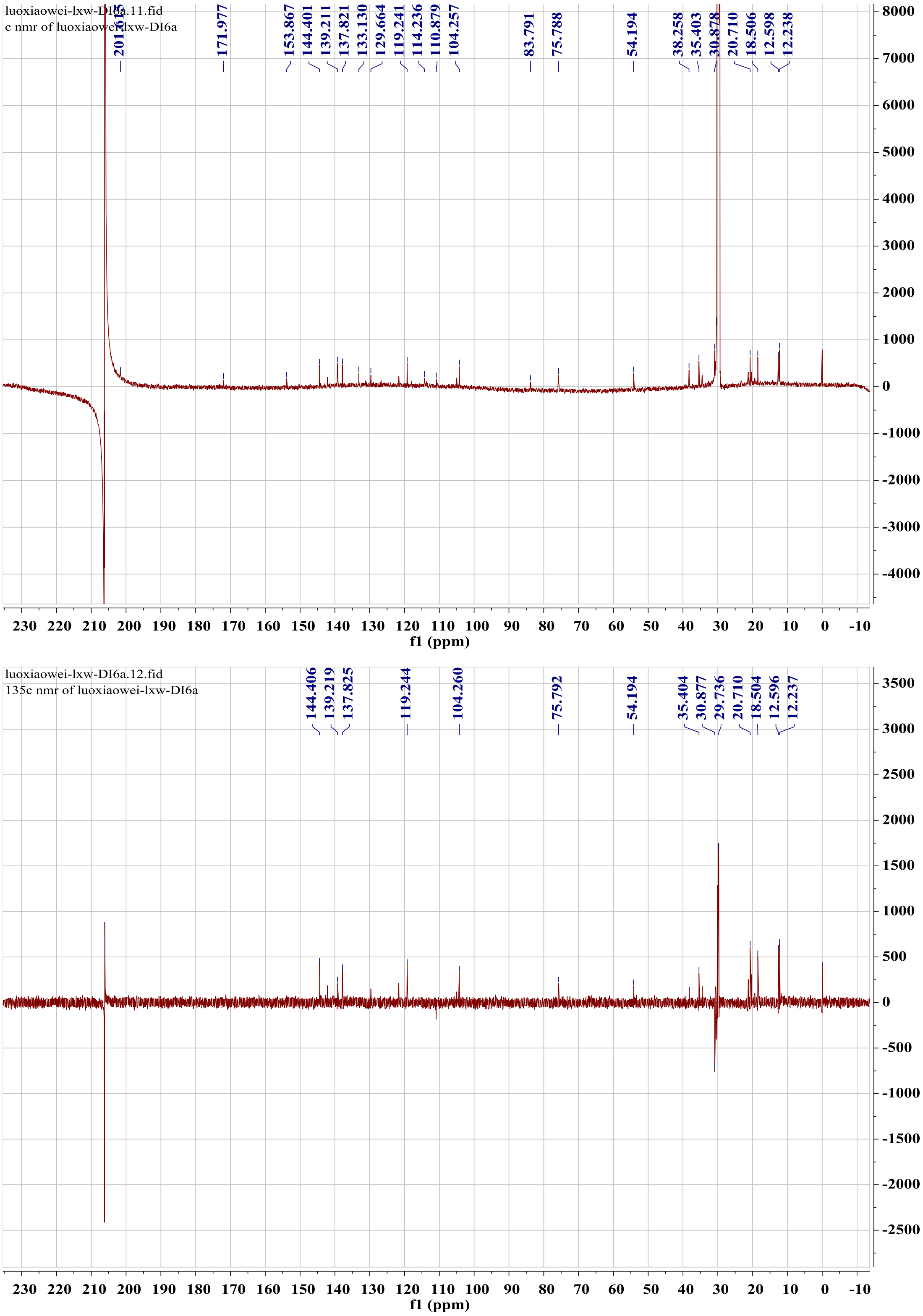


Figure S12. ${}^{13}C$ NMR and DEPT spectra of isochromophilone A (**1**) (acetone-d_6, 175 MHz)

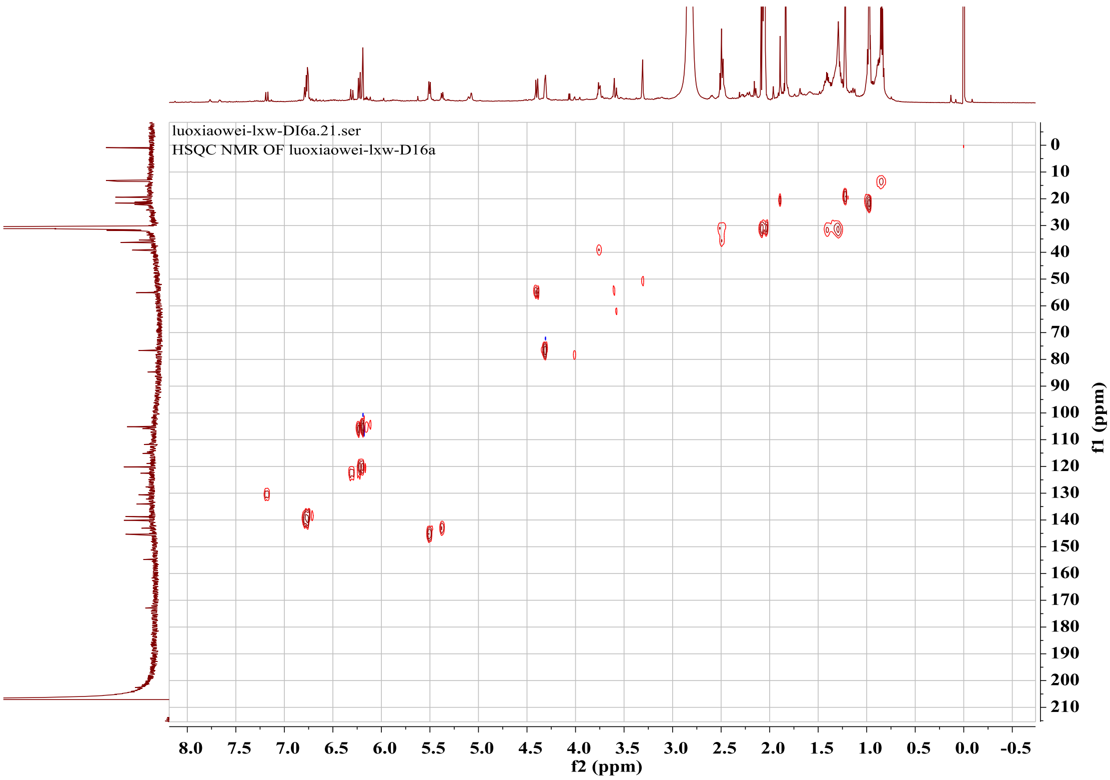
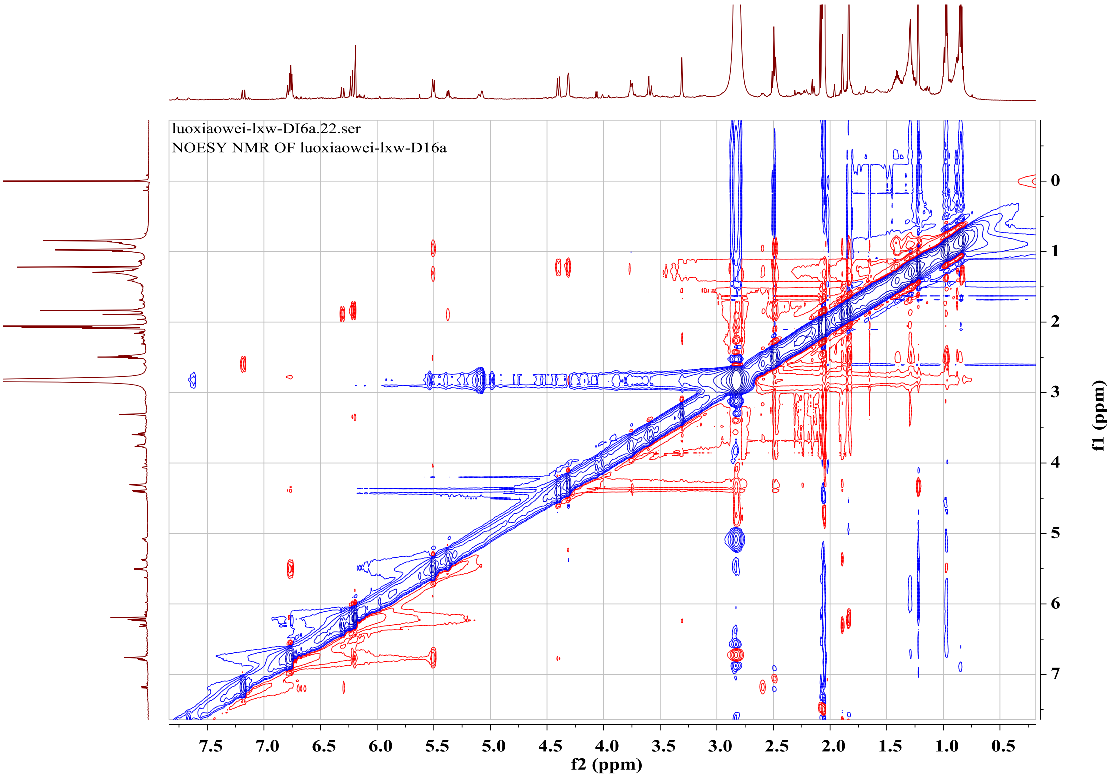


Figure S13. HSQC spectrum of isochromophilone A (**1**) (acetone-d_6)



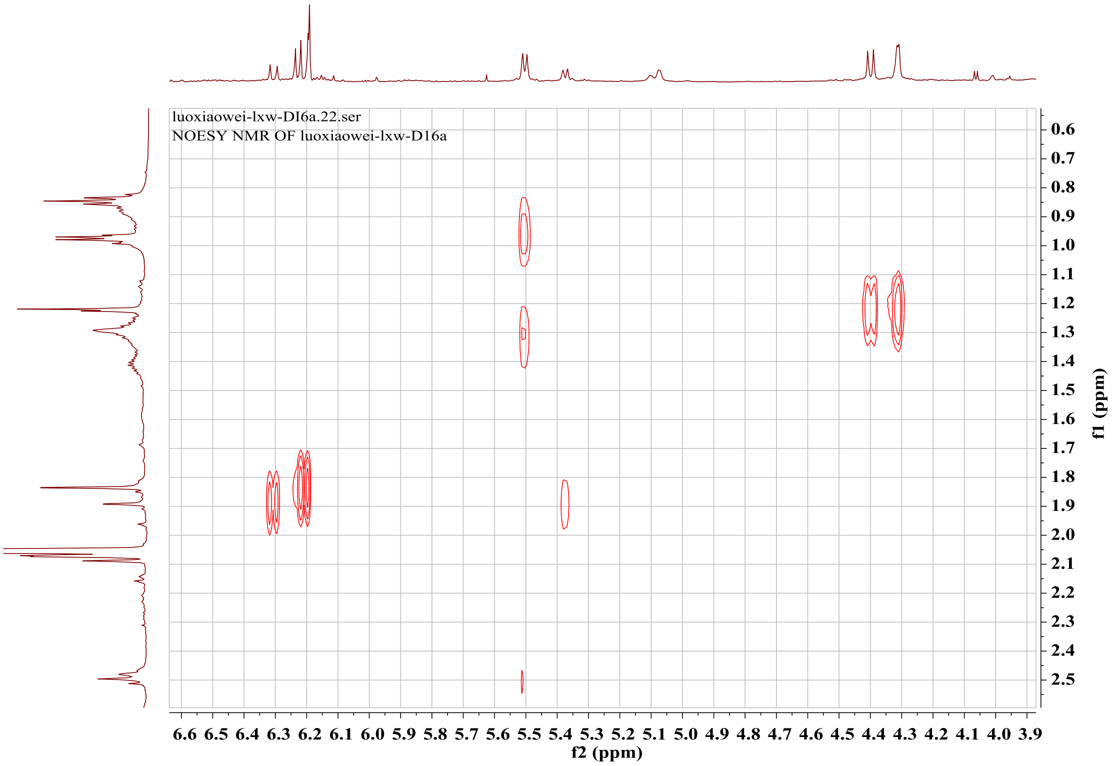


Figure S14. NOESY spectrum of isochromophilone A (**1**) (acetone-d_6)

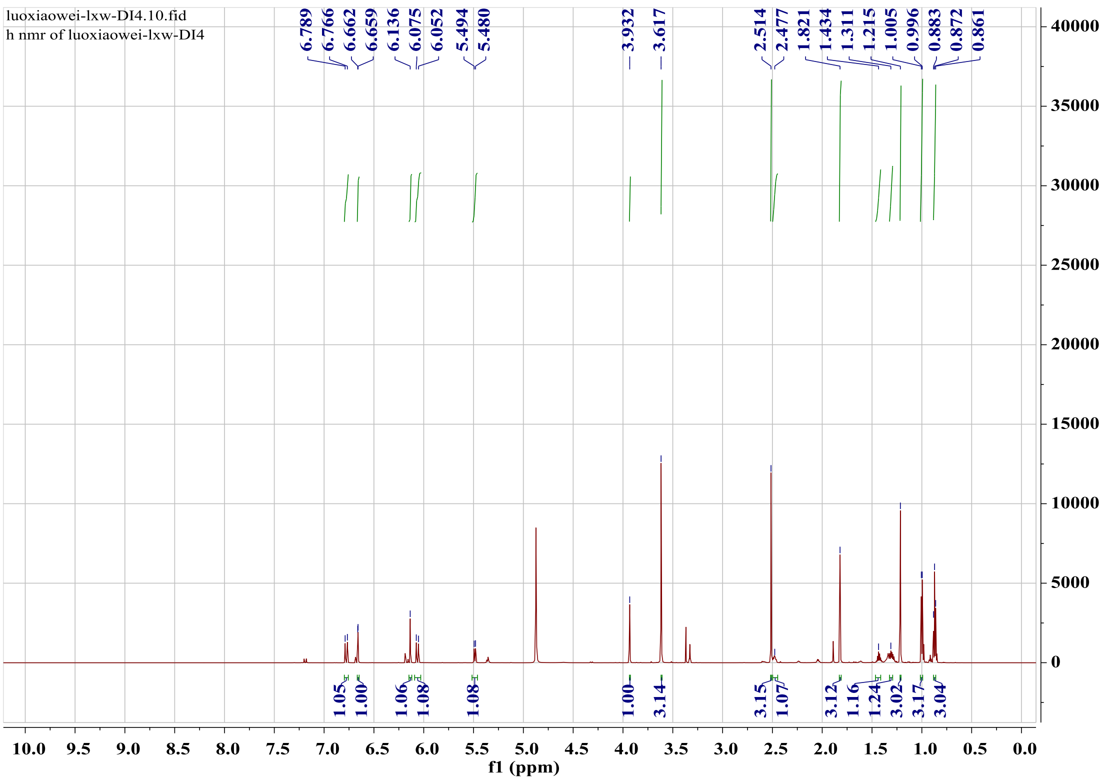


Figure S15. ^{1}H NMR spectrum of isochromophilone B (**2**) (CD_3OD, 700 MHz)

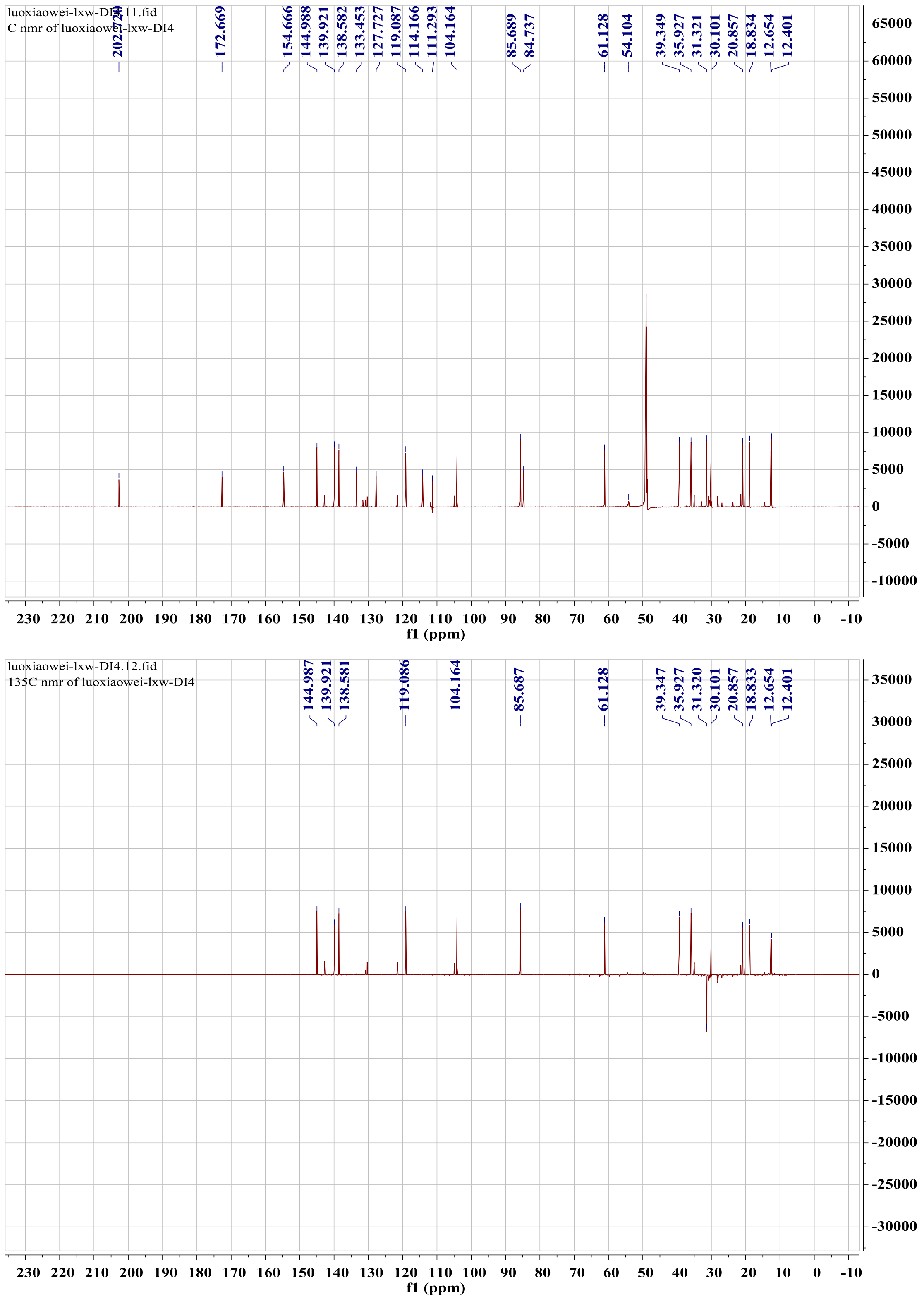


Figure S16. ^{13}C NMR and DEPT spectra of isochromophilone B (**2**) (CD_3OD, 175 MHz)

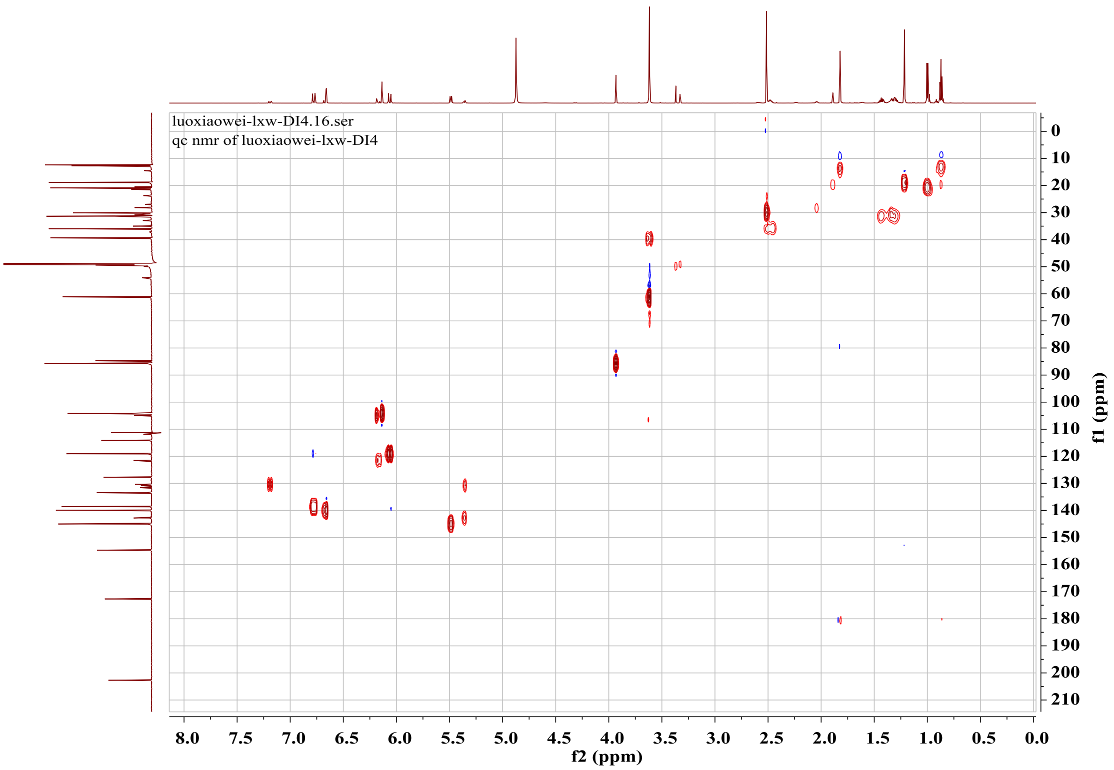


Figure S17. HSQC spectrum of isochromophilone B (**2**) (CD_3OD)

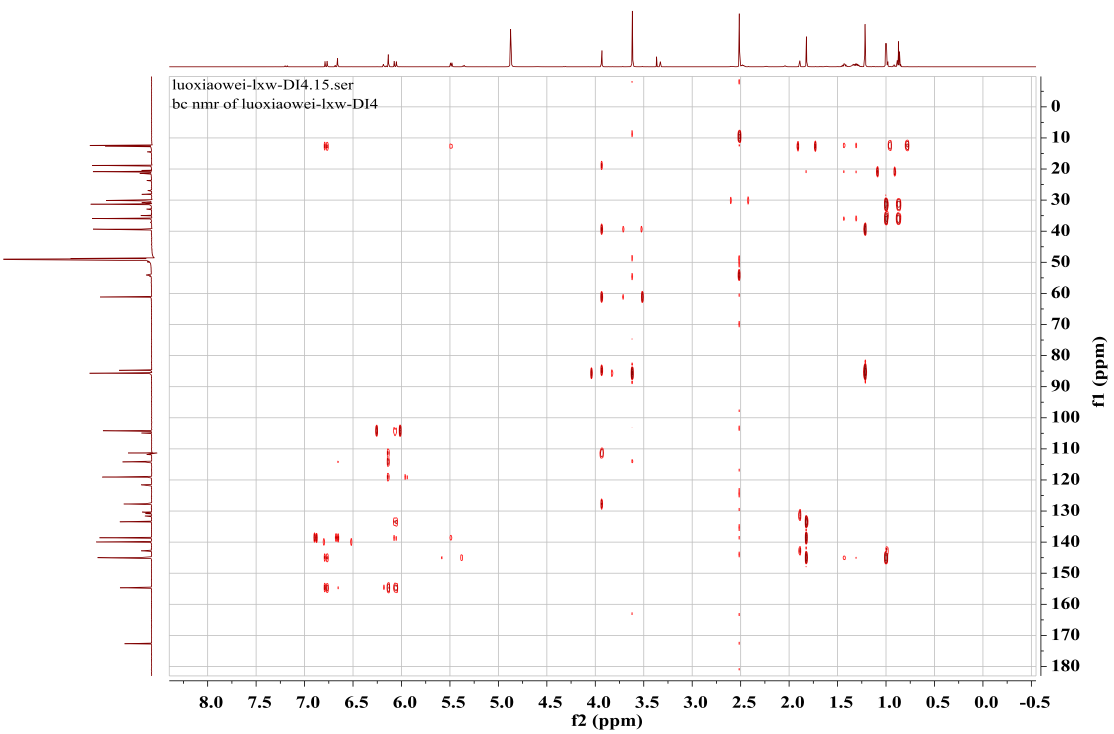


Figure S18. HMBC spectrum of isochromophilone B (**2**) (CD_3OD)

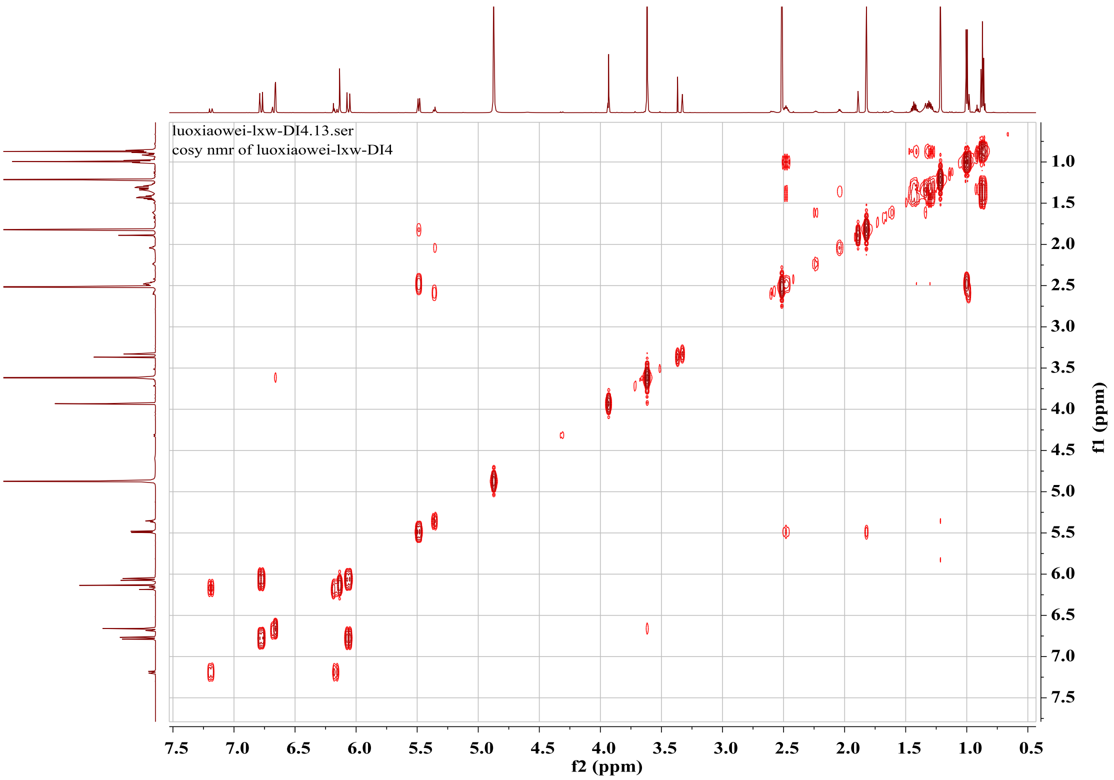
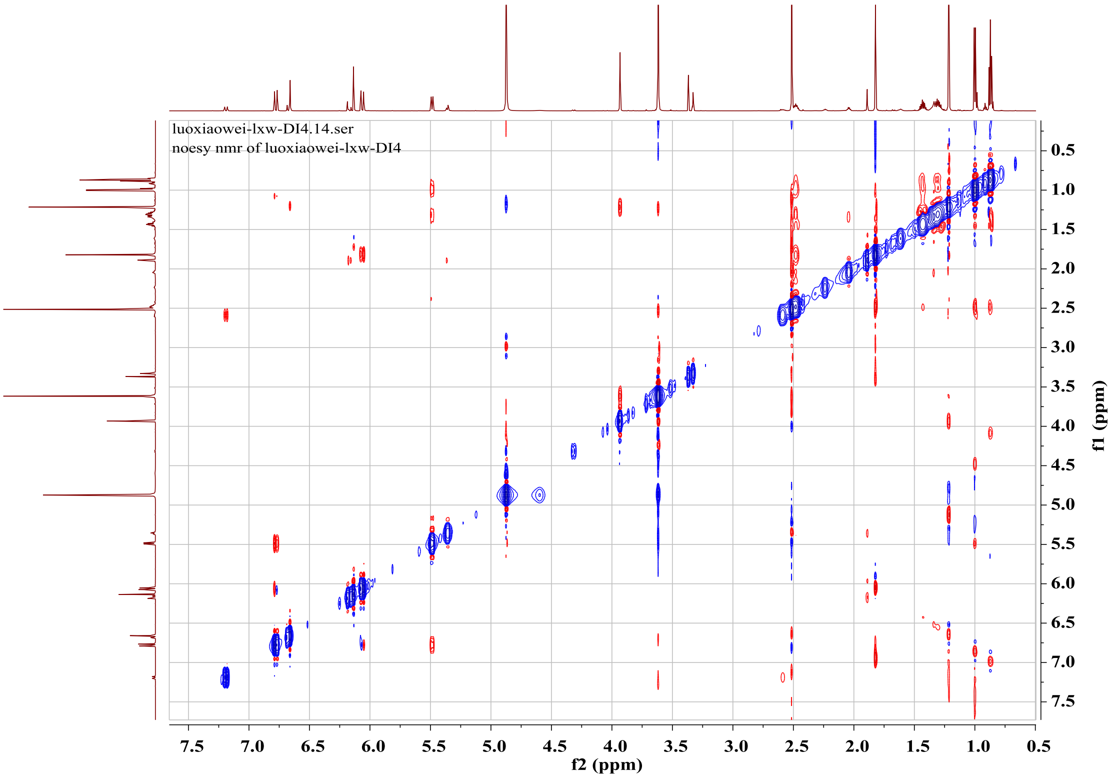


Figure S19. ¹H-¹H COSY spectrum of isochromophilone B (**2**) (CD_3OD)



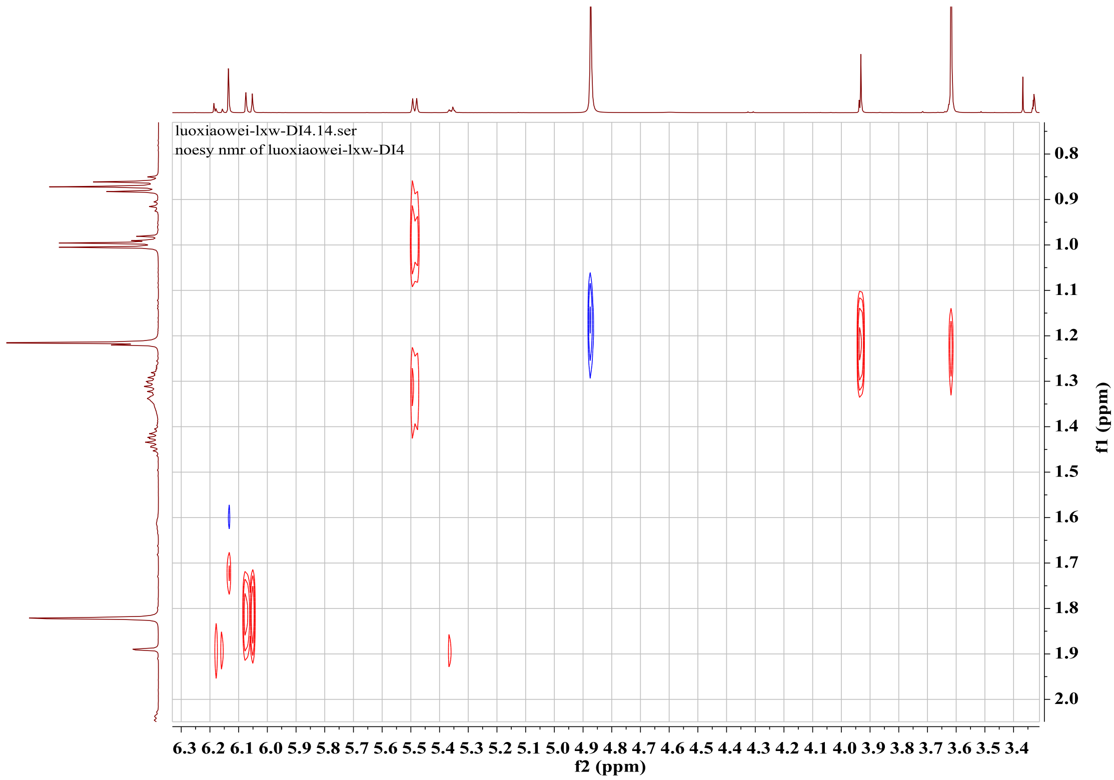
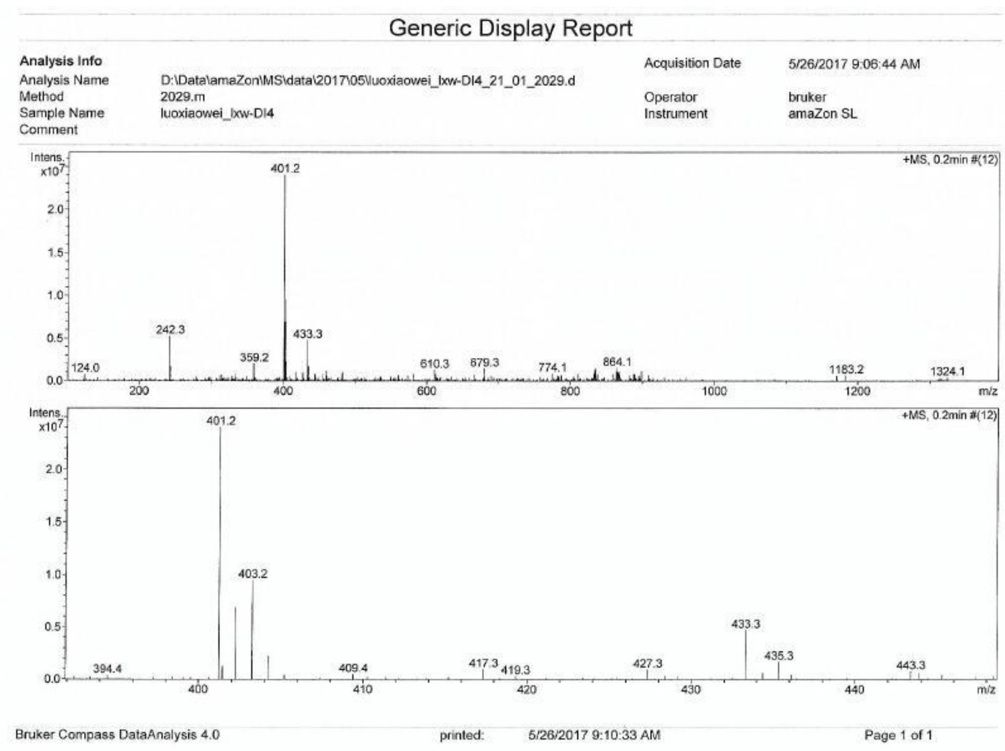


Figure S20. NOESY spectrum of isochromophilone B (**2**) (CD_3OD)



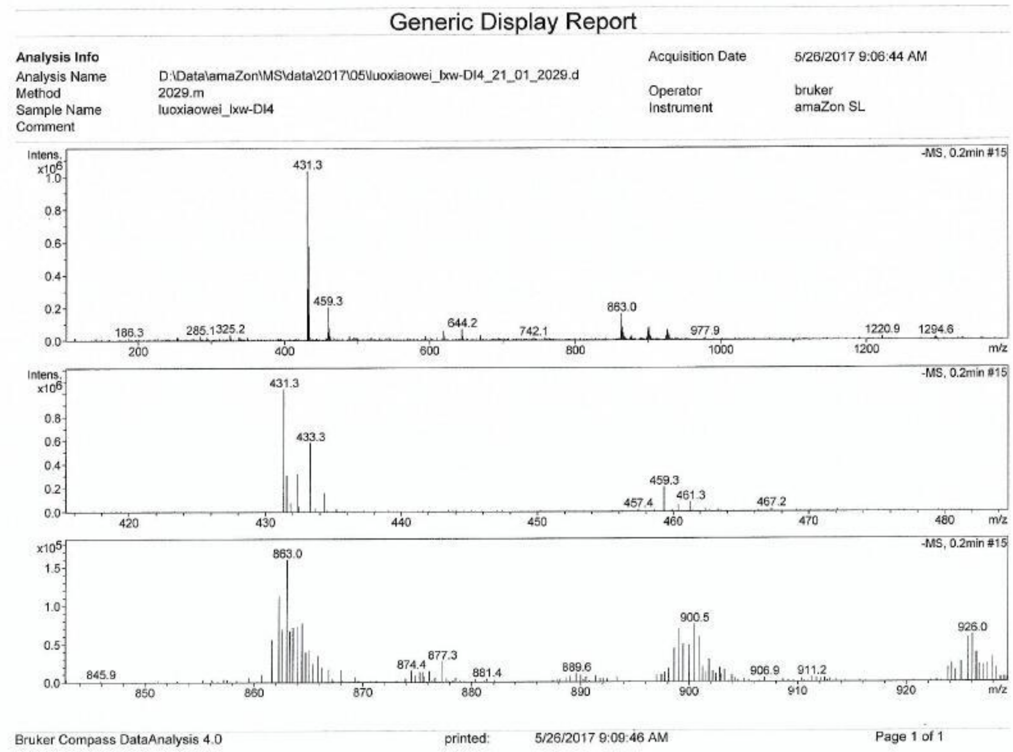
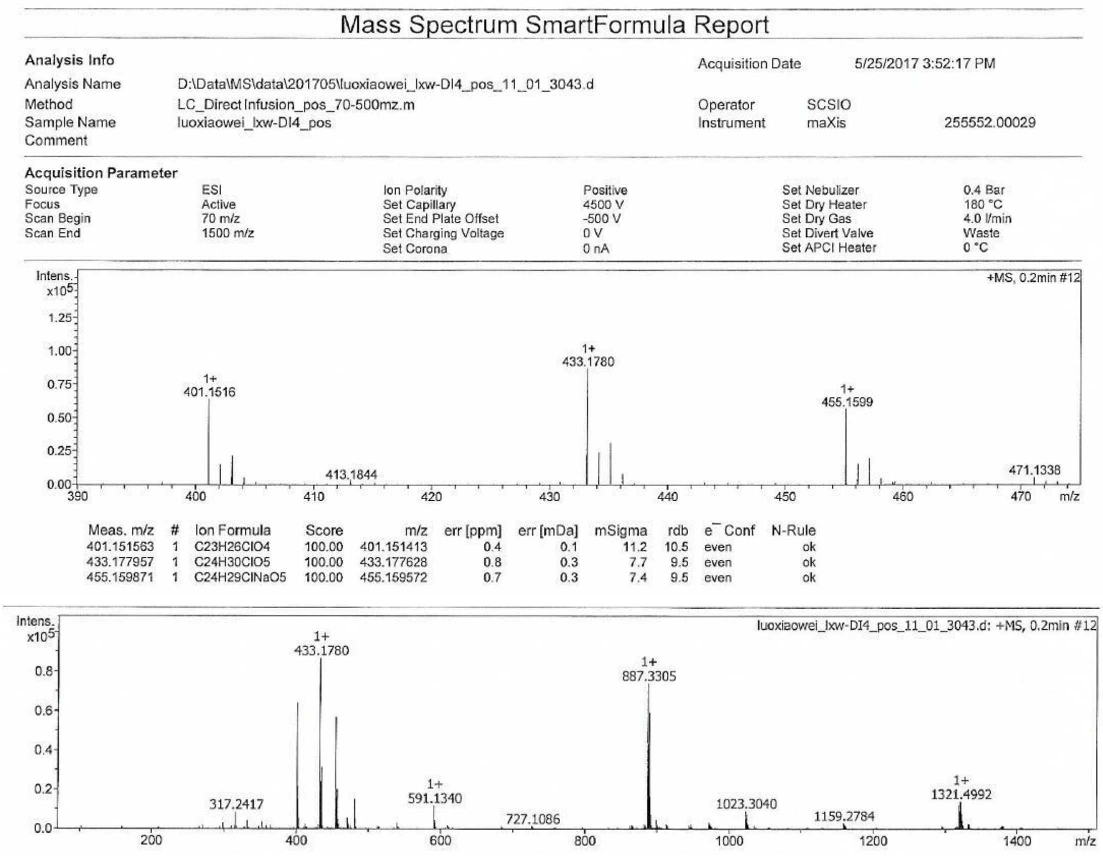


Figure S21. Positive and negative LR-ESI-MS spectra of isochromophilone B (**2**)



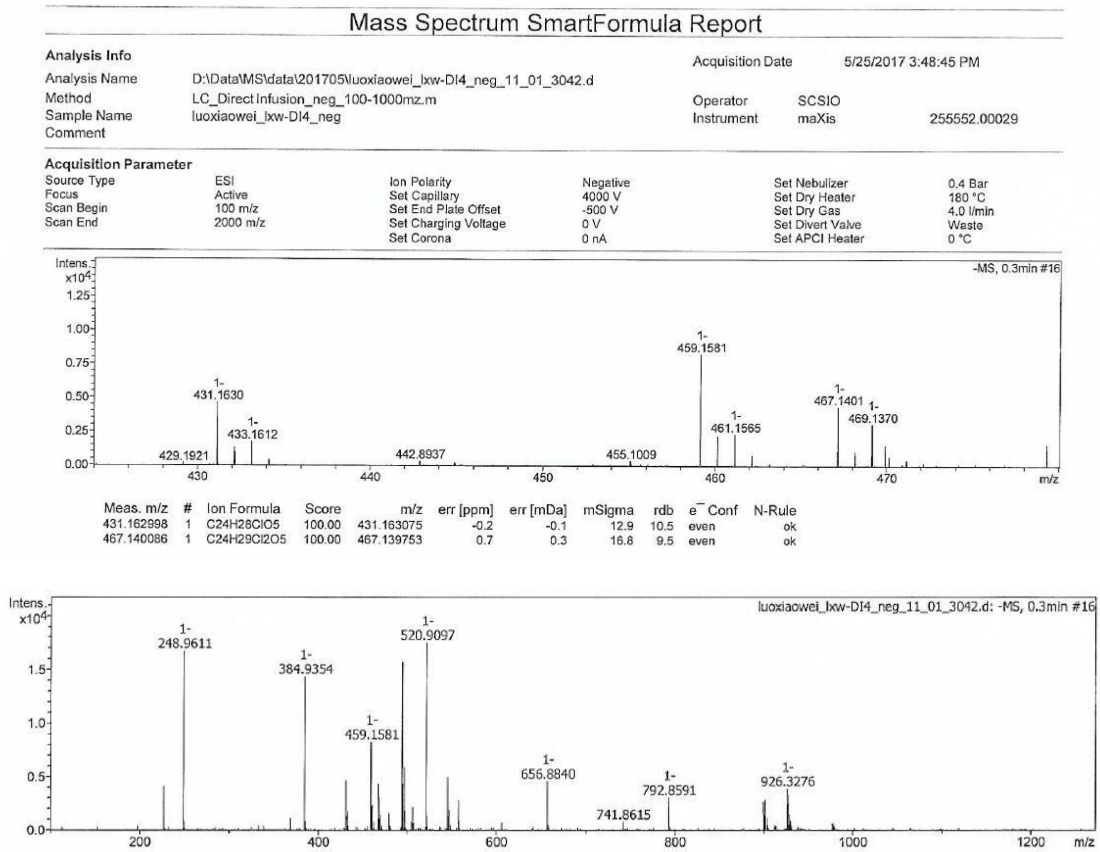


Figure S22. Positive and negative HR-ESI-MS spectra of isochromophilone B (**2**)

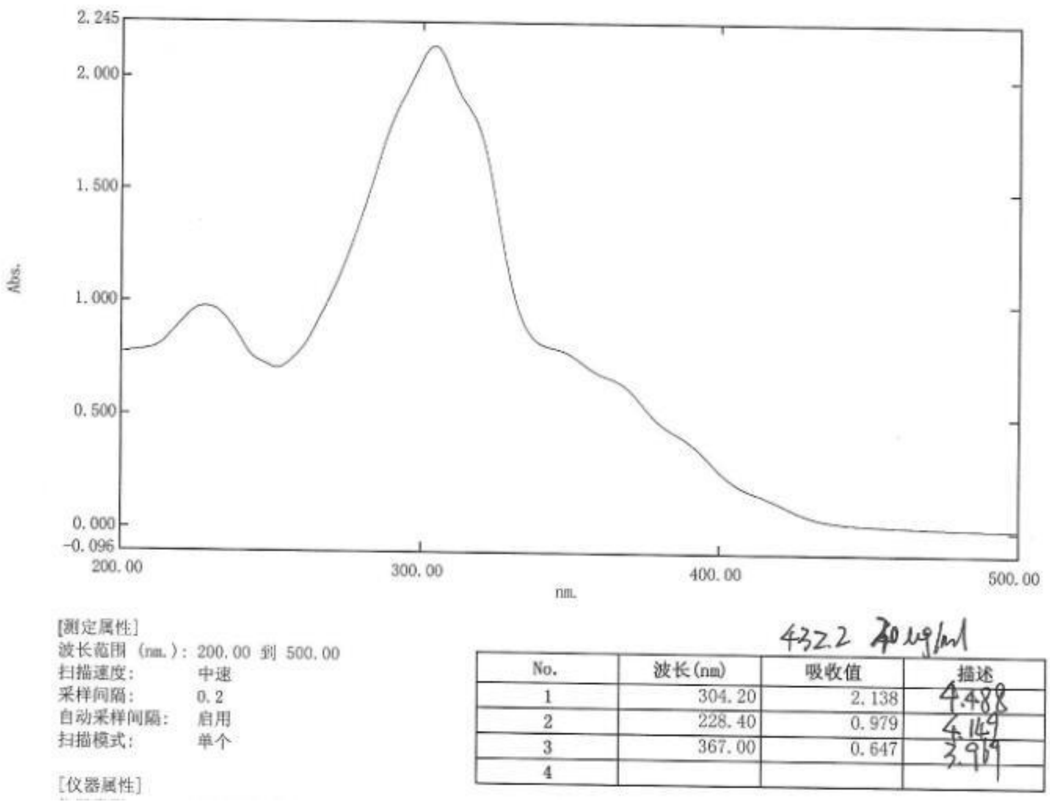


Figure S23. UV spectrum of isochromophilone B (**2**)

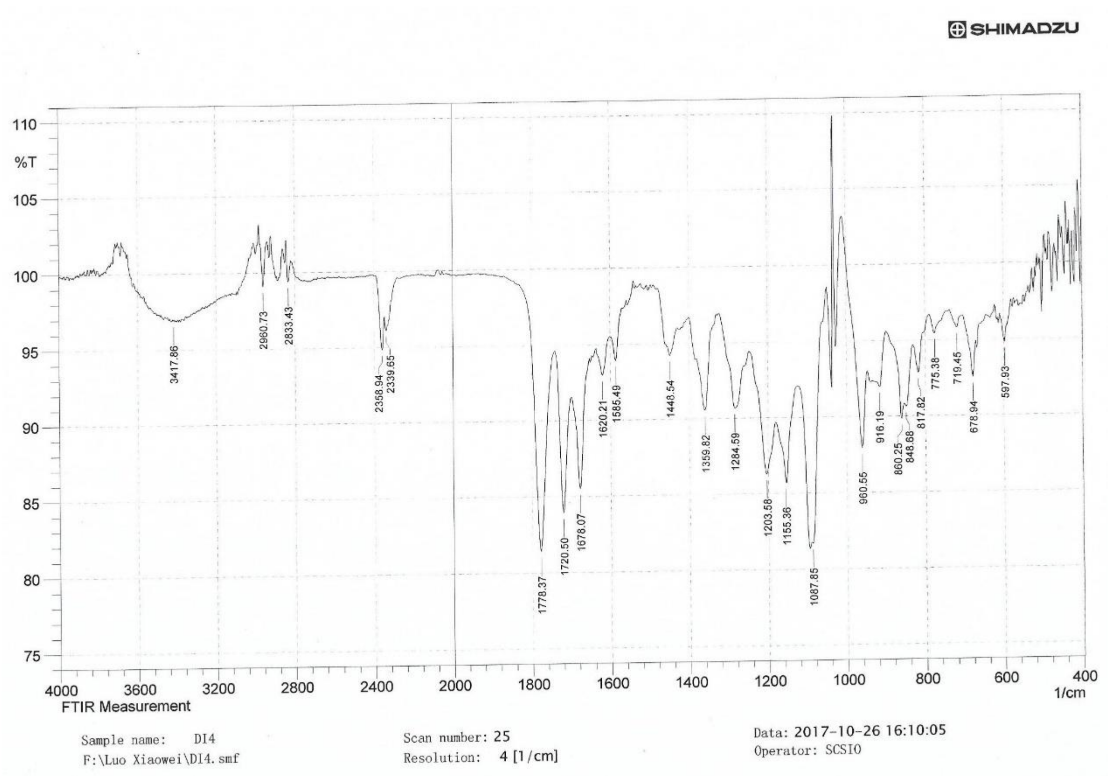


Figure S24. IR spectrum of isochromophilone B (**2**)

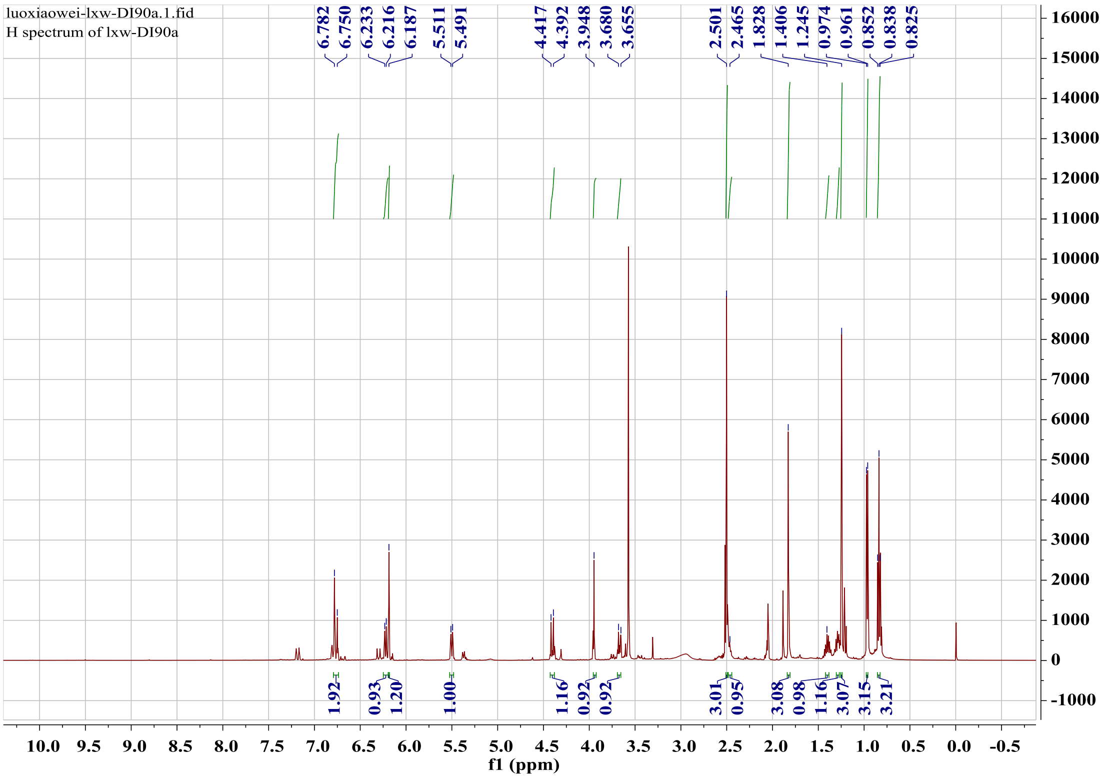


Figure S25. [1]H NMR spectrum of isochromophilone B (**2**) (acetone-d_6, 700 MHz)

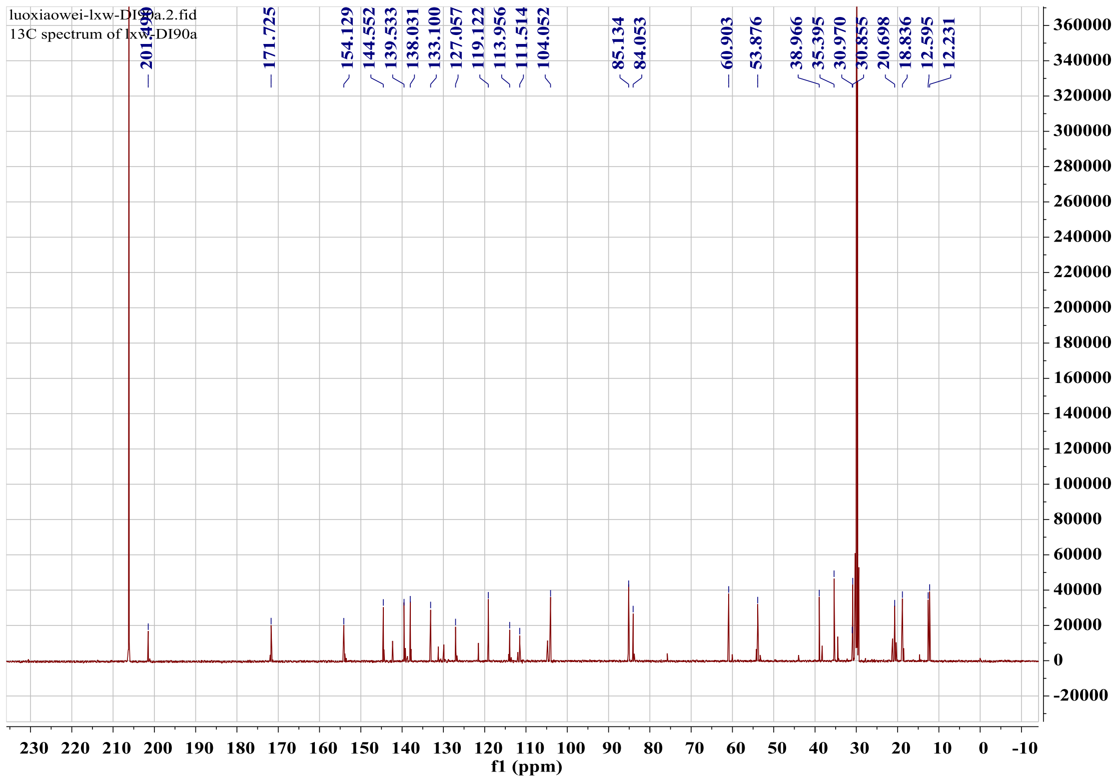


Figure S26. ^{13}C NMR spectrum of isochromophilone B (**2**) (acetone-d_6, 175 MHz)

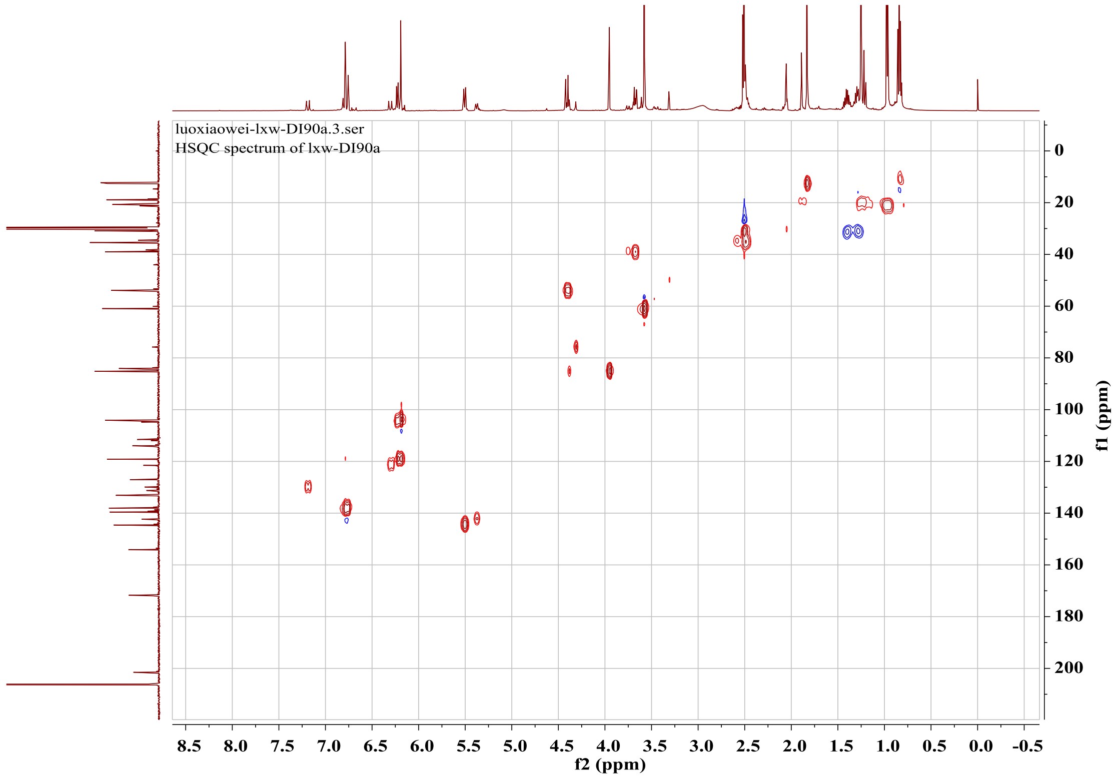


Figure S27. HSQC spectrum of isochromophilone B (**2**) (acetone-d_6)

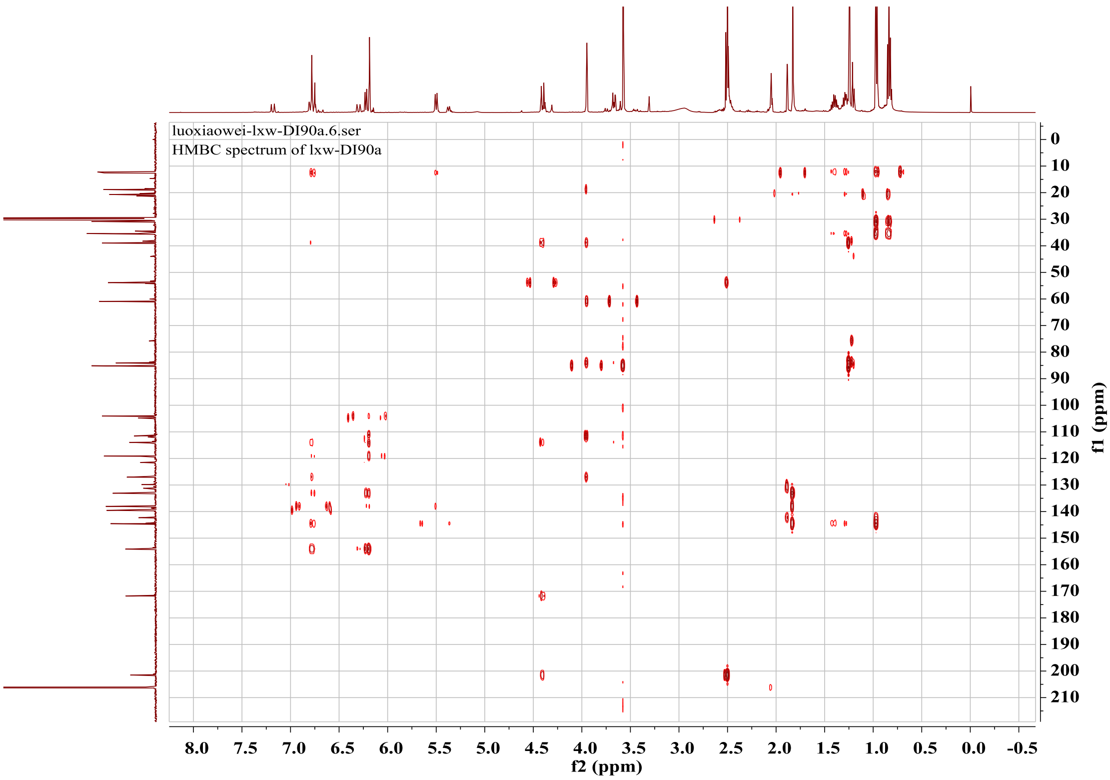


Figure S28. HMBC spectrum of isochromophilone B (**2**) (acetone-d_6)

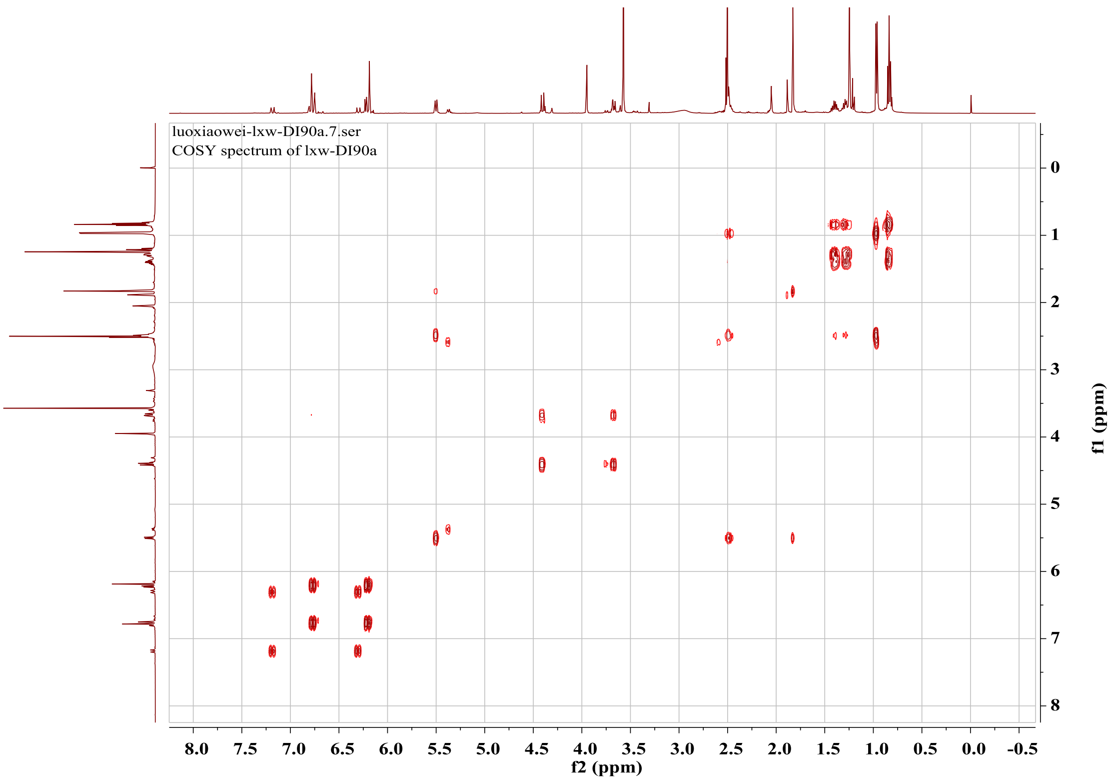
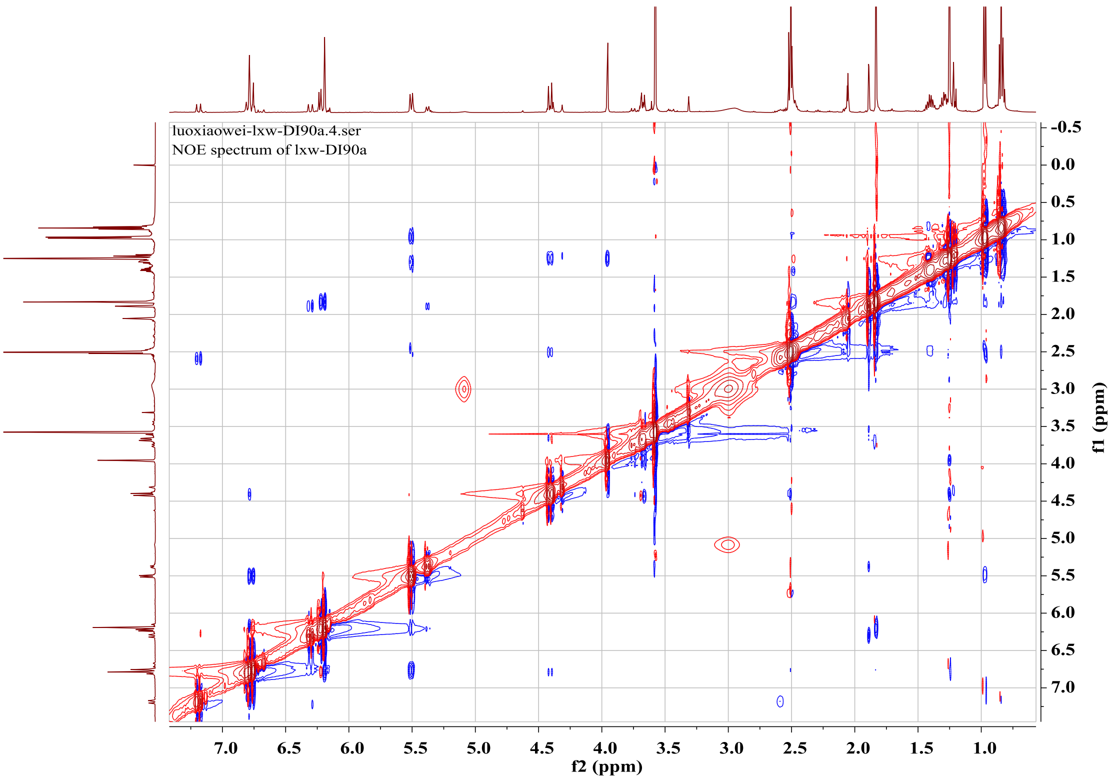


Figure S29. ^{1}H-^{1}H COSY spectrum of isochromophilone B (**2**) (acetone-d_6)



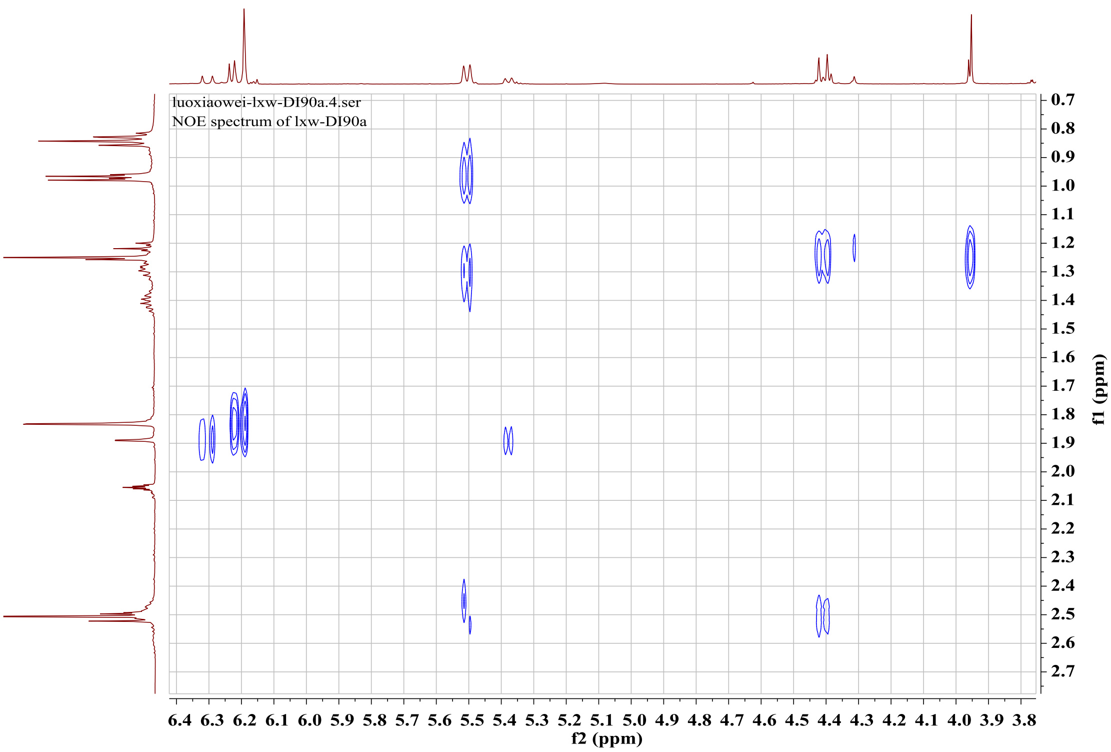


Figure S30. NOESY spectrum of isochromophilone B (**2**) (acetone-d_6)

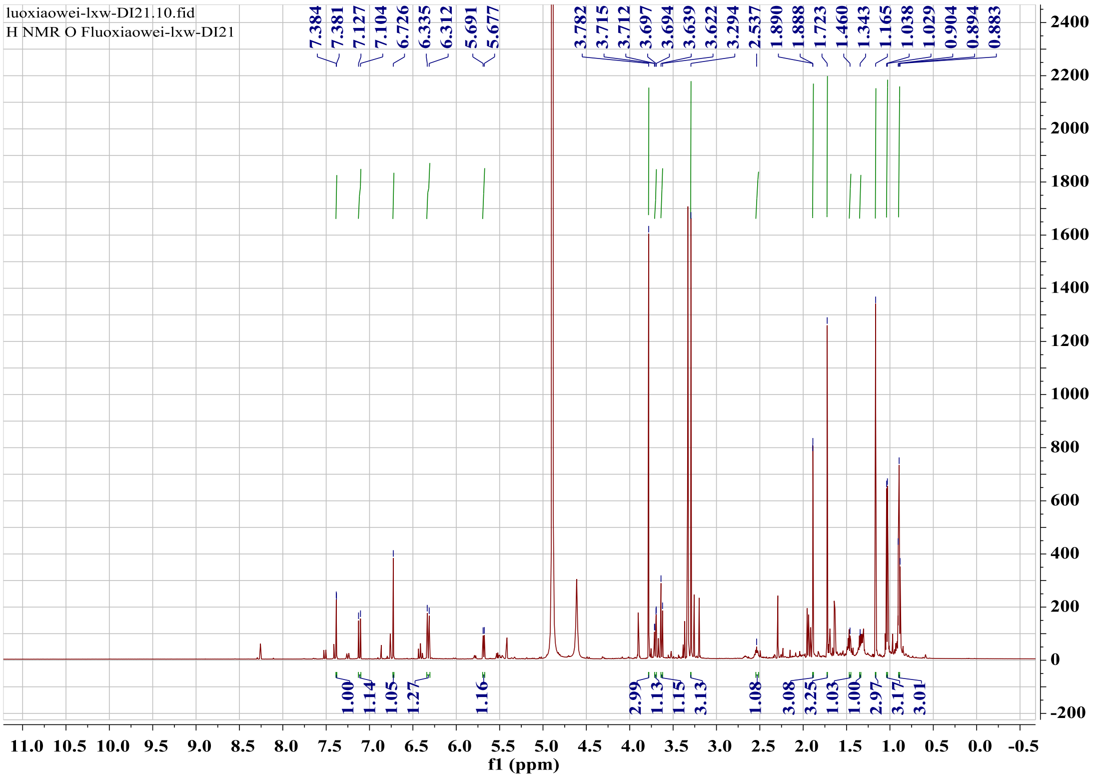
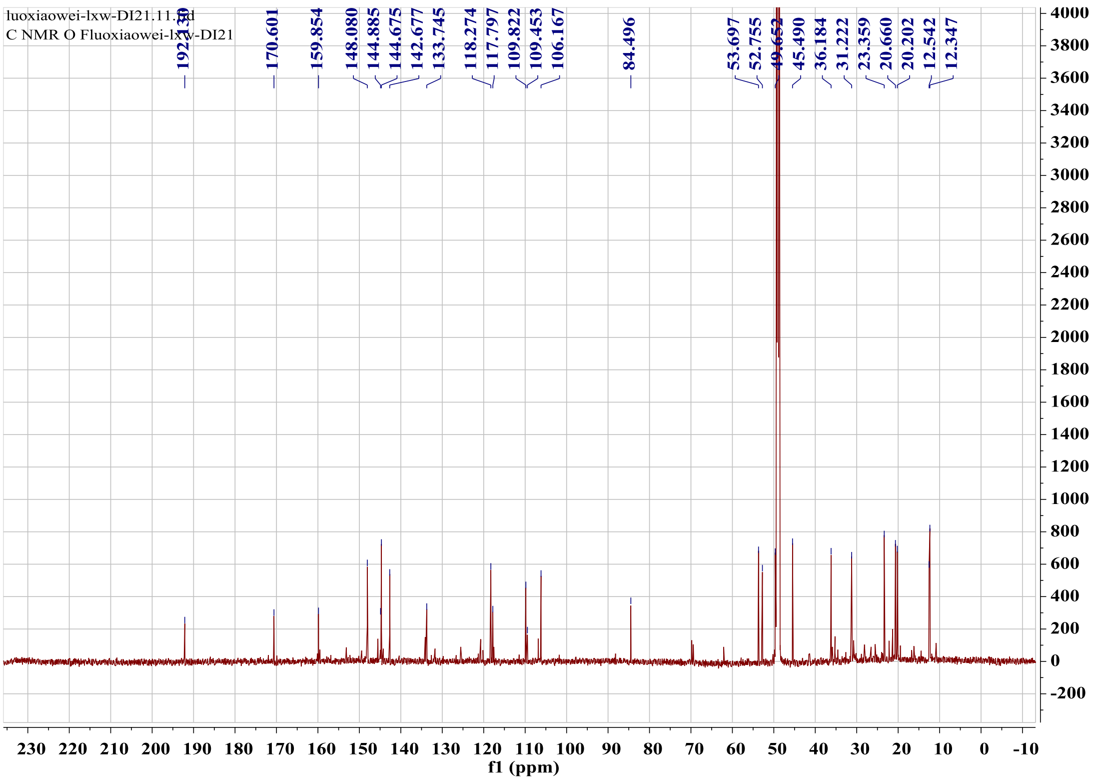


Figure S31. ^{1}H NMR spectrum of isochromophilone C (**3**) (CD_3OD, 700 MHz)



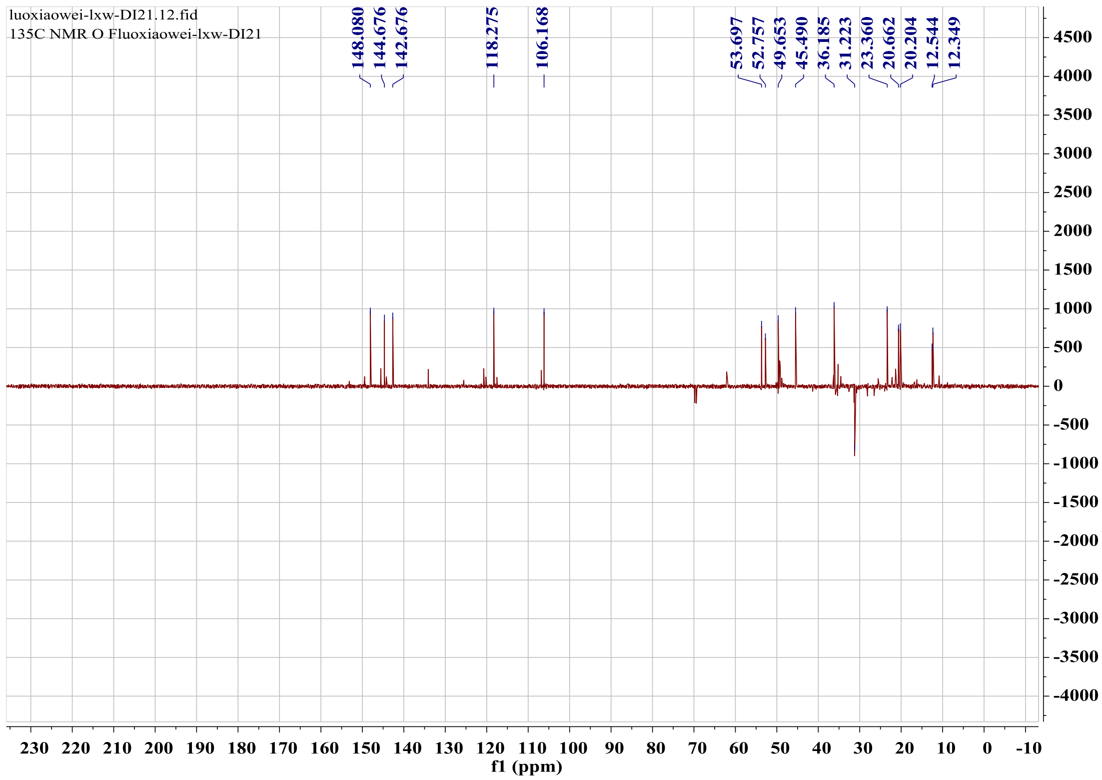


Figure S32. [13]C NMR and DEPT spectra of isochromophilone C (**3**) (CD_3OD, 175 MHz)

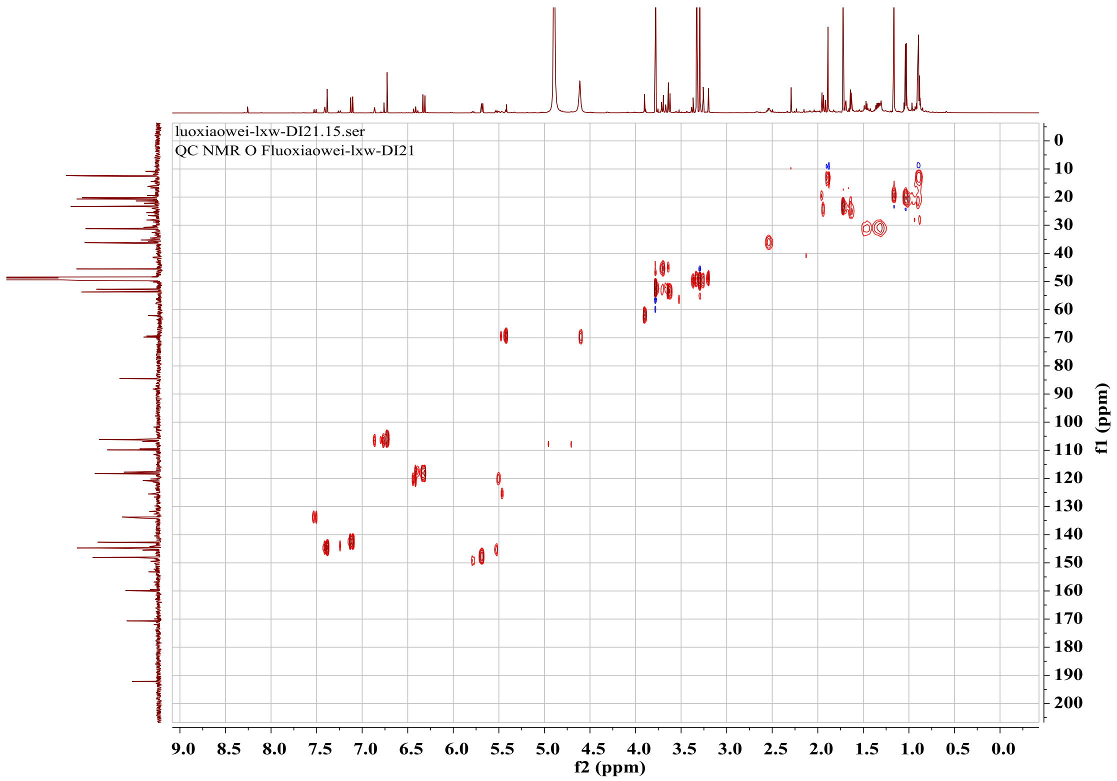


Figure S33. HSQC spectrum of isochromophilone C (**3**) (CD_3OD)

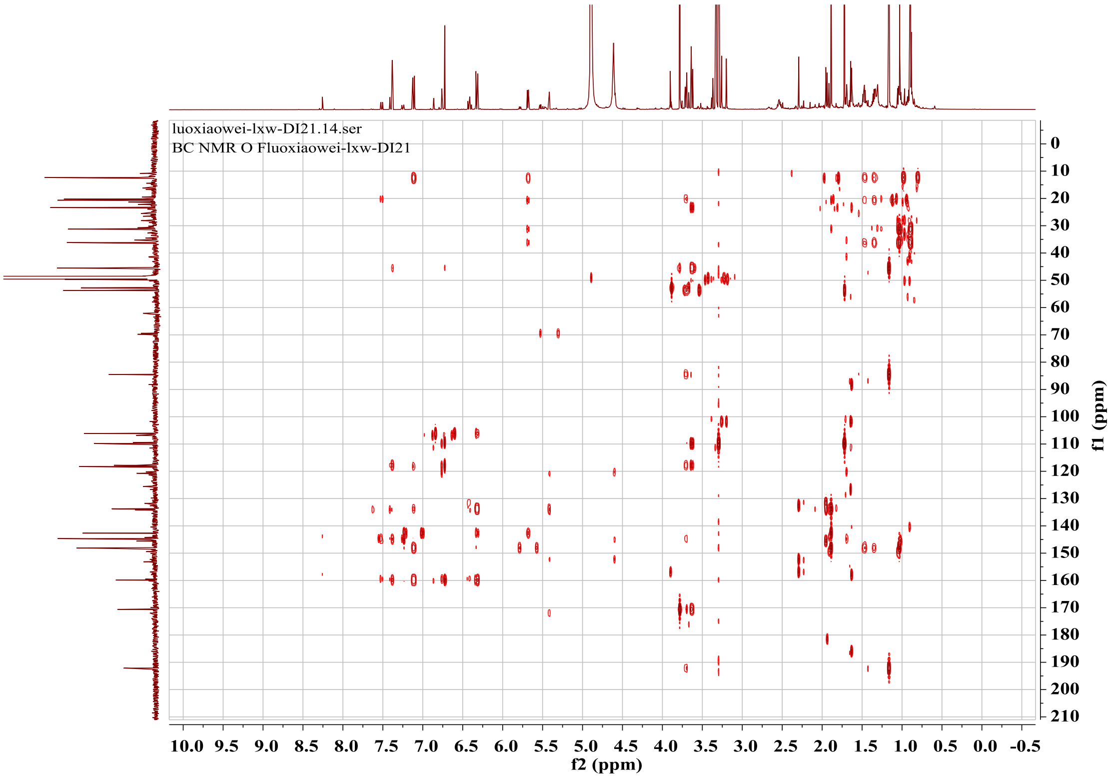


Figure S34. HMBC spectrum of isochromophilone C (**3**) (CD_3OD)

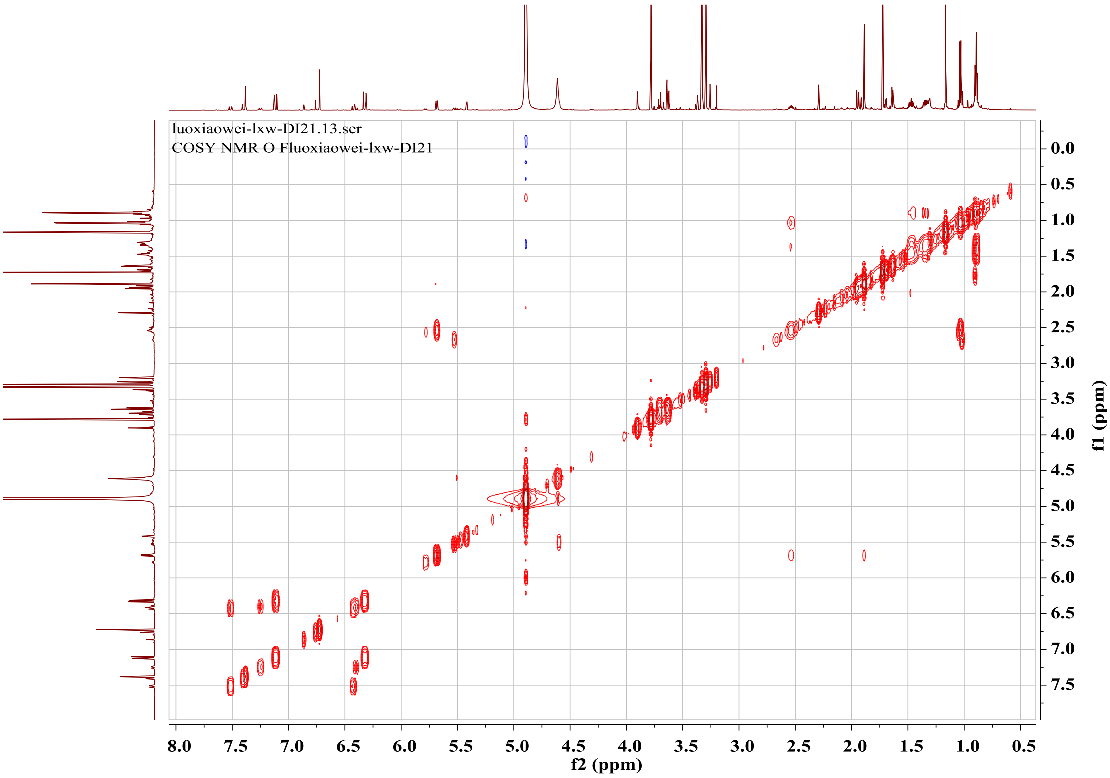
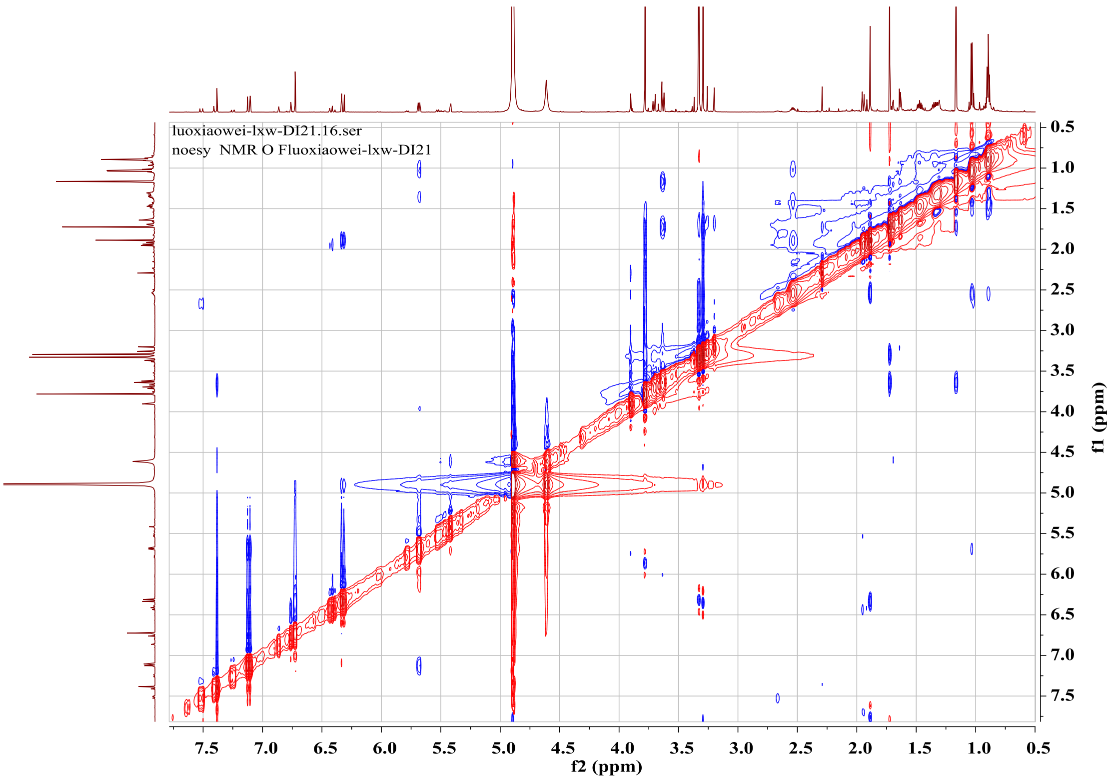


Figure S35. ^1H-^1H COSY spectrum of isochromophilone C (**3**) (CD_3OD)



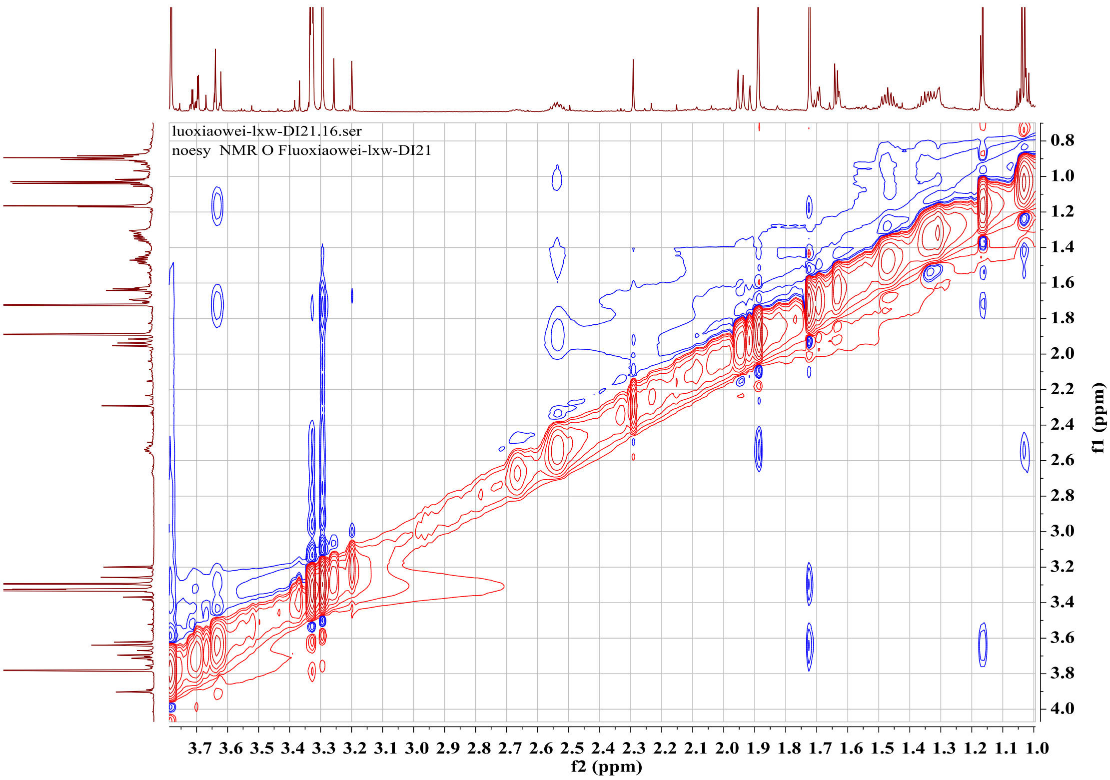


Figure S36. NOESY spectrum of isochromophilone C (**3**) (CD_3OD)

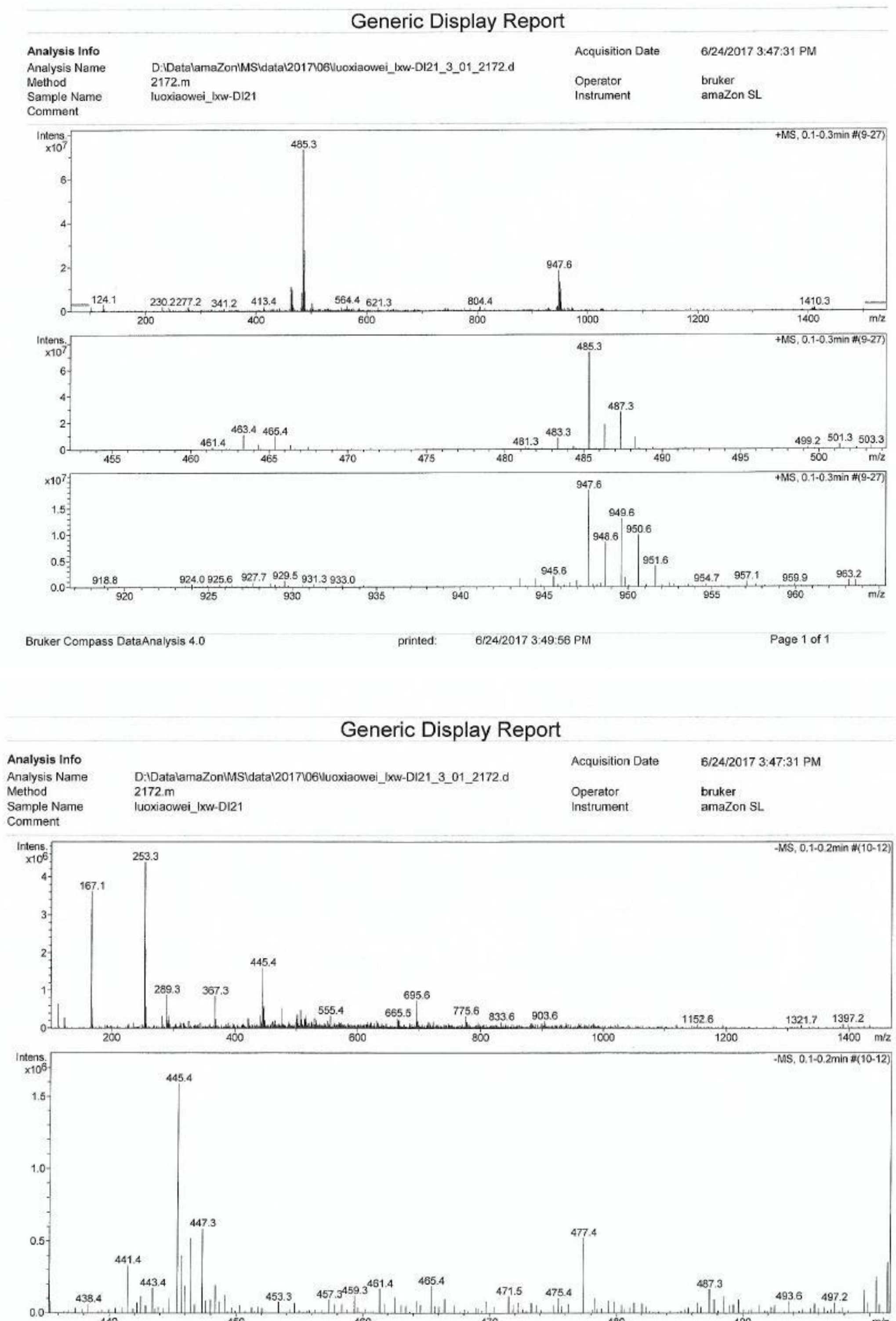
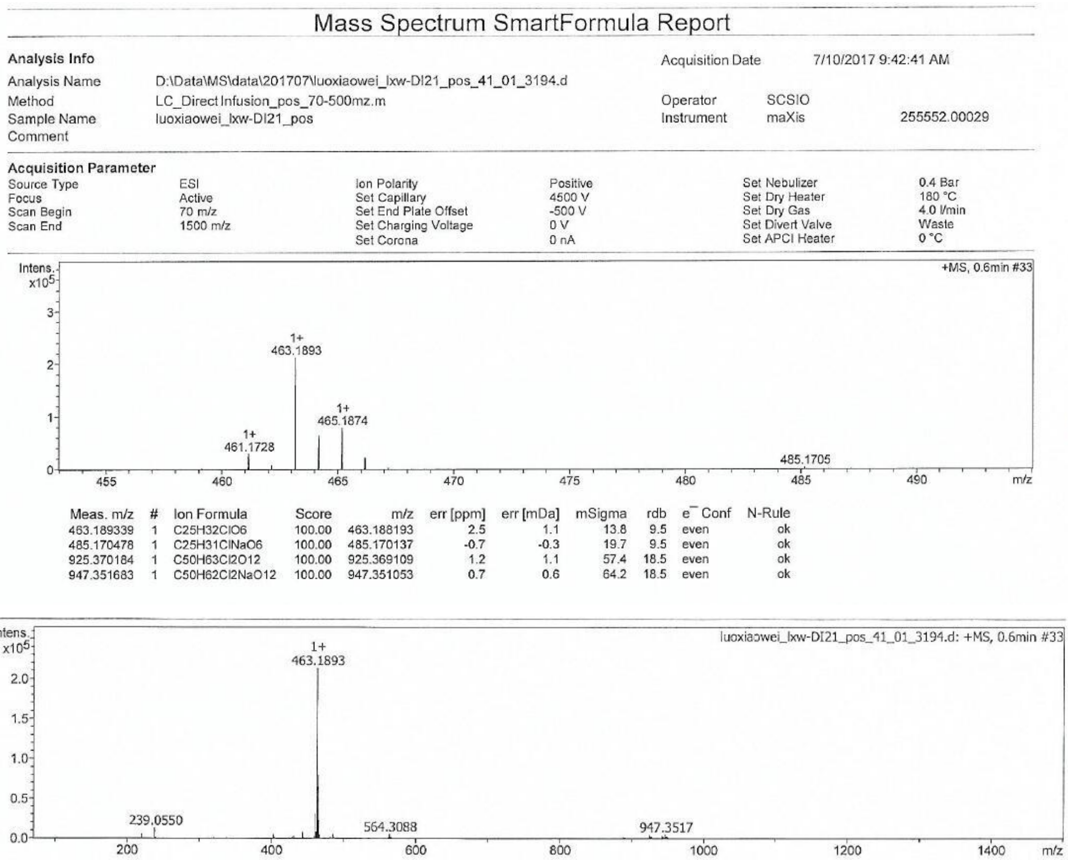


Figure S37. Positive and negative LR-ESI-MS spectra of isochromophilone C (**3**)



Mass Spectrum SmartFormula Report

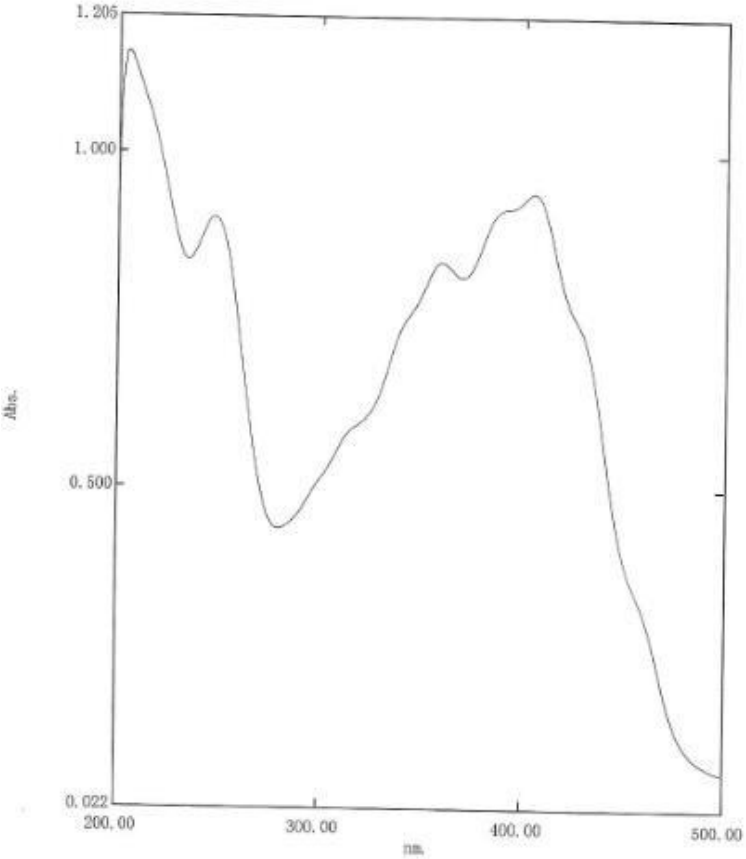
Analysis Info		Acquisition Date	7/10/2017 9:42:41 AM
Analysis Name	D:\Data\MS\data\201707\luoxiaowei_lxw-DI21_pos_41_01_3194.d		
Method	LC_Direct Infusion_pos_70-500mz.m	Operator	SCSIO
Sample Name	luoxiaowei_lxw-DI21_pos	Instrument	maXis 255552.00029
Comment			

Acquisition Parameter

Source Type	ESI	Ion Polarity	Positive	Set Nebulizer	0.4 Bar
Focus	Active	Set Capillary	4500 V	Set Dry Heater	180 °C
Scan Begin	70 m/z	Set End Plate Offset	-500 V	Set Dry Gas	4.0 l/min
Scan End	1500 m/z	Set Charging Voltage	0 V	Set Divert Valve	Waste
		Set Corona	0 nA	Set APCI Heater	0 °C

Meas. m/z	#	Ion Formula	Score	m/z	err [ppm]	err [mDa]	mSigma	rdb	e⁻ Conf	N-Rule
463.189339	1	C25H32ClO6	100.00	463.188193	2.5	1.1	13.8	9.5	even	ok
485.170478	1	C25H31ClNaO6	100.00	485.170137	-0.7	-0.3	19.7	9.5	even	ok
925.370184	1	C50H63Cl2O12	100.00	925.369109	1.2	1.1	57.4	18.5	even	ok
947.351683	1	C50H62Cl2NaO12	100.00	947.351053	0.7	0.6	64.2	18.5	even	ok

Figure S38. Positive HR-ESI-MS spectrum of isochromophilone C (**3**)



[测定属性]
波长范围 (nm.): 200.00 到 500.00
扫描速度: 中速
采样间隔: 0.2
自动采样间隔: 启用
扫描模式: 单个

[仪器属性]
仪器类型: UV-2600 系列
测定方式: 吸收值
狭缝宽: 2.0
积分时间: 0.1 秒.
光源转换波长: 323.0 nm
检测器单元: 直接
S/R 转换: 标准
阶梯校正: OFF

[附件属性]
附件: 无

[数据处理参数]
阈值: 0.0100000
点: 4
内插: 停用
平均: 停用

[样品准备属性]
重量:
体积:
稀释:
光程长:
附加信息:

462.2 30μg/ml

No.	P/V	波长(nm)	吸收值	描述
1		405.20	0.942	4.162
2		359.20	0.838	4.111
3		247.60	0.903	4.143
4		205.00	1.151	4.249

Figure S39. UV spectrum of isochromophilone C (**3**)

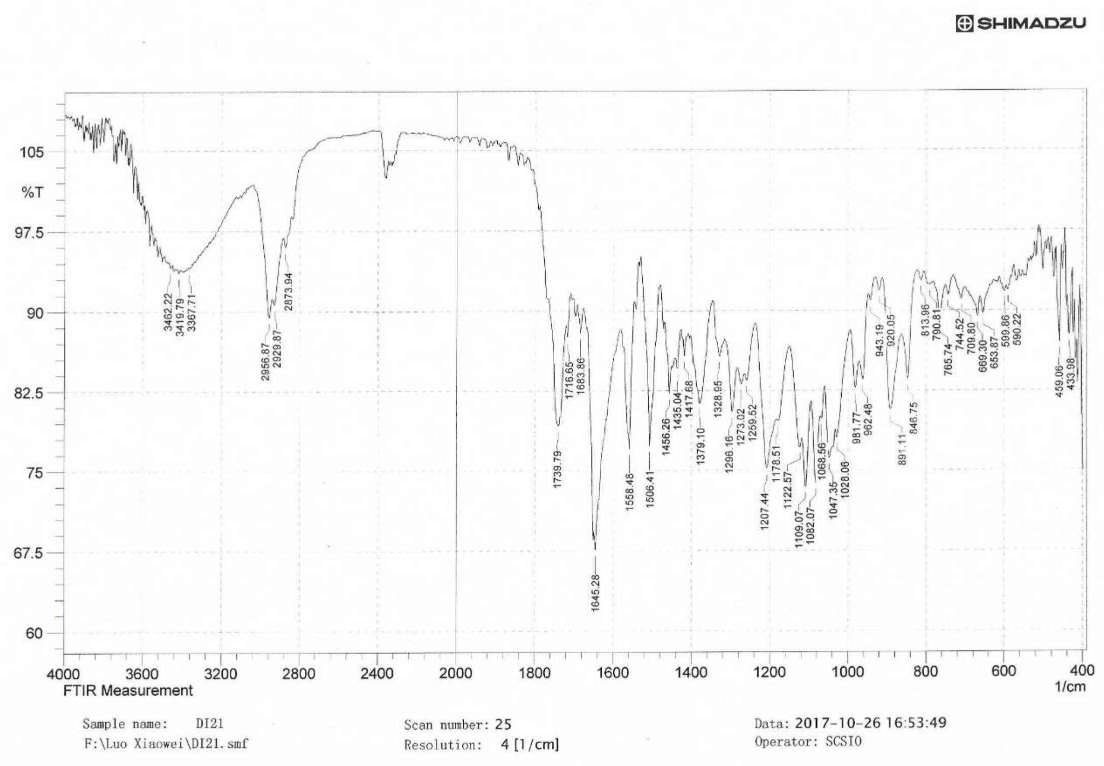


Figure S40. IR spectrum of isochromophilone C (**3**)

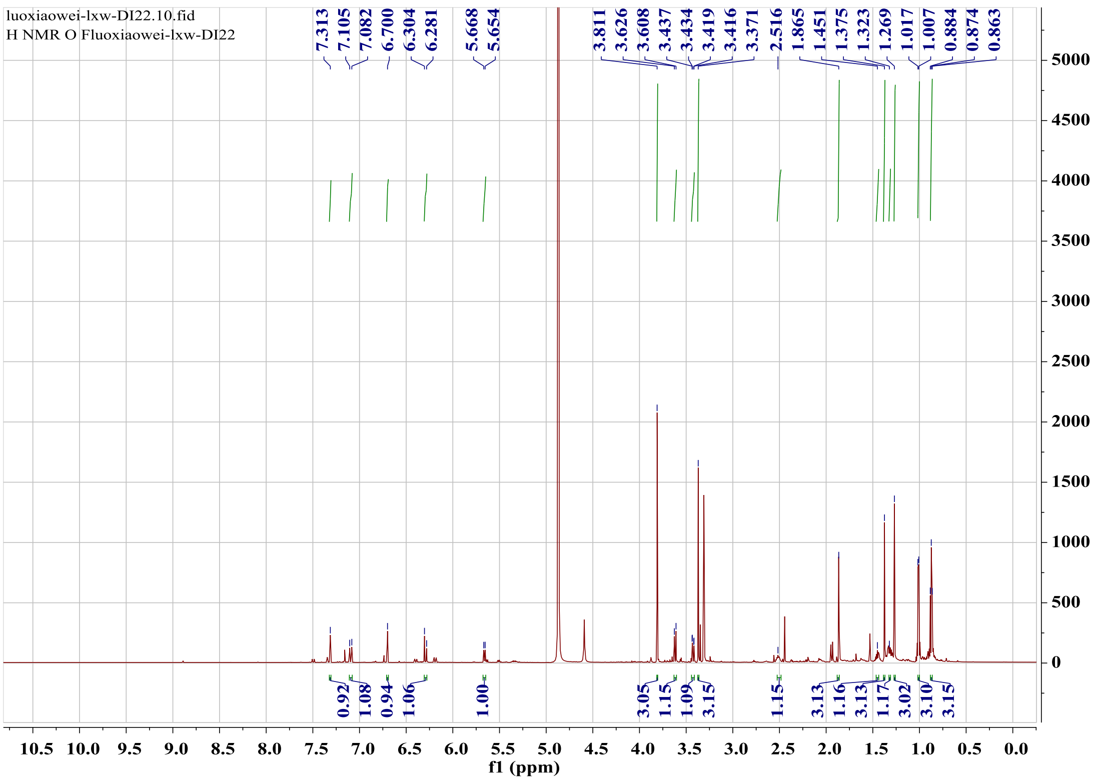


Figure S41. [1]H NMR spectrum of isochromophilone D (**4**) (CD_3OD, 700 MHz)

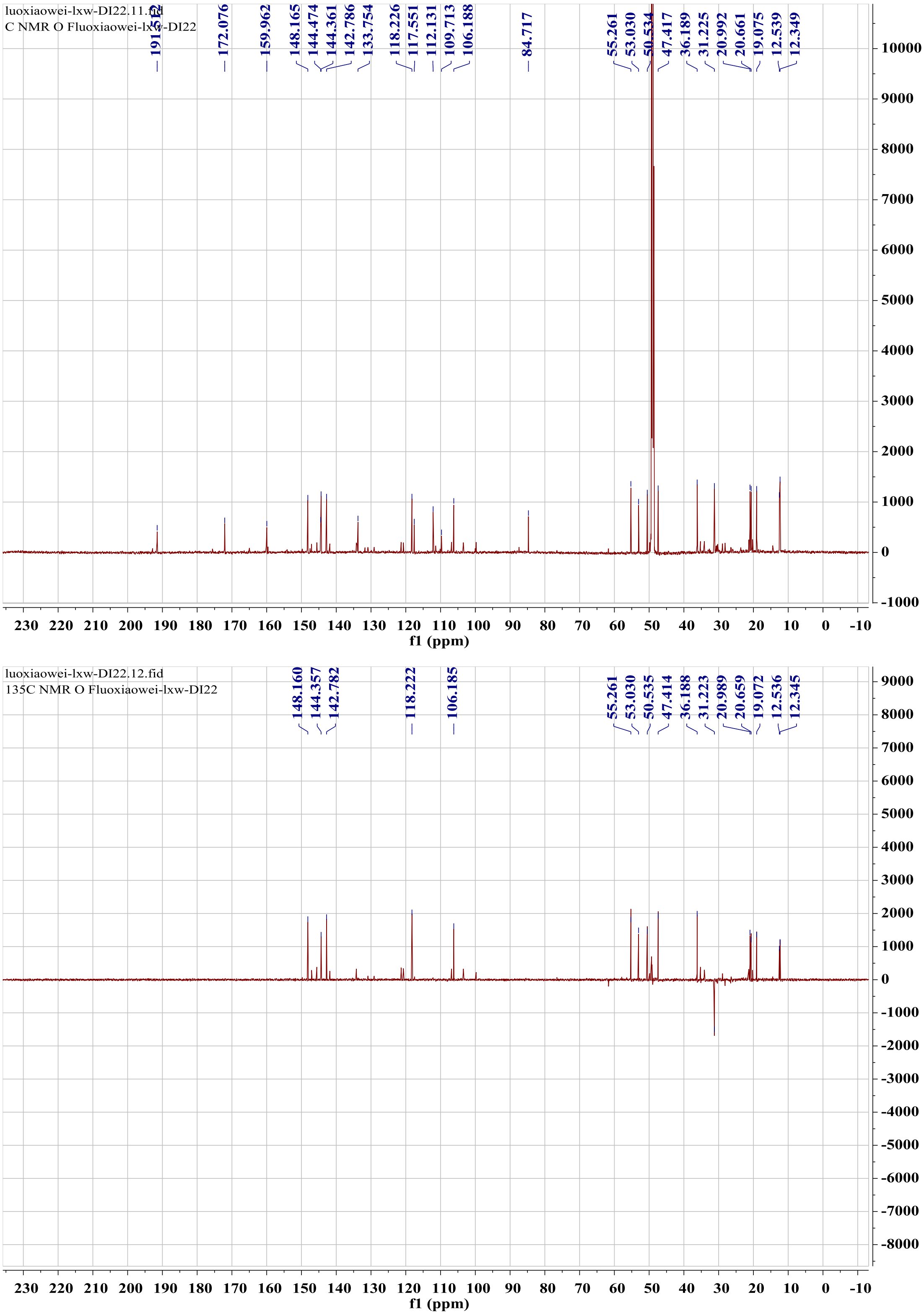


Figure S42. ^{13}C NMR and DEPT spectra of isochromophilone D (**4**) (CD_3OD, 175 MHz)

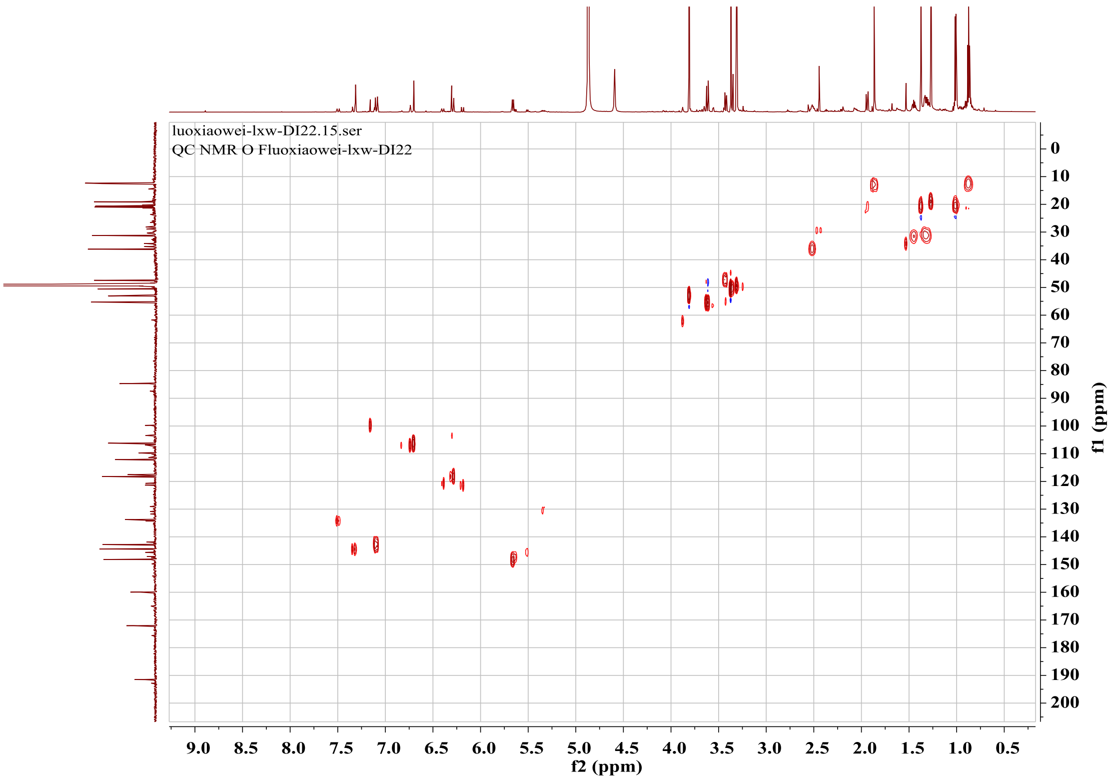


Figure S43. HSQC spectrum of isochromophilone D (**4**) (CD_3OD)

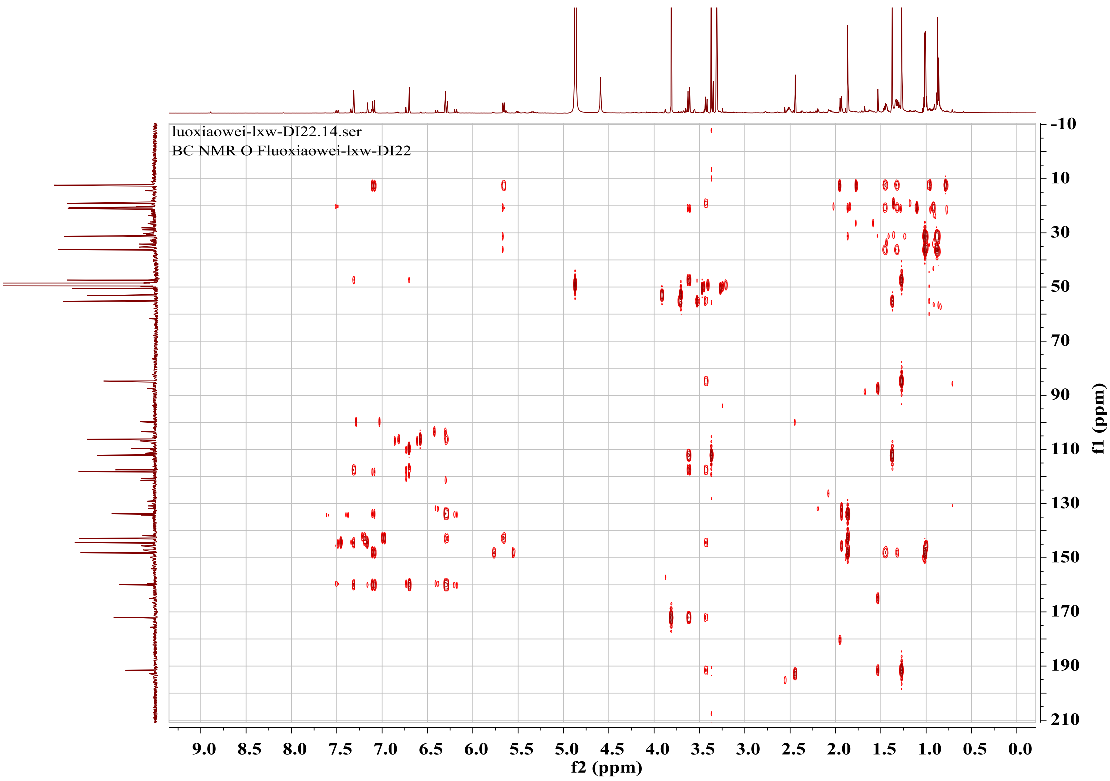


Figure S44. HMBC spectrum of isochromophilone D (**4**) (CD_3OD)

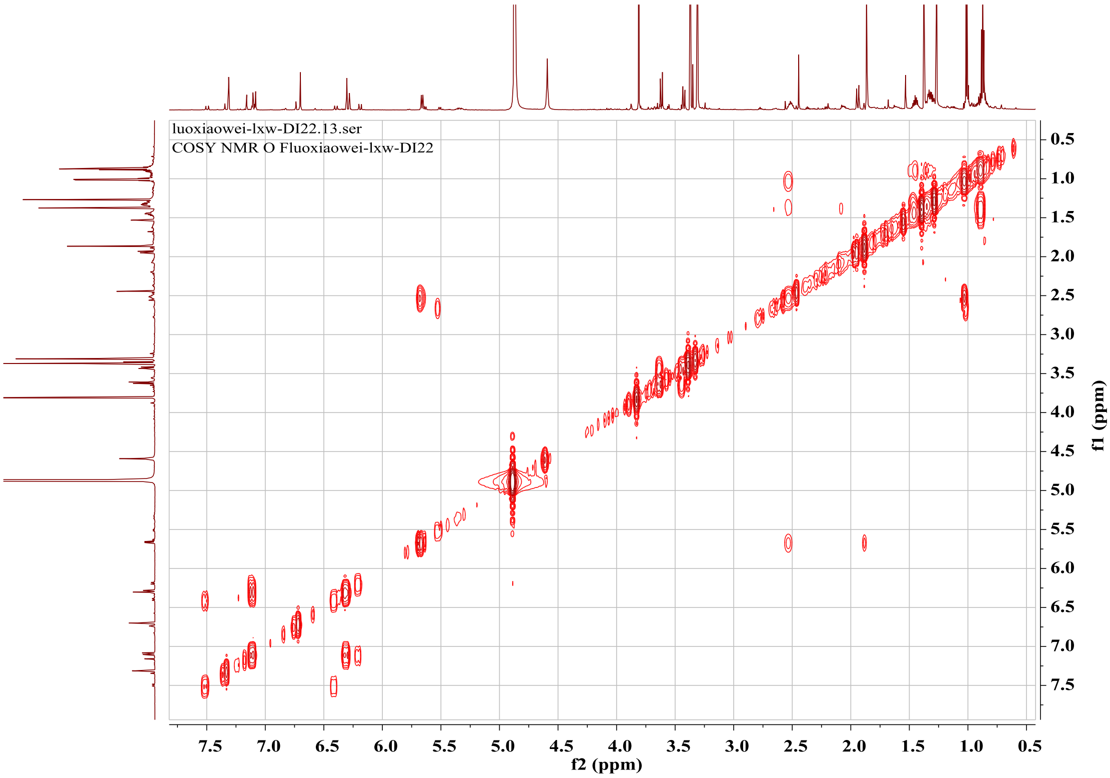
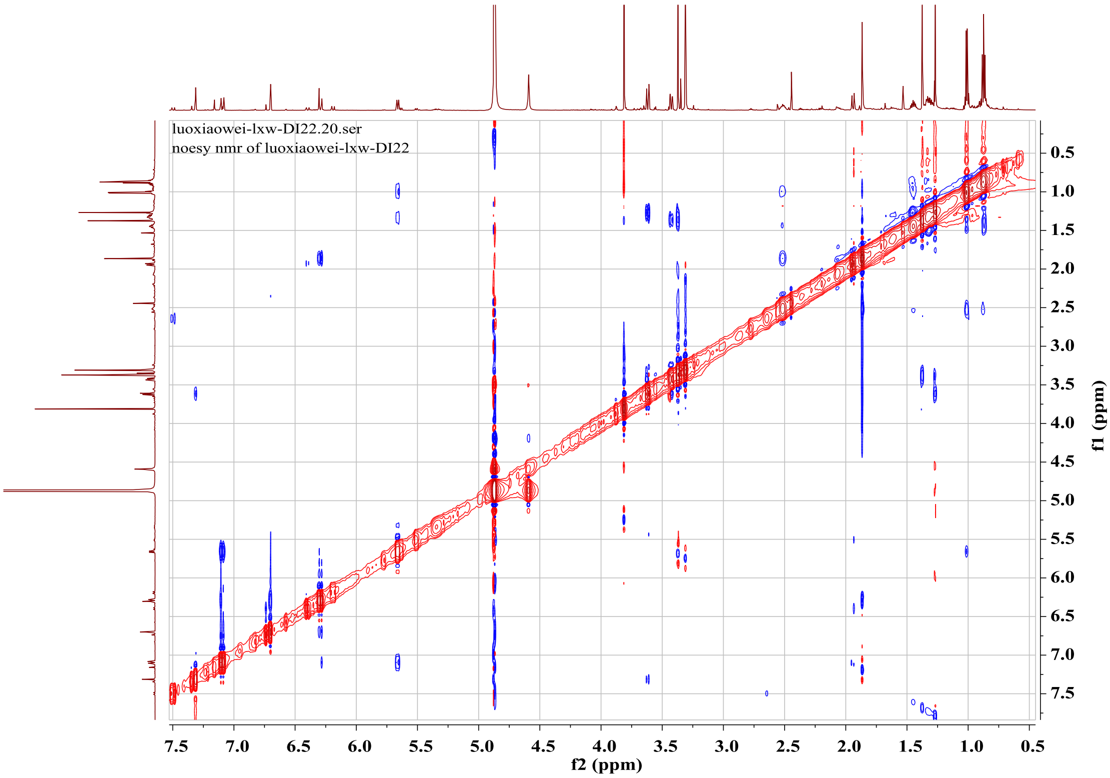


Figure S45. ^{1}H-^{1}H COSY spectrum of isochromophilone D (**4**) (CD_3OD)



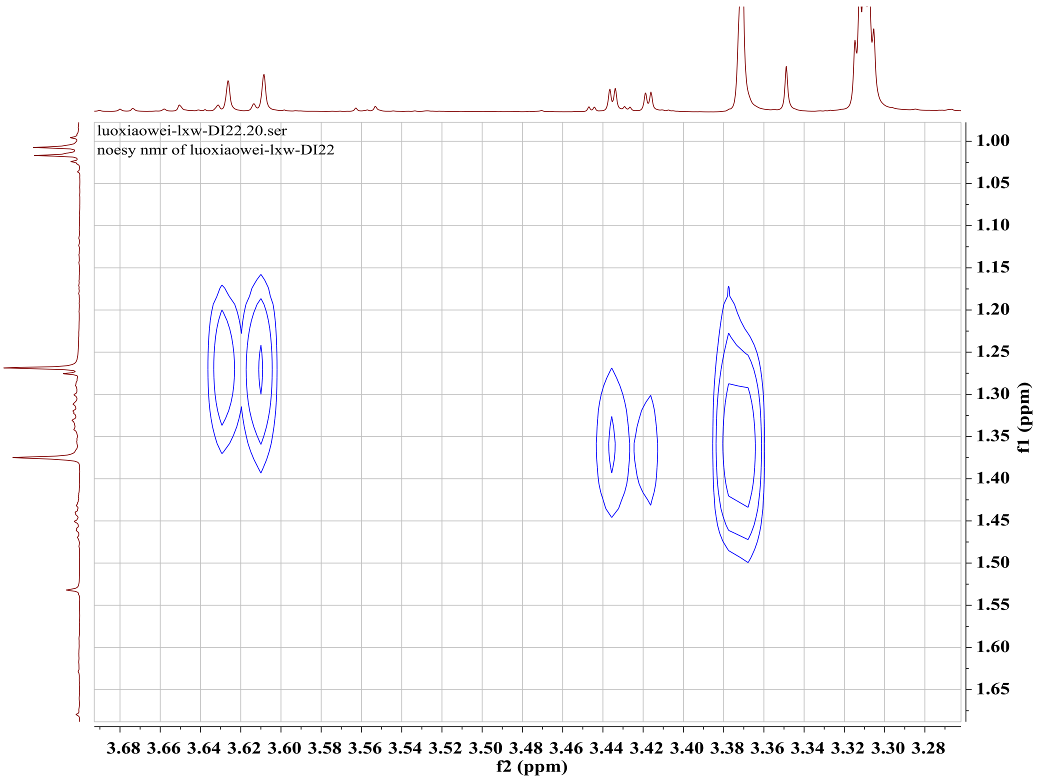
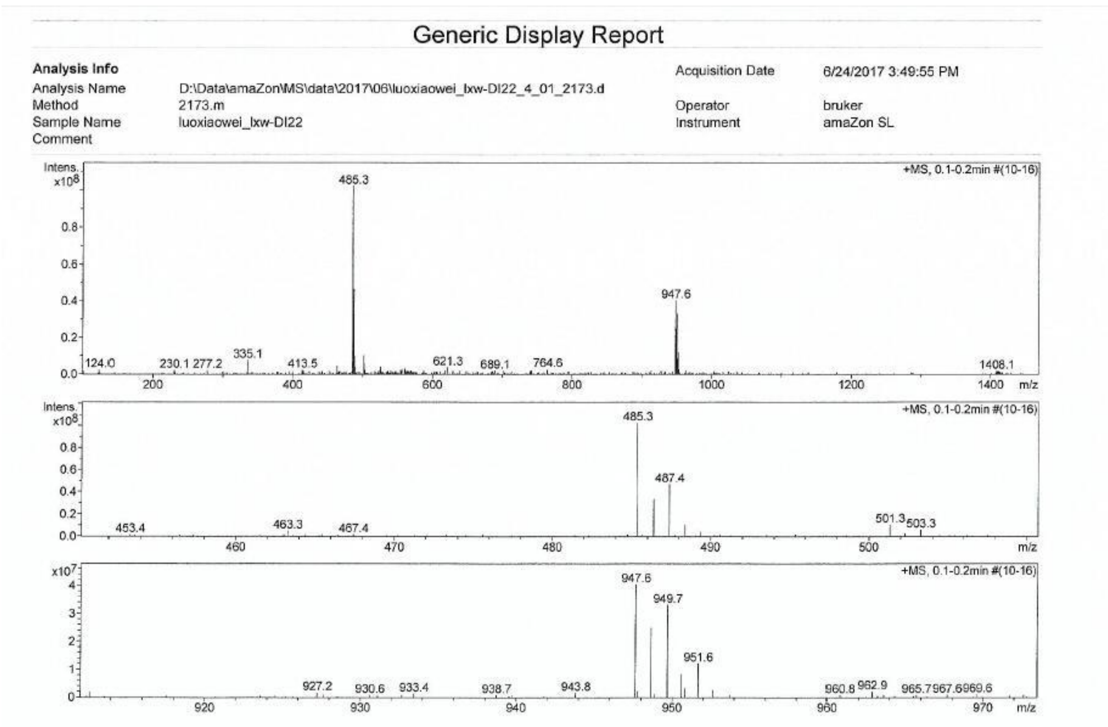


Figure S46. NOESY spectrum of isochromophilone D (**4**) (CD_3OD)



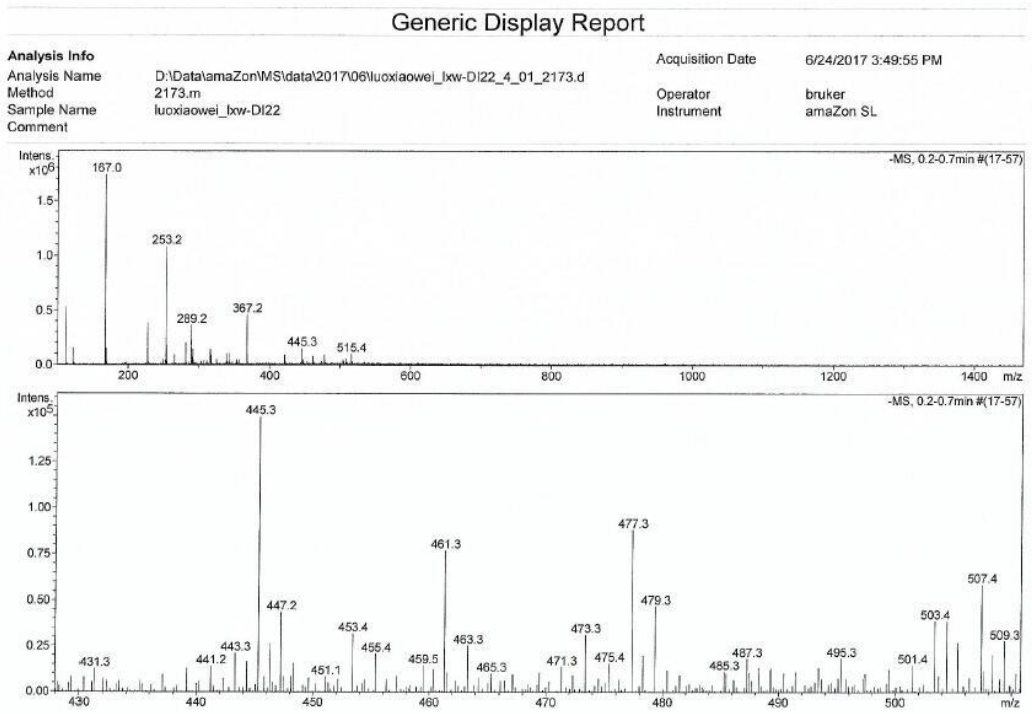
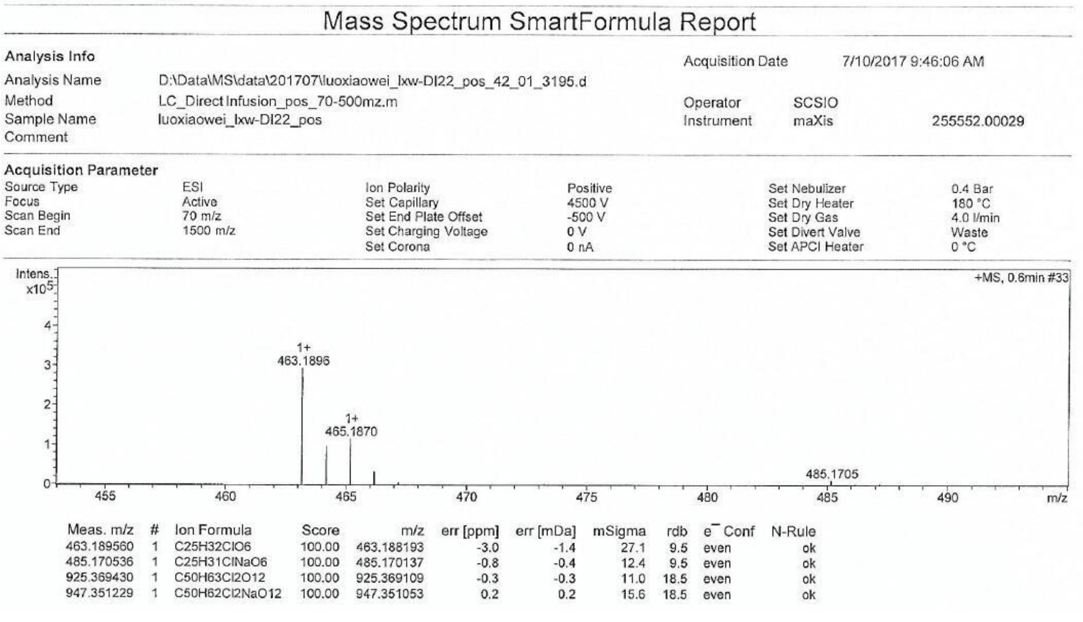
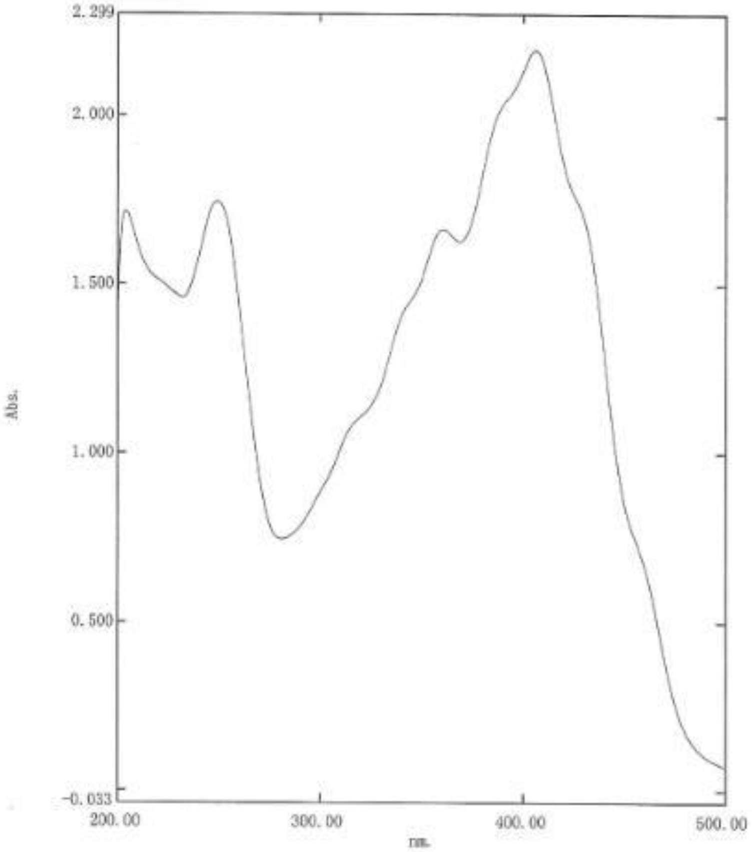


Figure S47. Positive and negative LR-ESI-MS spectra of isochromophilone D (**4**)



Meas. m/z	#	Ion Formula	Score	m/z	err [ppm]	err [mDa]	mSigma	rdb	e⁻ Conf	N-Rule
463.189560	1	C25H32ClO6	100.00	463.188193	-3.0	-1.4	27.1	9.5	even	ok
485.170536	1	C25H31ClNaO6	100.00	485.170137	-0.8	-0.4	12.4	9.5	even	ok
925.369430	1	C50H63Cl2O12	100.00	925.369109	-0.3	-0.3	11.0	18.5	even	ok
947.351229	1	C50H62Cl2NaO12	100.00	947.351053	0.2	0.2	15.6	18.5	even	ok

Figure S48. Positive HR-ESI-MS spectrum of isochromophilone D (**4**)



[测定属性]
波长范围 (nm.): 200.00 到 500.00
扫描速度: 中速
采样间隔: 0.2
自动采样间隔: 启用
扫描模式: 单个

[仪器属性]
仪器类型: UV-2600 系列
测定方式: 吸收值
狭缝宽: 2.0
积分时间: 0.1 秒.
光源转换波长: 323.0 nm
检测器单元: 直接
S/R 转换: 标准
阶梯校正: OFF

[附件属性]
附件: 无

[数据处理参数]
阈值: 0.0100000
点: 4
内插: 停用
平均: 停用

[样品准备属性]
重量:
体积:
稀释:
光程长:
附加信息:

462.2 40ug/ml

No.	P/V	波长(nm)	吸收值	描述
1	↑	406.40	2.193	4.404
2	↑	360.40	1.663	4.284
3	↑	249.60	1.743	4.304
4	↑	204.00	1.714	4.297

Figure S49. UV spectrum of isochromophilone D (**4**)

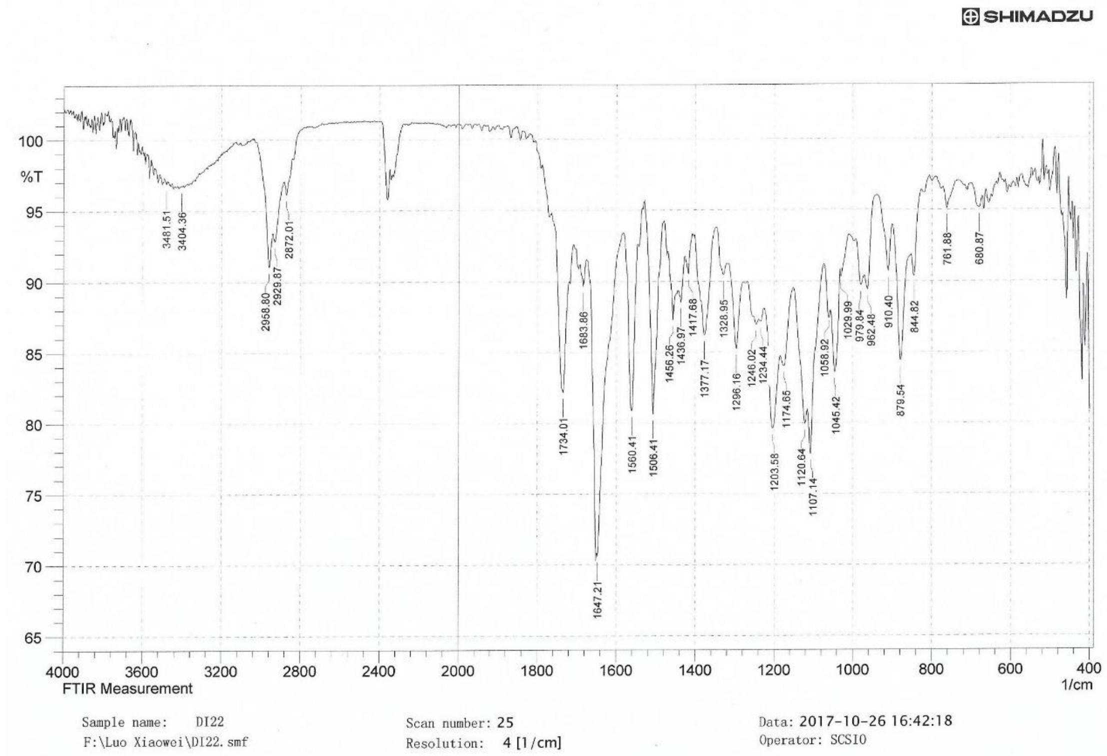


Figure S50. IR spectrum of isochromophilone D (**4**)

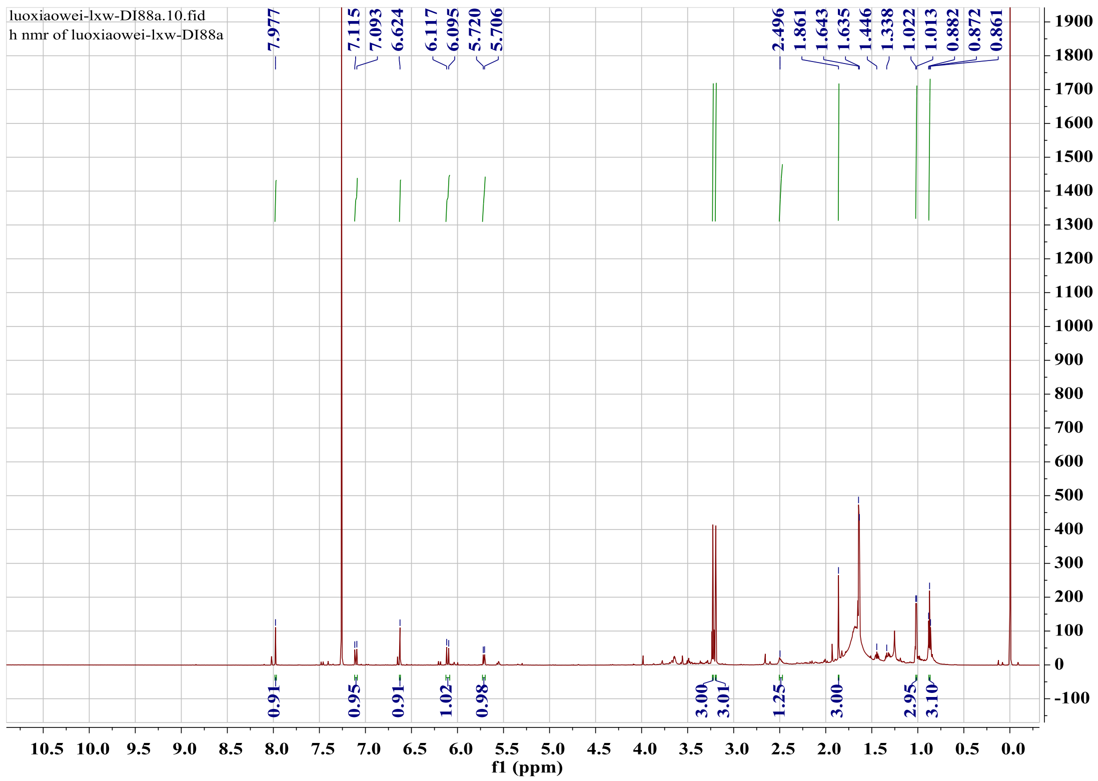


Figure S51. [1]H NMR spectrum of isochromophilone E (**5**) ($CDCl_3$, 700 MHz)

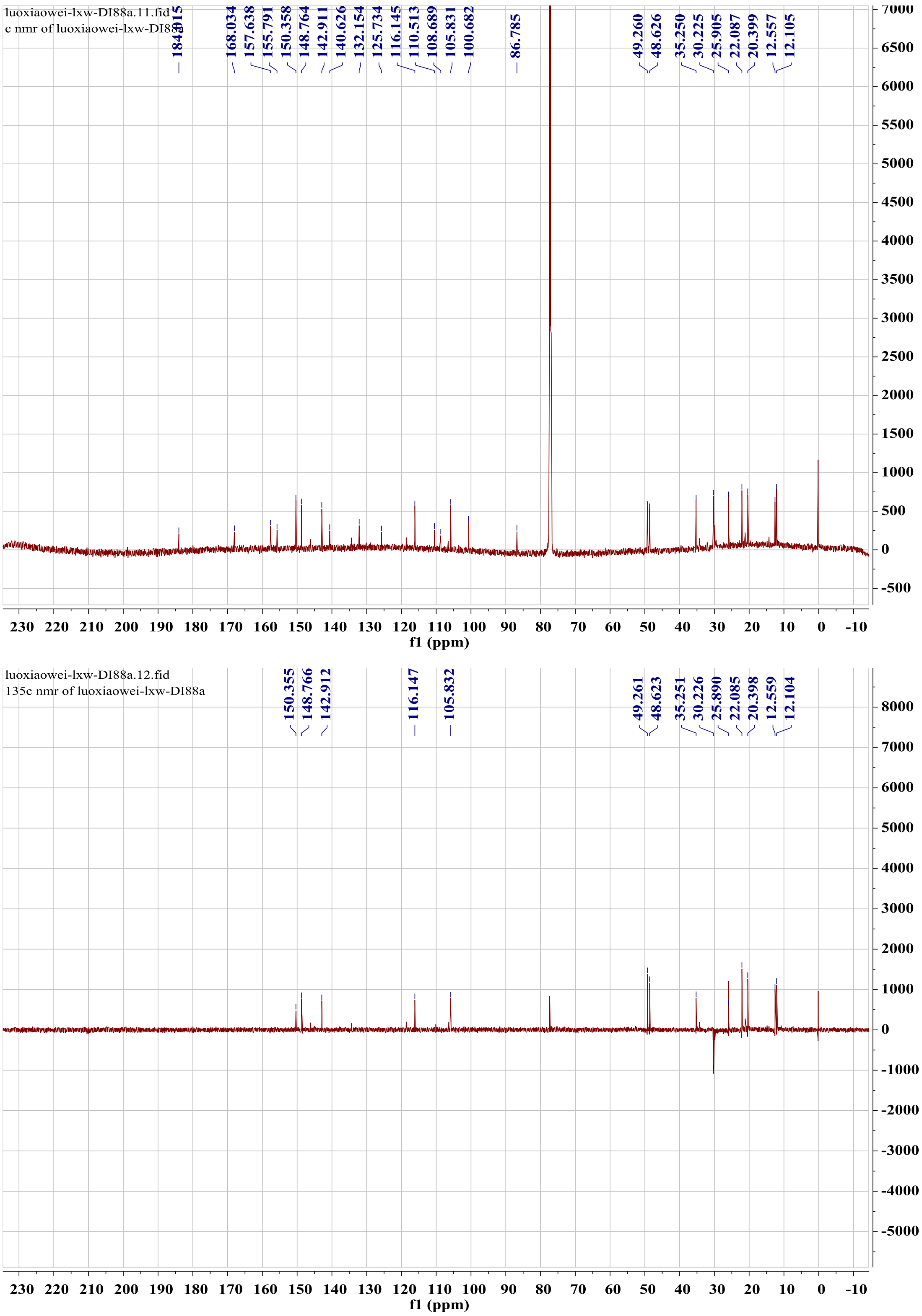


Figure S52. ^{13}C NMR and DEPT spectra of isochromophilone E (**5**) ($CDCl_3$, 175 MHz)

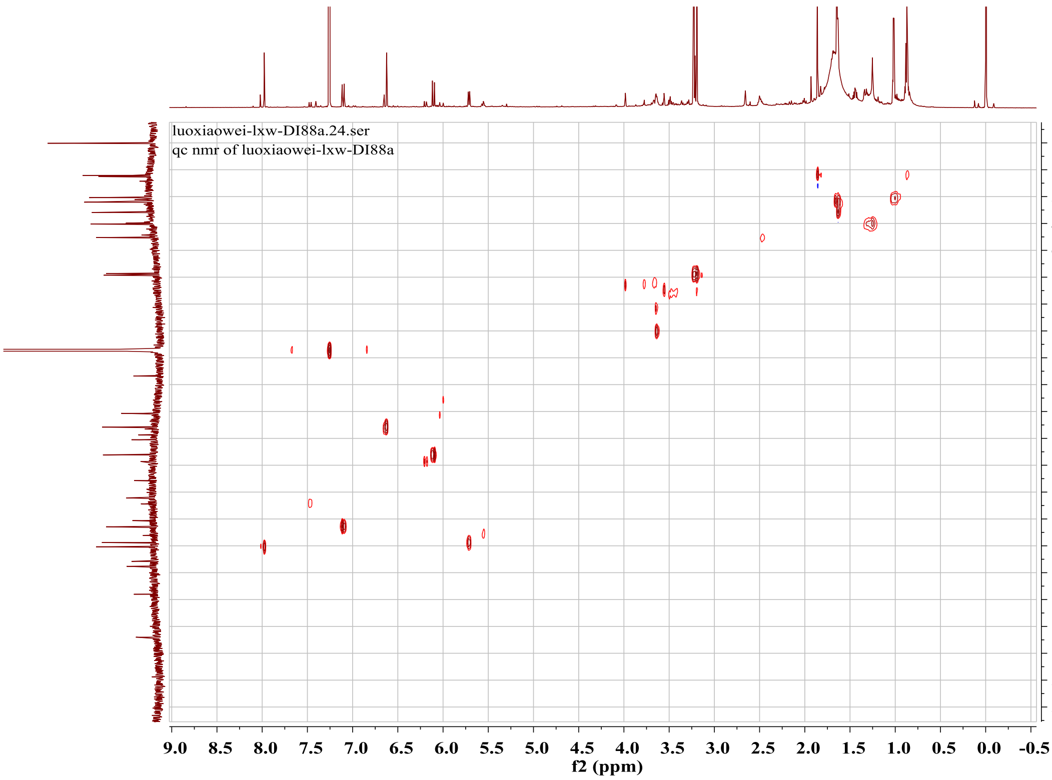


Figure S53. HSQC spectrum of isochromophilone E (**5**) ($CDCl_3$)

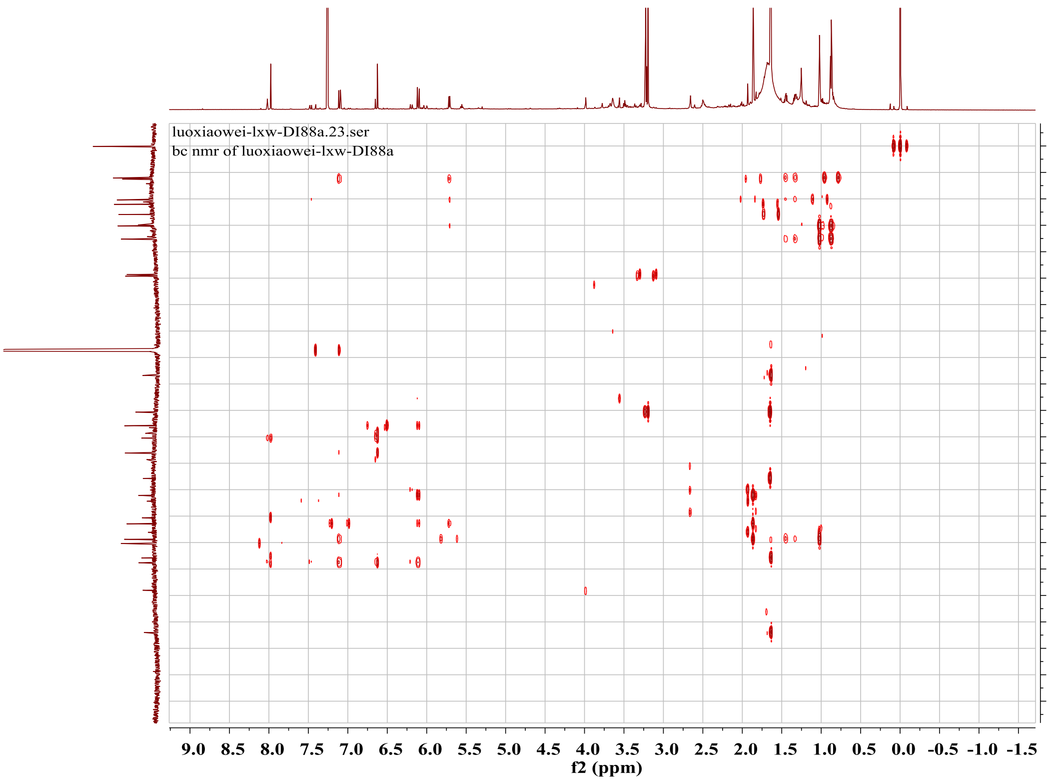


Figure S54. HMBC spectrum of isochromophilone E (**5**) ($CDCl_3$)

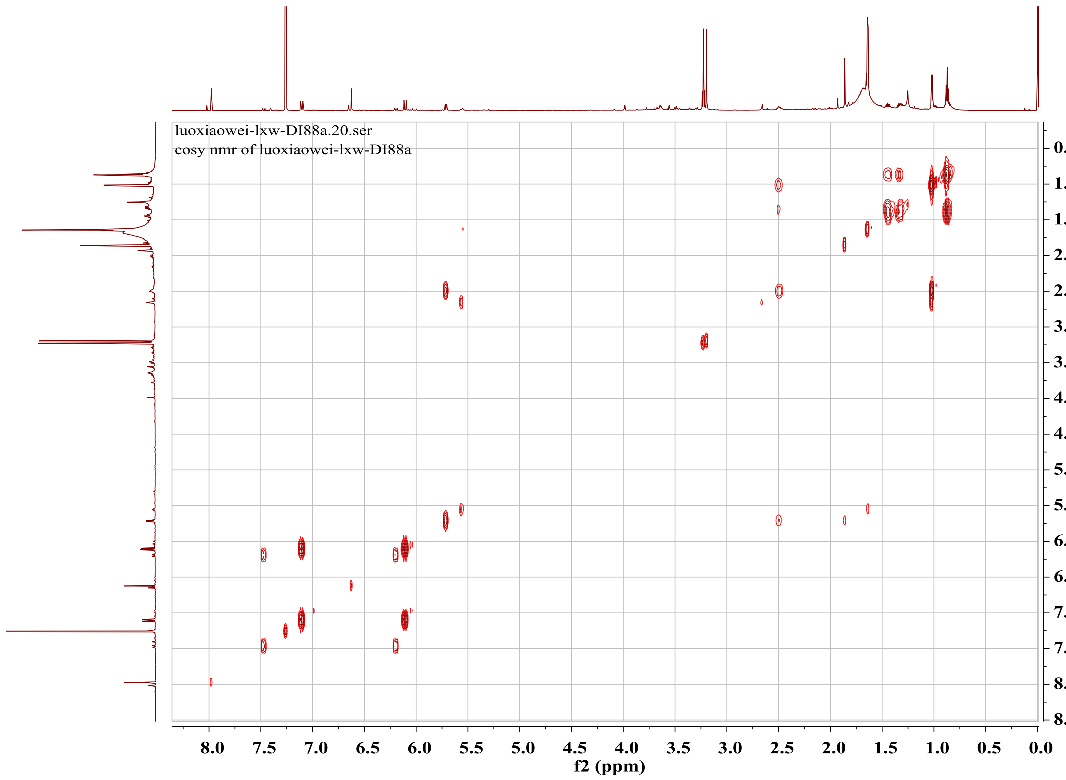
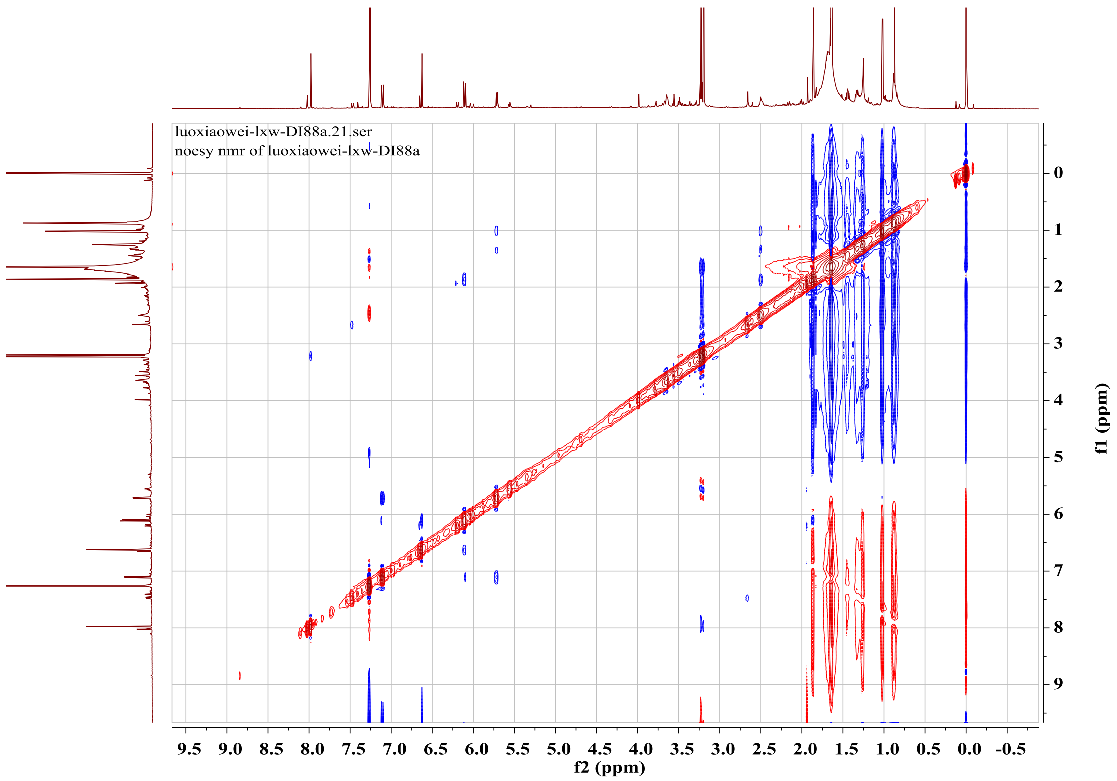


Figure S55. ^{1}H-^{1}H COSY spectrum of isochromophilone E (**5**) ($CDCl_3$)



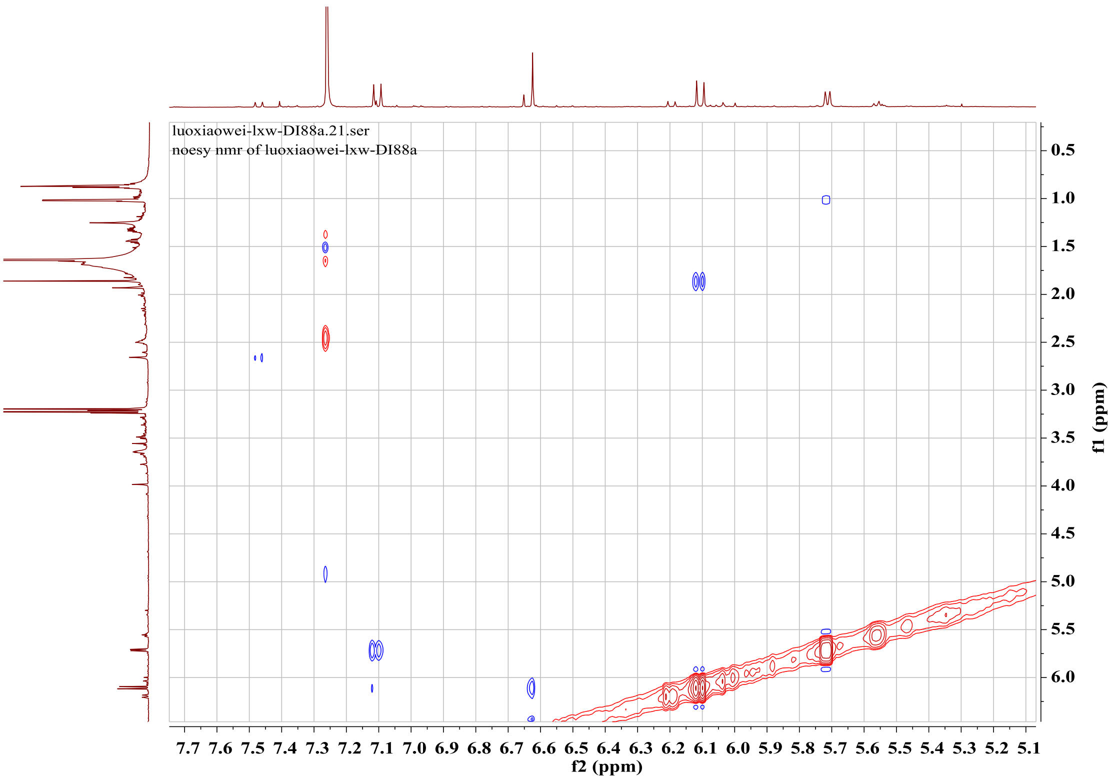


Figure S56. NOESY spectrum of isochromophilone E (**5**) ($CDCl_3$)

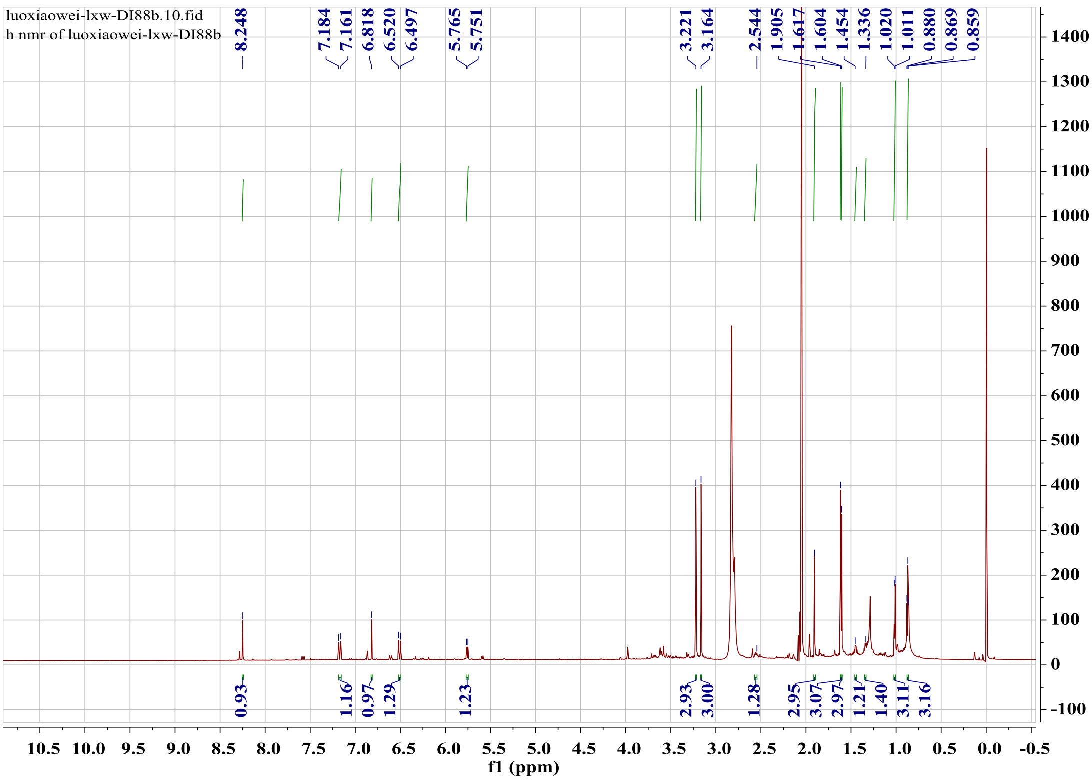
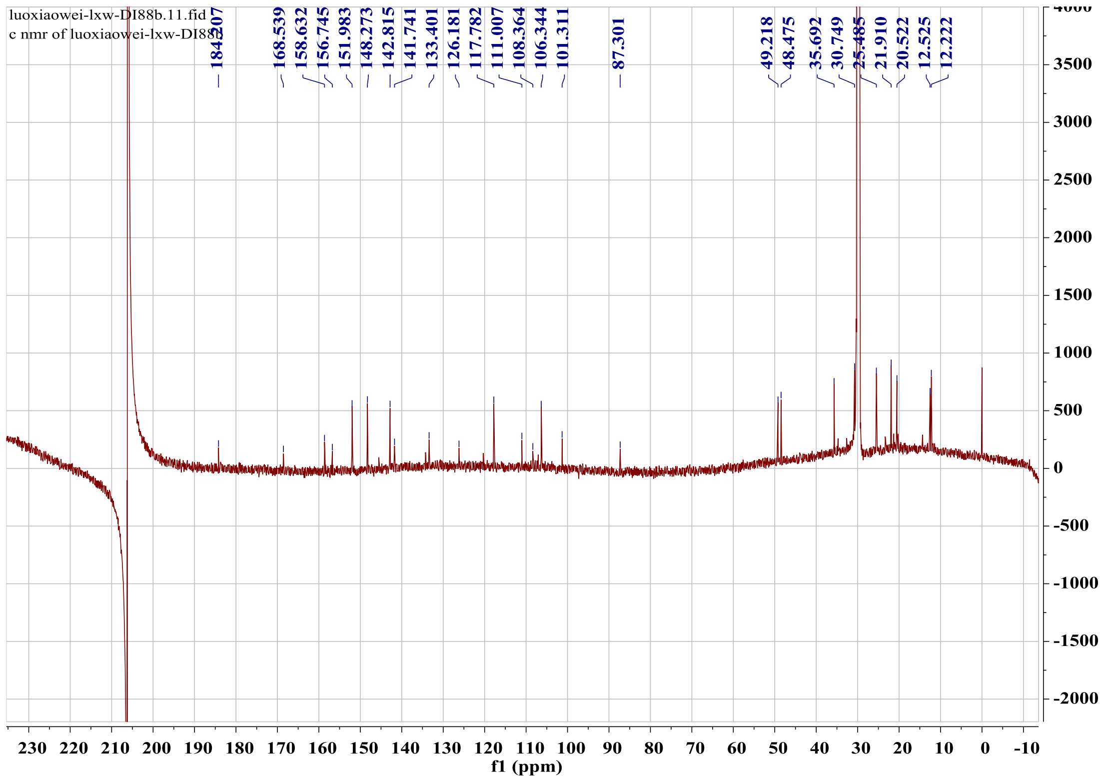


Figure S57. ^{1}H NMR spectrum of isochromophilone E (**5**) (Acetone-d_6, 700 MHz)



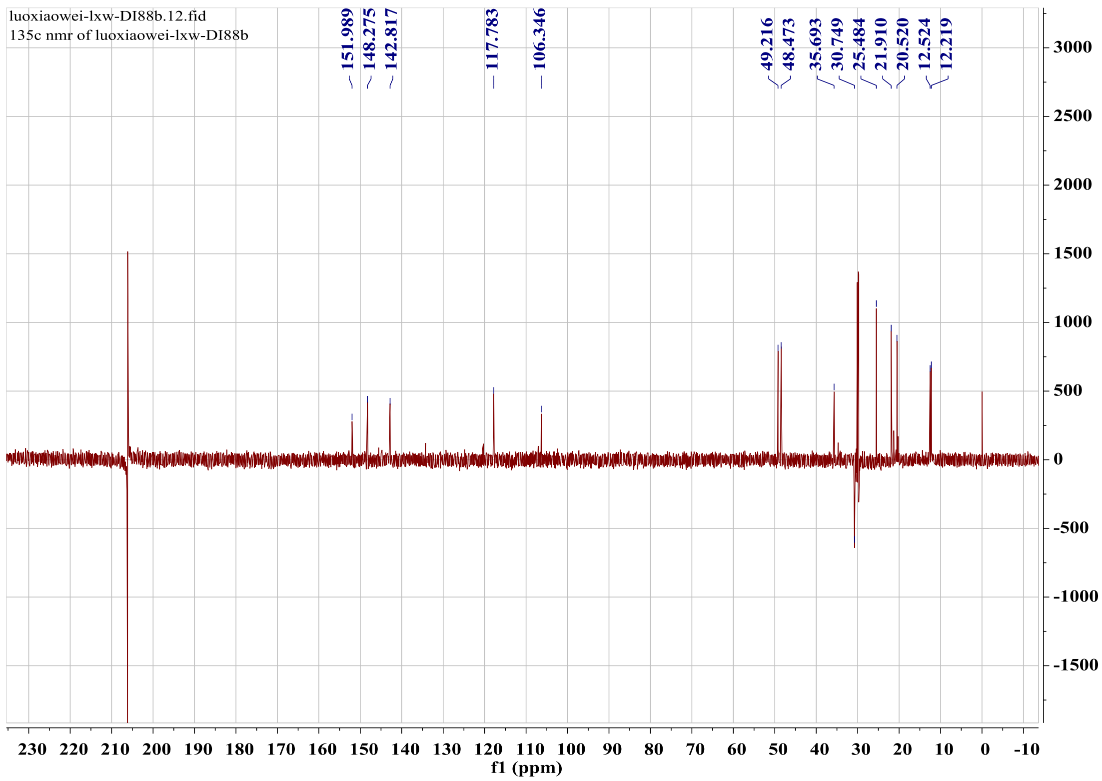


Figure S58. ^{13}C NMR and DEPT spectra of isochromophilone E (**5**) (acetone-d_6, 175 MHz)

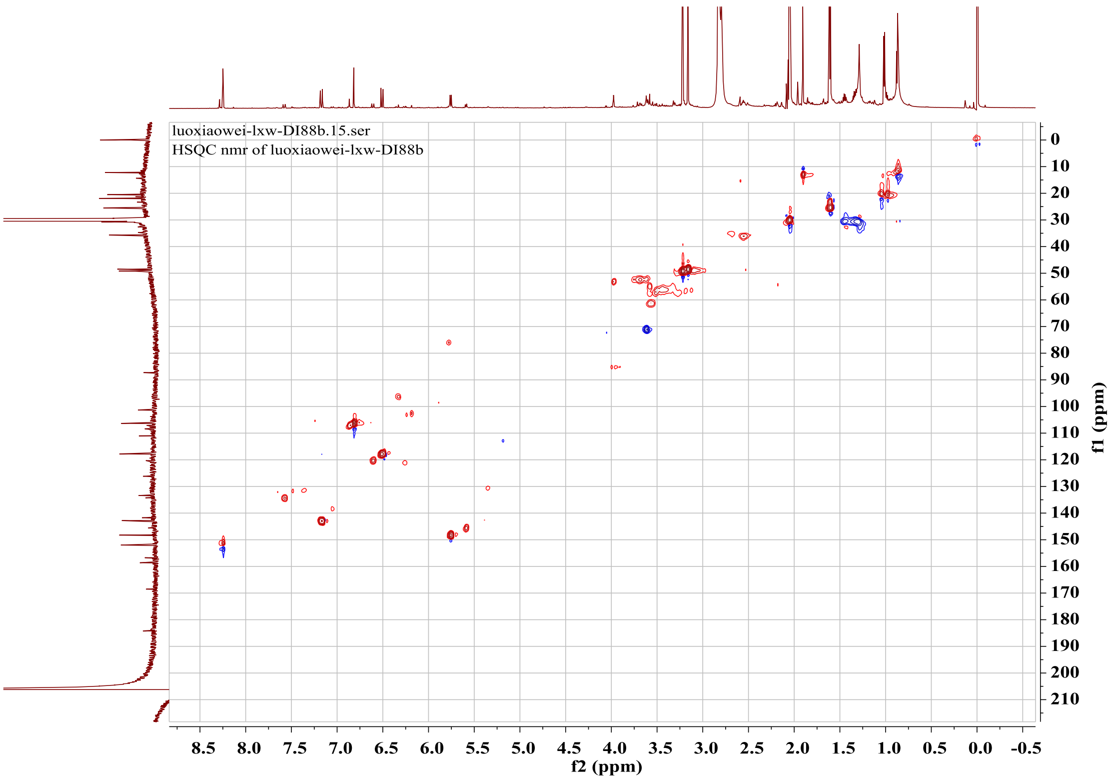


Figure S59. HSQC spectrum of isochromophilone E (**5**) (acetone-d_6)

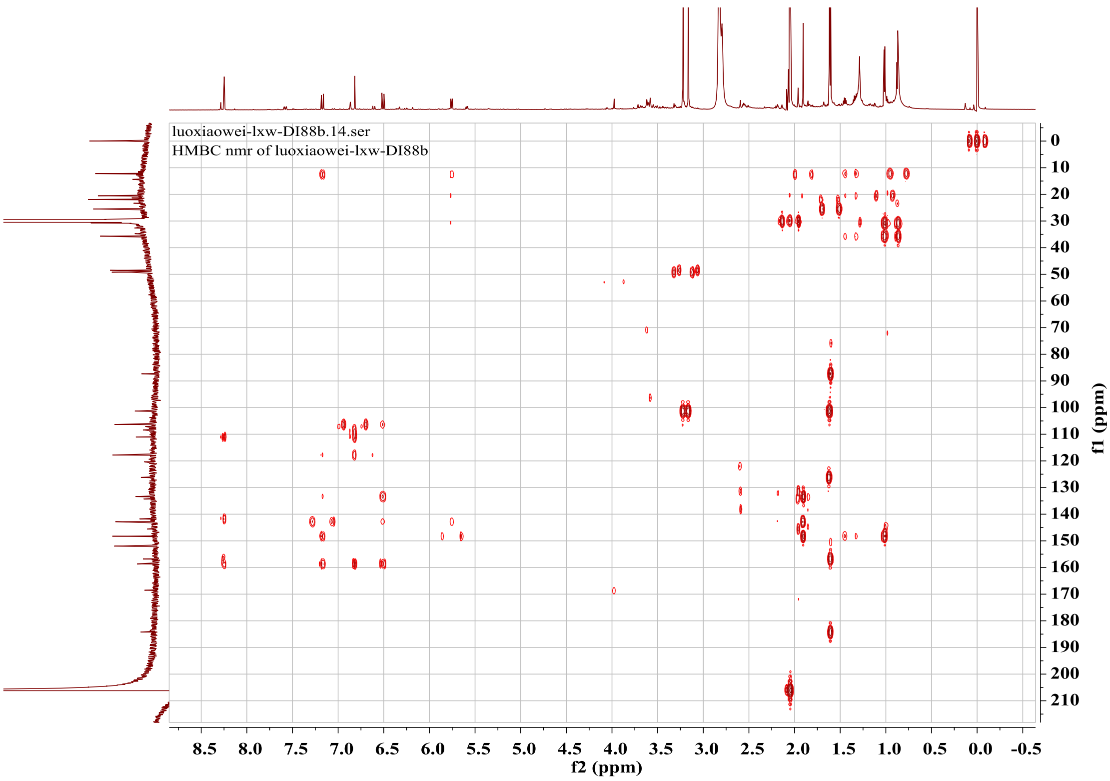


Figure S60. HMBC spectrum of isochromophilone E (**5**) (acetone-d_6)

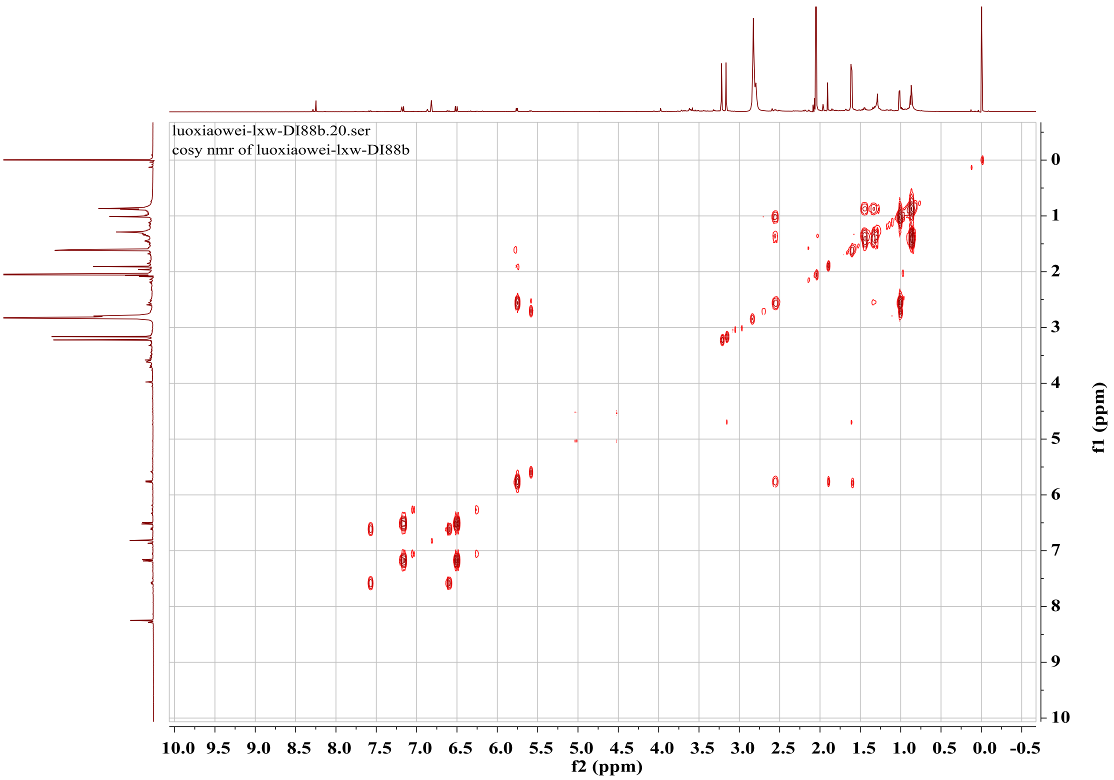
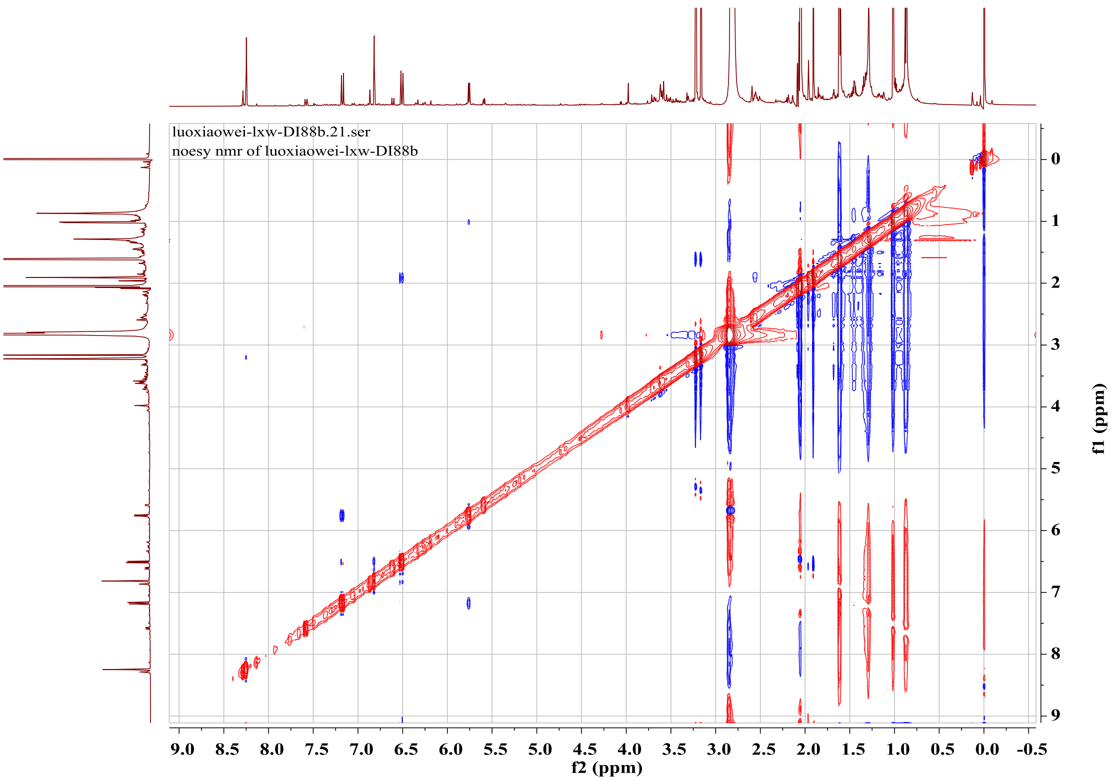


Figure S61. ^{1}H-^{1}H COSY spectrum of isochromophilone E (**5**) (acetone-d_6)



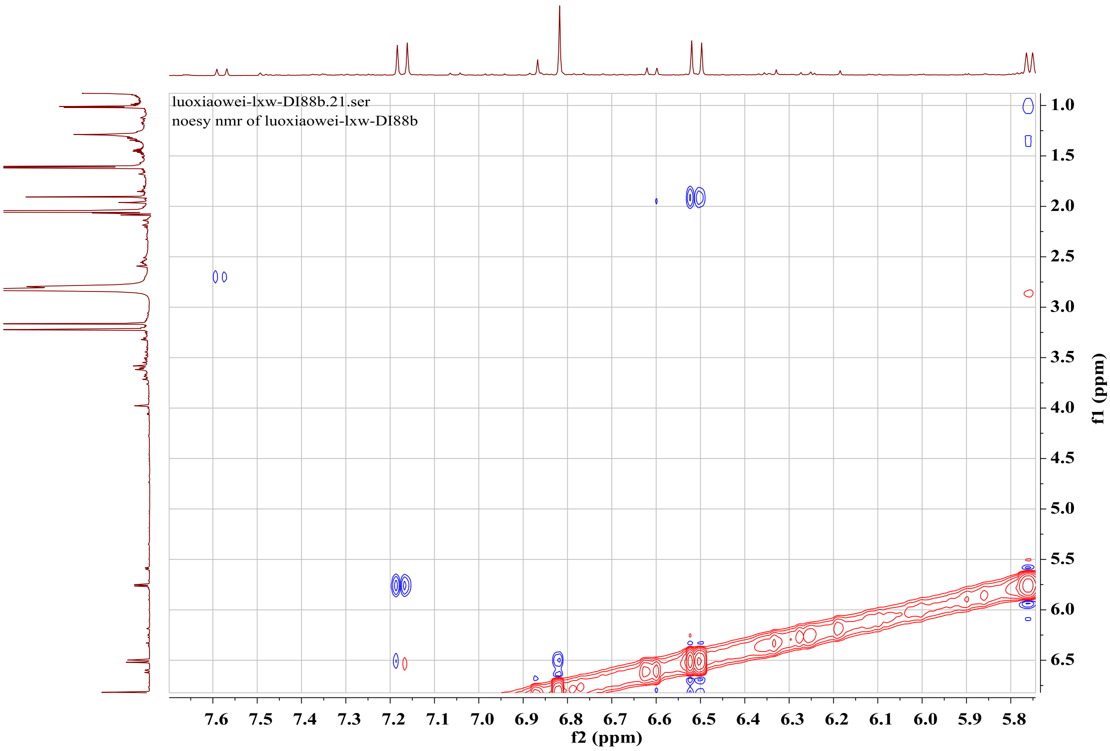


Figure S62. NOESY spectrum of isochromophilone E (**5**) (acetone-d_6)

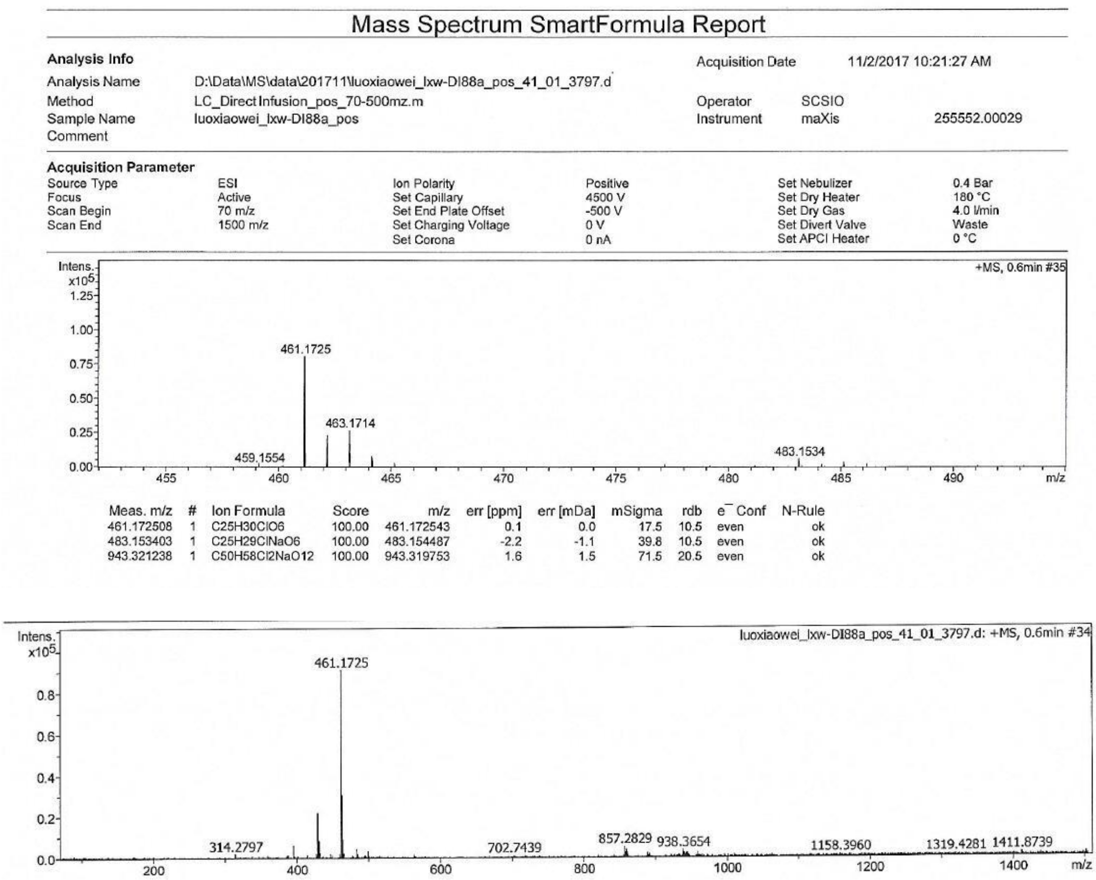
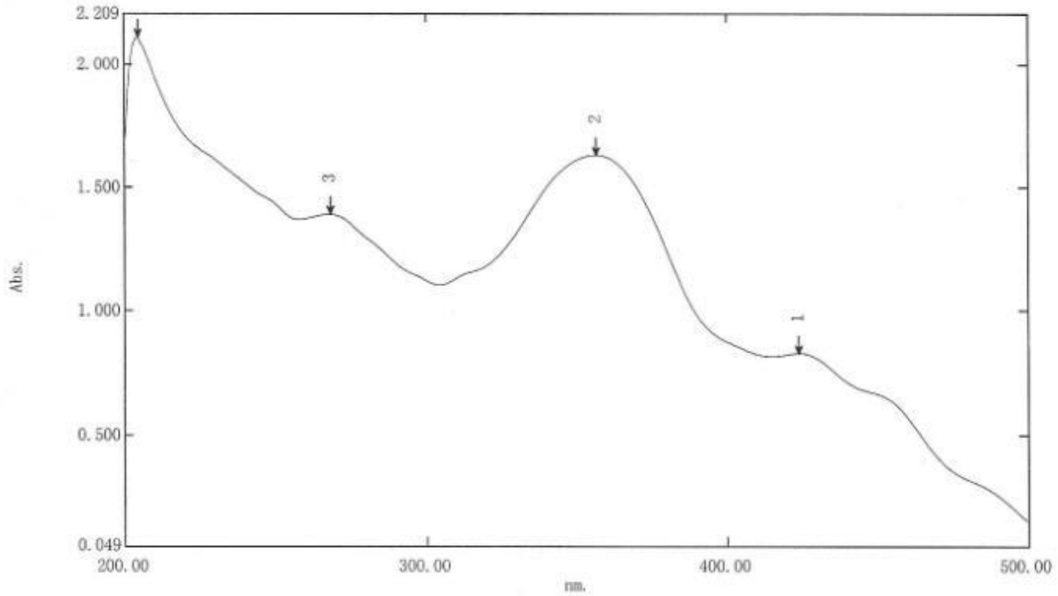


Figure S63. Positive HR-ESI-MS spectrum of isochromophilone E (**5**)



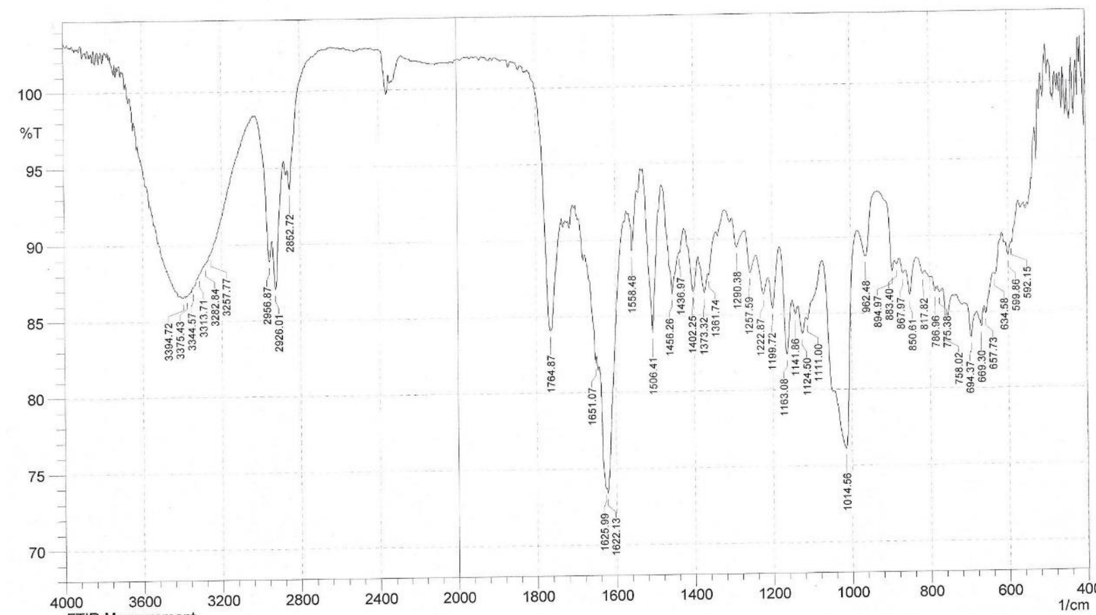
[测定属性]
波长范围 (nm.): 200.00 到 500.00
扫描速度: 中速
采样间隔: 0.2
自动采样间隔: 启用
扫描模式: 单个

[仪器属性]
仪器类型: UV-2600 系列
测定方式: 吸收值

No.	波长(nm)	吸收值	描述
1	424.40	0.829	
2	357.20	1.633	
3	268.80	1.391	
4	204.00	2.107	
5			

Figure S64. UV spectrum of isochromophilone E (**5**)

SHIMADZU



FTIR Measurement

Sample name: DI883
F:\Luo Xiaowei\DI883.smf

Scan number: 25
Resolution: 4 [1/cm]

Data: 2017-12-4 16:24:15
Operator: SCSIO

Figure S65. IR spectrum of isochromophilone E (**5**)

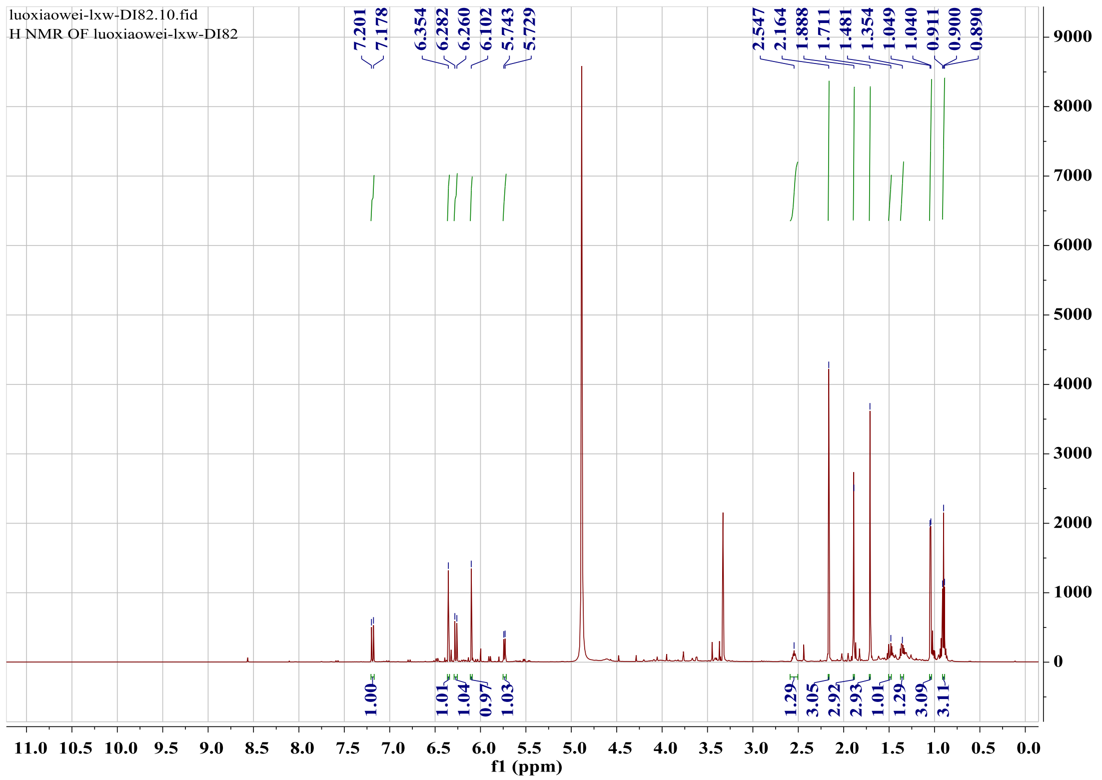
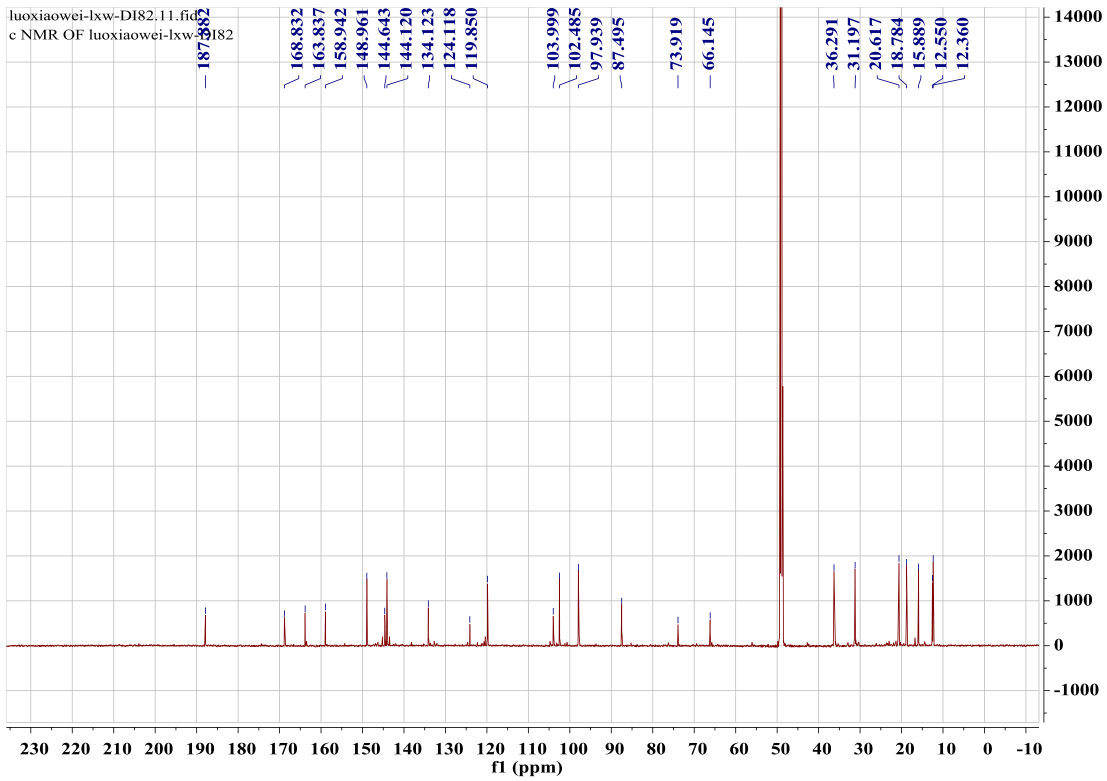


Figure S66. [1]H NMR spectrum of isochromophilone F (**6**) (CD_3OD, 700 MHz)



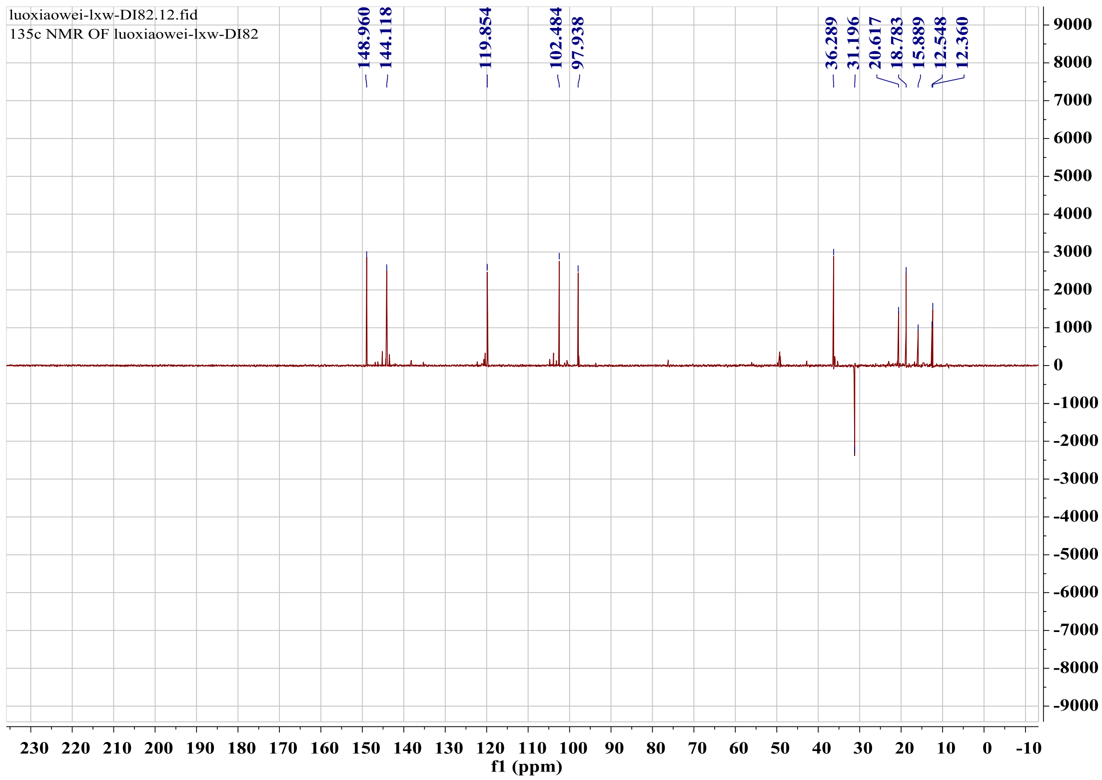


Figure S67. ^{13}C NMR and DEPT spectra of isochromophilone F (**6**) (CD_3OD, 175 MHz)

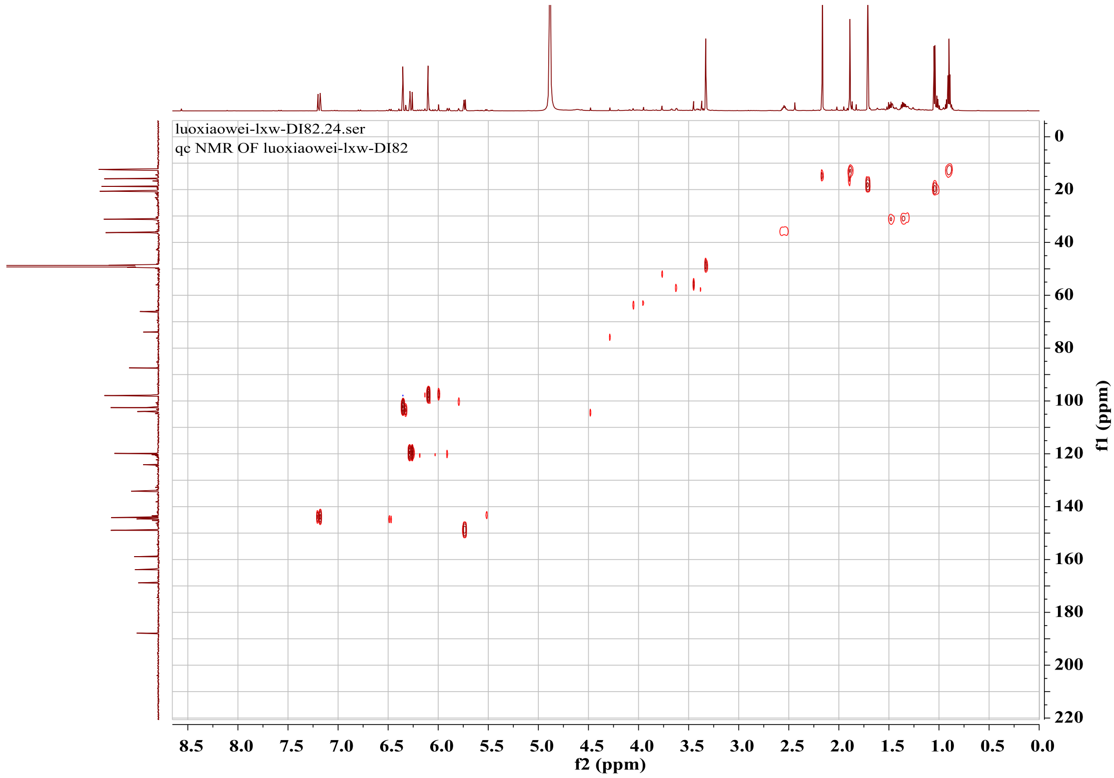


Figure S68. HSQC spectrum of isochromophilone F (**6**) (CD_3OD)

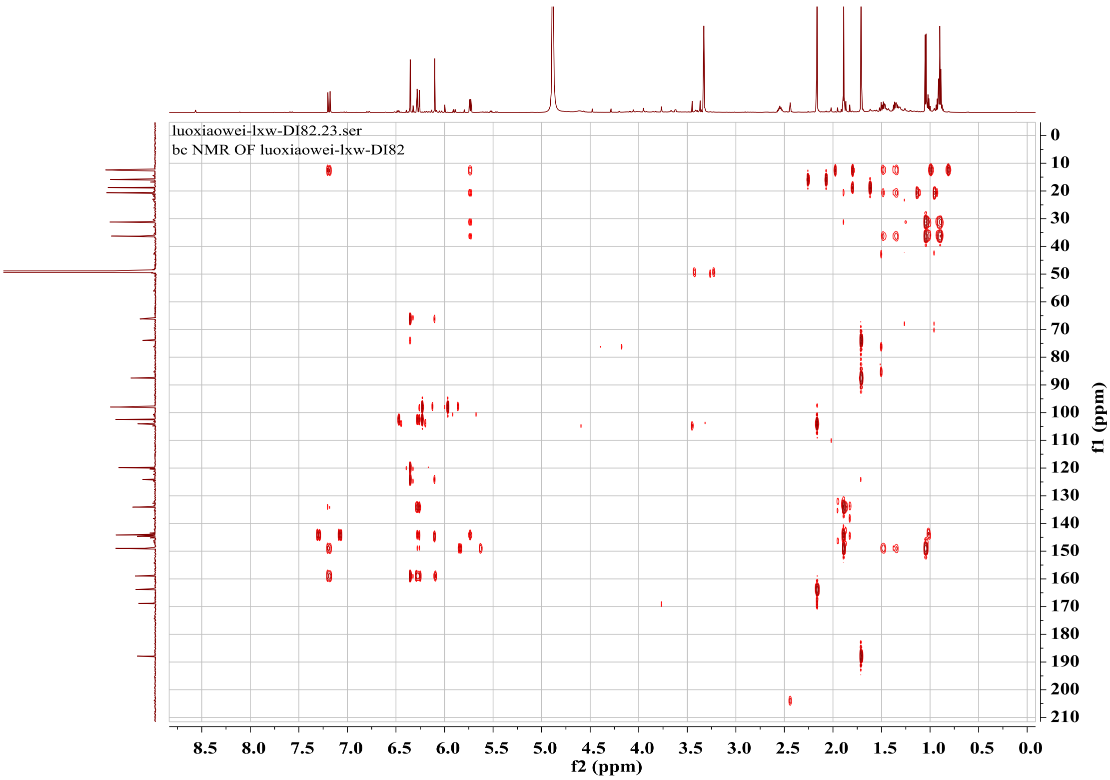


Figure S69. HMBC spectrum of isochromophilone F (**6**) (CD_3OD)

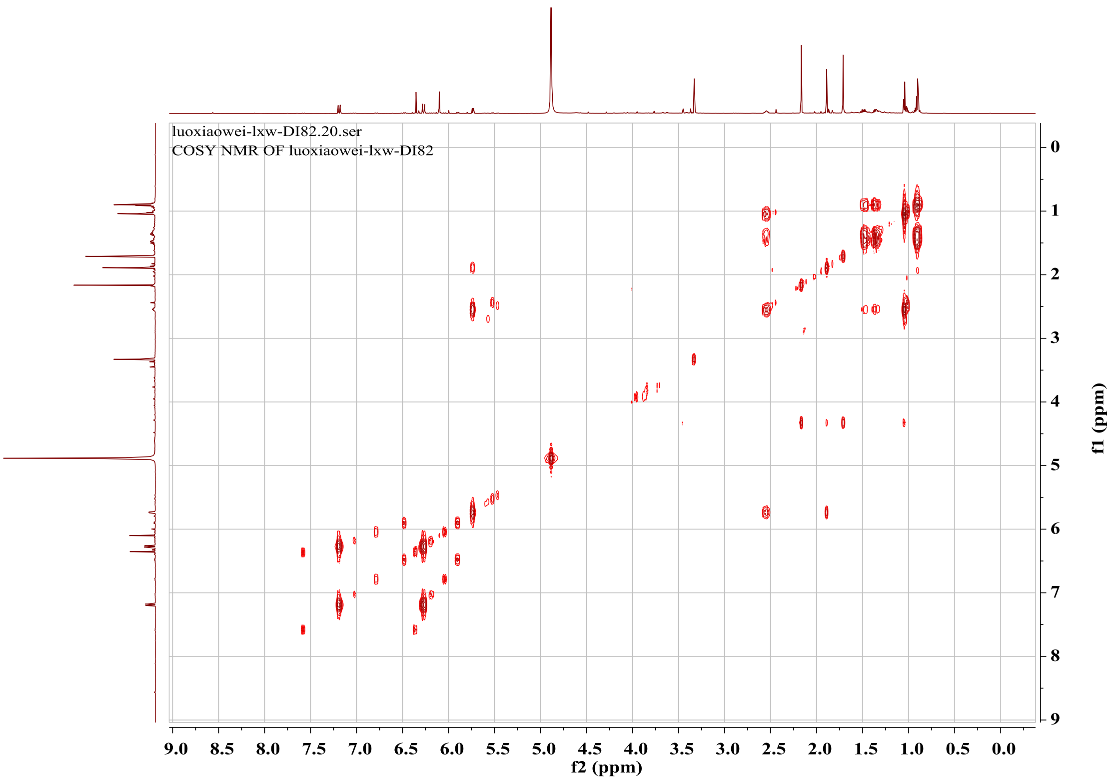
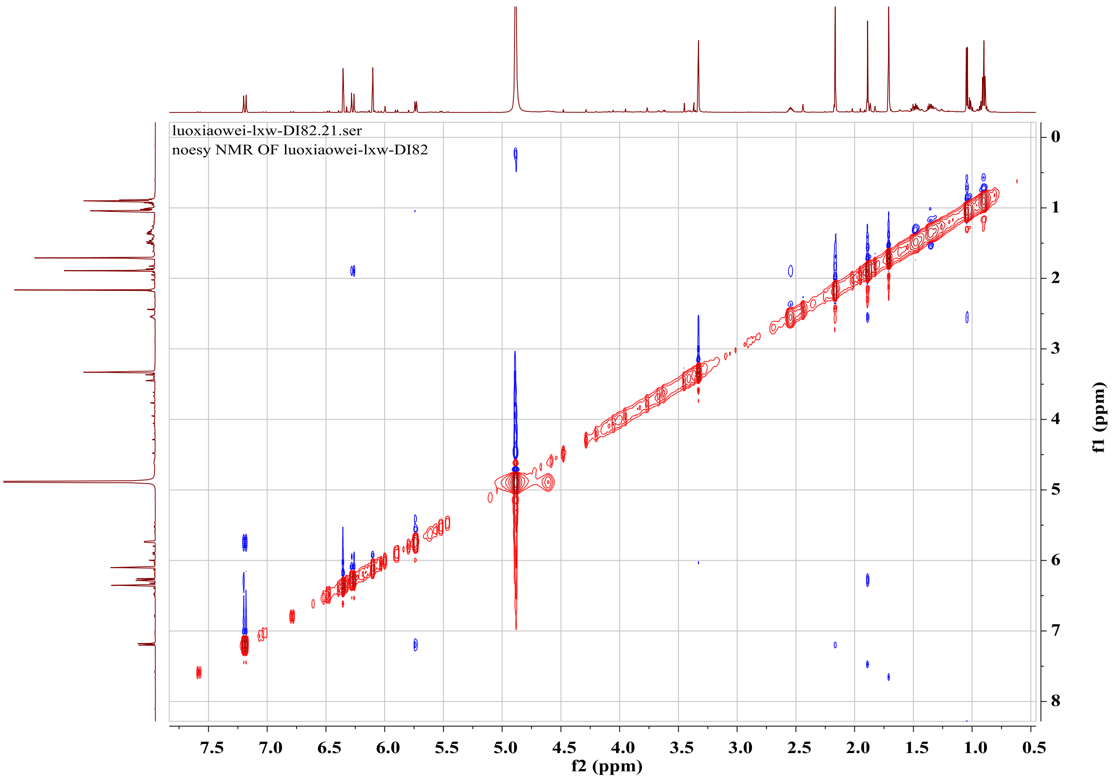


Figure S70. ^1H-^1H COSY spectrum of isochromophilone F (**6**) (CD_3OD)



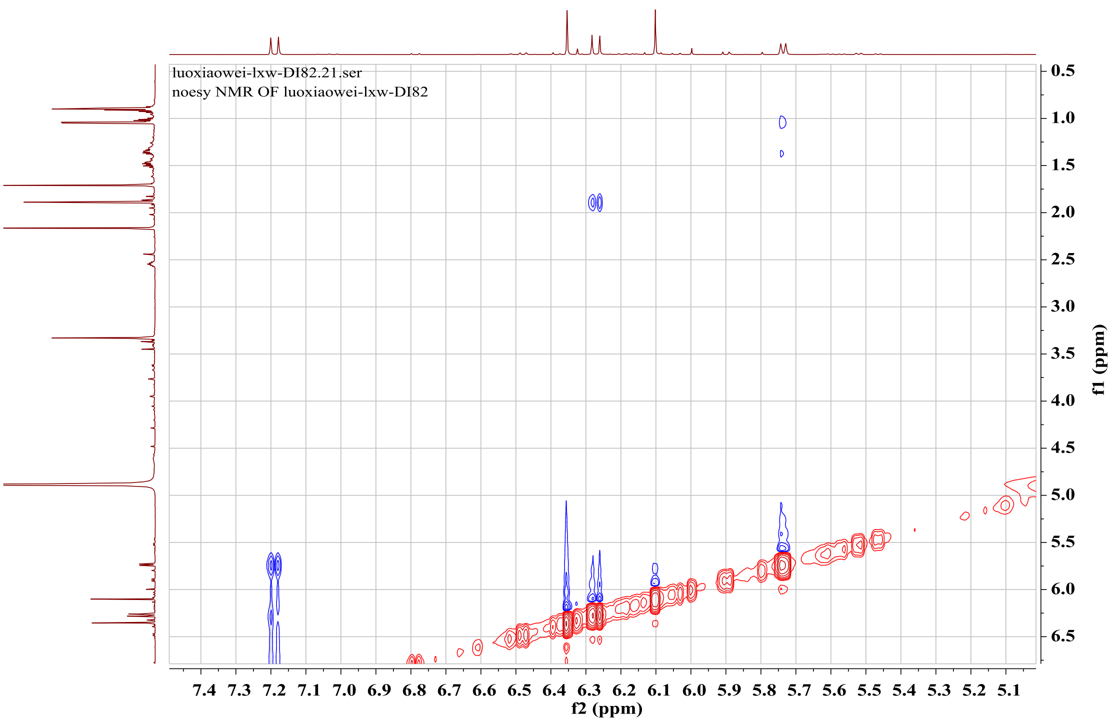


Figure S71. NOESY spectrum of isochromophilone F (**6**) (CD_3OD)

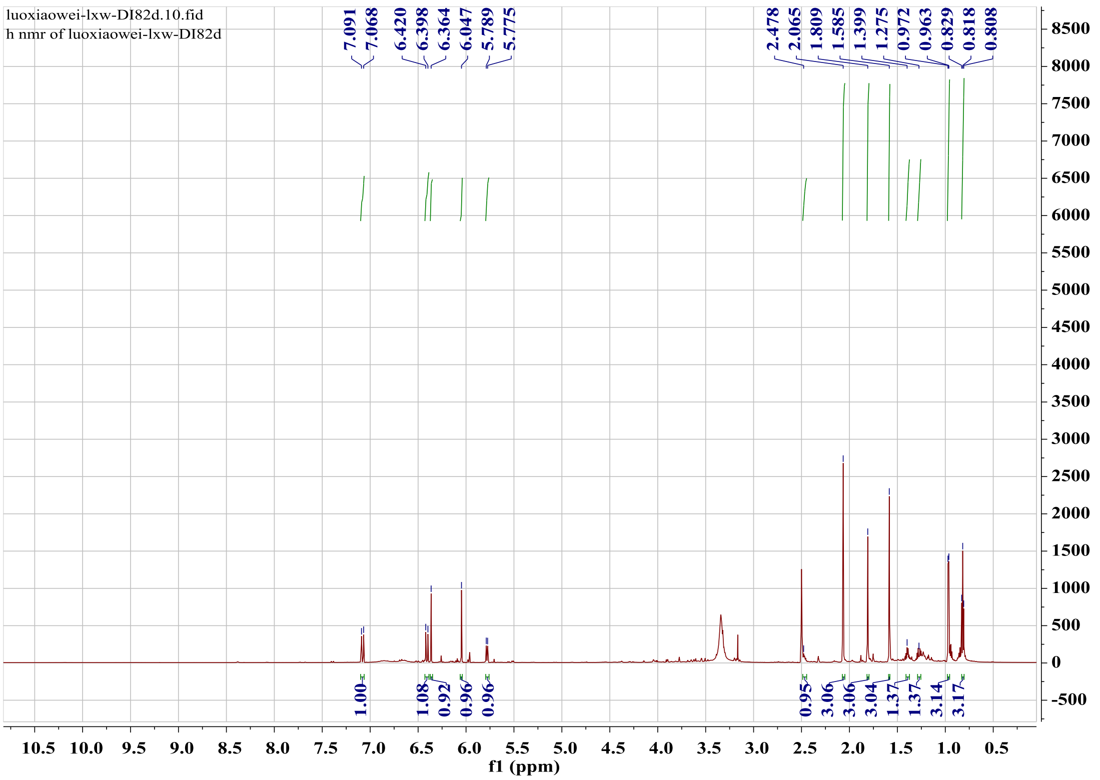
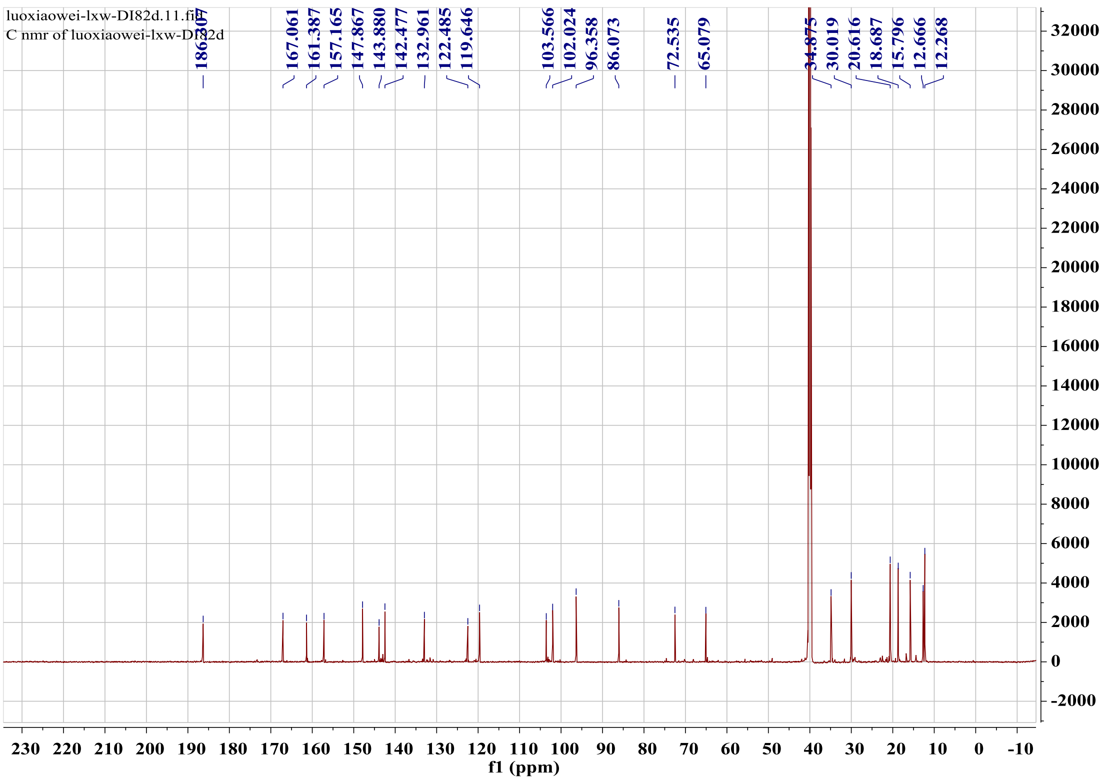


Figure S72. ^{1}H NMR spectrum of isochromophilone F (**6**) (DMSO-d_6, 700 MHz)



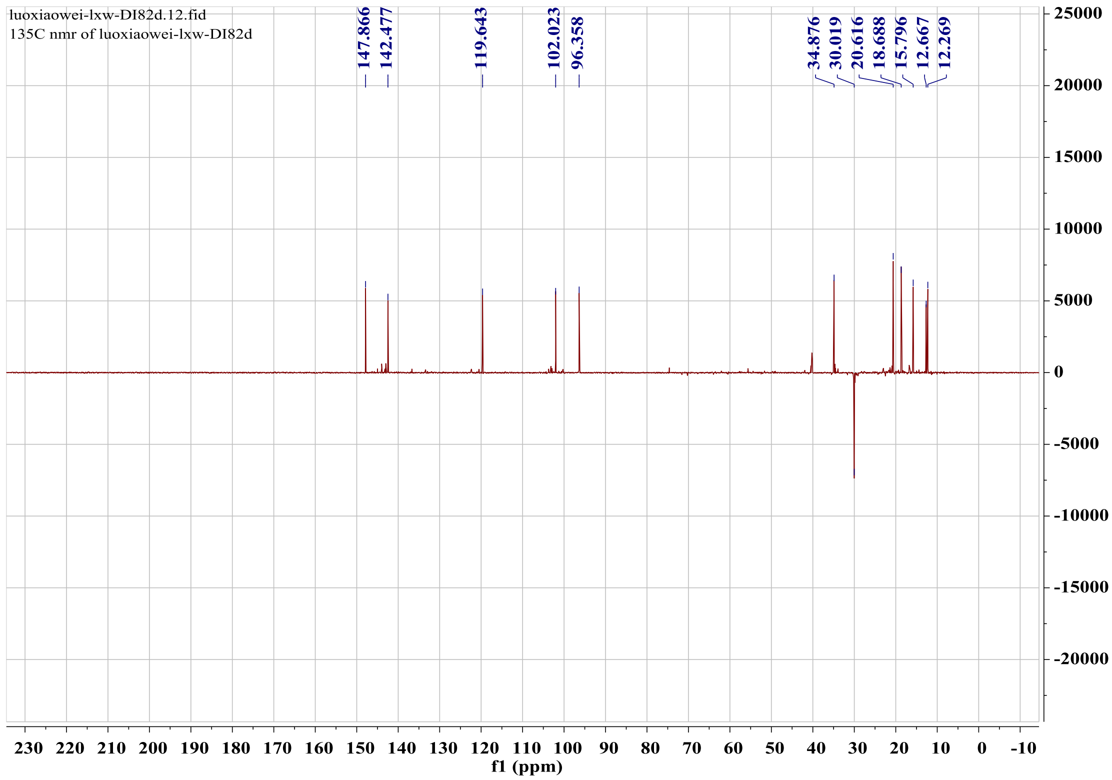


Figure S73. ^{13}C NMR and DEPT spectra of isochromophilone F (**6**) (DMSO-d_6, 175 MHz)

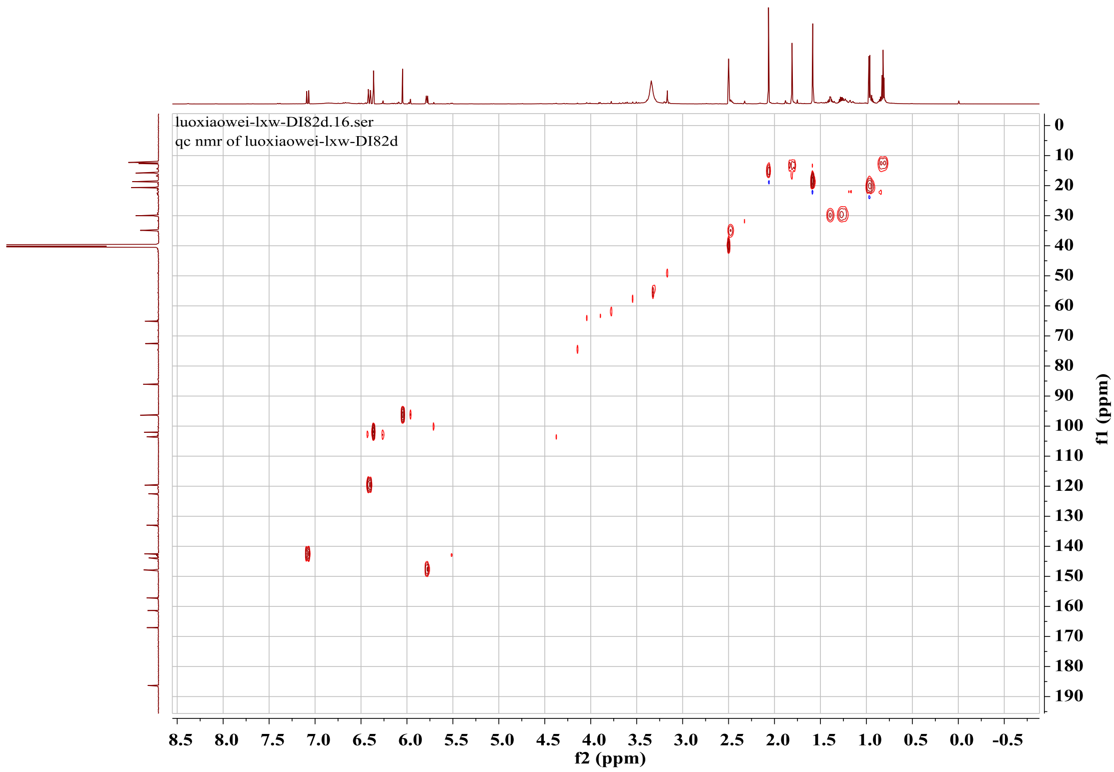


Figure S74. HSQC spectrum of isochromophilone F (**6**) (DMSO-d_6)

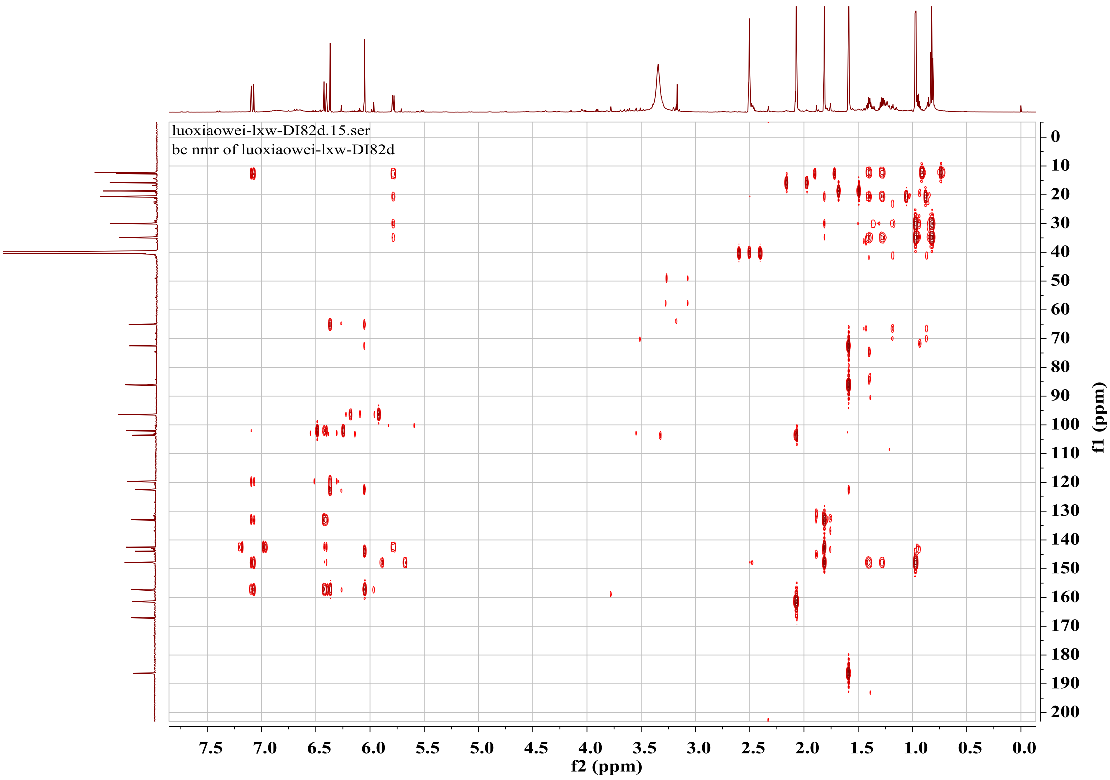


Figure S75. HMBC spectrum of isochromophilone F (**6**) (DMSO-d_6)

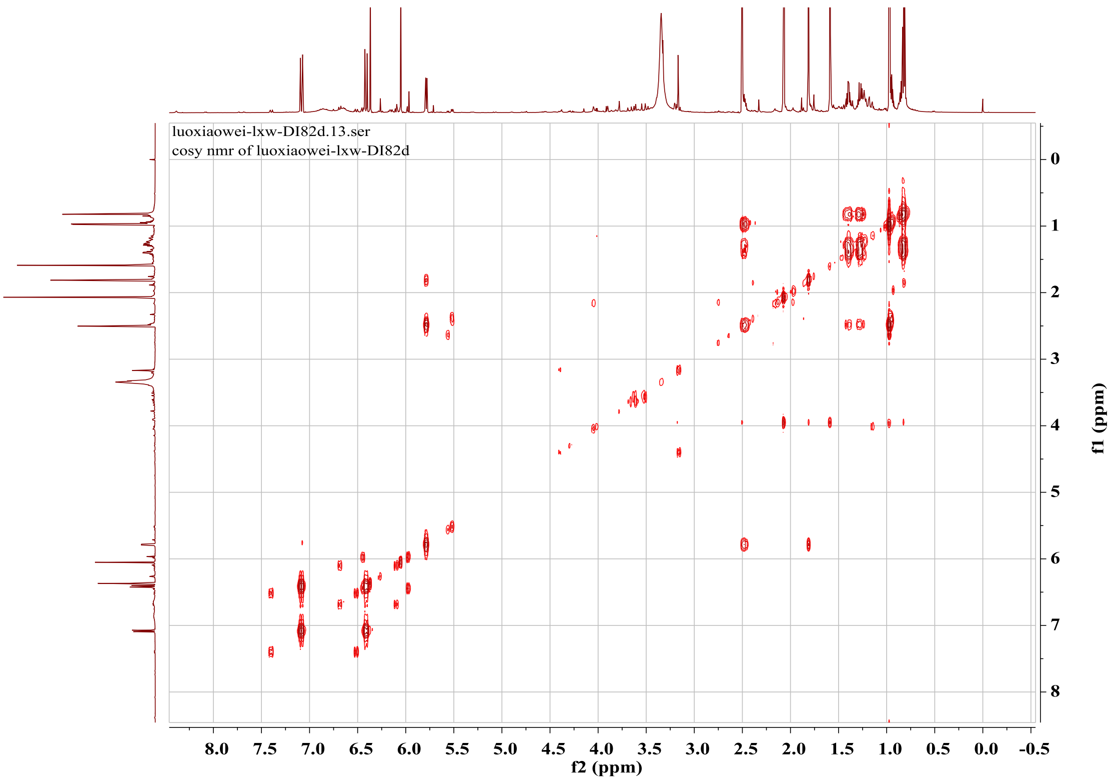


Figure S76. ^{1}H-^{1}H COSY spectrum of isochromophilone F (**6**) (DMSO-d_6)

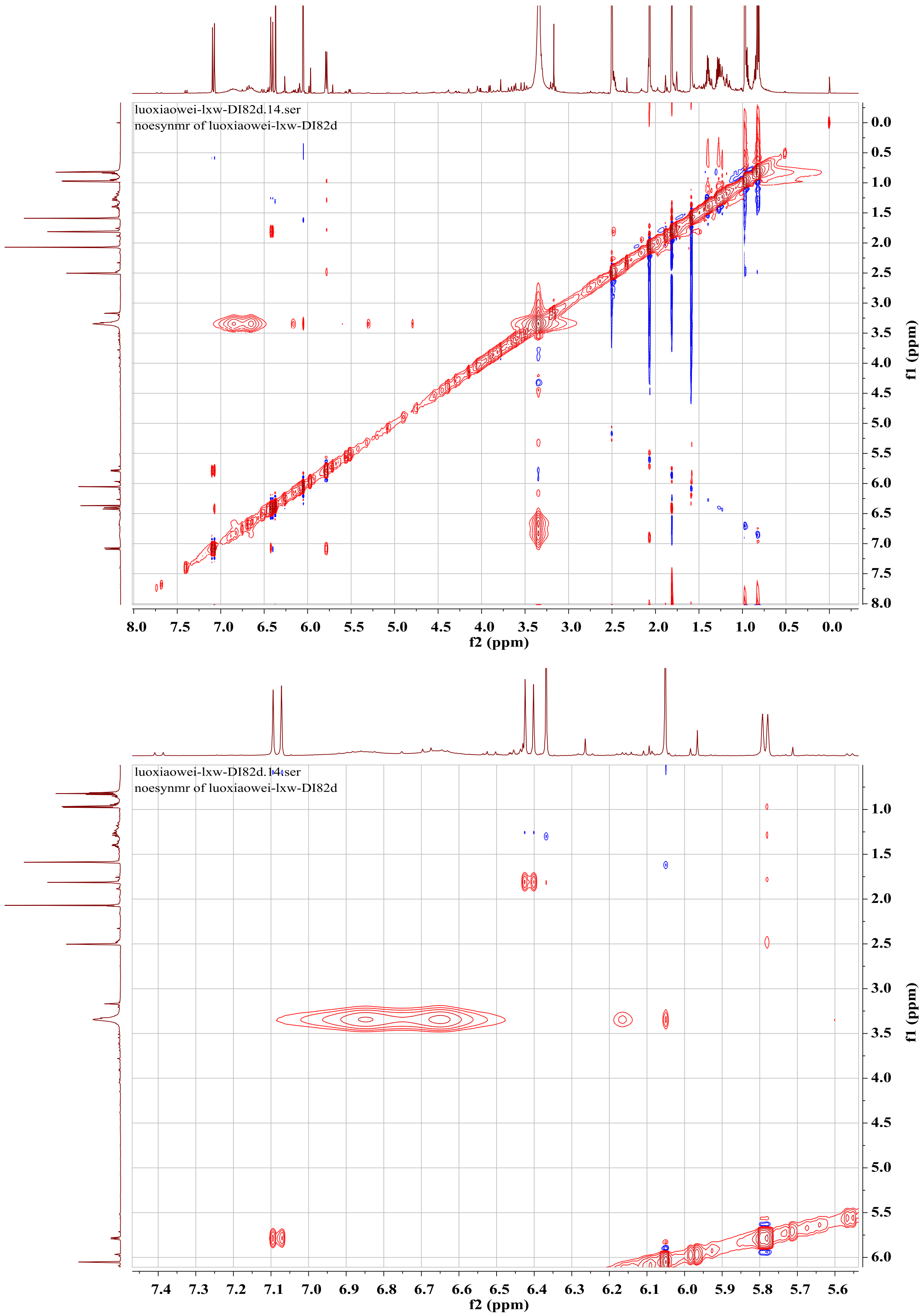
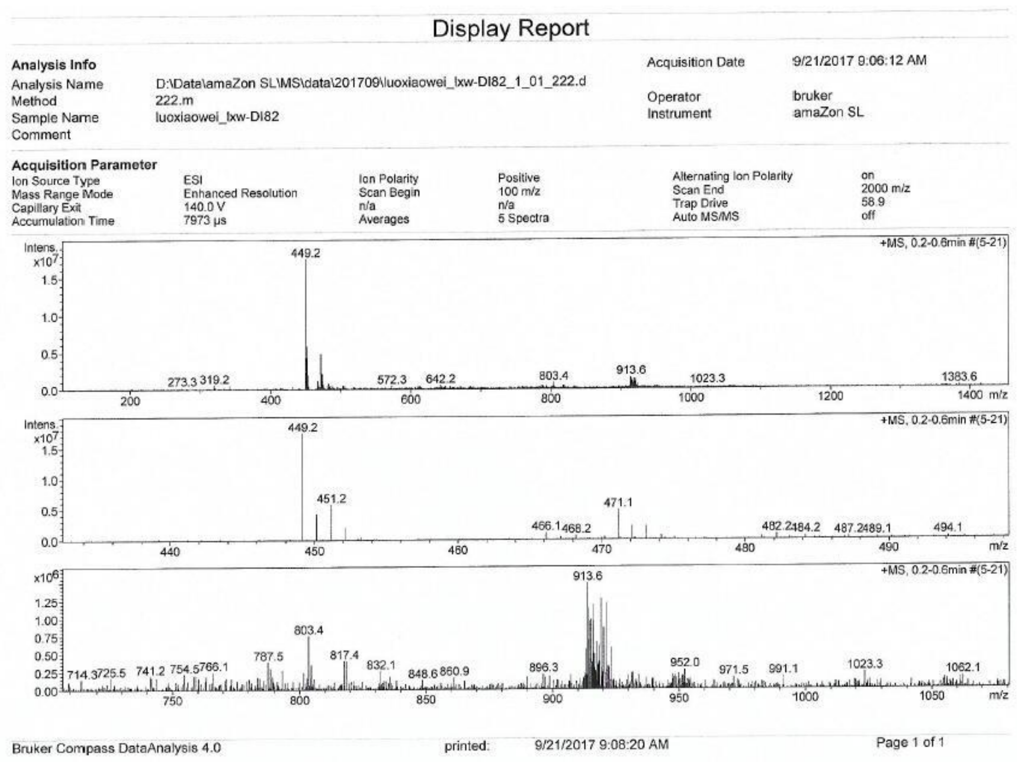


Figure S77. NOESY spectrum of isochromophilone F (**6**) (DMSO-d_6)



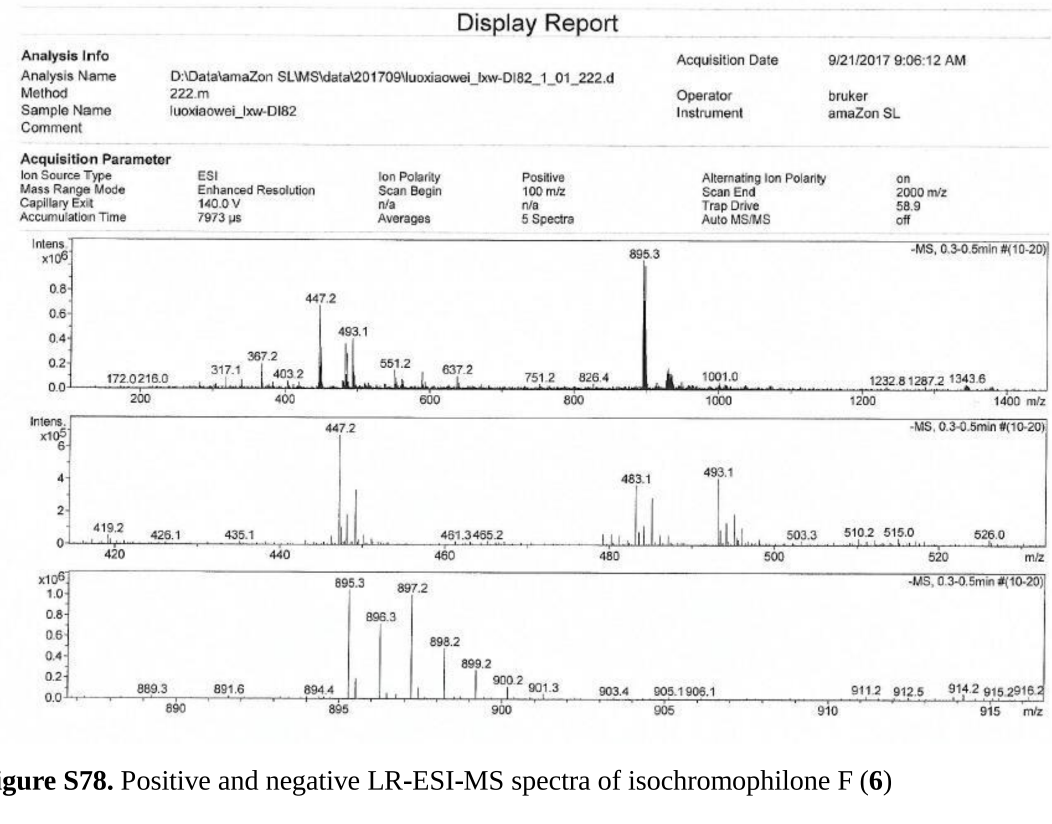


Figure S78. Positive and negative LR-ESI-MS spectra of isochromophilone F (**6**)

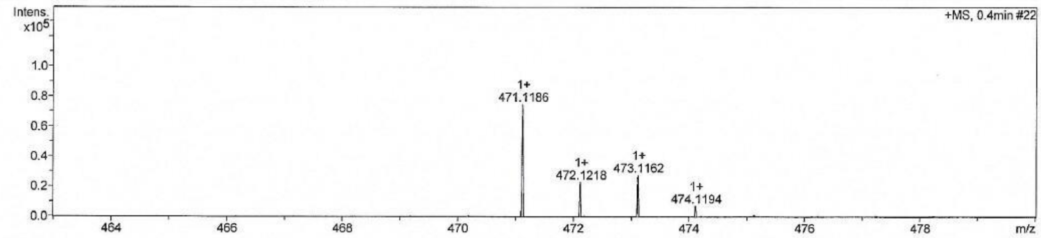
Mass Spectrum SmartFormula Report

Analysis Info

Analysis Name	D:\Data\MS\data\201709\luoxiaowei_lxw-DI82_pos_44_01_3603.d	Acquisition Date	9/21/2017 10:48:32 AM
Method	LC_Direct Infusion_pos_70-500mz.m	Operator	SCSIO
Sample Name	luoxiaowei_lxw-DI82_pos	Instrument	maXis 255552.00029
Comment			

Acquisition Parameter

Source Type	ESI	Ion Polarity	Positive	Set Nebulizer	0.4 Bar
Focus	Active	Set Capillary	4500 V	Set Dry Heater	180 °C
Scan Begin	70 m/z	Set End Plate Offset	-500 V	Set Dry Gas	4.0 l/min
Scan End	1500 m/z	Set Charging Voltage	0 V	Set Divert Valve	Waste
		Set Corona	0 nA	Set APCI Heater	0 °C



Meas. m/z	#	Ion Formula	Score	m/z	err [ppm]	err [mDa]	mSigma	rdb	e⁻ Conf	N-Rule
449.139525	1	C23H26ClO7	100.00	449.136157	-7.5	-3.4	76.4	10.5	even	ok
471.118592	1	C23H25ClNaO7	100.00	471.118102	1.0	0.5	25.5	10.5	even	ok
919.248267	1	C46H50Cl2NaO14	100.00	919.246982	1.4	1.3	56.1	20.5	even	ok

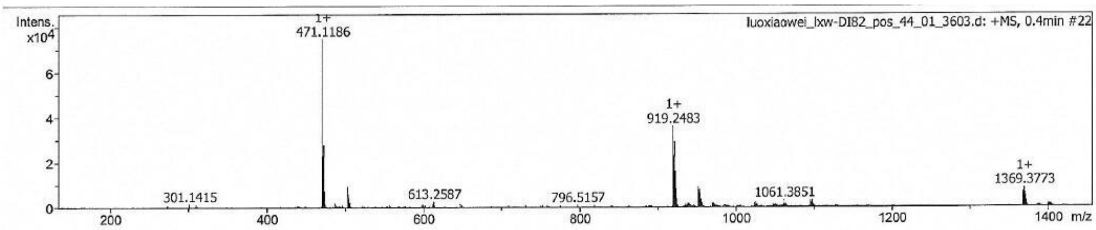
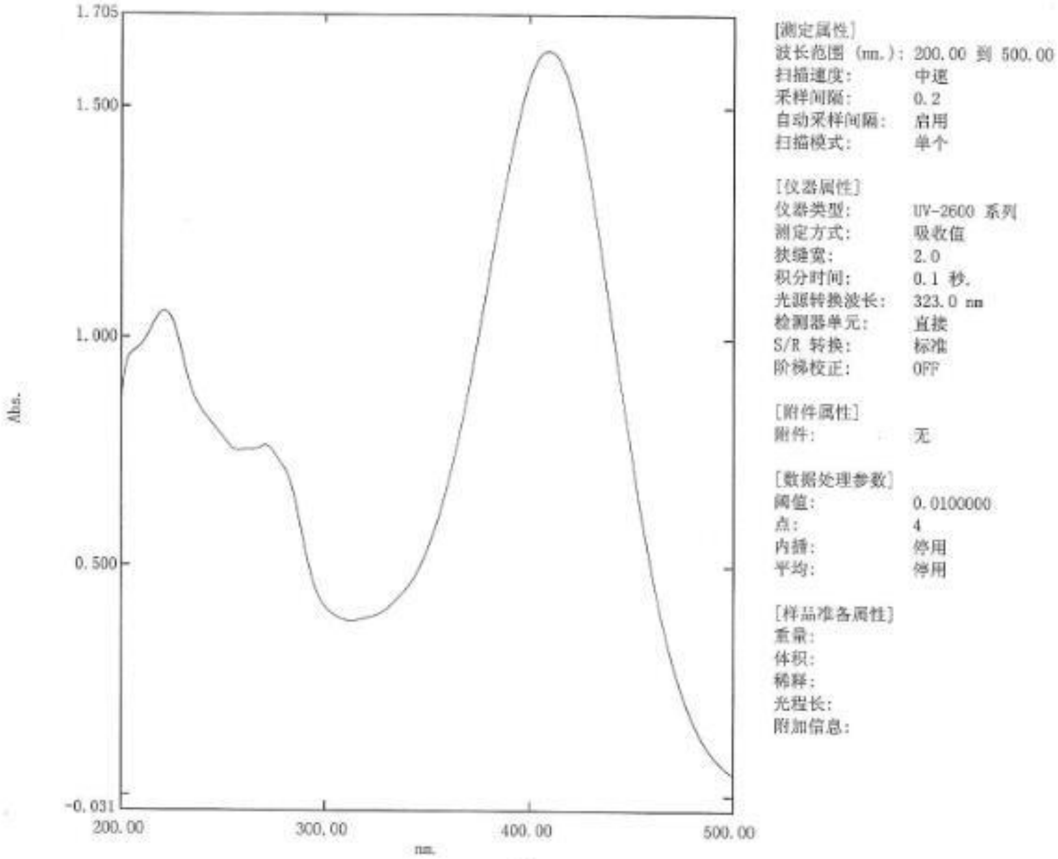


Figure S79. Positive HR-ESI-MS spectrum of isochromophilone F (**6**)



448.1 40ug/ml

No.	P/V	波长(nm)	吸收值	描述
1		409.60	1.626	4.260
2		270.80	0.763	3.932
3		221.60	1.056	4.073

Figure S80. UV spectrum of isochromophilone F (**6**)

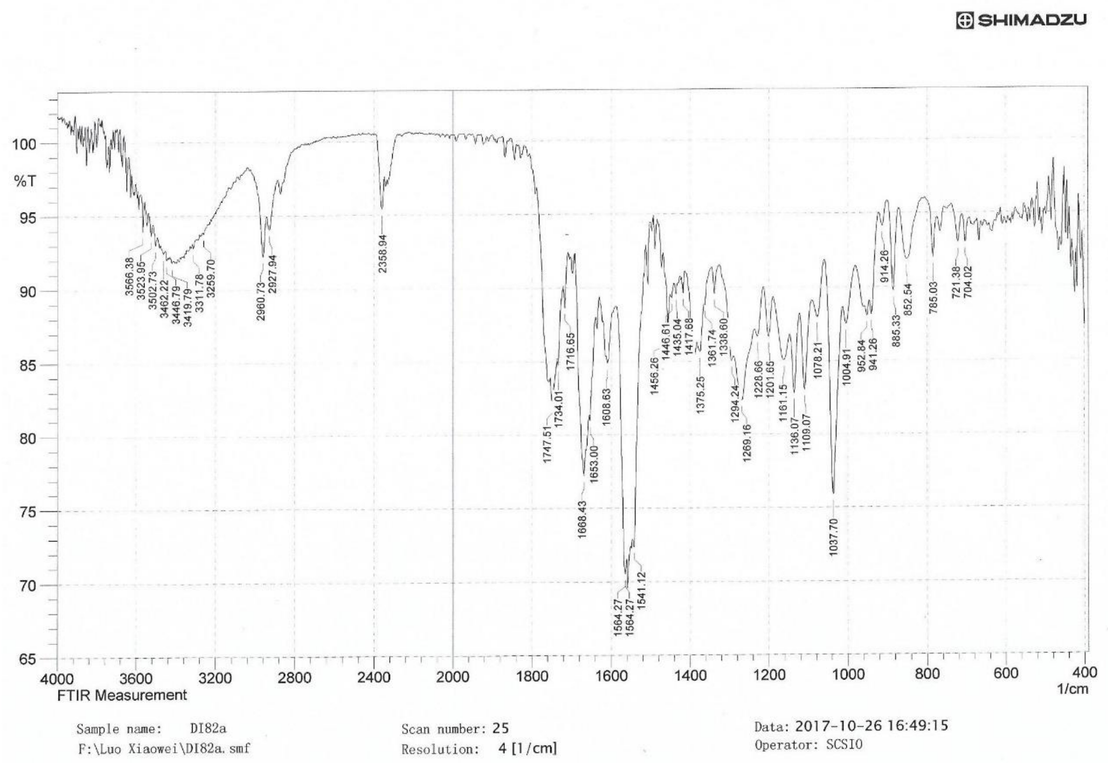


Figure S81. IR spectrum of isochromophilone F (**6**)

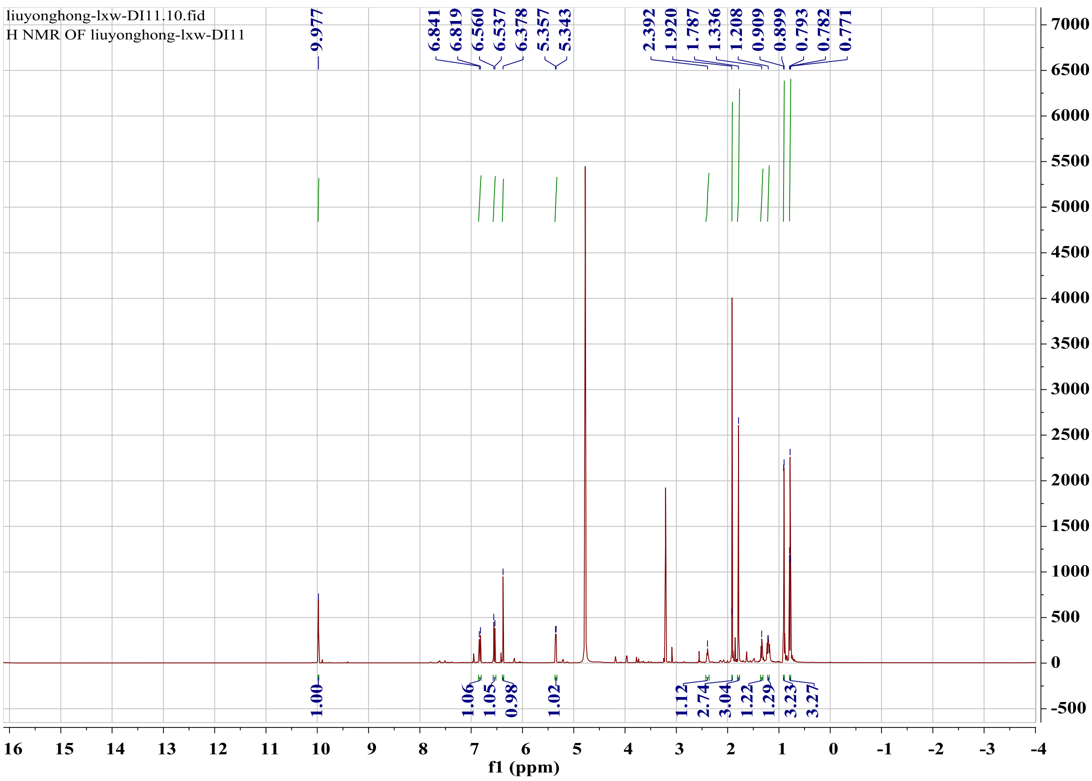
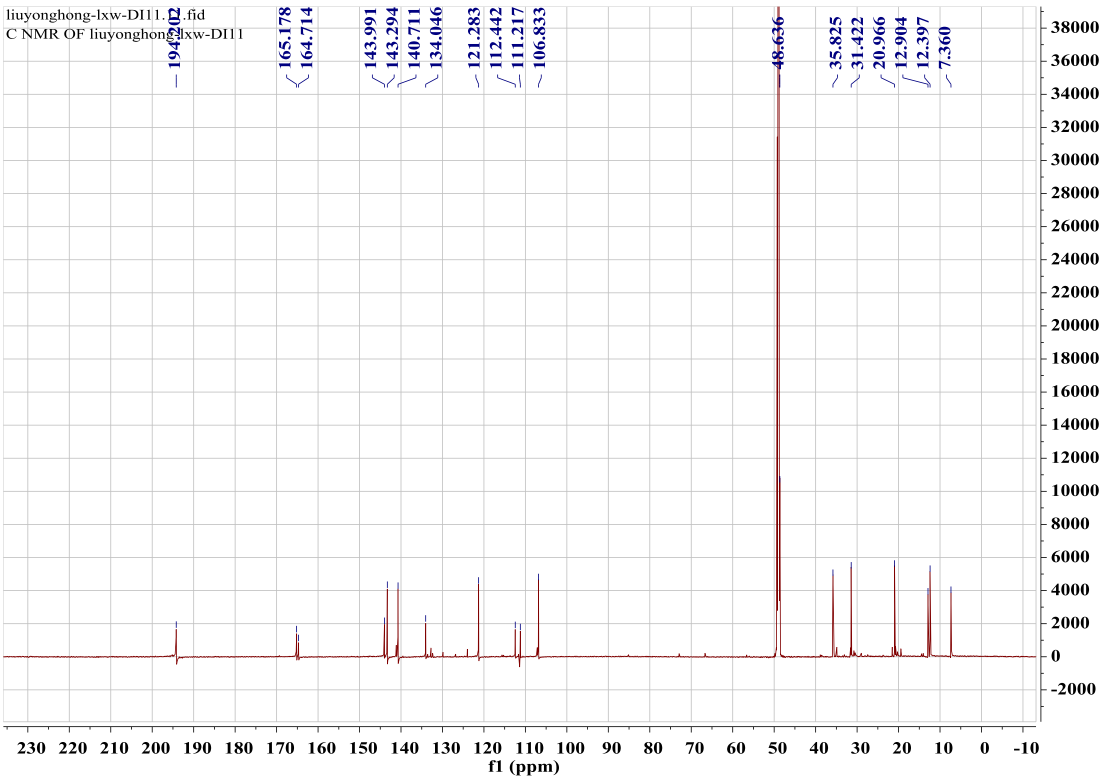


Figure S82. ^{1}H NMR spectrum of ((1*E*,3*E*)-3,5-dimethylhepta-1,3-dien-1-yl)-2,4-dihydroxy-3-methylbenzaldehyde (**11**) (CD_3OD, 700 MHz)



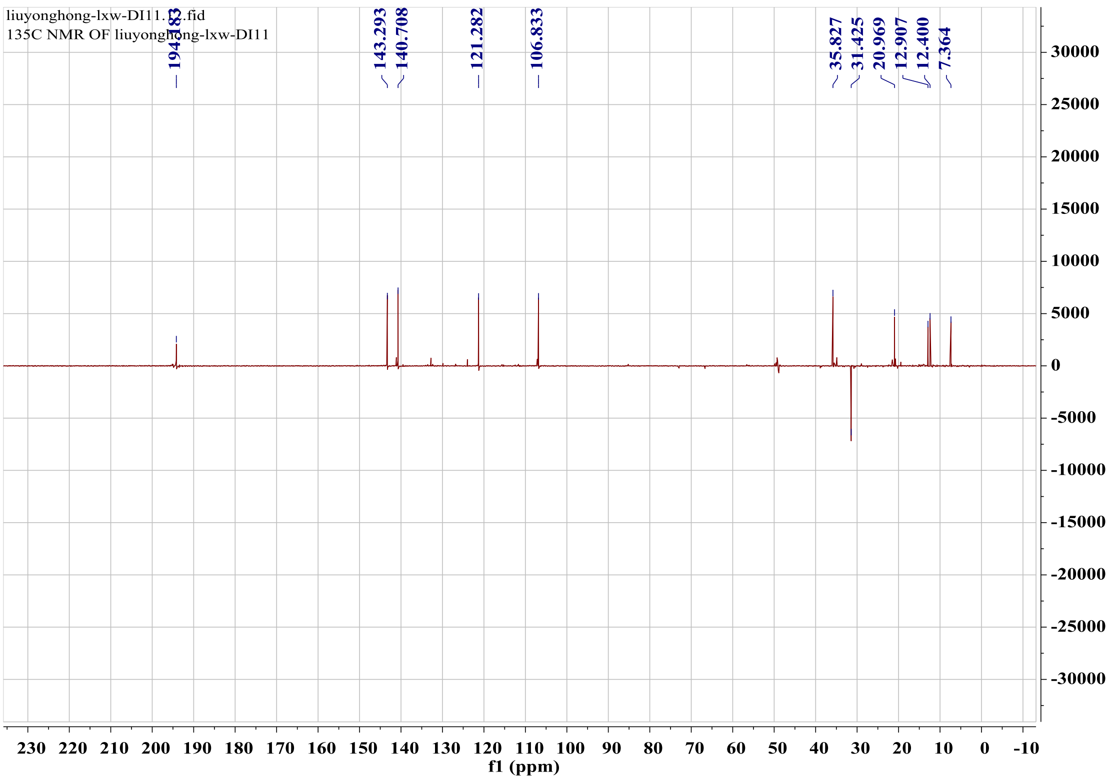


Figure S83. ^{13}C NMR and DEPT spectra of ((1*E*,3*E*)-3,5-dimethylhepta-1,3-dien-1-yl)-2,4-dihydroxy-3-methylbenzaldehyde (**11**) (CD_3OD, 175 MHz)

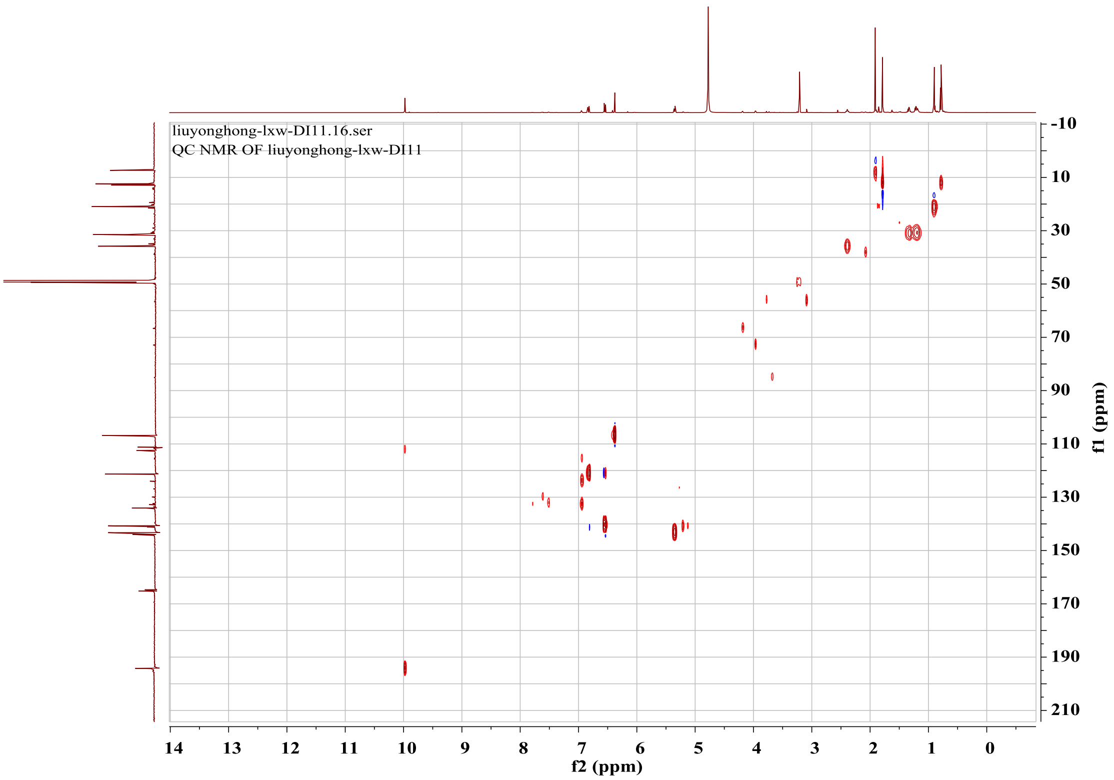


Figure S84. HSQC spectrum of ((1*E*,3*E*)-3,5-dimethylhepta-1,3-dien-1-yl)-2,4-dihydroxy-3-methylbenzaldehyde (**11**) (CD_3OD)

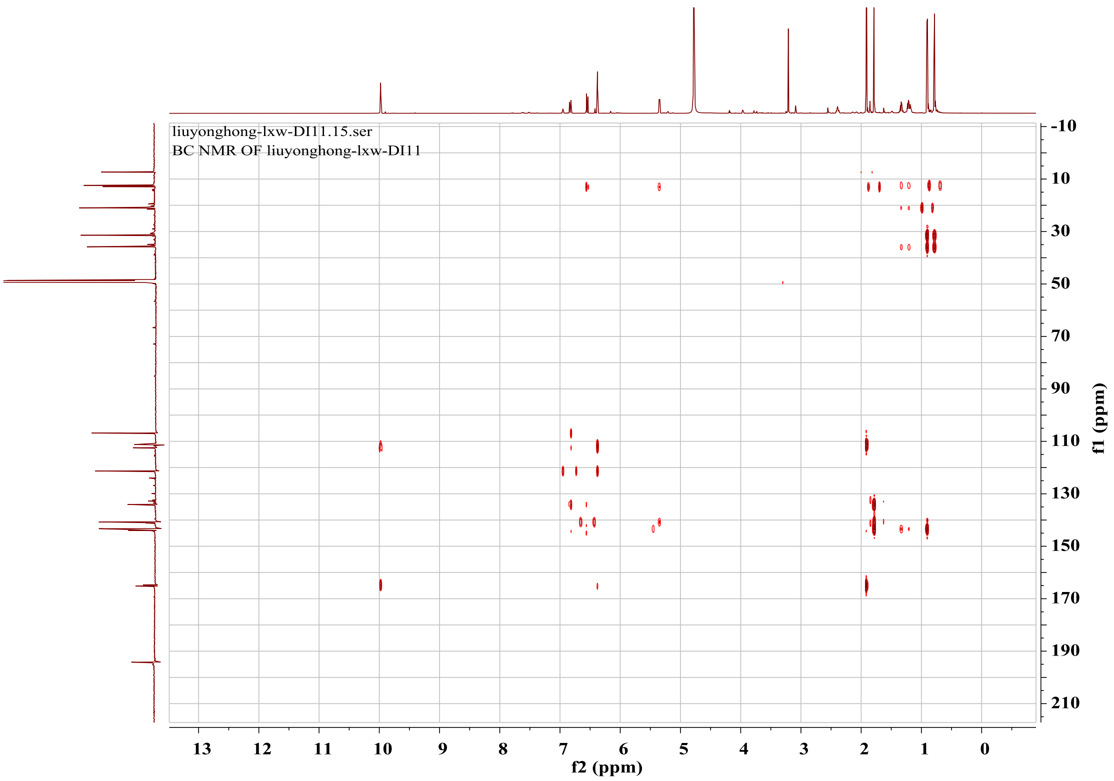


Figure S85. HMBC spectrum of ((1*E*,3*E*)-3,5-dimethylhepta-1,3-dien-1-yl)-2,4-dihydroxy-3-methylbenzaldehyde (**11**) (CD_3OD)

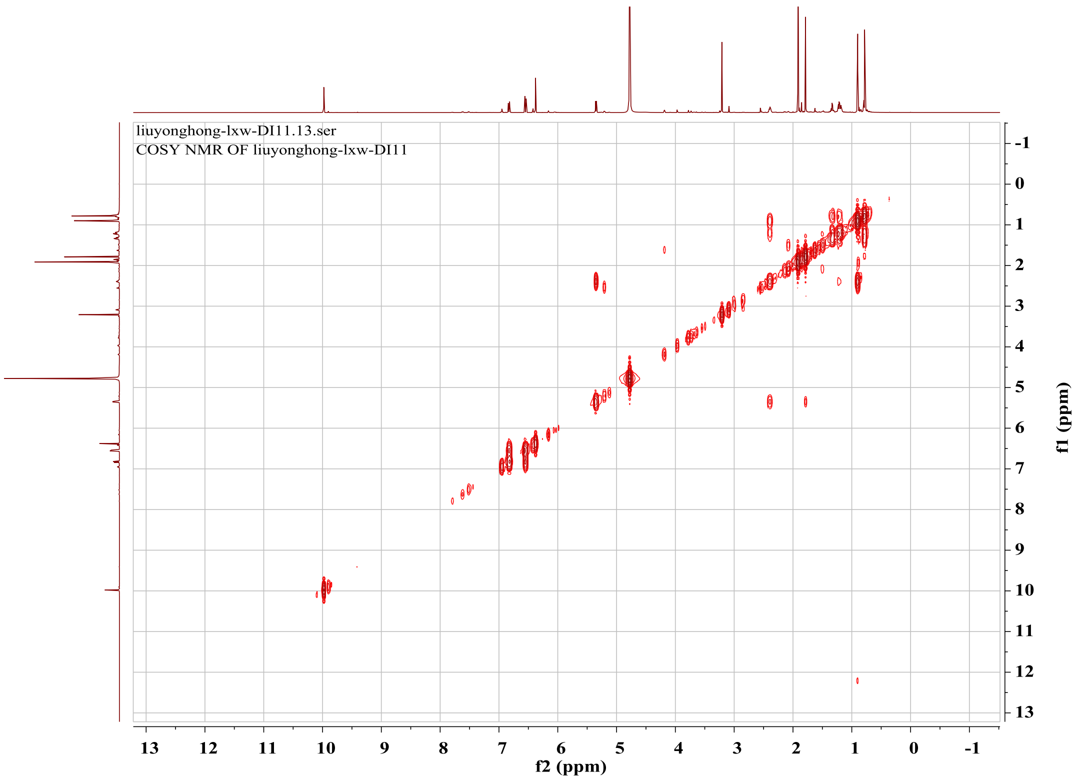


Figure S86. ^{1}H-^{1}H COSY spectrum of ((1*E*,3*E*)-3,5-dimethylhepta-1,3-dien-1-yl)-2,4-dihydroxy-3-methylbenzaldehyde (**11**) (CD_3OD)

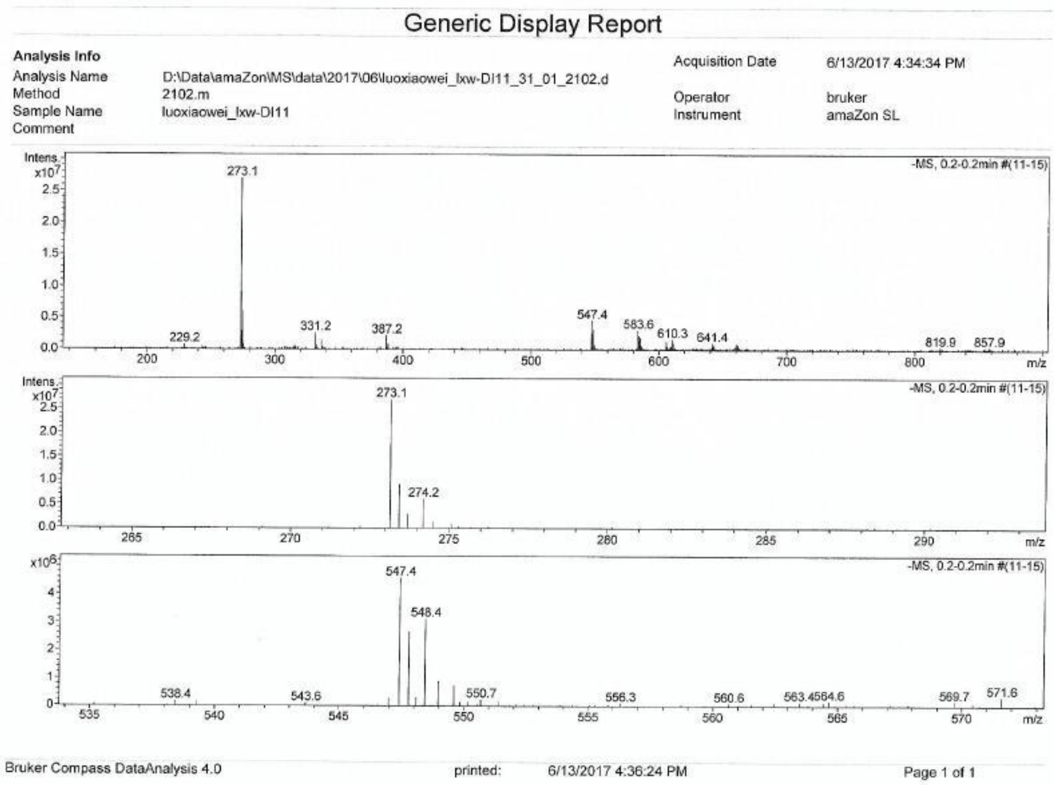


Figure S87. Negative LR-ESI-MS spectrum of ((1*E*,3*E*)-3,5-dimethylhepta-1,3-dien-1-yl)-2,4-dihydroxy-3-methylbenzaldehyde (**11**)

The optimized conformers and equilibrium populations of compounds (**1**, **3**−**6**)

The optimized conformers were calculated at the B3LYP/6-31+g(d, p) level. Equilibrium populations are in parentheses.

Table S2. Energies of 1 at MMFF94 force field.

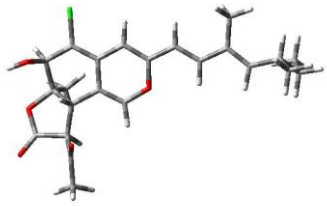
Configuration	Conformer	Energy (kcal/mol)	Population (%)
(6*R*,7*R*,8*S*,13*S*,2′*S*)-**1**	1	169.73	21.5
(6*R*,7*R*,8*S*,13*S*,2′*S*)-**1**	2	170.36	16.7
(6*R*,7*R*,8*S*,13*S*,2′*S*)-**1**	3	170.67	14.8
(6*R*,7*R*,8*S*,13*S*,2′*S*)-**1**	4	173.08	5.6
(6*R*,7*R*,8*S*,13*S*,2′*S*)-**1**	5	173.72	4.3
(6*R*,7*R*,8*S*,13*S*,2′*S*)-**1**	6	174.02	3.8
(6*S*,7*S*,8*R*,13*S*,2′*R*)-**1**	1	169.73	18.7
(6*S*,7*S*,8*R*,13*S*,2′*R*)-**1**	2	170.36	14.5
(6*S*,7*S*,8*R*,13*S*,2′*R*)-**1**	3	170.67	12.8
(6*S*,7*S*,8*R*,13*S*,2′*R*)-**1**	4	170.89	11.7
(6*S*,7*S*,8*R*,13*S*,2′*R*)-**1**	5	173.08	4.8
(6*S*,7*S*,8*R*,13*S*,2′*R*)-**1**	6	173.72	3.7
(6*S*,7*S*,8*R*,13*R*,2′*R*)-**1**	1	169.73	18.8
(6*S*,7*S*,8*R*,13*R*,2′*R*)-**1**	2	170.36	14.6
(6*S*,7*S*,8*R*,13*R*,2′*R*)-**1**	3	170.67	12.9
(6*S*,7*S*,8*R*,13*R*,2′*R*)-**1**	4	170.90	11.7
(6*S*,7*S*,8*R*,13*R*,2′*R*)-**1**	5	173.08	4.9
(6*S*,7*S*,8*R*,13*R*,2′*R*)-**1**	6	173.72	3.8

Table S3. Energies of 1 at B3LYP/6–31+g(d, p) level in methanol.

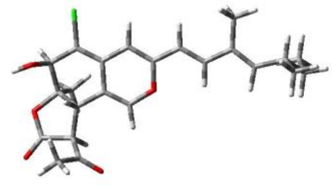
Configuration	Conformer	E (Hartree)	E (kcal/mol)	Population (%)
(6*R*,7*R*,8*S*,13*S*,2′*S*)-**1**	1	–1729.3803988	–1085203.49	64.23
(6*R*,7*R*,8*S*,13*S*,2′*S*)-**1**	2	–1729.3780158	–1085202.00	5.14
(6*R*,7*R*,8*S*,13*S*,2′*S*)-**1**	3	–1729.3761456	–1085200.83	0.71
(6*R*,7*R*,8*S*,13*S*,2′*S*)-**1**	4	–1729.3795967	–1085202.99	27.45
(6*R*,7*R*,8*S*,13*S*,2′*S*)-**1**	5	–1729.3772067	–1085201.49	2.18
(6*R*,7*R*,8*S*,13*S*,2′*S*)-**1**	6	–1729.3753364	–1085200.32	0.30
(6*S*,7*S*,8*R*,13*S*,2′*R*)-**1**	1	–1729.3804368	–1085203.53	59.02
(6*S*,7*S*,8*R*,13*S*,2′*R*)-**1**	2	–1729.3780390	–1085202.01	4.65
(6*S*,7*S*,8*R*,13*S*,2′*R*)-**1**	3	–1729.3761470	–1085200.83	0.63
(6*S*,7*S*,8*R*,13*S*,2′*R*)-**1**	4	–1729.3785771	–1085202.35	8.22
(6*S*,7*S*,8*R*,13*S*,2′*R*)-**1**	5	–1729.3796458	–1085203.02	25.52
(6*S*,7*S*,8*R*,13*S*,2′*R*)-**1**	6	–1729.3772282	–1085201.50	1.97
(6*S*,7*S*,8*R*,13*R*,2′*R*)-**1**	1	–1729.3803988	–1085203.49	59.04
(6*S*,7*S*,8*R*,13*R*,2′*R*)-**1**	2	–1729.3780159	–1085202.00	4.72
(6*S*,7*S*,8*R*,13*R*,2′*R*)-**1**	3	–1729.3761456	–1085200.83	0.65
(6*S*,7*S*,8*R*,13*R*,2′*R*)-**1**	4	–1729.3785557	–1085202.34	8.37

(6*S*,7*S*,8*R*,13*R*,2′*R*)-**1**	5	–1729.3795965	–1085202.99	25.22
(6*S*,7*S*,8*R*,13*R*,2′*R*)-**1**	6	–1729.3772067	–1085201.49	2.00

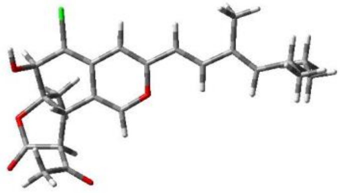
(6*R*,7*R*,8*S*,13*S*,2′*S*)-**1**



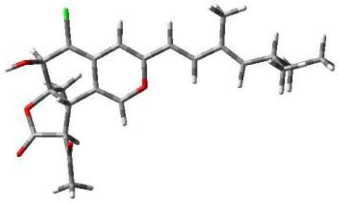
Conf.1 (64.23%)



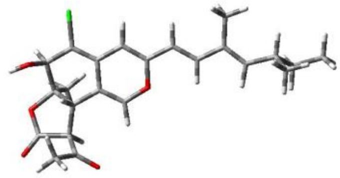
Conf.2 (5.14%)



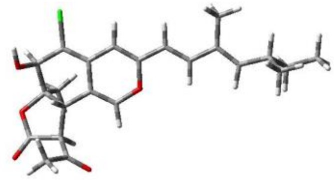
Conf.3 (0.71%)



Conf.4 (27.45%)

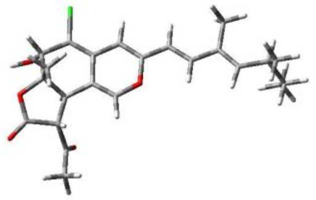


Conf.5 (2.18%)

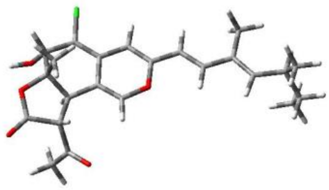


Conf.6 (0.30%)

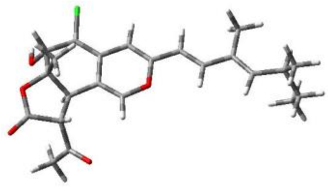
(6*S*,7*S*,8*R*,13*S*,2′*R*)-**1**



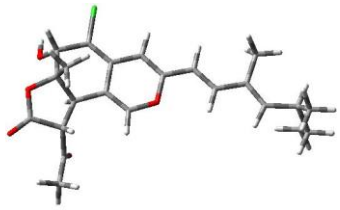
Conf.1 (59.02%)



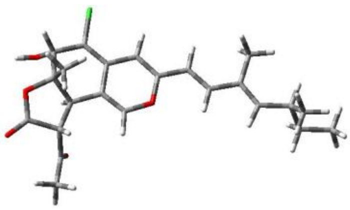
Conf.2 (4.65%)



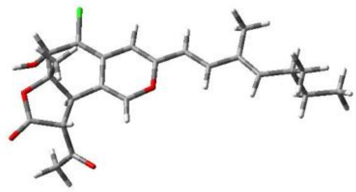
Conf.3 (0.63%)



Conf.4 (8.22%)

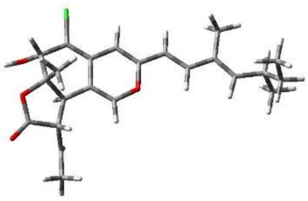


Conf.5 (25.52%)

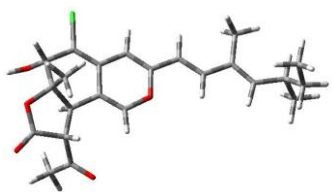


Conf.6 (1.97%)

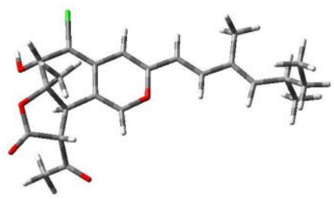
(6*S*,7*S*,8*R*,13*R*,2′*R*)-**1**



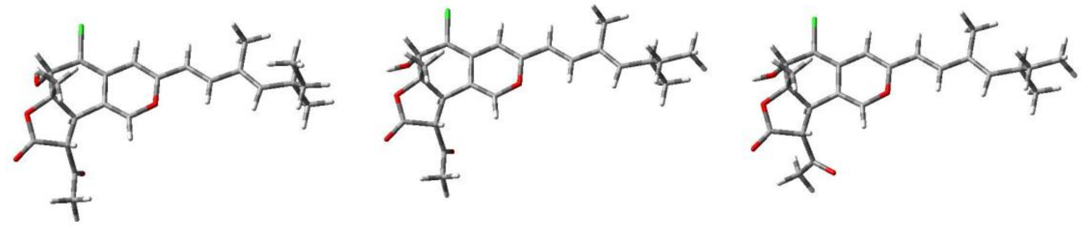
Conf.1 (59.04%)



Conf.2 (4.72%)



Conf.3 (0.65%)



Conf.4 (8.37%) Conf.5 (25.22%) Conf.6 (2.00%)

Figure S88. The optimized conformers and equilibrium populations of isochromophilone A (**1**)

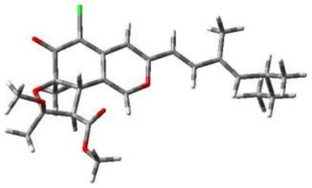
Table S4. Energies of 3 at MMFF94 force field.

Configuration	Conformer	Energy (kcal/mol)	Population (%)
(7*R*,8*S*,13*S*,1′*S*,2′*R*)-**3**	1	230.92	35.2%
(7*R*,8*S*,13*S*,1′*S*,2′*R*)-**3**	2	232.50	18.6%
(7*R*,8*S*,13*S*,1′*S*,2′*R*)-**3**	3	234.28	9.1%
(7*R*,8*S*,13*S*,1′*S*,2′*R*)-**3**	4	235.35	5.9%
(7*R*,8*S*,13*S*,1′*S*,2′*R*)-**3**	5	236.07	4.4%
(7*R*,8*S*,13*S*,1′*S*,2′*R*)-**3**	6	236.49	3.7%
(7*S*,8*R*,13*S*,1′*R*,2′*S*)-**3**	1	230.92	32.5%
(7*S*,8*R*,13*S*,1′*R*,2′*S*)-**3**	2	232.50	17.2%
(7*S*,8*R*,13*S*,1′*R*,2′*S*)-**3**	3	234.27	8.4%
(7*S*,8*R*,13*S*,1′*R*,2′*S*)-**3**	4	235.35	5.4%
(7*S*,8*R*,13*S*,1′*R*,2′*S*)-**3**	5	235.86	4.4%
(7*S*,8*R*,13*S*,1′*R*,2′*S*)-**3**	6	236.21	3.8%
(7*S*,8*R*,13*S*,1′*R*,2′*S*)-**3**	7	236.28	3.7%

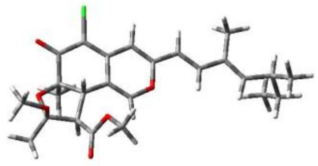
Table S5. Energies of 3 at B3LYP/6–31+g(d, p) level in methanol.

Configuration	Conformer	E (Hartree)	E (kcal/mol)	Population (%)
(7*R*,8*S*,13*S*,1′*S*,2′*R*)-**3**	1	–1883.2614337	–1181765.38	53.09
(7*R*,8*S*,13*S*,1′*S*,2′*R*)-**3**	2	–1883.2604074	–1181764.74	17.89
(7*R*,8*S*,13*S*,1′*S*,2′*R*)-**3**	3	–1883.2605962	–1181764.86	21.85
(7*R*,8*S*,13*S*,1′*S*,2′*R*)-**3**	4	–1883.2591219	–1181763.93	4.58
(7*R*,8*S*,13*S*,1′*S*,2′*R*)-**3**	5	–1882.9273271	–1181761.52	0.08
(7*R*,8*S*,13*S*,1′*S*,2′*R*)-**3**	6	–1883.2585576	–1181763.58	2.52
(7*S*,8*R*,13*S*,1′*R*,2′*S*)-**3**	1	–1883.2614274	–1181765.38	49.05
(7*S*,8*R*,13*S*,1′*R*,2′*S*)-**3**	2	–1883.2604423	–1181764.76	17.75
(7*S*,8*R*,13*S*,1′*R*,2′*S*)-**3**	3	–1883.2606114	–1181764.87	21.41
(7*S*,8*R*,13*S*,1′*R*,2′*S*)-**3**	4	–1883.2591585	–1181763.95	4.20
(7*S*,8*R*,13*S*,1′*R*,2′*S*)-**3**	5	–1883.2595864	–1181764.22	7.44
(7*S*,8*R*,13*S*,1′*R*,2′*S*)-**3**	6	–1883.2553047	–1181761.54	0.07
(7*S*,8*R*,13*S*,1′*R*,2′*S*)-**3**	7	–1883.2553621	–1181761.57	0.07

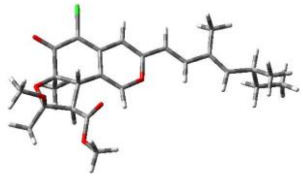
(7*R*,8*S*,13*S*,1′*S*,2′*R*)-**3**



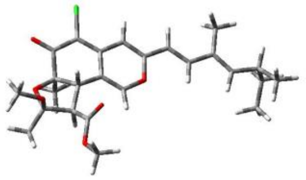
Conf.1 (53.09%)



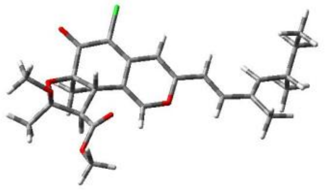
Conf.2 (17.89%)



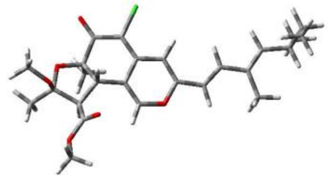
Conf.3 (21.85%)



Conf.4 (4.58%)

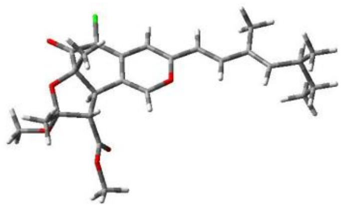


Conf.5 (0.08%)

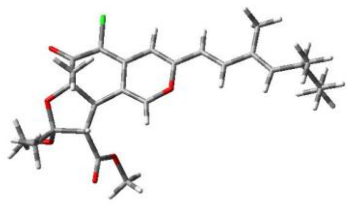


Conf.6 (2.52%)

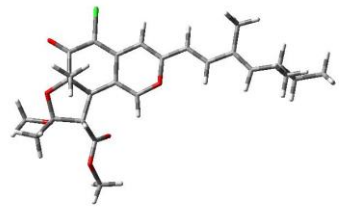
(7*S*,8*R*,13*S*,1′*R*,2′*S*)-**3**



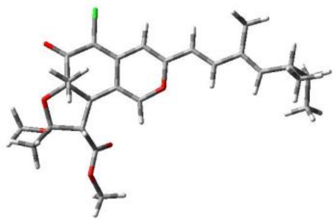
Conf.1 (49.05%)



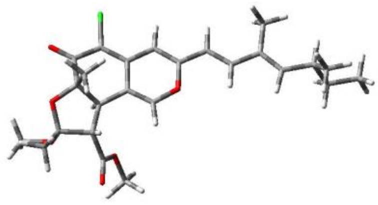
Conf.2 (17.75%)



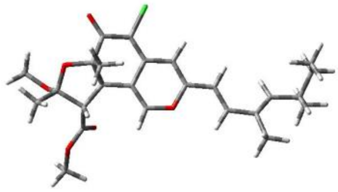
Conf.3 (21.41%)



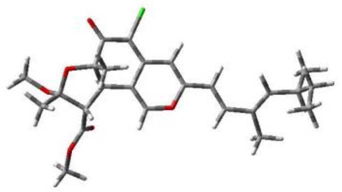
Conf.4 (4.20%)



Conf.5 (7.44%)



Conf.6 (0.07%)



Conf.7 (0.07%)

Figure S89. The optimized conformers and equilibrium populations of isochromophilone C (**3**)

Table S6. Energies of 4 at MMFF94 force field.

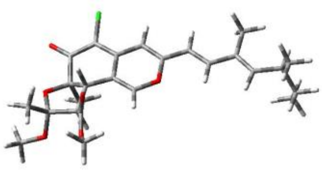
Configuration	Conformer	Energy (kcal/mol)	Population (%)
(7*R*,8*S*,13*S*,1′*R*,2′*R*)-**4**	1	226.33	48.5
(7*R*,8*S*,13*S*,1′*R*,2′*R*)-**4**	2	229.68	12.5
(7*R*,8*S*,13*S*,1′*R*,2′*R*)-**4**	3	230.76	8.1
(7*R*,8*S*,13*S*,1′*R*,2′*R*)-**4**	4	231.52	6.0
(7*R*,8*S*,13*S*,1′*R*,2′*R*)-**4**	5	231.78	5.4
(7*R*,8*S*,13*S*,1′*R*,2′*R*)-**4**	6	232.05	4.8

(7*R*,8*S*,13*S*,1′*R*,2′*R*)-**4**	7	232.28	4.4
(7*S*,8*R*,13*S*,1′*S*,2′*S*)-**4**	1	226.33	49.6
(7*S*,8*R*,13*S*,1′*S*,2′*S*)-**4**	2	229.68	12.8
(7*S*,8*R*,13*S*,1′*S*,2′*S*)-**4**	3	230.76	8.3
(7*S*,8*R*,13*S*,1′*S*,2′*S*)-**4**	4	231.57	6.0
(7*S*,8*R*,13*S*,1′*S*,2′*S*)-**4**	5	231.73	5.6
(7*S*,8*R*,13*S*,1′*S*,2′*S*)-**4**	6	232.08	4.9
(7*S*,8*R*,13*S*,1′*S*,2′*S*)-**4**	7	232.25	4.6

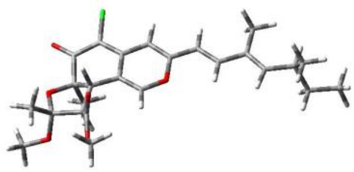
Table S7. Energies of **4** at B3LYP/6–31+g(d, p) level in methanol.

Configuration	Conformer	E (Hartree)	E (kcal/mol)	Population (%)
(7*R*,8*S*,13*S*,1′*R*,2′*R*)-**4**	1	–1883.2610978	–1181765.17	61.94
(7*R*,8*S*,13*S*,1′*R*,2′*R*)-**4**	2	–1883.2602894	–1181764.66	26.29
(7*R*,8*S*,13*S*,1′*R*,2′*R*)-**4**	3	–1883.2588291	–1181763.75	5.59
(7*R*,8*S*,13*S*,1′*R*,2′*R*)-**4**	4	–1883.2549615	–1181761.32	0.09
(7*R*,8*S*,13*S*,1′*R*,2′*R*)-**4**	5	–1883.2549735	–1181761.33	0.09
(7*R*,8*S*,13*S*,1′*R*,2′*R*)-**4**	6	–1883.2582402	–1181763.38	2.99
(7*R*,8*S*,13*S*,1′*R*,2′*R*)-**4**	7	–1883.2582402	–1181763.38	2.99
(7*S*,8*R*,13*S*,1′*S*,2′*S*)-**4**	1	–1883.2610907	–1181765.17	61.67
(7*S*,8*R*,13*S*,1′*S*,2′*S*)-**4**	2	–1883.2602977	–1181764.67	26.60
(7*S*,8*R*,13*S*,1′*S*,2′*S*)-**4**	3	–1883.2588443	–1181763.76	5.70
(7*S*,8*R*,13*S*,1′*S*,2′*S*)-**4**	4	–1883.2549643	–1181761.32	0.09
(7*S*,8*R*,13*S*,1′*S*,2′*S*)-**4**	5	–1883.2550169	–1181761.35	0.10
(7*S*,8*R*,13*S*,1′*S*,2′*S*)-**4**	6	–1883.2582135	–1181763.36	2.92
(7*S*,8*R*,13*S*,1′*S*,2′*S*)-**4**	7	–1883.2582135	–1181763.36	2.92

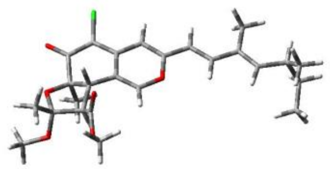
(7*R*,8*S*,13*S*,1′*R*,2′*R*)-**4**



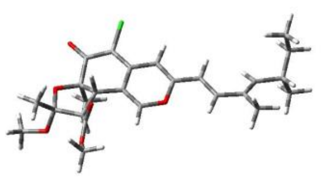
Conf.1 (61.94%)



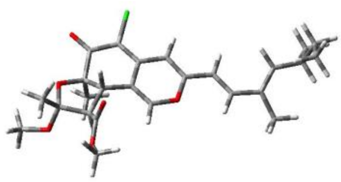
Conf.2 (26.29%)



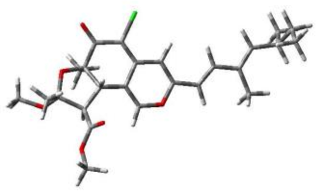
Conf.3 (5.59%)



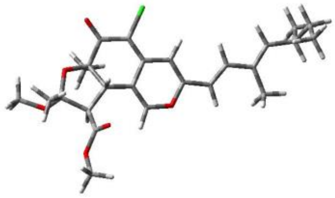
Conf.4 (0.09%)



Conf.5 (0.09%)

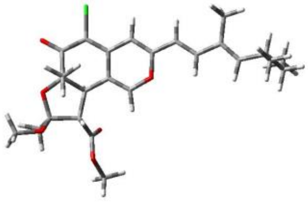


Conf.6 (2.99%)

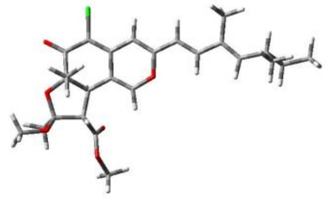


Conf.7 (2.99%)

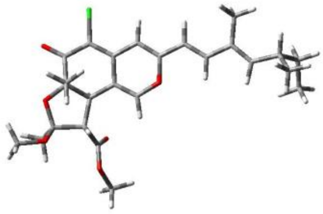
(7*S*,8*R*,13*S*,1′*S*,2′*S*)-**4**



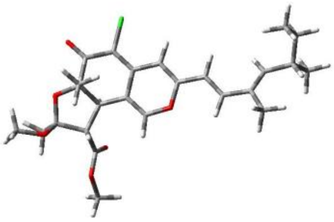
Conf.1 (61.67%)



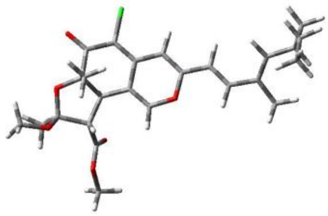
Conf.2 (26.60%)



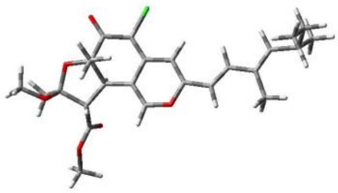
Conf.3 (5.70%)



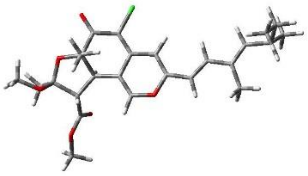
Conf.4 (0.09%)



Conf.5 (0.10%)



Conf.6 (2.92%)



Conf.7 (2.92%)

Figure S90. The optimized conformers and equilibrium populations of isochromophilone D (**4**)

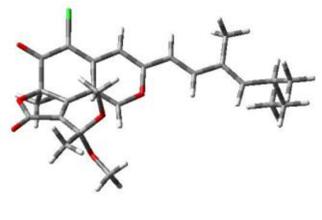
Table S8. Energies of 5 at MMFF94 force field.

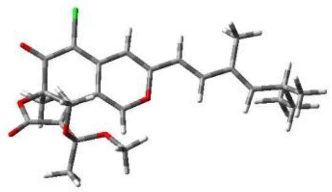
Configuration	Conformer	Energy (kcal/mol)	Population (%)
(7*R*,13*S*)-**5**	1	202.12	18.9
(7*R*,13*S*)-**5**	2	202.16	18.6
(7*R*,13*S*)-**5**	3	202.92	13.7
(7*R*,13*S*)-**5**	4	203.25	12.0
(7*R*,13*S*)-**5**	5	206.55	3.2
(7*R*,13*S*)-**5**	6	206.59	3.1
(7*S*,13*S*)-**5**	1	202.12	18.2
(7*S*,13*S*)-**5**	2	202.15	17.9
(7*S*,13*S*)-**5**	3	202.91	13.2
(7*S*,13*S*)-**5**	4	203.25	11.5
(7*S*,13*S*)-**5**	5	204.70	6.4
(7*S*,13*S*)-**5**	6	206.27	3.4

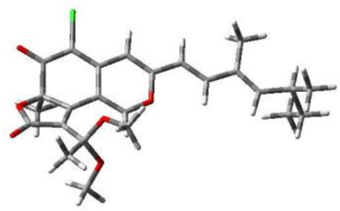
Table S9. Energies of 5 at B3LYP/6–31+g(d, p) level in methanol.

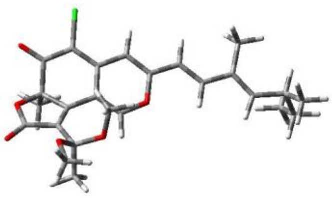
Configuration	Conformer	E (Hartree)	E (kcal/mol)	Population (%)
(7*R*,13*S*)-**5**	1	–1882.0381194	–1180997.74	2.36
(7*R*,13*S*)-**5**	2	–1882.0414787	–1180999.85	83.25
(7*R*,13*S*)-**5**	3	–1882.0375042	–1180997.35	1.23
(7*R*,13*S*)-**5**	4	–1882.0389323	–1180998.25	5.60
(7*R*,13*S*)-**5**	5	–1882.0357840	–1180996.27	0.20
(7*R*,13*S*)-**5**	6	–1882.0391901	–1180998.41	7.36
(7*S*,13*S*)-**5**	1	–1882.0381302	–1180997.75	1.12
(7*S*,13*S*)-**5**	2	–1882.0415116	–1180999.87	40.29
(7*S*,13*S*)-**5**	3	–1882.0374820	–1180997.34	0.56
(7*S*,13*S*)-**5**	4	–1882.039008	–1180998.30	2.84
(7*S*,13*S*)-**5**	5	–1882.0418043	–1181000.05	54.95
(7*S*,13*S*)-**5**	6	–1882.0366723	–1180996.83	0.24

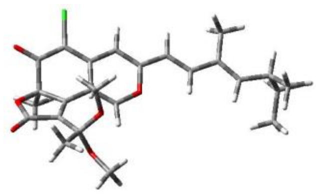
(7*R*,13*S*)-**5**

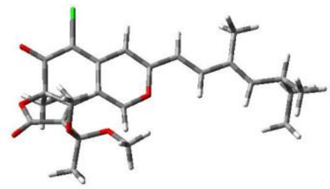

Conf.1 (2.36%)


Conf.2 (83.25%)

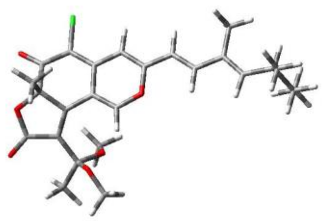

Conf.3 (1.23%)

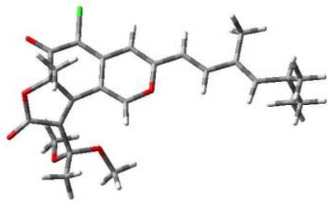

Conf.4 (5.60%)

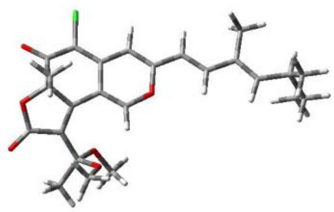

Conf.5 (0.20%)

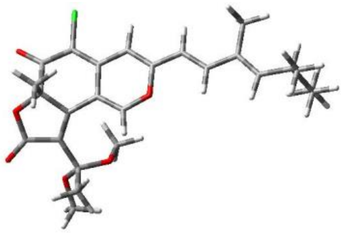

Conf.6 (7.36%)

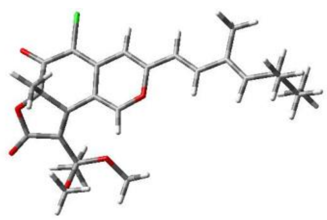
(7*S*,13*S*)-**5**

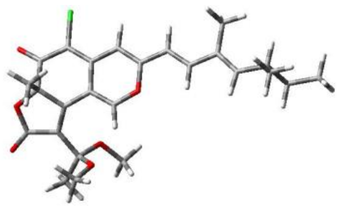

Conf.1 (1.12%)


Conf.2 (40.29%)


Conf.3 (0.56%)







Conf.4 (2.84%) Conf.5 (54.95%) Conf.5 (0.24%)

Figure S91. The optimized conformers and equilibrium populations of isochromophilone E (**5**)

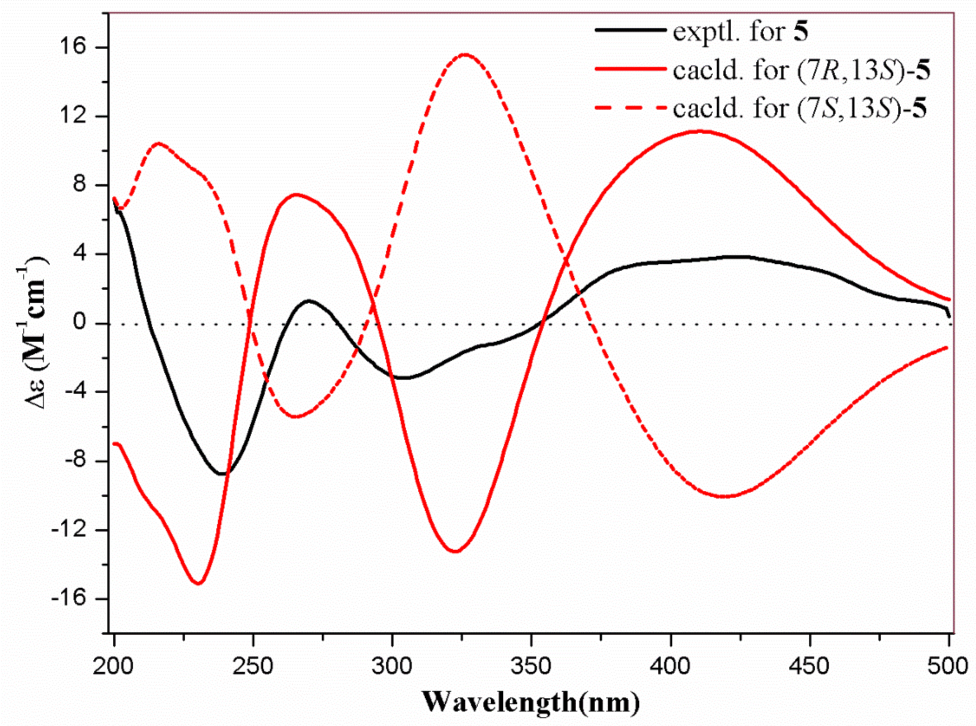


Figure S92. Experimental and calculated ECD spectra of compound **5**

Table S10. Energies of 6 at MMFF94 force field.

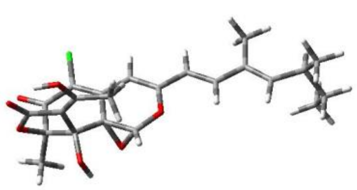
Configuration	Conformer	Energy (kcal/mol)	Population (%)
(1*R*,7*R*,8*S*,8a*S*,13*S*)-**6**	1	304.64	47.3
(1*R*,7*R*,8*S*,8a*S*,13*S*)-**6**	2	307.99	12.2
(1*R*,7*R*,8*S*,8a*S*,13*S*)-**6**	3	309.07	7.9
(1*R*,7*R*,8*S*,8a*S*,13*S*)-**6**	4	309.37	7.0
(1*R*,7*R*,8*S*,8a*S*,13*S*)-**6**	5	309.76	6.0
(1*R*,7*R*,8*S*,8a*S*,13*S*)-**6**	6	309.79	5.9
(1*R*,7*R*,8*S*,8a*S*,13*S*)-**6**	7	312.41	2.1
(1*S*,7*R*,8*R*,8a*R*,13*S*)-**6**	1	362.71	48.1
(1*S*,7*R*,8*R*,8a*R*,13*S*)-**6**	2	366.07	12.5
(1*S*,7*R*,8*R*,8a*R*,13*S*)-**6**	3	367.14	8.1
(1*S*,7*R*,8*R*,8a*R*,13*S*)-**6**	4	367.79	6.2
(1*S*,7*R*,8*R*,8a*R*,13*S*)-**6**	5	368.12	5.4
(1*S*,7*R*,8*R*,8a*R*,13*S*)-**6**	6	368.49	4.7
(1*S*,7*R*,8*R*,8a*R*,13*S*)-**6**	7	368.98	3.8
(1*R*,7*R*,8*R*,8a*S*,13*S*)-**6**	1	362.46	23.2
(1*R*,7*R*,8*R*,8a*S*,13*S*)-**6**	2	362.72	21.0
(1*R*,7*R*,8*R*,8a*S*,13*S*)-**6**	3	364.50	10.2
(1*R*,7*R*,8*R*,8a*S*,13*S*)-**6**	4	365.82	6.0
(1*R*,7*R*,8*R*,8a*S*,13*S*)-**6**	5	366.89	3.9
(1*R*,7*R*,8*R*,8a*S*,13*S*)-**6**	6	366.90	3.9

(1*S*,7*R*,8*S*,8a*R*,13*S*)-**6**	1	308.06	43.3
(1*S*,7*R*,8*S*,8a*R*,13*S*)-**6**	2	311.42	11.2
(1*S*,7*R*,8*S*,8a*R*,13*S*)-**6**	3	312.50	7.2
(1*S*,7*R*,8*S*,8a*R*,13*S*)-**6**	4	312.52	7.2
(1*S*,7*R*,8*S*,8a*R*,13*S*)-**6**	5	312.88	6.2
(1*S*,7*R*,8*S*,8a*R*,13*S*)-**6**	6	313.05	5.8

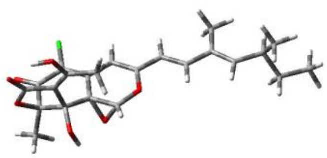
Table S11. Energies of 6 at B3LYP/6–31+g(d, p) level in methanol.

Configuration	Conformer	E (Hartree)	Energy (kcal/mol)	Population (%)
(1*R*,7*R*,8*S*,8a*S*,13*S*)-**6**	1	–1878.6417771	–1178866.50	58.32
(1*R*,7*R*,8*S*,8a*S*,13*S*)-**6**	2	–1878.6409624	–1178865.99	24.59
(1*R*,7*R*,8*S*,8a*S*,13*S*)-**6**	3	–1878.6394371	–1178865.03	4.88
(1*R*,7*R*,8*S*,8a*S*,13*S*)-**6**	4	–1878.6382607	–1178864.29	1.40
(1*R*,7*R*,8*S*,8a*S*,13*S*)-**6**	5	–1878.6354888	–1178862.56	0.07
(1*R*,7*R*,8*S*,8a*S*,13*S*)-**6**	6	–1878.6354791	–1178862.55	0.07
(1*R*,7*R*,8*S*,8a*S*,13*S*)-**6**	7	–1878.6401748	–1178865.50	10.67
(1*S*,7*R*,8*R*,8a*R*,13*S*)-**6**	1	–1878.6228859	–1178854.65	64.19
(1*S*,7*R*,8*R*,8a*R*,13*S*)-**6**	2	–1878.6220782	–1178854.14	27.27
(1*S*,7*R*,8*R*,8a*R*,13*S*)-**6**	3	–1878.6206160	–1178853.22	5.79
(1*S*,7*R*,8*R*,8a*R*,13*S*)-**6**	4	–1878.6167305	–1178850.78	0.09
(1*S*,7*R*,8*R*,8a*R*,13*S*)-**6**	5	–1878.6167063	–1178850.77	0.09
(1*S*,7*R*,8*R*,8a*R*,13*S*)-**6**	6	–1878.6191962	–1178852.33	1.28
(1*S*,7*R*,8*R*,8a*R*,13*S*)-**6**	7	–1878.6191951	–1178852.33	1.28
(1*R*,7*R*,8*R*,8a*S*,13*S*)-**6**	1	–1878.6228295	–1178854.61	28.79
(1*R*,7*R*,8*R*,8a*S*,13*S*)-**6**	2	–1878.6228298	–1178854.61	28.80
(1*R*,7*R*,8*R*,8a*S*,13*S*)-**6**	3	–1878.6226870	–1178854.52	24.75
(1*R*,7*R*,8*R*,8a*S*,13*S*)-**6**	4	–1878.6220360	–1178854.11	12.41
(1*R*,7*R*,8*R*,8a*S*,13*S*)-**6**	5	–1878.6205873	–1178853.20	2.67
(1*R*,7*R*,8*R*,8a*S*,13*S*)-**6**	6	–1878.6205543	–1178853.18	2.58
(1*S*,7*R*,8*S*,8a*R*,13*S*)-**6**	1	–1878.6379530	–1178864.10	51.29
(1*S*,7*R*,8*S*,8a*R*,13*S*)-**6**	2	–1878.6371254	–1178863.58	21.33
(1*S*,7*R*,8*S*,8a*R*,13*S*)-**6**	3	–1878.6356408	–1178862.65	4.42
(1*S*,7*R*,8*S*,8a*R*,13*S*)-**6**	4	–1878.6371407	–1178863.59	21.68
(1*S*,7*R*,8*S*,8a*R*,13*S*)-**6**	5	–1878.6344212	–1178861.88	1.21
(1*S*,7*R*,8*S*,8a*R*,13*S*)-**6**	6	–1878.6315568	–1178860.09	0.06

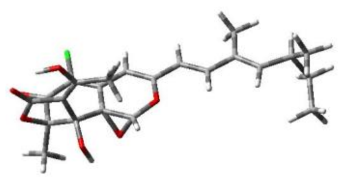
(1*R*,7*R*,8*S*,8a*S*,13*S*)-**6**



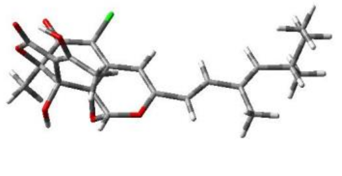
Conf.1 (58.32%)



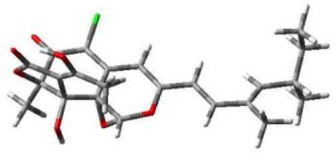
Conf.2 (24.59%)



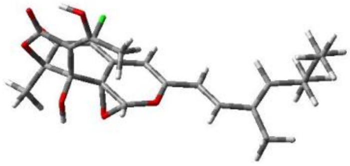
Conf.3 (4.88%)



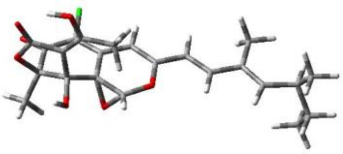
Conf.4 (1.40%)



Conf.5 (0.07%)

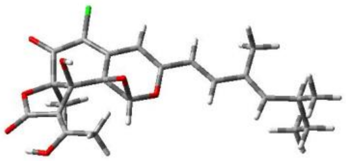


Conf.6 (0.07%)

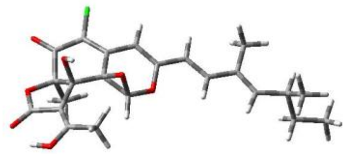


Conf.7 (10.67%)

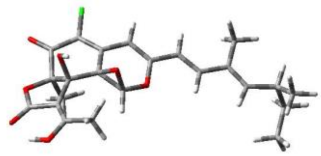
(1*S*,7*R*,8*R*,8a*R*,13*S*)-**6**



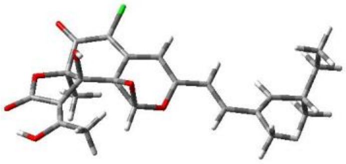
Conf.1 (64.19%)



Conf.2 (27.27%)

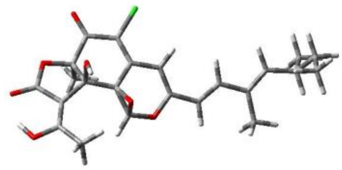


Conf.3 (5.79%)



Conf.4 (0.09%)

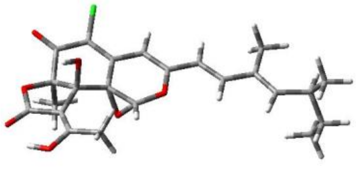
Conf.5 (0.09%)



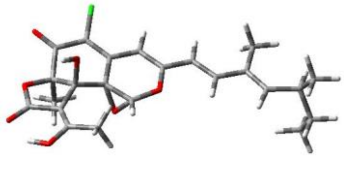
Conf.6 (1.28%)

Conf.7 (1.28%)

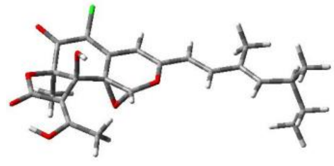
(1*R*,7*R*,8*R*,8a*S*,13*S*)-**6**



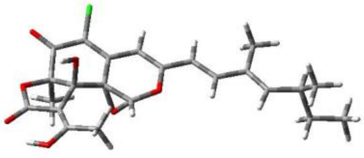
Conf.1 (28.79%)

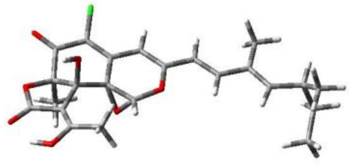


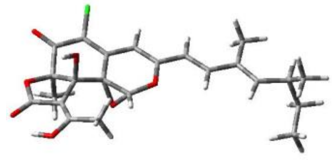
Conf.2 (28.80%)



Conf.3 (24.75%)

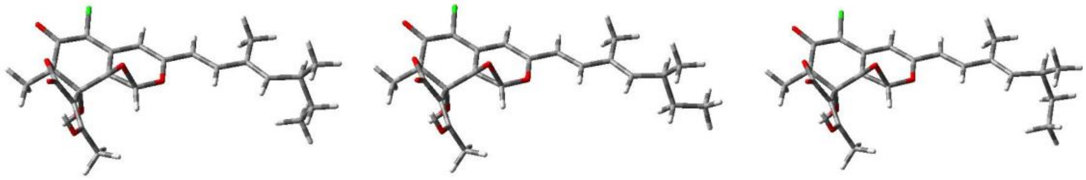




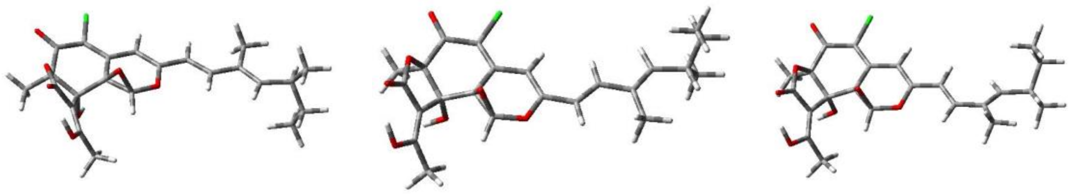


Conf.4 (12.41%) Conf.5 (2.67%) Conf.6 (2.58%)

(1*S*,7*R*,8*S*,8a*R*,13*S*)-**6**



Conf.1 (51.29%) Conf.2 (21.33%) Conf.3 (4.42%)



Conf.4 (21.68%) Conf.5 (1.21%) Conf.6 (0.06%)

Figure S93. The optimized conformers and equilibrium populations of isochromophilone F (**6**)

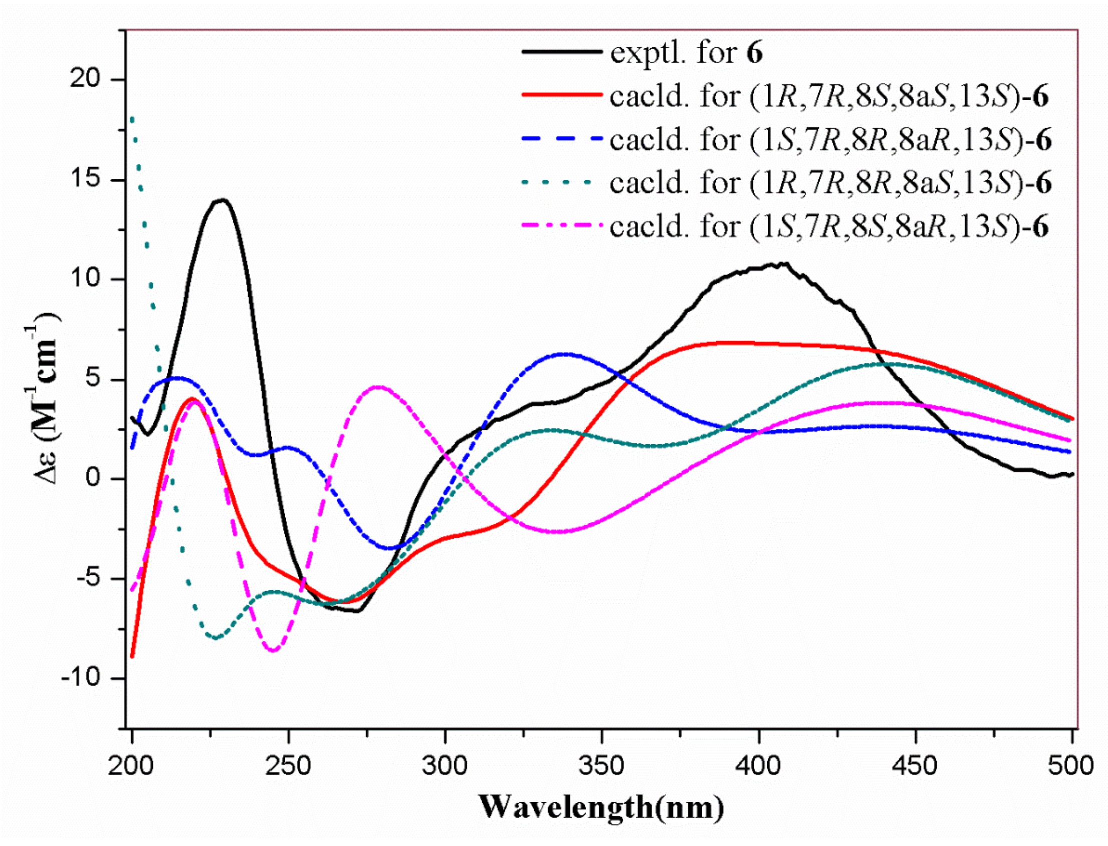


Figure S94. Experimental and calculated ECD spectra of compound **6**

Table S12. Specific data of the half-bandwidth and UV shifts for compounds 1, 3–6

Compounds	Half-bandwidth (eV)	UV shift (nm)
1	0.35	–20
3	0.30	+10
4	0.30	+10

5	0.30	–20
6	0.40	0

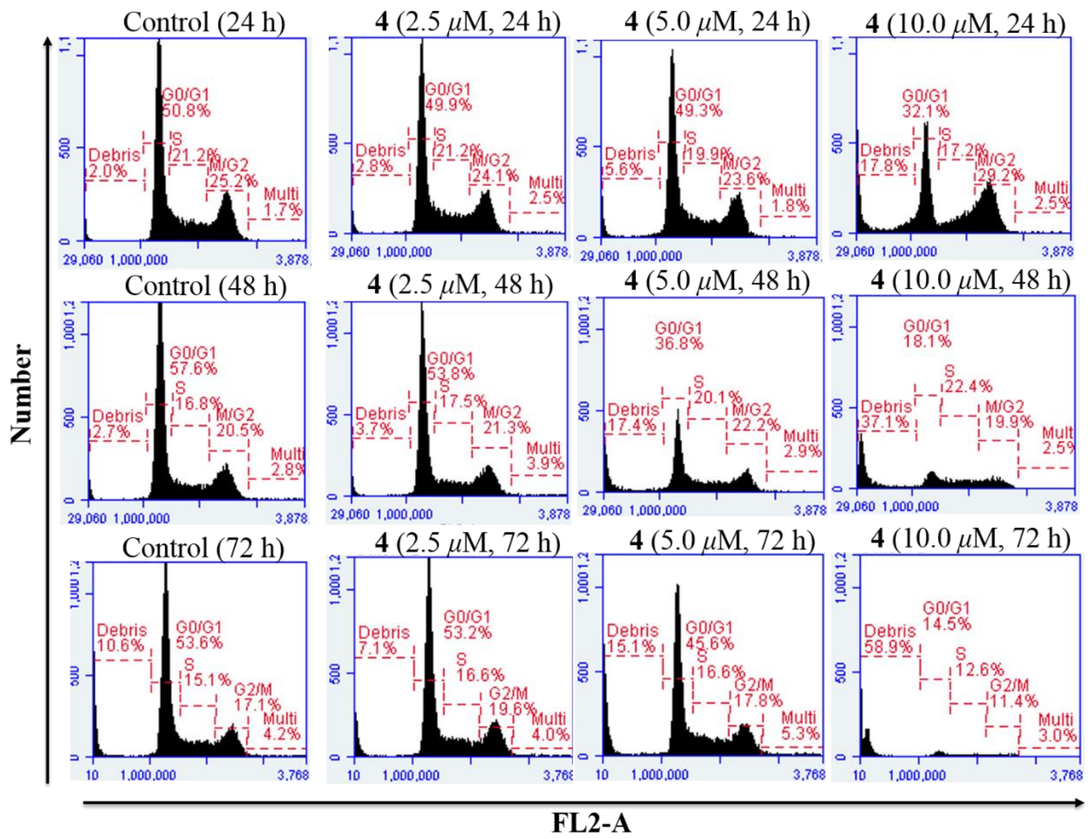


Figure S95. Effects of isochromophilone D (**4**) on cell cycle in 786-O cells.

The physicochemical data of the known compounds 7–12

5-chloroisorotiorin (7): yellow solid; $[\alpha]_D^{25}$ + 403 (c 0.10, MeOH), literature $[\alpha]_D^{20}$ + 405 (c 0.02, $CHCl_3$);[1] ^{1}H NMR (500 MHz, CD_3OD): 8.89 (1H, s, H-1), 6.80 (1H, s, H-4), 6.34 (1H, d, J = 16.0 Hz, H-9), 7.18 (1H, d, J = 16.0 Hz, H-10), 5.75 (1H, d, J = 9.8 Hz, H-12), 2.55 (1H, m, H-13), 1.48 (1H, m, H-14a), 1.37 (1H, m, H-14b), 0.90 (3H, t, J = 7.6 Hz, H_3-15), 1.06 (3H, d, J = 6.3 Hz, H_3-16), 1.89 (3H, s, H_3-17), 1.69 (3H, s, H_3-18), 2.58 (3H, s, H_3-4′); ^{13}C NMR (125 MHz, CD_3OD): 154.0 (qC, C-1), 160.0 (qC, C-3), 106.9 (CH, C-4), 142.2 (qC, C-4a), 118.8 (qC, C-5), 185.2 (qC, C-6), 88.6 (qC, C-7), 164.8 (qC, C-8), 111.4 (qC, C-8a), 117.4 (CH, C-9), 144.4 (CH, C-10), 133.8 (qC, C-11), 149.8 (CH, C-12), 36.3 (CH, C-13), 31.2 (CH_2, C-14), 12.3 (CH_3, C-15), 20.5 (CH_3, C-16), 12.5 (CH_3, C-17), 26.4 (CH_3, C-18), 169.6 (qC, C-1′), 124.7 (qC, C-2′), 195.2 (qC, C-3′), 30.0 (CH_3, C-4′); LRESIMS m/z 415.2 $[M+H]^+$, 417.2 $[M+H+2]^+$; 437.2 $[M+Na]^+$, 439.2 $[M+Na+2]^+$.

Epi-isochromophilone II (8): yellow solid; $[\alpha]_D^{25}$ + 350 (c 0.18, MeOH), literature $[\alpha]_D^{26}$ + 341 (c 0.15, $CHCl_3$);[2] ^{1}H NMR (700 MHz, CD_3OD): 7.22 (1H, s, H-1), 6.69 (1H, s, H-4), 3.62 (1H, overlapped, H-8), 6.31 (1H, d, J = 16.0 Hz, H-9), 7.10 (1H, d, J = 16.0 Hz, H-10), 5.68 (1H, d, J = 9.8 Hz, H-12), 2.53 (1H, m, H-13), 1.47 (1H, m, H-14a), 1.34 (1H, m, H-14b), 0.89 (3H, t, J = 7.0 Hz, H_3-15), 1.03 (3H, d, J = 7.0 Hz, H_3-16), 1.88 (3H, s, H_3-17), 1.15 (3H, s, H_3-18), 3.12 (1H, dd, J = 2.8, 16.8 Hz, H-1′a), 2.91 (1H, dd, J = 9.8, 16.8 Hz, H-1′b), 2.27 (3H, s, H_3-3′) ; ^{13}C NMR (175

MHz, CD_3OD): 145.8 (CH, C-1), 159.7 (qC, C-3), 105.8 (CH, C-4), 144.5 (qC, C-4a), 109.4 (qC, C-5), 193.5 (qC, C-6), 75.7 (qC, C-7), 41.5 (CH, C-8), 120.4 (qC, C-8a), 118.1 (CH, C-9), 142.7 (CH, C-10), 133.7 (qC, C-11), 148.0 (CH, C-12), 36.2 (CH, C-13), 31.2 (CH_2, C-14), 12.3 (CH_3, C-15), 20.9 (CH_3, C-16), 12.5 (CH_3, C-17), 20.6 (CH_3, C-18), 40.6 (CH_2, C-1′), 209.2 (qC, C-2′), 30.0 (CH_3, C-3′); HRESIMS *m/z* 413.1494 $[M+Na]^+$ (calcd for $C_{22}H_{27}ClNaO_4^+$, 413.1496), 803.3091 $[2M+Na]^+$ (calcd for $C_{44}H_{52}Cl_2NaO_8^+$, 803.3093).

*Isochromophilone III (**9**)*: yellow solid; $[\alpha]_D^{25}$ + 143 (*c* 0.05, MeOH), literature $[\alpha]_D$ + 150 (*c* 1.07, MeOH);[3] ^1H NMR (700 MHz, CD_3OD): 5.00 (1H, dd, *J* = 4.9, 11.2 Hz, H-1a), 4.80 (1H, dd, *J* = 11.2, 13.3 Hz, H-1b), 5.96 (1H, s, H-4), 3.90 (1H, d, *J* = 9.1 Hz, H-8), 4.73 (1H, d, *J* = 9.1 Hz, H-8a), 6.12 (1H, d, *J* = 16.0 Hz, H-9), 6.94 (1H, d, *J* = 16.0 Hz, H-10), 5.58 (1H, d, *J* = 9.8 Hz, H-12), 2.48 (1H, m, H-13), 1.43 (1H, m, H-14a), 1.29 (1H, m, H-14b), 0.87 (3H, t, *J* = 7.6 Hz, H_3-15), 1.00 (3H, d, *J* = 7.2 Hz, H_3-16), 1.82 (3H, s, H_3-17), 1.25 (3H, s, H_3-18); ^{13}C NMR (175 MHz, CD_3OD): 64.7 (CH_2, C-1), 163.4 (qC, C-3), 104.3 (CH, C-4), 149.3 (qC, C-4a), 115.3 (qC, C-5), 197.7 (qC, C-6), 78.9 (qC, C-7), 80.0 (CH, C-8), 61.7 (CH, C-8a), 119.6 (CH, C-9), 142.1 (CH, C-10), 133.9 (qC, C-11), 147.1 (CH, C-12), 36.1 (CH, C-13), 31.2 (CH_2, C-14), 12.3 (CH_3, C-15), 20.7 (CH_3, C-16), 12.5 (CH_3, C-17), 19.1 (CH_3, C-18); LRESIMS *m/z* 353.2 $[M+H]^+$, 355.2 $[M+H+2]^+$; 375.2 $[M+Na]^+$, 377.2 $[M+Na+2]^+$.

*Epi-isochromophilone III (**10**)*: yellow solid; $[\alpha]_D^{25}$ + 56 (*c* 0.10, MeOH), literature $[\alpha]_D^{26.3}$ + 49 (*c* 0.11, MeOH);[4] ^1H NMR (700 MHz, CD_3OD): 4.56 (1H, dd, *J* = 4.9, 11.2 Hz, H-1a), 4.24 (1H, dd, *J* = 11.2, 13.3 Hz, H-1b), 6.13(1H, s, H-4), 4.04 (1H, d, *J* = 2.8 Hz, H-8), 3.19 (1H, overlapped, H-8a), 6.14 (1H, d, *J* = 16.0 Hz, H-9), 7.00 (1H, d, *J* = 16.0 Hz, H-10), 5.59 (1H, d, *J* = 9.8 Hz, H-12), 2.50 (1H, m, H-13), 1.44 (1H, m, H-14a), 1.30 (1H, m, H-14b), 0.88 (3H, t, *J* = 7.6 Hz, H_3-15), 1.01 (3H, d, *J* = 7.2 Hz, H_3-16), 1.90 (3H, s, H_3-17), 1.34 (3H, s, H_3-18); ^{13}C NMR (175 MHz, CD_3OD): 69.7 (CH_2, C-1), 164.0 (qC, C-3), 103.1 (CH, C-4), 146.5 (qC, C-4a), 117.4 (qC, C-5), 195.2 (qC, C-6), 79.1(qC, C-7), 75.8 (CH, C-8), 38.8 (CH, C-8a), 120.5 (CH, C-9), 142.2 (CH, C-10), 133.9 (qC, C-11), 147.1 (CH, C-12), 36.1 (CH, C-13), 31.3 (CH_2, C-14), 12.3 (CH_3, C-15), 20.7 (CH_3, C-16), 12.6 (CH_3, C-17), 23.7 (CH_3, C-18); LRESIMS *m/z* 353.2 $[M+H]^+$, 355.2 $[M+H+2]^+$; 375.2 $[M+Na]^+$, 377.2 $[M+Na+2]^+$.

*6-((1E,3E)-3,5-dimethylhepta-1,3-dien-1-yl)-2,4-dihydroxy-3-methylbenzaldehyde (**11**)*: pale yellow solid, ^1H NMR (700 MHz, CD_3OD): 6.82 (1H, d, *J* = 16.1 Hz, H-1), 6.55 (1H, d, *J* = 16.1 Hz, H-2), 5.35 (1H, d, *J* = 9.8 Hz, H-4), 2.39 (1H, m, H-5), 1.34 (1H, m, H-6a),1.21 (1H, m, H-6b), 0.78 (3H, t, *J* = 7.7 Hz, H_3-7), 0.90 (3H, d, *J* = 7.0 Hz, H_3-8), 1.79 (3H, s, H_3-9), 6.37 (H, s, H-6′), 9.97 (H, s, H-7′), 1.91 (3H, s, H_3-8′); ^{13}C NMR (175 MHz, CD_3OD): 121.3 (CH, C-1), 140.7 (CH, C-2), 134.0 (qC, C-3), 143.3 (CH, C-4), 35.8 (CH, C-5), 31.4 (CH_2, C-6), 12.4 (CH_3, C-7), 21.0 (CH_3, C-8), 12.9 (CH_3, C-9), 143.3 (qC, C-1′), 112.4 (qC, C-2′), 164.7 (qC, C-3′), 111.2 (CH, C-4′), 165.2 (qC, C-5′), 106.8 (CH, C-6′), 194.2 (CH, C-7′), 7.4 (CH_3, C-8′). LRESIMS *m/z* 273.1 $[M-H]^-$; 547.4 $[2M-H]^-$.

*(2E,4E)-1-(2,6-dihydroxy-3,5-dimethyl-phenyl)hexa-2,4-dien-1-one) (**12**)*: yellow solid, ^1H NMR (700 MHz, CD_3OD): 7.12 (1H, d, *J* = 14.7 Hz, H-2), 7.42 (1H, dd, *J* = 11.2, 14.7 Hz, H-3), 6.46 (1H, dd, *J* = 11.2, 14.7 Hz, H-4), 6.32 (1H, m, H-5), 1.91 (3H, d, *J* = 7.0 Hz, H_3-6), 7.55 (3H, s, H_3-

4′), 2.18 (3H, s, H_3-7′), 2.07 (3H, s, H_3-8′); ^{13}C NMR (175 MHz, CD_3OD): 193.8 (qC, C-1), 123.5 (CH, C-2), 145.2 (CH, C-3), 132.0 (CH, C-4), 141.6 (CH, C-5), 18.9 (CH_3, C-6), 113.8 (qC, C-1′), 162.7 (qC, C-2′), 117.4 (qC, C-3′), 130.0 (CH, C-4′), 112.0 (qC, C-5′), 163.7 (qC, C-6′), 16.4 (CH_3, C-7′), 8.0 (CH_3, C-8′).

Figure S96. The strain's (*Diaporthe* sp. SCSIO 41011) ITS sequence of the rDNA

>**ITS4** (GenBank no. MG548388)

TCTGCCGGGGATCTACTGATCCGAGGTCAATTTCAGAAGTTTGGGGGTTTTACGGCTGG
TCCGCCGGGGCCTTCCGGAGC
GAGGGTTTGACTACTGCGCTCGGGGTCCCGGTGGGCTCGCCGCTGAATTTGAGGGCCT
GCTCCTGGGTGTAGCAGTGCCC
CAACACCAAGCAGTGCTTGAGGGGTGAAATGACGCTCGAACAGGCATGCCCTCCGGA
ATGCCAGAGGGCGCAATGTGCGT
TCAAAGATTCGATGATTCACTGAATTCTGCAATTCACATTACTTATCGCATTTCGCTGCG
TTCTTCATCGATGCCAGAAC
CAAGAGATCCGTTGTTGAAAGTTTTGATTCATTTTGTATTGCTCAGAGTTTCAGTATAAA
AACAGAGTTGTTTTGGCCGC
CGGCGTGCCTTGTCCTCACCGGGGTGAGGGGCCTAAAGACCAGCAGCGCCGAGGCAA
CAGAGGTATGGTTCACATAGGGT
TTCTGGGTGCGCCGGGGCGCGTTCCAGCAATGATCCCTCCGCTGGTTCACCAACGGAG
ACCTTGTTACGACTTTTTACTTCCA

>**ITS5** (GenBank no. MG548389)

TACCTTTTGTACGCGGAGGGATCATTGCTGGACGCGCCCCGGCGCACCCAGAAACCCT
ATGTGAACCATACCTCTGTTGC
CTCGGCGCTGCTGGTCTTTAGGCCCCTCACCCCGGTGAGGACAAGGCACGCCGGCGG
CCAAAACAACTCTGTTTTTATAC
TGAAACTCTGAGCAATACAAAATGAATCAAAACTTTCAACAACGGATCTCTTGGTTCT
GGCATCGATGAAGAACGCAGCG
AAATGCGATAAGTAATGTGAATTGCAGAATTCAGTGAATCATCGAATCTTTGAACGCAC
ATTGCGCCCTCTGGCATTCCG
GAGGGCATGCCTGTTCGAGCGTCATTTCACCCCTCAAGCACTGCTTGGTGTTGGGGCA
CTGCTACACCCAGGAGCAGGCC
CTCAAATTCAGCGGCGAGCCCACCGGGACCCCGAGCGCAGTAGTCAAACCCTCGCTC
CGGAAGGCCCCGGCGGACCAGCC
GTAAAACCCCCAAACTTCTGAAATTTGACCTCGGATCAGGTAGGAATACCCGCTGAAC
TTAAGCATATCAATAAGCGGAGGAA

References

1. Chong, R.; King, R. R.; Whalley, W. B. *J. Chem. Soc. C: Org.* **1971**, 3566-3571.
2. Kanokmedhakul, S.; Kanokmedhakul, K.; Nasomjai, P.; Louangsysouphanh, S.; Soytong, K.; Isobe, M.; Kongsaeree, P.; Prabpai, S.; Suksamrarn, A. *J. Nat. Prod.* **2006,** 69, 891-895.
3. Arai, N.; Shiomi, K.; Tomoda, H.; Tabata, N.; Yang, D. J.; Masuma, R.; Kawakubo, T.; Omura, S. *J. Antibiot.* **1995,** 48, 696-702.
4. Hemtasin, C.; Kanokmedhakul, S.; Moosophon, P.; Soytong, K.; Kanokmedhakul, K. *Phytochem. Lett.* **2016,** 16, 56-60.