Anti-neuroinflammatory asarone derivatives from the rhizomes of *Acorus tatarinowii*

Da-Peng Qin,[‡a] Xiao-Lin Feng,[‡a] Wei-Yang Zhang,[d] Hao Gao,[a] Xiao-Rui Cheng,[c] Wen-Xia Zhou,[c] Yang Yu,[a, b*] and Xin-Sheng Yao[a*]

[a] *Institute of Traditional Chinese Medicine & Natural Products, College of Pharmacy, Jinan University, Guangzhou 510632, P. R. China. E-mail: 1018yuyang@163.com; tyaoxs@jnu.edu.cn. Tel (Fax): +86-20-85221559*

[b] *State Key Laboratory of Bioactive Substance and Function of Natural Medicines, Institute of Materia Medica, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing 100050, P. R. China*

[c] *Beijing Institute of Pharmacology and Toxicology, Tai Ping Road 27, Beijing 100850, P. R. China*

[d] *State Key Laboratory of Quality Research in Chinese Medicine, Macau University of Science and Technology, Macau, P. R. China*

List of Supporting Information

UV, IR, HR-ESI-MS spectrum and NMR spectra of **1**.....1

UV, IR, HR-ESI-MS spectrum and NMR spectra of **2**.....5

UV, IR, HR-ESI-MS spectrum and NMR spectra of **3**.....8

UV, IR, HR-ESI-MS spectrum and NMR spectra of **4**.....12

UV, IR, HR-ESI-MS spectrum and NMR spectra of **5**.....15

UV, IR, HR-ESI-MS spectrum and NMR spectra of **6**.....18

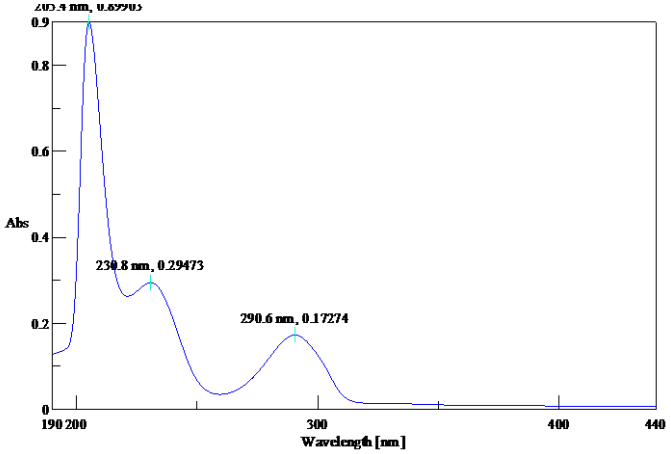
UV, IR, HR-ESI-MS spectrum and NMR spectra of **7**.....22

Chiral HPLC analytical chromatograms of compounds **2, 3, 7, 8, 14**.....26

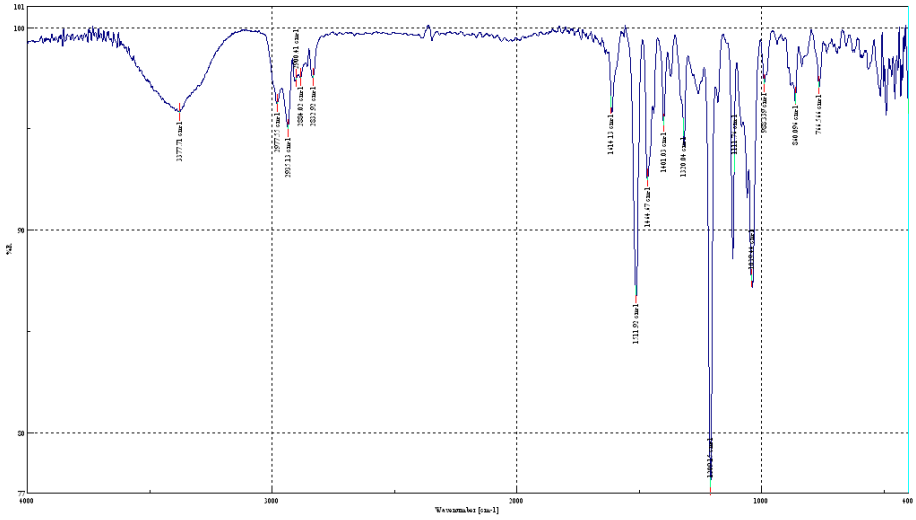
Purity of compound.....28

ECD spectrum of **8** and **14**.....28

UV spectrum of meso-asarolignan A (1) in CH_3OH.

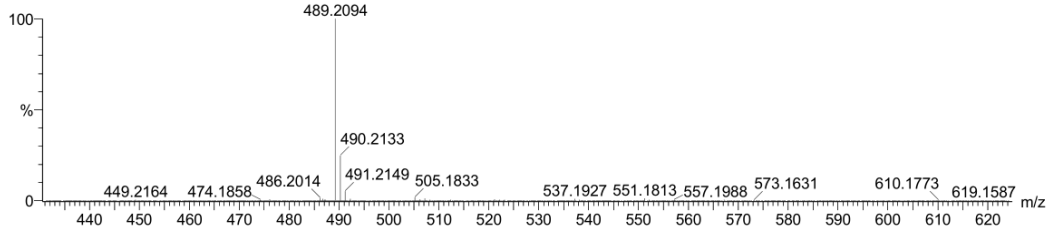


IR (KBr disc) spectrum of meso-asarolignan A (1).



HR-ESI-MS spectrum of meso-asarolignan A (1).

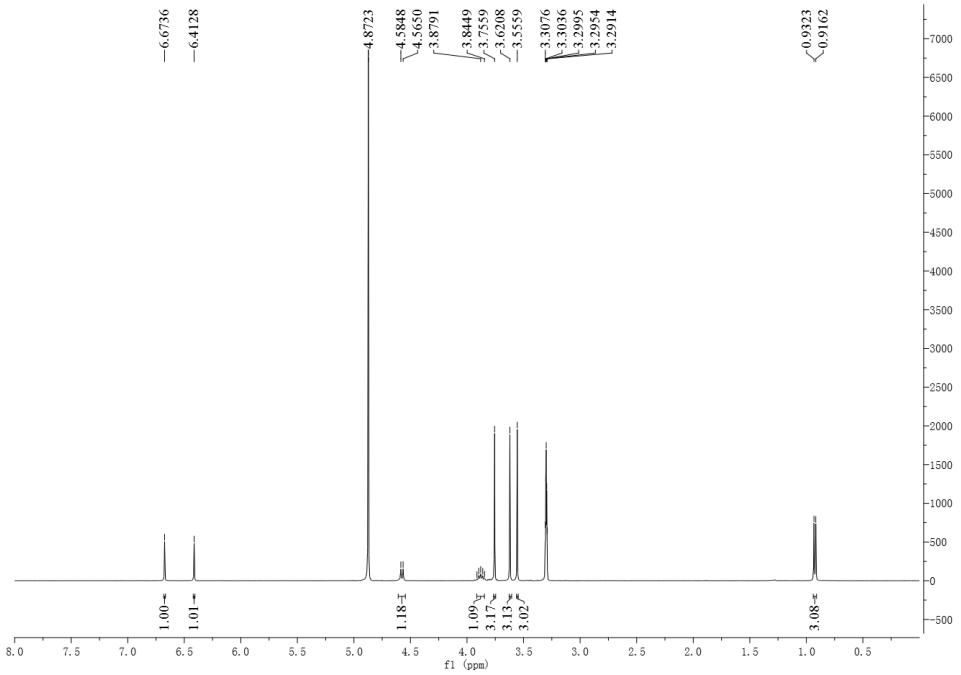
Monoisotopic Mass, Even Electron Ions
228 formula(e) evaluated with 1 results within limits (up to 50 closest results for each mass)
Elements Used:
C: 0-200 H: 0-1000 O: 0-200 Na: 0-1
AT-E2-(5-6)-17
20121126-11 109 (0.894) Cm (99:116)



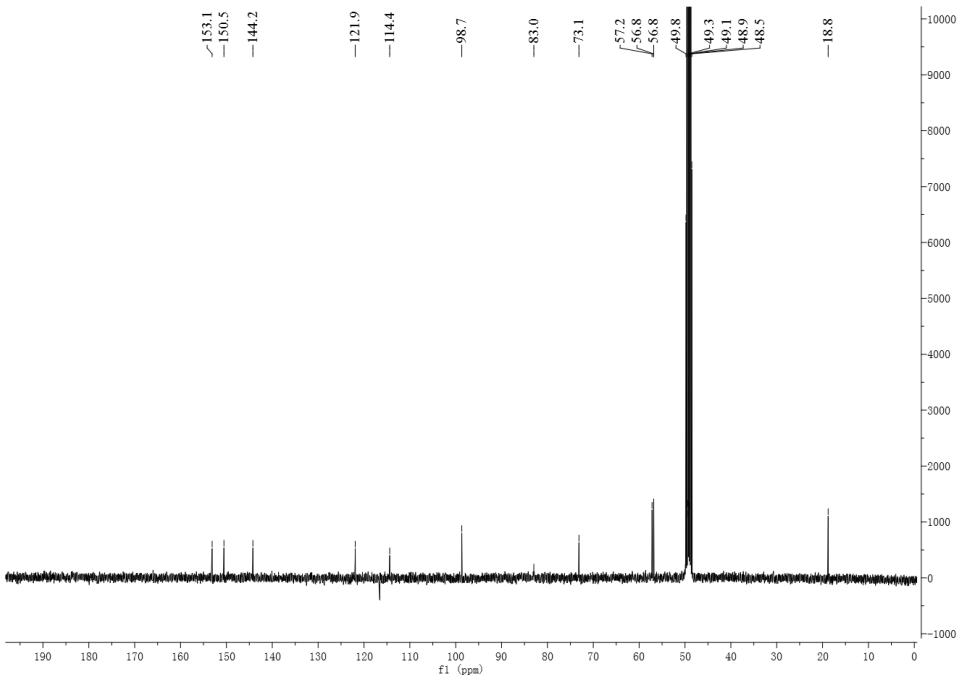
Minimum:				-1.5				
Maximum:		5.0	5.0	50.0				
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf(%)	Formula
489.2094	489.2101	-0.7	-1.4	7.5	510.4	n/a	n/a	C24 H34 O9 Na

The 1D and 2D NMR spectra of *meso*-asarolignan A (1)

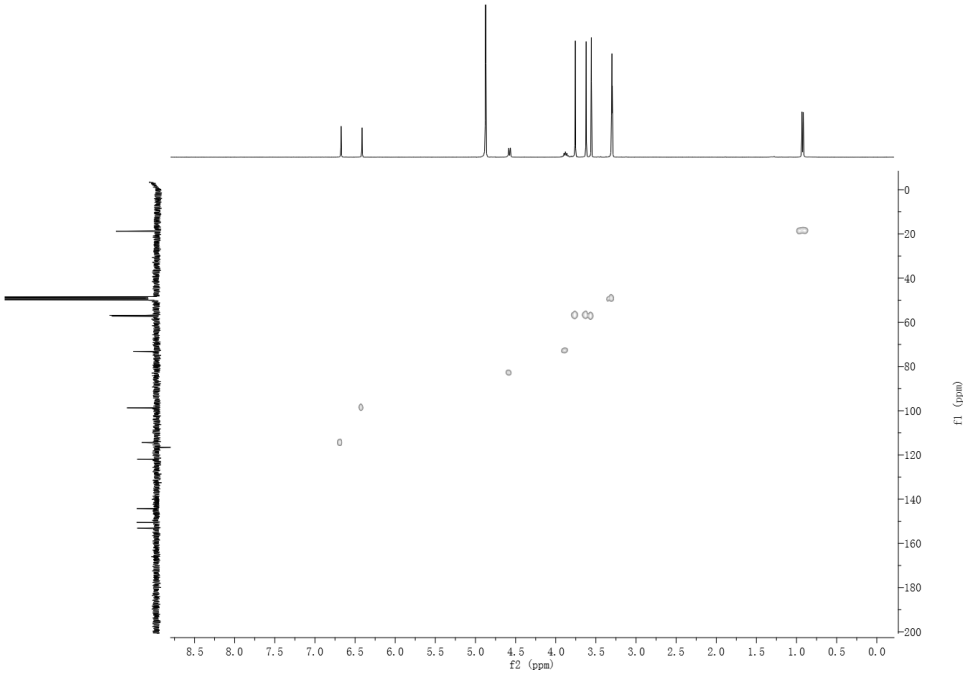
^{1}H NMR spectrum (AV-400, 400 MHz) of *meso*-asarolignan A (1) in CD_3OD



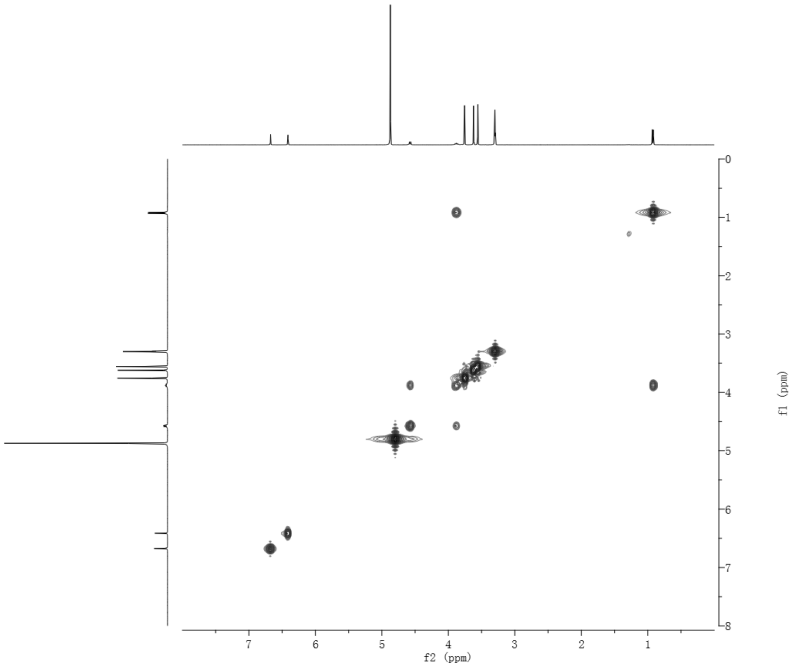
^{13}C NMR spectrum (AV-400, 100 MHz) of *meso*-asarolignan A (1) in CD_3OD



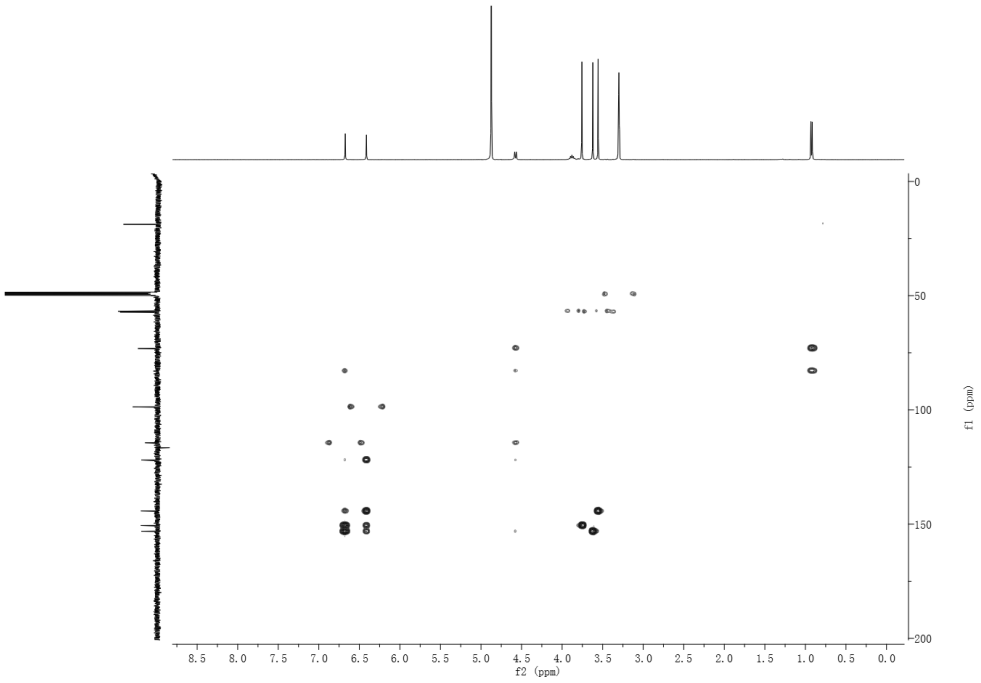
HSQC spectrum (AV-400) of *meso*-asarolignan A (1) in CD_3OD



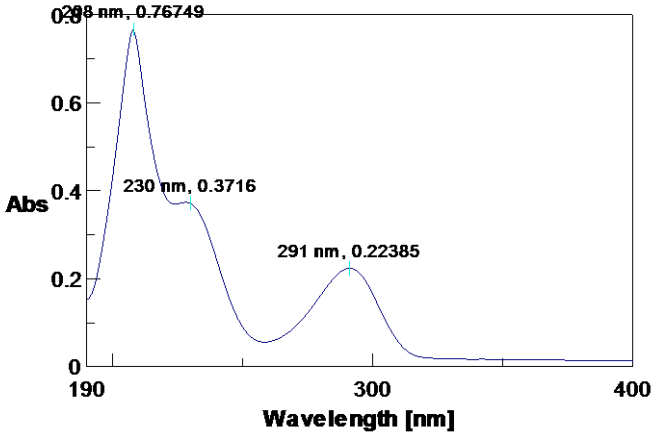
^{1}H-^{1}H COSY spectrum (AV-400) of *meso*-asarolignan A (1) in CD_3OD



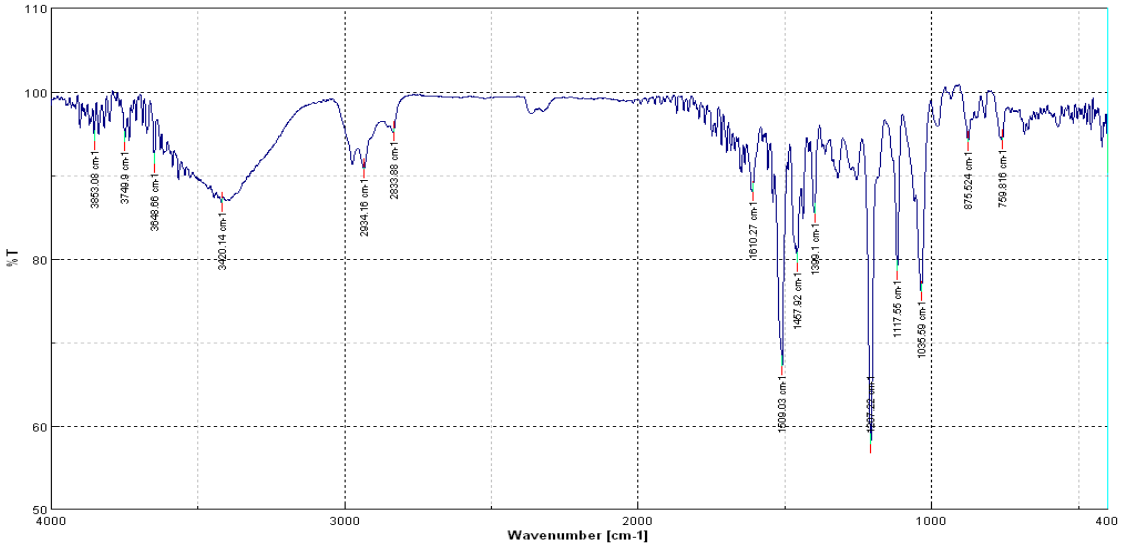
HMBC spectrum (AV-400) of *meso*-asarolignan A (1) in CD_3OD



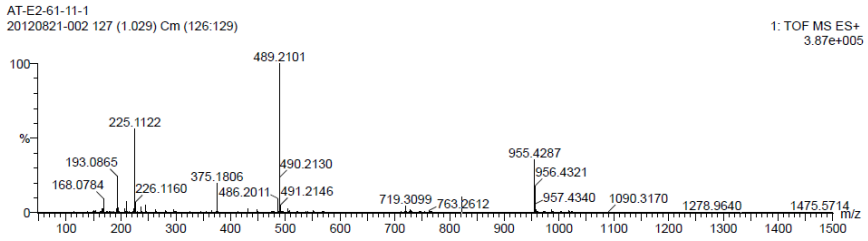
UV spectrum of (±)-asarolignan B (2) inCH_3OH.



IR (KBr disc) spectrum of (±)-asarolignan B (2).



HR-ESI-MS spectrum of (±)-asarolignan B (2).

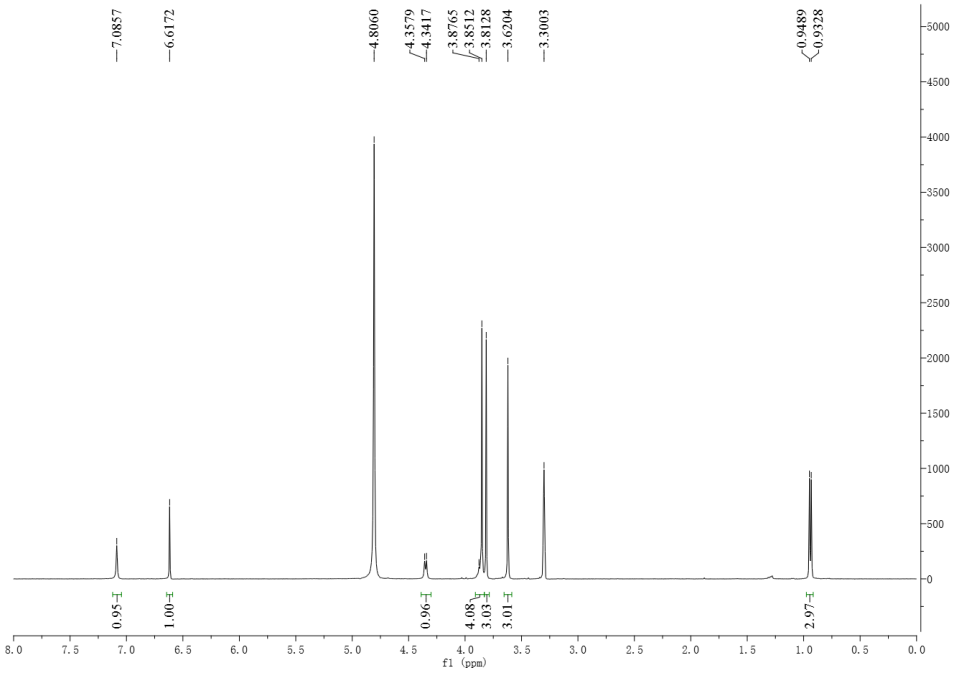


Minimum: -1.5
Maximum: 5.0 5.0 50.0

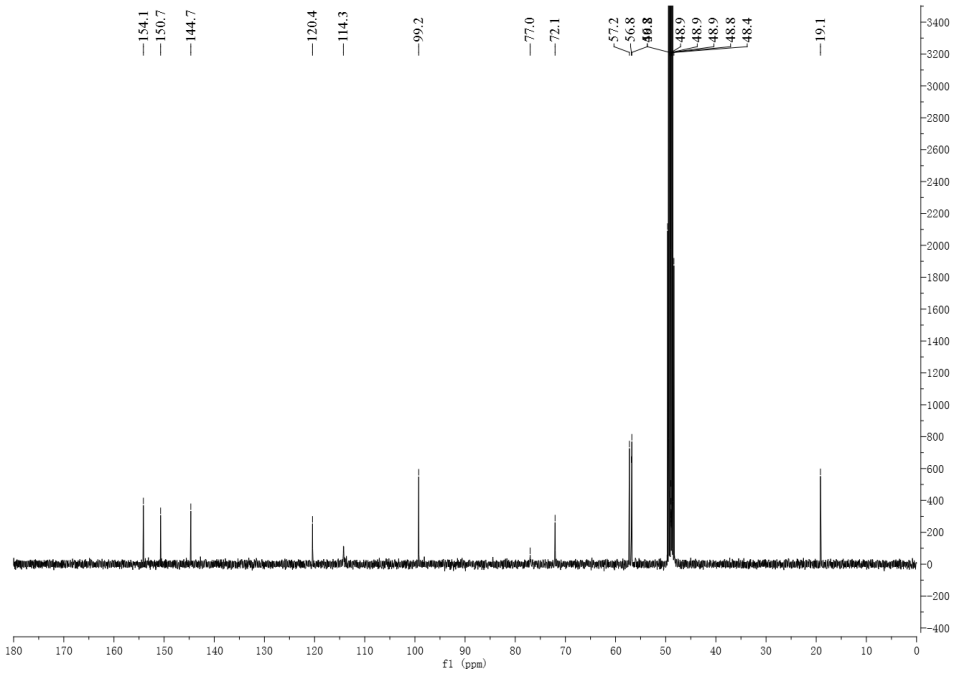
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf(%)	Formula
489.2101	489.2101	0.0	0.0	7.5	291.2	0.015	98.50	C24 H34 O9 Na
	489.2125	-2.4	-4.9	10.5	295.4	4.202	1.50	C26 H33 O9

The 1D and 2D NMR spectra of (±)-asarolignan B (2)

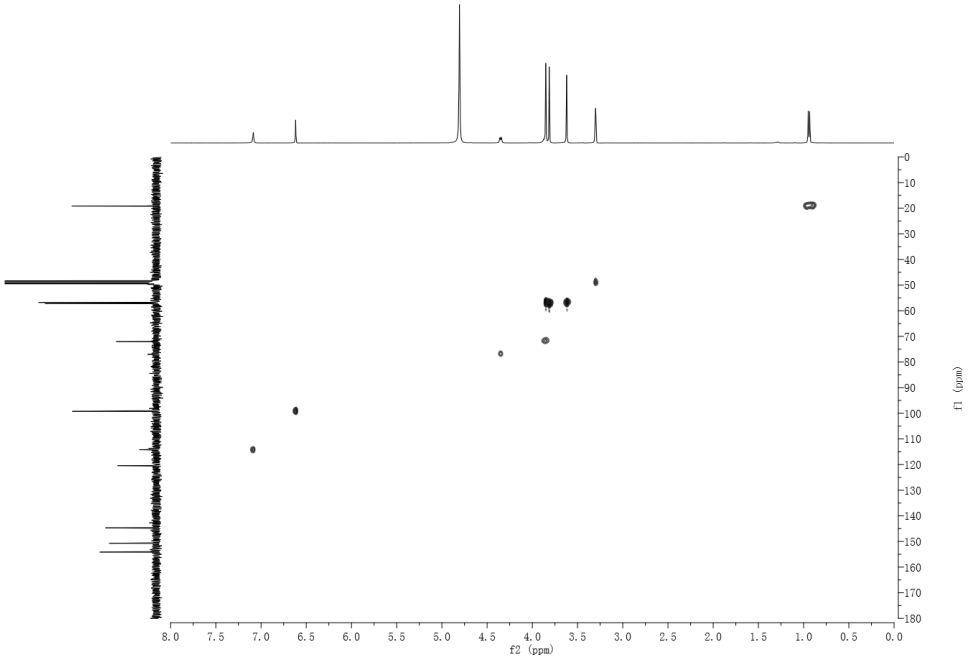
^{1}H NMR spectrum (AV-400, 400 MHz) of (±)-asarolignan B (2) in CD_3OD



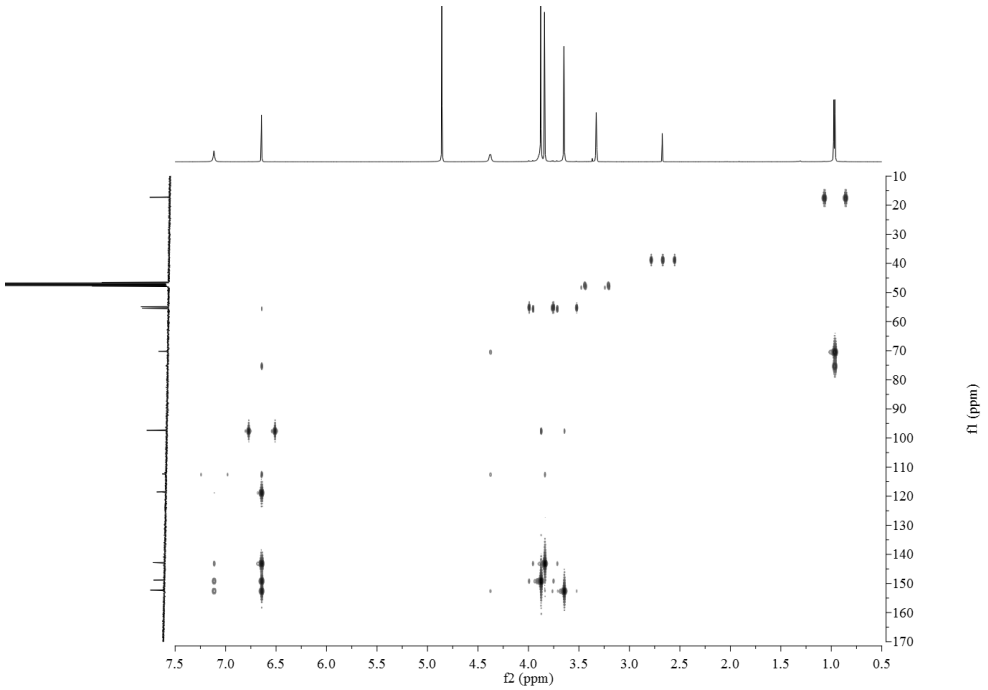
^{13}C NMR spectrum (AV-400, 100 MHz) of (±)-asarolignan B (2) in CD_3OD



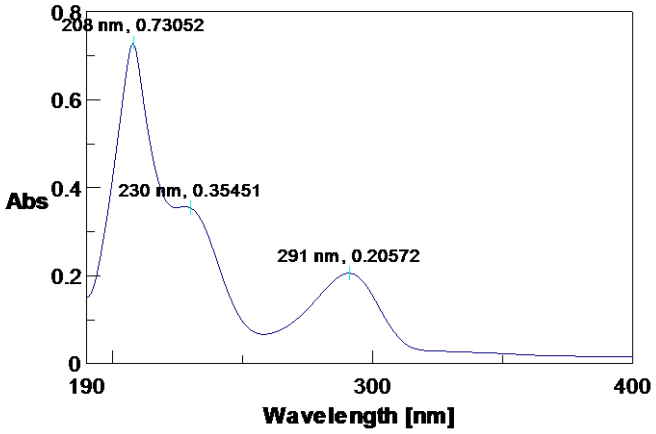
HSQC spectrum (AV-400) of (±)-asarolignan B (2) in CD_3OD



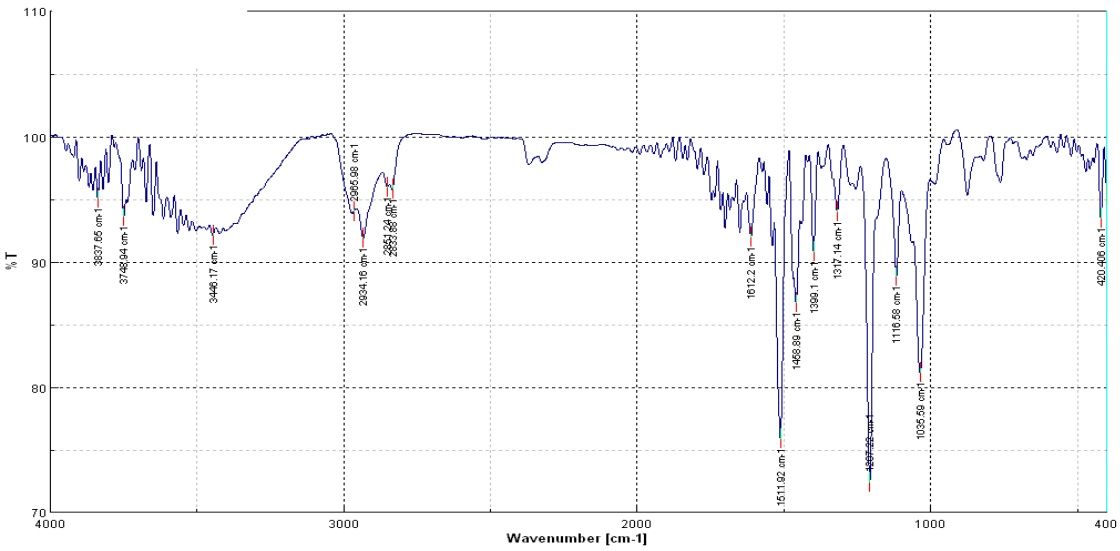
HMBC spectrum(AV-400) of (±)-asarolignan B (2) in CD_3OD



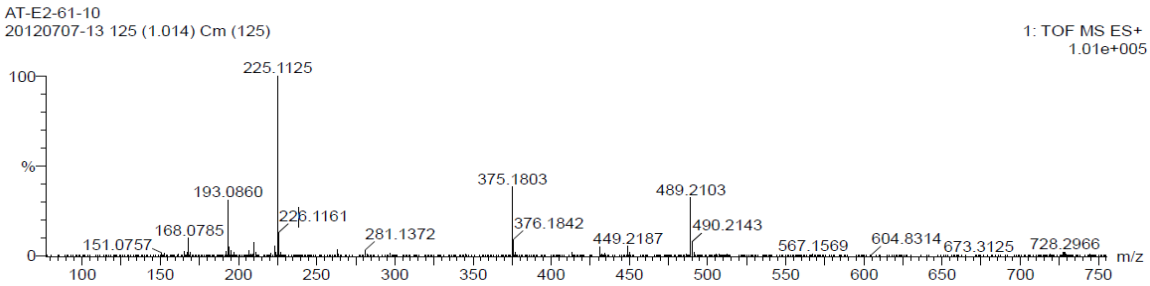
UV spectrum of (±)-asarolignan C (3) in CH_3OH



IR (KBr disc) spectrum of (±)-asarolignan C (3).



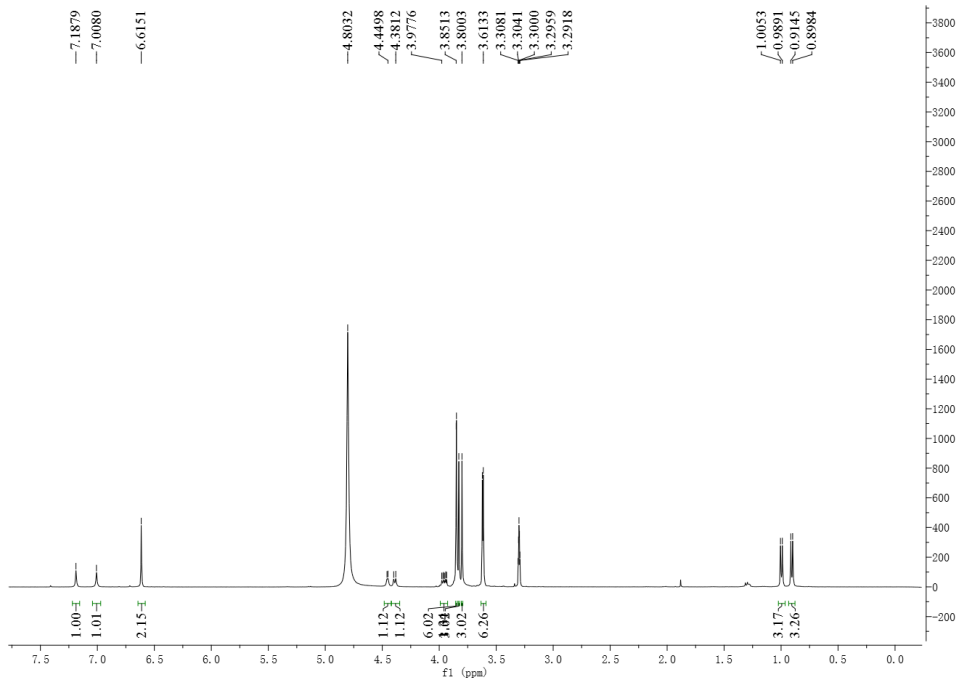
HR-ESI-MS spectrum of (±)-asarolignan C (3).



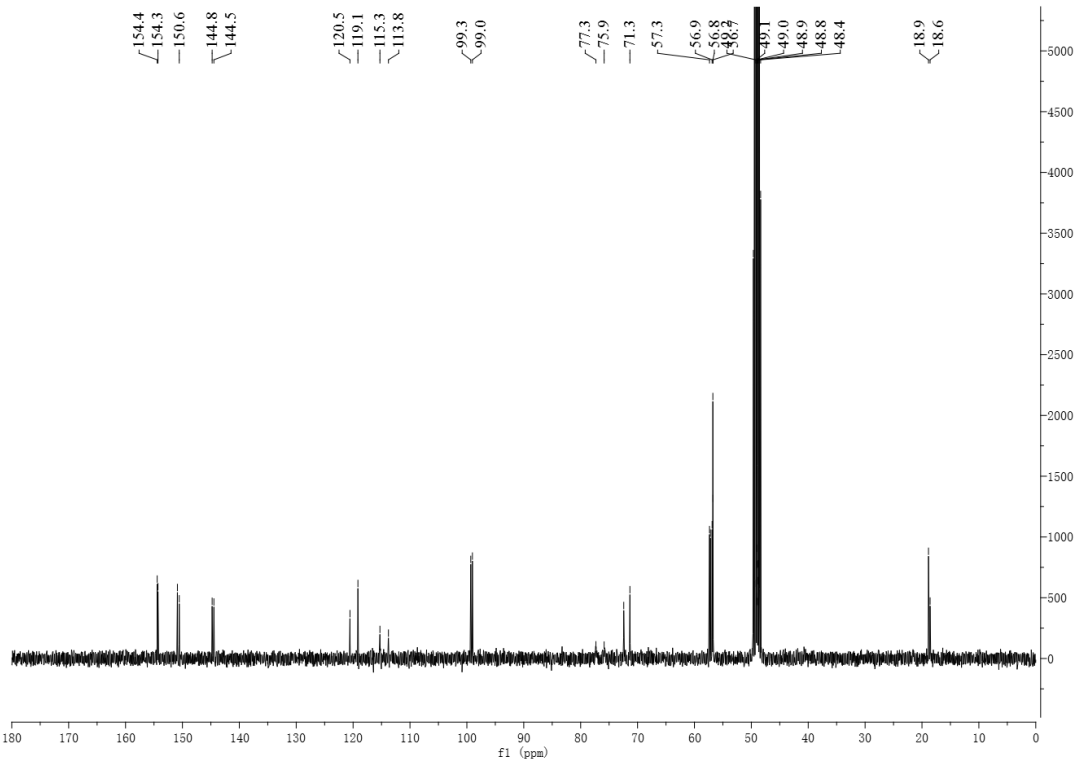
Minimum:				−1.5				
Maximum:		5.0	5.0	50.0				
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf(%)	Formula
489.2103	489.2101	0.2	0.4	7.5	41.9	0.054	94.74	C24 H34 O9 Na
	489.2125	−2.2	−4.5	10.5	44.8	2.946	5.26	C26 H33 O9

The 1D and 2D NMR spectra of (±)-asarolignan C (3)

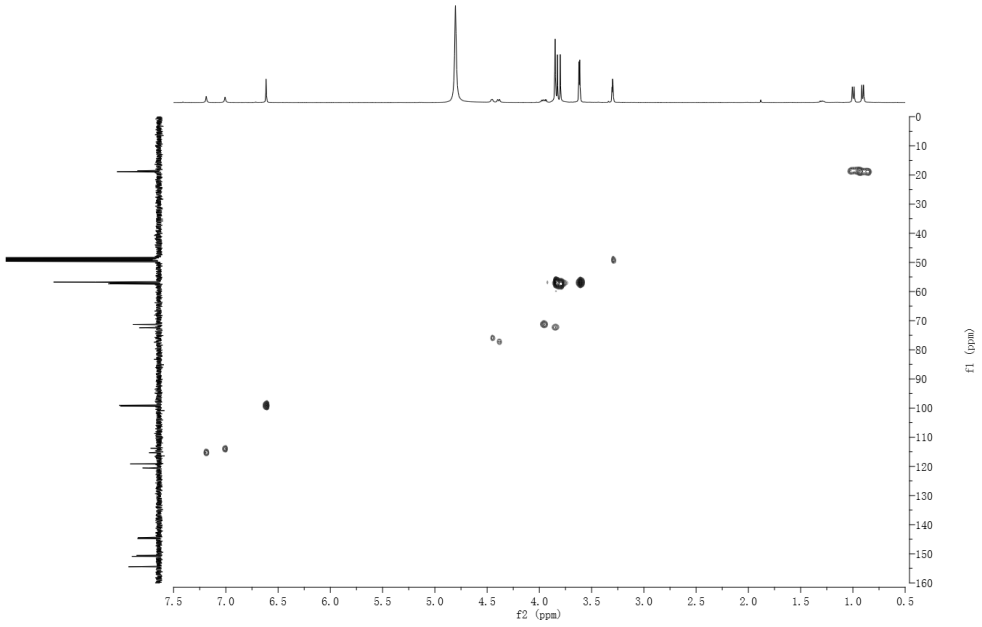
^{1}H NMR spectrum (AV-400, 400 MHz) of (±)-asarolignan C (3) in CD_3OD



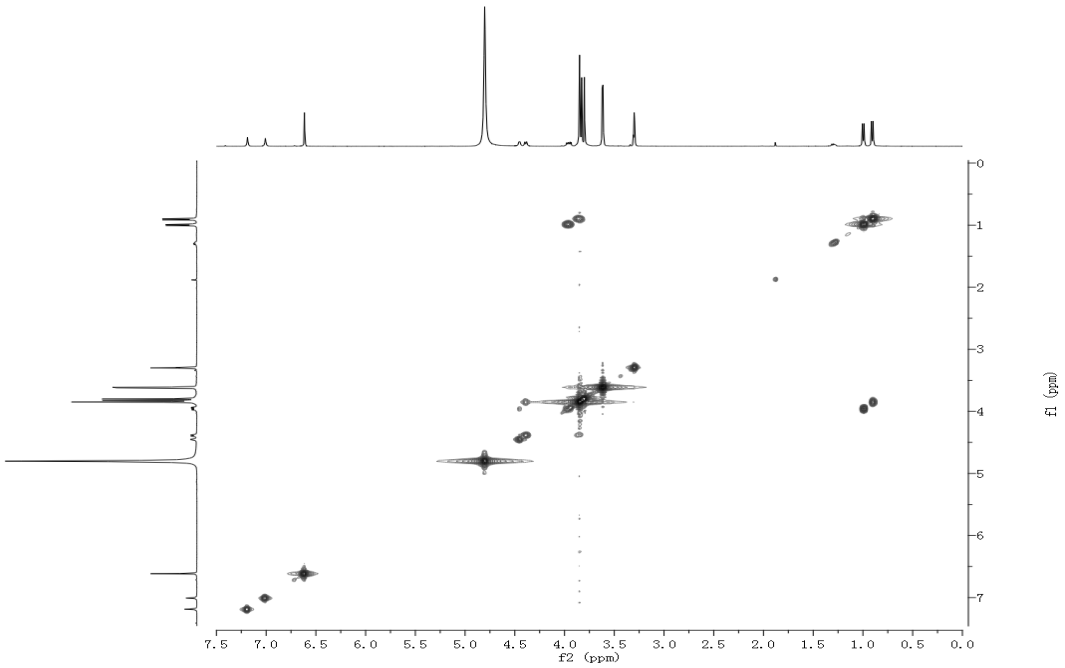
^{13}C NMR spectrum(AV-400, 400 MHz) of (±)-asarolignan C (3) in CD_3OD



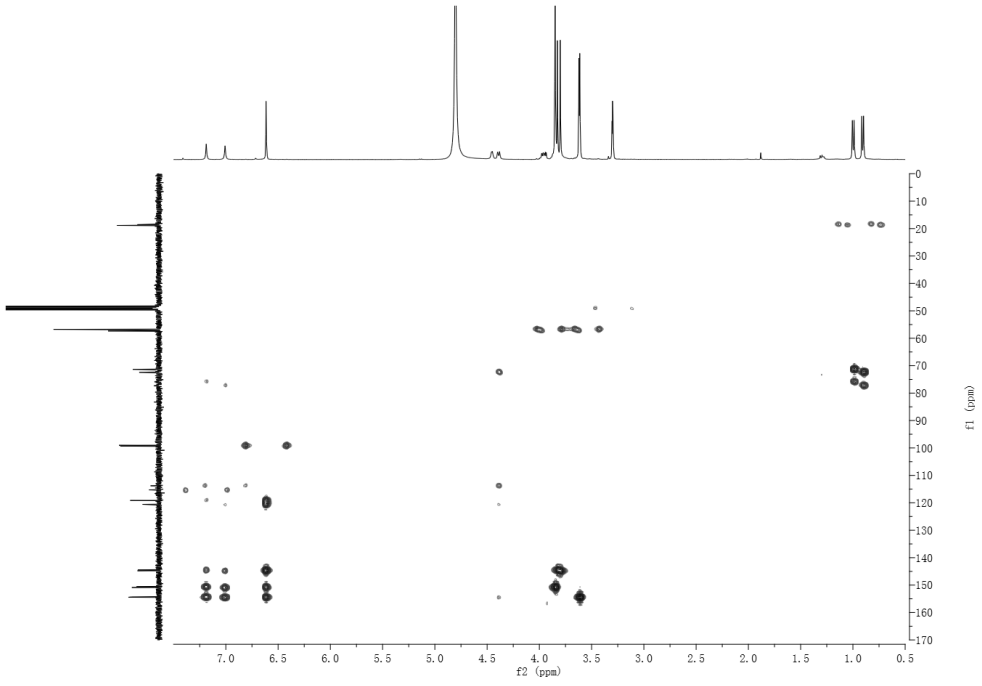
HSQC spectrum (AV-400) of (±)-asarolignan C (3) in CD_3OD



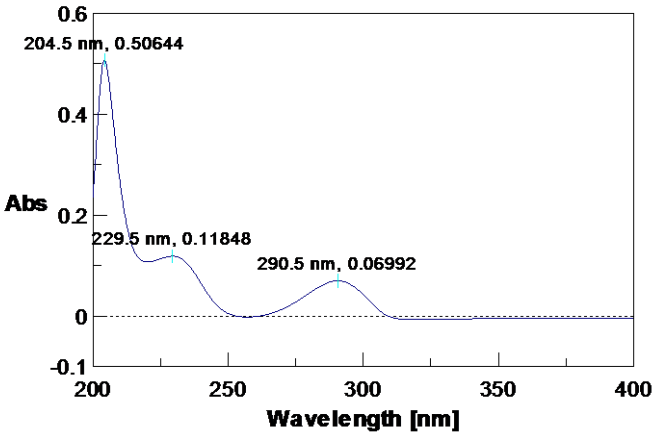
$^1H-^1H$ COSY spectrum (AV-400) of (±)-asarolignan C (3) in CD_3OD



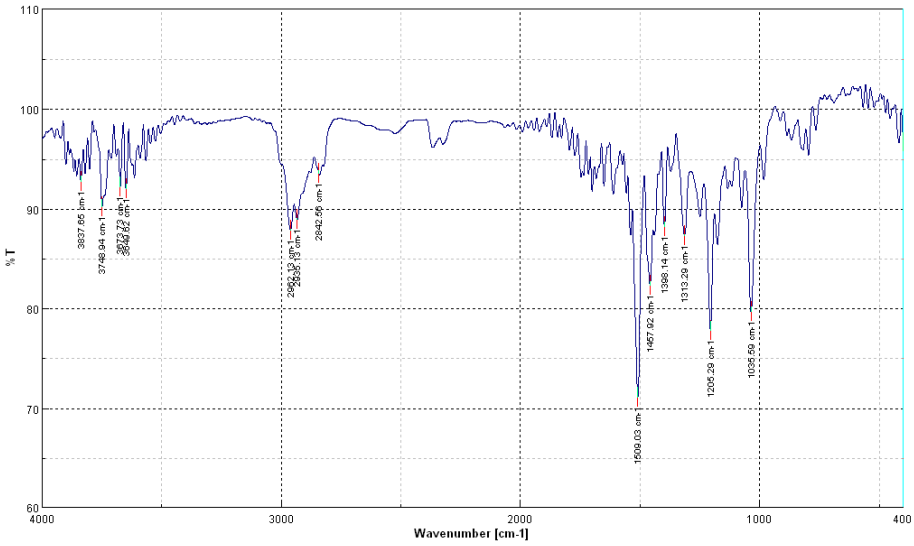
HMBC spectrum (AV-400) of (±)-asarolignan C (3) in CD_3OD



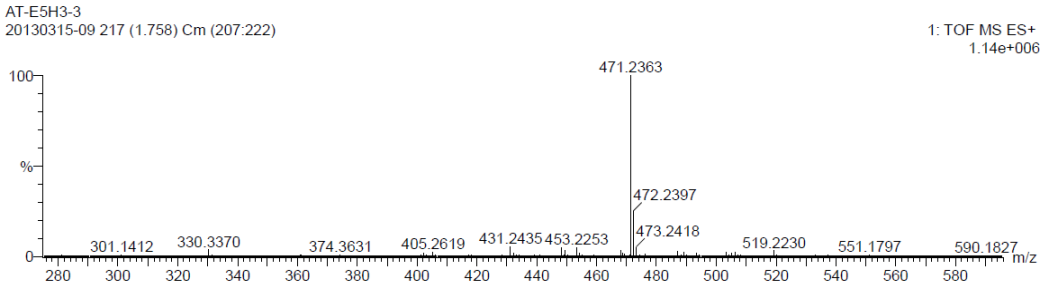
UV spectrum of (±)-asarolignan D (4) in CH_3OH



IR (KBr disc) spectrum of (±)-asarolignan D (4)



HR-ESI-MS spectrum of (±)-asarolignan D (4)

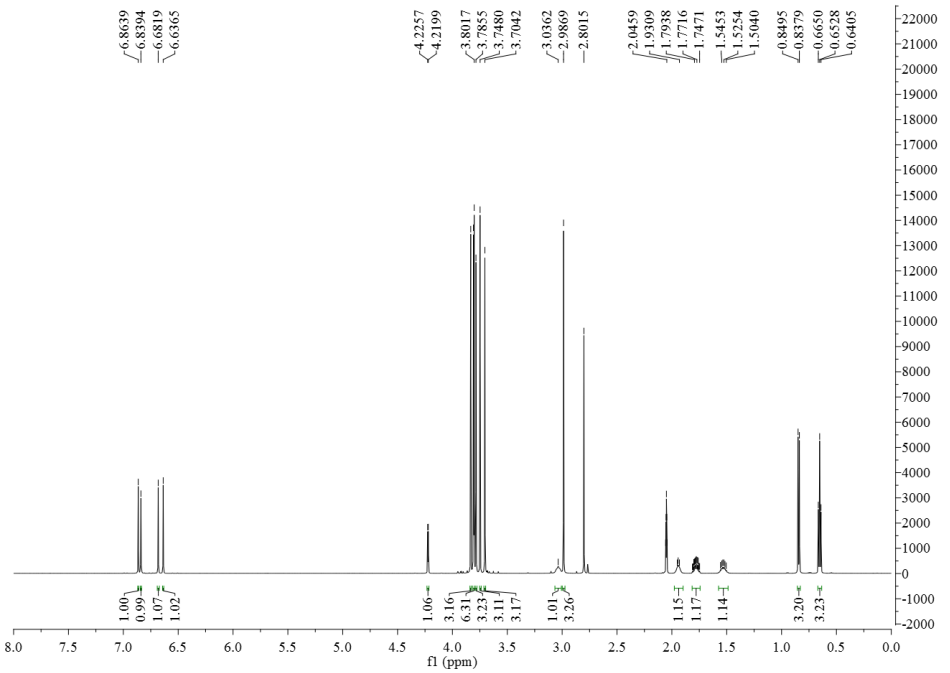


Minimum: -1.5
Maximum: 5.0 10.0 50.0

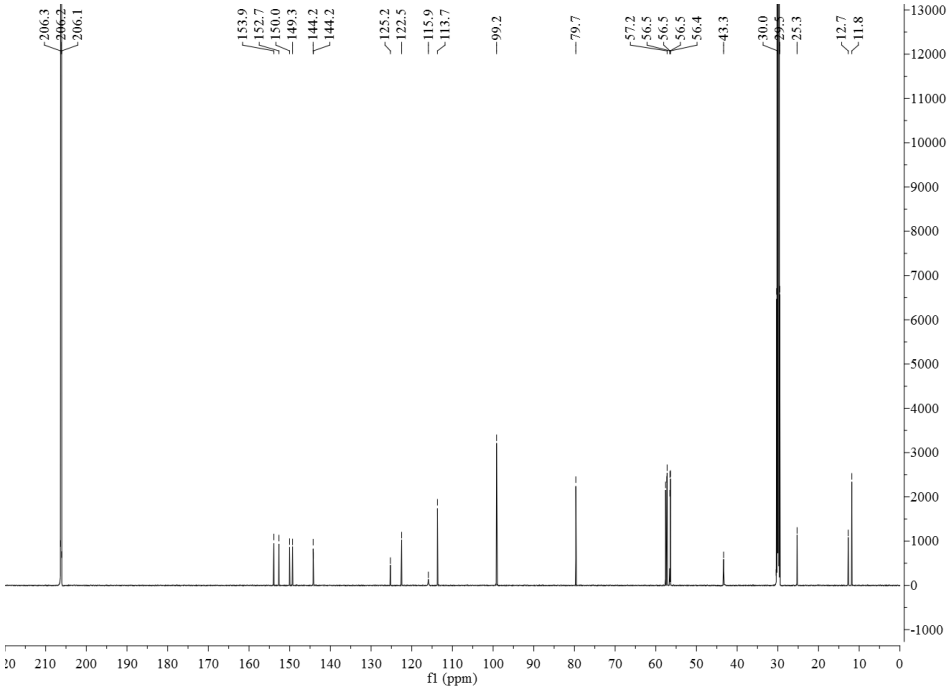
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf(%)	Formula
471.2363	471.2359	0.4	0.8	7.5	570.6	0.040	96.04	C25 H36 O7 Na
	471.2383	-2.0	-4.2	10.5	573.7	3.235	3.94	C27 H35 O7
	471.2324	3.9	8.3	19.5	578.8	8.247	0.03	C34 H31 O2

The 1D and 2D NMR spectra of (±)-asarolignan D (4)

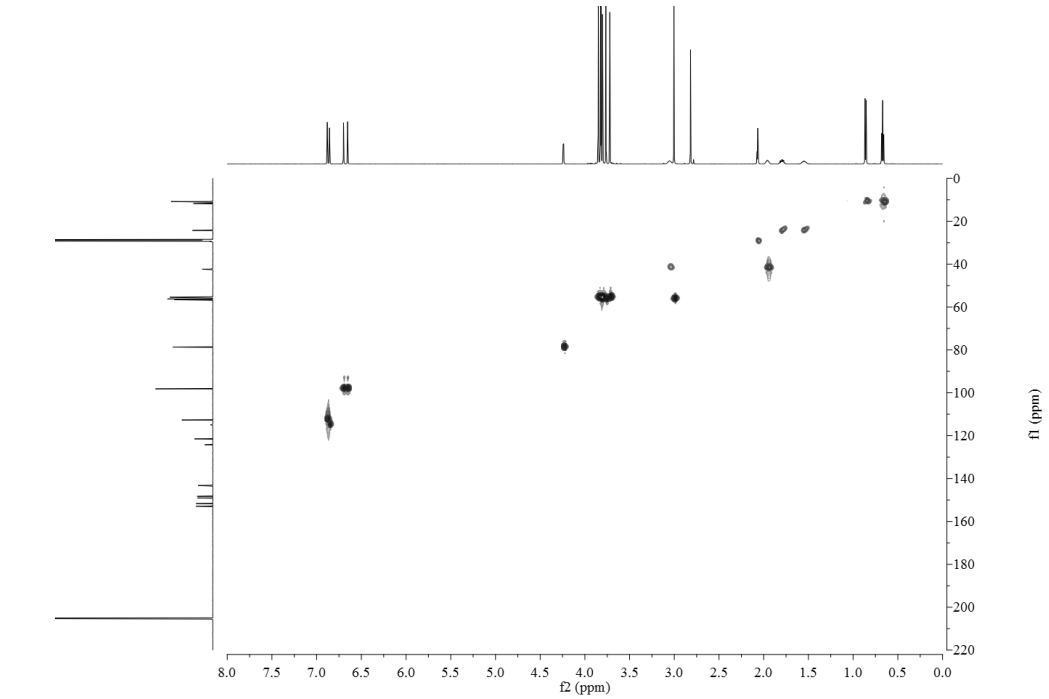
^{1}H NMR spectrum (AV-600, 600 MHz) of (±)-asarolignan D (4) in acetone-d_6



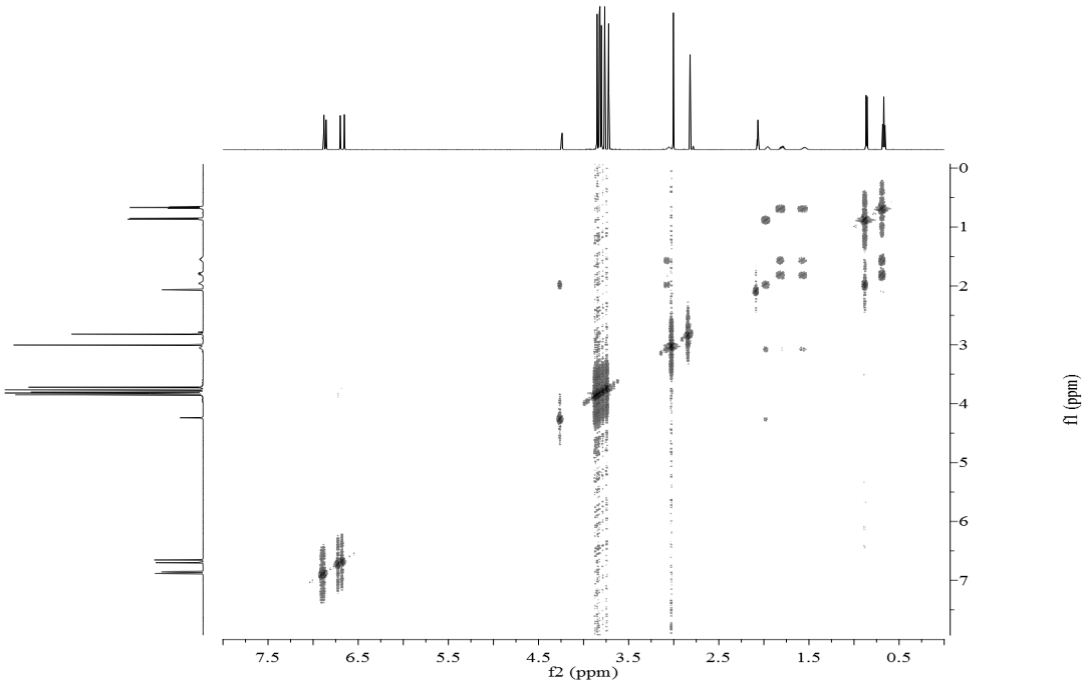
^{13}C NMR spectrum (AV-600, 150 MHz) of (±)-asarolignan D (4) in acetone-*d*$_6$



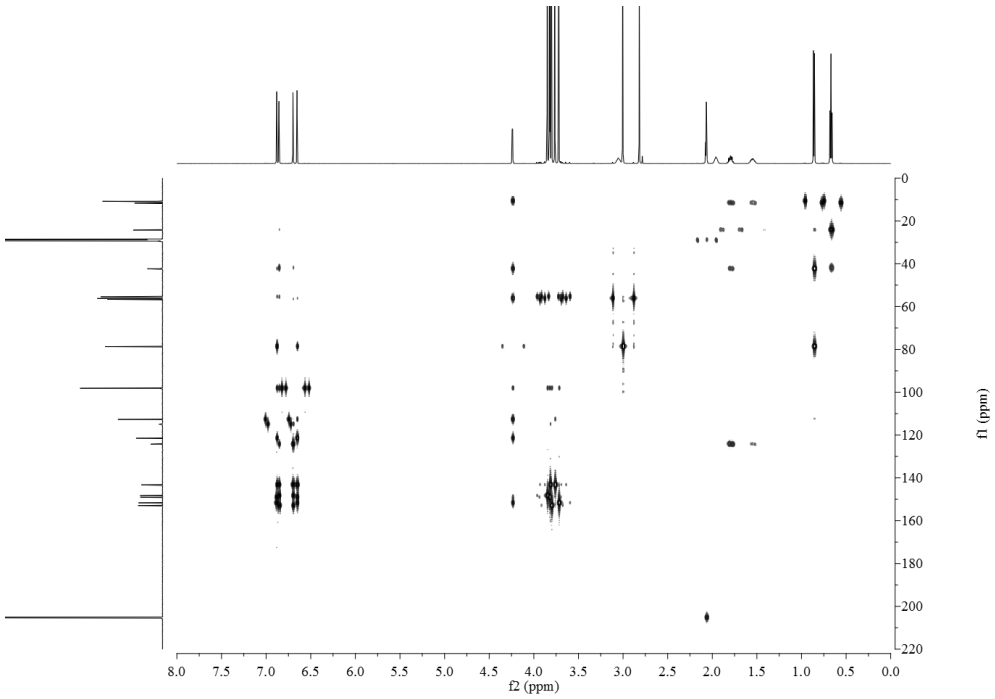
HSQC spectrum (AV-600) of (±)-asarolignan D (4) in acetone-*d*$_6$



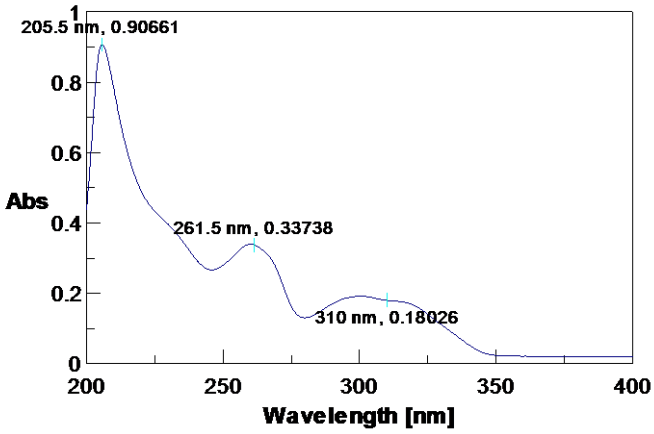
^{1}H–^{1}H COSY spectrum (AV-600) of (±)-asarolignan D (4) in acetone-*d*$_6$



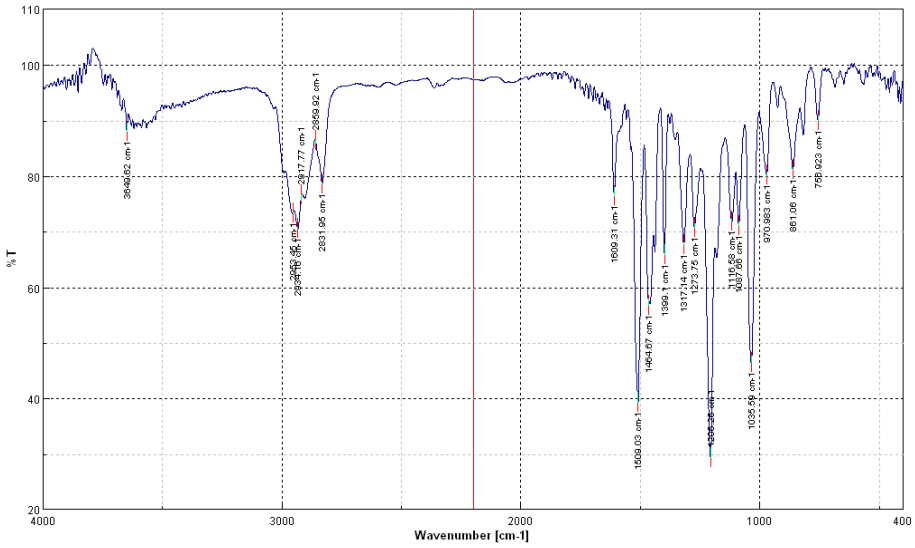
HMBC spectrum (AV-600) of (±)-asarolignan D (4) in acetone-*d*$_6$



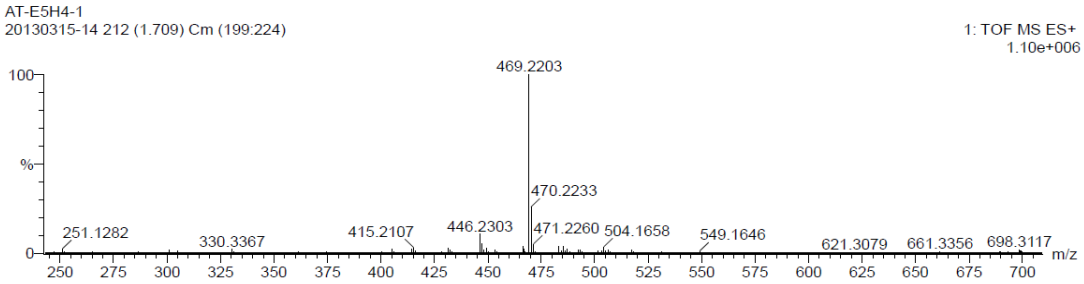
UV spectrum of (±)-asarolignan E (5) in CH_3OH



IR (KBr disc) spectrum of (±)-asarolignan E (5)



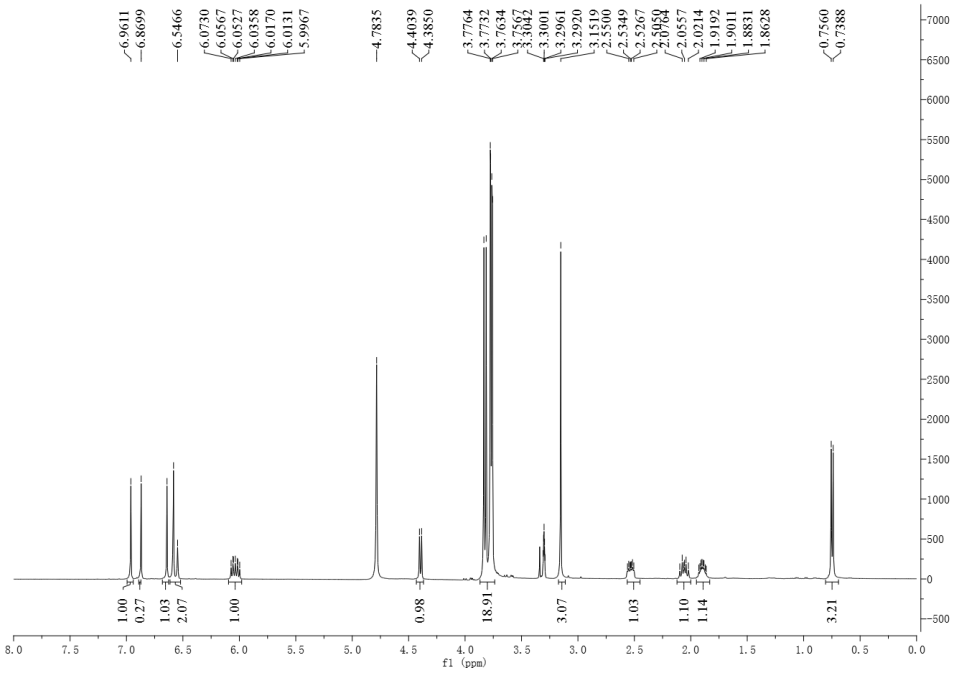
HR-ESI-MS spectrum of (±)-asarolignan E (5)



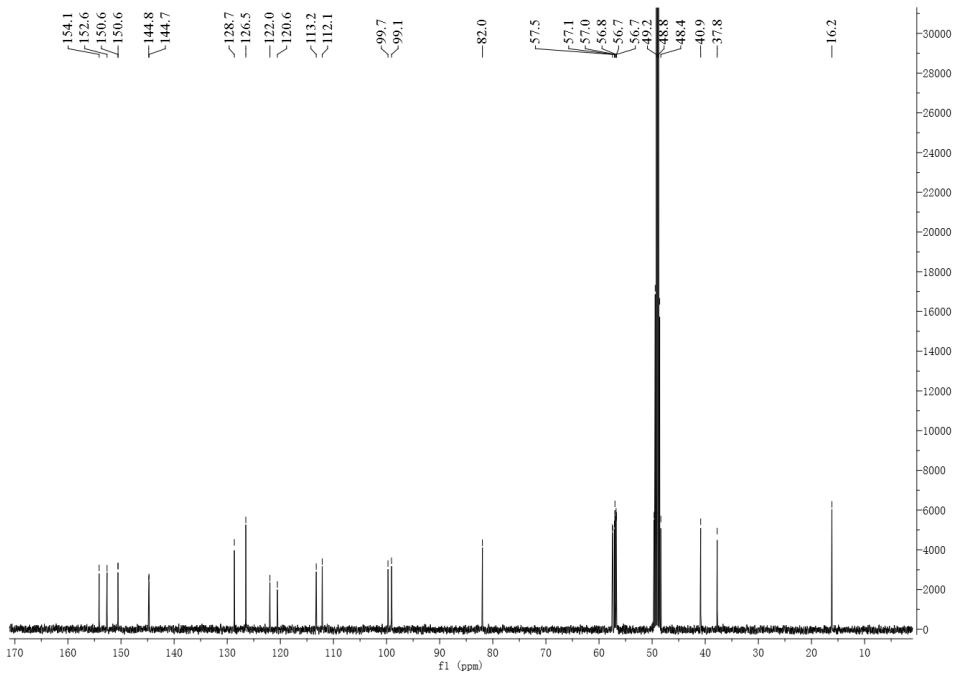
Minimum:				−1.5				
Maximum:		5.0	10.0	50.0				
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf(%)	Formula
469.2203	469.2202	0.1	0.2	8.5	550.5	0.018	98.25	C25 H34 O7 Na
	469.2226	−2.3	−4.9	11.5	554.5	4.056	1.73	C27 H33 O7
	469.2168	3.5	7.5	20.5	559.1	8.627	0.02	C34 H29 O2

The 1D and 2D NMR spectra of (±)-asarolignan E (5)

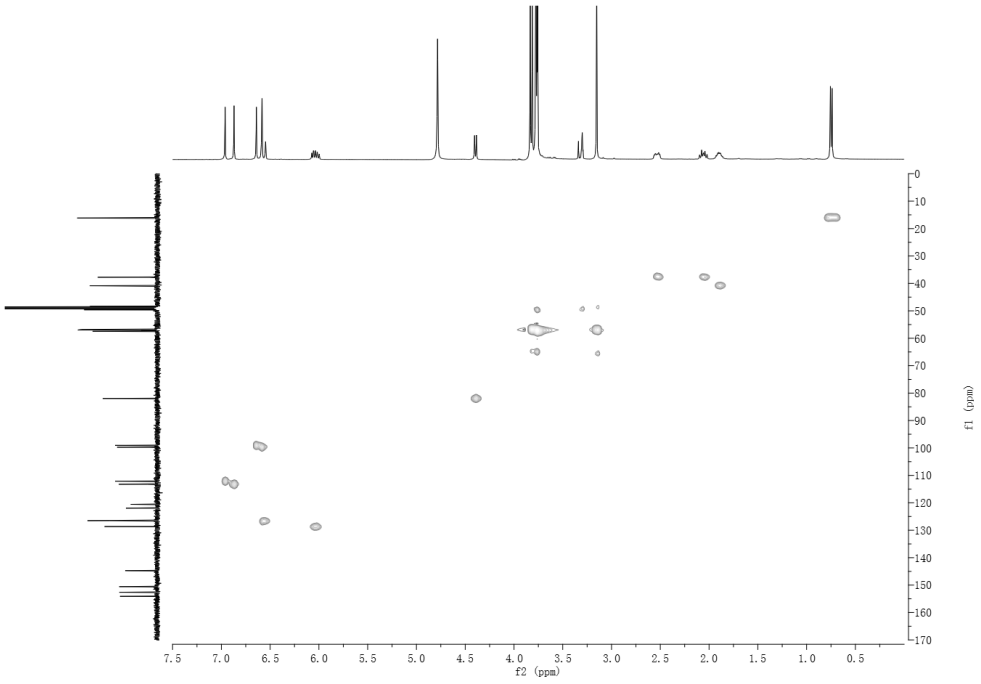
^{1}H NMR spectrum (AV-400, 400 MHz) of (±)-asarolignan E (5) in CD_3OD



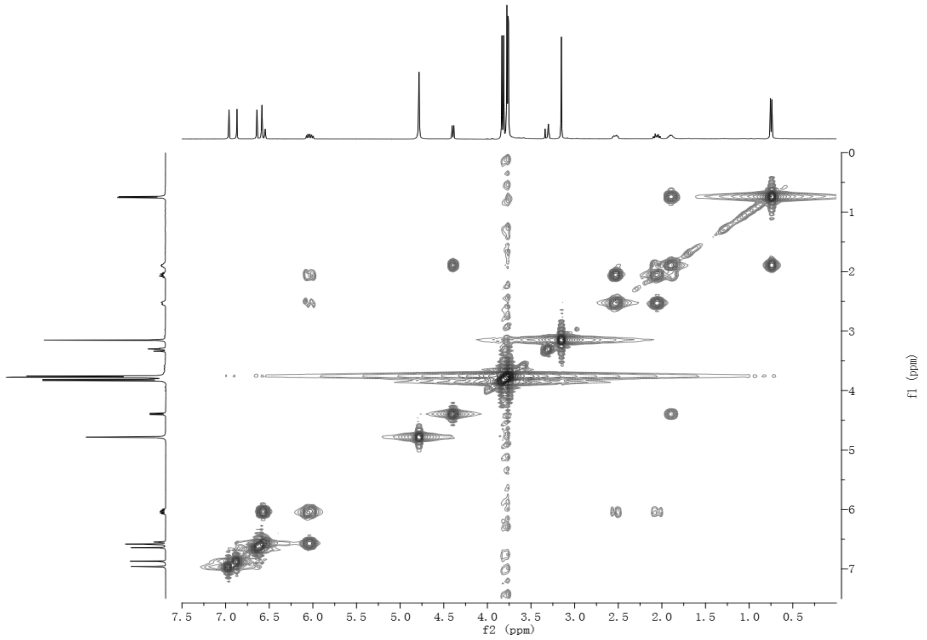
^{13}C NMR spectrum (AV-400, 100 MHz) of (±)-asarolignan E (5) in CD_3OD



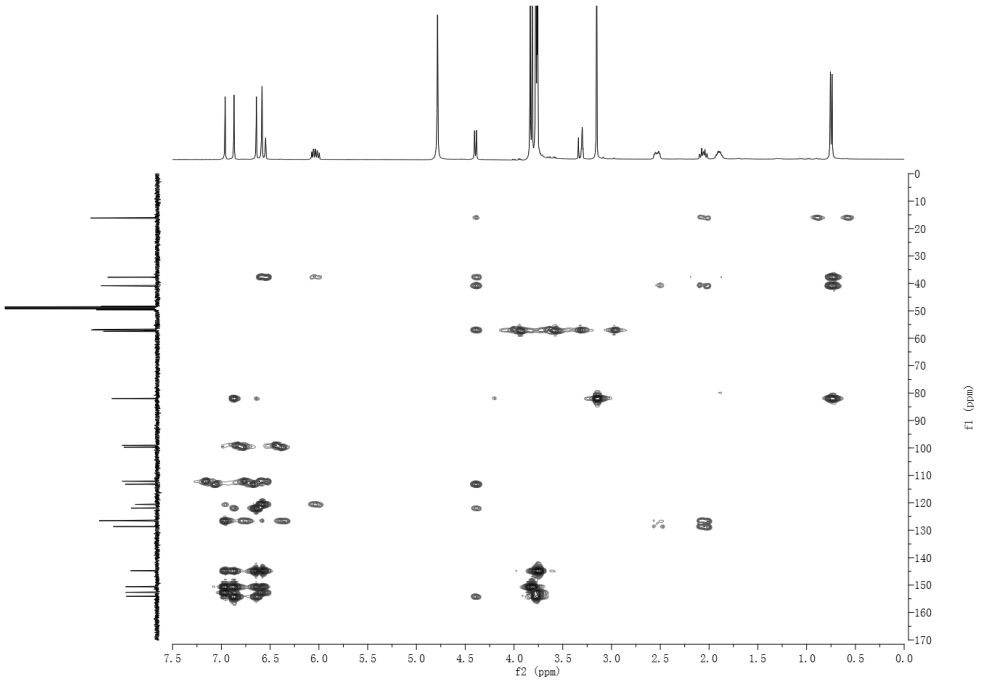
HSQC spectrum (AV-400) of (±)-asarolignan E (5) in CD_3OD



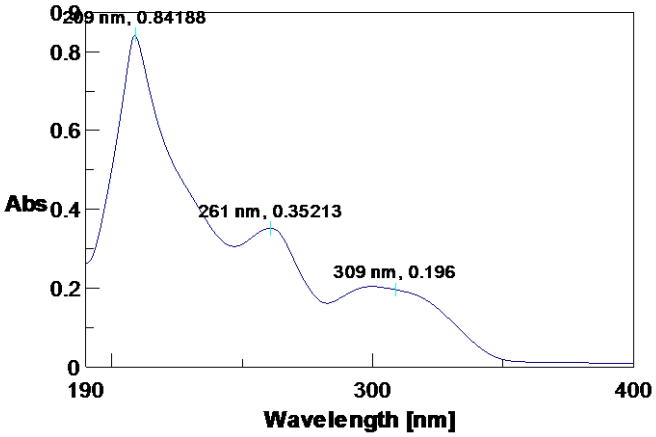
^1H-^1H COSY spectrum (AV-400) of (±)-asarolignan E (5) in CD_3OD



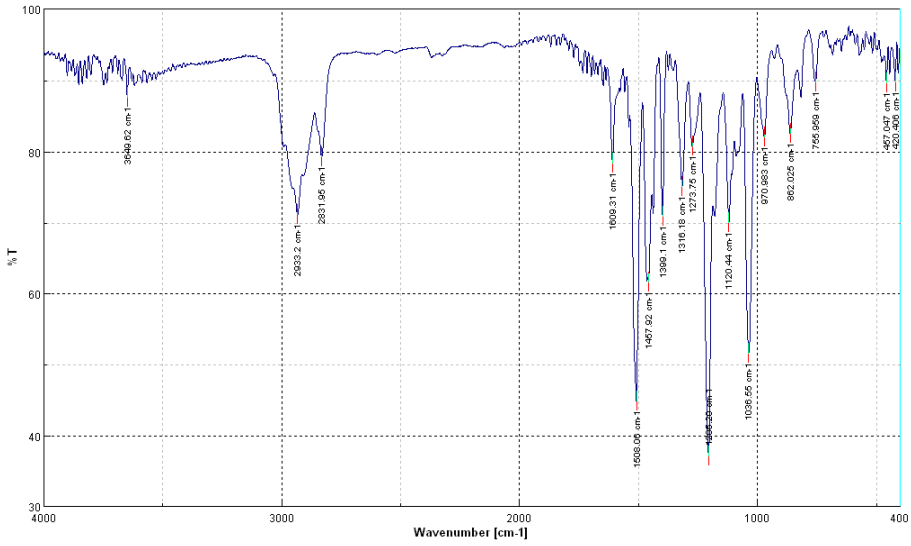
HMBC spectrum (AV-400) of (±)-asarolignan E (5) in CD_3OD



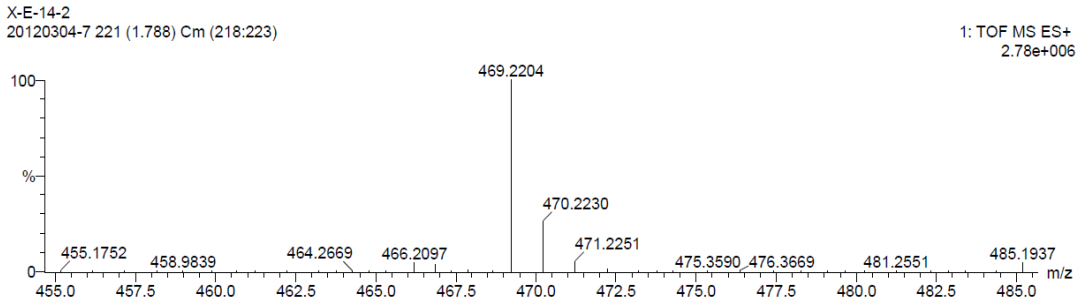
UV spectrum of (±)-asarolignan F (6) in CH_3OH



IR (KBr disc) spectrum of (±)-asarolignan F (6)



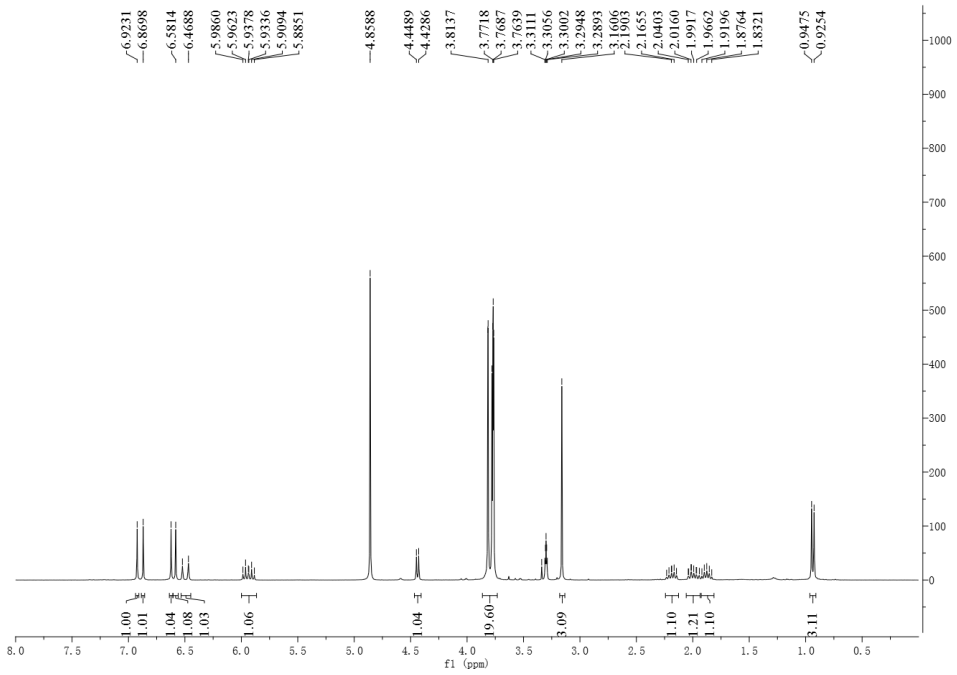
HR-ESI-MS spectrum of (±)-asarolignan F (6)



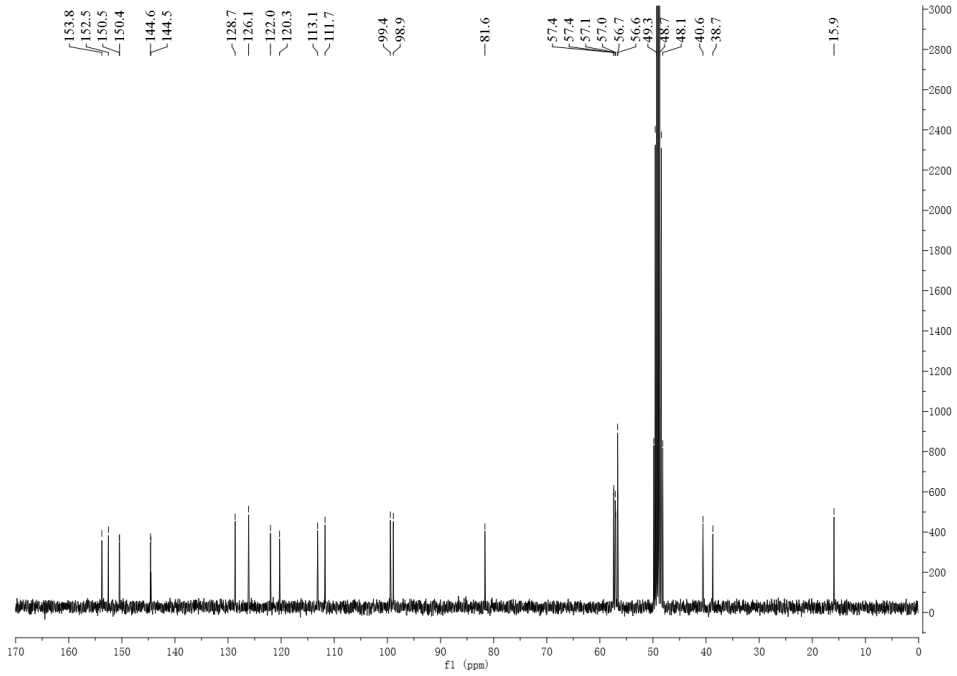
Minimum:				-1.5				
Maximum:		5.0	10.0	50.0				
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf(%)	Formula
469.2204	469.2202	0.2	0.4	8.5	26.5	0.015	98.51	C25 H34 O7 Na
	469.2226	-2.2	-4.7	11.5	30.7	4.216	1.48	C27 H33 O7
	469.2168	3.6	7.7	20.5	35.3	8.802	0.02	C34 H29 O2

The 1D and 2D NMR spectra of (±)-asarolignan F (6)

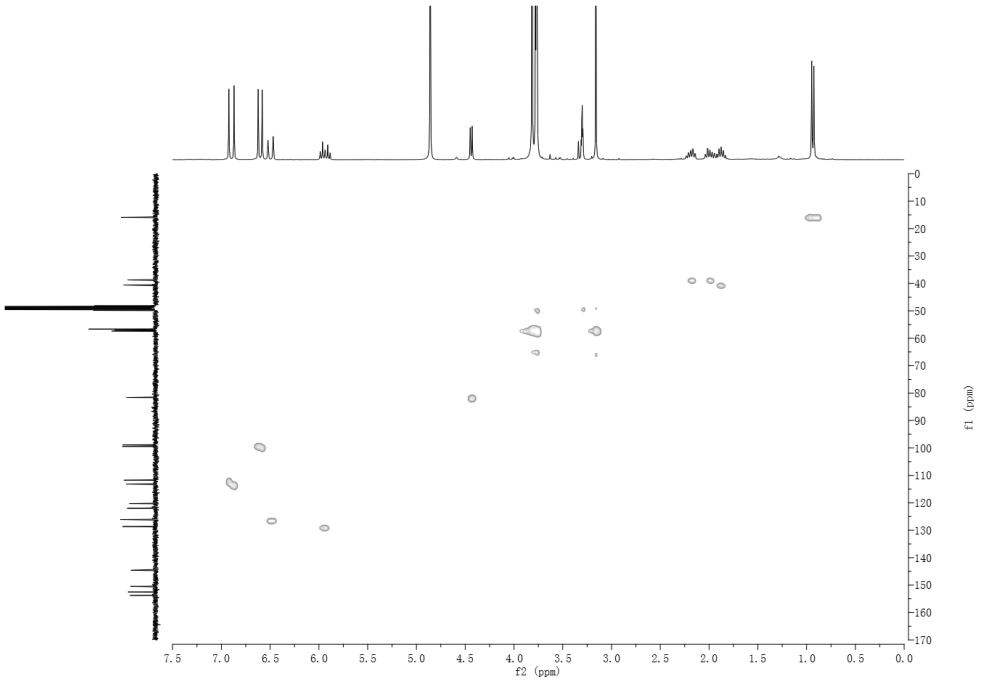
^{1}H NMR spectrum (AV-300, 300 MHz) of (±)-asarolignan F (6) in CD_3OD



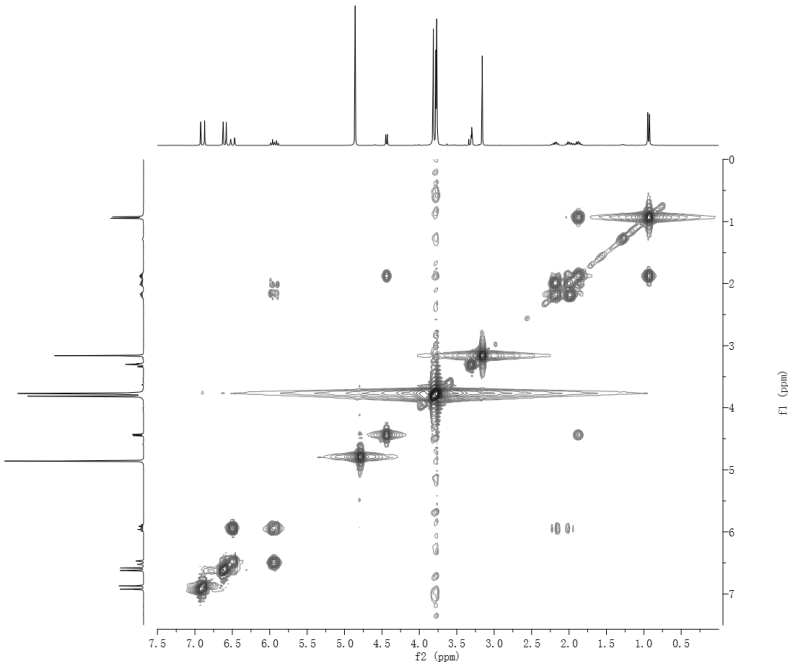
^{13}C NMR spectrum (AV-300, 75 MHz) of (±)-asarolignan F (6) in CD_3OD



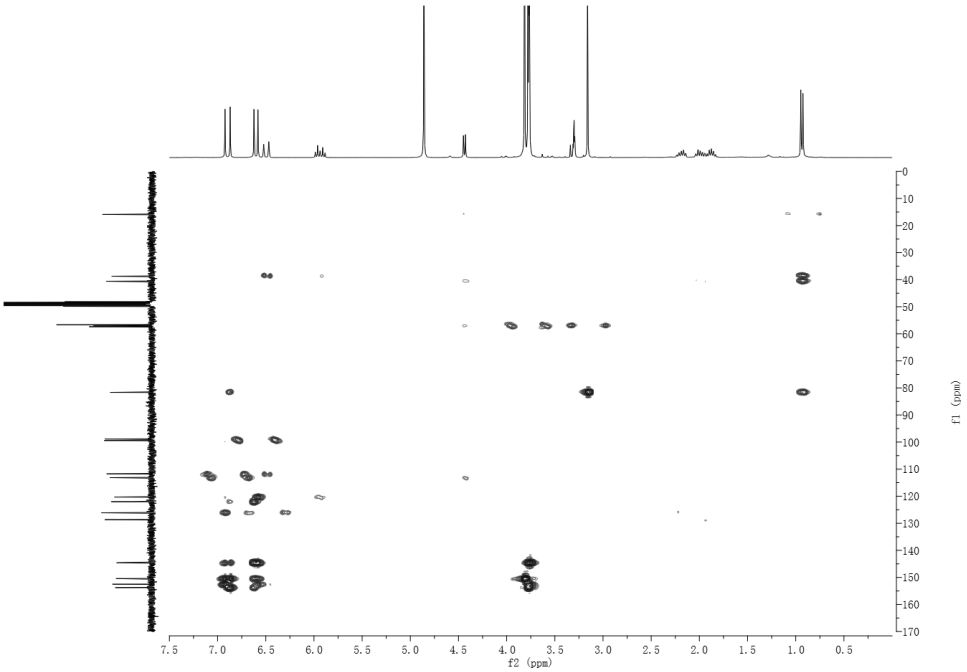
HSQC spectrum (AV-300) of (±)-asarolignan F (6) in CD_3OD



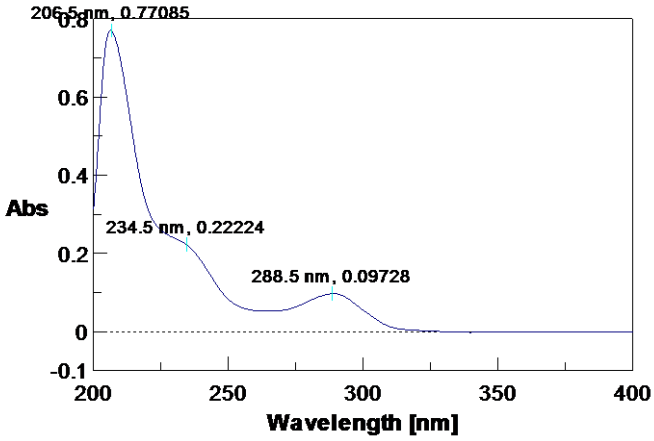
^{1}H-^{1}H COSY spectrum (AV-300) of (±)-asarolignan F (6) in CD_3OD



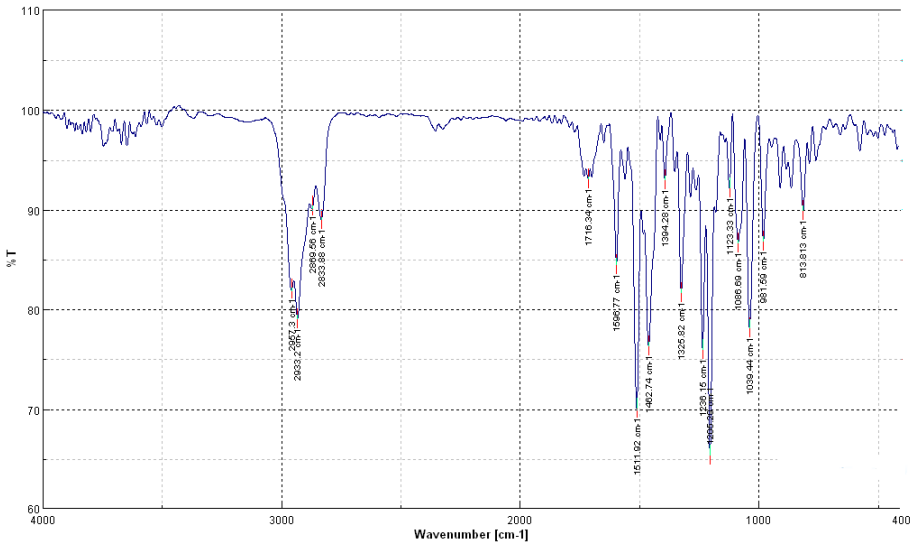
HMBC spectrum (AV-300) of (±)-asarolignan F (6) in CD_3OD



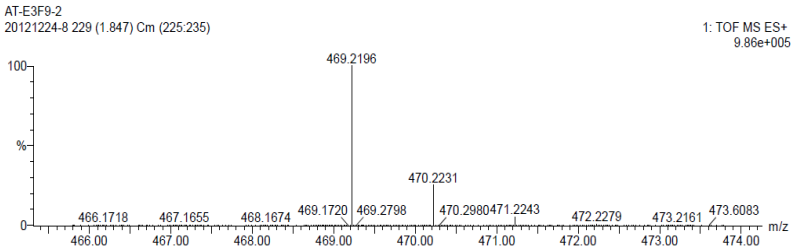
UV spectrum of (±)-asarolignan G (7) in CH_3OH



IR (KBr disc) spectrum of (±)-asarolignan G (7)



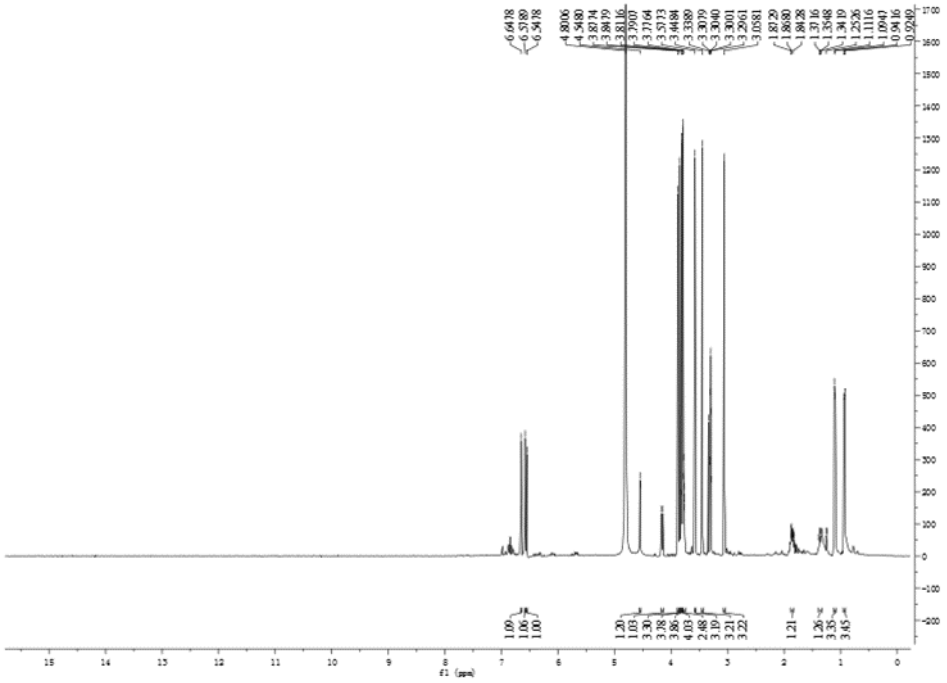
HR-ESI-MS spectrum of (±)-asarolignan G (7)



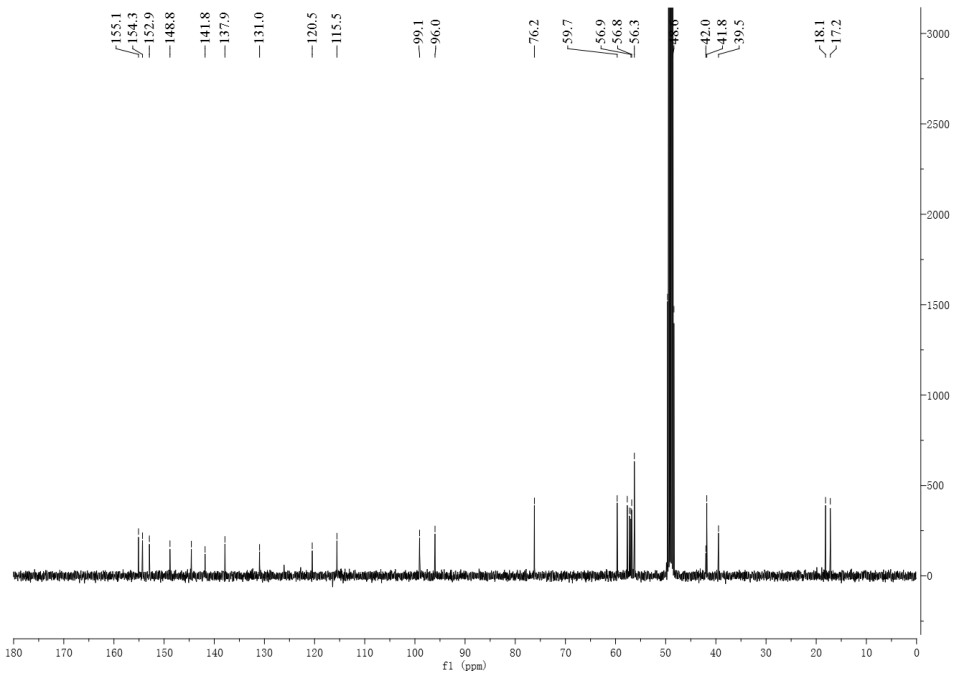
Minimum:			-1.5					
Maximum:		5.0	5.0	50.0				
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf(%)	Formula
469.2196	469.2202	-0.6	-1.3	8.5	850.6	n/a	n/a	C25 H34 O7 Na

The 1D and 2D NMR spectra of (±)-asarolignan G (7)

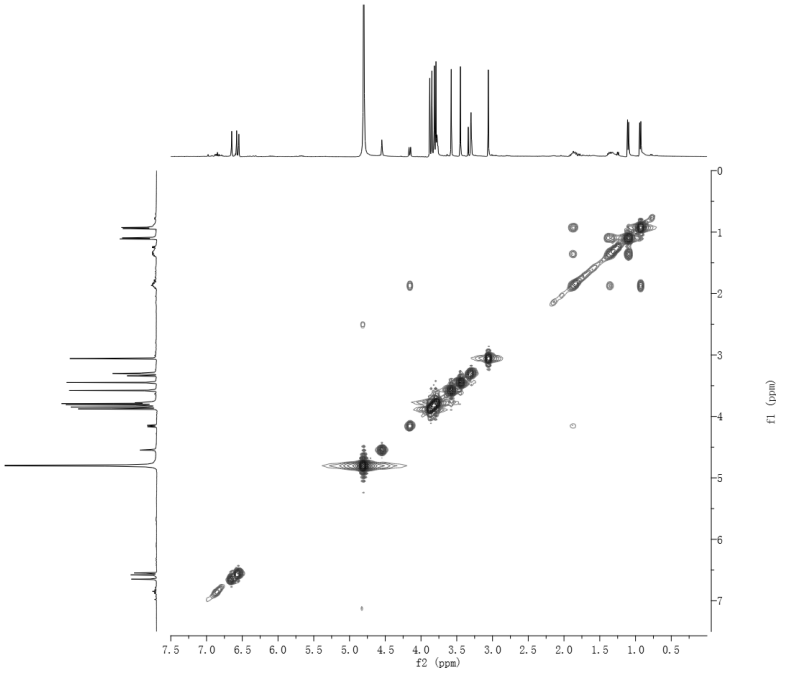
^{1}H NMR spectrum (AV-400, 400 MHz) of (±)-asarolignan G (7) in CD_3OD



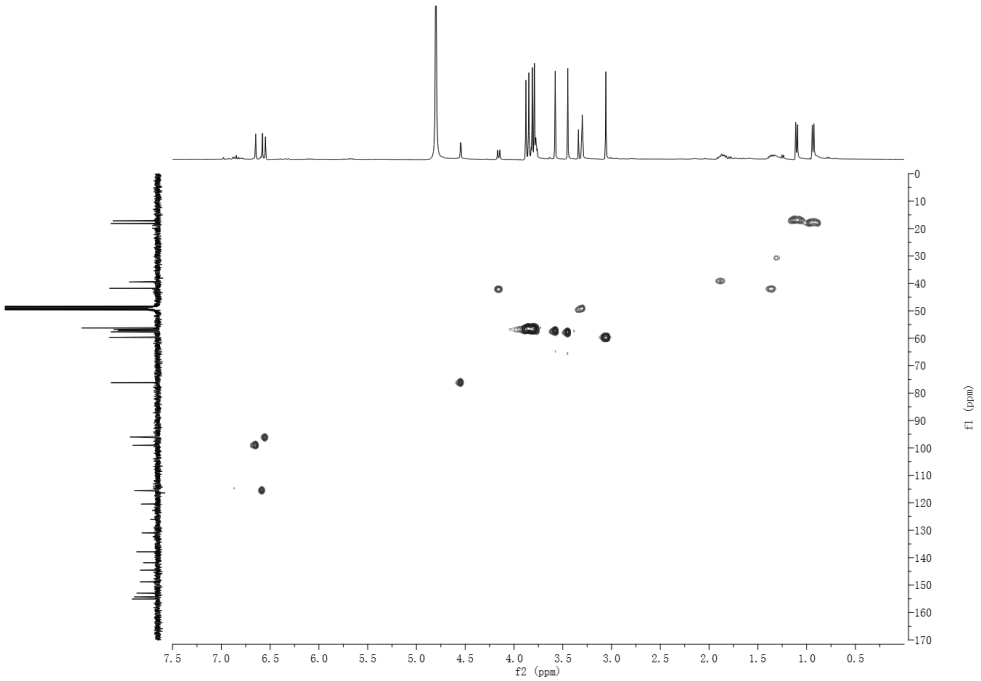
^{13}C NMR spectrum (AV-400, 100 MHz) of (±)-asarolignan G (7) in CD_3OD



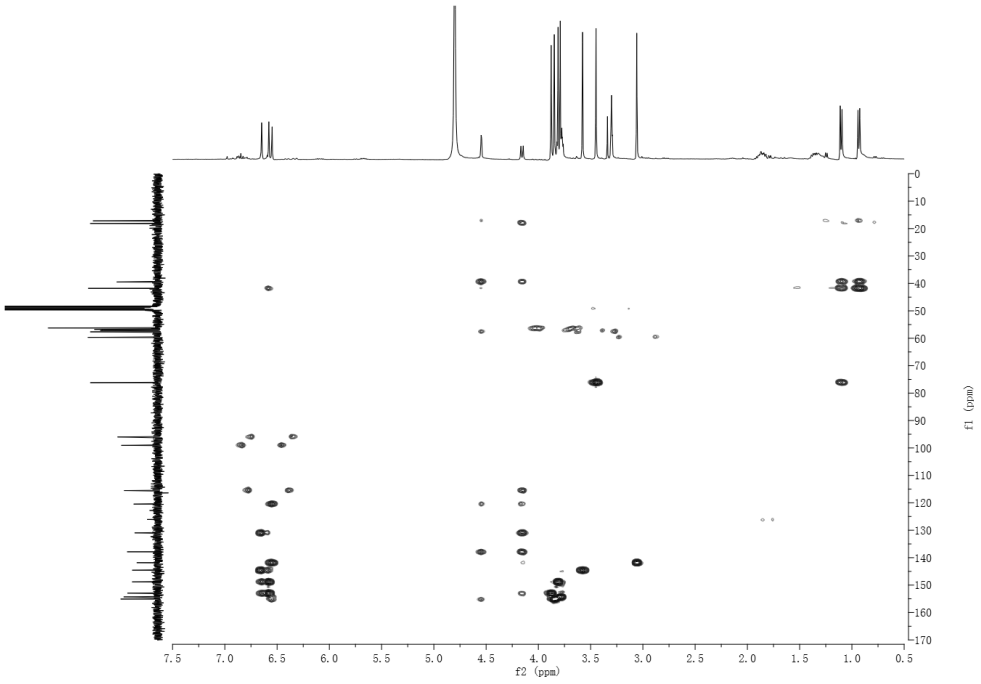
^{1}H–^{1}H COSY spectrum (AV-400) of (±)-asarolignan G (7) in CD_3OD



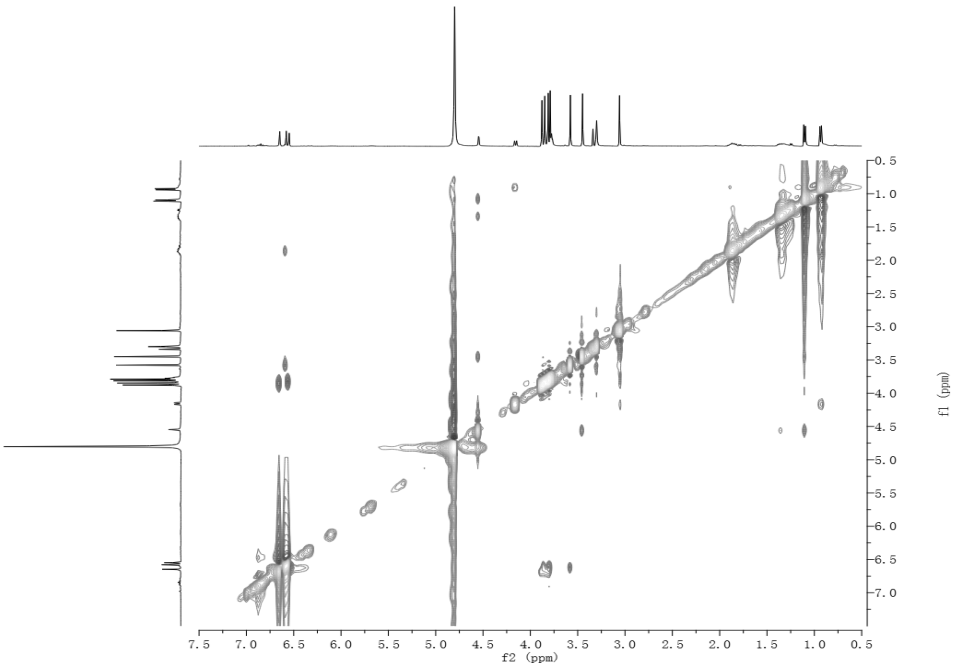
HSQC spectrum (AV-400) of (±)-asarolignan G (7) in CD_3OD



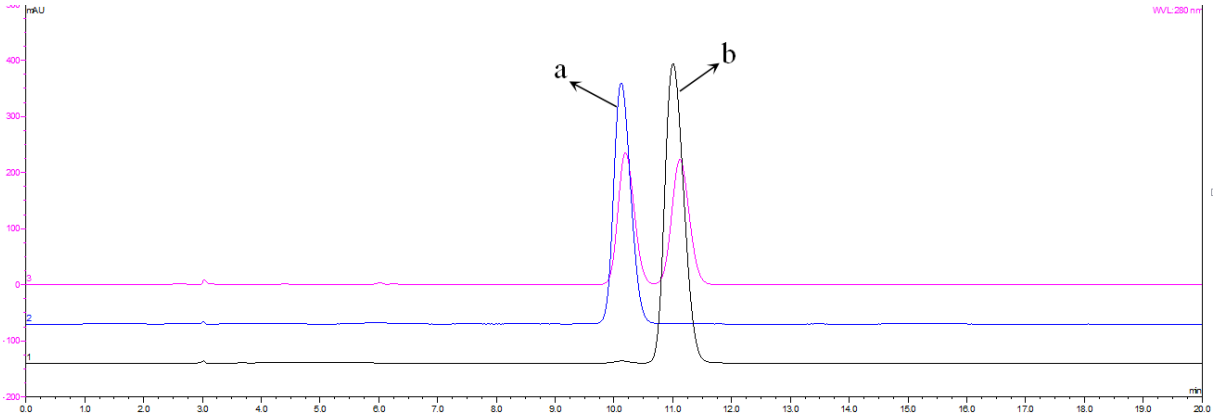
HMBC spectrum (AV-400) of (±)-asarolignan G (7) in CD_3OD



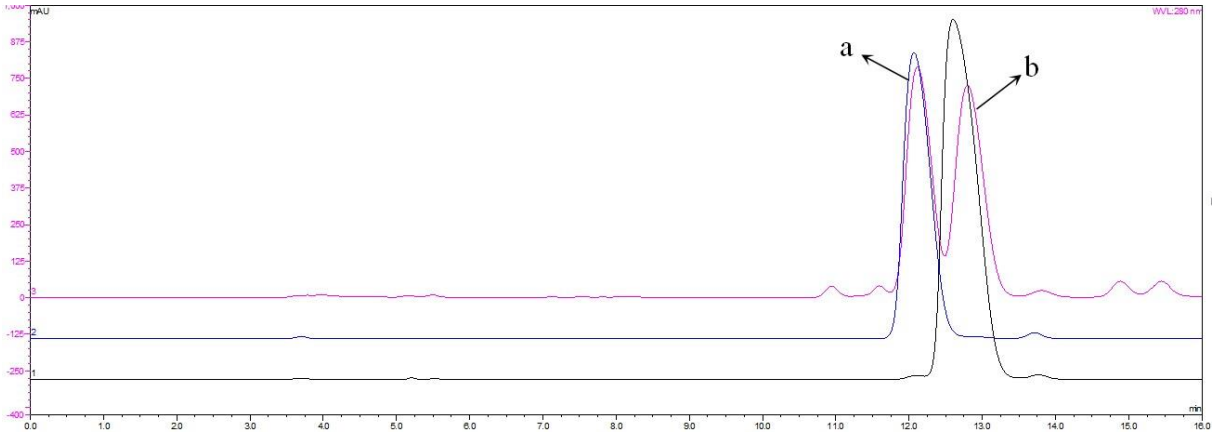
NOESY spectrum (AV-400) of (±)-asarolignan G (7) in CD_3OD



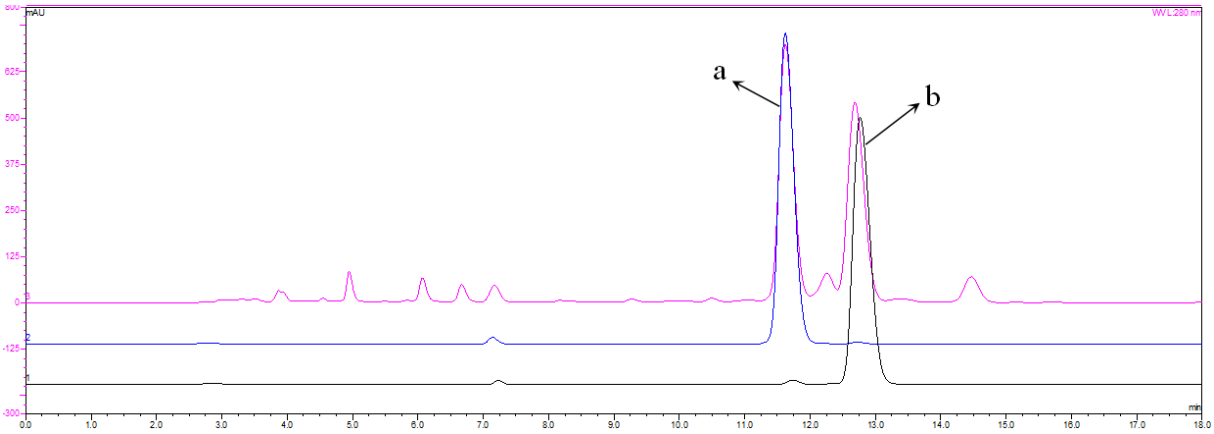
Chiral HPLC analytical chromatograms of compound 2, 3, 7, 8, 14



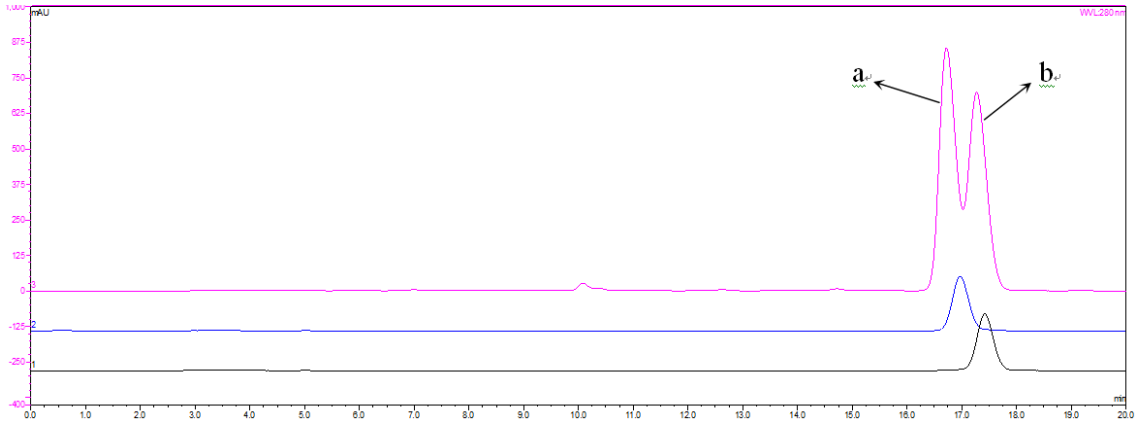
column, Lux Amylose-2 column (5 μm, 4.6 × 250 mm, Phenomenex); mobile phase, MeCN/H_2O = 35:75; flow rate: 0.7 mL/min; UV detection at 280 nm; peak area of **2a**:**2b** = 1:1; **2a**, t_R = 10.1 min; **2b**, t_R = 11.0 min.



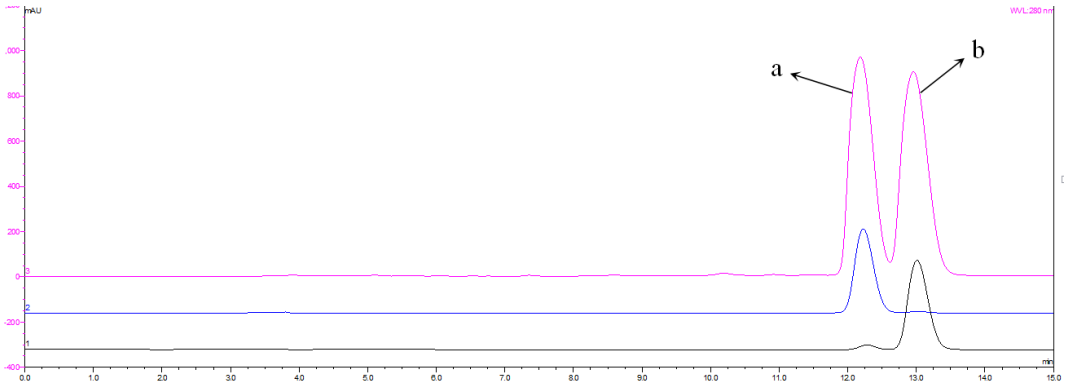
column, Lux Amylose-2 column (5 μm, 4.6 × 250 mm, Phenomenex); mobile phase, MeCN/H_2O = 3:7; flow rate: 0.7 mL/min; UV detection at 280 nm; peak area of **3a**:**3b** = 1:1; **3a**, t_R = 12.0 min; **3b**, t_R = 12.8 min.



column, Lux Amylose-2 column (5 μm, 4.6 × 250 mm, Phenomenex); mobile phase, MeCN/H_2O = 6:4; flow rate: 0.7 mL/min; UV detection at 280 nm; peak area of **7a**:**7b** = 1:1; **7a**, t_R = 11.5 min; **7b**, t_R = 12.8 min.



column, Lux Amylose-2 column (5 μm, 4.6 × 250 mm, Phenomenex); mobile phase, MeCN/H_2O = 4:6; flow rate: 0.7 mL/min; UV detection at 280 nm; peak area of **8a**:**8b** = 1:1; **8a**, t_R = 21.0 min; **8b**, t_R = 22.0 min.

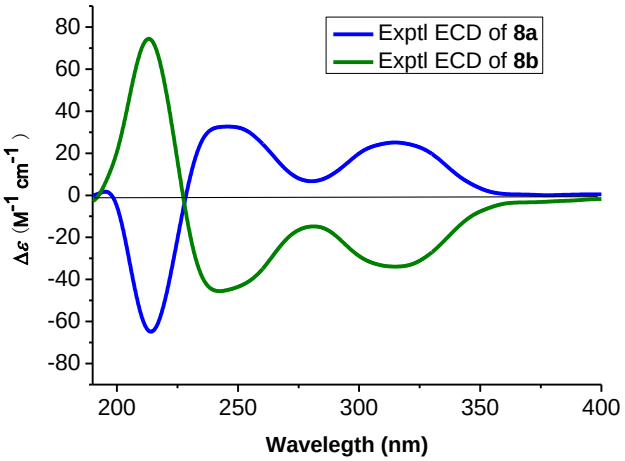


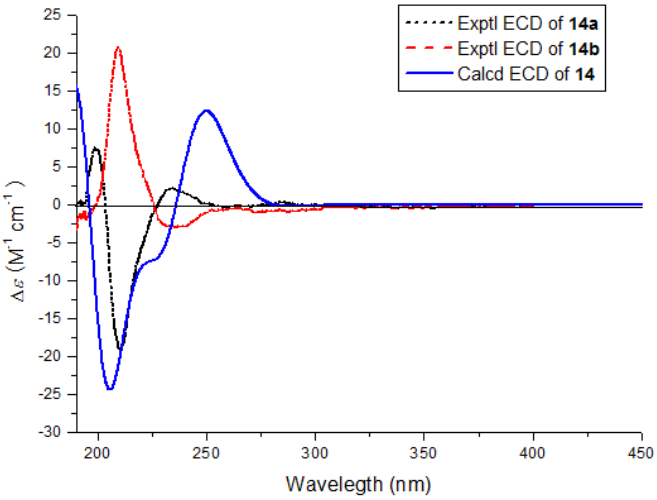
column, Lux Amylose-2 column (5 μm, 4.6 × 250 mm, Phenomenex); mobile phase, MeCN/H_2O = 4:6; flow rate: 0.7 mL/min; UV detection at 280 nm; peak area of **14a**:**14b** = 1:1; **14a**, t_R = 12.1 min; **14b**, t_R = 13.0 min.

Purity of compound

Purity of all the compounds were determined by HPLC using UV detection (peak area percentage represents the purity of compound), 1, 96.1% (208 nm); 2, 96.4% (208 nm); 2a, 96.4% (280 nm); 2b, 99.0% (280 nm); 3, 97.1% (208 nm); 3a, 98.2% (280 nm); 3b, 98.3% (280 nm); 4, 97.3% (208 nm); 5, 98.2% (208 nm); 6, 95.3% (208 nm); 7, 97.4% (208 nm); 7a, 97.4% (280 nm); 7b, 98.8% (280 nm); 8, 98.2% (208 nm);8a, 96.6% (280 nm); 8b, 97.4% (280 nm); 9, 95.2% (208 nm); 10, 94.7% (208 nm); 11, 98.9% (208 nm); 12, 96.3% (208 nm); 13, 90.1% (208 nm); 14, 96.7% (208 nm); 14a, 97.2% (280 nm); 14b, 95.1% (280 nm); 15, 97.2% (208 nm); 16, 97.7% (208 nm); 17, 98.7% (208 nm); 18, 97.8% (208 nm); 19, 95.8% (208 nm); 20, 97.3% (208 nm); 21, 96.3% (208 nm); 22, 97.8% (208 nm); 23, 97.7% (208 nm).

ECD spectrum of 8 and 14


Exptl ECD of 8a
Exptl ECD of 8b
Δε (M-1 cm-1)
Wavelegth (nm)


Exptl ECD of 14a
Exptl ECD of 14b
Calcd ECD of 14
Δε (M-1 cm-1)
Wavelegth (nm)