SUPPLEMENTARY MATERIAL

Two new sesquiterpenes from the rhizomes of *Atractylodes macrocephala* and their biological activities

Yi-Nan Zhao[a,#], Gai Gao[a,#], Jin-Lian Ma[a], Rui-Zhu Xu[a], Tao Guo[c], Li-Min Wu[a], Xin-Guang Liu[a], Zhi-Shen Xie[a], Jiang-Yan Xu[a], Zhen-Qiang Zhang[a,*] and Pan Wang[a,b,*]

[a] *Academy of Chinese Medical Sciences, Henan University of Chinese Medicine, Zhengzhou, China;* [b] *Zhongjing Wanxi Pharmaceutical Co., Ltd, Zhengzhou, China;* [c] *College of Pharmacy, Henan University of Chinese Medicine, Zhengzhou, China*

*Zhen-Qiang Zhang zhang_zhenqiang@126.com; *Pan Wang w.p1008@hotmail.com

[#] Yi-Nan Zhao and Gai Gao contributed equally to this work.

Abstract: Two new sesquiterpenes, named selina-4(14),7,11-trien-9-ol (**1**) and selina-4(14),11-dien-7-ol (**2**), along with two known compounds were isolated from rhizomes of *Atractylodes macrocephala* Koidz. All structures were assigned on the basis of detailed spectroscopic analyses. The absolute configuration of **1** was established by TDDFT-ECD calculations. Compound **1** was found to moderately inhibit LSD1 activity with IC_{50} value of 34.0 μM. Compounds **1** and **4** exhibited a regulate effect on Keap1-Nrf2-ARE pathway.

Keywords: *Atractylodes macrocephala*; sesquiterpenes; LSD1; Keap1-Nrf2-ARE

Table S1. ^{1}H (500 MHz) and ^{13}C (125 MHz) NMR data for **1** in methanol-d_4 and **2** in $CDCl_3$ (δ in ppm, J in Hz)[a]

Position		**1**			**2**		
		δ_H	δ_C	mult	δ_H	δ_C	mult
1	β	2.01 m	34.0	CH_2	1.46 m	41.5	CH_2
	α	1.29 br d (13.0)			1.40 dd (12.0, 6.0)		
2	β	1.74 m	23.3	CH_2	1.63 m	23.5	CH_2
	α	1.60 m			1.63 m		
3	β	2.38 m	36.8	CH_2	2.34 m	36.9	CH_2
	α	2.05 m			2.07 m		
4			150.2	C		150.8	C
5		2.36 m	38.1	CH	2.32 m	44.1	CH
6	β	2.32 dd (16.9, 12.0)	25.8	CH_2	1.71 dd (13.0, 4.8)	34.2	CH_2
	α	2.15 dd (16.9, 4.8)			1.49 m		
7			138.0	C		74.5	C
8	β	5.95 d (5.0)	123.4	CH	1.85 m	31.1	CH_2
	α				1.47 m		
9	β	3.62 d (5.0)	72.5	CH	1.67 m	36.2	CH_2
	α				1.34 m		
10			38.2	C		35.6	C
11			143.1	C		152.6	C
12	a	5.19 s	111.2	CH_2	5.08 s	108.8	CH_2
	b	5.00 s			4.84 s		
13		1.96 s	19.5	CH_3	1.86 s	19.1	CH_3
14	a	4.87 s	105.9	CH_2	4.73 s	105.1	CH_2
	b	4.70 s			4.41 s		
15		0.68 s	15.7	CH_3	0.74 s	15.3	CH_3

[a] overlapped signals assigned by $^{1}H–^{1}H$ COSY, HSQC, and HMBC spectra without designating multiplicity.

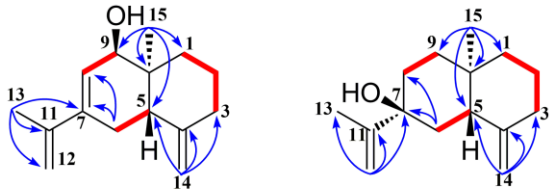


Figure S1. ^{1}H-^{1}H COSY (bold red bonds) and key HMBC (blue arrows) correlations of **1** and **2**.

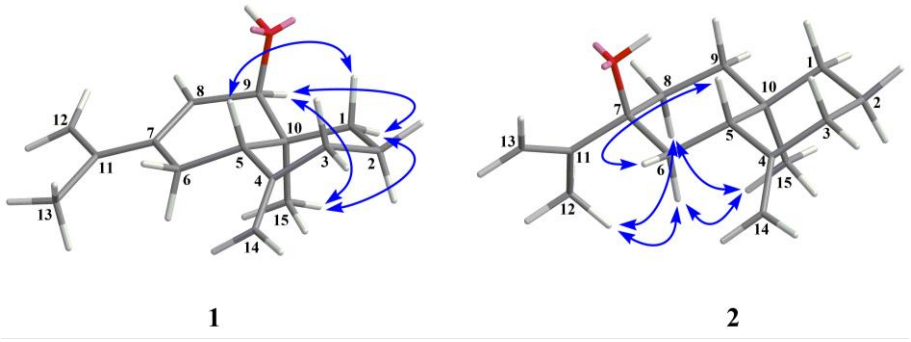


Figure S2. Key NOESY correlations for **1** and **2**.

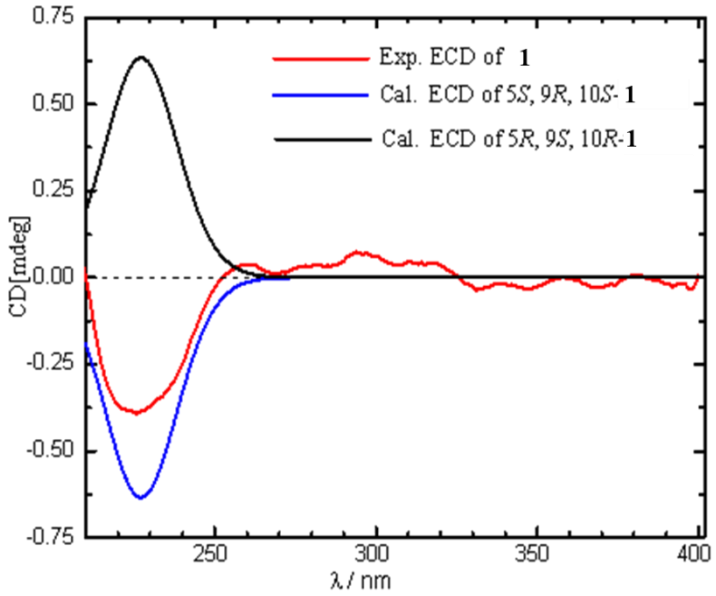


Figure S3. Experimental and calculated ECD spectra of **1**.

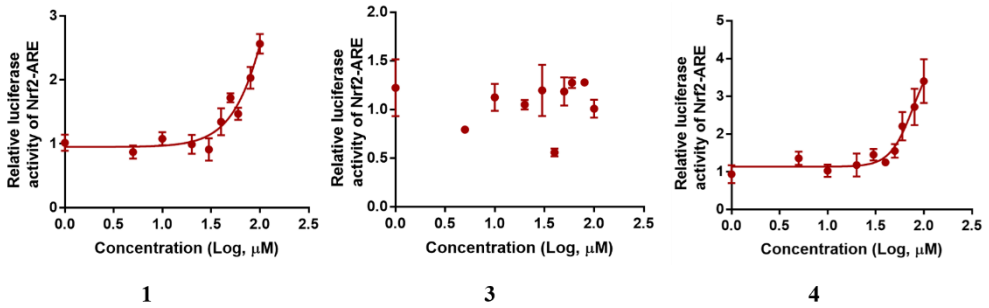


Figure S4. Compounds **1** and **4** activated Nrf2-ARE (n = 3).

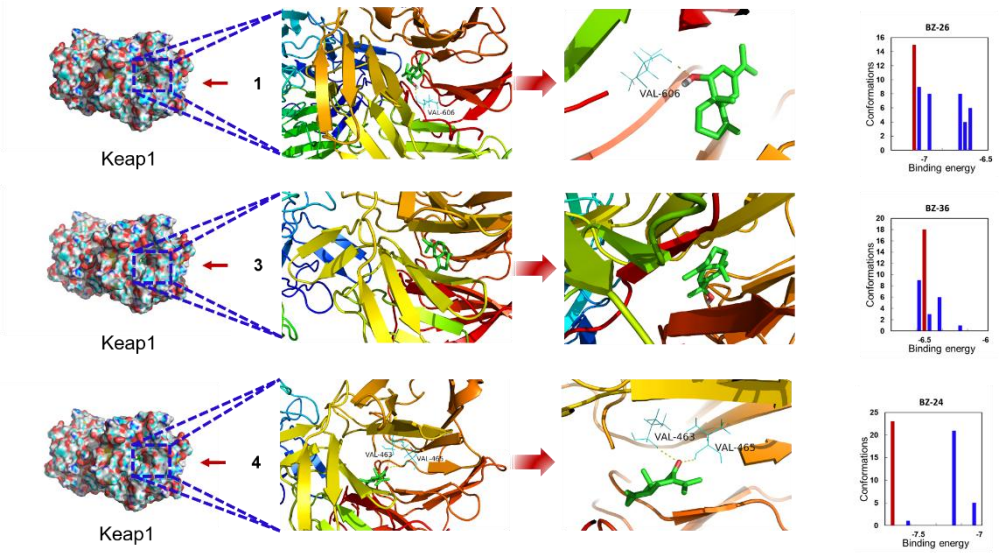
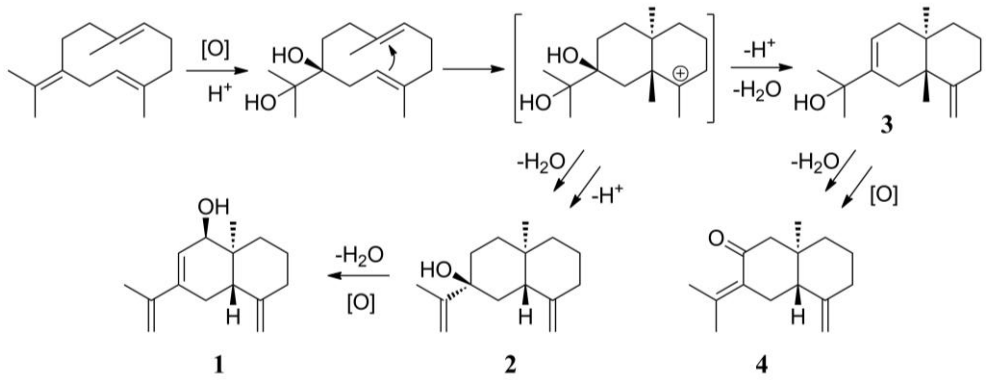


Figure S5. Compounds **1**, **3**, and **4** docking with Keap1.



Scheme S1. Proposed biosynthesis of the sesquiterpenes.

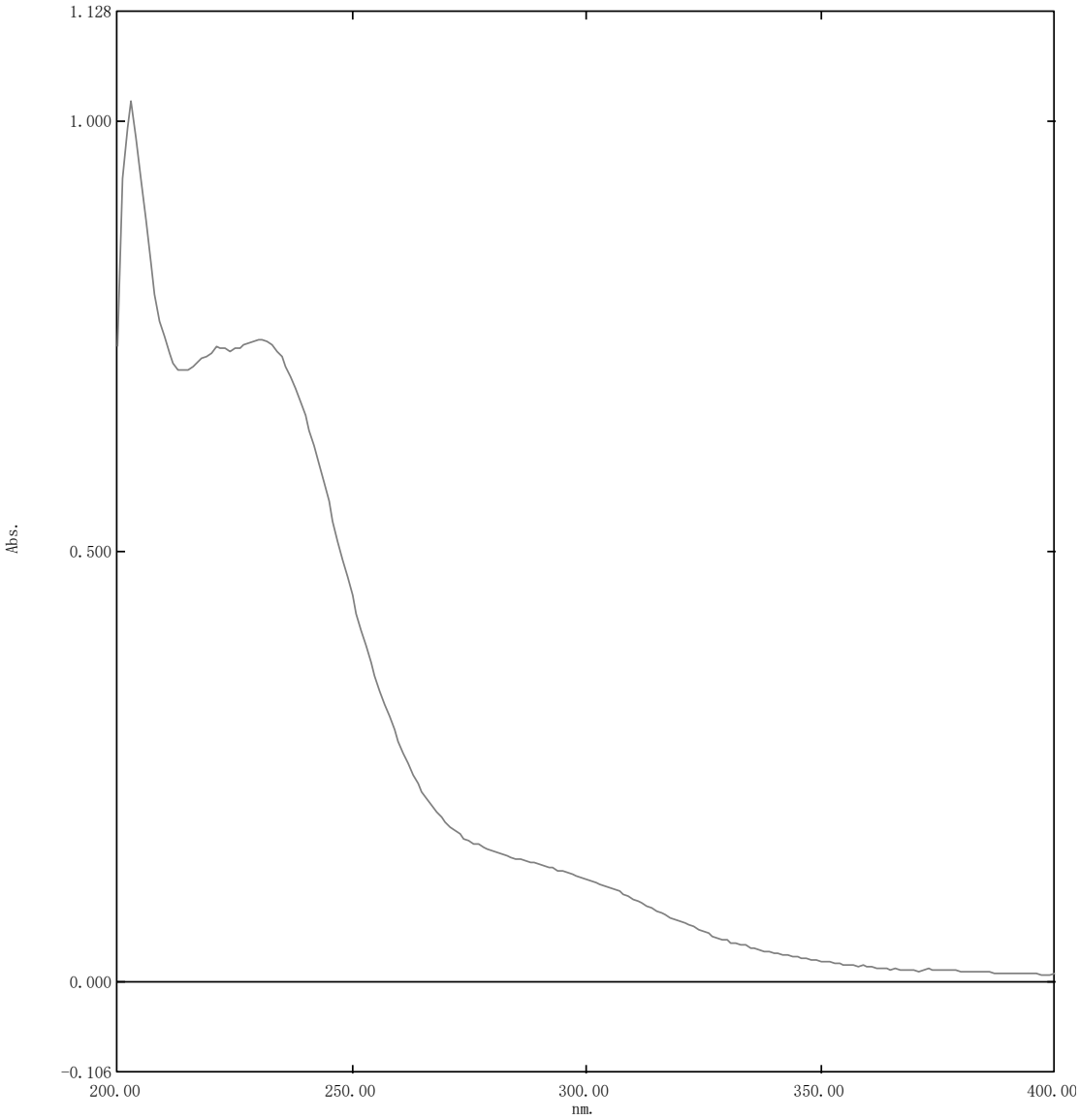


Figure S6 UV spectrum of compound **1**

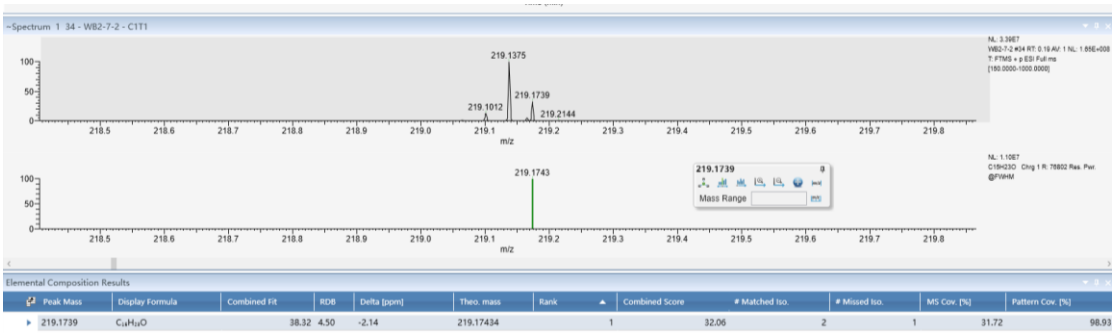


Figure S7 HRESIMS spectrum of compound **1**

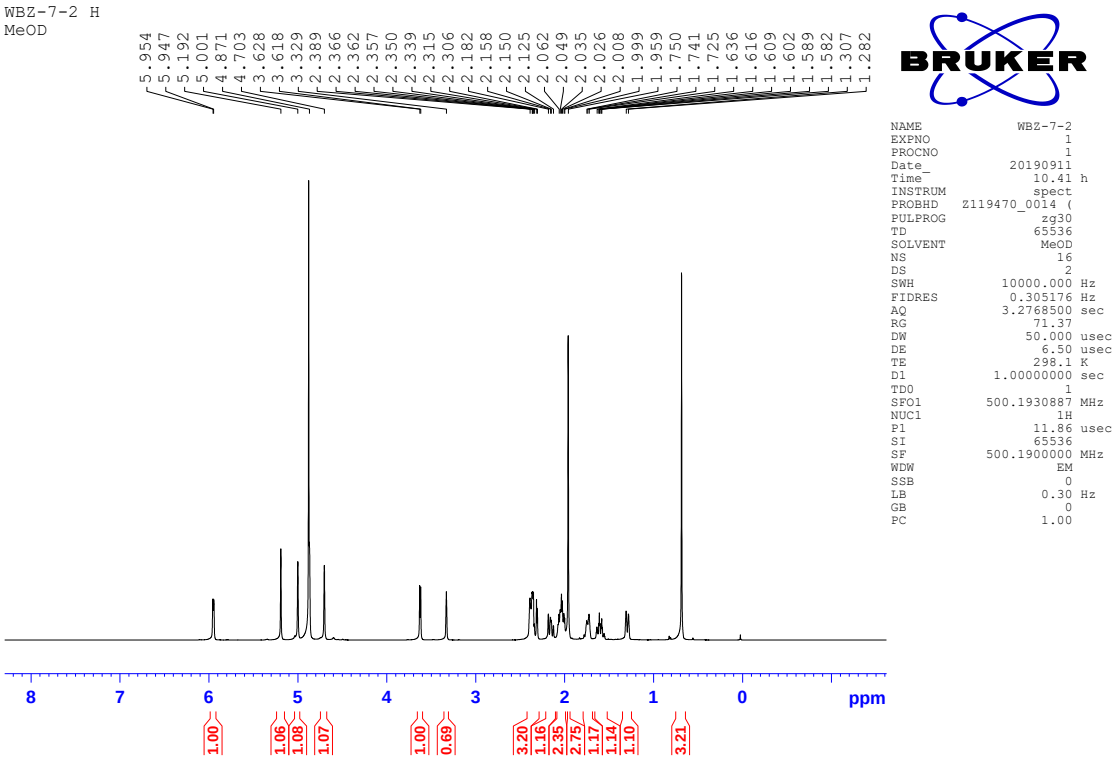


Figure S8 ^{1}H NMR (500 MHz) spectrum of compound **1** in methanol-d_4

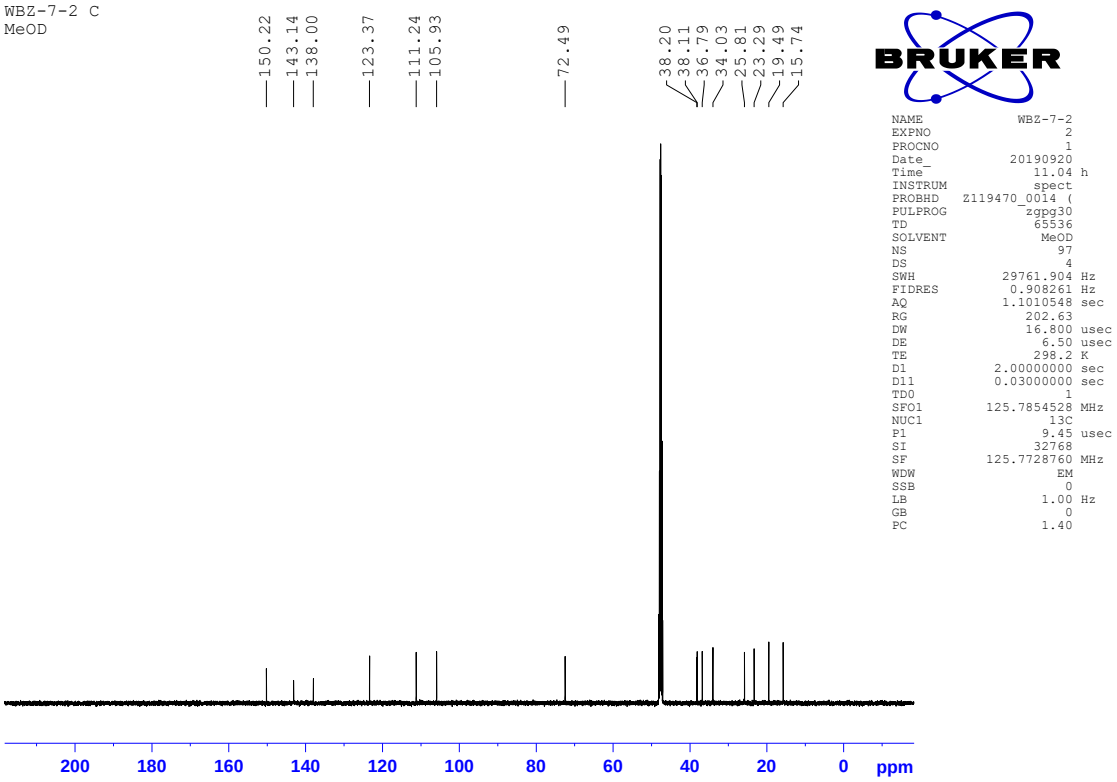


Figure S9 ^{13}C NMR (125 MHz) spectrum of compound **1** in methanol-d_4

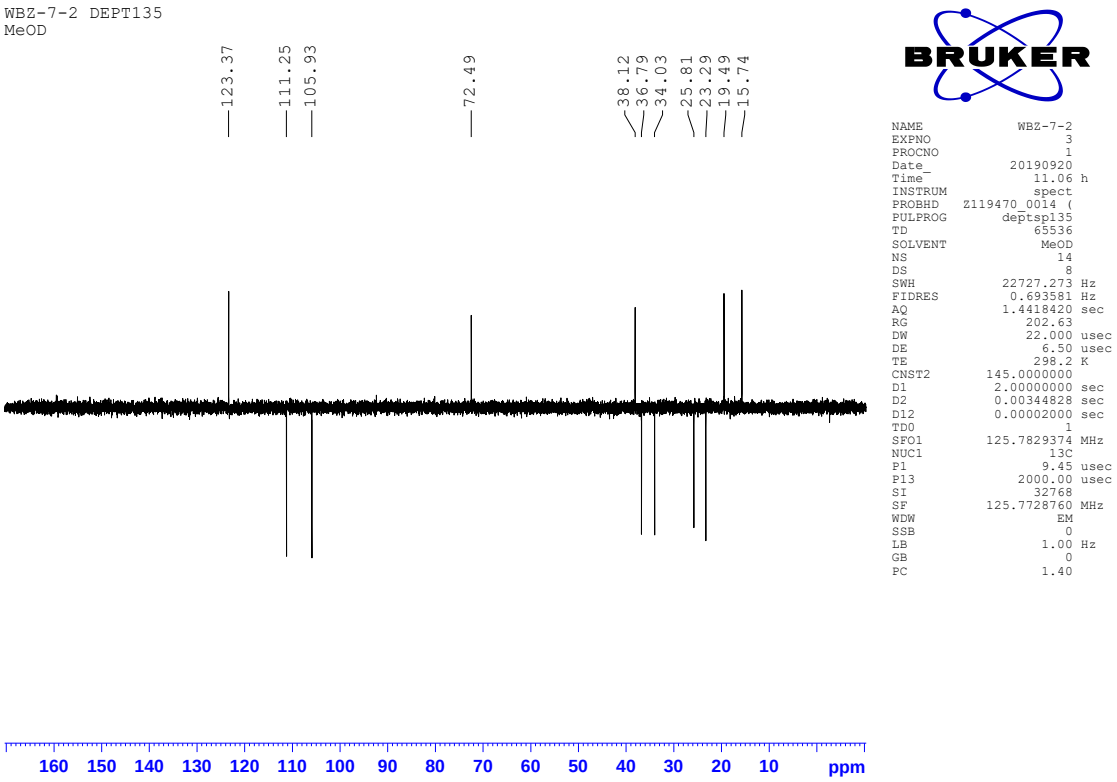


Figure S10 DEPT135 (125 MHz) spectrum of compound **1** in methanol-d_4

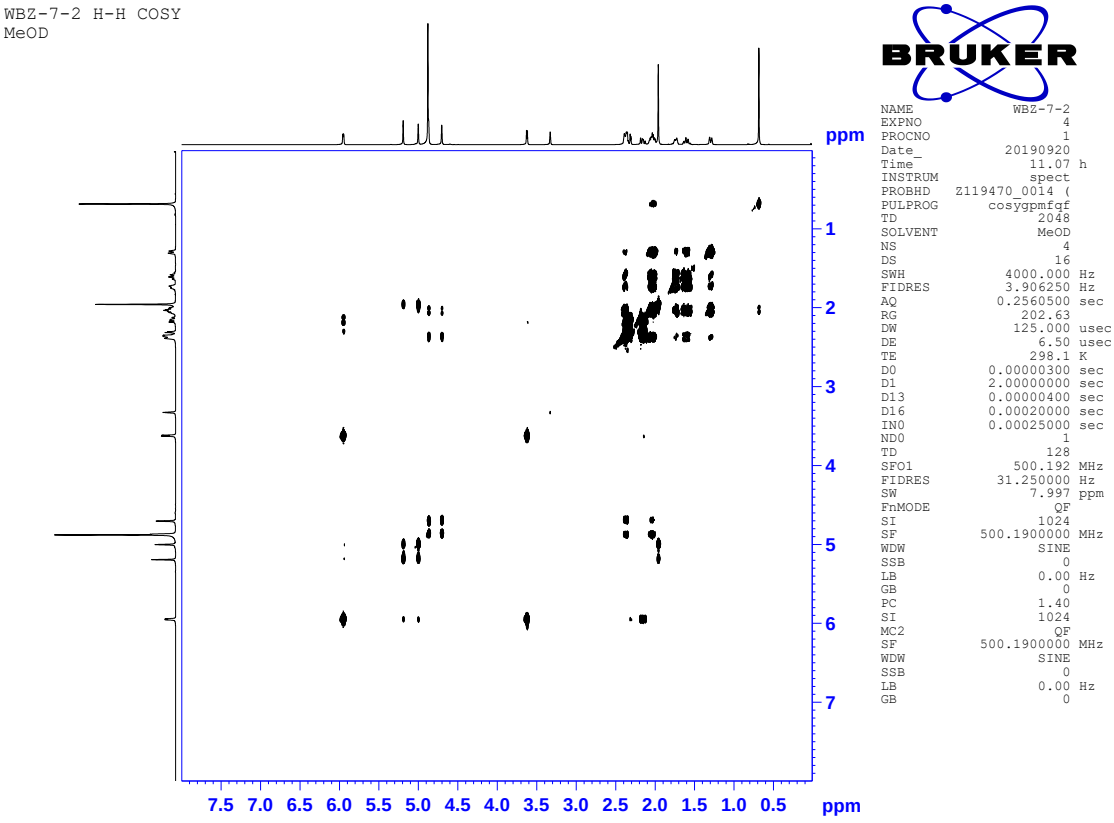


Figure S11 ^{1}H-^{1}H COSY (500 MHz) spectrum of compound **1** in methanol-d_4

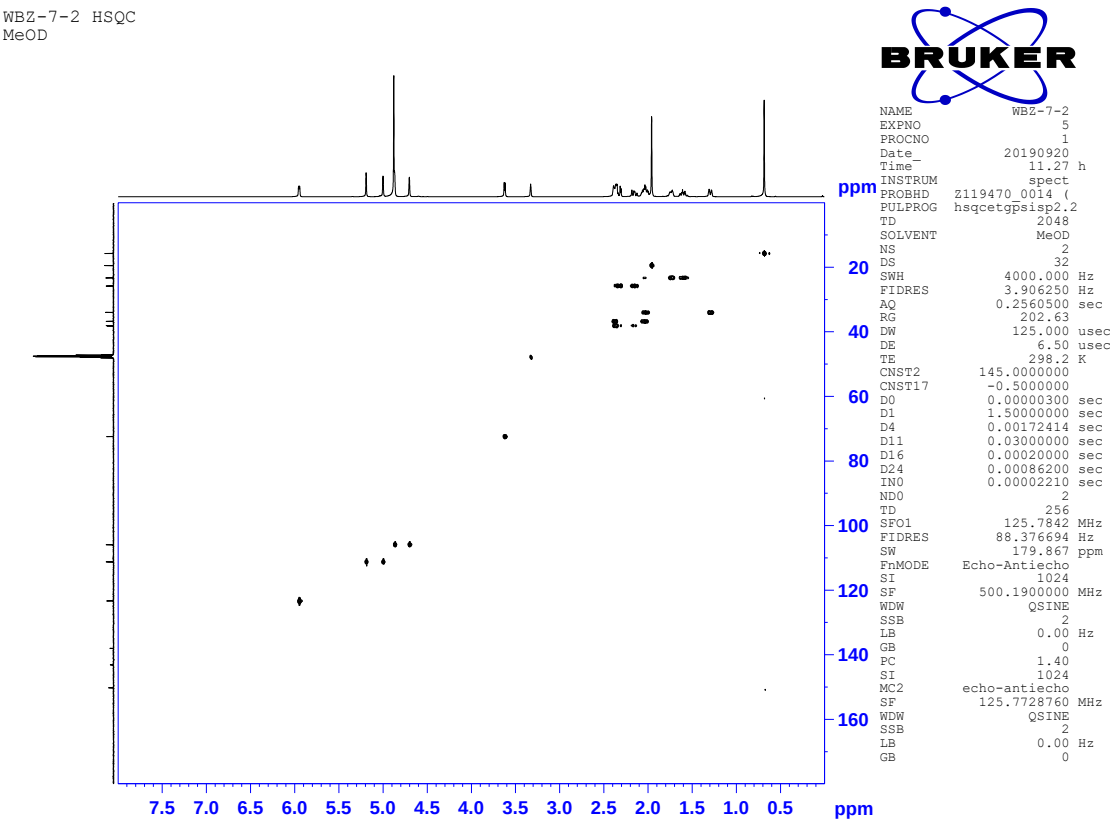


Figure S12 HSQC (500 MHz) spectrum of compound **1** in methanol-d_4

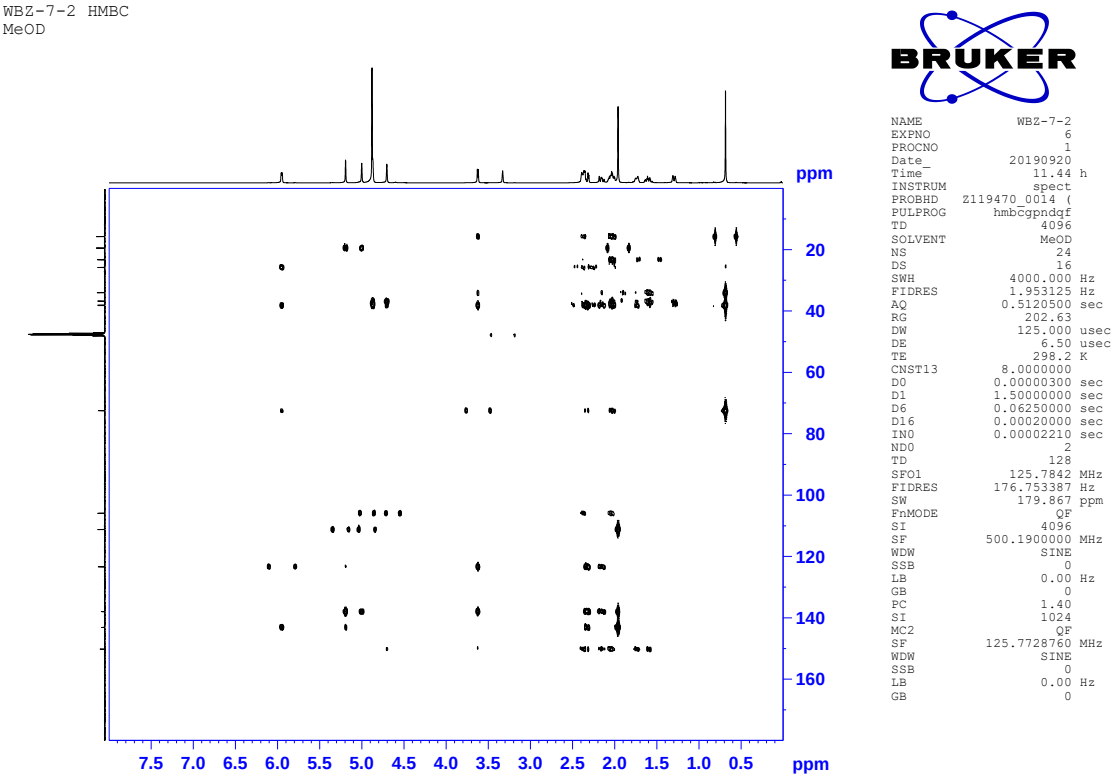


Figure S13 HMBC (500 MHz) spectrum of compound **1** in methanol-d_4

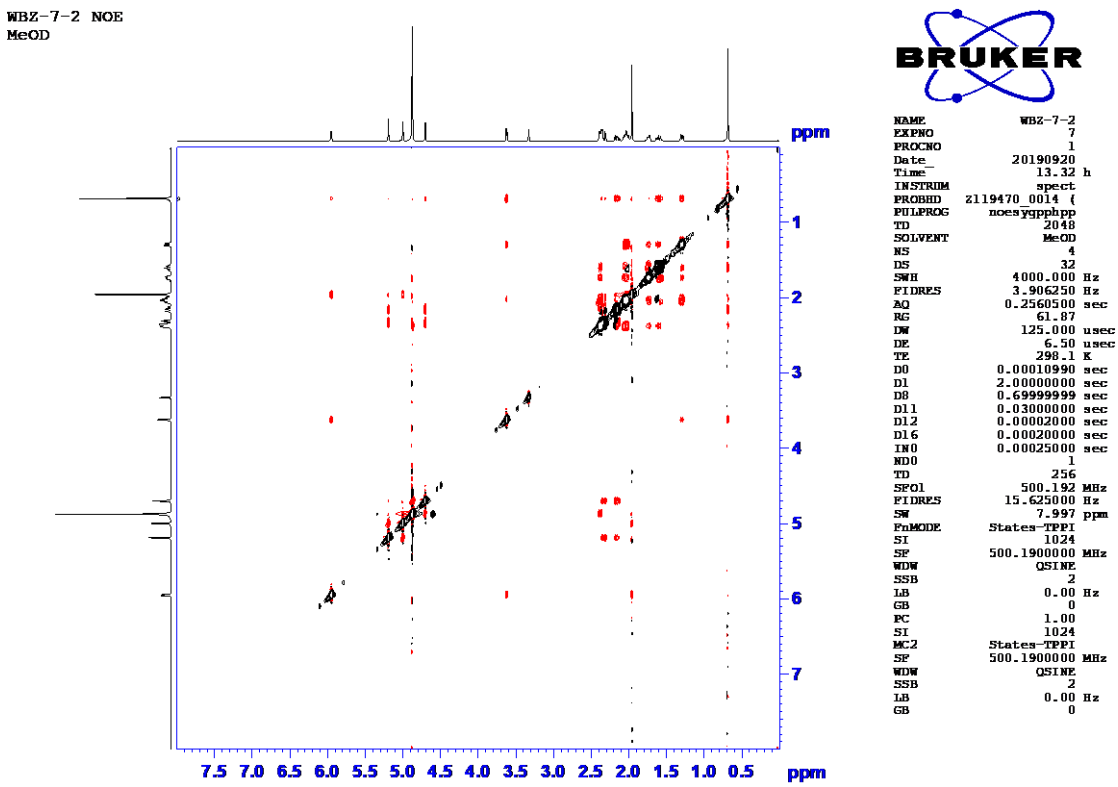


Figure S14 NOESY (500 MHz) spectrum of compound **1** in methanol-d_4

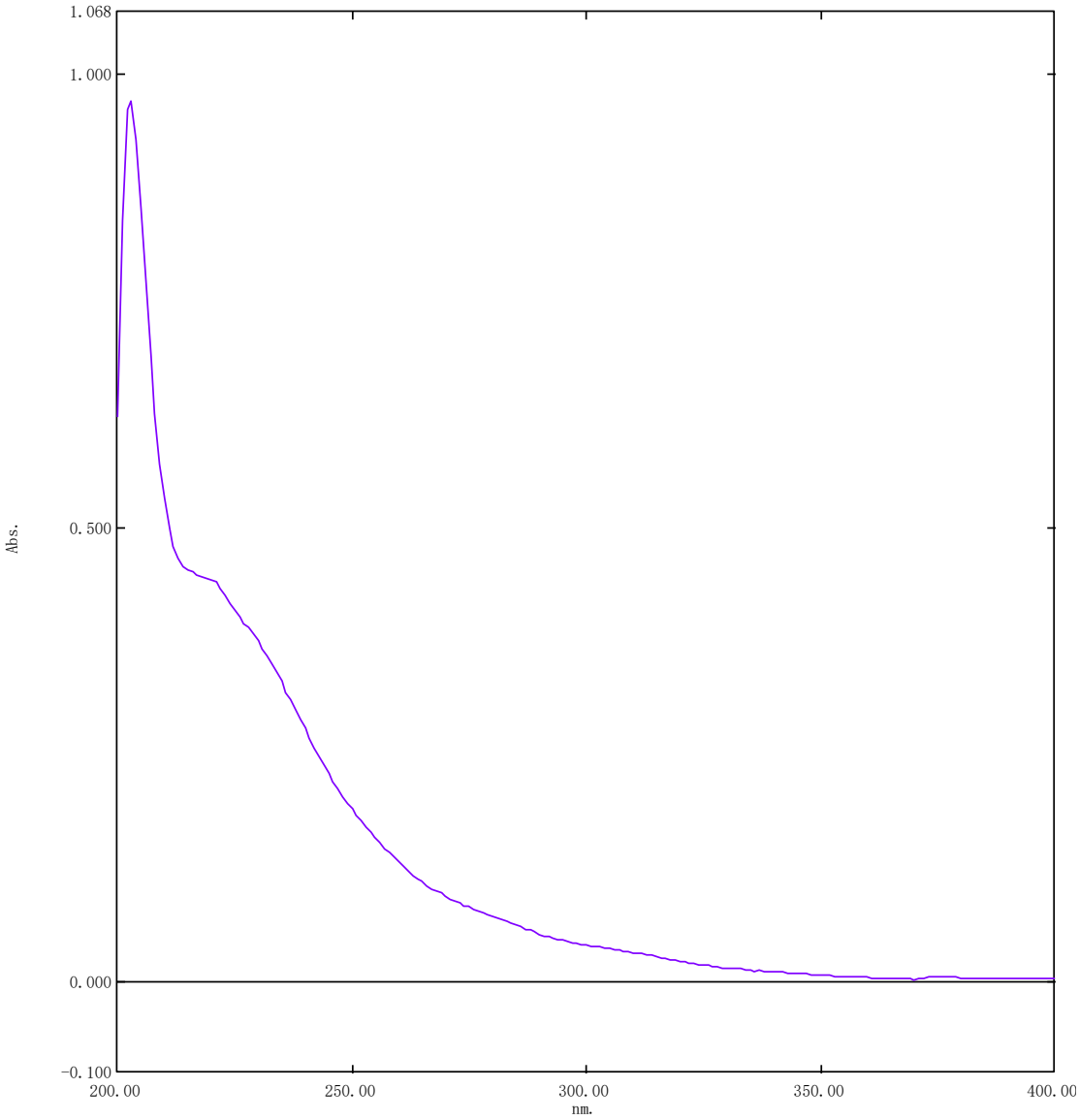


Figure S15 UV spectrum of compound **2**

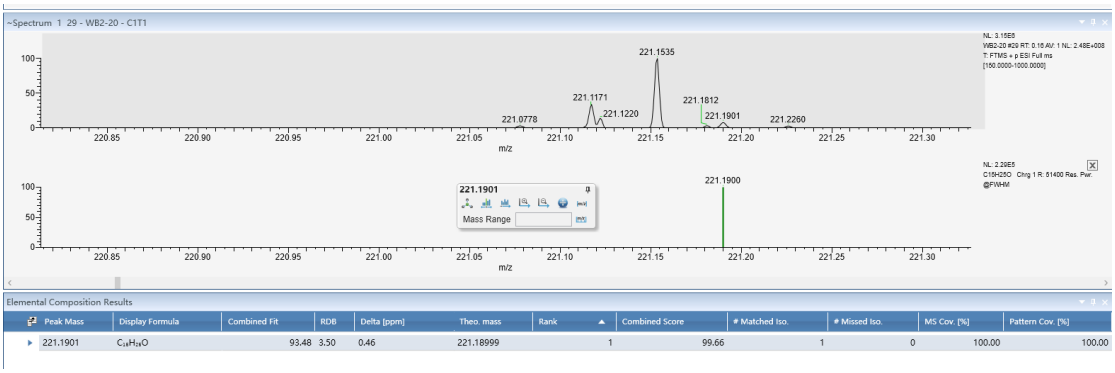


Figure S16 HRESIMS spectrum of compound **2**

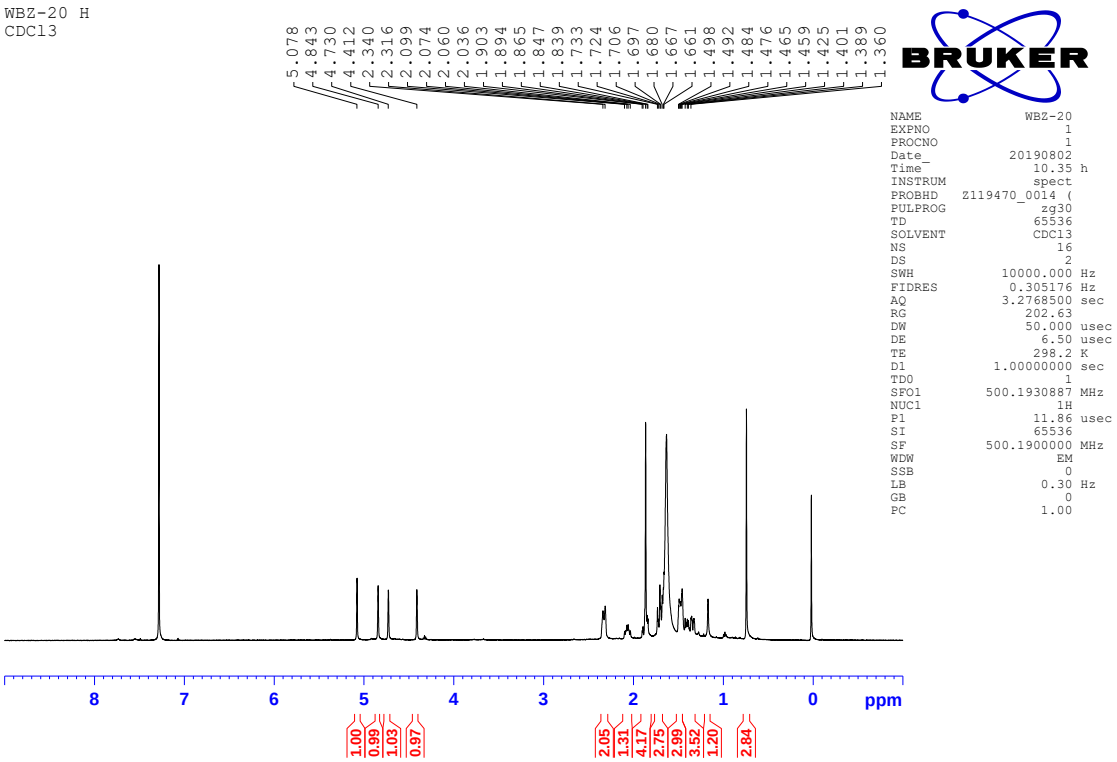


Figure S17 ^{1}H NMR (500 MHz) spectrum of compound **2** in $CDCl_3$

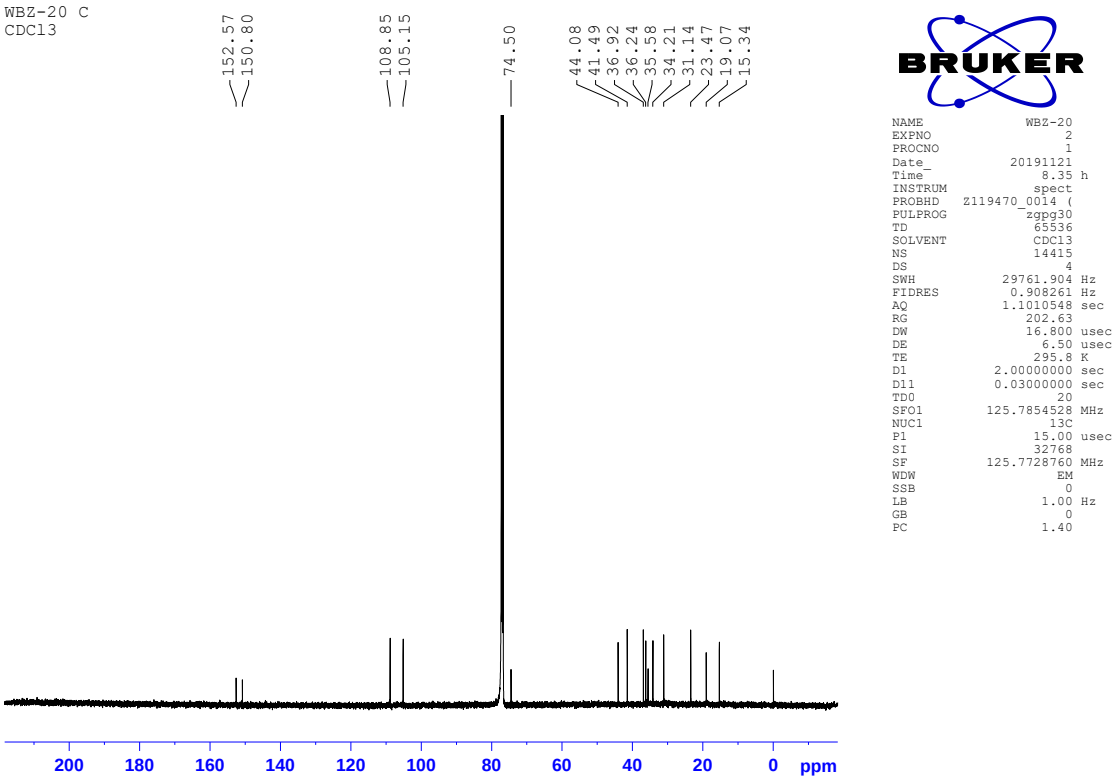


Figure S18 ^{13}C NMR (125 MHz) spectrum of compound **2** in $CDCl_3$

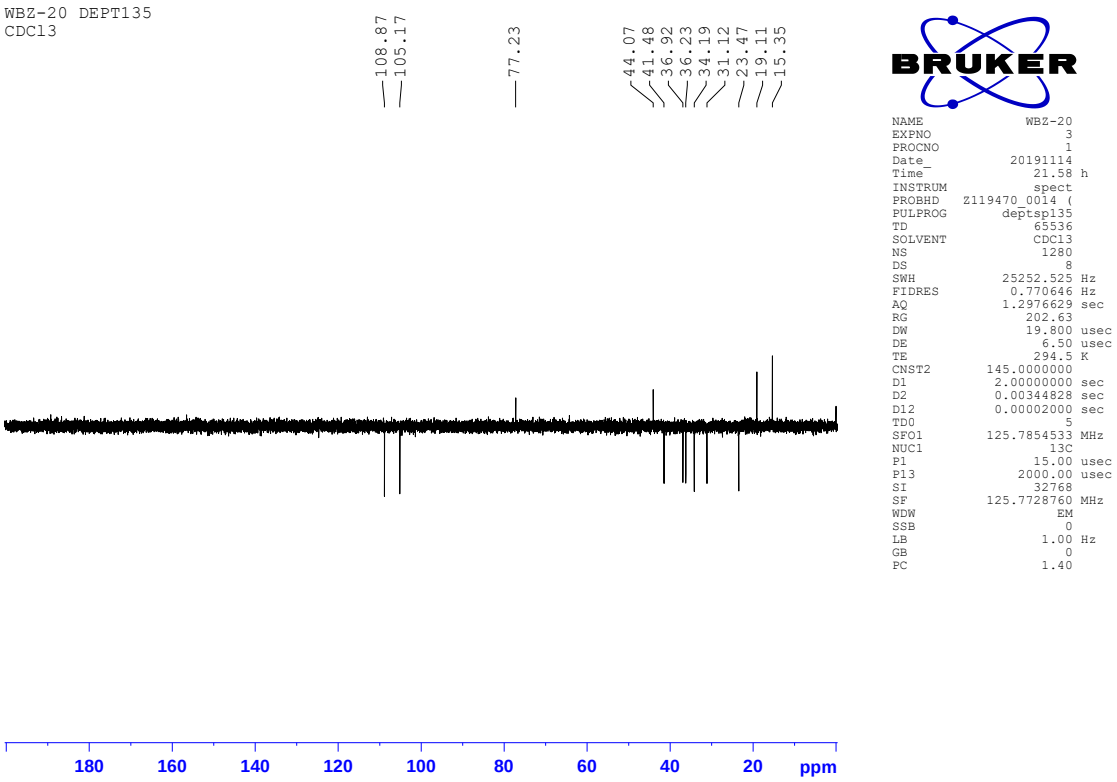


Figure S19 DEPT135 (125 MHz) spectrum of compound **2** in $CDCl_3$

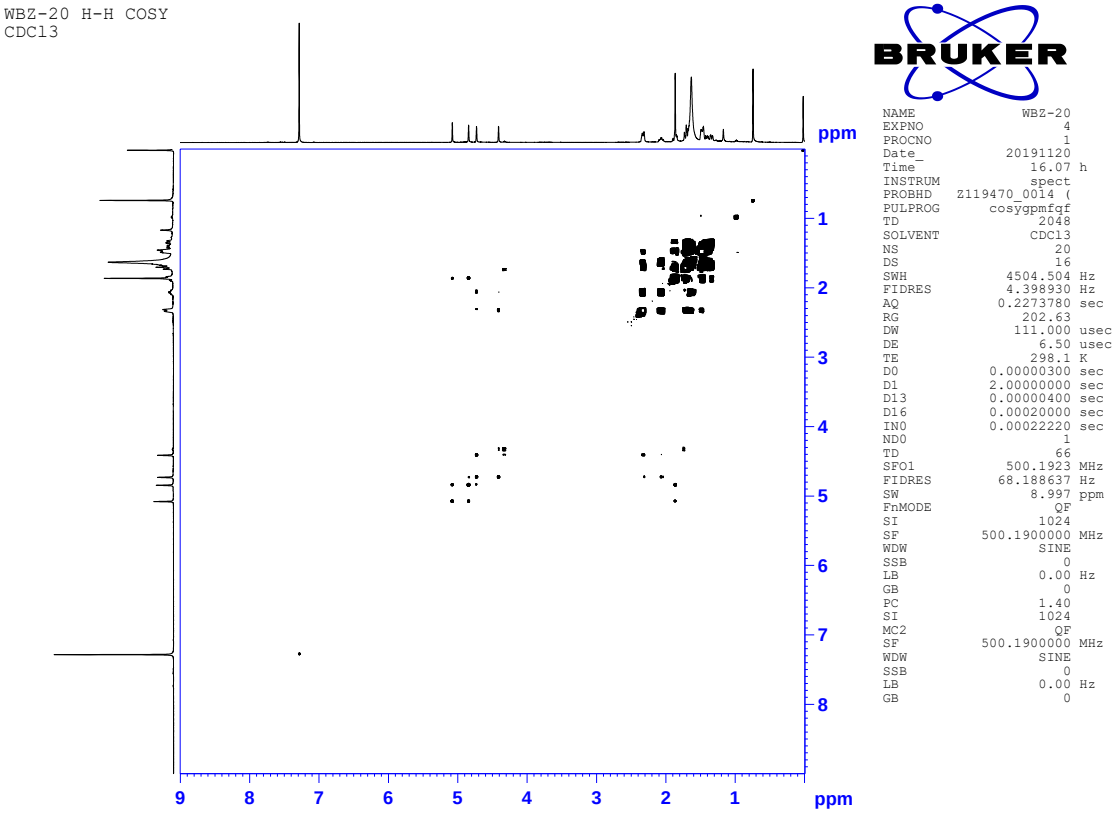


Figure S20 ^{1}H-^{1}H COSY (500 MHz) spectrum of compound **2** in $CDCl_3$

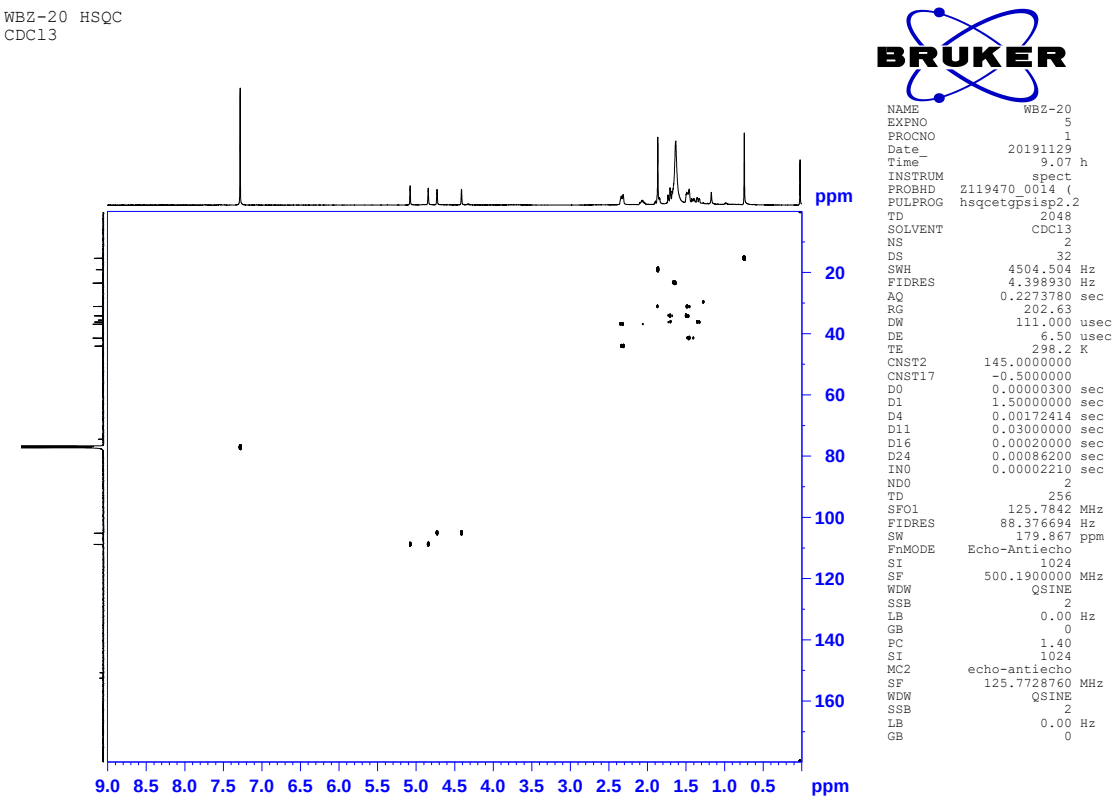


Figure S21 HSQC (500 MHz) spectrum of compound **2** in $CDCl_3$

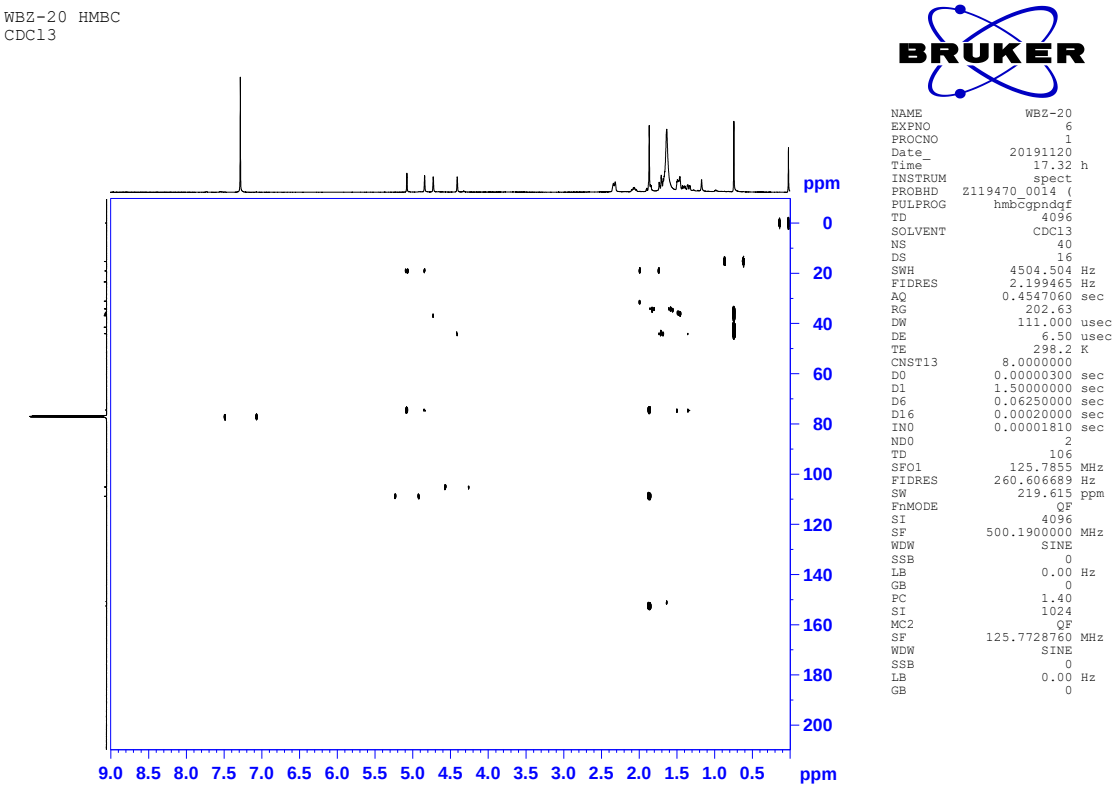


Figure S22 HMBC (500 MHz) spectrum of compound **2** in $CDCl_3$

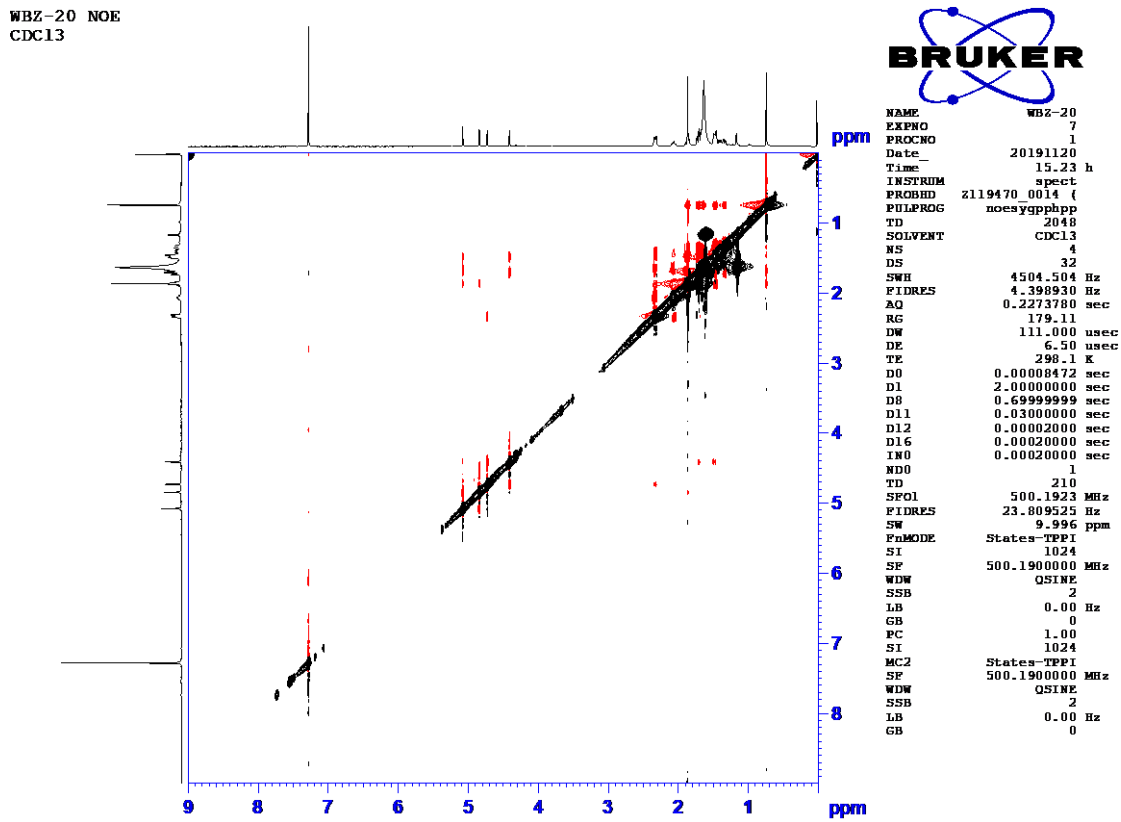


Figure S23 NOESY (500 MHz) spectrum of compound **2** in $CDCl_3$