

SUPPLEMENTARY MATERIAL

Antiplasmodial prenylated flavanonols from *Tephrosia subtriflora*

Lois M. Muiva-Mutisya^a, Yoseph Atilaw^a, Matthias Heydenreich^b, Andreas Koch^b, Hoseah M. Akala^c, Agnes C. Cheruiyot,^c Matthew L. Brown,^c Beatrice Irungu,^d Faith A. Okalebo^e, Solomon Derese^a, Charles Mutai^f, Abiy Yenesew^{a,*}

*Corresponding Author Tel.: +254 733 832576;

Email Address: ayenesew@uonbi.ac.ke (A. Yenesew)

Abstract

The CH₂Cl₂/MeOH (1:1) extract of the aerial parts of *Tephrosia subtriflora* afforded a new flavanonol, named subtriflavanonol (**1**), along with the known flavanone spinoflavanone B, and the known flavanonols MS-II (**2**) and mundulinol. The structures were elucidated by the use of NMR spectroscopy and mass spectrometry. The absolute configuration of the flavanonols was determined based on quantum chemical ECD calculations. In the antiplasmodial assay, compound **2** showed the highest activity against chloroquine sensitive *Plasmodium falciparum* reference clones (D6 and 3D7), artemisinin sensitive isolate (F32-TEM) as well as field isolate (KSM 009) with IC₅₀ values 1.4 - 4.6 μM without significant cytotoxicity against Vero and HEp2 cell-lines (IC₅₀ > 100 μM). The new compound (**1**) showed weak antiplasmodial active, IC₅₀ 12.5 – 24.2 μM, but also showed selective anticancer activity against HEp2 cell line (CC₅₀ 16.9 μM).

Keywords: *Tephrosia subtriflora*; Leguminosae; Prenylated flavanonol; Subtriflavanonol; Antiplasmodial; Cytotoxicity.

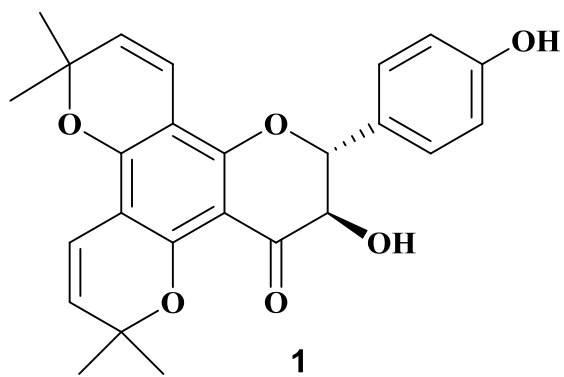


Figure. S1. Structure of compound **1** isolated from *Tephrosia subtriflora*.

Table of content

Table/Figure	Content	Page
Table S1	^1H and ^{13}C NMR data for compound 1	3
Fig. S1	Structure of compound 1 isolated from <i>Tephrosia subtriflora</i>	1
Fig. S2	^1H NMR spectrum of compound 1	4
Fig. S3	^{13}C NMR spectrum of compound 1	5
Fig. S4	^1H , ^1H -COSY spectrum of compound 1	6
Fig. S5	HMBC spectrum of compound 1	7
Fig. S6	HSQC spectrum of compound 1	8
Fig. S7	NOESY spectrum of compound 1	9
Fig. S8	EIMS and HRMS spectra of compound 1	10
Fig. S9	UV spectrum of compound 1	11
Fig. S10	ECD spectra of compounds 1 and 2	11

Table S1: ^1H (600 MHz) and ^{13}C (150 MHz) NMR data for compound **1** (in CDCl_3)

Position	δ_{H} , multiplicity(J in Hz)	δ_{C}	HMBC (2J , 3J)
2	4.92, <i>d</i> ($J = 12.1$)	82.9	C-3, C-4, C-2'
3	4.38, <i>dd</i> ($J = 12.1, 2.0$)	73.1	C-2, C-4, C-1'
4		190.6	
4a		102.6 ^a	
5		155.9	
6		104.8	
7		155.4	
8		102.7 ^a	
8a		157.5	
1'		129.1	
2'/6'	7.41, <i>m</i>	129.4	C-2, C-4'
3'/5'	6.87, <i>m</i>	115.6	C-1', C-4'
4'		156.8	
2''		78.5	
3''	5.50, <i>d</i> ($J = 10.0$)	126.9	C-8, C-2''
4''	6.58, <i>d</i> ($J = 10.0$)	115.9	C-7, C-8, C-8a, C-2''
2'''		78.4	
3'''	5.56, <i>d</i> ($J = 10.0$)	127.0	C-6, C-2'''
4'''	6.50, <i>d</i> ($J = 10.1$)	115.8	C-5, C-6, C-2'''
Me ₂ -2''	1.52 (3H, <i>s</i>), 1.45 (6H, <i>s</i>), 1.43 (3H <i>s</i>)	28.4, 28.2	
Me ₂ -2'''		28.2, 27.9	
3-OH	4.05 (1H, <i>d</i> , $J = 2.0$ Hz,)		C-2, C-3, C-4
4'-OH	5.61 (1H, <i>br s</i> ,)		

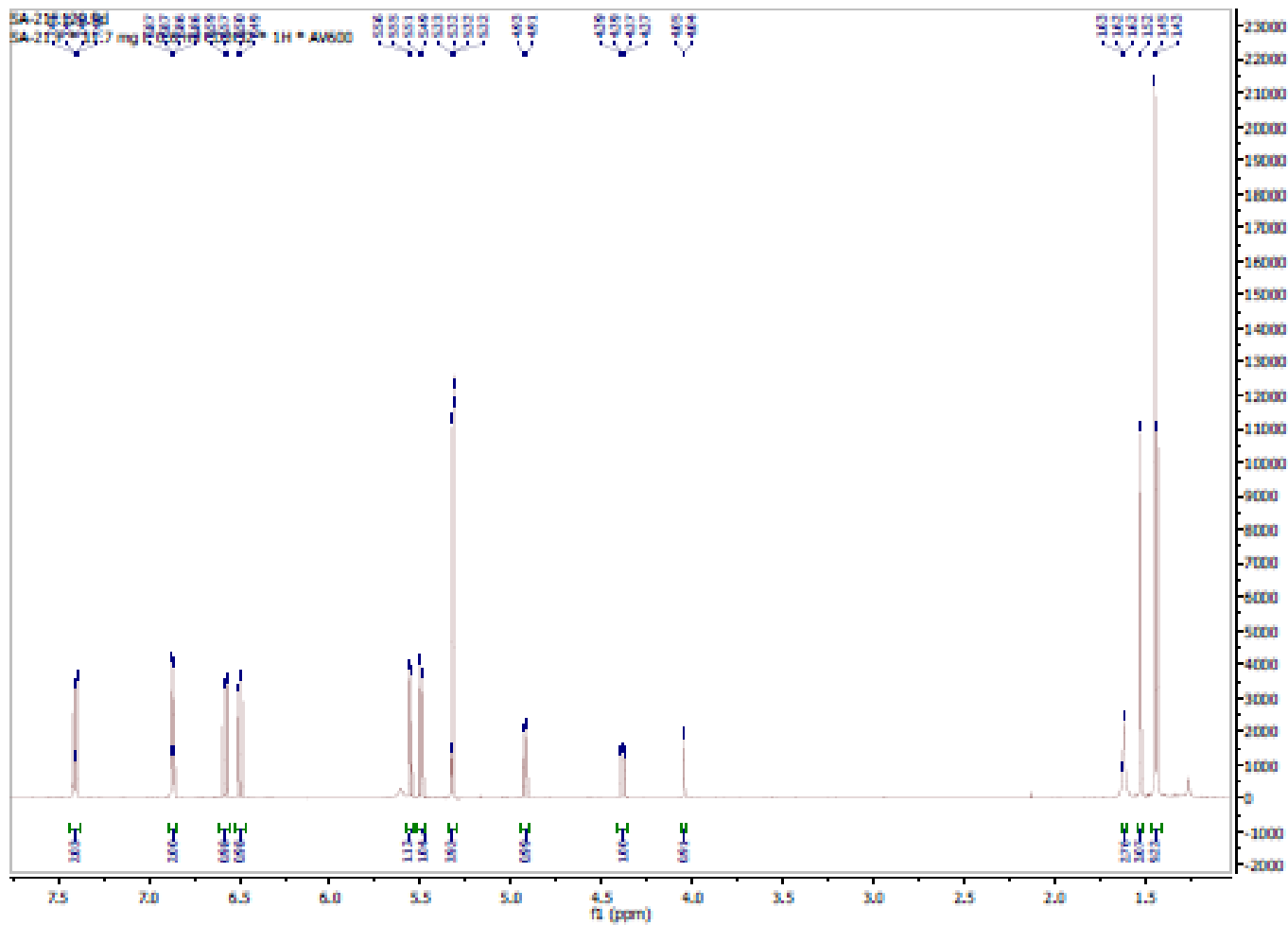


Figure. S2: ¹H NMR spectrum of compound **1** (CD₂Cl₂, 600 MHz)

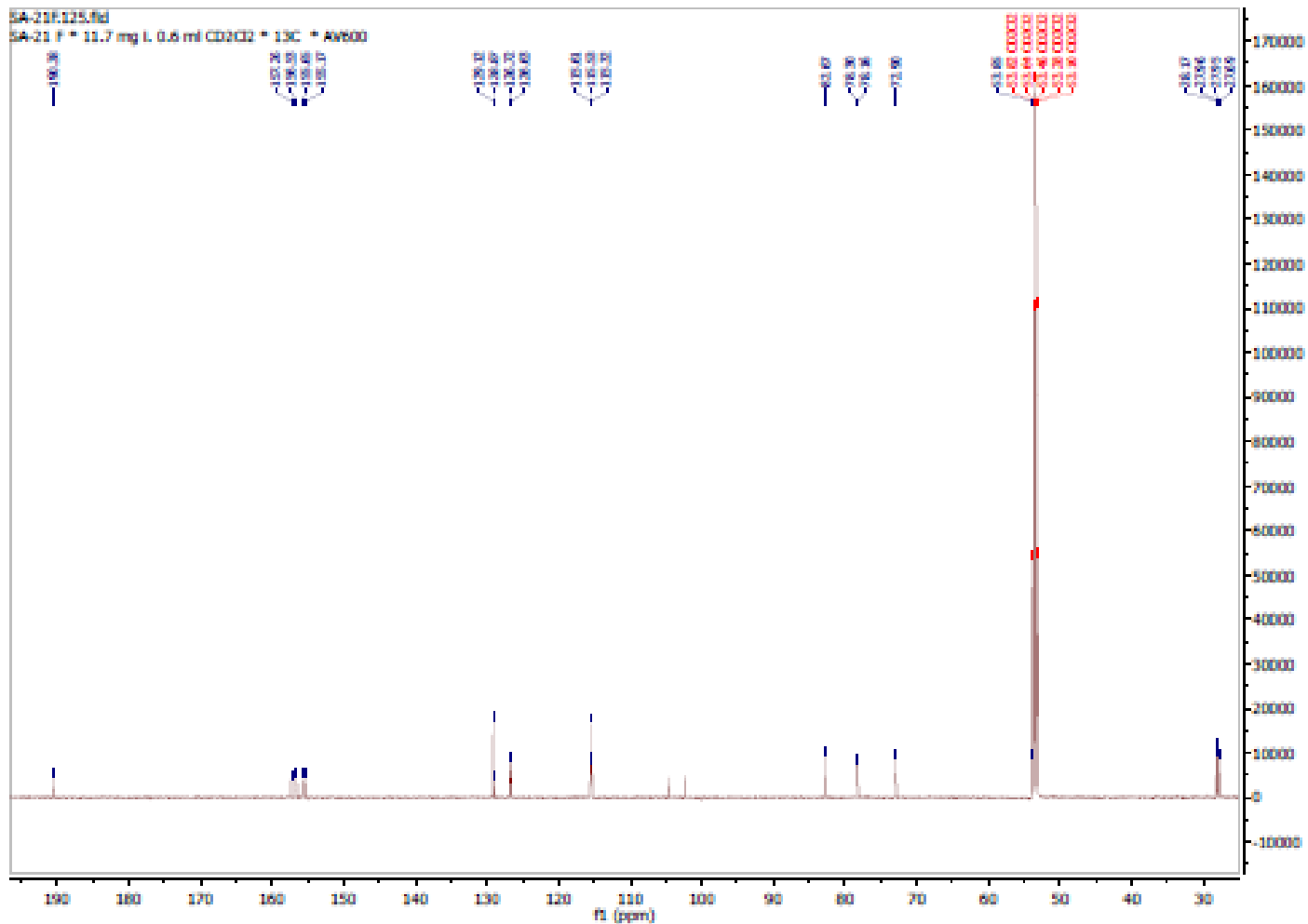


Figure. S3: ^{13}C NMR spectrum of compound **1** (CD_2Cl_2 , 150 MHz)

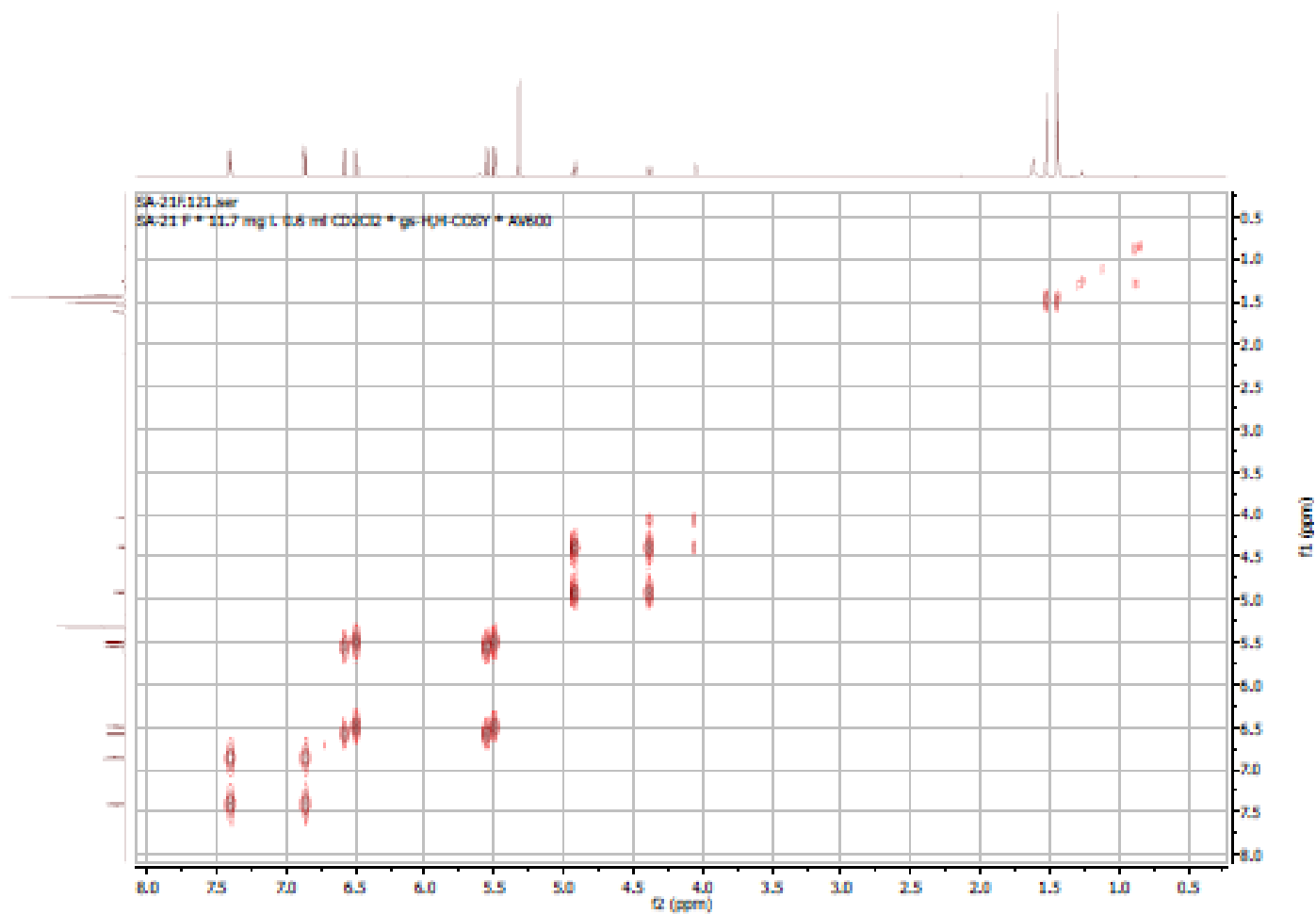


Figure. S4: ^1H - ^1H COSY spectrum of compound **1** (CD_2Cl_2 , 600 MHz)

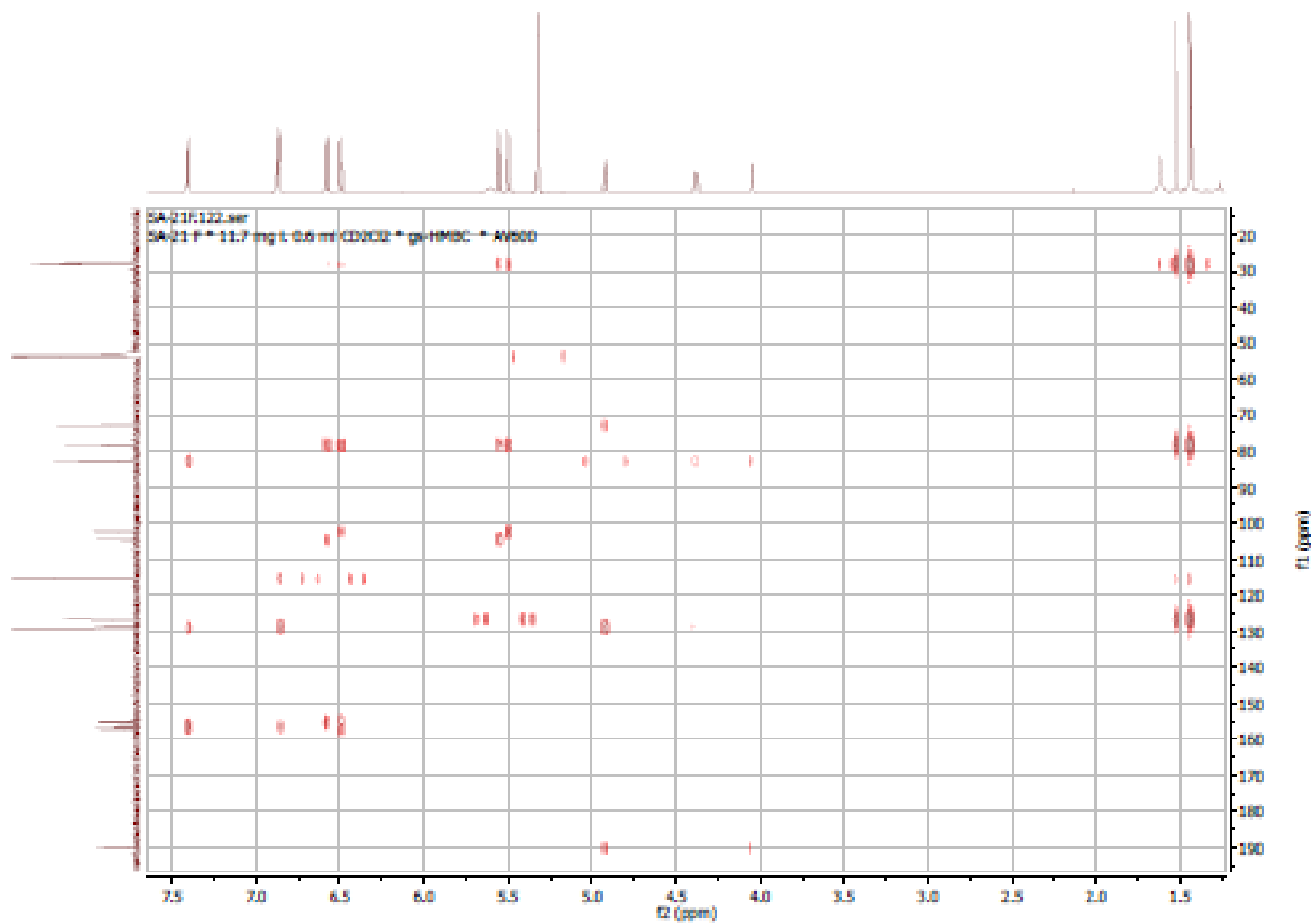


Figure. S5: HMBC spectrum of compound **1** (CD_2Cl_2 , 600 MHz)

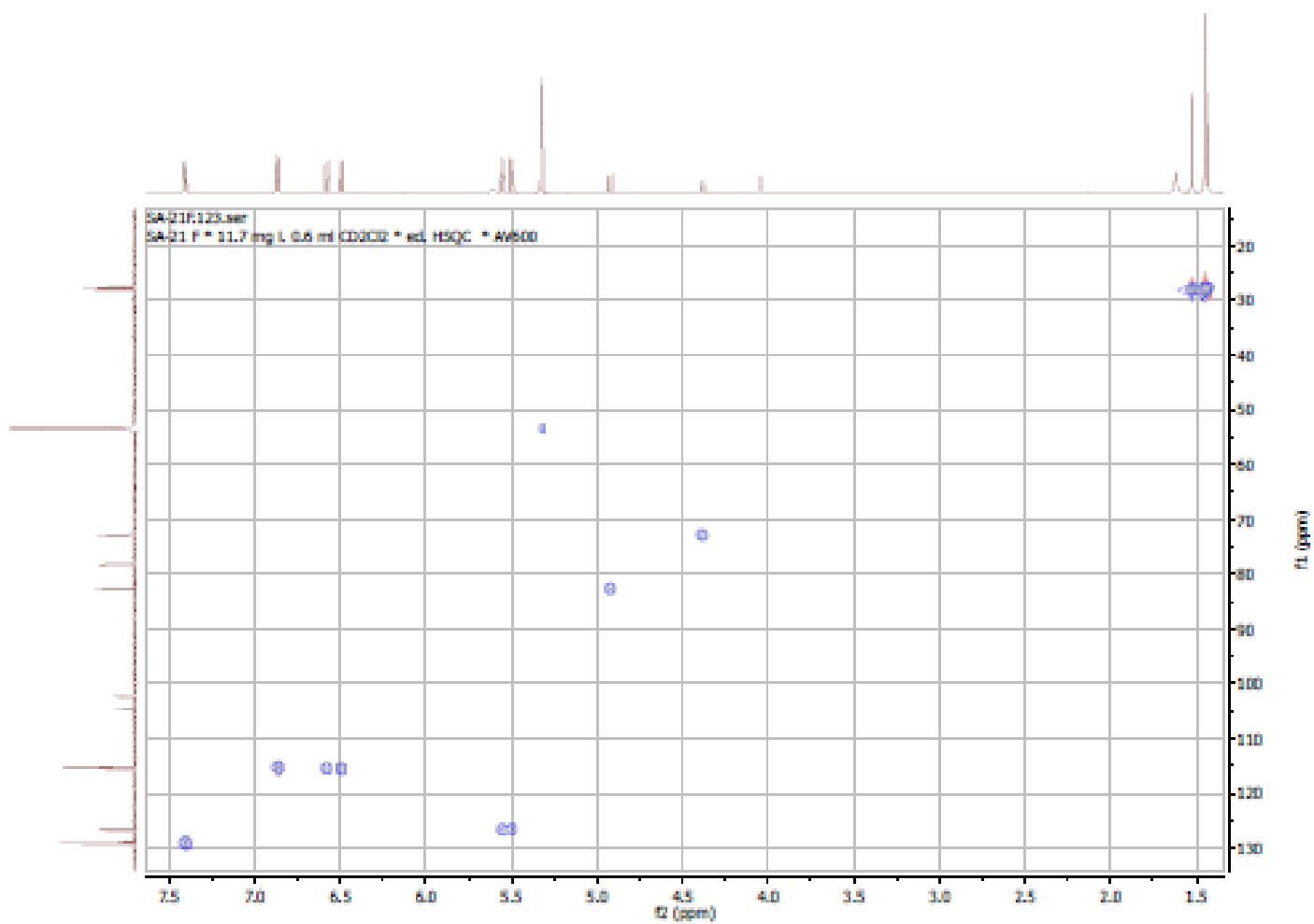


Figure. S6: HSQC spectrum of compound **1** (CD_2Cl_2 , 600 MHz)

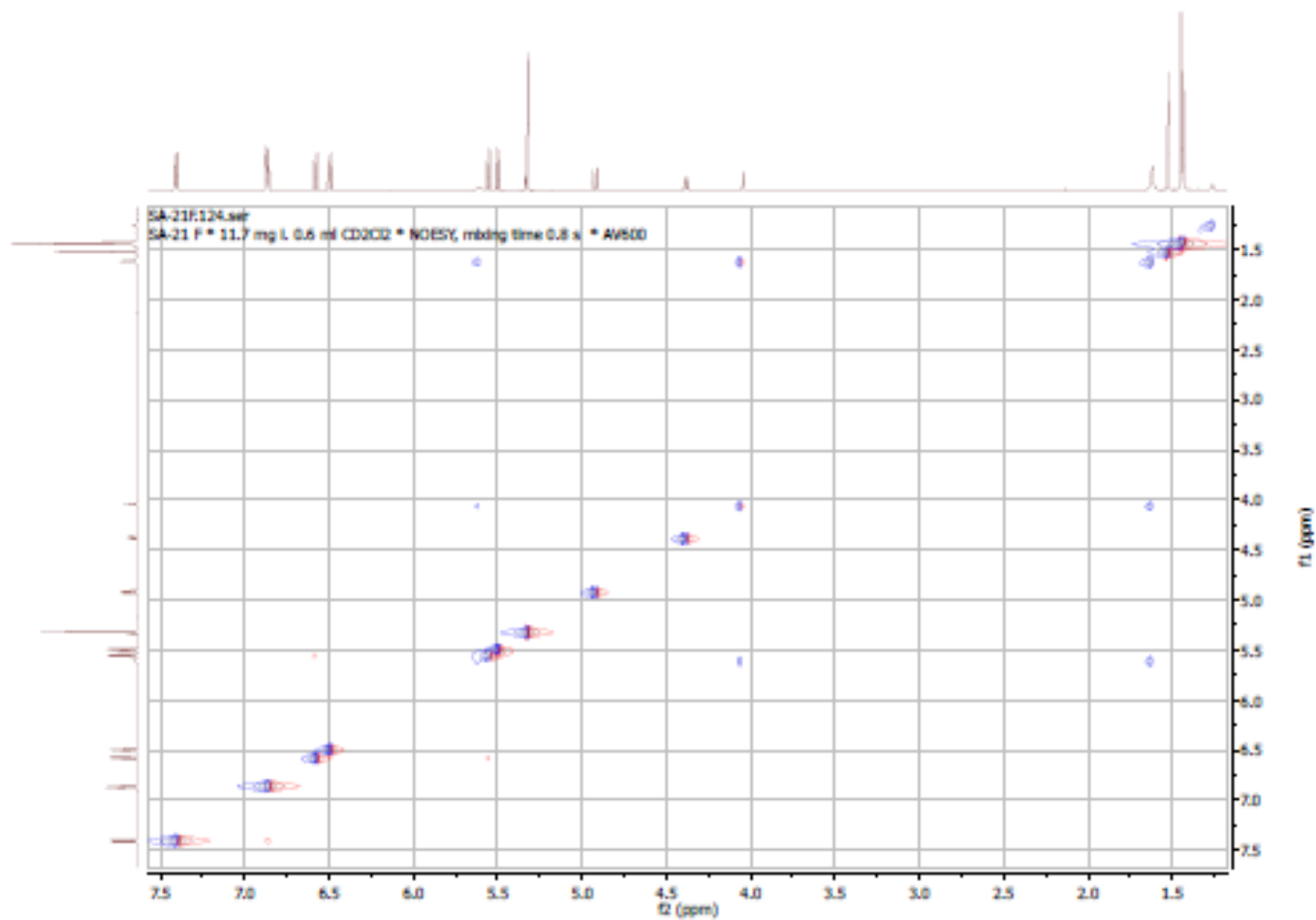
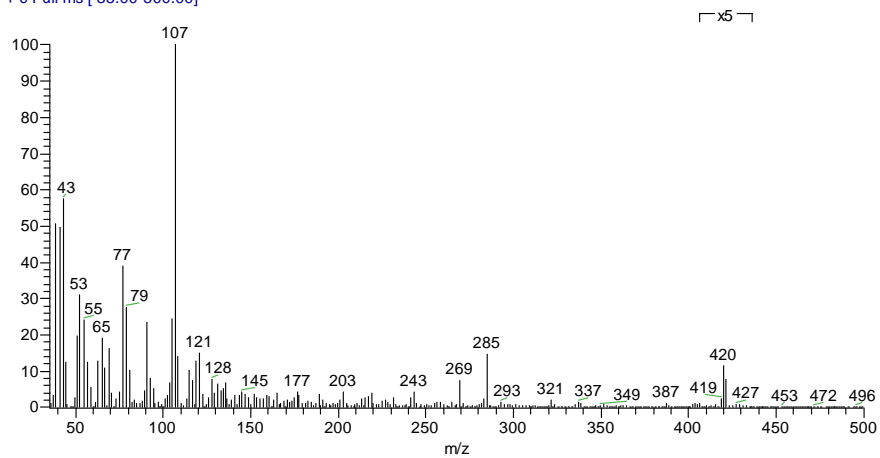


Figure. S7: NOESY spectrum of compound **1** (CD_2Cl_2 , 600 MHz)

Heydenreich_169 #197-202 RT: 0.72-0.74 AV
T: + c Full ms [35.00-500.00]



Heydenreich_169 #198-202 RT: 0.72-0.74 AV: 5 NL: 2.01E4
T: + c Full ms [35.00-500.00]

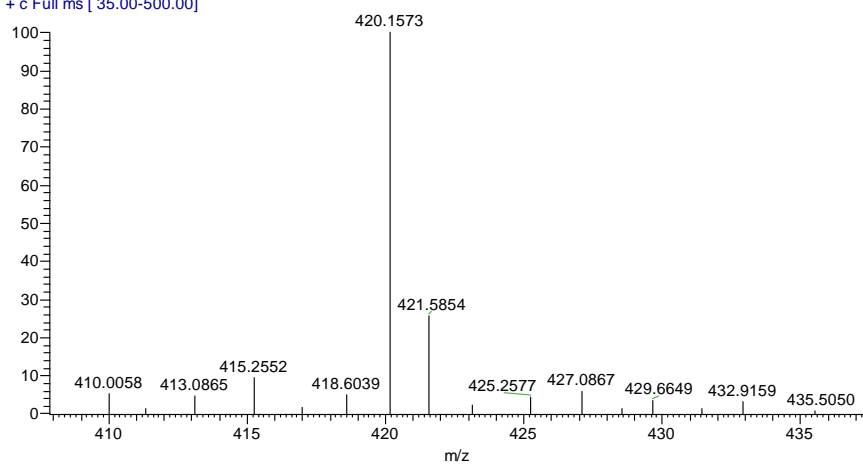


Figure. S8: EIMS and HRMS spectra of compound **1**

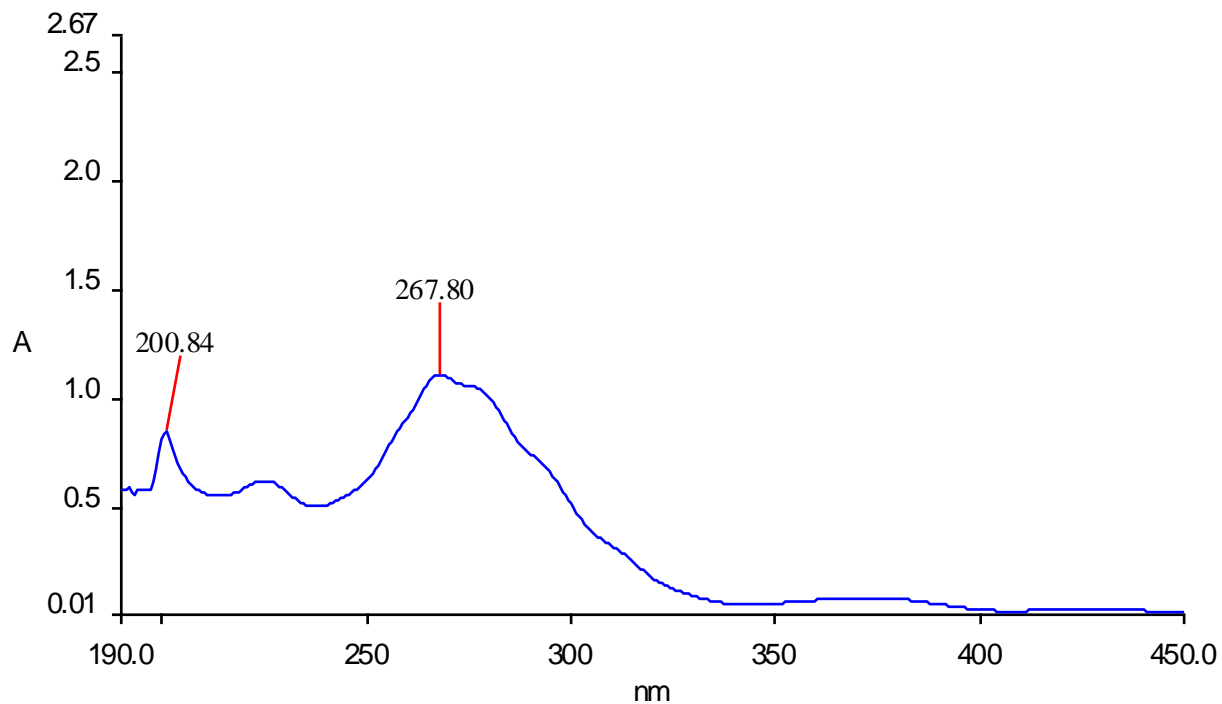


Figure. S9: UV spectrum of compound **1** (MeOH)

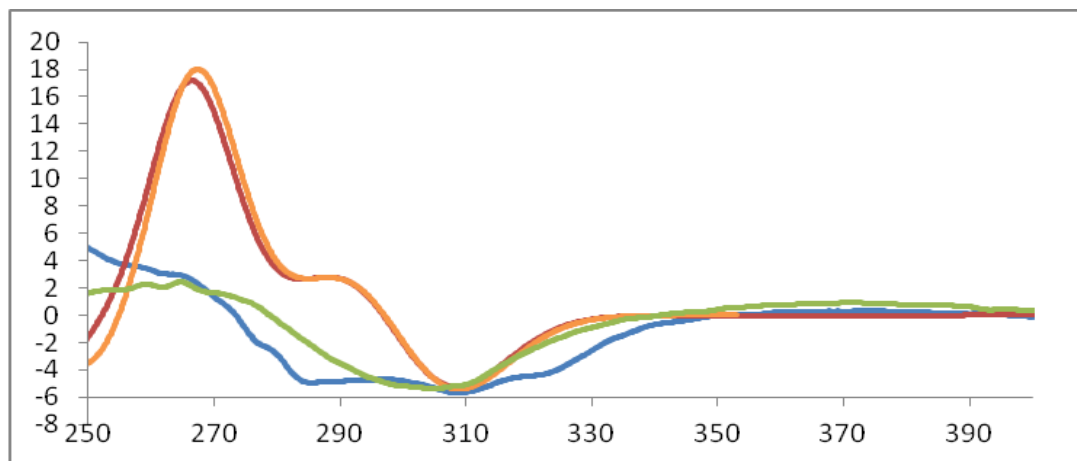


Figure. S10: The experimental ECD spectra of **1** (blue) and **2** (green), and the computationally (DFT) predicted spectra for the *trans*-fused (2*R*,3*R*)-**1** (orange) and *trans*-fused (2*R*,3*R*)-**2** (red).