Electronic Supplementary Material (ESI) for Organic Chemistry Frontiers.

Supporting Information

(+)- and (−)-Actinoxocine, and Actinaphthorans A−B, C-Ring Expansion and Cleavage Angucyclinones from a Marine-Derived *Streptomyces* sp.

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Experimental details

General Procedures. Opitical rotation was measured on an Autopol VI, Serial #91058. UV spectra were recorded by a Shimadzu UV-2401PC spectrometer. CD spectrum was recorded on a JASCO J-810 spectropolarimeter. ^{1}H and 2D NMR spectra were measured at 600 MHz in DMSO-d_6 by a Bruker AVANCE IIITM 600 spectrometer, and ^{13}C NMR spectra were acquired at 150 MHz, the chemical shifts were referenced to DMSO-d_6 (δ_H 2.50/δ_C 39.9). ESI-MS were performed through a Finnigan LCQ with quaternary pump Rheos 4000 (Flux Instrument). ESI-HRMS were recorded on a Bruker Daltonics on a Micromass LCT mass spectrometer. Single crystal X-ray crystallography was determined on SMART APEX II DUO X-ray single crystal diffractometer. Preparative HPLC was performed on a Waters 2489 series instrument with a UV/Visible detector, using a reversed-phase C18 column (Phenomenex, 250 × 21.2 mm, 5 μm). Sephadex LH-20 (GE Healthcare, Sweden), ODS-A (YMS, 100A, 50 μm), and silica gel (Yantai Chemical Industry Institute, Yantai, China) 200–300 mesh was used for column chromatography.

Cultivation and Culture Extraction. *Streptomyces* sp. strain KCB-132 was cultivated in seawater-based ISP2 media (10 g malt extract, 4 g yeast extract, 4 g glucose, 500 mL natural seawater, 500 mL deionized water, pH 7.8) with the addition of 50 μM lanthanum chloride, at a total volume of 110 L (220 × 0.5 L), and shaken at 200 rpm at 28 °C. After 10 days, the culture filtrate was absorbed by open column on amberlite XAD-16 resin, sequentially washed with deionized water and then eluted with methanol. The methanol eluent was removed under reduced pressure, the resulting aqueous layer was extracted with ethyl acetate. The EtOAc-soluble fraction was dried in vacuo to yield 35 g crude extract.

Isolation of Compounds 1−5. The crude extract (35g) was fractionated on silica gel column chromatography (CC) eluting with a step gradient of dichloromethane and methanol. The dichloromethane fraction (0.6 g) was subjected to ODS CC using a stepwise gradient of methanol and H_2O (10:90→100:0) to provide ten fractions (Fr1.1−Fr1.10). Fr1.8 (80 mg) was purified by semipreparative HPLC (Waters, SunFire, C18, 10 mm × 150 mm, 5 μm; 60% MeOH/H_2O; 3 mL/min) to yield elmenol G, **4** (5.6 mg, t_R = 84.5 min) and actinaphthoran B, **3** (3.9 mg, t_R = 100.3 min). The 1% methanol/dichloromethane fraction (4.0 g) was separated into ten fractions (Fr2.1−Fr2.10) by ODS CC using a stepwise gradient of methanol and H_2O. Fr2.8 (40 mg) was purified by semipreparative HPLC (Phenomenex Luna, C18, 21.2 mm × 250 mm, 5 μm; 60% MeOH/H_2O; 10 mL/min) to afford (±)-actinoxocine, (±)-**1** (10.8 mg, t_R = 63.4 min). Chiral seperation of (±)-**1** was performed on Agilent analytical HPLC system ((*R*,*R*) WHELK 01 column, 4.6 × 250 mm, 10 μm, 100 A, 20% isopropanol/n-hexane, 1.0 mL/min , UV = 210 nm) to give optically pure (+)-**1** (4.8 mg, t_R

= 17.5 min) and (–)-**1** (4.7 mg, t_R = 21.9 min). Fr2.9 (1.8 g) and Fr2.10 (0.7) were combined and subsequently purified by Sephadex LH-20, eluting with MeOH, to yield 8-*O*-methyltetrangulol, **5** (310 mg) as the major products. The 2% methanol/dichloromethane fraction (0.357 g) was also subjected to ODS CC to supply Fr3.1−Fr3.10, and Fr3.7 was further purified by semipreparative HPLC (Phenomenex Luna, C18, 21.2 mm × 250 mm, 5 μm; 70% MeOH/H_2O; 10 mL/min) to give actinaphthoran B, **2** (2.4 mg, t_R = 34.4 min).

(+)-Actinoxocine ((+)-**1**): colorless solid; $[\alpha]^{25}_D$ + 168.8 (CH_2Cl_2, *c* 0.08); UV (CH_2Cl_2) λ_{max} (log ε) 281 (2.65), 308 (2.54), 339 (2.52), 349 (2.50) nm; ^{1}D and ^{2}D-NMR see Table S1, HRESIMS $[M - H]^-$, *m/z* 319.0975 (Δ = 0.3 ppm).

(–)-Actinoxocine ((–)-**1**): colorless solid; $[\alpha]^{25}_D$ − 186.1 (CH_2Cl_2, *c* 0.08); UV (CH_2Cl_2) λ_{max} (log ε) 281 (2.49), 306 (2.33), 340 (2.22), 353 (2.23) nm; ^{1}D and ^{2}D-NMR see Table S1, HRESIMS $[M - H]^-$, *m/z* 319.0975 (Δ = 0.3 ppm).

Actinaphthoran A (**2**): colorless solid; $[\alpha]^{25}_D$ + 148.5 (CH_2Cl_2, *c* 0.06); UV (acetonitrile) λ_{max} (log ε) 202 (3.72), 221 (3.61), 248 (3.43), 289 (2.79), 302 (2.67), 332 (2.53), 345 (2.57) nm; ^{1}D and ^{2}D-NMR see Table S2, HRESIMS $[M - H]^-$, *m/z* 321.1131 (Δ = 0.3 ppm).

Actinaphtnoran B (**3**): colorless solid; $[\alpha]^{25}_D$ + 210.3 (CH_2Cl_2, *c* 0.10); UV (acetonitrile) λ_{max} (log ε) 202 (3.72), 221 (3.62), 248 (3.44), 289 (2.79), 302 (2.67), 332 (2.53), 345 (2.58) nm; ^{1}D and ^{2}D-NMR see Table S3, HRESIMS $[M - H]^-$, *m/z* 319.0974 (Δ = 0.6 ppm).

(±)-Elmenol G (**4**): colorless solid; $[\alpha]^{25}_D$ − 32.4 (CH_2Cl_2, *c* 0.10); this structure was identified by comparison with ^{1}H and ^{13}C NMR literature data of the known compound.

8-*O*-methyltetrangulol (**5**): brown solid; this structure was identified by comparison with ^{1}H and ^{13}C NMR literature data of the known compound.

Cytotoxicity Bioassay. The AGS (gastric adenocarcinoma), HepG2 (liver hepatocellular carcinoma), Hela (cervical cancer), U251 (gliomac), Hep3B (hepatoma), HCT116 and LS180 (colon cancer) cells were plated at a density of 5000 cells/well in 100 μL DMEM medium. All cell lines were incubated overnight then treated with various concentrations of **1**−**3** in triplicate. After cultured for 72 h, 20 μL/well of MTT solution (5 mg/mL, Sigma-Aldrich, USA) was added to each well, plate was cultured for 4 h at 37 °C in a 5% CO_2 atmosphere, which followed by adding 150 μL DMSO to dissolve the formazan crystals, and shaking for 5 min. The absorbance was recorded at 570 nm by a microplate Reader. IC_{50} value was taken using Graph pad Prism 5 software.

Antimicrobial Bioassay. The antimicrobial assays of **1**−**3** were tested against five Gram-positive bacteria,

Bacillus subtilis (CMCC63501), *Staphylococcus aureus* (CMCC 26003), *Enterococcus faecalis* ATCC 29212 and clinical isolated *Bacillus cereus* and *Nocardia*, three Gram-negative bacteria, *Shigella sonnei* (ATCC 25931), *Escherichia coli* (CMCC 44102), *Salmonella paratyphi* B (CMCC 50094), and a pathogenic fungus *Canidia albicans* (CMCC 98001), as well as a plant pathogenic fungi *Colletotrichum lagenarium* using a microplate assay. Penicillin and nystatin were used as positive controls, respectively.

Anti-inflammatory Activity Assay. Murine macrophage RAW264.7 cells (ATCC, Manassas, VA, USA) were cultured in 1640 containing 10% FBS in a humidified incubator of 5% CO_2 at 37 °C. For the cytotoxicity part, RAW264.7 cells were incubated with compounds or the media (0.1% DMSO in 1640 containing 10% FBS) for 24h. CCK-8 reagents (10 μL per well) were added and the OD values were collected after 3h incubation at 450 nm (650 nm calibration) by a microplate reader (BioTek, ELx808, USA). For the anti-inflammatory activity assay, RAW264.7 cells were incubated with compounds or the media (0.1% DMSO in 1640 containing 10% FBS), and then cells were primed with LPS (0.1 μg/mL) and Pam3CSK4 (50 nM) for 24 h, respectively. The supernatants were centrifuged and correspondingly measured using the mouse TNF-α ELISA kit. Dexamethasone was used as a positive control.

Table S1. NMR spectroscopic data for (±)-actinoxocine ((±)-1) in DMSO-d_6[a]

no.	δ_H mult (*J* in Hz)	δ_C[b]	COSY	HMBC
1		151.9, C		
2	6.86, d (1.8)	119.5, CH	3-Me	1, 4, 3-Me, 12b
3		132.8, C		
4	7.17, s	122.8, CH	3-Me	1, 2, 3-Me, 4a, 5, 12b
4a		131.8, C		
5	7.53, d (8.9)	129.7, CH	6	1, 4, 4a, 6a, 12b
6	7.12, d (8.9)	118.2, CH	5	4a, 6a, 12, 12a
6a		149.9, C		
7	6.88, s	100.6, C		11, 11a, 12
7a		124.3, C		
8		154.9, C		
9	6.83, d (7.8)	110.8, CH	8-OMe, 10	7, 7a, 8, 11, 11a
10	7.22, t (7.8)	132.5, CH	9, 11	7a, 8, 9, 11, 11a, 12
11	6.76, d (7.8)	112.5, CH	10	7a, 8, 9, 10, 11a, 12
11a		149.2, C		
12	7.02, s	79.5, C		7, 7a, 11, 11a, 12b
12a		121.5, C		
12b		121.0, C		
3-Me	2.28, s	20.7, CH_3	2, 4	2, 3, 4

8-OMe	3.85, s	56.0, CH_3	9	8
6a-OH	10.04, s			

[a]600 MHz for ^{1}H NMR and 150 MHz for ^{13}C NMR. [b]Numbers of attached protons were determined by analysis of 2D spectra.

Table S2. NMR spectroscopic data for actinaphthoran A (2) in DMSO-*d*$_6$[a]

no.	δ_H mult (*J* in Hz)	δ_C[b]	COSY	HMBC
1		159.9, C		
2	6.51, s	102.5, CH	3-Me	1, 3-Me, 4, 12b
3		136.2, C		
4	7.01, s	114.9, CH	3-Me	1, 2, 3, 3-Me, 12b
4a		121.4, C		
5	7.51, d (8.6)	125.4, CH	6	1, 4, 4a, 6a, 12a, 12b
6	6.99, d (8.6)	121.6, CH	5	4a, 6a, 12, 12a
6a		147.2, C		
7	5.04, dd (11.6, 3.6) 4.86, dd (11.6, 3.6)	53.7, CH_2	7-OH	7a, 8, 11a
7a		126.6, C		
8		157.3, C		
9	6.98, d (7.8)	111.4, CH	8-OMe, 10	7a, 8, 11
10	7.17, t (7.8)	129.6 CH	9, 11	8, 9, 11a
11	6.49, d (7.8)	119.1, CH	10	7a, 8, 9, 12
11a		139.5, C		
12	7.37, s	85.2, CH		1, 2, 4a, 6a, 7a, 11, 11a, 12b
12a		126.1, C		
12b		128.4, C		
3-Me	2.41, s	22.7, CH_3	2, 4	2, 3, 4
8-OMe	3.83, s	56.3, CH_3	9	8
6a-OH	9.70, s			5, 6, 6a
7-OH	5.96, t (3.6)		7	7, 7a

[a]600 MHz for ^{1}H NMR and 150 MHz for ^{13}C NMR. [b]Numbers of attached protons were determined by analysis of 2D spectra.

Table S3. NMR spectroscopic data for actinaphthoran B (3) in DMSO-*d*$_6$[a]

no.	δ_H mult (*J* in Hz)	δ_C[b]	COSY	HMBC
1		159.8, C		
2	6.59, s	102.6, CH		1, 3-Me, 4, 12b
3		136.5, C		
4	7.04, s	115.3, CH	3-Me	2, 3-Me, 12b
4a		126.7, C		
5	7.48, d (8.6)	125.5, CH	6	4, 6a, 12b
6	7.05, d (8.6)	121.4, CH	5	4a, 6a, 12a
6a		146.8, C		

7	10.67, s	197.6, C		7, 11, 11a
7a		122.8, C		
8		162.0, C		
9	6.92, d (8.2)	110.6, CH	10	7, 7a, 8, 11
10	7.47, t (8.2)	136.5 CH	9, 11	8, 11a
11	7.06, d (8.2)	119.3, CH	10	7, 7a, 9, 12
11a		142.0, C		
12	7.18, s	84.9, CH		1, 6a, 11, 11a, 12a
12a		121.1, C		
12b		127.4, C		
3-Me	2.49, s	22.7, CH_3	4	2, 3, 4
8-OMe	3.96, s	56.1, CH_3		8
6a-OH	7.91, s			5, 6, 6a

[a]600 MHz for ^{1}H NMR and 150 MHz for ^{13}C NMR. [b]Numbers of attached protons were determined by analysis of 2D spectra.

Table S4. Antimicrobial activity of compounds 1−3 (MIC, *μ*g/mL)

organism	(+)-**1**	(−)-**1**	**2**	**3**	penicillin	nystatin
Bacillus subtilis CMCC 63501	−	−	−	4	2	NT
Enterococcus faecalis ATCC 29212	16	16	32	8	2	NT
Bacillus cereus	−	−	64	2	4	NT
Nocardia	32	−	64	4	8	NT
Shigella sonnei ATCC 25931	−	−	−	−	−	NT
Salmonella paratyphi B CMCC 50094	−	−	−	−	−	NT
Staphylococcus aureus CMCC 26003	16	16	32	8	< 0.5	NT
Canidia albicans CMCC 98001	−	−	−	16	4	NT
Escherichia coli CMCC 44102	−	−	−	−	−	NT
Colletotrichum lagenarium	16	8	−	2	NT	0.75

"–" = inactive at 64 *μ*g/mL, "NT" = not tested.

Table S5. Cytotoxic activity of compounds 1−3 (IC_{50}, *μ*M)

cancer cell line	(+)-**1**	(−)-**1**	**2**	**3**
AGS	40.8	19.2	−	41.5
HeLa	−	−	−	51.6
HCT116	−	−	−	41.7
LS180	−	80.9	−	1.9
U251	−	−	31.7	74.6
HepG-2	−	−	−	–
Hep3B	−	−	−	48.2

"–" = inactive at 100 *μ*M.

Figure S1. ^{1}H NMR Spectrum (600 MHz) of (±)-Actinoxocine ((±)-**1**) in DMSO-d_6

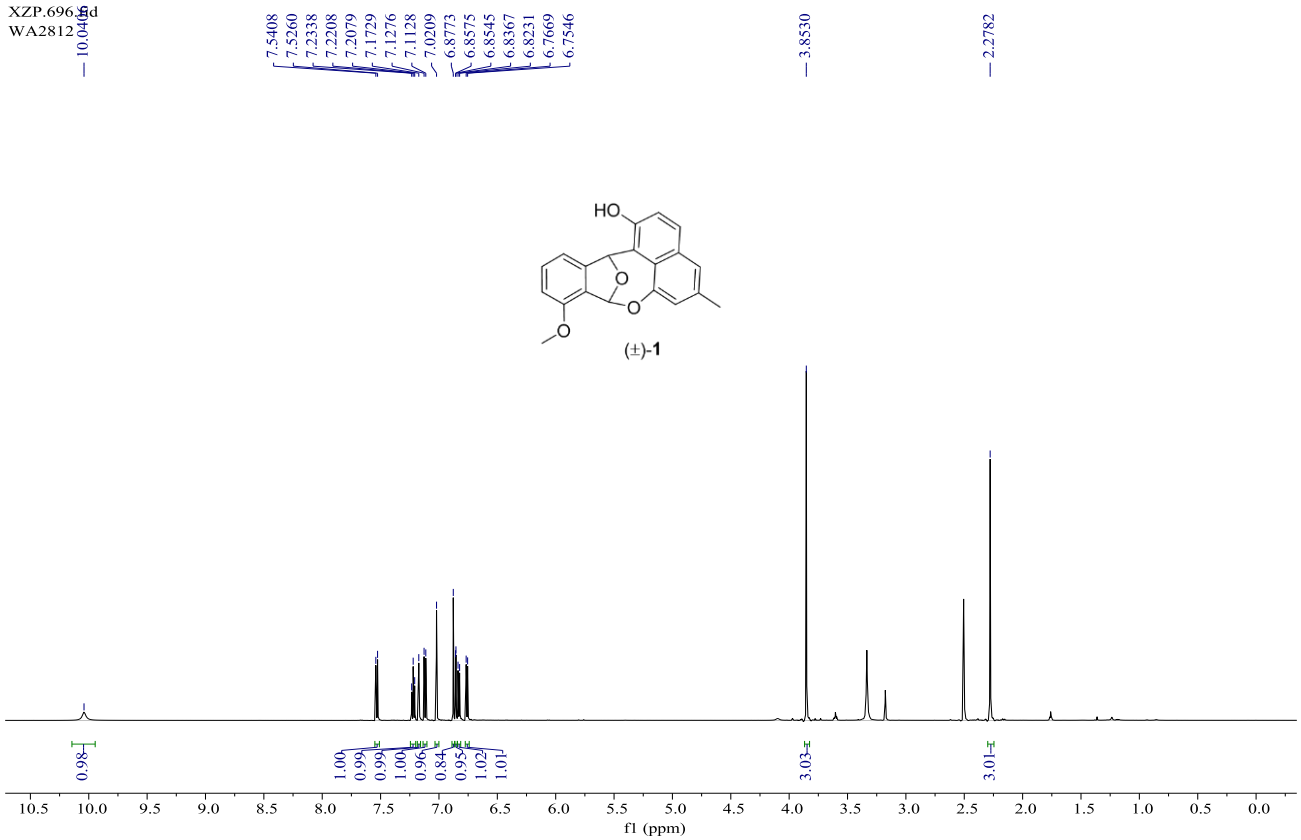


Figure S2. ^{13}C NMR Spectrum (150 MHz) of (±)-Actinoxocine ((±)-**1**) in DMSO-d_6

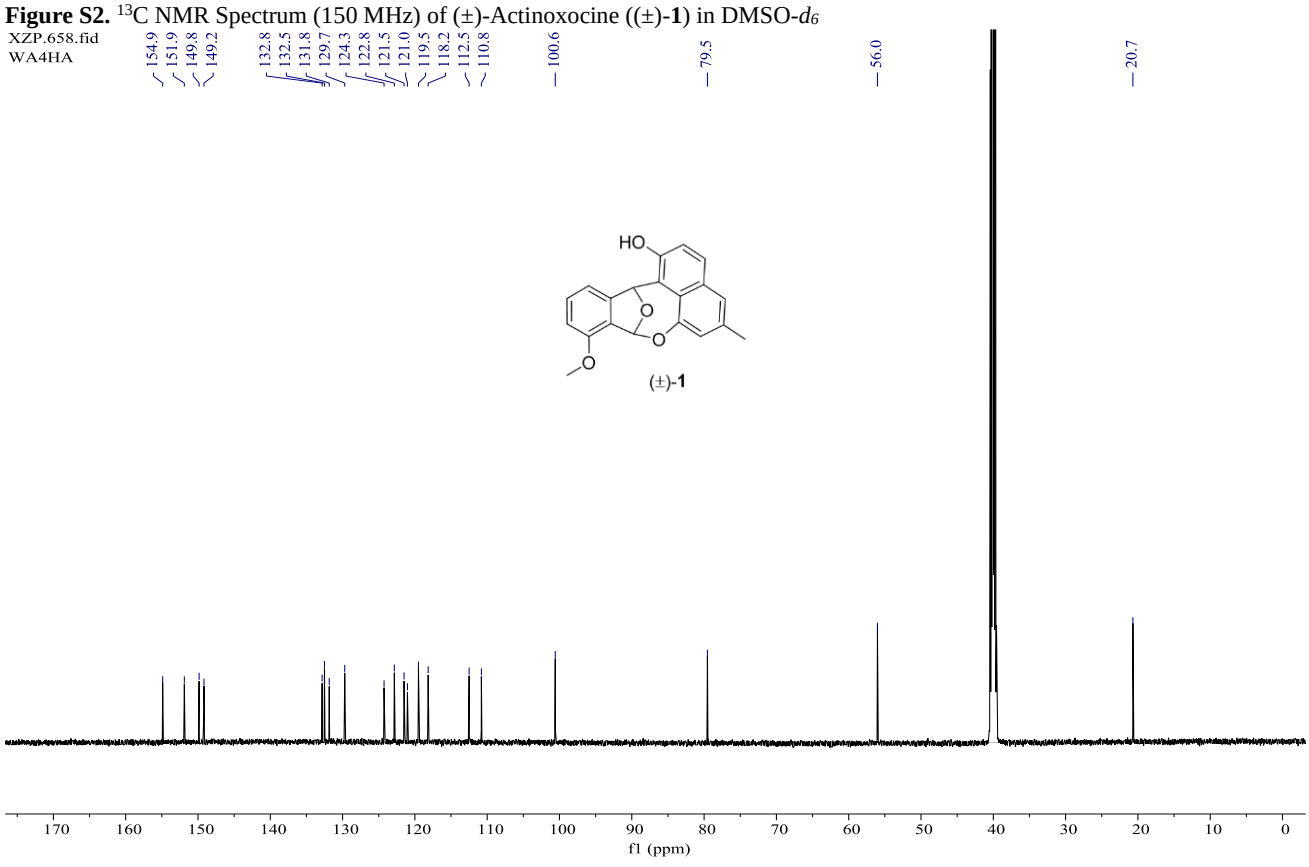


Figure S3. DEPT-135 NMR Spectrum (150 MHz) of (±)-Actinoxocine ((±)-**1**) in DMSO-d_6

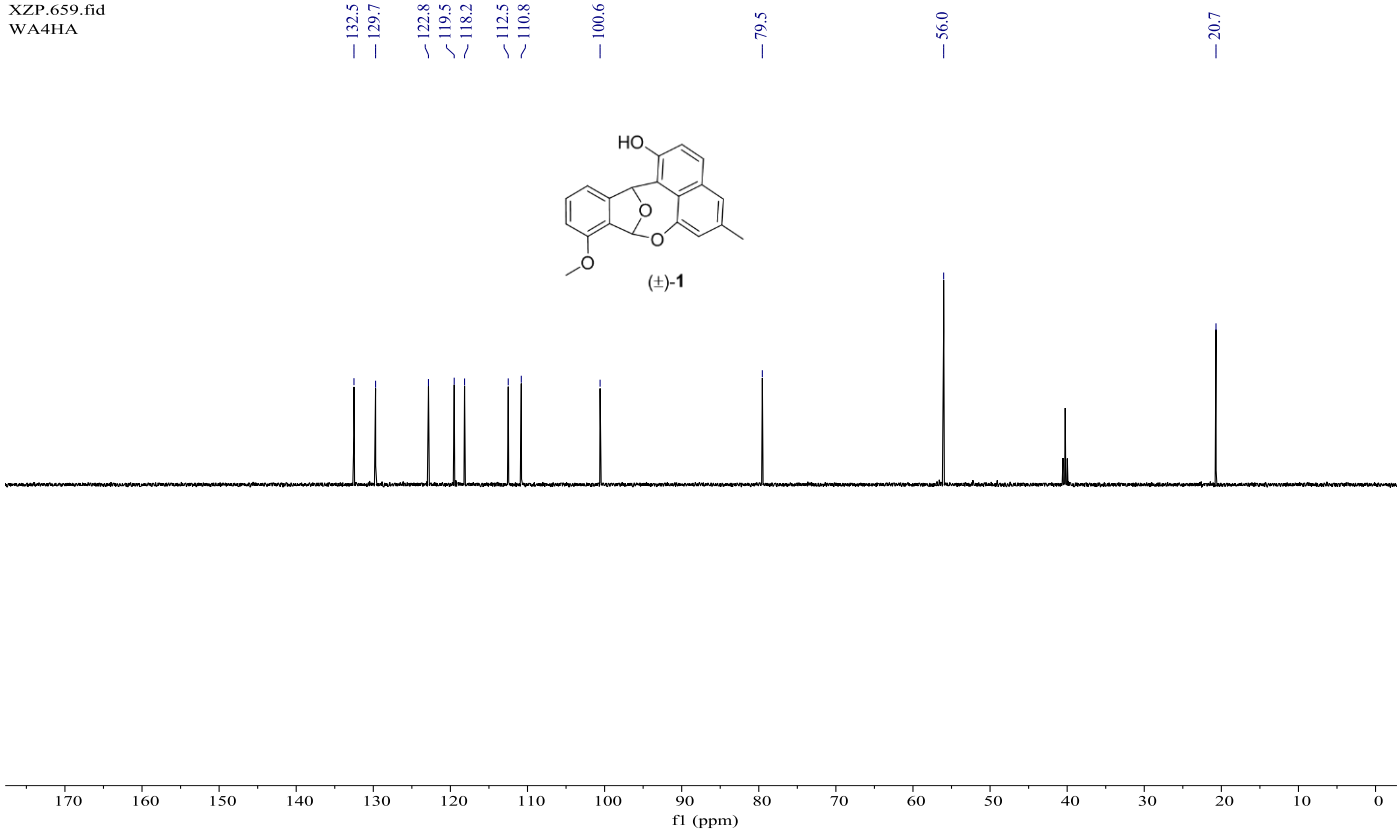


Figure S4. COSY Spectrum (600 MHz) of (±)-Actinoxocine ((±)-**1**) in DMSO-d_6

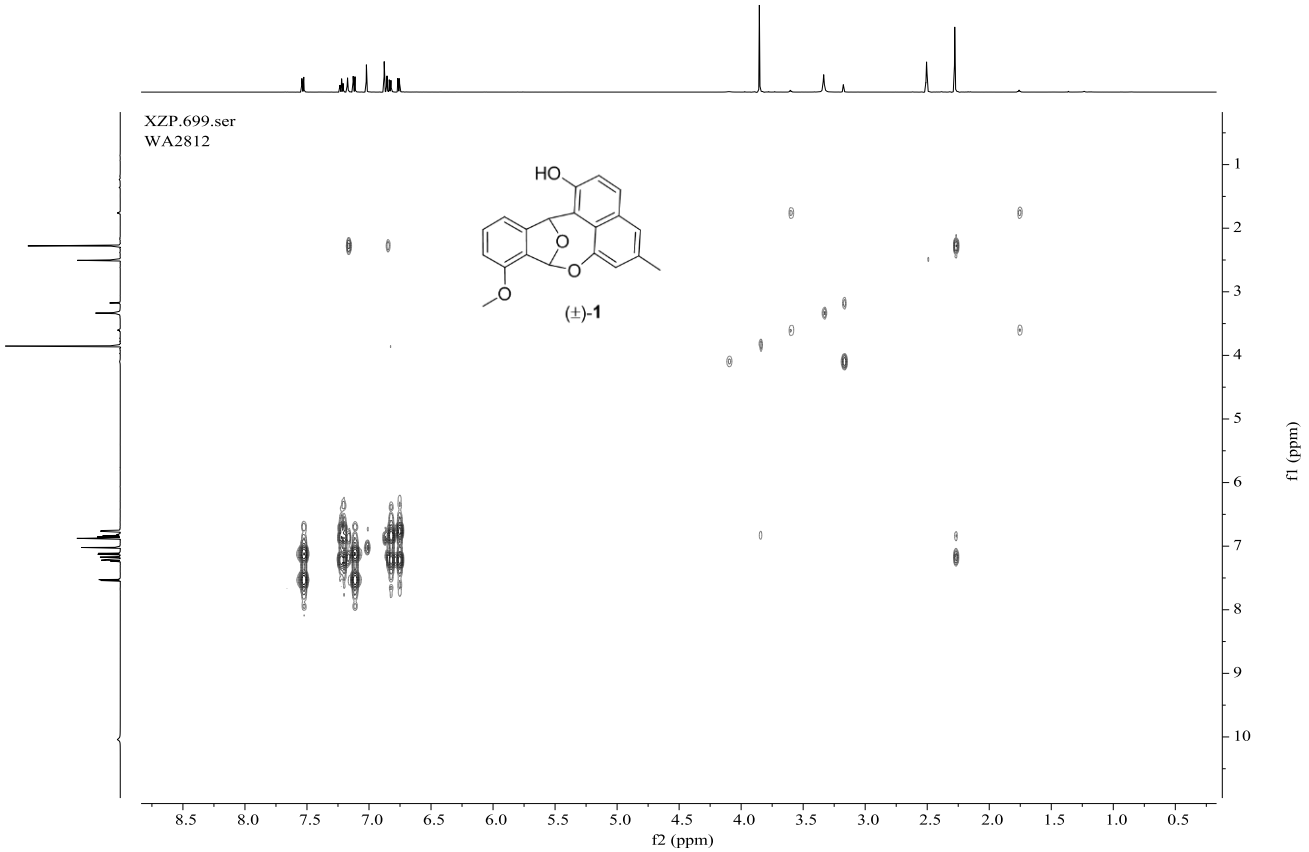


Figure S5. HSQC Spectrum (600 MHz) of (±)-Actinoxocine ((±)-**1**) in DMSO-d_6

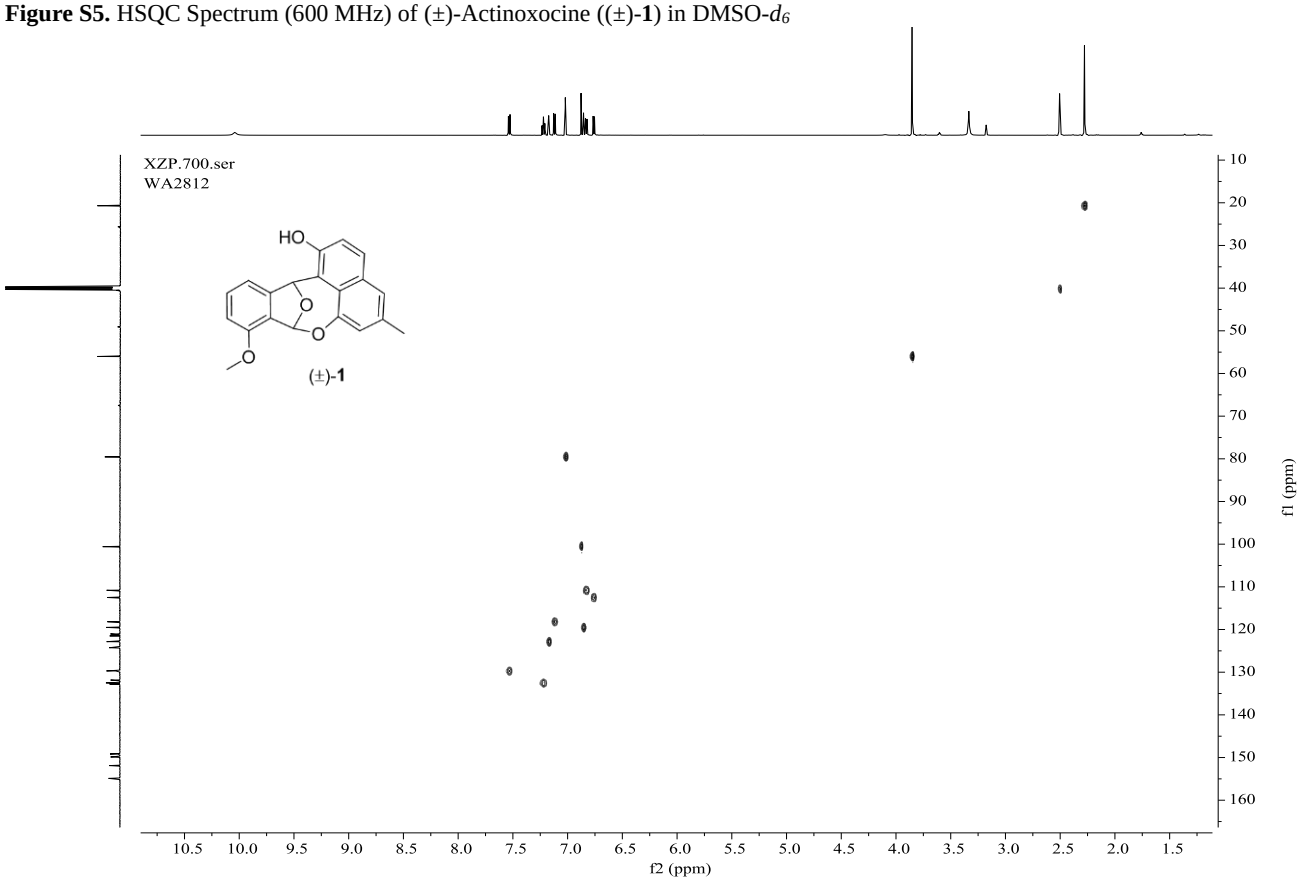


Figure S6. HMBC Spectrum (600 MHz) of (±)-Actinoxocine ((±)-**1**) in DMSO-d_6

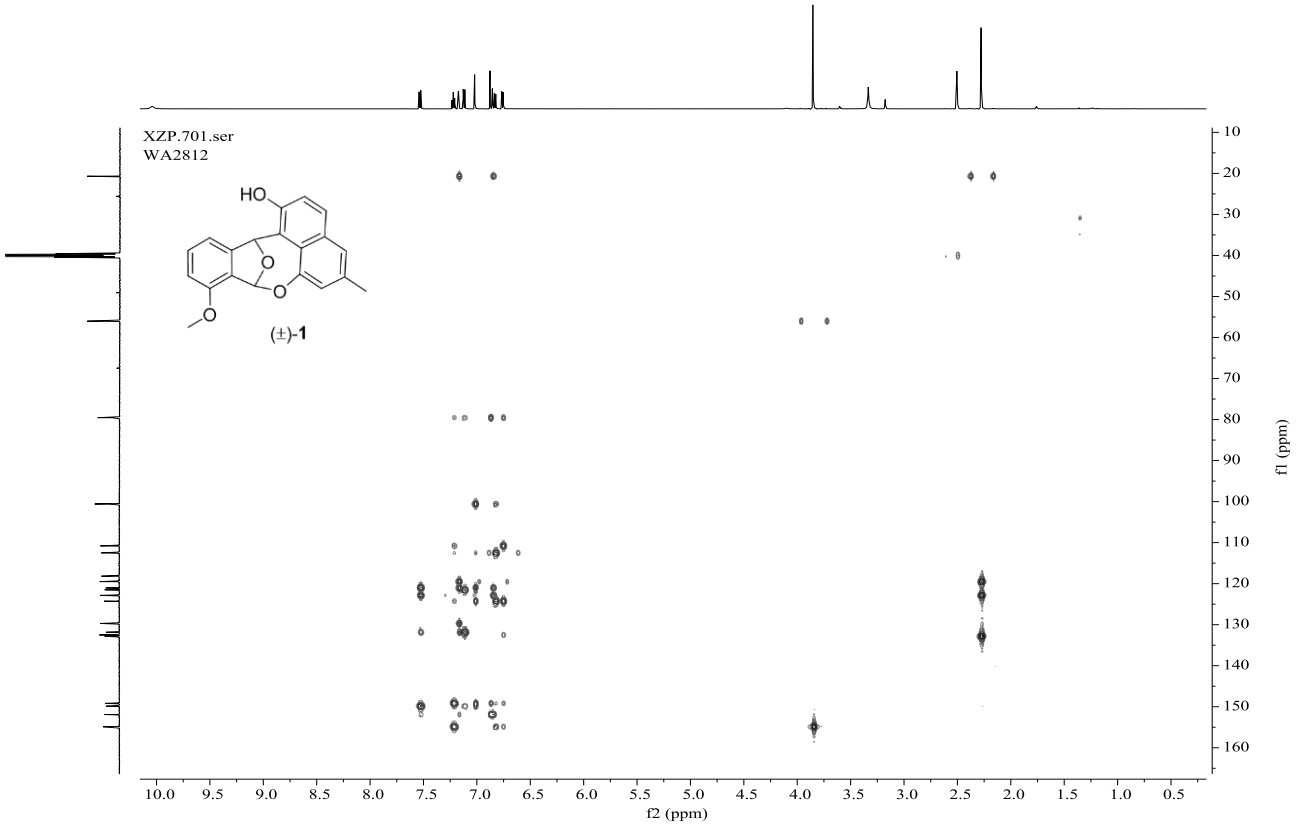


Figure S7. NOESY Spectrum (600 MHz) of (±)-Actinoxocine ((±)-**1**) in DMSO-d_6

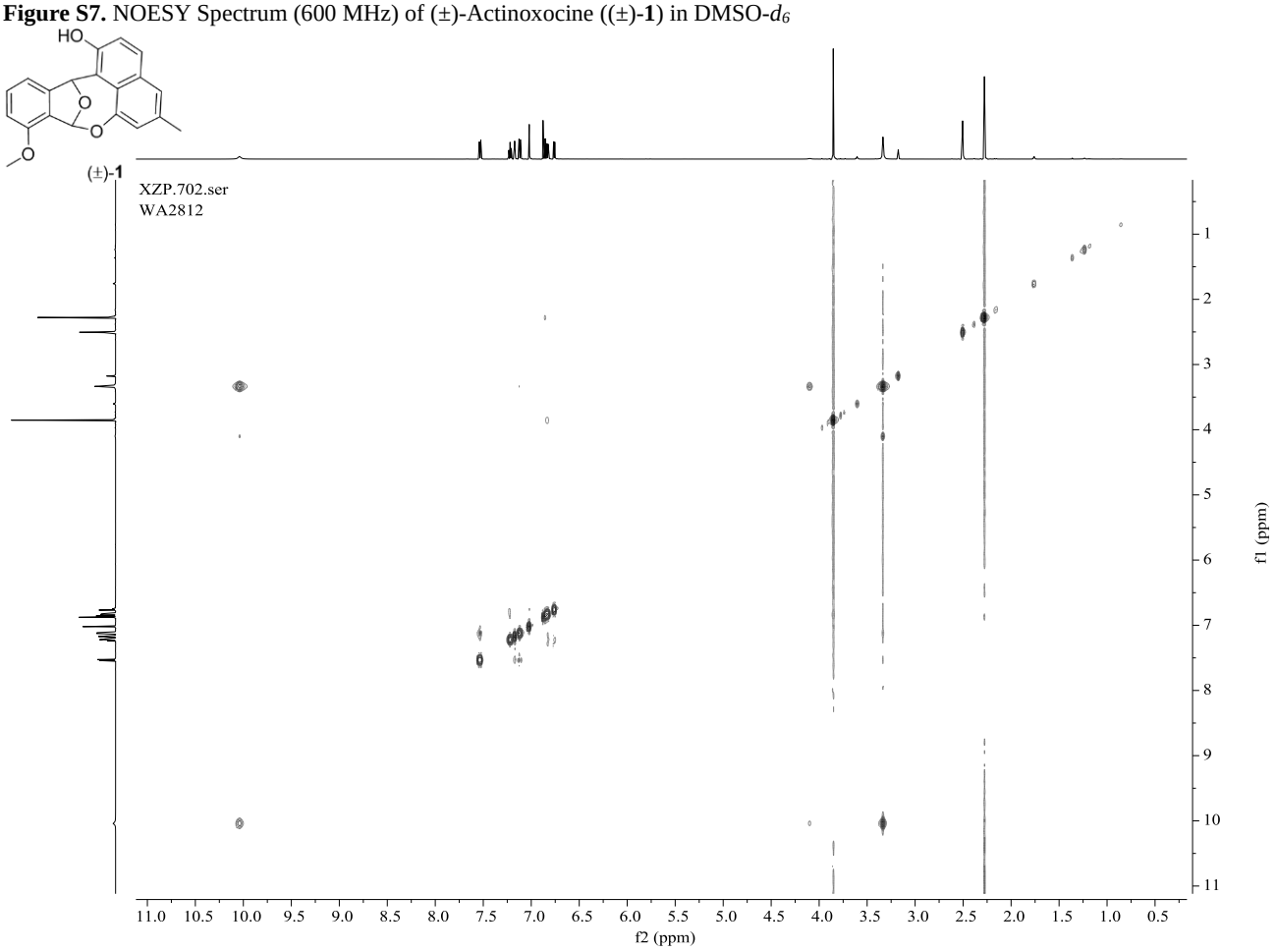


Figure S8. HRESIMS Spectrum of (±)-Actinoxocine ((±)-**1**)

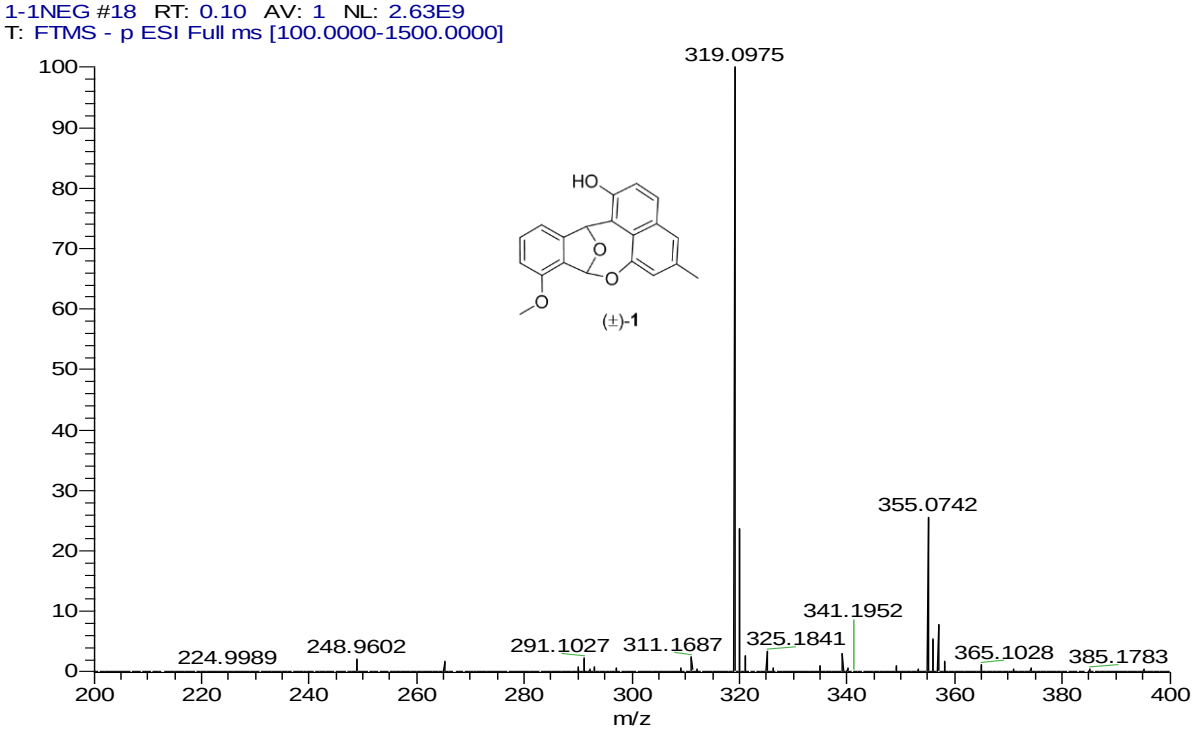


Figure S9. ^{1}H NMR Spectrum (600 MHz) of Actinaphthoran A (**2**) in DMSO-d_6

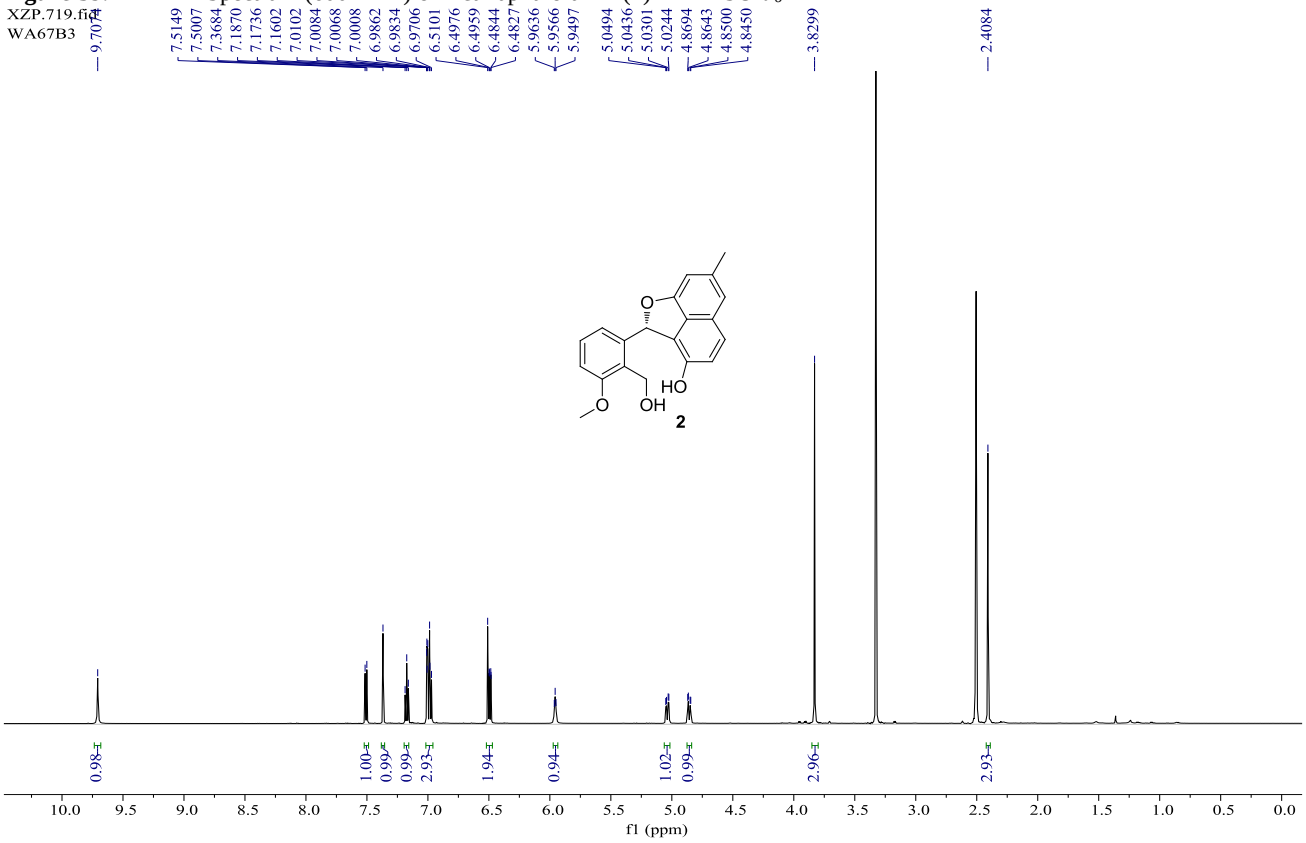


Figure S10. ^{13}C NMR Spectrum (150 MHz) of Actinaphthoran A (**2**) in DMSO-d_6

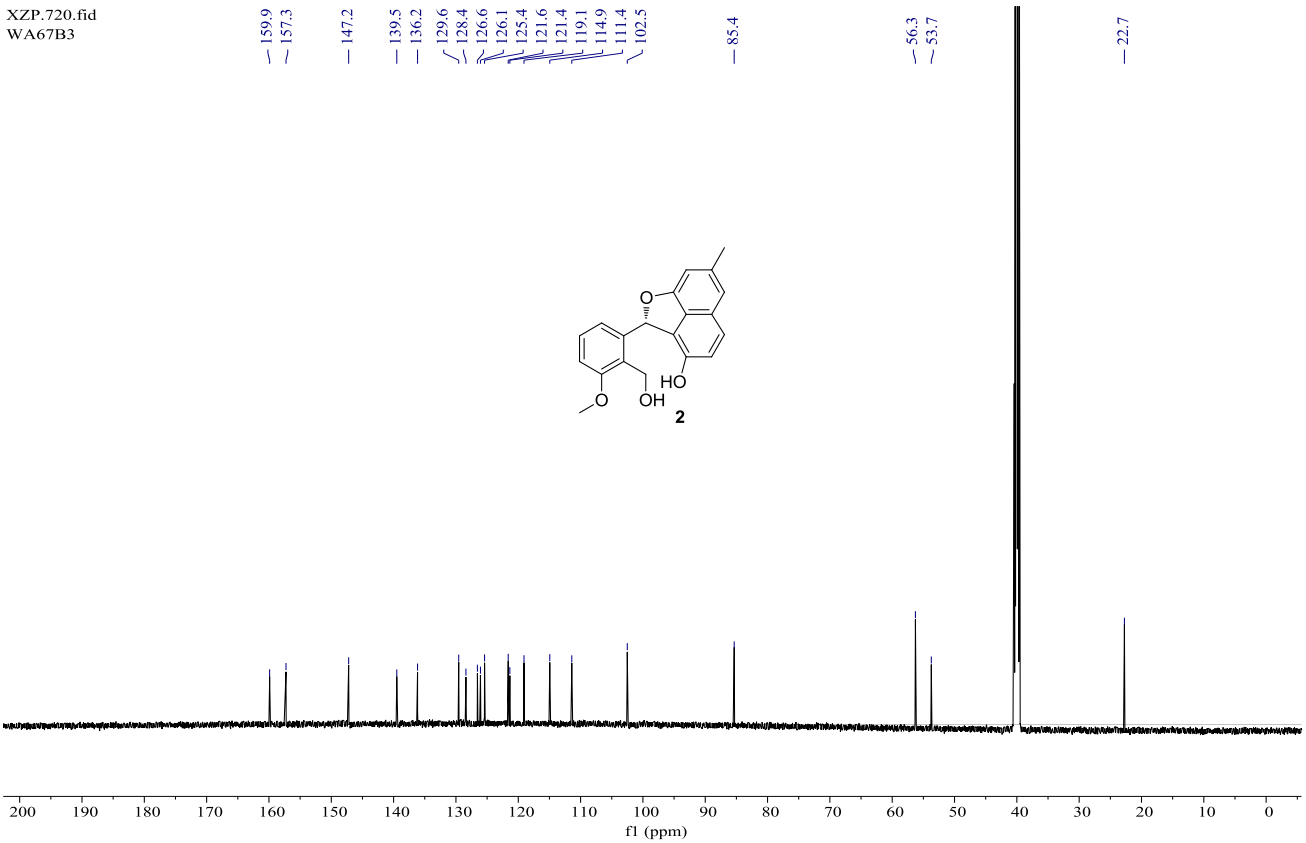


Figure S11. DEPT-135 NMR Spectrum (150 MHz) of Actinaphthoran A (**2**) in DMSO-d_6

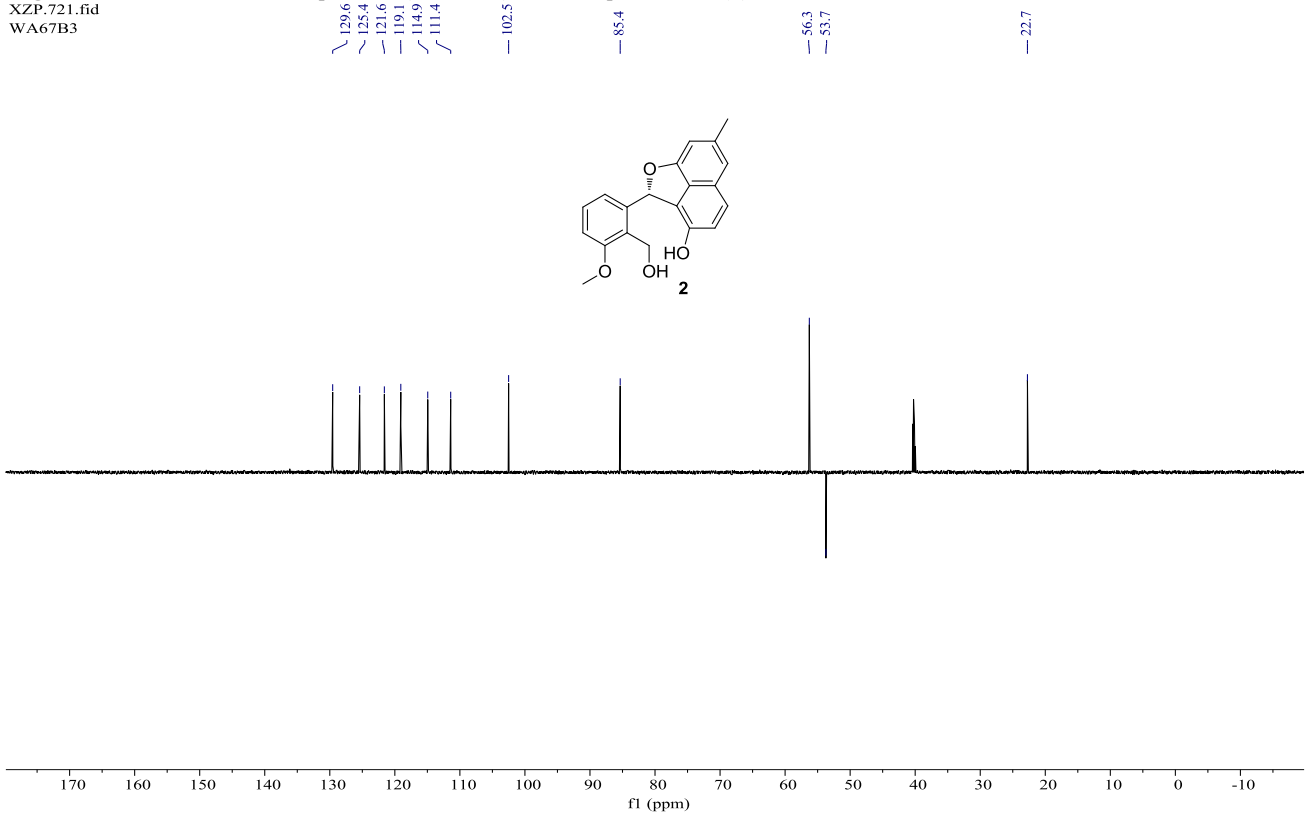


Figure S12. COSY Spectrum (600 MHz) of Actinaphthoran A (**2**) in DMSO-d_6

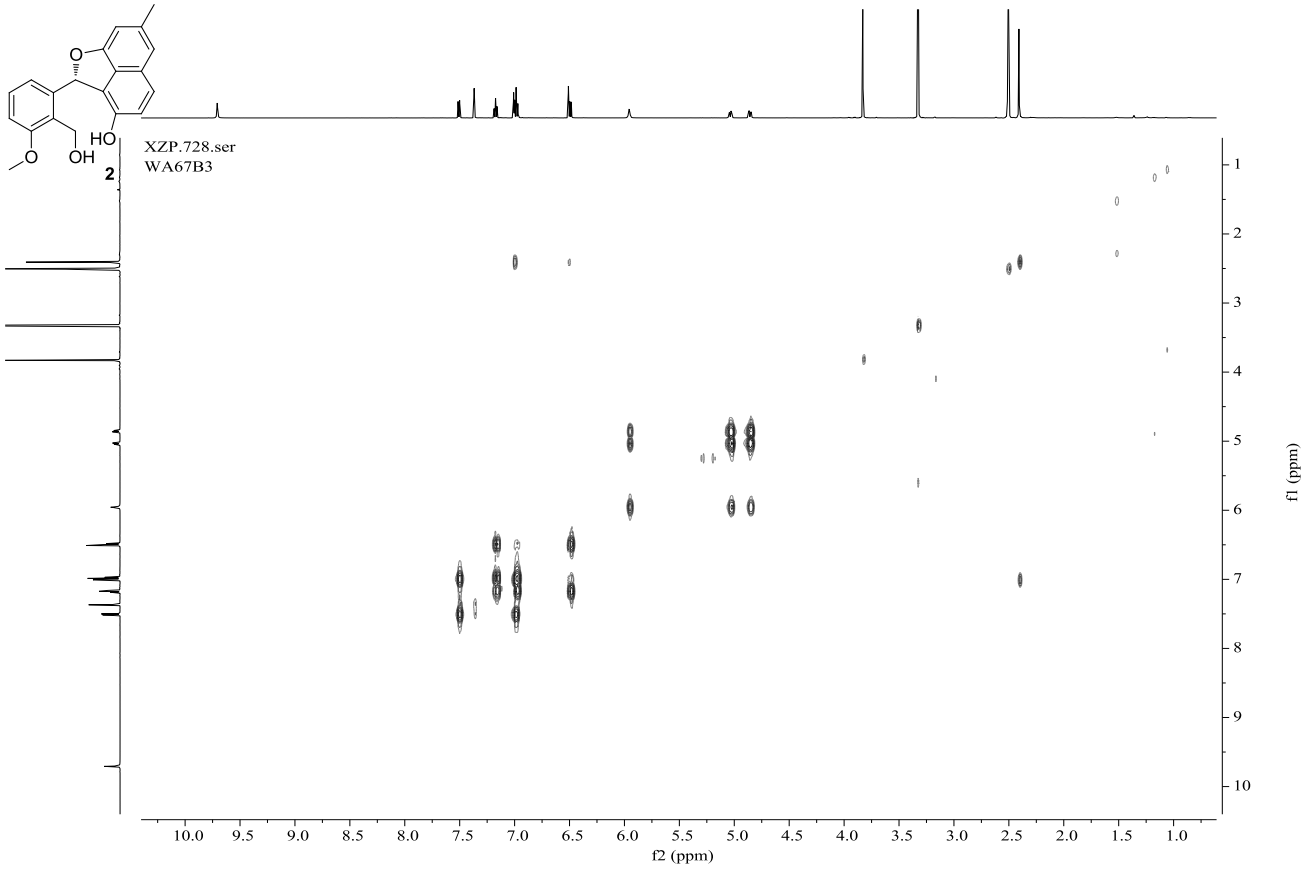


Figure S13. HSQC Spectrum (600 MHz) of Actinaphthoran A (**2**) in DMSO-d_6

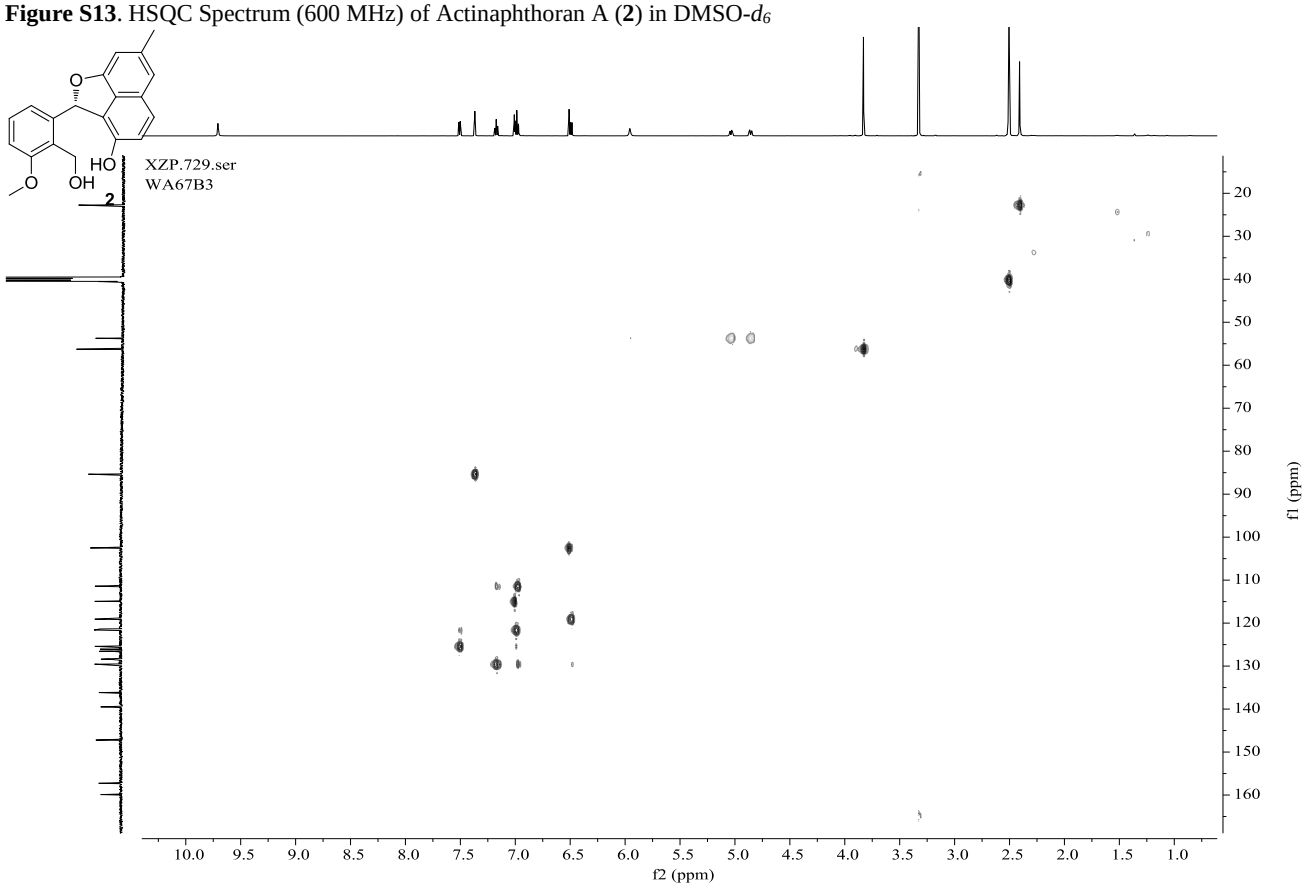


Figure S14. HMBC Spectrum (600 MHz) of Actinaphthoran A (**2**) in DMSO-d_6

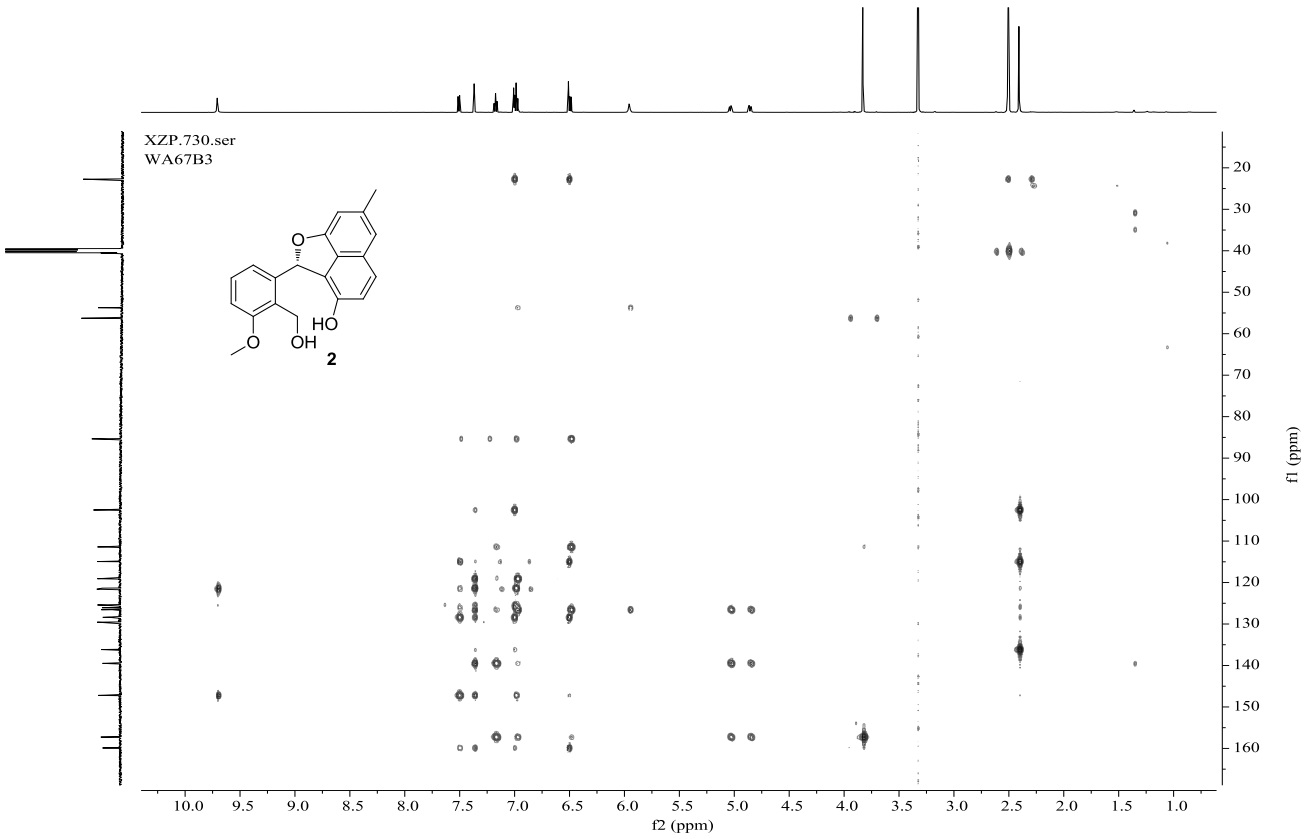


Figure S15. NOESY Spectrum (600 MHz) of Actinaphthoran A (**2**) in DMSO-d_6

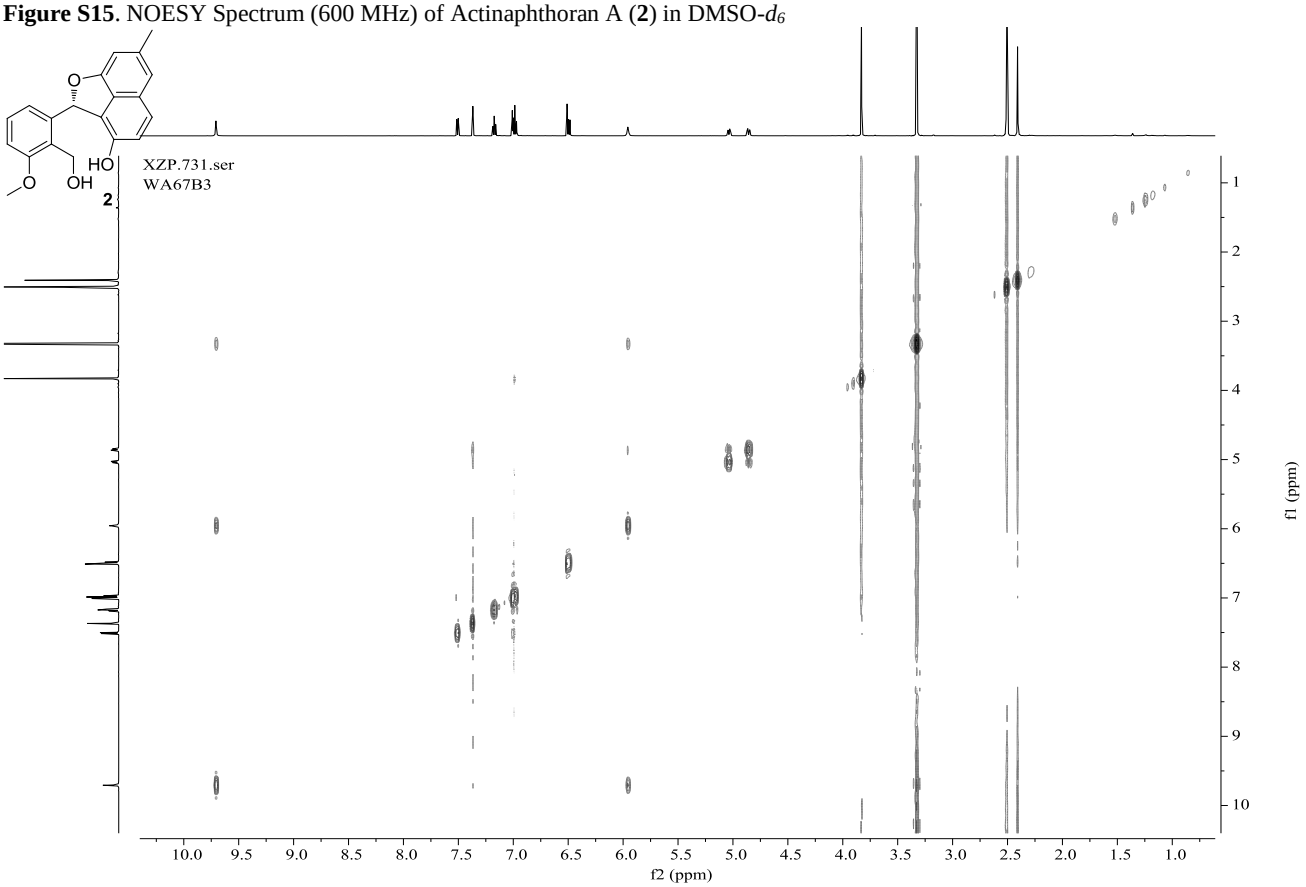


Figure S16. HRESIMS Spectrum of Actinaphthoran A (**2**)

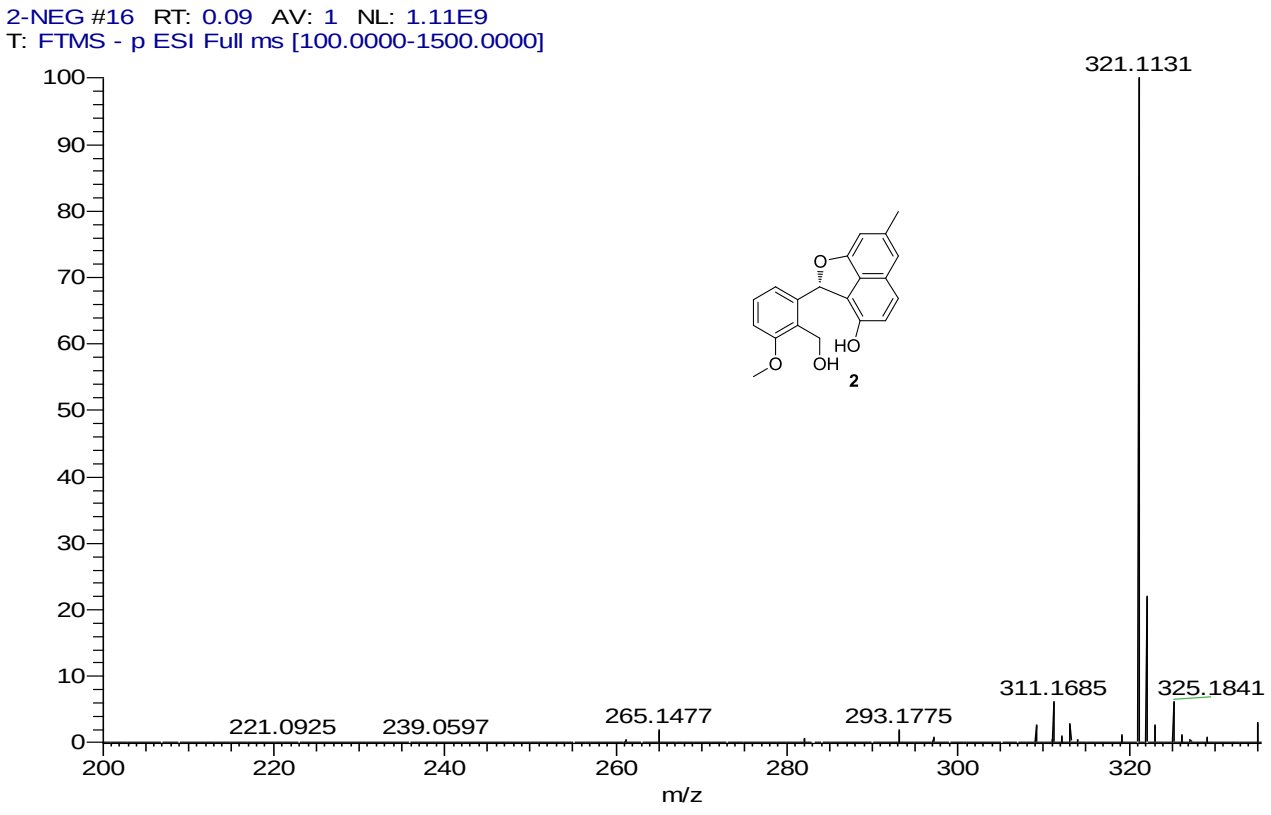


Figure S17. ^{1}H NMR Spectrum (600 MHz) of Actinaphthoran B (**3**) in DMSO-d_6

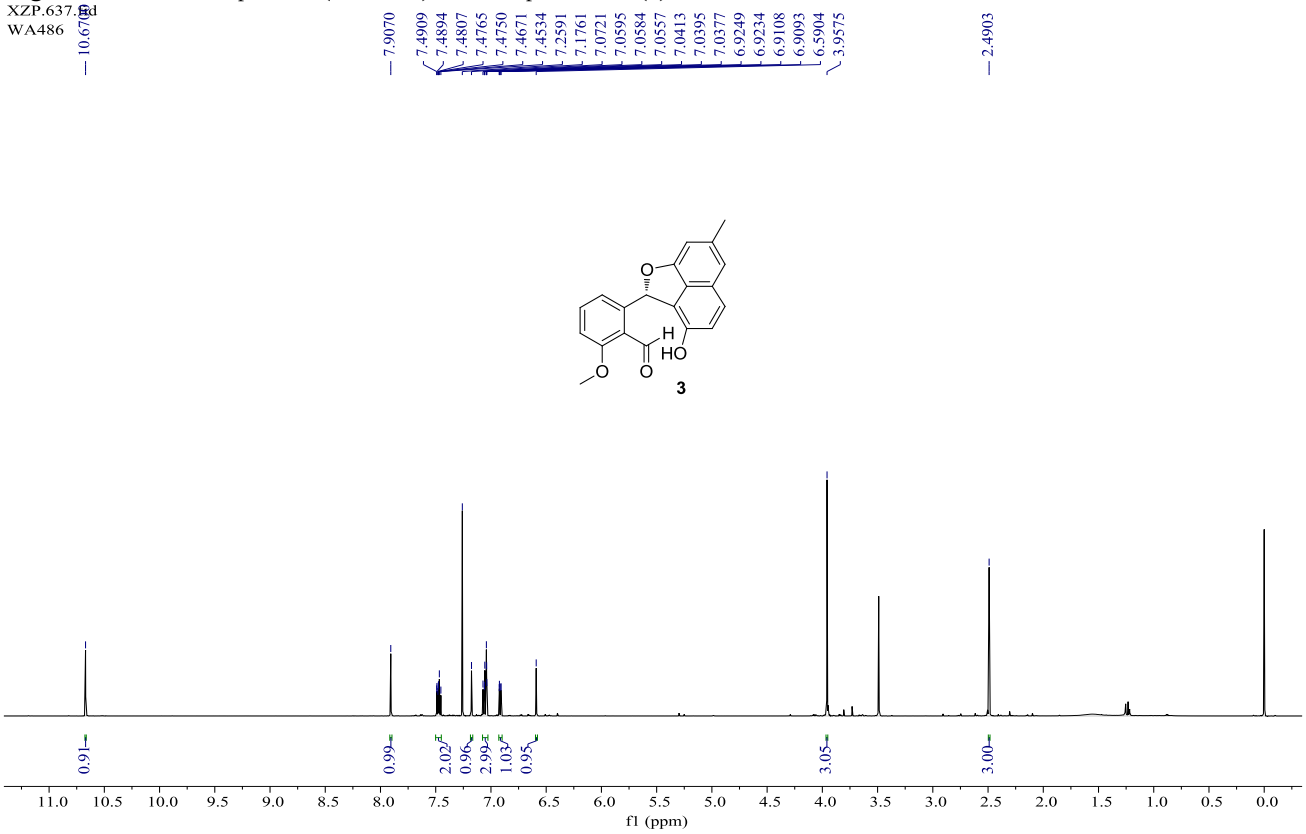


Figure S18. ^{13}C NMR Spectrum (150 MHz) of Actinaphthoran B (**3**) in DMSO-d_6

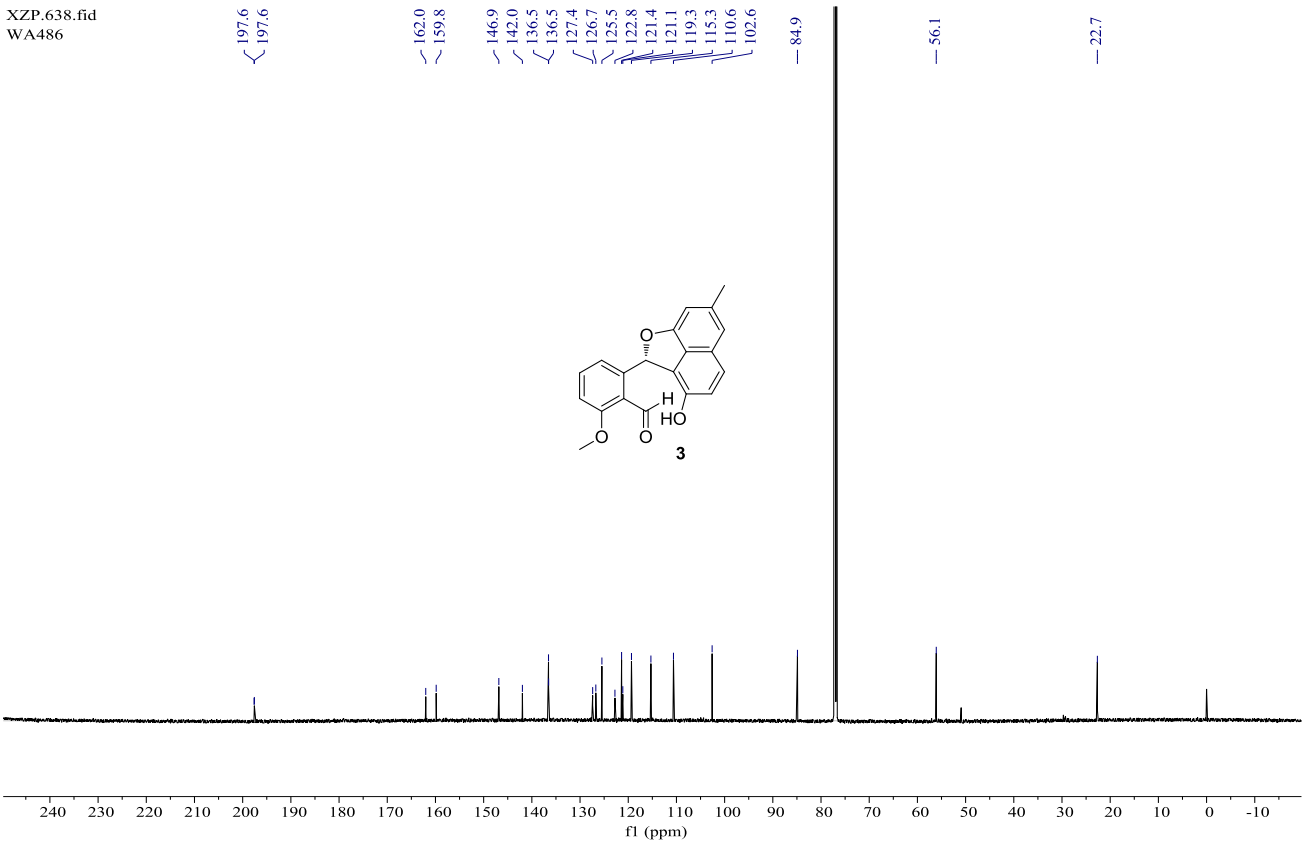


Figure S19. DEPT-135 NMR Spectrum (150 MHz) of Actinaphthoran B (**3**) in DMSO-d_6

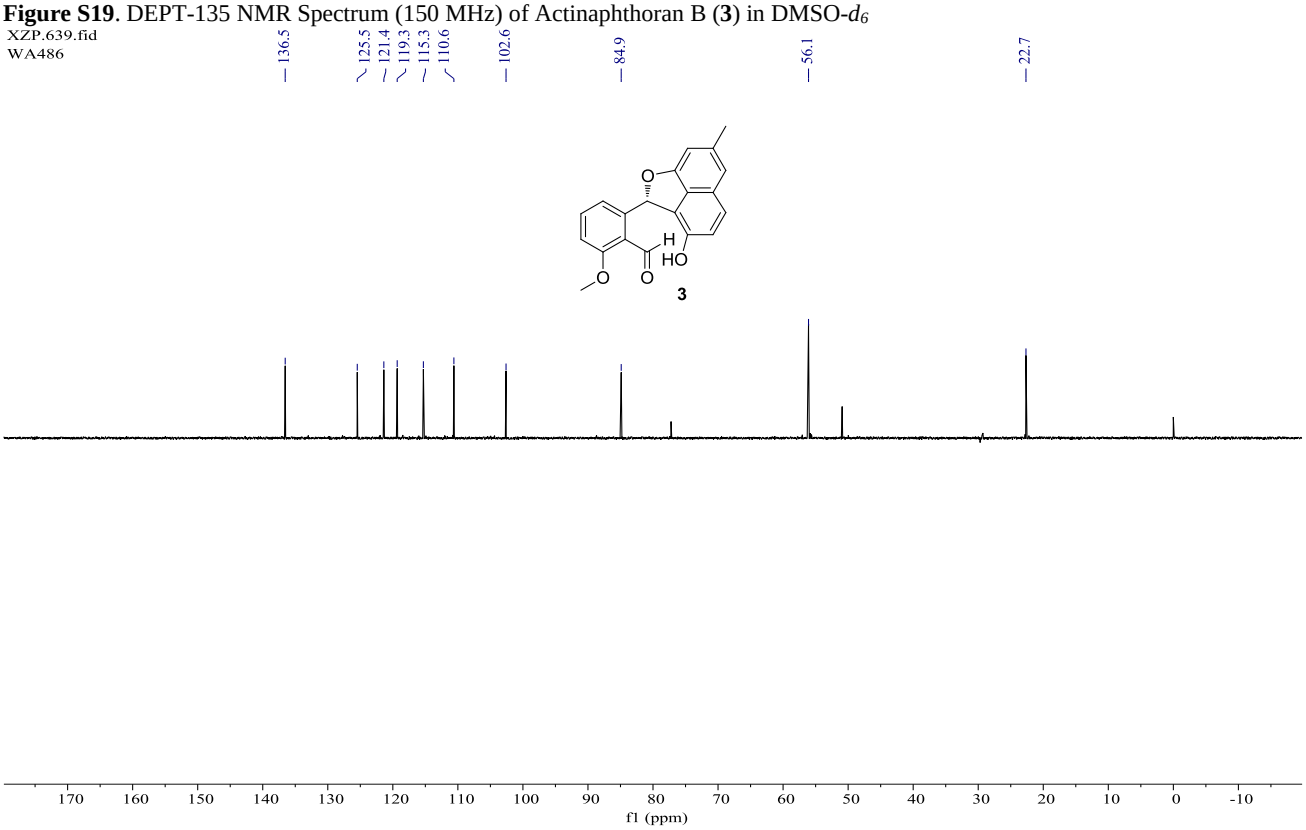


Figure S20. COSY Spectrum (600 MHz) of Actinaphthoran B (**3**) in DMSO-d_6

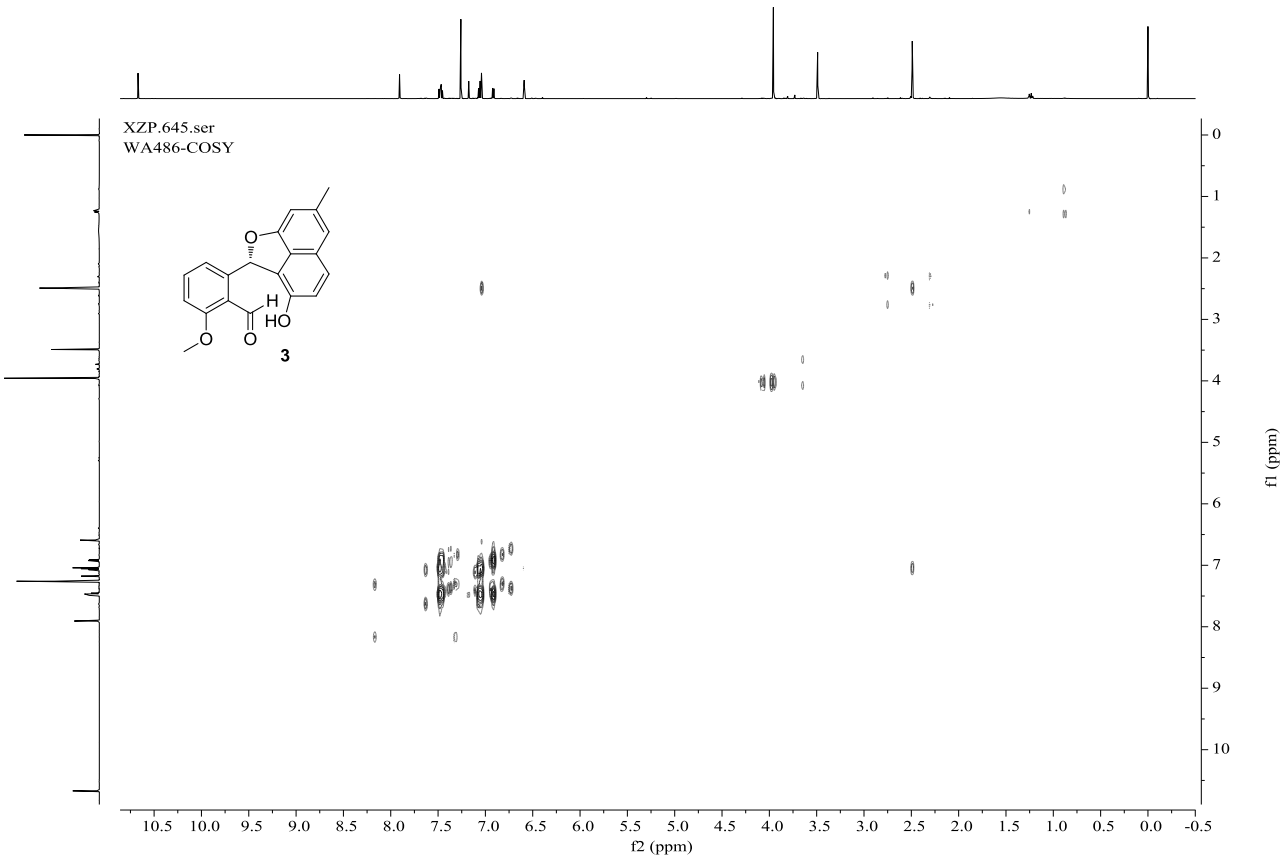


Figure S21. HSQC Spectrum (600 MHz) of Actinaphthoran B (**3**) in DMSO-d_6

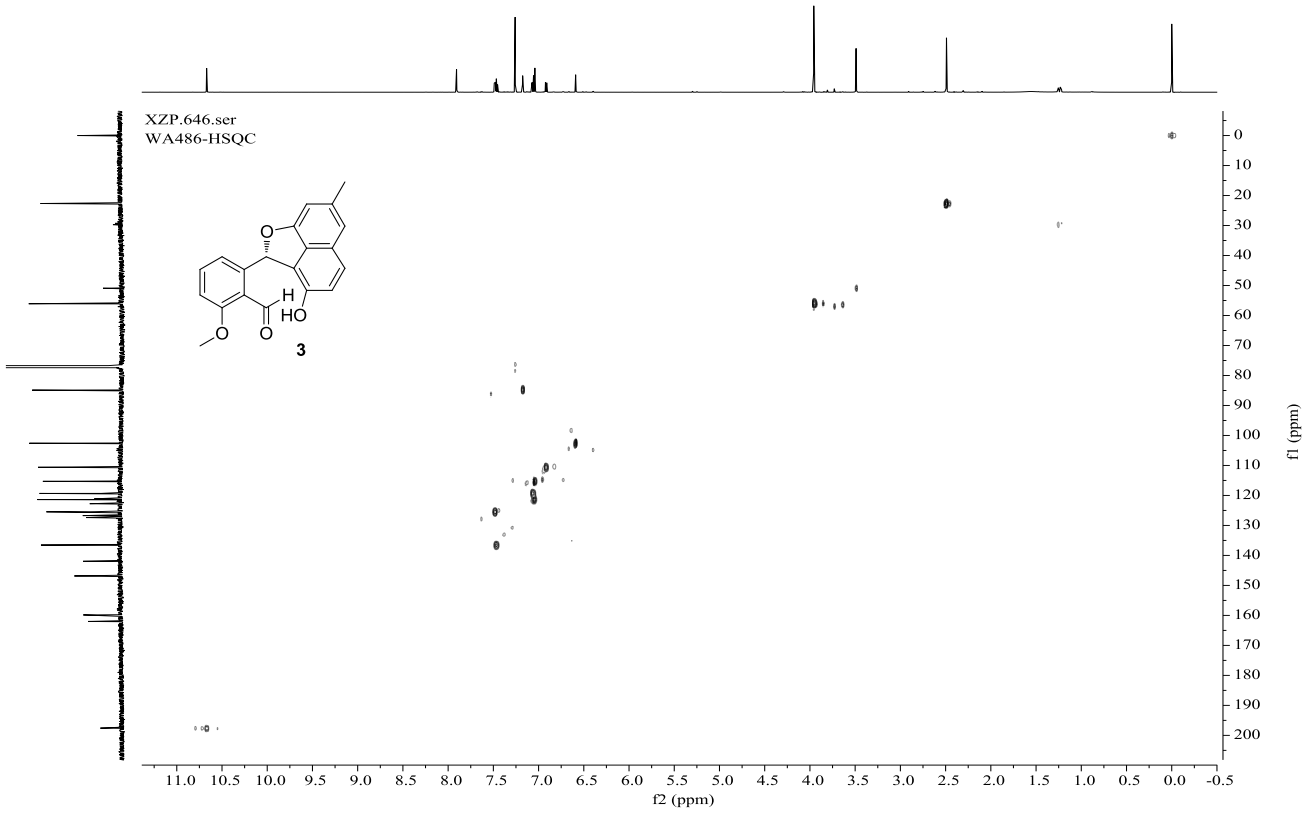


Figure S22. HMBC Spectrum (600 MHz) of Actinaphthoran B (**3**) in DMSO-d_6

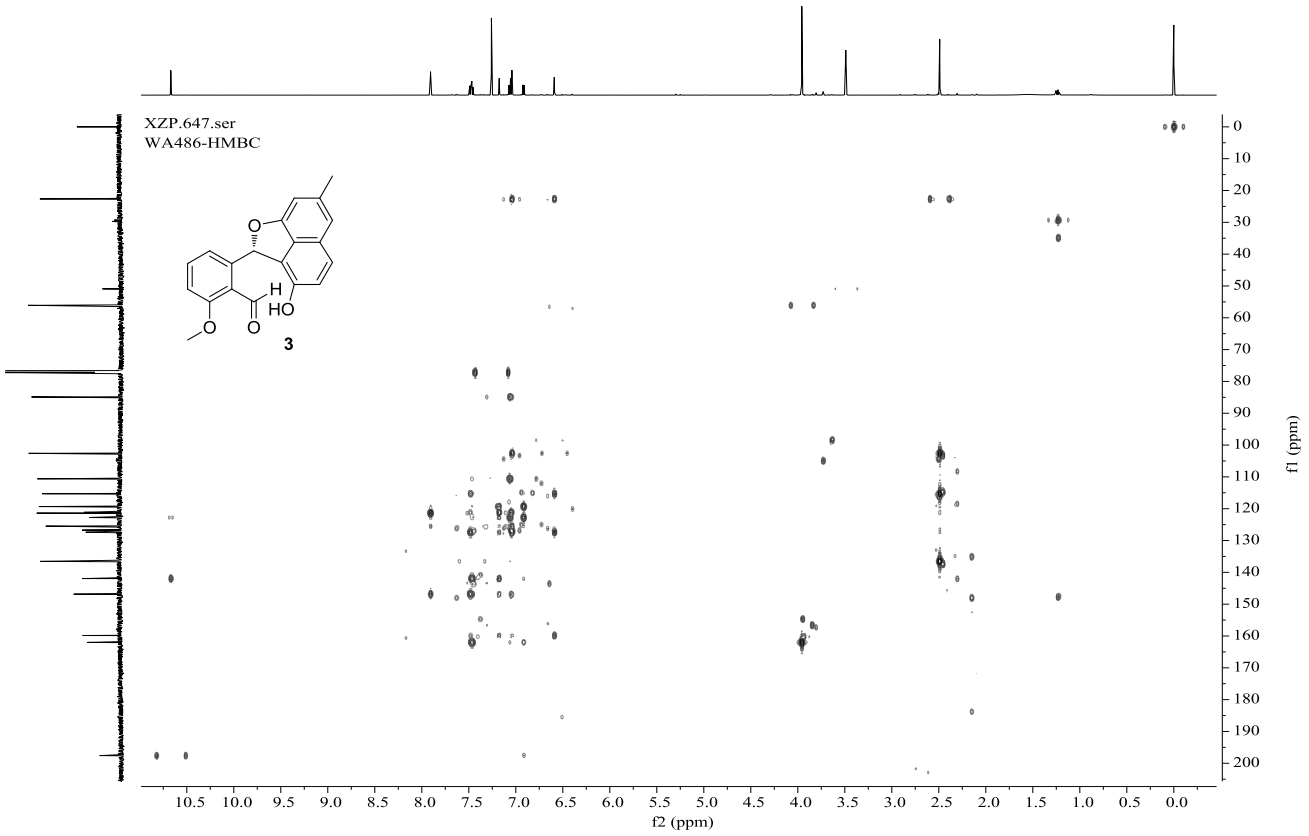


Figure S23. NOESY Spectrum (600 MHz) of Actinaphthoran B (3) in DMSO-d_6

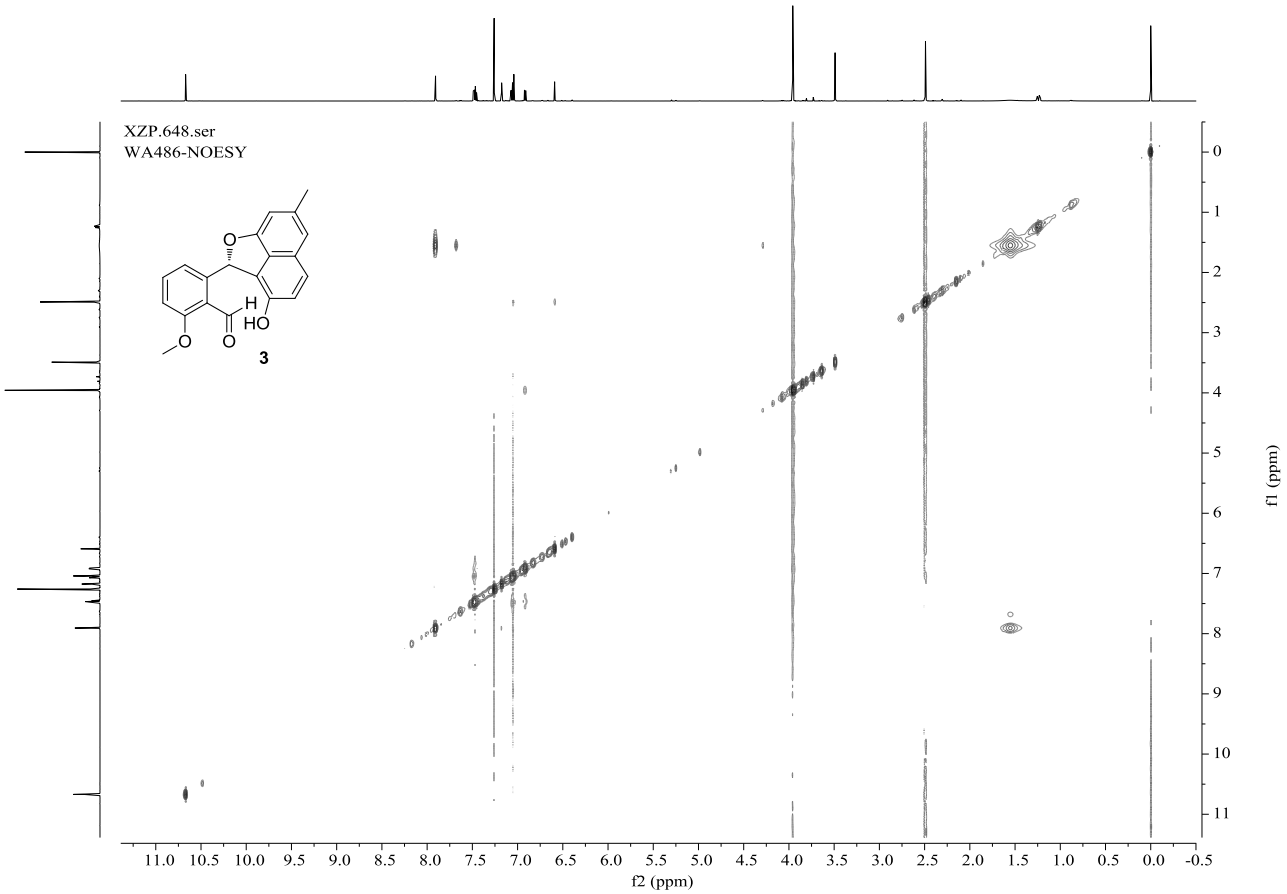
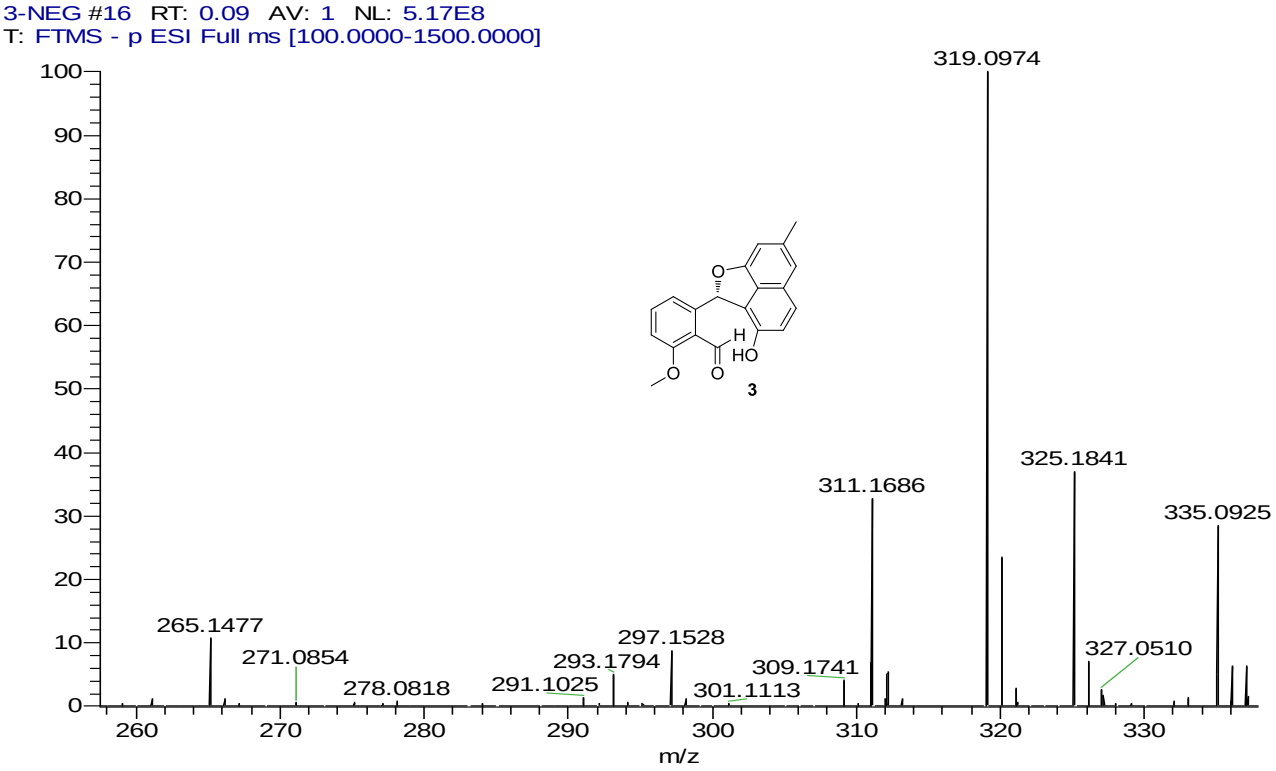


Figure S24. HRESIMS Spectrum of Actinaphthoran B (**3**)



X-ray Crystallographic Analysis of (±)-Actinoxocine ((±)-1). Crystal data for xzp5: $C_{20}H_{16}O_4$, M = 320.33, a = 7.8685(2) Å, b = 11.5144(2) Å, c = 16.5769(3) Å, α = 90°, β = 103.3720(10)°, γ = 90°, V = 1461.17(5) Å^3, T = 100.(2) K, space group $P121/n1$, Z = 4, μ(Cu Kα) = 0.828 mm^{-1}, 25663 reflections measured, 2876 independent reflections (R_{int} = 0.0245). The final R_1 values were 0.0382 ($I > 2\sigma(I)$). The final $wR(F^2)$ values were 0.1832 ($I > 2\sigma(I)$). The final R_1 values were 0.0384 (all data). The final $wR(F^2)$ values were 0.1837 (all data). The goodness of fit on F^2 was 1.810. (CCDC Number 1950508)

Table S6. Crystal data and structure refinement for (±)-Actinoxocine ((±)-1)

Identification code	global	
Empirical formula	$C_{20}H_{16}O_4$	
Formula weight	320.33	
Temperature	100(2) K	
Wavelength	1.54178 Å	
Crystal system	Monoclinic	
Space group	$P121/n1$	
Unit cell dimensions	a = 7.8685(2) Å	α = 90°.
	b = 11.5144(2) Å	β = 103.3720(10)°.
	c = 16.5769(3) Å	γ = 90°.
Volume	1461.17(5) Å^3	
Z	4	
Density (calculated)	1.456 Mg/m^3	
Absorption coefficient	0.828 mm^{-1}	
F(000)	672	
Crystal size	0.640 x 0.160 x 0.100 mm^3	
Theta range for data collection	4.72 to 72.36°.	
Index ranges	-8<=h<=9, -14<=k<=14, -20<=l<=20	
Reflections collected	25663	
Independent reflections	2876 [$R(int)$ = 0.0245]	
Completeness to theta = 72.36°	99.4 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.92 and 0.79	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	2876 / 0 / 221	

Goodness-of-fit on F^2	1.810
Final R indices [$I>2sigma(I)$]	R_1 = 0.0382, wR_2 = 0.1832
R indices (all data)	R_1 = 0.0384, wR_2 = 0.1837
Largest diff. peak and hole	0.354 and -0.230 e.Å^{-3}

X-ray Crystallographic Analysis of (+)-Actinoxocine ((+)-1). Crystal data for xzp5_1: $C_{20}H_{16}O_4$, M = 320.33, a = 7.6575(2) Å, b = 12.4737(3) Å, c = 15.9440(4) Å, α = 90°, β = 90°, γ = 90°, V = 1522.93(7) Å^3, T = 100.(2) K, space group $P212121$, Z = 4, μ(Cu Kα) = 0.794 mm^{-1}, 25301 reflections measured, 3025 independent reflections (R_{int} = 0.0376). The final R_1 values were 0.0261 ($I > 2\sigma(I)$). The final $wR(F^2)$ values were 0.0685 ($I > 2\sigma(I)$). The final R_1 values were 0.0269 (all data). The final $wR(F^2)$ values were 0.0694 (all data). The goodness of fit on F^2 was 1.032. Flack parameter = 0.00(4). (CCDC Number 1949848)

Figure S25. X-ray Crystal Data for (+)-Actinoxocine ((+)-**1**)

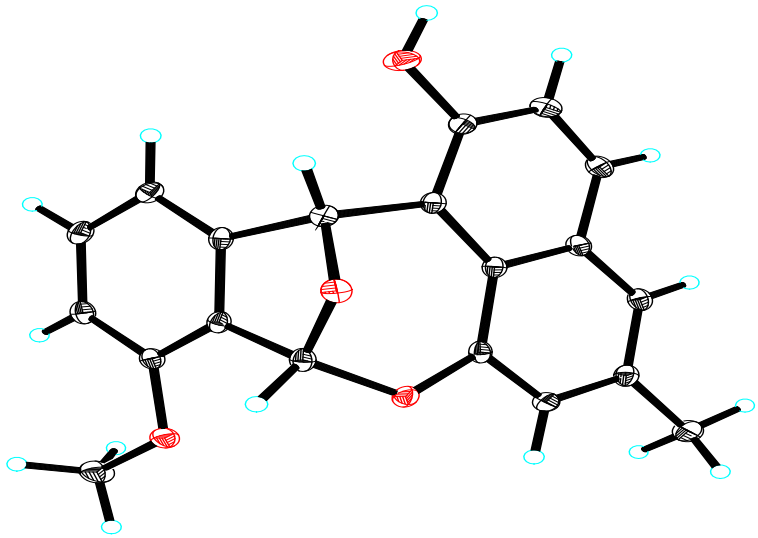


Table S7. Crystal data and structure refinement for (+)-Actinoxocine ((+)-1)

Identification code	global
Empirical formula	$C_{20}H_{16}O_4$
Formula weight	320.33
Temperature	100(2) K
Wavelength	1.54178 Å
Crystal system	Orthorhombic

Space group	$P2_12_12_1$	
Unit cell dimensions	a = 7.6575(2) Å	α = 90°.
	b = 12.4737(3) Å	β = 90°.
	c = 15.9440(4) Å	γ = 90°.
Volume	1522.93(7) Å^3	
Z	4	
Density (calculated)	1.397 Mg/m^3	
Absorption coefficient	0.794 mm^{-1}	
F(000)	672	
Crystal size	0.350 x 0.070 x 0.030 mm^3	
Theta range for data collection	4.50 to 72.43.	
Index ranges	-9<=h<=7, -15<=k<=15, -19<=l<=19	
Reflections collected	25301	
Independent reflections	3025 [$R(int)$ = 0.0376]	
Completeness to theta = 72.43°	100.0 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.98 and 0.86	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	3025 / 0 / 221	
Goodness-of-fit on F^2	1.032	
Final R indices [I>2$sigma$(I)]	R_1 = 0.0261, wR_2 = 0.0685	
R indices (all data)	R_1 = 0.0269, wR_2 = 0.0694	
Absolute structure parameter	0.00(4)	
Largest diff. peak and hole	0.166 and -0.166 e.Å^{-3}	

X-ray Crystallographic Analysis of (–)-Actinoxocine ((–)-1). Crystal data for xzp5_2: $C_{20}H_{16}O_4$, M = 320.33, a = 7.6647(2) Å, b = 12.4751(4) Å, c = 15.9554(5) Å, α = 90°, β = 90°, γ = 90°, V = 1525.62(8) Å^3, T = 100.(2) K, space group $P212121$, Z = 4, μ(Cu Kα) = 0.793 mm^{-1}, 29366 reflections measured, 3048 independent reflections (R_{int} = 0.1030). The final R_1 values were 0.0532 ($I > 2\sigma(I)$). The final $wR(F^2)$ values were 0.1387 ($I > 2\sigma(I)$). The final R_1 values were 0.0608 (all data). The final $wR(F^2)$ values were 0.1479 (all data). The goodness of fit on F^2 was 1.053. Flack parameter = 0.01(14). (CCDC Number 1950506)

Figure S26. X-ray Crystal Data for (–)-Actinoxocine ((–)-**1**)

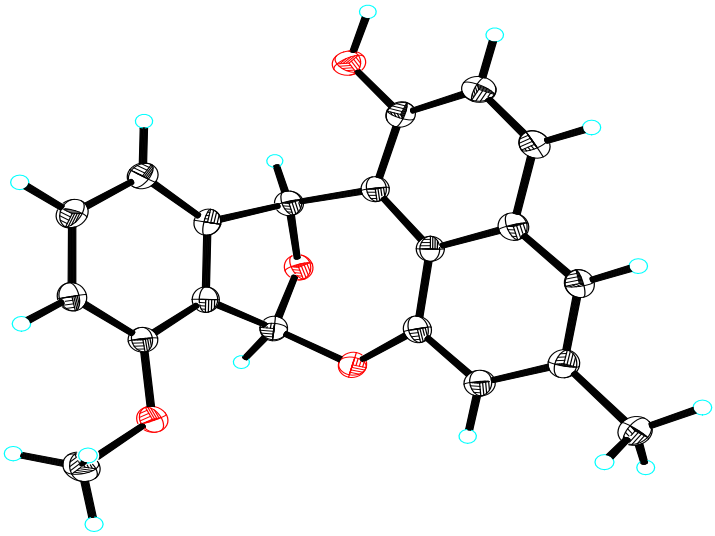


Table S8. Crystal data and structure refinement for (–)-Actinoxocine ((–)-1)

Identification code	global	
Empirical formula	$C_{20}H_{16}O_4$	
Formula weight	320.33	
Temperature	100(2) K	
Wavelength	1.54178 Å	
Crystal system	Orthorhombic	
Space group	$P2_12_12_1$	
Unit cell dimensions	a = 7.6647(2) Å	α = 90°.
	b = 12.4751(4) Å	β = 90°.
	c = 15.9554(5) Å	γ = 90°.
Volume	1525.62(8) $Å^3$	
Z	4	
Density (calculated)	1.395 Mg/m^3	
Absorption coefficient	0.793 mm^{-1}	
F(000)	672	
Crystal size	0.240 x 0.030 x 0.010 mm^3	
Theta range for data collection	4.50 to 73.17°.	

Index ranges	-9<=h<=9, -15<=k<=15, -19<=l<=19
Reflections collected	29366
Independent reflections	3048 [*R*(*int*) = 0.1030]
Completeness to theta = 73.17°	99.8 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.99 and 0.71
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	3048 / 0 / 222
Goodness-of-fit on F^2	1.053
Final R indices [*I*>2*sigma*(*I*)]	R_1 = 0.0532, wR_2 = 0.1387
R indices (all data)	R_1 = 0.0608, wR_2 = 0.1479
Absolute structure parameter	0.01(14)
Extinction coefficient	0.0019(7)
Largest diff. peak and hole	0.234 and -0.242 e.Å^{-3}

X-ray Crystallographic Analysis of Actinaphthoran A (2). Crystal data for xzp7: $C_{20}H_{18}O_4$, M = 322.34, a = 11.9282(8) Å, b = 4.7315(3) Å, c = 27.471(2) Å, α = 90°, β = 92.048(5)°, γ = 90°, V = 1549.43(19) Å^3, T = 100.(2) K, space group $P1211$, Z = 4, μ(Cu Kα) = 0.781 mm^{-1}, 15513 reflections measured, 5001 independent reflections (R_{int} = 0.2082). The final R_1 values were 0.0904 ($I > 2\sigma(I)$). The final $wR(F^2)$ values were 0.1702 ($I > 2\sigma(I)$). The final R_1 values were 0.1809 (all data). The final $wR(F^2)$ values were 0.2187 (all data). The goodness of fit on F^2 was 1.004. Flack parameter = -0.4(6). (CCDC Number 1950507)

Figure S27. X-ray Crystal Data for Actinaphthoran A (**2**)

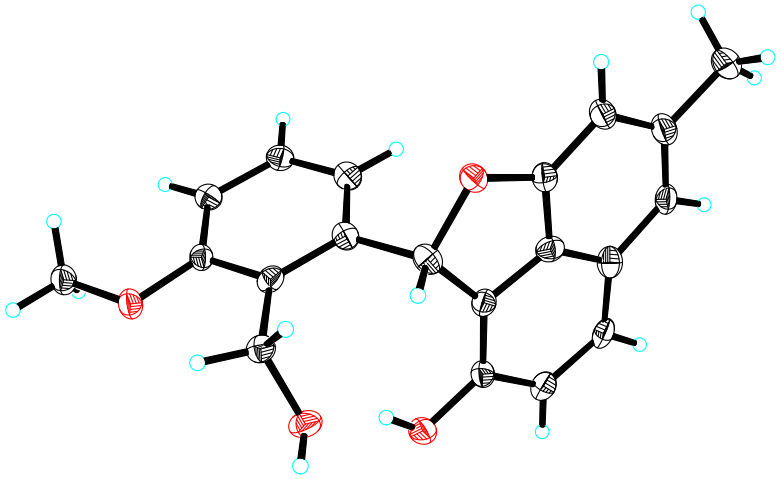


Table S9. Crystal data and structure refinement for Actinaphthoran A (2)

Identification code	global	
Empirical formula	$C_{20}H_{18}O_4$	
Formula weight	322.34	
Temperature	100(2) K	
Wavelength	1.54178 Å	
Crystal system	Monoclinic	
Space group	P1211	
Unit cell dimensions	a = 11.9282(8) Å	α = 90°.
	b = 4.7315(3) Å	β = 92.048(5)°.
	c = 27.471(2) Å	γ = 90°.
Volume	1549.43(19) Å^3	
Z	4	
Density (calculated)	1.382 Mg/m^3	
Absorption coefficient	0.781 mm^{-1}	
F(000)	680	
Crystal size	0.320 x 0.020 x 0.010 mm^3	
Theta range for data collection	3.22 to 72.54°.	
Index ranges	-14<=h<=14, -4<=k<=5, -33<=l<=33	

Reflections collected	15513
Independent reflections	5001 [$R(int)$ = 0.2082]
Completeness to theta = 72.54°	99.5 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.99 and 0.83
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	5001 / 0 / 439
Goodness-of-fit on F^2	1.004
Final R indices [$I>2sigma(I)$]	R_1 = 0.0904, wR_2 = 0.1702
R indices (all data)	R_1 = 0.1809, wR_2 = 0.2187
Absolute structure parameter	-0.4(6)
Largest diff. peak and hole	0.289 and -0.354 e.Å^{-3}

Figure S28. CD Spectrum of (+)-Actinoxocine ((+)-**1**) in CH_2Cl_2

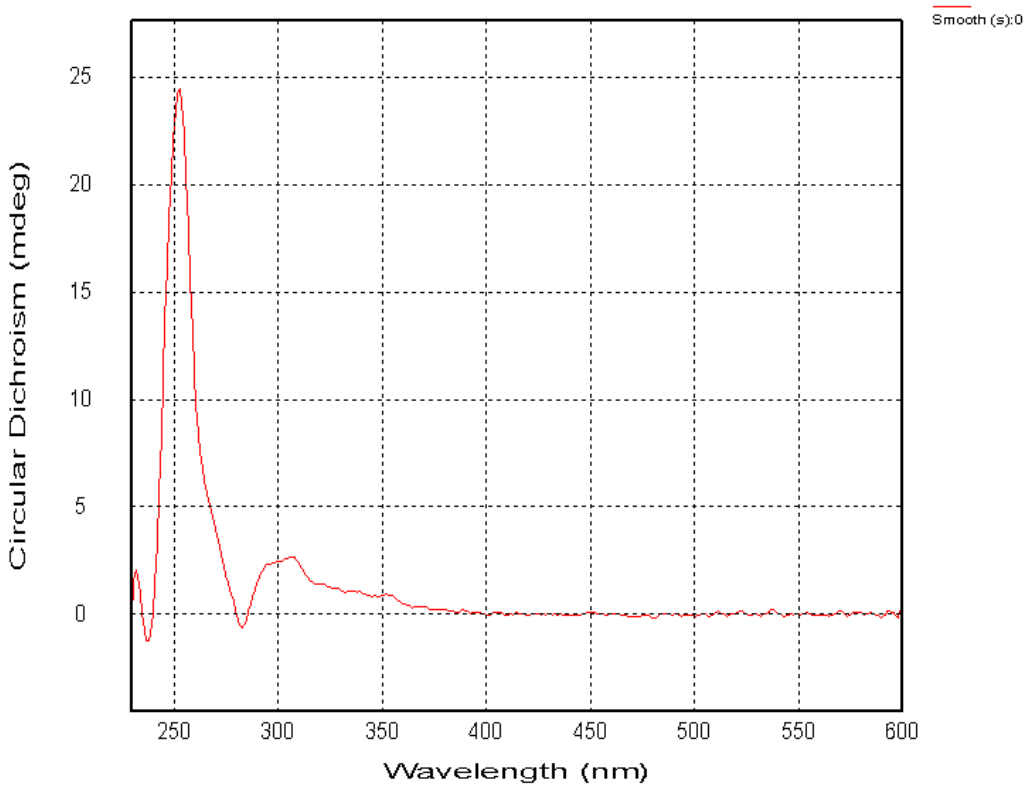


Figure S29. CD Spectrum of (–)-Actinoxocine ((–)-**1**) in CH_2Cl_2

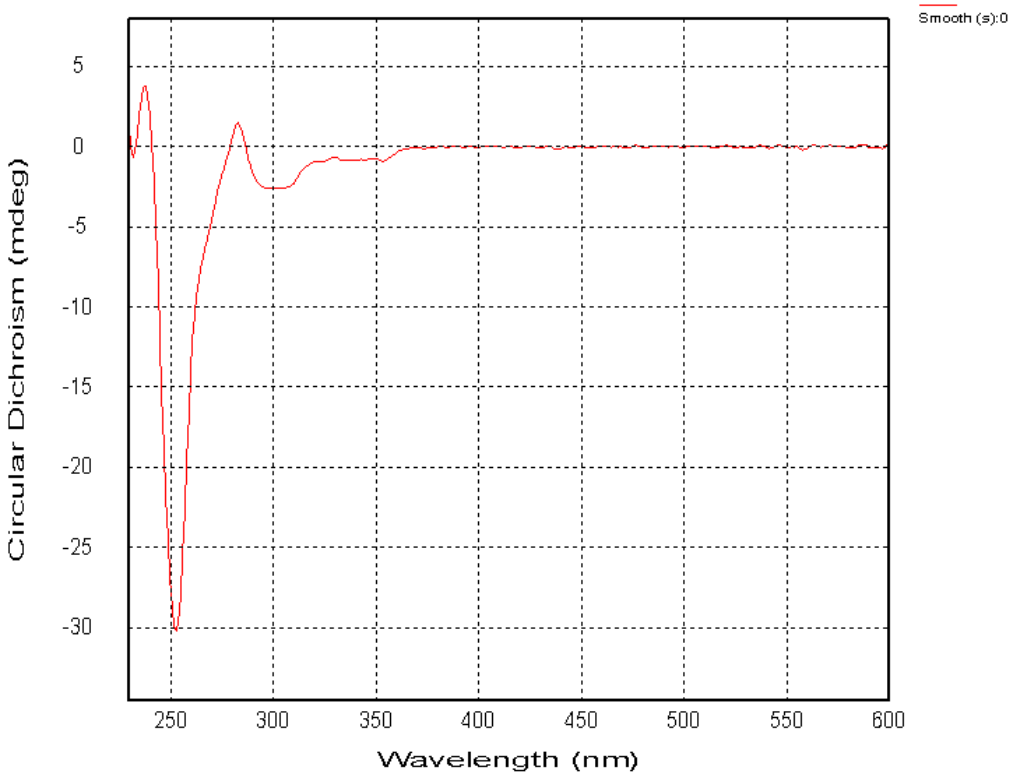


Figure S30. Experimental ECD spectra (200-400 nm) of actinaphthoran B (**3**) in acetonitrile and the calculated ECD spectra of the model molecules of **3** at the B3LYP/6-311+G(d, p) level.

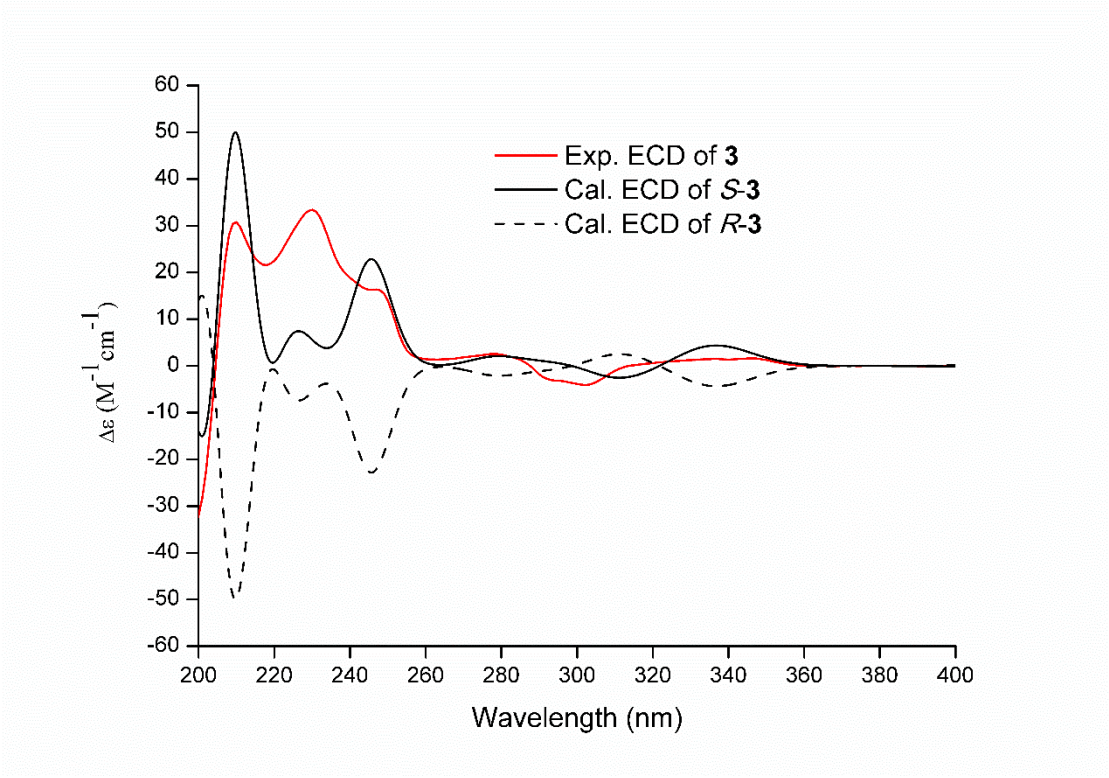


Figure S31. CD Spectrum of (±)-Elmenol G ((±)- **4**) in CH_2Cl_2

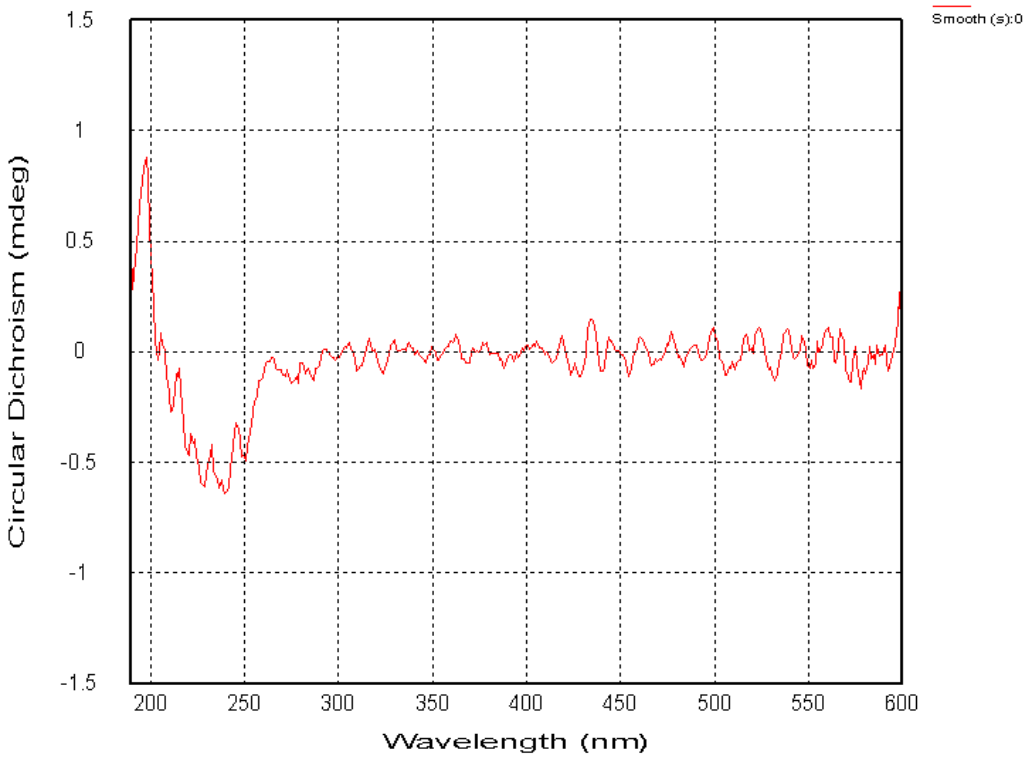


Figure S32. UV Spectra of (+)-Actinoxocine ((+)-**1**)

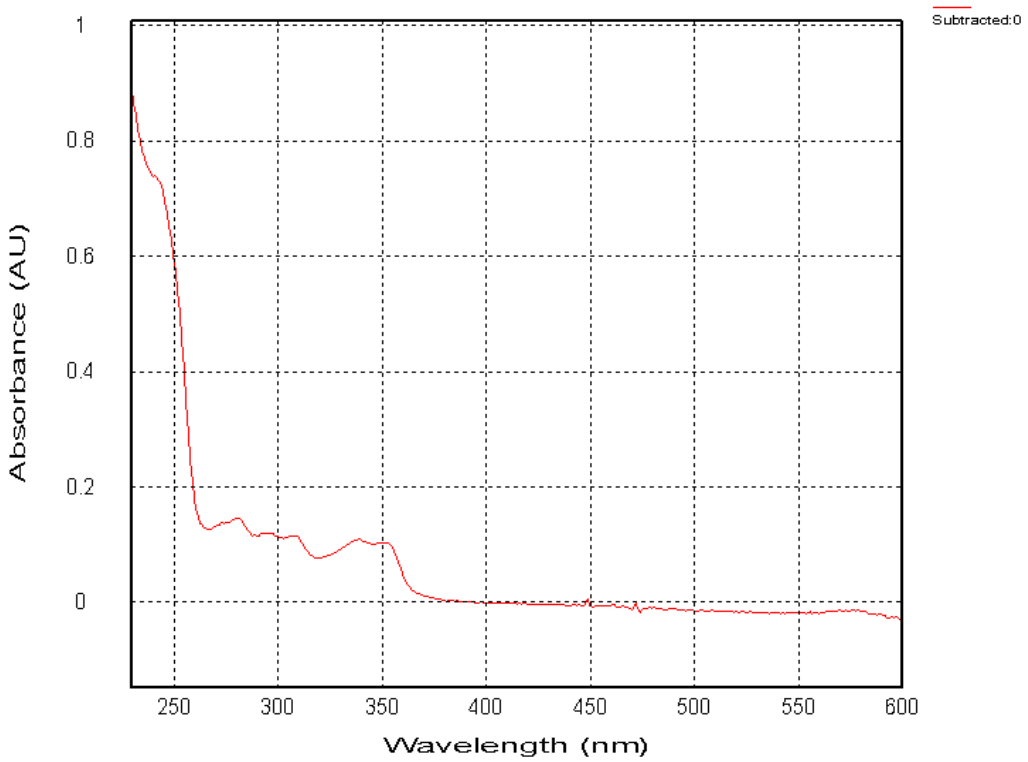


Figure S33. UV Spectra for (–)-Actinoxocine ((–)-**1**)

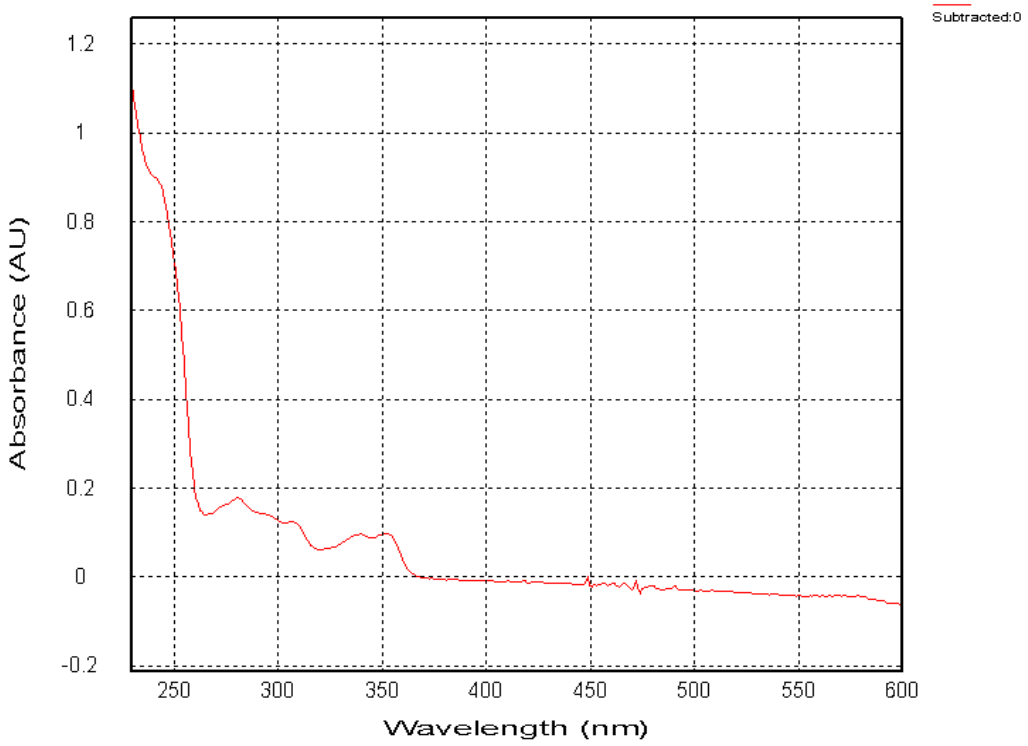


Figure S34. UV Spectra for Actinaphthoran A (**2**)

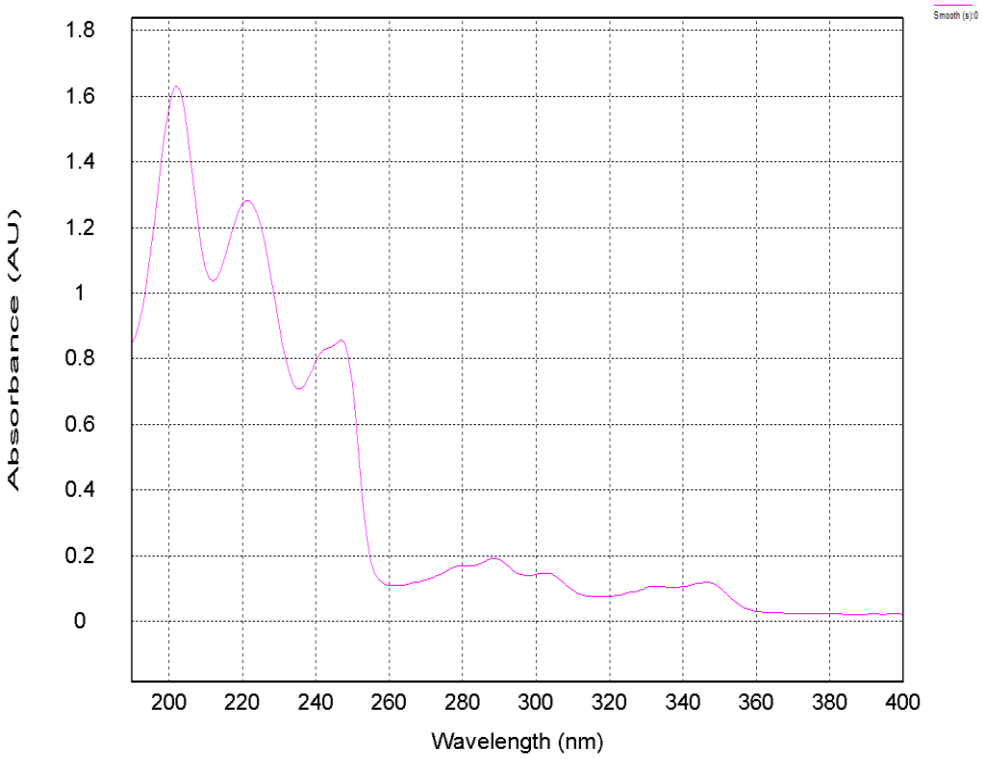


Figure S35. UV Spectra for Actinaphthoran B (**3**)