Supporting Information

Youssoufenes A2 and A3, Antibiotic Dimeric Cinnamoyl Lipids from the *ΔdtlA* Mutant of a Marine-Derived *Streptomyces* Strain

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Figure S1. HPLC-HRESIMS of the culture extract of the *ΔdtlA* mutant strain of marine-derived *S. youssoufiensis* OUC6819. HPLC conditions: Agilent Eclipse Plus C18 (100 × 2.1 mm, 3.5 μm); 20-100% gradient ACN/H_2O; wavelength 300 nm.
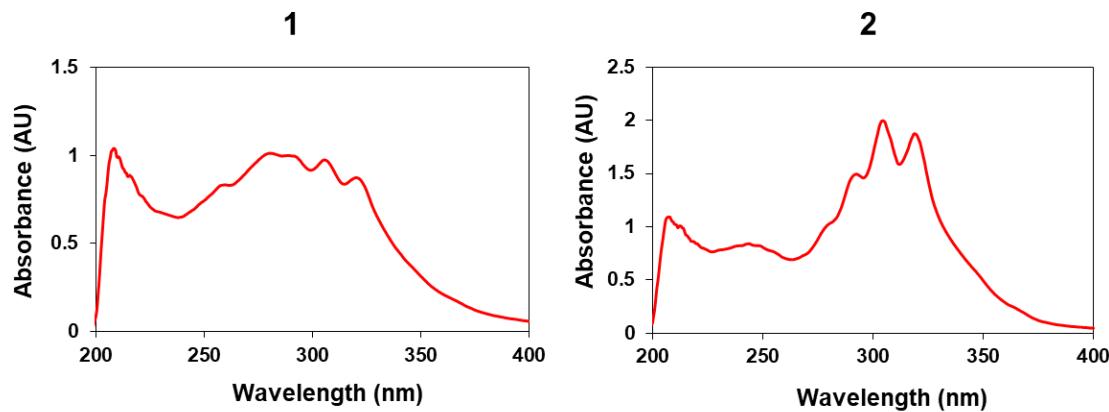
Figure S2. UV spectra of compounds **1** and **2**.
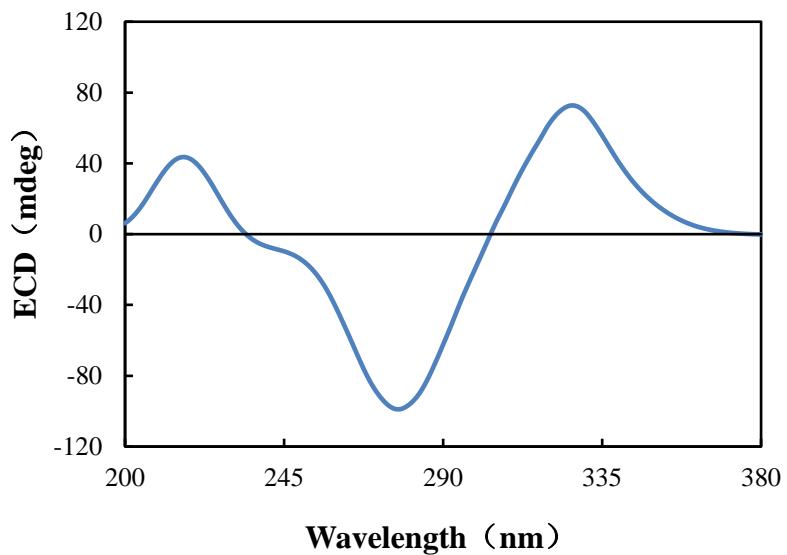
Figure S3. ECD spectrum of compound **1**
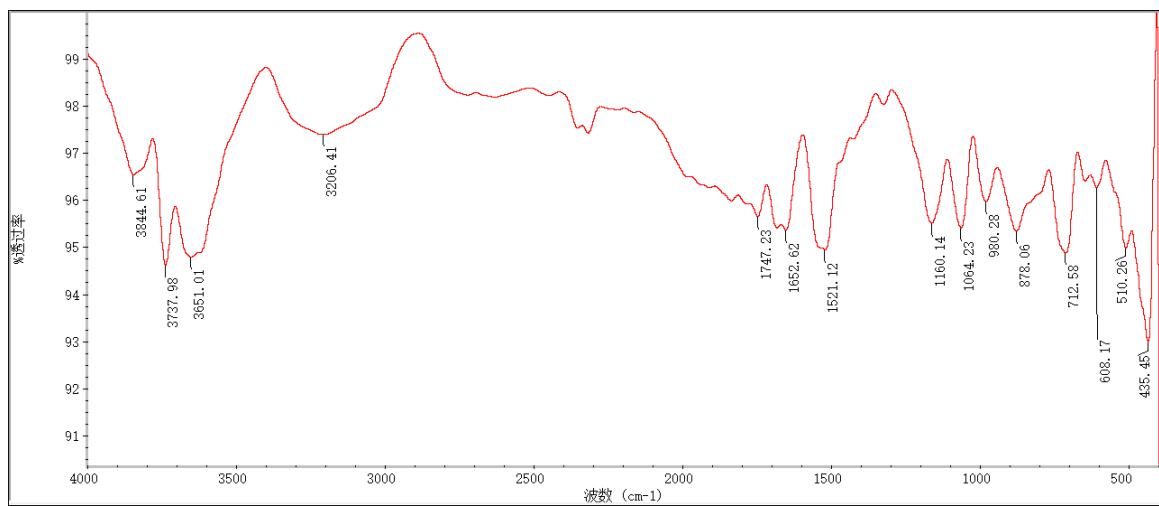
Figure S4. IR (KBr) spectrum of compound **1**
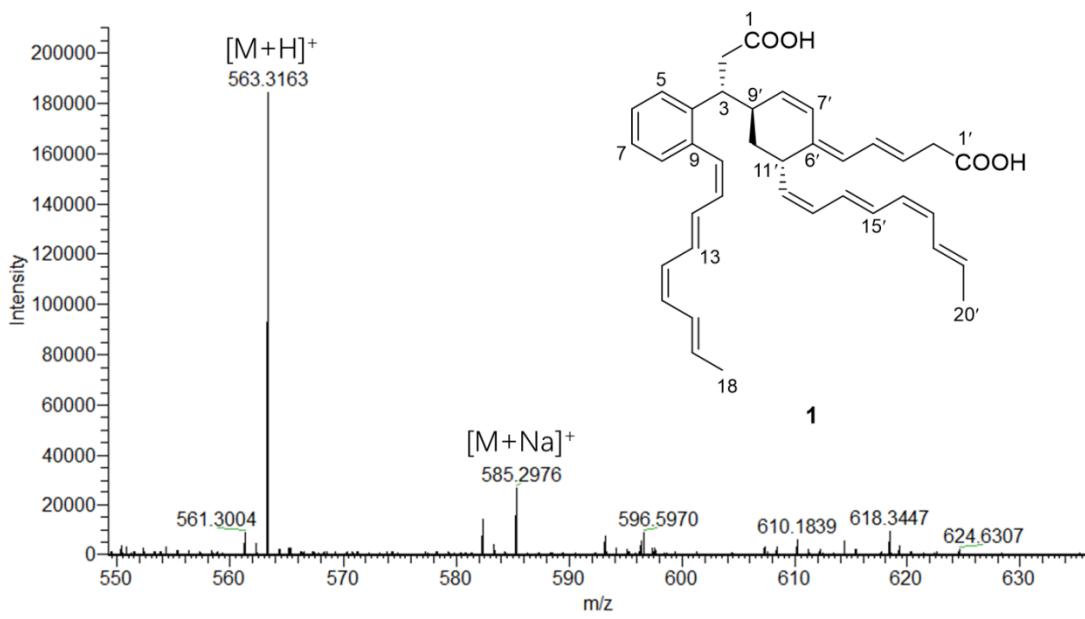
Figure S5. HR-ESIMS spectrum of compound **1**.
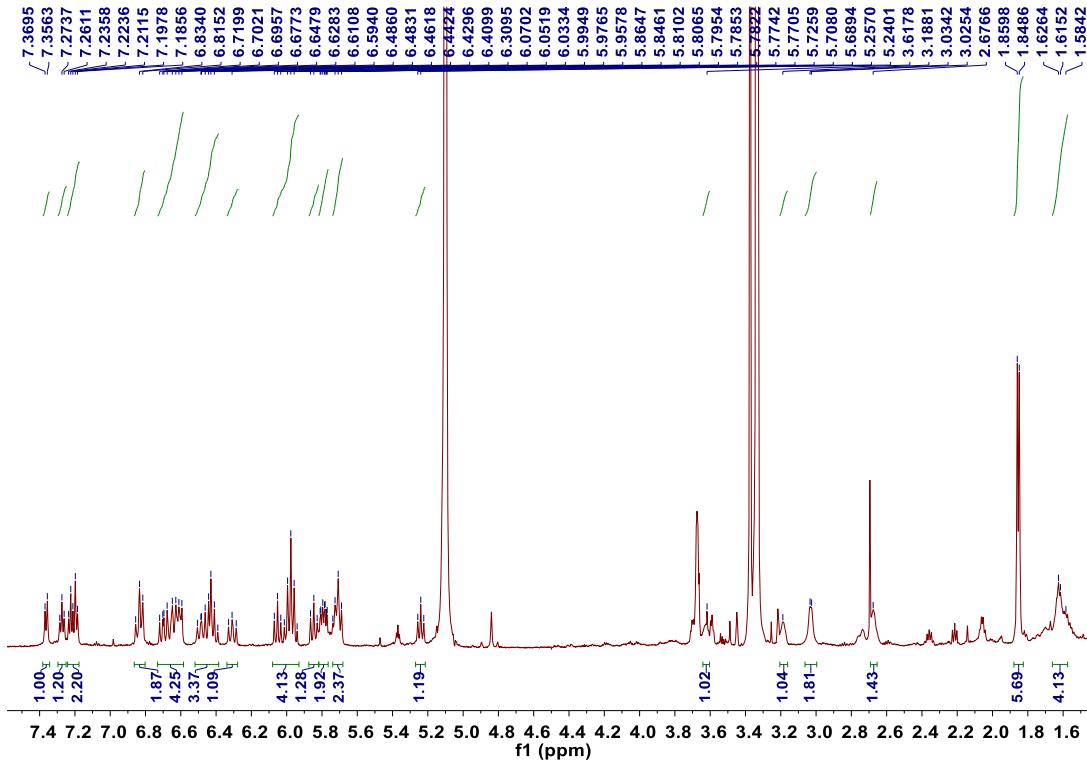
Figure S6. ^{1}H NMR spectrum of compound **1** in CD$_3$OD (600 MHz).
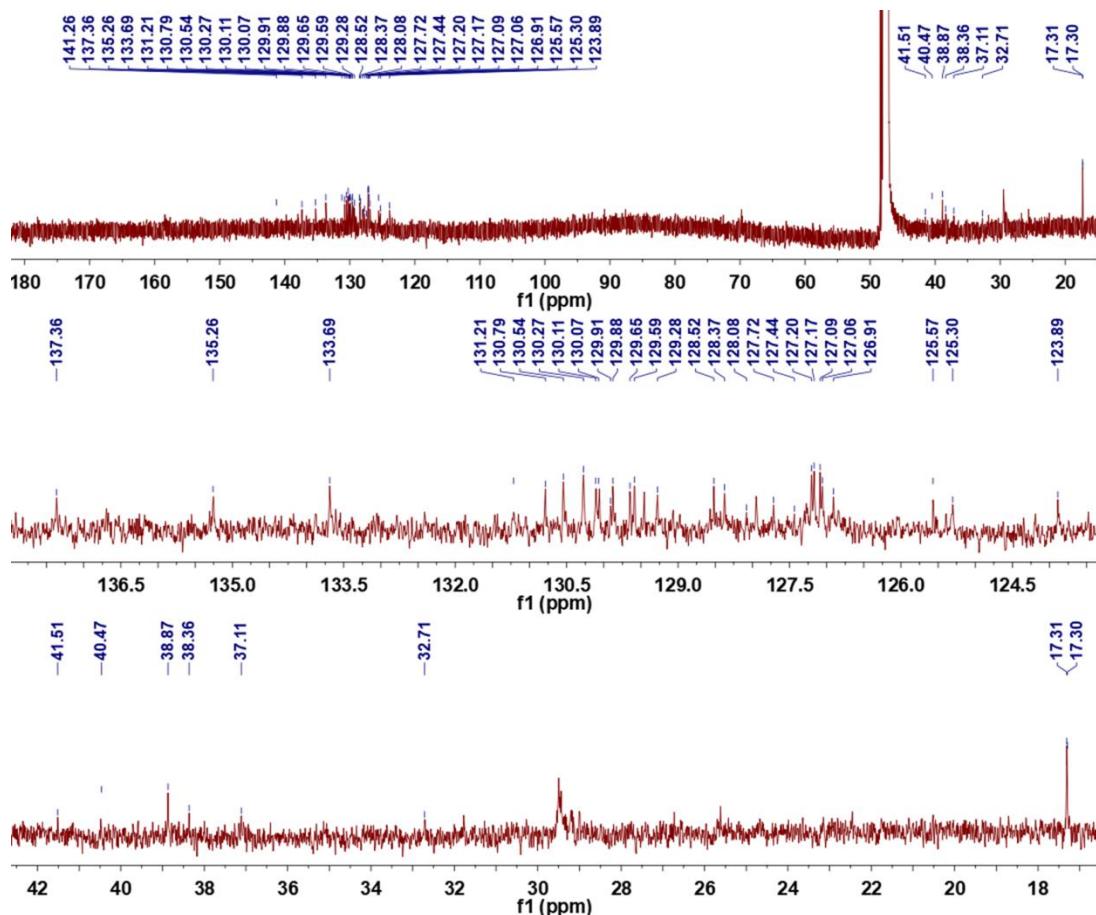
Figure S7. ^{13}C NMR spectrum of compound **1** in CD$_3$OD (150 MHz).
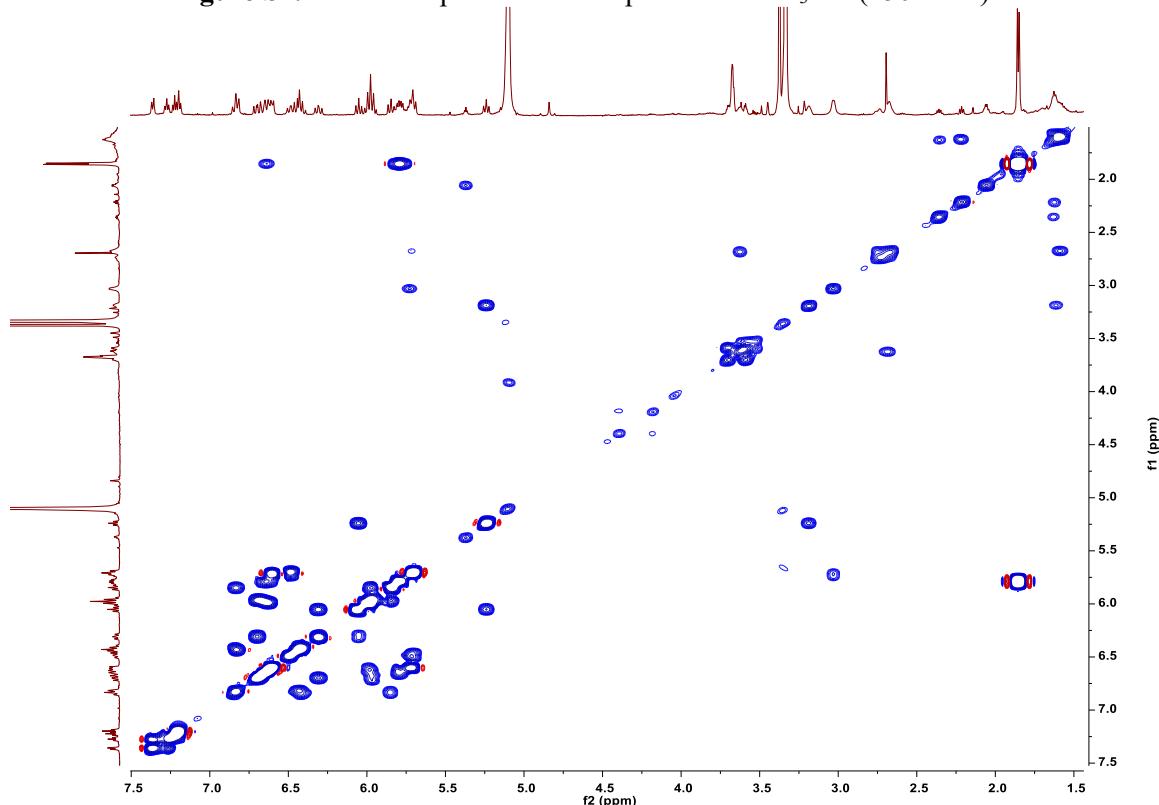
Figure S8. COSY spectrum of compound **1** in CD$_3$OD (600 MHz).
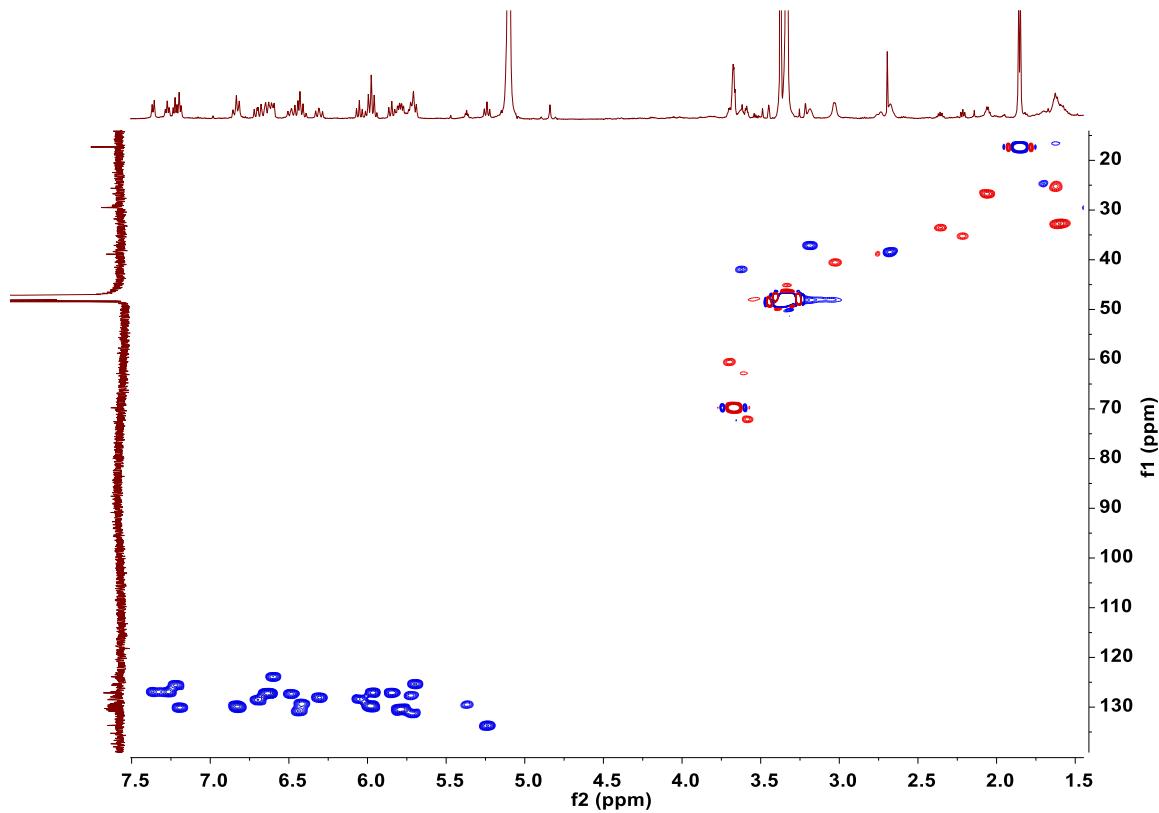
Figure S9. HSQC spectrum of compound **1** in CD₃OD (600 MHz).
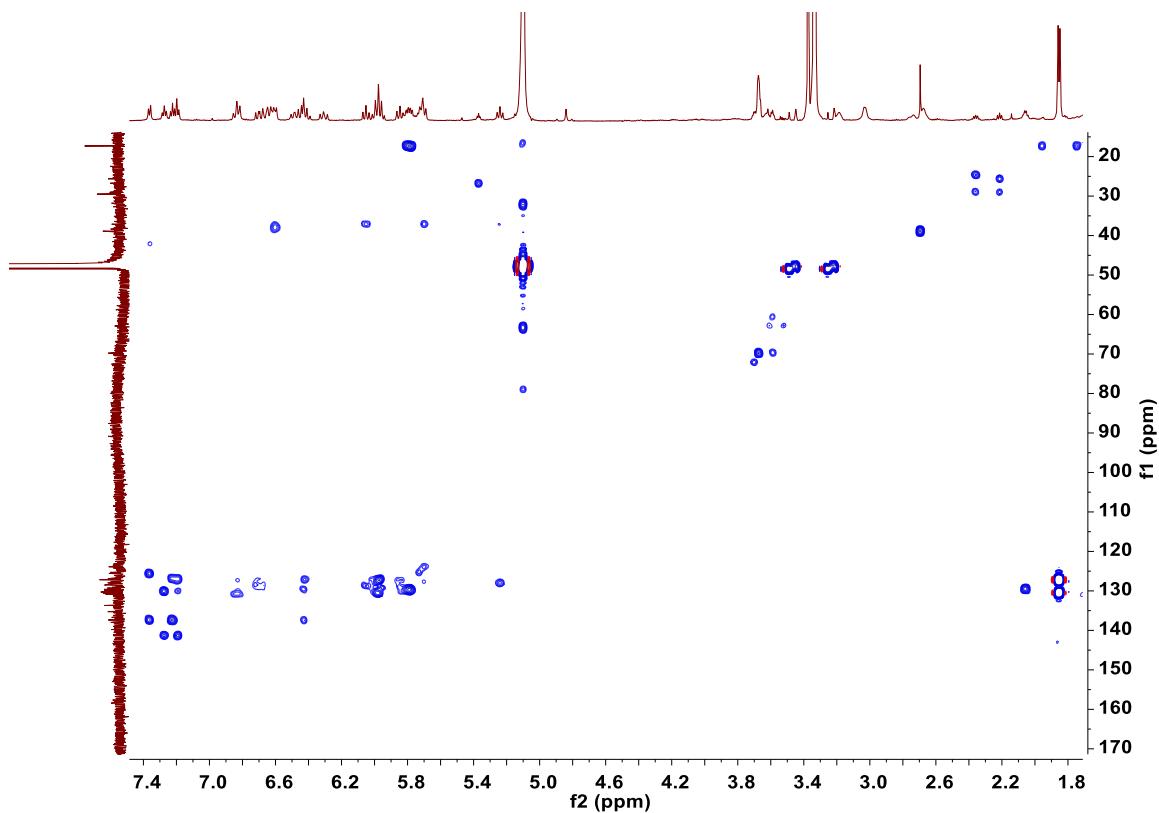
Figure S10. HMBC spectrum of compound **1** in CD₃OD (600 MHz).
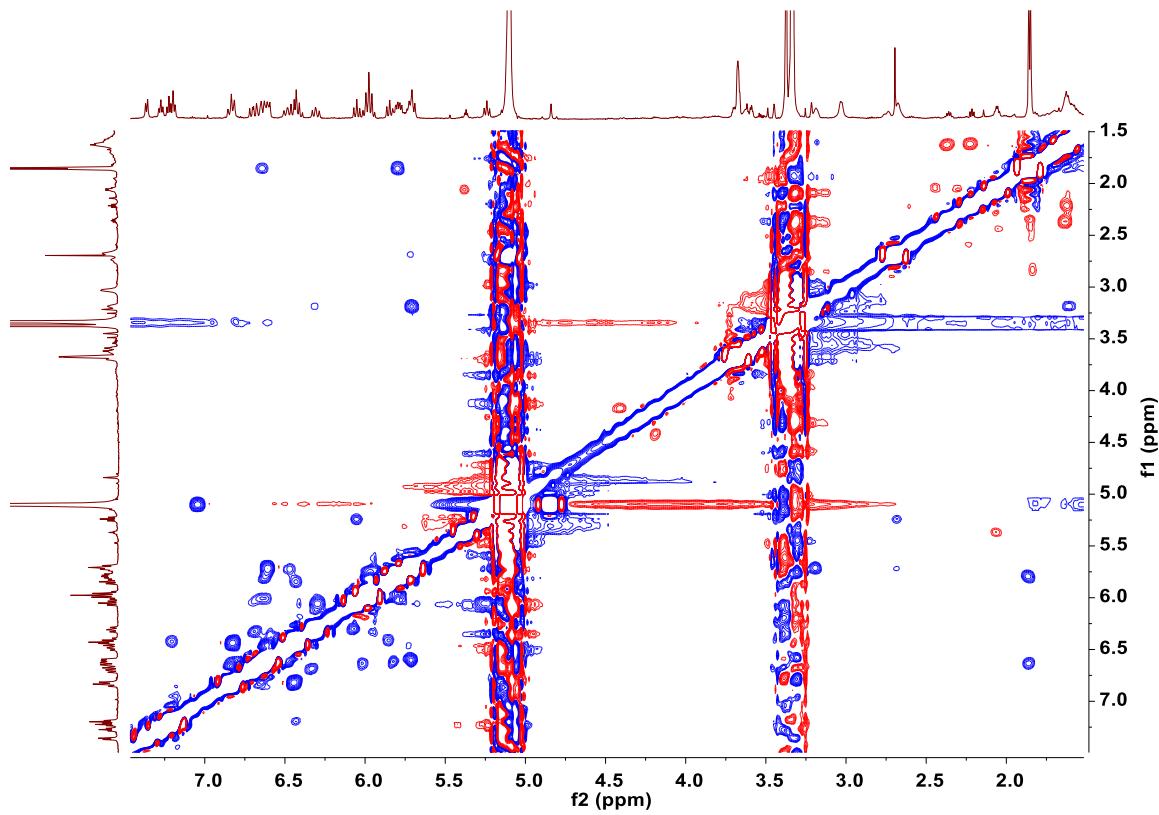
Figure S11. NOESY spectrum of compound **1** in CD₃OD (600 MHz)
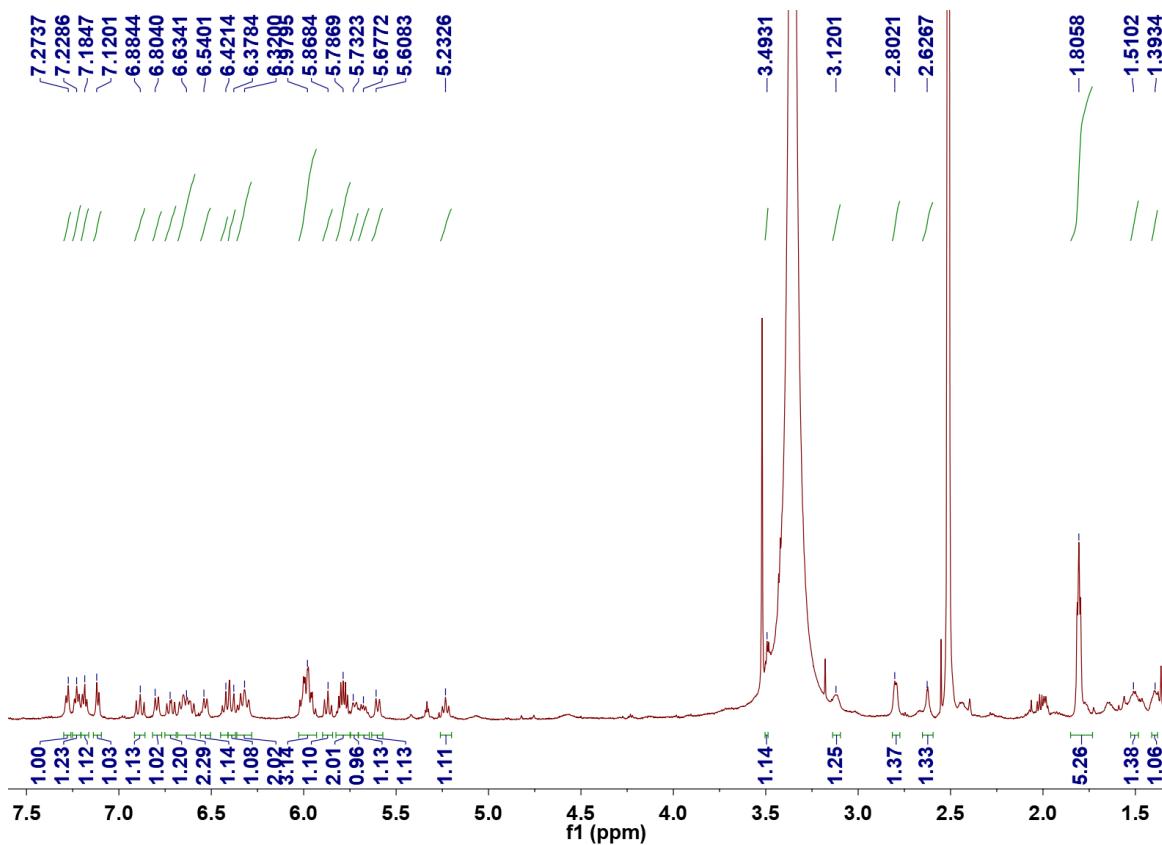
Figure S12. ¹H NMR spectrum of compound **1** in DMSO-d_6 (600 MHz).
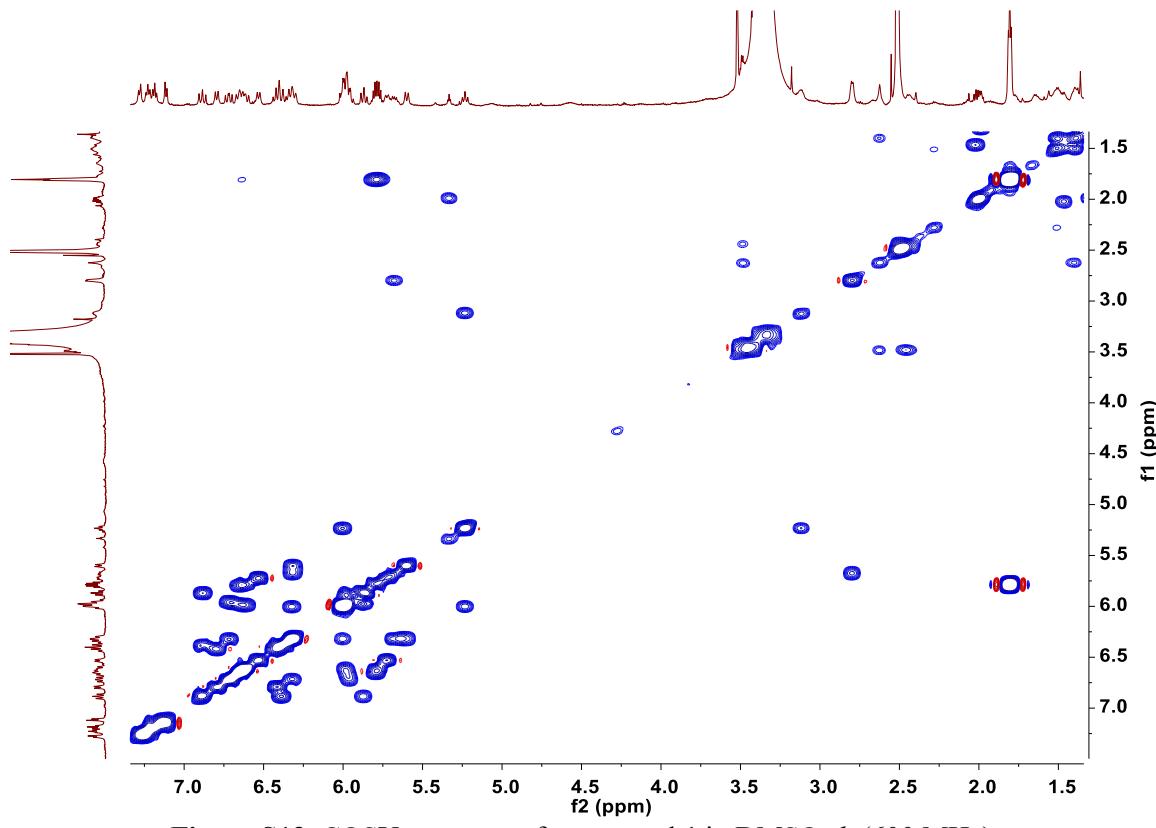
Figure S13. COSY spectrum of compound **1** in DMSO-d_6 (600 MHz).
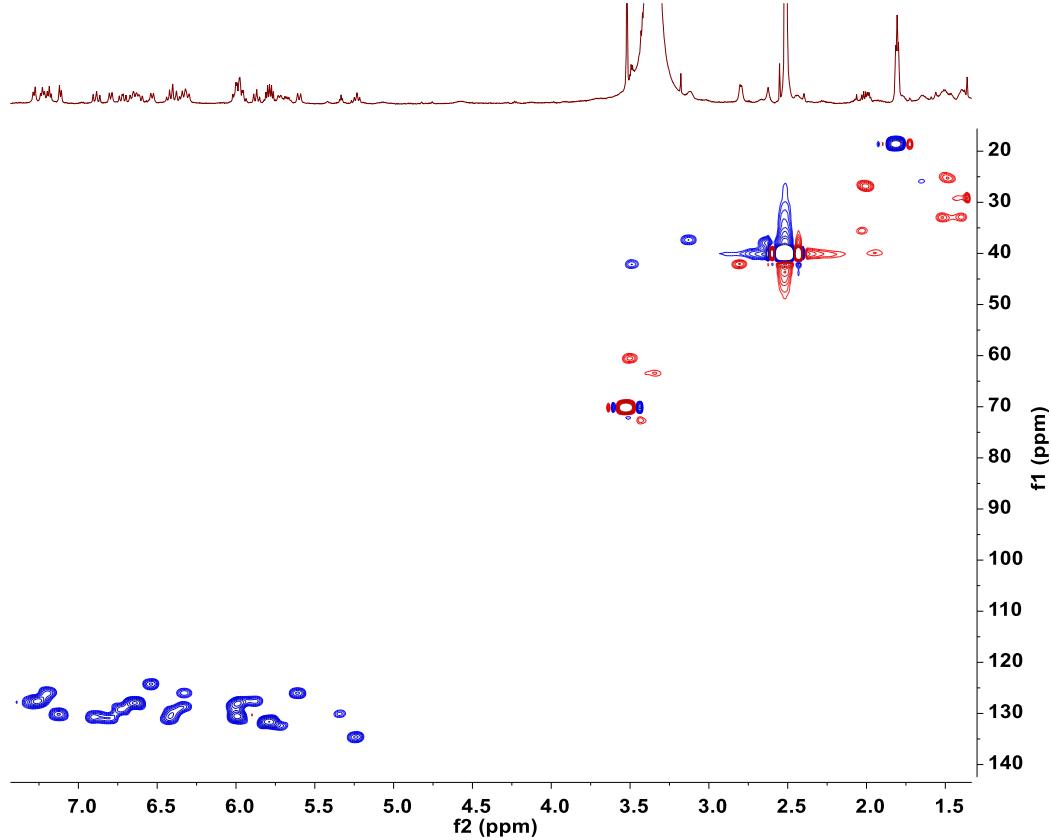
Figure S14. HSQC spectrum of compound **1** in DMSO-d_6 (600 MHz).
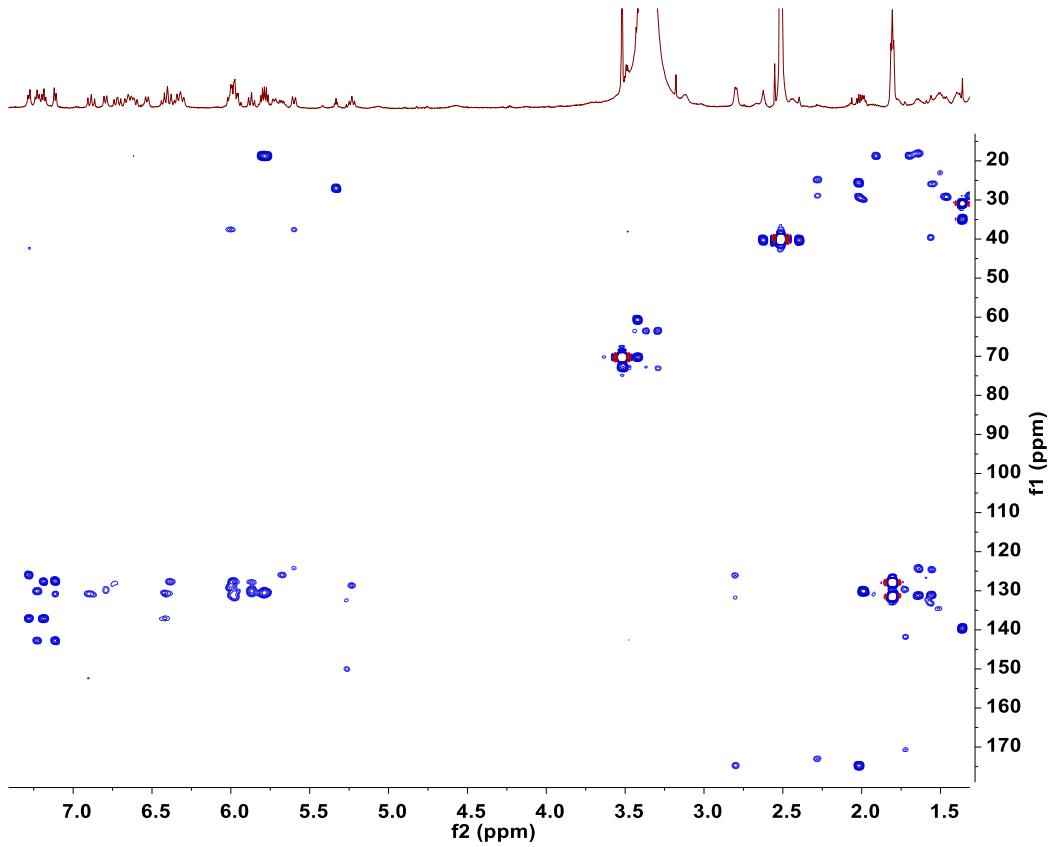
Figure S15. HMBC spectrum of compound **1** in DMSO-d_6 (600 MHz).
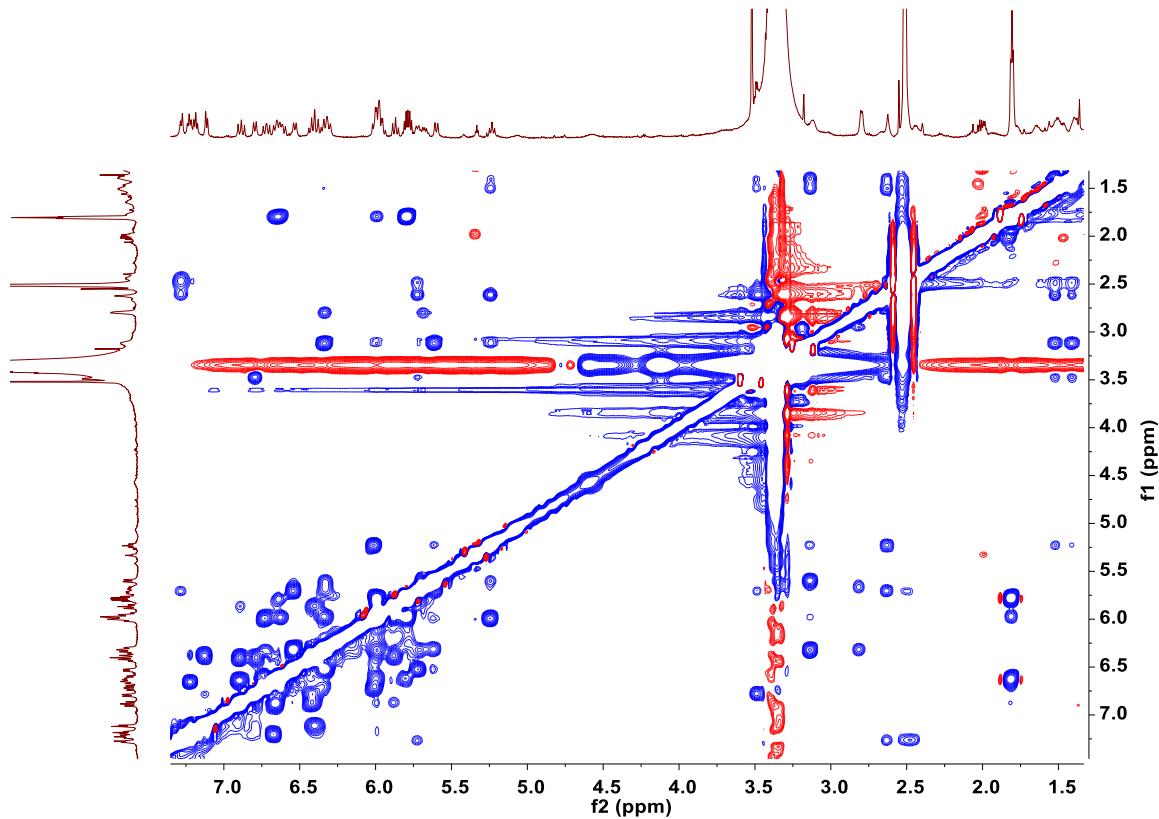
Figure S16. NOESY spectrum of compound **1** in DMSO-d_6 (600 MHz)
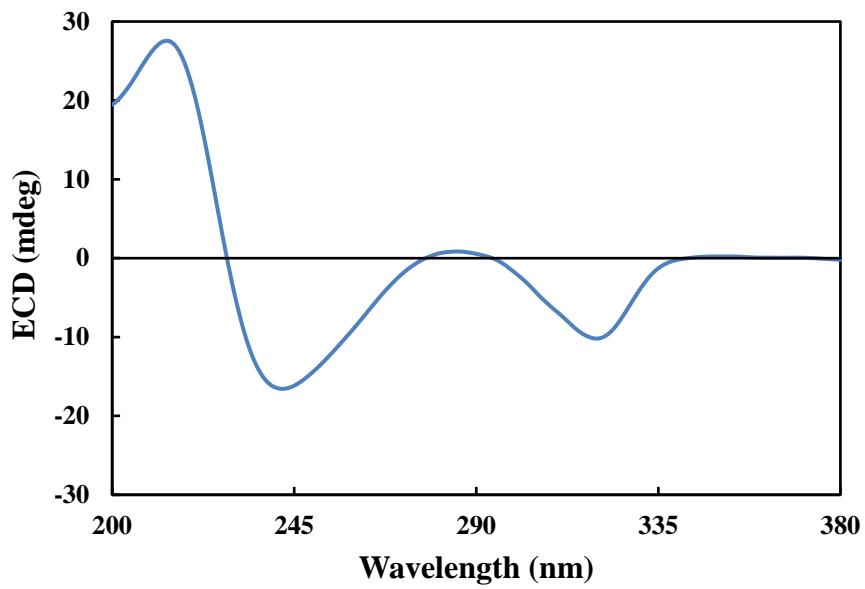
Figure S17. ECD spectrum of compound **2**
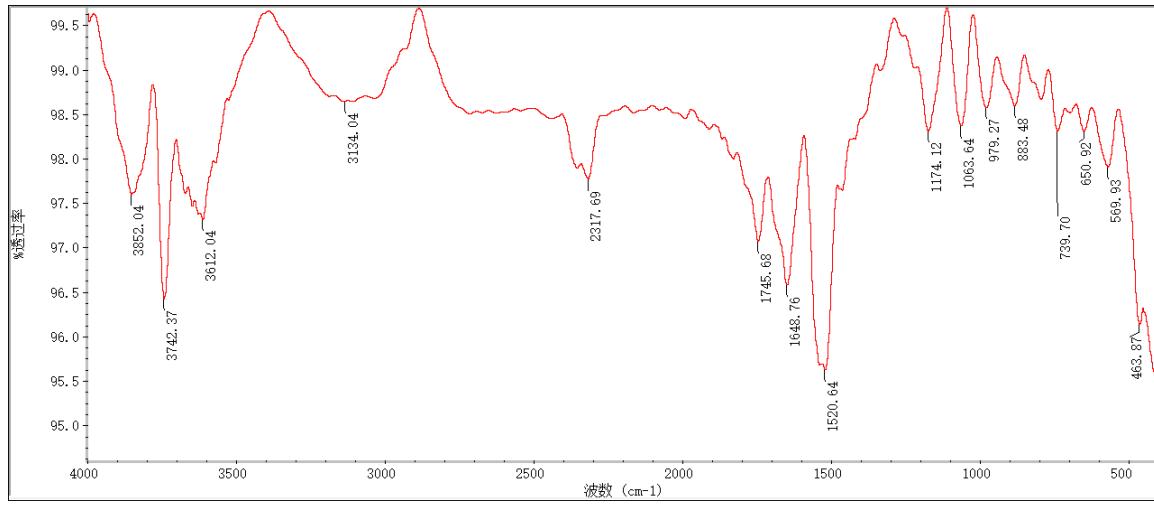
Figure S18. IR (KBr) spectrum of compound **2**
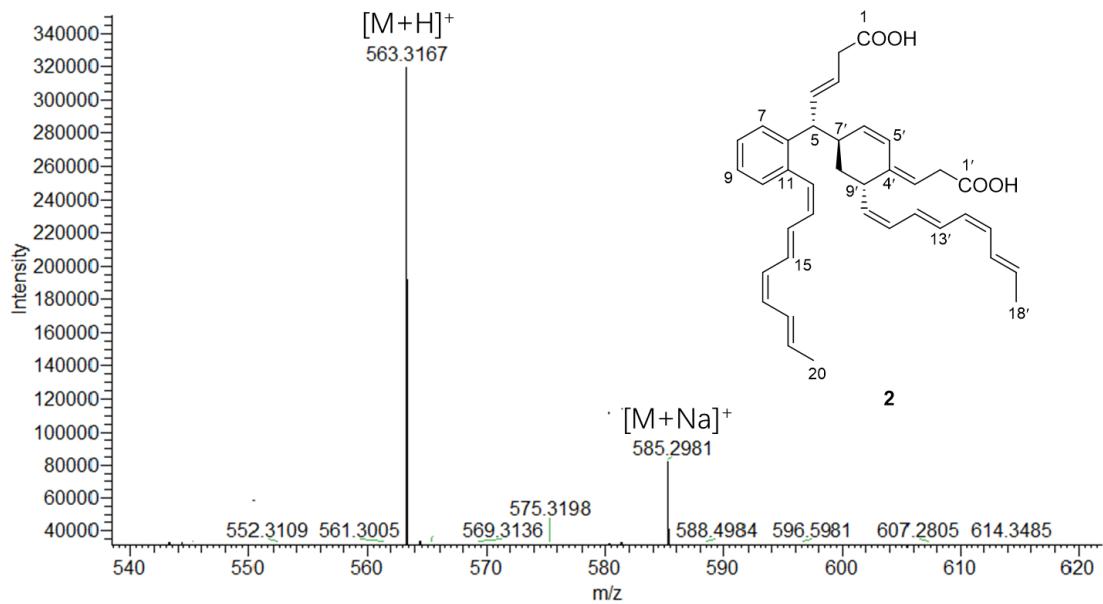
Figure S19. HR-ESIMS spectrum of compound **2**
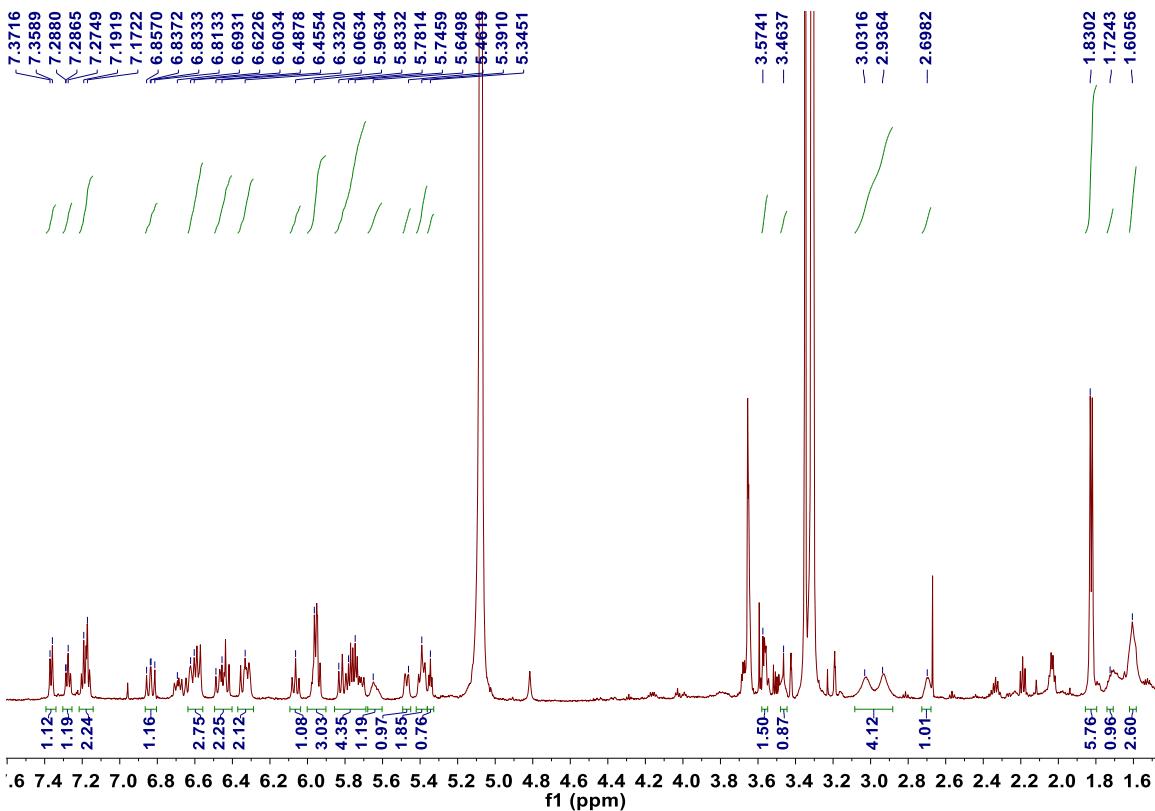
Figure S20. ¹H NMR spectrum of compound **2** in CD₃OD (600 MHz)
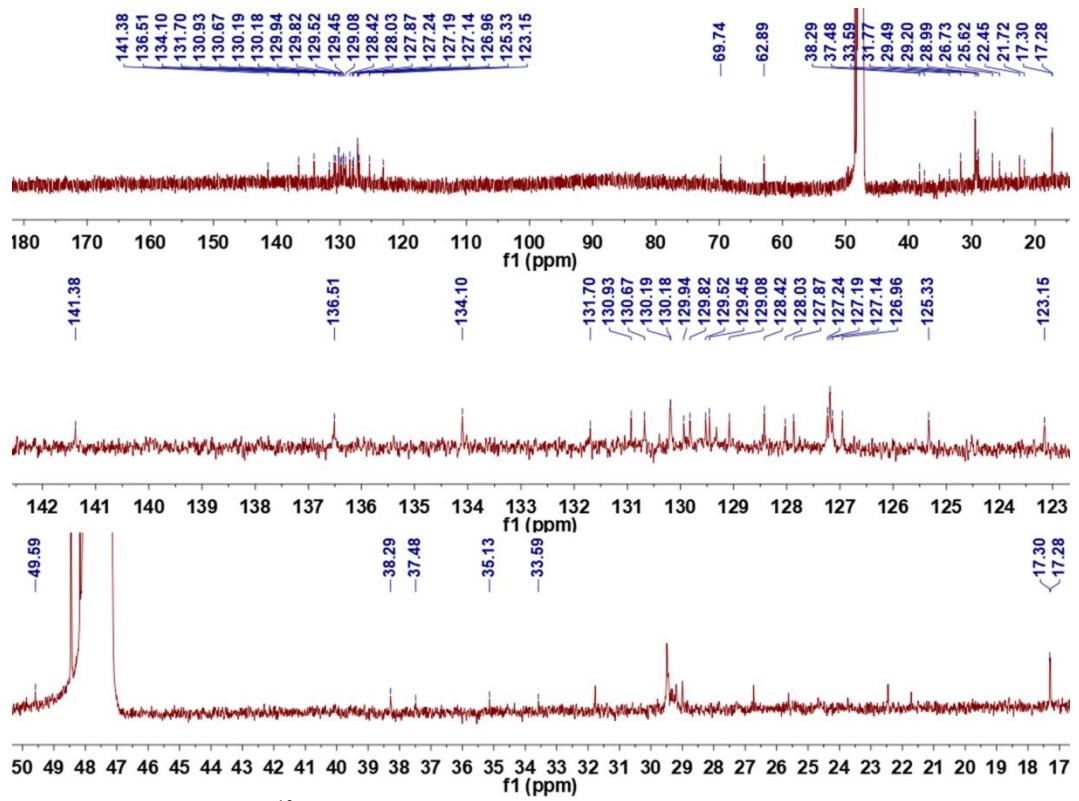
Figure S21. ^{13}C NMR spectrum of compound **2** in CD$_3$OD (150 MHz)
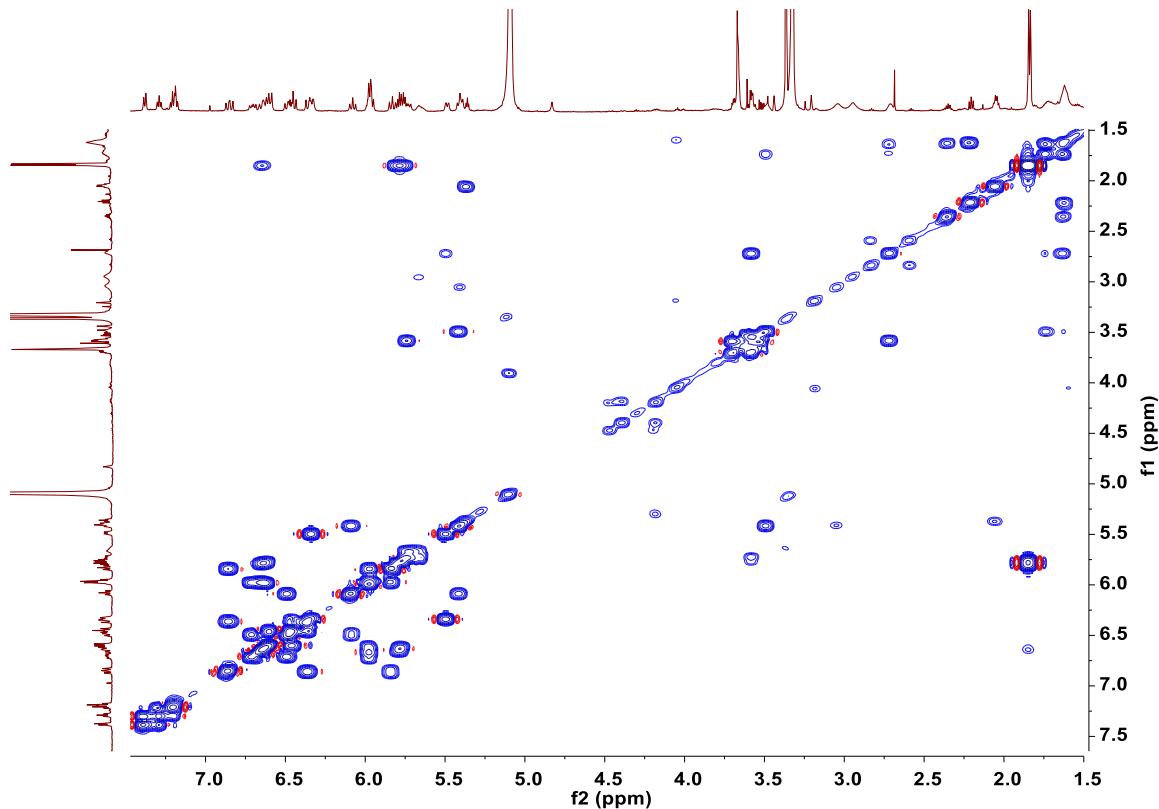
Figure S22. COSY spectrum of compound **2** in CD$_3$OD (600 MHz)
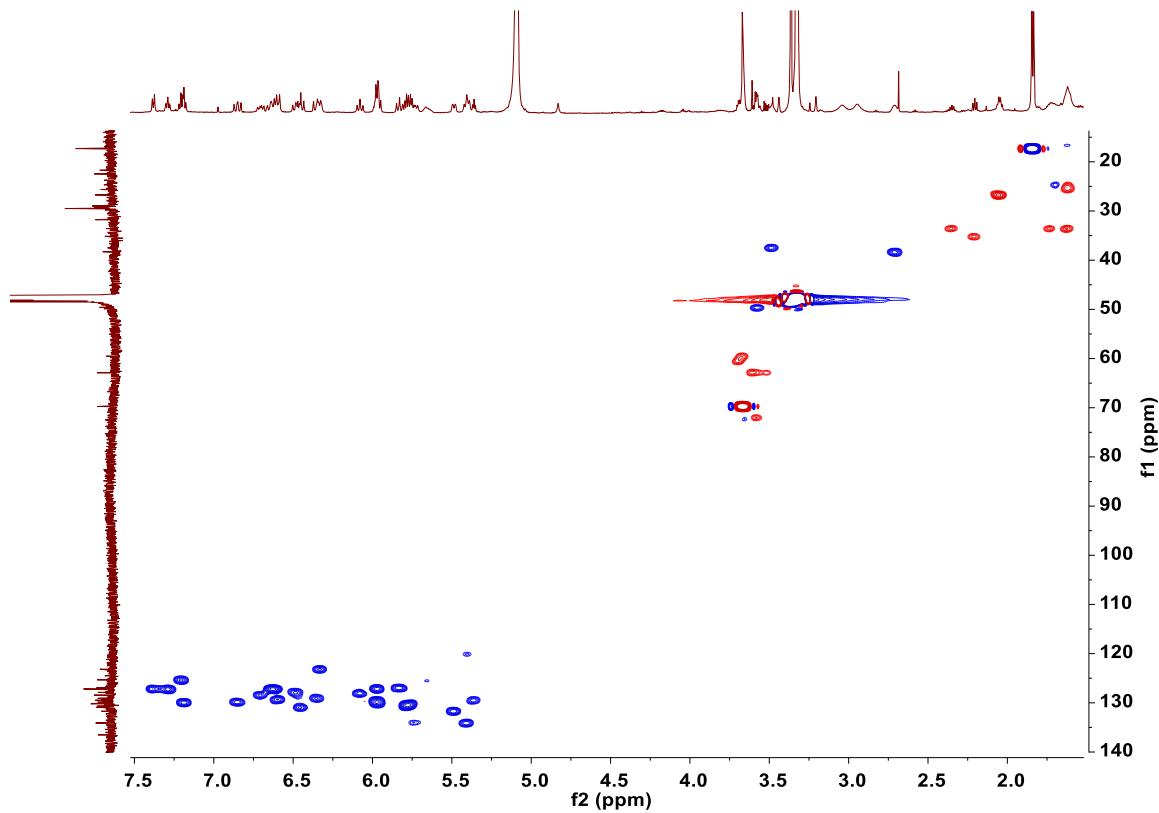
Figure S23. HSQC spectrum of compound **2** in CD₃OD (600 MHz)
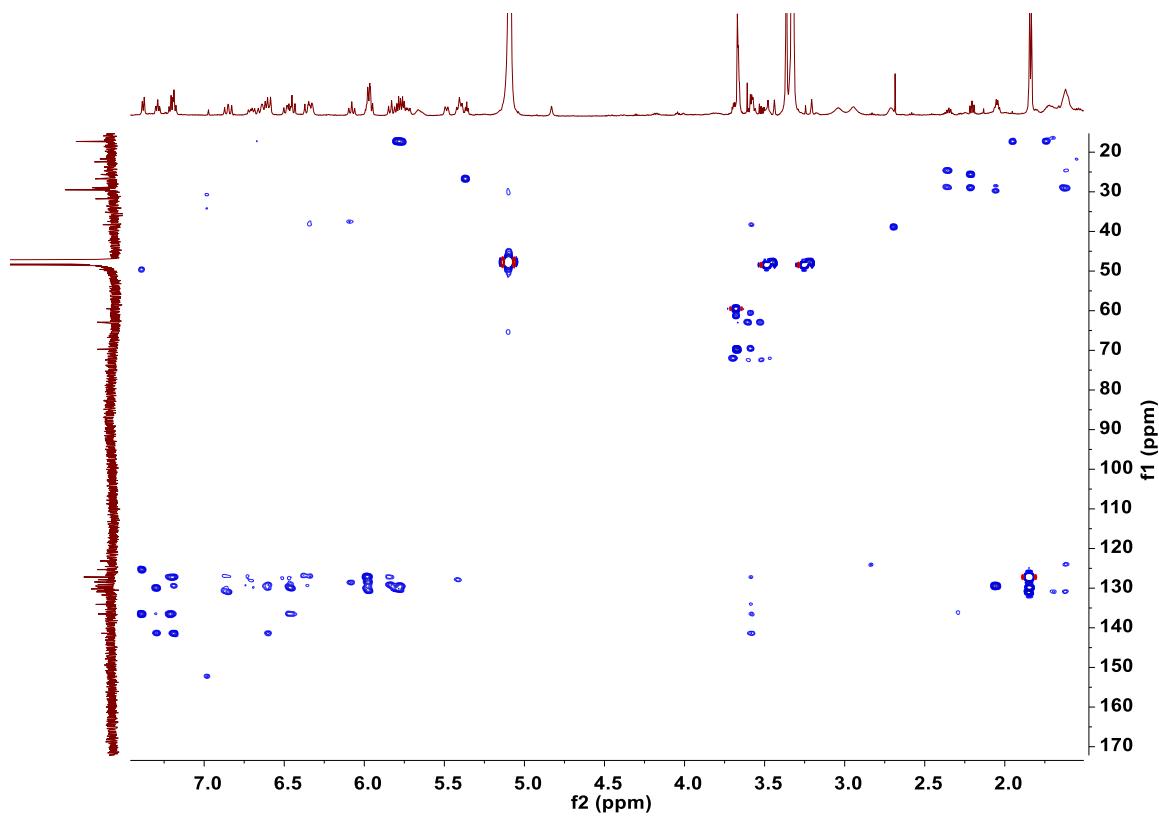
Figure S24. HMBC spectrum of compound **2** in CD₃OD (600 MHz)
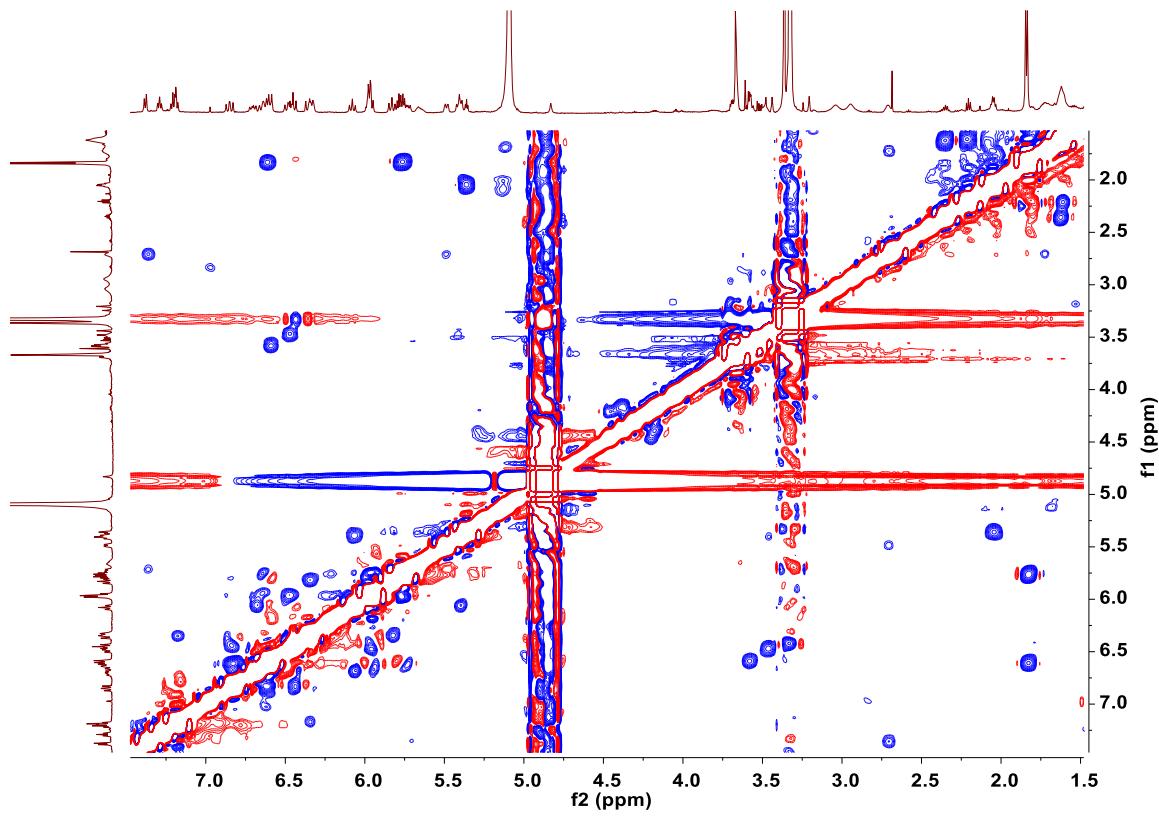
Figure S25. NOESY spectrum of compound **2** in CD$_3$OD (600 MHz)

Table S1. ^1H and ^{13}C NMR data of **1** in DMSO-d_6 (600 MHz)[a]

	1	
Position	δ_C, type	δ_H (J in Hz)
1	[b]	-
2	39.8, CH_2	2.60, m
		2.47, m
3	42.1, CH	3.49, m
4	142.8, C	-
5	127.7, CH	7.28, d (7.6)
6	127.5, CH	7.23, t (7.0)
7	126.0, CH	7.19, t (7.6)
8	130.2, CH	7.12, d (7.5)
9	137.1, C	-
10	130.9, CH	6.80, d (10.6)
11	130.9, CH	6.42, m
12	129.5, CH	6.38, m
13	130.7, CH	6.88, t (13.0)
14	127.6, CH	5.87, t (11.3)
15	130.6, CH	5.98, m
16	128.0, CH	6.64, m
17	131.6, CH	5.79, m
18	18.6, CH_3	1.81, d (5.28)
1'	174.7, C	-
2'	42.1, CH_2	2.80, m
3'	131.8, CH	5.68, m
4'	125.9, CH	6.32, m
5'	126.0, CH	5.60, d (11.4)
6'	[b]	-
7'	124.3, CH	6.54, d (9.7)
8'	132.3 CH	5.73, m
9'	38.0, CH	2.63, m
10'	32.9 CH_2	1.51, m
		1.40, m
11'	37.5 CH	3.12, m
12'	134.6 CH	5.24, m
13'	128.5, CH	6.00, m
14'	128.7, CH	6.32, m
15'	129.2 CH	6.72, dd (14.6, 10.7)
16'	127.9, CH	5.98, m
17'	130.6, CH	5.98, m
18'	127.2, CH	6.64, m
19'	131.6, CH	5.79, m
20'	18.6, CH_3	1.80, d (5.28)

[a] the ^{13}C chemical shifts were obtained by combination of HSQC and HMBC analysis

[b] not detected

Table S2. Antibacterial activity of compounds **1** and **2** against the multi-drug resistant *Enterococcus faecalis* CCARM 5172

Strain	MIC (μM)			
	1	**2**	Ciprofloxacin	Tetracycline
Enterococcus faecalis CCARM 5172	22.2	22.2	17.0	>112.5

Table S3. Bacteria and plasmids used in this study

Strains or plasmids	Description	Reference or source
S. youssoufiensis OUC6819	wild type, isolated from the reeds rhizosphere soil	[1, 2]
ΔdtlA	*dtlA* inactivation mutant of *S. youssoufiensis* OUC6819	[3]

Table S4. The computational method and coordinates of (3*R*,9'*R*,11'*S*)-**1** for ECD calculation

```
td(nstates=50) cam-b3lyp/6-31g(d) scrf=(solvent=methanol)
```

C	2.93553	1.57193	-1.56795
C	2.00222	1.51061	-2.59321
C	0.7781	2.14802	-2.43943
C	0.45205	2.84476	-1.27053
C	1.38924	2.88771	-0.21354
C	2.62315	2.25099	-0.39395
C	1.05815	3.57952	1.10421
C	0.46546	2.62776	2.19816
C	2.22959	4.39434	1.69627
C	-0.93223	2.20548	1.85859
C	-1.3238	0.94016	1.67836
C	-0.83734	3.57148	-1.2155
C	1.31405	1.41581	2.61658
C	1.06835	0.12132	1.81147
C	-0.41832	-0.20506	1.70986
C	1.87081	-0.99014	2.42998
C	-0.83995	-1.47881	1.5619
C	-2.20635	-1.92088	1.33549
C	-2.05375	3.04607	-1.43789
C	2.79842	-1.75929	1.84194
C	-2.36279	1.6409	-1.62516
C	-3.61288	1.17404	-1.80741
C	-3.92197	-0.23637	-1.93315
C	-5.14346	-0.7818	-2.1075
C	-6.41083	-0.07772	-2.21457
C	-7.58089	-0.70357	-2.39115
C	-8.90844	-0.02626	-2.50884
C	3.21229	-1.72455	0.44946
C	4.16168	-2.53315	-0.05735
C	4.57251	-2.50755	-1.44724
C	5.51275	-3.28249	-2.02459
C	6.31675	-4.30959	-1.38213
C	7.23162	-5.03714	-2.03441
C	8.08047	-6.1028	-1.4185
C	-2.54707	-3.20391	1.14103
C	-3.95294	-3.66642	0.89343
C	2.60709	5.64246	0.92097
O	2.72526	6.73011	1.43397
O	2.83225	5.50992	-0.39724
C	-4.60931	-4.34269	2.09103
O	-5.49687	-5.15606	1.99853
O	-4.17256	-3.95299	3.29807
H	3.90488	1.09547	-1.67262
H	2.23036	0.98809	-3.51654
H	0.05949	2.13567	-3.25224
```

| | | | | |
|---|---|---|---|---|
| H | 3.36124 | 2.26764 | 0.40138 |
| H | 0.25662 | 4.29807 | 0.90582 |
| H | 0.38004 | 3.27345 | 3.08242 |
| H | 3.13061 | 3.78202 | 1.81048 |
| H | 1.9605 | 4.74055 | 2.69515 |
| H | -1.67 | 2.99971 | 1.77839 |
| H | -2.37162 | 0.75514 | 1.46925 |
| H | -0.77809 | 4.63773 | -1.00678 |
| H | 2.38199 | 1.65379 | 2.58334 |
| H | 1.08614 | 1.20323 | 3.66774 |
| H | 1.41204 | 0.29336 | 0.78735 |
| H | 1.66725 | -1.16102 | 3.48652 |
| H | -0.09237 | -2.26826 | 1.5831 |
| H | -2.99456 | -1.17276 | 1.29145 |
| H | -2.90677 | 3.72237 | -1.42398 |
| H | 3.30265 | -2.50276 | 2.45814 |
| H | -1.53901 | 0.93295 | -1.57425 |
| H | -4.43323 | 1.88746 | -1.853 |
| H | -3.06994 | -0.91098 | -1.87311 |
| H | -5.20507 | -1.86628 | -2.18222 |
| H | -6.4044 | 1.00848 | -2.14934 |
| H | -7.58508 | -1.79186 | -2.45658 |
| H | -8.81379 | 1.06061 | -2.43241 |
| H | -9.38731 | -0.2627 | -3.46659 |
| H | -9.59531 | -0.36714 | -1.72492 |
| H | 2.72666 | -1.01283 | -0.21435 |
| H | 4.64593 | -3.24429 | 0.60893 |
| H | 4.05729 | -1.7832 | -2.07572 |
| H | 5.70363 | -3.1379 | -3.08659 |
| H | 6.16481 | -4.49348 | -0.32035 |
| H | 7.383 | -4.85215 | -3.0982 |
| H | 7.92042 | -7.06871 | -1.91245 |
| H | 9.14649 | -5.87005 | -1.52808 |
| H | 7.86433 | -6.22337 | -0.3532 |
| H | -1.77668 | -3.97314 | 1.17253 |
| H | -4.00839 | -4.37677 | 0.06475 |
| H | -4.59155 | -2.81469 | 0.62815 |
| H | 2.70845 | 4.58479 | -0.67988 |
| H | -3.44394 | -3.31328 | 3.18363 |

Standard orientation:

| Center Number | Atomic Number | Atomic Type | Coordinates (Angstroms) | | |
|---|---|---|---|---|---|
| | | | X | Y | Z |
| 1 | 6 | 0 | 2.935528 | 1.571925 | -1.567954 |
| 2 | 6 | 0 | 2.002220 | 1.510612 | -2.593205 |

| | | | | | |
|---|---|---|---|---|---|
| 3 | 6 | 0 | 0.778095 | 2.148017 | −2.439430 |
| 4 | 6 | 0 | 0.452052 | 2.844758 | −1.270528 |
| 5 | 6 | 0 | 1.389244 | 2.887708 | −0.213544 |
| 6 | 6 | 0 | 2.623146 | 2.250990 | −0.393949 |
| 7 | 6 | 0 | 1.058145 | 3.579523 | 1.104214 |
| 8 | 6 | 0 | 0.465461 | 2.627763 | 2.198160 |
| 9 | 6 | 0 | 2.229586 | 4.394342 | 1.696273 |
| 10 | 6 | 0 | −0.932228 | 2.205476 | 1.858588 |
| 11 | 6 | 0 | −1.323800 | 0.940161 | 1.678357 |
| 12 | 6 | 0 | −0.837343 | 3.571477 | −1.215497 |
| 13 | 6 | 0 | 1.314054 | 1.415812 | 2.616576 |
| 14 | 6 | 0 | 1.068345 | 0.121319 | 1.811469 |
| 15 | 6 | 0 | −0.418318 | −0.205057 | 1.709856 |
| 16 | 6 | 0 | 1.870806 | −0.990142 | 2.429977 |
| 17 | 6 | 0 | −0.839954 | −1.478805 | 1.561903 |
| 18 | 6 | 0 | −2.206350 | −1.920879 | 1.335486 |
| 19 | 6 | 0 | −2.053745 | 3.046074 | −1.437891 |
| 20 | 6 | 0 | 2.798420 | −1.759287 | 1.841941 |
| 21 | 6 | 0 | −2.362788 | 1.640902 | −1.625160 |
| 22 | 6 | 0 | −3.612880 | 1.174037 | −1.807414 |
| 23 | 6 | 0 | −3.921971 | −0.236374 | −1.933153 |
| 24 | 6 | 0 | −5.143457 | −0.781798 | −2.107503 |
| 25 | 6 | 0 | −6.410832 | −0.077721 | −2.214568 |
| 26 | 6 | 0 | −7.580891 | −0.703567 | −2.391146 |
| 27 | 6 | 0 | −8.908444 | −0.026257 | −2.508841 |
| 28 | 6 | 0 | 3.212291 | −1.724547 | 0.449462 |
| 29 | 6 | 0 | 4.161682 | −2.533149 | −0.057352 |
| 30 | 6 | 0 | 4.572514 | −2.507549 | −1.447238 |
| 31 | 6 | 0 | 5.512750 | −3.282491 | −2.024589 |
| 32 | 6 | 0 | 6.316747 | −4.309585 | −1.382134 |
| 33 | 6 | 0 | 7.231622 | −5.037135 | −2.034414 |
| 34 | 6 | 0 | 8.080474 | −6.102801 | −1.418503 |
| 35 | 6 | 0 | −2.547074 | −3.203911 | 1.141030 |
| 36 | 6 | 0 | −3.952940 | −3.666417 | 0.893428 |
| 37 | 6 | 0 | 2.607087 | 5.642464 | 0.920972 |
| 38 | 8 | 0 | 2.725260 | 6.730109 | 1.433966 |
| 39 | 8 | 0 | 2.832247 | 5.509918 | −0.397242 |
| 40 | 6 | 0 | −4.609306 | −4.342694 | 2.091034 |
| 41 | 8 | 0 | −5.496874 | −5.156057 | 1.998531 |
| 42 | 8 | 0 | −4.172560 | −3.952987 | 3.298072 |
| 43 | 1 | 0 | 3.904879 | 1.095473 | −1.672615 |
| 44 | 1 | 0 | 2.230362 | 0.988092 | −3.516537 |
| 45 | 1 | 0 | 0.059492 | 2.135675 | −3.252242 |
| 46 | 1 | 0 | 3.361236 | 2.267639 | 0.401376 |
| 47 | 1 | 0 | 0.256620 | 4.298066 | 0.905816 |
| 48 | 1 | 0 | 0.380037 | 3.273451 | 3.082422 |
| 49 | 1 | 0 | 3.130605 | 3.782015 | 1.810480 |
| 50 | 1 | 0 | 1.960502 | 4.740554 | 2.695153 |

| | | | | | |
|---|---|---|---|---|---|
| 51 | 1 | 0 | −1.669996 | 2.999707 | 1.778392 |
| 52 | 1 | 0 | −2.371619 | 0.755136 | 1.469251 |
| 53 | 1 | 0 | −0.778085 | 4.637730 | −1.006782 |
| 54 | 1 | 0 | 2.381987 | 1.653792 | 2.583336 |
| 55 | 1 | 0 | 1.086139 | 1.203225 | 3.667742 |
| 56 | 1 | 0 | 1.412039 | 0.293356 | 0.787349 |
| 57 | 1 | 0 | 1.667250 | −1.161020 | 3.486515 |
| 58 | 1 | 0 | −0.092368 | −2.268262 | 1.583100 |
| 59 | 1 | 0 | −2.994555 | −1.172759 | 1.291451 |
| 60 | 1 | 0 | −2.906766 | 3.722371 | −1.423976 |
| 61 | 1 | 0 | 3.302649 | −2.502756 | 2.458140 |
| 62 | 1 | 0 | −1.539014 | 0.932947 | −1.574247 |
| 63 | 1 | 0 | −4.433232 | 1.887462 | −1.852996 |
| 64 | 1 | 0 | −3.069940 | −0.910982 | −1.873113 |
| 65 | 1 | 0 | −5.205073 | −1.866275 | −2.182219 |
| 66 | 1 | 0 | −6.404404 | 1.008480 | −2.149335 |
| 67 | 1 | 0 | −7.585075 | −1.791861 | −2.456579 |
| 68 | 1 | 0 | −8.813788 | 1.060611 | −2.432414 |
| 69 | 1 | 0 | −9.387310 | −0.262696 | −3.466593 |
| 70 | 1 | 0 | −9.595309 | −0.367139 | −1.724917 |
| 71 | 1 | 0 | 2.726661 | −1.012833 | −0.214354 |
| 72 | 1 | 0 | 4.645926 | −3.244287 | 0.608928 |
| 73 | 1 | 0 | 4.057291 | −1.783202 | −2.075723 |
| 74 | 1 | 0 | 5.703626 | −3.137902 | −3.086588 |
| 75 | 1 | 0 | 6.164807 | −4.493477 | −0.320348 |
| 76 | 1 | 0 | 7.383004 | −4.852145 | −3.098202 |
| 77 | 1 | 0 | 7.920417 | −7.068707 | −1.912451 |
| 78 | 1 | 0 | 9.146493 | −5.870052 | −1.528081 |
| 79 | 1 | 0 | 7.864334 | −6.223366 | −0.353197 |
| 80 | 1 | 0 | −1.776678 | −3.973136 | 1.172525 |
| 81 | 1 | 0 | −4.008386 | −4.376768 | 0.064747 |
| 82 | 1 | 0 | −4.591546 | −2.814691 | 0.628152 |
| 83 | 1 | 0 | 2.708454 | 4.584787 | −0.679881 |
| 84 | 1 | 0 | −3.443937 | −3.313281 | 3.183629 |

--------------------------------------------------------------------------

**Table S5.** The computational method and coordinates of (3*S*,9'*S*,11'*R*)-**1** for ECD calculation

```
td(nstates=50) cam-b3lyp/6-31g(d) scrf=(solvent=methanol)
```

C	-3.0321	-1.5602	1.46882
C	-2.10124	-1.50483	2.49828
C	-0.88152	-2.15094	2.34822
C	-0.55846	-2.84538	1.17624
C	-1.48919	-2.87354	0.11685
C	-2.72059	-2.23853	0.29555
C	-1.16116	-3.56533	-1.19788
C	-0.54763	-2.638	-2.29843
C	-2.35848	-4.34471	-1.77158
C	0.87581	-2.28523	-1.98541
C	1.32718	-1.04228	-1.78927
C	0.71349	-3.60257	1.12705
C	-1.34371	-1.38148	-2.68721
C	-1.02793	-0.11513	-1.8623
C	0.47328	0.14257	-1.77809
C	-1.78496	1.04379	-2.44984
C	0.95424	1.39191	-1.60542
C	2.34245	1.77223	-1.39812
C	1.94267	-3.1168	1.36755
C	-2.68521	1.83096	-1.8432
C	2.29001	-1.72243	1.56815
C	3.54863	-1.2925	1.78002
C	3.89579	0.10792	1.91789
C	5.12692	0.61766	2.12769
C	6.36963	-0.12339	2.27027
C	7.55267	0.46658	2.48057
C	8.85548	-0.25051	2.63507
C	-3.10808	1.76869	-0.45444
C	-4.02514	2.59937	0.07569
C	-4.44401	2.54238	1.46234
C	-5.35314	3.33564	2.0641
C	-6.10964	4.41817	1.45574
C	-6.99588	5.1611	2.12979
C	-7.79578	6.28263	1.54831
C	2.73227	3.03193	-1.17127
C	4.16277	3.42872	-0.92065
C	-2.96947	-5.31076	-0.79028
O	-4.15142	-5.42409	-0.55762
O	-2.04263	-6.07752	-0.18898
C	4.72559	4.26751	-2.0542
O	5.58171	3.8953	-2.81765
O	4.19577	5.49749	-2.20565
H	-4.00041	-1.08094	1.57456
H	-2.32969	-0.98208	3.42178
H	-0.16663	-2.14933	3.16476
```

H	−3.45957	−2.26466	−0.49841
H	−0.38874	−4.31066	−0.99277
H	−0.51512	−3.27912	−3.1906
H	−3.15823	−3.69357	−2.12712
H	−2.01246	−4.92782	−2.63274
H	1.57818	−3.11351	−1.9339
H	2.38589	−0.90664	−1.59649
H	0.62301	−4.665	0.90861
H	−2.42092	−1.56995	−2.64077
H	−1.12031	−1.16137	−3.738
H	−1.36756	−0.29322	−0.83792
H	−1.5701	1.23779	−3.50023
H	0.24039	2.21252	−1.59013
H	3.10241	0.99503	−1.4065
H	2.7758	−3.81779	1.35959
H	−3.1569	2.61189	−2.4386
H	1.48767	−0.99119	1.50321
H	4.34684	−2.02956	1.84112
H	3.066	0.80719	1.83347
H	5.21812	1.69989	2.20446
H	6.33243	−1.20897	2.20383
H	7.58806	1.55427	2.54729
H	9.31429	−0.02897	3.60615
H	9.57426	0.06917	1.87105
H	8.73028	−1.33405	2.55502
H	−2.65858	1.01353	0.18629
H	−4.47536	3.35316	−0.56725
H	−3.96345	1.77422	2.06586
H	−5.55533	3.16157	3.11957
H	−5.94492	4.63209	0.40149
H	−7.16027	4.94597	3.18597
H	−7.59808	7.22318	2.07641
H	−8.87127	6.09145	1.64514
H	−7.56885	6.43107	0.48876
H	1.98506	3.82448	−1.15401
H	4.24041	4.00516	0.01064
H	4.79623	2.54588	−0.82446
H	−2.51281	−6.67388	0.42221
H	3.54945	5.692	−1.50774

Standard orientation:

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms)		
			X	Y	Z
1	6	0	−3.032099	−1.560196	1.468821
2	6	0	−2.101239	−1.504832	2.498278

3	6	0	−0.881520	−2.150936	2.348215
4	6	0	−0.558463	−2.845379	1.176236
5	6	0	−1.489185	−2.873541	0.116848
6	6	0	−2.720593	−2.238528	0.295545
7	6	0	−1.161157	−3.565330	−1.197878
8	6	0	−0.547634	−2.638002	−2.298432
9	6	0	−2.358477	−4.344713	−1.771583
10	6	0	0.875808	−2.285229	−1.985406
11	6	0	1.327178	−1.042275	−1.789268
12	6	0	0.713486	−3.602569	1.127049
13	6	0	−1.343706	−1.381483	−2.687209
14	6	0	−1.027934	−0.115130	−1.862296
15	6	0	0.473282	0.142568	−1.778086
16	6	0	−1.784959	1.043792	−2.449841
17	6	0	0.954235	1.391910	−1.605423
18	6	0	2.342451	1.772230	−1.398117
19	6	0	1.942670	−3.116802	1.367545
20	6	0	−2.685212	1.830964	−1.843200
21	6	0	2.290014	−1.722430	1.568151
22	6	0	3.548634	−1.292498	1.780017
23	6	0	3.895787	0.107919	1.917890
24	6	0	5.126918	0.617659	2.127691
25	6	0	6.369627	−0.123389	2.270269
26	6	0	7.552668	0.466578	2.480574
27	6	0	8.855482	−0.250509	2.635072
28	6	0	−3.108079	1.768687	−0.454435
29	6	0	−4.025137	2.599369	0.075692
30	6	0	−4.444014	2.542377	1.462344
31	6	0	−5.353137	3.335638	2.064096
32	6	0	−6.109643	4.418165	1.455740
33	6	0	−6.995883	5.161104	2.129793
34	6	0	−7.795775	6.282631	1.548310
35	6	0	2.732269	3.031925	−1.171268
36	6	0	4.162774	3.428719	−0.920653
37	6	0	−2.969469	−5.310755	−0.790280
38	8	0	−4.151421	−5.424088	−0.557616
39	8	0	−2.042627	−6.077524	−0.188978
40	6	0	4.725590	4.267513	−2.054202
41	8	0	5.581709	3.895300	−2.817653
42	8	0	4.195768	5.497490	−2.205653
43	1	0	−4.000407	−1.080941	1.574559
44	1	0	−2.329687	−0.982081	3.421779
45	1	0	−0.166625	−2.149330	3.164759
46	1	0	−3.459569	−2.264655	−0.498406
47	1	0	−0.388742	−4.310661	−0.992768
48	1	0	−0.515118	−3.279120	−3.190603
49	1	0	−3.158232	−3.693569	−2.127118
50	1	0	−2.012457	−4.927815	−2.632739

51	1	0	1.578178	−3.113508	−1.933899
52	1	0	2.385889	−0.906638	−1.596491
53	1	0	0.623005	−4.664997	0.908608
54	1	0	−2.420916	−1.569951	−2.640772
55	1	0	−1.120313	−1.161372	−3.738001
56	1	0	−1.367557	−0.293215	−0.837915
57	1	0	−1.570101	1.237792	−3.500230
58	1	0	0.240388	2.212515	−1.590133
59	1	0	3.102407	0.995025	−1.406504
60	1	0	2.775795	−3.817792	1.359591
61	1	0	−3.156904	2.611890	−2.438595
62	1	0	1.487669	−0.991189	1.503211
63	1	0	4.346837	−2.029557	1.841119
64	1	0	3.065998	0.807194	1.833472
65	1	0	5.218124	1.699891	2.204456
66	1	0	6.332431	−1.208974	2.203834
67	1	0	7.588057	1.554269	2.547290
68	1	0	9.314288	−0.028966	3.606147
69	1	0	9.574260	0.069173	1.871047
70	1	0	8.730280	−1.334049	2.555021
71	1	0	−2.658580	1.013534	0.186291
72	1	0	−4.475355	3.353163	−0.567247
73	1	0	−3.963447	1.774220	2.065858
74	1	0	−5.555327	3.161566	3.119570
75	1	0	−5.944922	4.632091	0.401491
76	1	0	−7.160272	4.945971	3.185968
77	1	0	−7.598078	7.223175	2.076413
78	1	0	−8.871266	6.091447	1.645138
79	1	0	−7.568854	6.431066	0.488757
80	1	0	1.985056	3.824484	−1.154007
81	1	0	4.240410	4.005158	0.010641
82	1	0	4.796234	2.545876	−0.824458
83	1	0	−2.512814	−6.673875	0.422207
84	1	0	3.549449	5.692004	−1.507741

Table S6. The computational method and coordinates of (5*R*,7'*R*,9'*S*)-**2** for ECD calculation

```
td(nstates=50) cam-b3lyp/6-31g(d) scrf=(solvent=methanol)
```

C	-1.48051	-2.38644	3.70146
C	-2.8198	-2.0489	3.73695
C	-3.5159	-1.92951	2.55287
C	-2.90035	-2.12779	1.3187
C	-1.53942	-2.45832	1.27923
C	-0.86028	-2.59127	2.48584
C	-0.81411	-2.70012	-0.04532
C	0.09824	-1.53886	-0.56492
C	-0.05002	-4.00612	-0.02377
C	-0.70716	-0.34264	-0.98953
C	-0.50614	0.89893	-0.58272
C	-3.73842	-2.06458	0.08954
C	1.29699	-1.11319	0.29916
C	1.02272	0.08684	1.22943
C	0.49124	1.2764	0.43645
C	2.197	0.3386	2.1576
C	0.82239	2.53113	0.70374
C	0.30097	3.78423	0.03868
C	-4.53243	-1.07393	-0.29553
C	3.43837	0.71018	1.8756
C	-4.69089	0.23141	0.34209
C	-5.55015	1.14834	-0.09273
C	-5.70033	2.45982	0.53134
C	-6.53343	3.43082	0.16313
C	-7.48674	3.41081	-0.94744
C	-8.27706	4.43317	-1.23505
C	-9.26927	4.46769	-2.35763
C	4.00097	1.05426	0.56988
C	5.2772	1.386	0.39922
C	5.84397	1.73404	-0.90085
C	7.10459	2.07489	-1.15967
C	8.21014	2.18148	-0.20613
C	9.43768	2.52498	-0.56345
C	10.60472	2.64917	0.3685
C	-0.33491	-5.03223	-0.79731
C	0.42278	-6.3358	-0.77061
C	1.10438	-6.63749	-2.08186
O	2.2702	-6.8246	-2.21519
O	0.25975	-6.68665	-3.09862
C	1.41663	4.47808	-0.70493
O	2.09025	5.35036	-0.25944
O	1.59651	3.99898	-1.92443
H	-0.92153	-2.49697	4.61221
H	-3.32118	-1.89586	4.67459
H	-4.56436	-1.70049	2.57941

H		0.17826	-2.85886	2.48607
H		-1.56814	-2.80803	-0.8101
H		0.51183	-1.95002	-1.48181
H		0.77537	-4.09103	0.6624
H		-1.48034	-0.52513	-1.71563
H		-1.11667	1.6739	-1.00463
H		-3.71509	-2.9395	-0.53645
H		1.65887	-1.94042	0.89466
H		2.10734	-0.85371	-0.37034
H		0.19874	-0.19922	1.87045
H		1.98894	0.13989	3.1952
H		1.54226	2.71669	1.47859
H		-0.50332	3.58795	-0.6512
H		-0.05021	4.47365	0.79485
H		-5.11024	-1.22402	-1.19213
H		4.12806	0.78154	2.70068
H		-4.0689	0.45372	1.19057
H		-6.16715	0.91758	-0.94319
H		-5.06249	2.64514	1.3789
H		-6.51583	4.34159	0.73777
H		-7.5431	2.52316	-1.55294
H		-8.2197	5.32279	-0.62707
H		-9.04711	5.28357	-3.03896
H		-9.2668	3.54145	-2.91919
H		-10.272	4.63604	-1.97631
H		3.34651	1.0467	-0.28206
H		5.9273	1.39946	1.2562
H		5.15551	1.70608	-1.72844
H		7.35591	2.30095	-2.18233
H		8.00989	1.96996	0.82968
H		9.63743	2.73699	-1.60247
H		11.01103	3.65583	0.34027
H		10.32415	2.42108	1.38956
H		11.40345	1.97553	0.07272
H		-1.15549	-4.97432	-1.49205
H		1.17967	-6.33207	-0.00134
H		-0.26259	-7.15503	-0.5744
H		0.73009	-6.87745	-3.90025
H		2.32577	4.44165	-2.33987

Standard orientation:

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms)		
			X	Y	Z
1	6	0	1.480510	2.386438	3.701459
2	6	0	2.819800	2.048896	3.736954

3	6	0	3.515901	1.929512	2.552874
4	6	0	2.900345	2.127786	1.318701
5	6	0	1.539420	2.458323	1.279232
6	6	0	0.860282	2.591265	2.485844
7	6	0	0.814110	2.700115	-0.045323
8	6	0	-0.098236	1.538855	-0.564921
9	6	0	0.050018	4.006116	-0.023768
10	6	0	0.707155	0.342636	-0.989529
11	6	0	0.506143	-0.898930	-0.582722
12	6	0	3.738418	2.064584	0.089540
13	6	0	-1.296992	1.113188	0.299164
14	6	0	-1.022723	-0.086843	1.229431
15	6	0	-0.491238	-1.276398	0.436451
16	6	0	-2.197004	-0.338596	2.157604
17	6	0	-0.822390	-2.531125	0.703737
18	6	0	-0.300970	-3.784225	0.038682
19	6	0	4.532427	1.073926	-0.295527
20	6	0	-3.438370	-0.710175	1.875601
21	6	0	4.690888	-0.231405	0.342091
22	6	0	5.550149	-1.148343	-0.092730
23	6	0	5.700333	-2.459815	0.531344
24	6	0	6.533428	-3.430819	0.163134
25	6	0	7.486739	-3.410807	-0.947441
26	6	0	8.277059	-4.433171	-1.235054
27	6	0	9.269268	-4.467690	-2.357626
28	6	0	-4.000971	-1.054257	0.569878
29	6	0	-5.277200	-1.385998	0.399215
30	6	0	-5.843973	-1.734040	-0.900845
31	6	0	-7.104594	-2.074890	-1.159673
32	6	0	-8.210144	-2.181481	-0.206133
33	6	0	-9.437679	-2.524981	-0.563454
34	6	0	-10.604723	-2.649174	0.368502
35	6	0	0.334905	5.032233	-0.797312
36	6	0	-0.422783	6.335804	-0.770614
37	6	0	-1.104380	6.637490	-2.081856
38	8	0	-2.270196	6.824595	-2.215192
39	8	0	-0.259746	6.686646	-3.098615
40	6	0	-1.416629	-4.478081	-0.704932
41	8	0	-2.090254	-5.350356	-0.259444
42	8	0	-1.596510	-3.998978	-1.924434
43	1	0	0.921525	2.496973	4.612205
44	1	0	3.321180	1.895864	4.674586
45	1	0	4.564363	1.700488	2.579407
46	1	0	-0.178264	2.858863	2.486070
47	1	0	1.568140	2.808029	-0.810100
48	1	0	-0.511832	1.950023	-1.481805
49	1	0	-0.775370	4.091033	0.662396
50	1	0	1.480337	0.525125	-1.715632

51	1	0	1.116673	−1.673897	−1.004626
52	1	0	3.715090	2.939496	−0.536450
53	1	0	−1.658866	1.940420	0.894655
54	1	0	−2.107337	0.853705	−0.370337
55	1	0	−0.198740	0.199217	1.870445
56	1	0	−1.988941	−0.139894	3.195195
57	1	0	−1.542262	−2.716689	1.478592
58	1	0	0.503315	−3.587953	−0.651200
59	1	0	0.050209	−4.473654	0.794845
60	1	0	5.110244	1.224024	−1.192125
61	1	0	−4.128057	−0.781537	2.700678
62	1	0	4.068896	−0.453724	1.190572
63	1	0	6.167152	−0.917580	−0.943189
64	1	0	5.062491	−2.645141	1.378901
65	1	0	6.515827	−4.341593	0.737767
66	1	0	7.543104	−2.523163	−1.552935
67	1	0	8.219701	−5.322791	−0.627070
68	1	0	9.047113	−5.283569	−3.038957
69	1	0	9.266805	−3.541445	−2.919188
70	1	0	10.272001	−4.636044	−1.976306
71	1	0	−3.346509	−1.046702	−0.282057
72	1	0	−5.927295	−1.399464	1.256198
73	1	0	−5.155514	−1.706080	−1.728443
74	1	0	−7.355907	−2.300952	−2.182327
75	1	0	−8.009894	−1.969962	0.829683
76	1	0	−9.637433	−2.736992	−1.602473
77	1	0	−11.011033	−3.655829	0.340271
78	1	0	−10.324147	−2.421076	1.389555
79	1	0	−11.403450	−1.975533	0.072721
80	1	0	1.155491	4.974324	−1.492046
81	1	0	−1.179670	6.332072	−0.001337
82	1	0	0.262589	7.155028	−0.574403
83	1	0	−0.730094	6.877446	−3.900246
84	1	0	−2.325768	−4.441653	−2.339866

Table S7. The computational method and coordinates of (5*S*,7'*S*,9'*R*)-**2** for ECD calculation

```
td(nstates=50) cam-b3lyp/6-31g(d) scrf=(solvent=methanol)
```

C	-3.12131	-3.94306	2.46963
C	-1.98228	-4.67227	2.18589
C	-1.13148	-4.23605	1.19245
C	-1.38538	-3.07117	0.47117
C	-2.53988	-2.33371	0.75572
C	-3.38961	-2.79239	1.7564
C	-2.90797	-1.06888	-0.02544
C	-3.14821	0.15166	0.91252
C	-4.10287	-1.37581	-0.90341
C	-3.76625	1.31851	0.18816
C	-3.18561	2.49307	0.01201
C	-0.45425	-2.68473	-0.62284
C	-1.87323	0.59739	1.64066
C	-0.99618	1.55114	0.80844
C	-1.80612	2.79073	0.44152
C	0.27848	1.84239	1.55672
C	-1.29231	4.01454	0.46607
C	-1.97434	5.30489	0.09483
C	0.8661	-2.56609	-0.54903
C	1.51599	1.84463	1.08381
C	1.70195	-2.69569	0.64304
C	3.03005	-2.64896	0.60387
C	3.86528	-2.76453	1.79591
C	5.19548	-2.74469	1.84715
C	6.12664	-2.60356	0.72668
C	7.44155	-2.60455	0.88062
C	8.44057	-2.46614	-0.2278
C	1.9318	1.61724	-0.30009
C	3.19813	1.69227	-0.69724
C	3.61441	1.47906	-2.08071
C	4.85158	1.55748	-2.56606
C	6.07638	1.87508	-1.82992
C	7.26641	1.93845	-2.40644
C	8.5498	2.26127	-1.70309
C	-4.06619	-1.39292	-2.21848
C	-5.19382	-1.75948	-3.15696
C	-6.54737	-1.89416	-2.49764
O	-7.09809	-2.92793	-2.318
O	-7.13557	-0.76935	-2.11059
C	-2.15342	6.26842	1.25481
O	-2.10647	7.44772	1.13399
O	-2.41654	5.74153	2.43972
H	-3.80111	-4.26931	3.2348
H	-1.76332	-5.5759	2.72384
H	-0.26009	-4.81578	0.95438

H	-4.28529	-2.24735	1.98716
H	-2.08598	-0.81395	-0.67666
H	-3.8694	-0.15185	1.66285
H	-5.01576	-1.61843	-0.38253
H	-4.76938	1.18836	-0.17499
H	-3.7431	3.26638	-0.48056
H	-0.90557	-2.50906	-1.5833
H	-1.28668	-0.26412	1.93236
H	-2.15593	1.10872	2.55599
H	-0.75812	1.05669	-0.12603
H	0.15005	2.0634	2.60402
H	-0.26834	4.12865	0.77143
H	-1.40127	5.83467	-0.6537
H	-2.96534	5.1517	-0.31149
H	1.3917	-2.32705	-1.45829
H	2.31462	2.0571	1.77519
H	1.20885	-2.82143	1.59014
H	3.51661	-2.52184	-0.34701
H	3.3326	-2.87971	2.72462
H	5.65415	-2.84446	2.81655
H	5.71836	-2.49552	-0.26289
H	7.84932	-2.71302	1.87375
H	7.95486	-2.36133	-1.19024
H	9.07337	-1.59873	-0.06571
H	9.09305	-3.33343	-0.2643
H	1.17224	1.39231	-1.02775
H	3.9558	1.92247	0.03078
H	2.82345	1.2363	-2.77007
H	4.98274	1.37123	-3.61877
H	5.99918	2.06614	-0.77387
H	7.34275	1.74729	-3.46571
H	9.00945	3.14592	-2.13364
H	8.39054	2.43737	-0.64624
H	9.26095	1.44805	-1.81285
H	-3.14666	-1.15389	-2.72544
H	-5.26506	-1.00999	-3.93888
H	-4.97545	-2.70279	-3.63879
H	-6.62145	-0.00014	-2.30616
H	-2.393	4.79451	2.41952

Standard orientation:

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms)		
			X	Y	Z
1	6	0	3.121311	-3.943062	-2.469626
2	6	0	1.982280	-4.672265	-2.185891

3	6	0	1.131483	-4.236052	-1.192451
4	6	0	1.385379	-3.071174	-0.471168
5	6	0	2.539879	-2.333712	-0.755718
6	6	0	3.389605	-2.792391	-1.756403
7	6	0	2.907966	-1.068882	0.025444
8	6	0	3.148212	0.151658	-0.912519
9	6	0	4.102871	-1.375814	0.903406
10	6	0	3.766254	1.318513	-0.188161
11	6	0	3.185609	2.493070	-0.012008
12	6	0	0.454248	-2.684730	0.622843
13	6	0	1.873230	0.597386	-1.640664
14	6	0	0.996183	1.551135	-0.808438
15	6	0	1.806123	2.790729	-0.441521
16	6	0	-0.278481	1.842391	-1.556715
17	6	0	1.292307	4.014535	-0.466070
18	6	0	1.974337	5.304891	-0.094825
19	6	0	-0.866099	-2.566091	0.549034
20	6	0	-1.515991	1.844629	-1.083812
21	6	0	-1.701946	-2.695692	-0.643039
22	6	0	-3.030050	-2.648964	-0.603872
23	6	0	-3.865276	-2.764526	-1.795907
24	6	0	-5.195480	-2.744690	-1.847147
25	6	0	-6.126643	-2.603561	-0.726683
26	6	0	-7.441550	-2.604552	-0.880615
27	6	0	-8.440572	-2.466139	0.227802
28	6	0	-1.931800	1.617244	0.300093
29	6	0	-3.198126	1.692266	0.697243
30	6	0	-3.614409	1.479059	2.080711
31	6	0	-4.851580	1.557475	2.566057
32	6	0	-6.076378	1.875076	1.829915
33	6	0	-7.266412	1.938448	2.406436
34	6	0	-8.549801	2.261267	1.703085
35	6	0	4.066192	-1.392915	2.218482
36	6	0	5.193824	-1.759478	3.156956
37	6	0	6.547372	-1.894155	2.497638
38	8	0	7.098091	-2.927928	2.318000
39	8	0	7.135569	-0.769349	2.110591
40	6	0	2.153425	6.268418	-1.254814
41	8	0	2.106465	7.447718	-1.133990
42	8	0	2.416544	5.741527	-2.439719
43	1	0	3.801108	-4.269307	-3.234803
44	1	0	1.763315	-5.575900	-2.723842
45	1	0	0.260087	-4.815784	-0.954383
46	1	0	4.285294	-2.247346	-1.987157
47	1	0	2.085985	-0.813950	0.676658
48	1	0	3.869400	-0.151853	-1.662850
49	1	0	5.015760	-1.618431	0.382534
50	1	0	4.769375	1.188356	0.174992

51	1	0	3.743095	3.266380	0.480562
52	1	0	0.905574	−2.509056	1.583301
53	1	0	1.286680	−0.264116	−1.932356
54	1	0	2.155929	1.108725	−2.555994
55	1	0	0.758123	1.056689	0.126032
56	1	0	−0.150046	2.063402	−2.604021
57	1	0	0.268341	4.128650	−0.771429
58	1	0	1.401274	5.834670	0.653698
59	1	0	2.965340	5.151695	0.311490
60	1	0	−1.391697	−2.327050	1.458285
61	1	0	−2.314623	2.057104	−1.775193
62	1	0	−1.208852	−2.821433	−1.590136
63	1	0	−3.516614	−2.521839	0.347010
64	1	0	−3.332596	−2.879705	−2.724621
65	1	0	−5.654151	−2.844464	−2.816552
66	1	0	−5.718356	−2.495515	0.262890
67	1	0	−7.849319	−2.713022	−1.873754
68	1	0	−7.954861	−2.361325	1.190245
69	1	0	−9.073365	−1.598725	0.065710
70	1	0	−9.093051	−3.333431	0.264301
71	1	0	−1.172238	1.392311	1.027749
72	1	0	−3.955802	1.922473	−0.030784
73	1	0	−2.823452	1.236295	2.770073
74	1	0	−4.982740	1.371229	3.618767
75	1	0	−5.999178	2.066137	0.773865
76	1	0	−7.342750	1.747285	3.465709
77	1	0	−9.009453	3.145920	2.133636
78	1	0	−8.390539	2.437369	0.646236
79	1	0	−9.260951	1.448050	1.812852
80	1	0	3.146658	−1.153894	2.725441
81	1	0	5.265058	−1.009990	3.938882
82	1	0	4.975449	−2.702788	3.638793
83	1	0	6.621451	−0.000136	2.306157
84	1	0	2.392999	4.794505	−2.419520 ----

References

1. Che, Q.; Zhu, T.; Qi, X.; Mándi, A.; Kurtán, T.; Mo, X.; Li, D. Hybrid Isoprenoids from a Reeds Rhizosphere Soil Derived Actinomycete *Streptomyces* sp. CHQ-64. *Org. Lett.* **2012**, *14*, 3438-3441.

2. Yao, T.; Liu, J.; Liu, Z.; Li, T.; Li, H.; Che, Q.; Zhu, T.; Li, D.; Li, W. Genome mining of cyclodipeptide synthases unravels unusual tRNA-dependent diketopiperazine-terpene biosynthetic machinery. *Nat. Commun.* **2018**, *9*, 4091

3. Li, H.; Liu, J.; Deng, Z.; Li, T.; Liu, Z.; Che, Q.; Li, W. Genetic Manipulation of an Aminotransferase Family Gene *dtlA* Activates Youssoufenes in Marine-Derived *Streptomyces youssoufiensis*. *Org Lett.* **2020**, *17*, 729-733.