Electronic Supplementary Material (ESI) for RSC Advances.

Supplementary Information

Two Pairs of Enantiomeric *α*-Pyrone Dimers from the Endophytic Fungus *Phoma* sp. YN02-P-3

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Contents

1. General experimental procedures

Optical rotation was measured with a JASCO P-2000 Series (Jasco Co., Ltd, Tokyo, Japan). The UV spectrum was recorded on a Shimadzu UV-2201 spectrophotometer (Shimadzu Corporation, Kyoto, Japan). The IR spectrum was obtained from a Bruker IFS-55 spectrophotometer using KBr pellet (Bruker Optik BmbH, Ettlingen, Germany). The HR-ESI-MS data were obtained on a microTOF-Q Bruker mass instrument (Bruker Daltonics, Billerica, MA, USA). CD spectra were recorded with a Biologic MOS-450 spectrometer using $CDCl_3$ as solvent. 1D and 2D NMR spectra were run on a Bruker AVANCE-400/-600 spectrometer (Bruker BioSpin GmbH, Rheinstetten, Germany). ^1H chemical shifts (δ_H) were measured in ppm, relative to TMS, and ^{13}C chemical shifts (δ_C) were measured relative to DMSO-d_6 and converted to TMS scale. Column chromatography (CC) was performed on Silica gel (200–300 mesh; Qingdao Marine Chemical Co., Qingdao, China) and Sephadex LH-20 (Pharmacia, Uppsala, Sweden) columns. Analytical and preparative thin-layer chromatographies (TLC) were carried out using silica gel plates (GF254 10-40 μm，Qingdao Marine Chemical Co., China). Analytical TLC was used to follow the separation and check the purity of isolated compounds. Spots on the plates were observed under UV light and visualized by spraying 10% H_2SO_4 in EtOH (v/v), followed by heating. HPLC was performed on a Shimadzu LC-10AVP liquid chromatograph with a YMC-pack C_{18} (ODS) column (10 × 250 mm, 5 μm, Japan) and a Shimadzu LC-8AVP liquid chromatograph with a Diamonsil C_{18} (ODS) column (4.6 × 250 mm, 5 μm, China). Reversed-phase HPLC (Shimadzu Corporation, Nakagyo-ku, Kyoto, Japan) was performed using a Shimadzu LC-8A HPLC pump equipped with SPD-10A detector, employing a YMC-Pack ODS-A column (250 × 10 mm, 5 mm, YMC Co., Ltd. Japan). All reagents were HPLC or analytical grade and were purchased from Tianjin Damao Chemical Company (Tianjin, China).

2. Fungal material and fermentation

The fungal strain YN02-P-3 was isolated from the plant *Sumbaviopsis* J. J. Smith in Yunnan, P.R. China in September 2013. It was identified as *Phoma* sp. YN02-P-3 (GenBank accession no. KU522468) and has been deposited in the School of Traditional

Chinese Materia Medica, Shenyang Pharmaceutical University.

The fungal strain YN02-P-3 was cultured on slants of potato dextrose agar at 25 °C for 10 days. Agar plugs were inoculated in 500 mL Erlenmeyer flask containing 120 mL of media (0.4% glucose,1% malt extract, and 0.4% yeast extract; the final pH of the media was adjusted to 6.5) before sterilization, and incubated at 25 °C on a rotary shaker at 170 rpm for one week. Large scale fermentation was carried out in one hundred and fifty 500 mL Fernbach flasks each containing 80 g of rice and 120 mL of distilled H_2O. Each flask was inoculated with 5.0 mL of the culture medium and incubated at 25 °C for 40 days.

3. Extraction and isolation

The solid culture of *Phoma* sp. YN02-P-3 on cooked rice was extracted with 95% EtOH (1×150 mL) under ultrasonic 2 times, and 85% EtOH (1×150 mL), each time for twenty minutes, respectively. The combined extracts were concentrated in vacuo to yield a residue, which was suspended in H_2O, successively partitioned with ethyl acetate and *n*-butanol. The EtOAc crude extracts (50.0 g) were applied on a silica gel column and eluted with Petroleum-Acetone gradient (from 100:0 to 0:100) to afford 9 fractions. Fr. 6 using silica gel column chromatography eluting with Petroleum-ethyl acetate (from 100:0 to 0:100) to give 3 subfractions. Fr.6-1 purified by semi-preparative HPLC on ODS column eluted with 32% MeOH-H_2O to yield compound **1** (30 mg), **2** (80mg) and **3** (100 mg), Compounds **1** and **2** further subjected to chiral HPLC with cyclohexane-isopropanol (85:25) to yield **1a** (2.0 mg), **1b** (2.1 mg), **2a** (2.0 mg), **2b** (2.1 mg).

Physicochemical data

Phomone A (**1**): a colorless block crystals (MeOH); $[\alpha]_D^{20}$ (c 0.20 MeOH) +30 (**1a**) and (c 0.20 MeOH) −39 (**1b**); UV (MeOH) λ_{max}(logε): 212 (3.40), 255 (3.28), 301 (3.08), nm; IR (KBr) ν_{max}: 3438, 2957, 1711, 1631, 1383 cm^{-1}; CD (MeOH) λ_{max} ($\Delta\varepsilon$) **1a** : 207 (+10.3), 244 (−67.9), 278 (+45.9) nm; **1b** : 208 (+1.6), 242 (+95.4), 277 (-34.9) nm; ^{13}C and ^{1}H NMR data, see Table 1; (+)-HRESIMS *m/z* 563.1352 $[M+Na]^+$ (calcd for $C_{24}H_{28}Na_1O_{14}$, 563.1371);

Phomone B (**2**): a colorless block crystals (MeOH); UV (MeOH) λ_{max}(logε): 209 (3.70), 254 (3.39), 298 (3.29) nm; IR (KBr) ν_{max}: 3424, 2920,1718, 1695,1623, 1383cm^{-1}; ^{13}C and ^{1}H NMR data, see Table 1; CD (MeOH) λ_{max} ($\Delta\varepsilon$) **2a** : 212 (+18.7), 247 (−34.9), 279 (+38.4) nm; **2b** : 212 (-25.2), 246 (+45.1), 278 (-51.6) nm (+)-HRESIMS *m/z* 563.1373 $[M+Na]^+$ (calcd for $C_{24}H_{28}Na_1O_{14}$, 563.1371);

4. Cytotoxic assay

Cytotoxic activities of isolated compounds **1-3** and the positive control 5-fluorouracil were evaluated by the trypan blue method[1, 2] against the human leukaemia cell lines (HL-60) and the MTT assay[3] using the prostate cancer cell lines (PC-3) and the human colon cancer (HCT-116). The cell lines were purchased from America Type Culture Collection, ATCC (Rockville, MD, USA) and cultured in RPMI-1640 medium (Gibco, New York, NY, USA) supplemented with 100 U/mL penicillin, 100 µg/mL streptomycin, 1 mM glutamine and 10% heat-inactivated foetal bovine serum (Gibco) at 37 °C in humidified atmosphere with 5% CO_2.

The human leukaemia cell lines (HL-60) (American Type Culture Collection, Rockville, MD, USA) were cultured in the above medium at a density of 5×10^4 cells/mL at 37 under an atmosphere of 5% CO_2. Cell growth inhibition assay was performed as reported previously. The compounds were dissolved in DMSO, and the amount of DMSO was controlled lower than 0.1% in the final concentration. Cells were incubated with various drug concentrations for 3 days. The number of cells was determined by hemocytometer, and its viability was determined using trypan blue staining. The growth inhibitory ability of the compound was calculated and expressed using the IC_{50} value (half-inhibitory concentration). 5-Fluorouracil (5-FU) and 0.1% DMSO were used as a positive control and a negative control, respectively.

In the MTT assay, briefly, cells suspensions, 200 µl, at a density of 2.5×104 cells/mL, were plated in 96-well microtiter plates and incubated for 24 h at 37 °C under 5% CO_2 and 95% air. Then the test compounds with different concentrations in DMSO were placed into each microtiter plates and further incubated for 72 h. Finally, 50 µl of a 0.4% MTT solution was added to each well and incubated for 4 h. Then, the MTT was

removed from the wells and the fromazan crystals were dissolved in DMSO (200 μl) for 10 min with shaking. Then the plate was read immediately on a microtiter plate reader (Bio-RAD) at a wavelength of 570 nm to record the optical density (OD). The IC_{50} value was defined as the concentration of the control in the MTT assay. 5-Fluorouracil (5-Fu) was used as a positive control.

References:

[1] F. Wang, H. M. Hua, Y. H. Pei, D. Chen, and Y. K. Jing, *J. Nat. Prod.*, 2006, **69**, 807-810.

[2] J. Hu, X. D. Shi, J. G. Chen, X. Mao, L. Zhu, L. YU, and J. Y. Shi, *Food Chem*., 2014, **148**, 437–444.

[3] K. B. Wang, Y. T. Di, Y. Bao, C.M. Yuan, G. Chen, D. H. Li, J. Bai, H. P. He, X. J. Hao, Y. H. Pei, Y. K. Jing, Z. L. Li, and H. M. Hua, *Org. Lett*., 2014, **16**, 4028−4031.

5. Computational details for ECD of compounds 1 and 2

Computational methods

The Spartan 14.0 (Wavefunction Inc., Irvine, CA, USA) searches using molecular mechanics MMFF were performed for **1** and **2**, which gave 100 conformers and 100 respectively. The low-energy conformers of **1** and **2** separately accounting for more than 6% and 5% Boltzmann distribution was further optimized successively in the gas phase by semi-empirical method and the Hartree-Fork (HF) method at the 6-31G (d) level in Gaussian 09 program package,[1] which was reoptimized and analysed frequency, orderly, using the density functional theory (DFT) at the B3LYP/6-31G (d, p) level and the same way in the methanol, resulted in no imaginary frequencies. Solvent effects were taken into consideration by using the conductor polarizable continuum model (CPCM). The conformers of **1** and **2** were calculated electronic circular dichroism (ECD) by the time-dependent density functional theory (TD-DFT) method at the B3LYP/6-31G (d, p) level with the CPCM model in methanol solution. The overall calculated ECD curves of the **1** and **2** were generated severally by Boltzmann weighting of their selected low-energy conformers using SpecDis 1.51 [2-3] with σ = 0.29eV at -6nm shift, together with σ = 0.30eV at 30nm shift.

Table S1 Energy analysis of compound the **1a**.

Label	MMFF	
	rel. E(Kal/mol)	Boltzmann Dist.
1a-1	0.00	0.194
1a-2	0.88	0.136
1a-3	1.02	0.128
1a-4	1.36	0.112
2a-5	2.05	0.085

Table S2 Energy analysis of compound the **2b**

Label	MMFF	
	rel. E(Kal/mol)	Boltzmann Dist.
2b-1	0.00	0.825
2b-2	5.03	0.109

Table S3 Computational methods for ECD of **1a**

1a-1
Standard orientation:

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms) X	Y	Z
1	8	0	2.069413	-0.947795	-0.878500
2	8	0	-1.951195	-2.095934	2.051661
3	8	0	-4.047562	2.089612	0.800105
4	8	0	-2.691812	0.390507	0.413952
5	8	0	-0.982162	-1.143056	-2.330690
6	8	0	5.214935	0.057174	1.535122
7	8	0	-4.521014	-3.007006	0.278562
8	8	0	3.358755	-2.195077	-2.201227
9	8	0	-0.032718	3.126270	-1.342608
10	8	0	-1.564360	4.896410	0.392567
11	8	0	1.486864	1.389473	2.769147
12	8	0	-4.949497	-1.347456	-1.190499
13	6	0	-3.006218	1.727231	0.285180
14	6	0	0.407402	0.243799	0.306301
15	6	0	-2.165791	-0.979580	-1.551249
16	6	0	-2.067701	2.618315	-0.398070
17	6	0	-4.162118	-2.281470	-0.626472

18	8	0	-0.380555	-0.766324	2.971413
19	6	0	-0.876301	2.177411	-0.885655
20	6	0	4.186058	-0.292060	0.702788
21	6	0	1.853860	-0.109691	0.181274
22	6	0	2.874012	0.240409	1.016408
23	6	0	2.779307	1.093961	2.281824
24	6	0	-0.314578	0.122709	-2.322880
25	6	0	-1.647472	-0.197998	-0.337104
26	6	0	-0.511620	0.724905	-0.895826
27	6	0	4.400127	-1.160134	-0.332435
28	6	0	1.236110	2.803637	-1.941878
29	6	0	-0.592093	-0.914129	0.556211
30	6	0	-0.944624	-1.227296	1.991358
31	6	0	-2.799050	-2.343809	-1.293556
32	6	0	-2.406007	4.095924	-0.439972
33	6	0	3.300459	-1.493082	-1.200120
34	6	0	-2.413766	-2.480379	3.366869
35	6	0	-6.267506	-1.203187	-0.621808
36	6	0	6.038693	1.149391	1.071190
37	8	0	6.165920	-1.513537	-1.981167
38	6	0	5.721625	-1.816456	-0.661706
39	1	0	-0.675225	4.831346	0.015610
40	1	0	1.024130	0.559763	2.993162
41	1	0	0.316225	0.983933	1.097982
42	1	0	-2.885417	-0.335681	-2.077414
43	1	0	3.259369	2.060979	2.093416
44	1	0	3.386379	0.593786	3.047019
45	1	0	0.722568	-0.050474	-2.598573
46	1	0	-0.782546	0.792168	-3.057197
47	1	0	1.756996	3.755283	-2.035462
48	1	0	1.820029	2.135511	-1.306326
49	1	0	1.098393	2.369612	-2.934483
50	1	0	-0.265845	-1.833535	0.061915
51	1	0	-2.926448	-2.839388	-2.263177
52	1	0	-2.157252	-2.976402	-0.678875
53	1	0	-3.424022	4.232739	-0.075088
54	1	0	-2.364233	4.445460	-1.480482
55	1	0	-3.266743	-3.131196	3.187430
56	1	0	-1.624782	-3.012193	3.901754
57	1	0	-2.712524	-1.596836	3.933223
58	1	0	-6.767987	-0.452325	-1.230909
59	1	0	-6.194939	-0.866389	0.414458
60	1	0	-6.806771	-2.151311	-0.660966
61	1	0	6.474967	0.919259	0.094739
62	1	0	5.458238	2.074773	1.002473
63	1	0	6.828016	1.265084	1.813384

64	1	0	5.468252	-1.851517	-2.566133
65	1	0	6.493242	-1.476206	0.029126
66	1	0	5.610994	-2.902855	-0.527342

1a-2

Standard orientation:

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms) X	Y	Z
1	8	0	1.925577	-1.127172	0.505544
2	8	0	-2.310779	-1.652202	2.410270
3	8	0	-4.739756	0.765829	-0.167560
4	8	0	-2.844824	-0.343847	-0.372573
5	8	0	0.226075	-0.524615	-2.091850
6	8	0	4.928057	1.584192	-0.016131
7	8	0	-1.815452	-4.160010	0.029220
8	8	0	3.267299	-2.888801	0.304917
9	8	0	-0.697399	3.278318	-0.404694
10	8	0	-4.588818	3.684221	-0.651075
11	8	0	2.723792	3.214005	-0.873010
12	8	0	-2.862037	-3.392320	-1.819984
13	6	0	-3.519790	0.829411	-0.179958
14	6	0	0.223521	0.527814	0.746386
15	6	0	-0.960060	-1.179107	-1.637124
16	6	0	-2.803886	2.107194	-0.022434
17	6	0	-1.813559	-3.489135	-0.983561
18	8	0	-1.745172	0.490682	2.846045
19	6	0	-1.473658	2.188892	-0.296899
20	6	0	4.021231	0.591758	0.104065
21	6	0	1.678648	0.208560	0.518697
22	6	0	2.687456	1.104075	0.358782
23	6	0	2.489488	2.603935	0.397965
24	6	0	0.040525	0.877598	-1.888907
25	6	0	-1.423545	-0.371924	-0.387368
26	6	0	-0.647920	0.961247	-0.521488
27	6	0	4.258379	-0.758393	-0.031508
28	6	0	-1.219906	4.593023	-0.687992
29	6	0	-0.725271	-0.680738	0.975234
30	6	0	-1.630927	-0.522191	2.182987
31	6	0	-0.639070	-2.664786	-1.472920
32	6	0	-3.733257	3.230977	0.396749
33	6	0	3.181126	-1.668322	0.259871
34	6	0	-3.251328	-1.618779	3.506792
35	6	0	-4.047131	-4.121055	-1.436028

36	6	0	6.318546	1.402481	0.320933
37	8	0	6.182090	-2.148943	0.593506
38	6	0	5.525788	-1.460330	-0.471004
39	1	0	-5.133652	2.915462	-0.880773
40	1	0	3.668399	3.100420	-1.055577
41	1	0	0.125718	1.257531	1.551934
42	1	0	-1.766496	-1.057750	-2.373964
43	1	0	3.150789	3.032427	1.161615
44	1	0	1.463111	2.851684	0.662357
45	1	0	1.014472	1.367844	-1.924645
46	1	0	-0.610672	1.304242	-2.665006
47	1	0	-2.136370	4.525195	-1.276918
48	1	0	-1.398515	5.140766	0.239508
49	1	0	-0.438013	5.094170	-1.258710
50	1	0	-0.256234	-1.661593	1.023990
51	1	0	-0.336306	-3.043212	-2.455068
52	1	0	0.196288	-2.809270	-0.786978
53	1	0	-3.179346	4.096929	0.751028
54	1	0	-4.325849	2.862637	1.243485
55	1	0	-3.698001	-2.610843	3.536087
56	1	0	-2.733599	-1.402632	4.443153
57	1	0	-4.014463	-0.859070	3.327012
58	1	0	-4.772331	-3.936929	-2.226805
59	1	0	-4.423509	-3.754234	-0.478945
60	1	0	-3.828886	-5.187707	-1.356642
61	1	0	6.443235	0.571080	1.016780
62	1	0	6.909487	1.236593	-0.582092
63	1	0	6.631891	2.335223	0.791230
64	1	0	5.550432	-2.823782	0.887433
65	1	0	5.247652	-2.164433	-1.266214
66	1	0	6.249147	-0.768652	-0.895884

1a-3

Standard orientation:

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms) X	Y	Z
1	8	0	-1.805429	0.802908	0.622854
2	8	0	2.068822	0.985620	3.333663
3	8	0	4.972623	-0.898680	0.094017
4	8	0	3.123571	0.227740	0.511832
5	8	0	1.311654	1.411485	-1.964894
6	8	0	-4.766802	-2.012836	0.294829
7	8	0	2.125095	4.568004	-1.567303

8	8	0	-3.272671	2.474350	0.688802
9	8	0	0.863440	-2.608766	-1.558293
10	8	0	4.522018	-3.682250	-0.844252
11	8	0	-1.889856	-3.420833	-0.968456
12	8	0	-0.034639	4.987484	-1.057528
13	6	0	3.780859	-0.772117	-0.141973
14	6	0	0.024227	-0.698850	0.685975
15	6	0	1.754561	1.857617	-0.675623
16	6	0	3.058023	-1.705175	-1.021108
17	6	0	1.089602	4.254836	-1.012764
18	8	0	1.605661	-1.210930	3.064120
19	6	0	1.700033	-1.672672	-1.068535
20	6	0	-3.795730	-1.047604	0.362701
21	6	0	-1.460924	-0.512083	0.577369
22	6	0	-2.411069	-1.478922	0.439552
23	6	0	-2.064232	-2.950058	0.371753
24	6	0	0.376414	0.352321	-1.784162
25	6	0	1.773828	0.566429	0.190129
26	6	0	0.935983	-0.476572	-0.593046
27	6	0	-4.155201	0.272041	0.446895
28	6	0	1.253841	-4.002922	-1.668646
29	6	0	0.828694	0.406116	1.427282
30	6	0	1.529690	-0.057518	2.690960
31	6	0	0.902995	3.016802	-0.154319
32	6	0	3.985402	-2.685940	-1.712492
33	6	0	-3.121380	1.269584	0.596402
34	6	0	2.819964	0.676047	4.528951
35	6	0	0.046137	6.223491	-1.799153
36	6	0	-4.996513	-2.581042	-1.024422
37	8	0	-6.556660	0.007067	-0.145299
38	6	0	-5.571568	0.819314	0.467643
39	1	0	5.042852	-3.193255	-0.188432
40	1	0	-1.165254	-2.907949	-1.360561
41	1	0	0.242872	-1.669277	1.131599
42	1	0	2.778947	2.214325	-0.801356
43	1	0	-2.887737	-3.530240	0.790394
44	1	0	-1.175104	-3.160028	0.975746
45	1	0	-0.625777	0.736138	-1.563340
46	1	0	0.330171	-0.217129	-2.713755
47	1	0	0.350037	-4.566736	-1.440396
48	1	0	1.576402	-4.217532	-2.688600
49	1	0	2.045087	-4.235646	-0.955089
50	1	0	0.257416	1.304940	1.650040
51	1	0	-0.158985	2.768899	-0.094119
52	1	0	1.232698	3.281786	0.858703
53	1	0	4.792970	-2.097172	-2.165033

54	1	0	3.479251	-3.207533	-2.522112
55	1	0	3.173368	1.633699	4.906562
56	1	0	2.177524	0.186806	5.263374
57	1	0	3.661771	0.024300	4.287160
58	1	0	-0.940093	6.677346	-1.718251
59	1	0	0.291254	6.024047	-2.844240
60	1	0	0.805724	6.878116	-1.367106
61	1	0	-5.449152	-1.820753	-1.666269
62	1	0	-4.062756	-2.948487	-1.453128
63	1	0	-5.693668	-3.404804	-0.870434
64	1	0	-6.508378	-0.857595	0.287162
65	1	0	-5.836376	1.045946	1.513793
66	1	0	-5.571476	1.776162	-0.061263

1a-4

Standard orientation:

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms) X	Y	Z
1	8	0	2.045588	-1.022479	-0.784982
2	8	0	-1.655269	-2.413357	2.061920
3	8	0	-4.054908	1.875928	1.142804
4	8	0	-2.693344	0.242697	0.554510
5	8	0	-0.962800	-1.023493	-2.308062
6	8	0	5.300905	0.853237	0.848639
7	8	0	-4.365291	-3.146513	0.267974
8	8	0	3.320082	-2.380853	-2.014602
9	8	0	-0.240151	3.182745	-1.228448
10	8	0	-3.946103	4.182949	-0.438958
11	8	0	3.285429	2.907145	1.326058
12	8	0	-4.910062	-1.489335	-1.165353
13	6	0	-3.022823	1.572252	0.560183
14	6	0	0.419393	0.229130	0.390572
15	6	0	-2.136975	-0.960815	-1.502279
16	6	0	-2.146890	2.553537	-0.074468
17	6	0	-4.064010	-2.389608	-0.632198
18	8	0	-0.562739	-0.664695	2.994660
19	6	0	-0.972337	2.204531	-0.668109
20	6	0	4.252510	0.174526	0.286933
21	6	0	1.867360	-0.037855	0.142214
22	6	0	2.934918	0.561621	0.739253
23	6	0	2.847730	1.636468	1.803928
24	6	0	-0.328376	0.255978	-2.213067
25	6	0	-1.629188	-0.243815	-0.245961

26	6	0	-0.549159	0.764735	-0.753711
27	6	0	4.443192	-0.756284	-0.696741
28	6	0	1.168468	3.036655	-1.494171
29	6	0	-0.535104	-0.973645	0.591971
30	6	0	-0.895578	-1.311938	2.022222
31	6	0	-2.711255	-2.363513	-1.322856
32	6	0	-2.619035	3.993234	0.041387
33	6	0	3.294828	-1.452644	-1.221216
34	6	0	-2.143395	-2.812372	3.361406
35	6	0	-6.222022	-1.422969	-0.568557
36	6	0	6.118280	0.102984	1.779790
37	8	0	6.131347	-2.494885	-1.002029
38	6	0	5.771986	-1.147147	-1.299229
39	1	0	-4.494773	3.608271	0.119145
40	1	0	4.230711	2.810143	1.132550
41	1	0	0.315933	0.889039	1.250218
42	1	0	-2.891973	-0.313666	-1.971908
43	1	0	3.439538	1.324850	2.673643
44	1	0	1.823386	1.773152	2.148298
45	1	0	0.715889	0.118317	-2.487518
46	1	0	-0.794574	0.962903	-2.911673
47	1	0	1.385569	2.140322	-2.077175
48	1	0	1.435283	3.912274	-2.084946
49	1	0	1.741241	3.034398	-0.563419
50	1	0	-0.191808	-1.866570	0.066857
51	1	0	-2.834613	-2.803068	-2.319306
52	1	0	-2.035941	-3.003944	-0.754063
53	1	0	-1.969851	4.638541	-0.550089
54	1	0	-2.537115	4.309468	1.092469
55	1	0	-2.797320	-3.661964	3.175565
56	1	0	-1.310233	-3.100643	4.005461
57	1	0	-2.697815	-1.994057	3.824378
58	1	0	-6.770422	-0.683783	-1.150014
59	1	0	-6.145167	-1.107190	0.474009
60	1	0	-6.715244	-2.395272	-0.620545
61	1	0	6.977214	0.735562	2.000481
62	1	0	5.557476	-0.098474	2.697313
63	1	0	6.448692	-0.839661	1.337843
64	1	0	5.437408	-3.040823	-1.404283
65	1	0	5.714996	-0.991242	-2.385647
66	1	0	6.566931	-0.507872	-0.914478

1a-5

Standard orientation:

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms) X	Y	Z
1	8	0	-1.841279	0.520018	-1.025630
2	8	0	1.846021	1.607237	2.376590
3	8	0	4.773956	-1.369040	0.537630
4	8	0	3.040279	-0.039204	0.236435
5	8	0	1.880662	0.480245	-2.761978
6	8	0	-4.955657	-1.262849	0.958162
7	8	0	0.809729	4.027958	0.205369
8	8	0	-3.227479	1.787632	-2.221937
9	8	0	0.968843	-3.322274	-1.316969
10	8	0	2.954581	-4.640996	0.381866
11	8	0	-2.053935	-1.614726	2.922261
12	8	0	2.949571	3.854642	-0.497841
13	6	0	3.648962	-1.264079	0.085575
14	6	0	-0.109546	-0.635187	0.110375
15	6	0	2.132539	1.269464	-1.599074
16	6	0	2.908068	-2.359412	-0.539732
17	6	0	1.639691	3.563247	-0.552658
18	8	0	0.488594	-0.116880	2.886322
19	6	0	1.635952	-2.195125	-0.983666
20	6	0	-3.929719	-0.652039	0.300315
21	6	0	-1.574668	-0.454674	-0.113246
22	6	0	-2.570911	-1.075842	0.578511
23	6	0	-2.295234	-2.144732	1.622508
24	6	0	0.752392	-0.351117	-2.498116
25	6	0	1.823783	0.298915	-0.418071
26	6	0	0.968296	-0.855336	-1.038894
27	6	0	-4.212237	0.285916	-0.658325
28	6	0	-0.247855	-3.325089	-2.085935
29	6	0	0.671250	0.619638	0.586796
30	6	0	0.986391	0.640984	2.068350
31	6	0	1.338449	2.588918	-1.674102
32	6	0	3.549912	-3.732463	-0.547327
33	6	0	-3.130238	0.916996	-1.368037
34	6	0	2.202933	1.729396	3.775635
35	6	0	3.354381	4.760024	0.552017
36	6	0	-5.197872	-0.789171	2.306845
37	8	0	-5.768401	2.140229	-1.006050
38	6	0	-5.608951	0.726432	-1.041930
39	1	0	2.047285	-4.780750	0.074819
40	1	0	-1.228348	-1.097314	2.894974
41	1	0	0.029561	-1.424291	0.846845
42	1	0	3.198939	1.501894	-1.584179
43	1	0	-1.470859	-2.789579	1.295655

44	1	0	-3.179493	-2.778353	1.706824
45	1	0	-0.188326	0.196970	-2.596970
46	1	0	0.770183	-1.148476	-3.240411
47	1	0	-0.712779	-4.289760	-1.887451
48	1	0	-0.930451	-2.530417	-1.781964
49	1	0	-0.021975	-3.242510	-3.151917
50	1	0	0.166018	1.557973	0.349346
51	1	0	1.621482	3.061952	-2.619920
52	1	0	0.260065	2.420766	-1.696780
53	1	0	4.595621	-3.632141	-0.256411
54	1	0	3.513045	-4.141733	-1.565661
55	1	0	2.908967	2.555678	3.822125
56	1	0	1.314550	1.945682	4.371023
57	1	0	2.666443	0.805604	4.125161
58	1	0	4.433819	4.858470	0.452190
59	1	0	3.093965	4.344640	1.527105
60	1	0	2.867727	5.729062	0.426014
61	1	0	-5.565304	0.241571	2.278745
62	1	0	-5.966071	-1.444339	2.716980
63	1	0	-4.287793	-0.846635	2.908761
64	1	0	-5.105411	2.487267	-1.625624
65	1	0	-5.838611	0.331468	-2.043844
66	1	0	-6.330728	0.297384	-0.346180

Table S4 Computational methods for ECD of **2b**.

2b-1

Standard orientation:

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms) X	Y	Z
1	6	0	-1.974341	0.607501	0.306850
2	6	0	-1.048597	-2.054857	0.793693
3	8	0	-2.710422	-0.277637	1.138597
4	6	0	-0.932065	-0.016184	-0.711012
5	6	0	-0.563345	-1.427892	-0.311840
6	6	0	-2.211189	-1.494378	1.501288
7	8	0	-2.807826	-2.088456	2.382732
8	6	0	-0.501328	-3.339716	1.407082
9	8	0	0.916348	-3.432479	1.413122
10	8	0	0.332132	-1.933115	-1.192487
11	6	0	0.392147	-3.351644	-1.486696
12	6	0	-1.215463	0.091448	-2.225379

13	8	0	-0.010907	0.087302	-2.992635
14	6	0	-0.774647	1.306793	1.045702
15	6	0	0.096132	1.088307	-0.208349
16	6	0	1.539581	0.760267	-0.027422
17	6	0	4.091826	-0.158020	0.630689
18	8	0	1.712817	-0.166772	0.951097
19	6	0	2.598412	1.272960	-0.715520
20	6	0	3.910347	0.763514	-0.372873
21	6	0	2.941866	-0.671495	1.316874
22	8	0	2.936305	-1.540559	2.190420
23	6	0	5.437045	-0.699230	1.065875
24	8	0	5.481875	-2.122078	1.066414
25	8	0	5.004298	1.268145	-1.006955
26	6	0	5.225164	0.793993	-2.359571
27	6	0	2.428461	2.353993	-1.768898
28	8	0	2.200656	1.852543	-3.079916
29	6	0	-0.930624	2.731427	1.526316
30	8	0	-1.385031	2.774714	2.784303
31	8	0	-0.702003	3.713813	0.843675
32	6	0	-1.624479	4.092507	3.329550
33	6	0	-4.162003	1.261613	-0.841822
34	6	0	-4.703215	-0.104600	-1.063520
35	8	0	-6.045593	-0.066342	-1.140464
36	6	0	-6.698650	-1.327057	-1.394056
37	8	0	-4.048267	-1.123267	-1.205284
38	6	0	-2.971036	1.564076	-0.308360
39	1	0	-0.856307	-4.224605	0.869048
40	1	0	-0.911988	-3.404181	2.419849
41	1	0	1.306988	-2.680100	1.892858
42	1	0	0.940293	-3.870543	-0.702741
43	1	0	-0.620061	-3.747654	-1.593350
44	1	0	0.918458	-3.420160	-2.438262
45	1	0	-1.705716	1.041873	-2.438741
46	1	0	-1.885860	-0.714099	-2.540216
47	1	0	0.435964	-0.748919	-2.784368
48	1	0	-0.460899	0.668711	1.872203
49	1	0	-0.002192	1.950415	-0.867322
50	1	0	5.672370	-0.299466	2.064413
51	1	0	6.209054	-0.347835	0.380628
52	1	0	4.775347	-2.400575	1.672014
53	1	0	5.499379	-0.265501	-2.339113
54	1	0	4.335223	0.940621	-2.975913
55	1	0	6.056645	1.382843	-2.746165
56	1	0	3.351131	2.936132	-1.813491
57	1	0	1.632382	3.042290	-1.458603
58	1	0	1.380672	1.318465	-3.062352

59	1	0	-2.369507	4.619464	2.730528
60	1	0	-0.696652	4.667107	3.347506
61	1	0	-1.992224	3.926013	4.340171
62	1	0	-4.805900	2.071945	-1.169590
63	1	0	-6.362152	-1.744202	-2.345476
64	1	0	-6.482916	-2.035517	-0.591636
65	1	0	-7.763260	-1.102704	-1.429605
66	1	0	-2.693313	2.613715	-0.284823

2b-2

Standard orientation:

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms) X	Y	Z
1	6	0	-1.896983	0.730275	0.264529
2	6	0	-1.268136	-1.963052	0.915911
3	8	0	-2.788380	-0.041155	1.063505
4	6	0	-0.866114	-0.033654	-0.666421
5	6	0	-0.624716	-1.437414	-0.159034
6	6	0	-2.469559	-1.304106	1.442979
7	8	0	-3.237417	-1.870205	2.208106
8	6	0	-0.948270	-3.255963	1.640973
9	8	0	-1.821683	-4.333787	1.307647
10	8	0	0.310442	-2.042600	-0.922911
11	6	0	0.410551	-3.483453	-1.039361
12	6	0	-1.072276	-0.009148	-2.196484
13	8	0	0.161101	-0.142938	-2.903386
14	6	0	-0.672927	1.320391	1.056119
15	6	0	0.220784	1.010388	-0.162028
16	6	0	1.641554	0.605323	0.059091
17	6	0	4.143917	-0.440877	0.743142
18	8	0	1.757795	-0.285475	1.076050
19	6	0	2.728771	1.035800	-0.640605
20	6	0	4.010160	0.461710	-0.280027
21	6	0	2.971249	-0.833264	1.490610
22	8	0	2.930215	-1.601890	2.435479
23	6	0	5.449466	-1.045970	1.227599
24	8	0	6.469549	-1.162440	0.249815
25	8	0	5.128530	0.896854	-0.943396
26	6	0	5.298637	0.370143	-2.288188
27	6	0	2.626979	2.098364	-1.721213
28	8	0	2.385138	1.583692	-3.025622
29	6	0	-0.715024	2.755872	1.527176
30	8	0	-1.190718	2.847239	2.774581

31	8	0	-0.383968	3.709719	0.845820
32	6	0	-1.319655	4.184164	3.310629
33	6	0	-3.917920	1.590725	-1.044681
34	6	0	-4.600770	0.289735	-1.268441
35	8	0	-5.918947	0.481663	-1.452771
36	6	0	-6.696987	-0.703178	-1.720245
37	8	0	-4.064035	-0.803558	-1.327642
38	6	0	-2.735891	1.772523	-0.440838
39	1	0	-1.000072	-3.041610	2.715701
40	1	0	0.066835	-3.587038	1.432930
41	1	0	-2.703965	-4.034483	1.577722
42	1	0	-0.544814	-3.955413	-0.807276
43	1	0	0.688856	-3.673545	-2.075924
44	1	0	1.195746	-3.854160	-0.378777
45	1	0	-1.485820	0.955144	-2.493263
46	1	0	-1.782009	-0.787318	-2.492657
47	1	0	0.549144	-0.986663	-2.622721
48	1	0	-0.451995	0.657809	1.893218
49	1	0	0.190837	1.857629	-0.846655
50	1	0	5.238393	-2.054681	1.591672
51	1	0	5.799073	-0.469103	2.099766
52	1	0	6.616398	-0.270090	-0.095531
53	1	0	6.135063	0.922449	-2.716814
54	1	0	5.544307	-0.693574	-2.224048
55	1	0	4.395899	0.524992	-2.882232
56	1	0	3.578676	2.631540	-1.769478
57	1	0	1.865621	2.834919	-1.435255
58	1	0	1.560829	1.056503	-2.996089
59	1	0	-0.343838	4.671933	3.344613
60	1	0	-1.720437	4.056982	4.314372
61	1	0	-2.001913	4.773562	2.695320
62	1	0	-4.440256	2.458616	-1.435220
63	1	0	-6.341628	-1.193288	-2.629030
64	1	0	-6.628798	-1.400443	-0.882652
65	1	0	-7.721352	-0.357443	-1.847150
66	1	0	-2.340786	2.783825	-0.423886

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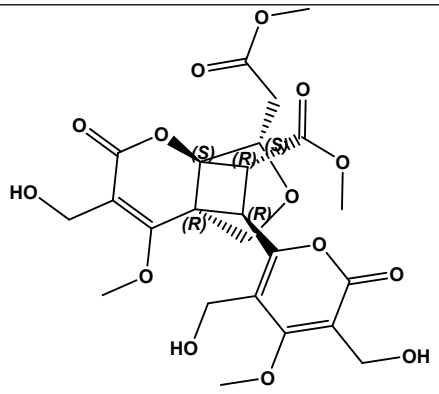
Table S5. 2D Structures of **1** and **2**.

label	structure
1a	

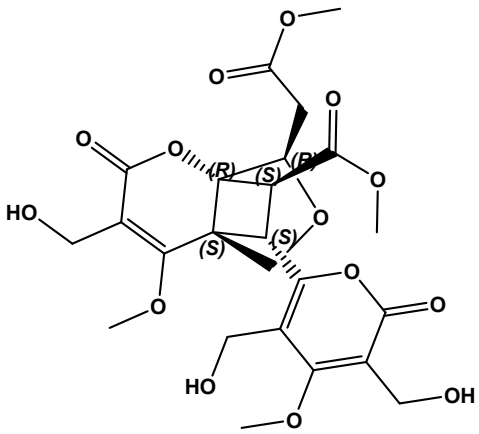
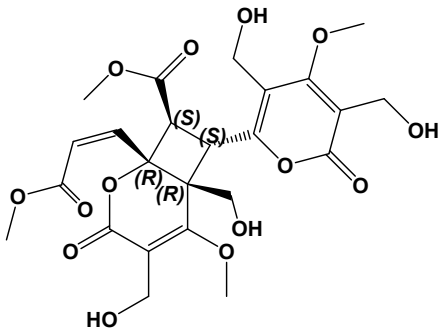
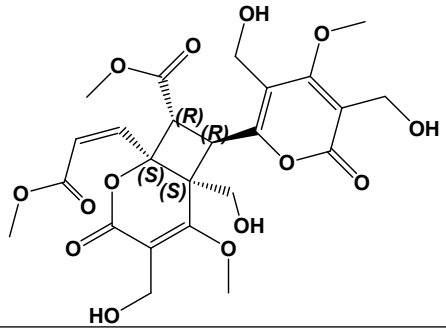
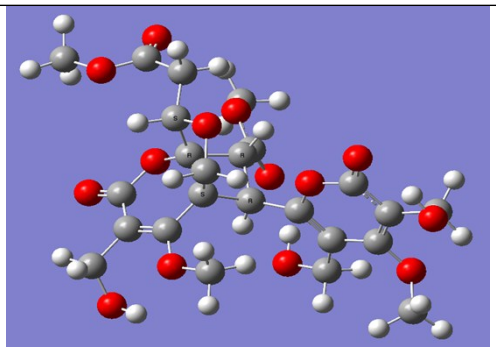
1b	
2b	
2a	

Table S6 B3LYP/6-31++G (d, p) optimized lowest energy 3D conformers of **1a**.

label	conformer	Boltzmann weighting factors
1a-1		9.5

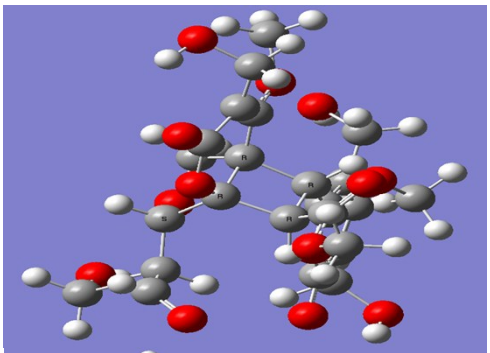
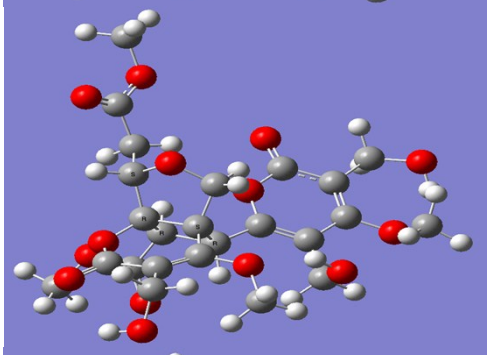
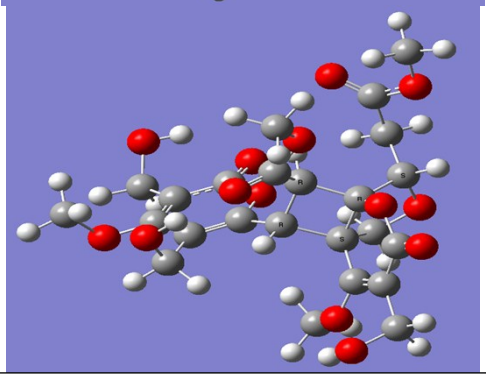
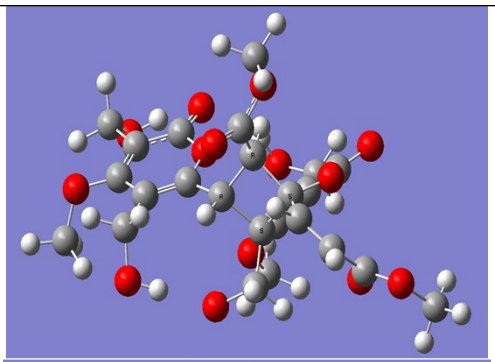
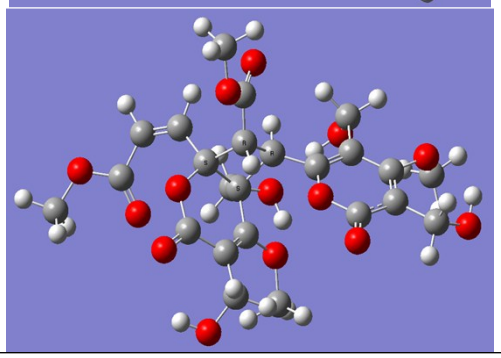
1a-2		14.37
1a-3		0.37
1a-4		75.72
1a-5		0.04

Table S7 B3LYP/6-31++G (d, p) optimized lowest energy 3D conformers of **2b**.

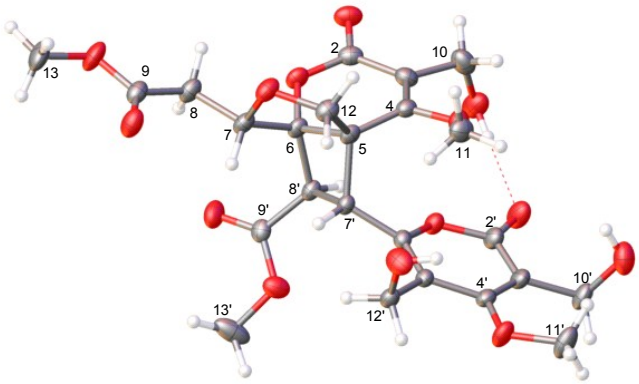
label	conformer	Boltzmann weighting factors

2b-1		99.69
2b-2		0.31

6. X-ray Crystallographic analyses of 1

X-ray quality crystal was cultivated upon slow evaporation of the MeOH by keeping the sample at room temperature for one month. Crystal data of **2**: $C_{24}H_{28}O_{14}$, M = 540.46, monoclinic, a = 11.6079 (8) Å, b = 8.1273(3) Å, c = 25.7149(10) Å, β = 92.286 (4) °, U = 2424.0 (2) Å^3, T = 106.4, space group P2$_1$/c, Z = 4, μ (Cu Kα) = 1.061, 11660 reflections measured, 4577 unique (R_{int} = 0.0268) which were used in all calculations. The final wR (F_2) was 0.1371 (all data).

X-ray crystal data for compound **1**



Identification code	exp_4022
Empirical formula	C24H28O14
Formula weight	540.46
Temperature / K	106.4
Crystal system	monoclinic
Space group	P21/c
a / Å, b / Å, c / Å	11.6079(8), 8.1273(3), 25.7149(10)
α/°, β/°, γ/°	90.00, 92.286(4), 90.00
Volume / Å3	2424.0(2)
Z	4
ρ_{calc} / mg mm^{-3}	1.481
μ / mm^{-1}	1.061
F(000)	1136
Crystal size / mm3	0.35 × 0.04 × 0.03
2Θ range for data collection	7.62 to 142.04°
Index ranges	-8 ⩽ h ⩽ 14, -9 ⩽ k ⩽ 8, -31 ⩽ l ⩽ 31
Reflections collected	11660
Independent reflections	4577[R(int) =
Data/restraints/parameters	4577/0/362
Goodness-of-fit on F2	1.029
Final R indexes [I>2σ (I) i.e. Fo>4σ (Fo)]	R1 = 0.0485, wR2 = 0.1300
Final R indexes [all data]	R1 = 0.0566, wR2 = 0.1371
Largest diff. peak/hole / e Å-3	0.708/-0.314

The crystallographic data for the structure of **1** have been deposited with the Cambridge Crystallographic Data Center as supplementary publication CCDC No. 1504985.

7. The spectra of phomone A (1)

Figure S1. The UV spectrum of compound **1**

NO.	ABSCISSA	PEAK	HEIGHT	ABSCISSA	VALLEY	HEIGHT
1	301.6	0.3592	0.1271	281.4	0.3090	-0.1313
2	255.0	0.5703	0.2117	230.2	0.4051	-0.2932
3	212.8	0.8316	0.2793	204.2	0.5193	-0.0823
4	202.6	0.6068	0.1096			

Figure S2. The IR spectrum of compound **1**

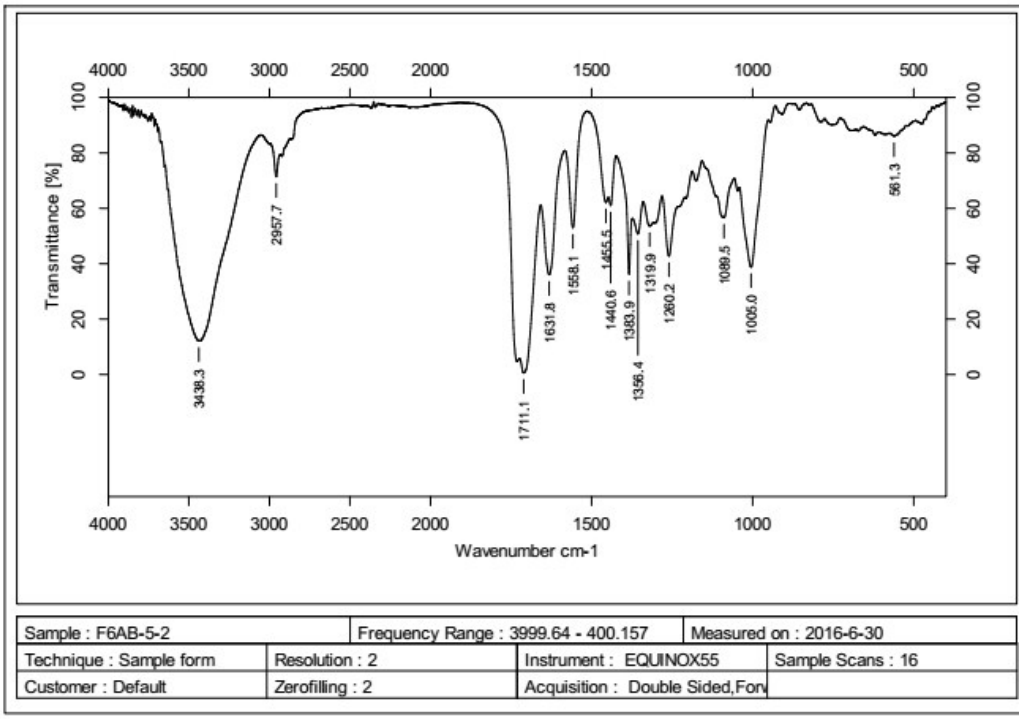
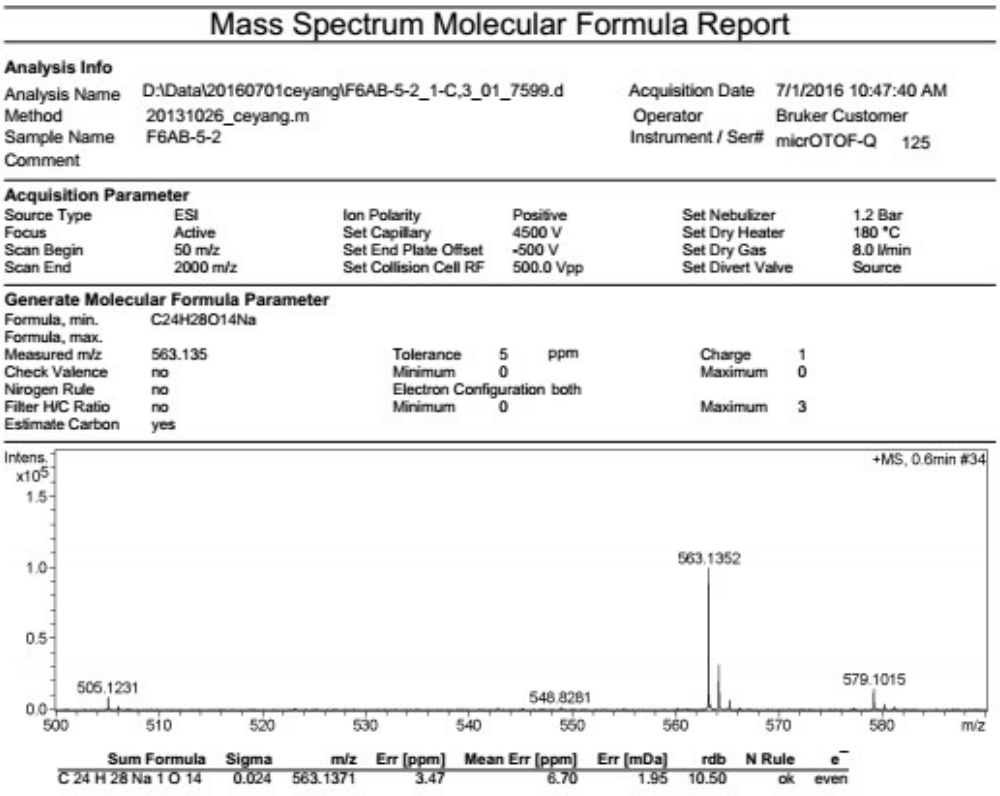


Figure S3. The HR-ESI-MS spectrum of compound **1**



Mass Spectrum Molecular Formula Report

Analysis Info

Analysis Name	D:\Data\20160701ceyang\F6AB-5-2_1-C,3_01_7599.d	Acquisition Date	7/1/2016 10:47:40 AM
Method	20131026_ceyang.m	Operator	Bruker Customer
Sample Name	F6AB-5-2	Instrument / Ser#	micrOTOF-Q 125
Comment			

Acquisition Parameter

Source Type	ESI	Ion Polarity	Positive	Set Nebulizer	1.2 Bar
Focus	Active	Set Capillary	4500 V	Set Dry Heater	180 °C
Scan Begin	50 m/z	Set End Plate Offset	-500 V	Set Dry Gas	8.0 l/min
Scan End	2000 m/z	Set Collision Cell RF	500.0 Vpp	Set Divert Valve	Source

Generate Molecular Formula Parameter

Formula, min.	C24H28O14Na						
Formula, max.							
Measured m/z	563.135	Tolerance	5	ppm	Charge	1	
Check Valence	no	Minimum	0		Maximum	0	
Nirogen Rule	no	Electron Configuration	both				
Filter H/C Ratio	no	Minimum	0		Maximum	3	
Estimate Carbon	yes						

Sum Formula	Sigma	m/z	Err [ppm]	Mean Err [ppm]	Err [mDa]	rdb	N Rule	e⁻
C 24 H 28 Na 1 O 14	0.024	563.1371	3.47	6.70	1.95	10.50	ok	even

Figure S4. The [1]H-NMR spectrum of compound **1**

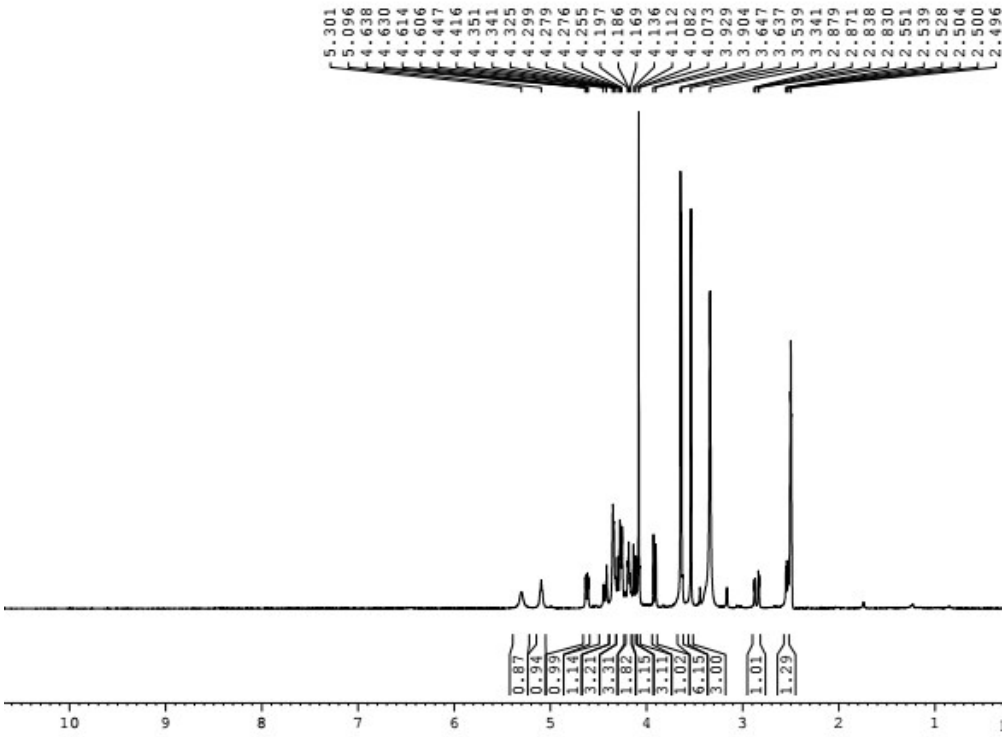


Figure S5. The [13]C-NMR spectrum of compound **1**

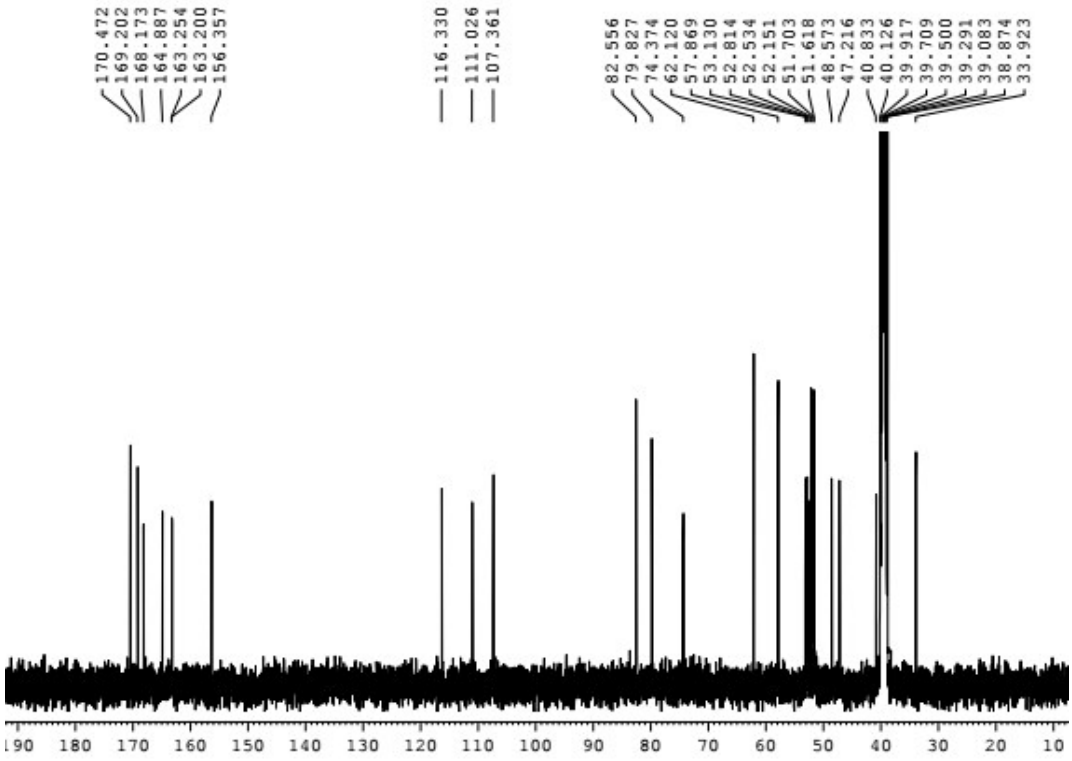


Figure S6. The HSQC spectrum of compound **1**

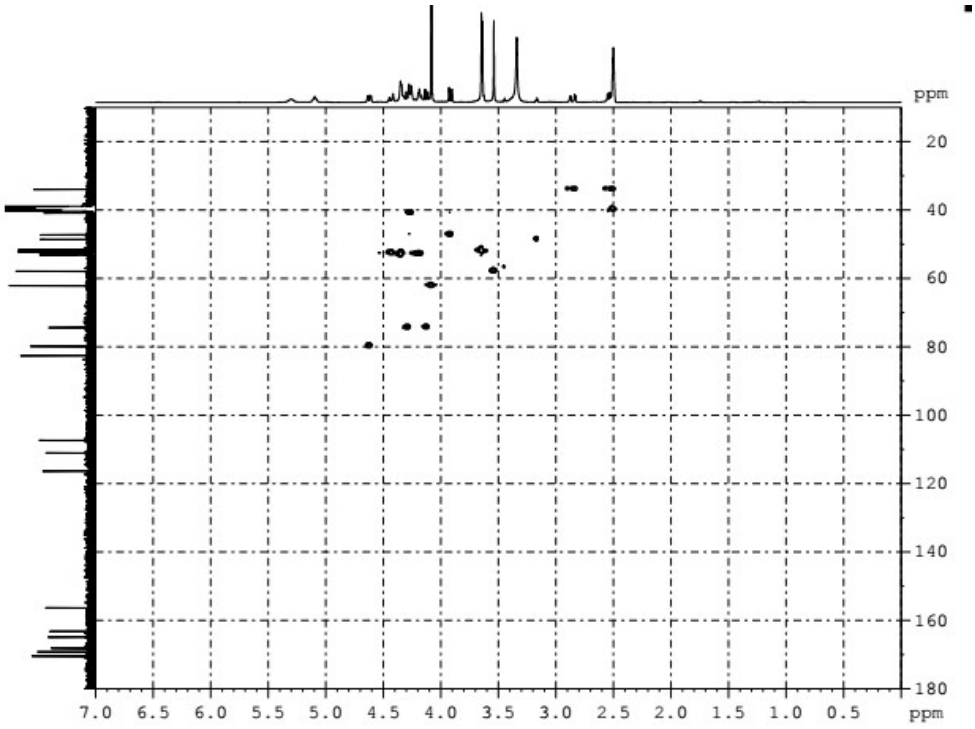


Figure S7. The HMBC spectrum of compound **1**

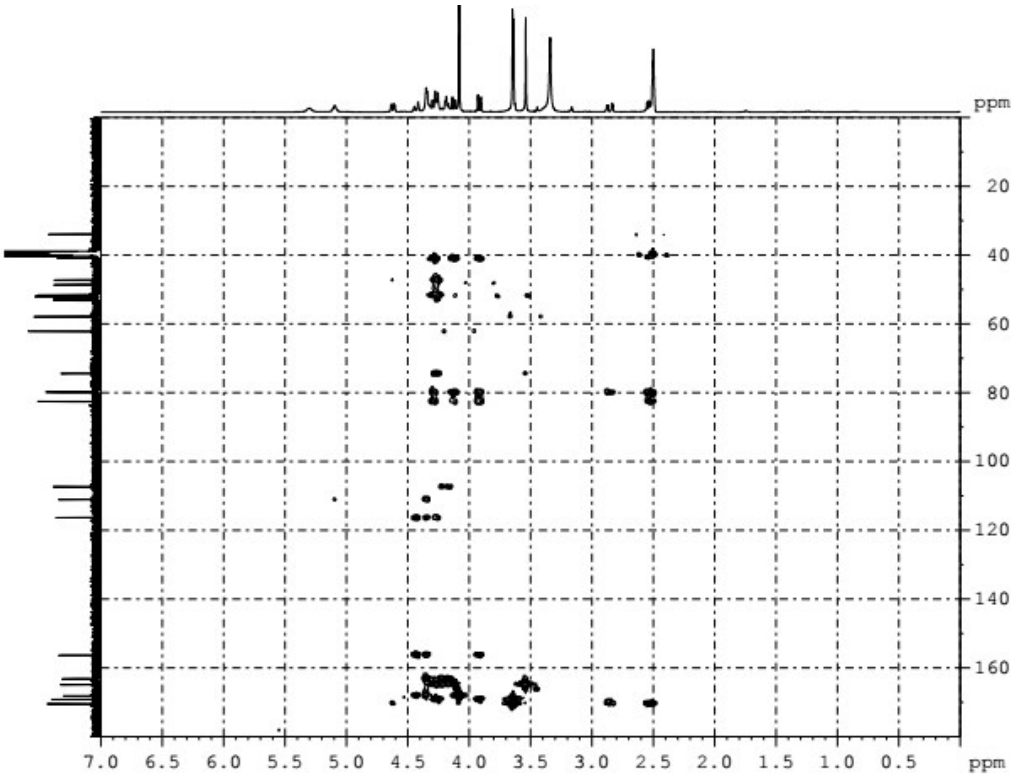


Figure S8. The NOESY spectrum of compound **1**

8. The spectra of phomone B (2)

Figure S9. The UV spectrum of compound **2**

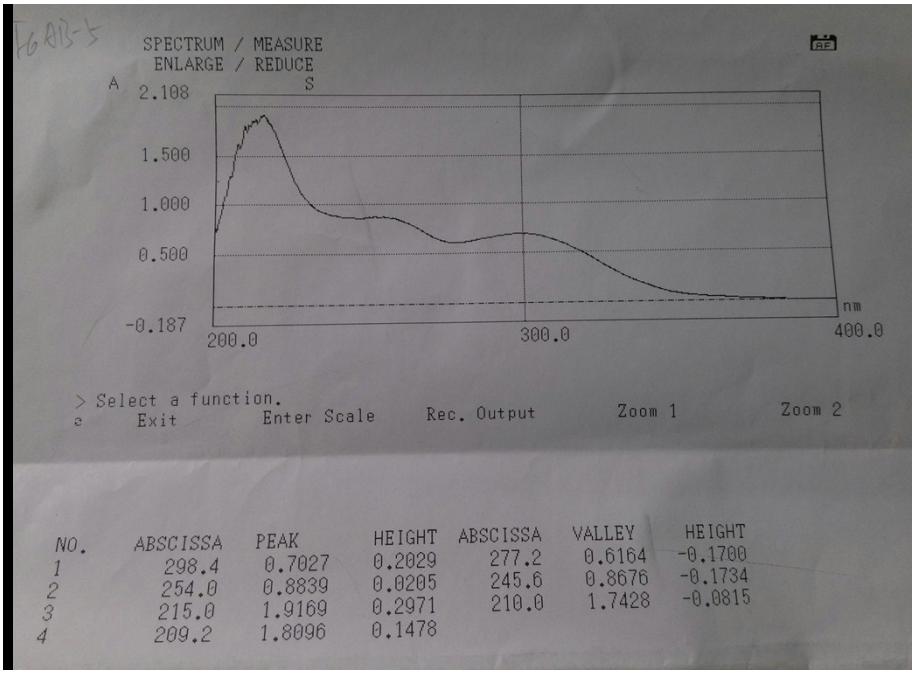
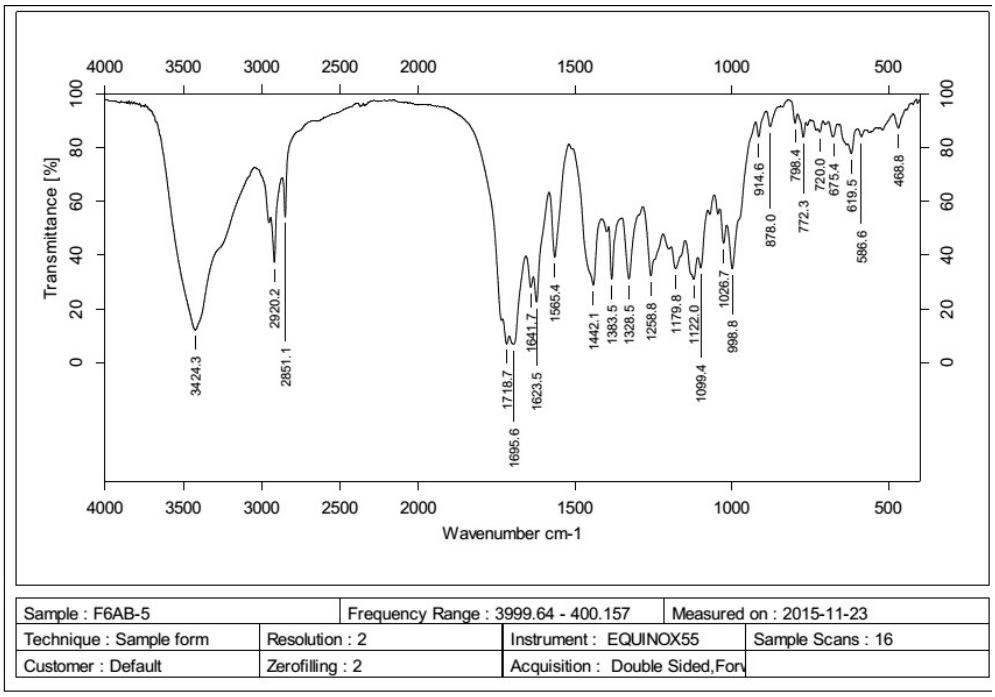


Figure S10. The IR spectrum of compound **2**



Sample : F6AB-5	Frequency Range : 3999.64 - 400.157	Measured on : 2015-11-23	
Technique : Sample form	Resolution : 2	Instrument : EQUINOX55	Sample Scans : 16
Customer : Default	Zerofilling : 2	Acquisition : Double Sided,For	

Figure S11. The HR-ESI-MS spectrum of compound **2**

Mass Spectrum Molecular Formula Report

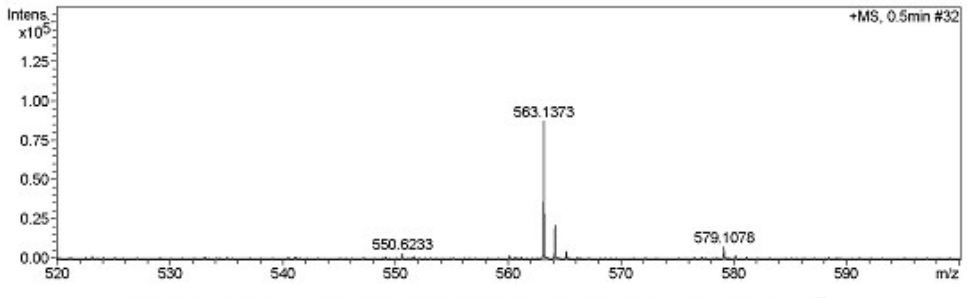
Analysis Info D:\Data\20150429CEYANG\F6-1-B-1_1-D,8_01_4993.d
Analysis Name
Method 20131026_ceyang.m
Sample Name F6-1-B-1
Comment
Acquisition Date 10/1/2014 3:24:21 PM
Operator micrOTOF-Q
Instrument / Ser# Bruker Customer 125

Acquisition Parameter

Source Type	ESI	Ion Polarity	Positive	Set Nebulizer	1.2 Bar
Focus	Active	Set Capillary	4500 V	Set Dry Heater	180 °C
Scan Begin	50 m/z	Set End Plate Offset	-500 V	Set Dry Gas	8.0 l/min
Scan End	3000 m/z	Set Collision Cell RF	600.0 Vpp	Set Divert Valve	Source

Generate Molecular Formula Parameter

Formula, min.	C24H28O14Na				
Formula, max.					
Measured m/z	563.137	Tolerance	5 ppm	Charge	1
Check Valence	no	Minimum	0	Maximum	0
Nirogen Rule	no	Electron Configuration	both		
Filter H/C Ratio	no	Minimum	0	Maximum	3
Estimate Carbon	yes				



Sum Formula	Sigma	m/z	Err [ppm]	Mean Err [ppm]	Err [mDa]	rdb	N Rule	e⁻
C 24 H 28 Na 1 O 14	0.014	563.1371	-0.36	1.15	-0.20	10.50	ok	even

Figure S12. The ^{1}H-NMR spectrum of compound **2**

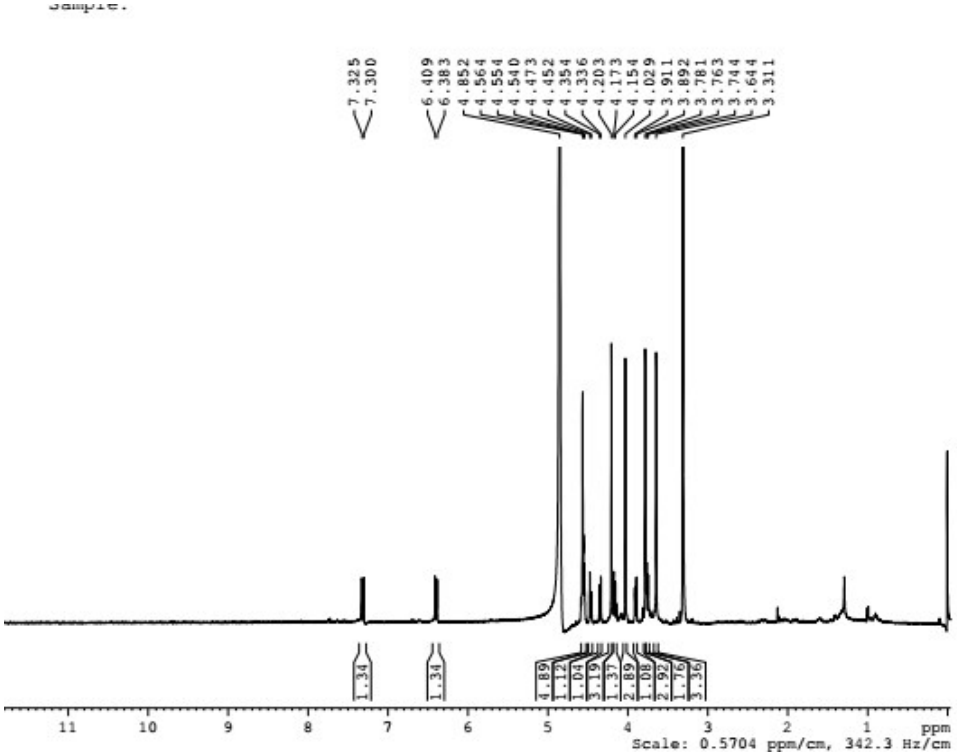


Figure S13. The ^{13}C-NMR spectrum of compound **2**

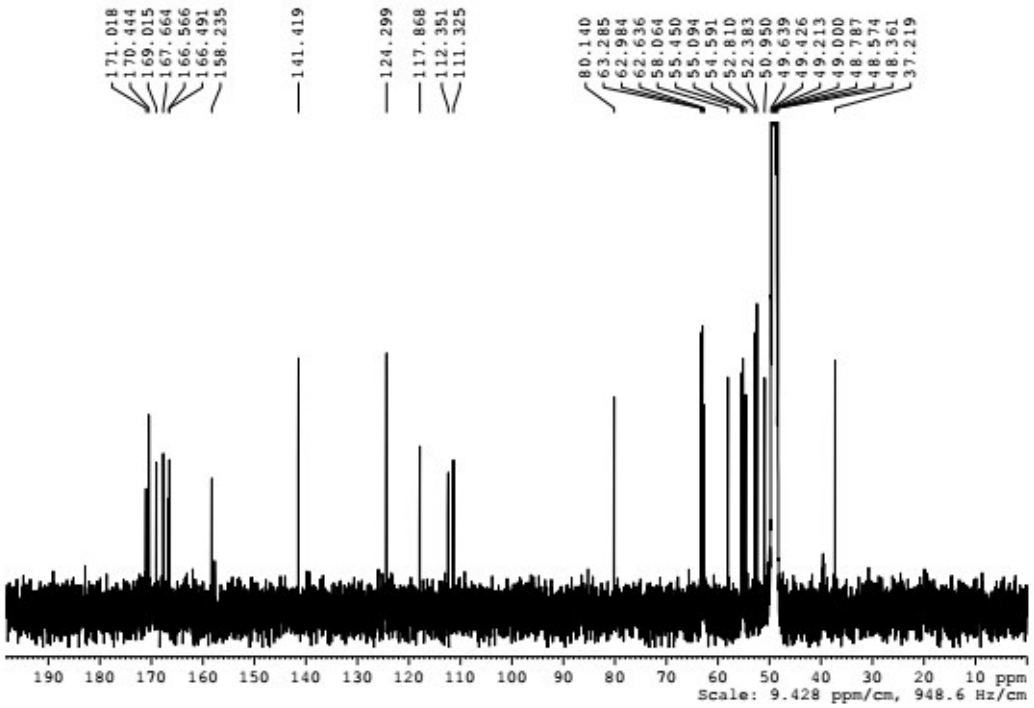


Figure S14. The HSQC spectrum of compound **2**

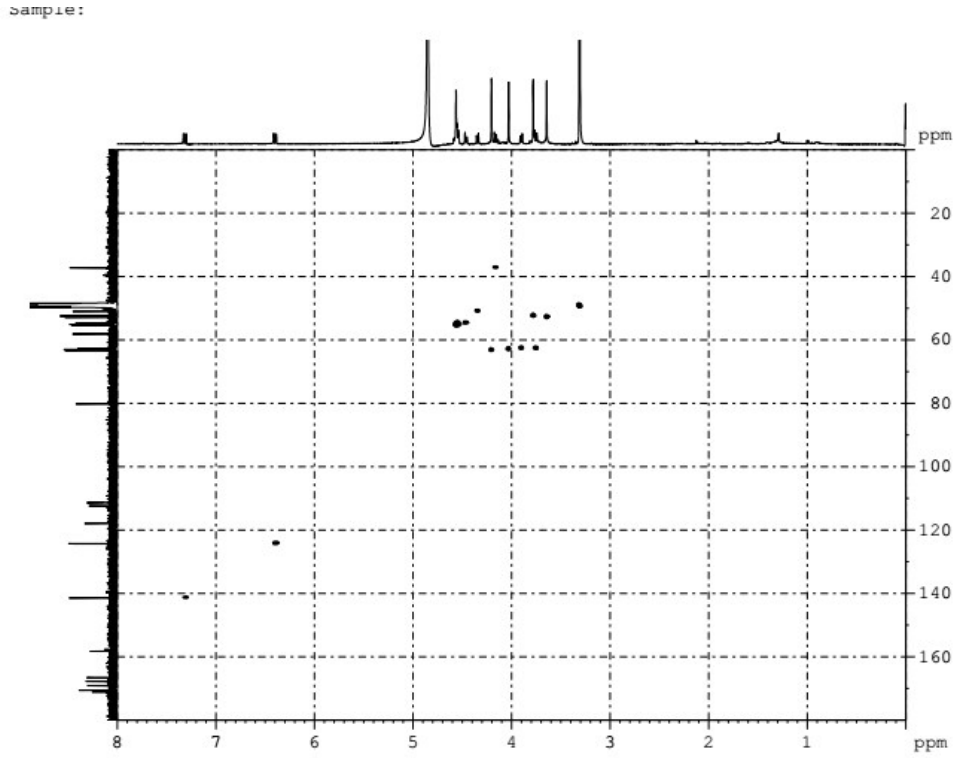


Figure S15. The HMBC spectrum of compound **2**

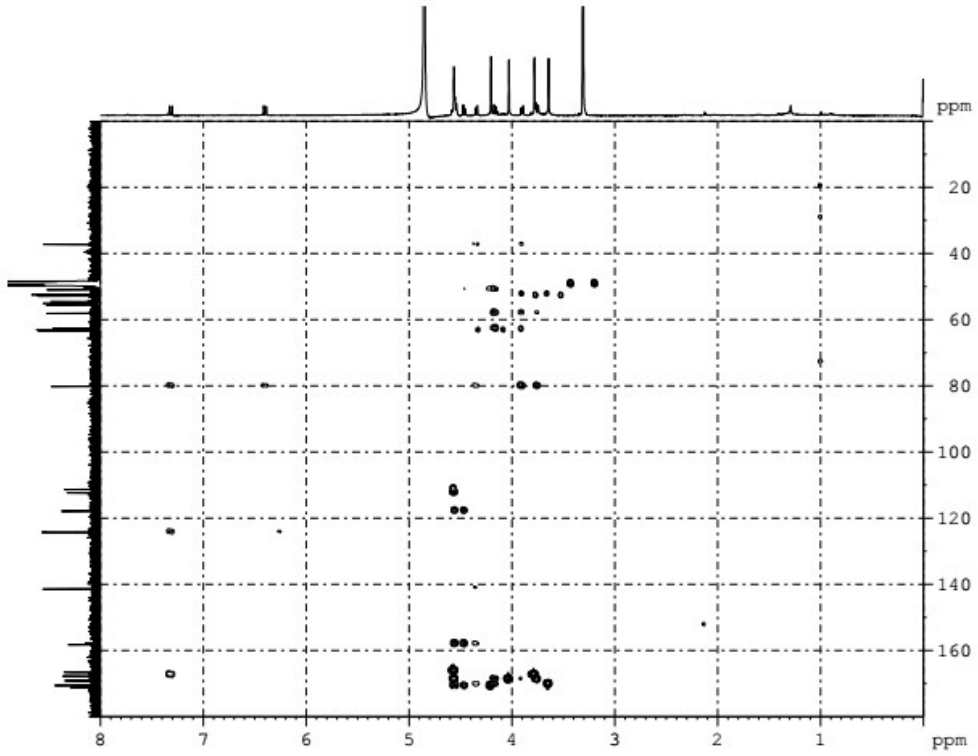
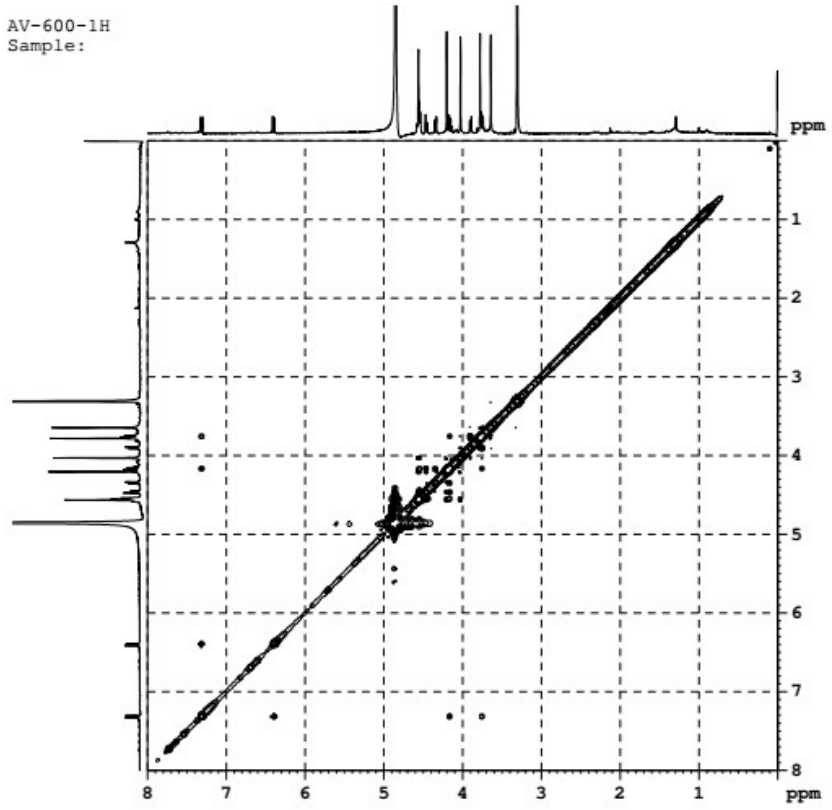


Figure S16. The NOESY spectrum of compound **2**



8. The spectra of compound 4

Figure S17. The ^{1}H-NMR spectrum of compound **4**

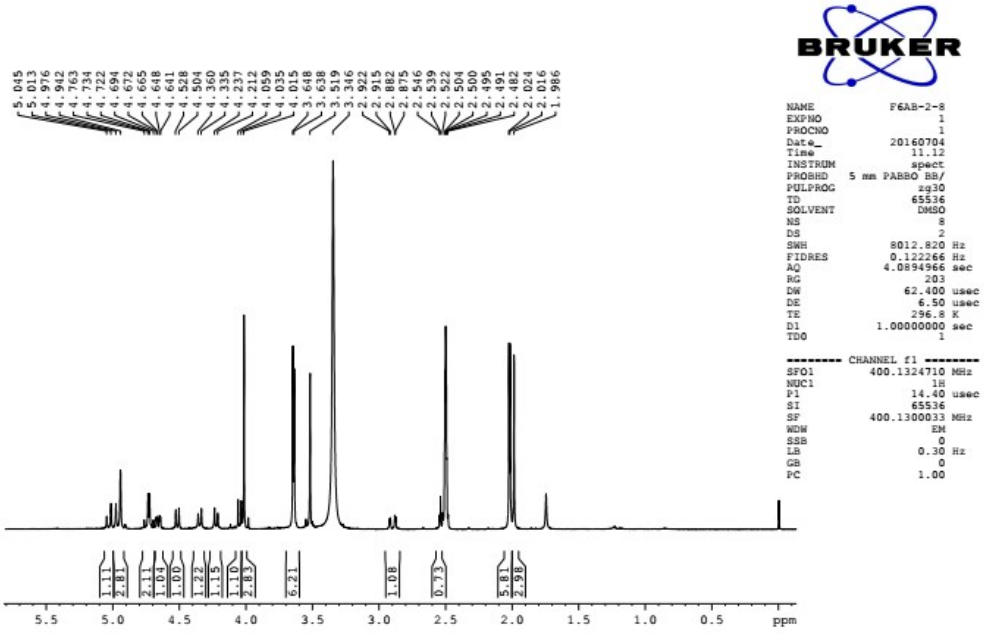


Figure S18. The^{13}C NMR spectrum of compound **4**

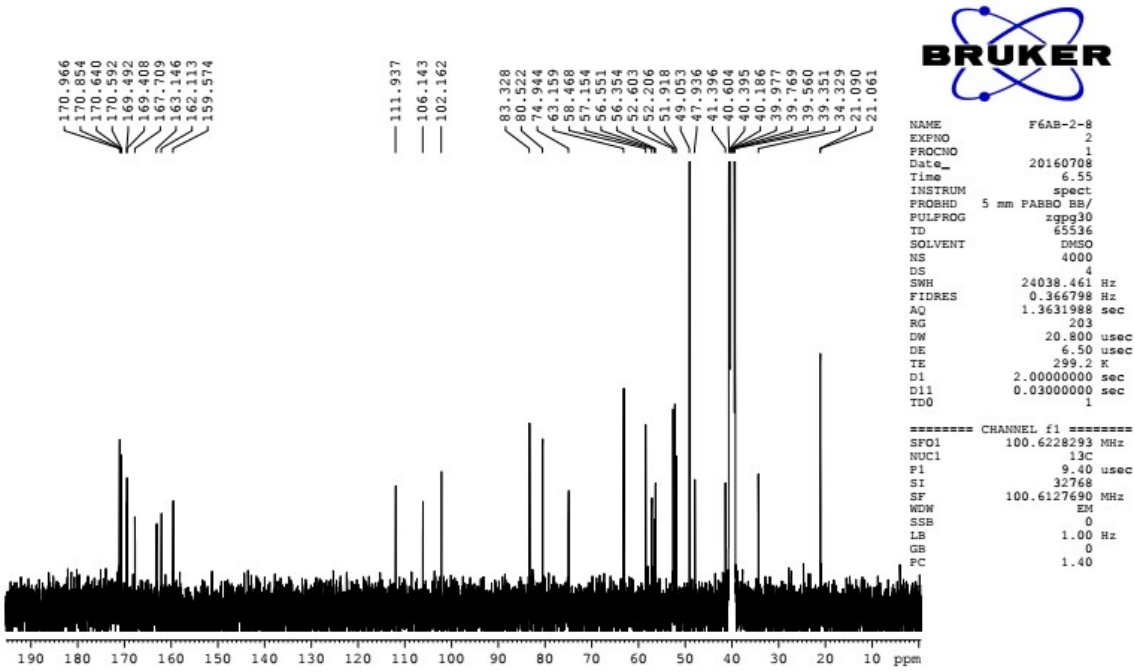
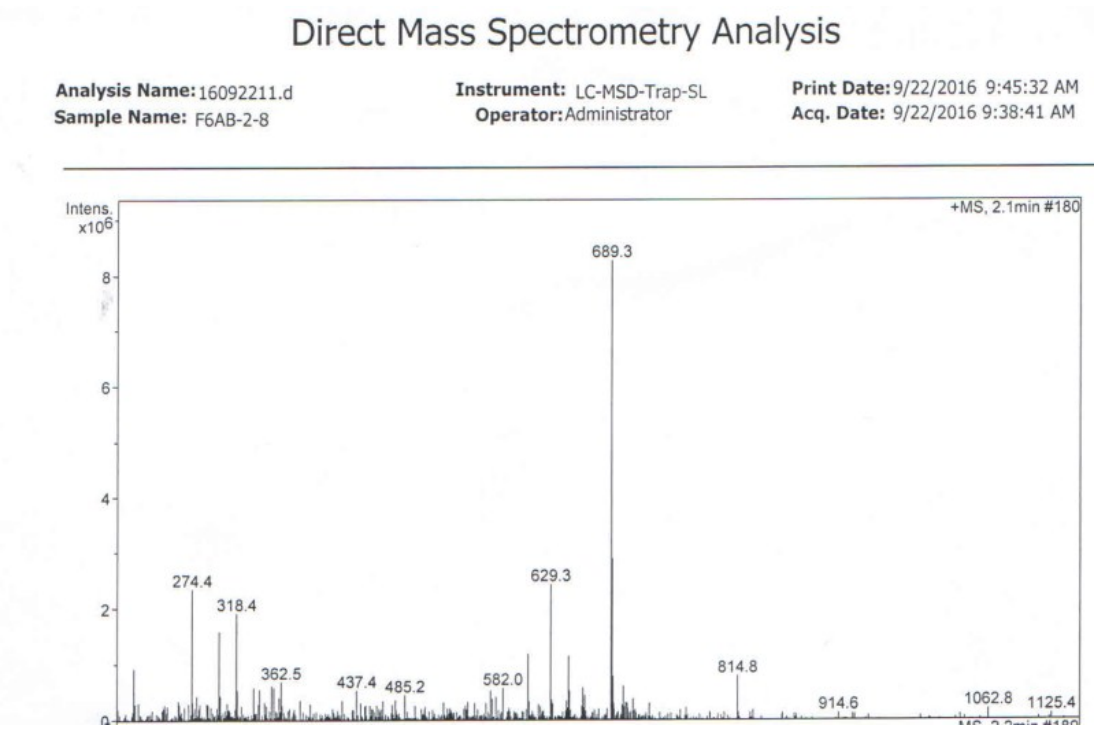
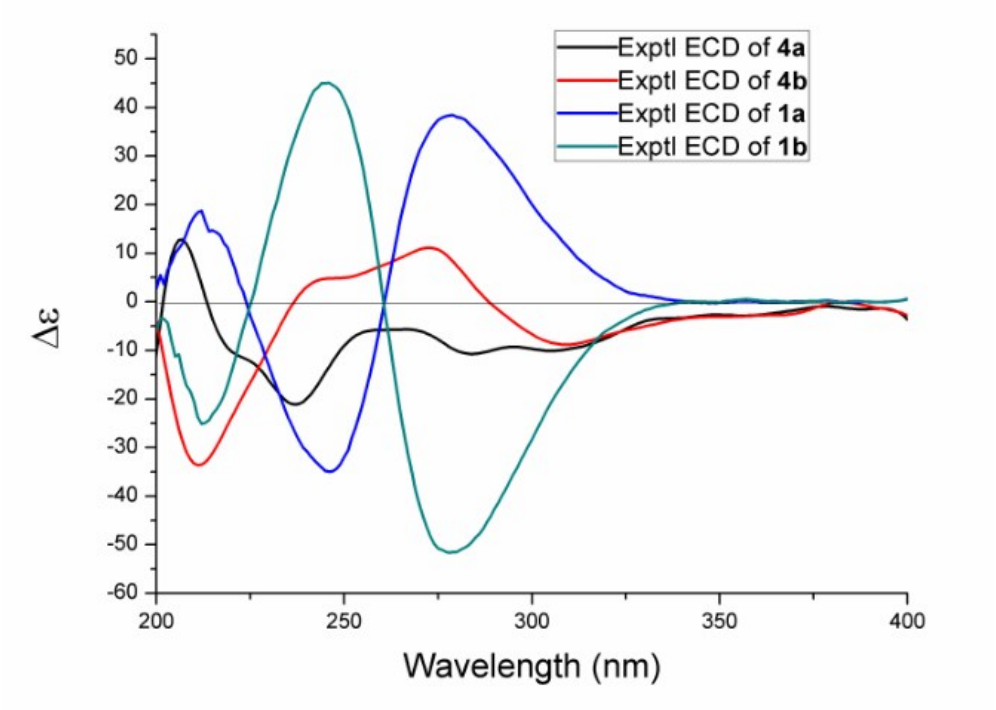


Figure S19. The ESI-MS spectrum of compound **4**



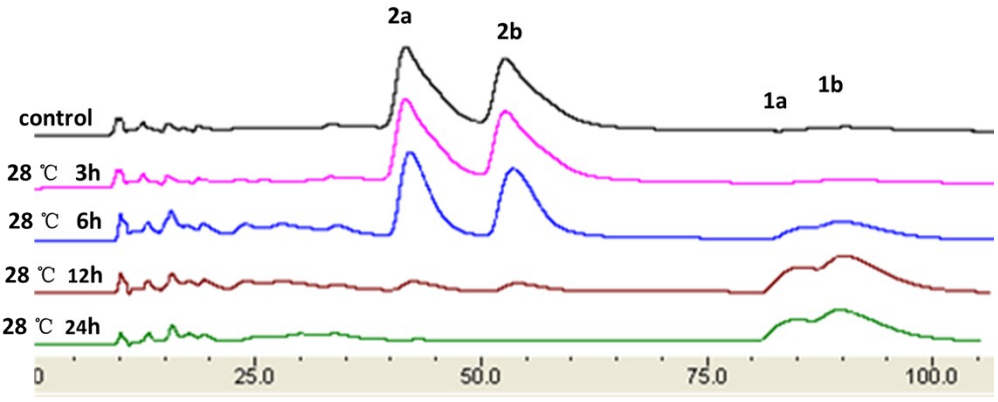
Figuer S20. Experimental ECD spectra of **4a** and **4b**



9. H_2O-, pH- and temperature-dependent epimerization effect

H_2O-dependent epimerization effect:

Figure S21. Dynamic chiral HPLC spectra of **2** dissolved in H_2O heating at 28 °C



pH-dependent epimerization effect:

Figure S22. Dynamic chiral HPLC spectra of compound **2** dissolved in anhydrous ethanol at pH = 8.0, 7.0, 5.0.

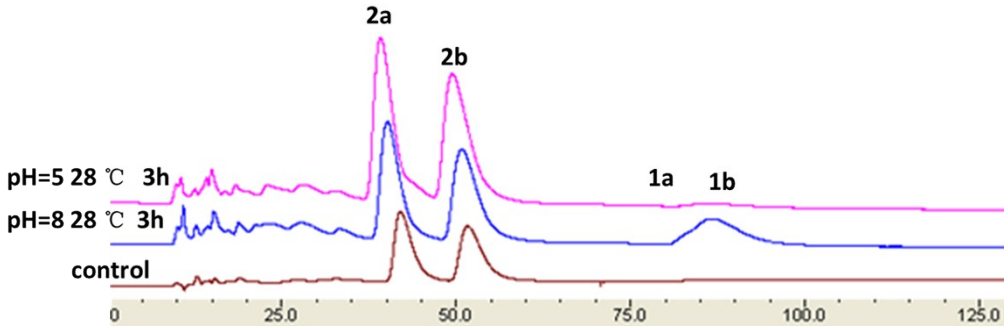


Figure S23. Dynamic chiral HPLC spectra of compound **1** dissolved in anhydrous ethanol at pH = 8.0, 7.0, 5.0.

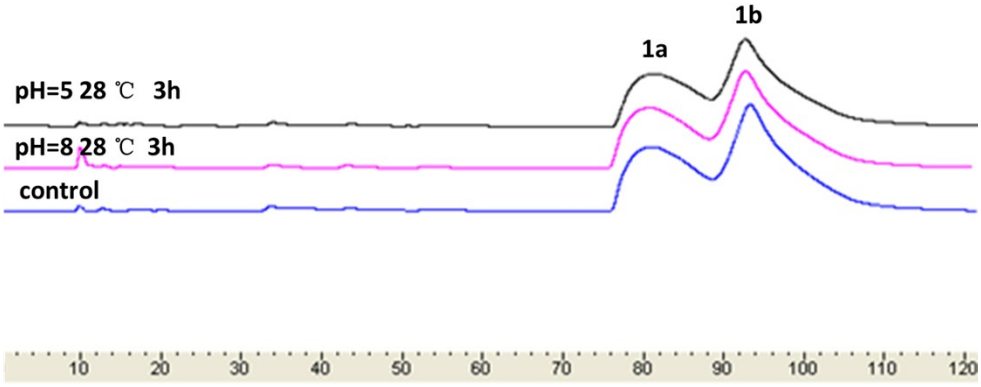
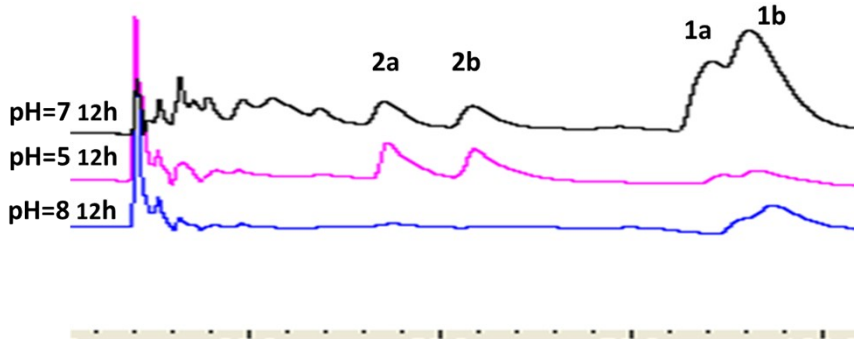


Figure S24. Chiral HPLC chromatogram of **2** dissolved in the H_2O at pH = 8.0, 7.0, 5.0



Temperature-dependent epimerizationeffect:

Figure S25. Dynamic chiral HPLC spectra: a) **2** dissolved in anhydrous ethanol heating at 50 °C