Electronic Supplementary Material (ESI) for Organic Chemistry Frontiers.

Isolation, structure elucidation, and synthesis of (±)-millpuline A with suppressive effect in miR-144 expression

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Shceme 1. The photochemical semi-synthesis from **2** to **1**

1. Experimental procedures

NMR spectra were recorded on a Bruker AV-300 and AV-600 spectrometer (Bruker Biospin, Rheinstetten, Germany), using TMS as an internal standard. CD spectra were acquired by Bio-logic MOS 450 spectropolarimeter. UV spectra were measured by a Shimadzu UV-2201 spectrometer. Specific rotation values were recorded on a Polarimeter (Model 341, Perkin Elmer, America). HRESIMS spectra were acquired from Waters ACQUITY UPLC and Xevo G2 Qtof system. Column chromatography was performed on silica gel (200-300 mesh, Qingdao Marine Chemical Plant, Qingdao, P. R. China). Sephadex LH-20 was purchased from Pharmacia company.

2. Plant material

The roots of *Millettia pulchra* Kurz var-laxior (Dunn) Z.Wei. were collected from Guangxi province of China, in June 2012. The plant material was authenticated by the professor Renbin Huang (Pharmaceutical College, Guangxi Medical University) and the Voucher specimen (no. 20121020) was deposited in School of Traditional Chinese Material Medica, Shenyang Pharmaceutical University.

3. Extraction and isolation

The small pieces of dried roots (4.5 kg) was refluxed with 95% (v/v) EtOH under reflux to afford the crude extract (1040 g), which was solved in hot water and then partitioned into ethyl acetate part (49.5 g) and *n*-butyl alcohol part (55.5 g) successively. The ethyl acetate extract was isolated by silica gel column chromatography (step with gradient PE/EtOAc 100:0, 100:1, 100:2, 100:3, 100:5, 100:6, 100:8, 100:10, 100:12, 100:20, 100:25, 100:33, 100:50, 100:100, 0:100) to afford 15 fractions (Fr.1–Fr.15). Fr.9 (250.0 mg) was purified by Sephadex LH-20 column chromatography and recrystallization to obtain **1** (20.0 mg, 0.04%) and **2** (140.0 mg), respectively.

4. The NMR data of compound 2

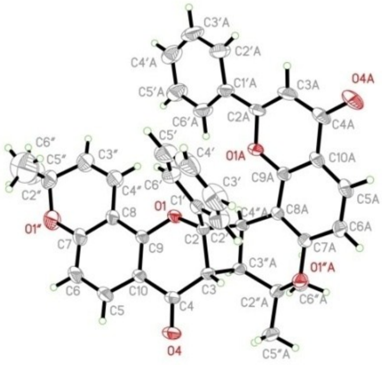
Compound 2: Yellow needle crystals (CH_2Cl_2:MeOH=1:1). The molecular formula of **2** was determined to be $C_{20}H_{16}O_3$. The ^{1}H NMR (300 MHz, $CDCl_3$): δ_H 7.99 (1 H, d,

J = 8.7 Hz, H-5), δ_H 7.90 (2 H, m, H-2′, 6′), δ_H 7.53 (3 H, m, H-3′, 4′, 5′), δ_H 6.94 (1 H, d, J = 10.0 Hz, H-4″), δ_H 6.86 (1 H, d, J = 8.7 Hz, H-6), δ_H 6.77 (1 H, s, H-3), δ_H 5.76 (1 H, d, J = 10.0 Hz, H-3″), δ_H 1.52 (6 H, s, 2″-Me2). The ^{13}C NMR (150 MHz, $CDCl_3$): δ_C 178.0 (C-4), 162.7 (C-2), 157.7 (C-7), 152.5 (C-9), 132.2 (C-1′), 131.6 (C-3″), 130.7 (C-4), 129.2 (C-3′, 5′), 126.3 (C-2′, 6′), 126.2 (C-5), 117.9 (C-10), 115.3 (C-6, 4″), 109.6 (C-8), 107.5 (C-3), 77.9 (C-2″), 28.3 (2″-Me2). It was elucidated to be 2″, 2″-dimethylchromene - [5″, 6″: 7, 8] flavone.

5. Single crystal X-ray data and structure of compound 1

Crystal data and structure refinement for compound1

Identification code	
Empirical formula	$C_{40}H_{32}O_6$
Formula weight	608.66
Temperature/K	296.15
Crystal system	triclinic
Space group	P-1
a/Å	10.438(5)
b/Å	10.700(5)
c/Å	15.172(7)
α/°	80.197(9)
β/°	70.129(9)
γ/°	79.638(9)
Volume/Å^3	1556.7(13)
Z	2
ρ_{calc}mg/mm^3	1.299
m/mm^{-1}	0.087
F(000)	640.0
Crystal size/mm^3	0.34 × 0.18 × 0.07
2Θ range for data collection	2.88 to 50.7°
Index ranges	$-12 \le h \le 12$, $-12 \le k \le 12$, $-18 \le l \le 18$
Reflections collected	16808
Independent reflections	5689[R(int) = 0.0442]
Data/restraints/parameters	5689/0/419
Goodness-of-fit on F^2	1.011
Final R indexes [I>=2σ (I)]	R_1 = 0.0518, wR_2 = 0.1225
Final R indexes [all data]	R1 = 0.1054, wR2 = 0.1483
Largest diff. peak/hole / e Å^{-3}	0.37/0.25



X-ray (MoKα) structure of **compound 1**

X-ray Crystallographic Analysis of 1. The X-ray crystallographic data of **1** was collected on a Bruker APEX DUO diffractomater and equipped with an APEX II CCD using Mo Kα radiation. **Crystal Data** for $C_{40}H_{32}O_6$ (M = 608.66): triclinic, space group P-1 (no. 2), a = 10.438(5) Å, b = 10.700(5) Å, c = 15.172(7) Å, α = 80.197(9)°, β = 70.129(9)°, γ = 79.638(9)°, V = 1556.7(13) Å^3, Z = 2, T = 296.15 K, μ(Mo Kα) = 0.087 mm^{-1}, $Dcalc$ = 1.299 g/mm^3, 16808 reflections measured ($2.88 \leq 2\Theta \leq 50.7$), 5689 unique ($R_{\mathrm{int}}$ = 0.0442) which were used in all calculations. The final R_1 was 0.0518 (>2sigma(I)) and wR_2 was 0.1483 (all data). 16808 reflections measured, 5689 unique (R_{int} = 0.0442) which were used in all calculations. The final $wR(F_2)$ was 0.1486 (all data). The crystal was kept at 296.15 K during data collection. Using Olex2,[1] the structure was solved with the olex2.solve[2] structure solution program using Charge Flipping and refined with the XL[3] refinement package using Least Squares minimisation.

Crystal data of **1** was deposited with the Cambrige Crystallographic Data Centre (1058399).

[1] O. V. Dolomanov, L. J. Bourhis, R. J. Gildea, J. A. K. Howard and H. Puschmann. *J. Appl. Cryst.* **2009**, *42*, 339-341.

[2] L. J. Bourhis, O. V. Dolomanov, R. J. Gildea, J. A. K. Howard, H. Puschmann, in preparation, **2011**

[3] G. M. Sheldrick. *Acta Cryst*. **2008**. *A64*, 112-122.

Table 1 Fractional Atomic Coordinates ($\times10^4$) and Equivalent Isotropic Displacement Parameters ($Å^2\times10^3$) for . U_{eq} is defined as 1/3 of of the trace of the orthogonalised U_{IJ} tensor.

Atom	*x*	*y*	*z*	U(eq)
O1	8490(2)	3762.3(18)	814.1(18)	106.8(8)
O2	8360.0(17)	-2141.7(16)	2190.9(15)	78.0(6)
O3	5319.0(14)	914.5(13)	2543.0(12)	54.1(5)
O4	4131.2(15)	-3274.9(13)	4309.7(12)	53.0(4)
O5	-1891.4(17)	-911(2)	4198.3(15)	81.5(6)
O6	1599.7(14)	668.8(14)	3611.2(10)	45.8(4)
C1	7397(3)	4792(3)	707(2)	75.5(8)
C2	7877(5)	5974(3)	828(4)	136.4(16)
C3	7328(6)	4838(6)	-259(3)	185(2)
C4	6076(4)	4566(3)	1403(3)	102.3(12)
C5	5810(3)	3424(3)	1835(3)	95.6(11)
C6	6862(2)	2331(2)	1661.5(18)	55.1(6)
C7	8197(3)	2554(3)	1142(2)	68.9(8)
C8	9269(3)	1571(3)	981(2)	83.8(10)
C9	9021(2)	343(3)	1345(2)	66.5(8)
C10	7699(2)	60(2)	1862.7(16)	44.5(6)
C11	6634(2)	1066(2)	2006.7(16)	43.7(6)
C12	7445(2)	-1248(2)	2269.8(17)	49.4(6)
C13	5965(2)	-1431(2)	2785.1(16)	44.4(6)
C14	4860(2)	-313.1(19)	2655.8(16)	41.5(5)
C15	4180(2)	-344(2)	1923.9(16)	51.3(6)
C16	3853(3)	744(3)	1375(2)	79.4(9)
C17	3211(4)	671(5)	714(3)	109.0(14)
C18	2886(4)	-445(6)	610(3)	112.0(15)
C19	3192(4)	-1529(5)	1159(3)	103.8(12)
C20	3840(3)	-1481(3)	1809(2)	73.4(8)
C21	4059(2)	-547(2)	3734.7(15)	38.9(5)
C22	5367(2)	-1400(2)	3869.2(16)	41.9(5)
C23	5135(2)	-2646(2)	4510.4(18)	50.7(6)
C24	6413(3)	-3617(2)	4323(2)	74.0(9)
C25	4554(3)	-2390(3)	5534.0(19)	69.2(8)
C26	2930(2)	-2549(2)	4265.5(16)	42.8(5)
C27	2854(2)	-1252(2)	3984.3(15)	38.2(5)
C28	1608(2)	-619(2)	3902.9(15)	39.8(5)
C29	461(2)	-1219(2)	4088.8(16)	45.6(6)
C30	582(2)	-2532(2)	4383.8(17)	53.4(6)

C31	1788(2)	-3191(2)	4473.7(17)	52.2(6)
C32	-804(2)	-459(3)	3973.2(17)	57.2(7)
C33	-672(2)	851(3)	3599.4(18)	61.1(7)
C34	463(2)	1385(2)	3450.0(16)	47.7(6)
C35	662(2)	2736(2)	3169.7(16)	53.8(6)
C36	-328(3)	3616(3)	2899(2)	80.1(9)
C37	-162(4)	4901(3)	2693(2)	93.1(11)
C38	960(4)	5324(3)	2745(2)	89.5(10)
C39	1947(4)	4460(3)	3002(2)	88.1(10)
C40	1801(3)	3180(3)	3205(2)	69.6(8)

6. ECD calculation methods

Computational methods for ECD of compounds 1a, 1b

The geometry determined from the X-ray analysis was used as the input for the structural optimization by the density functional theory (DFT) method at the B3LYP/6-31G(d) level in Gaussian 09 program package.[1] The optimized conformations were checked by frequency calculation. No imaginary frequencies were found. The ECD of the conformers of **1a** and **1b** were then calculated by the TDDFT method at the B3LYP/6-311++G (2d,p) level with the CPCM model in methanol solution. The calculated ECD curve was generated using SpecDis 1.6.2.[2]

Optimized conformation for compound **1a**

The energy of 1a is -1994.75218031 Hartree.

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                          Standard orientation:
---------------------------------------------------------------------
 Center     Atomic          Atomic              Coordinates (Angstroms)
 Number      Number            Type                  X                  Y
      Z
 ---------------------------------------------------------------------
      1          8             0          1.471329   -4.438460     0.958200
      2          6             0          1.397499   -3.259230     0.610730
      3          6             0          2.568459   -2.398440     0.434490
      4          6             0          3.867699   -2.889380     0.670640
      5          6             0          4.984409   -2.101130     0.466870
      6          6             0          4.814390   -0.782450     0.010100
      7          6             0          3.535870   -0.251840    -0.250670
      8          6             0          3.455480    1.097280    -0.800360
      9          6             0          4.551750    1.864190    -0.862140
     10          6             0          5.881260    1.407120    -0.308840
     11          6             0          6.107140    1.963300     1.105090
     12          6             0          7.035610    1.773799    -1.243870
     13          8             0          5.934140   -0.061080    -0.216620
     14          6             0          2.418550   -1.072460    -0.023750
```

15	8	0	1.204000	-0.534599	-0.332060
16	6	0	0.006180	-1.067379	0.284200
17	6	0	-0.319040	-0.285479	1.542320
18	6	0	0.247770	0.978311	1.767600
19	6	0	-0.062390	1.705831	2.917300
20	6	0	-0.949260	1.187011	3.862690
21	6	0	-1.524350	-0.066239	3.646510
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23	6	0	-1.017060	-1.175829	-0.920070
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45	6	0	-1.145801	-5.104769	-1.209440
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48	6	0	0.059009	-2.615649	0.323980
49	1	0	-0.674201	-3.019869	1.024700
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53	1	0	4.517350	2.866510	-1.280500
54	1	0	7.071950	1.624159	1.497880
55	1	0	6.104030	3.058400	1.085020
56	1	0	5.312560	1.631210	1.780820
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     59          1           0        7.980200     1.386539    -0.848870
     60          1           0        0.937500     1.392911     1.041680
     61          1           0        0.392300     2.680501     3.072710
     62          1           0       -1.189100     1.752811     4.758670
     63          1           0       -2.215770    -0.483689     4.373270
     64          1           0       -1.675661    -1.766179     2.356260
     65          1           0       -4.556849     3.703542    -0.032810
     66          1           0       -2.902869     5.091631     0.383990
     67          1           0       -1.271029     6.861611    -0.132150
     68          1           0        0.723531     6.359151    -1.533560
     69          1           0        1.058301     4.058541    -2.421240
     70          1           0       -0.585290     2.284231    -1.921660
     71          1           0       -6.229360    -0.834978     0.499820
     72          1           0       -5.159061    -3.079038     0.150720
     73          1           0       -1.311041    -3.684389    -3.602420
     74          1           0       -2.931931    -4.199979    -3.090930
     75          1           0       -2.494171    -2.479139    -3.066230
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     77          1           0       -1.975231    -5.800549    -1.371240
     78          1           0       -0.341691    -5.357639    -1.907950
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Optimized conformation for compound **1b**

The energy of **1b** is -1994.75218015 Hartree.

Standard orientation

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---------------------------------------------------------------------
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 Number      Number        Type             X           Y
     Z
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      4          6           0       -3.867700    -2.889379     0.670640
      5          6           0       -4.984410    -2.101129     0.466870
      6          6           0       -4.814390    -0.782449     0.010100
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      8          6           0       -3.455480     1.097281    -0.800360
      9          6           0       -4.551750     1.864191    -0.862140
     10          6           0       -5.881260     1.407121    -0.308840
     11          6           0       -7.035610     1.773801    -1.243870
     12          6           0       -6.107140     1.963301     1.105090
     13          8           0       -5.934140    -0.061079    -0.216620
     14          6           0       -2.418550    -1.072459    -0.023750
     15          8           0       -1.204000    -0.534599    -0.332060
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16	6	0	-0.006180	-1.067379	0.284200
17	6	0	0.319040	-0.285479	1.542320
18	6	0	-0.247770	0.978311	1.767600
19	6	0	0.062390	1.705831	2.917300
20	6	0	0.949260	1.187011	3.862690
21	6	0	1.524350	-0.066239	3.646510
22	6	0	1.211530	-0.795609	2.497900
23	6	0	1.017060	-1.175829	-0.920070
24	1	0	0.761750	-0.472639	-1.716560
25	6	0	2.473310	-1.090269	-0.566150
26	6	0	3.116080	0.147201	-0.390720
27	6	0	4.458580	0.261561	-0.009110
28	6	0	5.063580	1.592821	0.159290
29	6	0	4.159320	2.699031	-0.108780
30	6	0	2.861080	2.506751	-0.463140
31	6	0	1.871280	3.561651	-0.747170
32	6	0	2.049870	4.863541	-0.246850
33	6	0	1.121920	5.862551	-0.531120
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37	8	0	2.339310	1.255121	-0.606990
38	8	0	6.246110	1.755261	0.494130
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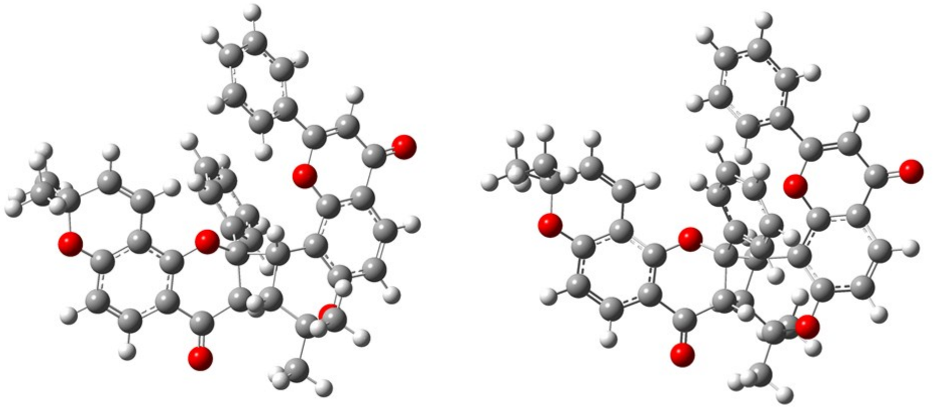
66	1	0	2.902870	5.091631	0.383990
67	1	0	1.271030	6.861611	-0.132150
68	1	0	-0.723530	6.359151	-1.533560
69	1	0	-1.058300	4.058541	-2.421240
70	1	0	0.585290	2.284231	-1.921660
71	1	0	6.229360	-0.834979	0.499820
72	1	0	5.159060	-3.079039	0.150720
73	1	0	2.931930	-4.199979	-3.090930
74	1	0	1.311040	-3.684389	-3.602420
75	1	0	2.494170	-2.479139	-3.066230
76	1	0	0.765780	-5.231899	-0.192410
77	1	0	0.341690	-5.357639	-1.907950
78	1	0	1.975230	-5.800549	-1.371240



(2*S*, 3*R*, 3"a*S*, 4"a*R*) (-) millpuline A

(2*R*, 3*S*, 3"a*R*, 4"a*S*) (+) millpuline A

B3LYP/6-31+G** optimized lowest energy 3D conformer of (2*S*, 3*R*, 3"a*S*, 4"a*R*) (-)-millpuline A and (2*R*, 3*S*, 3"a*R*, 4"a*S*) (+)-millpuline A

References

[1] Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Scalmani, G.; Barone, V.; Mennucci, B.; Petersson, G. A.; Nakatsuji, H.; Caricato, M.; Li, X.; Hratchian, H. P.; Izmaylov, A. F.; Bloino, J.; Zheng, G.; Sonnenberg, J. L.; Hada, M.; Ehara, M.; Toyota, K.; Fukuda, R.; Hasegawa, J.; Ishida,

M.; Nakajima, T.; Honda, Y.; Kitao, O.; Nakai, H.; Vreven, T.; Montgomery, J. A., Jr.; Peralta, J. E.; Ogliaro, F.; Bearpark, M.; Heyd, J. J.; Brothers, E.; Kudin, K. N.; Staroverov, V. N.; Kobayashi, R.; Normand, J.; Raghavachari, K.; Rendell, A.; Burant, J. C.; Iyengar, S. S.; Tomasi, J.; Cossi, M.; Rega, N.; Millam, J. M.; Klene, M.; Knox, J. E.; Cross, J. B.; Bakken, V.; Adamo, C.; Jaramillo, J.; Gomperts, R.; Stratmann, R. E.; Yazyev, O.; Austin, A. J.; Cammi, R.; Pomelli, C.; Ochterski, J. W.; Martin, R. L.; Morokuma, K.; Zakrzewski, V. G.; Voth, G. A.; Salvador, P.; Dannenberg, J.J.; Dapprich,S.; Daniels,A.D.;Farkas,O; Foresman, J. B.; Ortiz, J. V.; Cioslowski, J.; Fox, D. J. Gaussian 09, Revision C1; Gaussian, Inc.: Wallingford, CT, 2010.

[2] Bruhn, T.; Schaumlöffel, A.; Hemberger, Y.; Bringmann, G. Quantifying the Comparison of Calculated and Experimental Electronic Circular Dichroism Spectra, Chirality 2013, 25, 243–249.

7. The chiral separation of compound 1

Compound1 was separated by chiral HPLC method on a Daicel Chiralpak IF column (5 μm, 0.46 cm × 25 cm; Daicel, JPN) using Shimadzu UV detector (λ = 254 nm). The mobile phase was *n*-hexane: EtOH : TFA (75: 25: 0.1% v/v), and the flow rate was 1 mL/min. **Compound 1a** was obtained (t_R = 12.066 min, 1.5 mg) along with **compound 1b** (t_R =17.385 min, 1.3mg).

8. LC-MS analysis of the extract and compound 1

The fresh root of *M. pulchra* was immersed in 95% (v/v) EtOH in dark place at room temperature to afford the crude extract, which was solved in water and then partitioned by ethyl acetate to get the EtOAc extract. Liquid chromatography was performed on a Waters LC-MS Xevo G2 QTOF system. Chromatographic separation was achieved on a Waters system coupled with a DAD detection, conducting on an acquity H-class BEH-C18 column (1.7 μm, 100 × 2.1 mm) (Waters, America) at 30 °C. The mobile phase consisted of A (H_2O) and B (CH_3CN). For the EtOAc extract, a gradient program was used according to the following profile: 0-3 min, 30-45% B, 3-6 min, 45-60% B, 6-8 min, 60-85% B, 8-10 min, 85-100% B. The flow rate was 0.5 mL/min, the injection volume was 1 μL for each LC-MS analysis.

9. The synthesis of compound 1

5-hydroxy-2, 2-dimethyl-2H-chromene-6-carbaldehyde (II)

To a stirred solution of **I** (10.0 g, 72 mmol) in dry pyridine (8.04 mL) was added gradually 3-methyl-but-2-enal (6.1 g, 72 mmol) at room temperature. The reaction mixture was refluxed for 4 h at 150 °C, additional equivalent of 3-methyl-but-2-enal (6.1 g, 72 mmol) was added and refluxed for further 6 h. Excess pyridine, in the reaction mixture, was evaporated by rotary evaporator under reduced pressure. Then the crude product was subjected to silica gel column chromatography to afford desired compound **II**. Yield: 59%; ^{1}H NMR (600 MHz, $CDCl_3$) δ_H 11.65 (1 H, s, OH-3), 9.66 (1 H, s, H-1), 7.29 (1 H, d, *J* = 8.5 Hz, H-7), 6.69 (1 H, d, *J* = 10.1 Hz, H-11), 6.43 (1 H, d, *J* = 8.5 Hz, H-6), 5.61 (1 H, d, *J* = 10.1 Hz, H-10), 1.47 (6 H, s, 9-Me2).

1-(5-hydroxy-2,2-dimethyl-2H-chromen-6-yl)-3-phenylprop-2-yn-1-one (IV)

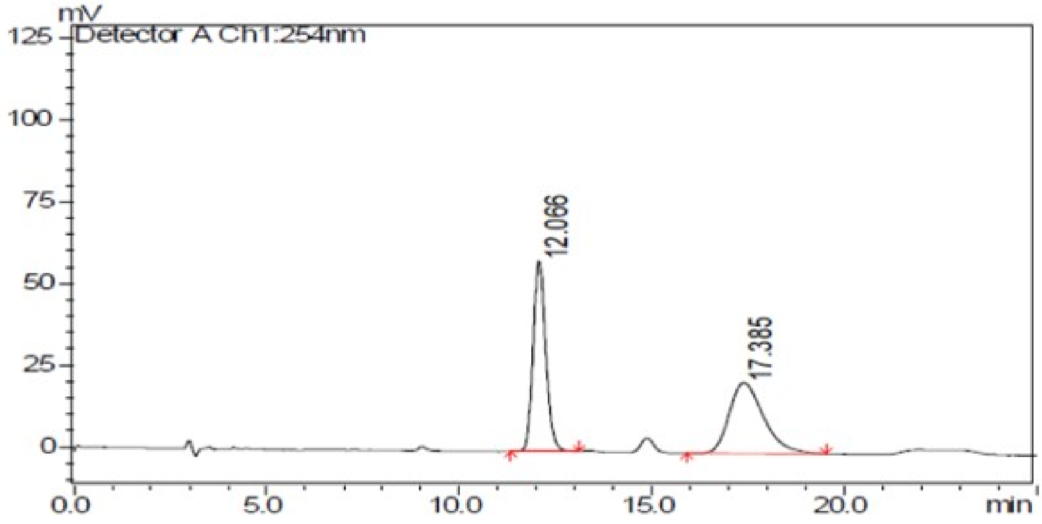
To a stirring solution of ethynylbenzene (8.5 g, 82 mmol) in THF (50 mL) was added a solution of *n*-BuLi (1.0 M in THF, 82 ml) dropwise at - 78 °C under nitrogen atmosphere. The reaction was stirred for 1 h at - 78 °C followed by the addition the solution of **II** (8.0 g, 39 mmol) in THF (10 mL) dropwise. After stirring at - 78 °C for 1h, the solution was warmed to 0 °C for another 1 h. The reaction mixture was quenched by the addition of a saturated aqueous solution of NH_4Cl. And the aqueous phase was extracted with ethyl acetate. The combined organic portions were washed with H_2O, saturated aqueous solution of NaCl, dried over anhydrous Na_2SO_4, filtered and reduced *in vacuo*. To a solution of the residue obtained above (**III**) in DCM (50 mL) was added activated MnO_2 (17.4 g, 200 mmol). The mixture was stirred at room temperature overnight. The reaction mixture was filtrated through Celite. Then the filtrate was concentrated and purified by a flash column chromatography on silica gel to afford the products **IV**. Yield: 61%; ^{1}H NMR (600 MHz, $CDCl_3$) δ_H 12.35 (1 H, s, OH-3), 7.82 (1 H, d, *J* = 8.8 Hz, H-7), 7.62 (2 H, m, H-2′, 6′), 7.41 (1 H, d, *J* = 7.5 Hz, H-4′), 7.36 (2 H, t, *J* = 7.5 Hz, H-3′, 5′), 6.65 (1 H, d, *J* = 10.1 Hz, H-11), 6.35 (1 H, d, *J* = 8.8 Hz, H-6), 5.54 (1 H, d, *J* = 10.1 Hz, H-10), 1.41 (6 H, s, 9-Me2).

2″, 2″- dimethylchromene - [5″, 6″: 7, 8] flavone (2)

To a stirring solution of **IV** in DMF (2 mL/mmol) was added DMAP (10 mol %) at 0 °C under argon. After 2 h being stirred at 30 °C, the reaction mixture was diluted with water. The aqueous layer was extracted twice with ethyl acetate. The organic layer was washed with 1 M HCl, saturated aqueous solution of $NaHCO_3$, saturated aqueous solution of NaCl, dried over anhydrous Na_2SO_4, filtered and reduced *in vacuo*, and then the resulting residue was purified by column chromatography on silica gel to afford 2″, 2″- dimethylchromene - [5″, 6″: 7, 8] flavone (**2**). Yield: 90%; ^{1}H NMR (600 MHz, $CDCl_3$) δ_H 7.99 (1 H, d, J = 8.6 Hz, H-5), 7.90 (2 H, m, H-2′, 6′), 7.53 (3 H, m, H-3′, 4′, 5′), 6.94 (1 H, d, J = 10.0 Hz, H-4″), 6.86 (1 H, d, J = 8.6 Hz, H-6), 6.76 (1 H, s, H-3), 5.76 (1 H, d, J = 10.0 Hz, H-3″), 1.52 (6 H, s, 2″-Me2).

(±)-**millpuline A (1)**

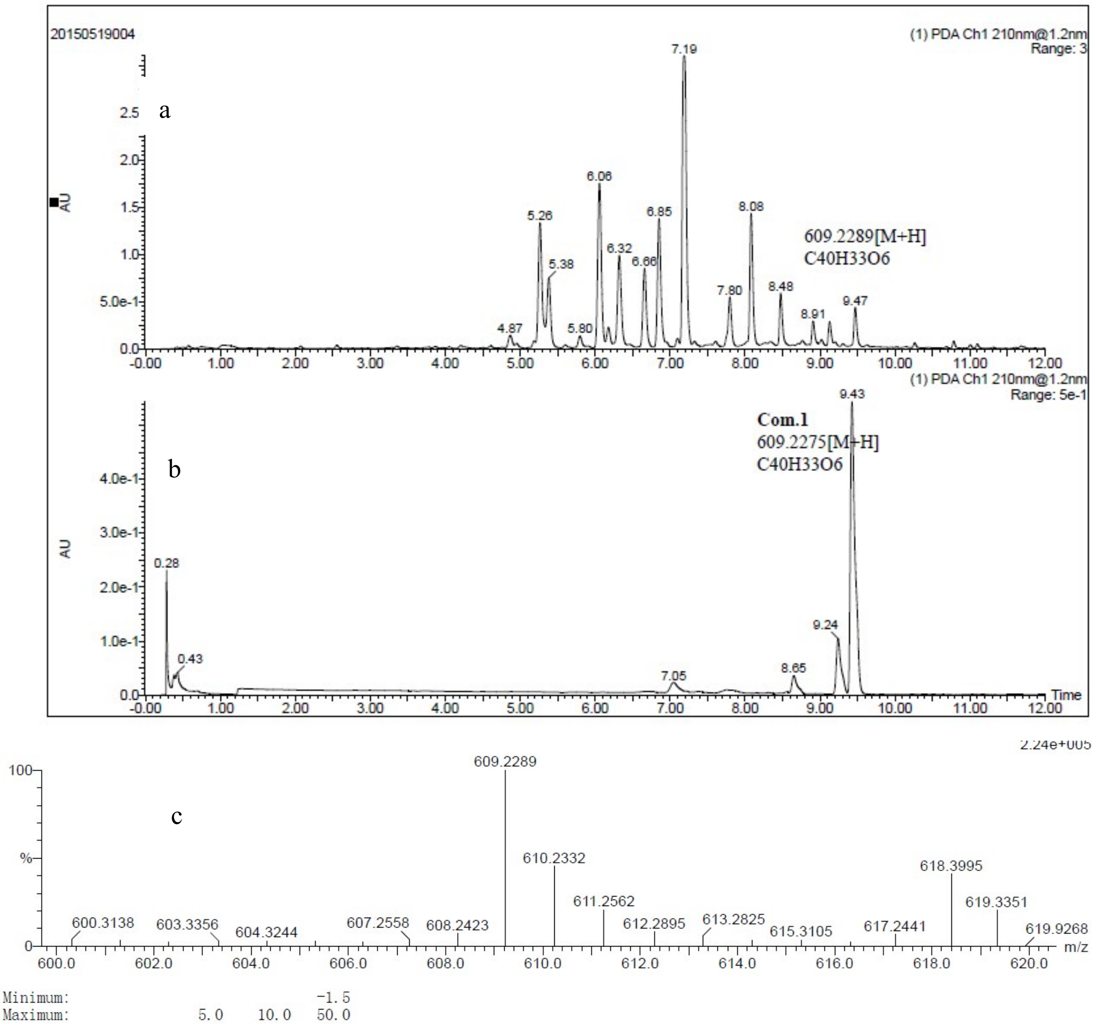
To a solution of **2** in DCM (1 mL/mmol) was irradiated with stirring using a 254 nm lamp at room temperature. The reaction was monitored by TLC, after 6 h the conversion was completed. The reaction mixture was concentrated *in vacuo* and then the resulting residue was purified by column chromatography on silica gel to afford (±)-Millpuline A (**1**). Yield: 55%; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.96 (1 H, d, J = 8.8 Hz, H-5a), 7.91 (2 H, m, H-2′a, 6′a), 7.66 (1 H, d, J = 8.6 Hz, H-5), 7.60 (3 H, d, J = 7.3 Hz, H-3′a, 4′a, 5′a), 7.03 (1 H, d, J = 10.0, H-4″), 7.02 (1H, d, J = 8.7 Hz, H-6a), 6.86 (1 H, m, H-4′), 6.80 (2 H, m, H-2′, 6′), 6.71 (2 H, m, H-3′, 5′), 6.52 (1 H, s, H-3a), 6.46 (1 H, d, J = 8.8 Hz, H-6), 5.82 (1 H, d, J = 10.0 Hz, H-3″), 4.58 (1 H, d, J = 8.6 Hz,H-4″a), 3.77 (1 H, d, J = 9.1 Hz, H-3), 3.43 (1 H, t, J = 9.1 Hz, H-3″a), 1.68 (3 H, s, CH_3-5″a), 1.54 (3 H, s, CH_3-5″), 1.49 (3 H, s, CH_3-6″), 1.27 (3 H, s, CH_3-6″a).



<Column Performance Report>

Peak No.	Time	Area	Area %	Plate number	Tailing	Resolution
1	12.066	1330874	49.8773	6529.849	1.177	--
2	17.385	1337424	50.1227	1909.478	1.373	4.861

Figure S1 The chiral separation of **compound 1**.



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Minimum:                          -1.5
Maximum:              5.0   10.0  50.0
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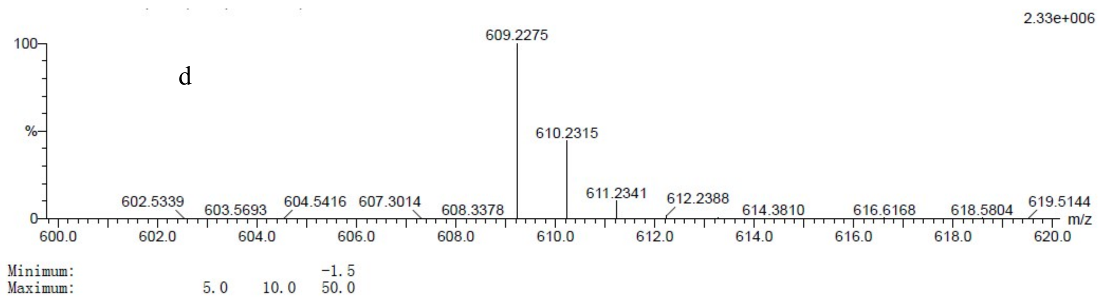


Figure S2 The LC-MS chromatogram of EtOAc extract (a, c) of *M.pulchra* and **compound 1** (b, d)

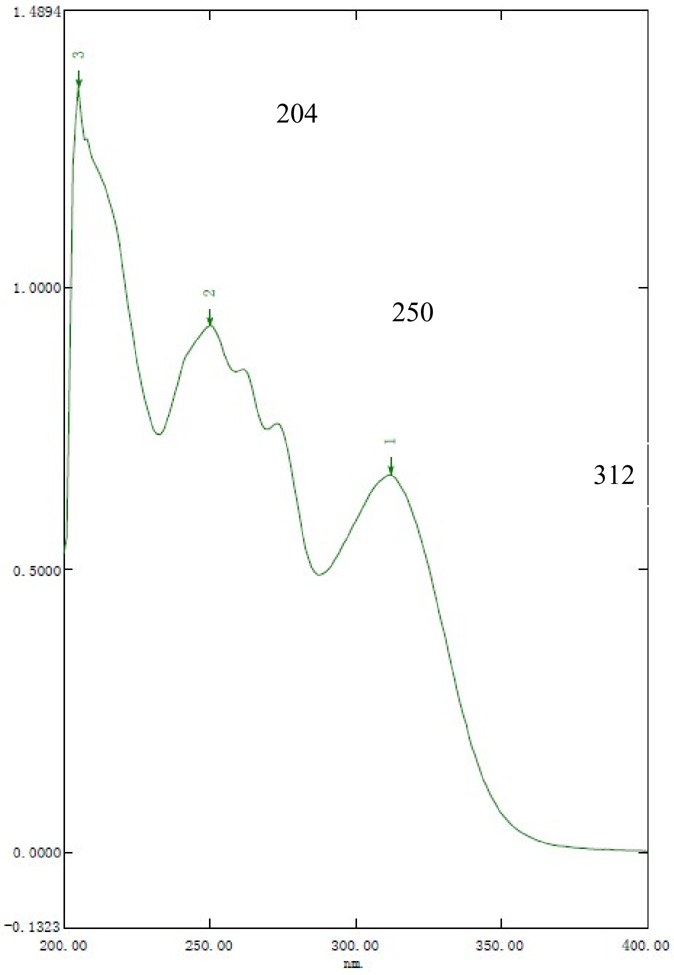
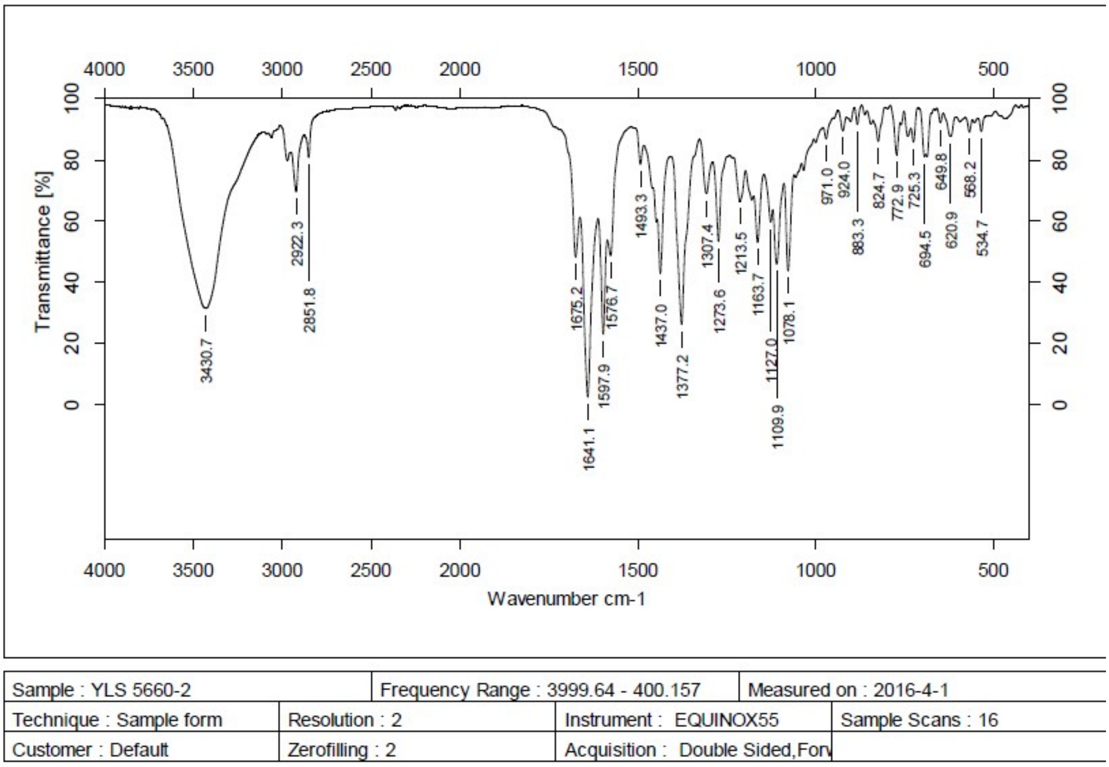
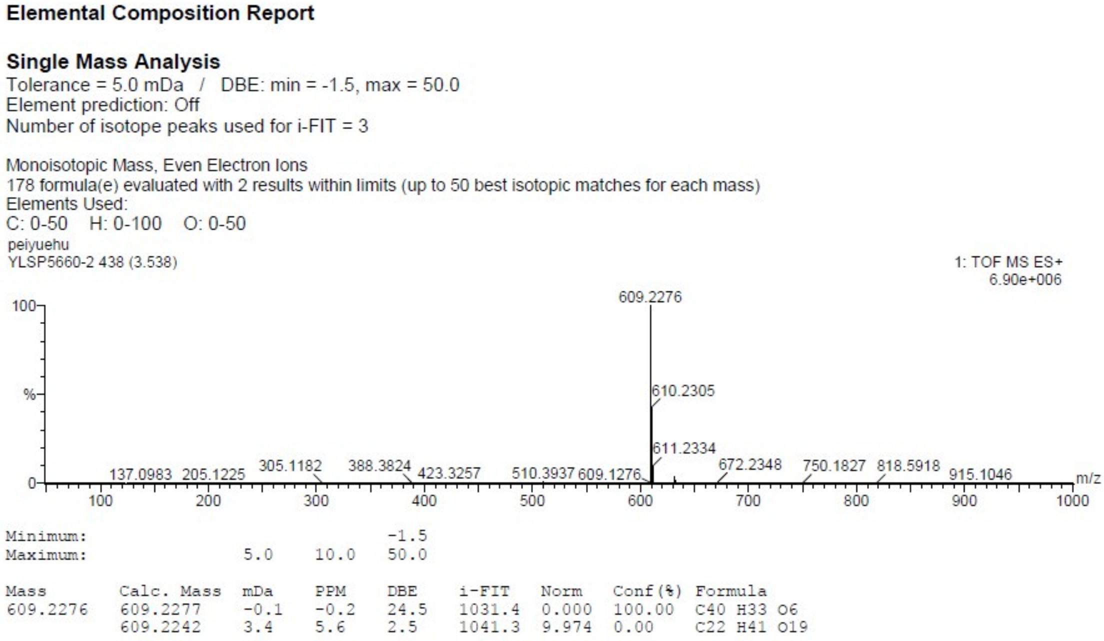


Figure S3 The UV spectrum of **compound 1** measured in MeOH.



Sample : YLS 5660-2	Frequency Range : 3999.64 - 400.157	Measured on : 2016-4-1	
Technique : Sample form	Resolution : 2	Instrument : EQUINOX55	Sample Scans : 16
Customer : Default	Zerofilling : 2	Acquisition : Double Sided,For	

Figure S4 The IR spectrum of **compound 1**.



Elemental Composition Report

Single Mass Analysis
Tolerance = 5.0 mDa / DBE: min = -1.5, max = 50.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions
178 formula(e) evaluated with 2 results within limits (up to 50 best isotopic matches for each mass)
Elements Used:
C: 0-50 H: 0-100 O: 0-50
peiyuehu
YLSP5660-2 438 (3.538)

1: TOF MS ES+
6.90e+006

```
Minimum:                              -1.5
Maximum:                5.0    10.0   50.0

Mass      Calc. Mass  mDa    PPM    DBE    i-FIT   Norm   Conf(%) Formula
609.2276  609.2277    -0.1   -0.2   24.5   1031.4  0.000  100.00  C40 H33 O6
          609.2242    3.4    5.6    2.5    1041.3  9.974  0.00    C22 H41 O19
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Figure S5 The HRESIMS spectrum of **compound 1** measured in MeOH.

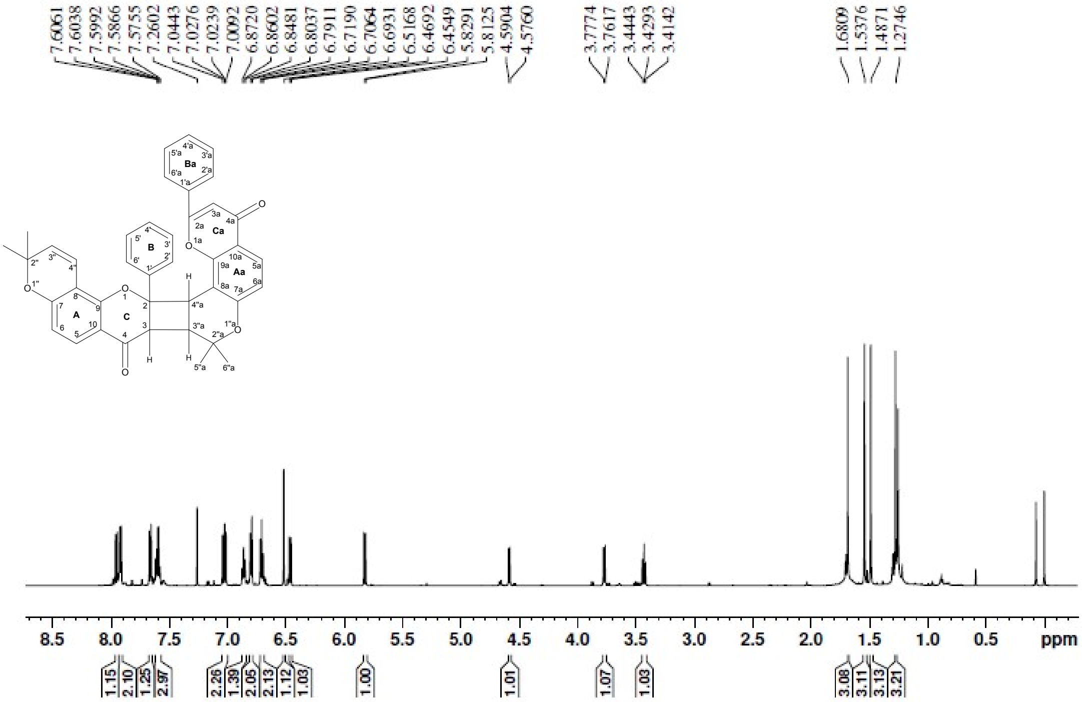


Figure S6 The ^{1}H NMR spectrum of **compound 1** measured in $CDCl_3$ (600 MHz).

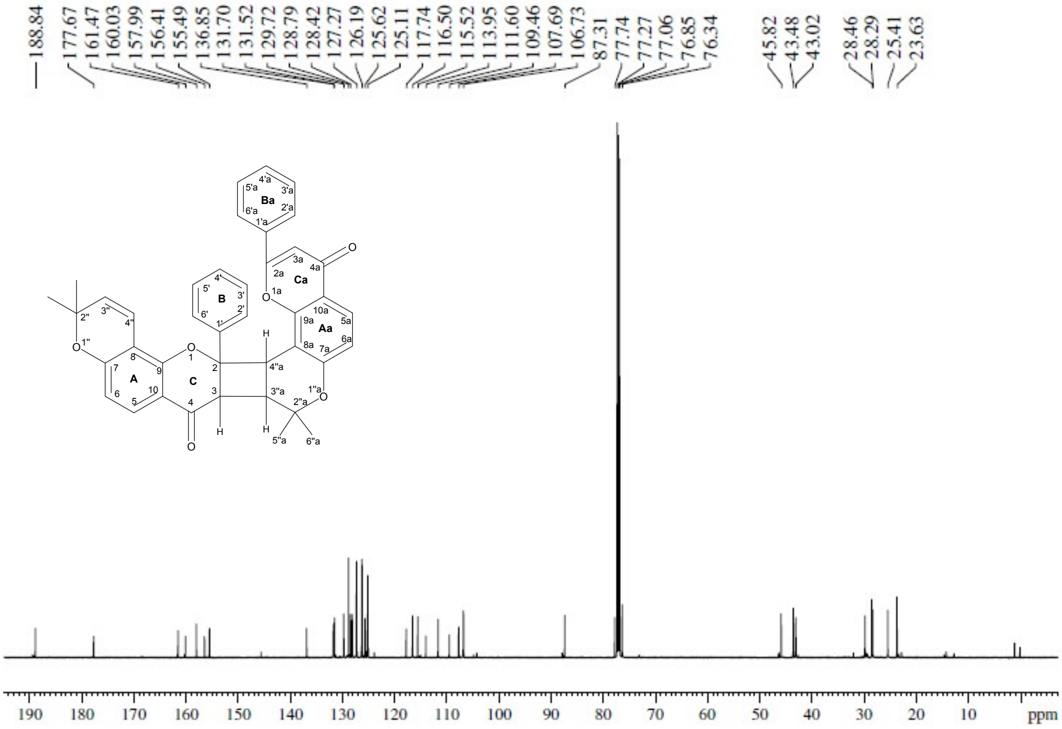


Figure S7 The ^{13}C NMR spectrum of **compound 1** measured in $CDCl_3$ (150 MHz).

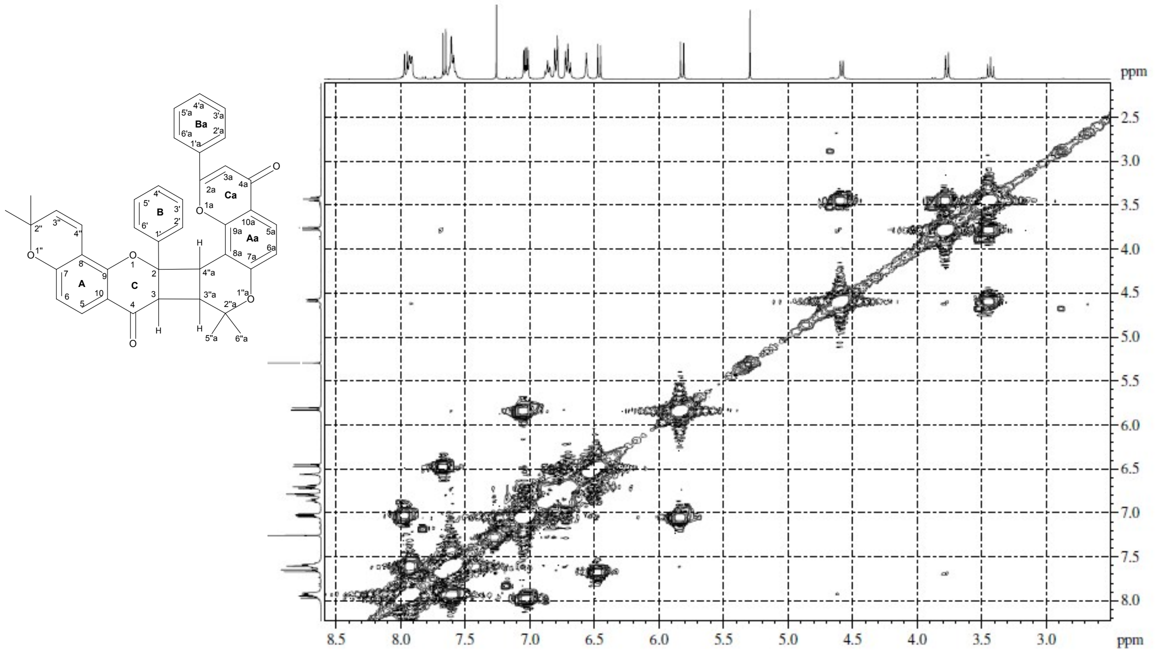


Figure S8 The ^1H-^1H COSY spectrum of **compound 1** measured in $CDCl_3$ (600 MHz).

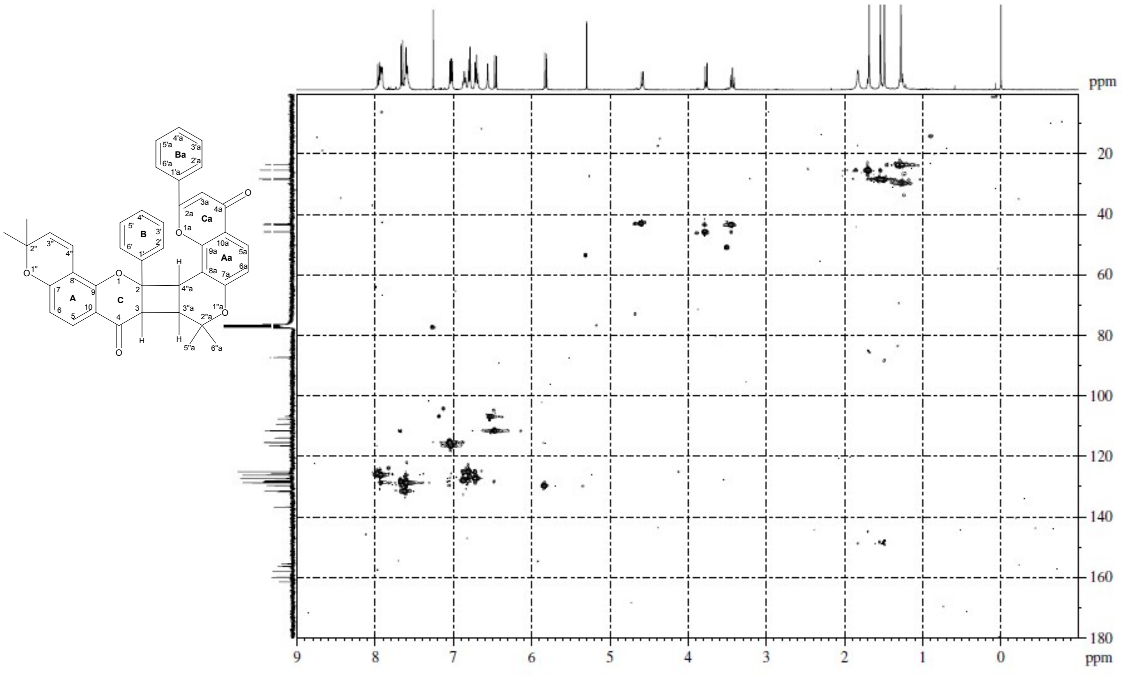


Figure S9 The HSQC spectrum of **compound 1** measured in $CDCl_3$ (600 MHz).

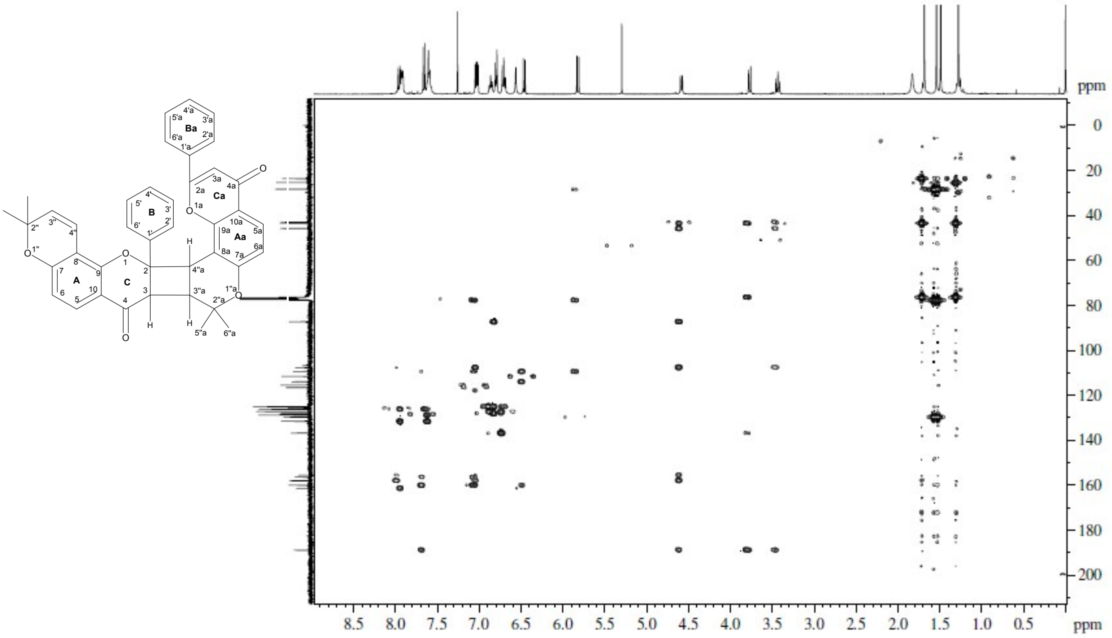


Figure S10 The HMBC spectrum of **compound 1** in $CDCl_3$ (600 MHz).

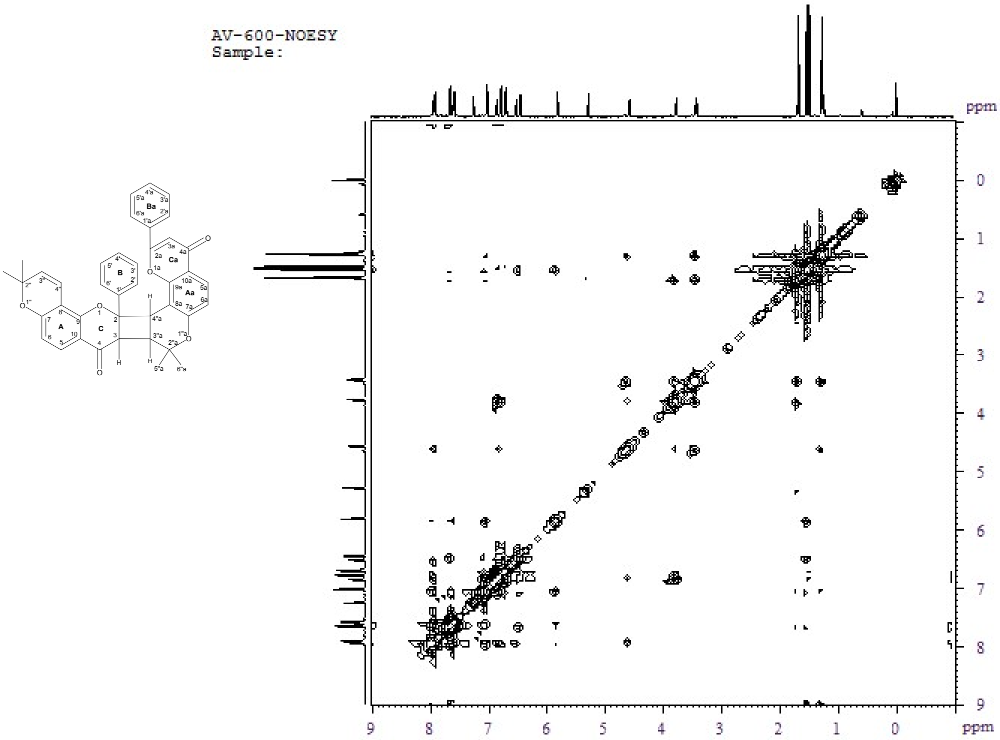


Figure S11 The NOESY spectrum of **compound 1** measured in $CDCl_3$ (600 MHz).

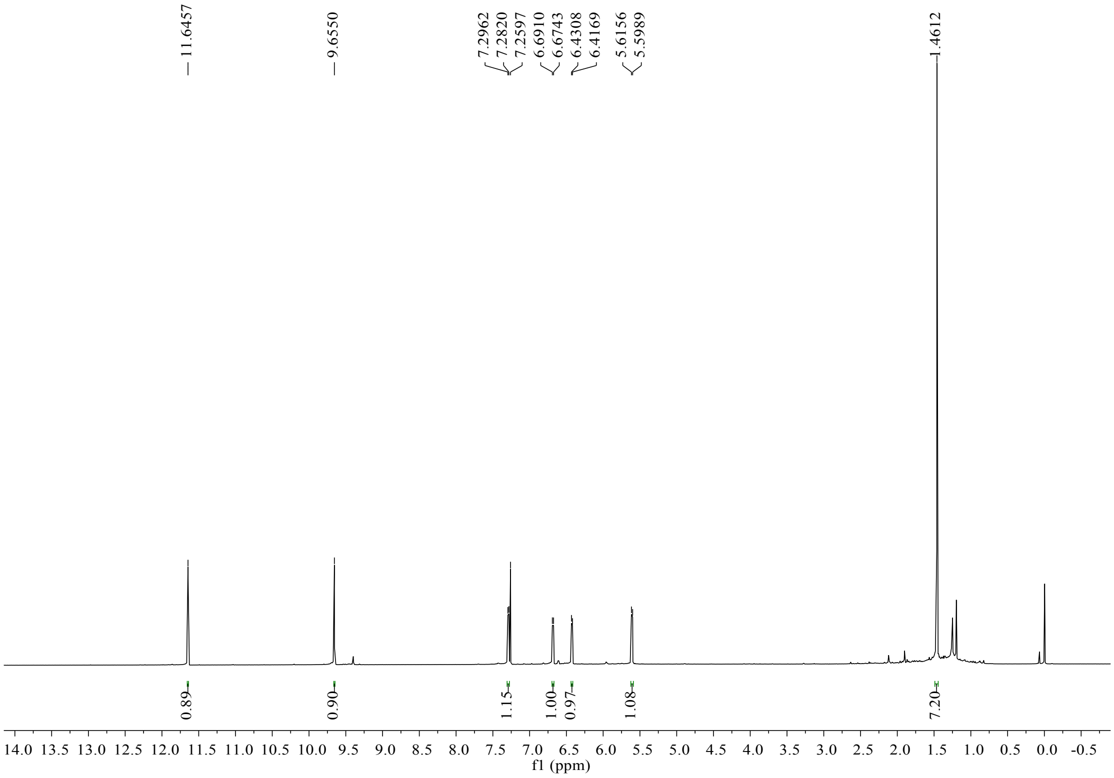


Figure S12 The ^{1}H NMR spectrum of **compound Ⅱ** measured in CDCl$_3$ (600 MHz).

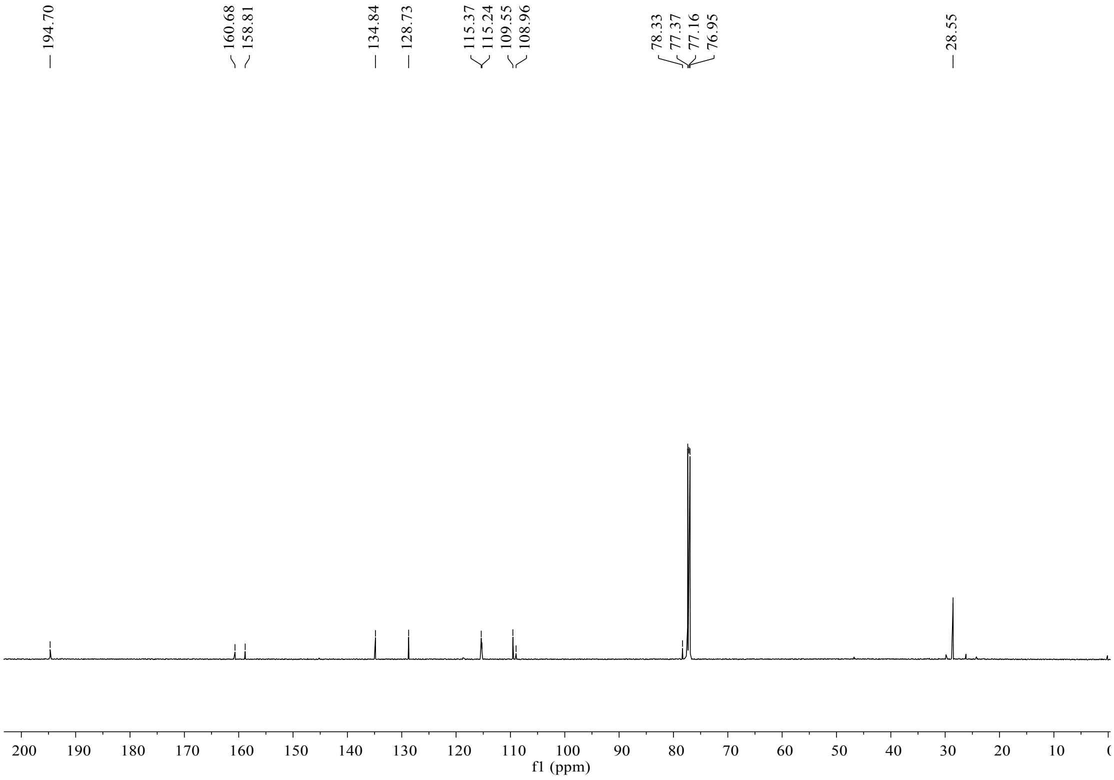


Figure S13 The ^{13}C NMR spectrum of **compound Ⅱ** measured in CDCl$_3$ (150 MHz).

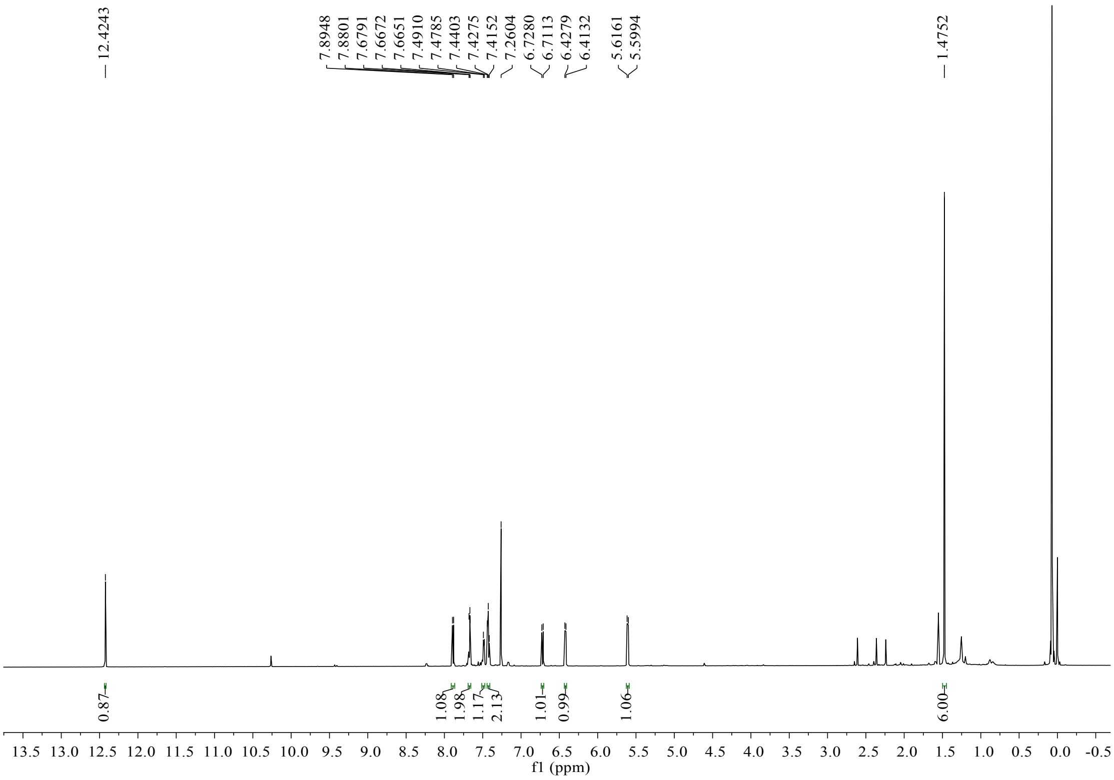


Figure S14 The ^{13}C NMR spectrum of **compound Ⅳ** measured in $CDCl_3$ (600 MHz).

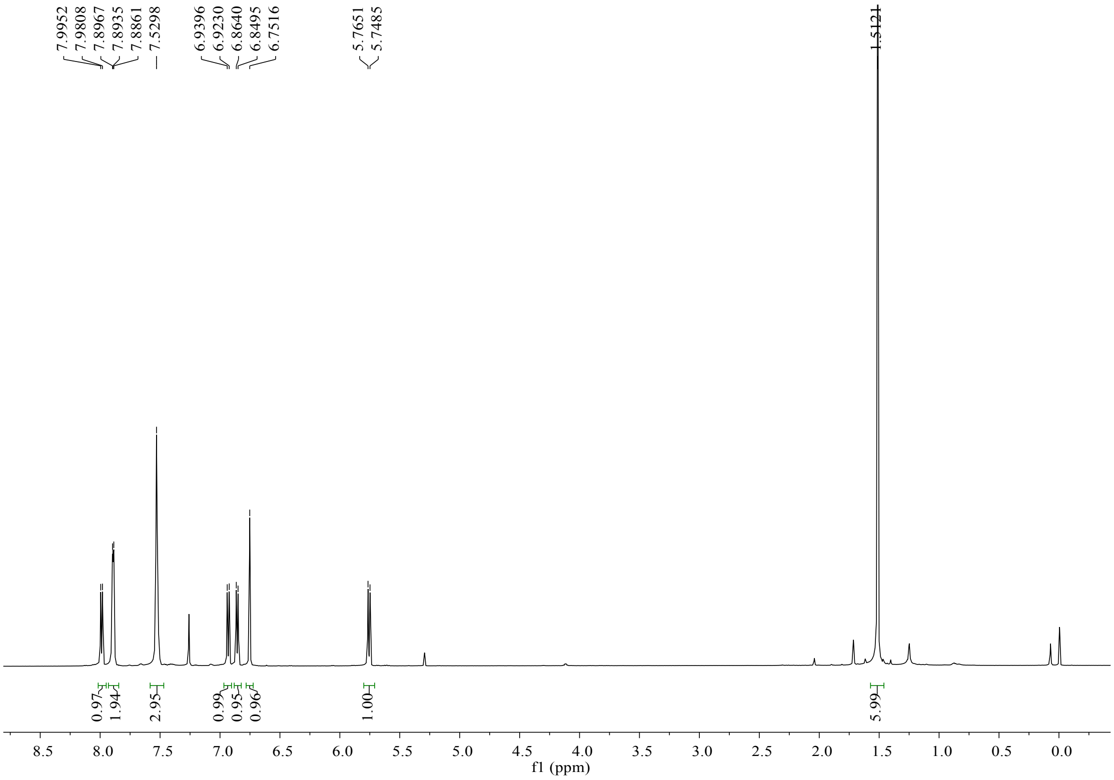


Figure S15 The ^{1}H NMR spectrum of **compound 2** (synthesis-product) measured in $CDCl_3$ (600 MHz).

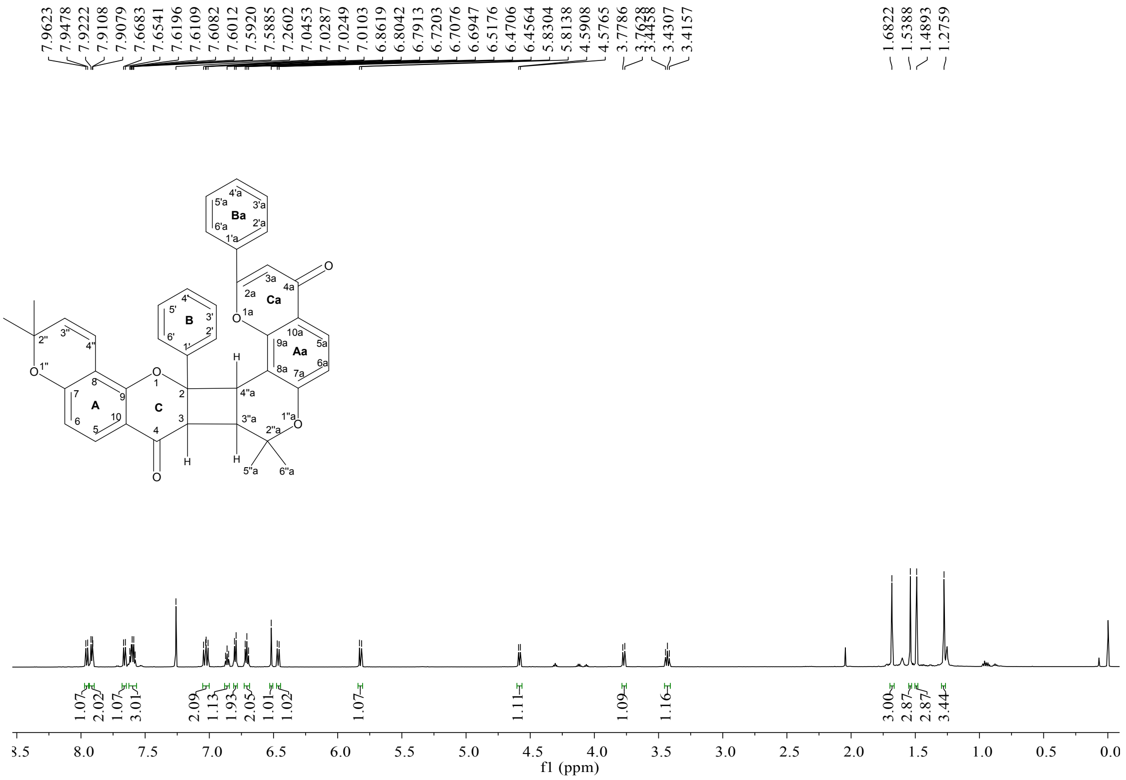


Figure S16 The ^{1}H NMR spectrum of **compound 1** (synthesis-product) measured in $CDCl_3$ (600 MHz).

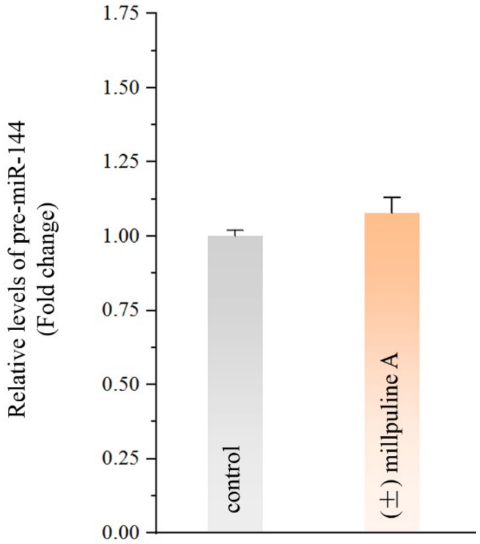
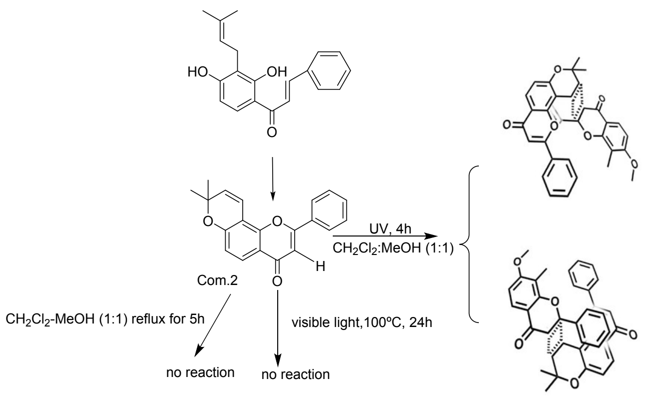


Figure S17 RT-qPCR results of pre-miR-144. 10 μM of (±) millpuline A was used to treat A549 cells for 48 h.



Shceme 1. The photochemical semi-synthesis from **2** to **1**.