Electronic Supplementary Material (ESI) for MedChemComm.

Supporting Information

Structural optimization and antibacterial evaluation of rhodomyrtosone B analogues against MRSA strains

Liyun Zhao[a, c,1], Hongxin Liu[a, b,1], Luqiong Huo[a, c], Miaomiao Wang[a, c], Bao Yang[a], Weimin Zhang[b], Zhifang Xu[a], Haibo Tan[a, *] Sheng-Xiang Qiu[a, *]

[a] *Key Laboratory of Plant Resources Conservation and Sustainable Utilization, South China Botanical Garden, Chinese Academy of Sciences, Guangzhou, 510650, People's Republic of China.*

[b] *State Key Laboratory of Applied Microbiology Southern China, Guangdong Provincial Key Laboratory of Microbial Culture Collection and Application, Guangdong Open Laboratory of Applied Microbiology, Guangdong Institute of Microbiology, Guangzhou 510070, People's Republic of China*

[c] *University of Chinese Academy of Sciences, Beijing 100049, People's Republic of China.*

Table of Contents

Abbreviations

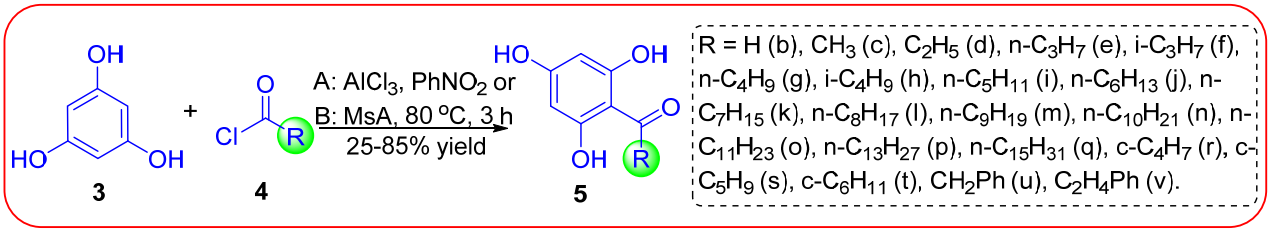
Ac	Acetyl
ACN	Acetonitrile
DCE	1,2-Dichloroethane
DMSO	Dimethylsulfoxide
DCM	Dichloromethane
THF	Tetrahydrofuran
TFA	Trifluoroacetic acid
PTSA	*p*-Toluenesulfonic acid
MSA	Methylsulphonic acid
HRMS	High resolution mass spectroscopy
NMR	Nuclear magnetic resonance
HPLC	High performance liquid chromatography
rt	Room temperature
ESI	Electron spray ionization
TLC	Thin layer chromatography

Experimental Procedures

All reactions were carried out under a nitrogen atmosphere with dry solvents under anhydrous conditions, unless otherwise noted. Reagents were purchased at high commercial quality, and used without further purification. Thin-layer chromatography (TLC) was conducted with 0.25 mm Tsingdao silica gel plates (60F-254) and visualized by exposure to UV light (254 nm) or stained with potassium permanganate. Silica gel (ZCX-II, 200-300 mesh) used for flash column chromatography was purchased from Qing Dao Hai Yang Chemical Industry Co. of China. ^{1}H NMR and ^{13}C NMR spectra were recorded on a Brüker Advance 500 (^{1}H: 500 MHz, ^{13}C: 125 MHz) or Brüker Advance 600 (^{1}H: 600 MHz, ^{13}C: 150 MHz). Chemical shifts reported in parts per million relative to $CDCl_3$ (^{1}H NMR; 7.28 ppm, ^{13}C NMR; 77.00 ppm), CD_3OD (^{1}H NMR; 3.33 ppm, ^{13}C NMR; 47.5 ppm), and DMSO-d_6 (^{1}H NMR; 2.50 ppm, ^{13}C NMR; 39.5 ppm). Mass spectrometric data were obtained using ABI-Q Star Elite high resolution mass spectrometer. Anhydrous THF was distilled from sodium-benzophenone until a deep blue color persisted, CH_2ClCH_2Cl (DCE) was distilled from calcium hydride. Yields referred to chromatographically purified products unless otherwise stated. The following abbreviations were used to explain the multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, brs = broad singlet.

Representative procedure for the preparation of rhodomyrtosone B analogues 11

The syntheses of acylphloroglucinols **5**



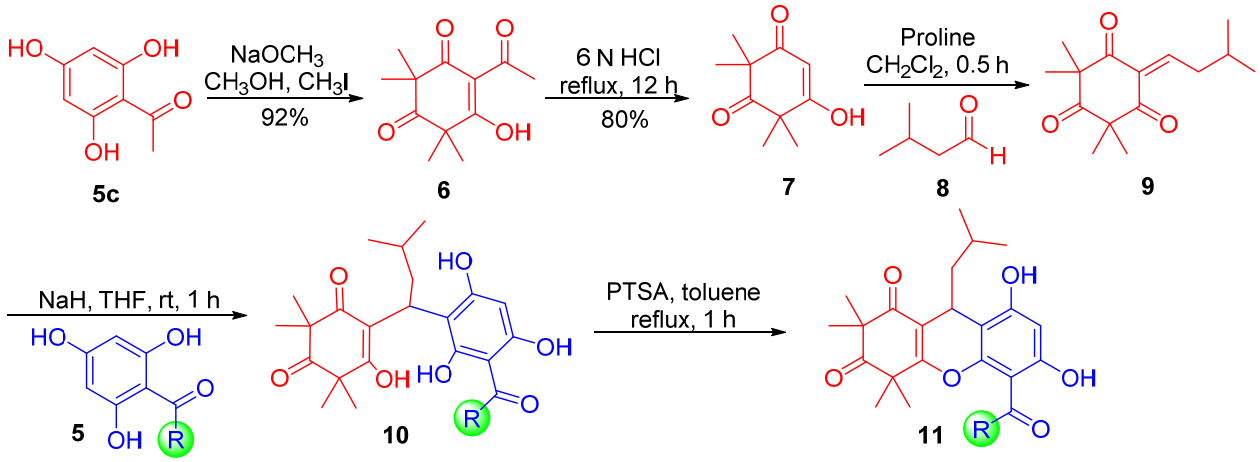
General procedure for the syntheses of intermediate compounds **5d-5k:**

$AlCl_3$ (1.33 g, 10 mmol) was slowly and carefully added to a solution of phloroglucinol **3** (315 mg, 2.5 mmol) in $CH_2ClCH_2Cl/PhNO_2$ (1:1, 10 mL) at 0 °C. After stirring at this temperature for 10 min under nitrogen atmosphere, acid chloride **4** (3.0 mmol) was added. The ice bath was removed, the mixture was stirred at 80 °C for 3 h. Then, the crude mixture was cooled to room temperature and quenched with water (25 mL). The mixture was extracted with EtOAc (5 x 25 mL), washed with brine, concentrated in *vacuo*. The crude product was purified by flash chromatography (silica gel, hexane/EtOAc = 2: l) to provide the correspounding acylphloroglucinols **5d-5k** with yields ranging from 60-80%.

General procedure for the syntheses of intermediate compounds **5l-5v**

To a solution of phloroglucinol **4** (315 mg, 2.5 mmol) in acid chloride **5** (3.0 mmol) was added methanesulfonic acid (720 mg, 7.5 mmol). After stirring at room temperature for 10 min under nitrogen atmosphere, the mixture was stirred at 80 °C for another 1 h. Then, the crude mixture was cooled to room temperature and quenched with water (25 mL). The mixture was extracted with EtOAc (5 x 25 mL), washed with brine, concentrated in *vacuo*. The crude product was purified by flash chromatography (silica gel, hexanes: EtOAc = 2 : 1) to provide compounds **5l-5v** with the yields ranging from 25%-80%.

The synthesis of rhodomyrtosone B analogues **11**



The syntheses of 4-acetyl-5-hydroxy-2,2,6,6-tetramethylcyclohex-4-ene-1,3-dione **6**

Sodium methoxide (7.18 g, 133 mmol) was slowly dissolved in anhydrous methanol (60 mL) at 0 ^{o}C. To this clear solution, acetylphloroglucinol **5c** (2.75 g, 16.5 mmol) was added carefully and stirred for 10 min under nitrogen atmosphere. Then, methyl iodide (32.4 g, 14.2 mL, 228 mmol) was slowly added. After finishing addition, the ice bath was removed and the mixture was stirred at room temperature for 24 h. The crude mixture was quenched with 2 N HCl (60 mL) and extracted with $CHCl_3$ (5 x 60 mL), washed with brine and concentrated in *vacuo*. The crude product was purified by flash chromatography (silica gel, hexanes: EtOAc = 5: l) to provide **6** (3.17 g, 14.2 mmol, 86% yield) as a yellow rod-like crystal. ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.33 (s, 6H), 1.42 (s, 6H), 2.57 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 23.8, 24.3, 27.4, 52.0, 56.7, 109.4, 196.7, 199.1, 201.7, 210.0.

The syntheses of syncarpic acid **7**

A flame-dried 50 mL flask was charged with 6 N HCl (30 mL) and **6** (3.17 g, 14.2 mmol). The reaction mixture was stirred vigorously and refluxed for 24 h. Then, the mixture was cooled to room temperature and extracted with EtOAc (5 x 50 mL). The combined organics were washed with brine (30 mL), dried over Na_2SO_4, and filtered. Removal of solvent by rotary evaporation and purification by a short flash column chromatography (silica gel, hexane: EtOAc = 1: l) to afford **7** (2.17 g, 11.4 mmol, 80% yield). ^{1}H NMR (500 MHz, $CDCl_3$): ketone: δ 1.31 (s, 12H), 3.61 (s, 2H); enol: δ 1.40 (s, 12H), 5.74 (br d, J = 2.3 Hz, 1H), 8.00 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): ketone: δ 21.8, 50.2, 59.1, 204.3, 208.9; enol：δ 24.5, 51.2, 59.1, 101.7, 191.9, 204.3, 212.6.

The syntheses of 2,2,4,4-tetramethyl-6-(3-methylbutylidene) cyclohexane-1,3,5-trione **9**

The syncarpic acid **7** (91 mg, 0.5 mmol) was dissolved in CH_2Cl_2 (5 mL), isovaleraldehyde **8** (86 mg, 1.0 mmol) and proline (5.7 mg, 0.5 mmol) were added. The resulting mixture was stirred for 30 min at room temperature, then purified by a 3 cm long flash chromatography (silica gel, CH_2Cl_2) to afford the desired product **9** (125 mg, 100% yield) as colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ 0.95 (d, J = 6.7 Hz, 6H), 1.30 (s, 6H), 1.31 (s, 6H), 1.89 (m, J = 6.7 Hz,1H), 2.59 (dd, J = 3.0, 3.0 Hz, 2H), 7.51 (dd, J = 3.0 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 21.9, 22.3, 22.6, 28.7, 38.9, 57.9, 58.6, 133.1, 159.1, 196.4, 199.5, 208.8.

General procedure for the syntheses of acyclic analogous **10**

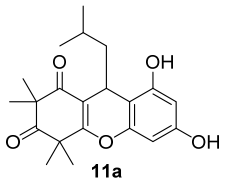
Sodium hydride (30.0 mg, 0.75 mmol, 60% in mineral oil) was carefully added to a solution of acetylphloroglucinol **5** (0.5 mmol) in THF (8 mL), then the unsaturated triketone **9** (62.5 mg, 0.25 mmol) in THF (2 mL) was slowly added. The resulting mixture was stirred for 0.5 h at room temperature. Then quenched it with 1 N HCl (3 mL) and extracted with EtOAc (3 x 5 mL), washed with

brine and concentrated in *vacuo*. The crude product was purified by flash chromatography (silica gel, hexanes : EtOAc = 10 : l to 2 : l) to provide **10** with yields ranging from 30% to 90%.

General procedure for the syntheses of rhodomyrtosone B analogues **11**

To a solution of acyclic analogous **11** (0.5 mmol) in toluene (6 mL) was carefully added PTSA (34 mg, 0.2 mmol), then the mixture was heated to reflux. After stirring at the reflux condition for 0.5 h, it was cooled to room temperature and directly purified by flash column chromatography (silica gel, hexanes: EtOAc = 10 : l to 2 : l) to provide **11** with yields ranging from 60% to 90%.

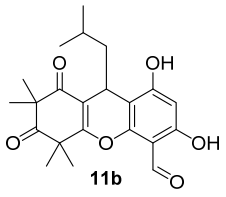
6,8-Dihydroxy-9-isobutyl-2,2,4,4-tetramethyl-4,9-dihydro-1H-xanthene-1,3(2H)-dione 11a:



11a

Following the typical procedure, **11a** were obtained in 46% overall yield for 3 steps as slight yellow oil. ^{1}H NMR (500 MHz, Acetone): δ 8.73 (s, 1H), 8.41 (s, 1H), 6.31 (d, J = 2.2 Hz, 1H), 6.22 (d, J = 2.3 Hz, 1H), 4.24 (t, J = 5.9 Hz, 1H), 1.66-1.29 (m, 15H), 0.84 (dd, J = 15.6, 6.5 Hz, 6H); ^{13}C NMR (126 MHz, Acetone): δ 211.8, 196.7, 167.5, 157.0, 155.6, 152.8, 113.5, 105.1, 99.1, 94.7, 55.4, 46.9, 46.1, 25.4, 24.8, 24.3, 24.2, 23.9, 23.6, 23.2, 22.8.

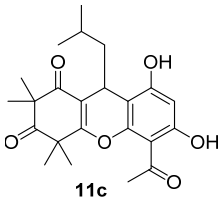
6,8-Dihydroxy-9-isobutyl-2,2,4,4-tetramethyl-1,3-dioxo-2,3,4,9-tetrahydro-1H-xanthene-5-carbaldehyde 11b:



11b

Following the typical procedure, **11b** were obtained in 46% overall yield for 3 steps as slight yellow oil. ^{1}H NMR (500 MHz, Acetone): δ 12.15 (s, 1H), 10.40 (s, 1H), 10.31 (s, 1H), 6.26 (s, 1H), 4.23 (t, J = 5.9 Hz, 1H), 1.64 (s, 3H), 1.59-1.33 (m, 12H), 0.86 (dd, J = 21.1, 6.5 Hz, 6H); ^{13}C NMR (125 MHz, Acetone): δ 211.1, 196.8, 190.8, 166.6, 163.6, 163.3, 154.1, 113.9, 105.9, 104.4, 98.3, 55.8, 47.2, 46.0, 25.0, 24.8, 24.3, 24.1, 24.1, 23.4, 22.9, 22.7.

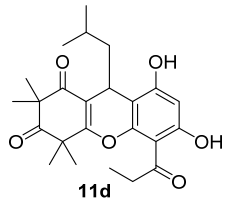
5-Acetyl-6,8-dihydroxy-9-isobutyl-2,2,4,4-tetramethyl-4,9-dihydro-1H-xanthene-1,3(2H)-dione 11c:



11c

Following the typical procedure, **11c** were obtained in 46% overall yield for 3 steps as slight yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ 13.53 (s, 1H), 6.29 (s, 1H), 4.33 (t, J = 6.1 Hz, 1H), 2.82 (s, 3H), 1.65 (s, 3H), 1.50 (d, J = 5.6 Hz, 4H), 1.45 (d, J = 3.7 Hz, 4H), 1.42 (d, J = 7.3 Hz, 4H), 1.39 (s, 1H), 0.89 (t, J = 6.3 Hz, 6H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 211.7, 201.6, 198.4, 167.3, 164.6, 160.1, 153.3, 114.6, 106.0, 105.4, 100.1, 56.1, 47.2, 46.9, 33.2, 25.4, 25.0, 24.8, 24.7, 24.5, 24.3, 23.4, 23.1.

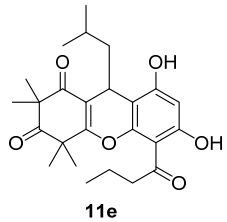
6,8-Dihydroxy-9-isobutyl-2,2,4,4-tetramethyl-5-propionyl-4,9-dihydro-1H-xanthene-1,3(2H)-dione 11d:



11d

Following the typical procedure, **11d** were obtained in 46% overall yield for 3 steps as slight yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ 13.57 (s, 1H), 6.30 (s, 1H), 4.34 (t, J = 6.0 Hz, 1H), 3.36-3.22 (m, 1H), 3.19-3.07 (m, 1H), 1.65 (s, 3H), 1.56-1.25 (m, 15H), 0.88 (t, J = 6.7 Hz, 6H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 211.8, 204.9, 198.5, 167.3, 164.4, 159.8, 153.2, 114.5, 105.9, 105.0 100.2, 56.1, 47.3, 46.8, 37.8, 25.4, 25.0, 24.8, 24.7, 24.5, 24.3, 23.4, 23.1, 8.6.

5-Butyryl-6,8-dihydroxy-9-isobutyl-2,2,4,4-tetramethyl-4,9-dihydro-1H-xanthene-1,3(2H)-dione 11e:

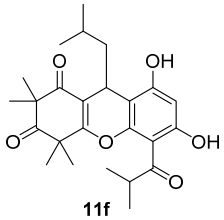


11e

Following the typical procedure, **11e** were obtained in 43% overall yield as slight yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ 13.58 (s, 1H), 7.66 (s, 1H), 6.32 (s, 1H), 4.36 (t, J = 6.0 Hz, 1H), 3.30 (ddd, J = 17.5, 9.0, 6.0 Hz, 1H), 3.10 (ddd, J = 17.5, 8.9, 5.9 Hz, 1H), 1.76 (ddd, J = 9.8, 8.5, 4.6 Hz, 2H), 1.66 (s, 3H), 1.45 (dd, J = 29.8, 12.2 Hz, 14H), 1.00 (t, J = 7.3 Hz, 3H), 0.89 (dd, J = 6.4, 4.4 Hz, 6H); ^{13}C

NMR (125 MHz, $CDCl_3$): δ 211.8, 204.5, 198.9, 167.6, 164.4, 159.9, 153.1, 114.6, 106.0, 105.1, 100.3, 56.1, 47.3, 46.9, 44.5, 26.3, 25.4, 25.0, 24.7, 24.6, 24.5, 23.5, 23.1, 22.4, 14.1.

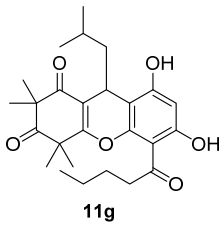
6,8-dihydroxy-9-isobutyl-5-isobutyryl-2,2,4,4-tetramethyl-4,9-dihydro-1H-xanthene-1,3(2H)-dione 11f:



11f

Following the typical procedure, **11f** were obtained in 43% overall yield as slight yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ 13.43 (s, 1H), 7.70 (s, 1H), 6.33 (s, 1H), 4.35 (t, J = 5.9 Hz, 1H), 3.93 (dt, J = 13.6, 6.8 Hz, 1H), 2.04 (s, 1H), 1.62 (s, 3H), 1.54 – 1.35 (m, 13H), 1.28 (dd, J = 6.8, 2.0 Hz, 6H), 0.93 – 0.84 (m, 6H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 211.8, 209.1, 198.7, 167.5, 164.7, 159.8, 152.7, 114.5, 106.0, 103.9, 100.4, 56.1, 47.2, 46.6, 39.6, 25.2, 25.0, 24.9, 24.6, 24.5, 24.3, 23.5, 23.2, 20.8, 18.0.

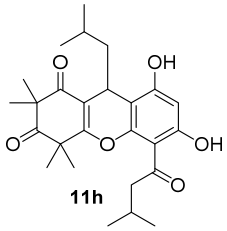
5-Pentanoyl-6,8-dihydroxy-9-isobutyl-2,2,4,4-tetramethyl-4,9-dihydro-1H-xanthene-1,3(2H)-dione 11g:



11g

Following the typical procedure, **11g** were obtained in 43% overall yield as slight yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ 13.58 (brs, 1H), 7.66 (s, 1H), 6.32 (s, 1H), 4.35 (t, J = 6.0 Hz, 1H), 3.29 (ddd, J = 17.5, 9.0, 6.0 Hz, 1H), 3.09 (ddd, J = 17.5, 9.0, 5.9 Hz, 1H), 1.90-1.72 (m, 2H), 1.66 (s, 3H), 1.58 -1.33 (m, 14H), 0.94 (dd, J = 8.3, 5.5 Hz, 3H), 0.88 (dd, J = 6.3, 5.2 Hz, 6H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 211.8, 204.5, 198.9, 167.5, 164.4, 160.0, 153.1, 114.6, 106.0, 105.1, 100.2, 56.1, 47.3, 46.9, 44.5, 26.3, 25.4, 25.0, 24.8, 24.7, 24.5, 24.3, 23.8, 23.4, 23.1, 22.4, 14.1.

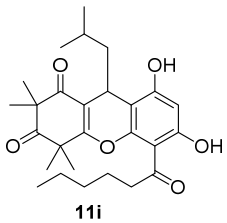
6,8-Dihydroxy-9-isobutyl-2,2,4,4-tetramethyl-5-(3-methylbutanoyl)-4,9-dihydro-1H-xanthene-1,3(2H)-dione 11h:



11h

Following the typical procedure, **11h** were obtained in 47% yield as slight yellow solid. ^{1}H NMR (500 MHz, $CDCl_3$): δ 13.52 (s, 1H), 7.51 (s, 1H), 6.31 (s, 1H), 4.34 (t, J = 6.1 Hz, 1H), 3.21 (dd, J = 17.2, 7.4 Hz, 1H), 2.98 (dd, J = 17.2, 6.2 Hz, 1H), 2.38 (dt, J = 13.5, 6.7 Hz, 1H), 1.66 (s, 3H), 1.50 (s, 3H), 1.46 (s, 3H), 1.42 (s, 4H), 1.41 (s, 3H), 1.04 (dd, J = 14.2, 6.6 Hz, 6H), 0.89 (t, J = 6.6 Hz, 6H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 211.8, 204.0, 198.7, 167.5, 164.3, 159.8, 153.1, 114.6, 106.0, 105.5, 100.2, 56.1, 53.4, 47.3, 46.9, 25.4, 25.0, 24.8, 24.7, 24.5, 24.4, 24.2, 23.4, 23.1, 22.9, 22.7.

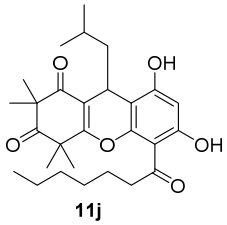
5-Hexanoyl-6,8-dihydroxy-9-isobutyl-2,2,4,4-tetramethyl-4,9-dihydro-1H-xanthene-1,3(2H)-dione 11i:



11i

Following the typical procedure, **11i** were obtained in 47% yield as slight yellow solid. ^{1}H NMR (500 MHz, $CDCl_3$): δ 13.58 (s, 1H), 7.76 (s, 1H), 6.32 (s, 1H), 4.35 (t, J = 6.0 Hz, 1H), 3.29 (ddd, J = 17.5, 9.0, 6.0 Hz, 1H), 3.09 (ddd, J = 17.5, 9.0, 5.9 Hz, 1H), 1.90 – 1.72 (m, 2H), 1.66 (s, 3H), 1.58 – 1.33 (m, 16H), 0.94 (dd, J = 8.3, 5.5 Hz, 3H), 0.88 (dd, J = 6.3, 5.2 Hz, 6H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 211.9, 204.5, 198.8, 167.5, 164.4, 156.0, 153.1, 114.6, 106.0, 105.1, 100.2, 56.1, 47.3, 46.8, 44.7, 31.4, 25.4, 25.0, 24.8, 24.7, 24.5, 24.3, 23.8, 23.5, 23.1, 22.7, 14.0.

5-Heptanoyl-6,8-dihydroxy-9-isobutyl-2,2,4,4-tetramethyl-4,9-dihydro-1H-xanthene-1,3(2H)-dione:

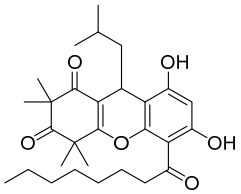


11j

Following the typical procedure, **11j** were obtained in 47% yield as slight yellow solid. ^{1}H NMR (500 MHz, Acetone): δ 13.47 (s, 1H), 10.06 (s, 1H), 6.30 (s, 1H), 4.29 (t, J = 6.0 Hz, 1H), 3.38 (ddd, J = 17.5,

8.7, 6.1 Hz, 1H), 3.19 (ddd, *J* = 17.6, 8.7, 6.1 Hz, 1H), 1.85-1.70 (m, 2H), 1.67 (s, 3H), 1.58-1.52 (m, 4H), 1.52-1.29 (m, 16H), 0.92-0.84 (m, 9H); ^{13}C NMR (126 MHz, Acetone): δ 211.26 (s), 204.43 (s), 196.83 (s), 166.59 (s), 164.43 (s), 160.93 (s), 153.34 (s), 114.07 (s), 105.90 (s), 104.61 (s), 99.29 (s), 55.69 (s), 46.99 (s), 46.57 (s), 44.38 (s), 31.67 (s), 28.67 (s), 24.78 (s), 24.73 (s), 24.66 (s), 24.29 (s), 23.95 (s), 23.91 (s), 23.54 (s), 22.92 (s), 22.71 (s), 22.32 (s).

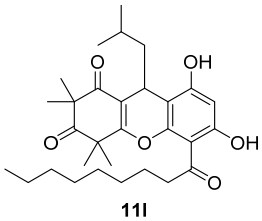
6, 8-Dihydroxy-9-isobutyl-2,2,4,4-tetramethyl-5-octanoyl-4,9-dihydro-1H-xanthene-1,3(2H) -dione 11k:



11k

Following the typical procedure, **11k** were obtained in 38% overall yield as slight yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$): *δ* 13.55 (s, 1H), 7.19 (s, 1H), 6.29 (s, 1H), 4.34 (t, *J* = 6.0 Hz, 1H), 3.75 (s, 1H), 3.29 (ddd, *J* = 17.5, 9.0, 6.0 Hz, 1H), 3.09 (ddd, *J* = 17.5, 9.0, 5.9 Hz, 1H), 1.82 – 1.71 (m, 2H), 1.65 (s, 3H), 1.50 (s, 4H), 1.46 (s, 3H), 1.43 (d, *J* = 8.1 Hz, 5H), 1.41 – 1.34 (m, 6H), 1.32 (dd, *J* = 6.4, 3.7 Hz, 4H), 0.90 (dt, *J* = 9.9, 6.8 Hz, 9H); ^{13}C NMR (125 MHz, $CDCl_3$): *δ* 211.8, 204.5, 198.5, 167.3, 164.4, 159.6, 153.1, 114.5, 105.9, 105.2, 100.2, 67.1, 56.1, 47.3, 46.9, 44.8, 31.7, 29.3, 29.2, 25.4, 25.0, 24.8, 24.7, 24.5, 24.3, 24.1, 23.4, 23.1, 22.6, 14.1.

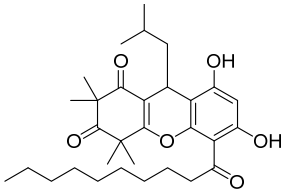
6,8-Dihydroxy-9-isobutyl-2,2,4,4-tetramethyl-5-nonanoyl-4,9-dihydro-1H-xanthene-1,3(2H)-dione 11l:



11l

Following the typical procedure, **11l** were obtained in 43% overall yield as slight yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$): *δ* 13.53 (s, 1H), 6.64 (s, 1H), 6.27 (s, 1H), 4.32 (t, *J* = 6.1 Hz, 1H), 3.29 (ddd, *J* = 17.5, 9.1, 5.9 Hz, 1H), 3.09 (ddd, *J* = 17.6, 9.0, 5.8 Hz, 1H), 1.87-1.27 (m, 27H), 0.90 (q, *J* = 6.7 Hz, 9H); ^{13}C NMR (125 MHz, $CDCl_3$): *δ* 211.7, 204.5, 198.2, 167.1, 164.4, 159.3, 153.1, 114.5, 105.8, 105.3, 100.2, 56.1, 47.2, 46.9, 44.8, 31.9, 29.6, 29.3, 29.2, 25.4, 25.0, 24.8, 24.7, 24.4, 24.3, 24.1, 23.4, 23.1, 22.7, 14.1.

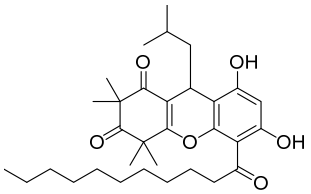
5-Decanoyl-6,8-dihydroxy-9-isobutyl-2,2,4,4-tetramethyl-4,9-dihydro-1H-xanthene-1,3(2H) -dione 11m:



11m

Following the typical procedure, **11m** were obtained in 43% overall yield as slight yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ 13.58 (s, 1H), 7.64 (s, 1H), 6.31 (s, 1H), 4.35 (t, J = 6.0 Hz, 1H), 3.29 (ddd, J = 17.4, 9.0, 6.0 Hz, 1H), 3.09 (ddd, J = 17.5, 9.0, 5.9 Hz, 1H), 1.86-1.70 (m, 3H), 1.66 (s, 3H), 1.62-1.24 (m, 29H), 0.92-0.86 (m, 9H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 211.8, 204.5, 198.7, 167.5, 164.4, 159.9, 153.1, 114.6, 106.0, 105.1, 100.2, 56.1, 47.3, 46.9, 44.7, 31.9, 29.6, 29.5, 29.3, 29.3, 25.4, 25.0, 24.8, 24.7, 24.5, 24.3, 24.1, 23.5, 23.1, 22.7, 14.1.

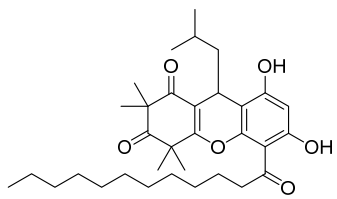
6,8-Dihydroxy-9-isobutyl-2,2,4,4-tetramethyl-5-undecanoyl-4,9-dihydro-1H-xanthene-1,3(2H)-dione 11n:



11n

Following the typical procedure, **11n** were obtained in 43% overall yield as slight yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ 13.54 (s, 1H), 6.75 (s, 1H), 6.27 (s, 1H), 4.31 (t, J = 6.0 Hz, 1H), 3.29 (ddd, J = 17.5, 9.0, 5.9 Hz, 1H), 3.09 (ddd, J = 17.6, 9.0, 5.8 Hz, 1H), 1.79 (dd, J = 15.1, 8.1 Hz, 2H), 1.65 (s, 3H), 1.53-1.25 (m, 31H), 0.90 (td, J = 6.8, 4.4 Hz, 9H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 211.8, 204.5, 198.1, 167.1, 164.4, 159.4, 153.2, 114.5, 105.8, 105.3, 100.2, 56.1, 47.2, 46.9, 44.8, 31.9, 29.7, 29.6, 29.5, 29.4, 29.3, 25.4, 25.0, 24.8, 24.7, 24.4, 24.3, 24.1, 23.4, 23.1, 22.7, 14.2.

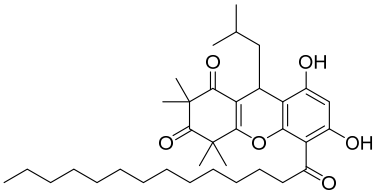
5-Dodecanoyl-6,8-dihydroxy-9-isobutyl-2,2,4,4-tetramethyl-4,9-dihydro-1H-xanthene-1,3(2H)-dione 11o:



11o

Following the typical procedure, **11o** were obtained in 43% overall yield as slight yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ 13.61 (s, 1H), 7.66 (s, 1H), 6.31 (s, 1H), 4.35 (t, J = 6.1 Hz, 1H), 3.29 (ddd, J = 17.5, 9.1, 5.9 Hz, 1H), 3.09 (ddd, J = 17.5, 9.0, 5.9 Hz, 1H), 1.89-1.69 (m, 2H), 1.66 (s, 3H), 1.60-1.22 (m, 33H), 0.89 (m, 9H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 211.8, 204.5, 198.8, 167.5, 164.4, 159.9, 153.1, 114.6, 106.0, 105.1, 100.3, 56.1, 47.3, 46.9, 44.8, 33.9, 31.9, 29.6, 29.6, 29.5, 29.5, 29.3, 29.3, 29.1, 25.4, 25.0, 24.7, 24.7, 24.5, 24.3, 24.1, 23.5, 23.1, 22.7, 14.1.

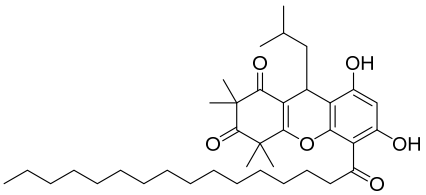
6, 8-Dihydroxy-9-isobutyl-2,2,4,4-tetramethyl-5-tetradecanoyl-4,9-dihydro-1H-xanthene-1,3(2H) -dione 11p:



11p

Following the typical procedure, **11p** were obtained in 43% overall yield as slight yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ 13.57 (brs, 1H), 7.50 (s, 1H), 6.30 (s, 1H), 4.34 (t, J = 6.0 Hz, 1H), 3.29 (ddd, J = 17.4, 9.0, 6.0 Hz, 1H), 3.09 (ddd, J = 17.5, 9.0, 5.9 Hz, 1H), 1.79 (dd, J = 11.3, 5.3 Hz, 2H), 1.65 (s, 3H), 1.56-1.21 (m, 37H), 0.89 (dd, J = 12.6, 6.6 Hz, 10H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 211.8, 204.5, 198.6, 167.4, 164.4, 159.8, 153.1, 114.6, 105.9, 105.2, 100.2, 56.1, 47.3, 46.8, 44.8, 31.9, 29.7, 29.7, 29.6, 29.6, 29.4, 29.3, 25.4, 25.0, 24.8, 24.7, 24.5, 24.3, 24.1, 23.5, 23.1, 22.7, 14.1.

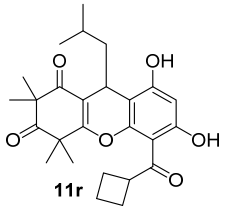
6, 8-Dihydroxy-9-isobutyl-2,2,4,4-tetramethyl-5-palmitoyl-4,9-dihydro-1H-xanthene-1,3(2H) -dione 11q:



11q

Following the typical procedure, **11q** were obtained in 43% overall yield as slight yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ 13.57 (s, 1H), 7.47 (s, 1H), 6.31 (s, 1H), 4.35 (t, J = 6.0 Hz, 1H), 3.29 (ddd, J = 17.5, 9.0, 6.0 Hz, 1H), 3.09 (ddd, J = 17.5, 9.0, 5.9 Hz, 1H), 1.88-1.70 (m, 2H), 1.50 (s, 3H), 1.46 (s, 3H), 1.45-1.23 (m, 35H), 0.89 (td, J = 6.4, 4.0 Hz, 9H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 211.8, 204.5, 198.7, 167.5, 164.4, 159.8, 153.1, 114.6, 106.0, 105.2, 100.2, 56.1, 47.3, 46.9, 44.8, 31.9, 29.7, 29.7, 29.7, 29.7, 29.7, 29.7, 29.6, 29.5, 29.4, 29.3, 25.4, 25.0, 24.8, 24.7, 24.5, 24.3, 24.1, 23.5, 23.1, 22.7, 14.1.

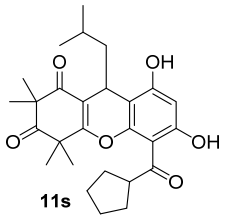
5-(Cyclobutanecarbonyl) -6,8-dihydroxy-9-isobutyl-2,2,4,4-tetramethyl-4,9-dihydro-1H-xanthene-1,3(2H) -dione 11r:



11r

Following the typical procedure, **11r** were obtained in 43% overall yield as slight yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ 13.26 (s, 1H), 6.68 (s, 1H), 6.28 (s, 1H), 4.30 (t, J = 6.0 Hz, 1H), 4.29-4.19 (m, 1H), 2.66 (dd, J = 11.2, 8.9 Hz, 1H), 2.51-2.43 (m, 1H), 2.20 (ddd, J = 11.3, 8.6, 3.8 Hz, 2H), 2.12-1.97 (m, 2H), 1.97-1.88 (m, 1H), 1.71 (s, 3H), 1.58-1.34 (m, 12H), 0.96-0.81 (m, 6H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 211.8, 205.8, 198.0, 167.3, 164.3, 159.3, 153.1, 114.6, 105.8, 103.8, 100.2, 56.1, 47.2, 46.5, 46.3, 28.1, 25.1, 25.0, 24.8, 24.7, 24.6, 24.0, 23.6, 23.2, 23.1, 17.9.

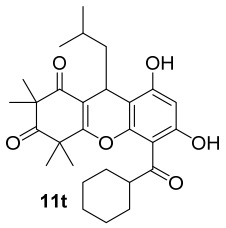
5-(Cyclopentanecarbonyl)-6,8-dihydroxy-9-isobutyl-2,2,4,4-tetramethyl-4,9-dihydro-1H-xanthene-1,3(2H)-dione 11s:



11s

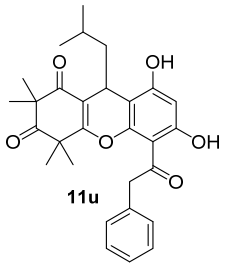
Following the typical procedure, **11s** were obtained in 43% overall yield as slight yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ 13.37 (s, 1H), 7.05 (s, 1H), 6.29 (s, 1H), 4.33 (t, J = 6.0 Hz, 1H), 4.17-4.07 (m, 1H), 2.28-2.18 (m, 1H), 2.18-2.09 (m, 1H), 1.90-1.65 (m, 8H), 1.61 (s, 3H), 1.59-1.34 (m, 14H), 0.96-0.85 (m, 6H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 211.8, 207.7, 198.3, 167.3, 164.4, 159.4, 153.0, 114.6, 106.0, 104.9, 100.3, 56.2, 50.9, 47.2, 46.7, 32.4, 28.3, 26.0, 25.9, 25.1, 25.0, 24.8, 24.6, 24.6, 24.2, 23.5, 23.1.

5-(Cyclohexanecarbonyl) -6,8-dihydroxy-9-isobutyl-2,2,4,4-tetramethyl-4,9-dihydro-1H-xanthene-1,3(2H) -dionee 11t:



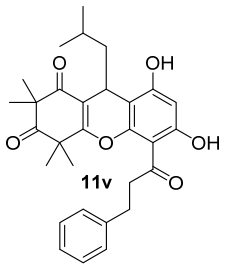
Following the typical procedure, **11s** were obtained in 43% overall yield as slight yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ 13.17 (s, 1H), 7.36 (s, 1H), 6.30 (s, 1H), 4.33 (t, J = 6.1 Hz, 1H), 3.77 (ddd, J = 11.1, 7.9, 3.1 Hz, 1H), 2.02 – 1.73 (m, 8H), 1.69 (s, 3H), 1.59 – 1.24 (m, 19H), 0.90 (dd, J = 6.4, 4.8 Hz, 6H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 211.8, 208.6, 198.4, 167.6, 164.3, 159.4, 152.9, 114.8, 106.2, 104.4, 100.3, 56.2, 49.2, 47.3, 46.7, 31.6, 27.7, 26.3, 25.8, 25.3, 25.1, 25.1, 28.5, 28.4, 24.6, 24.1, 23.5, 23.1, 21.1.

6,8-Dihydroxy-9-isobutyl-2,2,4,4-tetramethyl-5-(2-phenylacetyl)-4,9-dihydro-1H-xanthene-1,3(2H)-dione 11u:



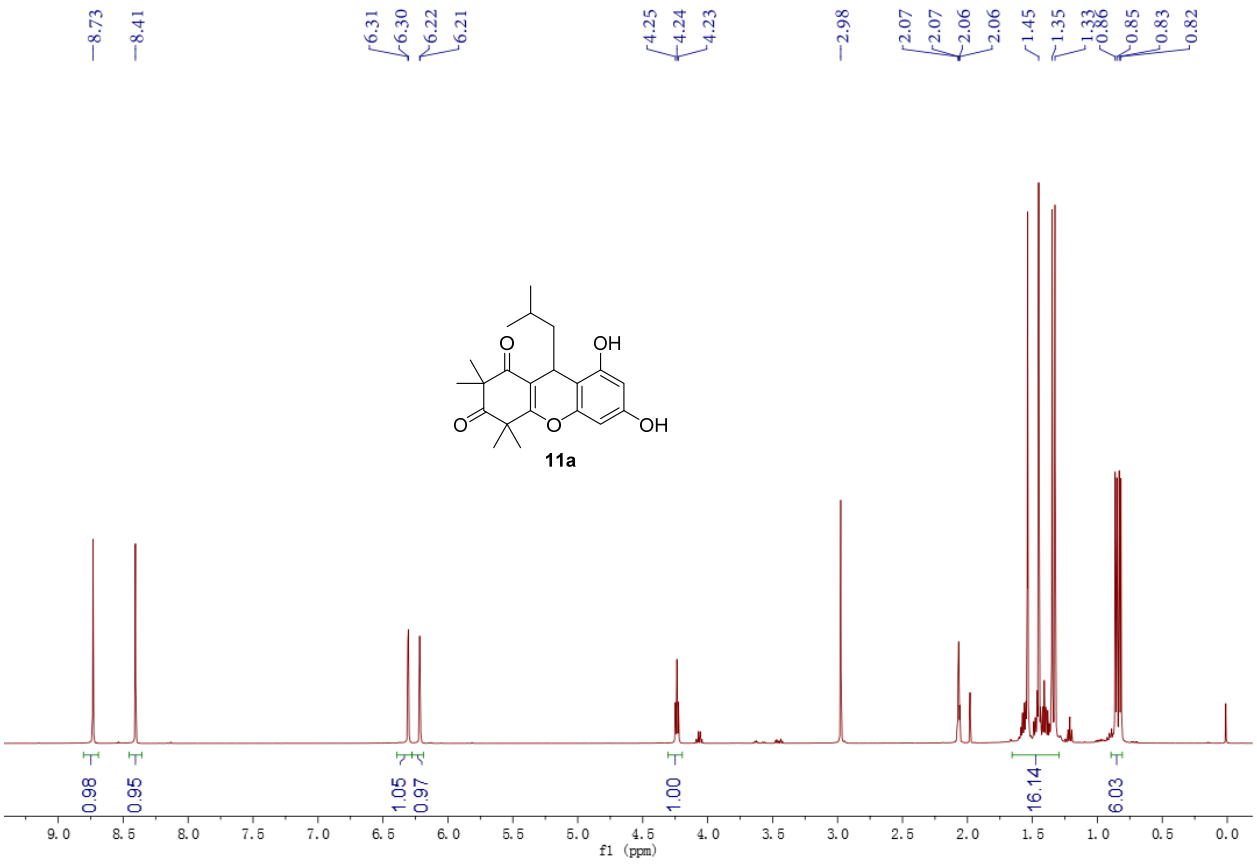
Following the typical procedure, **11u** were obtained in 43% overall yield as slight yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ 13.24 (s, 1H), 7.48 (s, 1H), 7.40 (t, J = 7.3 Hz, 2H), 7.34 (d, J = 7.3 Hz, 1H), 7.31-7.25 (m, 3H), 6.30 (s, 1H), 4.66 (d, J = 17.0 Hz, 1H), 4.38 (dd, J = 18.2, 11.6 Hz, 2H), 1.66 (s, 3H), 1.54 (s, 3H), 1.50 (s, 1H), 1.47 (d, J = 4.4 Hz, 3H), 1.44 (d, J = 4.0 Hz, 3H), 1.43-1.35 (m, 2H), 0.91 (dd, J = 6.4, 2.7 Hz, 6H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 211.6, 201.5, 198.6, 167.4, 164.6, 160.2, 153.2, 134.2, 129.9, 128.6, 127.3, 114.8, 106.3, 105.0, 100.3, 56.2, 50.5, 47.3, 47.0, 25.4, 25.1, 25.0, 24.8, 24.6, 24.2, 23.5, 23.1.

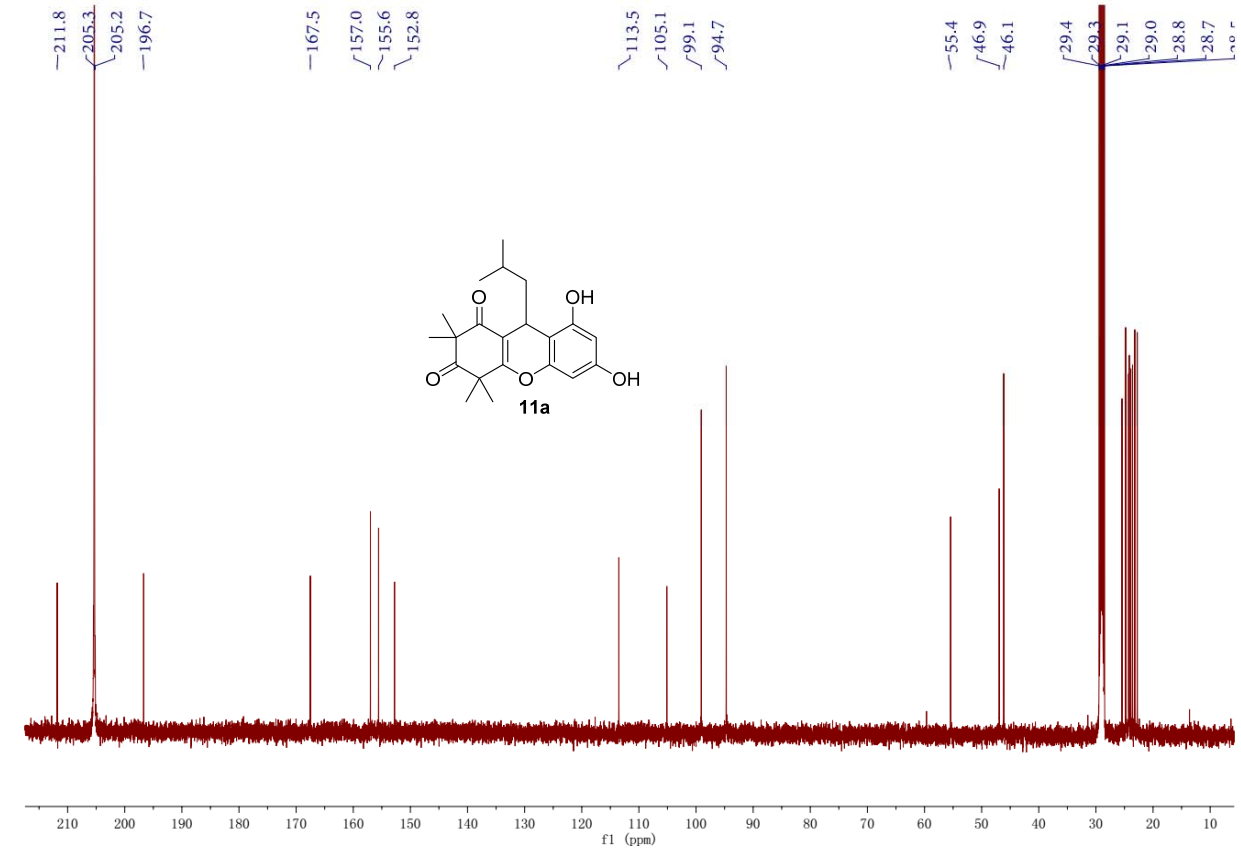
6,8-Dihydroxy-9-isobutyl-2,2,4,4-tetramethyl-5-(3-phenylpropanoyl)-4,9-dihydro-1H-xanthene-1,3(2H)-dione 11v:

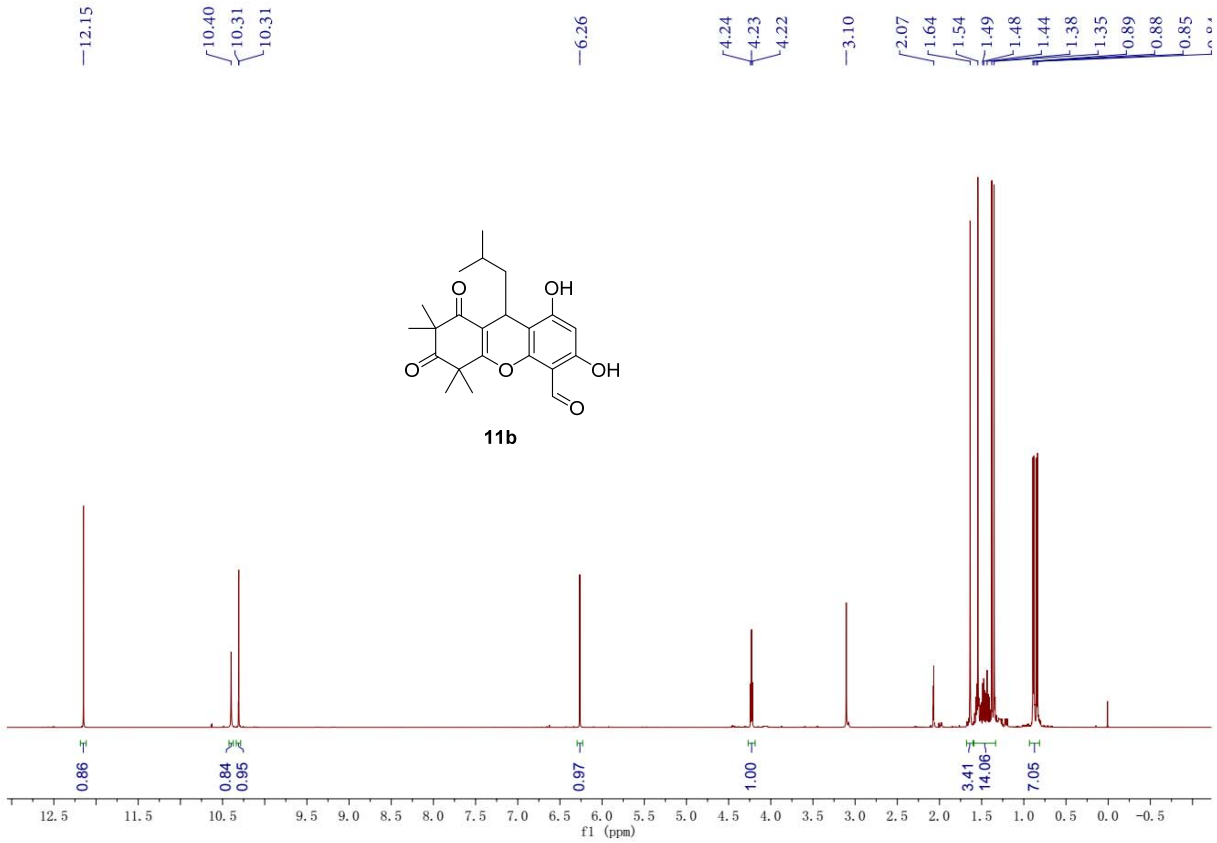


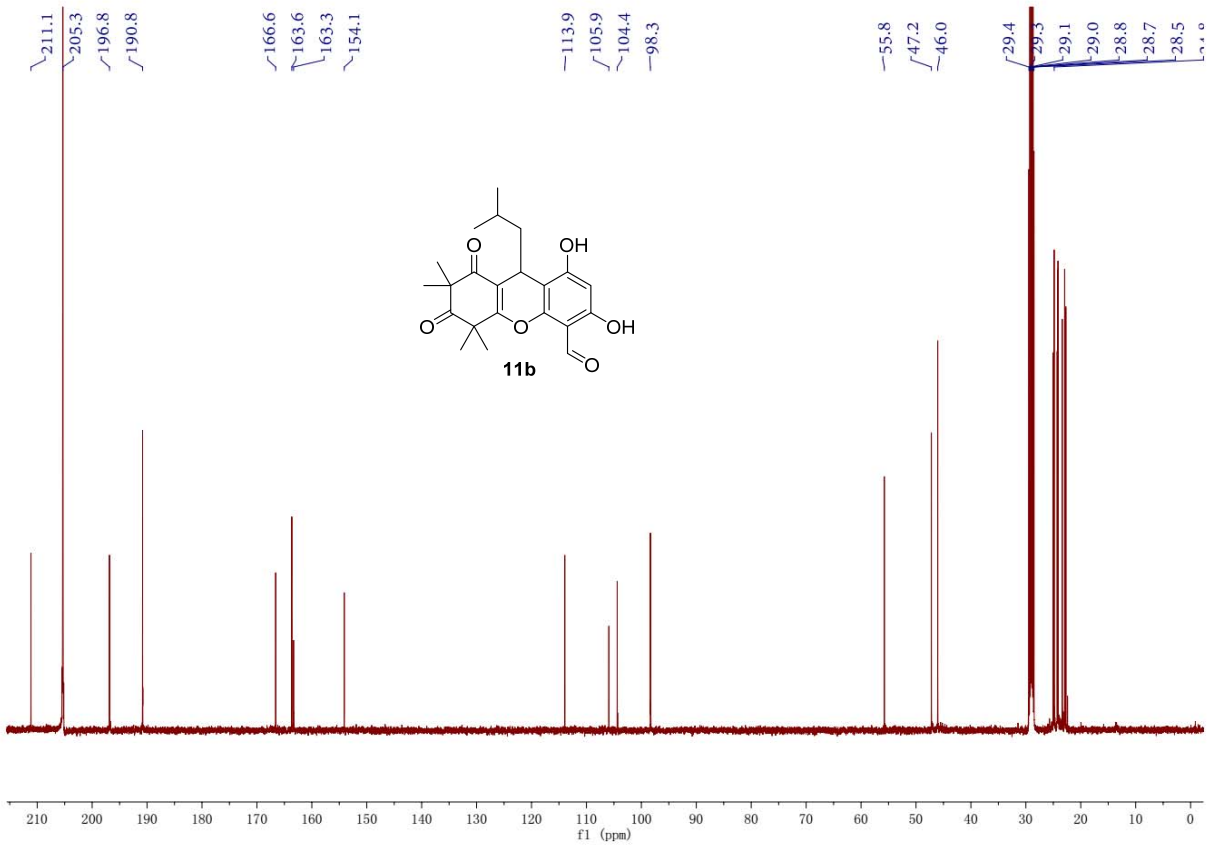
11v

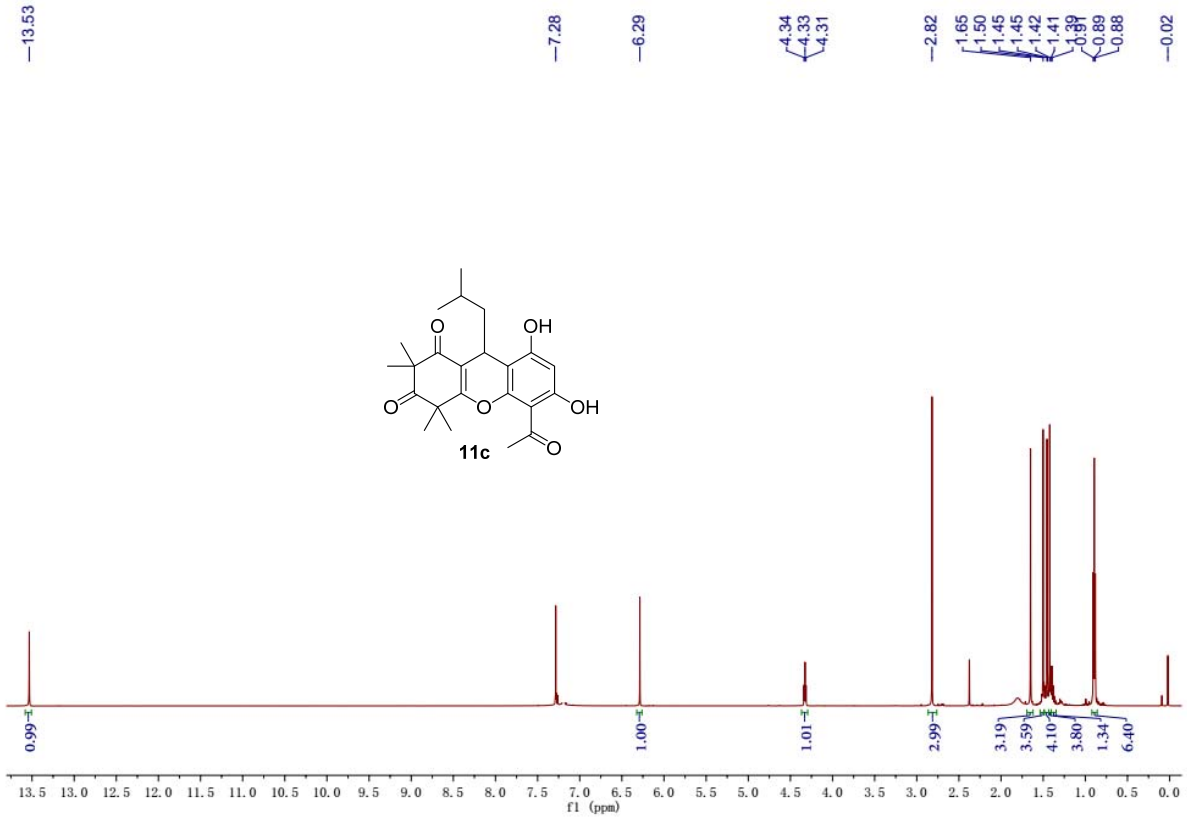
Following the typical procedure, **11v** were obtained in 43% overall yield as slight yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ 13.52 (s, 1H), 7.42 (s, 1H), 7.35-7.21 (m, 5H), 6.30 (s, 1H), 4.33 (t, J = 6.1 Hz, 1H), 3.52 (dddd, J = 47.5, 18.2, 9.6, 5.8 Hz, 2H), 3.22-3.03 (m, 2H), 1.54-1.33 (m, 16H), 0.88 (t, J = 6.1 Hz, 6H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 211.7, 202.9, 198.7, 167.4, 164.5, 159.9, 153.1, 141.0, 128.6, 128.4, 126.3, 114.6, 106.0, 105.0, 100.3, 56.1, 47.2, 46.9, 46.9, 30.1, 25.3, 25.0, 24.7, 24.5, 24.4, 24.2, 23.4, 23.1.

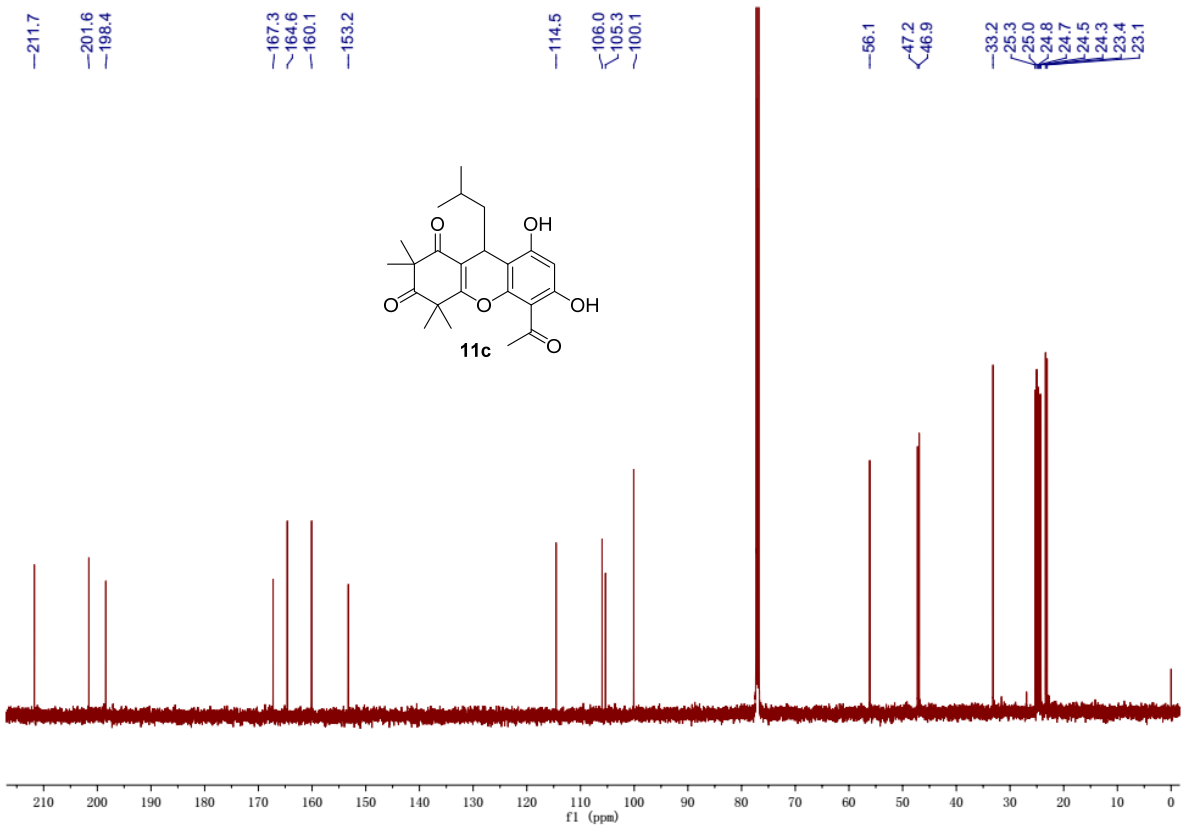

8.73
8.41
6.31
6.30
6.22
6.21
4.25
4.24
4.23
2.98
2.07
2.07
2.06
2.06
1.45
1.35
1.33
0.86
0.85
0.83
0.82
O
OH
O
O
OH
11a
0.98
0.95
1.05
0.97
1.00
16.14
6.03
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

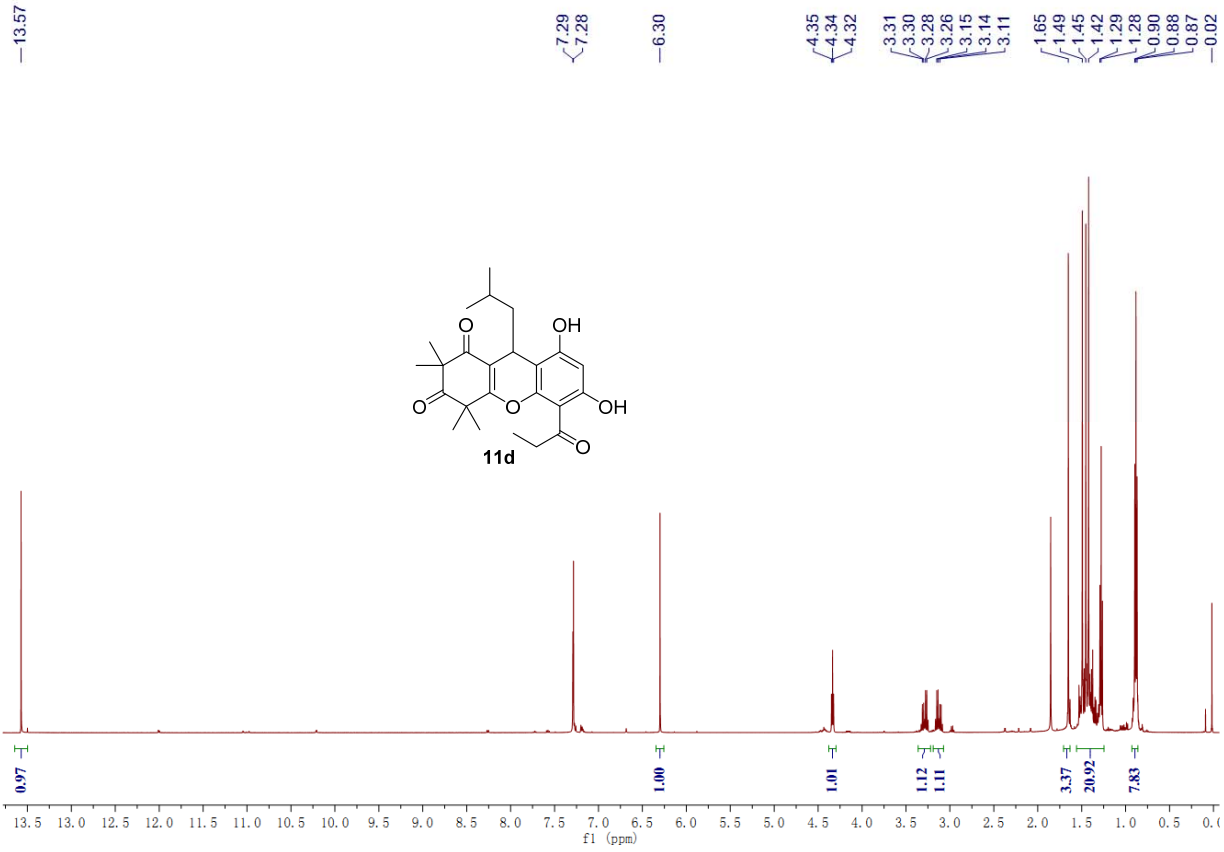

211.8
205.3
205.2
196.7
167.5
157.0
155.6
152.8
113.5
105.1
99.1
94.7
55.4
46.9
46.1
29.4
29.3
29.1
29.0
28.8
28.7
O
OH
O
O
OH
11a
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

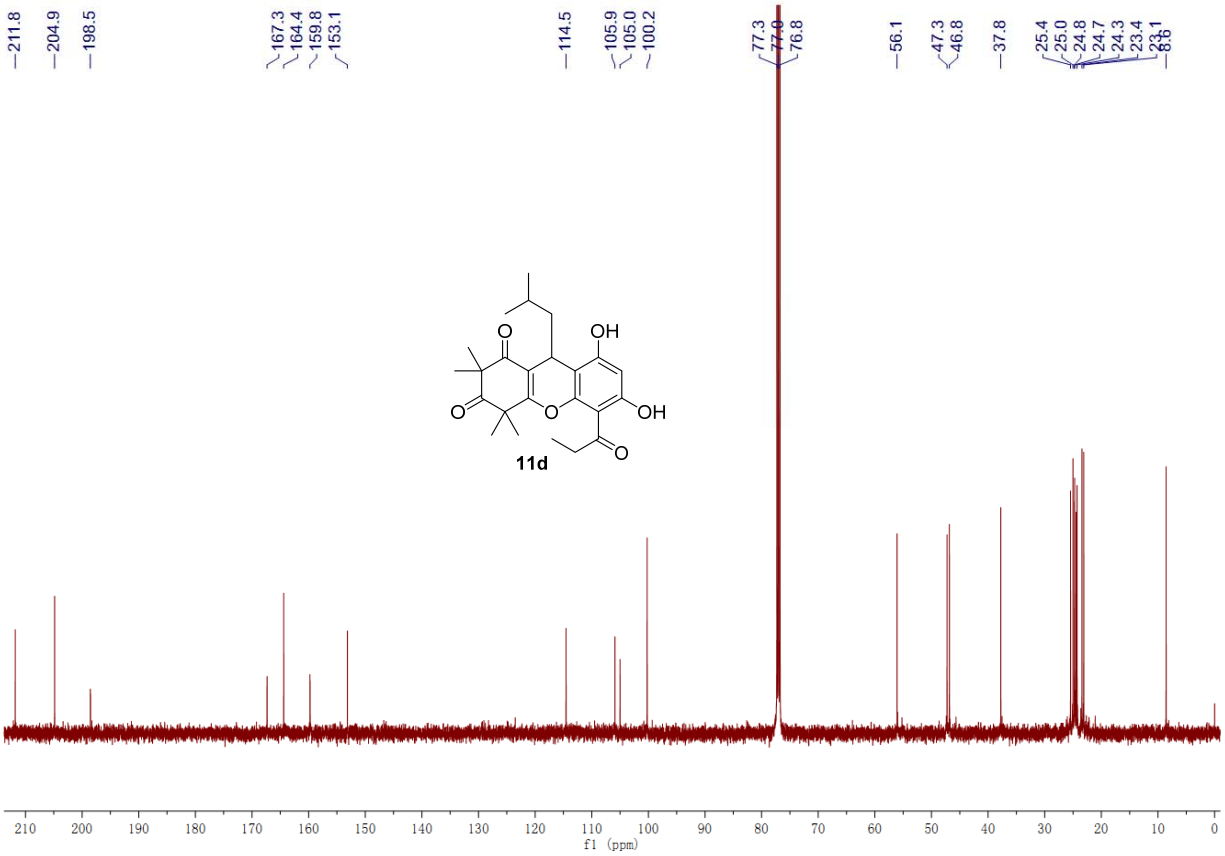

12.15
10.40
10.31
10.31
6.26
4.24
4.23
4.22
3.10
2.07
1.64
1.54
1.49
1.48
1.44
1.38
1.35
0.89
0.88
0.85
OH
O
O
O
OH
O
11b
0.86
0.84
0.95
0.97
1.00
3.41
14.06
7.05
f1 (ppm)

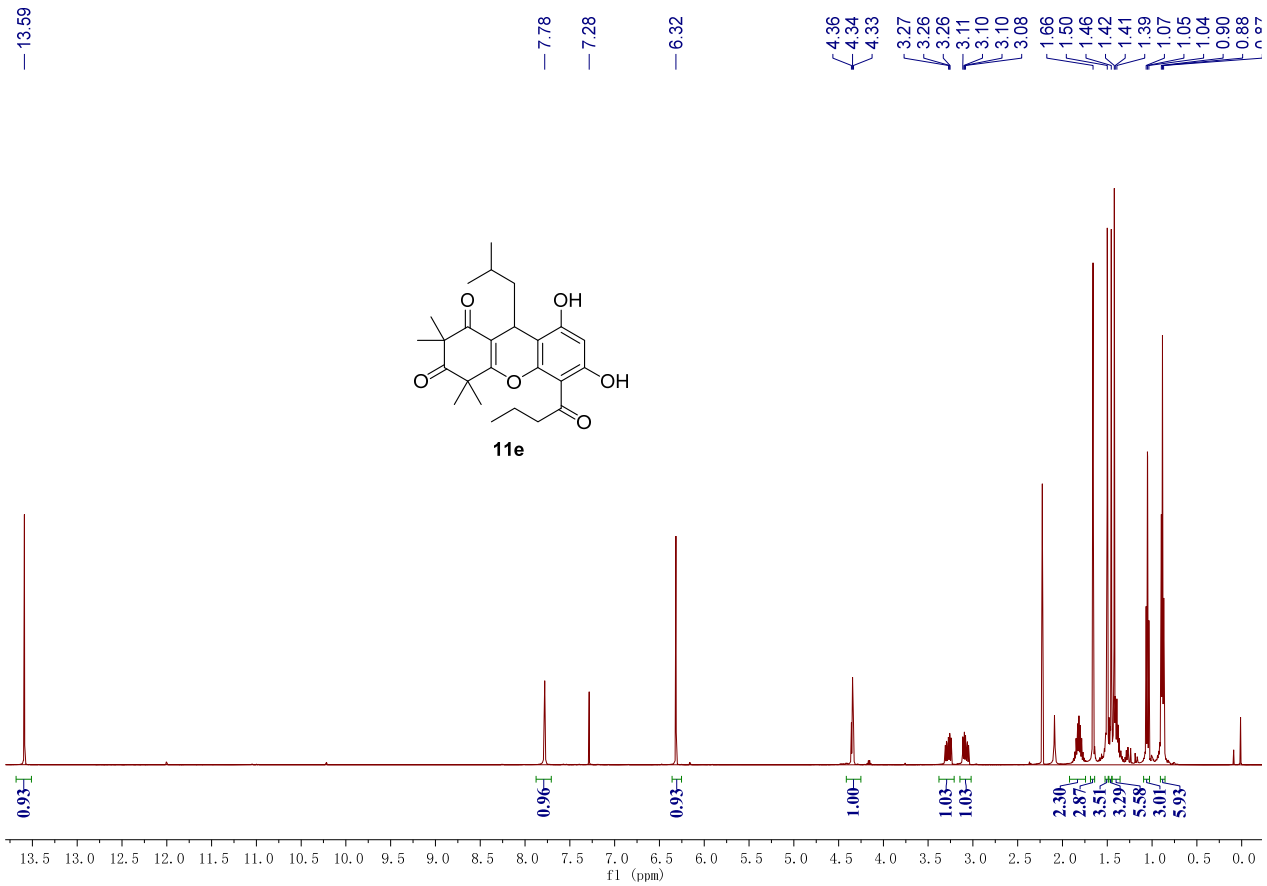

211.1
205.3
196.8
190.8
166.6
163.6
163.3
154.1
113.9
105.9
104.4
98.3
55.8
47.2
46.0
29.4
29.3
29.1
29.0
28.8
28.7
28.5
OH
O
O
O
OH
O
11b
f1 (ppm)

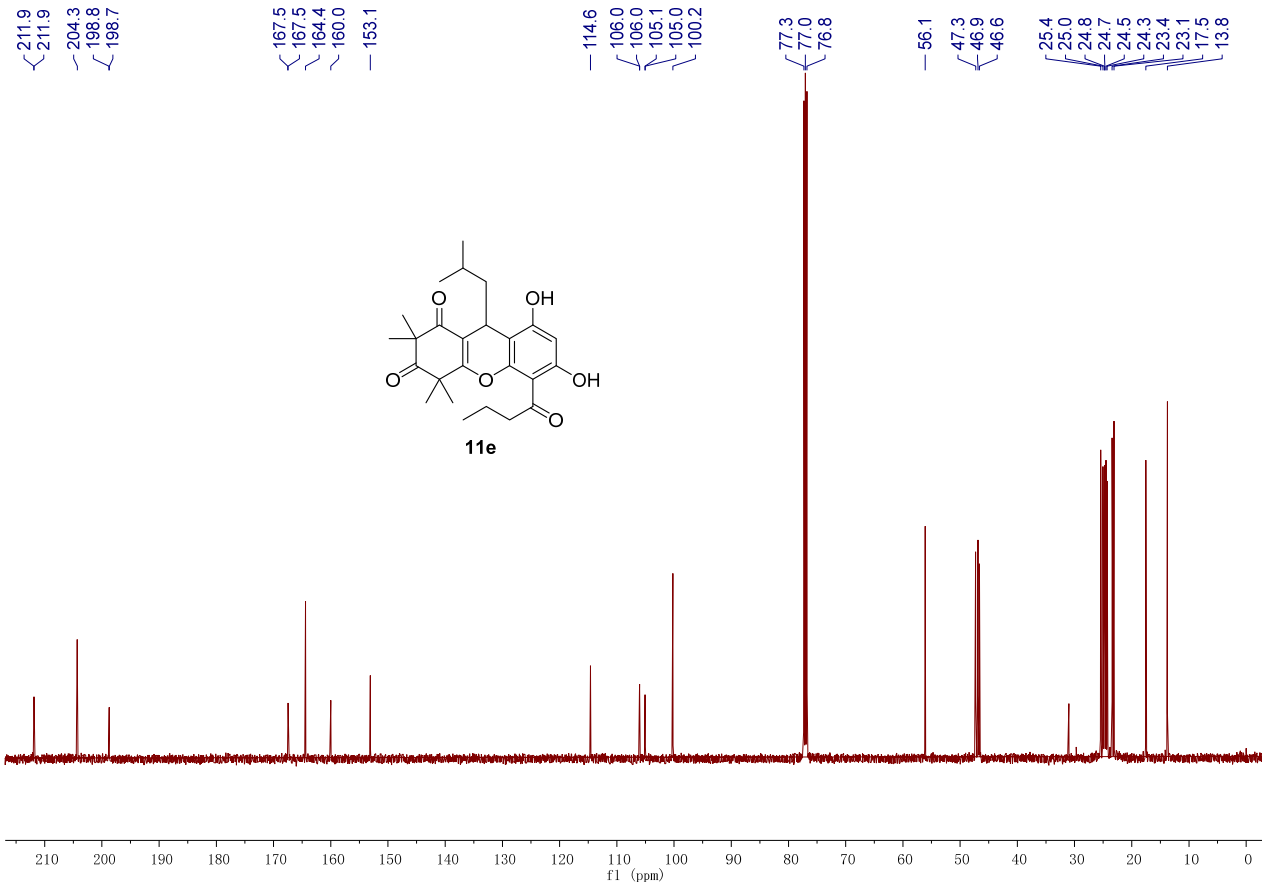

13.53
7.28
6.29
4.34
4.33
4.31
2.82
1.65
1.50
1.45
1.45
1.42
1.41
1.39
0.91
0.89
0.88
0.02
OH
O
O
O
OH
O
11c
0.99
1.00
1.01
2.99
3.19
3.59
4.10
3.80
1.34
6.40
f1 (ppm)

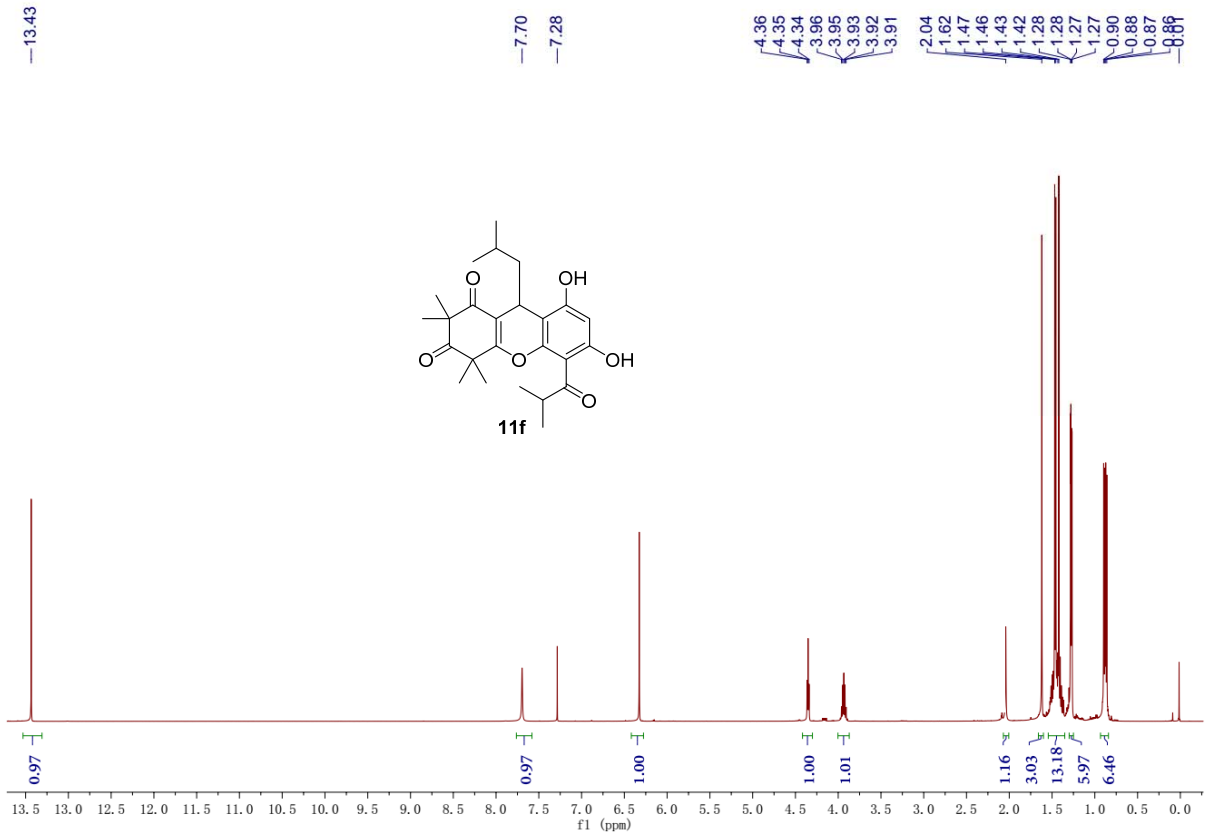

211.7
201.6
198.4
167.3
164.6
160.1
153.2
114.5
106.0
105.3
100.1
56.1
47.2
46.9
33.2
25.3
25.0
24.8
24.7
24.5
24.3
23.4
23.1
OH
O
O
O
OH
O
11c
f1 (ppm)

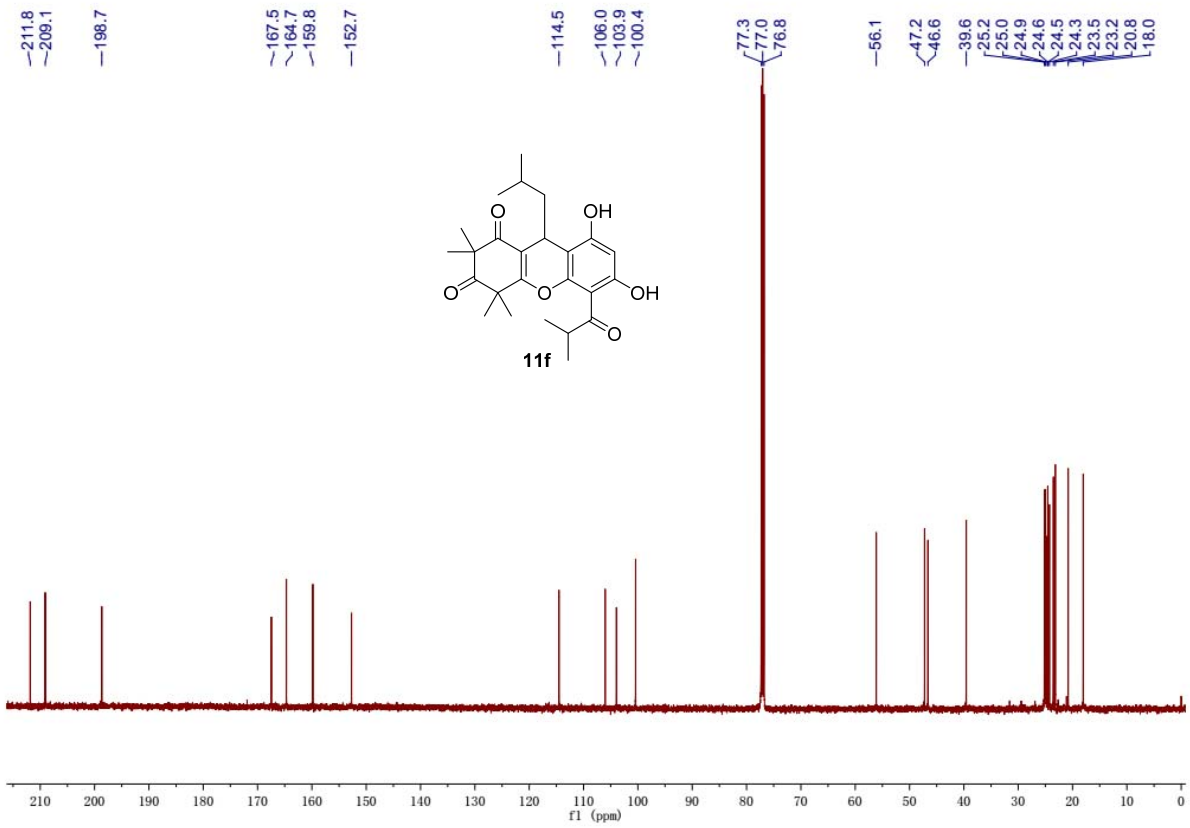

13.57
7.29
7.28
6.30
4.35
4.34
4.32
3.31
3.30
3.28
3.26
3.15
3.14
3.11
1.65
1.49
1.45
1.42
1.29
1.28
0.90
0.88
0.87
0.02
O
OH
O
O
OH
O
11d
0.97
1.00
1.01
1.12
1.11
3.37
20.92
7.83
f1 (ppm)

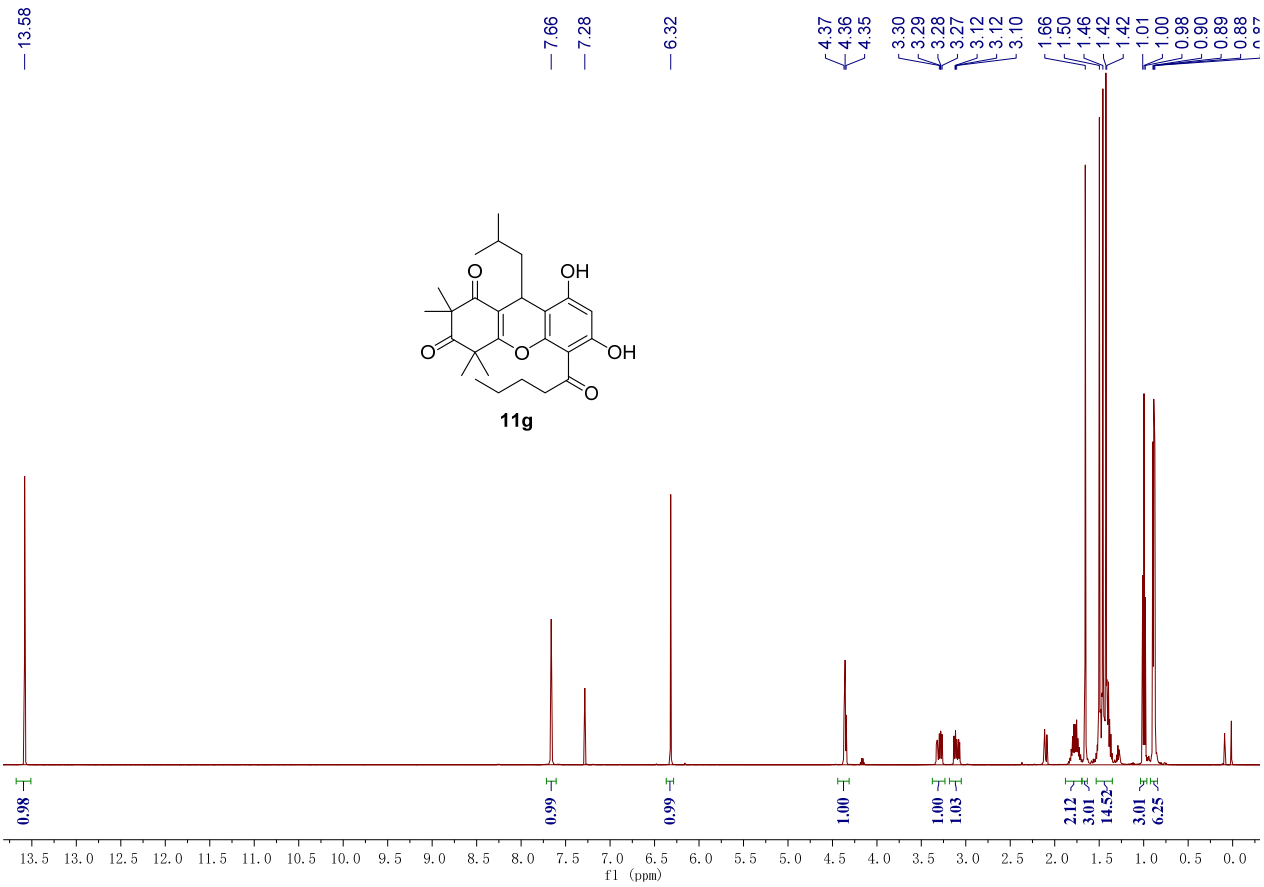

211.8
204.9
198.5
167.3
164.4
159.8
153.1
114.5
105.9
105.0
100.2
77.3
77.0
76.8
56.1
47.3
46.8
37.8
25.4
25.0
24.8
24.7
24.3
23.4
23.1
O
OH
O
O
OH
O
11d
f1 (ppm)


13.59
7.78
7.28
6.32
4.36
4.34
4.33
3.27
3.26
3.26
3.11
3.10
3.10
3.08
1.66
1.50
1.46
1.42
1.41
1.39
1.07
1.05
1.04
0.90
0.88
OH
O
O
O
OH
O
11e
0.93
0.96
0.93
1.00
1.03
1.03
2.30
2.87
3.51
3.29
5.58
3.01
5.93
f1 (ppm)

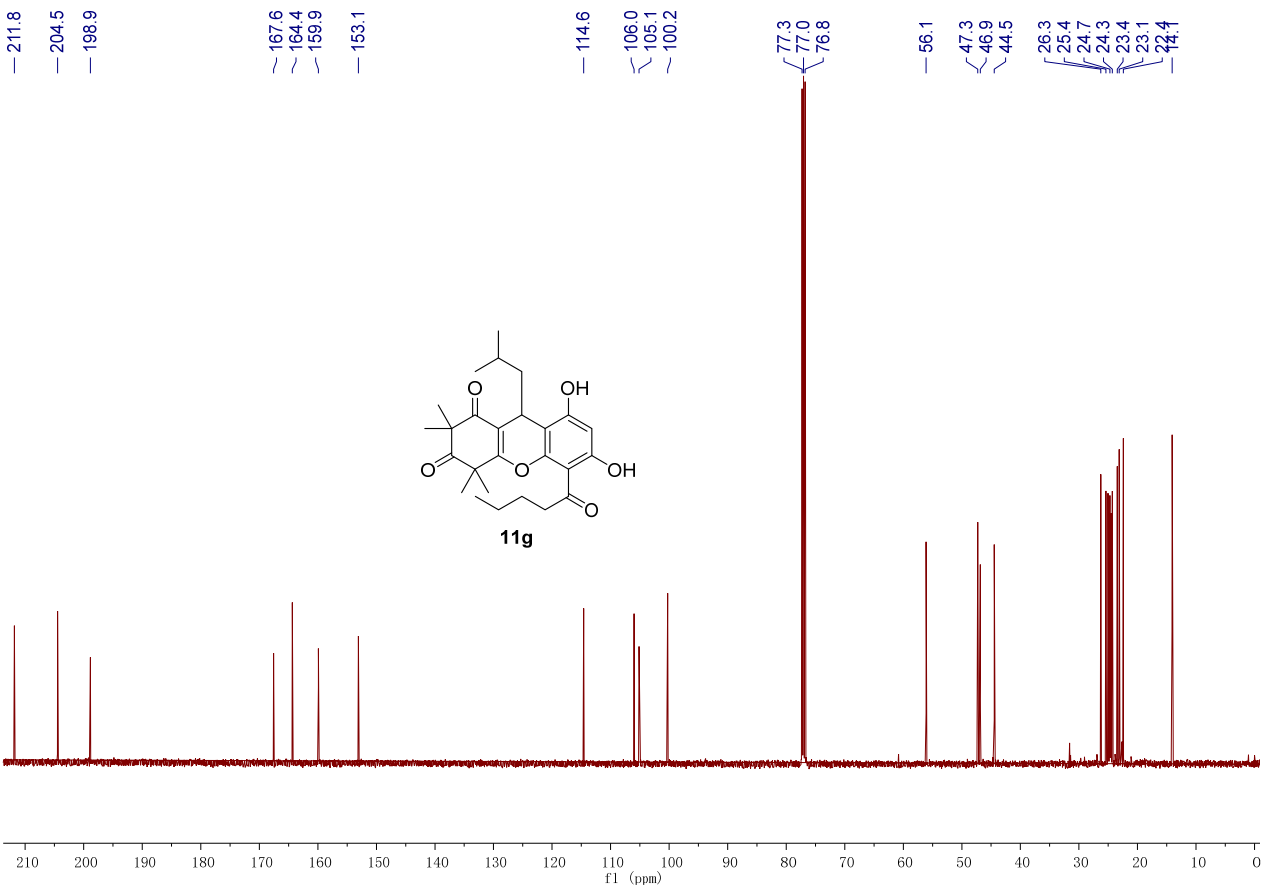

211.9
211.9
204.3
198.8
198.7
167.5
167.5
164.4
160.0
153.1
114.6
106.0
106.0
105.1
105.0
100.2
77.3
77.0
76.8
56.1
47.3
46.9
46.6
25.4
25.0
24.8
24.7
24.5
24.3
23.4
23.1
17.5
13.8
OH
O
O
O
OH
O
11e
f1 (ppm)


13.43
7.70
7.28
4.36
4.35
4.34
3.96
3.95
3.93
3.92
3.91
2.04
1.62
1.47
1.46
1.43
1.42
1.28
1.28
1.27
1.27
0.90
0.88
0.87
0.86
0.86
OH
O
O
O
OH
O
11f
0.97
0.97
1.00
1.00
1.01
1.16
3.03
13.18
5.97
6.46
f1 (ppm)

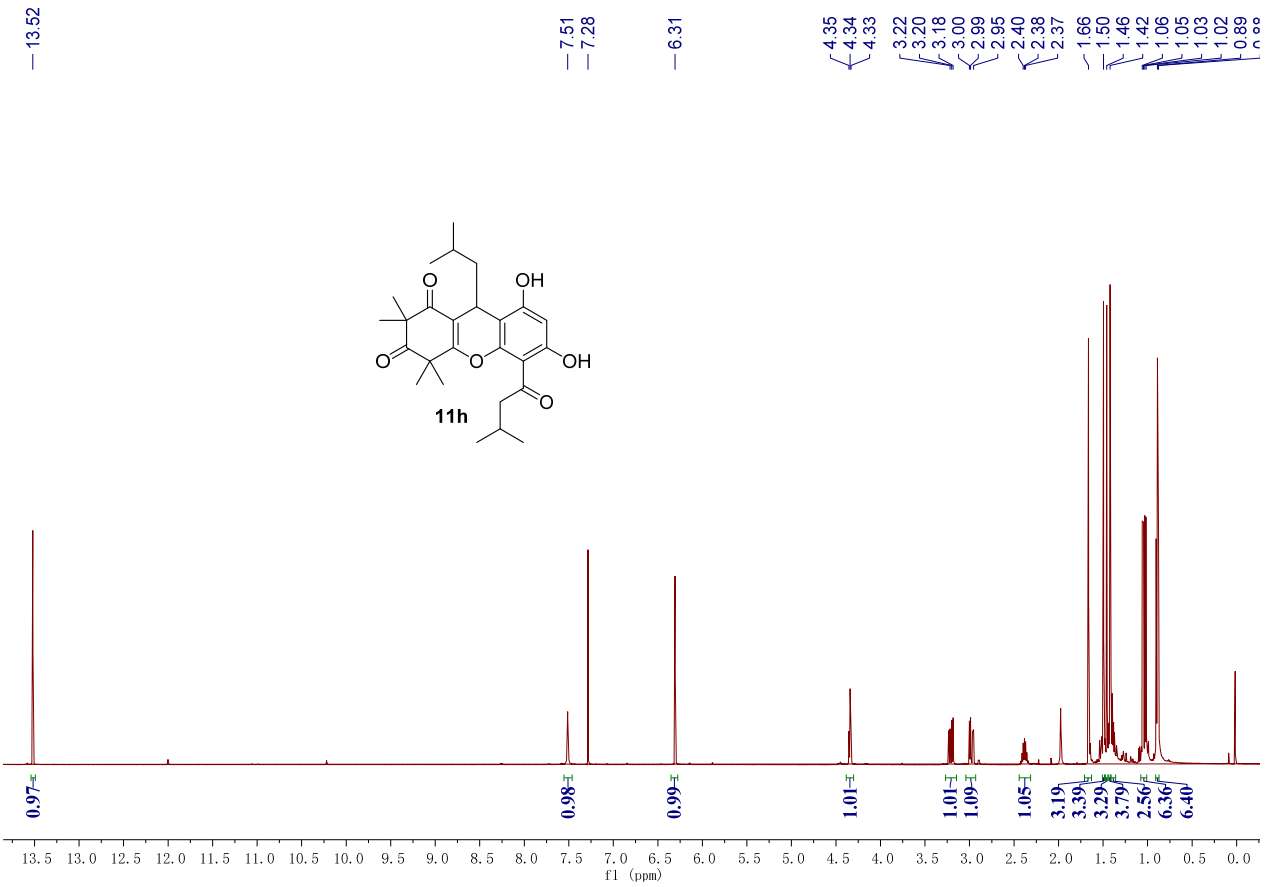

211.8
209.1
198.7
167.5
164.7
159.8
152.7
114.5
106.0
103.9
100.4
77.3
77.0
76.8
56.1
47.2
46.6
39.6
25.2
25.0
24.9
24.6
24.5
24.3
23.5
23.2
20.8
18.0
OH
O
O
O
OH
O
11f
f1 (ppm)

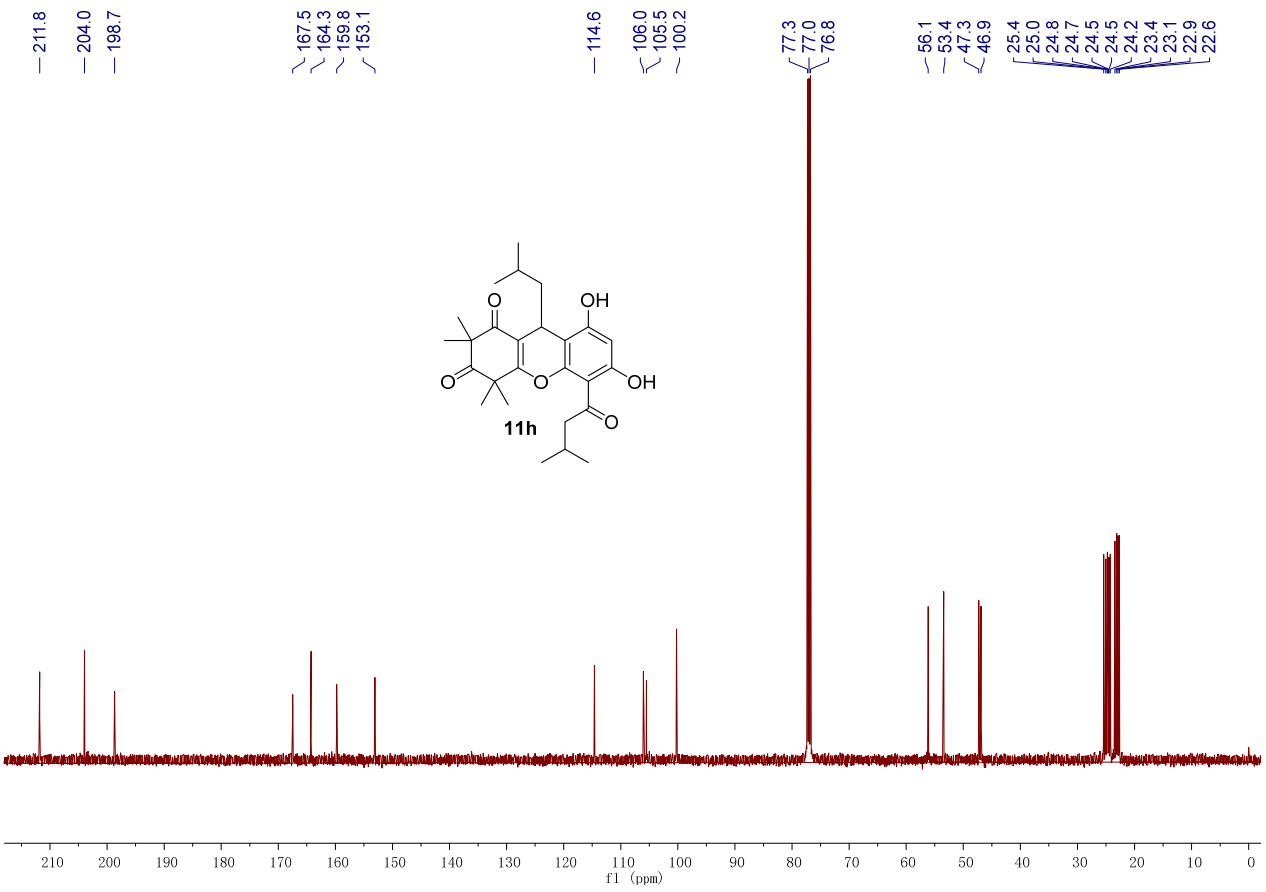

13.58
7.66
7.28
6.32
4.37
4.36
4.35
3.30
3.29
3.28
3.27
3.12
3.12
3.10
1.66
1.50
1.46
1.42
1.42
1.01
1.00
0.98
0.90
0.89
0.88
0.98
0.99
0.99
1.00
1.00
1.03
2.12
3.01
14.52
3.01
6.25
f1 (ppm)

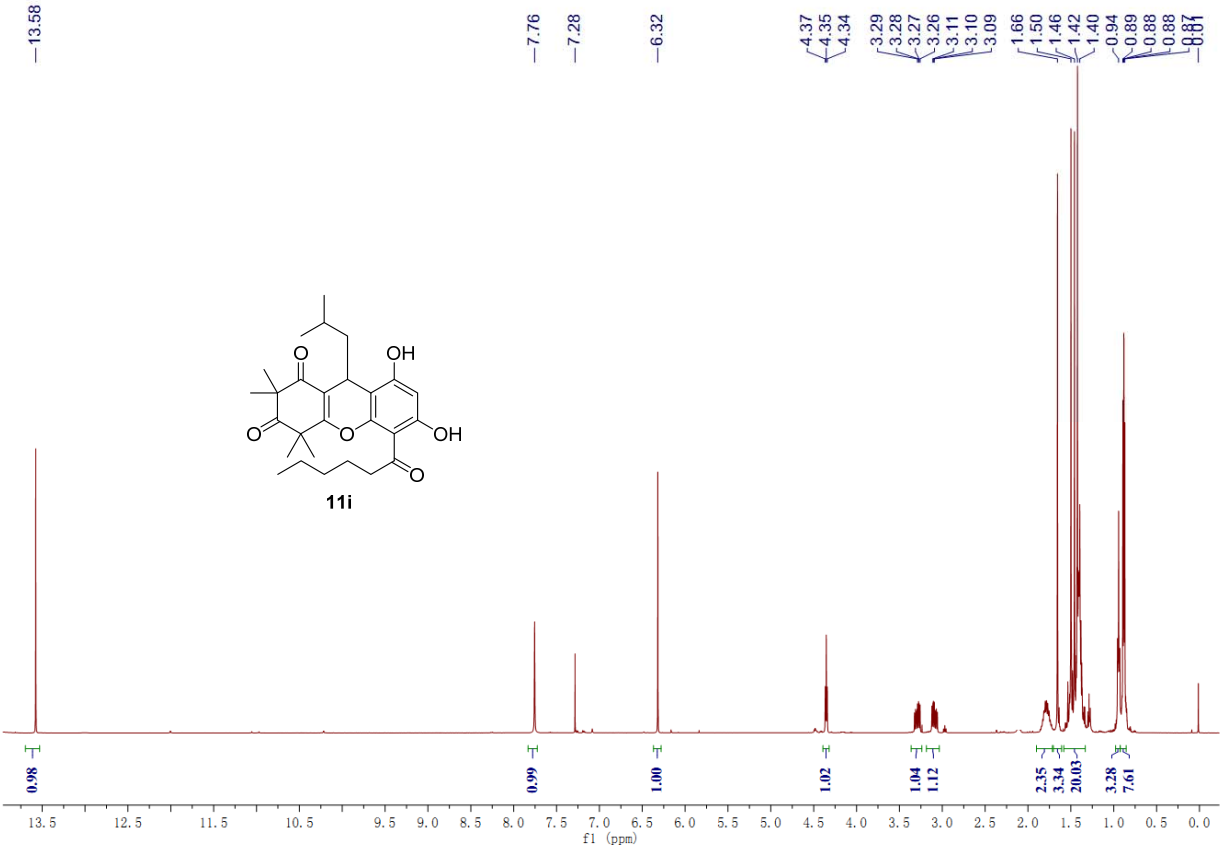
11g

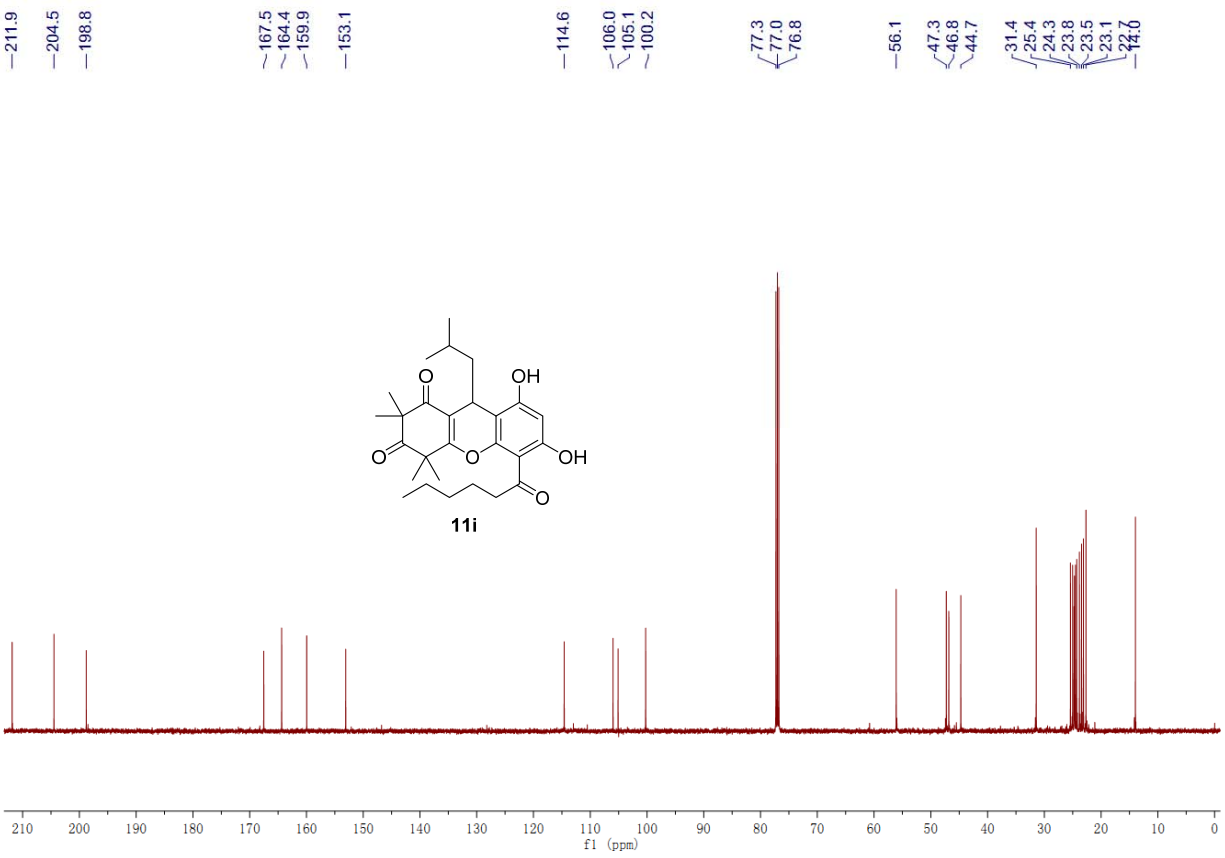

211.8
204.5
198.9
167.6
164.4
159.9
153.1
114.6
106.0
105.1
100.2
77.3
77.0
76.8
56.1
47.3
46.9
44.5
26.3
25.4
24.7
24.3
23.4
23.1
22.4
14.1
f1 (ppm)

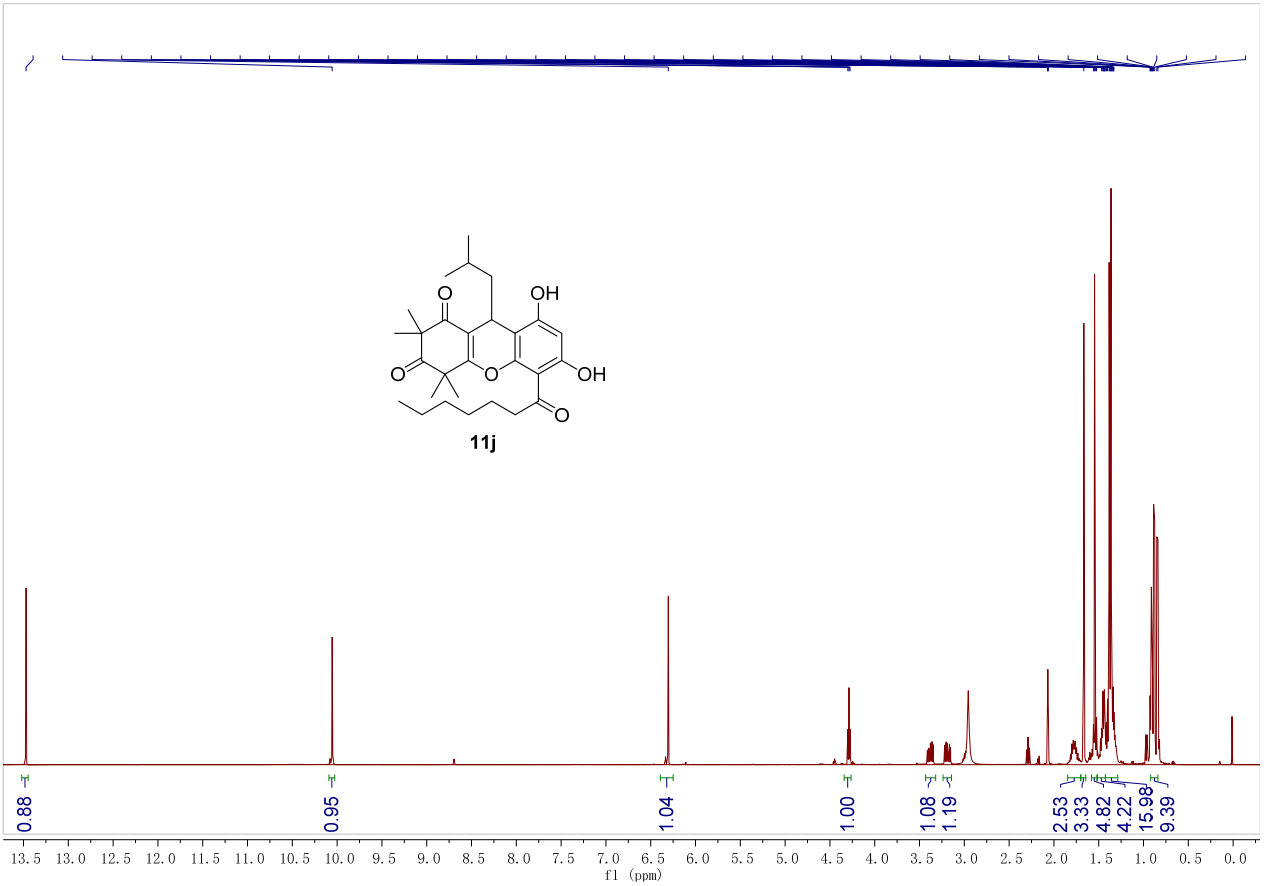
11g

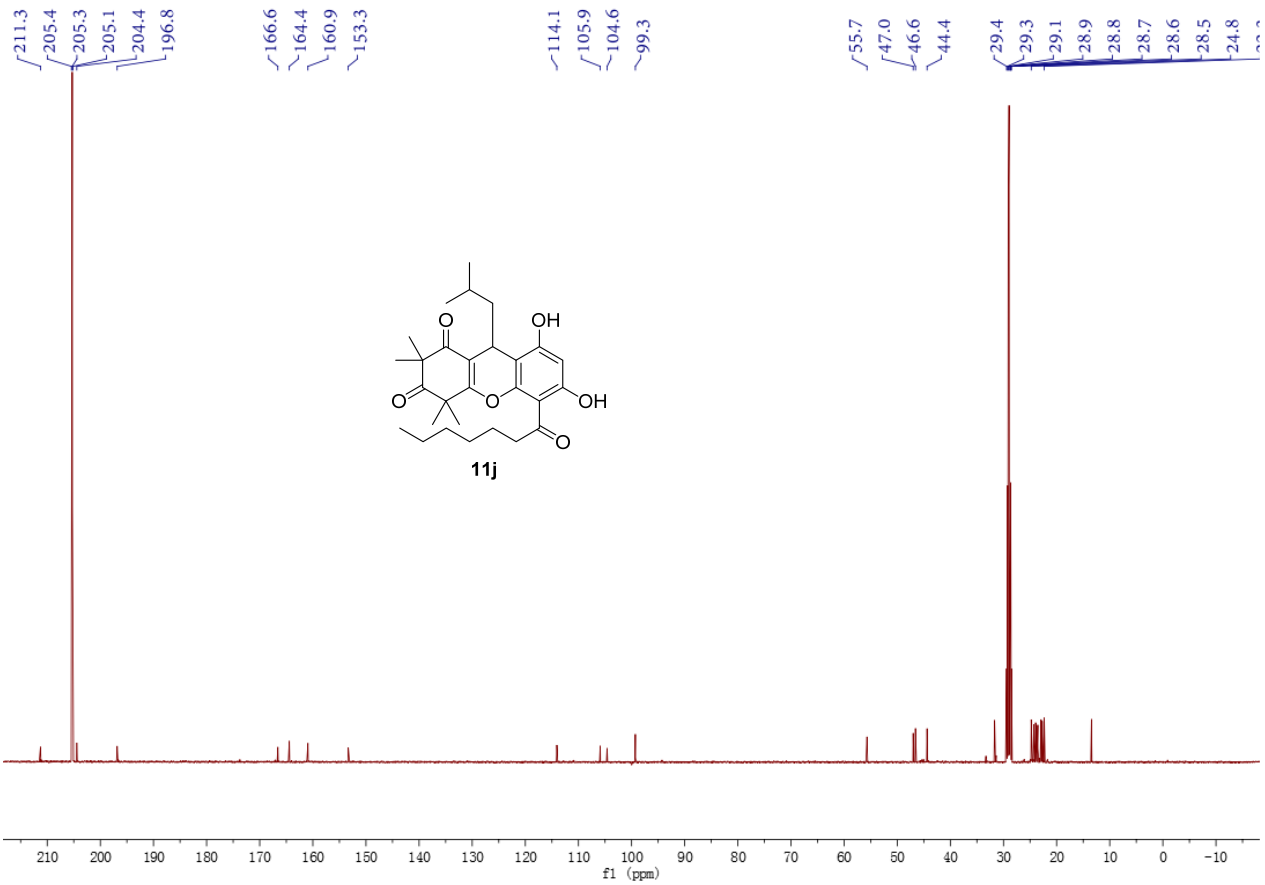

13.52
7.51
7.28
6.31
4.35
4.34
4.33
3.22
3.20
3.18
3.00
2.99
2.95
2.40
2.38
2.37
1.66
1.50
1.46
1.42
1.06
1.05
1.03
1.02
0.89
OH
O
O
O
OH
O
11h
0.97
0.98
0.99
1.01
1.01
1.09
1.05
3.19
3.39
3.29
3.79
2.56
6.36
6.40
f1 (ppm)

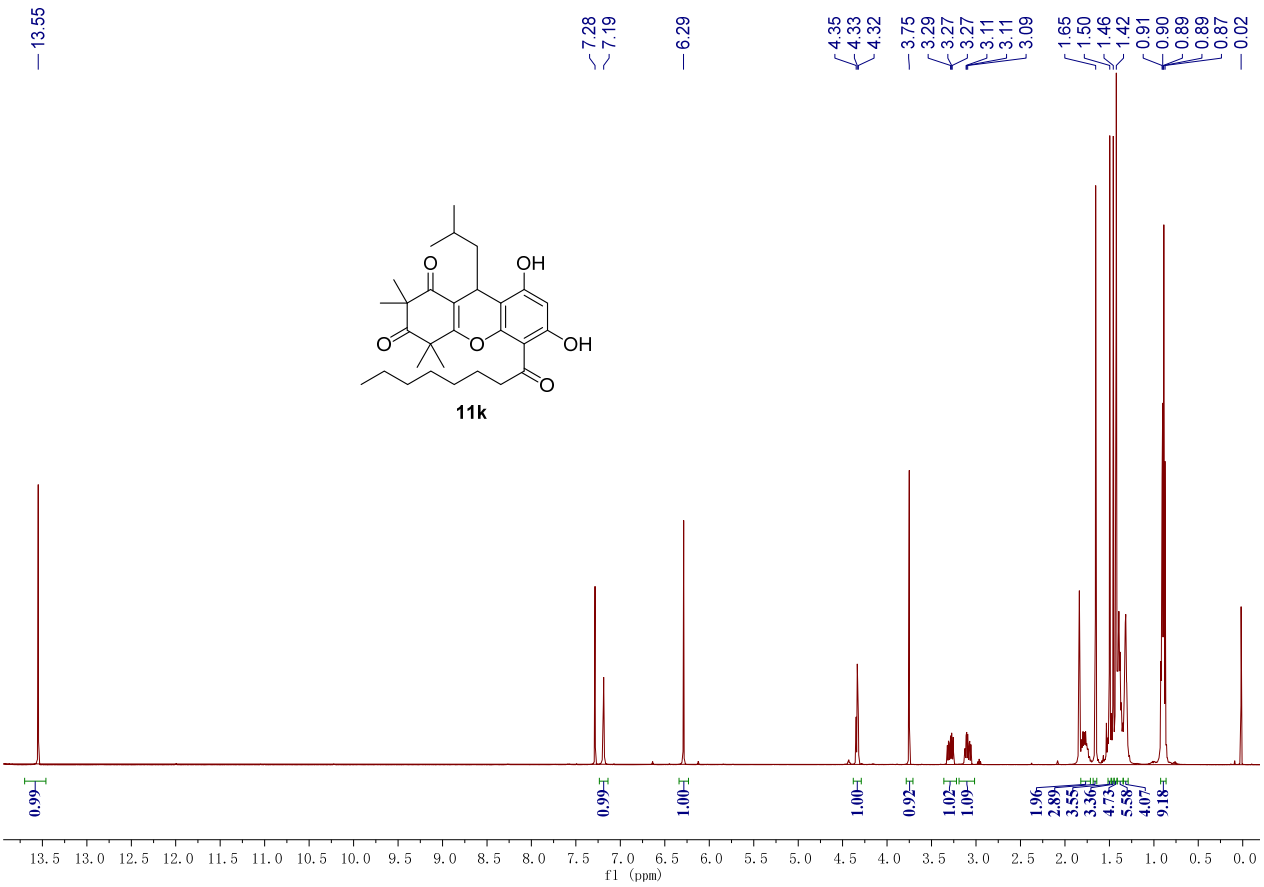

211.8
204.0
198.7
167.5
164.3
159.8
153.1
114.6
106.0
105.5
100.2
77.3
77.0
76.8
56.1
53.4
47.3
46.9
25.4
25.0
24.8
24.7
24.5
24.5
24.2
23.4
23.1
22.9
22.6
OH
O
O
O
OH
O
11h
f1 (ppm)

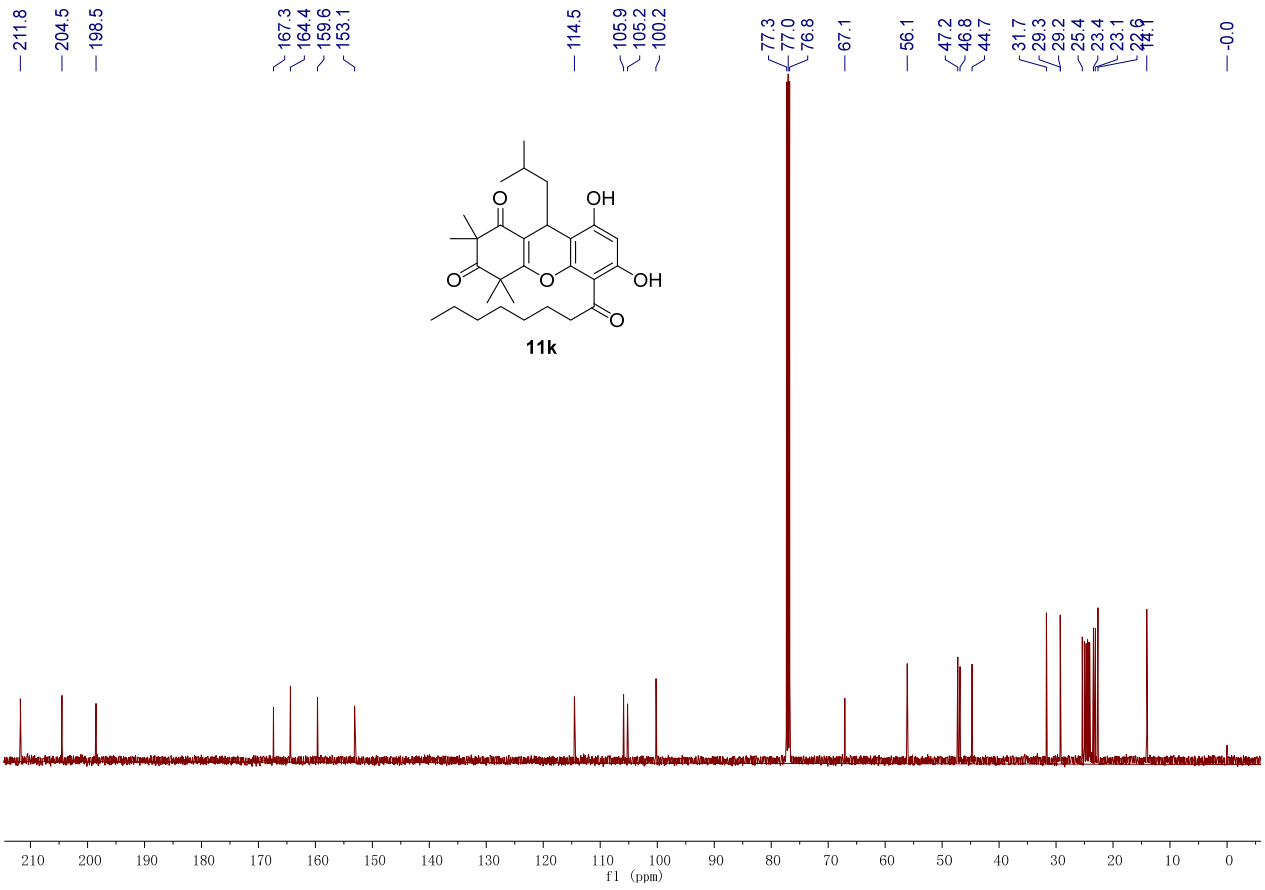

13.58
7.76
7.28
6.32
4.37
4.35
4.34
3.29
3.28
3.27
3.26
3.11
3.10
3.09
1.66
1.50
1.46
1.42
1.40
0.94
0.89
0.88
0.88
0.87
0.81
OH
O
O
O
OH
O
11i
0.98
0.99
1.00
1.02
1.04
1.12
2.35
3.34
20.03
3.28
7.61
f1 (ppm)

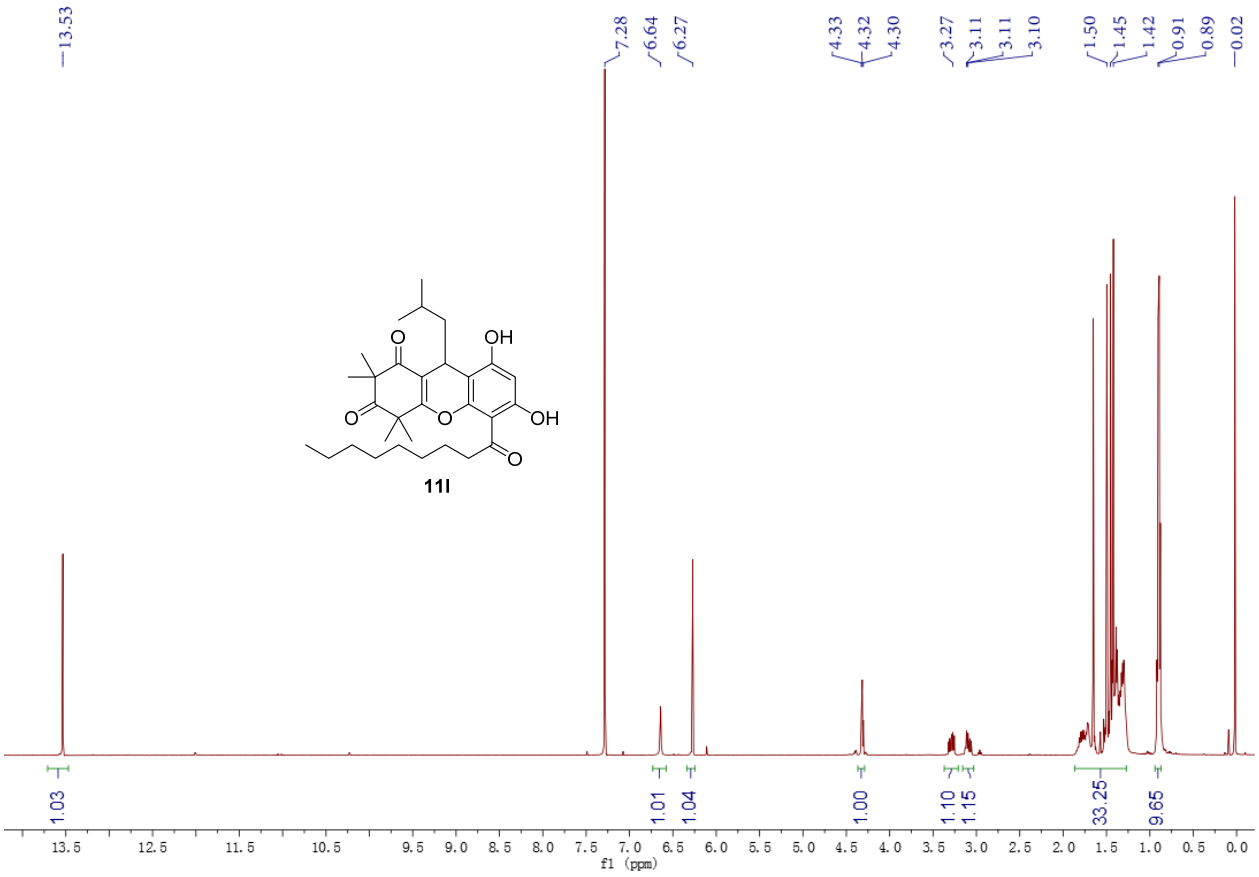

211.9
204.5
198.8
167.5
164.4
159.9
153.1
114.6
106.0
105.1
100.2
77.3
77.0
76.8
56.1
47.3
46.8
44.7
31.4
25.4
24.3
23.8
23.5
23.1
22.7
14.0
OH
O
O
O
OH
O
11i
f1 (ppm)

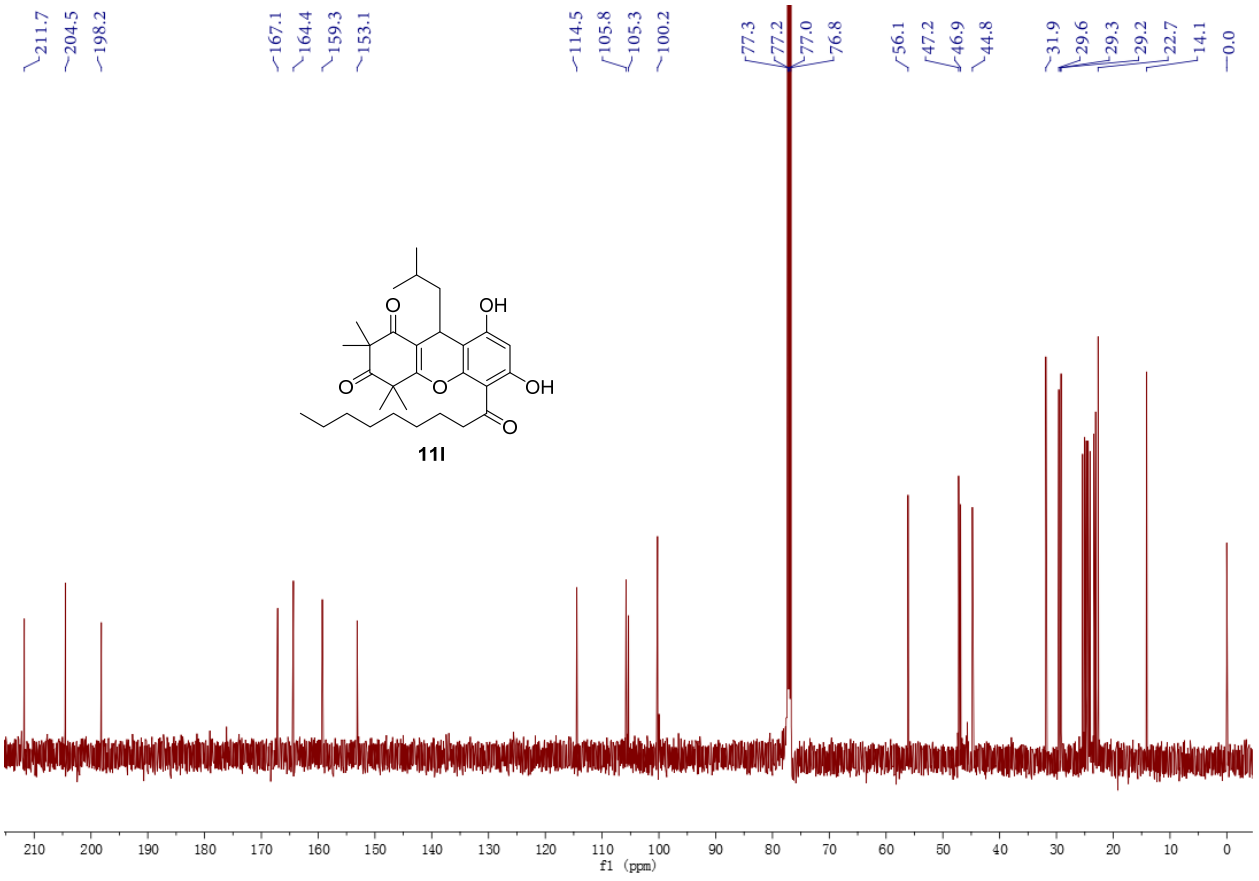

OH
O
O
O
OH
O
11j
0.88
0.95
1.04
1.00
1.08
1.19
2.53
3.33
4.82
4.22
15.98
9.39
f1 (ppm)

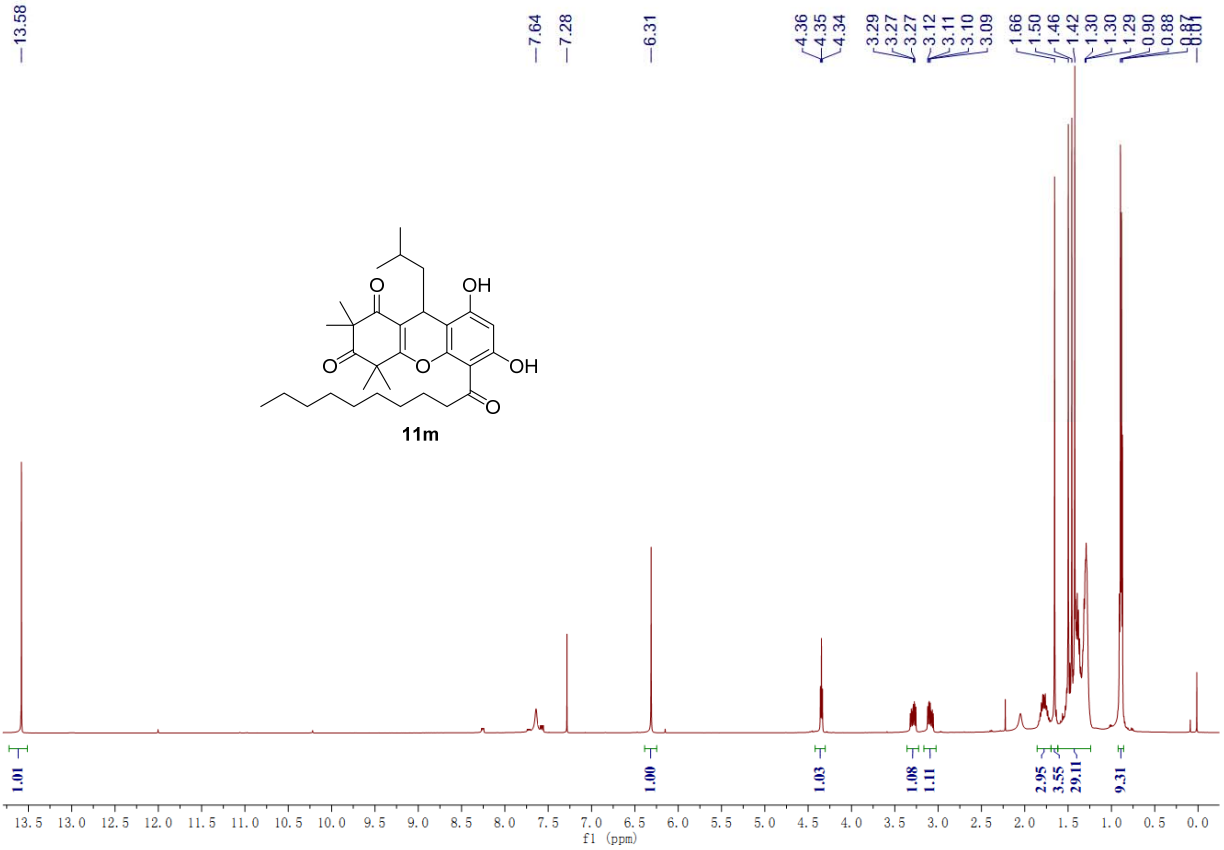

211.3
205.4
205.3
205.1
204.4
196.8
166.6
164.4
160.9
153.3
114.1
105.9
104.6
99.3
55.7
47.0
46.6
44.4
29.4
29.3
29.1
28.9
28.8
28.7
28.6
28.5
24.8
OH
O
O
O
OH
O
11j
f1 (ppm)

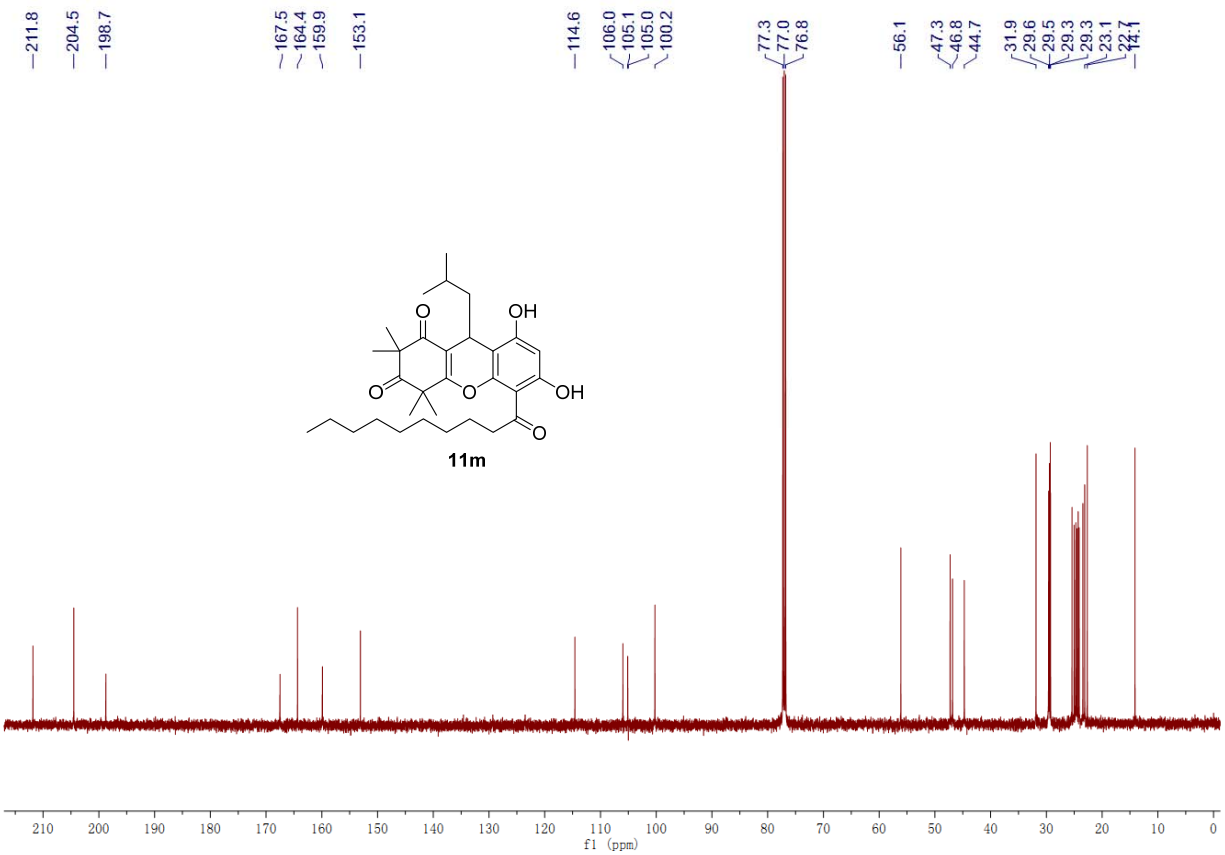

13.55
7.28
7.19
6.29
4.35
4.33
4.32
3.75
3.29
3.27
3.11
3.11
3.09
1.65
1.50
1.46
1.42
0.91
0.90
0.89
0.89
0.87
0.02
OH
O
O
O
OH
O
11k
0.99
0.99
1.00
1.00
0.92
1.02
1.09
1.96
2.89
3.55
3.36
4.73
5.58
4.07
9.18
f1 (ppm)

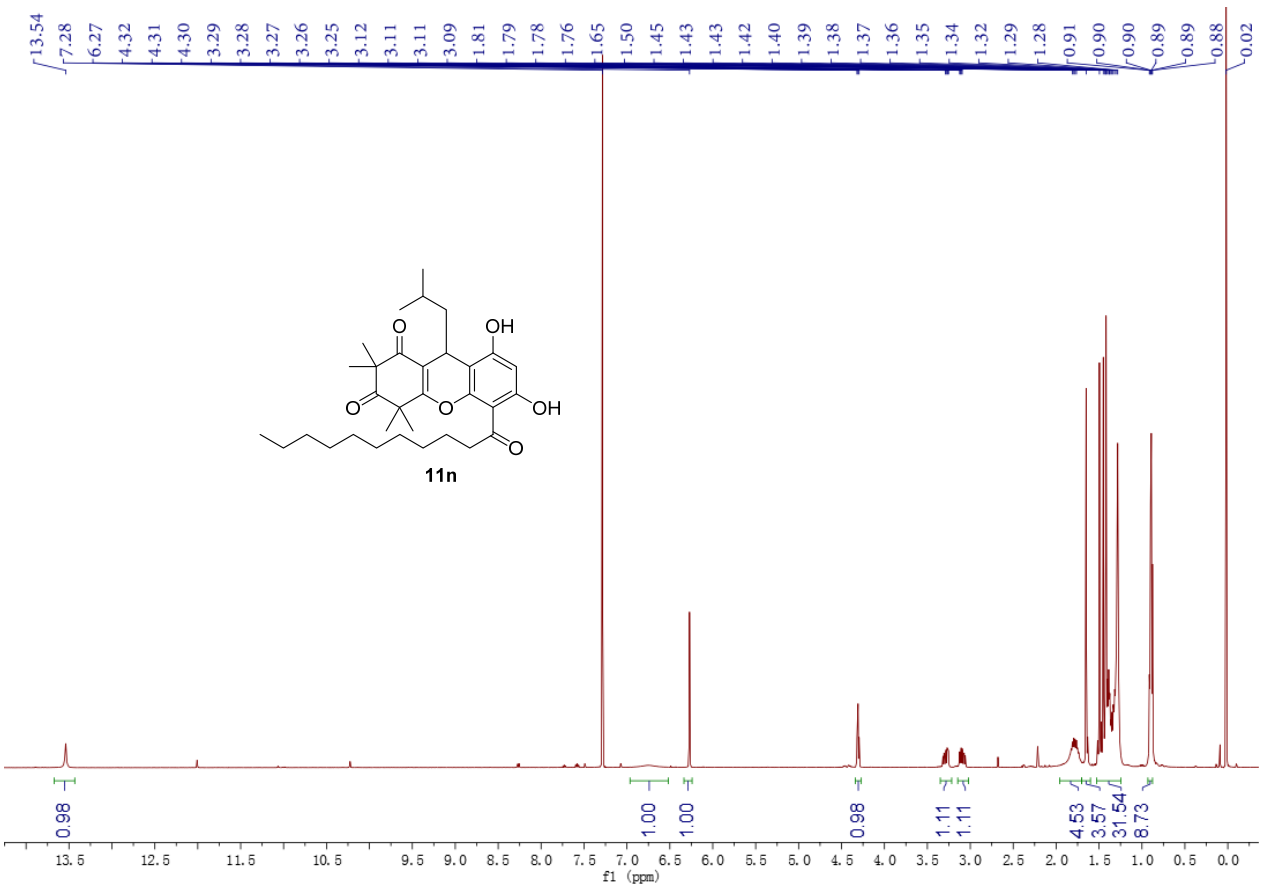

211.8
204.5
198.5
167.3
164.4
159.6
153.1
114.5
105.9
105.2
100.2
77.3
77.0
76.8
67.1
56.1
47.2
46.8
44.7
31.7
29.3
29.2
25.4
23.4
23.1
22.6
14.1
0.0
OH
O
O
O
OH
O
11k
f1 (ppm)

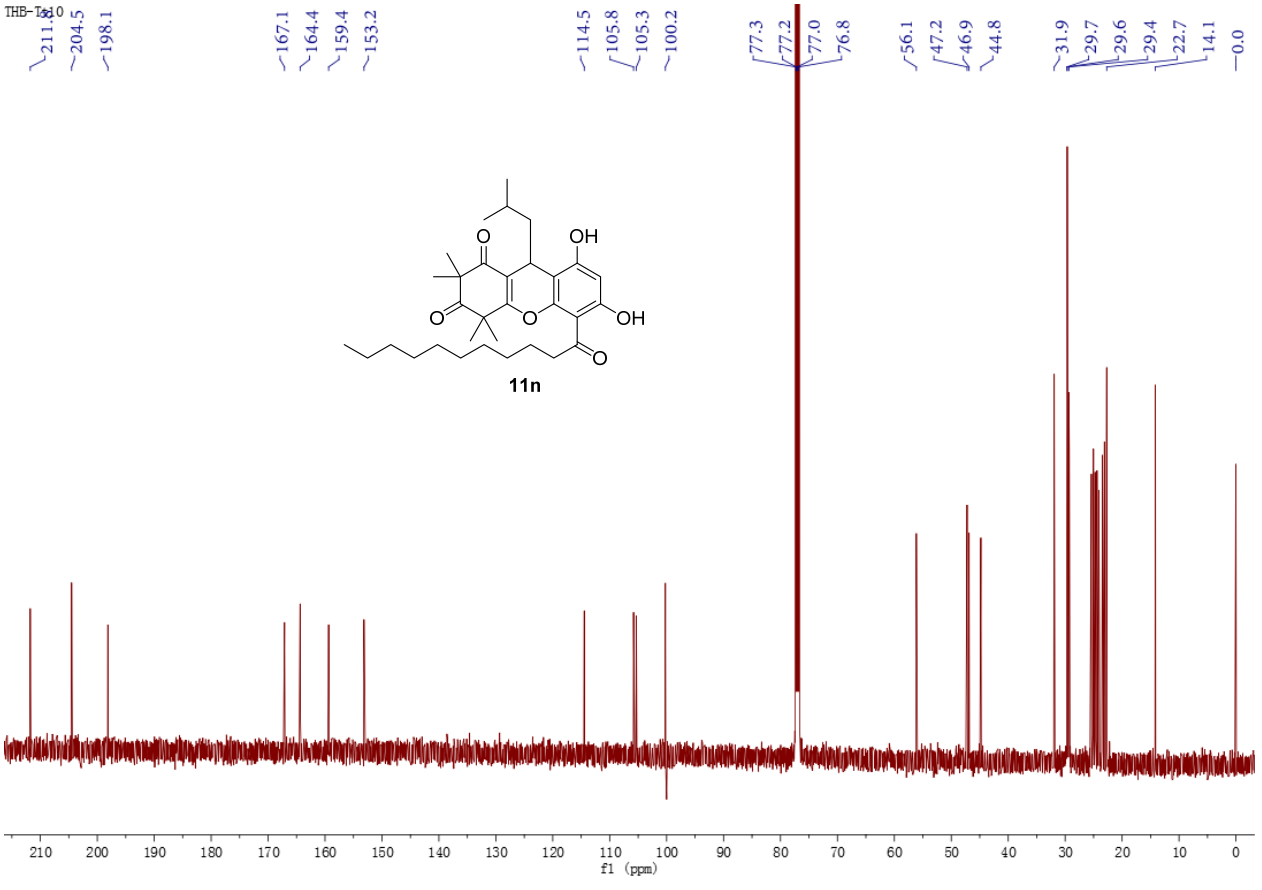

13.53
7.28
6.64
6.27
4.33
4.32
4.30
3.27
3.11
3.11
3.10
1.50
1.45
1.42
0.91
0.89
0.02
OH
O
O
O
OH
O
11l
1.03
1.01
1.04
1.00
1.10
1.15
33.25
9.65
f1 (ppm)

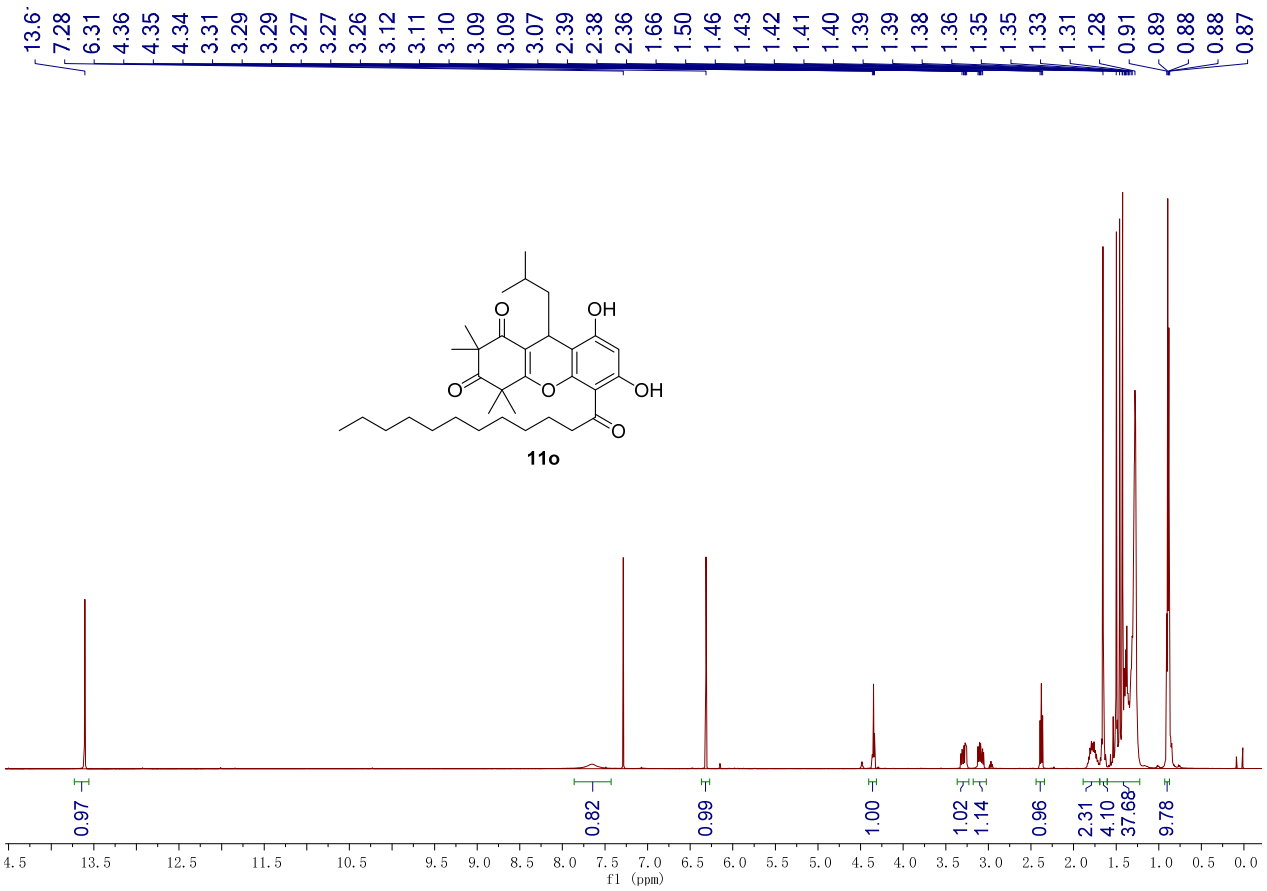

211.7
204.5
198.2
167.1
164.4
159.3
153.1
114.5
105.8
105.3
100.2
77.3
77.2
77.0
76.8
56.1
47.2
46.9
44.8
31.9
29.6
29.3
29.2
22.7
14.1
0.0
OH
O
O
O
OH
O
11l
f1 (ppm)

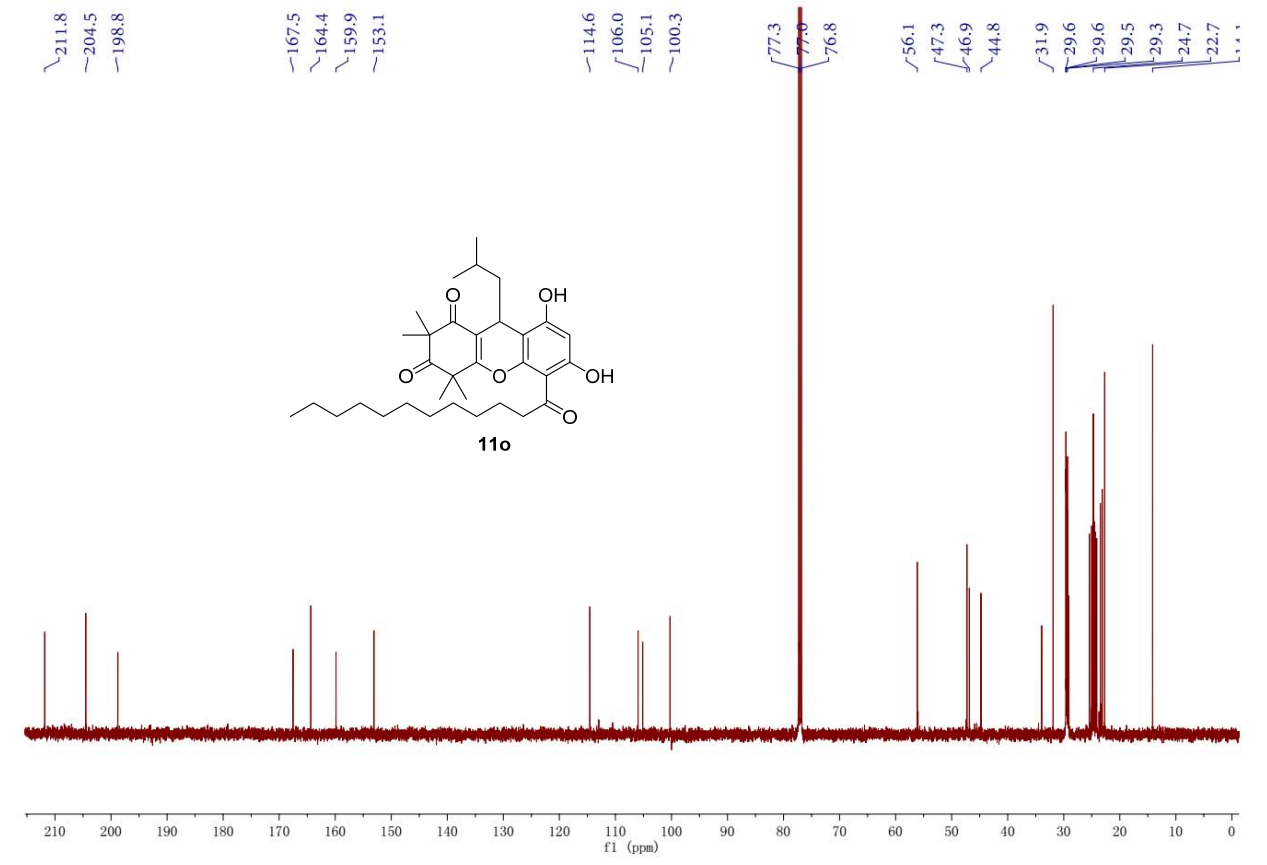

13.58
7.64
7.28
6.31
4.36
4.35
4.34
3.29
3.27
3.27
3.12
3.11
3.10
3.09
1.66
1.50
1.46
1.42
1.30
1.30
1.29
0.90
0.88
1.01
1.00
1.03
1.08
1.11
2.95
3.55
29.11
9.31
f1 (ppm)
11m

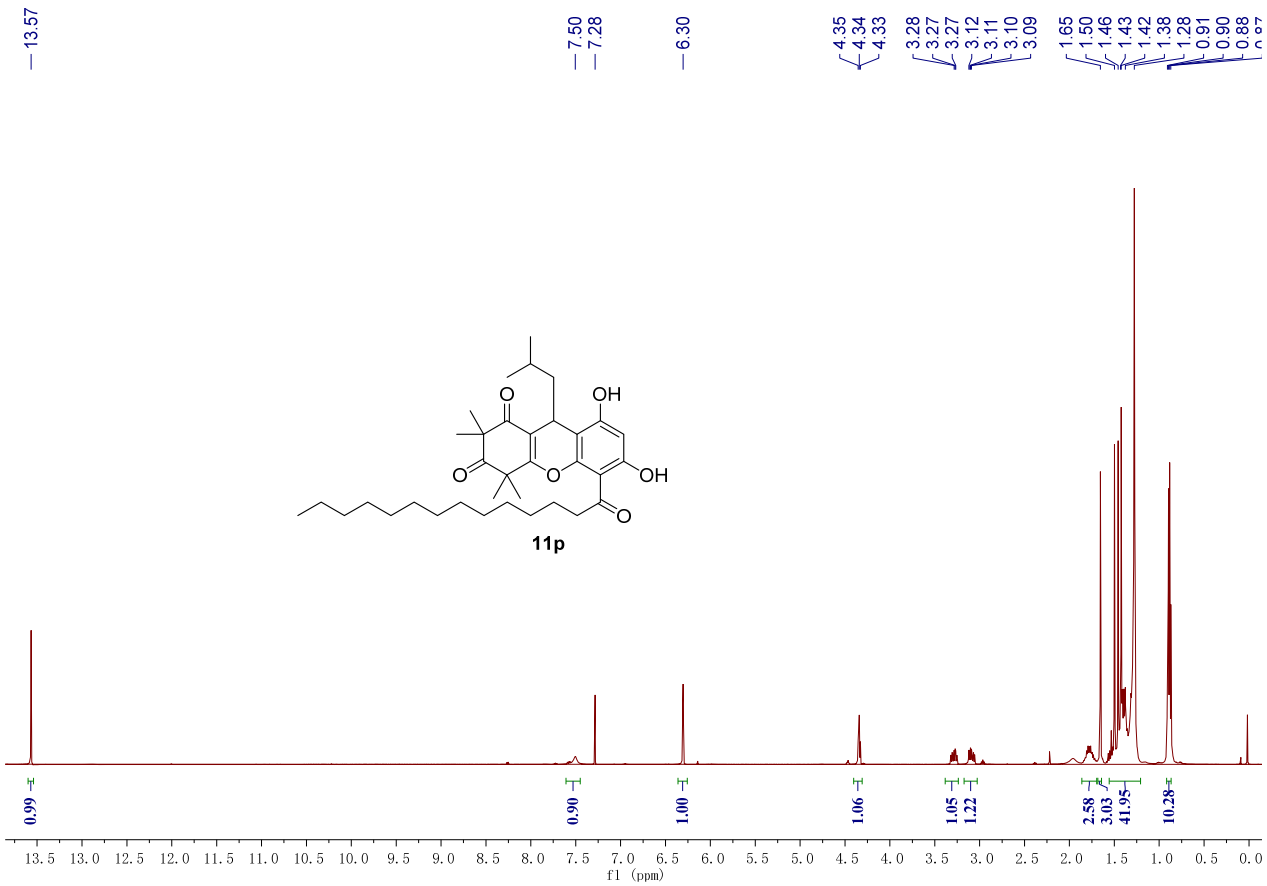

211.8
204.5
198.7
167.5
164.4
159.9
153.1
114.6
106.0
105.1
105.0
100.2
77.3
77.0
76.8
56.1
47.3
46.8
44.7
31.9
29.6
29.5
29.3
29.3
23.1
22.7
14.1
f1 (ppm)
11m

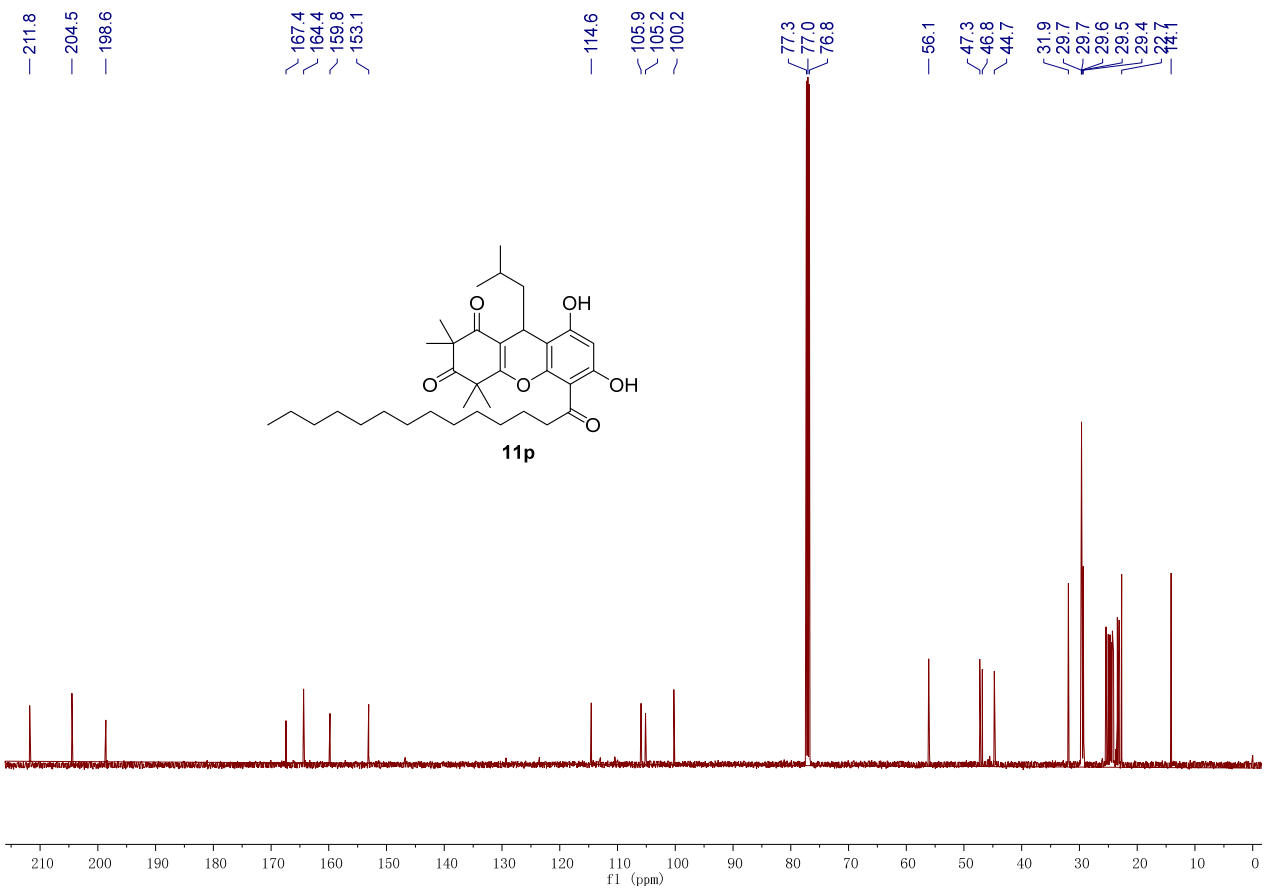

13.54
7.28
6.27
4.32
4.31
4.30
3.29
3.28
3.27
3.26
3.25
3.12
3.11
3.11
3.09
1.81
1.79
1.78
1.76
1.65
1.50
1.45
1.43
1.43
1.42
1.40
1.39
1.38
1.37
1.36
1.35
1.34
1.32
1.29
1.28
0.91
0.90
0.90
0.89
0.89
0.88
0.02
OH
O
O
O
OH
O
11n
0.98
1.00
1.00
0.98
1.11
1.11
4.53
3.57
31.54
8.73
f1 (ppm)

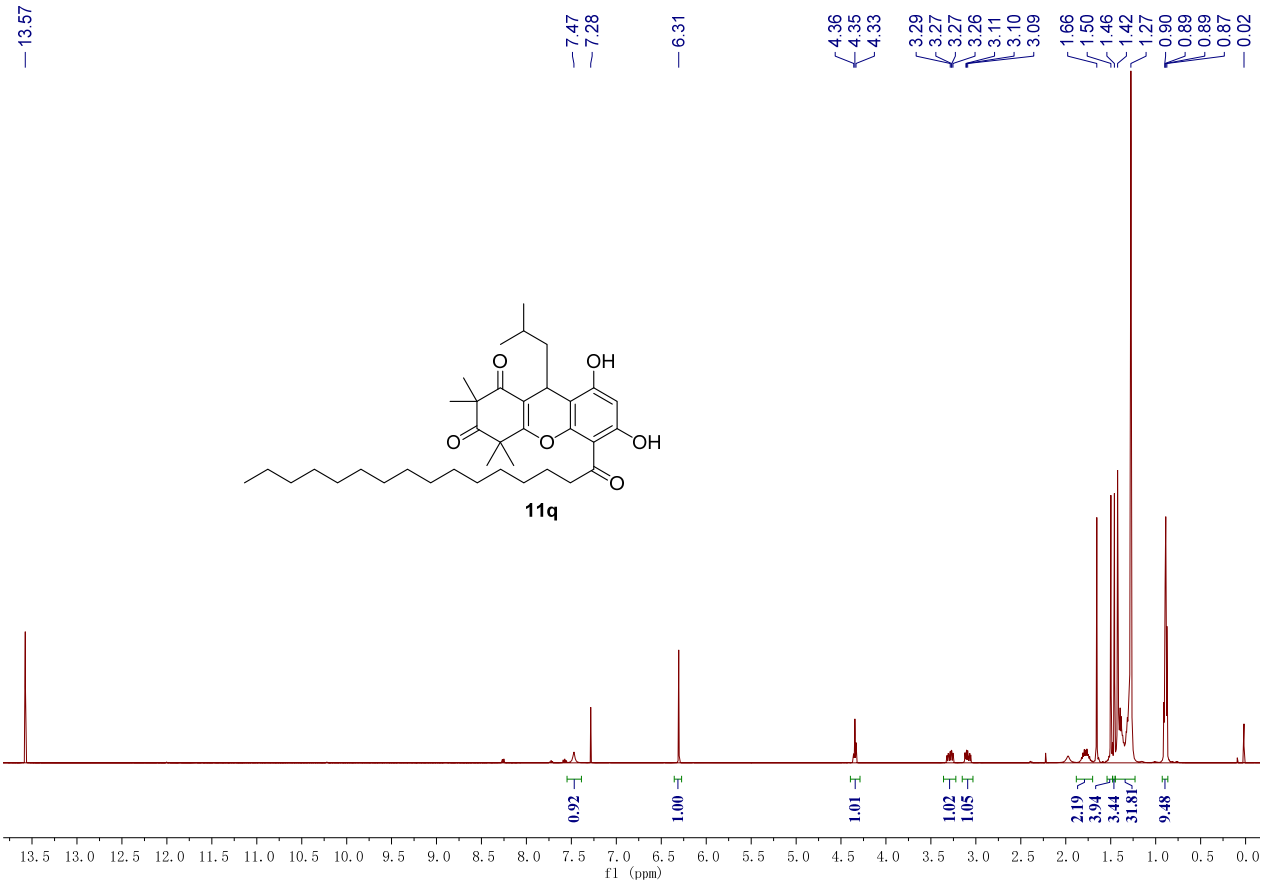

211.1
204.5
198.1
167.1
164.4
159.4
153.2
114.5
105.8
105.3
100.2
77.3
77.2
77.0
76.8
56.1
47.2
46.9
44.8
31.9
29.7
29.6
29.4
22.7
14.1
0.0
OH
O
O
O
OH
O
11n
f1 (ppm)

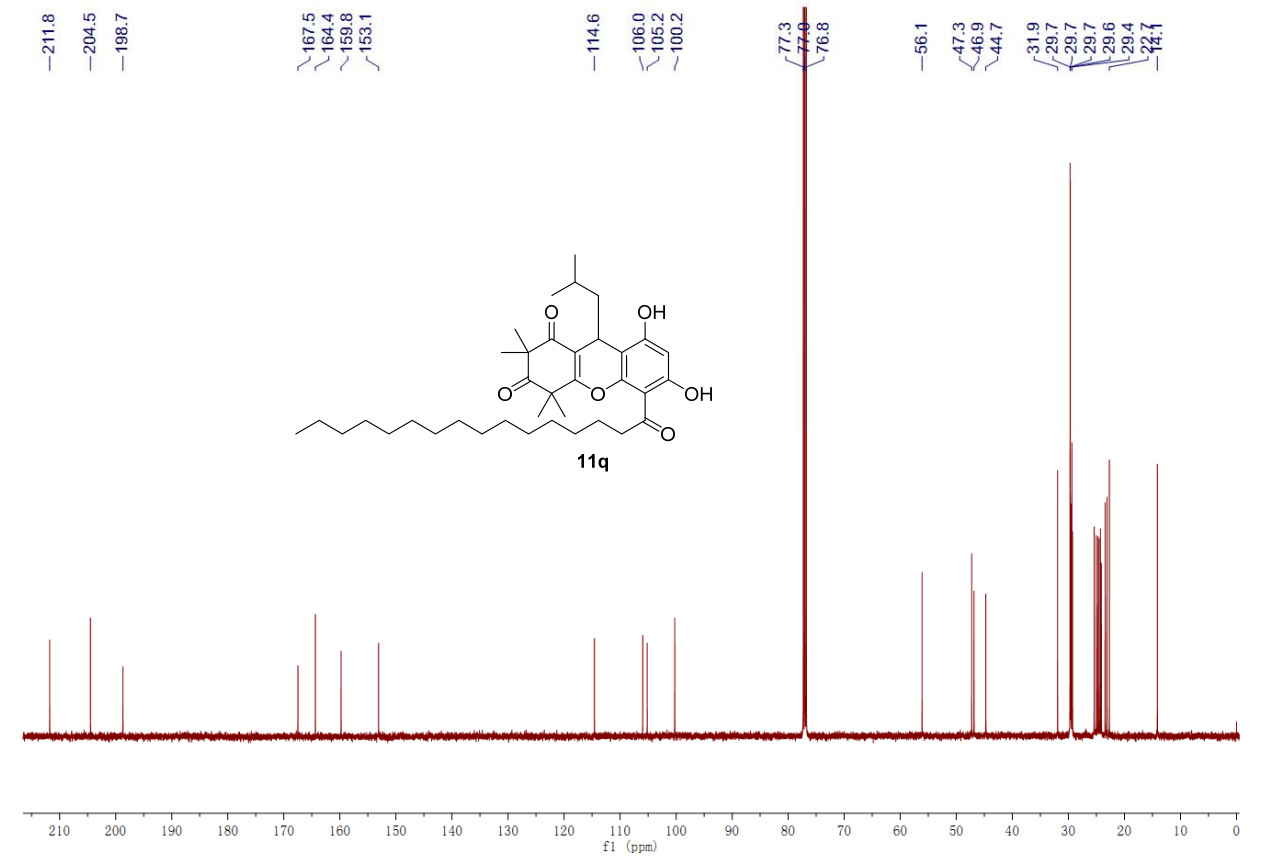

13.6
7.28
6.31
4.36
4.35
4.34
3.31
3.29
3.29
3.27
3.27
3.26
3.12
3.11
3.10
3.09
3.09
3.07
2.39
2.38
2.36
1.66
1.50
1.46
1.43
1.42
1.41
1.40
1.39
1.39
1.38
1.36
1.35
1.35
1.33
1.31
1.28
0.91
0.89
0.88
0.88
0.87
OH
O
O
O
OH
O
11o
0.97
0.82
0.99
1.00
1.02
1.14
0.96
2.31
4.10
37.68
9.78
f1 (ppm)

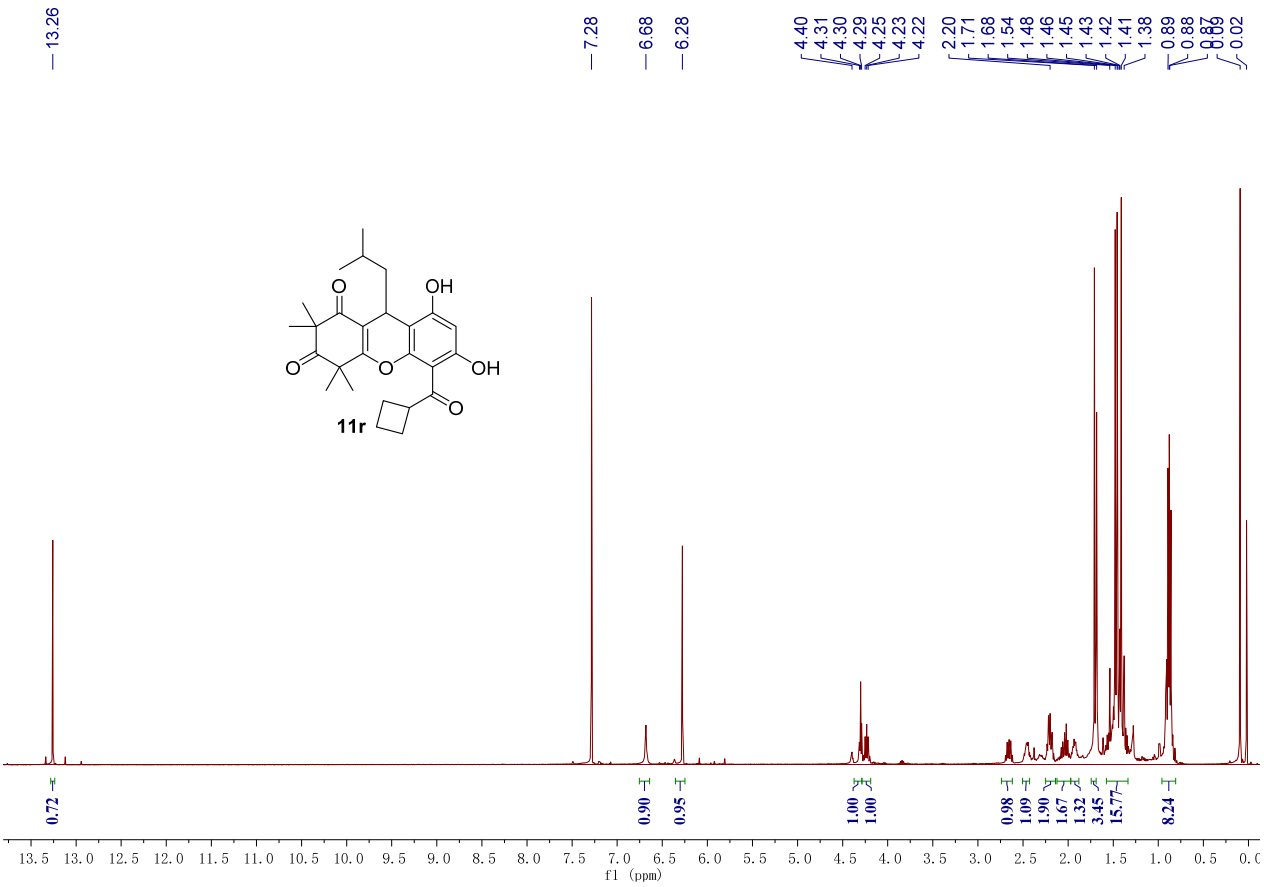

211.8
204.5
198.8
167.5
164.4
159.9
153.1
114.6
106.0
105.1
100.3
77.3
77.0
76.8
56.1
47.3
46.9
44.8
31.9
29.6
29.6
29.5
29.3
24.7
22.7
OH
O
O
O
OH
O
11o
f1 (ppm)

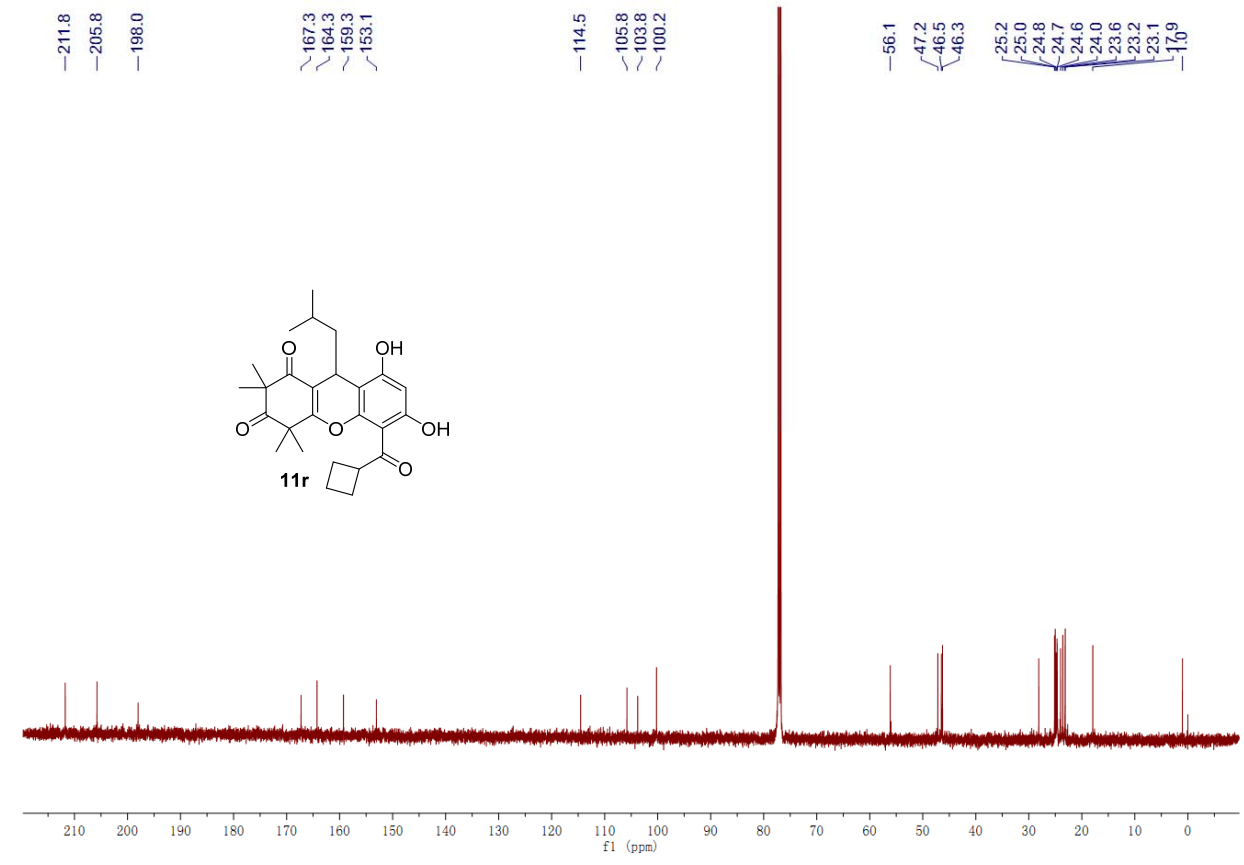

13.57
7.50
7.28
6.30
4.35
4.34
4.33
3.28
3.27
3.27
3.12
3.11
3.10
3.09
1.65
1.50
1.46
1.43
1.42
1.38
1.28
0.91
0.90
0.88
OH
O
O
O
OH
O
11p
0.99
0.90
1.00
1.06
1.05
1.22
2.58
3.03
41.95
10.28
f1 (ppm)


211.8
204.5
198.6
167.4
164.4
159.8
153.1
114.6
105.9
105.2
100.2
77.3
77.0
76.8
56.1
47.3
46.8
44.7
31.9
29.7
29.7
29.6
29.5
29.4
22.7
14.1
OH
O
O
O
OH
O
11p
f1 (ppm)

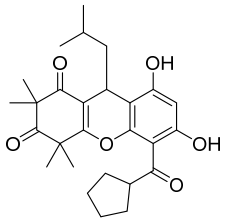

13.57
7.47
7.28
6.31
4.36
4.35
4.33
3.29
3.27
3.27
3.26
3.11
3.10
3.09
1.66
1.50
1.46
1.42
1.27
0.90
0.89
0.89
0.87
0.02
OH
O
O
O
OH
O
11q
0.92
1.00
1.01
1.02
1.05
2.19
3.94
3.44
31.81
9.48
f1 (ppm)


211.8
204.5
198.7
167.5
164.4
159.8
153.1
114.6
106.0
105.2
100.2
77.3
77.0
76.8
56.1
47.3
46.9
44.7
31.9
29.7
29.7
29.7
29.6
29.4
22.7
14.1
OH
O
O
O
OH
O
11q
f1 (ppm)

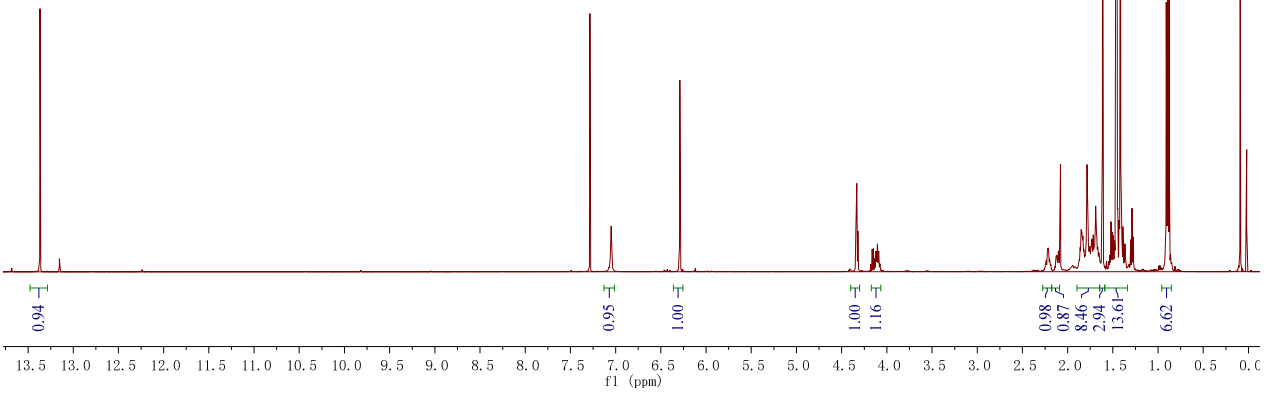

13.26
7.28
6.68
6.28
4.40
4.31
4.30
4.29
4.25
4.23
4.22
2.20
1.71
1.68
1.54
1.48
1.46
1.45
1.43
1.42
1.41
1.38
0.89
0.88
0.72
0.90
0.95
1.00
1.00
0.98
1.09
1.90
1.67
1.32
3.45
15.77
8.24
f1 (ppm)
11r

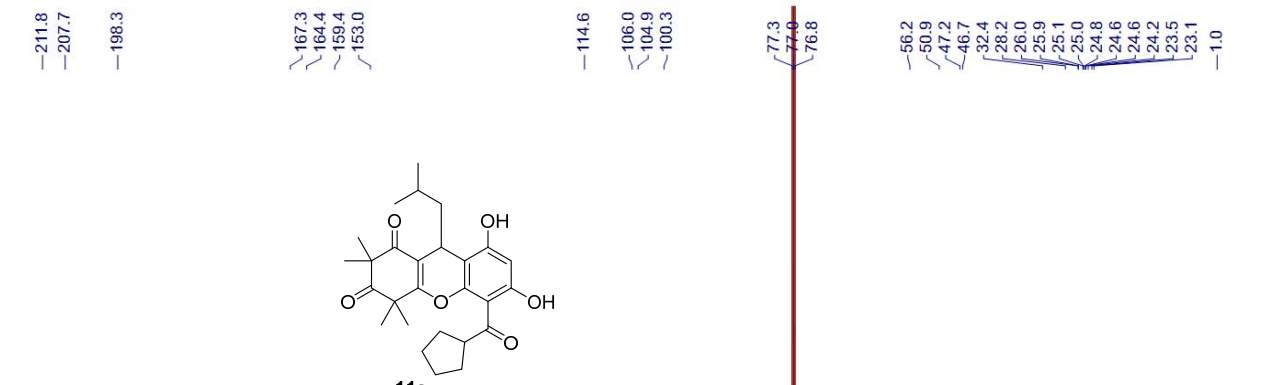

211.8
205.8
198.0
167.3
164.3
159.3
153.1
114.5
105.8
103.8
100.2
56.1
47.2
46.5
46.3
25.2
25.0
24.8
24.7
24.6
24.0
23.6
23.2
23.1
17.9
f1 (ppm)
11r


13.37
7.28
7.05
6.29
4.34
4.33
4.32
4.16
4.15
4.12
4.11
4.10
4.09
2.22
2.21
2.21
2.13
2.12
2.12
2.11
2.10
2.10
2.09
2.08
1.85
1.85
1.84
1.84
1.83
1.78
1.74
1.73
1.72
1.71
1.71
1.70
1.70
1.69
1.68
1.68
1.68
1.61
1.52
1.51
1.49
1.48
1.46
1.45
1.45
1.43
1.42
1.40
1.39
1.30
1.29
1.27
0.91
0.90
0.90
0.89
0.88
0.88
0.09
0.02


O
OH
O
O
OH
O

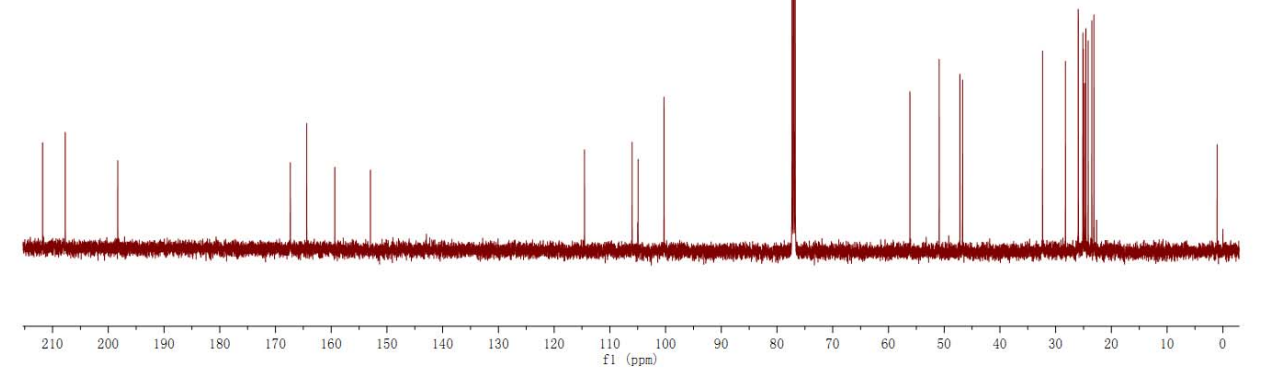
11s

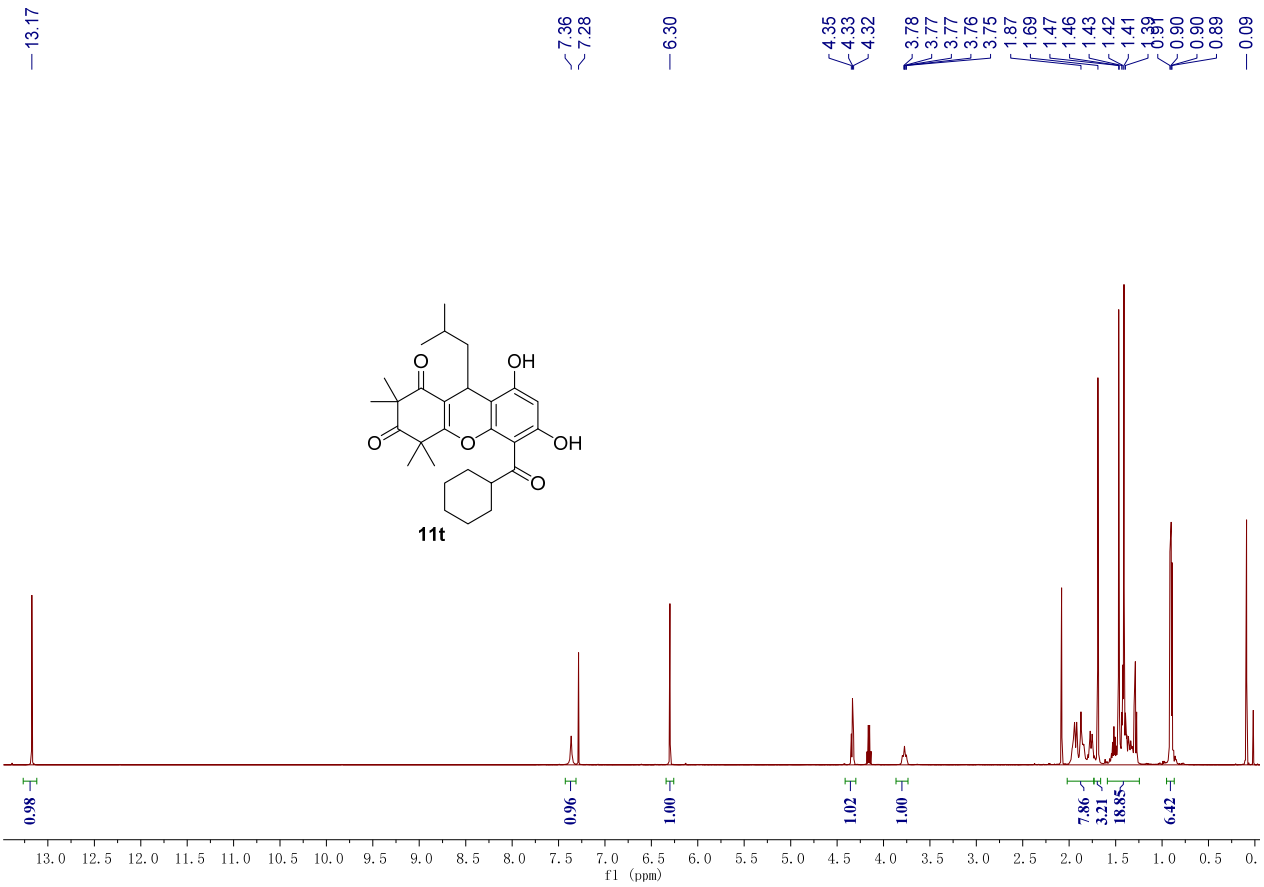

0.94
0.95
1.00
1.00
1.16
0.98
0.87
8.46
2.94
13.61
6.62
13.5 13.0 12.5 12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

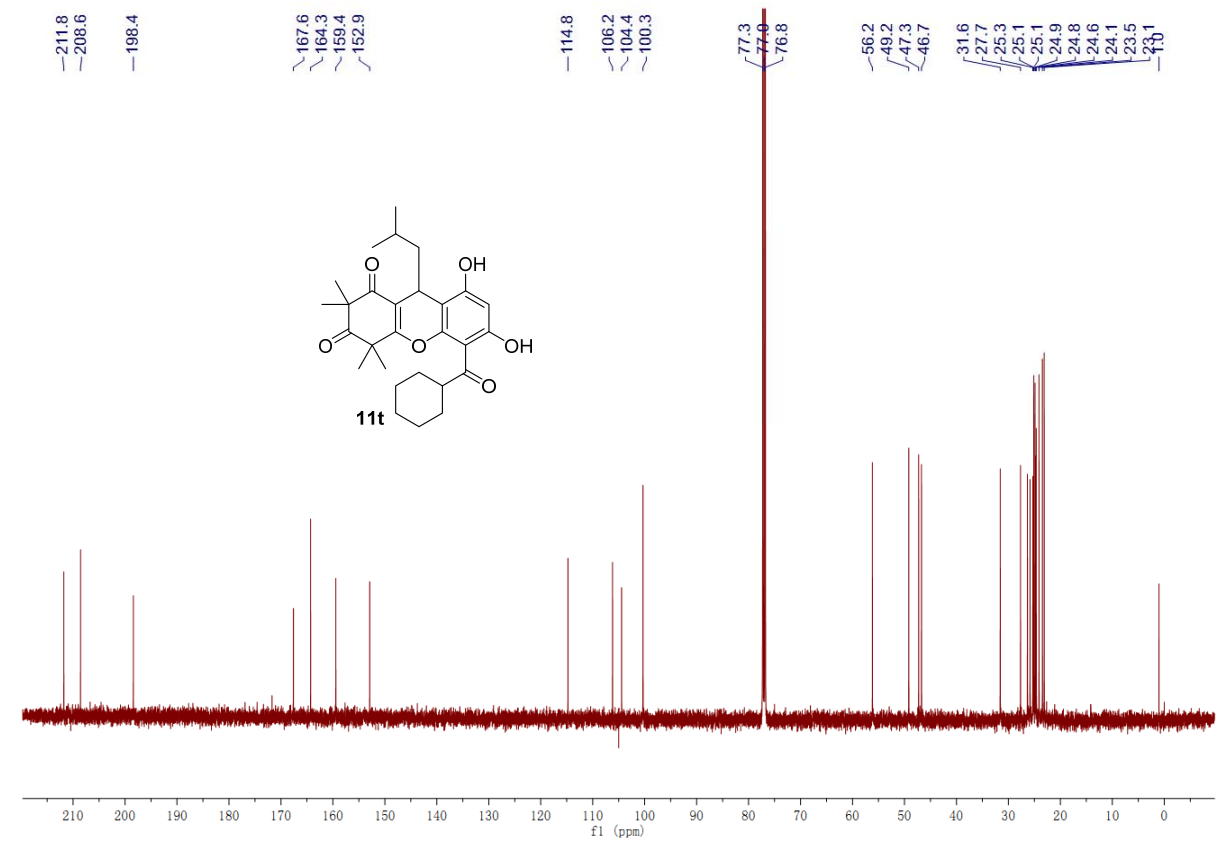

211.8
207.7
198.3
167.3
164.4
159.4
153.0
114.6
106.0
104.9
100.3
77.3
77.0
76.8
56.2
50.9
47.2
46.7
32.4
28.2
26.0
25.9
25.1
25.0
24.8
24.6
24.6
24.2
23.5
23.1
1.0

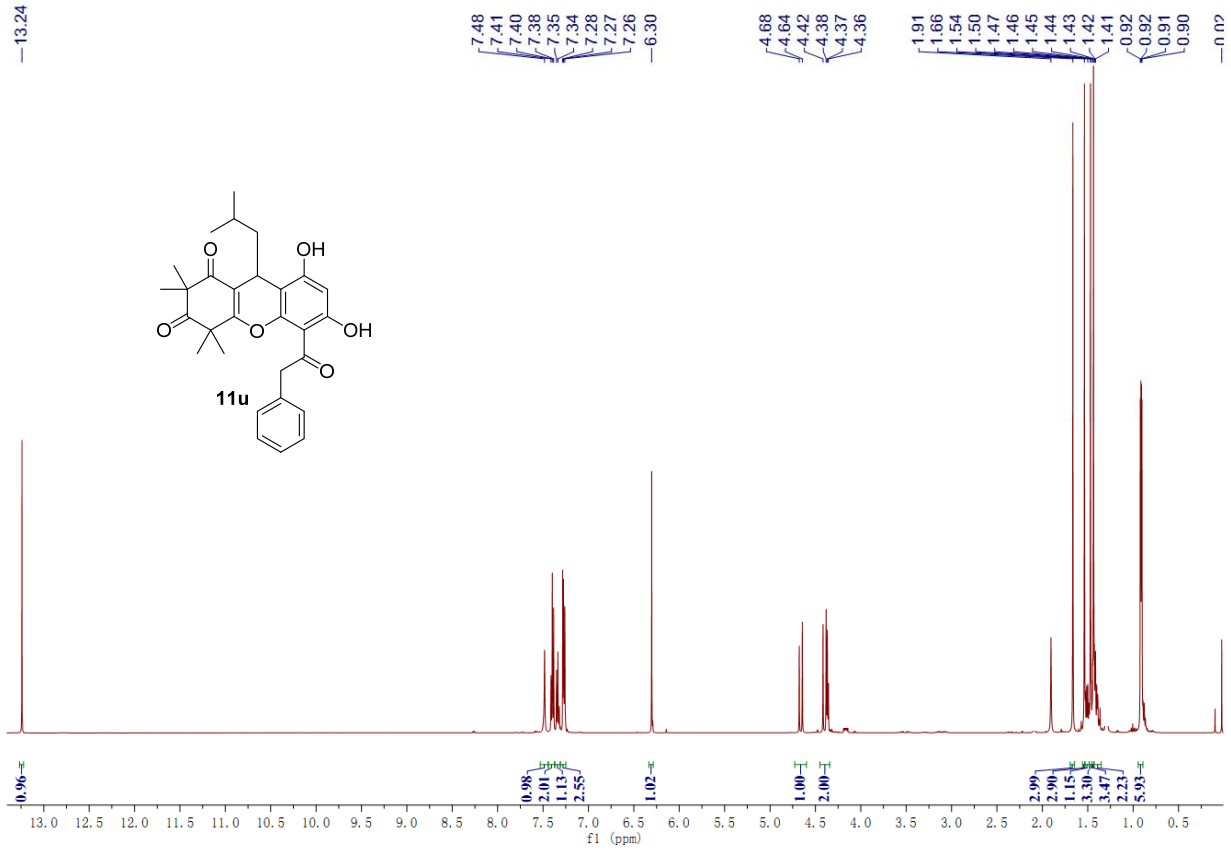
O
OH
O
O
OH
O

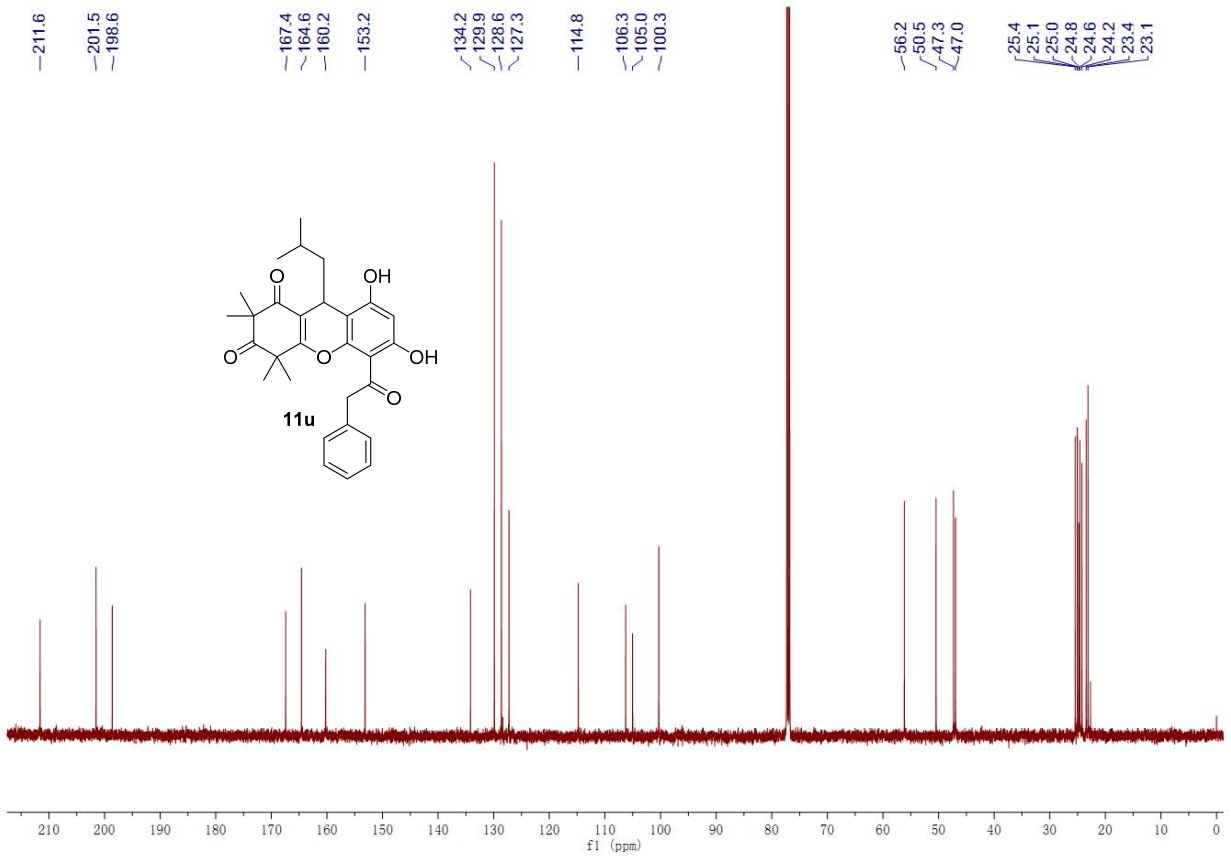
11s

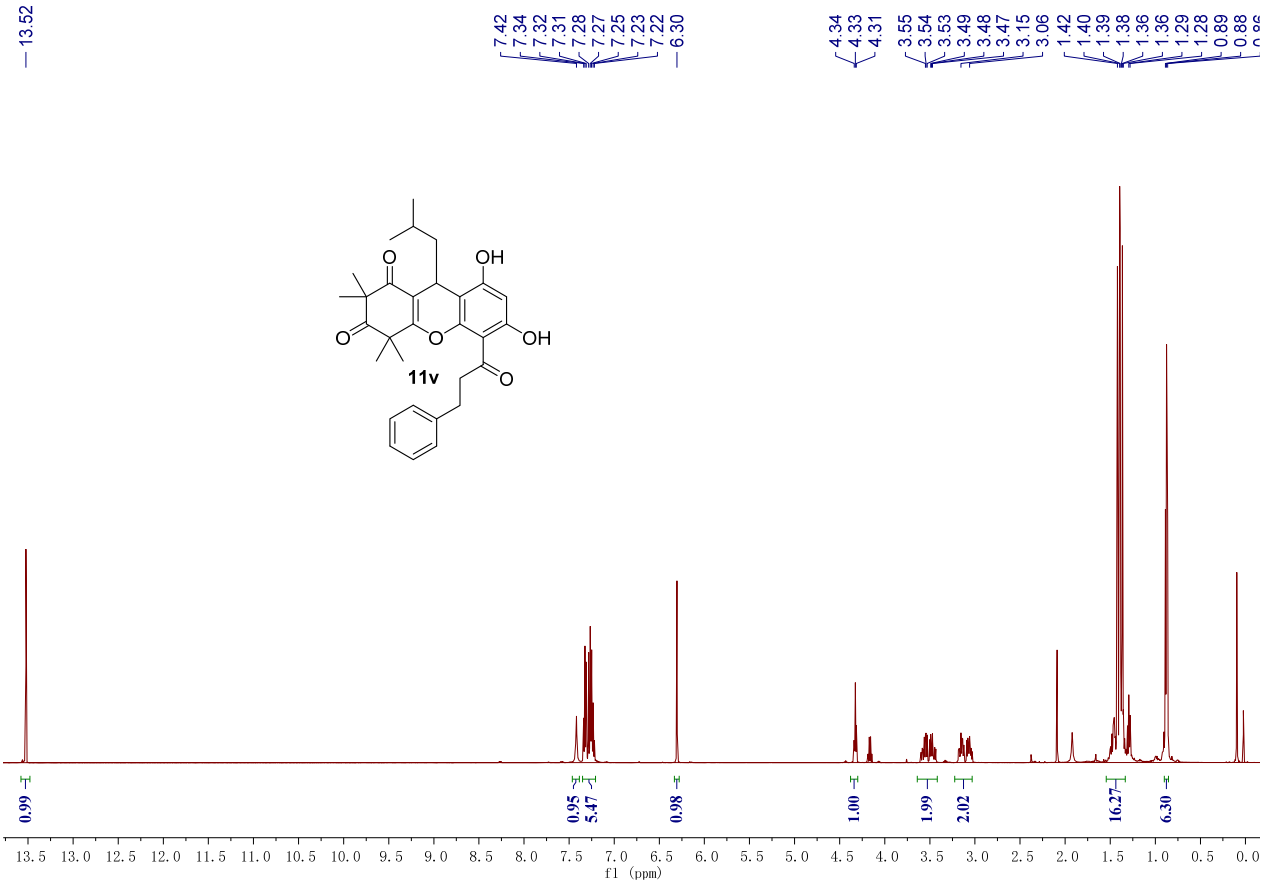

210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


13.17
7.36
7.28
6.30
4.35
4.33
4.32
3.78
3.77
3.77
3.76
3.75
1.87
1.69
1.47
1.46
1.43
1.42
1.41
0.90
0.90
0.89
0.09
11t
0.98
0.96
1.00
1.02
1.00
7.86
3.21
18.85
6.42
f1 (ppm)


211.8
208.6
198.4
167.6
164.3
159.4
152.9
114.8
106.2
104.4
100.3
77.3
77.0
76.8
56.2
49.2
47.3
46.7
31.6
27.7
25.3
25.1
25.1
24.9
24.8
24.6
24.1
23.5
23.1
11t
f1 (ppm)


13.24
7.48
7.41
7.40
7.38
7.35
7.34
7.28
7.27
7.26
6.30
4.68
4.64
4.42
4.38
4.37
4.36
1.91
1.66
1.54
1.50
1.47
1.46
1.45
1.44
1.43
1.42
1.41
0.92
0.92
0.91
0.90
0.96
0.98
2.01
1.13
2.55
1.02
1.00
2.00
2.99
2.90
1.15
3.30
3.47
2.23
5.93
f1 (ppm)
OH
OH
O
O
O
O
11u


211.6
201.5
198.6
167.4
164.6
160.2
153.2
134.2
129.9
128.6
127.3
114.8
106.3
105.0
100.3
56.2
50.5
47.3
47.0
25.4
25.1
25.0
24.8
24.6
24.2
23.4
23.1
f1 (ppm)
OH
OH
O
O
O
O
11u


13.52
7.42
7.34
7.32
7.31
7.28
7.27
7.25
7.23
7.22
6.30
4.34
4.33
4.31
3.55
3.54
3.53
3.49
3.48
3.47
3.15
3.06
1.42
1.40
1.39
1.38
1.36
1.36
1.29
1.28
0.89
0.88
OH
O
O
O
OH
11v
O
0.99
0.95
5.47
0.98
1.00
1.99
2.02
16.27
6.30
f1 (ppm)

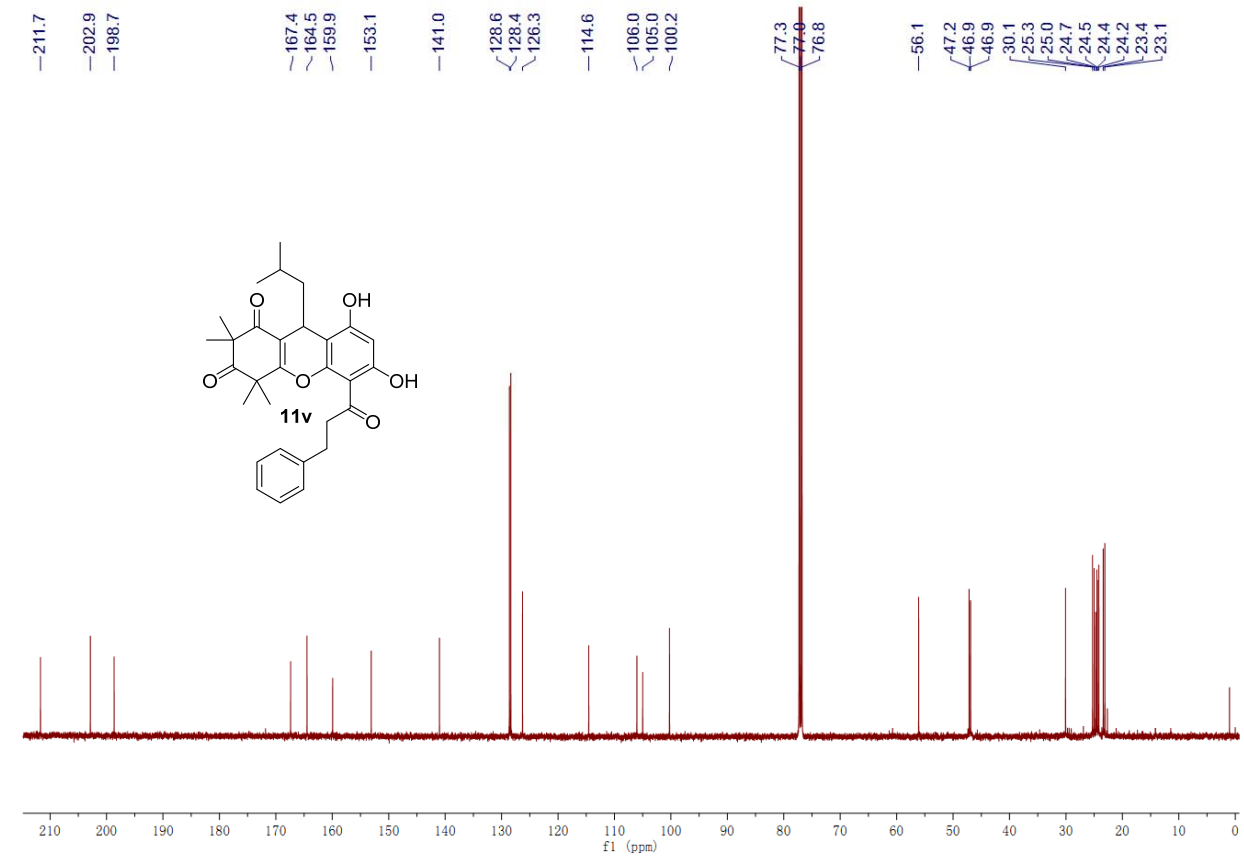

211.7
202.9
198.7
167.4
164.5
159.9
153.1
141.0
128.6
128.4
126.3
114.6
106.0
105.0
100.2
77.3
77.0
76.8
56.1
47.2
46.9
46.9
30.1
25.3
25.0
24.7
24.5
24.4
24.2
23.4
23.1
OH
O
O
O
OH
11v
O
f1 (ppm)

Table 1. *In vitro* antibacterial evaluation (MIC) of RDSB analogues **11a**-**11v** against MRSA (JCSC 4788) and standard SA (ATCC 6538).

Comp.	R	MIC_{MRSA} µg/mL	MIC_{SA} µg/mL	Comp.	R	MIC_{MRSA} µg/mL	MIC_{SA} µg/mL
11a	-	234.67±47.70	>256	**11l**	*n*-C_8H_{17}	0.58±0.19	0.29±0.09
11b	H	117.33±23.85	149.67±48.45	**11m**	*n*-C_9H_{19}	0.46±0.09	0.58±0.19
11c	CH_3	3.67±0.75	3.67±0.75	**11n**	*n*-$C_{10}H_{21}$	1.00±0.00	1.17±0.37
11d	C_2H_5	1.83±0.37	1.83±0.37	**11o**	*n*-$C_{11}H_{23}$	7.33±1.49	7.33±1.49
11e	*n*-C_3H_7	1.83±0.37	1.83±0.37	**11p**	*n*-$C_{13}H_{27}$	234.67±47.70	117.33±23.85
11f	*i*-C_3H_7	3.67±0.75	3.67±0.75	**11q**	*n*-$C_{15}H_{31}$	>256	>256
11g	*n*-C_4H_9	0.92±0.19	0.58±0.19	**11r**	*c*-C_4H_7	7.33±1.49	3.67±0.75
11h	*i*-C_4H_9	1.00±0.00	0.58±0.19	**11s**	*c*-C_5H_9	3.67±0.75	3.67±0.75
11i	*n*-C_5H_{11}	0.46±0.09	0.58±0.19	**11t**	*c*-C_6H_{11}	3.67±0.75	2.33±0.75
11j	*n*-C_6H_{13}	0.46±0.09	0.29±0.09	**11u**	CH_2Ph	4.67±1.49	3.67±0.75
11k	*n*-C_7H_{15}	0.25±0.00	0.29±0.09	**11v**	C_2H_4Ph	1.83±0.37	1.83±0.37
1	-	0.92±0.19	1.17±0.37	**Van.**	-	1.17±0.37	0.58±0.19

Table 2. Antibacterial spectrum of **11k** against various bacteria

Bacteria	G^+/G^-	MIC (μg/mL)		
		RDSB	**11k**	Vancomycin
S. aureus (ATCC 29213)	G^+	0.93±0.17	0.57±0.17	0.93±0.17
S. aureus (ATCC 6538)	G^+	1.14±0.35	0.23±0.04	0.93±0.17
S. aureus (CMCC 26003)	G^+	0.46±0.09	0.27±0.10	0.46±0.09
MRSA (JCSC 4788)	G^+	1.14±0.35	0.29±0.09	0.93±0.17
MRSA (JCSC 2172)	G^+	0.57±0.17	0.29±0.09	0.86±0.23
MRSA (JCSC 3063)	G^+	0.64±0.23	0.21±0.06	0.93±0.17
MRSA (JCSC 4469)	G^+	0.54±0.21	0.30±0.13	0.46±0.09
MRSA (JCSC 4744)	G^+	0.57±0.17	0.14±0.04	1.14±0.35
MRSA (NCTC 10442)	G^+	1.14±0.35	0.46±0.09	1.29±0.45
MRSA (N315)	G^+	1.07±0.42	0.23±0.04	1.14±0.35
MRSA (85/2082)	G^+	1.29±0.45	0.32±0.11	1.07±0.42
B. cereus (ATCC 10876)	G^+	0.57±0.17	0.57±0.17	0.57±0.17
P. acnes (ATCC 6919)	G^+	0.64±0.23	0.23±0.04	0.54±0.21
E. faecalis (ATCC 29212)	G^+	1.14±0.35	0.32±0.11	0.64±0.23
S. epidermids (ATCC 12228)	G^+	1.29±0.45	0.29±0.09	0.57±0.17
VRE (NO.151458137)	G^+	1.86±0.35	1.86±0.35	>32
B. polymyxa (GIM1.467)	G^+	>32	>32	>32
B. polymyxa (ATCC842)	G^+	>32	>32	>32
E. coli (ATCC 8739)	G^-	>32	>32	>32
S. typhi (CMCC 44102)	G^-	>32	>32	>32
S. dysenteriae (CMCC 51252)	G^-	>32	>32	>32
C. albicans (ATCC 10231)	Fungi	>32	>32	>32