Supporting Information for:

Synthesis and *in vitro* evaluation of zerumbone pendant derivatives: Potent candidates for anti-diabetic and anti-proliferative activities

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General Methods:

All the chemicals were of the best grade commercially available and were used without further purification. All the solvents were purified according to standard procedures; dry solvents were obtained according to the literature methods and stored over molecular sieves. Analytical thin layer chromatography was performed on glass plates coated with silica gel containing calcium sulfate binder. Gravity column chromatography was performed using 60-120 or 100-200 mesh silica gel, mixtures of hexane-ethyl acetate were used for elution. Melting point was determined on a Buchi melting point apparatus and is uncorrected. Proton nuclear magnetic resonance spectra (^{1}H NMR) were recorded on a Bruker AV 500 spectrophotometers ($CDCl_3$ as solvent). Chemical shifts for ^{1}H NMR spectra are reported as δ, in units of parts per million (ppm) downfield from $SiMe_4$ (δ 0.0) and relative to the signal of chloroform-d (δ 7.25, singlet). Multiplicities were given as: s (singlet); d (doublet); t (triplet); q (quartet); quin (quintet); dd (double doublet); m (multiplet). Coupling constants are reported as *J* value in Hz. Carbon nuclear magnetic resonance spectra (^{13}C NMR) are reported as δ in units of parts per million (ppm) downfield from $SiMe_4$ (δ 0.0) and relative to the signal of chloroform-d (δ 77.03, triplet). Mass spectra were recorded under ESI/HRMS at 61800 resolution using Thermo Scientific Exactive mass spectrometer. IR spectra were recorded on Bruker Alpha FT-IR spectrometer.

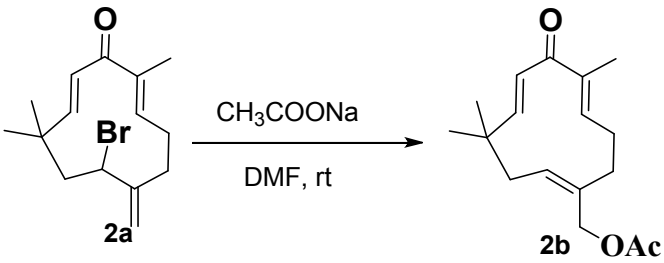
Synthesis of 7-Bromo-2,9,9-trimethyl-6-methyl-6-methylenecycloundeca-2,10-dienone (2a)

NBS (0.90g, 5.0mmol) was added to a solution of zerumbone (1.0 g, 4.6 mmol) in acetonitrile/H_2O (1:1, 15 mL) mixture, and stirred vigorously at room temperature for 1 min. H_2O (30 mL) was poured into the solution, filtered immediately, and washed with H_2O several times to afford 7-Bromo-2,9,9-trimethyl-6-methyl-6-methylenecycloundeca-2,10-dienone, **2a** as a colorless solid quantitatively

Synthesis of 6-acetoxymethyl- 2,9,9-trimethylcycloundeca-2,6,10-trienone (2b)

Sodium acetate (82.8 mg, 1.0 mmol) was added to a solution of 2**a** (200 mg, 0.67 mmol) in DMF (20 mL) at room temperature and stirred for 16 h. The progress of the reaction was monitored by TLC (hexane/ethyl acetate=3:2). The DMF solution was extracted with CH_2Cl_2 (3x30 mL) and

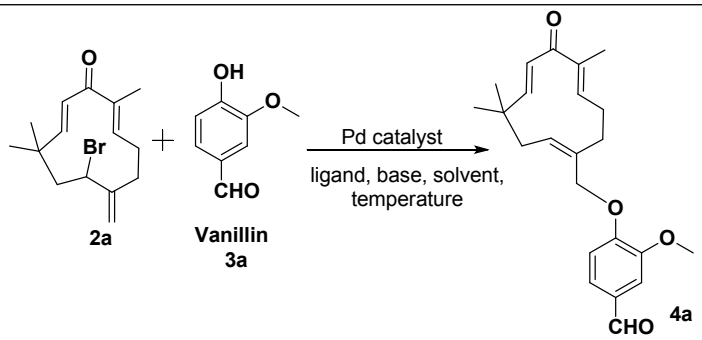
the combined organic extracts were washed with brine (2x30 mL), dried over anhydrous Na_2SO_4, and concentrated on a rotary evaporator. Chromatography on silica gel, eluting with a 2:1 mixture of hexane and ethyl acetate, afforded 6-acetoxymethyl- 2,9,9-trimethylcycloundeca-2,6,10-trienone, (**2b**) as a colorless oil in 91% yield.



General Procedure for the Synthesis of zerumbone pendant derivatives

6-Acetoxymethyl- 2,9,9-trimethylcycloundeca-2,6,10-trienone (0.137 mmol) and vanillin (0.137 mmol) were taken in a schlenk tube. $Pd_2(dba)_3.CHCI_3$(10 mol %), PPh_3 (40 mol %) as ligand, Cs_2CO_3(2.0 equiv.) as base were added followed by THF (2mL) and stirred the reaction for 12 h at room temperature. After the completion of the reaction as monitored by TLC, the reaction mixture was concentrated and the crude product was purified by column chromatography on silica gel (100-200 mesh) and hexane: ethylacetate as the eluent to afford the product as a crystalline solid.

Table S1 Optimization Studies for a Suitable Catalyst System



Entry	Catalyst	Ligand	Base	Solvent	Yield (%)[e]
1 [a]	-	-	Cs_2CO_3	THF	NR
2 [a]	$Pd_2(dba)_3$. $CHCl_3$	PPh_3	K_2CO_3	THF	Trace
3 [b]	$Pd_2(dba)_3$. $CHCl_3$	PPh_3	Cs_2CO_3	THF	43
4 [a]	$Pd_2(dba)_3$. $CHCl_3$	PPh_3	Cs_2CO_3	CH_3CN	44
5 [a]	$Pd_2(dba)_3$. $CHCl_3$	PPh_3	Cs_2CO_3	THF	24
6 [a]	$Pd(OAc)_2$	PPh_3	Cs_2CO_3	THF	Trace
7 [a]	$Pd(O_2C.CF_3)_2$	PPh_3	Cs_2CO_3	THF	21
8 [a]	$Pd(PPh_3)_4$	-	Cs_2CO_3	THF	24
9 [a]	$Pd_2(dba)_3$	PPh_3	Cs_2CO_3	THF	43
10 [c]	$Pd_2(dba)_3$. $CHCl_3$	PPh_3	Cs_2CO_3	THF	Trace
11 [d]	$Pd_2(dba)_3$. $CHCl_3$	PPh_3	Cs_2CO_3	THF	46
12 [e]	$Pd(OAc)_2$	dppf	NaH	THF	10

Reaction condition:

a :2a: 3a=1:1, Catalyst(10 mol%),Ligand (0.4 equiv.), Base (1equiv.), Solvent(2mL)

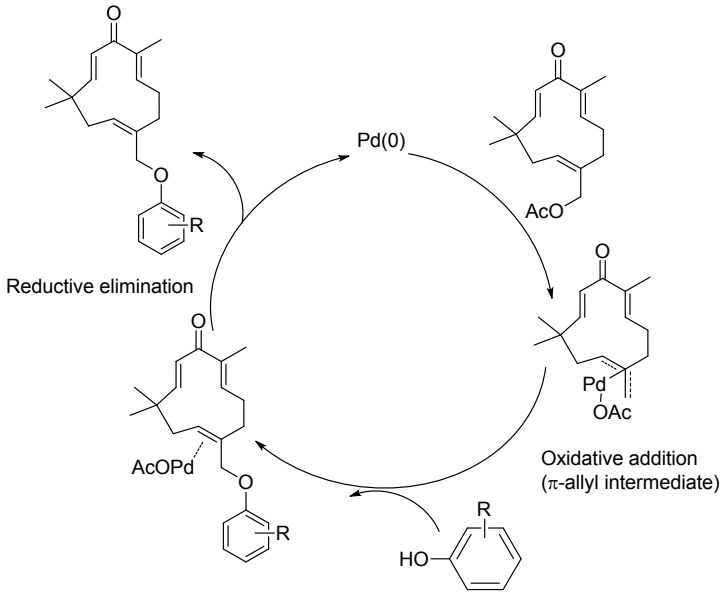
b: 2a: 3a=1:1Catalyst(10 mol%),Ligand (0.4 equiv.), Base (2 equiv.), Solvent (2mL)

c: 2a: 3a=1:2Catalyst(10 mol%),Ligand (0.4 equiv.), Base (1 equiv.), Solvent (2mL)

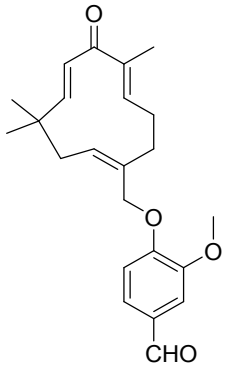
d: 2b: 3a=1:1Catalyst(10 mol%),Ligand (0.4 equiv.), Base (1 equiv.), Solvent (2mL)

e: Isolated Yield

Scheme 1: Proposed mechanism



3-methoxy-4-(((1Z,5E,8E)-4,4,8-trimethyl-7-oxocycloundeca-1,5,8 trienyl)methoxy)benzaldehyde (4a)



Yield: 46 % as a white solid; R_f: 0.14 (1:3 EtOAc: hexane), mp: 185-190°C

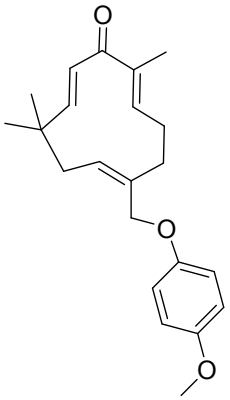
IR (neat) $\upsilon_{max:}$ 3268, 3032, 2958, 2953, 2857, 2366, 2336, 1651, 1498, 1467, 1366, 1268, 1232, 1173, 1106, 1038, 823, 736, 703, 631, 570, 528 cm^{-1}.

^{1}H NMR ($CDCl_3$, 500MHz): δ 9.85 (s, 1H), 7.43- 7.40 (m, 2H), 6.97 (d, *J*= 8Hz, 1H), 6.20 (d, *J*= 16Hz, 1H), 6.07- 6.03 (m, 1H), 6.02 (d, *J*= 16.5 Hz, 1H), 5.58- 5.54 (m, 1H), 4.64 (brs, 1H), 4.51 (brs, 1H), 3.88 (s, 3H), 2.69 (brs, 1H), 2.58 (brs, 1H), 2.41- 2.34 (m, 1H), 2.30- 2.25 (m, 2H), 2.07- 2.05 (m, 1H), 1.78 (s, 3H), 1.28 (s,3H), 1.09 (s, 3H) ppm.

^{13}C NMR ($CDCl_3$, 125MHz): δ 203.7, 190.5, 160.0, 153.6, 150.1, 148.9, 138.8, 134.6, 131.7, 130.4, 127.2, 126.3, 111.7, 109.1, 66.3, 55.5, 42.5, 37.3, 36.3, 24.8, 12.0 ppm.

HRMS (ESI): *m/z* Calcd for $C_{23}H_{28}NaO_4$: 391.18853, Found: 391.18878.

(2E,6Z,10E)-6-((4-methoxyphenoxy)methyl)-2,9,9-trimethylcycloundeca-2,6,10-trienone (4b)



Yield: 76 % as a white solid; R_f: 0.43 (1:3 EtOAc: hexane), mp: 110-115°C

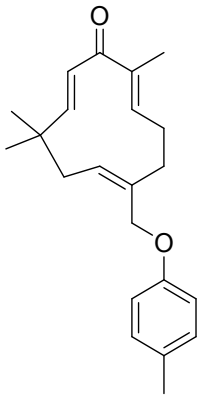
IR (neat) υ_{max}: 2924, 1742, 1652, 1508, 1462, 1365, 1226, 1106, 1038, 827, 625, 578 cm^{-1}.

^{1}H NMR ($CDCl_3$, 500MHz): δ 6.83 (s, 4H), 6.08- 6.06 (m, 1H), 6.06 (d, *J*= 16.5 Hz, 1H), 6.02 (d, *J*= 16.5 Hz, 1H), 5.51-5.47 (m, 1H), 4.50 (d, *J*= 9.5 Hz, 1H), 4.31 (d, *J*= 9 Hz, 1H), 3.78 (s, 3H), 2.74- 2.72 (m, 1H), 2.60-2.58 (m, 1H), 2.47-2.42 (m, 1H), 2.32- 2.23 (m, 2H), 2.05- 2.03 (m, 1H), 1.83 (s, 3H), 1.27 (s, 3H), 1.10 (s, 3H) ppm.

^{13}C NMR ($CDCl_3$, 125MHz): δ 203.9, 160.2, 154.0, 152.8, 149.3, 138.4, 135.9, 130.3, 127.4, 116.0, 115.5, 114.7, 65.8, 55.6, 42.4, 37.4, 36.2, 25.0, 12.2 ppm.

HRMS (ESI): *m/z* Calcd for $C_{22}H_{28}NaO_3$: 363.19361, Found: 363.23306.

(2E,6Z,10E)-2,9,9-trimethyl-6-(p-tolyloxymethyl)cycloundeca-2,6,10-trienone (4c)



Yield: 68 % as colourless liquid; R_f: 0.571 (1:3 EtOAc: hexane)

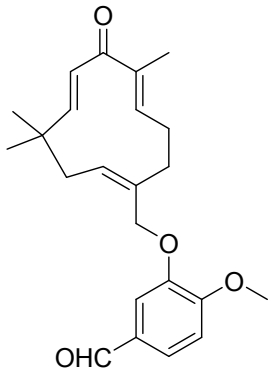
IR (neat) υ_{max}: 2925, 2852, 2394, 2356, 1714, 1555, 1509, 1430, 1362, 1331, 1232, 1178, 1102, 969, 816, 758, 702, 634, 574, 546 cm^{-1}.

^{1}H NMR ($CDCl_3$, 500MHz): δ 7.08 (d, *J*= 8.5 Hz, 2H), 6.79 (d, *J*= 8.5 Hz, 2H), 6.09- 6.07 (m, 1H), 6.07 (d, *J*= 16.5 Hz, 1H), 6.02 (d, *J*= 16 Hz, 1H), 5.52- 5.48 (m, 1H), 4.51 (d, *J*= 9.5 Hz, 1H), 4.34 (d, *J*= 9.5 Hz, 1H), 2.74- 2.72 (m, 1H), 2.60- 2.57 (m, 1H), 2.48- 2.43 (m, 1H), 2.31 (s, 3H), 2.28- 2.24 (m, 2H), 2.06- 2.03 (m, 1H), 1.83 (s, 3H), 1.27 (s, 3H), 1.10 (s,3H) ppm.

^{13}C NMR ($CDCl_3$, 125MHz): δ 203.5, 159.9, 156.6, 149.0, 138.5, 135.9, 130.3, 130.1, 129.9, 127.4, 114.3, 65.3, 42.4, 37.4, 36.3, 25.0, 20.5, 12.2 ppm.

HRMS (ESI): *m/z* Calcd for $C_{22}H_{28}NaO_2$: 347.19870, Found: 347.19887.

4-methoxy-3-(((1Z,5E,8E)-4,4,8-trimethyl-7-oxocycloundeca-1,5,8-trienyl)methoxy)benzaldehyde (4d)



Yield: 63 % as a white solid; R_f: 0.28 (1:3 EtOAc: hexane), mp: 85-90°C

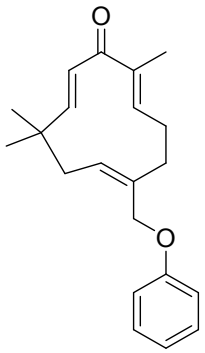
IR (neat) υ_{max}: 3351, 2960, 2864, 2724, 1686, 1645, 1588, 1510, 1439, 1395, 1342, 1269, 1161, 1129, 1015, 865, 808, 754, 700, 638, 583 cm^{-1}.

^{1}H NMR ($CDCl_3$, 500MHz): δ 9.86 (s, 1H), 7.46-7.40 (m, 2H), 6.98 (d, *J*= 8.5Hz, 1H), 6.26 (d, *J*= 16.5Hz, 1H), 6.06- 6.03 (m, 1H), 6.01 (d, *J*= 16.5Hz, 1H), 5.57- 5.54 (m, 1H), 4.57 (brs, 1H), 4.48 (brs, 1H), 3.89 (s, 3H), 2.67 (brs, 1H), 2.57 (brs, 1H), 2.45 (brs, 1H), 2.31- 2.25 (m, 2H), 2.07- 2.04 (m, 1H), 1.76 (s, 3H), 1.51(s, 6H) ppm.

^{13}C NMR ($CDCl_3$, 125MHz): δ 202.4, 190.4, 160.3, 158.0, 155.0, 149.1, 138.0, 133.7, 130.2, 127.2, 122.4, 114.7, 66.1, 55.7, 42.7, 37.3, 36.5, 29.7, 24.9, 12.2 ppm.

HRMS (ESI): *m/z* Calcd for $C_{23}H_{28}NaO_4$: 391.18853, Found: 391.18878

(2E,6Z,10E)-2,9,9-trimethyl-6-(phenoxymethyl)cycloundeca-2,6,10-trienone (4e)



Yield: 33 % as a white solid; R_f: 0.571 (1:3 EtOAc: hexane), mp: 60-63°C

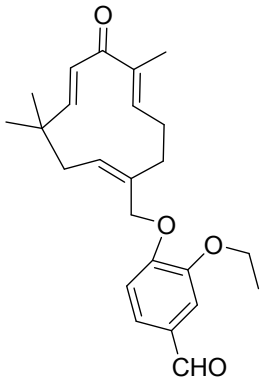
IR (neat) υ_{max}: 3390, 2922, 1590, 1462, 1420, 1121, 1040, 856, 540 cm^{-1}.

^{1}H NMR ($CDCl_3$, 500MHz): δ 7.30-7.26 (m, 2H), 6.96- 6.93 (m, 1H), 6.88- 6.87 (m, 2H), 6.07- 5.98 (m, 3H), 5.51- 5.48 (m, 1H), 4.51 (brs, 1H), 4.37 (brs, 1H), 2.71 (brs, 1H), 2.56 (brs, 1H), 2.44- 2.41 (m, 1H), 2.30- 2.23 (m, 2H), 2.05- 2.03 (m, 1H), 1.82 (s, 3H), 1.26 (s, 3H), 1.08 (s, 3H) ppm.

^{13}C NMR ($CDCl_3$, 125MHz): δ 203.7, 160.0, 158.7, 149.2, 138.5, 135.7, 130.5, 129.5, 127.4, 121.0, 114.5, 65.1, 42.5, 37.4, 36.3, 25.0, 12.2 ppm.

HRMS (ESI): *m/z* Calcd for $C_{21}H_{26}NaO_2$: 333.18305, Found: 333.18364.

3-ethoxy-4-(((1Z,5E,8E)-4,4,8-trimethyl-7-oxocycloundeca-1,5,8-trienyl)methoxy)benzaldehyde (4f)



Yield: 23 % as colourless liquid; R_f: 0.314 (1:3 EtOAc: hexane)

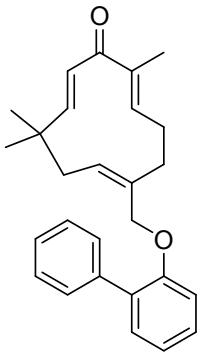
IR (neat) υ_{max}: 3384, 2922, 1586, 1514, 1468, 1425, 1367, 1317, 1266, 1120, 1038, 860, 661, 617, 547 cm^{-1}.

^{1}H NMR ($CDCl_3$, 500MHz): δ 9.84 (s, 1H), 7.42- 7.39 (m, 2H), 6.98 (d, *J*= 8 Hz, 1H), 6.30 (d, *J*= 16.5Hz, 1H), 6.04- 6.00 (m, 2H), 5.57- 5.53 (m, 1H), 4.60 (brs, 1H), 4.51 (brs, 1H), 4.14- 4.10 (q, 2H), 2.69 (s, 1H), 2.56 (brs, 1H), 2.45- 2.43 (m, 1H), 2.32- 2.26 (m, 2H), 2.06- 2.01(m, 1H), 1.77 (s, 3H), 1.41 (t, *J*= 7Hz, 3H), 1.27 (s, 3H), 1.11 (s, 3H) ppm.

^{13}C NMR ($CDCl_3$, 125MHz): δ 203.8, 190.4, 160.5, 153.7, 149.5, 148.5, 138.9, 134.5, 131.7, 130.4, 127.3, 126.0, 112.0, 110.2, 66.6, 64.2, 42.5, 37.4, 36.6, 24.8, 14.6, 12.2 ppm.

HRMS (ESI): *m/z* Calcd for $C_{24}H_{30}NaO_4$: 405.20418, Found: 405.20346.

. **(2E,6Z,10E)-6-((biphenyl-2-yloxy)methyl)-2,9,9-trimethylcycloundeca-2,6,10-trienone (4g)**



Yield: 76 % as colourless liquid; R_f : 0.571 (1:3 EtOAc: hexane)

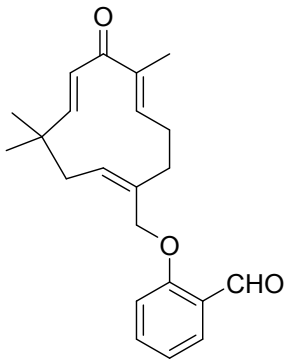
IR (neat) υ_{max}: 3372, 3059, 2962, 2929, 2870, 1897, 1709, 1646, 1504, 1479, 1457, 1434, 1388, 1366, 1267, 1223, 1119, 1054, 1007, 973, 912, 834, 754, 735, 700, 614, 566 cm^{-1}.

^{1}H NMR ($CDCl_3$, 500MHz): δ 7.53- 7.51 (m, 2H), 7.43- 7.40 (m, 2H), 7.36- 7.31 (m, 3H), 7.10- 7.09 (m, 1H), 7.03 (d, *J*= 5.5 Hz, 1H), 6.04- 6.02 (m, 1H), 5.99 (d, *J*= 16.5 Hz, 1H), 5.75 (d, *J*= 16.5 Hz, 1H), 5.43- 5.40 (m, 1H), 4.67 (brs, 1H), 4.16 (brs, 1H), 2.66 (brs, 1H), 2.38- 1.99 (m, 5H), 1.69 (s, 3H), 1.24 (s, 3H), 1.08 (s, 3H) ppm.

^{13}C NMR ($CDCl_3$, 125MHz): δ 203.2, 159.2, 155.6, 149.3, 138.3, 136.2, 131.0, 129.4, 128.8, 128.5, 127.8, 127.3, 126.9, 127.3, 126.9, 65.9, 42.2, 37.4, 35.2, 24.4, 11.7 ppm.

HRMS (ESI): *m/z* Calcd for $C_{27}H_{30}NaO_2$: 409.21435, Found: 409.21418.

2-(((1Z,5E,8E)-4,4,8-trimethyl-7-oxocycloundeca-1,5,8-trienyl)methoxy)benzaldehyde (4h)



Yield: 28% as viscous liquid; R_f : 0.40 (1:3 EtOAc: hexane)

IR (neat) υ_{max}: 3341, 2923, 2855, 1588, 1422, 1366, 1318, 1119, 1040, 858, 669, 618, 524 cm^{-1}.

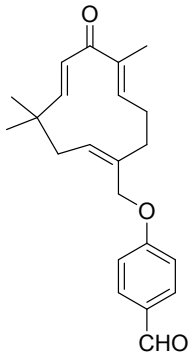
^{1}H NMR ($CDCl_3$, 500MHz): δ 10.5 (s, 1H), 7.87 (dd, *J*1= 7.5 Hz, *J*2=1.5 Hz, 1H), 7.57- 7.54 (m, 1H), 7.09- 7.06 (m, 1H), 7.00 (d, *J*= 8.5 Hz, 1H), 6.10- 6.08 (m, 1H), 6.04 (d, *J*= 16.5 Hz,

1H), 5.80 (d, *J*= 16.5Hz, 1H), 5.58- 5.55 (m, 1H), 4.83 (brs, 1H), 4.36 (brs, 1H), 2.81 (brs, 1H), 2.48- 2.37 (m, 3H), 2.27- 2.25 (m, 1H), 2.12-2.09 (m, 1H), 1.82 (s, 3H), 1.27 (s, 3H), 1.14 (s, 3H) ppm.

^{13}C NMR ($CDCl_3$, 125MHz): δ 203.0, 189.2, 160.8, 149.0, 135.7, 135.1, 128.9, 128.1, 125.2, 120.9, 112.6, 112.4, 64.9, 42.4, 37.4, 35.1, 29.6, 24.5, 11.7 ppm.

HRMS (ESI): *m/z* Calcd for $C_{22}H_{26}NaO_3$: 361.17796, Found: 361.17822.

4-(((1Z,5E,8E)-4,4,8-trimethyl-7-oxocycloundeca-1,5,8-trienyl)methoxy)benzaldehyde(4i)



Yield: 91 % as a colourless liquid; R_f : 0.42 (1:3 EtOAc: hexane)

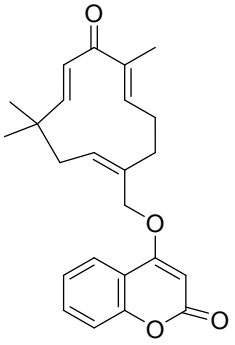
IR (neat) υ_{max}: 3341, 2923, 2855, 1588, 1422, 1366, 1318, 1119, 1040, 858, 669, 618, 524 cm^{-1}.

^{1}H NMR ($CDCl_3$, 500MHz): δ 9.88 (s, 1H), 7.83 (d, *J*= 8.5Hz, 2H), 6.99 (d, *J*= 8.5 Hz, 2H), 6.07- 6.06 (m, 1H), 6.02 (d, *J*= 16.5 Hz, 1H), 5.97 (d, *J*= 16.5 Hz, 1H), 5.56-5.53 (m, 1H), 4.63 (brs, 1H), 4.45 (brs, 1H), 2.68 (s, 1H), 2.53 (s, 1H), 2.42- 2.39 (m, 1H), 2.33- 2.26 (m, 2H), 2.09-2.07 (m, 1H), 1.82 (s, 3H), 1.27 (s, 3H), 1.10 (s, 3H) ppm.

^{13}C NMR ($CDCl_3$, 125MHz): δ 203.6, 190.4, 163.7, 159.7, 149.1, 137.9, 135.6, 132.0, 131.2, 130.1, 127.5, 114.9, 67.8, 42.5, 39.8, 37.4, 37.0, 31.8, 24.9, 21.2, 12.2 ppm.

HRMS (ESI): *m/z* Calcd for $C_{22}H_{26}NaO_3$: 361.17796, Found: 361.17822.

4-(((1Z,5E,8E)-4,4,8-trimethyl-7-oxocycloundeca-1,5,8-trienyl)methoxy)-2H-chromen-2-one (4j)



Yield: 31 % as pale yellow solid; R_f: 0.34 (1:3 EtOAc: hexane), mp: 165-167°C

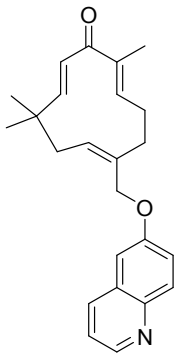
IR (neat) $\upsilon_{max:}$ 3391, 2960, 2924, 2854, 1724, 1649, 1436, 1382, 1283, 1099, 972, 747, 697 cm^{-1}.

^{1}H NMR ($CDCl_3$, 500MHz): δ 7.77 (d, *J*= 8Hz, 1H), 7.60- 7.57 (m, 1H), 7.36 (d, *J*= 8Hz, 1H), 7.30- 7.28 (m, 1H), 6.12- 6.09 (m, 1H), 6.06 (d, *J*= 16.5Hz, 1H), 5.84 (d, *J*= 16.5Hz, 1H), 5.71 (s, 1H), 5.66- 5.63 (m, 1H), 4.82 (brs, 1H), 4.47 (brs, 1H), 2.75 (brs, 1H), 2.51- 2.47 (m, 2H), 2.41- 2.31 (m, 3H), 1.84 (s, 3H), 1.27 (s, 3H), 1.16 (s, 3H) ppm.

^{13}C NMR ($CDCl_3$, 125MHz): δ 202.8, 165.1, 158.8, 153.3, 148.7, 138.7, 133.3, 132.5, 132.2, 127.5, 123.9, 122.7, 116.9, 115.5, 91.9, 66.0, 42.5, 37.5, 35.2, 29.6, 24.5, 12.1 ppm.

HRMS (ESI): *m/z* Calcd for $C_{24}H_{26}NaO_4$: 401.17288, Found: 434.24539.

(2E,6Z,10E)-2,9,9-trimethyl-6-((quinolin-6-yloxy)methyl)cycloundeca-2,6,10-trienone (4k)



Yield: 73 % as a white solid; R_f: 0.17 (1:3 EtOAc: hexane), mp: 125°C

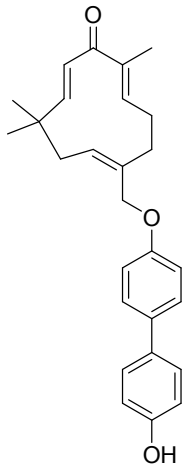
IR (neat) $\upsilon_{max:}$ 3012, 2918, 2383, 1868, 1829, 1796, 1744, 1652, 1541, 1521, 1422, 1366, 1317, 1272, 1209, 1161, 1119, 1018, 752, 601 cm^{-1}.

^{1}H NMR ($CDCl_3$, 500MHz): δ 8.75 (d, *J*= 3Hz, 1H), 8.02- 7.98 (m, 2H), 7.35- 7.31 (m, 2H), 7.05 (d, *J*= 2.5Hz, 1H), 6.09- 6.02 (m, 3H), 5.56- 5.53 (m, 1H), 4.65 (brs, 1H), 4.48 (brs, 1H), 2.75 (brs, 1H), 2.57 (brs, 1H), 2.48- 2.45 (m, 1H), 2.34- 2.27 (m, 2H), 2.24- 2.08 (m, 1H), 1.84 (s, 3H), 1.27 (s, 3H), 1.12 (s, 3H) ppm.

^{13}C NMR ($CDCl_3$, 125MHz): δ 203.3, 159.6, 156.7, 149.0, 148.0, 144.4, 138.5, 135.2, 134.7, 131.1, 130.9, 129.2, 127.5, 122.2, 121.4, 106.0, 65.5, 42.5, 37.4, 36.1, 25.0, 12.2 ppm.

HRMS (ESI): *m/z* Calcd for $C_{24}H_{28}NO_2$: 362.21200, Found: 362.21200

(2E,6Z,10E)-6-((4'-hydroxybiphenyl-4-yloxy)methyl)-2,9,9-trimethylcycloundeca-2,6,10-trienone (4l)



Yield: 26 % as viscous liquid; R_f: 0.371 (1:3 EtOAc: hexane)

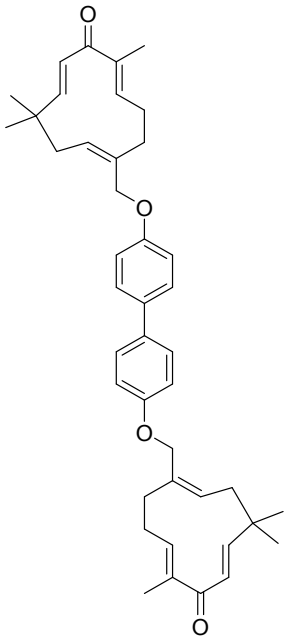
IR (neat) $\upsilon_{max:}$ 3341, 2923, 2854, 2369, 2338, 1742, 1589, 1503, 1461, 1422, 1368, 1316, 1268, 1163, 1118, 1038, 861, 823, 666, 620, 535 cm^{-1}.

^{1}H NMR ($CDCl_3$, 500MHz): δ 7.46 (d, *J*= 9 Hz, 2H), 7.42 (d, *J*= 8.5 Hz, 2H), 6.94 (d, *J*= 8.5 Hz, 2H), 6.89 (d, *J*= 8.5 Hz, 2H), 6.11- 6.08 (m, 2H), 6.04 (d, *J*= 16.5, Hz 1H), 5.55- 5.52 (m, 1H), 5.08 (s, 1H), 4.56 (brs, 1H), 4.42 (brs, 1H), 2.76- 2.75 (m, 1H), 2.62- 2.60 (m, 1H), 2.50- 2.45 (m, 1H), 2.37- 2.27 (m, 2H), 2.09- 2.06 (m, 1H), 1.85 (s, 3H), 1.28 (s, 3H), 1.11 (s, 3H) ppm.

^{13}C NMR ($CDCl_3$, 125MHz): δ 204.1, 160.2, 157.8, 154.9, 149.4, 138.5, 135.6, 133.8, 133.4, 130.6, 127.9, 127.8, 127.4, 115.6, 114.7, 65.3, 42.5, 37.4, 36.2, 25.0, 22.3, 12.2, 8.5 ppm.

HRMS (ESI): *m/z* Calcd for $C_{27}H_{30}NaO_3$: 425.20926, Found: 425.20904.

(2E,2'E,6Z,6'Z,10E,10'E)-6,6'-(biphenyl-4,4'-diylbis(oxy))bis(methylene)bis(2,9,9-trimethylcycloundeca-2,6,10-trienone) (4l')



Yield: 38 % as a white solid; R_f: 0.286 (1:3 EtOAc: hexane), mp: 150- 155°C

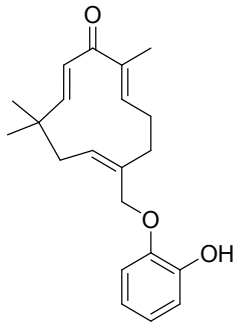
IR (neat) $\upsilon_{max:}$ 3268, 3032, 2958, 2953, 2857, 2366, 2336, 1651, 1498, 1467, 1366, 1268, 1232, 1173, 1106, 1038, 823, 736, 703, 631, 570, 528 cm^{-1}.

^{1}H NMR ($CDCl_3$, 500MHz): δ 7.47 (d, *J*= 8.5, Hz, 4H), 6.95 (d, *J*= 9Hz, 4H), 6.10-6.07 (m, 4H), 6.04 (d, *J*= 16.5 Hz, 2H), 5.55- 5.52 (m, 2H), 4.57 (brs, 2H), 4.42 (brs, 2H), 2.76- 2.74 (m, 2H), 2.62- 2.60 (m, 2H), 2.50- 2.45 (m, 2H), 2.37- 2.20 (m, 4H), 2.09- 2.07 (m, 2H), 1.85 (s, 6H), 1.28 (s, 6H), 1.11 (s, 6H) ppm.

^{13}C NMR ($CDCl_3$, 125MHz): δ 203.7, 160.0, 157.9, 149.2, 138.5, 135.6, 133.8, 130.6, 127.8, 127.5, 114.8, 65.3, 42.5, 37.4, 36.2, 25.0, 12.2 ppm.

HRMS (ESI): *m/z* Calcd for $C_{42}H_{50}NaO_4$: 641.36068, Found: 641.36.34.

(2E,6Z,10E)-6-((2-hydroxyphenoxy)methyl)-2,9,9-trimethylcycloundeca-2,6,10-trienone (3m)



Yield: 19 % as a white solid; R_f: 0.4 (1:3 EtOAc: hexane), mp: 100- 105°C

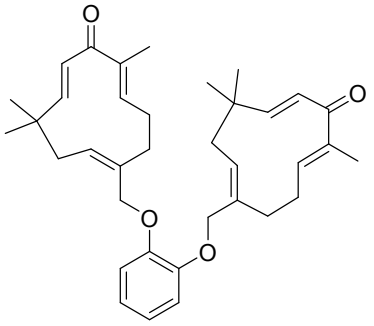
IR (neat) υ_{max}: 3395, 2923, 2854, 1587, 1463, 1420, 1364, 1121, 1041, 857, 619 cm^{-1}.

^{1}H NMR ($CDCl_3$, 500MHz): δ 6.94- 6.84 (m, 4H), 6.09- 6.08 (m, 1H), 6.03 (d, *J*= 16.5Hz, 1H), 5.82 (d, *J*= 16.5 Hz, 1H), 5.57- 5.59 (m, 1H), 5.51 (s, 1H), 4.71 (brs, 1H), 4.35 (brs, 1H), 2.76 (brs, 1H), 2.51- 2.37 (m, 3H), 2.29- 2.26 (m, 1H), 2.09 (brs, 1H), 1.83 (s, 3H), 1.28 (s, 3H), 1.13 (s, 3H) ppm.

^{13}C NMR ($CDCl_3$, 125MHz): δ 203.1, 159.2, 149.1, 145.9, 145.6, 138.5, 135.4, 130.8, 127.5, 122.1, 120.1, 114.9, 111.9, 65.5, 42.4, 37.5, 35.3, 24.8, 12.0 ppm.

HRMS (ESI): *m/z* Calcd for $C_{21}H_{26}NaO_3$: 349.17796, Found: 349.17866.

(2E,2'E,6Z,6'Z,10E,10'E)-6,6'-(1,2-phenylenebis(oxy))bis(methylene)bis(2,9,9-trimethylcycloundeca-2,6,10-trienone) (4m')



Yield: 15 % as a white solid; R_f: 0.4 (1:3 EtOAc: hexane), mp: 165- 170°C

IR (neat) $\upsilon_{max:}$ 3058, 3035, 2960, 2926, 1736, 1652, 1592, 1501, 1454, 1387, 1365, 1246, 1210, 1004, 907, 836, 742, 700, 623, 580 cm^{-1}.

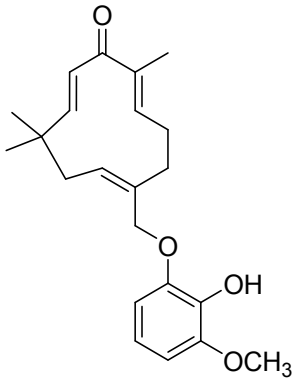
^{1}H NMR ($CDCl_3$, 500MHz): δ 6.92 (s, 4H), 6.06- 6.05 (m, 2H), 6.02 (d, *J*= 16.5 Hz, 2H), 5.95 (d, *J*= 16.5 Hz, 2H), 5.52- 5.48 (m, 2H), 4.65 (brs, 2H), 4.31 (brs, 2H), 2.78 (brs, 2H), 2.57 (brs, 2H), 2.48 (brs, 2H), 2.30 (brs, 2H), 2.19 (brs, 2H), 2.05 (brs, 2H), 1.79 (s, 6H), 1.27 (s, 6H), 1.12 (s, 6H) ppm.

^{13}C NMR ($CDCl_3$, 125MHz): δ 203.4, 159.6, 149.0, 148.9, 138.6, 136.0, 130.0, 127.4, 121.6, 114.3, 65.8, 42.4, 37.4, 35.6, 24.7, 12.1 ppm.

HRMS (ESI): *m/z* Calcd for $C_{36}H_{46}NaO_4$: 565.32938, Found: 565.32991.

(2E,6Z,10E)-6-((2-hydroxy-3-methoxyphenoxy)methyl)-2,9,9-trimethylcycloundeca-2,6,10-trienone (4n)

Yield: 15 % as a white solid; R_f: 0.25 (1:3 EtOAc: hexane), mp: 133-135^{o}C



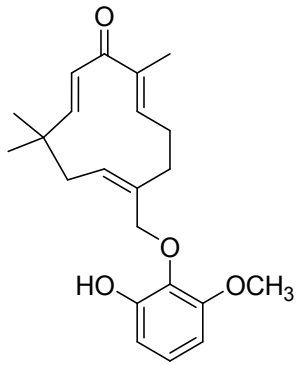
IR (neat) $\upsilon_{max:}$ 3377, 2924, 2032, 1590, 1473, 1421, 1313, 1120, 1090, 1040, 858, 779, 620, 539 cm^{-1}.

^{1}H NMR ($CDCl_3$, 500MHz): δ 6.78- 6.75 (m, 1H), 6.60- 6.58 (m, 2H), 6.06- 6.05 (m, 1H), 6.00- 5.99 (m, 2H), 5.53- 5.50 (m, 1H), 5.44 (s, 1H), 4.65 (brs, 1H), 4.40 (brs, 1H), 3.91 (s, 3H), 2.91- 2.78 (m, 1H), 2.61 (brs, 1H), 2.48 (brs, 1H), 2.33- 2.30 (m, 1H), 2.23 (brs, 1H), 2.06- 2.02 (m, 1H), 1.81 (s, 3H), 1.27 (s, 3H), 1.11 (s, 3H) ppm.

^{13}C NMR ($CDCl_3$, 125MHz): δ 203.6, 159.7, 153.4, 147.6, 146.1, 138.7, 135.7, 130.4, 127.5, 118.7, 114.2, 105.3, 66.4, 56.0, 42.2, 37.2, 36.0, 25.1, 12.1 ppm.

HRMS (ESI): *m/z* Calcd for $C_{22}H_{28}NaO_4$: 379.18853, Found: 379.18902.

(2E,6Z,10E)-6-((2-hydroxy-6-methoxyphenoxy)methyl)-2,9,9-trimethylcycloundeca-2,6,10-trienone (4n')



Yield: 13 % as a white solid; R_f: 0.28 (1:3 EtOAc: hexane), mp: 132-135°C

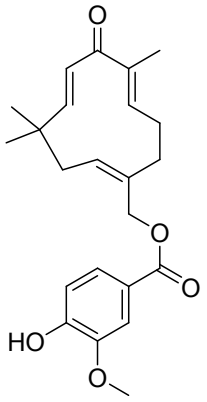
IR (neat) υ_{max}: 3377, 2924, 1590, 1473, 1421, 1313, 1120, 1090, 1040, 858, 779, 620, 539 cm^{-1}.

^{1}H NMR ($CDCl_3$, 500MHz): δ 6.94 (t, *J*= 8.5 Hz, 1H), 6.60 (dd, *J*1= 8.5 Hz, *J*2= 1Hz, 1H), 6.48 (dd, *J*1= 8.5 Hz, *J*2= 1Hz, 1H), 6.04- 6.02 (m, 1H), 6.00 (d, *J*= 16.5Hz, 1H), 5.82 (d, = 16.5Hz, 1H), 5.69 (s, 1H), 5.52- 5.48 (m, 1H), 4.58 (brs, 1H), 4.38 (brs, 1H), 3.89 (s, 3H), 2.89- 2.88 (m, 1H), 2.69- 2.68 (m, 1H), 2.57- 2.46 (m, 1H), 2.37- 2.35 (m, 1H), 2.26 (brs, 1H), 2.00- 1.97 (m, 1H), 1.81 (s, 3H), 1.25 (s, 3H), 1.09 (s, 3H) ppm.

^{13}C NMR ($CDCl_3$, 125MHz): δ 203.4, 159.6, 152.5, 149.8, 149.0, 138.4, 136.3, 134.2, 130.8, 127.3, 124.3, 108.3, 103.9, 68.9, 55.7, 42.2, 37.3, 35.7, 24.8, 12.0 ppm.

HRMS (ESI): *m/z* Calcd for $C_{22}H_{28}NaO_4$: 379.18853, Found: 379.18902.

2-(((1Z,5E,8E)-4,4,8-trimethyl-7-oxocycloundeca-1,5,8-trienyl)methoxy)benzaldehyde (6b)



Yield: 28 % as a white solid; R_f: 0.17 (1:3 EtOAc: hexane), mp: 110-112°C

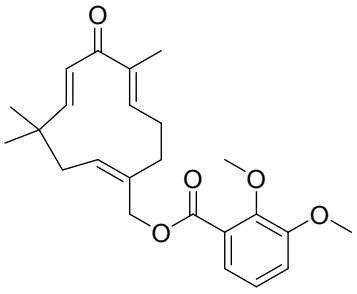
IR (neat) υ_{max}: 2922, 2856, 2404, 2300, 1707, 1641, 1600, 1514, 1458, 1366, 1282, 1215 1102, 1029, 970, 766 cm^{-1}.

^{1}H NMR ($CDCl_3$, 500MHz): δ 7.61 (dd, *J*1=8.5Hz, *J*2= 2 Hz, 1H), 7.52 (d, *J*= 1.5Hz, 1H), 6.93 (d, J= 8.5 Hz, 1H), 6.05- 6.04 (m, 2H), 6.01 (d, *J*= 16.5Hz, 1H), 5.94 (d, *J*= 16.5Hz, 1H), 5.52-5.48 (m, 1H), 4.89 (d, *J*= 12Hz, 1H), 4.68 (d, *J*= 12Hz, 1H), 3.94 (s, 3H), 2.70- 2.69 (m, 1H), 2.59- 2.45 (m, 2H), 2.31- 2.25 (m, 2H), 2.08- 2.04 (m, 1H), 1.70 (s, 3H), 1.26 (s, 3H), 1.13 (s, 3H) ppm.

^{13}C NMR ($CDCl_3$, 125MHz): δ 206.1, 161.1, 150.3, 146.1, 138.4, 134.6, 131.2, 127.2, 124.1, 122.0, 120.1, 114.0, 111.5, 61.3, 55.9, 42.4, 37.5, 35.7, 29.8, 24.7, 11.9 ppm.

HRMS (ESI): *m/z* Calcd for $C_{23}H_{28}NaO_5$: 407.18344, Found: 407.18428.

((1Z,5E,8E)-4,4,8-trimethyl-7-oxocycloundeca-1,5,8-trienyl)methyl 2,3-dimethoxybenzoate (6c)



Yield: 19 % as a white solid; R_f: 0.17 (1:3 EtOAc: hexane), mp: 65-67°C

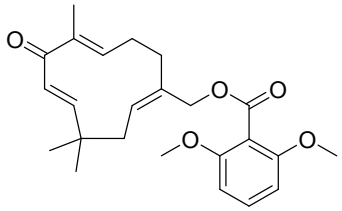
IR (neat) υ_{max}: 2919, 2850, 2370, 2341, 1974, 1798, 1741, 1649, 1582, 1373, 1160, 1119, 662, 619 cm^{-1}.

^{1}H NMR ($CDCl_3$, 500MHz): δ 7.29- 7.28 (m, 1H), 7.10- 7.06 (m, 2H), 6.07- 6.04 (m, 1H), 6.00 (d, *J*= 16.5 Hz, 1H), 5.88 (d, *J*= 16.5 Hz, 1H), 5.53- 5.49 (m, 1H), 4.92 (brs, 1H), 4.68 (brs, 1H), 3.91 (s, 3H), 3.90 (s, 3H), 2.77- 2.76 (m, 1H), 2.58- 2.54 (m, 2H), 2.32- 2.28 (m, 2H), 2.09- 2.06 (m, 1H), 1.71 (s, 3H), 1.27 (s, 3H), 1.14 (s, 3H) ppm.

^{13}C NMR ($CDCl_3$, 125MHz): δ 203.3, 159.9, 153.7, 148.7, 138.4, 134.8, 127.1, 125.7, 123.6, 121.9, 117.7, 115.9, 61.3, 55.9, 37.4, 35.4, 29.8, 24.7, 22.7, 12.1 ppm.

HRMS (ESI): *m/z* Calcd for $C_{24}H_{30}NaO_5$: 421.19909, Found: 421.19976.

((1Z,5E,8E)-4,4,8-trimethyl-7-oxocycloundeca-1,5,8-trienyl)methyl 2,6-dimethoxybenzoate (6d)



Yield: 14 % as a white solid; R_f: 0.28 (1:3 EtOAc: hexane), mp: 103-105^{o}C

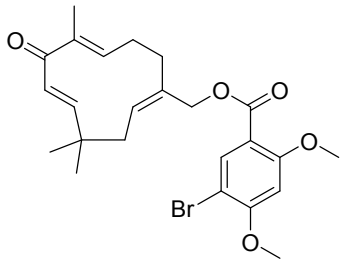
IR (neat) υ_{max}: 3363, 2924, 2852, 2038, 1739, 1648, 1423, 1370, 1230, 1122, 1040, 856, 780, 567, 527 cm^{-1}.

^{1}H NMR ($CDCl_3$, 500MHz): δ 7.30 (d, *J*=8Hz, 1H), 6.56 (d, *J*= 8.5 Hz, 2H), 6.03-6.01 (m, 1H), 5.99- 5.93 (m, 2H), 5.52-5.48 (m, 1H), 4.88 (d, *J*= 11.5Hz, 1H), 4.73 (d, *J*= 12Hz, 1H), 3.79 (s, 6H), 2.71- 2.69 (m, 1H), 2.54-2.49 (m, 2H), 2.26 (brs, 2H), 2.05- 2.03 (m, 1H), 1.52 (s, 3H), 1.24 (s, 3H), 1.10 (s, 3H) ppm.

^{13}C NMR ($CDCl_3$, 125MHz): δ 204.2, 166.5, 159.9, 157.2, 149.1, 138.4, 134.3, 131.6, 131.3, 127.2, 113.4, 103.8, 62.3, 55.8, 42.5, 37.3, 36.9, 36.6, 24.8, 11.5 ppm.

HRMS (ESI): *m/z* Calcd for $C_{24}H_{30}NaO_5$: 421.19909, Found: 421.19976.

((1Z,5E,8E)-4,4,8-trimethyl-7-oxocycloundeca-1,5,8-trienyl)methyl 5-bromo-2,4-dimethoxybenzoate (6e)



Yield: 10% as a pale yellow liquid; R_f: 0.171(1:3 EtOAc: hexane)

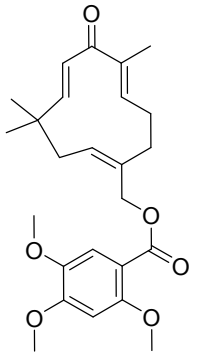
IR (neat) $\upsilon_{max:}$ 2924, 2370, 2118, 1705, 1650, 1597, 1463, 1402, 1319, 1279, 1238, 1181, 1111, 1024, 823, 624, 534 cm^{-1}.

^{1}H NMR ($CDCl_3$, 500MHz): δ 8.01 (s, 1H), 6.46 (s, 1H), 6.01- 5.97 (m, 1H), 5.90 (d, *J*= 16.5 Hz, 1H), 5.91 (d, *J*= 16Hz, 1H), 5.50- 5.47 (m, 1H), 4.89 (d, *J*= 11.5 Hz, 1H), 4.63 (d, *J*= 12 Hz, 1H), 3.96 (s, 3H), 3.91 (s, 3H), 2.71 (brs, 1 H), 2.55-2.49 (m, 2H), 2.30-2.27 (m, 2H), 2.06- 2.04 (m, 1H), 1.69 (s, 3H), 1.25 (s, 3H), 1.13 (s, 3H) ppm.

^{13}C NMR ($CDCl_3$, 125MHz): δ 203.7, 164.1, 159.7, 148.8, 138.4, 136.1, 134.6, 131.3, 127.2, 115.7, 115.1, 114.5, 102.1, 61.1, 56.0, 42.2, 37.2, 35.7, 31.0, 24.5, 11.8 ppm.

HRMS (ESI): *m/z* Calcd for $C_{24}H_{29}BrNaO_5$: 499.10961, Found: 499.10787.

((1Z,5E,8E)-4,4,8-trimethyl-7-oxocycloundeca-1,5,8-trienyl)methyl-2,4,5-trimethoxybenzoate (6f)



Yield: 17 % as a white solid; R_f: 0.412 (1:3 EtOAc: hexane), mp: 117-120°C

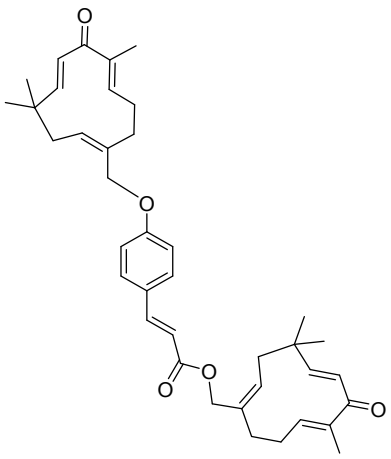
IR (neat) υ_{max}: 3402, 2959, 1716, 1691, 1648, 1611, 1516, 1462, 1405, 1360, 1244, 1212, 1161, 1072, 1030, 779, 700, 531 cm^{-1}.

^{1}H NMR ($CDCl_3$, 500MHz): 7.39 (S, 1H), 6.54 (S, 1H), 6.08-6.05 (m, 1H), 6.02 (d, *J*= 16.5Hz, 1H), 5.95 (d, *J*= 16.5Hz, 1H), 5.52-5.49 (m, 1H), 4.96 (d, *J*= 11.5 Hz, 1H), 4.62 (d, *J*= 12.Hz, 1H), 3.96 (s, 3H), 3.89 (s, 3H), 3.87 (s, 3H), 2.79-2.77 (m, 1H), 2.60- 2.55 (m, 2H), 2.82- 2.25 (m, 2H), 1.80-1.78 (m, 1H), 1.70 (s, 3H), 1.27 (s, 3H), 1.13 (s, 3H) ppm.

^{13}C NMR ($CDCl_3$, 500MHz): 203.5, 165.5, 159.7, 155.1, 153.7, 148.9, 142.5, 138.5, 134.9, 130.8, 127.2, 114.6, 110.4, 61.0, 56.6, 56.4, 55.9, 42.3, 37.3, 35.7, 24.7, 11.8 ppm.

HRMS (ESI): *m/z* Calcd for $C_{25}H_{32}NaO_6$: 451.20966, Found: 451.21035.

(E)-((1Z,5E,8E)-4,4,8-trimethyl-7-oxocycloundeca-1,5,8-trienyl)methyl 3-(4-(((1Z,5E,8E)-4,4,8-trimethyl-7-oxocycloundeca-1,5,8-trienyl)methoxy)phenyl)acrylate (8a)



Yield: 34 % as colourless liquid; R_f: 0.34 (1:3 EtOAc: hexane)

IR (neat) υ_{max}: 3403, 3037, 2960, 2926, 2866, 1708, 1652, 1601, 1510, 1453, 1388, 1362, 1305, 1244, 1159, 1105, 1064, 1001, 906, 831, 780, 736, 699, 632 cm^{-1}.

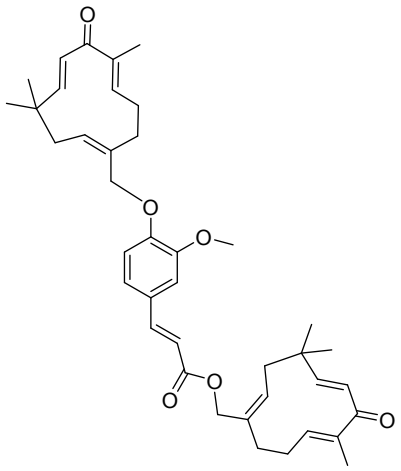
^{1}H NMR ($CDCl_3$, 500MHz): 7.64 (d, *J*=16Hz, 1H), 7.46 (d, *J*=8.5 Hz, 2H), 6.89 (d, *J*=8.5Hz, 2H), 6.28 (d, *J*=16Hz, 1H), 6.06-6.05 (m, 2H), 6.02-5.98 (m, 4H), 5.55-5.48 (m, 2H), 4.73 (brs,

1H), 4.65-4.62 (m, 1H), 4.57 (brs, 1H), 4.40- 4.38 (m, 1H), 2.69-2.66 (m, 2H), 2.53-2.36 (m, 4H), 2.32-2.17 (m, 4H), 2.06-2.05 (m, 2H), 1.83 (s, 3H), 1.79 (s, 3H), 1.27 (s, 6H), 1.12 (s, 6H).

^{13}C NMR ($CDCl_3$, 125MHz): 203.5, 203.4, 166.9, 160.6, 159.9, 149.0, 144.9, 138.5, 135.1, 134.6, 131.5, 131.0, 129.8, 127.3, 127.2, 115.2, 114.9, 65.3, 61.0, 42.5, 42.3, 37.4, 37.3, 36.0, 35.9, 24.8, 24.9, 12.7 ppm.

HRMS (ESI): *m/z* Calcd for $C_{39}H_{48}NaO_5$: 619.33994, Found: 619.33987.

(E)-((1Z,5E,8E)-4,4,8-trimethyl-7-oxocycloundeca-1,5,8-trienyl)methyl 3-(3-methoxy-4-(((1Z,5E,8E)-4,4,8-trimethyl-7-oxocycloundeca-1,5,8-trienyl)methoxy)phenyl)acrylate (8b)



Yield: 33 % as a colourless liquid; R_f : 0.28 (1:3 EtOAc: hexane)

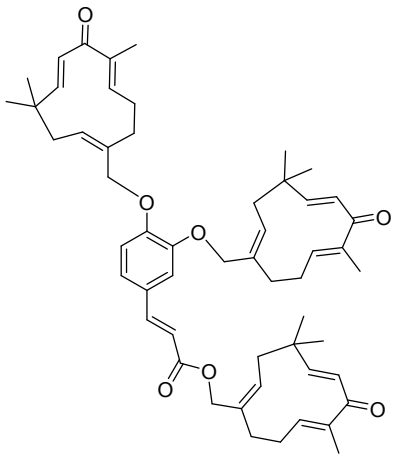
IR (neat) $\upsilon_{max:}$ 3398, 3057, 2963, 2922, 2412, 2356, 1710, 1640, 1512, 1464, 1424, 1363, 1266, 1161, 1033, 738, 704 cm^{-1}.

^{1}H NMR ($CDCl_3$, 500MHz): δ 7.05 (d, *J*= 8 Hz, 1H), 7.01 (d, *J*= 1 Hz, 1H), 6.86 (d, *J*= 8.5 Hz, 1H), 6.27 (d, *J*= 16 Hz, 1H), 6.20 (d, *J*= 16.5 Hz, 1H), 6.07- 6.04 (m, 2H), 5.99- 5.92 (m, 4H), 5.55- 5.48 (m, 2H), 4.72 (brs, 1H), 4.65- 4.63 (m, 1H), 4.56- 4.53 (m, 1H), 4.44 (brs, 1H), 3.84 (s, 3H), 2.69- 2.66 (m, 2H), 2.55- 2.52 (m, 4H), 2.46- 2.42 (m, 2H), 2.32- 2.24 (m, 4H), 1.80 (s, 3H), 1.77 (s, 3H), 1.27 (s, 3H), 1.26 (s, 3H), 1.12 (s, 3H), 1.09 (s, 3H) ppm.

^{13}C NMR ($CDCl_3$, 125MHz): δ 203.7, 203.4, 166.8, 160.1, 159.7, 150.4, 149.9, 149.0, 145.2, 145.2, 138.8, 138.4, 135.0, 134.6, 131.3, 127.6, 127.2, 122.1, 115.4, 112.9, 109.9, 66.3, 61.1, 55.4, 42.5, 42.4, 37.3, 36.3, 35.9, 29.7, 29.4, 24.9, 24.1, 14.2, 12.2, 12.1 ppm.

HRMS (ESI): *m/z* Calcd for $C_{40}H_{50}NaO_6$: 649.35051, Found: 649.35112.

(E)-((1Z,5E,8E)-4,4,8-trimethyl-7-oxocycloundeca-1,5,8-trienyl)methyl 3-(3,4-bis(((1Z,5E,8E)-4,4,8-trimethyl-7-oxocycloundeca-1,5,8-trienyl)methoxy)phenyl)acrylate (8c)



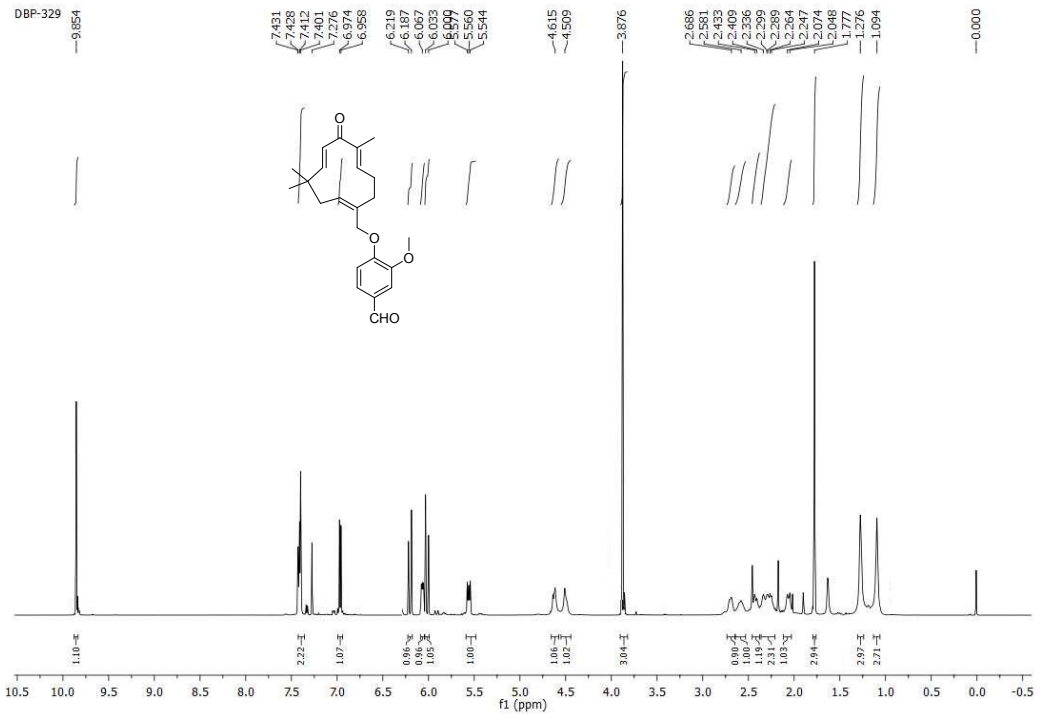
Yield:29 % as a colourless liquid; R_f: 0.17 (1:3 EtOAc: hexane)

IR (neat) $\upsilon_{max:}$ 3436, 2962, 2921, 2852, 2075, 1705, 1646, 1511, 1460, 1431, 1364, 1260, 1161, 1134, 1006, 738, 702, 530 cm^{-1}.

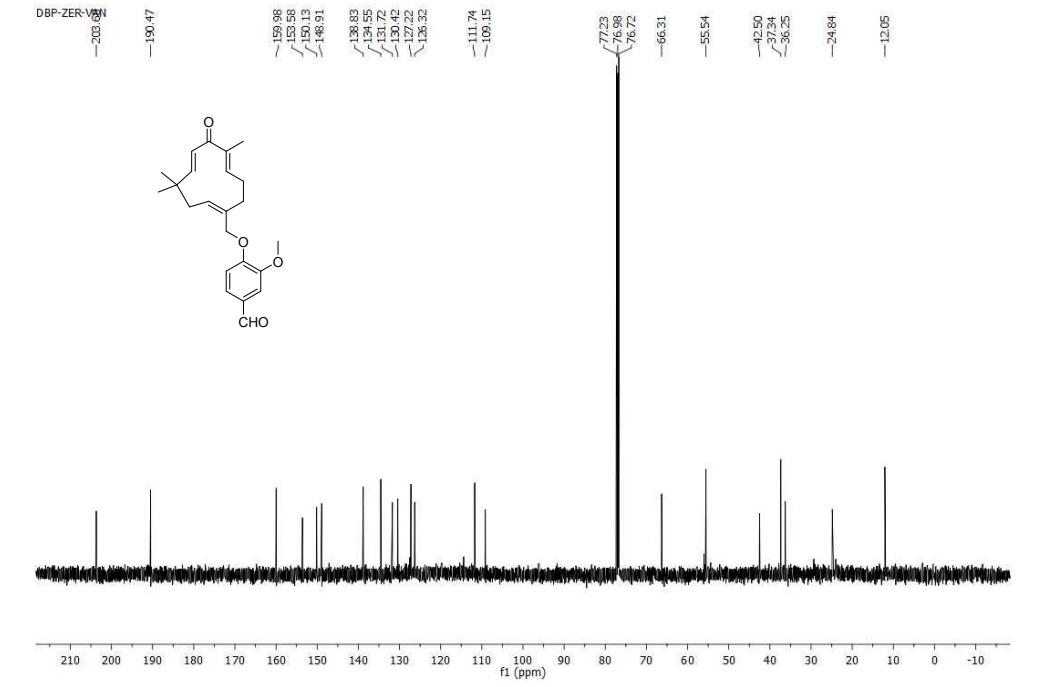
^{1}H NMR ($CDCl_3$, 500MHz): δ 7.58 (d, *J*= 16 Hz, 1H), 7.09 (d, *J*= 8 Hz, 1H), 7.02 (s, 1H), 6.88 (d, *J*= 8Hz, 1H), 6.24 (d, *J*= 16 Hz, 1H), 6.09- 5.91 (m, 9H), 5.54- 5.49 (m, 3H), 4.70- 4.67 (m, 4H), 4.35- 4.34 (m, 2H), 2.72- 2.65 (m, 3H), 2.52- 2.49 (m, 7H), 2.36- 2.27 (m, 8H), 1.79 (s, 9H), 1.26 (s, 9H), 1.12 (s, 9H) ppm.

^{13}C NMR ($CDCl_3$, 125MHz): δ 203.4, 203.3, 166.7, 159.6, 149.2, 148.9, 138.6, 138.6, 135.3, 135.2, 134.4, 131.8, 130.6, 127.4, 127.1, 122.4, 115.6, 11.33, 112.5, 65.7, 29.3, 24.8, 24.6, 24.0, 12.1, 12.0ppm.

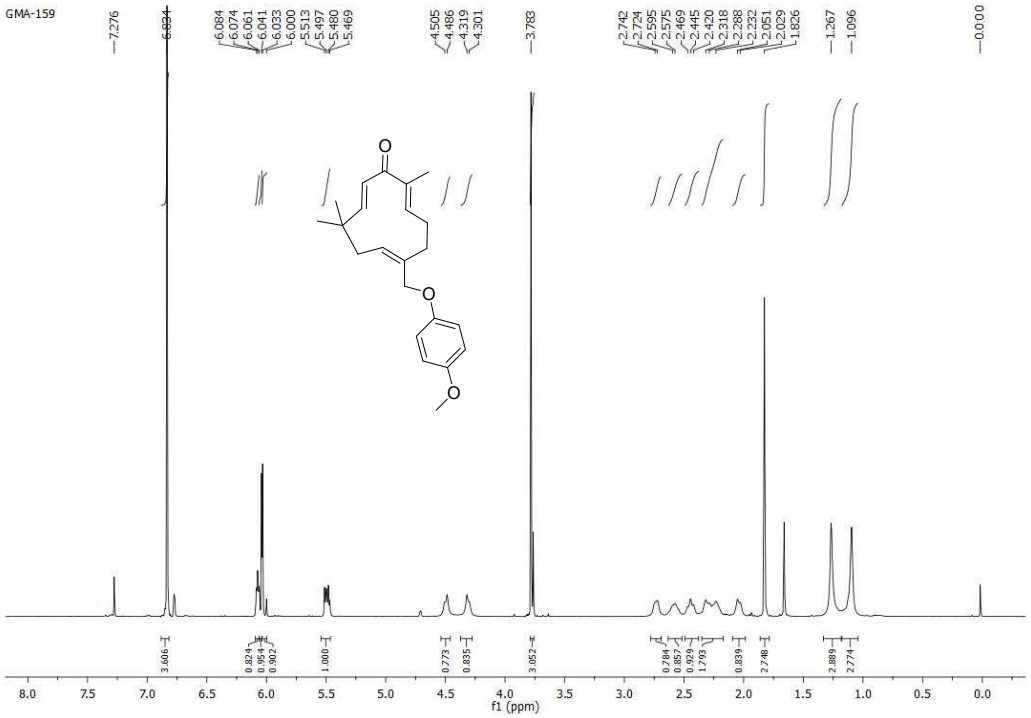
HRMS (ESI): *m/z* Calcd for $C_{54}H_{68}NaO_7$: 851.48627, Found: 851.48746.



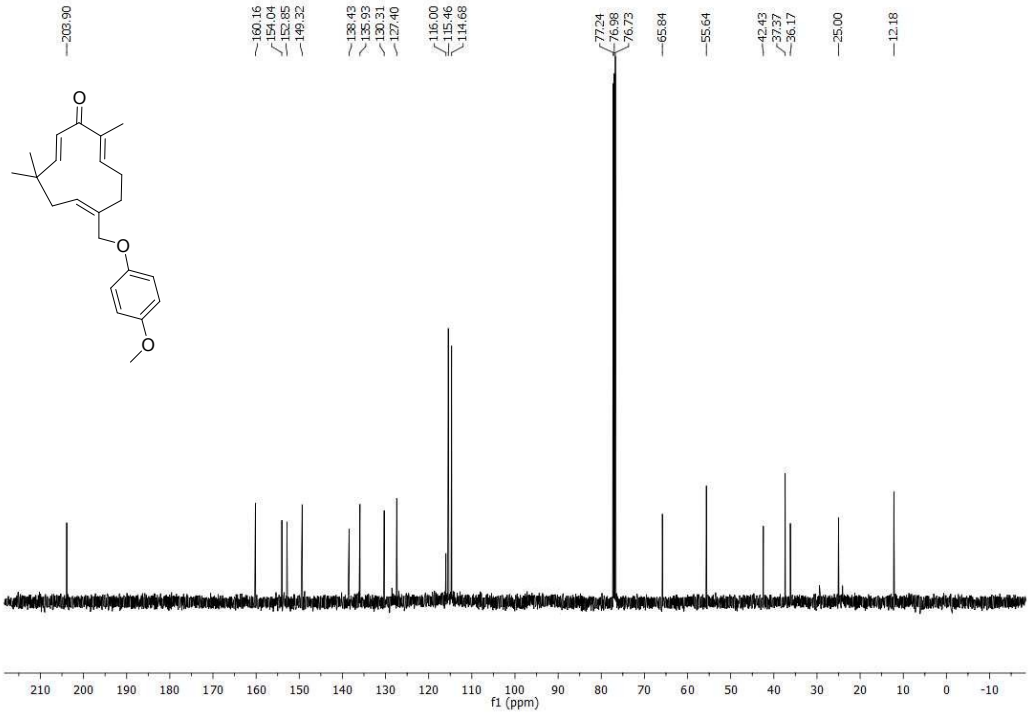
^{1}H NMR of 4a



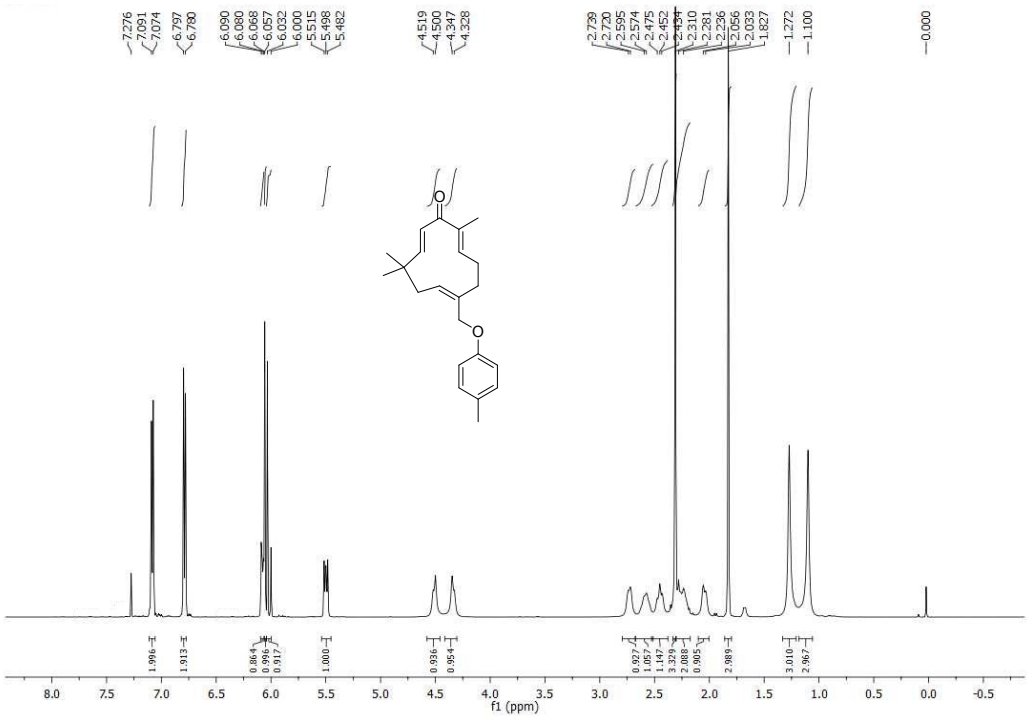
^{13}C NMR of 4a



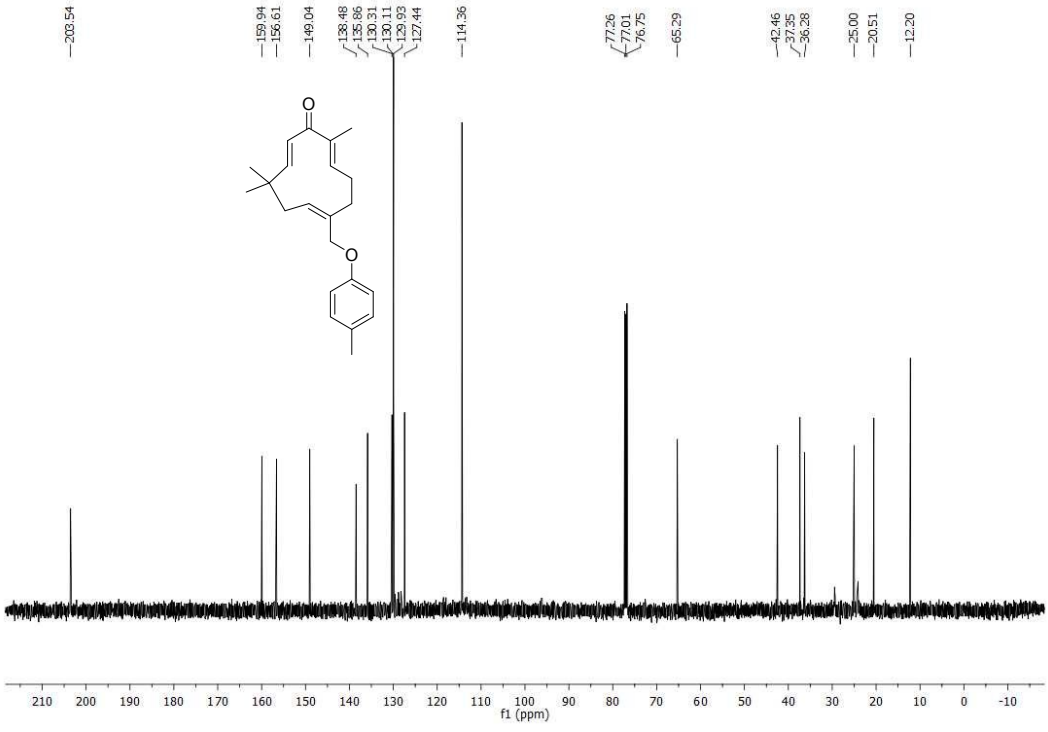
[1]H NMR of 4b



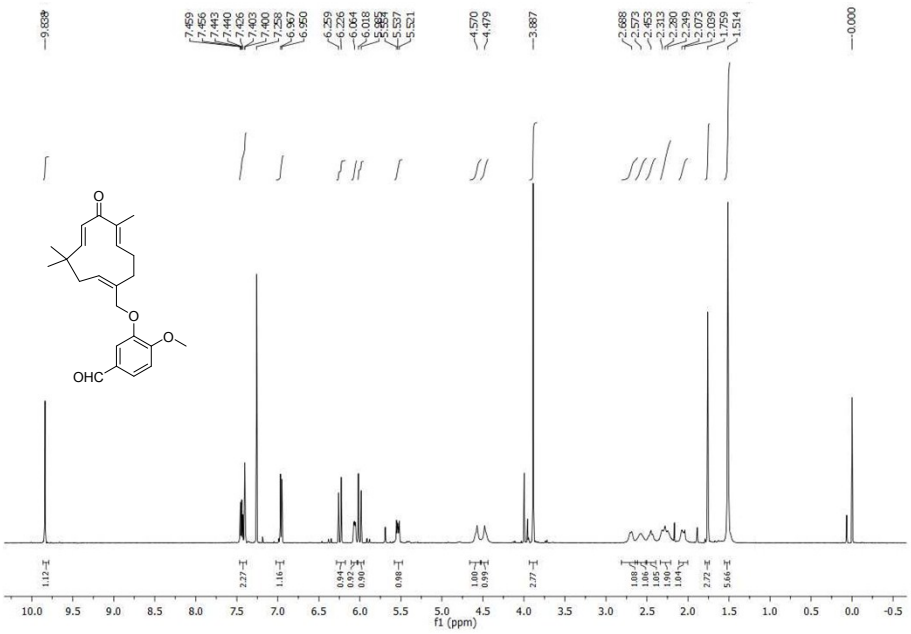
[13]C NMR of 4b



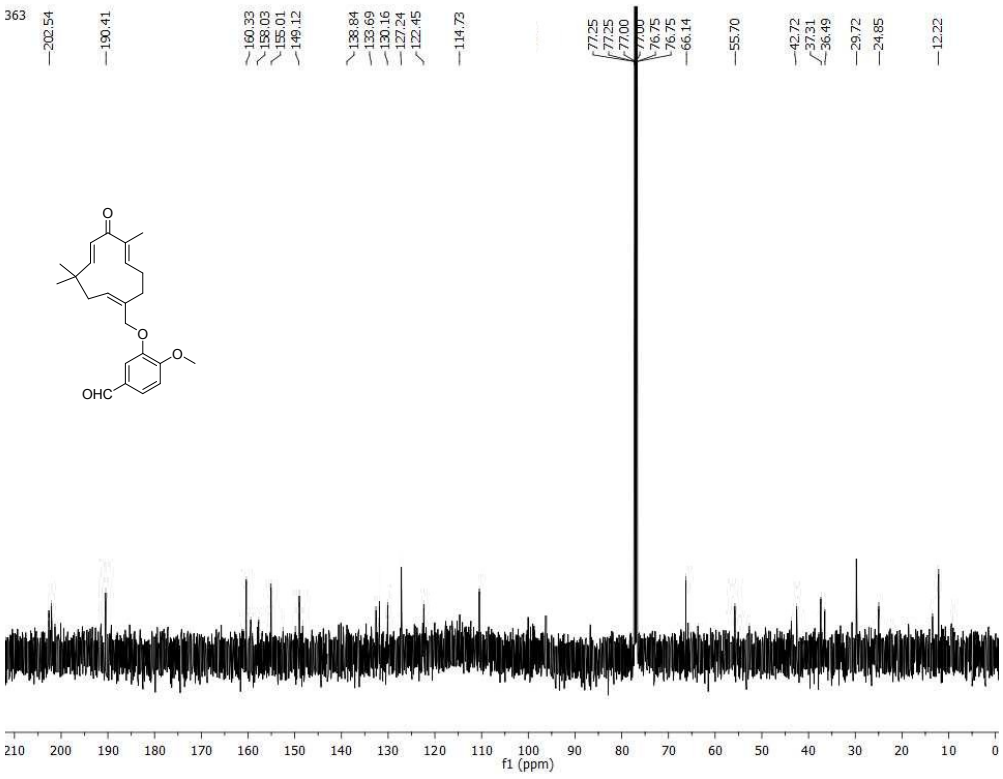
^{1}H NMR of 4c



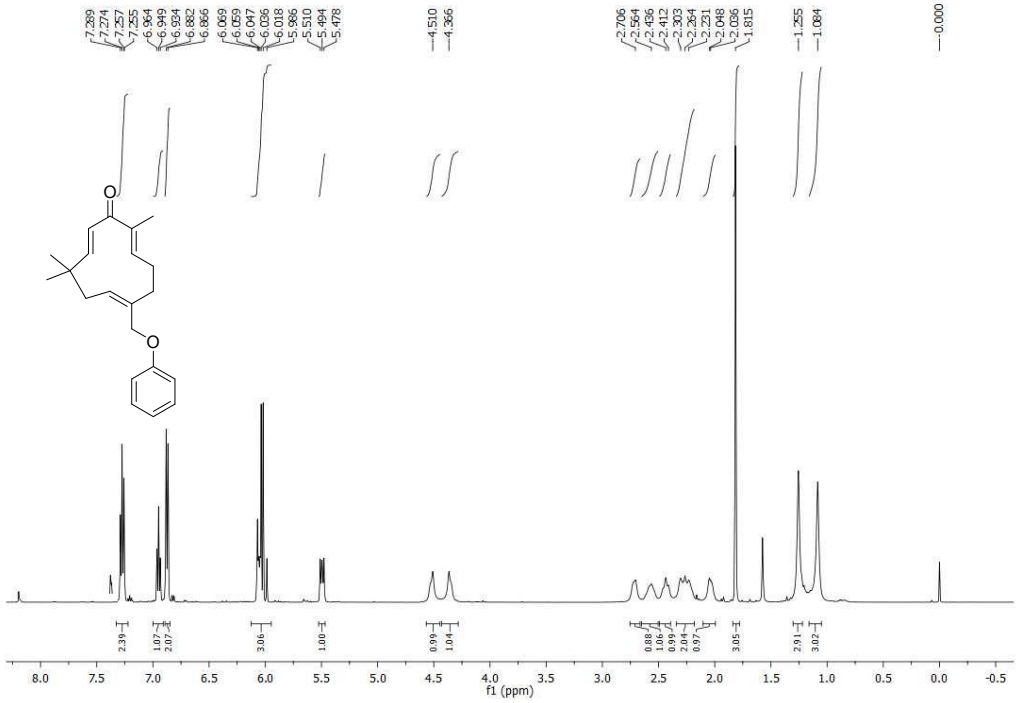
^{13}C NMR of 4c



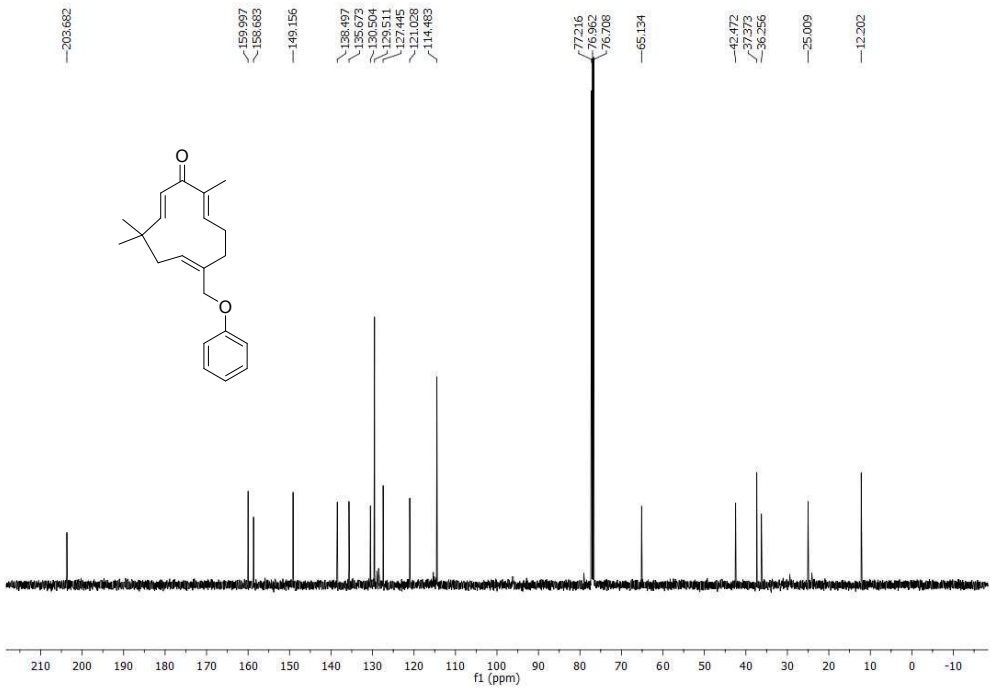
^{1}H NMR of 4d



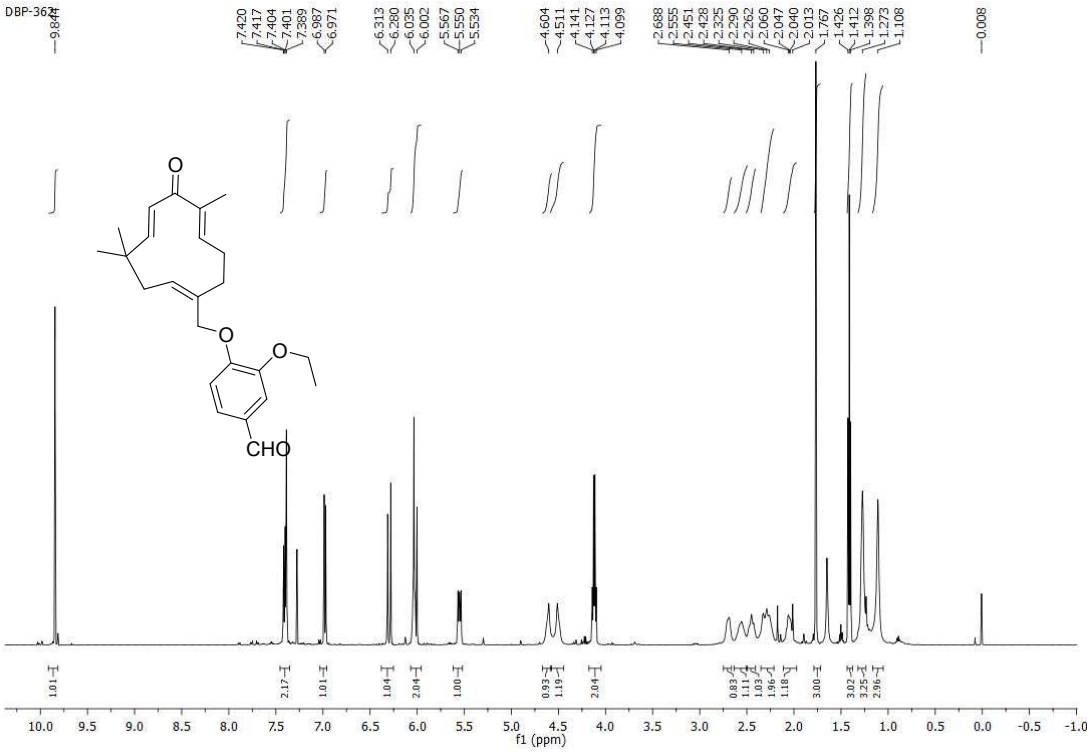
^{13}C NMR of 4d



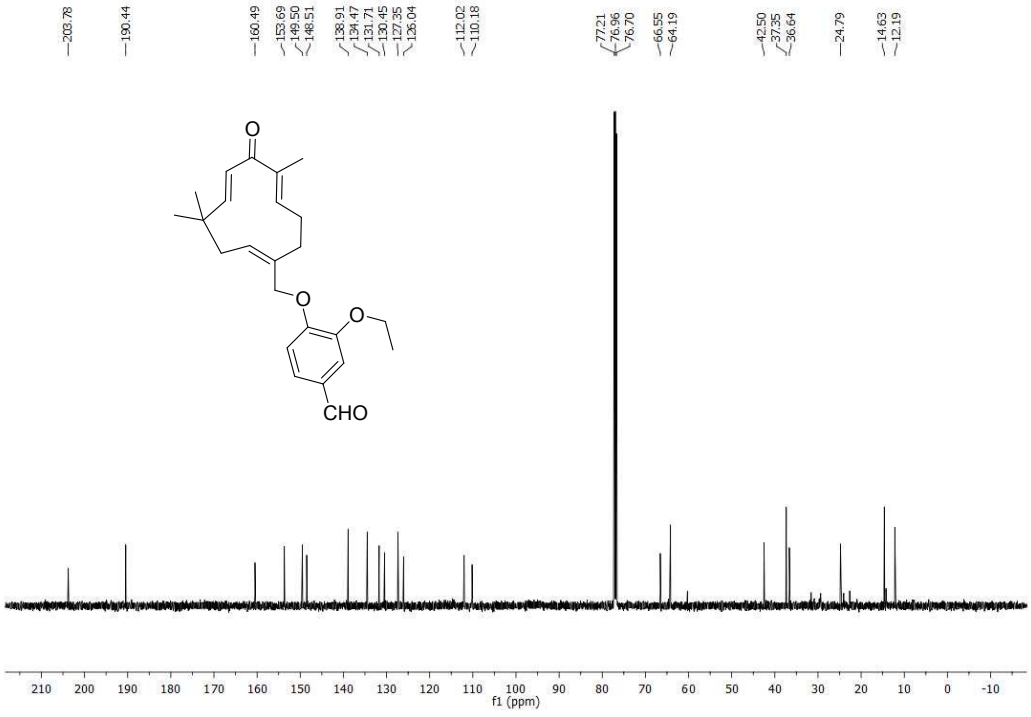
^{1}H NMR of 4e



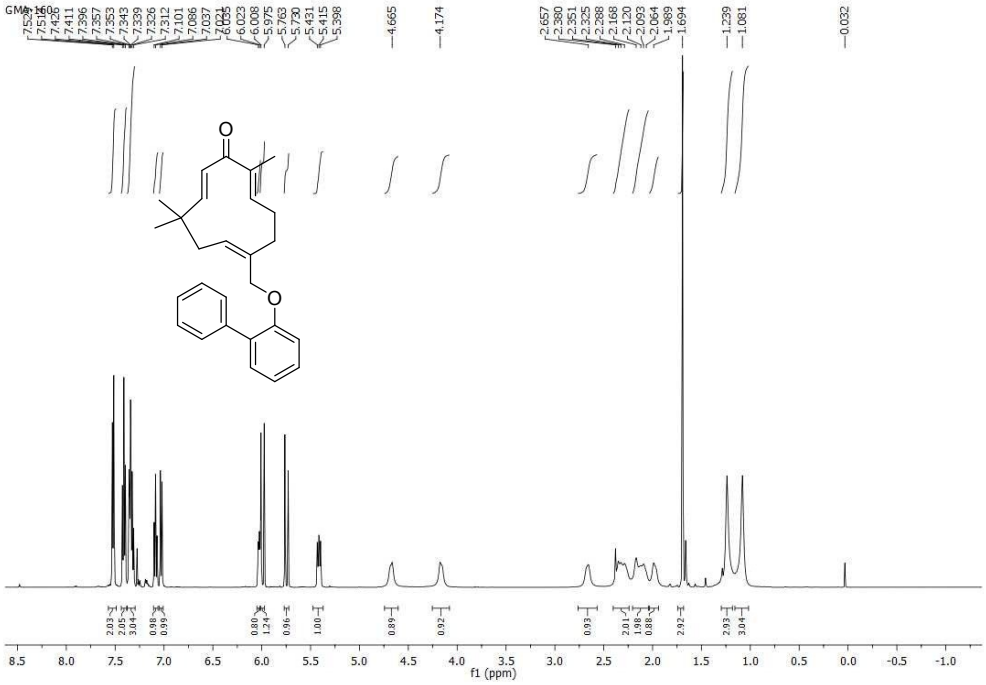
^{13}C NMR of 4e



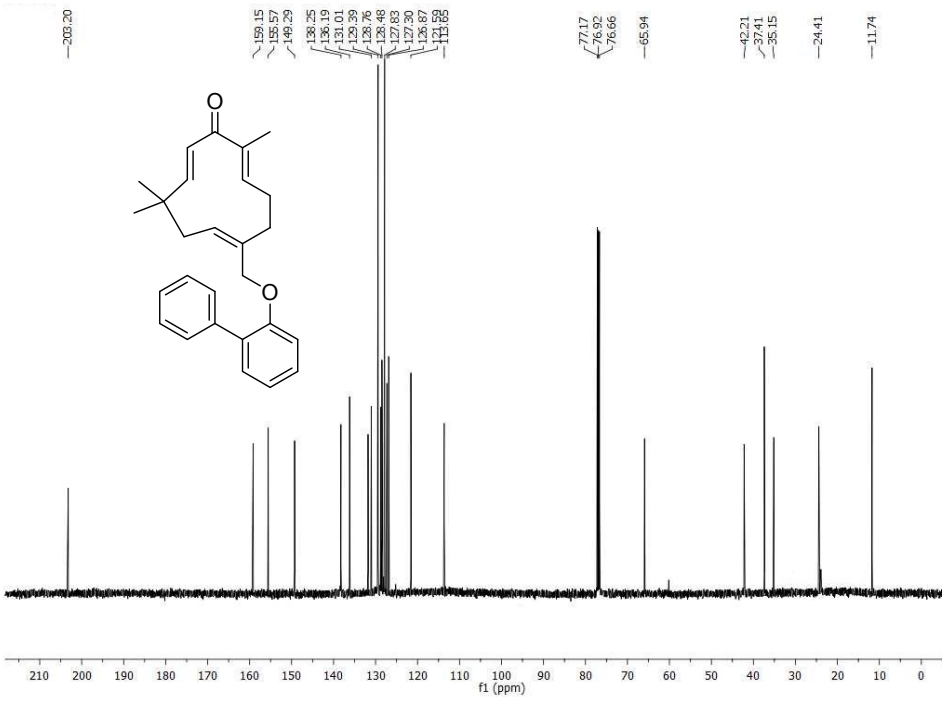
^{1}H NMR of 4f



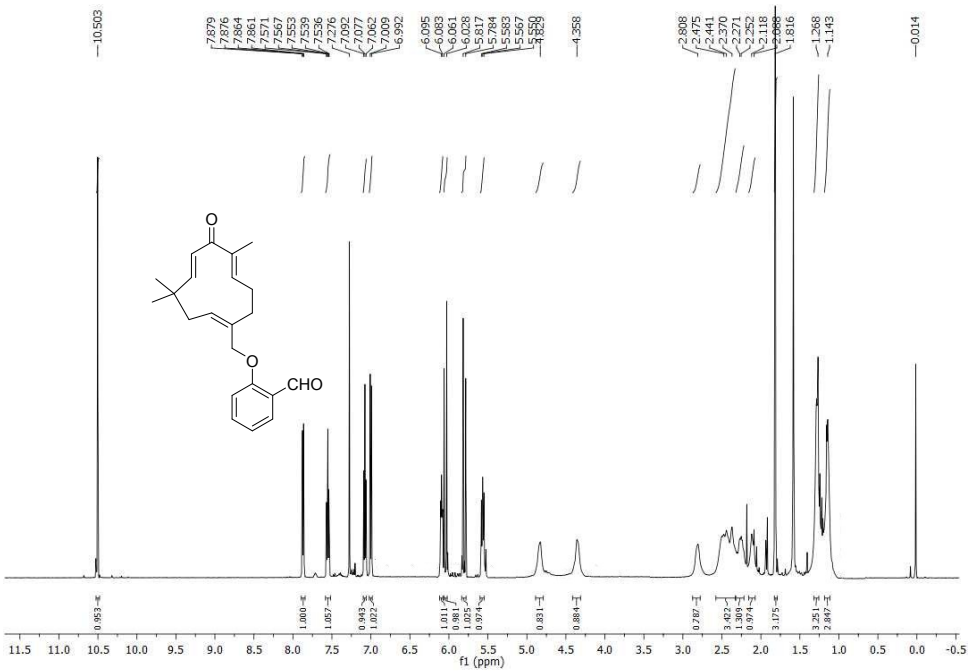
^{13}C NMR of 4f



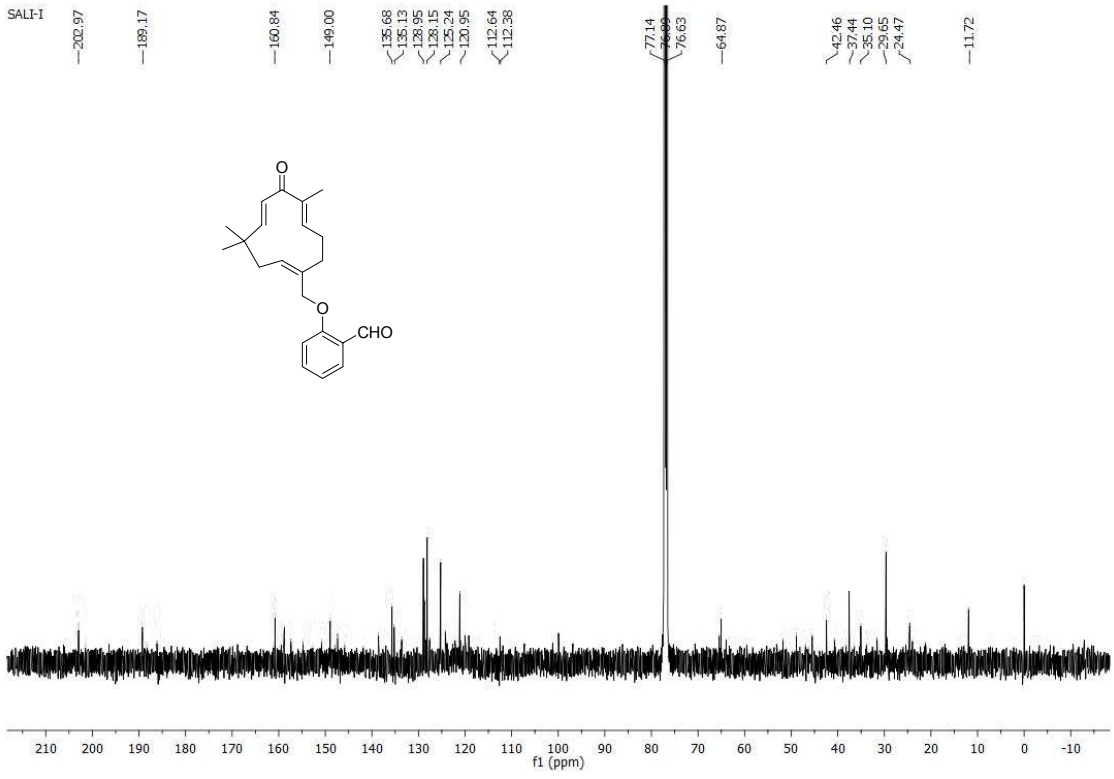
^{1}H NMR of 4g



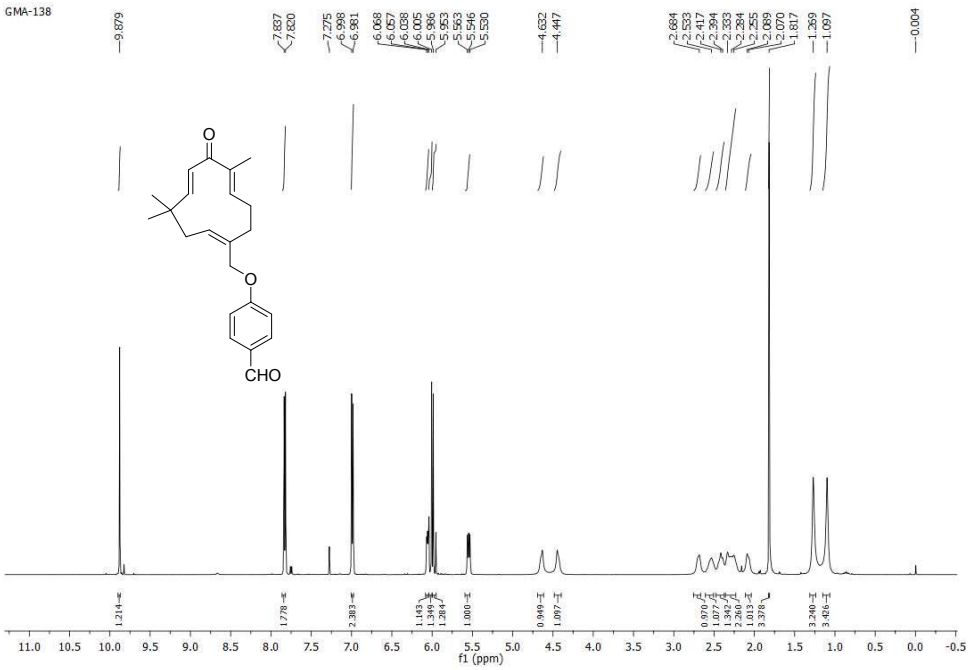
^{13}C NMR of 4g



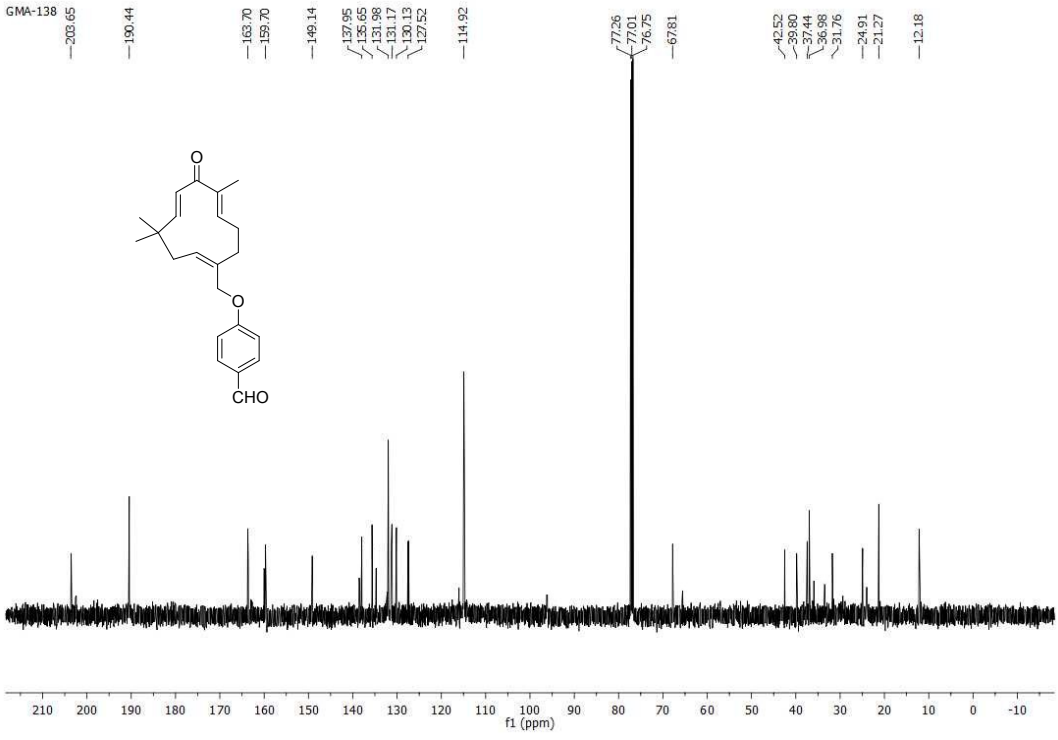
^{1}H NMR of 4h



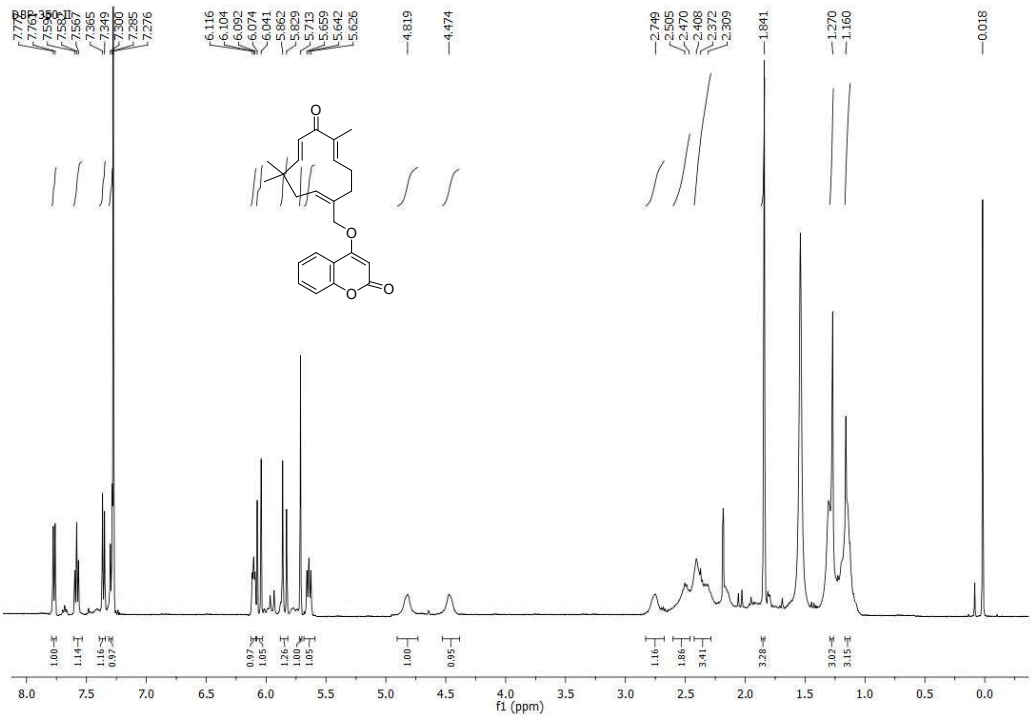
^{13}C NMR of 4h



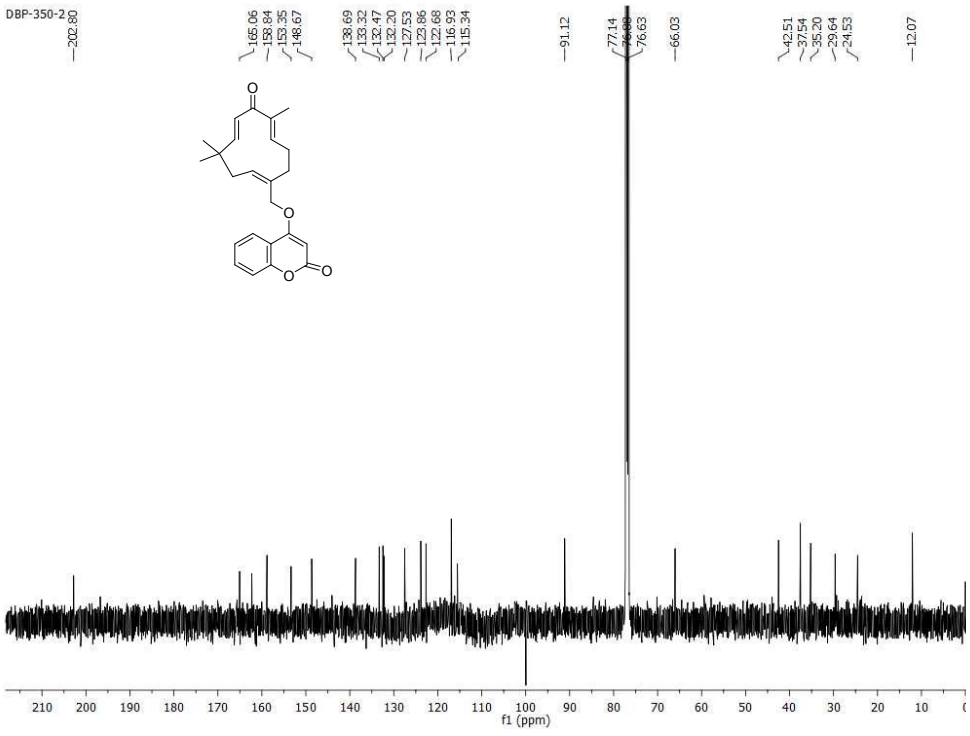
^{1}H NMR of 4i



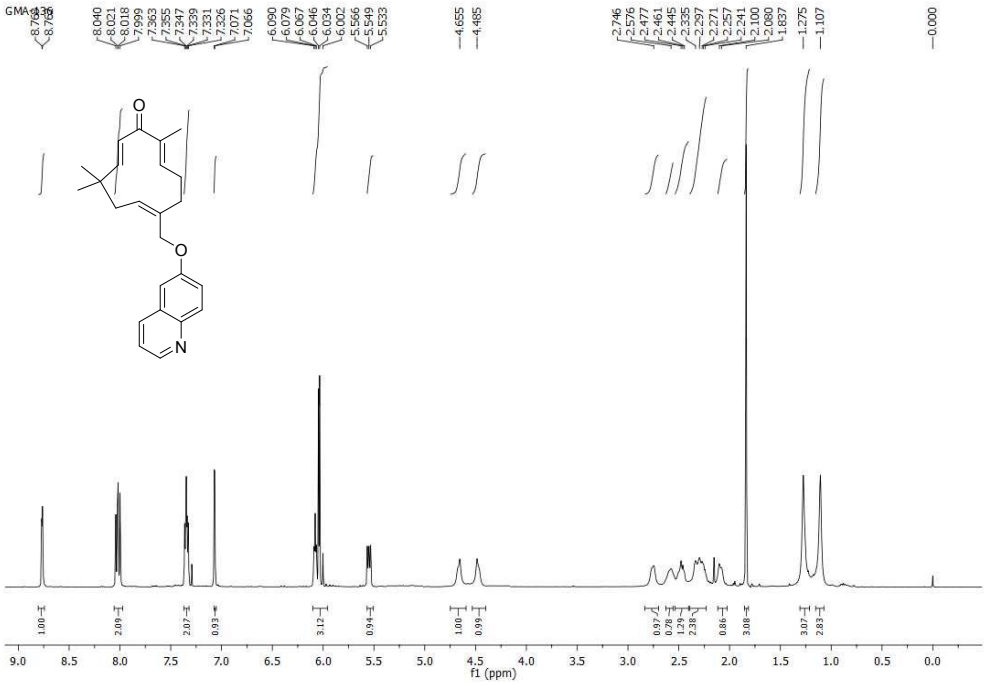
^{13}C NMR of 4i



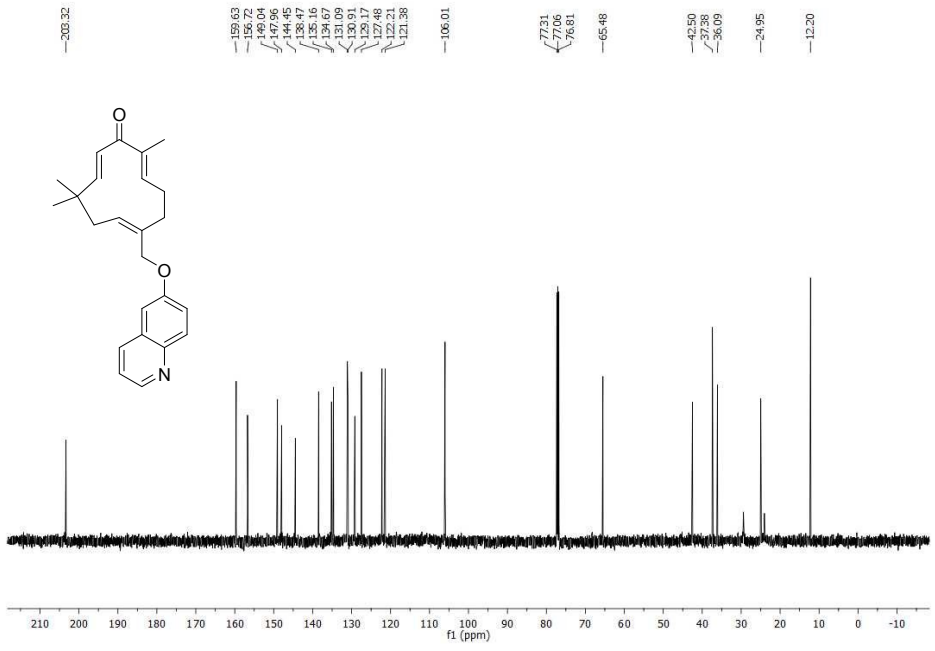
^{1}H NMR of 4j



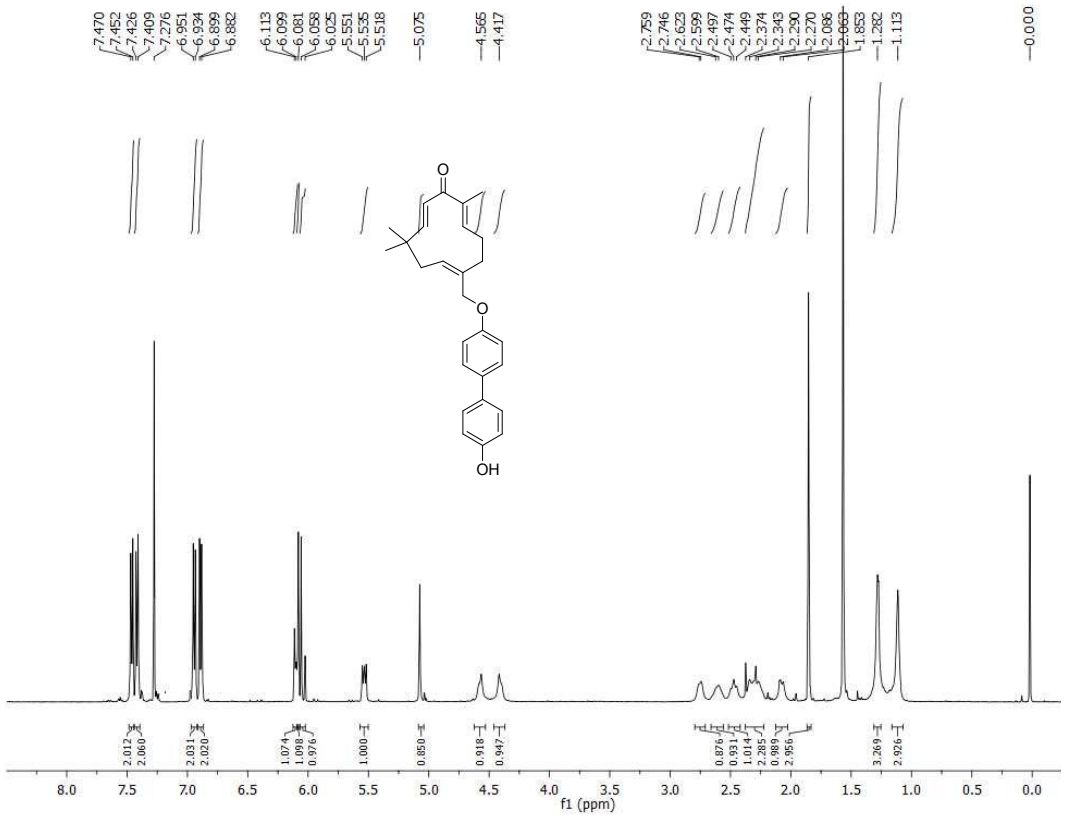
^{13}C NMR of 4j



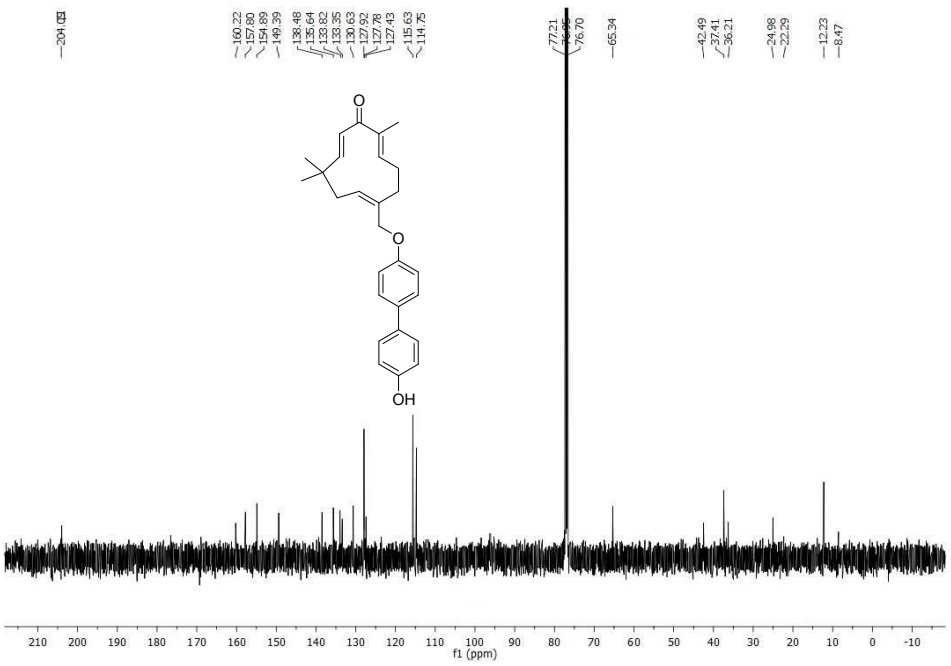
^{1}H NMR of 4k



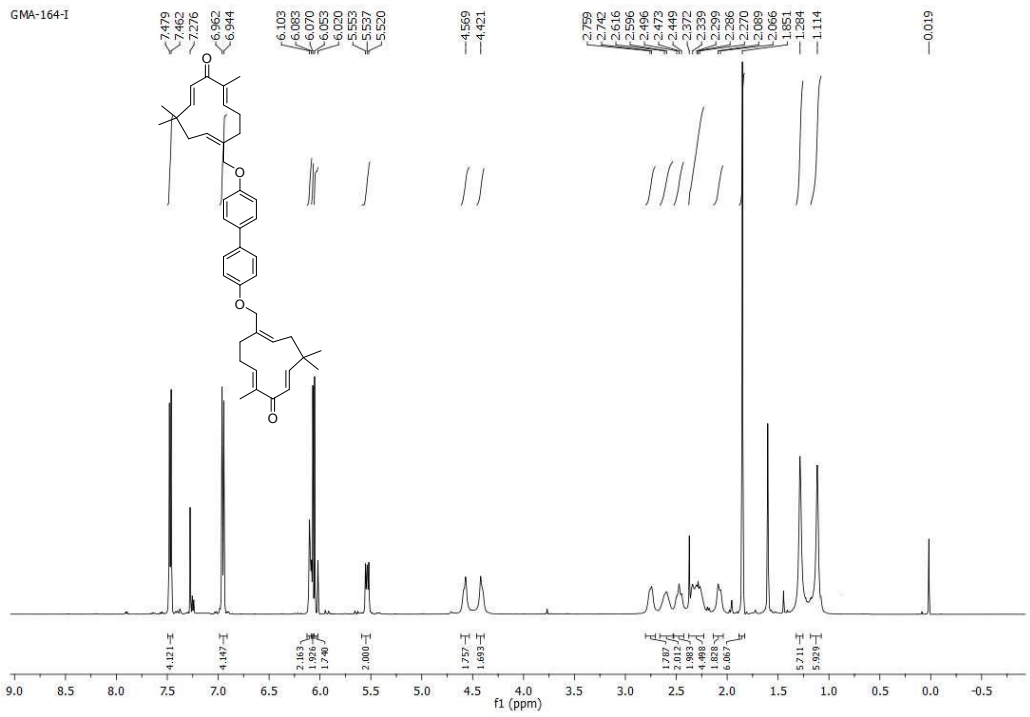
^{13}C NMR of 4k



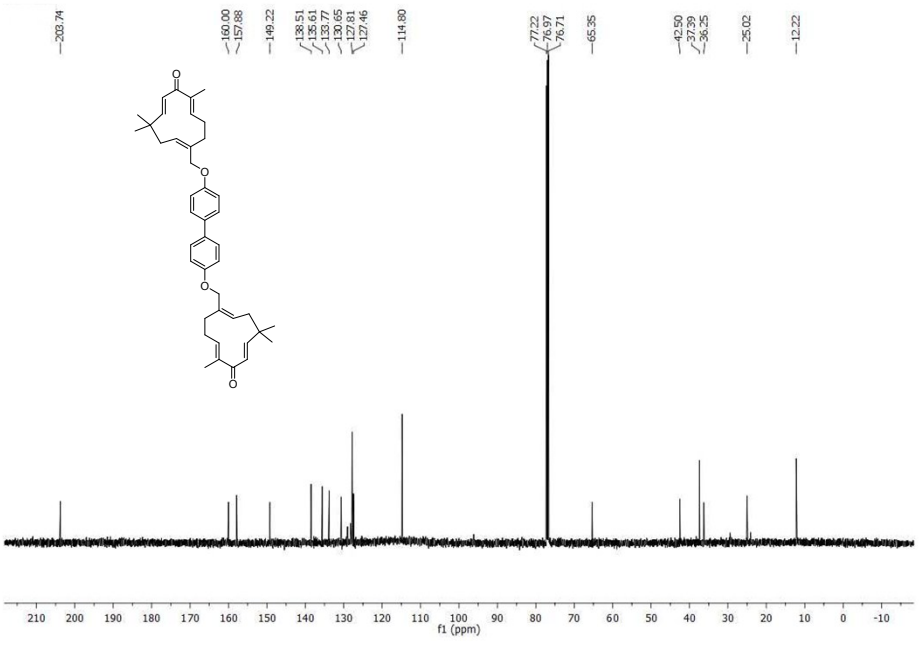
^{1}H NMR of 4l



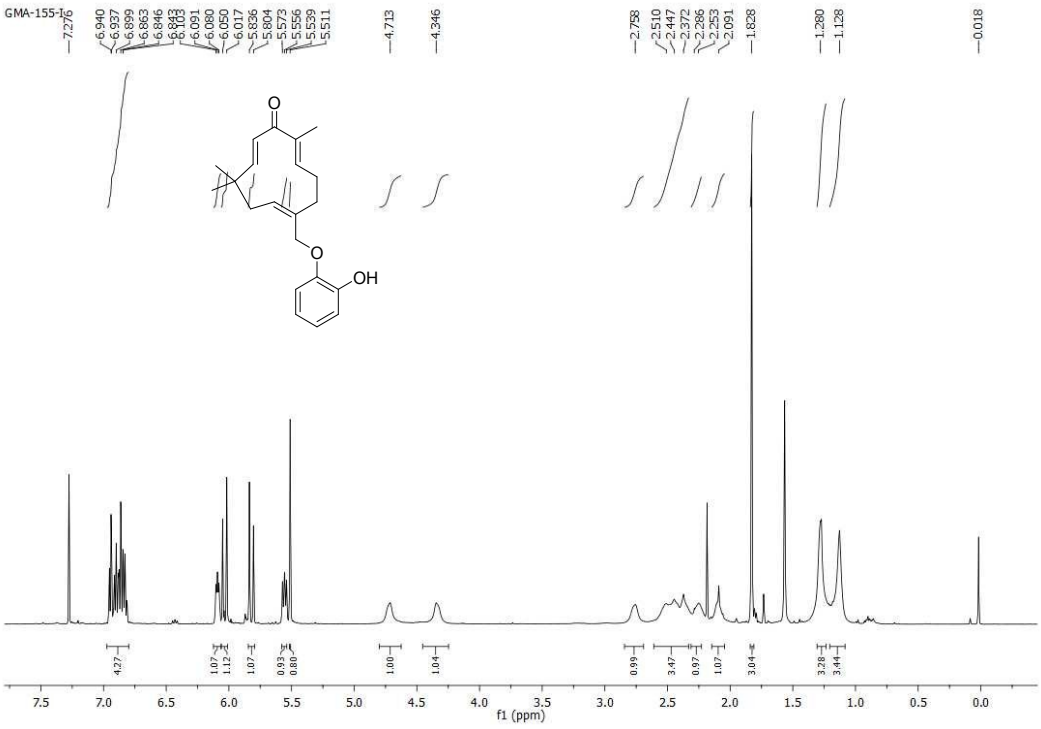
^{13}C NMR of 4l



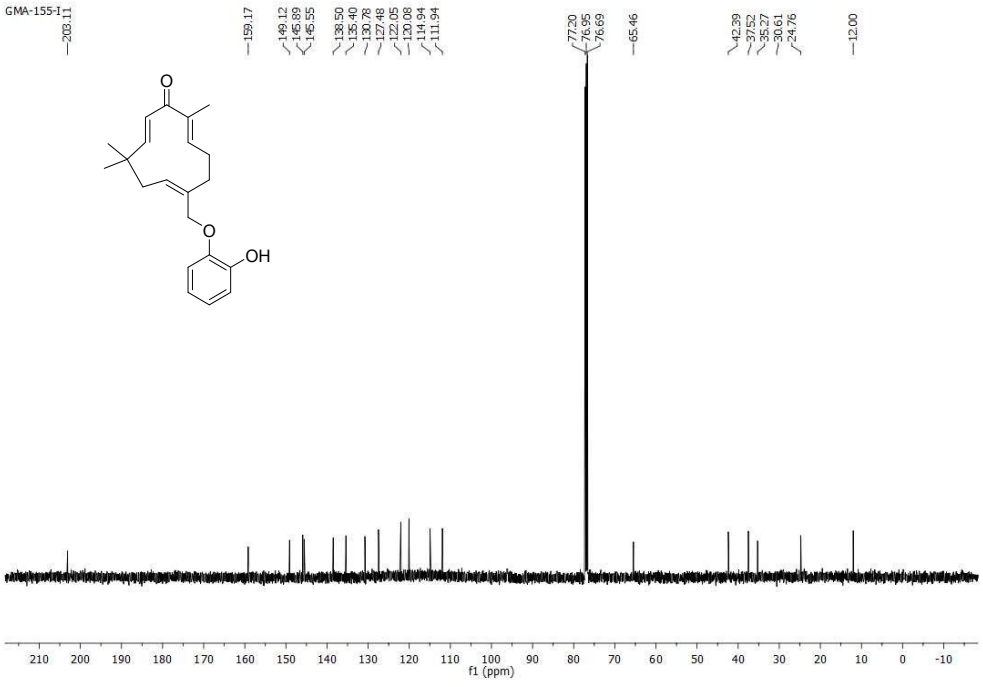
^{1}H NMR of 4l'



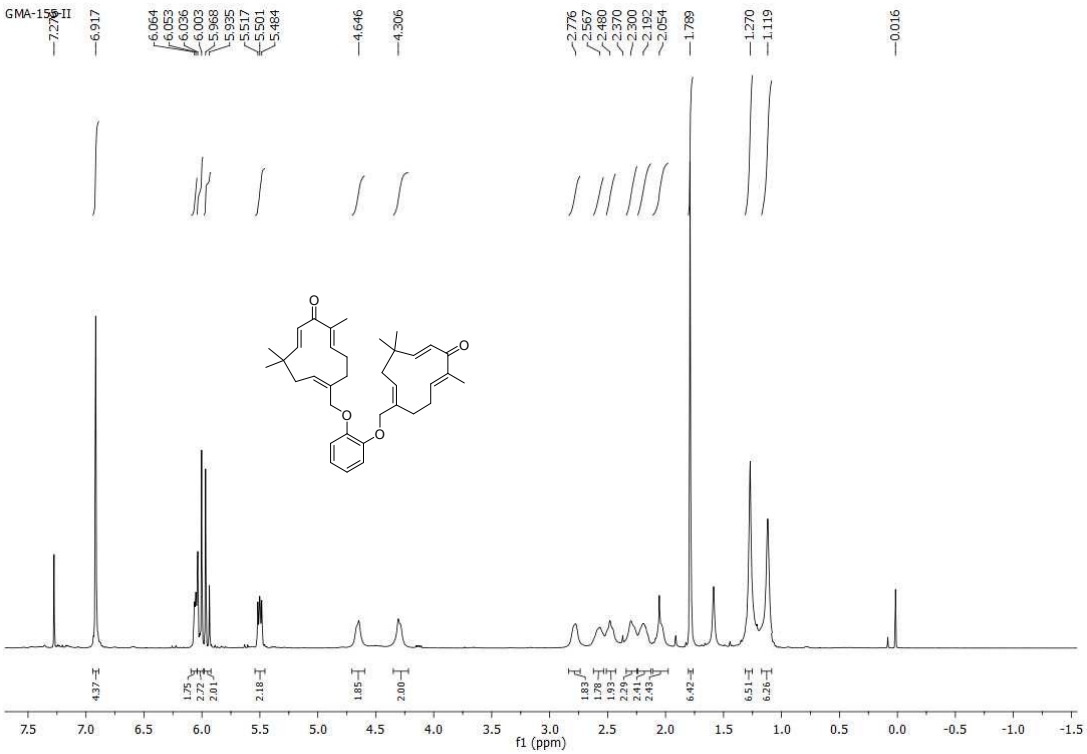
^{13}C NMR of 4l'



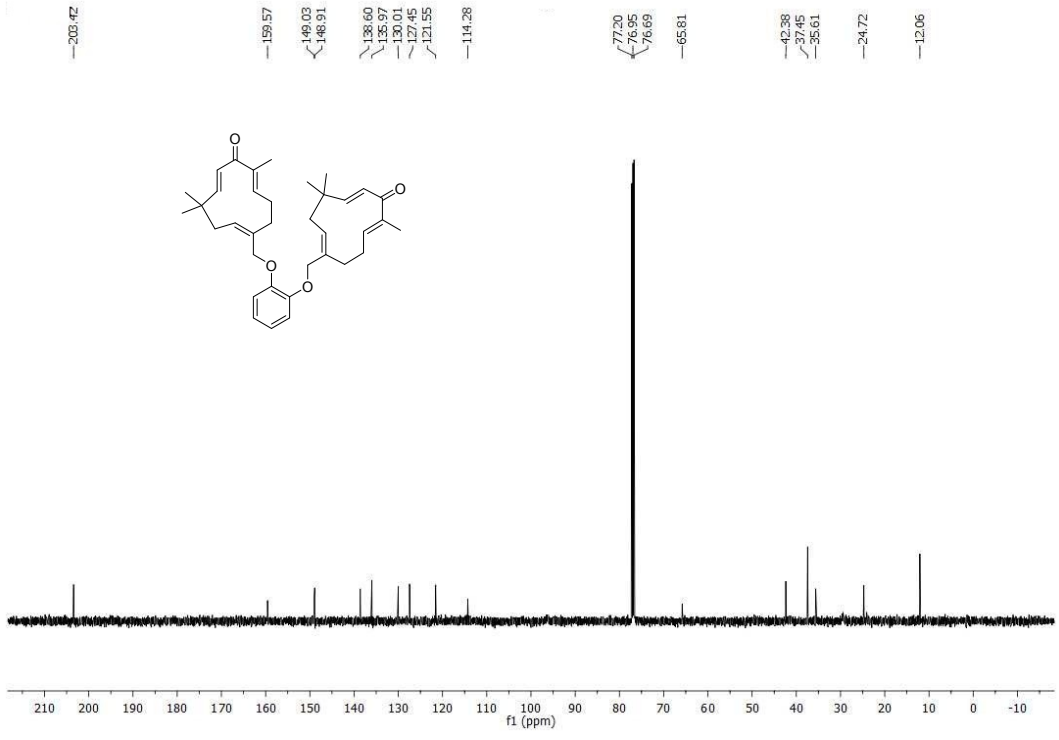
^{1}H NMR of 4m



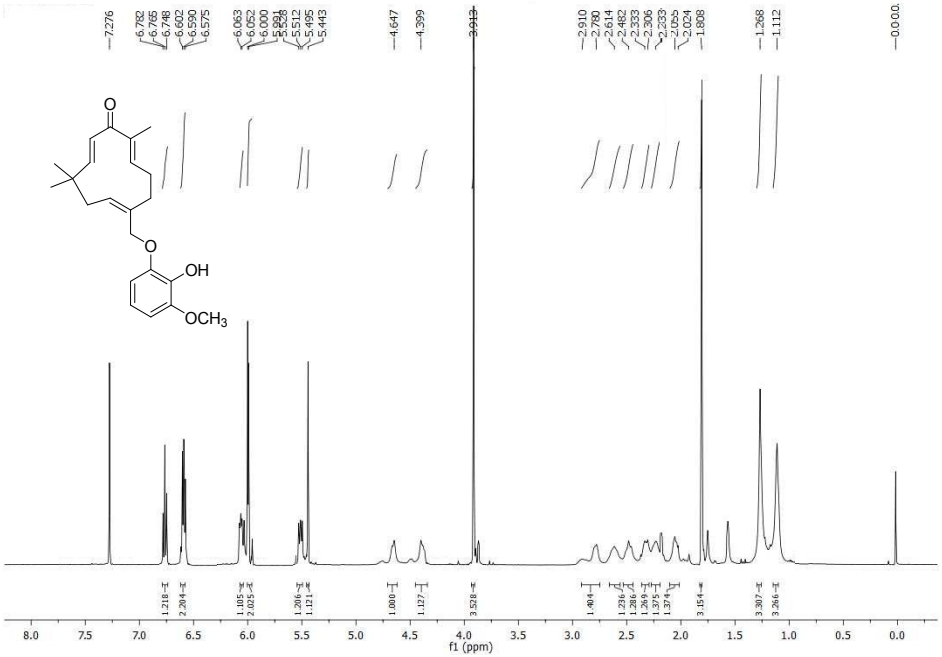
^{13}C NMR of 4m



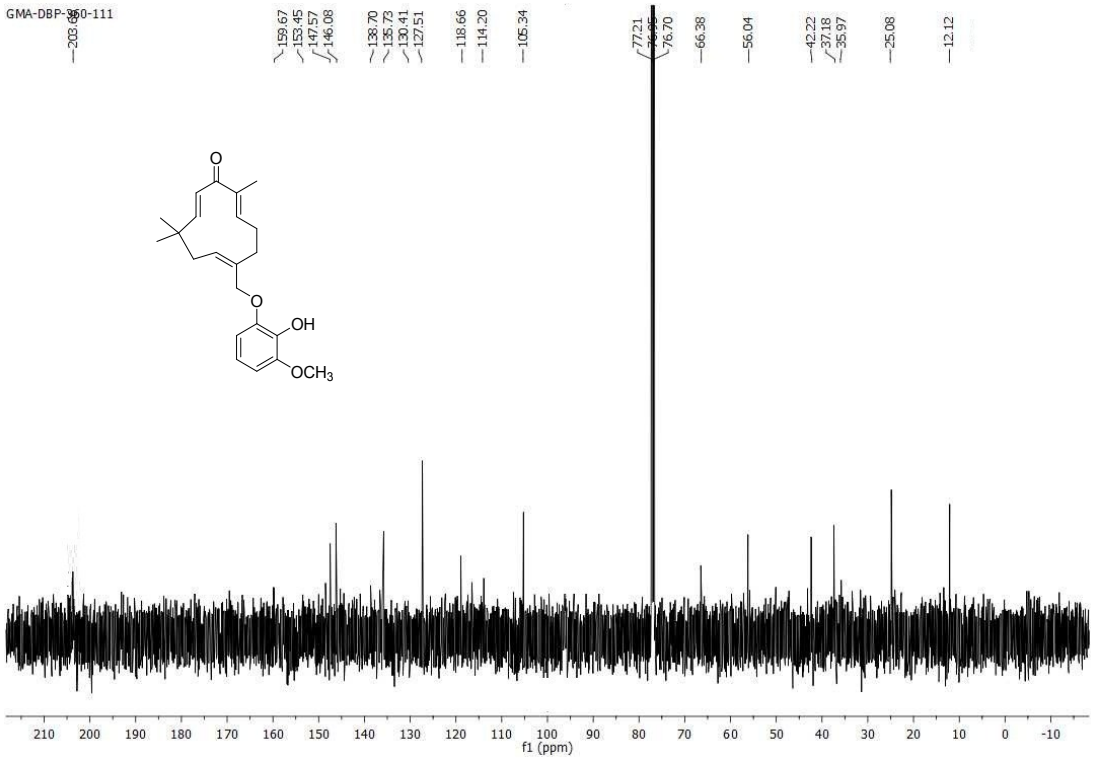
^{1}H NMR of 4m'



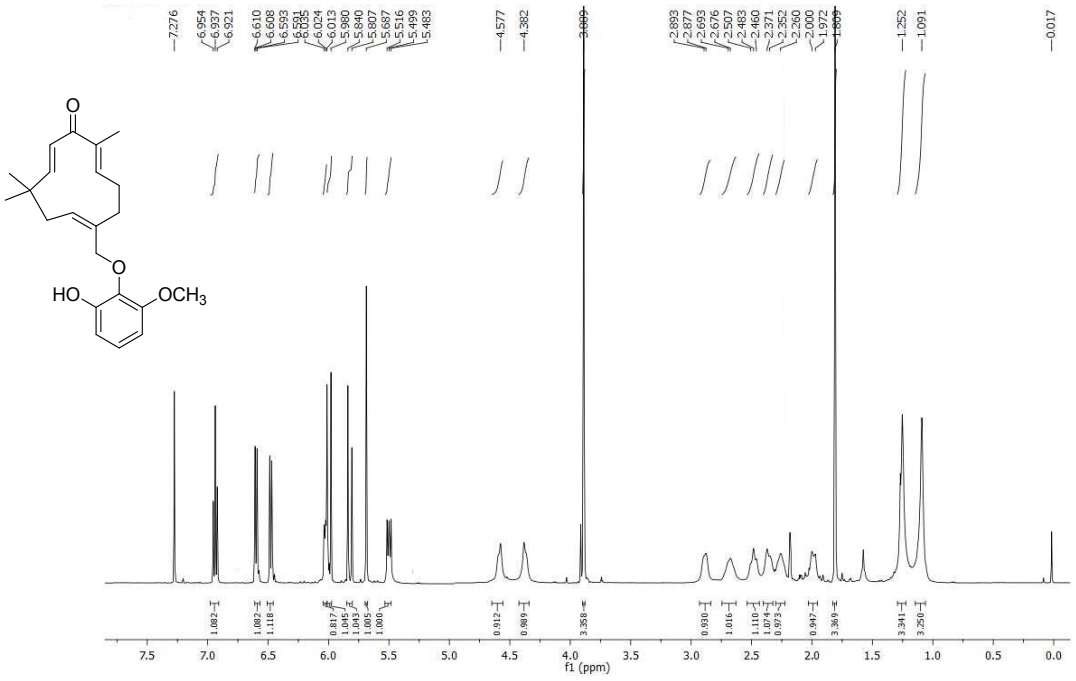
^{13}C NMR of 4m'



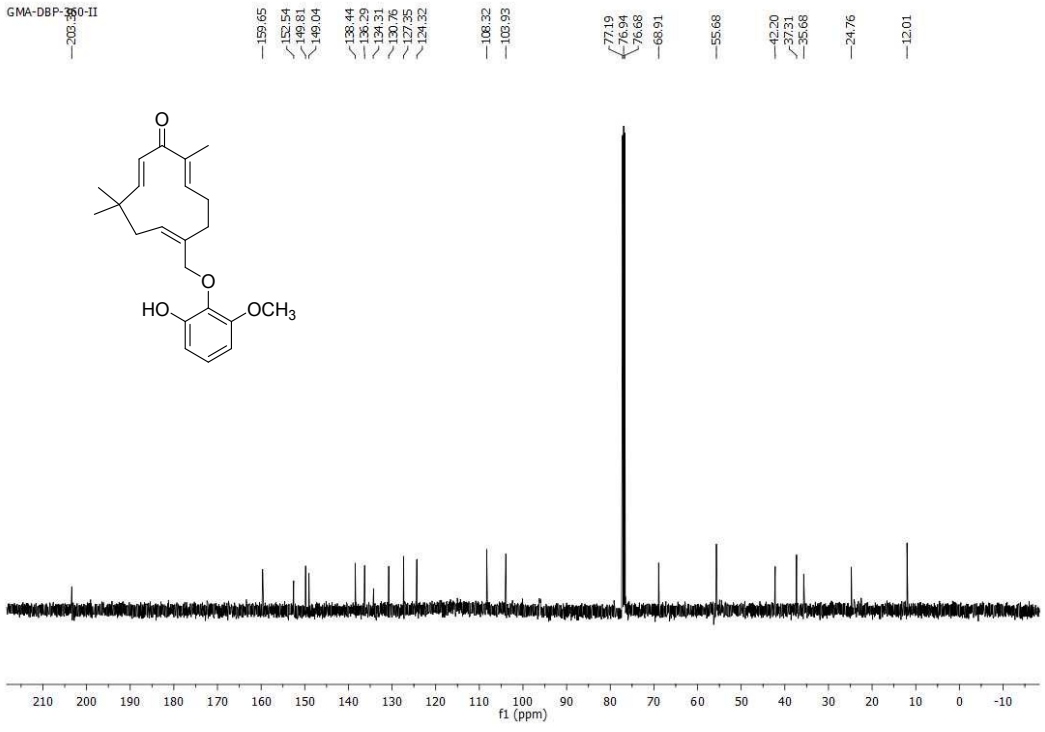
^{1}H NMR of 4n



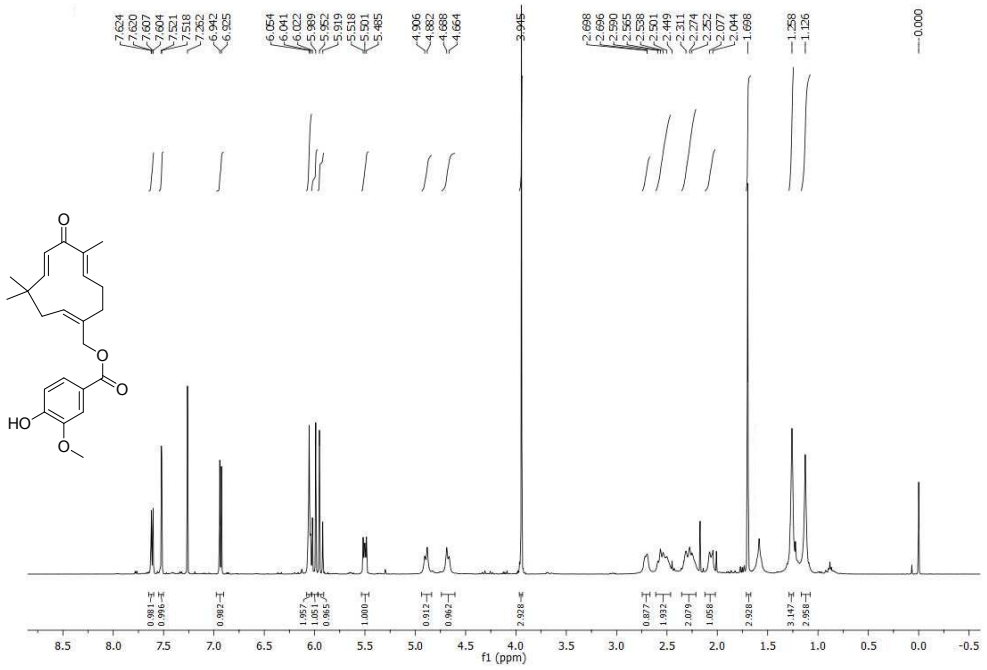
^{13}C NMR of 4n



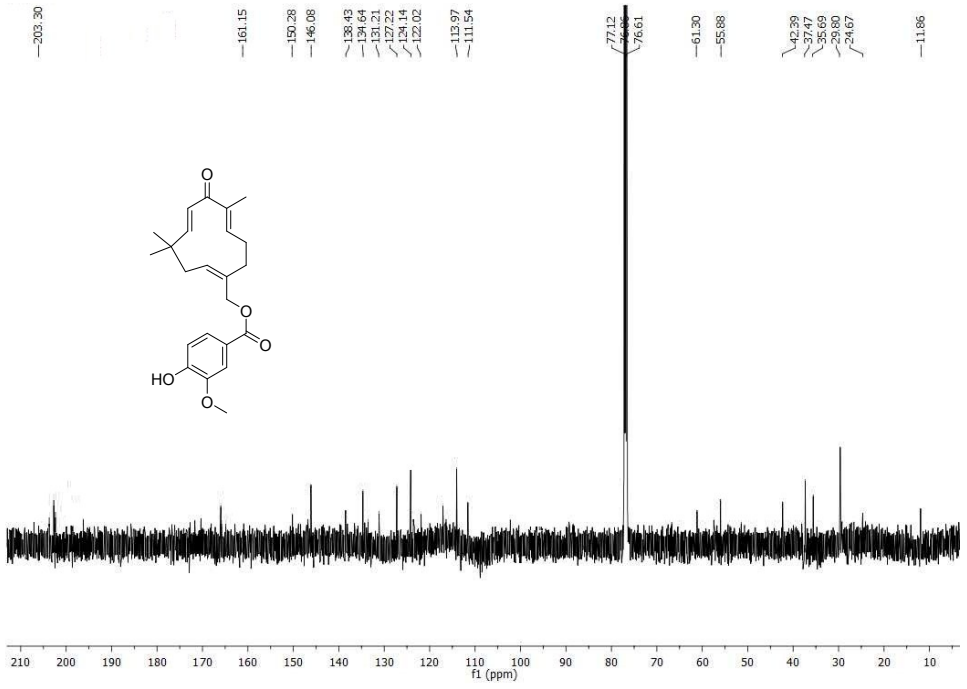
^{1}H NMR of 4n'



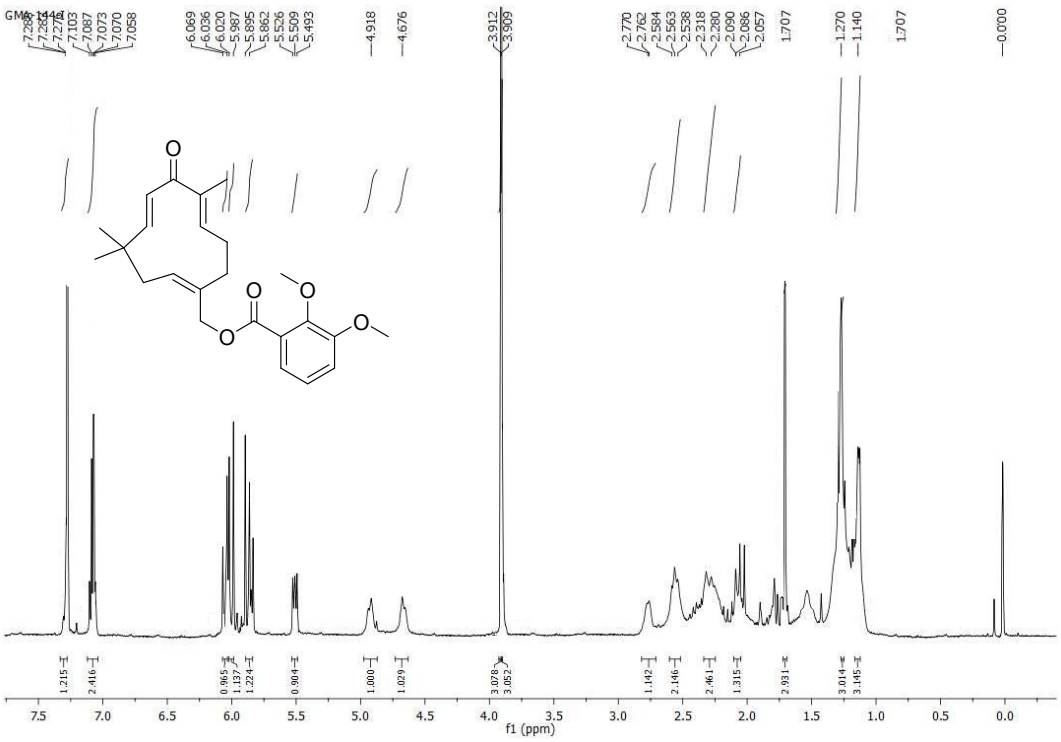
^{13}C NMR of 4n'



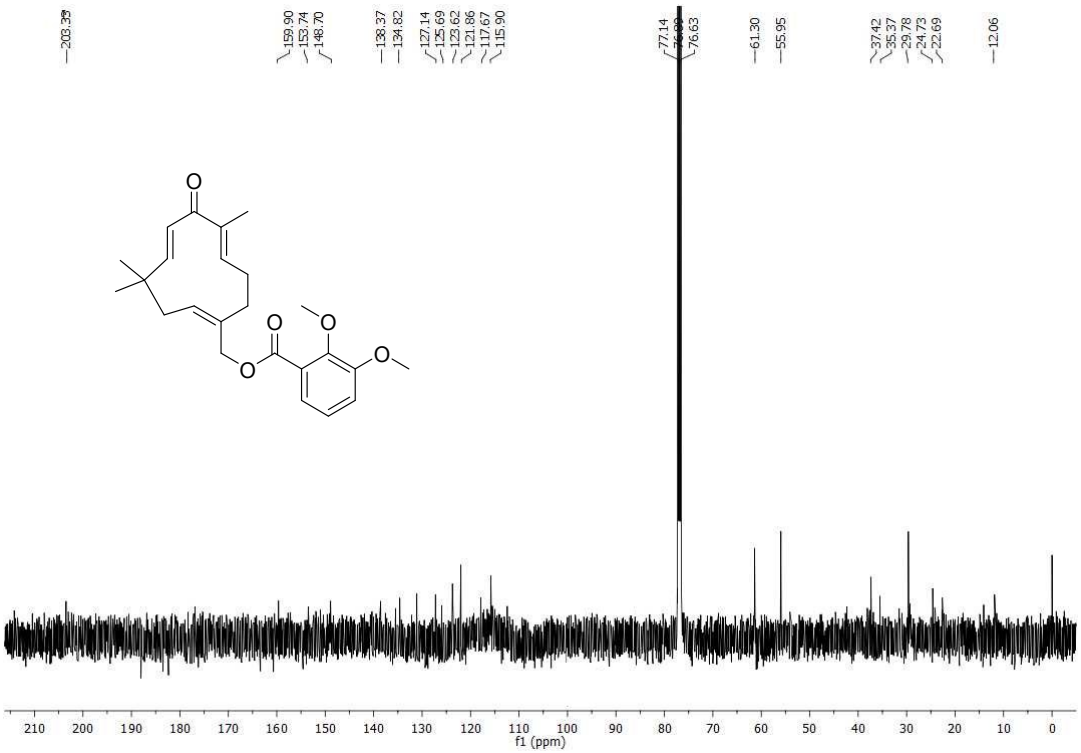
^{1}H NMR of 6b



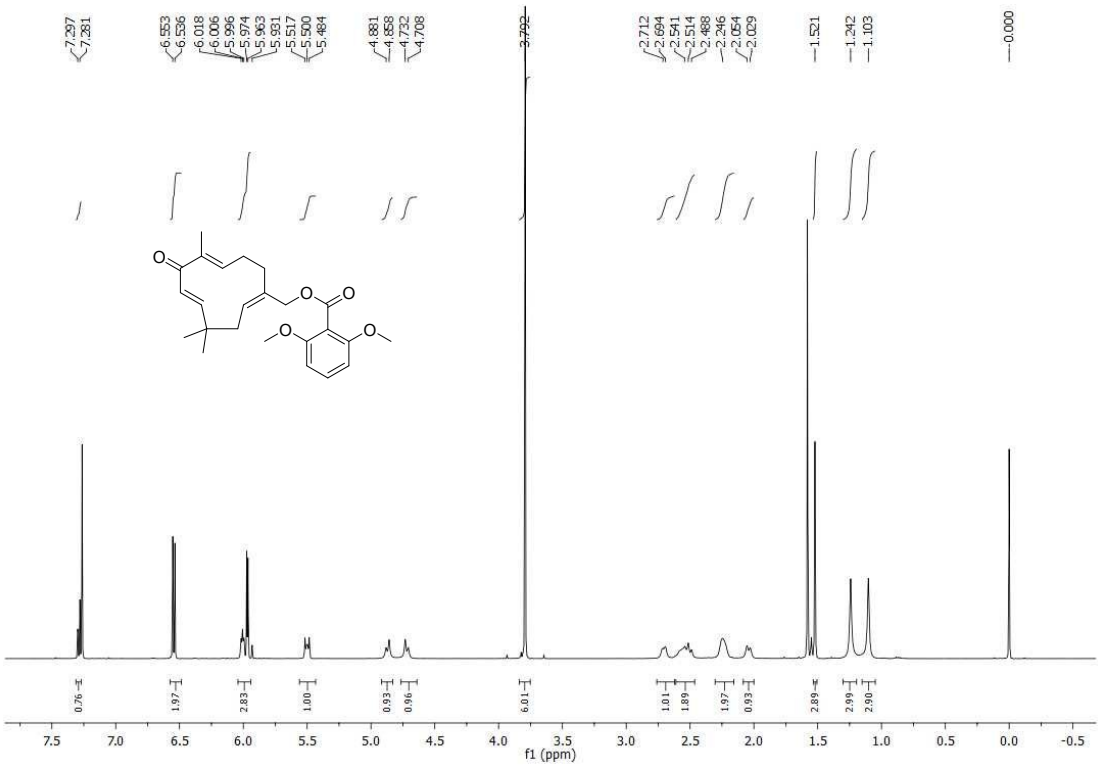
^{13}C NMR of 6b



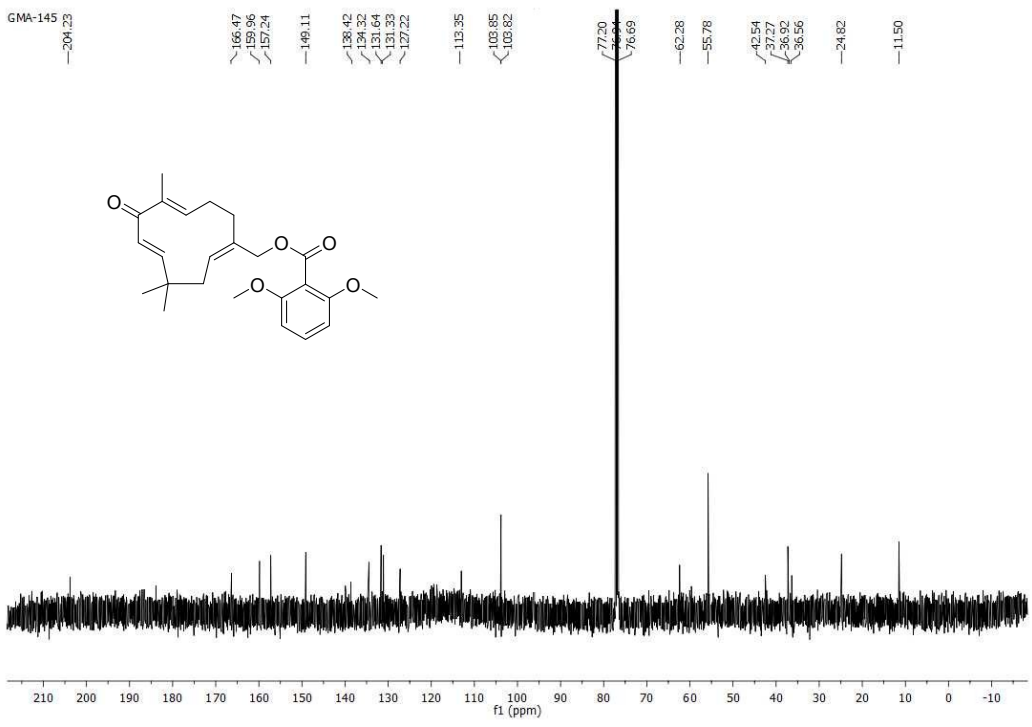
^{1}H NMR of 6c



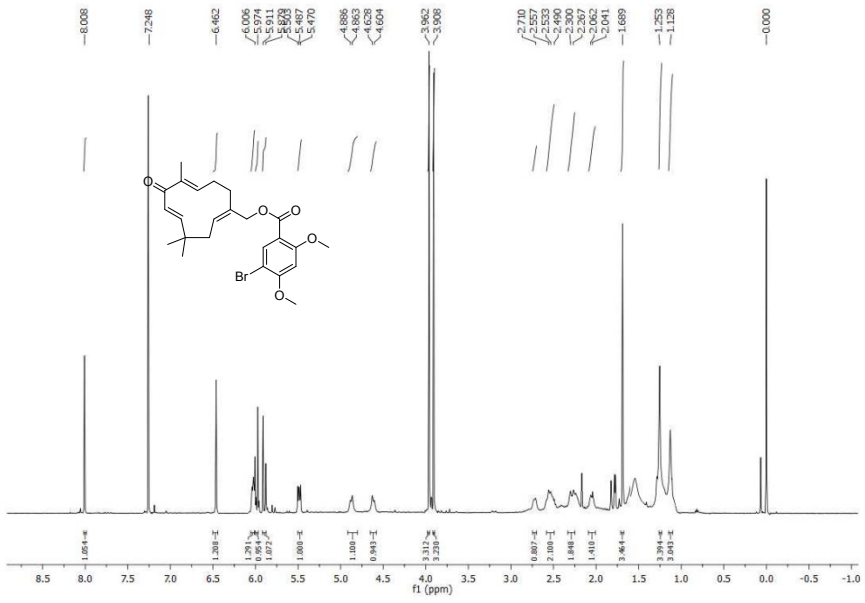
^{13}C NMR of 6c



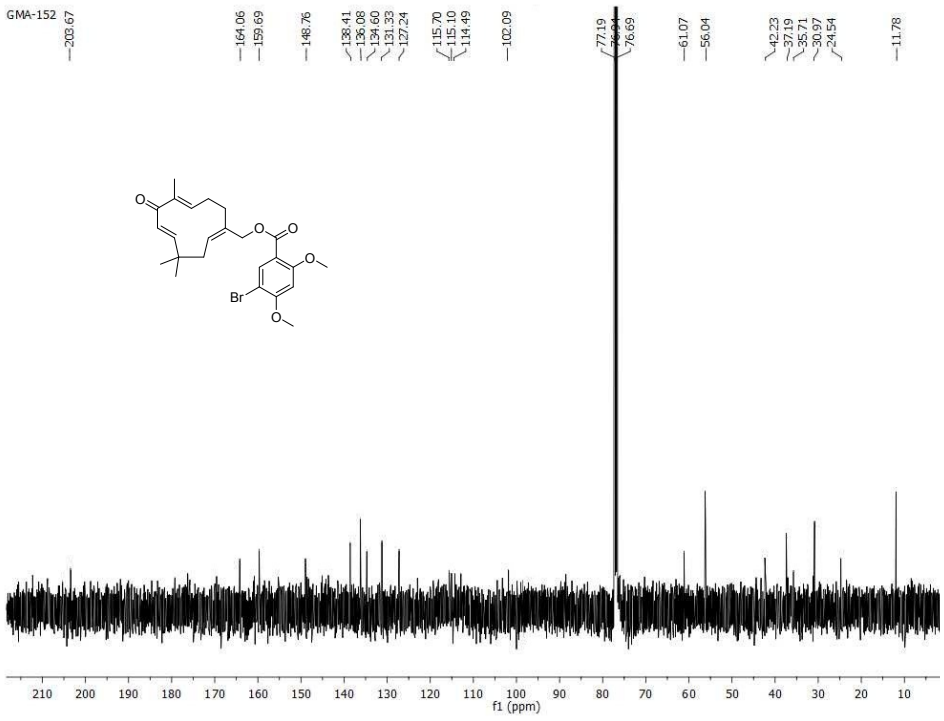
^{1}H NMR of 6d



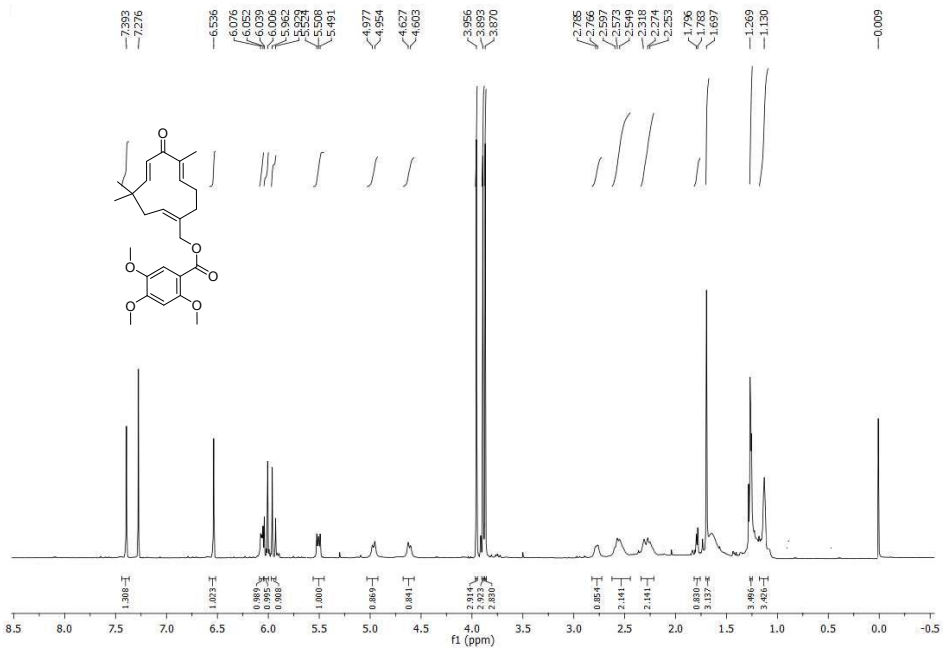
^{13}C NMR of 6d



^{1}H NMR of 6e



^{13}C NMR of 6e



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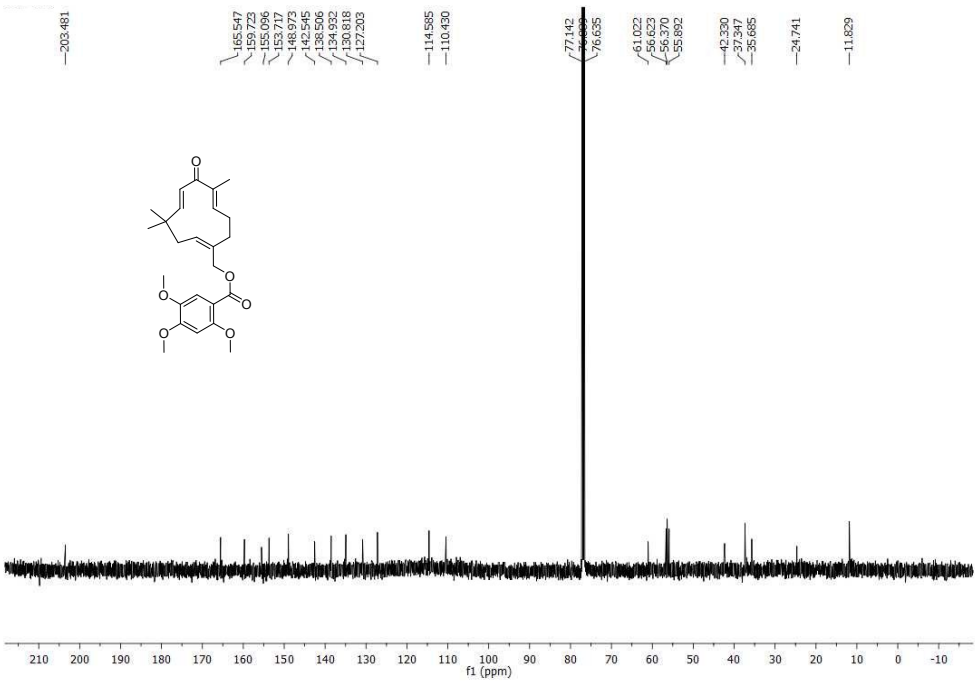

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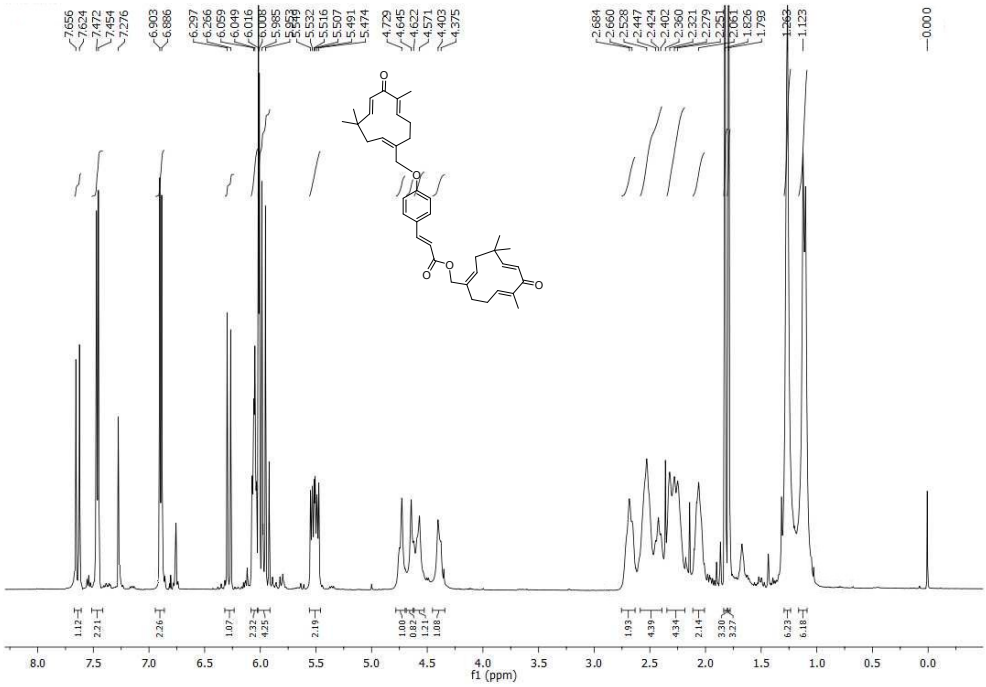
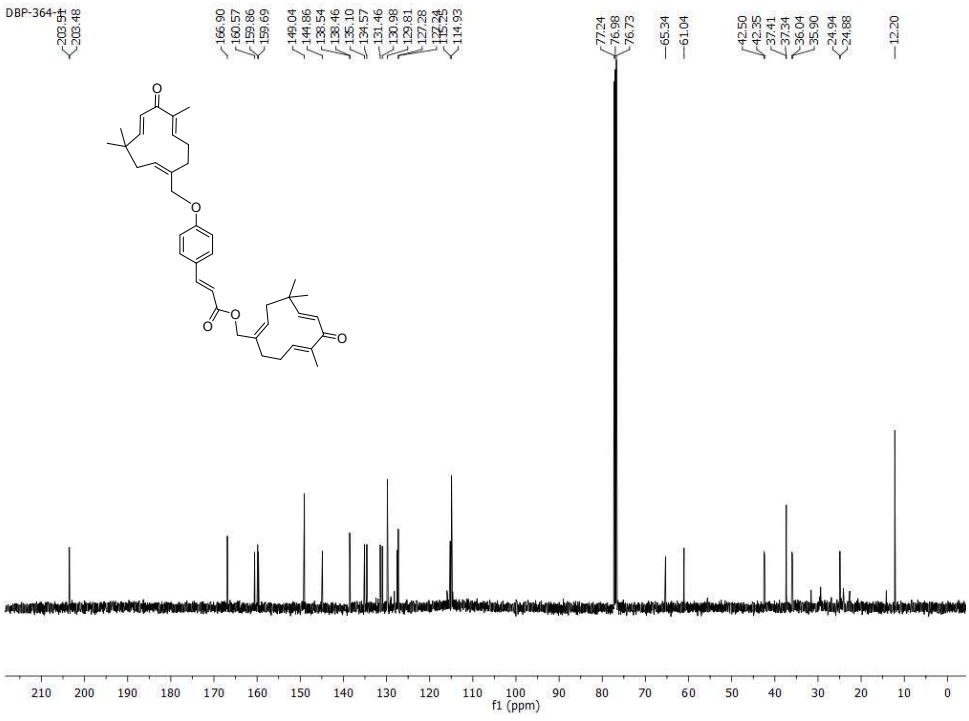
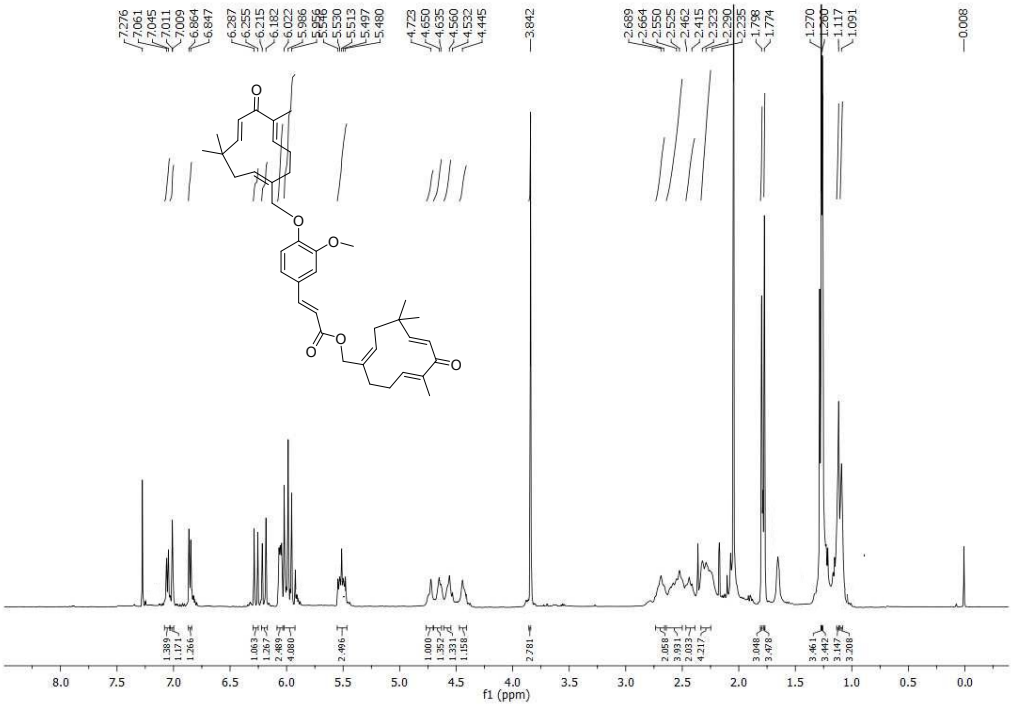


^{1}H NMR of 8a



^{13}C NMR of 8a



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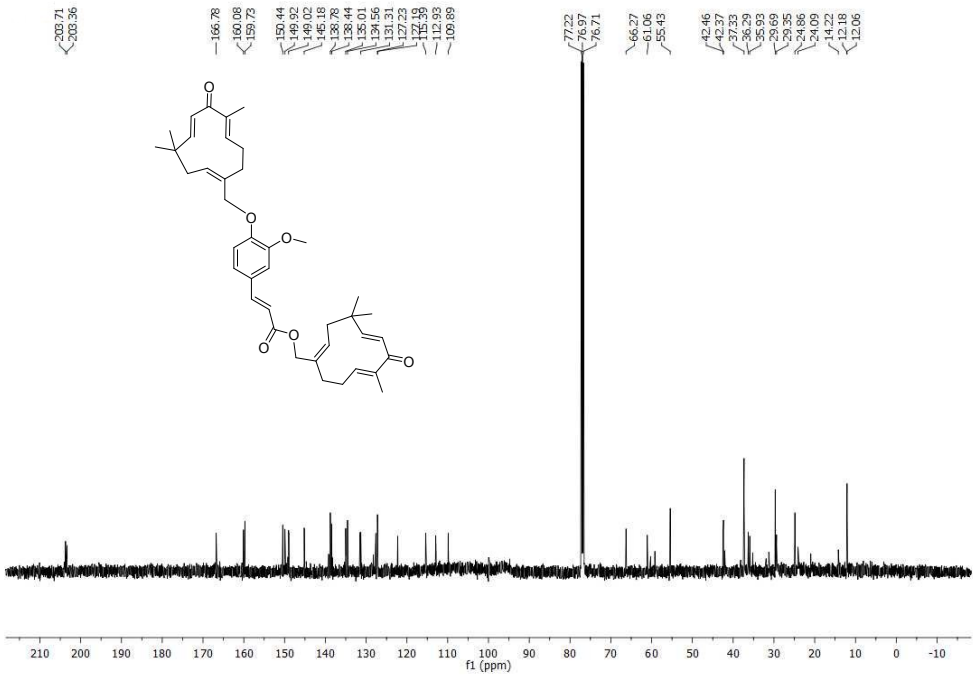
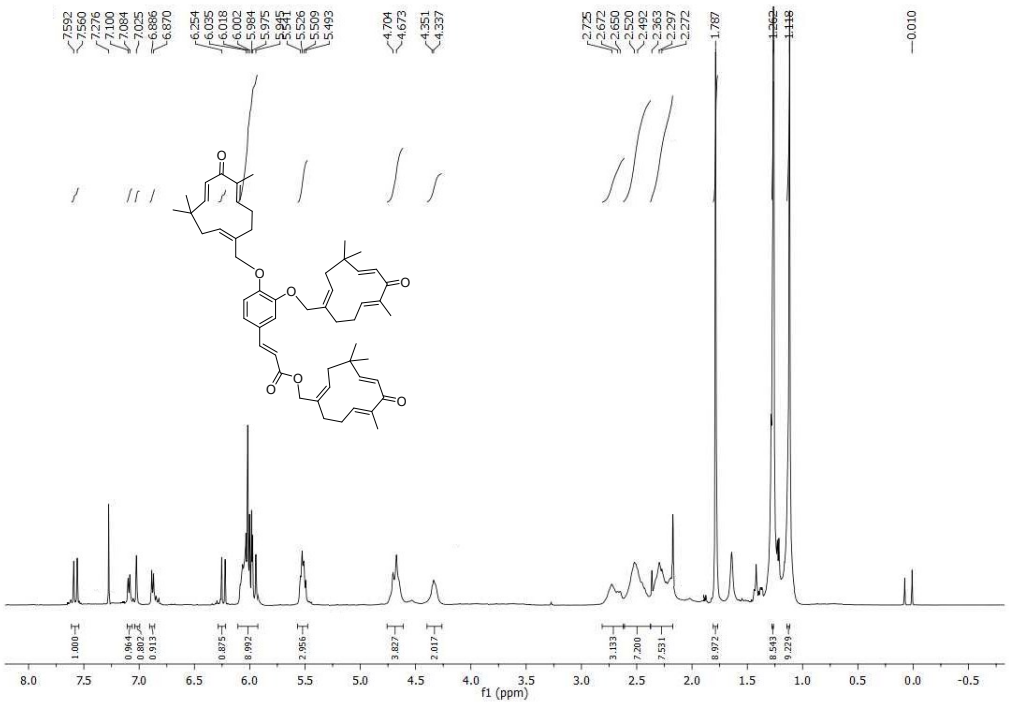
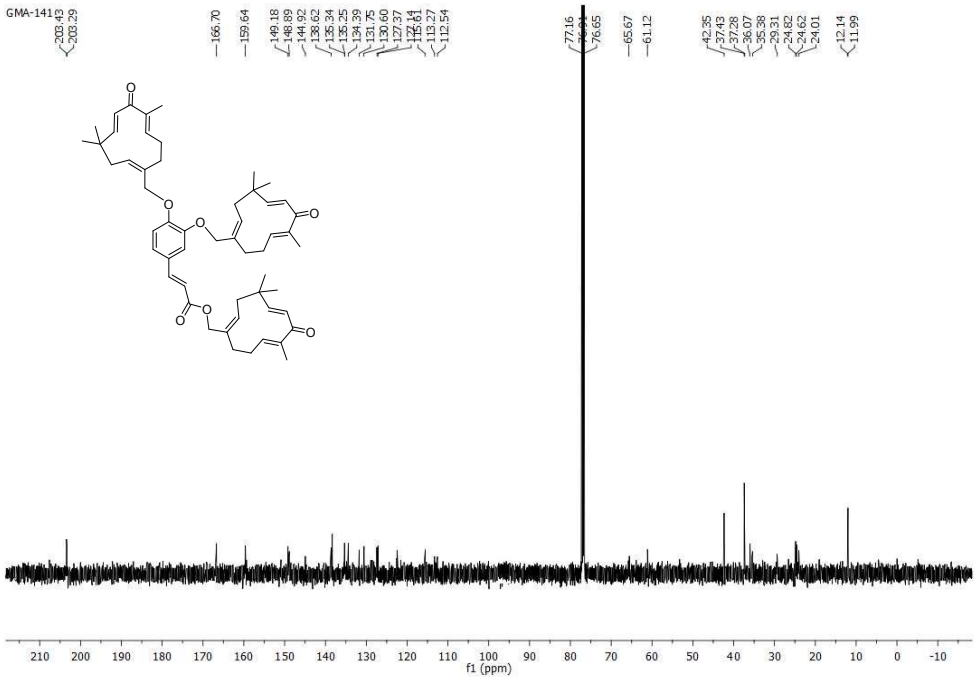


^{13}C NMR of 8b



^{1}H NMR of 8c



^{13}C NMR of 8c

Anti-diabetic assays

1. α-Amylase inhibition assay

α-Amylase inhibition assay was carried out according to Xiao et al.[25] based on the starch-iodine test. The total assay mixture composed of 40 µL 0.02 M sodium phosphate buffer (pH 6.9 containing 6 mM NaCl), 0.02 units of porcine pancreatic amylase solution and compounds / standard at different concentrations were incubated at 37°C for 10 min. Then 40 µL soluble starch (1%, w/v) was added to each reaction well and incubated at 37°C for 15 min. The reaction was stopped by addition of 1 M HCl (20 µL), followed by the addition of 100 µL of iodine reagent (5 mM I_2 and 5 mM KI), which will react with remaining starch. The absorbance was read at 600 nm on a microplate reader. The known α-amylase inhibitor, acarbose, was used a positive control.

2. α-Glucosidase enzyme inhibition assay

The α-glucosidase enzyme inhibition assay was carried out according to the method described by Apostolidis.[26] The enzyme inhibition assay mixture contained 50 µL p-nitrophenyl-α-D-glucopyranoside, different concentrations of compound/standard and the reaction mixture was made up to 2.8 mL with sodium phosphate buffer (pH 6.8; 50 mM). The reaction was initiated by adding 20 µL of α–glucosidase enzyme. The reaction was monitored by increase in absorbance at 405 nm.

3. Antiglycation assay

It was performed according to the methods reported by Matsuura et al. with slight modifications.[23] About 500 µL of albumin (1 mg/mL final concentration) was incubated with 400 µL of glucose (500 mM) in the presence of 100 µL of compound at different concentrations. The reaction was allowed to proceed at 60 °C for 24 h and thereafter reaction was stopped by adding 10µL of 100% TCA. Then the mixture was kept at 4 °C for 10 min before subjected to centrifugation at 10000g. The precipitate was redissolved in 500 µL alkaline PBS (pH10) and immediately quantified for relative amount of glycated BSA based on fluorescence intensity at 370 nm (excitation) and 440 nm (emission).

Table S2 Anti-diabetic assay

Compounds	α-amylase	α-glucosidase	Antiglycation
		IC 50 (µm/mL)	
4a	22.191±0.262	17.923±1.196	28.874±1.704
4b	27.532±1.291	25.723±0.726	27.597±1.895
4c	14.097±1.111	25.573±0.955	24.835±1.275
4d	12.975±0.815	27.839±0.594	32.217±0.346
4e	18.599±0.540	14.061±0.103	22.194±0.798
4f	18.231±1.230	23.754±0.453	29.254±0.302
4g	24.972±0.152	32.952±0.135	28.491±1.149
4h	11.933±1.540	29.591±0.922	25.411±0.208
4i	29.491±0.142	25.363±0.466	15.089±0.187
4j	17.585±1.120	33.215±0.132	29.781±0.222
4k	27.086±0.609	25.804±0.845	32.284±0.829
4l	43.657±1.610	46.940±0.910	46.433±0.067
4l'	19.46±0.098	25.581±0.065	29.281±0.252
4m	19.019±1.185	25.374±0.700	21.257±1.504
4m'	27.939±1.778	41.852±1.306	34.959±1.705
4n	12.504±0.621	26.528±0.585	27.864±0.225
4n'	19.466±1.389	19.573±1.977	25.931±1.547
6b	28.087±0.164	28.691±0.652	34.281±0.567
6c	33.230±0.591	27.090±0.447	30.108±1.293
6d	15.900±0.533	29.917±1.306	18.672±2.771
6e	26.462±1.469	33.766±0.687	35.247±1.982
6f	21.523±0.946	19.912±0.039	34.528±1.754
8a	24.739±1.310	52.180±0.750	47.141±0.033
8b	32.849±1.005	27.948±0.199	36.962±0.626
8c	35.070±1.028	37.563±0.554	62.697±0.080
Zerumbone	51.070±0.254	271.053±0.332	104.86±0.183
Standard	8.5±0.898 **(Acarbose)**	81.3±1.10 **(Acarbose)**	158.23±0.718 **(Ascorbic acid)**

4. MTT assay

The MTT (3-(4, 5-dimethylthiazole-2-yl)-2, 5- diphenyltetrazolium bromide) assay developed by Mosmann was used with slight modifications. In brief, the trypsinized cells from T-25 flask were seeded in each well of 96-well flat- bottomed tissue culture plate at a density of 1x104 cells/well in growth medium and cultured at 37°C in 5% CO2 to adhere. After 48hr incubation, the supernatant was discarded and the cells were pretreated with growth medium and were subsequently mixed with both standard (Paclitaxel) and (compound 4b, 4d, 4k, 4e, 8a, 8b and 8c) to achieve a final volume of 100 µl and then cultured for 24 hr. The compound was prepared as 1.0 mg/ml concentration stock solutions in DMSO. Each well then received 20µl of fresh MTT (5mg/ml in PBS) followed by incubation for 4hr at 37°C. The supernatant growth medium was removed from the wells and replaced with 100 µl of DMSO to solubilize the colored formazan product. After 30 min incubation, the absorbance (OD) of the culture plate was read at a wavelength of 570 nm on a microplate reader (Biotek Synergy 4, VT, USA). The percent cell viability was determined with respect to control, is calculated using formula. % Viability = corrected OD of sample /Control OD * 100 and percentage of inhibition was determined by using formula, % Inhibition = 100-%viability.