Divergent Synthetic Route to New Cyclopenta[*c*]pyran Iridoids: Syntheses of Jatamanin A, F, G, J, Gastrolactone, and Nepetalactone

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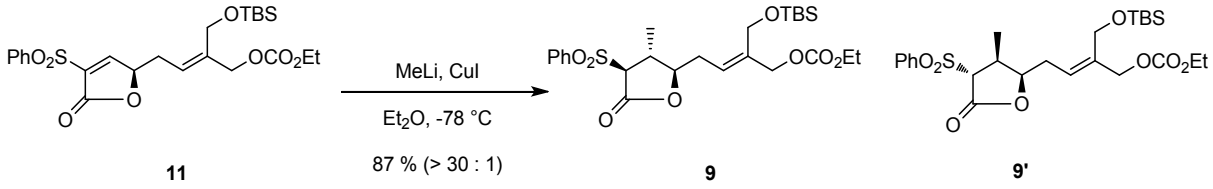
Supporting Information

Table of Contents

1. General Experimental

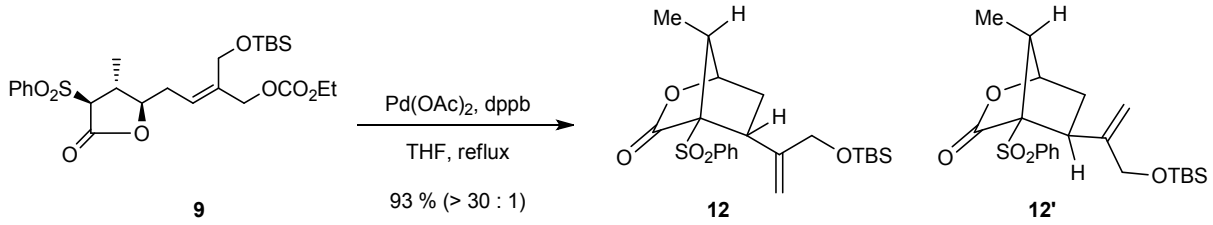
Unless noted otherwise, all starting materials and reagents were obtained from commercial suppliers and were used without further purification. Tetrahydrofuran and Et_2O were distilled from sodium benzophenone ketyl. Dichloromethane, chloroform, triethylamine, acetonitrile and pyridine were freshly distilled from calcium hydride. All solvents used for routine isolation of products and chromatography were reagent grade and glass distilled. Reaction flasks were dried at 100 °C. Air and moisture sensitive reactions were performed under argon atmosphere. Flash column chromatography was performed using silica gel 60 (230-400 mesh, Merck) with the indicated solvents. Thin-layer chromatography was performed using 0.25 mm silica gel plates (Merck). Optical rotations were measured with JASCO P-2000 digital polarimeter at ambient temperature using 100 mm cell of 2 mL capacity. Infrared spectra were recorded on a JASCO FT-IR-4200 spectrometer. Mass spectra were obtained with VG Trio-2 GC-MS instrument. High resolution mass spectra were obtained with JEOL JMS-700 instrument. 1H and 13C NMR spectra were recorded using JEOL JNM-ECA-600, JEOL JNM-LA 300, BRUKER AVANCE-800, BRUKER AVANCE-500, BRUKER AVANCE-400, and Varian Gemini-2000 spectrometer. Chemical shifts were expressed in parts per million (ppm, δ) downfield from tetramethylsilane and were referenced to the deuterated solvent ($CDCl_3$, Acetone-d_6, MeOD). 1H-NMR data were reported in the order of chemical shift, multiplicity (s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet and/or multiple resonances), number of protons, and coupling constant in hertz (Hz).

2. Experimental procedures



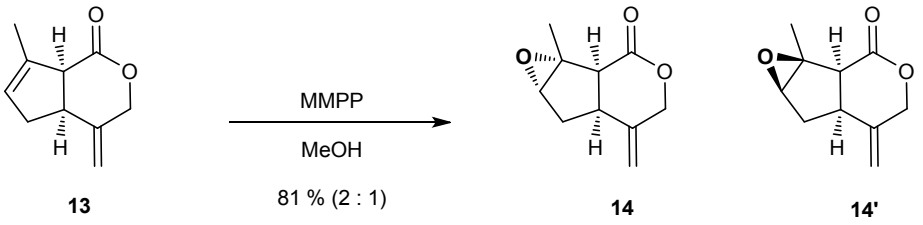
(*Z*)-2-(((tert-butyldimethylsilyl)oxy)methyl)-4-((2*R*,3*S*)-3-methyl-5-oxo-4-(phenylsulfonyl)tetrahydrofuran-2-yl)but-2-en-1-yl ethyl carbonate (9')

$[\alpha]_D^{20}$ 35.3 (c 1.15, MeOH); ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 7.91 (m, 2H), 7.68 (t, *J* = 7.4 Hz, 1H), 7.56 (t, *J* = 8.0 Hz, 2H), 5.56 (t, *J* = 7.2 Hz, 1H), 4.83 (q, *J* = 6.6 Hz, 1H), 4.61 (s, 2H), 4.22 (s, 2H), 4.12 (q, *J* = 7.1 Hz, 2H), 3.71 (d, *J* = 4.0 Hz, 1H), 3.37 (m, 1H), 2.47 (t, *J* = 6.8 Hz, 2H), 1.27 (t, *J* = 7.1 Hz, 3H), 1.20 (d, *J* = 7.3 Hz, 3H), 0.86 (s, 9H), 0.05 (s, 6H); ^{13}C-NMR ($CDCl_3$, 100 MHz) δ 167.1, 154.9, 137.2, 137.0, 134.6, 129.3, 129.2, 124.0, 81.7, 71.8, 69.0, 63.9, 58.8, 34.9, 28.4, 25.8, 25.8, 18.2, 14.4, 14.2, -5.5, -5.6; FT-IR (thin film, neat) ν_{max} 2930, 2885, 1777, 1463, 1323, 1312 cm^{-1}; LR-MS (FAB+) *m/z* 527 (M+H$^+$); HR-MS (FAB+) calcd for $C_{25}H_{39}O_8SSi$ (M+H$^+$) 527.2135; found 527.2143.



(1*R*,4*S*,5*S*,7*R*)-5-(3-((tert-butyldimethylsilyl)oxy)prop-1-en-2-yl)-7-methyl-4-(phenylsulfonyl)-2-oxabicyclo[2.2.1]heptan-3-one (12')

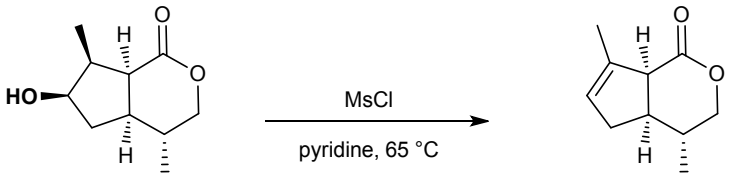
$[\alpha]_D^{20}$ -7.0 (c 0.45, MeOH); ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 8.18 (m, 2H), 7.61 (t, *J* = 7.5 Hz, 1H), 7.48 (t, *J* = 8.0 Hz, 2H), 5.22 (s, 1H), 4.83 (s, 1H), 4.59 (s, 1H), 4.08 (dd, *J* = 13.5 Hz, 32.2 Hz, 2H), 3.22 (q, *J* = 6.6 Hz, 1H), 2.68 (t, *J* = 7.2 Hz, 1H), 2.27 (d, *J* = 7.2 Hz, 2H), 1.42 (d, *J* = 6.6 Hz, 3H), 0.87 (s, 9H), 0.04 (s, 6H); ^{13}C-NMR ($CDCl_3$, 100 MHz) δ 170.3, 144.3, 138.1, 134.1, 130.5, 128.3, 117.4, 110.0, 82.7, 78.9, 65.5, 48.4, 44.3, 38.2, 25.8, 18.2, 11.5; FT-IR (thin film, neat) ν_{max} 2954, 2856, 1789, 1472, 1448, 1323 cm^{-1}; LR-MS (FAB+) *m/z* 437 (M+H$^+$); HR-MS (FAB+) calcd for $C_{22}H_{33}O_5SSi$ (M+H$^+$) 437.1818; found 437.1809.



13 14 14'

(1a*S*,1b*S*,5a*S*,6a*R*)-1a-methyl-5-methylenehexahydrooxireno[2',3':4,5]cyclopenta[1,2-c]pyran-2(1aH)-one (14').

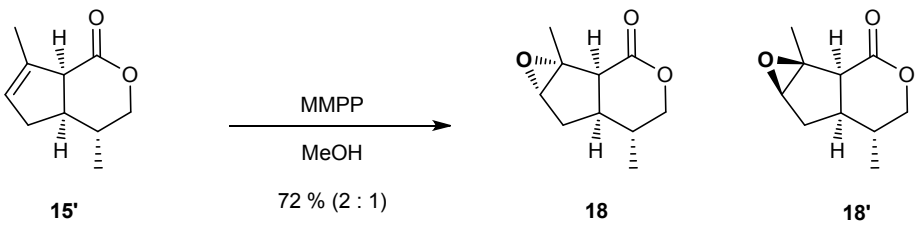
$[\alpha]_D^{20}$ -16.1 (c 0.12, MeOH); ^{1}H-NMR ($CDCl_3$, 500 MHz) δ 5.18 (d, *J* = 12.1 Hz, 1H), 5.04 (s, 1H), 4.99 (s, 1H), 4.41 (d, *J* = 12.0 Hz, 1H), 3.34 (s, 1H), 3.22 (t, *J* = 9.9 Hz, 1H), 3.06 (d, *J* = 9.9 Hz, 1H), 2.41 (dd, *J* = 14.9, 10.3 Hz, 1H), 2.04 (m, 1H), 1.58 (s, 3H); ^{13}C-NMR ($CDCl_3$, 75 MHz) δ 170.3, 142.7, 113.8, 71.2, 68.7, 63.5, 49.0, 38.8, 36.6, 16.5; FT-IR (thin film, neat) ν_{max} 3438, 2930, 1730, 1461, 1380, 1315 cm^{-1}; LR-MS (FAB+) *m/z* 181 (M+H$^+$); HR-MS (FAB+) calcd for $C_{10}H_{13}O_3$ (M+H$^+$) 181.0865; found 181.0867.



15 15'

(4*R*,4a*R*,7a*S*)-4,7-dimethyl-4,4a,5,7a-tetrahydrocyclopenta[c]pyran-1(3H)-one (15')

$[\alpha]_D^{20}$ -49.8 (c 0.09, MeOH); ^{1}H-NMR ($CDCl_3$, 600 MHz) δ 5.51 (s, 1H), 4.08 (t, *J* = 11.0 Hz, 1H), 4.01 (dq, *J* = 5.5 Hz, 3.7 Hz, 2.3 Hz, 1H), 3.49 (d, *J* = 9.6 Hz, 1H), 2.82 (m, 1H), 2.33 (m, 3H), 1.79 (s, 3H), 0.93 (d, *J* = 6.8 Hz, 3H); ^{13}C-NMR ($CDCl_3$, 150 MHz) δ 170.8, 136.8, 128.1, 69.9, 54.6, 39.4, 31.8, 31.3, 15.2, 13.6 ; FT-IR (thin film, neat) ν_{max} 3726, 2965, 2922, 1731, 1476, 1380 cm^{-1}; LR-MS (FAB+) *m/z* 167 (M+H$^+$); HR-MS (FAB+) calcd for $C_{10}H_{15}O_2$ (M+H$^+$) 167.1072; found 167.1070.

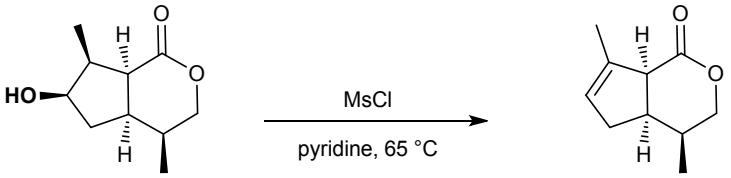


15' 18 18'

(1aS,1bS,5R,5aR,6aR)-1a,5-dimethylhexahydrooxireno[2',3':4,5]cyclopenta[1,2-

c]pyran-2(1aH)-one (18')

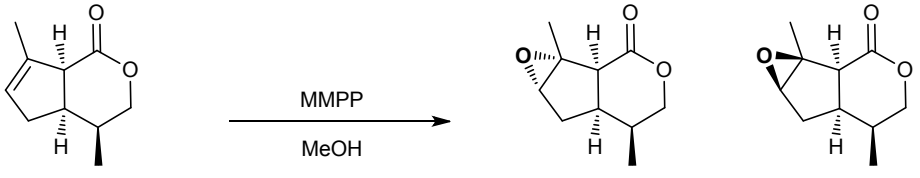
$[\alpha]_D^{20}$ 6.7 (c 0.4, MeOH); ^{1}H-NMR ($CDCl_3$, 600 MHz) δ 4.24 (t, *J* = 10.7 Hz, 1H), 3.90 (dq, *J* = 10.7, 3.6, 1.9 Hz, 1H), 3.34 (d, *J* = 2.3 Hz, 1H), 3.07 (d, *J* = 11.0 Hz, 1H), 2.91 (m, 1H), 2.07 (m, 1H), 1.99 (m, 1H), 1.92 (dd, *J* = 15.6, 5.5 Hz, 1H), 1.57 (s, 3H), 0.86 (d, *J* = 7.3 Hz, 3H); ^{13}C-NMR ($CDCl_3$, 150 MHz) δ 170.4, 70.4, 69.7, 65.5, 49.1, 40.8, 30.9, 27.9, 17.2, 13.3; FT-IR (thin film, neat) ν_{max} 3439, 2962, 2930, 1728, 1468, 1380 cm^{-1}; LR-MS (FAB+) *m/z* 183 (M+H$^+$); HR-MS (FAB+) calcd for $C_{10}H_{15}O_3$ (M+H$^+$) 183.1021; found 183.1021.



16 16'

(4*S*,4a*R*,7a*S*)-4,7-dimethyl-4,4a,5,7a-tetrahydrocyclopenta[c]pyran-1(3H)-one (16')

$[\alpha]_D^{20}$ -3.5 (c 0.18, MeOH); ^{1}H-NMR ($CDCl_3$, 600 MHz) δ 5.48 (s, 1H), 4.22 (dd, *J* = 11.0, 3.2 Hz, 1H), 3.93 (dd, *J* = 11.0, 7.8 Hz, 1H), 3.41 (d, *J* = 10.1 Hz, 1H), 2.65 (m, 1H), 2.43 (m, 1H), 2.10 (m, 1H), 1.84 (s, 3H), 1.76 (m, 1H), 1.03 (d, *J* = 6.9 Hz, 3H); ^{13}C-NMR ($CDCl_3$, 150 MHz) δ 171.8, 136.8, 127.2, 71.9, 52.0, 42.6, 38.2, 34.6, 16.2, 15.8 ; FT-IR (thin film, neat) ν_{max} 3371, 2966, 2930, 2350, 1714, 1404, 1321cm^{-1}; LR-MS (FAB+) *m/z* 167 (M+H$^+$); HR-MS (FAB+) calcd for $C_{10}H_{15}O_2$ (M+H$^+$) 167.1072; found 167.1073.



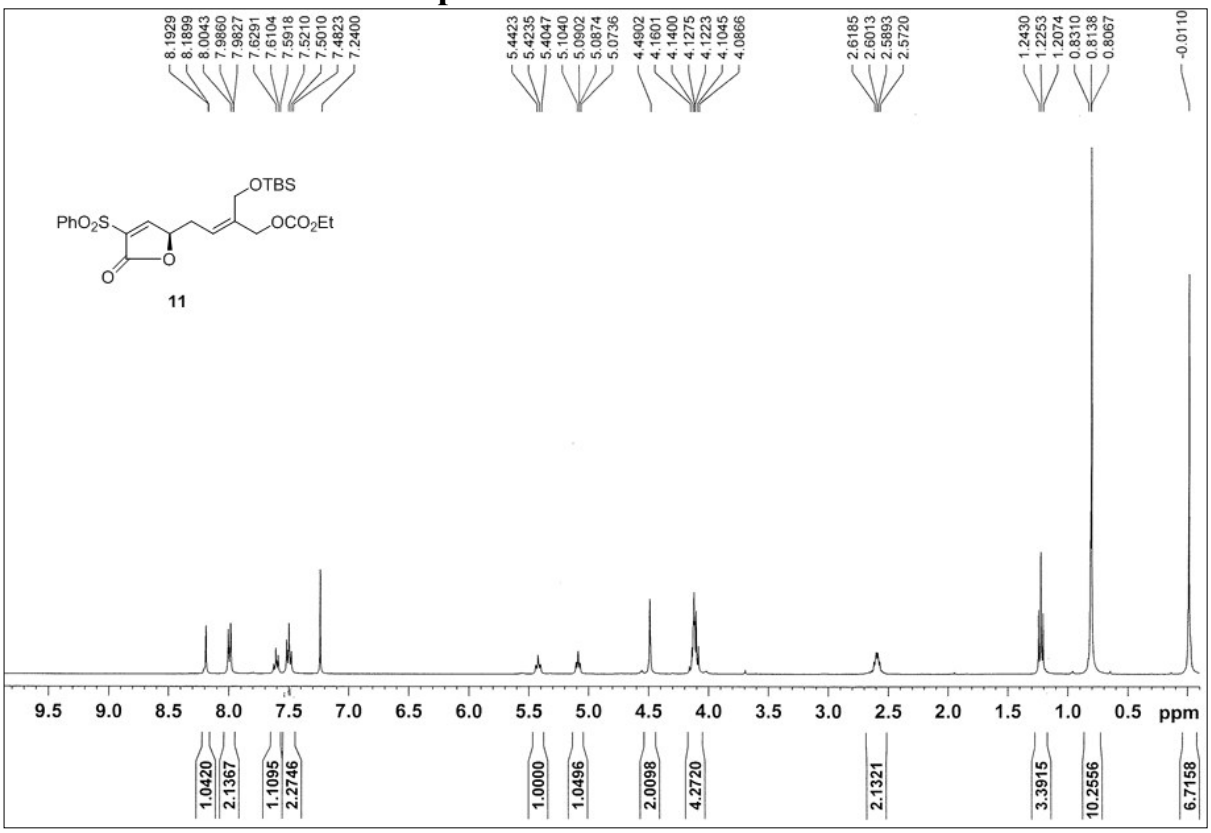
16' 19 19'

(1a*S*,1b*S*,5*S*,5a*R*,6a*R*)-1a,5-dimethylhexahydrooxireno[2',3':4,5]cyclopenta[1,2-c]pyran-2(1aH)-one (19')

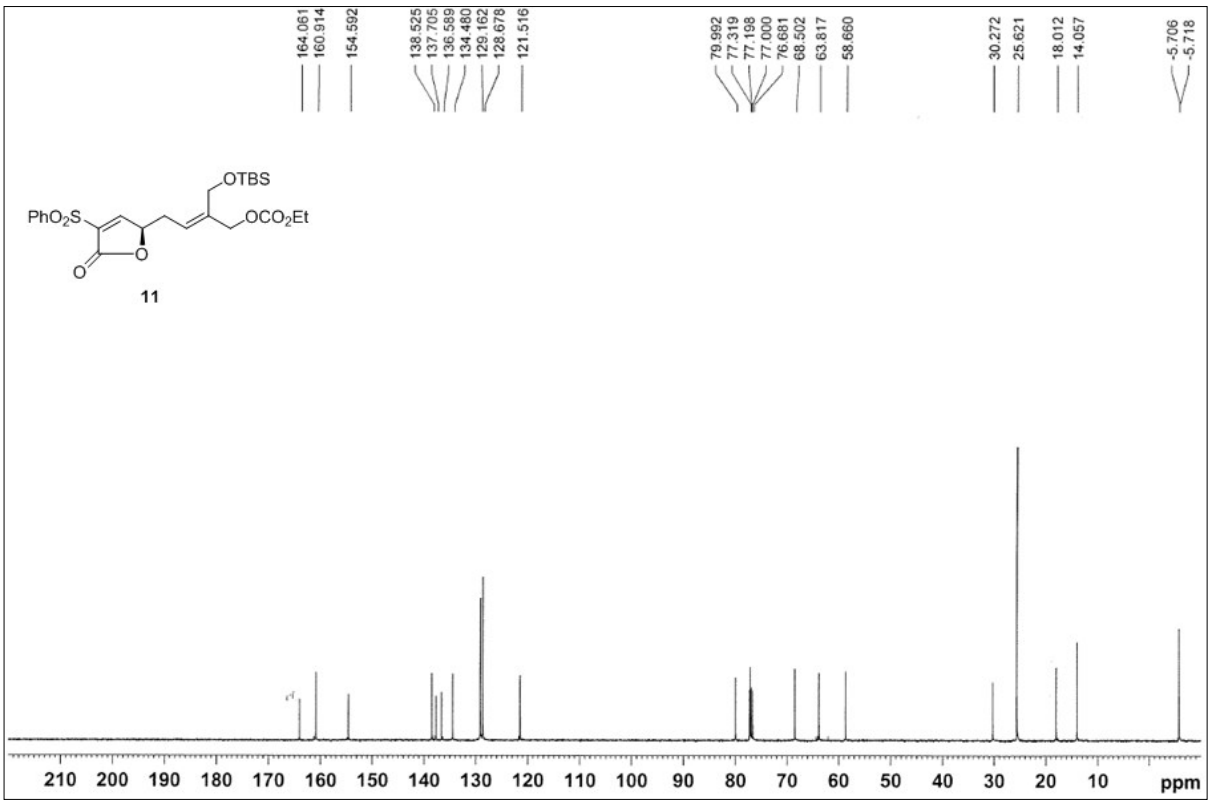
$[\alpha]_D^{20}$ -3.5 (c 0.13, MeOH); ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 4.20 (dd, *J* = 11.1, 3.8 Hz, 1H), 3.74 (t, *J* = 11.0 Hz, 1H), 3.29 (s, 1H), 2.93 (d, *J* = 9.0, 1H), 2.01 (m, 3H), 1.89 (m, 1H), 1.65 (s, 3H), 0.84 (d, *J* = 6.6 Hz, 3H); ^{13}C-NMR ($CDCl_3$, 125 MHz) δ 170.5, 74.0, 68.0, 64.1, 46.8, 41.7, 33.6, 30.4, 17.5, 14.8; FT-IR (thin film, neat) ν_{max} 3596, 2930, 1733, 1458, 1380 cm^{-1};

LR-MS (FAB+) *m/z* 183 ($M+H^+$); HR-MS (FAB+) calcd for $C_{10}H_{15}O_3$ ($M+H^+$) 183.1021; found 183.1018.

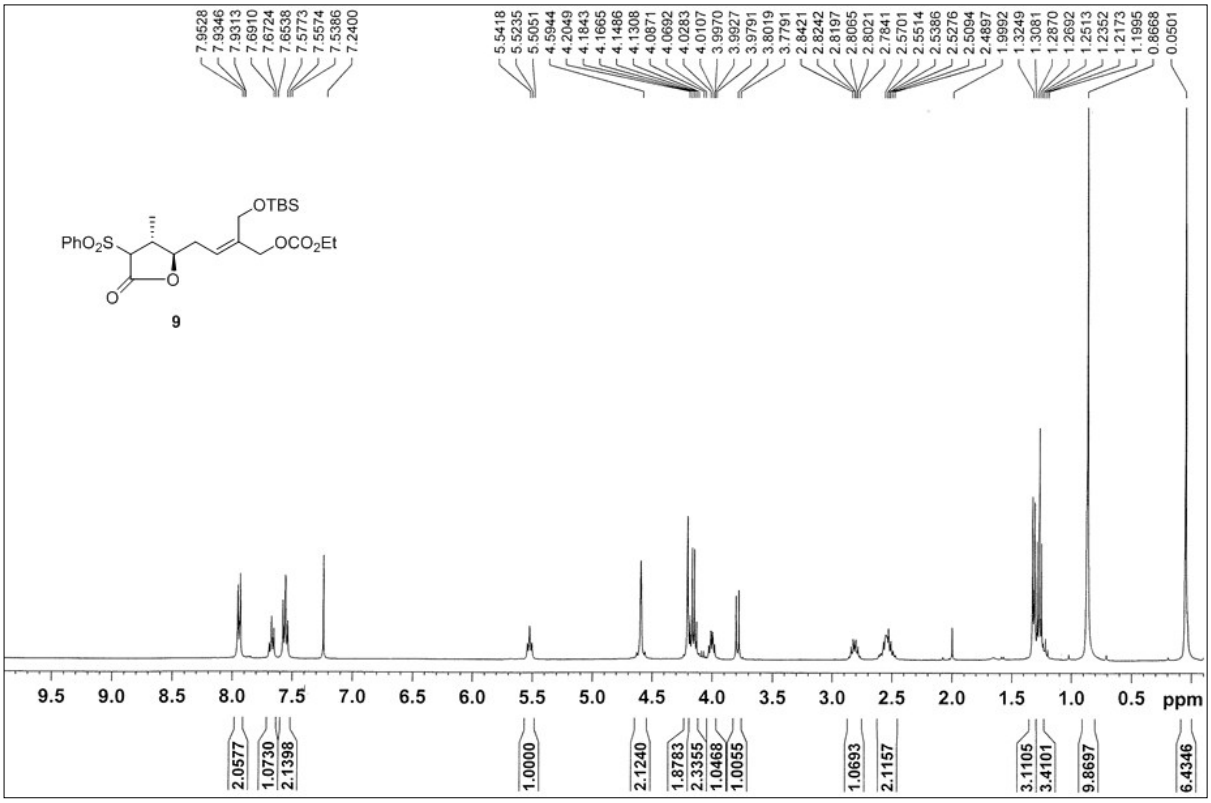
3. ^{1}H-NMR and ^{13}C-NMR Spectra



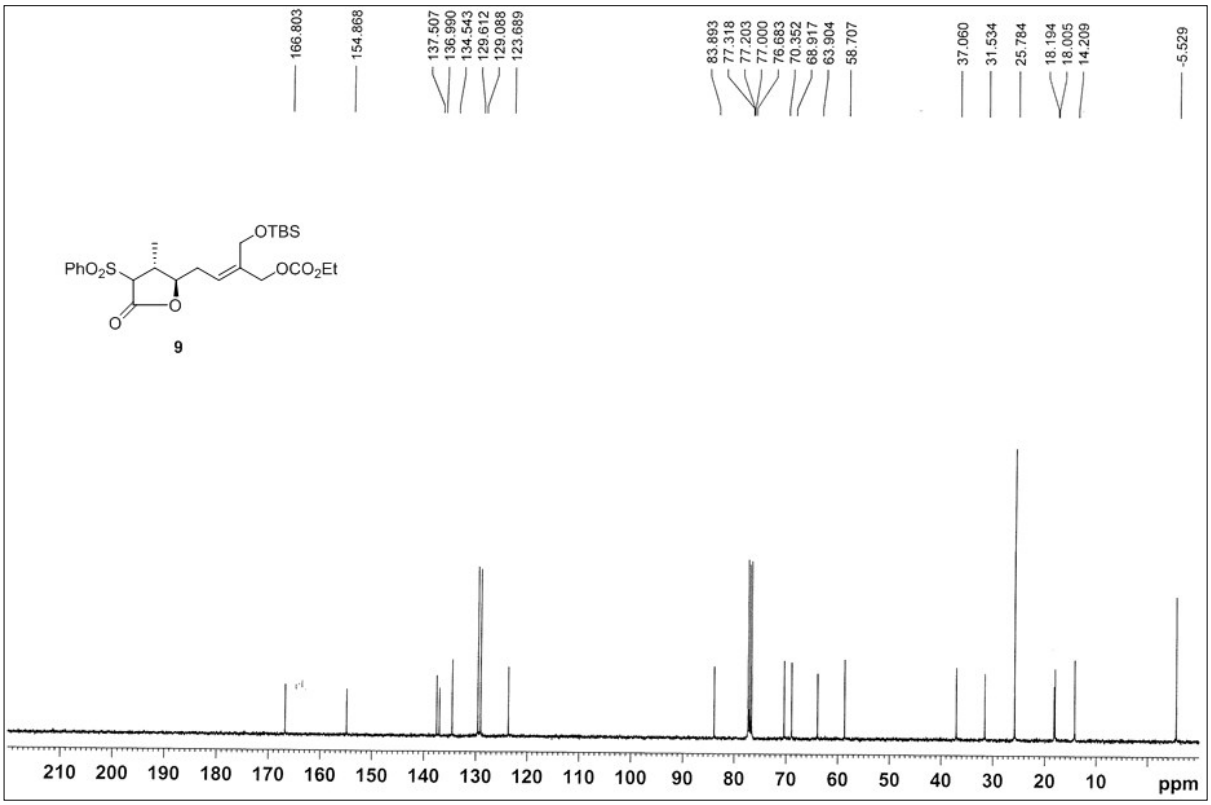
▲ ^{1}H-NMR (400 MHz, $CDCl_3$)



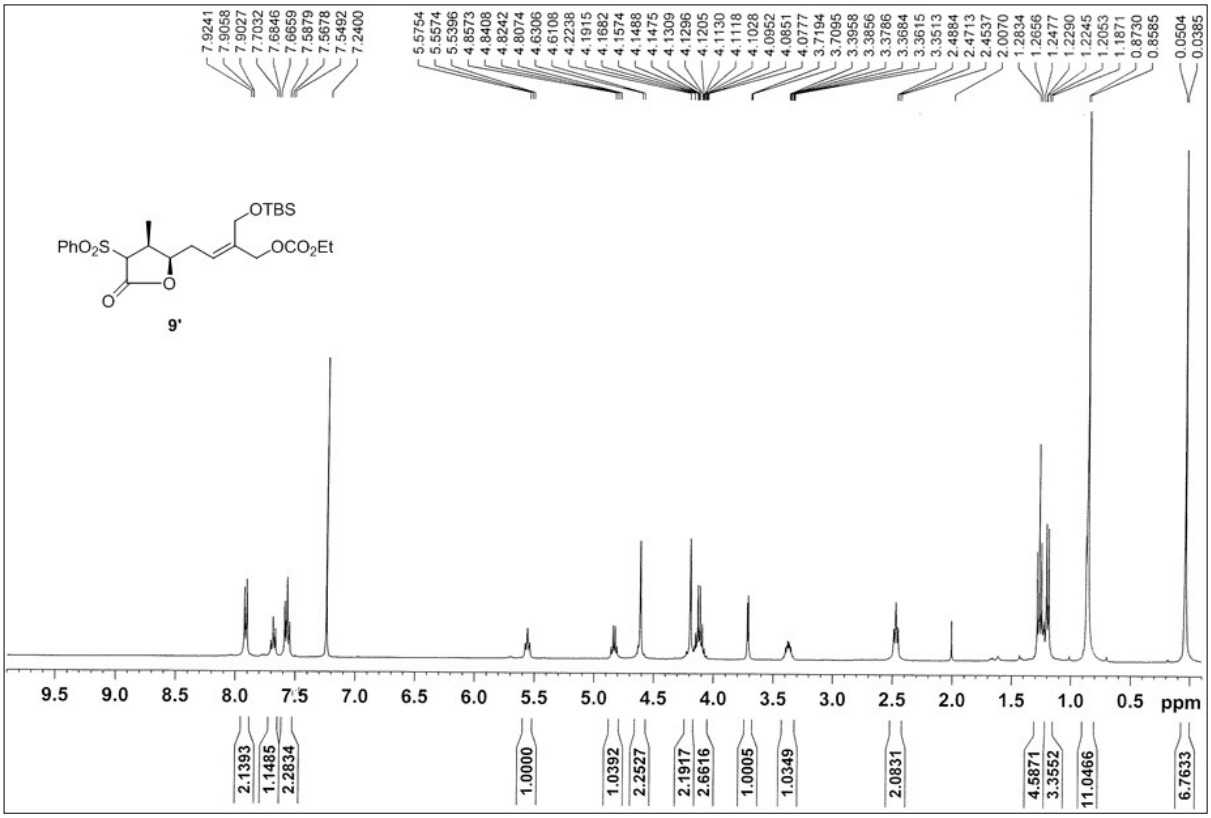
▲ ^{13}C-NMR (100 MHz, $CDCl_3$)



▲ ^{1}H-NMR (400 MHz, $CDCl_3$)



▲ ^{13}C-NMR (100 MHz, $CDCl_3$)



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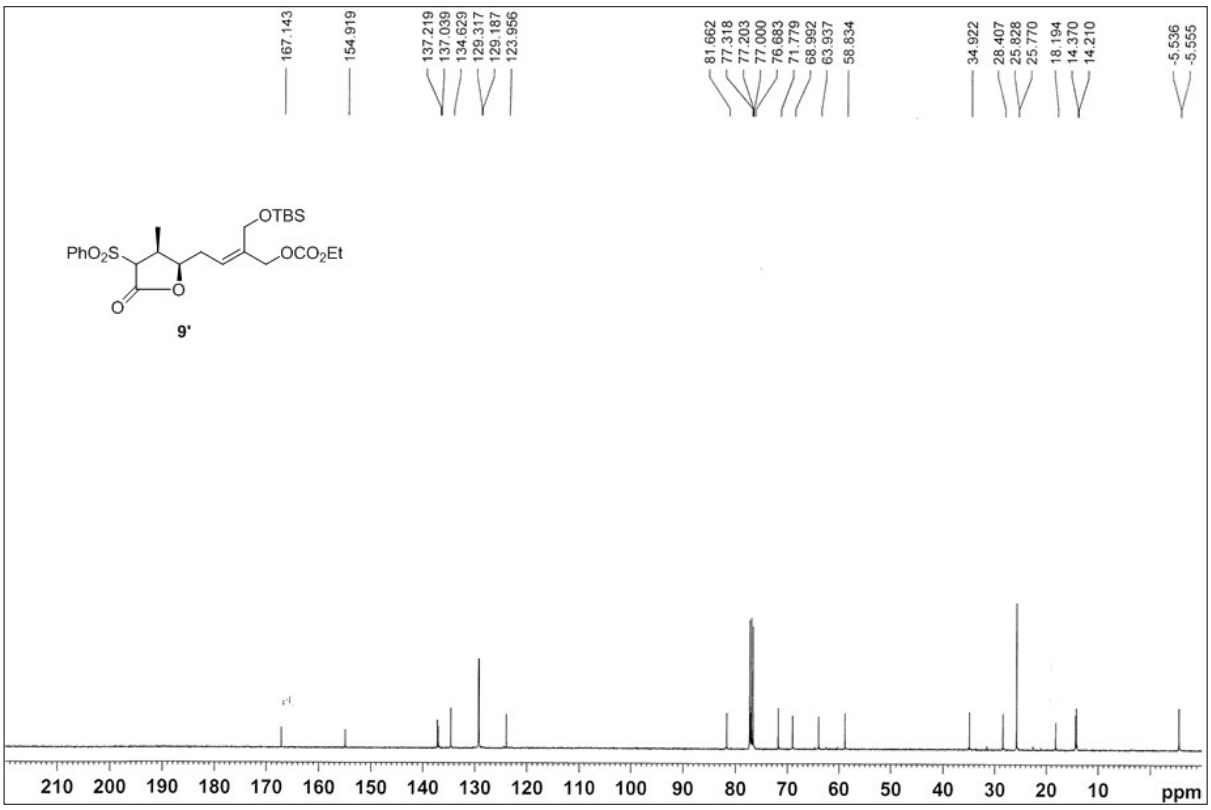

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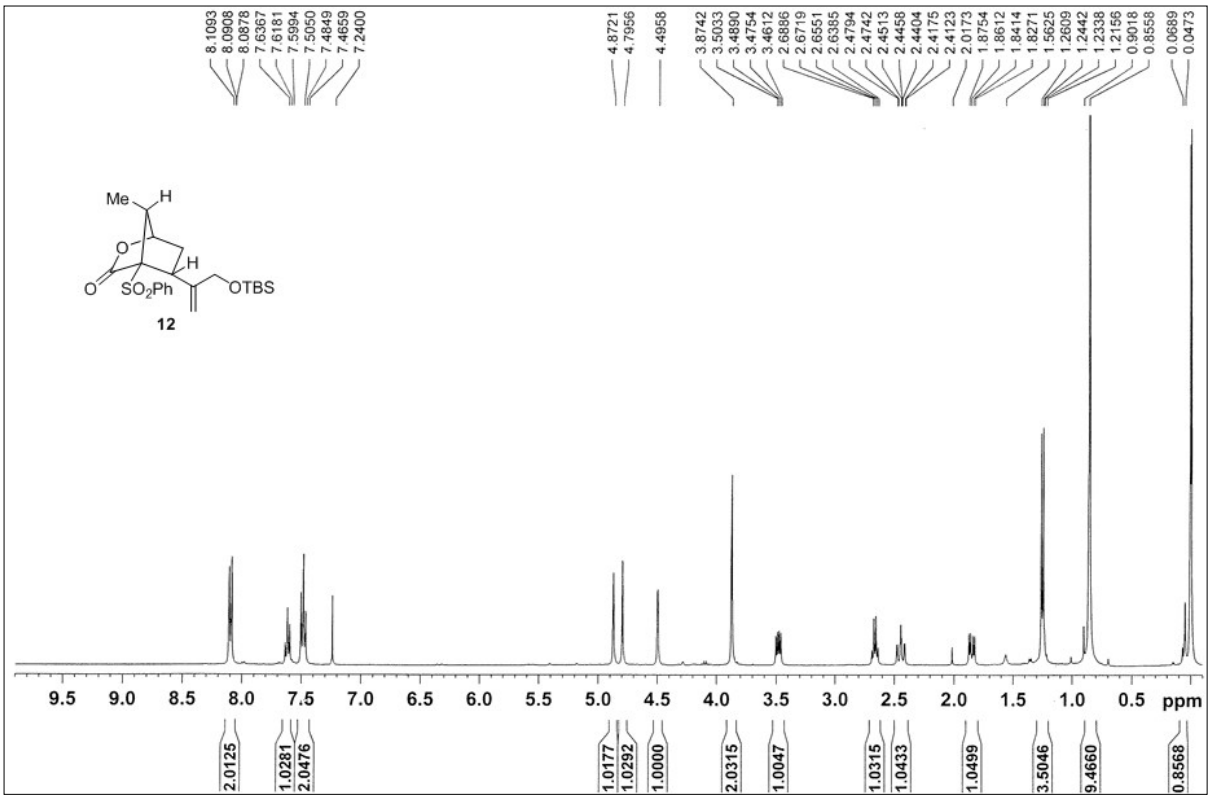

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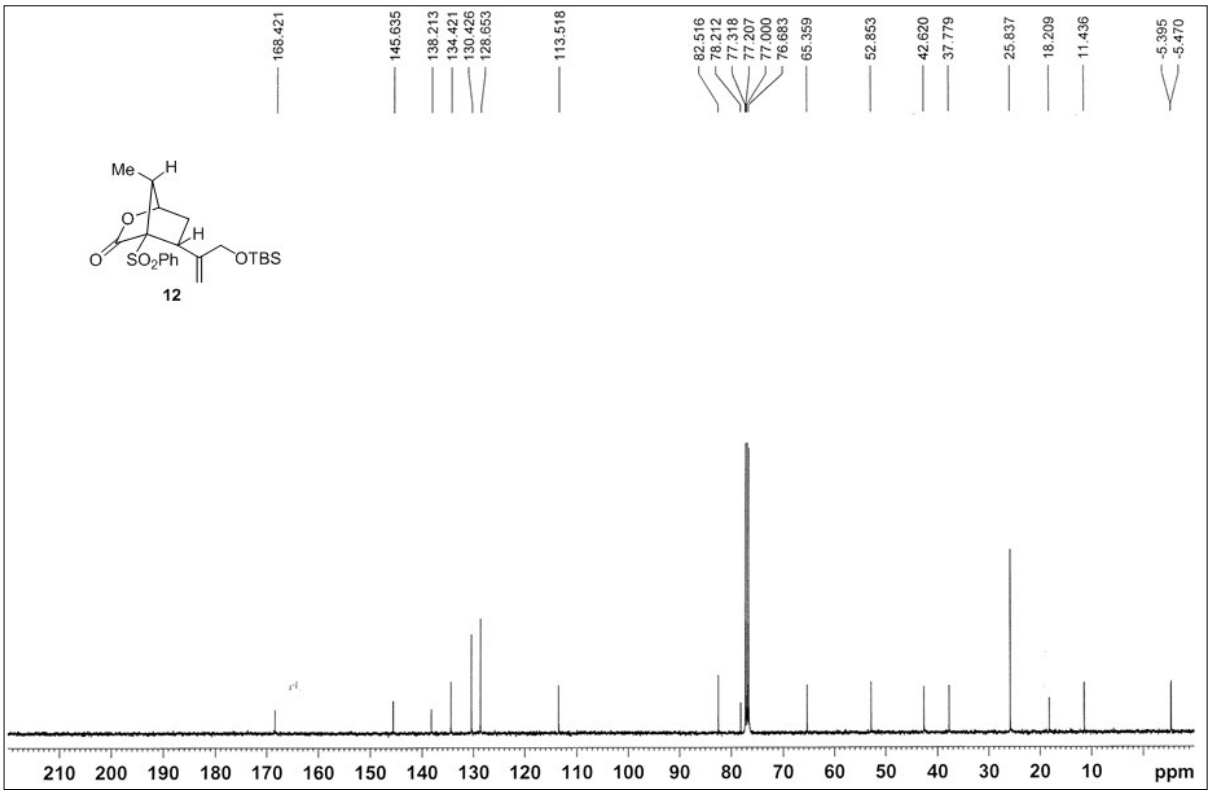
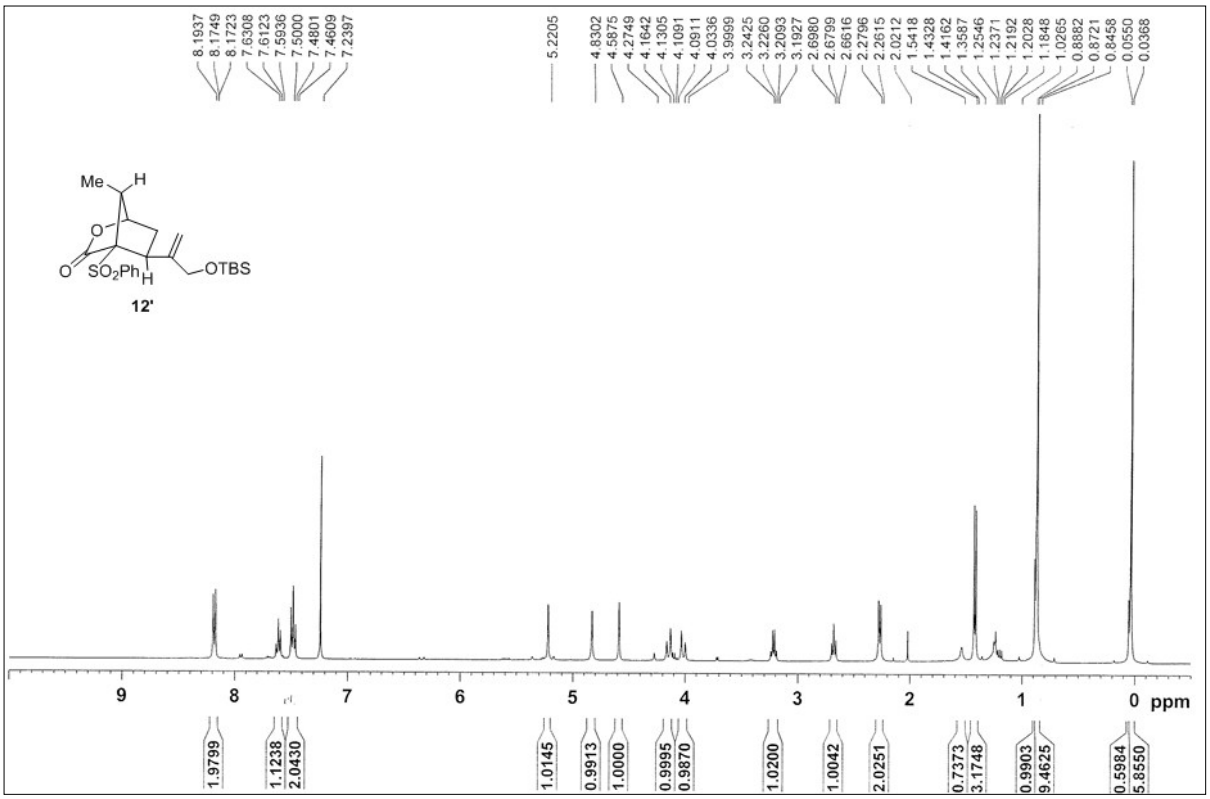
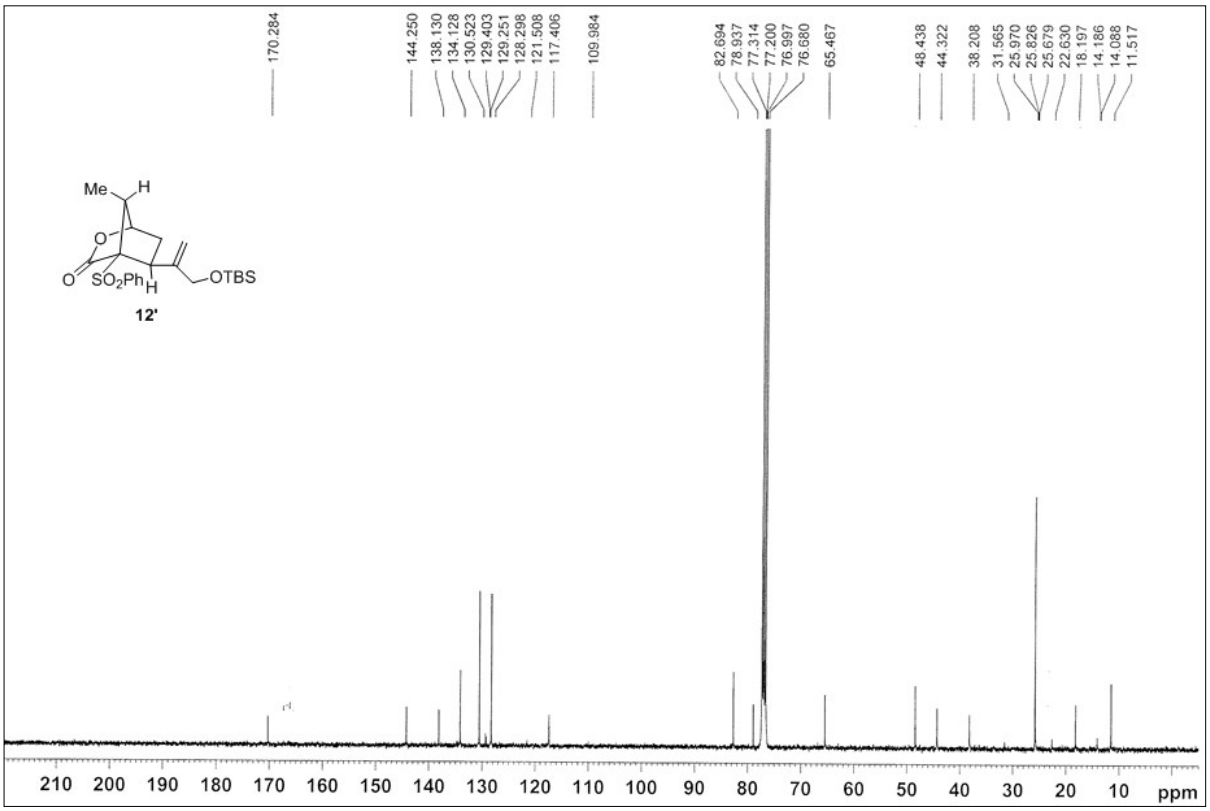


▲ ^{13}C-NMR (100 MHz, $CDCl_3$)



▲ ^{1}H-NMR (400 MHz, $CDCl_3$)



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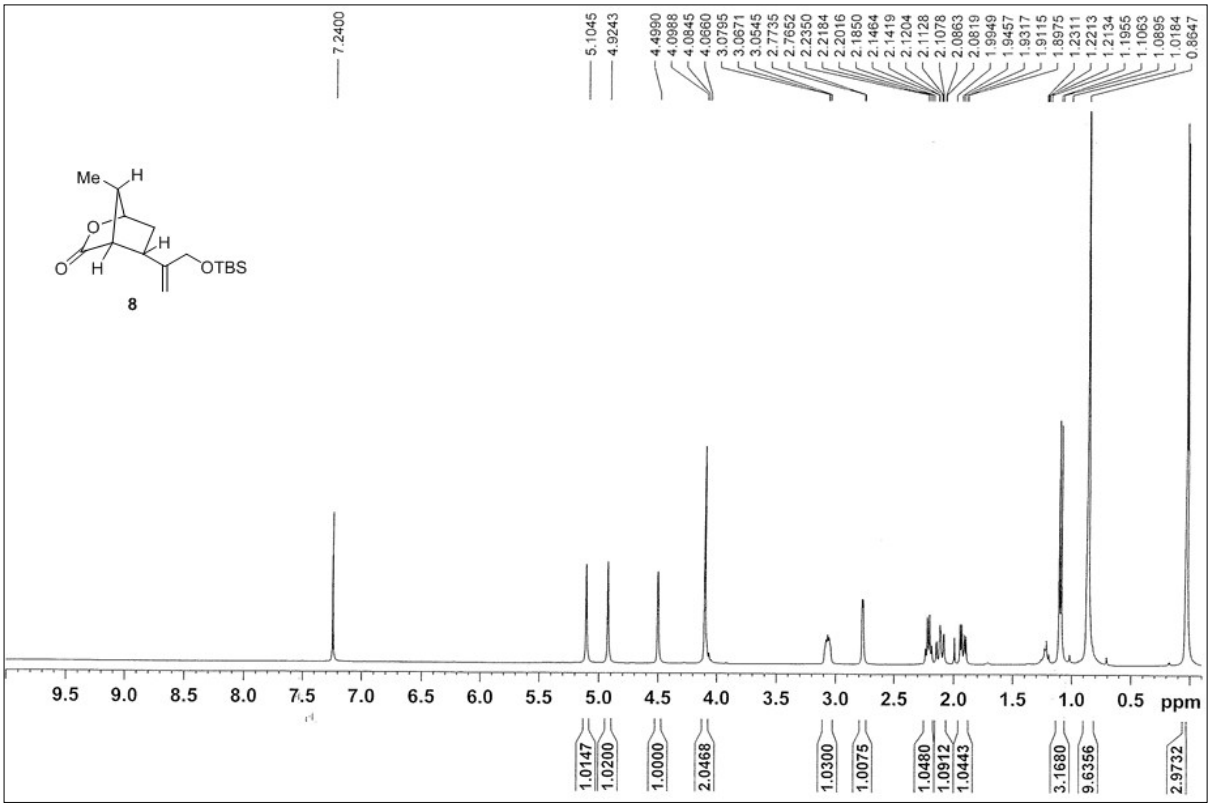

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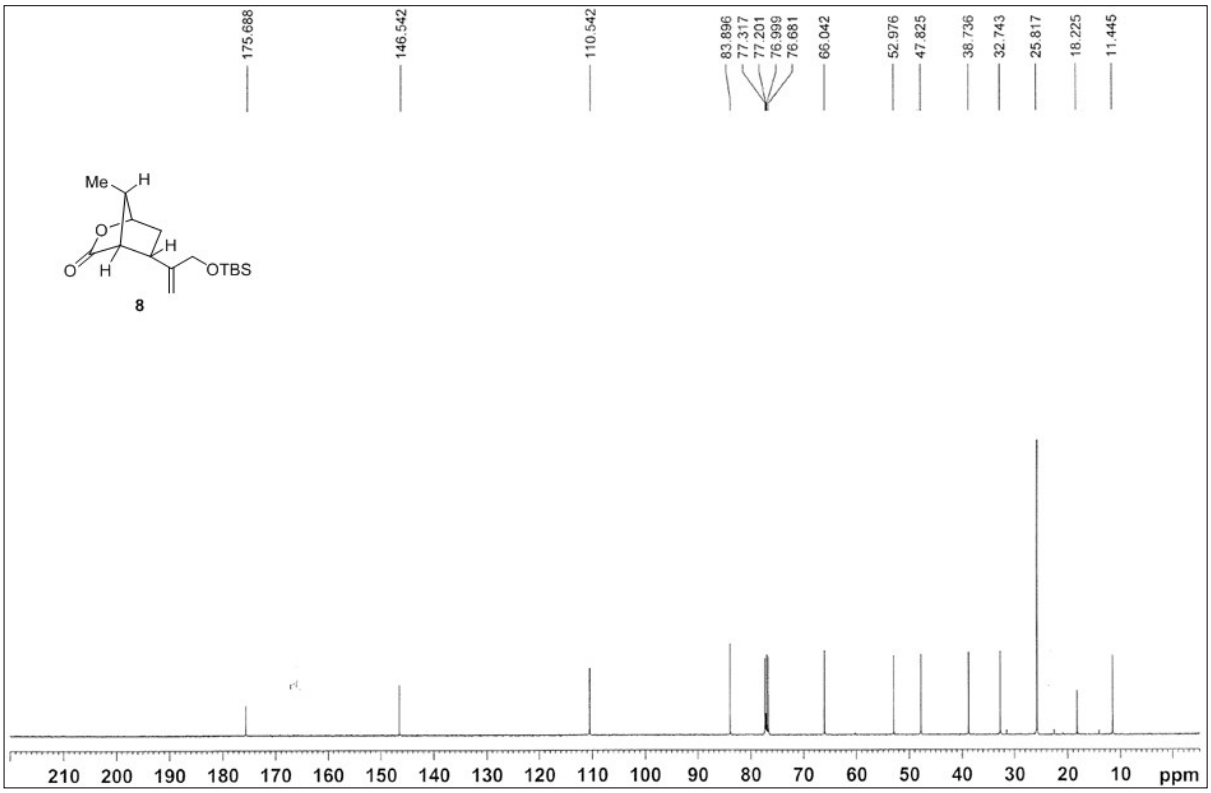
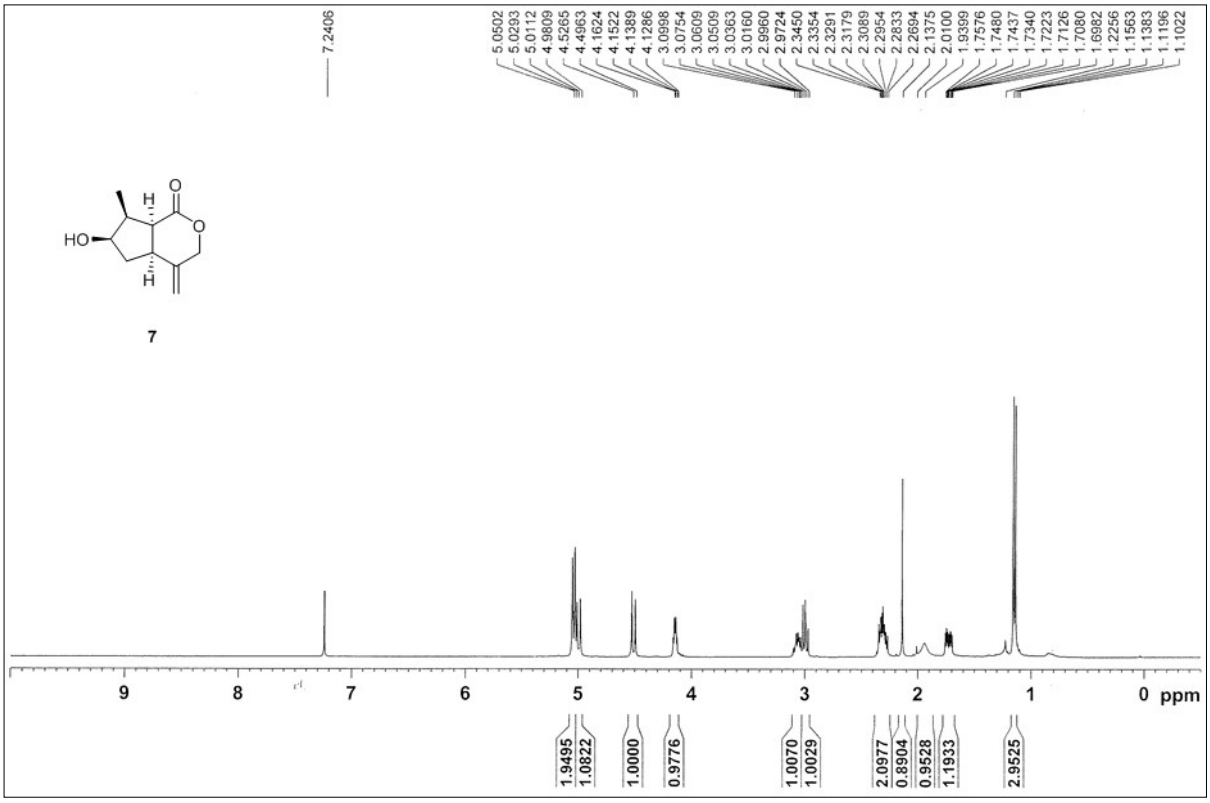
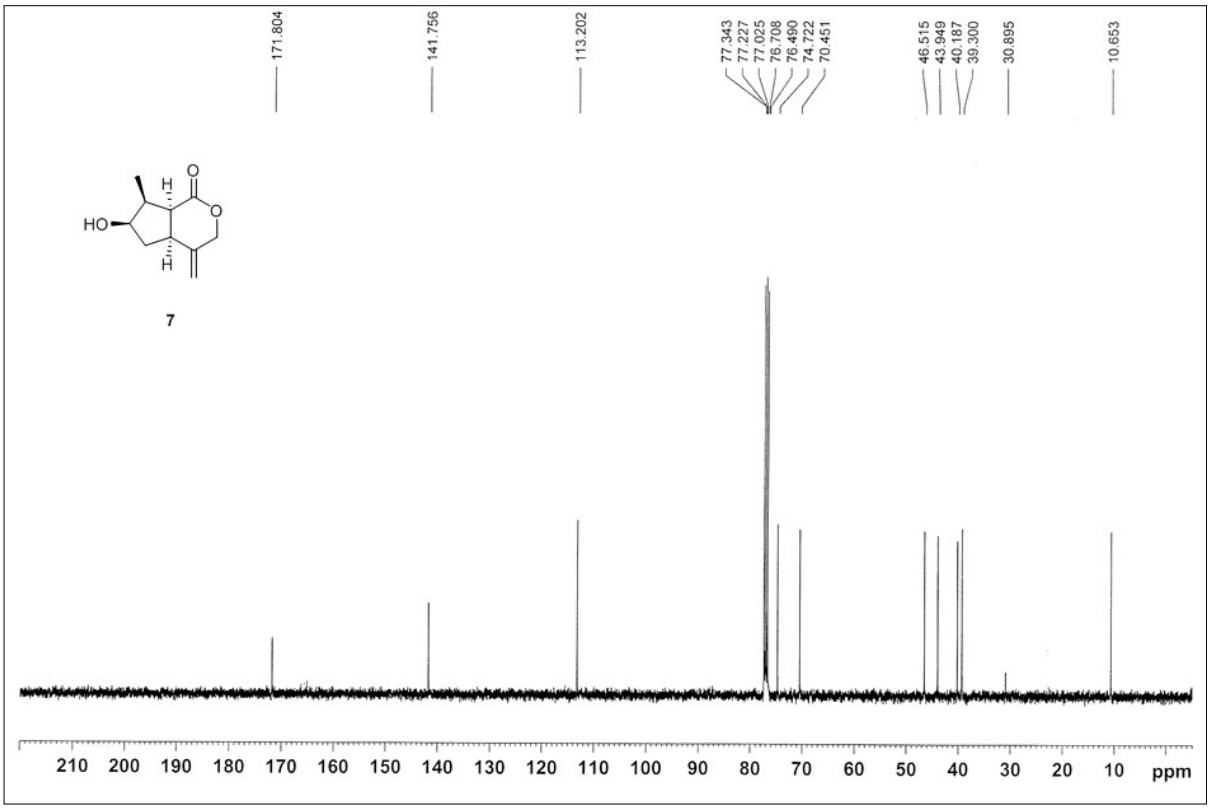


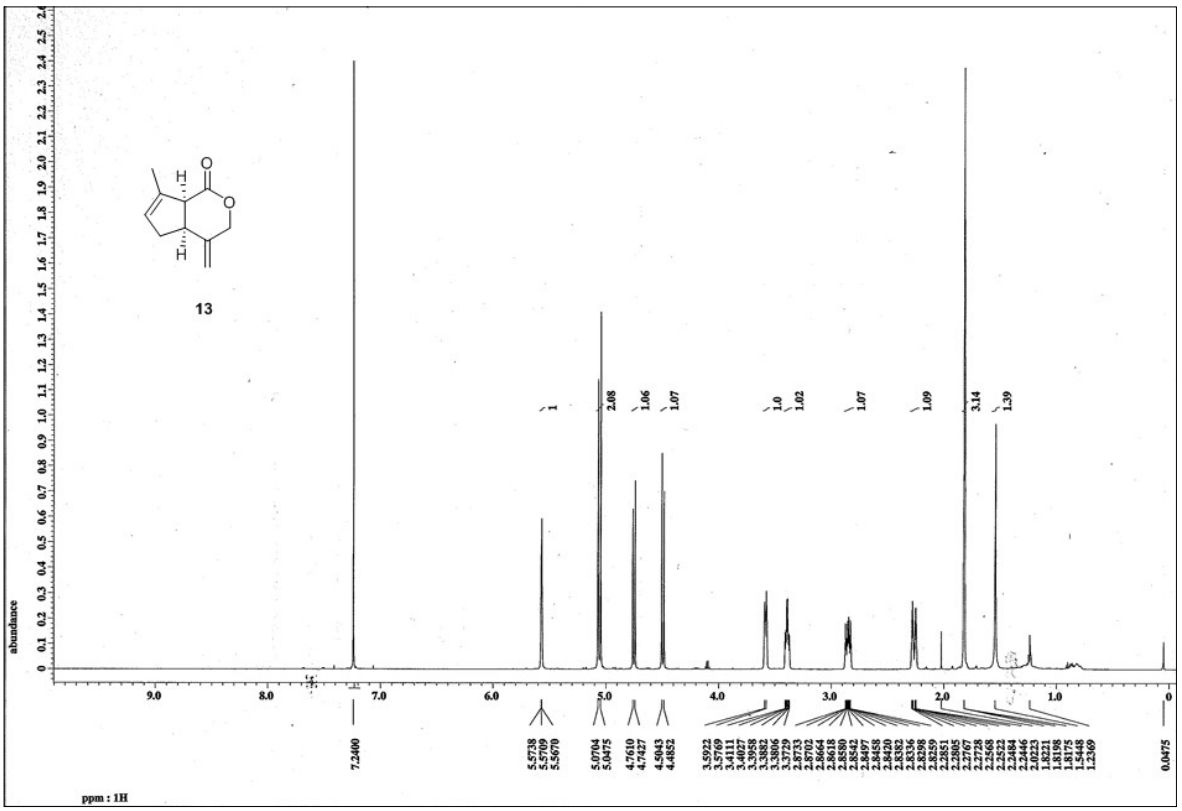
▲ ^{13}C-NMR (100 MHz, $CDCl_3$)



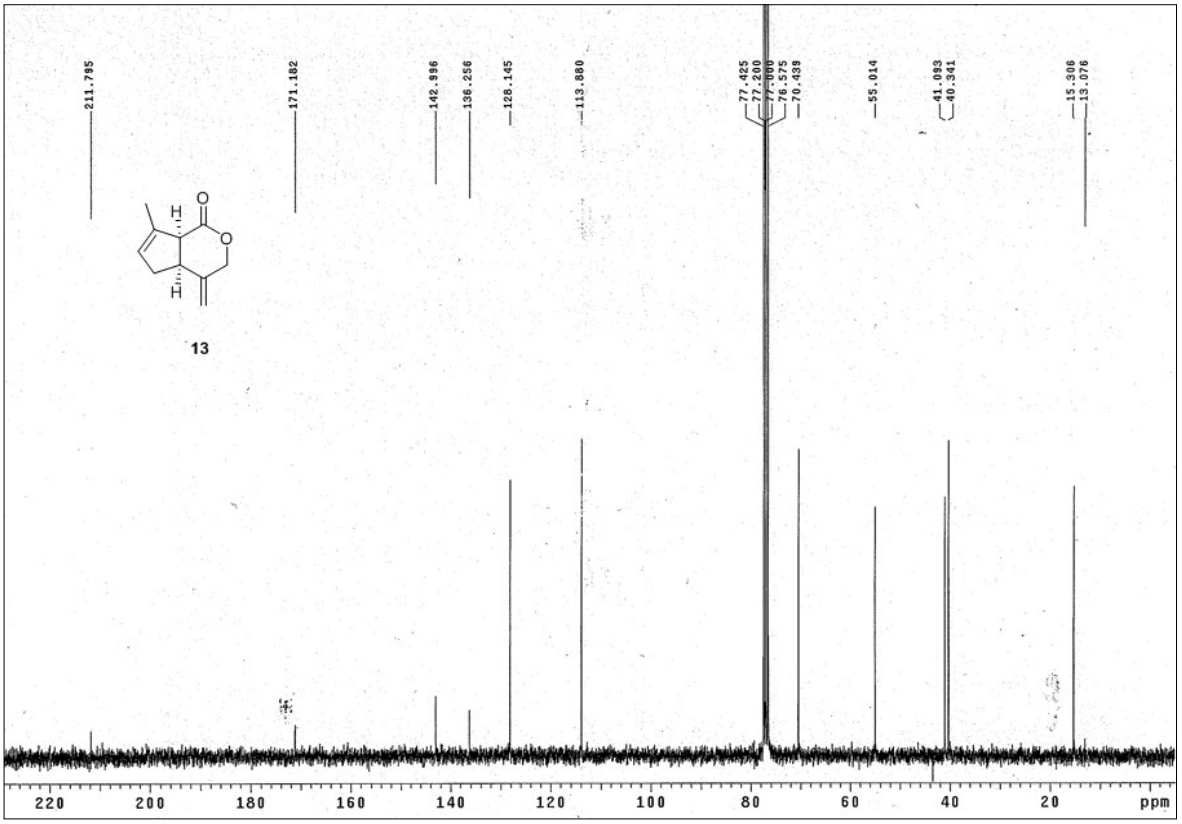
▲ ^{1}H-NMR (400 MHz, $CDCl_3$)



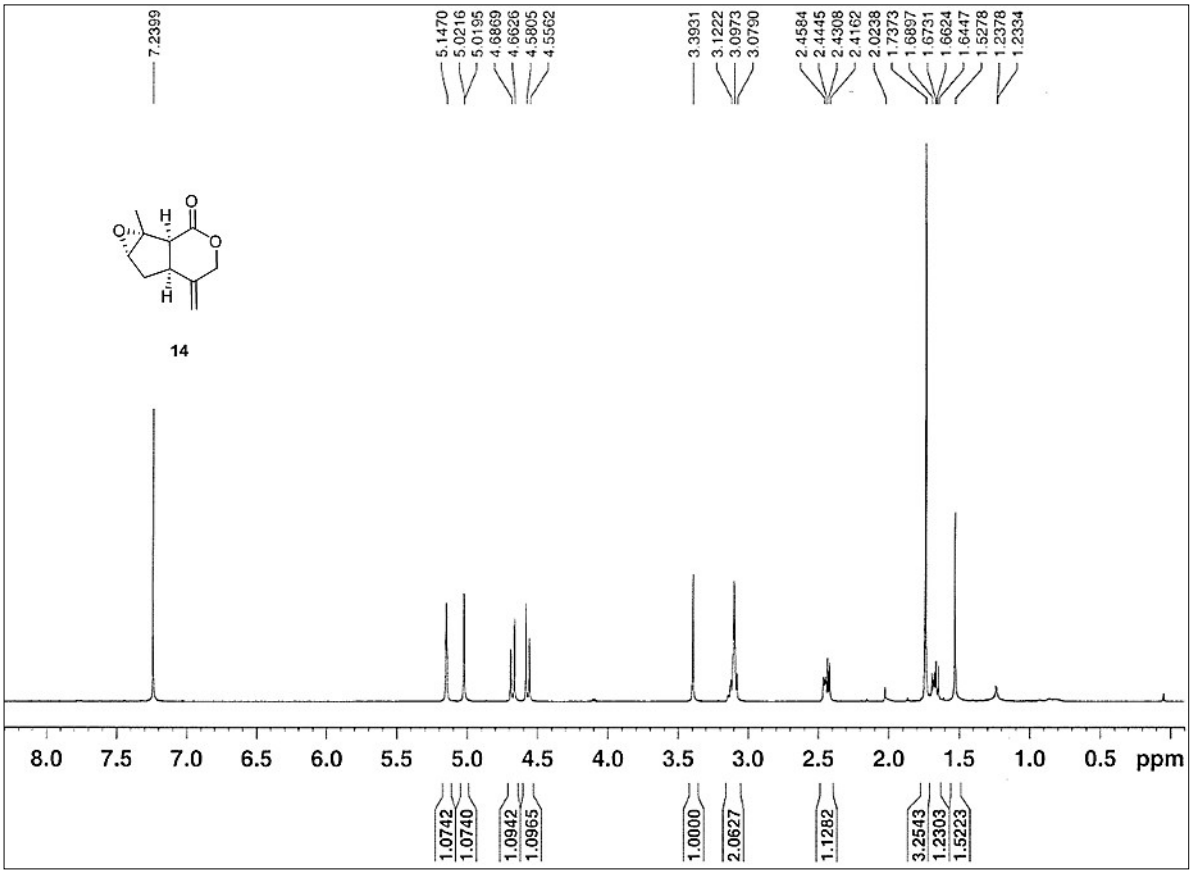
▲ ^{13}C-NMR (100 MHz, $CDCl_3$)



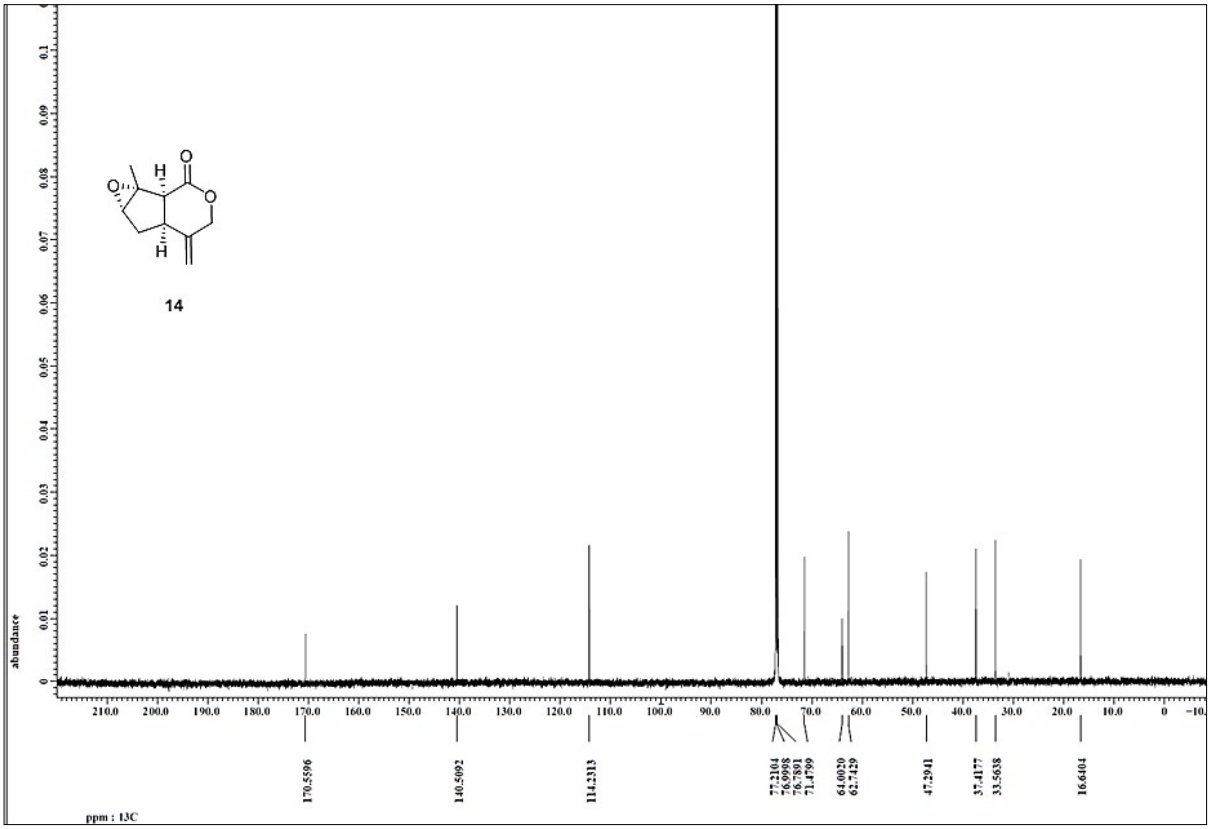
▲ ^{1}H-NMR (600 MHz, $CDCl_3$)



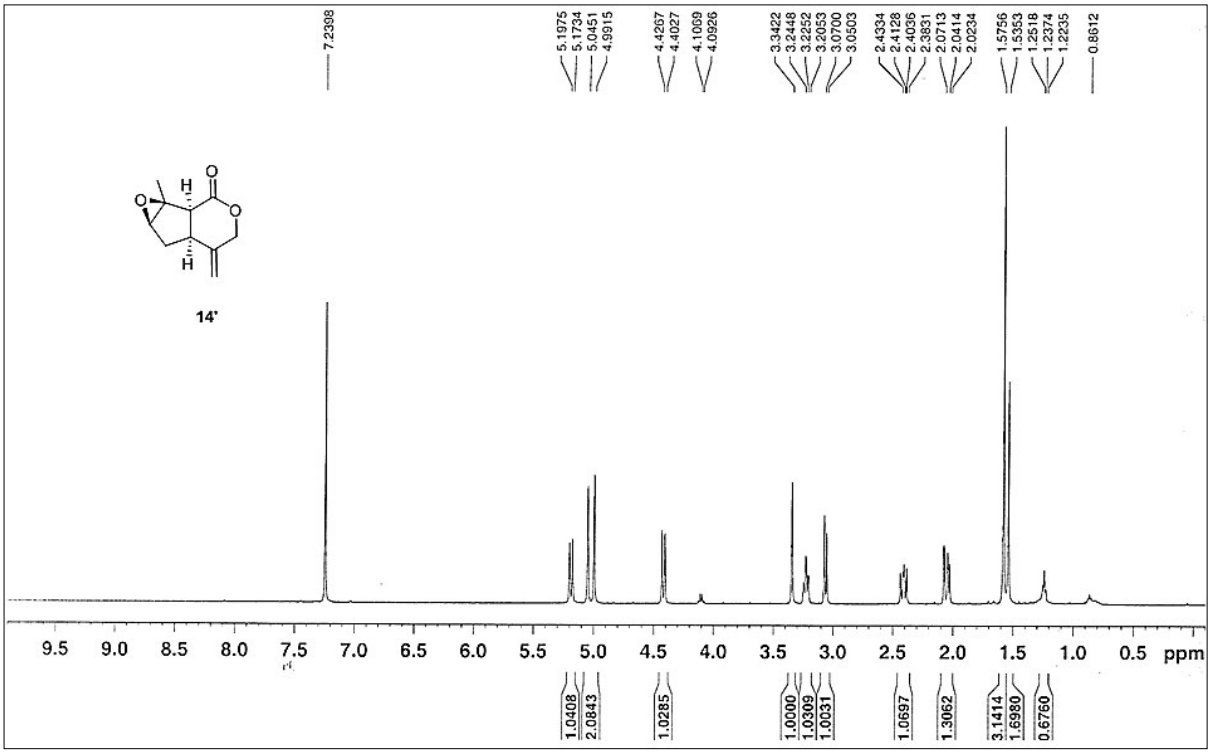
▲ ^{13}C-NMR (75 MHz, $CDCl_3$)



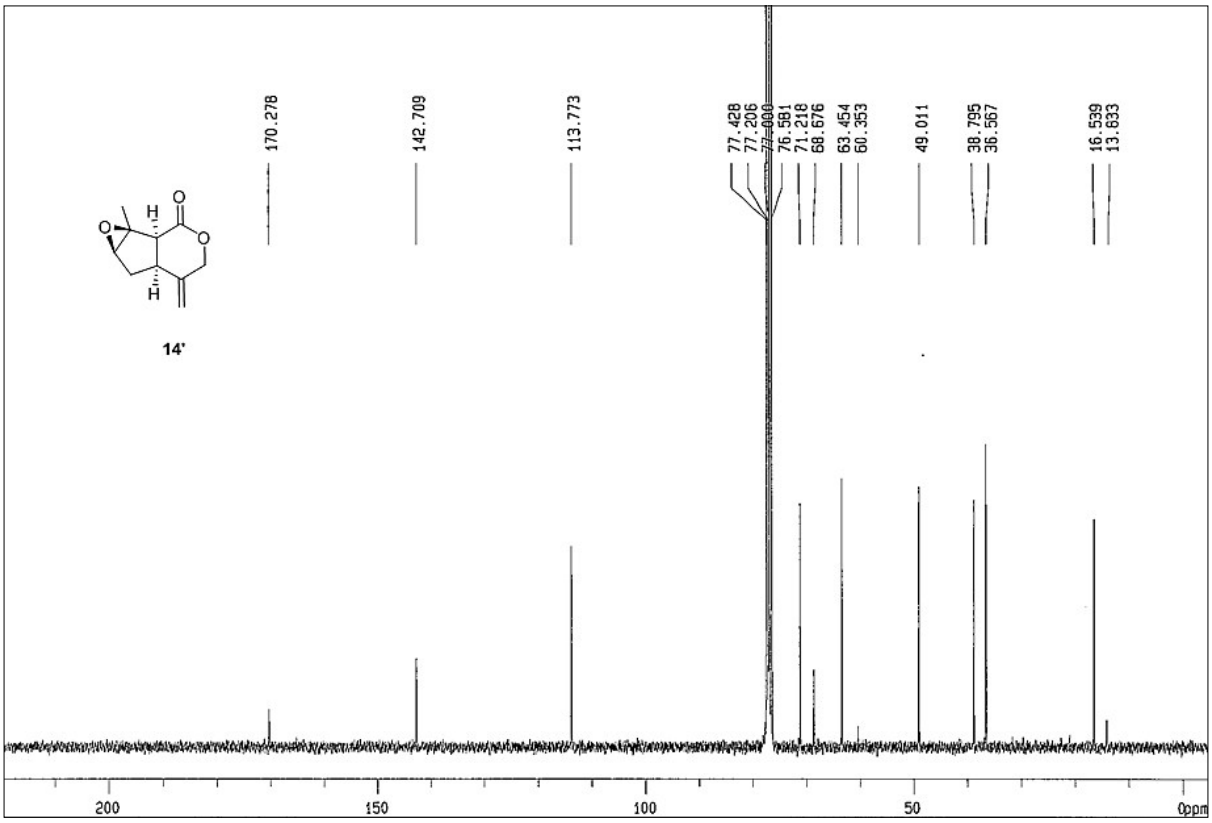
▲ ^{1}H-NMR (500 MHz, $CDCl_3$)



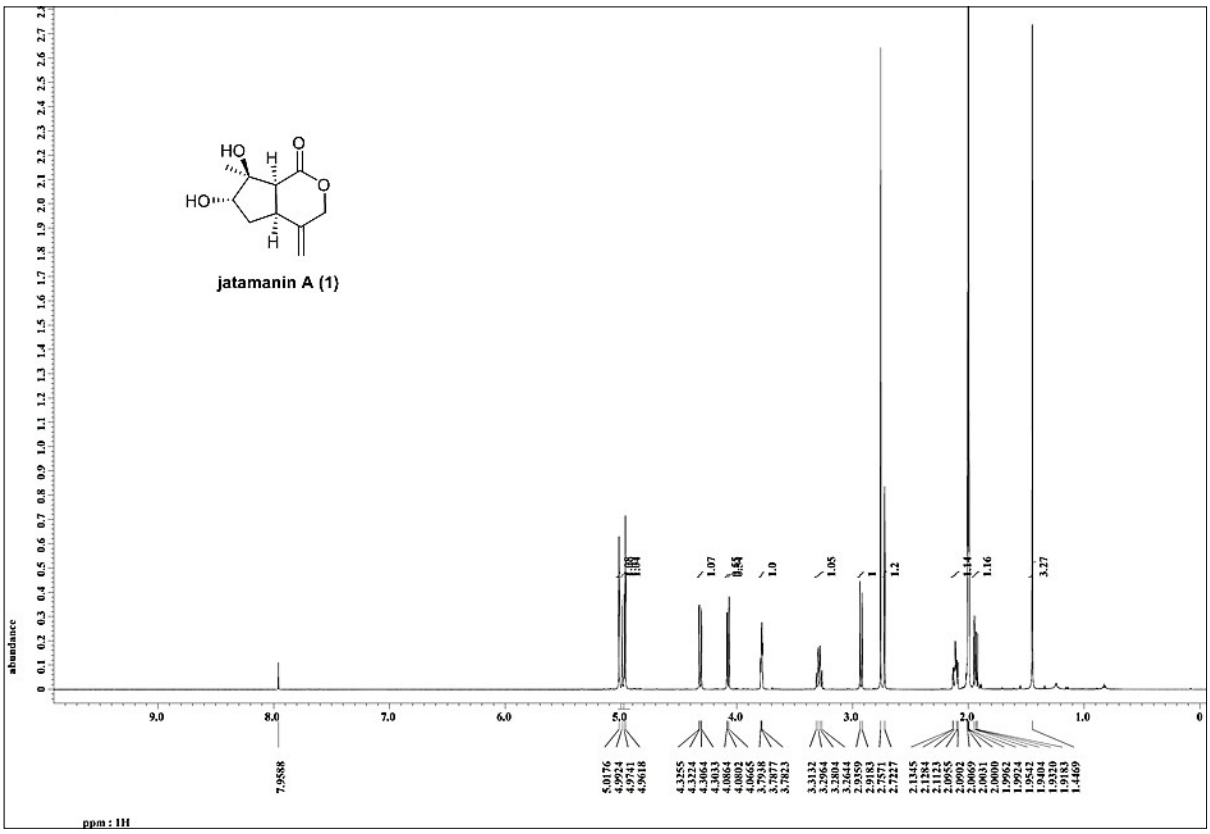
▲ ^{13}C-NMR (150 MHz, $CDCl_3$)



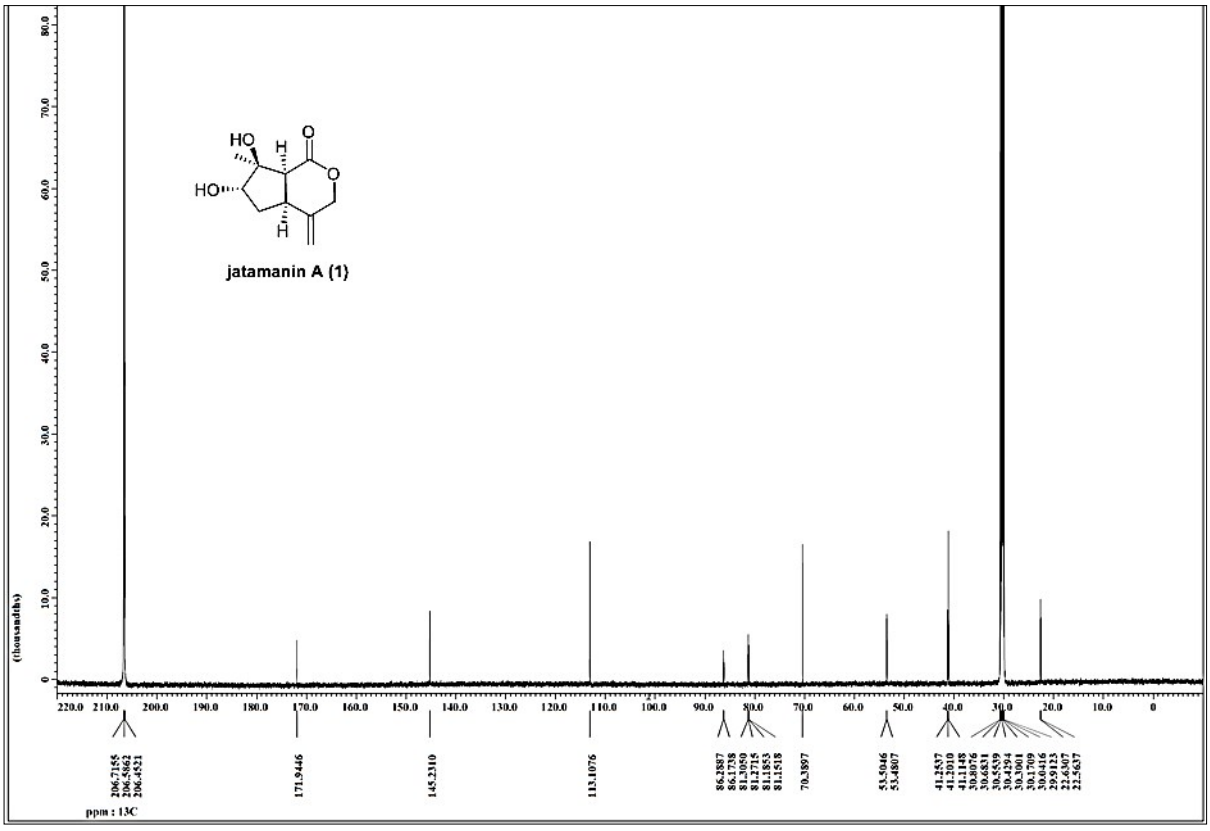
▲ ^{1}H-NMR (500 MHz, $CDCl_3$)



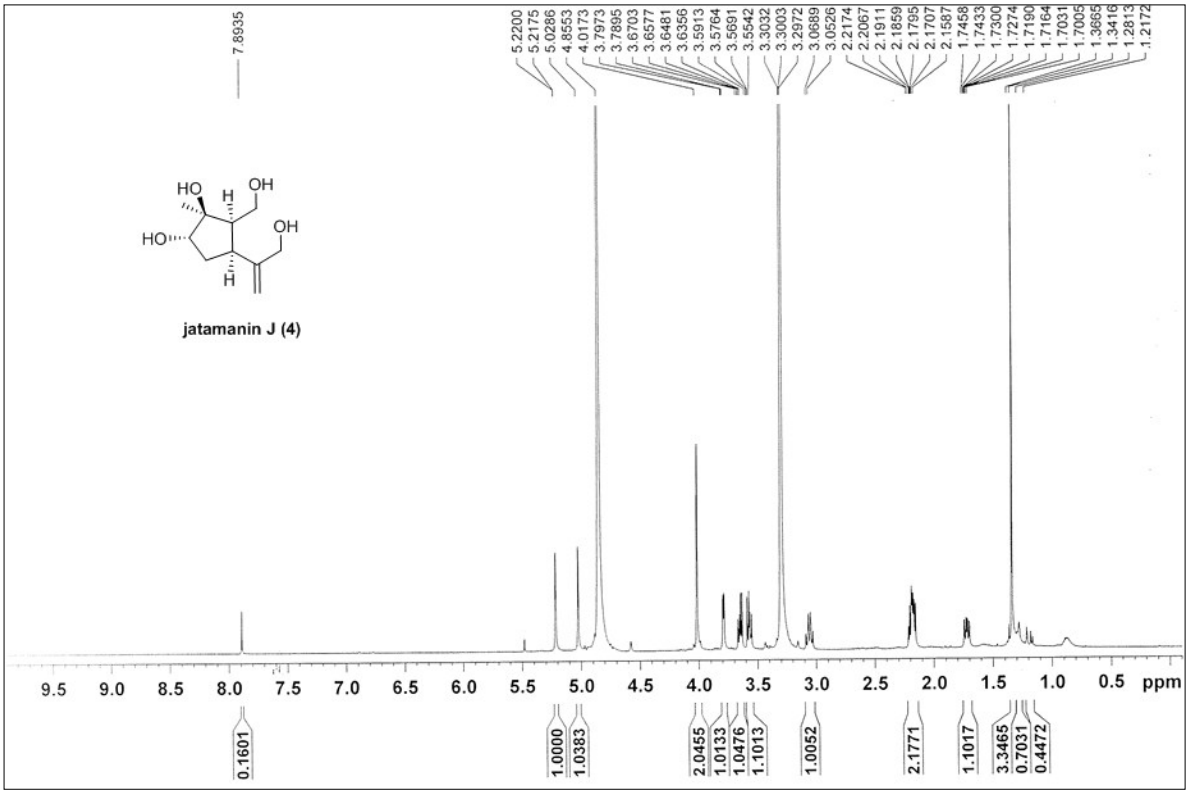
▲ ^{13}C-NMR (75 MHz, $CDCl_3$)



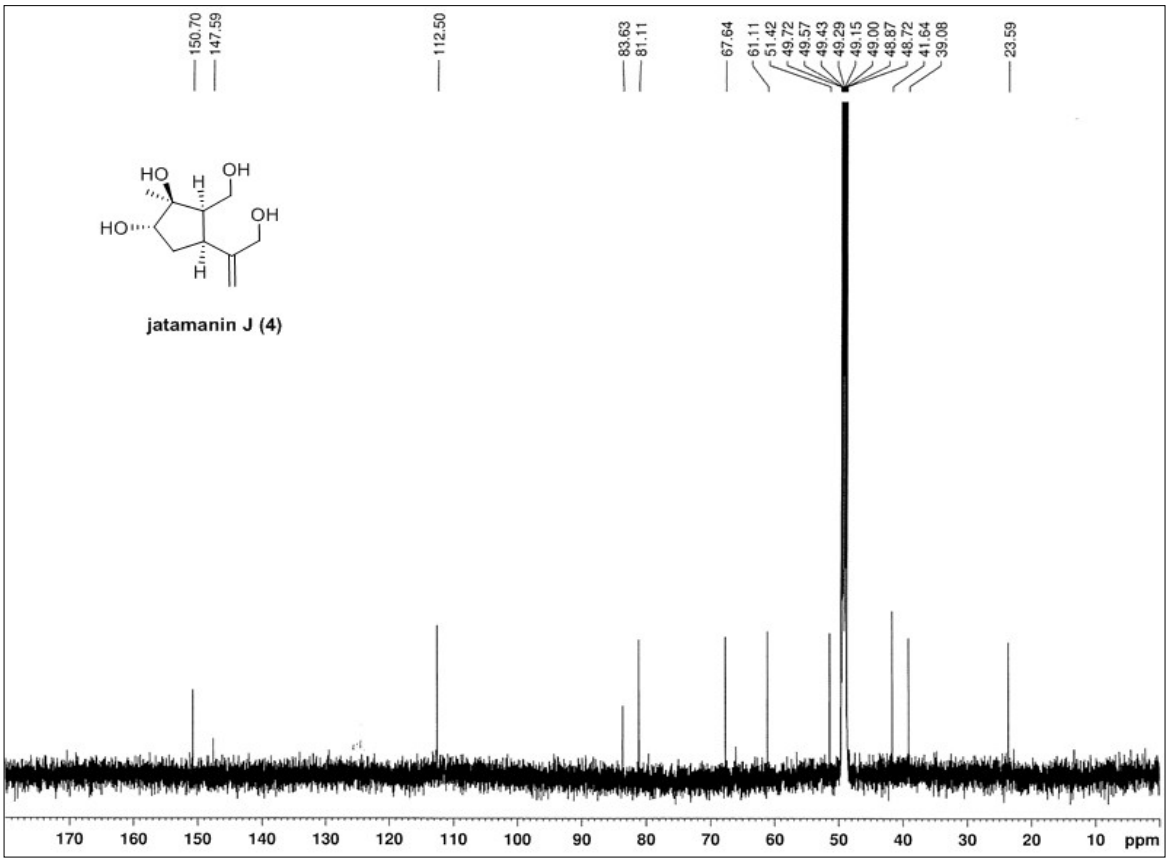
▲ ^{1}H-NMR (600 MHz, Acetone-d_6)



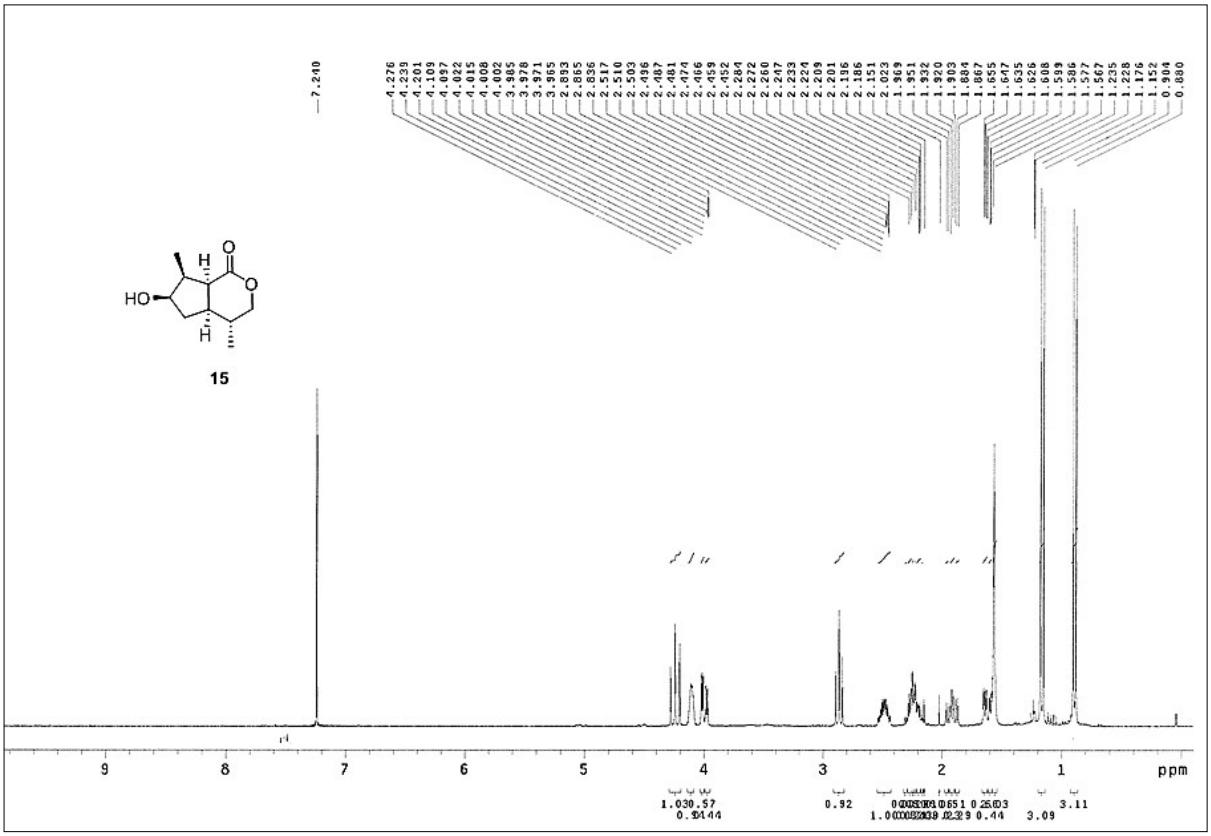
▲ ^{13}C-NMR (150 MHz, Acetone-d_6)



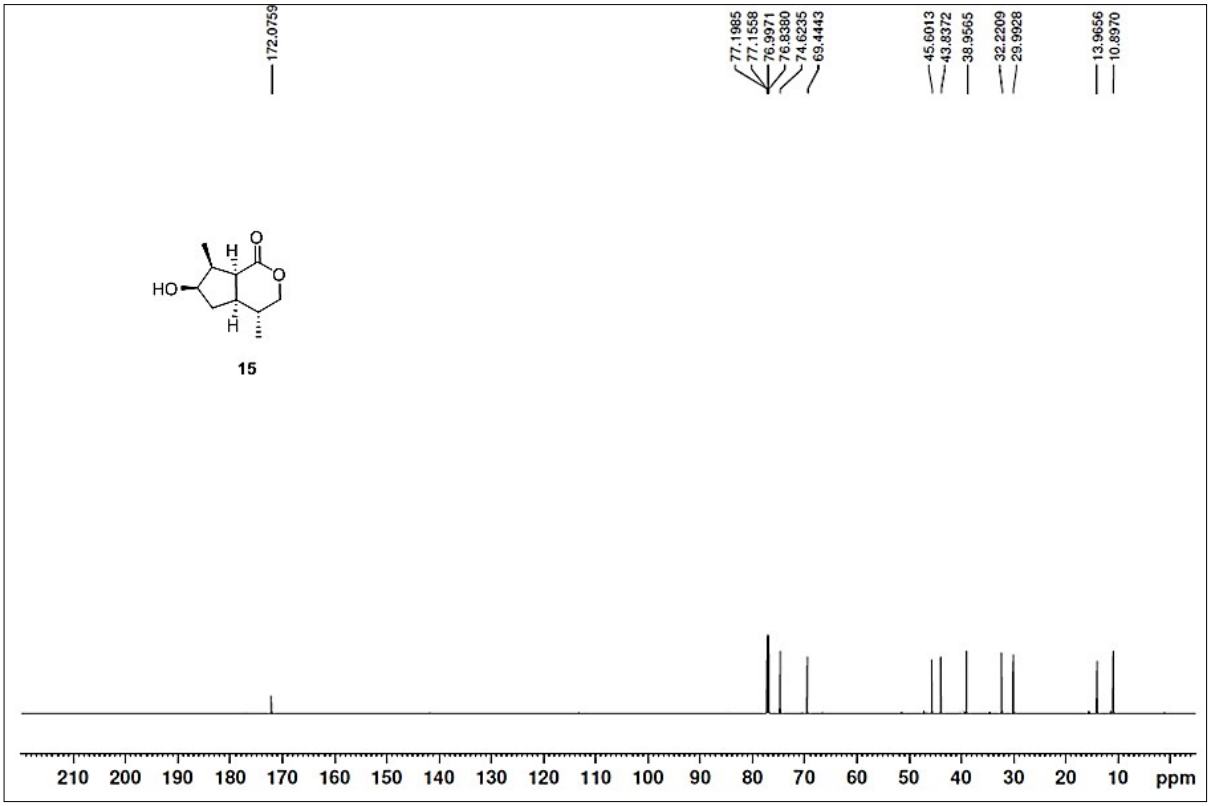
▲ ^{1}H-NMR (500 MHz, MeOD)



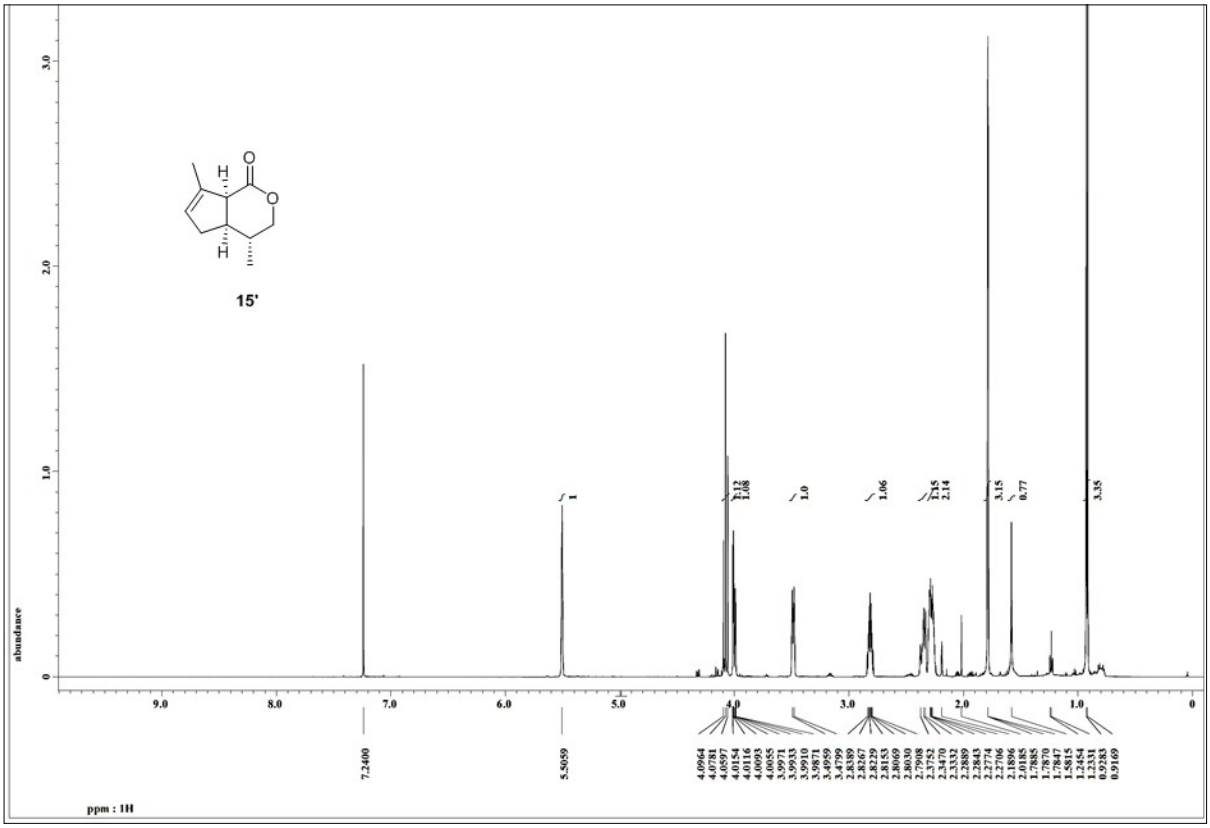
▲ ^{13}C-NMR (150 MHz, MeOD)



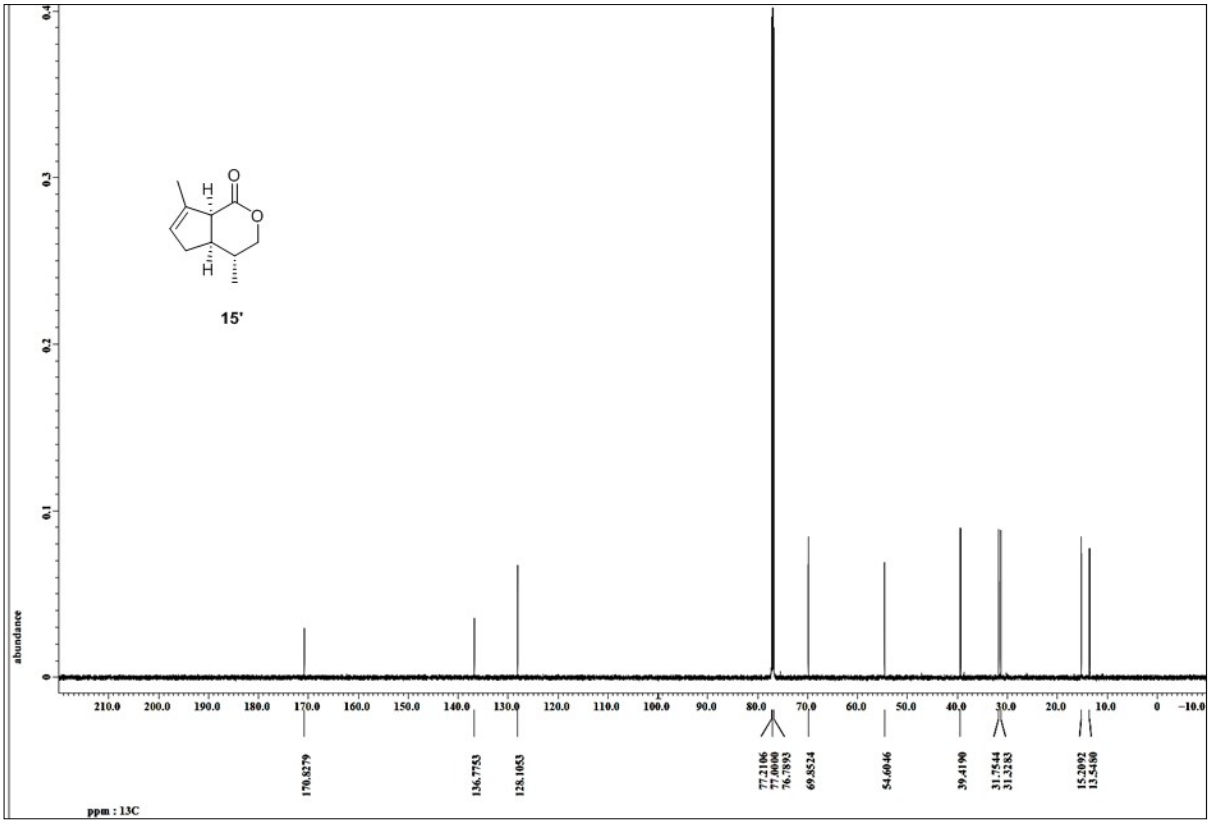
▲ ^{1}H-NMR (300 MHz, $CDCl_3$)



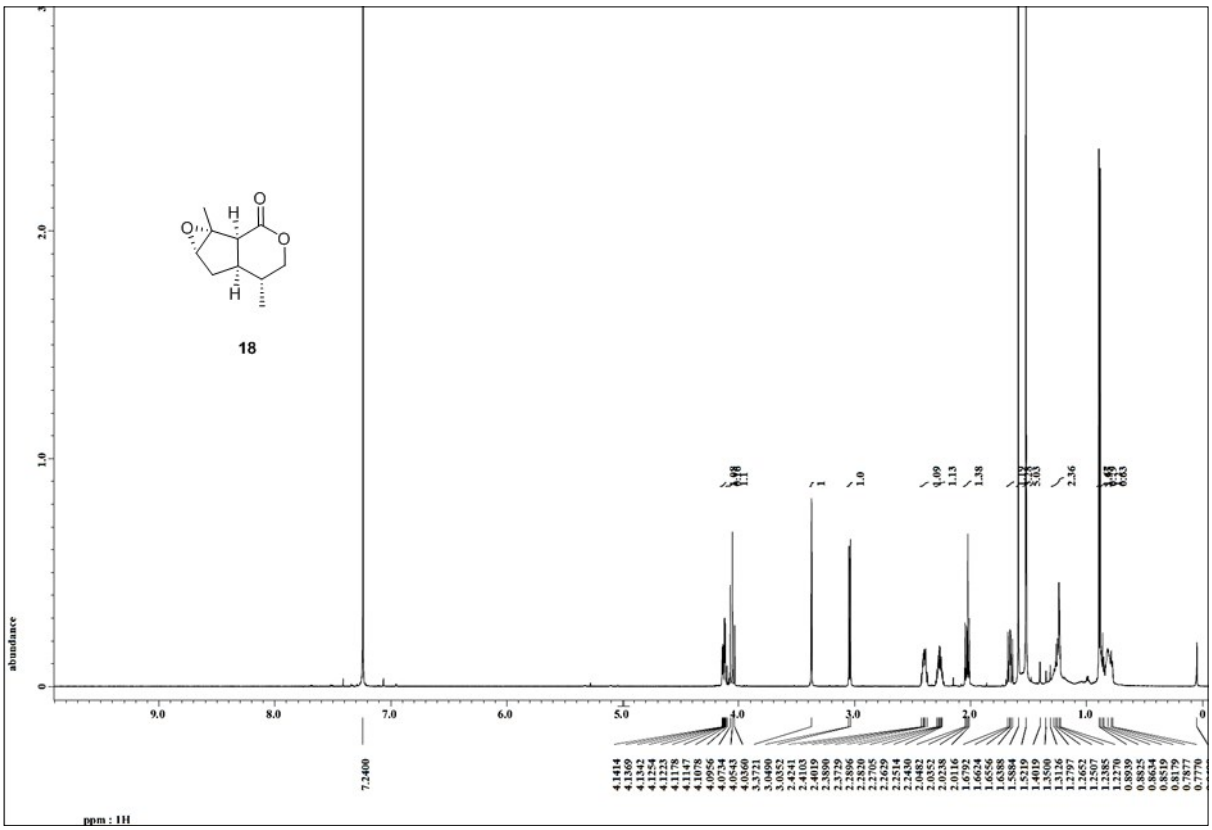
▲ ^{13}C-NMR (200 MHz, $CDCl_3$)



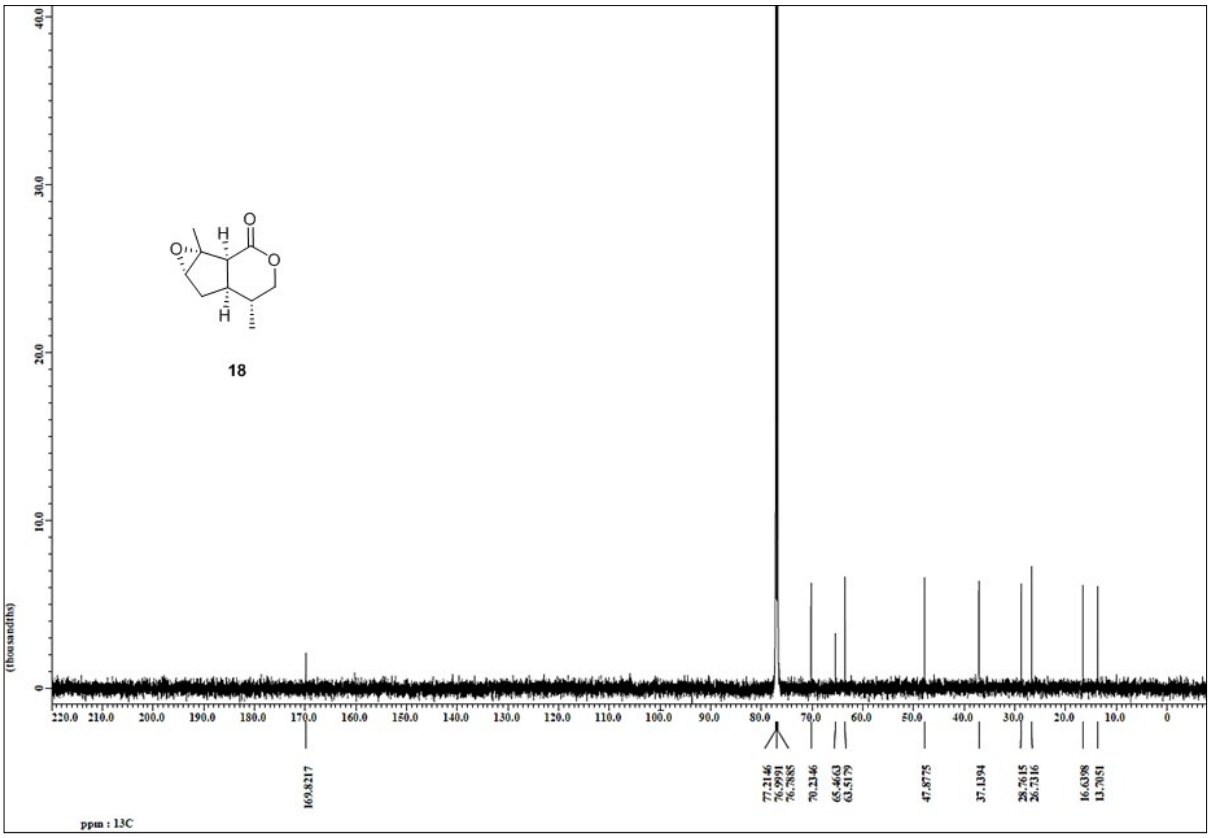
▲ ^{1}H-NMR (600 MHz, $CDCl_3$)



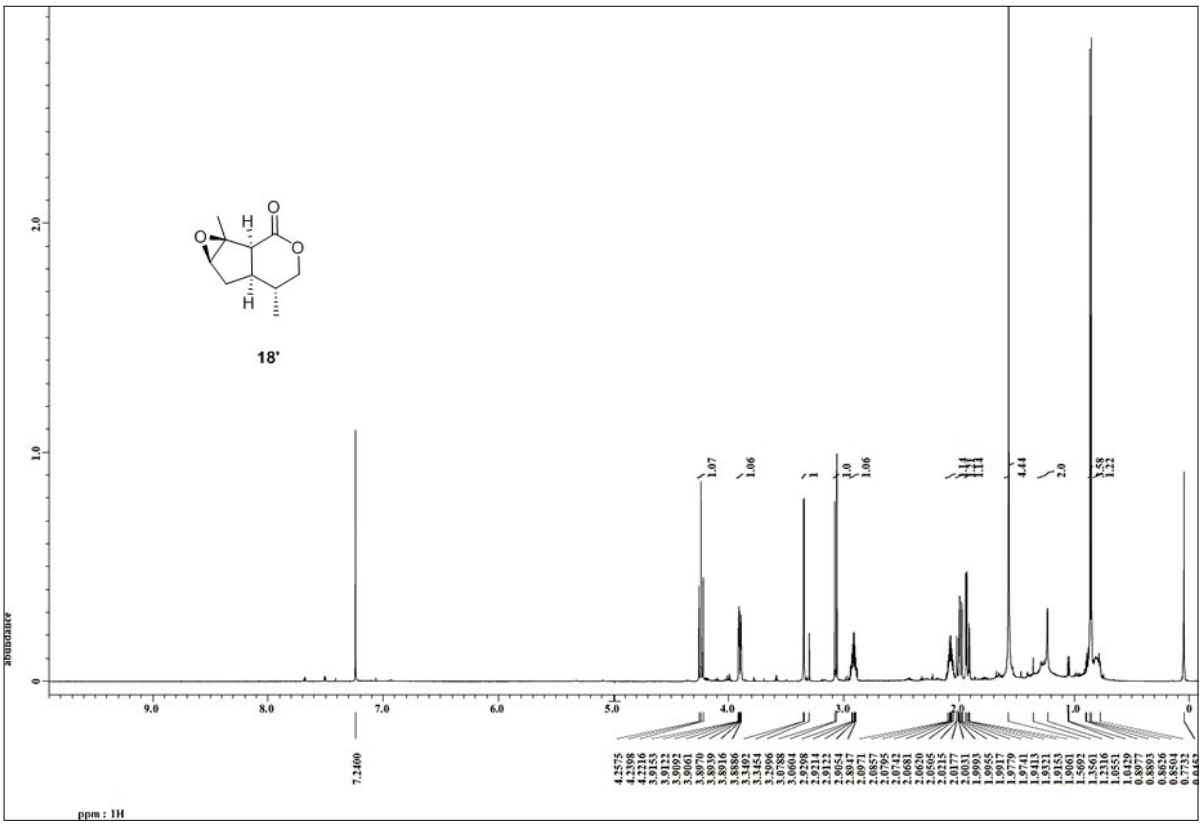
▲ ^{13}C-NMR (150 MHz, $CDCl_3$)



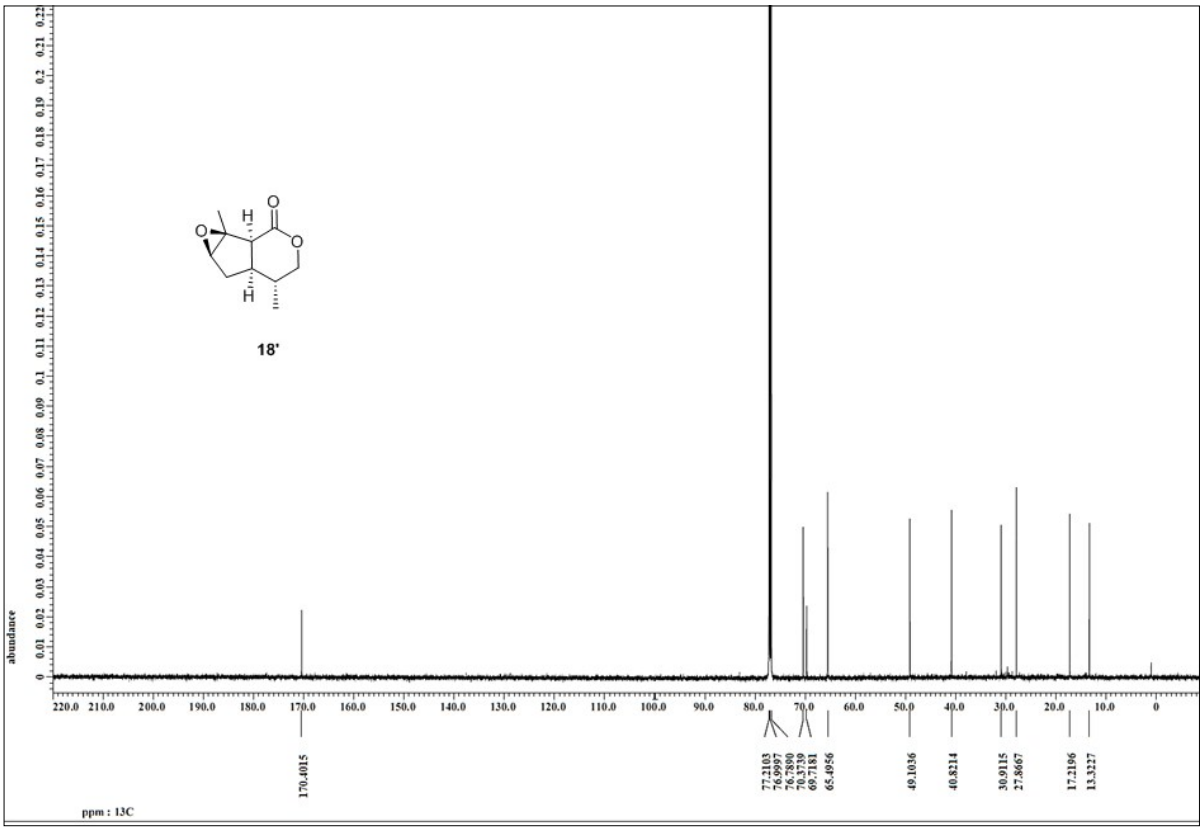
▲ ^{1}H-NMR (600 MHz, $CDCl_3$)



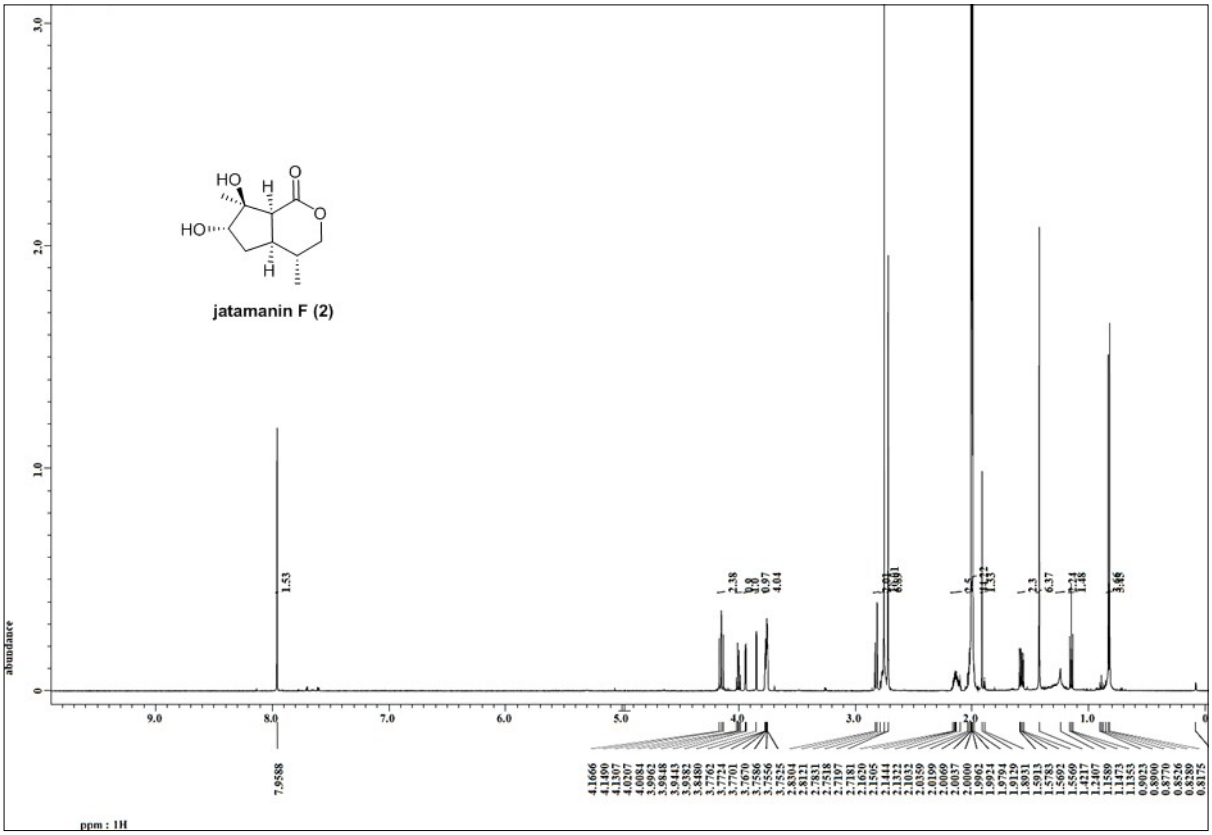
▲ ^{13}C-NMR (150 MHz, $CDCl_3$)



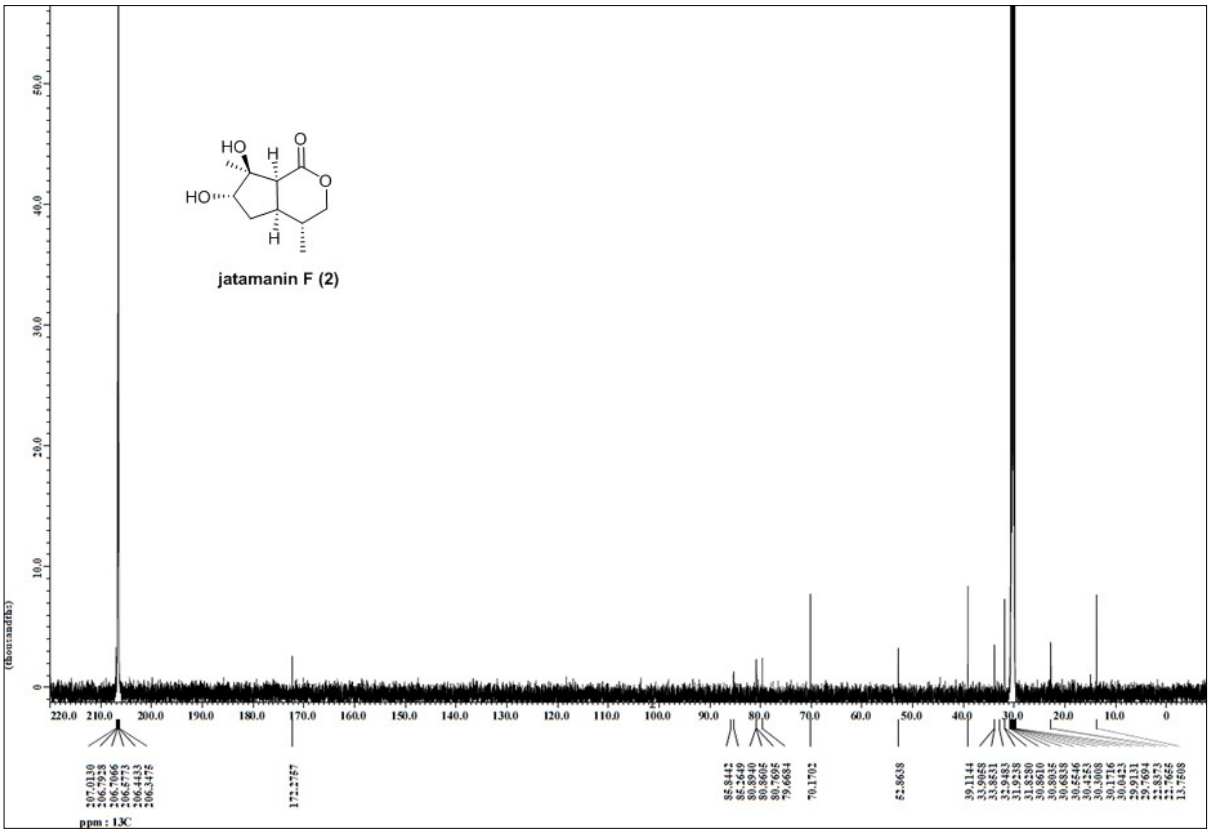
▲ ^{1}H-NMR (600 MHz, $CDCl_3$)



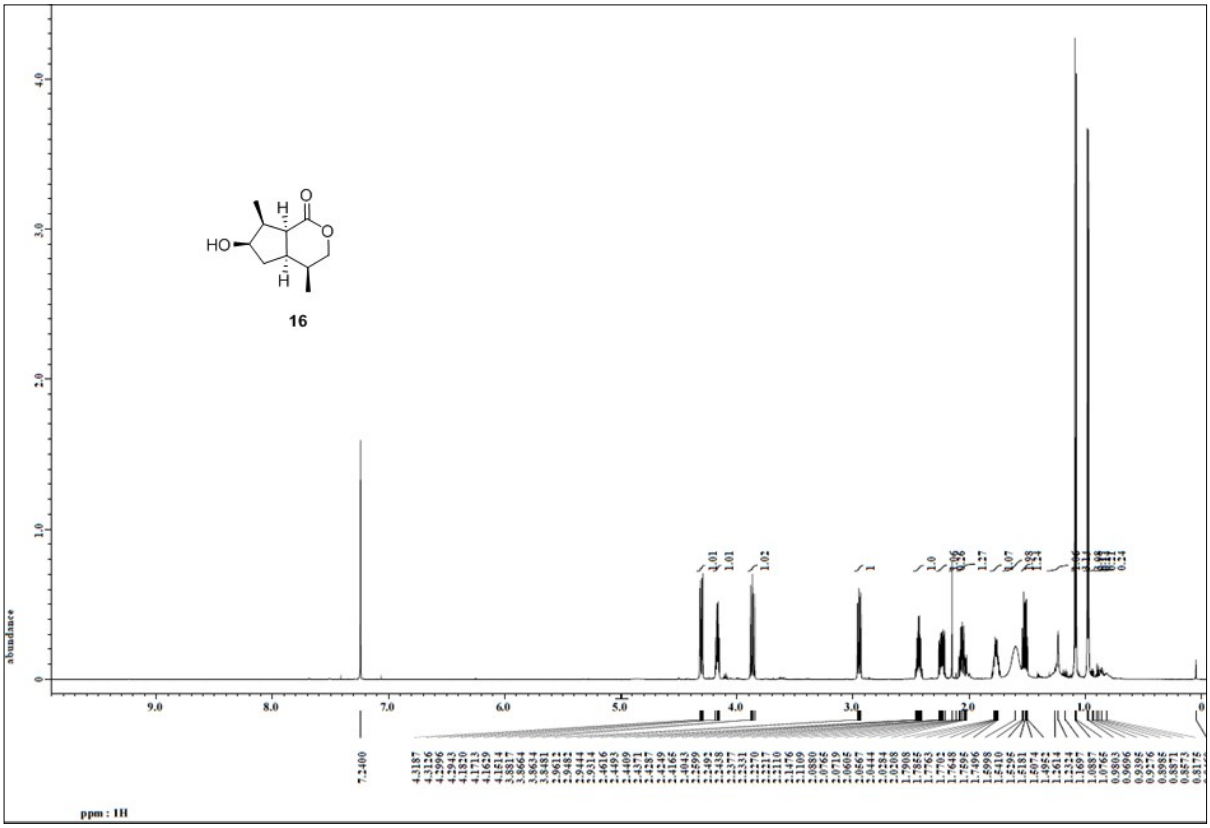
▲ ^{13}C-NMR (150 MHz, $CDCl_3$)



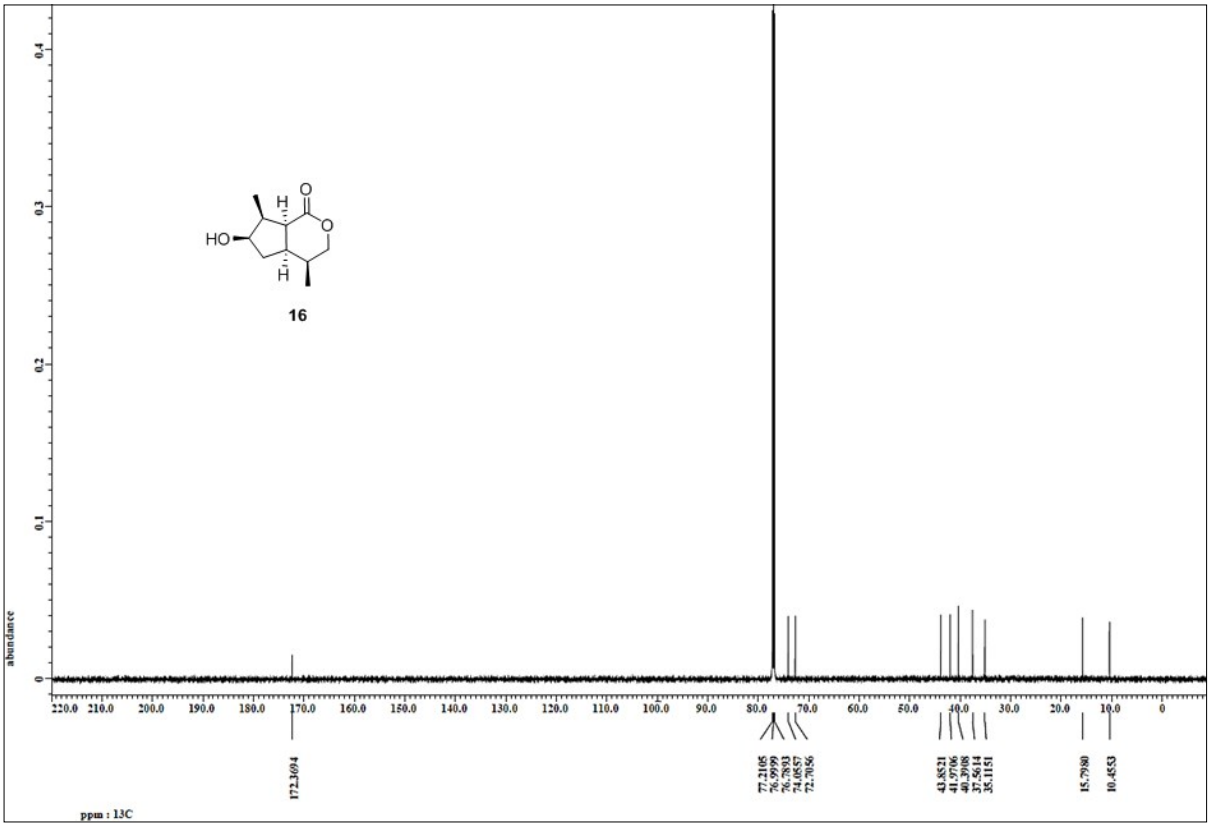
▲ ^{1}H-NMR (600 MHz, Acetone-d_6)



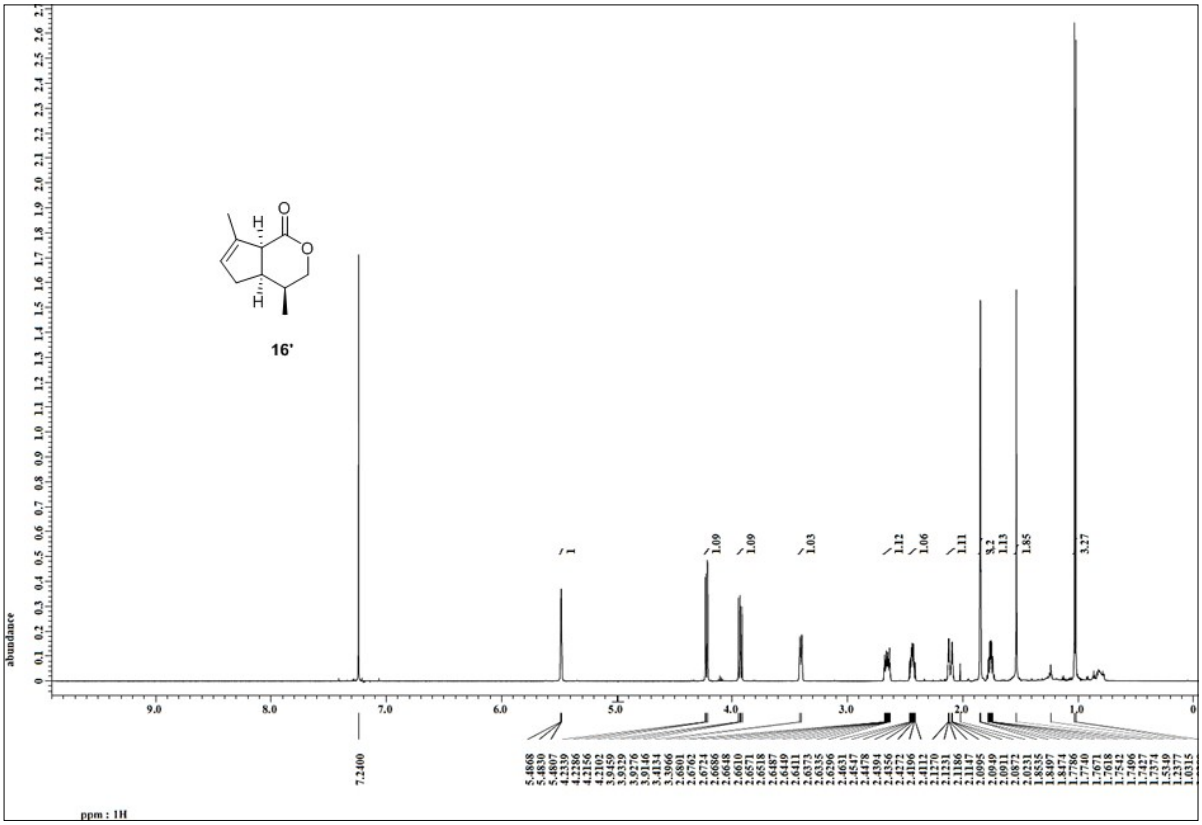
▲ ^{13}C-NMR (150 MHz, Acetone-d_6)



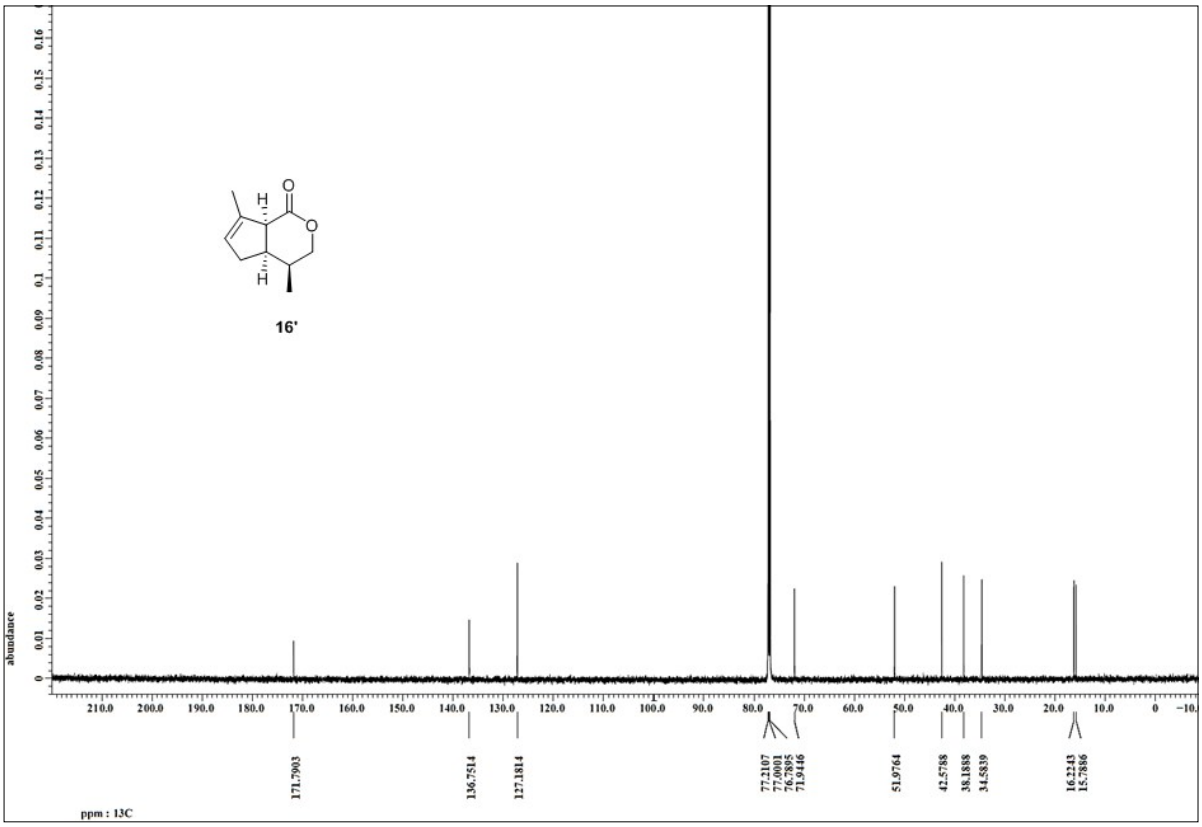
▲ ^{1}H-NMR (600 MHz, $CDCl_3$)



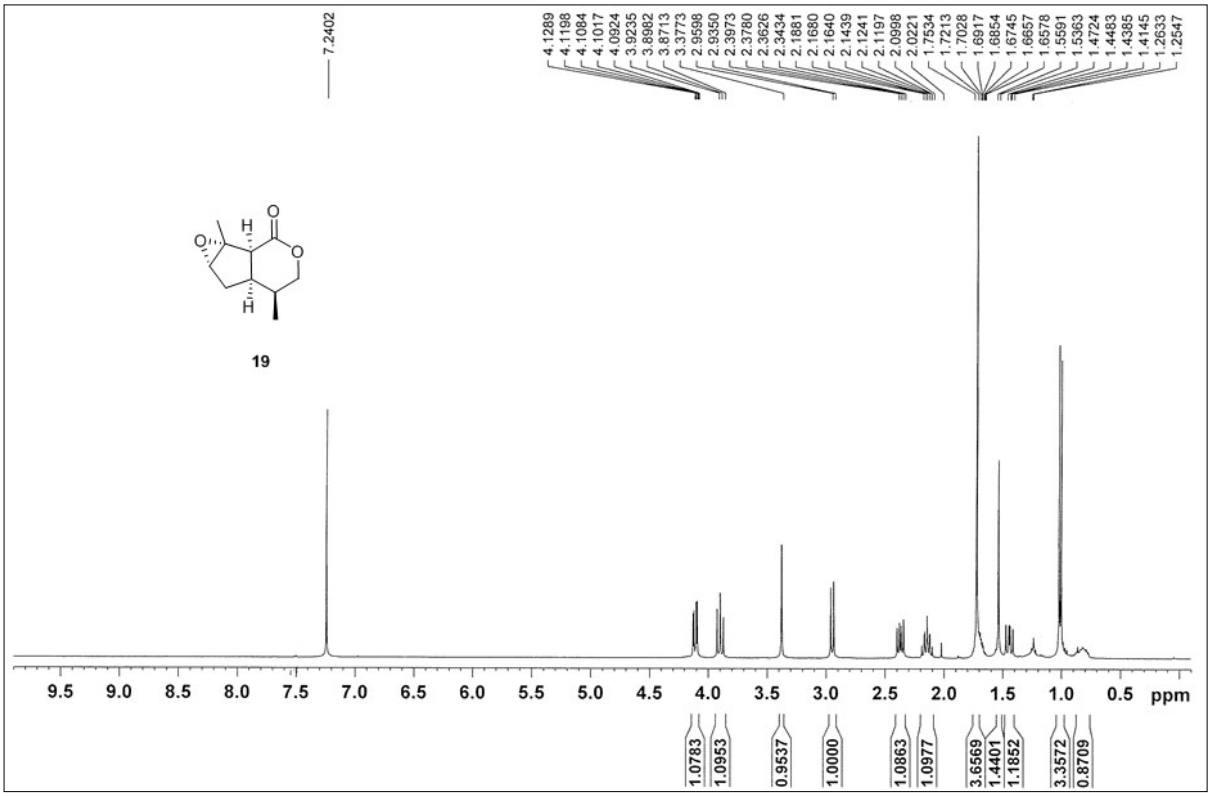
▲ ^{13}C-NMR (150 MHz, $CDCl_3$)



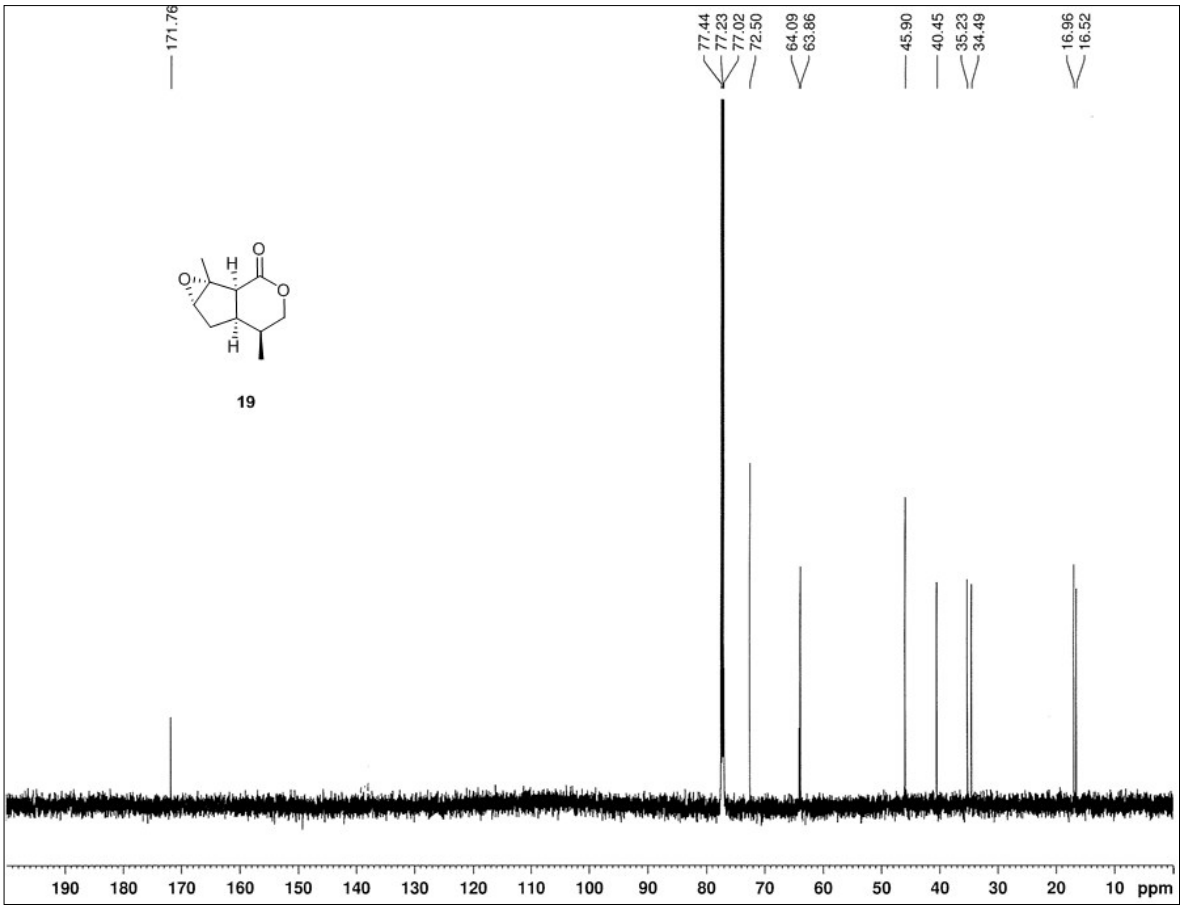
▲ ^{1}H-NMR (600 MHz, $CDCl_3$)



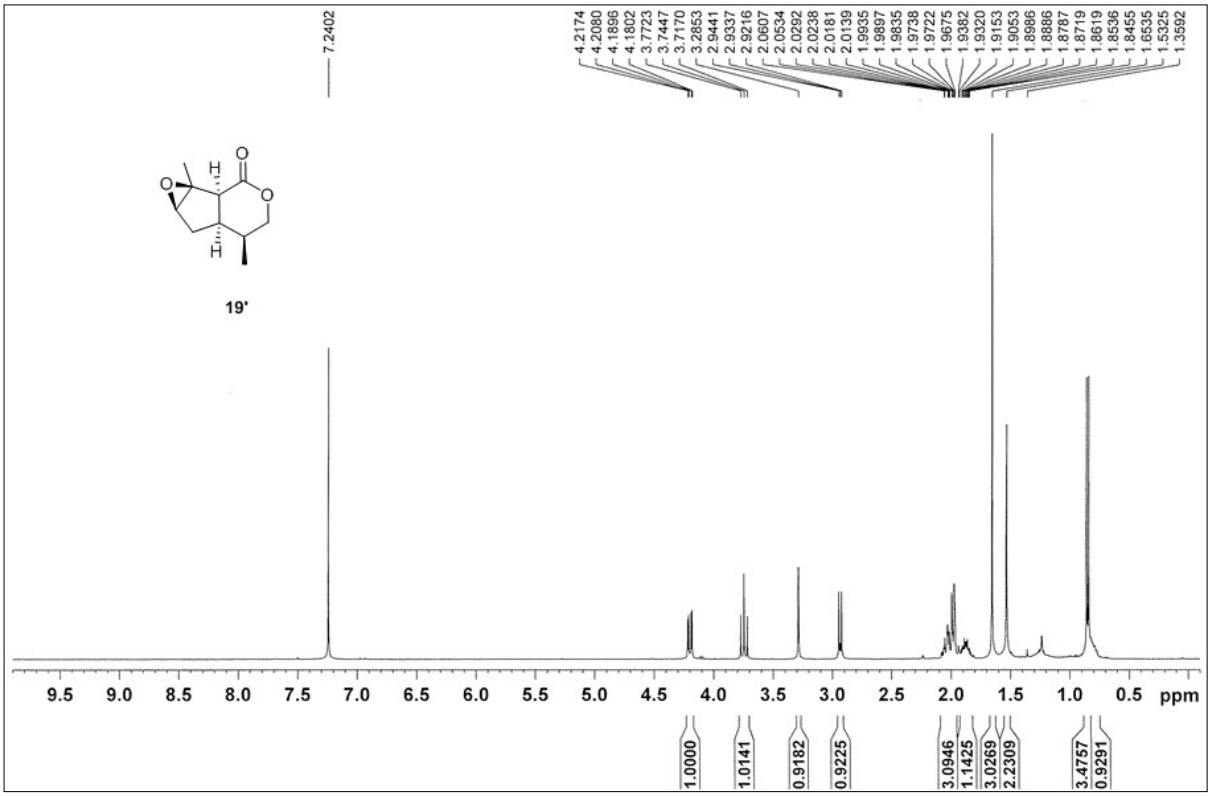
▲ ^{13}C-NMR (150 MHz, $CDCl_3$)



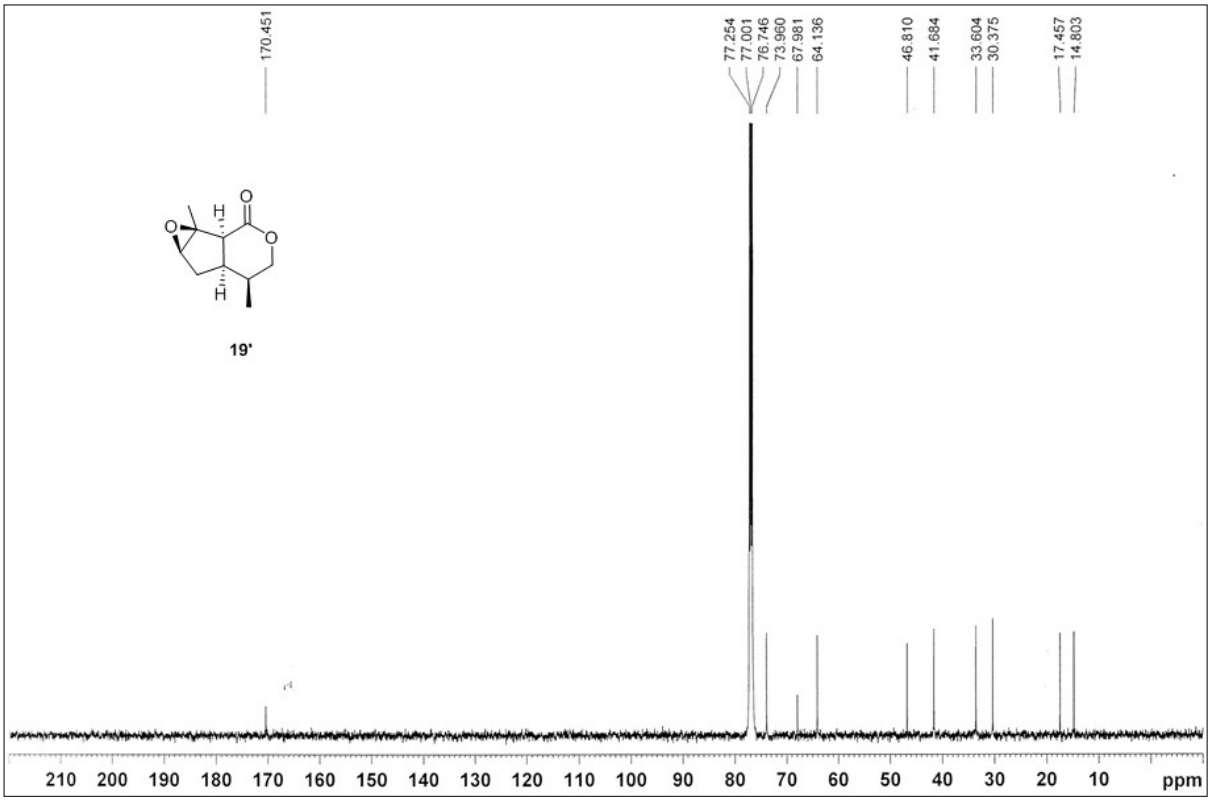
▲ ^{1}H-NMR (400 MHz, $CDCl_3$)



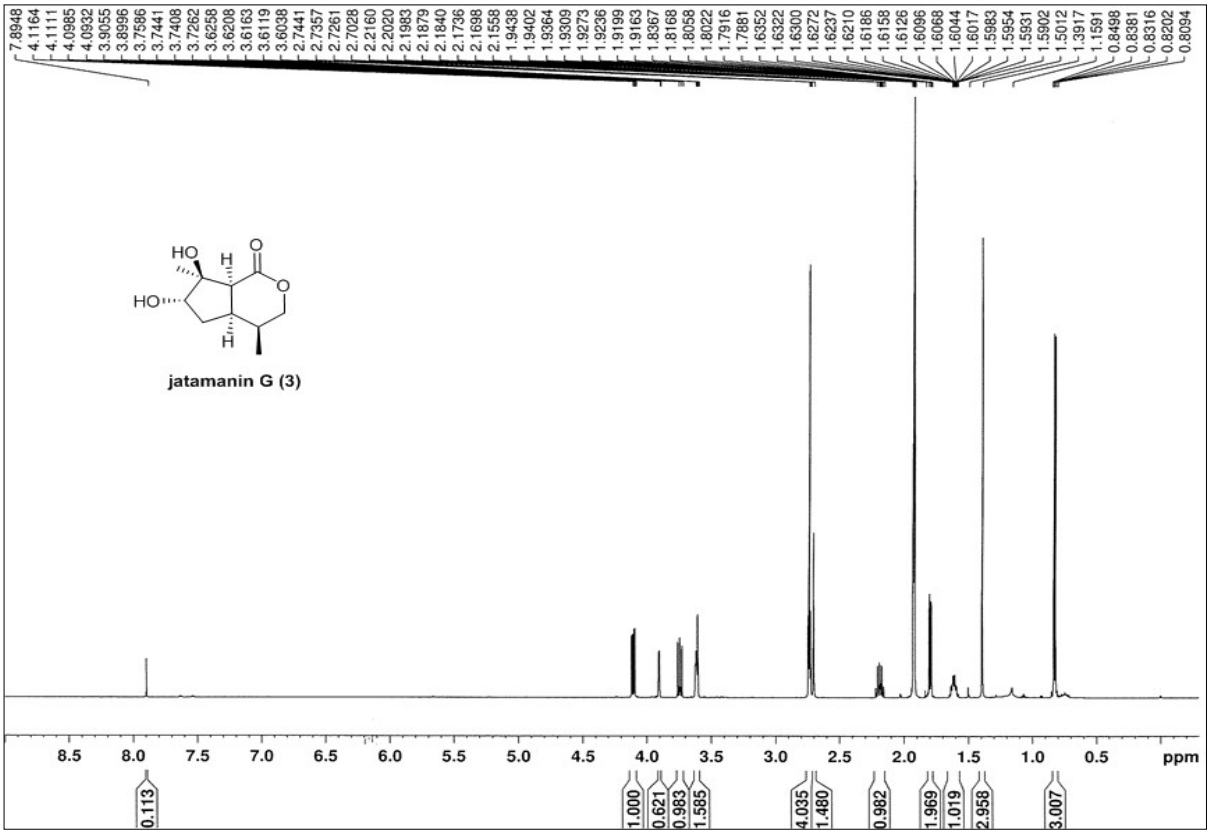
▲ ^{13}C-NMR (100 MHz, $CDCl_3$)



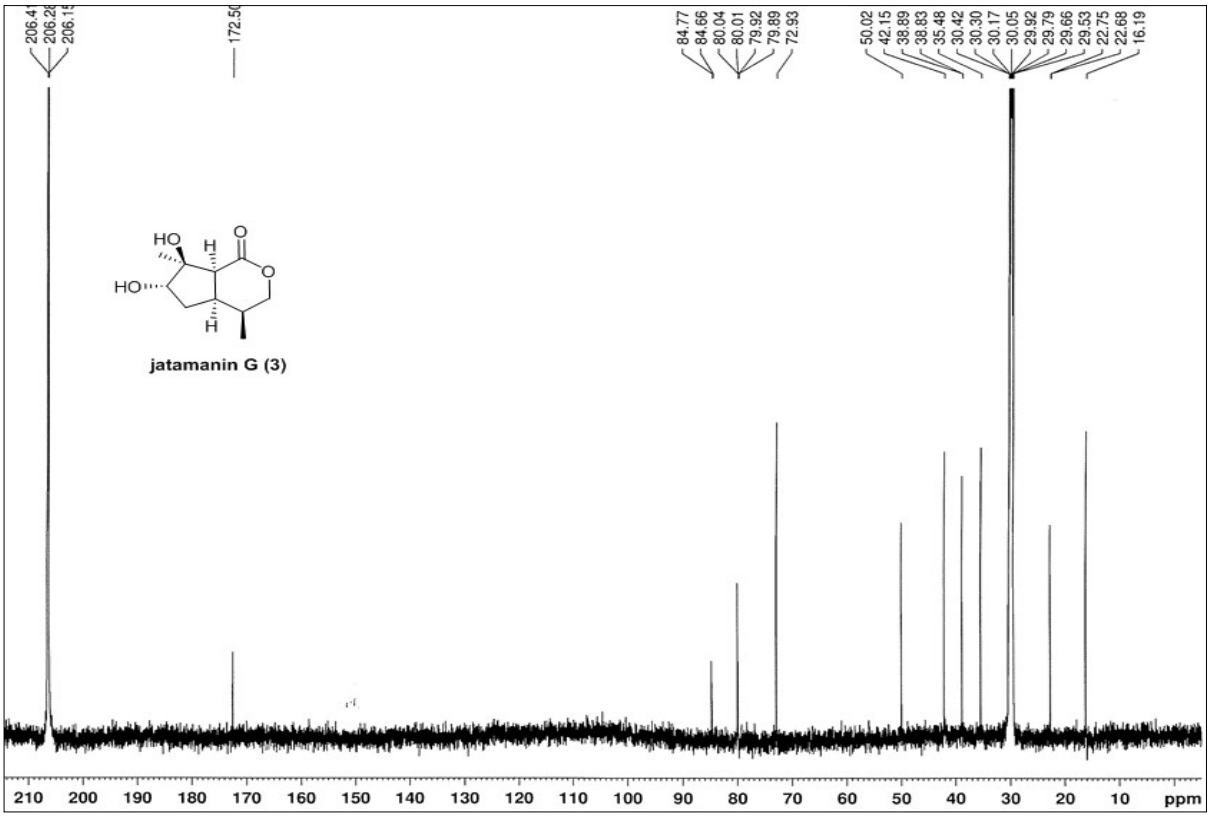
▲ ^{1}H-NMR (400 MHz, $CDCl_3$)



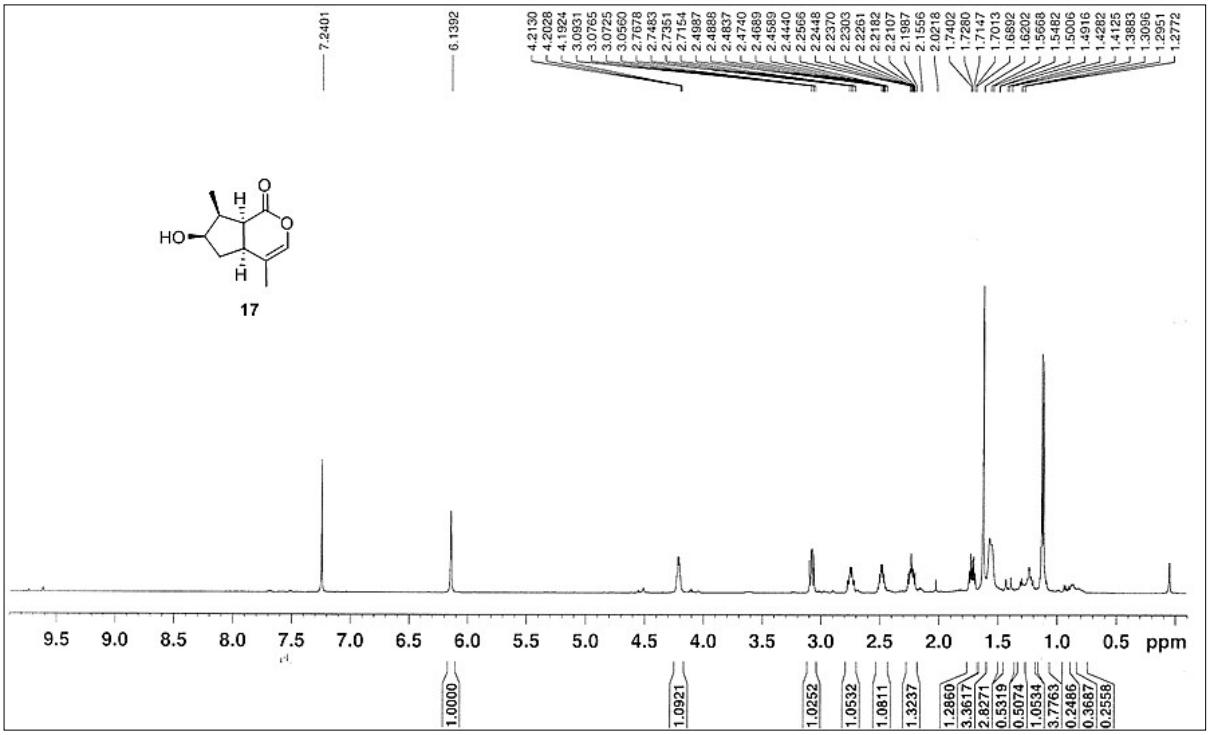
▲ ^{13}C-NMR (125 MHz, $CDCl_3$)



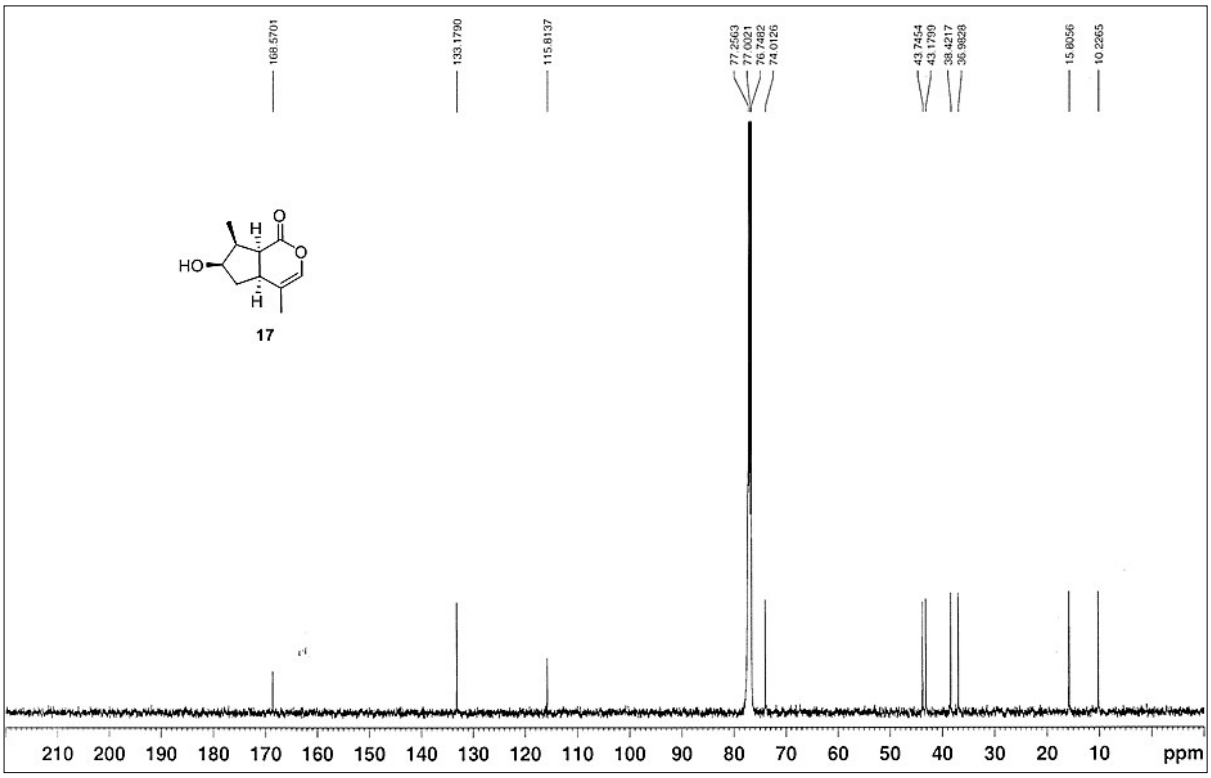
▲ ^{1}H-NMR (600 MHz, Acetone-d_6)



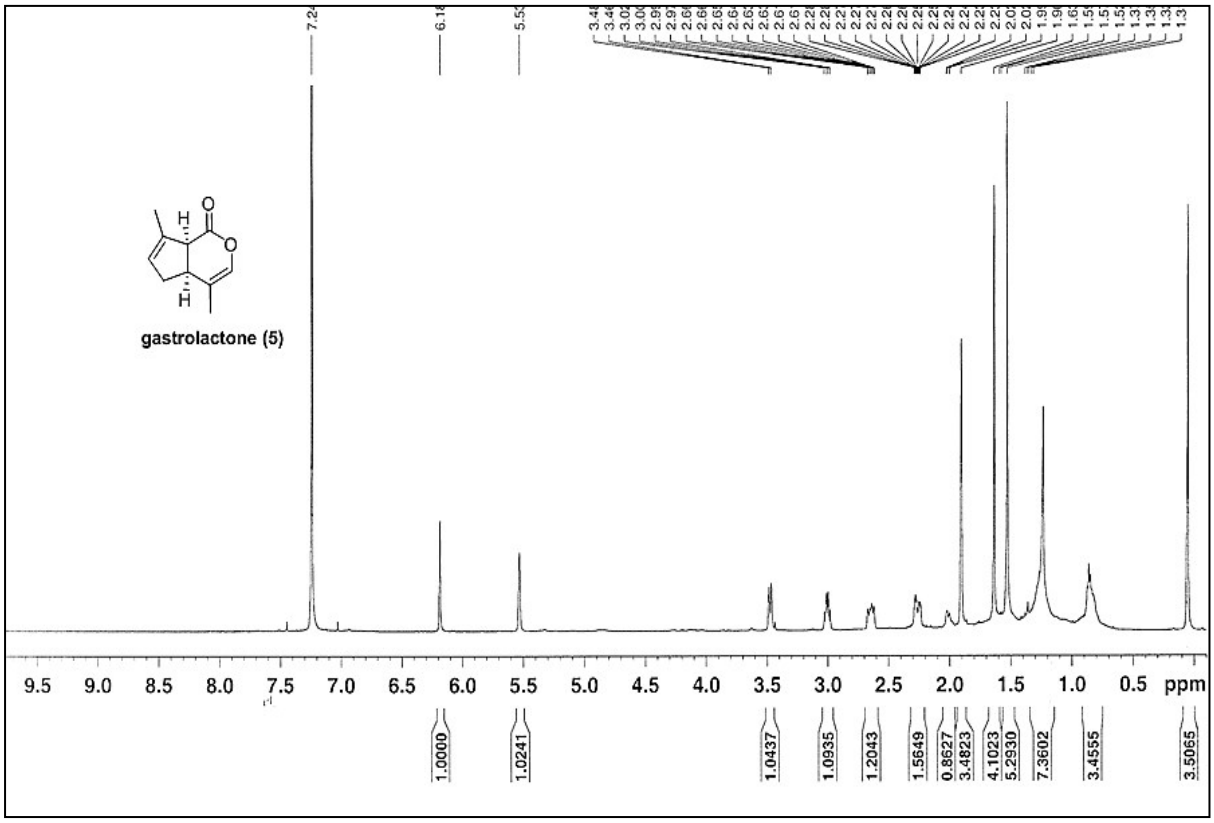
▲ ^{13}C-NMR (150 MHz, Acetone-d_6)



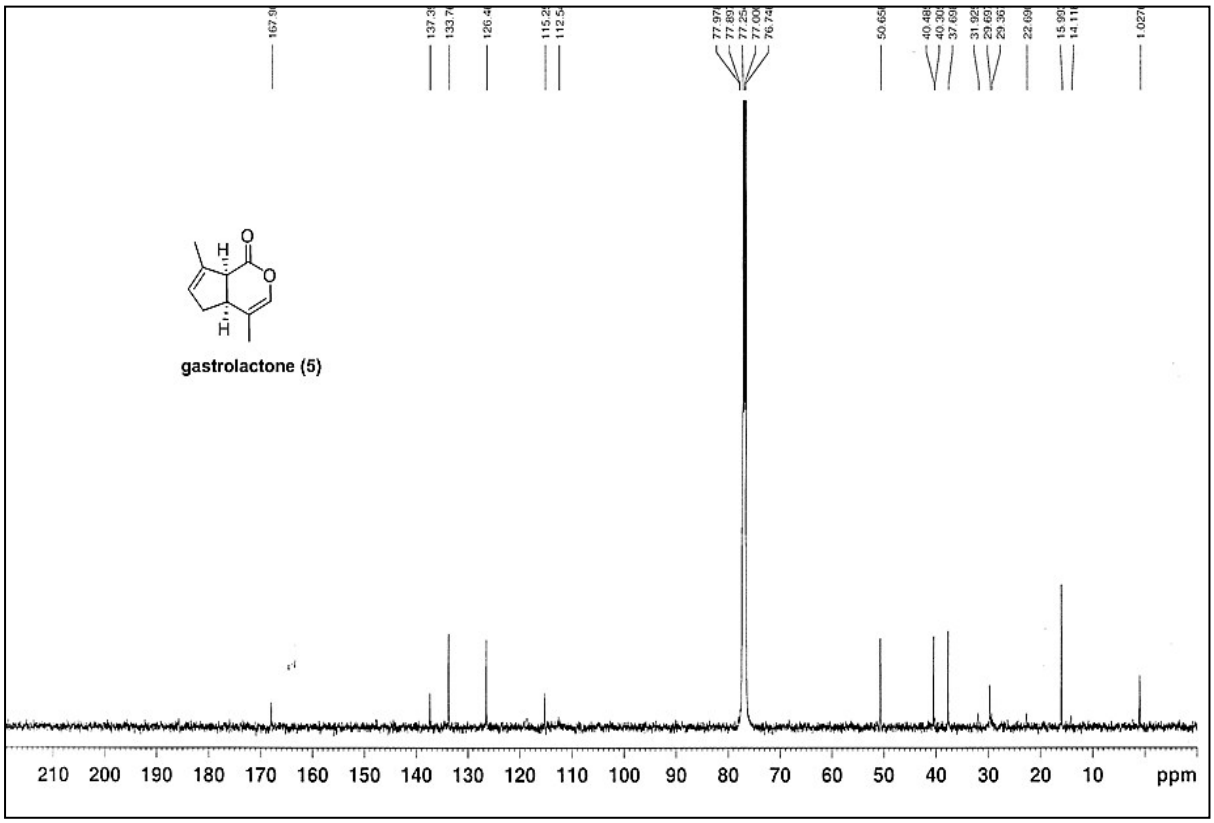
▲ ^{1}H-NMR (500 MHz, $CDCl_3$)



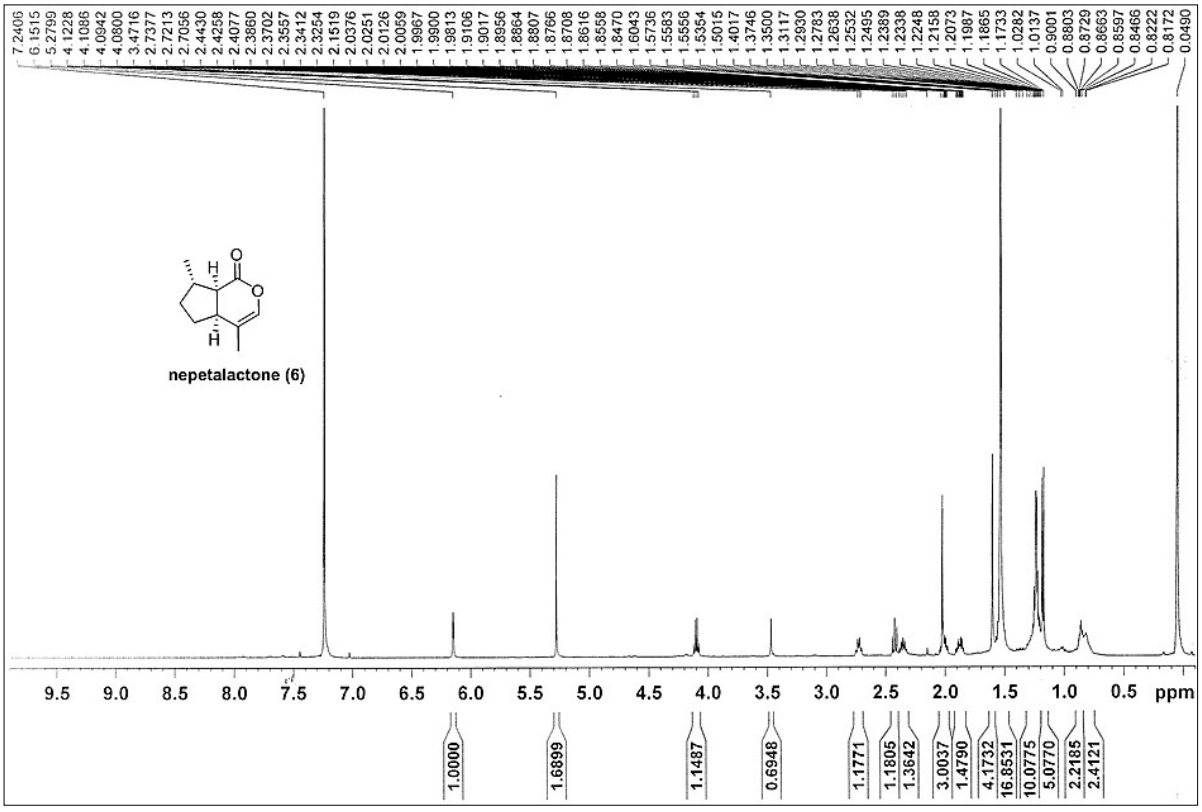
▲ ^{13}C-NMR (125 MHz, $CDCl_3$)



▲ ^{1}H-NMR (500 MHz, $CDCl_3$)



▲ ^{13}C-NMR (125 MHz, $CDCl_3$)



▲ ^{1}H-NMR (500 MHz, $CDCl_3$)