Synthesis of Bridged Inside-Outside Bicyclic Ethers through Oxidative Transannular Cyclization Reactions

Xun Han and Paul E. Floreancig*
Department of Chemistry, University of Pittsburgh, Pittsburgh, Pennsylvania 15260
florean@pitt.edu

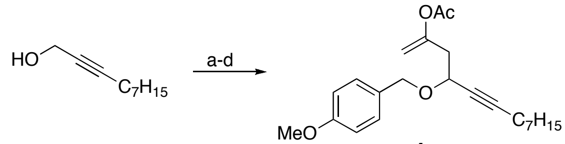
Supporting Information

Table of Contents

General Information

Proton (^{1}H NMR) and carbon (^{13}C NMR) nuclear magnetic resonance spectra were recorded on a Bruker Avance 300 spectrometer at 300 MHz and 75 MHz, a Bruker Avance 400 spectrometer at 400 MHz and 100 MHz, a Bruker Avance 500 spectrometer at 500 MHz and 125 MHz. The chemical shifts are reported in parts per million (ppm) on the delta (δ) scale. The solvent peak was used as a reference value, for ^{1}H NMR: $CDCl_3$ = 7.27 ppm, C_6D_6 = 7.16 ppm, for ^{13}C NMR: $CDCl_3$ = 77.23, C_6D_6 = 128.4 ppm. Data are reported as follows: (s = singlet; d = doublet; t = triplet; q = quartet; sept = septet; dd = doublet of doublets; ddd = doublet of doublet of doublets; dddd = doublet of doublet of doublet of doublet; td = triplet of doublets; dtd = doublet of triplet of doublets; br = broad). High resolution and low resolution mass spectra were recorded on a VG 7070 spectrometer. Infrared (IR) spectra were collected on a Mattson Cygnus 100 spectrometer. Samples for IR were prepared as a thin film on a NaCl plate by dissolving the compound in CH_2Cl_2 and then evaporating the CH_2Cl_2. Tetrahydrofuran and diethyl ether were distilled from sodium and benzophenone. Methylene chloride was distilled under N_2 from CaH_2. Analytical TLC was performed on E. Merck pre-coated (25 mm) silica gel 60F-254 plates. Visualization was done under UV (254 nm). Flash chromatography was done using ICN SiliTech 32-63 60 Å silica gel. Reagent grade ethyl acetate, diethyl ether, toluene and hexanes (commercial mixture) were purchased from EM Science and used as is for chromatography. All products in this manuscript are racemic mixtures but are drawn and named as single enantiomers to indicate their relative stereochemistry.

Experimental Section

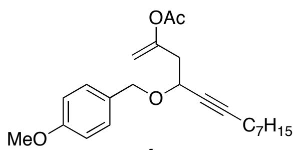


4

Reagents and conditions

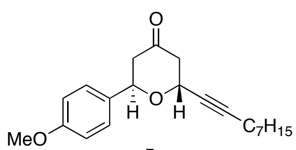
a) SO_3•Py, DMSO, Et_3N, CH_2Cl_2, 79%. b)[1] Propargyl bromide, Zn, ICH_2CH_2I, THF, sonication, 87%. c)[2] PMBOC(NH)CCl_3, $La(OTf)_3$, PhMe, 94%. d)[3] HOAc, $[(p\text{-cymene})RuCl_2]_2$, Fur_3P, Na_2CO_3, PhMe, 80 °C, 45%.

Scheme 1. Synthesis of **4**.

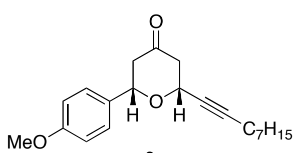


4

4-(4-methoxybenzyloxy)tridec-1-en-5-yn-2-yl acetate (4).
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.31-7.28 (m, 2H), 6.90-6.87 (m, 2H), 4.85 (s, 2H), 4.72 (d, 1H, J = 11.4 Hz), 4.45 (d, 1H, J = 11.4 Hz), 4.22 (ddt, 1H, J = 2.1, 6.3, 7.2 Hz), 3.81 (s, 3H), 2.66 (dd, 2H, J = 5.4, 7.2 Hz), 2.25 (td, 2H, J = 1.8, 6.9 Hz) 2.05 (s, 3H), 1.59-1.49 (m, 2H), 1.44-1.29 (m, 8H), 0.90 (t, 3H, J = 6.9 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.3, 159.4, 152.3, 130.1, 129.9, 113.9, 104.3, 87.4, 78.2, 70.1, 66.1, 55.5, 40.6, 32.0, 29.0, 28.9, 22.8, 21.2, 18.9, 14.3; IR (neat) 2930, 2857, 1758, 1667, 1613, 1586, 1514, 1464, 1369, 1341, 1302, 1249, 1206, 1137, 1081, 1036, 965, 875, 823, 758, 721 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{23}H_{32}O_4Na$ [M+Na]$^+$ 395.2198, found 395.2190.



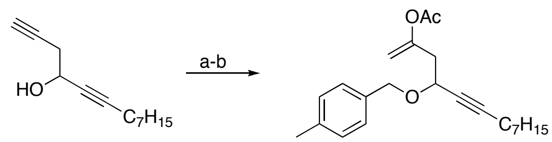
5



6

Cyclization of 4 to form 5 and 6.
To a suspension of substrate **4** (152 mg, 0.408 mmol), 2,6-dichloropypyridine (241 mg, 1.63 mmol), and 4 Å molecular sieves (304 mg) in anhydrous DCE (4 mL) was added DDQ (186 mg, 0.820 mmol) in one portion at rt. The mixture was stirred at rt for 1 h, and then was quenched by the addition of NEt_3. The mixture was loaded directly onto a short plug of silica gel and eluted with dichloromethane and EtOAc. The filtrate was concentrated and purified by flash chromatography (hexane:EtOAc, 30:1 to 15:1) to give the *trans* and *cis* products (97 mg, total mass, *trans*/*cis* = 2.8/1, 72% total yield). **5**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.35-7.30 (m, 2H), 6.94-6.89 (m, 2H), 5.26 (dd, 1H, J = 5.4, 8.4 Hz), 5.18 (ddt, 1H, J = 1.5, 1.8, 6.6 Hz), 3.82 (s, 3H), 2.81 (dd, 1H, J = 6.9, 14.1 Hz), 2.64-2.61 (m, 2H), 2.53 (d, 1H, J = 14.1 Hz), 2.23 (td, 2H, J = 2.1, 6.9 Hz), 1.54-1.47 (m, 2H), 1.40-1.26 (m, 8H), 0.89 (t, 3H, J = 6.9 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 205.3, 159.7, 132.8, 127.7, 114.2, 90.6, 76.6, 73.7, 65.8, 55.5, 49.4, 47.6, 31.9, 29.0, 29.0, 28.7, 22.8, 18.9, 14.3; IR (neat) 2929, 2856, 1724, 1613, 1515, 1463, 1367, 1334, 1304, 1248, 1177, 1104, 1054, 1035, 946, 829 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{21}H_{29}O_3$ [M]$^+$ 329.2117, found 329.2116.

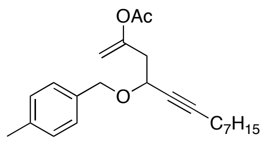
6: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.35-7.29 (m, 2H), 6.93-6.88 (m, 2H), 4.58 (dd, 1H, J = 3.3, 10.8 Hz), 4.53 (ddt, 1H, J = 1.8, 3.3, 11.1 Hz), 3.81 (s, 3H), 2.80-2.54 (m, 4H), 2.23 (td, 2H, J = 2.1, 7.2 Hz), 1.55-1.47 (m, 2H), 1.38-1.26 (m, 8H), 0.89 (t, 3H, J = 6.9 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 205.5, 159.8, 132.4, 127.7, 114.2, 88.0, 78.6, 67.8, 55.6, 53.6, 49.4, 48.5, 31.9, 29.0, 29.0, 28.6, 22.8, 19.0, 14.3; IR (neat) 2926, 2854, 1723, 1613, 1515, 1462, 1344, 1302, 1250, 1177, 1161, 1043, 952, 830 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{21}H_{29}O_3$ [M]$^+$ 329.2117, found 329.2108.



8

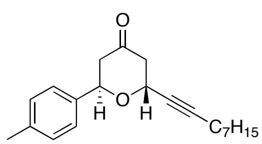
Reagents and conditions
a) NaH, THF, then p-methylbenzyl bromide, Bu_4NI, 99% b) HOAc, [(*p*-cymene)$RuCl_2$]$_2$, Fur_3P, Na_2CO_3, PhMe, 80 °C, 58%.

Scheme 2. Synthesis of **8**.

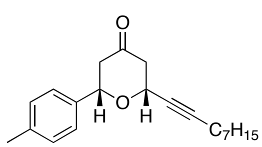


8

4-(4-methylbenzyloxy)tridec-1-en-5-yn-2-yl acetate (8).
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.25 (d, 2H, *J* = 8.0 Hz), 7.15 (d, 2H, *J* = 8.0 Hz), 4.85 (s, 2H), 4.74 (d, 1H, *J* = 11.6), 4.48 (d, 1H, *J* = 11.6 Hz), 4.23 (t, 1H, *J* = 6.8 Hz), 2.66 (app dd, 2H, *J* = 6.8, 8.0 Hz), 2.35 (s, 3H), 2.24 (app dd, 2H, *J* = 5.6, 6.8 Hz), 2.05 (s, 3H), 1.56-1.49 (m, 2H), 1.42-1.37 (m, 2H), 1.34-1.26 (m, 6H), 0.90 (t, 3H, *J* = 6.8 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 169.3, 152.3, 137.5, 135.0, 129.2, 128.4, 104.3, 87.5, 78.2, 70.3, 66.3, 40.6, 32.0, 29.0, 28.9, 22.9, 21.4, 21.3, 18.9, 14.3; IR (neat) 2928, 2857, 1759, 1668, 1458, 1433, 1369, 1340, 1204, 1083, 1020, 874, 803 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{23}H_{32}O_3Na$ [M+Na]$^+$ 379.2249, found 379.2222.



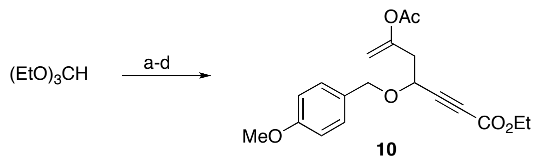
9



9'

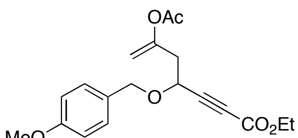
Cyclization of 8 to form 9 and 9'.
To a suspension of substrate **8** (29 mg, 0.081 mmol), 2,6-dichloropypyridine (47 mg, 0.32 mmol), 4 Å molecular sieves (57 mg) in anhydrous DCE (1 mL) was added DDQ (36 mg, 0.16 mmol) in one portion at rt. The mixture was stirred at rt for 6 h, and then was quenched by the addition of NEt_3. The mixture was loaded directly onto a short plug of silica gel and eluted with dichloromethane and EtOAc. The filtrate was concentrated and purified by flash chromatography to give both *trans* and *cis* products (18 mg, total mass, *trans*/*cis* = 3.3/1, 72% total yield). **9**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.28 (d, 2H, *J* = 8.4 Hz), 7.20 (d, 2H, *J* = 8.0 Hz), 5.27 (dd, 1H, *J* = 4.0, 10.0 Hz), 5.20 (ddt, 1H, *J* = 1.6, 2.4, 5.2 Hz), 2.89 (dd, 1H, *J* = 6.8, 14.0 Hz), 2.68-2.57 (m, 2H), 2.54 (dt, 1H, *J* = 1.6, 14.4 Hz), 2.36 (s, 3H), 2.23 (td, 2H, *J* = 2.0, 7.2 Hz), 1.55-1.47 (m, 2H), 1.39-1.33 (m, 2H), 1.31-1.28 (m, 6H), 0.89 (t, 3H, *J* = 6.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 205.3, 138.1, 137.7, 129.5, 126.2, 90.7, 76.5, 73.9, 65.8, 49.5, 47.6, 32.0, 29.0, 29.0, 28.7, 22.8, 21.4, 18.9, 14.3; IR (neat) 2927, 2856, 1724, 1516, 1459, 1415, 1365, 1333, 1225, 1161, 1104, 1055, 1021, 945, 809 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{21}H_{29}O_2$ [M]$^+$ 313.2168, found 313.2161.

9': ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29 (d, 2H, *J* = 8.0 Hz), 7.19 (d, 2H, *J* = 8.0 Hz), 4.60 (dd, 1H, *J* = 3.2, 10.8 Hz), 4.53 (ddt, 1H, *J* = 2.0, 2.8, 8.4 Hz), 2.76 (dd, 1H, *J* = 11.6, 14.4 Hz), 2.68-2.57 (m, 3H), 2.35 (s, 3H), 2.24 (td, 2H, *J* = 2.0, 7.2 Hz), 1.57-1.49 (m, 2H), 1.37-1.33 (m, 2H), 1.31-1.28 (m, 6H), 0.89 (t, 3H, *J* = 6.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 205.5, 138.3, 137.3, 129.5, 126.2, 88.0, 78.8, 77.6, 67.8, 49.4, 48.5, 31.9, 29.0, 29.0, 28.6, 22.8, 21.4, 19.0, 14.3; IR (neat) 2927, 2856, 1724, 1516, 1460, 1380, 1344, 1305, 1246, 1161, 1135, 1054, 953, 811, 719 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{21}H_{29}O_2$ [M]$^+$ 313.2168, found 313.2169.



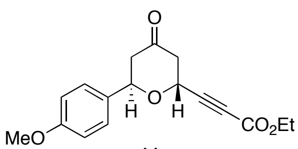
Reagents and conditions
a)[4] Ethyl propiolate, ZnI_2, 50-100 °C, then HCO_2H. b) Propargyl bromide, Zn, ICH_2CH_2I, THF, sonication. c) PMBOC(NH)CCl_3, La(OTf)$_3$, PhMe. d) HOAc, [(*p*-cymene)$RuCl_2$]$_2$, Fur$_3$P, Na_2CO_3, PhMe, 80 °C, 4% over 4 steps.

Scheme 3. Synthesis of **10**.

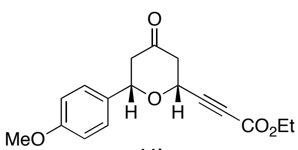


10

Ethyl 6-acetoxy-4-(4-methoxybenzyloxy)hept-6-en-2-ynoate (10).
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.29 (d, 2H, *J* = 8.5 Hz), 6.89 (d, 2H, *J* = 9.0 Hz), 4.90 (d, 1H, *J* = 2.0 Hz), 4.89 (s, 1H), 4.75 (d, 1H, *J* = 11.0 Hz), 4.46 (d, 1H, *J* = 11.0 Hz), 4.33 (t, 1H, *J* = 6.5 Hz), 4.26 (q, 2H, *J* = 7.0 Hz), 3.81 (s, 3H), 2.73-2.72 (m, 2H), 2.06 (s, 3H), 1.34 (t, 3H, *J* = 7.0 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 169.2, 159.7, 153.4, 150.9, 130.1, 129.1, 114.0, 105.3, 85.0, 78.2, 71.1, 65.5, 62.4, 55.5, 39.5, 21.2, 14.2; IR (neat) 2938, 2869, 2839, 2235, 1757, 1713, 1669, 1613, 1514, 1465, 1369, 1301, 1250, 1208, 1086, 1034, 882, 823, 752 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{19}H_{22}O_6Na$ [M+Na]$^+$ 369.1314, found 369.1331.

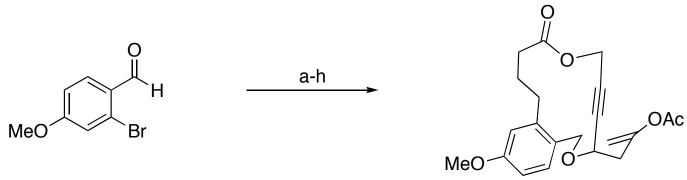


11



11'

Cyclization of 10 to form 11 and 11'.
To a suspension of substrate **10** (56 mg, 0.16 mmol), 2,6-dichloropypyridine (96 mg, 0.65 mmol) and 4 Å molecular sieves (113 mg) in anhydrous DCE (1.6 mL) was added DDQ (75 mg, 0.33 mmol) in one portion at rt. The mixture was stirred at rt for 9.5 h, and then was quenched by the addition of 0.1 mL NEt_3. The mixture was loaded directly onto a short plug of silica gel and eluted with dichloromethane and EtOAc. The filtrate was concentrated and purified by flash chromatography (hexane:EtOAc, 10:1 to 8:1) to give the desired product (22 mg, total mass, *trans*/*cis* = 1.6/1, 45% total yield) as an inseparable mixture. Mixture of **11** and **11'**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34-7.30 (m, 2H), 6.94-6.91 (m, 2H), 5.29 (dd, 0.6H, *J* = 2.0, 7.6 Hz), 5.22 (dd, 0.6H, *J* = 5.2, 9.2 Hz), 4.68 (dd, 0.4H, *J* = 3.2, 11.6 Hz), 4.62 (dd, 0.4H, *J* = 3.2, 10.8 Hz), 4.25 (q, 2H, *J* = 7.2 Hz), 3.82 (s, 1.8H), 3.82 (s, 1.2H), 2.94 (dd, 0.6H, *J* = 7.6, 14.8 Hz), 2.82 (dd, 0.4H, *J* = 12.0, 14.8 Hz), 2.75-2.62 (m, 3H), 1.33 (t, 1.8H, *J* = 6.8 Hz), 1.31 (t, 1.2H, *J* = 6.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 203.6, 203.5, 160.0, 159.9, 153.1, 152.9, 131.8, 131.7, 127.7, 127.5, 114.3, 83.0, 82.6, 80.2, 79.1, 78.0, 74.8, 66.7, 64.9, 62.6, 62.6, 55.5, 49.2, 49.0, 46.5, 45.7, 14.2; IR (neat) 2980, 2934, 2840, 1716, 1643, 1613, 1587, 1516, 1464, 1367, 1337, 1302, 1252, 1178, 1152, 1059, 1033, 950, 833, 751 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{17}H_{19}O_5$ [M]$^+$ 303.1232, found 303.1238.

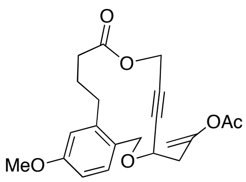


12

Reagents and conditions

a)[5] Methyl butenoate, 9-BBN, Pd(dppf)Cl_2, K_2CO_3, DMF, 50 °C. b) $NaBH_4$, MeOH, 0 °C, 80% (two steps). c) Cl_3CCN, DBU, CH_2Cl_2, 55%. d) 2,6-Heptadiyn-1-ol, La$(OTf)_3$, PhMe. e) *p*-TsOH, MeOH, 42% (two steps). f) LiOH, THF, MeOH, H_2O. g) 2,4,6-Trichlorobenzoyl chloride, Et_3N, THF, then DMAP, PhMe, 65 °C. h) HOAc, [Ru(*p*-cymene)Cl_2]$_2$, Fur_3P, 1-decyne, Na_2CO_3, PhMe, 80 °C, 11% (three steps).

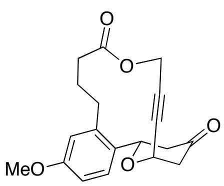
Scheme 4. Synthesis of **12**. Note: Compounds **14** and **16** were prepared through similar sequences.



12

Macrolactone substrate 12.

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.21 (d, 1H, *J* = 7.8 Hz), 6.74-6.70 (m, 2H), 4.89 (s, 1H), 4.85 (d, 1H, *J* = 1.5 Hz), 4.77 (d, 2H, *J* = 2.1), 4.76 (d, 1H, *J* = 9.6 Hz), 4.30 (tt, 1H, *J* = 2.1, 6.9 Hz), 4.17 (d, 1H, *J* = 9.3 Hz), 2.93-2.83 (m, 1H), 2.68 (dd, 1H, *J* = 6.9, 15.0), 2.62-2.37 (m, 3H), 2.08 (s, 3H), 2.00-1.88 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 173.3, 169.0, 160.0, 151.4, 143.1, 132.7, 127.1, 115.4, 111.2, 104.6, 84.8, 81.2, 68.0, 67.1, 55.2, 52.0, 39.4, 34.4, 31.2, 29.3, 21.1; IR (neat) 2922, 2852, 1745, 1667, 1611, 1579, 1503, 1461, 1439, 1368, 1324, 1258, 1215, 1132, 1110, 1044, 1025 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{21}H_{24}O_6Na$ $[M+Na]^+$ 395.1471, found 395.1475.

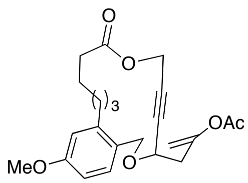


13

Cyclization of 12 to form 13.

To a suspension of macrolactone substrate **12** (46 mg, 0.12 mmol), 2,6-dichloropypyridine (77 mg, 0.52 mmol) and 4 Å molecular sieves (92 mg) in anhydrous DCE (1.3 mL) was added DDQ (59 mg, 0.26 mmol) in one portion at rt. The mixture was stirred at rt for 4 h, and then was quenched by the addition of 10 drops of NEt_3. The mixture was loaded directly onto a short plug of silica gel and eluted with dichloromethane and EtOAc. The filtrate was concentrated and purified by flash chromatography (hexane:EtOAc, 5:1 to 3:1) to give the desired product (29 mg, 72%). **13**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34 (d, 1H, *J* = 8.4 Hz), 6.81 (dd, 1H, *J* = 2.8, 8.8 Hz), 6.76 (d, 1H, *J* = 2.8 Hz), 5.36 (dd, 1H, *J* = 2.0, 12.4 Hz), 5.10 (app dt, 1H, *J* = 1.2, 7.2 Hz), 4.84 (dd, 1H, *J* = 3.2, 15.2 Hz), 4.69 (dd, 1H, *J* = 1.6, 14.8 Hz), 3.81 (s, 3H), 2.98-2.81 (m, 3H), 2.62-2.49 (m, 4H), 2.40 (ddd, 1H, *J* = 3.6, 11.2, 12.4 Hz), 2.01-1.79 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 204.7, 172.6, 159.9, 142.5, 128.3, 127.4, 115.8, 111.8, 84.2, 82.6, 69.2, 65.5, 55.2, 51.7, 46.8, 46.2, 34.5, 31.4, 29.1; IR (neat) 2923, 2851, 1740, 1611, 1579, 1504, 1441, 1368, 1334, 1275, 1255, 1233, 1158, 1131, 1110, 1048, 1024, 996, 952, 818, 733 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{19}H_{20}O_5Na$ $[M+Na]^+$ 351.1208, found 351.1199.

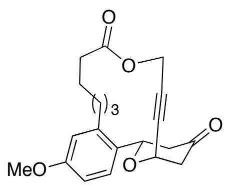
Macrolactone substrate 14.



14

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.23 (d, 1H, *J* = 8.8 Hz), 6.72-6.69 (m, 2H), 4.91 (s, 1H), 4.88 (d, 1H, *J* = 1.6 Hz), 4.84 (d, 1H, *J* = 10.4 Hz), 4.79 (d, 2H, *J* = 2.0 Hz), 4.36 (tt, 1H, *J* = 2.0, 6.4 Hz), 4.33 (d, 1H, *J* = 10.6 Hz), 3.79 (s, 3H), 2.77-2.71 (m, 2H), 2.65 (dd, 1H, *J* = 6.0, 14.8 Hz), 2.60-2.52 (m, 1H), 2.42-2.38 (m, 2H), 2.09 (s, 3H), 1.78-1.72 (m, 2H), 1.65-1.49 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.0, 169.3, 159.6, 151.7, 143.5, 130.8, 127.6, 115.1, 110.9, 104.9, 84.4, 81.0, 68.6, 66.8, 55.4, 51.7, 39.9, 33.8, 33.1, 30.4, 28.8, 24.5, 21.3; IR (neat) 2923, 2853, 1745, 1667, 1610, 1579, 1502, 1462, 1369, 1325, 1259, 1209, 1135, 1111, 1067, 1032 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{23}H_{28}O_6Na$ $[M+Na]^+$ 423.1784, found 423.1768.

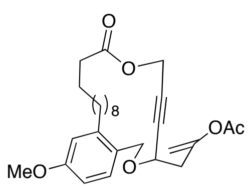
Cyclization of 14 to form 15.



15

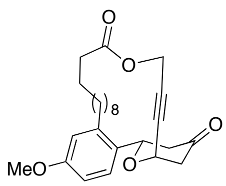
To a suspension of macrolactone substrate **14** (32 mg, 0.08 mmol), 2,6-dichloropypyridine (48 mg, 0.32 mmol), 4 Å molecular sieves (65 mg) in anhydrous DCE (0.85 mL) was added DDQ (37 mg, 0.16 mmol) in one portion at rt. The mixture was stirred at rt for 1 h, and then was quenched by the addition of 10 drops of NEt_3. The mixture was loaded directly onto a short plug of silica gel and eluted with dichloromethane and EtOAc. The filtrate was concentrated and purified by flash chromatography (hexane:EtOAc, 8:1 to 3:1) to give the desired product (23 mg, 81%). **15**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40 (d, 1H, *J* = 8.8 Hz), 6.80 (dd, 1H, *J* = 2.8, 8.4 Hz), 6.71 (d, 1H, *J* = 2.8 Hz), 5.43 (dd, 1H, *J* = 2.8, 11.6 Hz), (app d, 1H, *J* = 6.8 Hz), 4.83 (dd, 1H, *J* = 2.0, 15.2 Hz), 4.72 (dd, 1H, *J* = 3.2, 15.6 Hz), 3.80 (s, 3H), 2.92 (dd, 1H, *J* = 7.2, 14.4 Hz), 2.73-2.52 (m, 5H), 2.39 (t, 2H, *J* = 6.4 Hz), 1.81-1.75 (m, 1H), 1.73-1.57 (m, 3H), 1.53-1.46 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 204.9, 172.7, 159.7, 142.0, 130.0, 127.2, 115.0, 111.8, 83.2, 82.5, 70.7, 65.7, 55.4, 51.6, 49.1, 46.6, 33.7, 33.2, 30.7, 28.6, 24.4; IR (neat) 2934, 2861, 1739, 1610, 1580, 1503, 1458, 1371, 1333, 1266, 1229, 1158, 1113, 1056, 1023, 984, 947, 816, 731 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{21}H_{24}O_5Na$ $[M+Na]^+$ 379.1521, found 379.1543.

Macrolactone substrate 16



16

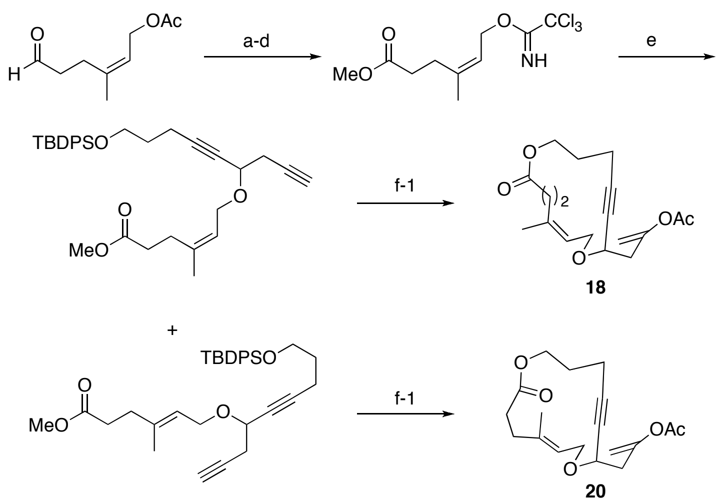
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.28 (d, 1H, *J* = 7.6 Hz), 6.73-6.71 (m, 2H), 4.88 (d, 2H, *J* = 3.6 Hz), 4.79 (d, 1H, *J* = 10.8 Hz), 4.76 (s, 2H), 4.36 (d, 1H, *J* = 10.8 Hz), 4.38-4.35 (m, 1H), 3.80 (s, 3H), 2.70 (dd, 2H, *J* = 7.2, 13.2 Hz), 2.64 (dd, 2H, *J* = 6.8, 10.0 Hz), 2.38 (t, 2H, 6.4 Hz), 2.06 (s, 3H), 1.72-1.68 (m, 2H), 1.62-1.58 (m, 2H), 1.38-1.26 (m, 12H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.4, 169.3, 159.5, 151.8, 143.4, 130.9, 127.7, 115.1, 111.1, 104.9, 85.2, 80.7, 68.4, 67.1, 55.4, 52.4, 40.2, 33.9, 33.2, 31.5, 29.2, 28.2, 27.8, 27.6, 27.5, 27.2, 24.5, 21.3; IR (neat) 2928, 2856, 1753, 1668, 1611, 1579, 1503, 1461, 1370, 1342, 1207, 1114, 1077, 1023, 875, 818 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{28}H_{38}O_6Na$ $[M+Na]^+$ 493.2566, found 493.2559.



17

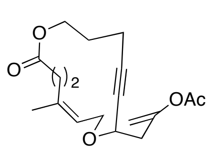
Cyclization of 16 to form 17.

To a suspension of macrolactone substrate **16** (50 mg, 0.11 mmol), 2,6-dichloropypyridine (63 mg, 0.42 mmol) and 4 Å molecular sieves (100 mg) in anhydrous DCE (1.3 mL) was added DDQ (48 mg, 0.21 mmol) in one portion at rt. The mixture was stirred at rt for 40 min, and then was quenched by the addition of 10 drops of NEt_3. The mixture was loaded directly onto a short plug of silica gel and eluted with dichloromethane and EtOAc. The filtrate was concentrated and purified by flash chromatography (hexane:EtOAc, 15:1 to 5:1) to give the desired product (30 mg, *trans*/*cis* = 6/1, 65% total yield; *cis* product has not been separated out from its *trans* isomer. *Trans*/*cis* ratio is based on integrating characteristic signals in the ^{1}H NMR spectrum.). **17**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39 (d, 1H, *J* = 8.4 Hz), 6.80 (dd, 1H, *J* = 2.8, 8.4 Hz), 6.74 (d, 1H, *J* = 2.8 Hz), 5.47 (dd, 1H, *J* = 2.8, 11.2 Hz), 5.25 (d, 1H, *J* = 6.0 Hz), 4.80 (dd, 1H, *J* = 1.2, 16.0 Hz), 4.70 (dd, 1H, *J* = 2.0, 16.0 Hz), 3.81 (s, 3H), 2.94 (dd, 1H, *J* = 7.2, 14.0 Hz), 2.77-2.70 (m, 2H), 2.63-2.55 (m, 3H), 2.39 (t, 2H, *J* = 6.8 Hz), 1.72-1.58 (m, 4H), 1.41-1.26 (m, 12H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 204.9, 173.4, 159.6, 142.5, 129.8, 127.7, 115.3, 111.8, 83.6, 83.4, 70.6, 65.5, 55.5, 52.3, 48.9, 46.9, 33.7, 33.2, 31.8, 29.7, 28.3, 27.5, 27.2, 26.9, 26.2, 24.1; IR (neat) 2928, 2855, 1739, 1610, 1579, 1504, 1461, 1335, 1230, 1160, 1052, 946, 816, 732, 705 cm^{-1}; $C_{26}H_{35}O_5$ $[M]^+$ 427.2484, found 427.2493.



Reagents and conditions
a)[6] $NaClO_2$, NaH_2PO_4, 2-methyl-2-butene, ^{t}BuOH, H_2O, –10 °C. b) K_2CO_3, MeOH. c) MeI, K_2CO_3, acetone. d) Cl_3CCN, DBU, CH_2Cl_2, 29% (4 steps). e) 4,8-Nonadiyne-1,6-diol, TMSOTf, C_6H_{12}, 0 °C, 18% *Z*, 21% *E*. f) LiOH, THF, MeOH, H_2O. g) Bu_4NF, THF. h)[7] 2-Chloro-1-methyl-pyridinium iodide, Et_3N, CH_3CN, reflux. i) HOAc, $[Ru(p\text{-cymene})Cl_2]_2$, 1-decyne, Na_2CO_3, PhMe, 80 °C, 11% **18**, 21% **20** (four steps).

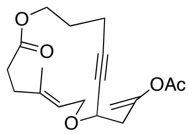
Scheme 5. Synthesis of **18** and **20**.



18

Macrolactone substrate 18.

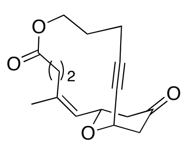
^{1}H NMR (400 MHz, $CDCl_3$) δ 5.44 (td, 1H, *J* = 1.2, 7.6 Hz), 4.88 (s, 1H), 4.85 (d, 1H, *J* = 1.6 Hz), 4.30-4.17 (m, 4H), 3.95 (dd, 1H, *J* = 7.2, 10.4 Hz), 2.62 (app dd, 2H, *J* = 4.8, 6.4 Hz), 2.59-2.49 (m, 3H), 2.47-2.43 (m, 2H), 2.42-2.35 (m, 1H), 2.14 (s, 3H), 1.90-1.84 (m, 2H), 1.79 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.3, 169.3, 152.2, 142.6, 121.8, 104.3, 86.4, 79.3, 66.1, 64.6, 64.0, 40.4, 34.7, 28.2, 26.8, 23.4, 21.3, 17.2; IR (neat) 2924, 2856, 1755, 1733, 1667, 1433, 1369, 1338, 1249, 1203, 1065, 1019, 969, 879 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{18}H_{24}O_5Na$ [M+Na]$^+$ 343.1521, found 343.1566.



20

Macrolactone substrate 20.

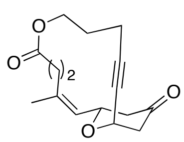
^{1}H NMR (400 MHz, $CDCl_3$) δ 5.55 (td, 1H, *J* = 1.2, 6.4 Hz), 4.85 (s, 1H), 4.84 (d, 1H, *J* = 1.6 Hz), 4.37 (dd, 1H, *J* = 6.0, 14.0 Hz), 4.27-4.12 (m, 3H), 4.02 (dd, 1H, *J* = 6.0, 14.0 Hz), 2.62-2.56 (m, 2H), 2.53-2.47 (m, 2H), 2.46-2.42 (m, 2H), 2.38-2.35 (m, 2H), 2.14 (s, 3H), 1.79 (p, 2H, *J* = 6.0 Hz), 1.66 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.6, 169.3, 152.2, 134.8, 124.0, 104.4, 84.1, 81.9, 67.8, 67.5, 62.3, 40.8, 35.1, 32.5, 25.0, 21.3, 16.1, 15.4; IR (neat) 2924, 2856, 1734, 1669, 1574, 1433, 1368, 1343, 1206, 1069, 1022, 969, 882 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{18}H_{24}O_5Na$ [M+Na]$^+$ 343.1521, found 343.1515.



19

Cyclization reaction of 18 to form 19.

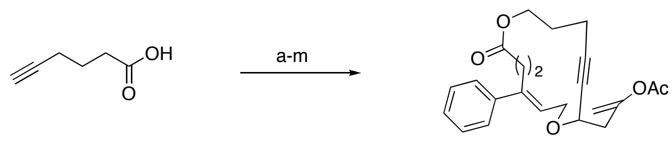
To a suspension of macrolactone substrate **18** (36 mg, 0.11 mmol), 2,6-dichloropyridine (100 mg, 0.674 mmol), $LiClO_4$ (3.0 mg, 0.028 mmol), 4 Å molecular sieves (72 mg) in anhydrous DCE (1.4 mL) was added DDQ (76 mg, 0.34 mmol) in one portion at rt. The mixture was stirred at rt for 23 hs, and then 26 mg DDQ (1.0 eq.) was added. The resulting mixture was stirred for 3 h at rt, and then was quenched with NEt_3. The black mixture was loaded directly onto a short plug of silica gel and eluted with dichloromethane and EtOAc. The filtrate was concentrated and purified by flash chromatography (hexane:EtOAc, 10:1 to 6:1) to give the desired *trans*-product (17 mg, 54%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.31 (dd, 1H, *J* = 1.2, 8.8 Hz), 5.08 (app dd, 1H, *J* = 1.2, 7.6 Hz), 4.95 (td, 1H, *J* = 5.6, 8.8 Hz), 4.28-4.23 (m, 1H), 4.14-4.09 (m, 1H), 2.78 (dd, 1H, *J* = 7.2, 14.0 Hz), 2.57-2.32 (m, 9H), 1.90-1.83 (m, 2H), 1.80 (d, 3H, *J* = 1.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 205.4, 172.8, 142.7, 125.4, 89.1, 77.8, 68.5, 65.9, 64.4, 48.2, 47.0, 34.7, 29.1, 26.2, 23.5, 16.9; IR (neat) 2922, 2852, 1731, 1436, 1380, 1332, 1249, 1154, 1106, 1051, 937, 893 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{16}H_{20}O_4Na$ [M+Na]$^+$ 299.1259, found 299.1248.



19

Cyclization reaction of 20 to form 19.

To a suspension of macrolactone substrate **20** (20 mg, 0.062 mmol), 2,6-dichloropypyridine (55 mg, 0.37 mmol), $LiClO_4$ (1.7 mg, 0.016 mmol), 4 Å molecular sieves (40 mg) in anhydrous DCE (0.8 mL) was added DDQ (42 mg, 0.19 mmol) in one portion at rt. The mixture was stirred at rt for 43 hours and then was quenched with NEt_3. The black mixture was loaded directly onto a short plug of silica gel and eluted with dichloromethane and EtOAc. The filtrate was concentrated and purified by flash chromatography to give the *trans*-product **19** (6.0 mg, 35%).

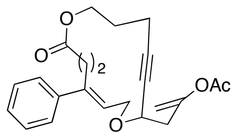


21

Reagents and conditions

a) (3-Methyloxetan-3-yl)methanol[8], DCC, DMAP, CH_2Cl_2. b) BF_3•OEt_2, CH_2Cl_2, 0 °C, 71% (two steps). c) ^nBuLi, THF, –78 °C, then $(CH_2O)_n$, 0 °C, 85%. d) HOAc, H_2O, THF. e) K_2CO_3, MeOH, 85% (two steps). f)[9] Dimethyl(thiophen-2-yl)silane, H_2PtCl_6, THF, 50 °C, 45% (+ 42% regioisomer). g)[10] PhI, Bu_4NF, $Pd_2(dba)_3$, THF, 76%. h) Cl_3CCN, DBU, CH_2Cl_2, 92%. i) TMSOTf, 4,8-Nonadiyne-1,6-diol, C_6H_{12}, 0 °C, 41%. j) Bu_4NF, THF, 78%. k) LiOH, THF, MeOH, H_2O. l) 2-Chloro-1-methylpyridinium iodide, Et_3N, CH_3CN, reflux 46% (two steps). m) HOAc, 1-decyne, $[Ru(p\text{-cymene})Cl_2]_2$, Fur_3P, Na_2CO_3, PhMe, 80 °C, 53%.

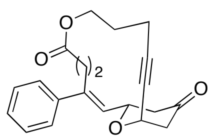
Scheme 6. Synthesis of **21**.



21

Macrolactone substrate 21.

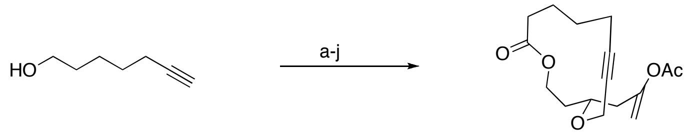
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39-7.25 (m, 5H), 5.82 (t, 1H, *J* = 6.4 Hz), 4.90 (s, 1H), 4.87 (d, 1H, *J* = 1.6 Hz), 4.39 (dd, 1H, *J* = 6.8 12.0 Hz), 4.35-4.28 (m, 3H), 4.18 (dd, 1H, *J* = 6.8, 12.0 Hz), 2.68-2.61 (m, 4H), 2.59-2.43 (m, 2H), 2.40-2.28 (m, 2H), 2.13 (s, 3H), 1.96-1.84 (m, 2H), 1.81-1.64 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.2, 169.3, 152.1, 143.4, 141.6, 128.6, 127.6, 126.7, 125.2, 104.6, 85.4, 80.0, 66.2, 64.9, 63.5, 40.3, 33.5, 28.8, 25.8, 24.1, 21.3, 16.2; IR (neat) 2929, 1755, 1730, 1667, 1493, 1433, 1368, 1245, 1204, 1080, 1020, 964, 917, 880, 761 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{24}H_{28}O_5Na$ $[M+Na]^+$ 419.1834, found 419.1841.



22

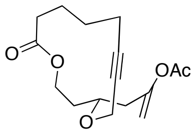
Cyclization reaction of 21 to form 22.

To a suspension of macrolactone **21** (38 mg, 0.096 mmol), 2,6-dichloropypyridine (57 mg, 0.38 mmol), $LiClO_4$ (3 mg, 0.03 mmol) and 4 Å molecular sieves (76 mg) in anhydrous DCE (1 mL) was added DDQ (44 mg, 0.19 mmol) in one portion at rt. The mixture was stirred at rt for 15 min, and then was quenched by with NEt_3. The mixture was loaded directly onto a short plug of silica gel and eluted with dichloromethane and EtOAc. The filtrate was concentrated and purified by flash chromatography (hexane:EtOAc, 8:1 to 4:1) to give the desired product **22** (24 mg, 72%). **22**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40-7.28 (m, 5H), 5.73 (d, 1H, *J* = 8.4 Hz), 5.14-5.10 (m, 2H), 4.37-4.24 (m, 2H), 2.83 (dd, 1H, *J* =7.2, 14.0 Hz), 2.63 (td, 2H, *J* = 4.0, 7.6 Hz), 2.56-2.37 (m, 6H), 2.32-2.25 (m, 1H), 1.93-1.81 (m, 2H), 1.80-1.68 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 204.9, 173.6, 144.6, 141.2, 128.7, 128.0, 127.3, 126.9, 88.5, 78.3, 69.2, 65.9, 63.4, 48.2, 47.2, 33.9, 29.5, 25.8, 23.9, 16.1; IR (neat) 2926, 1726, 1493, 1444, 1358, 1334, 1246, 1227, 1157, 1112, 1047, 937, 887, 764 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{22}H_{24}O_4Na$ $[M+Na]^+$ 375.1572, found 375.1584.



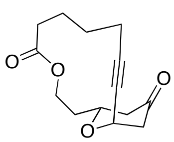
Reagents and conditions
a) TBSCl, imidazole, CH_2Cl_2. b) ^nBuLi, THF, –78 °C, then $(CH_2O)_n$, 0 °C, 93% (two steps). c) CBr_4, Ph_3P, CH_2Cl_2, MeOH, 0 °C. d) 5-Heptyne-1,3-diol 1-TBDPS ether, NaH, Bu_4NI, THF, 66%. e) PPTs, MeOH, CH_2Cl_2. f) Dess-Martin periodinane, $NaHCO_3$, CH_2Cl_2, 55% (two steps). g) $NaClO_2$, NaH_2PO_4, 2-methyl-2-butene, ^tBuOH, H_2O, –10 °C. h) Bu_4NF, THF. i) 2-Chloro-1-methylpyridinium iodide, Et_3N, CH_3CN, reflux. j) HOAc, $[Ru(p\text{-cymene})Cl_2]_2$, 1-decyne, Na_2CO_3, PhMe, 80 °C, 35% (four steps).

Scheme 7. Synthesis of **23**. Note: Compounds **25** and **27** were prepared through similar sequences.



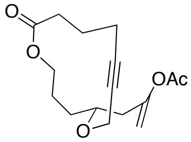
23

Macrolactone substrate 23.
^1H NMR (400 MHz, $CDCl_3$) δ 4.85 (d, 1H, J = 1.2 Hz), 4.83 (s, 1H), 4.30-4.19 (m, 2H), 4.14-4.05 (m, 3H), 2.58 (ddd, 1H, J = 2.0, 7.6, 14.4 Hz), 2.47 (t, 2H, J = 4.8 Hz), 2.37 (app dddd, 1H, J = 2.8, 5.6, 8.4, 17.2 Hz), 2.22-2.17 (m, 1H), 2.17 (s, 3H), 2.16-2.00 (m, 2H), 1.90 (ddt, 1H, J = 3.2, 12.0, 14.8 Hz), 1.83-1.76 (m, 1H), 1.74-1.67 (m, 2H), 1.51-1.44 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.8, 169.2, 153.0, 104.3, 86.0, 77.1, 69.6, 60.5, 56.8, 37.8, 35.0, 33.8, 27.7, 23.5, 21.3, 17.9; IR (neat) 2926, 2854, 1755, 1731, 1665, 1434, 1369, 1259, 1200, 1152, 1053 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{16}H_{22}O_5Na$ $[M+Na]^+$ 317.1365, found 317.1365.



24

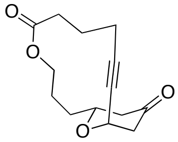
Cyclization of 23 to form 24.
To a suspension of macrolactone substrate **23** (177 mg, 0.60 mmol, **23**/regio-isomer = 8/1), 2,6-dichloropypyridine (888 mg, 6.0 mmol), $LiClO_4$ (51 mg, 0.48 mmol), 4 Å molecular sieves (355 mg) in anhydrous DCE (7 mL) was added DDQ (817 mg, 3.60 mmol) in one portion at rt. The mixture was stirred at 50 °C for 41.5 h, and then 272 mg DDQ (1.20 mmol) and 19 mg $LiClO_4$ was added. The resulting mixture was stirred at the same temperature for 20.5 h, and then was quenched by the addition of 1.5 mL NEt_3. The mixture was loaded directly onto a short plug of silica gel and eluted with dichloromethane and EtOAc. The filtrate was concentrated and purified by flash chromatography (hexane:EtOAc, 10:1 to 4:1) to give the desired product (49 mg, 36%) as colorless crystal. ^1H NMR (400 MHz, $CDCl_3$) δ 5.09-5.07 (m, 1H), 4.62-4.55 (m, 1H), 4.39-4.33 (m, 1H), 4.06 (dt, 1H, J = 4.0, 10.8 Hz), 2.74 (dd, 1H, J = 8.0, 14.8 Hz), 2.49 (ddd, 1H, J = 3.2, 6.8, 14.0 Hz), 2.45 (dt, 1H, J = 1.2, 14.4 Hz), 2.42-2.37 (m, 2H), 2.33-2.18 (m, 2H), 2.04 (ddt, 1H, J = 2.0, 11.2, 16.8 Hz), 1.96-1.79 (m, 4H), 1.76-1.66 (m, 1H), 1.51-1.40 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 205.4, 173.2, 89.0, 77.8, 67.2, 65.7, 60.0, 48.4, 46.2, 35.2, 34.4, 28.1, 24.7, 18.8; IR (neat) 2921, 2851, 1724, 1704, 1334, 1258, 1230, 1152, 1109, 1057, 1026, 860, 780 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{14}H_{18}O_4Na$ $[M+Na]^+$ 273.1103, found 273.1097.



25

Macrolactone substrate 25.
^1H NMR (400 MHz, $CDCl_3$) δ 4.80 (s, 2H), 4.34 (ddd, 1H, J = 3.6, 5.2, 11.2 Hz), 4.28 (dt, 1H, J = 2.0, 16.4 Hz), 4.12 (td, 1H, J = 2.8, 10.4 Hz), 4.04 (dt, 1H, J = 2.0, 16.4 Hz), 3.84 (p, 1H, J = 6.0 Hz), 2.48-2.44 (m, 2H), 2.43-2.31 (m, 4H), 2.16 (s, 3H), 2.02-1.84 (m. 3H), 1.83-1.73 (m, 2H), 1.61-1.52 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.4, 169.3, 153.4, 103.9, 84.8, 78.8, 75.0, 64.1,

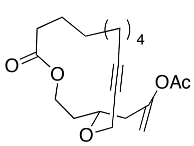
57.5, 38.2, 33.7, 31.1, 23.7, 21.9, 21.3, 18.4; IR (neat) 2929, 2855, 2032, 1962, 1754, 1732, 1666, 1574, 1436, 1369, 1201, 1159, 1069, 1019, 881 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{16}H_{22}O_5Na$ $[M+Na]^+$ 317.1365, found 317.1325.



26

Cyclization of 25 to form 26.

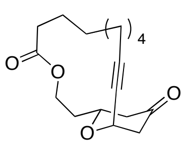
To a suspension of macrolactone substrate **25** (36 mg, 0.12 mmol), 2,6-dichloropypyridine (72 mg, 0.49 mmol), $LiClO_4$ (3.9 mg, 0.037 mmol), 4 Å molecular sieves (72 mg) in anhydrous DCE (1.5 mL) was added DDQ (56 mg, 0.25 mmol) in one portion at rt. The mixture was stirred at rt for 24 h, and then another 56 mg DDQ was added. The resulting mixture was stirred for 53 h at 40 °C, then was quenched by the addition of NEt_3. The black mixture was loaded directly onto a short plug of silica gel and eluted with dichloromethane and EtOAc. The filtrate was concentrated and purified by flash chromatography to give the desired *trans* product **26** (11 mg, 36%). **26**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.06 (app d, 1H, *J* = 7.2 Hz), 4.57 (ddd, 1H, *J* = 3.2, 4.8, 11.6 Hz), 4.42 (ddt, 1H, *J* = 2.4, 10.4, 11.6 Hz), 3.95 (td, 1H, *J* = 1.6, 11.2 Hz), 2.73 (dd, 1H, *J* = 7.6, 14.4 Hz), 2.52 (ddd, 1H, *J* = 2.8, 8.8, 16.8 Hz), 2.14 (app d, 2H, *J* = 14.4 Hz), 2.38-2.17 (m, 4H), 2.06-1.97 (m, 1H), 1.92-1.77 (m, 2H), 1.65-1.57 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 205.7, 173.8, 87.6, 78.6, 70.9, 67.0, 65.6, 49.2, 47.0, 35.5, 33.0, 23.3, 21.1, 18.8; IR (neat) 2922, 2852, 1727, 1554, 1452, 1390, 1341, 1230, 1196, 1159, 1110, 1052, 967, 910 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{14}H_{19}O_4$ $[M]^+$ 251.1283, found 251.1314.



27

Macrolactone substrate 27.

^{1}H NMR (400 MHz, $CDCl_3$) δ 4.84 (s, 2H), 4.30-4.14 (m, 4H), 4.04 (p, 1H, *J* = 6.0 Hz), 2.47 (d, 2H, *J* = 5.6 Hz), 2.34 (t, 2H, *J* = 6.8 Hz), 2.29-2.28 (m, 2H), 2.14 (s, 3H), 1.91-1.82 (m, 2H), 1.78-1.65 (m, 2H), 1.57-149 (m, 4H), 1.44-1.33 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.1, 169.2, 152.8, 104.5, 86.9, 76.4, 70.7, 60.8, 55.9, 36.6, 33.9, 33.3, 27.4, 26.9, 26.5, 26.0, 24.0, 21.3, 18.2; IR (neat) 2930, 2857, 1756, 1733, 1666, 1435, 1369, 1199, 1065, 1022, 965, 878 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{19}H_{29}O_5$ $[M]^+$ 337.2015, found 337.1962.

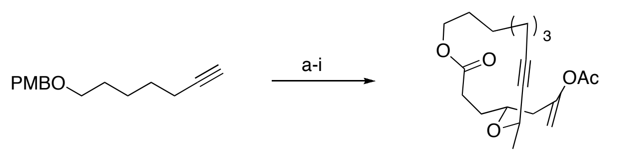


28

Cyclization of 27 to form 28.

To a suspension of macrolactone substrate **27** (30 mg, 0.090 mmol), 2,6-dichloropypyridine (53 mg, 0.36 mmol), $LiClO_4$ (2.8 mg, 0.027 mmol), 4 Å molecular sieves (60 mg) in anhydrous DCE (1 mL) was added DDQ (81 mg, 0.36 mmol) in one portion at rt. The mixture was stirred at 40 °C for 46 h, then was quenched by adding 3 drops of NEt_3. The mixture was loaded directly onto a short plug of silica gel and eluted with dichloromethane and EtOAc. The filtrate was concentrated and purified by flash chromatography (hexane:EtOAc, 10:1 to 4:1) to give both *trans*- and *cis*-products (12 mg total mass, *trans*/*cis* = 2/1, 46% total yield). **28**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.11 (dd, 1H, *J* = 1.6, 6.8), 4.48 (app ddt, 1H, *J* = 2.4, 8.8, 13.6 Hz), 4.26-4.17 (m, 2H), 2.80 (dd, 1H, *J* = 6.8, 13.6 Hz), 2.49-2.43 (m, 2H), 2.34 (t, 2H, *J* = 6.8 Hz), 2.32-2.29 (m, 2H), 2.21 (dd, 1H, *J* = 7.2, 14.0 Hz), 2.04-1.96 (m, 1H), 1.90-1.82 (m, 1H), 1.71 (p, 2H, *J* = 6.8 Hz), 1.51-1.44 (m, 4H), 1.41-1.28 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 205.0, 174.0, 90.0, 77.1, 68.3, 66.0, 59.7, 47.9, 47.8, 35.7, 33.6, 27.8, 26.8, 26.7, 26.0, 24.4, 18.0; IR (neat) 2929, 2857, 1729, 1459, 1337, 1226, 1187, 1147, 1097, 1053, 980, 932, 863 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{17}H_{25}O_4$ $[M]^+$ 293.1753, found 292.1720.

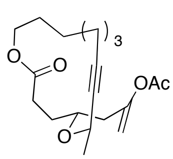
28': ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.38-4.21 (m, 3H), 3.78 (ddt, 1H, J = 2.4, 9.2, 11.2 Hz), 2.63-2.52 (m, 2H), 2.46-2.38 (m, 2H), 2.36-2.24 (m, 4H), 2.13-2.04 (m, 1H), 1.85-1.68 (m, 3H), 1.60-1.34 (m, 8H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 205.3, 174.4, 86.7, 78.8, 67.5, 62.1, 48.1, 47.7, 35.2, 33.7, 26.4, 25.7, 24.8, 24.5, 22.5, 17.9; HRMS (ESI) *m/z* calcd for $C_{17}H_{24}O_4$ $[M]^+$ 292.1675, found 292.1700



29

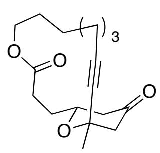
Reagents and conditions
a) ^{n}BuLi, THF, –78 °C, then $(CH_2O)_n$, rt. b) SO_3•Py, DMSO, Et_3N, CH_2Cl_2, 33% (two steps). c)[11] 5-Hexyne-1,3-diol bis-trimethylsilyl ether, TMSOTf, CH_2Cl_2, –78 °C, 30%. d)[12] Me_3Al, PhMe, 0 °C, 68%. e) Dess-Martin periodinane, $NaHCO_3$, CH_2Cl_2, 83%. f) $NaClO_2$, NaH_2PO_4, 2-methyl-2-butene, ^{t}BuOH, H_2O, –10 °C. g) DDQ, CH_2Cl_2, H_2O. h) 2-Chloro-1-methylpyridinium iodide, Et_3N, CH_3CN, reflux. i) HOAc, 1-decyne, Na_2CO_3, $[Ru(p\text{-cymene})Cl_2]_2$, Fur_3P, PhMe, 80 °C, 29% (four steps).

Scheme 8. Synthesis of **29**. Note: Compound **31** was synthesized through a very similar sequence.



29

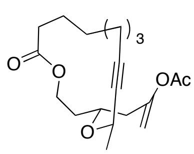
Macrolactone substrate 29.
^{1}H NMR (400 MHz, $CDCl_3$) δ 4.89 (d, 1H, J = 1.2 Hz), 4.85 (d, 1H, J = 1.2 Hz), 4.64-4.58 (m, 1H), 4.44 (ddt, 1H, J = 2.0, 6.4, 12.8 Hz), 4.25 (ddd, 1H, J = 2.8, 8.0, 11.2 Hz), 4.12-4.07 (m, 1H), 2.71 (dd, 1H, J = 4.8, 14.0 Hz), 2.50 (d, 2H, J = 6.4 Hz), 2.41 (dd, 1H, J = 6.8, 14.0 Hz), 2.30 (td, 2H, J = 1.6, 6.0 Hz), 2.15 (s, 3H), 1.80-1.45 (m, 8H), 1.36 (d, 3H, J = 6.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.8, 169.2, 152.8, 104.2, 87.2, 80.1, 69.8, 65.6, 62.5, 40.0, 39.8, 27.4, 26.8, 26.7, 26.0, 22.6, 21.4, 18.3; IR (neat) 2933, 2859, 1756, 1733, 1668, 1434, 1370, 1332, 1194, 1091, 1050, 1021, 877 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{18}H_{27}O_5$ $[M]^+$ 323.1858, found 323.1856.



30

Cyclization of 29 to form 30.
To a suspension of macrolactone substrate **29** (36 mg, 0.11 mmol), 2,6-dichloropypyridine (66 mg, 0.45 mmol), $LiClO_4$ (3.6 mg, 0.034 mmol), and 4 Å molecular sieves (72 mg) in anhydrous DCE (1.4 mL) was added DDQ (51 mg, 0.22 mmol) in one portion at rt. The mixture was stirred at rt for 10 h, then was warmed to 30 °C. 25 mg (0.11 mmol) DDQ was added after the reaction was stirred at 30 °C for 43 h. The reaction was quenched with 3 drops of NEt_3. The black mixture was loaded directly onto a short plug of silica gel and eluted with dichloromethane and EtOAc. The filtrate was concentrated and purified by flash chromatography (hexane:EtOAc, 10:1 to 8:1) to give the desired *trans*-product **30** (12.4 mg, 40%). **30:** ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.80-4.73 (m, 1H), 4.21-4.07 (m, 2H), 2.57 (d, 1H, J = 1.6 Hz), 2.56 (s, 1H), 2.52 (dd, 1H, J = 2.0, 14.0 Hz), 2.43 (d, 1H, J = 13.6 Hz), 2.39 (dt, 1H, J = 2.0, 14.0 Hz), 2.27-2.20 (m, 3H), 1.84-1.75 (m, 1H), 1.68-1.62 (m, 3H), 1.59 (s, 3H), 1.56-1.39 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 205.2, 170.3, 87.3, 80.7, 72.6, 70.2, 64.5, 53.6, 47.1, 42.7, 30.6, 27.6, 26.7, 26.3, 24.8, 17.5; IR (neat) 2920, 2858, 1731, 1468, 1449, 1426, 1375, 1316, 1275, 1259, 1204, 1162, 1129, 1100, 1071, 1029, 968 cm^{-1}; HRMS (EI) *m/z* calcd for $C_{16}H_{22}O_4$ $[M]^+$ 278.1518, found 278.1505.

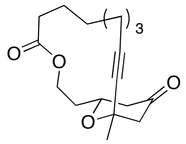
Macrolactone substrate 31.



31

^{1}H NMR (400 MHz, $CDCl_3$) δ 4.88 (s, 1H), 4.83 (d, 1H, *J* = 1.2 Hz), 4.50 (ddt, 1H, *J* = 2.0, 6.4, 12.8 Hz), 4.35-4.26 (m, 2H), 4.16 (td, 1H, *J* = 2.4, 11.6 Hz), 2.67 (dd, 1H, *J* = 3.2, 15.2 Hz), 2.43-2.37 (m, 3H), 2.30-2.18 (m, 3H), 2.14 (s, 3H), 1.71-1.57 (m, 4H), 1.54-1.46 (m, 4H), 1.37 (d, 3H, *J* = 6.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.7, 169.3, 153.4, 103.8, 86.9, 80.3, 69.1, 61.9, 60.8, 38.1, 34.4, 31.4, 27.1, 26.8, 24.3, 22.8, 21.4, 18.2; IR (neat) 2933, 2862, 1754, 1731, 1667, 1436, 1369, 1332, 1202, 1085, 1021, 966, 874 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{18}H_{26}O_5Na$ $[M+Na]^+$ 345.1678, found 345.1668.

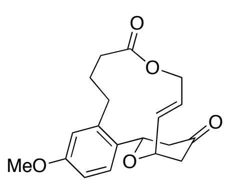
Cyclization of 31 to form 32.



32

To a suspension of macrolactone substrate **31** (40 mg, 0.12 mmol), 2,6-dichloropypyridine (73 mg, 0.50 mmol), $LiClO_4$ (4.0 mg, 0.037 mmol), and 4 Å molecular sieves (80 mg) in anhydrous DCE (1.5 mL) was added DDQ (56 mg, 0.25 mmol) in one portion at rt. The mixture was stirred at rt for 8 h, and then warmed to 30 °C. 27 mg (0.12 mmol) DDQ was added after the reaction was stirred at 30 °C for 26 h. The resulting mixture was stirred for 14 h at 30 °C, and then quenched with NEt_3. The black mixture was loaded directly onto a short plug of silica gel and eluted with dichloromethane and EtOAc. The filtrate was concentrated and purified by flash chromatography to give the desired *trans*-product **32** (13.4 mg, 39%). **32**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.50-4.37 (m, 2H), 4.05 (dt, 1H, *J* = 4.0, 11.2 Hz), 2.53 (dd, 1H, *J* = 2.0, 14.0 Hz), 2.48-2.36 (m, 3H), 2.36-2.25 (m. 2H), 2.24-2.20 (m, 1H), 2.18-2.12 (m, 1H), 1.93-1.88 (m, 2H), 1.72-1.61 (m, 2H), 1.58 (s, 1H), 1.56-1.41 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 205.8, 173.9, 87.5, 80.7, 72.4, 68.3, 60.3, 54.0, 47.5, 34.9, 34.7, 30.2, 27.2, 26.8, 24.8, 18.1; IR (neat) 2928, 2859, 1728, 1441, 1357, 1303, 1254, 1166, 1142, 1085, 1033, 1001, 865, 784 cm^{-1}; HRMS (EI) *m/z* calcd for $C_{16}H_{23}O_4$ $[M]^+$ 279.1596, found 279.1582.

Reduction of macrolactone 13 to form 33.[13]



33

To a solution of macrolactone **13** (14 mg, 0.044 mmol) in dry DCM (0.1 mL) was added $HSi(OEt)_3$ (9.7 μL, 0.053 mmol) under argon atmosphere. The resulting solution was cooled to 0 °C and added $[Cp^*Ru(NCCH_3)_3]PF_6$ (cat.). Then the reaction was warmed to rt and stirred at rt for 30 min then was diluted with 2 mL dry Et_2O. The resulting mixture was filtered through a plug of florisil (2 cm), washed with 2 ml dry Et_2O and concentrated *in vacuo*. The residue was re-dissolved in 0.3 mL dry THF. Under argon atmosphere, CuI (1 mg, cat.) was added followed by Bu_4NF (84 μL, 0.084 mmol) at rt. The resulting mixture was stirred at rt for 4 h, then was diluted with EtOAc, filtered through a pad of silica gel and concentrated in vacuum. The residue was purified by flash chromatography (hexane:EtOAc, 6:1 to 4:1) to give the desired alkene (7.2 mg, 49%) as yellowish oil. **33**: ^{1}H NMR (400 MHz, C_6D_6) δ 7.25 (d, 1H, *J* = 8.4 Hz), 6.68 (dd, 1H, *J* = 2.8, 8.4 Hz), 6.59 (d, 1H, *J* = 2.8 Hz), 5.92 (ddd, 1H, *J* = 0.8, 4.4, 16.0 Hz), 5.81 (dddd, 1H, *J* = 0.8, 4.4, 5.6, 16.4 Hz), 4.90 (dd, 1H, *J* = 2.4, 12.0 Hz), 4.44-4.43 (m, 1H), 4.36 (dd, 1H, *J* = 6.4, 12.4 Hz), 4.07 (ddt, 1H, *J* = 1.2, 4.4, 12.0 Hz), 2.61-2.48 (m, 2H), 2.43-2.29 (m, 4H), 2.04 (ddd, 1H, *J* = 3.2, 9.6, 12.4 Hz), 1.94 (ddd, 1H, *J* = 3.2, 9.6, 12.4 Hz), 1.62-1.58 (m, 1H), 1.50-1.43 (m, 1H); ^{13}C NMR (100 MHz, C_6D_6) δ 205.0, 172.8, 160.4, 142.4, 135.7, 131.9, 130.6, 116.0, 112.3, 72.6, 67.6, 61.5, 55.1, 48.6, 43.5, 34.8, 32.1, 30.6, 29.2; IR (neat) 2923, 2852, 1730, 1611, 1579, 1504, 1459, 1375, 1264, 1235, 1156, 1133, 1101, 1042, 995, 954, 810 cm^{-1}; HRMS (EI) *m/z* calcd for $C_{19}H_{22}O_5Na$ $[M+Na]^+$ 353.1365, found 353.1374.

References

1. Lee, A. S.-Y.; Chu, S.-F.; Chang, Y.-T.; Wang, S.-H. *Tetrahedron Lett.* **2004**, *45*, 1551.
2. Rai, A. N.; Basu, A. *Tetrahedron Lett.* **2003**, *44*, 2267.
3. Goossen, L. J.; Paetzold, J.; Koley, D. *Chem. Commun*. **2003**, 706.
4. Dunn, P. J.; Rees, C. W. *J. Soc. Chem. Perkin Trans. 1*, **1987**, 1579.
5. Miyaura, N.; Ishiyama, T.; Sasaki, H.; Ishikawa, M.; Satoh, M.; Suzuki, A. *J. Am. Chem. Soc.* **1989**, *111*, 314.
6. Fillion, E.; Beingessner, R. L. *J. Org. Chem.* **2003**, *68*, 9485.
7. a) Mukaiyama, T.; Usui, M.; Saigo, K. *Chem. Lett.* **1976**, 49; b) Sawamura, K.; Yoshida, K.; Suzuki, A.; Motozaki, T.; Kozawa, I.; Hayamizu, T.; Munakata, R.; Takao, K.; Tadano, K. *J. Org. Chem.* **2007**, *72*, 6143.
8. Zhdanko, A. G.; Nenajdenko, V. G. *J. Org. Chem.* **2009**, *74*, 884-887.
9. Commandeur, C.; Thorimbert, S.; Malacria, M. *J. Org. Chem.* **2003**, *68*, 5588.
10. Hatanaka, Y.; Hiyama, T. *J. Org. Chem.* **1988**, *53*, 918-920.
11. Noyori, R.; Murata, S.; Suzuki, M. *Tetrahedron*, **1981**, *37*, 3899-3910.
12. Ishihara, K.; Hanaki, N.; Yamamoto, H. *J. Am. Chem. Soc.* **1993**, *115*, 10695-10704.
13. Trost, B. M.; Ball, Z. T.; Jöge, T. *J. Am. Chem. Soc.* **2002**, *124*, 7922-7923.

Crystal data (macrolactone 24)

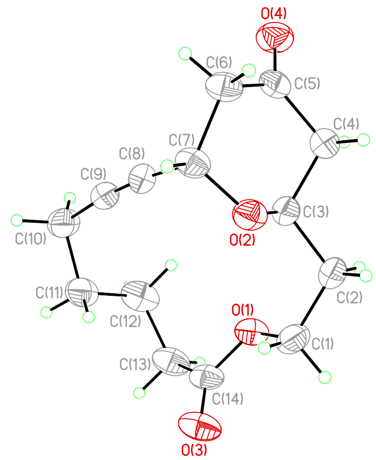


Table 1. Crystal data and structure refinement for xhflor1.

Empirical formula	C14 H18 O4	
Formula weight	250.28	
Temperature	203(2) K	
Wavelength	0.71073 Å	
Crystal system	Orthorhombic	
Space group	P c a 21	
Unit cell dimensions	a = 15.563(7) Å	a= 90°.
	b = 5.224(3) Å	b= 90°.
	c = 32.605(15) Å	g = 90°.
Volume	2651(2) $Å^3$	
Z	8	
Density (calculated)	1.254 Mg/m^3	
Absorption coefficient	0.091 mm^{-1}	
F(000)	1072	
Crystal size	0.36 x 0.20 x 0.05 mm^3	
Theta range for data collection	2.50 to 25.00°.	
Index ranges	-18<=h<=18, -6<=k<=6, -38<=l<=38	
Reflections collected	19056	
Independent reflections	2379 [R(int) = 0.0781]	
Completeness to theta = 25.00°	100.0 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.9955 and 0.9679	
Refinement method	Full-matrix least-squares on F^2	

Data / restraints / parameters	2379 / 1 / 325
Goodness-of-fit on F^2	0.877
Final R indices [I>2sigma(I)]	R1 = 0.0426, wR2 = 0.1184
R indices (all data)	R1 = 0.0589, wR2 = 0.1303
Absolute structure parameter	?
Largest diff. peak and hole	0.147 and -0.155 e.Å^{-3}

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (Å^{2}x 10^3) for xhflor1. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
O(1)	1266(2)	353(6)	1782(1)	63(1)
C(1)	1118(3)	2511(10)	2047(2)	69(1)
O(2)	2874(2)	4255(5)	2224(1)	57(1)
C(2)	1616(3)	2058(11)	2439(1)	75(1)
C(3)	2577(2)	1819(8)	2367(1)	53(1)
O(3)	615(2)	2394(5)	1271(1)	75(1)
O(4)	4503(2)	-657(6)	2767(1)	71(1)
C(4)	3071(3)	1048(9)	2751(1)	60(1)
C(5)	4026(3)	1057(8)	2658(1)	52(1)
C(6)	4349(3)	3340(8)	2429(1)	57(1)
C(7)	3746(2)	4155(8)	2078(1)	53(1)
C(8)	3807(2)	2455(8)	1720(1)	52(1)
C(9)	3791(2)	1136(9)	1422(1)	59(1)
C(10)	3681(3)	-346(12)	1045(2)	76(2)
C(11)	2737(3)	-375(10)	920(1)	69(1)
C(12)	2212(3)	-2279(8)	1164(2)	70(1)
C(13)	1234(3)	-1708(9)	1151(2)	69(1)
C(14)	1005(2)	565(8)	1393(2)	55(1)
O(1')	3660(2)	-4764(6)	4433(1)	64(1)
C(1')	3531(3)	-2670(9)	4154(2)	69(1)
O(2')	5288(2)	-1023(5)	3962(1)	59(1)
C(2')	4028(3)	-3290(12)	3772(2)	77(1)
C(3')	4986(2)	-3518(8)	3847(1)	53(1)
O(3')	3040(2)	-2561(6)	4940(1)	79(1)
O(4')	6931(2)	-5947(6)	3422(1)	70(1)
C(4')	5494(3)	-4461(9)	3478(1)	61(1)
C(5')	6440(3)	-4303(8)	3544(1)	52(1)
C(6')	6758(3)	-1962(8)	3762(1)	59(1)
C(7')	6156(2)	-1086(7)	4103(1)	54(1)
C(8')	6233(2)	-2642(8)	4481(1)	55(1)
C(9')	6224(2)	-3906(10)	4784(1)	62(1)
C(10')	6116(3)	-5298(12)	5166(2)	80(2)

C(11')	5154(3)	-5288(10)	5297(1)	67(1)
C(12')	4622(3)	-7256(8)	5065(2)	73(1)
C(13')	3668(3)	-6683(9)	5082(2)	72(1)
C(14')	3408(3)	-4421(8)	4821(1)	56(1)

Table 3. Bond lengths [Å] and angles [°] for xhflor1.

O(1)-C(14)	1.337(6)
O(1)-C(1)	1.439(6)
C(1)-C(2)	1.512(7)
C(1)-H(1A)	0.9800
C(1)-H(1B)	0.9800
O(2)-C(3)	1.433(5)
O(2)-C(7)	1.438(5)
C(2)-C(3)	1.519(6)
C(2)-H(2A)	0.9800
C(2)-H(2B)	0.9800
C(3)-C(4)	1.524(6)
C(3)-H(3A)	0.9900
O(3)-C(14)	1.200(5)
O(4)-C(5)	1.216(5)
C(4)-C(5)	1.516(6)
C(4)-H(4A)	0.9800
C(4)-H(4B)	0.9800
C(5)-C(6)	1.495(6)
C(6)-C(7)	1.539(5)
C(6)-H(6A)	0.9800
C(6)-H(6B)	0.9800
C(7)-C(8)	1.470(6)
C(7)-H(7A)	0.9900
C(8)-C(9)	1.192(6)
C(9)-C(10)	1.465(8)
C(10)-C(11)	1.525(6)
C(10)-H(10A)	0.9800
C(10)-H(10B)	0.9800
C(11)-C(12)	1.514(7)
C(11)-H(11A)	0.9800
C(11)-H(11B)	0.9800
C(12)-C(13)	1.551(6)
C(12)-H(12A)	0.9800
C(12)-H(12B)	0.9800
C(13)-C(14)	1.469(7)
C(13)-H(13A)	0.9800
C(13)-H(13B)	0.9800
O(1')-C(14')	1.335(6)

O(1')-C(1')	1.437(6)
C(1')-C(2')	1.502(7)
C(1')-H(1'A)	0.9800
C(1')-H(1'B)	0.9800
O(2')-C(7')	1.428(5)
O(2')-C(3')	1.436(5)
C(2')-C(3')	1.515(6)
C(2')-H(2'A)	0.9800
C(2')-H(2'B)	0.9800
C(3')-C(4')	1.521(6)
C(3')-H(3'A)	0.9900
O(3')-C(14')	1.193(5)
O(4')-C(5')	1.217(5)
C(4')-C(5')	1.490(6)
C(4')-H(4'A)	0.9800
C(4')-H(4'B)	0.9800
C(5')-C(6')	1.499(6)
C(6')-C(7')	1.525(6)
C(6')-H(6'A)	0.9800
C(6')-H(6'B)	0.9800
C(7')-C(8')	1.481(6)
C(7')-H(7'A)	0.9900
C(8')-C(9')	1.187(6)
C(9')-C(10')	1.455(8)
C(10')-C(11')	1.557(6)
C(10')-H(10C)	0.9800
C(10')-H(10D)	0.9800
C(11')-C(12')	1.522(7)
C(11')-H(11C)	0.9800
C(11')-H(11D)	0.9800
C(12')-C(13')	1.516(6)
C(12')-H(12C)	0.9800
C(12')-H(12D)	0.9800
C(13')-C(14')	1.513(7)
C(13')-H(13C)	0.9800
C(13')-H(13D)	0.9800
C(14)-O(1)-C(1)	117.2(4)
O(1)-C(1)-C(2)	107.6(4)
O(1)-C(1)-H(1A)	110.2
C(2)-C(1)-H(1A)	110.2
O(1)-C(1)-H(1B)	110.2
C(2)-C(1)-H(1B)	110.2
H(1A)-C(1)-H(1B)	108.5
C(3)-O(2)-C(7)	112.4(3)
C(3)-C(2)-C(1)	112.8(4)
C(3)-C(2)-H(2A)	109.0

C(1)-C(2)-H(2A)	109.0
C(3)-C(2)-H(2B)	109.0
C(1)-C(2)-H(2B)	109.0
H(2A)-C(2)-H(2B)	107.8
O(2)-C(3)-C(2)	107.2(3)
O(2)-C(3)-C(4)	109.9(3)
C(2)-C(3)-C(4)	113.1(3)
O(2)-C(3)-H(3A)	108.8
C(2)-C(3)-H(3A)	108.8
C(4)-C(3)-H(3A)	108.8
C(5)-C(4)-C(3)	109.3(3)
C(5)-C(4)-H(4A)	109.8
C(3)-C(4)-H(4A)	109.8
C(5)-C(4)-H(4B)	109.8
C(3)-C(4)-H(4B)	109.8
H(4A)-C(4)-H(4B)	108.3
O(4)-C(5)-C(6)	121.9(4)
O(4)-C(5)-C(4)	122.5(4)
C(6)-C(5)-C(4)	115.6(3)
C(5)-C(6)-C(7)	112.8(3)
C(5)-C(6)-H(6A)	109.0
C(7)-C(6)-H(6A)	109.0
C(5)-C(6)-H(6B)	109.0
C(7)-C(6)-H(6B)	109.0
H(6A)-C(6)-H(6B)	107.8
O(2)-C(7)-C(8)	110.1(3)
O(2)-C(7)-C(6)	109.9(3)
C(8)-C(7)-C(6)	112.6(3)
O(2)-C(7)-H(7A)	108.0
C(8)-C(7)-H(7A)	108.0
C(6)-C(7)-H(7A)	108.0
C(9)-C(8)-C(7)	174.8(4)
C(8)-C(9)-C(10)	173.6(4)
C(9)-C(10)-C(11)	110.0(4)
C(9)-C(10)-H(10A)	109.7
C(11)-C(10)-H(10A)	109.7
C(9)-C(10)-H(10B)	109.7
C(11)-C(10)-H(10B)	109.7
H(10A)-C(10)-H(10B)	108.2
C(12)-C(11)-C(10)	112.7(4)
C(12)-C(11)-H(11A)	109.1
C(10)-C(11)-H(11A)	109.1
C(12)-C(11)-H(11B)	109.1
C(10)-C(11)-H(11B)	109.1
H(11A)-C(11)-H(11B)	107.8
C(11)-C(12)-C(13)	112.9(4)

C(11)-C(12)-H(12A)	109.0
C(13)-C(12)-H(12A)	109.0
C(11)-C(12)-H(12B)	109.0
C(13)-C(12)-H(12B)	109.0
H(12A)-C(12)-H(12B)	107.8
C(14)-C(13)-C(12)	112.3(3)
C(14)-C(13)-H(13A)	109.2
C(12)-C(13)-H(13A)	109.2
C(14)-C(13)-H(13B)	109.2
C(12)-C(13)-H(13B)	109.2
H(13A)-C(13)-H(13B)	107.9
O(3)-C(14)-O(1)	122.2(4)
O(3)-C(14)-C(13)	126.1(4)
O(1)-C(14)-C(13)	111.7(4)
C(14')-O(1')-C(1')	117.1(4)
O(1')-C(1')-C(2')	106.8(4)
O(1')-C(1')-H(1'A)	110.4
C(2')-C(1')-H(1'A)	110.4
O(1')-C(1')-H(1'B)	110.4
C(2')-C(1')-H(1'B)	110.4
H(1'A)-C(1')-H(1'B)	108.6
C(7')-O(2')-C(3')	111.9(3)
C(1')-C(2')-C(3')	112.9(4)
C(1')-C(2')-H(2'A)	109.0
C(3')-C(2')-H(2'A)	109.0
C(1')-C(2')-H(2'B)	109.0
C(3')-C(2')-H(2'B)	109.0
H(2'A)-C(2')-H(2'B)	107.8
O(2')-C(3')-C(2')	107.0(3)
O(2')-C(3')-C(4')	109.3(3)
C(2')-C(3')-C(4')	114.2(4)
O(2')-C(3')-H(3'A)	108.7
C(2')-C(3')-H(3'A)	108.7
C(4')-C(3')-H(3'A)	108.7
C(5')-C(4')-C(3')	112.4(4)
C(5')-C(4')-H(4'A)	109.1
C(3')-C(4')-H(4'A)	109.1
C(5')-C(4')-H(4'B)	109.1
C(3')-C(4')-H(4'B)	109.1
H(4'A)-C(4')-H(4'B)	107.8
O(4')-C(5')-C(4')	122.3(4)
O(4')-C(5')-C(6')	121.6(4)
C(4')-C(5')-C(6')	116.1(4)
C(5')-C(6')-C(7')	112.8(3)
C(5')-C(6')-H(6'A)	109.0
C(7')-C(6')-H(6'A)	109.0

C(5')-C(6')-H(6'B)	109.0
C(7')-C(6')-H(6'B)	109.0
H(6'A)-C(6')-H(6'B)	107.8
O(2')-C(7')-C(8')	110.9(3)
O(2')-C(7')-C(6')	110.7(4)
C(8')-C(7')-C(6')	113.1(3)
O(2')-C(7')-H(7'A)	107.3
C(8')-C(7')-H(7'A)	107.3
C(6')-C(7')-H(7'A)	107.3
C(9')-C(8')-C(7')	174.7(4)
C(8')-C(9')-C(10')	173.0(5)
C(9')-C(10')-C(11')	110.2(4)
C(9')-C(10')-H(10C)	109.6
C(11')-C(10')-H(10C)	109.6
C(9')-C(10')-H(10D)	109.6
C(11')-C(10')-H(10D)	109.6
H(10C)-C(10')-H(10D)	108.1
C(12')-C(11')-C(10')	112.5(4)
C(12')-C(11')-H(11C)	109.1
C(10')-C(11')-H(11C)	109.1
C(12')-C(11')-H(11D)	109.1
C(10')-C(11')-H(11D)	109.1
H(11C)-C(11')-H(11D)	107.8
C(11')-C(12')-C(13')	112.3(4)
C(11')-C(12')-H(12C)	109.1
C(13')-C(12')-H(12C)	109.1
C(11')-C(12')-H(12D)	109.1
C(13')-C(12')-H(12D)	109.1
H(12C)-C(12')-H(12D)	107.9
C(14')-C(13')-C(12')	113.3(3)
C(14')-C(13')-H(13C)	108.9
C(12')-C(13')-H(13C)	108.9
C(14')-C(13')-H(13D)	108.9
C(12')-C(13')-H(13D)	108.9
H(13C)-C(13')-H(13D)	107.7
O(3')-C(14')-O(1')	124.0(4)
O(3')-C(14')-C(13')	125.5(4)
O(1')-C(14')-C(13')	110.5(4)

Symmetry transformations used to generate equivalent atoms:

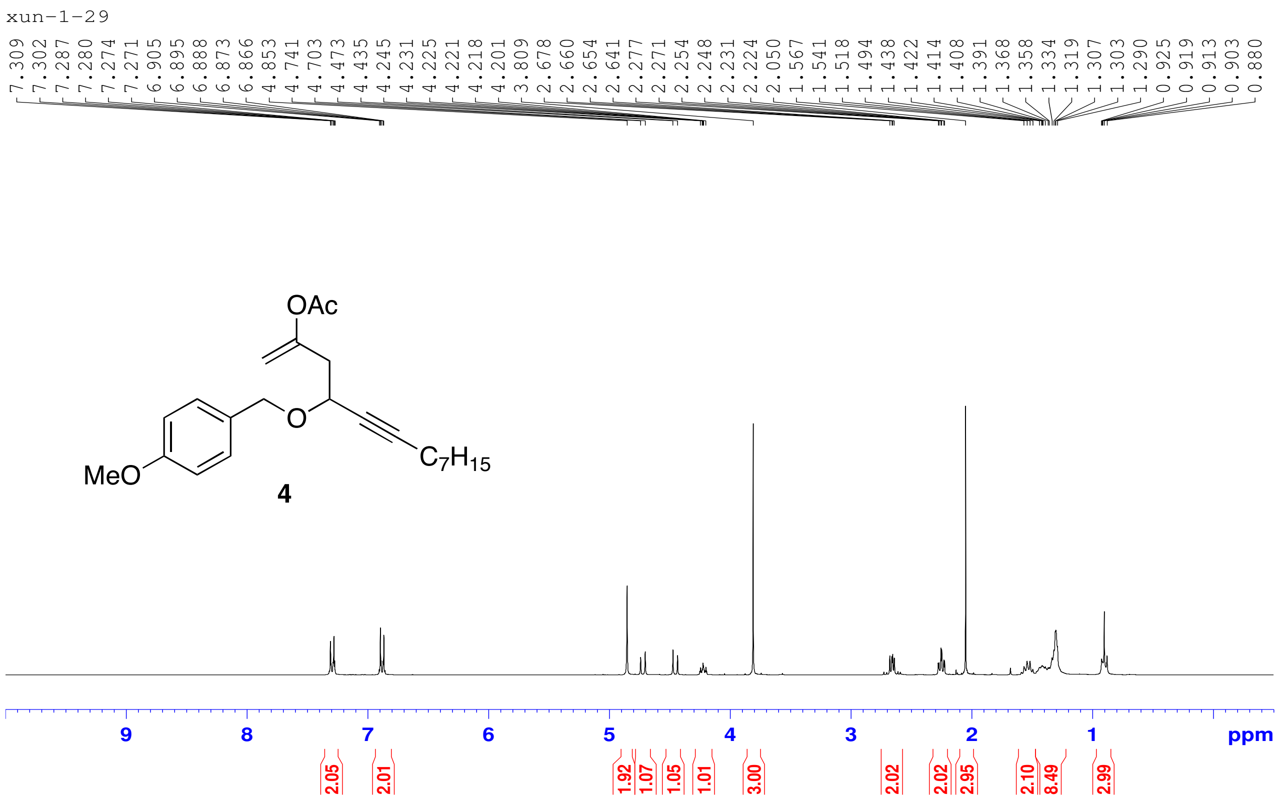
Table 4. Anisotropic displacement parameters ($Å^2$x 10^3) for xhflor1. The anisotropic displacement factor exponent takes the form: $-2p^2[h^2 a^{*2}U^{11} + ... + 2 h k a^* b^* U^{12}]$

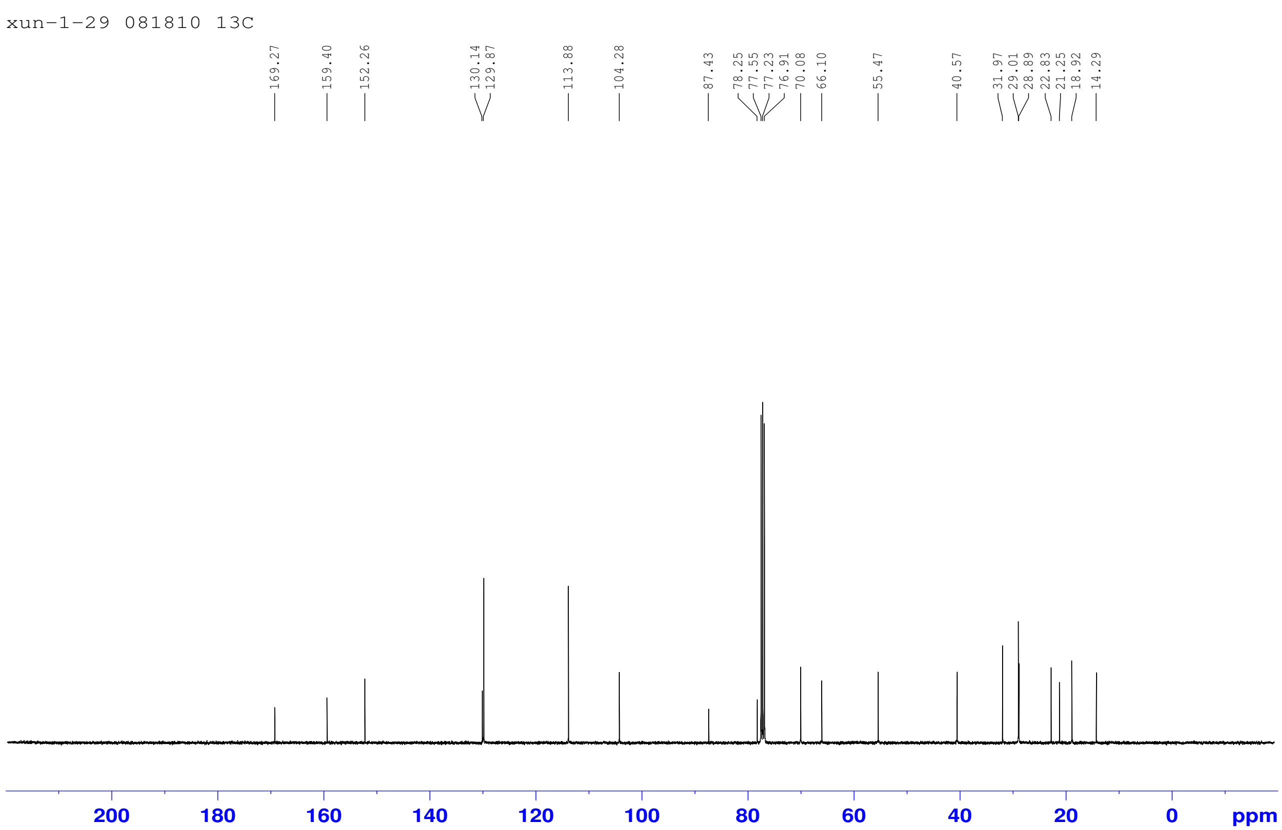
	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
O(1)	56(2)	67(2)	65(2)	4(2)	-13(1)	7(1)
C(1)	47(2)	91(3)	69(3)	-16(2)	-1(2)	14(2)
O(2)	59(2)	55(2)	56(2)	-10(1)	-7(1)	14(1)
C(2)	49(2)	122(4)	53(2)	-9(3)	7(2)	11(2)
C(3)	47(2)	65(2)	47(2)	-5(2)	3(2)	4(2)
O(3)	78(2)	56(2)	90(2)	15(2)	-33(2)	-2(2)
O(4)	63(2)	70(2)	80(2)	18(2)	-10(2)	11(2)
C(4)	54(2)	75(3)	49(2)	1(2)	-1(2)	5(2)
C(5)	57(2)	55(2)	44(2)	-5(2)	-12(2)	-1(2)
C(6)	56(2)	53(2)	62(2)	-3(2)	-16(2)	-6(2)
C(7)	57(2)	47(2)	55(2)	1(2)	-13(2)	-10(2)
C(8)	45(2)	61(2)	48(2)	4(2)	5(2)	-1(2)
C(9)	43(2)	84(3)	49(2)	0(2)	1(2)	7(2)
C(10)	59(3)	115(4)	53(3)	-23(3)	-1(2)	23(2)
C(11)	71(3)	85(3)	52(3)	-18(2)	-8(2)	24(2)
C(12)	93(3)	44(2)	74(3)	-18(2)	-23(3)	15(2)
C(13)	77(3)	57(2)	74(3)	-3(2)	-32(2)	-9(2)
C(14)	40(2)	50(2)	74(3)	13(2)	-18(2)	-17(2)
O(1')	58(2)	74(2)	60(2)	-5(2)	15(1)	2(1)
C(1')	37(2)	96(3)	75(3)	11(3)	-1(2)	14(2)
O(2')	56(2)	60(2)	59(2)	15(1)	8(1)	12(1)
C(2')	46(2)	125(4)	59(3)	13(3)	-6(2)	5(2)
C(3')	46(2)	72(2)	43(2)	12(2)	1(2)	2(2)
O(3')	80(2)	59(2)	98(2)	-19(2)	33(2)	-2(2)
O(4')	65(2)	64(2)	81(2)	2(2)	8(2)	10(2)
C(4')	59(2)	78(3)	46(2)	7(2)	-2(2)	4(2)
C(5')	57(2)	56(2)	43(2)	18(2)	8(2)	6(2)
C(6')	54(2)	56(2)	67(3)	11(2)	16(2)	-4(2)
C(7')	48(2)	51(2)	63(3)	4(2)	9(2)	-3(2)
C(8')	41(2)	67(3)	56(3)	1(2)	4(2)	-3(2)
C(9')	43(2)	89(3)	55(3)	7(3)	-4(2)	6(2)
C(10')	72(3)	117(4)	51(3)	23(3)	-3(2)	25(3)
C(11')	72(3)	80(3)	50(3)	18(2)	13(2)	20(2)
C(12')	96(4)	49(2)	72(3)	16(2)	27(3)	15(2)
C(13')	82(3)	54(2)	80(3)	6(2)	31(3)	-16(2)
C(14')	46(2)	56(2)	67(3)	-11(2)	15(2)	-16(2)

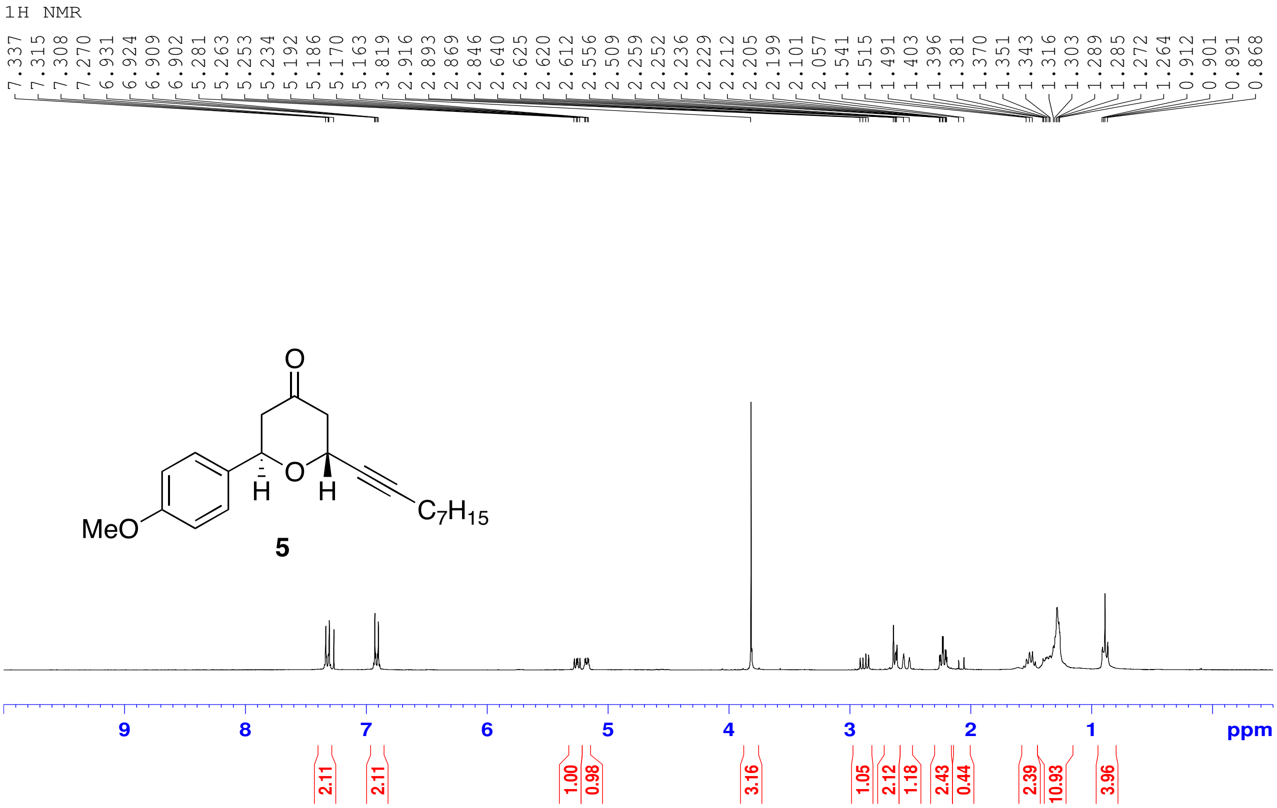
Table 5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$x 10^3) for xhflor1.

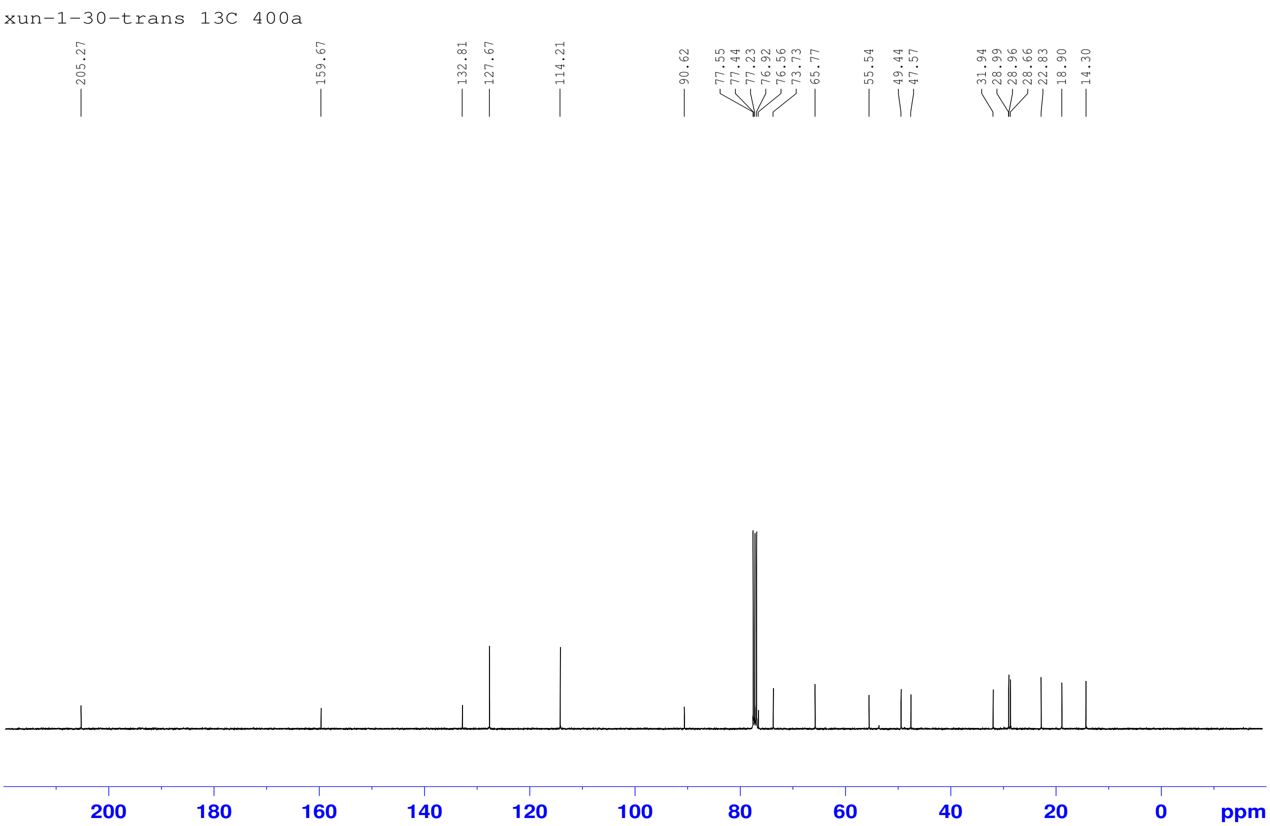
	x	y	z	U(eq)
H(1A)	504	2676	2107	83
H(1B)	1314	4090	1915	83
H(2A)	1509	3480	2628	90
H(2B)	1406	487	2569	90
H(3A)	2679	523	2151	64
H(4A)	2947	2252	2974	71
H(4B)	2893	-665	2839	71
H(6A)	4917	2949	2315	69
H(6B)	4415	4772	2621	69
H(7A)	3914	5900	1991	63
H(10A)	3882	-2104	1088	91
H(10B)	4027	414	825	91
H(11A)	2495	1341	958	83
H(11B)	2695	-799	627	83
H(12A)	2406	-2257	1449	84
H(12B)	2314	-4001	1055	84
H(13A)	1057	-1445	866	83
H(13B)	920	-3192	1258	83
H(1'A)	3740	-1070	4275	83
H(1'B)	2919	-2477	4090	83
H(2'A)	3926	-1947	3567	92
H(2'B)	3816	-4907	3658	92
H(3'A)	5082	-4709	4079	64
H(4'A)	5337	-6242	3421	73
H(4'B)	5340	-3434	3238	73
H(6'A)	6825	-571	3563	71
H(6'B)	7325	-2322	3880	71
H(7'A)	6319	690	4175	65
H(10C)	6465	-4498	5381	96
H(10D)	6313	-7067	5132	96
H(11C)	5115	-5645	5592	80
H(11D)	4913	-3581	5249	80
H(12C)	4728	-8956	5181	87
H(12D)	4808	-7286	4777	87
H(13C)	3350	-8198	4991	87
H(13D)	3506	-6342	5367	87

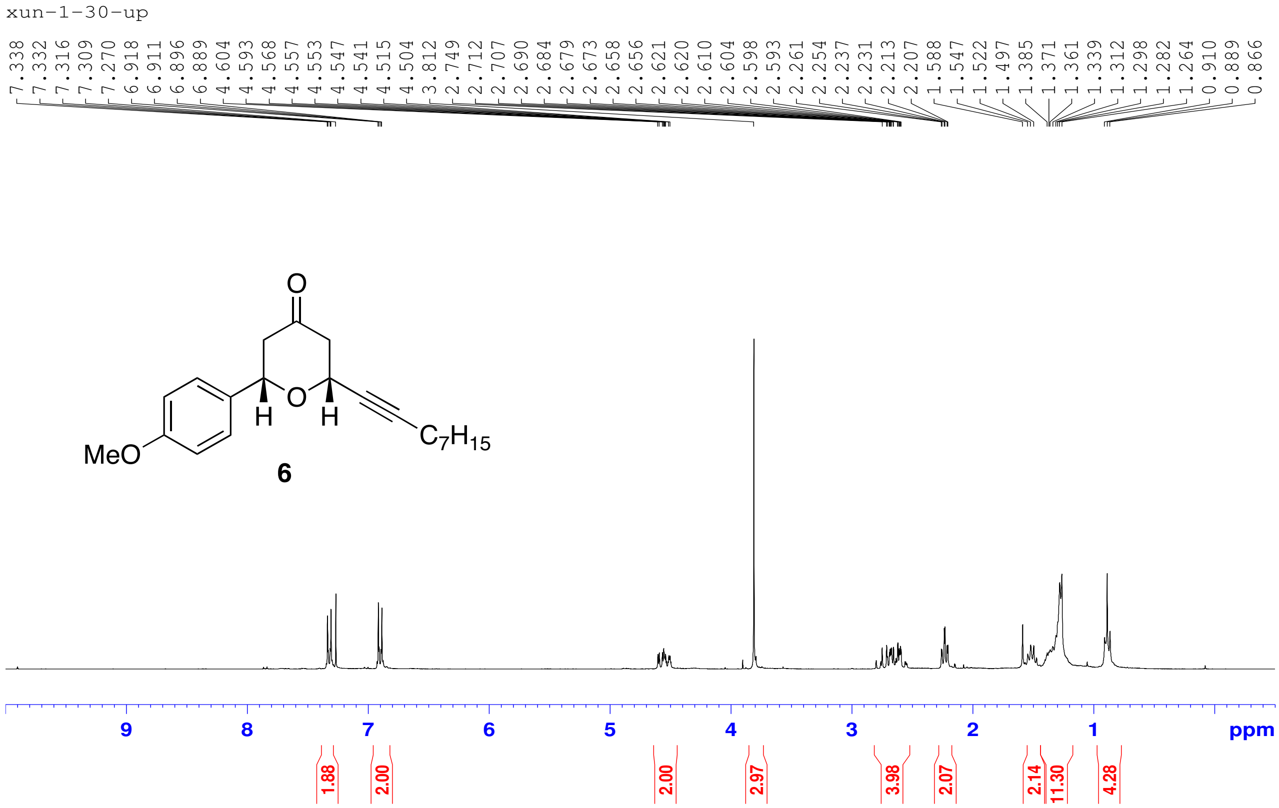
Spectral data

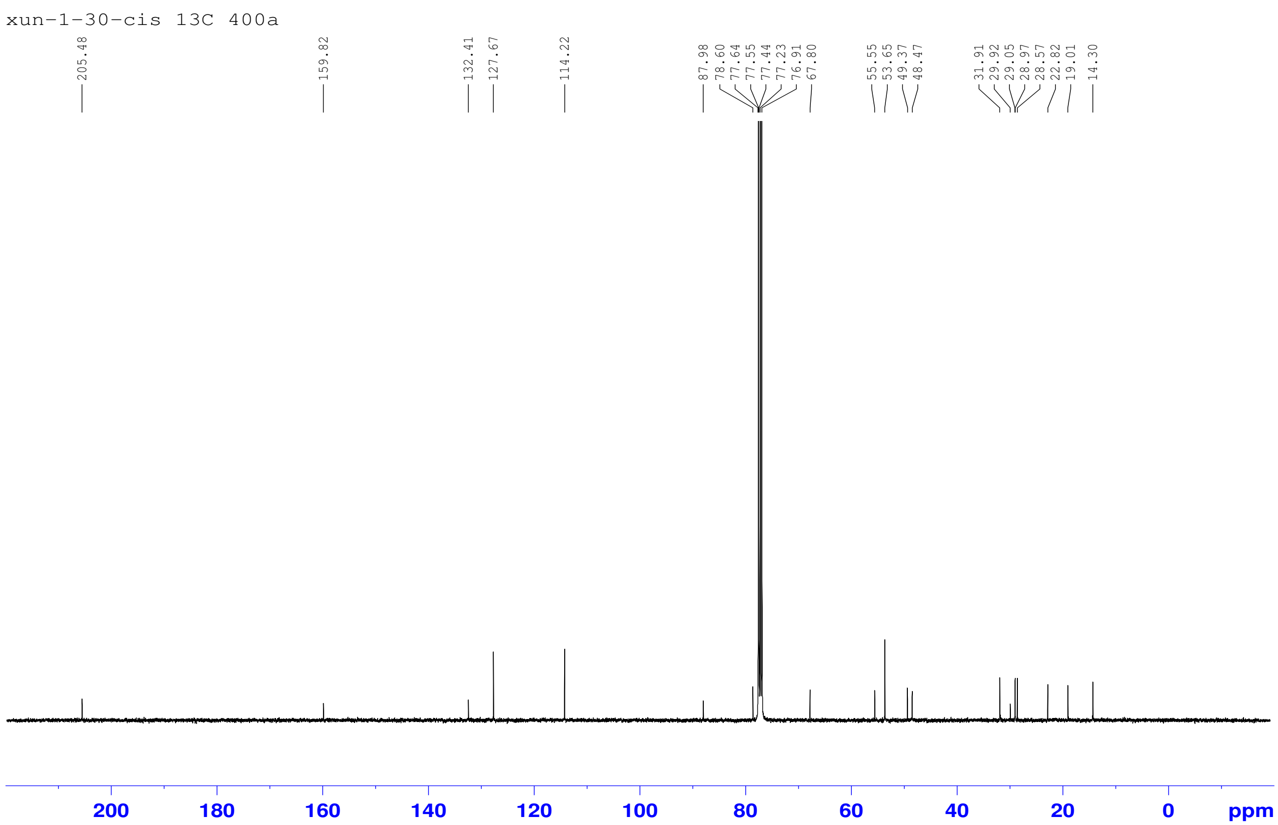




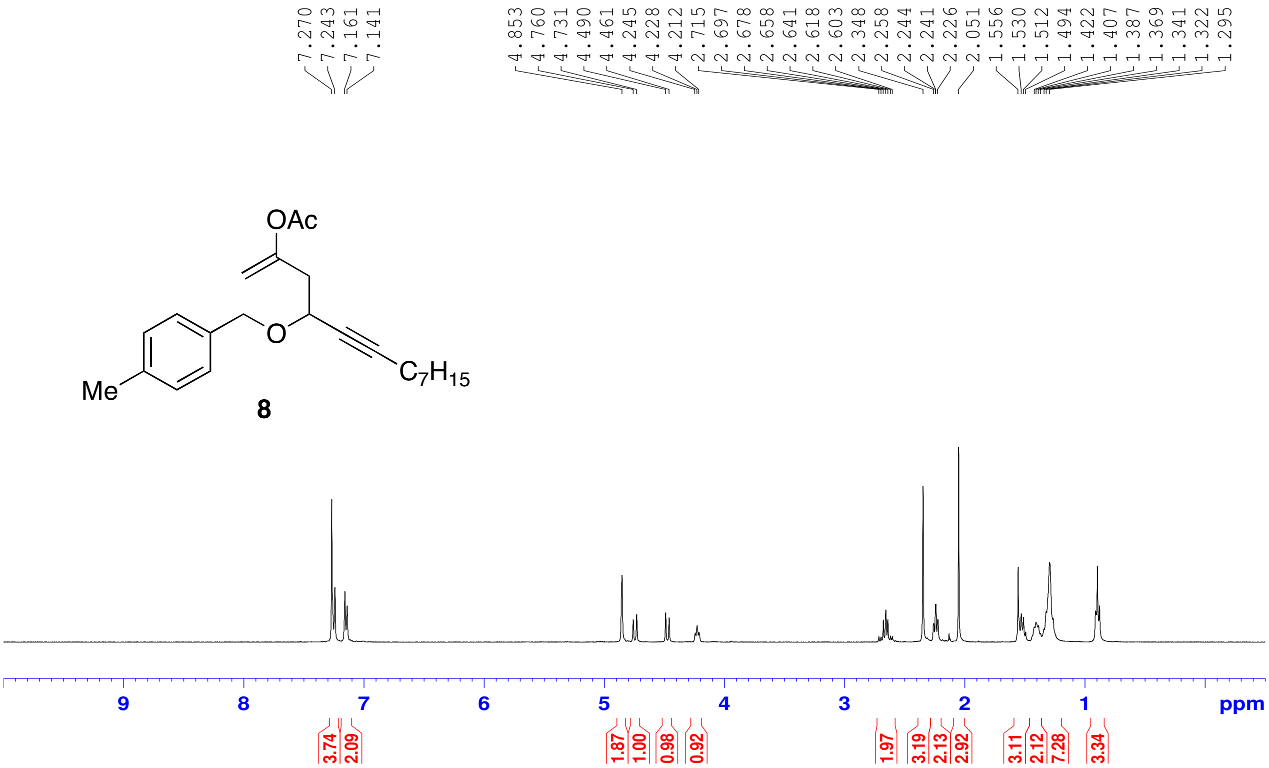

1H NMR
7.337
7.315
7.308
7.270
6.931
6.924
6.909
6.902
5.281
5.263
5.253
5.234
5.192
5.186
5.170
5.163
3.819
2.916
2.893
2.869
2.846
2.640
2.625
2.620
2.612
2.556
2.509
2.259
2.252
2.236
2.229
2.212
2.205
2.199
2.101
2.057
1.541
1.515
1.491
1.403
1.396
1.381
1.370
1.351
1.343
1.316
1.303
1.289
1.285
1.272
1.264
0.912
0.901
0.891
0.868
O
H
O
H
MeO
C7H15
5
9
8
7
6
5
4
3
2
1
ppm
2.11
2.11
1.00
0.98
3.16
1.05
2.12
1.18
2.43
0.44
2.39
10.93
3.96


xun-1-30-trans 13C 400a
205.27
159.67
132.81
127.67
114.21
90.62
77.55
77.44
77.23
76.92
76.56
73.73
65.77
55.54
49.44
47.57
31.94
28.99
28.96
28.66
22.83
18.90
14.30
200
180
160
140
120
100
80
60
40
20
0
ppm

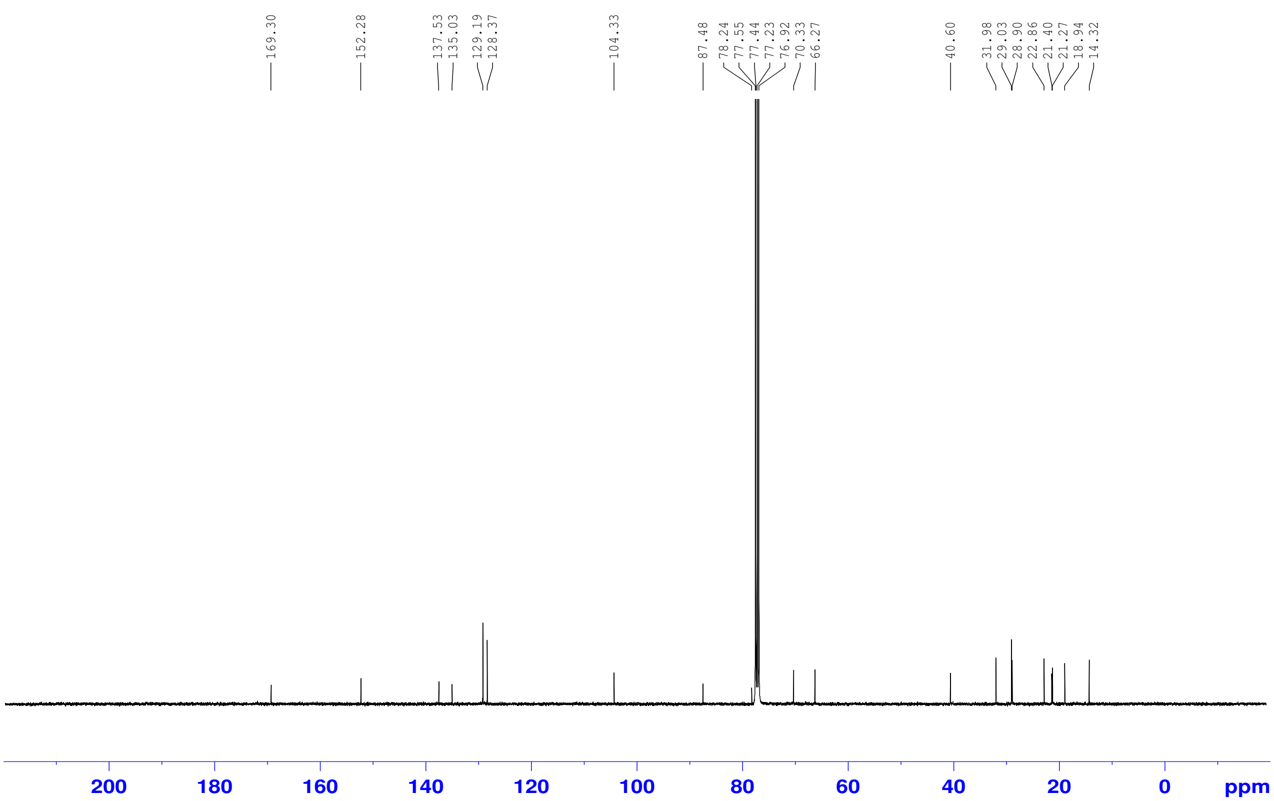

xun-1-30-up
7.338
7.332
7.316
7.309
7.270
6.918
6.911
6.896
6.889
4.604
4.593
4.568
4.557
4.553
4.547
4.541
4.515
4.504
3.812
2.749
2.712
2.707
2.690
2.684
2.679
2.673
2.658
2.656
2.621
2.620
2.610
2.604
2.598
2.593
2.261
2.254
2.237
2.231
2.213
2.207
1.588
1.547
1.522
1.497
1.385
1.371
1.361
1.339
1.312
1.298
1.282
1.264
0.910
0.889
0.866
O
O
H
H
MeO
C7H15
6
9
8
7
6
5
4
3
2
1
ppm
1.88
2.00
2.00
2.97
3.98
2.07
2.14
11.30
4.28

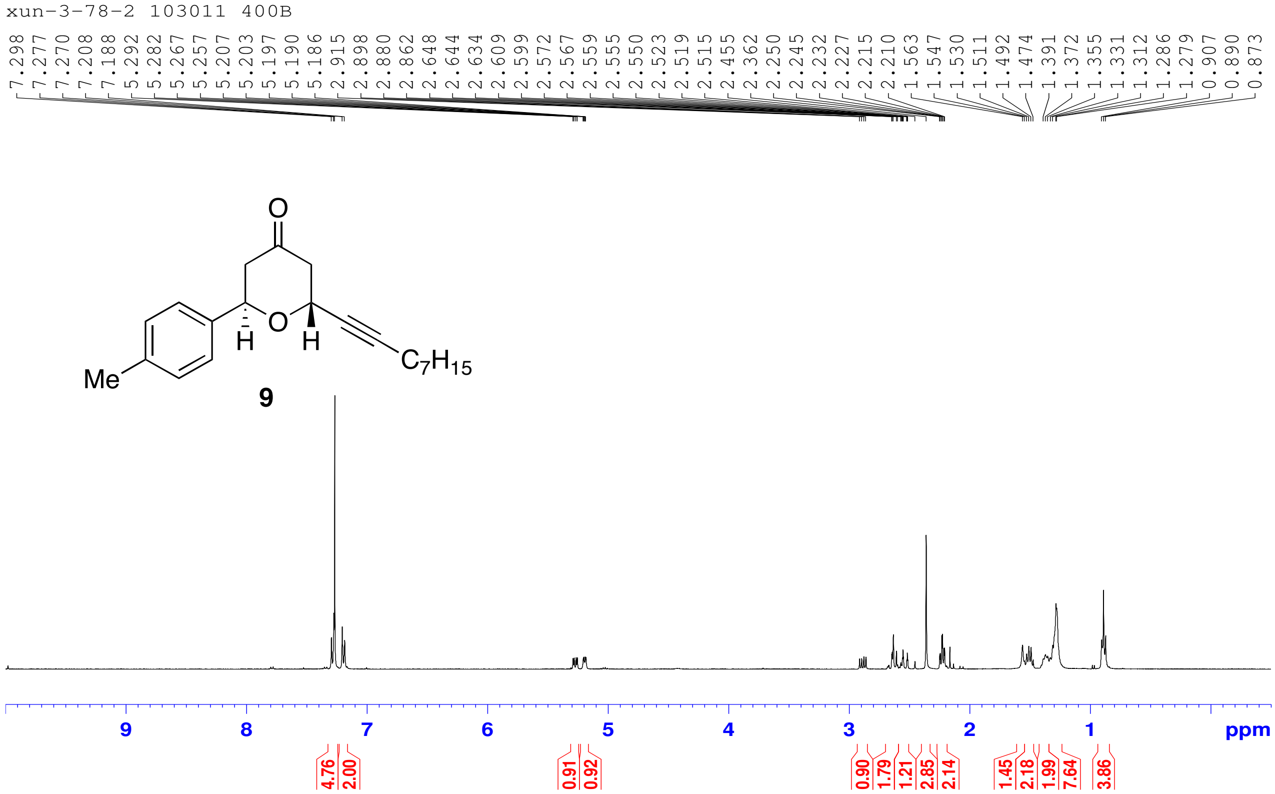

xun-1-30-cis 13C 400a
205.48
159.82
132.41
127.67
114.22
87.98
78.60
77.64
77.55
77.44
77.23
76.91
67.80
55.55
53.65
49.37
48.47
31.91
29.92
29.05
28.97
28.57
22.82
19.01
14.30
200
180
160
140
120
100
80
60
40
20
0
ppm

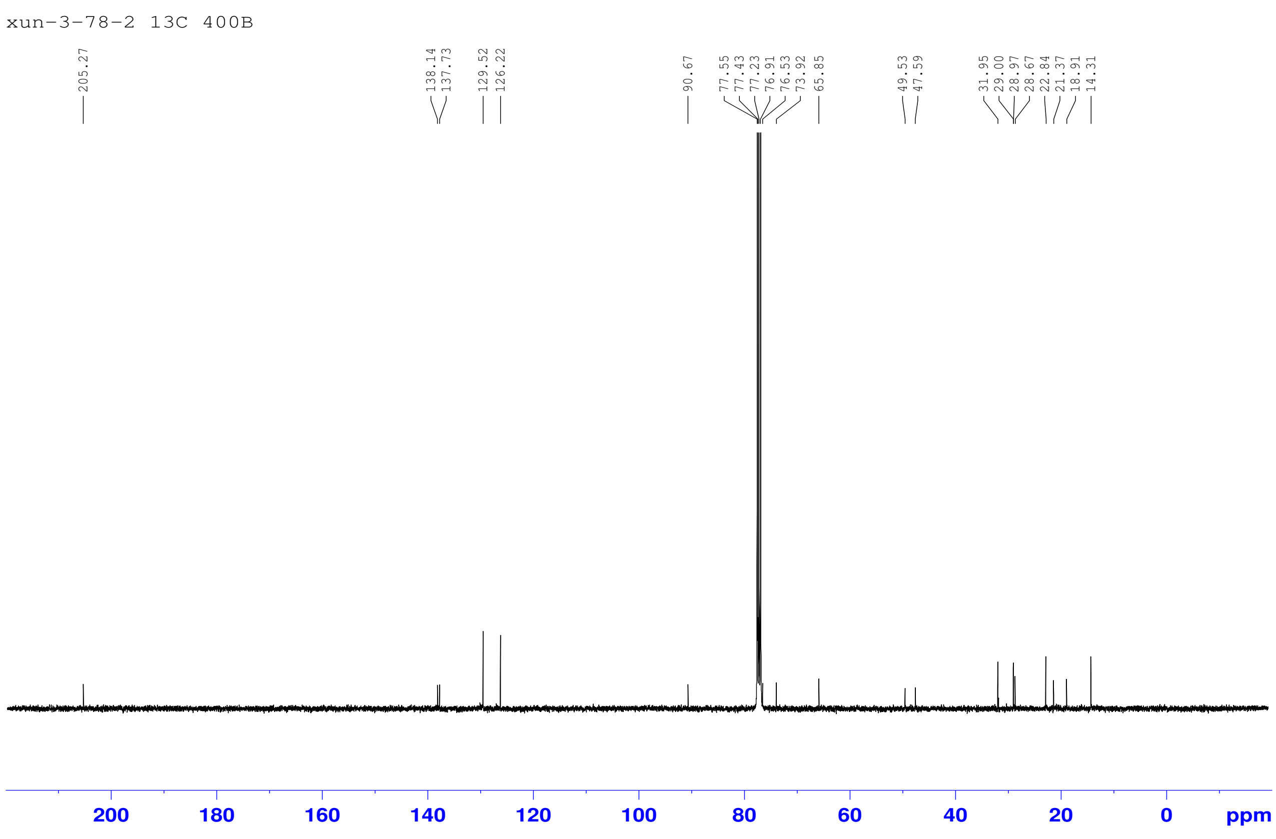
xun-1-262 400A

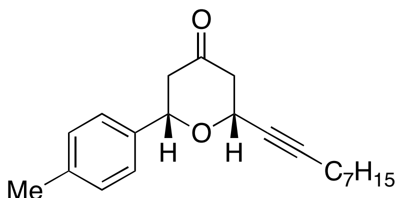


xun-1-262 13C 400B

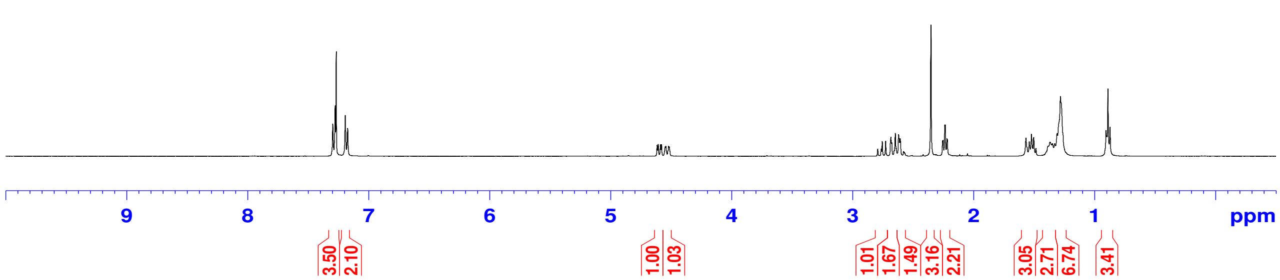


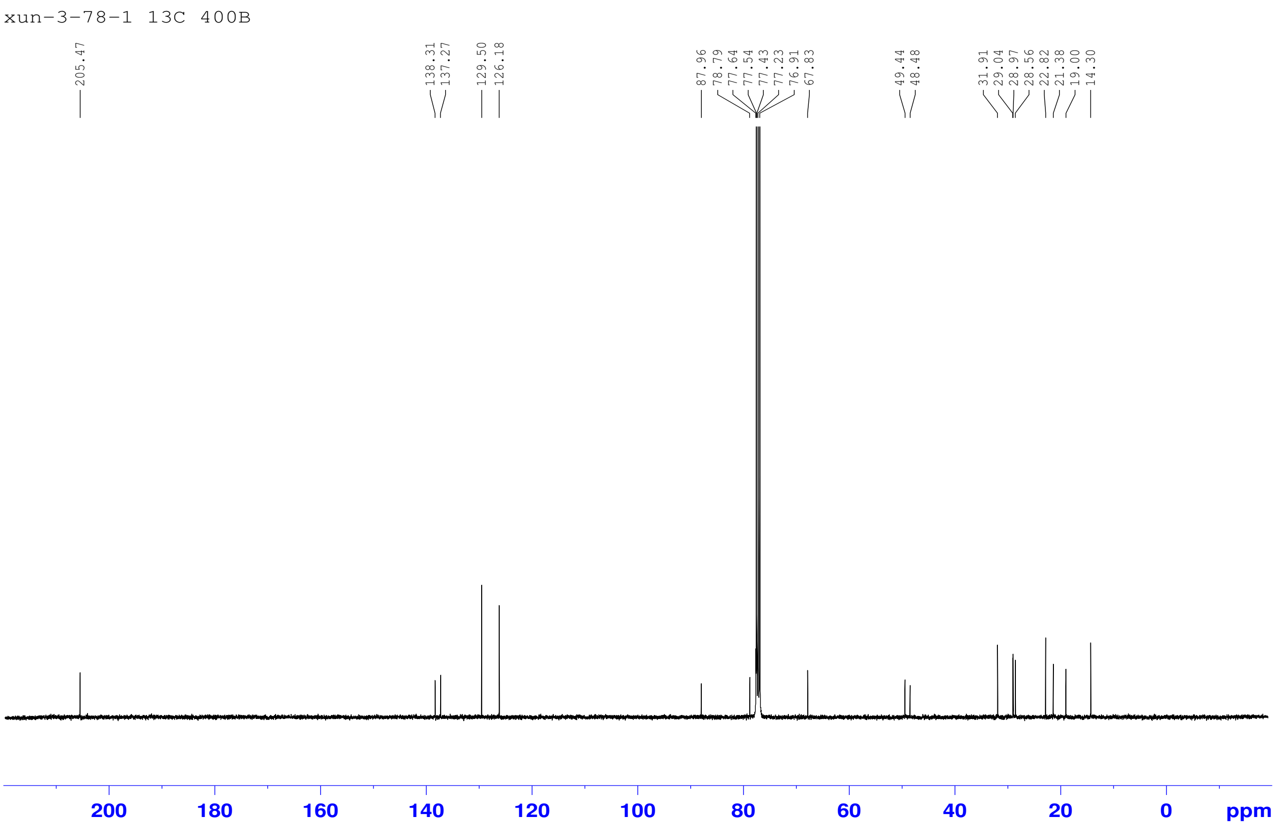

xun-3-78-2 103011 400B
7.298
7.277
7.270
7.208
7.188
5.292
5.282
5.267
5.257
5.207
5.203
5.197
5.190
5.186
2.915
2.898
2.880
2.862
2.648
2.644
2.634
2.609
2.599
2.572
2.567
2.559
2.555
2.550
2.523
2.519
2.515
2.455
2.362
2.250
2.245
2.232
2.227
2.215
2.210
1.563
1.547
1.530
1.511
1.492
1.474
1.391
1.372
1.355
1.331
1.312
1.286
1.279
0.907
0.890
0.873
O
H
O
H
Me
C_7H_{15}
9
9
8
7
6
5
4
3
2
1
ppm
4.76
2.00
0.91
0.92
0.90
1.79
1.21
2.85
2.14
1.45
2.18
1.99
7.64
3.86


xun-3-78-2 13C 400B
205.27
138.14
137.73
129.52
126.22
90.67
77.55
77.43
77.23
76.91
76.53
73.92
65.85
49.53
47.59
31.95
29.00
28.97
28.67
22.84
21.37
18.91
14.31
200
180
160
140
120
100
80
60
40
20
0
ppm

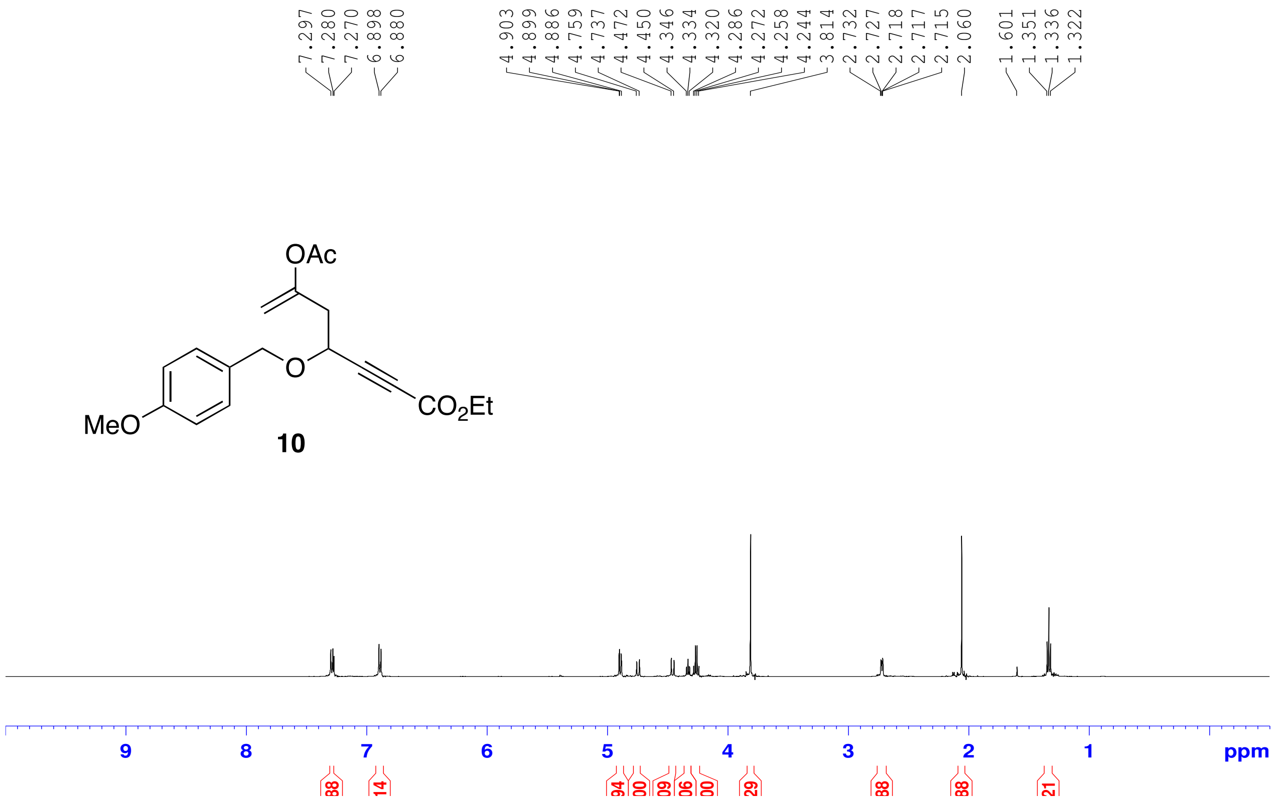

O
H
O
H
Me
C7H15

9'

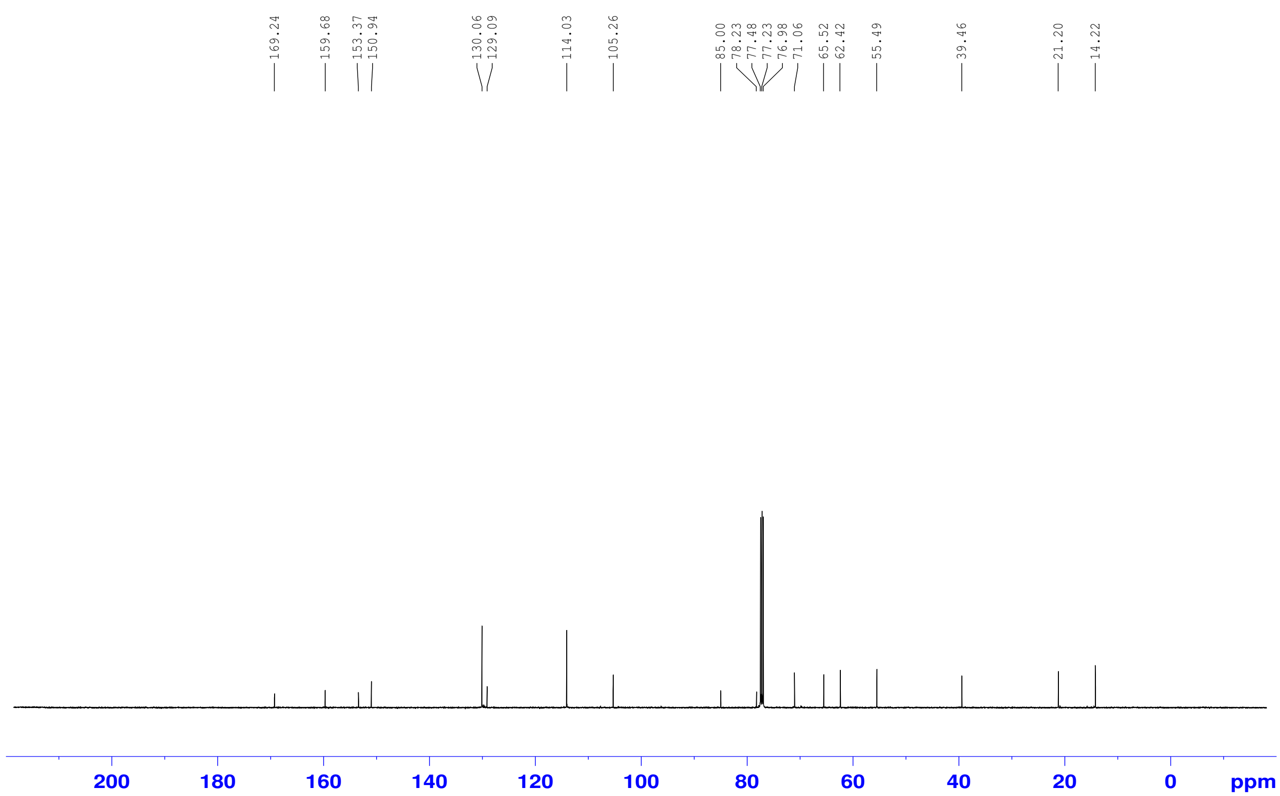

xun-3-78-1 400A
PROTON CDCl3 C:\Bruker\TOPSPIN floreancig 2
7.299 7.279 7.270 7.196 7.176 4.617 4.609 4.590 4.581 4.552 4.549 4.545 4.540 4.523 4.519 4.516 2.793 2.764 2.757 2.728 2.685 2.682 2.678 2.648 2.640 2.621 2.618 2.613 2.608 2.605 2.581 2.576 2.572 2.568 2.354 2.258 2.253 2.240 2.235 2.222 2.217 1.568 1.541 1.523
9 8 7 6 5 4 3 2 1 ppm
3.50 2.10 1.00 1.03 1.01 1.67 1.49 3.16 2.21 3.05 2.71 6.74 3.41

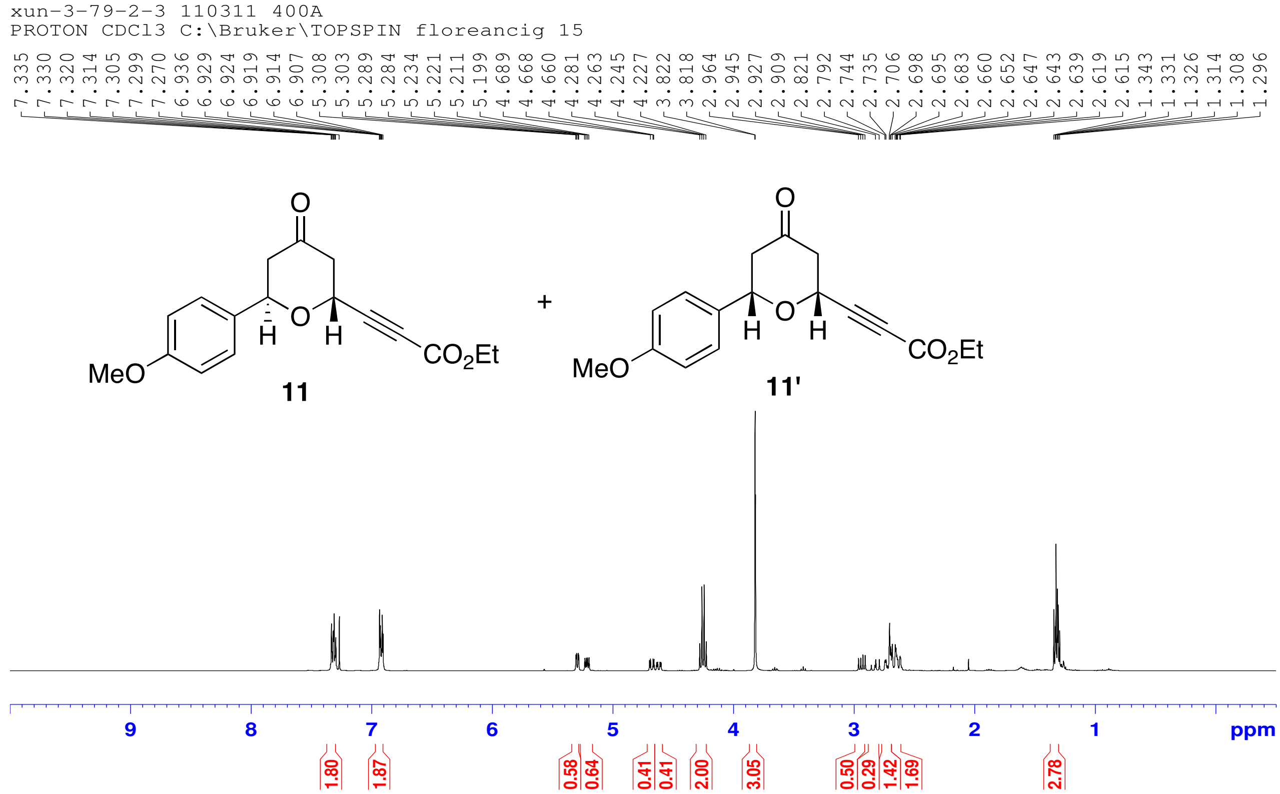

xun-3-78-1 13C 400B
205.47
138.31 137.27 129.50 126.18
87.96 78.79 77.64 77.54 77.43 77.23 76.91 67.83
49.44 48.48
31.91 29.04 28.97 28.56 22.82 21.38 19.00 14.30
200 180 160 140 120 100 80 60 40 20 0 ppm

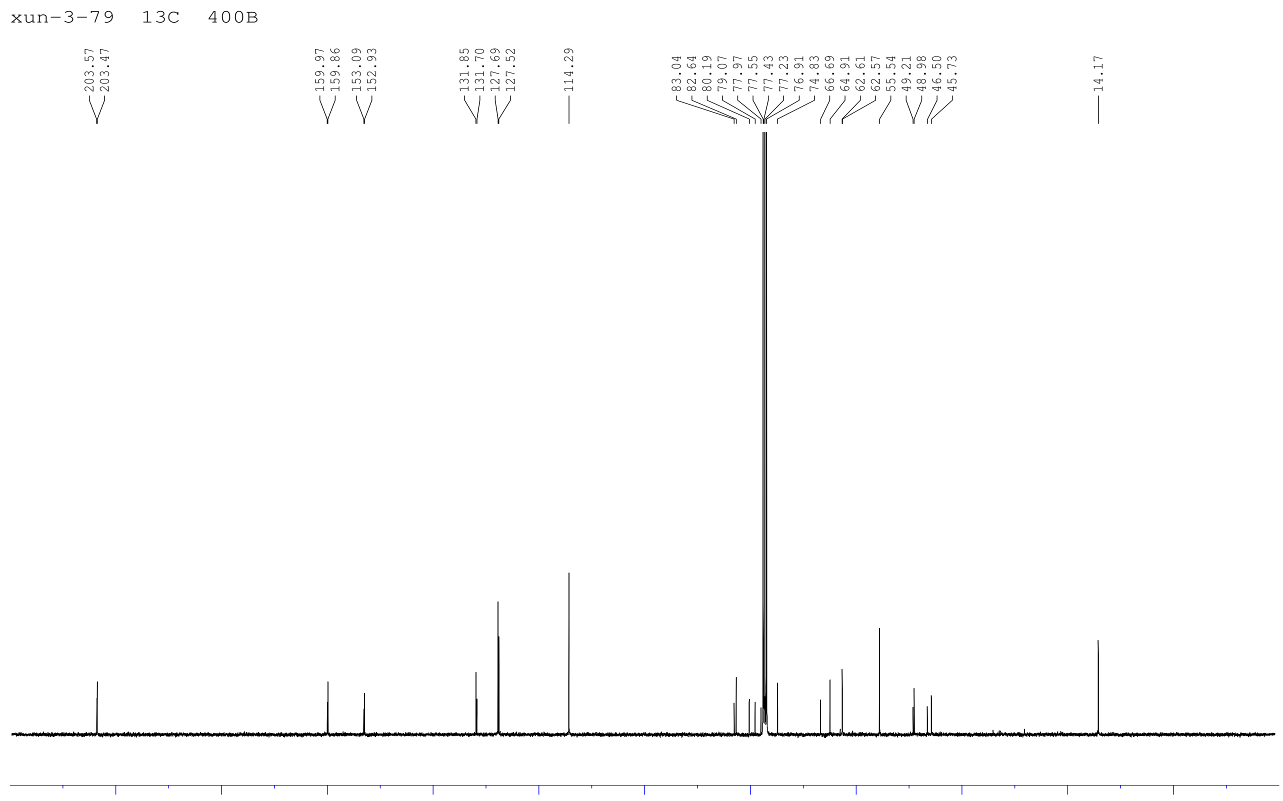
xun-1-259 1H 500

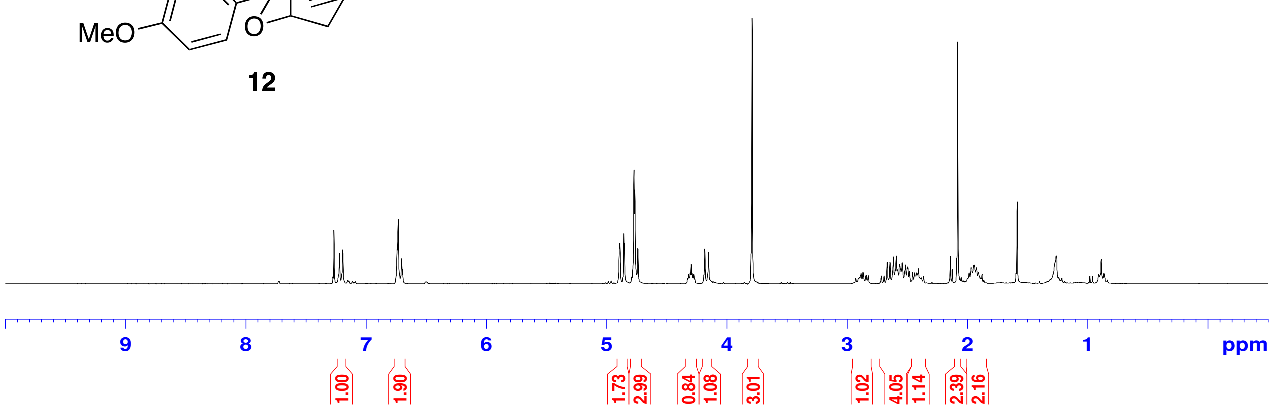


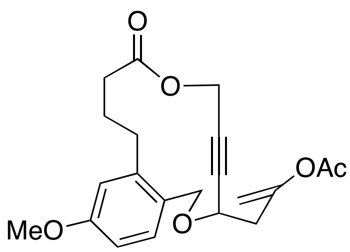
xun-1-259 13C 500



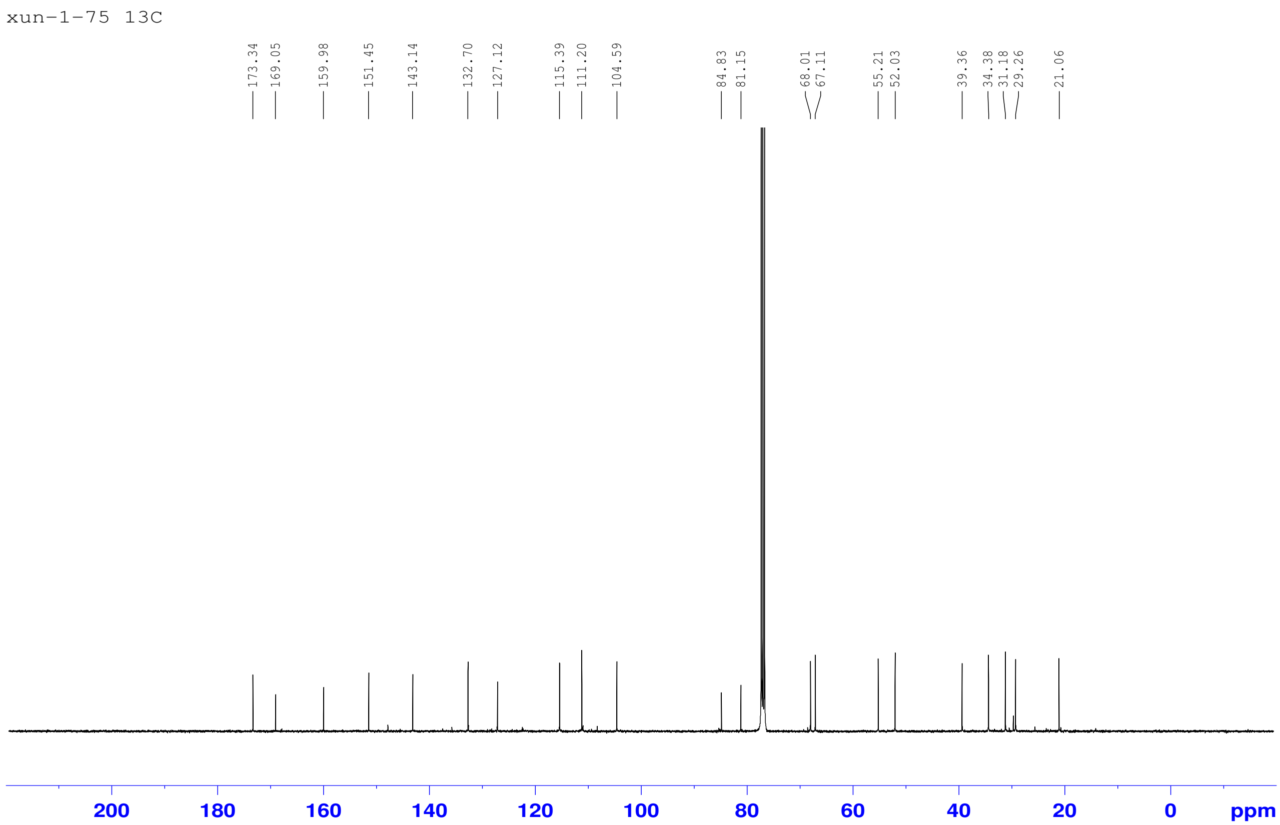

xun-3-79-2-3 110311 400A
PROTON CDCl3 C:\Bruker\TOPSPIN floreancig 15
7.335 7.330 7.320 7.314 7.305 7.299 7.270 6.936 6.929 6.924 6.919 6.914 6.907 5.308 5.303 5.289 5.284 5.234 5.221 5.211 5.199 4.689 4.668 4.660 4.281 4.263 4.245 4.227 3.822 3.818 2.964 2.945 2.927 2.909 2.821 2.792 2.744 2.735 2.706 2.698 2.695 2.683 2.660 2.652 2.647 2.643 2.639 2.619 2.615 1.343 1.331 1.326 1.314 1.308 1.296
O
O
H
H
MeO
CO2Et
11
+
O
O
H
H
MeO
CO2Et
11'
9
8
7
6
5
4
3
2
1
ppm
1.80
1.87
0.58
0.64
0.41
0.41
2.00
3.05
0.50
0.29
1.42
1.69
2.78

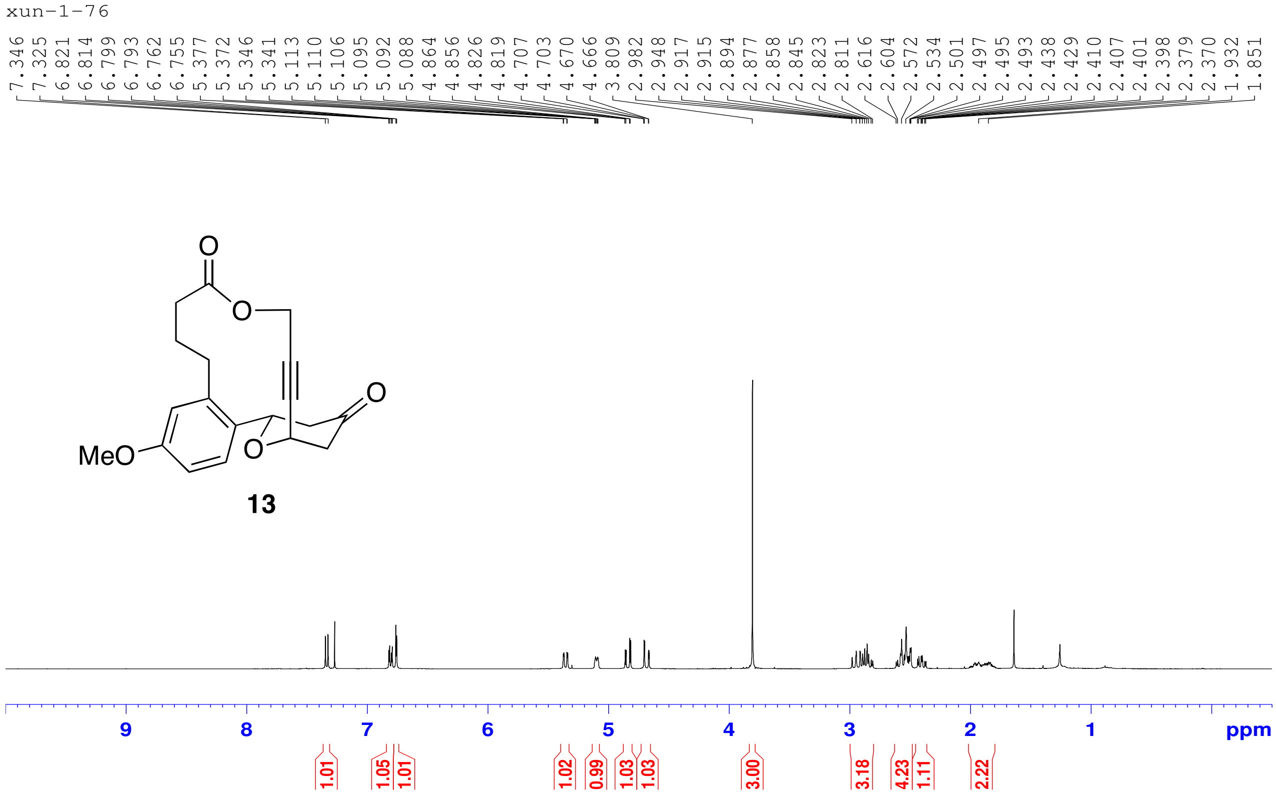

xun-3-79 13C 400B
203.57 203.47 159.97 159.86 153.09 152.93 131.85 131.70 127.69 127.52 114.29 83.04 82.64 80.19 79.07 77.97 77.55 77.43 77.23 76.91 74.83 66.69 64.91 62.61 62.57 55.54 49.21 48.98 46.50 45.73 14.17
200
180
160
140
120
100
80
60
40
20
0
ppm


xun-1-75
7.269 7.223 7.197 6.743 6.735 6.725 6.707 6.698 4.892 4.858 4.853 4.774 4.767 4.742 4.322 4.307 4.299 4.292 4.276 4.185 4.154 3.792 2.886 2.870 2.668 2.645 2.617 2.602 2.594 2.585 2.566 2.544 2.523 2.517 2.502 2.498 2.483 2.457 2.441 2.424 2.415 2.409 2.144 2.127 2.091 2.082 1.988 1.970 1.951 1.945 1.925 1.911 1.880 1.587
9 8 7 6 5 4 3 2 1 ppm
1.00 1.90 1.73 2.99 0.84 1.08 3.01 1.02 4.05 1.14 2.39 2.16

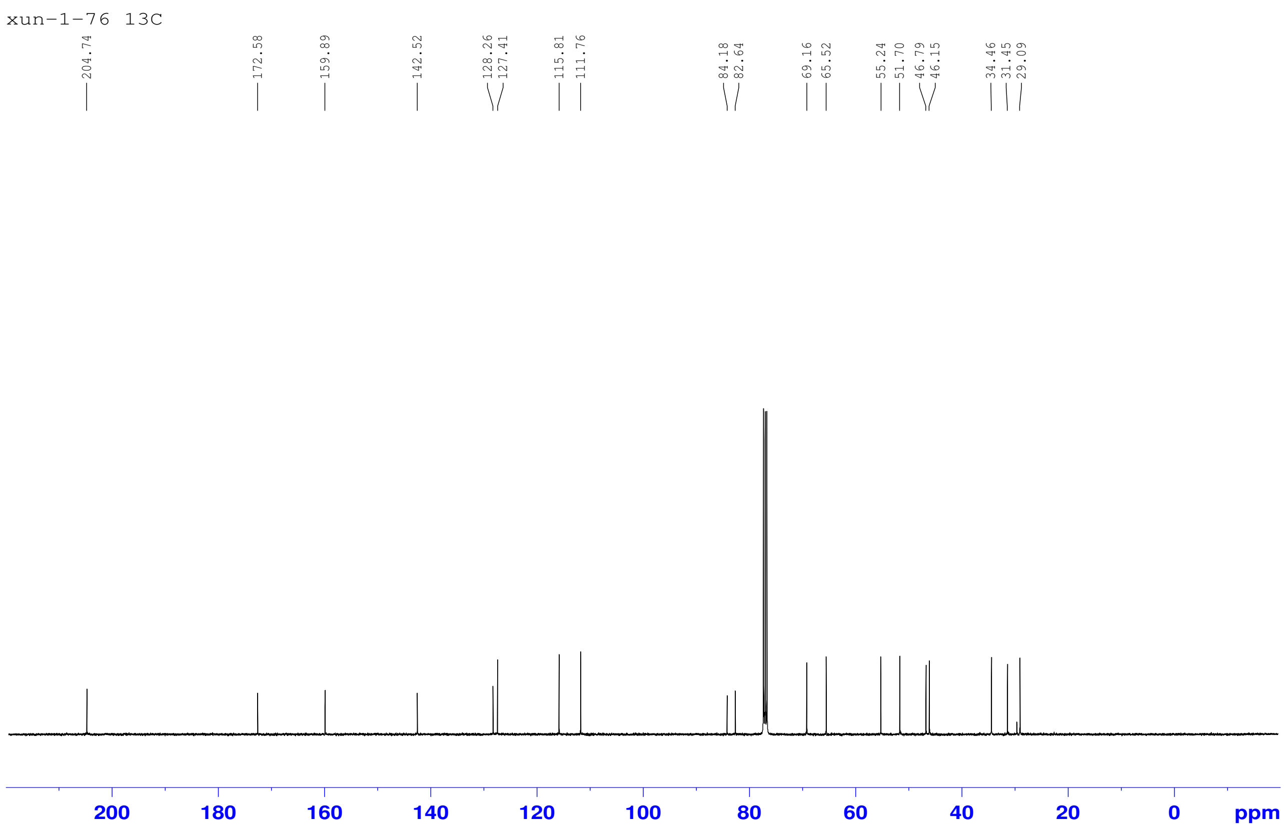

O
O
OAc
MeO
O

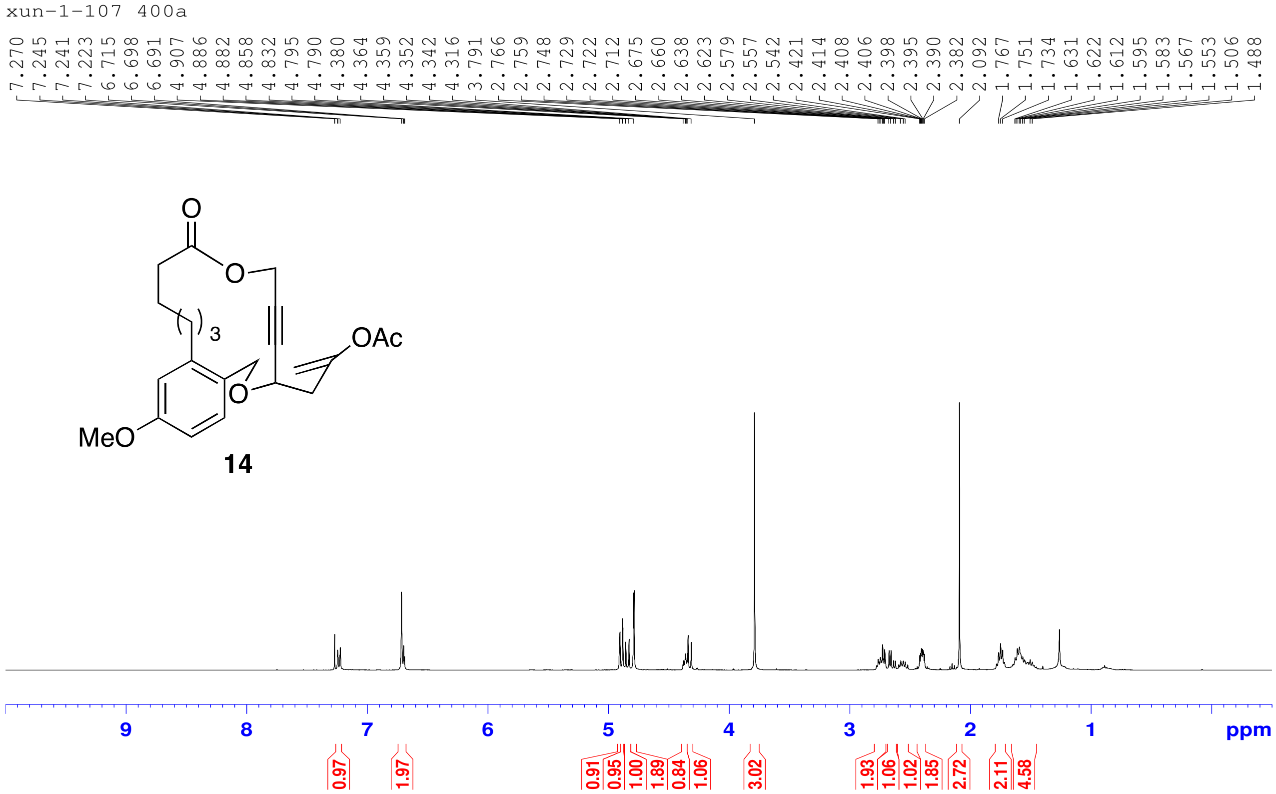
12


xun-1-75 13C
173.34 169.05 159.98 151.45 143.14 132.70 127.12 115.39 111.20 104.59 84.83 81.15 68.01 67.11 55.21 52.03 39.36 34.38 31.18 29.26 21.06
200 180 160 140 120 100 80 60 40 20 0 ppm

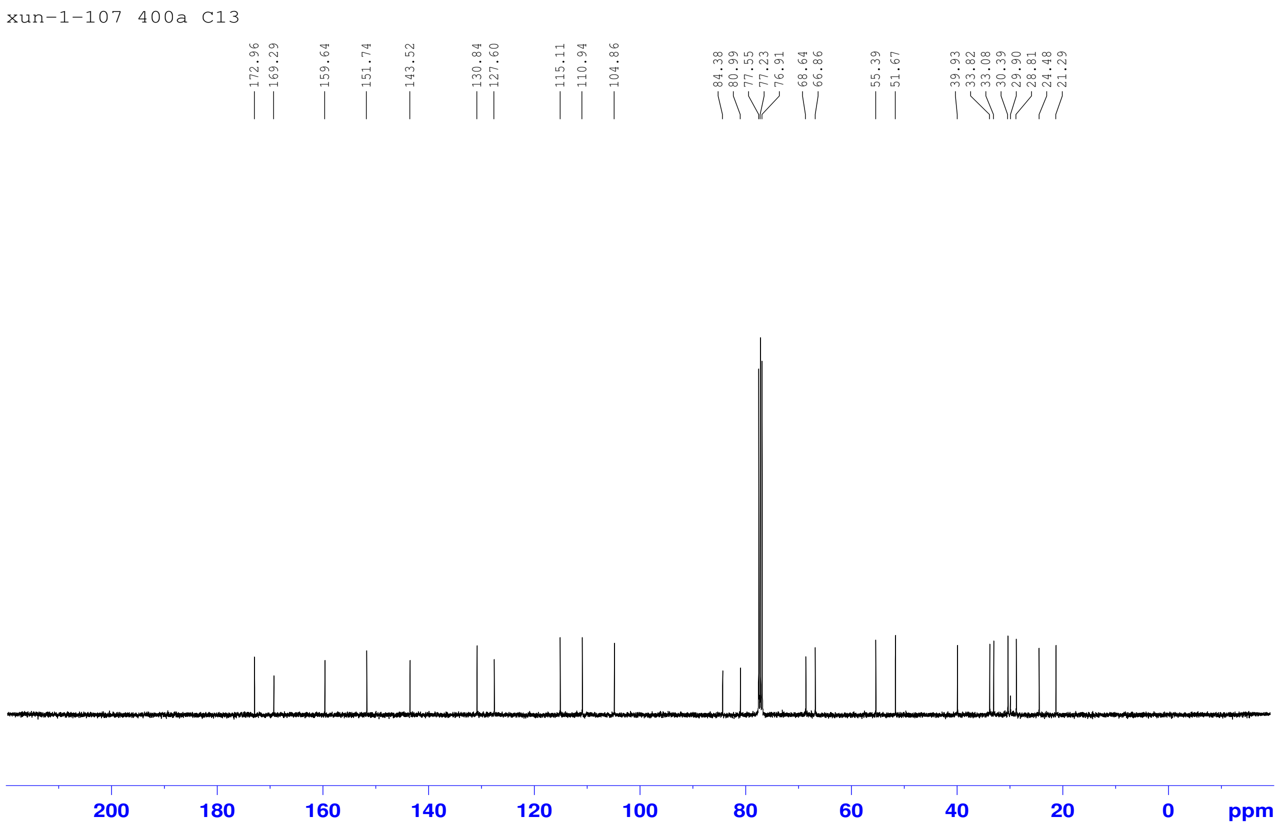

xun-1-76
7.346 7.325 6.821 6.814 6.799 6.793 6.762 6.755 5.377 5.372 5.346 5.341 5.113 5.110 5.106 5.095 5.092 5.088 4.864 4.856 4.826 4.819 4.707 4.703 4.670 4.666 3.809 2.982 2.948 2.917 2.915 2.894 2.877 2.858 2.845 2.823 2.811 2.616 2.604 2.572 2.534 2.501 2.497 2.495 2.493 2.438 2.429 2.410 2.407 2.401 2.398 2.379 2.370 1.932 1.851
9 8 7 6 5 4 3 2 1 ppm
1.01 1.05 1.01 1.02 0.99 1.03 1.03 3.00 3.18 4.23 1.11 2.22
O
O
O
MeO
O

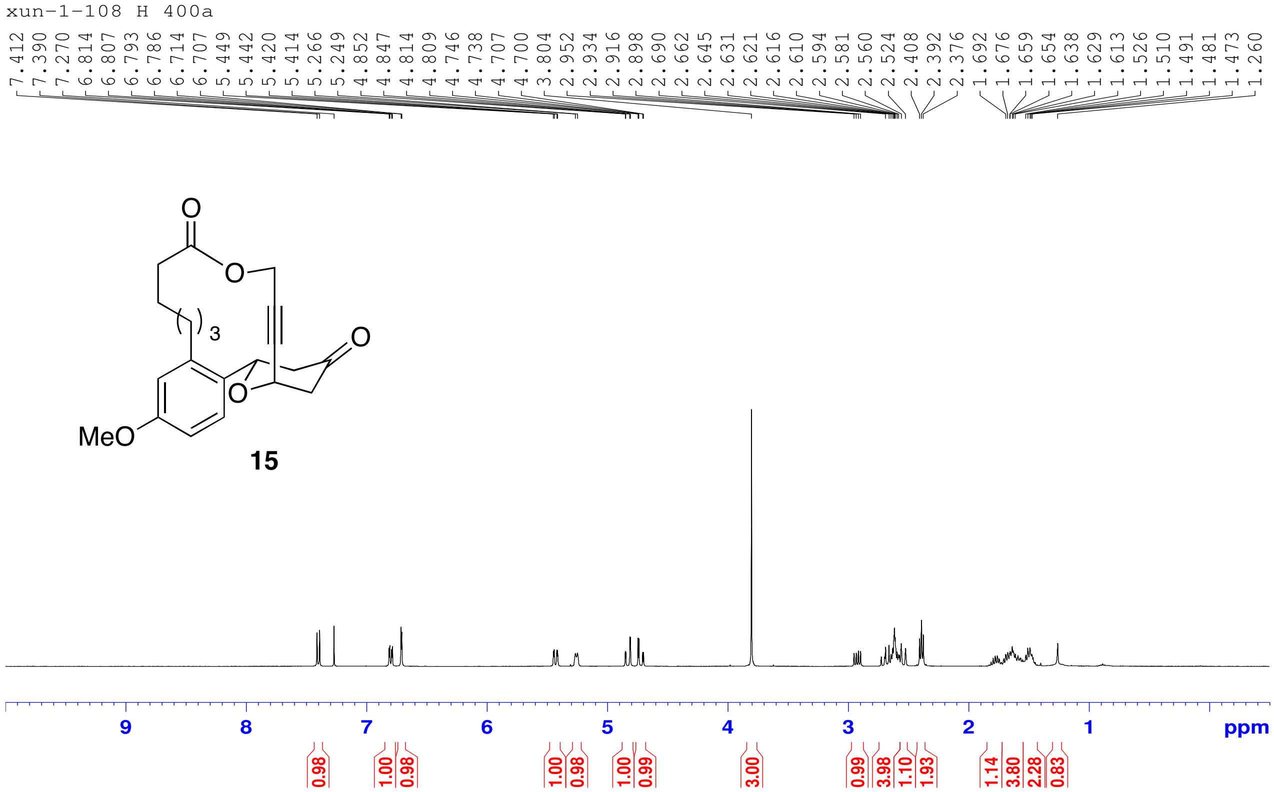
13

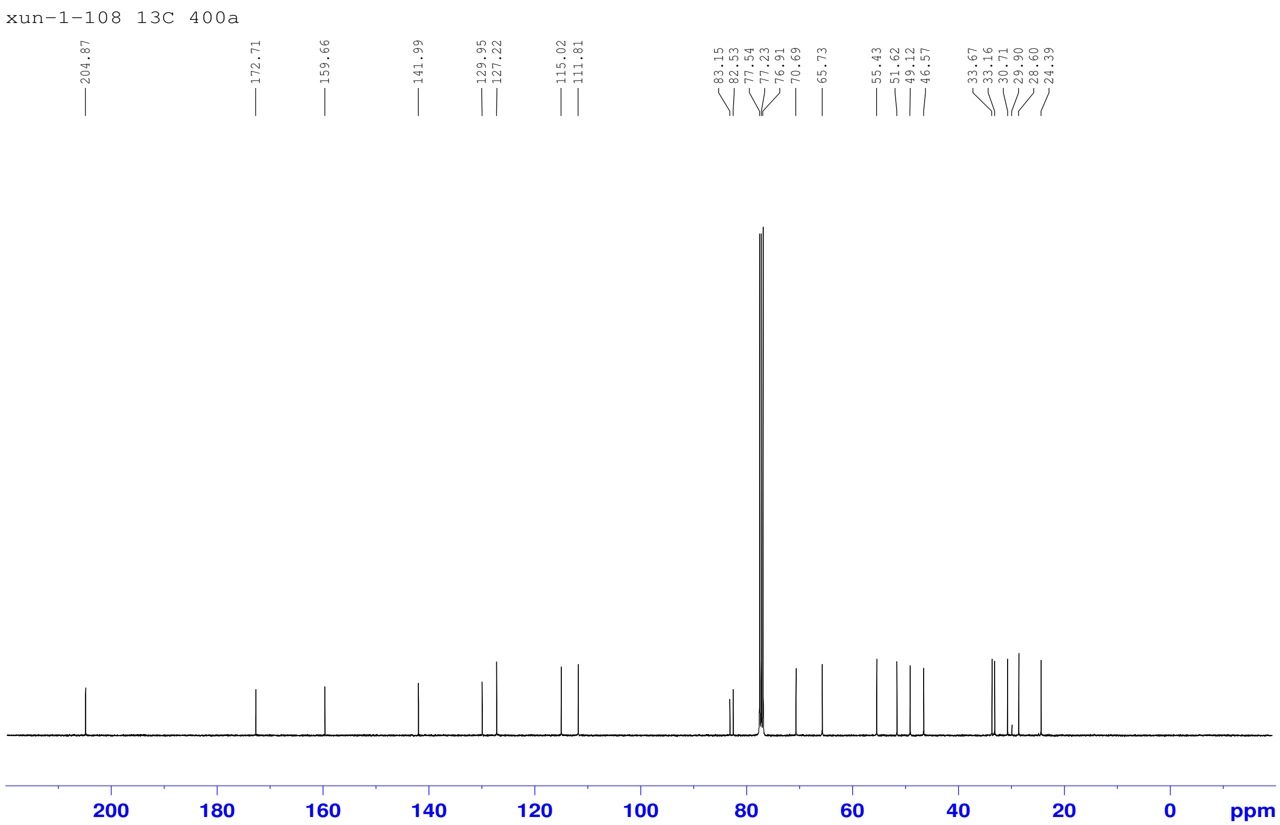

xun-1-76 13C
204.74 172.58 159.89 142.52 128.26 127.41 115.81 111.76 84.18 82.64 69.16 65.52 55.24 51.70 46.79 46.15 34.46 31.45 29.09
200 180 160 140 120 100 80 60 40 20 0 ppm


xun-1-107 400a
7.270 7.245 7.241 7.223 6.715 6.698 6.691 4.907 4.886 4.882 4.858 4.832 4.795 4.790 4.380 4.364 4.359 4.352 4.342 4.316 3.791 2.766 2.759 2.748 2.729 2.722 2.712 2.675 2.660 2.638 2.623 2.579 2.557 2.542 2.421 2.414 2.408 2.406 2.398 2.395 2.390 2.382 2.092 1.767 1.751 1.734 1.631 1.622 1.612 1.595 1.583 1.567 1.553 1.506 1.488
9 8 7 6 5 4 3 2 1 ppm
0.97 1.97 0.91 0.95 1.00 1.89 0.84 1.06 3.02 1.93 1.06 1.02 1.85 2.72 2.11 4.58
O
O
3
OAc
O
MeO

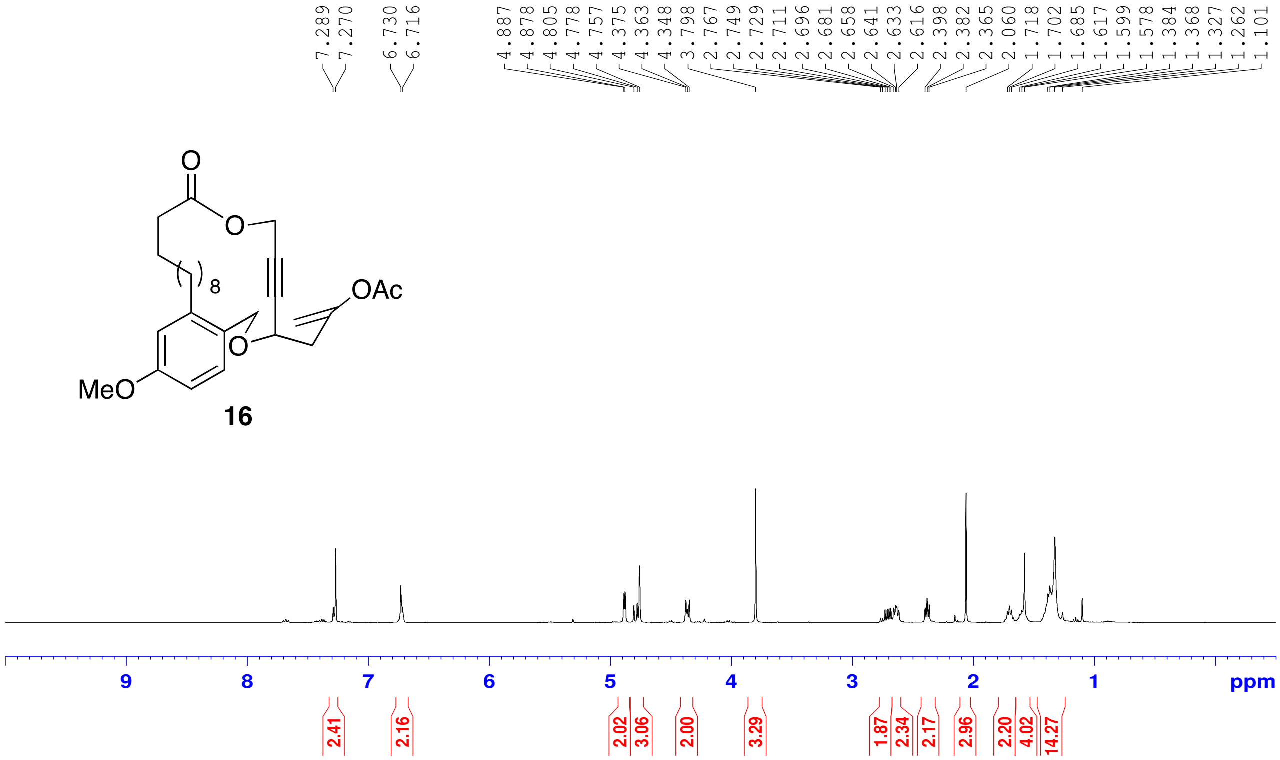
14


xun-1-107 400a C13
172.96 169.29 159.64 151.74 143.52 130.84 127.60 115.11 110.94 104.86 84.38 80.99 77.55 77.23 76.91 68.64 66.86 55.39 51.67 39.93 33.82 33.08 30.39 29.90 28.81 24.48 21.29
200 180 160 140 120 100 80 60 40 20 0 ppm

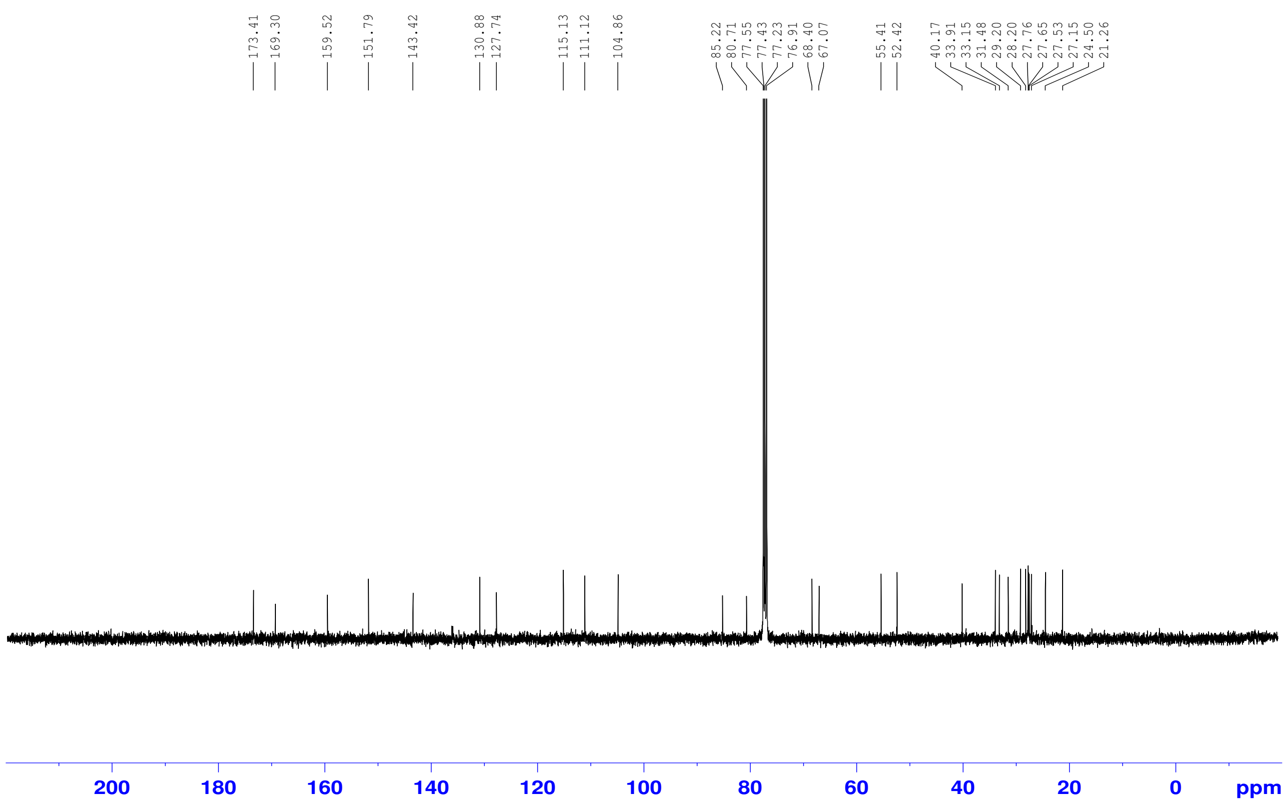

xun-1-108 H 400a
MeO
15
ppm

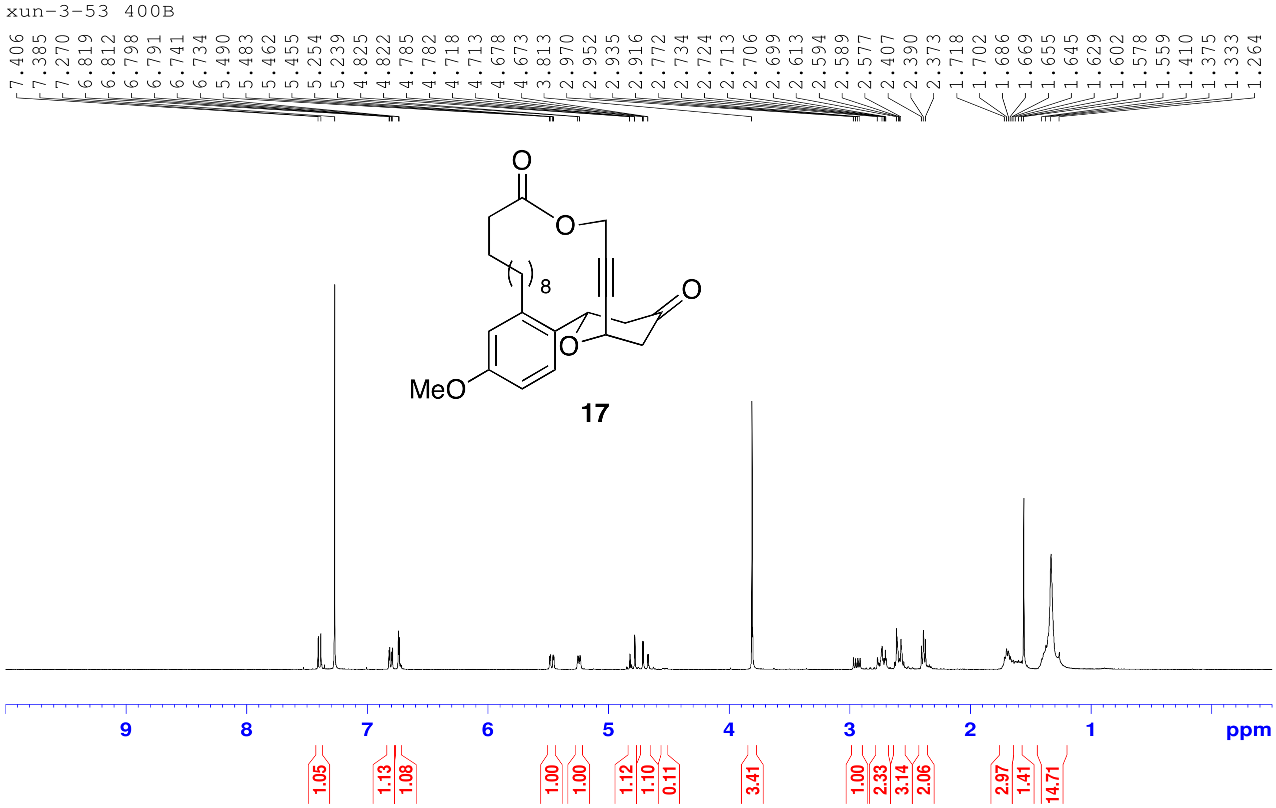

xun-1-108 13C 400a
204.87
172.71
159.66
141.99
129.95
127.22
115.02
111.81
83.15
82.53
77.54
77.23
76.91
70.69
65.73
55.43
51.62
49.12
46.57
33.67
33.16
30.71
29.90
28.60
24.39
ppm

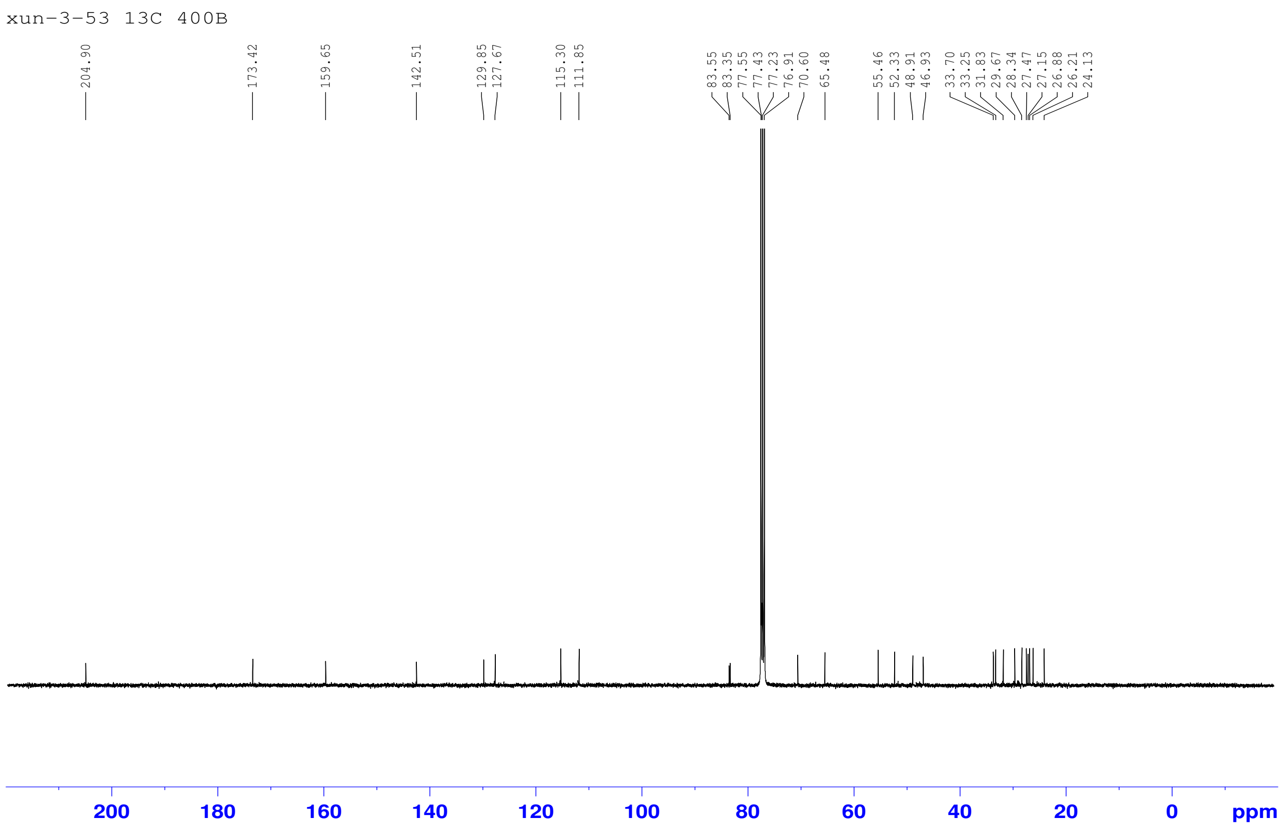
xun-3-52 400A
PROTON CDCl3 C:\Bruker\TOPSPIN floreancig 14



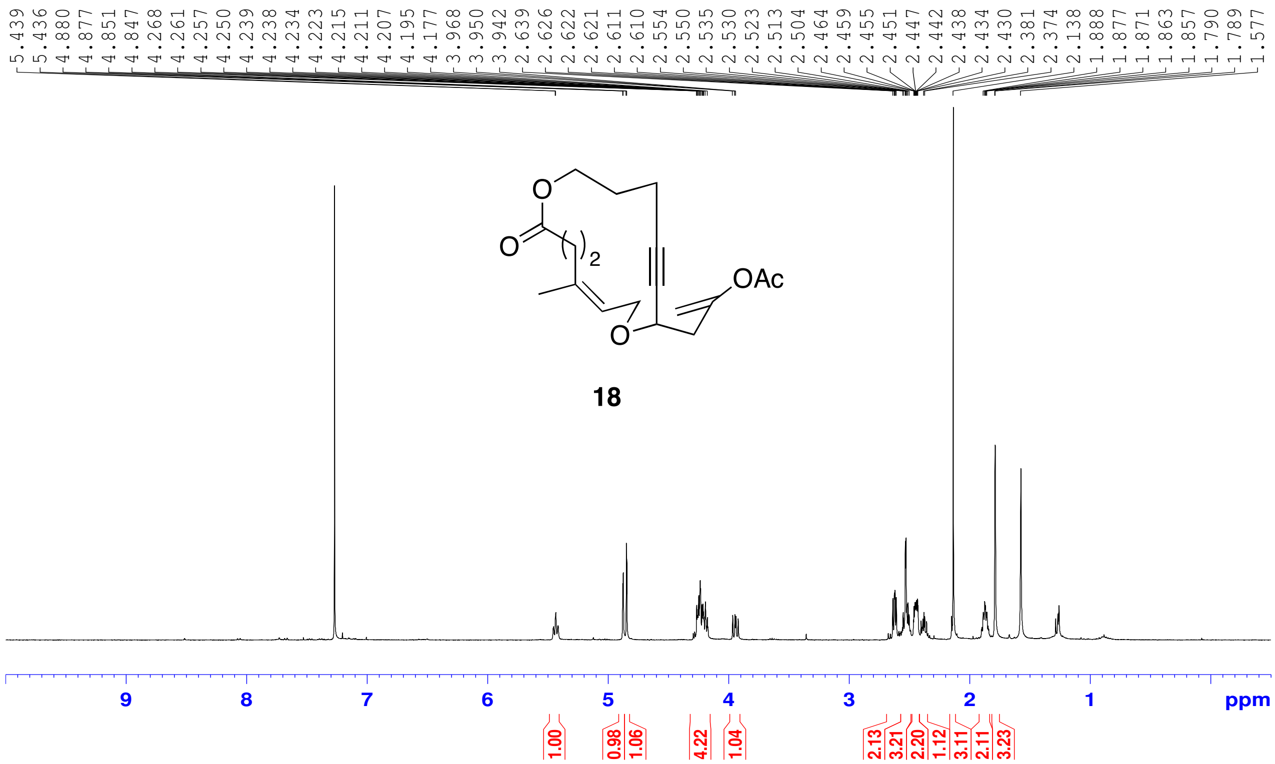
xun-3-52 13C 400B



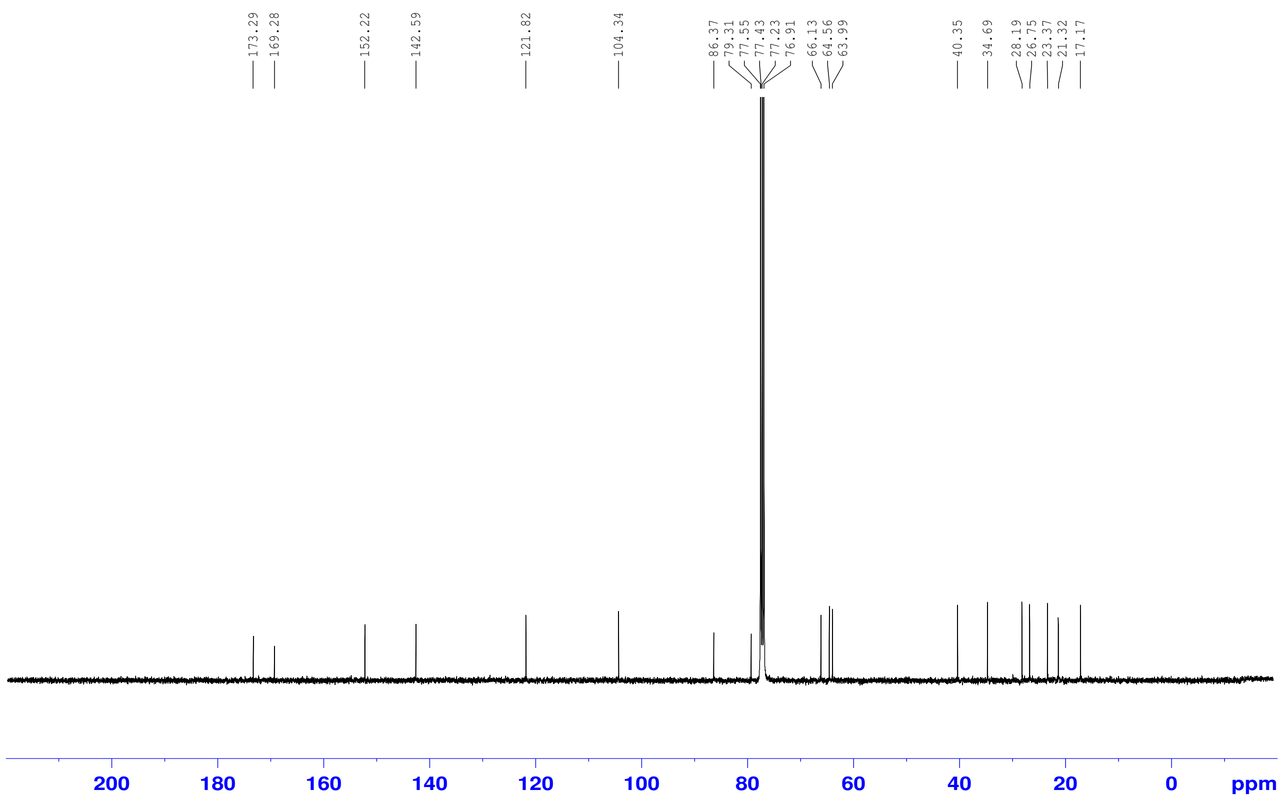

xun-3-53 400B
7.406
7.385
7.270
6.819
6.812
6.798
6.791
6.741
6.734
5.490
5.483
5.462
5.455
5.254
5.239
4.825
4.822
4.785
4.782
4.718
4.713
4.678
4.673
3.813
2.970
2.952
2.935
2.916
2.772
2.734
2.724
2.713
2.706
2.699
2.613
2.594
2.589
2.577
2.407
2.390
2.373
1.718
1.702
1.686
1.669
1.655
1.645
1.629
1.602
1.578
1.559
1.410
1.375
1.333
1.264
O
O
8
O
O
MeO
17
9
8
7
6
5
4
3
2
1
ppm
1.05
1.13
1.08
1.00
1.00
1.12
1.10
0.11
3.41
1.00
2.33
3.14
2.06
2.97
1.41
14.71


xun-3-53 13C 400B
204.90
173.42
159.65
142.51
129.85
127.67
115.30
111.85
83.55
83.35
77.55
77.43
77.23
76.91
70.60
65.48
55.46
52.33
48.91
46.93
33.70
33.25
31.83
29.67
28.34
27.47
27.15
26.88
26.21
24.13
200
180
160
140
120
100
80
60
40
20
0
ppm

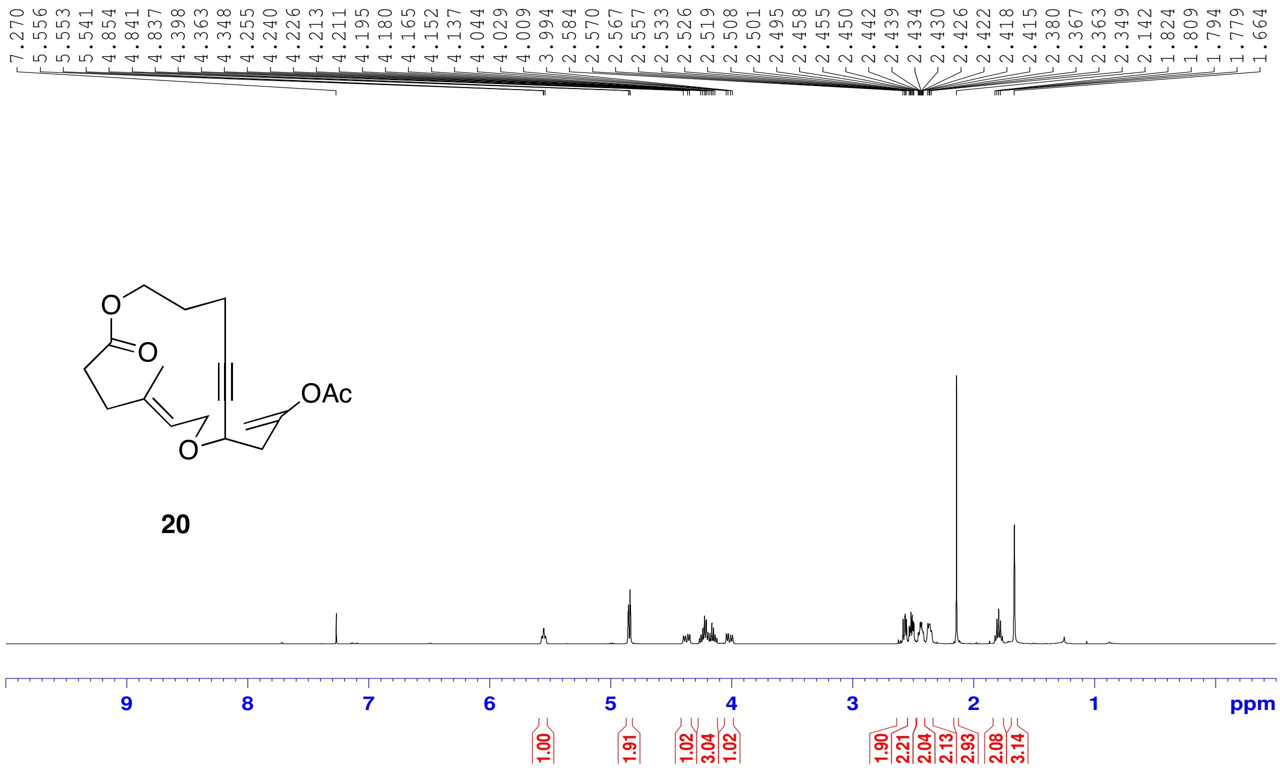
xun-2-222 1H NMR 400B



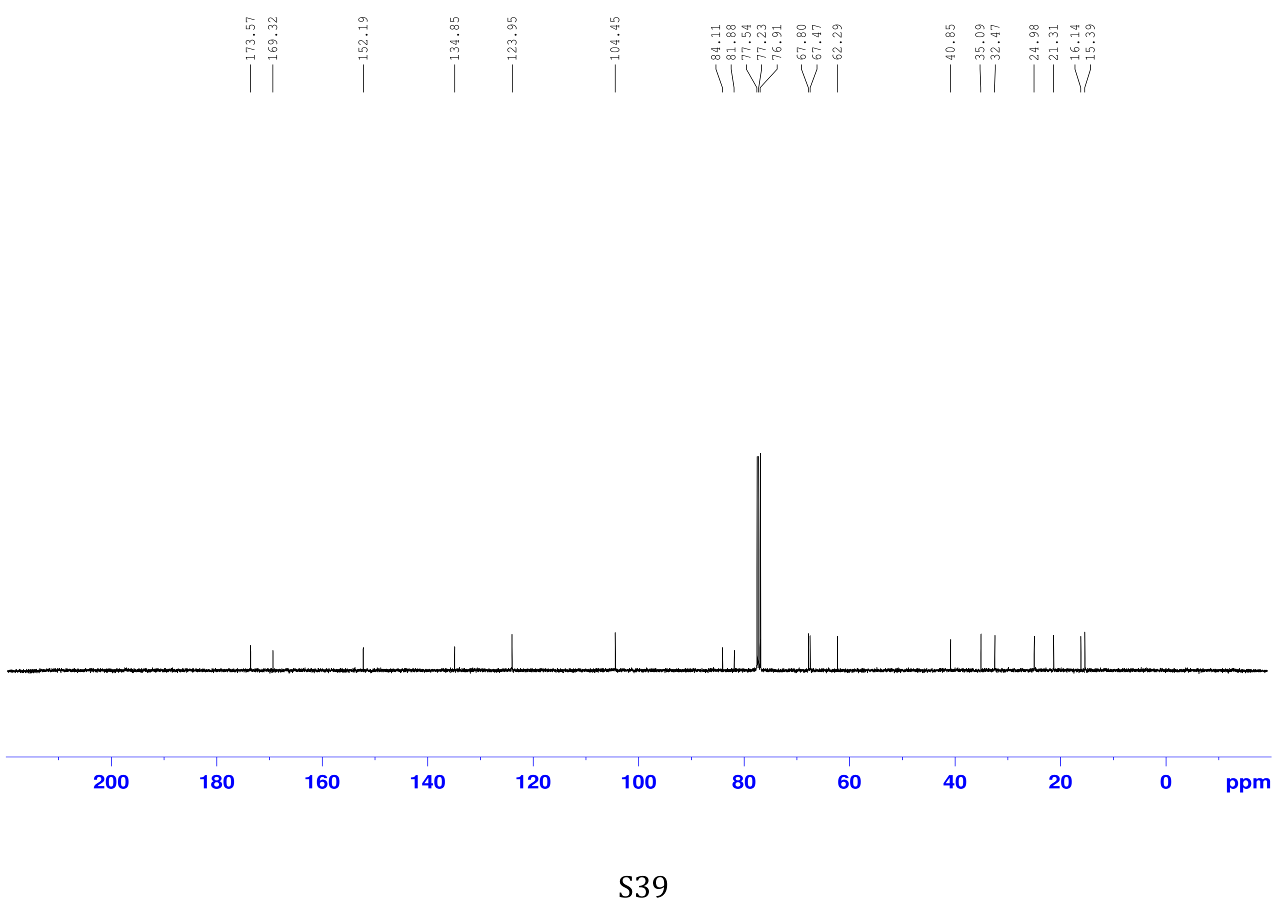
xun-2-222 13C NMR 400B

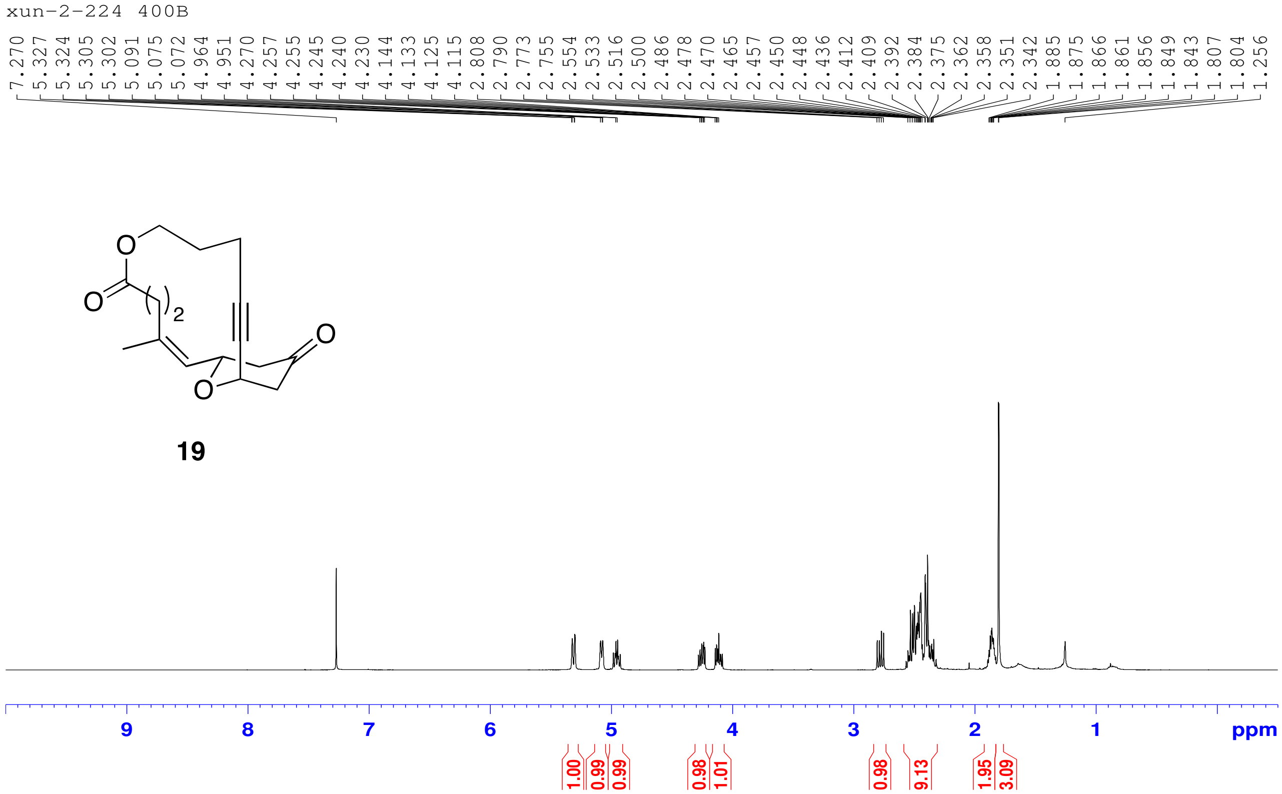


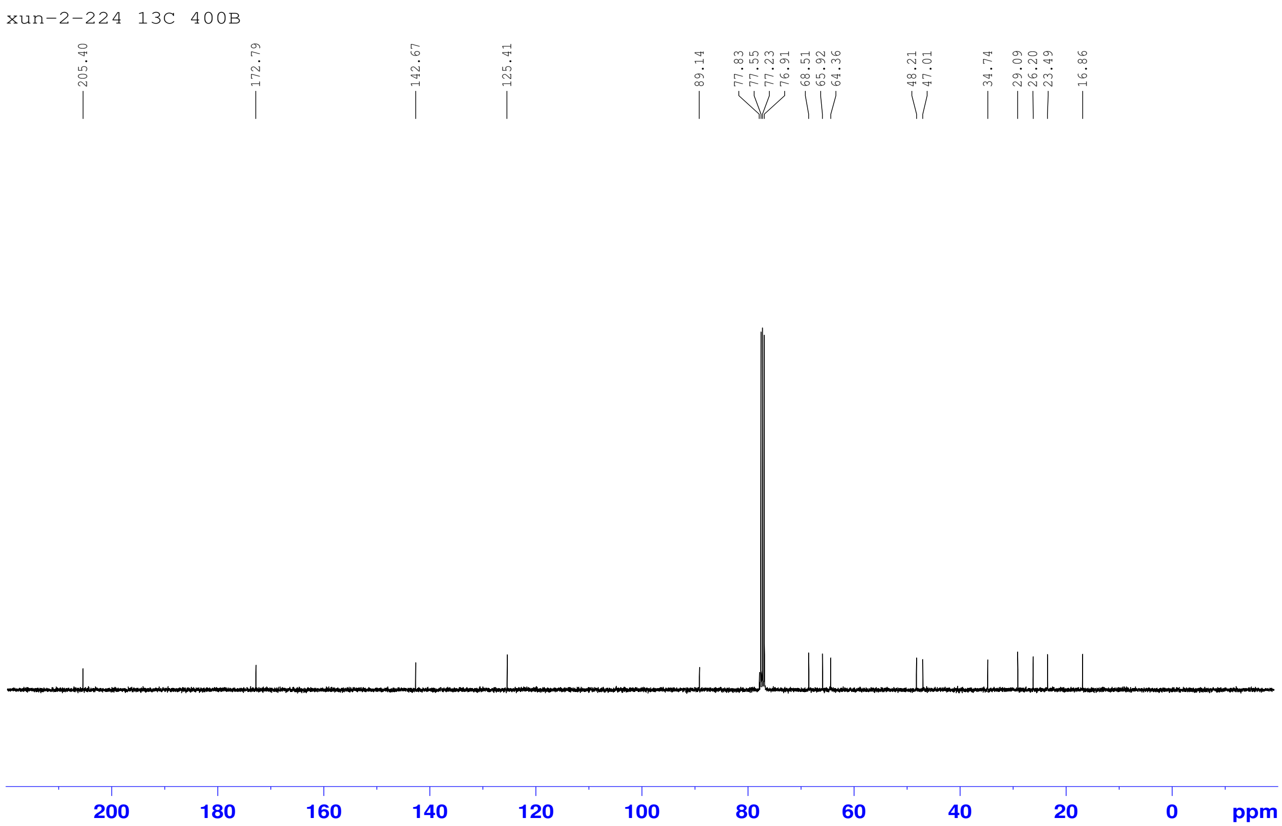
xun-2-227 400B

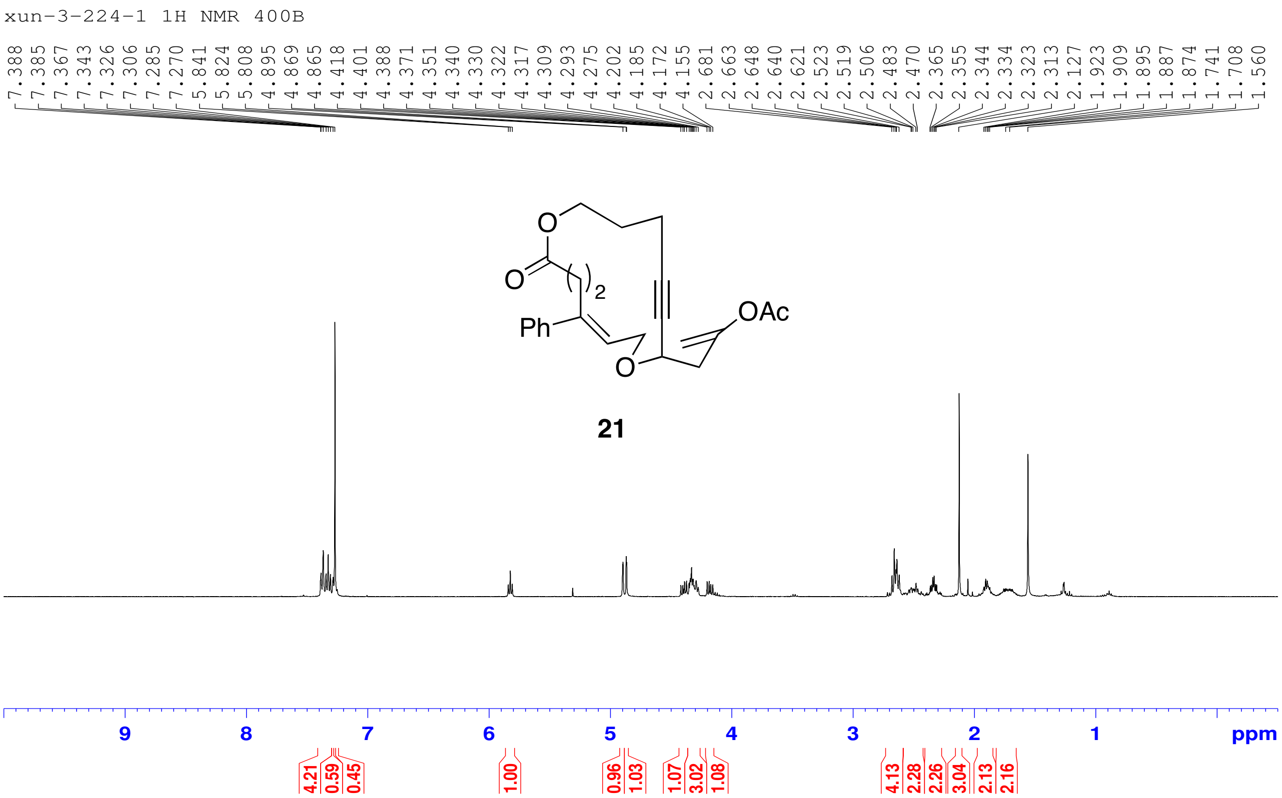


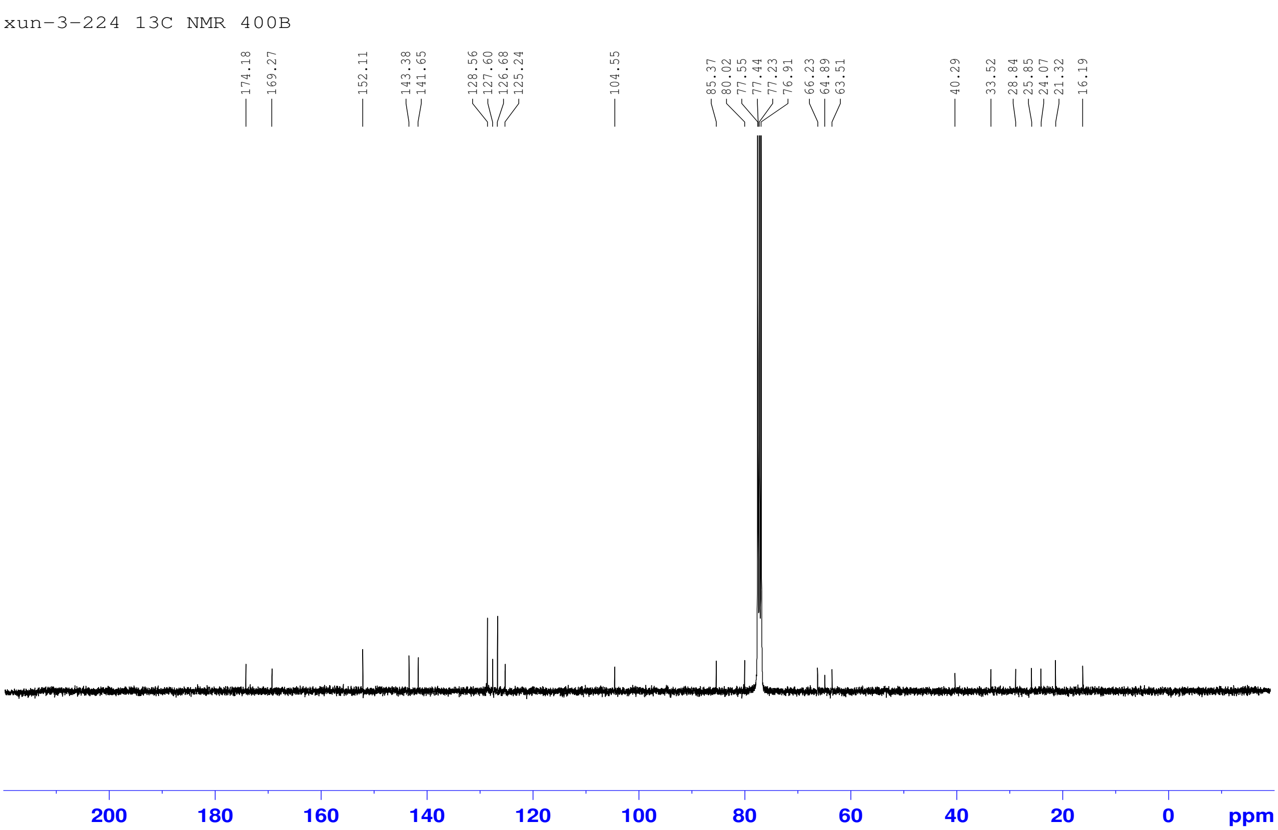
xun-2-227 13C 400B

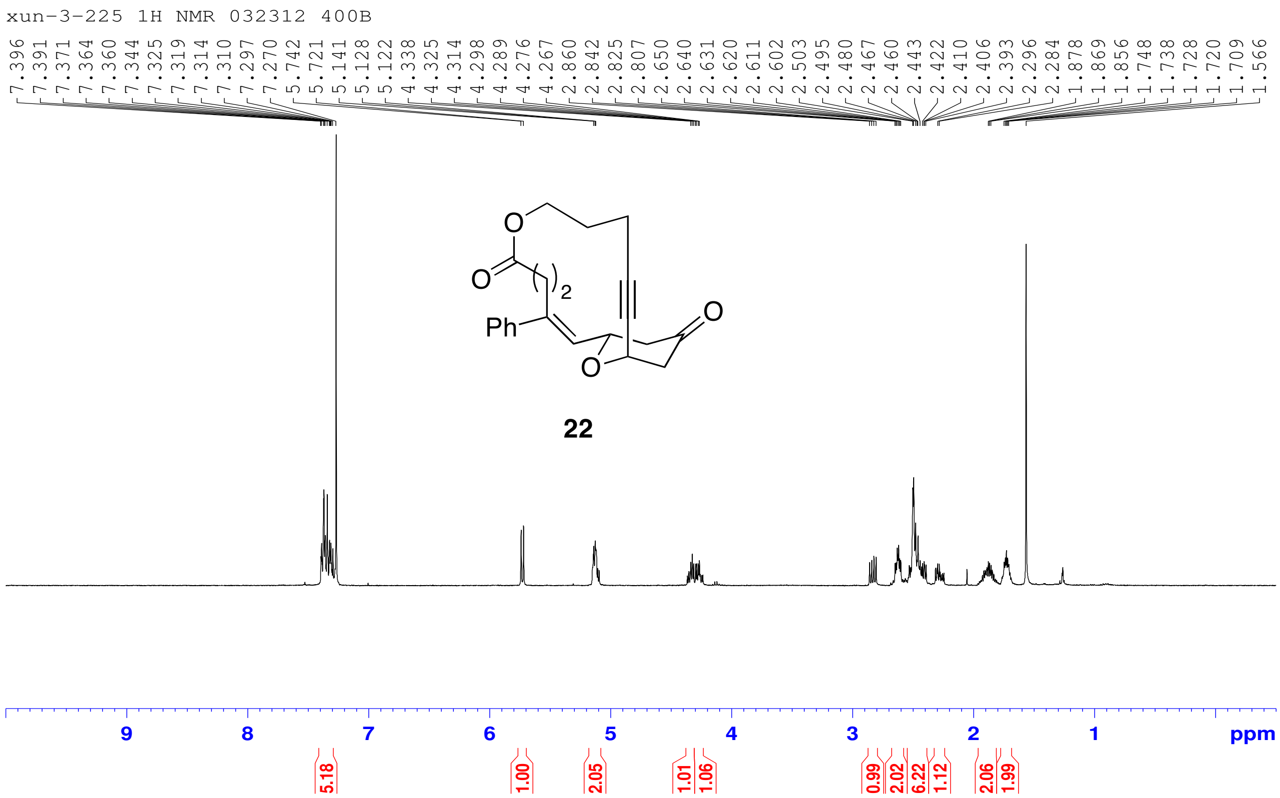


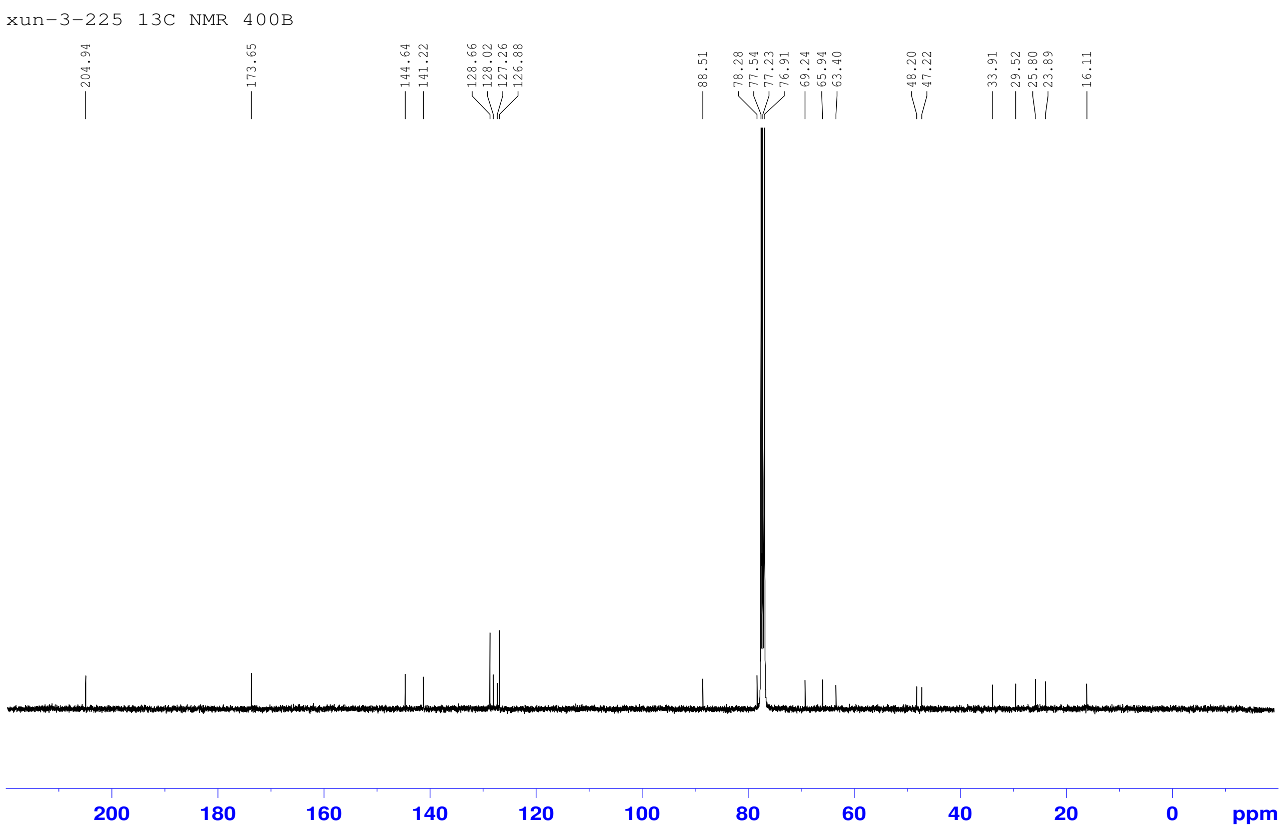

xun-2-224 400B
7.270 5.327 5.324 5.305 5.302 5.091 5.075 5.072 4.964 4.951 4.270 4.257 4.255 4.245 4.240 4.230 4.144 4.133 4.125 4.115 2.808 2.790 2.773 2.755 2.554 2.533 2.516 2.500 2.486 2.478 2.470 2.465 2.457 2.450 2.448 2.436 2.412 2.409 2.392 2.384 2.375 2.362 2.358 2.351 2.342 1.885 1.875 1.866 1.861 1.856 1.849 1.843 1.807 1.804 1.256
O
O
2
O
O
19
9
8
7
6
5
4
3
2
1
ppm
1.00
0.99
0.99
0.98
1.01
0.98
9.13
1.95
3.09

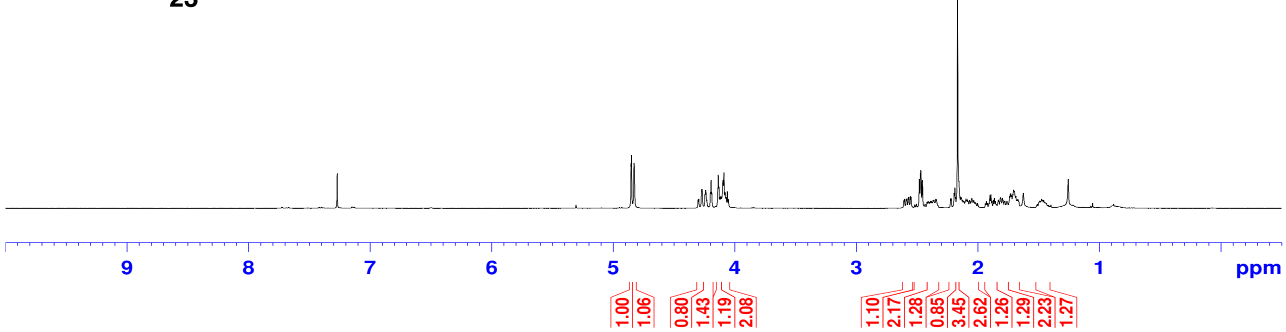

xun-2-224 13C 400B
205.40
172.79
142.67
125.41
89.14
77.83
77.55
77.23
76.91
68.51
65.92
64.36
48.21
47.01
34.74
29.09
26.20
23.49
16.86
200
180
160
140
120
100
80
60
40
20
0
ppm

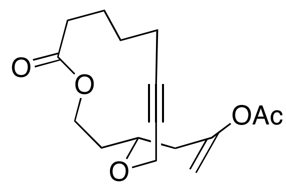

xun-3-224-1 1H NMR 400B
7.388 7.385 7.367 7.343 7.326 7.306 7.285 7.270 5.841 5.824 5.808 4.895 4.869 4.865 4.418 4.401 4.388 4.371 4.351 4.340 4.330 4.322 4.317 4.309 4.293 4.275 4.202 4.185 4.172 4.155 2.681 2.663 2.648 2.640 2.621 2.523 2.519 2.506 2.483 2.470 2.365 2.355 2.344 2.334 2.323 2.313 2.127 1.923 1.909 1.895 1.887 1.874 1.741 1.708 1.560
O
O
2
Ph
OAc
O
21
9
8
7
6
5
4
3
2
1
ppm
4.21 0.59 0.45 1.00 0.96 1.03 1.07 3.02 1.08 4.13 2.28 2.26 3.04 2.13 2.16


xun-3-224 13C NMR 400B
174.18 169.27 152.11 143.38 141.65 128.56 127.60 126.68 125.24 104.55 85.37 80.02 77.55 77.44 77.23 76.91 66.23 64.89 63.51 40.29 33.52 28.84 25.85 24.07 21.32 16.19
200
180
160
140
120
100
80
60
40
20
0
ppm

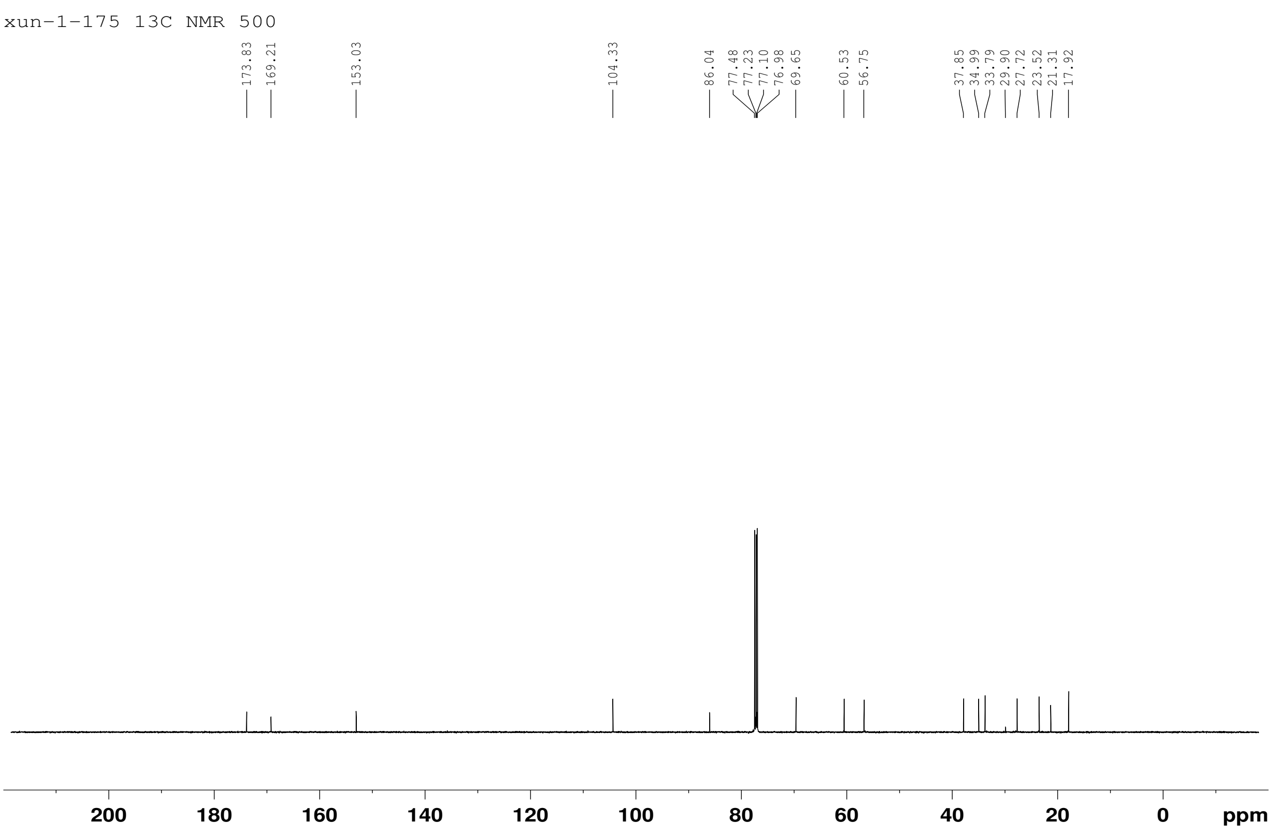

xun-3-225 1H NMR 032312 400B
7.396 7.391 7.371 7.364 7.360 7.344 7.325 7.319 7.314 7.310 7.297 7.270 5.742 5.721 5.141 5.128 5.122 4.338 4.325 4.314 4.298 4.289 4.276 4.267 2.860 2.842 2.825 2.807 2.650 2.640 2.631 2.620 2.611 2.602 2.503 2.495 2.480 2.467 2.460 2.443 2.422 2.410 2.406 2.393 2.296 2.284 1.878 1.869 1.856 1.748 1.738 1.728 1.720 1.709 1.566
O
O
2
Ph
O
O
22
9
8
7
6
5
4
3
2
1
ppm
5.18
1.00
2.05
1.01
1.06
0.99
2.02
6.22
1.12
2.06
1.99

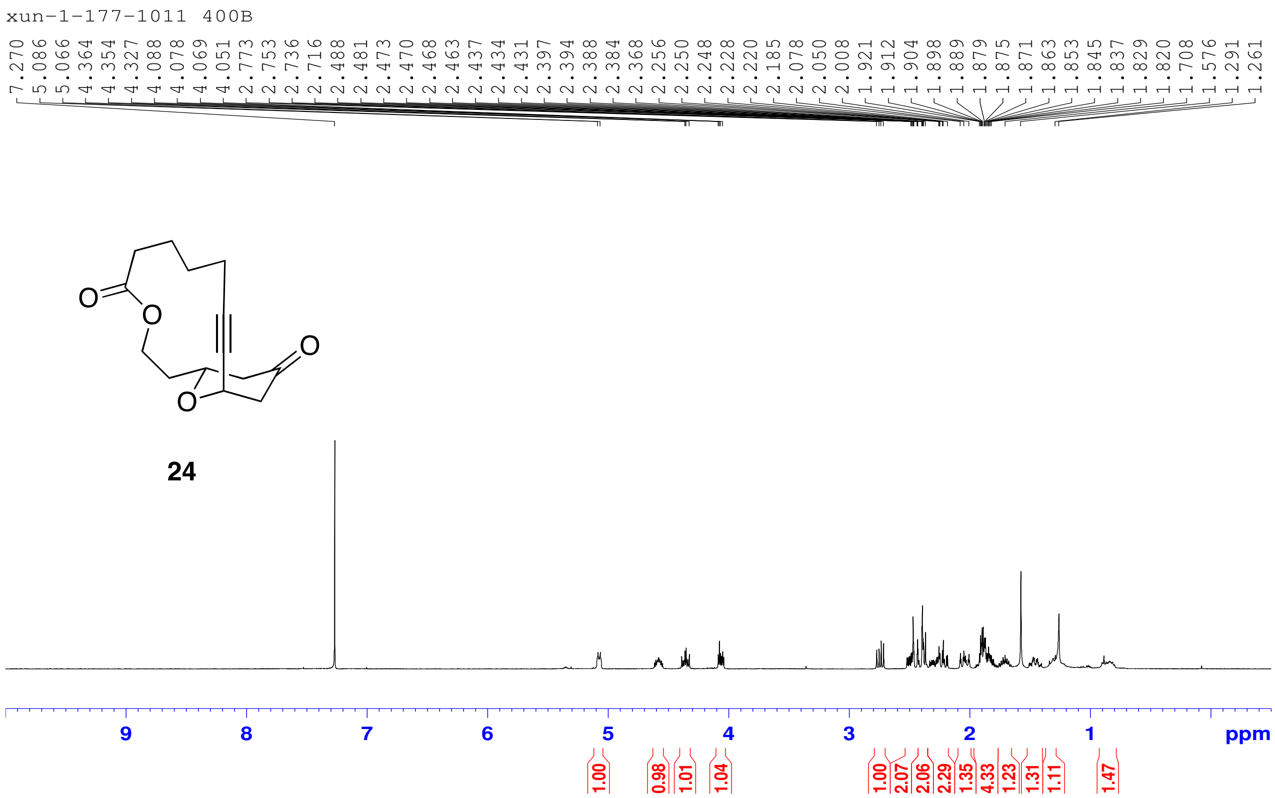

xun-3-225 13C NMR 400B
204.94
173.65
144.64
141.22
128.66 128.02 127.26 126.88
88.51
78.28 77.54 77.23 76.91
69.24
65.94
63.40
48.20 47.22
33.91
29.52
25.80
23.89
16.11
200
180
160
140
120
100
80
60
40
20
0
ppm

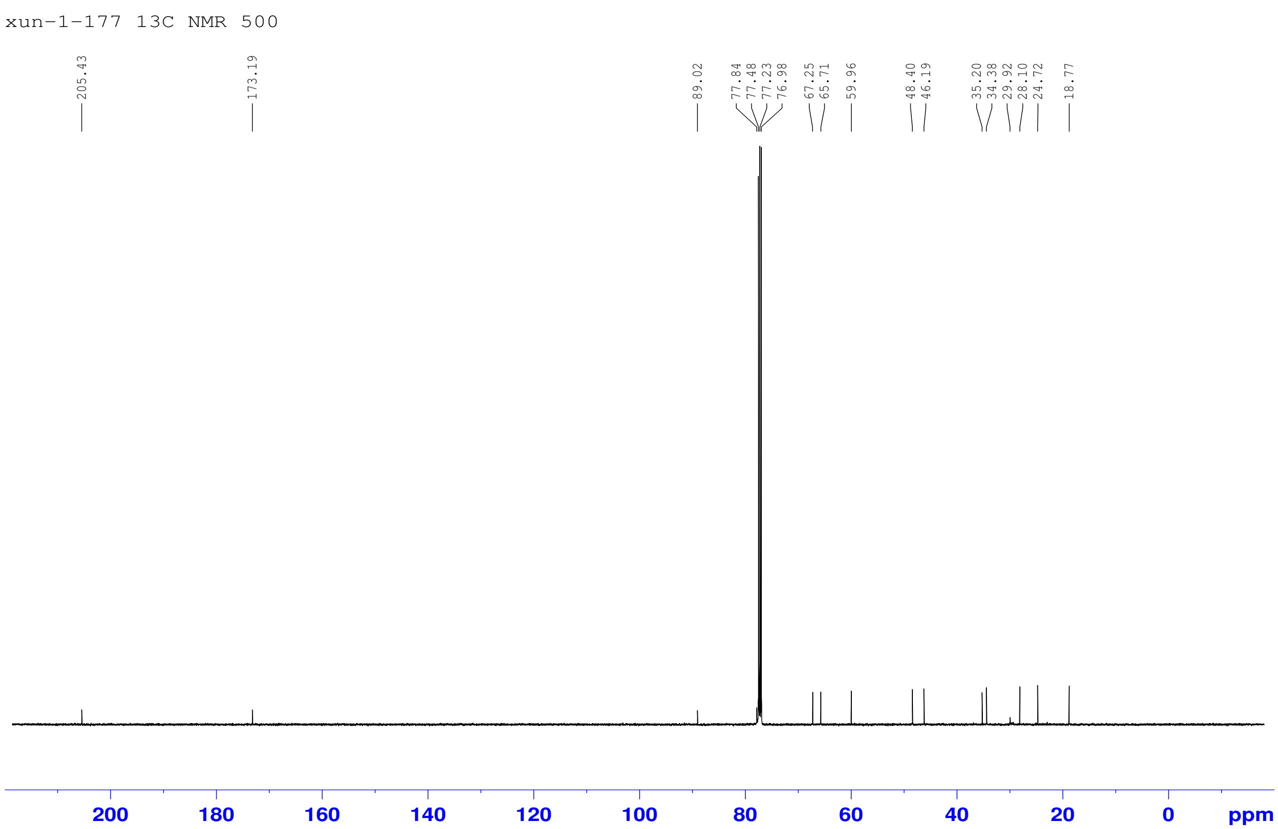

xun-1-175 1H 400B
7.270 4.852 4.849 4.828 4.272 4.268 4.244 4.239 4.235 4.199 4.194 4.189 4.135 4.130 4.121 4.114 4.095 4.088 4.079 4.070 4.061 2.572 2.567 2.553 2.548 2.480 2.470 2.456 2.224 2.219 2.195 2.189 2.183 2.166 2.155 2.140 2.134 2.097 2.050 1.900 1.892 1.863 1.816 1.811 1.797 1.738 1.732 1.729 1.723 1.713 1.705 1.698 1.687 1.625 1.256
1.00 1.06 0.80 1.43 1.19 2.08 1.10 2.17 1.28 0.85 3.45 2.62 1.26 1.29 2.23 1.27
ppm

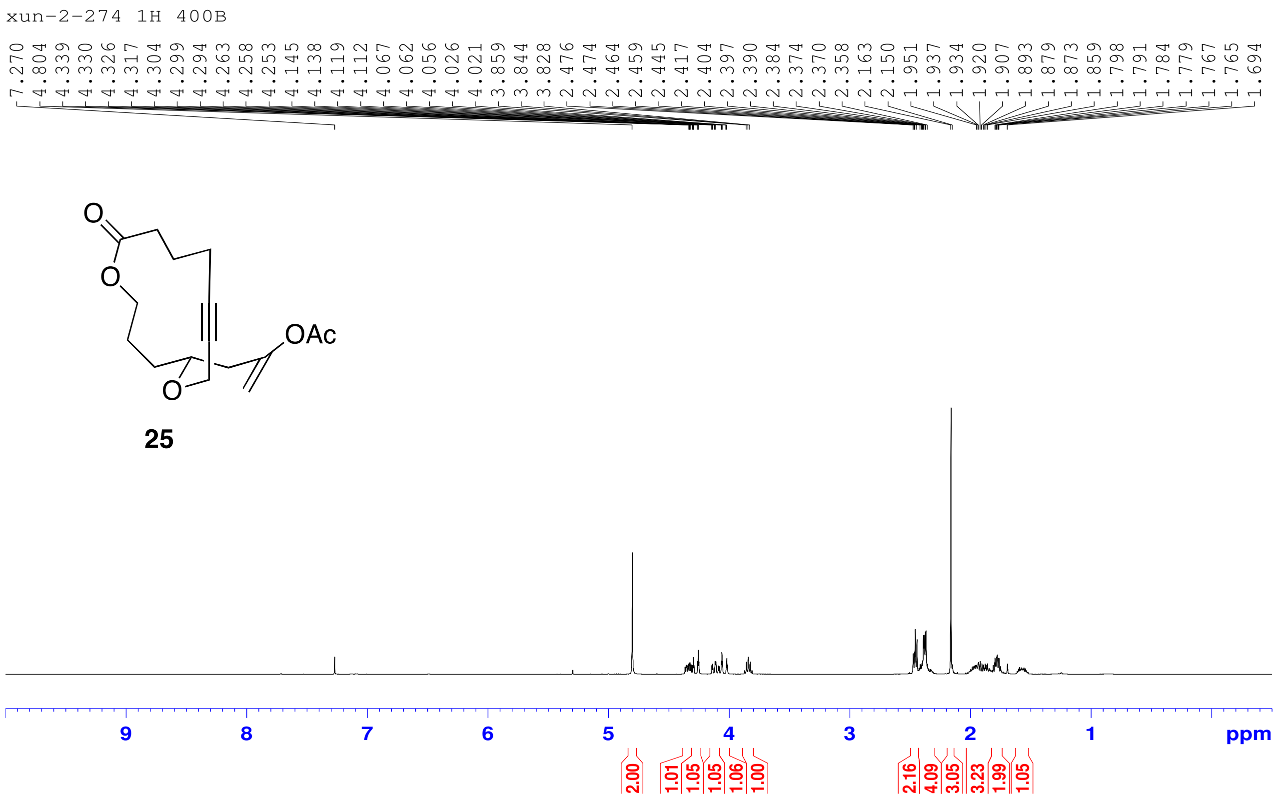

OAc

23

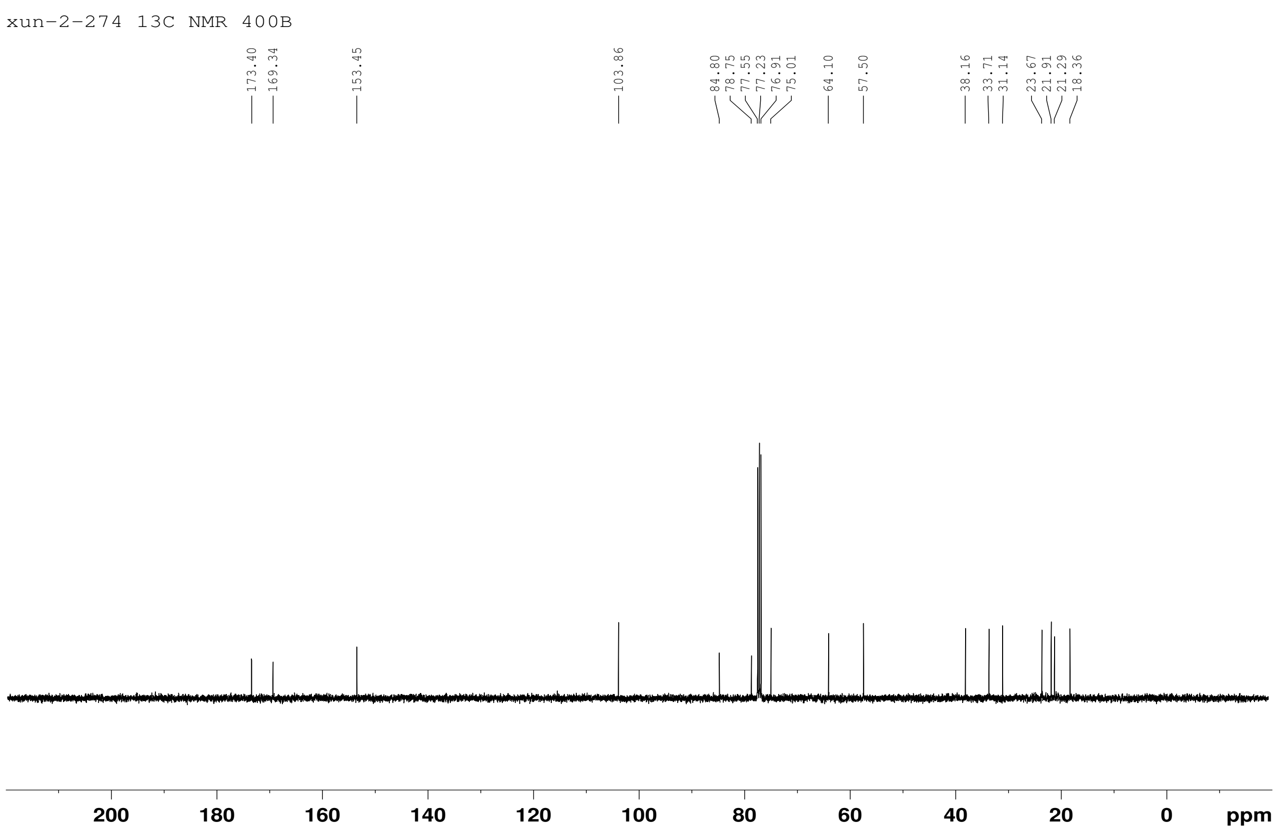

xun-1-175 13C NMR 500
173.83 169.21 153.03 104.33 86.04 77.48 77.23 77.10 76.98 69.65 60.53 56.75 37.85 34.99 33.79 29.90 27.72 23.52 21.31 17.92
200 180 160 140 120 100 80 60 40 20 0 ppm

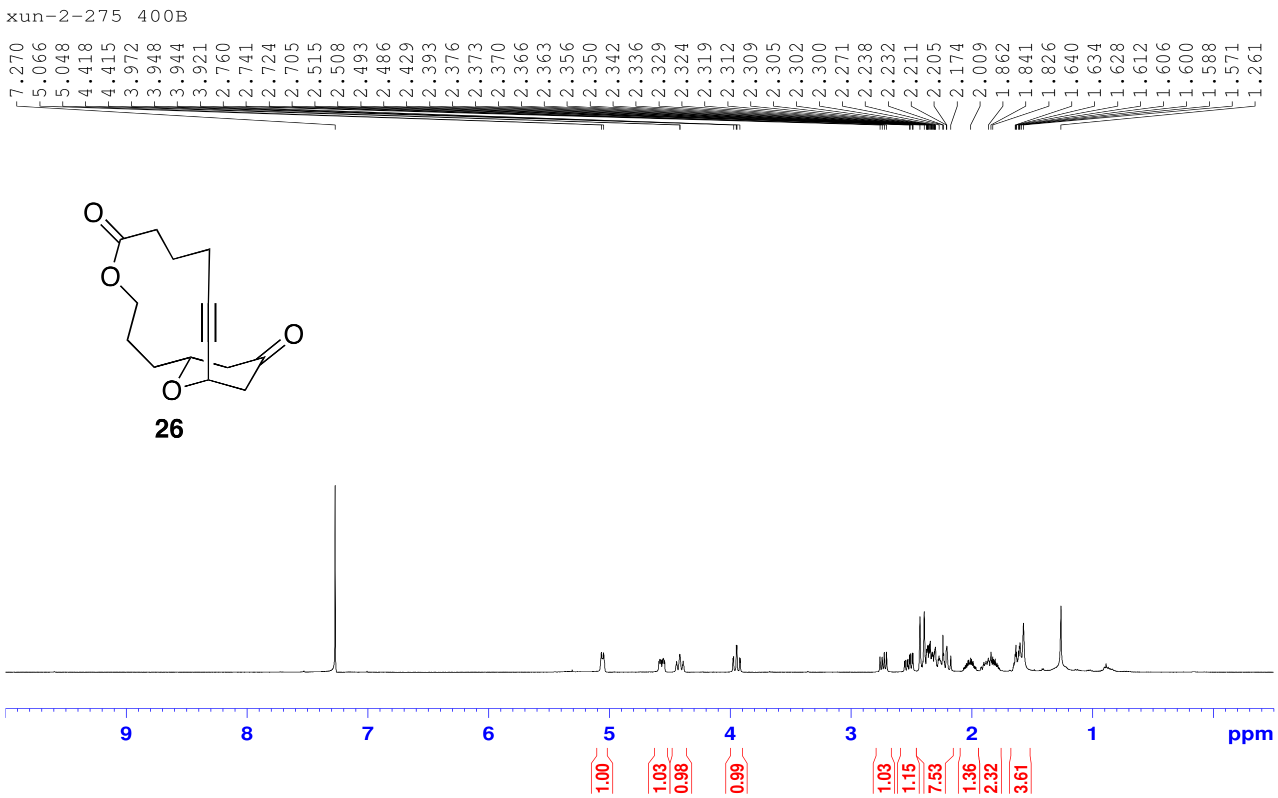

24
xun-1-177-1011 400B
7.270
5.086
5.066
4.364
4.354
4.327
4.088
4.078
4.069
4.051
2.773
2.753
2.736
2.716
2.488
2.481
2.473
2.470
2.468
2.463
2.437
2.434
2.431
2.397
2.394
2.388
2.384
2.368
2.256
2.250
2.248
2.228
2.220
2.185
2.078
2.050
2.008
1.921
1.912
1.904
1.898
1.889
1.879
1.875
1.871
1.863
1.853
1.845
1.837
1.829
1.820
1.708
1.576
1.291
1.261
9
8
7
6
5
4
3
2
1
ppm
1.00
0.98
1.01
1.04
1.00
2.07
2.06
2.29
1.35
4.33
1.23
1.31
1.11
1.47


xun-1-177 13C NMR 500
205.43
173.19
89.02
77.84
77.48
77.23
76.98
67.25
65.71
59.96
48.40
46.19
35.20
34.38
29.92
28.10
24.72
18.77
200
180
160
140
120
100
80
60
40
20
0
ppm

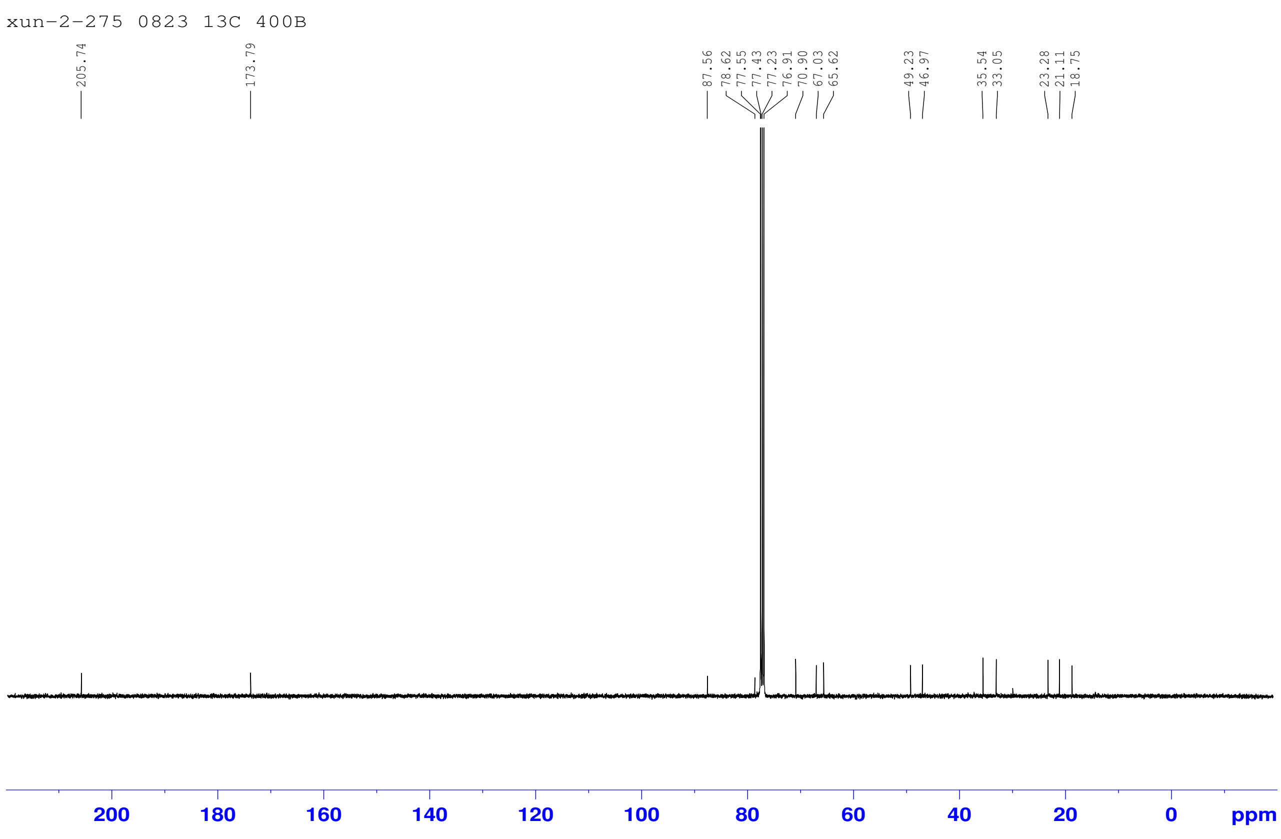

xun-2-274 1H 400B
7.270 4.804 4.339 4.330 4.326 4.317 4.304 4.299 4.294 4.263 4.258 4.253 4.145 4.138 4.119 4.112 4.067 4.062 4.056 4.026 4.021 3.859 3.844 3.828 2.476 2.474 2.464 2.459 2.445 2.417 2.404 2.397 2.390 2.384 2.374 2.370 2.358 2.163 2.150 1.951 1.937 1.934 1.920 1.907 1.893 1.879 1.873 1.859 1.798 1.791 1.784 1.779 1.767 1.765 1.694
9 8 7 6 5 4 3 2 1 ppm
2.00 1.01 1.05 1.05 1.06 1.00 2.16 4.09 3.05 3.23 1.99 1.05

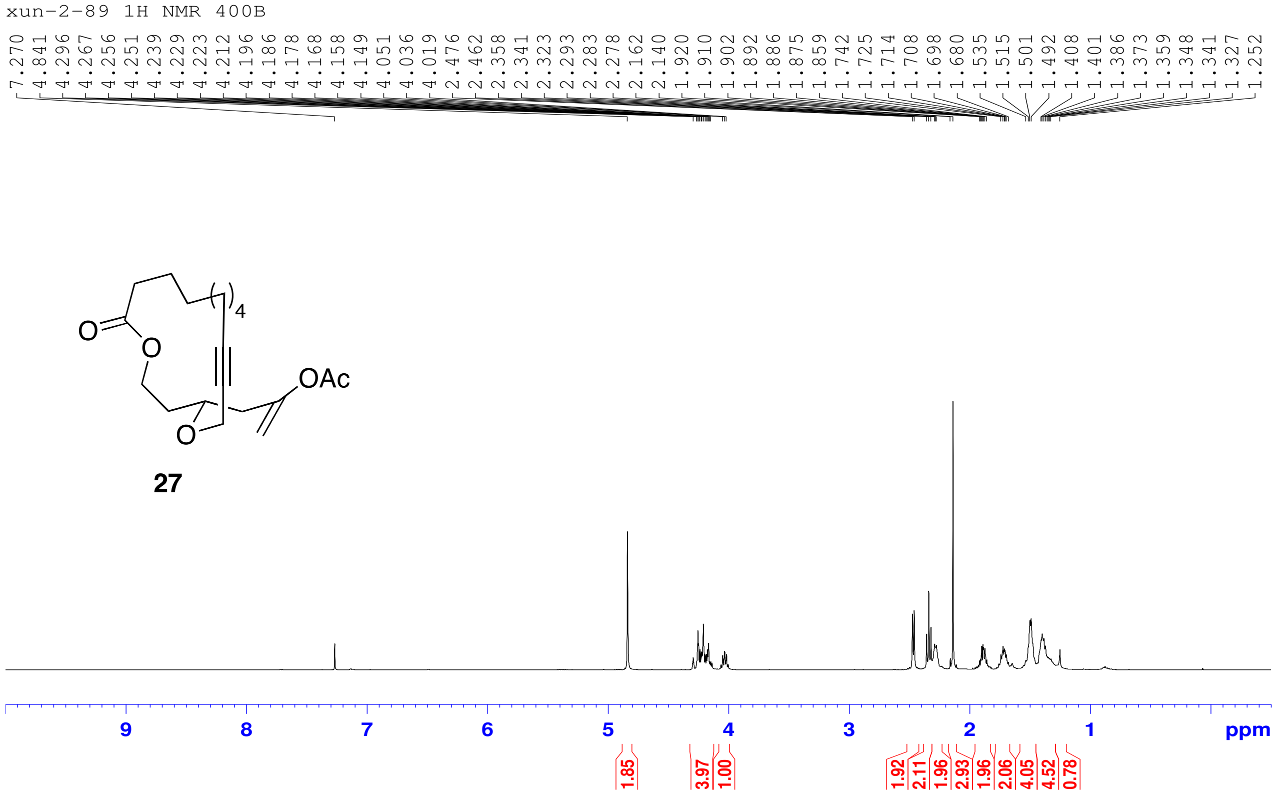
25


xun-2-274 13C NMR 400B
173.40 169.34 153.45 103.86 84.80 78.75 77.55 77.23 76.91 75.01 64.10 57.50 38.16 33.71 31.14 23.67 21.91 21.29 18.36
200 180 160 140 120 100 80 60 40 20 0 ppm

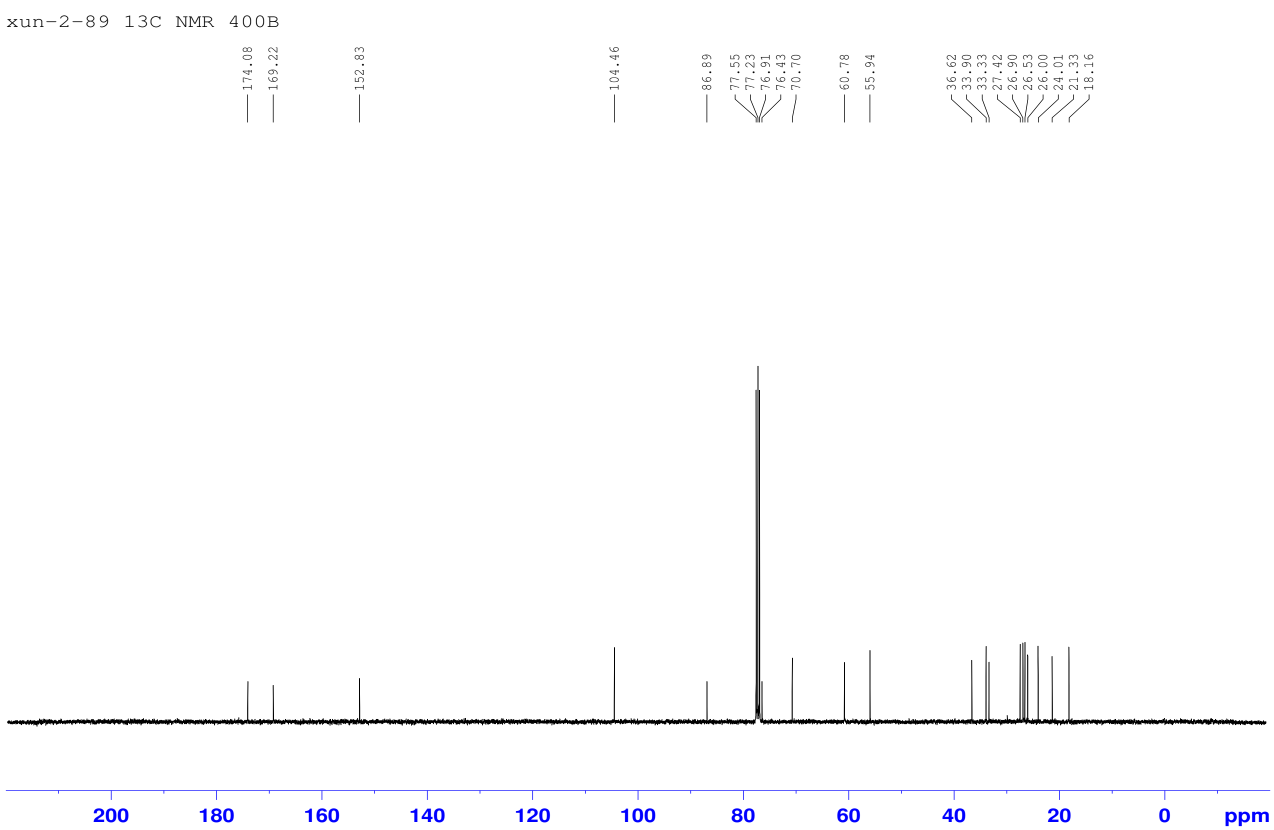

xun-2-275 400B
7.270
5.066
5.048
4.418
4.415
3.972
3.948
3.944
3.921
2.760
2.741
2.724
2.705
2.515
2.508
2.493
2.486
2.429
2.393
2.376
2.373
2.370
2.366
2.363
2.356
2.350
2.342
2.336
2.329
2.324
2.319
2.312
2.309
2.305
2.302
2.300
2.271
2.238
2.232
2.211
2.205
2.174
2.009
1.862
1.841
1.826
1.640
1.634
1.628
1.612
1.606
1.600
1.588
1.571
1.261
1.00
1.03
0.98
0.99
1.03
1.15
7.53
1.36
2.32
3.61
ppm

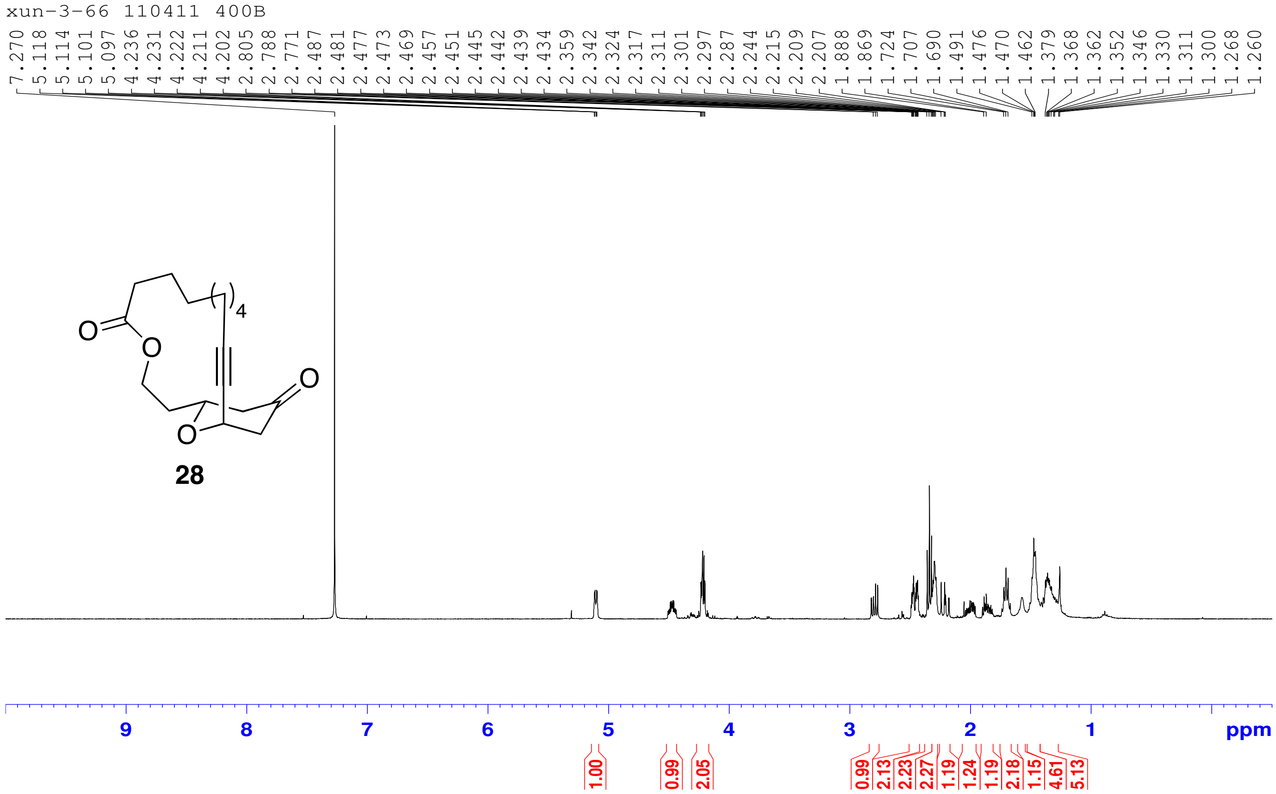
26


xun-2-275 0823 13C 400B
205.74
173.79
87.56
78.62
77.55
77.43
77.23
76.91
70.90
67.03
65.62
49.23
46.97
35.54
33.05
23.28
21.11
18.75
ppm

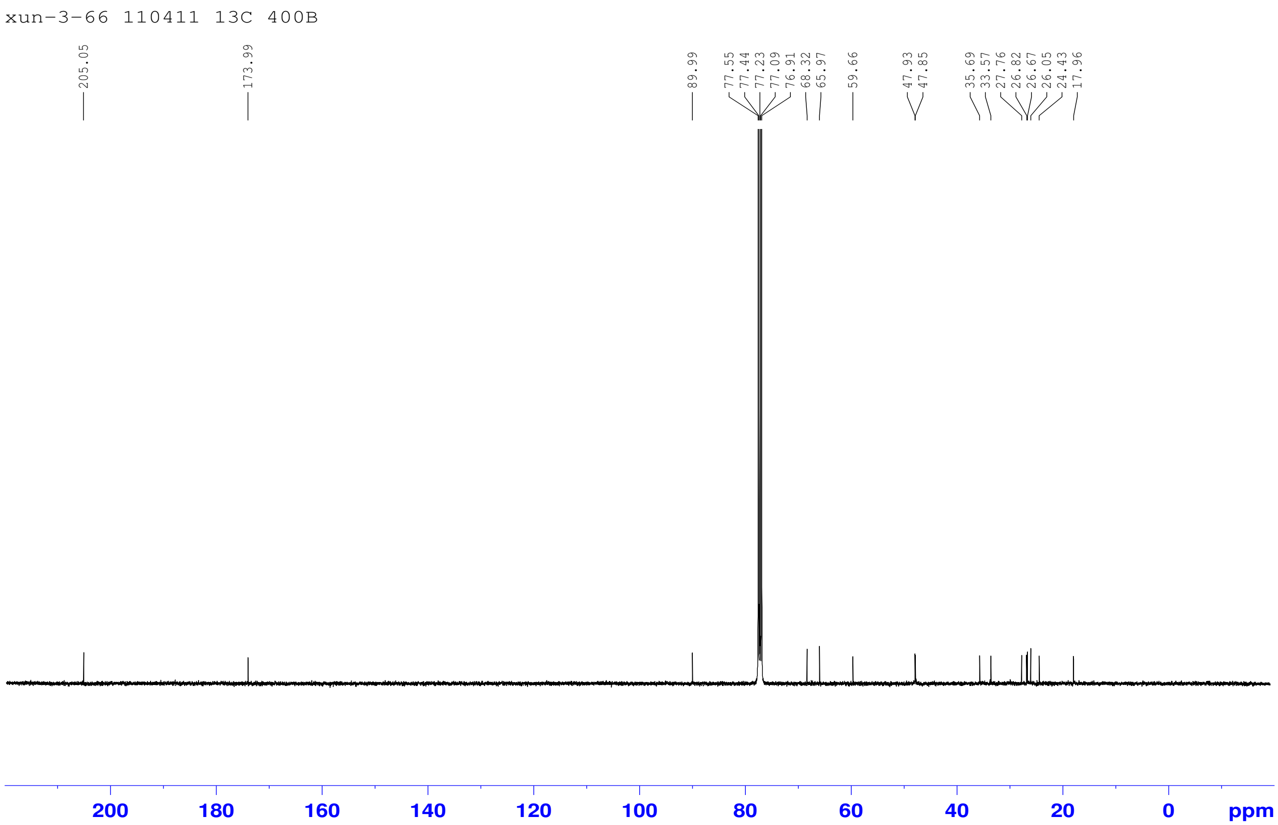

xun-2-89 1H NMR 400B
7.270
4.841
4.296
4.267
4.256
4.251
4.239
4.229
4.223
4.212
4.196
4.186
4.178
4.168
4.158
4.149
4.051
4.036
4.019
2.476
2.462
2.358
2.341
2.323
2.293
2.283
2.278
2.162
2.140
1.920
1.910
1.902
1.892
1.886
1.875
1.859
1.742
1.725
1.714
1.708
1.698
1.680
1.535
1.515
1.501
1.492
1.408
1.401
1.386
1.373
1.359
1.348
1.341
1.327
1.252
9
8
7
6
5
4
3
2
1
ppm
1.85
3.97
1.00
1.92
2.11
1.96
2.93
1.96
2.06
4.05
4.52
0.78
O
O
4
OAc
O

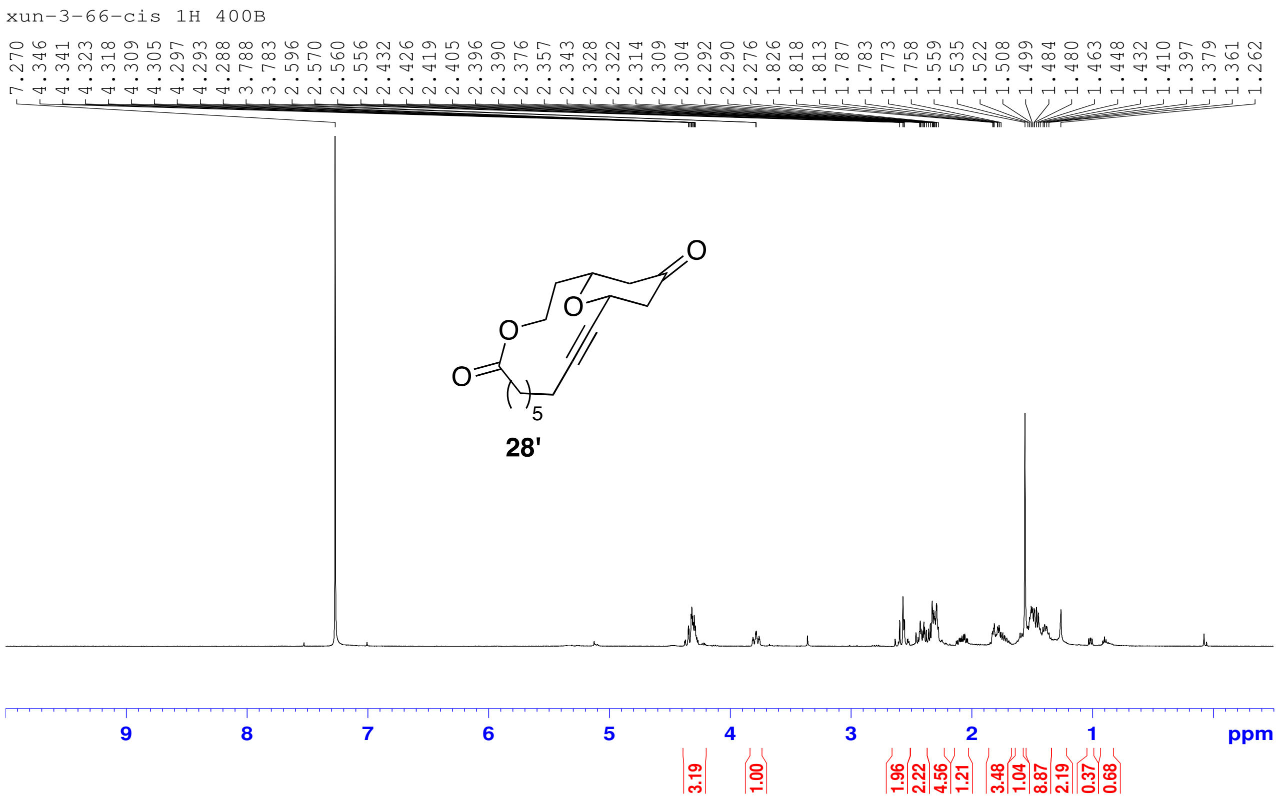
27

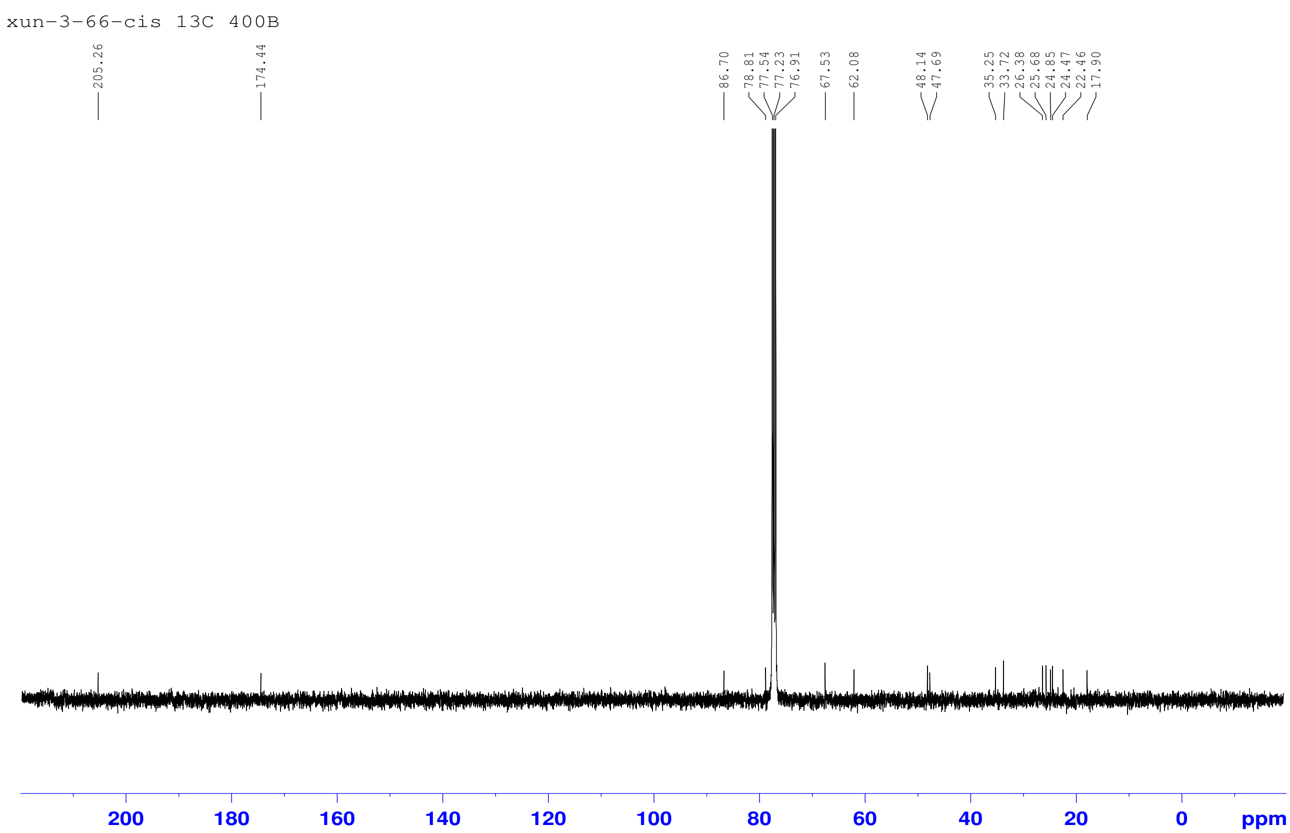

xun-2-89 13C NMR 400B
174.08
169.22
152.83
104.46
86.89
77.55
77.23
76.91
76.43
70.70
60.78
55.94
36.62
33.90
33.33
27.42
26.90
26.53
26.00
24.01
21.33
18.16
200
180
160
140
120
100
80
60
40
20
0
ppm


xun-3-66 110411 400B
7.270
5.118
5.114
5.101
5.097
4.236
4.231
4.222
4.211
4.202
2.805
2.788
2.771
2.487
2.481
2.477
2.473
2.469
2.457
2.451
2.445
2.442
2.439
2.434
2.359
2.342
2.324
2.317
2.311
2.301
2.297
2.287
2.244
2.215
2.209
2.207
1.888
1.869
1.724
1.707
1.690
1.491
1.476
1.470
1.462
1.379
1.368
1.362
1.352
1.346
1.330
1.311
1.300
1.268
1.260
9
8
7
6
5
4
3
2
1
ppm
1.00
0.99
2.05
0.99
2.13
2.23
2.27
1.19
1.24
1.19
2.18
1.15
4.61
5.13

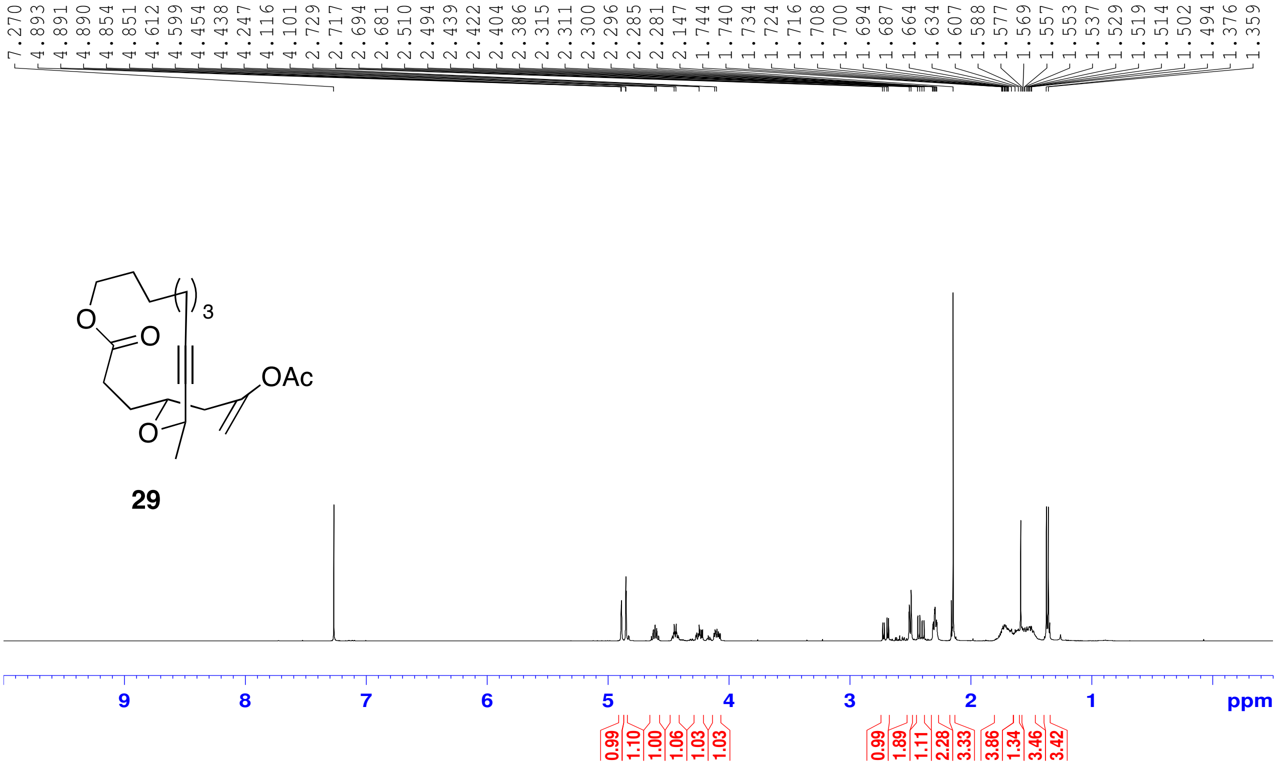
28


xun-3-66 110411 13C 400B
205.05
173.99
89.99
77.55
77.44
77.23
77.09
76.91
68.32
65.97
59.66
47.93
47.85
35.69
33.57
27.76
26.82
26.67
26.05
24.43
17.96
200
180
160
140
120
100
80
60
40
20
0
ppm

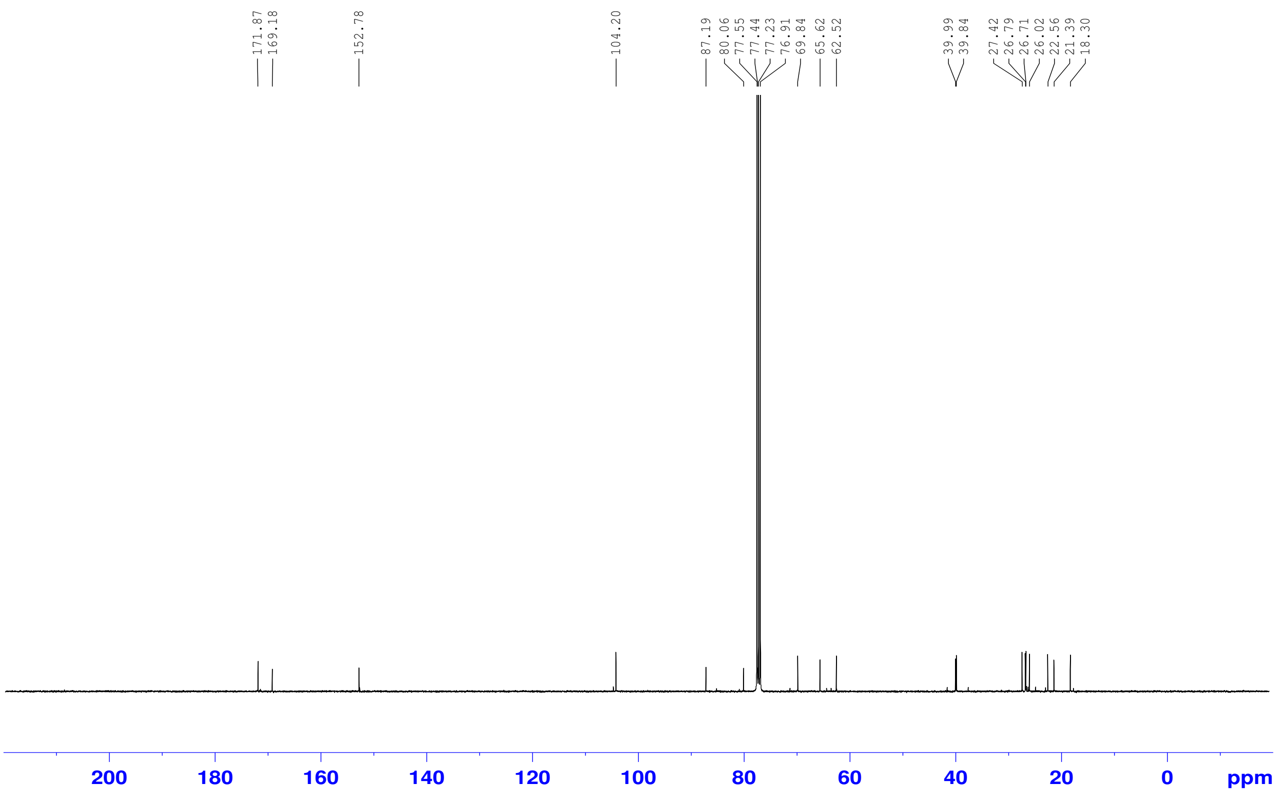

xun-3-66-cis 1H 400B
7.270
4.346
4.341
4.323
4.318
4.309
4.305
4.297
4.293
4.288
3.788
3.783
2.596
2.570
2.560
2.556
2.432
2.426
2.419
2.405
2.396
2.390
2.376
2.357
2.343
2.328
2.322
2.314
2.309
2.304
2.292
2.290
2.276
1.826
1.818
1.813
1.787
1.783
1.773
1.758
1.559
1.535
1.522
1.508
1.499
1.484
1.480
1.463
1.448
1.432
1.410
1.397
1.379
1.361
1.262
O
O
O
O
5
28'
9
8
7
6
5
4
3
2
1
ppm
3.19
1.00
1.96
2.22
4.56
1.21
3.48
1.04
8.87
2.19
0.37
0.68


xun-3-66-cis 13C 400B
205.26
174.44
86.70
78.81
77.54
77.23
76.91
67.53
62.08
48.14
47.69
35.25
33.72
26.38
25.68
24.85
24.47
22.46
17.90
200
180
160
140
120
100
80
60
40
20
0
ppm

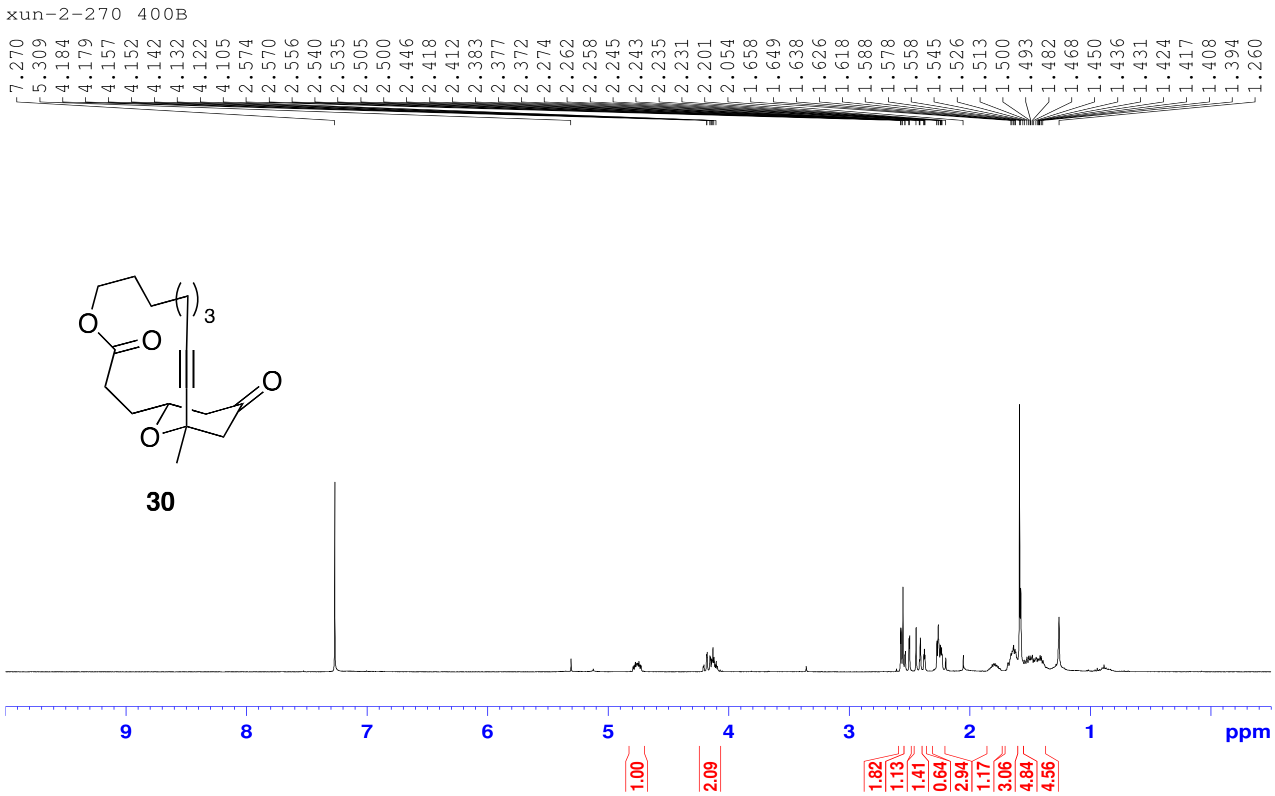
xun-2-269 400B

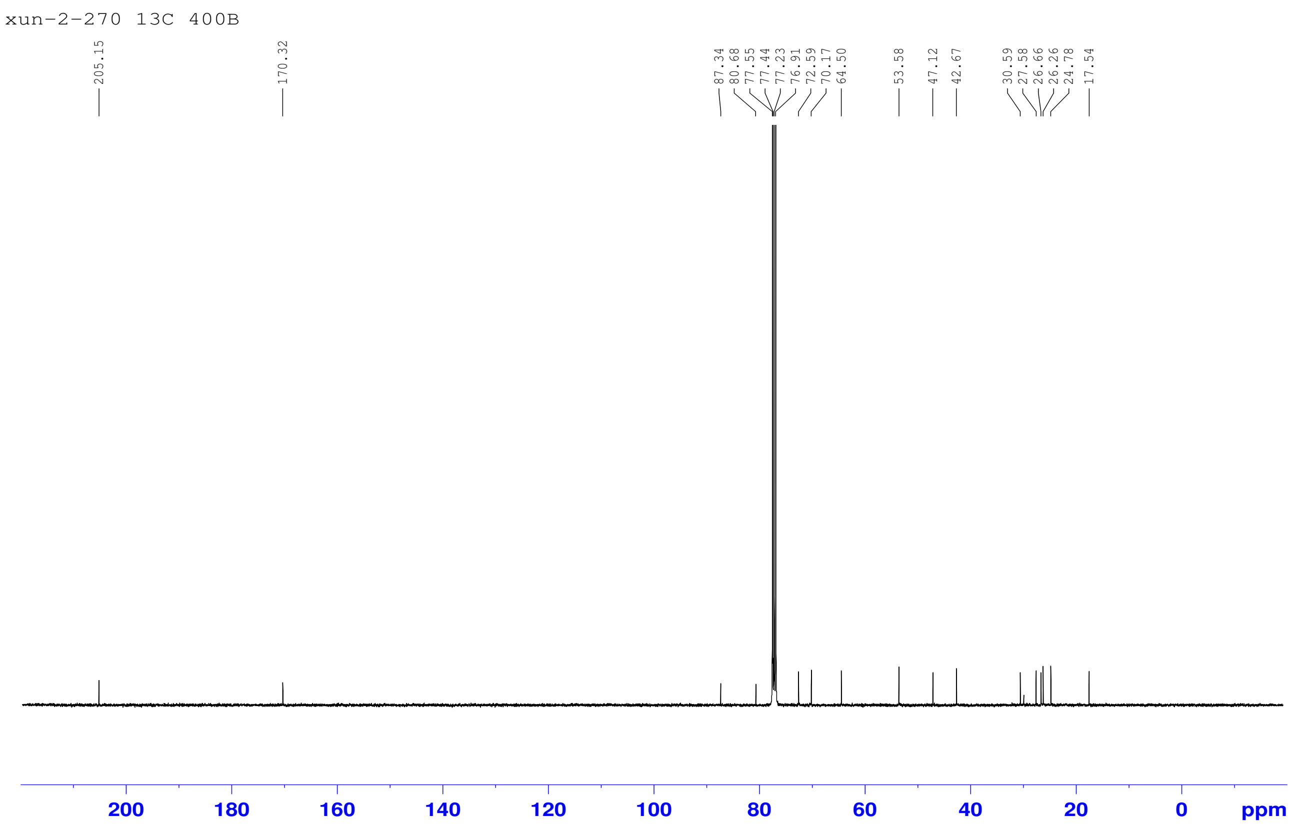


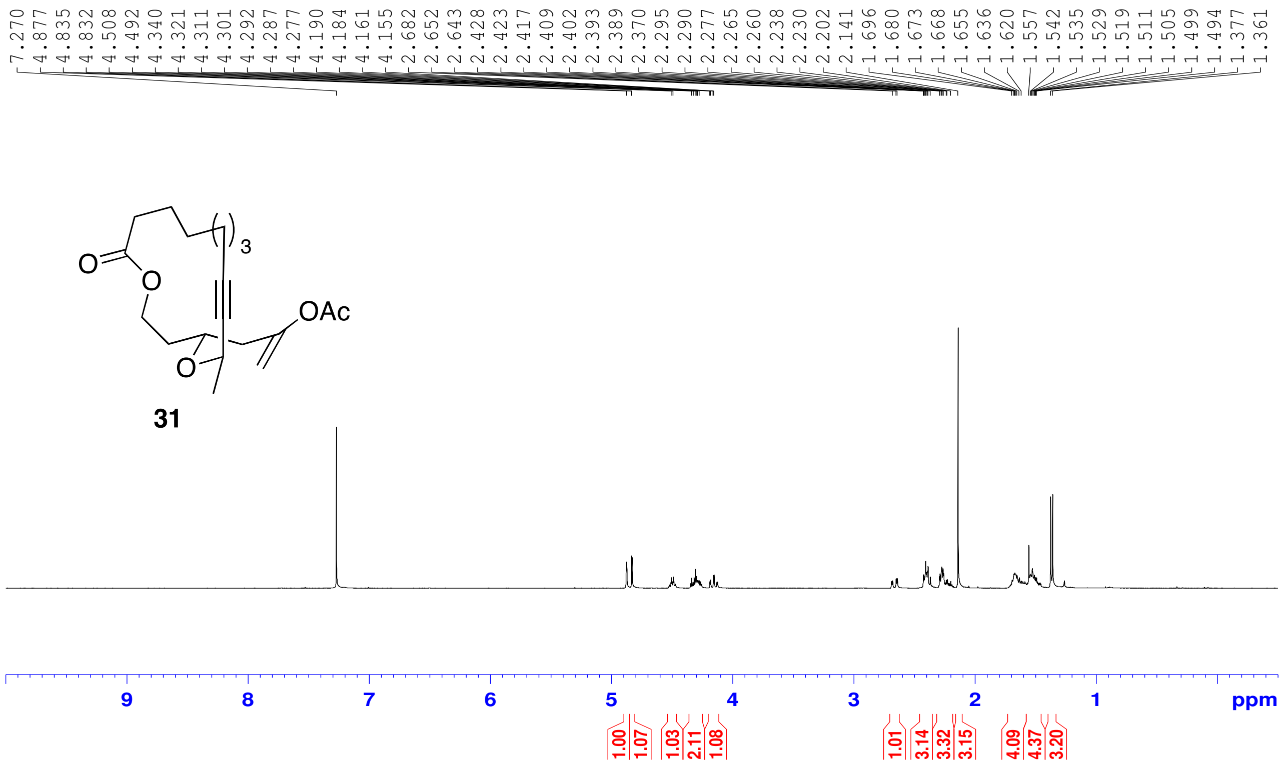
xun-2-269 13C 400B

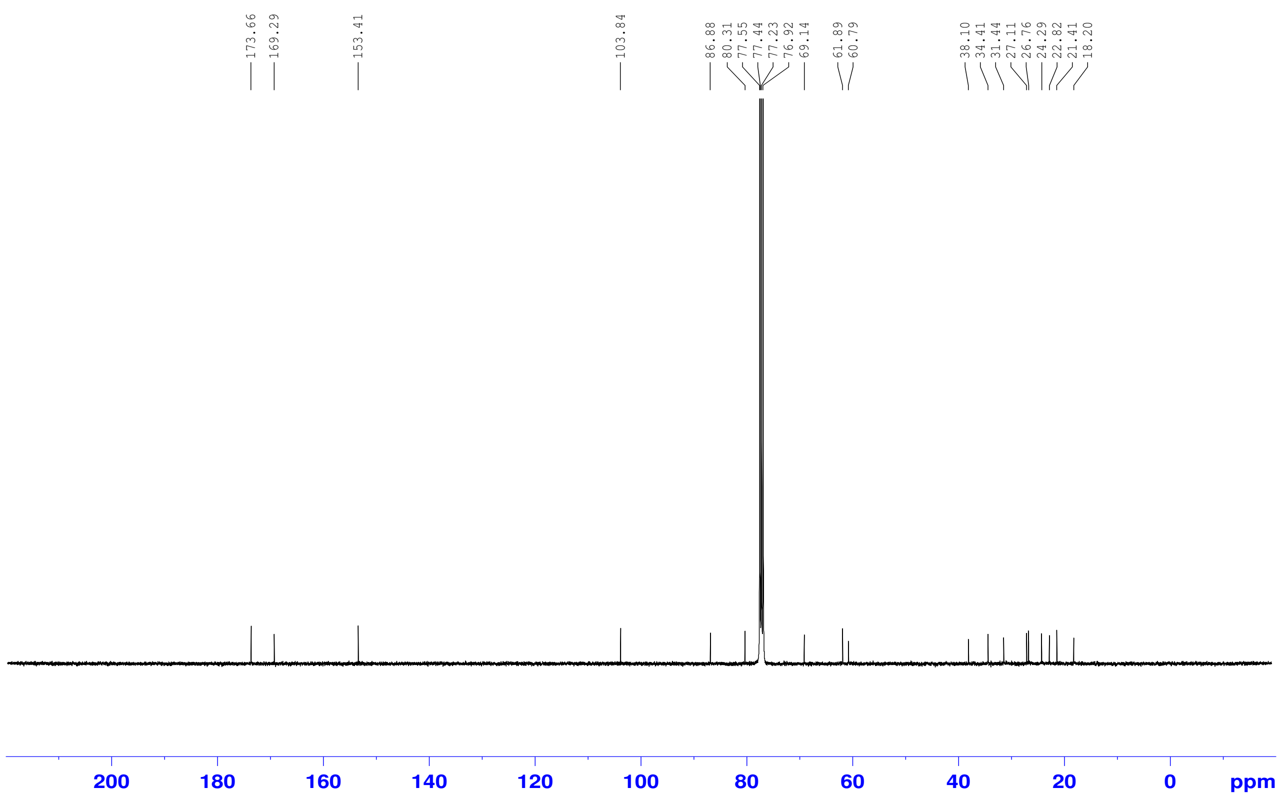


30

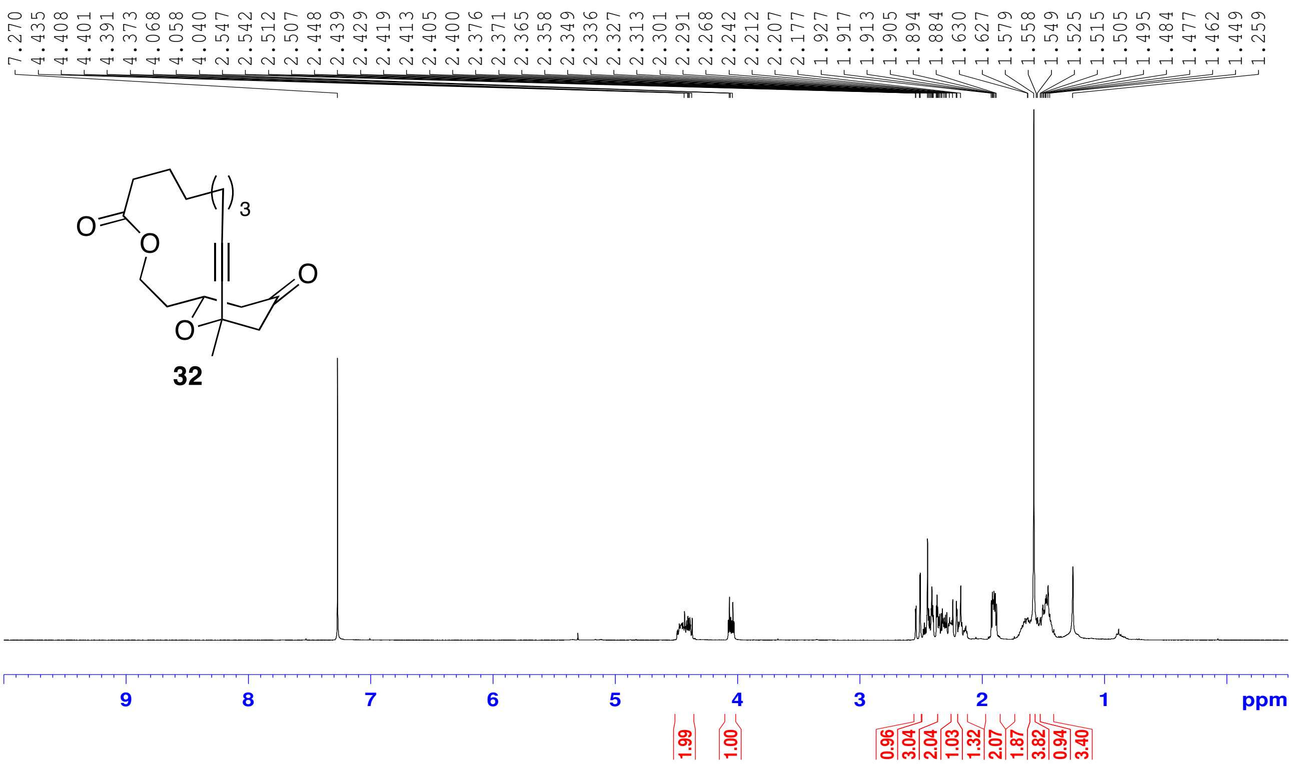

xun-2-270 400B
7.270
5.309
4.184
4.179
4.157
4.152
4.142
4.132
4.122
4.105
2.574
2.570
2.556
2.540
2.535
2.505
2.500
2.446
2.418
2.412
2.383
2.377
2.372
2.274
2.262
2.258
2.245
2.243
2.235
2.231
2.201
2.054
1.658
1.649
1.638
1.626
1.618
1.588
1.578
1.558
1.545
1.526
1.513
1.500
1.493
1.482
1.468
1.450
1.436
1.431
1.424
1.417
1.408
1.394
1.260
9
8
7
6
5
4
3
2
1
ppm
1.00
2.09
1.82
1.13
1.41
0.64
2.94
1.17
3.06
4.84
4.56


xun-2-270 13C 400B
205.15
170.32
87.34
80.68
77.55
77.44
77.23
76.91
72.59
70.17
64.50
53.58
47.12
42.67
30.59
27.58
26.66
26.26
24.78
17.54
200
180
160
140
120
100
80
60
40
20
0
ppm

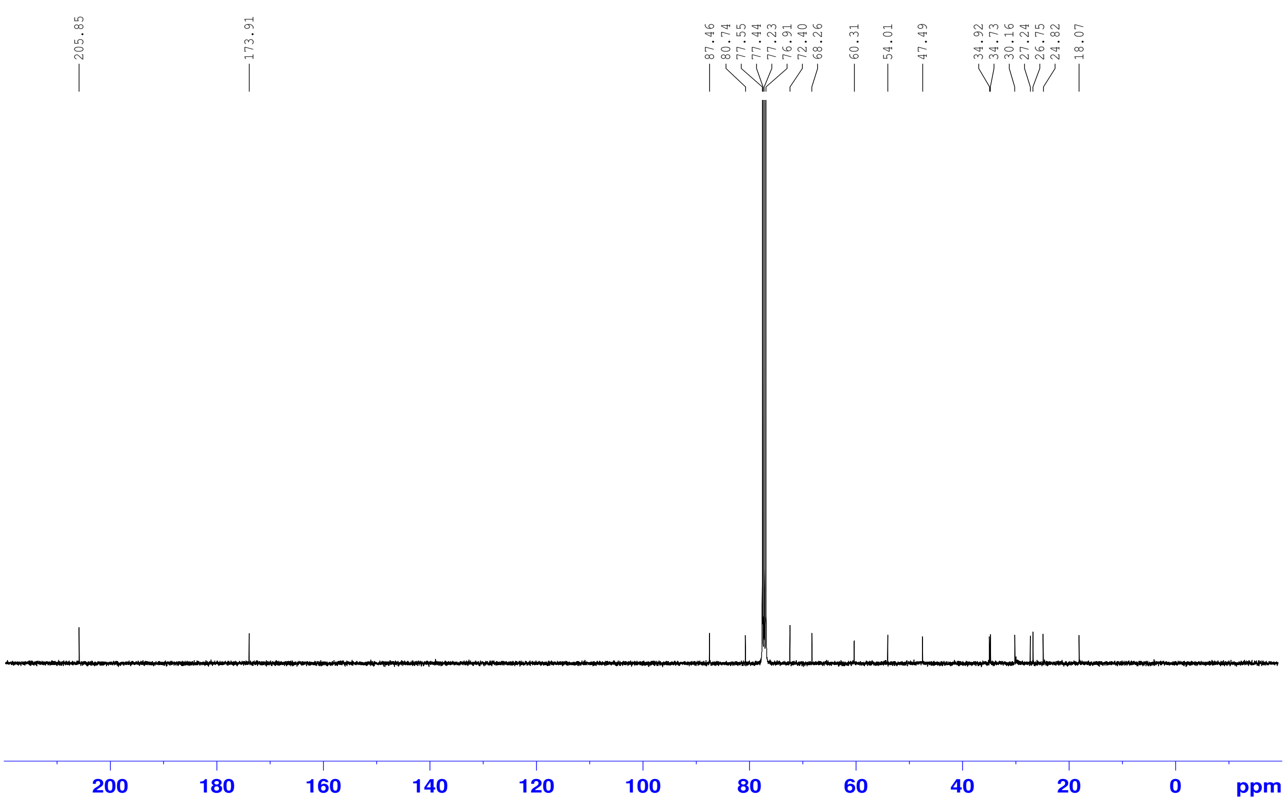

xun-3-201 1H 400B
7.270 4.877 4.835 4.832 4.508 4.492 4.340 4.321 4.311 4.301 4.292 4.287 4.277 4.190 4.184 4.161 4.155 2.682 2.652 2.643 2.428 2.423 2.417 2.409 2.402 2.393 2.389 2.370 2.295 2.290 2.277 2.265 2.260 2.238 2.230 2.202 2.141 1.696 1.680 1.673 1.668 1.655 1.636 1.620 1.557 1.542 1.535 1.529 1.519 1.511 1.505 1.499 1.494 1.377 1.361
O
O
3
OAc
O
31
9 8 7 6 5 4 3 2 1 ppm
1.00 1.07 1.03 2.11 1.08 1.01 3.14 3.32 3.15 4.09 4.37 3.20

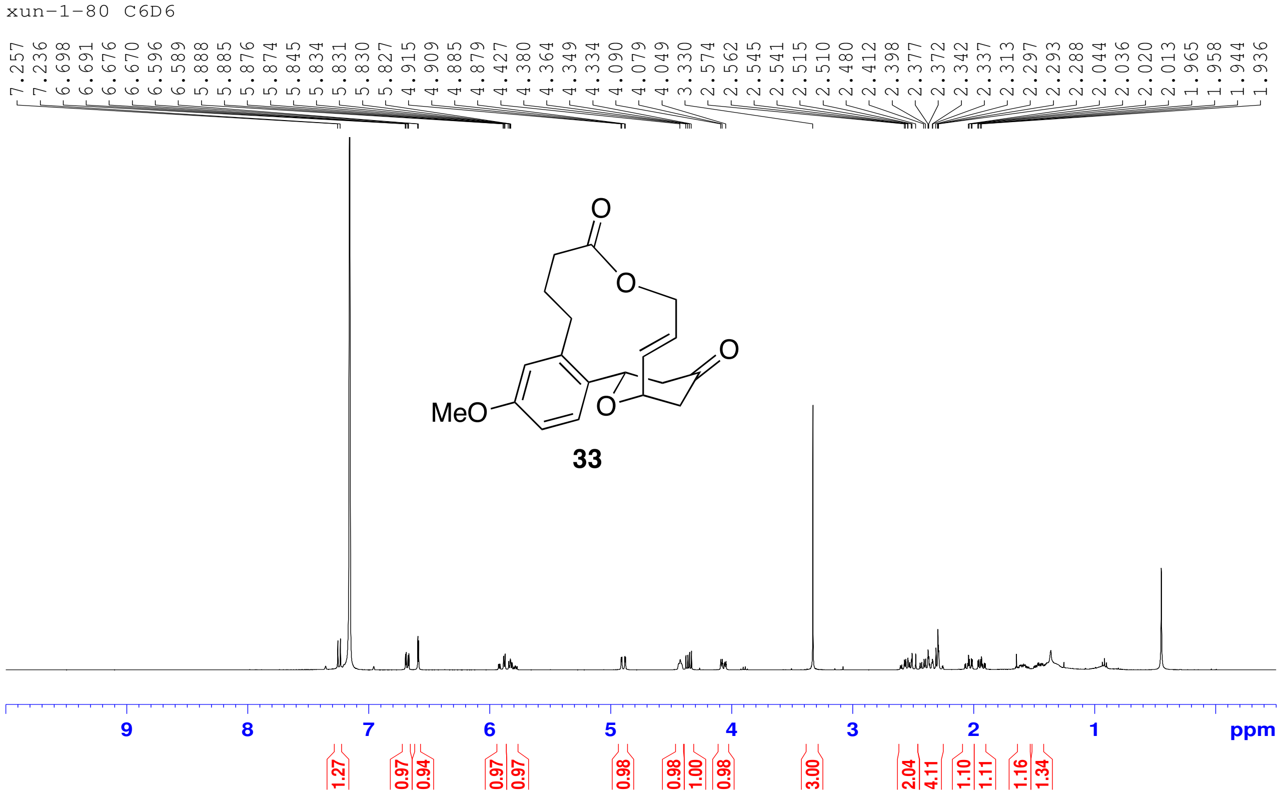

xun-3-201 13C NMR 400B
173.66 169.29 153.41 103.84 86.88 80.31 77.55 77.44 77.23 76.92 69.14 61.89 60.79 38.10 34.41 31.44 27.11 26.76 24.29 22.82 21.41 18.20
200 180 160 140 120 100 80 60 40 20 0 ppm

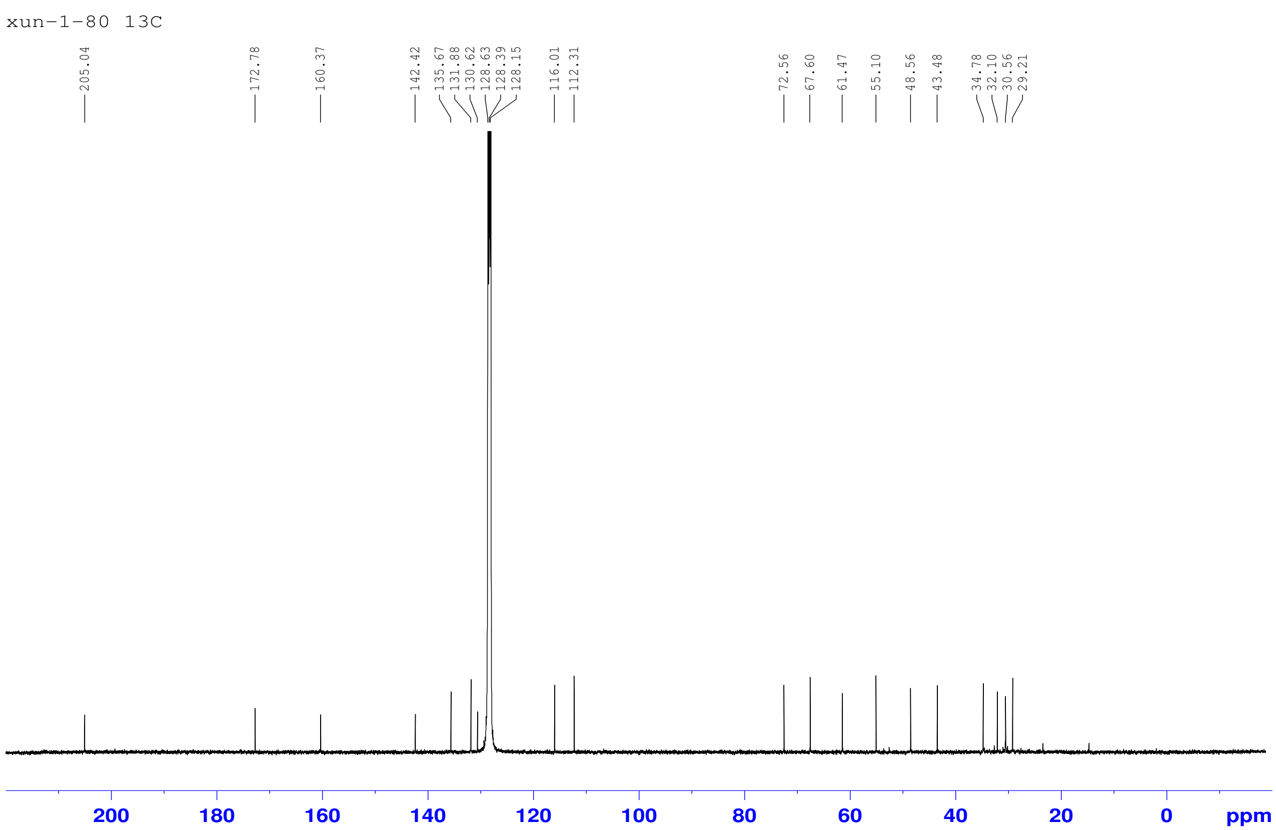
xun-3-202 1H 400B



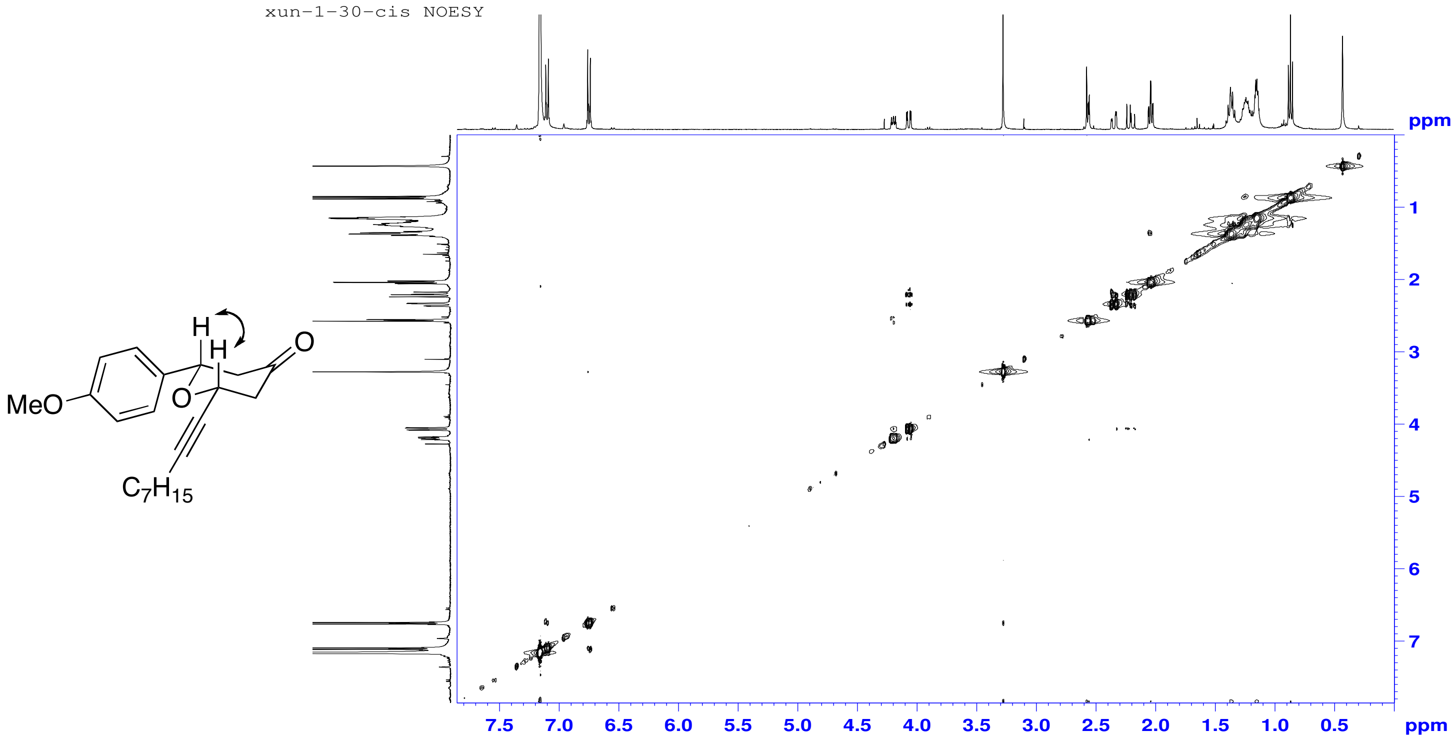
xun-3-202 13C 400B



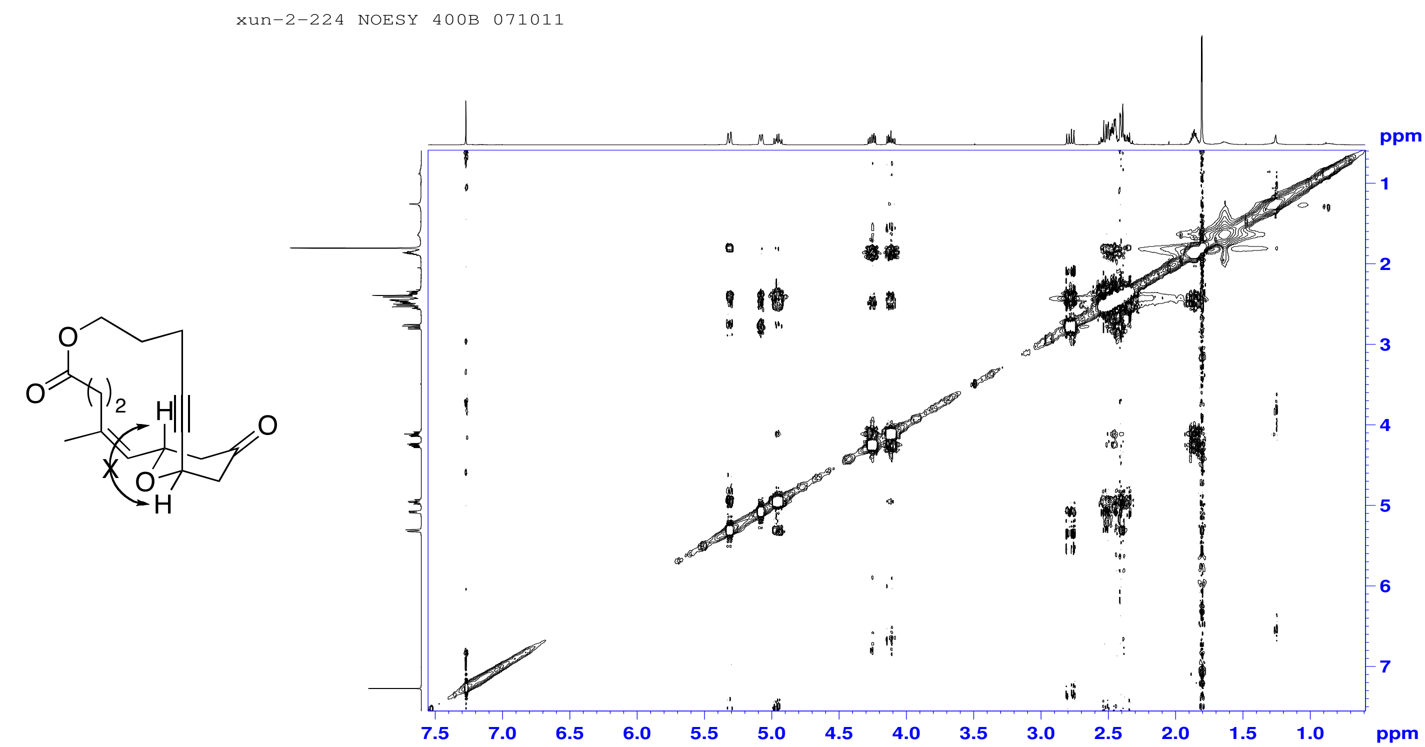

xun-1-80 C6D6
7.257
7.236
6.698
6.691
6.676
6.670
6.596
6.589
5.888
5.885
5.876
5.874
5.845
5.834
5.831
5.830
5.827
4.915
4.909
4.885
4.879
4.427
4.380
4.364
4.349
4.334
4.090
4.079
4.049
3.330
2.574
2.562
2.545
2.541
2.515
2.510
2.480
2.412
2.398
2.377
2.372
2.342
2.337
2.313
2.297
2.293
2.288
2.044
2.036
2.020
2.013
1.965
1.958
1.944
1.936
O
O
O
MeO
O
33
9
8
7
6
5
4
3
2
1
ppm
1.27
0.97
0.94
0.97
0.97
0.98
0.98
1.00
0.98
3.00
2.04
4.11
1.10
1.11
1.16
1.34


xun-1-80 13C
205.04
172.78
160.37
142.42
135.67
131.88
130.62
128.63
128.39
128.15
116.01
112.31
72.56
67.60
61.47
55.10
48.56
43.48
34.78
32.10
30.56
29.21
200
180
160
140
120
100
80
60
40
20
0
ppm

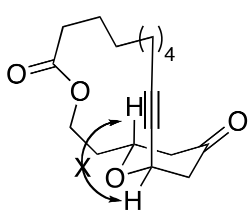
NOESY of compound 6 (CDCl$_3$)

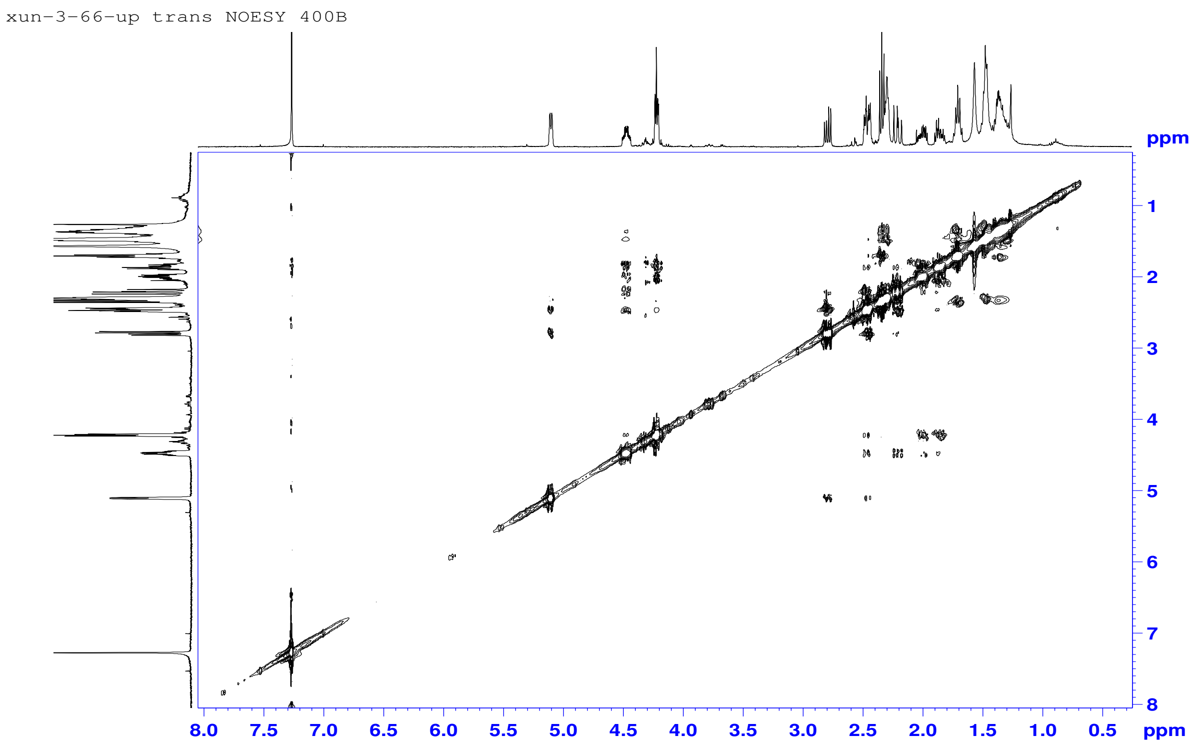


NOESY of compound 19 (CDCl$_3$)

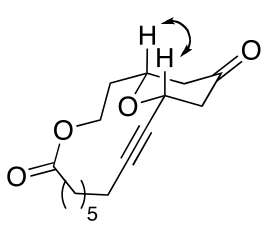


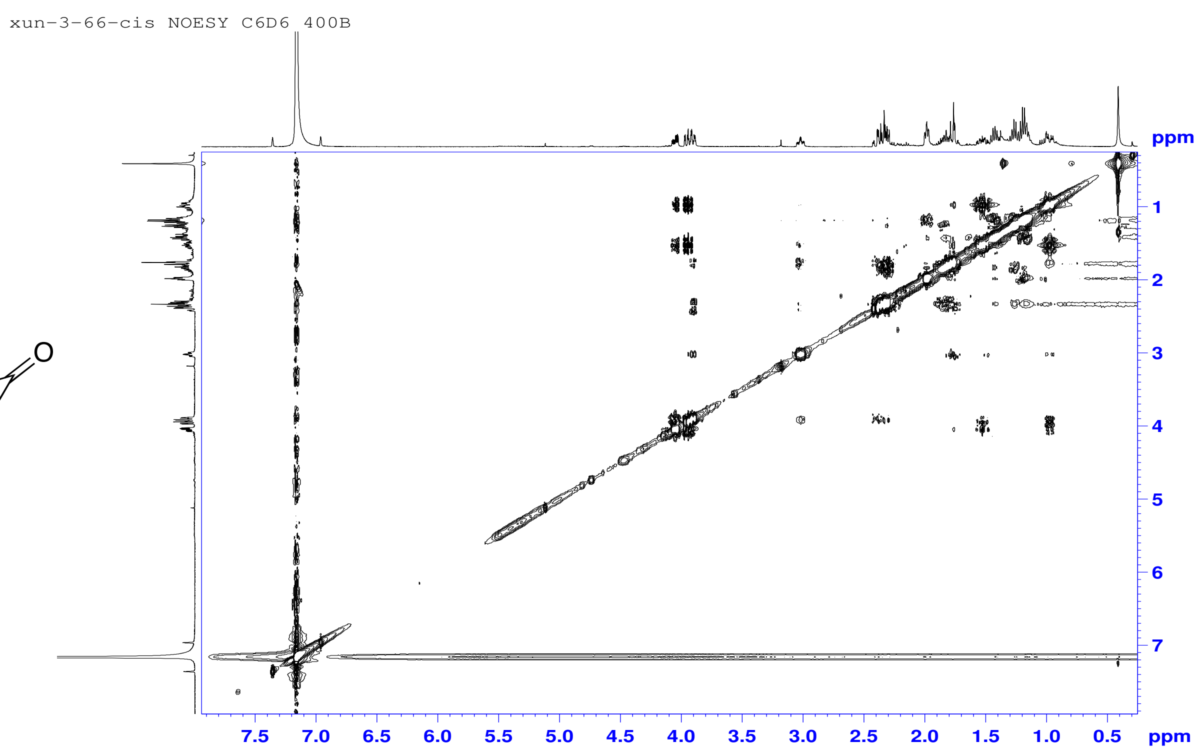
NOESY of compound 28 ($CDCl_3$)





NOESY of compound 28' (C_6D_6)





NOESY of compound 30 ($CDCl_3$)