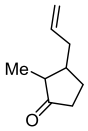
Construction of the Basic Skeleton of Ophiobolin A and Variecolin

Ke Li,[†] Cheng Wang,[†] Gang Yin,[†] Shuanhu Gao*[, †, ‡]

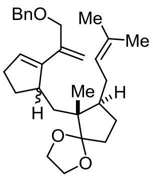
Shanghai Key Laboratory of Green Chemistry and Chemical Processes, Department of Chemistry, East China Normal University, 3663N Zhongshan Road, Shanghai 200062, China, and State Key Laboratory of Bioorganic and Natural Products Chemistry, Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences, 345 Lingling Road, Shanghai 200032, China
Email: shgao@chem.ecnu.edu.cn
Fax: (+) 86-21-62604784

Supporting Information

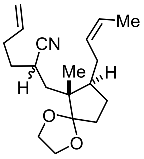
General Experimental Procedures. All reactions were carried out under nitrogen except noted. Anhydrous dichloromethane (CH_2Cl_2) was distilled from calcium hydride. Tetrahydrofuran (THF) was distilled from sodium-benzophenone ketyl, and anhydrous toluene was prepared from sodium. Flash column chromatography was performed as described by Still (Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923–2925), employing Qingdao Haiyang silica gel 60 (200–300 mesh). TLC analyses were performed on EMD 250 μm Silica Gel $HSGF_{254}$ plates and visualized by quenching of UV fluorescence (λ_{max}= 254 nm), or by staining ceric ammonium molybdate, ammonium molybdate, or potassium permanganate. ^1H and ^{13}C NMR spectra were recorded on a Bruker-500, 400 spectrometer. Chemical shifts for ^1H and ^{13}C NMR spectra are reported in ppm (δ) relative to residue protium in the solvent ($CDCl_3$: δ 7.26, 77.00 ppm;) and the multiplicities are presented as follows: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet. High-resolution mass spectra (HRMS) were acquired on a waters GCT premier.



Ketone **11**+**11'** (dr = 1.2:1).[1] To a round-bottom flask equipped with dry LiCl (1.32 g, 31.1 mmol, 2.3 equiv.) was added CuBr·DMS (6.40 g, 31.1 mmol, 2.3 equiv.) and dry THF (70 mL) under nitrogen. The mixture was stirred at 25 °C until the suspension turned to be a homogeneous phase. To the above mixture was added a solution of allylmagnesium bromide (1.0 M diethyl ether solution, 27 mL, 27.0 mmol, 2.0 equiv.) at -78 °C. After stirring for 1 hour, a solution of 2-methyl-2-cyclopenten-1-one (1.30 g, 13.5 mmol, 1.0 euiv.) in THF (5 mL) was added and the mixture was stirred at -78 °C for 3 hours. Then saturated NH_4Cl (20 mL) was added at -78 °C to quench the reaction. The mixture was extracted with diethyl ether (50 mL x 3), the organic layer was washed with brine (50 mL x 3), dried over anhydrous magnesium sulfate, filtered, concentrated, and purified by silica gel column chromatography (2~5% diethyl ether - petroleum ether) to give ketone **11**+**11'** (1.80 g, 96%) as a mixture of inseparable diastereomers as colorless oil: R_f = 0.47 (10% ethyl acetate - petroleum ether); ^1H NMR (400 MHz, $CDCl_3$) δ 5.81 – 5.73 (m, 2H) (**11**+**11'**), 5.07 – 4.99 (m, 4H) (**11**+**11'**), 2.41 – 2.28 (m, 4H) (**11**+**11'**), 2.19 – 2.01 (m, 6H) (**11**+**11'**), 1.91 – 1.82 (m, 2H) (**11**+**11'**), 1.76 – 1.31 (m, 4H) (**11**+**11'**), 1.03 (d, *J* = 6.8 Hz, 3H) (**11**), 0.97 (d, *J* = 6.8 Hz, 3H) (**11'**); ^{13}C NMR (100 MHz, $CDCl_3$) δ (221.6) 221.0, (136.6) 135.7, 116.6 (116.2), 49.6 (46.9), 44.3 (39.4), 38.2 (37.2), (35.7) 33.6, (26.7) 24.9, 12.5 (9.6) ppm; MS (m/z): EI [M] calcd for $C_9H_{14}O$ 138.10; found 138.0 (36%), 123.0 (6%), 97.0 (62%).

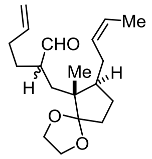


Triene **22**+**22’** (dr = 1:1). To benzyl ether **20** and **20’** (19 mg, 0.045 mmol, 1.0 equiv.) was added Grubbs II (4 mg, 0.0045 mmol, 0.1 equiv.) in degassed CH_2Cl_2 (1 mL) at 40 °C under nitrogen. The mixture was stirred for 12 hours. The solvent was removed under reduced pressure. The residue was purified by silica gel column chromatography (5% ethyl acetate - petroleum ether) to give triene **22** and **22’** (15 mg, 79%) as a mixture of inseparable diastereomers as colorless oil: R_f = 0.47 (10% ethyl acetate - petroleum ether); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40 – 7.26 (m, 10H) (**22**+**22’**), 5.80 (s, 2H) (**22**+**22’**), 5.27 (s, 2H) (**22**), 5.22 (d, *J* = 48 Hz, 2H) (**22’**), 5.06 (d, *J* = 5.6 Hz, 2H) (**22**+**22’**), 4.53 (s, 4H) (**22**+**22’**), 4.18 (s, 4H) (**22**+**22’**), 4.00 – 3.80 (m, 8H) (**22**+**22’**), 3.08 (q, *J* = 9.2 Hz, 2H) (**22**+**22’**), 2.52 – 2.40 (m, 2H) (**22**+**22’**), 2.36 – 2.24 (m, 2H) (**22**+**22’**), 2.22 – 2.10 (m, 2H) (**22**+**22’**), 1.91 – 1.79 (m, 8H) (**22**+**22’**), 1.79 – 1.71 (m, 4H) (**22**+**22’**), 1.67 (s, 6H) (**22**+**22’**), 1.60 (s, 6H) (**22**+**22’**), 1.04 (s, 3H) (**22’**), 0.99 (s, 3H) (**22**); ^{13}C NMR (100 MHz, $CDCl_3$) δ (146.7) 146.6, 139.5 (2 C), 138.5 (2 C), 131.6 (131.5), 128.3 (4 c), 127.8 (4 c), 127.5 (4 c), 123.5 (2 C), (120.4) 120.0, (113.6) 113.2, (71.9) 71.9, 64.3 (63.9), 63.3 (63.2), 47.7 (47.6), (46.5) 46.1, (41.0) 40.7, (37.2) 36.7, (31.8) 31.7, (31.4) 31.3, (31.0) 30.2, (29.7) 29.5, 25.8 (2 C), 25.6 (25.4), 17.9 (2 C), (16.6) 16.2 ppm; HRMS (m/z): Exact mass calcd for $C_{29}H_{40}O_3$ $[M]^+$: 436.2977; found 436.2979.

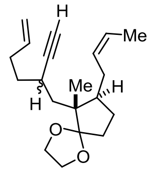


Diene **26**+**26’** (dr = 1.5:1). To a solution of diisopropylamine (162 μL, 1.15 mmol, 1.4 equiv.) in dry THF (4 mL) was added *n*-BuLi (1.6 M THF solution, 0.7 mL, 1.06 mmol, 1.3 equiv.) at -78 °C under nitrogen. The mixture was stirred for 30 minutes. To the above mixture was added olefin **25** (204 mg, 0.82 mmol, 1.0 equiv.) in THF (0.5 mL), and 4-bromo-1-butene (100 μL, 0.98 mmol, 1.2 equiv.) dropwise at -78 °C. The mixture was stirred for 2 hours at 25 °C. Water (5 mL) was added to quench the reaction and the mixture was extracted with ethyl acetate (10 mL x 3). The combined organic layer was dried over anhydrous magnesium sulfate, filtered, concentrated, and purified by silica gel column chromatography (10% ethyl acetate - petroleum ether) to give diene **26** and **26’** (203 mg, 82%) as a mixture of inseparable diastereomers as colorless oil: R_f = 0.29 (10% ethyl acetate - petroleum ether); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.83 – 5.68 (m, 2H) (**26**+**26’**), 5.50 – 5.40 (m, 2H) (**26**+**26’**), 5.38 – 5.26 (m, 2H) (**26**+**26’**), 5.14 – 4.99 (m, 4H) (**26**+**26’**), 4.14 – 3.78 (m, 8H) (**26**+**26’**), 2.93 – 2.78 (m, 2H) (**26**+**26’**), 2.30 – 2.16 (m, 4H) (**26**+**26’**), 2.08 (t, *J* = 8.4 Hz, 2H) (**26**+**26’**), 1.92 – 1.84 (m, 4H) (**26**+**26’**), 1.85 – 1.65

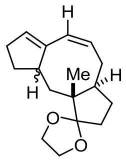
(m, 12H) (**26**+**26’**), 1.60 (d, *J* = 6.4 Hz, 6H) (**26**+**26’**), 1.37 – 1.25 (m, 2H) (**26**+**26’**), 1.11 (s, 3H) (**26**), 0.93 (s, 3H) (**26’**); ^{13}C NMR (100 MHz, $CDCl_3$) δ 136.6 (2 C), (128.8) 128.8, 124.6 (124.5), 123.9 (123.4), 119.6 (119.0), 116.0 (116.0), (63.8) 63.8, 63.1 (62.9), (46.8) 46.3, 37.8 (37.8), (34.4) 33.7, 31.9 (31.5), (31.0) 30.9, (27.7) 27.5, (25.4) 25.4, 25.4 (25.1), (15.4) 15.3, 12.9 (12.9) ppm; HRMS (m/z): Exact mass calcd for $C_{19}H_{29}NO_2$ $[M]^+$: 303.2198; found 303.2200.



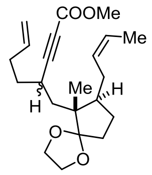
Aldehyde **27**+**27’** (dr = 1.5:1). To a solution of diene **26** and **26’** (142 mg, 0.47 mmol, 1.0 equiv.) in dry PhMe (3 mL) was added diisobutylaluminum hydride (1.0 M PhMe solution, 0.6 mL, 0.56 mmol, 1.2 equiv.) at -78 ^{o}C under nitrogen. The mixture was stirred for 2 hours at -78 ^{o}C. Potassium sodium tartrate solution (3 mL) was added to quench the reaction and the mixture was extracted with ethyl acetate (10 mL x 3). The combined organic layer was dried over anhydrous magnesium sulfate, filtered, concentrated, and purified by silica gel column chromatography (10% ethyl acetate - petroleum ether) to give aldehyde **27** and **27’** (123 mg, 87%) as a mixture of inseparable diastereomers as colorless oil: R_f = 0.29 (10% ethyl acetate - petroleum ether); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.55 (d, *J* = 3.6 Hz, 1H) (**27**), 9.37 (d, *J* = 3.6 Hz, 1H) (**27’**), 5.84 – 5.70 (m, 2H) (**27**+**27’**), 5.50 – 5.48 (m, 2H) (**27**+**27’**), 5.36 – 5.24 (m, 2H) (**27**+**27’**), 4.98 (dd, *J* = 18.3, 13.9 Hz, 4H) (**27**+**27’**), 3.98 – 3.71 (m, 8H) (**27**+**27’**), 2.78 – 2.61 (m, 1H) (**27**), 2.61 – 2.45 (m, 1H) (**27’**), 2.19 – 1.96 (m, 8H) (**27**+**27’**), 1.97 – 1.74 (m, 8H) (**27**+**27’**), 1.74 – 1.64 (m, 4H) (**27**+**27’**), 1.61 (d, *J* = 6.8 Hz, 6H) (**27**+**27’**), 1.50 – 1.17 (m, 8H) (**27**+**27’**), 0.89 (s, 3H) (**27’**), 0.82 (s, 3H) (**27**); ^{13}C NMR (100 MHz, $CDCl_3$) δ 205.6 (205.4), (137.8) 137.8, (129.1) 129.0, 124.4 (2 C), 119.6 (119.1), (115.2) 115.1, 63.9 (63.3), 63.1 (62.6), 47.0 (47.0), 46.9 (46.8), (46.6) 45.6, 35.2 (34.1), 32.1 (31.7), (31.5) 31.1, (30.9) 30.8, (27.7) 27.6, (25.5) 25.2, (16.6) 15.6, 12.9 (2 C) ppm; HRMS (m/z): Exact mass calcd for $C_{19}H_{30}O_3$ $[M]^+$: 306.2195; found 306.2196.



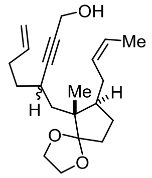
Dienyne **28**+**28’** (dr = 1:1). To a solution of aldehyde **27** and **27’** (58 mg, 0.19 mmol, 1.0 equiv.) in MeOH (1 mL) was added dimethyl (1-diazo-2-oxopropyl) phosphonate (73 mg, 0.38 mmol, 2.0 equiv.), anhydrous potassium carbonate (79 mg, 0.57 mmol, 3.0 equiv.) at 25 ^{o}C. The mixture was stirred for 4 hours at 25 ^{o}C. The solvent was removed under reduced pressure and the residue was added ethyl acetate (10 mL) and water (10 mL). The organic layer was separated and the water layer was extracted with ethyl acetate (10 mL x 2). The combined organic layer was dried over anhydrous magnesium sulfate, filtered, concentrated, and purified by silica gel column chromatography (2~4% ethyl acetate - petroleum ether) to give dienyne **28** and **28’** (56 mg, 98%) as a mixture of inseparable diastereomers as colorless oil: R_f = 0.51 (10% ethyl acetate - petroleum ether); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.87 – 5.74 (m, 2H) (**28**+**28’**), 5.52 – 5.26 (m, 4H) (**28**+**28’**), 5.11 – 4.89 (m, 4H) (**28**+**28’**), 4.02 – 3.79 (m, 8H) (**28**+**28’**), 2.79 – 2.56 (m, 2H) (**28**+**28’**), 2.30 – 2.10 (m, 6H) (**28**+**28’**), 2.05 (dd, *J* = 8.0, 2.4 Hz, 2H) (**28**+**28’**), 1.97 – 1.62 (m, 14H) (**28**+**28’**), 1.59 (d, *J* = 6.8 Hz, 6H) (**28**+**28’**), 1.58 – 1.42 (m, 4H) (**28**+**28’**), 1.34 – 1.20 (m, 2H) (**28**+**28’**), 1.08 (s, 3H) (**28**), 0.95 (s, 3H) (**28’**); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.3 (138.3), (129.5) 129.4, 124.2 (124.1), (120.0) 120.0, 114.7 (2 C), 89.8 (89.6), 69.1 (68.7), (64.5) 64.0, (63.7) 63.5, (47.6) 47.4, 46.4 (44.6), (40.7) 40.5, (36.8) 36.5, (32.5) 32.3, (31.4) 31.1, (28.4) 27.9, (26.3) 25.8, (25.4) 25.1, (16.5) 15.4, (13.0) 12.9 ppm; HRMS (m/z): Exact mass calcd for $C_{20}H_{30}O_2$ $[M]^+$: 302.2246; found 302.2245.



Diene **21**+**21’** (dr = 1:1). To a mixture of dienyne **28** and **28’** (21 mg, 0.069 mmol, 1.0 equiv.) and Grubbs II (6 mg, 0.0069 mmol, 0.1 equiv.) was added degassed CH_2Cl_2 at 40 ^{o}C under nitrogen. The mixture was stirred for 12 hours. The solvent was removed under reduced pressure, and purified by silica gel column chromatography (2% ethyl acetate - petroleum ether) to give diene **21** and **21’** (14 mg, 78%) as a mixture of inseparable diastereomers as colorless oil: R_f = 0.59 (10% ethyl acetate - petroleum ether); ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.10 – 6.00 (m, 2H) (**21**+**21’**), 5.73 – 5.60 (m, 2H) (**21**+**21’**), 5.68 (dt, *J* = 13.7, 4.5 Hz, 1H) (**21**), 5.29 (dt, *J* = 13.7, 4.5 Hz, 1H) (**21’**), 4.01 – 3.79 (m, 8H) (**21**+**21’**), 3.30 – 3.22 (m, 1H) (**21’**), 3.05 – 2.96 (m, 1H) (**21**), 2.76 – 2.66 (m, 1H) (**21**), 2.48 – 2.36 (m, 1H) (**21’**), 2.23 – 2.10 (m, 8H) (**21**+**21’**), 1.94 – 1.69 (m, 10H) (**21**+**21’**), 1.68 – 1.56 (m, 4H) (**21**+**21’**), 1.56 – 1.36 (m, 4H) (**21**+**21’**), 1.36 – 1.12 (m, 4H) (**21**+**21’**), 0.98 (s, 3H) (**21’**), 0.82 (s, 3H) (**21**); ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.1 (147.1), 134.6 (132.4), (128.8) 126.7, (126.4) 124.4, (121.7) 120.1, 65.3 (65.2), 64.1 (2 C), 47.8 (2 C), (47.1) 46.1, (41.9) 41.5, (39.2) 38.5, (38.0) 37.8, (36.0) 33.3, (32.9) 32.6, (30.2) 30.0, (27.6) 27.2, 18.8 (14.6) ppm; MS (m/z): EI [M] calcd for $C_{17}H_{24}O_2$ 260.18; found 260.0 (32%), 198.0 (9%), 141.0 (47%).

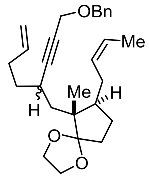


Ester **29**+**29’** (dr = 1:1). To a mixture of dienyne **28** and **28’** (46 mg, 0.15 mmol, 1.0 equiv.) in dry THF (0.8 mL) was added *n*-BuLi (1.6 M THF solution, 190 μL, 0.30 mmol, 2.0 equiv.) at -78 ^{o}C under nitrogen. The mixture was stirred for 30 minutes. To the above mixture was added methyl chloroformate (19 μL, 0.24 mmol, 1.6 equiv.) dropwise at -78 ^{o}C. The mixture was stirred for 0.5 hours at -78 ^{o}C and for further 0.5 hours at 25 ^{o}C. Water (1 mL) was added to quench the reaction and the mixture was extracted with ethyl acetate (10 mL x 3). The combined organic layer was dried over anhydrous magnesium sulfate, filtered, concentrated, and purified by silica gel column chromatography (2~5% ethyl acetate - petroleum ether) to give ester **29** and **29’** (45 mg, 82%) as a mixture of inseparable diastereomers as colorless oil: R_f = 0.42 (10% ethyl acetate - petroleum ether); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.87 – 5.71 (m, 2H) (**29**+**29’**), 5.50 – 5.40 (m, 2H) (**29**+**29’**), 5.37 – 5.26 (m, 2H) (**29**+**29’**), 5.01 (dd, *J* = 13.7, 11.5, 4H) (**29**+**29’**), 4.08 – 3.81 (m, 8H) (**29**+**29’**), 3.74 (d, *J* = 5.1 Hz, 6H) (**29**+**29’**), 2.93 – 2.76 (m, 2H) (**29**+**29’**), 2.29 – 2.06 (m, 6H) (**29**+**29’**), 1.95 – 1.84 (m, 4H) (**29**+**29’**), 1.80 – 1.67 (m, 8H) (**29**+**29’**), 1.60 (d, *J* = 7.0 Hz, 6H) (**29**+**29’**), 1.52 – 1.44 (m, 2H) (**29**+**29’**), 1.35 – 1.18 (m, 4H) (**29**+**29’**), 1.07 (s, 3H) (**29’**), 0.94 (s, 3H) (**29**); ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.5 (2 C), 137.7 (137.6), (129.2) 129.2, 124.4 (124.3), 119.9 (119.7), 115.2 (2 C), (94.7) 94.7, 73.9 (73.3), 64.3 (63.9), 63.4 (63.4), (52.5) 52.4, 47.3 (47.2), (46.5) 45.1, (39.8) 39.8, 36.1 (35.6), 32.2 (32.1), 31.3 (31.1), 28.1 (27.8), 26.3 (26.0), 25.4 (25.1), 16.1 (15.5), 13.0 (12.9) ppm; HRMS (m/z): Exact mass calcd for $C_{22}H_{32}O_4$ $[M]^+$: 360.2301; found 360.2300.

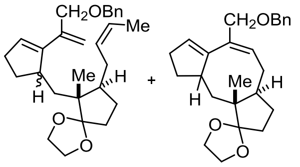


Alcohol **30**+**30’** (dr = 1:1). To a solution of ester **29** and **29’** (58 mg, 0.16 mmol, 1.0 equiv.) in dry Et_2O (0.8 mL) was added diisobutylaluminum hydride (1.0 M PhMe solution, 0.4 mL, 0.40 mmol, 2.5 equiv.) at -78 ^{o}C under nitrogen. The mixture was stirred for 2 hours at -78 ^{o}C, and 30 minutes at 25 ^{o}C. Potassium sodium tartrate solution (1 mL) was added to quench the reaction and the mixture was extracted with ethyl acetate (10 mL x 3). The organic layer was dried over anhydrous magnesium sulfate, filtered, concentrated, and purified by silica gel column chromatography (20% ethyl acetate - petroleum ether) to give alcohol **30** and **30’** (51 mg, 96%) as a mixture of inseparable diastereomers as colorless oil: R_f = 0.37 (20% ethyl acetate - petroleum ether); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.87 – 5.75 (m, 2H) (**30**+**30’**), 5.53 – 5.40 (m, 2H) (**30**+**30’**), 5.40 – 5.28 (m, 2H) (**30**+**30’**), 5.10 – 4.91 (m, 4H) (**30**+**30’**), 4.31 – 4.23 (m, 4H)

(**30**+**30’**), 3.99 – 3.82 (m, 8H) (**30**+**30’**), 2.81 – 2.73 (m, 1H) (**30**), 2.70 – 2.62 (m, 1H) (**30’**), 2.33 – 2.07 (m, 6H) (**30**+**30’**), 2.07 – 1.67 (m, 12H) (**30**+**30’**), 1.61 (dd, *J* = 13.1, 6.3 Hz, 10H) (**30**+**30’**), 1.56 – 1.46 (m, 6H) (**30**+**30’**), 1.31 – 1.20 (m, 2H) (**30**+**30’**), 1.06 (s, 3H) (**30**), 0.94 (s, 3H) (**30’**); ^{13}C NMR (100 MHz, CDCl$_3$) δ 138.4 (138.3), 129.7 (129.5), (124.5) 124.3, (120.2) 120.1, 114.7 (2 C), (91.6) 91.4, 79.4 (78.9), (64.6) 64.0, 63.7 (63.5), 51.6 (51.5), (47.6) 47.4, 46.3 (44.2), 40.7 (40.6), (36.8) 36.5, 32.6 (32.3), (31.5) 31.3, (28.5) 28.1, (26.8) 26.1, 25.4 (25.2), (16.9) 15.5, (13.1) 13.0 ppm; HRMS (m/z): Exact mass calcd for $C_{21}H_{32}O_3$ [M]$^+$: 332.2351; found 332.2352.



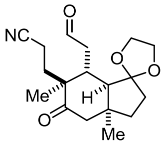
Benzyl ether **31**+**31’** (dr = 1:1). To a solution of alcohol **30** and **30’** (53 mg, 0.16 mmol, 1.0 equiv.) in dry DMF (0.8 mL) was added sodium hydride (57% - 63% oil dispersion, 10 mg, 0.24 mmol, 1.5 equiv.) at 0 ^{o}C under nitrogen. The mixture was stirred for 30 minutes at 0 ^{o}C. To the above mixture was added benzyl bromide (23 µL, 0.19 mmol, 1.2 equiv.). The mixture was stirred for 30 minutes at 0 ^{o}C. Water (1 mL) was added to quench the reaction and the mixture was extracted with ethyl acetate (10 mL x 5). The combined organic layer was washed with brine (20 mL x 3), dried over anhydrous magnesium sulfate, filtered, concentrated, and purified by silica gel column chromatography (10% ethyl acetate - petroleum ether) to give benzyl ether **31** and **31’** (63 mg, 97%) as a mixture of inseparable diastereomers as colorless oil: R_f = 0.42 (10% ethyl acetate - petroleum ether); ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.42 – 7.28 (m, 10H) (**31**+**31’**), 5.90 – 5.79 (m, 2H) (**31**+**31’**), 5.52 – 5.29 (m, 4H) (**31**+**31’**), 5.11 – 4.93 (m, 4H) (**31**+**31’**), 4.60 (d, *J* = 5.5 Hz, 4H) (**31**+**31’**), 4.19 (dd, *J* = 6.9, 1.9 Hz, 4H) (**31**+**31’**), 4.00 –3.85 (m, 8H) (**31**+**31’**), 2.83 – 2.65 (m, 2H) (**31**+**31’**), 2.36 – 2.13 (m, 6H) (**31**+**31’**), 1.99 – 1.88 (m, 2H) (**31**+**31’**), 1.88 – 1.70 (m, 10H) (**31**+**31’**), 1.70 – 1.65 (m, 2H) (**31**+**31’**), 1.62 (d, *J* = 6.5 Hz, 6H) (**31**+**31’**), 1.59 – 1.49 (m, 4H) (**31**+**31’**), 1.35 – 1.22 (m, 2H) (**31**+**31’**), 1.12 (s, 3H) (**31**), 0.99 (s, 3H) (**31’**); ^{13}C NMR (100 MHz, CDCl$_3$) δ 138.4 (138.3), 137.8 (137.7), (129.6) 129.4 , 128.3 (4 c), 128.0 (4 c), 127.7 (127.7), 124.2 (124.1), (120.1) 120.0, (114.7) 114.7, 92.3 (92.2), 76.8 (76.4), (71.1) 71.0, (64.6) 64.0, (63.7) 63.5, 57.8 (57.7), (47.6) 47.4, 46.4 (44.6), (40.8) 40.6, (36.9) 36.6, (32.5) 32.4, (31.6) 31.3, (28.5) 28.0, (26.7) 26.1, (25.4) 25.1, (16.5) 15.5, (13.0) 12.9 ppm; HRMS (m/z): Exact mass calcd for $C_{28}H_{38}O_3$ [M]$^+$: 422.2821; found 422.2824.



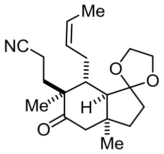
Triene **32**+**32’** (dr = 8:1) and diene **24**. To a solution of benzyl ether **31** and **31’** (18 mg, 0.042 mmol, 1.0 equiv.) was added Grubbs II (4 mg, 0.0042 mmol, 0.1 equiv.) in degassed CH_2Cl_2 (0.8 mL) at 40 ^oC under nitrogen. After refluxing for 15 hours, the solvent was removed under reduced pressure, and purified by silica gel column chromatography (2% ethyl acetate - petroleum ether) to give triene **32**+**32’** and diene **24** totally 79% yield.

Triene **32** and **32’** as a mixture of inseparable diastereomers as colorless oil: R_f = 0.42 (10% ethyl acetate - petroleum ether); ^1H NMR (400 MHz, $CDCl_3$) δ 7.40 – 7.26 (m, 10H) (**32**+**32’**), 5.80 (s, 2H) (**32**+**32’**), 5.49 – 5.39 (m, 2H) (**32**+**32’**), 5.39 – 5.31 (m, 2H) (**32**+**32’**), 5.27 (s, 2H) (**32**), 5.15 (d, *J* = 48 Hz, 2H) (**32’**), 4.53 (s, 4H) (**32**+**32’**), 4.18 (s, 4H) (**32**+**32’**), 4.00 – 3.80 (m, 8H) (**32**+**32’**), 3.14 – 3.02 (m, 2H) (**32**+**32’**), 2.52 – 2.36 (m, 2H) (**32**+**32’**), 2.36 – 2.10 (m, 4H) (**32**+**32’**), 2.06 – 1.67 (m, 14H) (**32**+**32’**), 1.60 (d, *J* = 6.7 Hz, 6H) (**32**+**32’**), 1.47 – 1.36 (m, 2H) (**32**+**32’**), 1.34 – 1.19 (m, 4H) (**32**+**32’**), 1.06 (s, 3H) (**32**), 1.01 (s, 3H) (**32’**); ^{13}C NMR (100 MHz, $CDCl_3$) δ (146.7) 146.6, 139.6 (139.6), (138.5) 138.5, 129.5 (2 C), 128.3 (4 c), 127.7 (6 c), (127.5) 127.5, 124.2 (124.1), (120.3) 119.9, (113.5) 113.1, (72.0) 71.9, 71.9 (2 C), 64.3 (63.9), 63.4 (63.2), 47.8 (47.6), (46.2) 45.8, 41.0 (40.7), (37.3) 36.8, (31.8) 31.7, (31.4) 31.3, 31.0 (2 C), 29.0 (28.4), 25.5 (25.4), (16.7) 16.1, 13.0 (2 C) ppm; HRMS (m/z): Exact mass calcd for $C_{28}H_{38}O_3$ $[M]^+$: 422.2821; found 422.2820.

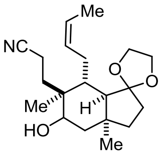
Diene **24** as a colorless oil (**24** was isolated as a single diastereomer, it’s relative configuration was not assigned.): R_f = 0.33 (10% ethyl acetate - petroleum ether). ^1H NMR (400 MHz, $CDCl_3$) δ 7.39 – 7.28 (m, 5H), 5.90 (t, *J* = 8.2 Hz, 2H), 4.48 (s, 2H), 4.07 (s, 2H), 3.90 – 3.82 (m, 4H), 3.06 (m, 1H), 2.47 – 2.30 (m, 2H), 2.18 (dd, *J* = 15.1, 10.0 Hz, 2H), 1.93 (dd, *J* = 15.9, 8.7 Hz, 1H), 1.86 (d, *J* = 12.0 Hz, 1H), 1.80 – 1.67 (m, 5H), 1.40 (d, *J* = 13.9 Hz, 1H), 0.96 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 146.0, 138.6, 131.5, 130.7, 129.4, 128.3 (2 C), 127.9 (2 C), 127.4, 119.8, 76.1, 71.5, 65.2, 64.2, 47.0, 46.9, 40.6, 40.5, 37.7, 33.7, 30.4, 27.5, 26.8, 14.7 ppm; HRMS (m/z): Exact mass calcd for $C_{25}H_{32}O_3$ $[M]^+$: 380.2351; found 380.2349.



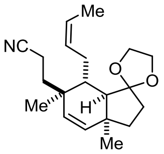
Aldehyde **40**. To a solution of nitrile **39** (307 mg, 0.97 mmol, 1.0 equiv.) in CH_2Cl_2 (10 mL) was bubbled with O_3 at -78 ^{o}C until the system turned to blue, then the mixture was bubbled with O_2 until the mixture turned to colorless. To the above mixture was added triphenylphosphine (507 mg, 1.93 mmol, 2.0 equiv.) at -78 ^{o}C. The mixture was stirred for 15 minutes, then stirred at 25 ^{o}C for another 3 hours. The organic layer was dried over anhydrous magnesium sulfate, filtered, concentrated, and purified by silica gel column chromatography (20~30% ethyl acetate - petroleum ether) to give aldehyde **40** (272 mg, 88%) as a colorless solid: R_f = 0.15 (30% ethyl acetate - petroleum ether); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.68 (d, *J* = 2.4 Hz, 1H), 3.83 (s, 4H), 2.90 (dt, *J* = 12.2, 4.2 Hz, 1H), 2.73 – 2.53 (m, 3H), 2.32 – 2.13 (m, 3H), 2.00 – 1.90 (m, 2H), 1.83 (dt, *J* = 11.9, 4.3 Hz, 1H), 1.72 – 1.64 (m, 1H), 1.63 – 1.50 (m, 3H), 1.02 (s, 3H), 1.00 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 215.4, 200.8, 119.4, 118.2, 63.2 (2 C), 51.8, 51.2, 48.3, 43.5, 38.7, 38.4, 33.0, 32.7, 32.3, 29.9, 18.6, 12.1 ppm; HRMS (m/z): Exact mass calcd for $C_{18}H_{25}NO_4$ $[M]^+$: 319.1784; found 319.1781.



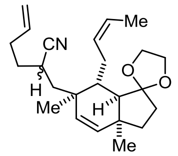
Olefin **41**. To a solution of ethyltriphenylphosphonium bromide (506 mg, 1.36 mmol, 1.6 equiv.) in dry THF (17 mL) was added sodium bis(trimethylsilyl)amide (0.6 mL, 2.0 M solution in THF, 1.28 mmol, 1.5 equiv.) at -78 ^{o}C under nitrogen. After stirring for 20 minutes at 0 ^{o}C, to the above mixture was added aldehyde **40** (272 mg, 0.85 mmol, 1.0 equiv.) at -78 ^{o}C. The mixture was stirred for 10 minutes at -78 ^{o}C, then 20 minutes at 25 ^{o}C. water (20 mL) was added to quench the reaction and the mixture was extracted with ethyl acetate (40 mL x 2). The combined organic layer was washed with brine (40 mL), dried over anhydrous magnesium sulfate, filtered, concentrated, and purified by silica gel column chromatography (10~20% ethyl acetate - petroleum ether) to give olefin **41** (245 mg, 87%) as a colorless solid: R_f = 0.39 (30% ethyl acetate - petroleum ether); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.52 – 5.37 (m, 2H), 4.06 – 3.88 (m, 4H), 2.48 (d, *J* = 13.6 Hz, 1H), 2.44 – 2.22 (m, 3H), 2.19 (d, *J* = 13.6 Hz, 1H), 2.16 – 2.02 (m, 3H), 1.93 (d, *J* = 11.9 Hz, 1H), 1.82 (dt, *J* = 7.9, 4.2 Hz, 1H), 1.76 – 1.66 (m, 2H), 1.64 (d, *J* = 5.9 Hz, 3H), 1.54 (dd, *J* = 10.4, 4.9 Hz, 2H), 1.07 (s, 3H), 1.01 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 216.8, 131.1, 123.5, 119.6, 118.9, 63.9, 63.6, 51.6, 51.6, 49.2, 38.8, 38.6, 38.0, 33.6, 33.4, 30.1, 25.9, 19.6, 13.1, 12.4 ppm; MS (m/z): EI [M] calcd for $C_{20}H_{29}NO_3$ 331.21; found 331.0 (7%), 291.0 (2%), 276.0 (3%).



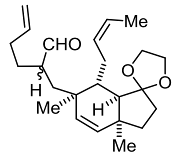
Alcohol **S1**+**S1'** (dr = 5:1). To a solution of olefin **41** (245 mg, 0.74 mmol, 1.0 equiv.) in MeOH (4 mL) was added sodium borohydride (168 mg, 4.43 mmol, 6.0 equiv.) partially at 0 °C. After the SM disappeared, acetone (1 mL) was carefully added at 0 °C to quench the reaction. Concentrated, the residue was extracted with ethyl acetate (20 mL x 3). The combined organic layer was dried over anhydrous magnesium sulfate, filtered, concentrated, to give crude alcohol **S1** and **S1'**(dr = 5:1) (242 mg, 98% without purification) as a mixture of inseparable diastereomers as colorless oil: R_f = 0.34 (30% ethyl acetate - petroleum ether); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.54 – 5.44 (m, 2H) (**S1**+**S1'**), 5.44 – 5.28 (m, 2H) (**S1**+**S1'**), 4.00 – 3.74 (m, 8H) (**S1**+**S1'**), 3.71 – 3.47 (m, 2H) (**S1**+**S1'**), 2.42 – 2.22 (m, 4H) (**S1**+**S1'**), 2.20 – 1.96 (m, 4H) (**S1**+**S1'**), 1.92 – 1.73 (m, 12H) (**S1**+**S1'**), 1.72 – 1.53 (m, 14H) (**S1**+**S1'**), 1.54 – 1.35 (m, 4H) (**S1**+**S1'**), 1.16 (s, 3H) (**S1**), 1.12 (s, 3H) (**S1'**), 0.93 (s, 3H) (**S1**), 0.80 (s, 3H) (**S1'**); ^{13}C NMR (100 MHz, $CDCl_3$) δ (132.0) 131.2, 124.0 (122.7), 121.2 (2 C), (120.6) 119.6, 71.8 (69.1), 64.7 (63.9), 63.6 (63.5), (55.9) 53.6, (40.3) 39.5, (39.2) 39.1, 38.9 (2 C), 38.3(2 C), 37.6 (36.3), (35.4) 34.5, 32.2 (30.9), (30.4) 30.3, 29.3 (29.0), 21.4 (2 C), (13.2) 13.1, 12.3 (11.5) ppm; MS (m/z): EI [M] calcd for $C_{20}H_{31}NO_3$ 333.23; found 333.0 (3%), 316.0 (2%), 278.0 (3%).



Diene **42**.[5] To the crude alcohol **S1** and **S1'** (185 mg, 0.56 mmol, 1.0 equiv.) was added bis[alpha,alpha-bis(trifluoromethyl)benzenemethanolato]diphenylsulfur (597 mg, 0.89 mmol, 1.6 equiv.) (weighted in glove box) in $CHCl_3$ (3 mL) under nitrogen. The mixture was stirred for 6 hours at 25 °C. Concentrated, the residue was purified by silica gel column chromatography (10~20% ethyl acetate - petroleum ether) to give diene **42** (120 mg, 90% with recovery of 44 mg SM) as a colorless solid: R_f = 0.29 (10% ethyl acetate - petroleum ether); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.52 (d, *J* = 9.8 Hz, 1H), 5.49 – 5.35 (m, 2H), 5.29 (d, *J* = 9.9 Hz, 1H), 3.98 – 3.82 (m, 4H), 2.41 – 2.32 (m, 1H), 2.23 – 2.09 (m, 2H), 1.97 (dd, *J* = 10.8, 6.9 Hz, 2H), 1.90 – 1.81 (m, 1H), 1.81 – 1.71 (m, 2H), 1.71 – 1.66 (m, 1H), 1.65 (d, *J* = 6.7 Hz, 3H), 1.61 – 1.38 (m, 2H), 1.13 (s, 3H), 0.94 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 136.3, 132.8, 131.8, 123.0, 120.6, 119.4, 63.7, 63.6, 53.4, 40.9, 38.1, 37.5, 36.7, 36.1, 34.4, 30.2, 27.4, 23.3, 13.2, 12.5 ppm; MS (m/z): EI [M] calcd for $C_{20}H_{29}NO_2$ 315.22; found 315.0 (2%), 275.0 (2%), 224.0 (11%).

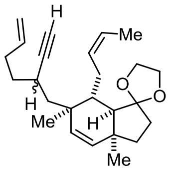


Triene **43**+**43’** (dr = 1.5:1). To a solution of diene **42** (95 mg, 0.30 mmol, 1.0 equiv.) in dry THF (0.5 mL) was added LDA (2.0 M THF solution, 0.2 mL, 0.42 mmol, 1.4 equiv.) at -78 °C under nitrogen. After stirring for 30 minutes, to the above mixture was added 4-bromo-1-butene (40 μL, 0.39 mmol, 1.3 equiv.) dropwise at -78 °C. The mixture was stirred for 1 hours at 25 °C. Water (1 mL) was added to quench the reaction and the mixture was extracted with ethyl acetate (10 mL x 3). The combined organic layer was dried over anhydrous magnesium sulfate, filtered, concentrated, and purified by silica gel column chromatography (5% ethyl acetate - petroleum ether) to give triene **43** and **43’** (105 mg, 94%) as a mixture of inseparable diastereomers as colorless oil: R_f = 0.40 (10% ethyl acetate - petroleum ether); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.36 – 5.25 (m, 2H) (**43**+**43’**), 5.66 (d, *J* = 9.9 Hz, 2H) (**43**+**43’**), 5.65 – 5.36 (m, 4H) (**43**+**43’**), 5.36 – 5.25 (m, 2H) (**43**+**43’**), 5.15 – 4.98 (m, 4H) (**43**+**43’**), 3.97 – 3.83 (m, 8H) (**43**+**43’**), 2.68 – 2.54 (m, 2H) (**43**+**43’**), 2.36 – 2.23 (m, 2H) (**43**+**43’**), 2.22 – 2.12 (m, 4H) (**43**+**43’**), 2.00 – 1.88 (m, 4H) (**43**+**43’**), 1.87 – 1.70 (m, 6H) (**43**+**43’**), 1.69 – 1.54 (m, 12H) (**43**+**43’**), 1.54 – 1.40 (m, 6H) (**43**+**43’**), 1.13 (s, 6H) (**43**+**43’**), 0.94 (s, 6H) (**43**+**43’**); ^{13}C NMR (100 MHz, $CDCl_3$) δ 136.6 (2 C), 135.1 (2 C), (132.8) 132.7, 132.7 (132.0), 122.9 (2 C), (122.5) 122.4, 119.5 (119.3), 116.0 (2 C), (63.9) 63.6, 63.5 (2 C), 53.8 (53.1), (42.8) 42.7, 40.8 (40.4), 38.6 (38.4), 38.3 (38.3), (36.8) 36.7, 34.5 (34.4), 33.1 (33.0), (31.0) 30.8, (30.6) 30.2, (28.2) 27.6, (26.5) 25.8, 23.7 (23.5), 13.1 (2 C) ppm; MS (m/z): EI [M] calcd for $C_{24}H_{35}NO_2$ 369.27; found 369.0 (2%), 314.0 (2%), 278.0 (8%).

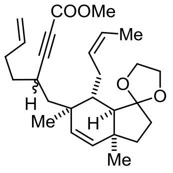


Aldehyde **44**+**44’** (dr = 1.5:1). To a solution of triene **43** and **43’** (142 mg, 0.47 mmol, 1.0 equiv.) in dry PhMe (3 mL) was added diisobutylaluminum hydride (1.0 M PhMe solution, 0.6 mL, 0.56 mmol, 1.2 equiv.) at -78 °C under nitrogen. The mixture was stirred for 2 hours at -78 °C. Potassium sodium tartrate solution (3 mL) was added to quench the reaction and the mixture was extracted with ethyl acetate (10 mL x 3), the organic layer was dried over anhydrous magnesium sulfate, filtered, concentrated, and purified by silica gel column chromatography (10% ethyl acetate - petroleum ether) to give aldehyde **44** and **44’** (123 mg, 87%) as a mixture of inseparable diastereomers as colorless oil: R_f = 0.29 (10% ethyl acetate - petroleum ether); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.59 (d, *J* = 3.6 Hz, 1H) (**44**), 9.54 (d, *J* = 3.6 Hz, 1H) (**44’**), 5.82 – 5.68 (m, 2H) (**44**+**44’**), 5.60 – 5.20 (m, 8H) (**44**+**44’**), 4.98 (t, *J* = 13.8 Hz, 4H) (**44**+**44’**), 4.01 – 3.77 (m, 8H) (**44**+**44’**), 2.56 – 2.50 (m, 1H) (**44**), 2.50 – 2.44 (m, 1H) (**44’**), 2.30 –

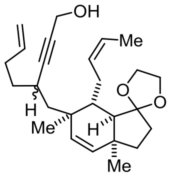
2.14 (m, 2H) (**44**+**44’**), 2.09 – 1.70 (m, 16H) (**44**+**44’**), 1.63 (dd, J = 17.9, 10.7 Hz, 8H) (**44**+**44’**), 1.56 – 1.28 (m, 8H) (**44**+**44’**), 1.12 (s, 3H) (**44’**), 1.10 (s, 3H) (**44**), 0.91 (s, 3H) (**44’**), 0.87 (s, 3H) (**44**); ^{13}C NMR (100 MHz, CDCl$_3$) δ 205.7 (205.2), 137.9 (2 C), 134.9 (134.5), 133.6 (133.4), 133.0 (132.7), (122.2) 121.9, 119.6 (119.5), (115.2) 115.2, (63.8) 63.7, 63.6 (2 C), 53.8 (53.5), (47.7) 47.6, 41.0 (2 C), 40.9 (40.6), (39.5) 39.5, (38.6) 38.5, (36.8) 36.6, 34.5 (34.5), (31.0) 30.9, 30.6 (30.5), 30.3 (30.2), (28.0) 27.9, 23.5 (23.5), 13.1 (2 C) ppm; MS (m/z): EI [M] calcd for $C_{24}H_{36}O_3$ 372.27; found 372.0 (2%), 317.0 (1%), 281.0 (7%).



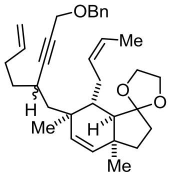
Trienyne **45**+**45’** (dr = 1.3:1). To a solution of aldehyde **44** and **44’** (44 mg, 0.12 mmol, 1.0 equiv.) in MeOH (0.6 mL) was added dimethyl(1-diazo-2-oxopropyl) phosphonate (45 mg, 0.24 mmol, 2.0 equiv.), anhydrous potassium carbonate (49 mg, 0.35 mmol, 3.0 equiv.) at 25 $^{\circ}$C. The mixture was stirred for 4 hours at 25 $^{\circ}$C. The solvent was removed under reduced pressure and the residue was added ethyl acetate (10 mL) and water (10 mL). The organic layer was separated and the water layer was extracted with ethyl acetate (10 mL x 2). The combined organic layer was dried over anhydrous magnesium sulfate, filtered, concentrated, and purified by silica gel column chromatography (2~5% ethyl acetate - petroleum ether) to give trienyne **45** and **45’** (37 mg, 85%) as a mixture of inseparable diastereomers as colorless oil: R_f = 0.54 (10% ethyl acetate - petroleum ether); ^{1}H NMR (400 MHz, CDCl$_3$) δ 5.89 – 5.67 (m, 4H) (**45**+**45’**), 5.66 – 5.56 (m, 1H) (**45’**), 5.55 – 5.44 (m, 1H) (**45**), 5.44 – 5.24 (m, 4H) (**45**+**45’**), 5.10 – 4.90 (m, 4H) (**45**+**45’**), 3.99 – 3.80 (m, 8H) (**45**+**45’**), 2.53 – 2.38 (m, 2H) (**45**+**45’**), 2.30 – 2.10 (m, 6H) (**45**+**45’**), 2.06 (dd, J = 19.5, 2.4 Hz, 2H) (**45**+**45’**), 2.00 – 1.90 (m, 4H) (**45**+**45’**), 1.88 – 1.70 (m, 6H) (**45**+**45’**), 1.61 (d, J = 6.8 Hz, 6H) (**45**+**45’**), 1.59 – 1.52 (m, 4H) (**45**+**45’**), 1.50 – 1.40 (m, 6H) (**45**+**45’**), 1.13 (s, 6H) (**45**+**45’**), 0.93 (s, 3H) (**45**), 0.90 (s, 3H) (**45’**); ^{13}C NMR (100 MHz, CDCl$_3$) δ 138.4 (138.3), 134.2 (134.0), (133.9) 133.4, 133.2 (132.8), 121.7 (121.6), 119.7 (119.6), (114.7) 114.6, (89.1) 88.9, 70.0 (69.7), (63.8) 63.7, 63.6 (2 C), 54.0 (53.3), (45.5) 45.4, 40.8 (40.5), 39.6 (39.5), 38.7 (2 C), (36.9) 36.9, 36.0 (35.9), 34.6 (34.5), (31.2) 31.1, (30.7) 30.4, (28.1) 27.9, (26.7) 26.1, 23.5 (22.9), 13.1 (2 C) ppm; HRMS (m/z): Exact mass calcd for $C_{25}H_{36}O_2$ $[M]^+$: 368.2715; found 368.2717.



Ester **46**+**46’** (dr = 1.3:1). To a solution of trienyne **45** and **45’** (41 mg, 0.11 mmol, 1.0 equiv.) in dry THF (0.8 mL) was added *n*-BuLi (1.6 M THF solution, 139 μL, 0.22 mmol, 2.0 equiv.) at -78 °C under nitrogen. After stirring for 30 minutes, to the above mixture was added methyl chloroformate (14 μL, 0.19 mmol, 1.6 equiv.) dropwise at -78 °C. The mixture was stirred for 0.5 hours at -78 °C and for further 0.5 hours at 25 °C. Water (1 mL) was added to quench the reaction and the mixture was extracted with ethyl acetate (10 mL x 3). The combined organic layer was dried over anhydrous magnesium sulfate, filtered, concentrated, and purified by silica gel column chromatography (2~5% ethyl acetate - petroleum ether) to give ester **46** and **46’** (45 mg, 96%) as a mixture of inseparable diastereomers as colorless oil: R_f = 0.42 (10% ethyl acetate - petroleum ether); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.85 – 5.70 (m, 2H) (**46**+**46’**), 5.67 (d, *J* = 9.9 Hz, 2H) (**46**+**46’**), 5.54 – 5.24 (m, 6H) (**46**+**46’**), 5.00 (dd, *J* = 26.2, 13.6 Hz, 4H) (**46**+**46’**), 3.96 – 3.80 (m, 8H) (**46**+**46’**), 3.74 (s, 6H) (**46**+**46’**), 2.66 – 2.56 (m, 2H) (**46**+**46’**), 2.30 – 2.10 (m, 6H) (**46**+**46’**), 2.06 – 1.89 (m, 4H) (**46**+**46’**), 1.90 – 1.70 (m, 6H) (**46**+**46’**), 1.61 (d, *J* = 7.0 Hz, 6H) (**46**+**46’**), 1.58 – 1.38 (m, 12H) (**46**+**46’**), 1.13 (s, 6H) (**46**+**46’**), 0.92 (s, 3H) (**46**), 0.90 (s, 3H) (**46’**); ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.4 (2 C), 137.7 (137.7), (134.6) 133.9, 133.7 (133.6), 133.0 (132.4), 122.0 (2 C), 119.7 (119.5), (115.2) 115.2, (93.8) 93.8, 75.0 (74.3), (63.8) 63.7, 63.6 (2 C), 54.0 (2 C), (53.0) 52.4, (44.9) 44.8, 40.8 (40.5), 39.1 (2 C), 38.7 (38.6), (36.9) 36.8, 35.1 (35.0), 34.6 (34.4), (31.2) 31.0, (30.7) 30.4, (28.0) 27.8, (27.0) 26.5, 23.6 (23.3), 13.1 (13.1); HRMS (m/z): Exact mass calcd for $C_{27}H_{38}O_4$ $[M]^+$: 426.2770; found 426.2769.



Alcohol **S2**+**S2’** (dr = 1.3:1). To a solution of ester **46** and **46’** (47 mg, 0.11 mmol, 1.0 equiv.) in dry PhMe (0.6 mL) was added diisobutylaluminum hydride (1.0 M PhMe solution, 0.3 mL, 0.28 mmol, 2.5 equiv.) at -78 °C under nitrogen. The mixture was stirred for 2 hours at -78 °C, and for 30 minutes at 25 °C. Potassium sodium tartrate solution (0.5 mL) was added to quench the reaction and the mixture was extracted with ethyl acetate (10 mL x 3). The combined organic layer was dried over anhydrous magnesium sulfate, filtered, concentrated, and purified by silica gel column chromatography (20% ethyl acetate - petroleum ether) to give alcohol **S2** and **S2’** (44 mg, 100%) as a mixture of inseparable diastereomers as colorless oil: R_f = 0.32 (20% ethyl acetate - petroleum ether); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.88 – 5.69 (m, 4H) (**S2**+**S2’**), 5.55 – 5.27 (m, 6H) (**S2**+**S2’**), 4.99 (dd, *J* = 28.2, 13.5 Hz, 4H) (**S2**+**S2'**), 4.21 (d, *J* = 5.0 Hz, 4H) (**S2**+**S2'**), 3.99 – 3.83 (m, 8H) (**S2**+**S2'**), 2.72 – 2.45 (m, 2H) (**S2**+**S2'**), 2.30 – 2.18 (m, 4H) (**S2**+**S2'**), 2.18 (dt, *J* = 14.4, 11.5 Hz, 2H) (**S2**+**S2'**), 2.01 – 1.87 (m, 6H) (**S2**+**S2'**), 1.86 – 1.70 (m, 4H) (**S2**+**S2'**), 1.61 (d, *J* = 5.8 Hz, 6H) (**S2**+**S2'**), 1.58 – 1.39 (m, 14H) (**S2**+**S2'**), 1.14 (s, 6H) (**S2**+**S2'**), 0.92 (s, 3H) (**S2**), 0.87 (s, 3H) (**S2'**); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.4 (138.4), 135.2 (2 C), 134.1 (133.6), 133.0 (132.8), 121.8 (121.4), (120.2) 119.8, (114.7) 114.6, 90.7 (90.6), (81.2) 80.5, (63.7) 63.6, 63.6 (2 C), 54.0 (53.4), 51.6 (51.4), 45.7 (44.2), 40.8 (2 C), 38.7 (38.5), (37.1) 37.0, 36.9 (2 C), (36.0) 35.8, (34.7) 34.6, 31.2 (2 C), (30.7) 30.5, (28.5) 28.0, (27.4) 26.6, (24.5) 23.9, 13.1 (2 C) ppm; HRMS (m/z): Exact mass calcd for $C_{26}H_{38}O_3$ $[M]^+$: 398.2821; found 398.2824.



Benyl ether **47**+**47'** (dr = 1.3:1). To a solution of alcohol **S2** and **S2'** (66 mg, 0.17 mmol, 1.0 equiv.) in dry DMF (1.7 mL) was added sodium hydride (57% - 63% oil dispersion, 10 mg, 0.25 mmol, 1.5 equiv.) at 0 °C under nitrogen. After stirring for 30 minutes at 0 °C, to the above mixture was added benzyl bromide (24 µL, 0.20 mmol, 1.2 equiv.). The mixture was stirred for 30 minutes at 0 °C. Water (2 mL) was added to quench the reaction and the mixture was extracted with ethyl acetate (10 mL x 5). The combined organic layer was washed with brine (20 mL x 3), dried over anhydrous magnesium sulfate, filtered, concentrated, and purified by silica gel column chromatography (5% ethyl acetate - petroleum ether) to give benyl ether **47** and **47'** (75 mg, 93%) as a mixture of inseparable diastereomers as colorless oil: R_f = 0.39 (10% ethyl acetate - petroleum ether); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41 – 7.26 (m, 10H) (**47**+**47'**), 5.88 – 5.66 (m, 4H) (**47**+**47'**), 5.66 – 5.45 (m, 2H) (**47**+**47'**), 5.41 (d, *J* = 9.9 Hz, 1H) (**47'**), 5.36 (d, *J* = 10.0 Hz, 1H) (**47**), 5.32 – 5.23 (m, 2H) (**47**+**47'**), 4.99 (dd, *J* = 29.2, 13.7 Hz, 4H) (**47**+**47'**), 4.58 (s, 4H) (**47**+**47'**), 4.20 (s, 2H) (**47'**), 4.17 (s, 2H) (**47**), 3.94 – 3.76 (m, 8H) (**47**+**47'**), 2.60 – 2.48 (m, 2H) (**47**+**47'**), 2.33 – 2.03 (m, 8H) (**47**+**47'**), 2.02 – 1.86 (m, 4H) (**47**+**47'**), 1.83 – 1.70 (m, 4H) (**47**+**47'**), 1.61 (d, *J* = 6.5 Hz, 6H) (**47**+**47'**), 1.58 – 1.48 (m, 4H) (**47**+**47'**), 1.48 – 1.33 (m, 6H) (**47**+**47'**), 1.13 (s, 6H) (**47**+**47'**), 0.94 (s, 3H) (**47**), 0.91 (s, 3H) (**47'**); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.4 (138.4), 137.8 (2 C), 134.6 (134.0) , 132.9 (132.8), 128.3 (6 c), 128.0 (4 c), 127.6 (2 C), 121.7 (121.5), 119.7 (119.6), (114.7) 114.6, (91.6) 91.3, 77.9 (77.5), (71.1) 71.1, (63.7) 63.6, 63.5 (2 C), 57.8 (2 C), 54.0 (53.2), 45.7 (45.5), 40.8 (40.5), 39.2 (2 C), (38.7) 38.6, (36.9) 36.9, (36.1)

36.0, 34.6 (34.4), (31.4) 31.2, (30.6) 30.4, (28.0) 27.8, (27.0) 26.5, 23.7 (23.0), 13.1 (2 C) ppm; HRMS (m/z): Exact mass calcd for $C_{33}H_{44}O_3$ $[M]^+$: 488.3290; found 488.3289.

Reference:

[1] B. H. Lipshutz, C. Hackmann, *J. Org. Chem.* **1994**, *59*, 7437–7444.

[2] A. Marquet, H. B. Kagan, M. Dvolaitzky, J. Lematre, J. Jacques, *Bull. Soc. Chim. Fr.* **1960**, 539–547.

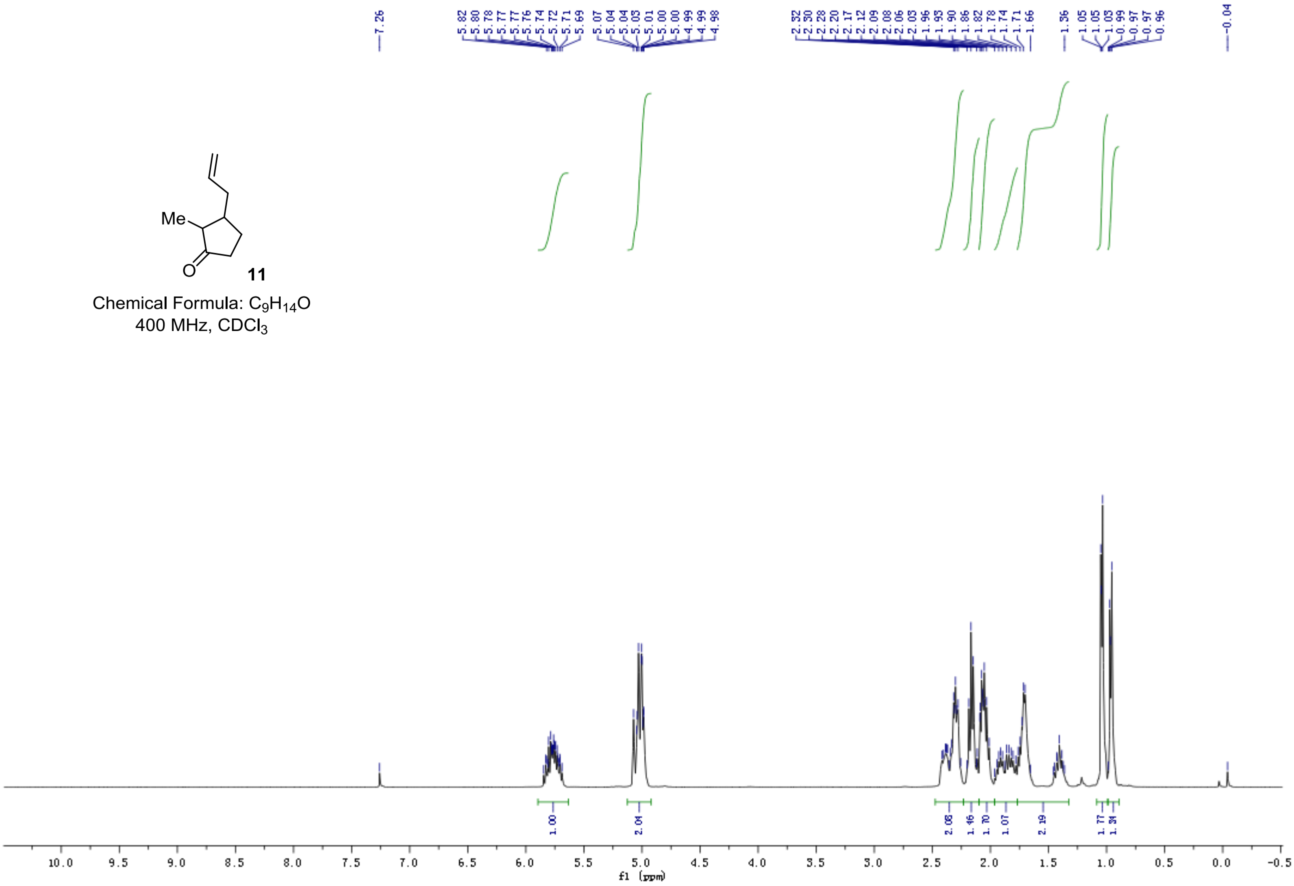
[3] A. K. Chatterjee, D. P. Sanders, R. H. Grubbs, *Org. Lett.* **2002**, *4* , 1939–1942.

[4] (a) R. H. Grubbs, S. J. Miller, G. C. Fu, *Acc. Chem. Res.* **1995**, *28*, 446–452. (b) P. Schwab, M. B. France, J. W. Ziller, R. H. Grubbs, *Angew. Chem., Int. Ed.* **1995**, *34*, 2039–2041. (c) S. H. Kim, N. Bowden, R. H. Grubbs, *J. Am. Chem. Soc.* **1994**, *116*, 10801–10802.

[5] J. C. Martin, R. J. Arhart, *J. Am. Chem. Soc.* **1971**, *93* , 4327–4329.

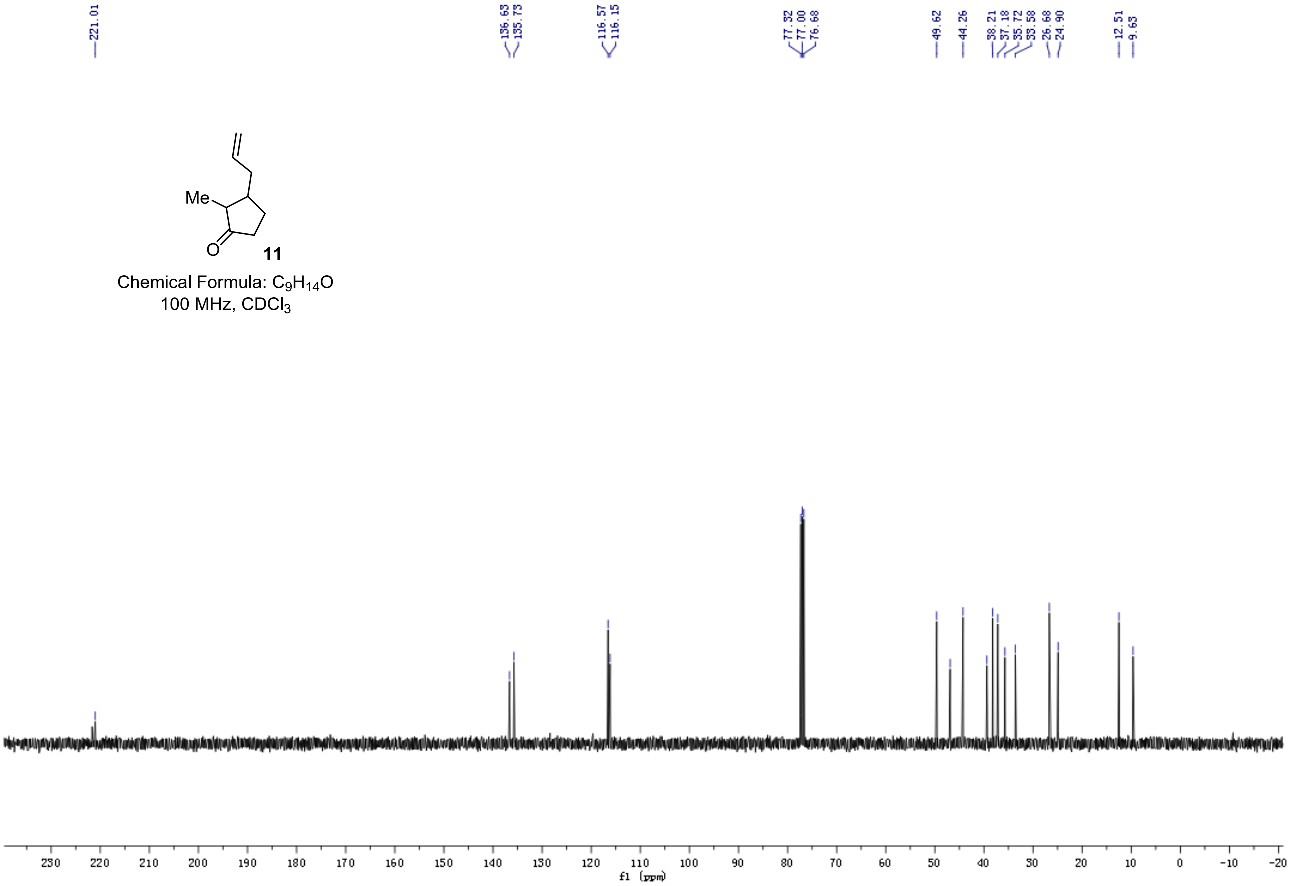
11

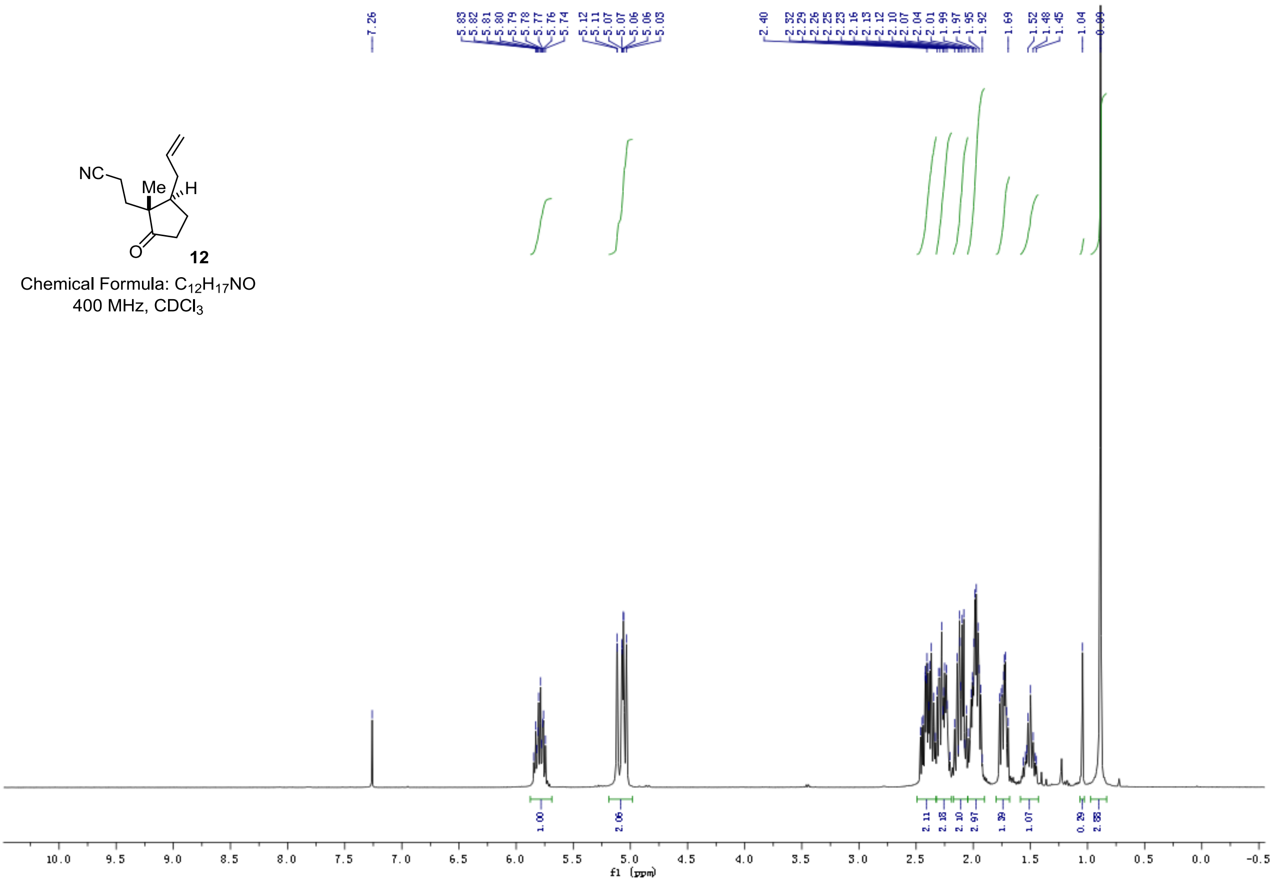
Chemical Formula: $C_9H_{14}O$
400 MHz, $CDCl_3$



11

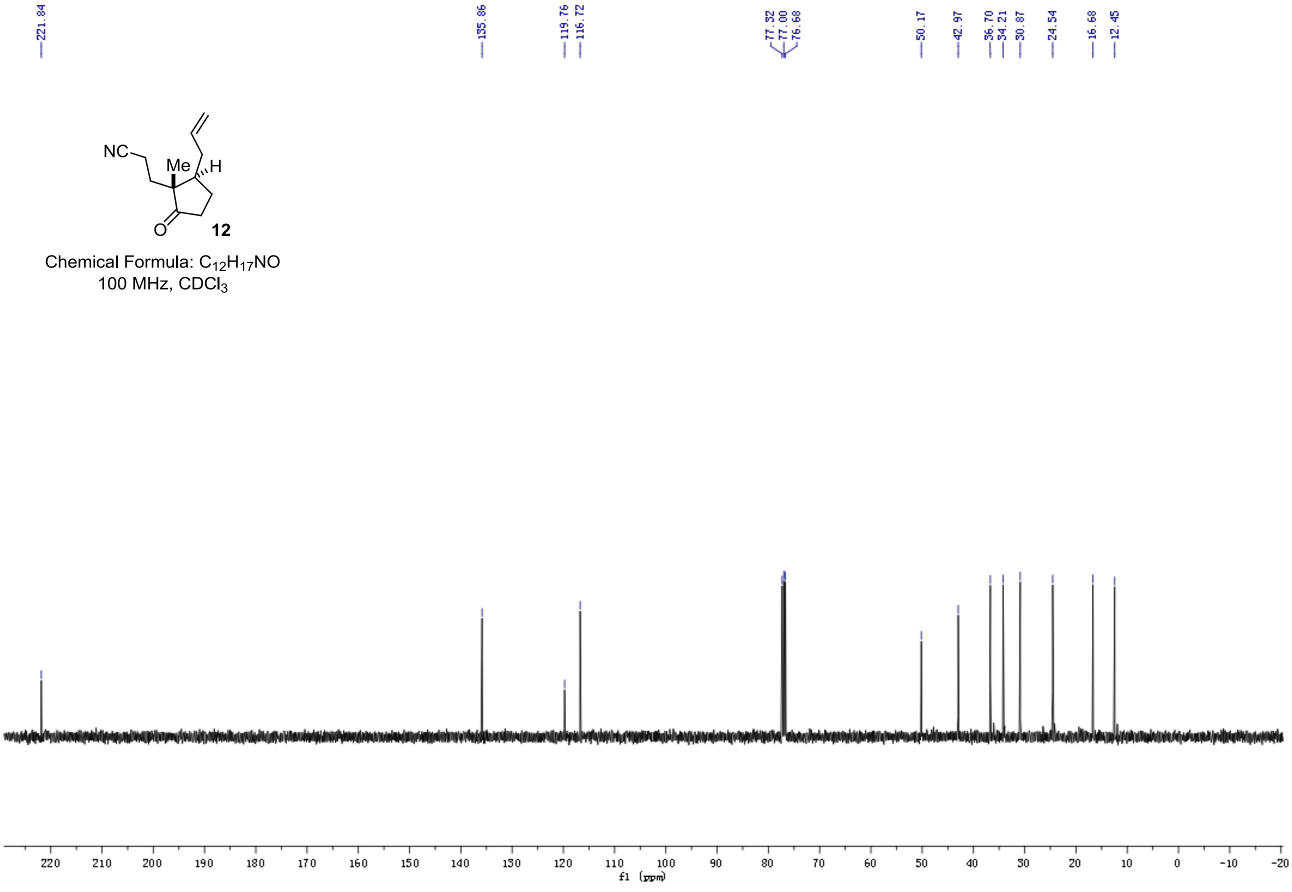
Chemical Formula: $C_9H_{14}O$
100 MHz, $CDCl_3$





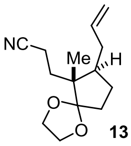
12

Chemical Formula: $C_{12}H_{17}NO$
400 MHz, $CDCl_3$



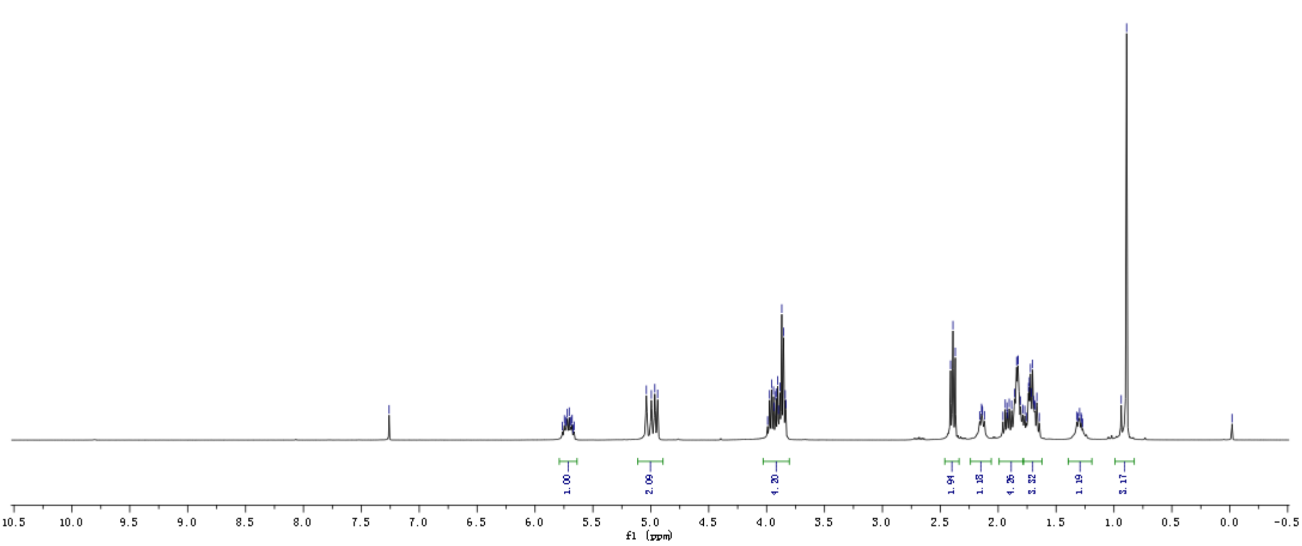
12

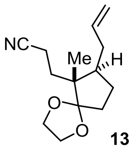
Chemical Formula: $C_{12}H_{17}NO$
100 MHz, $CDCl_3$



13

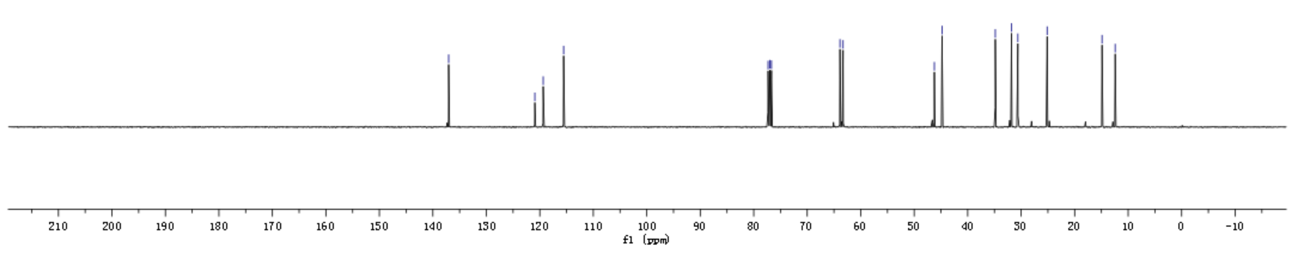
Chemical Formula: $C_{14}H_{21}NO_2$
400 MHz, $CDCl_3$

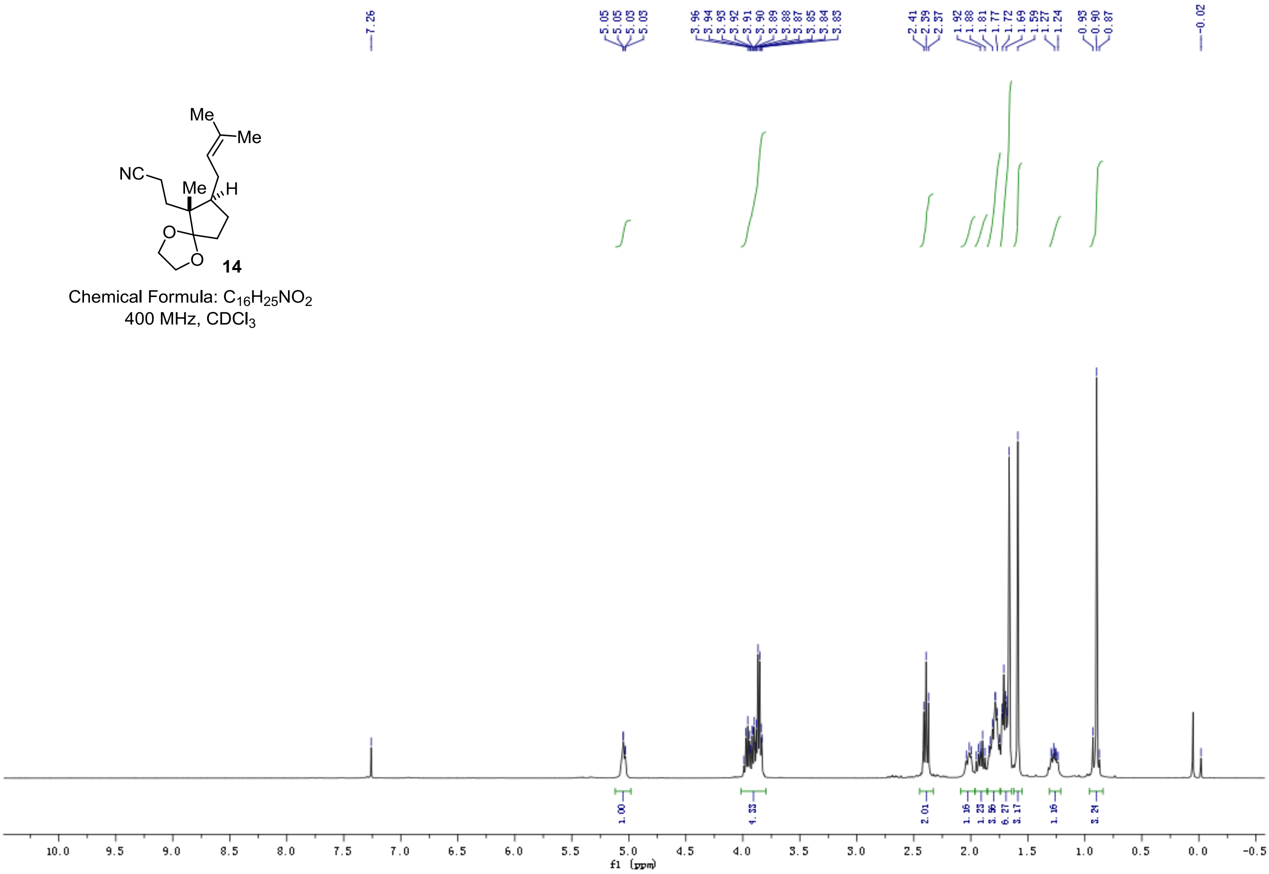




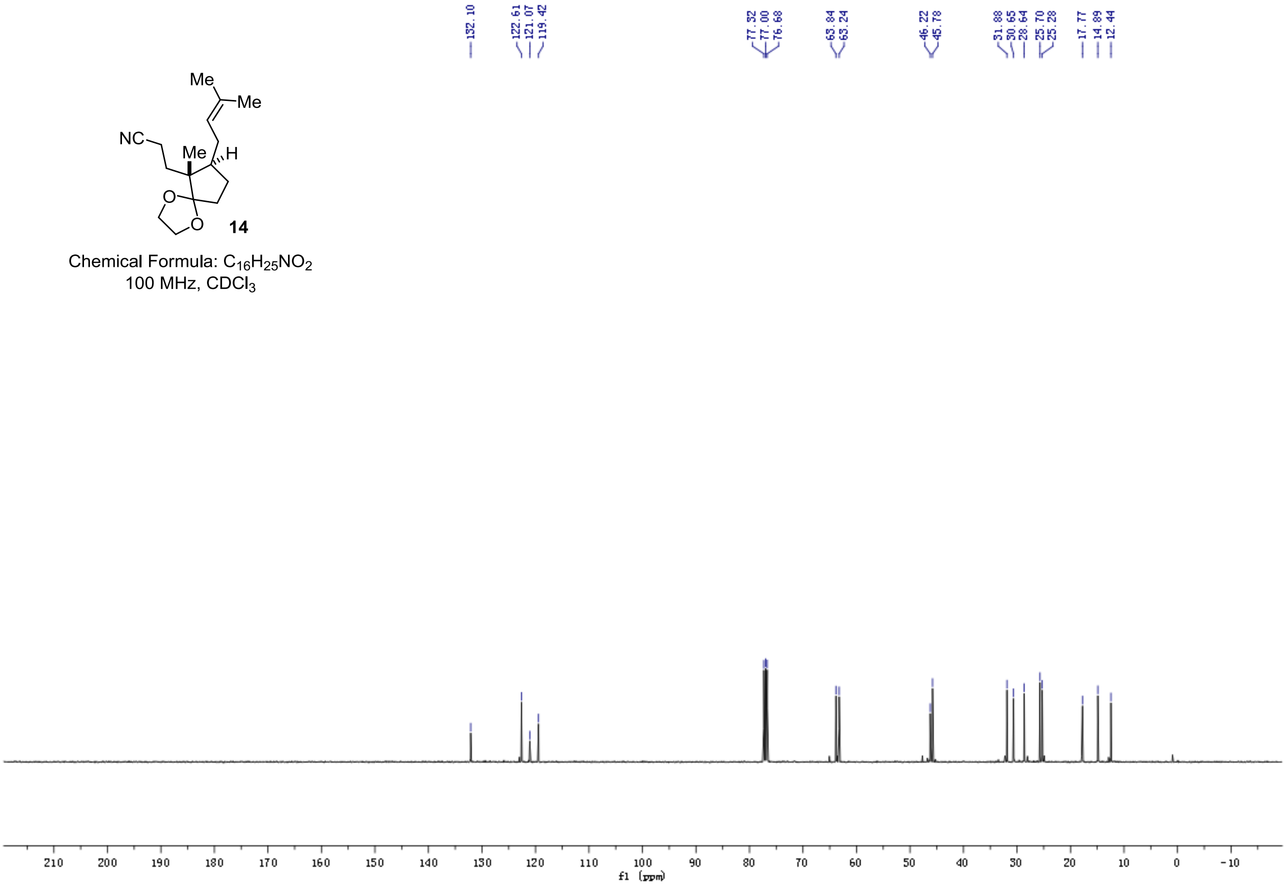
13

Chemical Formula: $C_{14}H_{21}NO_2$
100 MHz, $CDCl_3$

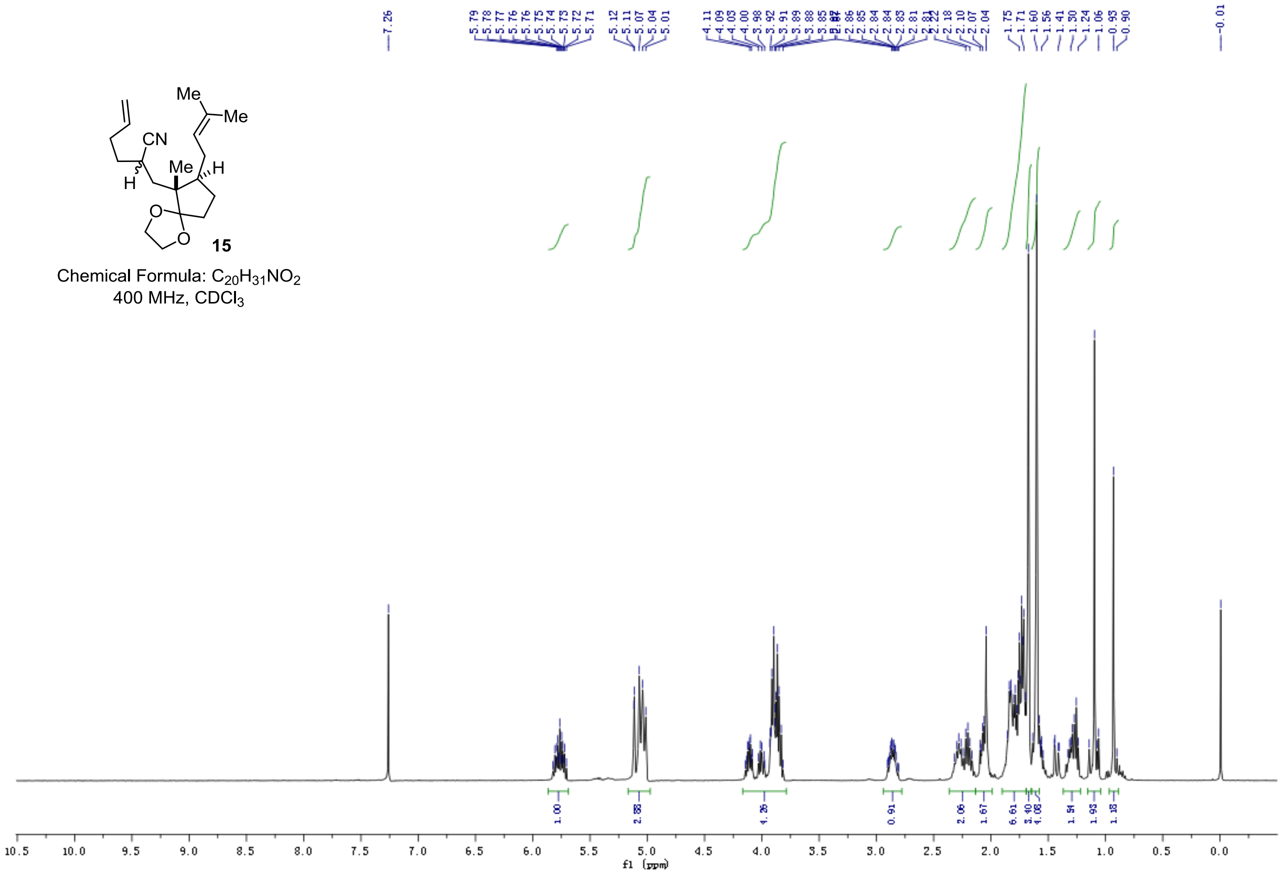




Chemical Formula: $C_{16}H_{25}NO_2$
400 MHz, $CDCl_3$

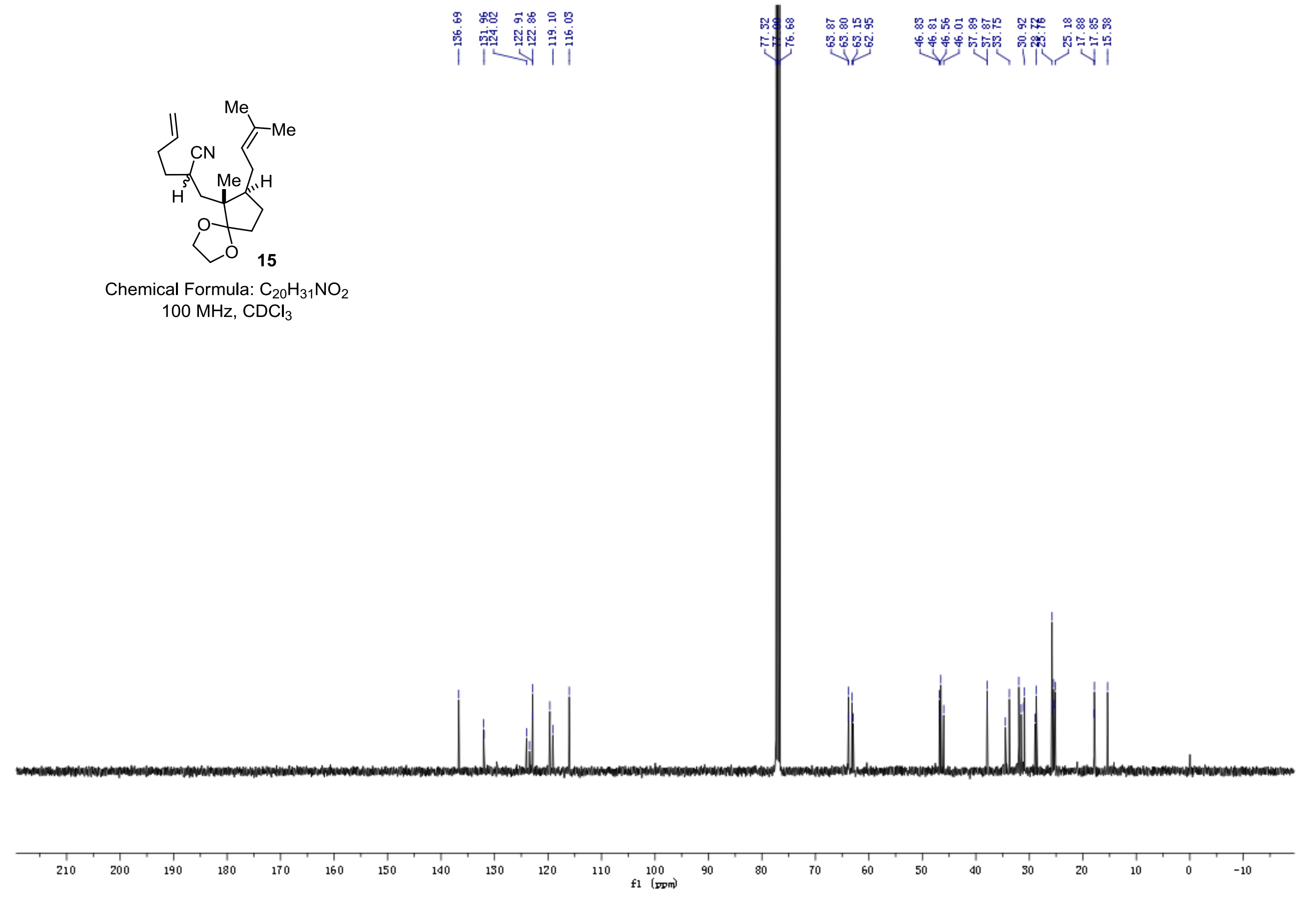


Chemical Formula: $C_{16}H_{25}NO_2$
100 MHz, $CDCl_3$



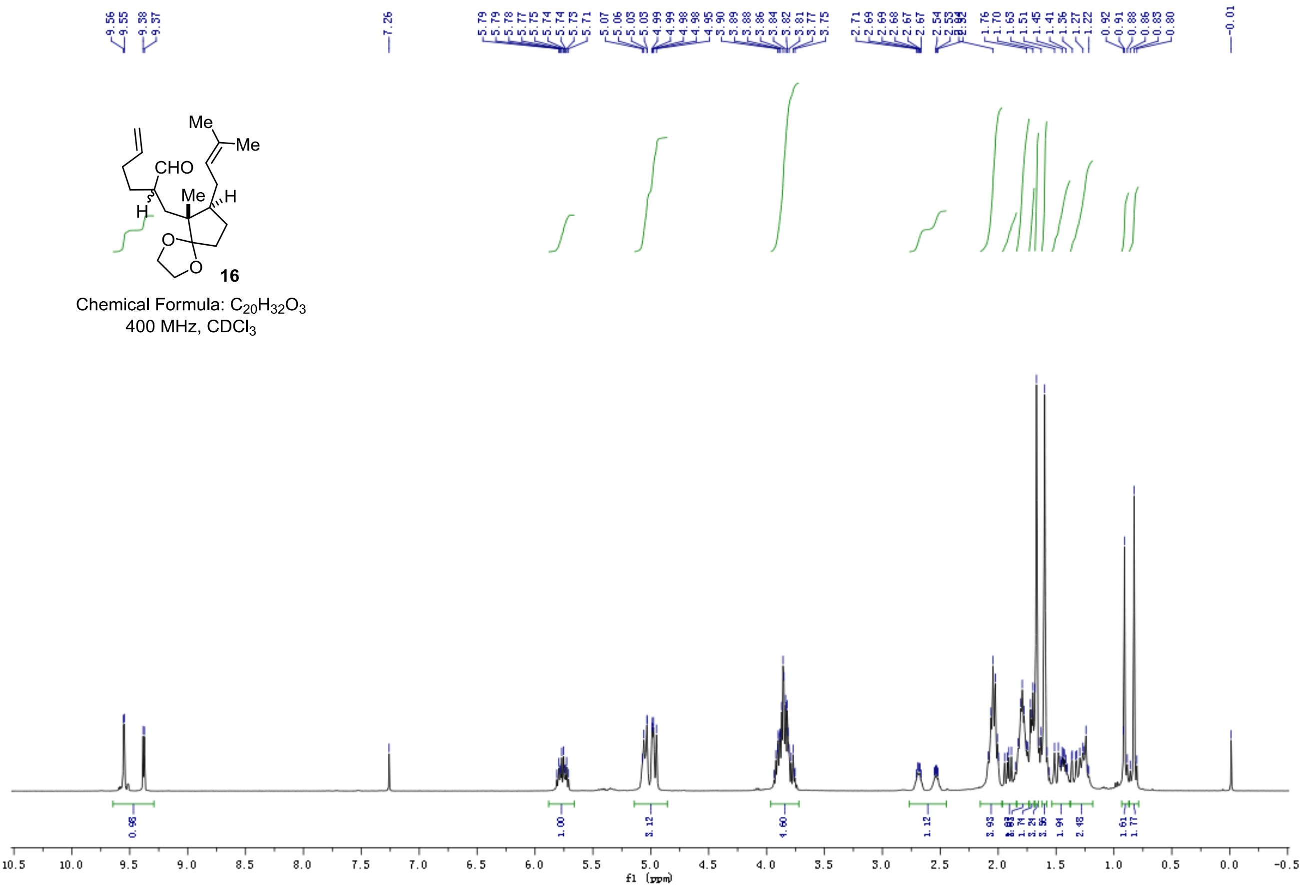
15

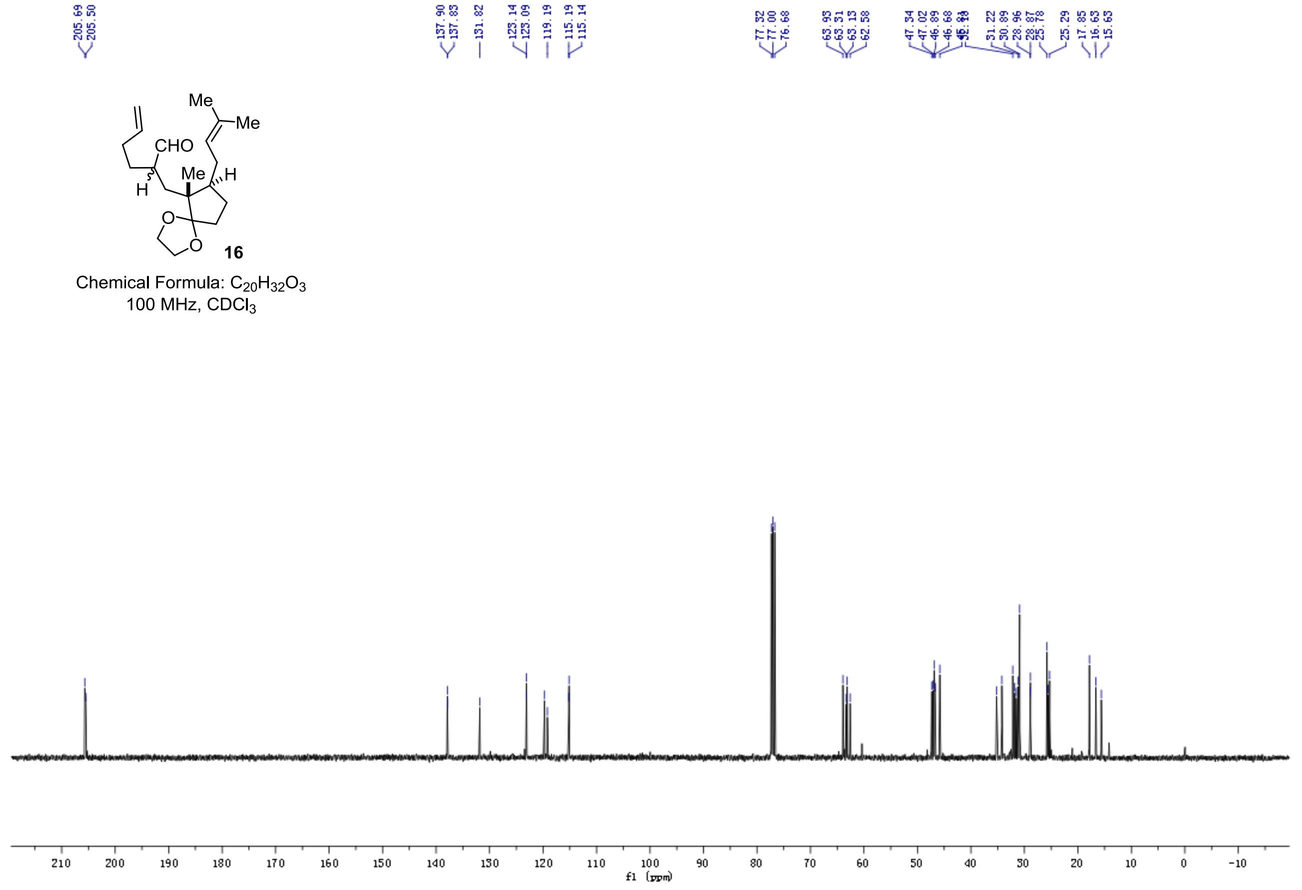
Chemical Formula: $C_{20}H_{31}NO_2$
400 MHz, $CDCl_3$



15

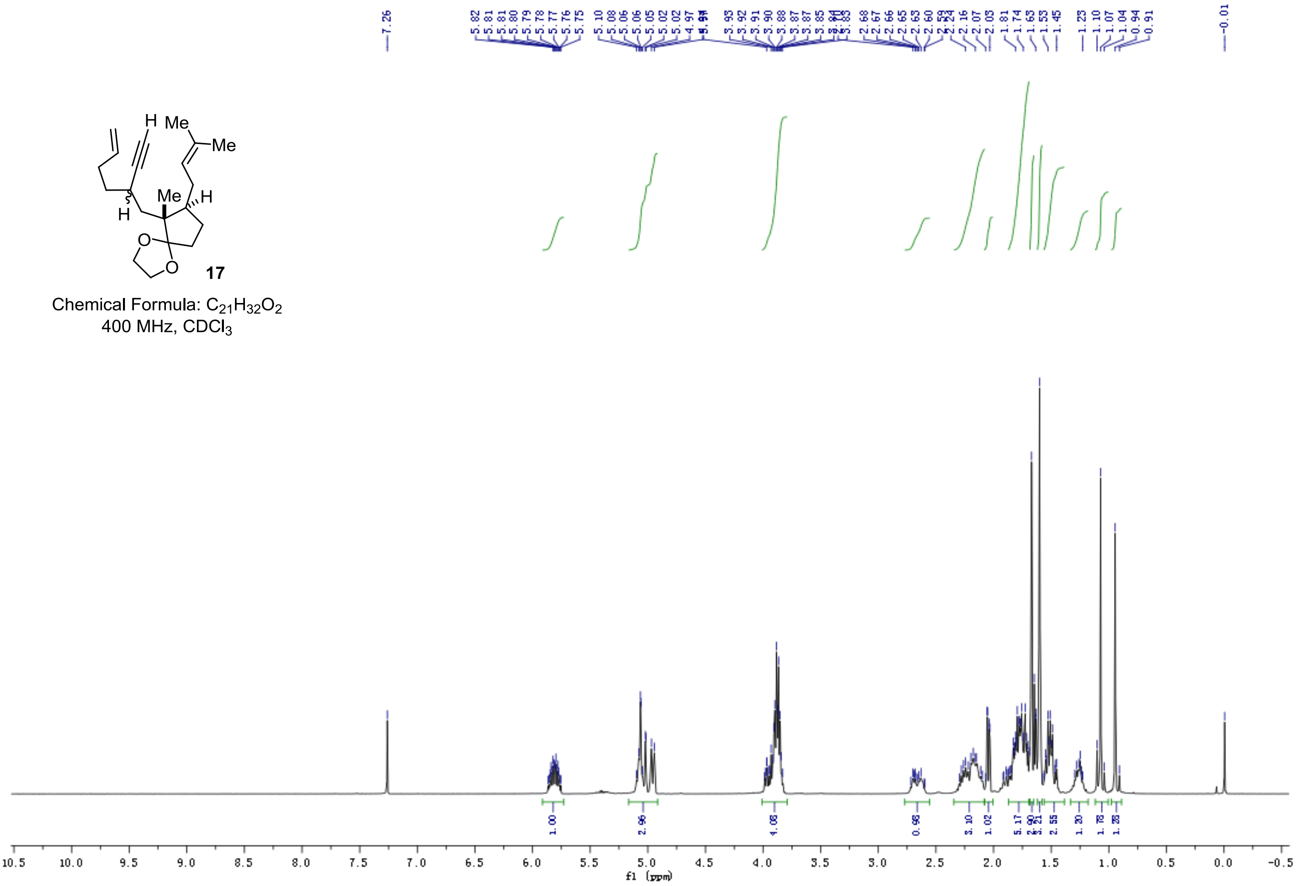
Chemical Formula: $C_{20}H_{31}NO_2$
100 MHz, $CDCl_3$


9.56
9.55
9.38
9.37
7.26
5.79
5.79
5.78
5.77
5.75
5.74
5.74
5.73
5.71
5.07
5.06
5.03
5.03
4.99
4.99
4.98
4.98
4.95
3.90
3.89
3.88
3.86
3.84
3.82
3.81
3.77
3.75
2.71
2.69
2.69
2.68
2.67
2.67
2.54
2.53
1.76
1.70
1.63
1.51
1.45
1.41
1.36
1.27
1.22
0.92
0.91
0.88
0.86
0.83
0.80
-0.01
Me
Me
CHO
Me
H
H
O
O
16
Chemical Formula: $C_{20}H_{32}O_3$
400 MHz, $CDCl_3$
0.98
1.00
3.12
4.60
1.12
3.93
1.74
3.24
3.56
1.94
2.48
1.61
1.77
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)


205.69
205.50
137.90
137.83
131.82
123.14
123.09
119.19
115.19
115.14
77.32
77.00
76.68
63.93
63.51
63.13
62.58
47.34
47.02
46.89
46.68
31.22
30.89
28.96
28.87
25.78
25.29
17.85
16.63
15.63
Me
Me
CHO
Me
H
H
O
O
16
Chemical Formula: $C_{20}H_{32}O_3$
100 MHz, $CDCl_3$
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

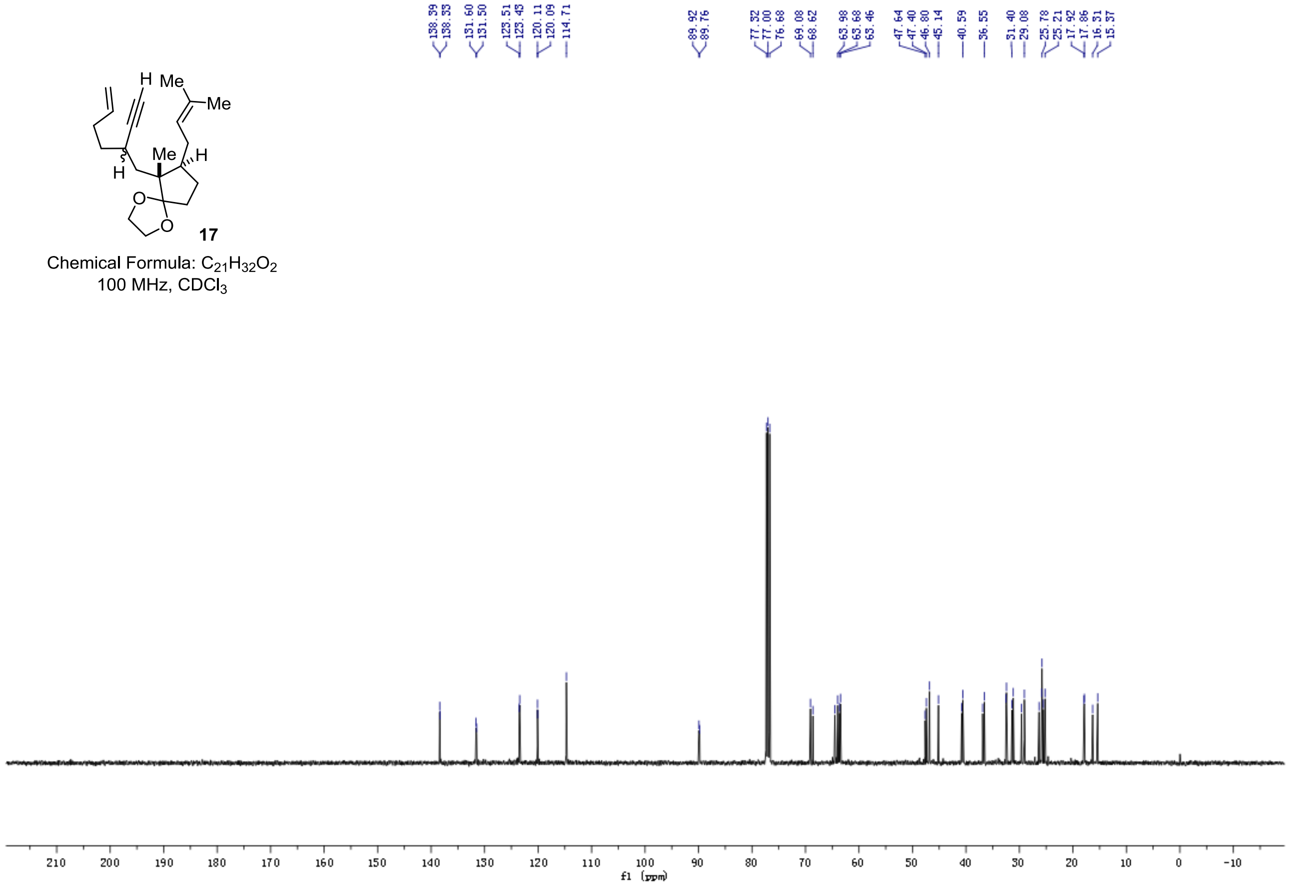
17

Chemical Formula: $C_{21}H_{32}O_2$
400 MHz, $CDCl_3$



17

Chemical Formula: $C_{21}H_{32}O_2$
100 MHz, $CDCl_3$

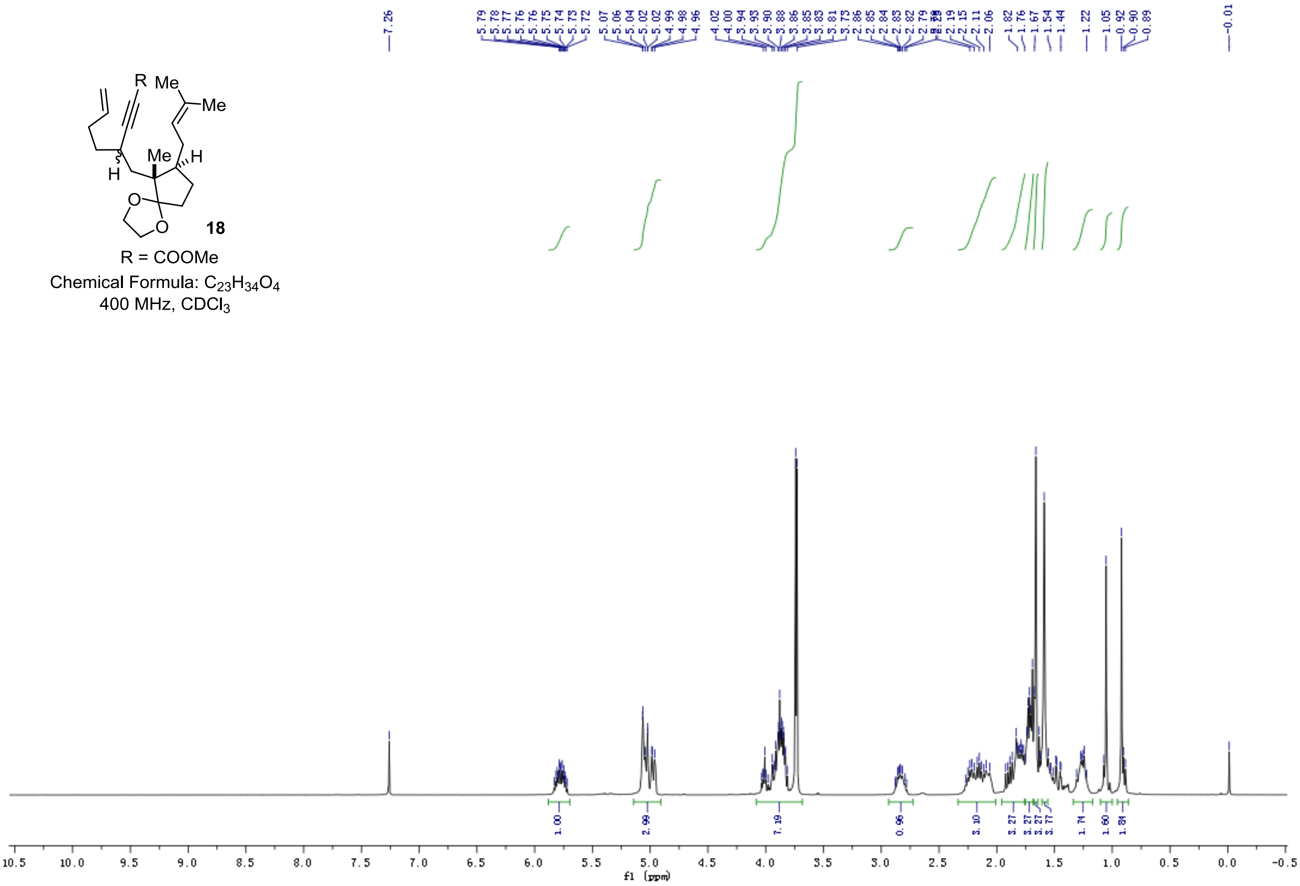


18

R = COOMe

Chemical Formula: $C_{23}H_{34}O_4$

400 MHz, $CDCl_3$

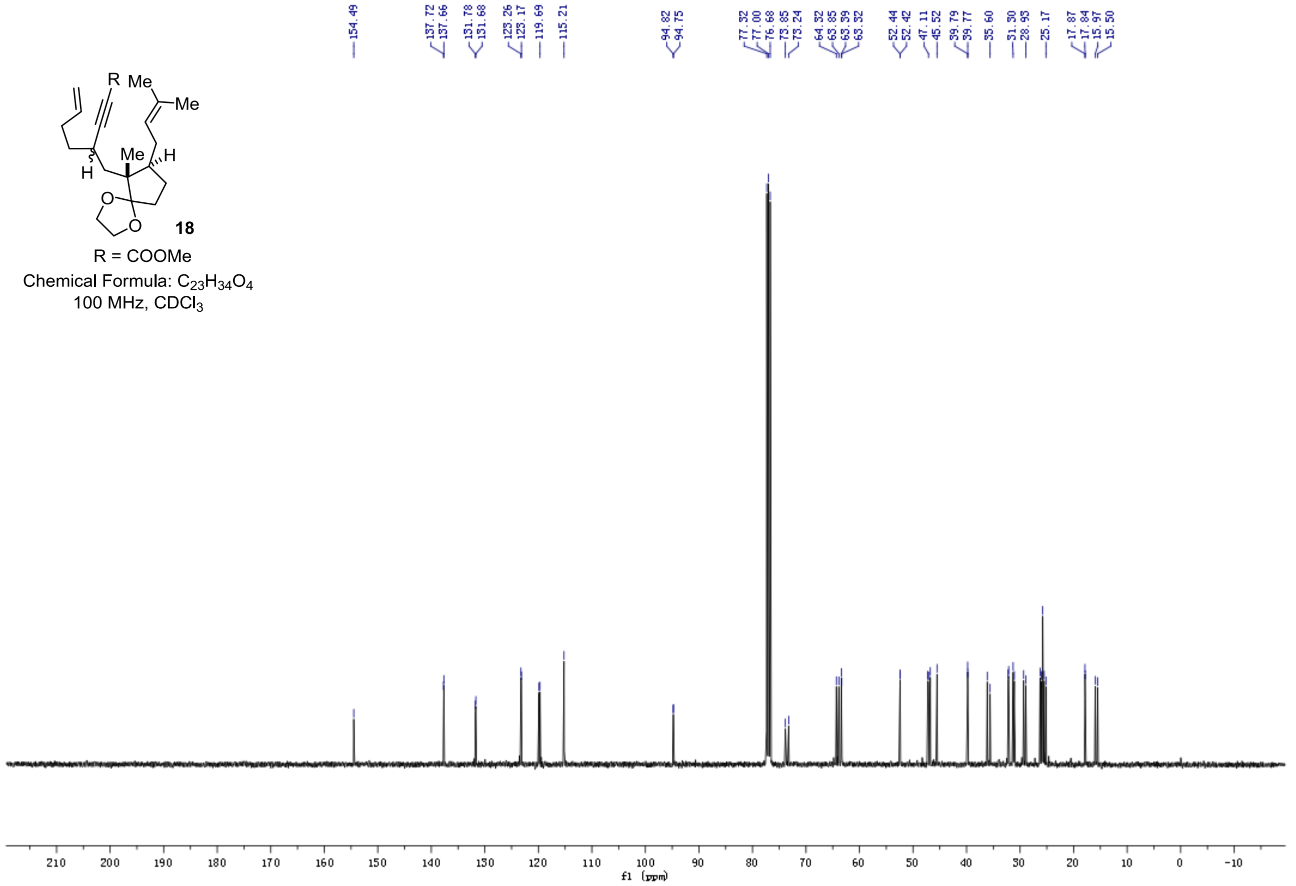


18

R = COOMe

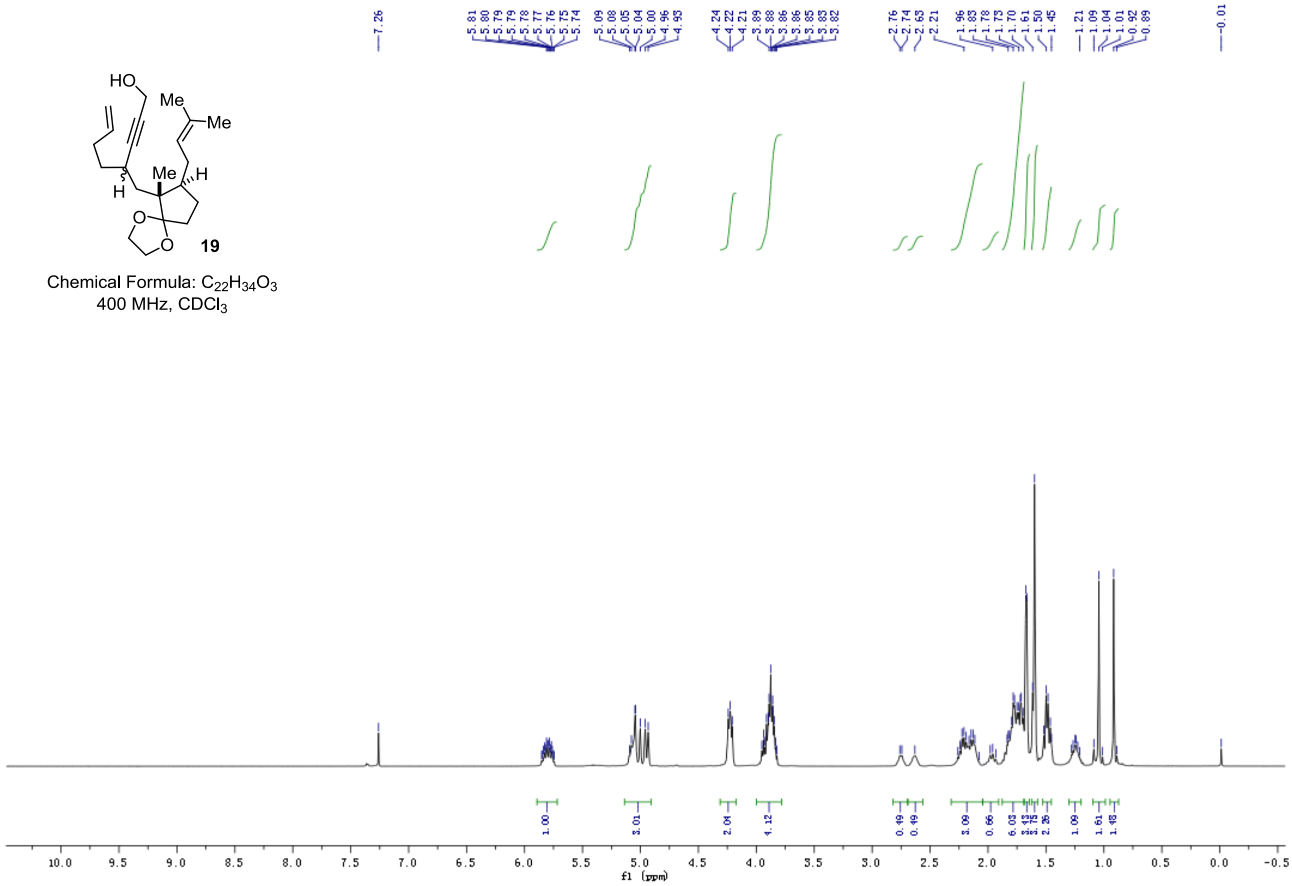
Chemical Formula: $C_{23}H_{34}O_4$

100 MHz, $CDCl_3$



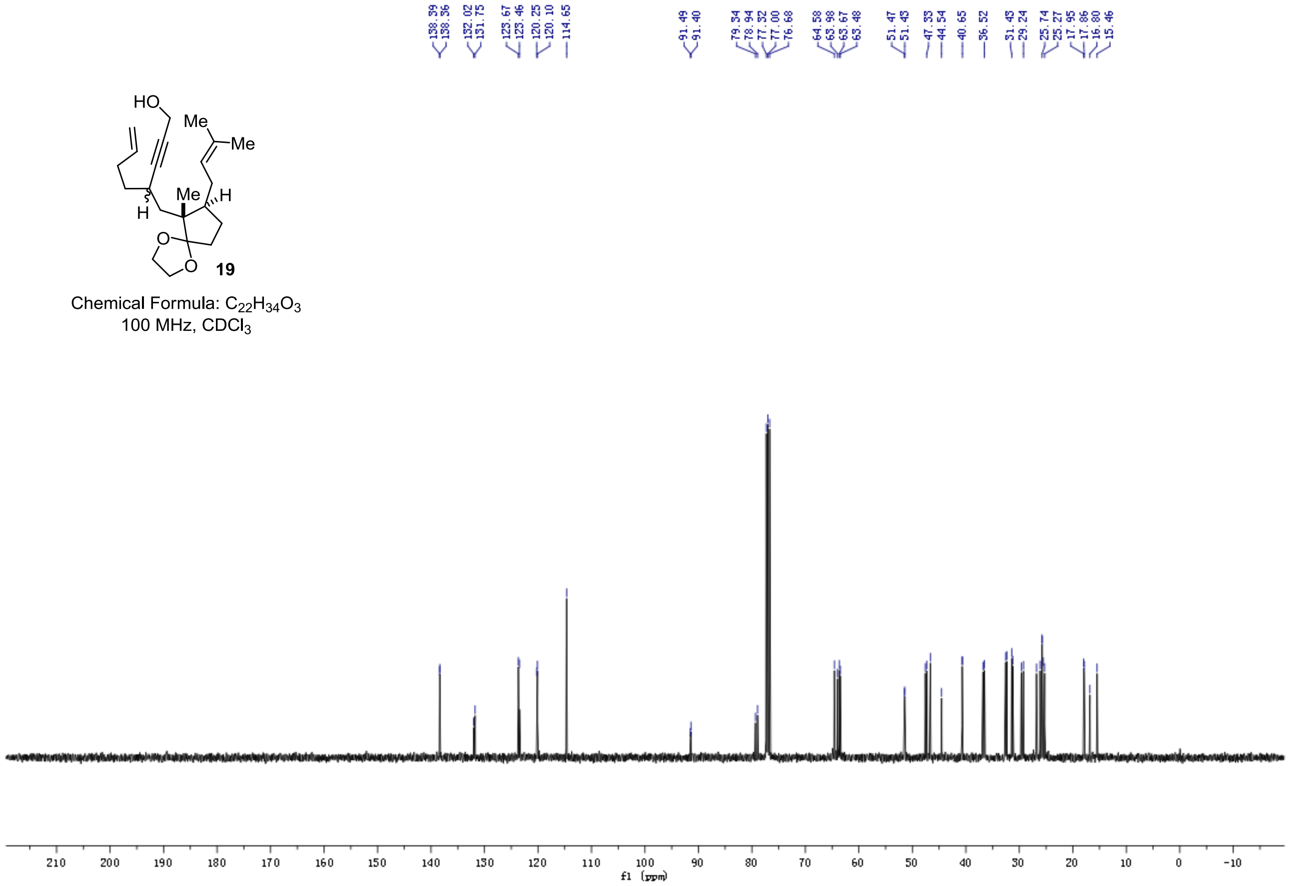
19

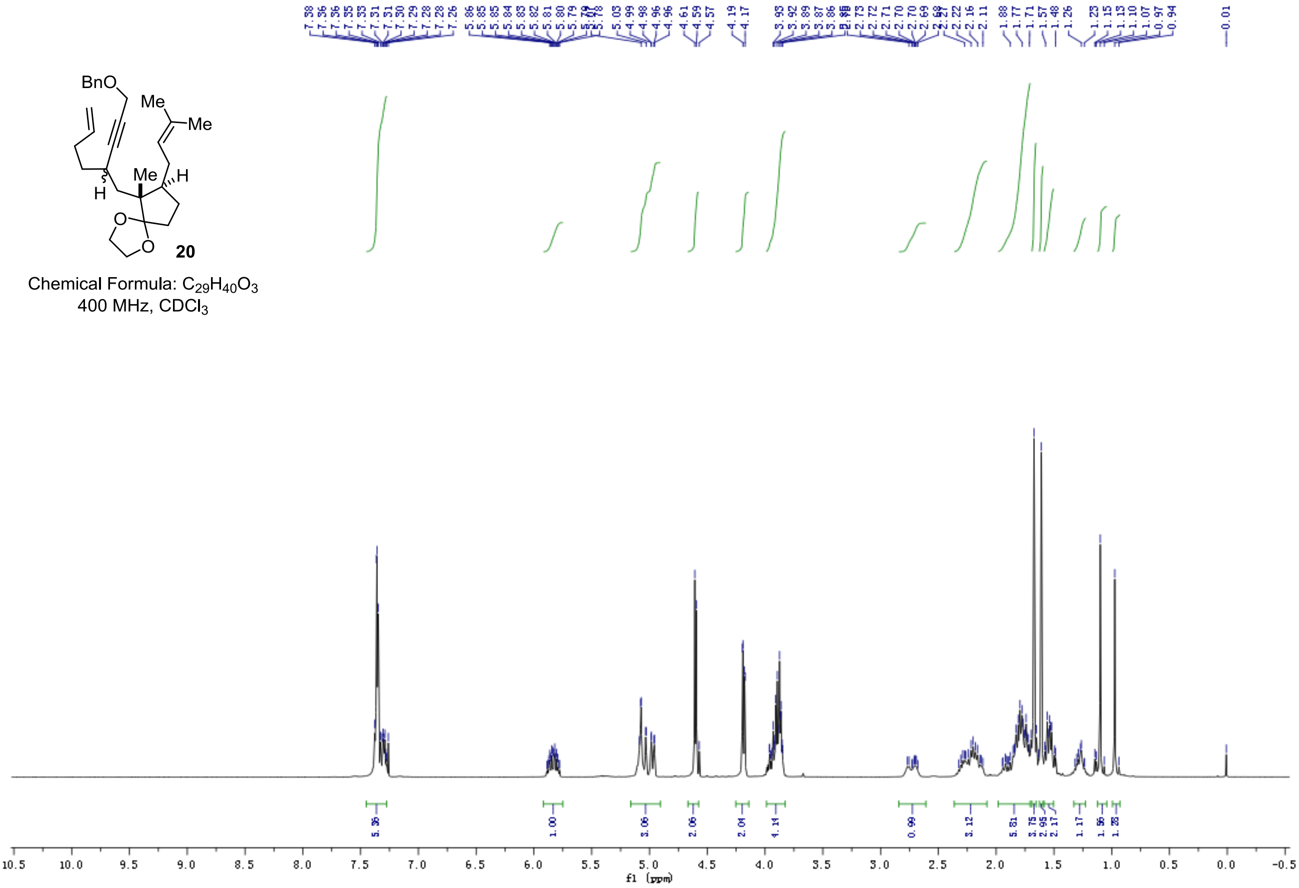
Chemical Formula: $C_{22}H_{34}O_3$
400 MHz, $CDCl_3$



19

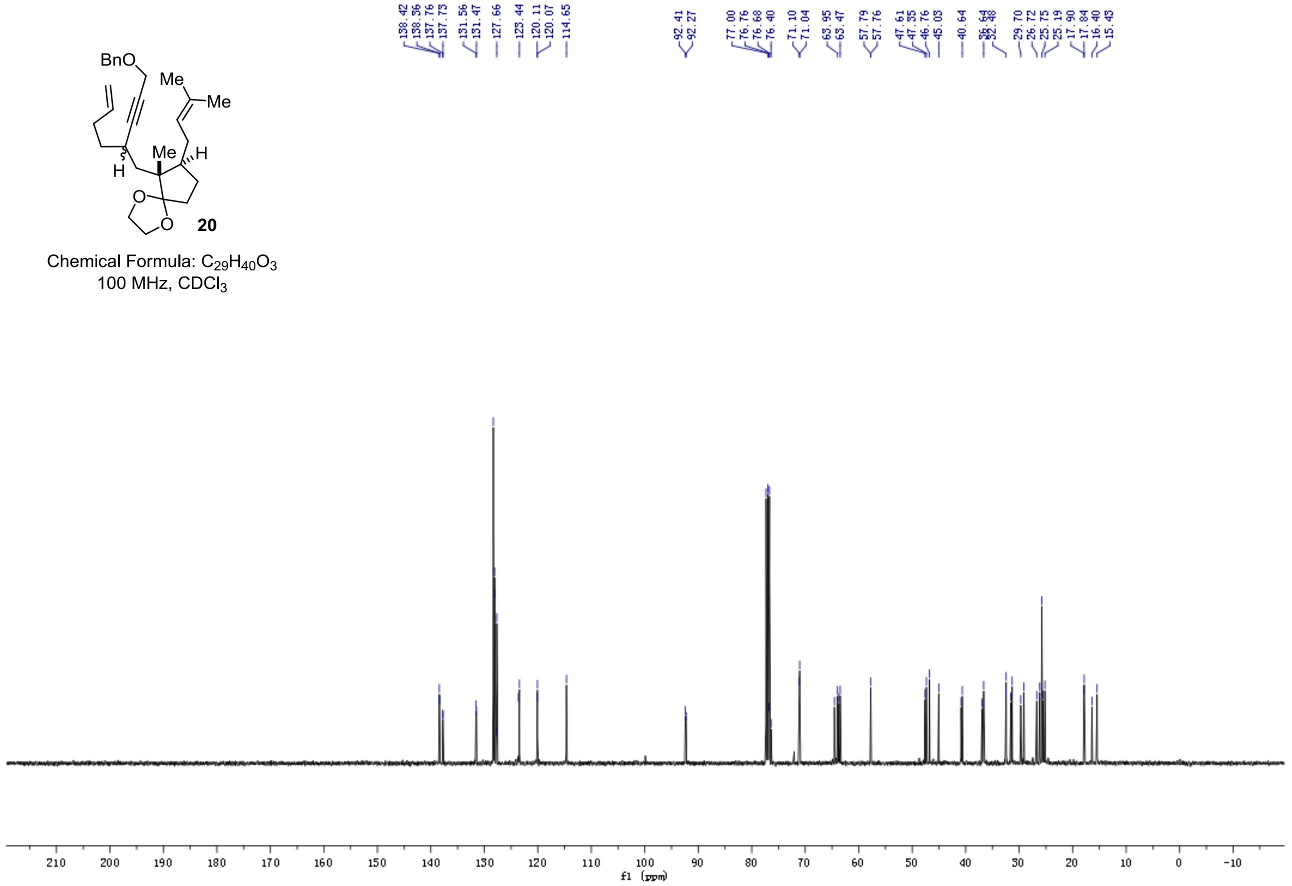
Chemical Formula: $C_{22}H_{34}O_3$
100 MHz, $CDCl_3$





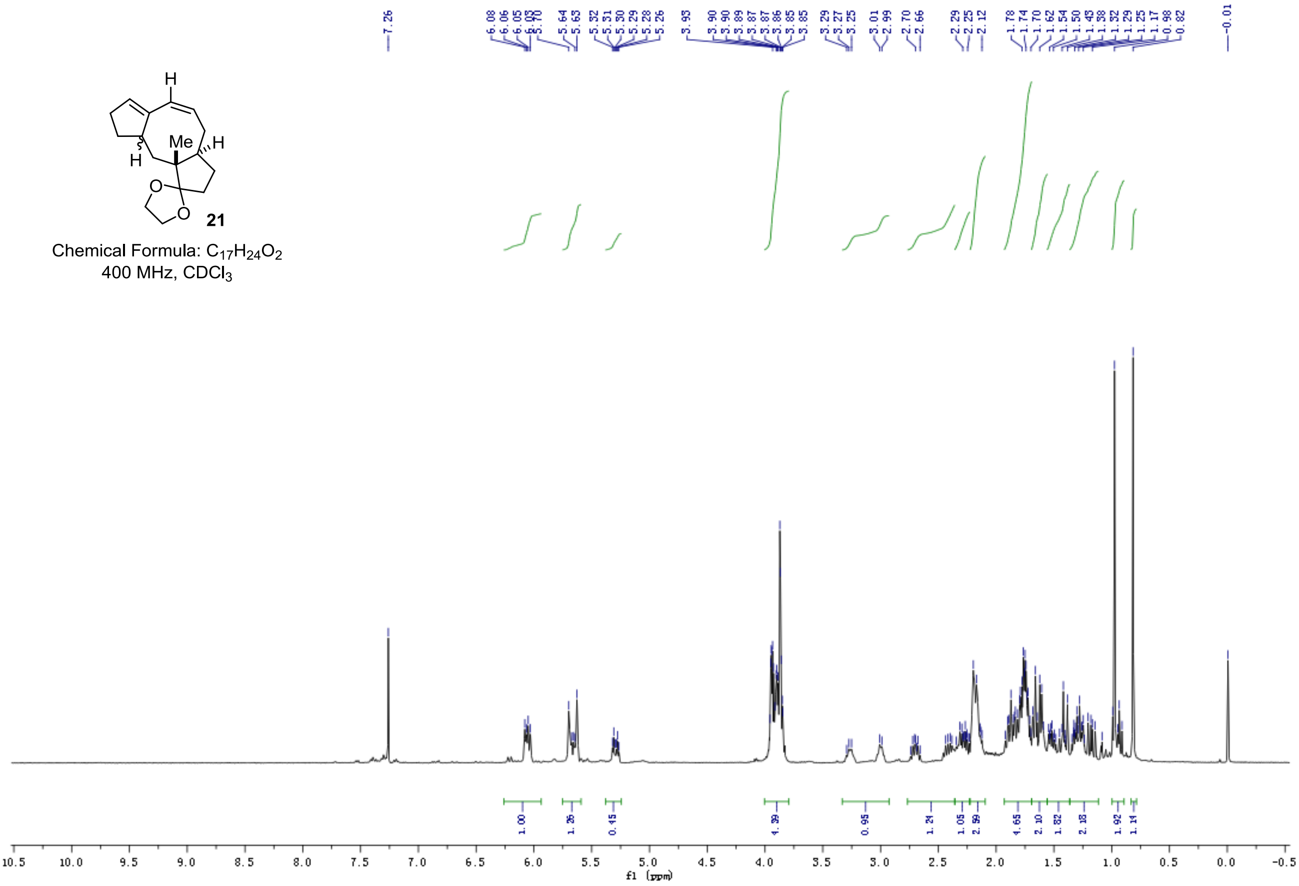
20

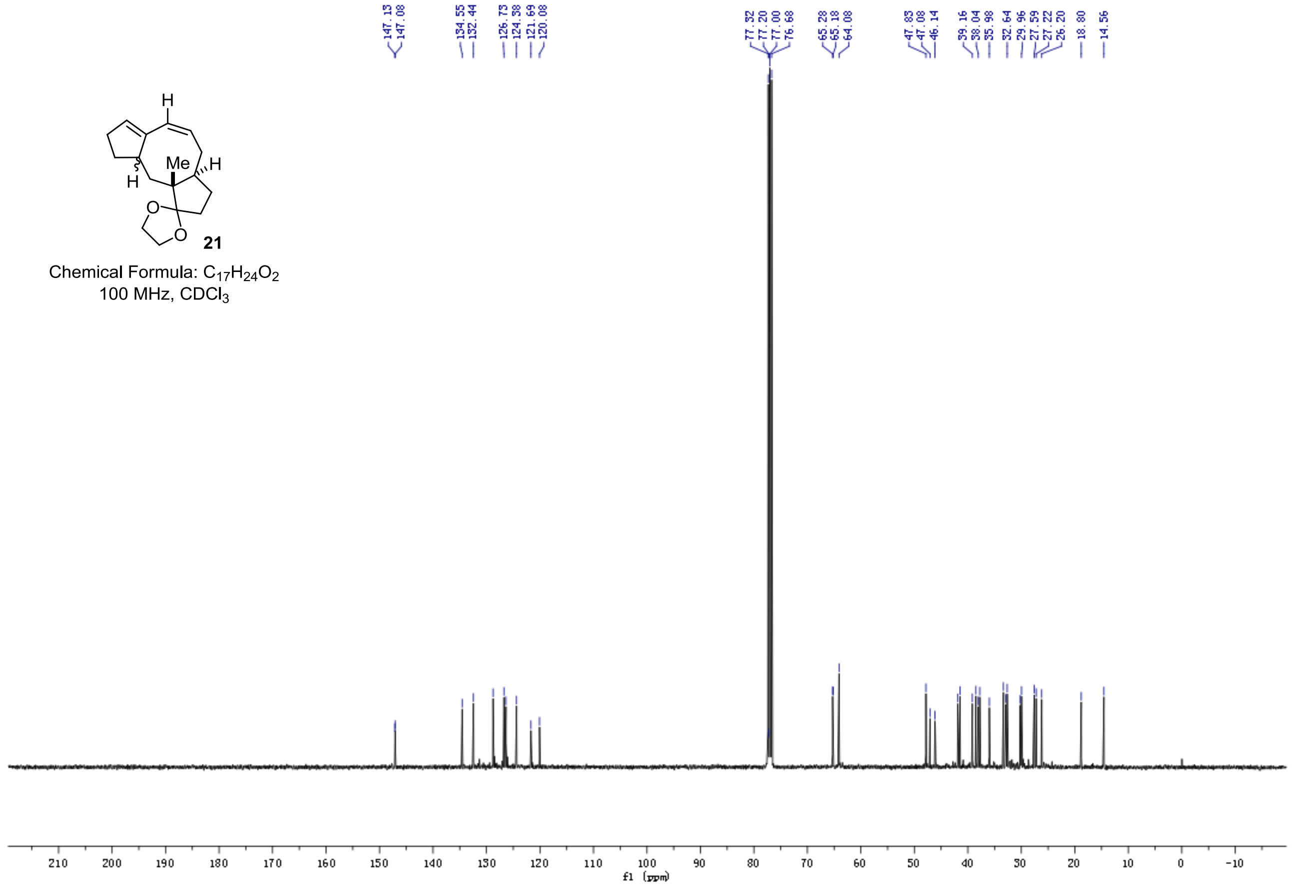
Chemical Formula: $C_{29}H_{40}O_3$
400 MHz, $CDCl_3$

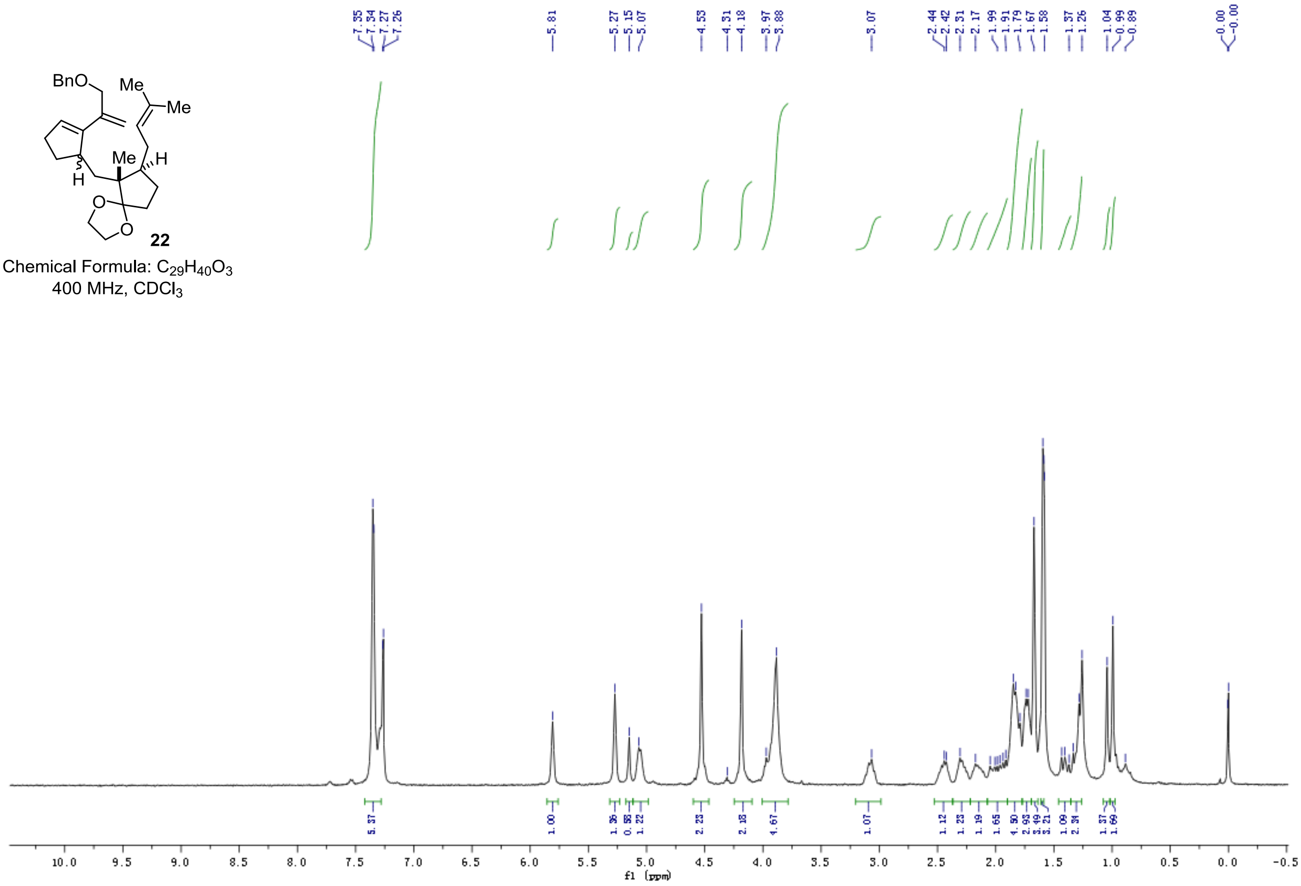


20

Chemical Formula: $C_{29}H_{40}O_3$
100 MHz, $CDCl_3$

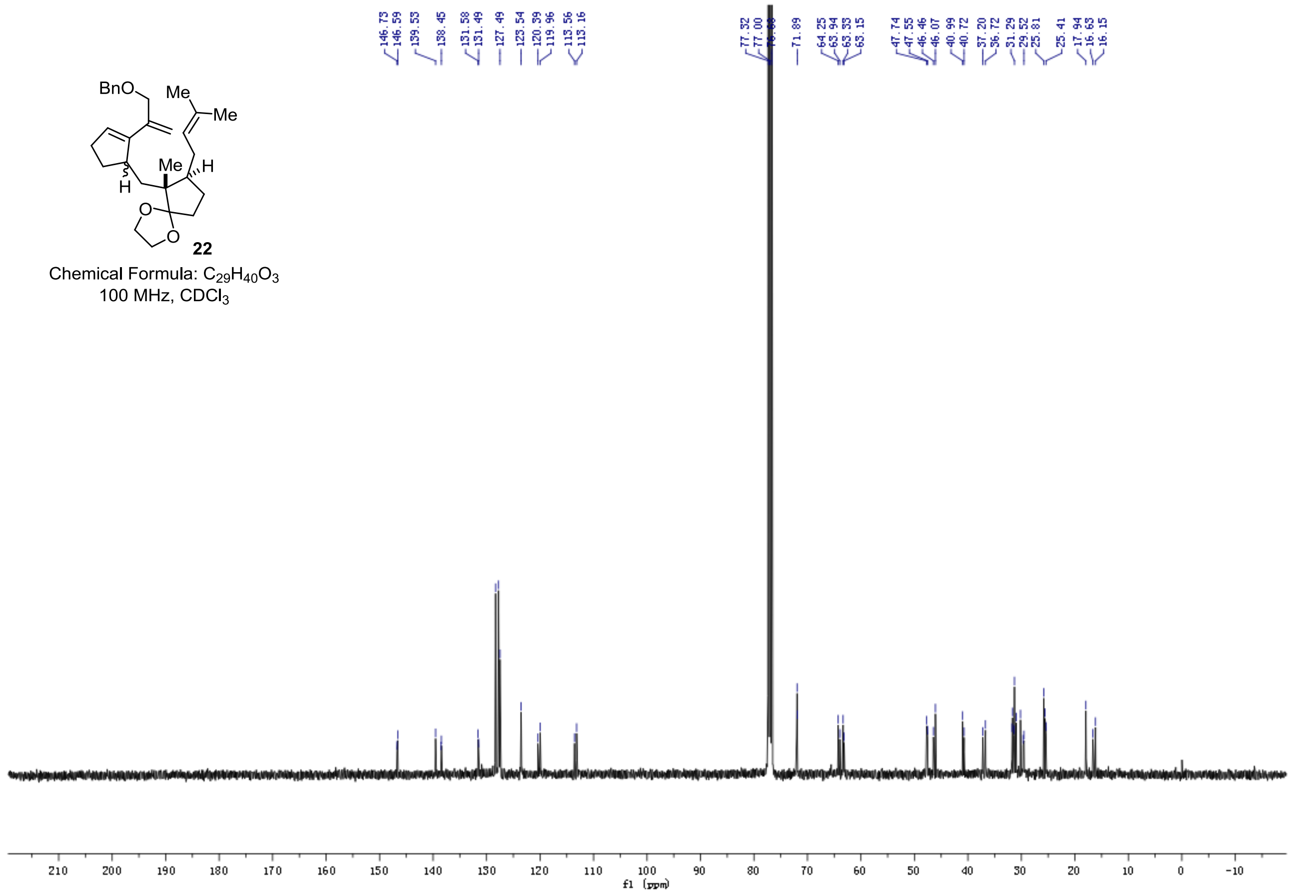

H
Me
H
H
O
O
21
Chemical Formula: C17H24O2
400 MHz, CDCl3
7.26
6.08
6.06
6.05
6.03
5.70
5.64
5.63
5.32
5.31
5.30
5.29
5.28
5.26
3.93
3.90
3.90
3.89
3.87
3.87
3.86
3.85
3.85
3.29
3.27
3.25
3.01
2.99
2.70
2.66
2.29
2.25
2.12
1.78
1.74
1.70
1.62
1.54
1.50
1.43
1.38
1.32
1.29
1.25
1.17
0.98
0.82
-0.01
1.00
1.26
0.45
4.39
0.95
1.21
1.05
2.59
4.65
2.10
1.82
2.18
1.92
1.14
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)


H
Me
H
H
O
O
21
Chemical Formula: C17H24O2
100 MHz, CDCl3
147.13
147.08
134.55
132.44
126.73
124.38
121.69
120.08
77.32
77.20
77.00
76.68
65.28
65.18
64.08
47.83
47.08
46.14
39.16
38.04
35.98
32.64
29.96
27.59
27.22
26.20
18.80
14.56
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)



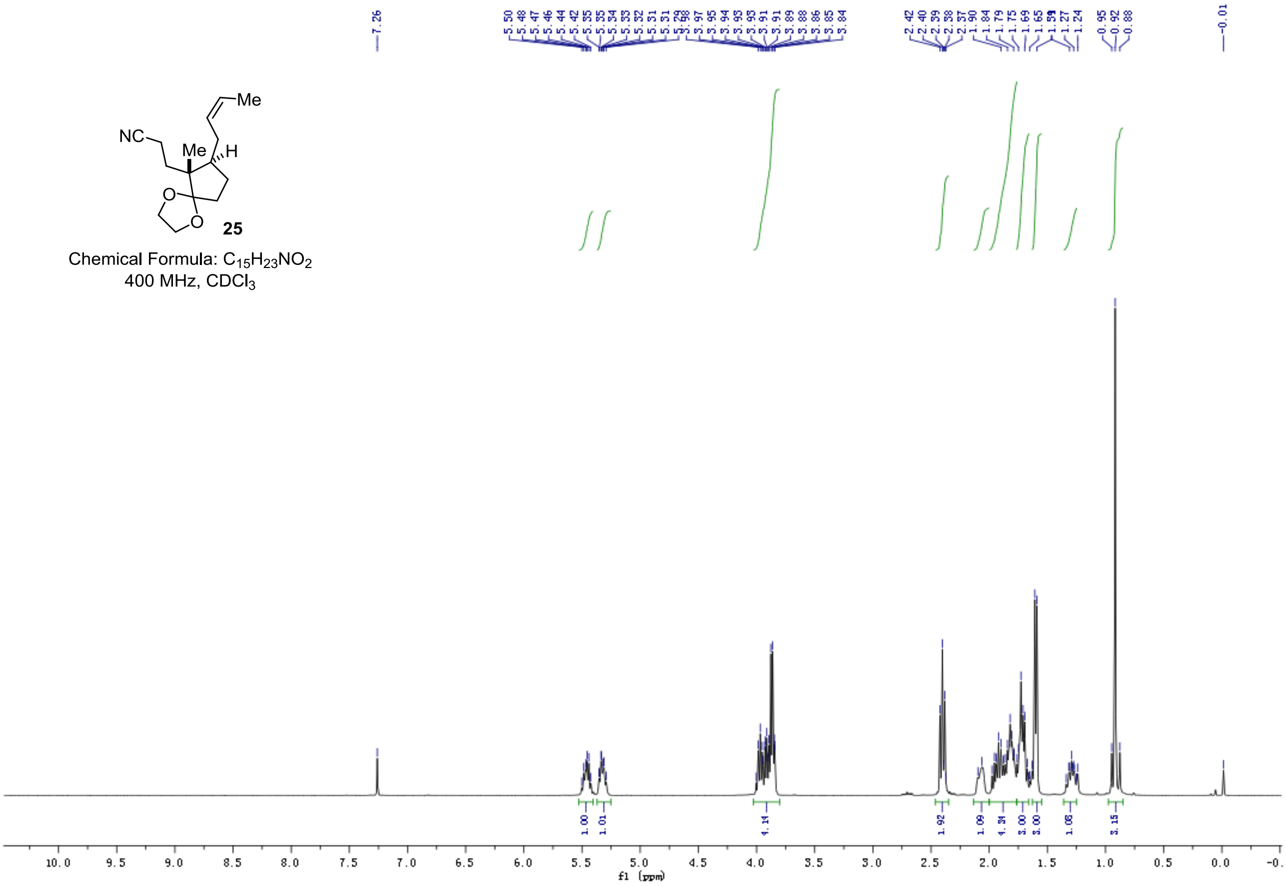
22

Chemical Formula: $C_{29}H_{40}O_3$
400 MHz, $CDCl_3$



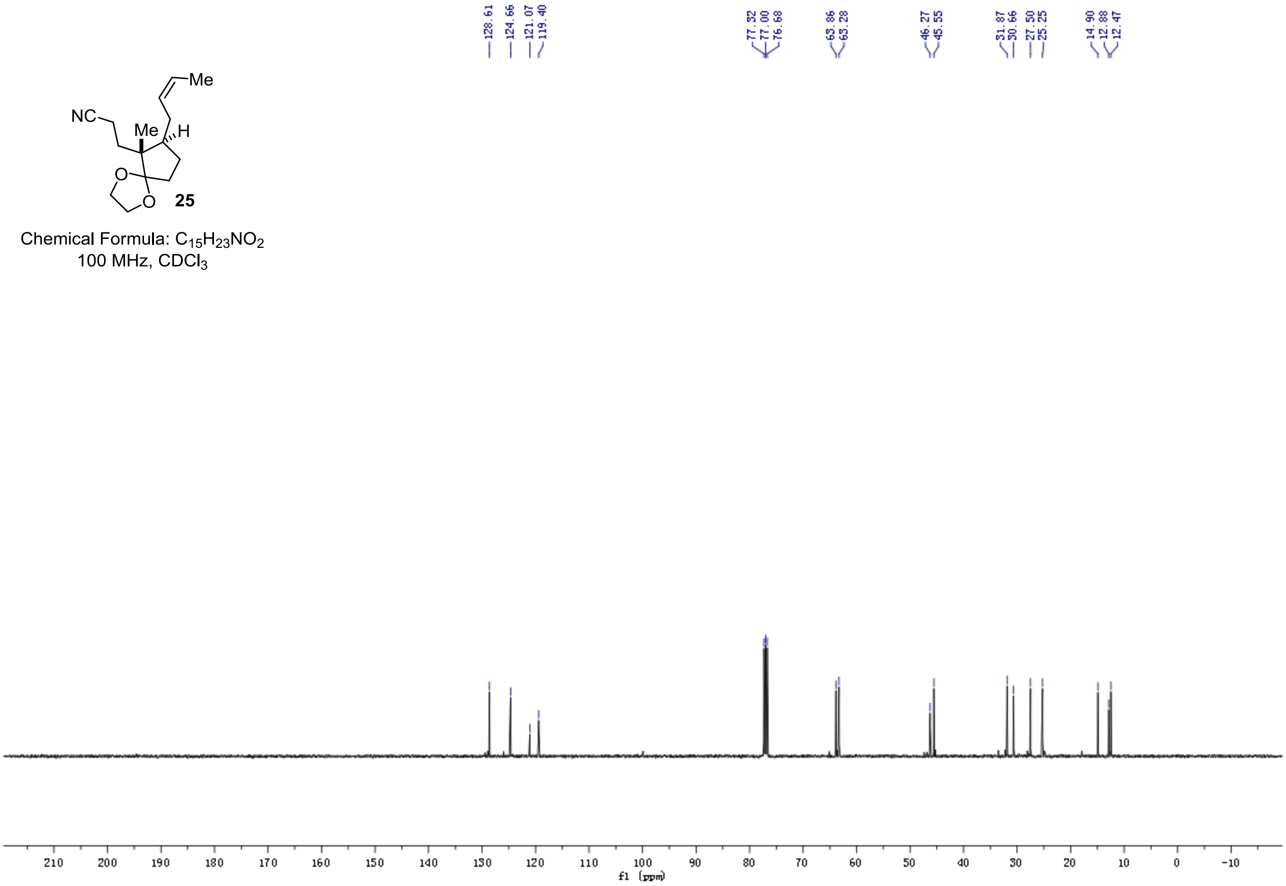
22

Chemical Formula: $C_{29}H_{40}O_3$
100 MHz, $CDCl_3$



25

Chemical Formula: $C_{15}H_{23}NO_2$
400 MHz, $CDCl_3$

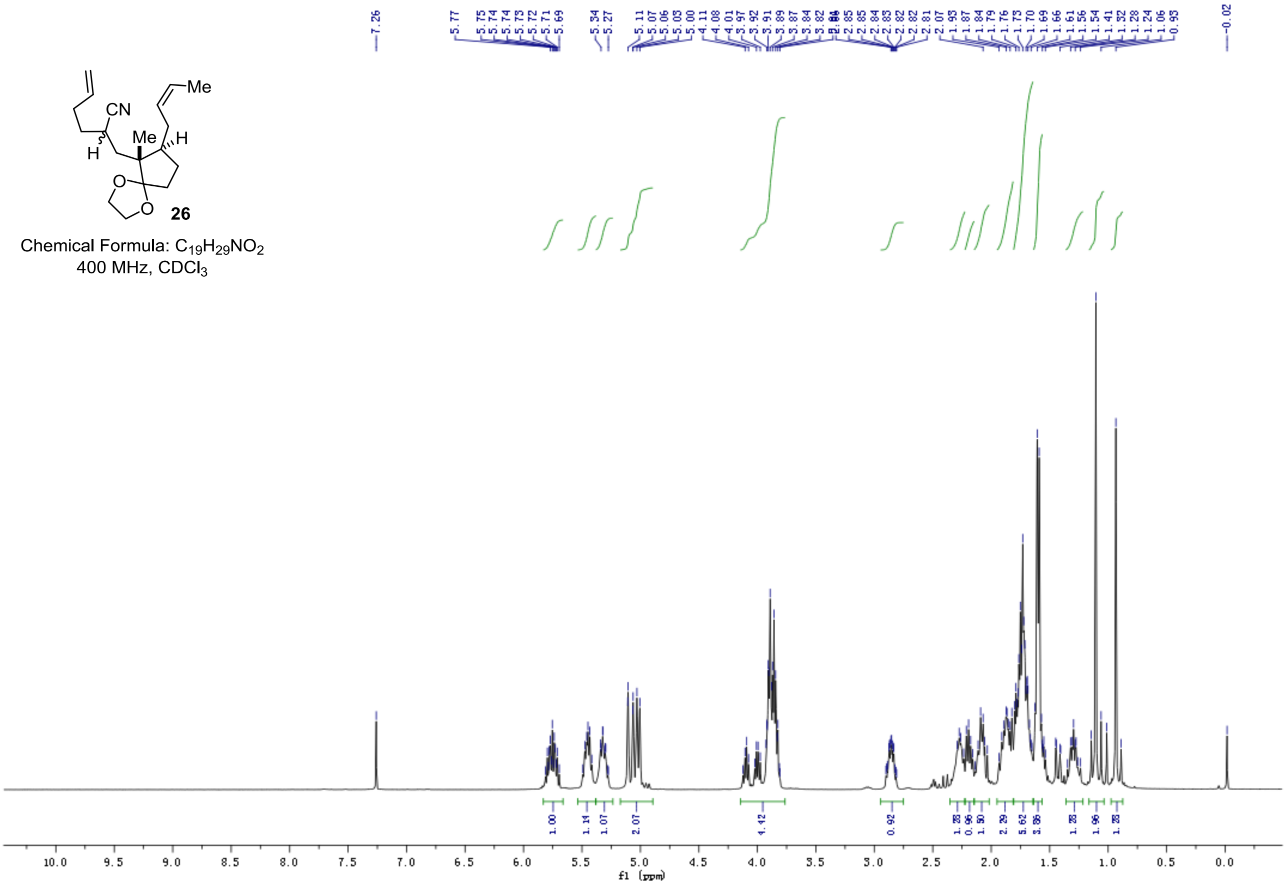


25

Chemical Formula: $C_{15}H_{23}NO_2$
100 MHz, $CDCl_3$

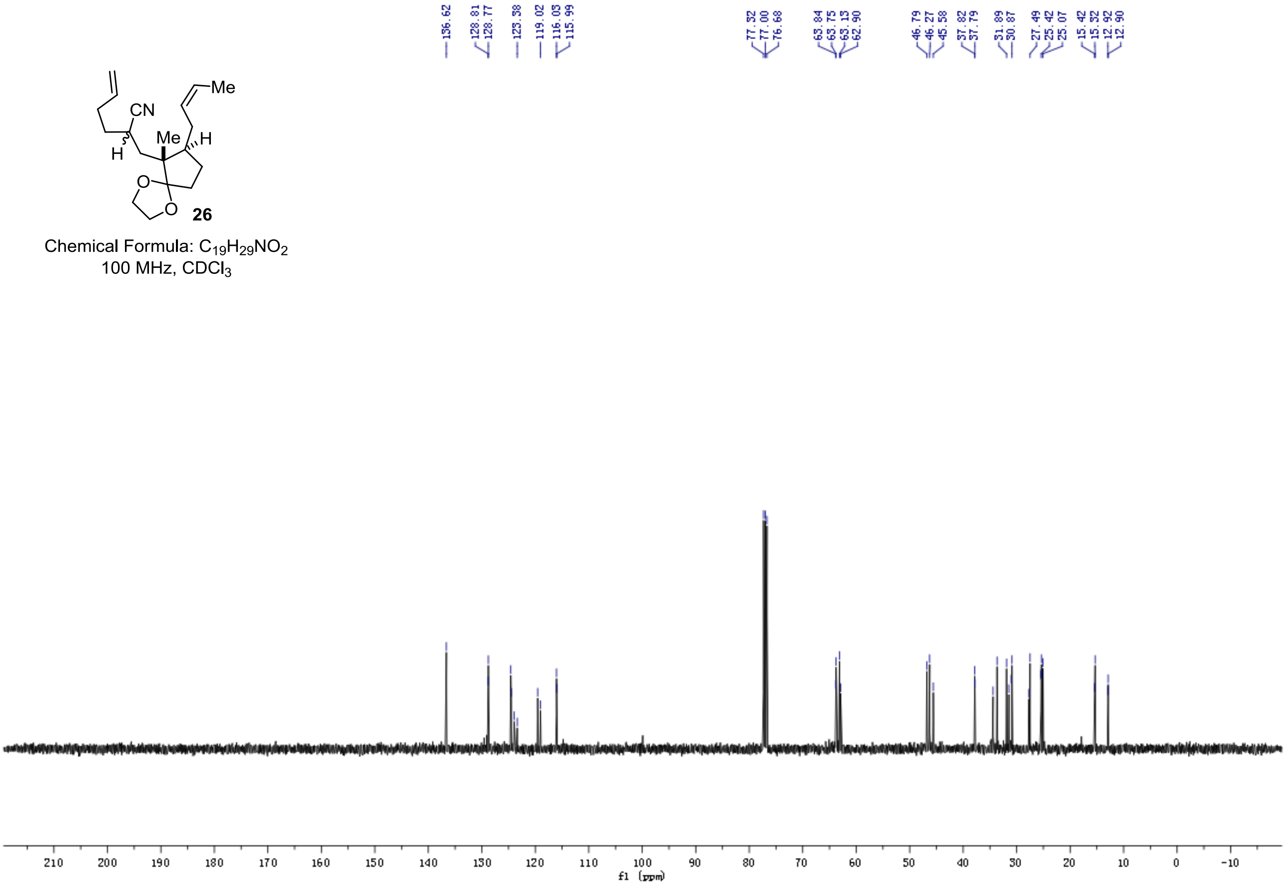
26

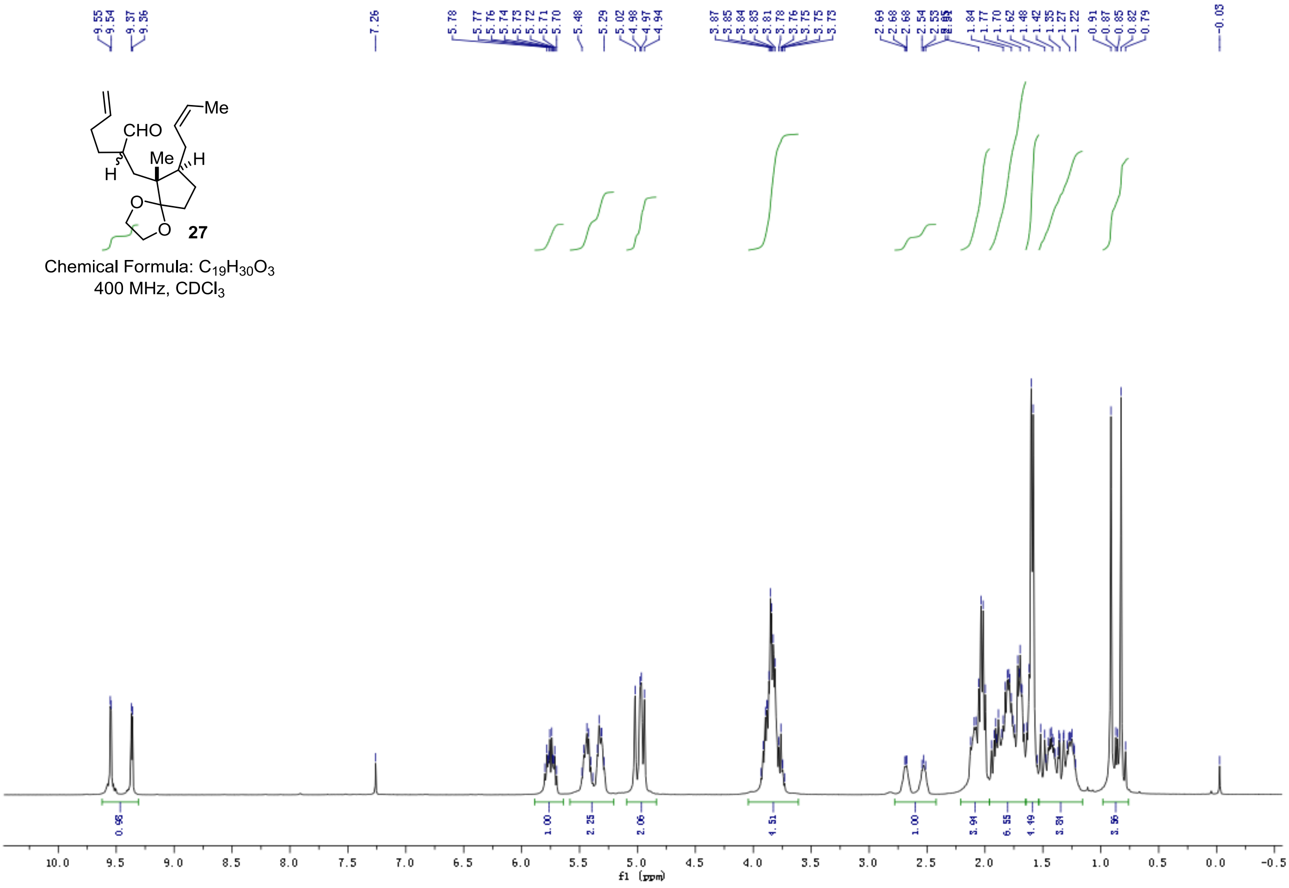
Chemical Formula: $C_{19}H_{29}NO_2$
400 MHz, $CDCl_3$



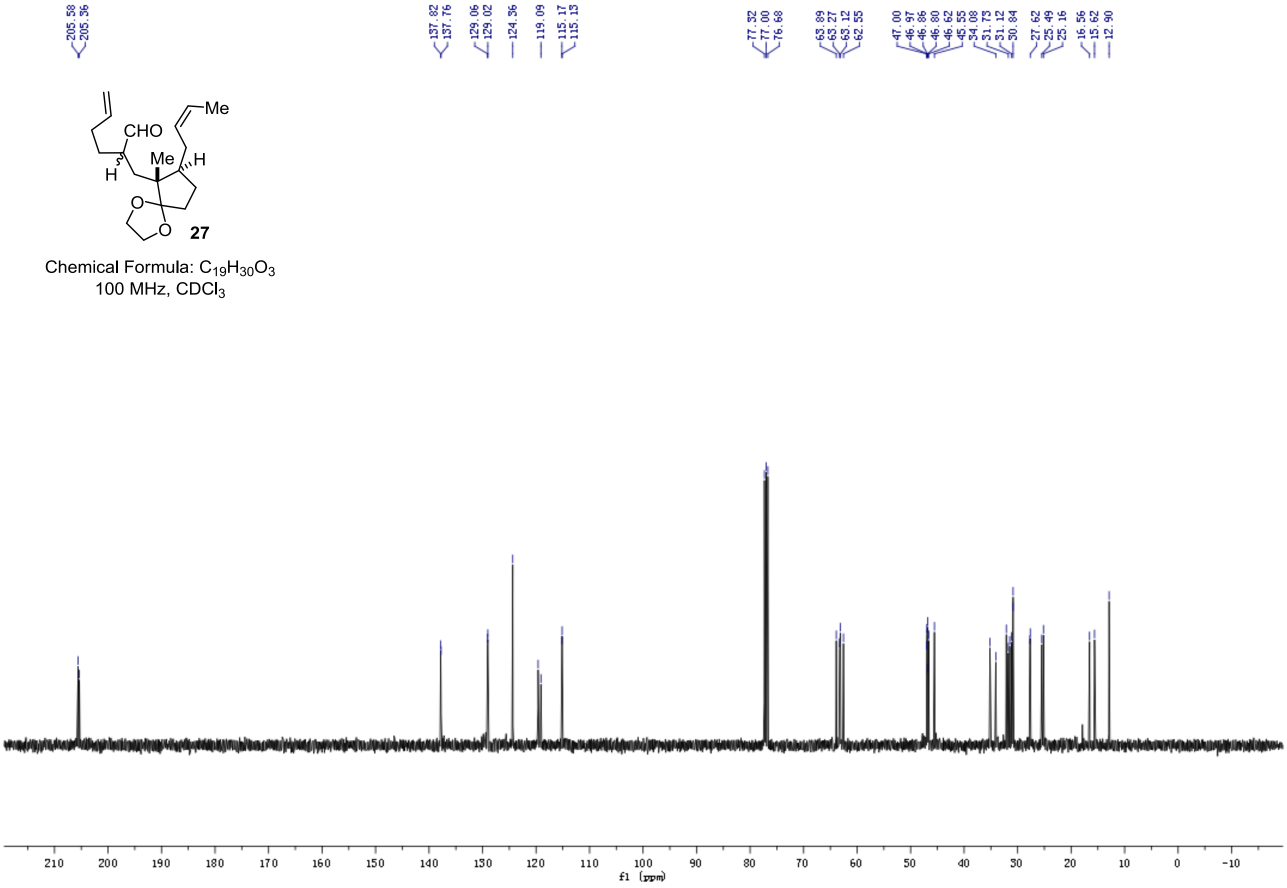
26

Chemical Formula: $C_{19}H_{29}NO_2$
100 MHz, $CDCl_3$





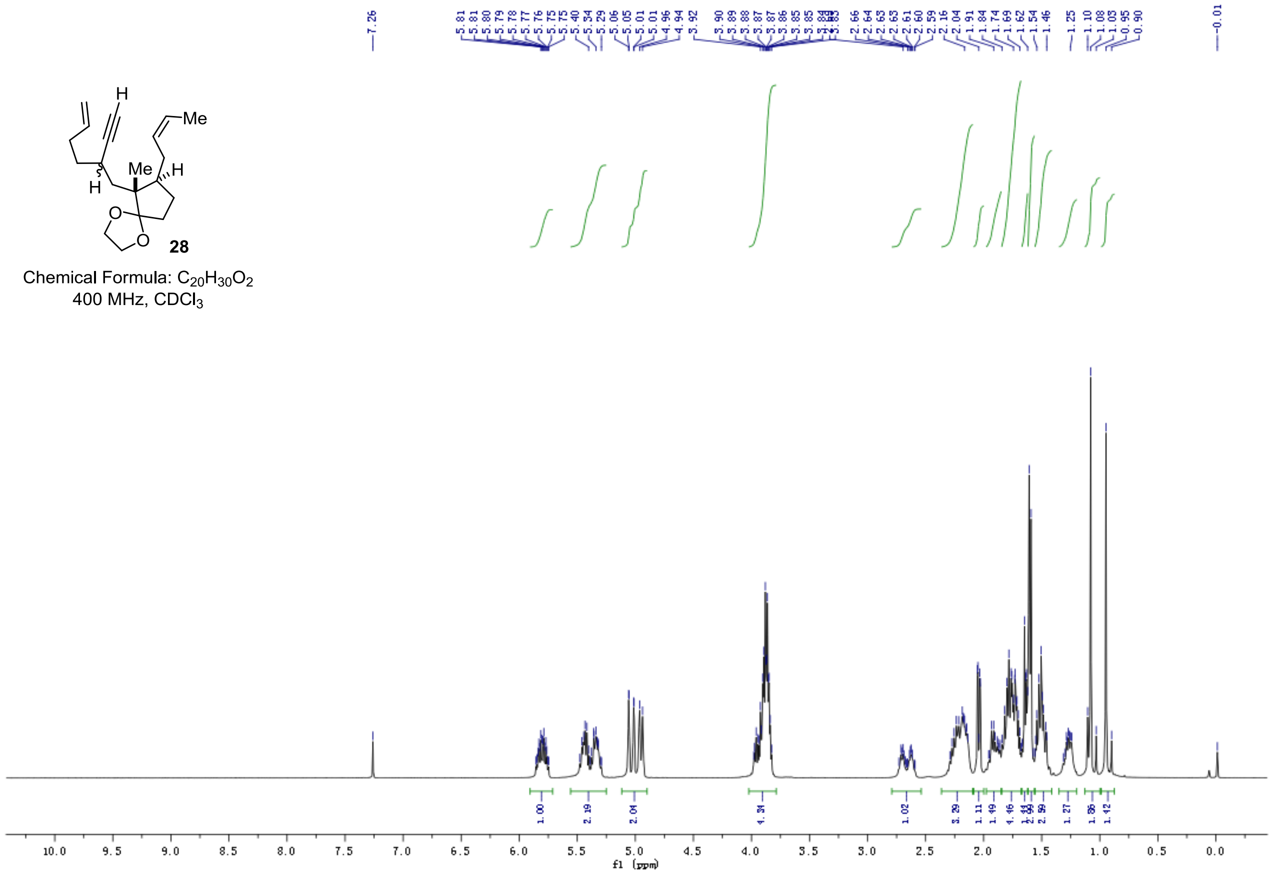
Chemical Formula: $C_{19}H_{30}O_3$
400 MHz, $CDCl_3$



Chemical Formula: $C_{19}H_{30}O_3$
100 MHz, $CDCl_3$

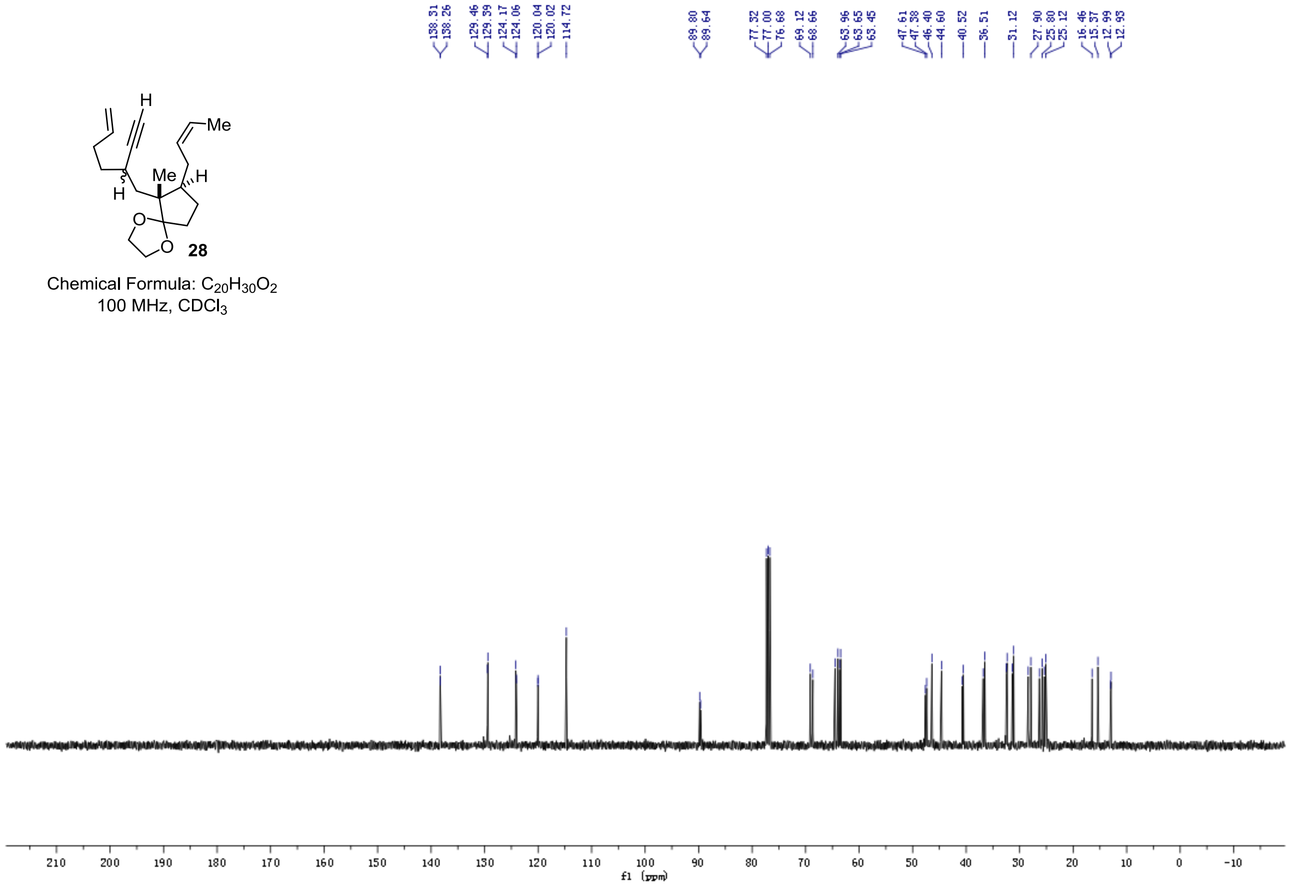
28

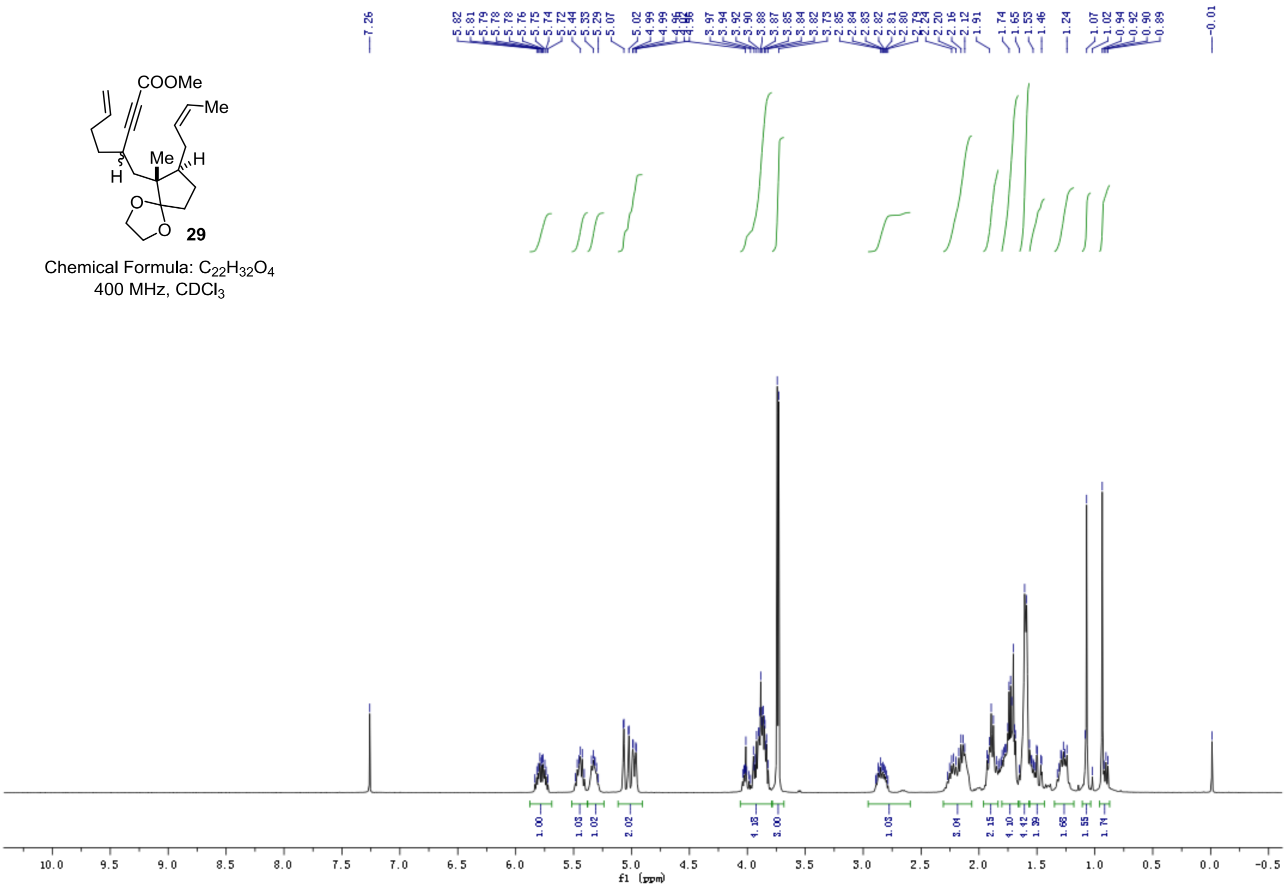
Chemical Formula: $C_{20}H_{30}O_2$
400 MHz, $CDCl_3$



28

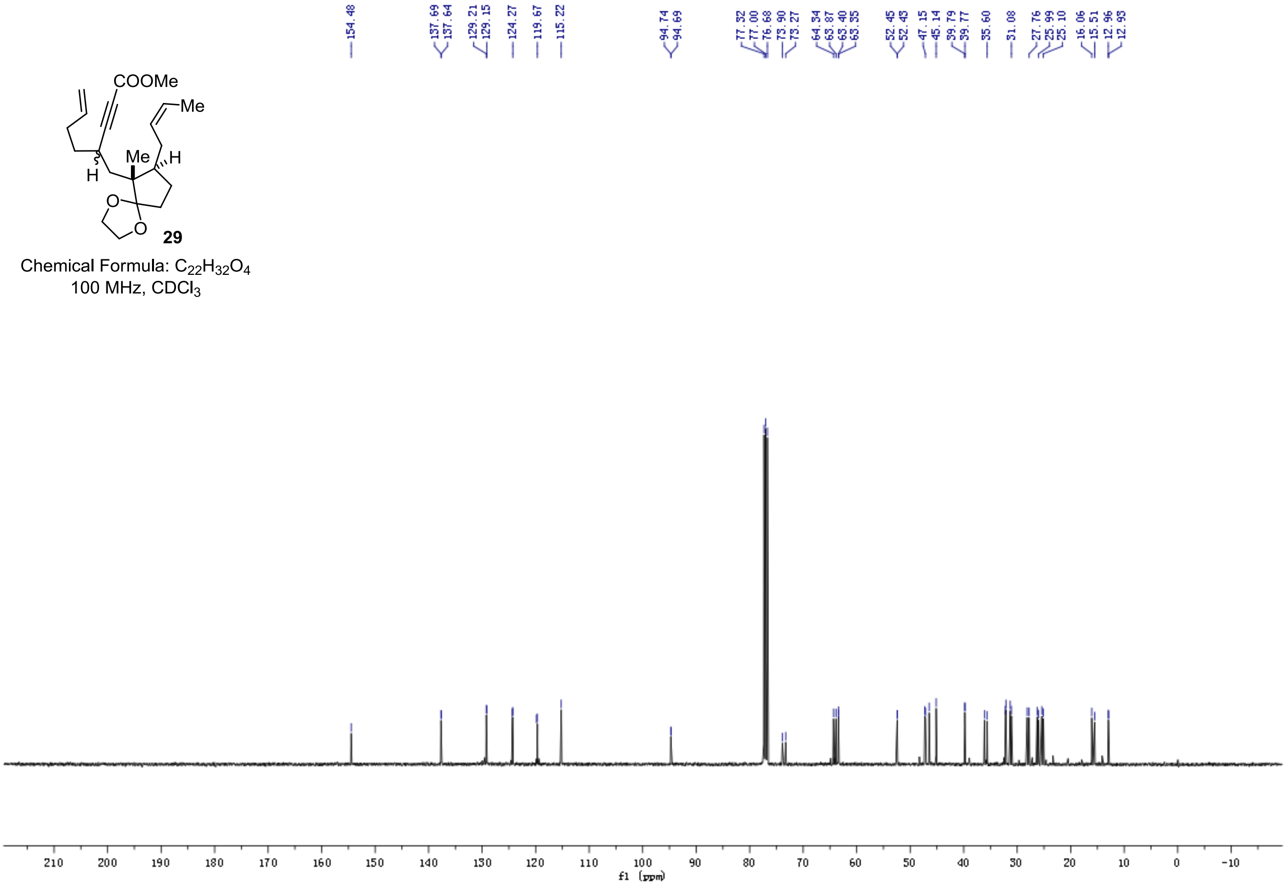
Chemical Formula: $C_{20}H_{30}O_2$
100 MHz, $CDCl_3$





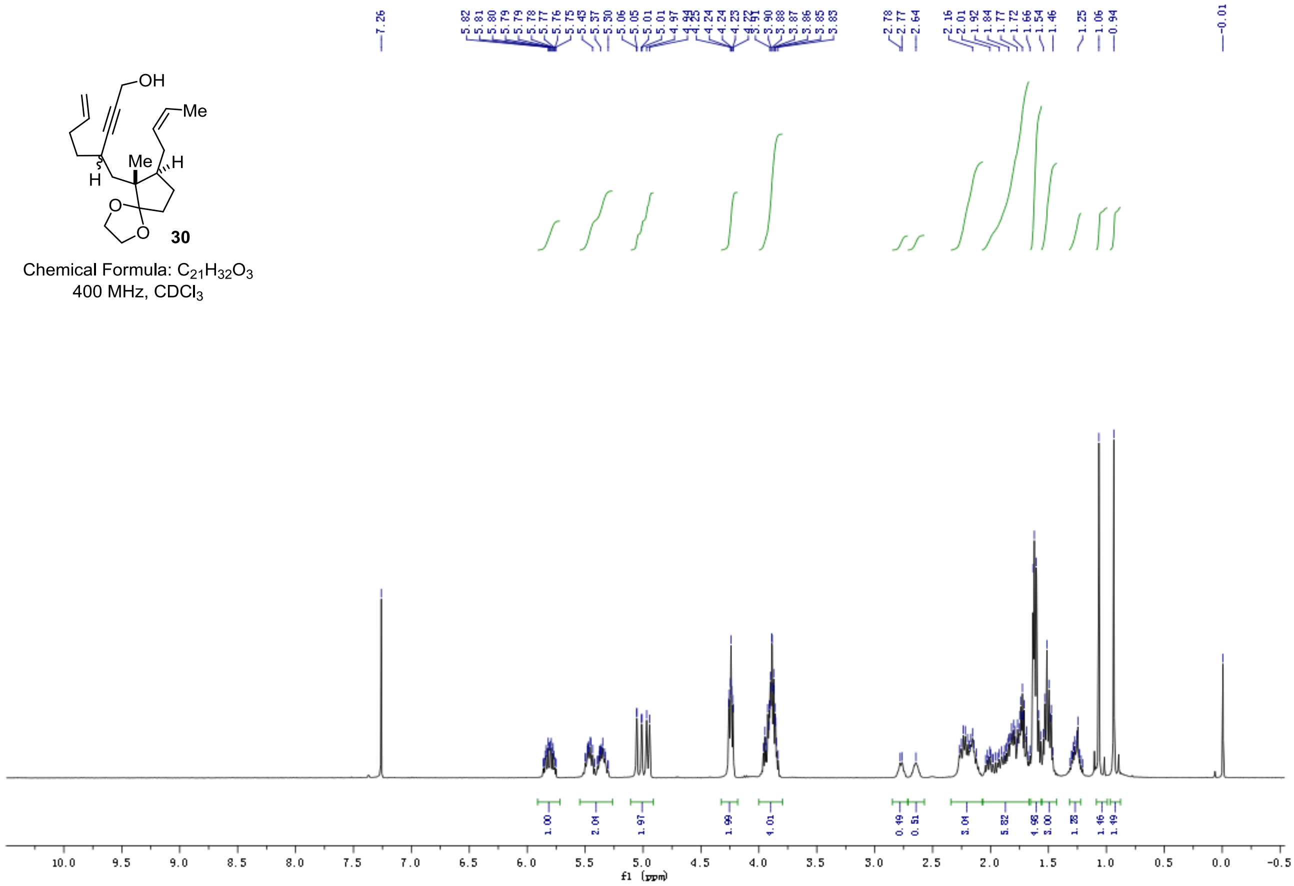
29

Chemical Formula: $C_{22}H_{32}O_4$
400 MHz, $CDCl_3$



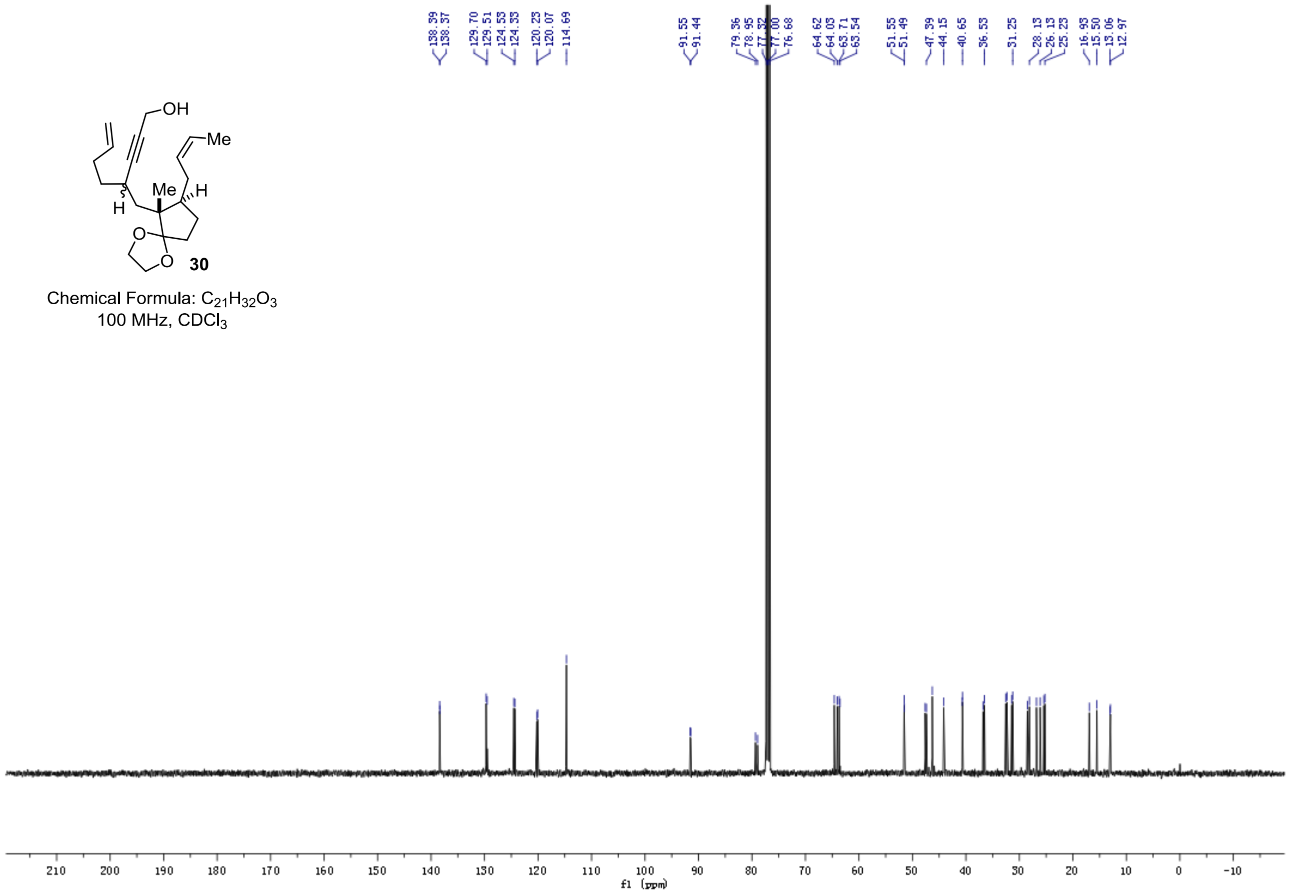
29

Chemical Formula: $C_{22}H_{32}O_4$
100 MHz, $CDCl_3$



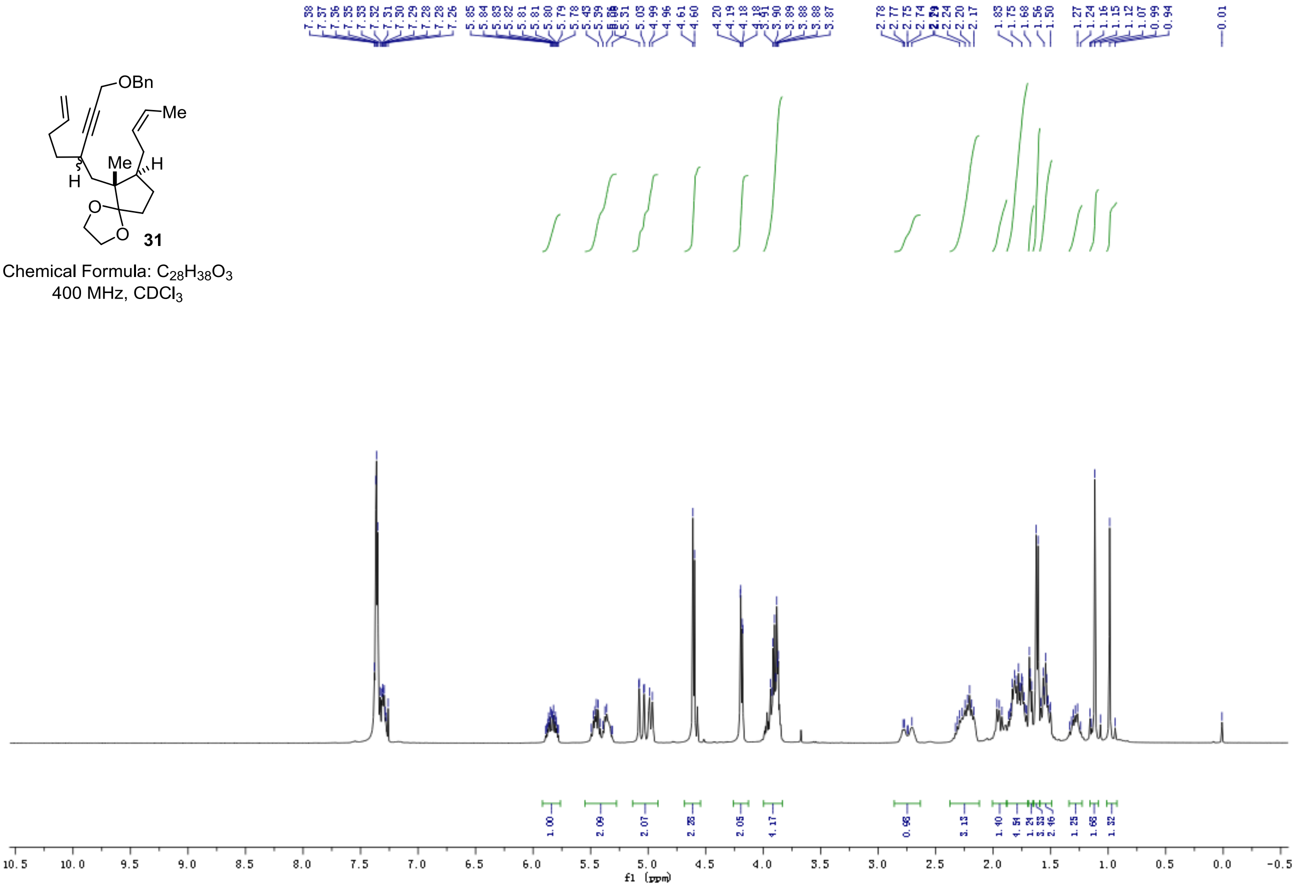
30

Chemical Formula: $C_{21}H_{32}O_3$
400 MHz, $CDCl_3$



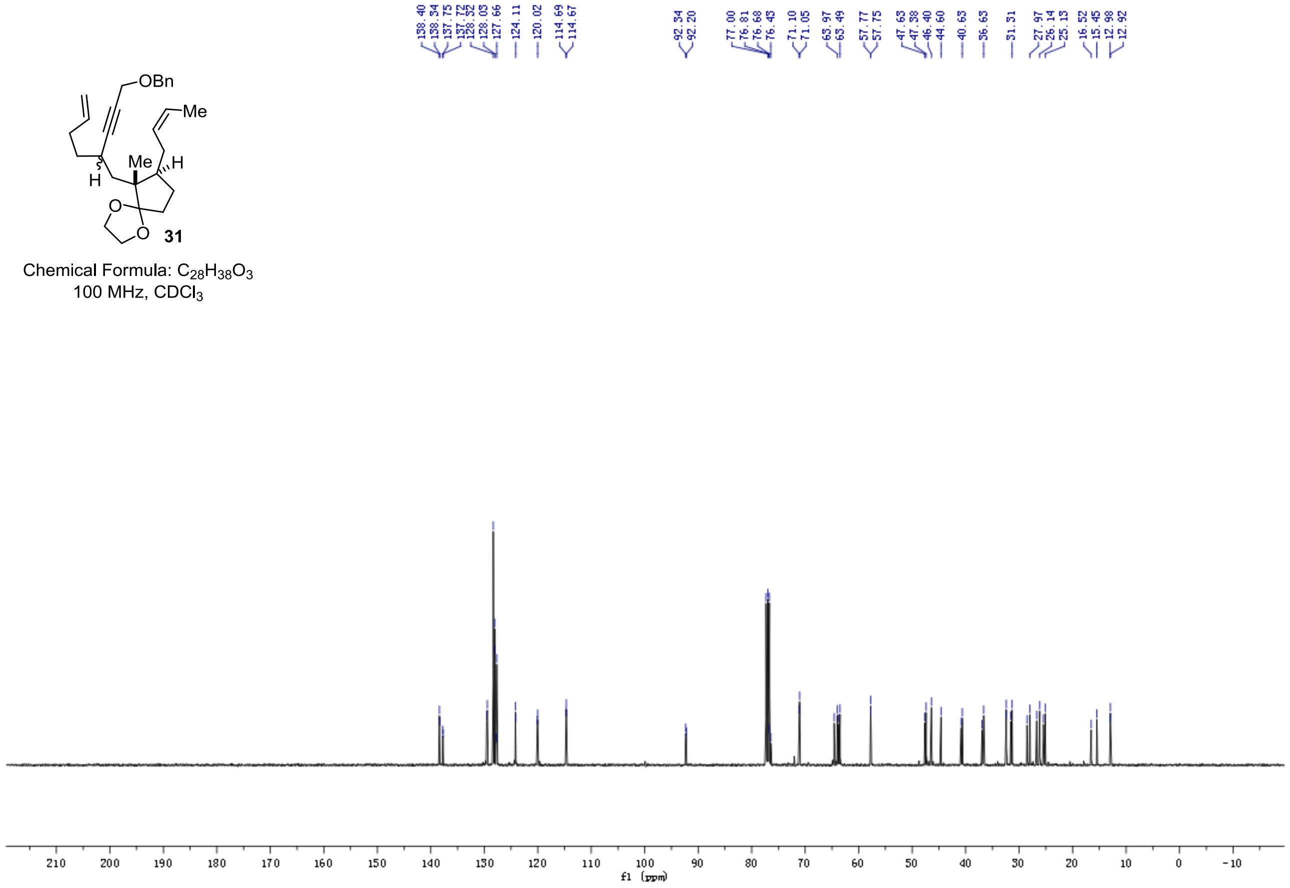
30

Chemical Formula: $C_{21}H_{32}O_3$
100 MHz, $CDCl_3$



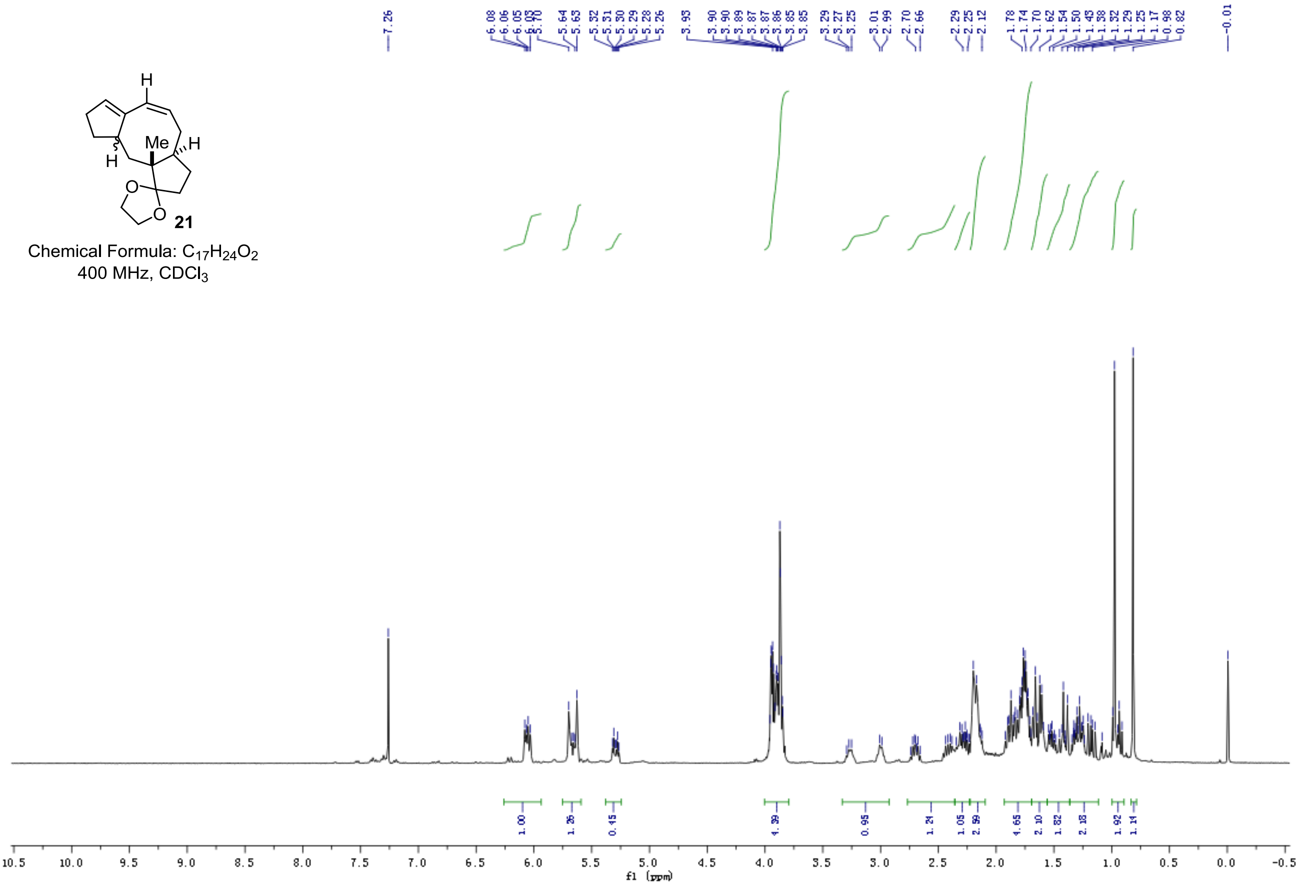
31

Chemical Formula: $C_{28}H_{38}O_3$
400 MHz, $CDCl_3$



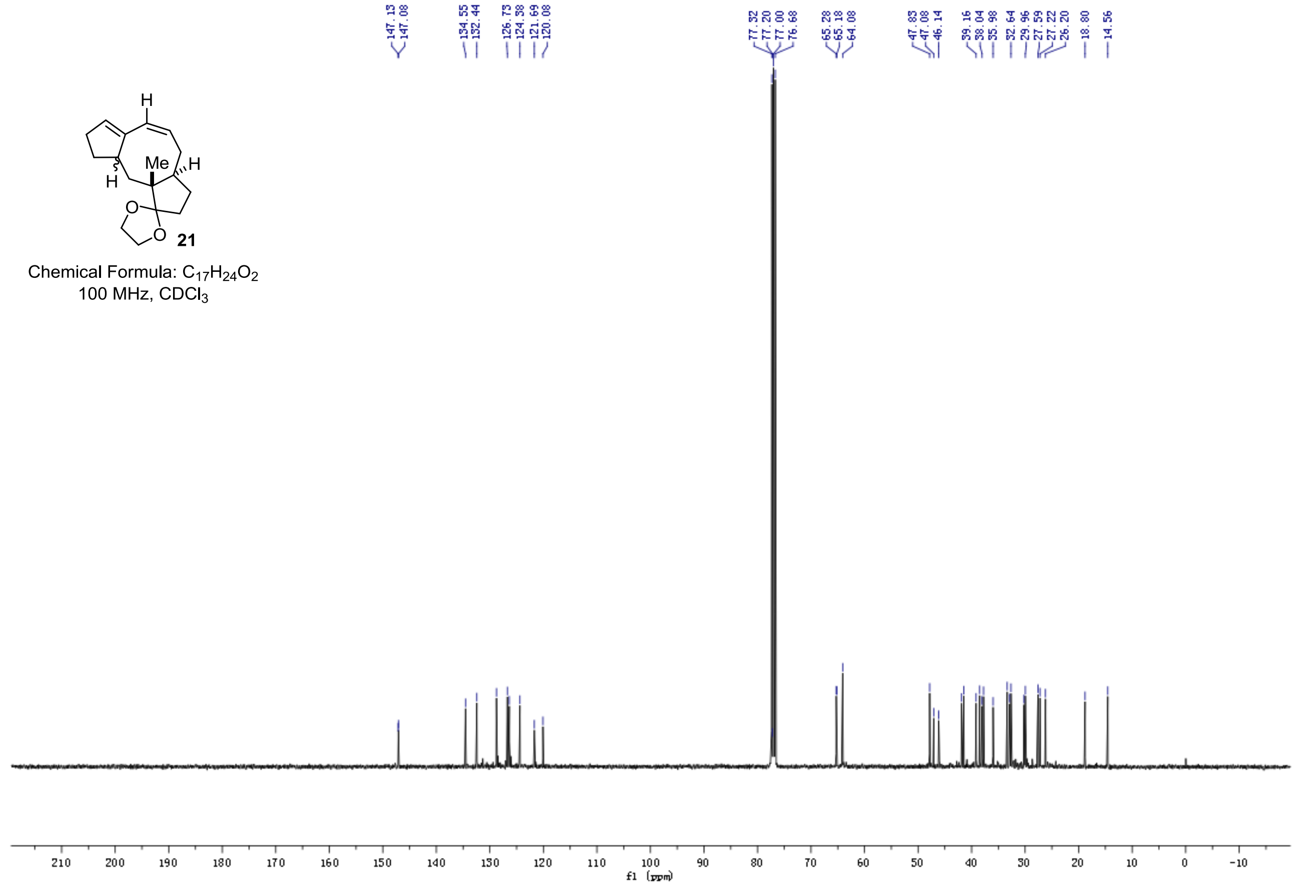
31

Chemical Formula: $C_{28}H_{38}O_3$
100 MHz, $CDCl_3$



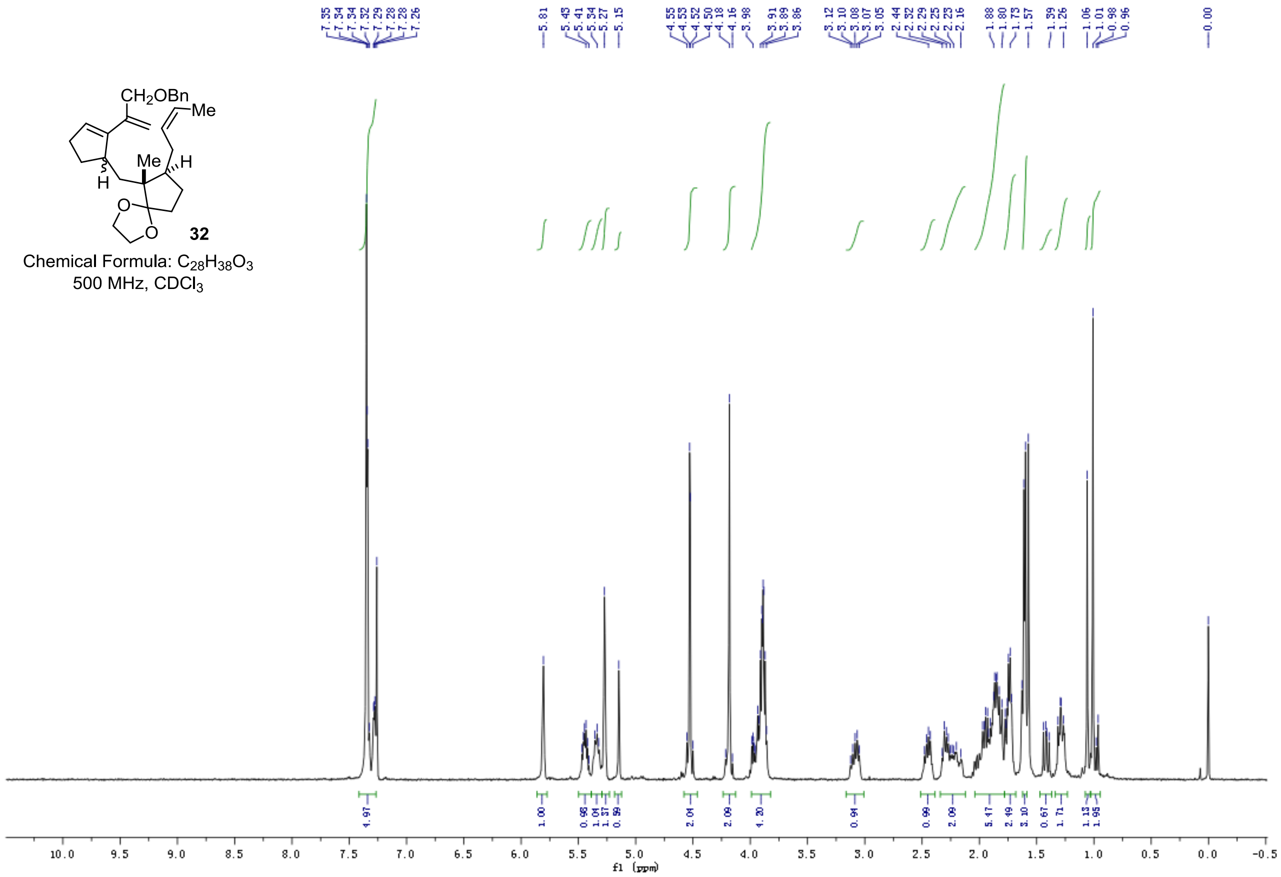
21

Chemical Formula: $C_{17}H_{24}O_2$
400 MHz, $CDCl_3$



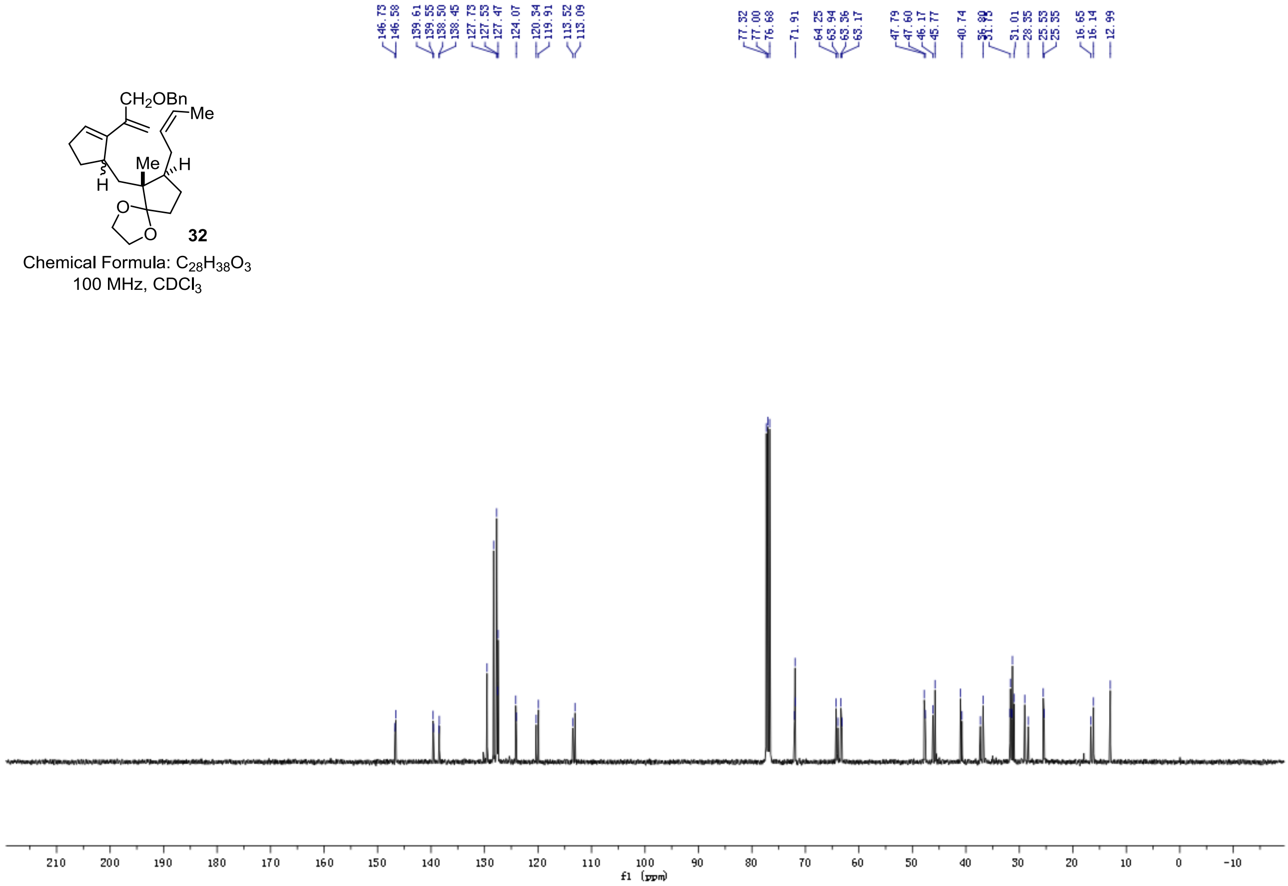
21

Chemical Formula: $C_{17}H_{24}O_2$
100 MHz, $CDCl_3$



32

Chemical Formula: $C_{28}H_{38}O_3$
500 MHz, $CDCl_3$

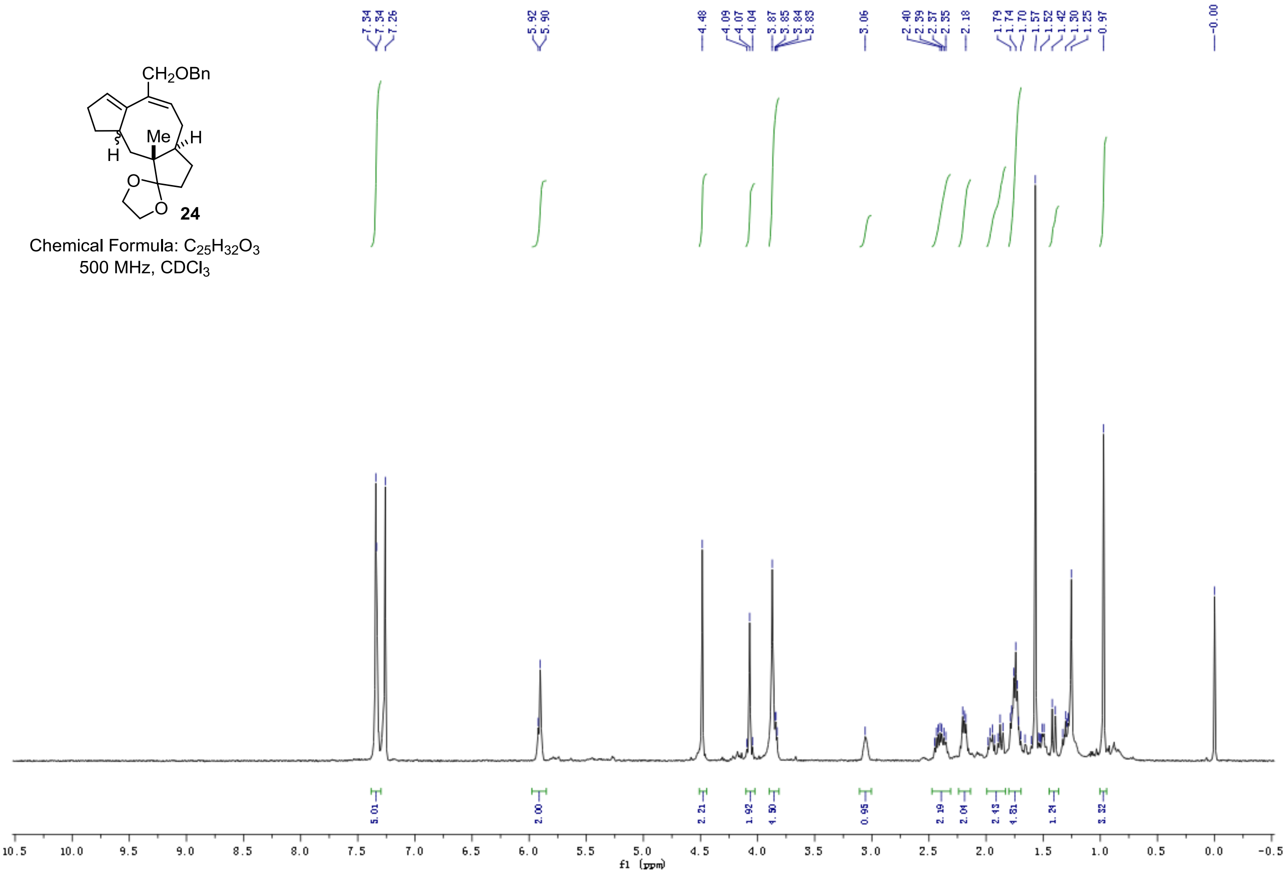


32

Chemical Formula: $C_{28}H_{38}O_3$
100 MHz, $CDCl_3$

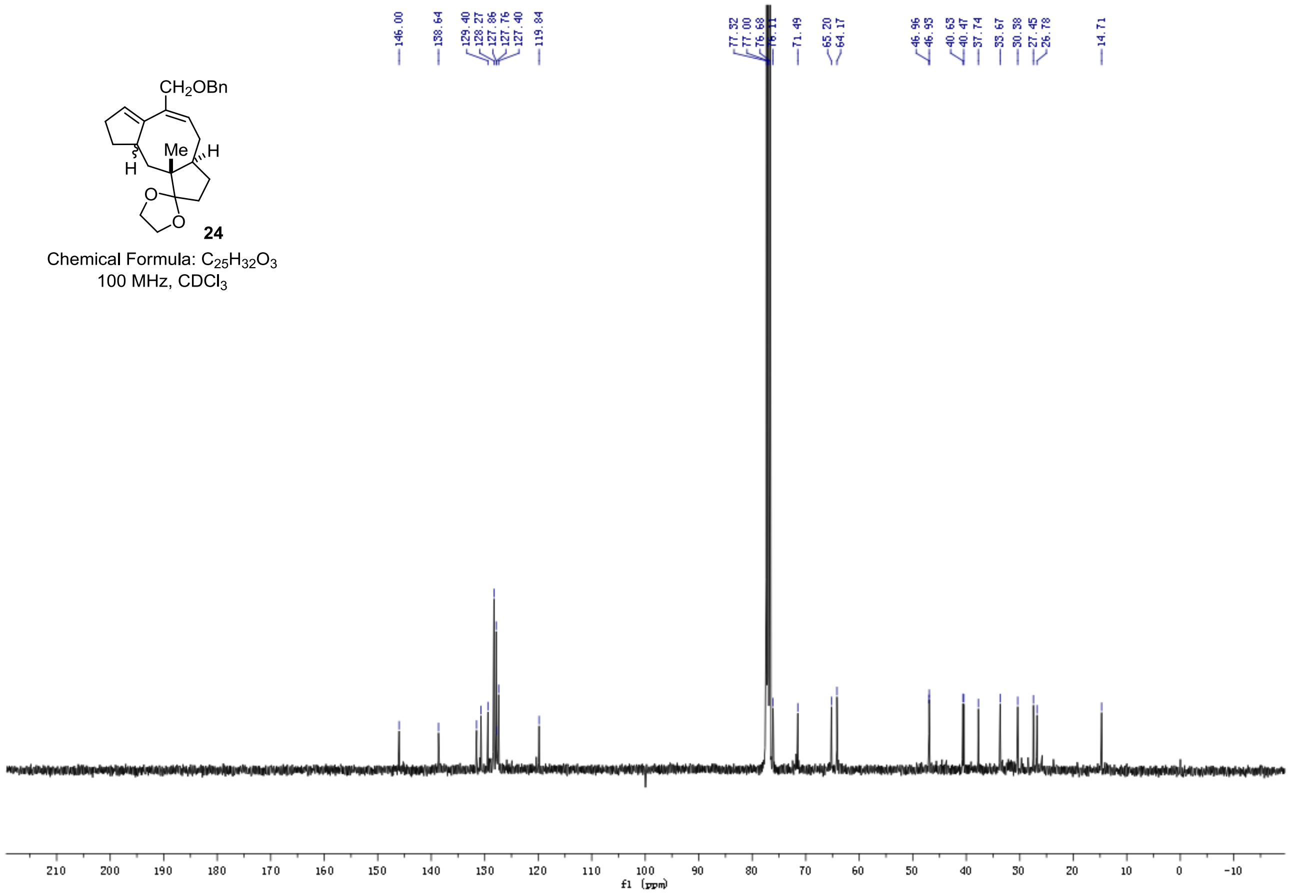
24

Chemical Formula: $C_{25}H_{32}O_3$
500 MHz, $CDCl_3$

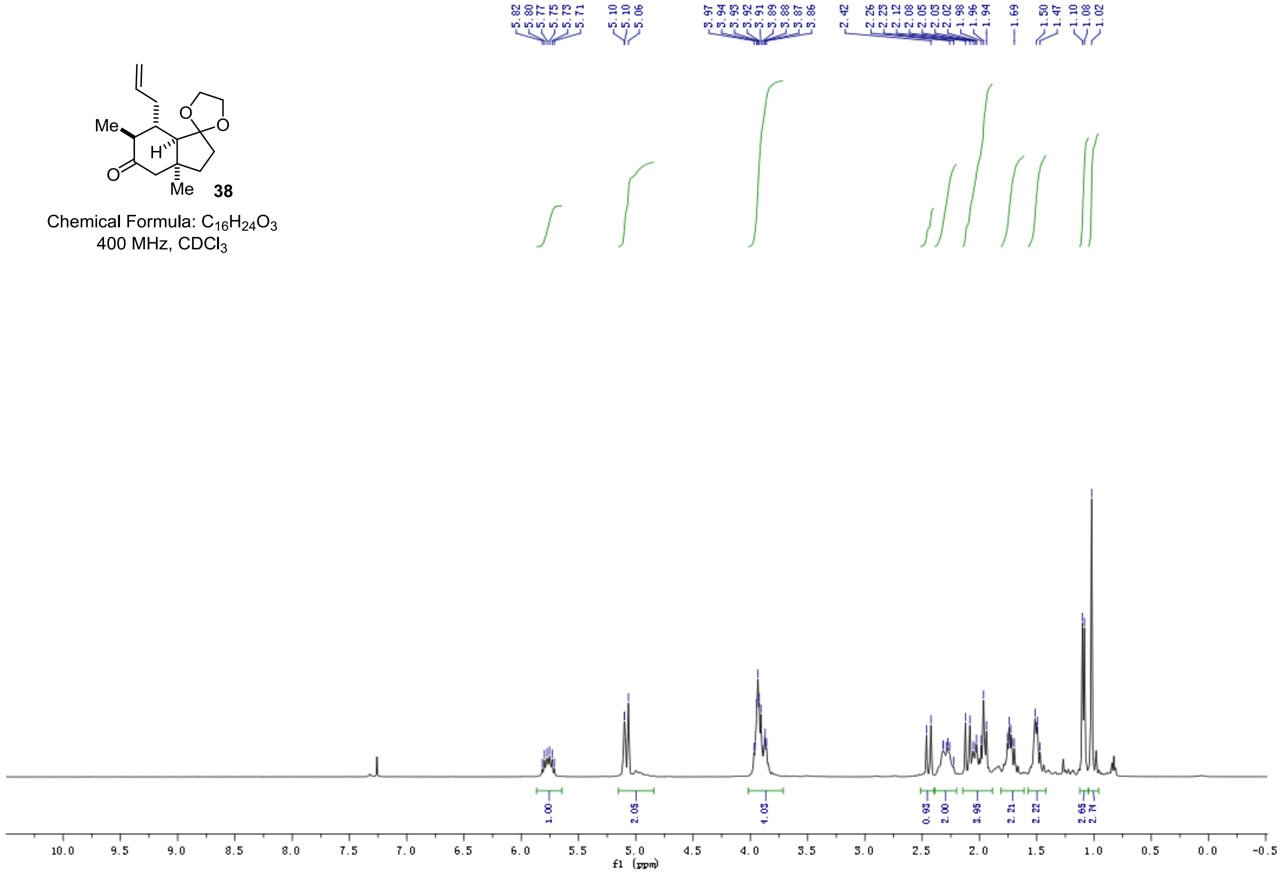


24

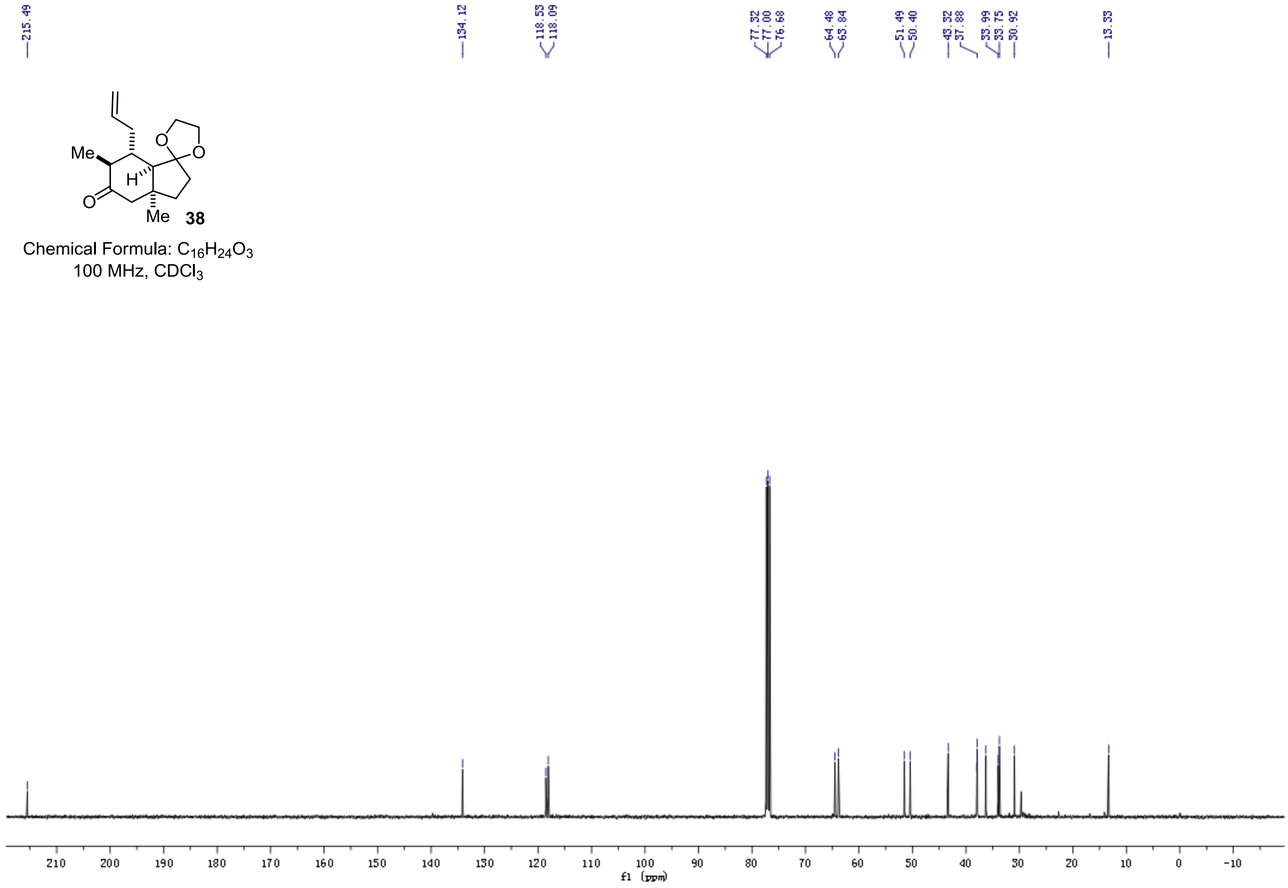
Chemical Formula: $C_{25}H_{32}O_3$
100 MHz, $CDCl_3$

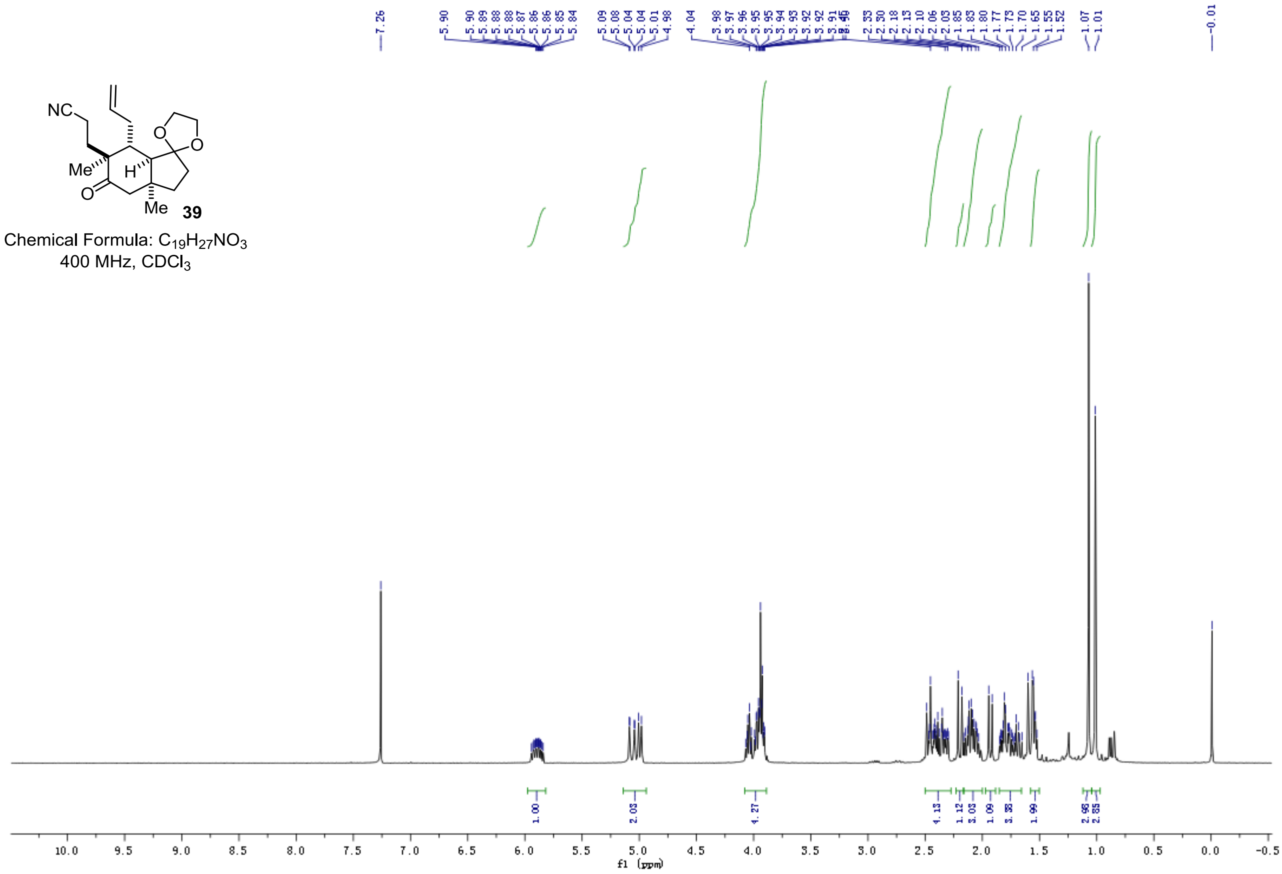


Chemical Formula: $C_{16}H_{24}O_3$
400 MHz, $CDCl_3$

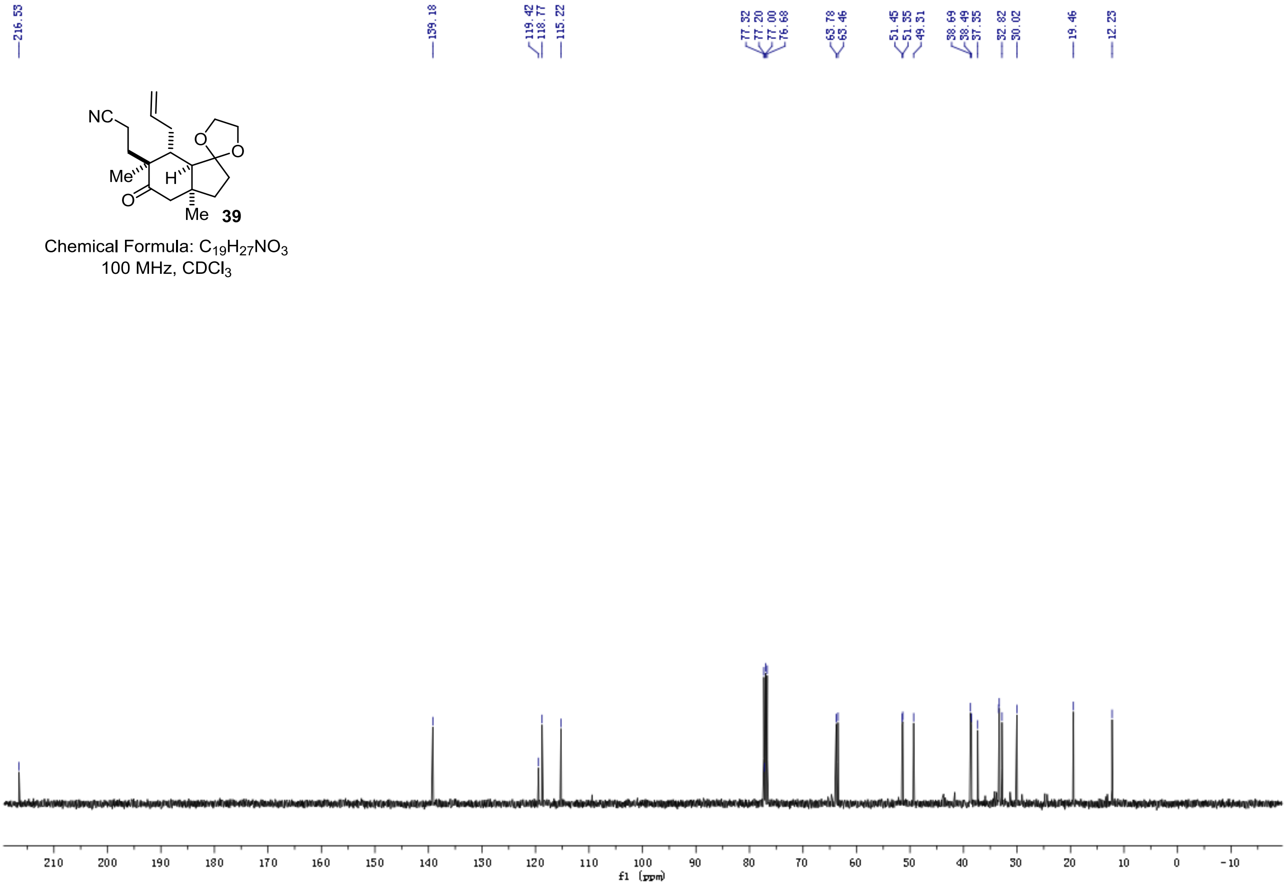


Chemical Formula: $C_{16}H_{24}O_3$
100 MHz, $CDCl_3$

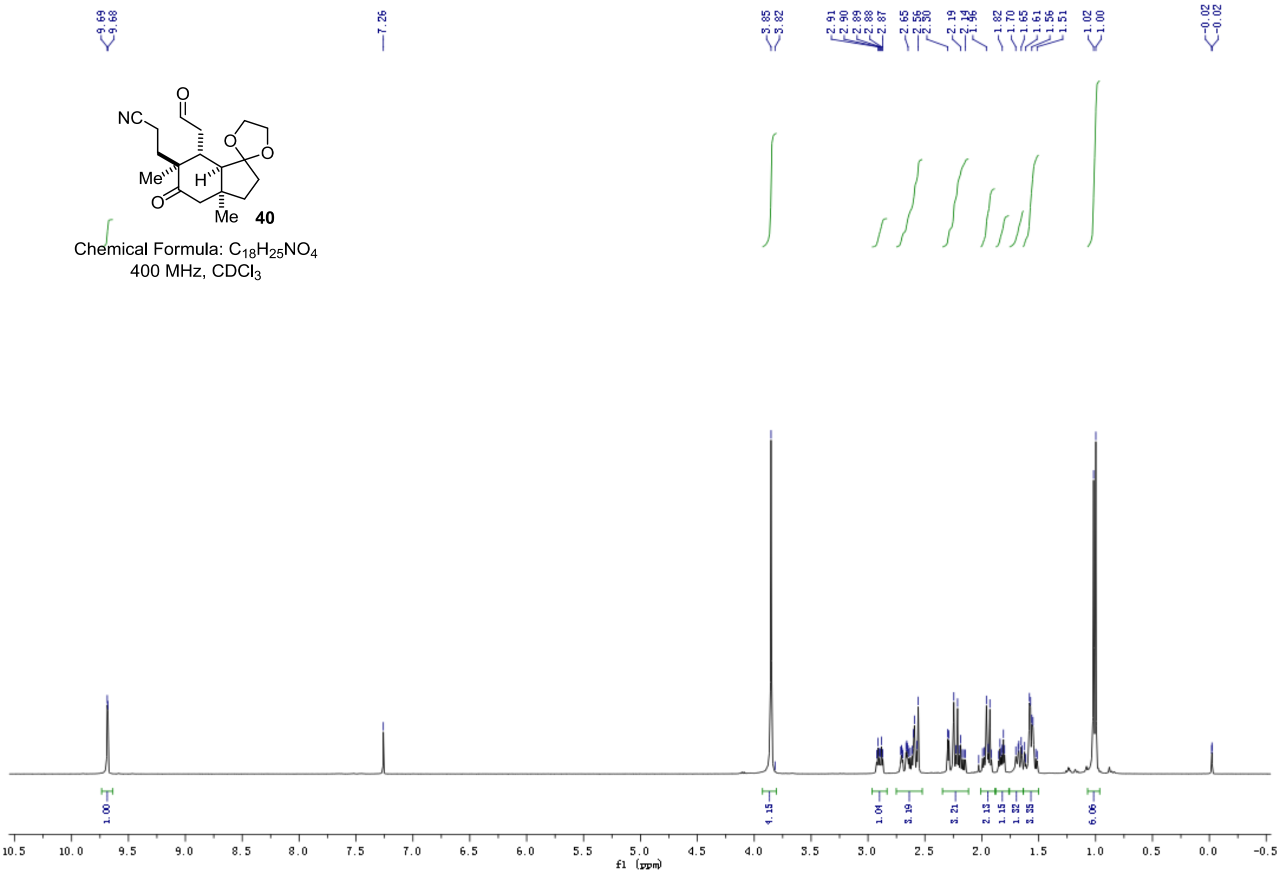




Chemical Formula: $C_{19}H_{27}NO_3$
400 MHz, $CDCl_3$

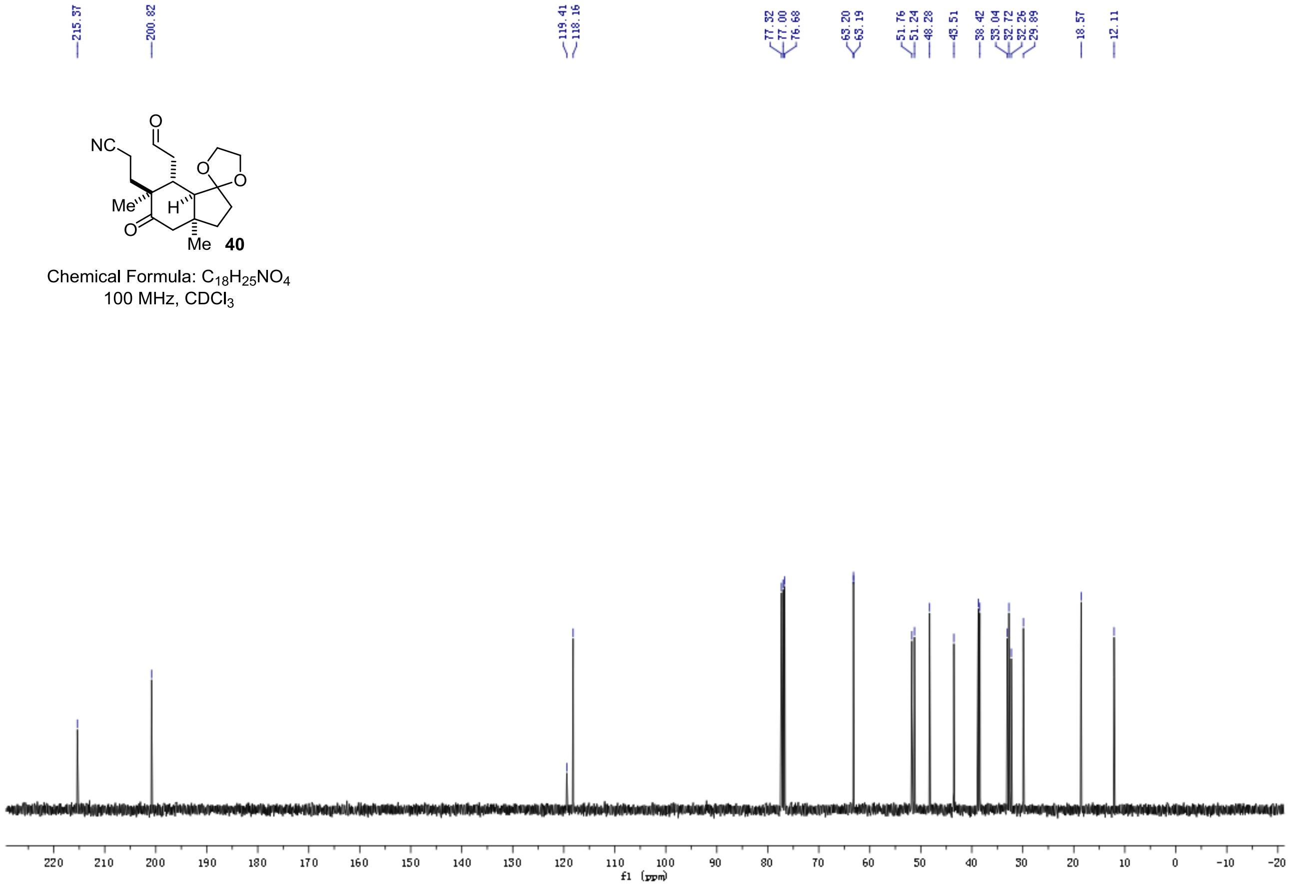


Chemical Formula: $C_{19}H_{27}NO_3$
100 MHz, $CDCl_3$



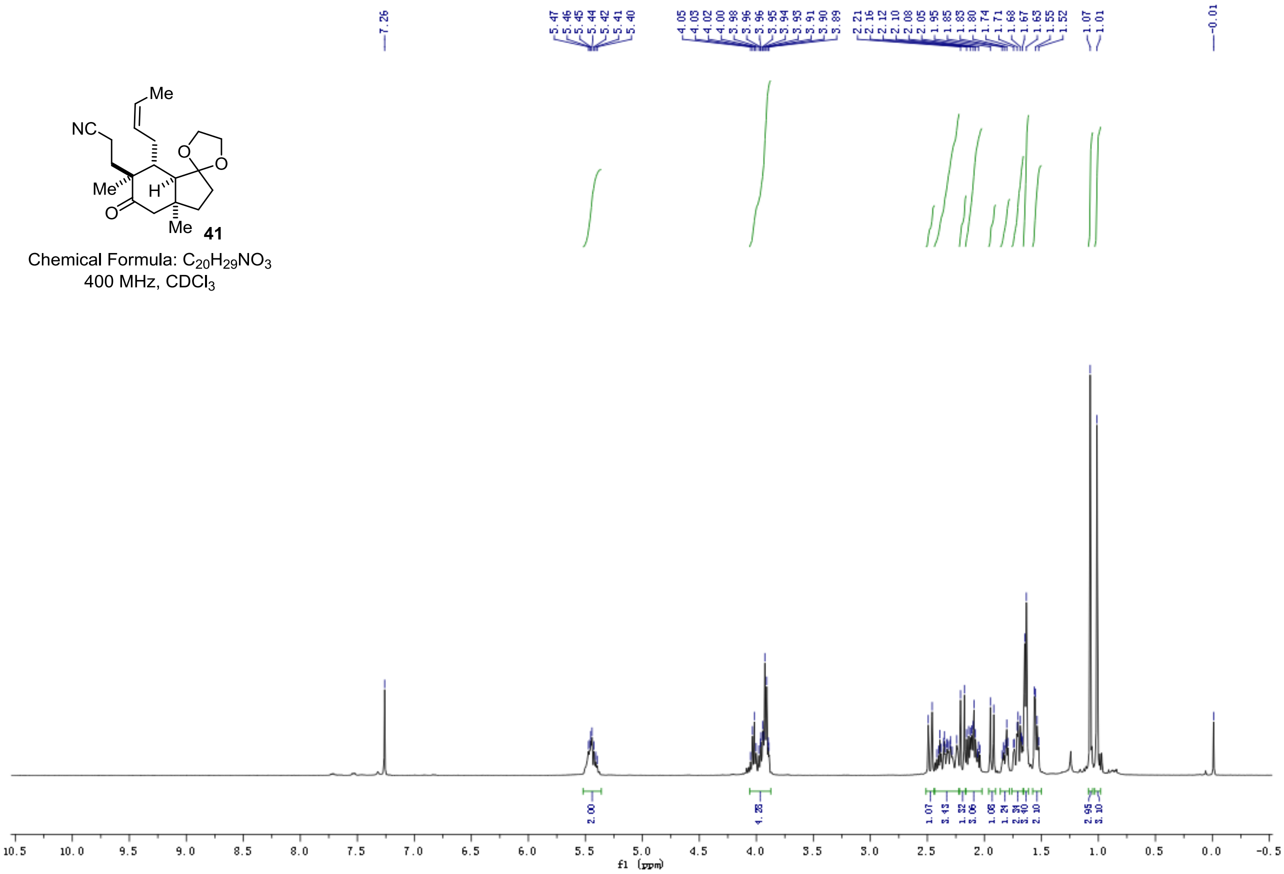
40

Chemical Formula: $C_{18}H_{25}NO_4$
400 MHz, $CDCl_3$



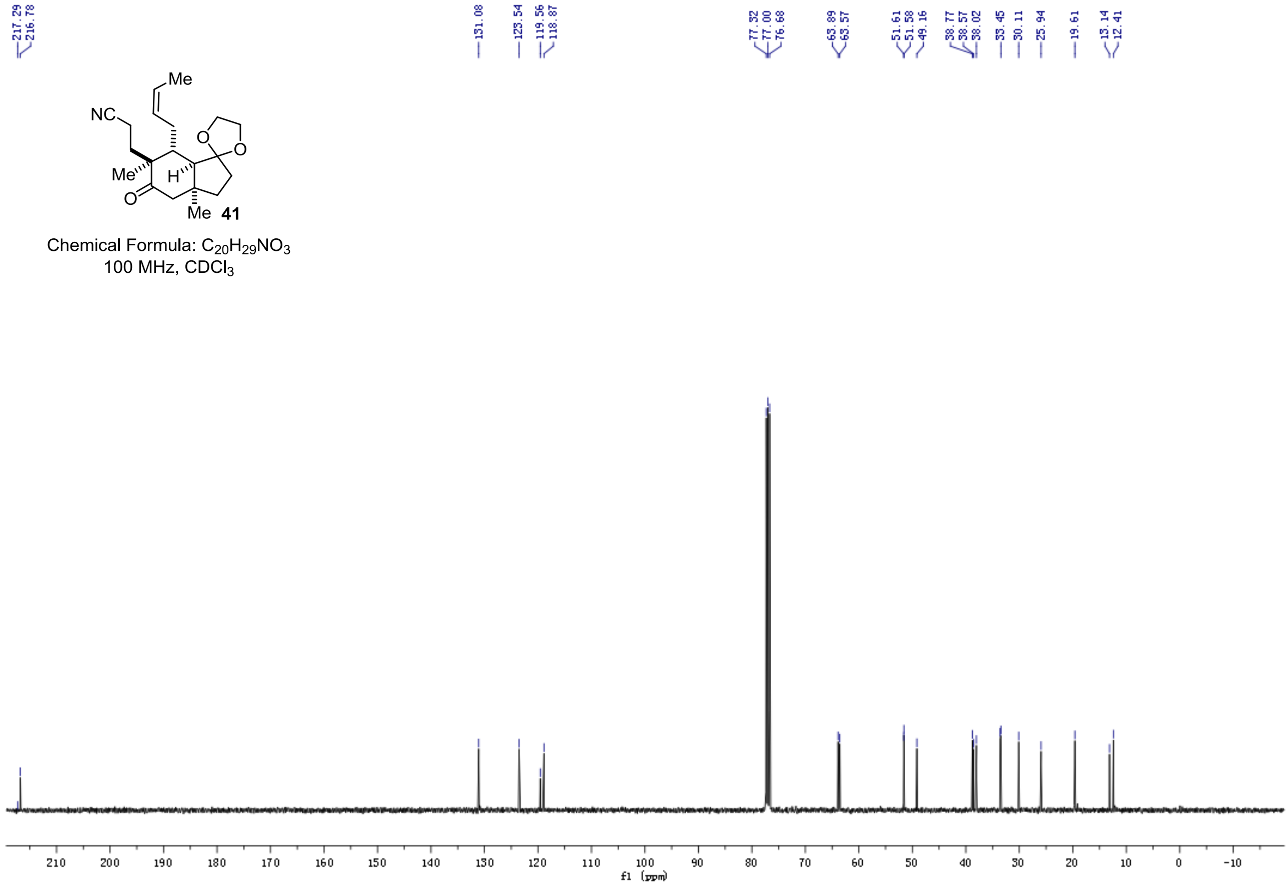
40

Chemical Formula: $C_{18}H_{25}NO_4$
100 MHz, $CDCl_3$



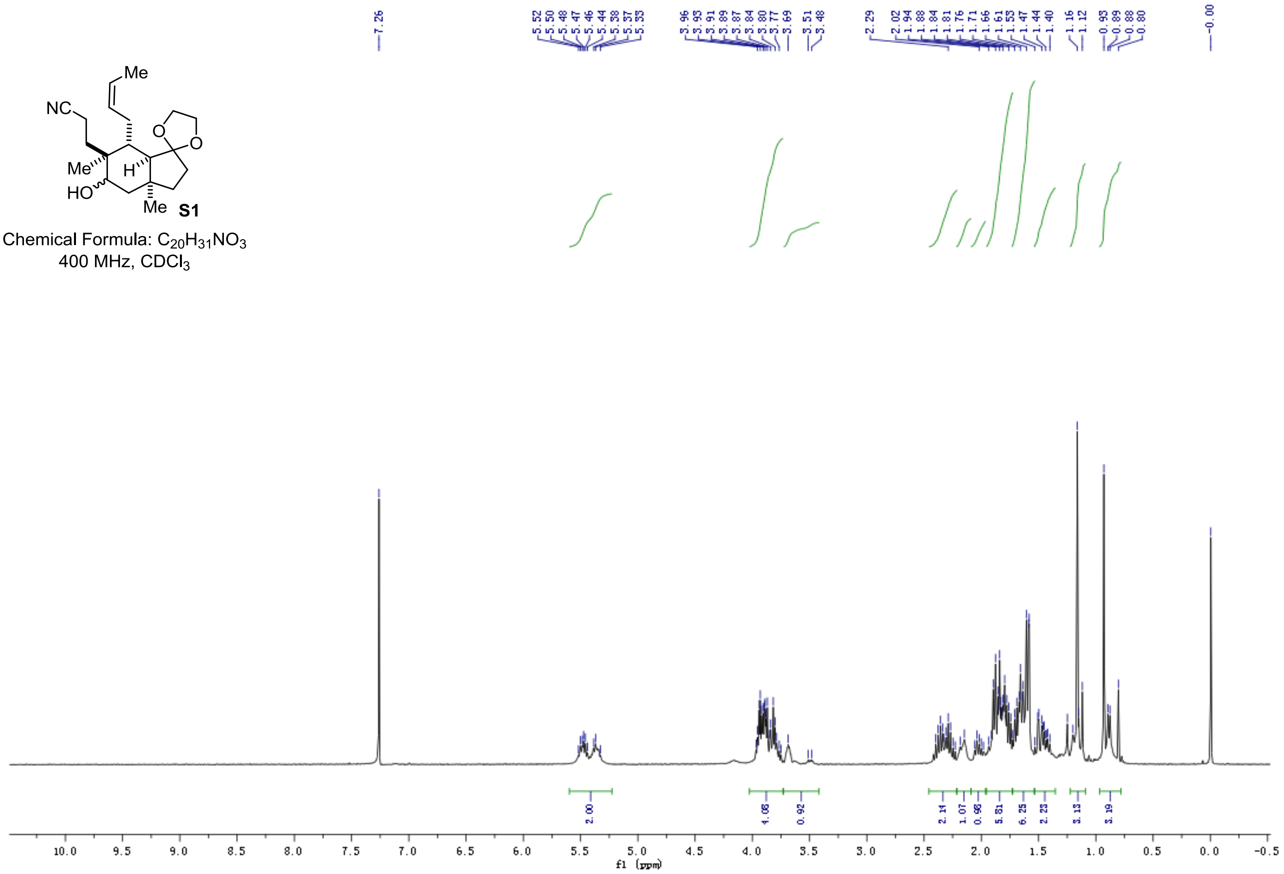
41

Chemical Formula: $C_{20}H_{29}NO_3$
400 MHz, $CDCl_3$



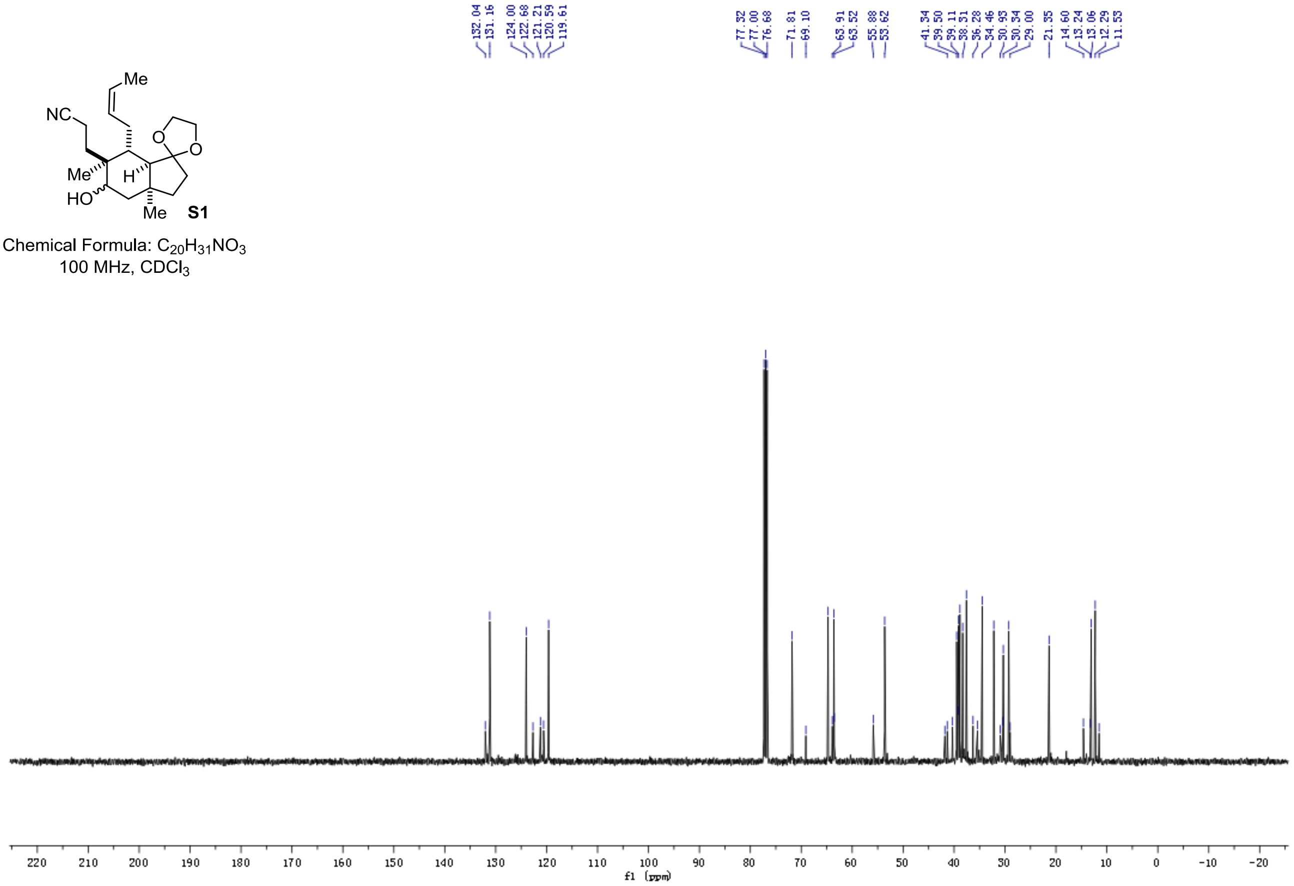
41

Chemical Formula: $C_{20}H_{29}NO_3$
100 MHz, $CDCl_3$



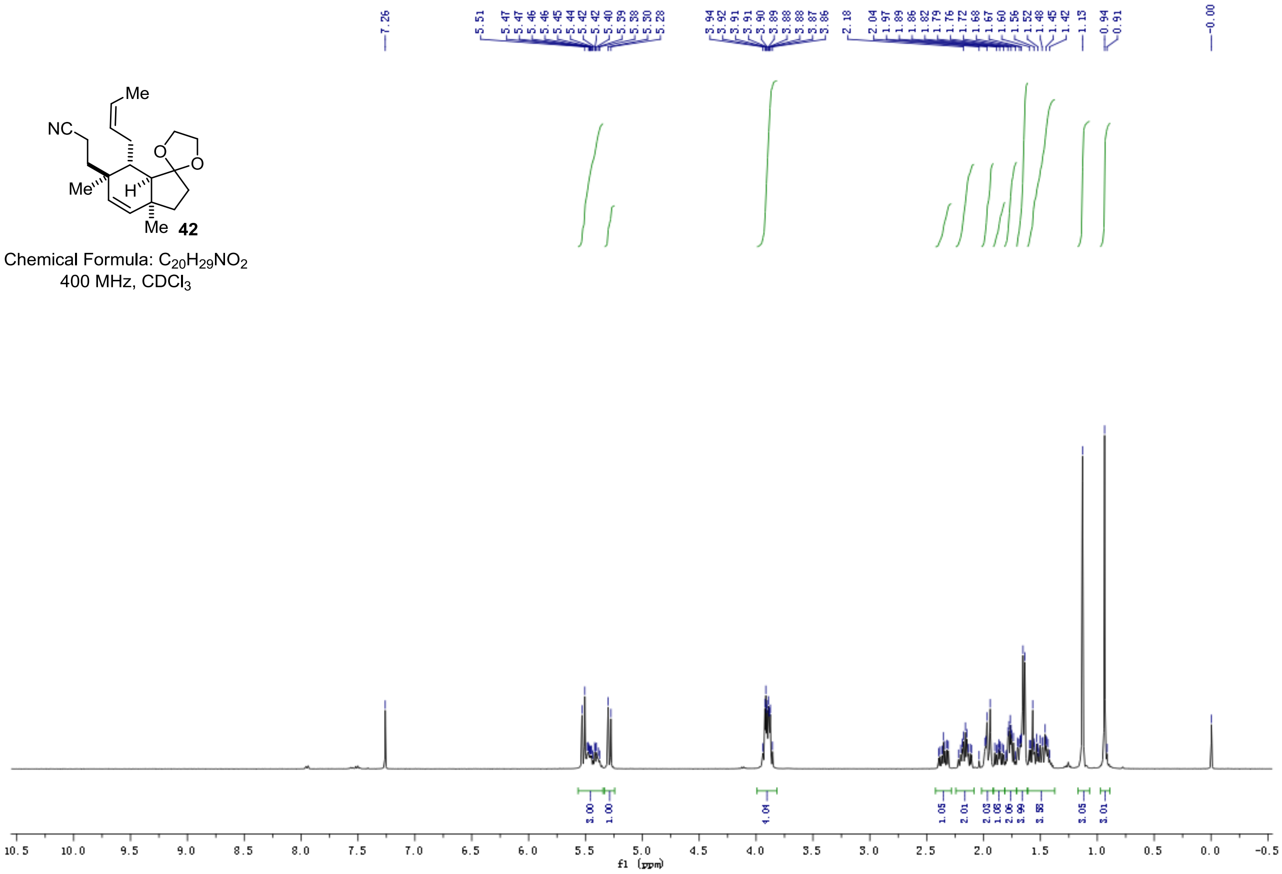
S1

Chemical Formula: $C_{20}H_{31}NO_3$
400 MHz, $CDCl_3$



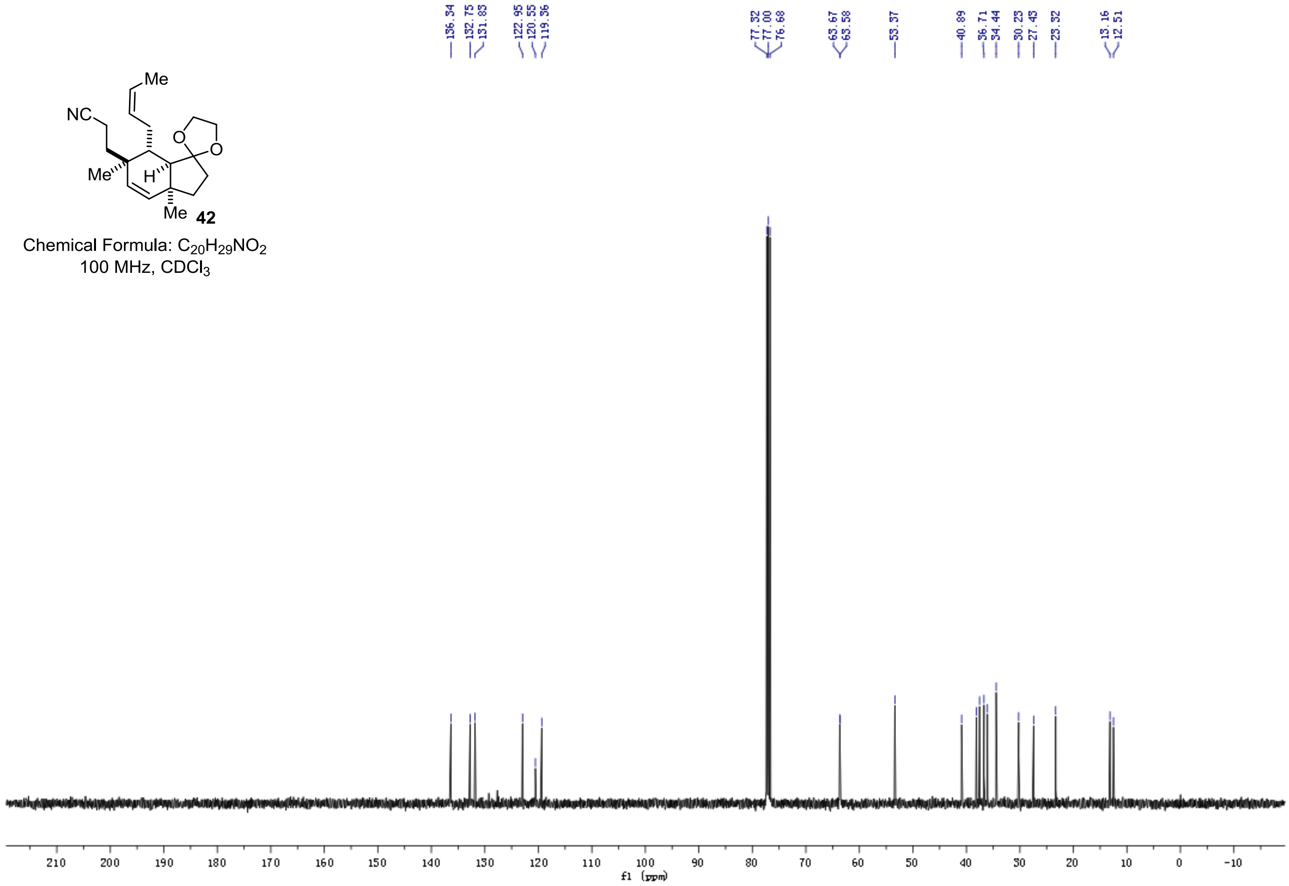
S1

Chemical Formula: $C_{20}H_{31}NO_3$
100 MHz, $CDCl_3$



42

Chemical Formula: $C_{20}H_{29}NO_2$
400 MHz, $CDCl_3$

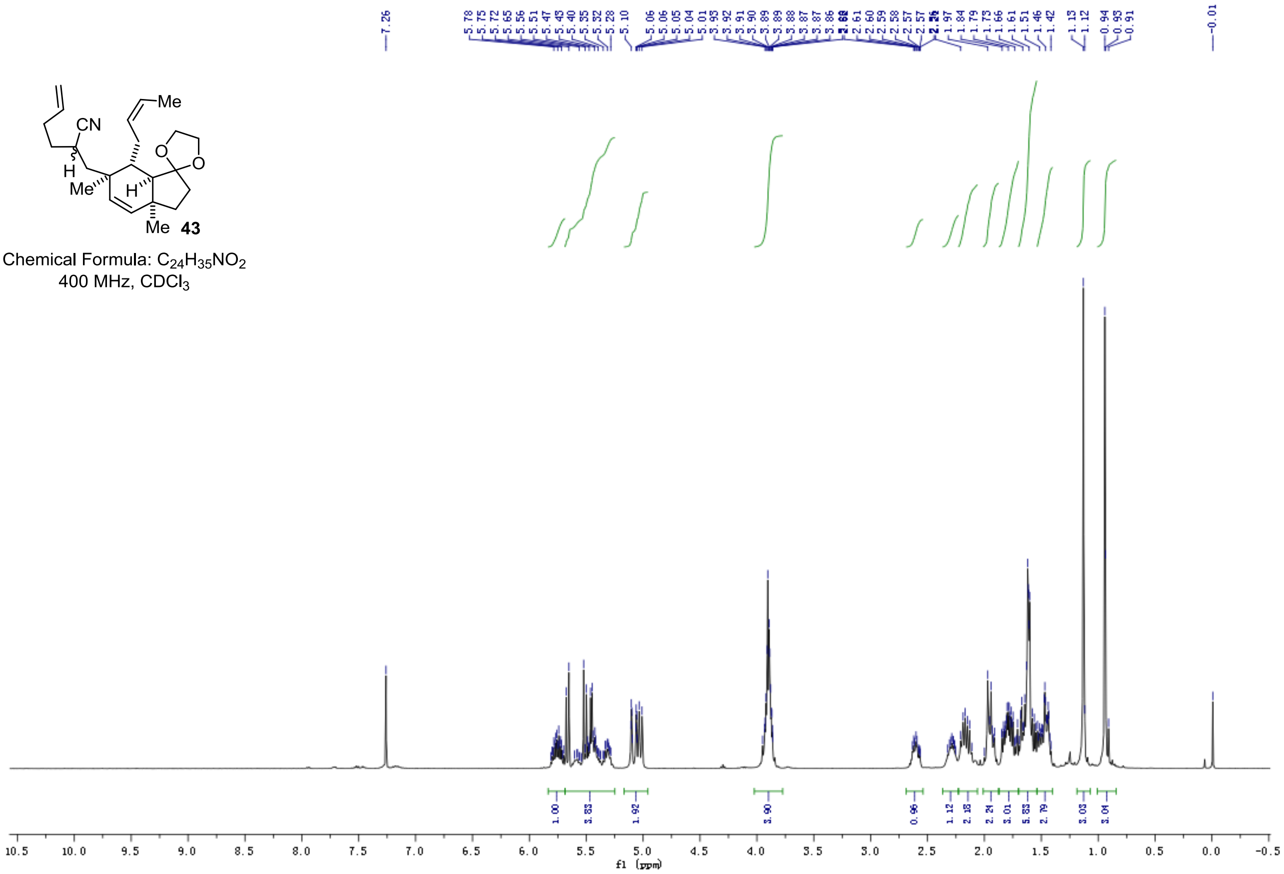


42

Chemical Formula: $C_{20}H_{29}NO_2$
100 MHz, $CDCl_3$

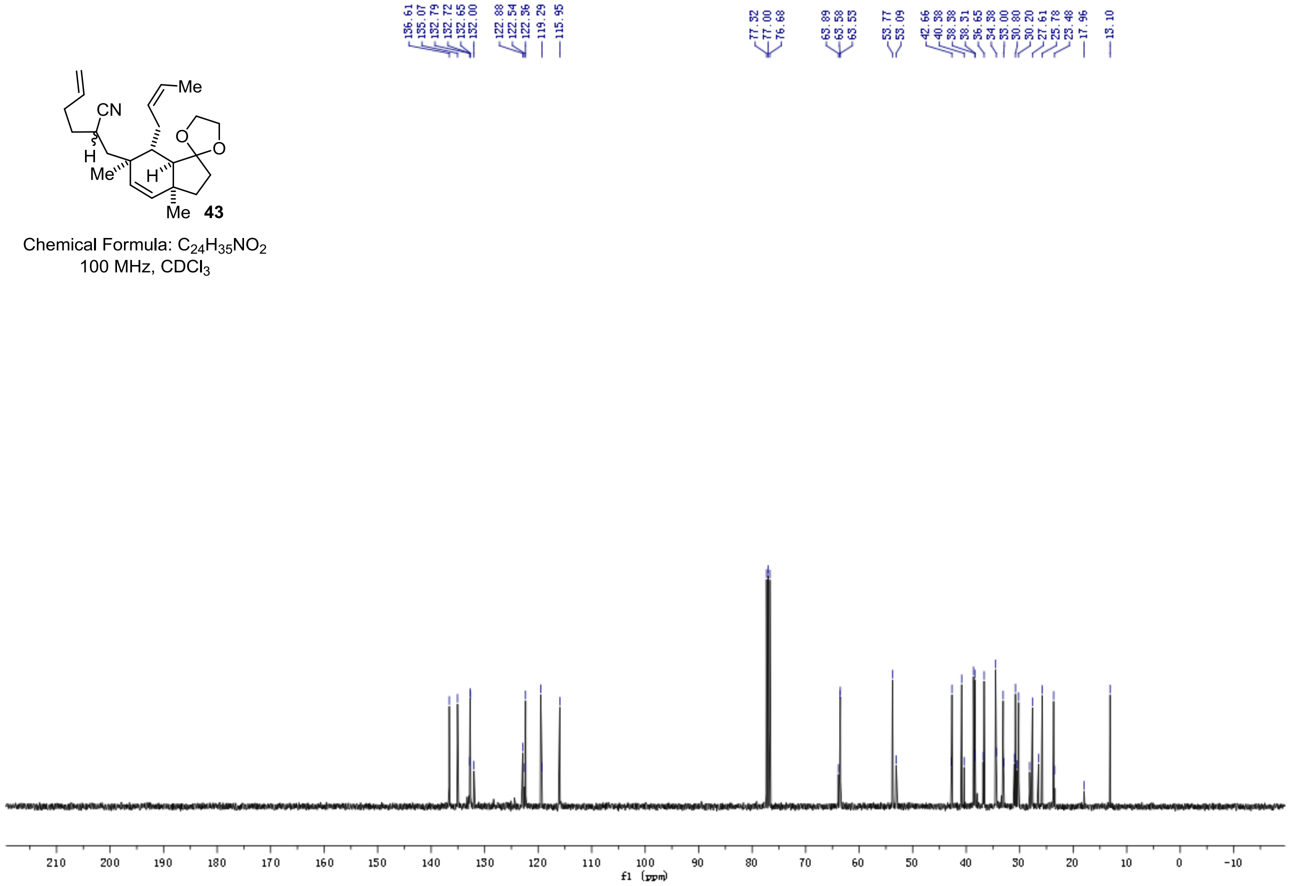
43

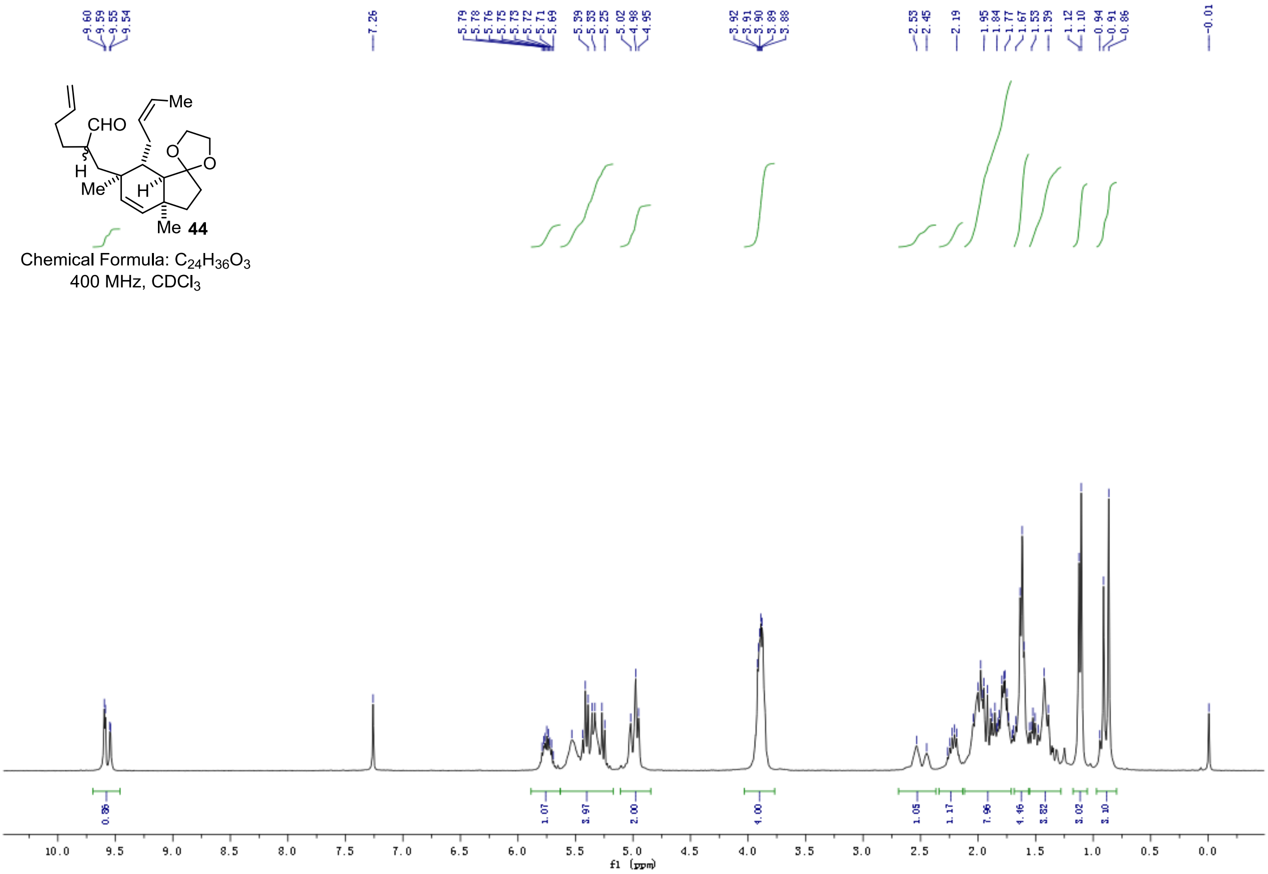
Chemical Formula: $C_{24}H_{35}NO_2$
400 MHz, $CDCl_3$



43

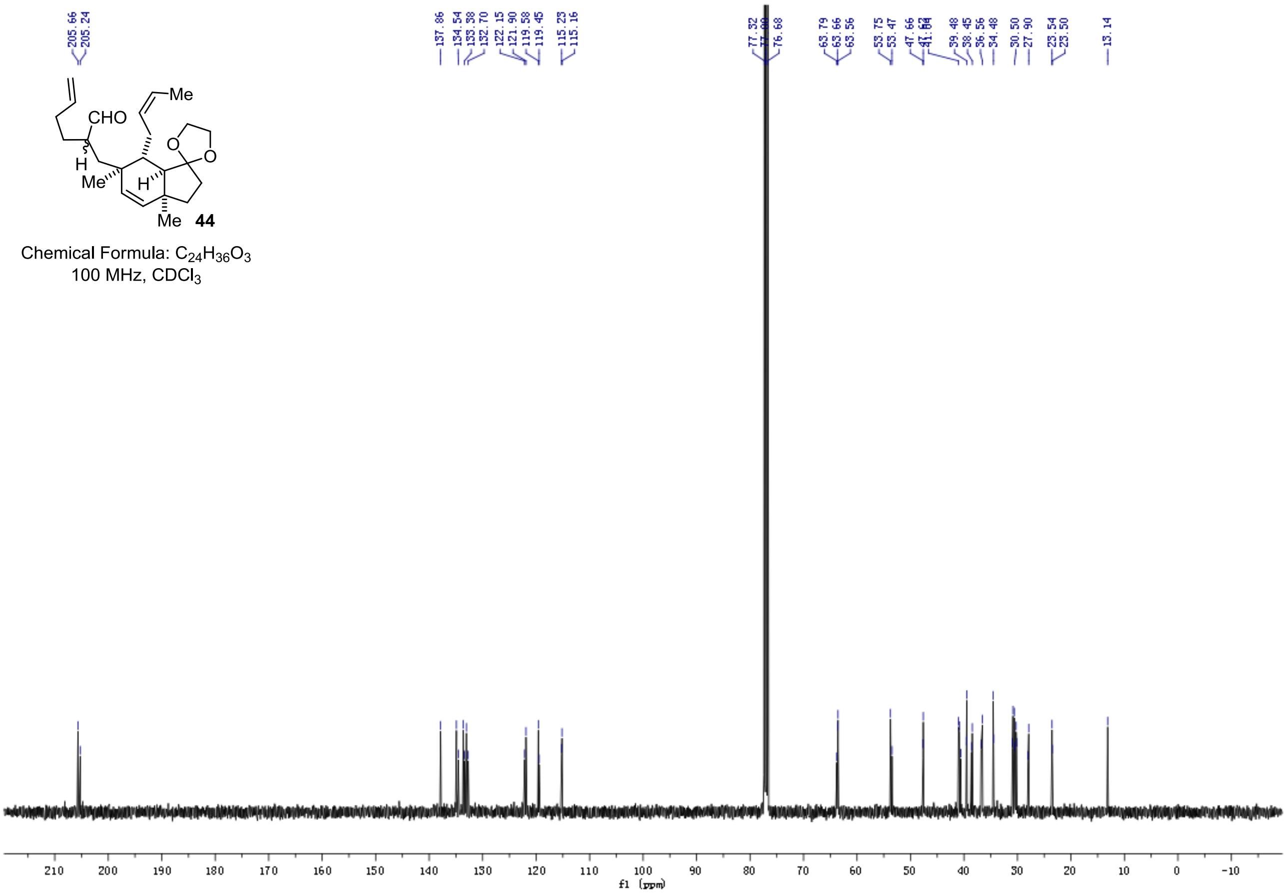
Chemical Formula: $C_{24}H_{35}NO_2$
100 MHz, $CDCl_3$





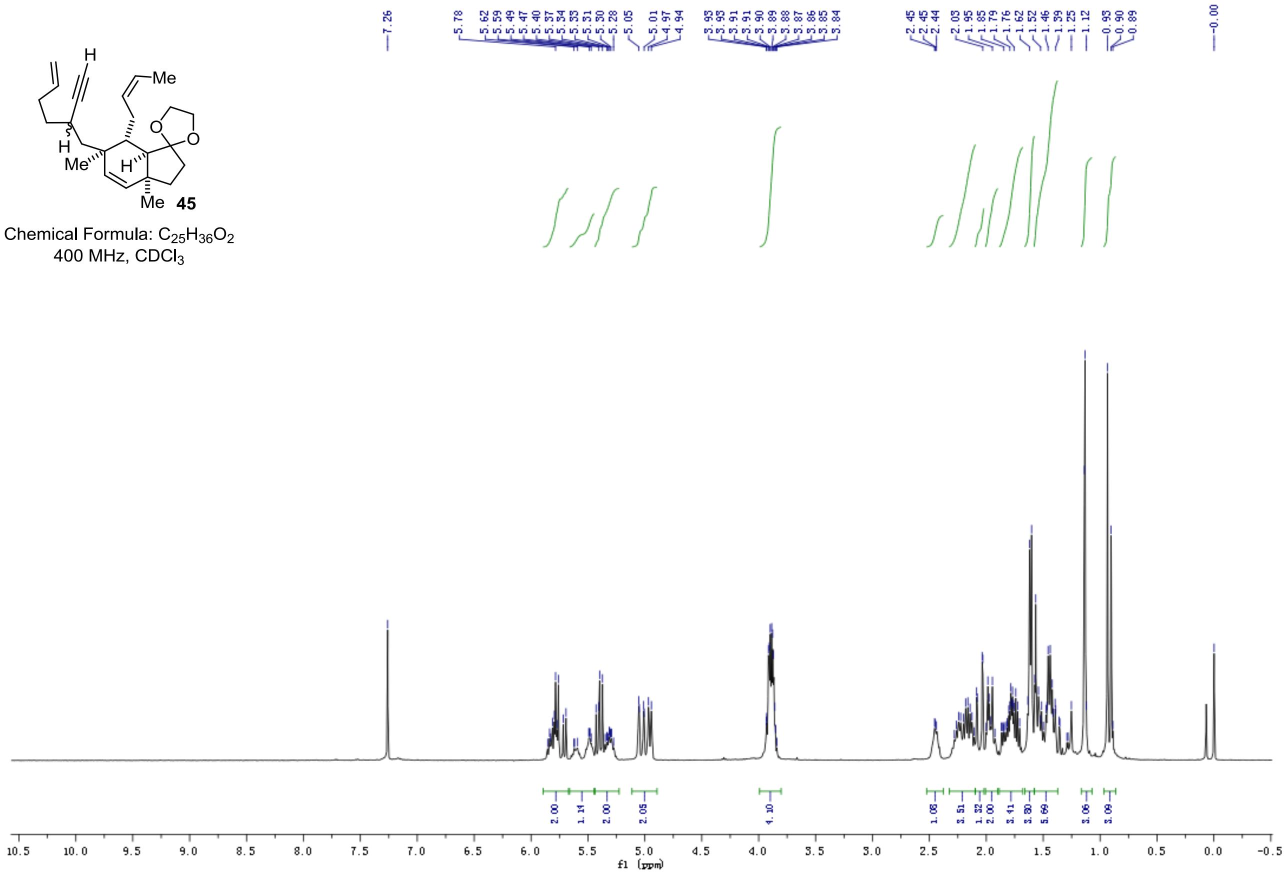
44

Chemical Formula: $C_{24}H_{36}O_3$
400 MHz, $CDCl_3$



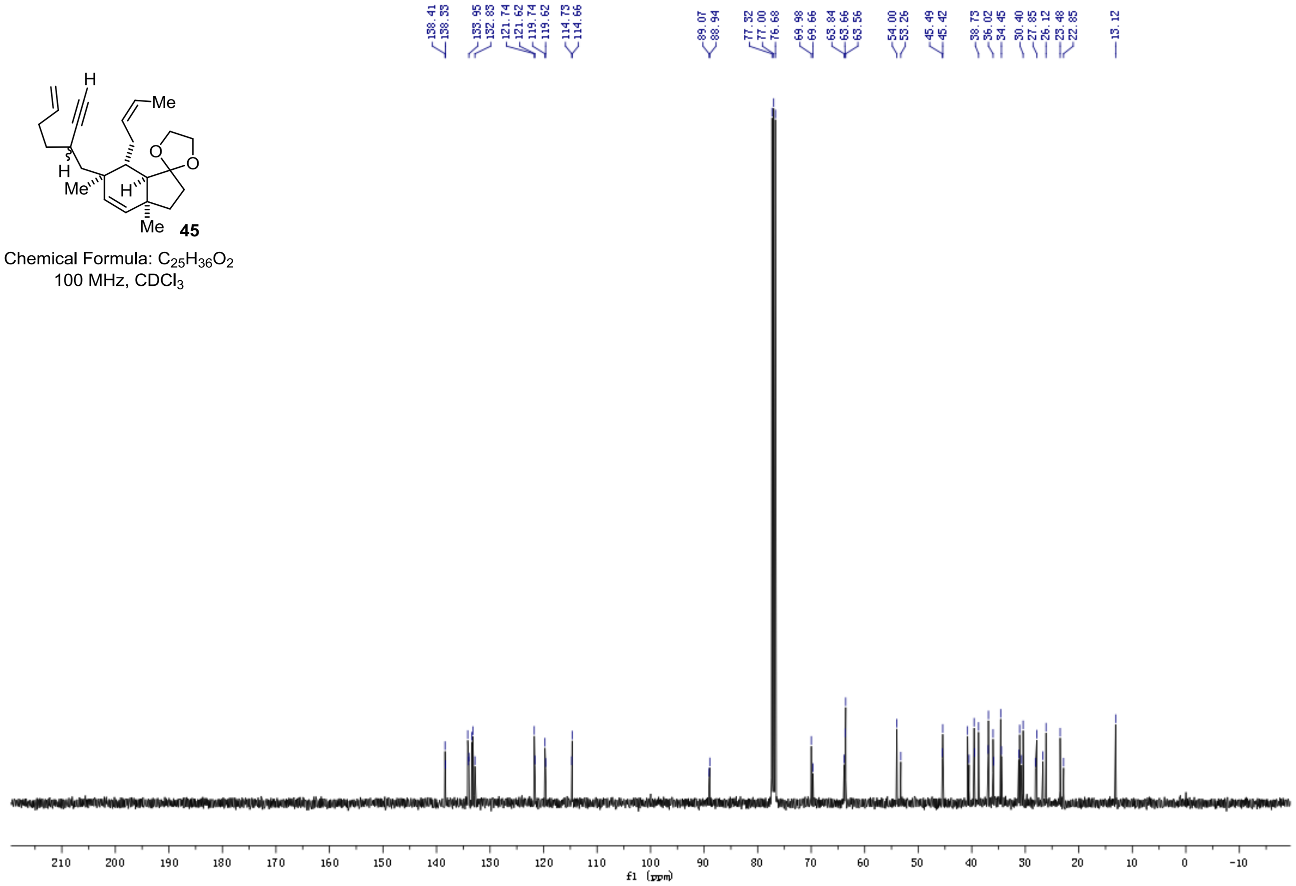
44

Chemical Formula: $C_{24}H_{36}O_3$
100 MHz, $CDCl_3$



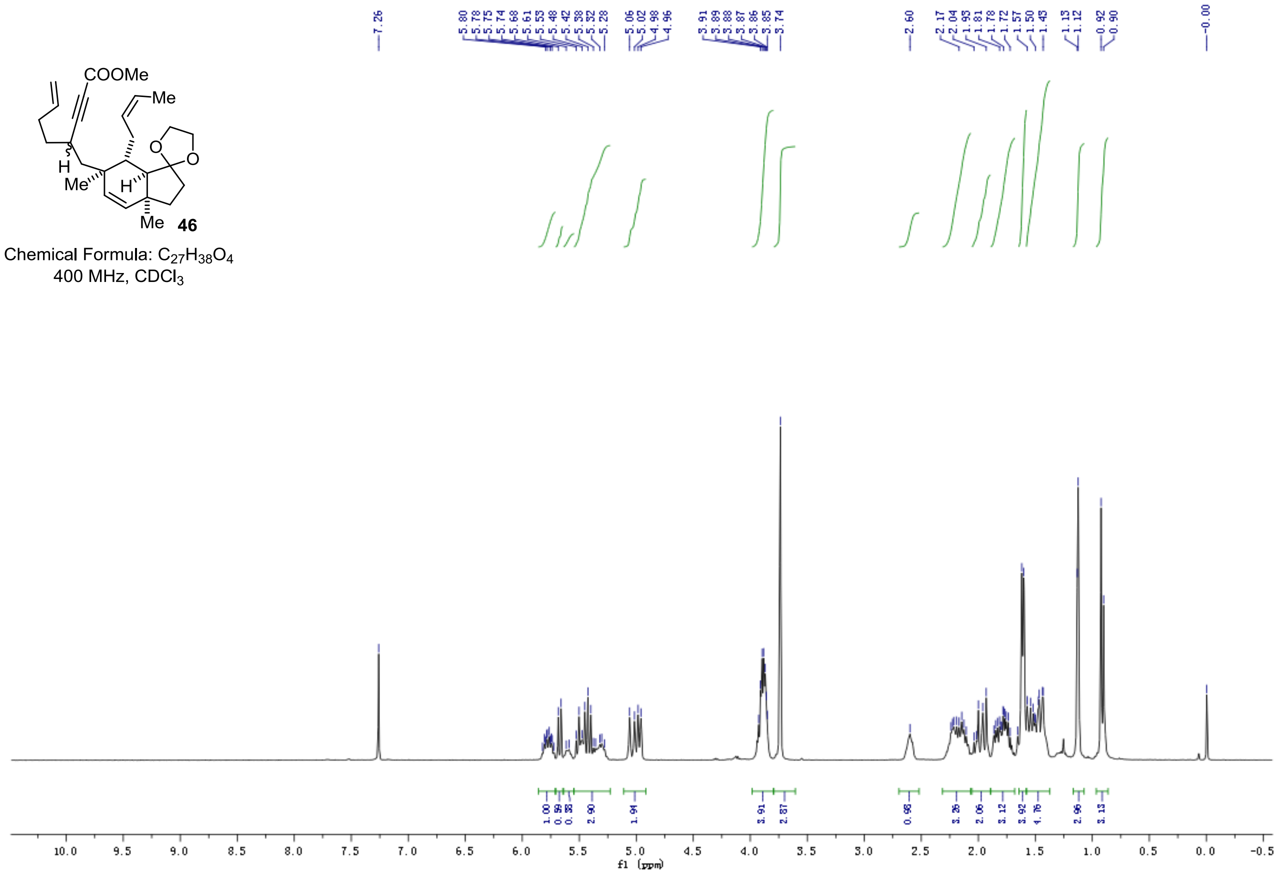
45

Chemical Formula: $C_{25}H_{36}O_2$
400 MHz, $CDCl_3$

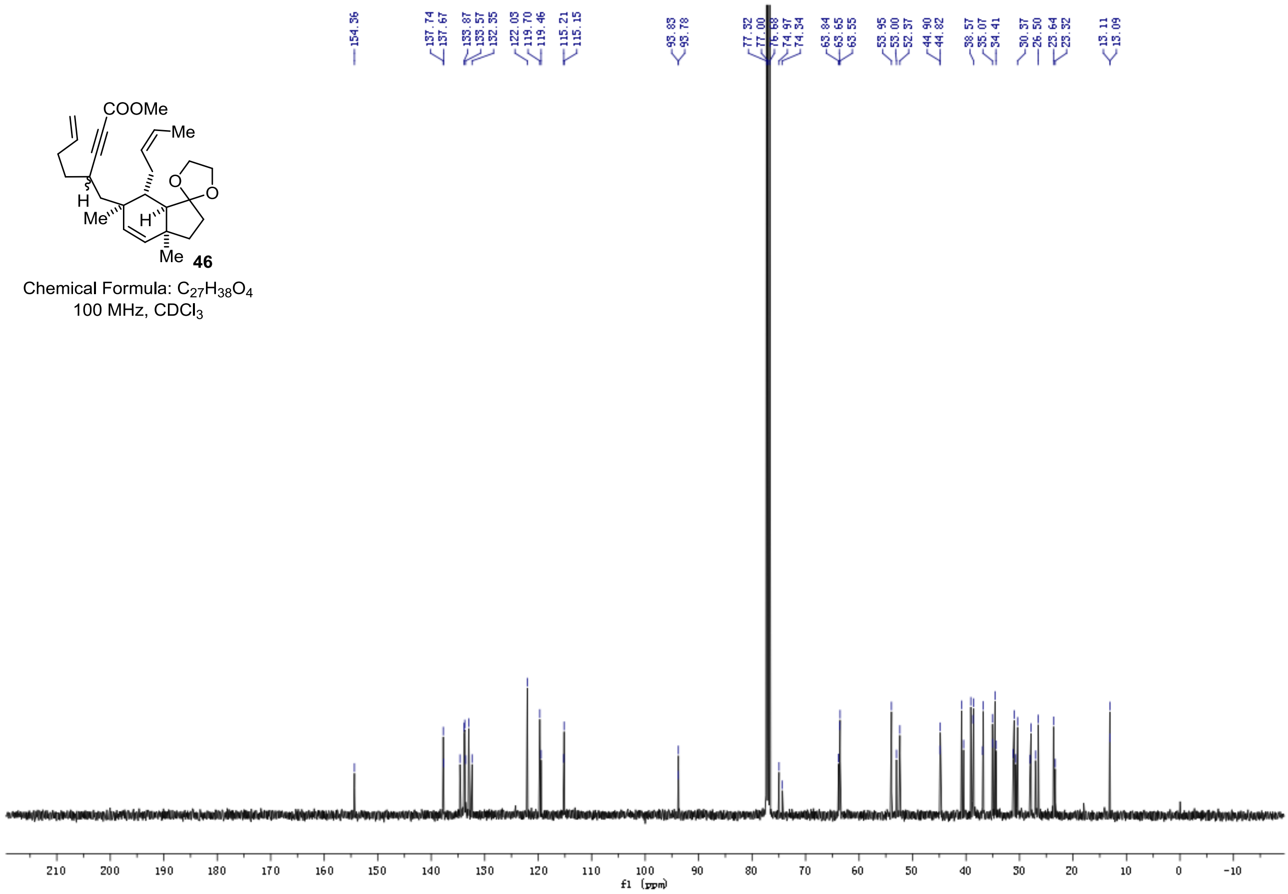


45

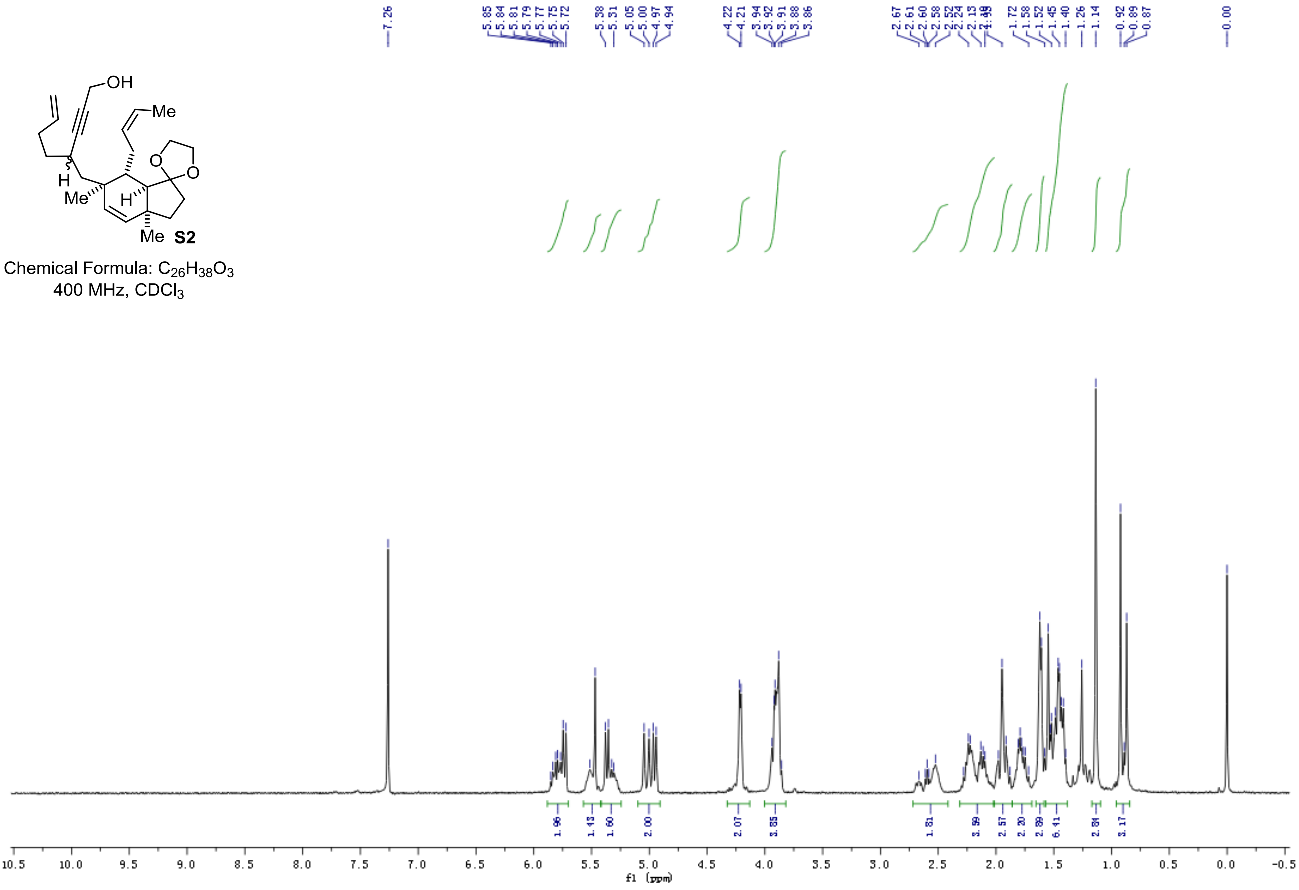
Chemical Formula: $C_{25}H_{36}O_2$
100 MHz, $CDCl_3$



Chemical Formula: $C_{27}H_{38}O_4$
400 MHz, $CDCl_3$

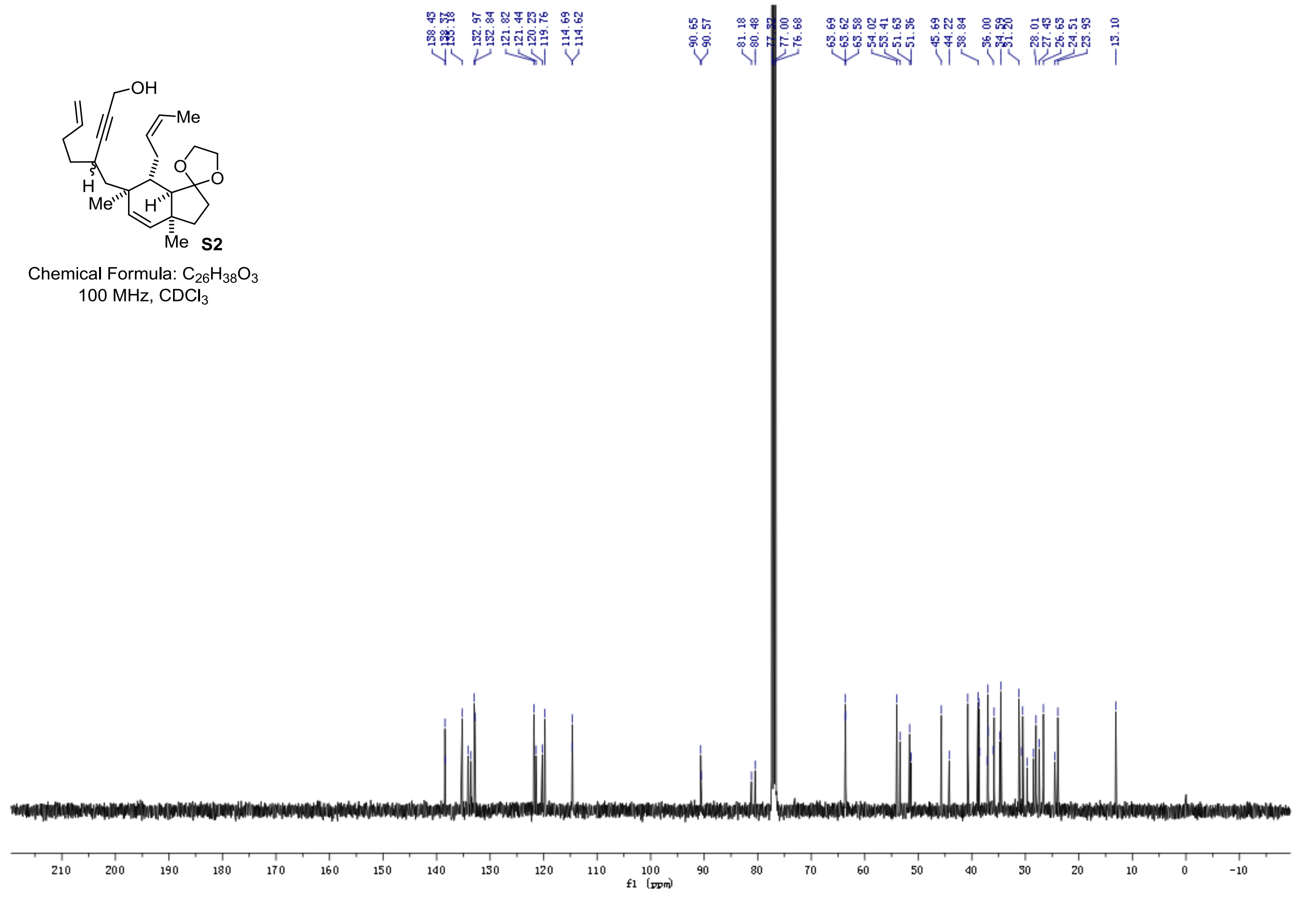


Chemical Formula: $C_{27}H_{38}O_4$
100 MHz, $CDCl_3$



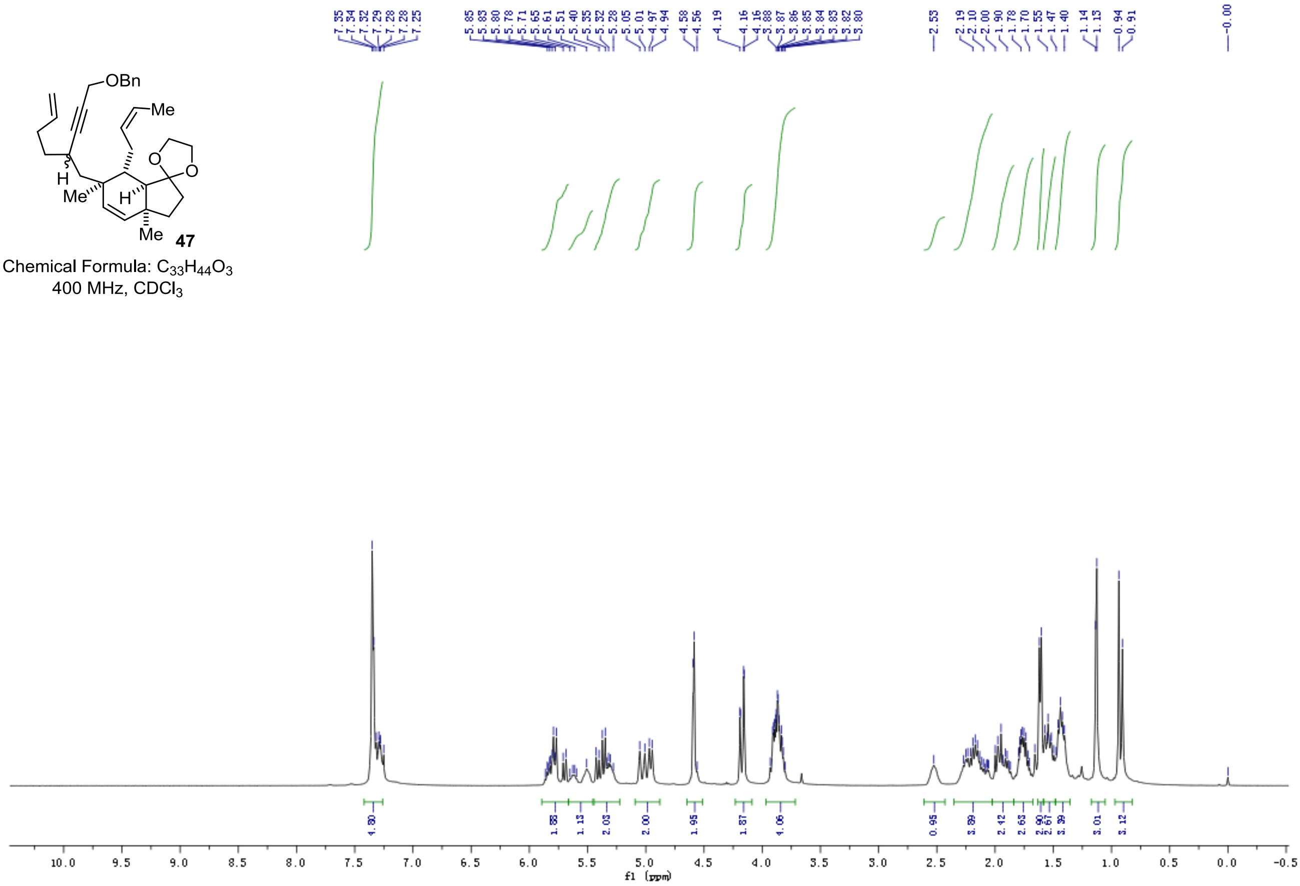
S2

Chemical Formula: $C_{26}H_{38}O_3$
400 MHz, $CDCl_3$



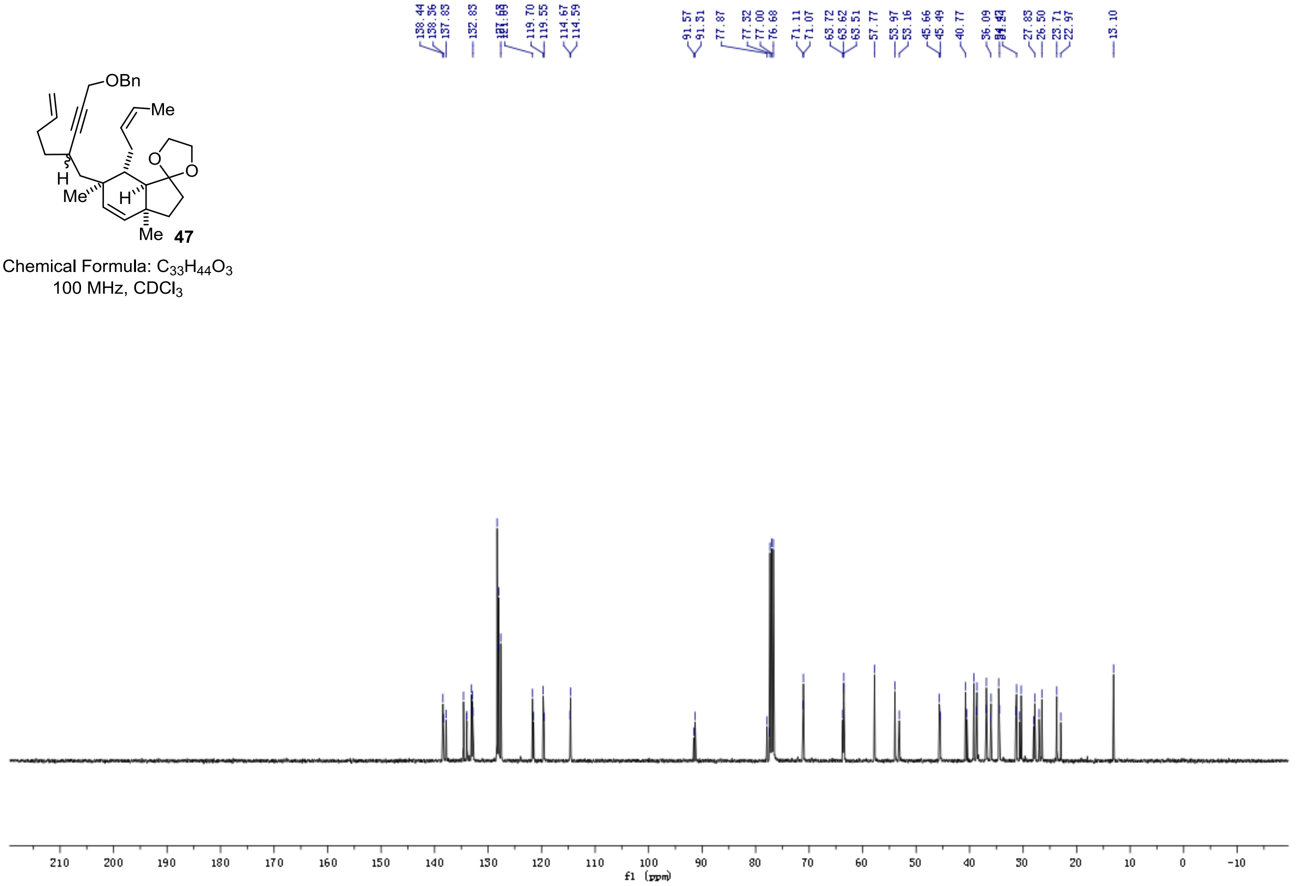
S2

Chemical Formula: $C_{26}H_{38}O_3$
100 MHz, $CDCl_3$



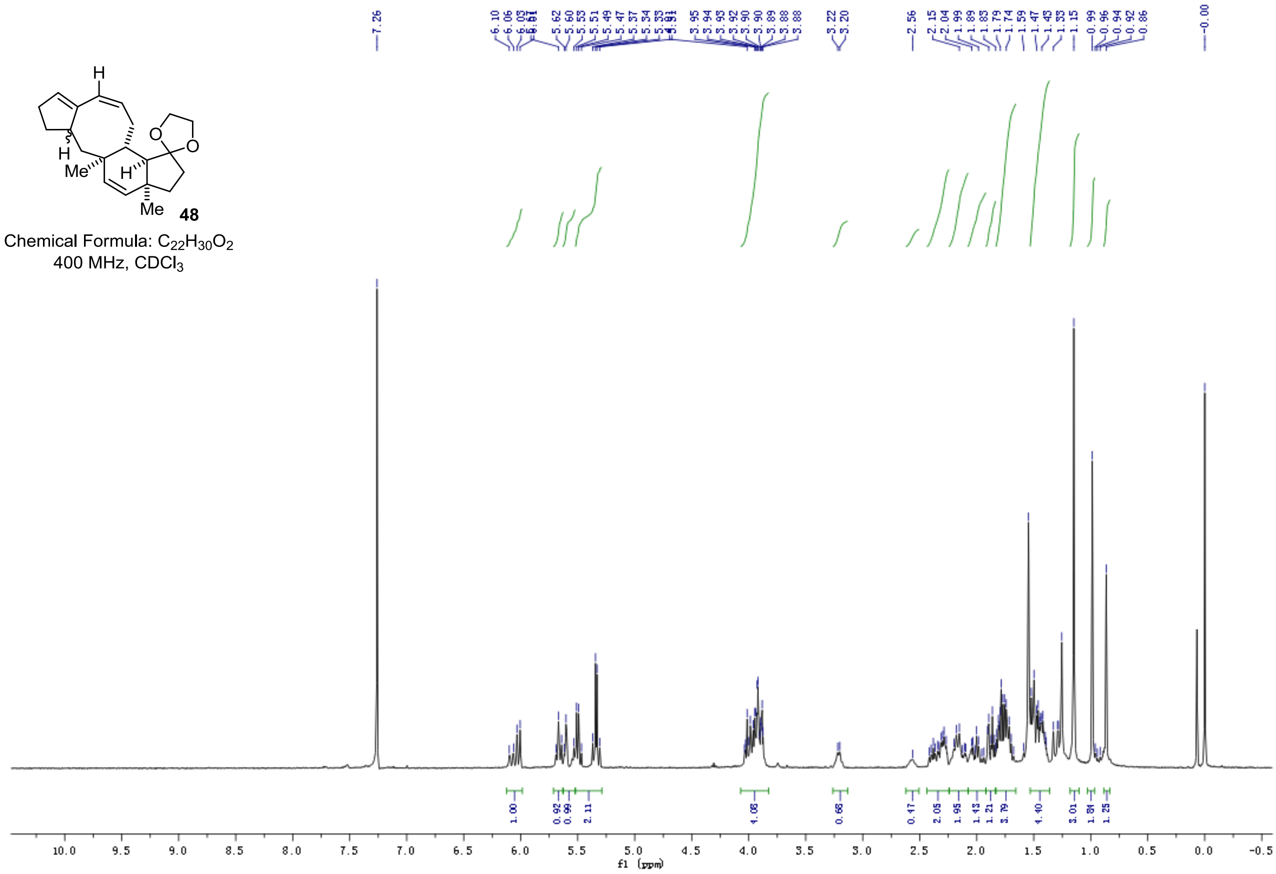
47

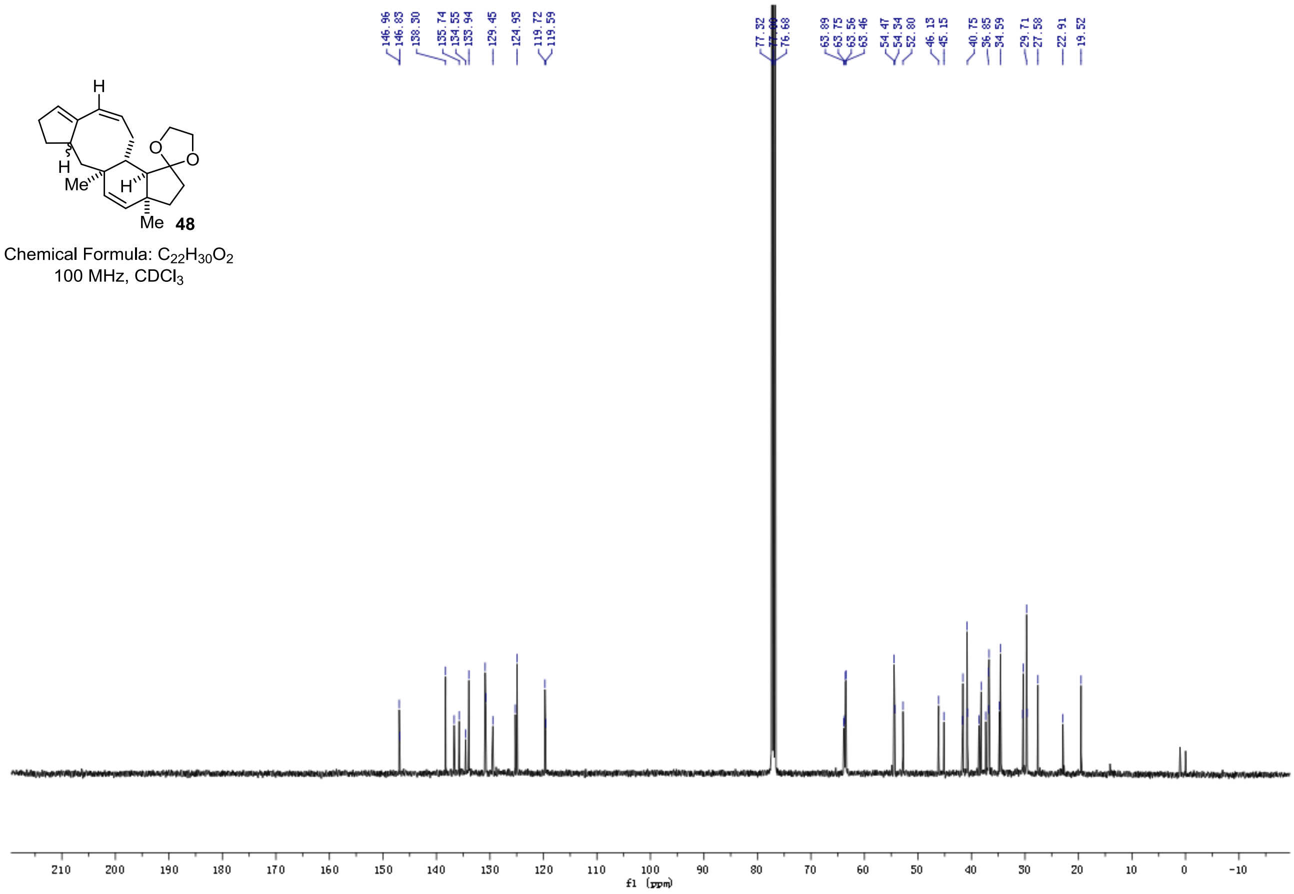
Chemical Formula: $C_{33}H_{44}O_3$
400 MHz, $CDCl_3$

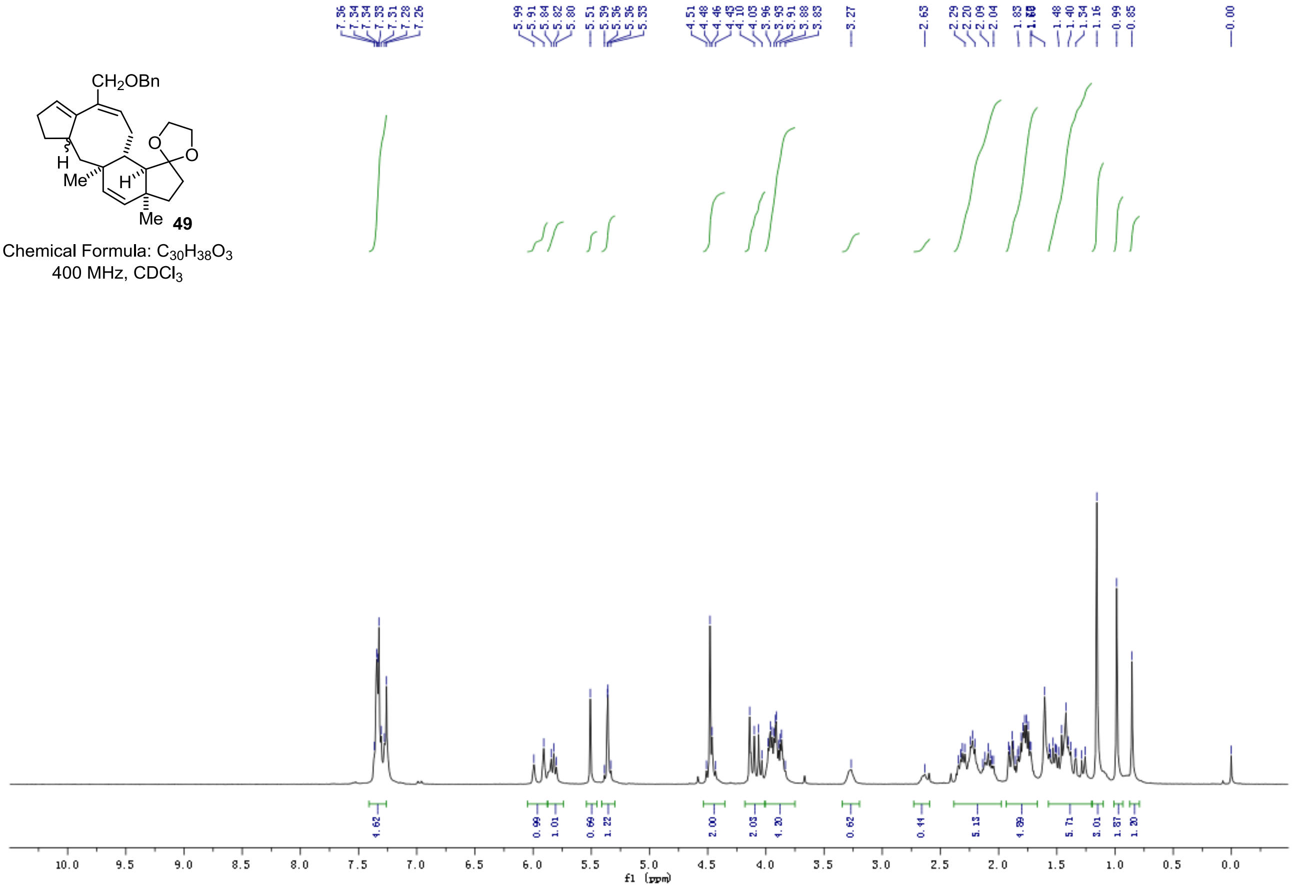


47

Chemical Formula: $C_{33}H_{44}O_3$
100 MHz, $CDCl_3$

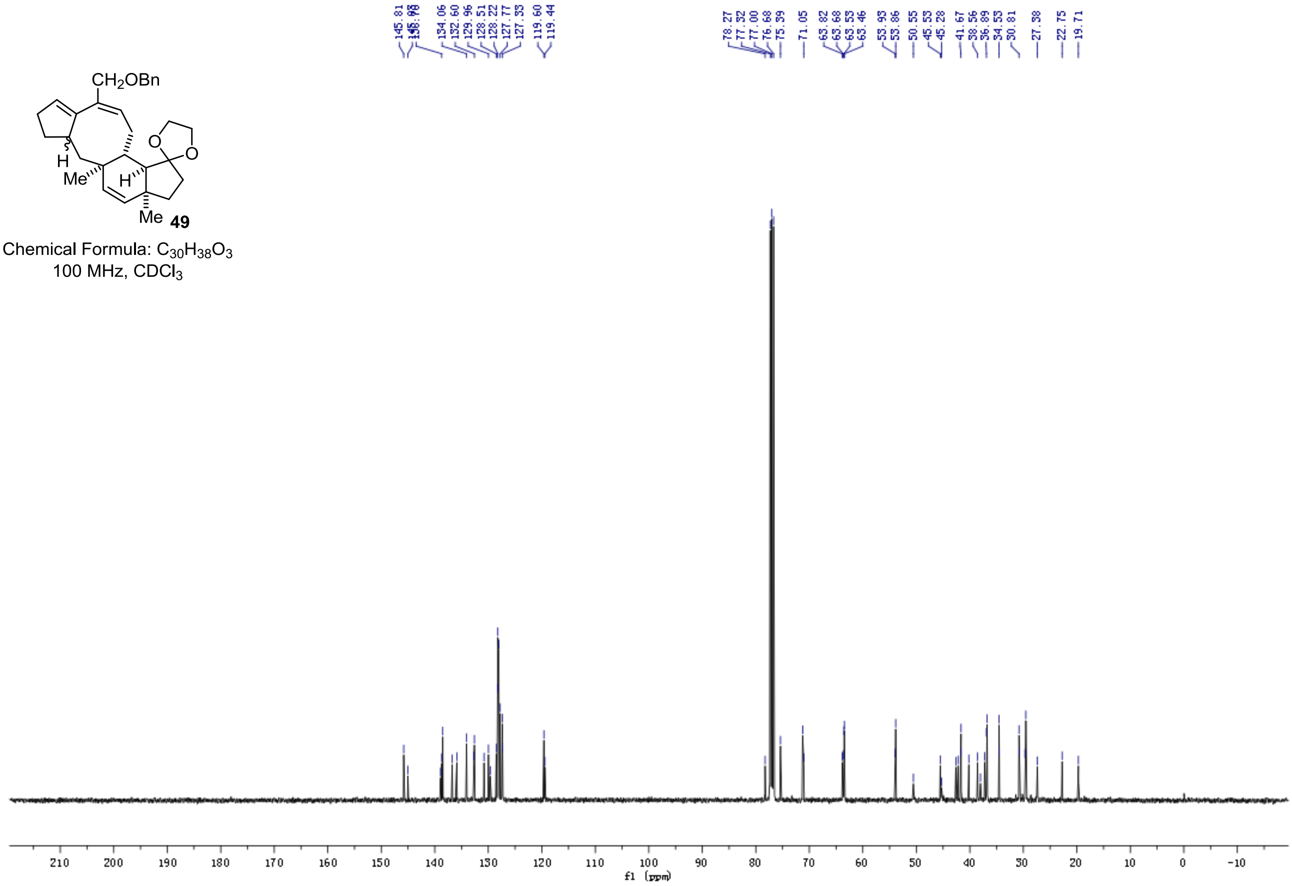

H
O
O
H
Me
H
Me
48
Chemical Formula: $C_{22}H_{30}O_2$
400 MHz, $CDCl_3$
7.26
6.10
6.06
6.03
6.01
5.62
5.60
5.53
5.51
5.49
5.47
5.37
5.34
5.33
3.95
3.94
3.93
3.92
3.90
3.90
3.89
3.88
3.88
3.22
3.20
2.56
2.15
2.04
1.99
1.89
1.83
1.79
1.74
1.59
1.47
1.43
1.33
1.15
0.99
0.96
0.94
0.92
0.86
-0.00
1.00
0.92
0.99
2.11
4.08
0.68
0.47
2.05
1.95
1.43
1.21
3.79
4.40
3.01
1.81
1.25
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)


H
O
O
H
Me
H
Me
48
Chemical Formula: $C_{22}H_{30}O_2$
100 MHz, $CDCl_3$
146.96
146.83
138.30
135.74
134.55
133.94
129.45
124.93
119.72
119.59
77.32
77.00
76.68
63.89
63.75
63.56
63.46
54.47
54.34
52.80
46.13
45.15
40.75
36.85
34.59
29.71
27.58
22.91
19.52
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)



49

Chemical Formula: $C_{30}H_{38}O_3$
400 MHz, $CDCl_3$



49

Chemical Formula: $C_{30}H_{38}O_3$
100 MHz, $CDCl_3$