Electronic Supplementary Material (ESI) for Organic Chemistry Frontiers.

Supporting Information

Stereoselective Total Synthesis of Orientalol F via Gold-Catalyzed Cycloisomerization

Yueqing Gu ‡[a], Jun Huang ‡[a], Jianxian Gong*[a] and Zhen Yang*[a, b]

[a]*Laboratory of Chemical Genomics, School of Chemical Biology and Biotechnology, Peking University Shenzhen Graduate School, Shenzhen 518055, China.*

[b]*Key Laboratory of Bioorganic Chemistry and Molecular Engineering of Ministry of Education, Beijing National Laboratory for Molecular Science, College of Chemistry and Molecular Engineering, and Peking-Tsing hua Center for Life Sciences, Peking University, Beijing 100871, China.*

‡*These authors contributed equally to this work.*

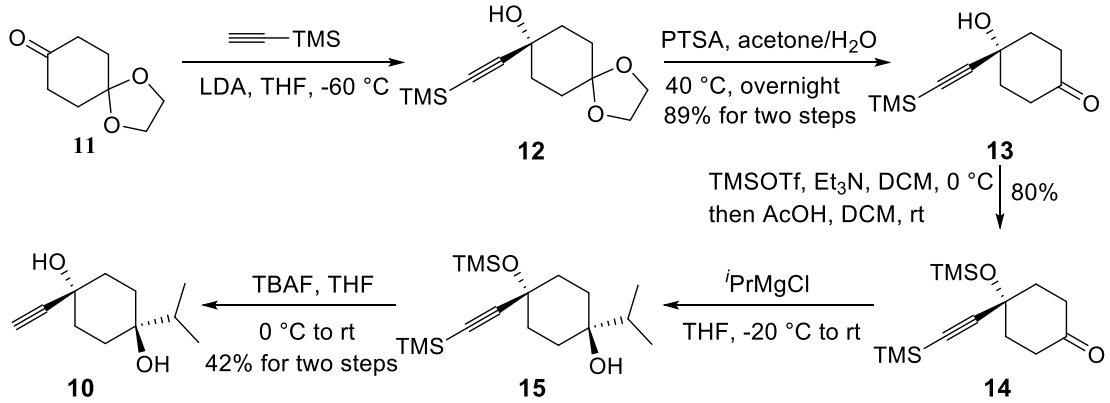
E-mail: zyang@pku.edu.cn
E-mail: gongjx@pku.edu.cn

Table of Contents

Part 1: General information

Unless otherwise mentioned, all reactions were carried out under a nitrogen atmosphere with dry solvents, unless otherwise noted. Reagents were purchased at the highest commercial quality and used without further purification, unless otherwise stated. Solvents purification was conducted according to Purification of Laboratory Chemicals (Peerrin, D. D.; Armarego, W. L. and Perrins, D. R., Pergamon Press: Oxford, 1980). Yields refer to chromatographically and spectroscopically (^{1}H NMR) homogeneous materials. Reactions were monitored by thin-layer chromatography (TLC) carried out on 0.25 mm Tsingdao silica gel plates (GF-254) and visualized under UV light at 254 nm. Staining was performed with an ethanolic solution of phosphomolybdic acid (PMA) and cerium sulfate, or by oxidative staining with an aqueous basic potassium permanganate ($KMnO_4$) solution and subsequent heating. Tsingdao silica gel (60, particle size 0.040-0.063 mm) was used for flash column chromatography. NMR spectra were recorded on either a Brüker Advance 400 (^{1}H: 400 MHz, ^{13}C: 100 MHz) or Brüker Advance 500 (^{1}H: 500 MHz, ^{13}C: 125 MHz) and were calibrated using residual undeuterated solvent as an internal reference ($CDCl_3$: ^{1}H NMR = 7.26 ppm, ^{13}C NMR = 77.0 ppm; CD_3OD: ^{1}H NMR = 3.31 ppm, ^{13}C NMR = 49.0 ppm; CD_2Cl_2: ^{1}H NMR =5.35 ppm, ^{13}C NMR = 53.3 ppm). The following abbreviations were used to explain the multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad. IR spectra were recorded on an IR Prestige-21 FTIR spectrometer with a KBr disc. High resolution mass spectrometric (HRMS) data were recorded on a Brüker Apex IV RTMS instrument and a VG Auto Spec-3000 spectrometer, respectively. CD spectrum was measured using the Applied Photophysics Chirascan with a 150W Xe lamp (165 nm – 900 nm). Optical rotation values were recorded on a Rudolph Research Analytical Autopol I polarimeter (Rudolph Research Co.).

Part 2: Experimental Procedures and Spectroscopic Date of Synthesized Compounds



Compound 13. To a stirred solution of ethynyltrimethylsilane (13.4 mL, 96.0 mmol, 1.5 equiv) in anhydrous THF (600 mL) at -60 °C was added LDA (44.8 mL, 89.6 mmol, 1.4 equiv, 2.0 M in THF). The mixture was stirred at -60 °C for 30 min, and then a solution of 1,4-dioxaspiro[4.5]decan-8-one **11** (10.0 g, 64.0 mmol, 1.0 equiv) in THF (40 mL) was added dropwise. After 20 min, the reaction was warmed up to ambient temperature slowly during 4 h, and quenched with saturated aqueous ammonium chloride (200 mL). The mixture was extracted with ethyl acetate (250 mL × 3), and the combined organic layers were dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The residue was directly dissolved in acetone/H_2O (360 mL/120 mL), and PTSA (2.20 g, 12.8 mmol, 0.2 equiv) was added into the solution at ambient temperature. The mixture was warmed up to 40 °C, and stirred overnight. After cooled to ambient temperature, the reaction was

quenched by careful addition of saturated aqueous sodium bicarbonate (100 mL). The mixture was extracted with ethyl acetate (200 mL × 4), and the combined organic layers were dried over Na_2SO_4, filtered, and concentrated *in vacuo*. Purification by flash column chromatography afforded ketone **13** (12.0 g, 57.0 mmol) as colorless oil in 89% yield for two steps.

Compound 13:

R_f = 0.40 (silica gel, hexane/EtOAc = 4:1).

^{1}H NMR (500 MHz, $CDCl_3$) δ = 3.09 (br, 1H), 2.51 – 2.42 (m, 4H), 2.22 – 2.06 (m, 4H), 0.13 (s, 9H).

^{13}C NMR (125 MHz, $CDCl_3$) δ = 210.5, 107.3, 89.3, 66.4, 38.7, 37.4, -0.2 ppm.

IR ν_{max} (film): 3286, 2953, 2928, 2158, 1738, 1722, 1694, 1420, 1364, 1256, 1229, 1126, 1092, 962, 841, 762 cm^{-1}.

HRMS (ESI): m/z calcd for $C_{11}H_{18}O_2NaSi$ $[M+Na]^+$: 233.0968; found: 233.0969.

Compound 14. To a solution of ketone **13** (5.45 g, 25.9 mmol, 1.0 equiv) in anhydrous DCM (200 mL) at 0 °C was added dried triethylamine (21.8 mL, 155.4 mmol, 6.0 equiv) followed by the addition of TMSOTf (14.1 mL, 77.7 mmol, 3.0 equiv). The reaction mixture was warmed up to ambient temperature slowly during 3 h, and then quenched with water (100 mL). The organic layer was separated, and the aqueous phase was extracted with DCM (150 mL × 2). The combined organic extracts were dried over Na_2SO_4 and filtered, and the solvents were removed *in vacuo*. The residue was dissolved in DCM (100 mL), and acetic acid (8.0 mL) was added. The mixture was stirred at ambient temperature overnight, and then quenched by careful addition of saturated aqueous sodium bicarbonate (100 mL) at 0 °C until no gas generated. The mixture was extracted with DCM (150 mL × 2), and the combined organic layers were dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The residue was purified by flash column chromatography to afford **14** (5.84 g, 20.7 mmol) in 80% yield as colorless oil.

Compound 14:

R_f = 0.53 (silica gel, hexane/EtOAc = 16:1).

^{1}H NMR (500 MHz, $CDCl_3$) δ = 2.51 – 2.41 (m, 2H), 2.43 – 2.33 (m, 2H), 2.08 (t, J = 6.8 Hz, 4H), 0.21 (s, 9H), 0.17 (s, 9H).

^{13}C NMR (125 MHz, $CDCl_3$) δ = 210.4, 107.7, 90.5, 67.5, 40.1, 37.3, 1.7, -0.3 ppm.

IR ν_{max} (film): 2963, 1724, 1350, 1252, 1103, 1043, 999, 951, 879, 843, 760 cm^{-1}.

HRMS (ESI): m/z calcd for $C_{14}H_{26}O_2NaSi_2$ $[M+Na]^+$: 305.1364; found: 305.1363.

Compound 10. To a flame dried round-bottom flask containing ketone **14** (2.00 g, 7.09 mmol, 1.0 equiv) was added anhydrous THF (70 mL), and the mixture was cooled to -20 °C. Isopropylmagnesium chloride (4.3 mL, 8.51 mmol, 1.2 equiv, 2.0 M in THF) was added into the solution, and the reaction mixture was warmed up to ambient temperature slowly during 4 h. The reaction was quenched with saturated aqueous ammonium chloride (40 mL), and the organic layer was separated. The aqueous phase was extracted with ethyl acetate (60 mL × 3). The combined organic extracts were washed with brine (20 mL), dried over Na_2SO_4 and filtered, and the solvents were removed *in vacuo*. The residue was dissolved in THF (50 ml), TBAF (7.80 ml, 7.80 mmol, 1.1 equiv, 1.0 M in THF) was added at 0 °C, and the reaction mixture was warmed up to ambient temperature slowly during 2 h. Next the reaction was quenched with saturated aqueous ammonium chloride (40 ml), and the organic layer was separated. The aqueous phase was extracted with ethyl acetate (60 mL × 3). The combined organic extracts were dried over Na_2SO_4 and filtered, and the solvents were removed *in vacuo*. Purification by flash column chromatography afforded the desired alcohol **10** (542 mg, 2.98 mmol) in 42% yield along with its diastereoisomer **10'** (400 mg, 2.20 mmol) in 31% yield as thick oil.

Compound 10:

R_f = 0.60 (silica gel, hexane/EtOAc = 2:1).

^{1}H NMR (400 MHz, *d*$_4$-MeOD) δ = 2.72 (s, 1H), 2.09 – 1.95 (m, 2H), 1.81 – 1.66 (m, 4H), 1.66 – 1.51 (m, 1H), 1.48 – 1.38 (m, 2H), 0.92 (s, 3H), 0.90 (s, 3H).

^{13}C NMR (100 MHz, *d*$_4$-MeOD) δ = 90.3, 73.1, 71.1, 66.4, 38.9, 35.2, 29.4, 17.3 ppm.

IR ν_{max} (film): 3358, 3306, 2963, 2936, 2884, 2492, 2241, 2075, 1437, 1370, 1260, 1123, 978, 820 cm^{-1}.

HRMS (ESI): m/z calcd for $C_{11}H_{18}O_2Na$ $[M+Na]^+$: 205.1199; found: 205.1199.

Compound 10':

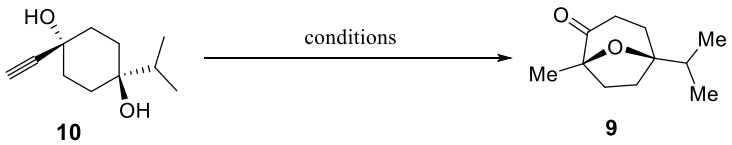
R_f = 0.40 (silica gel, hexane/EtOAc = 2:1).

^{1}H NMR (400 MHz, *d*$_4$-MeOD) δ 2.81 (s, 1H), 1.95 – 1.84 (m, 2H), 1.79 – 1.67 (m, 4H), 1.65 – 1.51 (m, 3H), 0.92 (d, J = 6.9 Hz, 3H), 0.92 (d, J = 6.9 Hz, 3H).

^{13}C NMR (100 MHz, *d*$_4$-MeOD) δ 87.8, 73.4, 72.9, 69.6, 39.3, 36.1, 32.1, 17.4 ppm.

IR ν_{max} (film): 3358, 3306, 2963, 2936, 2884, 2492, 2241, 2075, 1437, 1370, 1260, 1123, 978, 820 cm^{-1}.

HRMS (ESI): m/z calcd for $C_{11}H_{18}O_2Na$ $[M+Na]^+$: 205.1199; found: 205.1199.



10 **9**

entry	catalyst	solvent	time	yield(%)[a]
1	$(Ph_3P)AuCl / AgBF_4$	DCM	2h	75
2	$(Ph_3P)AuCl / AgOTf$	DCM	2h	72
3	$(Ph_3P)AuCl / AgSbF_6$	DCM	2h	80
4	$(Ph_3P)AuCl / AgNTf_2$	DCM	2h	85
5	$IPrAuCl / AgNTf_2$	DCM	2h	46
6	$(t\text{-}Bu)_3PAuCl / AgNTf_2$	DCM	2h	50
7	$(Ph_3P)AuCl / AgNTf_2$	DCE	2h	79
8	$(Ph_3P)AuCl / AgNTf_2$	THF	3h	0
9	$(Ph_3P)AuCl / AgNTf_2$	CH_3CN	3h	0
10	$(Ph_3P)AuCl / AgNTf_2$	Toluene	3h	0
11	$(Ph_3P)AuCl$	DCM	3h	trace
12	$AgNTf_2$	DCM	3h	0
13	$PtCl_2$	DCM	3h	0
14	PTSA	DCM	3h	0

[a]Isolated yield

Procedure for entry 1 to 4:

A mixture of Ph_3PAuCl (10.9 mg, 0.022 mmol, 0.05 equiv) and $AgBF_4$ (4.3 mg, 0.022 mmol, 0.05 equiv for entry 1) or AgOTf (5.7 mg, 0.022 mmol, 0.05 equiv for entry 2) or $AgSbF_6$ (7.6 mg, 0.022 mmol, 0.05 equiv for entry 3) or $AgNTf_2$ (8.4 mg, 0.022 mmol, 0.05 equiv for entry 4) in DCM (2.0 mL) was stirred for 0.5 h to generate the active gold catalyst in situ. Then the mixture was added into a stirred solution of the substrate (80 mg, 0.44 mmol, 1.0 equiv) in DCM (8.0 mL), and the reaction was stirred at ambient temperature for 2 h. next most of the solvents were removed *in vacuo*. Direct purification by flash column chromatography afforded the desired ketone **9** as colorless oil in 75% yield (for entry 1) or 72% yield (for entry 2) or 80% yield (for entry 3) or 85% yield (for entry 4).

Procedure for entry 5 to 6:

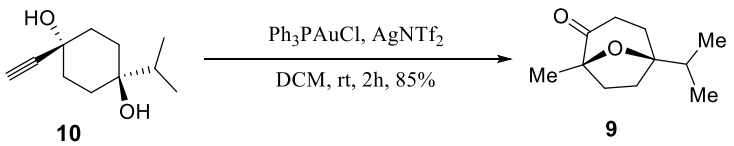
A mixture of IprAuCl (13.7 mg, 0.022 mmol, 0.05 equiv for entry 5) or $(t\text{-Bu})_3PAuCl$ (9.6 mg, 0.022 mmol, 0.05 equiv for entry 6) and $AgNTf_2$ (8.4 mg, 0.022 mmol, 0.05 equiv) in DCM (2.0 mL) was stirred for 0.5 h to generate the active gold catalyst in situ. Then the mixture was added into a stirred solution of the substrate (80 mg, 0.44 mmol, 1.0 equiv) in DCM (8.0 mL), and the reaction was stirred at ambient temperature for 2 h. next most of the solvents were removed *in vacuo*. Direct purification by flash column chromatography afforded the desired ketone **9** as colorless oil in 46% yield (for entry 5) or 50% yield (for entry 6).

Procedure for entry 7 to 10:

A mixture of Ph_3PAuCl (10.9 mg, 0.022 mmol, 0.05 equiv) and $AgNTf_2$ (8.4 mg, 0.022 mmol, 0.05 equiv) in DCE (2.0 mL for entry 7) or THF (2.0 ml for entry 8) or CH_3CN (2.0 ml for entry 9) or toluene (2.0 ml for entry 10) was stirred for 0.5 h to generate the active gold catalyst in situ. Then the mixture was added into a stirred solution of the substrate (80 mg, 0.44 mmol, 1.0 equiv) in DCE (8.0 mL for entry 7) or THF (8.0 ml for entry 8) or CH_3CN (8.0 ml for entry 9) or toluene (8.0 ml for entry 10), and the reaction was stirred at ambient temperature for 2 h or 3 h. next most of the solvents were removed *in vacuo*. Direct purification by flash column chromatography afforded the desired ketone **9** as colorless oil in 79% yield (for entry 7). No desired ketone **9** was obtained (for entry 8 to 10).

Procedure for entry 11 to 14:

To a stirred solution of the substrate (80 mg, 0.44 mmol, 1.0 equiv) in DCM (8.0 mL) was added Ph_3PAuCl (10.9 mg, 0.022 mmol, 0.05 equiv for entry 11) or $AgNTf_2$ (8.4 mg, 0.022 mmol, 0.05 equiv for entry 12) or $PtCl_2$ (5.9 mg, 0.022 mmol, 0.05 equiv for entry 13) or PTSA (3.8 mg, 0.022 mmol, 0.05 equiv for entry 14), and the reaction was stirred at ambient temperature for 3 h. No desired ketone **9** was obtained.



10 **9**

Compound 9. A mixture of Ph_3PAuCl (68.3 mg, 0.138 mmol, 0.05 equiv) and $AgNTf_2$ (52.4 mg, 0.138 mmol, 0.05 equiv) in DCM (5.0 mL) was stirred for 0.5 h to generate the active gold catalyst in situ. Then the

mixture was added into a stirred solution of the substrate (500 mg, 2.75 mmol, 1.0 equiv) in DCM (50.0 mL), and the reaction was stirred at ambient temperature for 2 h. next most of the solvents were removed *in vacuo*. Direct purification by flash column chromatography afforded the desired alcohol **9** (425 mg, 2.34 mmol) in 85% yield as colorless oil.

Compound 9:

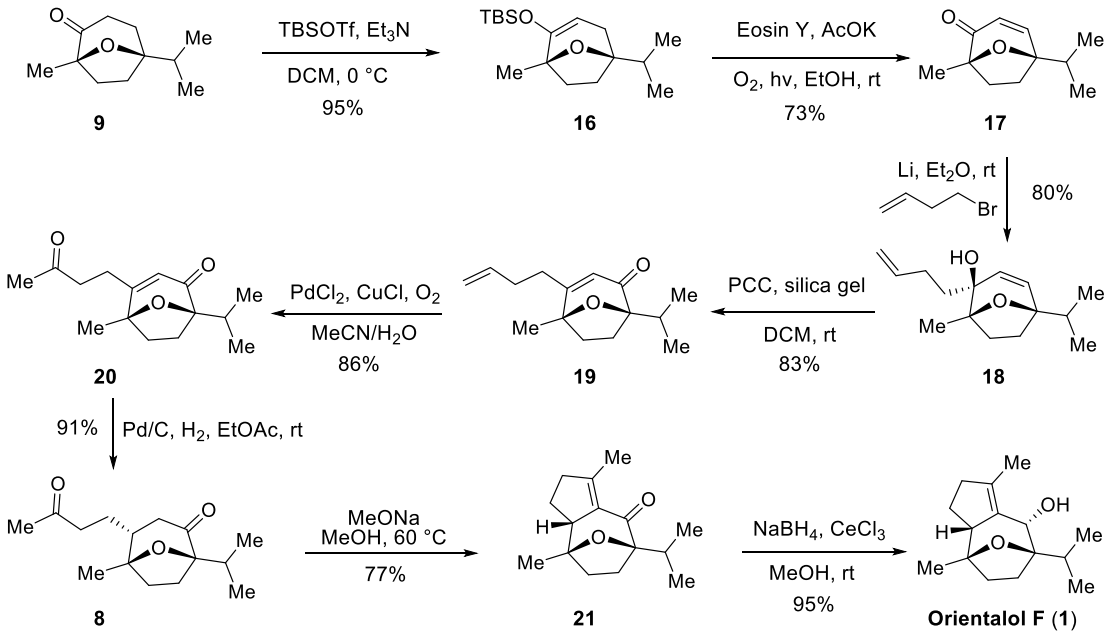
R_f = 0.80 (silica gel, hexane/EtOAc = 4:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ = 2.43 – 2.34 (m, 2H), 2.06 – 1.81 (m, 6H), 1.81 – 1.69 (m, 1H), 1.29 (s, 3H), 0.94 (d, J = 6.4 Hz, 3H), 0.92 (d, J = 6.4 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ = 209.9, 85.9, 85.7, 36.0, 35.8, 32.9, 32.9, 31.8, 19.1, 17.8, 17.3 ppm.

IR ν_{max} (film): 2926, 2961, 2851, 1452, 1273, 1261, 762, 750 cm^{-1}.

HRMS (ESI): m/z calcd for $C_{11}H_{18}O_2Na$ $[M+Na]^+$: 205.1199; found: 205.1197



Compound 16. To a solution of **9** (1.56 g, 8.57 mmol, 1.0 equiv) in anhydrous DCM (40 mL) was added dried triethylamine (3.6 mL, 25.7 mmol, 3.0 equiv) at 0 °C, followed by the addition of TBSOTf (3.0 mL, 12.9 mmol, 1.5 equiv), and the reaction mixture was then gradually warmed up to room temperature during 3 h. The reaction was quenched with water (20 mL), and the mixture was extracted with DCM (40 mL × 2). The combined organic extracts were dried over Na_2SO_4, then filtered off, and concentrated under vacuum, The residue was purified by a flash column chromatography on silica gel (pre-treated with Et_3N) to give **16** (2.42 g, 8.1 mmol) in 95% yield as colorless oil.

Compound 16:

R_f = 0.80 (silica gel, hexane/EtOAc = 20:1).

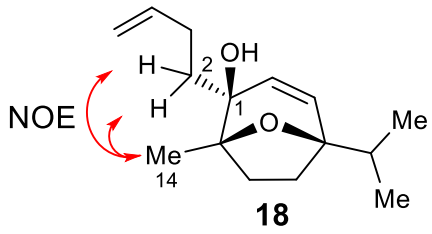
^{1}H NMR (500 MHz, CD_2Cl_2) δ 4.56 (dd, J = 5.0, 2.3 Hz, 1H), 2.34 (d, J = 15.8 Hz, 1H), 2.13 – 2.08 (m, 1H), 1.92 – 1.80 (m, 3H), 1.74 – 1.70 (m, 1H), 1.60 – 1.54 (m, 1H), 1.33 (s, 3H), 0.96 (s, 9H), 0.94 (d, J = 2.8 Hz, 3H), 0.93 (d, J = 2.8 Hz, 3H), 0.21 (s, 3H), 0.18 (s, 3H).

^{13}C NMR (125 MHz, CD_2Cl_2) δ 155.5, 96.2, 84.5, 81.0, 41.3, 36.2, 35.0, 32.4, 25.5, 19.7, 18.0, 17.3, 16.7, -4.5, -5.4 ppm.

IR ν_{max} (film): 2959, 2930, 2858, 1772, 1654, 1635, 1472, 1377, 1247, 1202, 1057, 839 cm^{-1}.
HRMS (ESI): m/z calcd for $C_{17}H_{33}O_2Si$ $[M+H]^+$: 297.2244; found: 297.2244.

Compound 17. To a solution of **16** (750 mg, 2.53 mmol, 1.0 equiv) in EtOH (10 ml) was added AcOK (297 mg, 3.03 mmol, 1.2 equiv) and Eosin Y (16 mg, 0.025 mmol, 0.01 equiv), and the reaction mixture was degassed with oxygen three times. And the round-bottom flask containing the reaction mixture was placed next to (2 cm) a housedhold florescent bulb (Philip, Torado-48W) at room temperature. The reaction was stirred under an oxygen balloon for 48 h, then the solvent was removed and the residue was purified by flash gel chromatography to give **17** (332 mg, 1.84 mmol) in 73% yield as colorless oil.
Compound 17:
R_f = 0.40 (silica gel, hexane/EtOAc = 20:1).
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.19 (d, J = 9.9 Hz, 1H), 6.02 (d, J = 9.9 Hz, 1H), 2.01 – 1.96 (m, 1H), 1.95 – 1.89 (m, 2H), 1.88 – 1.81 (m, 2H), 1.47 (s, 3H), 1.05 (d, J = 7.0 Hz, 3H), 1.02 (d, J = 7.0 Hz, 3H).
^{13}C NMR (125 MHz, $CDCl_3$) δ 199.2, 153.2, 126.5, 86.2, 85.8, 34.4, 33.0, 32.8, 19.7, 17.8, 17.7 ppm.
IR ν_{max} (film): 2957, 2916, 2849, 1706, 1469, 1377, 1250, 1123, 869, 771 cm^{-1}.
HRMS (ESI): m/z calcd for $C_{11}H_{17}O_2$ $[M+H]^+$: 181.1223; found: 181.1225.

Compound 18. To a solution of lithium particle (174 mg, 25.0 mmol, 15.0 equiv) in ether (10 ml) was added 4-bromo-1-butene (2.54 ml, 25.0 mmol, 15.0 equiv) and substrate **17** (300 mg, 1.67 mmol, 1.0 equiv) in ether (3 ml) slowly under argon at 0 °C, the resultant mixture was stirred at room temperature for further 16 h. The reaction was worked up by filtration to remove the remained lithium particle, and the filtrate was then quenched by addition of a saturated aqueous solution of ammonium chloride (5 mL). The mixture was extracted with ethyl acetate (10 mL × 3), and the combined organic extracts were dried over Na_2SO_4, and filtered off. The filtrate was concentrated under vacuum, and the residue was purified by a flash chromatography to give product **18** (315 mg, 1.33 mmol) as a single isomer in 80% yield as colorless oil.
Compound 18:
R_f = 0.40 (silica gel, hexane/EtOAc = 8:1).
^{1}H NMR (400 MHz, $CDCl_3$) δ 5.96 – 5.75 (m, 2H), 5.48 (d, J = 10.0 Hz, 1H), 5.04 (dd, J = 17.2, 1.8 Hz, 1H), 4.95 (dd, J = 17.2, 1.8 Hz, 1H), 2.42 (ddd, J = 12.6, 8.9, 7.5 Hz, 1H), 2.33 – 2.05 (m, 2H), 1.98 – 1.91 (m, 1H), 1.87 – 1.69 (m, 2H), 1.66 – 1.54 (m, 3H), 1.49 (s, 1H), 1.31 (s, 3H), 0.95 (d, J = 4.1 Hz, 3H), 0.94 (d, J = 4.1 Hz, 3H).
^{13}C NMR (100 MHz, $CDCl_3$) δ 139.4, 131.2, 130.7, 114.2, 86.0, 84.3, 75.7, 37.4, 35.9, 34.1, 32.8, 28.7, 20.8, 17.9, 17.8 ppm.
IR ν_{max} (film): 2960, 2927, 1684, 1654, 1560, 1300, 1266, 1202, 1107, 1071, 1022, 911 cm^{-1}.
HRMS (ESI): m/z calcd for $C_{15}H_{25}O_2$ $[M+H]^+$: 237.1849; found: 237.1848.
The relative stereostructure of **18** was characterized by NOESY experiment, the correlations between the protons on C-2 and C-14 was observed which suggests that the butenyl group and the methyl are located on the same side.



18

Compound 19. To a solution of the allylic alcohol **18** (80 mg, 0.34 mmol, 1.0 equiv) in DCM (5 ml) was added PCC (218 mg, 1.02 mmol, 3.0 equiv) and silica gel (400 mg). The reaction mixture was stirred at room temperature for 8 h. Then the mixture was directly purification by a flash column chromatography to give the product **19** (66 mg, 0.28 mmol) in 83% yield as colorless oil.

Compound 19:

R_f = 0.60 (silica gel, hexane/EtOAc = 8:1).

^{1}H NMR (500 MHz, $CDCl_3$) δ 5.85 – 5.79 (m, 1H), 5.77 (s, 1H), 5.13 – 4.99 (m, 2H), 2.50 – 2.37 (m, 1H), 2.30 – 2.13 (m, 5H), 1.89 – 1.84 (m, 1H), 1.77 – 1.69 (m, 1H), 1.67 – 1.60 (m, 1H), 1.53 (s, 3H), 1.04 (d, J = 6.9 Hz, 3H), 1.03 (d, J = 6.9 Hz, 3H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 199.4, 168.2, 136.8, 122.8, 115.8, 90.5, 82.2, 36.4, 31.0, 30.5, 30.4, 29.6, 21.7, 17.9, 16.6 ppm.

IR ν_{max} (film): 2981, 2968, 2932, 1687, 1658, 1618, 1273, 1211, 1181, 1126, 1071, 999, 914 cm^{-1}.

HRMS (ESI): m/z calcd for $C_{15}H_{23}O_2$ $[M+H]^+$: 235.1693; found: 235.1696.

Compound 20. To a solution of alkene **19** (60 mg, 0.26 mmol, 1.0 equiv) in CH_3CN/H_2O (3/1, 8 mL) was added $PdCl_2$ (2.3 mg, 0.013 mmol, 0.05 equiv) and CuCl (31 mg, 0.31 mmol, 1.2 equiv), and the reaction mixture was degassed by oxygen, and then stirred at room temperature for 12 h. The mixture was diluted with water (6.0 mL), and extracted with diethyl ether (15 mL × 4). The combined organic extracts were dried over Na_2SO_4 and filtered off. The filtrate was removed under vacuum, and the residue was purified by a flash chromatography on silica gel to give product **20** (55 mg, 0.22 mmol) in 86% yield as colorless oil.

Compound 20:

R_f = 0.20 (silica gel, hexane/EtOAc = 8:1).

^{1}H NMR (500 MHz, $CDCl_3$) δ 5.62 (s, 1H), 2.73 – 2.52 (m, 3H), 2.49 – 2.36 (m, 1H), 2.28 – 2.22 (m, 1H), 2.20 (s, 3H), 2.19 – 2.13 (m, 1H), 1.96 – 1.89 (m, 1H), 1.78 – 1.70 (m, 1H), 1.67 – 1.60 (m, 1H), 1.53 (s, 3H), 1.03 (d, J = 6.7 Hz, 3H), 1.03 (d, J = 6.7 Hz, 3H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 206.2, 199.1, 167.7, 124.4, 90.5, 82.4, 39.6, 36.2, 30.5, 30.0, 29.6, 24.8, 21.6, 17.9, 16.6 ppm.

IR ν_{max} (film): 2956, 2925, 2869, 2854, 1720, 1687, 1654, 1459, 1380, 1263, 1162, 1071, 1032, 739 cm^{-1}.

HRMS (ESI): m/z calcd for $C_{15}H_{23}O_3$ $[M+H]^+$: 251.1642; found: 251.1643.

Compound 8. To a solution of the substrate **20** (40 mg, 0.16 mmol, 1.0 equiv) in ethyl acetate (5 ml) was added palladium on carbon (17 mg, 0.016 mmol, 0.1 equiv, palladium 10% on carbon), the reaction was degassed by hydrogen, and resultant mixture was stirred at room temperature for 8 h. The mixture was filtered off through a silica gel pad, and the filtrate was concentrated under vacuum. The residue was purified by a flash chromatography to give product **8** (37 mg, 0.15 mmol) in 91% yield as a single isomer.

Compound 8:

R_f = 0.60 (silica gel, hexane/EtOAc = 2:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 2.51 – 2.31 (m, 3H), 2.15 (s, 3H), 2.13 – 2.07 (m, 2H), 2.00 – 1.98 (m, 3H), 1.83 – 1.73 (m, 1H), 1.73 – 1.66 (m, 1H), 1.64 – 1.55 (m, 1H), 1.38 (s, 3H), 1.37 – 1.28 (m, 1H), 0.95 (d, J = 2.1 Hz, 3H), 0.94 (d, J = 2.1 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 208.0, 207.4, 89.9, 84.0, 48.0, 40.7, 40.0, 30.7, 30.5, 30.0, 29.8, 25.5, 24.4, 17.9, 16.6 ppm.

IR ν_{max} (film): 2957, 2925, 2854, 1736, 1720, 1511, 1276, 1263, 1045, 1016, 761, 751 cm^{-1}.

HRMS (ESI): m/z calcd for $C_{15}H_{25}O_3$ $[M+H]^+$: 253.1798; found: 253.1799.

Compound 21. To a solution of diketone **8** (25 mg, 0.1 mmol, 1.0 equiv) in anhydrous MeOH (4 mL) was added NaOMe (16 mg, 0.3 mmol, 3.0 equiv) at room temperature. The reaction mixture was warmed up to 60 °C, and after stirred for 5 h, the reaction was quenched with saturated aqueous ammonium chloride (4 mL). The organic layer was separated, and the aqueous phase was extracted with ethyl acetate (5 mL × 3). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated *in vacuo*. Purification by flash column chromatography afforded the enone **21** (18 mg, 0.077 mmol) in 77% yield as colorless oil.

Compound 21:

R_f = 0.70 (silica gel, hexane/EtOAc = 4:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 3.22 (t, J = 7.5 Hz, 1H), 2.57 – 2.43 (m, 1H), 2.35 – 2.25 (m, 1H), 2.20 (m, 1H), 2.08 (s, 3H), 2.06 – 1.95 (m, 2H), 1.95 – 1.84 (m, 1H), 1.69 – 1.58 (m, 1H), 1.53 – 1.38 (m, 2H), 1.34 (s, 3H), 1.03 (d, J = 6.9 Hz, 3H), 1.02 (d, J = 6.9 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 199.9, 154.4, 131.9, 91.1, 84.4, 57.9, 38.8, 33.3, 30.5, 30.0, 26.0, 24.6, 18.4, 17.3, 15.9 ppm.

IR ν_{max} (film): 2965, 2944, 2876, 1736, 1720, 1658, 1459, 1420, 1117, 1032 cm^{-1}.

HRMS (ESI): m/z calcd for $C_{15}H_{23}O_2$ $[M+H]^+$: 235.1693; found: 235.1694.

Orientalol F (1). To a solution of **21** (18 mg, 0.077 mmol, 1.0 equiv) in MeOH (4 ml) was added $CeCl_3.(H_2O)_7$ (32 mg, 0.085 mmol, 1.1 equiv) and $NaBH_4$ (3 mg, 0.085 mmol, 1.1 equiv) at room temperature. After stirring the mixture for 36 h the reaction was quenched by the addition of saturated aqueous solution of ammonium chloride (1 mL). The mixture was extracted with ethyl acetate (8 mL× 3). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated *in vacuo*. Purification by flash column chromatography afforded Orientalol F (**1**) (17 mg, 0.073 mmol) in 95% yield as colorless oil.

Orientalol F (**1**):

R_f = 0.30 (silica gel, hexane/EtOAc = 4:1).

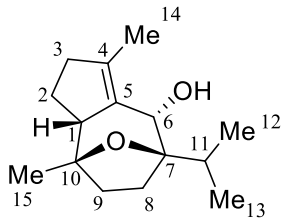
^{1}H NMR (500 MHz, $CDCl_3$) δ 4.44 (s, 1H), 2.68 (t, J = 7.5 Hz, 1H), 2.35 – 2.27 (m, 1H), 2.24 – 2.17 (m, 1H), 1.98 – 1.93 (m, 1H), 1.89 (s, 3H), 1.84 – 1.79 (m, 2H), 1.76 – 1.58 (m, 2H), 1.47 (s, 1H), 1.36 – 1.22 (m, 2H), 1.19 (s, 3H), 1.04 (d, J = 7.0 Hz, 3H), 1.02 (d, J = 7.0 Hz, 3H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 133.6, 132.9, 86.7, 84.4, 74.0, 57.7, 39.1, 31.8, 31.7, 28.6, 24.0, 23.9, 18.1, 17.3, 14.6 ppm.

IR ν_{max} (film): 2965, 2929, 2880, 2854, 1684, 1654, 1374, 1254, 1176, 1110, 1074, 1016, 973 cm^{-1}.

HRMS (ESI): m/z calcd for $C_{15}H_{25}O_2$ $[M+H]^+$: 237.1849; found: 237.1839.

Part 3: Comparison of the Spectra of Natural and Synthetic Orientalol F

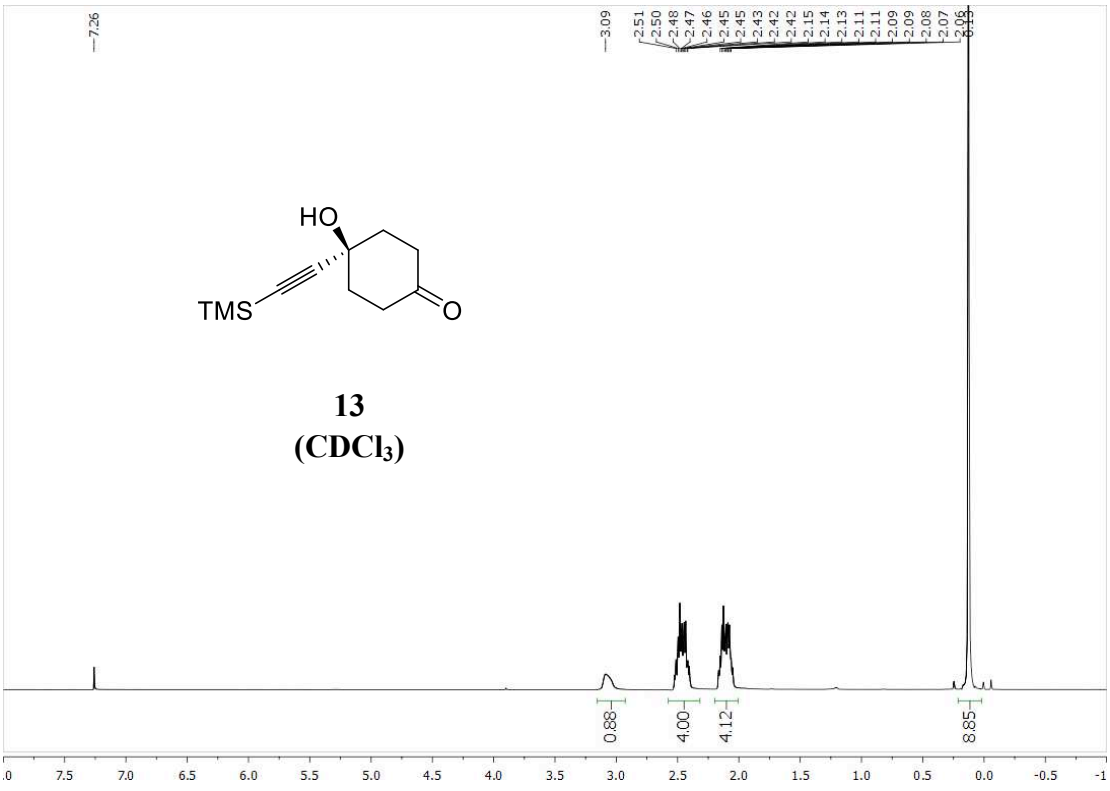


Orientalol F (1)

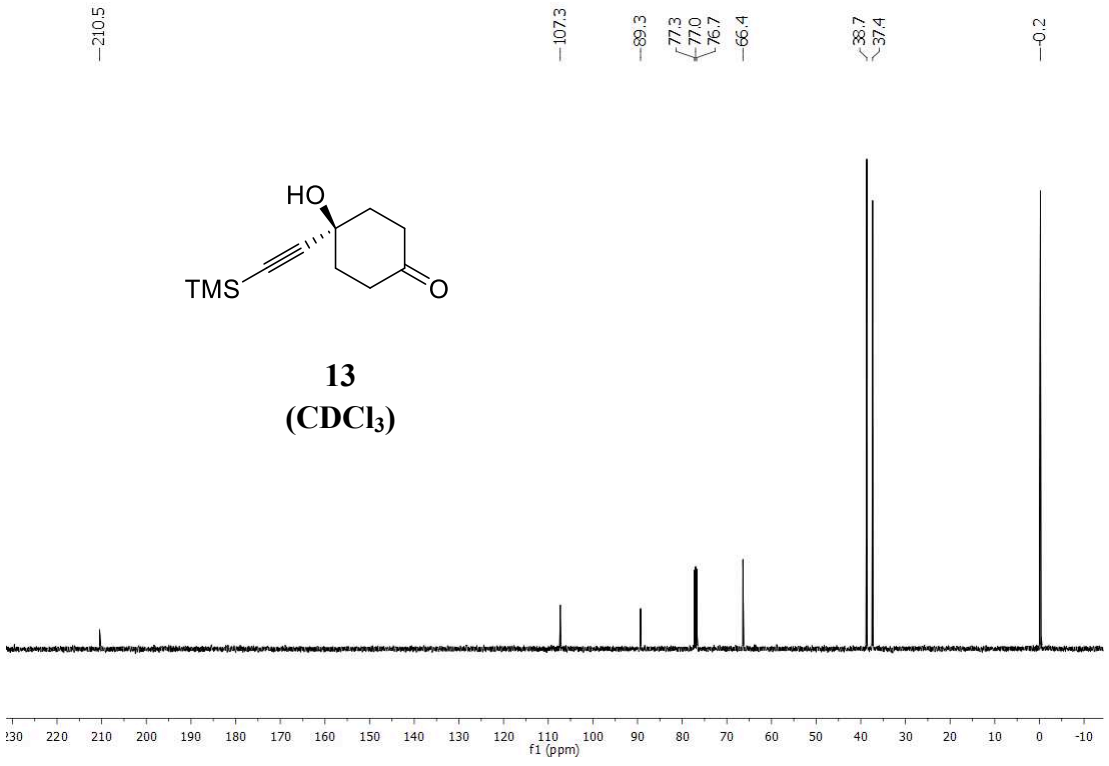
	^{1}H NMR ($CDCl_3$)			^{13}C NMR ($CDCl_3$)		
	Natural δ^{1H} [ppm] 400 MHz	Synthetic δ^{1H} [ppm, mult, J(Hz)] 500 MHz	Δδ ppm	Natural δ^{13C} [ppm] 100 MHz	Synthetic δ^{13C} [ppm] 125 MHz	Δδ ppm
1	2.69	2.68 (t, 7.5)	0.01	57.7 CH	57.7 CH	0
2	1.21, 1.81	1.26 – 1.20 (m) 1.82 – 1.79 (m)	/	24.0 CH_2	23.9 CH_2	0.1
3	2..31, 2.20	2.35 – 2.27 (m) 2.24 – 2.17 (m)	/	39.1 CH_2	39.1 CH_2	0
4				133.6 qC	133.6 qC	0
5				133.0 qC	132.9 qC	0.1
6	4.44	4.44 (s)	0	74.0 CH	74.0 CH	0
7				86.7 qC	86.7 qC	0
8	1.71, 1.60	1.73 – 1.69 (m) 1.64 – 1.58 (m)	/	28.6 CH_2	28.6 CH_2	0
9	1.83, 1.29	1.84 – 1.82 (m) 1.32 – 1.27 (m)	/	31.7 CH_2	31.7 CH_2	0
10				84.5 qC	84.4 qC	0.1
11	1.95	1.98 – 1.93 (m)	/	31.8 CH	31.8 CH	0
12	1.01	1.02 (d, 7.0)	0.01	17.3 CH_3	17.3 CH_3	0
13	1.03	1.04 (d, 7.0)	0.01	18.2 CH_3	18.1 CH_3	0.1
14	1.89	1.89 (s)	0	14.7 CH_3	14.6 CH_3	0.1
15	1.19	1.19 (s)	0	24.1 CH_3	24.0 CH_3	0

Part 4: NMR spectra

^{1}H and ^{13}C NMR spectra for 13

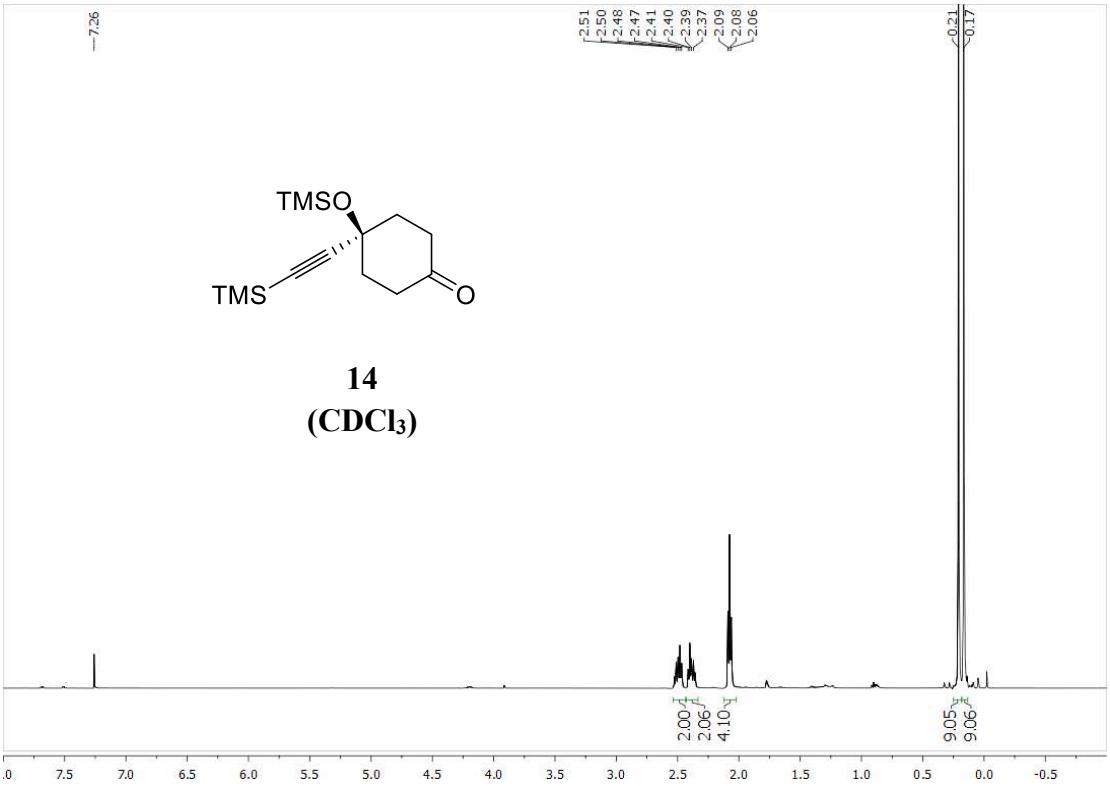


13
($CDCl_3$)

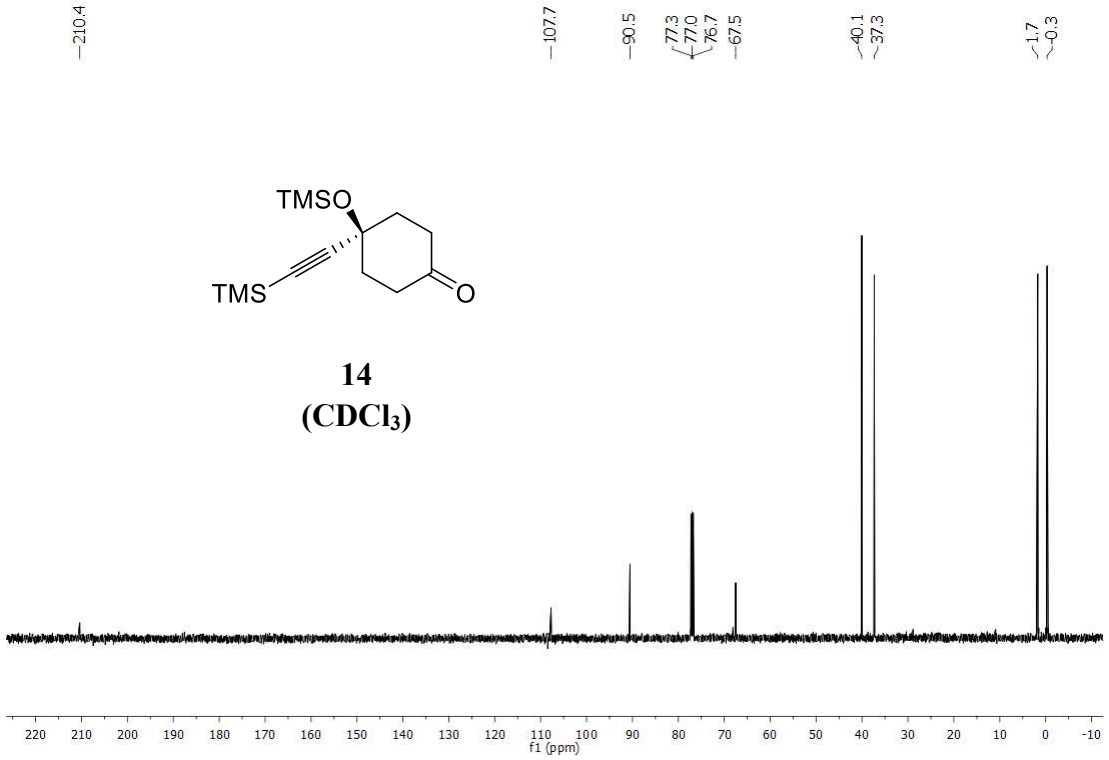


13
($CDCl_3$)

^{1}H and ^{13}C NMR spectra for 14

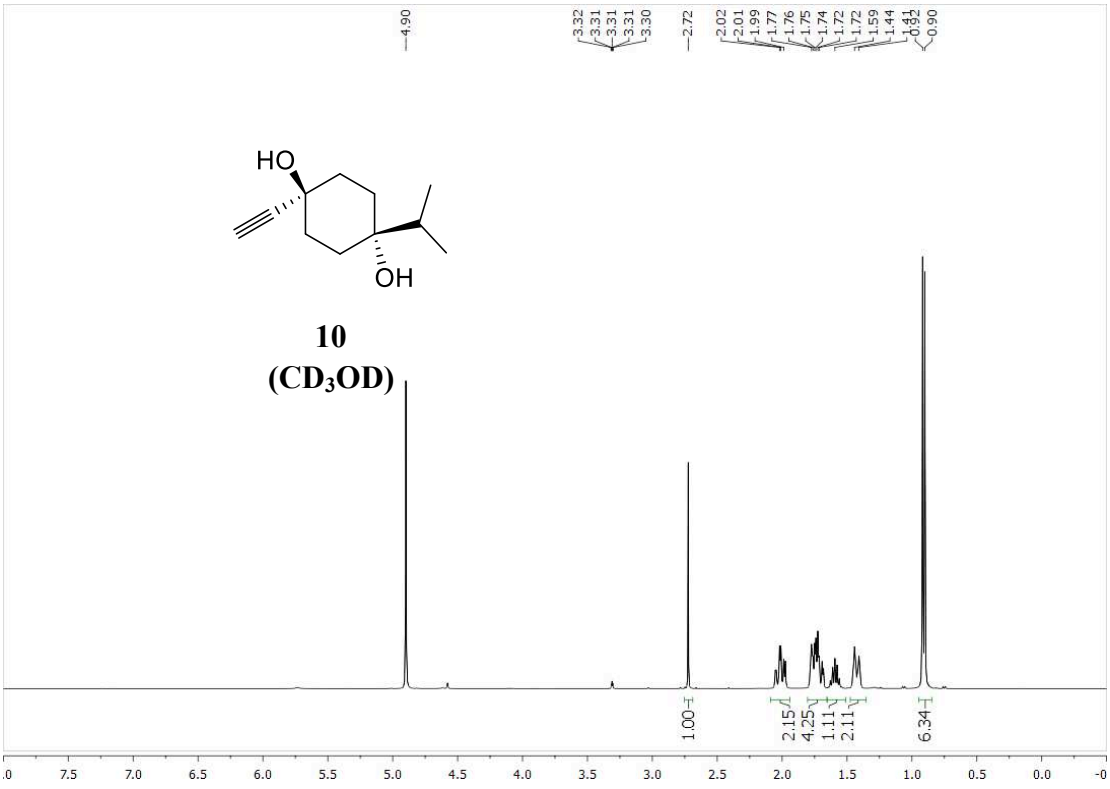


14
($CDCl_3$)

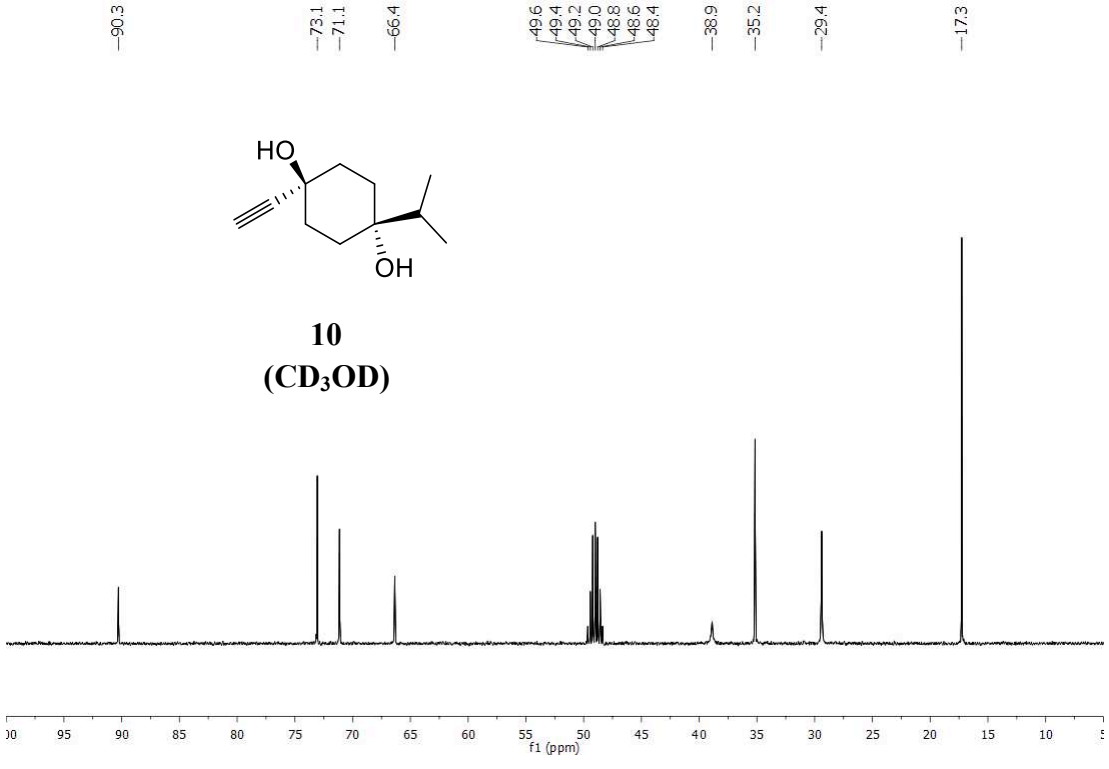


14
($CDCl_3$)

^{1}H and ^{13}C NMR spectra for 10

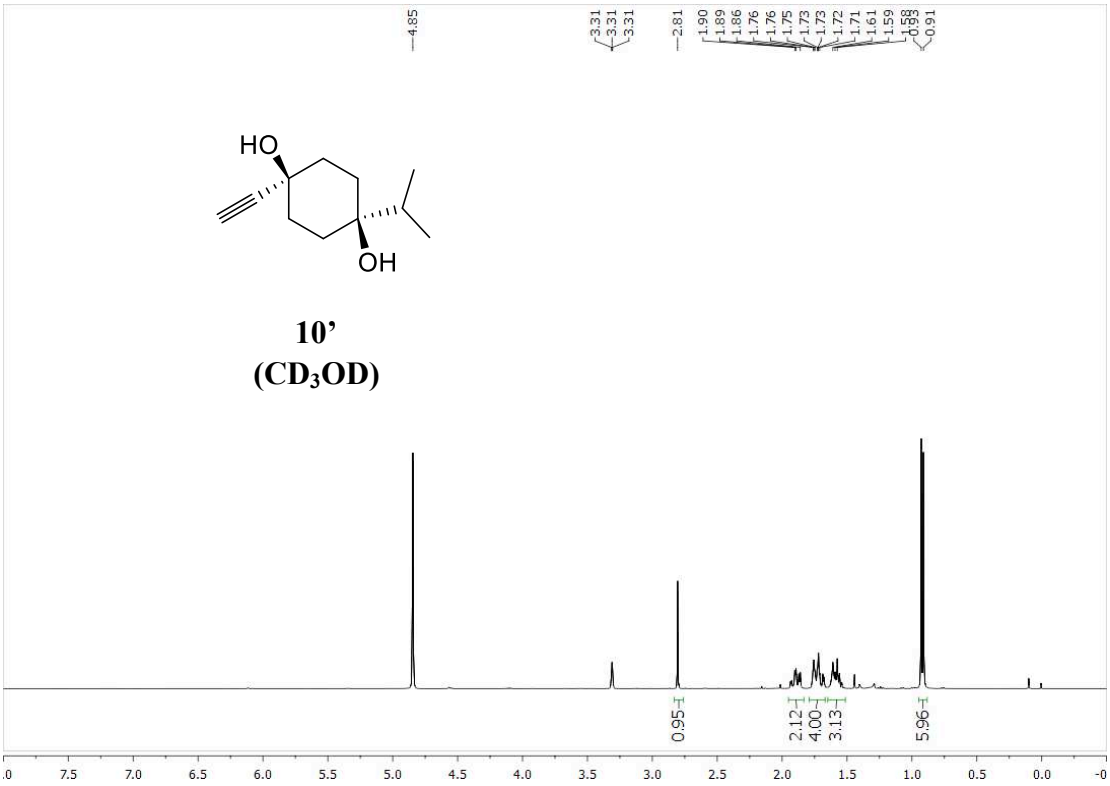


10
(CD_3OD)

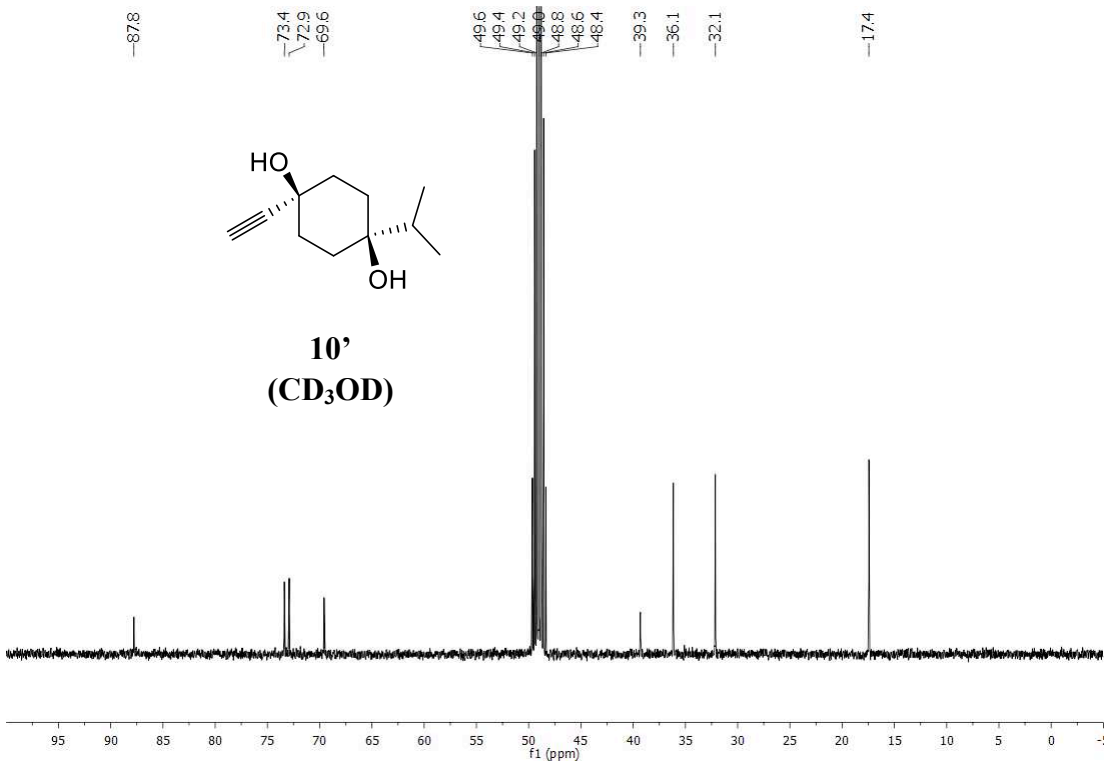


10
(CD_3OD)

^{1}H and ^{13}C NMR spectra for 10’

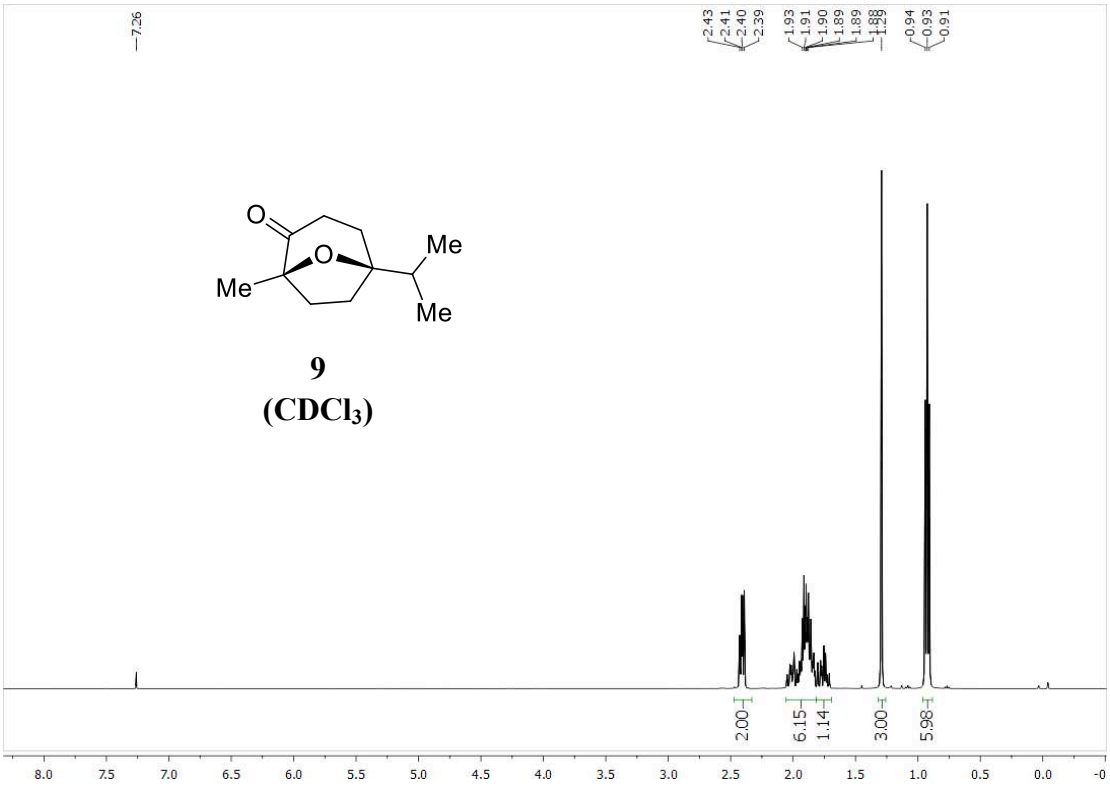


10’
(CD_3OD)



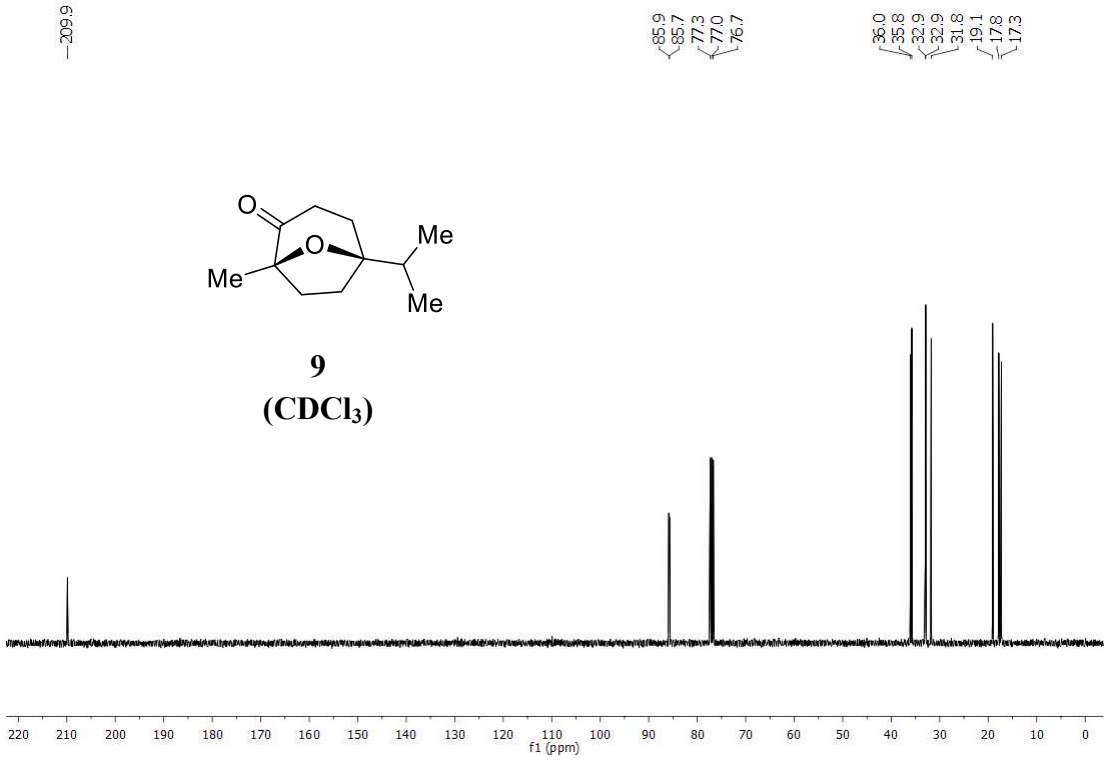
10’
(CD_3OD)

^{1}H and ^{13}C NMR spectra for 9



9

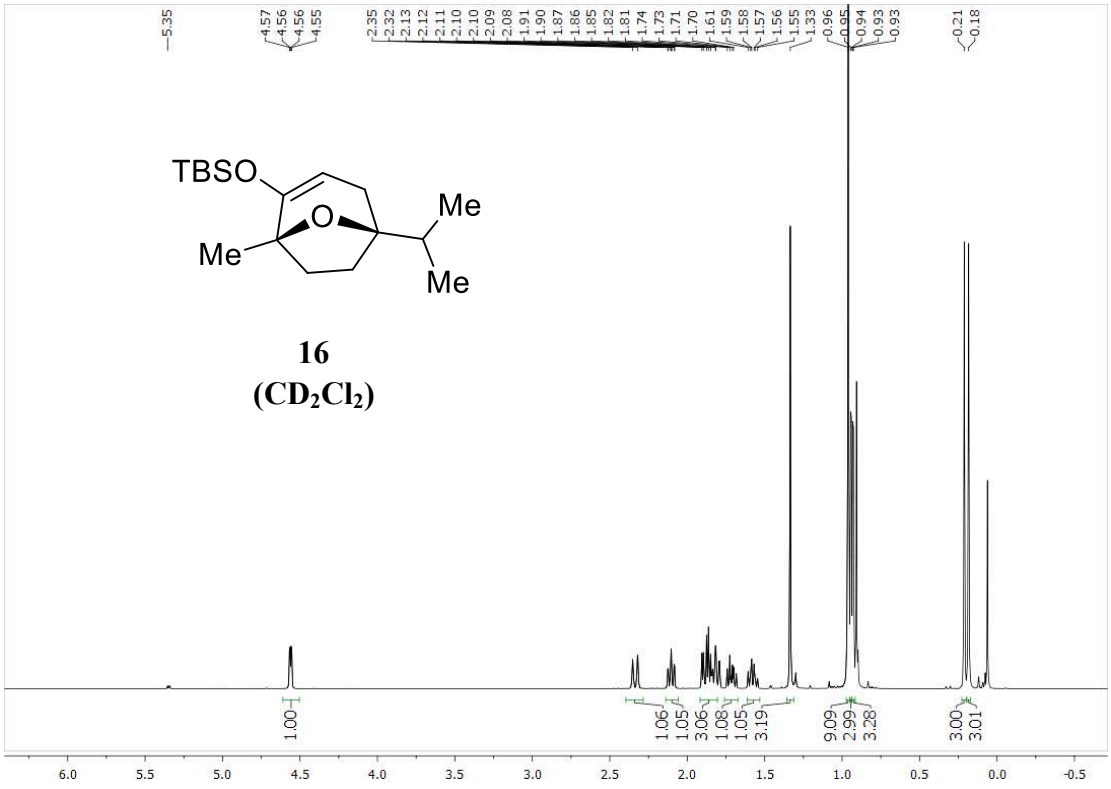
($CDCl_3$)



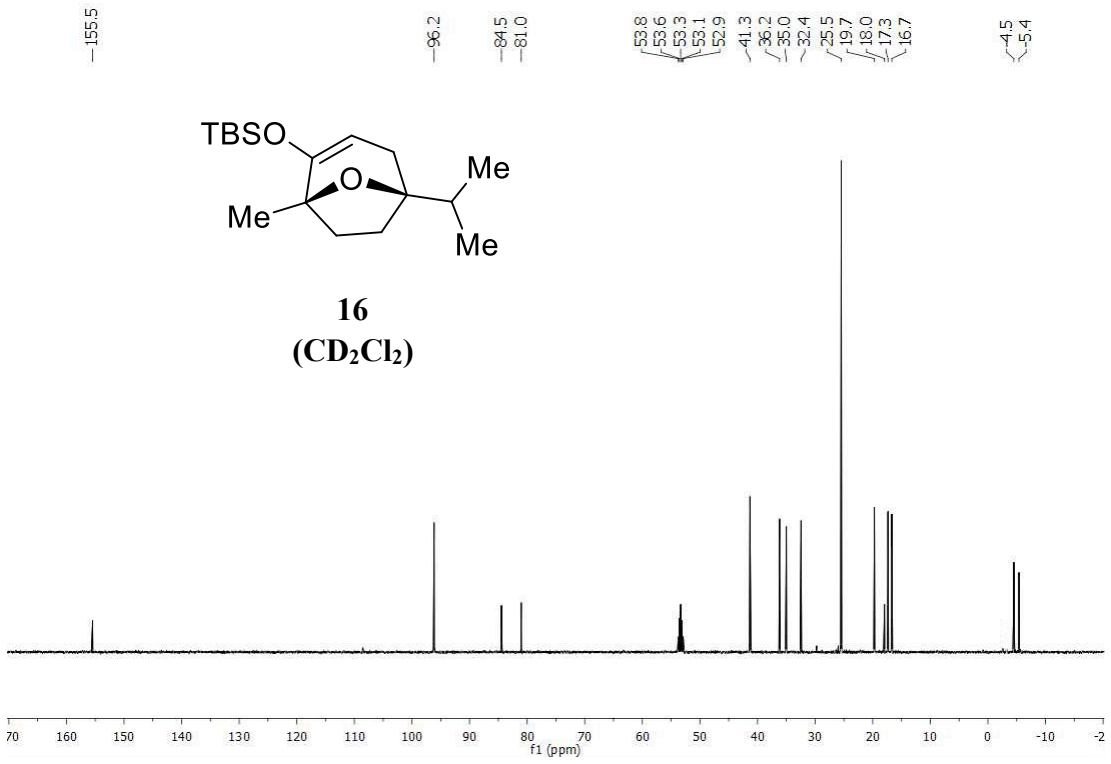
9

($CDCl_3$)

^{1}H and ^{13}C NMR spectra for 16

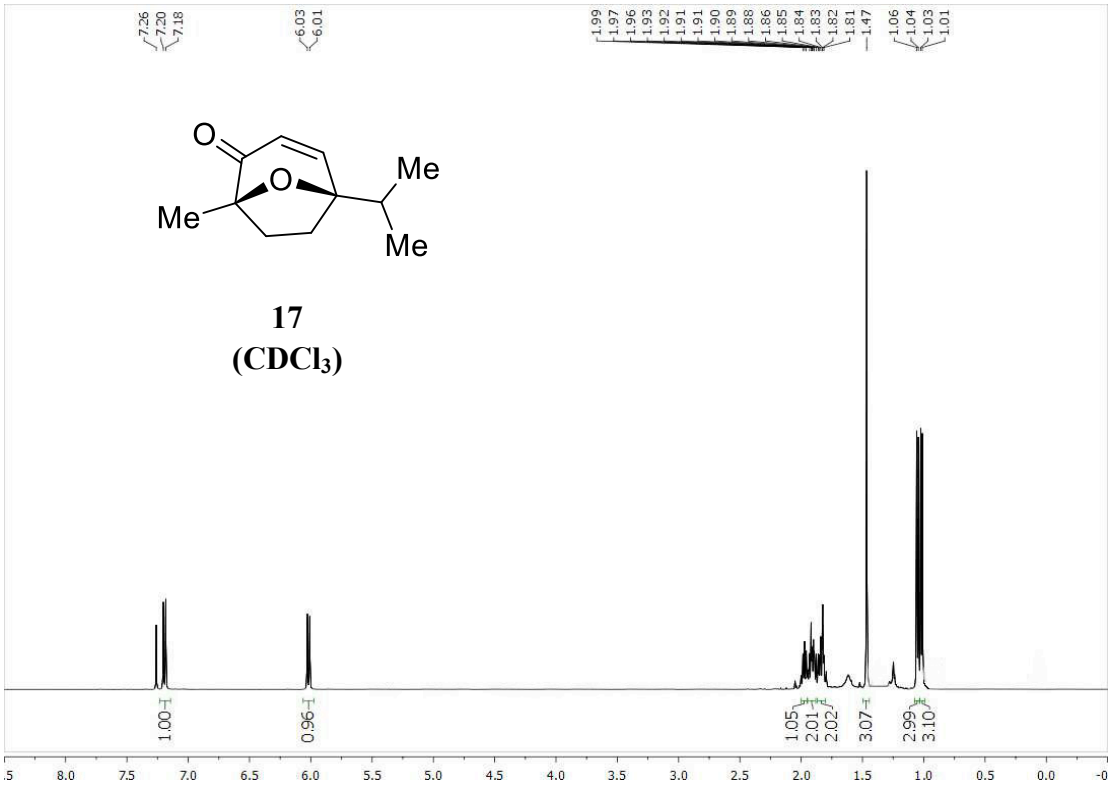


16
(CD_2Cl_2)

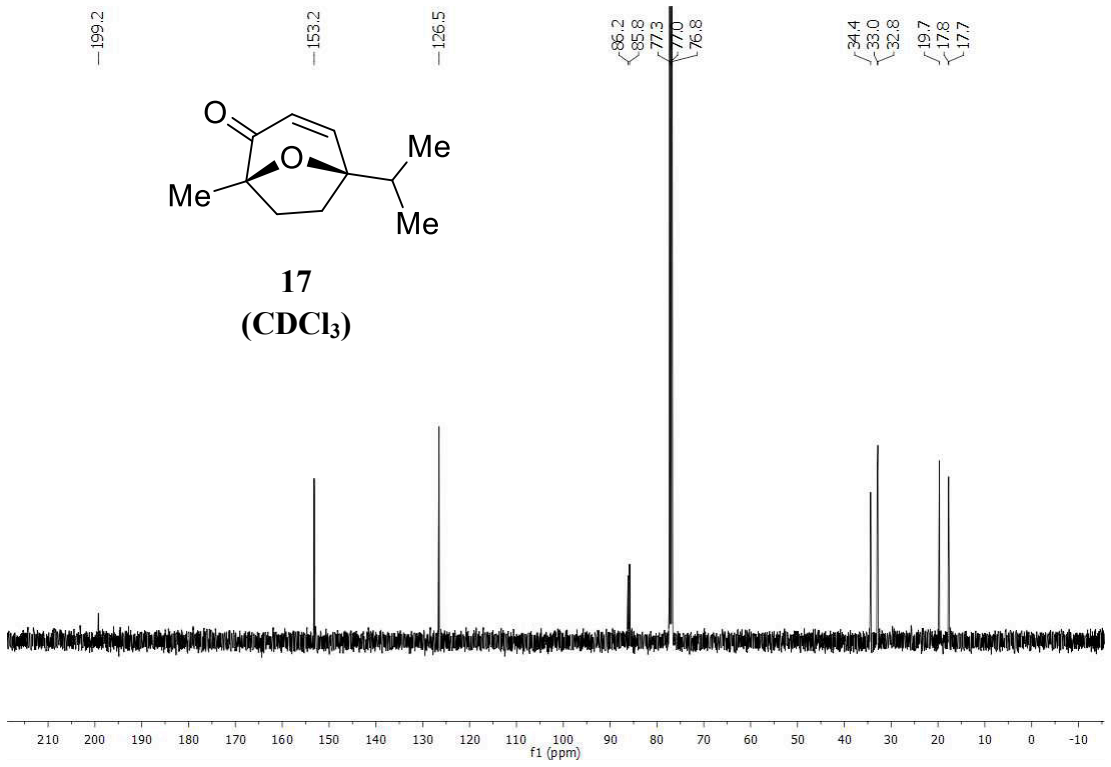


16
(CD_2Cl_2)

^{1}H and ^{13}C NMR spectra for 17

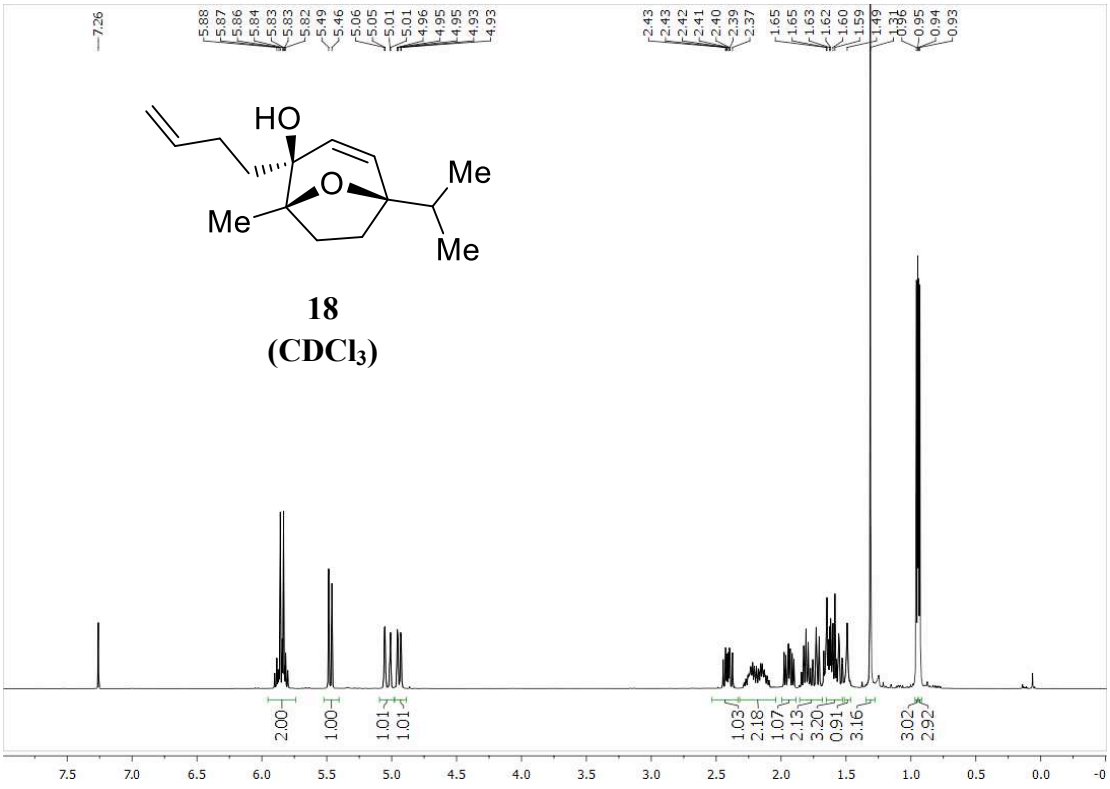


17
($CDCl_3$)

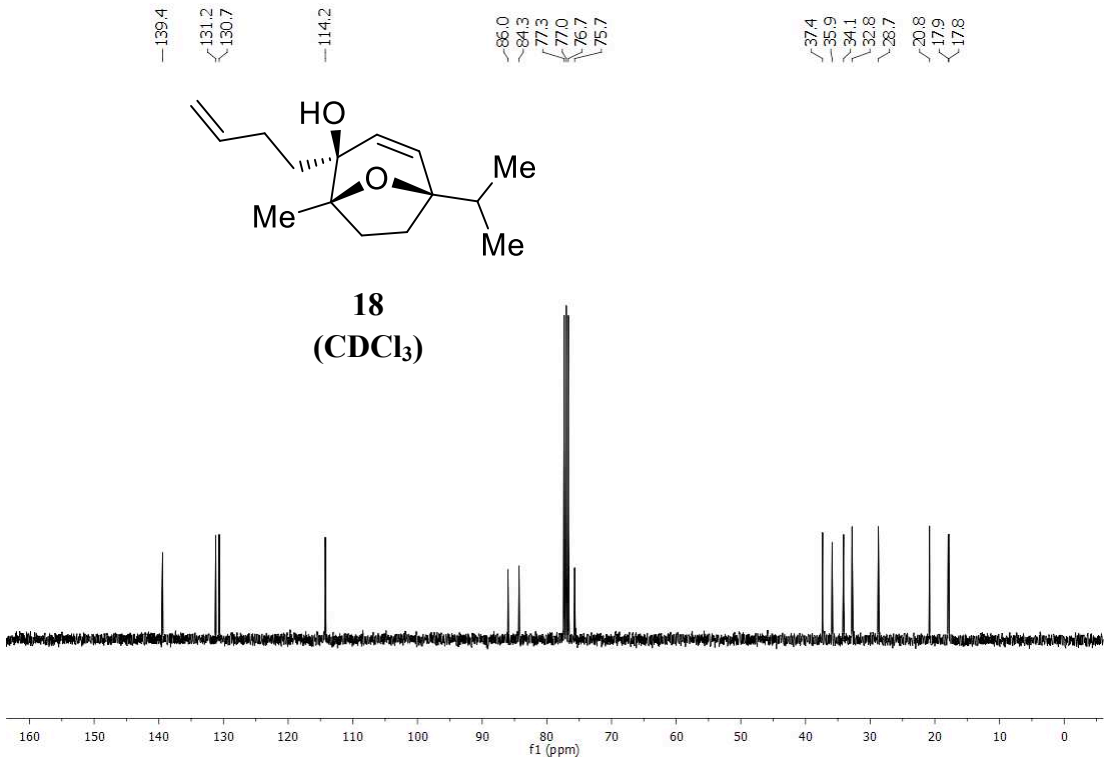


17
($CDCl_3$)

^{1}H and ^{13}C NMR spectra for 18

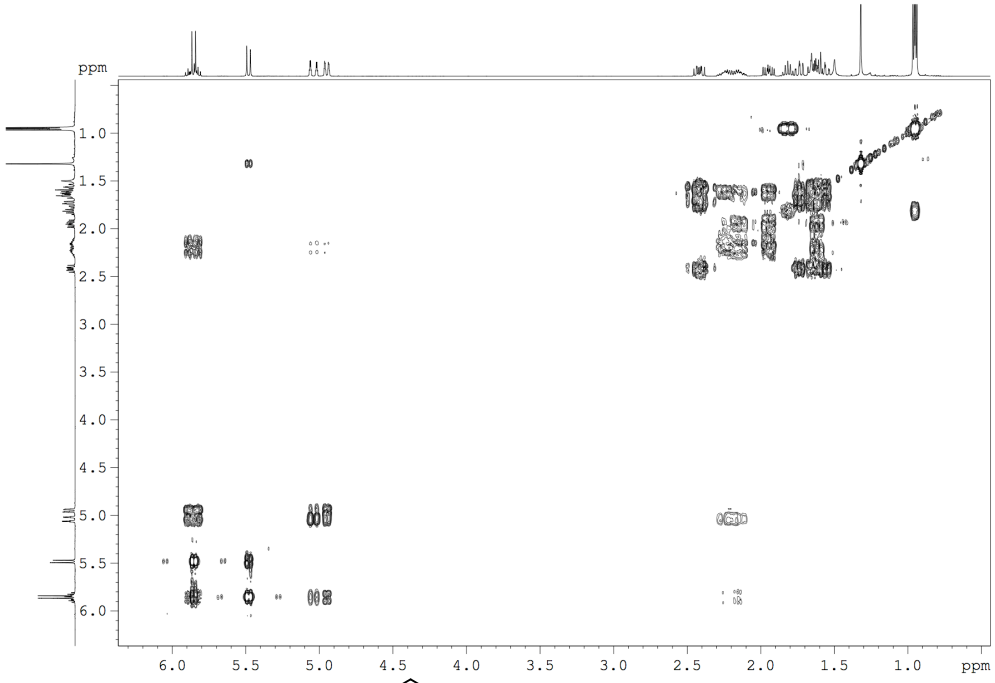


18
($CDCl_3$)

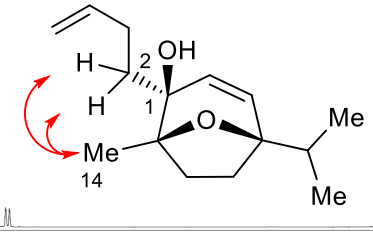


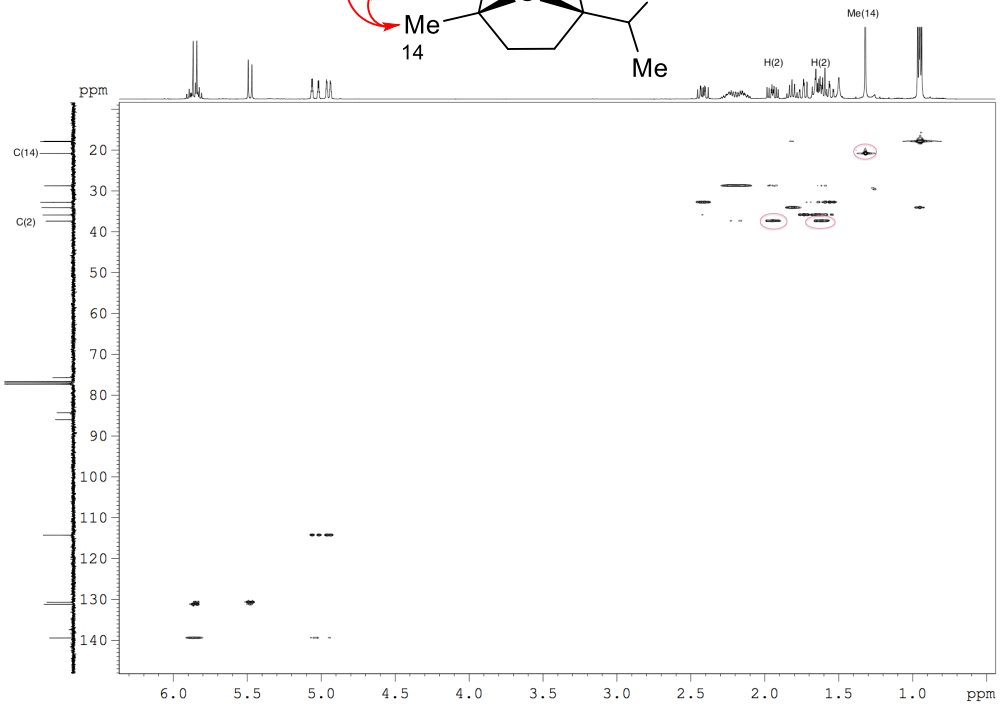
18
($CDCl_3$)

COSY NMR spectra for 18

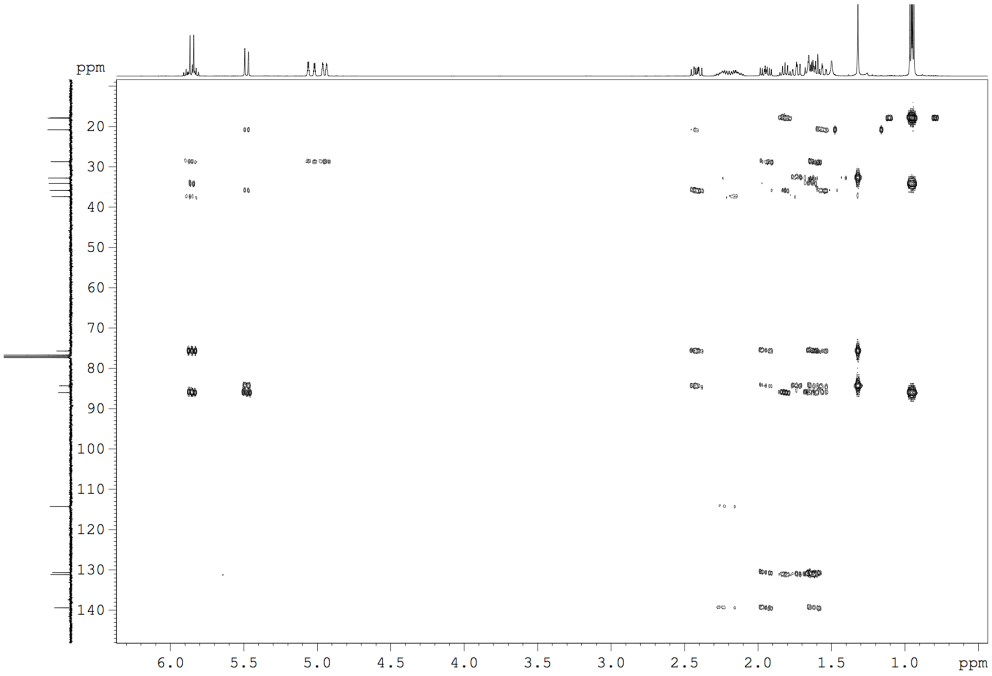


HSQC NMR spectra for 18

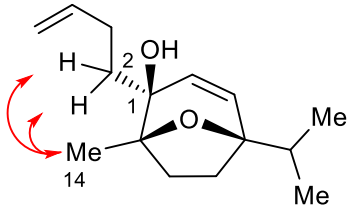




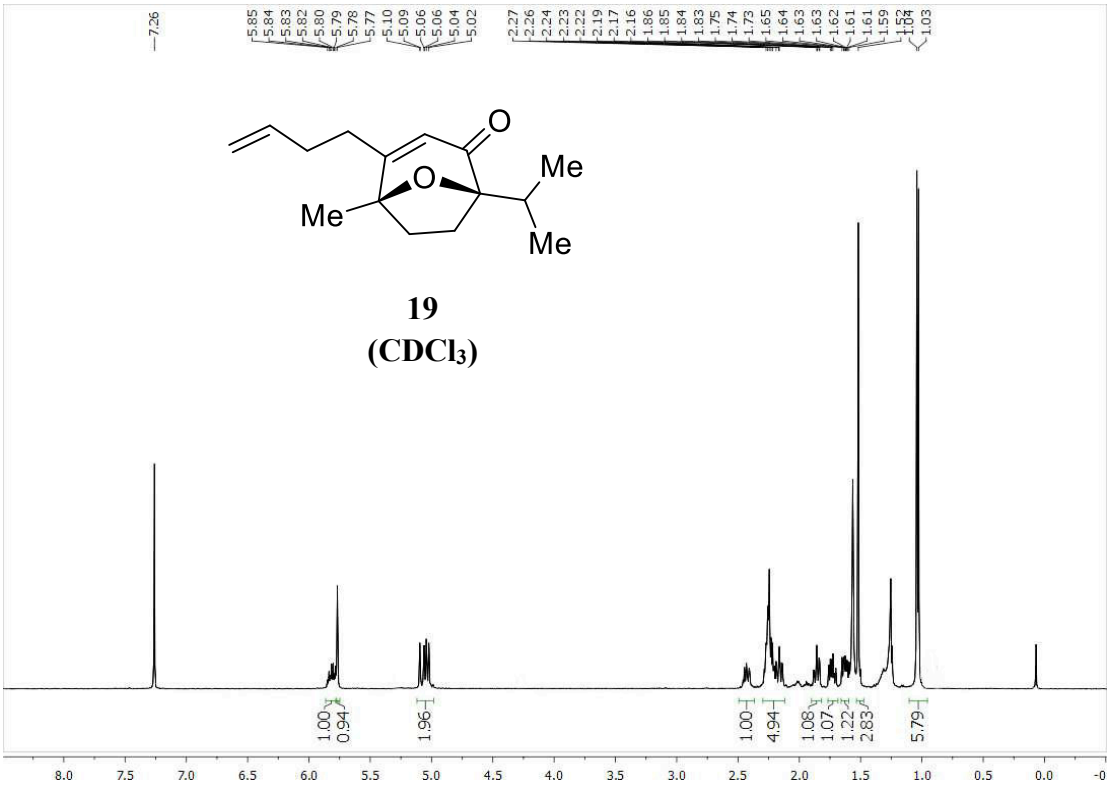
HMBC NMR spectra for 18



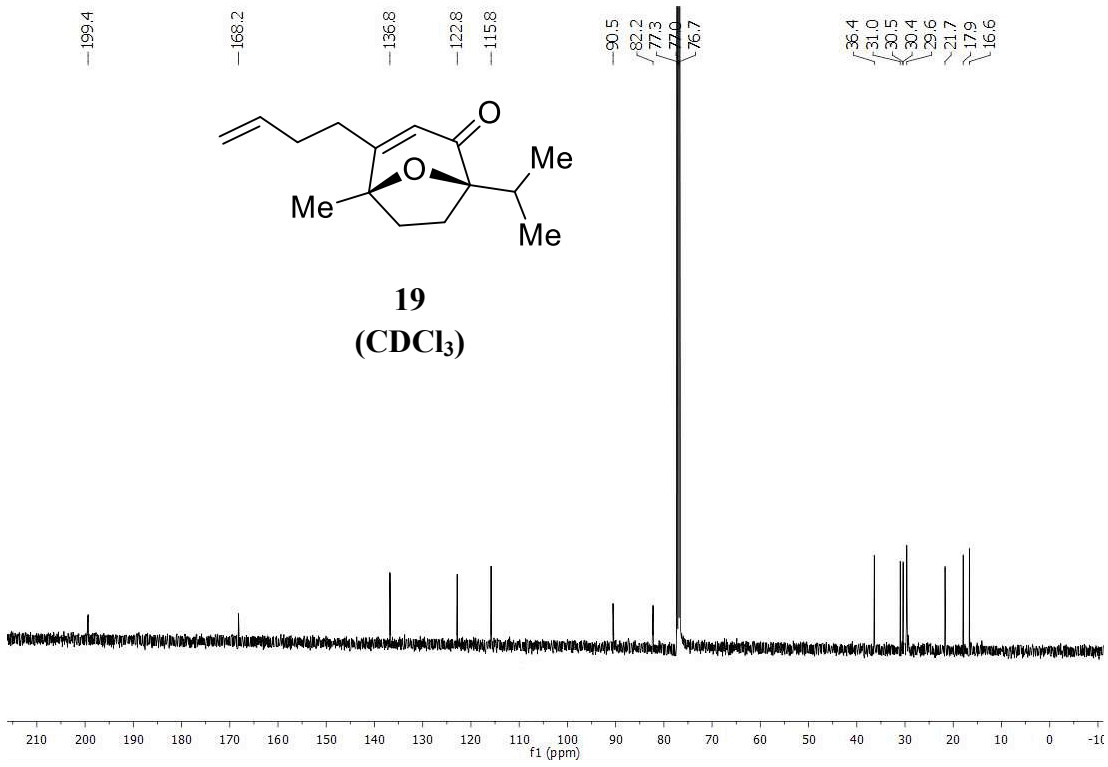
NOESY NMR spectra for 18



^{1}H and ^{13}C NMR spectra for 19

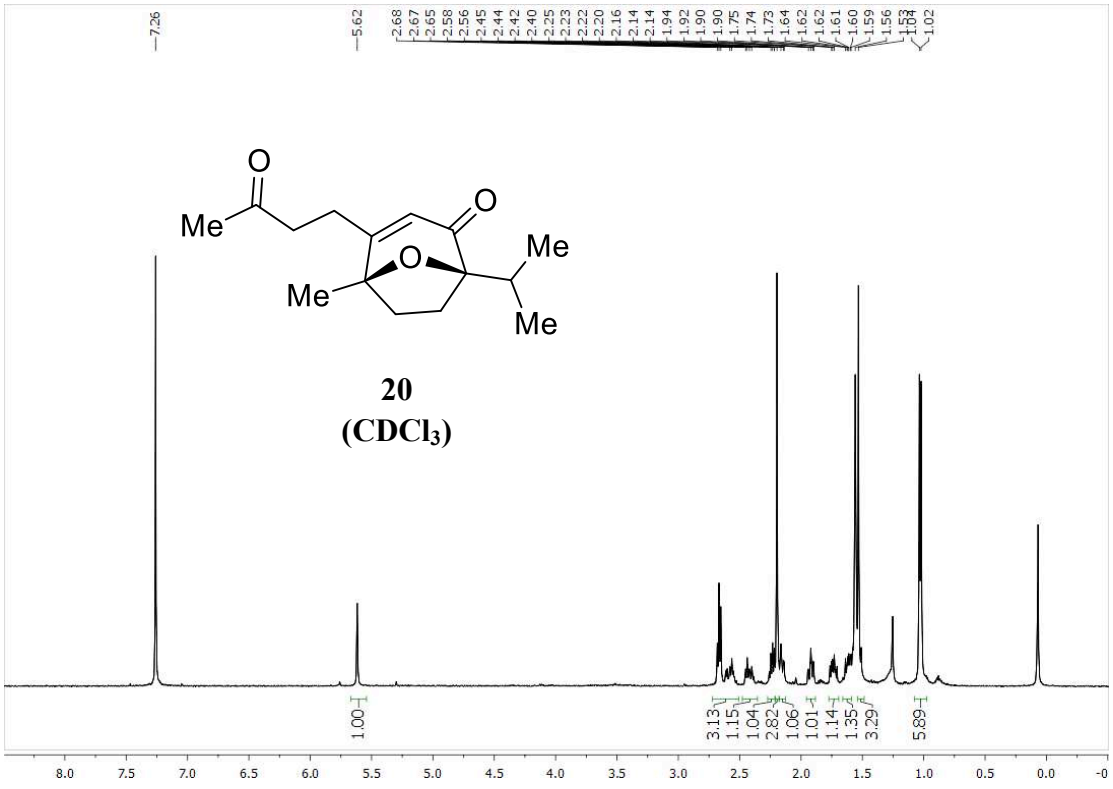


19
($CDCl_3$)

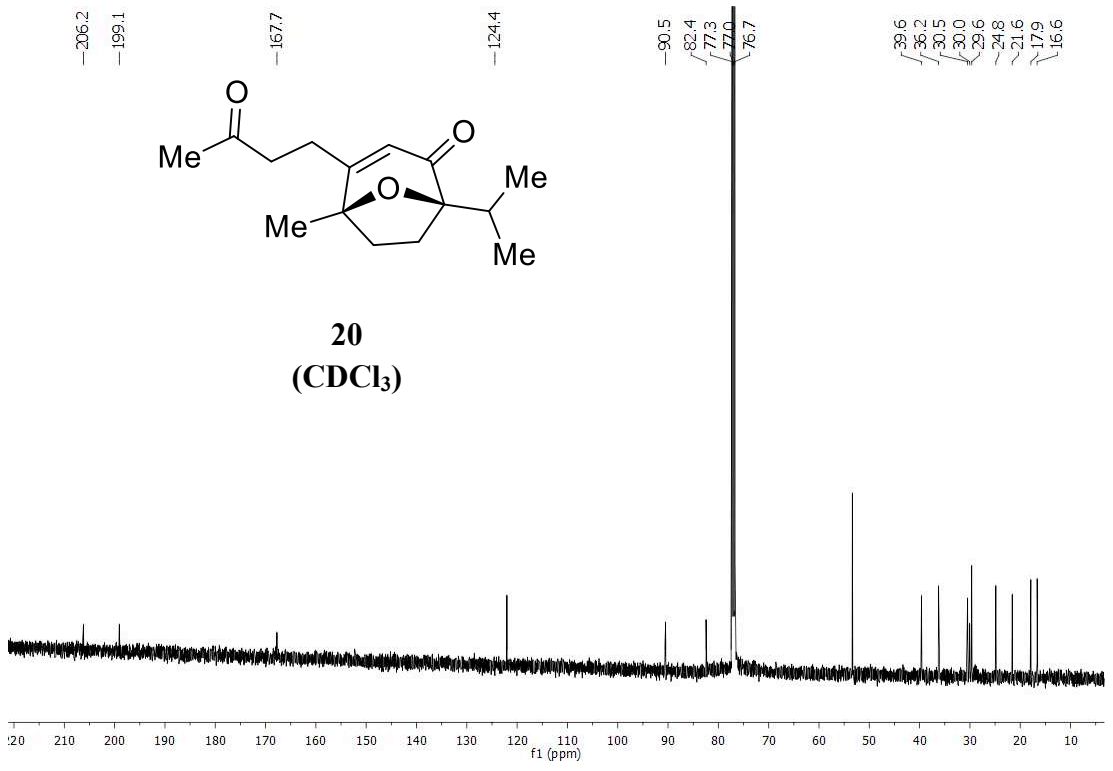


19
($CDCl_3$)

^{1}H and ^{13}C NMR spectra for 20

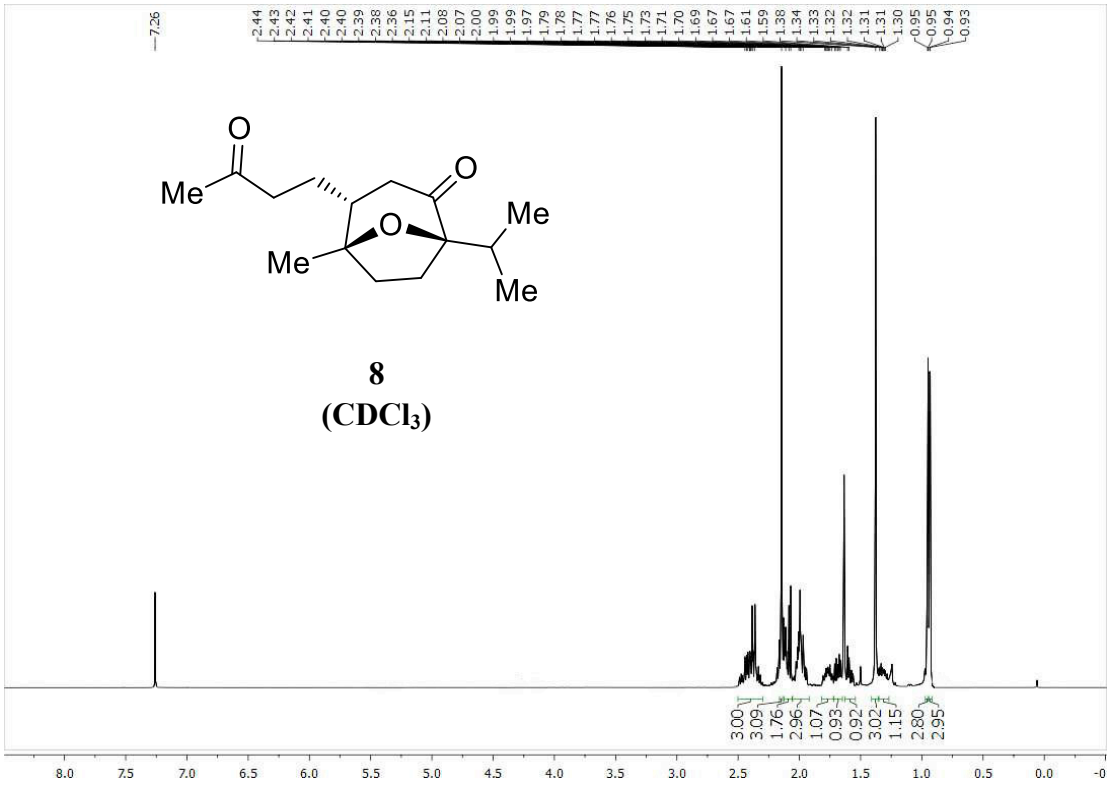


20
($CDCl_3$)

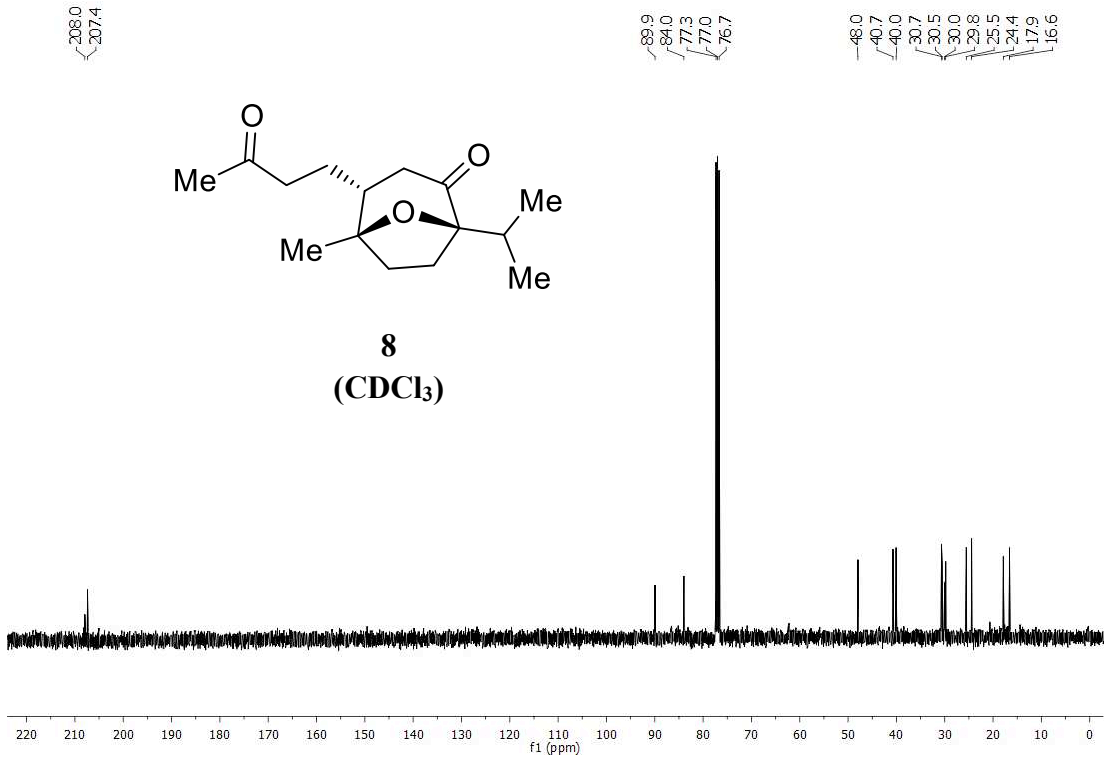


20
($CDCl_3$)

^{1}H and ^{13}C NMR spectra for 8

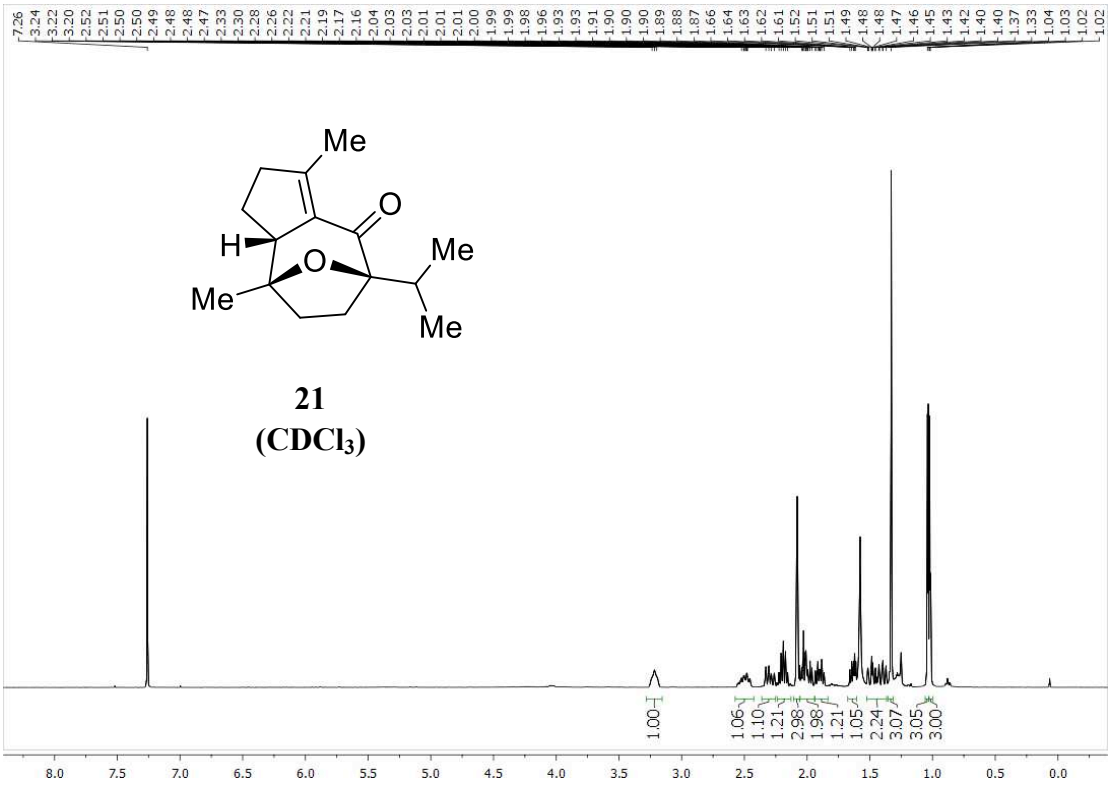


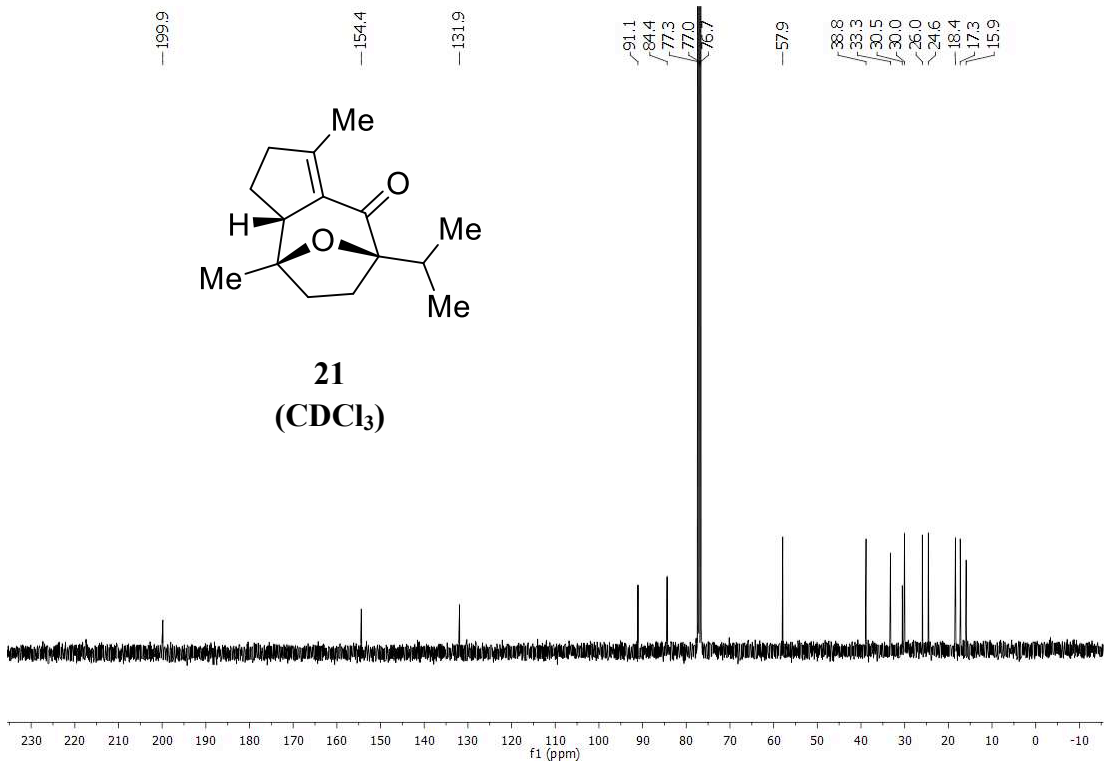
8
($CDCl_3$)



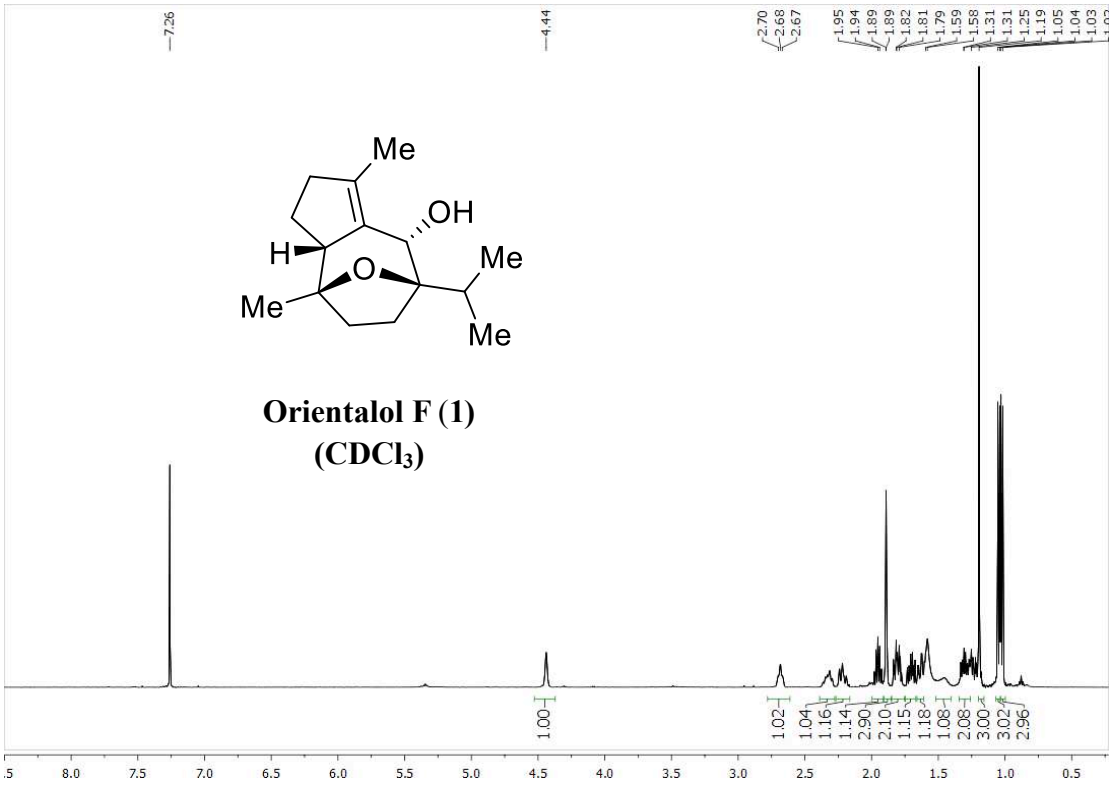
8
($CDCl_3$)

^{1}H and ^{13}C NMR spectra for 21

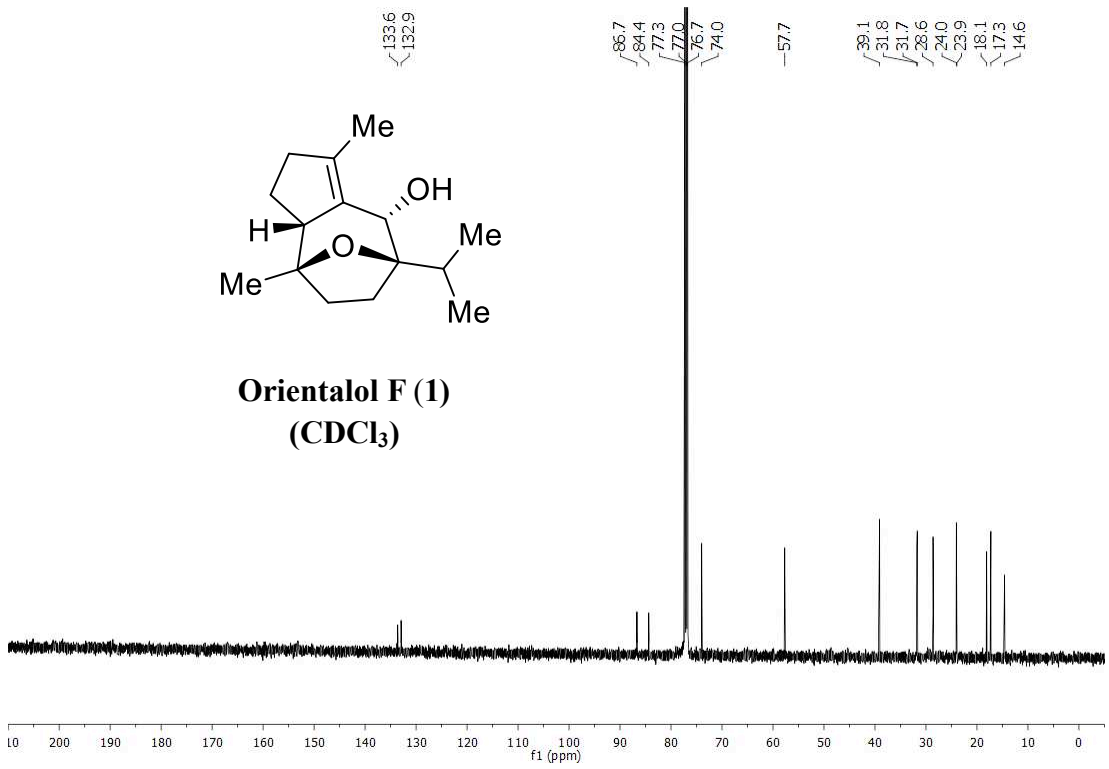




^{1}H and ^{13}C NMR spectra for 1



Orientalol F (1)
($CDCl_3$)



Orientalol F (1)
($CDCl_3$)