Supporting Information

Synthetic Study Toward Diterpenoid Aberrarone

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Table of Contents

1. General Experimental Details

Unless otherwise stated, all reactions were performed with magnetic stirring under a positive pressure of nitrogen or argon gas. Over-dried glassware (over temperature of 150 ºC) was further dried with a heat-gun at 650 ºC under vacuum, followed by back-filling with inert gas, three times and fitted with rubber septa prior to use. Solids were added under inert gas counter flow or were dissolved and transferred in the appropriate solvent. Solutions and liquids reagents were transferred to reaction vessels by oven-dried stainless-steel cannulas or nitrogen flushed syringes. Low temperature reactions were carried out in a Dewar vessel filled with acetone/dry ice (−78 ºC) or distilled water/ice (0 ºC). High temperature reactions were conducted using a heated silicon oil bath in reaction vessels equipped with a reflux condenser.

1.1 Materials

Dry Tetrahydrofuran (THF), Dichloromethane (CH_2Cl_2), ethanol (EtOH), toluene (PhMe) and methanol (MeOH) were purchased from Tansoole company and stored over molecular sieves. Ethyl acetate (EtOAc), Petroleum ether (PE), methyl tert-butyl ether (*t*-BuOMe) used specifically for extraction and flash column chromatography were purchased from commercial sources. All other solvents and regents were also purchased from commercial sources (Sigma Aldrich, Energy chemical, 3A, Adamasect.).

Reactions were monitored by thin-layer chromatography (TLC) using silica gel F254 pre-coated glass plates (*Merck*) and visualized by exposure to ultraviolet light ($\lambda = 254$ nm) or by staining with aqueous potassium permanganate ($KMnO_4$) solution (7.5 g $KMnO_4$, 50 g K_2CO_3, 6.25 mL aqueous 10% NaOH, 1000 mL distilled H_2O), Phosphomolybdic acid hydrate (PMA) solution (10.0 g PMA, 100 mL EtOH) followed by heating with a heat gun (150-600 ºC). Flash column chromatography was performed using silica gel (60 Å, 40-63 µm, *Merck*) and a forced flow of eluent.

1.2 Instrumentation

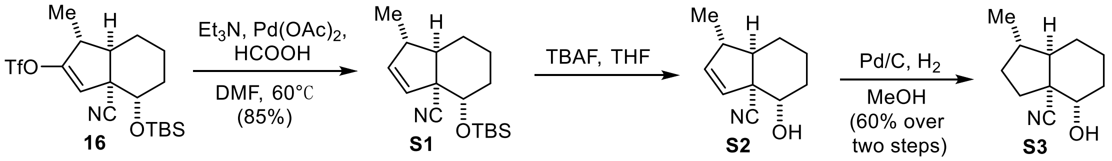
NMR spectra were recorded on a Brucker Avance III HD 500 MHz and 400 MHz spectrometer equipped with a CroProbe TM. Chemical shifts were reported in parts per million (ppm) respectively to the residual solvent signal (^1H NMR: $CDCl_3$: 7.26 ppm C_6D_6: 7.16 ppm);. ^{13}C NMR: $CDCl_3$ 77.2 ppm; C_6D_6: 128.06 ppm). The reported data is represented as follows: chemical shift in parts per million (ppm, δ scale), multiplicity, coupling constants J in Hz, integration intensity and proton assignment. Abbreviations used for analysis of multiplets are as follows: s (singlet), br (broad singlet), d (doublet), t (triplet), q (quartet), quin (quintet), h (hextet), and m (multiplet). Variable temperature NMR spectroscopy was performed at the Northwest A&F University NMR facility.

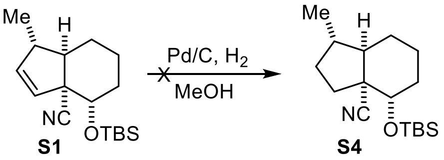
Mass spectroscopy (MS) experiments were performed in high resolution with an AB SCIEX Triple TOF 5600+ spectrometer (AB SCIEX, Boston, MA, USA). IR spectra were recorded on a Perkin-Elmer Frontier FT-IR spectrometer.

Single-crystal X-ray diffraction data of compound was collected on a Bruker D8-Quest diffractometer equipped with a photon 100 detector by using a graphite monochromator utilizing Mo-Kα radiation (λ = 0.71073 Å). Data integration and absorption correction were processed by the SAINT [1] and SADABS [2] programs. The structures were solved by intrinsic phasing with the SHELXS [3] and refined by full-matrix least-squares methods on F2 by using the SHELXL-2018 program [4]. The hydrogen atoms on C atoms were fixed at the calculated positions and refined by a riding model, with Uiso(H) = 1.2Ueq(C).

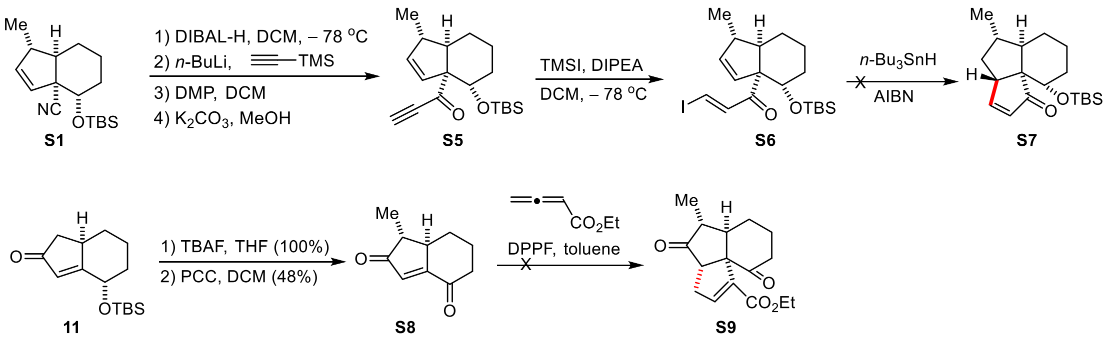
2. Experimental Procedures

Hydrogenation was tried on compounds S1 and S2. To our surprise, hydrogenation of S1 failed in our hand.

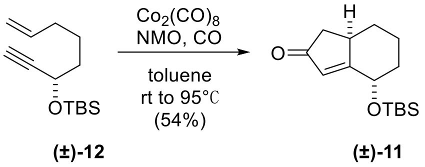




Construction the C ring through radical cyclization or [3+2] cycloaddition was also tried but failed.

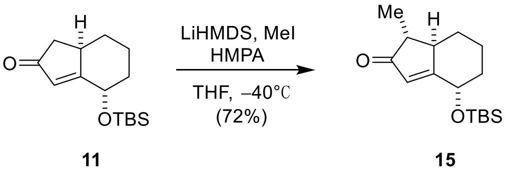


Synthesis of compound 11



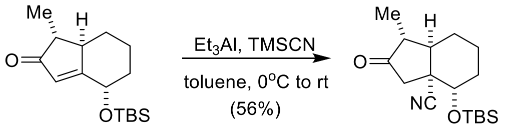
To a stirred solution of **12**[1] (635 mg, 2.66 mmol) in dry toluene (20 mL) at r.t was added $Co_2(CO)_8$ (999 mg, 2.93 mmol) under 1 atm of CO, the mixture was stirred at r.t. for 1 h. After the complete transformation of the starting material, the reaction mixture was added NMO (1.563 g, 13.3 mmol) and heated at 95 °C overnight. The reaction mixture was cooled to room temperature, and concentrated under reduced pressure, the residue was purified by flash column chromatography on silica gel (EtOAc / petroleum ether = 1 / 25) to give product **11** (380 mg, 1.43 mmol, 54%) as a yellow oil. **Data for 11:** R_f = 0.28 (silica, EtOAc: petroleum ether = 1: 20, stains with PMA); **^{1}H NMR (500 MHz, Chloroform-*d*):** δ 5.82 (s, 1H), 4.73 (s, 1H), 3.10 – 3.02 (m, 1H), 2.57 (dd, J_1 = 19.1 Hz, J_2 = 6.2 Hz, 1H), 2.19 – 2.13 (m, 1H), 1.99 – 1.93 (m, 3H), 1.60 – 1.45 (m, 3H), 1.06 (q, J_1 = 25.4Hz, J_2 = 12.7 Hz, 1H), 0.88 (s, 9H), 0.07 (s, 3H), 0.00 (s, 3H); **^{13}C NMR (100 MHz, Chloroform-*d*)**: δ 209.5, 184.0, 125.7, 66.8, 42.2, 37.6, 35.6, 35.4, 25.7, 19.2, 18.1, –4.8, –5.0; **HRMS ESI** calcd for $C_{15}H_{26}O_2SiNa^+$ $[M+Na]^+$ 289.1594, found 289.1594; **IR (neat)** Vmax 2940, 2861, 1705, 1709, 1255, 1020, 839, 781 cm^{-1}.

Synthesis of compound 15



To a solution of the compound **11** (283 mg, 1.06 mmol) in tetrahydrofuran (10 mL) was added LiHMDS (1.27 ml, 1M) at -40°C. After stirred for an hour, HMPA (0.35 mL, 1.27 mmol) and MeI (0.08 mL, 1.27 mmol) was added to the reaction mixture. The reaction was quenched by saturated NH$_4$Cl aqueous solution and extracted with EtOAc (3 × 10 mL). The combined organic extract was dried over anhydrous Na$_2$SO$_4$ and concentrated *in vacuo*. The crude product was purified via flash chromatography (EtOAc: petroleum ether = 1 / 30) to provide **15** (214 mg, 0.763 mmol, 72%) as a yellow oil. **Data for 15:** R_f = 0.37 (silica, EtOAc: petroleum ether = 1: 20, stains with PMA); **^{1}H NMR (500 MHz, Chloroform-*d*):** δ 5.75 (s, 1H), 4.71 – 4.66 (m, 1H), 2.62 – 2.52 (m, 1H), 2.21 – 2.11 (m, 1H), 1.95 – 1.83 (m, 3H), 1.55 – 1.40 (m, 2H), 1.12 (d, J = 7.7 Hz, 3H), 0.84 (s, 9H) 0.03 (s, 3H), -0.05 (s, 3H); **^{13}C NMR (125 MHz, Chloroform-*d*)**: δ 211.7, 181.5, 124.7, 66.7, 47.9, 46.4, 35.2, 34.5, 25.6, 19.2, 18.0, 15.1, –4.8, –5.0; **HRMS ESI** calcd for C$_{16}$H$_{28}$O$_2$SiNa$^+$ [M+Na]$^+$ 303.1751, found 303.1747; **IR (neat)** Vmax 2934, 2859, 1711, 1254, 1165, 1078, 837, 779 cm^{-1}.

Synthesis of compound 10



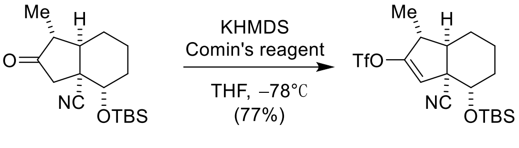
15 **10**

Preparation of Nagata reagent: To a solution of Et$_3$Al (1.0 mL, 1.0 M in toluene, 1.0 mmol) was added TMSCN (125 µL 1.0 mmol) at r.t.. Then the solution was heated to 110 °C. After 1 h, the formed Nagata reagent was cooled down to r.t. and used for next step.

To a stirred solution of **15** (50.6 mg, 0.18 mmol) in dry toluene (2 mL) at 0°C was added Et$_2$AlCN (0.9 mL, 0.9 mmol), After 2 hours, the reaction mixture was quenched by saturated NaHCO$_3$ aqueous solution (2 mL) and extract with EtOAc (3 × 2 mL). The combined organic layers were washed with brine, concentrated and purified by flash chromatography (EtOAc / petroleum ether = 1 / 25) to afford product **10** (31 mg, 0.100 mmol, 56%) as a white solid. **Data for 10:** R_f = 0.50 (silica, EtOAc: petroleum ether = 1: 8, stains with PMA); **^{1}H NMR (125 MHz, Chloroform-*d*):** δ 3.38 (dd, J_1 = 11.4 Hz, J_2 = 4.0 Hz, 1H), 2.88-2.81 (m, 1H), 2.63 – 2.56 (m, 1H), 2.39 – 2.33 (m, 1H), 2.18 – 2.10 (m, 1H), 1.94 – 1.87 (m, 2H), 1.79 – 1.68 (m, 3H), 1.47 – 1.39 (m, 1H), 1.10 (d, J = 6.9 Hz, 3H), 0.91 (s, 9H), 0.08 (s, 3H), 0.05 (s, 3H); **^{13}C NMR (125**

MHz, Chloroform-*d*): δ 214.5, 120.9, 71.3, 49.2, 46.7, 45.3, 43.4, 32.6, 25.6, 22.2, 19.3, 18.0, 13.3, -3.7, -4.9; **HRMS ESI** calcd for $C_{17}H_{29}NO_2SiNa^+$ $[M+Na]^+$ 330.1860, found 330.1856; **IR (neat)** Vmax 2935, 2861, 2239, 1747, 1466, 1257, 1116, 838, 778 cm^{-1}.

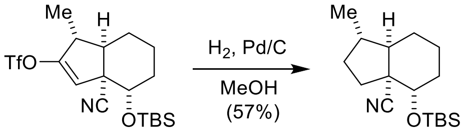
Synthesis of compound 16



10 **16**

A solution of **10** (593 mg, 1.93 mmol) in dry THF (20 mL) at – 78°C was added dropwise the KHMDS (2.9 mL, 1.0 M solution in THF, 2.9 mmol). After 40 min, a solution of N, N-bis(trifluoromethanesulfonyl)-2-amine-5-chloropyridine (1.137 g, 2.9 mmol) in dry THF (10 mL) was added. The reaction mixture was stirred at – 78°C for 2 h. Then the reaction mixture was quenched with saturated aqueous NH_4Cl, extracted with t-BuOMe (3 × 20 mL), dried over anhydrous Na_2SO_4 and concentrated *in vacuo*. The residue was purified by flash chromatography (EtOAc / petroleum ether = 1 / 60) to give compound **16** (652 mg, 1.49 mmol, 77% yield)as a yellow-oil. Compound 16 was used immediately due to the instability.

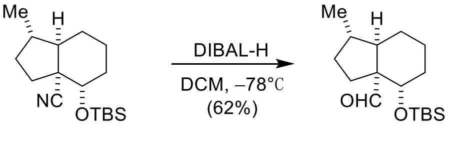
Synthesis of compound 17



16 **17**

To a solution of the compound **16** (62 mg, 0.142 mmol) in dry methanol (4 mL) were added 16% Pd/C (10 mg) as the catalyst. The mixture was hydrogenated at 1 atm of H_2 until the starting material disappeared on TLC. Then the catalyst was filtered off, the solvent was evaporated *in vacuo*, and the residue was purified by flash column chromatography on silica gel (EtOAc / petroleum ether = 1 / 40) to give product **17** (24 mg, 0.08 mmol, 57% yield) as a colorless oil. **Data for 17**:R_f = 0.61 (silica, EtOAc: petroleum ether = 1: 20, stains with PMA); **^{1}H NMR (400 MHz, Benzene-*d*$_6$)** δ 3.17 (dd, J_1 = 10.6, J_1 = 5.0, 1H), 2.07 – 1.99 (m, 1H), 1.85 – 1.76 (m, 1H), 1.71 – 1.50 (m, 6H), 1.47 – 1.32 (m, 2H), 1.28 – 1.21 (m, 2H), 1.01 (s, 9H), 0.63 (d, J = 6.4, 3H), 0.03 (s, 3H), 0.00 (s, 3H); **^{13}C NMR (100 MHz, Benzene-*d$_6$*)** δ 122.1, 70.8, 52.8, 50.0, 33.4, 32.8, 32.5, 30.3, 25.6, 21.8, 19.7, 19.1, 17.9, -4.0, -5.2; **HRMS ESI** calcd for $C_{17}H_{31}NOSiNa^+$ $[M+Na]^+$ 316.2067, found 316.2066.

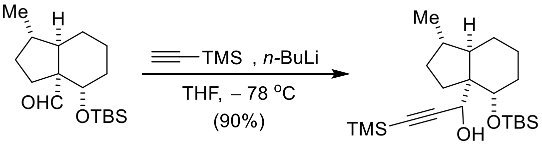
Synthesis of compound S10



17 **S10**

To a solution of alcohol **17** (162 mg, 0.55 mmol) in dry DCM (8 mL) was added DIBAL-H (0.83 ml, 0.83 mmol) at – 78 °C under argon. After completing the reaction, the mixture was quenched by MeOH (1 mL) and then saturated Rochelle's salt solution (10 mL) was added, and the mixture was stirred vigorously for 2 h at room temperature until the two layers were clear and the aqueous phase was extracted with *t*-BuOMe (3 × 10 mL). The combined organic layers was washed with brine, dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. Afterwards, the residue was purified through flash column chromatography (EtOAc / petroleum ether = 1 / 8) to yield **S10** (100 mg, 0.34 mmol, 62%) as a colorless oil. Aldehyde **S10** was directly used for next step.

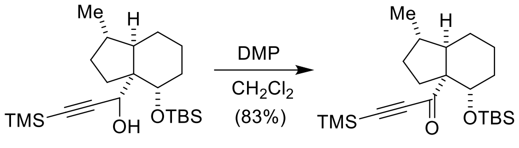
Synthesis of compound S11



S10 **S11**

In a 50 mL flask fitted with a Ar inlet adapter, a magnetic stir bar was placed trimethylsilylacetylene (0.4 mL, 2.82 mmol) in THF (6 mL) at –78 °C, *n*-BuLi (1.6 M in hexane, 1.73 mL, 2.77 mmol, 5.0 equiv) was then added slowly. After complete addition of *n*-BuLi, the mixture was stirred for 60 min and aldehyde **S10** (162 mg, 2.82 mmol, 1.0 equiv) in THF (5 ml) was added dropwise. The mixture was stirred for 1 h at –78 °C. The mixture was quenched by saturated aqueous NH_4Cl solution (10 mL) and the aqueous layer was extracted with *t*-BuOMe (3 x 10 mL). The combined organic layers were washed with brine (20 mL), dried by Na_2SO_4. The solvent was removed by rotary evaporation to give crude product, which was purified through flash column chromatography (EtOAc / petroleum ether = 1 / 80) to yield **S11** (198 mg, 0.5 mmol, 90%) as a light-yellow oil. Compound **S11** was obtained as a single diastereomer and directly used for the next step.

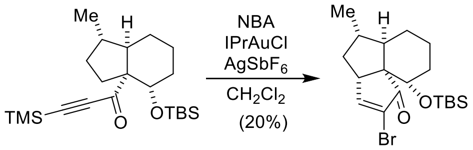
Synthesis of compound 9



S11 **9**

To a stirred solution of **S11** (51 mg, 0.13 mmol) in dichloromethane (3 mL) were added Dess-Martin reagents (92 mg, 0.2 mmol) at room temperature. After 1 h, the reaction mixture was quenched with saturated aqueous Na_2SO_3 and extracted with t-BuOMe (3 ×5 mL). The combined organic layer was washed with brine, dried over anhydrous Na_2SO_4 and concentrated *in vacuo*. The residue was purified by flash column chromatography (EtOAc / petroleum ether = 1 / 100) to produce **9** (42 mg, 0.11 mmol, 83%) as a light-yellow oil. **Data for 9**: R_f = 0.95 (silica, EtOAc: petroleum ether = 1: 30, stains with PMA); **^{1}H NMR (500 MHz, Benzene-d_6):** δ 3.75 (dd, J_1 = 10.0 Hz, J_2 = 3.8 Hz, 1H), 2.61 – 2.54 (m, 1H), 2.09 – 2.03 (m, 2H), 1.85 – 1.80 (m, 1H), 1.78 – 1.72 (m, 1H), 1.63 – 1.53 (m, 3H), 1.36 – 1.28 (m, 2H), 1.26 – 1.22 (m, 1H), 1.15 – 1.09 (m, 1H), 1.01 (s, 9H), 0.83 (d, J = 6.7 Hz, 3H), 0.11 (s, 3H), 0.09 (s, 9H), 0.06 (s, 3H); **^{13}C NMR (125 MHz, Benzene-d_6)**: δ 190.6, 103.8, 95.8, 74.5, 62.9, 49.0, 36.5, 33.2, 31.2, 30.9, 25.8, 23.8, 19.6, 18.1, -1.1, -4.1, -5.2; **HRMS ESI** calcd for $C_{22}H_{40}O_2Si_2Na^+$ $[M+Na]^+$ 415.2459, found 415.2459; **IR (neat)** Vmax 2952, 2866,1667, 1422, 1254, 1216, 1137, 1092, 848 cm^{-1}.

Synthesis of compound 8



9 **8**

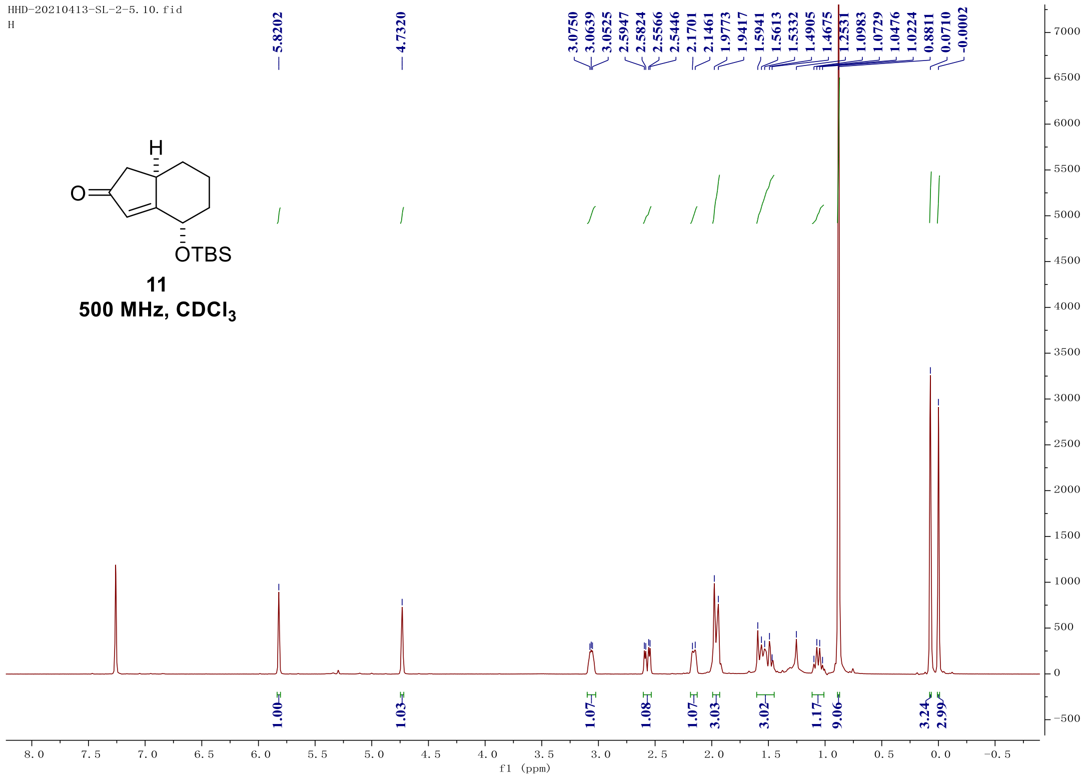
NBA (12.5 mg , 1.5 equiv), IPrAuCl (1.9 mg, 0.05 equiv), and $AgSbF_6$ (2.1 mg, 0.1 equiv) were added in this order to a mixture of ynone **9**(23.3 mg, 0.06 mmol) and DCM (2 mL) in a vial at room temperature. The reaction mixture was stirred at room temperature for 10 hours. Upon completion, the mixture was concentrated and the residue was purified by chromatography on silica gel (EtOAc / petroleum ether = 1 / 80) to afford the desired product **8** (5 mg, 0.012 mmol, 20%) as a colorless oil. **Data for 8**: R_f = 0.62 (silica, EtOAc: petroleum ether = 1: 30, stains with

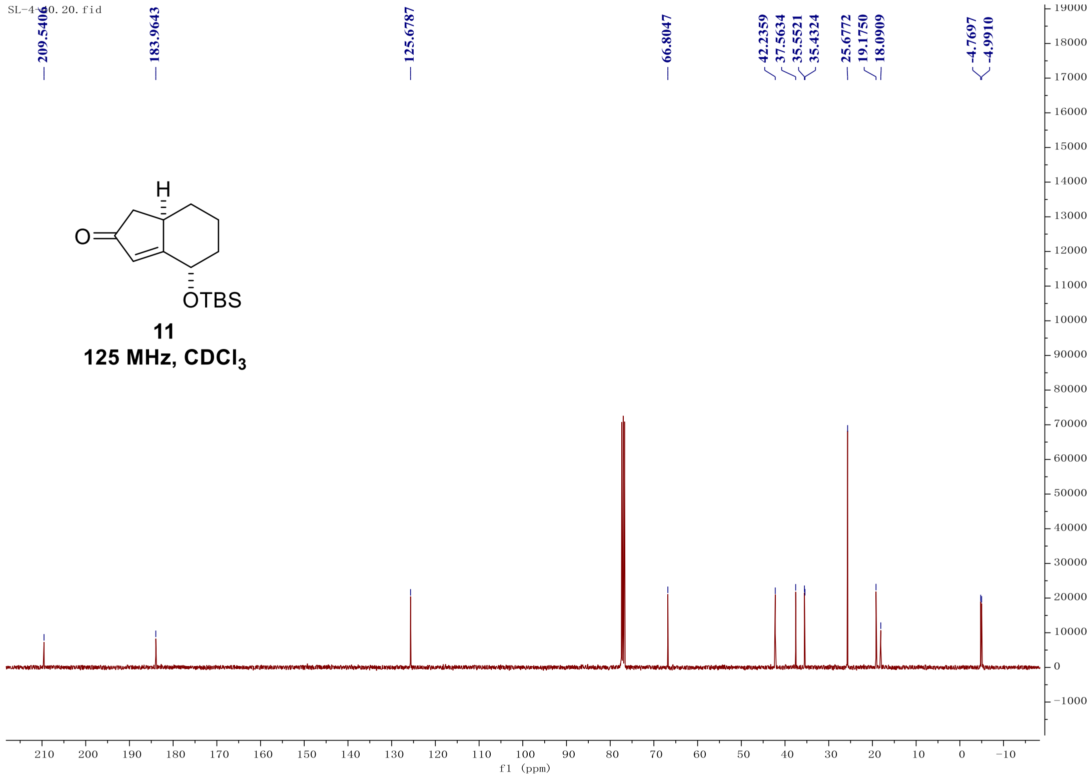
PMA); **^{1}H NMR (400 MHz, Benzene-*d_6*):** δ =6.94 (d, J = 2.84 Hz ,1H), 3.55 (dd, J_1 = 11.9, J_2=4.7 Hz ,1H), 2.76 (td, J_1 = 5.5 Hz, J_2 = 2.9 Hz, 1H), 2.45 (qd, J_1 = 12.4, J_2 = 3.4 Hz, 1H), 1.77 (tdd, J_1 = 14.1, J_2 = 6.1, J_3 = 4.3 Hz, 1H), 1.65 – 1.60 (m, 2H), 1.47 (dt, J_1 = 13.6, J_2 = 3.6 Hz, 1H), 1.34 – 1.29 (m, 2H), 1.06 – 1.01 (m, 2H), 0.9 (s, 9H), 0.58 (d, J = 2.8 Hz, 3H), 0.02 (s, 3H), -0.03 (s, 3H); **^{13}C NMR (100 MHz, Benzene-*d_6*):** δ =199.8, 160.1, 122.4, 74.0, 59.1, 52.1, 50.1, 46.8, 37.9, 36.5, 30.3, 24.7, 20.5, 19.4, 17.0, 16.2, -4.5, -6.2; **HRMS ESI** calcd for $C_{19}H_{31}BrO_2SiNa^+$ $[M+Na]^+$ 421.1169, found 421.1170. **IR (neat)** Vmax 2926, 2856,1716, 1257, 1103, 841, 815 cm^{-1}.

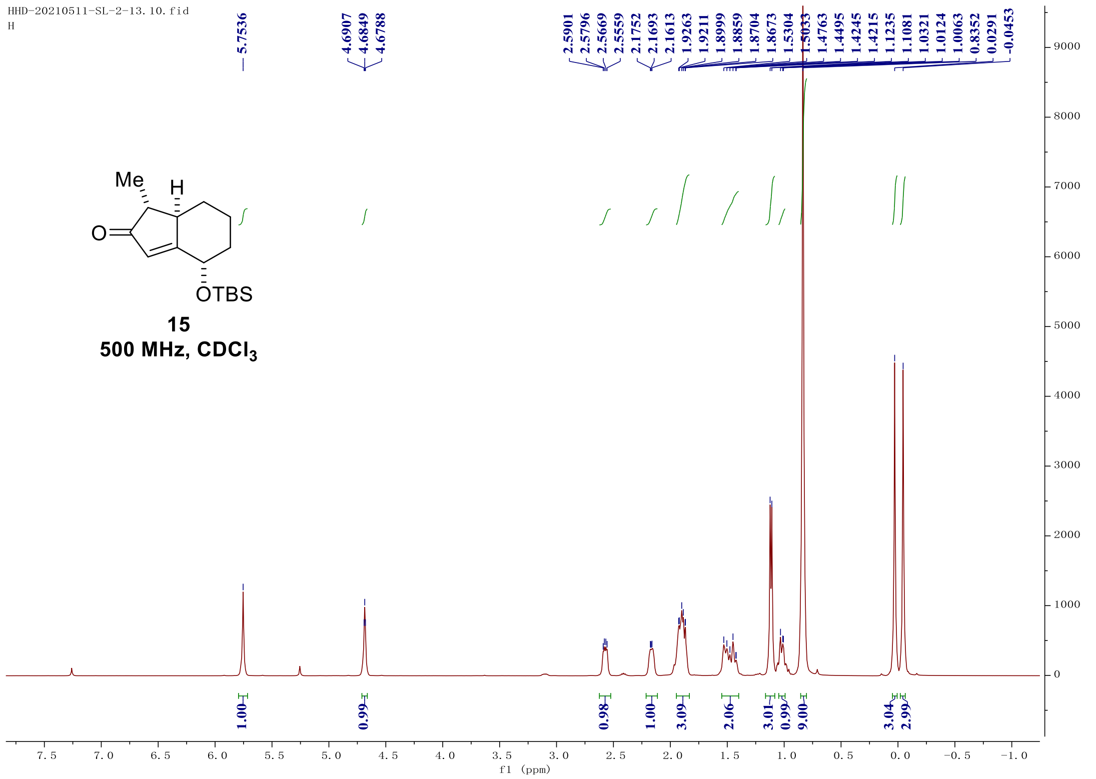
3. References

1. Cantagrel, G.; Meyer, C.; Cossy, J. *Synlett* **2007**, 2983-2986.

4. ^{1}H and ^{13}C NMR Spectra



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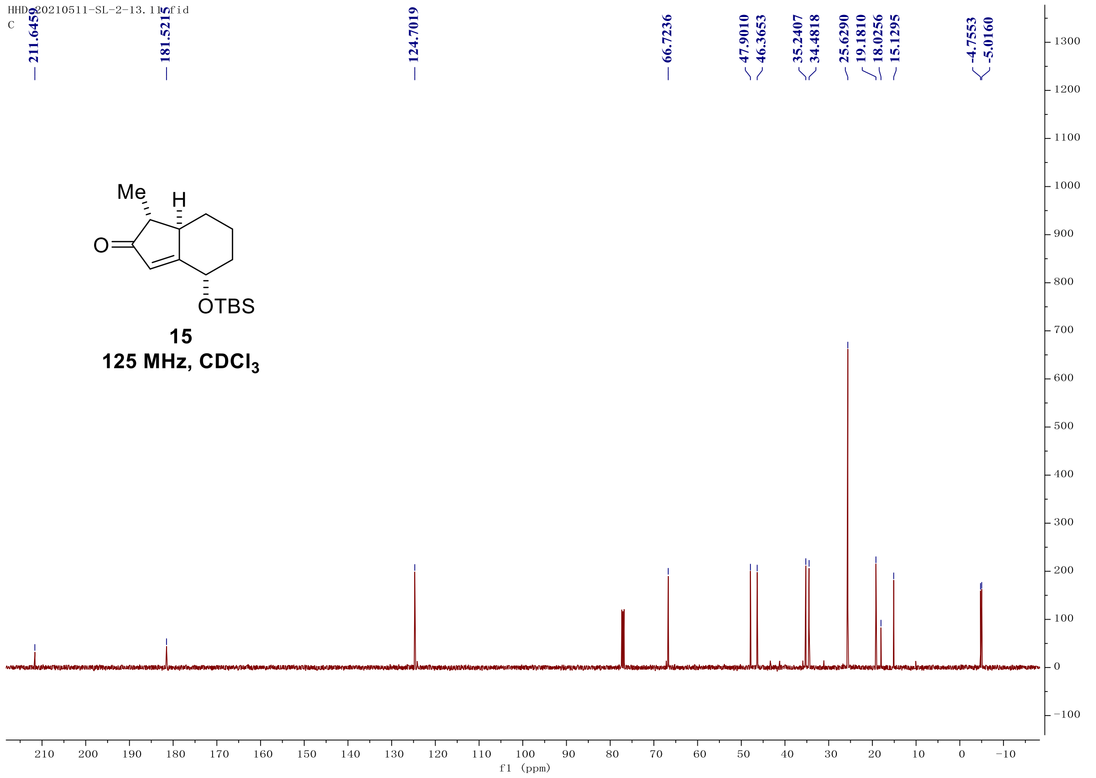
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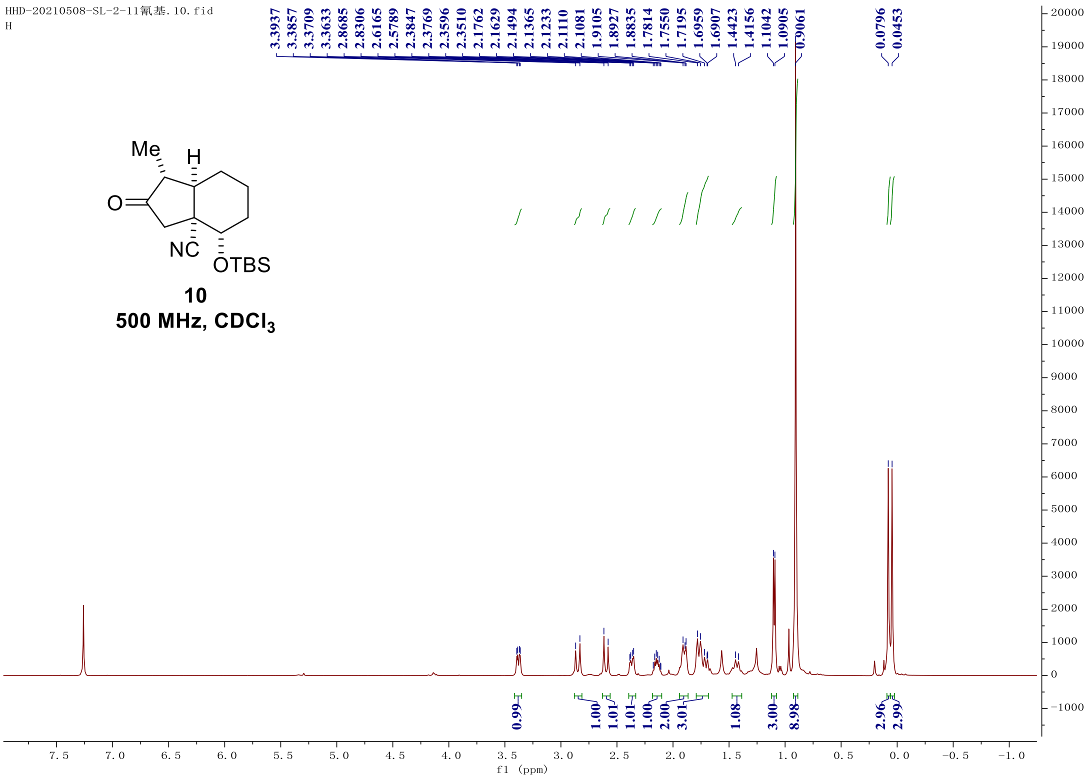

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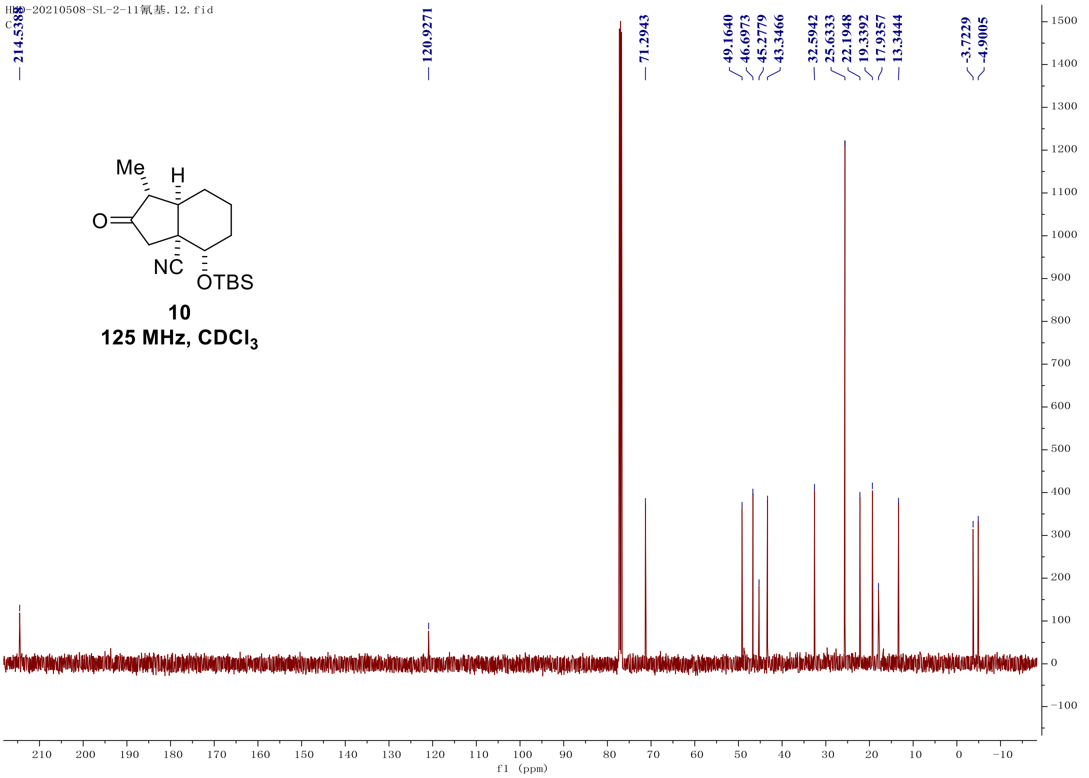

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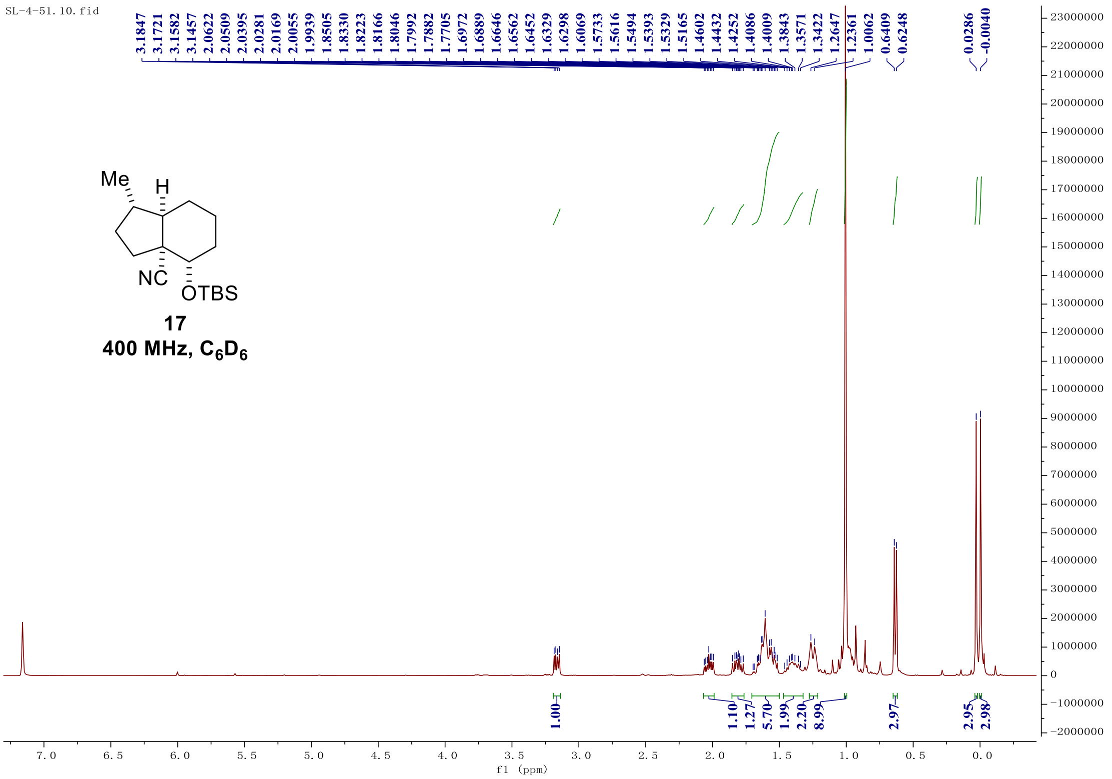
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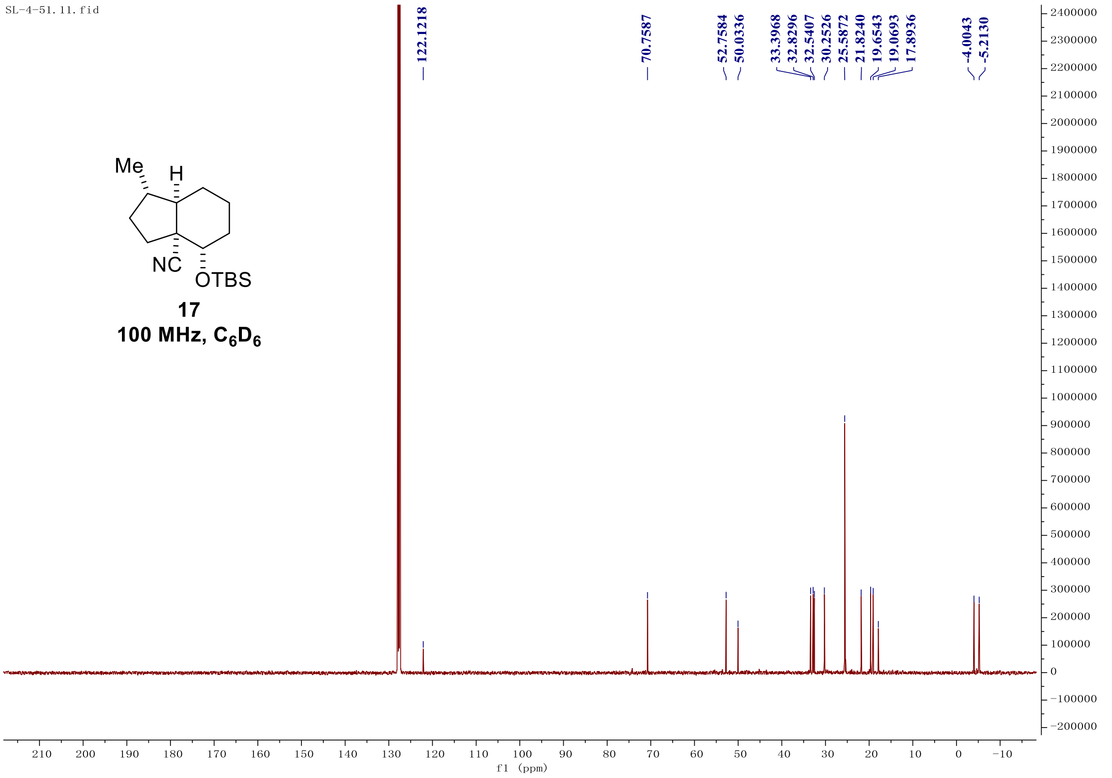
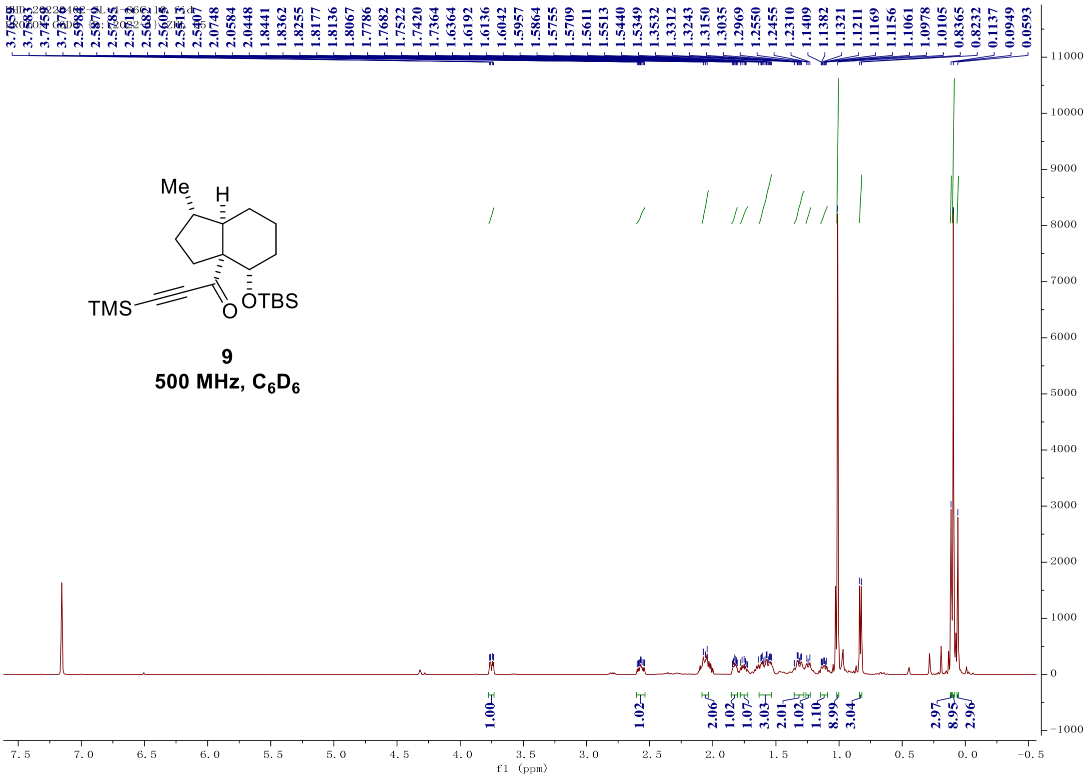
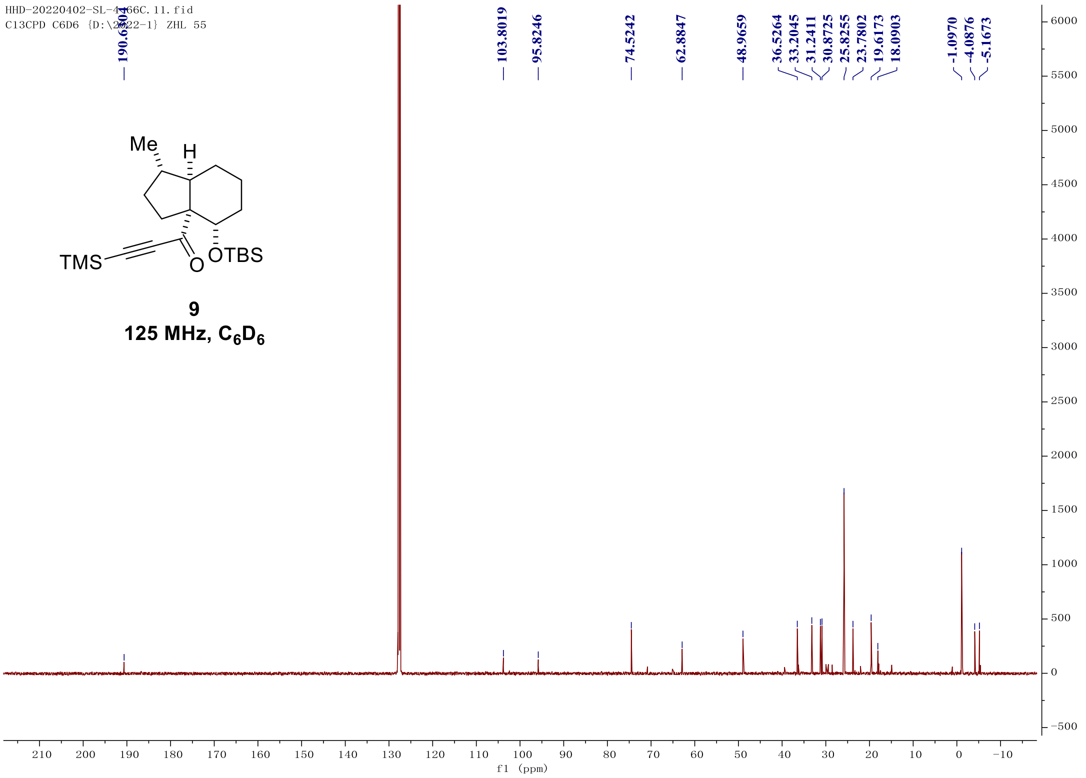
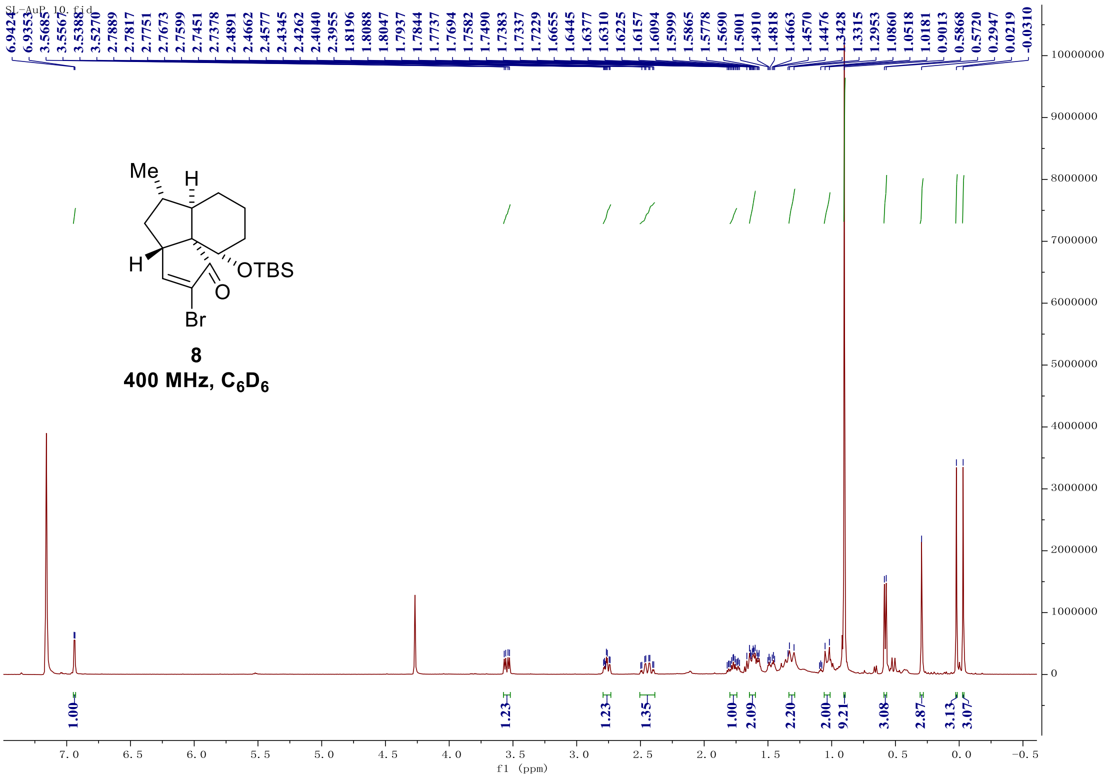
1.4009
1.3843
1.3571
1.3422
1.2647
1.2361
1.0062
0.6409
0.6248
0.0286
-0.0040
Me
H
NC
OTBS
17
400 MHz, C6D6
1.00
1.10
1.27
5.70
1.99
2.20
8.99
2.97
2.95
2.98
f1 (ppm)


SL-4-51.11.fid
122.1218
70.7587
52.7584
50.0336
33.3968
32.8296
32.5407
30.2526
25.5872
21.8240
19.6543
19.0693
17.8936
-4.0043
-5.2130
Me
H
NC
OTBS
17
100 MHz, C6D6
f1 (ppm)

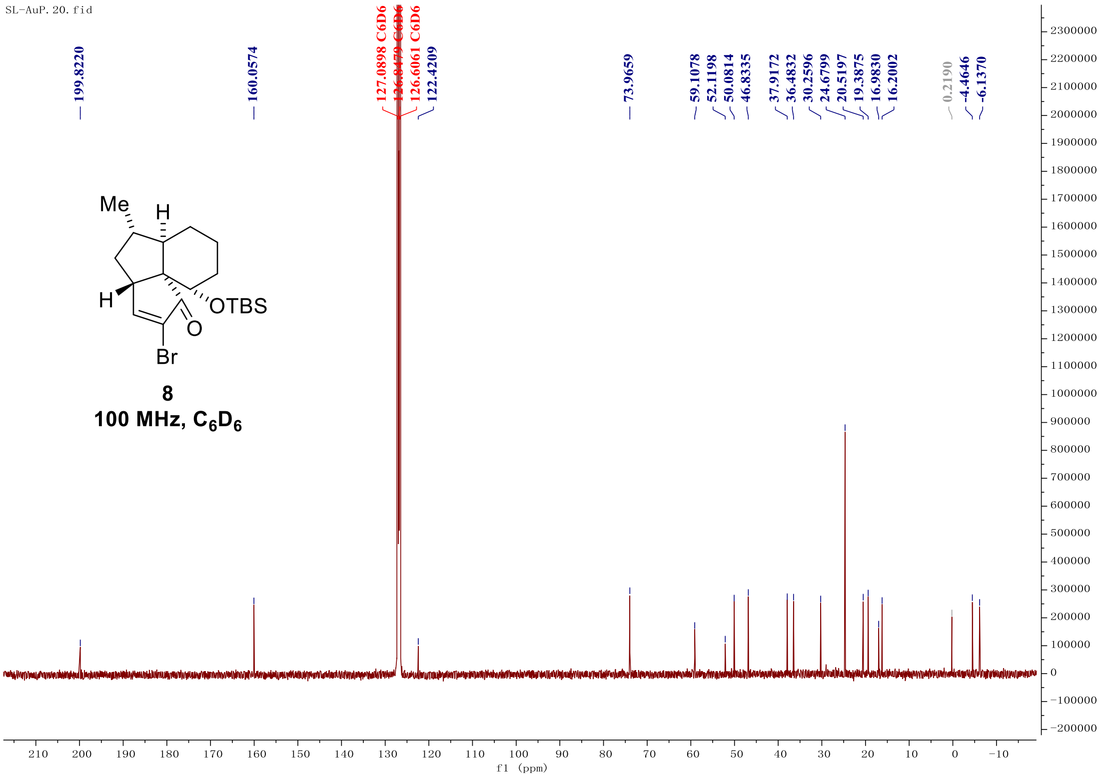

HHD-20220402-SL-4466C.10.fid
PROTON C6D6 {D:\2022-1} ZHL 55
3.7659
3.7583
3.7459
3.7376
2.5984
2.5870
2.5785
2.5712
2.5682
2.5605
2.5513
2.5407
2.0748
2.0584
2.0448
1.8441
1.8362
1.8255
1.8177
1.8136
1.8067
1.7786
1.7682
1.7522
1.7420
1.7364
1.6364
1.6192
1.6136
1.6042
1.5957
1.5864
1.5755
1.5709
1.5611
1.5513
1.5440
1.5349
1.3532
1.3312
1.3243
1.3150
1.3035
1.2969
1.2550
1.2455
1.2310
1.1409
1.1382
1.1321
1.1211
1.1169
1.1156
1.1061
1.0978
1.0105
0.8365
0.8232
0.1137
0.0949
0.0593
Me
H
TMS
O
OTBS
9
500 MHz, C_6D_6
1.00
1.02
2.06
1.02
1.07
3.03
2.01
1.02
1.10
8.99
3.04
2.97
8.95
2.96
f1 (ppm)


HHD-20220402-SL-4466C.11.fid
C13CPD C6D6 {D:\2022-1} ZHL 55
190.6304
103.8019
95.8246
74.5242
62.8847
48.9659
36.5264
33.2045
31.2411
30.8725
25.8255
23.7802
19.6173
18.0903
-1.0970
-4.0876
-5.1673
Me
H
TMS
O
OTBS
9
125 MHz, C_6D_6
f1 (ppm)



8

400 MHz, C_6D_6



8

100 MHz, C_6D_6