Electronic Supplementary Information

Cascade cyclization of 1,2,7,8-tetraones and total synthesis of (±)-nesteretal A

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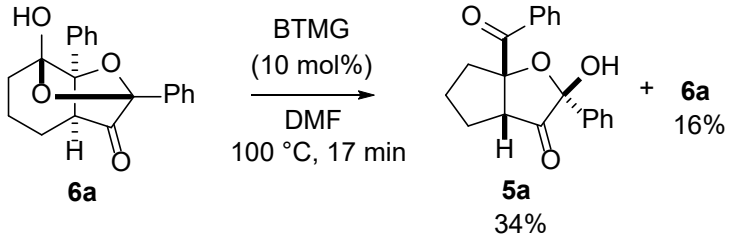
Contents

Scheme S1. Isomerization of **6a** to **5a**.



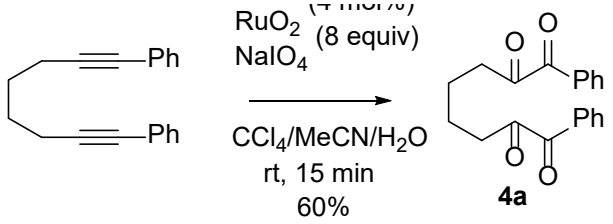
6a

5a
34%

General

All melting points were determined on Yanagimoto micro melting point apparatus. Infrared spectra (IR) were recorded on Horiba IR-710. ^{1}H NMR spectra were recorded on a JEOL JNM ECA600 (600 MHz), JEOL JNM ECZ 600 (600 MHz), or a JEOL JNM ECS400 (400 MHz) spectrometer at room temperature; chemical shifts (δ) are reported in parts per million relative to tetramethylsilane. Splitting pattern are designated as s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; br, broad. ^{13}C NMR spectra were recorded on a JEOL JNM ECA600 (150 MHz), JEOL JNM ECZ 600 (150 MHz), or JEOL JNM ECS400 (100 MHz) spectrometer with complete proton decoupling. Chemical shifts are reported in parts per million relative to tetramethylsilane with the solvent resonance as the internal standard $CDCl_3$. HRMS data were recorded on JEOL JMS-T100TD. Elemental analysis was performed with J-Science Lab Micro Coder JM-10. X-ray crystallographic analysis was performed on Rigaku R-AXIS RAPIDII-S. UV spectrum was recorded on Shimadzu UV-2600i spectormeter. ECD spectrum was obtained on JASCO J-820 spectrometer. Analytical TLC was performed on Merck precoated TLC plates (silica gel 60 GF254, 0.25 mm). Silica gel column chromatography was carried out on silica gel 60 N (Kanto Kagaku Co., Ltd., spherical, neutral, 63-210 μm). All reactions were carried out under nitrogen atmosphere in a dried glassware with magnetic stirring. 1-Propynylmagnesium bromide (0.5 M solution in THF) was purchased from Aldrich. The aldol cyclization of 1,2,7,8-tetraones should be carried out under shielding lights.

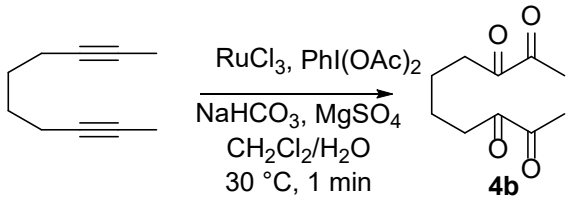
Synthesis of 1,8-diphenyloctan-1,2,7,8-tetraone (4a)



To a stirred mixture of 1,8-diphenylocta-1,7-diyne[1] (224 mg, 0.87 mmol) in acetonitrile (4.5 mL), tetrachloromethane (4.5 mL), and water (6.8 mL) were added $NaIO_4$ (1.5 g, 7.1 mmol) and RuO_2 (5.1 mg, 0.038 mmol) successively at room temperature. After stirring the resulting mixture for 15 min at room temperature, H_2O (30 mL) was added, and the mixture was extracted with CH_2Cl_2. The organic layer was dried over anhydrous Na_2SO_4, filtered through Celite, and concentrated. The crude product was purified by chromatography on silica gel (silica gel:20 g, eluent: benzene) to afford 1,8-diphenyloctan-1,2,7,8-tetraone (**4a**) (168 mg, 0.52 mmol, 60%) as a yellow oil.

^{1}H NMR (600 MHz, $CDCl_3$): δ 7.99 (4H, d, J = 7.2 Hz), 7.65 (2H, t, J = 7.2 Hz), 7.50 (4H, t, J = 7.2 Hz), 2.95 (4H, m), 1.81 (4H, m); ^{13}C NMR (100 MHz, $CDCl_3$): δ 202.6, 192.1, 134.6, 131.9, 130.2, 128.9, 38.3, 22.3; IR ($CHCl_3$) cm^{-1}: 1714, 1674; Anal. calcd for $C_{20}H_{18}O_4$: C, 74.52; H, 5.63, found C, 74.21, H, 5.33.

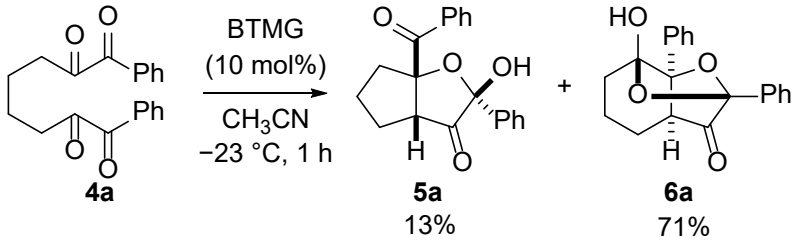
Synthesis of decan-2,3,8,9-tetraone (4b)



To a stirred mixture of deca-2,8-diyne[2] (50 mg, 3.73 mmol) in CH_2Cl_2 (1.5 mL) and H_2O (0.3 mL) were added $NaHCO_3$ (2.4 mg, 0.029 mmol), $MgSO_4$ (11.1 mg, 0.092 mmol), and $PhI(OAc)_2$ (721.5 mg, 2.24 mmol) at room temperature. Then, $RuCl_3$ (0.16 mg, 0.75 μmol) in H_2O (0.1 mL) was added at room temperature, and the resulting mixture was stirred at 30 °C for 1 min. The mixture was extracted with AcOEt, and the organic layer was washed with H_2O, dried over anhydrous Na_2SO_4, filtered, and concentrated. The crude product was purified by chromatography on silica gel (hexane/AcOEt = 5:1) to afford decan-2,3,8,9-tetraone (**4b**) (31.4 mg, 0.158 mmol, 42%) as a yellow powder.

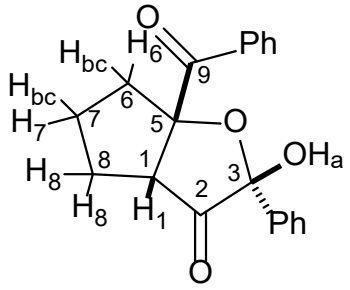
Mp: 79.5-81.0 °C (recryst. from Hexane/AcOEt); ^{1}H NMR (600 MHz, $CDCl_3$): δ 2.77 (4H, m), 2.34 (6H, s), 1.62 (4H, m); ; ^{13}C NMR (100 MHz, $CDCl_3$): δ 198.8, 197.4, 35.3, 23.6, 22.3; IR ($CHCl_3$) cm^{-1}: 1714, 1356; Anal. calcd for $C_{10}H_{14}O_4$: C, 60.59; H, 7.12, found C, 60.29, H, 7.21.

The cyclization of 4a under kinetic conditions



To a stirred solution of **4a** (20 mg, 62 μmol) in CH_3CN (0.4 mL) was added a solution of BTMG (1.1 mg, 6.2 μmol) in CH_3CN (0.2 mL) at −23 °C, and the mixture was stirred at −23 °C for 1 h. The reaction was quenched by the addition of saturated aqueous NH_4Cl solution, and the resulting mixture was extracted with AcOEt (three times). The combined organic extracts were dried over anhydrous Na_2SO_4, filtered, and concentrated. The yields of **5a** (13%) and **6a** (71%) was determined by ^{1}H NMR spectra by using 1,3,5-trimethoxybenzene as an internal standard. Compounds **5a** and **6a** were isolated by purification with column chromatography on silica gel.

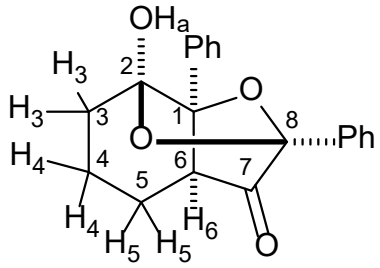
(1*R,3*R**,5*S**)-5-Benzoyl-3-hydroxy-3-phenyl-4-oxabicyclo[3.3.0]octan-2-one (5a)**



5a

White solid; mp: 117.0-119.5 ° C (recryst from $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.22 (2H, d, *J* = 7.6 Hz), 7.60-7.39 (8H, m), 3.95 (1H, t, *J* = 6.3 Hz, H_1), 2.77 (1H, brs, H_a), 2.69-2.65 (1H, m, H_6), 2.13-2.09 (2H, m, H_8, H_8), 2.05-1.97 (2H, m, H_b, H_c), 1.86-1.76 (1H, m, H_7); ^{13}C NMR (150 MHz, $CDCl_3$): δ 207.6 (C2), 200.3 (C9), 136.5, 134.8, 133.0, 130.3, 129.4, 128.3, 128.3, 126.3, 100.4 (C3), 96.1 (C5), 51.1 (C1), 40.6 (C6), 30.2 (C8), 26.5 (C7); IR ($CHCl_3$) cm^{-1}: 3558, 1768 (C=O), 1678 (PhCO); HRMS (DART) *m/z* calcd for $C_{20}H_{17}O_3$ [(M-OH)$^+$]: 305.11777, found 305.11819.

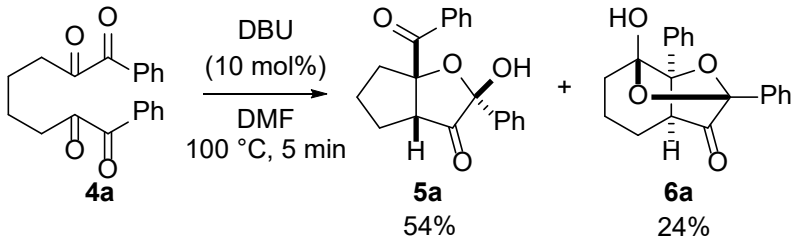
(1*R,2*R**,6*R**,8*R**)-2-Hydroxy-1,8-diphenyl-9,10-dioxatricyclo[4.3.0.1^{2,8}]decan-7-one (6a)**



6a

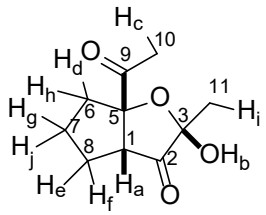
Colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.69-7.67 (4H, m), 7.48-7.42 (6H, m), 2.99 (1H, brs, H_a), 2.77 (1H, brs, H_6), 2.34 (1H, d, *J* = 14.4 Hz, H_3), 2.22 (1H, d, *J* = 14.8 Hz, H_5), 2.07 (1H, dt, *J* = 4.8, 13.9 Hz, H_3), 1.88 (1H, tt, *J* = 4.6, 14.0 Hz, H_5), 1.78 (1H, d, *J* = 14.0 Hz, H_4), 1.66 (1H, tt, *J* = 4.4, 13.8 Hz, H_4); ^{13}C NMR (100 MHz, $CDCl_3$): δ 202.0 (C7), 134.5, 130.0, 129.4, 128.8, 128.6, 128.4, 127.1, 126.2, 102.7 (C8 or C2), 102.4 (C8 or C2), 88.2 (C1), 50.3 (C6), 30.9 (C3), 22.5 (C5), 18.2 (C4); IR ($CHCl_3$) cm^{-1}: 3566, 1774; HRMS (DART) *m/z* calcd for $C_{20}H_{17}O_3$ [(M-OH)$^+$]: 305.11777, found 305.11819.

The cyclization of 4a under thermodynamic conditions



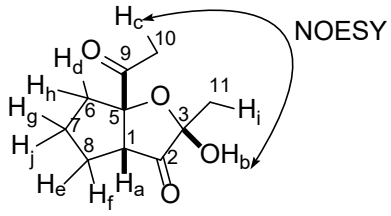
To a stirred solution of **4a** (20 mg, 62 μmol) in DMF (0.4 mL) was added a solution of DBU (0.9 mg, 6.2 μmol) in DMF (0.2 mL) at 100 °C, and the mixture was stirred at 100 °C for 5 min. The reaction was quenched by the addition of saturated aqueous NH_4Cl solution, and the resulting mixture was extracted with AcOEt (three times). The combined organic extracts were dried over anhydrous Na_2SO_4, filtered, and concentrated. The yields of **5a** (54%) and **6a** (24%) was determined by ^1H NMR by using 1,3,5-trimethoxybenzene as an internal standard. The recovery of **4a** (2%) was also detected by ^1H NMR.

(1*R,3*R**,5*S**)-5-acetyl-3-hydroxy-3-methyl-4-oxabicyclo[3.3.0]octan-2-one (5b)**



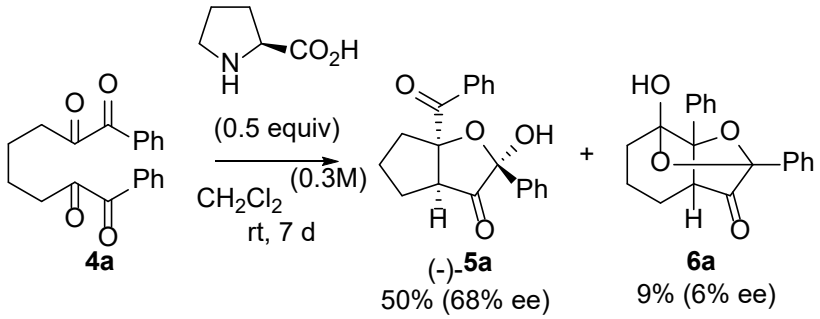
5b

66% yield; white solid; mp 111.0-114.5° C (recryst from $CHCl_3$); ^1H NMR (600 MHz, $CDCl_3$): δ 3.31 (1H, d, J = 10.8 Hz, H_a), 3.13 (1H, brs, H_b), 2.37 (3H, s, H_c), 2.20-2.08 (2H, m, H_d and H_e), 2.02-1.95 (1H, m, H_f), 1.86-1.82 (1H, m, H_g), 1.75-1.70 (1H, m, H_h), 1.50 (3H, s, Hi), 1.49-1.45 (1H, m, H_j); ^{13}C NMR (150 MHz, $CDCl_3$): δ 210.9 (C9), 209.9 (C2), 99.3 (C3), 95.6 (C5), 49.4 (C1), 38.7 (C6), 30.7 (C8), 26.1 (C10), 25.3 (C7), 20.7 (C11); IR ($CHCl_3$) cm^{-1}: 3586, 1766, 1712, 1214, HRMS (DART) *m/z* calcd for $C_{10}H_{13}O_3$ [$(M\text{-}OH)^+$]: 181.08647, found 181.08666.



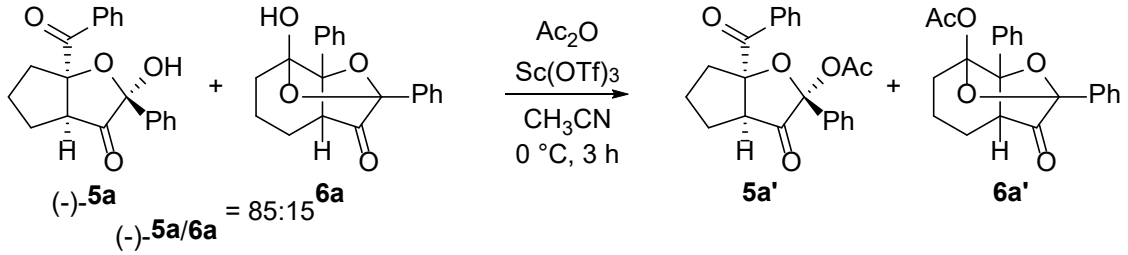
We could not purify compound **6b** by column chromatography on silica gel and preparative TLC on silica gel. Its presence and yield was deduced by ^1H NMR analysis with reference to the data of compound **6a**.

L-Proline-catalyzed enantioselective cyclization of 4a

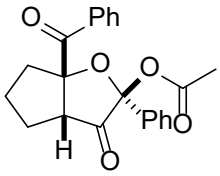


The mixture of **4a** (30 mg, 93 μmol) and L-proline (5.4 mg, 47 μmol) in dichloromethane (0.3 mL) was stirred at 25°C for 7 days. The reaction was quenched by adding water, and the resulting mixture was extracted with ethyl acetate. The combined extracts were washed with brine, dried over anhydrous Na_2SO_4, filtered, and concentrated. The yields of **5a** (50%), **6a** (9%), and recovered **4a** (2%) were determined by ^1H NMR analysis of the crude product by using 1,3,5-trimethoxybenzene (15.6 mg) as an internal standard. $[\alpha]_D^{21} = -34.8°$ (*c* 0.145, $CHCl_3$) for (-)-**5a** (68% ee).

Acetylation of (-)-5a and 6a



To a stirred solution of **5a** and **6a** (17.7 mg, 0.055 mmol, **5a**/**6a** = 85:15) in Ac_2O (0.1 mL, 1.06 mmol) was added a solution of $Sc(OTf)_3$ (1.8 mg, 3.6 μmol) in CH_3CN (0.05 mL) at 0 °C. The mixture was stirred at 0 °C for 3 h, and the reaction was quenched by adding a saturated aqueous solution of $NaHCO_3$. The resulting mixture was extracted with ether. The combined organic extracts were washed with brine, dried over anhydrous Na_2SO_4, filtered, and concentrated. The crude product was purified by preparative TLC (CH_2Cl_2 and hexane/ethyl acetate = 5:1) to afford **5a'** (12.8 mg, 0.04 mmol) as a colorless solid and **6a'** (1.9 mg, 6.2 μmol).

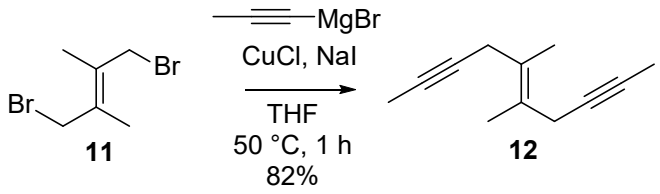


5a'

Mp: 153.0-155.0 °C (recryst. from CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.15 (2H, d, *J* = 7.2 Hz), 7.73-7.71 (2H, m), 7.55-7.41 (6H, m), 4.00 (1H, dd, *J* = 11.6, 2.8 Hz), 2.68 (1H, dd, *J* = 13.2, 6.0 Hz), 2.20-2.10 (2H, m), 1.94-1.85 (2H, m), 1.75-1.64 (1H, m), 1.59 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) : δ 208.4, 200.8, 170.7, 135.5, 134.6, 132.6, 129.9, 129.5, 128.3, 128.0, 126.2, 101.1, 100.1, 54.4, 42.2, 31.4, 26.9, 19.9; IR ($CHCl_3$) cm^{-1}: 2927, 1766, 1738, 1246; HRMS (DART) *m/z* calcd for $C_{20}H_{17}O_3$ [(M-OAc)$^+$]: 305.11777, found 305.11695; $[\alpha]_D^{22}$ = +179° (*c* 0.058, $CHCl_3$) for **5a'** (68% ee)

The optical purity of **5a'** was determined by chiral HPLC (Daicel chiralpac AD-H (15 cm × 0.46 cm ID), hexane/2-propanol = 99:1, flow rate = 1 mL/min, 254 nm) t_{major} = 22.3 min, t_{minor} = 31.7 min.

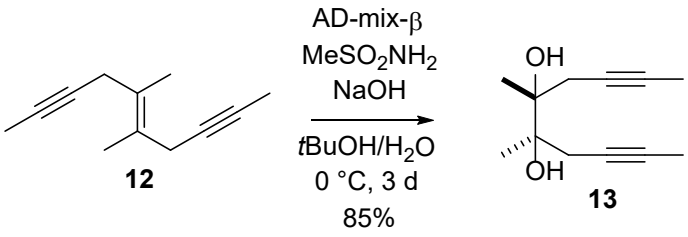
(*E*)-5,6-dimethyldeca-5-en-2,8-diyne (12)



To a stirred mixture of NaI (282 mg, 1.88 mmol) and CuCl (326 mg, 3.29 mmol) was added 1-propynylmagnesium bromide (0.5 M solution in THF, 45 mL, 22.5 mmol) at 50 °C, and the resulting mixture was stirred at 50 °C for 30 min. The solution of **11** (680 mg, 2.81 mmol) in THF (14.1 mL) was then added at 50°C, and the mixture was stirred at 50 °C for 1 h. The reaction was quenched by the addition with ice, and the mixture was filtered through a Celite pad. After evaporation of THF in the filtrate, the residue was extracted with ethyl acetate. The combined organic extracts were washed with brine, dried over anhydrous Na_2SO_4, filtered, and concentrated carefully because of the low boiling point of **12**. The crude product was purified by column chromatography on silica gel (hexane/ethyl acetate = 50 : 1) to afford **12** (369 mg, 2.31 mmol, 82%) as a colorless oil.

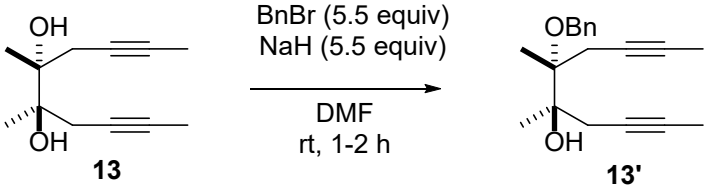
^{1}H NMR (400 MHz, $CDCl_3$): δ 2.88 (4H, m), 1.72 (12H, m); ^{13}C NMR (100 MHz, $CDCl_3$): δ 125.5, 77.0, 75.5, 24.0, 17.9, 3.6; IR ($CHCl_3$) cm^{-1}: 3008, 2922, 1442, 1230; HRMS (ESI+) (*m/z*) calcd for $C_{12}H_{17}$ [(M+H)$^+$]: 161.13303, found 161.13235.

(5*R,6*R**)-5,6-dimethyldeca-2,8-diyne-5,6-diol (13)**



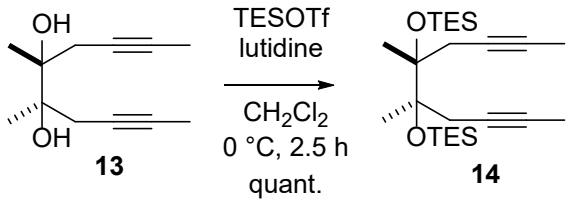
To a stirred solution of **12** (50 mg, 0.31 mmol) in *t*BuOH (1.6 mL) and H_2O (1.6 mL) were added $MeSO_2NH_2$ (89 mg, 0.94 mmol) and AD-mix-β (1.06 g) at 0°C. The pH of the reaction mixture was adjusted to 12 by adding the 2 M aqueous solution of NaOH (2.4 mL) at 0 °C. The resulting orange solution was stirred at 0 °C for 3 days. The reaction was quenched by the addition of the saturated aqueous solution of $Na_2S_2O_3$ and NaCl. The mixture was extracted with ethyl acetate. The organic extracts were washed with the saturated aqueous solution of NH_4Cl and brine, dried over anhydrous Na_2SO_4, filtered, and concentrated. The crude product was purified by column chromatography on silica gel (hexane/ethyl acetate = 50:1 to 10:1) to afford **13** (52 mg, 0.27 mmol, 85%) as a while solid. M.p.: 57-59 °C; ^{1}H NMR (600 MHz, $CDCl_3$): δ 2.73 (2H, br, s), 2.65 (2H, dq, J = 2.4 Hz, J = 16.8 Hz), 2.37 (2H, dq, J = 2.4 Hz, J = 16.8 Hz), 1.82 (6H, t, J = 2.4 Hz), 1.27 (6H, s); ^{13}C NMR (150 MHz, $CDCl_3$): δ 79.1, 75.5, 75.4, 28.1, 21.9, 3.5; IR ($CHCl_3$) cm^{-1}: 3546; HRMS (ESI+) (*m/z*) calcd for $C_{12}H_{19}O_2$ [$(M+H)^+$]: 195.13850, found 195.13864.

It was found that thus obtained **13** was racemic. The optical purity of **13** was determined by chiral HPLC analysis of its monobenzylated derivative **13'**.



The optical purity of **13'** was determined by chiral HPLC (Daicel chiralpac OJ-H (15 cm × 0.46 cm ID), hexane/2-propanol = 9:1, flow rate = 1 mL/min, 254 nm) t = 3.9 min, t = 4.5 min.

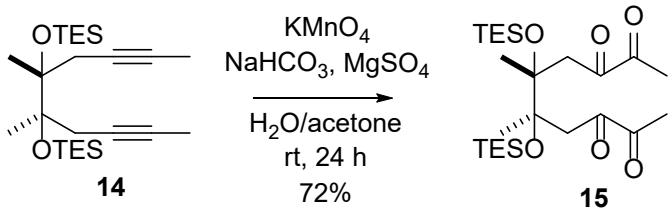
(5*R,6*R**)-5,6-di(but-2-yn-1-yl)-3,3,8,8-tetraethyl-5,6-dimethyl-4,7-dioxa-3,8-disiladecane (14)**



To a solution of diol **13** (389 mg, 2.0 mmol) in CH_2Cl_2 (17 mL) cooled in an ice bath was added 2,6-lutidine (0.69 mL, 6.0 mmol) and triethylsilyl trifluoromethanesulfonate (1.35 mL, 6.0 mmol). Et_2O was added to the reaction mixture, and the organic layer was separated. The organic layer was washed with saturated aqueous $NaHCO_3$, brine, and dried over anhydrous Na_2SO_4. The solvent was removed under reduced pressure and the residue was purified by silica gel column chromatography (Hexane 100%) to furnish compound **14** (876 mg, quant.) as a colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ 2.58 (2H, dq, J = 2.4 Hz, J = 16.8 Hz), 2.41 (2H, dq, J = 2.4 Hz, J = 16.8 Hz), 1.79 (6H, t, J = 2.4 Hz), 1.30 (6H, s), 0.92-0.97 (18H, t, J = 8.0 Hz), 0.59-0.73 (12H, m, J = 8.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 80.0, 78.3, 78.1, 27.7, 22.5, 7.3, 6.8, 3.8; IR ($CHCl_3$) cm^{-1}: 2051; Anal. calcd for $C_{24}H_{46}O_2Si_2$: C, 68.18; H, 10.97, found C, 66.37, H, 10.74.

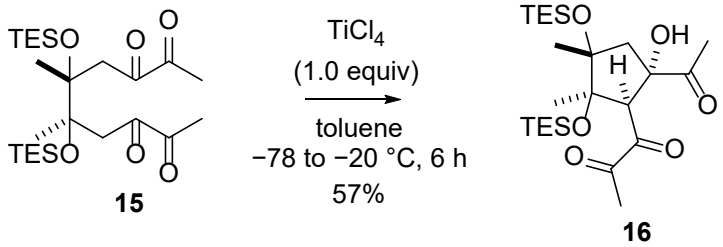
(5*R,6*R**)-5,6-dimethyl-5,6-bis((triethylsilyl)oxy)decane-2,3,8,9-tetraone (15)**



To a solution of **14** (31.4 mg, 0.074 mmol) in acetone (2.5 mL) and a buffer solution (1.0 mL) that was prepared from of $NaHCO_3$ (4.93 mg), $MgSO_4$ (49.3 mg), and water (1.0 mL) was added at room temperature $KMnO_4$ (94 mg, 0.60 mmol) in portions over 24 h. After Celite filtration with ethyl acetate, the organic layer was separated. The aqueous layer was extracted with ethyl acetate and the combined organic layers were washed with brine and dried over anhydrous Na_2SO_4. The solvent was removed under reduced pressure and the residue was purified by column chromatography on silica gel (2% ethyl acetate/hexane) to afford tetraone **15** (26 mg, 72%) as a yellow oil.

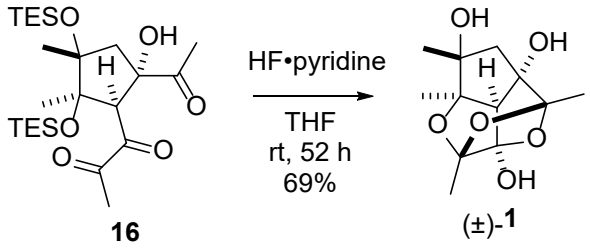
^{1}H NMR (600 MHz, $CDCl_3$): δ 3.90 (2H, d, *J* = 13.6 Hz), 2.40 (2H, d, *J* = 13.6 Hz), 2.34 (6H, s), 1.42 (6H, s), 0.90 (18H, t, *J* = 7.6 Hz), 0.55 (12H, q, *J* = 7.6 Hz); ^{13}C NMR (150 MHz, $CDCl_3$): δ 196.9, 195.9, 81.8, 23.5, 22.9, 22.6, 14.1, 6.9, 6.5; IR ($CHCl_3$) cm^{-1}: 1708; Anal. calcd for $C_{24}H_{46}O_6Si_2$: C, 59.22; H, 9.53, found C, 58.93, H, 9.26.

1-((1*R,2*R**,3*R**,5*S**)-5-acetyl-5-hydroxy-2,3-dimethyl-2,3-bis((triethylsilyl)oxy)cyclopentyl)propane-1,2-dione (16)**



To a solution of tetraone **15** (144 mg, 0.3 mmol) in toluene (6 mL) was added $TiCl_4$ (1.0 M solution of dichloromethane, 0.3 mL, 0.3 mmol) at −78 °C under argon atmosphere. The mixture was stirred at −78 °C for 1 h and at −20 °C for 5 h, and the reaction was quenched by adding saturated aqueous solution of $NaHCO_3$ at −20 °C. The organic layer was separated, and the aqueous layer was extracted with ethyl acetate. The combined organic layers were washed with brine and dried over anhydrous Na_2SO_4. The solvent was removed under reduced pressure and the residue was purified by column chromatography on silica gel (2% ethyl acetate/hexane) to afford **16** (82.3 mg, 57%) as a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.80 (1H, s), 3.53 (1H, s), 2.40 (3H, s), 2.20 (1H, d, *J* = 14 Hz), 2.14 (3H, s), 2.04 (1H, d, *J* = 14 Hz), 1,46 (3H, s), 1.23 (3H, s), 0.97 (9H, t, *J* = 8.0 Hz), 0.88 (9H, t, *J* = 8.0 Hz), 0.59-0.68 (12H, m); ^{13}C NMR (100 MHz, $CDCl_3$): δ 207.9, 203.1, 194.8, 88.3, 87.9, 83.9, 62.4, 49.0, 23.8, 23.7, 20.0, 18.7, 7.2, 7.1, 6.6, 6.5; IR ($CHCl_3$) cm^{-1}: 3478, 1774, 1708, 1602; Anal. calcd for $C_{24}H_{46}O_6Si_2$: C, 59.22; H, 9.52, found C, 58.90, H, 9.80.

(±)-Nesteretal A (1)[3]



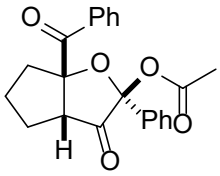
16 (±)-**1**

To a solution of **16** (35 mg, 0.071 mmol) in dry THF (0.35 mL) was added pyridine (0.096 mL, 1.20 mmol) and HF·pyridine (0.071 mL) at 0 ℃. The mixture was stirred at the room temperature for 52 h. The reaction was quenched with saturated aqueous solution of $NaHCO_3$ and the resulting mixture was extracted with AcOEt (three times) and THF (twice). The combined organic extracts were washed with brine, dried over Na_2SO_4, and concentrated in vacuo. The residue was purified by column chromatography on silica gel (AcOEt 100%) to afford **1** (12.6 mg, 69%) as amorphous powder.

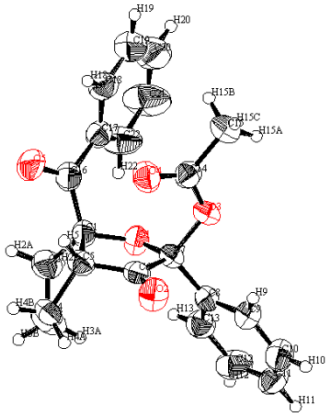
^{1}H NMR (400 MHz, DMSO-d_6): δ 7.67 (1H, s), 5.16 (1H, s), 4.54 (1H, s), 2.55 (1H, s), 2.11 (1H, d, J = 14 Hz), 1.51 (1H, d, J = 14 Hz), 1.20 (3H, s), 1.15 (3H, s), 1.13 (3H, s), 1.04 (3H, s); ^{13}C NMR (400 MHz, DMSO-d_6): δ 111.6, 107.0, 104.1, 90.3, 90.2, 84.3, 64.3, 47.4, 21.0, 19.4, 18.1 ,13.3.

The ^{1}H an ^{13}C NMR data of our synthesized **1** were accordance with the literature values.[3]

X-ray Crystallography of 5a'



5a'



Crystallographic data (excluding structure factors) for **5a'** have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication CCDC 2141535. Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK, (fax: +44-(0)1223-336033 or e-mail: deposit@ccdc.cam.ac.Uk).

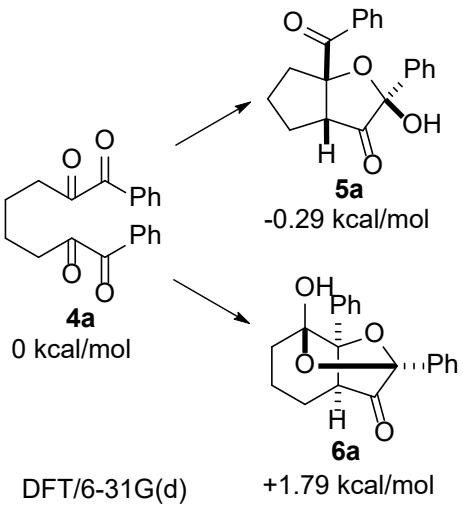


Figure S1. DFT calculations of **4a**, **5a**, and **6a**.

Geometry optimization was performed with Spartan '18[4] and the Gaussian 09 packages.[5] The ground-state geometries of all compounds were determined by means of the following successive steps: Conformational search with MMFF,[6] then DFT calculation with B3LYP functionals.[7] The basis set employed for DFT geometry optimization was the native 6-31G(d).

Compound 4a: 0 kcal/mol

SCF Done: E(RB3LYP) = -1073.85384809 A.U. after 7 cycles

Standard orientation:

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms) X	Y	Z
1	6	0	-1.716688	-0.817644	-4.095689
2	6	0	-1.815898	-0.677725	-2.555082
3	6	0	-0.509737	-0.380902	-1.847439
4	1	0	0.173944	-1.221310	-2.046677
5	1	0	-0.045241	0.474665	-2.354280
6	6	0	-0.669222	-0.141569	-0.345993
7	1	0	-1.152982	-1.013888	0.111864
8	1	0	-1.359637	0.696881	-0.187874
9	6	0	0.669222	0.141569	0.345993
10	1	0	1.359637	-0.696881	0.187874
11	1	0	1.152982	1.013888	-0.111864

12	6	0	0.509737	0.380902	1.847439
13	1	0	0.045241	-0.474665	2.354280
14	1	0	-0.173944	1.221310	2.046677
15	6	0	1.815898	0.677725	2.555082
16	6	0	1.716688	0.817644	4.095689
17	6	0	2.646422	1.700239	4.851722
18	6	0	4.278074	3.357584	6.412408
19	6	0	2.514202	1.717848	6.252554
20	6	0	3.605692	2.526962	4.240945
21	6	0	4.414364	3.350502	5.023251
22	6	0	3.325533	2.537967	7.027259
23	1	0	1.765366	1.077909	6.707577
24	1	0	3.726947	2.513616	3.165523
25	1	0	5.154820	3.986004	4.545687
26	1	0	3.217830	2.543406	8.108380
27	1	0	4.912109	4.000867	7.016954
28	6	0	-2.646422	-1.700239	-4.851722
29	6	0	-4.278074	-3.357584	-6.412408
30	6	0	-2.514202	-1.717848	-6.252554
31	6	0	-3.605692	-2.526962	-4.240945
32	6	0	-4.414364	-3.350502	-5.023251
33	6	0	-3.325533	-2.537967	-7.027259
34	1	0	-1.765366	-1.077909	-6.707577
35	1	0	-3.726947	-2.513616	-3.165523
36	1	0	-5.154820	-3.986004	-4.545687
37	1	0	-3.217830	-2.543406	-8.108380
38	1	0	-4.912109	-4.000867	-7.016954
39	8	0	0.851914	0.152215	4.651648
40	8	0	2.889346	0.741041	1.984483
41	8	0	-2.889346	-0.741041	-1.984483
42	8	0	-0.851914	-0.152215	-4.651648

Compound 5a: -0.29 kcal/mol

SCF Done: E(RB3LYP) = -1073.85431499 A.U. after 7 cycles

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms) X	Y	Z
1	6	0	-0.692339	1.282122	0.304641
2	6	0	0.149632	2.298628	-0.509421
3	6	0	0.477207	3.474380	0.444444
4	6	0	0.274261	2.890349	1.853140
5	6	0	-0.933346	1.953298	1.675026
6	1	0	-0.375033	2.633047	-1.408229
7	1	0	1.484388	3.863377	0.265529
8	1	0	-0.232482	4.290817	0.269167
9	1	0	0.103734	3.657257	2.615628
10	1	0	1.153867	2.310016	2.157132
11	1	0	-1.858241	2.540878	1.624024
12	1	0	-1.047481	1.210600	2.470478
13	8	0	0.180963	0.138039	0.515801
14	6	0	1.372663	1.495974	-0.932058
15	8	0	2.393052	1.920570	-1.413805
16	6	0	1.075249	0.011578	-0.572803
17	6	0	-2.016936	0.899701	-0.391381
18	8	0	0.420909	-0.488003	-1.725970
19	1	0	0.184592	-1.414861	-1.546308
20	8	0	-2.526357	1.725196	-1.136243
21	6	0	2.277230	-0.811986	-0.171948
22	6	0	4.554735	-2.299929	0.495474
23	6	0	2.576743	-1.078833	1.168880
24	6	0	3.131129	-1.286218	-1.176715
25	6	0	4.264083	-2.026833	-0.842790
26	6	0	3.709009	-1.824667	1.498946
27	1	0	1.918198	-0.708582	1.946568
28	1	0	2.900893	-1.070591	-2.214754
29	1	0	4.921084	-2.389302	-1.628777
30	1	0	3.929536	-2.034359	2.542309
31	1	0	5.437246	-2.878788	0.754725
32	6	0	-2.718320	-0.395327	-0.109082
33	6	0	-4.215476	-2.727674	0.339408

34	6	0	-3.864946	-0.670671	-0.875519
35	6	0	-2.333763	-1.306726	0.889320
36	6	0	-3.084287	-2.461652	1.112232
37	6	0	-4.603719	-1.828595	-0.658465
38	1	0	-4.157571	0.046043	-1.635442
39	1	0	-1.446128	-1.123959	1.480772
40	1	0	-2.780517	-3.157013	1.890061
41	1	0	-5.484176	-2.030806	-1.262314
42	1	0	-4.793294	-3.631707	0.513192

Compound 6a: +1.79 kcal/mol

SCF Done: E(RB3LYP) = -1073.85099898 A.U. after 6 cycles

Standard orientation:

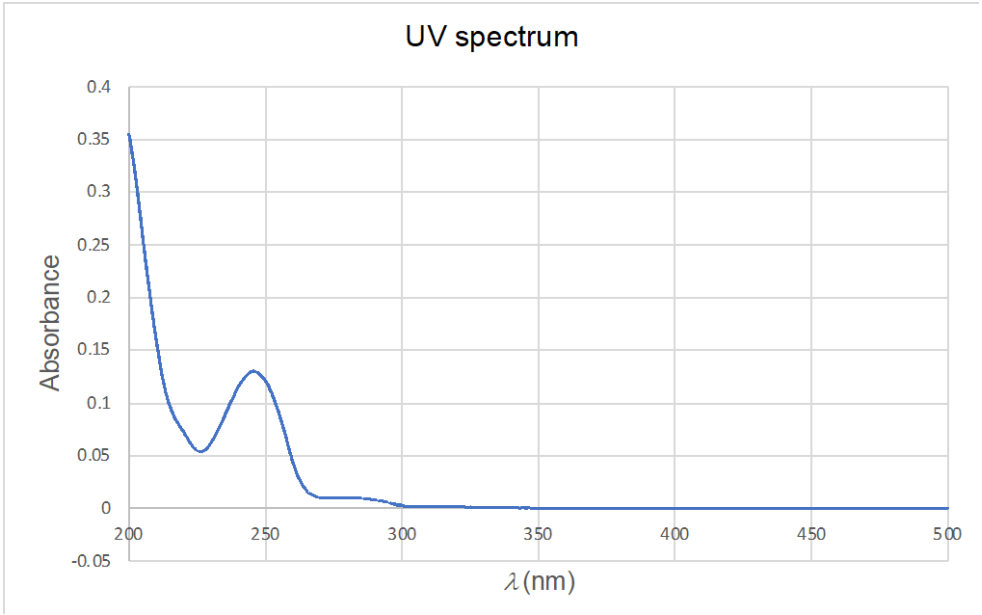
Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms) X	Y	Z
1	6	0	0.688341	0.935619	-1.340639
2	6	0	0.843307	3.159549	-0.123442
3	6	0	0.560584	0.985176	1.168302
4	6	0	1.120925	2.405822	1.183207
5	6	0	0.973197	0.102800	-0.056621
6	6	0	1.285555	2.349966	-1.351371
7	1	0	1.359317	4.126246	-0.107157
8	1	0	0.678143	2.923589	2.040699
9	1	0	0.973995	2.853885	-2.273167
10	1	0	1.034575	0.369147	-2.213327
11	1	0	-0.228742	3.375041	-0.195496
12	1	0	2.200064	2.349480	1.366587
13	1	0	2.380522	2.270191	-1.379328
14	8	0	-0.146697	-0.842562	-0.044478
15	6	0	-0.848558	0.925047	-1.341171
16	6	0	-1.198166	0.099249	-0.077814
17	8	0	-0.877285	1.036784	0.980521
18	8	0	-1.595902	1.484372	-2.105987

19	8	0	0.849961	0.394195	2.399348
20	1	0	0.488806	-0.508966	2.370614
21	6	0	2.277868	-0.655884	-0.045608
22	6	0	4.693542	-2.088808	-0.188770
23	6	0	2.434711	-1.709574	-0.960536
24	6	0	3.343726	-0.340354	0.806066
25	6	0	4.544768	-1.049550	0.728285
26	6	0	3.629701	-2.421750	-1.030476
27	1	0	1.605990	-1.979963	-1.608259
28	1	0	3.233890	0.436203	1.552603
29	1	0	5.361555	-0.790537	1.396562
30	1	0	3.729588	-3.237617	-1.741297
31	1	0	5.627942	-2.640774	-0.243850
32	6	0	-2.565122	-0.484199	0.060307
33	6	0	-5.145767	-1.535181	0.274287
34	6	0	-3.663083	0.374322	0.194193
35	6	0	-2.762526	-1.868118	0.026774
36	6	0	-4.051898	-2.390564	0.135059
37	6	0	-4.948586	-0.152628	0.303720
38	1	0	-3.506362	1.447657	0.215483
39	1	0	-1.908046	-2.528115	-0.079902
40	1	0	-4.200156	-3.466860	0.112256
41	1	0	-5.797491	0.517093	0.410436
42	1	0	-6.149318	-1.943635	0.358792

Determination of the absolute configuration of (-)-5a

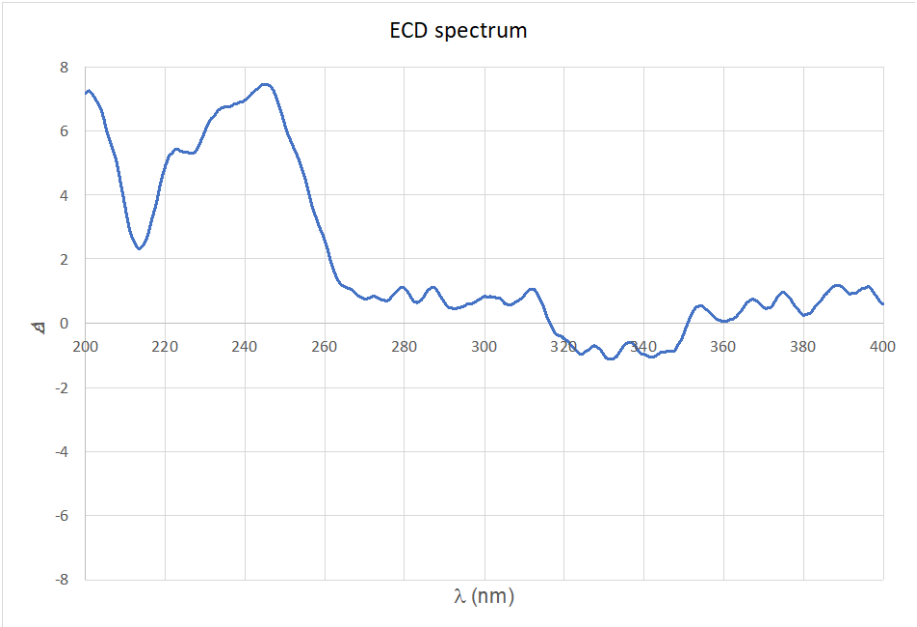
The absolute configuration of (-)-**5a** was determined by comparing the experimental and calculated ECD spectra using the TDDFT method at the B3LYP/6-31+G(d) level. The calculated ECD curves of (1*S*,3*S*,5*R*)-**5a** was in good agreement with the experimental one of (-)-**5a** (**Figure S6**).

Figure S2. UV spectrum of compound **5a**[a]



[a]Conditions:A 1.33 x 10^{-5} M of **5a** in MeCN at 20 ˚C.

Figure S3. ECD spectrum of compoun (-)-**5a**[b]



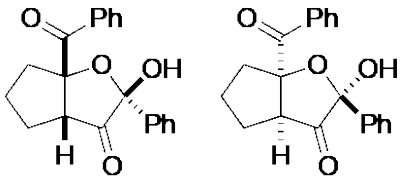
[b]Conditions: A 1.33 x 10^{-5} M solution of (-)-**5a** (68% ee) in MeCN at 20 ˚C.

Computational experiments: The all conformers of (1*S*,3*S*,5*R*)-**5a** and (1*R*,3*R*,5*S*)-**5a** were systematically generated by Spartan '18[1] package using MMFF molecular force field[6] within an energy from the global minima to 9.56 kcal/mol (40 kJ/mol). These comformers were optimized by Gaussian 09[2] using DFT calculation at B3LYP/6-31G(d) level and an energy minimum of each conformers was confirmed by frequency calculation at the same level. ECD calculations for all of the optimized conformers were carried out by Gaussian 09 using TDDFT calculation at B3LYP/6-31G(d) level by considering the first 20 excitations. The ECD spectra corrrected with regard to Boltzmann weighted average of each conformer at 20 ˚C were produced by excel program (UV-VIS peak half-width at height: 0.333 eV).

Results

conformers	G (hartree)	ΔG (kcal/mol)	Boltzmann distribution (%)
(1*R*,3*R*,5*S*)-**5a-01**	–1073.85431497	0	97.73
(1*R*,3*R*,5*S*)-**5a-02**	–1073.85034767	2.49	1.36
(1*R*,3*R*,5*S*)-**5a-03**	–1073.84997352	2.72	0.91
(1*S*,3*S*,5*R*)-**5a-01**	–1073.85431495	0	97.73
(1*S*,3*S*,5*R*)-**5a-02**	–1073.85034767	2.49	1.36
(1*S*,3*S*,5*R*)-**5a-03**	–1073.84997351	2.72	0.91

Figure S4. Structures of (1*R*,3*R*,5*S*)-**5a** and (1*S*,3*S*,5*R*)-**5a**.



(1*R*,3*R*,5*S*)-**5a** (1*S*,3*S*,5*R*)-**5a**

Figure S5. Optimized conformers of (1*R*,3*R*,5*S*)-**5a** and (1*S*,3*S*,5*R*)-**5a** within an energy from global minima to 9.56 kcal/mol

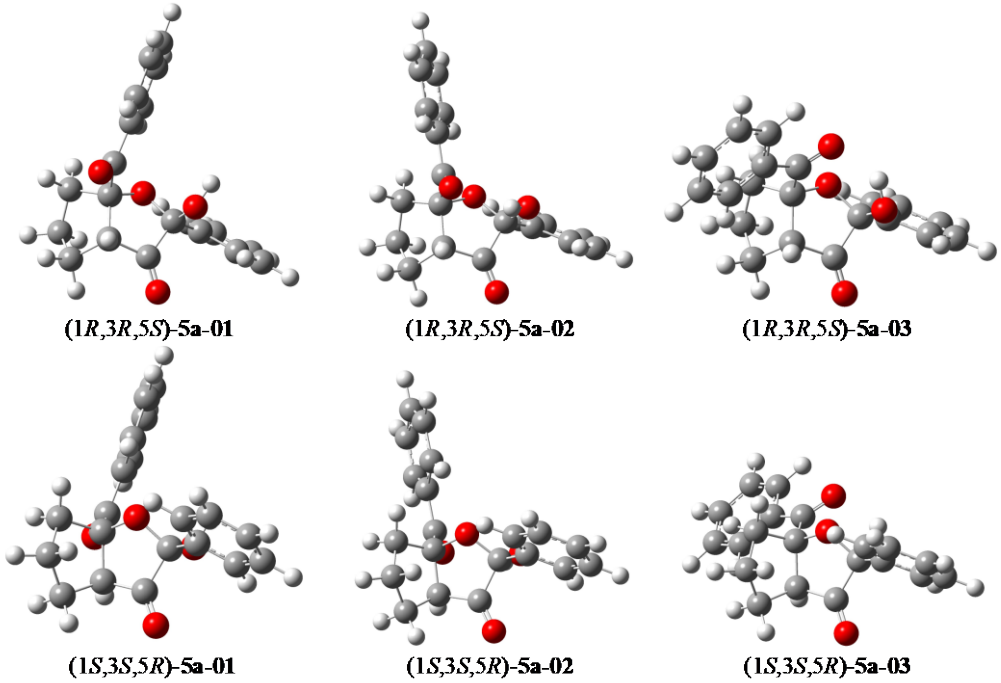
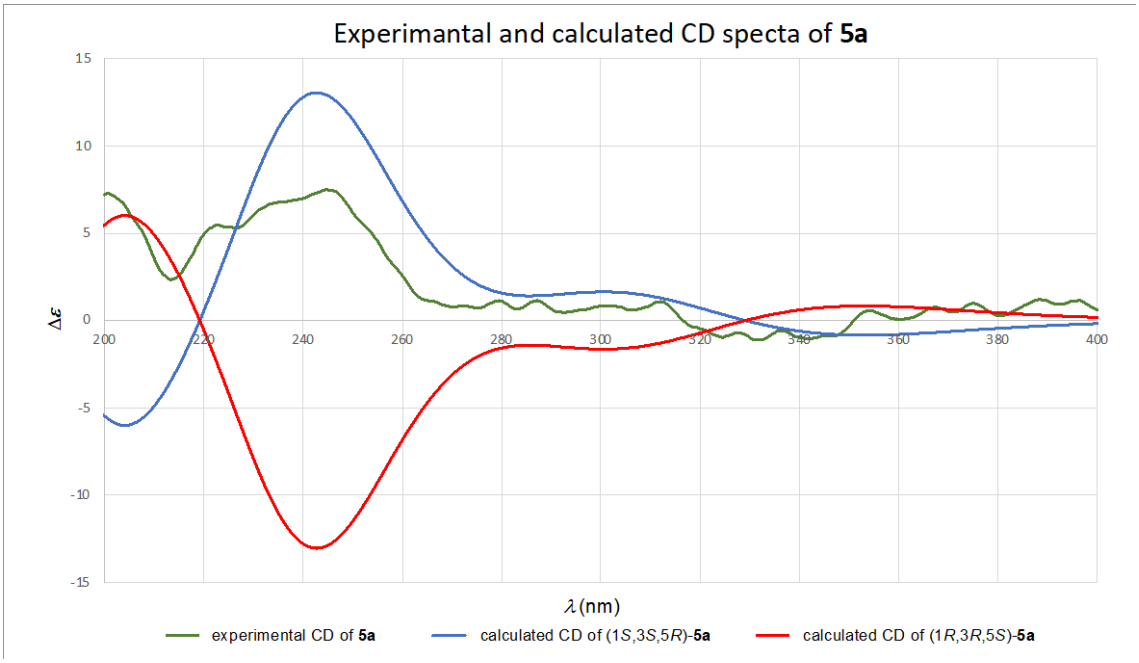


Figure S6. Superimposed ECD spectra of the experimental spectrum of (-)-**5a** and the caluculated spectra of (1*R*,3*R*,5*S*)-**5a** and (1*S*,3*S*,5*R*)-**5a**.[c,d]



[c]Conditions: The experimental ECD spectrum was measured using a 1.33 x 10^{-5} M solution of (-)-**5a** (68% ee) in MeCN at 20 ˚C. [d]The calculation of ECD spectra were carried out with the B3LYP/6-

31G(d).

Results of optimization of each conformers

Conformer (1*R*,3*R*,5*S*)-**5a-01**: ΔG = 0 kcal/mol

SCF Done: E(RB3LYP) = -1073.85431497 A.U. after 7 cycles

Standard orientation:

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms) X	Y	Z
1	1	0	-0.374907	2.632781	-1.408405
2	6	0	0.149593	2.298654	-0.509387
3	6	0	0.476641	3.474586	0.444388
4	6	0	0.273861	2.890515	1.853089
5	6	0	-0.933505	1.953166	1.674967
6	6	0	-0.692358	1.282031	0.304580
7	1	0	-0.233384	4.290720	0.269049
8	1	0	1.483676	3.863960	0.265479
9	1	0	1.153622	2.310394	2.157058
10	1	0	0.103168	3.657362	2.615602
11	1	0	-1.858536	2.540534	1.623968
12	1	0	-1.047491	1.210453	2.470427
13	6	0	1.372932	1.496228	-0.931576
14	8	0	0.180973	0.137979	0.515718
15	6	0	1.075413	0.011703	-0.572808
16	8	0	0.421224	-0.487542	-1.726162
17	1	0	0.185216	-1.414574	-1.546997
18	6	0	2.277305	-0.811982	-0.171987
19	6	0	4.554695	-2.300142	0.495373
20	6	0	3.131348	-1.285967	-1.176747
21	6	0	2.576623	-1.079195	1.168814
22	6	0	3.708829	-1.825128	1.498848
23	6	0	4.264243	-2.026692	-0.842859
24	1	0	2.901289	-1.070057	-2.214769
25	1	0	1.917972	-0.709140	1.946506

26	1	0	3.929207	-2.035098	2.542186
27	1	0	4.921352	-2.388959	-1.628848
28	1	0	5.437161	-2.879079	0.754608
29	8	0	2.393582	1.921040	-1.412571
30	6	0	-2.016921	0.899571	-0.391507
31	8	0	-2.526313	1.725008	-1.136450
32	6	0	-2.718342	-0.395436	-0.109159
33	6	0	-4.215528	-2.727761	0.339342
34	6	0	-3.865002	-0.670739	-0.875554
35	6	0	-2.333760	-1.306863	0.889203
36	6	0	-3.084297	-2.461778	1.112122
37	6	0	-4.603797	-1.828649	-0.658489
38	1	0	-4.157649	0.045994	-1.635450
39	1	0	-1.446106	-1.124133	1.480638
40	1	0	-2.780506	-3.157168	1.889916
41	1	0	-5.484286	-2.030822	-1.262305
42	1	0	-4.793354	-3.631787	0.513135

Conformers (1*R*,3*R*,5*S*)-**5a-02**: ΔG = 2.49 kcal/mol

SCF Done: E(RB3LYP) = -1073.85034767 A.U. after 7 cycles

Standard orientation:

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms) X	Y	Z
1	1	0	-0.267913	2.706354	-1.147501
2	6	0	0.171823	2.236853	-0.263021
3	6	0	0.331842	3.232384	0.911956
4	6	0	0.017325	2.394962	2.163337
5	6	0	-1.102736	1.453467	1.688777
6	6	0	-0.687105	1.058983	0.259316
7	1	0	-0.398068	4.043350	0.806161
8	1	0	1.329074	3.682805	0.916349
9	1	0	0.895263	1.807461	2.458147
10	1	0	-0.277680	3.002803	3.024608
11	1	0	-2.057468	1.994874	1.646359

12	1	0	-1.249257	0.578821	2.327236
13	6	0	1.480579	1.569421	-0.678101
14	8	0	0.209864	-0.088511	0.329132
15	6	0	1.246324	0.032671	-0.640610
16	8	0	0.839146	-0.402333	-1.922051
17	1	0	0.159879	0.204363	-2.267460
18	6	0	2.454064	-0.769176	-0.219050
19	6	0	4.759904	-2.167356	0.537130
20	6	0	3.433872	-1.079271	-1.169614
21	6	0	2.639026	-1.155584	1.112444
22	6	0	3.786322	-1.855884	1.487018
23	6	0	4.580326	-1.776384	-0.791195
24	1	0	3.288323	-0.778874	-2.200841
25	1	0	1.878516	-0.918654	1.848102
26	1	0	3.917139	-2.159229	2.522479
27	1	0	5.334373	-2.014935	-1.536474
28	1	0	5.653788	-2.711924	0.829888
29	8	0	2.509607	2.126511	-0.973497
30	6	0	-1.853640	0.672079	-0.684923
31	8	0	-1.950676	1.222773	-1.776925
32	6	0	-2.848300	-0.358950	-0.267987
33	6	0	-4.804542	-2.246771	0.405833
34	6	0	-4.100840	-0.345741	-0.906100
35	6	0	-2.579586	-1.342291	0.698887
36	6	0	-3.554549	-2.283342	1.026770
37	6	0	-5.076383	-1.275905	-0.562796
38	1	0	-4.288695	0.406433	-1.665347
39	1	0	-1.598015	-1.398041	1.154020
40	1	0	-3.334770	-3.050727	1.763695
41	1	0	-6.046391	-1.249636	-1.051452
42	1	0	-5.563995	-2.977764	0.670342

Conformers (1*R*,3*R*,5*S*)-**5a-03**: ΔG = 2.72 kcal/mol

SCF Done: E(RB3LYP) = -1073.84997351 A.U. after 7 cycles

Standard orientation:

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms) X	Y	Z
1	1	0	1.036000	0.810416	1.709974
2	6	0	0.359749	1.102314	0.900967
3	6	0	0.455676	2.612079	0.564169
4	6	0	0.212943	2.685085	-0.953917
5	6	0	0.901862	1.419214	-1.497276
6	6	0	0.586666	0.336564	-0.439701
7	1	0	1.455165	2.992096	0.808501
8	1	0	-0.262195	3.187811	1.156590
9	1	0	-0.861429	2.645413	-1.166945
10	1	0	0.604163	3.603080	-1.403814
11	1	0	1.981146	1.576399	-1.581898
12	1	0	0.533739	1.099118	-2.476508
13	6	0	-1.065233	0.696069	1.308297
14	8	0	-0.709795	-0.198674	-0.794013
15	6	0	-1.493698	-0.444920	0.354236
16	8	0	-1.073385	-1.621752	1.025587
17	1	0	-0.552950	-2.124411	0.366006
18	6	0	-2.962142	-0.466042	-0.007147
19	6	0	-5.706045	-0.456696	-0.568868
20	6	0	-3.856398	-1.135825	0.835330
21	6	0	-3.449542	0.211527	-1.130129
22	6	0	-4.816282	0.211533	-1.411394
23	6	0	-5.222283	-1.129582	0.554933
24	1	0	-3.471575	-1.666897	1.698980
25	1	0	-2.756147	0.719954	-1.791538
26	1	0	-5.184802	0.731309	-2.292044
27	1	0	-5.909328	-1.653802	1.213984
28	1	0	-6.770637	-0.455210	-0.788068
29	8	0	-1.713844	1.195307	2.193082
30	6	0	1.599873	-0.835427	-0.390741
31	8	0	1.198177	-1.981990	-0.542252
32	6	0	3.067445	-0.599075	-0.187062
33	6	0	5.839828	-0.359241	0.200833

34	6	0	3.925449	-1.683612	-0.443405
35	6	0	3.623493	0.605522	0.274680
36	6	0	4.999229	0.721042	0.471933
37	6	0	5.298608	-1.563067	-0.259175
38	1	0	3.487980	-2.614681	-0.786704
39	1	0	2.992901	1.457734	0.496824
40	1	0	5.412986	1.656345	0.838156
41	1	0	5.948531	-2.407755	-0.469751
42	1	0	6.912054	-0.264830	0.349645

Conformer (1*S*,3*S*,5*R*)-**5a-01**: ΔG = 0 kcal/mol

SCF Done: E(RB3LYP) = -1073.85431495 A.U. after 7 cycles

Standard orientation:

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms) X	Y	Z
1	6	0	0.692241	1.281922	0.304552
2	6	0	-0.149751	2.298587	-0.509322
3	6	0	-0.476842	3.474462	0.444483
4	6	0	-0.274061	2.890281	1.853146
5	6	0	0.933304	1.952952	1.674992
6	1	0	0.374753	2.632728	-1.408341
7	1	0	0.233124	4.290660	0.269209
8	1	0	-1.483904	3.863786	0.265604
9	1	0	-1.153856	2.310178	2.157063
10	1	0	-0.103376	3.657079	2.615713
11	1	0	1.047280	1.210182	2.470401
12	1	0	1.858344	2.540317	1.624061
13	8	0	-0.180832	0.137693	0.515455
14	6	0	-1.373054	1.496130	-0.931525
15	6	0	-1.075399	0.011534	-0.573022
16	6	0	-2.277271	-0.812125	-0.172047
17	6	0	-4.554690	-2.300118	0.495521
18	6	0	-3.131284	-1.286294	-1.176748
19	6	0	-2.576610	-1.079098	1.168796

20	6	0	-3.708835	-1.824941	1.498935
21	6	0	-4.264205	-2.026943	-0.842753
22	1	0	-2.901208	-1.070554	-2.214801
23	1	0	-1.917909	-0.708944	1.946401
24	1	0	-3.929270	-2.034728	2.542298
25	1	0	-4.921304	-2.389354	-1.628684
26	1	0	-5.437158	-2.879004	0.754866
27	8	0	-0.421407	-0.487528	-1.726454
28	1	0	-0.185661	-1.414689	-1.547635
29	8	0	-2.393829	1.920902	-1.412289
30	6	0	2.016830	0.899634	-0.391644
31	6	0	2.718424	-0.395288	-0.109207
32	6	0	4.216048	-2.727272	0.339575
33	6	0	3.864872	-0.670707	-0.875887
34	6	0	2.334252	-1.306457	0.889549
35	6	0	3.085025	-2.461180	1.112625
36	6	0	4.603869	-1.828465	-0.658702
37	1	0	4.157184	0.045845	-1.636081
38	1	0	1.446694	-1.123683	1.481122
39	1	0	2.781605	-3.156351	1.890762
40	1	0	5.484157	-2.030767	-1.262768
41	1	0	4.794053	-3.631155	0.513520
42	8	0	2.525978	1.725029	-1.136789

Conformers (1*S*,3*S*,5*R*)-**5a-02**: ΔG = 2.49 kcal/mol

SCF Done: E(RB3LYP) = -1073.85034767 A.U. after 7 cycles

Standard orientation:

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms) X	Y	Z
1	6	0	0.687104	1.058981	0.259318
2	6	0	-0.171823	2.236853	-0.263013
3	6	0	-0.331836	3.232383	0.911965
4	6	0	-0.017325	2.394956	2.163343
5	6	0	1.102733	1.453457	1.688782

6	1	0	0.267911	2.706353	-1.147495
7	1	0	0.398079	4.043345	0.806171
8	1	0	-1.329065	3.682809	0.916358
9	1	0	-0.895266	1.807458	2.458150
10	1	0	0.277682	3.002793	3.024616
11	1	0	1.249246	0.578807	2.327237
12	1	0	2.057469	1.994857	1.646370
13	8	0	-0.209865	-0.088515	0.329127
14	6	0	-1.480582	1.569424	-0.678090
15	6	0	-1.246327	0.032674	-0.640611
16	6	0	-2.454066	-0.769175	-0.219052
17	6	0	-4.759903	-2.167362	0.537124
18	6	0	-3.433886	-1.079246	-1.169612
19	6	0	-2.639015	-1.155610	1.112436
20	6	0	-3.786308	-1.855913	1.487007
21	6	0	-4.580338	-1.776362	-0.791195
22	1	0	-3.288348	-0.778828	-2.200835
23	1	0	-1.878495	-0.918697	1.848090
24	1	0	-3.917116	-2.159280	2.522464
25	1	0	-5.334395	-2.014894	-1.536470
26	1	0	-5.653785	-2.711933	0.829881
27	8	0	-0.839153	-0.402321	-1.922056
28	1	0	-0.159885	0.204376	-2.267462
29	8	0	-2.509612	2.126517	-0.973474
30	6	0	1.853640	0.672081	-0.684921
31	6	0	2.848302	-0.358948	-0.267989
32	6	0	4.804547	-2.246770	0.405823
33	6	0	4.100843	-0.345734	-0.906100
34	6	0	2.579589	-1.342295	0.698879
35	6	0	3.554553	-2.283346	1.026758
36	6	0	5.076387	-1.275898	-0.562800
37	1	0	4.288698	0.406445	-1.665343
38	1	0	1.598017	-1.398049	1.154012
39	1	0	3.334774	-3.050736	1.763679
40	1	0	6.046395	-1.249625	-1.051455
41	1	0	5.564000	-2.977763	0.670328

42	8	0	1.950675	1.222776	-1.776923

Conformers (1*S*,3*S*,5*R*)-**5a-03**: ΔG = 2.72 kcal/mol

SCF Done: E(RB3LYP) = -1073.84997351 A.U. after 7 cycles

Standard orientation:

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms) X	Y	Z
1	6	0	-0.586733	0.336603	-0.439732
2	6	0	-0.359633	1.102590	0.900818
3	6	0	-0.455354	2.612301	0.563620
4	6	0	-0.212656	2.684903	-0.954475
5	6	0	-0.901978	1.419077	-1.497434
6	1	0	-1.035965	0.811056	1.709886
7	1	0	-1.454836	2.992431	0.807831
8	1	0	0.262535	3.188115	1.155935
9	1	0	0.861687	2.644821	-1.167561
10	1	0	-0.603631	3.602895	-1.404586
11	1	0	-0.534270	1.098727	-2.476741
12	1	0	-1.981256	1.576501	-1.581718
13	8	0	0.709730	-0.198628	-0.794093
14	6	0	1.065237	0.696182	1.308202
15	6	0	1.493640	-0.444840	0.354155
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24	1	0	5.184647	0.728330	-2.293718
25	1	0	5.909429	-1.651268	1.216010
26	1	0	6.770634	-0.455537	-0.787809
27	8	0	1.073335	-1.621649	1.025536

28	1	0	0.552566	-2.124124	0.366043
29	8	0	1.713839	1.195287	2.193078
30	6	0	-1.599874	-0.835380	-0.390544
31	6	0	-3.067461	-0.599041	-0.186877
32	6	0	-5.839867	-0.359266	0.200943
33	6	0	-3.925435	-1.683613	-0.443179
34	6	0	-3.623553	0.605558	0.274805
35	6	0	-4.999296	0.721047	0.472016
36	6	0	-5.298603	-1.563101	-0.258987
37	1	0	-3.487936	-2.614686	-0.786429
38	1	0	-2.992999	1.457797	0.496964
39	1	0	-5.413081	1.656358	0.838187
40	1	0	-5.948485	-2.407828	-0.469531
41	1	0	-6.912097	-0.264861	0.349723
42	8	0	-1.198134	-1.981957	-0.541905

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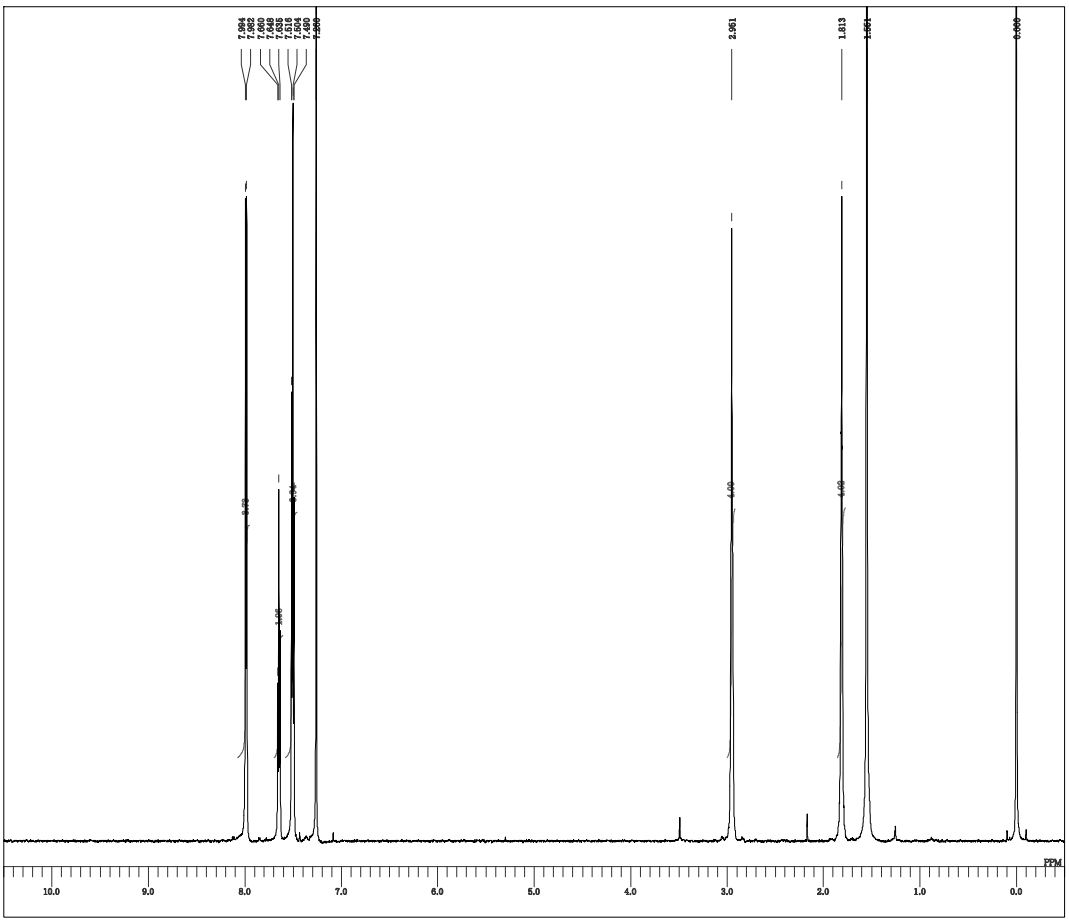


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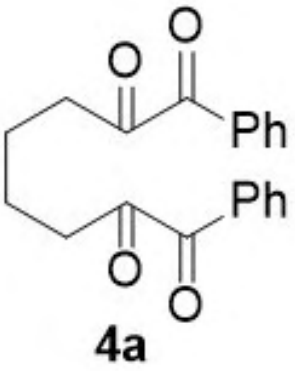
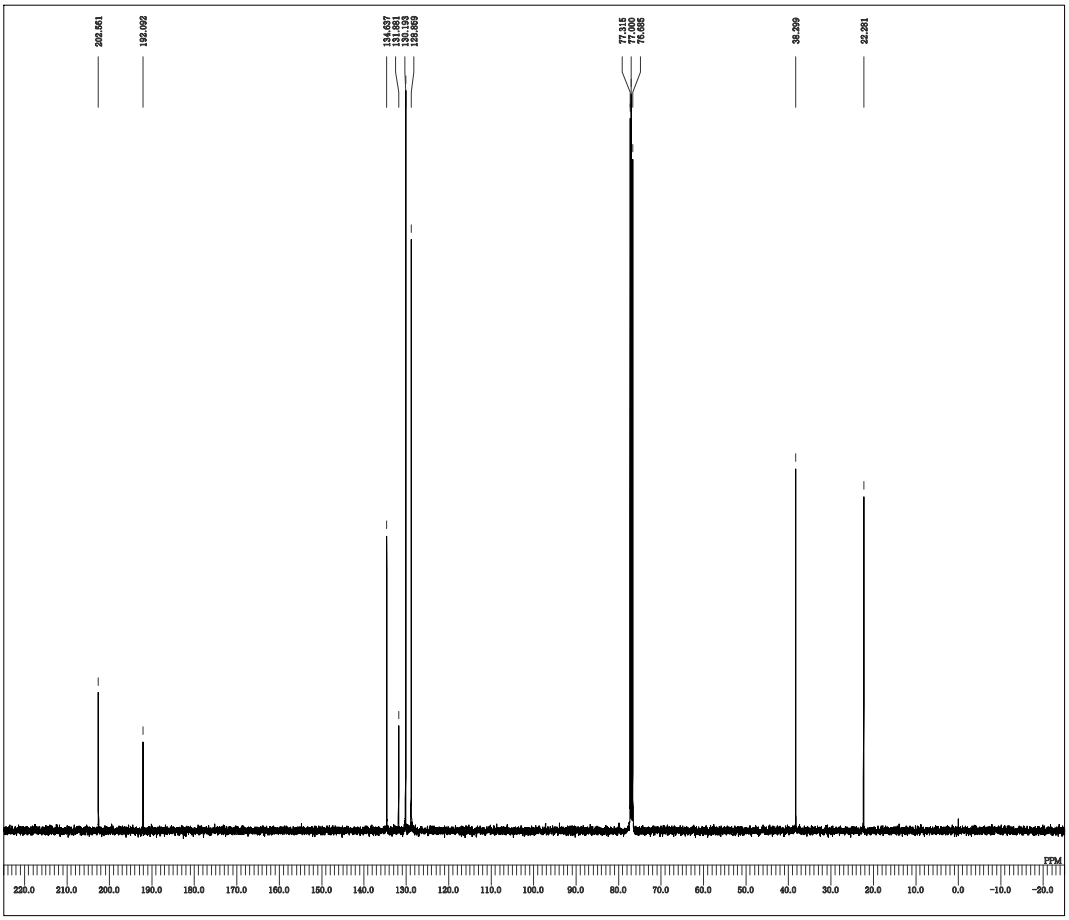
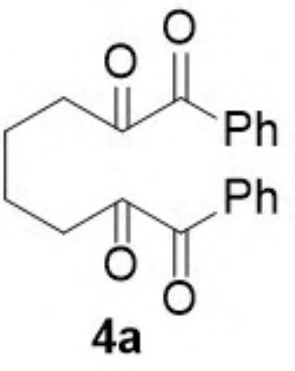


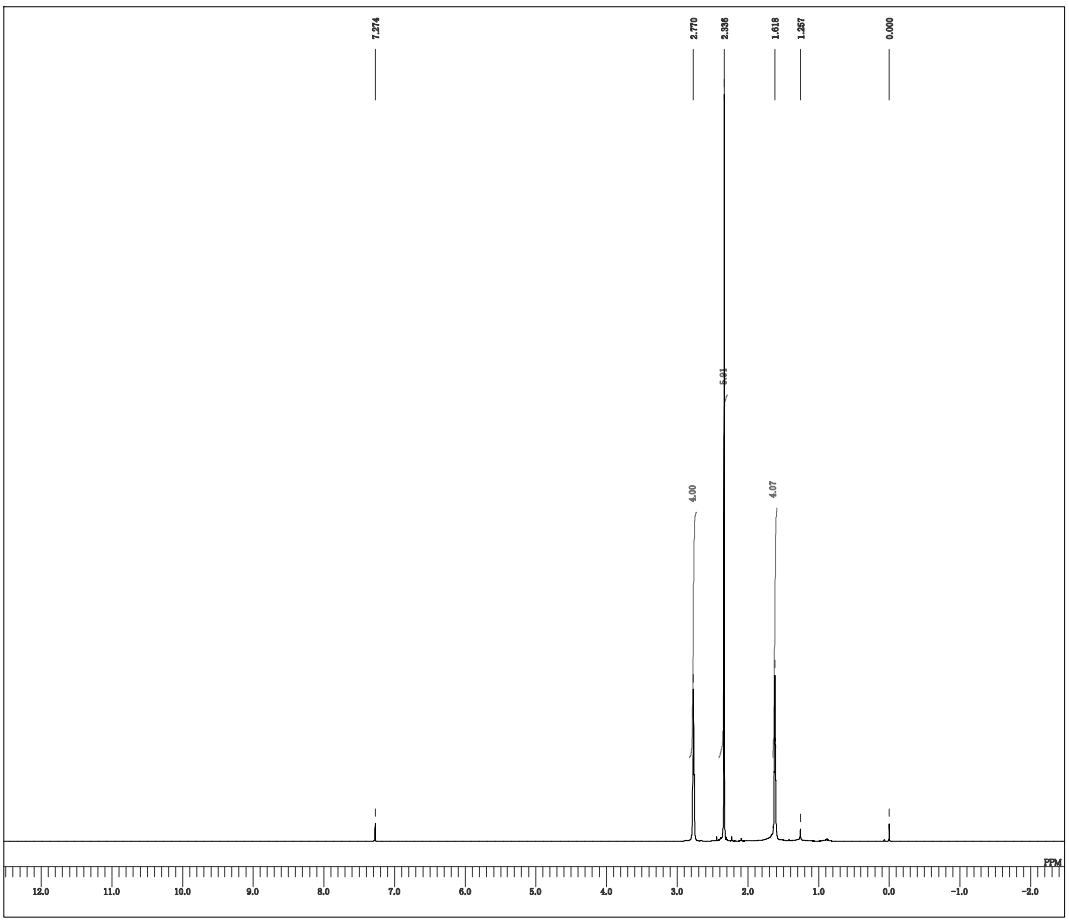
4a



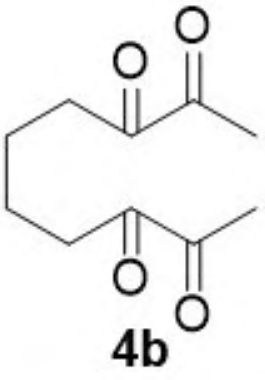

```
DPILE     TD81_sm_13C-1.als
COMNT
DATIM     2021-08-17 14:29:10
OBNUC     13C
EXMOD     single_pulse_dec
OBFRQ      100.53 MHz
OBSET        5.35 KHz
OBFIN        5.86 Hz
POINT       26214
FREQU     25125.24 Hz
SCANS         1000
ACQTM      1.0433 sec
PD         1.2000 sec
PW1        2.98 usec
IRNUC     1H
CTEMP       25.4 c
SLVNT     CDCL3
EXREF       77.00 ppm
BF          1.40 Hz
RGAIN         60
```



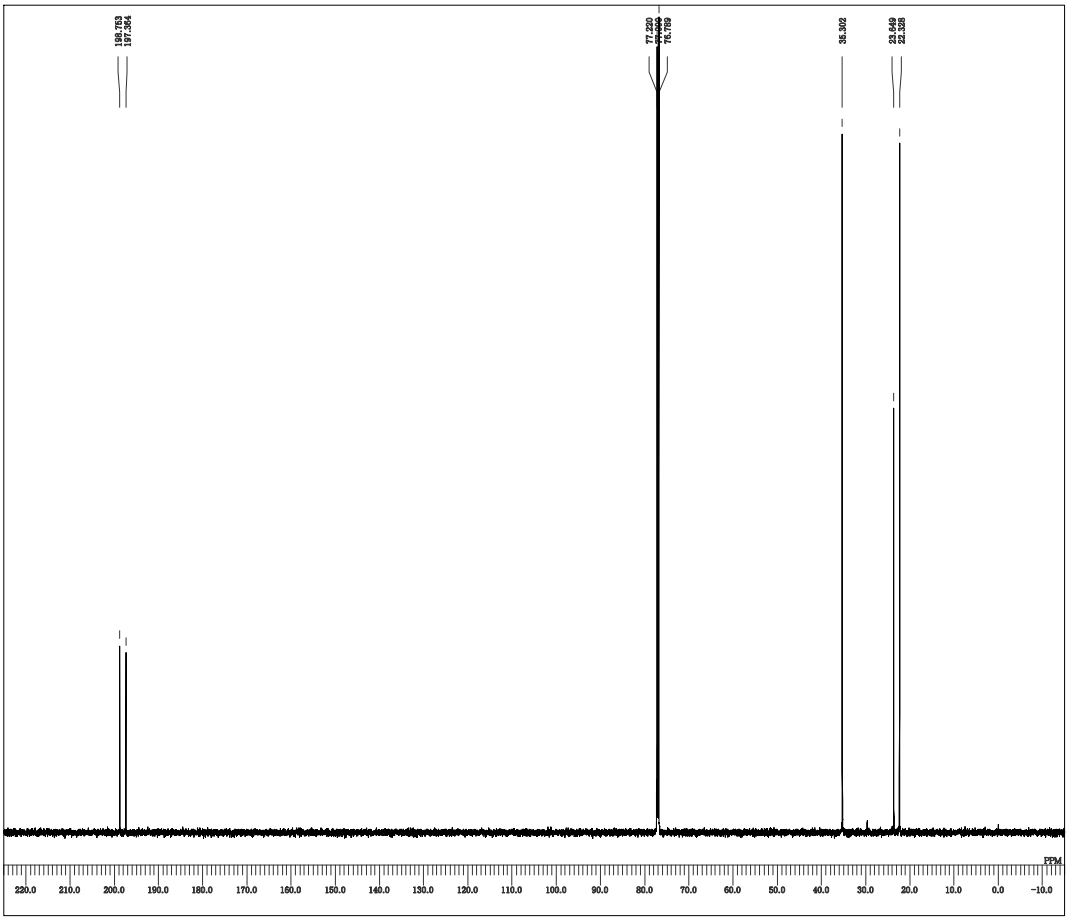
4a



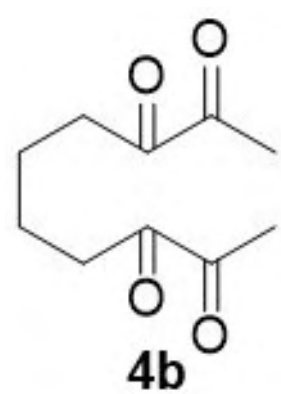

```
DPILE     MK52_sm_Ma_1H-1.als
COMNT
DATIM     2021-08-17 15:14:34
OBNUC     1H
EXMOD     single_pulse.ex2
OBFRQ      600.17 MHz
OBSET        5.30 KHz
OBFIN        5.47 Hz
POINT       26214
FREQU     9006.87 Hz
SCANS           8
ACQTM       2.9098 sec
PD          2.0000 sec
PW1         6.90 usec
IRNUC     1H
CTEMP       25.0 c
SLVNT     CDCL3
EXREF       0.00 ppm
BF          1.40 Hz
RGAIN         40
```



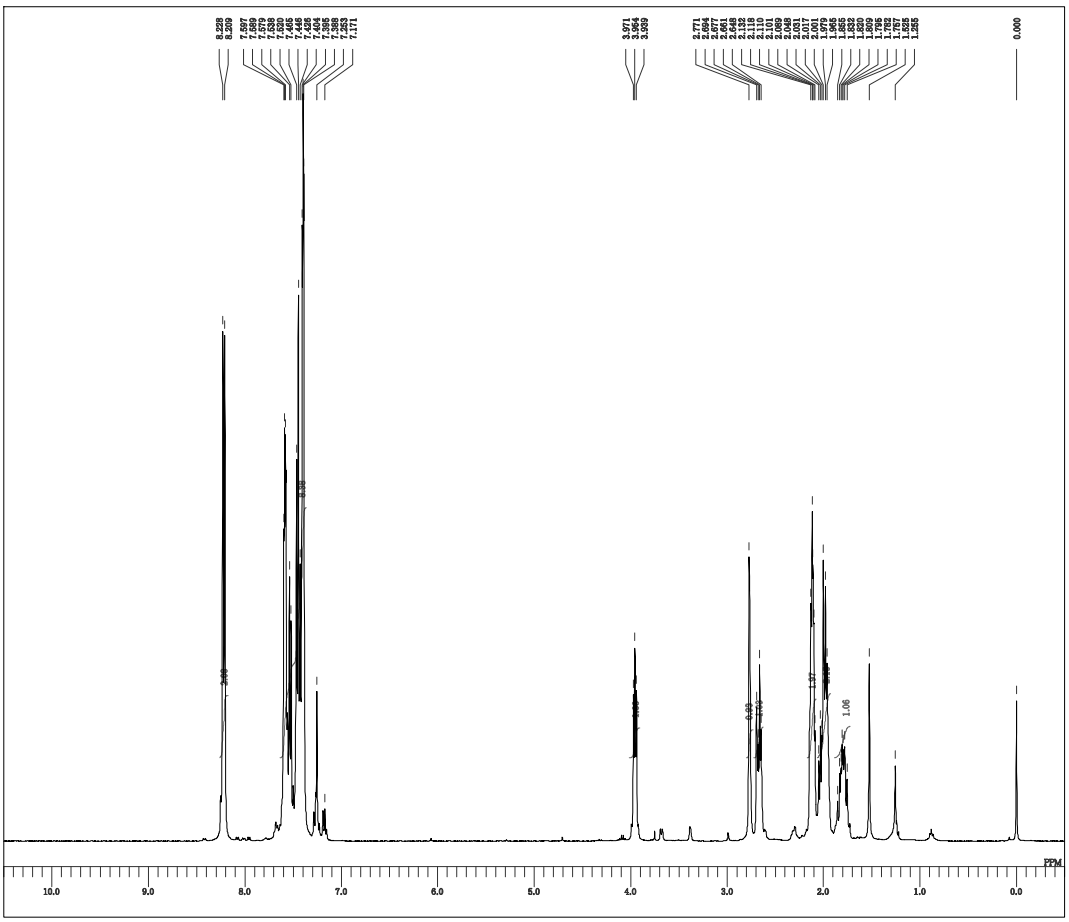
4b



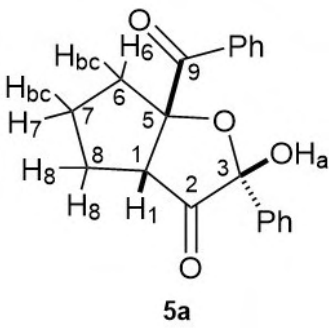

```
DPILE     MK52_sm_Ma_13C-1.als
COMNT
DATIM     2021-08-17 15:13:14
OBNUC     13C
EXMOD     single_pulse_dec
OBFRQ      150.92 MHz
OBSET        8.52 KHz
OBFIN        1.74 Hz
POINT       26214
FREQU     37978.21 Hz
SCANS         1000
ACQTM       0.6921 sec
PD          1.2000 sec
PW1         3.60 usec
IRNUC     1H
CTEMP       25.3 c
SLVNT     CDCL3
EXREF       77.00 ppm
BF          1.40 Hz
RGAIN         56
```



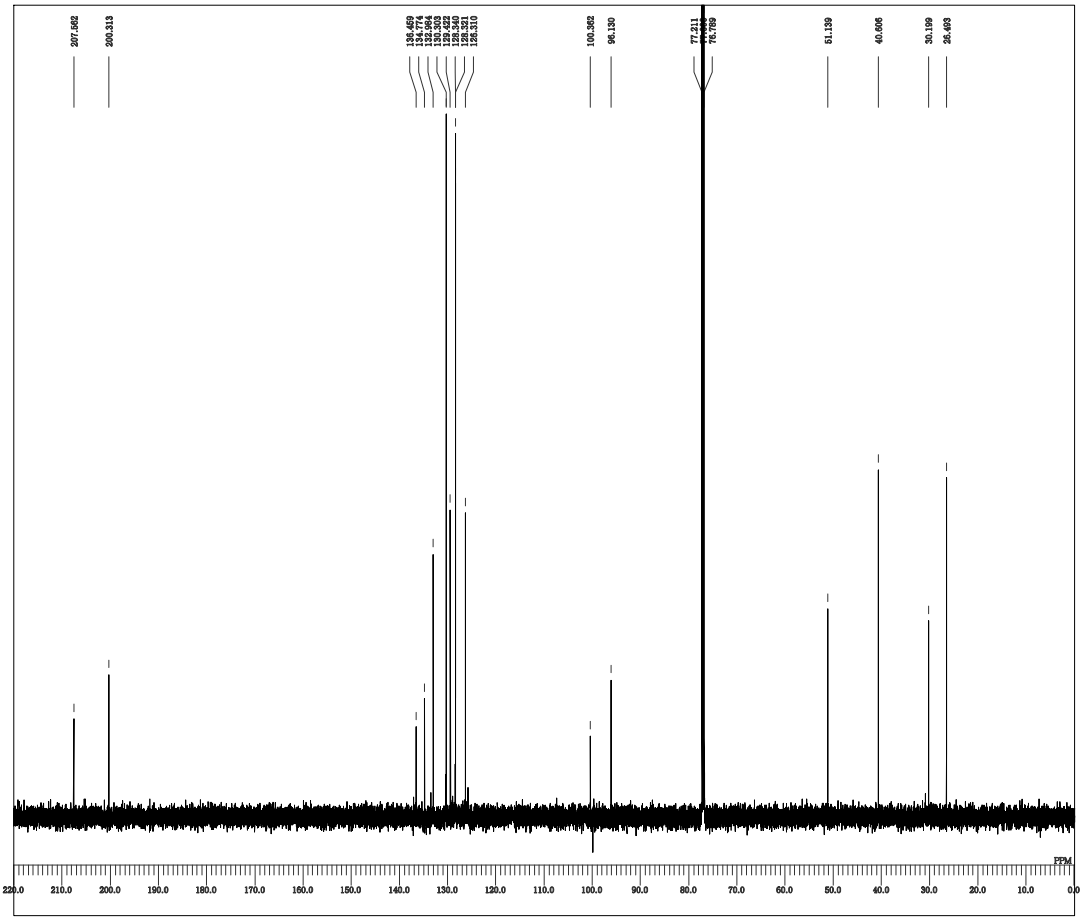
4b



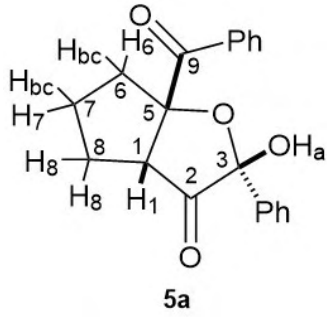

```
DPILE     MK 76-78_A-1.als
COMNT
DATIM     2020-12-03 09:22:07
OBNUC     1H
EXMOD     single_pulse.ex2
OBFRQ       399.78 MHz
OBSET         4.19 KHz
OBFIN         7.29 Hz
POINT        13107
FREQU      6002.31 Hz
SCANS           8
ACQTM       2.1837 sec
PD          2.0000 sec
PW1         5.00 usec
IRNUC     1H
CTEMP       21.1 c
SLVNT     CDCL3
EXREF       0.00 ppm
BF          1.40 Hz
RGAIN         36
```



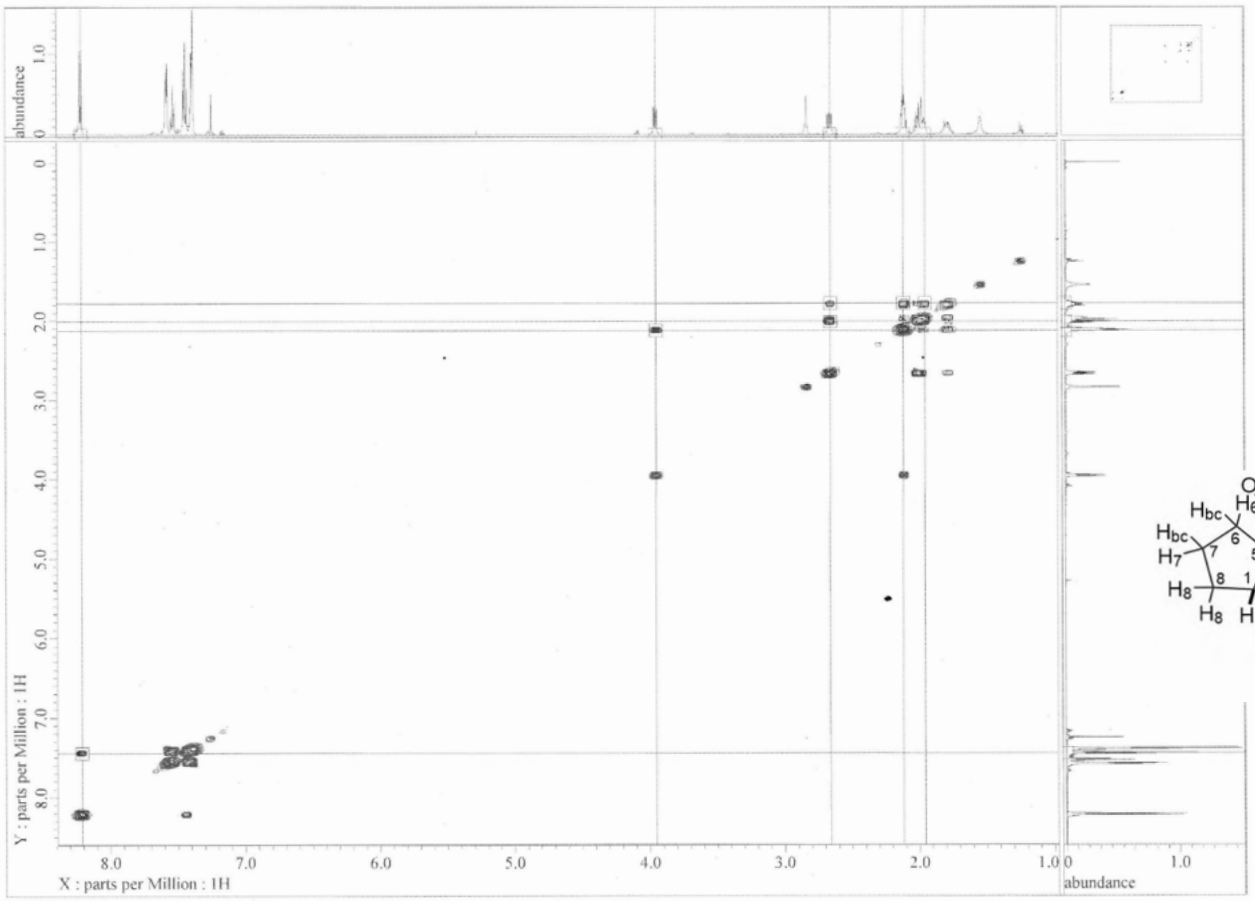
5a



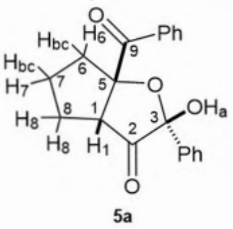

```
DPILE     MK 45-A_8-10silu_36silu_13c-1.als
COMNT
DATIM     2020-07-03 10:22:03
OBNUC     13C
EXMOD     single_pulse_dec
OBFRQ       150.92 MHz
OBSET         8.52 KHz
OBFIN         1.74 Hz
POINT        26214
FREQU      37878.21 Hz
SCANS          151
ACQTM       0.6921 sec
PD          1.2000 sec
PW1         3.67 usec
IRNUC     1H
CTEMP       23.1 c
SLVNT     CDCL3
EXREF       77.00 ppm
BF          0.12 Hz
RGAIN         56
```



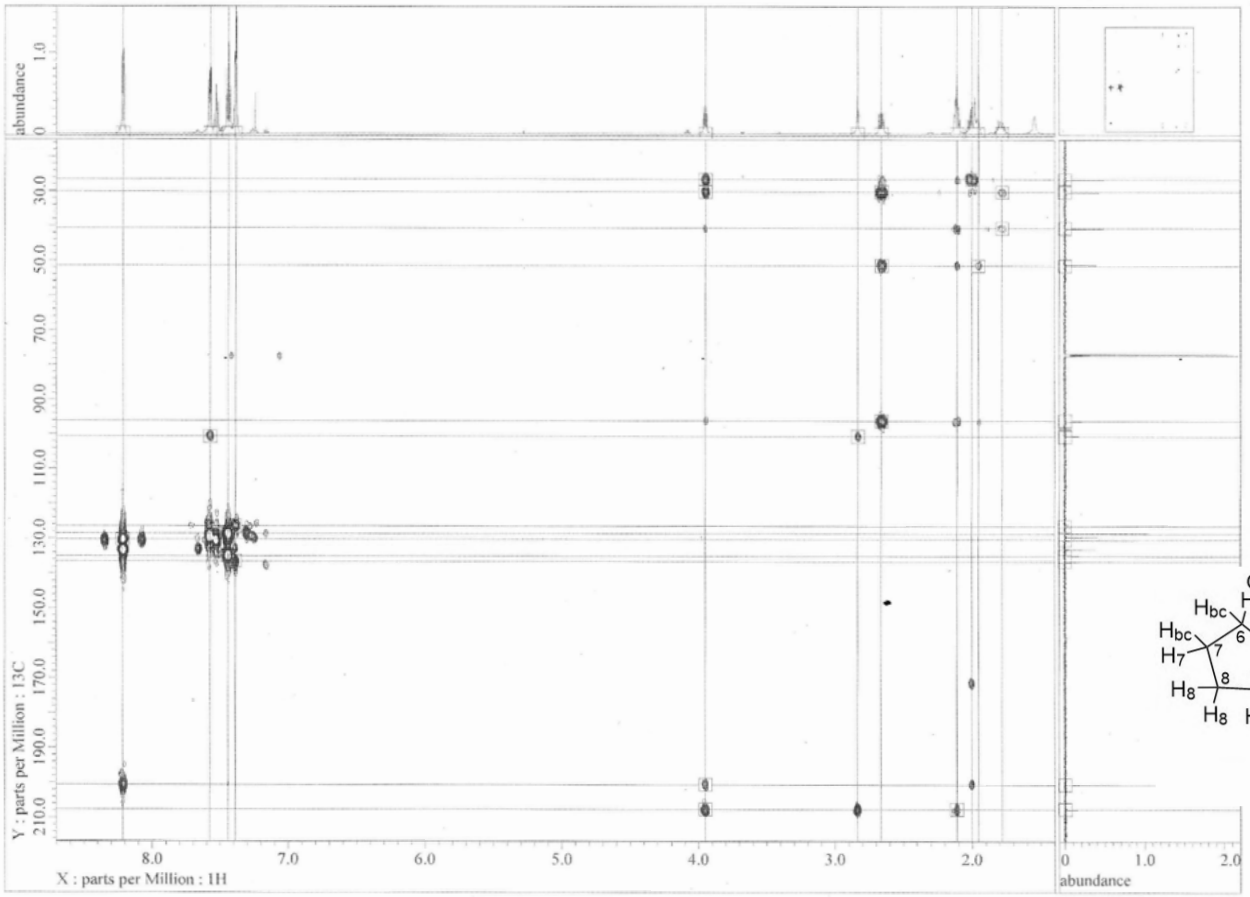
5a



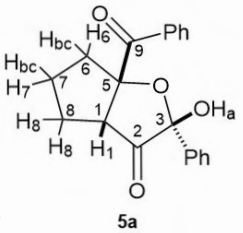
H-H COSY



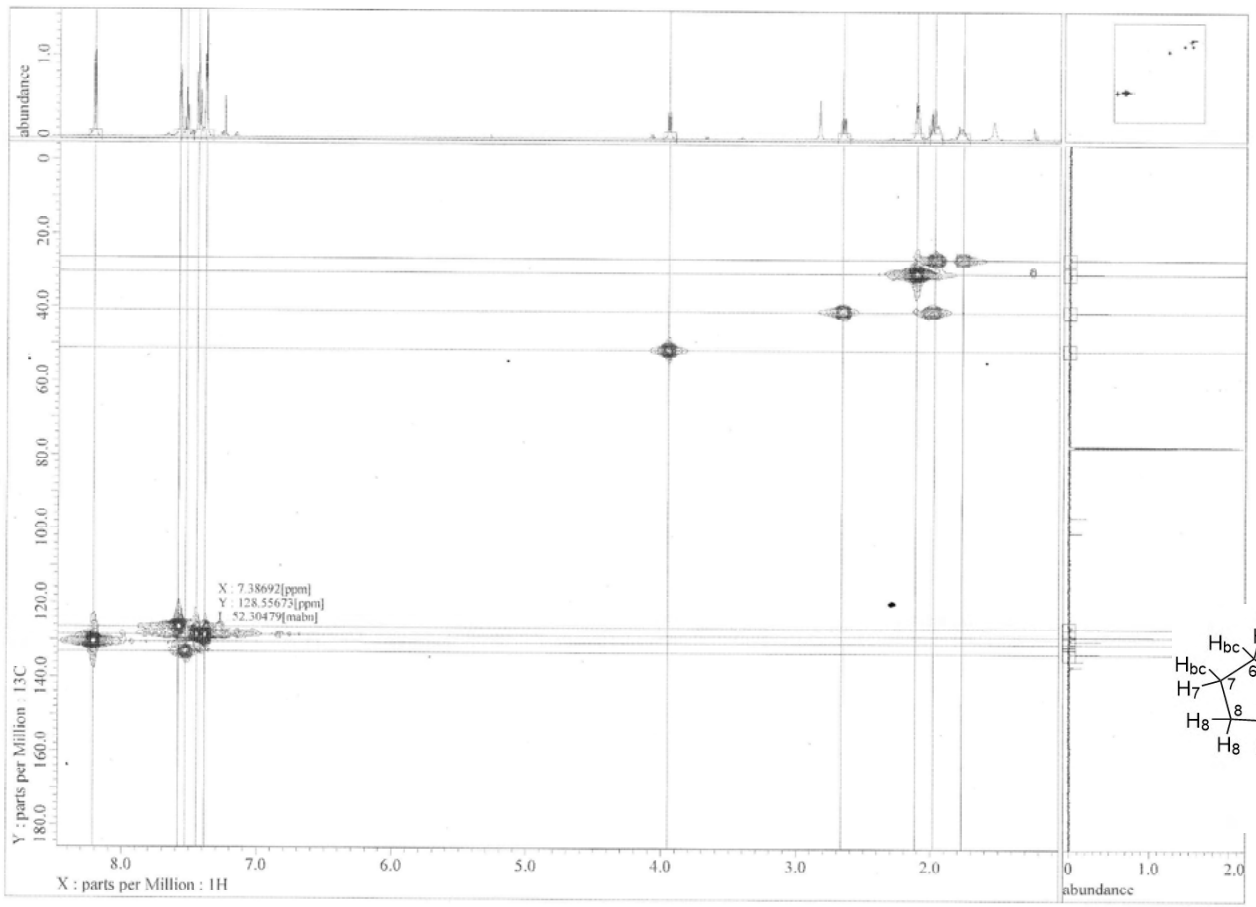
5a



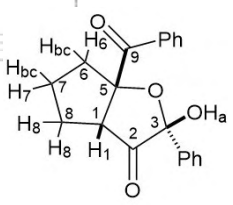
HMBC



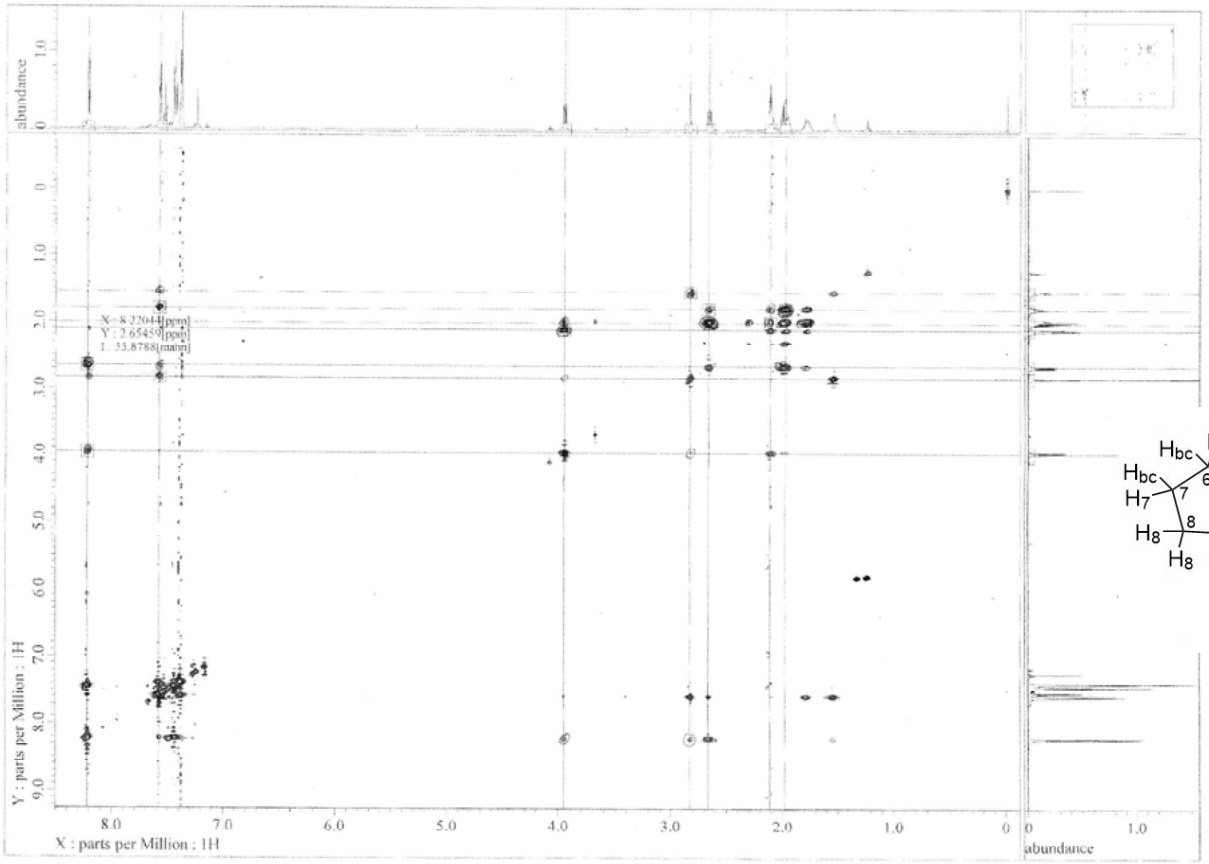
5a



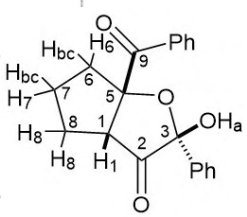
HMQC



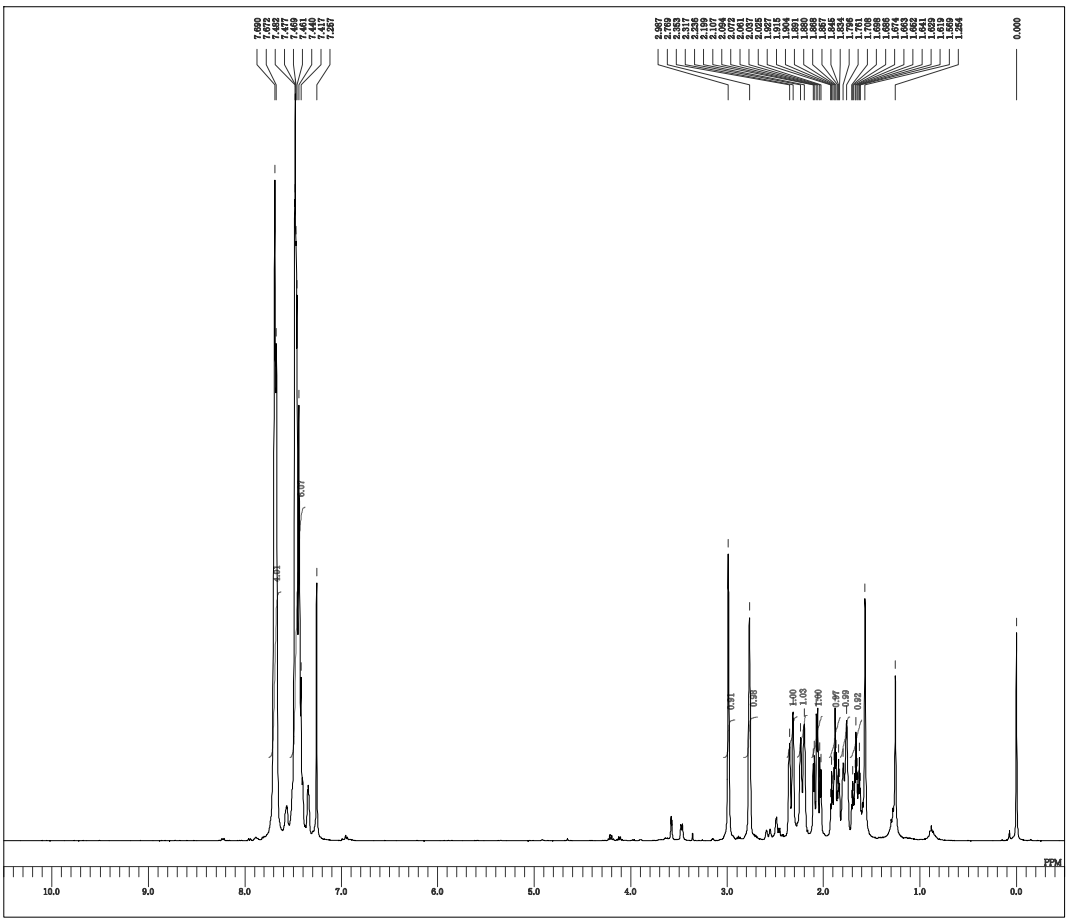
5a

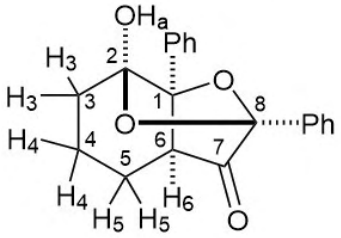


NOESY

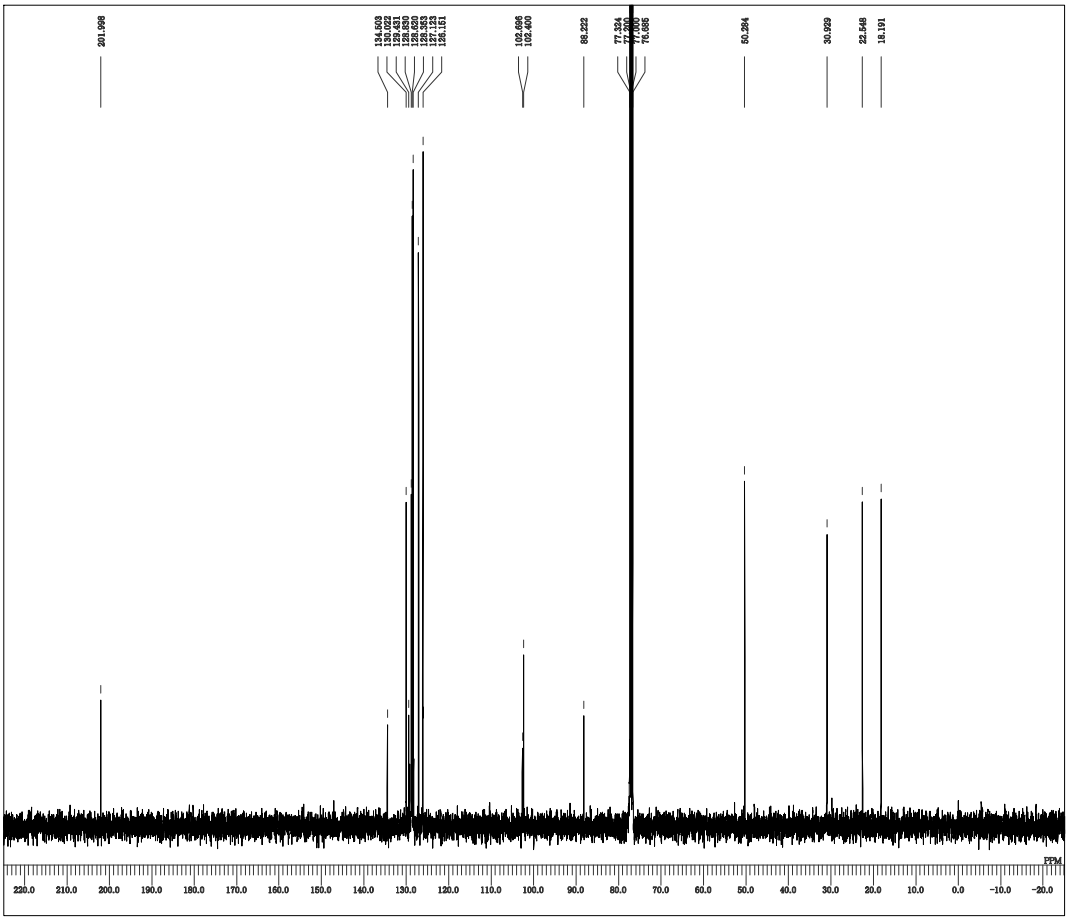


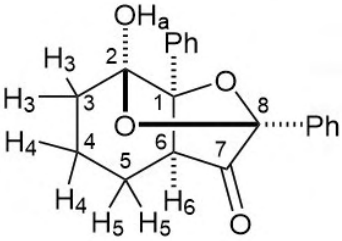
5a


DPULS MK 76-78_B-1.als
COMNT
DATIM 2020-12-07 11:22:45
OBNUC 1H
EXMOD single_pulse.ex2
OBFRQ 399.78 MHz
OBSET 4.19 KHz
OBFIN 7.29 Hz
POINT 13107
FREQU 6002.31 Hz
SCANS 8
ACQTM 2.1837 sec
PD 2.0000 sec
PW1 5.00 usec
IRNUC 1H
CTEMP 21.3 c
SLVNT CDCL3
EXREF 0.00 ppm
BF 1.40 Hz
RGAIN 40
PPM

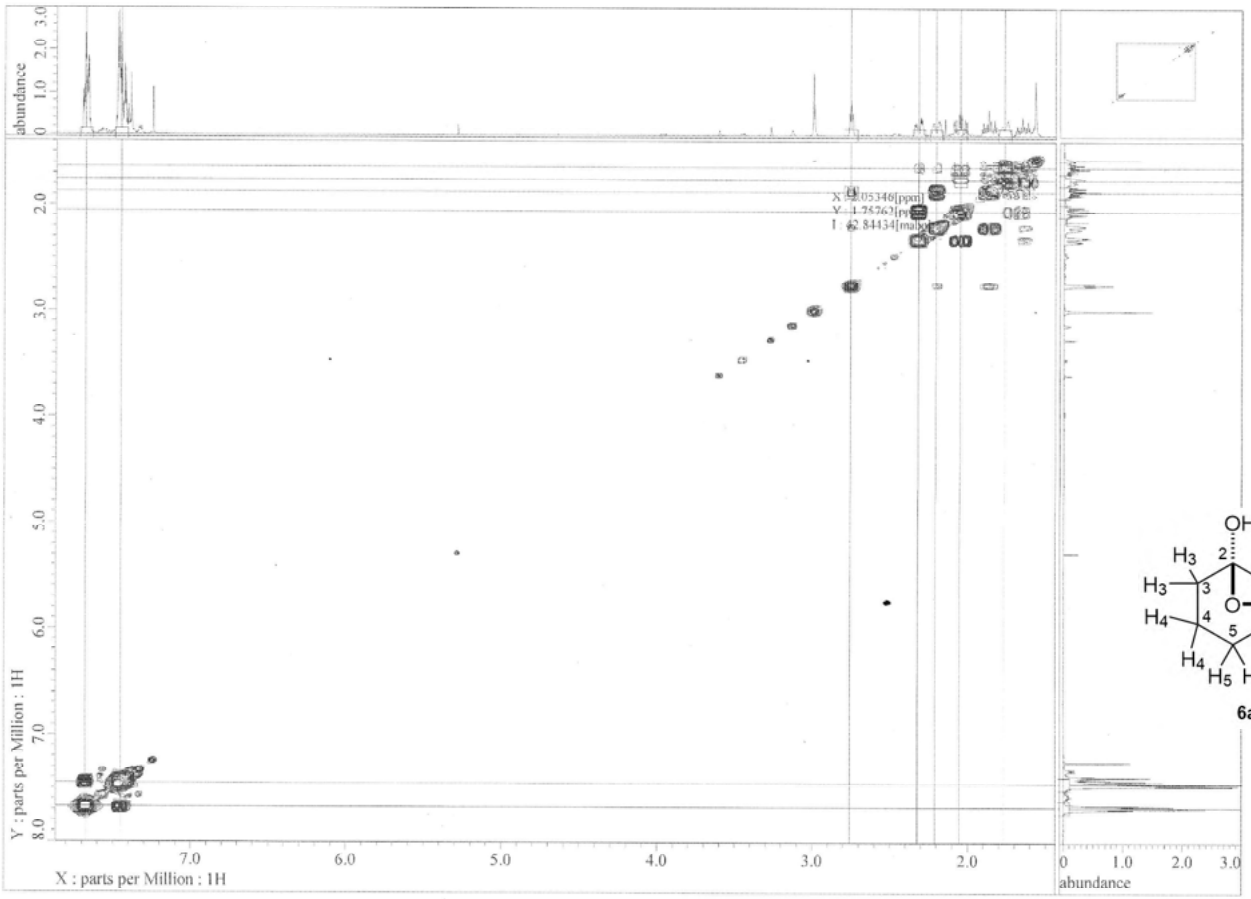

OHa
Ph
H3
H3
H4
O
Ph
H4
H5
H5
H6
O

6a

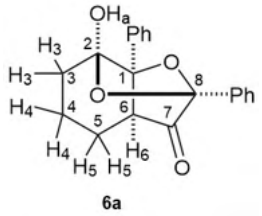

DPULS MK 76-78_B_13C-1.als
COMNT
DATIM 2020-12-07 13:19:16
OBNUC 13C
EXMOD single_pulse_dec
OBFRQ 100.53 MHz
OBSET 5.35 KHz
OBFIN 5.86 Hz
POINT 26214
FREQU 25125.24 Hz
SCANS 568
ACQTM 1.0433 sec
PD 1.2000 sec
PW1 2.98 usec
IRNUC 1H
CTEMP 21.5 c
SLVNT CDCL3
EXREF 77.00 ppm
BF 1.40 Hz
RGAIN 60
PPM


OHa
Ph
H3
H3
H4
O
Ph
H4
H5
H5
H6
O

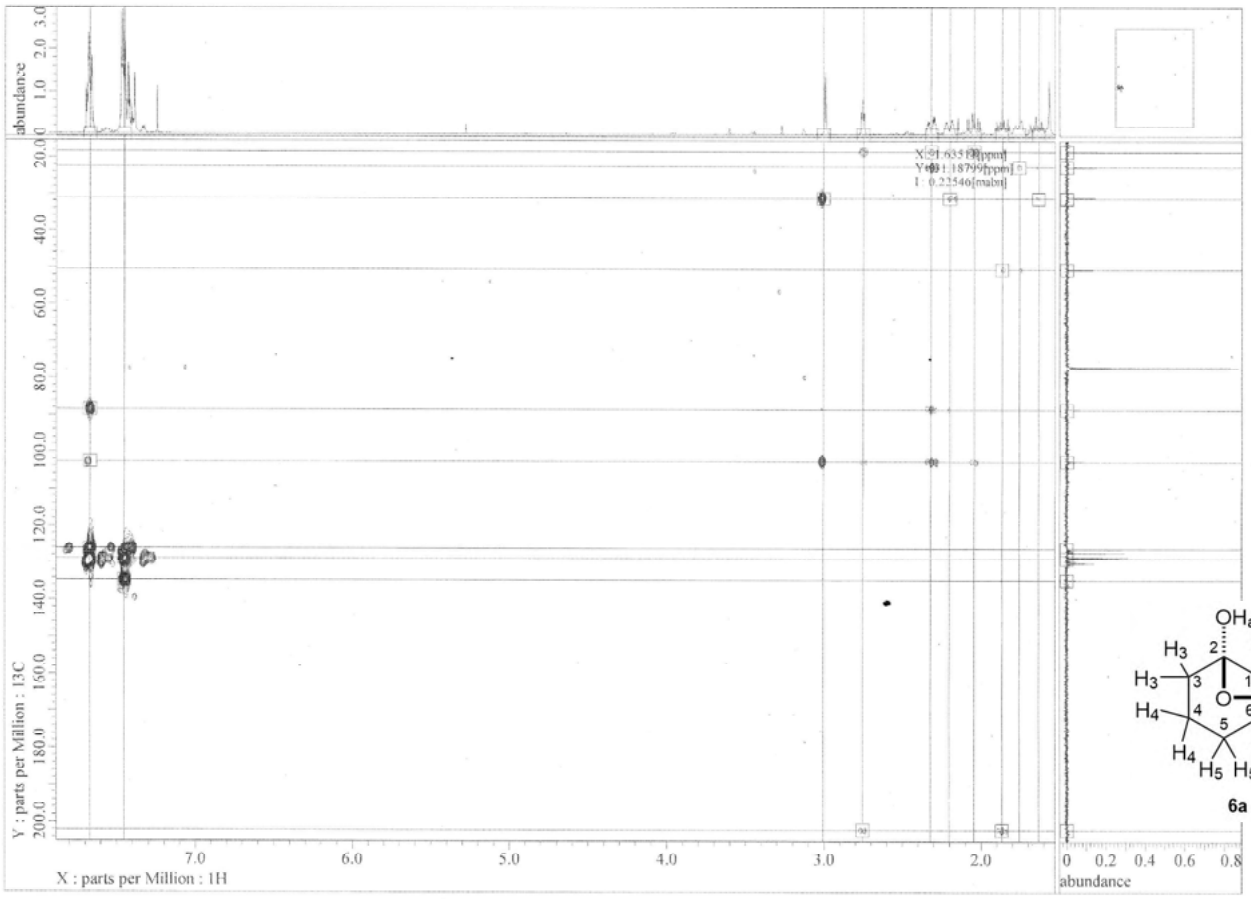
6a



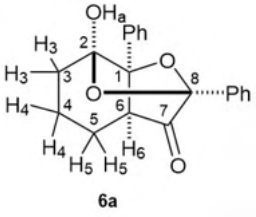
H-H COSY



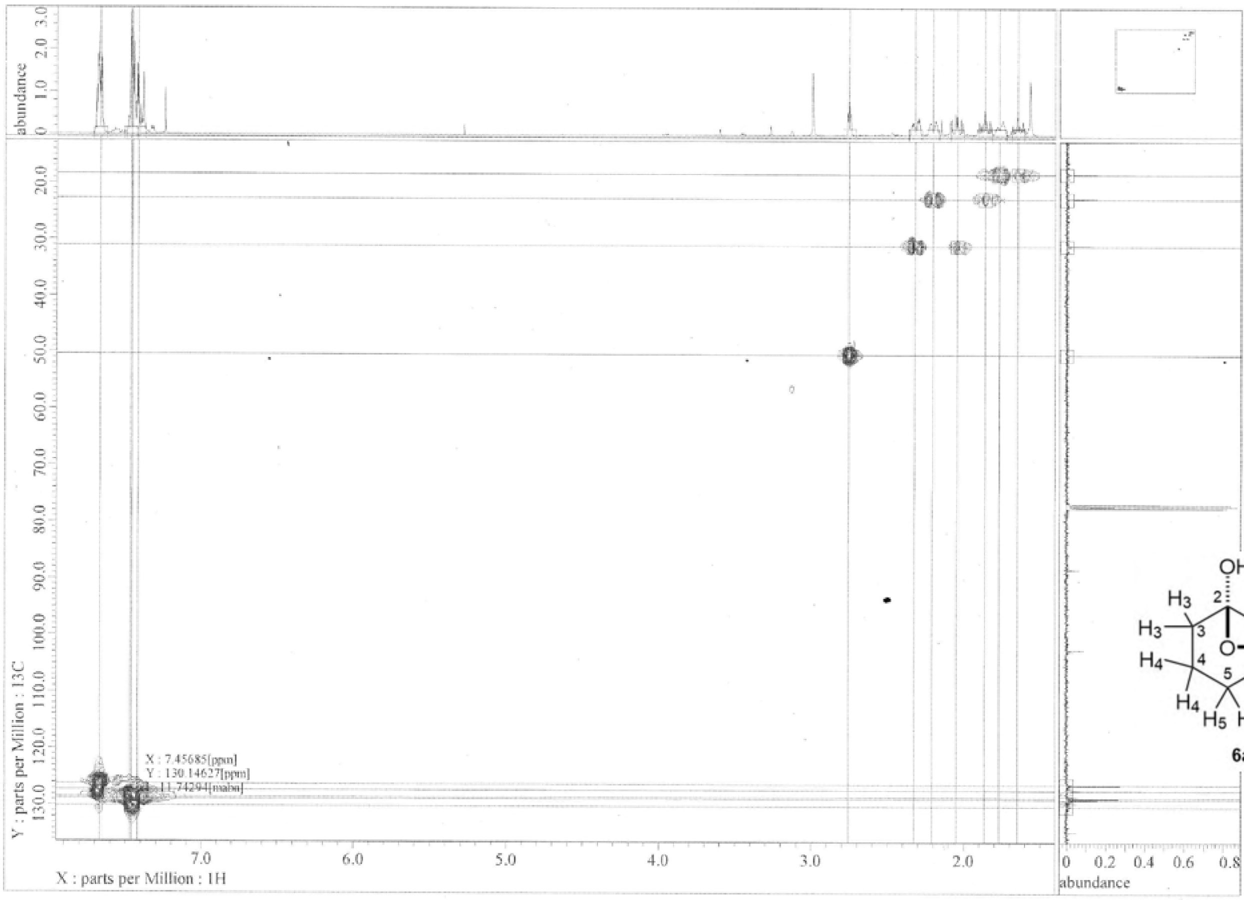
6a



HMBC

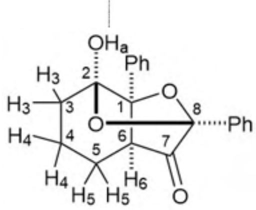


6a

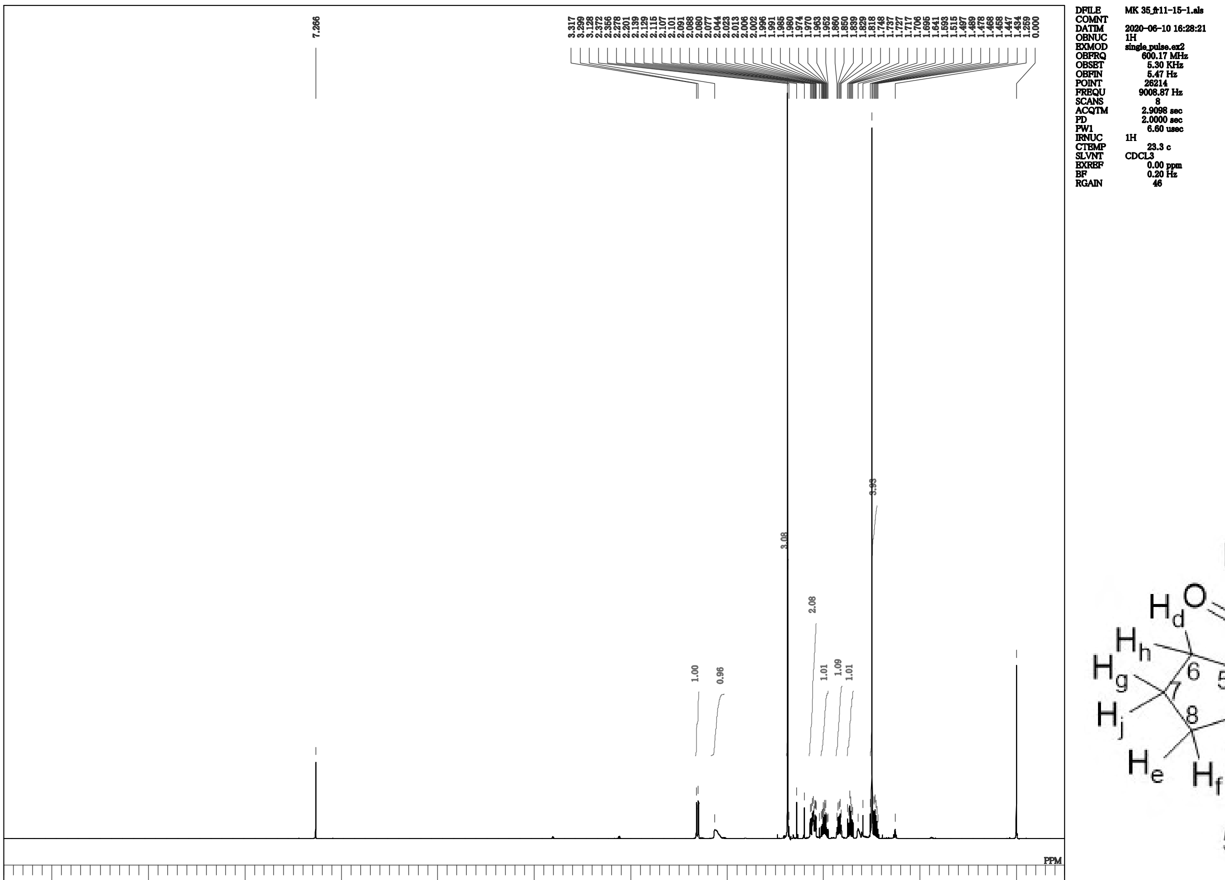


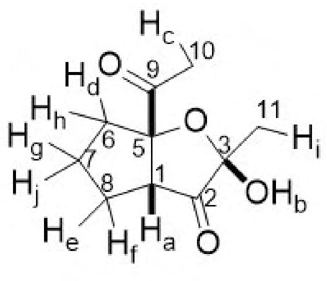
abundance
Y : parts per Million : 13C
X : parts per Million : 1H
X : 7.45685[ppm]
Y : 130.14627[ppm]

HMQC

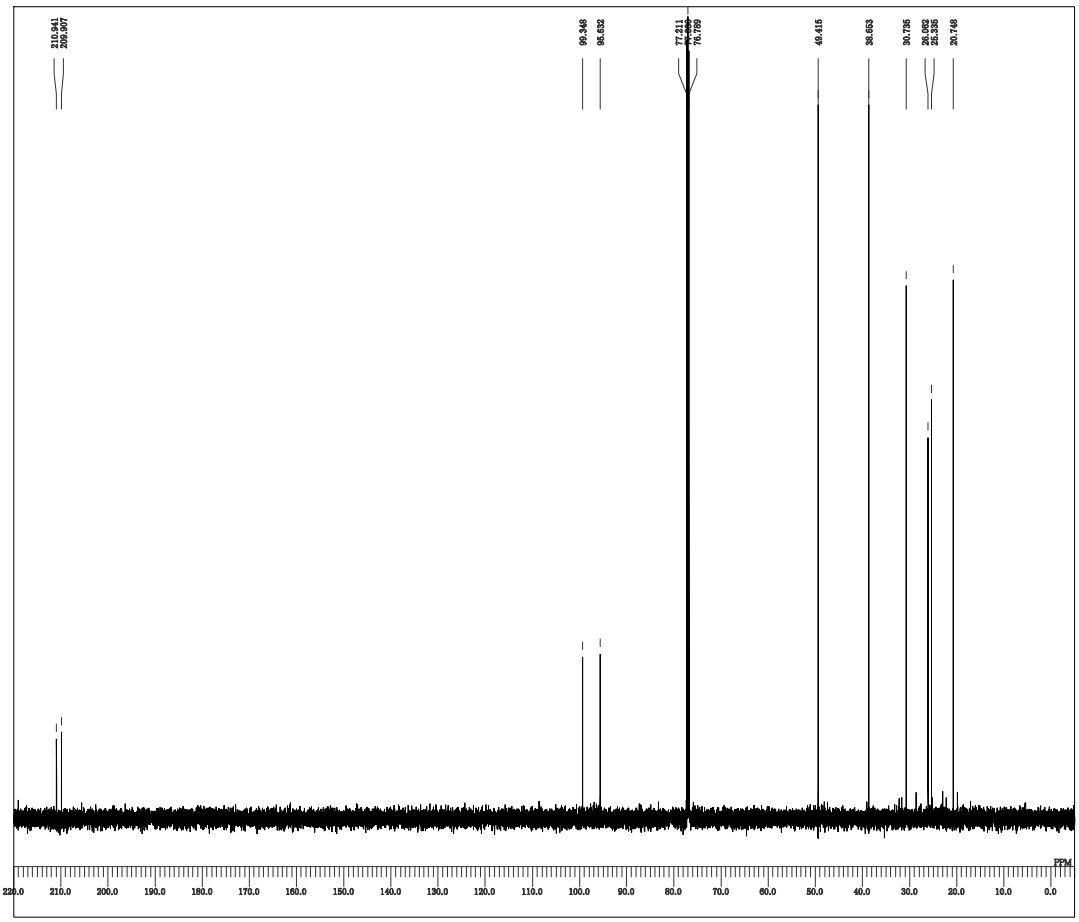


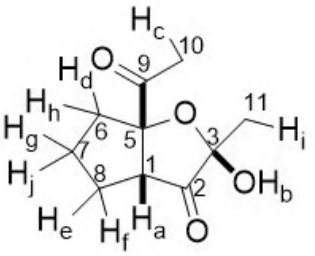
6a



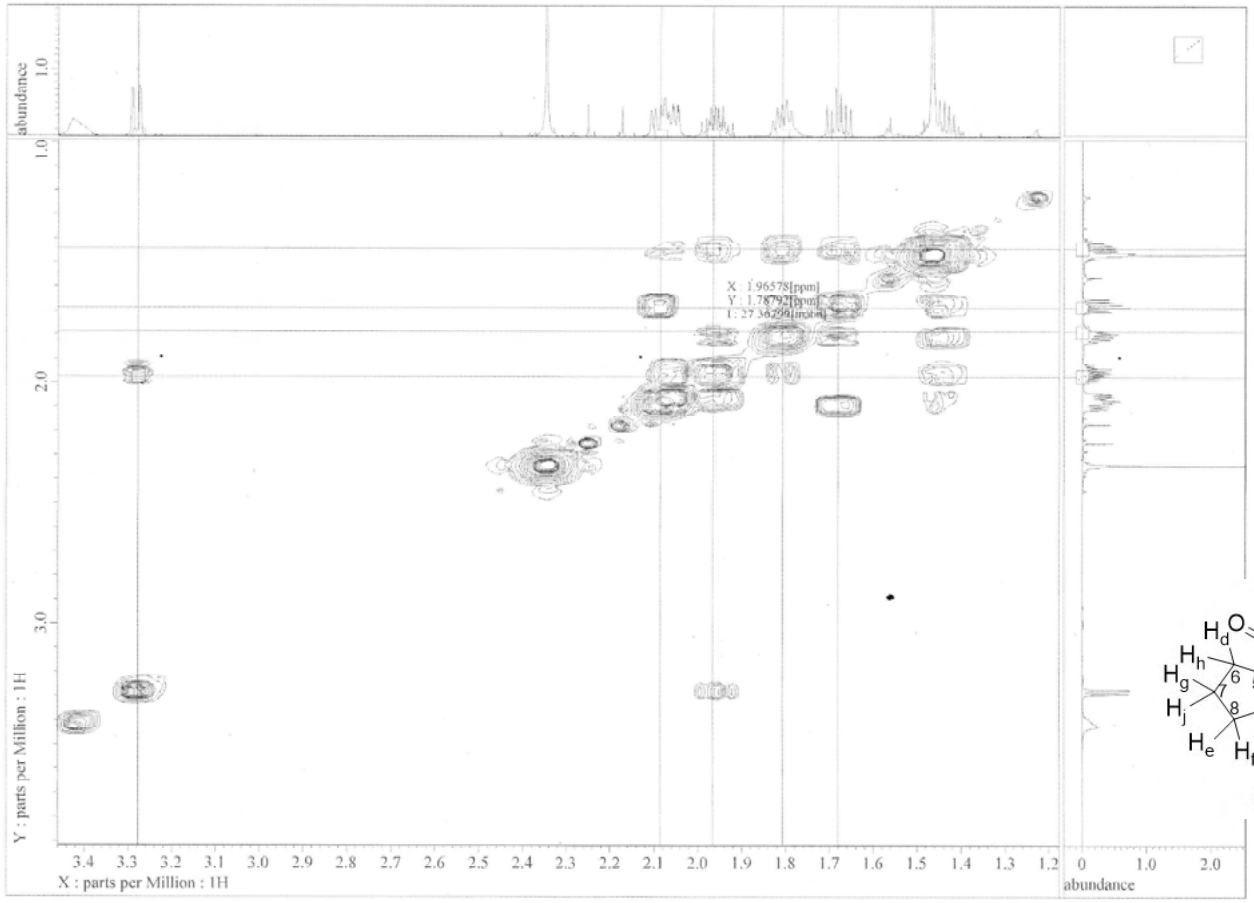


5b

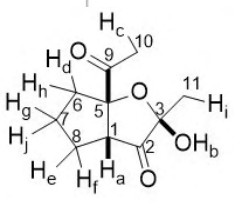

210.941
208.907
99.348
95.632
77.211
76.789
49.415
38.653
30.735
26.052
25.335
20.748
PPM



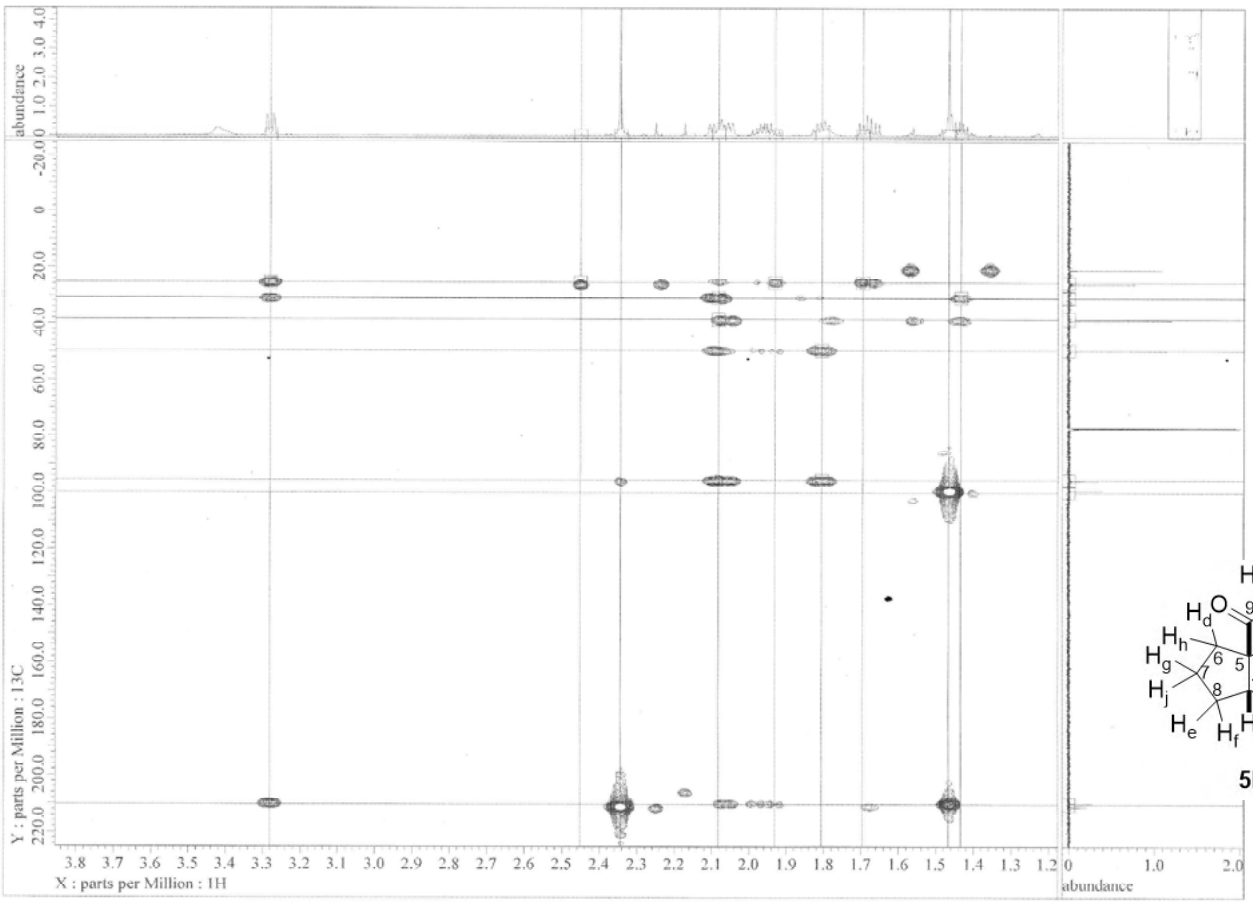
5b


abundance
X : 1.96578[ppm]
Y : 1.78792[ppm]
Y : parts per Million : 1H
X : parts per Million : 1H
abundance

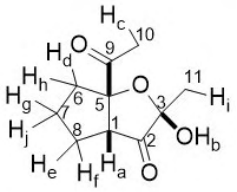
H-H COSY



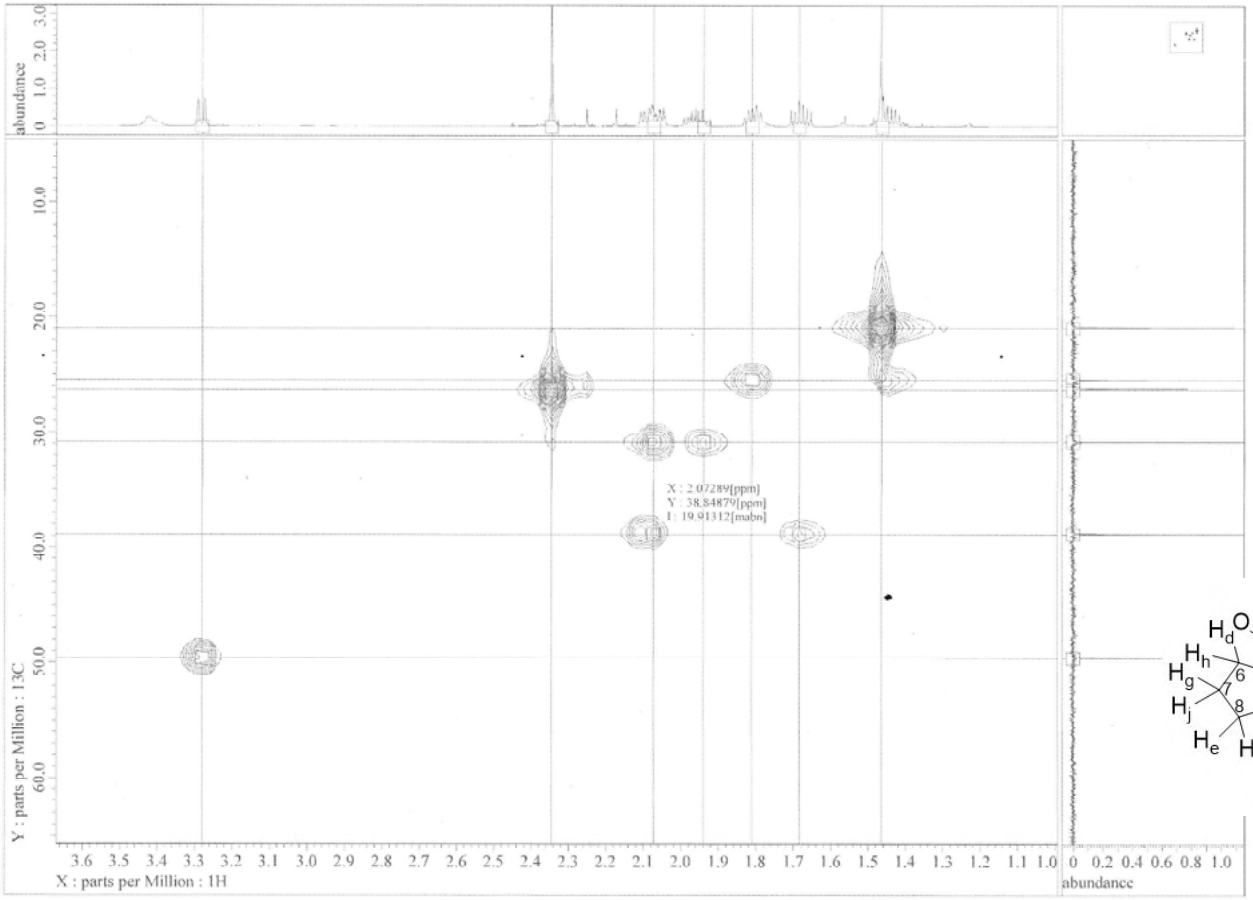
5b



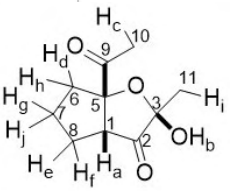
HMBC



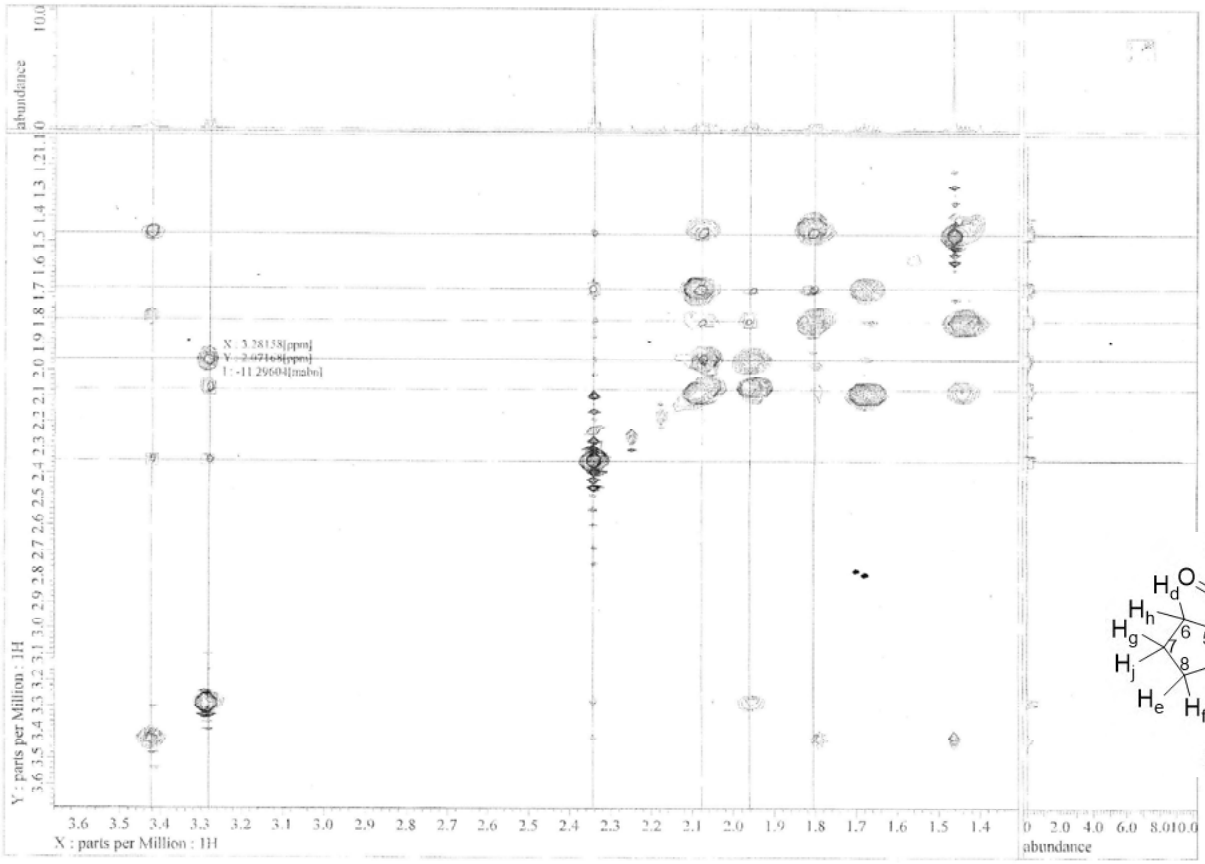
5b



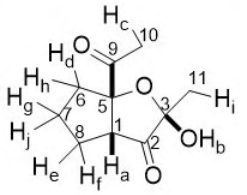
HMQC



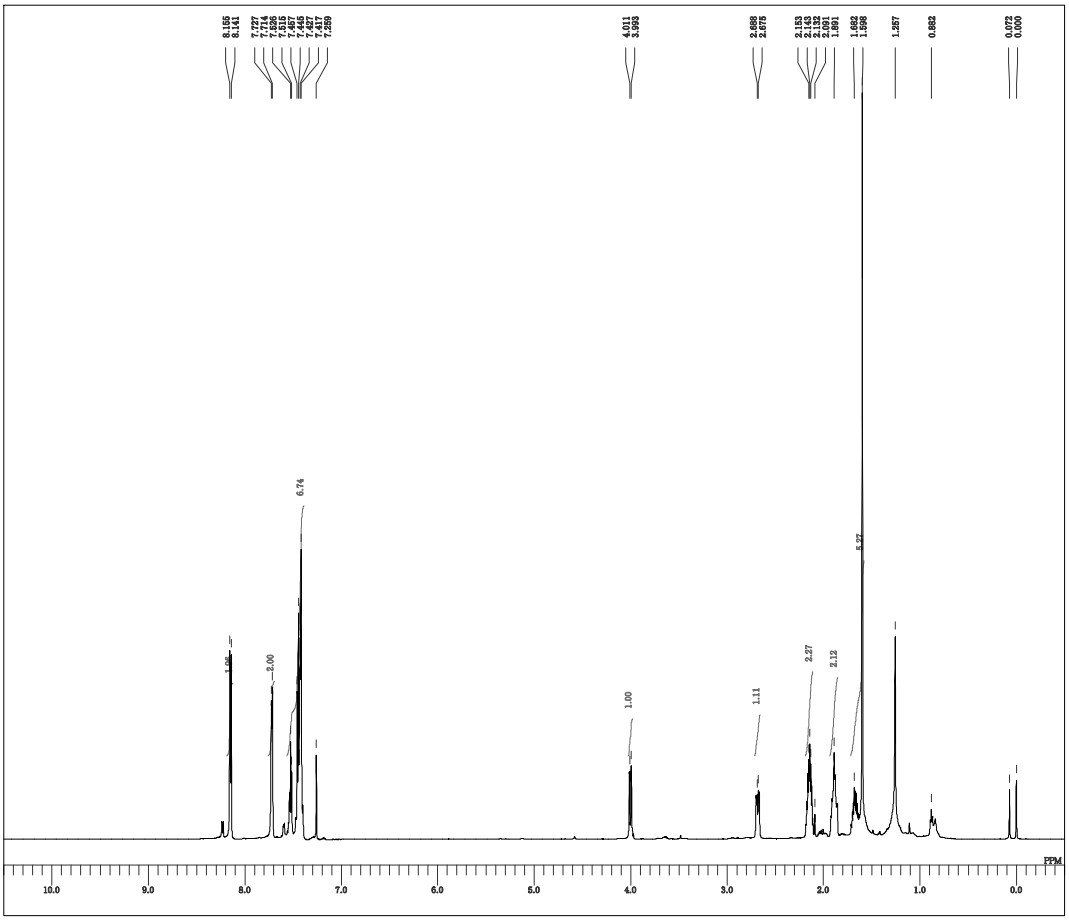
5b



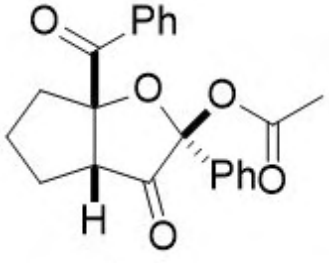
NOESY



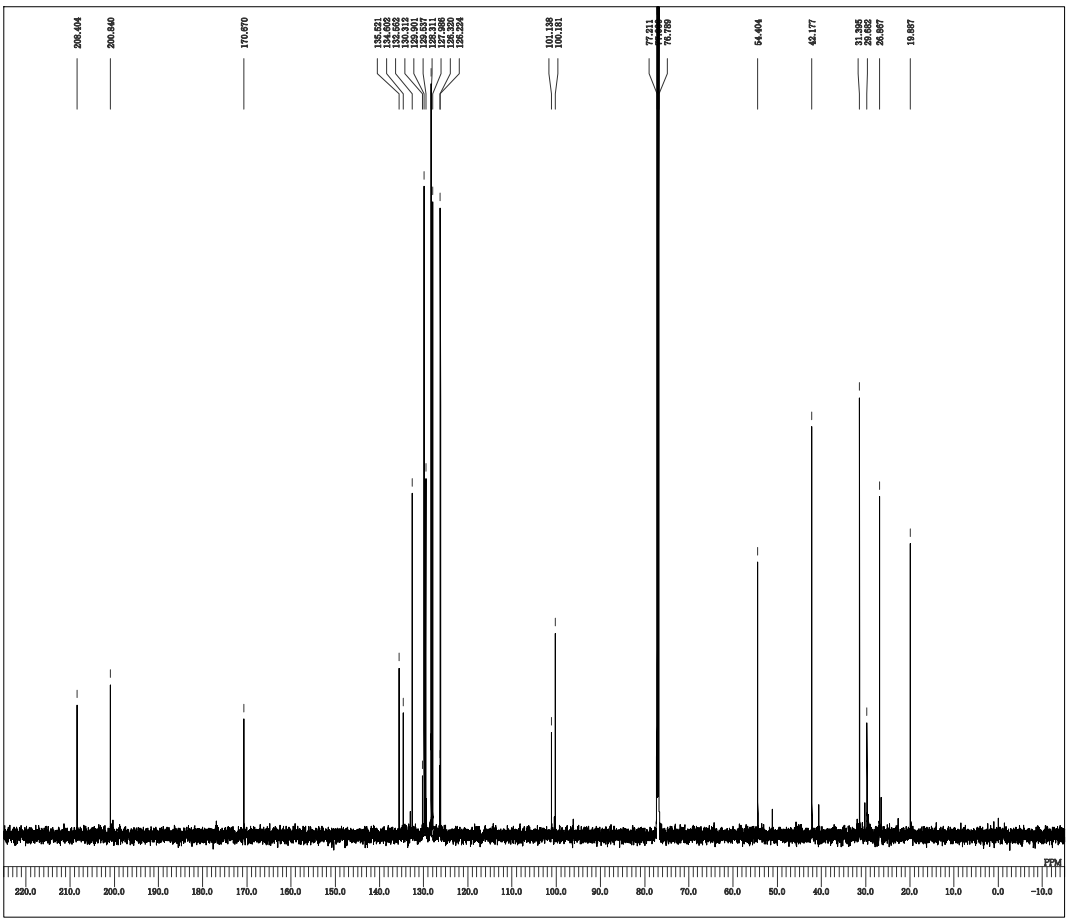
5b



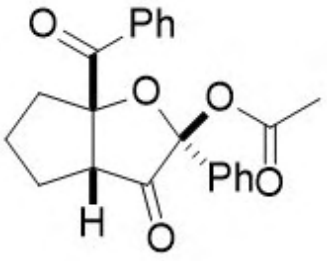
DPULE TD82_55sc_1H-1.als
COMNT
DATIM 2021-09-06 15:28:03
OBNUC 1H
EXMOD single_pulse.ex2
OBFRQ 600.17 MHz
OBSET 5.30 KHz
OBFIN 5.47 Hz
PONT 20214
FREQU 9006.57 Hz
SCANS 8
ACQTM 2.0098 sec
PD 2.0000 sec
PW1 6.90 usec
IRNUC 1H
CTEMP 24.2 c
SLVNT CDCL3
EXREF 0.00 ppm
BF 1.40 Hz
RGAIN 44



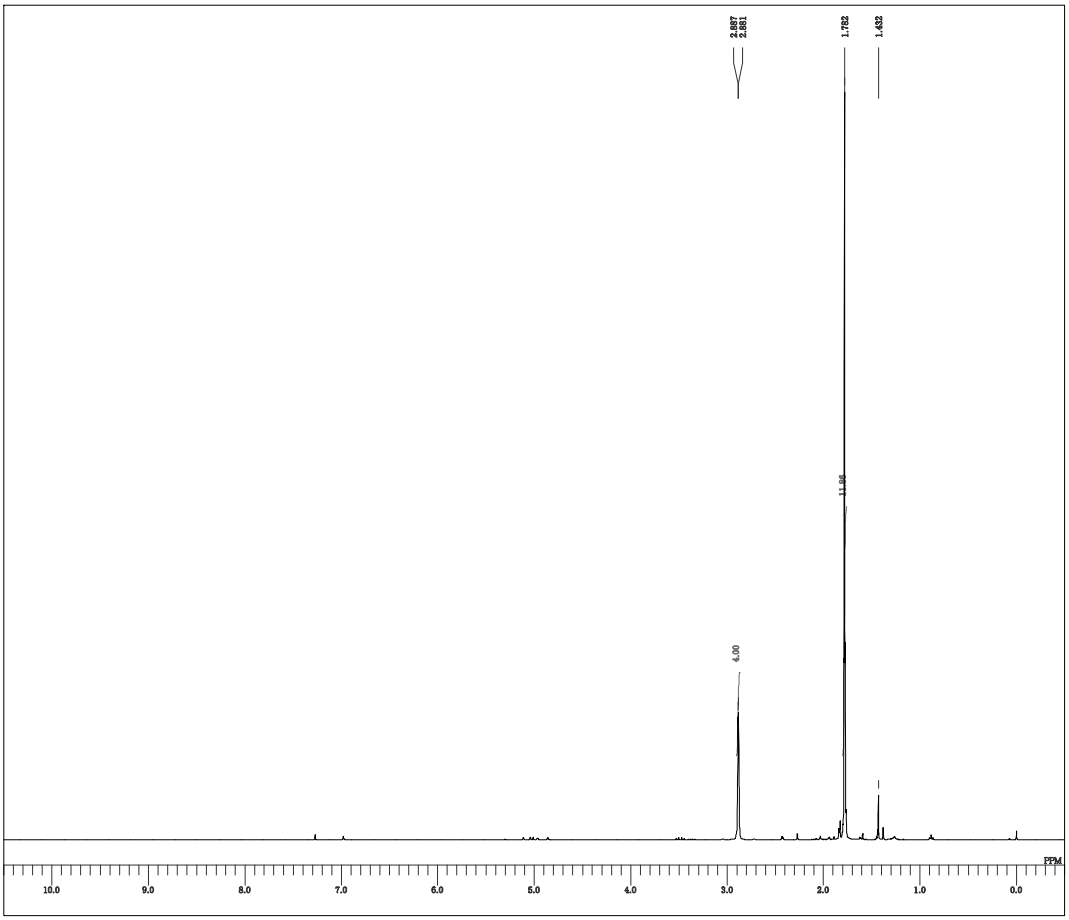
5a'



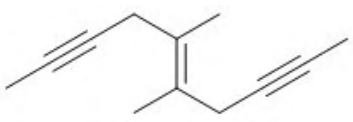
DPILE TD82_55ac_13C-1.als
COMNT
DATIM 2021-09-06 15:26:44
OBNUC 13C
EXMOD single_pulse_dec
OBFRQ 150.92 MHz
OBSET 8.52 KHz
OBFIN 1.74 Hz
POINT 26214
FREQU 37878.21 Hz
SCANS 1000
ACQTM 0.6921 sec
PD 1.2000 sec
PW1 3.50 usec
IRNUC 1H
CTEMP 24.5 c
SLVNT CDCL3
EXREF 77.00 ppm
BF 1.40 Hz
RGAIN 56



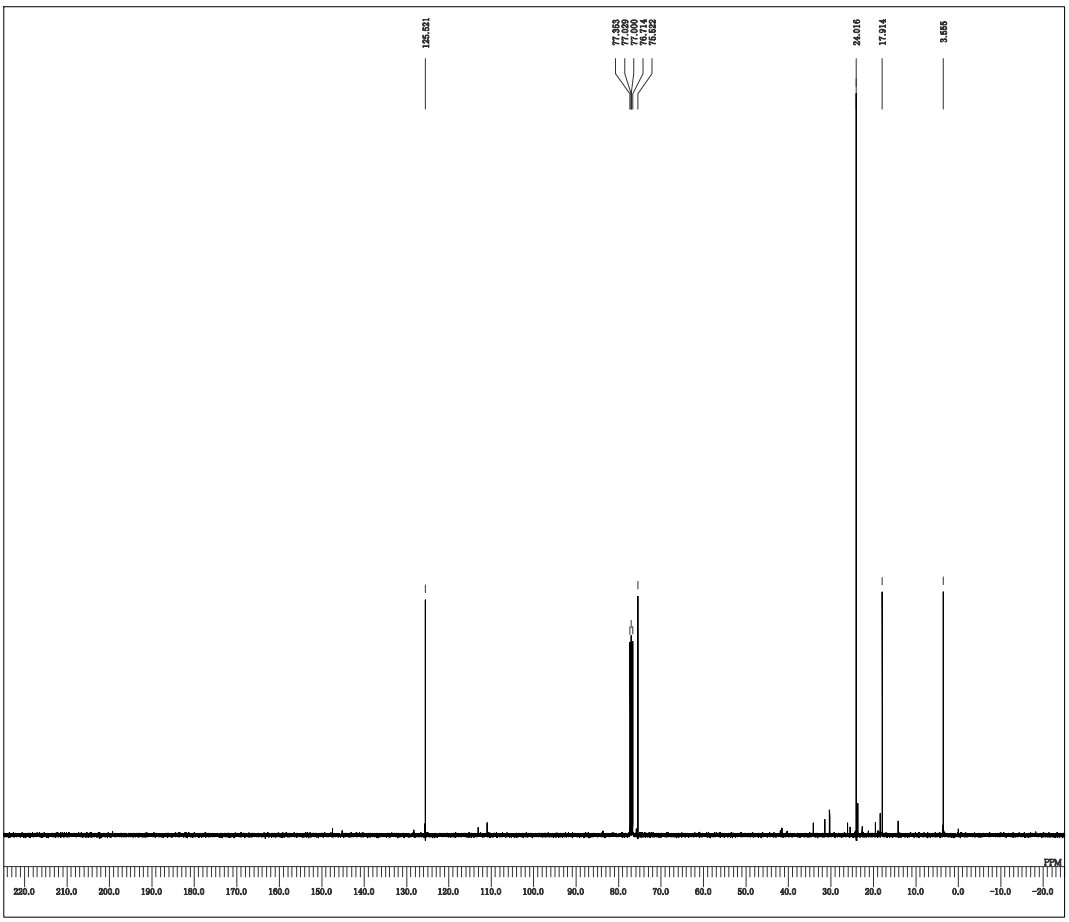
5a'



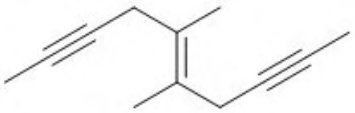
DPILE TD139_9.4-9-1.als
COMNT
DATIM 2022-01-13 15:33:42
OBNUC 1H
EXMOD single_pulse.ex2
OBFRQ 399.78 MHz
OBSET 4.19 KHz
OBFIN 7.29 Hz
POINT 13107
FREQU 6002.31 Hz
SCANS 8
ACQTM 2.1837 sec
PD 2.0000 sec
PW1 5.00 usec
IRNUC 1H
CTEMP 20.4 c
SLVNT CDCL3
EXREF 0.00 ppm
BF 0.30 Hz
RGAIN 28



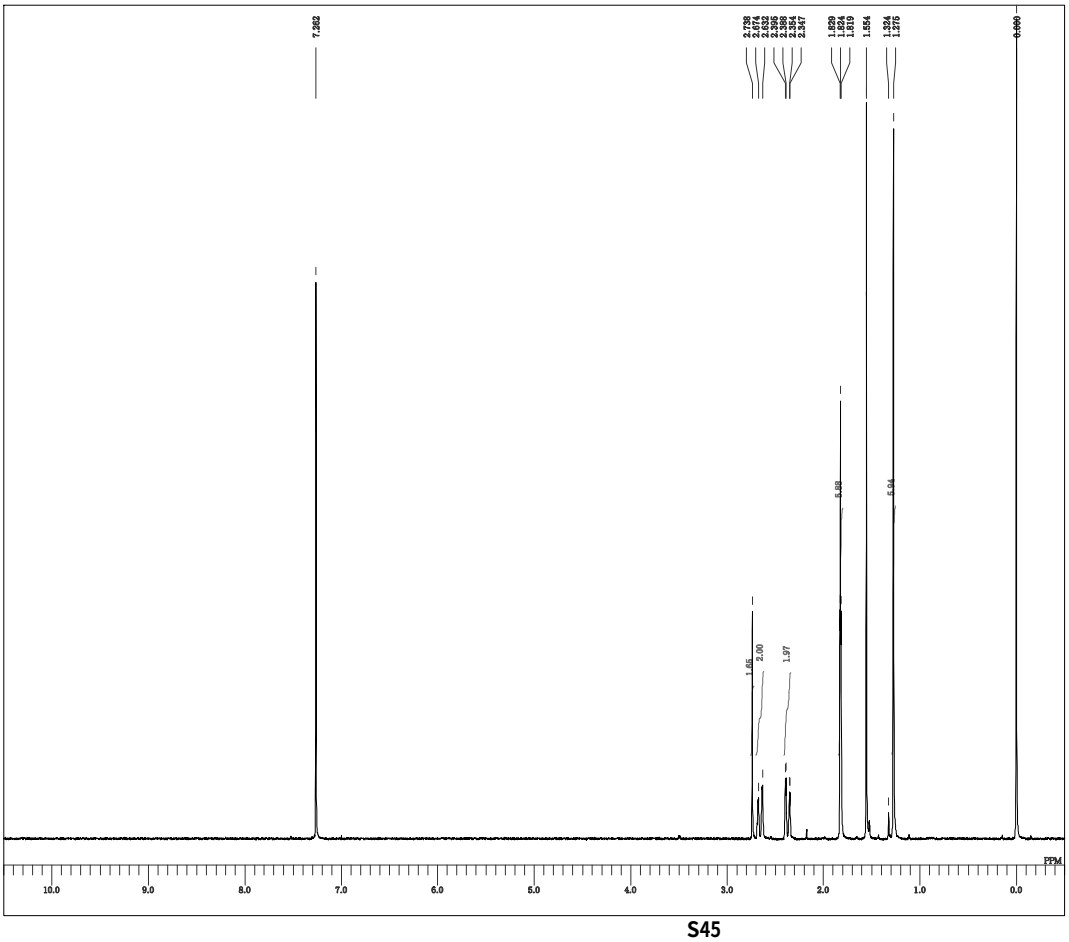
12



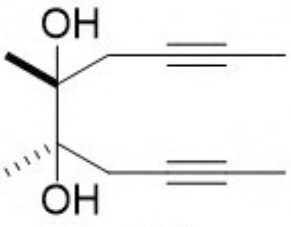
DPILE TD139_13C_fr.4-9-1.als
COMNT
DATIM 2022-01-13 17:17:04
OBNUC 13C
EXMOD single_pulse_dec
OBFRQ 100.63 MHz
OBSET 5.35 KHz
OBFIN 5.86 Hz
POINT 26214
FREQU 25125.24 Hz
SCANS 714
ACQTM 1.0433 sec
PD 1.2000 sec
PW1 2.98 usec
IRNUC 1H
CTEMP 20.9 c
SLVNT CDCL3
EXREF 77.00 ppm
BF 0.20 Hz
RGAIN 60



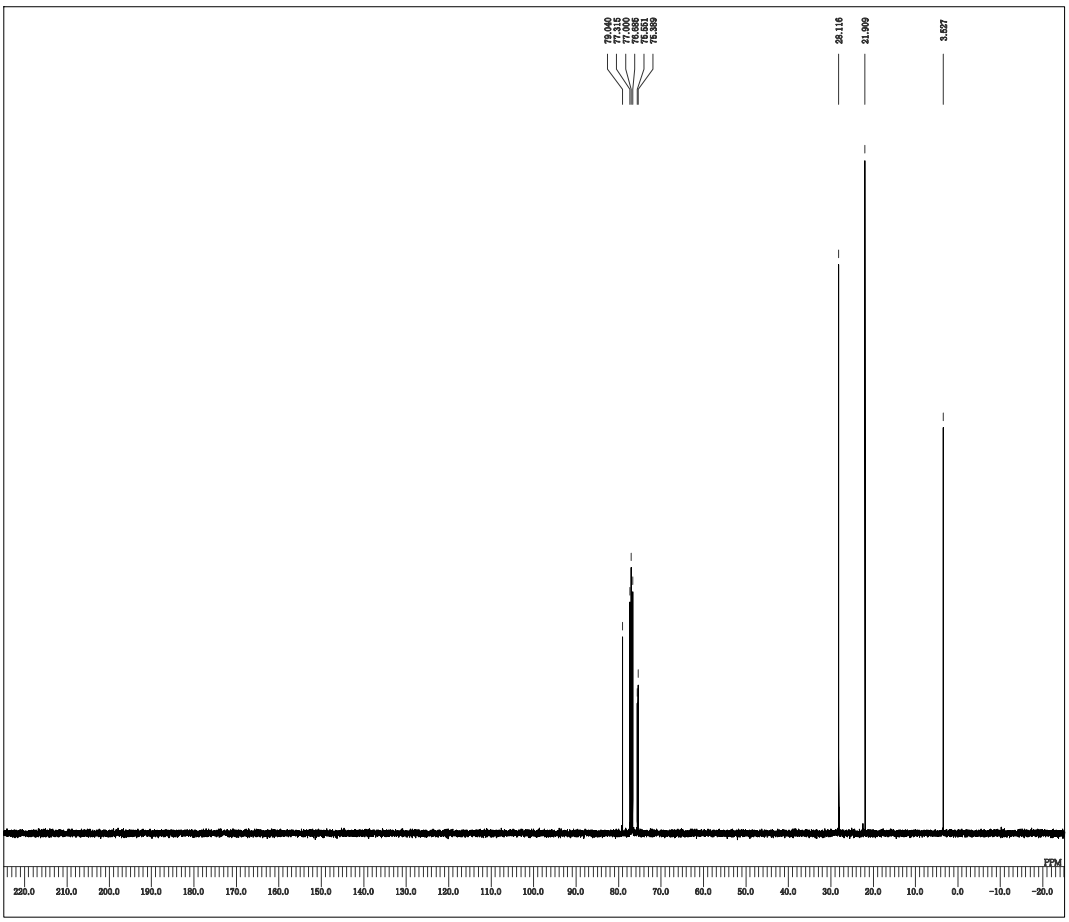
12



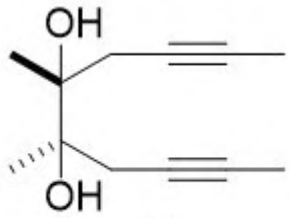
DPILE AK_dcl2-1.als
COMNT
DATIM 2021-12-21 11:17:10
OBNUC 1H
EXMOD single_pulse.ex2
OBFRQ 399.78 MHz
OBSET 4.19 KHz
OBFIN 7.29 Hz
POINT 13107
FREQU 6002.31 Hz
SCANS 8
ACQTM 2.1837 sec
PD 2.0000 sec
PW1 5.00 usec
IRNUC 1H
CTEMP 21.0 c
SLVNT CDCL3
EXREF 0.00 ppm
BF 0.20 Hz
RGAIN 52



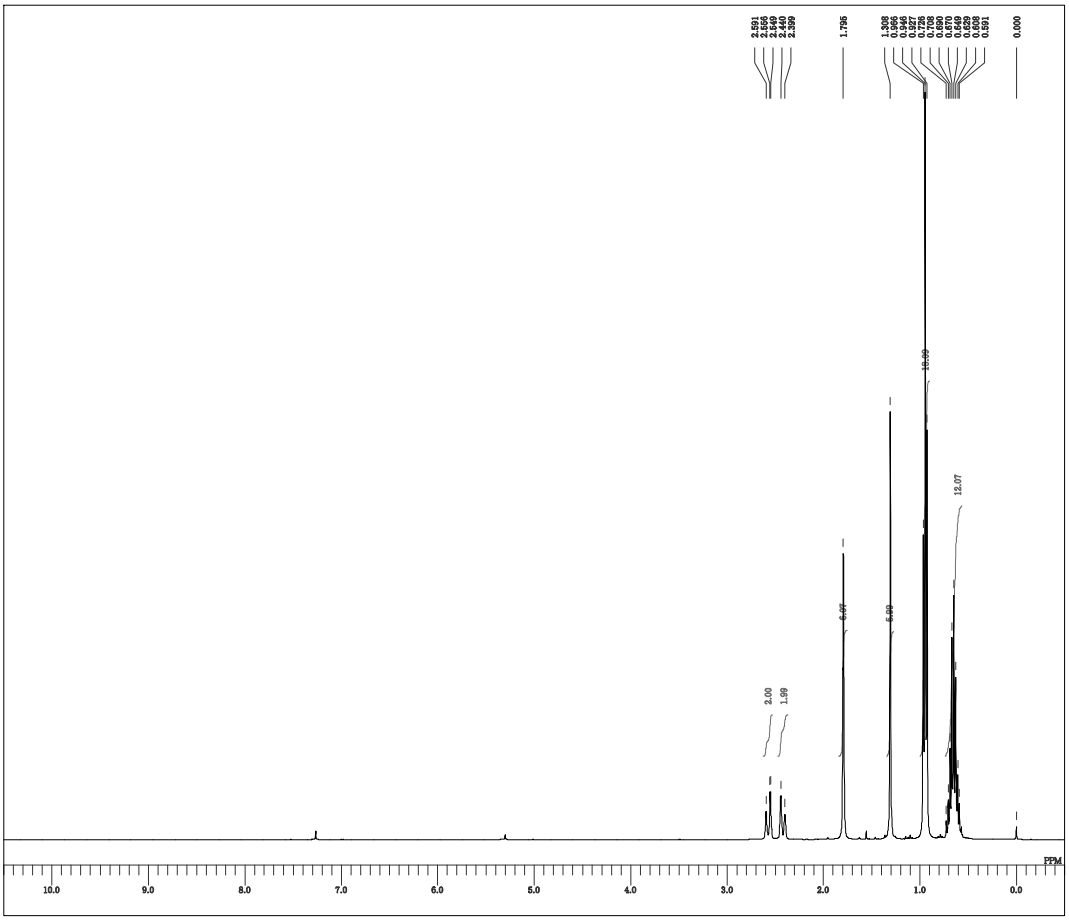
13



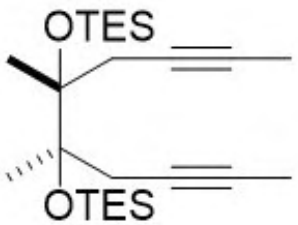
DPILE AK_diol2_13C-1.als
COMNT
DATIM 2022-02-02 15:06:23
OBNUC 13C
EXMOD single_pulse_dec
OBFRQ 100.53 MHz
OBSET 5.35 KHz
OBFIN 5.35 Hz
POINT 26214
FREQU 25125.24 Hz
SCANS 377
ACQTM 1.0433 sec
PD 1.2000 sec
PW1 2.98 usec
IRNUC 1H
CTEMP 20.6 c
SLVNT CDCL3
EXREF 77.00 ppm
BF 0.20 Hz
RGAIN 60



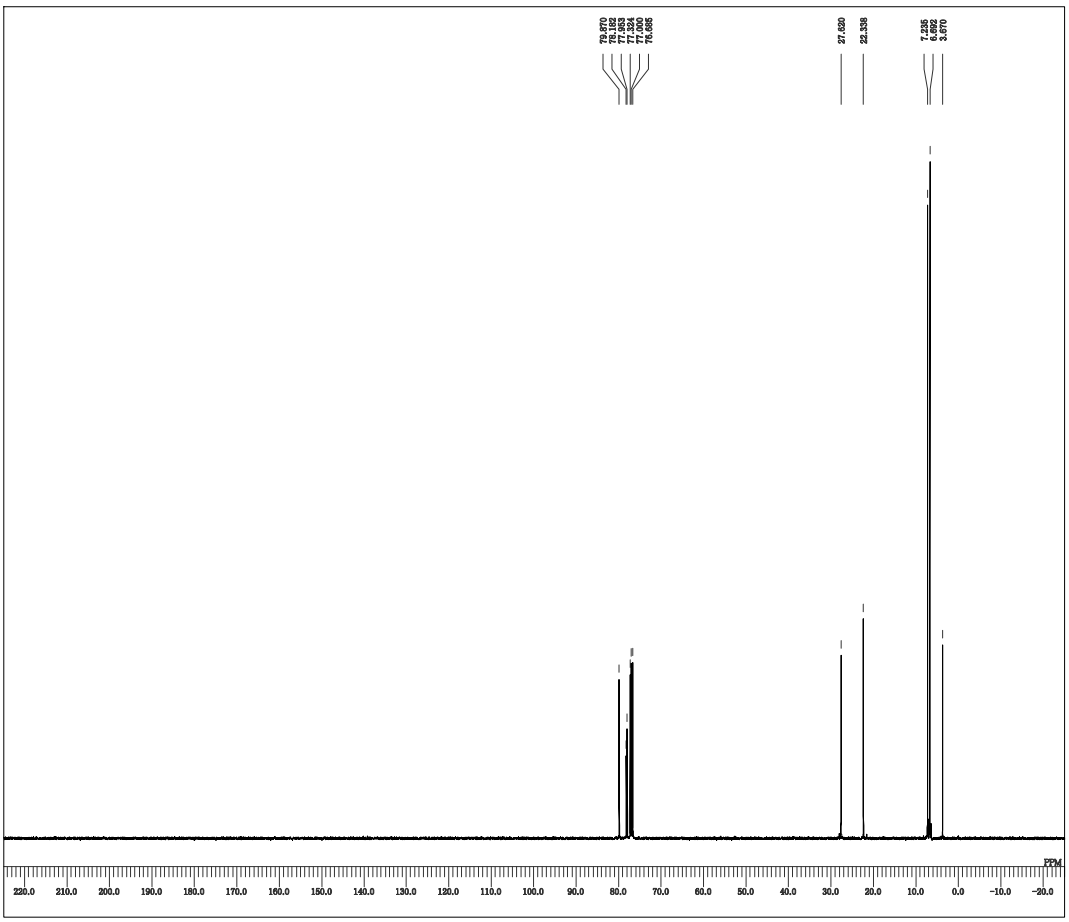
13



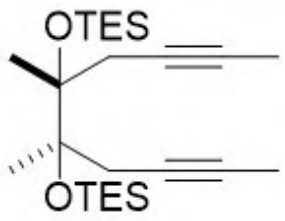
DPILE AK_TESAlkyne_1H-1.als
COMNT
DATIM 2022-02-02 11:31:28
OBNUC 1H
EXMOD single_pulse.ex2
OBFRQ 399.78 MHz
OBSET 4.19 KHz
OBFIN 7.29 Hz
POINT 13107
FREQU 6005.31 Hz
SCANS 8
ACQTM 2.1837 sec
PD 2.0000 sec
PW1 5.00 usec
IRNUC 1H
CTEMP 20.1 c
SLVNT CDCL3
EXREF 0.00 ppm
BF 1.40 Hz
RGAIN 24



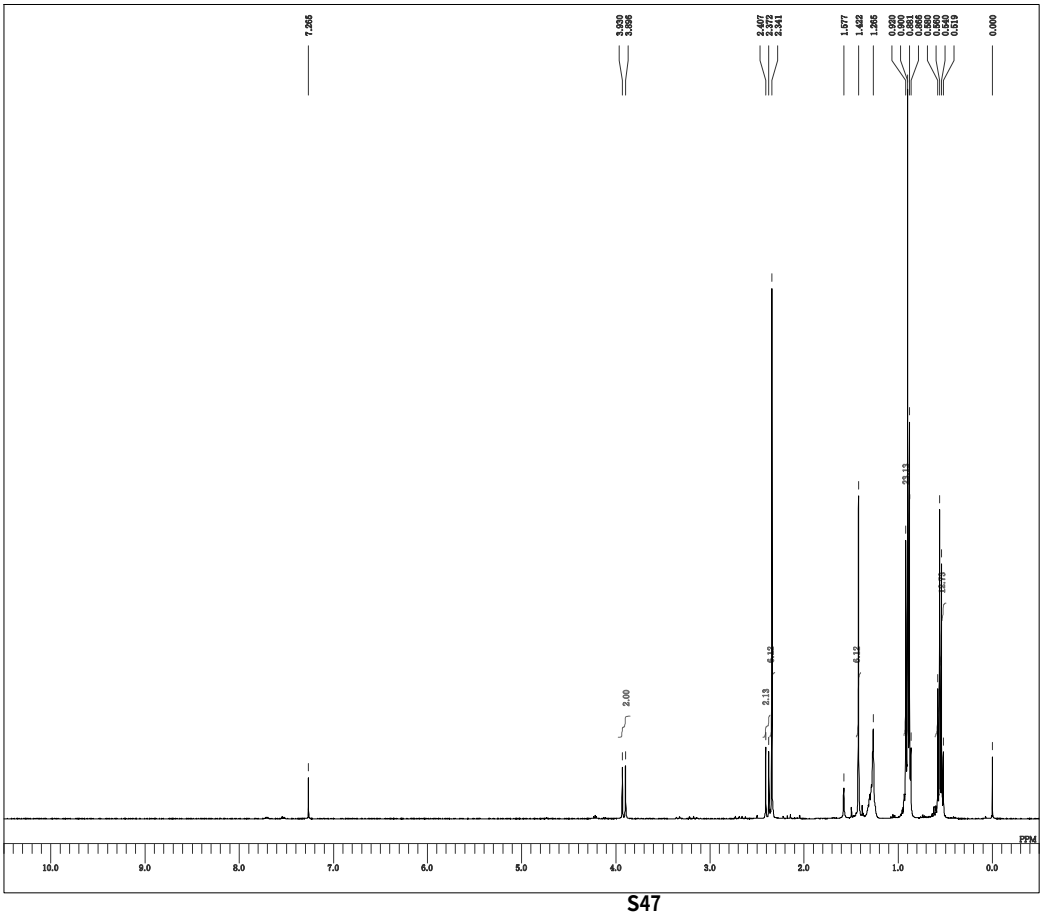
14



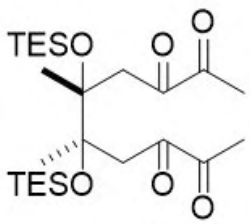
DFILE AK_TBSAlkyne_13C-1.als
COMNT
DATIM 2022-02-02 11:58:27
OBNUC 13C
EXMOD single_pulse_dec
OBFRQ 100.63 MHz
OBSET 5.35 KHz
OBFIN 5.35 Hz
POINT 26214
FREQU 25125.24 Hz
SCANS 710
ACQTM 1.0433 sec
PD 1.2000 sec
PW1 2.98 usec
IRNUC 1H
CTEMP 20.8 c
SLVNT CDCL3
EXREF 77.00 ppm
BF 1.40 Hz
RGAIN 60



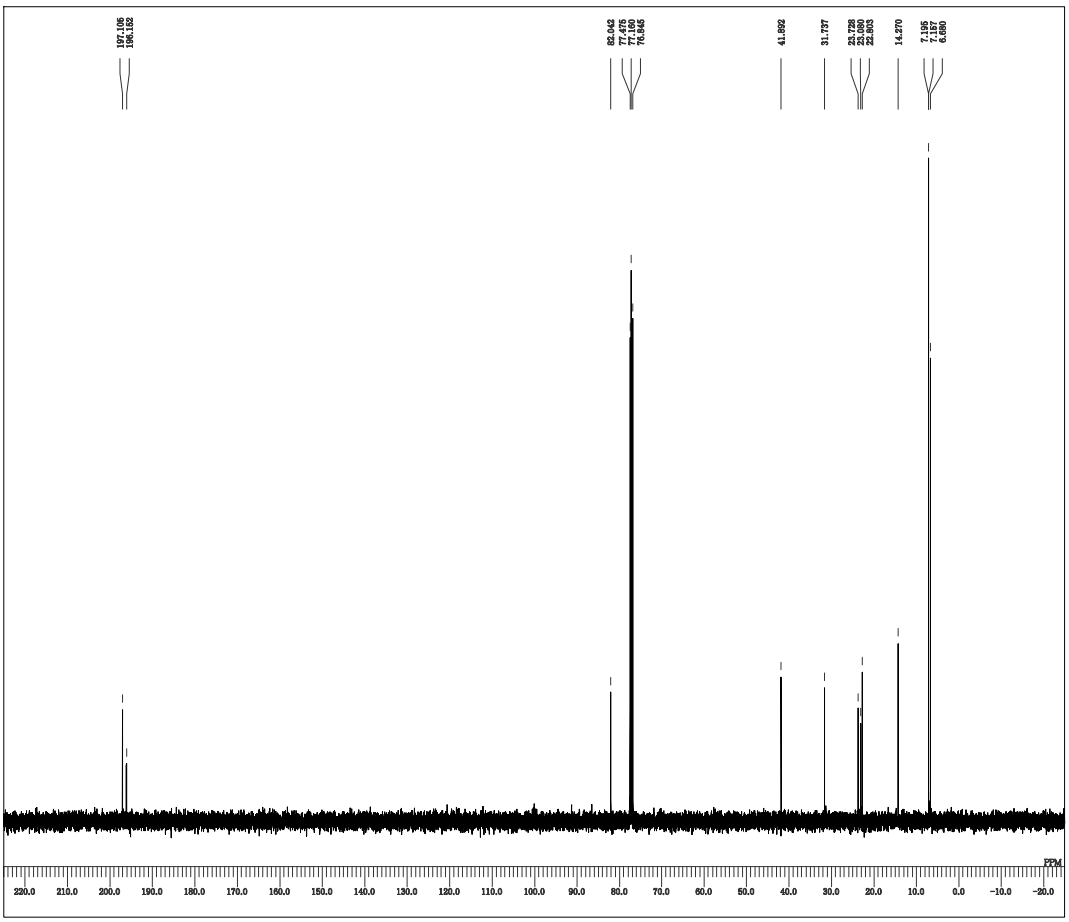
14

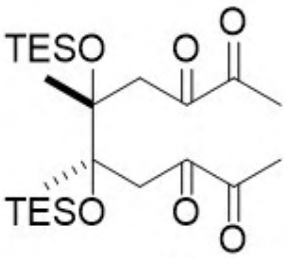


DFILE ak-323-tetra-1.als
COMNT
DATIM 2021-10-13 15:58:08
OBNUC 1H
EXMOD single_pulse.ex2
OBFRQ 399.78 MHz
OBSET 4.19 KHz
OBFIN 7.29 Hz
POINT 13107
FREQU 6002.31 Hz
SCANS 8
ACQTM 2.1837 sec
PD 2.0000 sec
PW1 5.00 usec
IRNUC 1H
CTEMP 22.6 c
SLVNT CDCL3
EXREF 0.00 ppm
BF 0.20 Hz
RGAIN 36

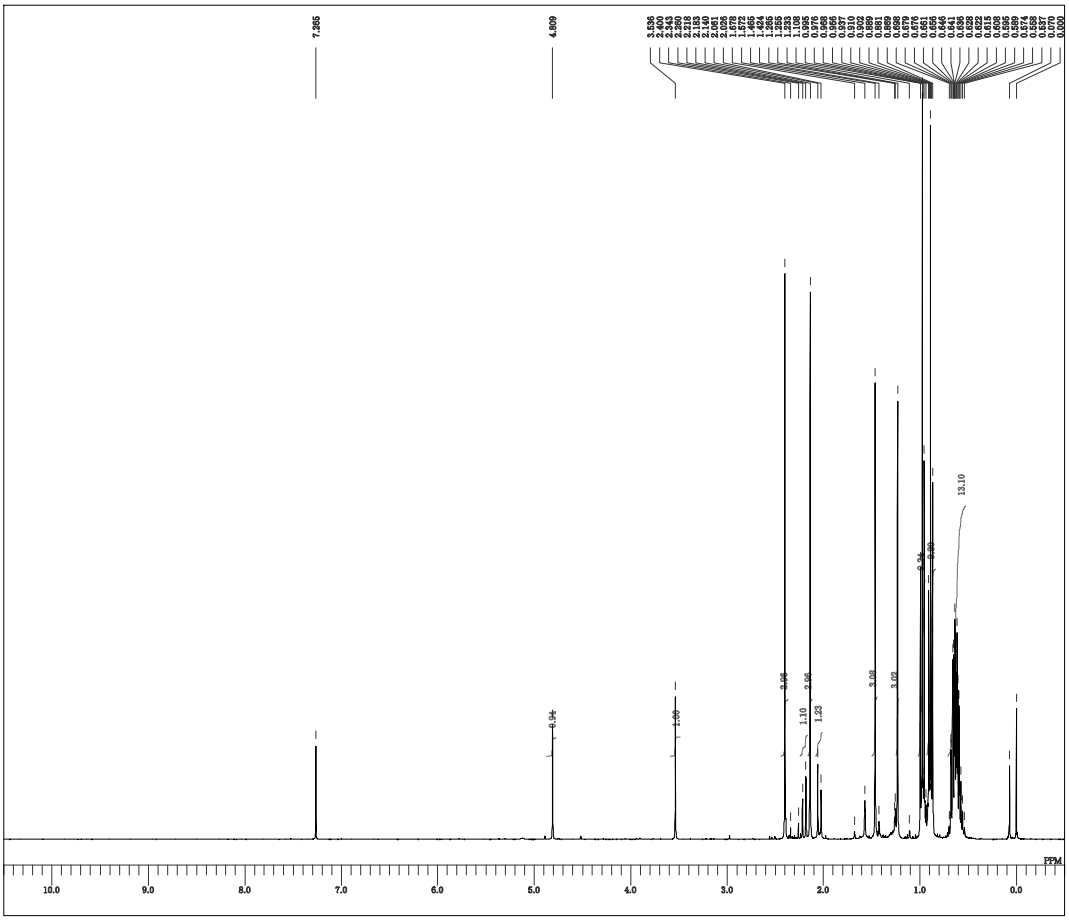


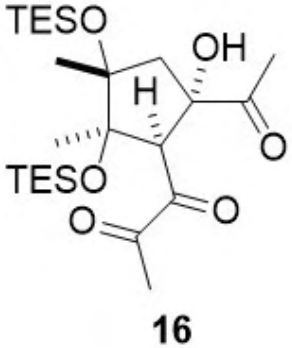
15


197.105
196.182
77.475
77.160
76.845
41.892
31.737
23.728
22.803
14.270
7.195
6.880
PPM

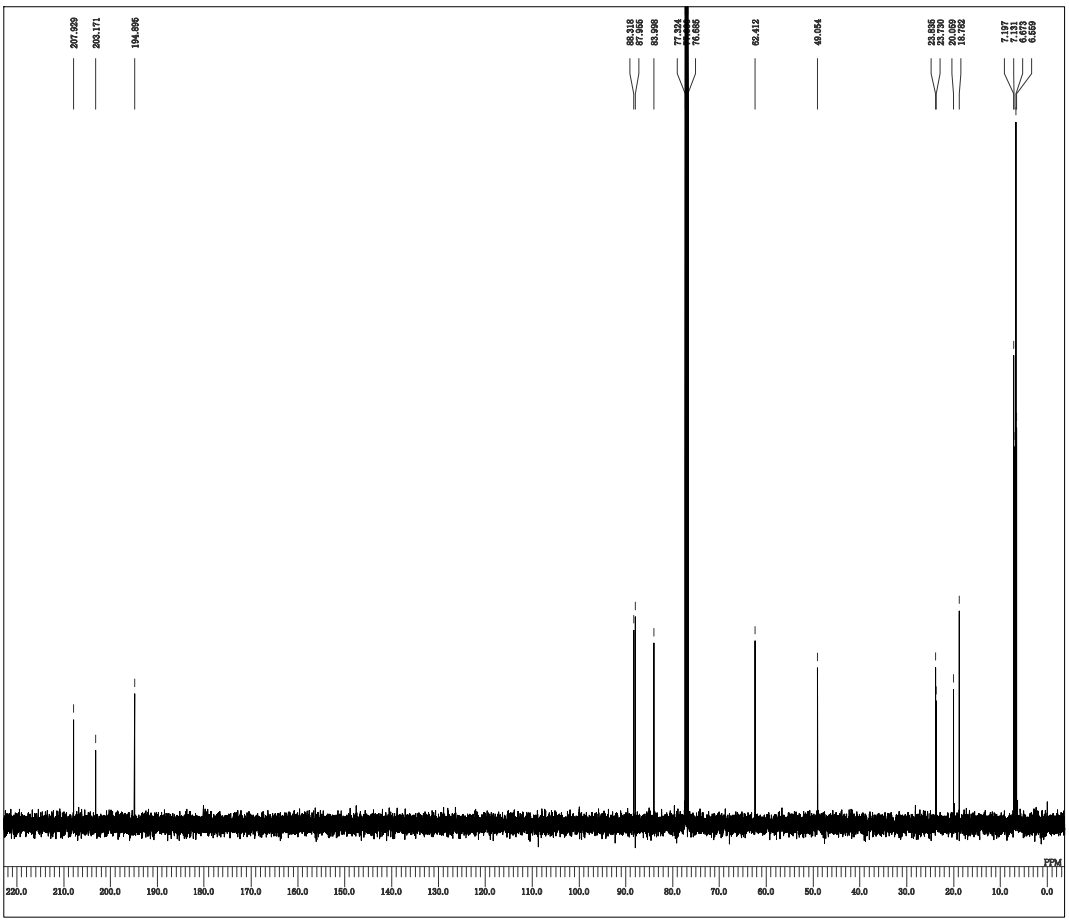

TESO
O
O
TESO
O
O

15

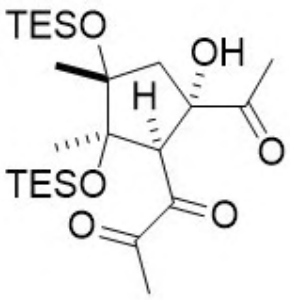

7.265
4.809
6.94
1.00
2.66
1.10
2.66
1.23
3.00
3.02
13.10
PPM


TESO
OH
H
TESO
O
O
O

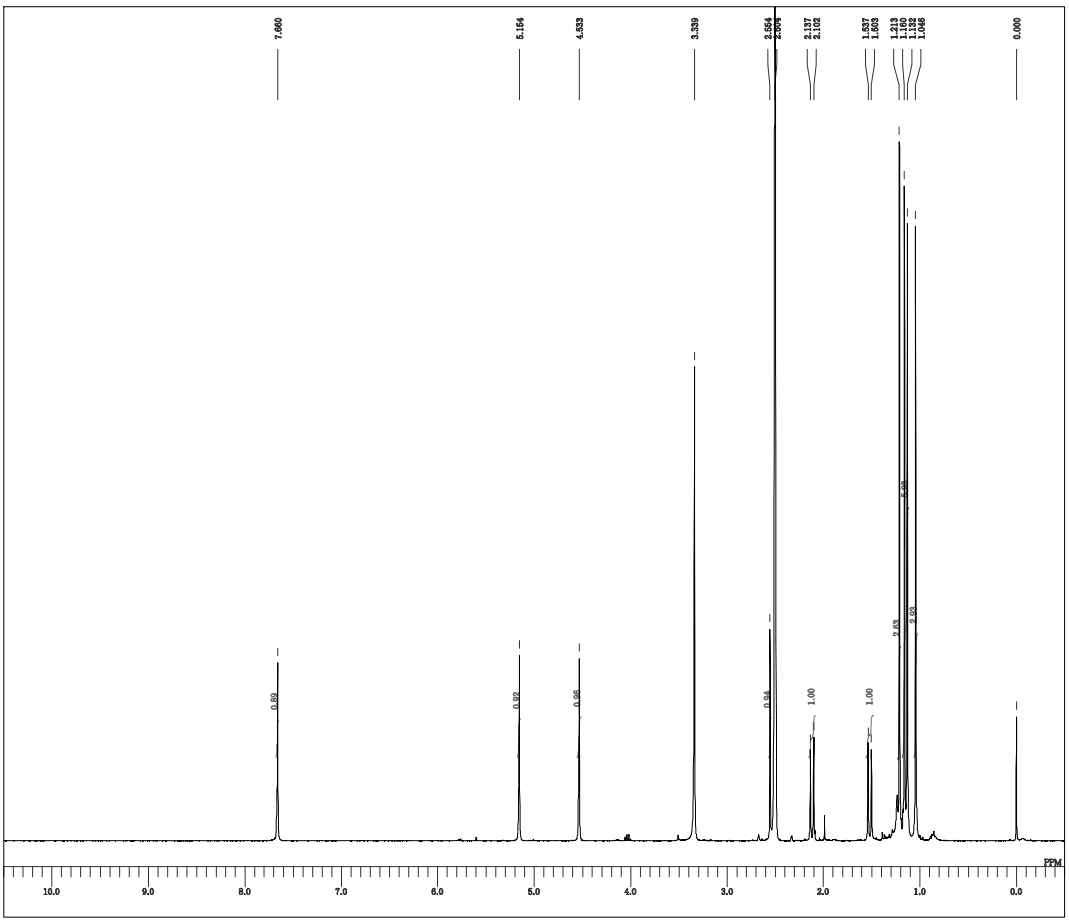
16



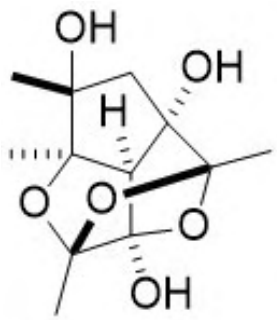

```
DFILE     sk-337-Ti-1-C-1.als
COMNT
DATIM     2021-10-28 17:15:02
OBNUC     13C
EXMOD     single_pulse_dec
OBFRQ       100.53 MHz
OBSET         5.35 KHz
OBFIN         5.35 Hz
POINT        26214
FREQU     25125.24 Hz
SCANS          690
ACQTM       1.0433 sec
PD          1.2000 sec
PW1         2.98 usec
IRNUC      1H
CTEMP      21.7 c
SLVNT      CDCL3
EXREF       77.00 ppm
RF           0.20 Hz
RGAIN          60
```



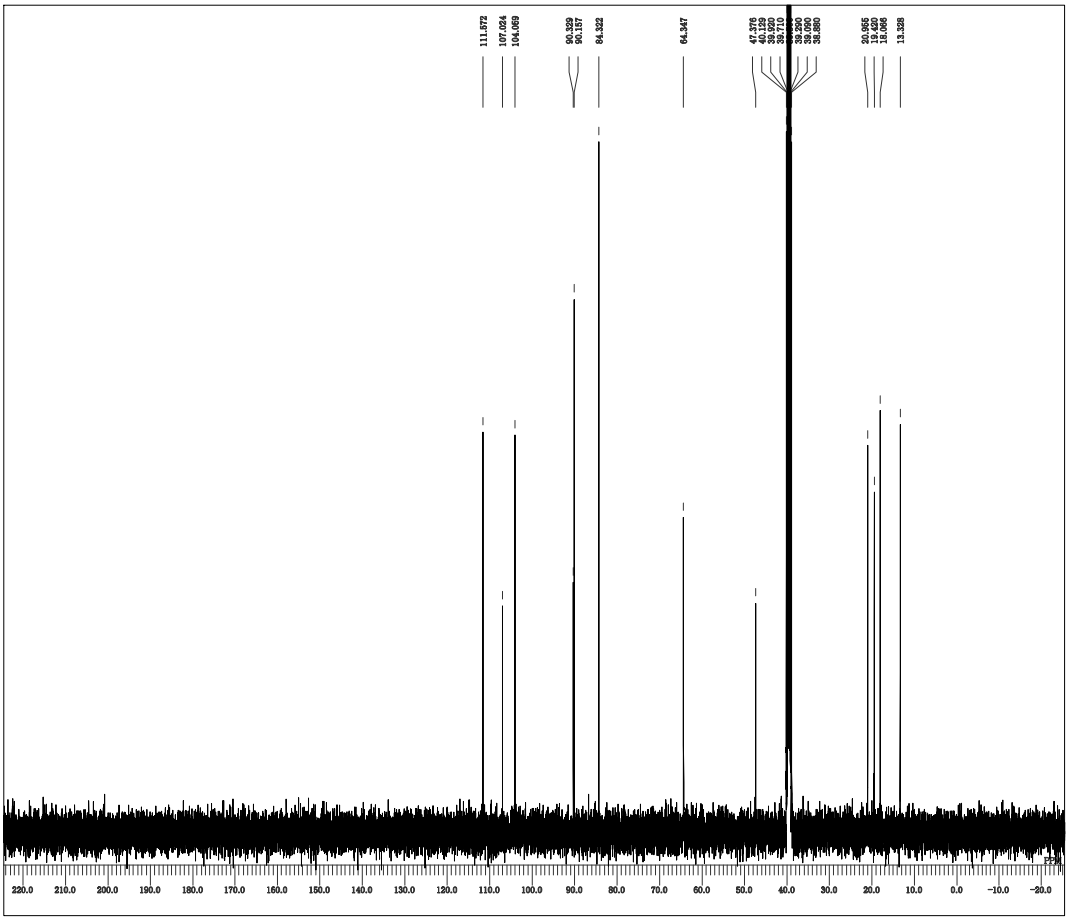
16



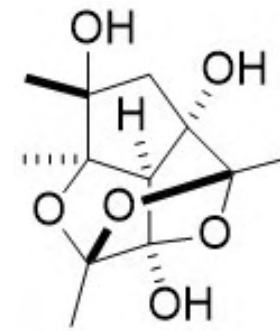
DPILE Nasteretal A_recolumn_1H-1.als
COMNT
DATIM 2022-04-06 11:18:24
OBNUC 1H
EXMOD single_pulse.ex2
OBFRQ 399.78 MHz
OBSET 4.19 KHz
OBFIN 7.29 Hz
POINT 13107
FREQU 6002.31 Hz
SCANS 8
ACQTM 2.1837 sec
PD 2.0000 sec
PW1 5.00 usec
IRNUC 1H
CTEMP 21.6 c
SLVNT DMSO
EXREF 0.00 ppm
BF 0.20 Hz
RGAIN 42



(±)-**1**

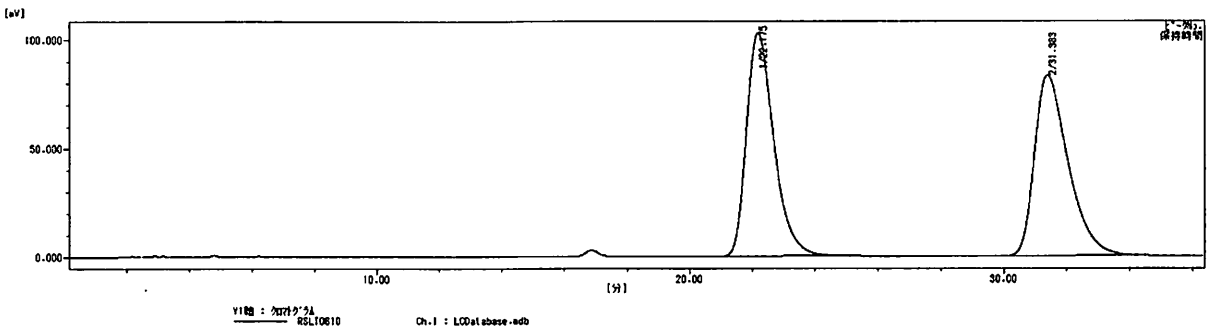


DPILE Nasteretal A_13C-1.als
COMNT
DATIM 2022-02-07 12:10:11
OBNUC 13C
EXMOD single_pulse_dec
OBFRQ 100.53 MHz
OBSET 5.35 KHz
OBFIN 5.86 Hz
POINT 26214
FREQU 25125.24 Hz
SCANS 1000
ACQTM 1.0433 sec
PD 1.2000 sec
PW1 2.98 usec
IRNUC 1H
CTEMP 20.6 c
SLVNT DMSO
EXREF 39.50 ppm
BF 0.20 Hz
RGAIN 60

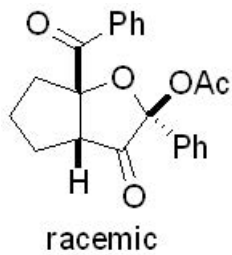


(±)-**1**

タイトル　　: td 55acr
データ　　: C:¥LC¥Database¥LCDatabase.mdb　RSLT0356
日時　　: 収集 2021/09/09
カップ番号　　:
収集属性　　:
計算方法　　: 百分率法
希釈率　　: 1.00000



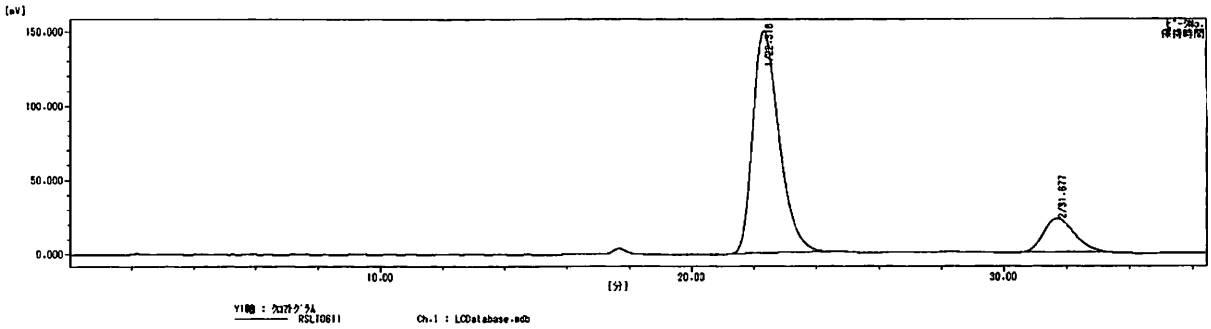
Conditions:
Solvent: IPA/Hexane = 1/99
Detect: 254 nm
Column: chiralpak AD-H
Flow: 1 mL/min



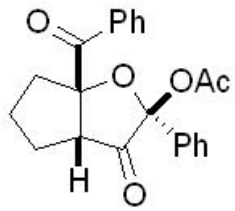
racemic

ﾋﾟｰｸNo.	保持時間	成分名	面積[mV×秒]	高さ[mV]	面積比[%]
1	22.175		6265.955	102.963	50.057
2	31.383		6251.754	83.287	49.943
ALL			0.000	0.000	100.000

タイトル　　: td 55acee
データ　　: C:¥LC¥Database¥LCDatabase.mdb　RSLT0356
日時　　: 収集 2021/09/09
カップ番号　　:
収集属性　　:
計算方法　　: 百分率法
希釈率　　: 1.00000

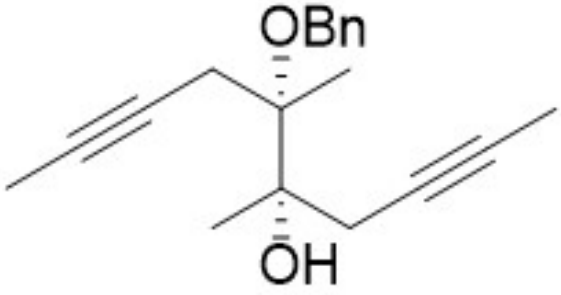


Conditions:
Solvent: IPA/Hexane = 1/99
Detect: 254 nm
Column: chiralpak AD-H
Flow: 1 mL/min

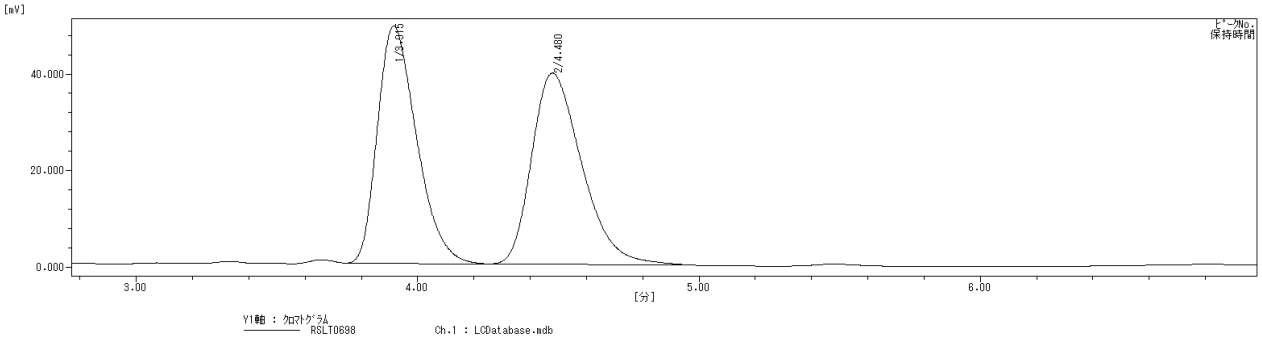


69% ee

ﾋﾟｰｸNo.	保持時間	成分名	面積[mV×秒]	高さ[mV]	面積比[%]
1	22.318		8712.257	149.621	84.674
2	31.677		1576.905	22.735	15.326
ALL			0.000	0.000	100.000



タイトル　　: td144
データ　　: C:¥LC¥Database¥LCDatabase.mdb　RSLT0356
日時　　: 収集 2022/02/01
カップ番号　　:
収集属性　　:
計算方法　　: 百分率法
希釈率　　: 1.00000



Conditions:
Solvent: IPA/Hexane = 1/9
Detect: 254 nm
Column: chiralpak OJ-H
Flow: 1 mL/min

ﾋﾟｰｸNo.	保持時間	成分名	面積[mV×秒]	高さ[mV]	面積比[%]
1	3.915		474.827	49.180	49.288
2	4.480		488.546	39.543	50.712
ALL			0.000	0.000	100.000