Supporting Information

A Tunable Cyclization Strategy for the Synthesis of Zizaene, *allo*-Cedrane, *seco*-Kaurane and *seco*-Atesane type Skeletons

Qianqian Yang, Wenjing Ma, Gaopeng Wang, Wenli Bao, Xiaoshu Dong, Xuefeng Liang, Lizhi Zhu* and Chi-Sing Lee*

Laboratory of Chemical Genomics, School of Chemical Biology and Biotechnology, Peking University Shenzhen Graduate School, Shenzhen University Town, Xili, Shenzhen 518055, China, e-mail: lizc@szpku.edu.cn

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General Information

All air and water sensitive reactions were carried out under a nitrogen atmosphere with dry solvents under anhydrous conditions, unless otherwise noted. All the chemicals were purchased commercially and used without further purification. Anhydrous THF and was distilled from sodium-benzophenone, toluene was distilled from sodium, and dichloromethane was distilled from calcium hydride. Yields refer to chromatographically, unless otherwise stated. Reactions were monitored by thin-layer chromatography (TLC) carried out on 0.25 mm silica gel plates (60F-254) that were analyzed by staining with $KMnO_4$ (200 mL H_2O of 1.5 g $KMnO_4$, 10 g K_2CO_3 and 1.25 mL of 10% aq NaOH), fluorescence upon 254 nm irradiation or by staining with anisaldehyde (450mL of 95% EtOH, 25 mL of conc.H_2SO_4, 15 mL of acetic acid, and 25 mL of anisaldehyde). Silica gel (60, particle size 0.040–0.063 mm) was used for flash chromatography. IR spectra were obtained using FT-IR Spectrometer. NMR spectra were recorded on either a 300 (^{1}H: 300 MHz, ^{13}C: 75 MHz), 400 (^{1}H: 400 MHz, ^{13}C: 100 MHz), or 500 (^{1}H: 500 MHz, ^{13}C: 125 MHz). The following abbreviations were used to explain the multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, b = broad. High resolution mass spectra were obtained from a MALDI-TOF mass spectrometer. Crystallographic data were obtained from a single crystal X-ray diffractometer.

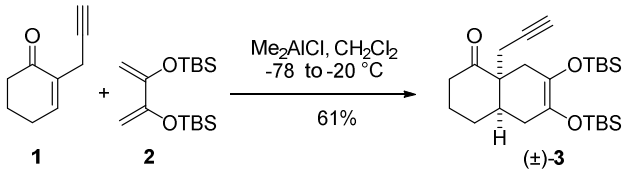
Synthetic Procedures

General procedure for synthesis of dienes 2,[1] 6,[2] 8,[3] 10 and 12

To a stirred solution of the diketone (56.1 mmol) and TEA (75 mL, 560 mmol) in CH_2Cl_2 (300 mL) was added TMSOTf, TBSOTf or TIPSOTf (145 mmol) at 0 ºC. The resulting solution was stirred at rt for 11 h and the concentrated. The remaining brown liquid was diluted with hexanes (300 mL) and wait until the layers separated. The upper layer was decanted and the lower layer was extracted with hexanes (300 mL × 3). After reducing the volume of the combined organic extracts to about 100 mL, the

solution was filtered through a plug of silica gel and the silica gel was washed by hexanes (300 mL × 3). The combined filtrates and washings were concentrated to give the product dienes. **2**[1] (a colorless oil, 17.3 g, 55.0 mmol, 98% from 2,3-butanedione). **6**[2] (a colorless oil, 9.6 g, 42.1 mmol, 75% from 2,3-butanedione). **8**[3] (a colorless oil, 22.0 g, 55.1 mmol, 98% from 2,3-butanedione). **10** (a colorless oil, 18.9 g, 55.5 mmol, 93% from 1,2-cyclohexanedione): ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.00 (s, 2H), 2.07 (dd, *J* = 3.0, 1.6 Hz, 4H), 0.95 (s, 19H), 0.16 (s, 12H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 146.9, 105.2, 26.0, 25.7, 22.5, -3.0, -4.5. IR (neat, cm^{-1}): 2930, 2858, 1724, 1472, 1255, 1078, 837, 782; HRMS (ESI/[M+H]$^+$) calcd. for $C_{18}H_{36}O_2Si_2$: 340.2254, found 340.2258. **12** (a colorless oil, 14.7 g, 43.1 mmol, 78% from 3-methylcyclopentane-1,2-dione): ^{1}H NMR (300 MHz, $CDCl_3$) δ4.97 (d, *J* = 2.1 Hz, 1H), 2.59 (d, *J* = 2.1 Hz, 2H), 1.84 (s, 3H), 0.99 (s, 9H), 0.96 (s, 9H), 0.87 (s, 3H), 0.21 (s, 3H), 0.15 (s, 3H), 0.02 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 152.1, 145.4, 116.9, 99.2, 73.5, 34.7, 26.0, 25.7, 18.5, 12.7, -2.9, -4.5. IR (neat, cm^{-1}): 2947, 2752, 1756, 1439, 1268, 1029, 857, 753; HRMS (ESI/[M+H]$^+$) calcd. for $C_{18}H_{36}O_2Si_2$: 340.2254, found 340.2259.

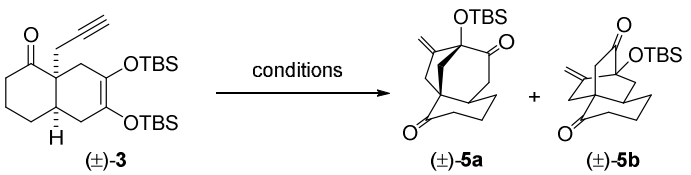
Synthesis of compd (±)-3



To a stirred mixture of **1**[4] (1.07 g, 8.0 mmol) in CH_2Cl_2 (40 mL) was added Me_2AlCl (9.8 mL, 8.8 mmol) dropwise at 0 ºC over 0.5 h. The mixture was then treated with a solution of **2**[1] (7.55 g, 24.0 mmol) in CH_2Cl_2 (15 mL) at –78 ºC over 1 h. After stirring at –20 ºC for 1 h, the reaction was quenched by addition of a saturated $NaHCO_3$ aq solution (20 mL), and the aq phase was extracted with ethyl acetate (100 mL × 3). The combined organic extracts were washed with brine, dried over Na_2SO_4, filtered and concentrated. Silica gel flash column chromatography (hexanes/ethyl acetate = 200:1) of the residue gave a yellow oil (2.2 g, 4.9 mmol, 61%) as the

product. (±)-**3**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.79 (dd, *J* = 16.6, 2.6 Hz, 1H), 2.62 – 2.43 (m, 2H), 2.43 – 2.23 (m, 4H), 2.08 – 1.72 (m, 4H), 1.70 – 1.61 (m, 3H), 0.91 (s, 9H), 0.89 (s, 9H), 0.13 – 0.12, (d, *J* = 3 Hz, 6H), 0.11 (s, 6H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 211.1, 129.8, 127.1, 81.1, 77.5, 77.1, 76.6, 70.2, 52.2, 37.8, 37.1, 35.2, 33.0, 27.6, 26.3, 25.0, 24.5, 22.7, 18.2, -3.3, -3.8. IR (neat, cm^{-1}): 3289, 2963, 2930, 1707, 1251, 1219, 838, 780, 676; HRMS (ESI/$[M+H]^+$) calcd. for $C_{25}H_{44}O_3Si_2$: 448.2829, found 448.2835. If the reaction mixture is stirred at rt for 1 h, another white solid (1.5 g, 4.5 mmol, 56%) will be obtained as the major side-product. (±)-**4**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.62 (d, *J* = 15.0 Hz, 1H), 2.31 – 2.22 (m, 4H), 2.03 – 2.01 (t, *J* = 5.0 Hz, 1H), 1.94 (s, 1H), 1.89 – 1.81 (m, 2H), 1.76 – 1.72 (t, *J* = 10.0 Hz, 1H), 1.70 – 1.62 (m, 3H), 1.40 – 1.48 (m, 1H), 0.93 (s, 9H), 0.79 (s, 9H), 0.29 (s, 3H), 0.10 (s, 3H), 0.09 (s, 6H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 210.6, 89.6, 84.9, 80.3, 69.8, 45.8, 44.1, 37.0, 32.5, 27.0, 26.2, 25.8, 24.3, 18.4, 18.4, 18.3, 17.9, -1.7, -2.1, -2.6, -3.2. IR (neat, cm^{-1}): 2970, 2680, 1769, 1439, 1369, 1028, 718, 665; HRMS (ESI/$[M+Na]^+$) calcd. for $C_{25}H_{44}O_3Si_2$: 448.2829, found 448.2838.

General procedures for carbocyclization of (±)-3 (Table 1)



(±)-**3** (±)-**5a** (±)-**5b**

To a stirred mixture of (±)-**3** (100 mg, 0.22 mmol) in CH_2Cl_2 (4 mL) was added the indicated Lewis acid (0.11 mmol) at the indicated temp. After stirring at the specified temp for the specified time, the reaction was quenched by addition of a saturated $NaHCO_3$ aq solution (2 mL). The aq phase was extracted with CH_2Cl_2 (5 mL × 3). The combined organic extracts were washed with brine, dried over Na_2SO_4, filtered and concentrated. Silica gel flash column chromatography (hexanes/ethyl acetate = 15:1) of the residue gave a white solid as the cyclized product(s) in the indicated ratio. With $PtCl_2$ (0.5 equiv)/CH_2Cl_2 at -78 °C, 52.8 mg (0.16 mmol, 72%**)** of a 7.8:1 mixture of (±)-**5a**/(±)-**5b** was obtained (Table 1, entry 23). (±)-**5a**: ^{1}H NMR (500 MHz,

$CDCl_3$) δ 5.14 (t, *J* = 2.6 Hz, 1H), 5.02 (s, 1H), 3.55 (dt, *J* = 17.9, 2.7 Hz, 1H), 2.79 (q, *J* = 10, 1H), 2.44 – 2.29 (m, 4H), 2.25 – 2.20 (m, 2H), 2.12 – 2.05 (m, 2H), 1.89 (dd, *J* = 13.6, 11.1 Hz, 1H), 1.75 – 1.65 (m, 2H), 0.88 (s, 9H), 0.22 (s, 3H), 0.06 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 209.9, 205.7, 148.8, 108.6, 88.3, 54.6, 45.4, 43.2, 42.3, 38.8, 35.9, 29.3, 25.8, 18.4, -2.7, -2.9. IR (neat, cm^{-1}): 2953, 2930, 2856, 1735, 1710, 1251, 1163, 1123, 893; HRMS (ESI/$[M+H]^+$) calcd. for $C_{19}H_{30}O_3Si$: 334.1964, found 334.1968. (±)-**5b** (a white solid): ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.39 (dd, *J* = 3.5, 2.3 Hz, 1H), 5.00 (d, *J* = 1.3 Hz, 1H), 2.95 (dd, *J* = 18.6, 3.6 Hz, 1H), 2.86 (dt, *J* = 17.7, 2.4 Hz, 1H), 2.61 (ddt, *J* = 17.7, 3.8, 2.1 Hz, 1H), 2.52 – 2.40 (m, 1H), 2.38 – 2.31 (m, 1H), 2.25- 2.21 (m, 1H), 2.20 (s, 1H), 2.19 – 2.11 (m, 1H), 2.10 – 2.04(m, 1H), 1.86 (dd, *J* = 13.1, 2.2 Hz, 1H), 1.74 – 1.53 (m, 3H), 0.92 (s, 18H), 0.20 (s, 6H), 0.09 (s, 6H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 210.6, 206.6, 142.7, 110.3, 82.0, 48.0, 42.4, 41.2, 40.4, 38.2, 36.7, 30.1, 26.1, 25.6, 18.8, -2.5. IR (neat, cm^{-1}): 2926, 2854, 1733, 1706, 1245, 1202, 1174, 1139, 833, 776; HRMS (ESI/$[M+Na]^+$) calcd. for $C_{19}H_{30}O_3Si$: 334.1964, found 334.1969. The structure of (±)-**5b** was also characterized by X-ray crystallography.

General procedure for the cascade cyclization reactions (Table 2)

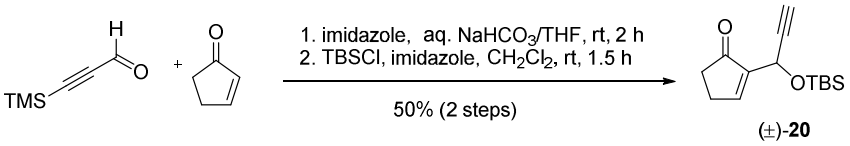
To a stirred solution of enone (**1**,[4] (±)-**14**[4], **16**[5] or **18**[6]) (1.0 mmol) in CH_2Cl_2 (5 mL) was added anhydrous $ZnBr_2$ (0.22 g, 1.0 mmol) at rt and diene (**2**,[1] **6**,[2] **8**,[3] **10** or **12**) (2.0 mmol). The resulting mixture was stirred at rt for 3 h, and the reaction was quenched by addition of a saturated $NaHCO_3$ aq solution. The aq phase was extracted with CH_2Cl_2 (50 mL × 3). The combined organic extracts were washed with brine, dried over Na_2SO_4, filtered and concentrated. Silica gel flash column chromatography (hexanes/ethyl acetate = 100:1) of the residue provided the cascade cyclized product(s). (±)-**5b** (a white solid, 0.31 g, 0.93 mmol, 93% from **1** and **2**): see the above characterization data. (±)-**7a** and (±)-**7b** (a white solid, 77.1 mg, 0.35 mmol, 35% from **1** and **6**, a 1:2 mixture): ^{1}H NMR (500 MHz, CD_3OD) δ 5.32 (d, *J* = 2.9 Hz, 0.7H), 5.13 (t, *J* = 2.7 Hz, 0.3H), 5.06 (s, 0.3H), 5.02 (s, 0.7H), 3.51 (dt, *J* = 18.0, 2.8 Hz, 0.3H), 3.31 (t, *J* = 1.5Hz, 0.7H), 3.17 (dd, *J* = 19.0, 3.5 Hz, 0.7H), 2.88 (q, *J* = 10

Hz, 0.3H), 2.81 (dt, *J* = 17.7, 2.5 Hz, 0.7H), 2.68 – 2.58 (m, 1.4H), 2.55 – 2.43 (m, 0.7H), 2.45 (dd, *J* = 18.0, 2.1 Hz, 0.3H), 2.27 – 2.15 (m, 3.5H), 2.07 – 2.06 (m, 0.9H), 1.95 – 1.89 (m, 0.3H), 1.83 (dd, *J* = 11.7, 1.6 Hz, 0.9H), 1.77 – 1.62 (m, 1.8H), 1.57 (d, *J* = 6.4 Hz, 0.7H). ^{13}C NMR (125 MHz, CD_3OD) δ 211.6, 210.7, 208.2, 206.9, 149.0, 143.2, 108.4, 107.0, 85.8, 79.1, 53.9, 45.5, 42.5, 41.5, 41.0, 40.8, 38.8, 38.2, 37.7, 36.4 , 35.9, 29.3, 28.8. IR (neat, cm^{-1}): 3474, 2930, 1730, 1707, 1437, 1123, 1064, 898; HRMS (ESI/$[M+Na]^+$) calcd. for $C_{13}H_{16}O_3$: 220.1099, found 220.1102. (±)-**9a** and (±)-**9b** (a white solid, 0.29 g, 0.78 mmol, 78% from **1** and **8**, a 1:16 mixture, only the signals of (±)-**9b** were listed). ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.40 (d, *J* = 0.8 Hz, 1H), 5.01 (d, *J* = 1.3 Hz, 1H), 2.94 (dd, *J* = 18.6, 3.6 Hz, 1H), 2.82 (dt, *J* = 17.7, 2.5 Hz, 1H), 2.61 (ddt, *J* = 17.7, 3.7, 2.0 Hz, 1H), 2.49-2.41 (m, 1H), 2.36 – 2.29 (m, 1H), 2.22 – 2.18 (m, 2H), 2.18 – 2.10 (m, 1H), 2.08 – 2.01 (m, 1H), 1.87 – 1.81 (m, 1H), 1.69-1.66, (m, 1H), 1.66 – 1.50 (m, 2H), 1.20-1.12 (m, 3H), 1.02 (dd, *J* = 7.4, 1.3 Hz, 18H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 210.8, 206.4, 142.5, 110.4, 81.9, 77.3, 77.1, 76.8, 47.9, 42.4, 41.0, 40.4, 38.2, 36.8, 30.0, 25.6, 18.6, 13.8. IR (neat, cm^{-1}): 2940, 2864, 1706, 1462, 1246, 1198, 996, 883, 669, 641; HRMS (ESI/$[M+H]^+$) calcd. for $C_{22}H_{36}O_3Si$: 376.2434, found 376.2439. (±)-**11a** (a white solid, 0.28 g, 0.79 mmol, 79% from **1** and **10**): ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.39 (dd, *J* = 3.2, 1.6 Hz, 1H), 5.13 (dd, *J* = 2.7, 1.4 Hz, 1H), 2.65 (q, *J* = 2.4 Hz, 1H), 2.63 – 2.58 (m, 1H), 2.58 – 2.54 (m, 1H), 2.39 – 2.28 (m, 2H), 2.25 (q, *J* = 2.9 Hz, 1H), 2.17 – 2.00 (m, 2H), 2.01 – 1.82 (m, 2H), 1.75 – 1.61 (m, 3H), 1.60 – 1.47 (m, 2H), 0.88 (s, 9H), 0.21 (s, 3H), 0.03 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 213.2, 211.9, 146.4, 113.2, 87.0, 77.2, 76.8, 76.5, 52.6, 49.1, 47.9, 46.0, 40.8, 37.8, 25.6, 20.9, 19.1, 18.1, 13.9, -2.9, -3.4. IR (neat, cm^{-1}): 2941, 2865, 1735, 1696, 1465, 1199, 1174, 882, 665; HRMS (ESI/$[M+H]^+$) calcd. for $C_{21}H_{32}O_3Si$: 360.2121, found 360.2129. The structure of (±)-**11a** were also characterized by X-ray crystallography. **13**: (a white solid, 0.13 g, 0.35 mmol, 35% from **1** and **12**, a single diastereomer, relative configurations were not determined): ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.30 – 3.11 (m, 1H), 2.83 (d, *J* = 17.2 Hz, 1H), 2.71 – 2.59 (m, 2H), 2.53 (ddd, *J* = 17.2, 5.6, 2.6 Hz, 1H), 2.43 (dd, *J* = 14.0, 1.3 Hz, 1H), 2.28 (td, *J* = 13.7, 6.3 Hz, 1H), 2.19-2.11 (m, 2H), 2.06 – 1.98 (m, 1H),

1.96 (s, 3H), 1.91 (t, J = 2.6 Hz, 1H), 1.68 (d, J = 13.1 Hz, 1H), 1.63 – 1.48 (m, 1H), 1.40 (ddd, J = 24.8, 12.5, 3.0 Hz, 1H), 0.95 (s, 9H), 0.17 (d, J = 1.9 Hz, 6H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 209.5, 204.2, 149.6, 81.8, 77.3, 77.0, 76.8, 69.5, 50.2, 43.6, 42.0, 41.3, 33.3, 25.7, 24.9, 18.3, 15.6, 14.7, -4.0. IR (neat, cm^{-1}): 3292, 2930, 1706, 1710, 1645, 1391, 1340, 1220, 841; HRMS (ESI/$[M+H]^+$) calcd. for $C_{21}H_{32}O_3Si$: 360.2121, found 360.2125. **(±)-15b** (a white solid, 0.36 g, 0.79 mmol, 79% from (±)-**14** and **2**, a single diastereomer, the relative configuration of the OTBS was not determined): ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.60 (s, 1H), 5.28 (s, 1H), 4.86 (s, 1H), 2.96 – 2.90 (m, 1H), 2.71 (d, J = 19.0 Hz, 1H), 2.39 – 2.20 (m, 2H), 2.10 (dd, J = 19.0, 1.2 Hz, 1H), 2,06 – 1.91 (m, , 1H), 1.87 (dd, J = 12.9, 3.5 Hz, 1H), 1.55 (dd, J = 12.9, 6.0 Hz, 10H), 1.26 (s, 2H), 0.92 (s, 9H), 0.86 (s, 9H), 0.19 (s, 6H), 0.10 (d, J = 4.4 Hz, 6H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 209.5, 206.1, 147.4, 115.0, 81.6, 77.5, 77.0, 76.6, 71.3, 53.5, 40.1, 39.7, 38.4, 31.9, 29.7, 28.3, 26.1, 23.4, 18.7, 18.3, -2.5, -3.9, -4.4. IR (neat, cm^{-1}): 2930, 2955, 2856, 1741, 1713, 1253, 1148, 1092, 858; HRMS (ESI/$[M+Na]^+$) calcd. for $C_{25}H_{44}O_4Si_2$: 464.2778, found 464.2779. **(±)-17a** (a yellow oil, 0.18 g, 0.57 mmol, 57% from **16** and **2**). ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.26 (dd, J = 3.2, 1.9 Hz, 1H), 5.12 (s, 1H), 3.10 (dt, J = 16.6, 3.0 Hz, 1H), 2.81 (dd, J = 18.7, 9.2 Hz, 1H), 2.53 – 2.45 (m, 1H), 2.41 (dd, J = 18.7, 3.8 Hz, 1H), 2.36 – 2.19 (m, 4H), 2.06 (dd, J = 11.4, 2.1 Hz, 1H), 1.88 (dd, J = 11.5, 0.9 Hz, 1H), 1.73 – 1.68 (m, 1H). 0.89 (s, 9H), 0.16 (s, 3H), 0.01 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 217.3, 206.1, 147.6, 111.2, 86.9, 54.1, 41.3, 40.7, 40.2, 38.5, 37.7, 27.9, 25.8, 18.3, -2.9. IR (neat, cm^{-1}): 2955, 2928, 2855, 1769, 1735, 1463, 1247, 1167, 1053, 837, 778; HRMS (ESI/$[M+H]^+$) calcd. for $C_{18}H_{28}O_3Si$: 320.1808, found 320.1818. (±)-**17b** (a yellow oil, 44.8 mg, 0.14 mmol, 14% from **16** and **2**): ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.49 (s, 1H), 5.07 (s, 1H), 2.71 (dt, J = 16.6, 2.5 Hz, 1H), 2.65 (dd, J = 18.6, 3.5 Hz, 1H), 2.57 – 2.46 (m, 2H), 2.41 – 2.13 (m, 5H), 1.86 (dd, J = 13.0, 7.9 Hz, 1H), 1.74-1.63(m, 1H), 0.93 (s, 9H), 0.21 (s, 3H), 0.09 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 216.2, 206.8, 142.5, 112.2, 82.1, 48.2, 40.5, 40.2, 39.3, 37.8, 36.0, 26.5, 26.1, 18.8, -2.5. IR (neat, cm^{-1}): 2950, 2855, 1743, 1471, 1248, 1154, 1051, 837, 776, 672; HRMS (ESI/$[M+H]^+$) calcd. for $C_{18}H_{28}O_3Si$: 320.1808, found 320.1812. The structure of (±)-**17b** was also

characterized by X-ray crystallography. (±)-**19a** (a yellow oil, 0.16 g, 0.45 mmol, 45% from **18** and **2**, single isomer, the geometry of the alkene was not determined): ^{1}H NMR (300 MHz, $CDCl_3$) δ5.77-5.75 (m, 1H), 3.12 (q, 1H), 3.00 (dt, *J* = 18.0, 3.0 Hz, 1H), 2.61-2.50 (m, 2H), 2.43 (d, *J* = 15.0, 1H), 2.29 – 2.13 (m, 3H), 1.88 (dd, *J* = 19.5, 1.8 Hz, 1H), 1.81-1.67(m, 1H), 0.92 (t, *J* = 7.2, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 217.0, 211.4, 142.3, 123.8, 73.5, 51.0, 46.2, 38.3, 37.6, 36.0, 32.8, 29.7, 25.2, 23.4, 12.3. IR (neat, cm^{-1}): 3201, 2984, 1749, 1398, 1204, 1003, 932, 869, 790, 621; HRMS (ESI/$[M+Na]^+$) calcd. for $C_{14}H_{18}O_3$: 234.1256, found 234.1263.

Synthesis of compd (±)-20

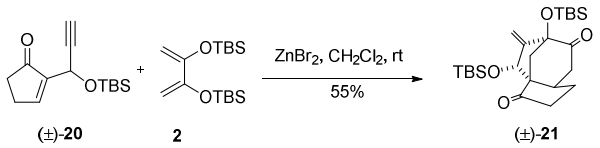


(±)-**20**

To a stirred mixture of 3-(trimethylsilyl) propiolaldehyde[4] (5 g, 39.6 mmol), imidazole (3.6 g, 52.8 mmol) in THF (50 mL) and a 1 N aq solution of $NaHCO_3$ (50 mL) was added 2-cyclopentenone (2.2 mL, 26.4 mmol) dropwise at rt. The resulting mixture was stirred at rt for 1.5 h, and the reaction was quenched by addition of a 1 N HCl aq solution (50 mL). The aq phase was extracted with CH_2Cl_2 (100 mL× 3). The combined organic extracts were washed with brine, dried over Na_2SO_4, filtered and concentrated. To a stirred solution of the residue in CH_2Cl_2 (50 mL) was added imidazole (1.5 g, 22.2 mmol) and TBSCl (2.5 g, 16.5 mmol). The resulting mixture was stirred at rt for 3 h, and the reaction was quenched by addition of a saturated $NaHCO_3$ aq solution (20 mL). The aq phase was extracted with CH_2Cl_2 (50 mL × 3) and the combined organic extracts were washed with brine, dried over $MgSO_4$, filtered and concentrated. Silica gel flash column chromatography (hexanes/ethyl acetate = 20:1) of the residue gave a yellow oil (3.3 g, 13.2 mmol, 50% in 2 steps) as the product. (±)-**20**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.80 – 7.56 (m, 1H), 5.13 – 5.12 (m, 1H), 2.61 – 2.60 (m, 2H), 2.50 – 2.42 (m, 3H), 0.87 (s, 10H), 0.14 (s, 3H), 0.10 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 206.4, 159.7, 146.0, 82.7, 72.9, 57.4, 35.3, 26.4,

25.7, 18.2, -4.8, -5.2. IR (neat, cm^{-1}): 3309, 2930, 2857, 1709, 1251, 1078, 839, 780; HRMS (ESI/$[M+H]^+$) calcd. for $C_{14}H_{22}O_2Si$: 250.1389, found 250.1392.

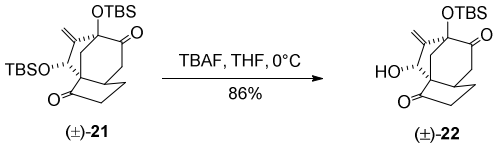
Synthesis of compd (±)-21



(±)-**20** **2** (±)-**21**

The general procedures of the cascade cyclization reaction were followed. (±)-**21** (a yellow oil, 0.25 g, 0.55 mmol, 55%): ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.30 (d, *J* = 2.8 Hz, 1H), 5.24 (d, *J* = 2.3 Hz, 1H), 4.92 (t, *J* = 2.4 Hz, 1H), 2.89 – 2.85 (m, 1H), 2.78 (dd, *J* = 18.4, 9.3 Hz, 1H), 2.44 (dd, *J* = 18.6, 7.8 Hz, 1H), 2.34 – 2.29 (m, 2H), 2.16 – 2.10 (m, 1H), 1.99 (d, *J* = 11.9 Hz, 1H), 1.82 (d, *J* = 11.8 Hz, 1H), 1.65 – 1.52 (m, 1H), 0.88 (d, *J* = 2.6 Hz, 18H), 0.14 (d, *J* = 8.2 Hz, 6H), 0.00 (d, *J* = 7.9 Hz, 6H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 217.2, 205.8, 151.0, 112.9, 84.3, 74.4, 59.1, 40.0, 38.9, 37.3, 31.4, 27.8, 25.8, 18.2, 17.9, -2.87, -2.88, -4.58, -4.60. IR (neat, cm^{-1}): 2956, 2857, 1743, 1472, 1254, 1111, 838; HRMS (ESI/$[M+H]^+$) calcd. for $C_{24}H_{42}O_4Si_2$: 450.2622, found 450.2629.

Synthesis of compd (±)-22

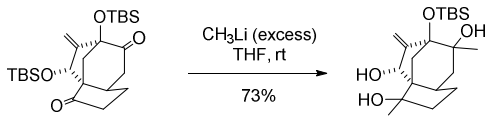


(±)-**21** (±)-**22**

To a stirred solution of (±)-**21** (100 mg, 0.22 mmol) in THF (2.5 mL) was added TBAF (0.45 mL of a 1 M solution in THF, 0.44 mmol) at 0 ºC. The resulting mixture was stirred at 0 ºC for 1 h and the reaction was quenched by addition of water (3 mL). The aq phase was extracted with ethyl acetate (5 mL × 3). The combined organic extracts were washed with brine, dried over Na_2SO_4, filtered and concentrated. Silica gel flash column chromatography (hexanes/ethyl acetate = 1:1) of the residue gave a yellow oil (64 mg, 0.19 mmol, 86%) as the product. (±)-**22**: ^{1}H NMR (500 MHz,

$CDCl_3$) δ 5.40 (d, *J* = 3.0 Hz, 1H), 5.38 (d, *J* = 3.0 Hz, 1H), 5.00 (s, 1H), 2.87-2.80 (m, 1H), 2.77 (dd, *J* = 9.5 Hz, 2.6 Hz, 1H), 2.49 (dd, *J* = 9.0 Hz, 3.0 Hz, 1H), 2.35 (dt, *J* = 7.0 Hz, 2.0 Hz, 1H), 2.29 – 1.01 (m, 2H), 2.05 (d, *J* = 12.0 Hz, 1H), 1.83 (d, *J* = 12.0 Hz, 1H), 1.72 – 1.65 (m, 1H), 0.89 (s, 9H), 0.15 (s, 3H), 0.01 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 217.1, 205.5, 150.6, 113.0, 84.5, 74.0, 58.9, 39.9, 38.4, 37.4, 31.2, 31.0, 29.6, 27.8, 25.7, 18.2, 1.0, -2.8, -2.9. IR (neat, cm^{-1}): 2950, 1749, 1523, 1109, 1003, 812, 716, 629; HRMS (ESI/$[M+Na]^+$) calcd. for $C_{18}H_{28}O_4Si$: 336.1757, found 336.1759. The structure of (±)-**22** was also characterized by X-ray crystallography.

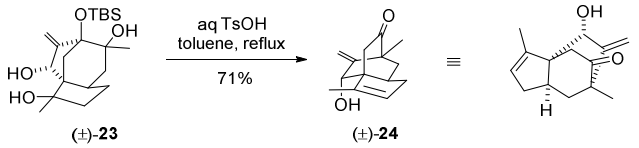
Synthesis of compd (±)-23



(±)-**21** (±)-**23**

To a stirred solution of **21** (1.0 g g, 2.22 mmol) in THF (25 mL) was added MeLi (8.9 mL of a 2.5 M solution in THF, 22.2 mmol) dropwise at rt. The resulting mixture was stirred at rt for 2 h, and the reaction was quenched by addition of H_2O (10 mL). The aq phase was extracted with ethyl acetate (50 mL × 3). The combined organic extracts were washed with brine, dried over Na_2SO_4, filtered and concentrated. Silica gel flash column chromatography (hexanes/ethyl acetate = 2:1) of the residue gave a yellow oil (0.60 g, 1.6 mmol, 73%), single diastereomer, the relative configurations were not determined) as the product. (±)-**23**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.40 (d, *J* = 1.9 Hz, 1H), 5.34 (d, *J* = 2.8 Hz, 1H), 4.56 (s, 1H), 2.73 (dd, *J* = 17.7, 8.7 Hz, 1H), 2.01 – 1.92 (m, 1H), 1.90 – 1.75 (m, 3H), 1.75 – 1.65 (m, 3H), 1.56 – 1.49 (m, 1H), 1.36 (s, 3H), 1.22 (s, 3H), 0.90 (s, 13H), 0.07 (s, 7H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.4, 112.1, 82.8, 82.3, 76.0, 72.9, 57.2, 40.1, 37.0, 36.5, 35.2, 26.3, 26.0, 25.6, 23.4, 18.4, -2.4, -2.5. IR (neat, cm^{-1}): 2859, 1633, 1459, 1257, 1129, 824, 745, 669; HRMS (ESI/$[M+Na]^+$) calcd. for $C_{18}H_{32}O_4Si$: 340.2070, found 340.2075.

Synthesis of compd (±)-24

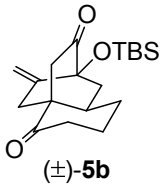


(±)-**23** (±)-**24**

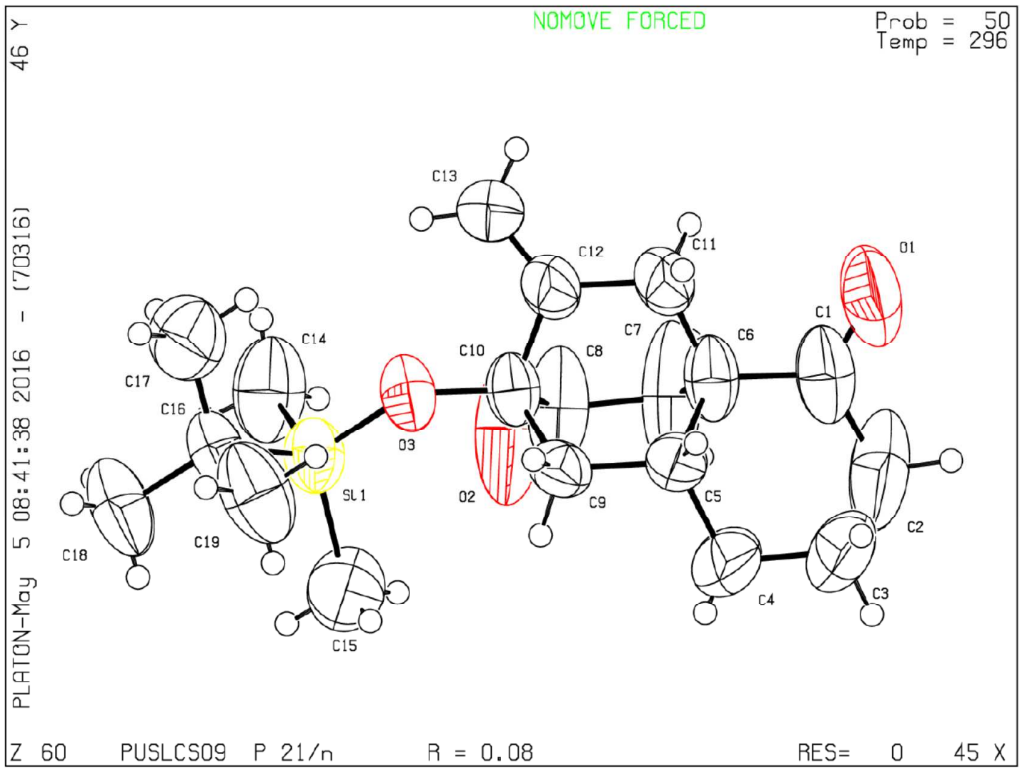
To a stirred mixture of (±)-**23** (50 mg, 0.14 mmol) in toluene (1.5 mL) was added an aq solution of TsOH (0.5 mL of a 1.8 M aq solution, 0.91 mmol) at rt. The reaction mixture was stirred at 110℃ for 2 h, and the reaction was quenched by addition of a saturated $NaHCO_3$ aq solution (2 mL). The aq phase was extracted with ethyl acetate (10 mL× 3). The combined organic extracts were washed with brine, dried over Na_2SO_4, filtered and concentrated. Silica gel flash column chromatography (hexanes/ethyl acetate = 10:1) of the residue gave a yellow oil (21.6 mg, 0.1 mmol, 71%) as the product. (±)-**24**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.50 (d, *J* = 1.2 Hz, 1H), 5.46 (d, *J* = 2.0 Hz, 1H), 5.26 (d, *J* = 2.4 Hz, 1H), 4.31 (s, 1H), 2.60 – 2.47 (m, 1H), 2.46 – 2.40 (m, 1H), 2.37 (d, *J* = 19.0 Hz, 1H), 2.14 (dd, *J* = 18.9, 1.1 Hz, 1H), 2.01 – 1.92 (m, 1H), 1.89 (dd, *J* = 13.3, 9.7 Hz, 1H), 1.77 – 1.74 (m, 3H), 1.72 – 1.68 (m, 1H), 1.14 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 211.3, 151.3, 141.9, 128.1, 113.1, 72.2, 55.3, 51.7, 40.0, 38.5, 35.6, 34.8, 16.4, 13.1. IR (neat, cm^{-1}): 2898, 1635, 1705, 1425, 1139, 1039, 796; HRMS (ESI/$[M+Na]^+$) calcd. for $C_{14}H_{18}O_2$: 218.1307, found 218.1309. The structure of (±)-**24** was also characterized by X-ray crystallography.

X-ray structures

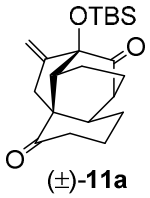
Crystals of (±)-**5b** (CCDC-1563450) were obtained by recrystallization from *n*-hexane and CH_2Cl_2.



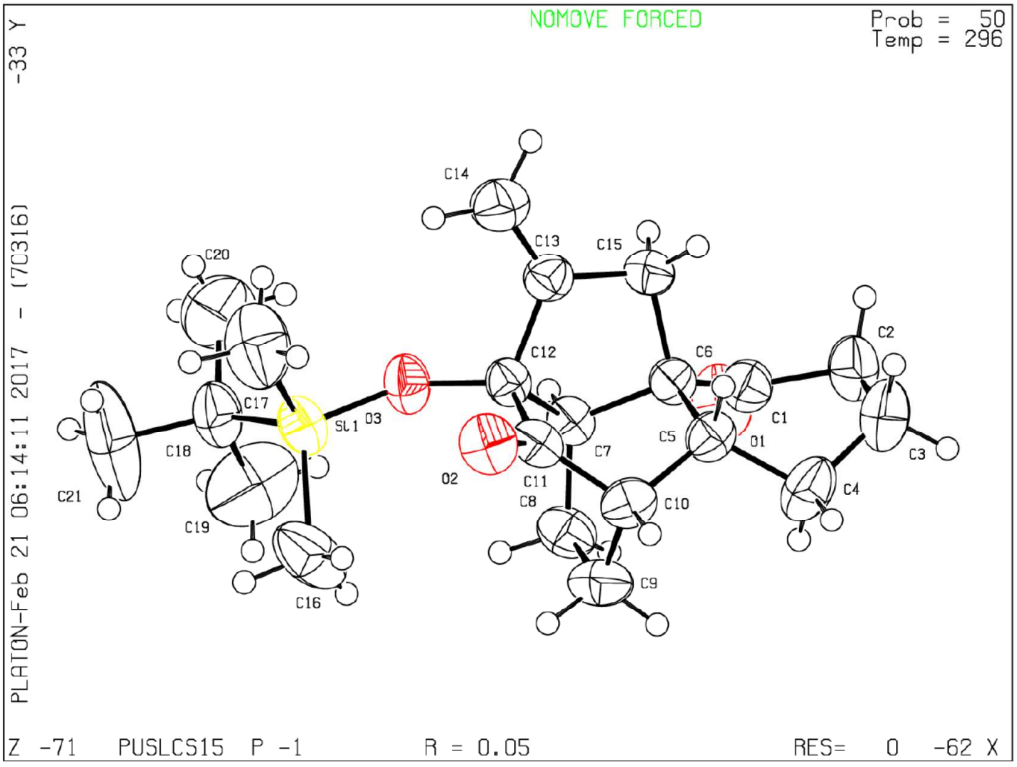
(±)-**5b**



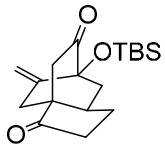
Crystals of (±)-**11a** (CCDC-1563462) were obtained by recrystallization from *n*-hexane and CH_2Cl_2.



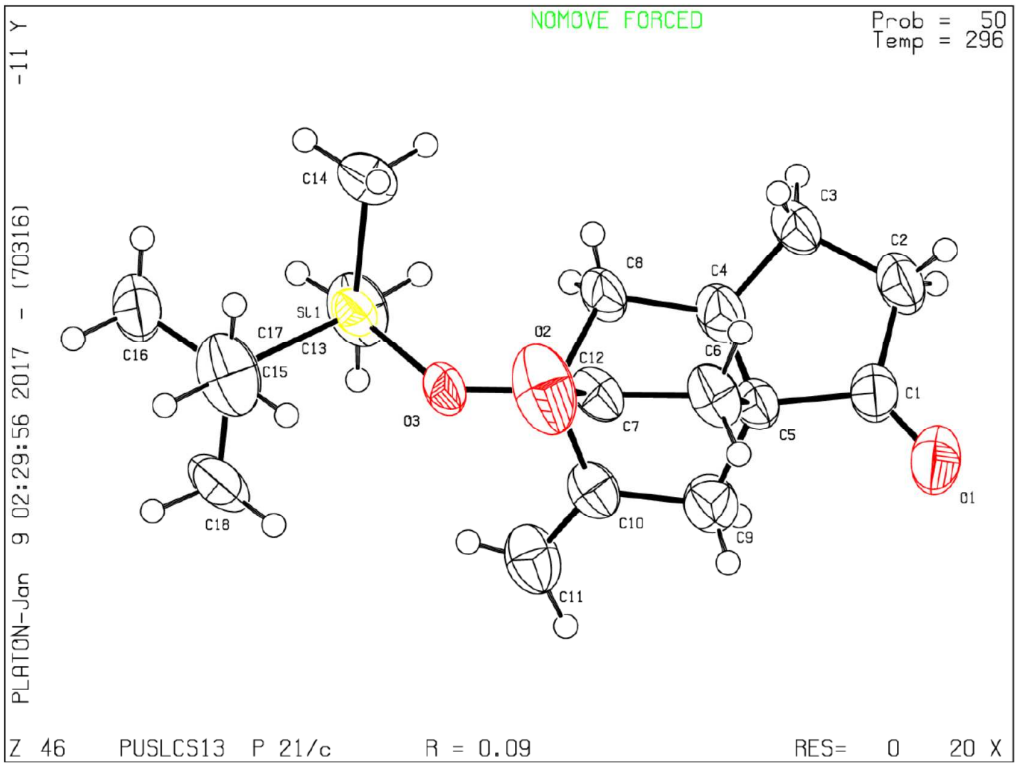
(±)-**11a**



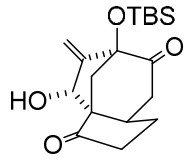
Crystals of (±)-**17b** (CCDC-1563456) were obtained by recrystallization from *n*-hexane and CH_2Cl_2.



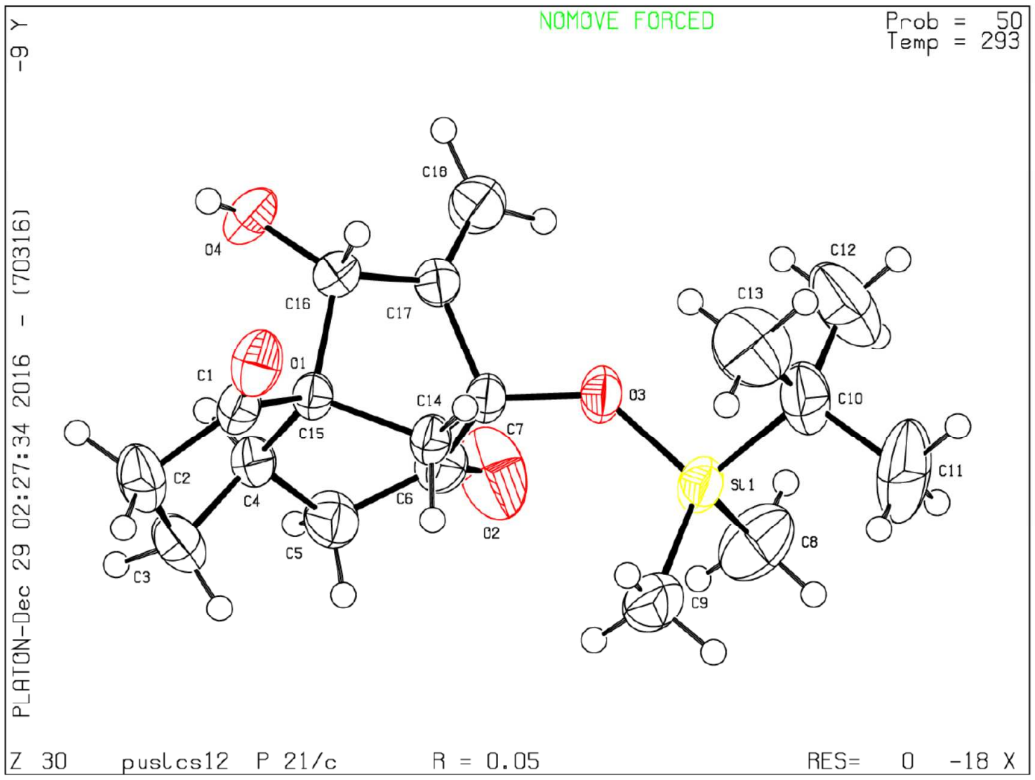
(±)-**17b**



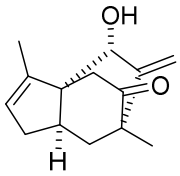
Crystals of (±)-**22 (**CCDC-1563454) were obtained by recrystallization from *n*-hexane and CH_2Cl_2.



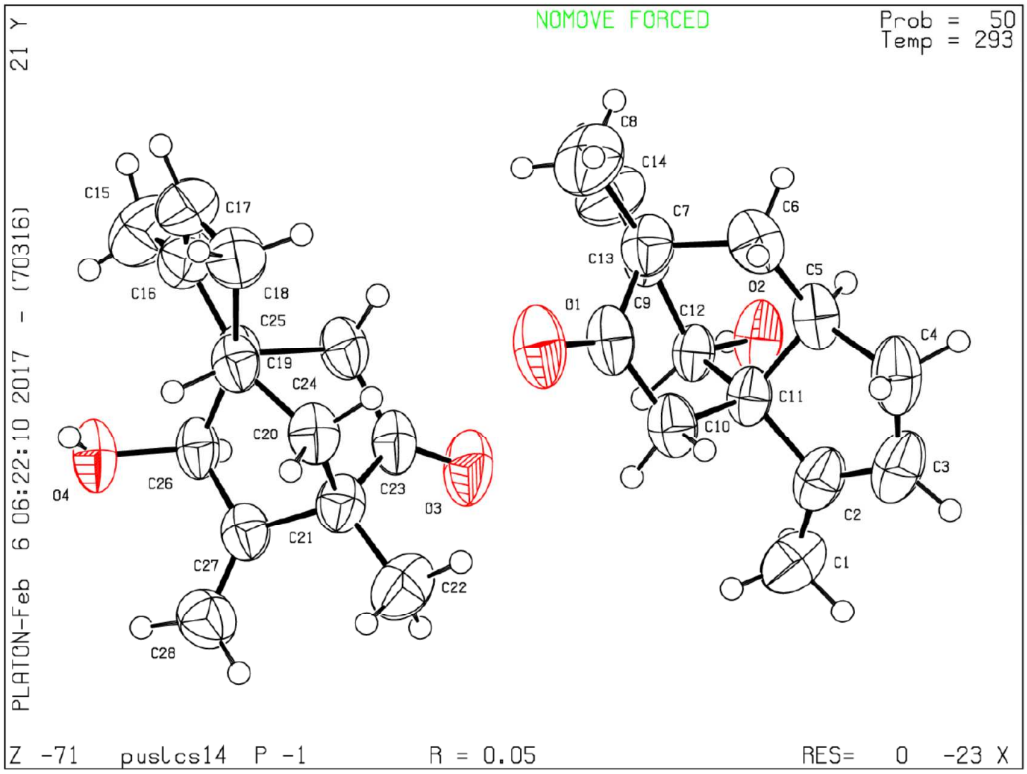
(±)-**22**



Crystals of (±)-**24** (CCDC-1563457) were obtained by recrystallization from *n*-hexane.

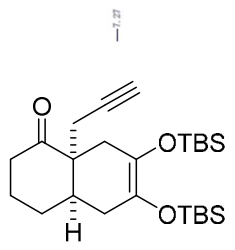


(±)-**24**

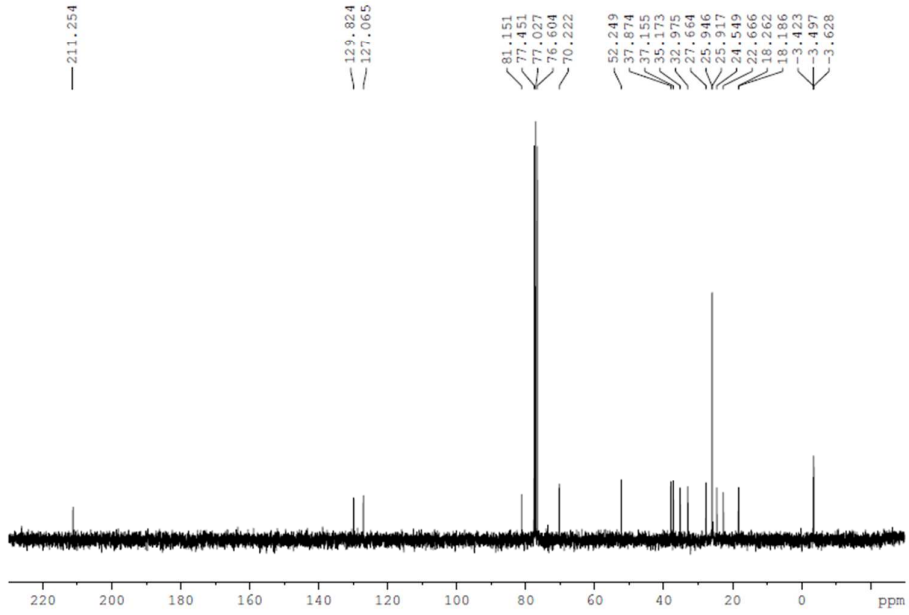


NMR Spectra

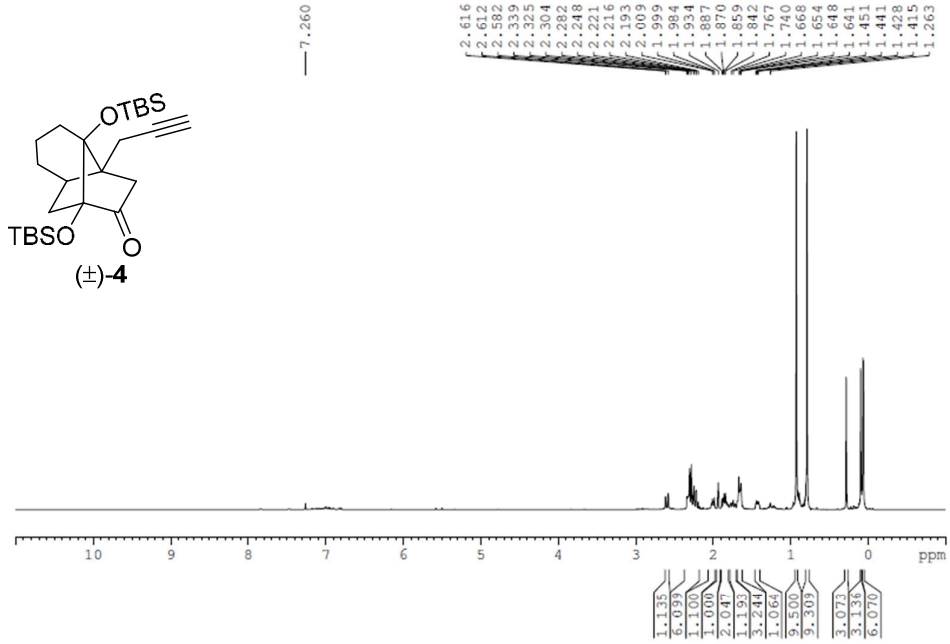
^{1}H and ^{13}C NMR spectra of (±)-3 in $CDCl_3$

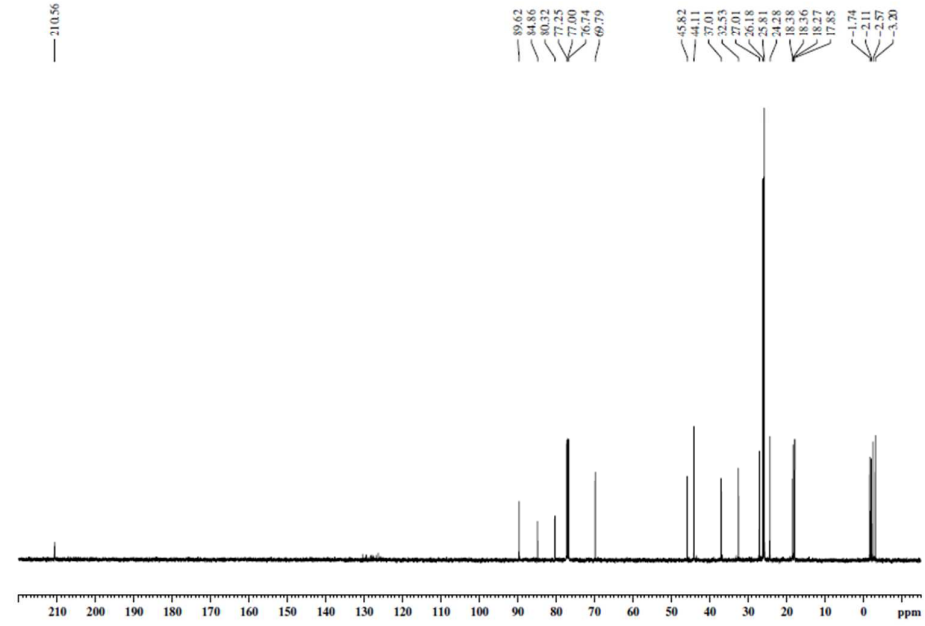


(±)-**3**

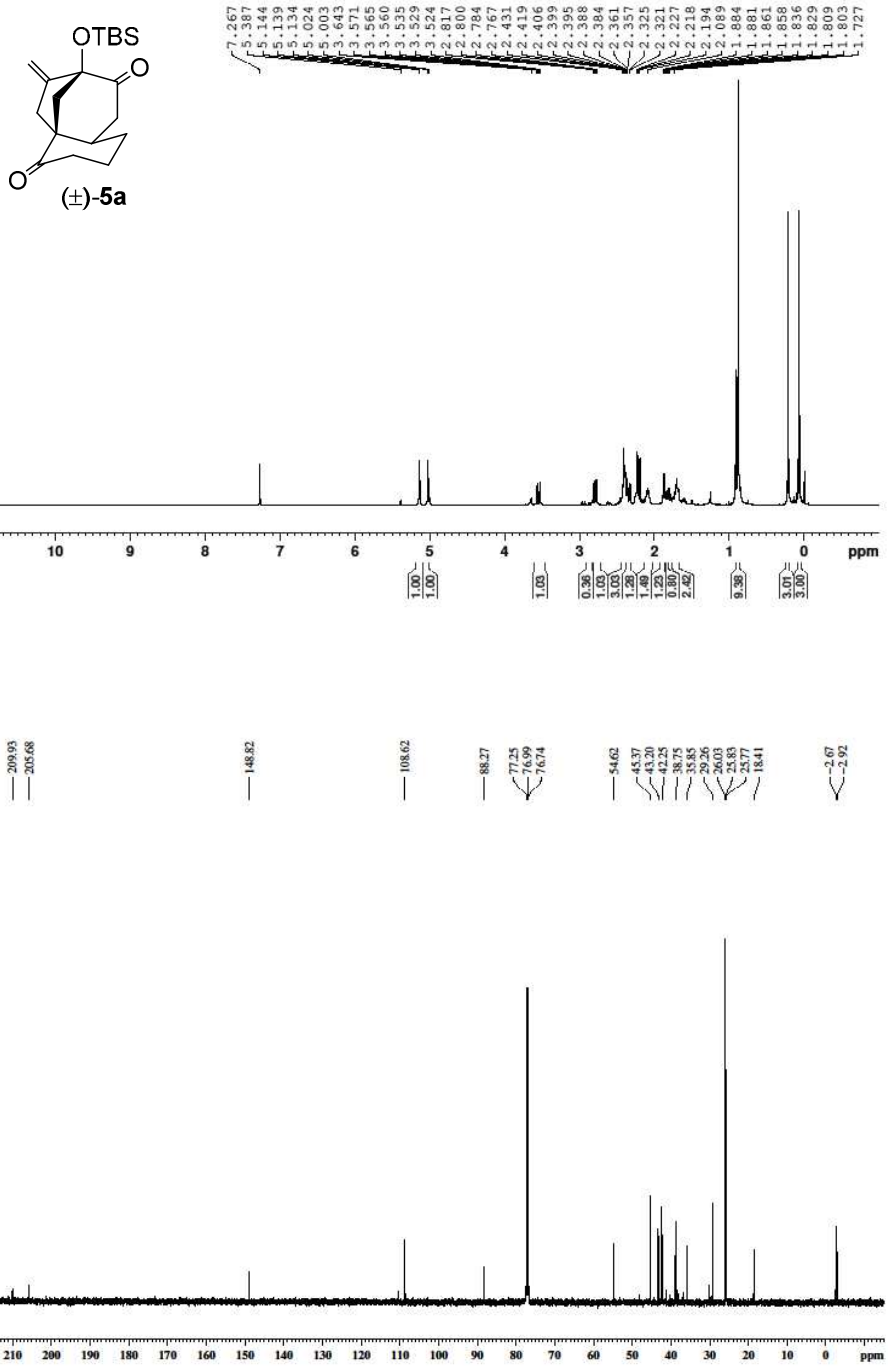


^{1}H and ^{13}C NMR spectra of (±)-4 in $CDCl_3$

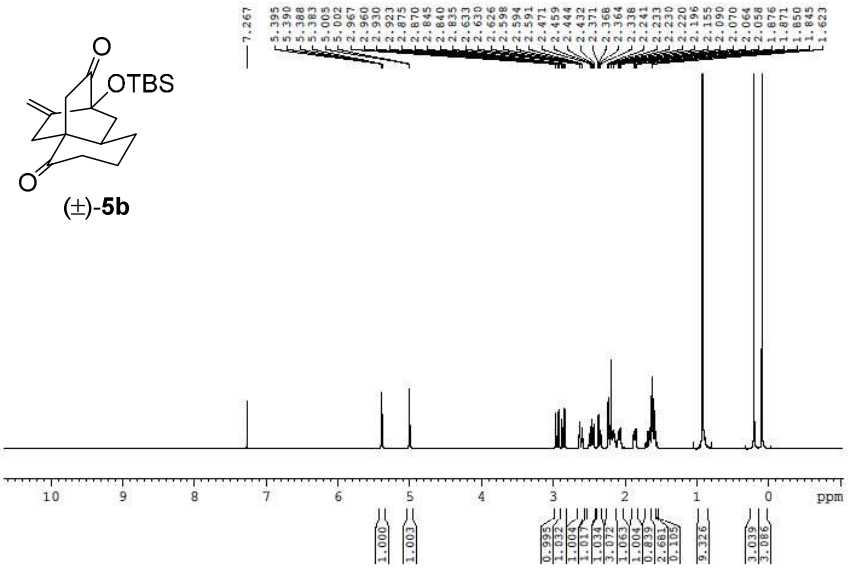


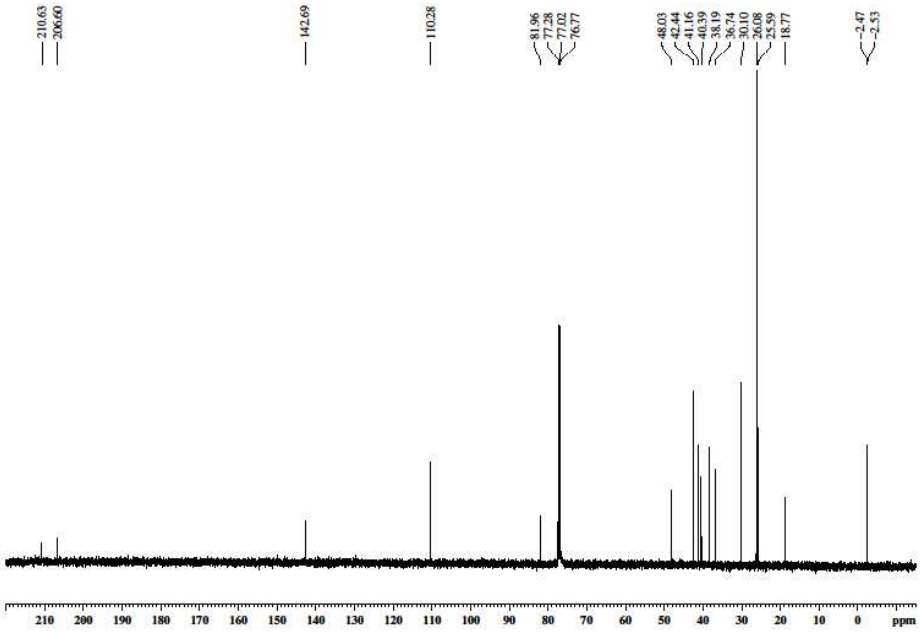


^{1}H an ^{13}C NMR spectra of (±)-5a in $CDCl_3$

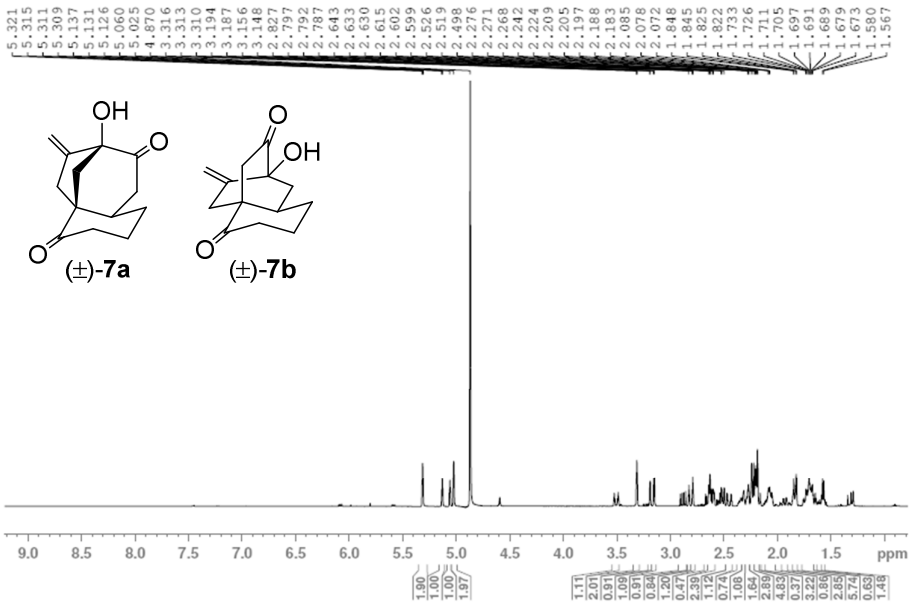


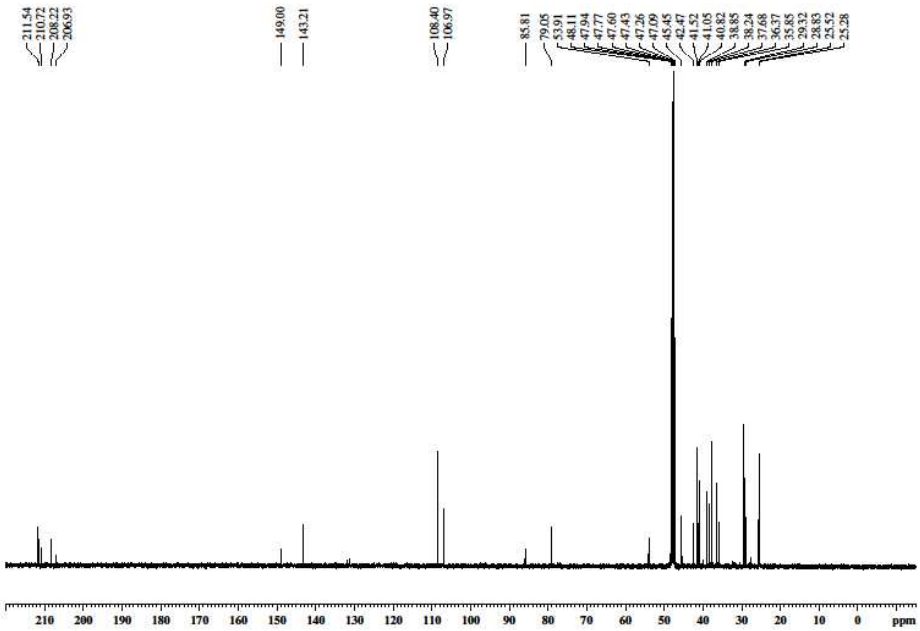
^{1}H and ^{13}C NMR spectra of (±)-5b in $CDCl_3$



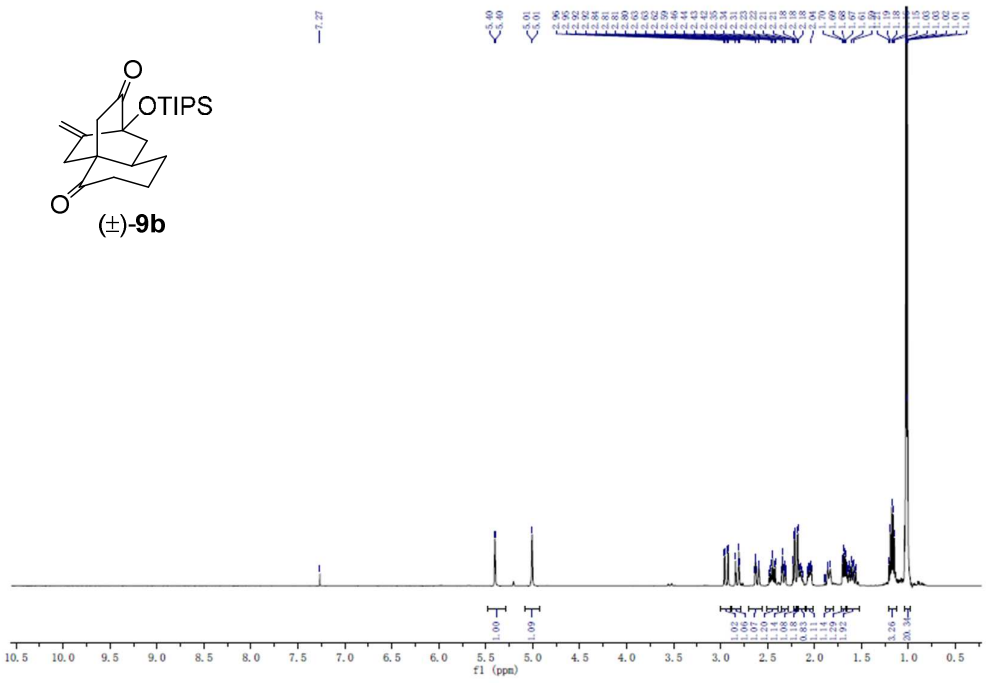


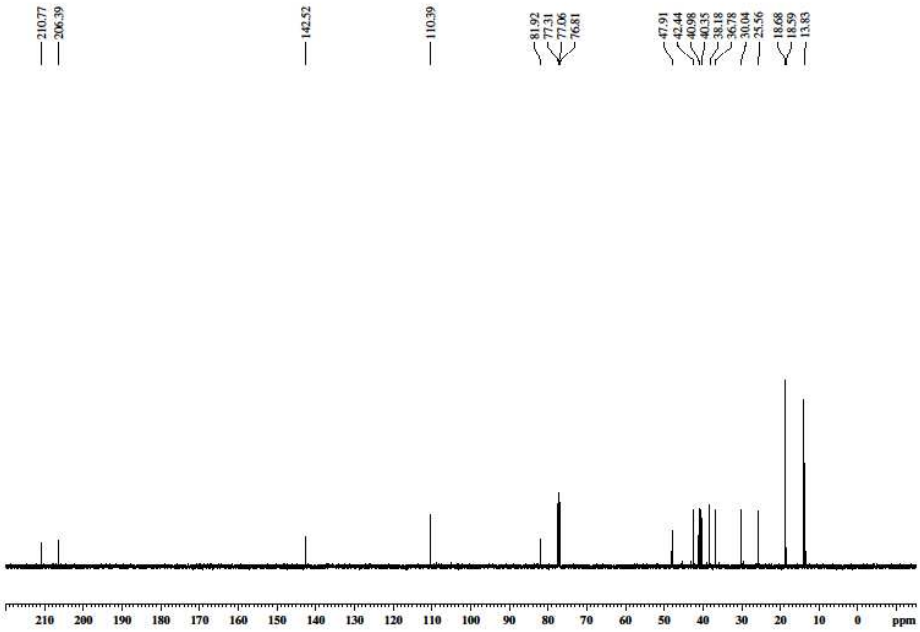
^{1}H and ^{13}C NMR spectra of (±)-7a and (±)-7b (a 1:2 mixture) in CD_3OD



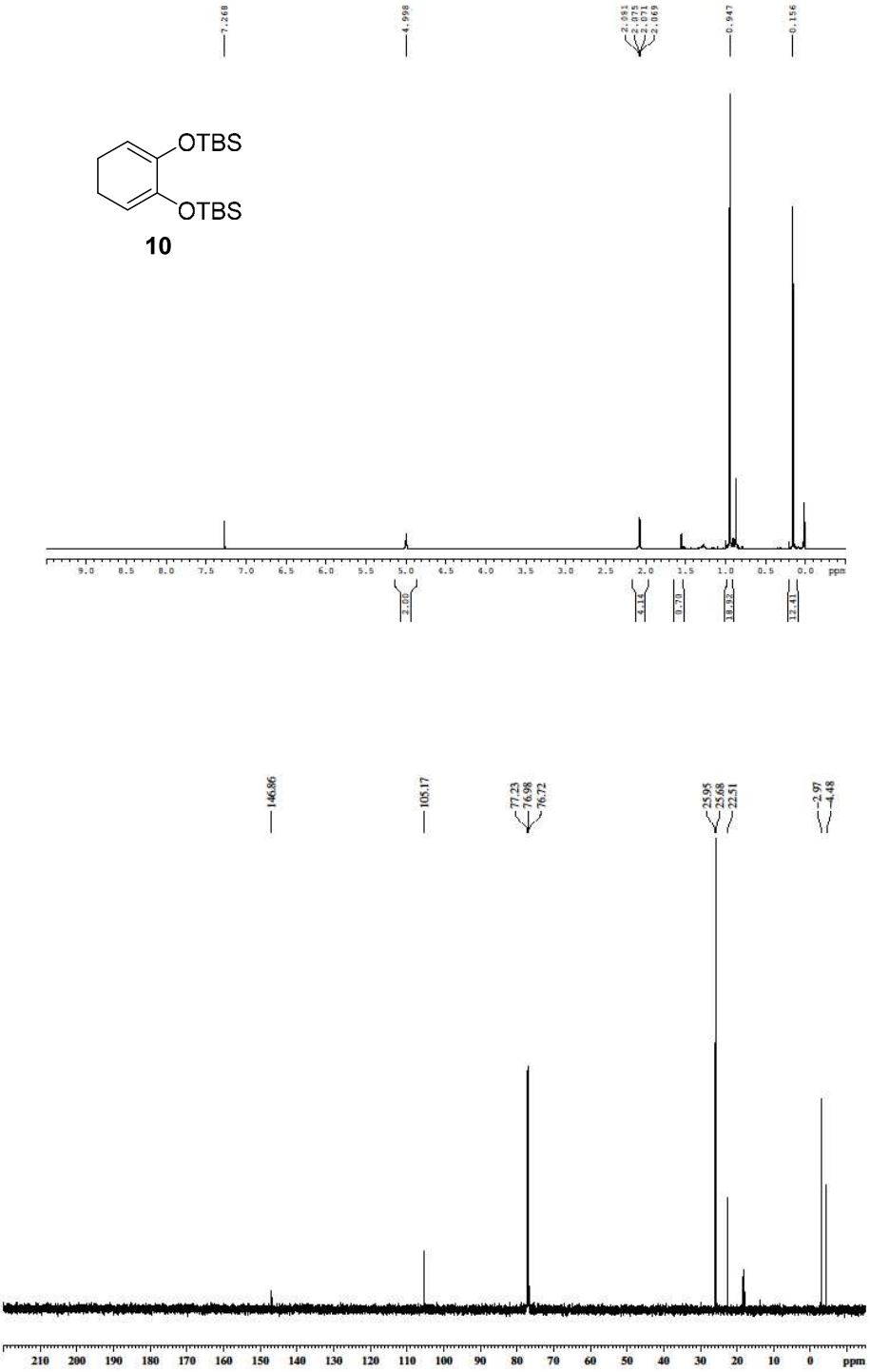


^{1}H and ^{13}C NMR spectra of (±)-9b (a 1:16 mixture) in $CDCl_3$



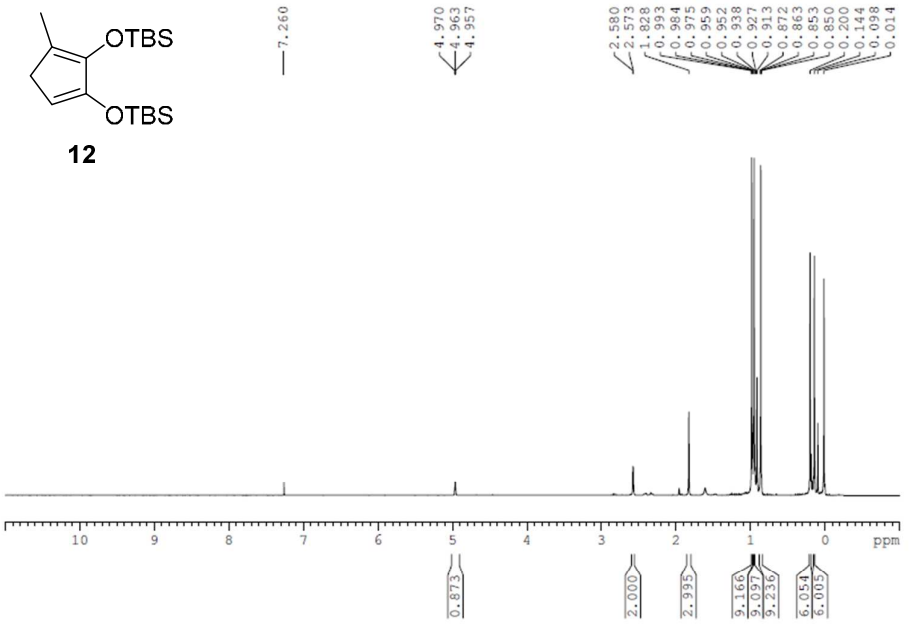


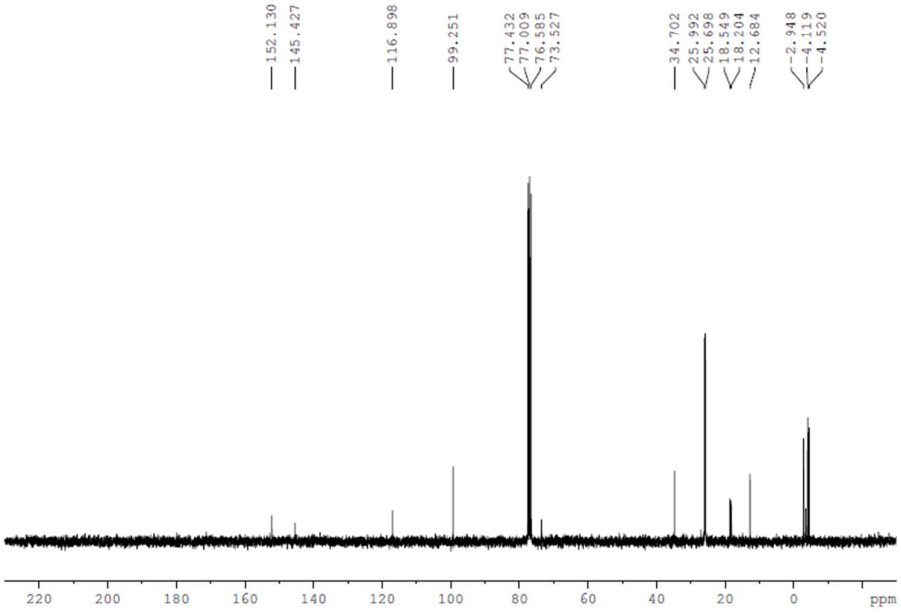
^{1}H and ^{13}C NMR spectra of 10 in $CDCl_3$



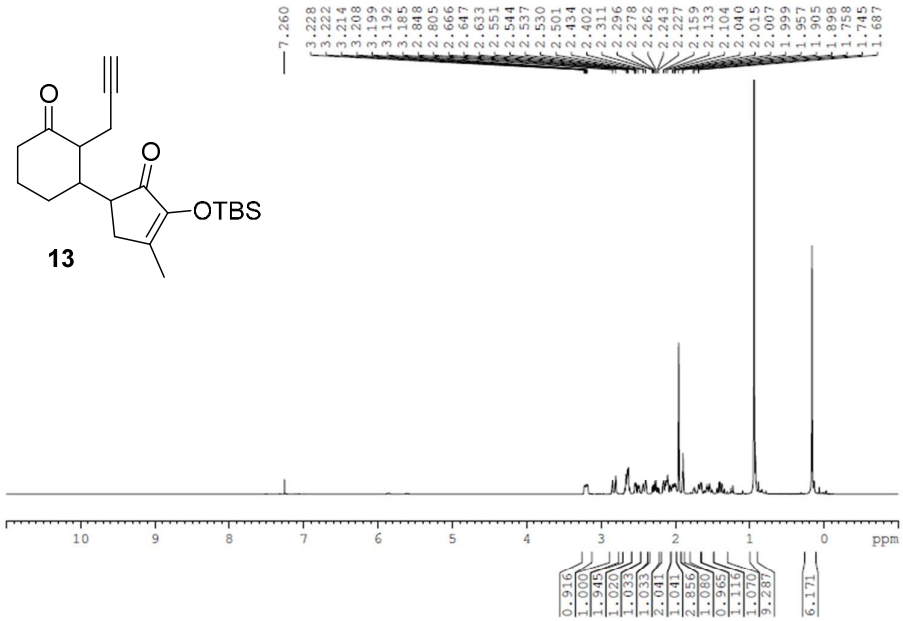
^{1}H and ^{13}C NMR spectra of (±)-11a in $CDCl_3$

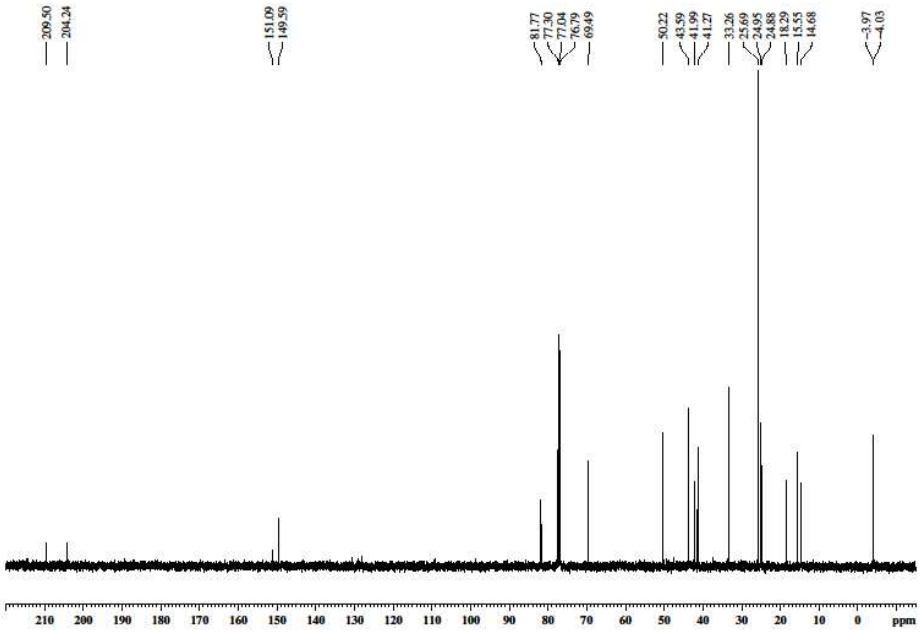
^{1}H and ^{13}C NMR spectra of 12 in $CDCl_3$



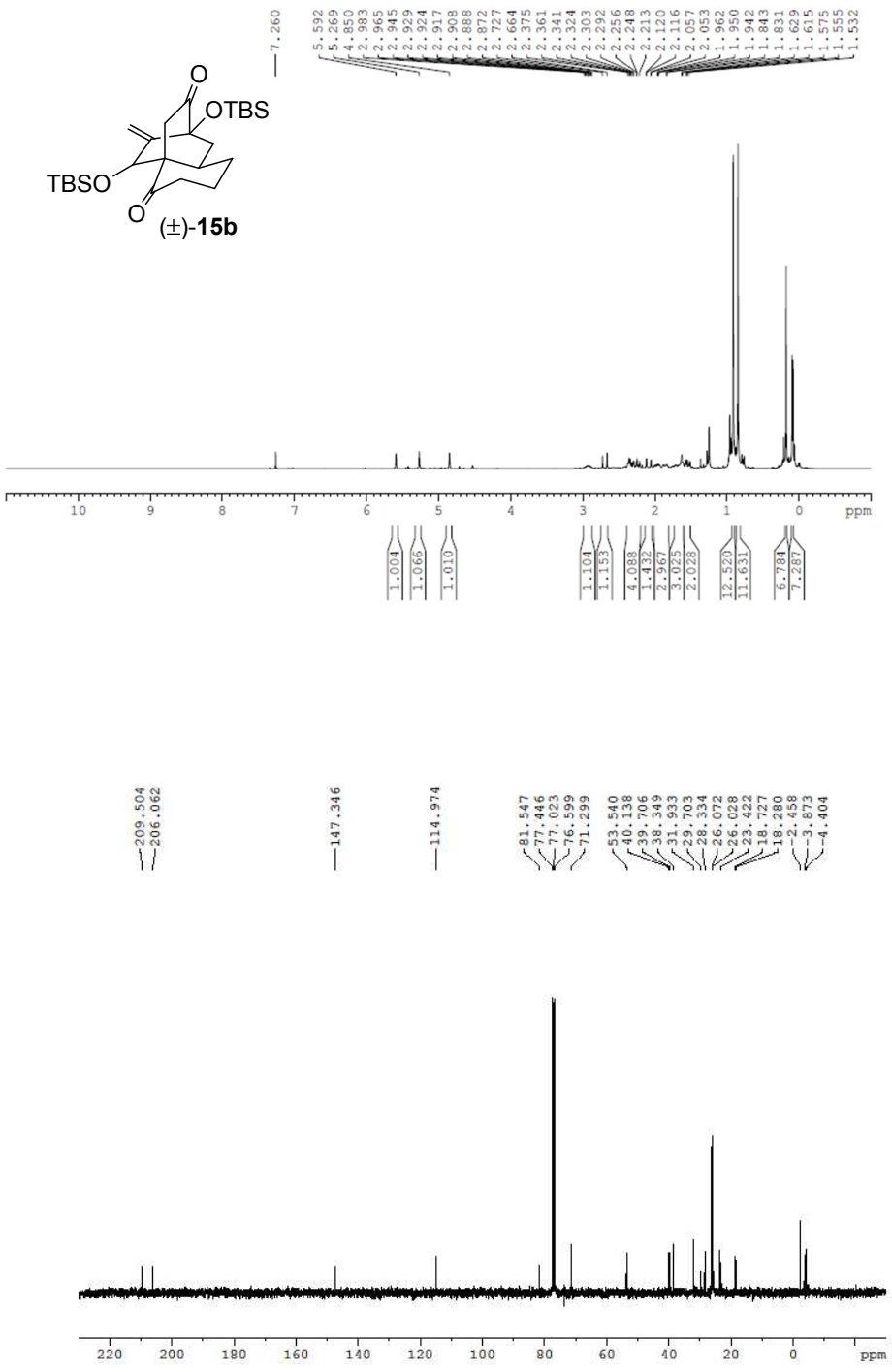


^{1}H and ^{13}C NMR spectra of 13 (a single diastereomer) in $CDCl_3$

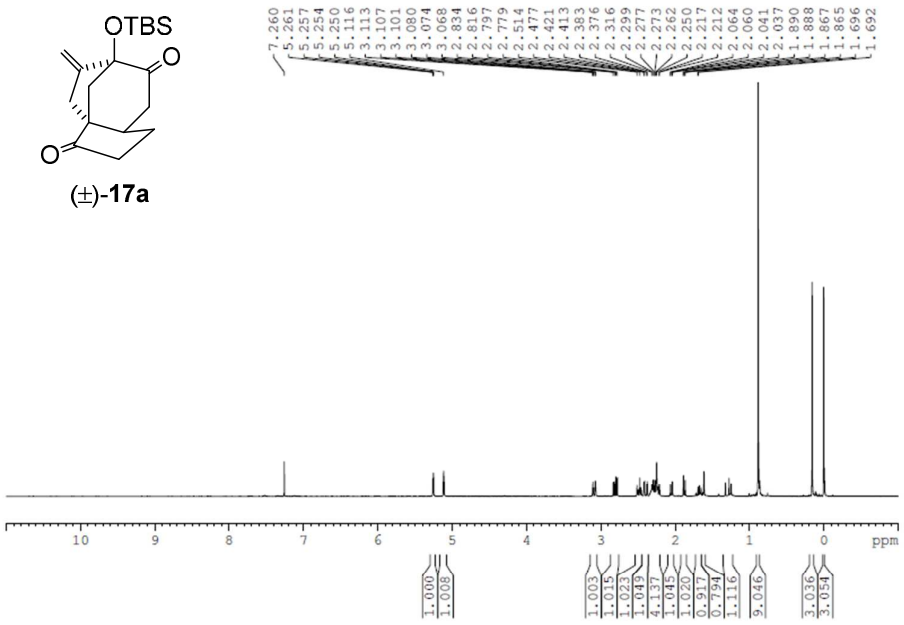


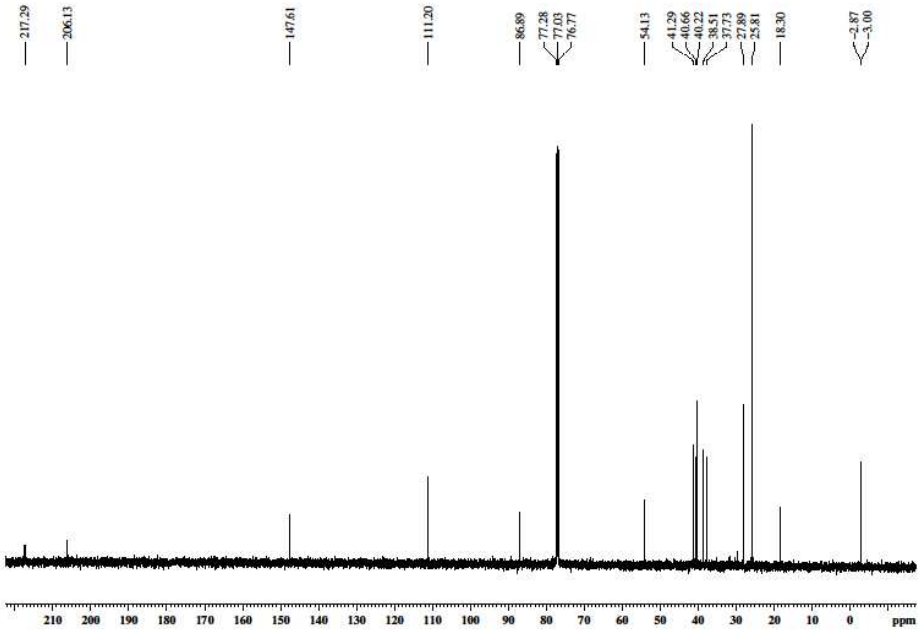


^{1}H and ^{13}C NMR spectra of (±)-15b (a single diastereomer) in $CDCl_3$

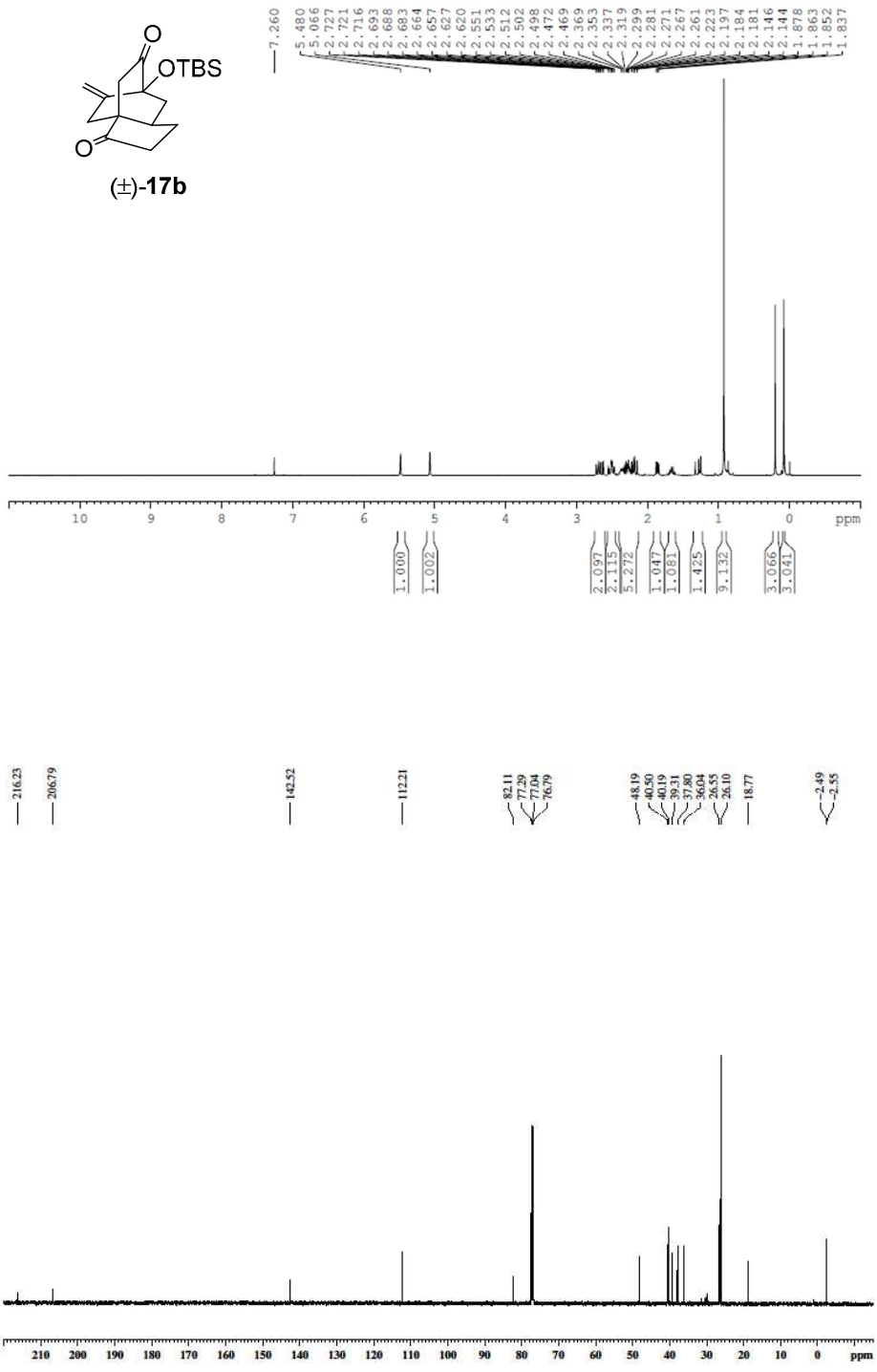


^{1}H and ^{13}C NMR spectra of (±)-17a in $CDCl_3$

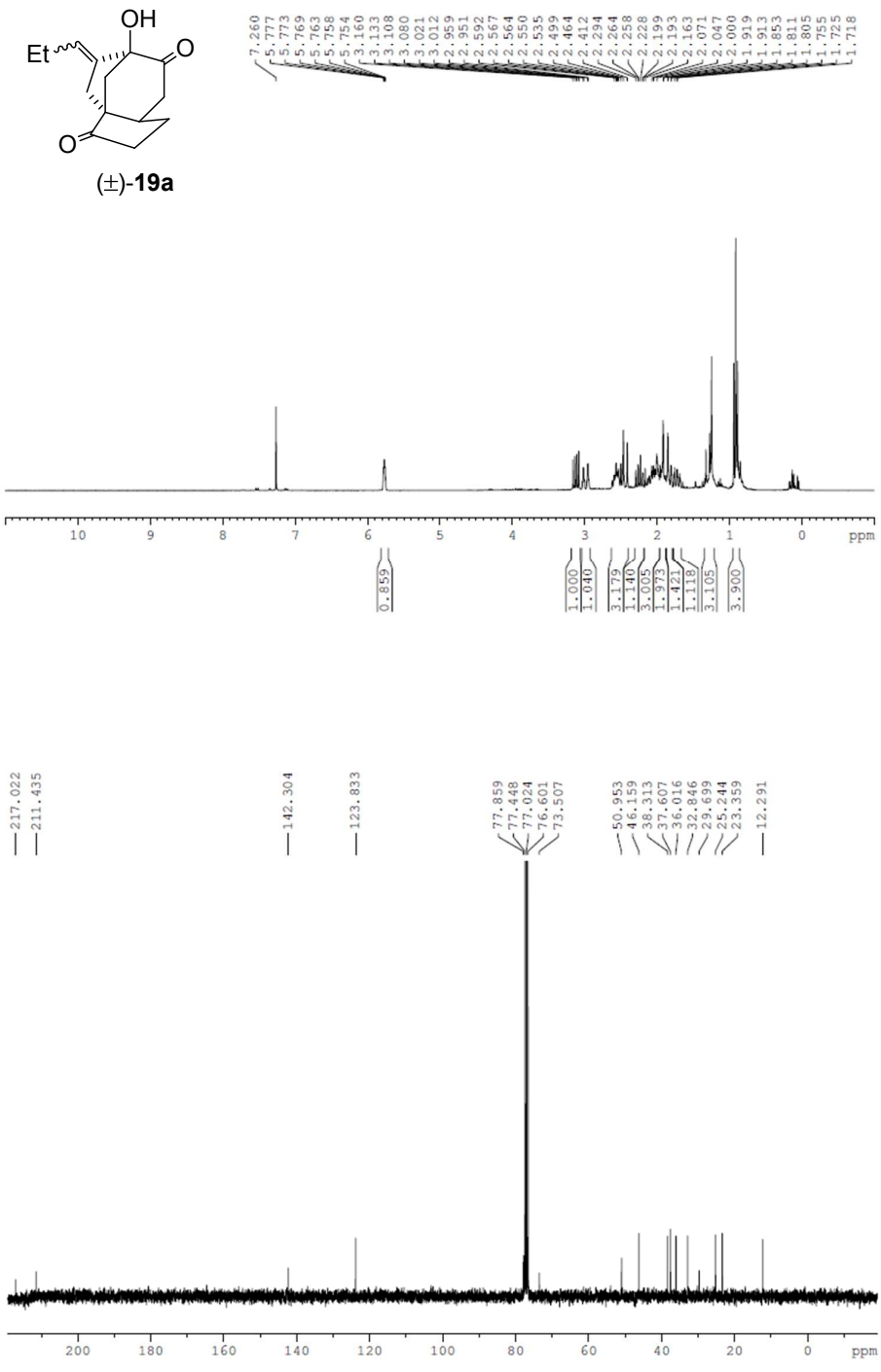




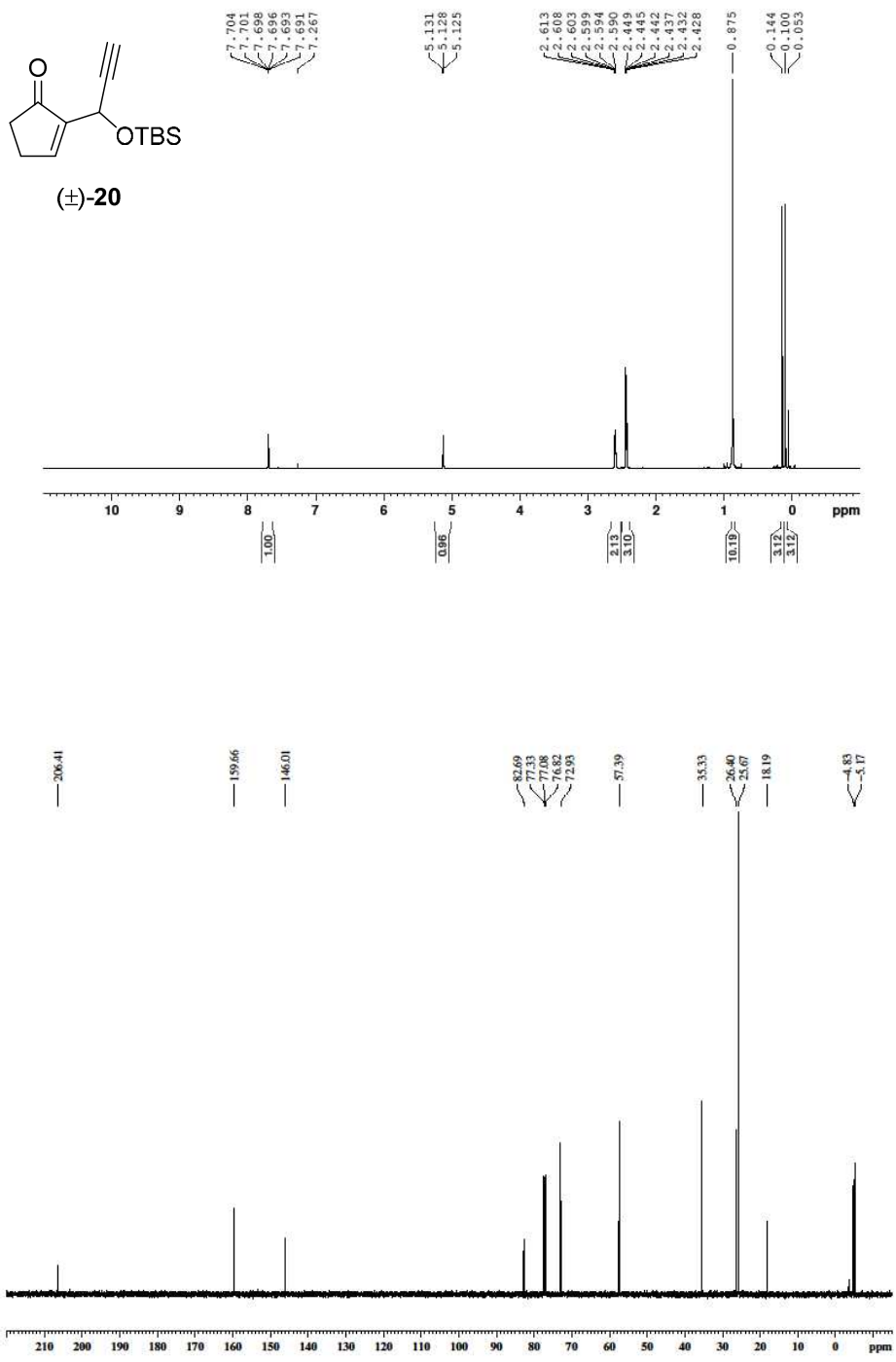
^{1}H and ^{13}C NMR spectra of (±)-17b in $CDCl_3$



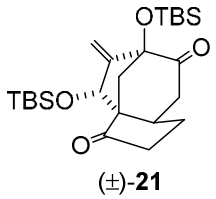
^{1}H and ^{13}C NMR spectra of (±)-19a (single isomer) in $CDCl_3$



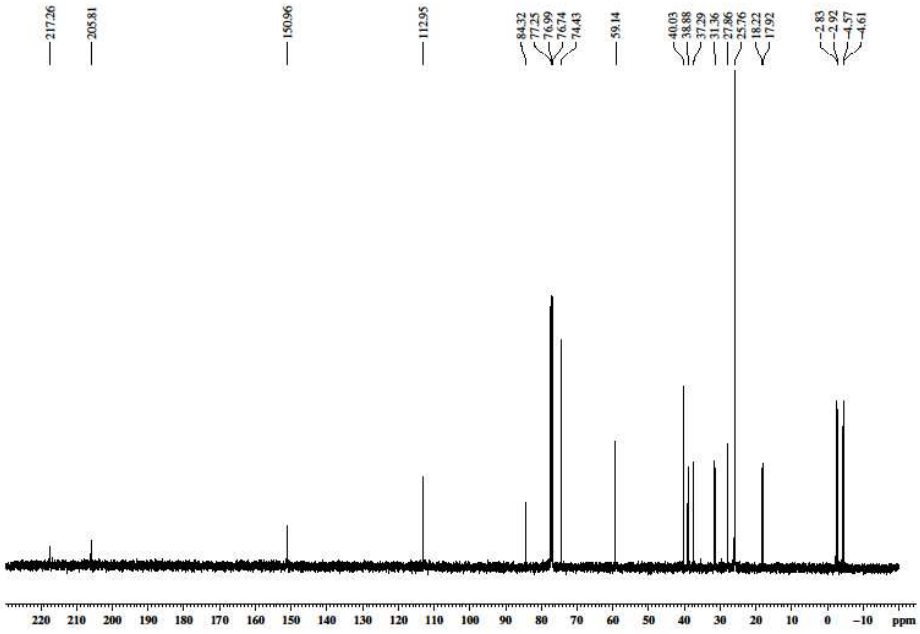
^{1}H and ^{13}C NMR spectra of (±)-20 in $CDCl_3$



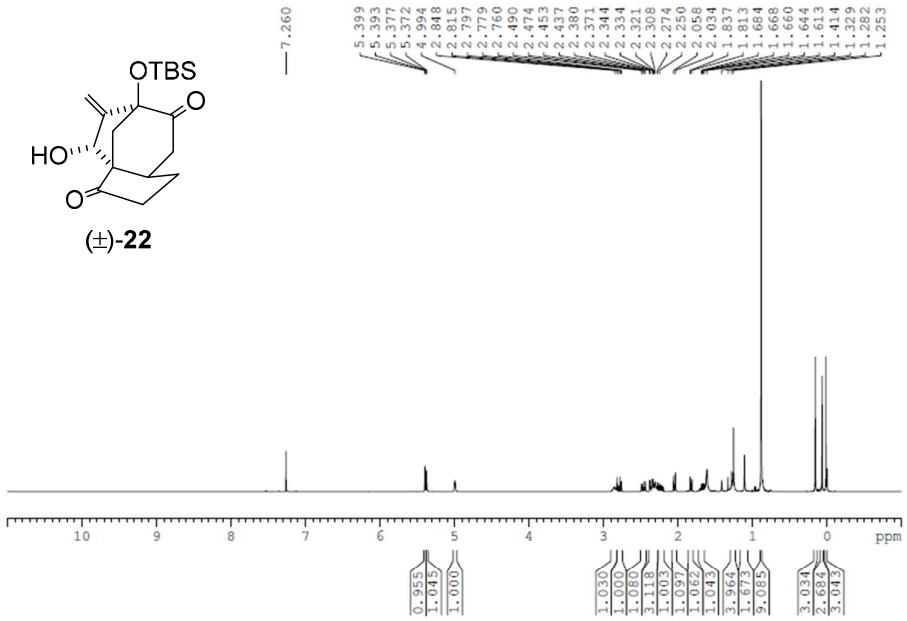
^{1}H and ^{13}C NMR spectra of (±)-21 in $CDCl_3$

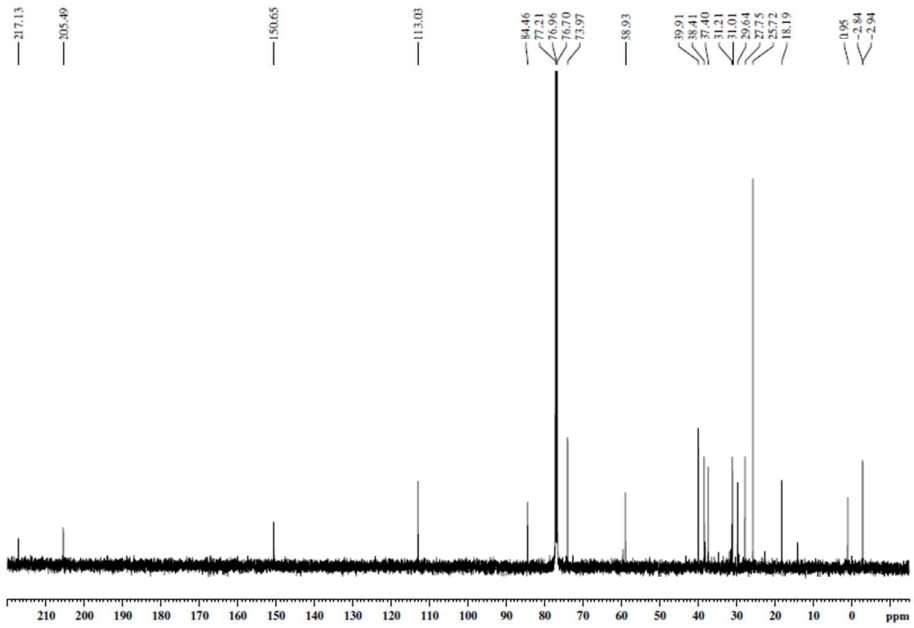


(±)-**21**

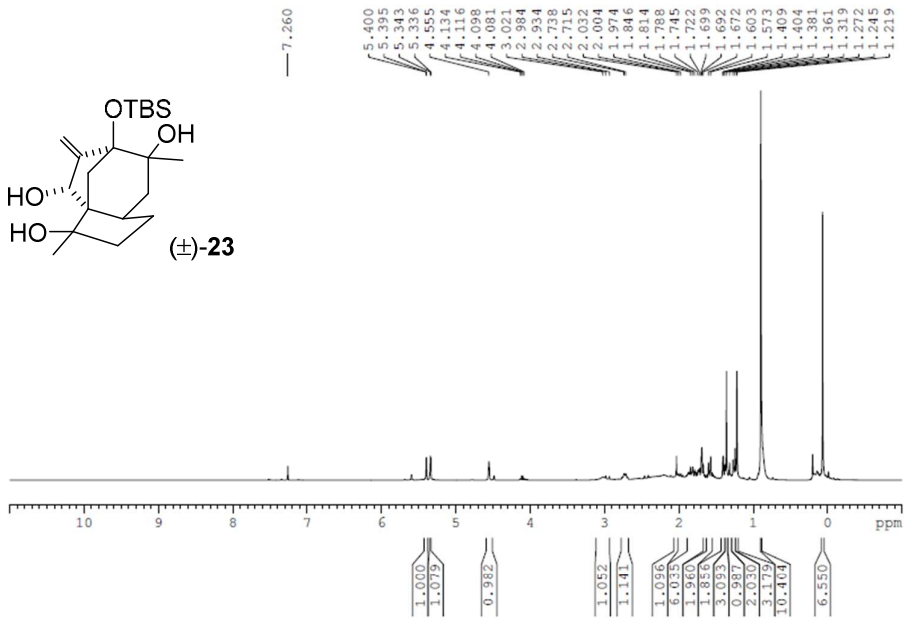


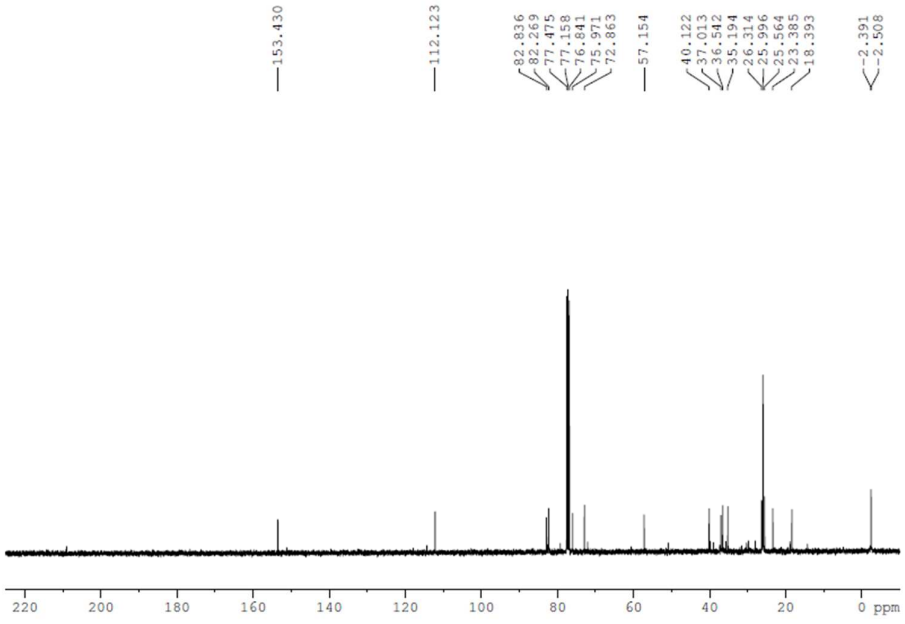
^{1}H and ^{13}C NMR spectra of (±)-22 in $CDCl_3$



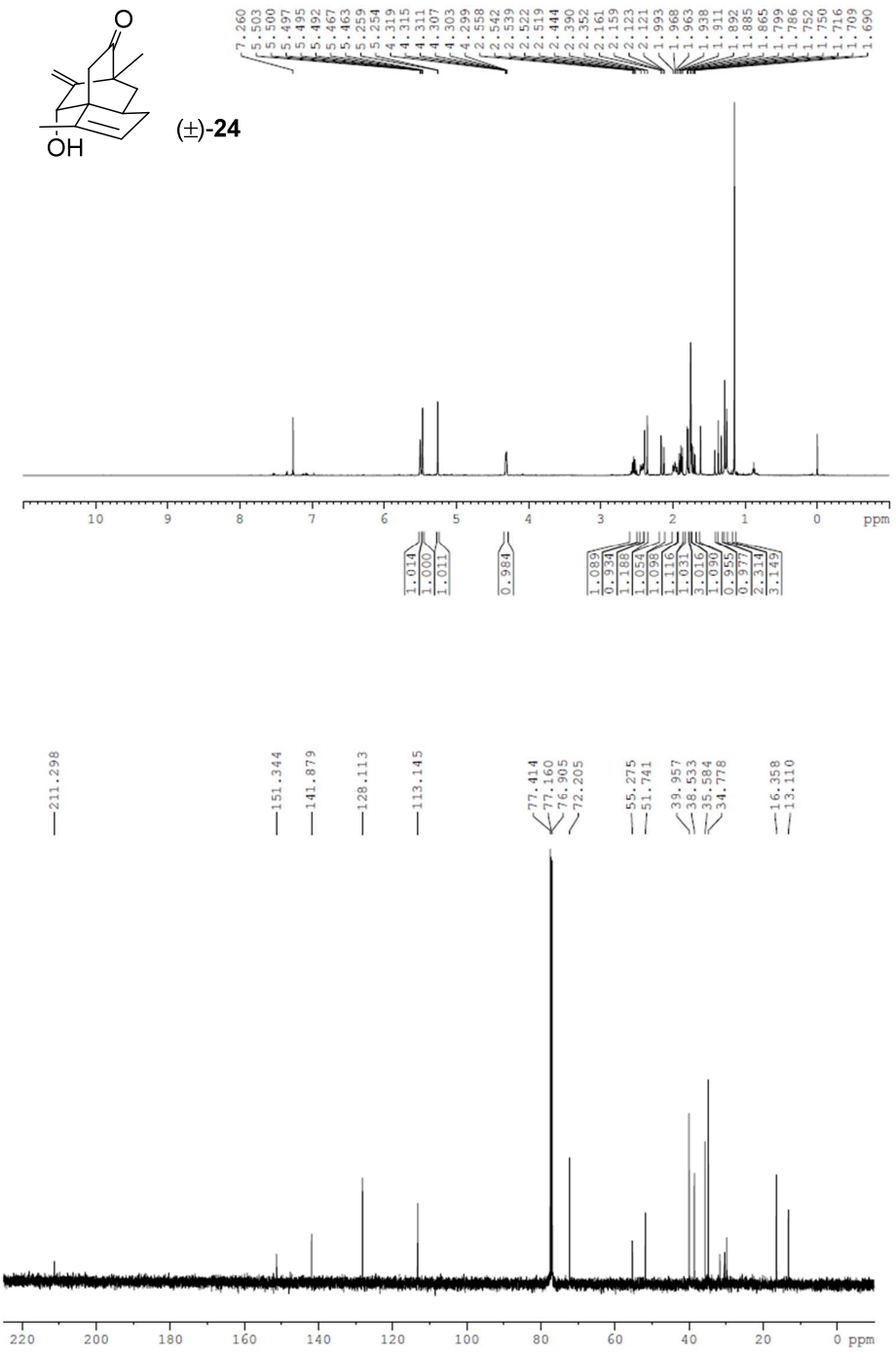


^{1}H and ^{13}C NMR spectra of (±)-23 (single diastereomer) in $CDCl_3$





^{1}H and ^{13}C NMR spectra of (±)-24 in $CDCl_3$



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