Electronic Supplementary Material (ESI) for Organdic and Biomolecular Chemistry

Supporting Information

Total Synthesis and Absolute Configuration of Malyngamide W

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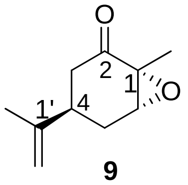
General. All reactions that required anhydrous conditions were carried by standard procedures under argon atmosphere. Commercially available reagents were used as received. The solvents were dried by distillation over the appropriate drying reagents. Petroleum ether used had a bp range of 60–90 °C. Reactions were monitored by TLC on silica gel plates. Column chromatography was generally performed through silica gel (200–300 mesh). IR spectra were reported in wave numbers (cm^{-1}). ^1H and ^{13}C NMR, DEPT 135, ^1H–^1H COSY and NOE experiments were recorded on 400 MHz or 600 MHz spectrometer. Chemical shifts (δ) were reported in ppm relative to TMS (δ_H 0.00) for the ^1H NMR and to chloroform (δ_C 77.0) for the ^{13}C NMR measurements. High resolution mass spectra (HRMS) and mass spectra (MS) were obtained on the mass spectrometer.

Experimental Section

(1*R*,4*R*,6*R*)-1-Methyl-4-(1-methylethenyl)-7-oxa-bicyclo[4.1.0]heptan-2-one (9)[1]

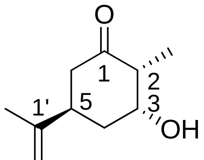


9

To a stirred solution (*R*)-(−)-carvone **8** (5.00 g, 33.28 mmol) in methanol (80 mL) was added 4 M sodium hydroxide (2.5 mL) at −20 °C, followed by the dropwise addition of hydrogen peroxide solution (4.6 mL, 30% purity, 39.94 mmol) over 50 min. Upon completion of the reaction by TLC monitored, the reaction mixture was quenched by the slow addition of saturated sodium sulfite solution. The aqueous phase was extracted with dichloromethane (100 mL × 4). The organic layer was washed with brine, dried over $MgSO_4$, filtered, and concentrated in vacuo. Flash chromatography of the residue over silica gel (petroleum ether/EtOAc 50:1) afforded epoxy ketone

9 (5.42 g, 98%) as a colorless oil: $[\alpha]_D^{20}$ +31.7 (*c* 2.0 in $CHCl_3$); IR (KBr, ν_{max}/cm^{-1}): 2978, 2936, 1709, 1441, 1118, 892, 815; δ_H (400 MHz; $CDCl_3$; Me_4Si) 1.42 (s, 3H, CH_3), 1.72 (s, 3H, CH_3), 1.91 (dd, *J* 11.1, 15.0, 1H, 5a-H), 2.03 (dd, *J* 11.1, 17.4, 1H, 3a-H), 2.38 (dt, *J* 3.0, 15.0, 1H, 5b-H), 2.59 (dd, *J* 4.5, 17.4, 1H, 3b-H), 2.67–2.76 (m, 1H, 4-H), 3.46 (d, *J* 2.7, 1H, 6-H), 4.72 (s, 1H, 2a′-H), 4.79 (s, 1H, 2b′-H); δ_C (400 MHz; $CDCl_3$; Me_4Si) 15.2 (CH_3), 20.5 (CH_3), 28.6 (CH_2, 5-C), 34.9 (CH, 4-C), 41.7 (CH_2, 3-C), 58.7 (C, 1-C), 61.2 (CH, 6-C), 110.4 (CH_2, 2′-C), 146.2 (C, 1′-C), 205.4 (CO); MS (EI) *m*/*z* (%): 166 (M^+, 1), 85 (18), 67 (20), 43 (100).

(2*R*,3*R*,5*R*)-3-Hydroxy-2-methyl-5-(1-methylethenyl)-cyclohexanone (10)[2]

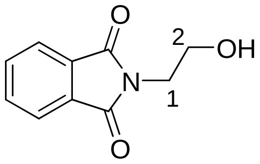


10

To a stirred and degassed solution of epoxy ketone **9** (0.33 g, 1.99 mmol), *N*-acethyl-L-cysteine (0.97 g, 5.97 mmol), and diphenyldiselenide (0.03 g, 0.01 mmol) in methanol (24 mL) under argon was added sodium hydroxide (1.0 mL, 6 M, 5.97 mmol) and stirred continued for 1.5 h. The reaction mixture was then diluted with water (20 mL), saturated with sodium chloride, and extracted with dichloromethane (20 mL × 4). The organic layer was dried over $MgSO_4$, filtered, and concentrated in vacuo. Flash chromatography of the residue over silica gel (petroleum ether/EtOAc 5:1) afforded ketone **10** (0.22 g, 65%) as a white solid: mp 67–69 °C; $[\alpha]_D^{20}$ –18 (*c* 1.0 in $CHCl_3$); IR (KBr, ν_{max}/cm^{-1}): 3473, 2949, 1697, 1396, 1057, 725, 535; δ_H (400 MHz; $CDCl_3$; Me_4Si) 1.07 (d, *J* 6.8, 3H, CH_3), 1.72 (s, 3H, CH_3), 1.79 (t, *J* 13.2, 1H, 4b-H), 2.09 (dd, *J* 1.8, 10.8, 1H, 6b-H), 2.24 (t, *J* 13.2, 1H, 4a-H), 2.41 (br, 1H), 2.43 (dd, *J* 1.8, 10.8, 1H, 6a-H), 2.49–2.53 (m, 1H, 2-H), 2.84–2.92 (m, 1H, 5-H), 4.26 (d, *J* 2.4, 1H, 3-H), 4.72 (s, 1H, 2′b-H), 4.75 (s, 1H, 2′a-H);

δ_C (400 MHz; $CDCl_3$; Me_4Si) 10.6 (CH_3), 20.5 (CH_3), 37.6 (CH_2, 4-C), 39.8 (CH, 2-C), 46.4 (CH_2, 6-C), 49.2 (CH, 5-C), 73.4 (CH, 3-C), 109.8 (CH_2, 2′-C), 147.1 (C, 1′-C), 211.4 (CO); IR (KBr): 3460, 2937, 1709, 1449, 1210, 984, 892 cm^{-1}; MS (EI) *m*/*z* (%): 168 (M^+, 17), 150 (100), 107 (49), 93 (89), 67 (51), 55 (52).

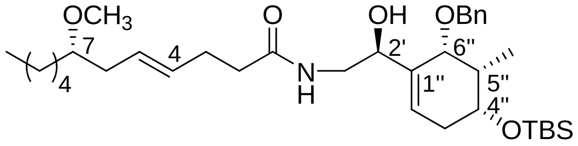
2-(2-Hydroxyethyl)isoindoline-1,3-dione (15)[3]



15

To the flask was added phthalic anhydride **7** (3.70 g, 25.00 mmol) and pure monoethanolamine **6** (1.5 mL, 25.00 mmol) at such a rate that the reaction did not too vigorous. The reaction mixture was then heated to 175 °C and kept at this temperature until no water take-off. The melt was cooled and recrystallized out of 50 mL of water, afforded the compound **15** (4.2 g, 89%) as a sheet solid: mp 126–127 °C; δ_H (400 MHz; $CDCl_3$; Me_4Si) 2.73 (br, 1H, OH), 3.84 (s, 4H, 1-H and 2-H), 7.66–7.70 (m, 2H, ArH), 7.77–7.80 (m, 2H, ArH); δ_C (400 MHz; $CDCl_3$; Me_4Si) 40.7 (CH_2, 1-C), 60.7 (CH_2, 2-C), 123.2 (2 × ArCH), 131.9 (ArC), 134.0 (2 × ArCH), 168.7 (2 × CO); MS (EI) *m*/*z* (%): 191 (M^+, 2), 160 (100), 148 (45), 133 (24), 104 (16).

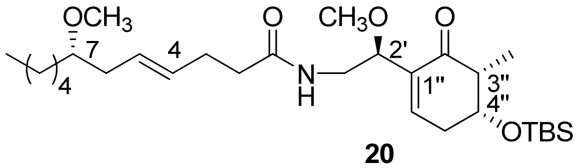
(4*E*,7*S*)-*N*-{(2*S*)-[(4*R*,5*S*,6*R*)-6-Benzyloxy-4-*tert*-butyldimethylsilyloxy-5-methyl-1-cyclohexenyl]-2-hydroxyethyl}-7-methoxydodec-4-enamide (17)



17

To a stirred compound **3** (200 mg, 0.38 mmol) in ethanol (4 mL) was added hydrazine monohydrate (1.1 mL, 2.28 mmol), then the mixture was stirred for 2 h at 60 °C. The precipitate formed was filtered off and the filtrate was evaporated to give crude amine, which was immediately used in the next step without further purification. To the crude amine was added a solution of acid **2** (105 mg, 0.46 mmol) in dichloromethane (10 mL), *N*,*N*′-dicyclohexylcarbodiimide (DCC) (95 mg, 0.46 mmol), 1-hydroxybenzotriazole (HOBt) (51 mg, 0.38 mmol) and 4-methylmorpholine (NMM) (38 mg, 0.38 mmol) at 0 °C. After stirred for 30 min at the same temperature. The reaction was warmed to room temperature and stirred for 8 h. Then the reaction mixture was concentrated in vacuo. Flash chromatography of the residue over silica gel (petroleum ether/EtOAc 2:1) afforded amide **17** (185 mg, 80%) as a colorless oil: $[\alpha]_D^{20}$ –4 (*c* 0.5 in $CHCl_3$); IR (KBr, ν_{max}/cm^{-1}): 3375, 3031, 2928, 1560, 1419, 1068, 838; δ_H (400 MHz; $CDCl_3$; Me_4Si) 0.04 (s, 3H, CH_3), 0.05 (s, 3H, CH_3), 0.86–0.89 (m, 3H, CH_3), 0.89 (s, 9H, 3 × CH_3), 0.92 (d, *J* 6.8, 3H, CH_3), 1.25–1.43 (m, 8H, 8-H, 9-H, 10-H, and 11-H), 2.15–2.21 (m, 4H, 2-H and 6-H), 2.09–2.11 (m, 2H, 3-H), 2.40–2.44 (m, 1H, 5″-H), 2.28–2.33 (m, 2H, 3″-H), 3.09–3.16 (m, 2H, 1b′-H and 7-H), 3.30 (s, 3H, OCH_3), 3.63–3.69 (m, 1H, 1a′-H), 3.79–3.84 (m, 1H, 4″-H), 3.89 (br, 1H, OH), 4.03 (br, 1H, 6″-H), 4.39 (d, *J* 10.8, 1H, ArCH), 4.41 (t, *J* 2.8, 1H, 2′-H), 4.66 (d, *J* 10.8, 1H, ArCH), 5.44–5.46 (m, 2H, 4-H and 5-H), 5.66 (br, 1H, 2″-H), 5.99 (dd, *J* 3.2, 4.0, 1H, NH), 7.30–7.35 (m, 5H, ArH); δ_C (400 MHz; $CDCl_3$; Me_4Si) −4.9 (CH_3), −4.7 (CH_3), 5.3 (CH_3), 14.0 (CH_3, 12-C), 18.0 (C), 22.6 (CH_2, 11-C), 24.8 (CH_2, 9-C), 25.7 (3 × CH_3), 28.7 (CH_2, 3-C), 30.7 (CH_2, 3″-C), 31.9 (CH_2, 10-C), 33.2 (CH_2, 8-C), 36.2 (CH_2, 6-C), 36.4 (CH_2, 2-C), 36.6 (CH, 5″-C), 44.9 (CH_2, 1′-C), 56.4 (OCH_3), 68.3 (CH, 7-C), 70.3 (CH_2), 75.1 (CH, 4″-C), 78.9 (CH, 2′-C), 80.6 (CH, 6″-C), 125.4 (CH, 2″-C), 127.4 (CH, 5-C), 127.99 (ArCH), 128.01 (2 × ArCH), 128.5 (2 × ArCH), 130.7 (CH, 4-C), 135.4 (C, 1″-C), 137.3 (C), 172.9 (CO); HRMS (ESI) *m*/*z* calcd for $C_{35}H_{60}NO_5Si$ $[M + H]^+$ 602.4235, found 602.4241.

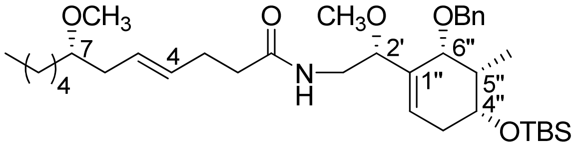
(4*E*,7*S*)-*N*-{(2*S*)-[(3*R*,4*R*)-4-*tert*-Butyldimethylsilyoxy-3-methyl-2-oxocyclohex-1-enyl]-2-methoxyethyl}-7-methoxydodec-4-enamide (20)



20

To a stirred suspension of amide **19** (87 mg, 0.14 mmol) in dichloromethane (4.5 mL) and water (0.5 mL) was added DDQ (190 mg, 0.84 mmol) and the stirring was continued for 12 h. The reaction was quenched by saturated bicarbonate solution. The aqueous phase was extracted with dichloromethane (40 mL × 6). The organic layer was washed with brine, dried over $MgSO_4$, filtered, and concentrated in vacuo. Flash chromatography of the residue over silica gel (petroleum ether/ EtOAc 2:1) afforded amide **20** (56 mg, 75%) as a pale yellow oil: $[\alpha]_D^{20}$ +5 (*c* 0.4 in $CHCl_3$); IR (KBr, ν_{max}/cm^{-1}): 2926, 1383, 1099, 838; δ_H (400 MHz; $CDCl_3$; Me_4Si) 0.04 (s, 6H, 2 × CH_3), 0.85 (s, 9H, 3 × CH_3), 0.89 (t, *J* 8.0, 3H, CH_3), 1.12 (d, *J* 7.2, 3H, CH_3), 1.26–1.44 (m, 8H, 8-H, 9-H, 10-H, and 11-H), 2.18–2.22 (m, 4H, 3-H and 6-H), 2.30–2.33 (m, 2H, 2-H), 2.46–2.66 (m, 3H, 3″-H and 5″-H), 3.11–3.24 (m, 2H, 1′b-H and 7-H), 3.26 (s, 3H, OCH_3), 3.32 (s, 3H, OCH_3), 3.49–3.55 (m, 1H, 1′a-H), 4.19–4.22 (m, 2H, 2′-H and 4″-H), 5.47–5.48 (m, 2H, 4-H and 5-H), 5.76 (br, 1H, NH), 6.76 (t, *J* 4.0, 1H, 6″-H); δ_C (400 MHz; $CDCl_3$; Me_4Si) –4.9 (CH_3), –4.7 (CH_3), 10.7 (CH_3), 14.0 (CH_2, 12-C), 17.9 (C), 22.6 (CH_2, 11-C), 24.9 (CH_2, 9-C), 25.6 (CH_3), 28.7 (CH_2, 3-C), 32.0 (CH_2, 10-C), 33.3 (CH_2, 8-C), 33.5 (CH_2, 5″-C), 36.4 (CH_2, 6-C), 36.5 (CH_2, 2-C), 43.1 (CH_2, 1′-C), 48.5 (CH, 3″-C), 56.5 (OCH_3), 57.0 (OCH_3), 70.9 (CH, 4″-C), 76.4 (CH, 2′-C), 80.7 (CH, 7-C), 127.4 (CH, 5-C), 130.9 (CH, 4-C), 136.1 (C, 1″-C), 141.6 (CH, 6″-C), 172.1 (CO, 1-C), 200.6 (CO, 2″-C); HRMS (ESI) *m/z* calcd for $C_{29}H_{54}NO_5Si$ $[M + H]^+$ 524.3766, found 524.3777.

(4*E*,7*S*)-*N*-{(2*R*)-[(4*R*,5*S*,6*R*)-6-Benzyloxy-4-*tert*-butyldimethylsilyoxyl-5-methyl-1-cyclohexenyl]-2-methoxyethyl}-7-methoxydodec-4-enamide (2′-*epi*-19)

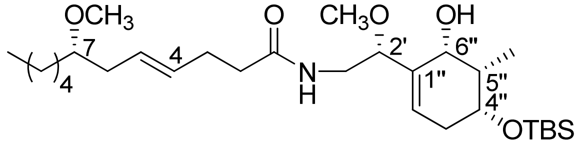


2'-*epi*-**19**

As the procedure for the preparation of **18**, amide 2′-*epi*-**17** (78 mg, 0.13 mmol), MeI (5.0 mL), calcium sulfate (230 mg, 1.69 mmol), and silver oxide (151 mg, 0.65 mmol) afforded pure 2′-*epi*-**19** (56 mg, 70%) as a colorless oil (The reaction condition had a little of difference: the reaction mixture was stirred for 12 h at 40 °C, and then another equivalent of dry calcium sulfate (230 mg, 1.69 mmol) and silver oxide (151 mg, 0.65 mmol) was added and the reaction stirred for another 12 h): $[\alpha]_D^{20}$ –20 (*c* 0.8 in $CHCl_3$); IR (KBr, ν_{max}/cm^{-1}): 2984, 2937, 1742, 1374, 1098, 84; δ_H (400 MHz; $CDCl_3$; Me_4Si) 0.05 (s, 3H, CH_3), 0.06 (s, 3H, CH_3), 0.87–0.93 (m, 15H, 5 × CH_3), 1.27–1.44 (m, 8H, 8-H, 9-H, 10-H, and 11-H), 2.11–2.20 (m, 6H, 2-H, 3-H, and 6-H), 2.28–2.40 (m, 3H, 3″-H and 5″-H), 3.12–3.16 (m, 1H, 7-H), 3.25–3.33 (m, 1H, 1′b-H), 3.29 (s, 3H, OCH_3), 3.33 (s, 3H, OCH_3), 3.44–3.49 (m, 1H, 1′a-H), 3.78–3.83 (m, 1H, 4″-H), 4.07 (br, 1H, 6″-H), 4.16

(t, *J* 2.4, 1H, 2′-H), 4.45 (d, *J* 11.6, 1H, ArCH), 4.64 (d, *J* 11.6, 1H, ArCH), 5.46–5.48 (m, 2H, 4-H and 5-H), 5.60 (br, 1H, 2″-H), 5.79 (dt, *J* 5.2, 5.6, 1H, NH), 7.39–7.28 (m, 5H, 5 × ArH); δ_C (400 MHz; CDCl$_3$; Me$_4$Si) –4.8 (CH$_3$), –4.6 (CH$_3$), 5.7 (CH$_3$), 14.1 (CH$_3$, 12-C), 18.0 (C), 22.6 (CH$_2$, 11-C), 24.9 (CH$_2$, 9-C), 25.8 (3 × CH$_3$), 28.9 (CH$_2$, 3-C), 30.8 (CH$_2$, 10-C), 32.0 (CH$_2$, 8-C), 33.3 (CH$_2$, 3″-C), 36.3 (CH$_2$, 6-C), 36.6 (CH$_2$, 2-C), 37.1(CH, 5″-C), 42.3 (CH$_2$, 1′-C), 56.5 (OCH$_3$), 57.0 (OCH$_3$), 68.7 (CH, 4″-C), 70.8 (CH$_2$), 76.7 (CH, 2′-C), 79.4 (CH, 6″-C), 80.7 (CH, 7-C), 122.4 (CH, 2″-C), 127.3 (CH, 5-C), 127.6 (ArCH), 127.9 (2 × ArCH), 128.4 (2 × ArCH), 130.9 (CH, 4-C), 134.4 (C, 1″-C), 138.3 (C), 172.3 (CO); HRMS (ESI) *m/z* calcd for $C_{36}H_{61}NO_5SiK$ [M + K]$^+$ 654.3951, found 654.3938.

(4*E*,7*S*)-*N*-{(2*R*)-[(4*R*,5*S*,6*R*)-4-*tert*-Butyldimethylsilyoxy-6-hydroxyl-5-methyl-1-cyclohex1enyl]-2-methoxyethyl}-7-methoxydodec-4-enamide (22)



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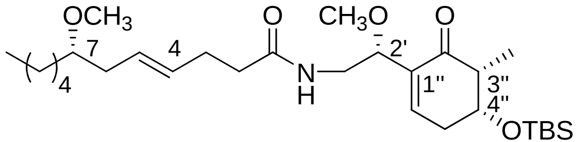
To a stirred suspension of amide 2′-*epi*-**19** (50 mg, 0.08 mmol) in dichloromethane (3.6 mL) and water (0.4 mL) was added DDQ (145 mg, 0.64 mmol) and the stirring was continued for 12 h. The reaction was quenched by saturated sodium bicarbonate solution. The aqueous phase was extracted with dichloromethane (40 mL × 4). The organic layer was washed with brine, dried over MgSO$_4$, filtered, and concentrated in vacuo. Flash chromatography of the residue over silica gel (petroleum ether/EtOAc 2:1) afforded amide **22** (33 mg, 77%) as a colorless oil: $[\alpha]_D^{20}$ –10 (*c* 0.2 in CHCl$_3$); IR (KBr, ν_{max}/cm^{-1}): 3323, 2929, 1650, 1461, 1102, 837; δ_H (400 MHz; CDCl$_3$; Me$_4$Si) 0.09 (s, 3H, CH$_3$), 0.12 (s, 3H, CH$_3$), 0.88 (br, 12H, 4 × CH$_3$), 1.22–1.44 (m, 11H, 8-H, 9-H, 10-H, 11-H, and

CH_3), 1.70–1.71 (m, 1H, 5″-H), 2.19–2.33 (m, 8H, 2-H, 3-H, 6-H, and 3″-H), 3.13–3.16 (m, 1H, 7-H), 3.23 (s, 3H, OCH_3), 3.33 (s, 3H, OCH_3), 3.45–3.50 (m, 2H, 1′-H), 3.80–3.83 (m, 2H, 2′-H and 4″-H), 4.05 (br, 1H, 6″-H), 5.47–5.48 (m, 2H, 4-H and 5-H), 5.62 (br, 1H, 2″-H), 6.21 (br, 1H, NH); δ_C (100 MHz; $CDCl_3$; Me_4Si) –5.1 (CH_3), –4.8 (CH_3), 14.1 (CH_3), 14.9 (CH_2, 12-C), 17.8 (C), 22.7 (CH_2, 11-C), 24.9 (CH_2, 9-C), 25.7 (CH_3), 28.8 (CH_2, 3-C), 32.0 (CH_2, 10-C), 33.3 (CH_2, 8-C), 34.9 (CH_2, 3″-C), 36.4 (CH_2, 6-C), 36.6 (CH_2, 2-C), 36.9 (CH_2, 1′-C), 42.4 (CH, 5″-C), 56.2 (OCH_3), 56.5 (OCH_3), 66.8 (CH, 4″-C), 72.0 (CH, 2′-C), 80.8 (CH, 7-C), 82.1 (CH, 6″-C), 123.3 (CH, 2″-C), 127.3 (CH, 5-C), 130.9 (CH, 4-C), 137.9 (C, 1″-C), 172.4 (CO, 1-C); HRMS (ESI) *m/z* calcd for $C_{29}H_{56}NO_5Si$ $[M + H]^+$ 526.3922, found 526.3935.

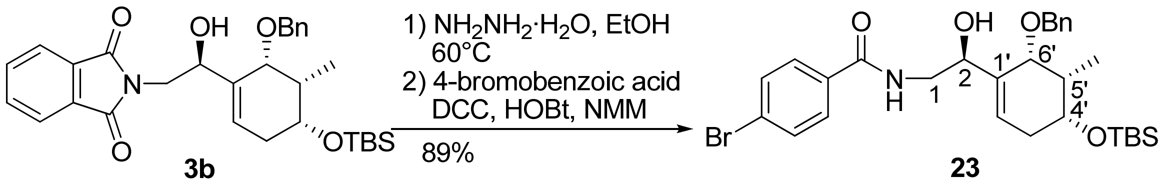
(4*E*,7*S*)-*N*-{(2*R*)-[(3*R*,4*R*)-4-*tert*-Butyldimethylsilyoxy-3-methyl-2-oxocyclohex-1-enyl]-2-methoxyethyl}-7-methoxydodec-4-enamide (2′-*epi*-20)



2'-*epi*-**20**

To a stirred solution of amide **22** (26 mg, 0.05 mmol) in dichloromethane (4 mL) was added Dess-Martin periodinane (25 mg, 0.06 mmol) at room temperature. The reaction mixture was stirred for 1 h, and the solution was then concentrated in vacuo. Flash chromatography of the residue over silica gel (petroleum ether/EtOAc 3:1) afforded amide 2′-*epi*-**20** (26 mg, 99%) as colorless oil: $[\alpha]_D^{20}$ –21 (*c* 0.7 in $CHCl_3$); IR (KBr): 2925, 1762, 1654, 1382, 1100, 1064; δ_H (400 MHz; $CDCl_3$; Me_4Si) 0.05 (s, 6H, 2 × CH_3), 0.84 (s, 9H, 3 × CH_3), 0.89 (d, *J* 7.2, 3H, CH_3), 1.14 (d, *J* 6.8, 3H, CH_3), 1.27–1.45 (m, 8H, 8-H, 9-H, 10-H, and 11-H), 2.20–2.32 (m, 6H, 2-H, 3-H, and 6-H), 2.54–2.59 (m, 3H, 3″-H and 5″-H), 3.14–3.17 (m, 1H, 7-H), 3.24 (s, 3H, OCH_3), 3.27–3.32 (m, 1H, 1′b-H), 3.33 (s, 3H, OCH_3), 3.39–3.45 (m, 1H, 1′a-H), 4.20–4.21 (m, 1H, 4″-H), 4.33 (dt, *J* 4.4, 5.2, 1H, 2′-H), 5.47–5.49 (m, 2H, 4-H and 5-H), 5.79 (br, 1H, NH), 6.66 (dt, *J* 3.6, 4.4, 1H, 6″-H); δ_C (100 MHz; $CDCl_3$; Me_4Si) –4.9 (CH_3), –4.7 (CH_3), 11.1 (CH_3), 14.1 (CH_2, 12-C), 17.9 (C), 22.7 (CH_2, 11-C), 24.9 (CH_2, 9-C), 25.6 (CH_3), 28.8 (CH_2, 3-C), 32.0 (CH_2, 10-C), 33.3 (CH_2, 8-C), 34.0 (CH_2, 5″-C), 36.4 (CH_2, 6-C), 36.6 (CH_2, 2-C), 43.2 (CH_2, 1′-C), 48.3 (CH, 3″-C), 56.5 (OCH_3), 56.7 (OCH_3), 71.6 (CH, 4″-C), 75.9 (CH, 2′-C), 80.7 (CH, 7-C), 127.5 (CH, 5-C), 130.9 (CH, 4-C), 135.9 (C, 1″-C), 140.3 (CH, 6″-C), 172.3 (CO, 1-C), 200.2 (CO, 2″-C); HRMS (ESI) *m/z* calcd for $C_{29}H_{54}NO_5Si$ $[M + H]^+$ 524.3766, found 524.3775.

***N*-{(2*S*)-[(4*R*,5*S*,6*R*)-6-Benzyloxy-4-*tert*-butyldimethylsilyloxy-5-methyl-1-cyclohexenyl]-2-hydroxyethyl}-4-bromobenzamide (23)**



As the procedure for the preparation of **17**, **3b** (82 mg, 0.16 mmol) afforded amide **23** (80 mg, 89 %) as a colorless oil: $[\alpha]_D^{20} = -6$ (*c* 1.0 in $CHCl_3$); IR (KBr, ν_{max}/cm^{-1}): 3410, 2928, 1641, 1254, 1110, 1069, 838, 777; δ_H (400 MHz; $CDCl_3$; Me_4Si) 0.05 (s, 3H, CH_3), 0.06 (s, 3H, CH_3), 0.90 (s, 9H, 3 × CH_3), 0.94 (d, *J* 6.8, 3H, CH_3), 2.43–2.47 (m, 1H, 5′-H), 2.11–2.13 (m, 2H, 3′-H), 3.31–3.38 (m, 1H, 4′-H), 3.91 (d, *J* 11.2, 1H, 6′-H), 3.78–3.87 (m, 2H, 1-H), 4.18–4.21 (m, 1H, 2-H), 4.45 (d, *J* 11.6, 1H, ArCH), 4.66 (d, *J* 2.4, 1H, 6′-H), 4.69 (d, *J* 11.6, 1H, ArCH), 6.73 (d, *J* 4.0, 1H, NH), 5.72 (br, 1H, 2′-H), 7.29–7.35 (m, 5H, 5 × ArH), 7.50 (d, *J* 8.4, 2H, 2 × ArH), 7.58 (d, *J* 8.4, 2H, 2 × ArH); δ_C (100 MHz; $CDCl_3$; Me_4Si) –4.8 (CH_3), –4.6 (CH_3), 5.4 (CH_3), 18.0 (C), 25.7 (3 × CH_3), 30.8 (CH_2, 3′-C), 36.7 (CH, 5′-C), 45.7 (CH_2, 1-C), 68.3(CH, 4′-C), 70.5 (CH_2, $ArCH_2$), 74.6 (CH, 2-C), 78.9 (CH, 6′-C), 125.7 (CH, 2′-C), 126.0 (ArC), 128.1 (2 × ArCH), 128.2 (2 × ArCH), 128.5 (ArCH), 128.6 (2 × ArCH), 131.6 (2 × ArCH), 133.2 (ArC), 135.5 (C, 1′-C), 137.2 (ArC), 166.8 (CO); HRMS (ESI) *m/z* calcd for $C_{29}H_{40}BrNNaO_4Si$ $[M + Na]^+$ 596.1802, found 596.1810. This compound was used to get crystal, though it didn't succeed, it's mosher's ester **24a** and **24b** was obtained for the determination of compound **3**.

(1) (a) E. Klein, G. Ohloff, *Tetrahedron* 1963, **19**, 109; (b) S. Hatakeyama, H. Numata, K. Osanai, S. Takano, *J. Org. Chem*. 1989, **54**, 3515.
(2) L. Engman, D. Stern, *J. Org. Chem*. 1994, **59**, 5179.
(3) J. H. Billman, E. E. Parker, *J. Am. Chem. Soc*. 1943, **65**, 761.
(4) K. L. McPhail, W. H. Gerwick, *J. Nat. Prod.* 2003, **66**, 132.
(5) I. Ohtani, T. Kusumi, Y. Kashman, H. Kakisawa, *J. Am. Chem. Soc*. 1991, **113**, 4092.

Comparison of ^{1}H NMR spectral data for malyngamide W (isolated **1**, synthetic **1**) and 2′-*epi*-**1**

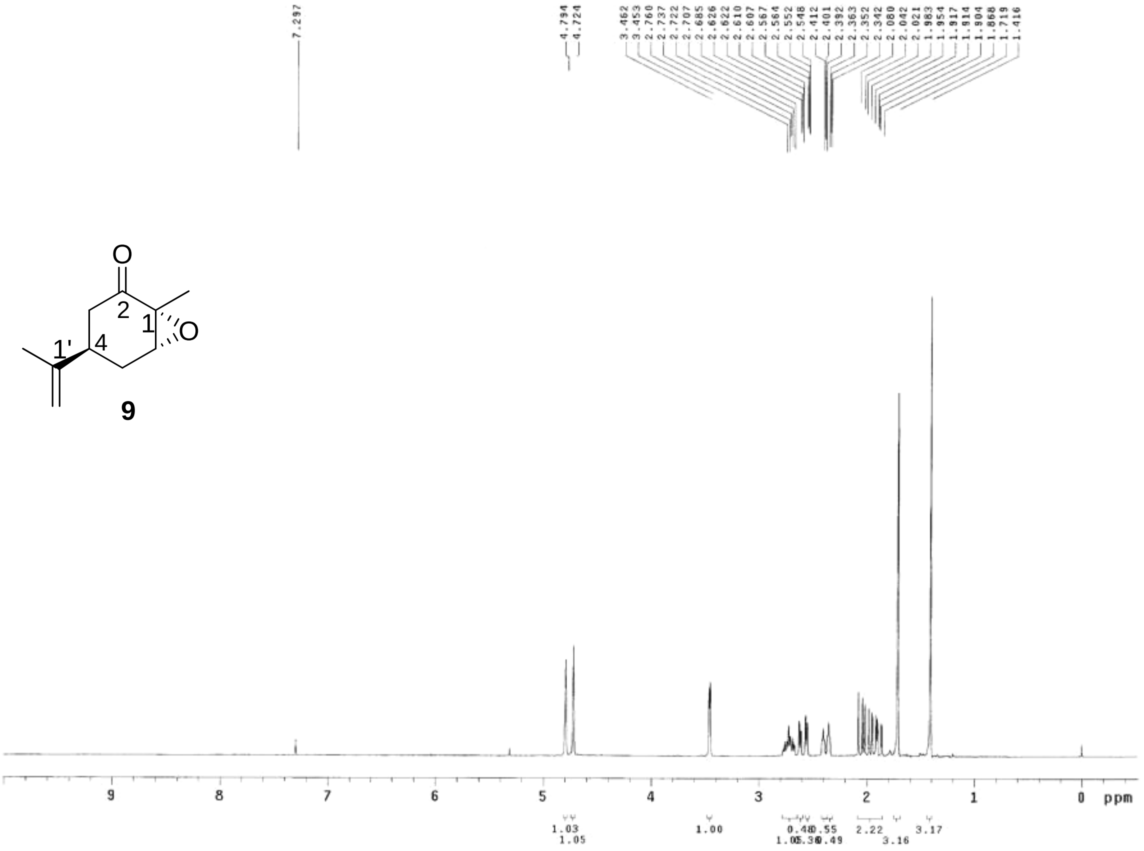
Position	Isolated **1**	Synthetic **1**		2′-*epi*-**1**
		(*c* = 1.6 mg/mL)	(*c* = 3.3 mg/mL)	
1				
2	2.20 (m)	2.31–2.18 (m)	2.30–2.17 (m)	2.31–2.18 (m)
3	2.31 (m)	2.31–2.18 (m)	2.30–2.17 (m)	2.31–2.18 (m)
4	5.47 (m)	5.49–5.46 (m)	5.47–5.46 (m)	5.47–5.44 (m)
5	5.47 (m)	5.49–5.46 (m)	5.47–5.46 (m)	5.47–5.44 (m)
6	2.20 (m)	2.31–2.18 (m)	2.30–2.17 (m)	2.31–2.18 (m)
7	3.16 (m)	3.17–3.14 (m)	3.17–3.14 (m)	3.25–3.14 (m)
8	1.44 (m)	1.46–1.34 (m)	1.45–1.41 (m)	1.45–1.41 (m)
9	1.29 (m)	1.32–1.26 (m)	1.33–1.26 (m)	1.30–1.28 (m)
10	1.27 (m)	1.32–1.26 (m)	1.33–1.26 (m)	1.30–1.28 (m)
11	1.31 (m)	1.32–1.26 (m)	1.33–1.26 (m)	1.30–1.28 (m)
12	0.91 (t, 7.3)	0.89 (t, 6.8)	0.89 (t, 6.8)	0.89 (dt, 7.2, 6.4)
OCH_3	3.33 (s)	3.33 (s)	3.33 (s)	3.32 (s)
1′	3.40 (dd, 4.9, 6.0)	3.40 (t, 5.2)	3.42–3.34 (m)	3.80–3.74 (m, 1′a)
				3.25–3.14 (m, 1′b)
2′	4.31 (td, 1.1, 4.7)	4.32–4.26 (m)	4.29–4.26 (m)	4.28 (br, s)
1″				
2″				
3″	2.7 (dq, 3.0, 7.0)	2.72–2.64 (m)	2.71–2.65 (m)	2.75–2.59 (m)
4″	4.27 (m)	4.32–4.26 (m)	4.29–4.26 (m)	4.14 (br, s)
5″	2.66 (m)	2.72–2.64 (m)	2.71–2.65 (m)	2.71–2.65 (m)
6″	6.67 (br t, 4)	6.67 (br t, 4.4)	6.69 (br, s)	6.66 (br, s)
OCH_3	3.28 (s)	3.28 (s)	3.27 (s)	3.27 (s)
CH_3	1.22 (d, 7.0)	1.21 (d, 7.2)	1.20 (d, 6.8)	1.30–1.28 (m)
NH	5.75 (br t, 5.5)	5.80 (br s)	5.85 (br s)	5.90 (br, s)
OH	1.81 (br, s)			2.71–2.65 (m)

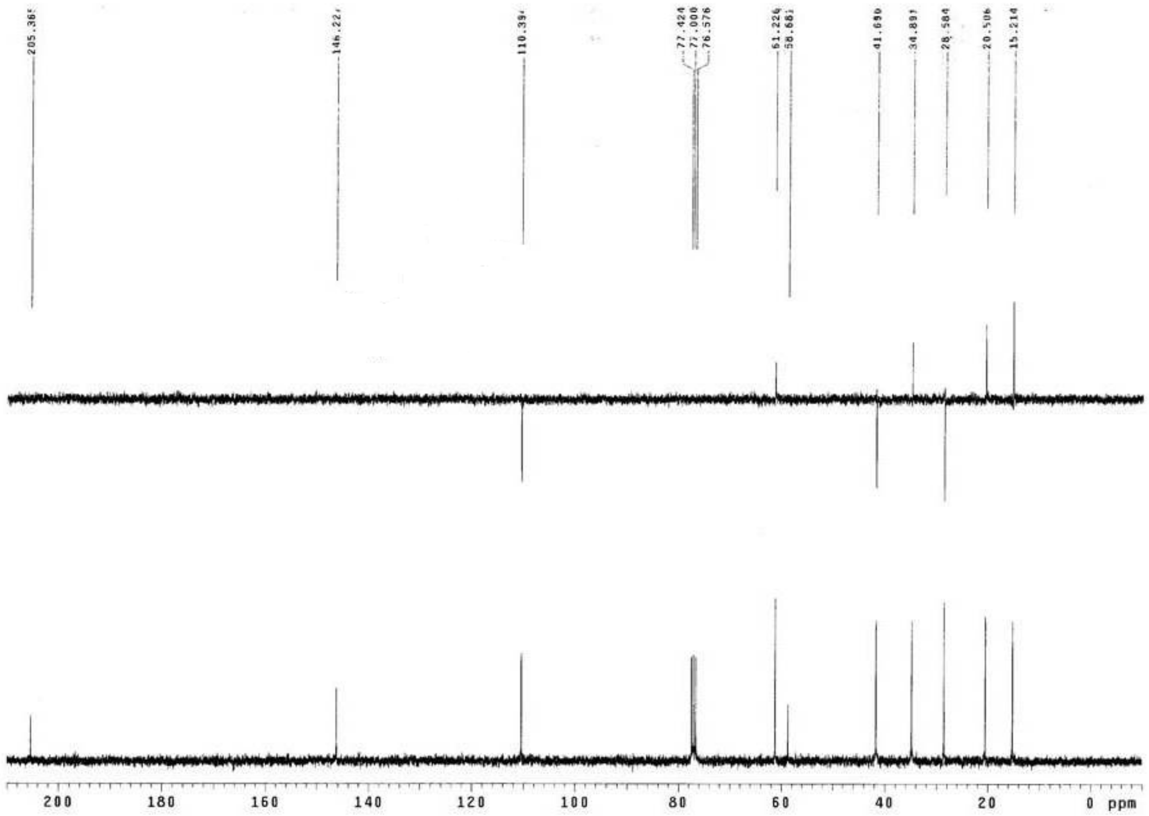
Comparison of ^{13}C NMR spectral data for malyngamide W (isolated **1**, synthetic **1**) and 2′-*epi*-**1**

Position	Isolated **1**	Synthetic **1**		2′-*epi*-**1**
		(*c* = 1.6 mg/mL)	(*c* = 3.3 mg/mL)	
1	172.8	172.8	173.2	174.8
2	36.9	36.9	36.9	36.9
3	29.1	29.1	29.1	28.8
4	131.2	131.2	131.2	131.1
5	127.9	127.9	127.9	128.0
6	36.8	36.8	36.8	36.7
7	81.1	81.1	81.1	81.1
8	33.69	33.70	33.68	33.6
9	25.4	25.4	25.3	25.4
10	32.4	32.4	32.4	32.4
11	23.0	23.0	23.0	23.0
12	14.4	14.5	14.4	14.4
OCH_3	56.9	56.9	56.9	56.8
1′	43.0	43.0	43.2	43.0
2′	76.9	77.0	77.1	76.4
OCH_3	57.4	57.4	57.4	57.4
1″	136.3	136.3	136.2	136.1
2″	200.1	200.0	200.4	199.7
3″	48.0	48.0	48.0	48.4
4″	71.5	71.6	71.4	71.9
5″	33.74	33.78	33.68	34.9
6″	140.4	140.4	140.0	140.3
CH_3	11.0	11.0	11.0	11.6

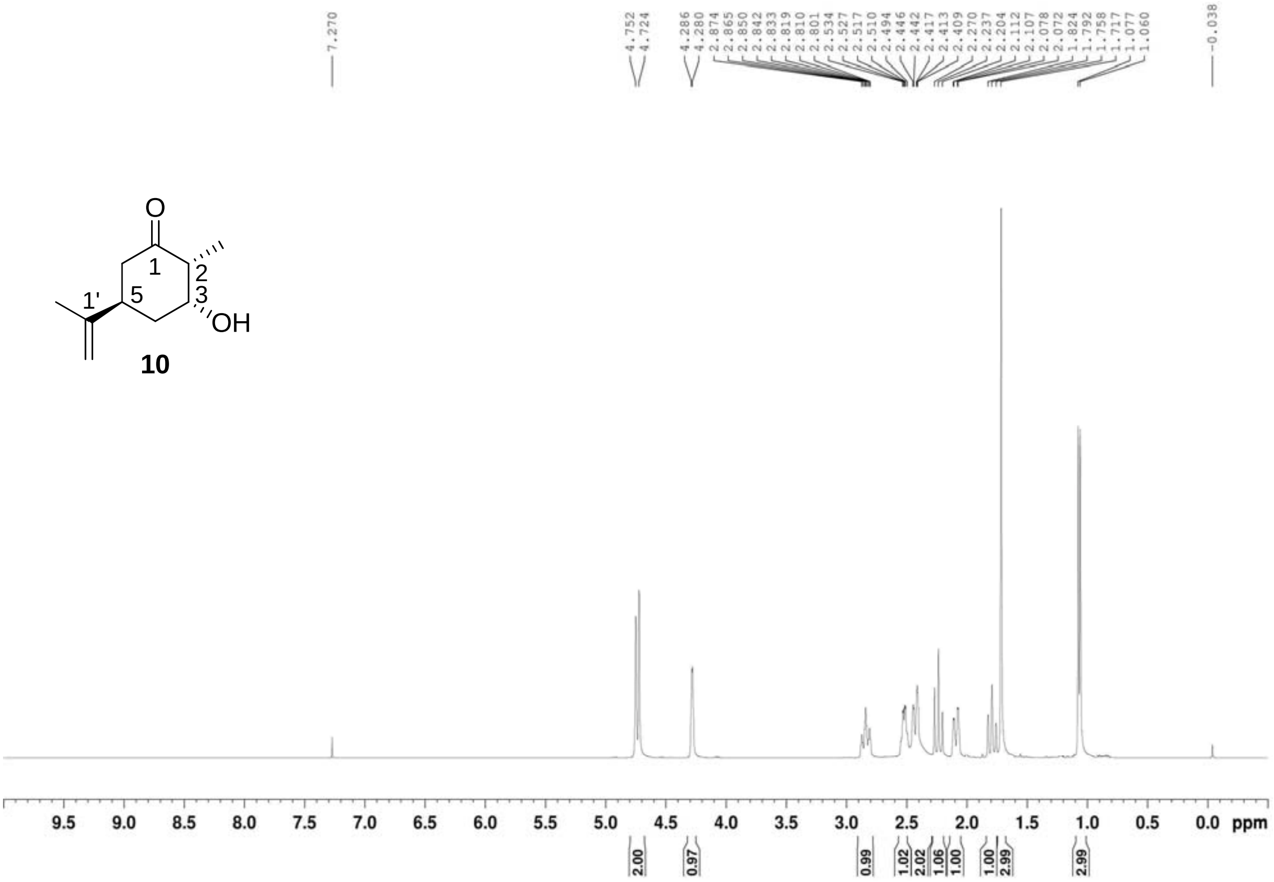
It was very interesting that the different consistence of synthetic **1** showed different chemical shift (δ) of the ^{1}H and ^{13}C NMR. When c = 1.6 mg/mL, the δ value was more consistent with the literature reported[4] compare to c = 3.3 mg/mL. eg: NH, H-1′, H-2′, H-6″, C-1, C-2″, and C-6″.

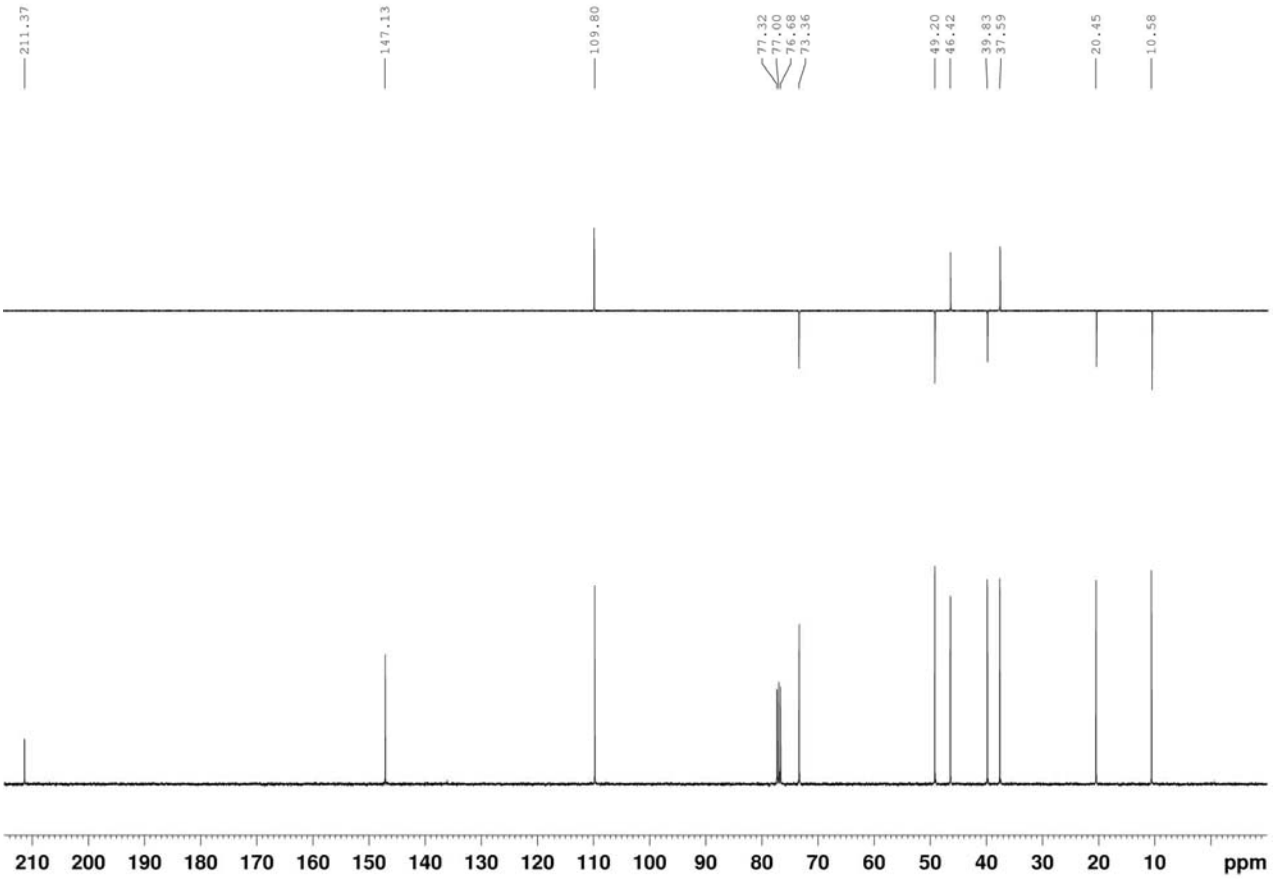
^{1}H NMR (CDCl$_3$, 400 MHz) and ^{13}C NMR (CDCl$_3$, 100 MHz) of **9**





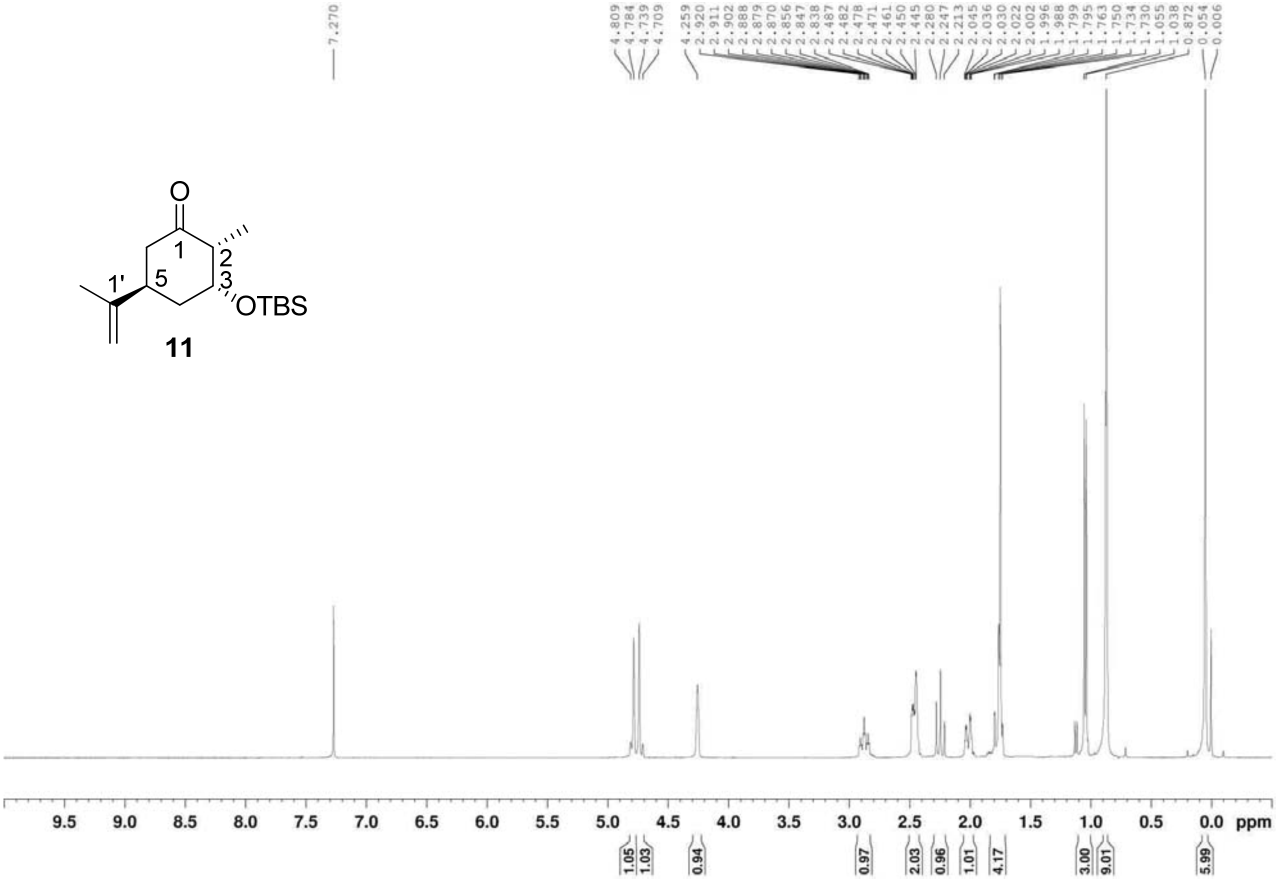
^{1}H NMR (CDCl$_3$, 400 MHz) and ^{13}C NMR (CDCl$_3$, 100 MHz) of **10**

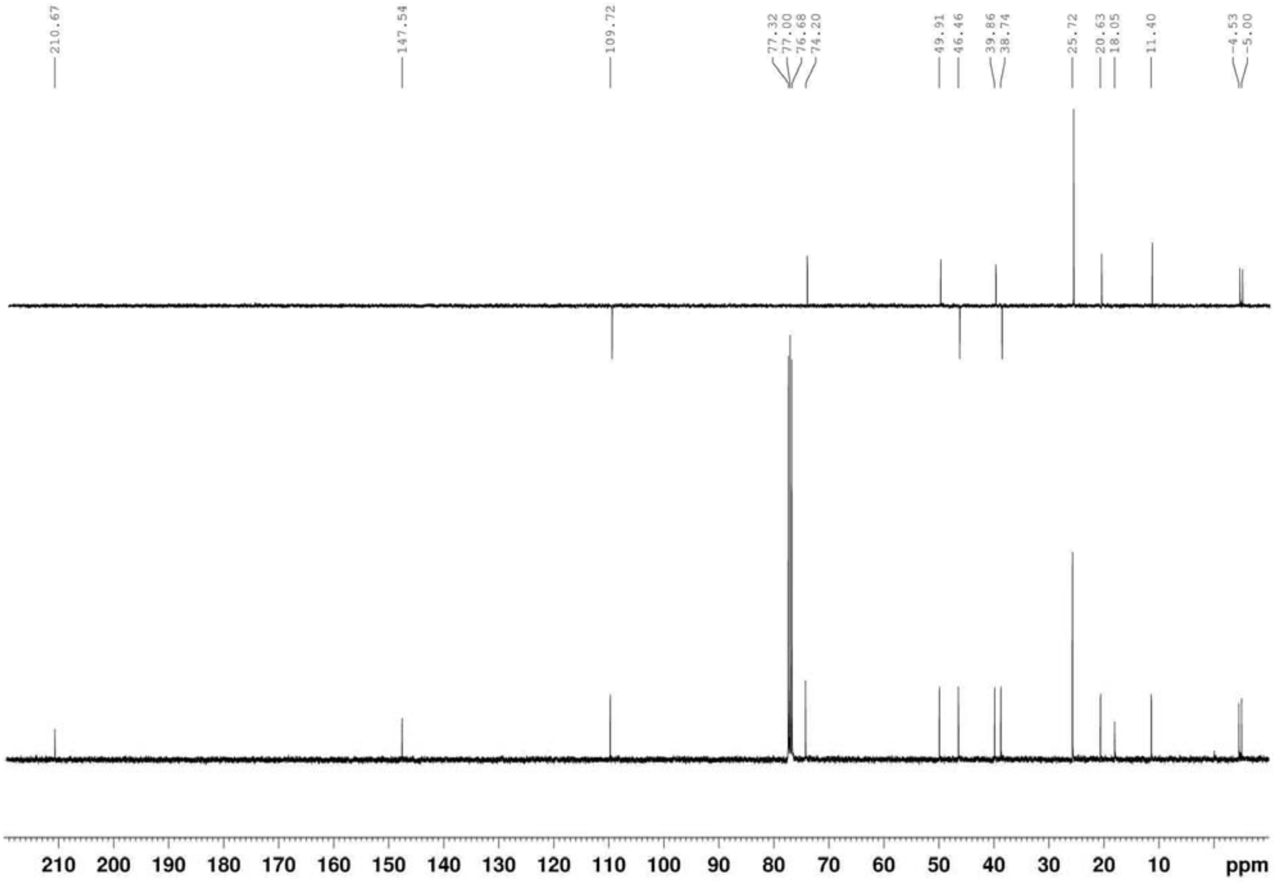




^{1}H NMR (CDCl$_3$, 400 MHz) and ^{13}C NMR (CDCl$_3$, 100 MHz) of **11**

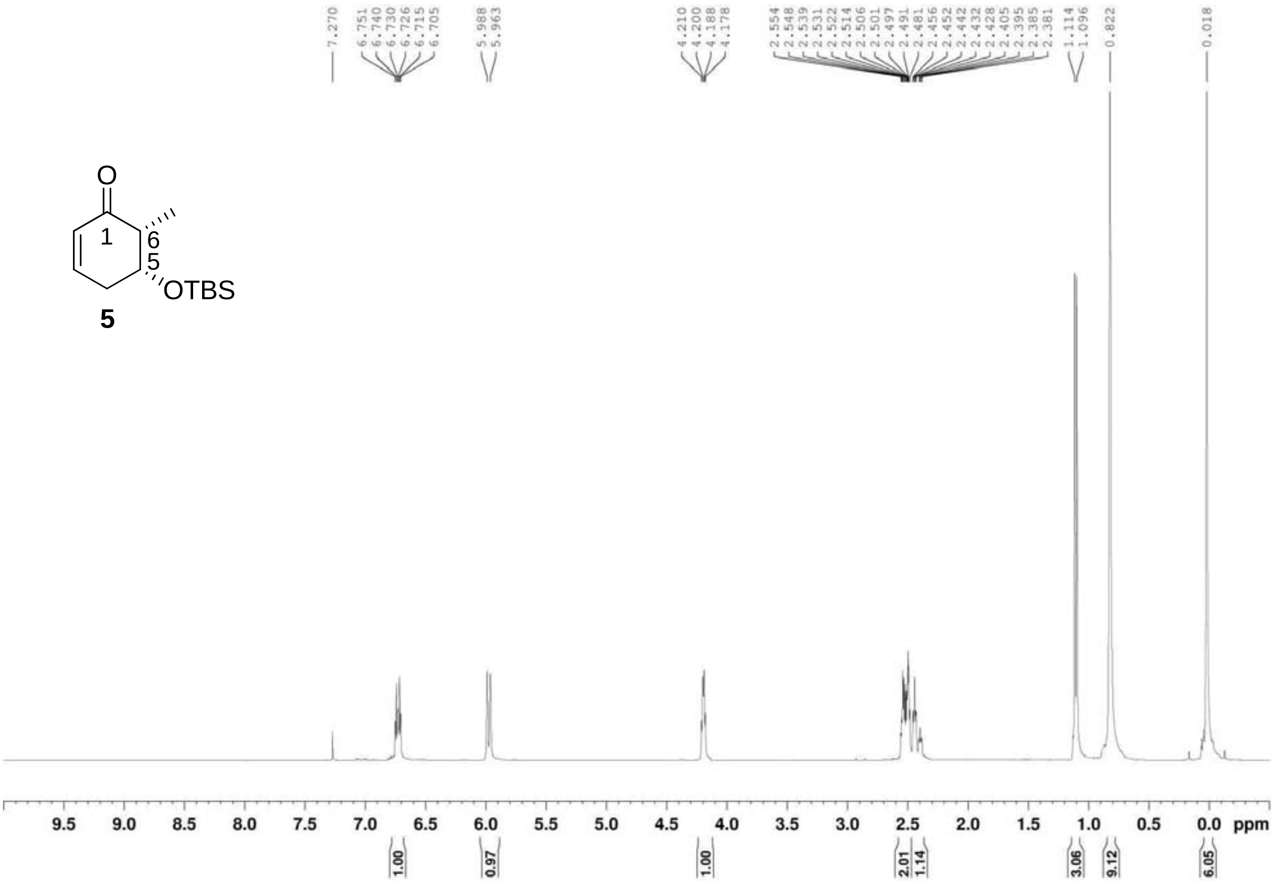
11

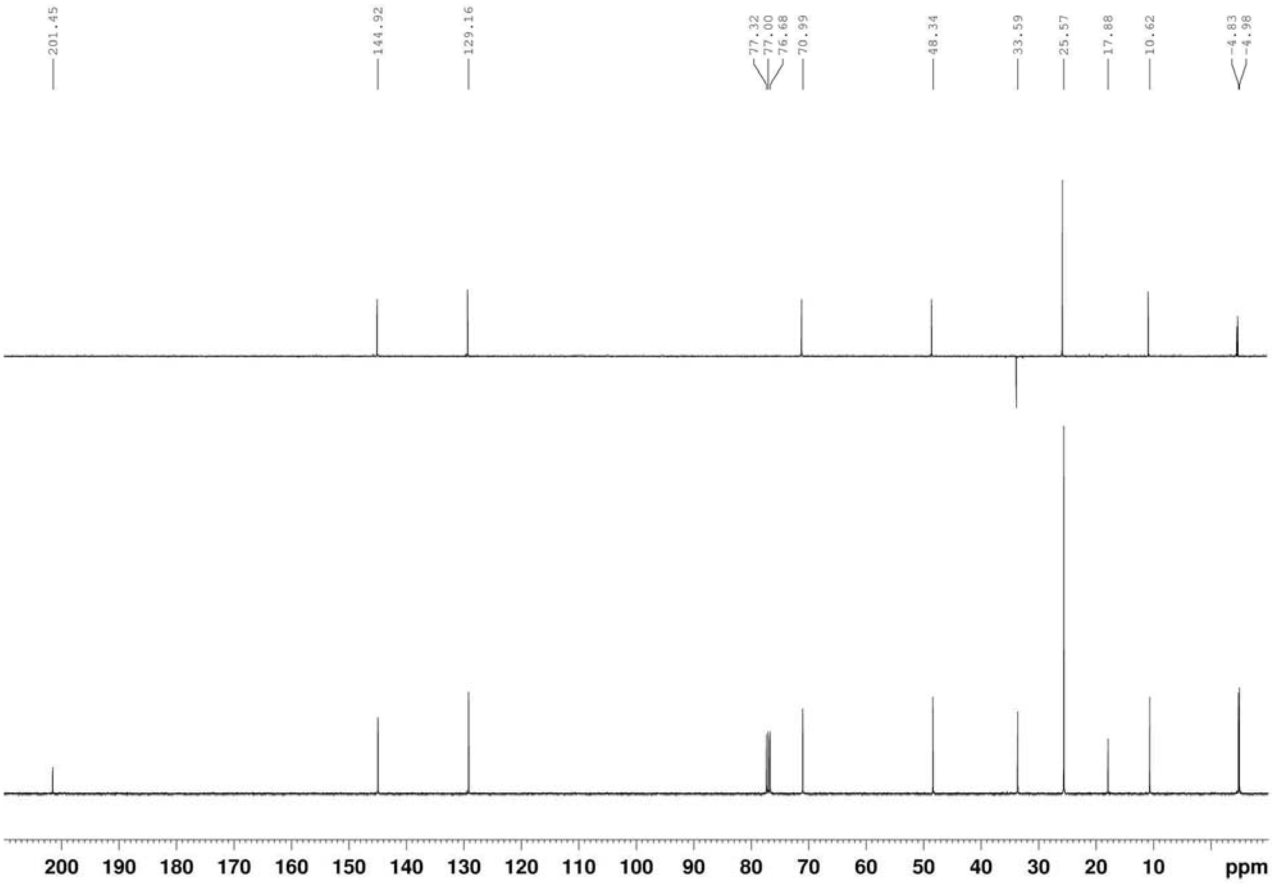




^{1}H NMR (CDCl$_3$, 400 MHz) and ^{13}C NMR (CDCl$_3$, 100 MHz) of **5**

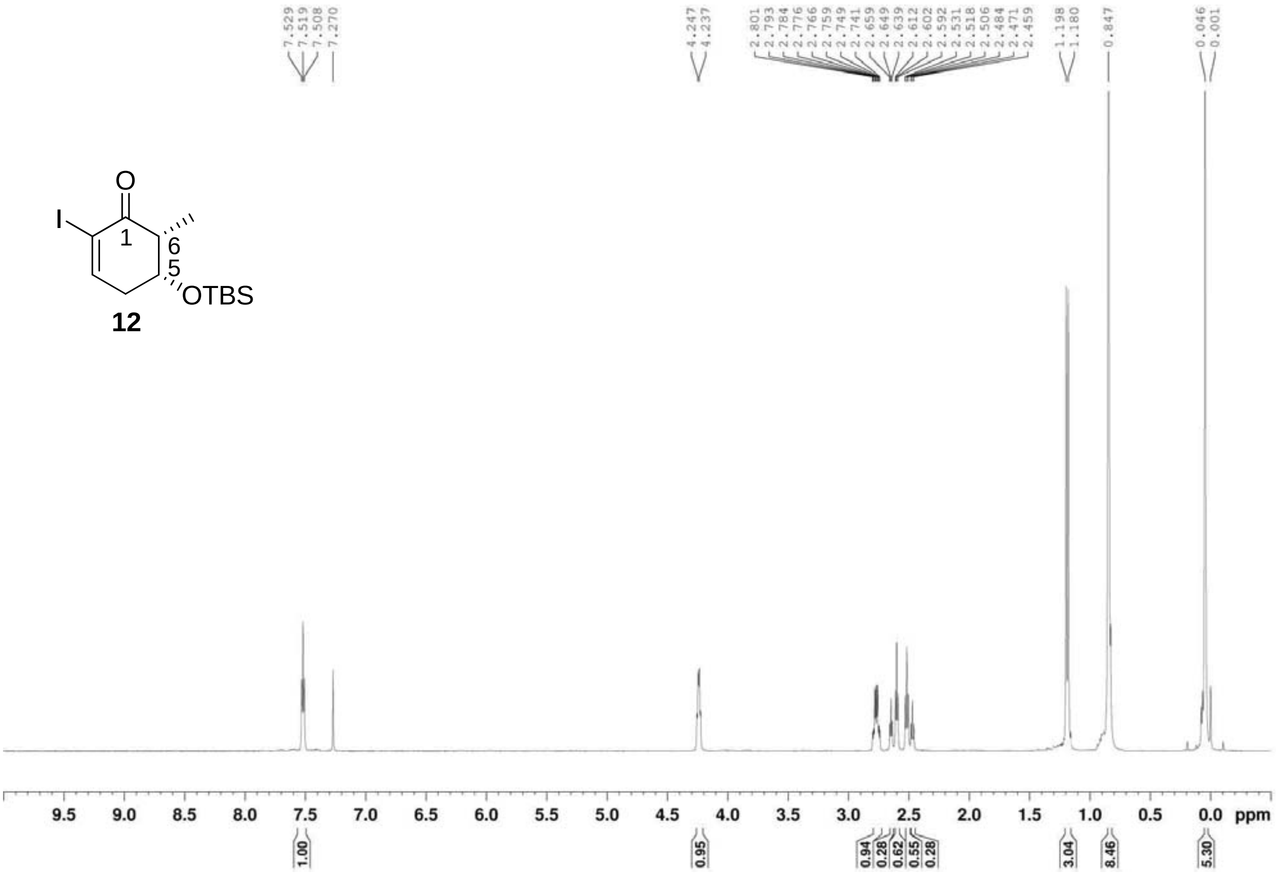
5

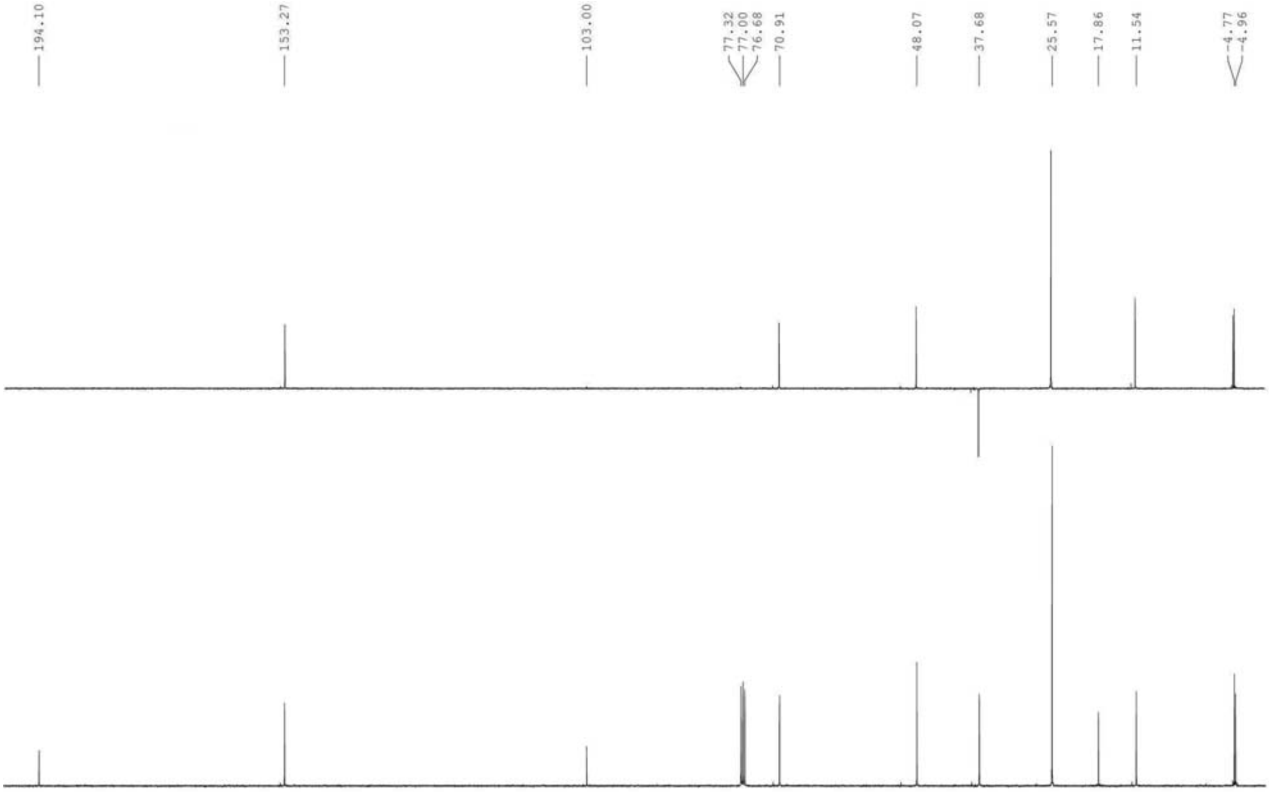




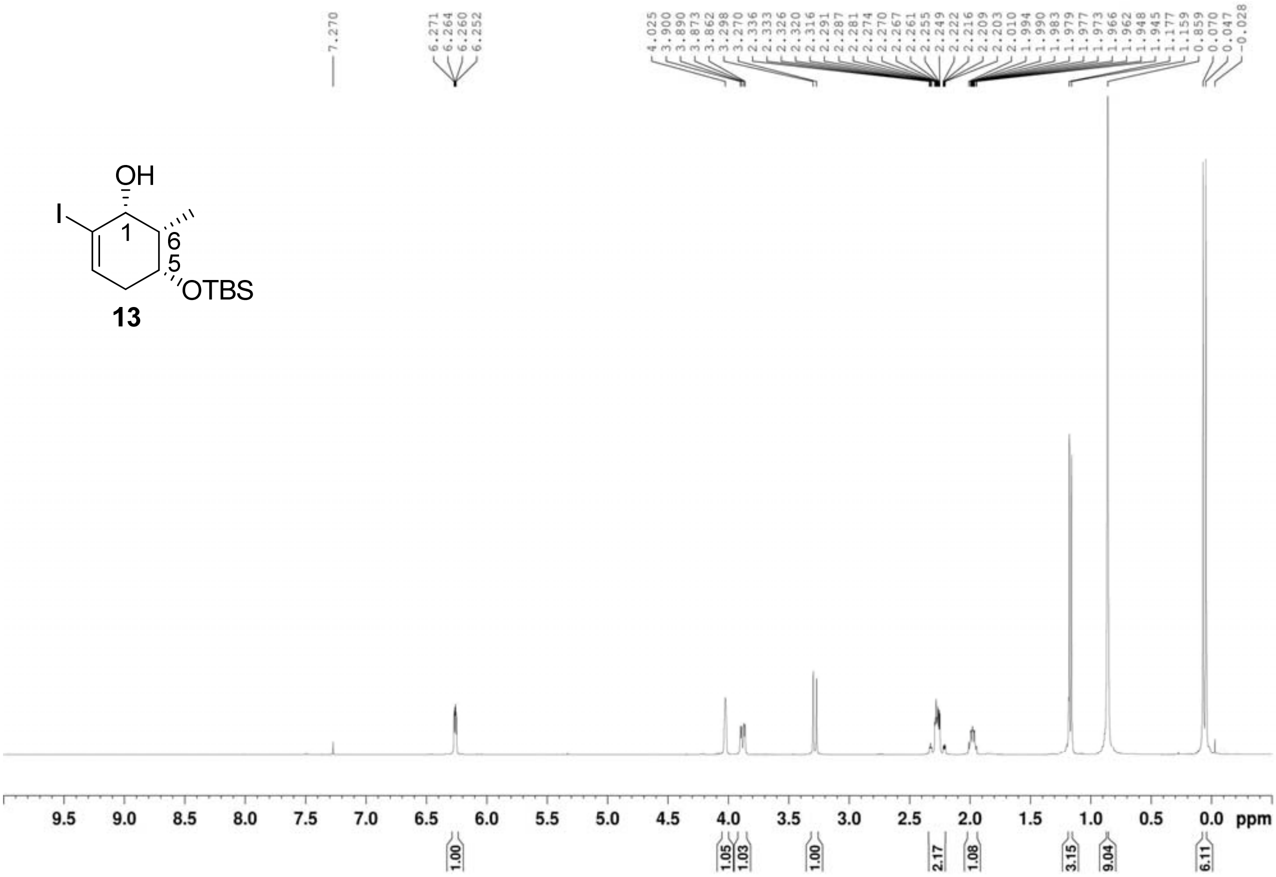
^{1}H NMR (CDCl$_3$, 400 MHz) and ^{13}C NMR (CDCl$_3$, 100 MHz) of **12**

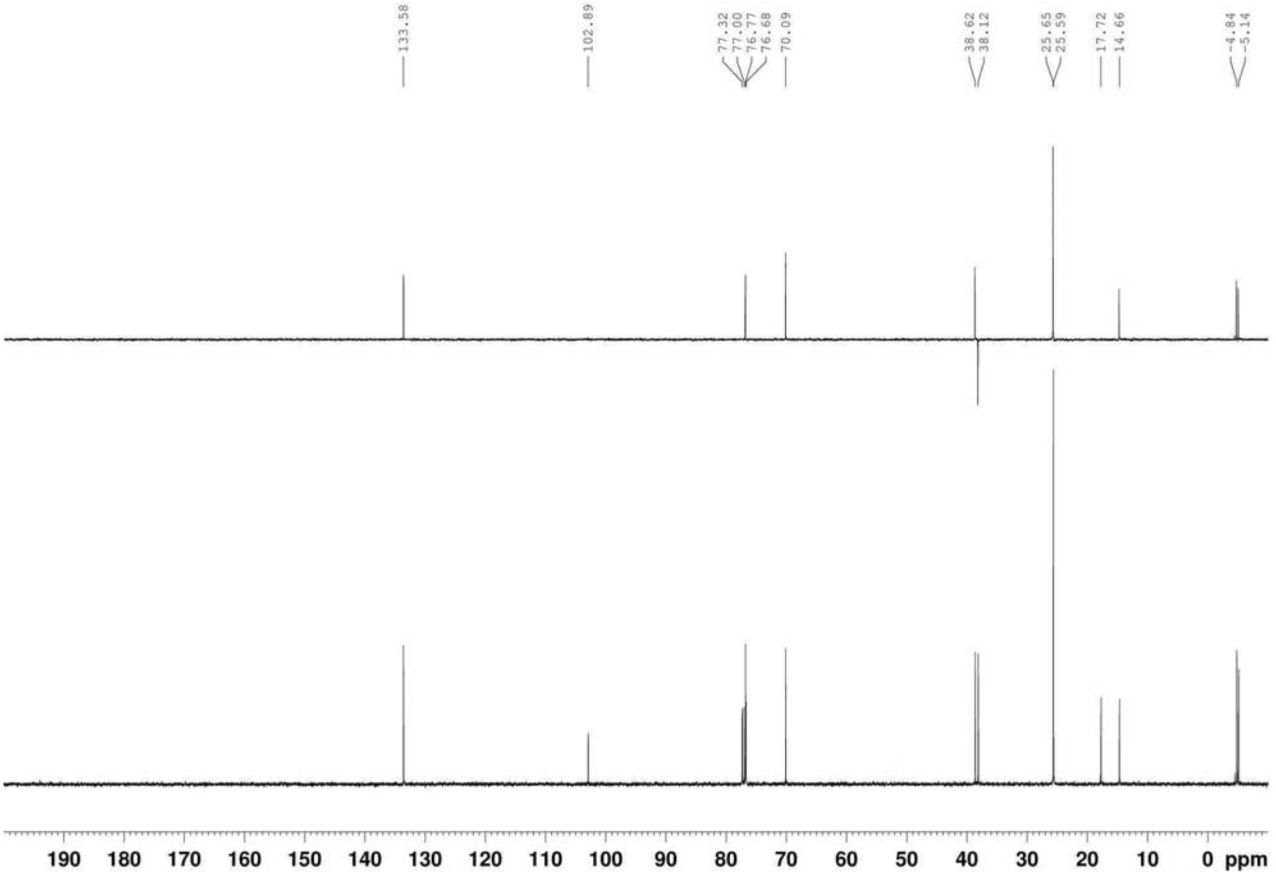
12



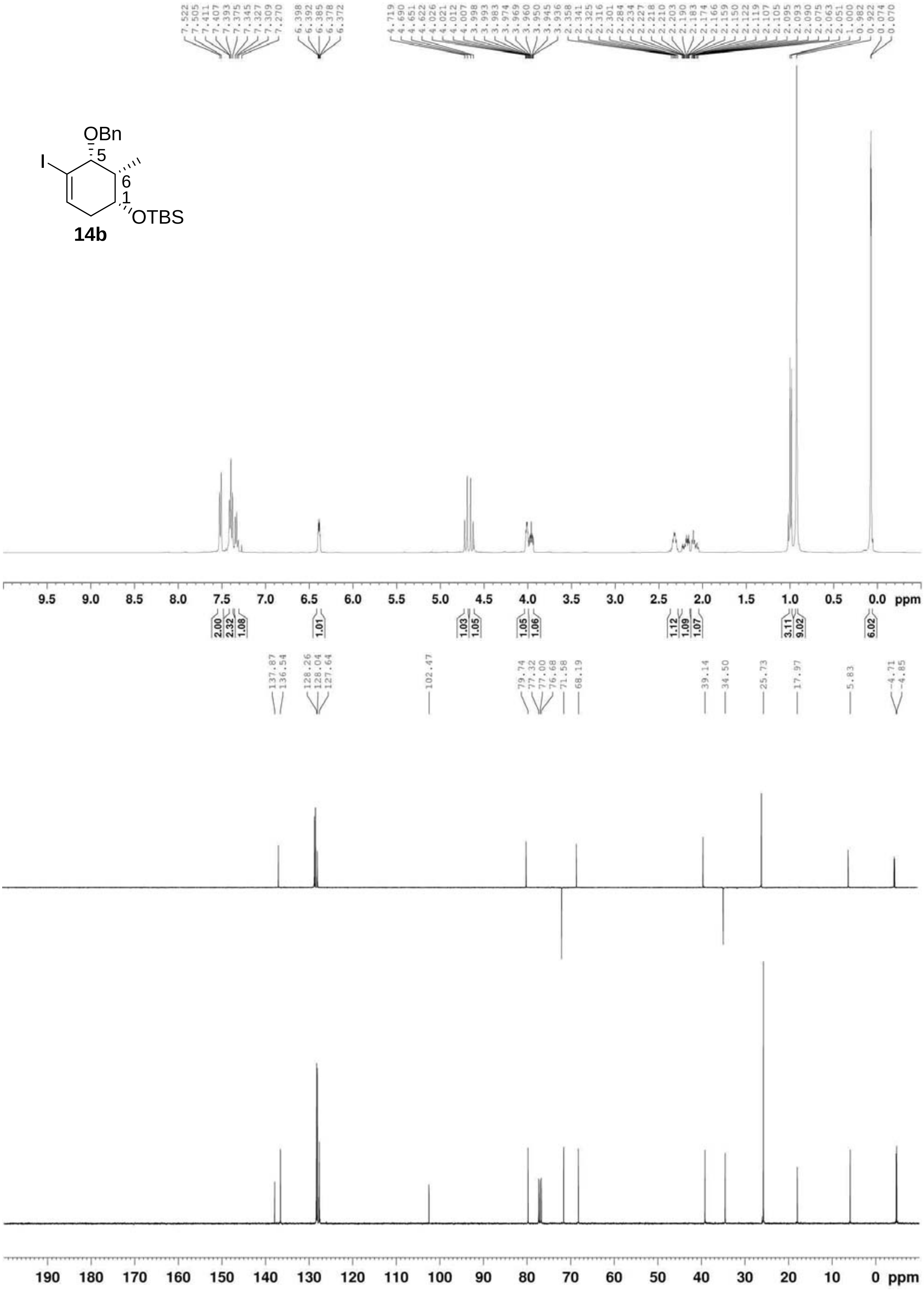


^{1}H NMR (CDCl$_3$, 400 MHz) and ^{13}C NMR (CDCl$_3$, 100 MHz) of **13**

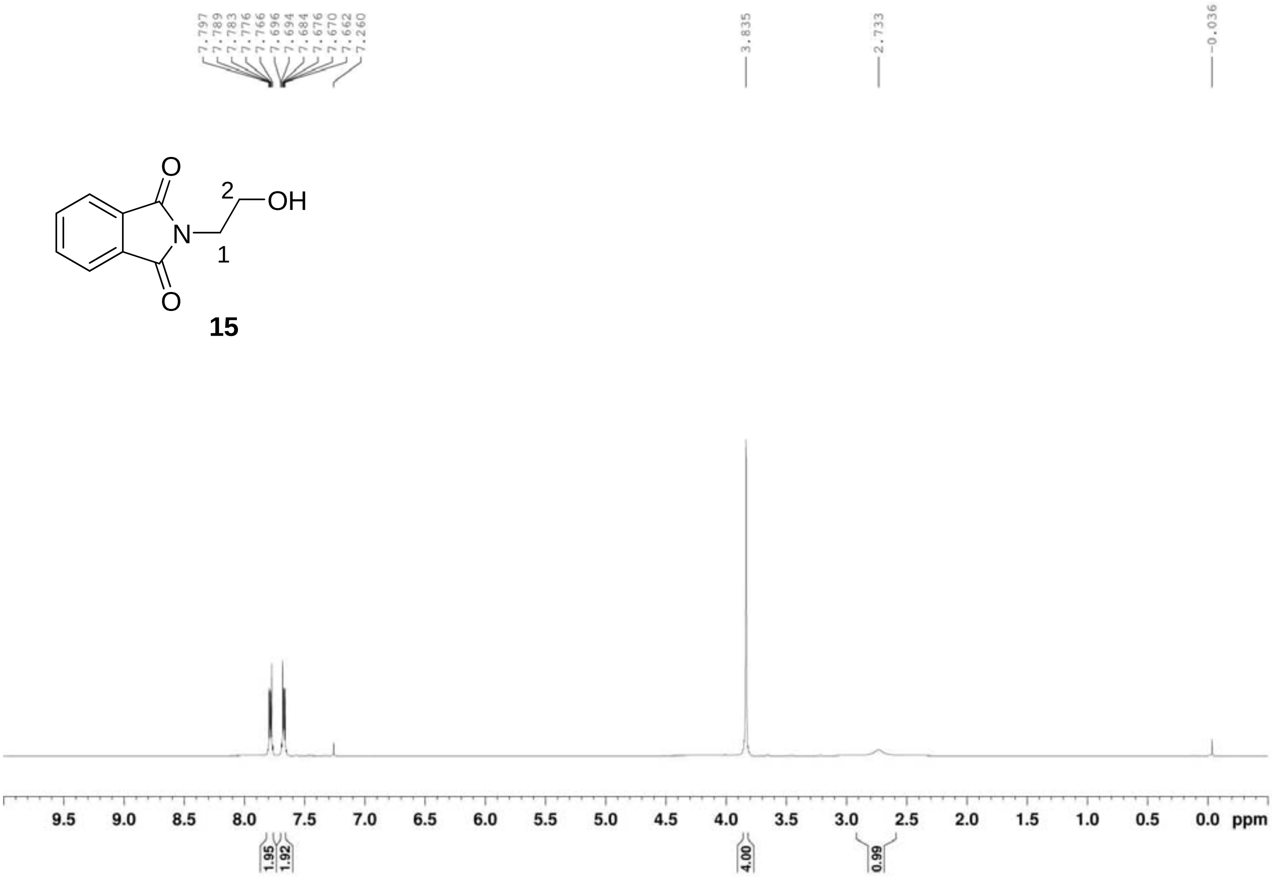


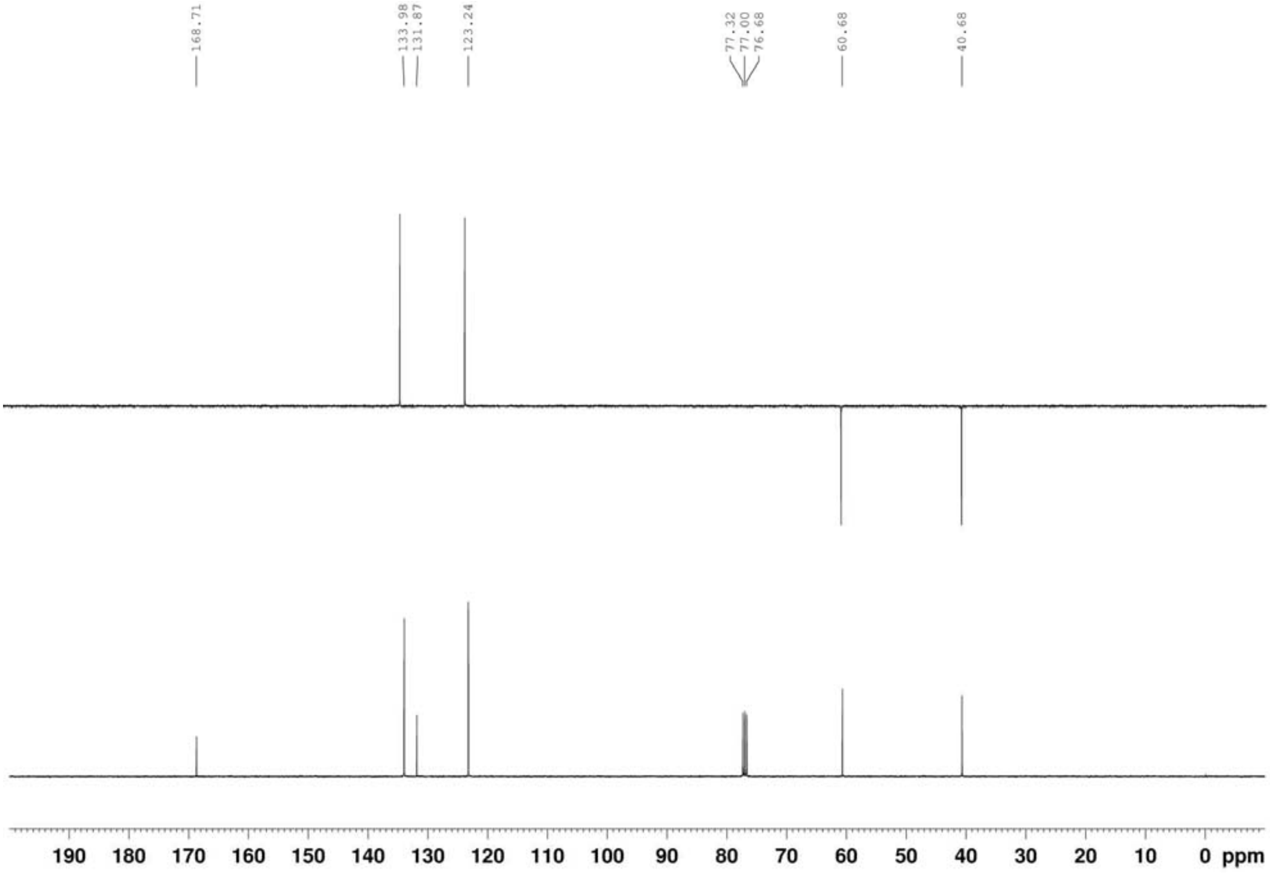


^{1}H NMR ($CDCl_3$, 400 MHz) and ^{13}C NMR ($CDCl_3$, 100 MHz) of **14b**

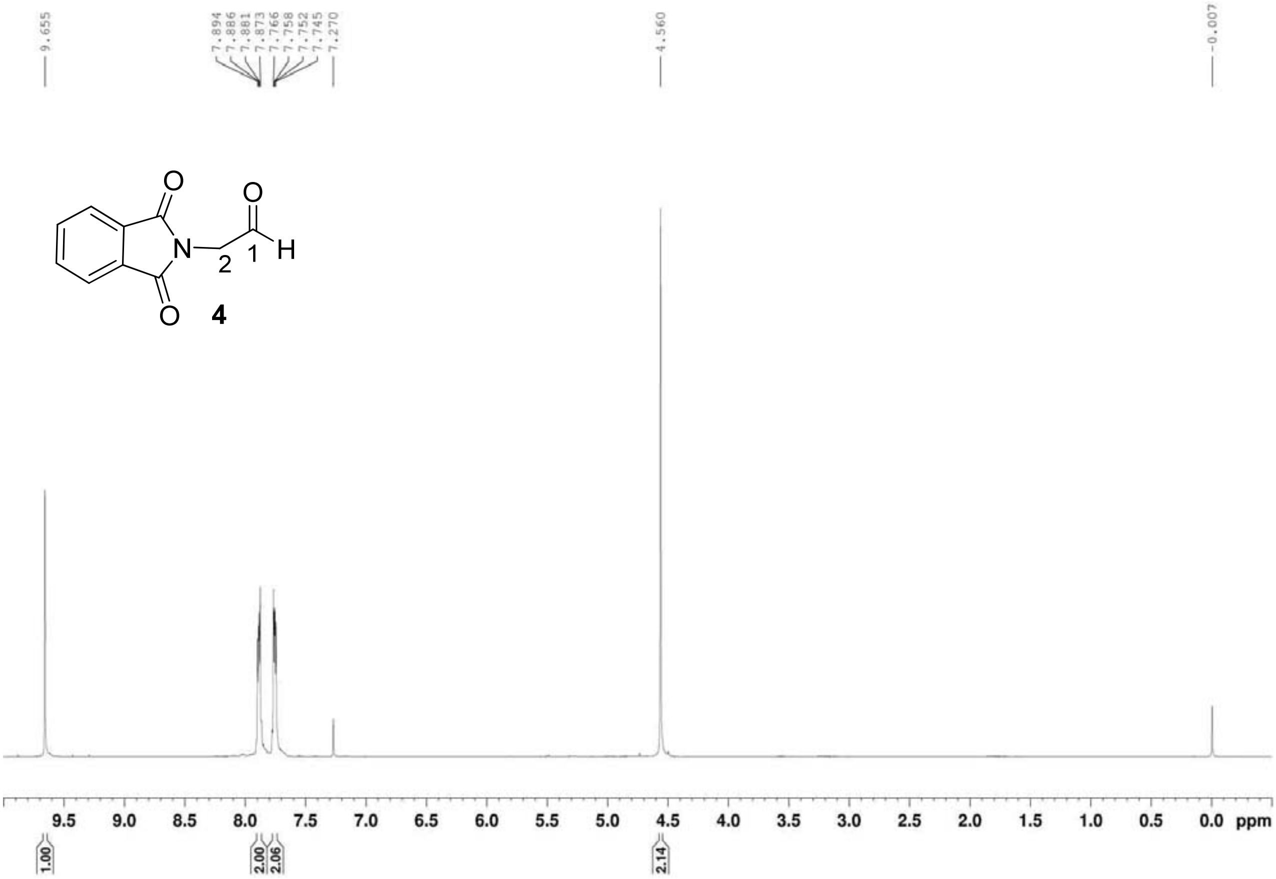


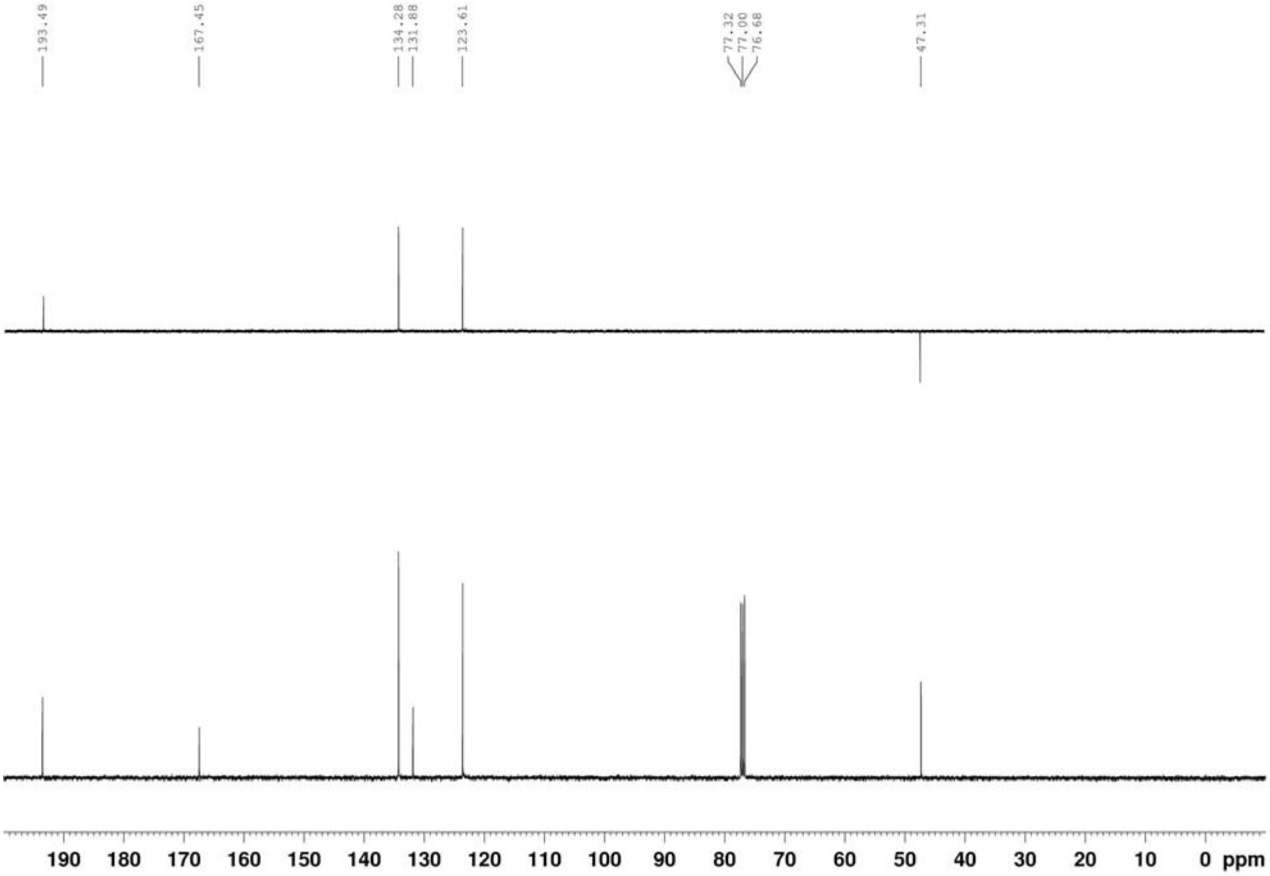
^{1}H NMR ($CDCl_3$, 400 MHz) and ^{13}C NMR ($CDCl_3$, 100 MHz) of **15**



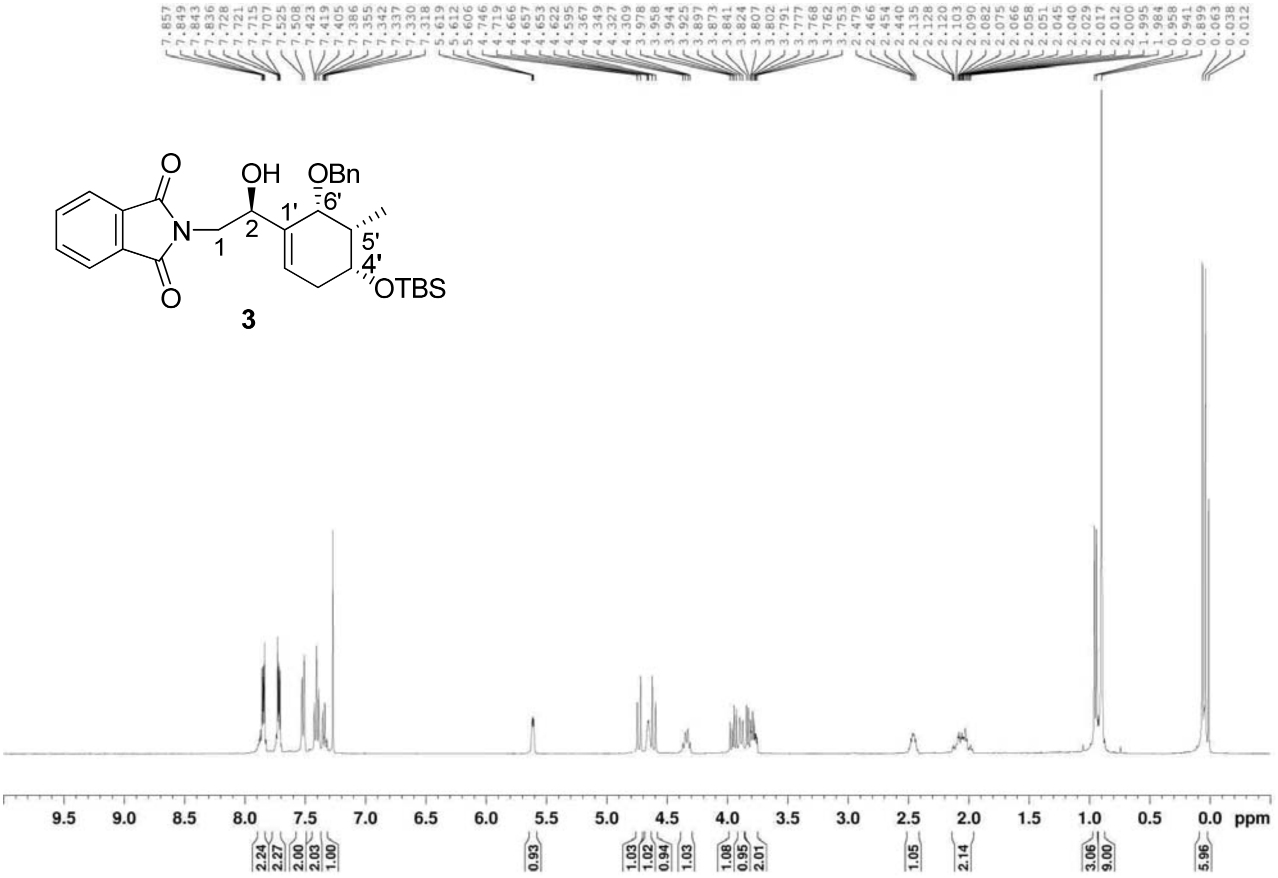


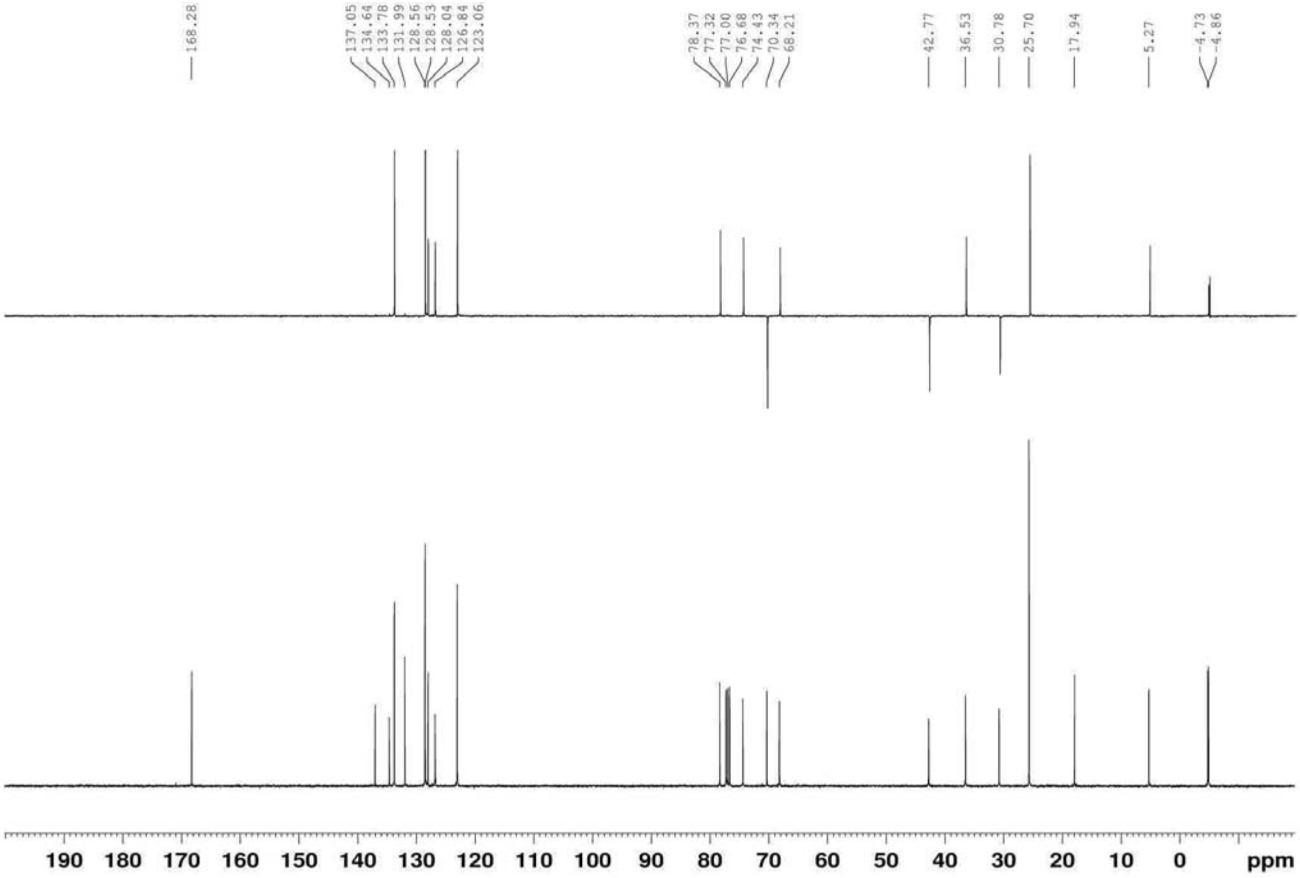
^{1}H NMR (CDCl$_3$, 400 MHz) and ^{13}C NMR (CDCl$_3$, 100 MHz) of **4**



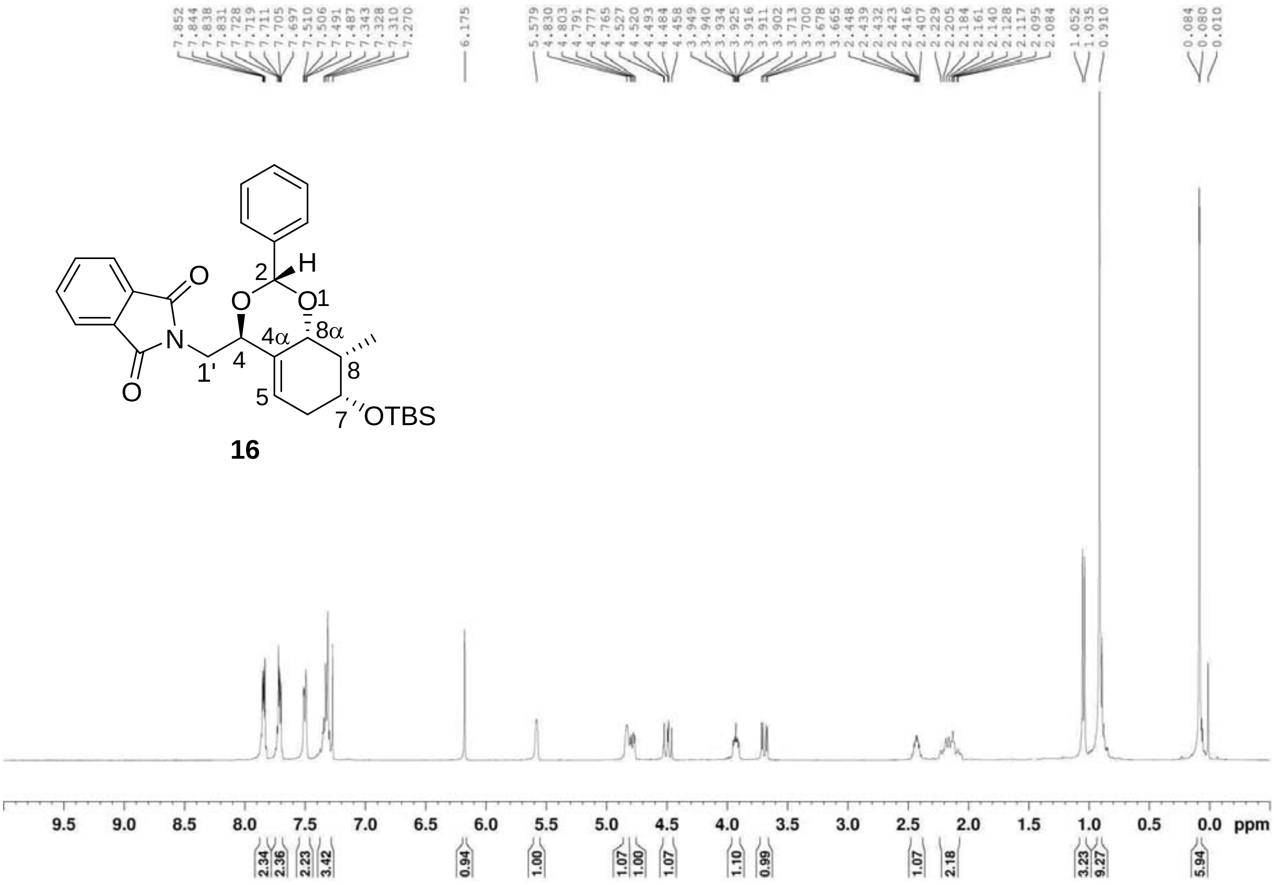


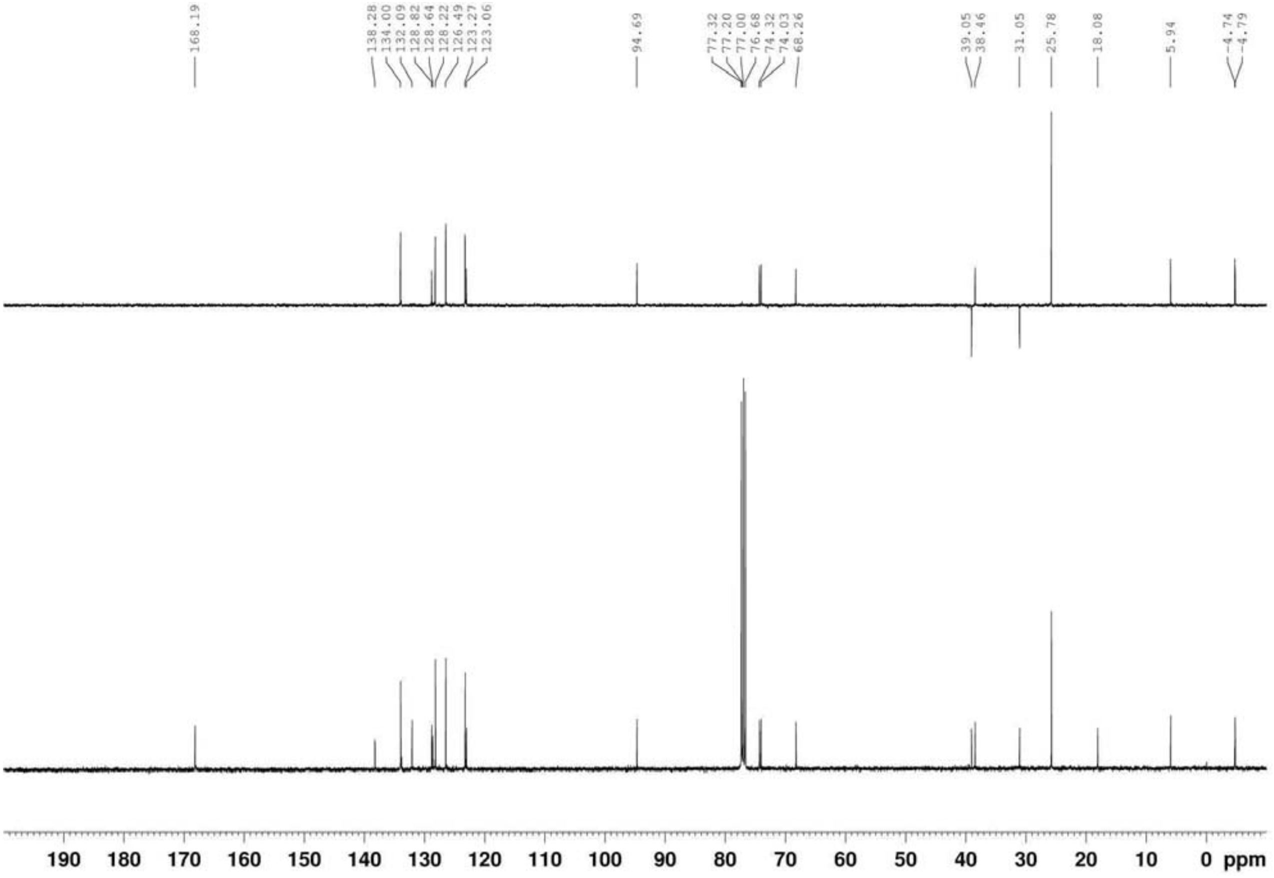
^{1}H NMR ($CDCl_3$, 400 MHz) and ^{13}C NMR ($CDCl_3$, 100 MHz) of **3**



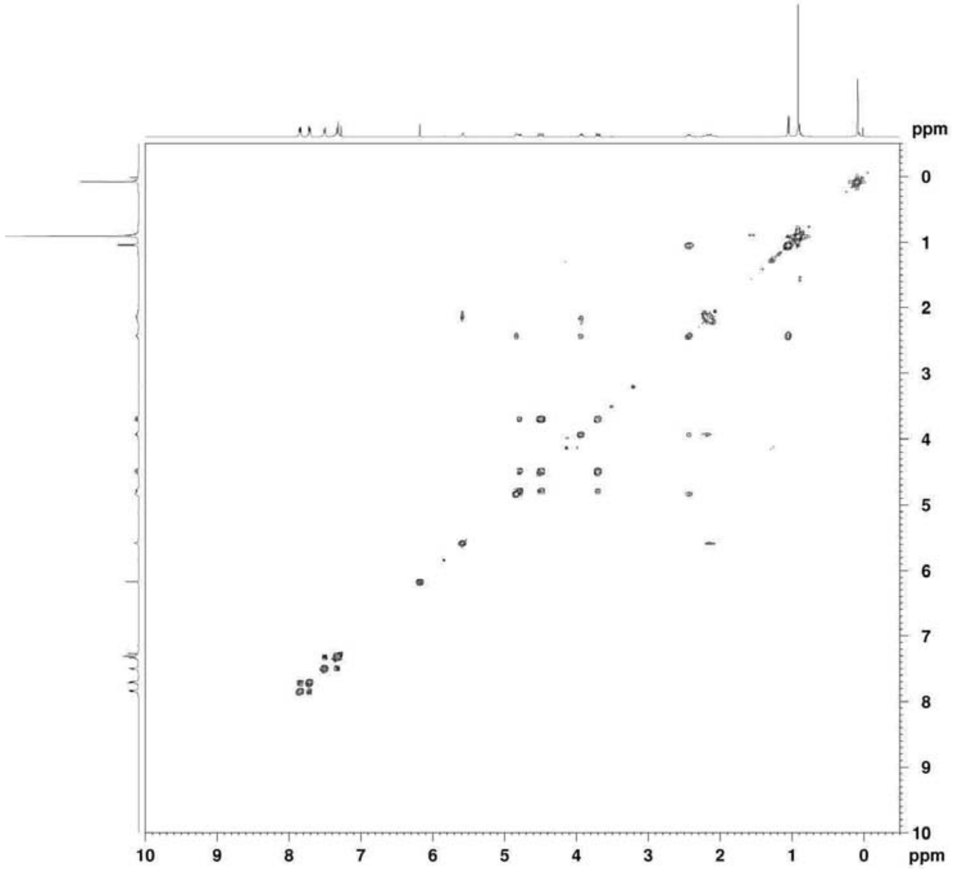


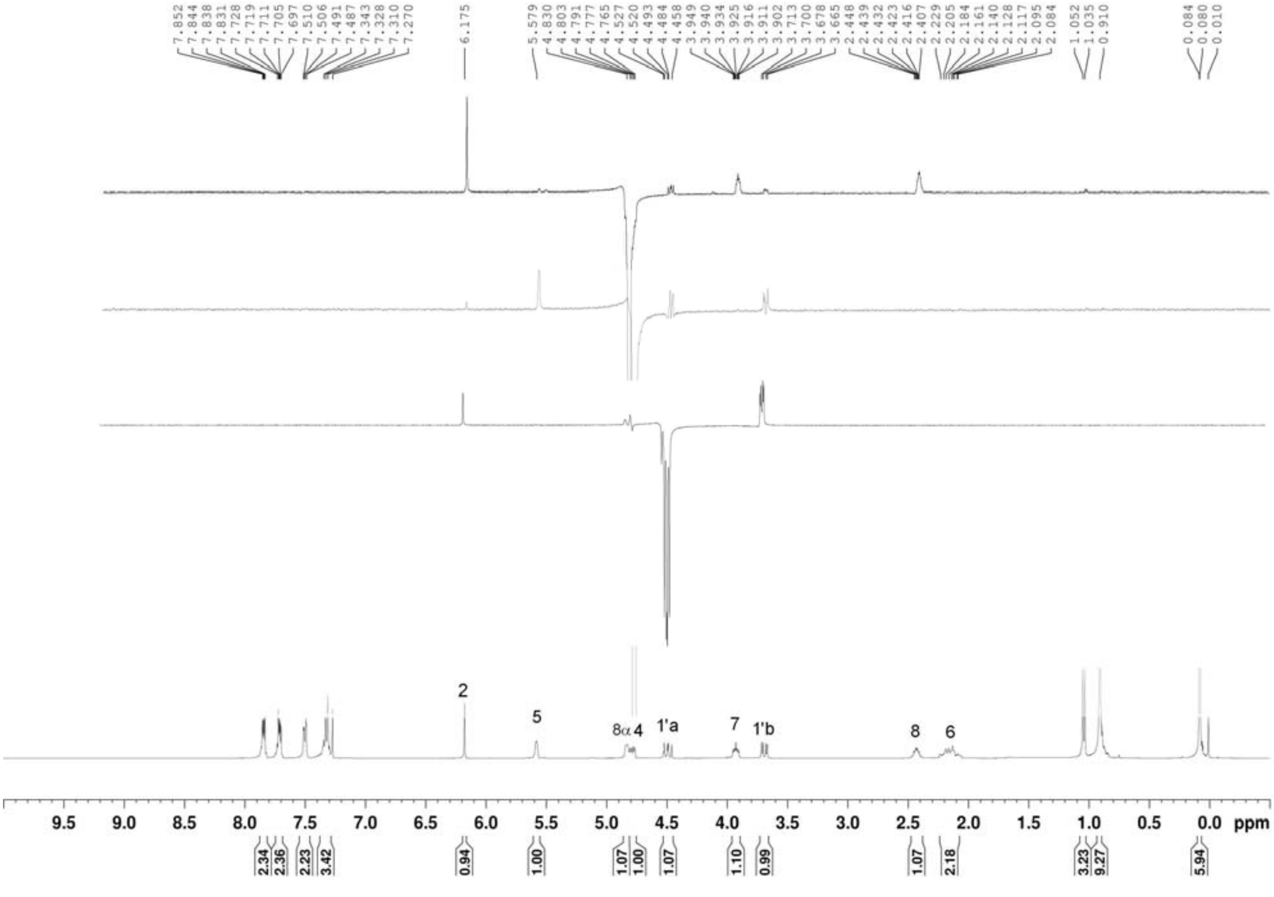
^{1}H NMR (CDCl$_3$, 400 MHz) and ^{13}C NMR (CDCl$_3$, 100 MHz) of **16**



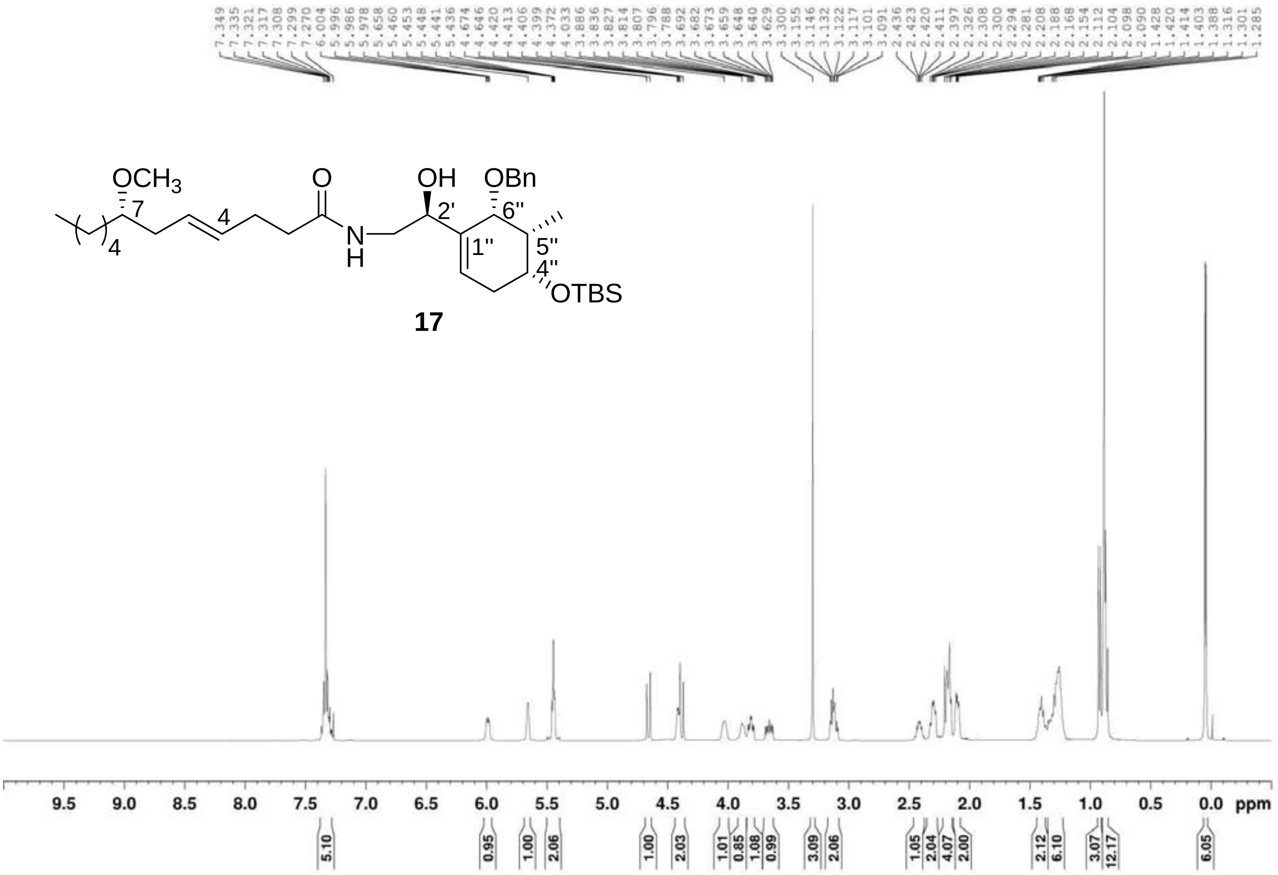


^{1}H–^{1}H COSY NMR ($CDCl_3$, 400 MHz) and NOE NMR ($CDCl_3$, 150 MHz) of **16**

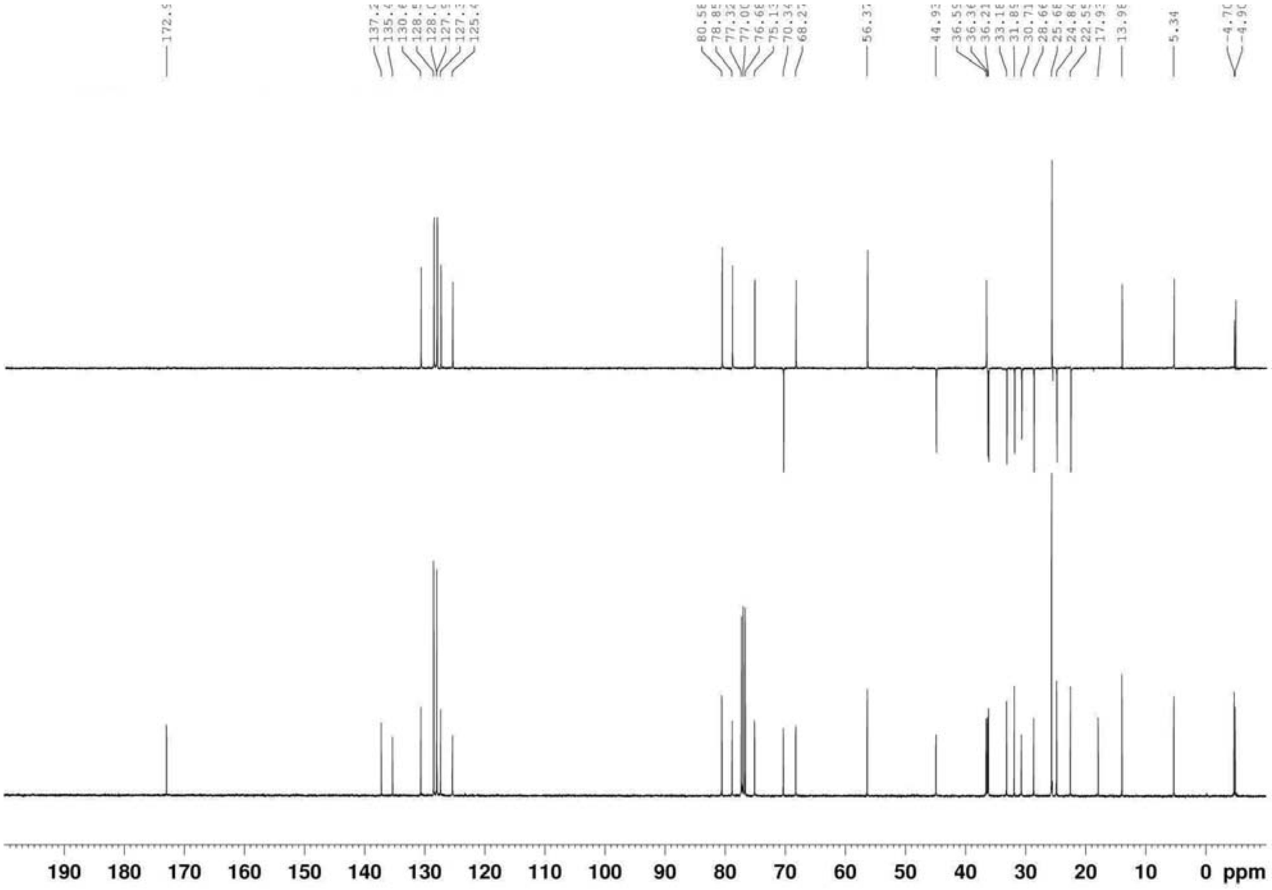




^{1}H NMR (CDCl$_3$, 400 MHz) and ^{13}C NMR (CDCl$_3$, 100 MHz) of **17**

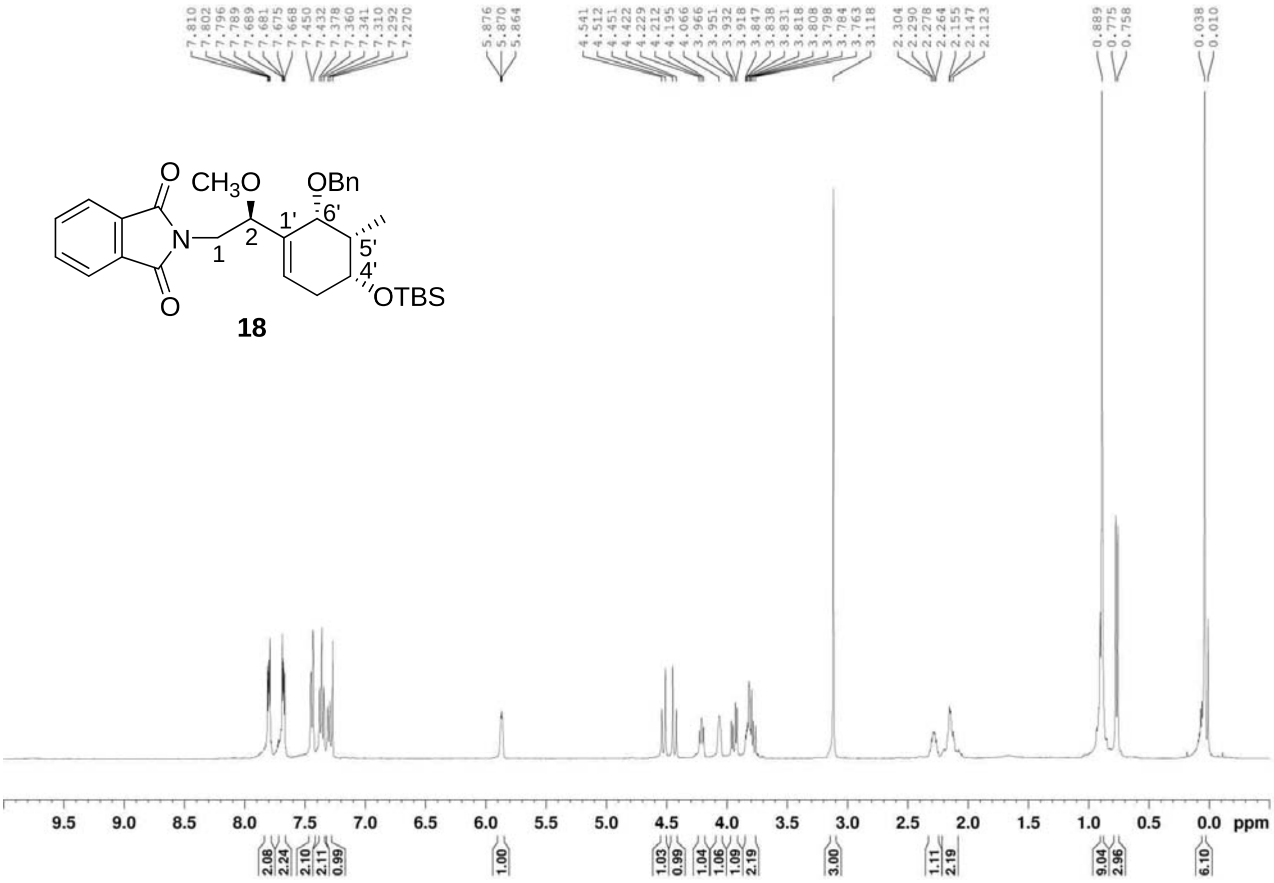


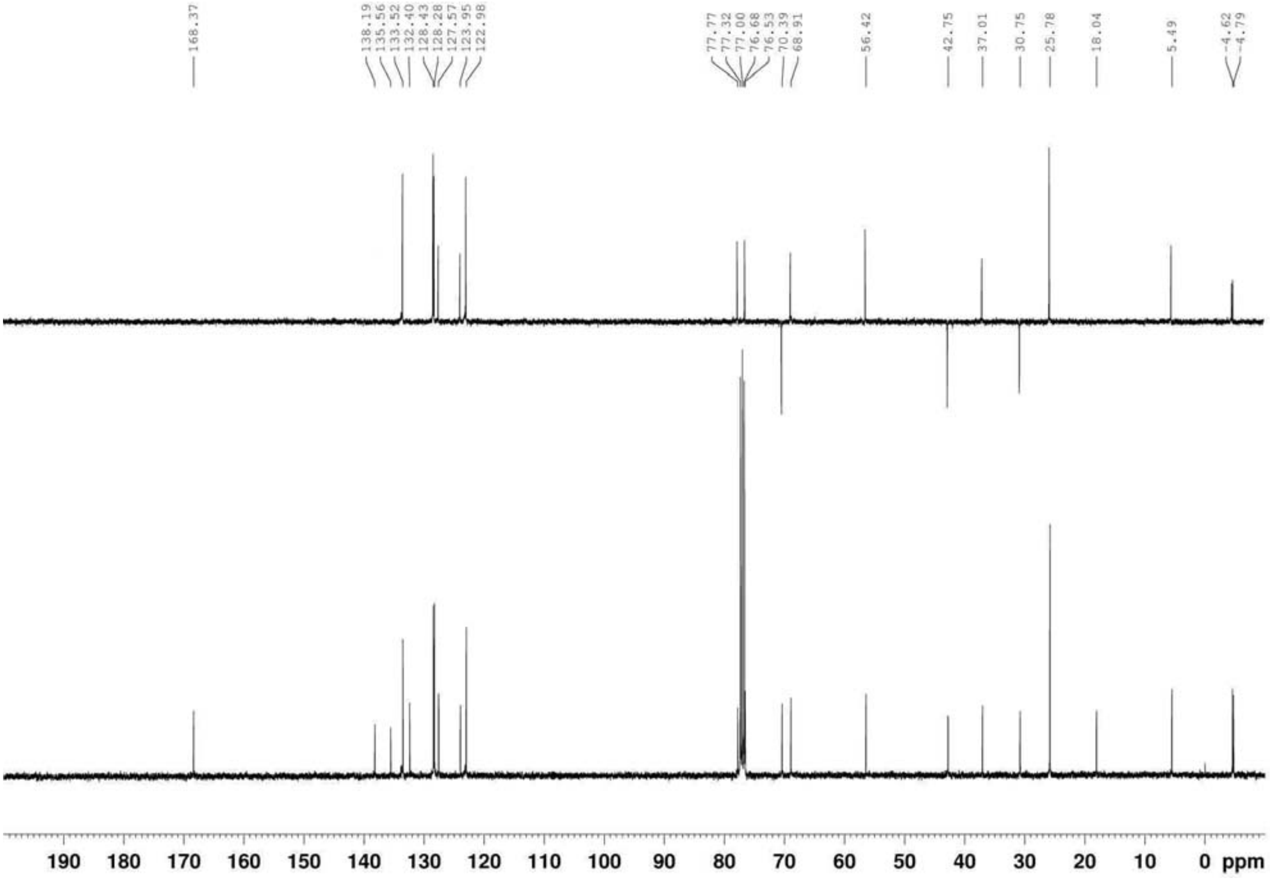
17



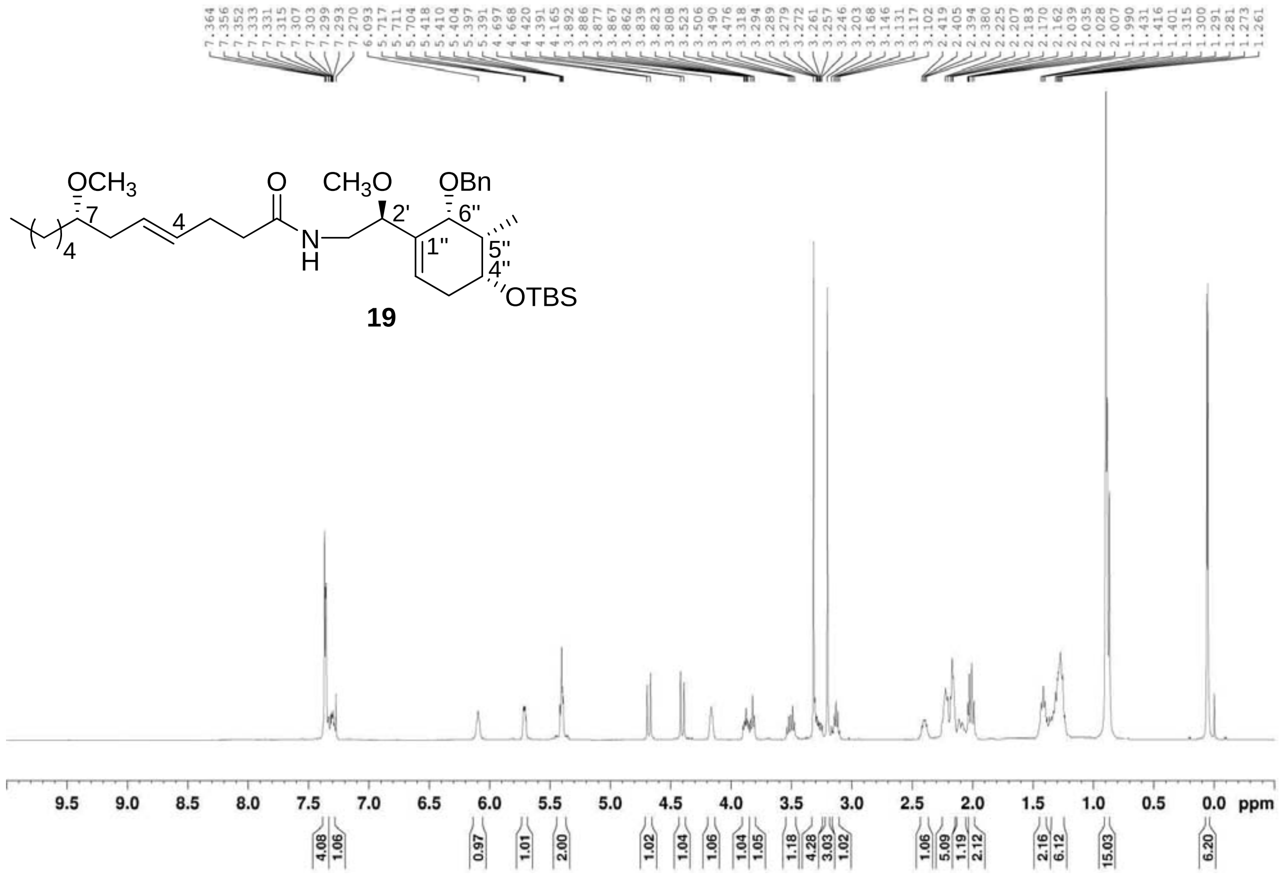
^{1}H NMR (CDCl$_3$, 400 MHz) and ^{13}C NMR (CDCl$_3$, 100 MHz) of **18**

18

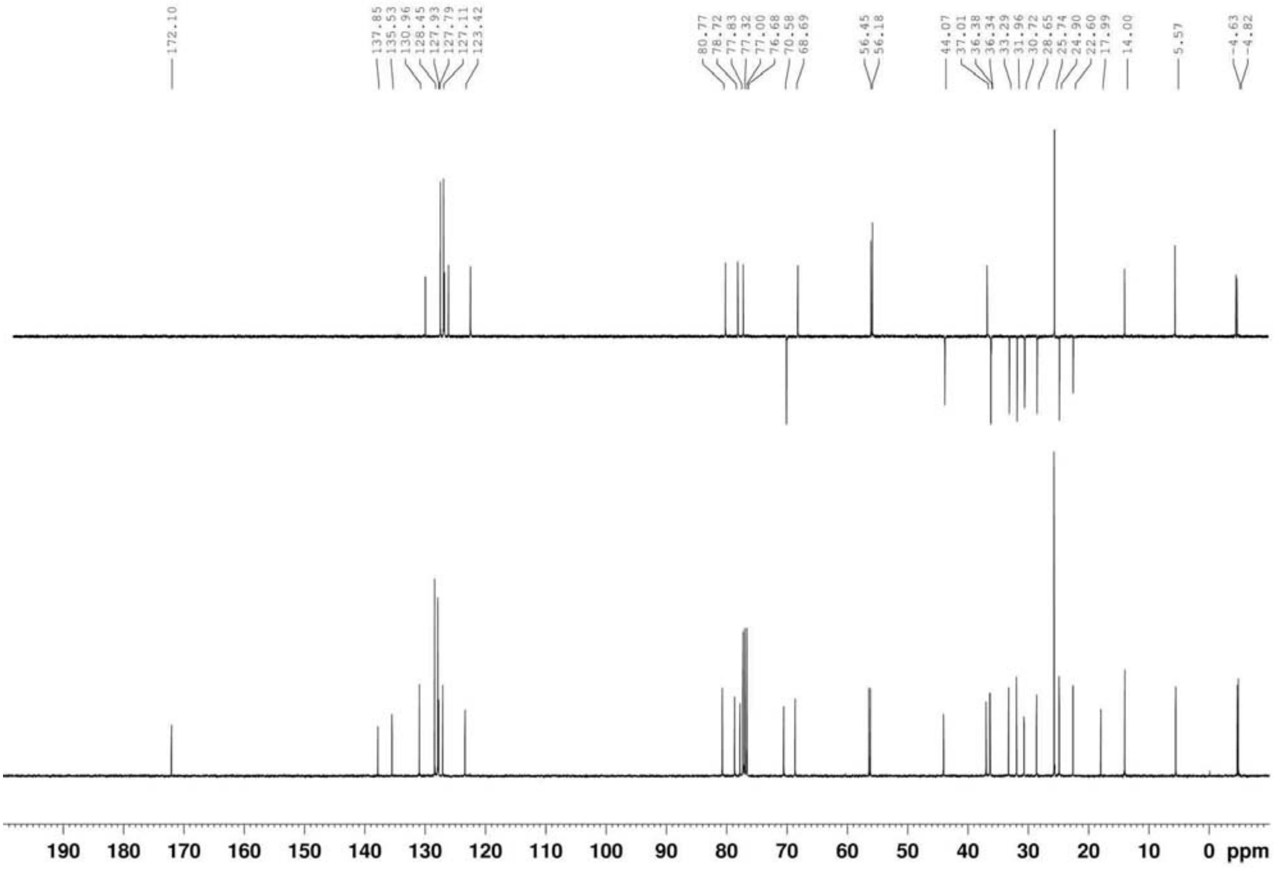




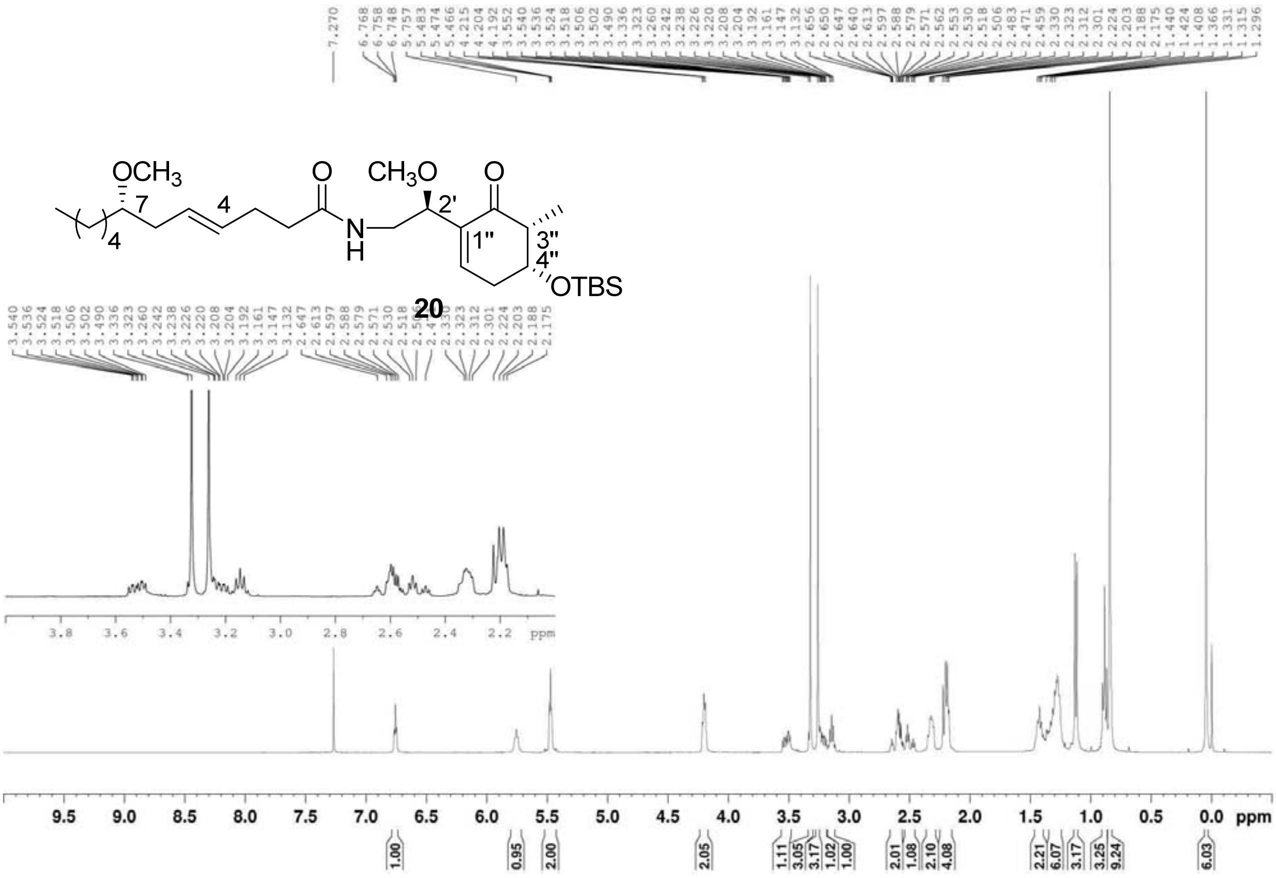
^{1}H NMR (CDCl$_3$, 400 MHz) and ^{13}C NMR (CDCl$_3$, 100 MHz) of **19**



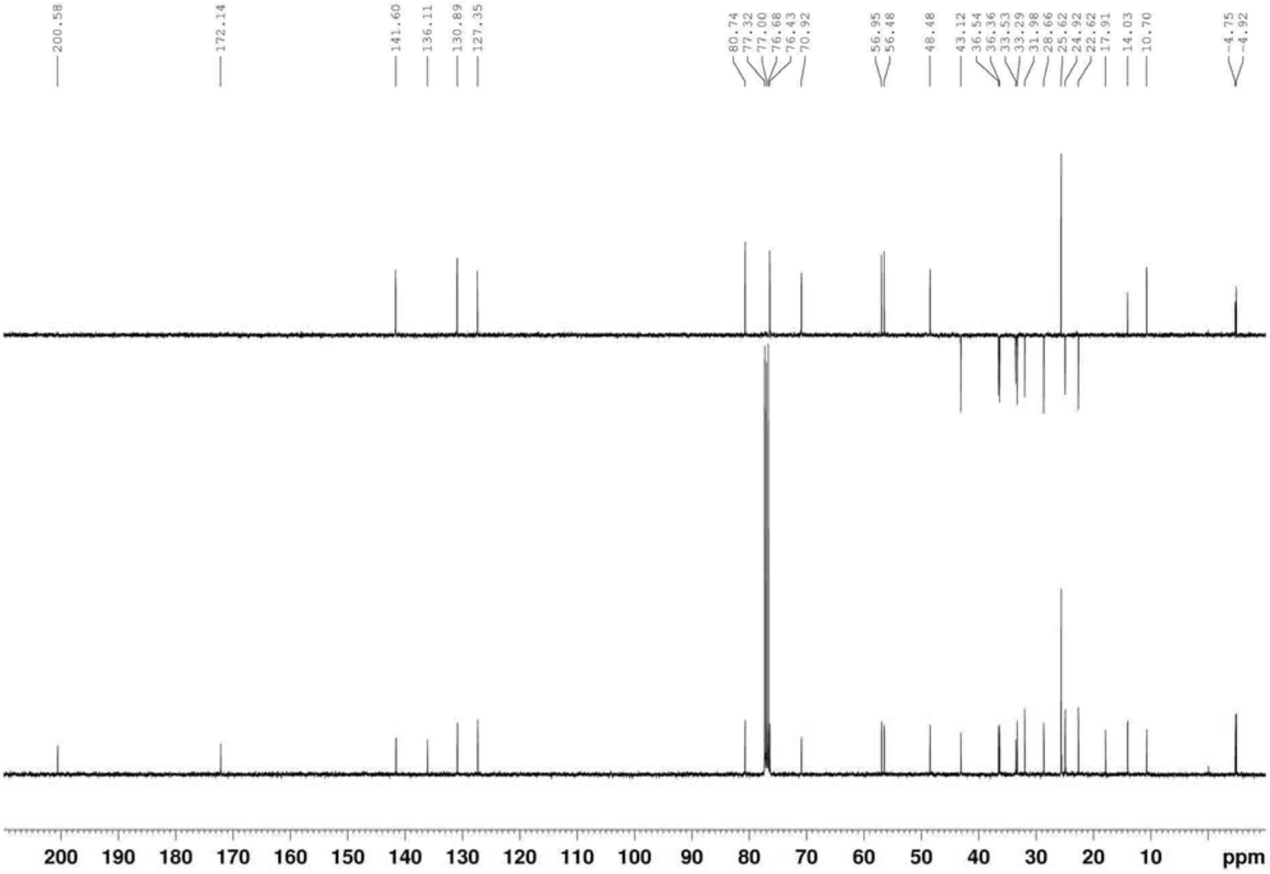
19



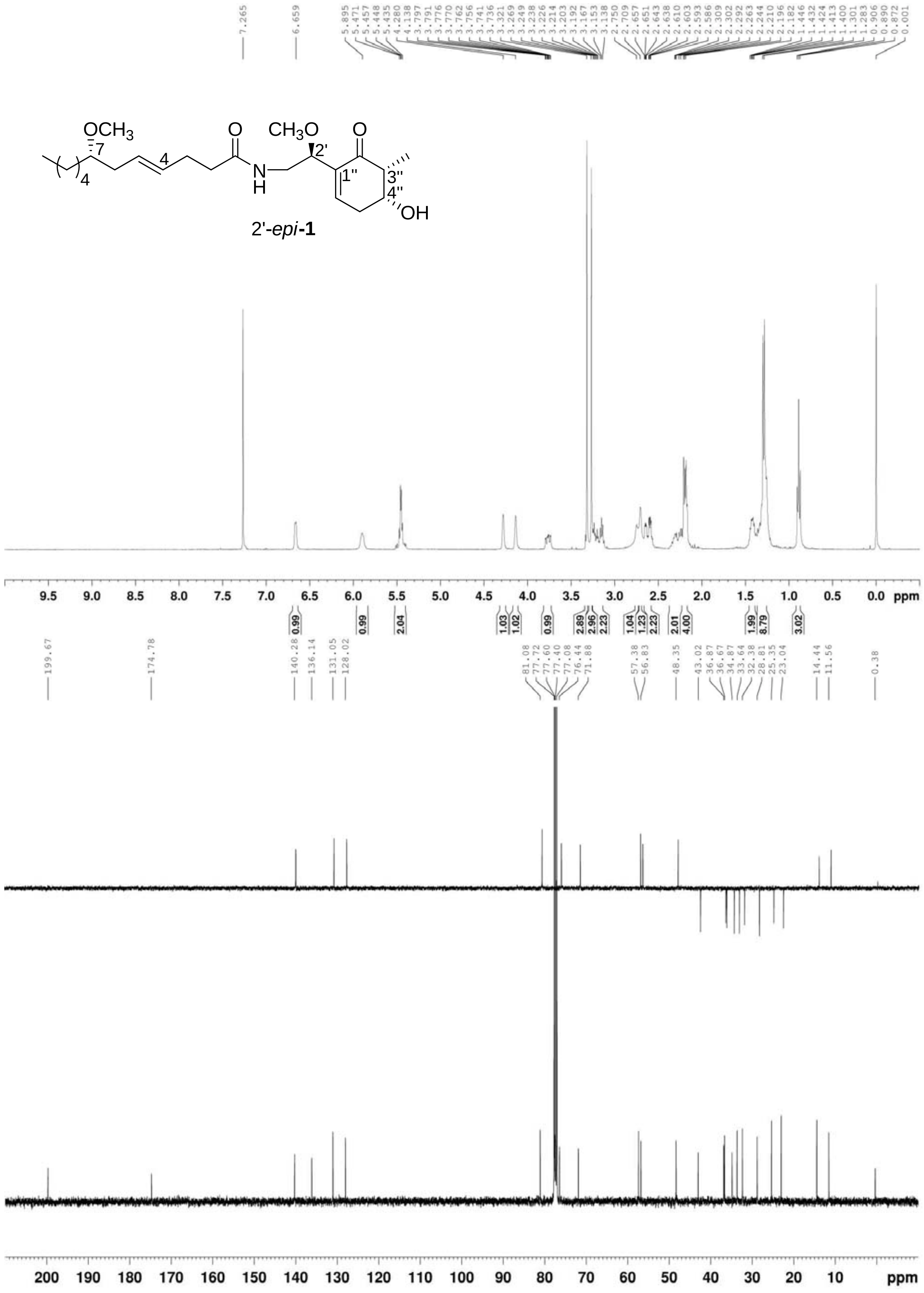
^{1}H NMR (CDCl$_3$, 400 MHz) and ^{13}C NMR (CDCl$_3$, 100 MHz) of **20**



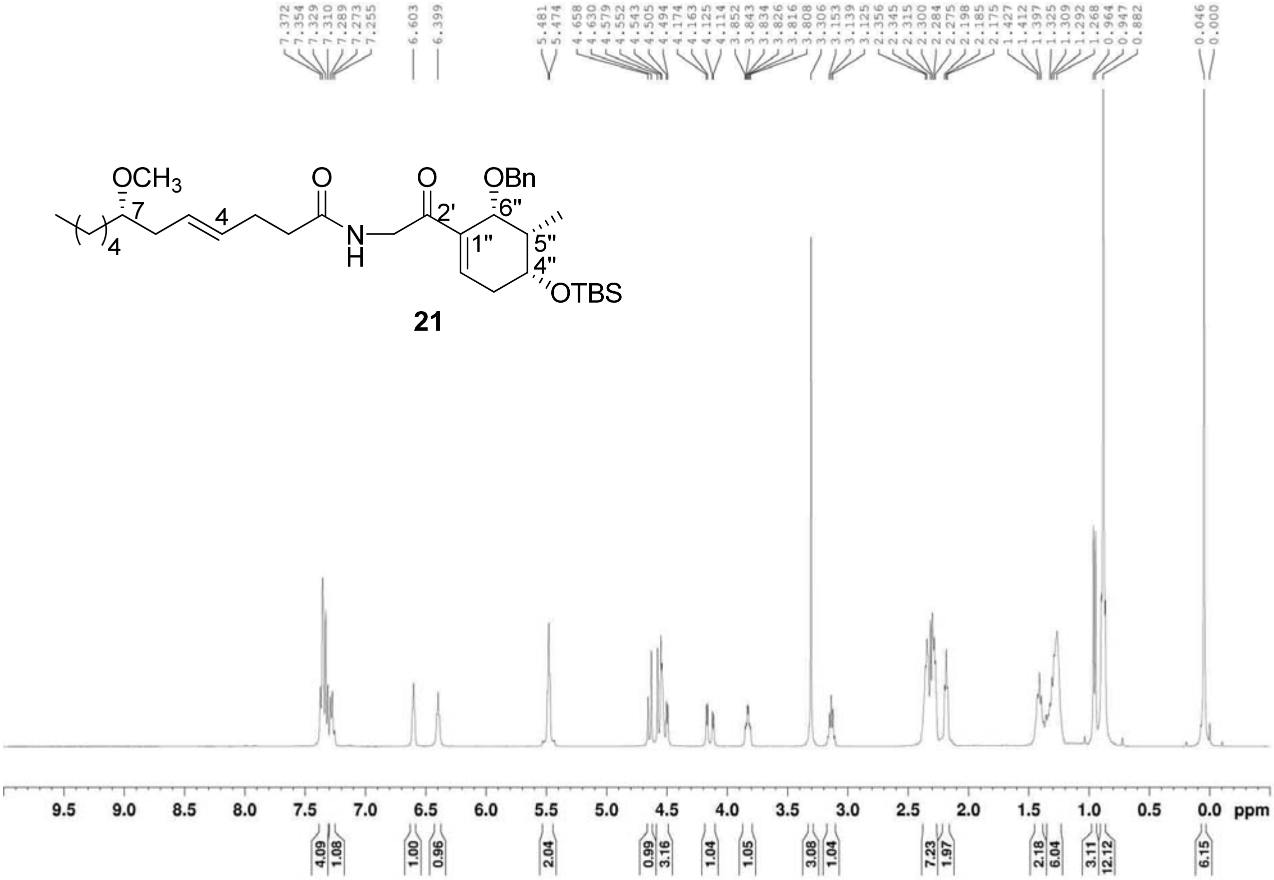
20



^{1}H NMR (CDCl$_3$, 400 MHz) and ^{13}C NMR (CDCl$_3$, 100 MHz) of 2′-*epi*-**1**



^{1}H NMR (CDCl$_3$, 400 MHz) and ^{13}C NMR (CDCl$_3$, 100 MHz) of **21**



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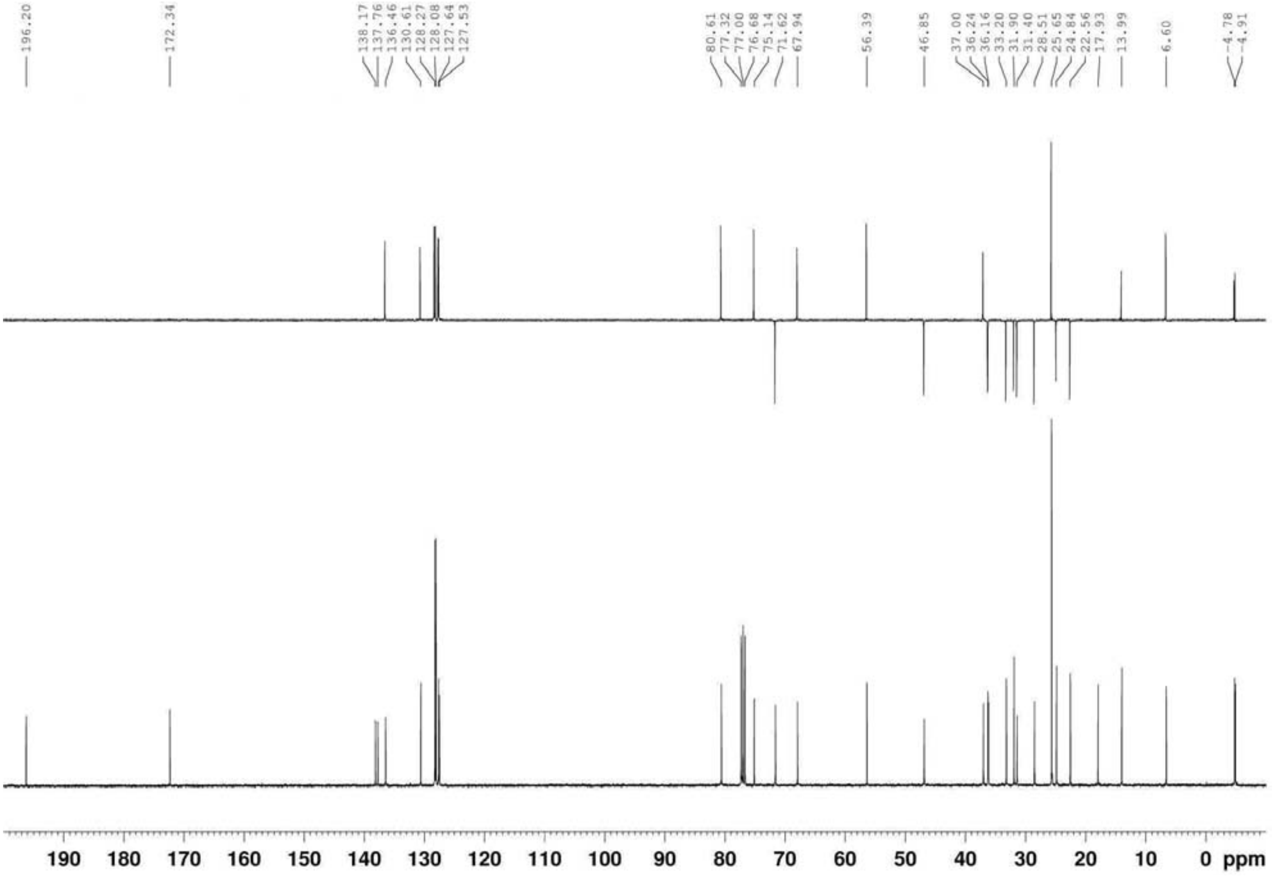
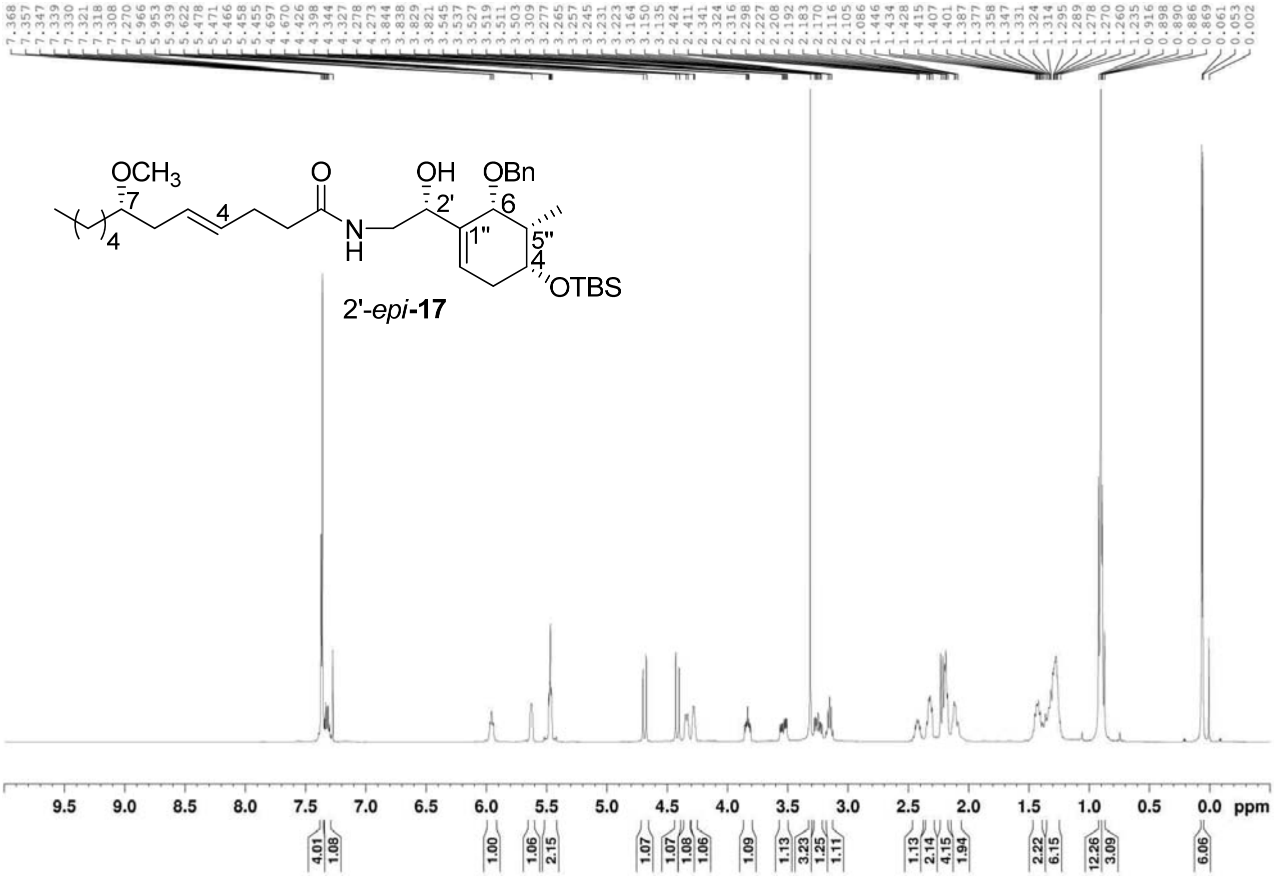
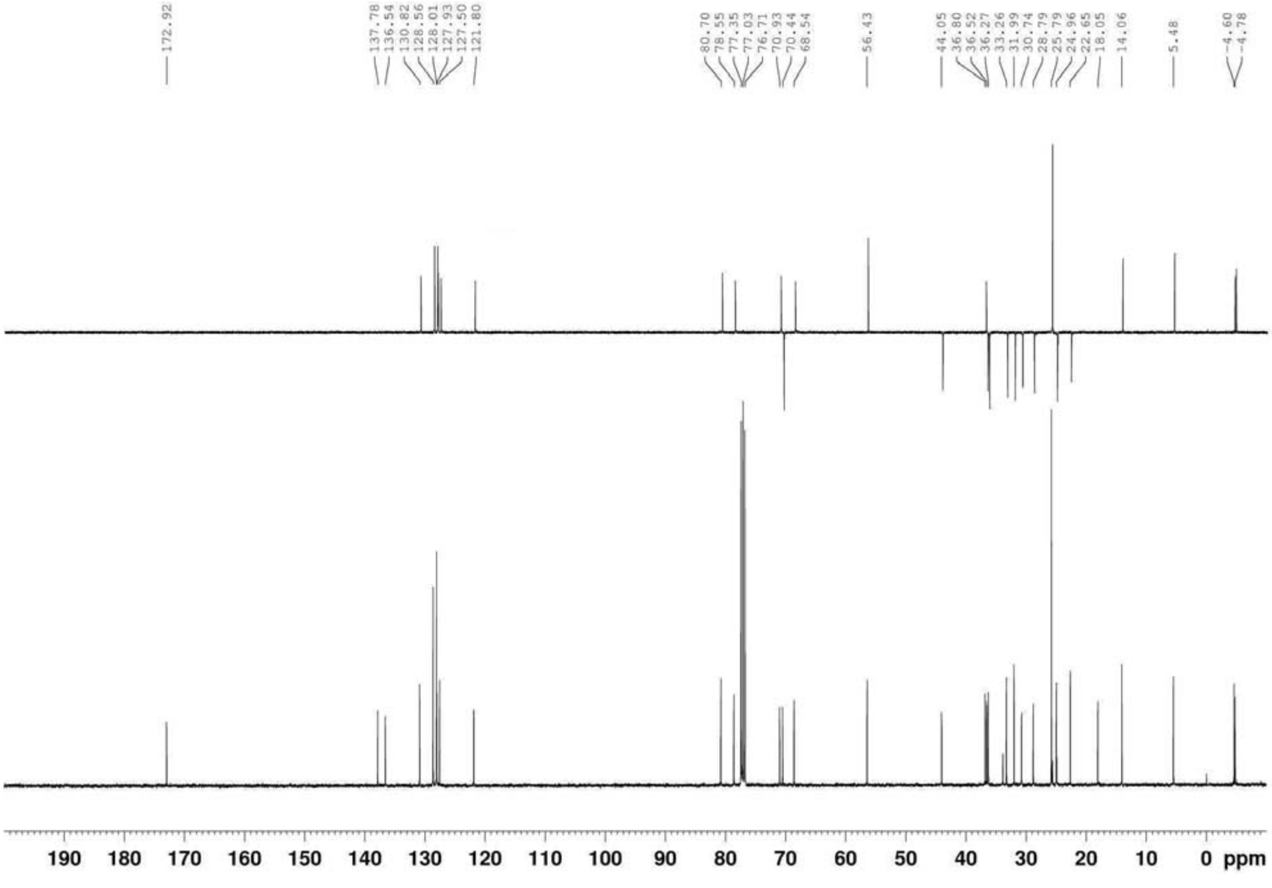
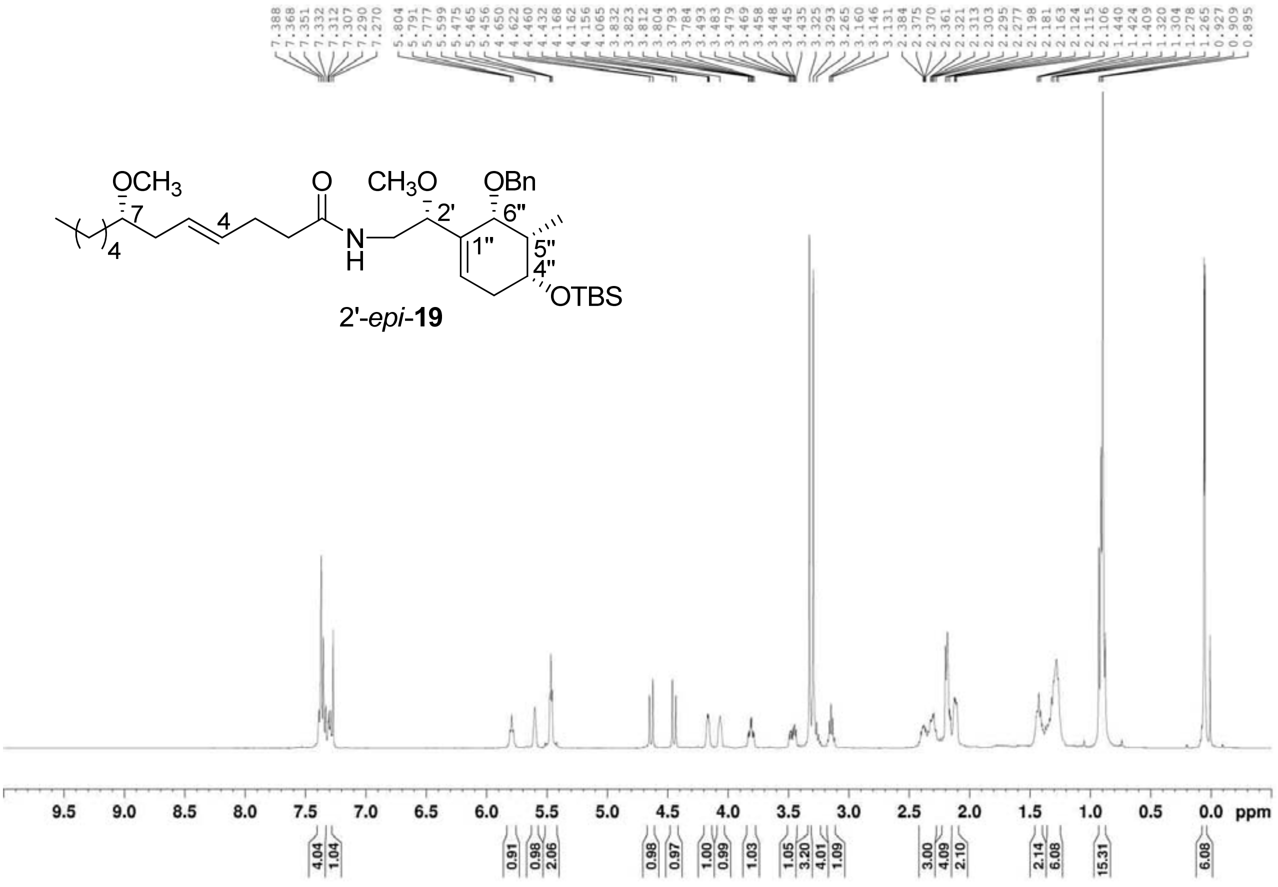


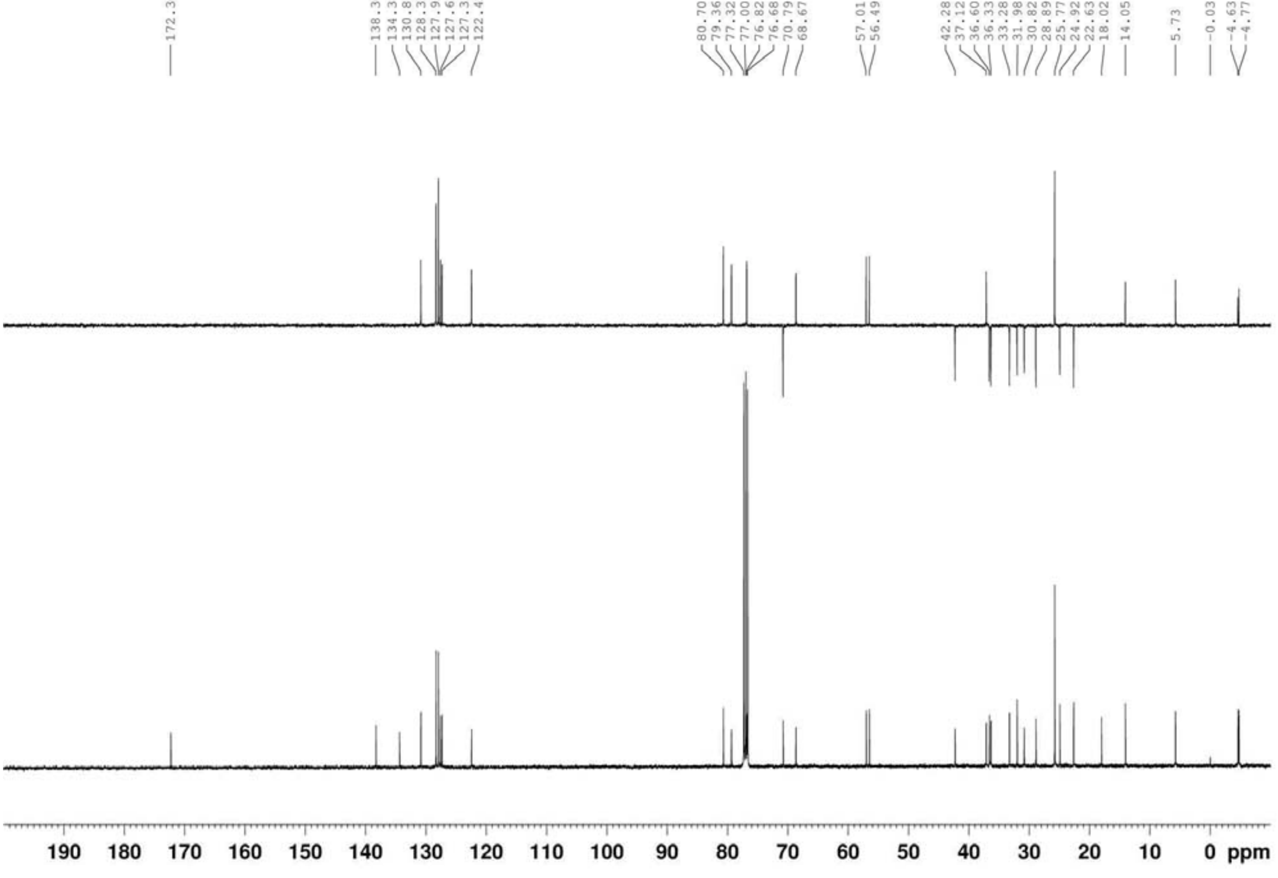
^{1}H NMR (CDCl$_3$, 400 MHz) and ^{13}C NMR (CDCl$_3$, 100 MHz) of 2′-*epi*-**17**



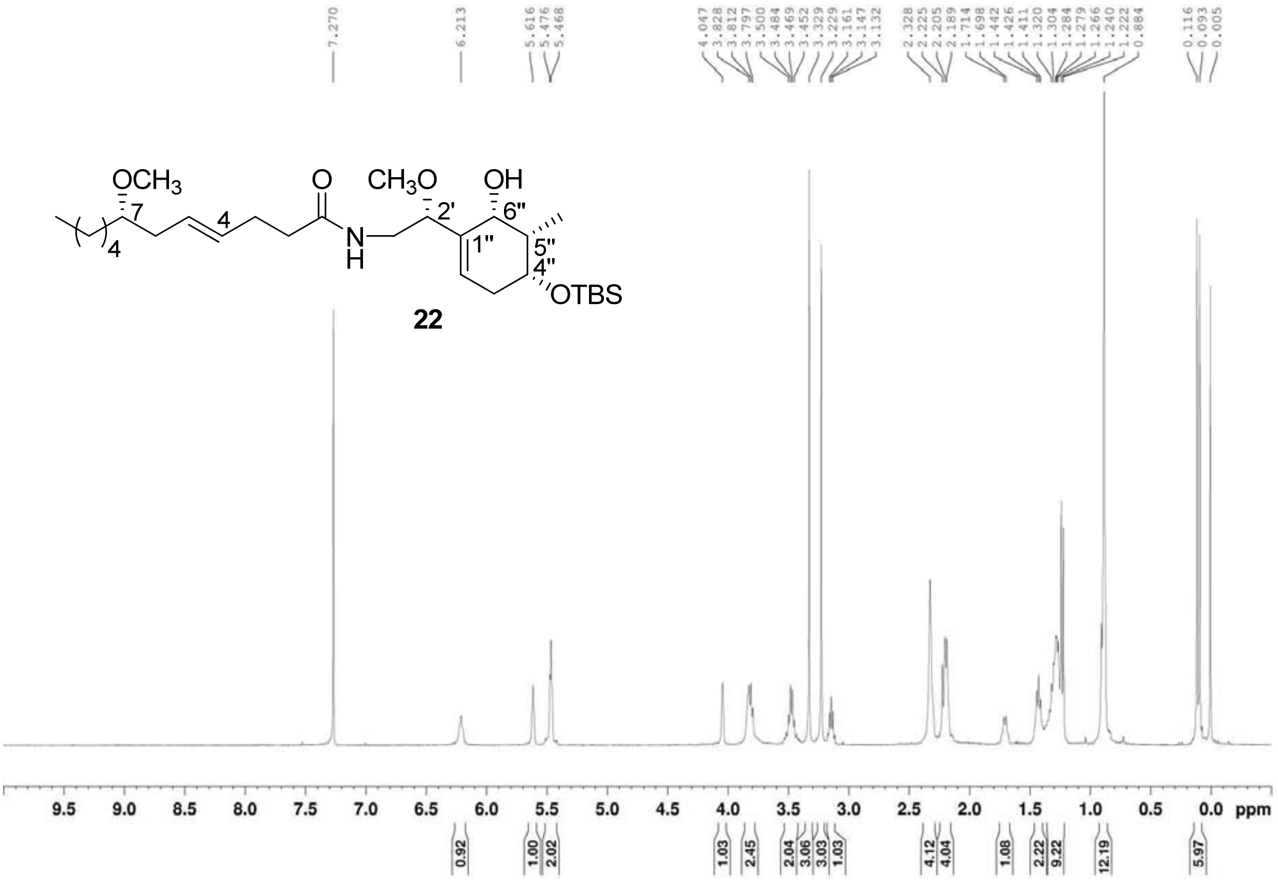


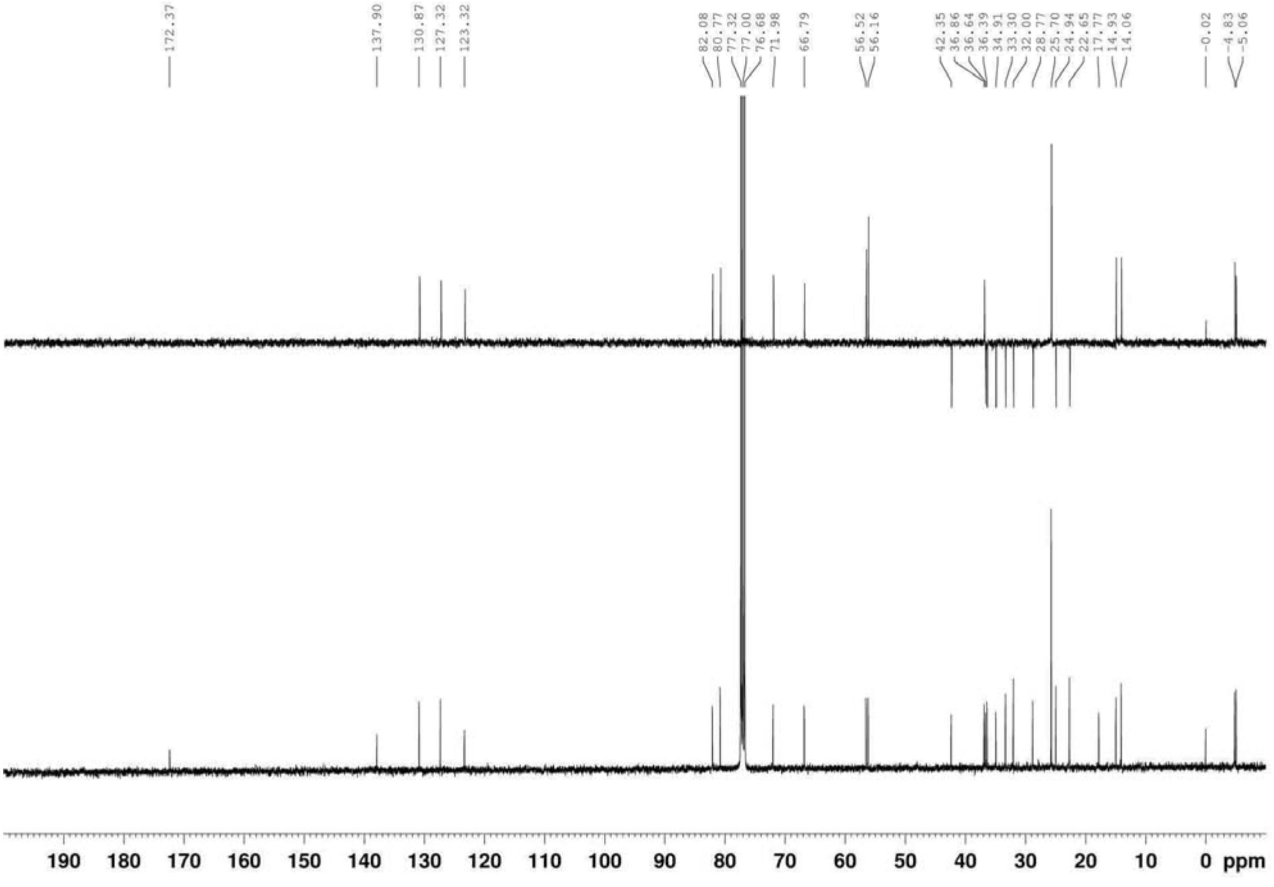
^{1}H NMR (CDCl$_3$, 400 MHz) and ^{13}C NMR (CDCl$_3$, 100 MHz) of 2′-*epi*-**19**



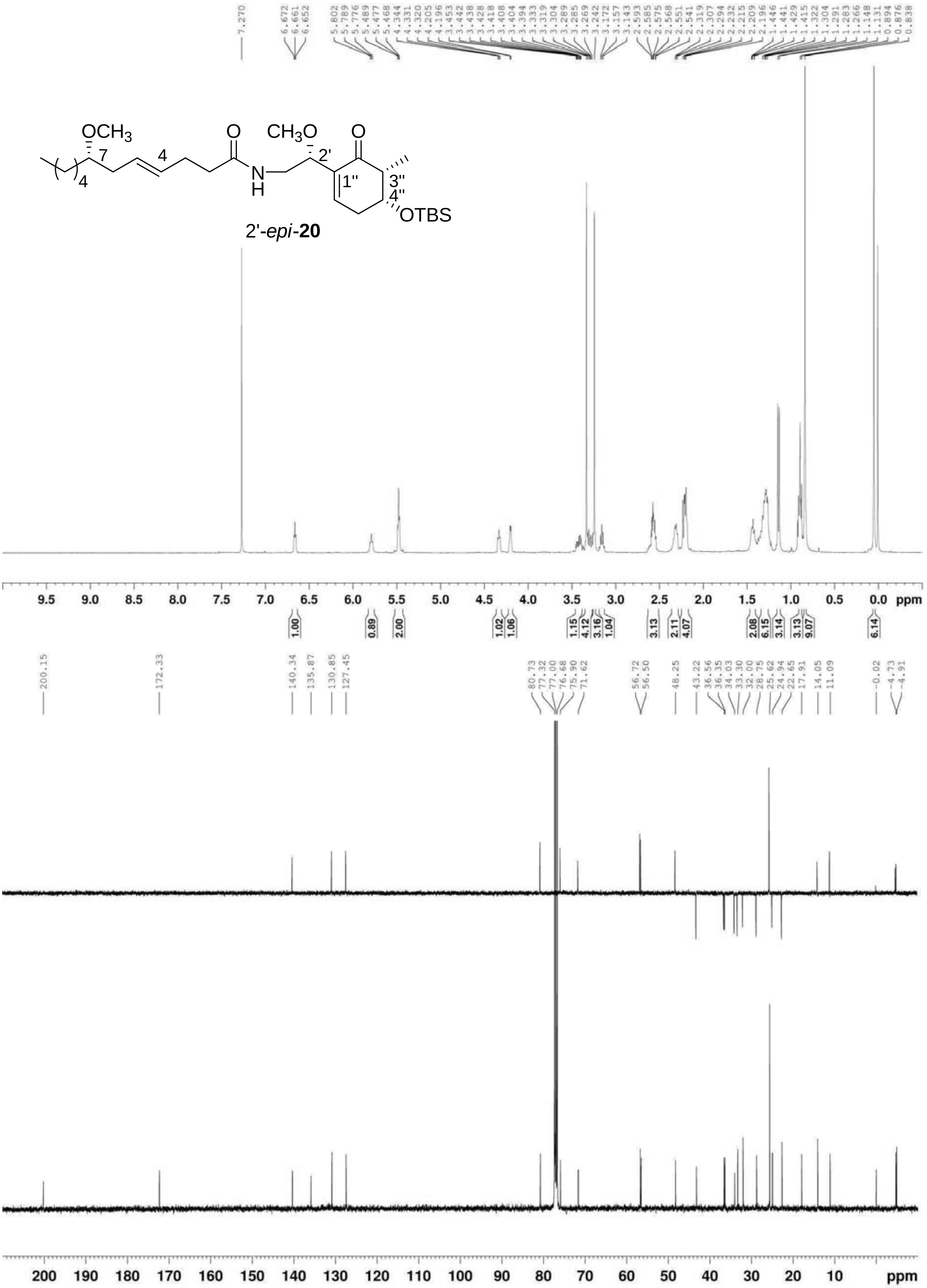


^{1}H NMR (CDCl$_3$, 400 MHz) and ^{13}C NMR (CDCl$_3$, 100 MHz) of **20**

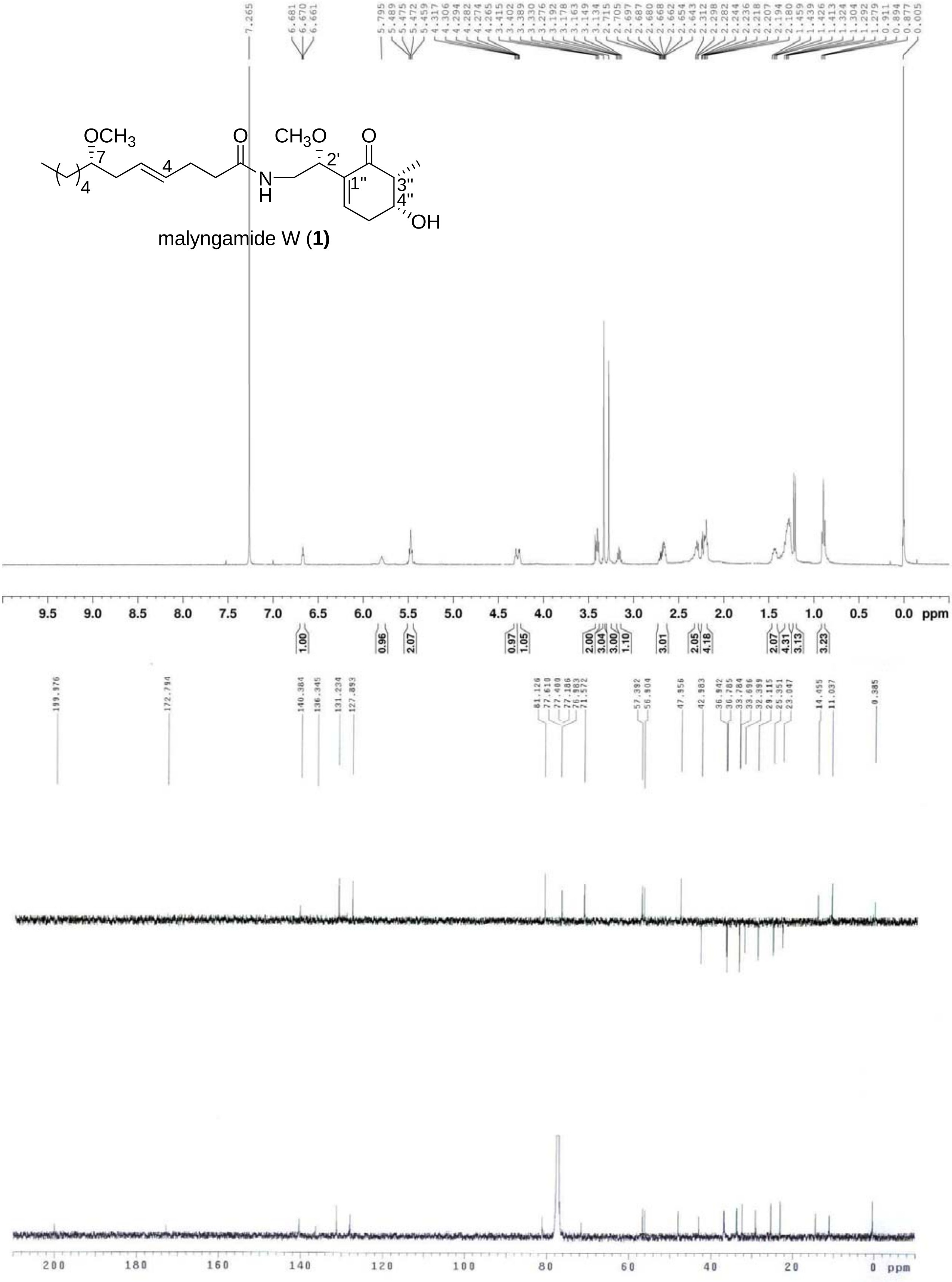




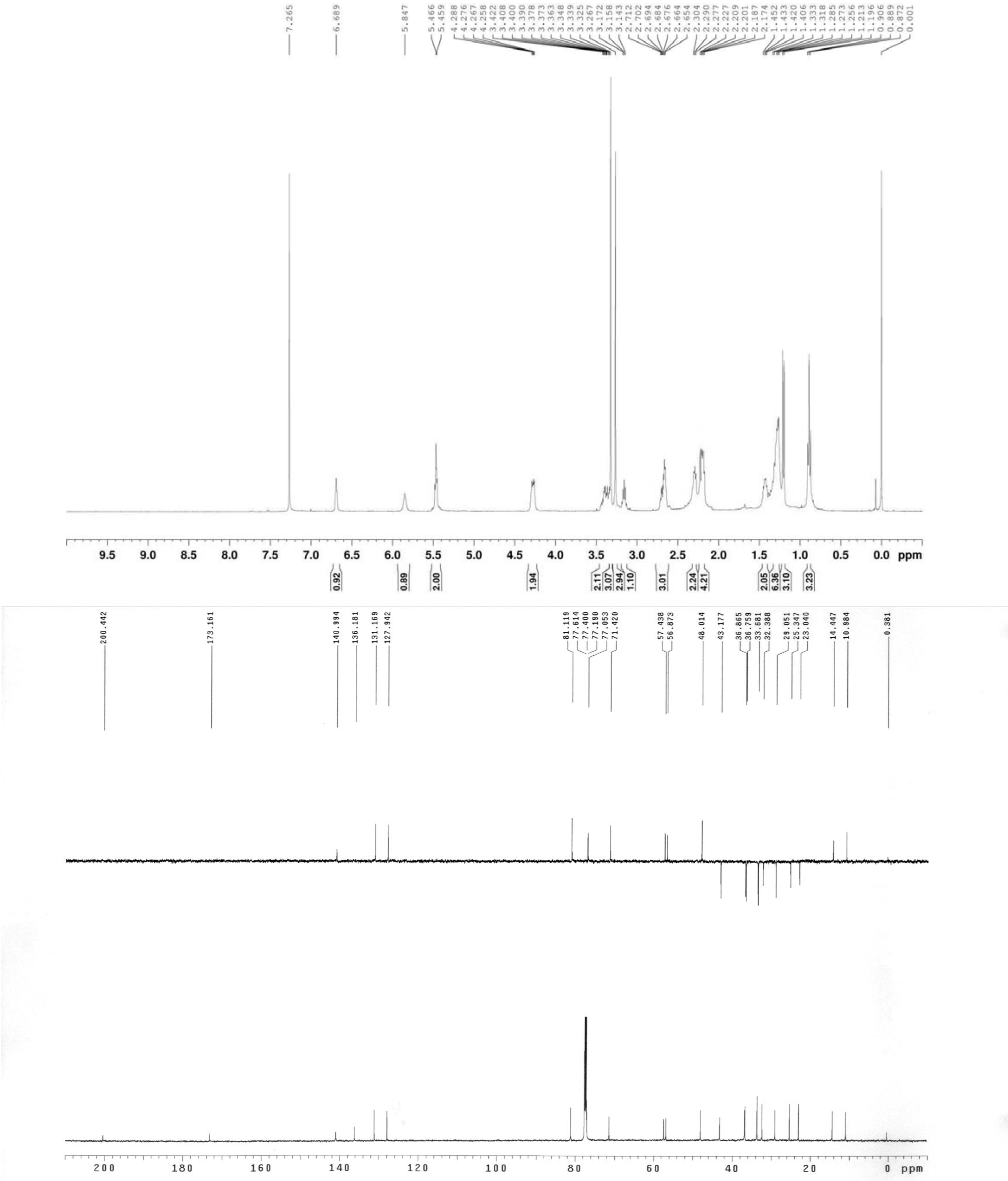
^{1}H NMR (CDCl$_3$, 400 MHz) and ^{13}C NMR (CDCl$_3$, 100 MHz) of 2′-*epi*-**20**



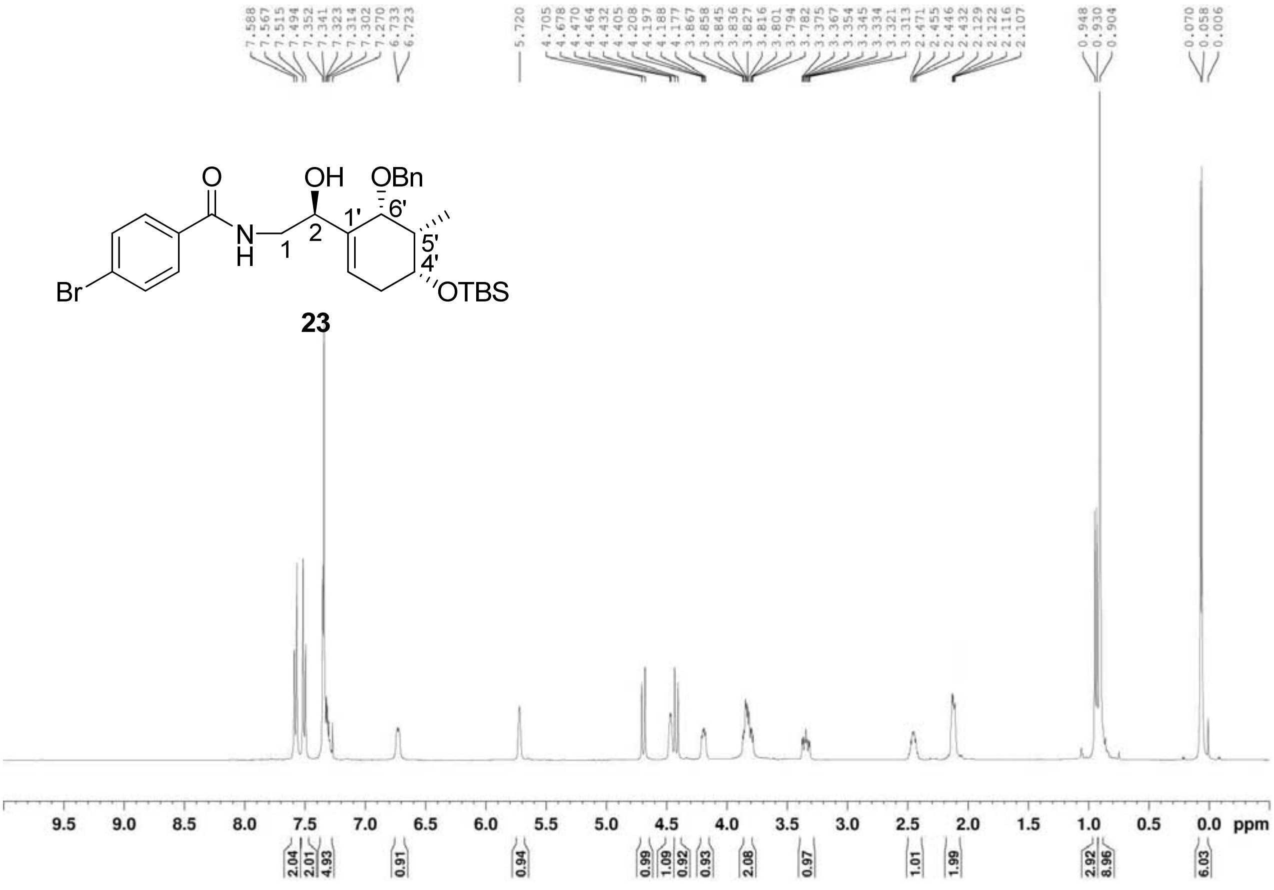
^{1}H NMR ($CDCl_3$, 400 MHz) and ^{13}C NMR ($CDCl_3$, 150 MHz) of **1** (c = 1.6 mg/mL)

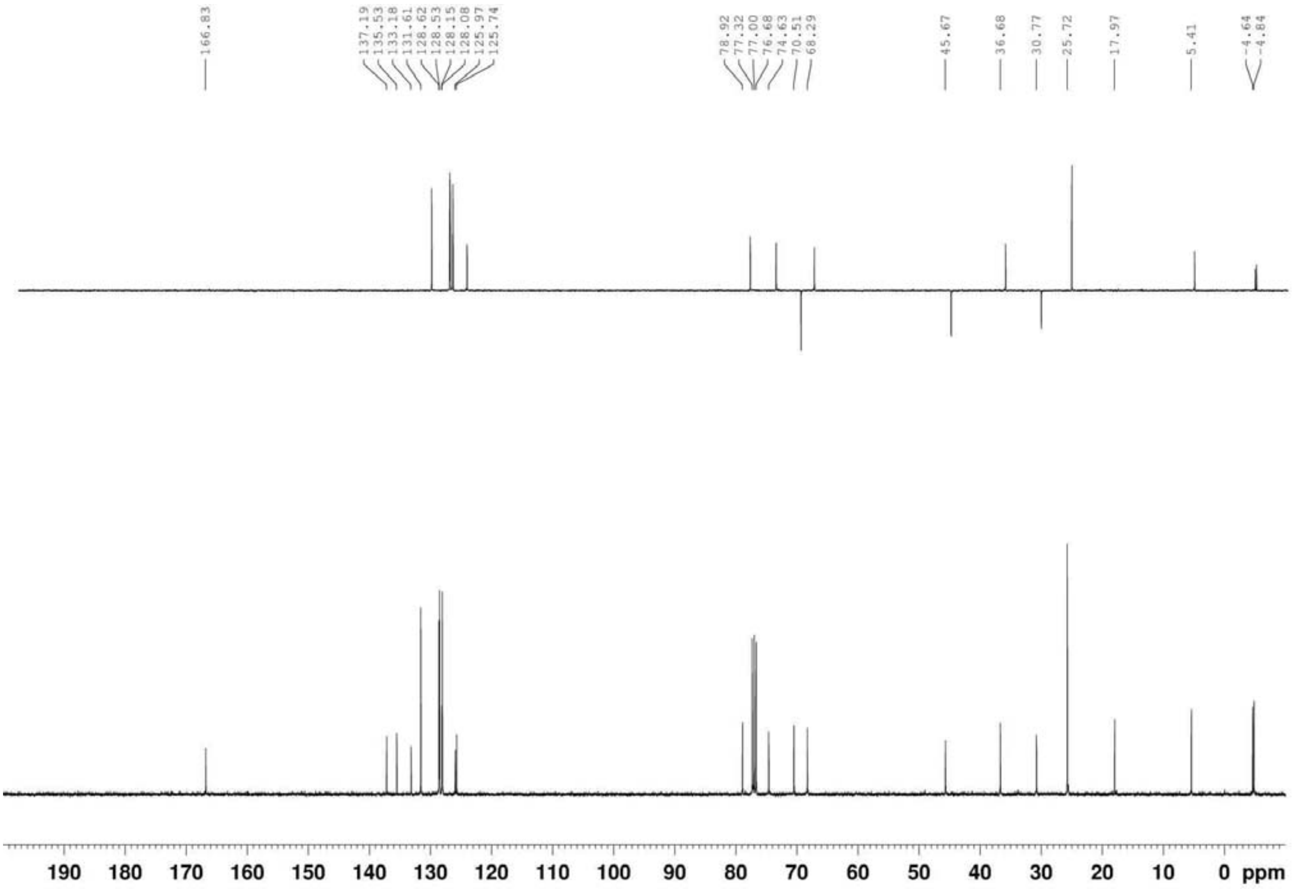


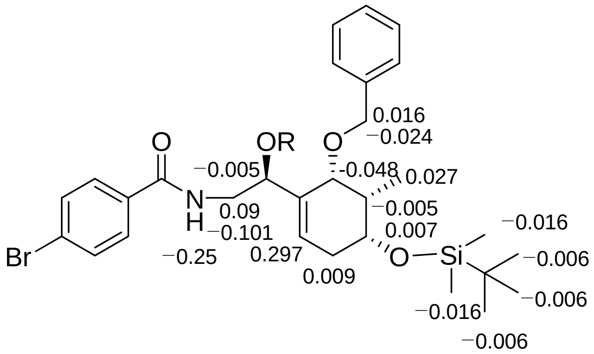
^{1}H NMR (CDCl$_3$, 400 MHz) and ^{13}C NMR (CDCl$_3$, 150 MHz) of **1** (c = 3.3 mg/mL)



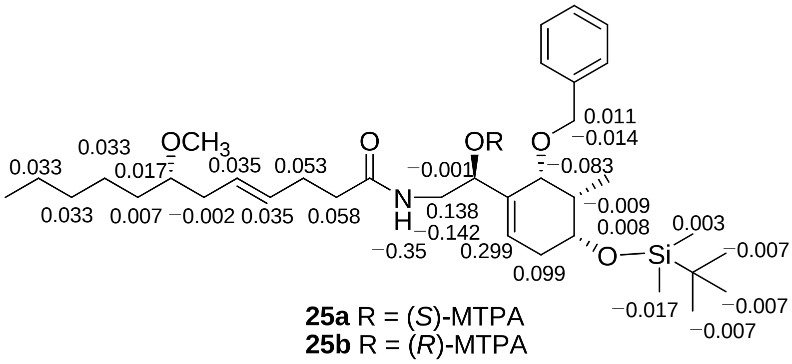
^{1}H NMR (CDCl$_3$, 400 MHz) and ^{13}C NMR (CDCl$_3$, 100 MHz) of **23**







24a R = (*S*)-MTPA
24b R = (*R*)-MTPA

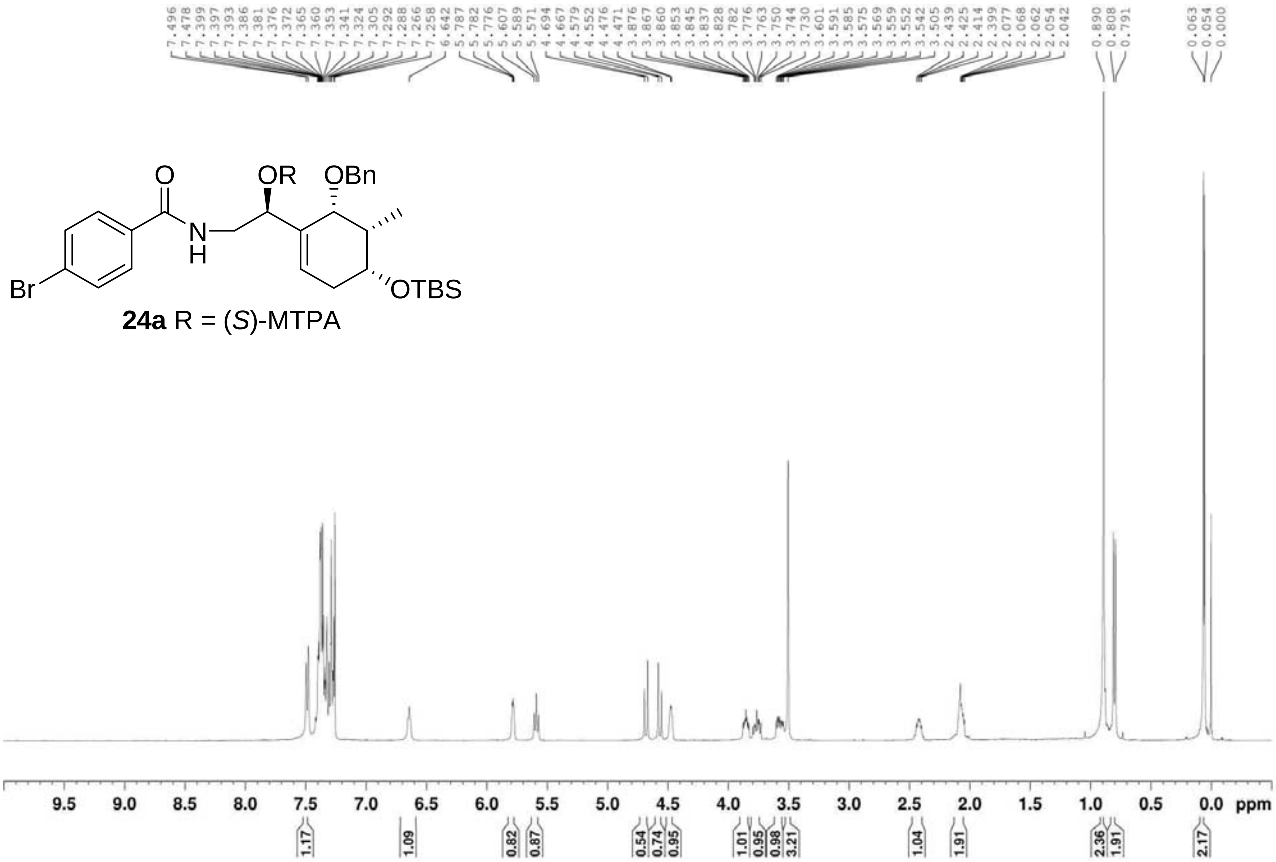


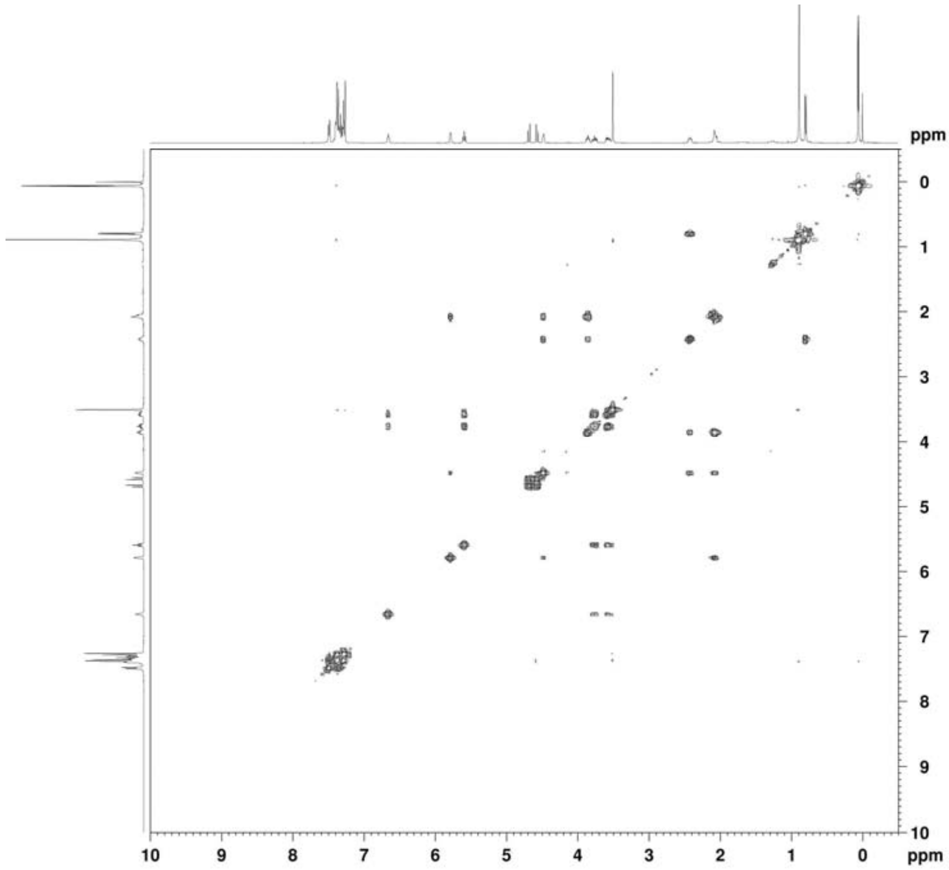
25a R = (*S*)-MTPA
25b R = (*R*)-MTPA

FIGURE 1. The determination of absolute configuration of **3b** and **17** using mosher′s method.[5] (compound **24a** and **24b** were derived from compound **23**, compound **25a** and **25b** were derived from compound **17**)

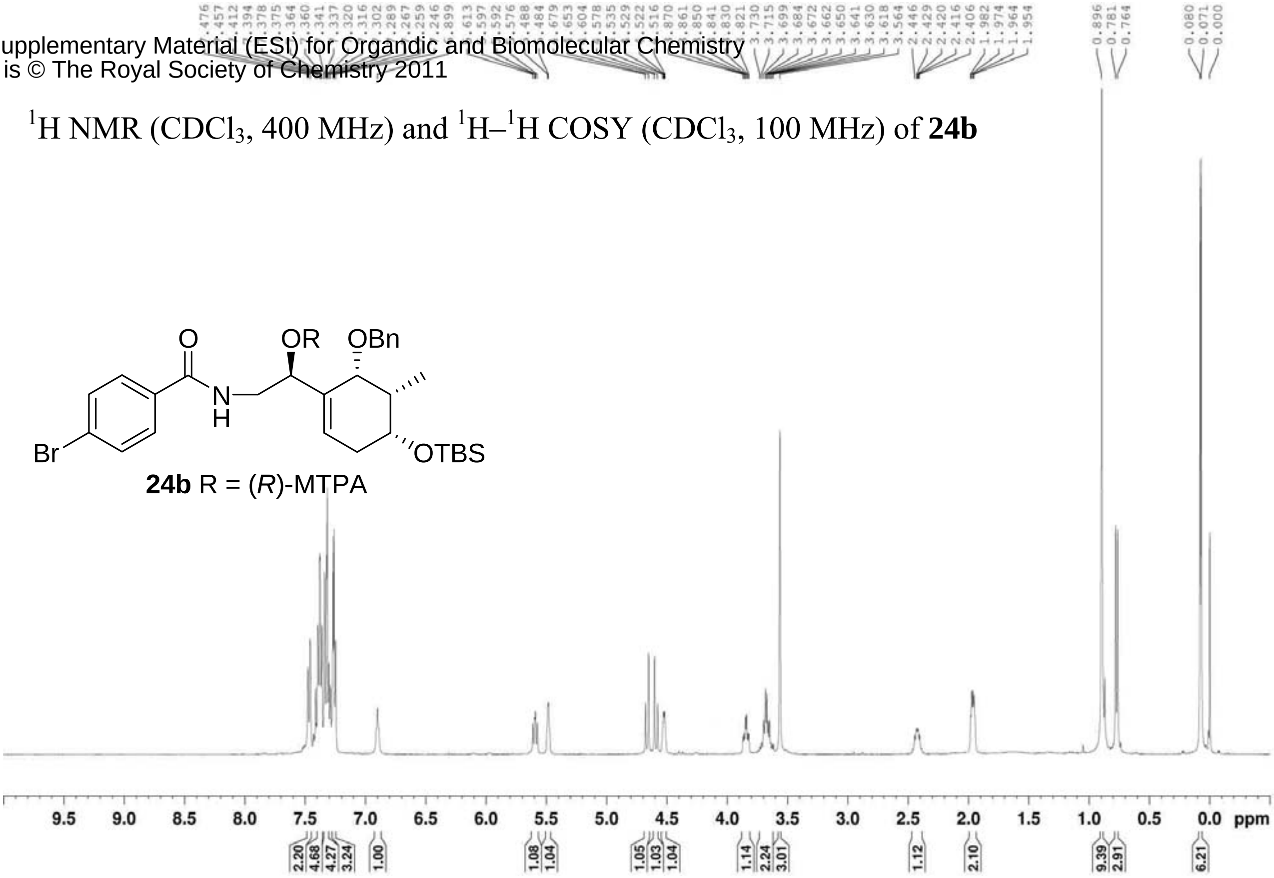
^{1}H NMR (CDCl$_3$, 400 MHz) and ^{1}H–^{1}H COSY (CDCl$_3$, 100 MHz) of **24a**

24a R = (*S*)-MTPA

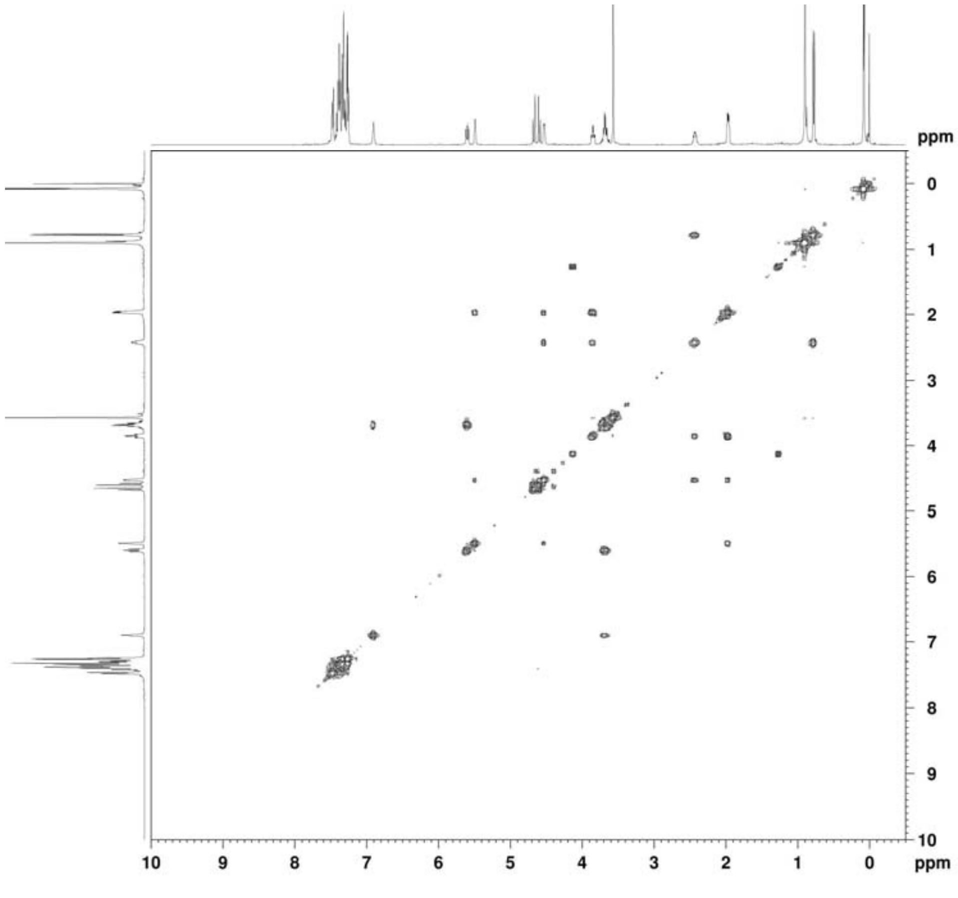




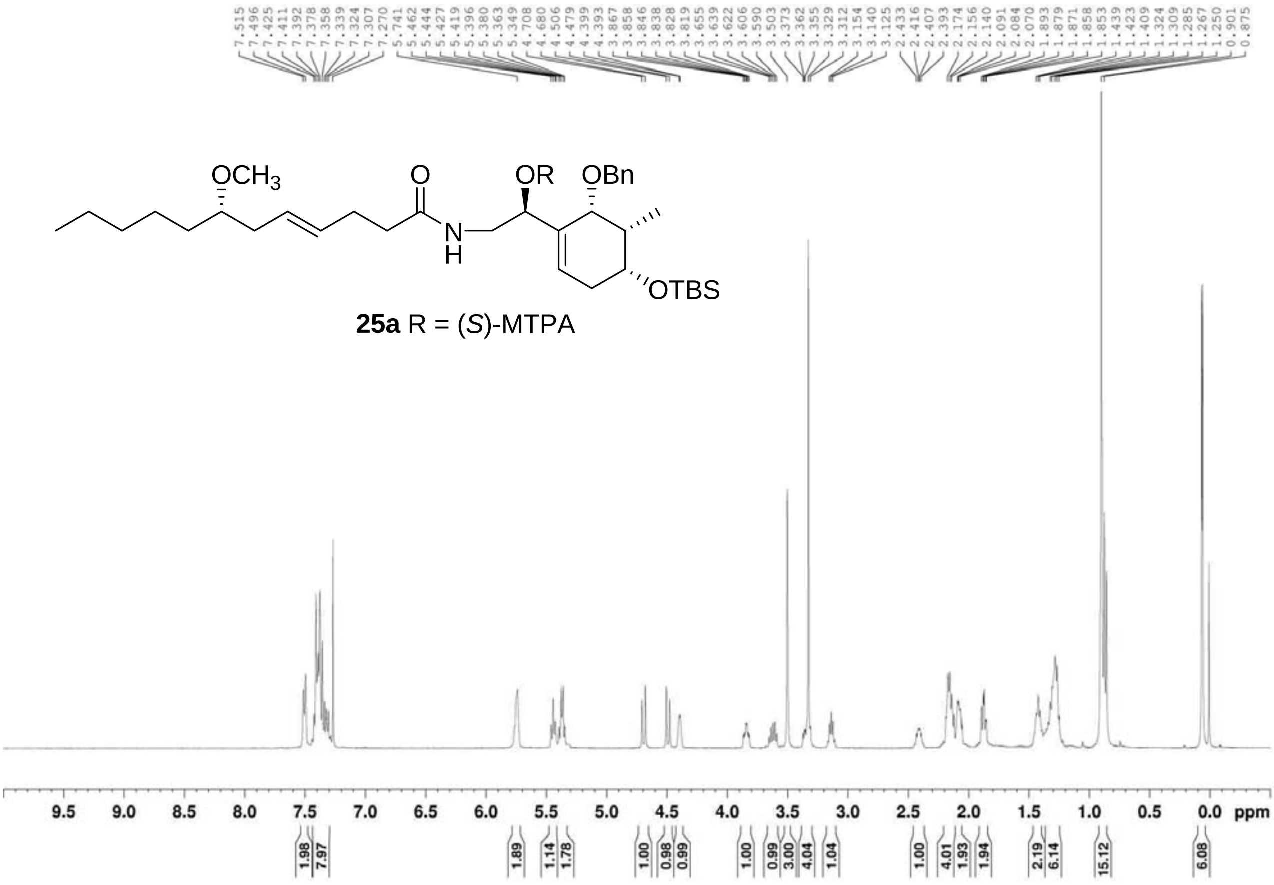
^{1}H NMR (CDCl$_3$, 400 MHz) and ^{1}H–^{1}H COSY (CDCl$_3$, 100 MHz) of **24b**



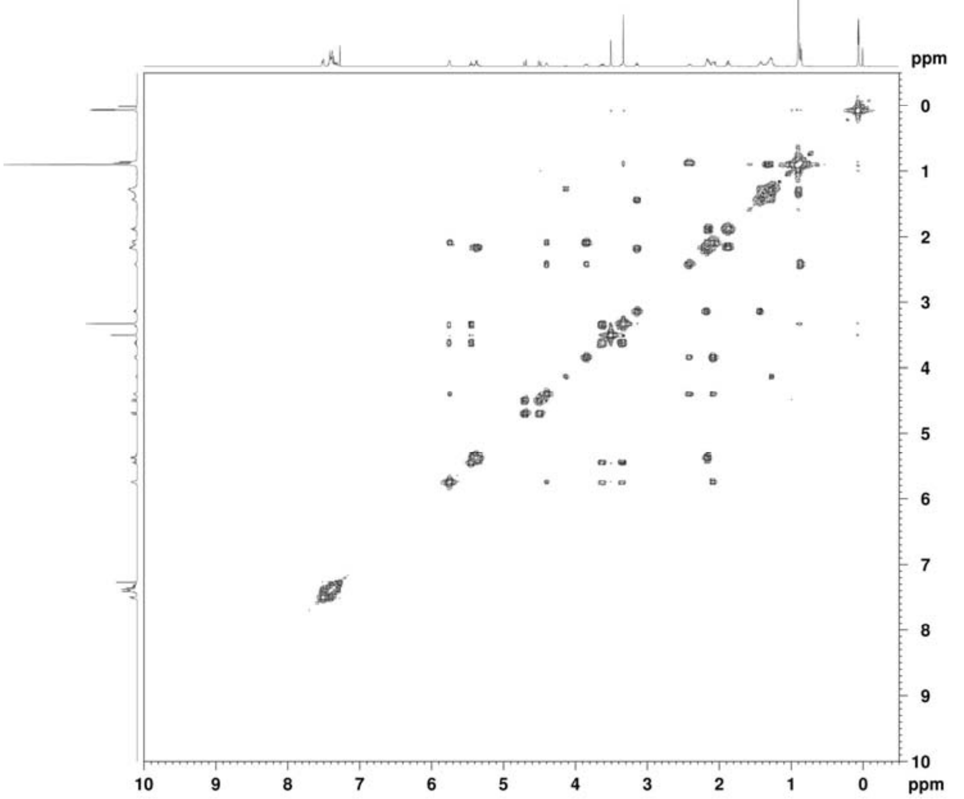
24b R = (*R*)-MTPA



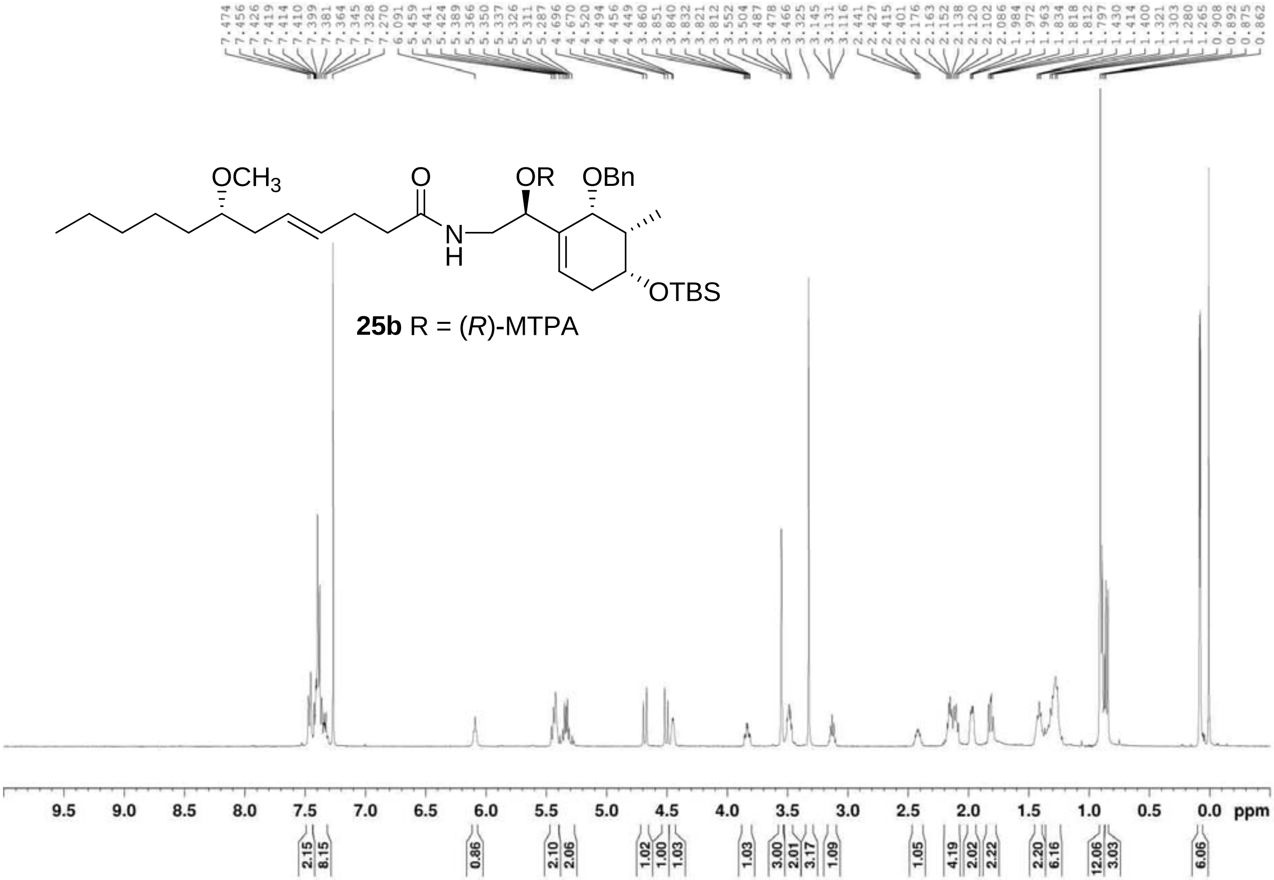
^{1}H NMR (CDCl$_3$, 400 MHz) and ^{1}H–^{1}H COSY (CDCl$_3$, 100 MHz) of **25a**



25a R = (*S*)-MTPA



^{1}H NMR ($CDCl_3$, 400 MHz) and ^{1}H–^{1}H COSY ($CDCl_3$, 100 MHz) of **25b**



25b R = (*R*)-MTPA