Supplementary Material

Stereoselective synthesis of megastigmatrien-3-one using catalytic olefin isomerization as key step

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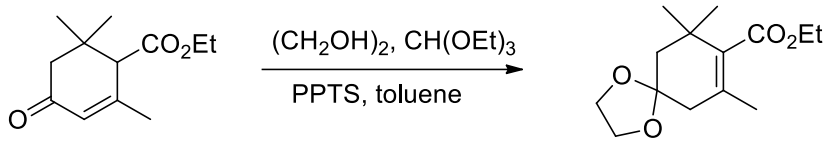
1 General Information

The NMR spectra were recorded on Bruker AC-500 spectrometer (500 MHz for ^{1}H NMR and 125 MHz for ^{13}C NMR) with $CDCl_3$ as the solvent and TMS as internal reference. ^{1}H NMR spectral data were reported as follows: chemical shift (δ, ppm), multiplicity, integration, and coupling constant (Hz). ^{13}C NMR spectral data were reported in terms of the chemical shift. The following abbreviations were used to indicate multiplicities: s = singlet; d = doublet; t = triplet; q = quartet; m = multiplet. Low-resolution mass spectra were obtained on a Shimadzu LCMS-2010EV spectrometer in ESI mode and reported as m/z. High-resolution mass spectra (HRMS) were recorded on a Bruker Daltonics, Inc. APEXIII 7.0 TESLA FTMS instrument. GC analysis was detected on an Agilent 8890B instrument. Melting points were obtained on a X-4 digital melting point apparatus without correction. Purification of products was accomplished by column chromatography packed with silica gel. Unless otherwise stated, all reagents were commercially purchased and used without further purification.

2 General Procedure

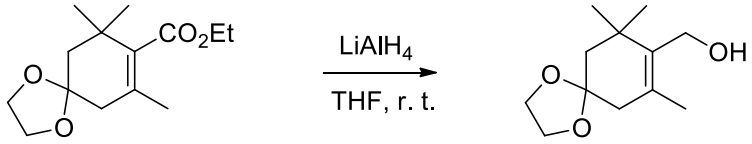
a) **General Procedure for the synthesis of compound 2**



1 **2**

A round bottom flask was charged with 3,5,5-trimethoxy-2-cyclohexen-1-one-4-carboxylic acid ethyl ester **1** (1.05 g, 5 mmol), Ethylene glycol (40 mmol, 3.09 mL), triethyl orthoformate (20 mmol, 3.32 mL), 4-methylbenzenesulfonic acid pyridine (0.5 mmol, 120.6 mg) in toluene (60 mL) , and the reaction vessel placed in an oil bath at 120 °C for 15 h. After the reaction was completed, it was cooled to room temperature and monitored by TLC. The solvent was then removed under reduced pressure and the residue was purified by column chromatography on silica gel to afford product **2.**

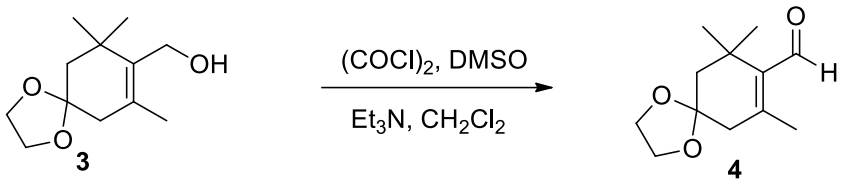
b) **General Procedure for the synthesis of compound 3**



2 **3**

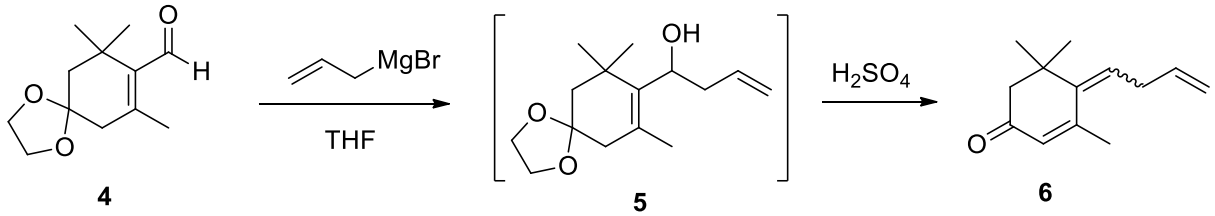
A round bottom flask was charged with lithium aluminum hydride (7.5 mmol, 0.285 g) and 7,9,9-trimethyl-1,4-dioxaspiro[4.5]dec-7-ene-8-carboxylic acid ethyl ester **2** (4 mmol, 1.27 g) in dry THF (20 mL), and the reaction mixture was stirred at room temperature overnight. The reaction was quenched with water and diluted with ethyl acetate. The layers were separated, and the aqueous layer was extracted with two additional portions of ethyl acetate. The combined organics were washed with brine before drying over anhydrous Na_2SO_4. The solvent was removed under reduced pressure, and the residual oil was purified by column chromatography on silica gel (eluent: PE:EA = 5: 1) to afford **3**.

c) **General Procedure for the synthesis of compound 4**



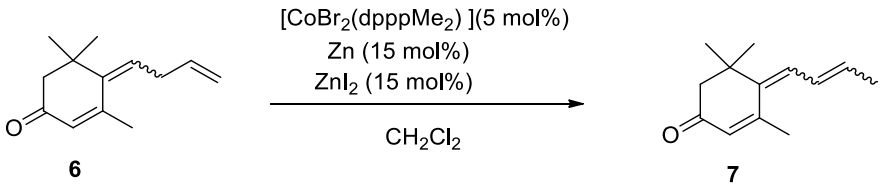
To a solution of oxalyl chloride (0.51 mL, 6 mmol) in 30 mL of CH_2Cl_2 at –78 °C was added DMSO (0.85 mL, 12 mmol) dropwise. After 5 min, a solution of **3a** (4 mmol, 0.848 g) in 10 mL of CH_2Cl_2 was added, and stirring was continued at –78 °C for 15 min. Et_3N (37 mL, 264 mmol, 5 eq.) was then added, the cooling bath was removed, and stirring was continued. After 1 h, TLC analysis indicated complete consumption of the starting material and formation of the product. The reaction was quenched with saturated sodium bicarbonate and diluted with CH_2Cl_2. The layers were separated, and the aqueous layer was extracted with two additional portions of CH_2Cl_2. The combined organics were washed with brine before drying over anhydrous Na_2SO_4. The solvent was removed under reduced pressure, and the residual oil was purified by column chromatography on silica gel (eluent: PE:EA = 10: 1) to afford **4**.

d) **General Procedure for the synthesis of compound 6**



In a Schlenk flask filled nitrogen the compound **4** (2 mmol, 0.42 g) in dry THF (10 mL) was carefully added Allyl magnesium bromide (4 mmol, 8 mL, 0.5 M in THF). The reaction mixture was stirring at 0 °C for 3 h. Then the residue was quenched with saturated NH_4Cl solution, extracted with ethyl acetate and dried on $MgSO_4$. After removal of the solvent under reduced pressure, the crude product put into a solution in 10 mL of THF followed by the addition of 36% sulfuric acid aqueous solution (4 mL) dropwise. The reaction mixture was stirring at at room temperature for 4 h. Then the residue was quenched with Saturated sodium bicarbonate aqueous solution, extracted with ethyl acetate and dried on $MgSO_4$. After removal of the solvent under reduced pressure, the crude product was purified by column chromatography (eluent: PE:EA = 10: 1) to give **6**.

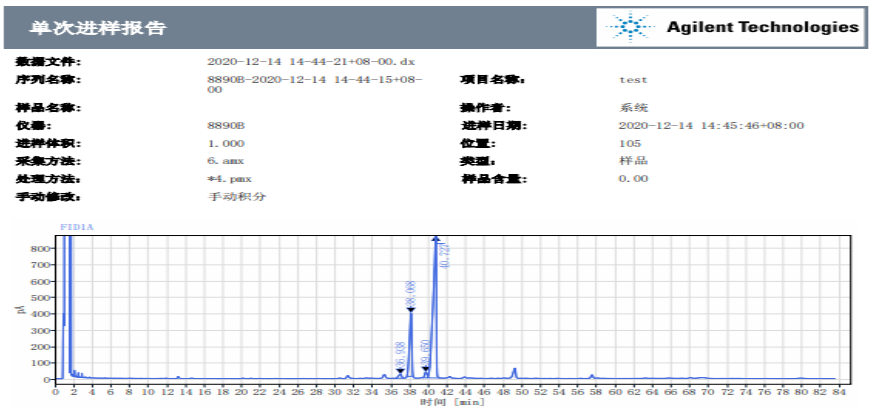
e) **General Procedure for the synthesis of compound 7**



The cobalt catalyst (5 mol %), zinc powder (15 mol %) and zinc iodide (15 mol %) were combined under an atmosphere of nitrogen and suspended in CH_2Cl_2. Then compound **6** (0.95 g， 5 mmol) was added and the reaction mixture was stirred at room temperature until complete conversion of the starting material was observed. The reaction was quenched with saturated sodium bicarbonate and diluted with CH_2Cl_2. The layers were separated, and the aqueous layer was extracted with two additional portions of CH_2Cl_2. The combined organics were washed with brine before drying over

anhydrous Na_2SO_4. The solvent was removed under reduced pressure, and the residual oil was purified by column chromatography on silica gel (eluent: PE:EA = 10: 1) to afford megastigmatrien-3-one **7**.

Ratio of four isomers under r.t.



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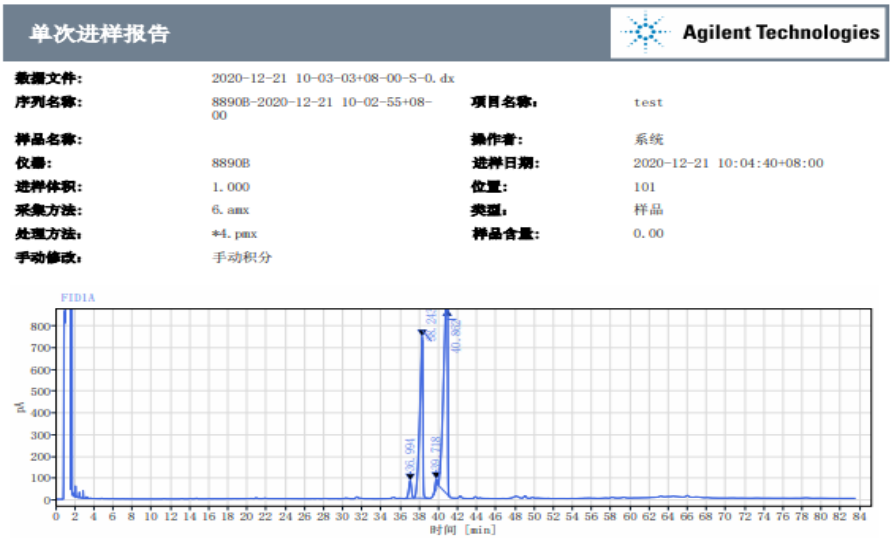
Ratio of four isomers under 40 °C.



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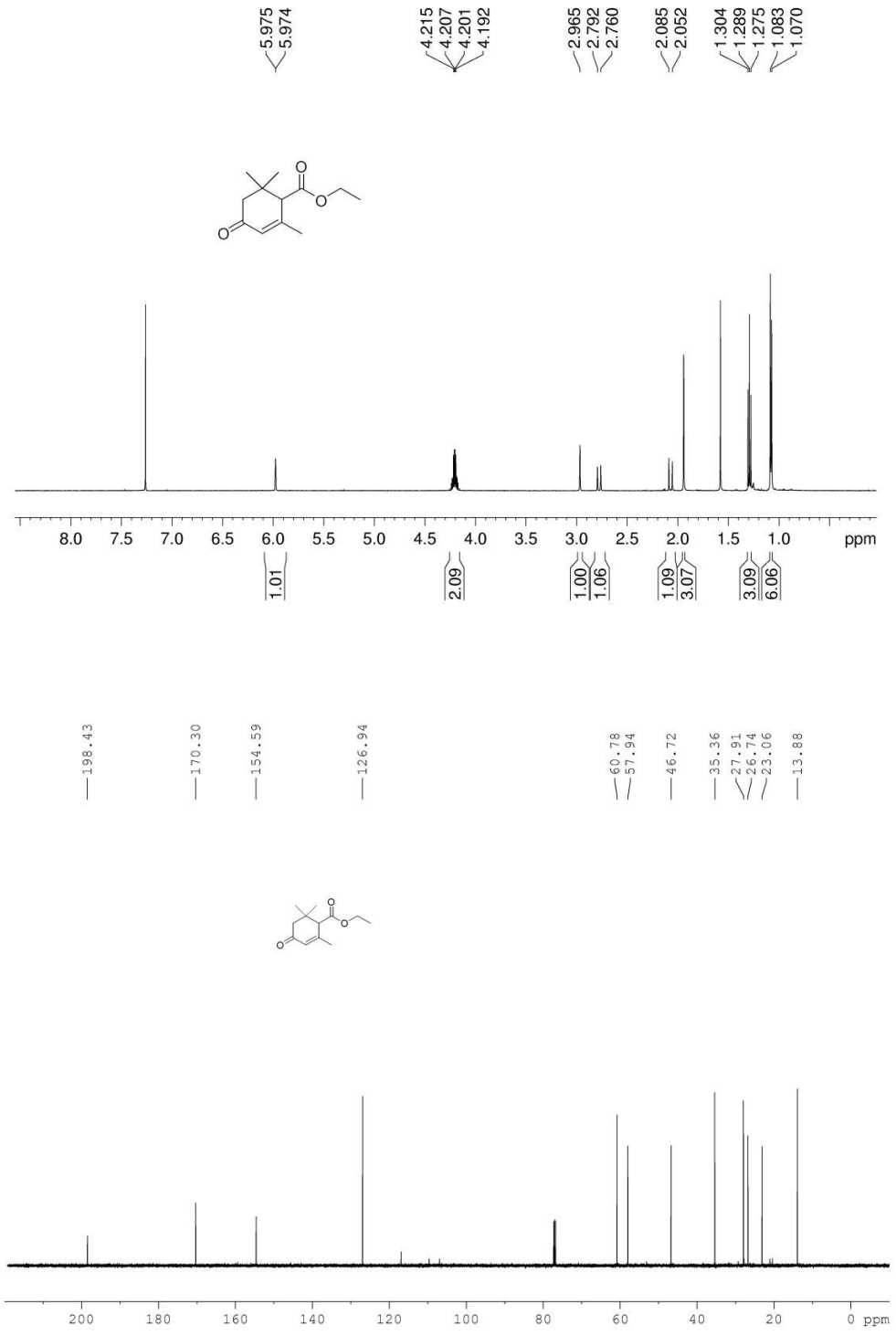
39.718	BV	0.33	422.77	45.00	0.89	
40.862	BB m	0.30	29108.62	1123.69	61.46	
		总和	47362.81			

f) **General Procedure for the synthesis of compound 8**

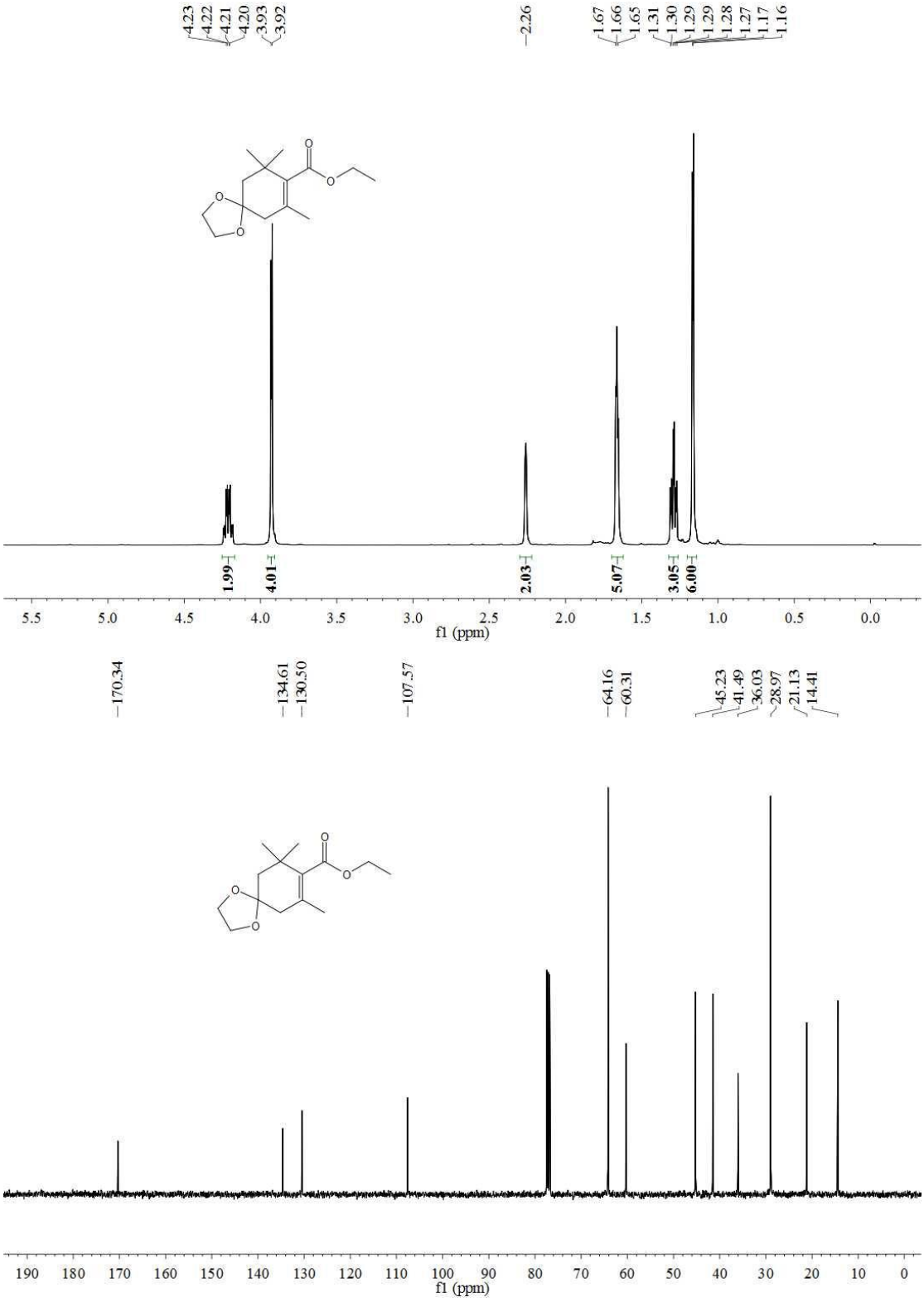
To a cold solution (0 ^{o}C) of **7** (187.5 mg, 1 mmol) in dry dichloromethane (5 mL) was added *m*-chilrlperbenzoic acid (215.8 mg, 1.25 mmol) and the mixture was stirred at 0 ^{o}C for 2 h. The mixture was washed with a 1 % solution of NaOH and brine, dried over $MgSO_4$, and concentrated. The resdue was added to a mixture of zinc power (326.7 mg) and acetic acid (1.5 mL) at room temperature. After the mixture was stirred for 2 h at room temperature, the precipitata was filtered off and washed with ether (10 mL). The filtrate was washed with a saturated solution of $NaHCO_3$ and brine, dried over $MgSO_4$, and then concentrated. Purification by silica-gel column chromatography (hexane-ether) afford **8** (65%).

3 ^{1}H NMR and ^{13}C NMR Spectra of All Compounds

Compound **1**



Compound **2**



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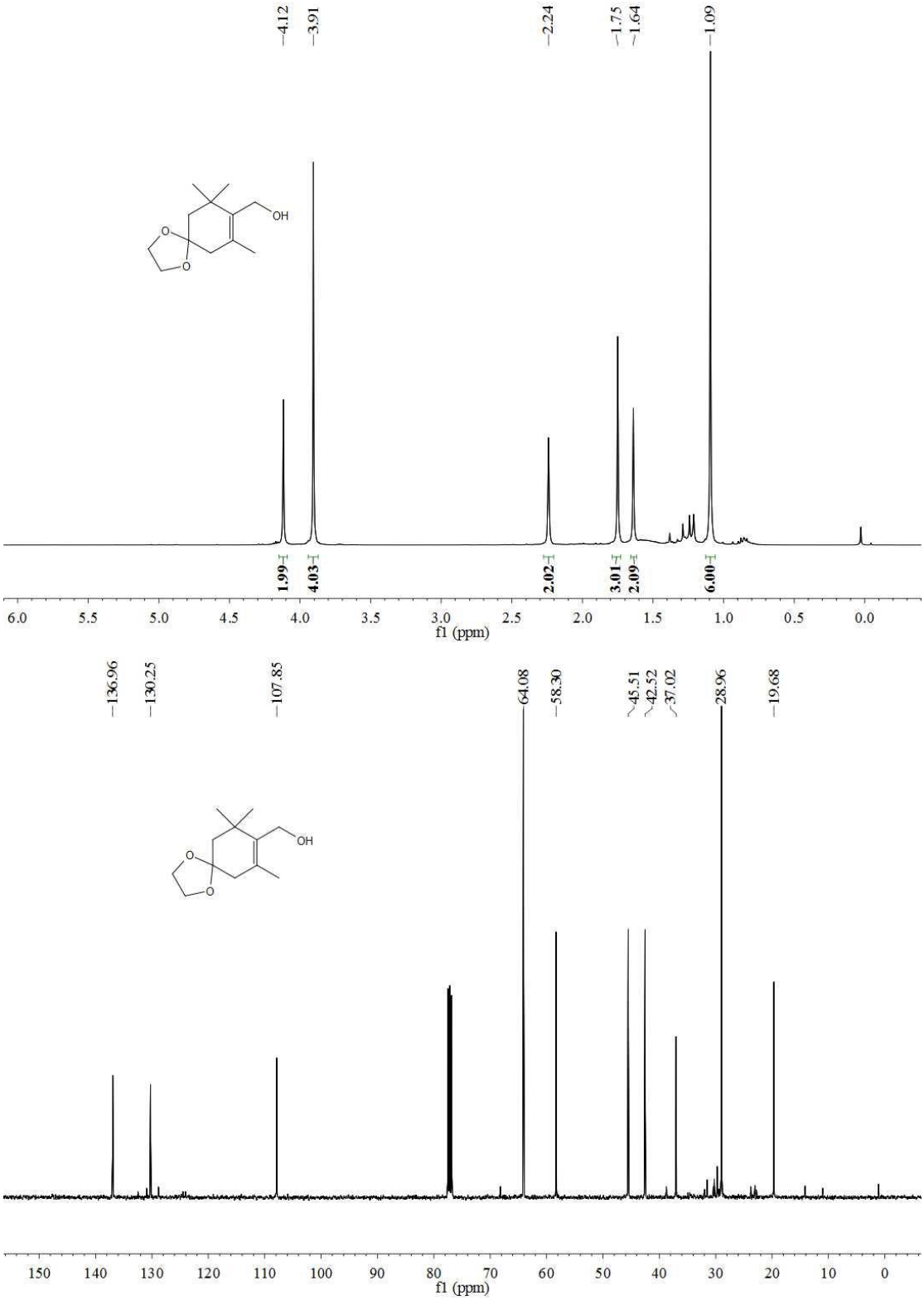
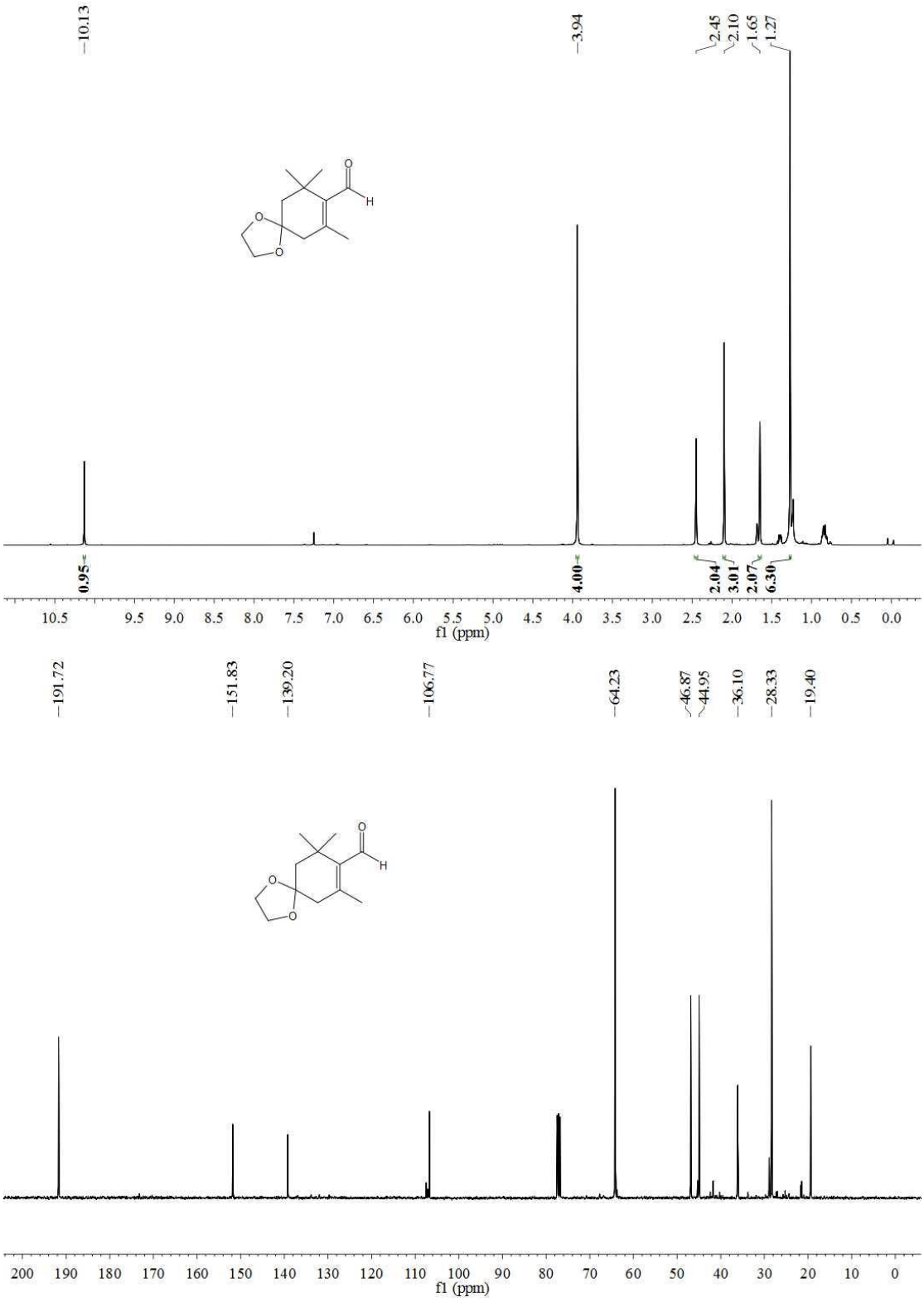
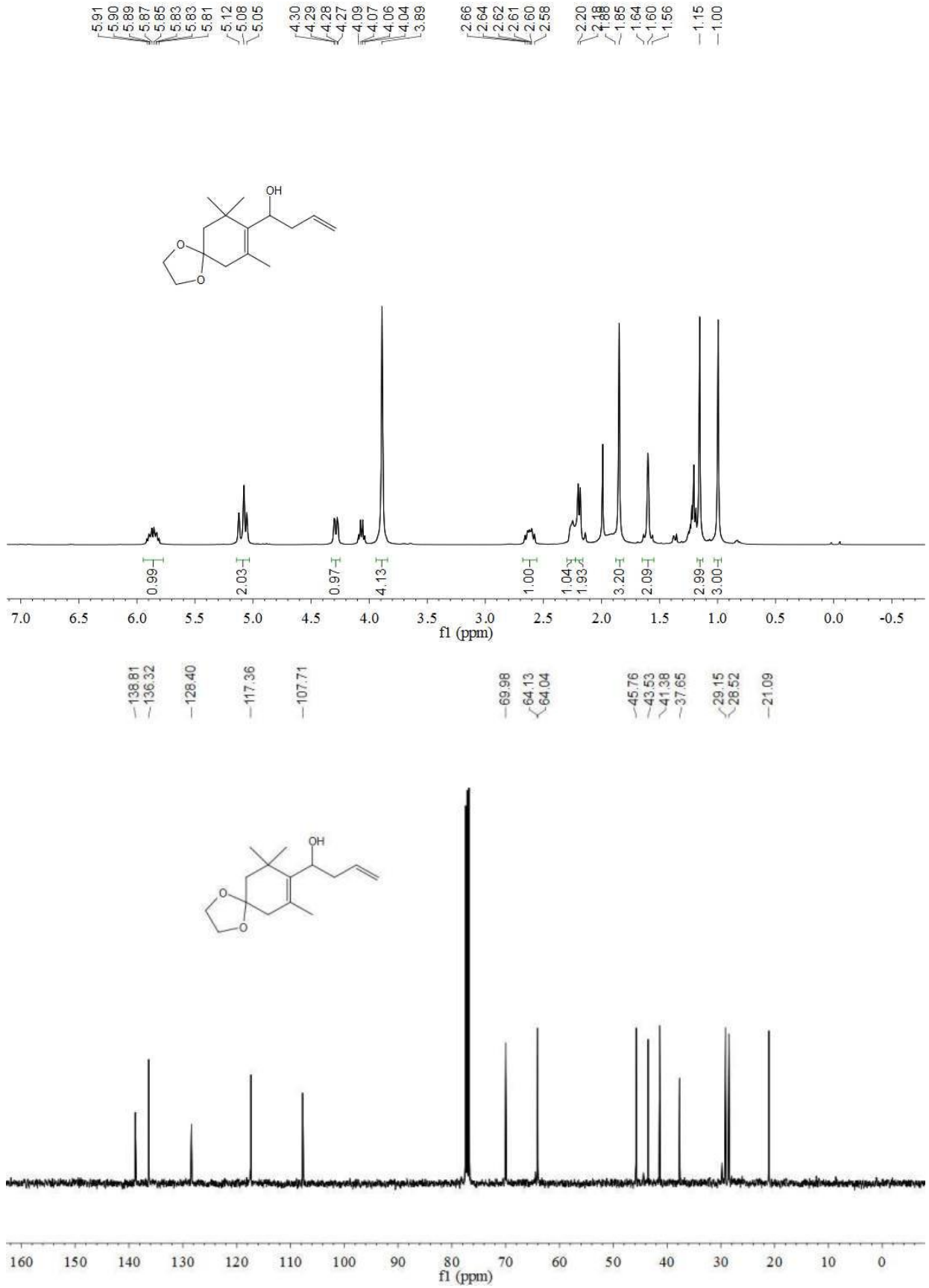


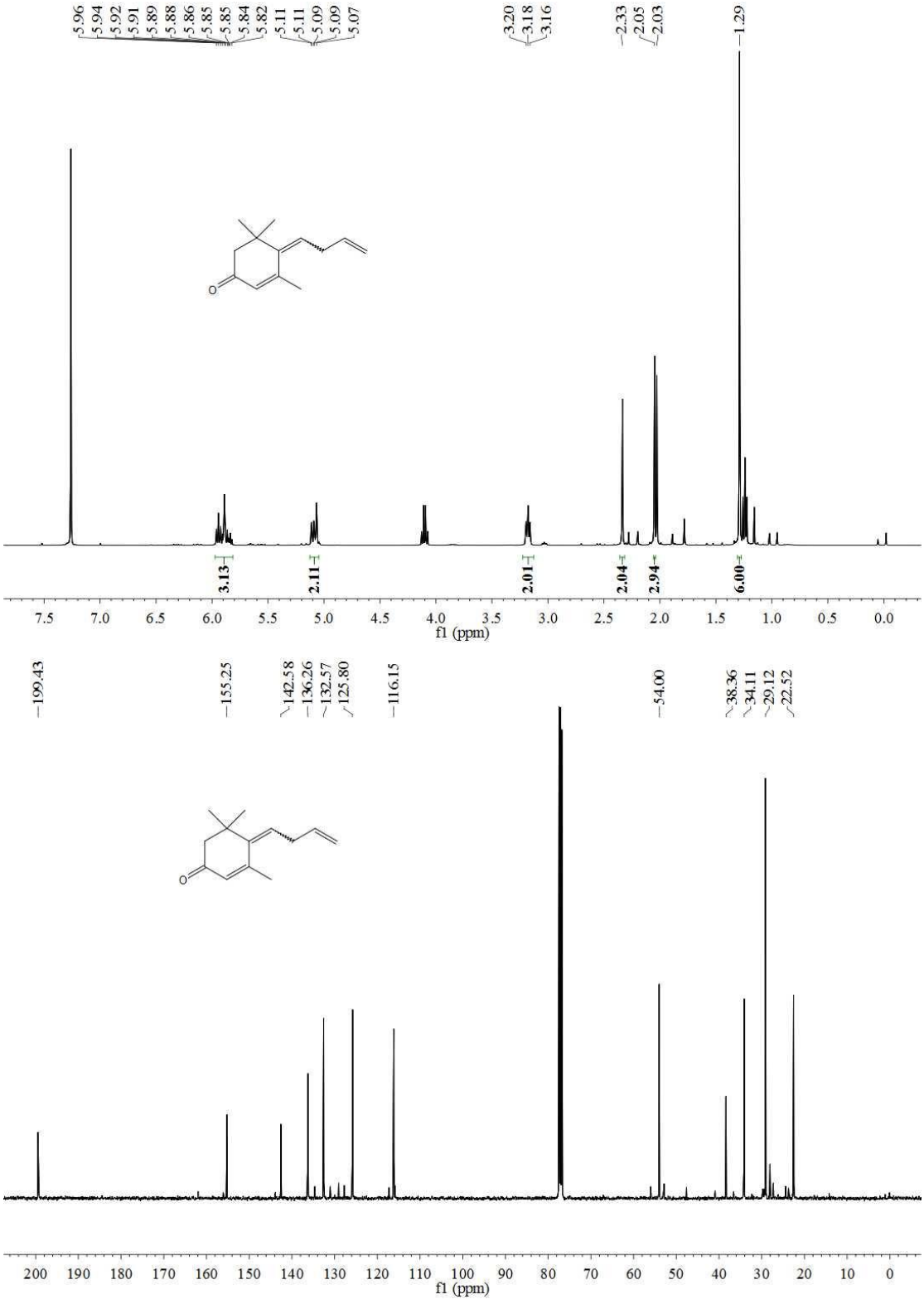
Compound **4**



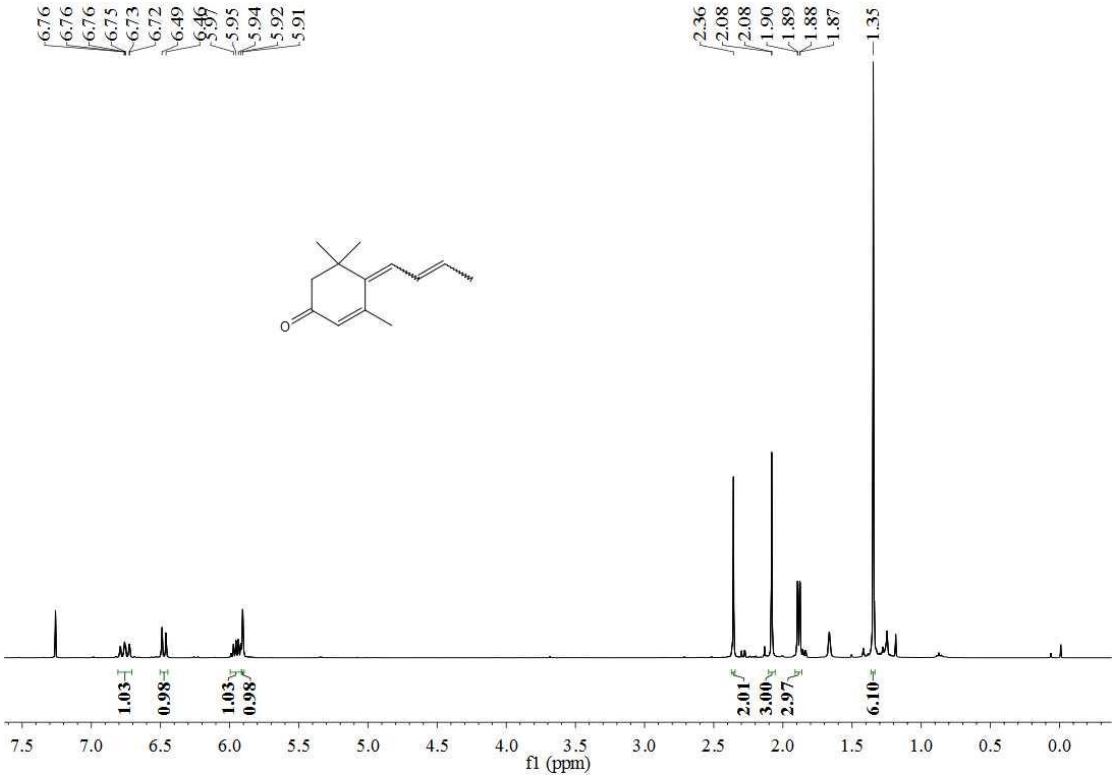
Compound **5**

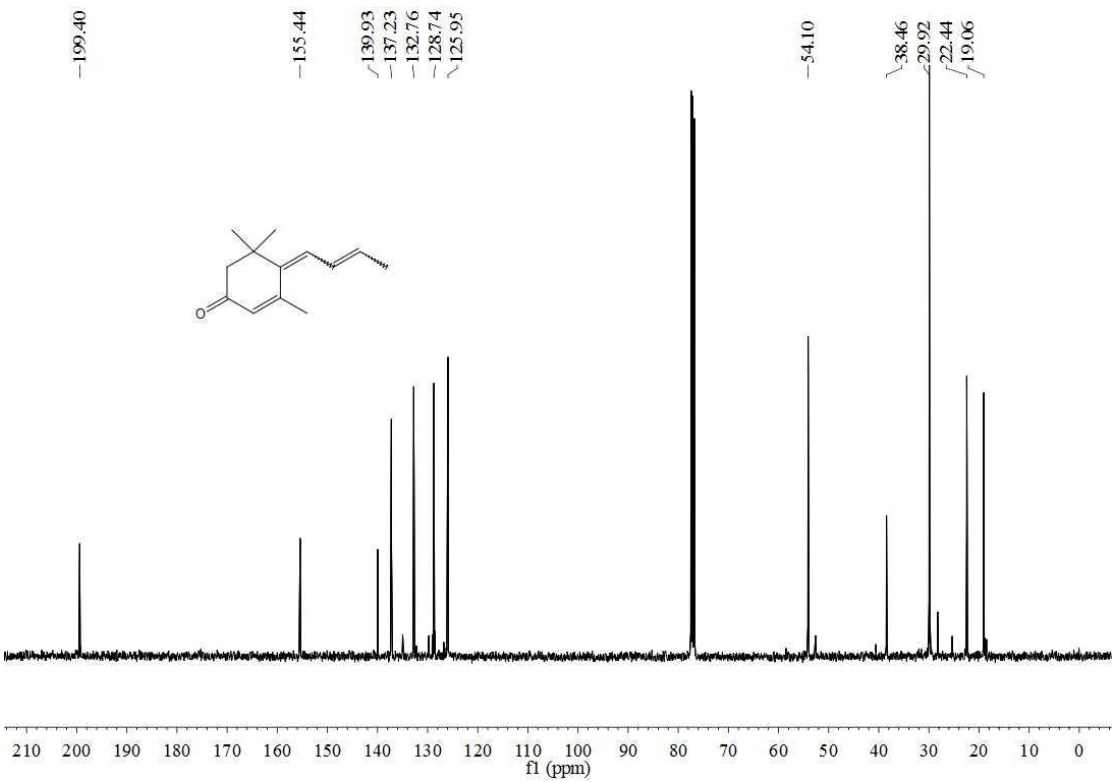


Compound **6**

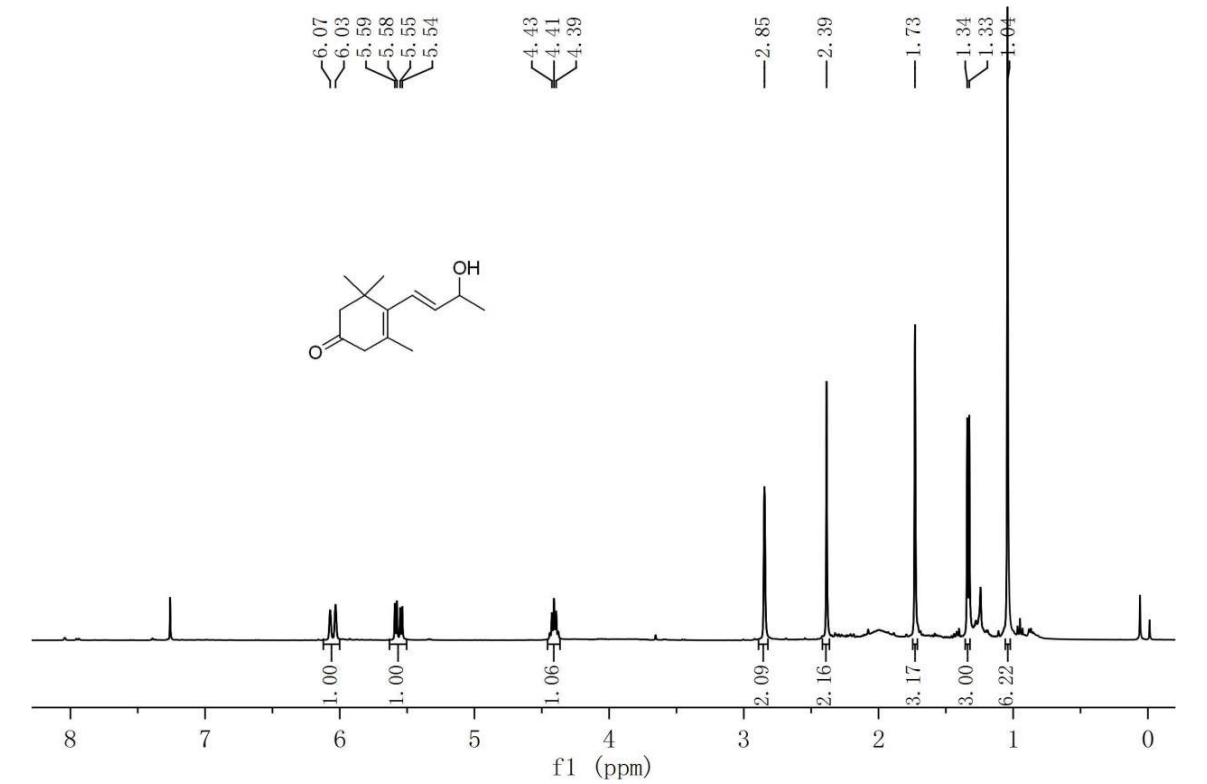


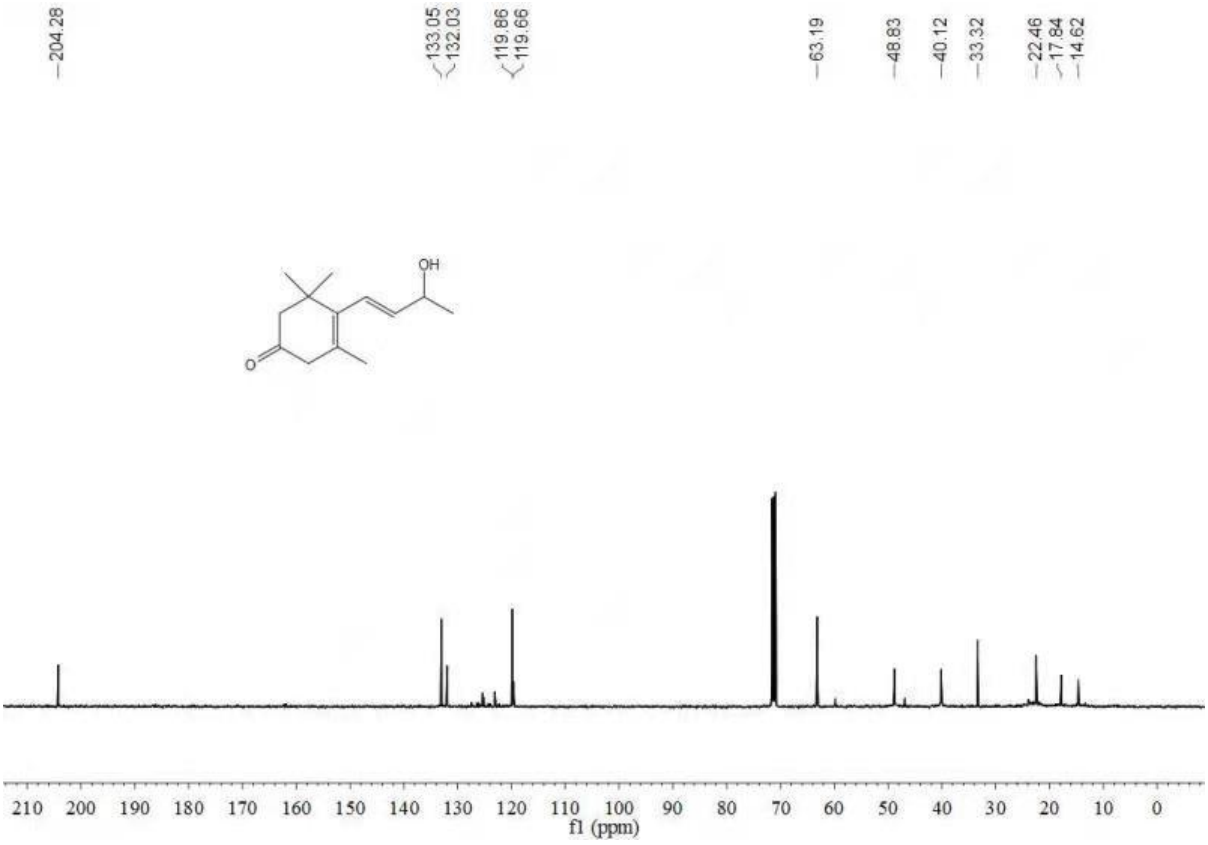
Compound **7**





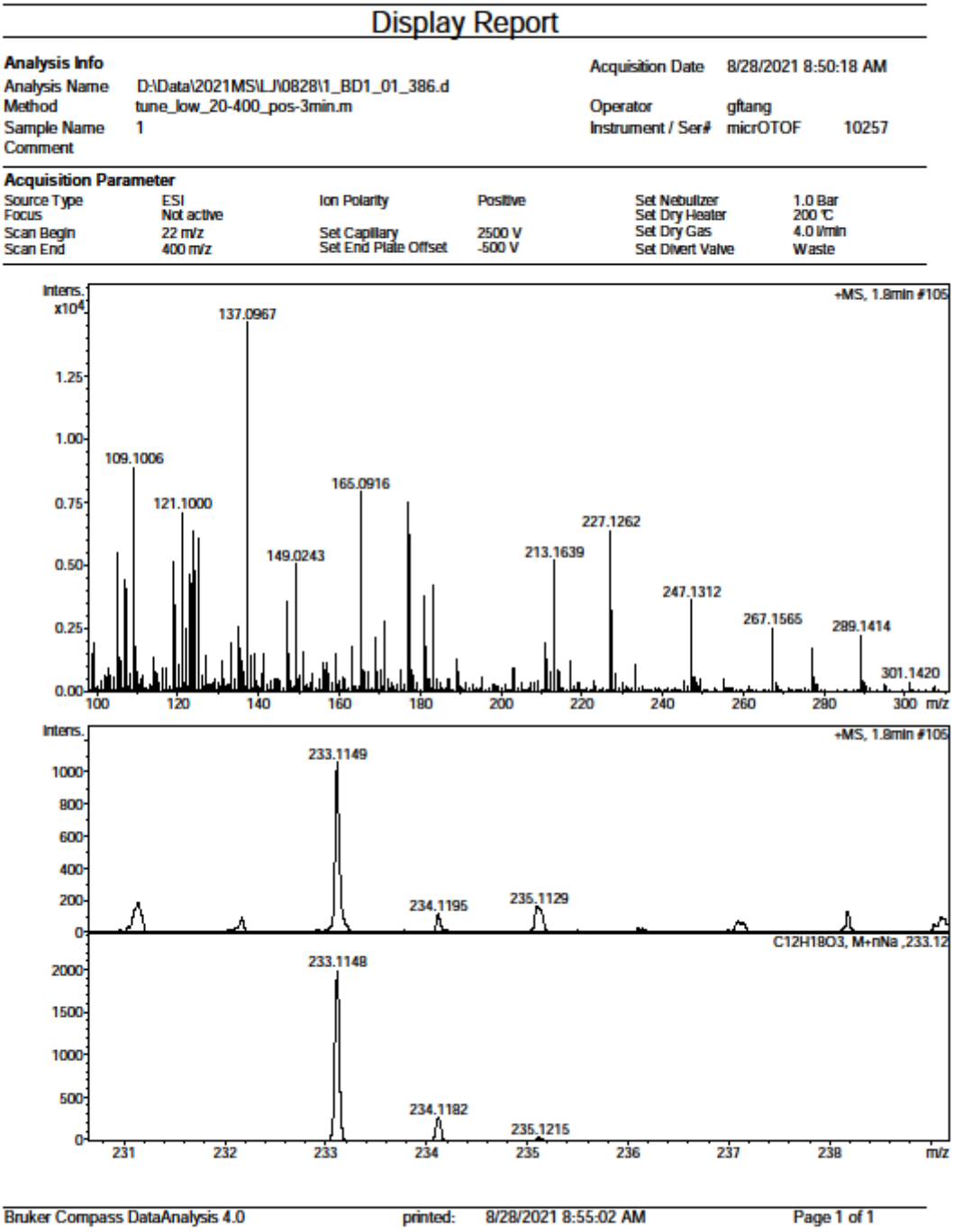
Compound **8**



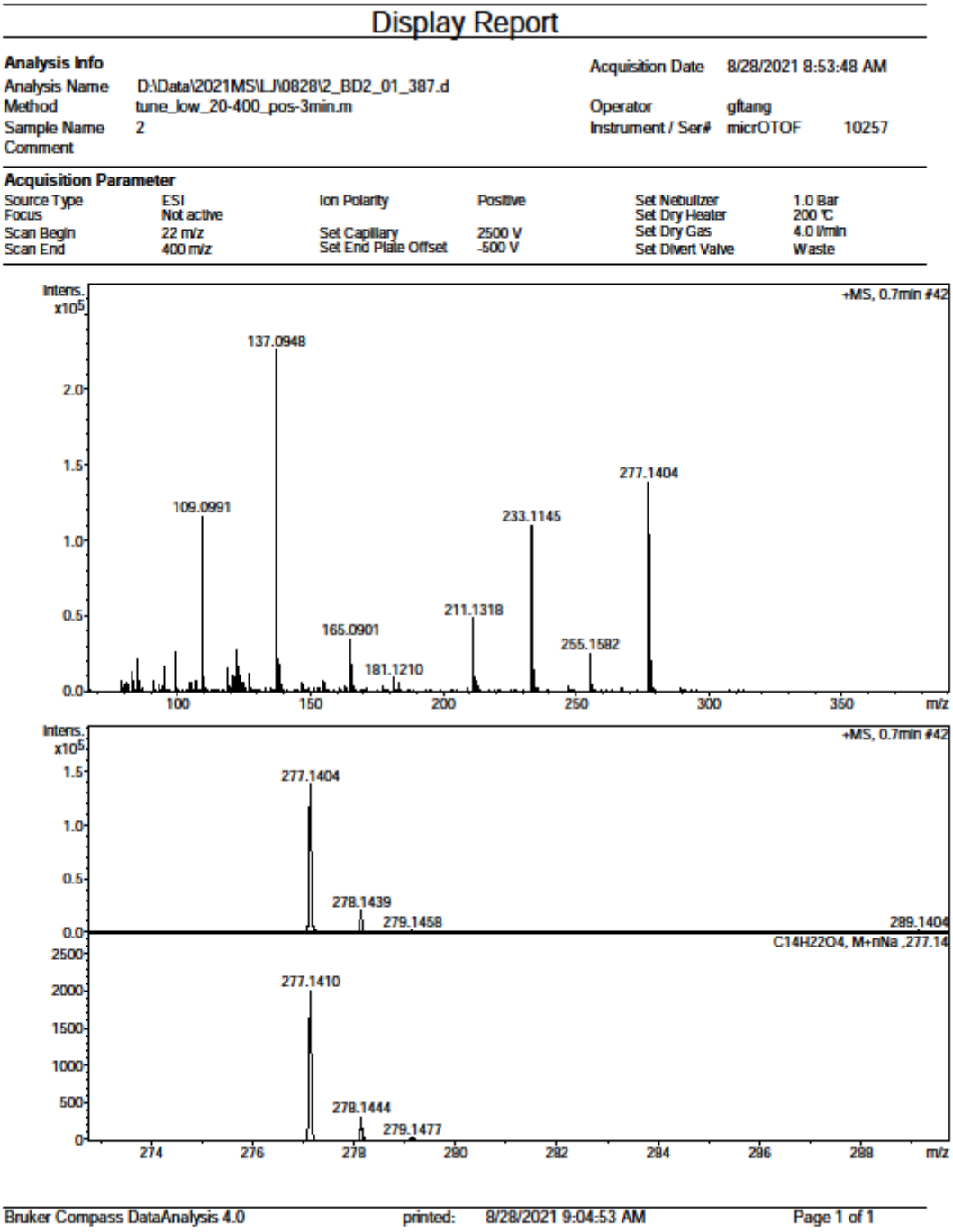


4 HRMS of new compounds and significant compounds

HRMS of compound 1



HRMS of compound 2



HRMS of compound 3

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Comment			

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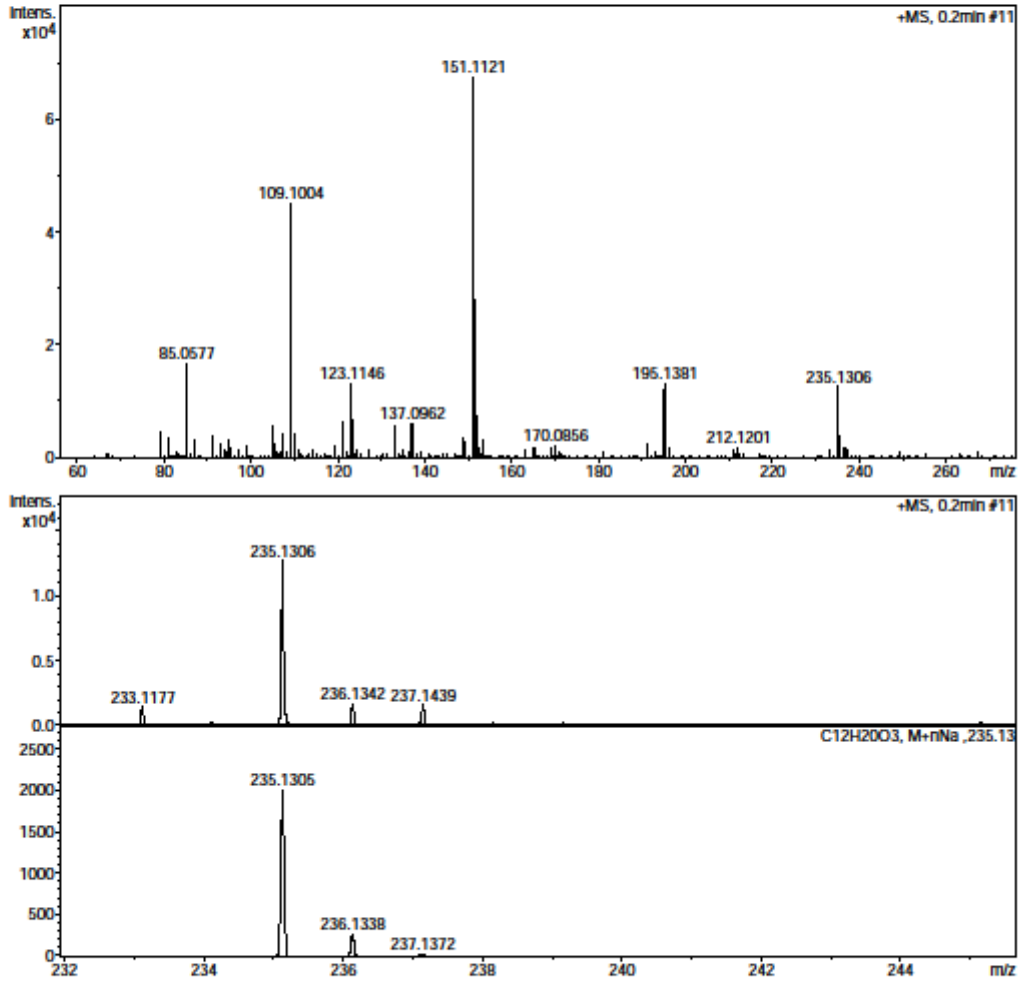

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HRMS of compound 4

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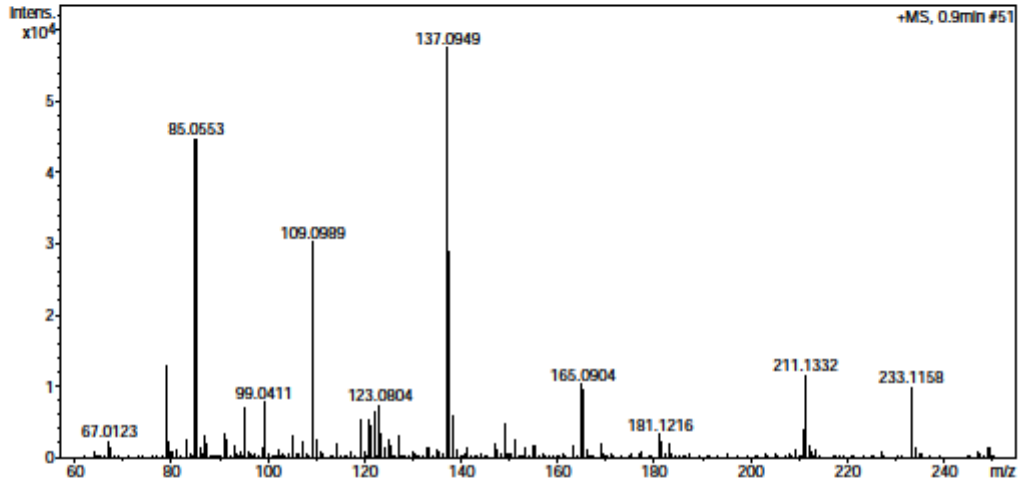

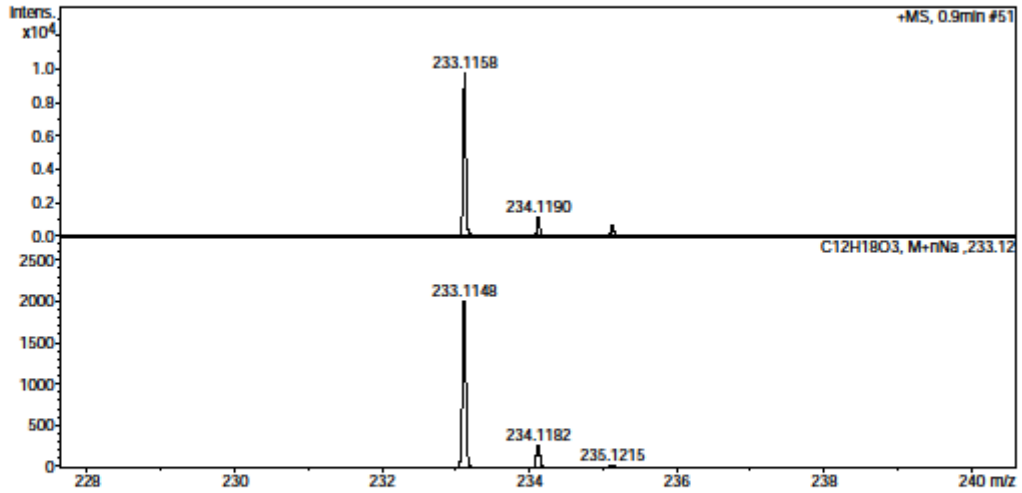

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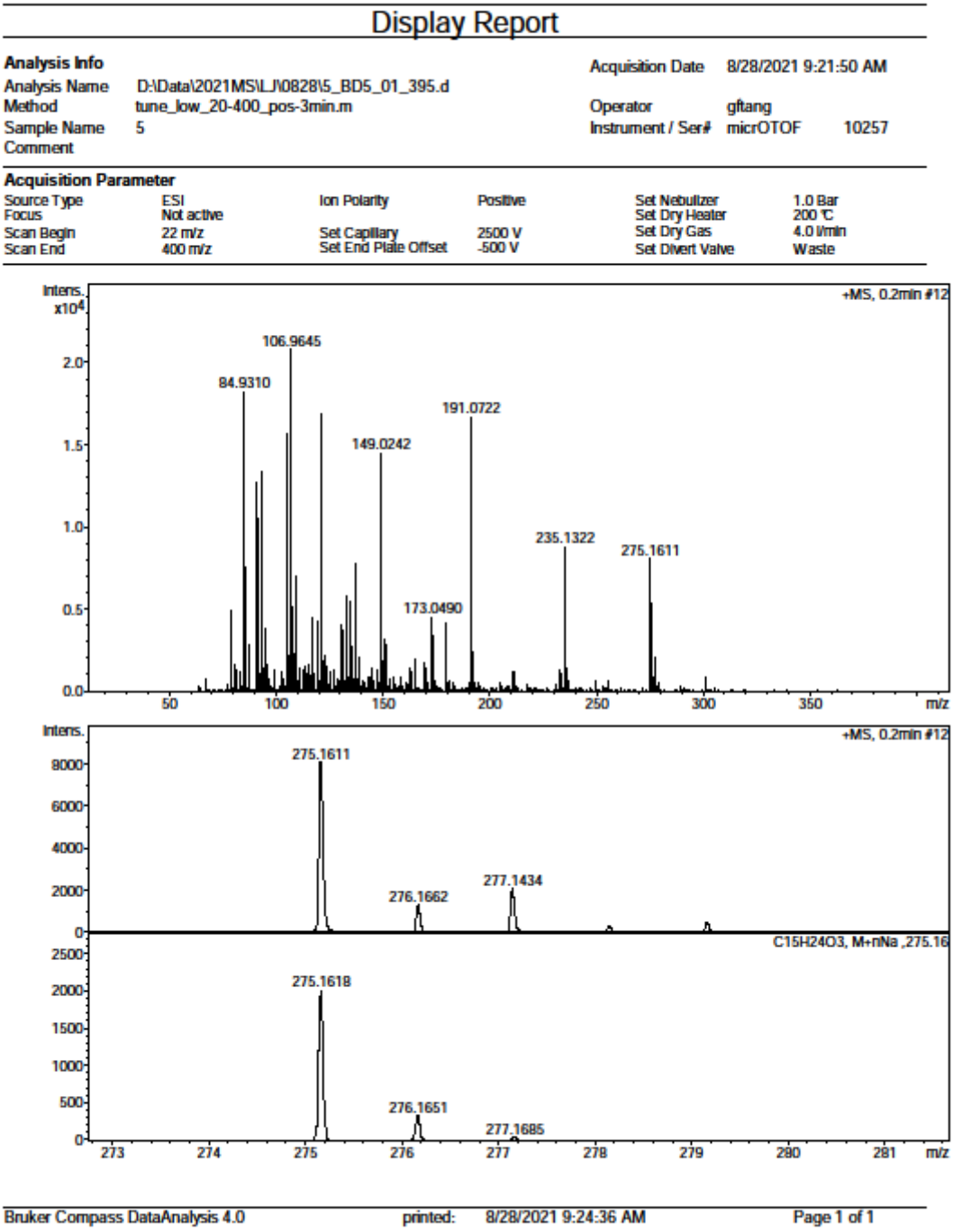
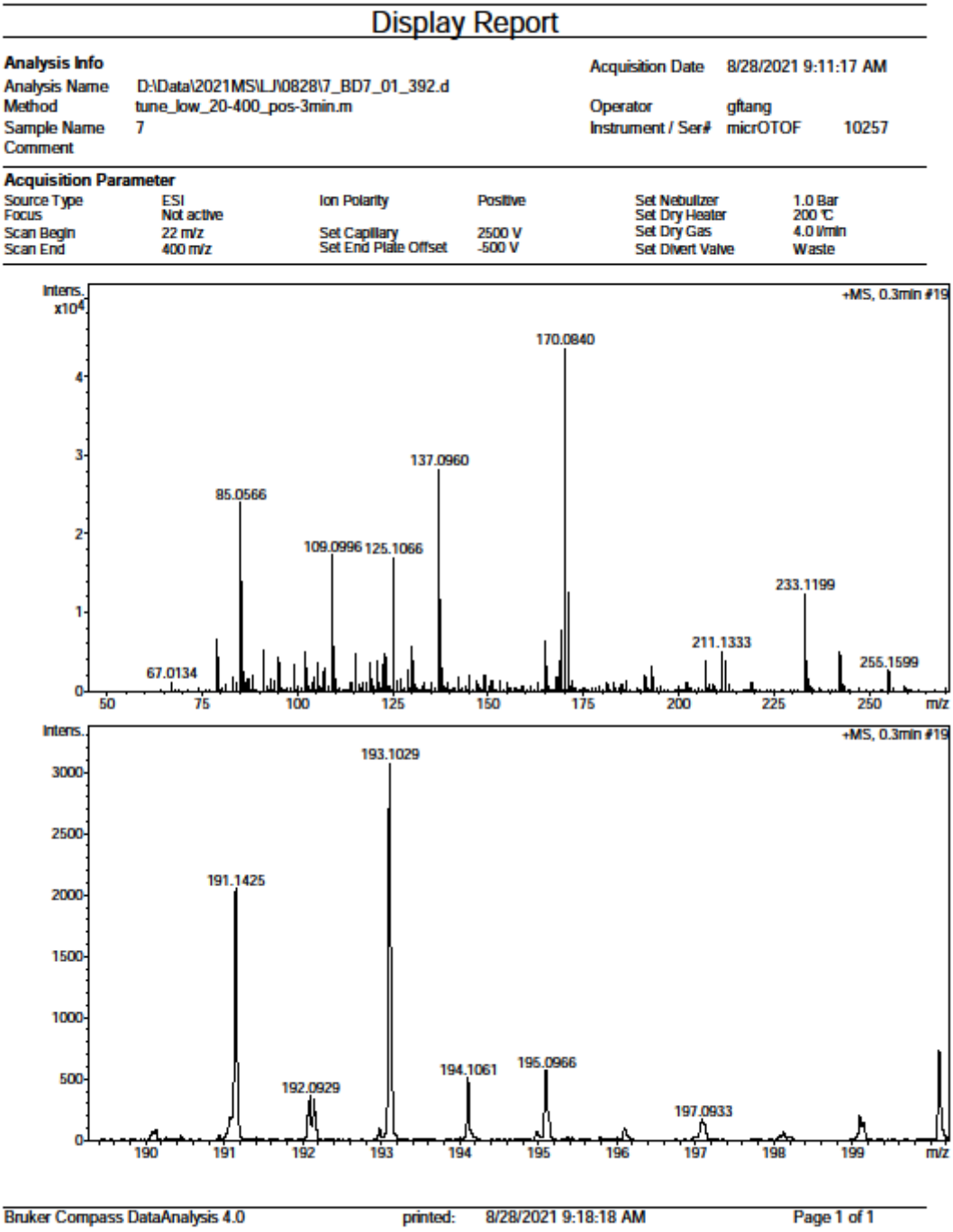
HRMS of compound 5



HRMS of compound 6



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Comment			

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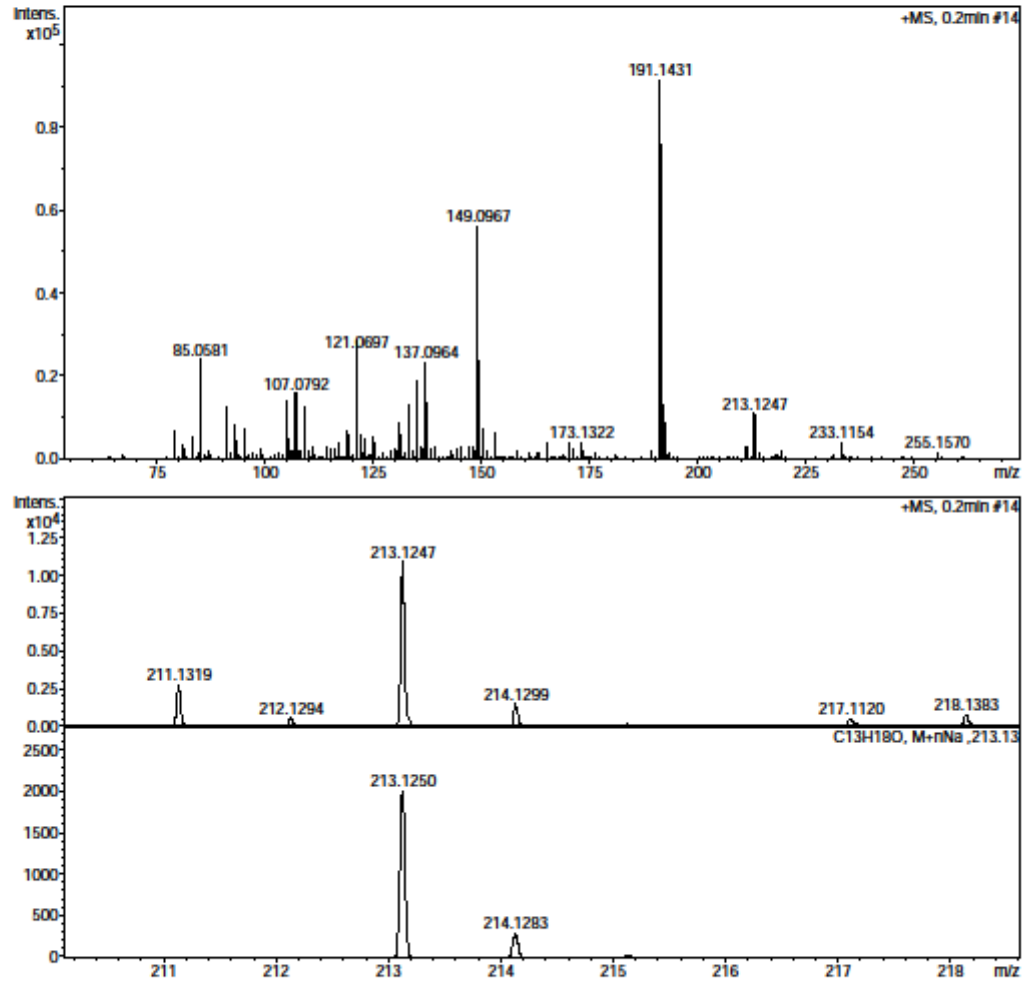

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