Supporting Information

Cooperative NHC/LA Catalysis for Stereoselective Strain-Release gem-Difunctionalization of Bicyclo[1.1.0]butanes to 1,1,3,3-Tetrasubstituted Cyclobutanes

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1. General Information

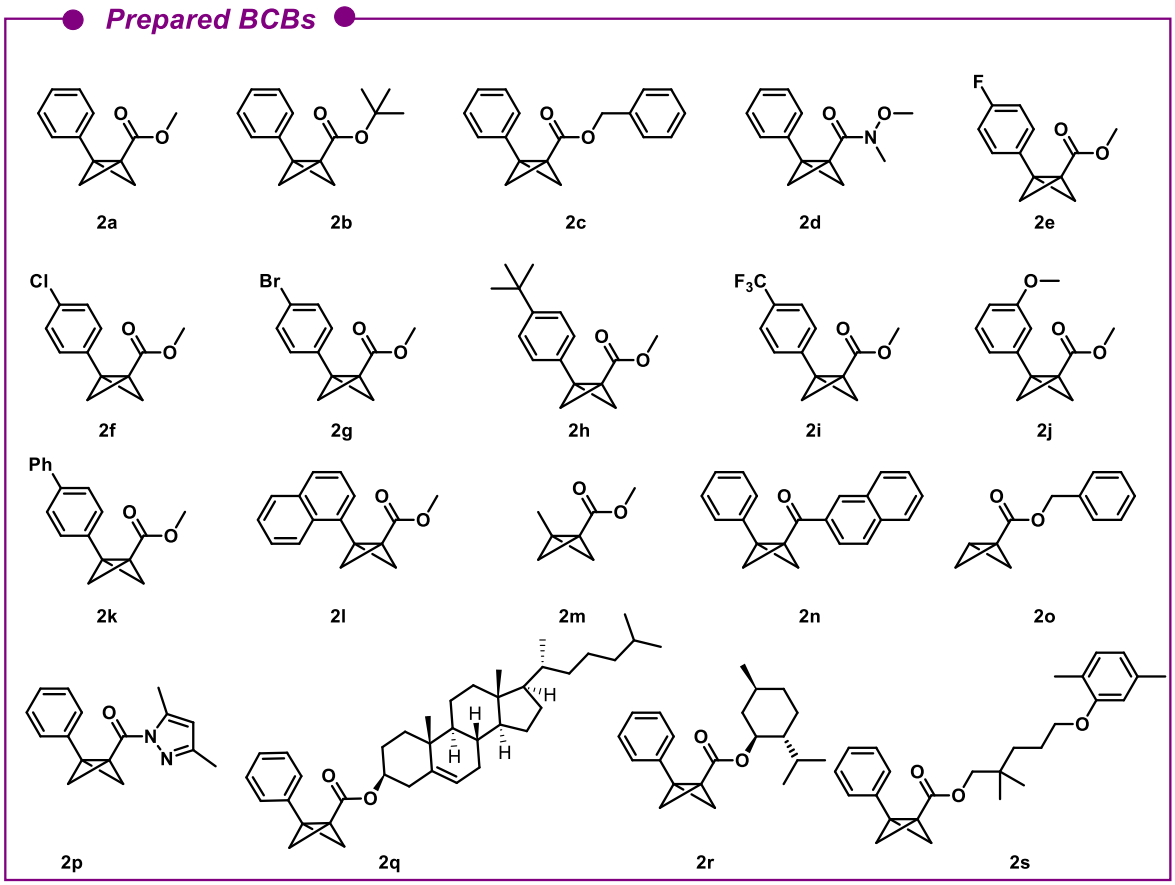
All reagents were used as received from commercial sources without additional purification. Solvents were purified and dried by standard techniques. All glassware were stored in an oven or flame-dried (60-70 °C) for at least 3 h before use. Room temperature (rt) corresponds to the 25-35 °C, when the experiments were performed. Catalytic reactions were performed under an inert atmosphere of argon using schlenk tube. Thin layer chromatography (TLC) was performed using silica gel precoated aluminium foil, which was visualized with UV light at 254 nm or under iodine / 2,4-DNP / $KMnO_4$ charring. Column chromatography was performed with flash silica-gel (230-400 mesh). ^1H NMR (400, or 500 MHz), $^{13}C\{^1H\}$ NMR (100.6, or 126 MHz) spectra were recorded on the NMR spectrometer. The flip angle of the DEPT spectra are 135 degrees. Deuterated chloroform was used as solvent, and chemical shift values (δ) are reported in parts per million relative to the residual signal of the chloroform [δ 7.27 for ^1H (chloroform-*d*), δ 77.0 for $^{13}C\{^1H\}$ (chloroform-*d*)]. Abbreviations used in the NMR data: br, broad. s, singlet. br s, broad singlet. d, doublet. t, triplet. q, quartet. quint, quintet. sext, sextet. m, multiplet. Coupling constants (*J*) are reported in hertz. Melting points were measured using a melting point apparatus in open glass capillaries. High-resolution mass spectrometry (HRMS) was performed on QTOF/ESI-TOF mass spectrometer.

Abbreviations: NHC - N-Heterocyclic carbene, THF - Tetrahydrofuran, DCM -Dichloromethane, ACN: Acetonitrile, DCM: Dichloromethane, DCE: Dichloroethane, DMF: *N*, *N*-Dimethylformamide, EtOAc: Ethyl Acetate, NHC: N-Heterocyclic carbene, DIPEA- N, N-Diisopropylethylamine, DBU- 1,8-Diazabicyclo[5.4.0]undec-7-ene, rt - room temperature.

2. Experimental section

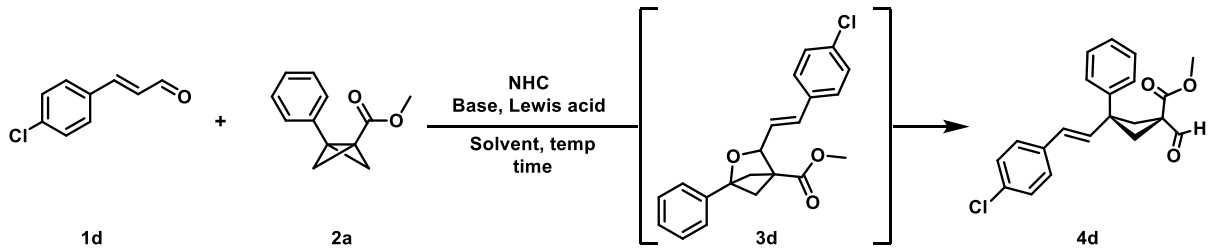
2.1. Preparation of starting materials

The *α,β*-unsaturated aldehydes **1a-b**, **1d-g**, **1k-1l**, **1o** were purchased from commercial sources. All other *α,β*-unsaturated aldehydes **1c**, **1h**, **1i-j**, **1m-n and 1p** were synthesized by following the literature procedure.[1-3] BCBs (**2a-2s**) are known in the literature and were prepared according to corresponding literature procedures and all the spectral data are in agreement with the reported values[4-8]. The achiral N-heterocyclic carbene precursor NHCs (**C, I & J**) was prepared following the literature procedure.[9-11] The chiral NHCs (**A, B, D-H**) and achiral NHC **L** were purchased from commercial sources.



2.2. Protocol optimization:

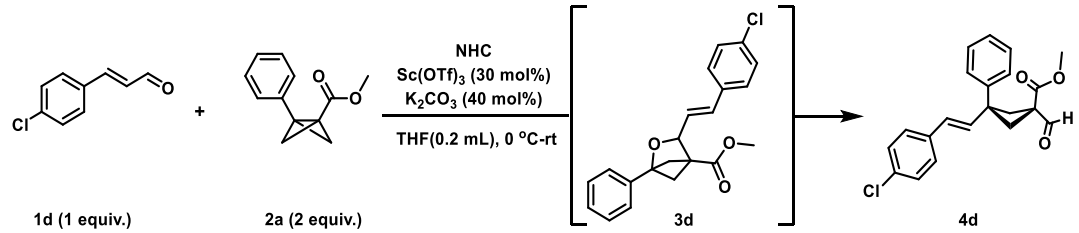
2.2. A) General procedure for the optimization of the reaction condition for methyl (1s,3s)-3-((E)-4-chlorostyryl)-1-formyl-3-phenylcyclobutane-1-carboxylate (4d):

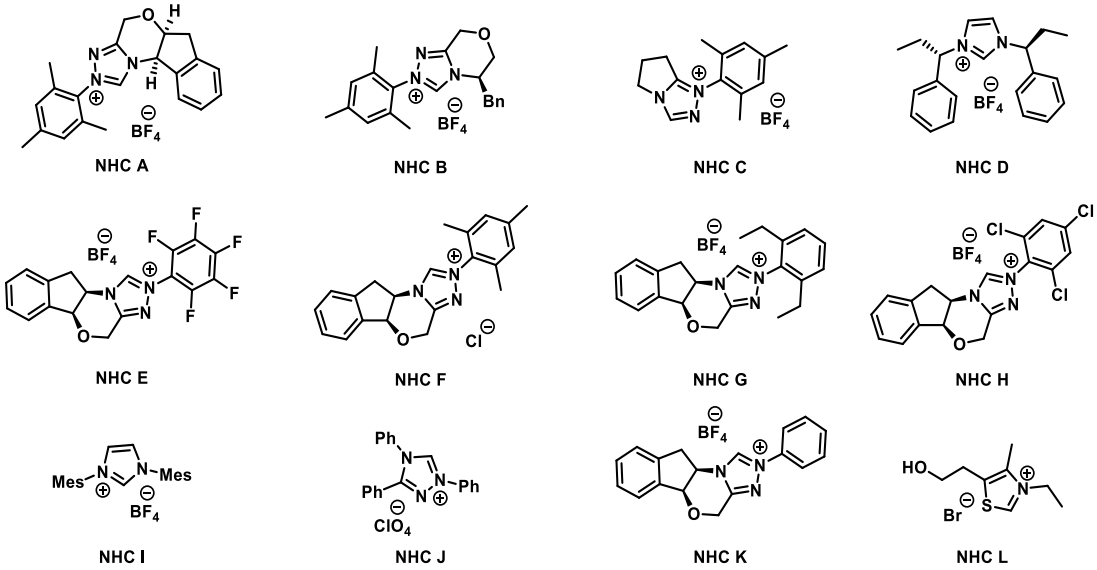


An oven-dried schlenk tube equipped with a magnetic stirring bar was charged with a NHC and base. The reaction vessel was evacuated and backfilled with argon three times. Under an argon atmosphere, (E)-3-(4-Chlorophenyl)acrylaldehyde (**1d**) and methyl 3-phenylbicyclo[1.1.0]butane-1-carboxylate (**2a**) were added followed by addition of dry solvent. The reaction vessel was evacuated and backfilled with argon three times. The schlenk tube was placed in an ice bath and the reaction mixture was stirred for 5 minutes. After this, Lewis acid was added and the tube was tightly closed with a glass stopper. The resulting mixture was kept for stirring at rt for completion of the reaction. Upon completion of the reaction as observed by TLC, the reaction mixture was directly subjected to column chromatography using ethyl acetate:pet ether over 230-400 flash silica gel to afford the corresponding product **4d.**

Various permutations and combinations attempted are provided in the Table S1-S4.

Table S1: Screening of different NHCs:[a]



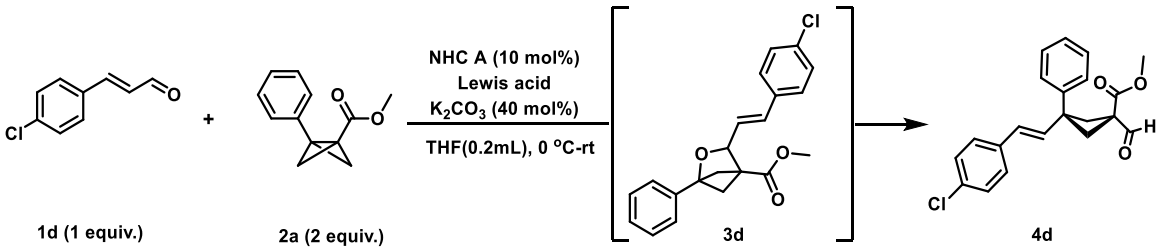


Entry	Variation of NHCs from Standard Reaction Condition	Yield 3d(%)[b]	Yield 4d(%)[b]
1.	NHC A (20 mol%)	trace	76%
2.	NHC B (20 mol%)	5%	80%
3.	NHC C (20 mol%)	trace	78%
4.	NHC D (20 mol%)	trace	74%
5.	NHC E (20 mol%)	21%	58%
6.	NHC F (20 mol%)	trace	trace

7.	NHC G (20 mol%)	36%	29%
8.	NHC H (20 mol%)	40%	20%
9.	NHC I (20 mol%)	14%	53%
10	NHC J (20 mol%)	N.R.	N.R.
11.	NHC K (20 mol%)	28%	43%
12.	NHC L (20 mol%)	N.R.	N.R.
13.	**NHC A (10 mol%)**	-	**85%**
14.	NHC B (10 mol%)	7%	71%
15.	NHC C (10 mol%)	45%	33%

[a]Standard Reaction conditions: **1d** (1 equiv., 0.16 mmol), **2a** (2 equiv., 0.32 mmol), NHC-**A** (10 mol%, 0.016 mmol), K_2CO_3 (40 mol%, 0.064 mmol), $Sc(OTf)_3$ (30 mol%, 0.045 mmol), THF (0.2 mL), 0°C-rt, 15 min. [b]Isolated yield. N.R.: No reaction

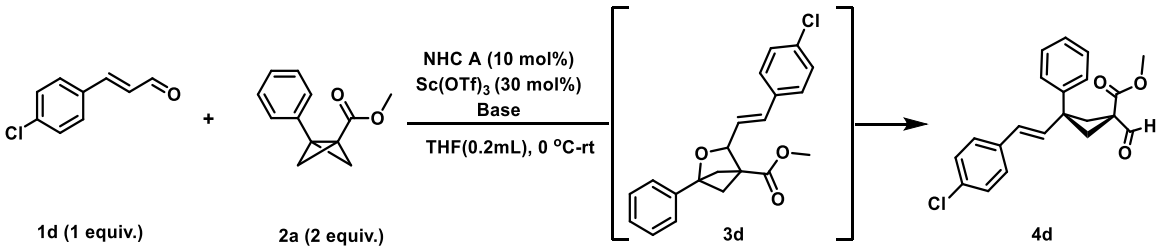
Table S2: Screening of different Lewis acids:[a]



Entry	Variation of Lewis acids from Standard Reaction Condition	Yield 3d(%)[b]	Yield 4d(%)[b]
1.	**$Sc(OTf)_3$ (30 mol%)**	**-**	**85%**
2.	$Sc(OTf)_3$ (20 mol%)	20%	57%
3.	$Bi(OTf)_3$ (30 mol%)	N.R.	N.R.
4.	$Cu(OTf)_2$ (30 mol%)	N.R.	N.R.
5.	AgOTf (30 mol%)	N.R.	N.R.
6.	$Yb(OTf)_3$ (30 mol%)	N.R.	N.R.
7.	$BF_3.OEt_2$ (10-30 mol%)	50-65%	-

[a]Standard Reaction conditions: **1d** (1 equiv., 0.16 mmol), **2a** (2 equiv., 0.32 mmol), NHC-**A** (10 mol%, 0.016 mmol), K_2CO_3 (40 mol%, 0.064 mmol), $Sc(OTf)_3$ (30 mol%, 0.045 mmol), THF (0.2 mL), 0°C-rt, 15 min. [b]Isolated yield. N.R.: No reaction

Table S3: Screening of different bases:[a]

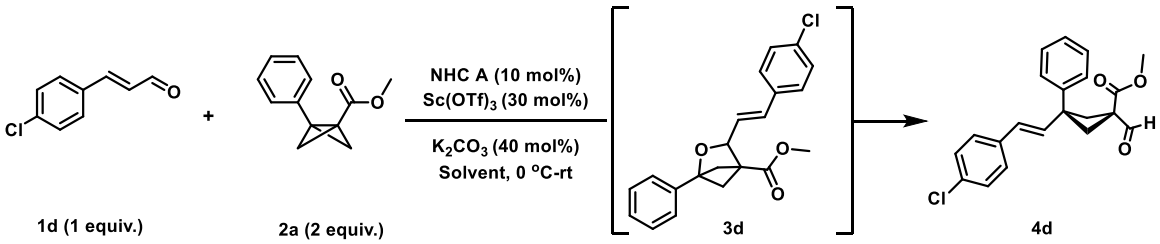


Entry	Variation of bases from Standard Reaction Condition	Yield 3d(%)[b]	Yield 4d(%)[b]
1.	**K_2CO_3 (40 mol%)**	**-**	**85%**

2.	K_3PO_4 (40 mol%)	N.R.	N.R.
3.	Cs_2CO_3 (40 mol%)	-	24%
4.	DBU (40 mol%)	-	18%
5.	DIPEA (40 mol%)	trace	trace
6.	Na_2CO_3 (40 mol%)	63%	19%
7.	Without base	80%	10%

[a]Standard Reaction conditions: **1d**(1 equiv., 0.16 mmol), **2a** (2 equiv., 0.32 mmol), NHC-**A** (10 mol%, 0.016 mmol), K_2CO_3 (40 mol%, 0.064 mmol), $Sc(OTf)_3$ (30 mol%, 0.045 mmol), THF (0.2 mL), 0°C-rt, 15 min. [b]Isolated yield. N.R.: No reaction

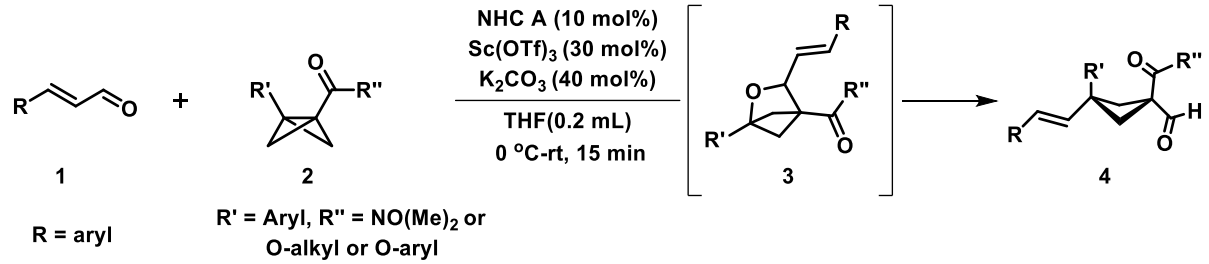
Table S4: Screening of different solvents:[a]



Entry	Variation of solvents from Standard Reaction Condition	Yield 3d(%)[b]	Yield 4d(%)[b]
1.	**THF (0.2 mL)**	**-**	**85%**
2.	Toluene (0.2 mL)	trace	49.4%
3.	DCM (0.2 mL)	N.R.	N.R.
4.	Chloroform (0.2 mL)	10%	48%
5.	ACN (0.2 mL)	89%	-
6.	1,4-dioxane (0.2 mL)	trace	47%
7.	THF (0.5 mL)	12%	70%
8.	THF (0.7 mL)	56%	27%

[a]Standard Reaction conditions: **1d** (1 equiv., 0.16 mmol), **2a** (2 equiv., 0.32 mmol), NHC-**A** (10 mol%, 0.016 mmol), K_2CO_3 (40 mol%, 0.064 mmol), $Sc(OTf)_3$ (30 mol%, 0.045 mmol), THF (0.2 mL), 0°C-rt, 15 min. [b]Isolated yield. N.R.: No reaction

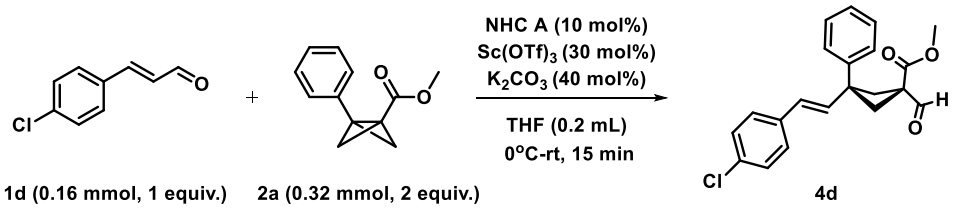
2.2. B) General optimized procedure for the synthesis of polyfunctionalised cyclobutane derivatives 4



An oven-dried schlenk tube equipped with a magnetic stirring bar was charged with the NHC precatalyst-**A** (10 mol%) and K_2CO_3 (40 mol%). The reaction vessel was evacuated and backfilled with argon three times. Under an argon atmosphere, *α,β*-unsaturated aldehyde **1** (1 equiv.) and bicyclobutane derivative **2** (2 equiv.) were added followed by addition of THF (0.2 mL). The reaction vessel was evacuated and backfilled with argon three times. The schlenk tube was placed in an ice

bath and the reaction mixture was stirred for 5 minutes. After this, $Sc(OTf)_3$ (30 mol%) was added and the tube was tightly closed with a glass stopper. The resulting mixture was kept for stirring at rt for completion of the reaction. Upon completion of the reaction as observed by TLC, the reaction mixture was directly subjected to column chromatography using ethyl acetate:pet ether over 230-400 flash silica gel to afford the desired products **4** in good to excellent yields**.**

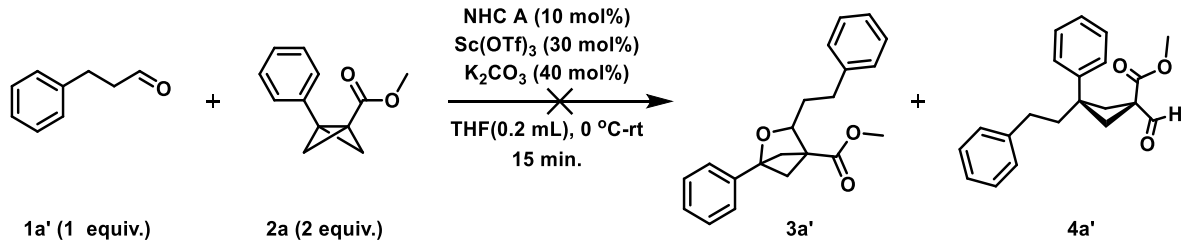
2.2. C) Typical procedure for the synthesis of representative product 4d



An oven-dried schlenk tube equipped with a magnetic stirring bar was charged with NHC precatalyst-**A** (6.7 mg, 0.016 mmol, 10 mol%) and K_2CO_3 (8.8 mg, 0.064 mmol, 40 mol%). The reaction vessel was evacuated and backfilled with argon three times. Under an argon atmosphere, (E)-3-(4-Chlorophenyl)acrylaldehyde (**1d**, 27 mg, 0.16 mmol, 1 equiv.), methyl 3-phenylbicyclo[1.1.0]butane-1-carboxylate (**2a**, 60 mg, 0.32 mmol, 2 equiv.) were added followed by addition of dry THF (0.2 mL). The schlenk tube was placed in an ice bath and the reaction mixture was stirred for 5 minutes. After this, $Sc(OTf)_3$ (24 mg, 0.048 mmol, 30 mol%) was added and the tube was tightly closed with a glass stopper. The resulting mixture was kept for stirring at rt for 15 min. Upon completion of the reaction as observed by TLC, the reaction mixture was directly subjected to column chromatography using ethyl acetate:pet ether (1:4) over 230-400 flash silica gel to afford the methyl (1s,3s)-3-((E)-4-chlorostyryl)-1-formyl-3-phenylcyclobutane-1-carboxylate (**4d)** as a yellow oil with 85% yield (48 mg, >19:1 d.r.).

3. Mechanistic Studies and Control Experiments

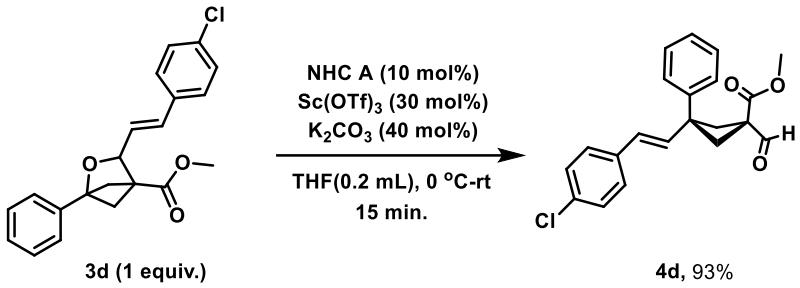
3.1 Reaction with saturated aldehyde



An oven-dried schlenk tube equipped with a magnetic stirring bar was charged with NHC precatalyst-**A** (6.7 mg, 0.016 mmol, 10 mol%) and K_2CO_3 (8.8 mg, 0.064 mmol, 40 mol%). The reaction vessel was evacuated and backfilled with argon three times. Under an argon atmosphere, 3-phenylpropanal

(**1a'**, 21 mg, 0.16 mmol, 1 equiv.), methyl 3-phenylbicyclo[1.1.0]butane-1-carboxylate (**2a**, 60 mg, 0.32 mmol, 2 equiv.) were added followed by addition of dry THF (0.2 mL). The schlenk tube was placed in an ice bath and the reaction mixture was stirred for 5 minutes. After this, $Sc(OTf)_3$ (24 mg, 0.048 mmol, 30 mol%) was added and the tube was tightly closed with a glass stopper. The resulting mixture was stirred at room temperature for 24 h. After monitoring the reaction for different time intervals, no formation of **3a′** and/or **4a′** was observed.

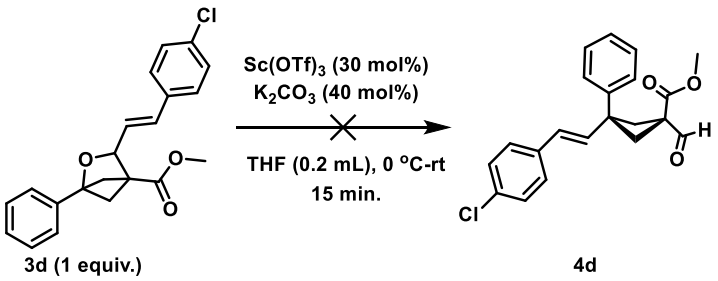
3.2 Reactivity of Intermediate under standard reaction conditions



An oven-dried schlenk tube equipped with a magnetic stirring bar was charged with NHC precatalyst-**A** (3.5 mg, 0.008 mmol, 10 mol%) and K_2CO_3 (4.6 mg, 0.033 mmol, 40 mol%). The reaction vessel was evacuated and backfilled with argon three times. Under an argon atmosphere, methyl (E)-3-(4-chlorostyryl)-1-phenyl-2-oxabicyclo[2.1.1]hexane-4-carboxylate (**3d**, 30 mg, 0.085 mmol, 1 equiv.) was added followed by addition of dry THF (0.2 mL). The schlenk tube was placed in an ice bath and the reaction mixture was stirred for 5 minutes. After this, $Sc(OTf)_3$ (12.5 mg, 0.025 mmol, 30 mol%) was added and the tube was tightly closed with a glass stopper. The resulting mixture was kept for stirring at rt for 15 min. Upon completion of the reaction as observed by TLC, the reaction mixture was directly subjected to column chromatography using ethyl acetate:pet ether (1:4) over 230-400 flash silica gel to afford the methyl (1s,3s)-3-((E)-4-chlorostyryl)-1-formyl-3-phenylcyclobutane-1-carboxylate (**4d)** as a yellow solid with 93% yield (28 mg, >19:1 d.r.).

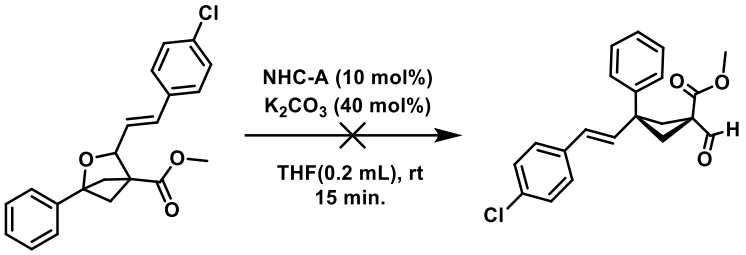
Note: Intermediate **3d** was obtained during the initial screening of ACN as a solvent (Table S4, entry 5)

3.3 Reactivity of Intermediate under Standard Reaction Conditions in the Absence of NHC precatalyst



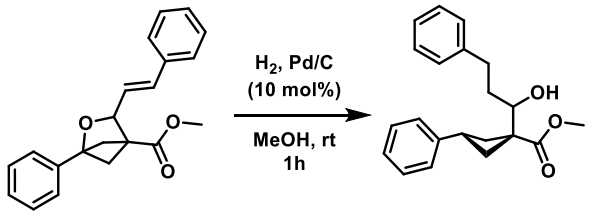
An oven-dried schlenk tube equipped with a magnetic stirring bar was charged with K_2CO_3 (7.8 mg, 0.056 mmol, 40 mol%). The reaction vessel was evacuated and backfilled with argon three times. Under an argon atmosphere, methyl (E)-3-(4-chlorostyryl)-1-phenyl-2-oxabicyclo[2.1.1]hexane-4-carboxylate (**3d**, 50 mg, 0.14 mmol, 1 equiv.) was added followed by addition of dry THF (0.5 mL). The schlenk tube was placed in an ice bath and the reaction mixture was stirred for 5 minutes. After this, $Sc(OTf)_3$ (21 mg, 0.042 mmol, 30 mol%) was added and the tube was tightly closed with a glass stopper. The resulting mixture was stirred at room temperature for 24 h. After monitoring the reaction for different time intervals, no formation of **4d** was observed.

3.4 Reactivity of Intermediate under Standard Reaction Conditions in the Absence of $Sc(OTf)_3$



An oven-dried schlenk tube equipped with a magnetic stirring bar was charged with NHC precatalyst-**A** (5.9 mg, 0.014 mmol, 10 mol%) and K_2CO_3 (7.8 mg, 0.056 mmol, 40 mol%). The reaction vessel was evacuated and backfilled with argon three times. Under an argon atmosphere, methyl (E)-3-(4-chlorostyryl)-1-phenyl-2-oxabicyclo[2.1.1]hexane-4-carboxylate (**3d**, 50 mg, 0.14 mmol, 1 equiv.) was added followed by addition of dry THF (0.5 mL). The resulting mixture was stirred at room temperature for 24 h. After monitoring the reaction for different time intervals, no formation of **4d** was observed.

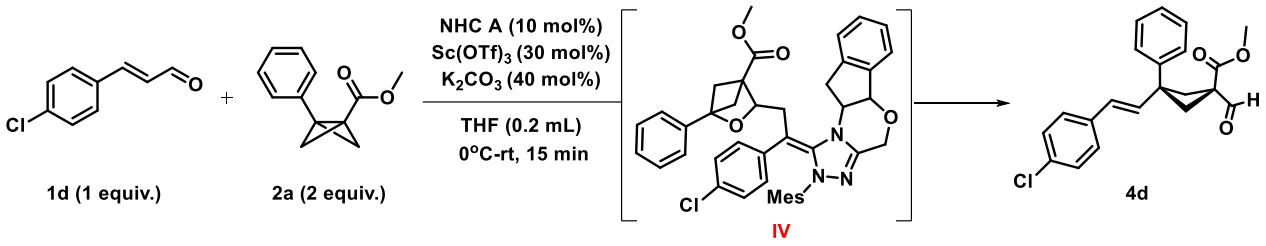
3.5 Reactivity of intermediate under hydrogenation condition



To a solution of methyl (E)-1-phenyl-3-styryl-2-oxabicyclo[2.1.1]hexane-4-carboxylate (**3a**, 76 mg, 0.24 mmol, 1 equiv.) in MeOH (8 mL), 10% Pd/C (25.3 mg, 0.023 mmol, 10 mol%) was added and the resulting mixture was stirred at room temperature for 1 h. After complete consumption of the starting material as observed by TLC, the reaction mixture was filtered through a pad of celite and concentrated under reduced pressure. The reaction mixture was then subjected to column chromatography using ethyl acetate:pet ether (1: 9) over 230-400 flash silica gel to afford the methyl

(1s,3s)-1-(1-hydroxy-3-phenylpropyl)-3-phenylcyclobutane-1-carboxylate (**3a"**) as a colourless oil (73 mg, 95% yield).

3.6 HRMS Analysis of Reaction Aliquots for the Proposed Intermediate IV

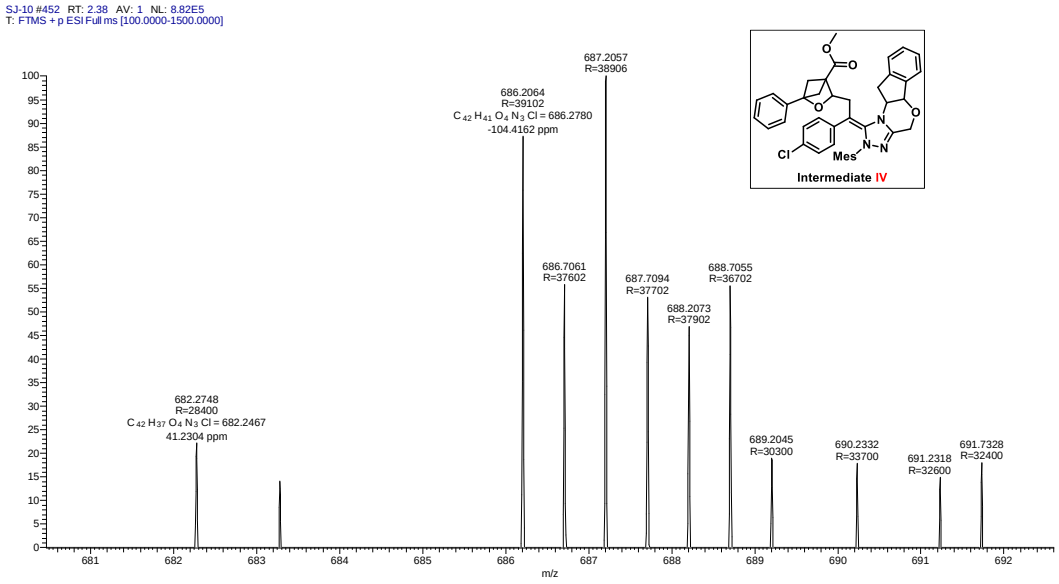


An oven-dried schlenk tube equipped with a magnetic stirring bar was charged with NHC precatalyst-**A** (6.7 mg, 0.016 mmol, 10 mol%) and K_2CO_3 (8.8 mg, 0.064 mmol, 40 mol%). The reaction vessel was evacuated and backfilled with argon three times. Under an argon atmosphere, (E)-3-(4-Chlorophenyl)acrylaldehyde (**1d**, 27 mg, 0.16 mmol, 1 equiv.), methyl 3-phenylbicyclo[1.1.0]butane-1-carboxylate (**2a**, 60 mg, 0.32 mmol, 2 equiv.) were added followed by addition of dry THF (0.2 mL). The schlenk tube was placed in an ice bath and the reaction mixture was stirred for 5 minutes. After this, $Sc(OTf)_3$ (24 mg, 0.048 mmol, 30 mol%) was added and the tube was tightly closed with a glass stopper. The resulting mixture was kept for stirring at room temperature. The progress of the reaction was monitored by TLC and HRMS at 3, 5, and 10 min. At each specified time interval, a 30 µL aliquot was withdrawn from the reaction mixture, filtered, and subsequently analyzed by HRMS.

After HRMS analysis of the samples collected at the specified time intervals (3 min, 5 min and 10 min) and quenched with methanol. We observed the following HRMS data:

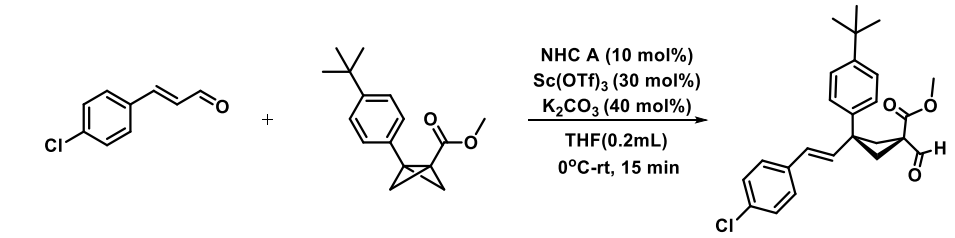
HRMS (ESI) m/z calcd for $C_{42}H_{41}ClN_3O_4$ $[M+H]^+$: 686.2780, found: 686.2064. The HRMS data provide evidence supporting the plausible formation of the proposed intermediate **IV**. However, the observed mass deviation (ppm error) is relatively high, possibly due to the limited stability of the intermediate under the analytical conditions.

HRMS spectra of the crude reaction mixture for detection of intermediate (IV)



4. Gram Scale Experiments

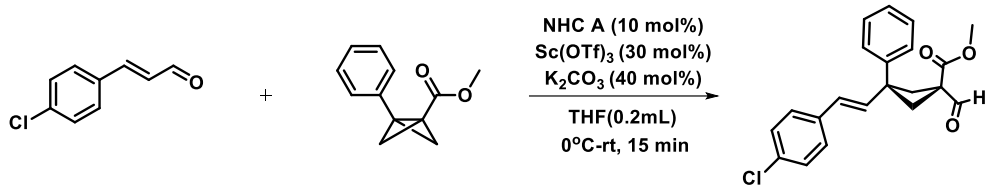
4.1. Gram Scale synthesis of Methyl (1*s*,3*s*)-3-(4-(*tert*-butyl)phenyl)-3-((*E*)-4-chlorostyryl)-1-formylcyclobutane-1-carboxylate (4x)



1d (500 mg, 3 mmol, 1 equiv.) **2x (1.46 g, 6 mmol, 2 equiv.)** **4x** (1.1g, 89%)

A 25mL round bottom flask was charged with NHC precatalyst-**A** (126 mg, 0.3 mmol, 10 mol%) and K_2CO_3 (166 mg, 1.2 mmol, 40 mol%). The reaction vessel was evacuated and backfilled with argon three times. Under an argon atmosphere, (E)-3-(4-Chlorophenyl)acrylaldehyde (**1d**, 500 mg, 3 mmol, 1 equiv.), methyl 3-(4-(*tert*-butyl)phenyl)bicyclo[1.1.0]butane-1-carboxylate (**2x**, 1.46 g, 6 mmol, 2 equiv.) were added followed by addition of dry THF (4 mL). The reaction vessel was placed in an ice bath and the reaction mixture was stirred for 5 minutes. After this, $Sc(OTf)_3$ (443 mg, 0.9 mmol, 30 mol%) was added and the resulting mixture was kept for stirring at rt for 15 min. After 15 min, the reaction mixture was directly subjected to column chromatography using ethyl acetate:pet ether (1:19) over 230-400 flash silica gel to afford the Methyl (1s,3s)-3-(4-(*tert*-butyl)phenyl)-3-((E)-4-chlorostyryl)-1-formylcyclobutane-1-carbox-ylate (**4x**) as a white solid with 89% yield (1.1 g, >19:1 d.r.).

4.2. Gram Scale synthesis of Methyl (1*s*,3*s*)-3-((*E*)-4-chlorostyryl)-1-formyl-3-phenyl cyclobutane-1-carboxylate (4d)

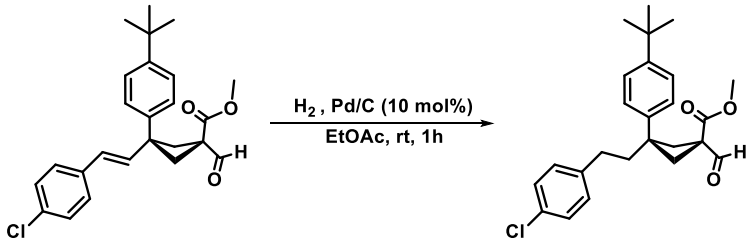


1d (1 g, 6 mmol, 1 equiv.) **2a** (2.26 g, 12 mmol, 2 equiv.) **4d** (1.51 g, 71%)

A 25mL round bottom flask was charged with NHC precatalyst-**A** (251 mg, 0.6 mmol, 10 mol%) and K_2CO_3 (331 mg, 1.2 mmol, 40 mol%). The reaction vessel was evacuated and backfilled with argon three times. Under an argon atmosphere, (E)-3-(4-Chlorophenyl)acrylaldehyde (**1d**, 1 g, 6 mmol, 1 equiv.), methyl 3-phenylbicyclo[1.1.0]butane-1-carboxylate (**2a**, 2.26 g, 12 mmol, 2 equiv.) were added followed by addition of dry THF (4 mL). The reaction vessel was placed in an ice bath and the reaction mixture was stirred for 5 minutes. After this, $Sc(OTf)_3$ (886 mg, 0.9 mmol, 30 mol%) was added and the resulting mixture was kept for stirring at rt for 15 min. The reaction mixture was then directly subjected to column chromatography using ethyl acetate:pet ether (1:19) over 230-400 flash silica gel to afford the Methyl (1s,3s)-3-((E)-4-chlorostyryl)-1-formyl-3-phenyl cyclo-butane-1-carboxylate (**4d**) as a yellow solid. (1.51 g, 71% yield, >19:1 d.r.).

5. Synthetic Transformations

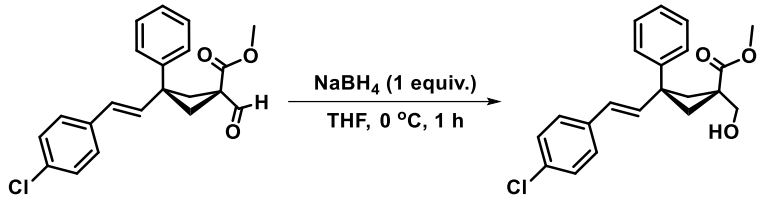
5.1 Synthesis of compound 5



4x **5**, 85%

To a solution of methyl (1s,3s)-3-(4-(*tert*-butyl)phenyl)-3-((*E*)-4-chlorostyryl)-1-formylcyclobutane-1-carboxylate (**4x**, 100 mg, 0.24 mmol) in EtOAc (8 mL), 10% Pd/C (25.9 mg, 0.024 mmol, 0.1 equiv.) was added and the resulting mixture was stirred under H_2 atmosphere for 1 h. After complete consumption of the starting material, the reaction mixture was filtered through a pad of celite and concentrated under reduced pressure. The reaction mixture was then subjected to column chromatography using ethyl acetate:pet ether (1: 9) over 230-400 flash silica gel to afford the methyl (1r,3s)-3-(4-(*tert*-butyl)phenyl)-3-(4-chlorophenethyl)-1-formylcyclobutane-1-carboxylate (**5**) as a colourless oil (85 mg, 85% yield, >19:1 d.r.).

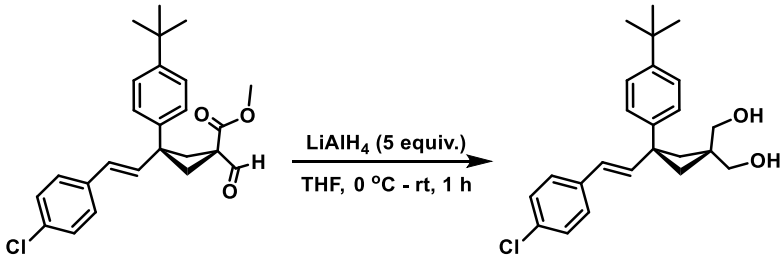
5.2 Synthesis of compound 6



4d **6**, 96%

To the solution of Methyl (1s,3s)-3-((E)-4-chlorostyryl)-1-formyl-3-phenylcyclobutane-1-carboxylate (**4d**, 30 mg, 0.085 mmol, 1 equiv.) in dry THF (0.5 mL) at 0 °C was added $NaBH_4$ (3.2 mg, 0.085 mmol, 1.0 equiv.). The reaction mixture was warmed to rt and stirred for 1 h. after completion of reaction as monitored by TLC, the resulting reaction mixture was quenched with brine (5 mL) and extracted with ethyl acetate (10 mL × 3). The combined organic layer was dried over anhydrous Na_2SO_4, and concentrated in vacuo. The obtained crude product was purified by flash chromatography (20% EtOAc in petroleum ether) to yield methyl (1s,3s)-3-((E)-4-chlorostyryl)-1-(hydroxymethyl)-3-phenylcyclobutane-1-carboxylate (**6**, 29 mg, 96% yield, >19:1 d.r.) as a yellow oil.

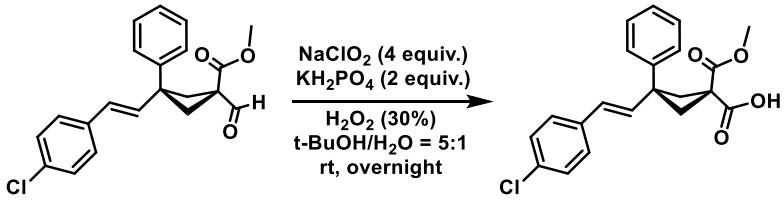
5.3 Synthesis of compound 7



4x **7**, 94%

To a solution of methyl (1s,3s)-3-(4-(*tert*-butyl)phenyl)-3-((*E*)-4-chlorostyryl)-1-formylcyclobutane-1-carboxylate (**4x**, 50 mg, 0.12 mmol, 1 equiv.) in dry THF (0.5 mL) at 0 °C was added $LiAlH_4$ (23 mg, 0.61 mmol, 5 equiv.) portion wise. The reaction mixture was allowed to warm to room temperature and stirred for 1 h. After completion, as monitored by TLC, the reaction was quenched with water (5 mL) and extracted with EtOAc (3 × 15 mL). The combined organic layers were dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The crude product was purified by flash column chromatography using 40% ethyl acetate in petroleum ether as the eluent to afford (*E*)-(3-(4-(*tert*-butyl)phenyl)-3-(4-chlorostyryl)cyclobutane-1,1-diyl)dimethanol (**7**, 44 mg, 94% yield, >19:1 d.r.) as a white solid.

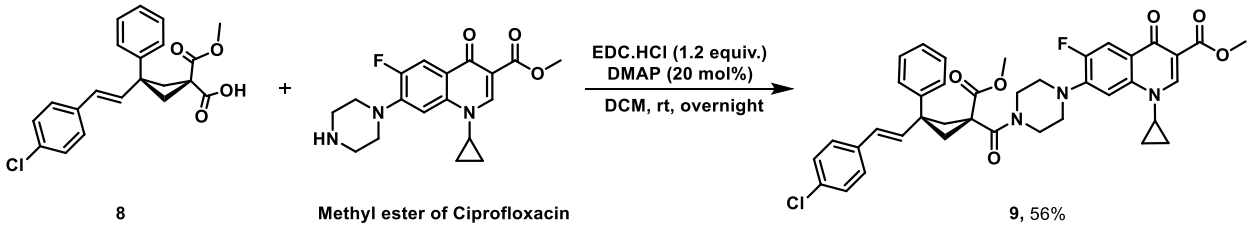
5.4 Synthesis of compound 8



4d **8**, 38%

A 25 mL round bottom flask was charged with methyl (1s,3s)-3-((*E*)-4-chlorostyryl)-1-formyl-3-phenylcyclobutane-1-carboxylate (**4d**, 230 mg, 0.64 mmol, 1.0 equiv) and a magnetic stir bar. Next, tert-butanol:H_2O (5 mL:1.5 mL), KH_2PO_4 (176 mg, 1.29 mmol, 2.0 equiv), hydrogen peroxide (0.6 mL, 30%), and $NaClO_2$ (234 mg, 2.59 mmol, 4.0 equiv) were added sequentially. The reaction mixture was stirred at room temperature for 12 hours. The reaction was quenched with hydrochloric acid solution (6 mL, 1 M), and the aqueous phase was extracted with EtOAc (3 x 20 mL). The combined organic layers were concentrated, and the residue was purified by flash chromatography (1:19 MeOH/DCM) to afford the desired product, (1s,3s)-3-((*E*)-4-chlorostyryl)-1-(methoxycarbonyl)-3-phenylcyclobutane-1-carboxylic acid (**8**, 90 mg, 38% yield, >19:1 d.r.) as a white solid.

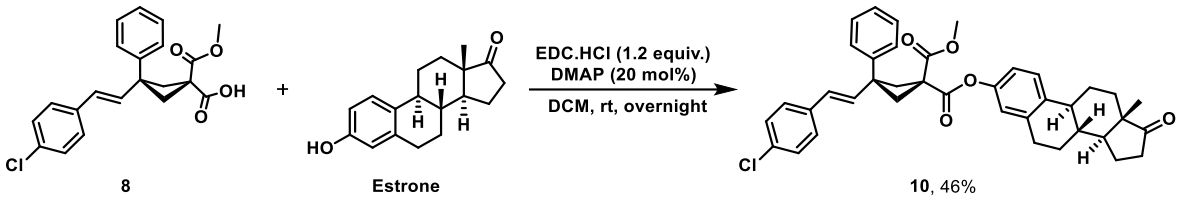
5.5 Synthesis of compound 9



8 Methyl ester of Ciprofloxacin **9**, 56%

A 10 mL round-bottom flask equipped with a magnetic stir bar was charged with (1s,3s)-3-((E)-4-chlorostyryl)-1-(methoxycarbonyl)-3-phenylcyclobutane-1-carboxylic acid (**8**, 37 mg, 0.1 mmol, 1.0 equiv.), methyl ester of ciprofloxacin (34.5 mg, 0.1mmol, 1.0 equiv.), 4-dimethylaminopyridine (2.4 mg, 0.02 mmol, 20 mol%), and 1-(3-Dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (23 mg, 0.12 mmol, 1.2 equiv.). DCM (2mL) was added and the reaction was stirred at rt for 12 h. Afterward, saturated NH_4Cl aqueous solution (3 mL) was added and the reaction mixture was extracted with DCM (5 mL×3). The combined organic layers were concentrated, and the residue was purified by flash chromatography (1:19 MeOH/DCM) to afford the desired product, methyl 7-(4-((1s,3s)-3-((E)-4-chlorostyryl)-1-(methoxycarbonyl)-3-phenylcyclobutane-1-carbonyl)piperazin-1-yl)-1-cyclopropyl-6-fluoro-4-oxo-1,4-dihydroquinoline-3-carboxylate (**9**, 39 mg, 56% yield, >19:1 d.r.) as a white solid.

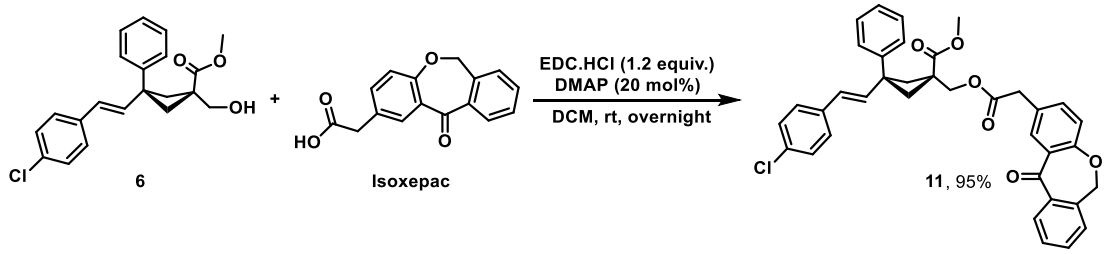
5.6 Synthesis of compound 10



8 Estrone **10**, 46%

A 10 mL round-bottom flask equipped with a magnetic stir bar was charged with (1s,3s)-3-((*E*)-4-chlorostyryl)-1-(methoxycarbonyl)-3-phenylcyclobutane-1-carboxylic acid (**8**, 37 mg, 0.1 mmol, 1.0 equiv.), estrone (30.4 mg, 0.1mmol, 1.0 equiv.), 4-dimethylaminopyridine (2.4 mg, 0.02 mmol, 20 mol%), and 1-(3-Dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (23 mg, 0.12 mmol, 1.2 equiv.). DCM (2mL) was added and the reaction was stirred at r.t. for 12 h. Afterward, saturated NH_4Cl aqueous solution (3 mL) was added and the reaction mixture was extracted with DCM (5 mL×3). The combined organic layers were concentrated, and the residue was purified by flash chromatography (1:4 EtOAc/Pet ether) to afford the desired product, 1-methyl 1-((8R,9S,13S,14S)-13-methyl-17-oxo-7,8,9,11,12,13,14,15,16,17-decahydro-6H-cyclopenta[a]phenanthren-3-yl) (1r,3S)-3-((E)-4-chlorostyryl)-3-phenylcyclobutane-1,1-dicarboxylate (**10**, 29 mg, 46% yield, >19:1 d.r.) as a yellow oil.

5.7 Synthesis of compound 11

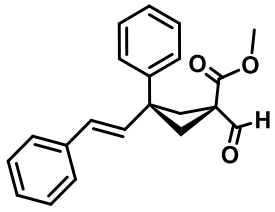


6 Isoxepac **11**, 95%

A 10 mL round-bottom flask equipped with a magnetic stir bar was charged with methyl (1s,3s)-3-((E)-4-chlorostyryl)-1-(hydroxymethyl)-3-phenylcyclobutane-1-carboxylate (**6**, 56 mg, 0.16 mmol, 1.0 equiv.), isoxepac (46 mg, 0.18 mmol, 1.1 equiv.), 4-dimethylaminopyridine (3.8 mg, 0.032 mmol, 20 mol%), and 1-(3-Dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (33 mg, 0.17 mmol, 1.1 equiv.). DCM (3mL) was added and the reaction was stirred at rt for 12 h. Afterward, saturated NH_4Cl aqueous solution (5 mL) was added and the reaction mixture was extracted with DCM (10 mL×3). The combined organic layers were concentrated, and the residue was purified by flash chromatography (1:4 EtOAc/Pet ether) to afford the desired product, Methyl (1s,3s)-3-((E)-4-chlorostyryl)-1-((2-(11-oxo-6,11-dihydrodibenzo[b,e]oxepin-2-yl)acetoxy)methyl)-3-phenylcyclobutane-1-carboxylate (**11**, 100 mg, 95% yield, >19:1 d.r.) as a yellow oil.

6. Characterization Data

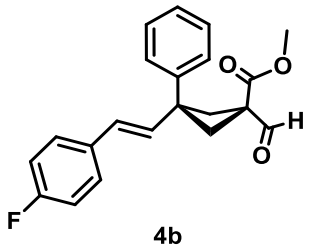
Methyl (1*s*,3*s*)-1-formyl-3-phenyl-3-((*E*)-styryl)cyclobutane-1-carboxylate (4a)



4a

Yellow oil, 88% (45 mg) isolated yield, R_f = 0.6 in 20% EtOAc: Pet Ether. **^{1}H NMR** (400MHz, CHLOROFORM-*d*): δ ppm 9.82 (s, 1 H), 7.38 - 7.33 (m, 2 H), 7.29 (t, J = 2.2 Hz, 2 H), 7.26 - 7.22 (m, 5 H), 7.21 - 7.16 (m, 1 H), 6.38 (d, J = 15.9 Hz, 1 H), 6.10 (d, J = 16.0 Hz, 1 H), 3.68 (s, 3 H), 3.17 - 3.07 (m, 4 H). **^{13}C{^{1}H} NMR** (101MHz, CHLOROFORM-*d*): δ ppm 196.3, 171.3, 146.4, 136.7, 136.4, 128.5 (2C), 128.4, 127.4, 126.3, 126.0, 52.8, 52.7, 43.6, 37.7. **HRMS (ESI-TOF) m/z:** $[M+H]^+$ Calcd for $C_{21}H_{21}O_3$ 321.1485; Found 321.1485.

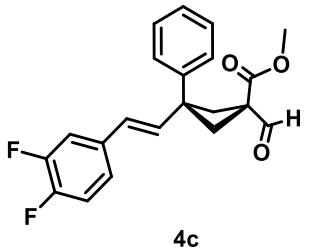
Methyl (1*s*,3*s*)-3-((*E*)-4-fluorostyryl)-1-formyl-3-phenylcyclobutane-1-carboxylate (4b)



4b

Yellow oil, 85% (46 mg) isolated yield, R_f = 0.4 in 20% EtOAc: Pet Ether. **^{1}H NMR** (400MHz, CHLOROFORM-*d*): δ ppm 9.84 (s, 1 H), 7.40 - 7.35 (m, 2 H), 7.25 (m, 5 H), 6.96 (t, J = 8.6 Hz, 2 H), 6.31 (d, J = 15.9 Hz, 1 H), 6.05 (d, J = 15.9 Hz, 1 H), 3.70 (s, 3 H), 3.17 - 3.08 (m, 4 H). **^{13}C{^{1}H} NMR** (101MHz, CHLOROFORM-*d*): δ ppm 196.3, 171.3, 162.2 (d, $J_{C\text{-}F}$ = 246.4 Hz), 146.3, 136.3, 136.3, 132.8 (d, $J_{C\text{-}F}$ = 3.81 Hz), 128.5, 127.8 (d, $J_{C\text{-}F}$ = 8.39 Hz), 127.3, 126.4, 126.0, 115.3 (d, $J_{C\text{-}F}$ = 22.13 Hz), 52.7, 43.5, 37.7. **HRMS (ESI-TOF) m/z:** $[M+H]^+$ Calcd for $C_{21}H_{20}O_3F$ 339.1391; Found 339.1388.

Methyl (1*s*,3*s*)-3-((*E*)-3,4-difluorostyryl)-1-formyl-3-phenylcyclobutane-1-carboxylate (4c)

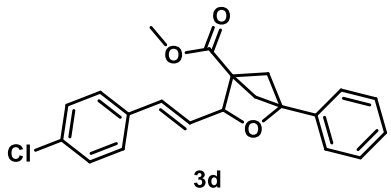


4c

Yellow oil, 79% (45 mg) isolated yield, R_f = 0.41 in 20% EtOAc: Pet Ether. **^{1}H NMR** (400MHz, CHLOROFORM-*d*): δ ppm 9.84 (s, 1 H), 7.40 - 7.36 (m, 2 H), 7.26 - 7.22 (m, 3 H), 7.11 - 7.06 (m,

1 H), 7.06 - 7.01 (m, 1 H), 6.99 - 6.95 (m, 1 H), 6.31 (d, *J* = 16.0 Hz, 1 H), 5.99 (d, *J* = 16.0 Hz, 1 H), 3.71 (s, 3 H), 3.17 - 3.08 (m, 4 H). **^{13}C{^{1}H} NMR** (101MHz, CHLOROFORM-*d*): *δ* ppm 196.2, 171.2, 151.6, 150.2 (dd, $J_{C\text{-}F}$ = 247.2, 13.0 Hz, 149.6 (dd, $J_{C\text{-}F}$ = 248.7, 12.2 Hz), 146.0, 137.6 (d, $J_{C\text{-}F}$ = 2.3 Hz), 134.0 (dd, $J_{C\text{-}F}$ = 6.1, 3.8 Hz), 128.6, 126.5, 126.0, 122.5 (dd, $J_{C\text{-}F}$ = 6.1, 3.0 Hz), 117.1 (d, $J_{C\text{-}F}$ = 17.5 Hz), 114.6 (d, $J_{C\text{-}F}$ = 17.5 Hz), 52.8, 52.7, 43.5, 37.5. **HRMS (ESI-TOF) m/z:** $[M+H]^+$ Calcd for $C_{21}H_{19}O_3F_2$ 357.1297; Found 357.1290.

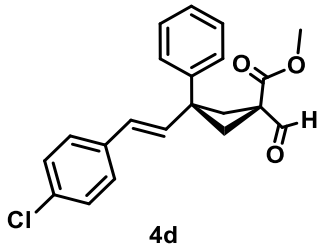
Methyl (E)-3-(4-chlorostyryl)-1-phenyl-2-oxabicyclo[2.1.1]hexane-4-carboxylate (3d)



3d

Colorless oil, 89% (50 mg) isolated yield, R_f = 0.5 in 10% EtOAc: Pet Ether. **^{1}H NMR** (400MHz, CHLOROFORM-*d*): *δ* ppm 7.49 - 7.44 (m, 2 H), 7.41 (t, *J* = 7.2 Hz, 2 H), 7.38 - 7.33 (m, 3 H), 7.32 - 7.28 (m, 2 H), 6.78 (d, *J* = 15.8 Hz, 1 H), 6.35 (dd, *J* = 6.1, 15.8 Hz, 1 H), 4.99 - 4.91 (m, 1 H), 3.77 (s, 3 H), 2.53 (d, *J* = 7.0 Hz, 1 H), 2.47 - 2.32 (m, 3 H). **^{13}C{^{1}H} NMR** (101MHz, CHLOROFORM-*d*): *δ* ppm 170.2, 136.8, 135.0, 133.4, 132.6, 128.7, 128.4, 128.3, 127.9, 127.3, 126.1, 86.8, 79.6, 53.3, 52.0, 49.7, 41.6. **HRMS (ESI-TOF) m/z:** $[M+H]^+$ Calcd for $C_{21}H_{20}O_3{}^{35}Cl$ 355.1095; Found 355.1086.

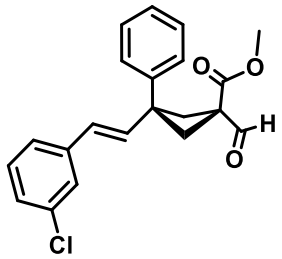
Methyl (1*s*,3*s*)-3-((*E*)-4-chlorostyryl)-1-formyl-3-phenylcyclobutane-1-carboxylate (4d)



4d

Yellow solid, mp 56-58 ºC, 85% (48 mg) isolated yield, R_f = 0.3 in 10% EtOAc: Pet Ether. **^{1}H NMR** (400MHz, CHLOROFORM-*d*): *δ* ppm 9.86 (s, 1 H), 7.43 - 7.36 (m, 2 H), 7.28 (d, *J* = 7.1 Hz, 3 H), 7.26 - 7.21 (m, 4 H), 6.39 (d, *J* = 16.0 Hz, 1 H), 6.05 (d, *J* = 15.9 Hz, 1 H), 3.72 (s, 3 H), 3.20 - 3.09 (m, 4 H). **^{13}C{^{1}H} NMR** (101MHz, CHLOROFORM-*d*): *δ* ppm 196.3, 171.3, 146.1, 137.2, 135.2, 133.0, 128.6, 128.5, 127.5, 127.3, 126.4, 126.0, 52.8, 52.7, 43.6, 37.6. **HRMS (ESI-TOF) m/z:** $[M+H]^+$ Calcd for $C_{21}H_{20}O_3{}^{35}Cl$ 355.1095; Found 355.1096.

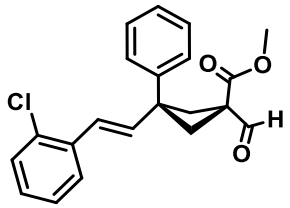
Methyl (1*s*,3*s*)-3-((*E*)-3-chlorostyryl)-1-formyl-3-phenylcyclobutane-1-carboxylate (4e)



4e

Colorless oil, 69% (39 mg) isolated yield, R_f = 0.6 in 10% EtOAc: Pet Ether. **^{1}H NMR** (400MHz, CHLOROFORM-*d*): δ ppm 9.83 (s, 1 H), 7.40 - 7.35 (m, 2 H), 7.27 - 7.22 (m, 4 H), 7.22 - 7.11 (m, 3 H), 6.40 (d, *J* = 15.9 Hz, 1 H), 6.03 (d, *J* = 16.0 Hz, 1 H), 3.70 (s, 3 H), 3.18 - 3.07 (m, 4 H). **^{13}C{^{1}H} NMR** (101MHz, CHLOROFORM-*d*): δ ppm 196.2, 171.3, 146.0, 138.6, 138.0, 134.4, 129.7, 128.6, 127.4, 127.2, 126.5, 126.3, 126.0, 124.6, 52.8, 52.7, 43.6, 37.5. **HRMS (ESI-TOF) m/z:** $[M+H]^+$ Calcd for $C_{21}H_{20}O_3{}^{35}Cl$ 355.1095; Found 355.1092.

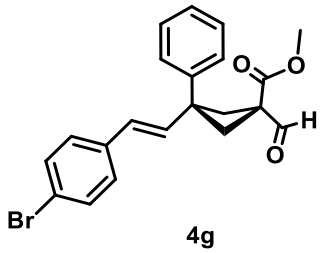
Methyl (1s,3s)-3-((E)-2-chlorostyryl)-1-formyl-3-phenylcyclobutane-1-carboxylate (4f)



4f

Yellow oil, 20% (11 mg) isolated yield, R_f = 0.41 in 20% EtOAc: Pet Ether. **^{1}H NMR** (400MHz, CHLOROFORM-*d*): δ ppm 9.83 (s, 1 H), 7.44 - 7.35 (m, 3 H), 7.33 - 7.27 (m, 3 H), 7.26 - 7.21 (m, 1 H), 7.16 (m, 2 H), 6.38 (d, *J* = 15.9 Hz, 1 H), 6.01 (d, *J* = 15.9 Hz, 1 H), 3.70 (s, 3 H), 3.17 - 3.07 (m, 4 H). **^{13}C{^{1}H} NMR** (101MHz, CHLOROFORM-*d*): δ ppm 196.3, 171.3, 146.1, 139.1, 134.9, 133.1, 129.5, 128.6, 128.5, 126.9, 126.8, 126.5, 126.0, 124.9, 52.8, 52.8, 43.9, 37.6. **HRMS (ESI-TOF) m/z:** $[M+H]^+$ Calcd for $C_{21}H_{20}O_3{}^{35}Cl$ 355.1095; Found 355.1095.

Methyl (1*s*,3*s*)-3-((*E*)-4-bromostyryl)-1-formyl-3-phenylcyclobutane-1-carboxylate (4g)

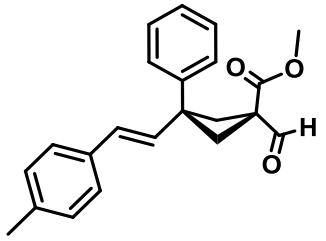


4g

White solid, mp 91-93 ºC, 82% (52 mg) isolated yield, R_f = 0.6 in 20% EtOAc: Pet Ether. **^{1}H NMR** (400MHz, CHLOROFORM-*d*): δ ppm 9.83 (s, 1 H), 7.41 - 7.35 (m, 4 H), 7.24 (d, *J* = 8.1 Hz, 2 H), 7.15 (d, *J* = 8.5 Hz, 2 H), 6.38 (d, *J* = 15.9 Hz, 1 H), 6.01 (d, *J* = 15.9 Hz, 1 H), 3.70 (s, 3 H), 3.17 - 3.07 (m, 4 H). **^{13}C{^{1}H} NMR** (101MHz, CHLOROFORM-*d*): δ ppm 196.3, 171.3, 146.1, 137.3,

135.7, 131.5, 128.5, 127.9, 127.3, 126.4, 126.0, 121.2, 52.8, 52.7, 43.6, 37.6. **HRMS (ESI-TOF) m/z:** $[M+H]^+$ Calcd for $C_{21}H_{20}O_3{}^{81}Br$ 401.0570; Found 401.0562.

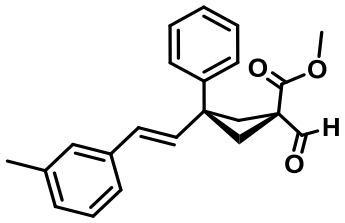
Methyl (1*s*,3*s*)-1-formyl-3-((*E*)-4-methylstyryl)-3-phenylcyclobutane-1-carboxylate (4h)



4h

Colorless oil, 68% (36 mg) isolated yield, R_f = 0.3 in 10% EtOAc: Pet Ether. **^{1}H NMR** (400MHz, CHLOROFORM-*d*): δ ppm 9.82 (s, 1 H), 7.37 - 7.32 (m, 2 H), 7.25 - 7.21 (m, 3 H), 7.17 (d, *J* = 8.0 Hz, 2 H), 7.06 (d, *J* = 8.0 Hz, 2 H), 6.32 (d, *J* = 15.9 Hz, 1 H), 6.06 (d, *J* = 16.0 Hz, 1 H), 3.68 (s, 3 H), 3.11 (s, 4 H), 2.30 (s, 3 H). **^{13}C{^{1}H} NMR** (101MHz, CHLOROFORM-*d*): δ ppm 196.4, 171.4, 146.5, 137.3, 135.4, 133.9, 129.2, 128.4, 128.3, 126.3, 126.2, 126.1, 52.8, 52.7, 43.6, 37.8, 21.1. **HRMS (ESI-TOF) m/z:** $[M+H]^+$ Calcd for $C_{22}H_{23}O_3$ 335.1642; Found 335.1637.

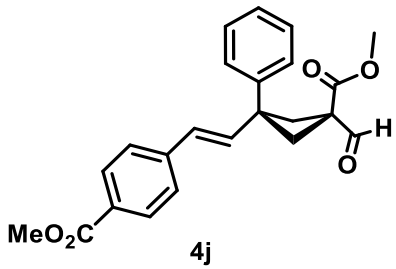
Methyl (1*s*,3*s*)-1-formyl-3-((*E*)-3-methylstyryl)-3-phenylcyclobutane-1-carboxylate (4i)



4i

Yellow oil, 73% (39 mg) isolated yield, R_f = 0.35 in 10% EtOAc: Pet Ether. **^{1}H NMR** (400MHz, CHLOROFORM-*d*): δ ppm 9.84 (s, 1 H), 7.40 - 7.34 (m, 2 H), 7.27 (s, 1 H), 7.27 - 7.21 (m, 2 H), 7.20 - 7.15 (m, 1 H), 7.14 - 7.08 (m, 2 H), 7.02 (d, *J* = 7.4 Hz, 1 H), 6.38 (d, *J* = 16.0 Hz, 1 H), 6.09 (d, *J* = 16.0 Hz, 1 H), 3.71 (s, 3 H), 3.20 - 3.09 (m, 4 H), 2.32 (s, 3 H). **^{13}C{^{1}H} NMR** (101MHz, CHLOROFORM-*d*): δ ppm 196.4, 171.3, 146.4, 138.0, 136.6, 136.2, 128.5, 128.5, 128.4, 128.2, 127.0, 126.3, 126.0, 123.5, 52.8, 52.7, 43.6, 37.7, 21.3. **HRMS (ESI-TOF) m/z:** $[M+H]^+$ Calcd for $C_{22}H_{23}O_3$ 335.1642; Found 335.1637.

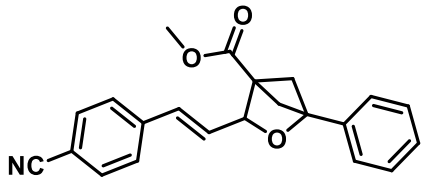
Methyl 4-((*E*)-2-((1*s*,3*s*)-3-formyl-3-(methoxycarbonyl)-1-phenylcyclobutyl)vinyl) benzoate (4j)



4j

Yellow oil, 70% (42 mg) isolated yield, R_f = 0.26 in 20% EtOAc: Pet Ether. **^{1}H NMR** (400MHz, CHLOROFORM-*d*): δ ppm 9.84 (s, 1 H), 7.93 (d, *J* = 8.4 Hz, 2 H), 7.40 - 7.36 (m, 2 H), 7.34 (d, *J* = 8.4 Hz, 2 H), 7.25 (d, *J* = 8.0 Hz, 3 H), 6.51 (d, *J* = 16.0 Hz, 1 H), 6.11 (d, *J* = 16.0 Hz, 1 H), 3.90 (s, 3 H), 3.70 (s, 3 H), 3.18 - 3.10 (m, 4 H). **^{13}C{^{1}H} NMR** (101MHz, CHLOROFORM-*d*): δ ppm 196.2, 171.3, 166.9, 145.9, 141.2, 139.2, 129.8, 128.9, 128.6, 127.6, 126.5, 126.2, 126.1, 52.8, 52.7, 52.0, 43.7, 37.5. **HRMS (ESI-TOF) m/z:** $[M+H]^+$ Calcd for $C_{23}H_{23}O_5$ 379.1540; Found 379.1524.

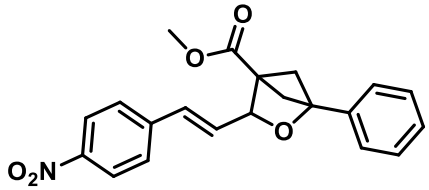
Methyl (*E*)-3-(4-cyanostyryl)-1-phenyl-2-oxabicyclo[2.1.1]hexane-4-carboxylate (3k)



3k

Colourless oil, 85% (47 mg) isolated yield, R_f = 0.5 in 20% EtOAc: Pet Ether. **^{1}H NMR** (400MHz, CHLOROFORM-*d*): δ ppm 7.61 (d, *J* = 8.4 Hz, 2 H), 7.52 - 7.44 (m, 4 H), 7.44 - 7.35 (m, 3 H), 6.84 (d, *J* = 15.9 Hz, 1 H), 6.53 (dd, *J* = 5.5, 15.9 Hz, 1 H), 4.98 (dd, *J* = 1.1, 5.6 Hz, 1 H), 3.78 (s, 3 H), 2.56 (d, *J* = 7.1 Hz, 1 H), 2.46 - 2.39 (m, 2 H), 2.34 - 2.30 (m, 1 H). **^{13}C{^{1}H} NMR** (101MHz, CHLOROFORM-*d*): δ ppm 169.9, 140.9, 136.6, 132.3, 131.9, 130.8, 128.4, 128.4, 127.1, 126.0, 118.8, 110.9, 86.9, 79.0, 53.2, 52.0, 49.7, 41.6. **HRMS (ESI-TOF) m/z:** $[M+H]^+$ Calcd for $C_{22}H_{20}O_3N$ 346.1438; Found 346.1426.

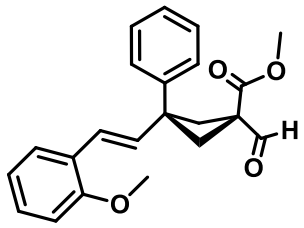
Methyl (*E*)-3-(4-nitrostyryl)-1-phenyl-2-oxabicyclo[2.1.1]hexane-4-carboxylate (3l)



3l

Yellow oil, 93% (54 mg) isolated yield, R_f = 0.5 in 20% EtOAc: Pet Ether. **^{1}H NMR** (400MHz, CHLOROFORM-*d*): δ ppm 8.28 - 8.10 (m, *J* = 8.6 Hz, 2 H), 7.58 - 7.51 (m, *J* = 8.8 Hz, 2 H), 7.50 - 7.44 (m, 2 H), 7.44 - 7.34 (m, 3 H), 6.90 (d, *J* = 15.9 Hz, 1 H), 6.60 (dd, *J* = 5.4, 15.8 Hz, 1 H), 5.00 (d, *J* = 5.3 Hz, 1H), 3.79 (s, 3 H), 2.57 (d, *J* = 7.1 Hz, 1 H), 2.49 - 2.40 (m, 2 H), 2.36 - 2.30 (m, 1 H). **^{13}C{^{1}H} NMR** (101MHz, CHLOROFORM-*d*): δ ppm 169.9, 147.0, 142.9, 136.6, 131.8, 131.5, 128.4, 128.4, 127.2, 126.0, 123.9, 87.0, 79.0, 53.2, 52.1, 49.7, 41.7. **HRMS (ESI-TOF) m/z:** $[M+H]^+$ Calcd for $C_{21}H_{20}O_5N$ 366.1336; Found 366.1324.

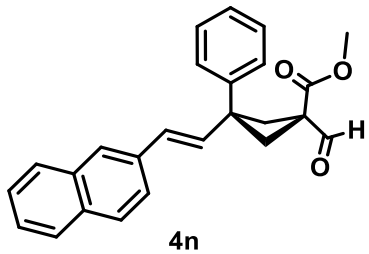
Methyl (1*s*,3*s*)-1-formyl-3-((*E*)-2-methoxystyryl)-3-phenylcyclobutane-1-carboxylate (4m)



4m

Yellow oil, 66% (35 mg) isolated yield, R_f = 0.23 in 10% EtOAc: Pet Ether. **^{1}H NMR** (400MHz, CHLOROFORM-*d*): δ ppm 9.84 (s, 1 H), 7.39 - 7.32 (m, 3 H), 7.29 (d, *J* = 1.4 Hz, 2 H), 7.25 - 7.16 (m, 2 H), 6.91 - 6.80 (m, 2 H), 6.56 (d, *J* = 16.1 Hz, 1 H), 6.36 (d, *J* = 16.1 Hz, 1 H), 3.81 (s, 3 H), 3.70 (s, 3 H), 3.19 - 3.10 (m, 4 H). **^{13}C{^{1}H} NMR** (101MHz, CHLOROFORM-*d*): δ ppm 196.5, 171.4, 156.6, 146.7, 136.6, 128.5, 128.5, 126.6, 126.2, 126.0, 125.8, 123.1, 120.6, 110.9, 55.5, 52.9, 52.7, 44.0, 37.9**. HRMS (ESI-TOF) m/z:** $[M+H]^+$ Calcd for $C_{22}H_{23}O_4$ 351.1591; Found 351.1586.

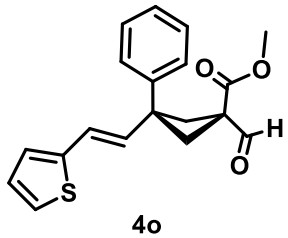
Methyl (1*s*,3*s*)-1-formyl-3-((*E*)-2-(naphthalen-2-yl)vinyl)-3-phenylcyclobutane-1-carboxylate (4n)



4n

Yellow solid, mp 125-127 ºC, 49% (29 mg) isolated yield, R_f = 0.5 in 10% EtOAc: Pet Ether. **^{1}H NMR** (400MHz, CHLOROFORM-*d*): δ ppm 9.88 (s, 1 H), 7.79 - 7.73 (m, 3 H), 7.64 (s, 1 H), 7.53 (dd, *J* = 1.6, 8.6 Hz, 1 H), 7.46 - 7.38 (m, 4 H), 7.33 - 7.27 (m, 3 H), 6.53 (d, *J* = 16.0 Hz, 1 H), 6.26 (d, *J* = 15.9 Hz, 1 H), 3.71 (s, 3 H), 3.19 (s, 4 H). **^{13}C{^{1}H} NMR** (101MHz, CHLOROFORM-*d*): δ ppm 196.4, 171.4, 146.3, 136.9, 134.1, 133.5, 132.9, 128.6, 128.5, 128.1, 127.9, 127.6, 126.4, 126.2, 126.2, 126.1, 125.7, 123.5, 52.8, 52.7, 43.7, 37.8. **HRMS (ESI-TOF) m/z:** $[M+H]^+$ Calcd for $C_{25}H_{23}O_3$ 371.1642; Found 371.1635.

Methyl (1*s*,3*s*)-1-formyl-3-phenyl-3-((*E*)-2-(thiophen-2-yl)vinyl)cyclobutane-1-carboxylate (4o)

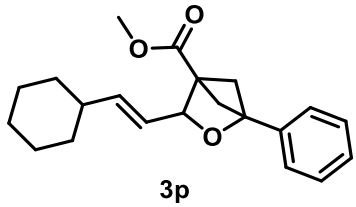


4o

Yellow oil, 48% (25 mg) isolated yield, R_f = 0.2 in 10% EtOAc: Pet Ether. **^{1}H NMR** (400MHz, CHLOROFORM-*d*): δ ppm 9.83 (s, 1 H), 7.39 - 7.35 (m, 2 H), 7.27 - 7.23 (m, 3 H), 7.11 (d, *J* = 4.9

Hz, 1 H), 6.93 - 6.89 (m, 1 H), 6.86 (d, *J* = 2.4 Hz, 1 H), 6.29 - 6.15 (m, 2 H), 3.69 (s, 3 H), 3.17 - 3.05 (m, 4 H). **^{13}C{^{1}H} NMR** (101MHz, CHLOROFORM-*d*): *δ* ppm 196.3, 171.3, 146.0, 141.8, 136.2, 128.5, 127.3, 126.4, 126.1, 125.6, 124.0, 122.0, 52.7 (2C), 43.5, 37.7. **HRMS (ESI-TOF) m/z:** $[M+H]^+$ Calcd for $C_{19}H_{19}O_3S$ 327.1049; Found 327.1045

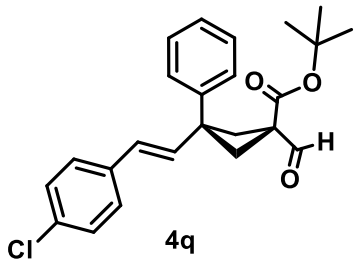
Methyl (*E*)-3-(2-cyclohexylvinyl)-1-phenyl-2-oxabicyclo[2.1.1]hexane-4-carboxylate (3p)



3p

Colorless oil, 33% (17 mg) isolated yield, R_f = 0.43 in 20% EtOAc: Pet Ether. **^{1}H NMR** (400MHz, CHLOROFORM-*d*): *δ* ppm 7.47 (d, *J* = 7.1 Hz, 2 H), 7.38 (t, *J* = 7.6 Hz, 2 H), 7.31 - 7.28 (m, 1 H), 6.54 (dd, *J* = 10.8, 15.2 Hz, 1 H), 5.97 (d, *J* = 15.3 Hz, 1 H), 5.85 (d, *J* = 10.8 Hz, 1 H), 3.61 (s, 3 H), 3.28 - 3.22 (m, 2 H), 2.68 - 2.62 (m, 2 H), 2.34 - 2.28 (m, 2 H), 2.20 - 2.09 (m, 3 H), 1.58 (br. s., 6 H). **^{13}C{^{1}H} NMR** (101MHz, CHLOROFORM-*d*): *δ* ppm 175.5, 145.2, 144.3, 132.2, 128.5, 127.5, 126.2, 125.1, 121.1, 73.0, 52.2, 46.0 (2C), 42.8, 37.3, 29.3, 28.4, 27.6, 26.7. **HRMS (ESI-TOF) m/z:** $[M+H]^+$ Calcd for $C_{21}H_{27}O_3$ 327.1955; Found 327.1943.

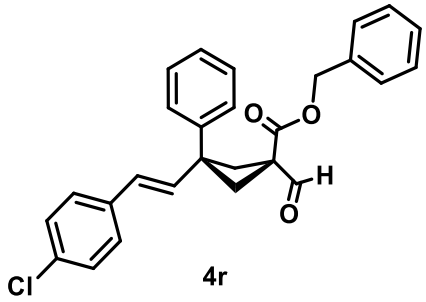
***Tert*-butyl (1*s*,3*s*)-3-((*E*)-4-chlorostyryl)-1-formyl-3-phenylcyclobutane-1-carboxylate (4q)**



4q

Yellow oil, 74% (47 mg) isolated yield, R_f = 0.4 in 5% EtOAc: Pet Ether. **^{1}H NMR** (400MHz, CHLOROFORM-*d*): *δ* ppm 9.79 (s, 1 H), 7.39 - 7.35 (m, 2 H), 7.28 (br. s., 1 H), 7.25 (d, *J* = 5.9 Hz, 2 H), 7.23 - 7.19 (m, 4 H), 6.36 (d, *J* = 15.9 Hz, 1 H), 5.99 (d, *J* = 15.9 Hz, 1 H), 3.10 - 3.01 (m, 4 H), 1.35 (s, 9 H). **^{13}C{^{1}H} NMR** (101MHz, CHLOROFORM-*d*): *δ* ppm 197.1, 170.0, 146.0, 137.8, 135.3, 133.0, 128.6, 128.5, 127.5, 127.1, 126.4, 126.3, 82.5, 53.5, 43.5, 37.8, 27.8. **HRMS (ESI-TOF) m/z:** $[M+H]^+$ Calcd for $C_{24}H_{26}O_3{}^{35}Cl$ 397.1565; Found 397.1561.

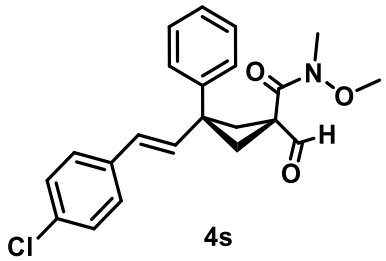
Benzyl (1*s*,3*s*)-3-((*E*)-4-chlorostyryl)-1-formyl-3-phenylcyclobutane-1-carboxylate (4r)



4r

Colorless oil, 79% (54 mg) isolated yield, R_f = 0.6 in 10% EtOAc: Pet Ether. **^{1}H NMR** (400MHz, CHLOROFORM-*d*): δ ppm 9.76 (s, 1 H), 7.30 - 7.22 (m, 5 H), 7.19 - 7.14 (m, 4 H), 7.14 - 7.11 (m, 5 H), 6.29 (d, *J* = 16.0 Hz, 1 H), 5.93 (d, *J* = 15.9 Hz, 1 H), 5.03 (s, 2 H), 3.09 - 3.00 (m, 4 H). **^{13}C{^{1}H} NMR** (101MHz, CHLOROFORM-*d*): δ ppm 196.3, 170.7, 145.9, 137.3, 135.2, 135.0, 133.0, 128.6 (2C), 128.5, 128.4, 128.0, 127.5, 127.2, 126.4, 126.1, 67.4, 52.7, 43.5, 37.7. **HRMS (ESI-TOF) m/z:** $[M+H]^+$ Calcd for $C_{27}H_{24}O_3{}^{35}Cl$ 431.1408; Found 431.1406.

(1*s*,3*s*)-3-((*E*)-4-chlorostyryl)-1-formyl-N-methoxy-*N*-methyl-3-phenylcyclobutane-1-carboxamide (4s)

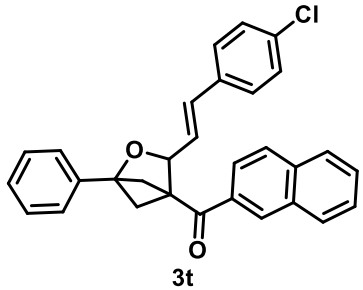


4s

Yellow solid, mp 102-104 ºC, 49% (30 mg) isolated yield, R_f = 0.4 in 30% EtOAc: Pet Ether. **^{1}H NMR** (400MHz, CHLOROFORM-*d*): δ ppm 9.77 (s, 1 H), 7.38 - 7.32 (m, 3 H), 7.24 (s, 5 H), 7.22 (s, 1 H), 6.47 (d, *J* = 16.0 Hz, 1 H), 6.11 (d, *J* = 15.9 Hz, 1 H), 3.59 (s, 3 H), 3.24 - 3.19 (m, 2 H), 3.18 (s, 3 H), 3.10 - 3.05 (m, 2 H). **^{13}C{^{1}H} NMR** (101MHz, CHLOROFORM-*d*): δ ppm 196.4, 146.9, 137.4, 135.3, 133.0, 128.6, 128.5, 128.3, 127.5, 127.1, 126.3, 125.9, 61.2, 52.9, 43.2, 37.7, 32.9. **HRMS (ESI-TOF) m/z:** $[M+H]^+$ Calcd for $C_{22}H_{23}O_3N^{35}Cl$ 384.1361; Found 384.1353.

(The reaction mixture was stirred at 50 °C for 10 h)

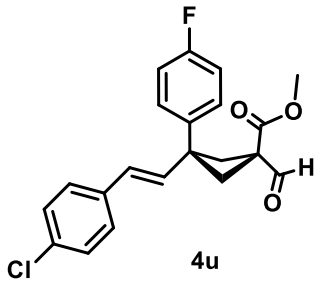
(*E*)-(3-(4-chlorostyryl)-1-phenyl-2-oxabicyclo[2.1.1]hexan-4-yl)(naphthalen-2-yl) methanone (3t)



3t

White solid, mp 140-142 ºC, 49% (35 mg) isolated yield, R_f = 0.4 in 40% EtOAc: Pet Ether. **^{1}H NMR** (400MHz, CHLOROFORM-*d*): δ ppm 8.35 (s, 1 H), 7.96 - 7.86 (m, 4 H), 7.67 - 7.53 (m, 2 H), 7.44 (d, *J* = 7.4 Hz, 2 H), 7.32 (t, *J* = 7.6 Hz, 2 H), 7.25 - 7.20 (m, 3 H), 7.17 - 7.12 (m, 2 H), 6.35 (d, *J* = 15.8 Hz, 1 H), 6.06 (dd, *J* = 6.8, 15.8 Hz, 1 H), 5.17 (d, *J* = 6.8 Hz, 1 H), 3.59 (d, *J* = 13.9 Hz, 1 H), 3.38 - 3.27 (m, 2 H), 2.84 (dd, *J* = 3.5, 14.0 Hz, 1 H). **^{13}C{^{1}H} NMR** (101MHz, CHLOROFORM-*d*): δ ppm 200.9, 145.3, 135.4, 134.4, 133.7, 132.3, 132.0, 131.6, 131.0, 129.6, 128.7, 128.7, 128.5, 128.4, 127.9, 127.8, 127.5, 127.2, 126.9, 125.0, 124.8, 74.8, 72.3, 51.4, 47.0, 40.4. **HRMS (ESI-TOF) m/z:** $[M+H]^+$ Calcd for $C_{30}H_{24}O_2{}^{35}Cl$ 451.1459; Found 451.1443.

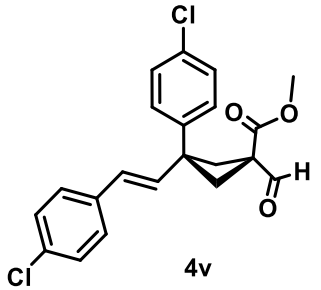
Methyl (1*s*,3*s*)-3-((*E*)-4-chlorostyryl)-3-(4-fluorophenyl)-1-formylcyclobutane-1-carboxylate (4u)



4u

Yellow oil, 79% (47 mg) isolated yield, R_f = 0.5 in 20% EtOAc: Pet Ether. **^{1}H NMR** (400MHz, CHLOROFORM-*d*): δ ppm 9.83 (s, 1 H), 7.26 - 7.19 (m, 6 H), 7.08 - 7.03 (m, 2 H), 6.35 (d, *J* = 15.9 Hz, 1 H), 5.99 (d, *J* = 15.9 Hz, 1 H), 3.71 (s, 3 H), 3.09 (s, 4 H). **^{13}C{^{1}H} NMR** (101MHz, CHLOROFORM-*d*): δ ppm 196.1, 171.3, 161.3 (d, $J_{C\text{-}F}$ = 246.4 Hz), 141.7 (d, $J_{C\text{-}F}$ = 3.8 Hz), 137.1, 135.0, 133.1, 128.6, 127.8 (d, $J_{C\text{-}F}$ = 7.6 Hz), 127.5, 127.4, 115.4, 115.2, 52.8, 52.4, 43.1, 37.7. **HRMS (ESI-TOF) m/z:** $[M+H]^+$ Calcd for $C_{21}H_{19}O_3{}^{35}ClF$ 373.1001; Found 373.0997.

Methyl (1*s*,3*s*)-3-(4-chlorophenyl)-3-((*E*)-4-chlorostyryl)-1-formylcyclobutane-1-carboxylate (4v)

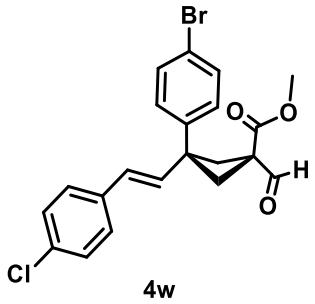


4v

Yellow oil, 56% (35 mg) isolated yield, R_f = 0.4 in 20% EtOAc: Pet Ether. **^{1}H NMR** (400MHz, CHLOROFORM-*d*): δ ppm 9.83 (s, 1 H), 7.34 (d, *J* = 8.5 Hz, 2 H), 7.25 - 7.20 (m, 4 H), 7.19 - 7.17 (m, 2 H), 6.34 (d, *J* = 16.0 Hz, 1 H), 5.99 (d, *J* = 16.0 Hz, 1 H), 3.71 (s, 3 H), 3.09 (s, 4 H). **^{13}C{^{1}H} NMR** (101MHz, CHLOROFORM-*d*): δ ppm 196.1, 171.2, 144.5, 136.7, 135.0, 133.2, 132.3, 128.7,

128.6, 127.6 (2C), 127.5, 52.9, 52.4, 43.1, 37.6. **HRMS (ESI-TOF) m/z:** $[M+H]^+$ Calcd for $C_{21}H_{19}O_3{}^{35}Cl_2$ 389.0706; Found 389.0700.

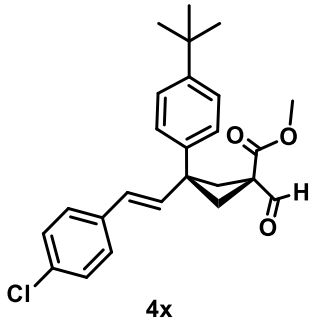
Methyl(1*s*,3*s*)-3-(4-bromophenyl)-3-((*E*)-4-chlorostyryl)-1-formylcyclobutane-1-carboxylate (4w)



4w

Yellow oil, 81% (56 mg) isolated yield, R_f = 0.3 in 20% EtOAc: Pet Ether. **^{1}H NMR** (400MHz, CHLOROFORM-*d*): δ ppm 9.82 (s, 1 H), 7.54 - 7.47 (m, *J* = 8.5 Hz, 2 H), 7.25 - 7.18 (m, 4 H), 7.15 - 7.10 (m, 2 H), 6.33 (d, *J* = 16.0 Hz, 1 H), 5.99 (d, *J* = 16.0 Hz, 1 H), 3.71 (s, 3 H), 3.08 (s, 4 H). **^{13}C{^{1}H} NMR** (101MHz, CHLOROFORM-*d*): δ ppm 196.0, 171.2, 145.1, 136.6, 135.0, 133.2, 131.6, 128.6, 128.0, 127.6, 127.5, 120.4, 52.8, 52.4, 43.2, 37.6. **HRMS (ESI-TOF) m/z:** $[M+H]^+$ Calcd for $C_{21}H_{19}O_3{}^{35}Cl^{81}Br$ 435.0180; Found 435.0173.

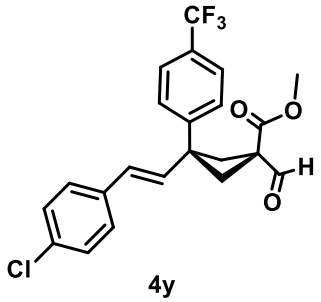
Methyl (1*s*,3*s*)-3-(4-(*tert*-butyl)phenyl)-3-((*E*)-4-chlorostyryl)-1-formylcyclobutane-1-carboxylate (4x)



4x

White solid, mp 124-126 ºC, 93% (61 mg) isolated yield, R_f = 0.32 in 10% EtOAc: Pet Ether. **^{1}H NMR** (400MHz, CHLOROFORM-*d*): δ ppm 9.82 (s, 1 H), 7.38 (d, *J* = 8.4 Hz, 2 H), 7.23 (s, 4 H), 7.17 (d, *J* = 8.5 Hz, 2 H), 6.35 (d, *J* = 16.0 Hz, 1 H), 6.10 (d, *J* = 16.0 Hz, 1 H), 3.70 (s, 3 H), 3.15 - 3.07 (m, 4 H), 1.33 (s, 9 H). **^{13}C{^{1}H} NMR** (101MHz, CHLOROFORM-*d*): δ ppm 196.3, 171.3, 149.2, 143.1, 137.1, 135.3, 133.0, 128.6, 127.5, 127.0, 125.6, 125.4, 52.8, 52.7, 43.2, 37.6, 34.4, 31.3. **HRMS (ESI-TOF) m/z:** $[M+H]^+$ Calcd for $C_{25}H_{28}O_3{}^{35}Cl$ 411.1721; Found 411.1719.

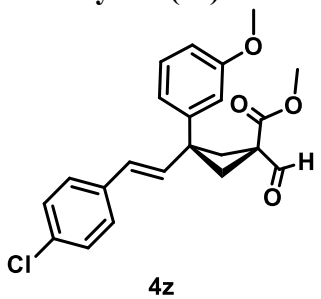
Methyl (1*s*,3*s*)-3-((*E*)-4-chlorostyryl)-1-formyl-3-(4-(trifluoromethyl)phenyl)cyclo- butane-1-carboxylate (4y)



4y

Yellow oil, 42% (28 mg) isolated yield, R_f = 0.5 in 20% EtOAc: Pet Ether. **^{1}H NMR** (400MHz, CHLOROFORM-*d*): δ ppm 9.84 (s, 1 H), 7.66 - 7.62 (m, J = 8.4 Hz, 2 H), 7.38 - 7.35 (m, J = 8.3 Hz, 2 H), 7.22 (q, J = 8.6 Hz, 4 H), 6.34 (d, J = 16.0 Hz, 1 H), 6.01 (d, J = 16.0 Hz, 1 H), 3.72 (s, 3 H), 3.17 - 3.09 (m, 4 H). **^{13}C{^{1}H} NMR** (101MHz, CHLOROFORM-*d*): δ ppm 196.9, 171.2, 150.2, 136.2, 134.8, 133.4, 128.8 (q, $J_{C\text{-}F}$ = 32.4 Hz), 128.7, 128.0, 127.6, 126.5, 125.6 (q, $J_{C\text{-}F}$ = 3.8 Hz), 124.1 (q, $J_{C\text{-}F}$ = 272.4 Hz), 52.9, 52.4, 43.5, 37.5. **HRMS (ESI-TOF) m/z:** $[M+H]^+$ Calcd for $C_{22}H_{19}{}^{35}ClF_3O_3$ 423.0969; Found 423.0969.

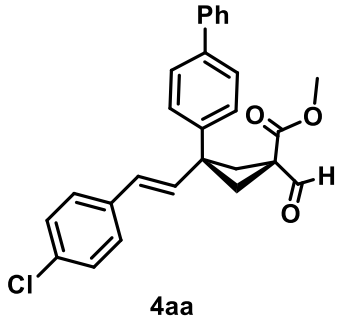
Methyl (1*s*,3*s*)-3-((*E*)-4-chlorostyryl)-1-formyl-3-(3-methoxyphenyl)cyclobutane-1-carboxylate (4z)



4z

Colorless oil, 82% (50 mg) isolated yield, R_f = 0.5 in 20% EtOAc: Pet Ether. **^{1}H NMR** (400MHz, CHLOROFORM-*d*): δ ppm 9.79 (s, 1 H), 7.26 - 7.22 (m, 1 H), 7.22 - 7.15 (m, 4 H), 6.79 (d, J = 7.6 Hz, 1 H), 6.77 - 6.71 (m, 2 H), 6.31 (d, J = 15.9 Hz, 1 H), 6.02 (d, J = 16.0 Hz, 1 H), 3.78 (s, 3 H), 3.67 (s, 3 H), 3.15 - 3.00 (m, 4 H). **^{13}C{^{1}H} NMR** (101MHz, CHLOROFORM-*d*): δ ppm 196.3, 171.3, 159.7, 147.9, 136.9, 135.2, 133.0, 129.6, 128.6, 127.5, 127.3, 118.4, 112.4, 111.3, 55.2, 52.8, 52.6, 43.6, 37.6. **HRMS (ESI-TOF) m/z:** $[M+H]^+$ Calcd for $C_{22}H_{22}O_4{}^{35}Cl$ 385.1201; Found 385.1196.

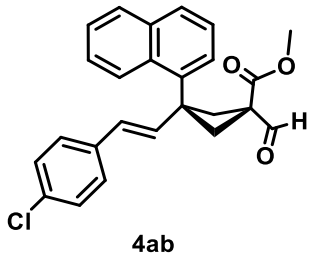
Methyl(1*s*,3*s*)-3-([1,1'-biphenyl]-4-yl)-3-((*E*)-4-chlorostyryl)-1-formylcyclobutane-1-carboxylate (4aa)



4aa

White solid, mp 104-106 ºC, 93% (64 mg) isolated yield, R_f = 0.24 in 10% EtOAc: Pet Ether. **^{1}H NMR** (400MHz, CHLOROFORM-*d*): δ ppm 9.86 (s, 1 H), 7.62 (d, J = 8.1 Hz, 4 H), 7.46 (t, J = 7.6 Hz, 2 H), 7.40 - 7.32 (m, 3 H), 7.25 (s, 4 H), 6.41 (d, J = 16.0 Hz, 1 H), 6.11 (d, J = 16.0 Hz, 1 H), 3.73 (s, 3 H), 3.23 - 3.11 (m, 4 H). **^{13}C{^{1}H} NMR** (101MHz, CHLOROFORM-*d*): δ ppm 196.2, 171.3, 145.1, 140.6, 139.3, 137.0, 135.2, 133.0, 128.8, 128.6, 127.5, 127.3, 127.3, 127.2, 127.0, 126.5, 52.8, 52.7, 43.4, 37.6. **HRMS (ESI-TOF) m/z:** $[M+H]^+$ Calcd for $C_{27}H_{24}{}^{35}ClO_3$ 431.1408; Found 431.1405.

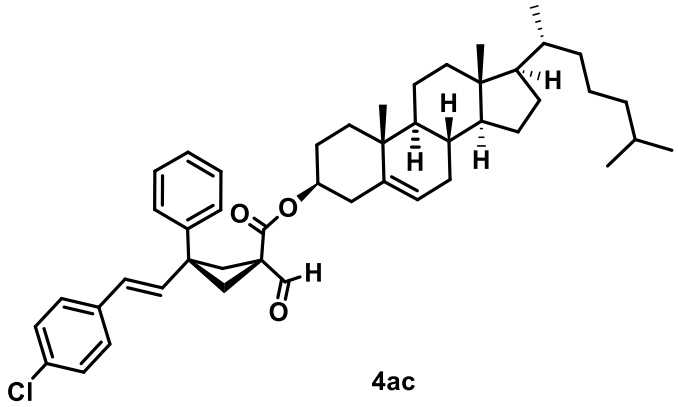
Methyl (1*s*,3*s*)-3-((*E*)-4-chlorostyryl)-1-formyl-3-(naphthalen-1-yl)cyclobutane-1-carboxylate (4ab)



4ab

Yellow oil, 74% (48 mg) isolated yield, R_f = 0.5 in 20% EtOAc: Pet Ether. **^{1}H NMR** (400MHz, CHLOROFORM-*d*): δ ppm 9.97 (s, 1 H), 7.92 - 7.88 (m, 1 H), 7.81 (d, *J* = 8.1 Hz, 1 H), 7.68 (d, *J* = 8.3 Hz, 1 H), 7.54 - 7.49 (m, 1 H), 7.48 - 7.41 (m, 3 H), 7.20 - 7.12 (m, 4 H), 6.67 (d, *J* = 16.0 Hz, 1 H), 5.94 (d, *J* = 15.9 Hz, 1 H), 3.69 (s, 3 H), 3.42 - 3.34 (m, 4 H). **^{13}C{^{1}H} NMR** (101MHz, CHLOROFORM-*d*): δ ppm 196.6, 171.2, 141.8, 136.7, 135.2, 134.4, 132.9, 130.3, 129.1, 128.5, 128.1, 127.8, 127.5, 125.6, 125.5(2C), 125.1, 124.3, 52.9, 52.8, 43.9, 39.0. **HRMS (ESI-TOF) m/z:** $[M+H]^+$ Calcd for $C_{25}H_{22}O_3{}^{35}Cl$ 405.1252; Found 405.1248.

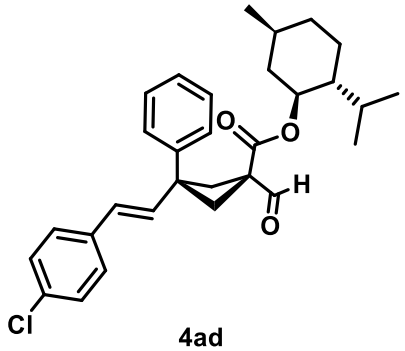
(3S,8S,9S,10R,13R,14S,17R)-10,13-dimethyl-17-((R)-6-methylheptan-2-yl)-2,3,4,7,8,9,10,11, 12,13,14,15,16,17-tetradecahydro-1H-cyclopenta[a]phenanthren-3-yl(1s,3R)-3-((E)-4-chloro styryl)-1-formyl-3-phenylcyclobutane-1-carboxylate (4ac)



4ac

White solid, mp 164-166 ºC, 94% (106 mg) isolated yield, R_f = 0.44 in 5% EtOAc: Pet Ether. **^{1}H NMR** (400MHz, CHLOROFORM-*d*): δ ppm 9.83 (s, 1 H), 7.40 - 7.34 (m, 2 H), 7.27 (s, 1 H), 7.26 - 7.15 (m, 6 H), 6.38 (d, *J* = 16.0 Hz, 1 H), 6.01 (d, *J* = 15.9 Hz, 1 H), 5.34 (d, *J* = 4.4 Hz, 1 H), 4.63 - 4.54 (m, 1 H), 3.14 - 3.05 (m, 4 H), 2.18 (d, *J* = 7.1 Hz, 2 H), 2.04 - 1.93 (m, 2 H), 1.87 - 1.79 (m, 2 H), 1.76 - 1.70 (m, 1 H), 1.57 - 1.31 (m, 11 H), 1.19 - 0.99 (m, 10 H), 0.98 (s, 3 H), 0.92 (d, *J* = 6.5 Hz, 3 H), 0.88 (d, *J* = 1.5 Hz, 3 H), 0.87 (d, *J* = 1.5 Hz, 3 H), 0.68 (s, 3 H). **^{13}C{^{1}H} NMR** (101MHz, CHLOROFORM-*d*): δ ppm 196.8, 170.4, 146.0, 139.2, 137.6, 135.3, 133.0, 128.6, 128.5, 127.5, 127.1, 126.4, 126.3, 122.9, 75.5, 56.6, 56.1, 52.8, 49.9, 43.5, 42.3, 39.7, 39.5, 37.8, 37.7, 36.8, 36.5, 36.2, 35.8, 31.9, 31.8, 28.2, 28.0, 27.4, 24.2, 23.8, 22.8, 22.5, 21.0, 19.2, 18.7, 11.8. **HRMS (ESI-TOF) m/z:** $[M+Na]^+$ Calcd for $C_{47}H_{61}O_3{}^{35}ClNa$ 731.4201; Found 731.4251 (due to poor solubility). **MALDI-TOF-MS m/z:** $[M + Na]^+$ Calcd for $C_{47}H_{61}O_3{}^{35}ClNa$ 731.4207; Found 731.6881.

(1S,2R,5S)-2-isopropyl-5-methylcyclohexyl (1s,3R)-3-((E)-4-chlorostyryl)-1-formyl-3-phenylcyclobutane-1-carboxylate (4ad)

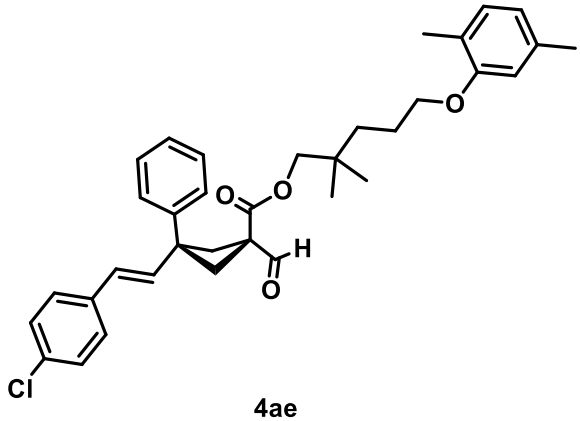


4ad

Yellow oil, 90% (69 mg) isolated yield, R_f = 0.6 in 10% EtOAc: Pet Ether. **^{1}H NMR** (400MHz, CHLOROFORM-*d*): δ ppm 9.82 (s, 1 H), 7.40 - 7.34 (m, 2 H), 7.28 (br. s., 1 H), 7.27 - 7.24 (m, 2 H), 7.24 - 7.18 (m, 4 H), 6.38 (d, *J* = 15.9 Hz, 1 H), 6.00 (d, *J* = 16.0 Hz, 1 H), 4.69-4.62 (m, 1 H), 3.17 - 3.05 (m, 4 H), 1.85 - 1.79 (m, 1 H), 1.69 - 1.61 (m, 3 H), 1.48 - 1.39 (m, 1 H), 1.36 - 1.25 (m,

3 H), 1.06-0.95 (m, 1 H), 0.87 (d, *J* = 6.5 Hz, 3 H), 0.83 (d, *J* = 7.0 Hz, 3 H), 0.66 (d, *J* = 7.0 Hz, 3 H). **^{13}C{^{1}H} NMR** (101MHz, CHLOROFORM-*d*): *δ* ppm 196.7, 170.4, 145.8, 137.7, 135.2, 133.0, 128.6, 128.5, 127.5, 127.1, 126.4, 126.2, 75.9, 52.9, 46.7, 43.5, 40.4, 37.7, 34.0, 31.3, 26.1, 23.1, 21.9, 20.7, 15.9. **HRMS (ESI-TOF) m/z:** $[M+H]^+$ Calcd for $C_{30}H_{36}{}^{35}ClO_3$ 479.2347; Found 479.2347.

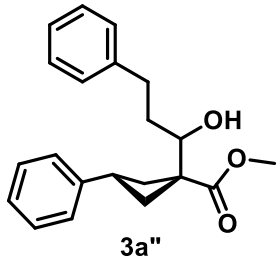
5-(2,5-dimethylphenoxy)-2,2-dimethylpentyl (1s,3s)-3-((E)-4-chlorostyryl)-1-formyl-3-phenylcyclobutane-1-carboxylate (4ae)



4ae

Yellow oil, 45% (40 mg) isolated yield, R_f = 0.29 in 10% EtOAc: Pet Ether. **^{1}H NMR** (400MHz, CHLOROFORM-*d*): *δ* ppm 9.87 (s, 1 H), 7.39 - 7.34 (m, 2 H), 7.27 - 7.20 (m, 7 H), 7.03 (d, *J* = 7.4 Hz, 1 H), 6.69 (d, *J* = 7.5 Hz, 1 H), 6.63 (s, 1 H), 6.39 (d, *J* = 16.0 Hz, 1 H), 6.02 (d, *J* = 16.0 Hz, 1 H), 3.91 - 3.85 (m, 4 H), 3.19 - 3.09 (m, 4 H), 2.34 (s, 3 H), 2.20 (s, 3 H), 1.75 - 1.67 (m, 2 H), 1.38 - 1.33 (m, 2 H), 0.88 (s, 6 H). **^{13}C{^{1}H} NMR** (101MHz, CHLOROFORM-*d*): *δ* ppm 196.3, 170.9, 156.9, 146.1, 137.4, 136.4, 135.2, 133.0, 130.3, 128.6, 128.5, 127.5, 127.2, 126.4, 126.1, 123.5, 120.7, 111.9, 73.4, 68.1, 52.6, 43.5, 37.6, 35.2, 33.7, 24.0, 21.4, 15.8. **HRMS (ESI-TOF) m/z:** $[M+H]^+$ Calcd for $C_{35}H_{40}{}^{35}ClO_4$ 559.2610; Found 559.2589.

Methyl (1s,3s)-1-(1-hydroxy-3-phenylpropyl)-3-phenylcyclobutane-1-carboxylate (3a")

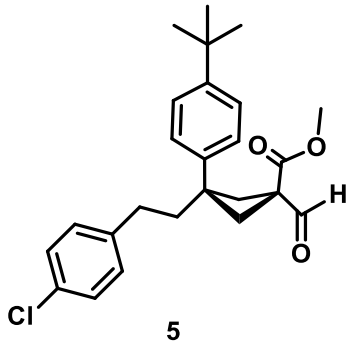


3a"

Colourless oil, 95% (73 mg) isolated yield, R_f = 0.43 in 20% EtOAc: Pet Ether. **^{1}H NMR** (400MHz, CHLOROFORM-*d*): *δ* ppm 7.33 - 7.23 (m, 4 H), 7.18 (m, 6 H), 3.79 (s, 3 H), 3.69 (br. s., 1 H), 3.57 (quin, *J* = 9.3 Hz, 1 H), 2.96 - 2.86 (m, 1 H), 2.82 - 2.69 (m, 2 H), 2.69 - 2.58 (m, 2 H), 2.46 (t, *J* = 10.8 Hz, 1 H), 2.11 (t, *J* = 10.5 Hz, 1 H), 1.76 - 1.64 (m, 1 H), 1.63 - 1.51 (m, 1 H).**^{13}C{^{1}H} NMR**

(101MHz, CHLOROFORM-*d*): δ ppm 176.7, 144.7, 141.8, 128.4 (2C), 128.3, 126.3, 126.1, 125.8, 76.2, 52.2, 48.7, 35.8, 35.3, 34.4, 33.8, 32.4. **HRMS (ESI-TOF) m/z:** $[M+Na]^+$ Calcd for $C_{21}H_{24}O_3Na$ 347.1618; Found 347.1611.

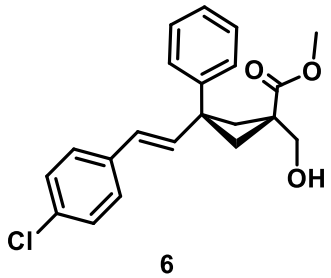
Methyl (1*r*,3*s*)-3-(4-(*tert*-butyl)phenyl)-3-(4-chlorophenethyl)-1-formylcyclobutane-1-carboxylate (5)



5

Colourless oil, 85% (85 mg) isolated yield, R_f = 0.5 in 10% EtOAc: Pet Ether. **^{1}H NMR** (400MHz, CHLOROFORM-*d*): δ ppm 9.84 (s, 1 H), 7.38 (d, *J* = 8.4 Hz, 2 H), 7.21 - 7.17 (m, *J* = 8.4 Hz, 2 H), 7.14 - 7.10 (m, *J* = 8.5 Hz, 2 H), 6.97 (d, *J* = 8.4 Hz, 2 H), 3.69 (s, 3 H), 2.94 (d, *J* = 13.1 Hz, 2 H), 2.80 (d, *J* = 13.3 Hz, 2 H), 2.28 - 2.21 (m, 2 H), 1.96 - 1.89 (m, 2 H), 1.35 (s, 9 H). **^{13}C{^{1}H} NMR** (101MHz, CHLOROFORM-*d*): δ ppm 196.6, 171.5, 148.8, 143.9, 140.3, 131.3, 129.6, 128.3, 125.3, 125.1, 52.6, 52.6, 44.7, 40.8, 36.9, 34.3, 31.3, 30.0. **HRMS (ESI-TOF) m/z:** $[M+H]^+$ Calcd for $C_{25}H_{30}{}^{35}ClO_3$ 413.1878; Found 413.1870.

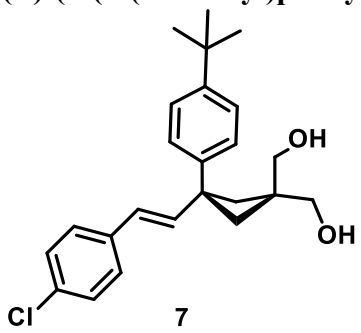
Methyl (1s,3s)-3-((*E*)-4-chlorostyryl)-1-(hydroxymethyl)-3-phenylcyclobutane-1-carboxylate (6)



6

Yellow oil, 96% (29 mg) isolated yield, R_f = 0.4 in 40% EtOAc: Pet Ether. **^{1}H NMR** (400MHz, CHLOROFORM-*d*): δ ppm 7.40 - 7.34 (m, 2 H), 7.29 (s, 4 H), 7.27(s, 3H), 7.25 - 7.21 (m, 1 H), 6.46 (d, *J* = 16.0 Hz, 1 H), 6.29 (d, *J* = 16.0 Hz, 1 H), 3.97 (s, 2 H), 3.69 (s, 3 H), 3.07 (d, *J* = 13.3 Hz, 2 H), 2.68 (d, *J* = 13.3 Hz, 2 H), 2.36 (br. s., 1 H). **^{13}C{^{1}H} NMR** (101MHz, CHLOROFORM-*d*): δ ppm 176.4, 147.7, 138.9, 135.4, 132.9, 128.6, 128.5, 127.5, 126.2, 126.1, 125.9, 67.0, 52.2, 43.2 (2C), 38.2. **HRMS (ESI-TOF) m/z:** $[M+Na]^+$ Calcd for $C_{21}H_{21}{}^{35}ClO_3Na$ 379.1071; Found 379.1069.

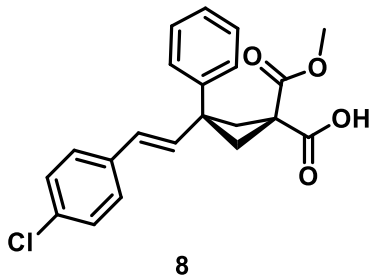
(*E*)-(3-(4-(*tert*-butyl)phenyl)-3-(4-chlorostyryl)cyclobutane-1,1-diyl)dimethanol (7)



7

White solid, mp 129-131 ºC, 94% (44 mg) isolated yield, R_f = 0.5 in 40% EtOAc: Pet Ether. **^{1}H NMR** (400MHz, CHLOROFORM-*d*): δ ppm 7.38 - 7.33 (m, 2 H), 7.23 (s, 4 H), 7.20 - 7.15 (m, 2 H), 6.42 (d, *J* = 16.0 Hz, 1 H), 6.18 (d, *J* = 15.9 Hz, 1 H), 3.85 (s, 2 H), 3.63 (s, 2 H), 2.62 (br. s., 2 H), 2.50 - 2.41 (m, 4 H), 1.33 (s, 9 H). **^{13}C{^{1}H} NMR** (101MHz, CHLOROFORM-*d*): δ ppm 148.6, 145.0, 140.4, 135.7, 132.6, 128.5, 127.4, 125.7, 125.3, 124.9, 70.4, 69.9, 42.6, 37.6, 37.6, 34.3, 31.4. **HRMS (ESI-TOF) m/z:** $[M-H]^+$ Calcd for $C_{24}H_{28}{}^{35}ClO_2$ 383.1772; Found 383.1768.

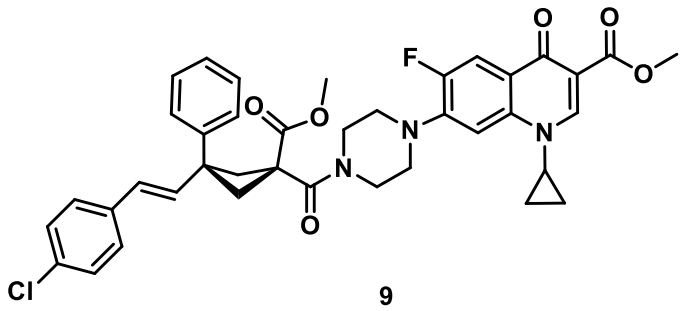
(1s,3s)-3-((E)-4-chlorostyryl)-1-(methoxycarbonyl)-3-phenylcyclobutane-1-carboxylic acid (8)



8

White solid, mp 182-184 ºC, 38% (90 mg) isolated yield, R_f = 0.25 in 5% MeOH: DCM. **^{1}H NMR** (400MHz, CHLOROFORM-*d*): δ ppm 7.40 - 7.33 (m, 2 H), 7.26 - 7.18 (m, 7 H), 6.42 (d, *J* = 15.9 Hz, 1 H), 6.11 (d, *J* = 16.0 Hz, 1 H), 3.66 (s, 3 H), 3.23 (d, *J* = 13.0 Hz, 2 H), 3.13 (d, *J* = 13.0 Hz, 2 H). **^{13}C{^{1}H} NMR** (101MHz, CHLOROFORM-*d*): δ ppm 176.0, 171.3, 145.8, 137.4, 135.4, 132.9, 128.6, 128.5, 127.6, 127.0, 126.4, 126.1, 53.0, 48.1, 43.9, 40.3. **HRMS (ESI-TOF) m/z:** $[M+Na]^+$ Calcd for $C_{21}H_{19}{}^{35}ClO_4Na$ 393.0864; Found 393.0865.

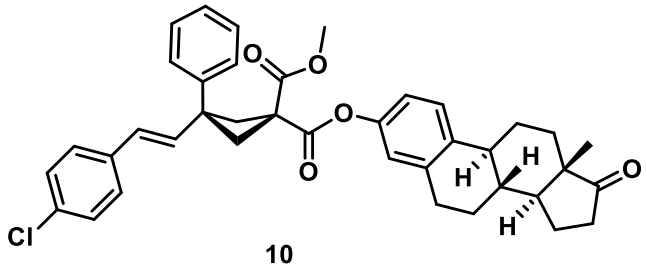
Methyl 7-(4-((1s,3s)-3-((E)-4-chlorostyryl)-1-(methoxycarbonyl)-3-phenylcyclobutane-1-carbonyl)piperazin-1-yl)-1-cyclopropyl-6-fluoro-4-oxo-1,4-dihydroquinoline-3-carboxylate (9)



9

White solid, mp 170-172 ºC, 56% (39 mg) isolated yield, R_f = 0.33 in 5% MeOH: DCM. **^{1}H NMR** (400MHz, CHLOROFORM-*d*): δ ppm 8.49 (s, 1 H), 7.96 (d, *J* = 13.1 Hz, 1 H), 7.40 - 7.34 (m, 2 H), 7.27 - 7.18 (m, 8 H), 6.46 (d, *J* = 15.9 Hz, 1 H), 5.98 (d, *J* = 15.9 Hz, 1 H), 3.89 (s, 5 H), 3.65 (s, 3 H), 3.55 - 3.45 (m, 2 H), 3.45 - 3.38 (m, 1 H), 3.34 - 3.14 (m, 8 H), 1.31 (q, *J* = 6.6 Hz, 2 H), 1.17 - 1.09 (m, 2 H). **^{13}C{^{1}H} NMR** (101MHz, CHLOROFORM-*d*): δ ppm **HRMS (ESI-TOF) m/z:** $[M+H]^+$ Calcd for $C_{39}H_{38}O_6N_3{}^{35}ClF$ 698.2428; Found 698.2416.

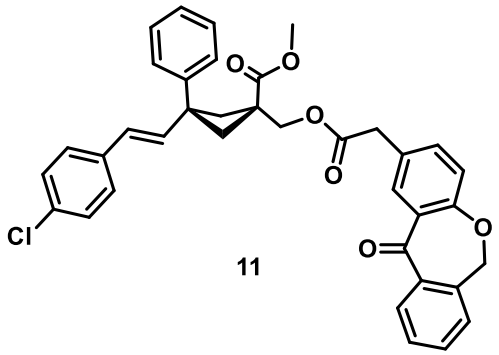
1-Methyl 1-((8R,9S,13S,14S)-13-methyl-17-oxo-7,8,9,11,12,13,14,15,16,17-decahydro-6H-cyclopenta[a]phenanthren-3-yl) (1r,3S)-3-((E)-4-chlorostyryl)-3-phenylcyclobutane-1,1-dicarboxylate (10)



10

Yellow oil, 46% (29 mg) isolated yield, R_f = 0.53 in 25% EtOAc: Pet Ether. **^{1}H NMR** (400MHz, CHLOROFORM-*d*): δ ppm 7.42 - 7.34 (m, 2 H), 7.27 - 7.21 (m, 8 H), 6.79 (dd, *J* = 2.4, 8.5 Hz, 1 H), 6.65 (d, *J* = 2.3 Hz, 1 H), 6.52 (d, *J* = 16.0 Hz, 1 H), 6.31 (d, *J* = 16.0 Hz, 1 H), 3.77 (s, 3 H), 3.31 (s, 4 H), 2.82 - 2.66 (m, 2 H), 2.52 (dd, *J* = 8.7, 18.9 Hz, 1 H), 2.45 - 2.36 (m, 1 H), 2.30 - 2.22 (m, 1 H), 2.22 - 2.12 (m, 1 H), 2.12 - 2.00 (m, 2 H), 1.99 - 1.95 (m, 1 H), 1.70 - 1.58 (m, 2 H), 1.56 - 1.48 (m, 3 H), 1.46 - 1.36 (m, 1 H), 0.92 (s, 3 H). **^{13}C{^{1}H} NMR** (101MHz, CHLOROFORM-*d*): δ ppm 220.8, 171.3, 170.5, 148.5, 146.4, 138.1, 137.7, 136.8, 135.3, 133.1, 128.6 (2C), 127.6, 127.1, 126.4 (2C), 125.8, 121.2, 118.2, 53.0, 50.4, 48.9, 47.9, 44.2, 44.1, 40.4, 37.9, 35.8, 31.5, 29.2, 26.2, 25.7, 21.5, 13.8. **HRMS (ESI-TOF) m/z:** $[M+H]^+$ Calcd for $C_{39}H_{40}O_5{}^{35}Cl$ 623.2559; Found 623.2548.

Methyl (1s,3s)-3-((E)-4-chlorostyryl)-1-((2-(11-oxo-6,11-dihydrodibenzo[b,e]oxepin-2-yl) acetoxy)methyl)-3-phenylcyclobutane-1-carboxylate (11)



11

Yellow oil, 95% (100 mg) isolated yield, R_f = 0.3 in 20% EtOAc: Pet Ether. **^{1}H NMR** (400MHz, CHLOROFORM-*d*): δ ppm 8.13 (d, *J* = 2.3 Hz, 1 H), 7.90 (dd, *J* = 1.1, 7.8 Hz, 1 H), 7.57 (m, 1 H), 7.48 (m, 1 H), 7.41 (dd, *J* = 2.4, 8.4 Hz, 1 H), 7.33 (d, *J* = 7.4 Hz, 2 H), 7.37 (d, *J* = 8.5 Hz, 1 H), 7.26 - 7.18 (m, 7 H), 7.04 (d, *J* = 8.4 Hz, 1 H), 6.43 (d, *J* = 16.0 Hz, 1 H), 6.25 (d, *J* = 16.0 Hz, 1 H), 5.19 (s, 2 H), 4.52 (s, 2 H), 3.65 (s, 2 H), 3.60 (s, 3 H), 3.09 (d, *J* = 13.4 Hz, 2 H), 2.66 (d, *J* = 13.4 Hz, 2 H).**^{13}C{^{1}H} NMR** (101MHz, CHLOROFORM-*d*): δ ppm 190.7, 174.6, 171.1, 160.4, 147.2, 140.4, 138.5, 136.3, 135.5, 135.3, 132.9, 132.8, 132.4, 129.4, 129.2, 128.6, 128.4, 127.8, 127.5, 127.5, 126.3, 126.1, 125.9, 125.1, 121.0, 73.6, 68.2, 52.2, 42.9, 41.8, 40.0, 38.4. **HRMS (ESI-TOF) m/z:** $[M-H]^+$ Calcd for $C_{37}H_{30}O_6{}^{35}Cl$ 605.1725; Found 605.1724.

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8. X-Ray Crystallographic Data

8.1 X-Ray Crystallographic Data of Compound 3g

A colourless, needle-shaped crystal was mounted on the goniometer. Data for mo_**3g** were collected from a single crystal in n/a hours at 100(2) K on a Bruker D8 VENTURE Kappa Duo PHOTON II CPAD \k-geometry diffractometer with a micro-focus sealed tube using a multilayer mirrors as monochromator and a Photon II CPAD Area Detector detector. The diffractometer used MoKα radiation (λ = 0.71073 Å). All data were integrated with SAINT (Bruker,, yielding 39429 reflections of which 4324 where independent and 90.7% were greater than 2σ(F2).[1] A multi-scan absorption correction using SADABS 2016/2 was applied.[2] The structure was solved by intrinsic phasing method methods with SHELXT 2018/2 and refined by full-matrix least-squares methods against F2 using SHELXL-2019/2.[3,4] All non-hydrogen atoms were refined with anisotropic displacement parameters. All hydrogen atoms were refined isotropic on calculated positions using a riding model with their Uiso values constrained to 1.5 times the Ueq of their pivot atoms for terminal sp3 carbon atoms and 1.2 times for all other carbon atoms. Crystallographic data for the structures reported in this paper have been deposited with the Cambridge Crystallographic Data Centre.[5] CCDC contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/structures. This report and the CIF file were generated using Final Cif.[6]

Table 1. Crystal data and structure refinement for mo_**3g**

CCDC number	2588893
Empirical formula	$C_{21}H_{19}BrN_0O_3$
Formula weight	399.27
Temperature [K]	100(2)
Crystal system	monoclinic
Space group (number)	$P2_1/c$ (14)
a [Å]	16.5799(4)
b [Å]	6.04510(10)
c [Å]	17.4355(4)
α [°]	90
β [°]	95.5860(10)
γ [°]	90
Volume [Å^3]	1739.21(6)
Z	4
ρ_{calc} [gcm^{-3}]	1.525
μ [mm^{-1}]	2.381
F(000)	816
Crystal size [mm^3]	0.12×0.14×0.33
Crystal colour	colourless
Crystal shape	needle
Radiation	MoK_α (λ=0.71073 Å)

2θ range [°]	4.94 to 56.72 (0.75 Å)
Index ranges	$-21 \le h \le 22$ $-8 \le k \le 8$ $-23 \le l \le 23$
Reflections collected	39429
Independent reflections	4324 R_{int} = 0.0545 R_{sigma} = 0.0319
Completeness to θ = 25.242°	99.6
Data / Restraints / Parameters	4324 / 0 / 227
Goodness-of-fit on F^2	1.024
Final R indexes [$I \ge 2\sigma(I)$]	R_1 = 0.0256 wR_2 = 0.0629
Final R indexes [all data]	R_1 = 0.0298 wR_2 = 0.0650
Largest peak/hole [eÅ^{-3}]	0.46/−0.39

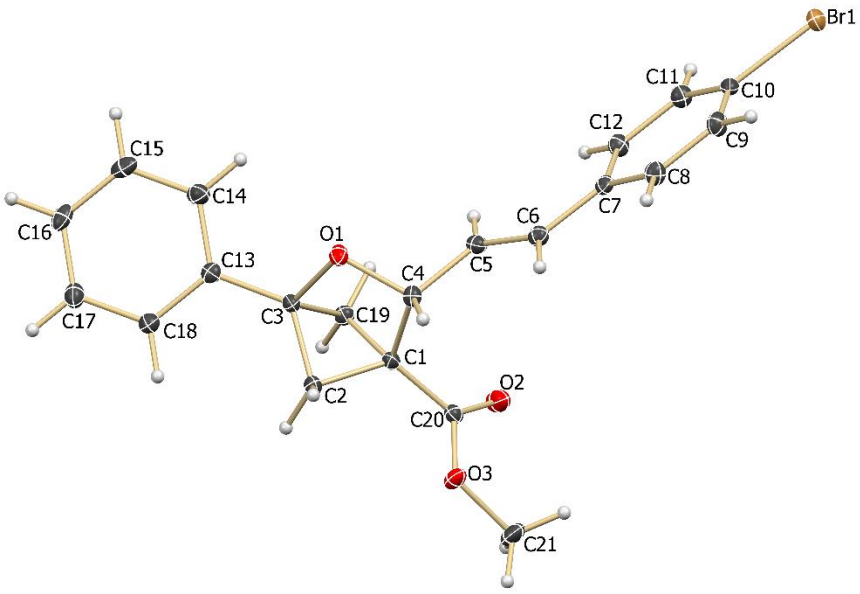


Figure 1. ORTEP view of compound **3g** showing the atom-numbering scheme, Displacement ellipsoids are drawn at the 50% probability level and H atoms are shown as small spheres with arbitrary radii. The compound crystallizes in the monoclinic space group $P2_1/c$ containing one molecule in the asymmetric unit.

Table 2. Bond lengths and angles for mo_**3g**

Atom–Atom	**Length [Å]**
Br1–C10	1.9030(15)
O1–C3	1.4558(18)
O1–C4	1.4633(18)
O2–C20	1.2037(19)
O3–C20	1.3415(18)
O3–C21	1.4538(19)
C1–C20	1.491(2)
C1–C19	1.547(2)
C1–C4	1.552(2)
C1–C2	1.556(2)
C1–C3	2.014(2)
C2–C3	1.550(2)
C3–C13	1.490(2)
C3–C19	1.551(2)
C4–C5	1.489(2)
C5–C6	1.338(2)
C6–C7	1.466(2)
C7–C8	1.396(2)
C7–C12	1.400(2)
C8–C9	1.386(2)
C9–C10	1.382(2)
C10–C11	1.387(2)
C11–C12	1.389(2)
C13–C18	1.388(2)
C13–C14	1.396(2)
C14–C15	1.389(2)
C15–C16	1.390(2)
C16–C17	1.387(2)
C17–C18	1.397(2)
Atom–Atom–Atom	**Angle [°]**
C3–O1–C4	102.23(11)
C20–O3–C21	114.84(13)
C20–C1–C19	120.74(13)
C20–C1–C4	117.03(12)
C19–C1–C4	101.42(12)
C20–C1–C2	125.25(12)
C19–C1–C2	87.13(11)
C4–C1–C2	99.14(12)
C20–C1–C3	164.81(12)
C19–C1–C3	49.53(8)
C4–C1–C3	77.96(9)
C2–C1–C3	49.45(8)
C3–C2–C1	80.85(10)
O1–C3–C13	112.02(12)
O1–C3–C2	102.96(12)

C13–C3–C2	125.10(13)
O1–C3–C19	101.78(11)
C13–C3–C19	123.11(13)
C2–C3–C19	87.20(11)
O1–C3–C1	80.88(9)
C13–C3–C1	167.01(12)
C2–C3–C1	49.70(8)
C19–C3–C1	49.37(8)
O1–C4–C5	111.65(12)
O1–C4–C1	98.81(11)
C5–C4–C1	116.61(12)
C6–C5–C4	121.11(14)
C5–C6–C7	127.84(15)
C8–C7–C12	118.07(14)
C8–C7–C6	118.25(14)
C12–C7–C6	123.66(14)
C9–C8–C7	121.70(15)
C10–C9–C8	118.65(14)
C9–C10–C11	121.60(14)
C9–C10–Br1	118.54(12)
C11–C10–Br1	119.85(12)
C10–C11–C12	118.93(15)
C11–C12–C7	121.05(14)
C18–C13–C14	119.20(14)
C18–C13–C3	120.30(14)
C14–C13–C3	120.42(14)
C15–C14–C13	120.22(15)
C14–C15–C16	120.38(15)
C17–C16–C15	119.72(15)
C16–C17–C18	119.89(15)
C13–C18–C17	120.59(15)
C1–C19–C3	81.10(11)
O2–C20–O3	123.52(14)
O2–C20–C1	124.21(14)
O3–C20–C1	112.26(13)

Bonds and angles to hydrogen atoms were omitted.

Table 3. Torsion angles for mo_**3g**

Atom–Atom–Atom–Atom	**Torsion Angle [°]**
C20–C1–C2–C3	−161.92(15)
C19–C1–C2–C3	−35.67(10)
C4–C1–C2–C3	65.45(11)
C4–O1–C3–C13	179.13(12)
C4–O1–C3–C2	42.29(13)
C4–O1–C3–C19	−47.53(13)
C4–O1–C3–C1	−2.54(10)
C1–C2–C3–O1	−65.88(11)

C1–C2–C3–C13	164.92(15)
C1–C2–C3–C19	35.57(10)
C3–O1–C4–C5	126.60(13)
C3–O1–C4–C1	3.30(13)
C20–C1–C4–O1	175.07(12)
C19–C1–C4–O1	41.55(13)
C2–C1–C4–O1	−47.35(12)
C3–C1–C4–O1	−2.38(9)
C20–C1–C4–C5	55.39(18)
C19–C1–C4–C5	−78.13(15)
C2–C1–C4–C5	−167.02(13)
C3–C1–C4–C5	−122.06(13)
O1–C4–C5–C6	124.42(15)
C1–C4–C5–C6	−123.06(16)
C4–C5–C6–C7	−176.93(14)
C5–C6–C7–C8	167.01(16)
C5–C6–C7–C12	−11.2(3)
C12–C7–C8–C9	0.4(2)
C6–C7–C8–C9	−177.83(15)
C7–C8–C9–C10	−0.6(2)
C8–C9–C10–C11	0.3(2)
C8–C9–C10–Br1	−178.67(12)
C9–C10–C11–C12	0.2(2)
Br1–C10–C11–C12	179.15(12)
C10–C11–C12–C7	−0.4(2)
C8–C7–C12–C11	0.1(2)
C6–C7–C12–C11	178.25(15)
O1–C3–C13–C18	−138.99(14)
C2–C3–C13–C18	−13.5(2)
C19–C3–C13–C18	99.23(18)
C1–C3–C13–C18	48.4(6)
O1–C3–C13–C14	44.29(19)
C2–C3–C13–C14	169.73(15)
C19–C3–C13–C14	−77.49(19)
C1–C3–C13–C14	−128.3(5)
C18–C13–C14–C15	−0.8(2)
C3–C13–C14–C15	175.98(15)
C13–C14–C15–C16	0.4(2)
C14–C15–C16–C17	0.4(2)
C15–C16–C17–C18	−0.9(2)
C14–C13–C18–C17	0.4(2)
C3–C13–C18–C17	−176.40(15)
C16–C17–C18–C13	0.5(2)
C20–C1–C19–C3	165.60(14)
C4–C1–C19–C3	−63.12(11)
C2–C1–C19–C3	35.62(10)
O1–C3–C19–C1	66.89(11)
C13–C3–C19–C1	−166.72(14)

C2–C3–C19–C1	−35.77(10)
C21–O3–C20–O2	−2.3(2)
C21–O3–C20–C1	177.22(13)
C19–C1–C20–O2	38.9(2)
C4–C1–C20–O2	−85.30(19)
C2–C1–C20–O2	149.33(16)
C3–C1–C20–O2	85.1(5)
C19–C1–C20–O3	−140.62(14)
C4–C1–C20–O3	95.17(15)
C2–C1–C20–O3	−30.2(2)
C3–C1–C20–O3	−94.4(5)

Bonds and angles to hydrogen atoms were omitted.

Table 4. Hydrogen bonds for mo_**3g**

D–H---A [Å]	d(D–H) [Å]	d(H---A) [Å]	d(D---A) [Å]	<(DHA) [°]
C5–H5---O3$^{\#1}$	0.95	2.65	3.5676(19)	161.9
C21–H21B---O2$^{\#2}$	0.98	2.52	3.488(2)	170.7

Symmetry transformations used to generate equivalent atoms:
#1: +X, -1+Y, +Z; #2: +X, 1+Y, +Z;

5.2 X-Ray Crystallographic Data of Compound 4g

A colourless, cube-shaped crystal was mounted on the goniometer. Data for cu_**4g** were collected from a single crystal in n/a hours at 100(2) K on a Bruker D8 VENTURE Kappa Duo PHOTON II CPAD \k-geometry diffractometer with a micro-focus sealed tube using a multilayer mirrors as monochromator and a Photon II CPAD Area Detector detector. The diffractometer used CuK_α radiation (λ = 1.54178 Å). All data were integrated with SAINT V8.41, yielding 261745 reflections of which 7571 where independent and 88.3% were greater than 2σ(F^2).[1] A Multi-Scan absorption correction using TWINABS Bruker was applied.[2] The structure was solved by Intrinsic Phasing methods with SHELXT 2018/2 and refined by full-matrix least-squares methods against F^2 using SHELXL-2019/2.[3,4] All non-hydrogen atoms were refined with anisotropic displacement parameters. All hydrogen atoms were refined isotropic on calculated positions using a riding model with their U_{iso} values constrained to 1.5 times the U_{eq} of their pivot atoms for terminal sp^3 carbon atoms and 1.2 times for all other carbon atoms. Crystallographic data for the structures reported in this paper have been deposited with the Cambridge Crystallographic Data Centre.[5] CCDC ?????? contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/structures. This report and the CIF file were generated using FinalCif.[6]

Table 5: Crystal data and structure refinement for cu_**4g**

CCDC number	2588894
Empirical formula	$C_{21}H_{19}BrO_3$
Formula weight	399.27
Temperature [K]	100(2)
Crystal system	triclinic
Space group (number)	$P\overline{1}$ (2)
a [Å]	11.2175(5)
b [Å]	11.6447(5)
c [Å]	15.3731(6)
α [°]	78.532(2)
β [°]	81.760(2)
γ [°]	65.099(2)
Volume [Å^3]	1781.04(13)
Z	4
ρ_{calc} [gcm^{-3}]	1.489
μ [mm^{-1}]	3.282
F(000)	816
Crystal size [mm^3]	0.16×0.18×0.22
Crystal colour	colourless
Crystal shape	cube
Radiation	CuK_α (λ=1.54178 Å)
2θ range [°]	5.88 to 158.31 (0.78 Å)
Index ranges	−13 ≤ h ≤ 14 −14 ≤ k ≤ 14 0 ≤ l ≤ 19
Reflections collected	261745
Independent reflections	7571 R_{int} = 0.0995 R_{sigma} = 0.0287
Completeness to θ = 67.679°	99.7
Data / Restraints / Parameters	7571 / 0 / 462
Goodness-of-fit on F^2	1.029
Final *R* indexes [$I \geq 2\sigma(I)$]	R_1 = 0.0426 wR_2 = 0.1115
Final *R* indexes [all data]	R_1 = 0.0503 wR_2 = 0.1205
Largest peak/hole [eÅ^{-3}]	0.61/−0.68

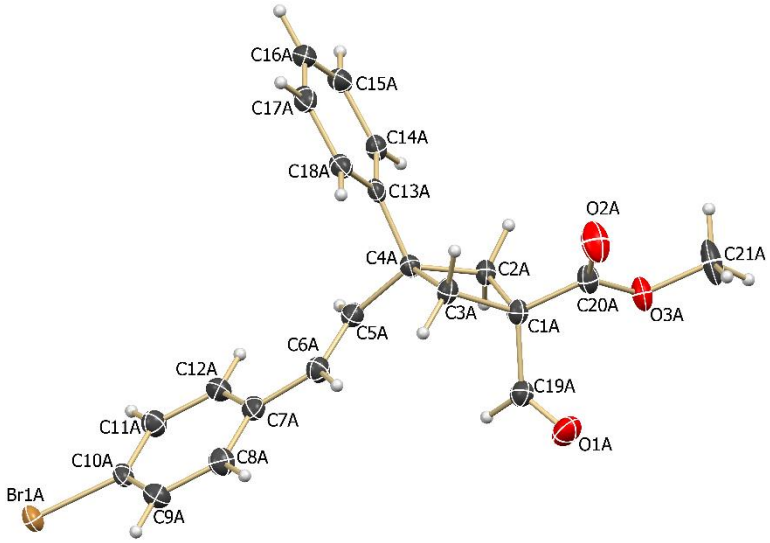


Figure 2. ORTEP view of compound **4g** showing the atom-numbering scheme, Displacement ellipsoids are drawn at the 50% probability level and H atoms are shown as small spheres with arbitrary radii. The compound crystallizes in the triclinic space group $P\overline{1}$ containing two molecules in the asymmetric unit, of which only molecule labelled with A suffix is shown. The Bromine atom also showed thermal disorder over two positions with occupanices 95% and 5%.

Refinement details for cu_4g

Refined as a 2-component twin.

Table 6. Bond lengths and angles for cu_**4g**

Atom–Atom	Length [Å]
Br1A–C10A	1.900(3)
Br2A–C10A	1.876(12)
O1A–C19A	1.202(4)
O2A–C20A	1.201(4)
O3A–C20A	1.341(3)
O3A–C21A	1.448(3)
C1A–C19A	1.510(4)
C1A–C20A	1.517(4)
C1A–C3A	1.559(4)
C1A–C2A	1.561(4)
C2A–C4A	1.565(4)
C3A–C4A	1.558(4)
C4A–C5A	1.509(4)
C4A–C13A	1.519(4)
C5A–C6A	1.329(4)
C6A–C7A	1.473(4)

C7A–C8A	1.391(4)
C7A–C12A	1.406(4)
C8A–C9A	1.386(4)
C9A–C10A	1.388(4)
C10A–C11A	1.382(4)
C11A–C12A	1.392(4)
C13A–C18A	1.392(4)
C13A–C14A	1.400(4)
C14A–C15A	1.391(4)
C15A–C16A	1.390(4)
C16A–C17A	1.388(4)
C17A–C18A	1.393(4)
Br1B–C10B	1.901(3)
Br2B–C10B	1.928(9)
O1B–C19B	1.193(4)
O2B–C20B	1.204(4)
O3B–C20B	1.338(4)
O3B–C21B	1.448(3)
C1B–C20B	1.507(4)
C1B–C19B	1.511(4)
C1B–C3B	1.559(4)
C1B–C2B	1.559(4)
C2B–C4B	1.573(4)
C3B–C4B	1.567(4)
C4B–C13B	1.512(4)
C4B–C5B	1.521(4)
C5B–C6B	1.320(4)
C6B–C7B	1.481(4)
C7B–C8B	1.392(4)
C7B–C12B	1.393(4)
C8B–C9B	1.398(4)
C9B–C10B	1.379(4)
C10B–C11B	1.383(4)
C11B–C12B	1.382(4)
C13B–C18B	1.394(4)
C13B–C14B	1.394(4)
C14B–C15B	1.391(4)
C15B–C16B	1.390(4)
C16B–C17B	1.391(4)
C17B–C18B	1.392(4)
Atom–Atom–Atom	**Angle [°]**
C20A–O3A–C21A	115.8(2)
C19A–C1A–C20A	112.4(2)
C19A–C1A–C3A	109.5(2)
C20A–C1A–C3A	116.5(2)
C19A–C1A–C2A	113.8(2)
C20A–C1A–C2A	113.6(2)

C3A–C1A–C2A	89.07(19)
C1A–C2A–C4A	89.89(19)
C4A–C3A–C1A	90.2(2)
C5A–C4A–C13A	105.3(2)
C5A–C4A–C3A	118.1(2)
C13A–C4A–C3A	115.6(2)
C5A–C4A–C2A	112.9(2)
C13A–C4A–C2A	116.0(2)
C3A–C4A–C2A	88.93(19)
C6A–C5A–C4A	127.2(3)
C5A–C6A–C7A	126.4(3)
C8A–C7A–C12A	117.7(3)
C8A–C7A–C6A	118.8(2)
C12A–C7A–C6A	123.3(3)
C9A–C8A–C7A	121.7(3)
C8A–C9A–C10A	119.0(3)
C11A–C10A–C9A	121.4(2)
C11A–C10A–Br2A	122.9(4)
C9A–C10A–Br2A	114.4(4)
C11A–C10A–Br1A	119.4(2)
C9A–C10A–Br1A	119.2(2)
C10A–C11A–C12A	118.7(3)
C11A–C12A–C7A	121.5(3)
C18A–C13A–C14A	119.3(3)
C18A–C13A–C4A	120.1(2)
C14A–C13A–C4A	120.5(2)
C15A–C14A–C13A	120.4(3)
C16A–C15A–C14A	120.2(3)
C17A–C16A–C15A	119.4(3)
C16A–C17A–C18A	120.8(3)
C13A–C18A–C17A	119.9(3)
O1A–C19A–C1A	124.2(3)
O2A–C20A–O3A	124.5(3)
O2A–C20A–C1A	125.6(3)
O3A–C20A–C1A	109.8(2)
C20B–O3B–C21B	116.3(2)
C20B–C1B–C19B	111.6(2)
C20B–C1B–C3B	116.2(2)
C19B–C1B–C3B	110.7(2)
C20B–C1B–C2B	114.7(2)
C19B–C1B–C2B	113.0(2)
C3B–C1B–C2B	89.05(19)
C1B–C2B–C4B	90.3(2)
C1B–C3B–C4B	90.5(2)
C13B–C4B–C5B	111.3(2)
C13B–C4B–C3B	115.8(2)
C5B–C4B–C3B	111.1(2)
C13B–C4B–C2B	115.5(2)

C5B–C4B–C2B	113.0(2)
C3B–C4B–C2B	88.29(19)
C6B–C5B–C4B	124.6(3)
C5B–C6B–C7B	127.3(3)
C8B–C7B–C12B	118.3(3)
C8B–C7B–C6B	123.3(3)
C12B–C7B–C6B	118.3(3)
C7B–C8B–C9B	121.0(3)
C10B–C9B–C8B	118.7(3)
C9B–C10B–C11B	121.6(3)
C9B–C10B–Br1B	119.5(2)
C11B–C10B–Br1B	118.9(2)
C9B–C10B–Br2B	126.3(3)
C11B–C10B–Br2B	110.4(3)
C12B–C11B–C10B	118.8(3)
C11B–C12B–C7B	121.6(3)
C18B–C13B–C14B	119.0(3)
C18B–C13B–C4B	119.6(2)
C14B–C13B–C4B	121.4(2)
C15B–C14B–C13B	120.5(3)
C16B–C15B–C14B	120.0(3)
C15B–C16B–C17B	119.9(3)
C16B–C17B–C18B	119.9(3)
C17B–C18B–C13B	120.7(3)
O1B–C19B–C1B	125.0(3)
O2B–C20B–O3B	124.7(3)
O2B–C20B–C1B	125.7(3)
O3B–C20B–C1B	109.6(2)

Bonds and angles to hydrogen atoms were omitted.

Bibliography

[1] Bruker, *SAINT*, *(Bruker*,, Bruker AXS Inc., Madison, Wisconsin, USA.

[2] L. Krause, R. Herbst-Irmer, G. M. Sheldrick, D. Stalke, *J. Appl. Cryst.* **2015**, *48*, 3–10, doi:10.1107/S1600576714022985.

[3] G. M. Sheldrick, *Acta Cryst.* **2015**, *A71*, 3–8, doi:10.1107/S2053273314026370.

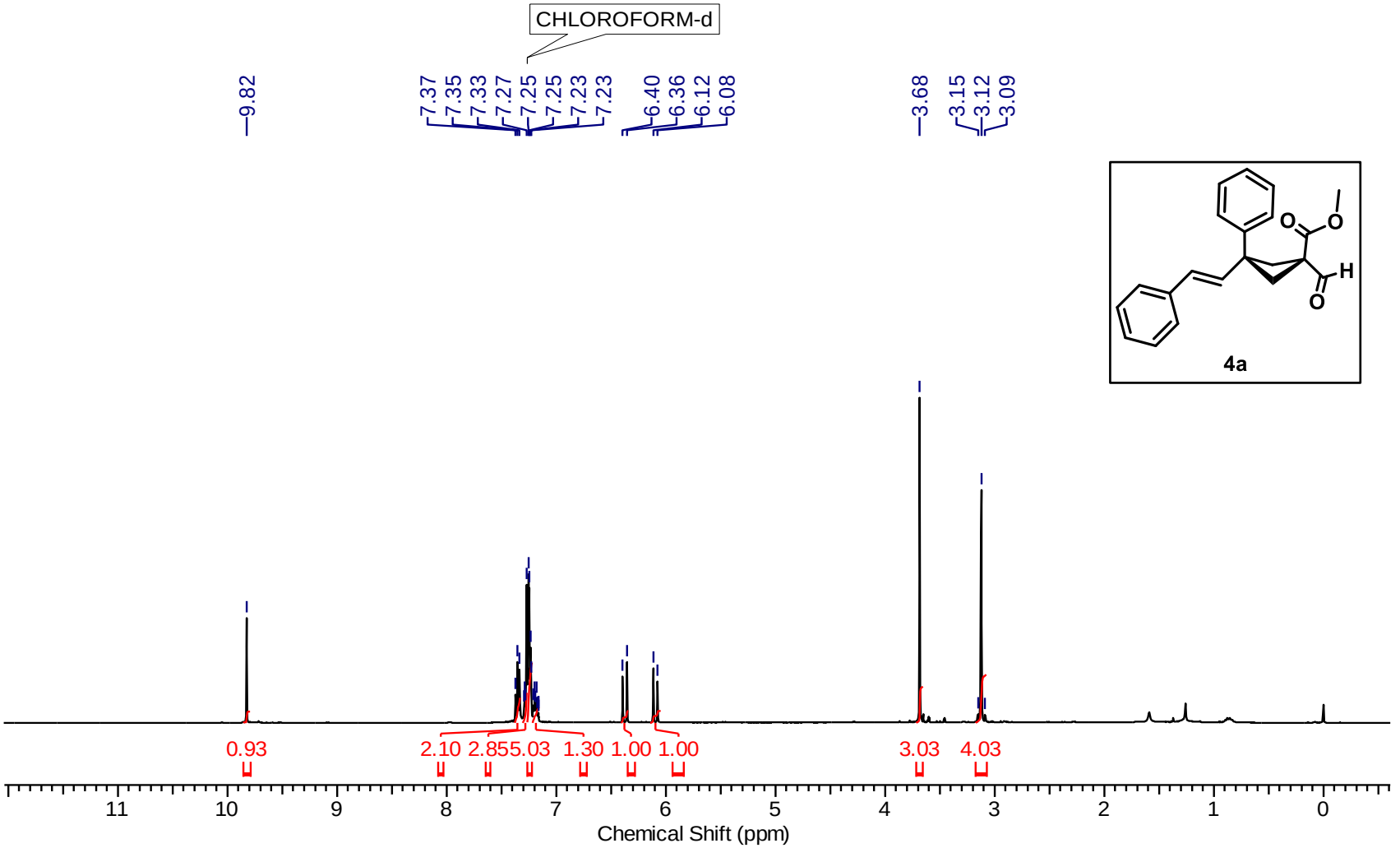
[4] G. M. Sheldrick, *Acta Cryst.* **2015**, *C71*, 3–8, doi:10.1107/S2053229614024218.

[5] C. R. Groom, I. J. Bruno, M. P. Lightfoot, S. C. Ward, *Acta Cryst.* **2016**, *B72*, 171–179, doi:10.1107/S2052520616003954.

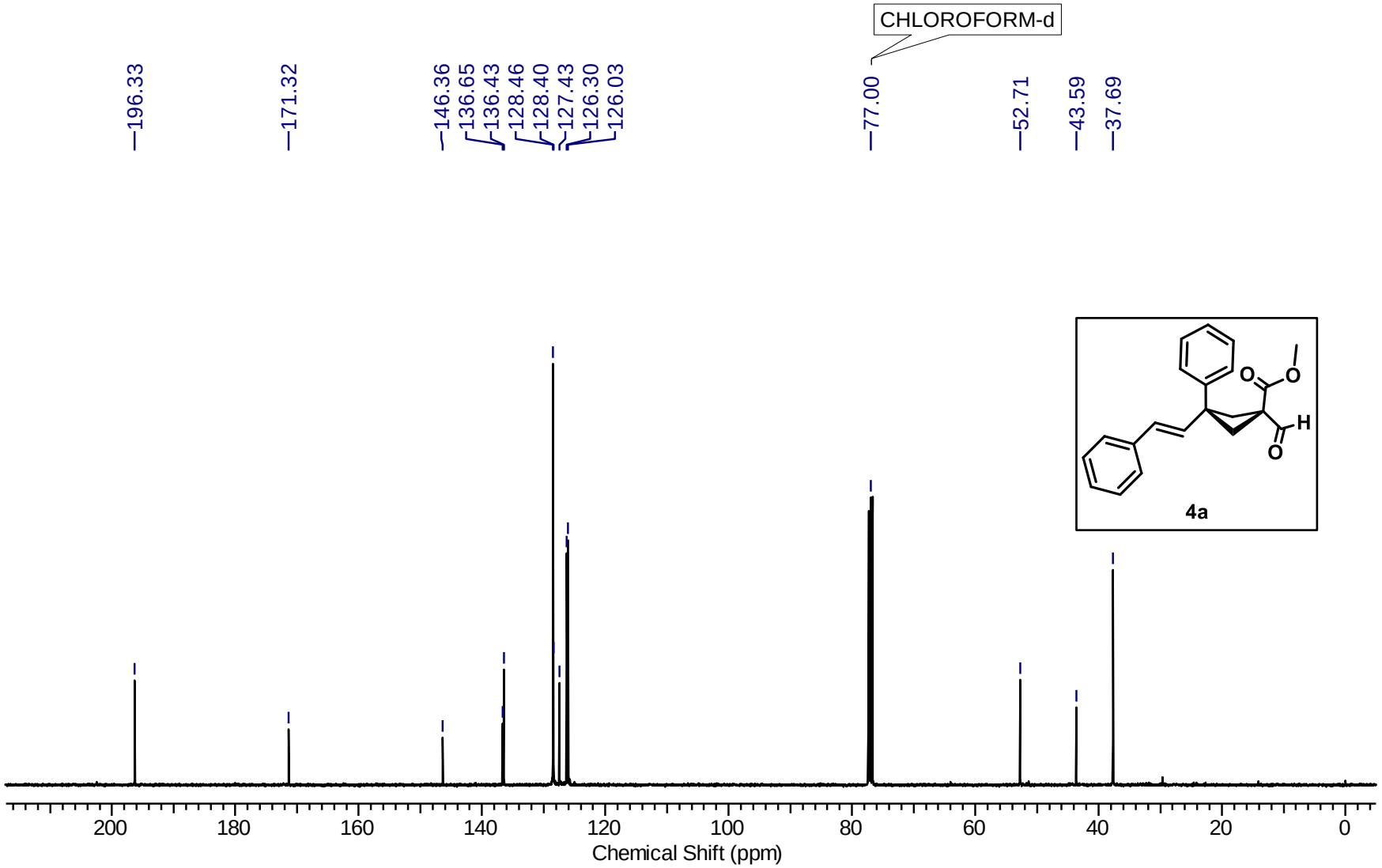
[6] D. Kratzert, *FinalCif*, *(Bruker Edition)*, https://dkratzert.de/finalcif.html.

9. Copies of ^{1}H, ^{13}C NMR spectra:

^{1}H NMR (400 MHz, $CDCl_3$) spectrum of Methyl (1s,3s)-1-formyl-3-phenyl-3-((E)-styryl)cyclobutane-1-carboxylate (4a)

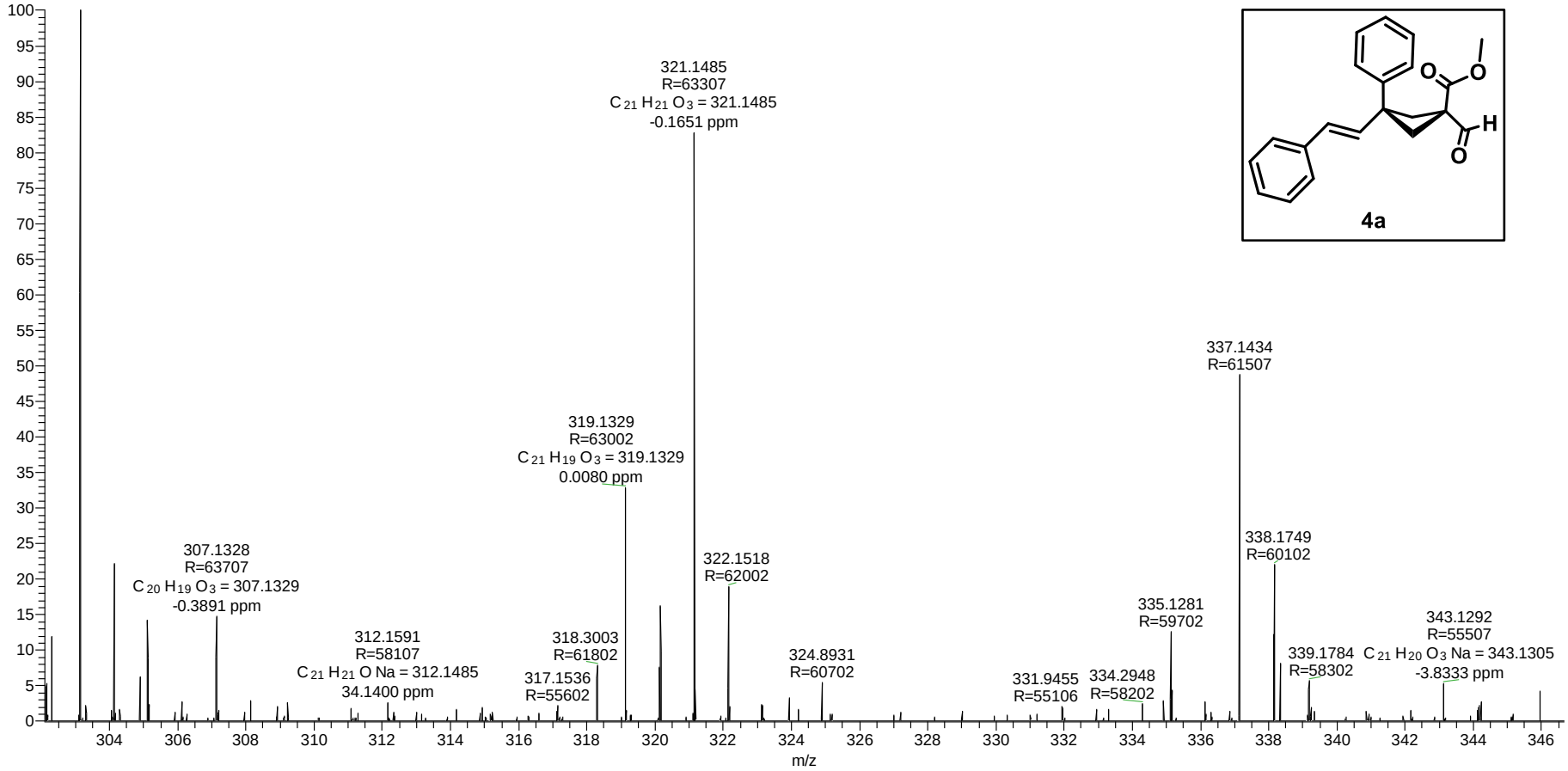


$^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) spectrum of Methyl (1s,3s)-1-formyl-3-phenyl-3-((E)-styryl)cyclobutane-1-carboxylate (4a)

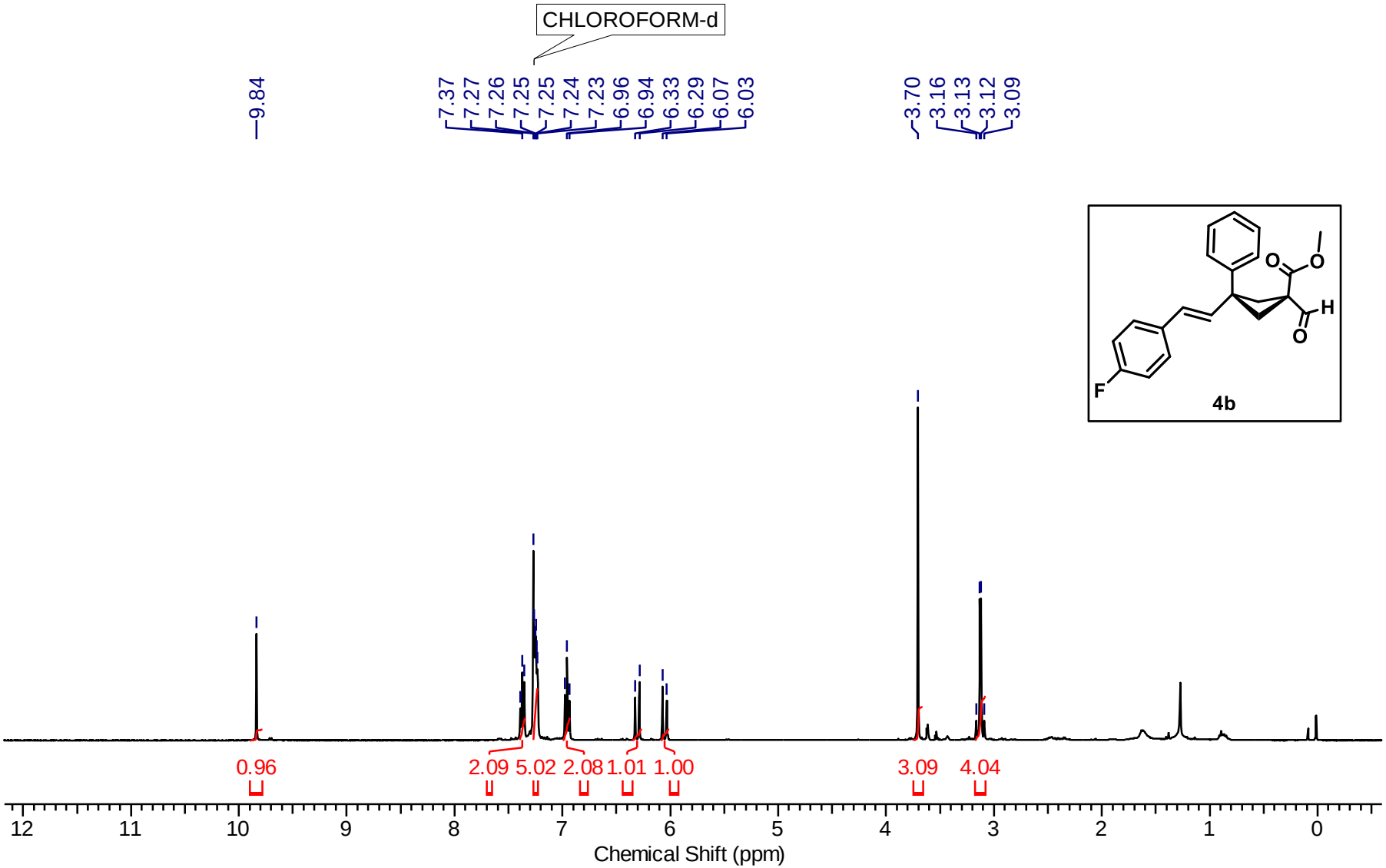


HRMS Spectrum of Methyl (1s,3s)-1-formyl-3-phenyl-3-((E)-styryl)cyclobutane-1-carboxylate (4a)

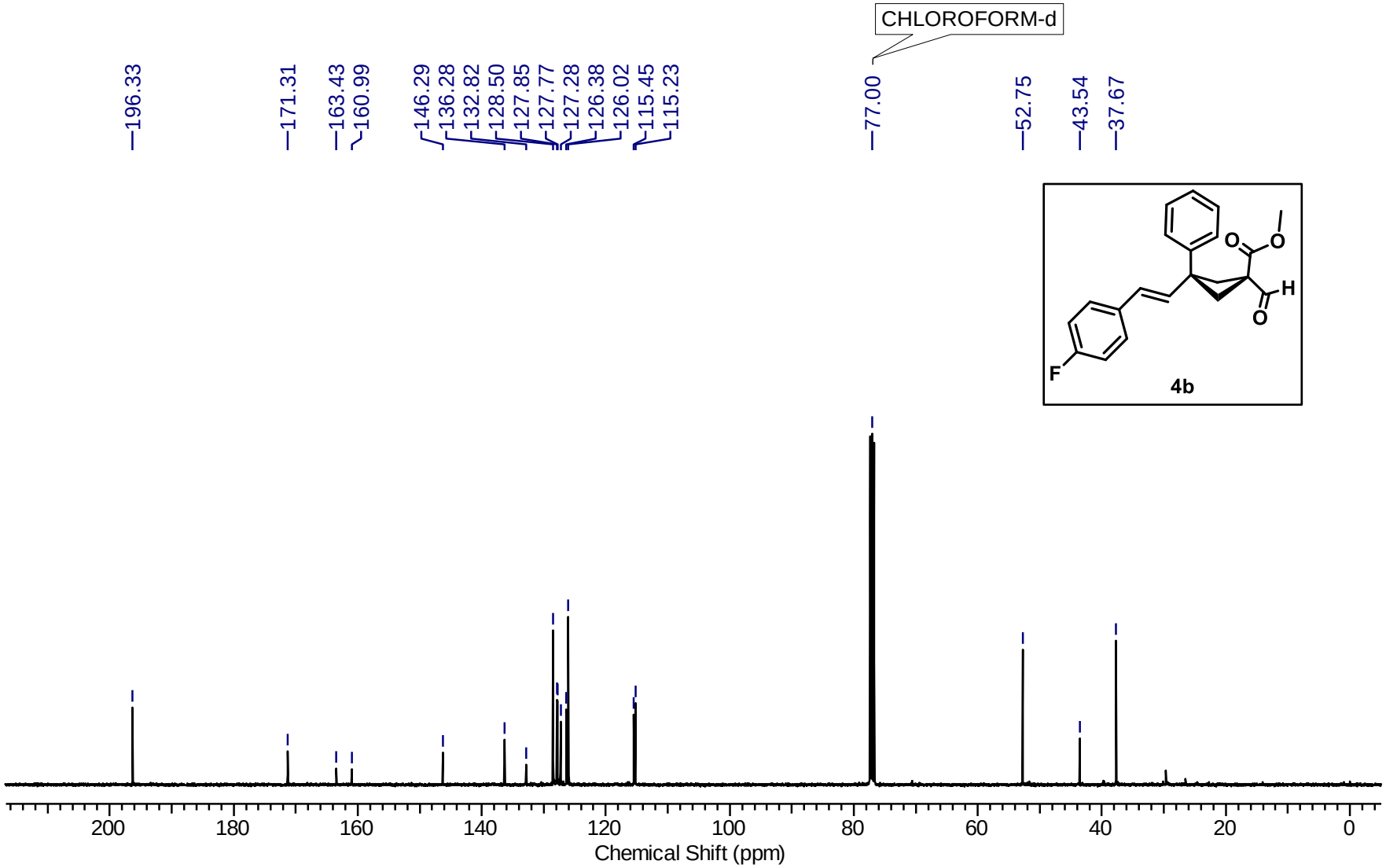
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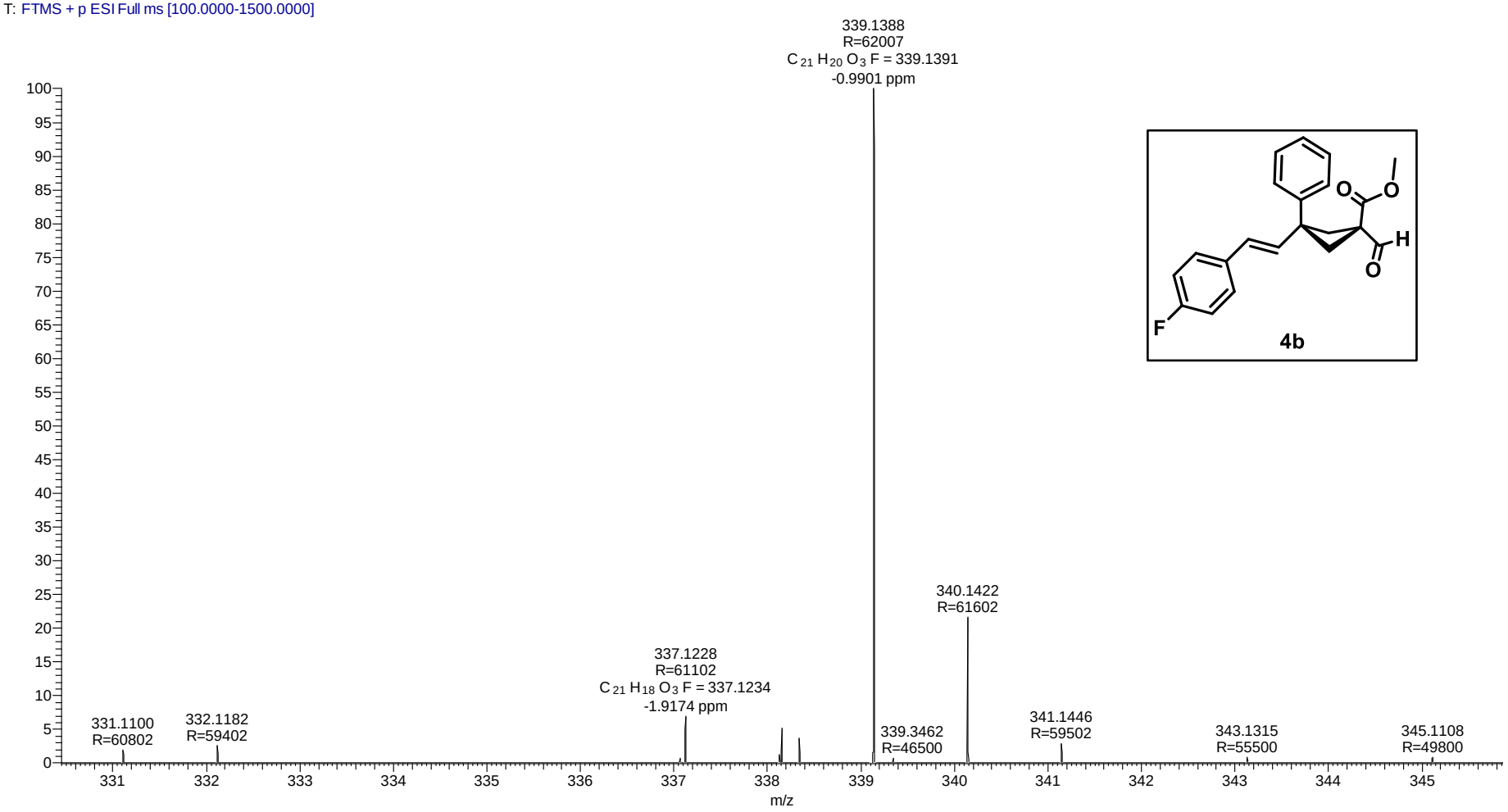
^{1}H NMR (400 MHz, $CDCl_3$) spectrum of Methyl (1s,3s)-3-((E)-4-fluorostyryl)-1-formyl-3-phenylcyclobutane-1-carboxylate (4b)



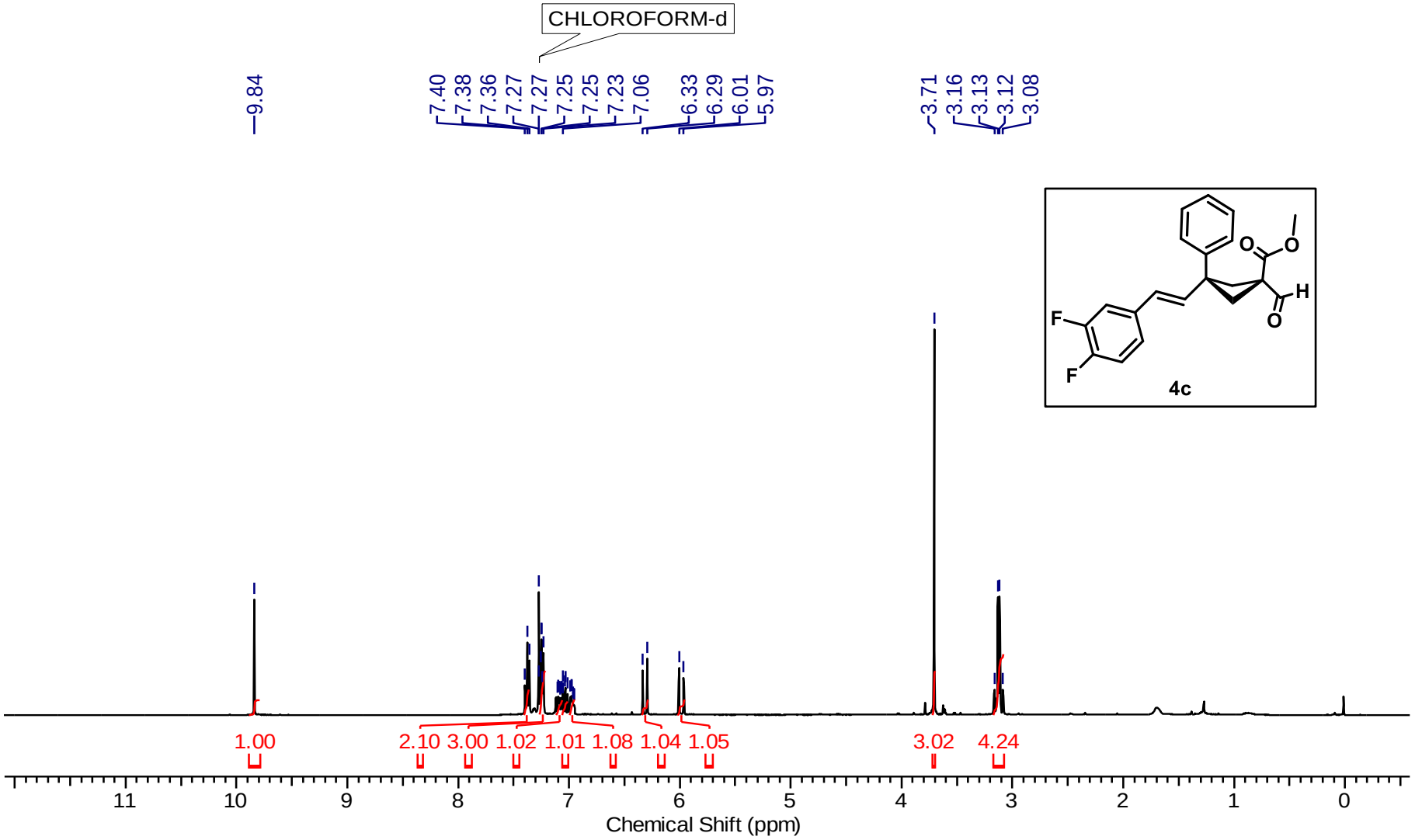
$^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) spectrum of Methyl (1s,3s)-3-((E)-4-fluorostyryl)-1-formyl-3-phenylcyclobutane-1-carboxylate (4b)



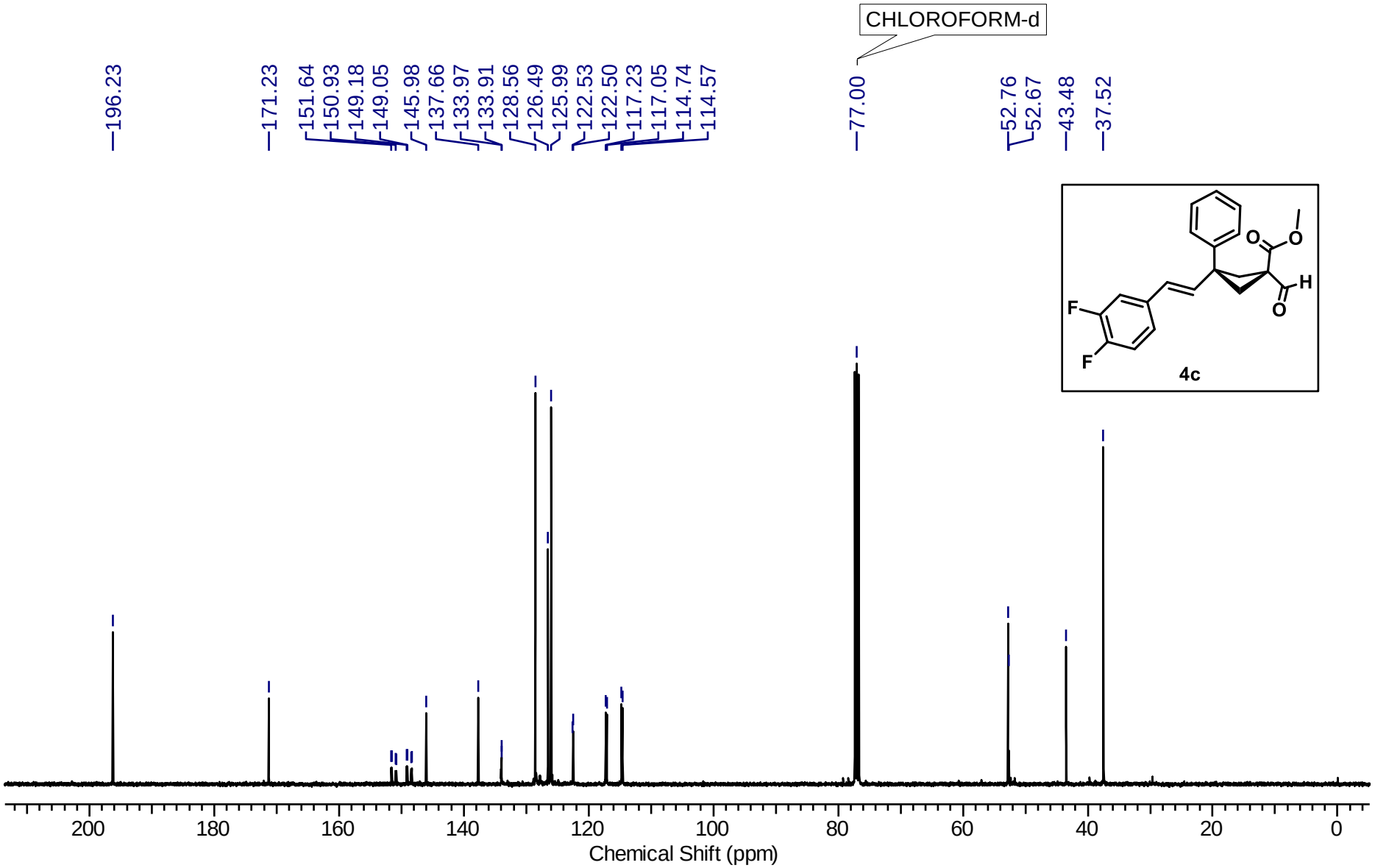
HRMS Spectrum of Methyl (1s,3s)-3-((E)-4-fluorostyryl)-1-formyl-3-phenylcyclobutane-1-carboxylate (4b)



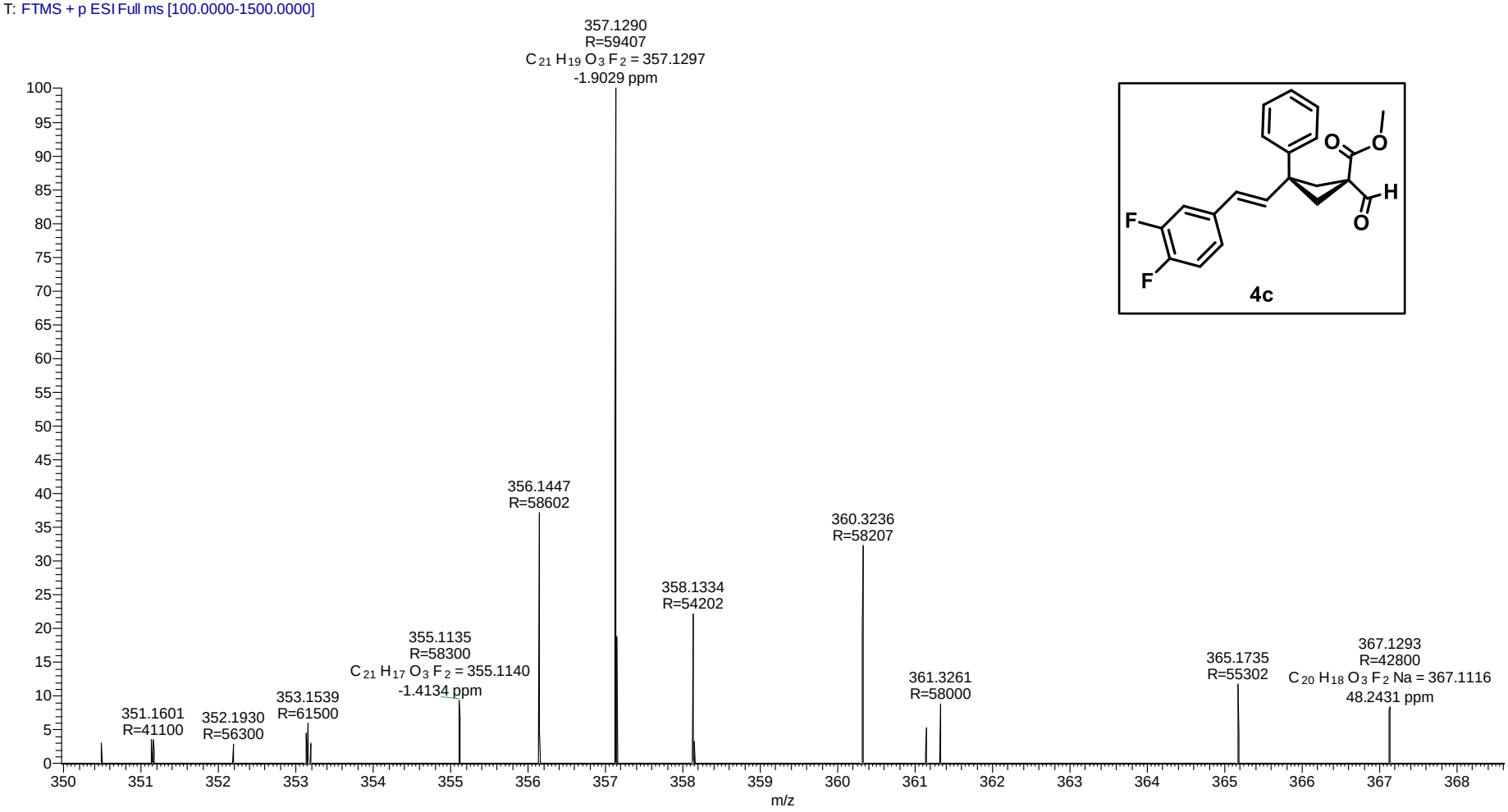
^{1}H NMR (400 MHz, $CDCl_3$) spectrum of Methyl (1s,3s)-3-((E)-3,4-difluorostyryl)-1-formyl-3-phenylcyclobutane-1-carboxylate (4c)



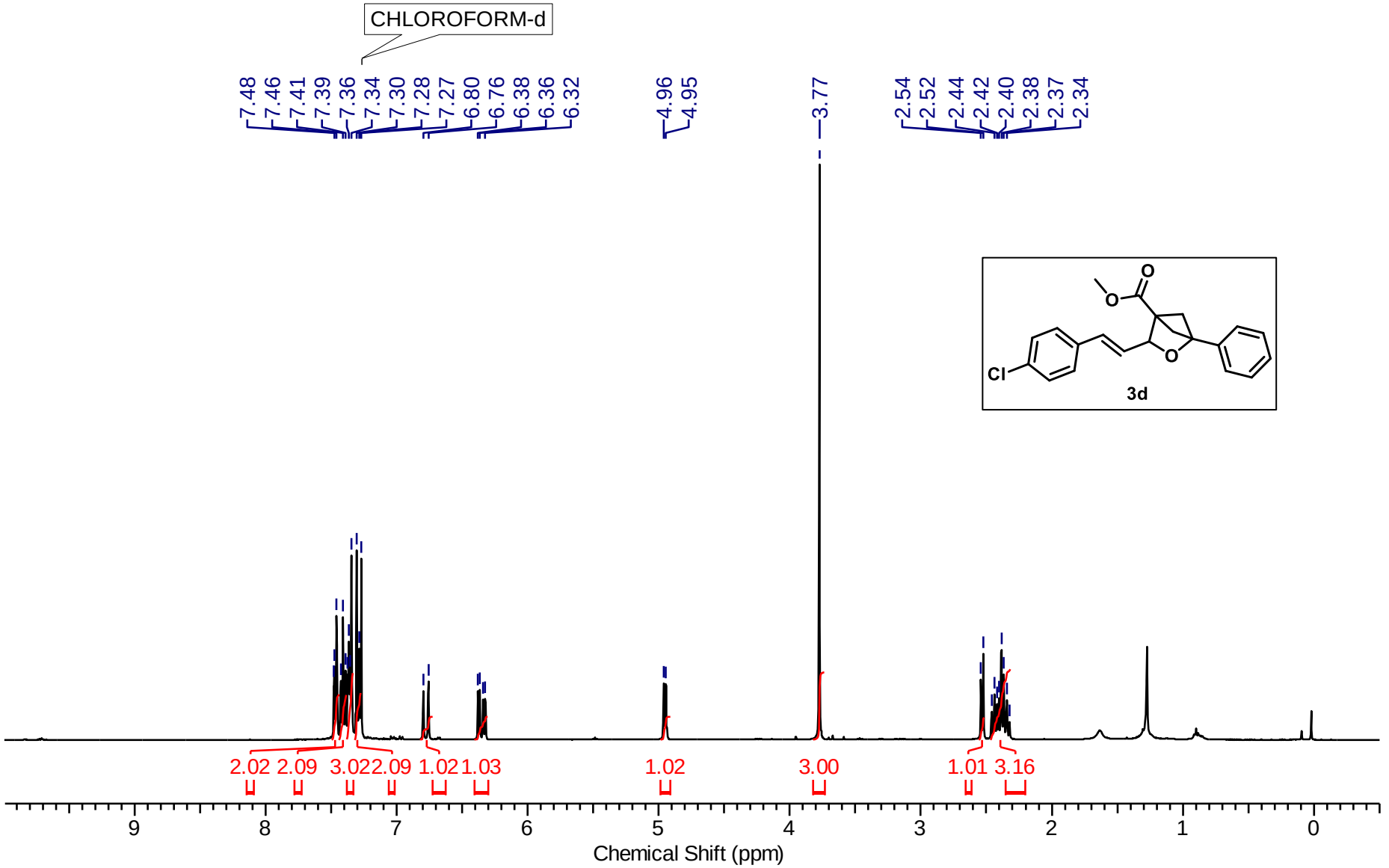
$^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) spectrum of Methyl (1s,3s)-3-((E)-3,4-difluorostyryl)-1-formyl-3-phenylcyclobutane-1-carboxylate (4c)



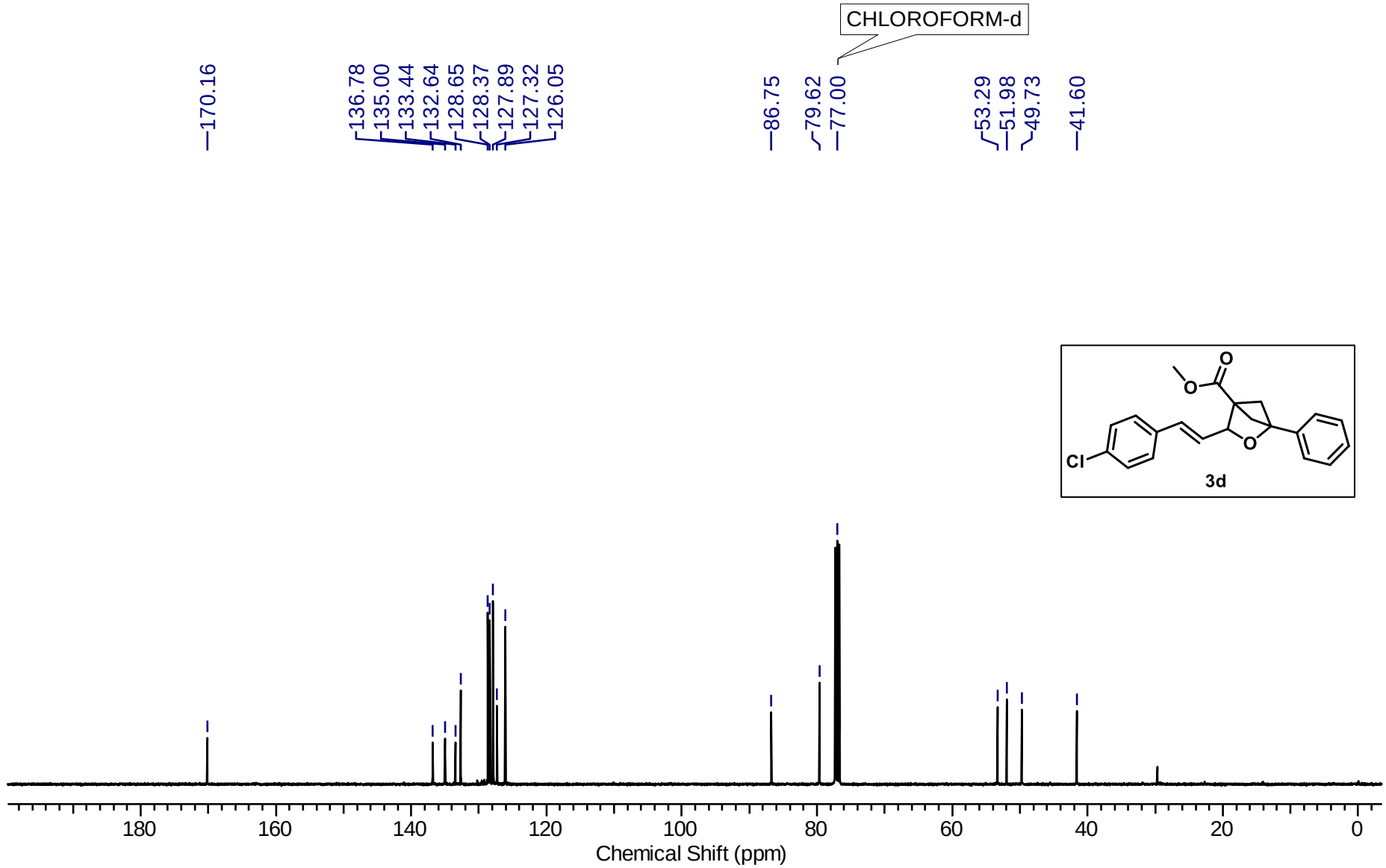
HRMS Spectrum of Methyl (1s,3s)-3-((E)-3,4-difluorostyryl)-1-formyl-3-phenylcyclobutane-1-carboxylate (4c)



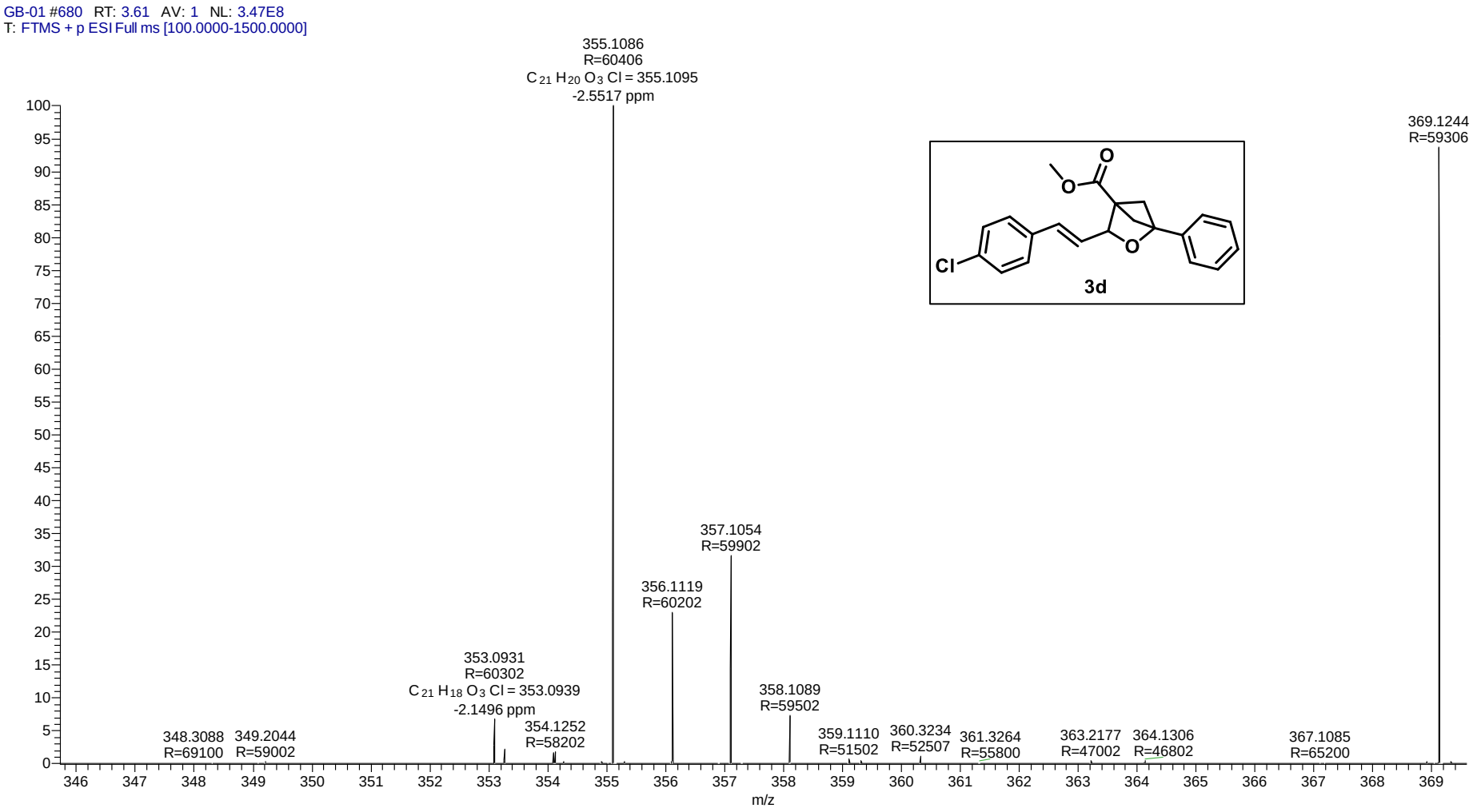
^{1}H NMR (400 MHz, $CDCl_3$) spectrum of Methyl (E)-3-(4-chlorostyryl)-1-phenyl-2-oxabicyclo[2.1.1]hexane-4-carboxylate (3d)



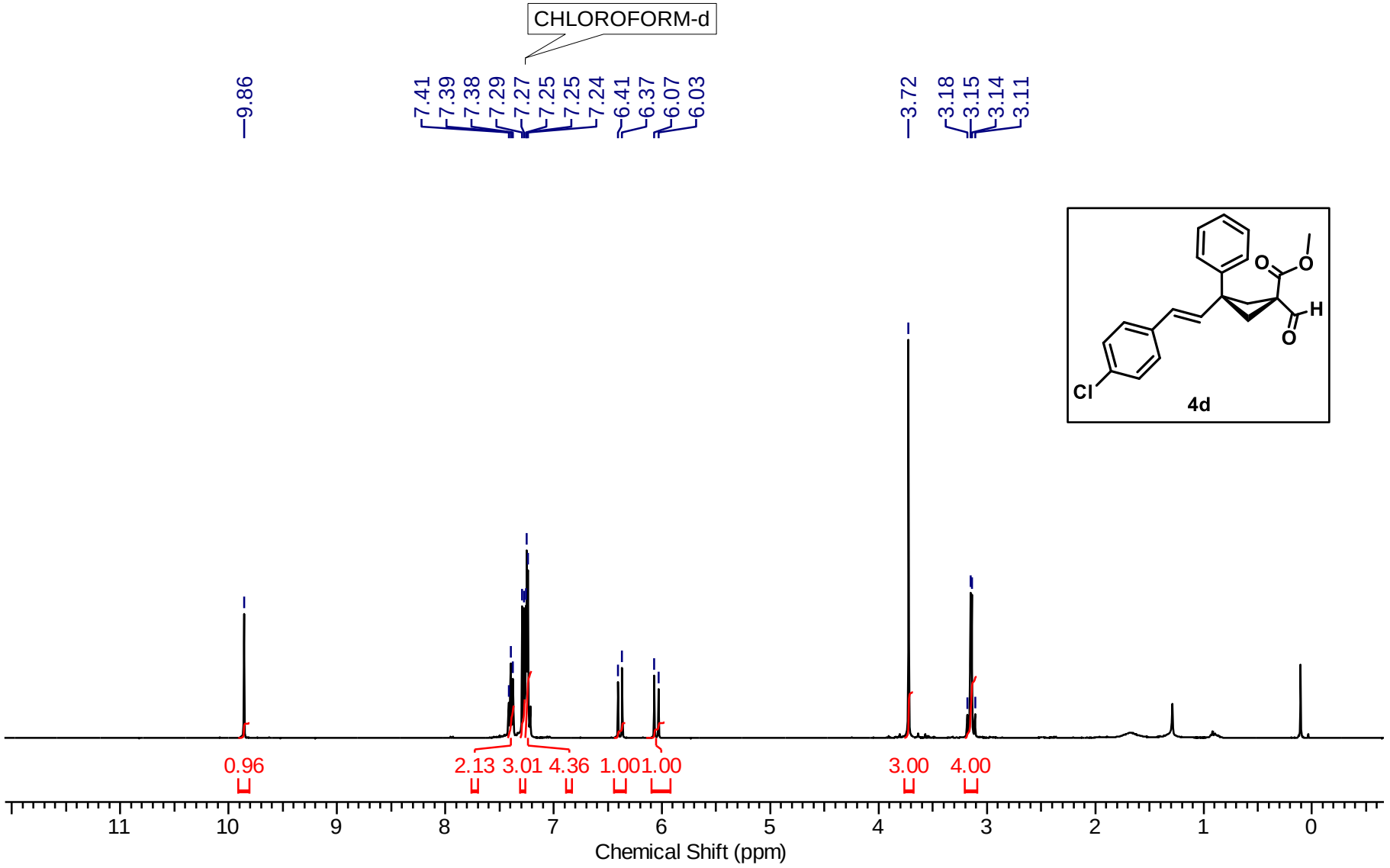
$^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) spectrum of Methyl (E)-3-(4-chlorostyryl)-1-phenyl-2-oxabicyclo[2.1.1]hexane-4-carboxylate (3d)



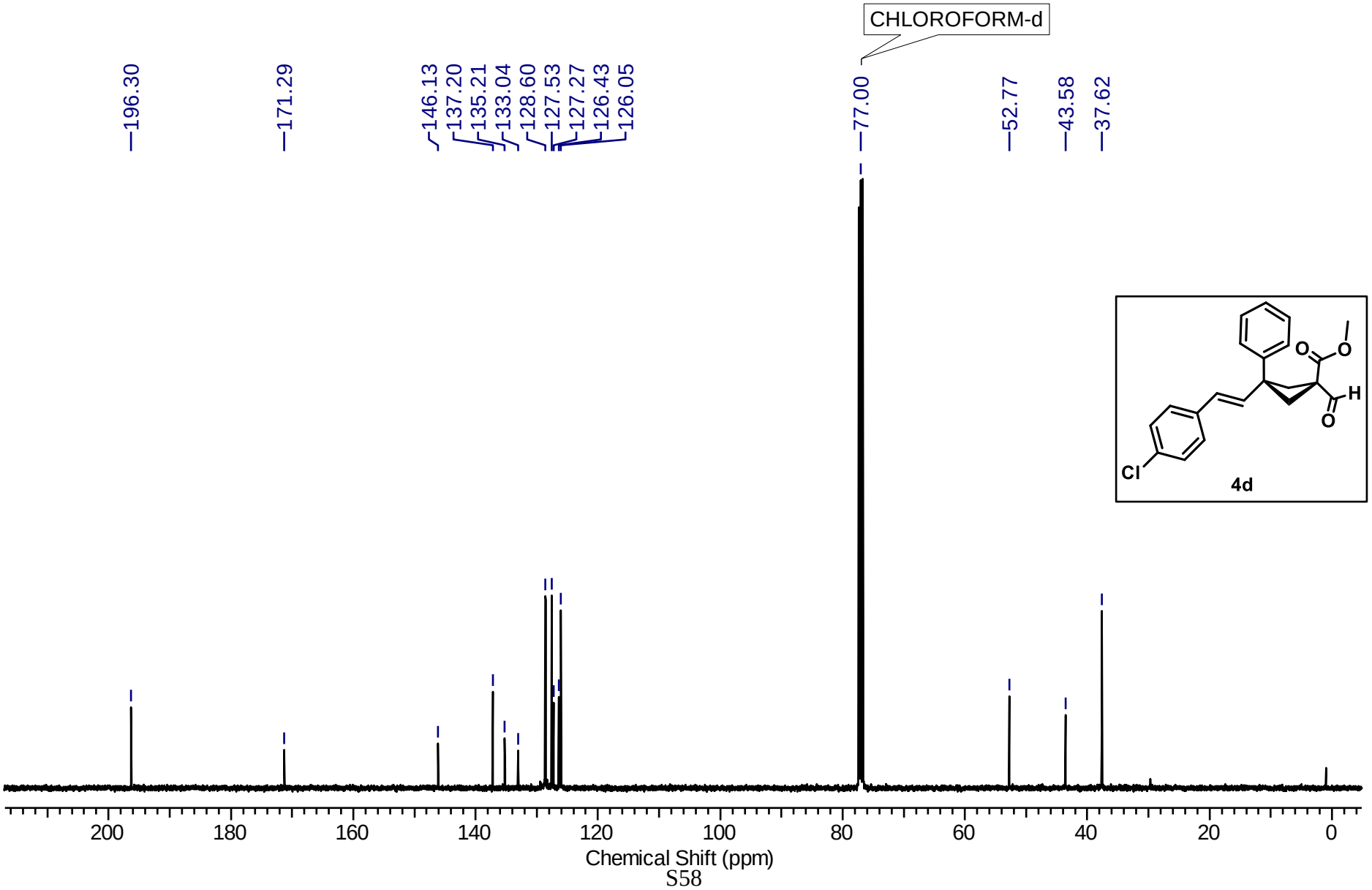
HRMS Spectrum of Methyl (E)-3-(4-chlorostyryl)-1-phenyl-2-oxabicyclo[2.1.1]hexane-4-carboxylate (3d)



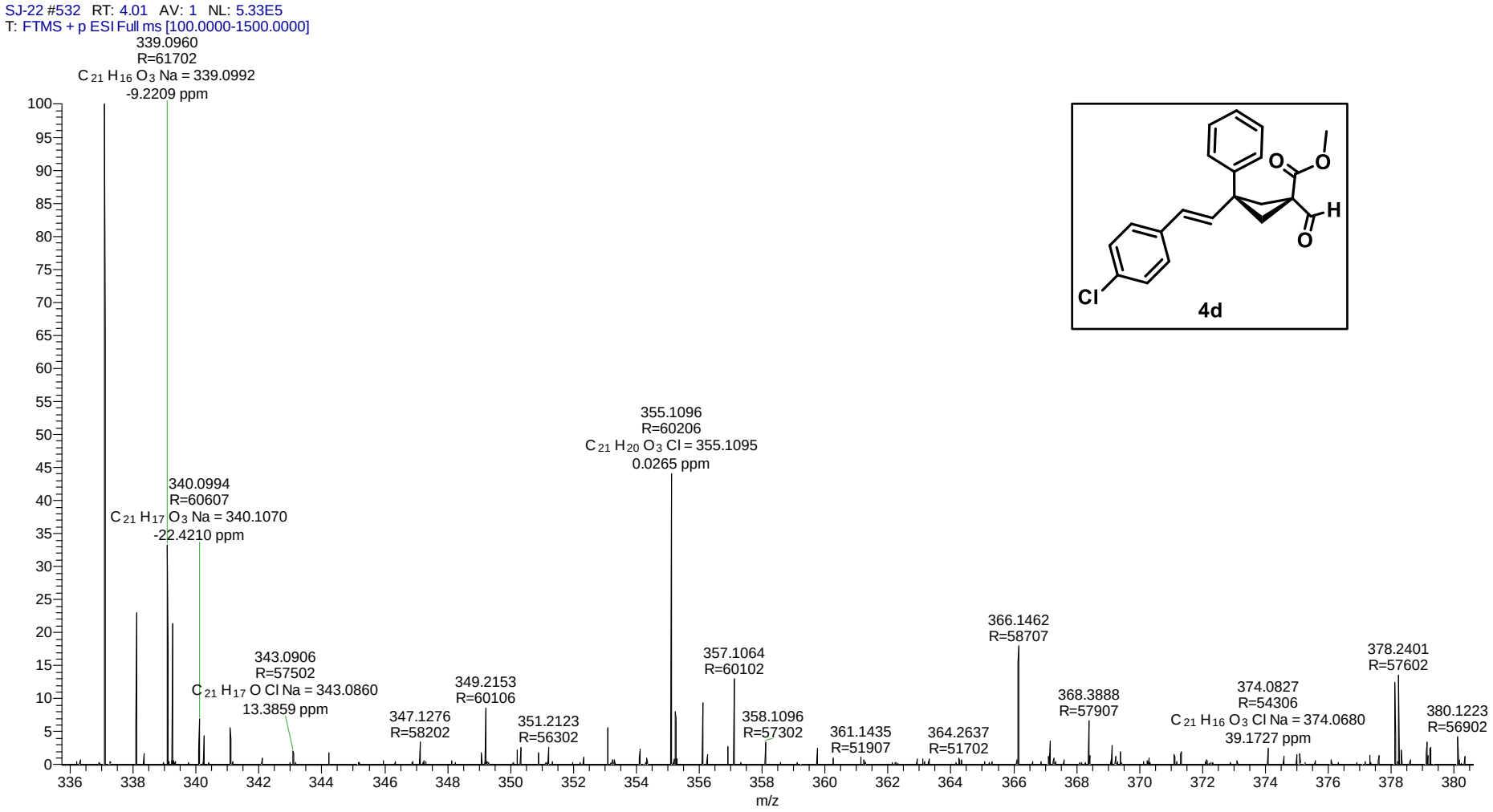
^{1}H NMR (400 MHz, $CDCl_3$) spectrum of Methyl (1s,3s)-3-((E)-4-chlorostyryl)-1-formyl-3-phenylcyclobutane-1-carboxylate (4d)



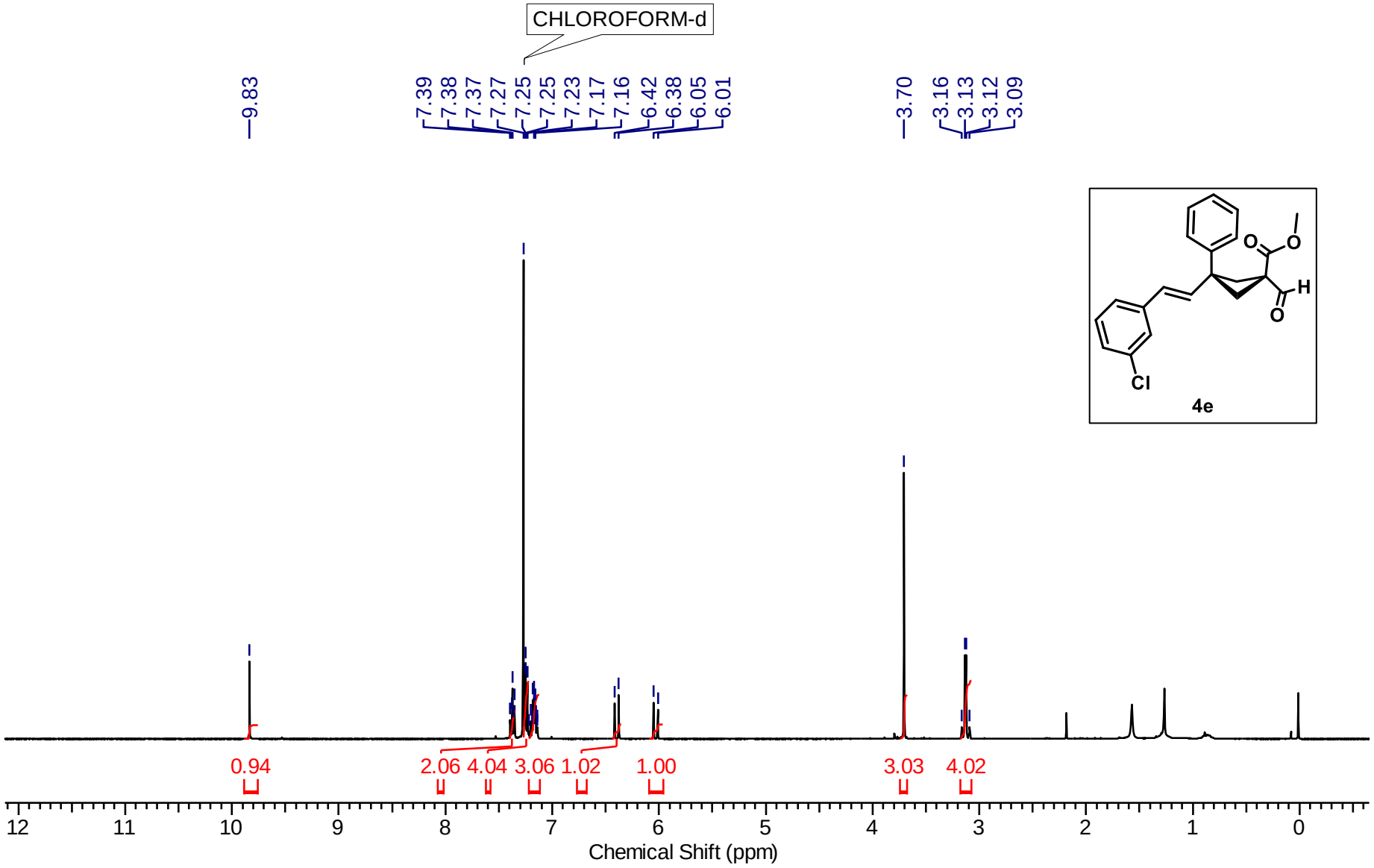
$^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) spectrum of Methyl (1s,3s)-3-((E)-4-chlorostyryl)-1-formyl-3-phenylcyclobutane-1-carboxylate (4d)



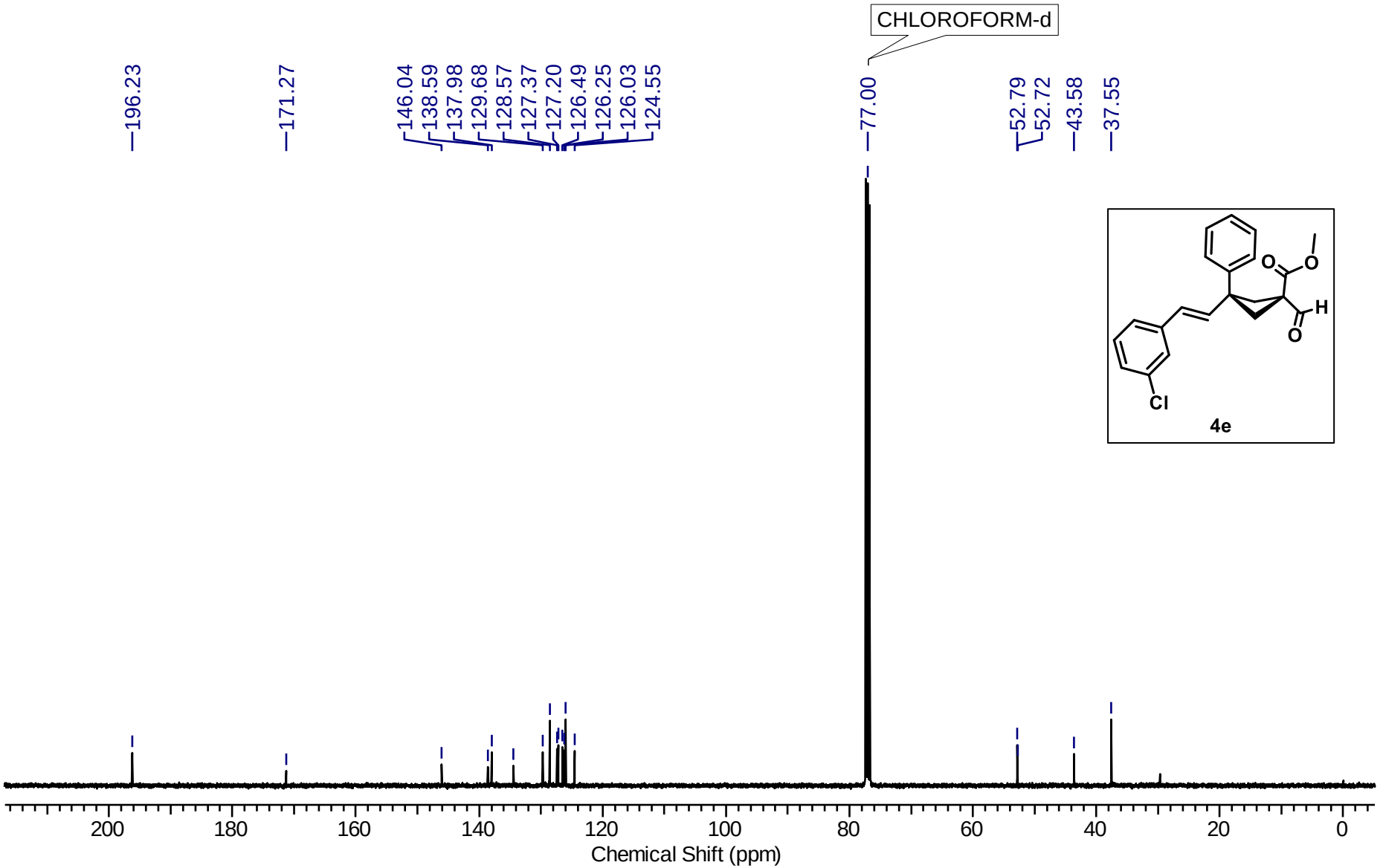
HRMS Spectrum of Methyl (1s,3s)-3-((E)-4-chlorostyryl)-1-formyl-3-phenylcyclobutane-1-carboxylate (4d)



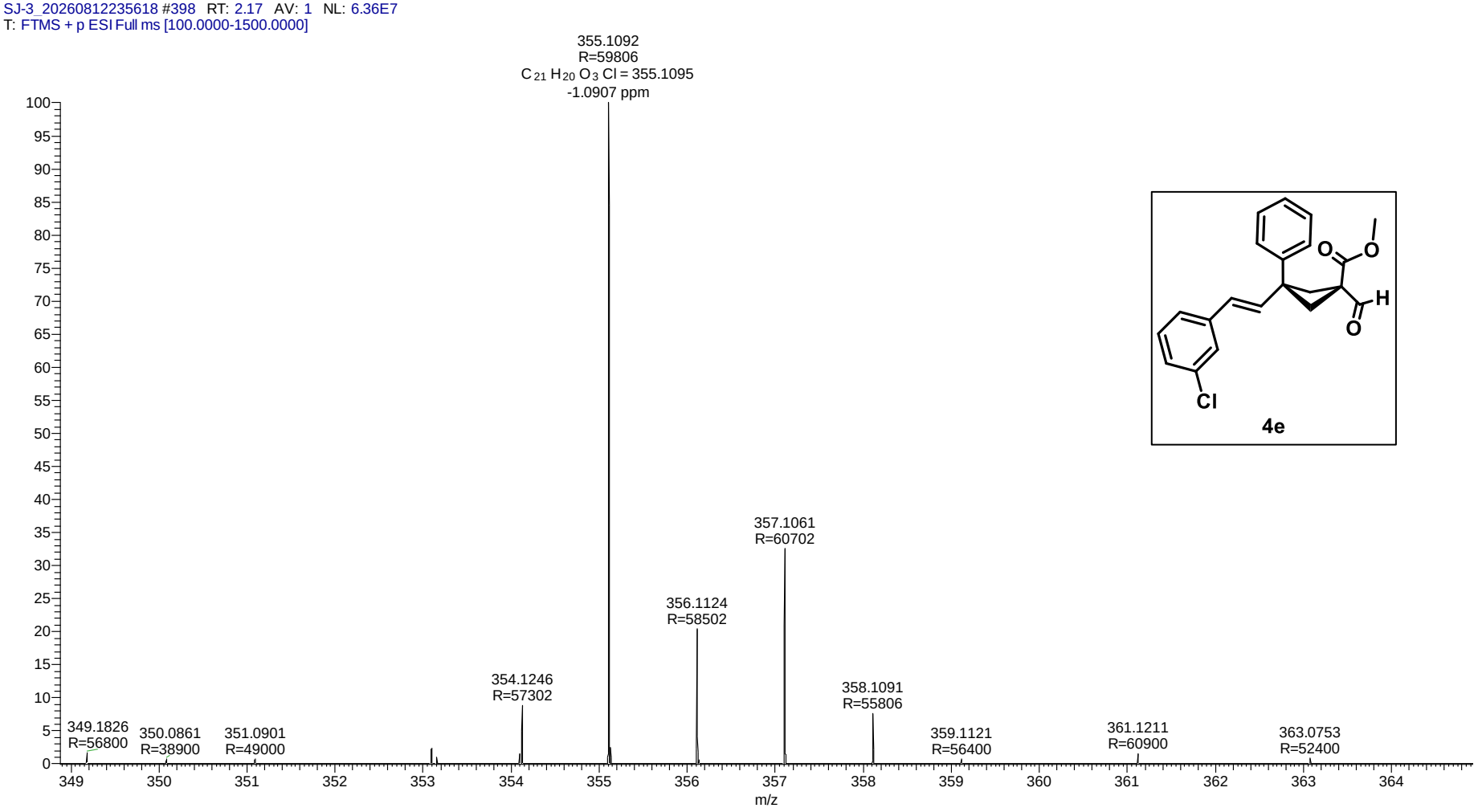
^{1}H NMR (400 MHz, $CDCl_3$) spectrum of Methyl (1s,3s)-3-((E)-3-chlorostyryl)-1-formyl-3-phenylcyclobutane-1-carboxylate (4e)



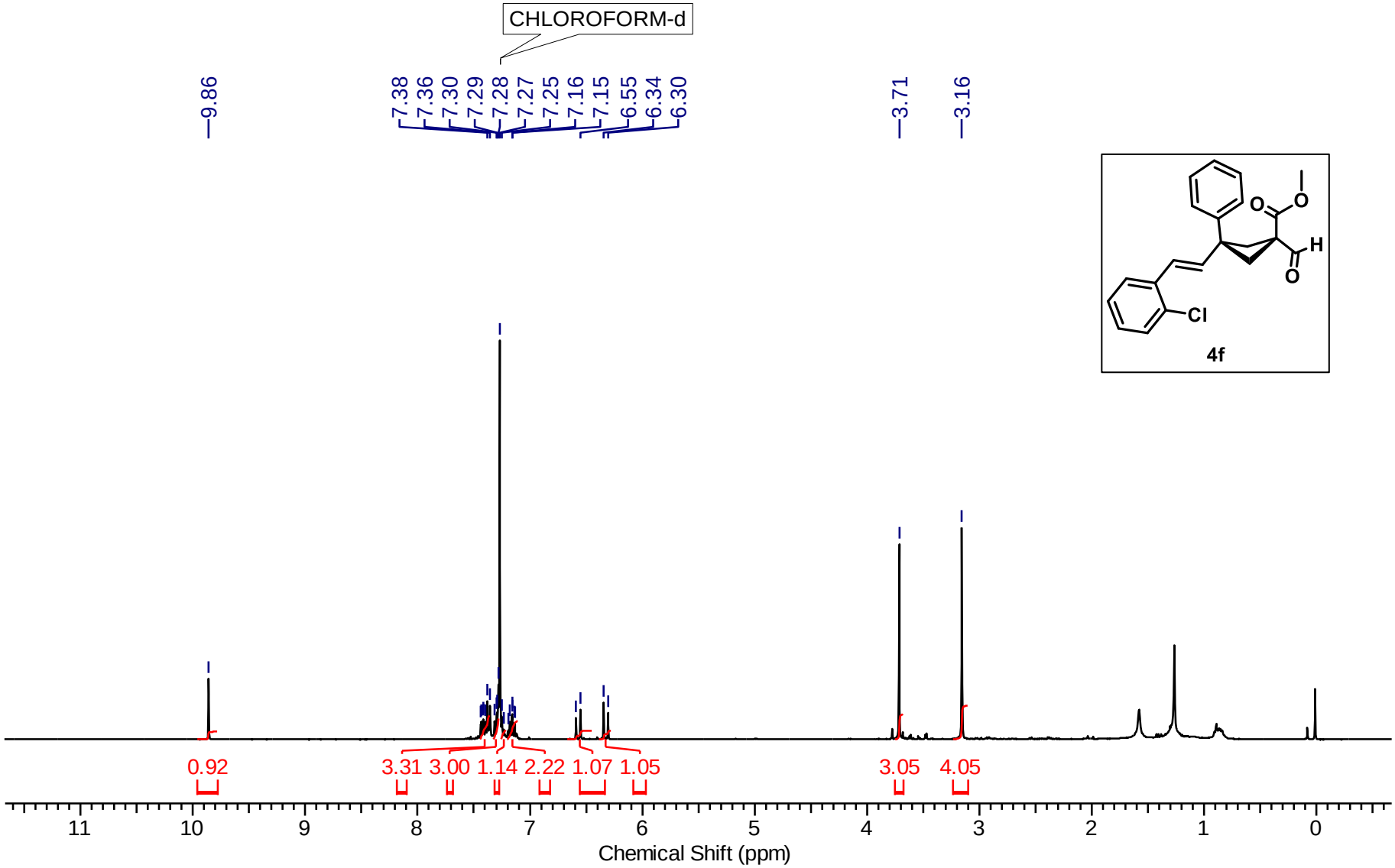
$^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) spectrum of Methyl (1s,3s)-3-((E)-3-chlorostyryl)-1-formyl-3-phenylcyclobutane-1-carboxylate (4e)



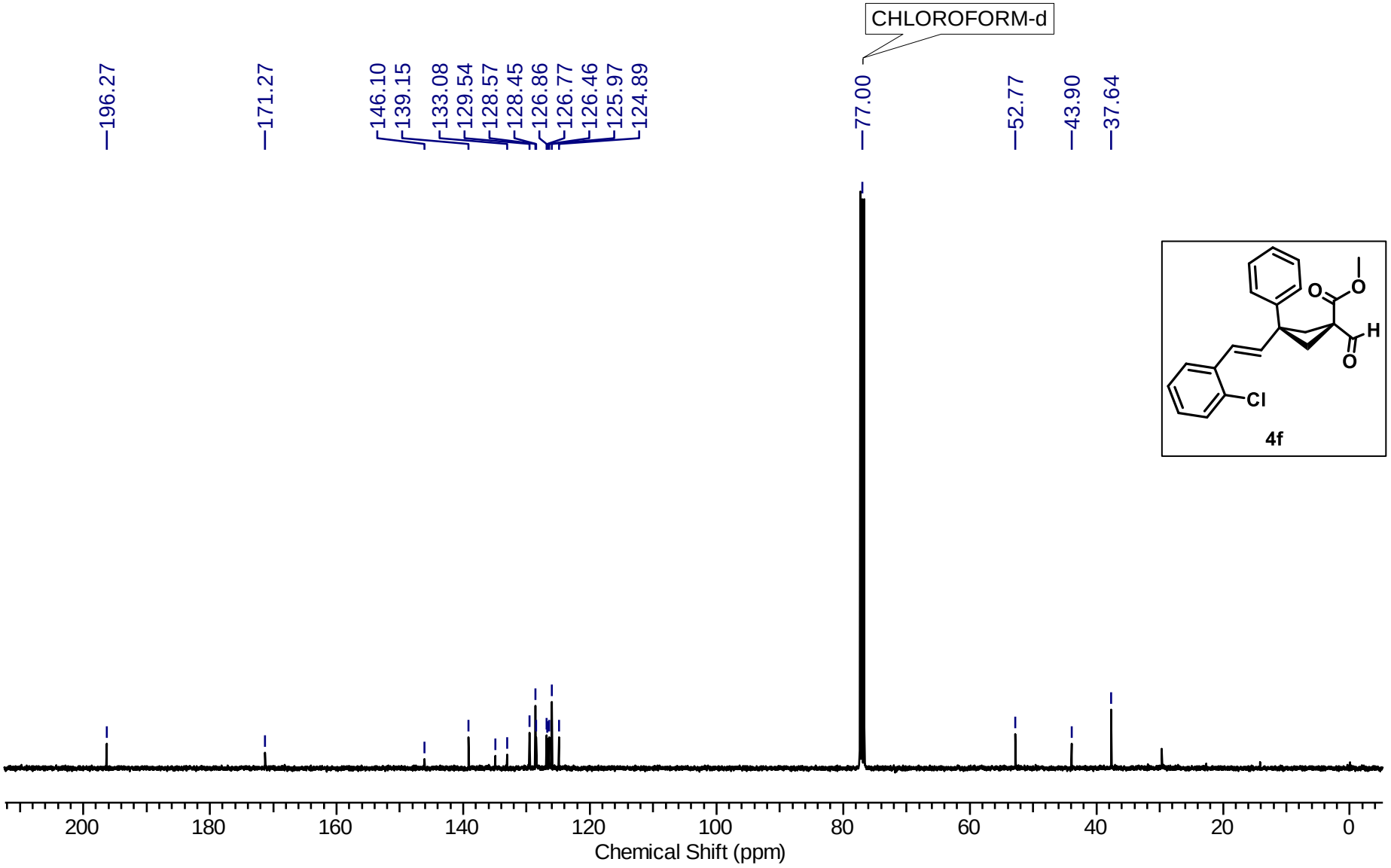
HRMS Spectrum of Methyl (1s,3s)-3-((E)-3-chlorostyryl)-1-formyl-3-phenylcyclobutane-1-carboxylate (4e)



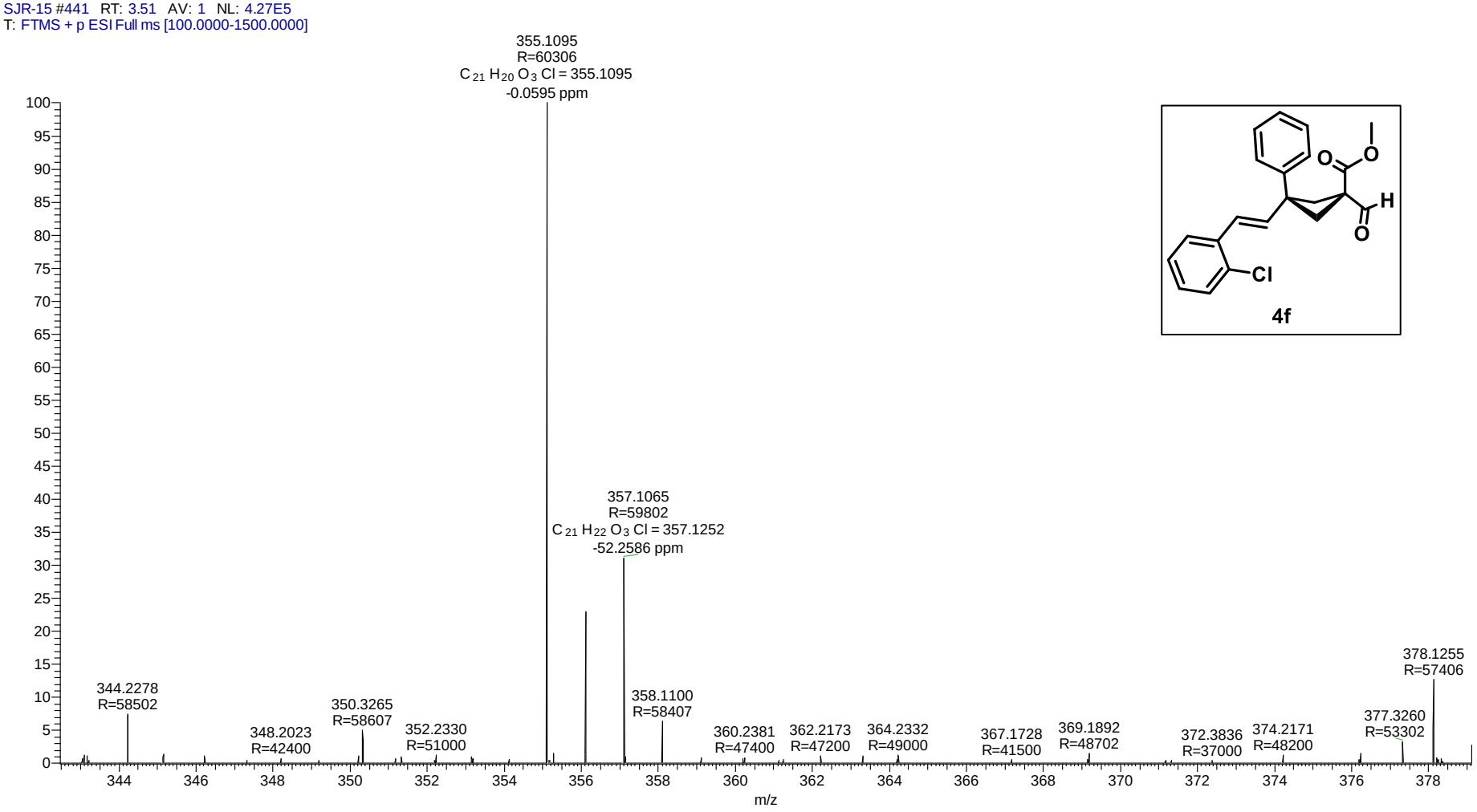
^{1}H NMR (400 MHz, $CDCl_3$) spectrum of Methyl (1s,3s)-3-((E)-2-chlorostyryl)-1-formyl-3-phenylcyclobutane-1-carboxylate (4f)



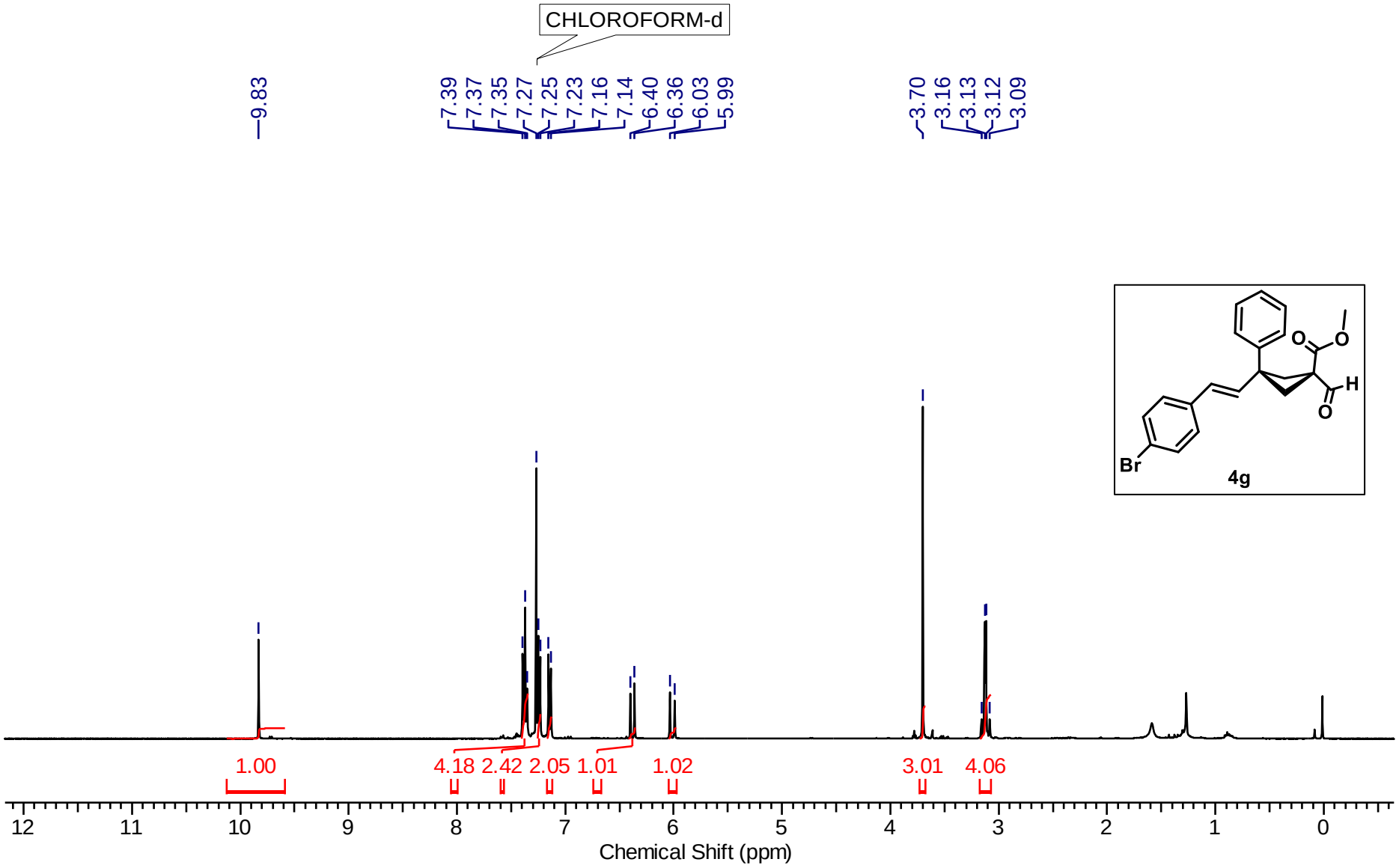
$^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) spectrum of Methyl (1s,3s)-3-((E)-2-chlorostyryl)-1-formyl-3-phenylcyclobutane-1-carboxylate (4f)



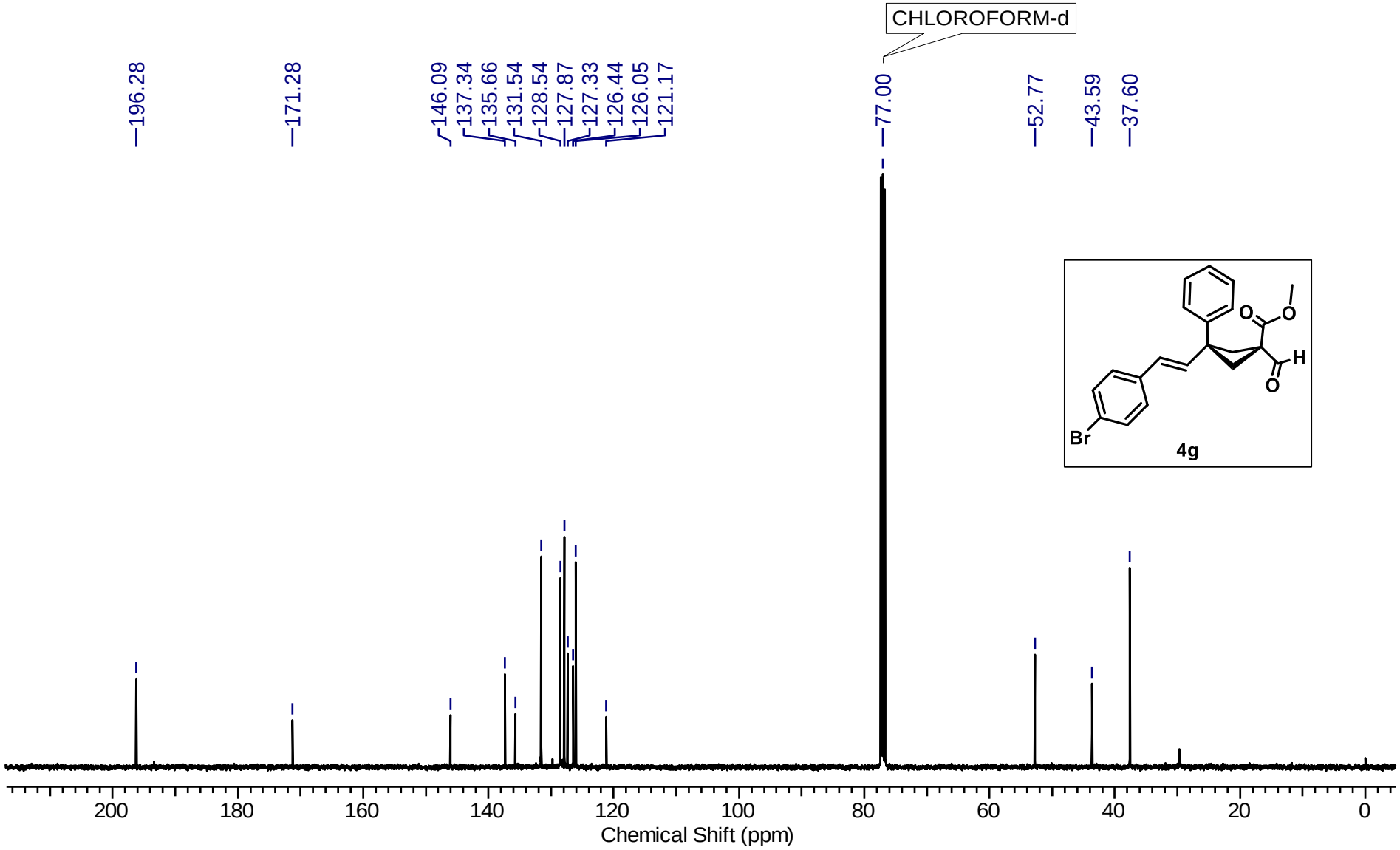
HRMS spectrum of Methyl (1s,3s)-3-((E)-2-chlorostyryl)-1-formyl-3-phenylcyclobutane-1-carboxylate (4f)



^{1}H NMR (400 MHz, $CDCl_3$) spectrum of Methyl (1s,3s)-3-((E)-4-bromostyryl)-1-formyl-3-phenylcyclobutane-1-carboxylate (4g)

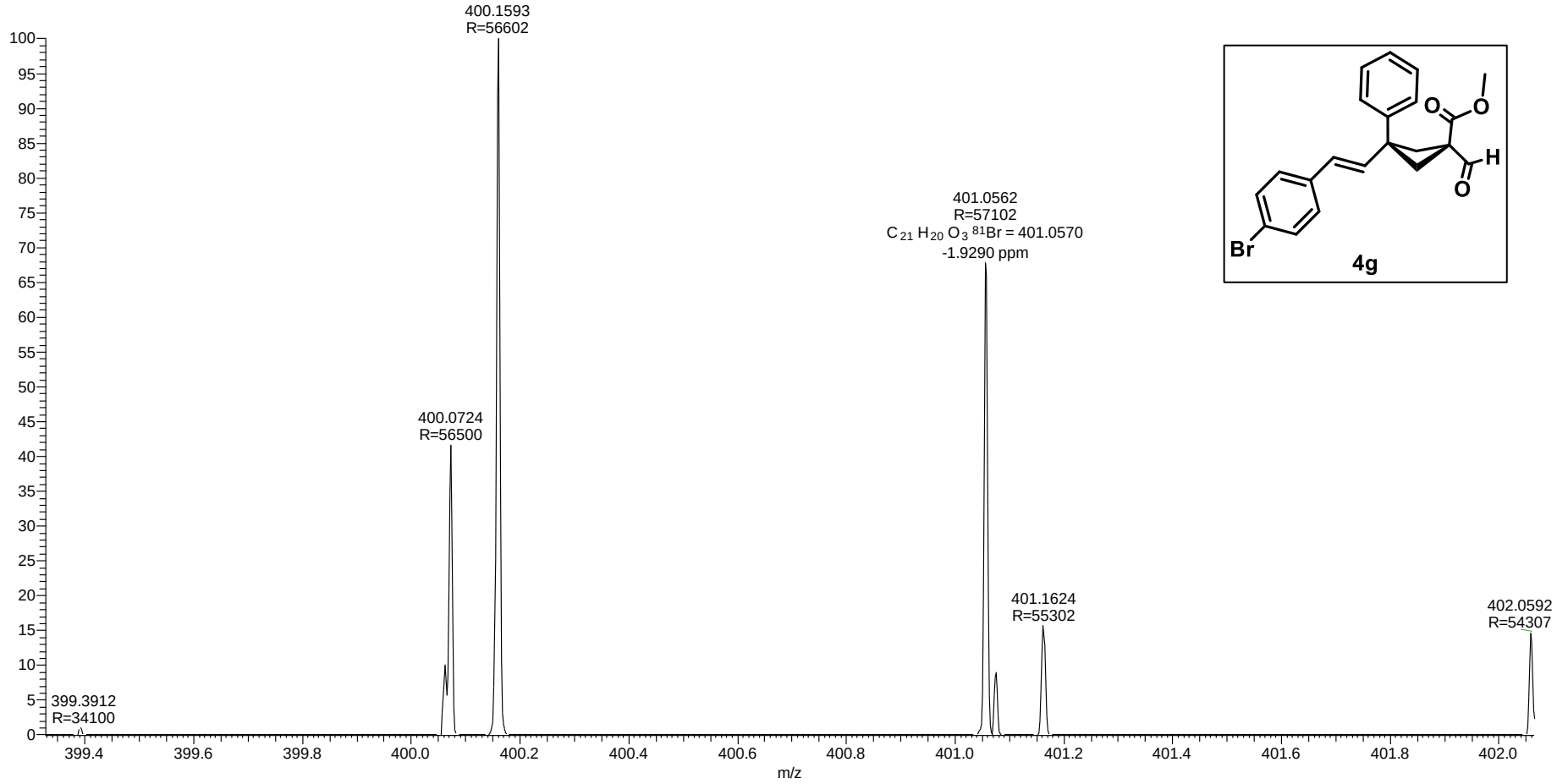


$^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) spectrum of Methyl (1s,3s)-3-((E)-4-bromostyryl)-1-formyl-3-phenylcyclobutane-1-carboxylate (4g)

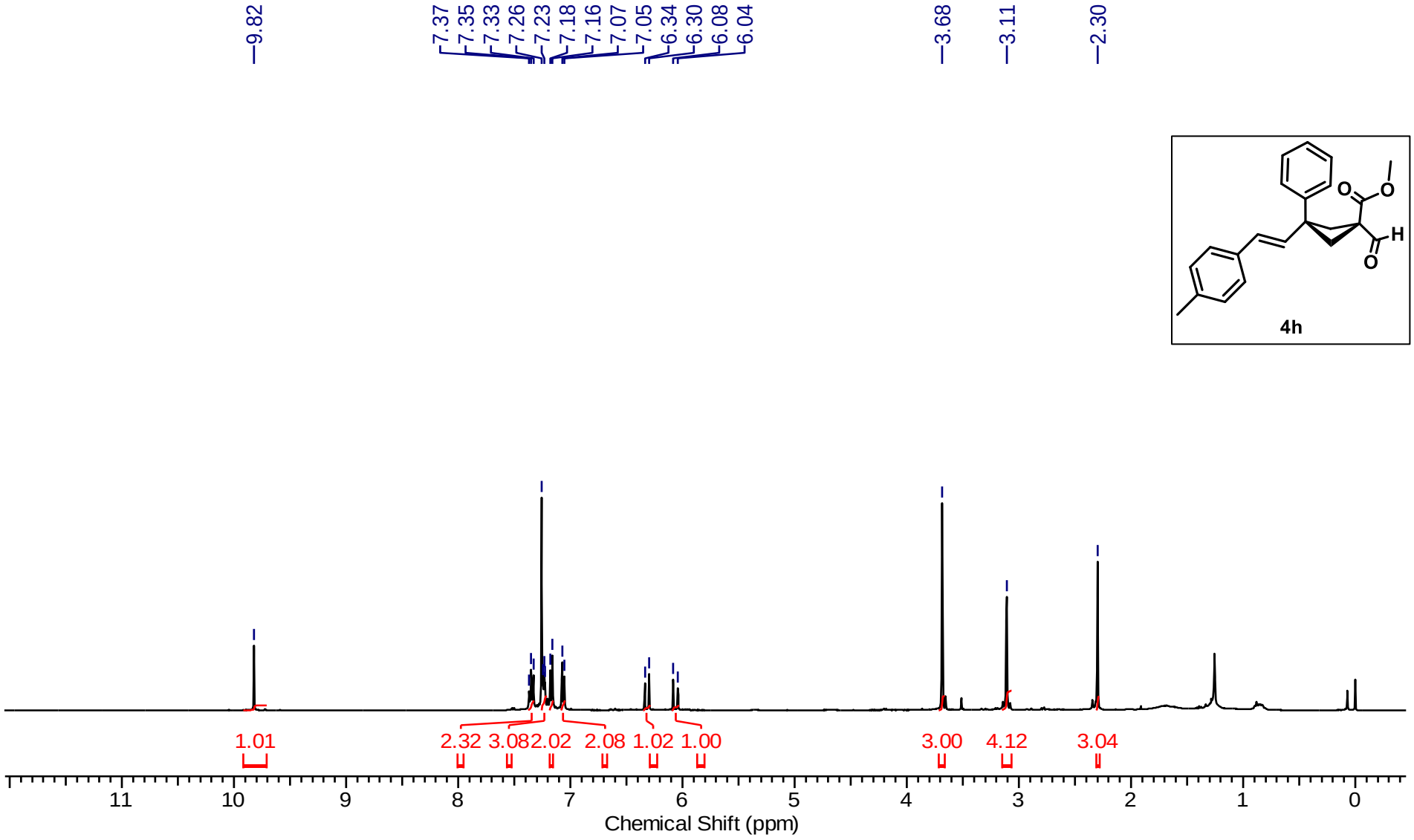


HRMS spectrum of Methyl (1s,3s)-3-((E)-4-bromostyryl)-1-formyl-3-phenylcyclobutane-1-carboxylate (4g)

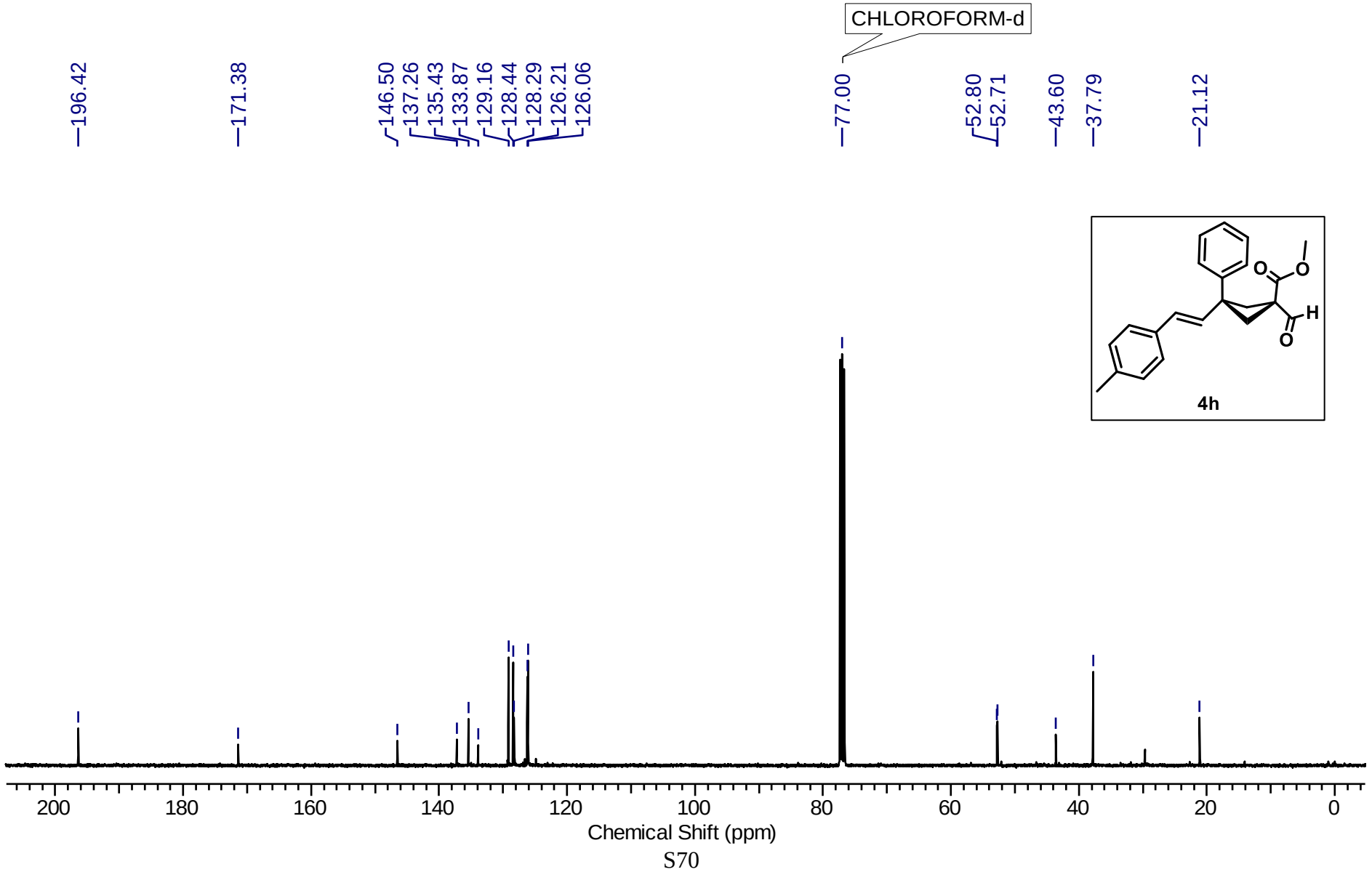
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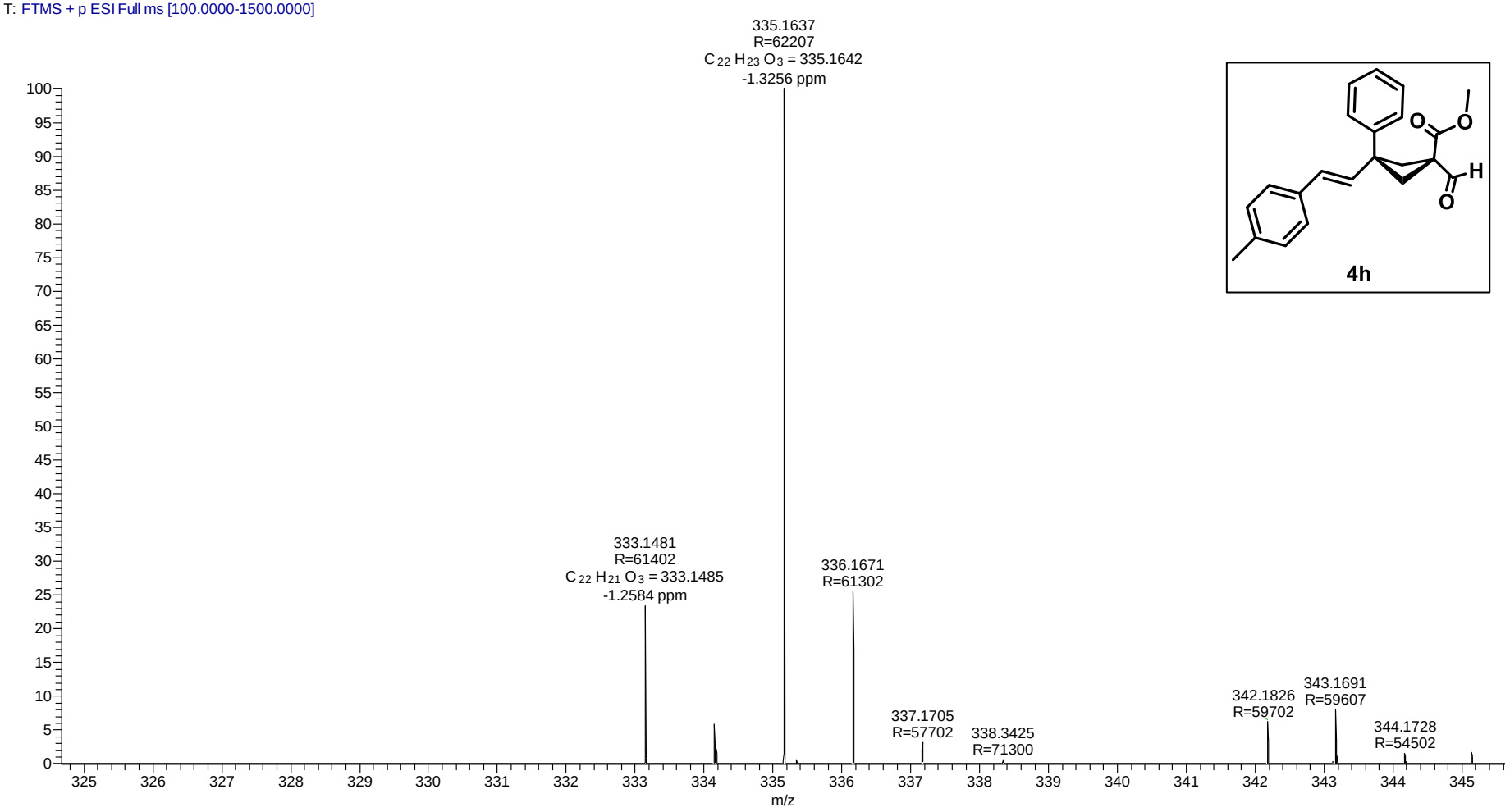
^{1}H NMR (400 MHz, $CDCl_3$) spectrum of Methyl (1s,3s)-1-formyl-3-((E)-4-methylstyryl)-3-phenylcyclobutane-1-carboxylate (4h)



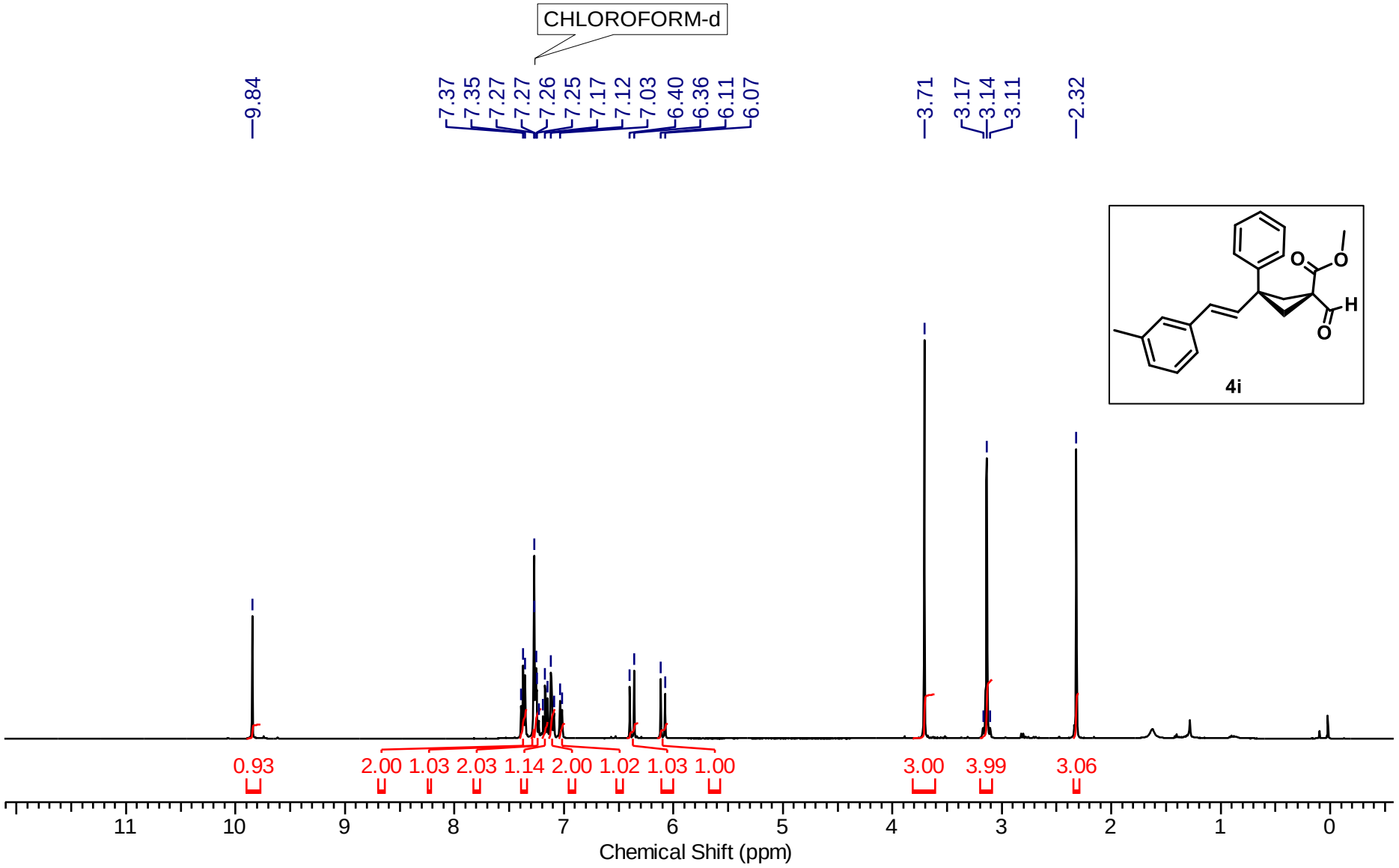
$^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) spectrum of Methyl (1s,3s)-1-formyl-3-((E)-4-methylstyryl)-3-phenylcyclobutane-1-carboxylate (4h)



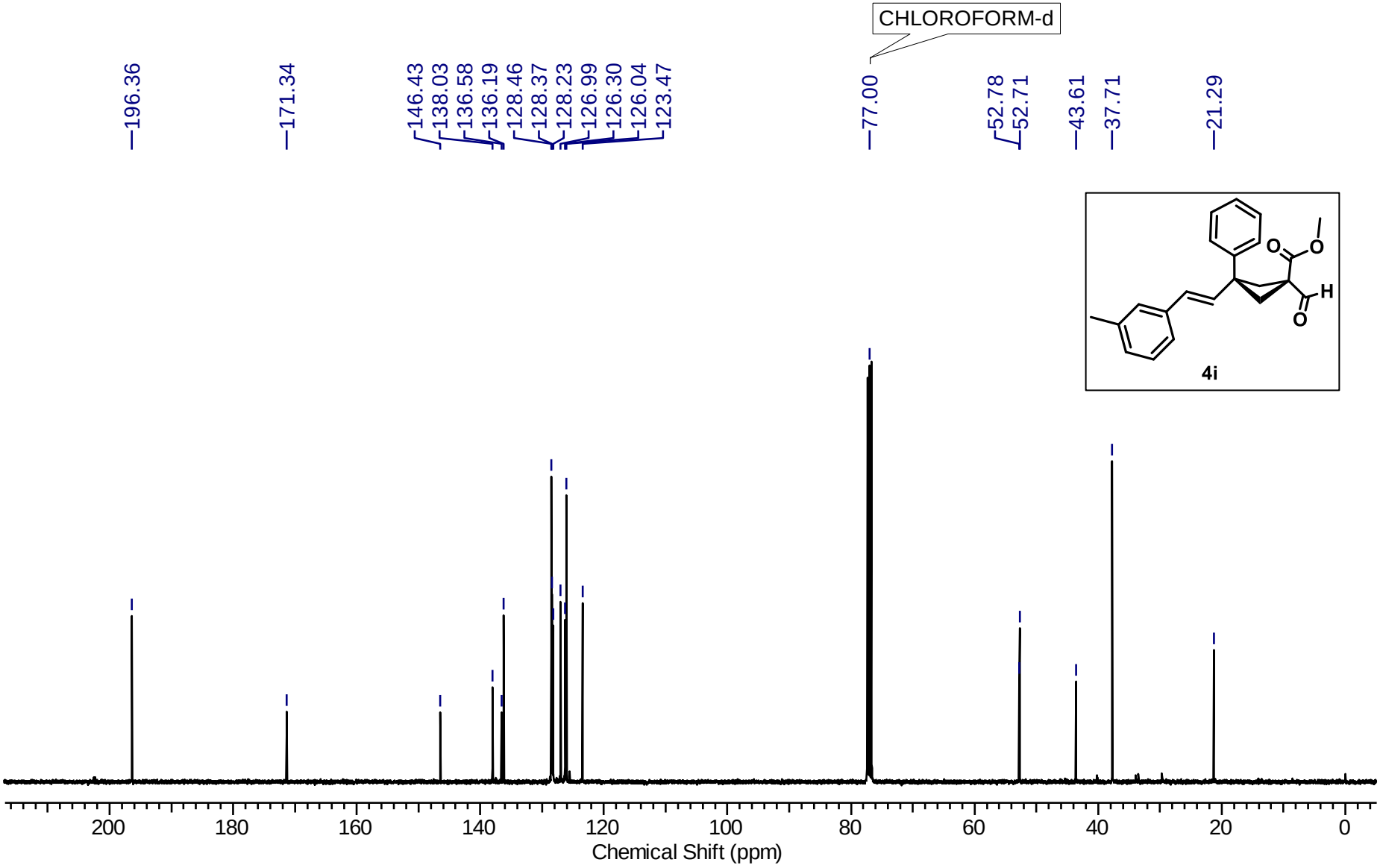
HRMS spectrum of Methyl (1s,3s)-1-formyl-3-((E)-4-methylstyryl)-3-phenylcyclobutane-1-carboxylate (4h)



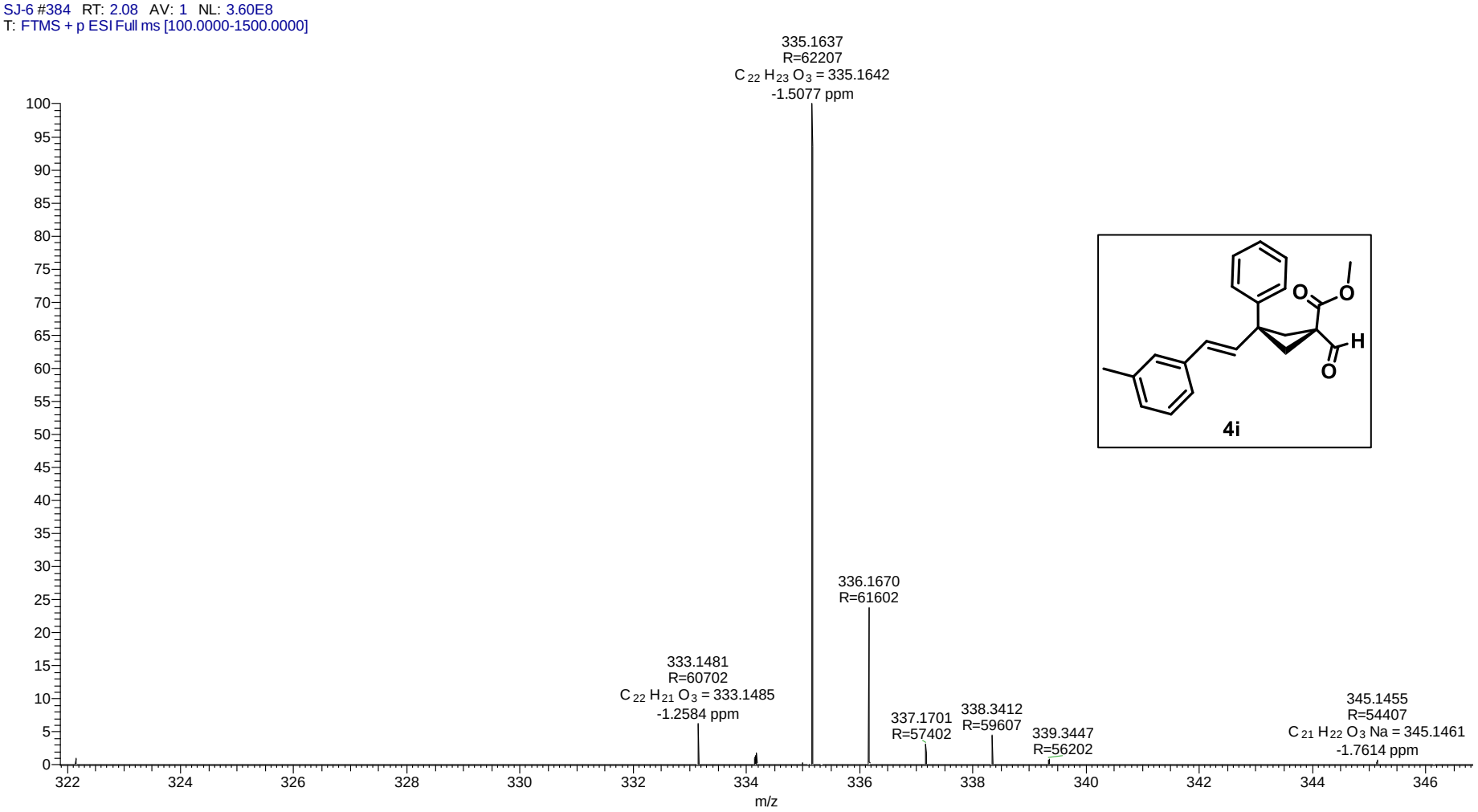
^{1}H NMR (400 MHz, $CDCl_3$) spectrum of Methyl (1s,3s)-1-formyl-3-((E)-3-methylstyryl)-3-phenylcyclobutane-1-carboxylate (4i)



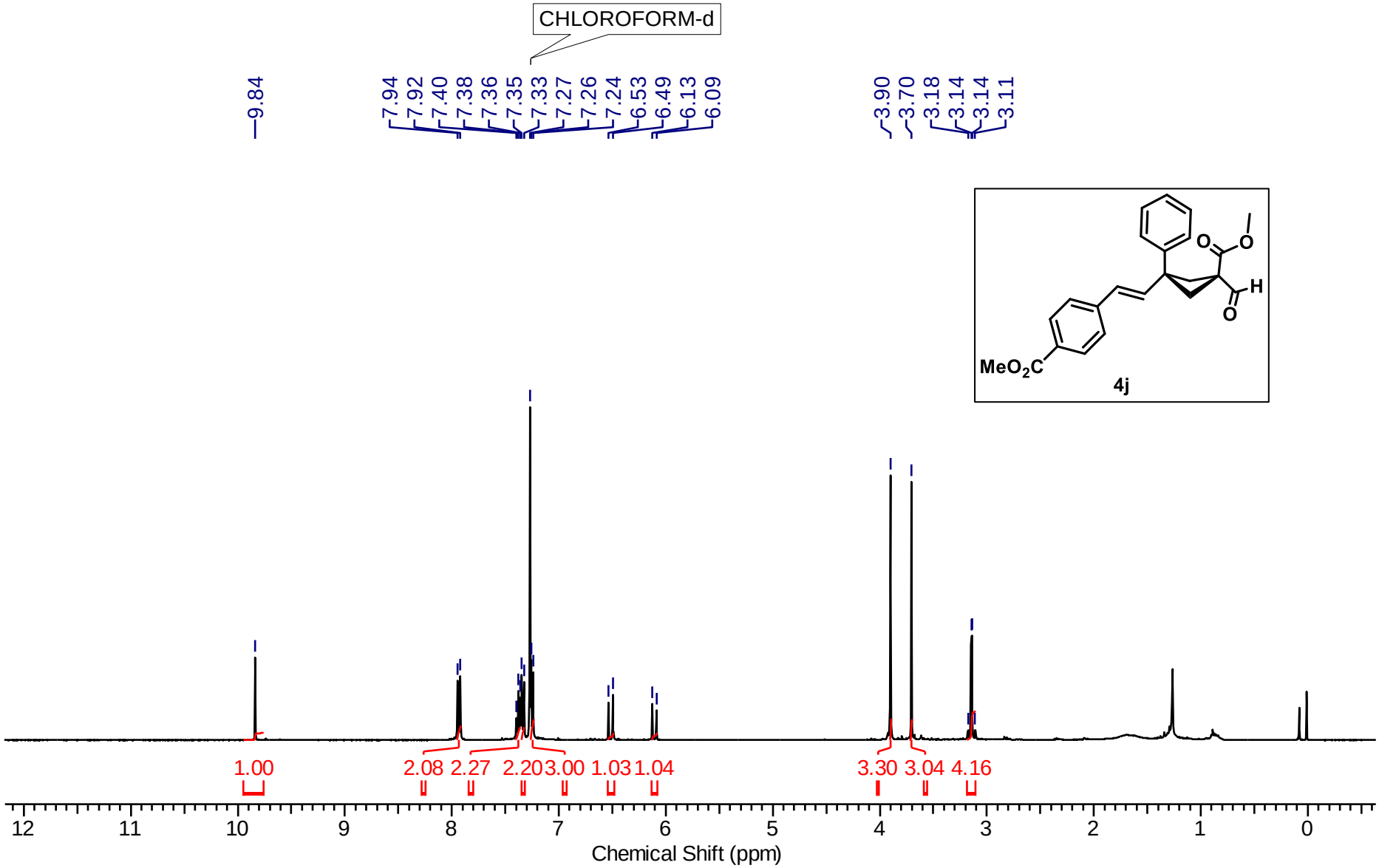
$^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) spectrum of Methyl (1s,3s)-1-formyl-3-((E)-3-methylstyryl)-3-phenylcyclobutane-1-carboxylate (4i)



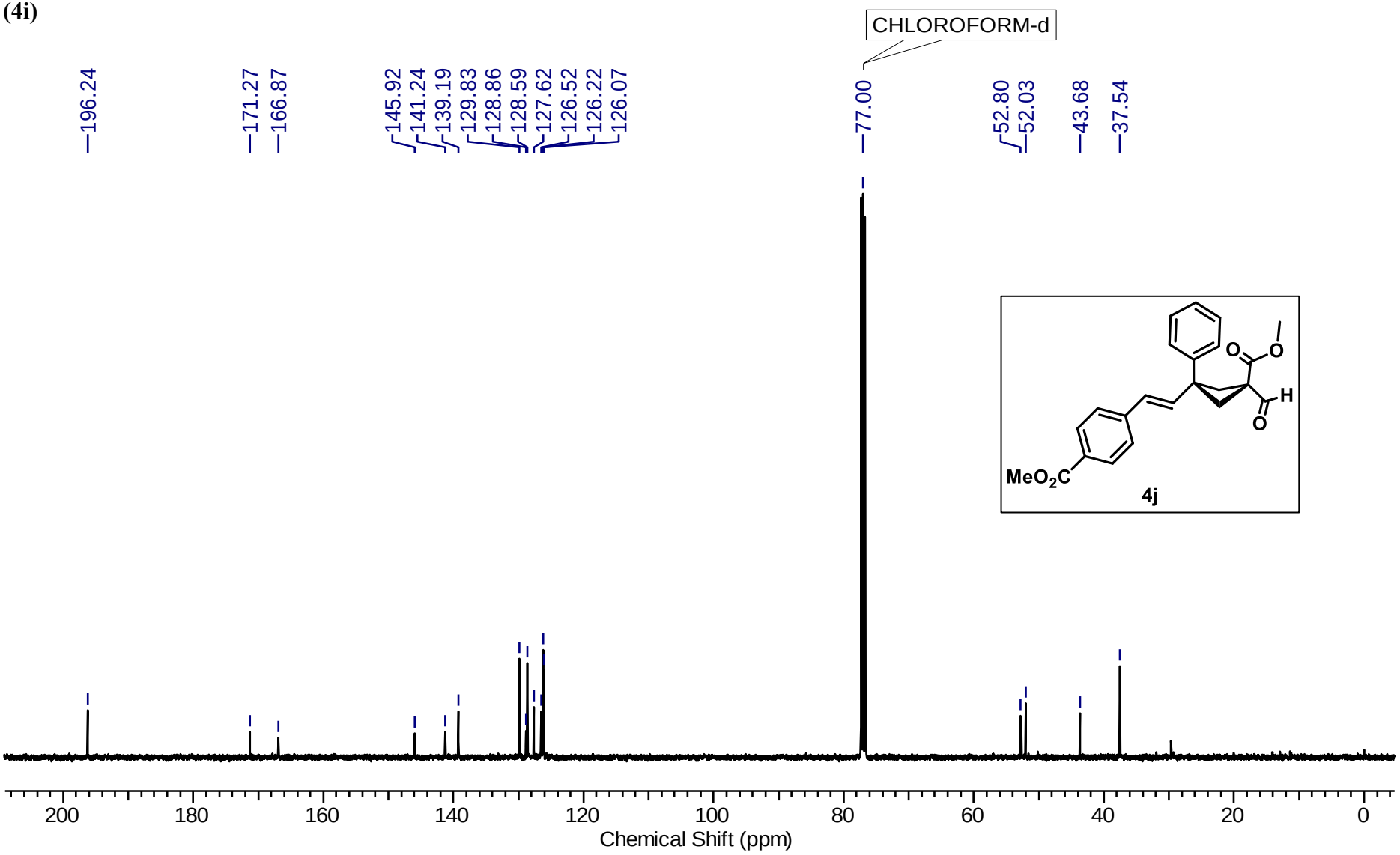
HRMS spectrum of Methyl (1s,3s)-1-formyl-3-((E)-3-methylstyryl)-3-phenylcyclobutane-1-carboxylate (4i)



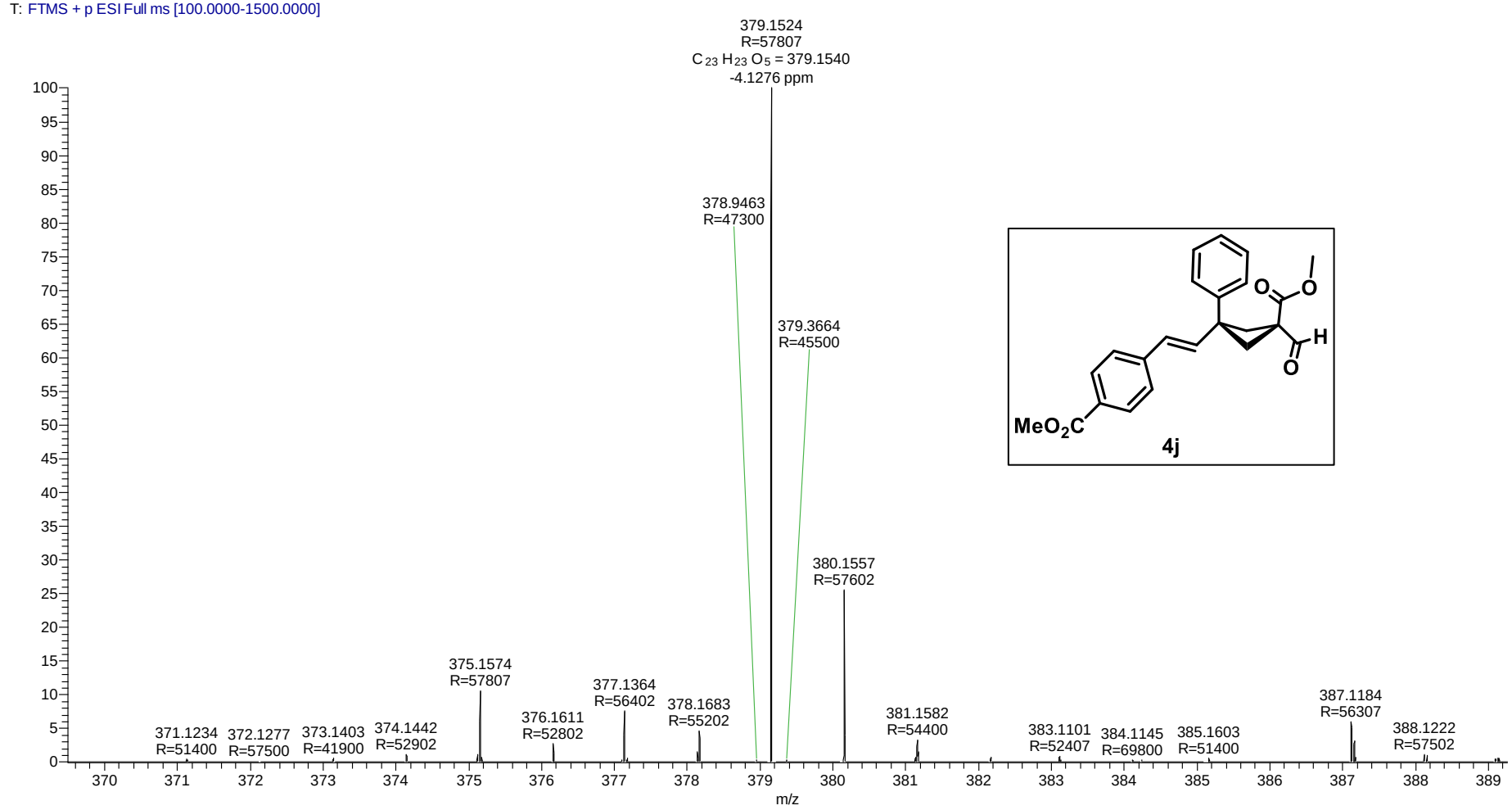
^{1}H NMR (400 MHz, $CDCl_3$) spectrum of Methyl 4-((E)-2-((1s,3s)-3-formyl-3-(methoxycarbonyl)-1-phenylcyclobutyl)vinyl)benzoate (4j)



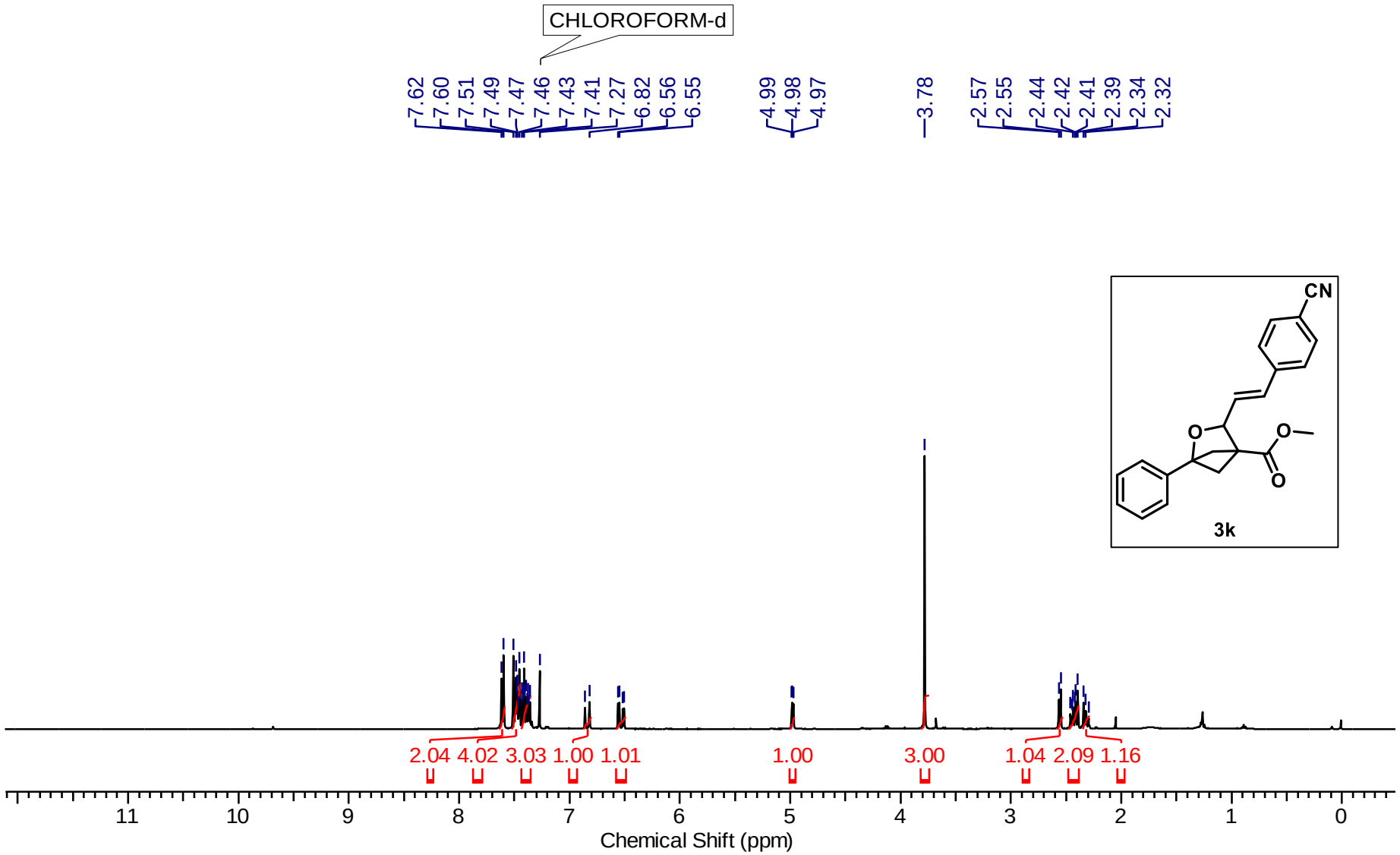
$^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) spectrum of Methyl 4-((E)-2-((1s,3s)-3-formyl-3-(methoxycarbonyl)-1-phenylcyclobutyl)vinyl)benzoate (4i)



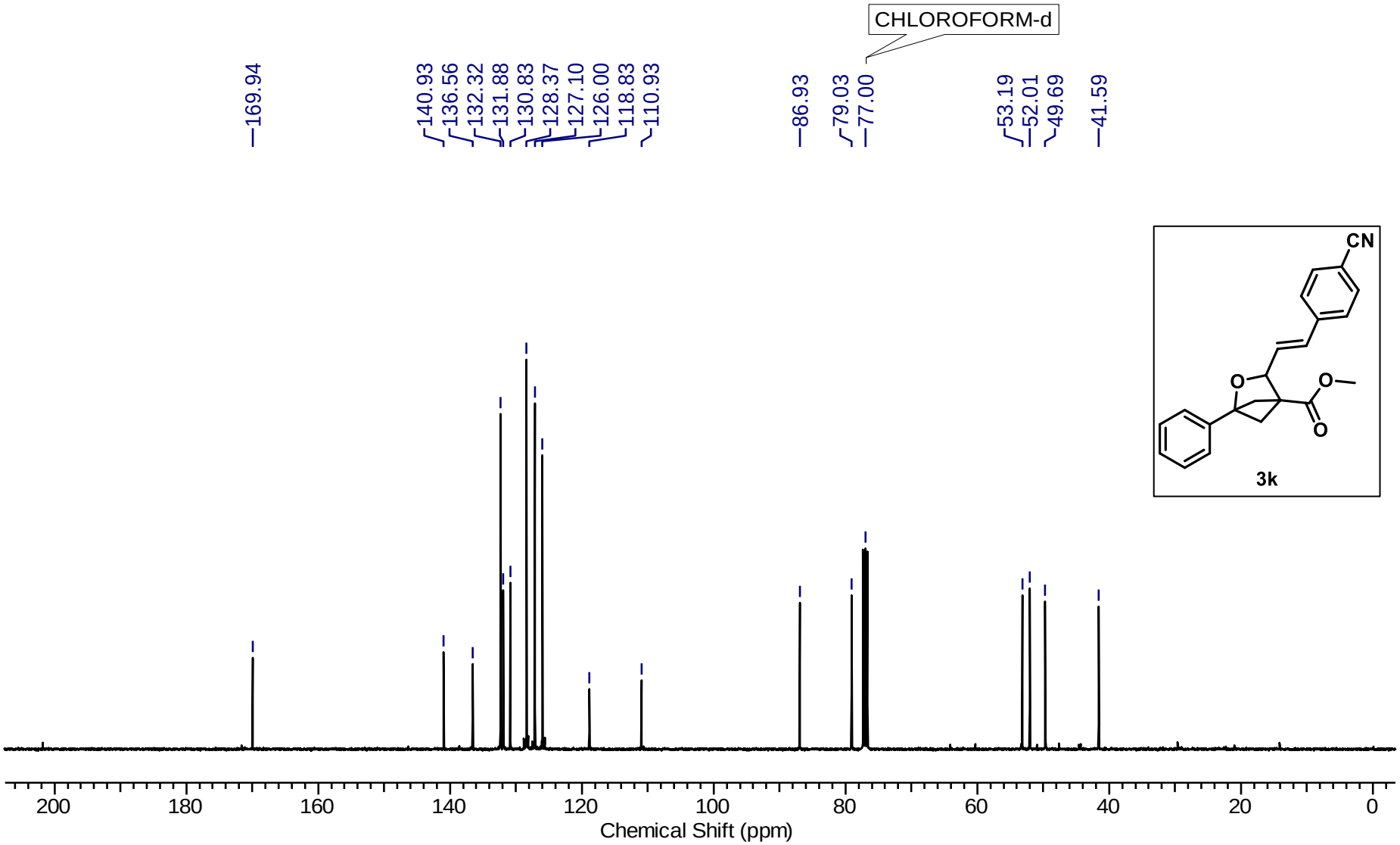
HRMS spectrum of Methyl 4-((E)-2-((1s,3s)-3-formyl-3-(methoxycarbonyl)-1-phenylcyclobutyl)vinyl)benzoate (4i)



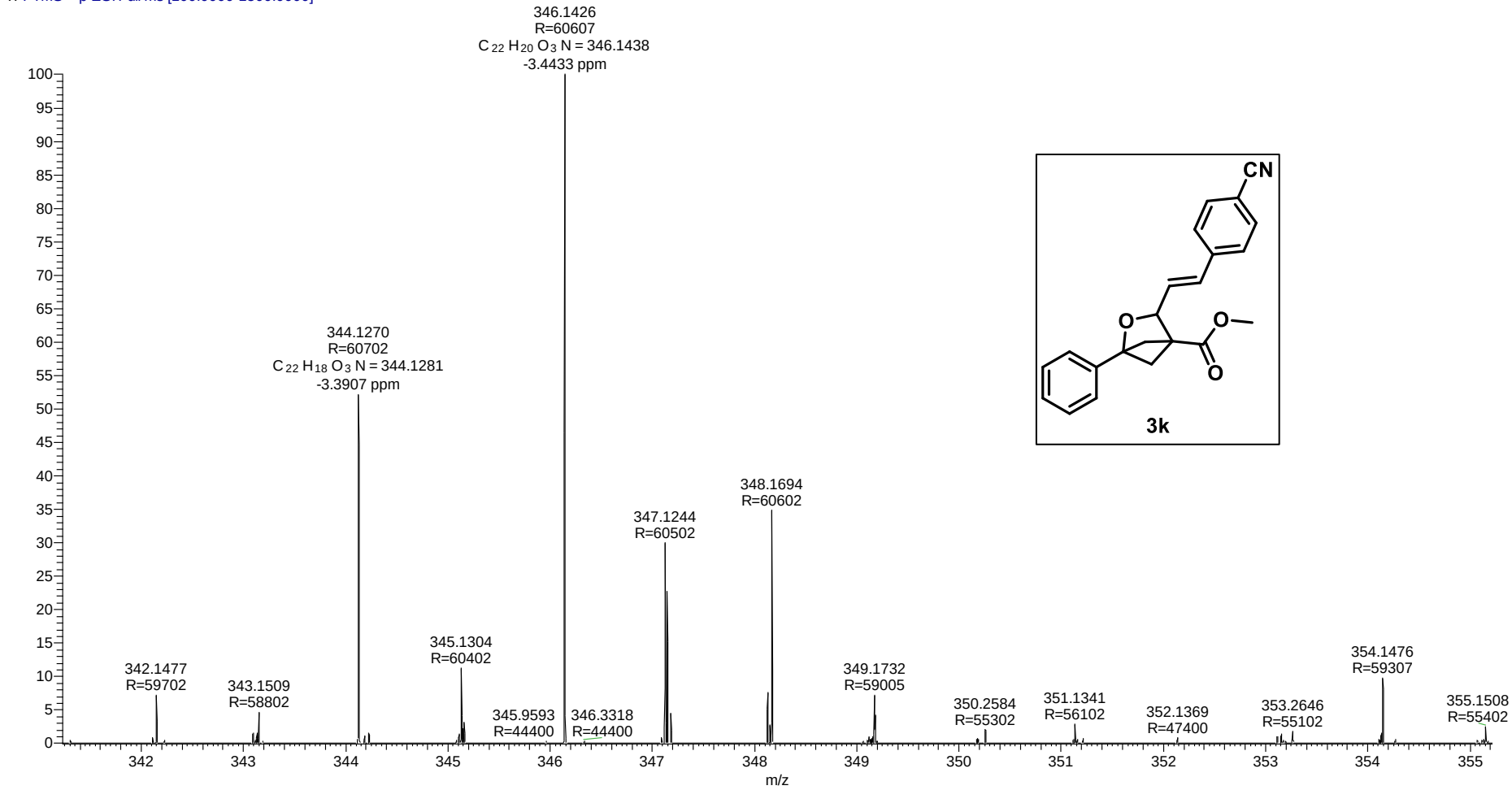
^{1}H NMR (400 MHz, $CDCl_3$) spectrum of Methyl (E)-3-(4-cyanostyryl)-1-phenyl-2-oxabicyclo[2.1.1]hexane-4-carboxylate (3k)



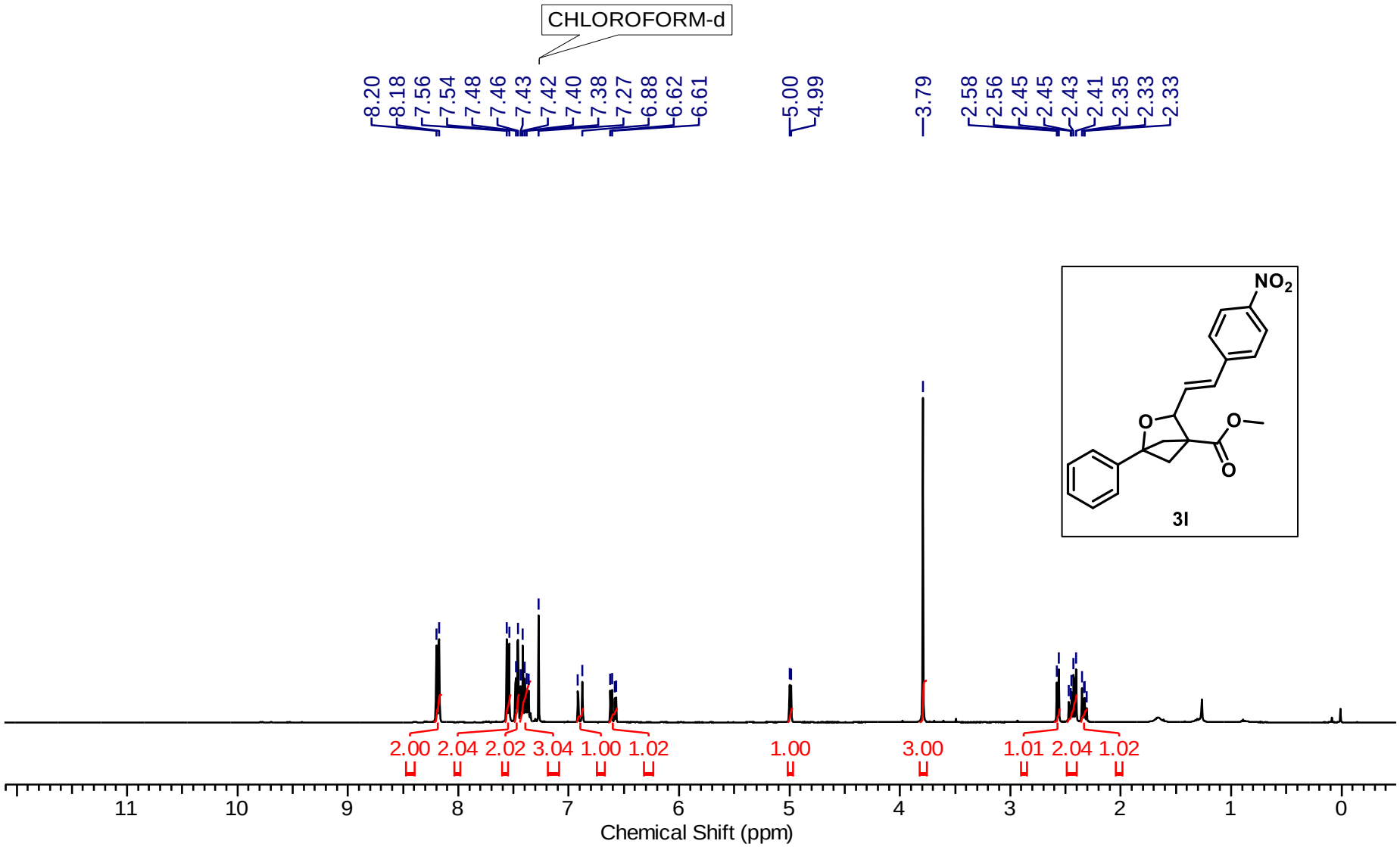
$^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) spectrum of Methyl (E)-3-(4-cyanostyryl)-1-phenyl-2-oxabicyclo[2.1.1]hexane-4-carboxylate (3k)



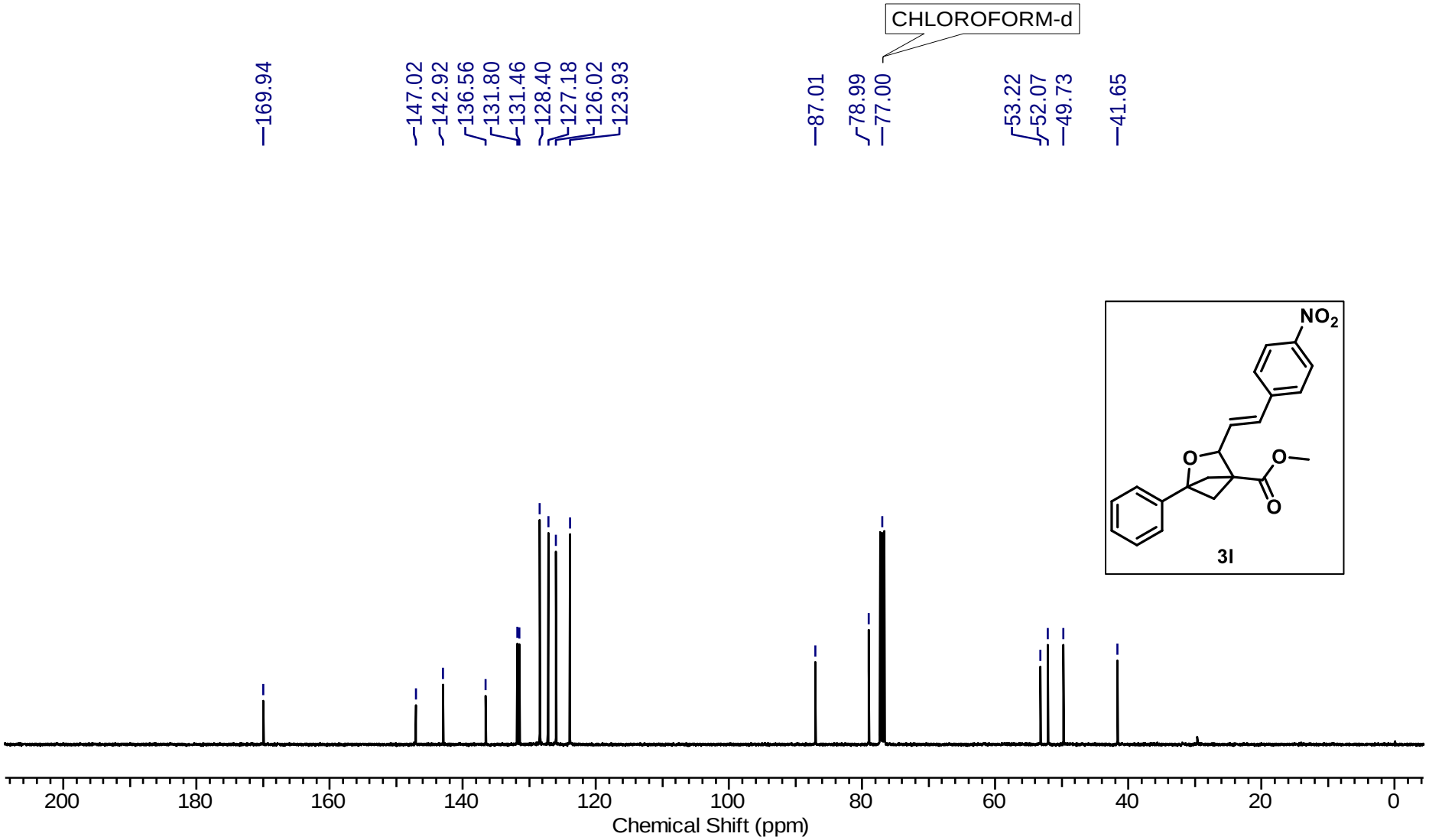
HRMS spectrum of Methyl (E)-3-(4-cyanostyryl)-1-phenyl-2-oxabicyclo[2.1.1]hexane-4-carboxylate (3k)



^{1}H NMR (400 MHz, $CDCl_3$) spectrum of Methyl (E)-3-(4-nitrostyryl)-1-phenyl-2-oxabicyclo[2.1.1]hexane-4-carboxylate (3l)

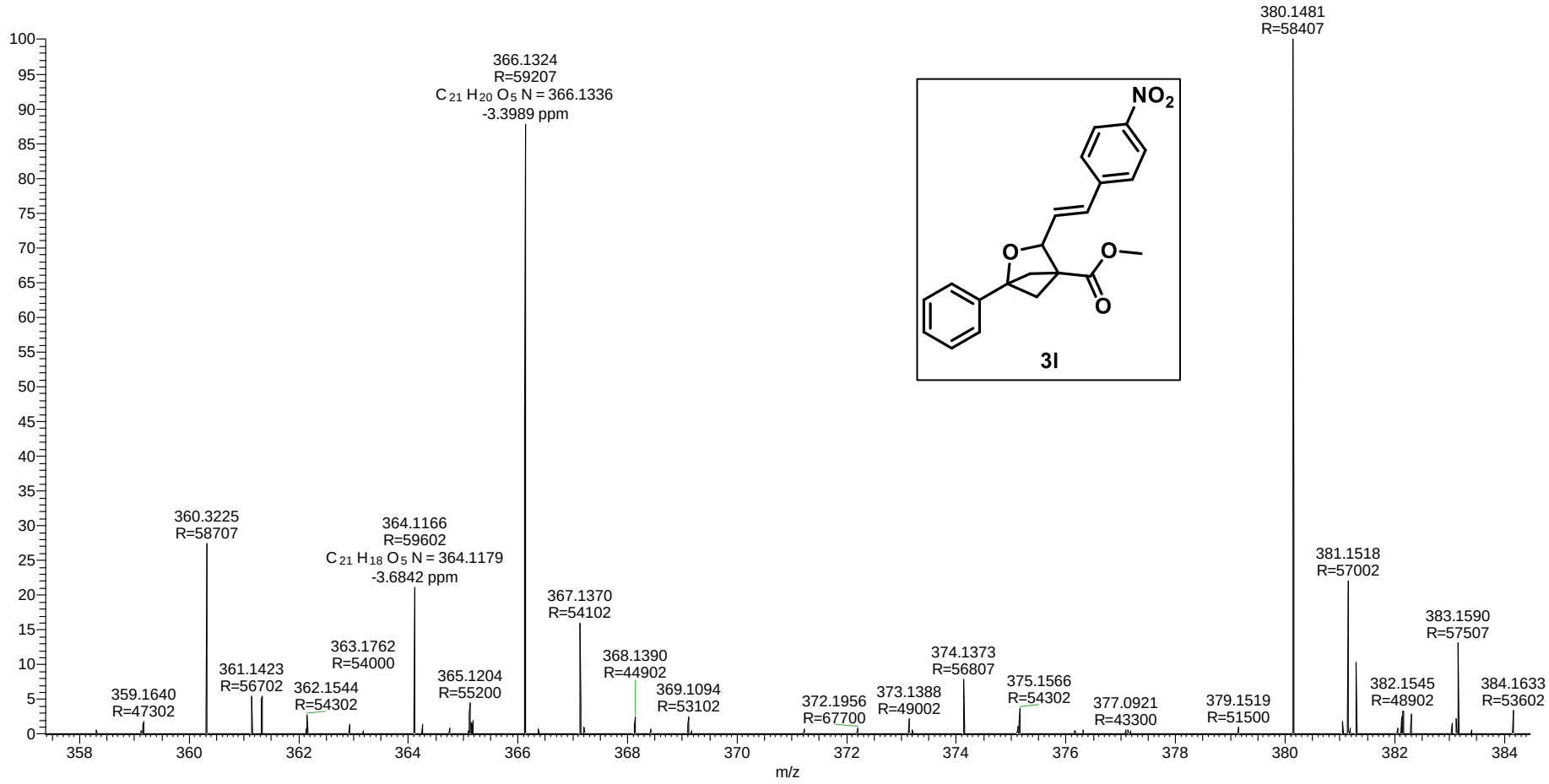


$^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) spectrum of Methyl (E)-3-(4-nitrostyryl)-1-phenyl-2-oxabicyclo[2.1.1]hexane-4-carboxylate (3l)

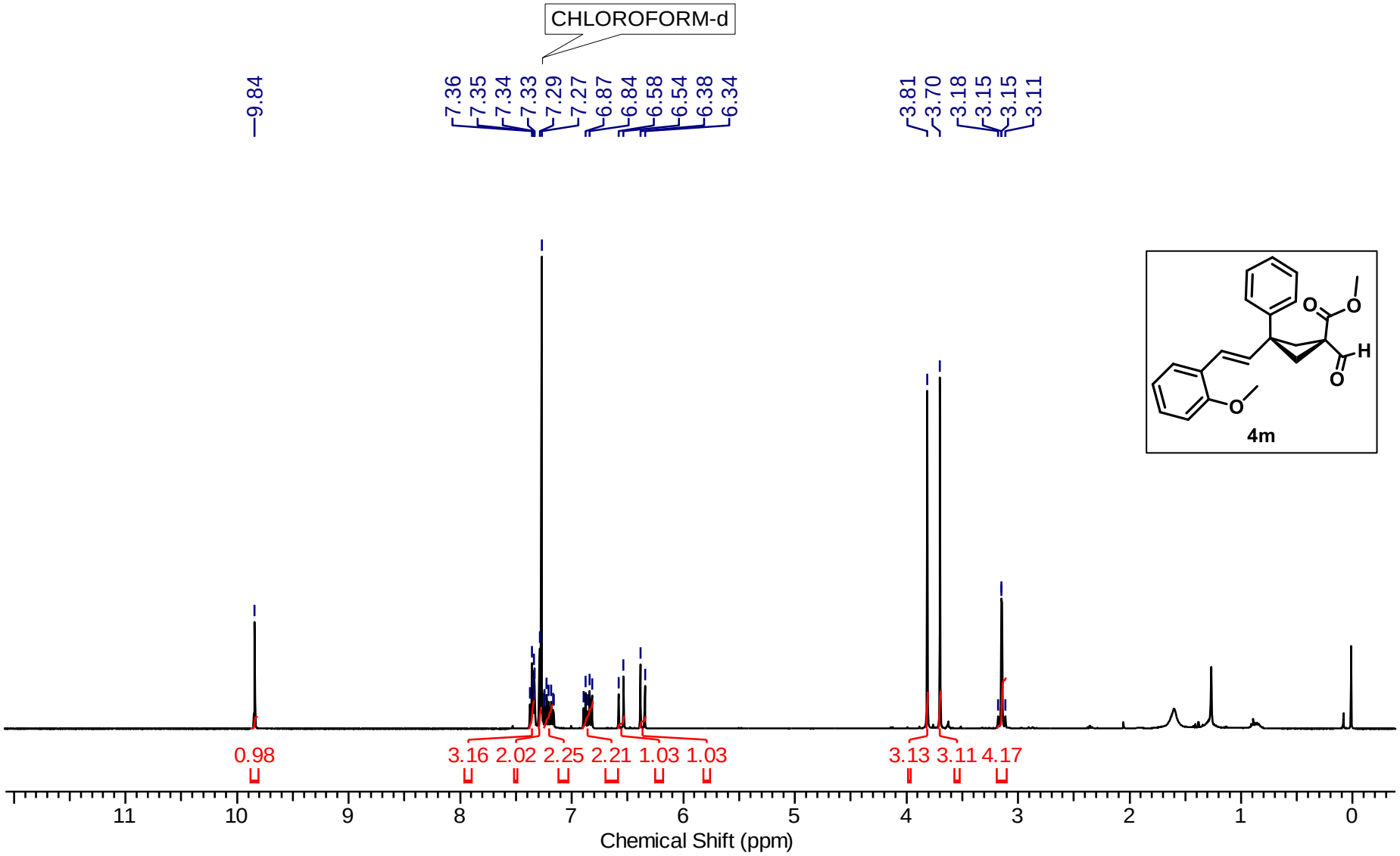


HRMS spectrum of Methyl (E)-3-(4-nitrostyryl)-1-phenyl-2-oxabicyclo[2.1.1]hexane-4-carboxylate (3l)

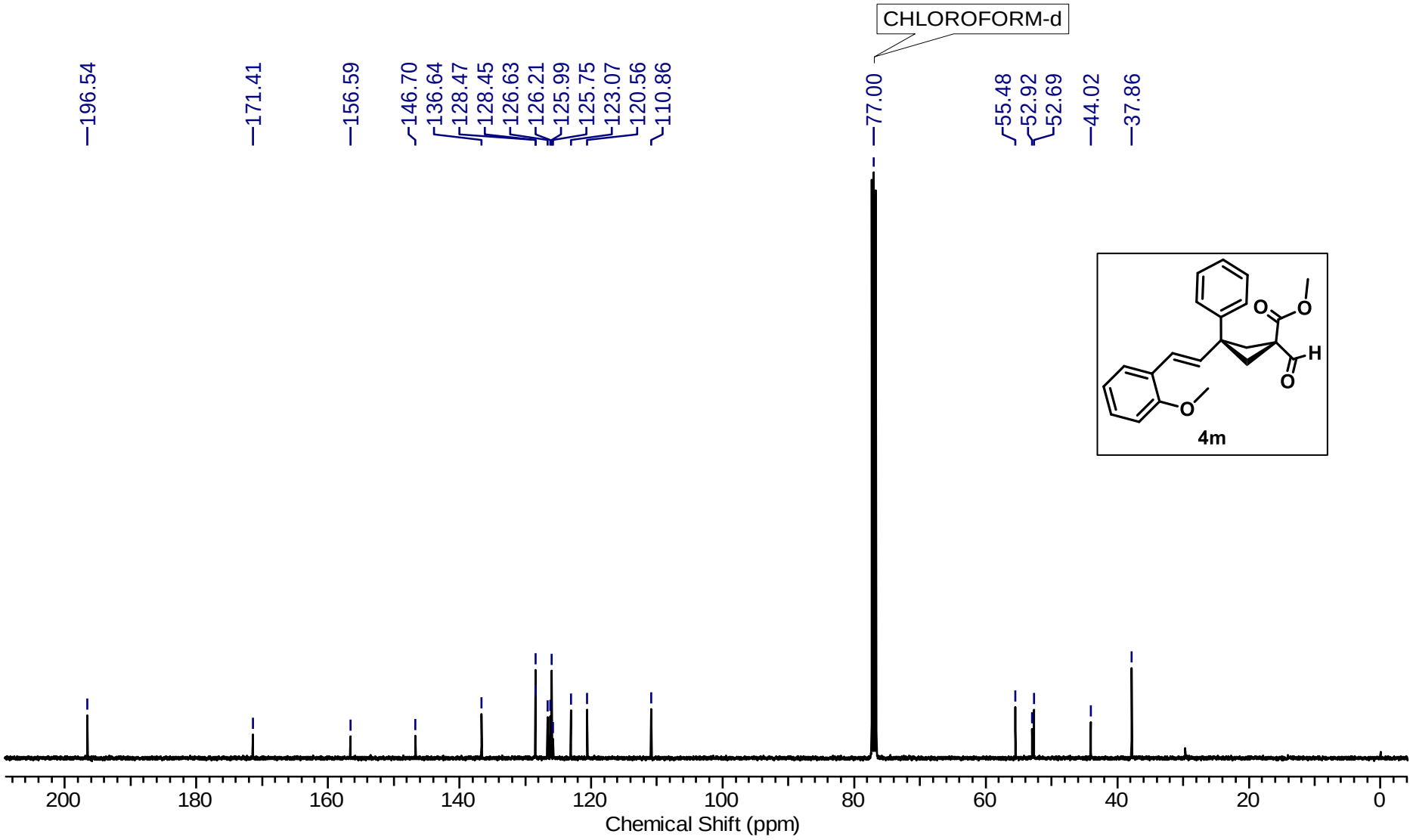
SJ-19 #363 RT: 1.96 AV: 1 NL: 1.74E7
T: FTMS + p ESI Full ms [100.0000-1500.0000]



^{1}H NMR (400 MHz, $CDCl_3$) spectrum of Methyl (1s,3s)-1-formyl-3-((E)-2-methoxystyryl)-3-phenylcyclobutane-1-carboxylate (4m)

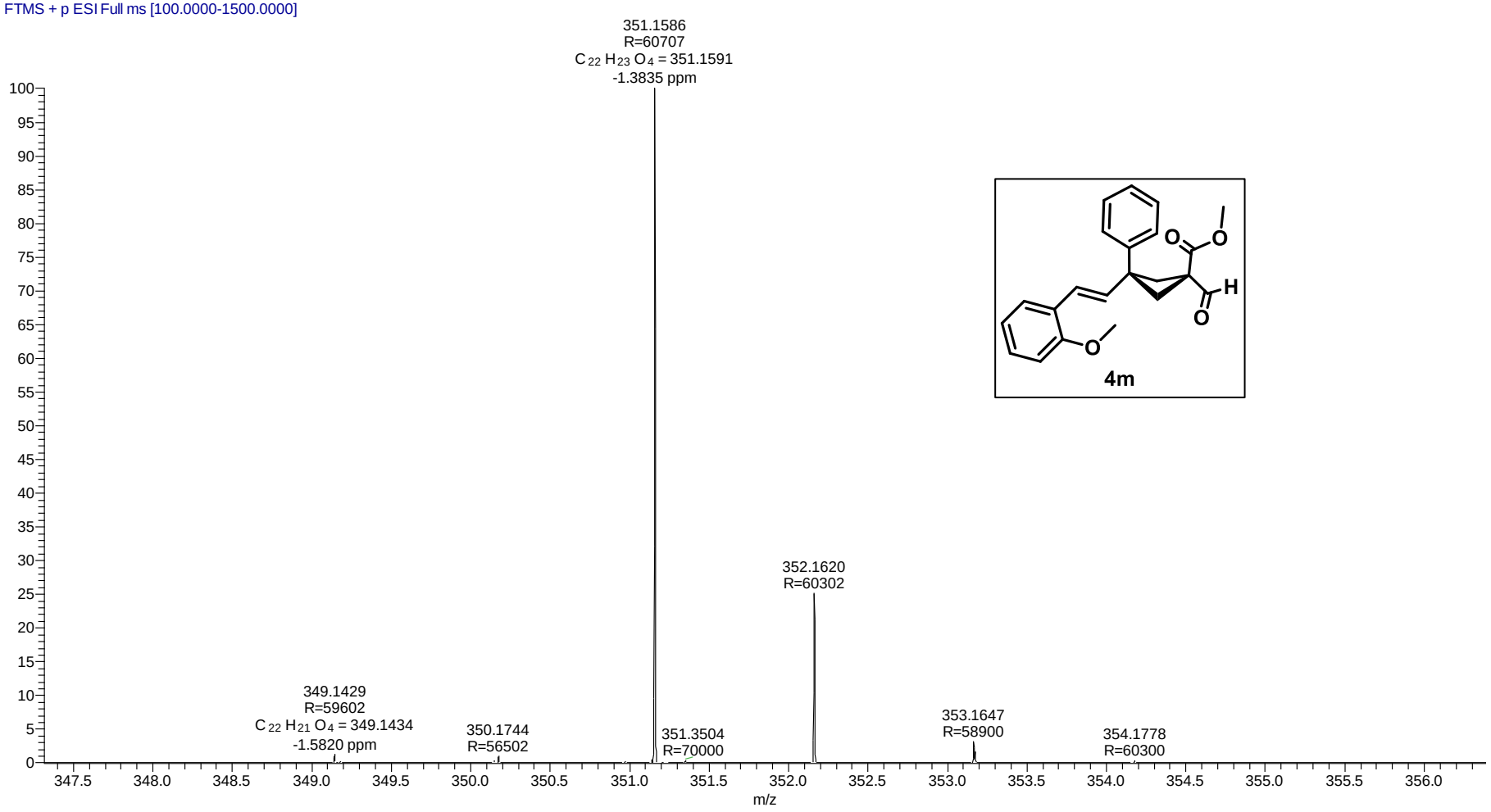


$^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) spectrum of Methyl (1s,3s)-1-formyl-3-((E)-2-methoxystyryl)-3-phenylcyclobutane-1-carboxylate (4m)

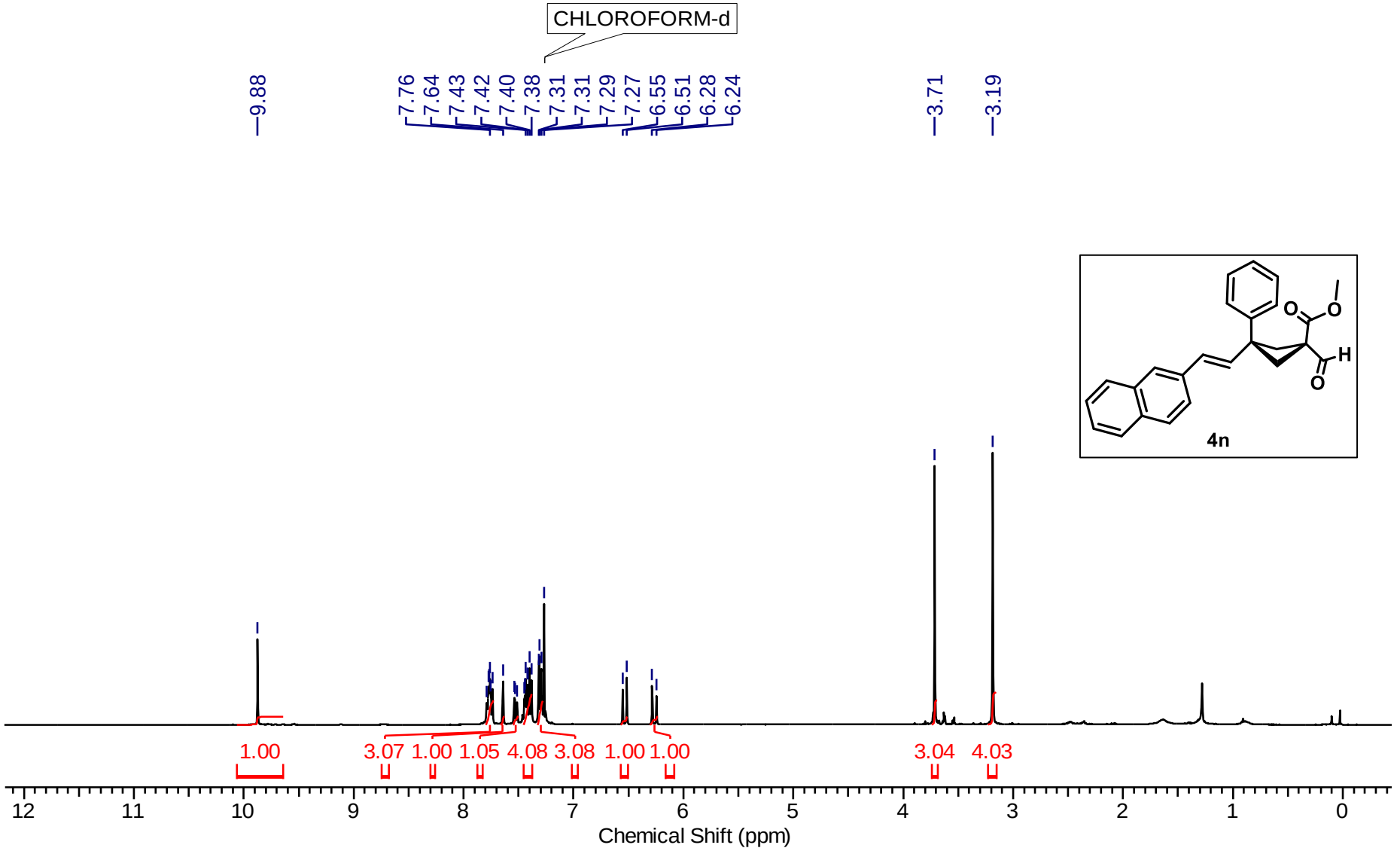


HRMS spectrum of Methyl (1s,3s)-1-formyl-3-((E)-2-methoxystyryl)-3-phenylcyclobutane-1-carboxylate (4m)

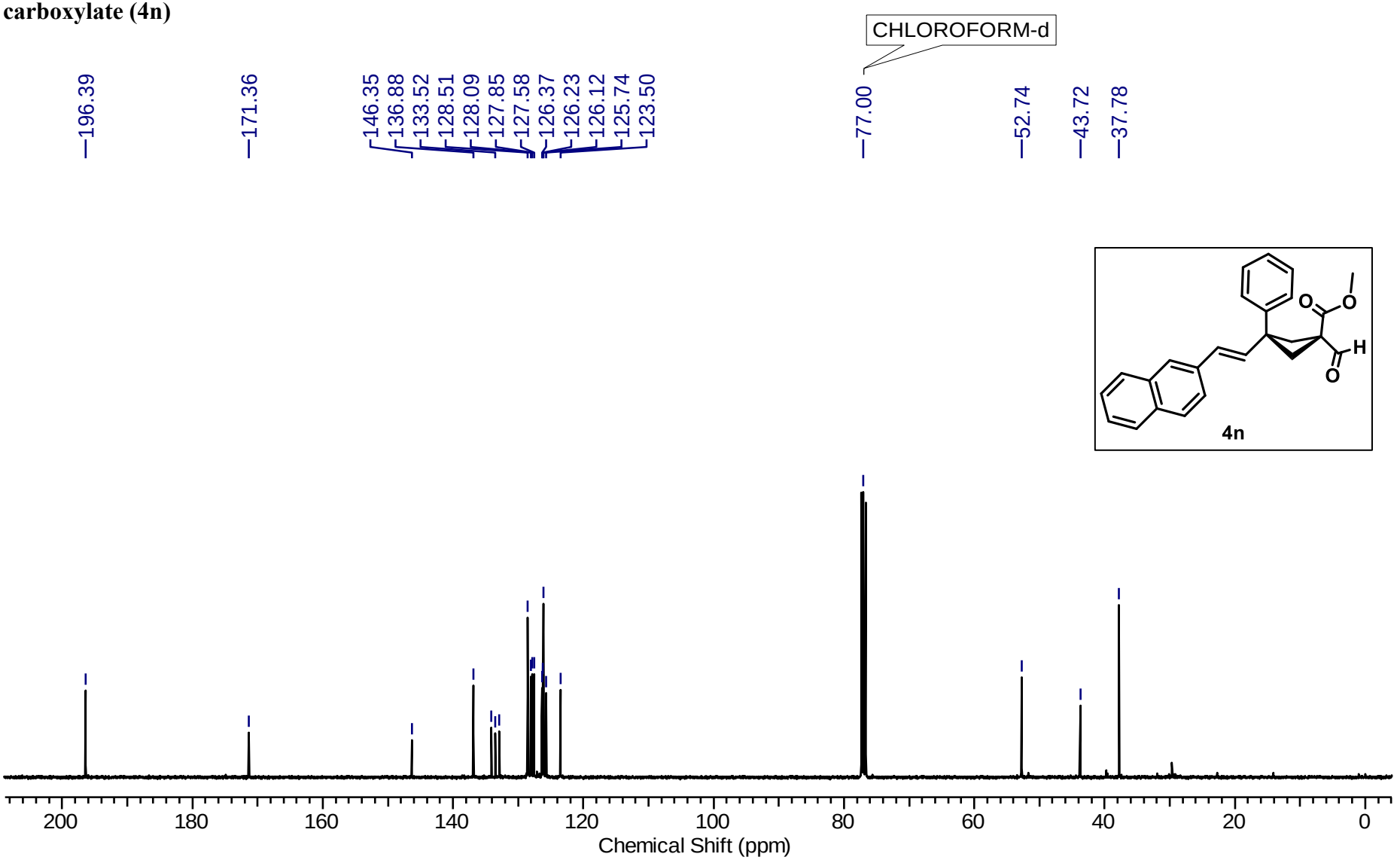
SJ-7 #349 RT: 1.90 AV: 1 NL: 4.53E8
T: FTMS + p ESI Full ms [100.0000-1500.0000]



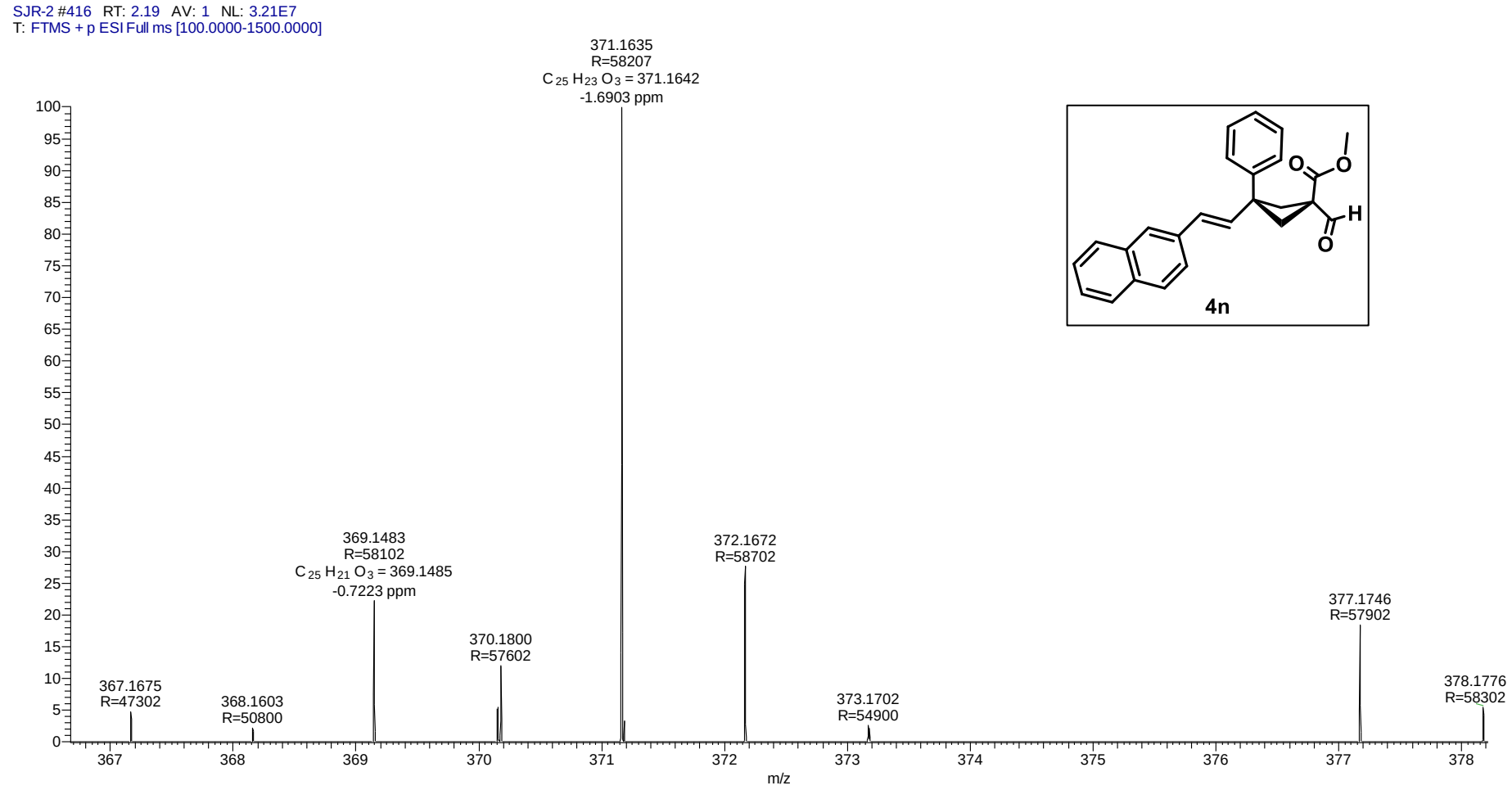
^{1}H NMR (400 MHz, $CDCl_3$) spectrum of Methyl (1s,3s)-1-formyl-3-((E)-2-(naphthalen-2-yl)vinyl)-3-phenylcyclobutane-1-carboxylate (4n)



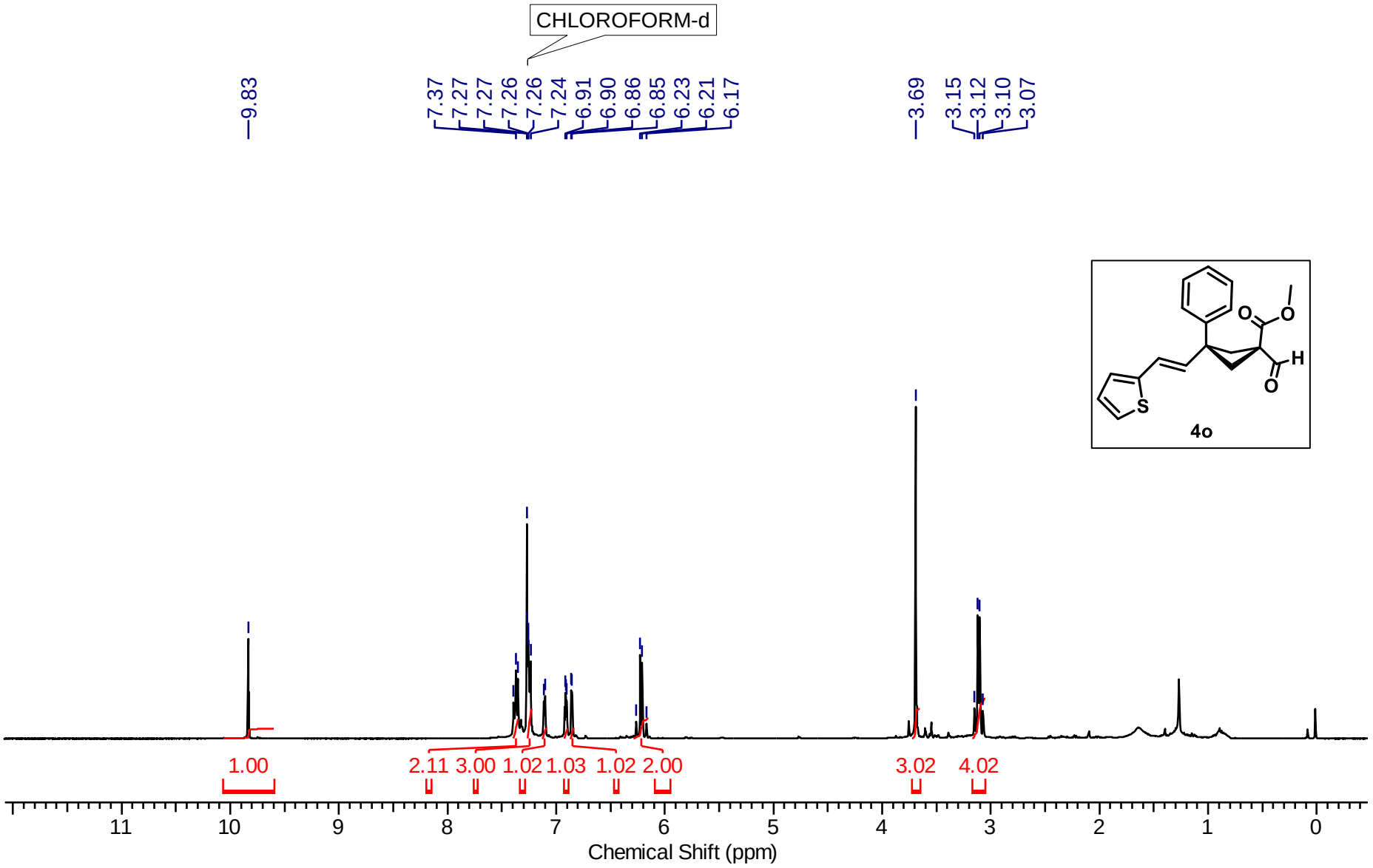
$^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) spectrum of Methyl (1s,3s)-1-formyl-3-((E)-2-(naphthalen-2-yl)vinyl)-3-phenylcyclobutane-1-carboxylate (4n)



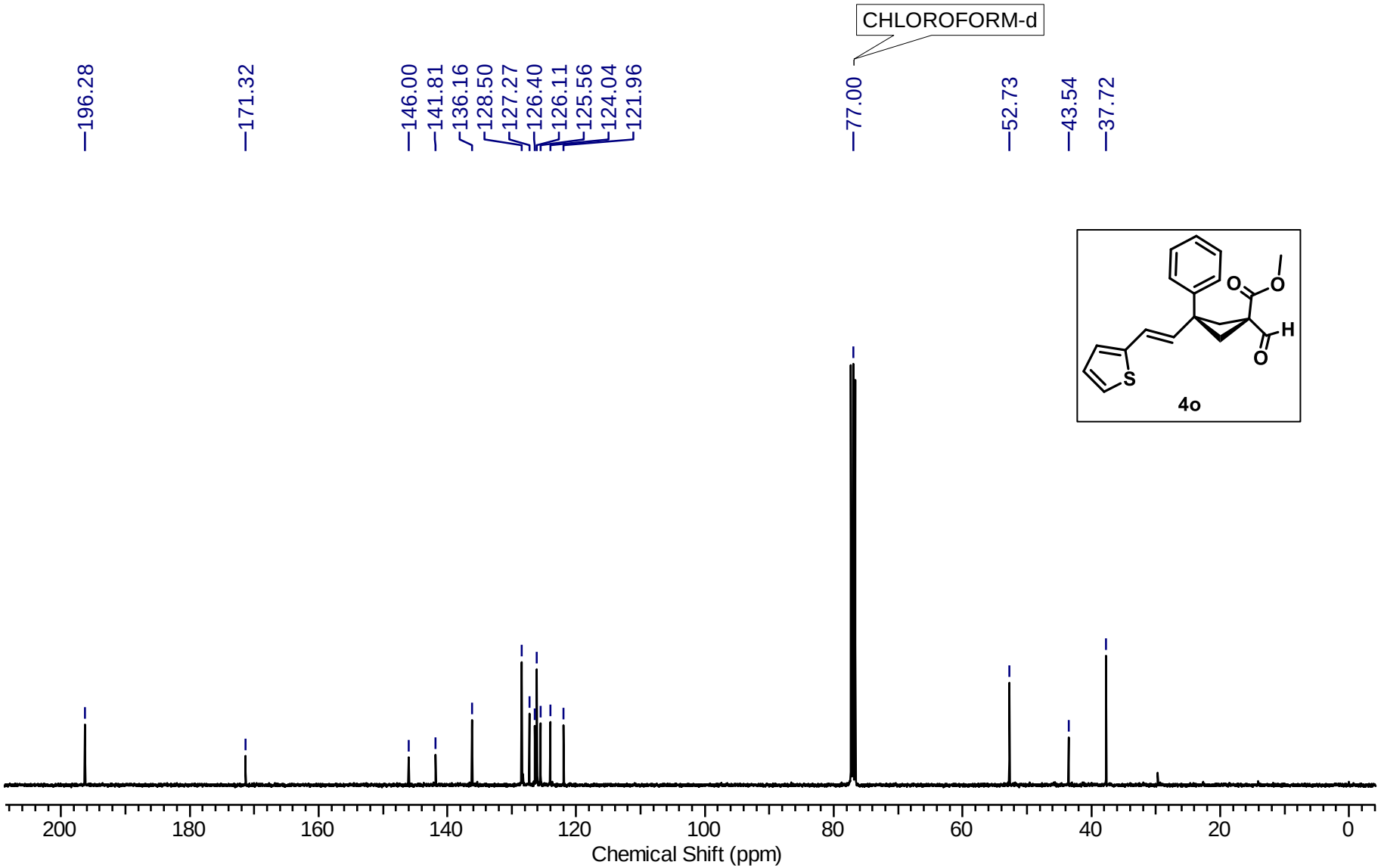
HRMS spectrum of Methyl (1s,3s)-1-formyl-3-((E)-2-(naphthalen-2-yl)vinyl)-3-phenylcyclobutane-1-carboxylate (4n)



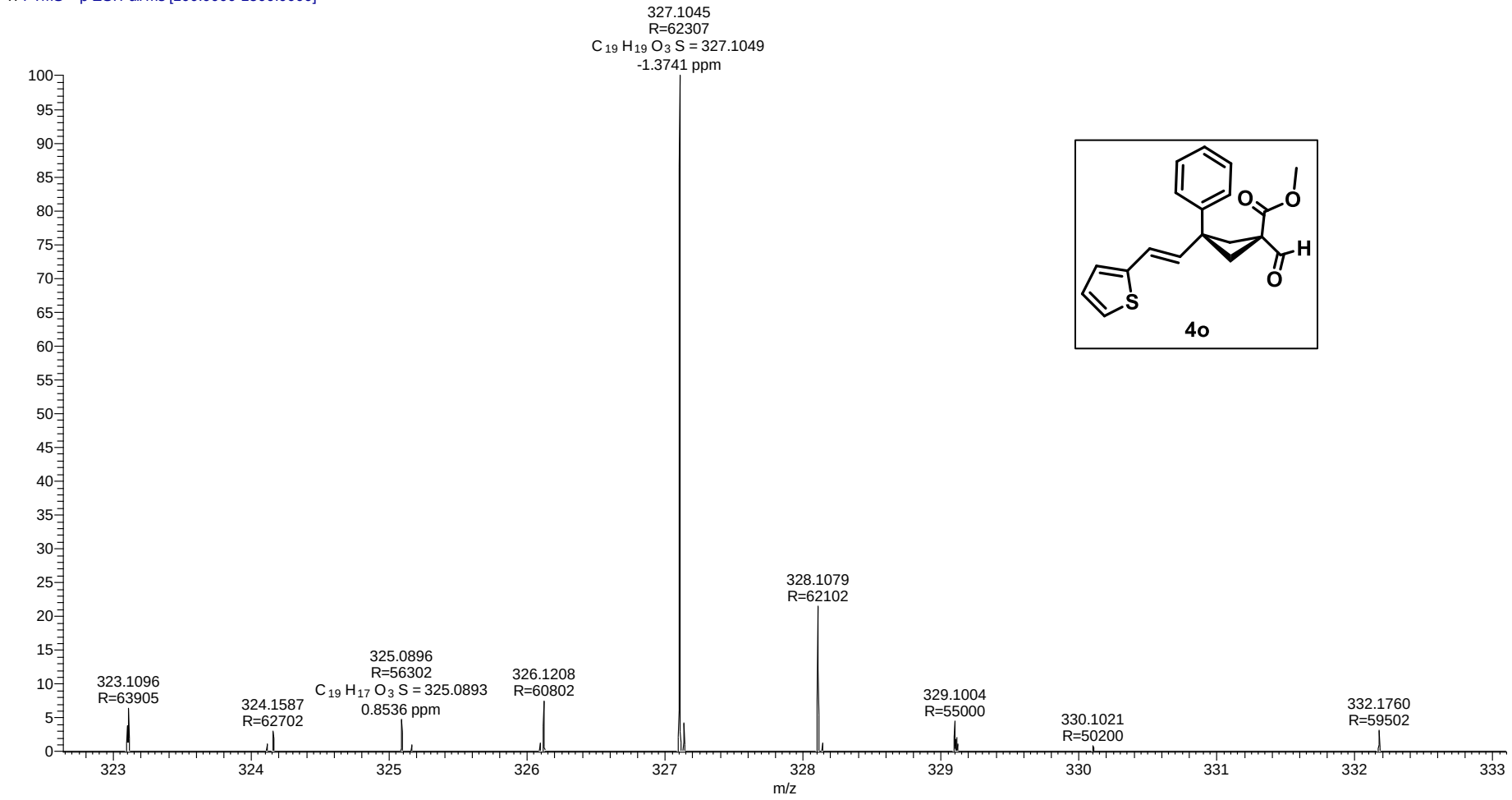
^{1}H NMR (400 MHz, $CDCl_3$) spectrum of Methyl (1s,3s)-1-formyl-3-phenyl-3-((E)-2-(thiophen-2-yl)vinyl)cyclobutane-1-carboxylate (4o)



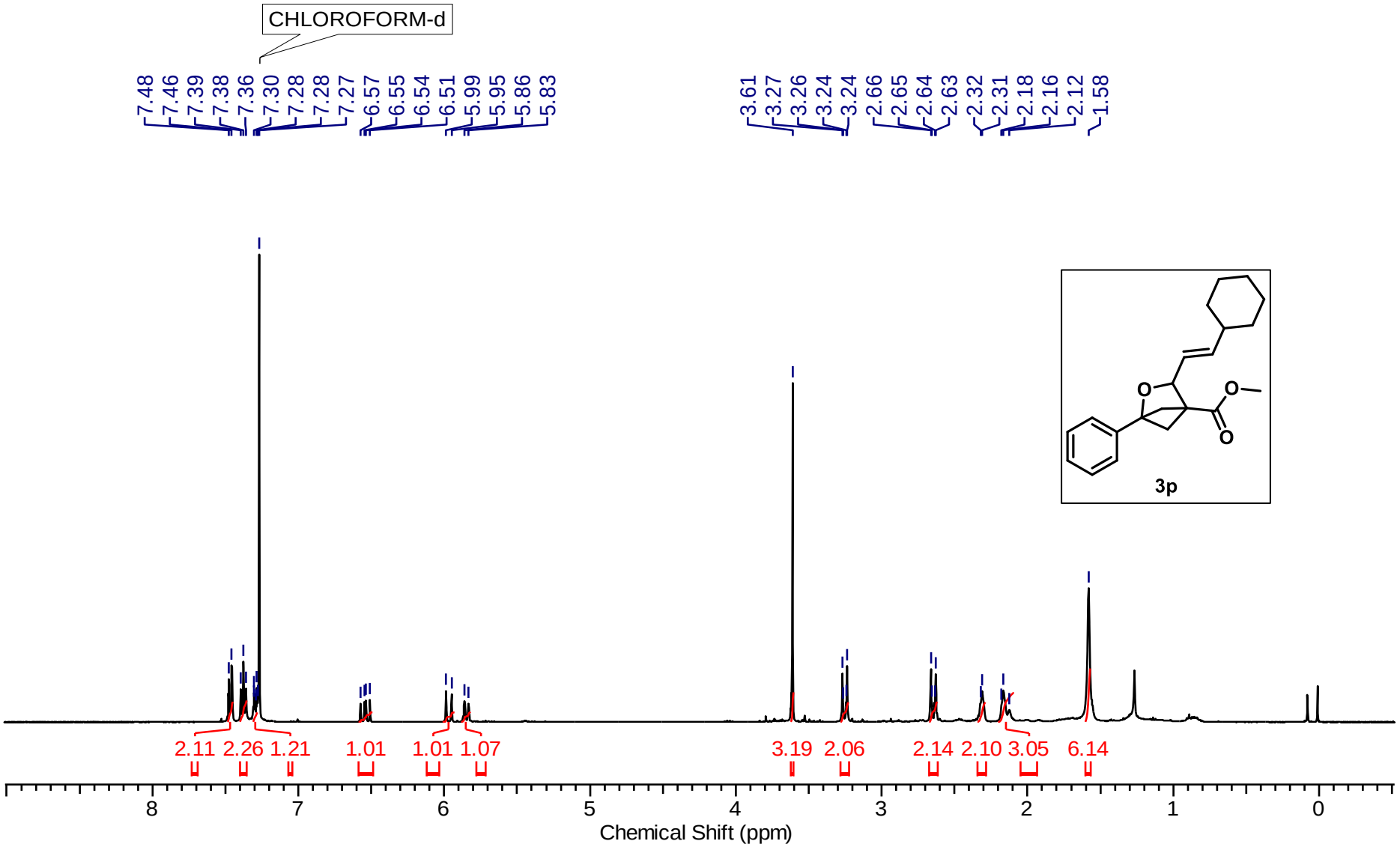
$^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) spectrum of Methyl (1s,3s)-1-formyl-3-phenyl-3-((E)-2-(thiophen-2-yl)vinyl)cyclobutane-1-carboxylate (4o)



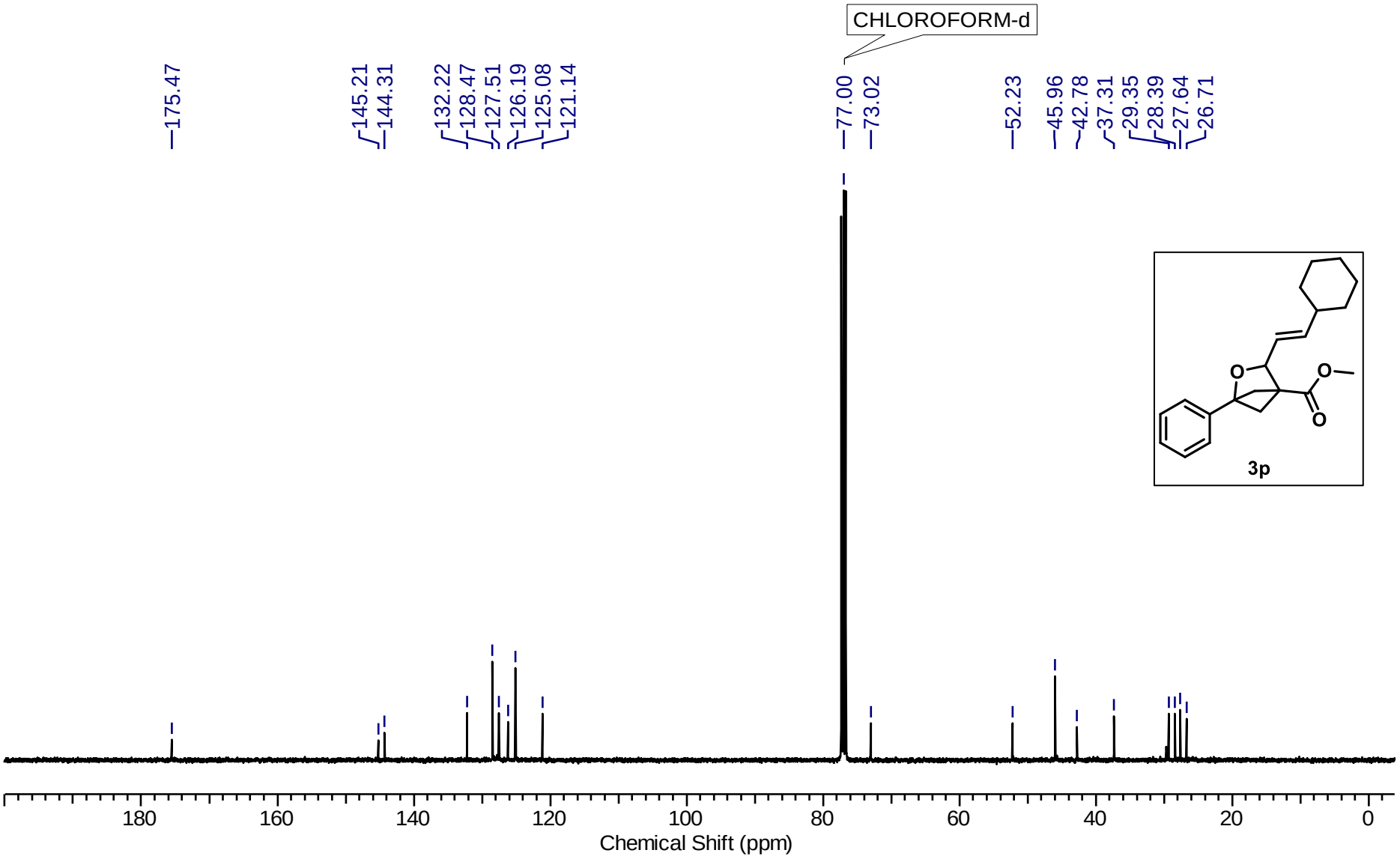
HRMS spectrum of Methyl (1s,3s)-1-formyl-3-phenyl-3-((E)-2-(thiophen-2-yl)vinyl)cyclobutane-1-carboxylate (4o)



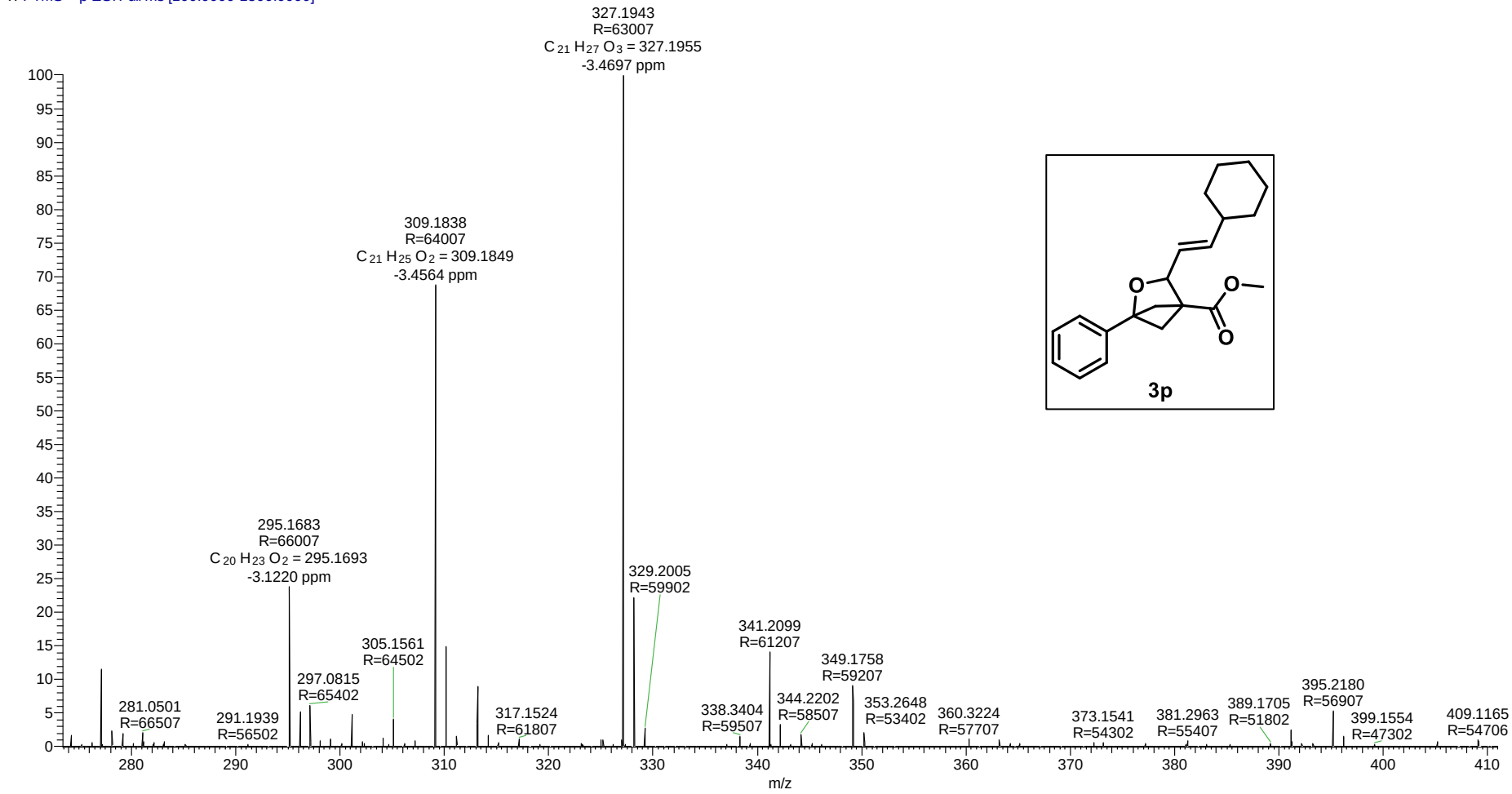
^{1}H NMR (400 MHz, $CDCl_3$) spectrum of Methyl (E)-3-(2-cyclohexylvinyl)-1-phenyl-2-oxabicyclo[2.1.1]hexane-4-carboxylate (3p)



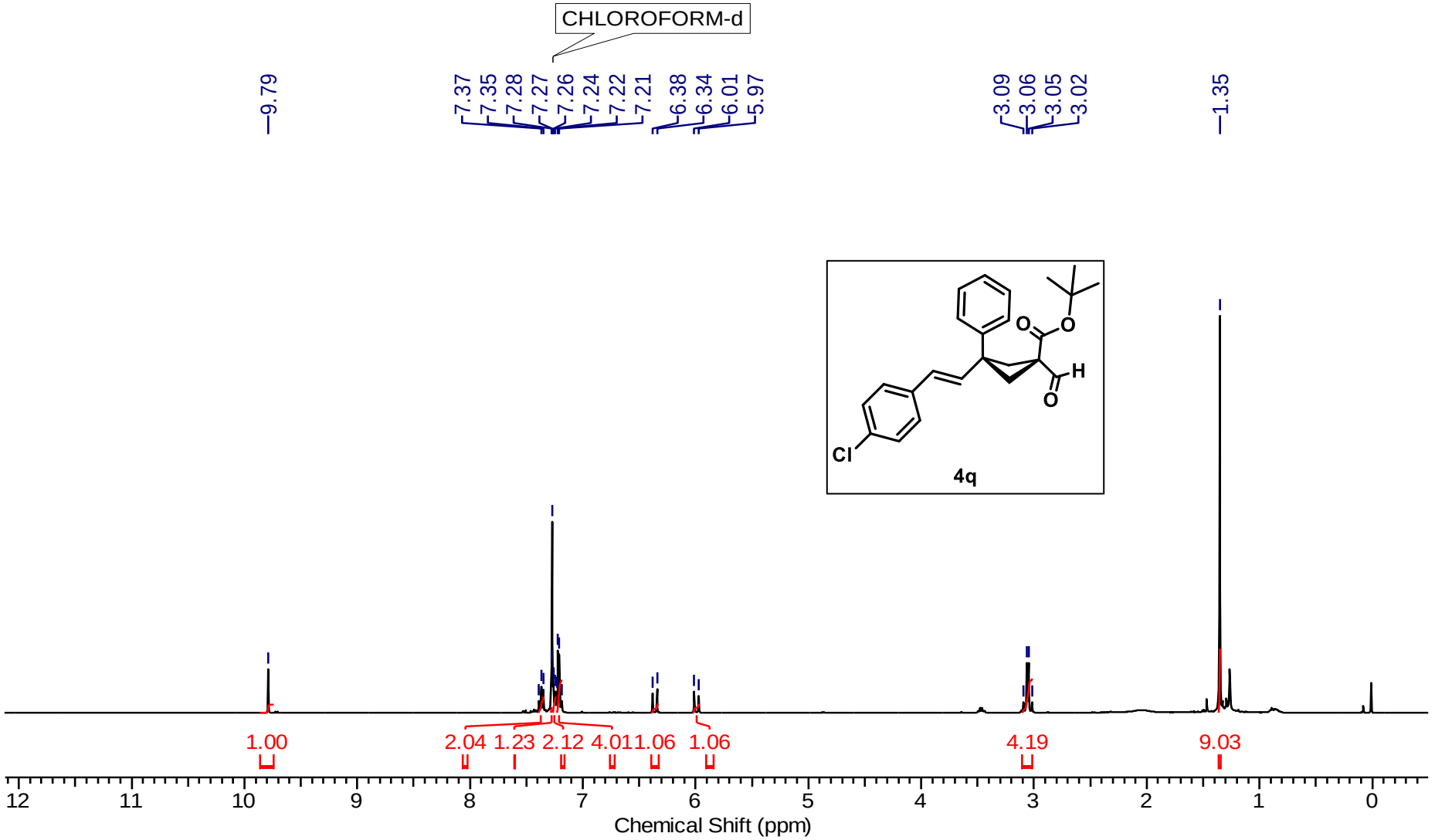
$^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) spectrum of Methyl (E)-3-(2-cyclohexylvinyl)-1-phenyl-2-oxabicyclo[2.1.1]hexane-4-carboxylate (3p)



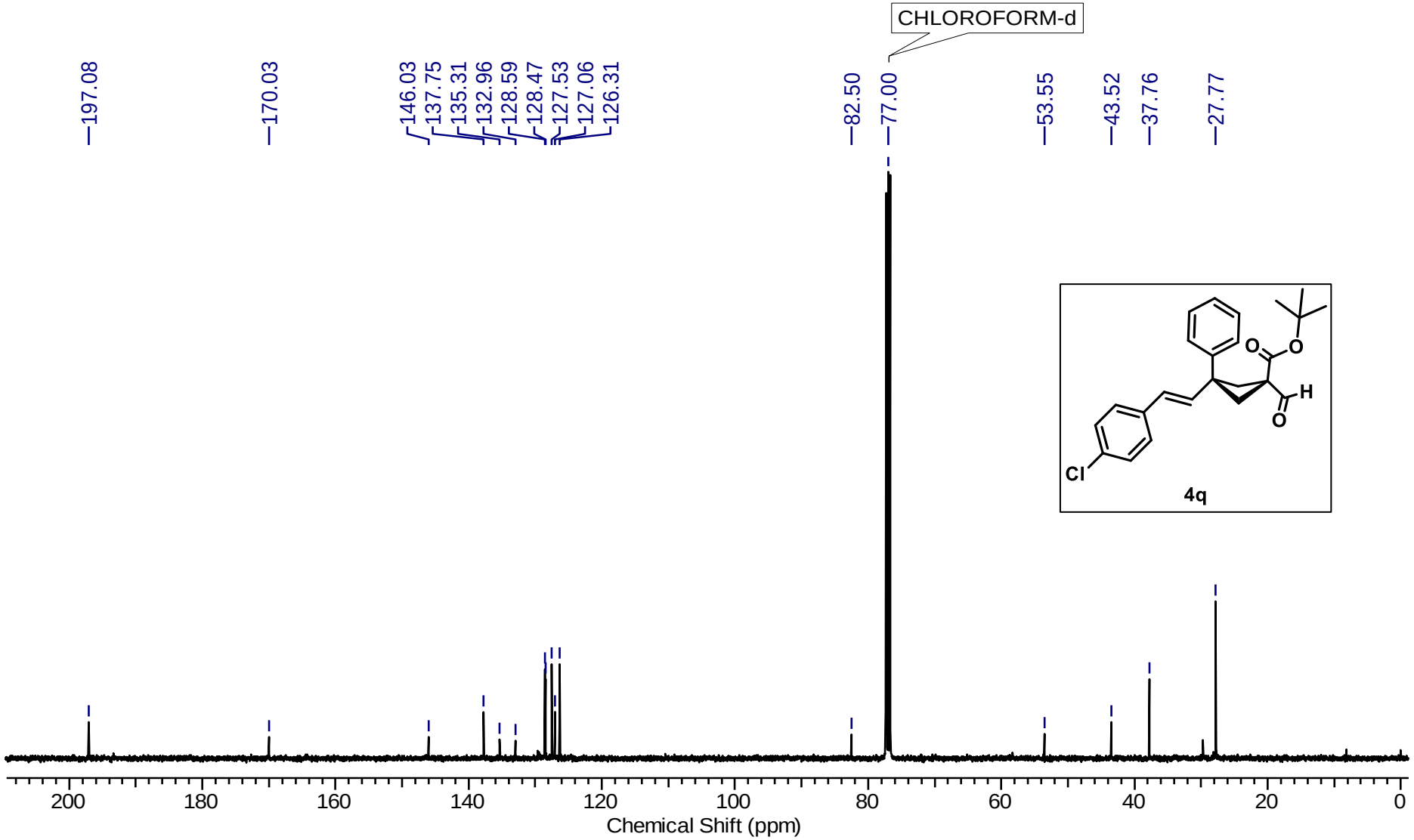
HRMS spectrum of Methyl (E)-3-(2-cyclohexylvinyl)-1-phenyl-2-oxabicyclo[2.1.1]hexane-4-carboxylate (3p)



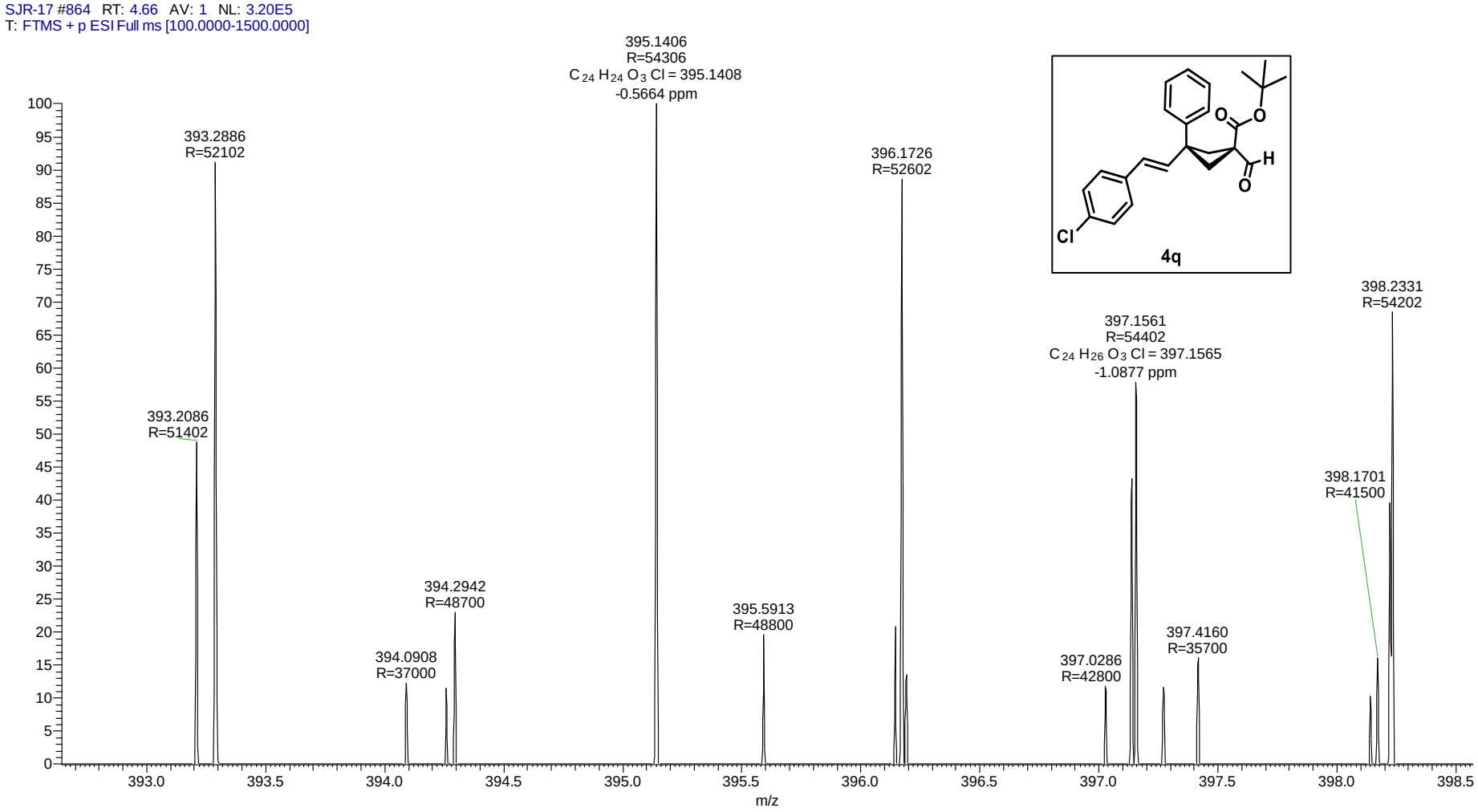
^{1}H NMR (400 MHz, $CDCl_3$) spectrum of *Tert*-butyl (1s,3s)-3-((*E*)-4-chlorostyryl)-1-formyl-3-phenylcyclobutane-1-carboxylate (4q)



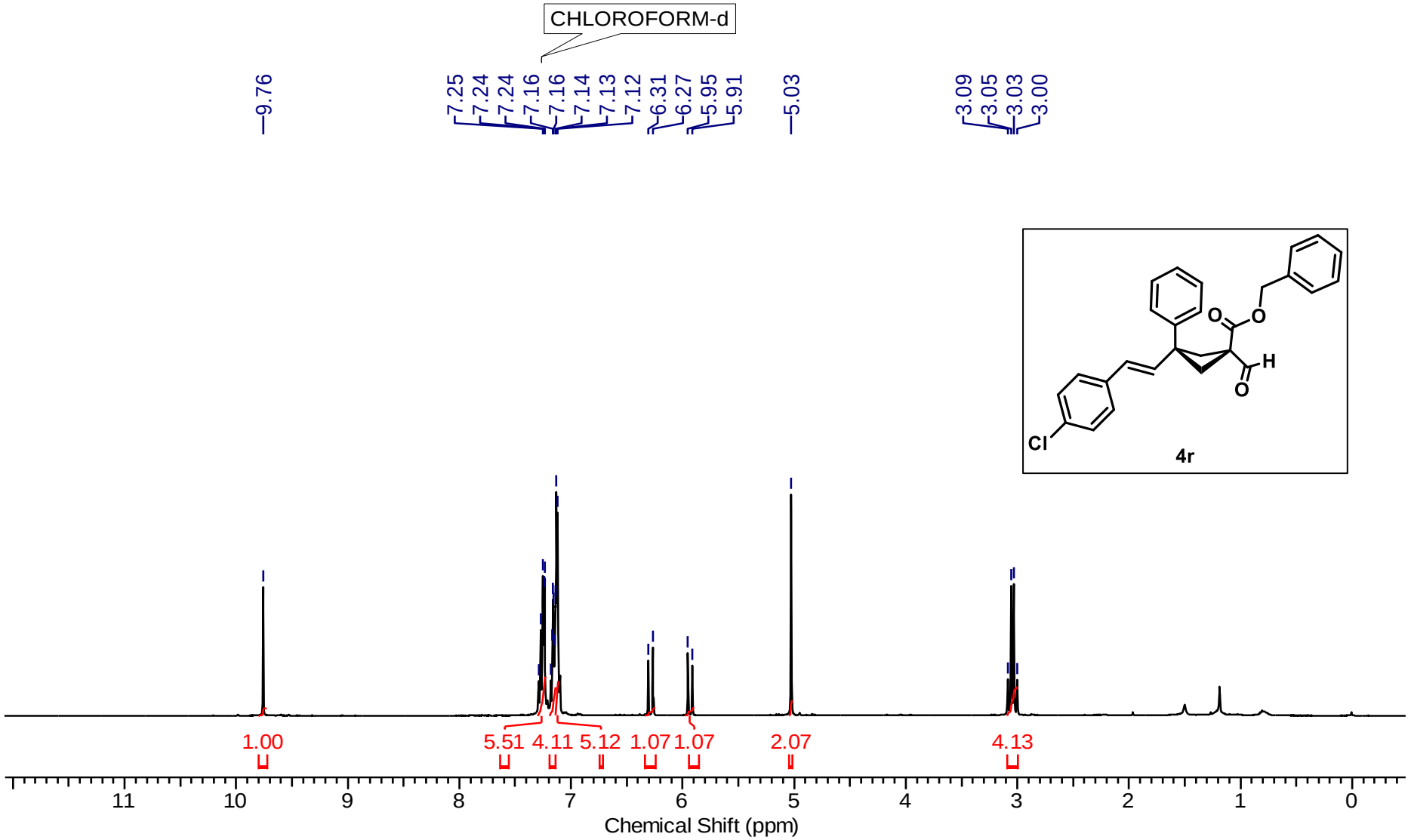
$^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) spectrum of *Tert*-butyl (1s,3s)-3-((*E*)-4-chlorostyryl)-1-formyl-3-phenylcyclobutane-1-carboxylate (4q)



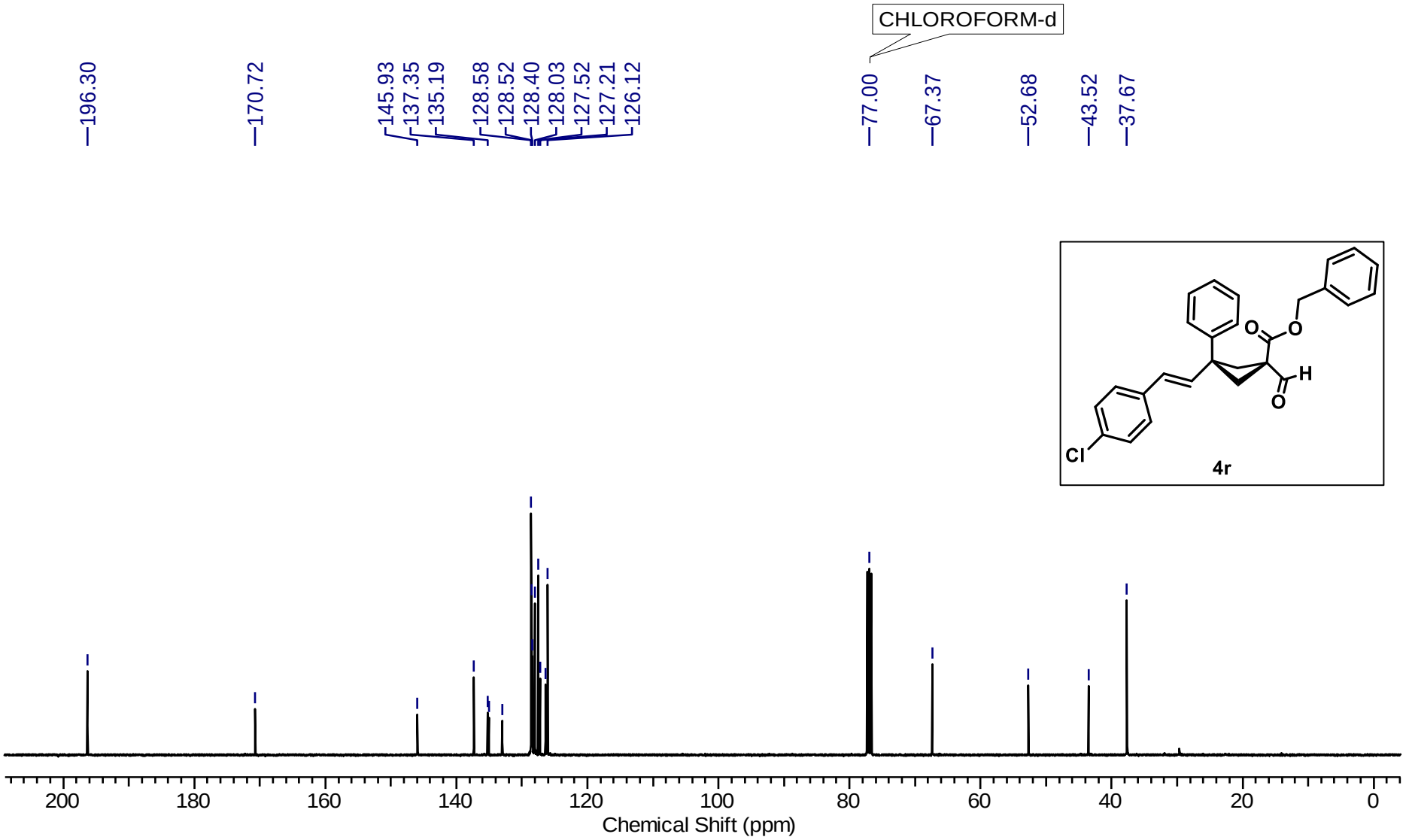
HRMS spectrum of *Tert*-butyl (1s,3s)-3-((*E*)-4-chlorostyryl)-1-formyl-3-phenylcyclobutane-1-carboxylate (4q)



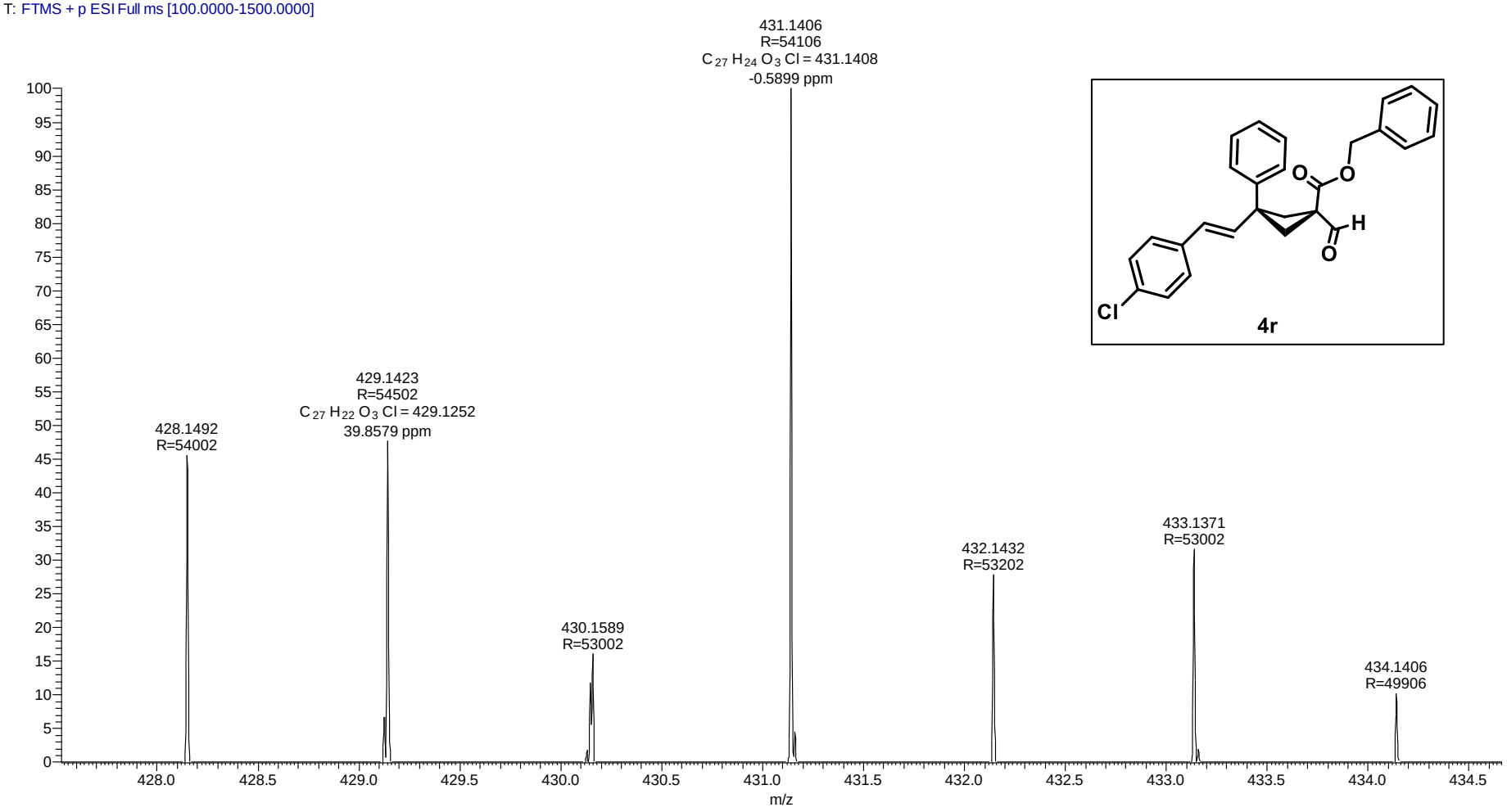
^{1}H NMR (400 MHz, $CDCl_3$) spectrum of Benzyl (1s,3s)-3-((E)-4-chlorostyryl)-1-formyl-3-phenylcyclobutane-1-carboxylate (4r)



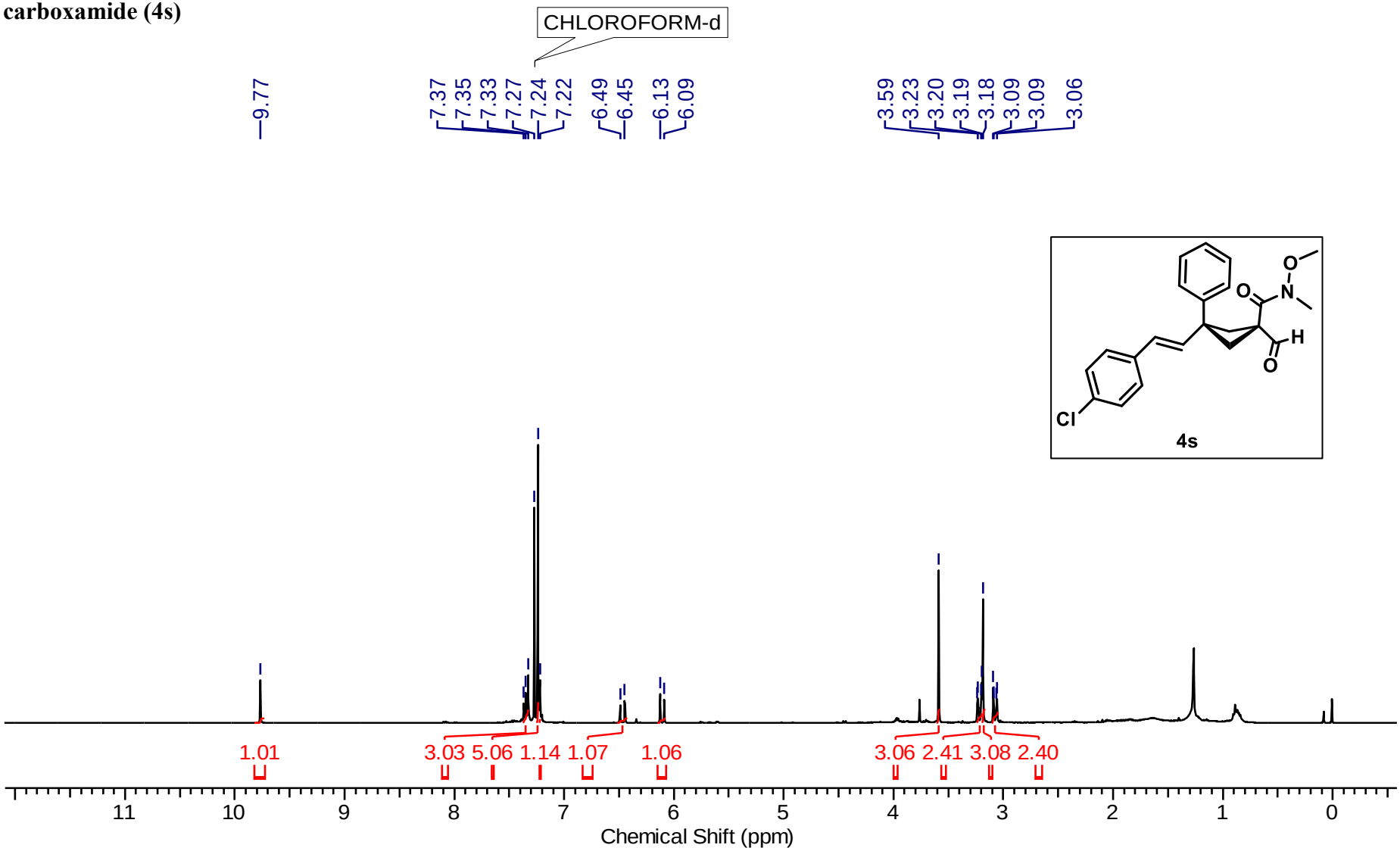
$^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) spectrum of Benzyl (1s,3s)-3-((E)-4-chlorostyryl)-1-formyl-3-phenylcyclobutane-1-carboxylate (4r)



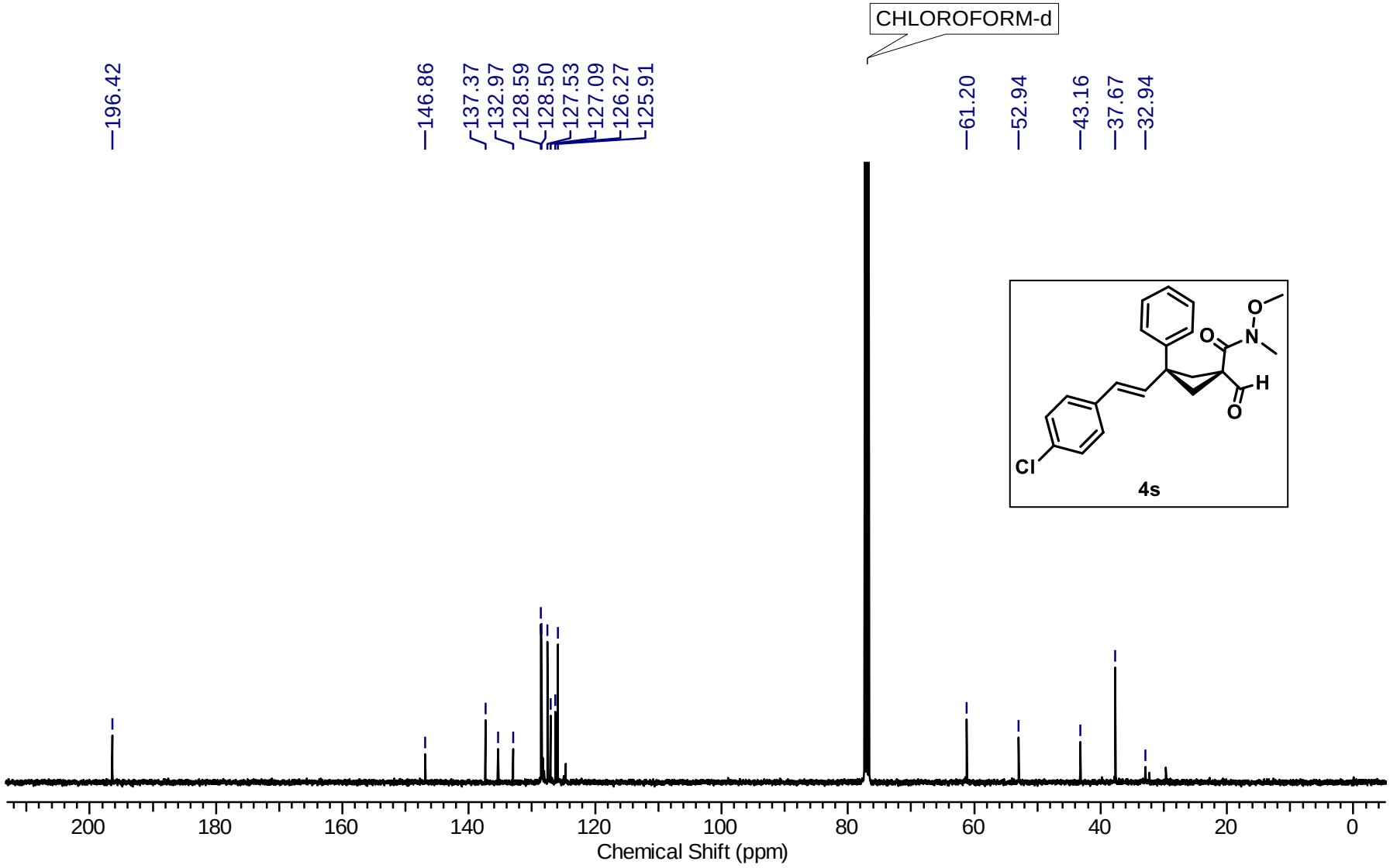
HRMS spectrum of Benzyl (1s,3s)-3-((E)-4-chlorostyryl)-1-formyl-3-phenylcyclobutane-1-carboxylate (4r)



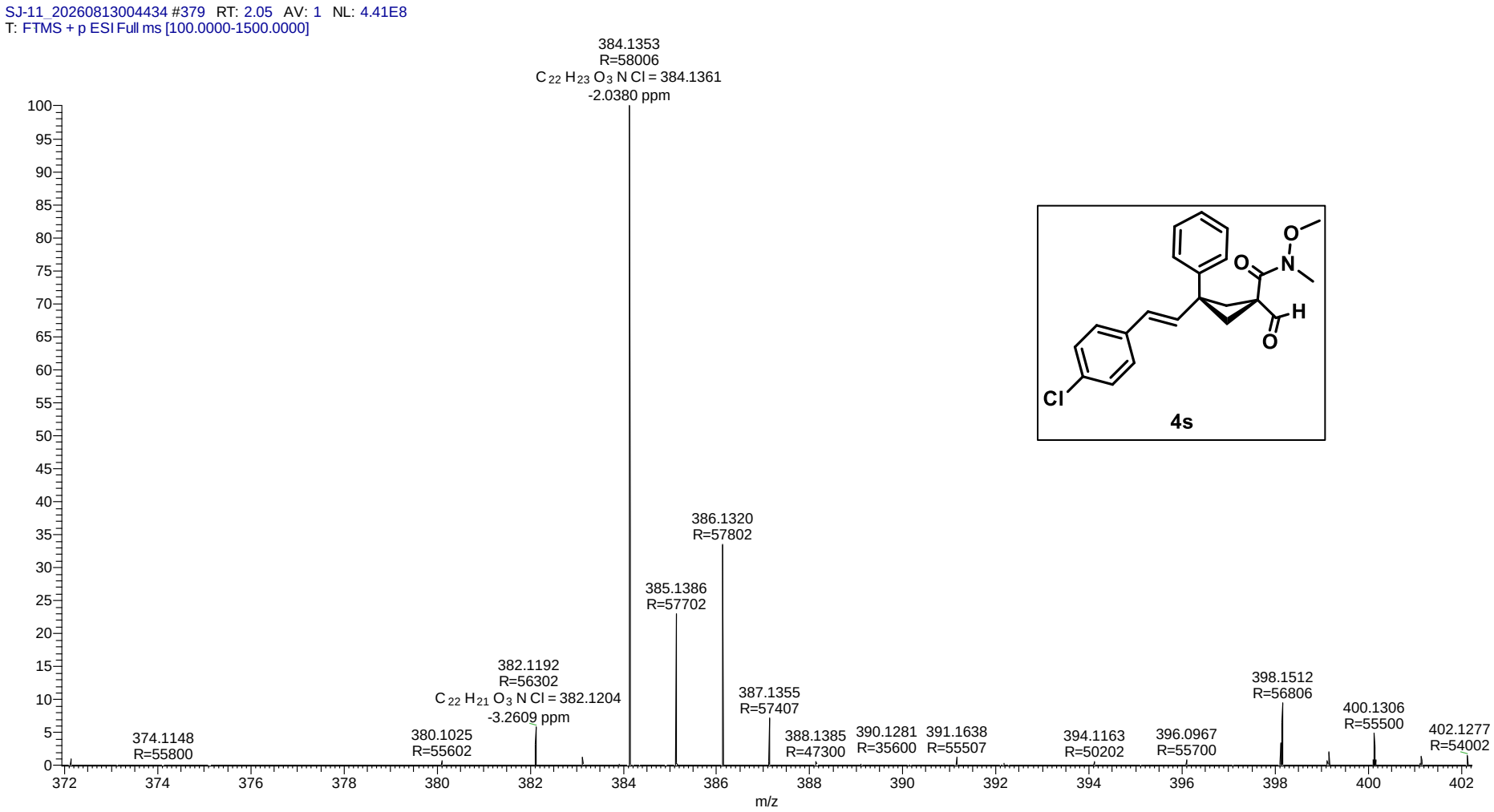
^{1}H NMR (400 MHz, $CDCl_3$) spectrum of (1s,3s)-3-((E)-4-chlorostyryl)-1-formyl-N-methoxy-N-methyl-3-phenylcyclobutane-1-carboxamide (4s)



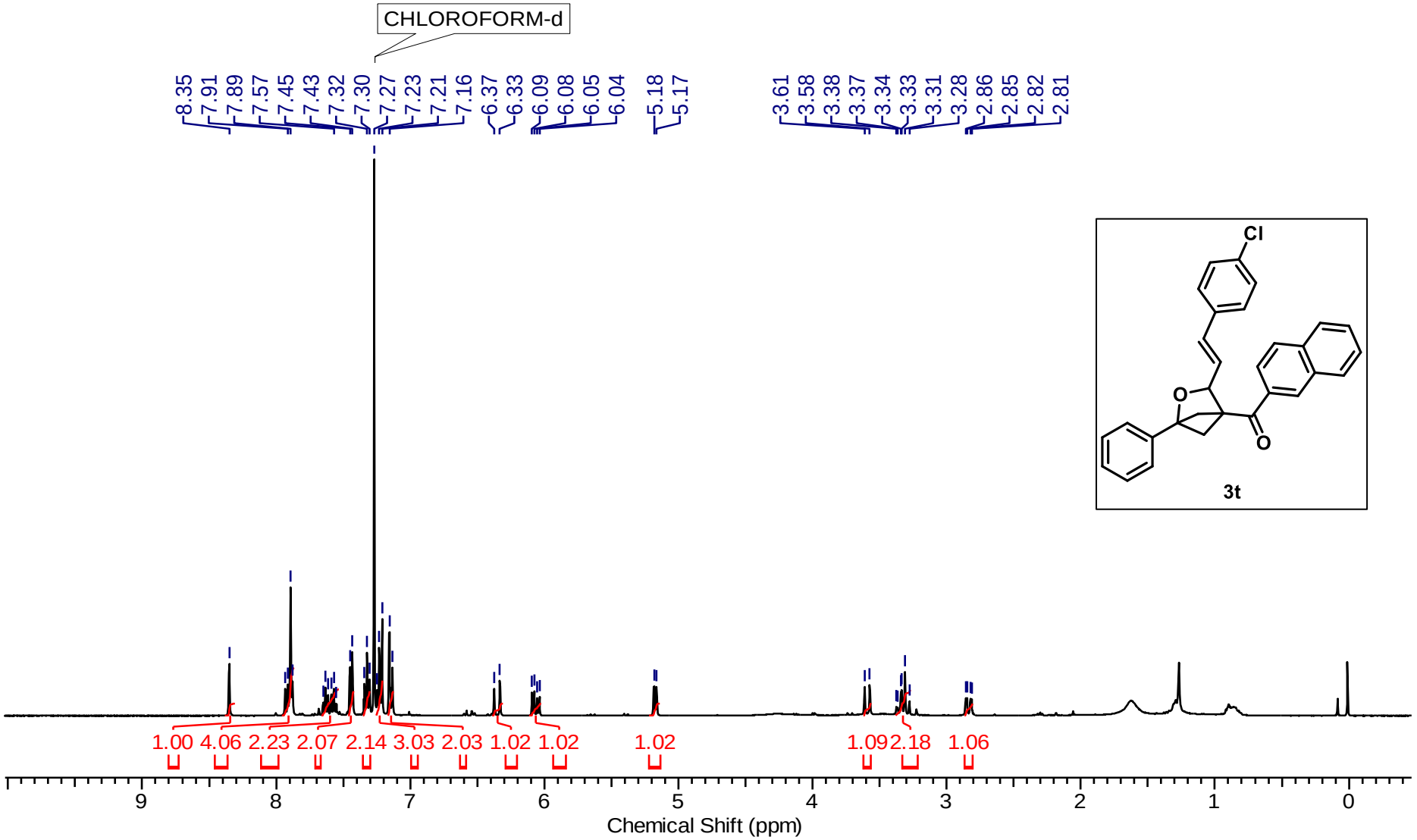
$^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) spectrum of (1s,3s)-3-((E)-4-chlorostyryl)-1-formyl-N-methoxy-N-methyl-3-phenylcyclobutane-1-carboxamide (4s)



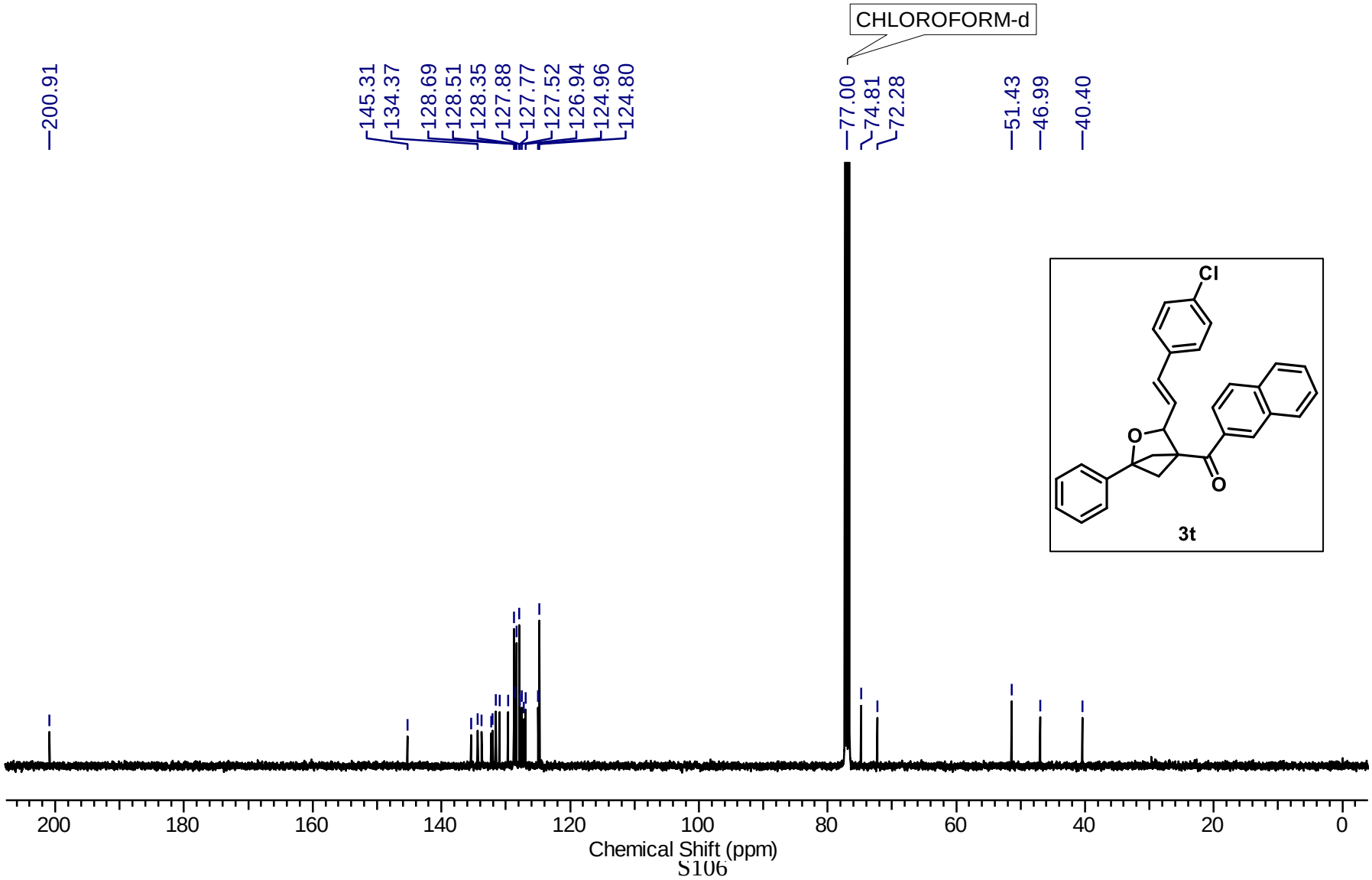
HRMS spectrum of (1s,3s)-3-((E)-4-chlorostyryl)-1-formyl-N-methoxy-N-methyl-3-phenylcyclobutane-1-carboxamide (4s)



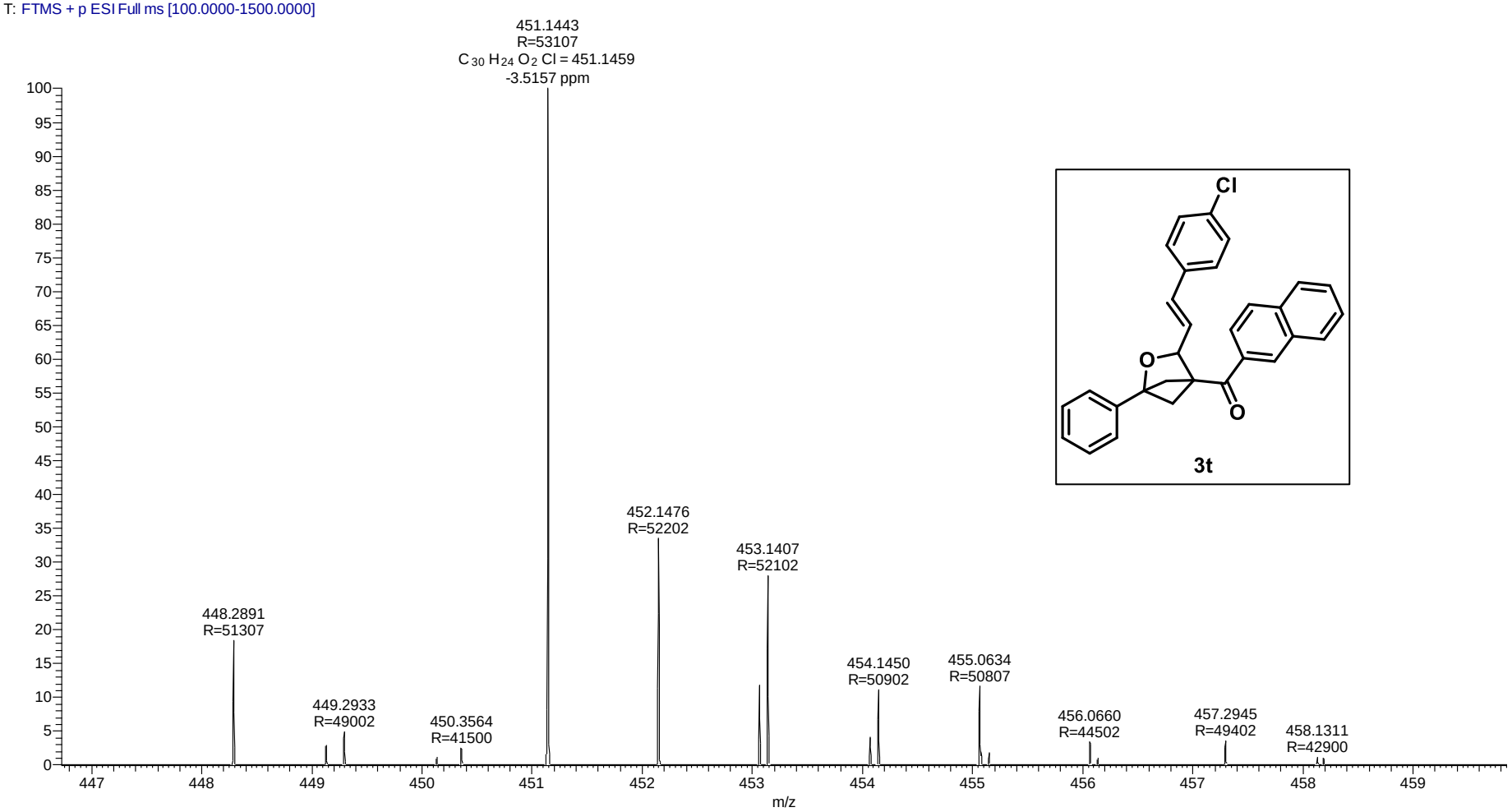
^{1}H NMR (400 MHz, $CDCl_3$) spectrum of (E)-(3-(4-chlorostyryl)-1-phenyl-2-oxabicyclo[2.1.1]hexan-4-yl)(naphthalen-2-yl)methanone (3t)



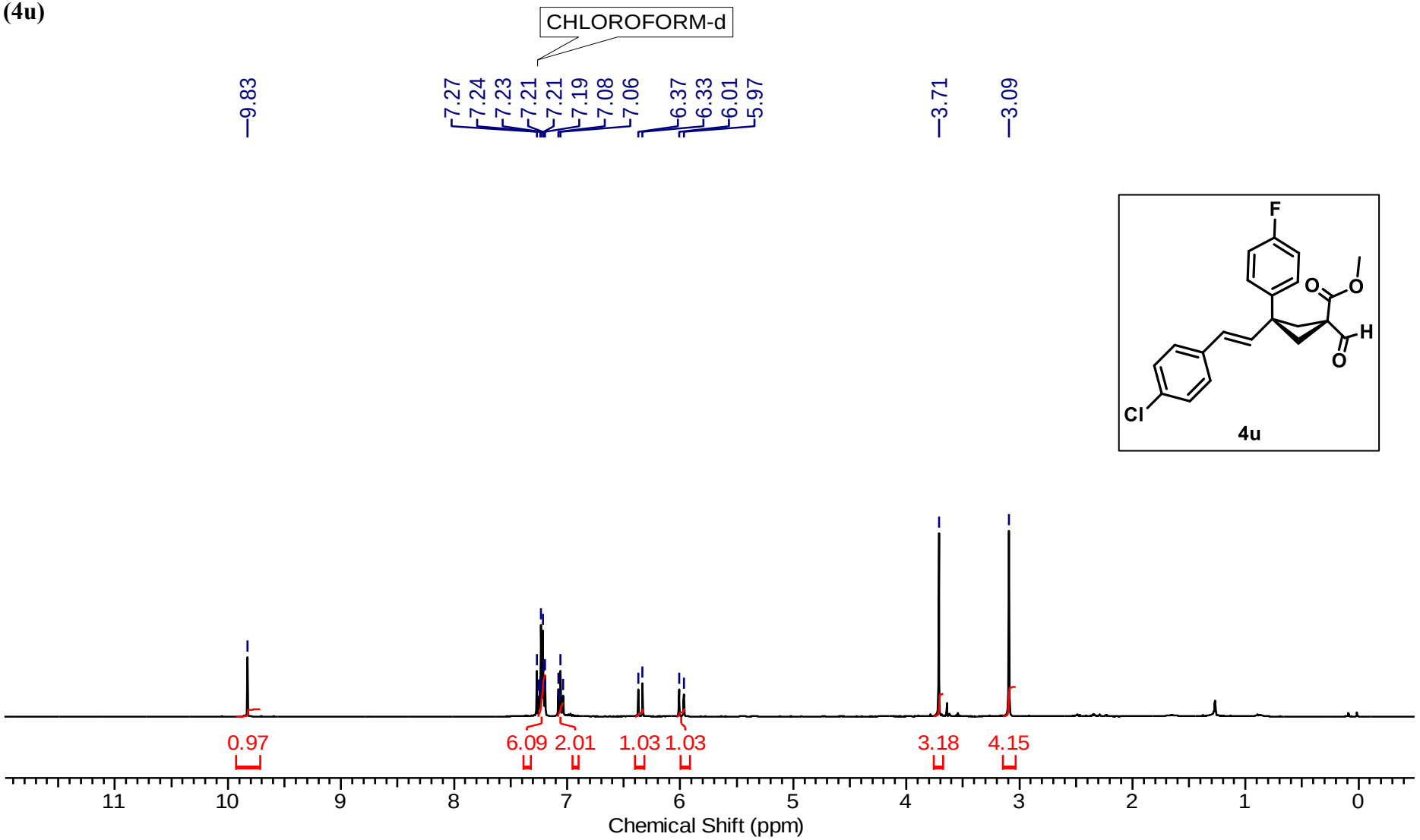
$^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) spectrum of (E)-(3-(4-chlorostyryl)-1-phenyl-2-oxabicyclo[2.1.1]hexan-4-yl)(naphthalen-2-yl)methanone (3t)



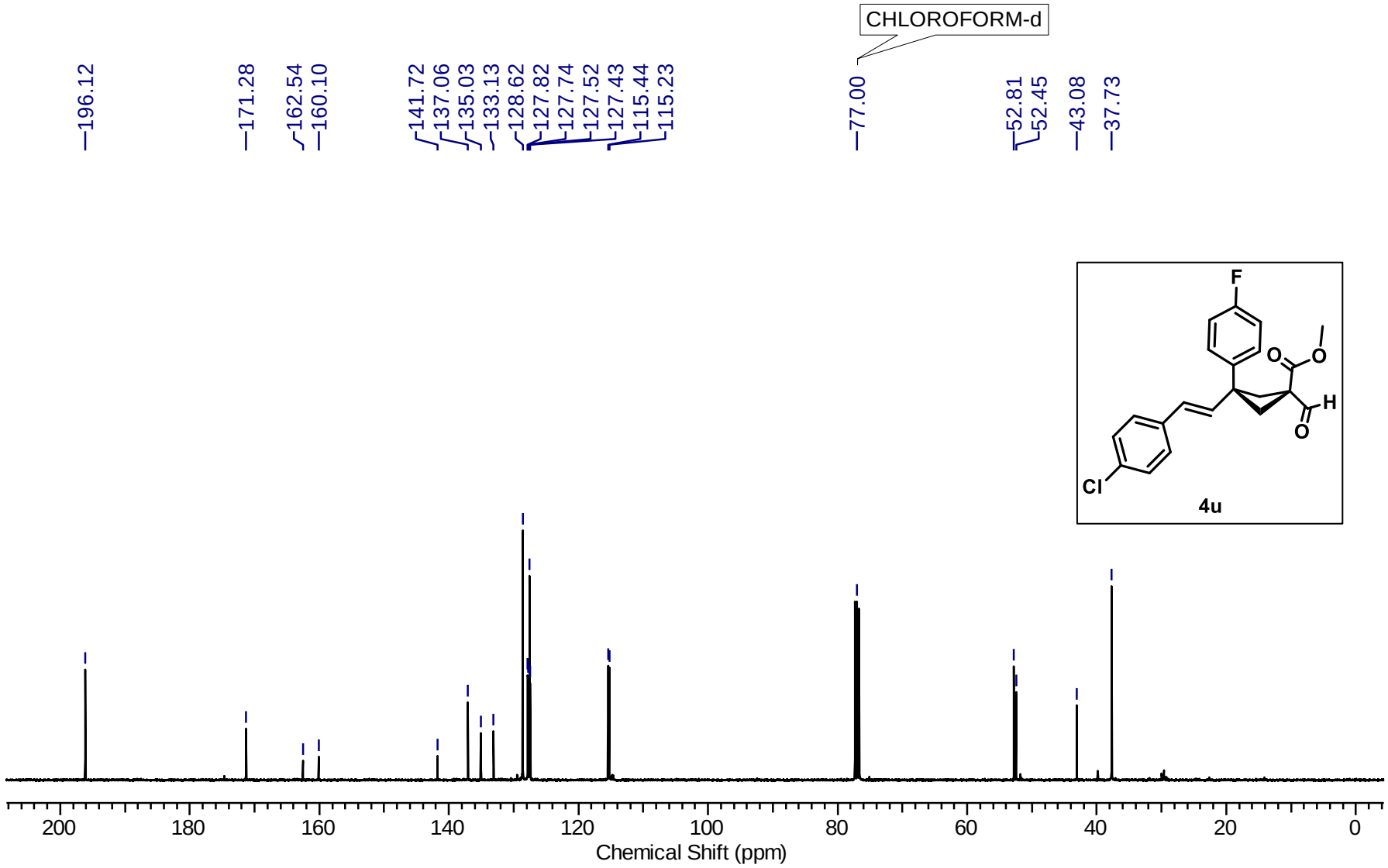
HRMS spectrum of (E)-(3-(4-chlorostyryl)-1-phenyl-2-oxabicyclo[2.1.1]hexan-4-yl)(naphthalen-2-yl)methanone (3t)



^{1}H NMR (400 MHz, $CDCl_3$) spectrum of Methyl (1s,3s)-3-((E)-4-chlorostyryl)-3-(4-fluorophenyl)-1-formylcyclobutane-1-carboxylate (4u)

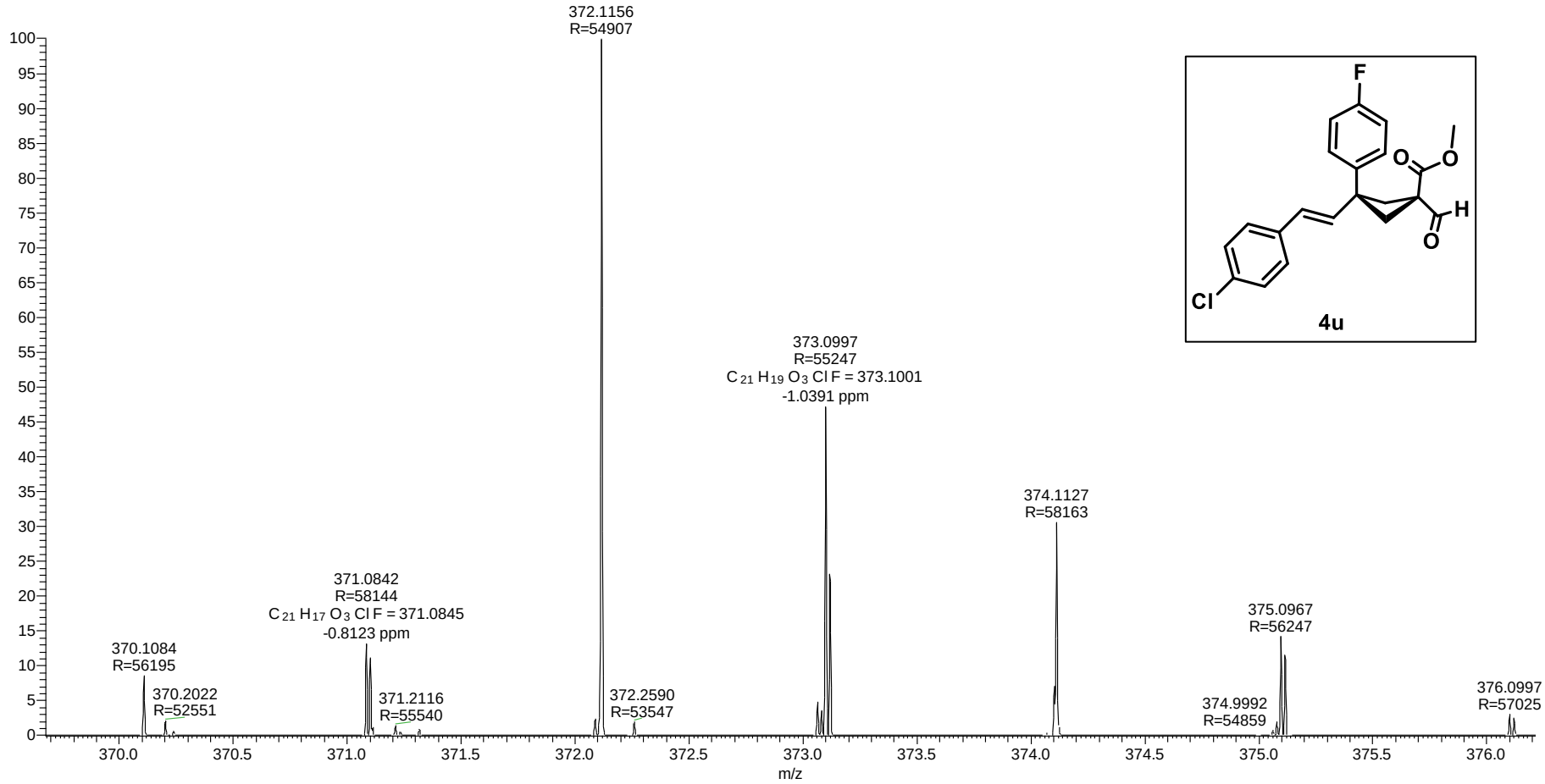


$^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) spectrum of Methyl (1s,3s)-3-((E)-4-chlorostyryl)-3-(4-fluorophenyl)-1-formylcyclobutane-1-carboxylate (4u)

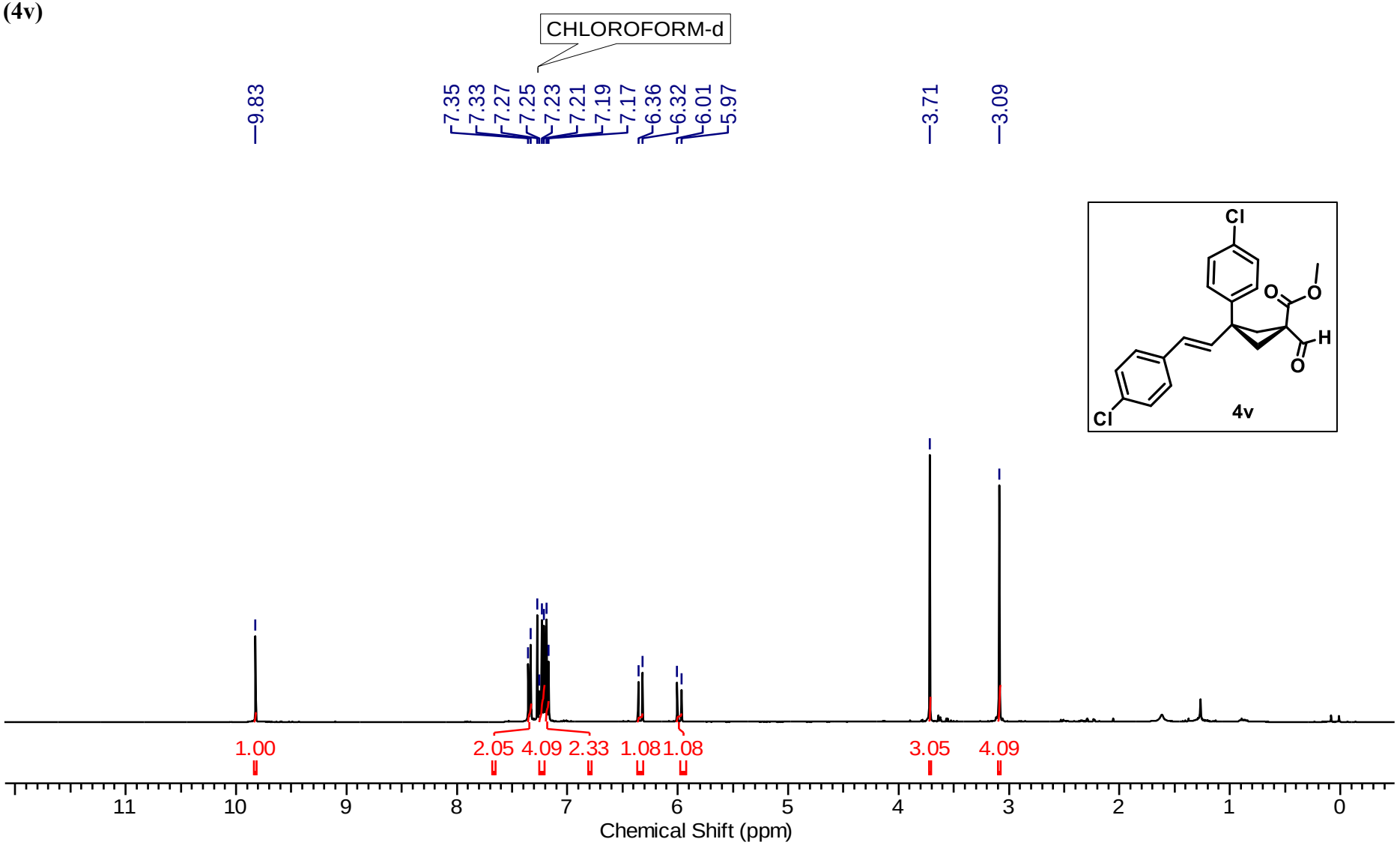


HRMS spectrum of Methyl (1s,3s)-3-((E)-4-chlorostyryl)-3-(4-fluorophenyl)-1-formylcyclobutane-1-carboxylate (4u)

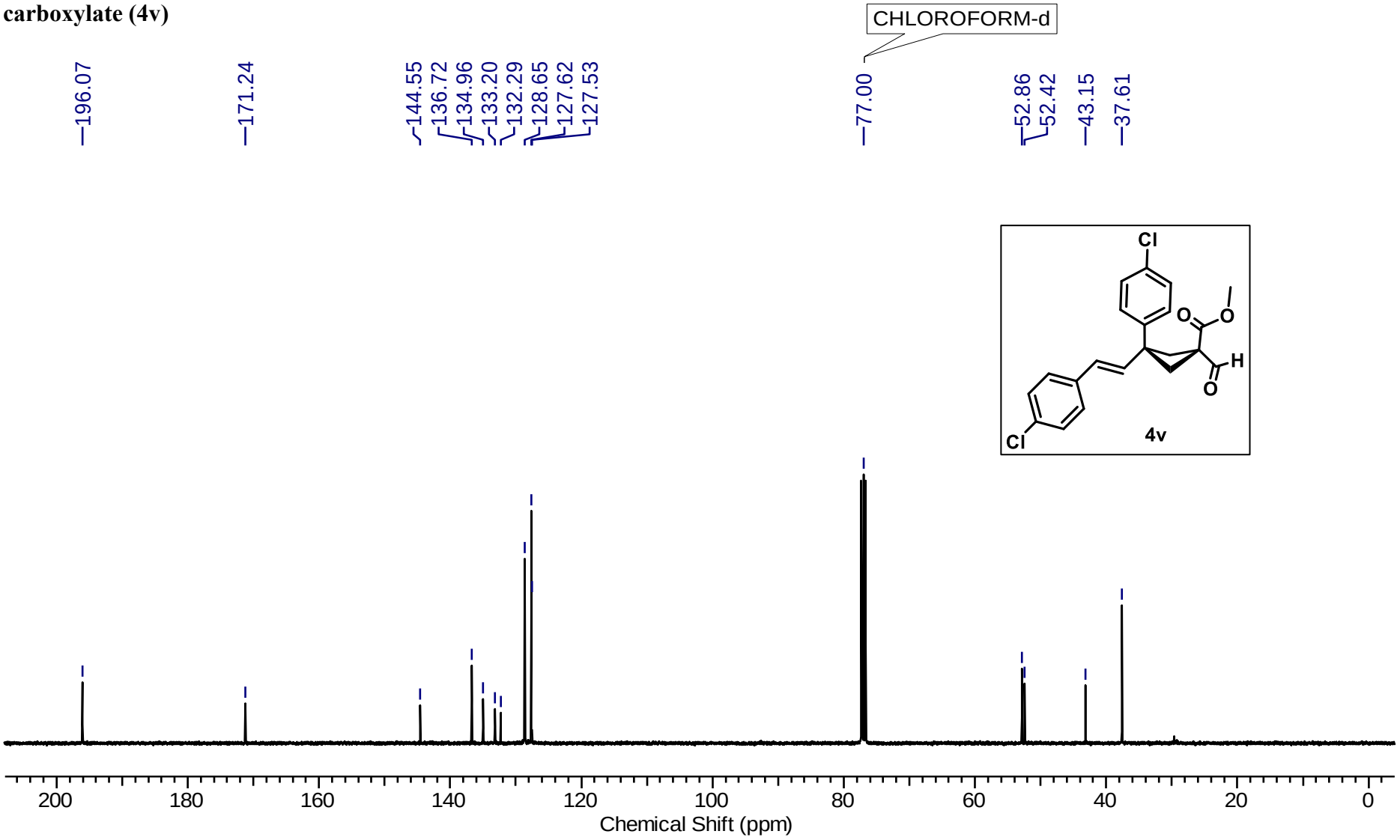
SJR-19 #384-387 RT: 2.09-2.11 AV: 4 NL: 6.60E6
T: FTMS + p ESI Full ms [100.0000-1500.0000]



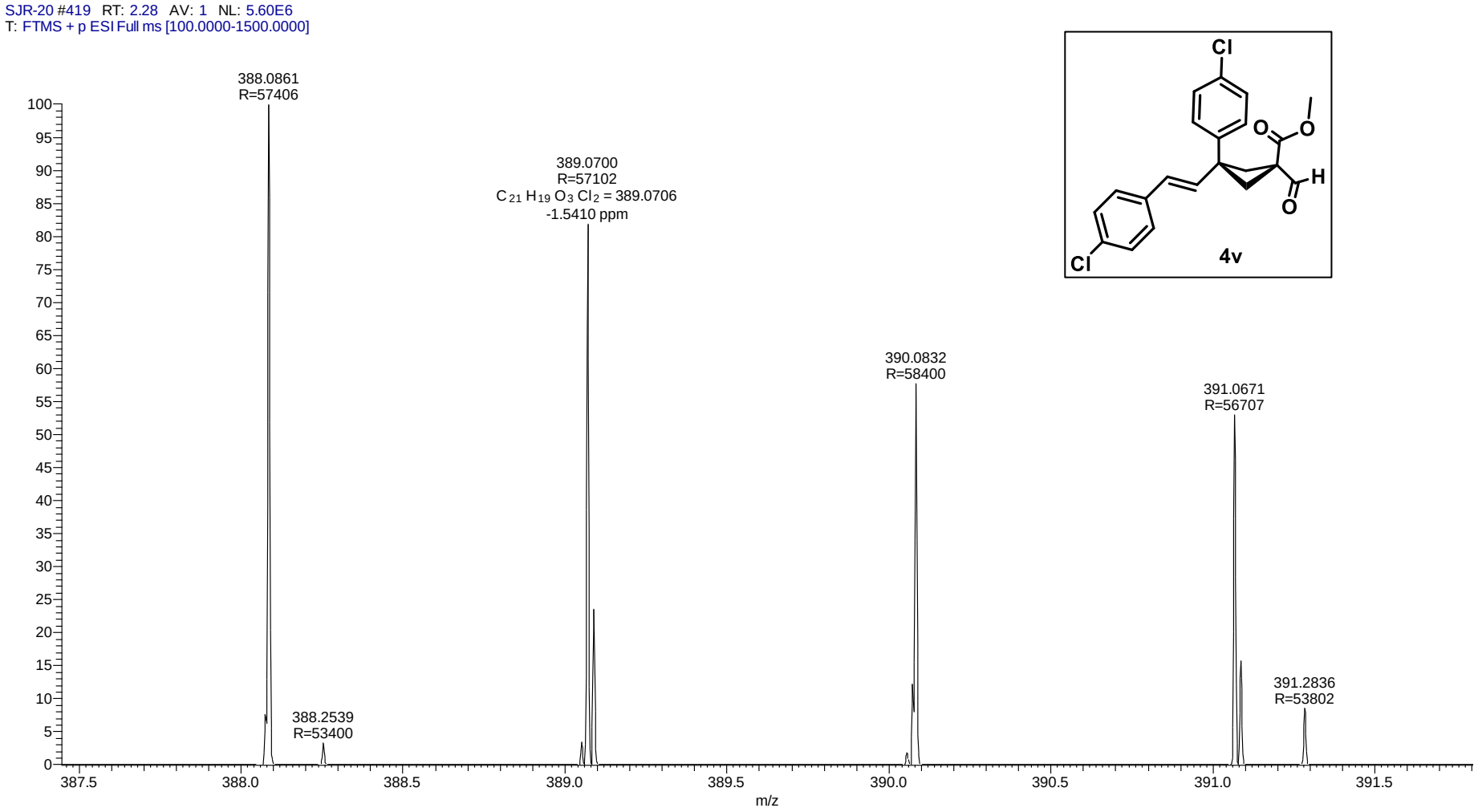
^{1}H NMR (400 MHz, $CDCl_3$) spectrum of Methyl (1s,3s)-3-(4-chlorophenyl)-3-((E)-4-chlorostyryl)-1-formylcyclobutane-1-carboxylate (4v)



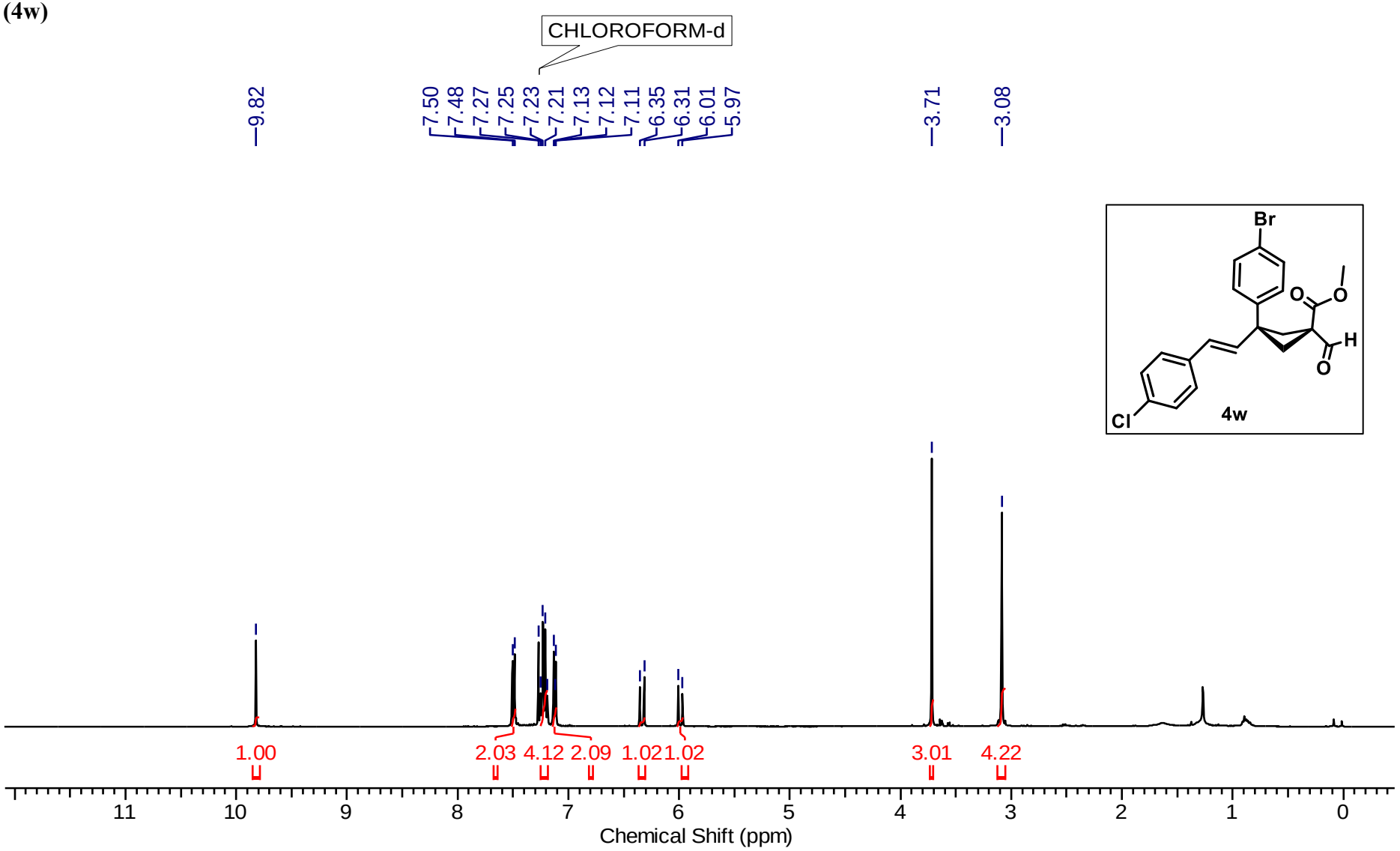
$^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) spectrum of Methyl (1s,3s)-3-(4-chlorophenyl)-3-((E)-4-chlorostyryl)-1-formylcyclobutane-1-carboxylate (4v)



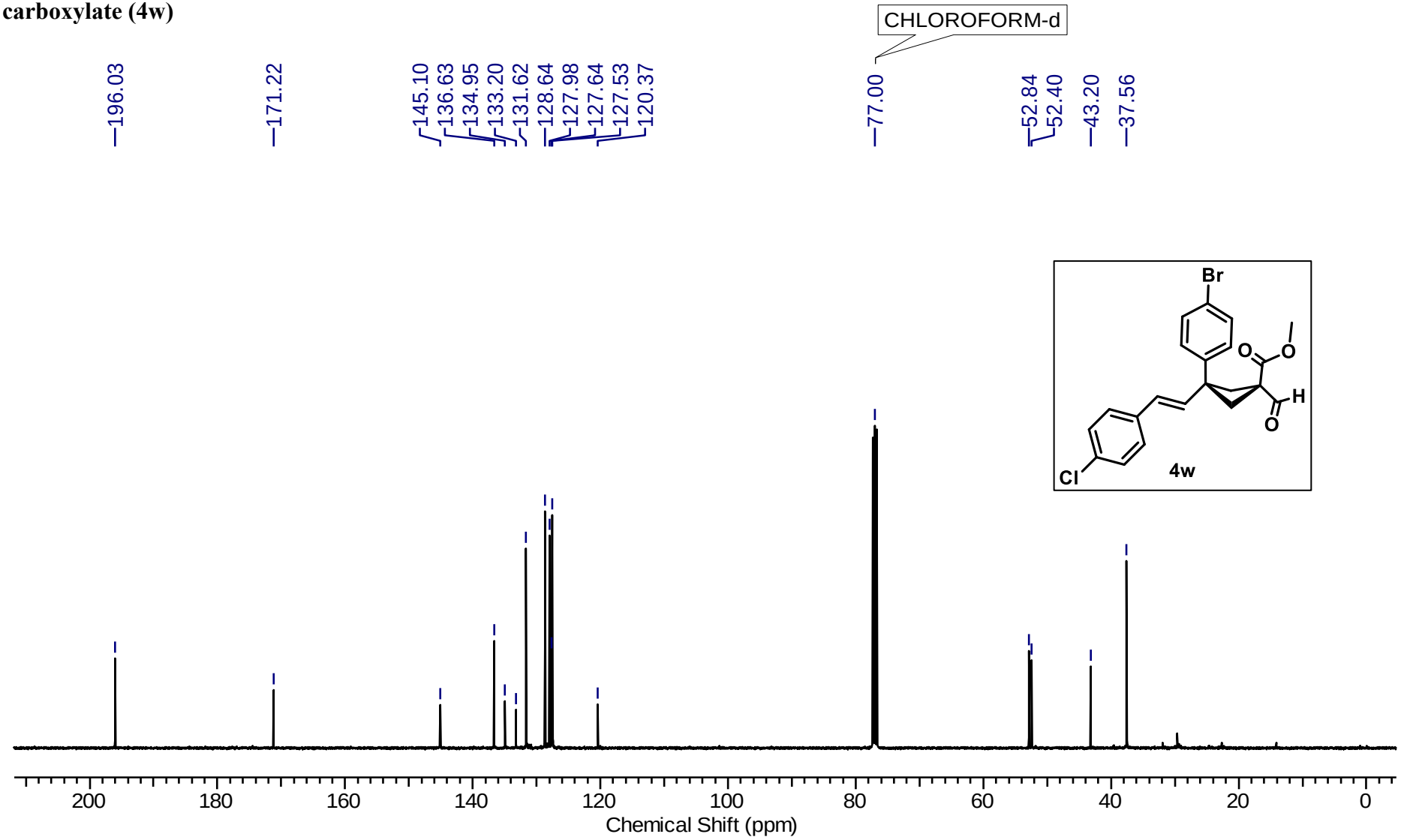
HRMS spectrum of Methyl (1s,3s)-3-(4-chlorophenyl)-3-((E)-4-chlorostyryl)-1-formylcyclobutane-1-carboxylate (4v)



^{1}H NMR (400 MHz, $CDCl_3$) spectrum of Methyl (1s,3s)-3-(4-bromophenyl)-3-((E)-4-chlorostyryl)-1-formylcyclobutane-1-carboxylate (4w)

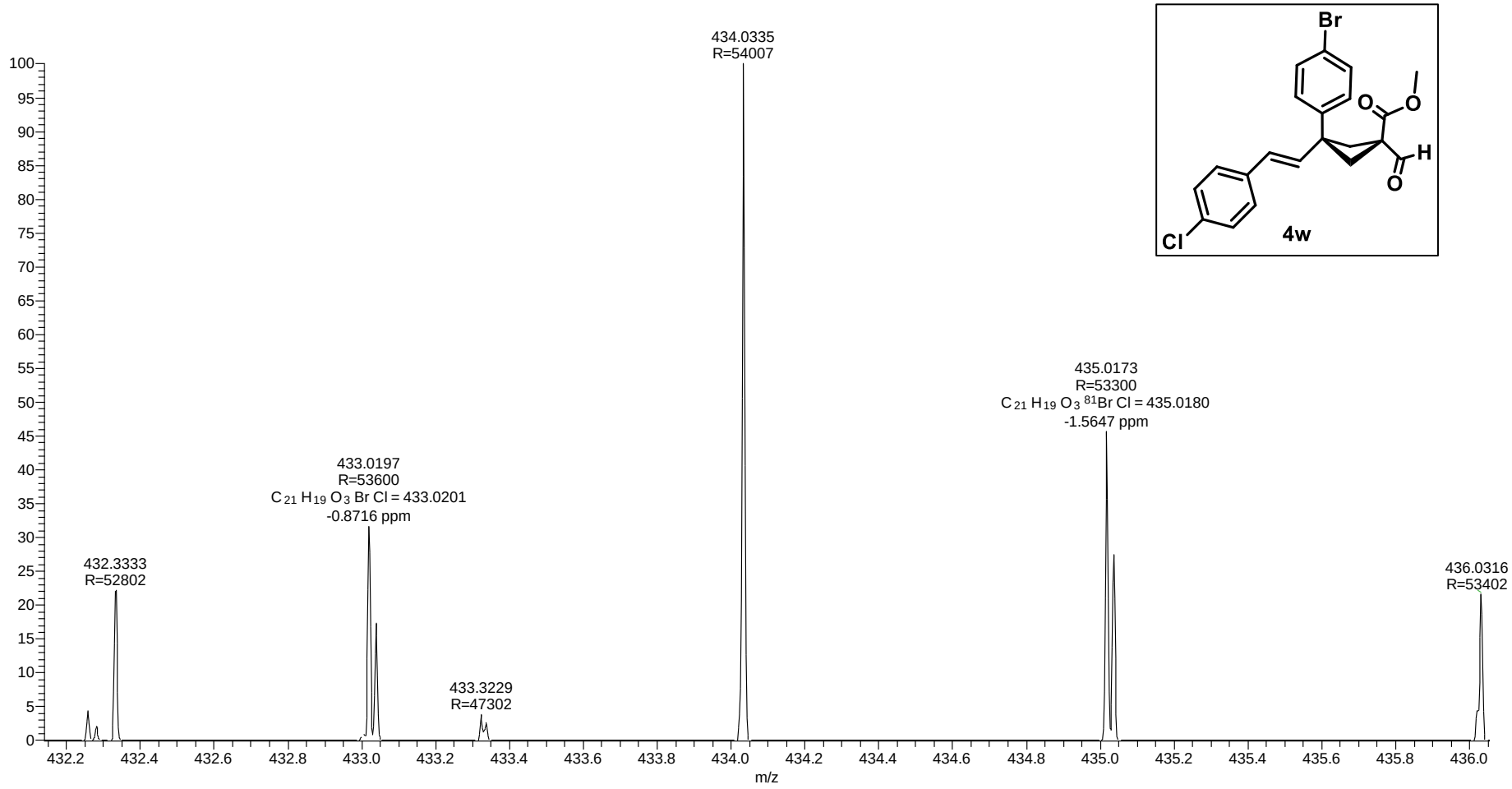


$^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) spectrum of Methyl (1s,3s)-3-(4-bromophenyl)-3-((E)-4-chlorostyryl)-1-formylcyclobutane-1-carboxylate (4w)

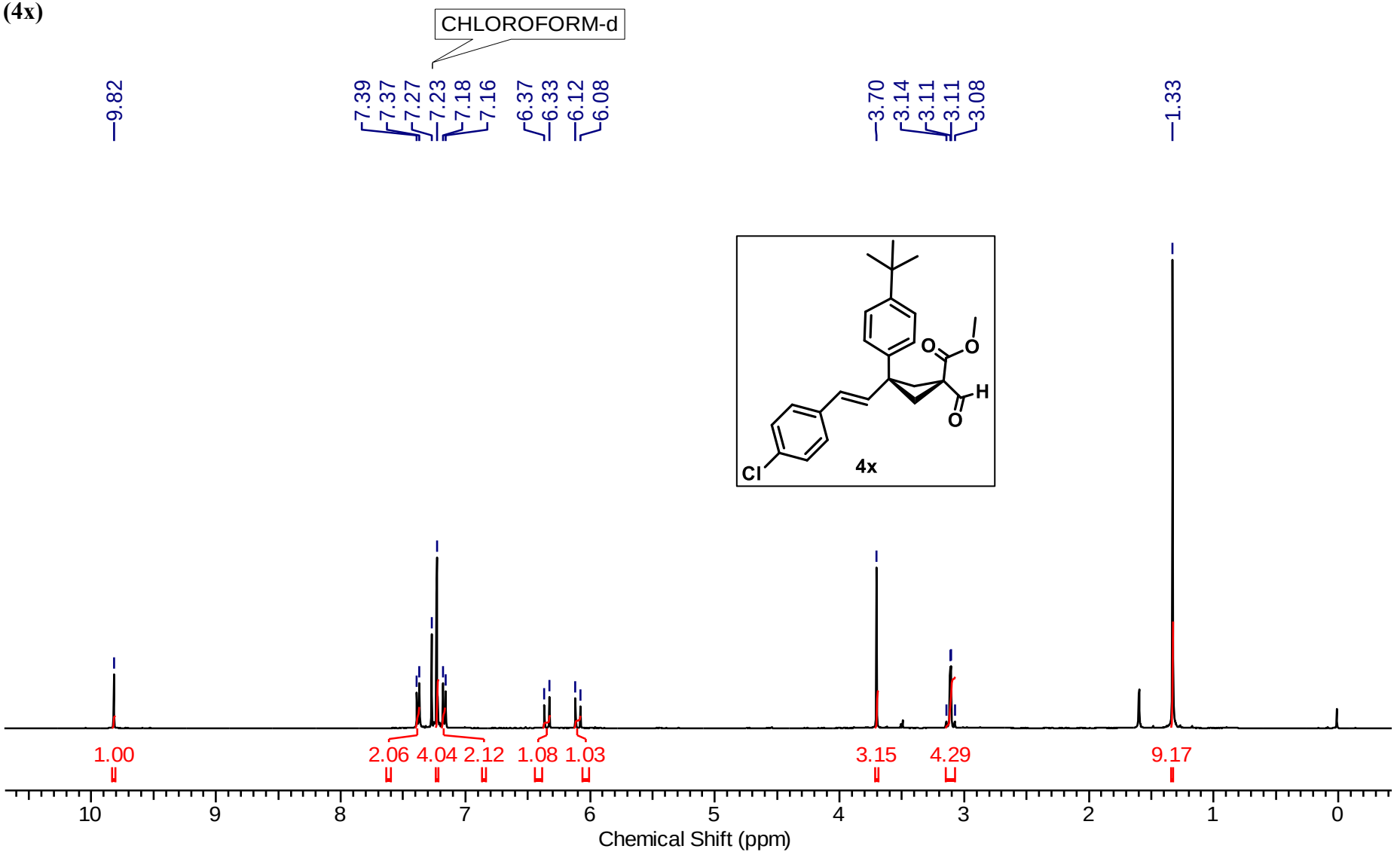


HRMS spectrum of Methyl (1s,3s)-3-(4-bromophenyl)-3-((E)-4-chlorostyryl)-1-formylcyclobutane-1-carboxylate (4w)

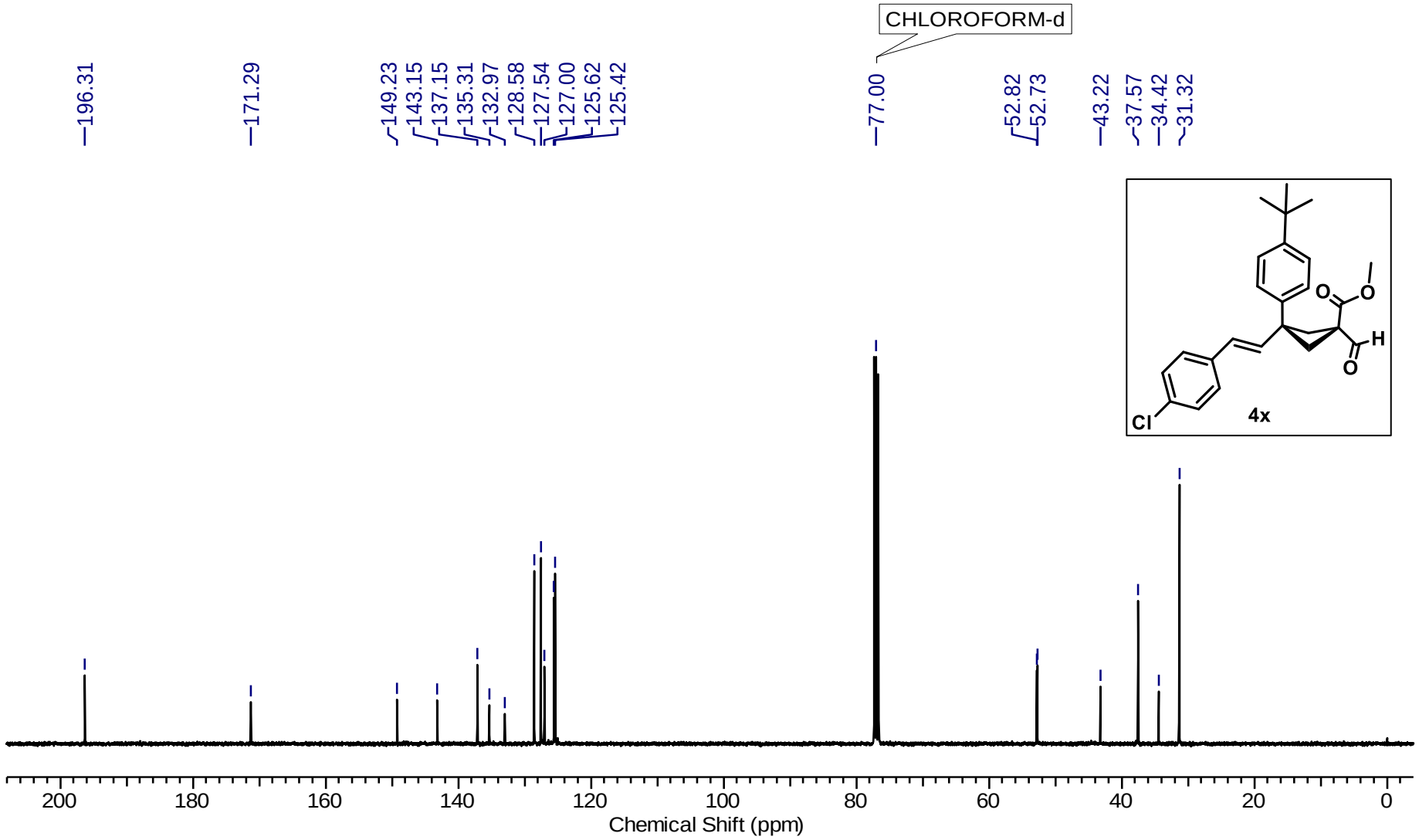
SJR-18 #437 RT: 2.37 AV: 1 NL: 4.00E6
T: FTMS + p ESI Full ms [100.0000-1500.0000]



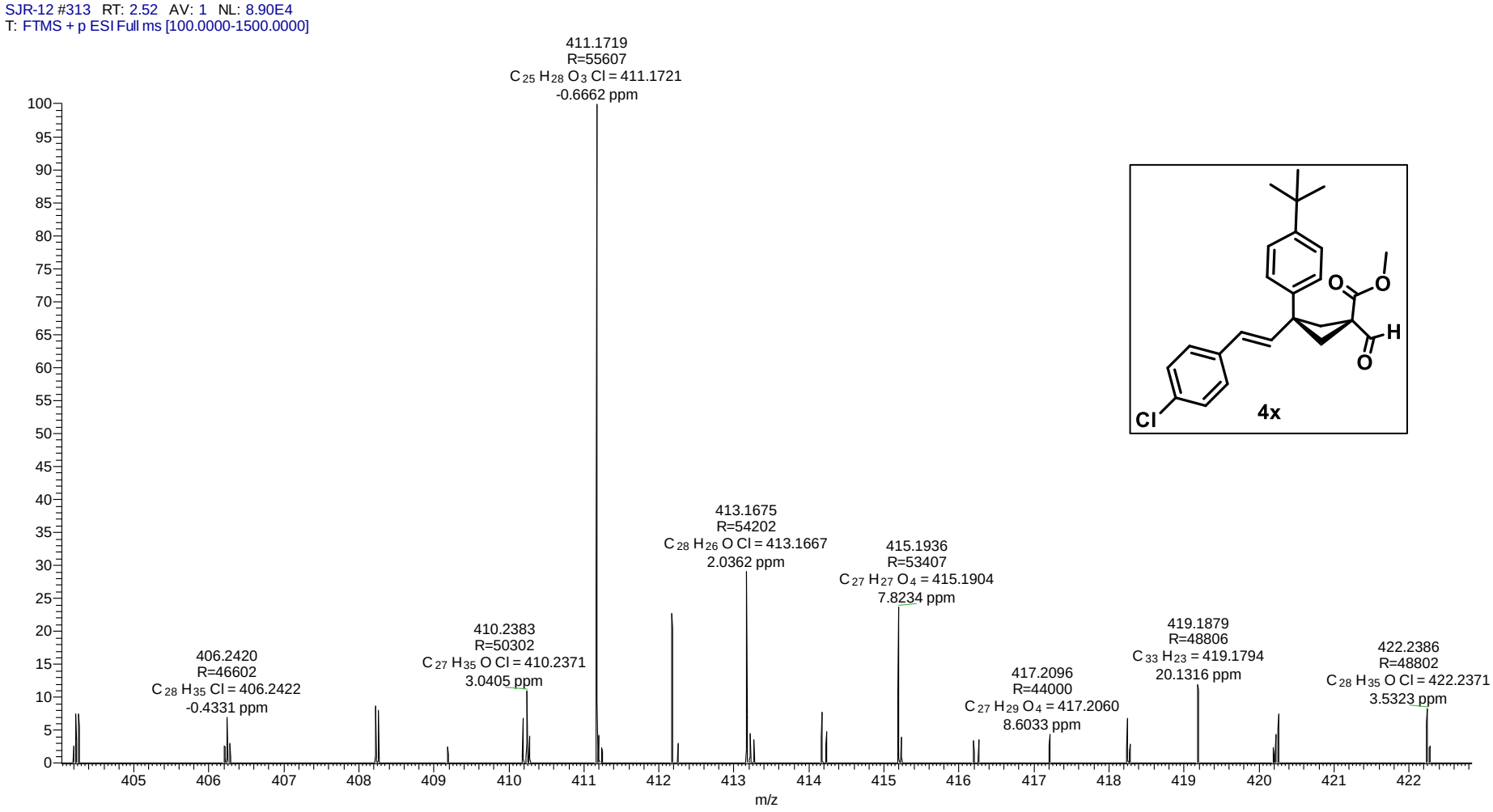
^{1}H NMR (400 MHz, $CDCl_3$) spectrum of Methyl (1s,3s)-3-(4-(*tert*-butyl)phenyl)-3-((*E*)-4-chlorostyryl)-1-formylcyclobutane-1-carboxylate (4x)



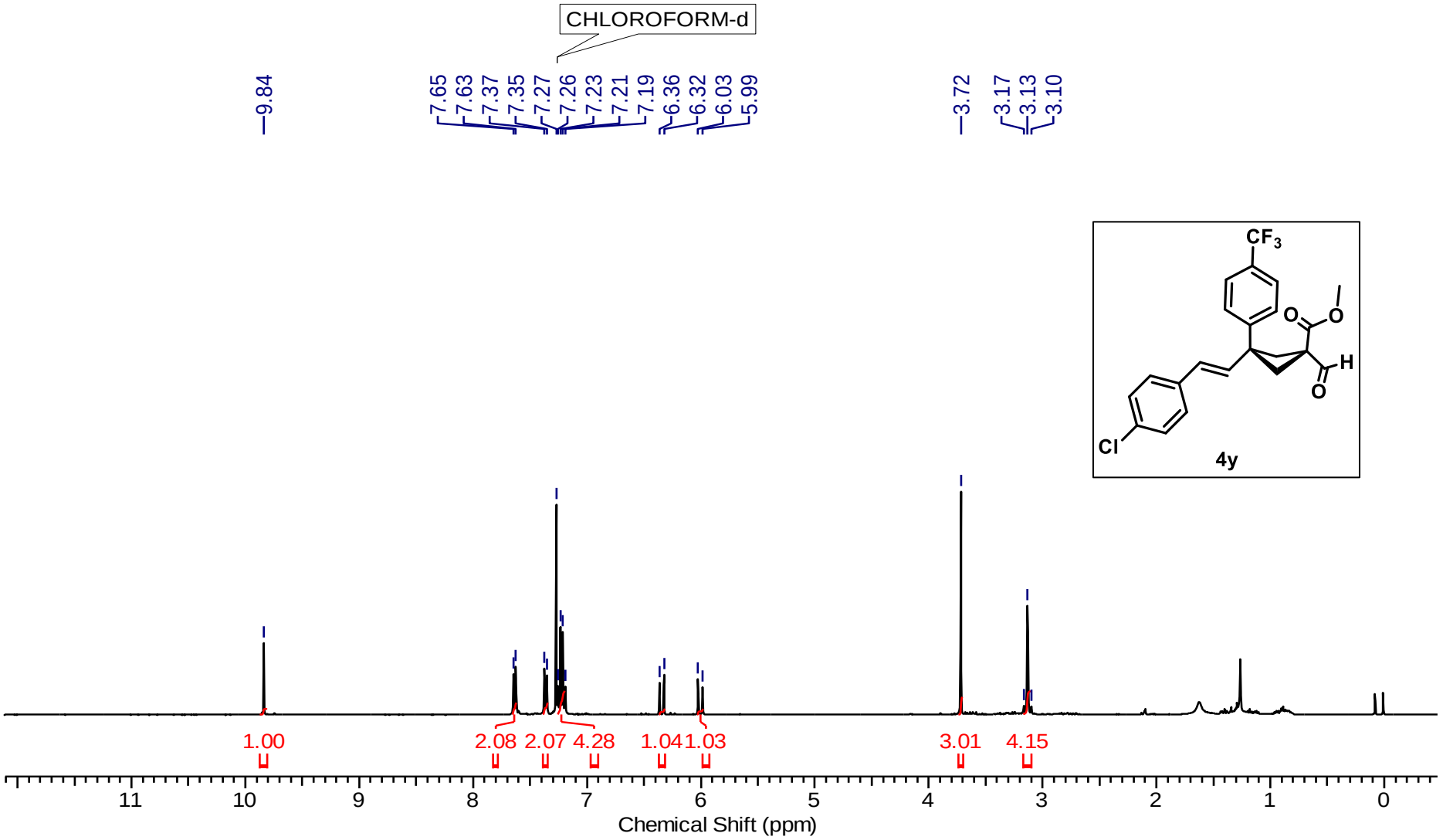
$^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) spectrum of Methyl (1s,3s)-3-(4-(*tert*-butyl)phenyl)-3-((*E*)-4-chlorostyryl)-1-formylcyclobutane-1-carboxylate (4x)



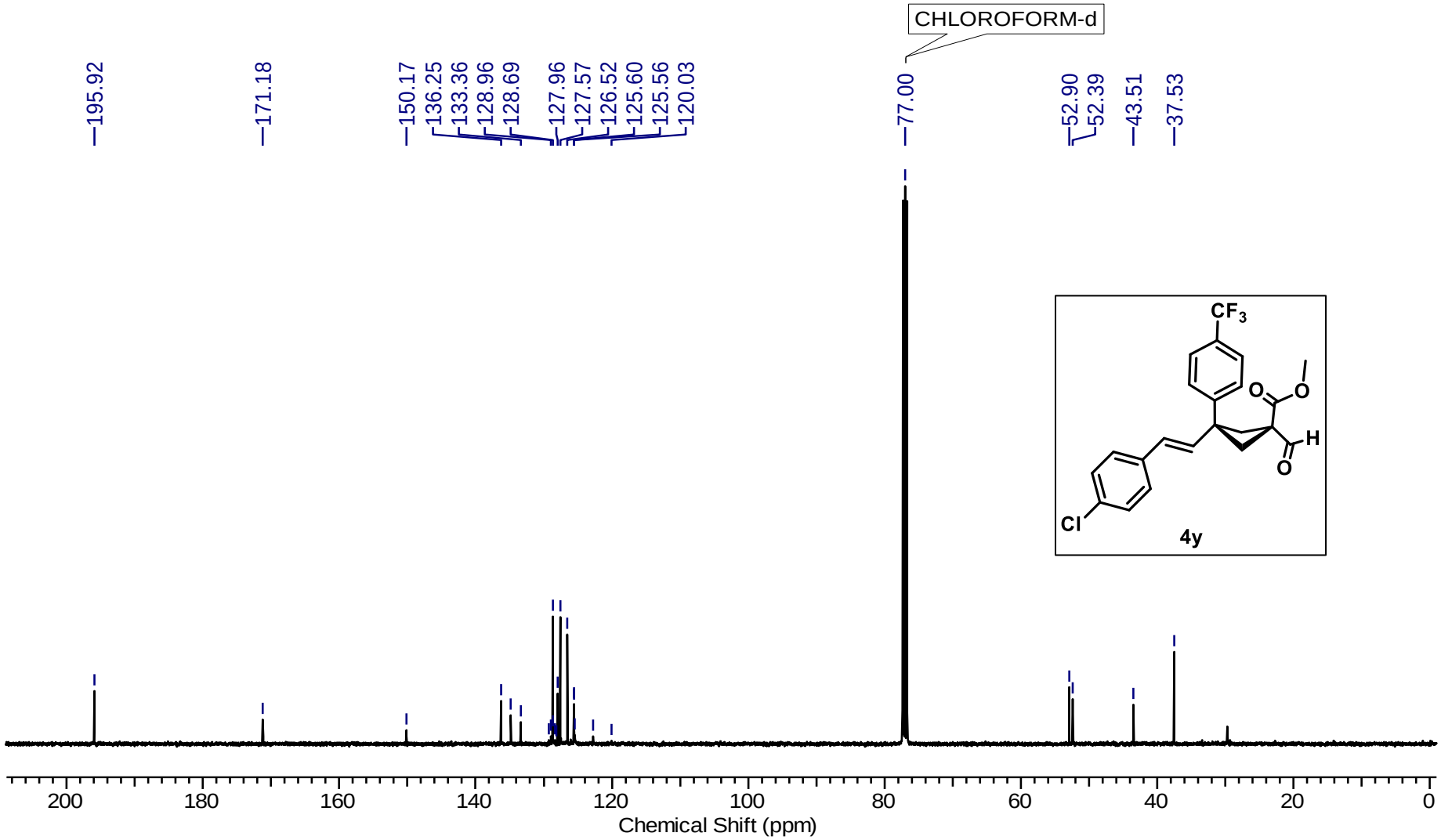
HRMS spectrum of Methyl (1s,3s)-3-(4-(*tert*-butyl)phenyl)-3-((*E*)-4-chlorostyryl)-1-formylcyclobutane-1-carboxylate (4x)



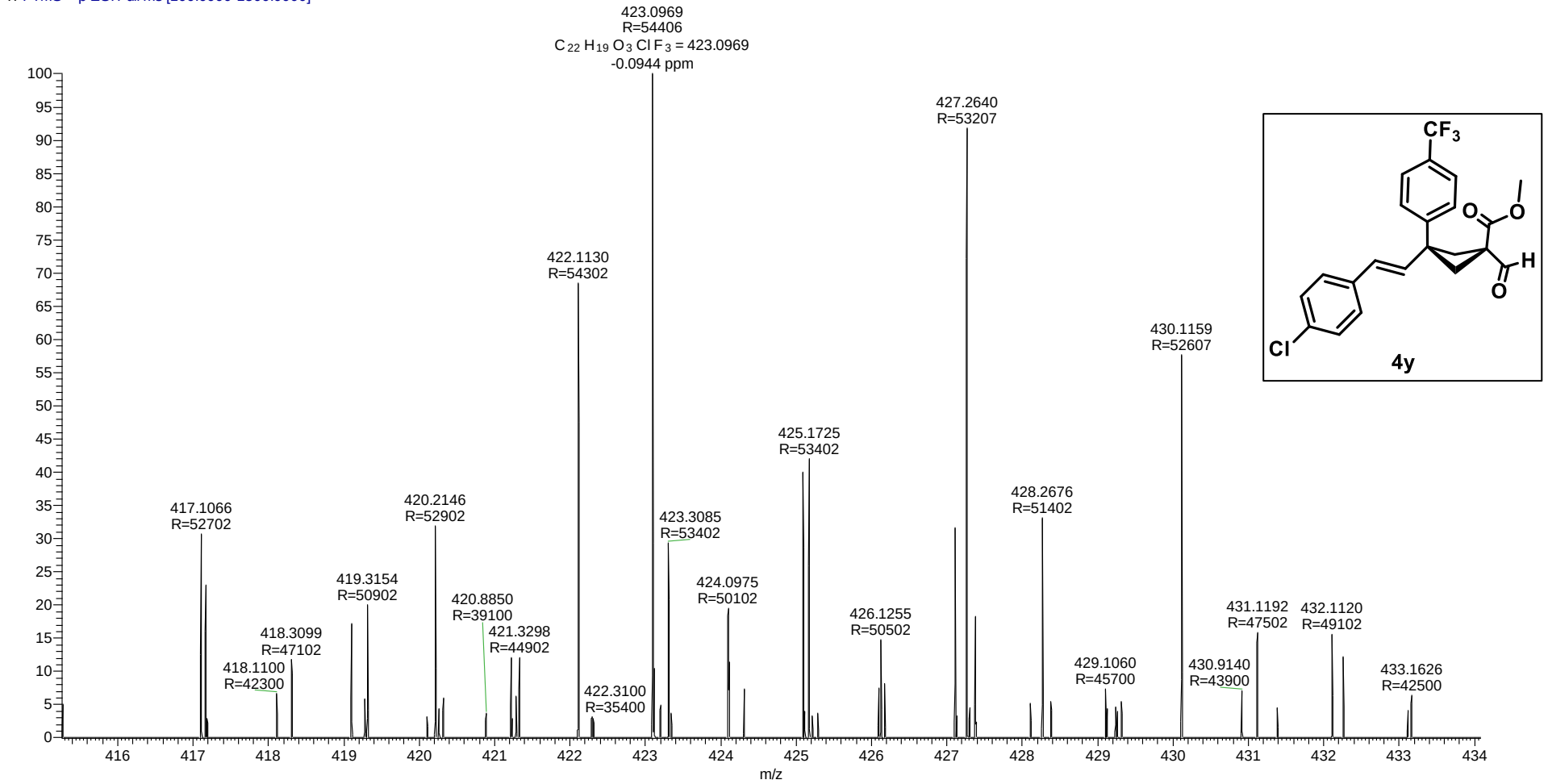
^{1}H NMR (400 MHz, $CDCl_3$) spectrum of Methyl (1s,3s)-3-((E)-4-chlorostyryl)-1-formyl-3-(4-(trifluoromethyl)phenyl)cyclobutane-1-carboxylate (4y)



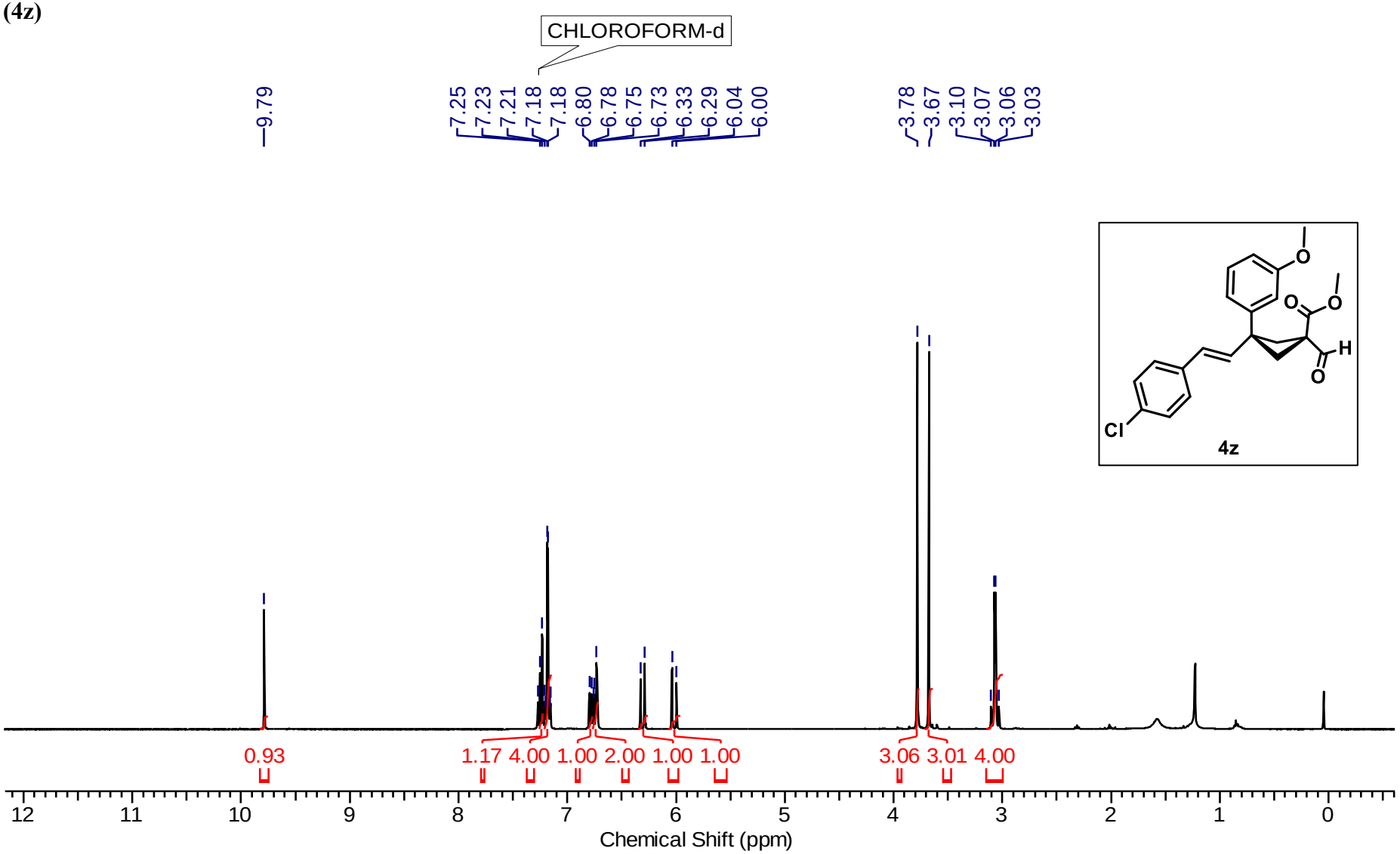
$^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) spectrum of Methyl (1s,3s)-3-((E)-4-chlorostyryl)-1-formyl-3-(4-(trifluoromethyl)phenyl)cyclobutane-1-carboxylate (4y)



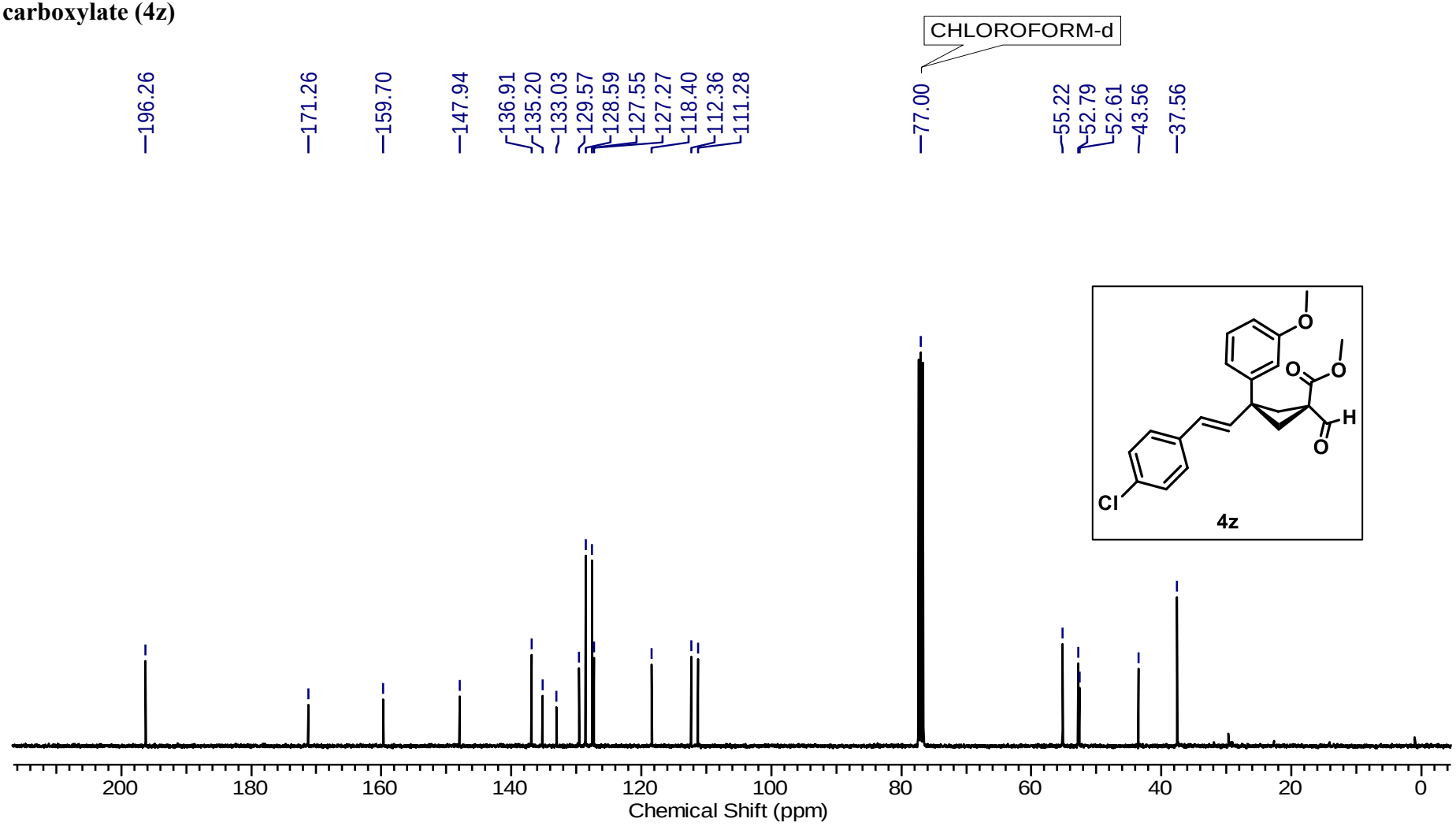
HRMS spectrum of Methyl (1s,3s)-3-((E)-4-chlorostyryl)-1-formyl-3-(4-(trifluoromethyl)phenyl)cyclobutane-1-carboxylate (4y)



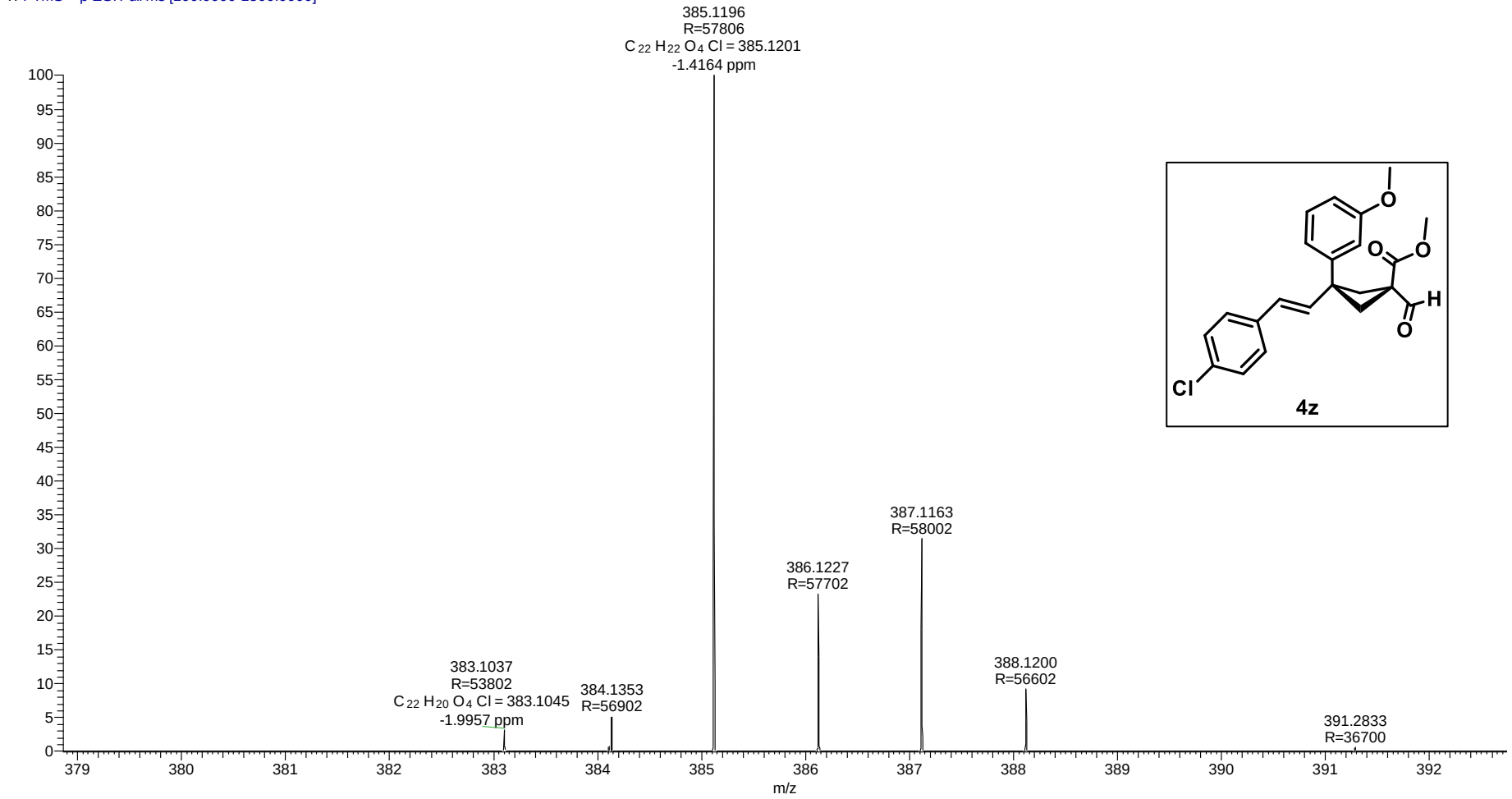
^{1}H NMR (400 MHz, $CDCl_3$) spectrum of Methyl (1s,3s)-3-((E)-4-chlorostyryl)-1-formyl-3-(3-methoxyphenyl)cyclobutane-1-carboxylate (4z)



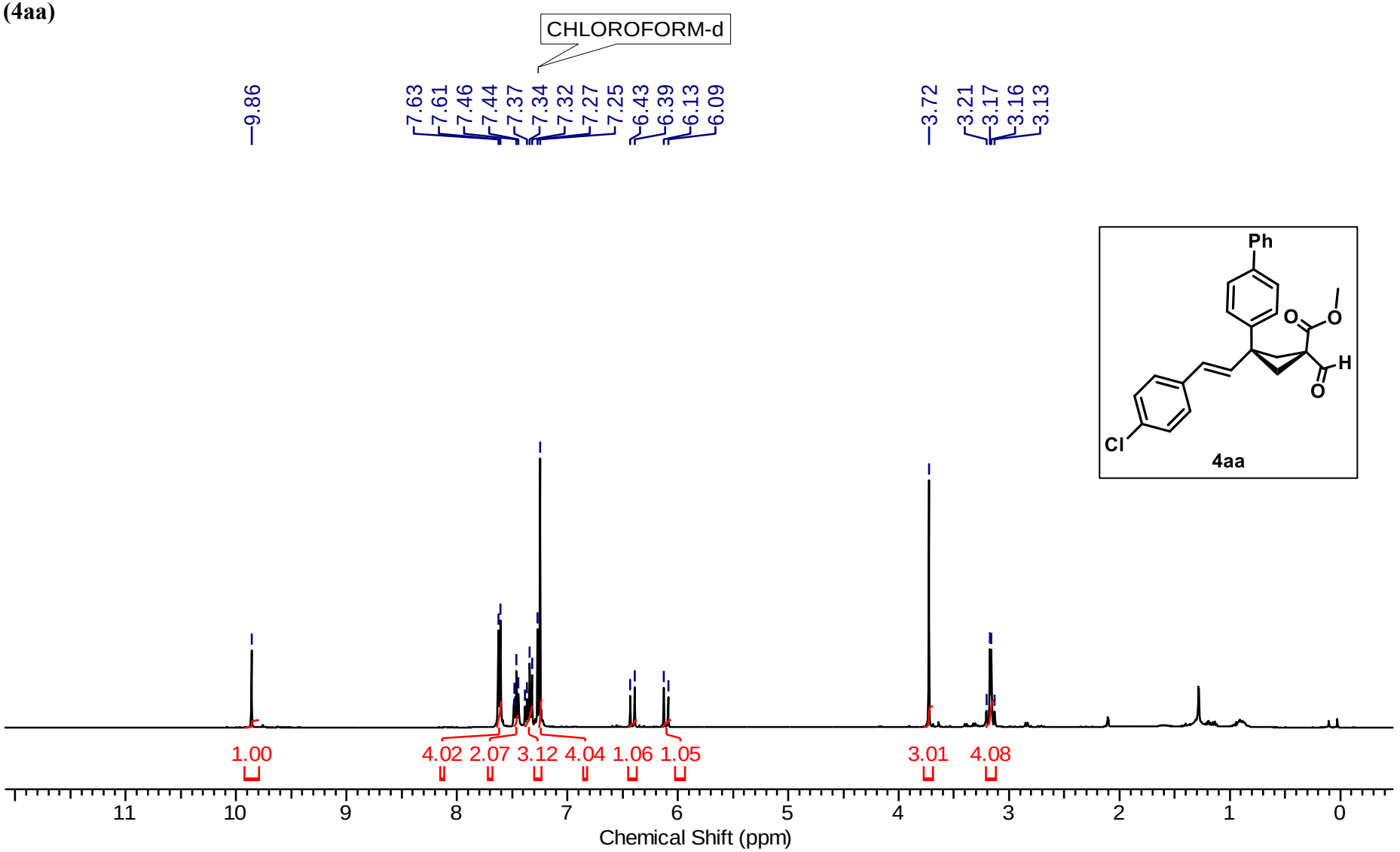
$^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) spectrum of Methyl (1s,3s)-3-((E)-4-chlorostyryl)-1-formyl-3-(3-methoxyphenyl)cyclobutane-1-carboxylate (4z)



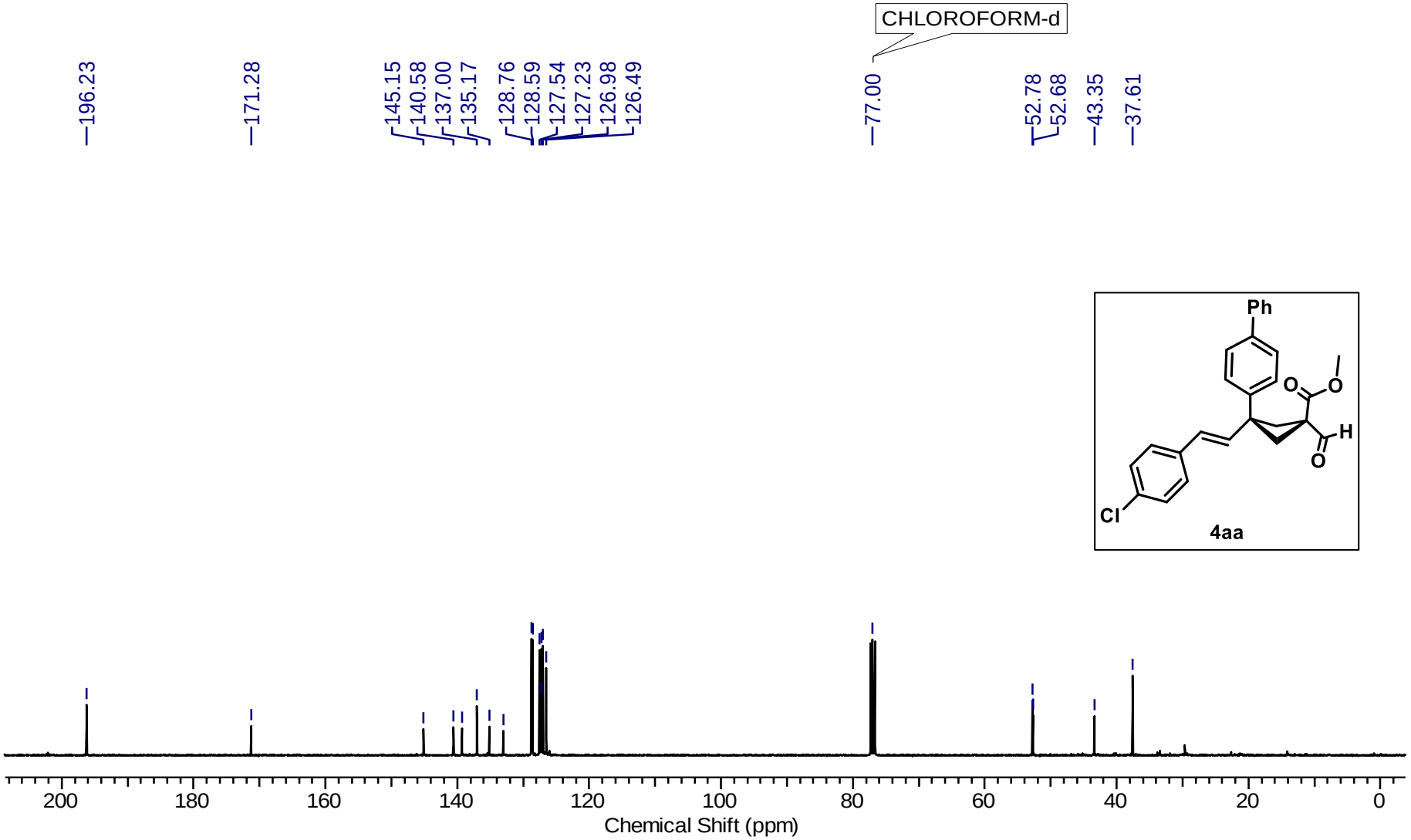
HRMS spectrum of Methyl (1s,3s)-3-((E)-4-chlorostyryl)-1-formyl-3-(3-methoxyphenyl)cyclobutane-1-carboxylate (4z)



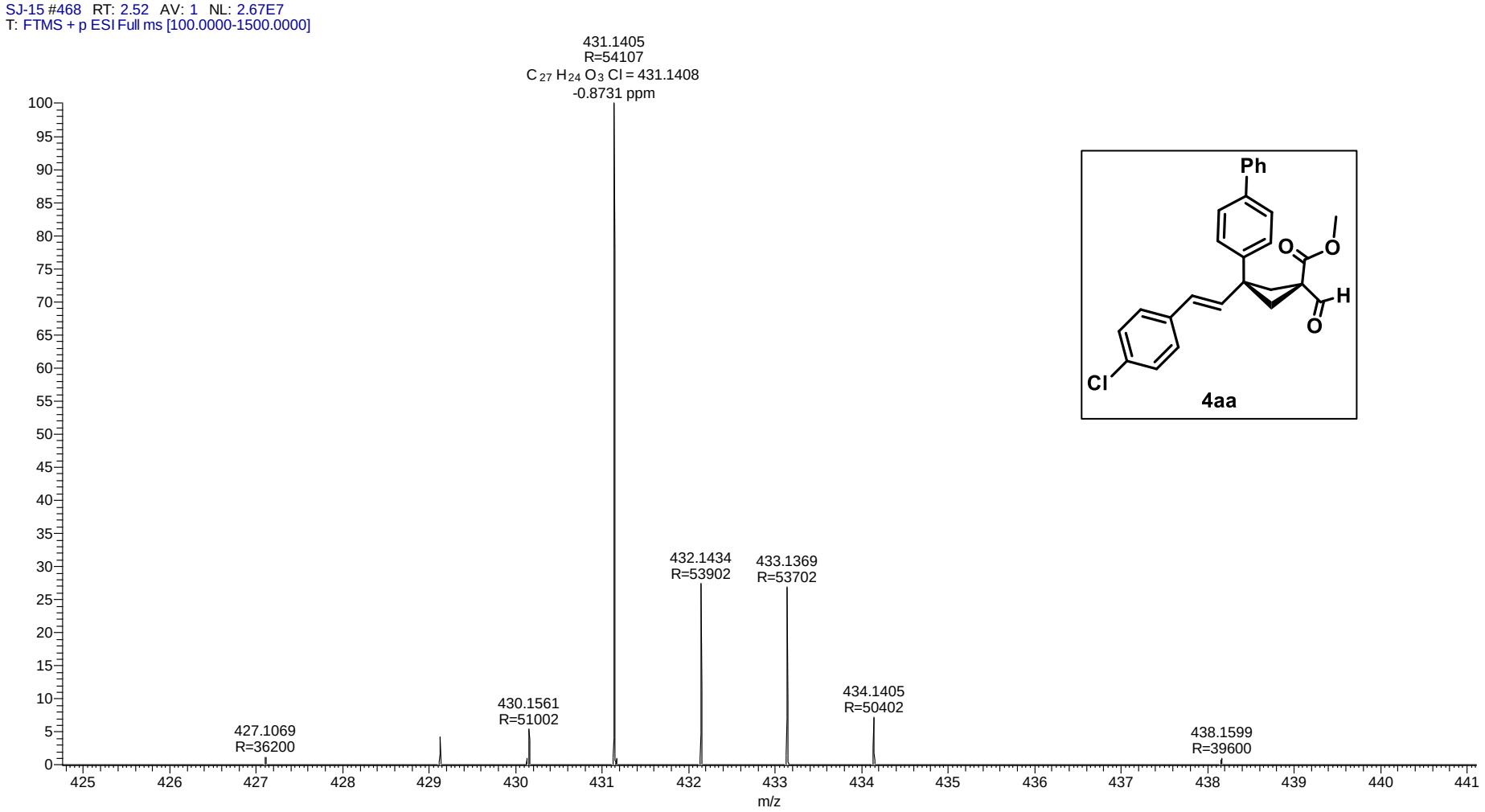
^{1}H NMR (400 MHz, $CDCl_3$) spectrum of Methyl(1s,3s)-3-([1,1'-biphenyl]-4-yl)-3-((E)-4-chlorostyryl)-1-formylcyclobutane-1-carboxylate (4aa)



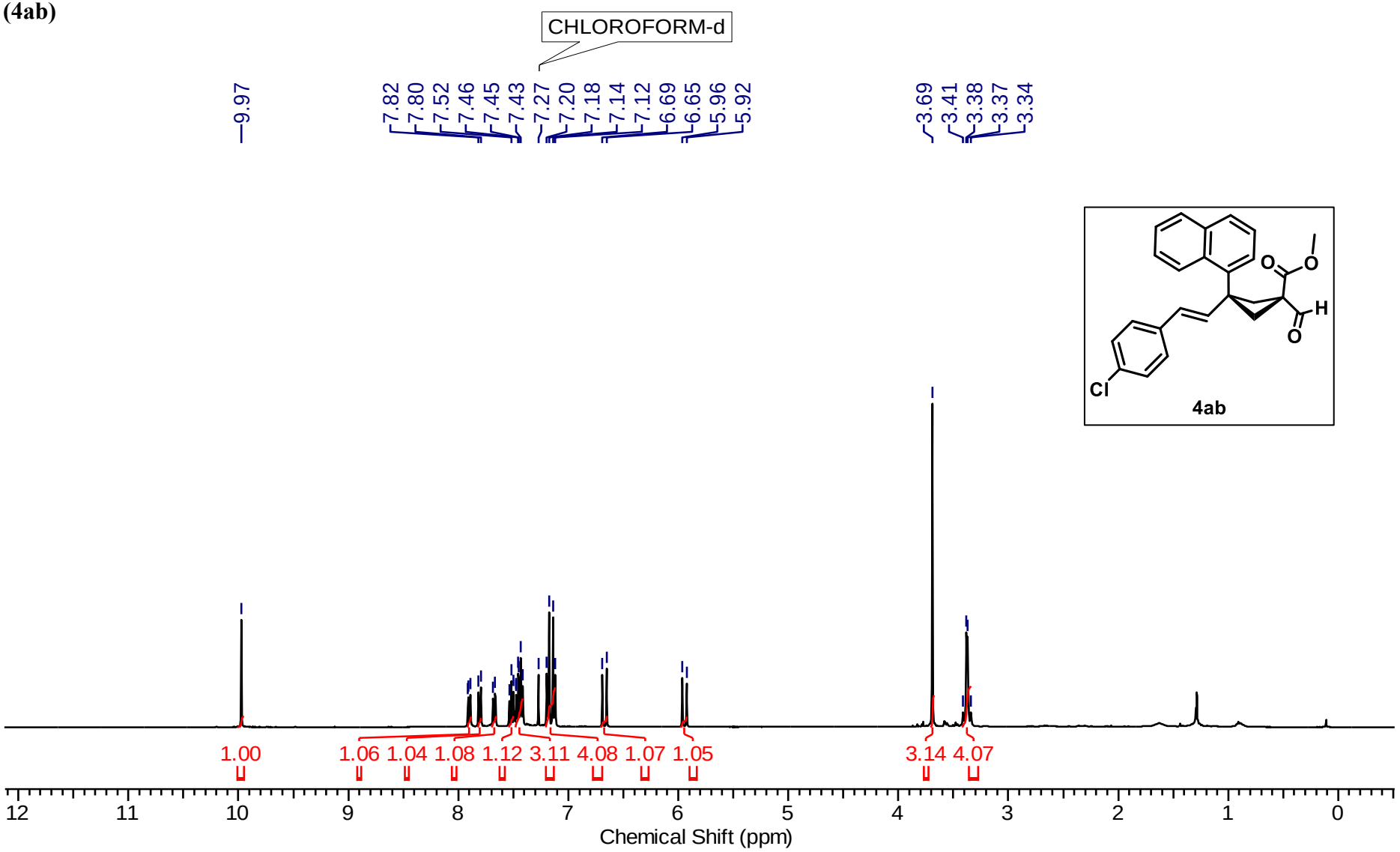
$^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) spectrum of Methyl(1s,3s)-3-([1,1'-biphenyl]-4-yl)-3-((E)-4-chlorostyryl)-1-formylcyclobutane-1-carboxylate (4aa)



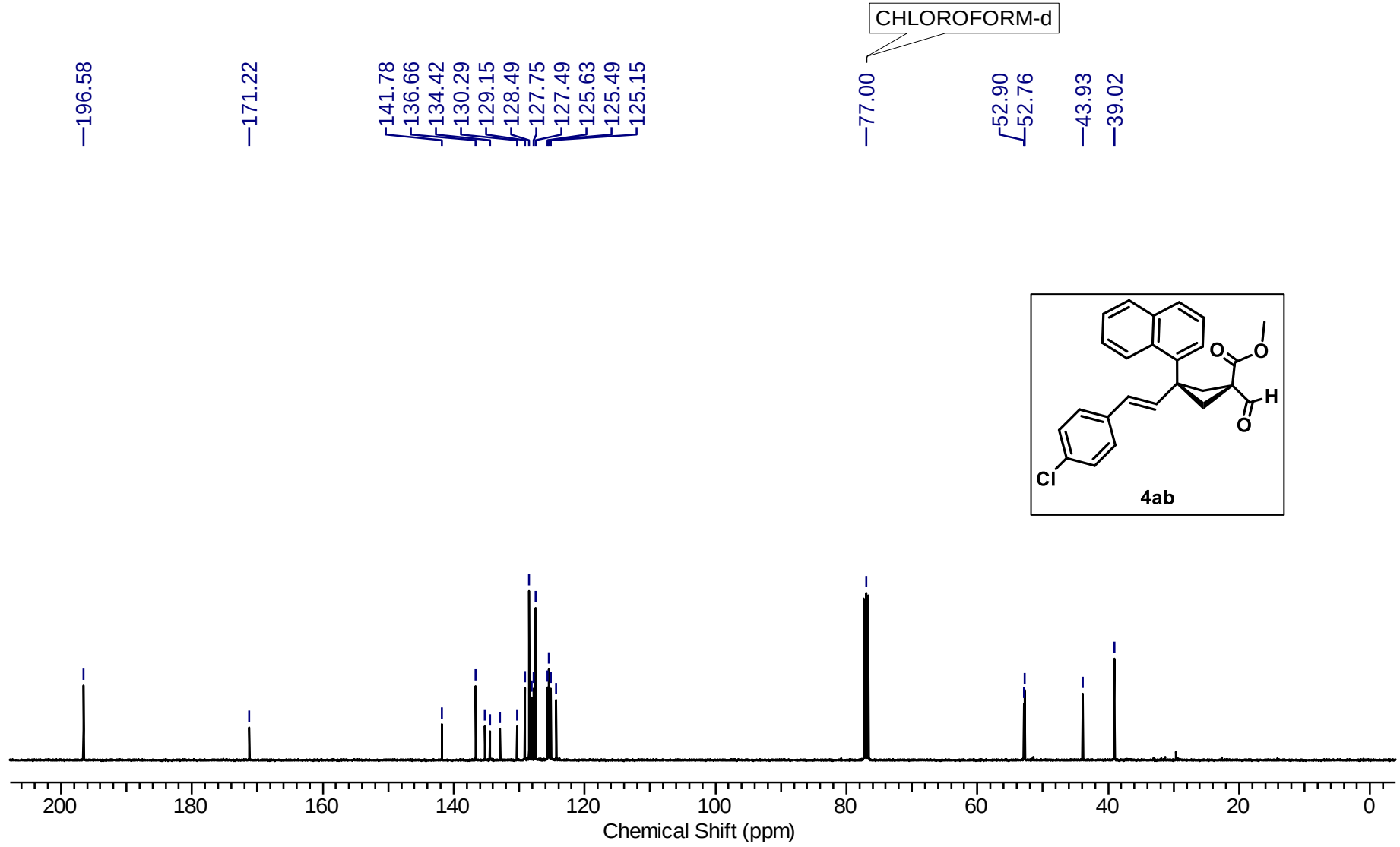
HRMS spectrum of Methyl(1s,3s)-3-([1,1'-biphenyl]-4-yl)-3-((E)-4-chlorostyryl)-1-formylcyclobutane-1-carboxylate (4aa)



^{1}H NMR (400 MHz, $CDCl_3$) spectrum of Methyl (1s,3s)-3-((E)-4-chlorostyryl)-1-formyl-3-(naphthalen-1-yl)cyclobutane-1-carboxylate (4ab)

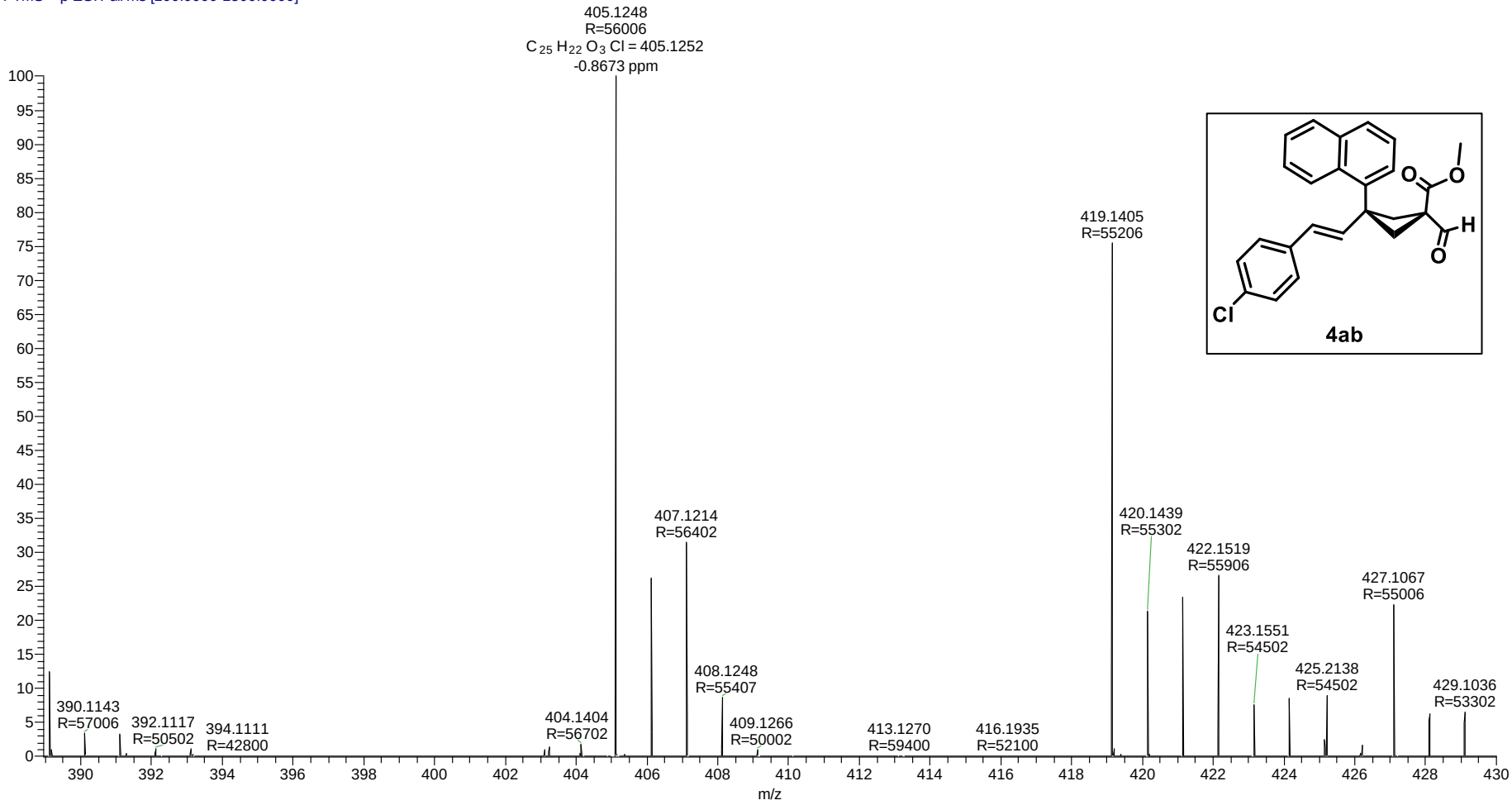


$^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) spectrum of Methyl (1s,3s)-3-((E)-4-chlorostyryl)-1-formyl-3-(naphthalen-1-yl)cyclobutane-1-carboxylate (4ab)

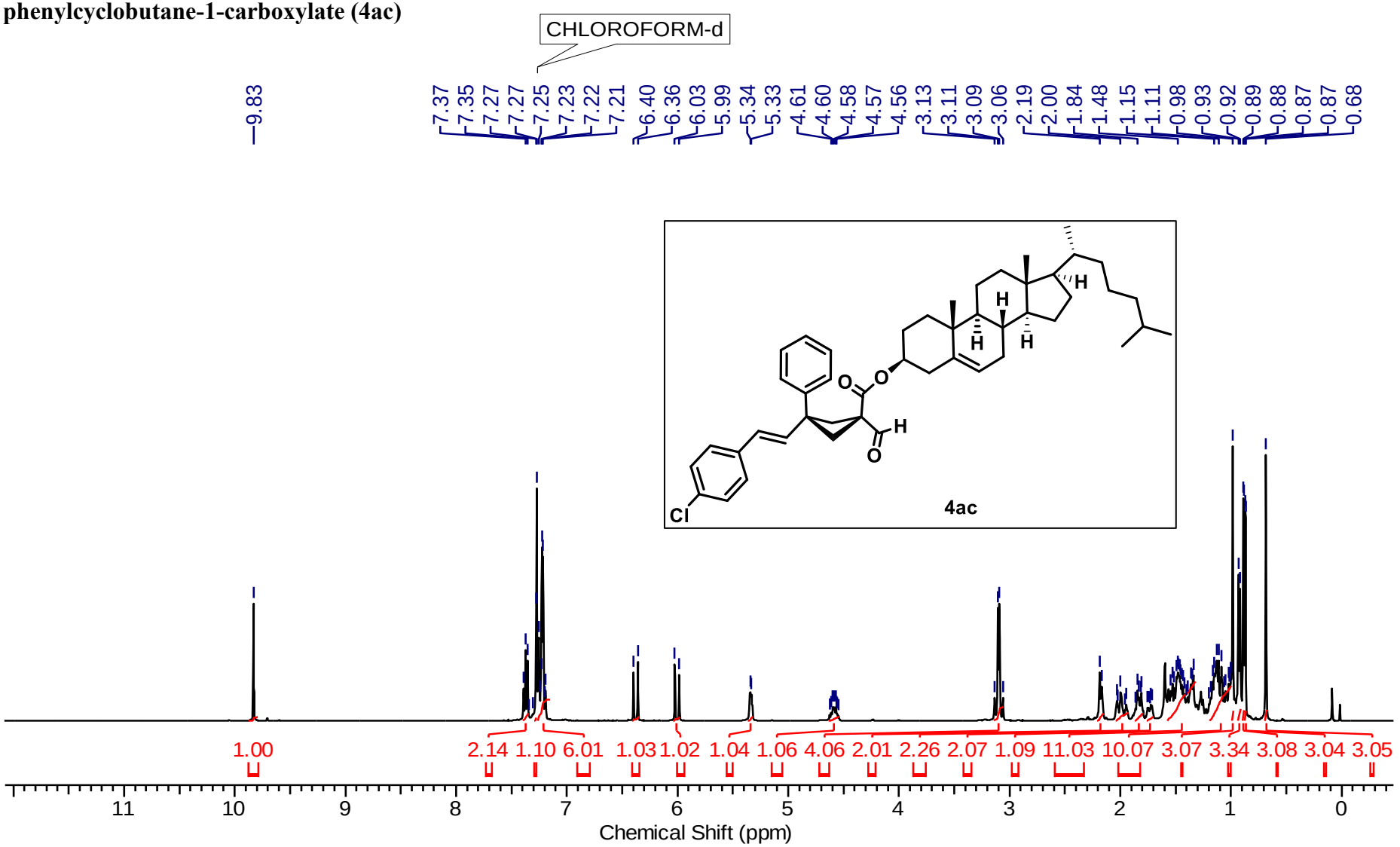


HRMS spectrum of Methyl (1s,3s)-3-((E)-4-chlorostyryl)-1-formyl-3-(naphthalen-1-yl)cyclobutane-1-carboxylate (4ab)

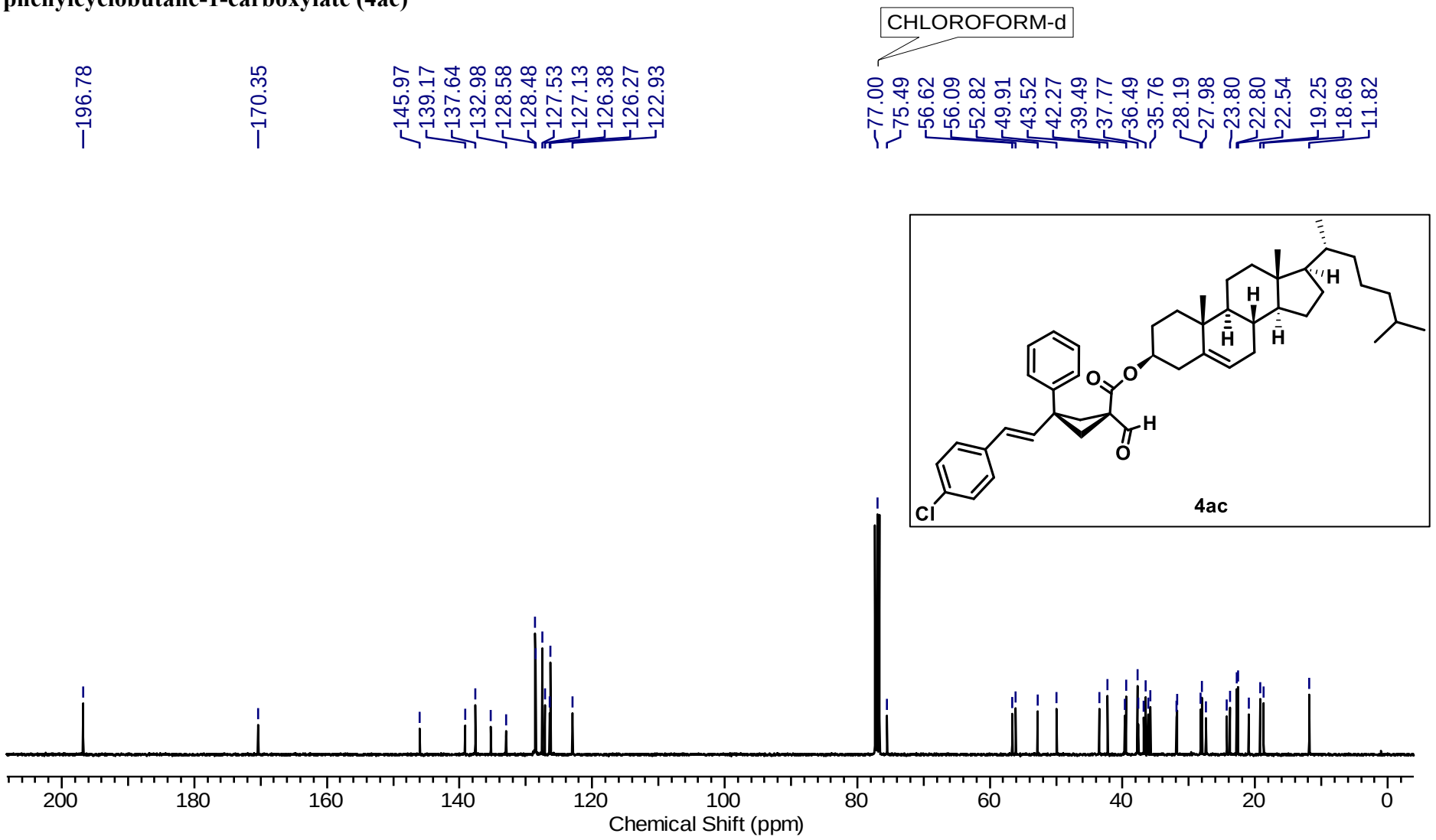
SJ-13 #415 RT: 2.26 AV: 1 NL: 1.66E8
T: FTMS + p ESI Full ms [100.0000-1500.0000]



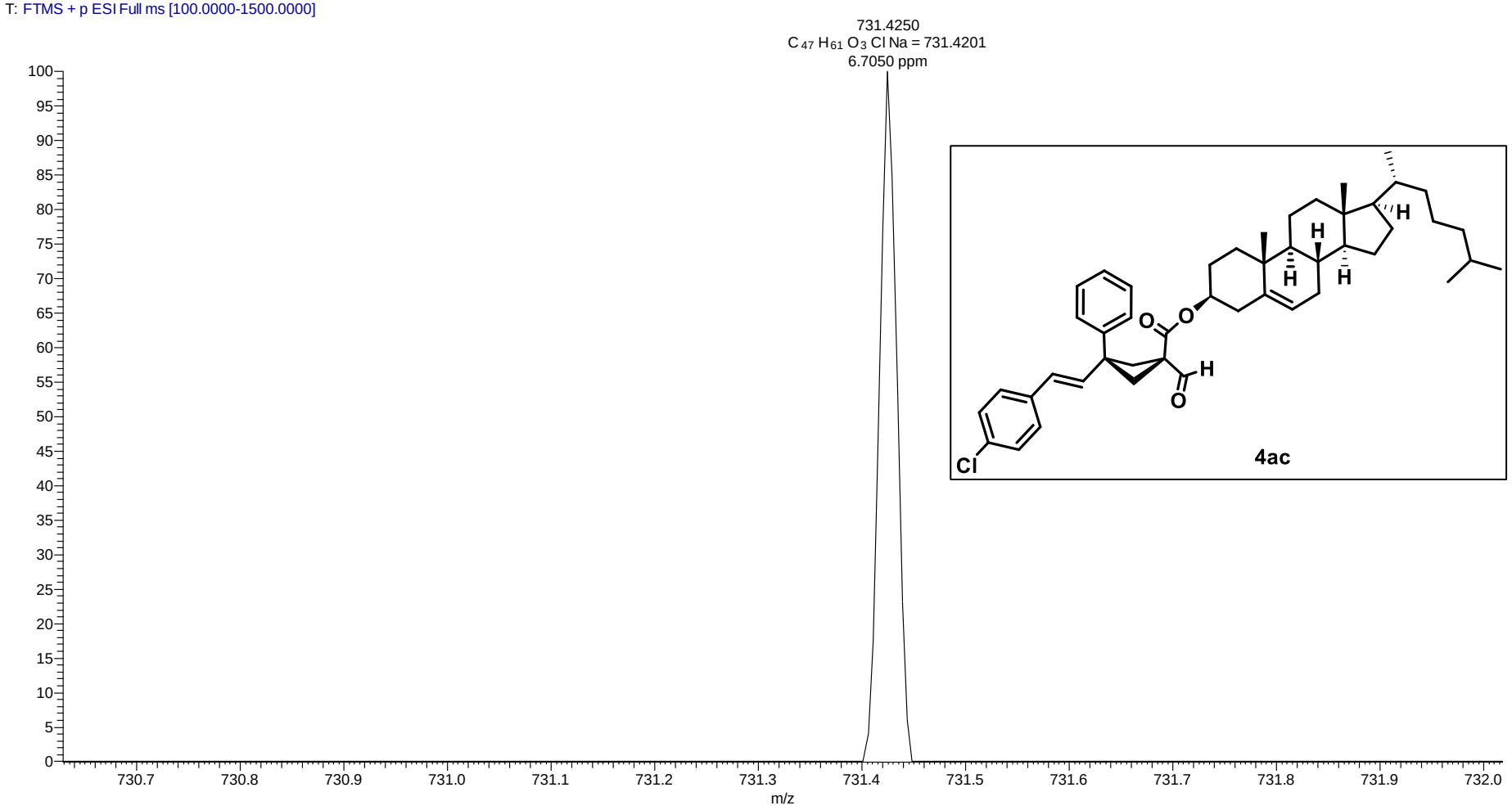
^{1}H NMR (400 MHz, $CDCl_3$) spectrum of (3S,8S,9S,10R,13R,14S,17R)-10,13-dimethyl-17-((R)-6-methylheptan-2-yl)-2,3,4,7,8,9,10,11,12,13,14,15,16,17-tetradecahydro-1H-cyclopenta[a]phenanthren-3-yl (1s,3R)-3-((E)-4-chlorostyryl)-1-formyl-3-phenylcyclobutane-1-carboxylate (4ac)



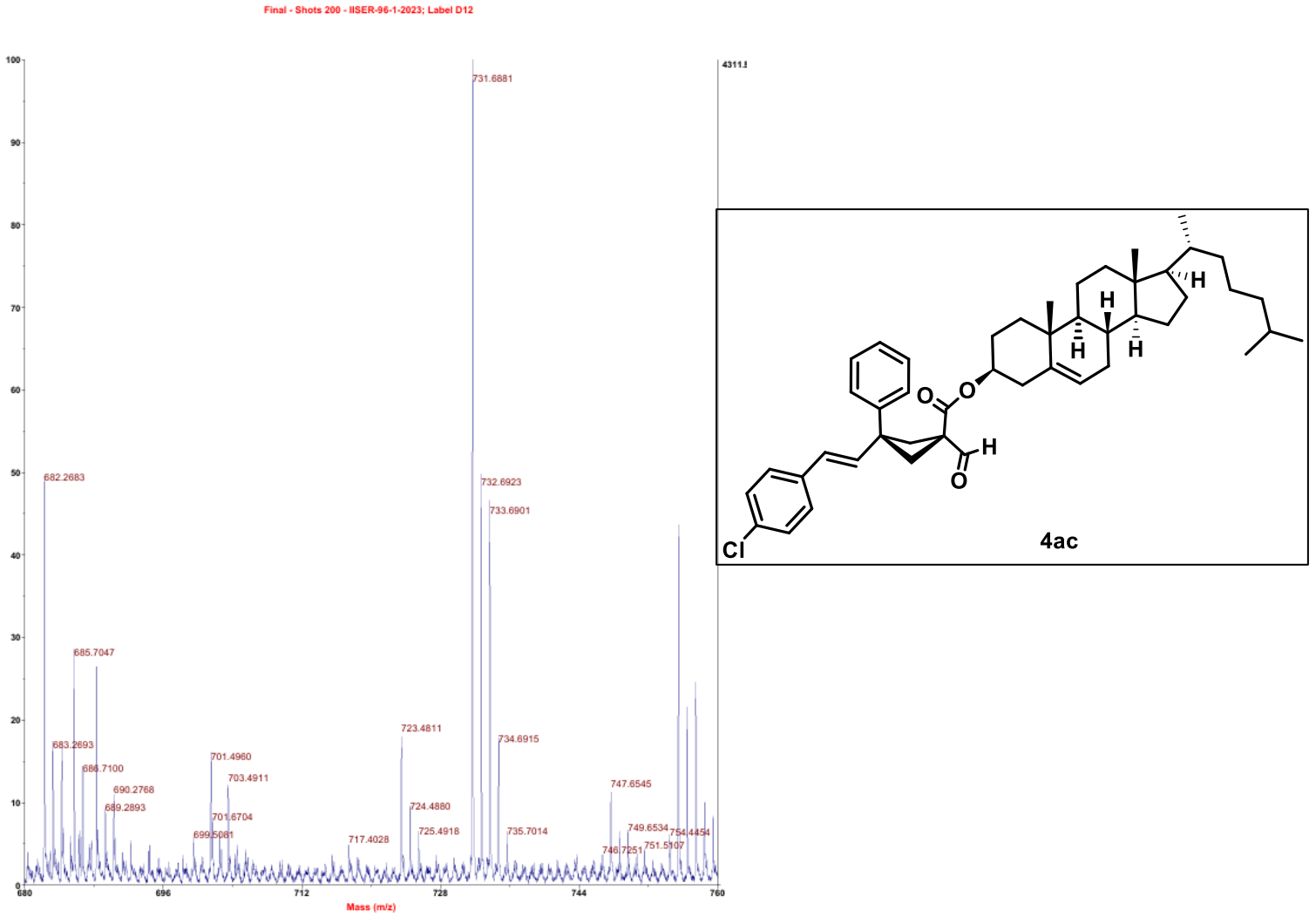
$^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) spectrum of (3S,8S,9S,10R,13R,14S,17R)-10,13-dimethyl-17-((R)-6-methylheptan-2-yl)-2,3,4,7,8,9,10,11,12,13,14,15,16,17-tetradecahydro-1H-cyclopenta[a]phenanthren-3-yl (1s,3R)-3-((E)-4-chlorostyryl)-1-formyl-3-phenylcyclobutane-1-carboxylate (4ac)



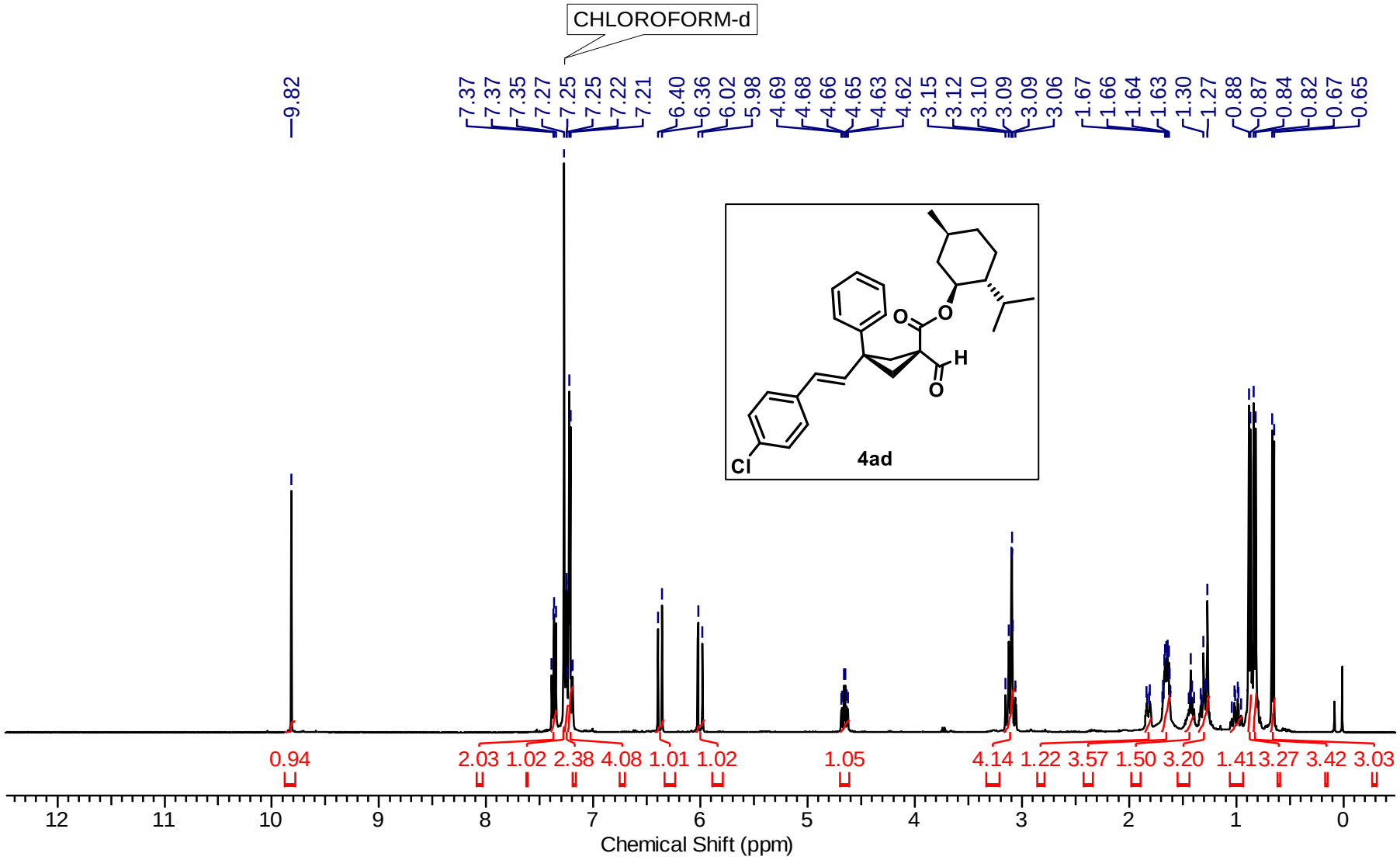
HRMS spectrum of (3S,8S,9S,10R,13R,14S,17R)-10,13-dimethyl-17-((R)-6-methylheptan-2-yl)-2,3,4,7,8,9,10,11,12,13,14,15,16,17-tetradecahydro-1H-cyclopenta[a]phenanthren-3-yl (1s,3R)-3-((E)-4-chlorostyryl)-1-formyl-3-phenylcyclobutane-1-carboxylate(4ac)



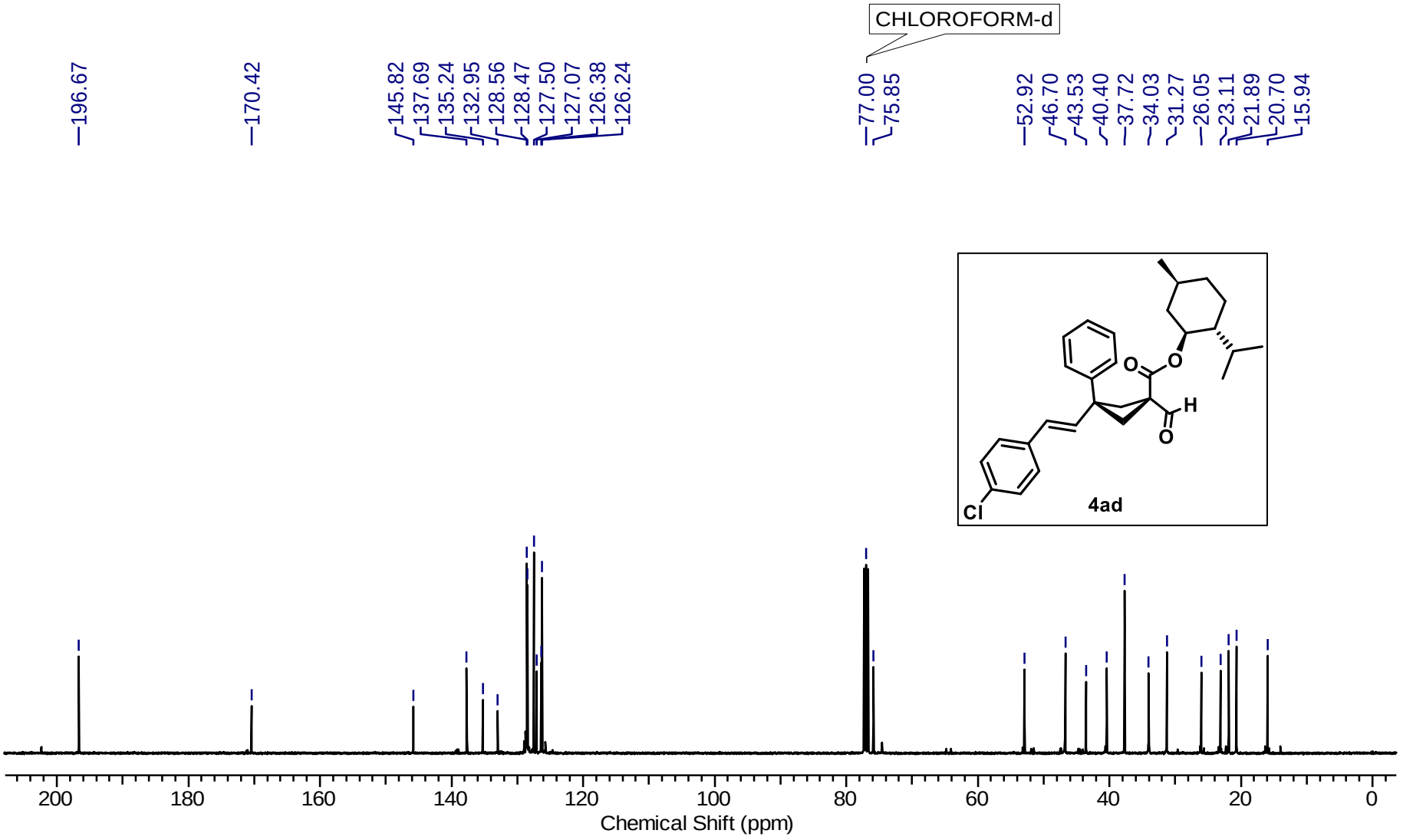
MALDI-TOF Mass Spectrum of (3S,8S,9S,10R,13R,14S,17R)-10,13-dimethyl-17-((R)-6-methylheptan-2-yl)-2,3,4,7,8,9,10,11,12,13,14,15,16,17-tetradecahydro-1H-cyclopenta[a]phenanthren-3-yl (1s,3R)-3-((E)-4-chlorostyryl)-1-formyl-3-phenylcyclobutane-1-carboxylate(4ac)



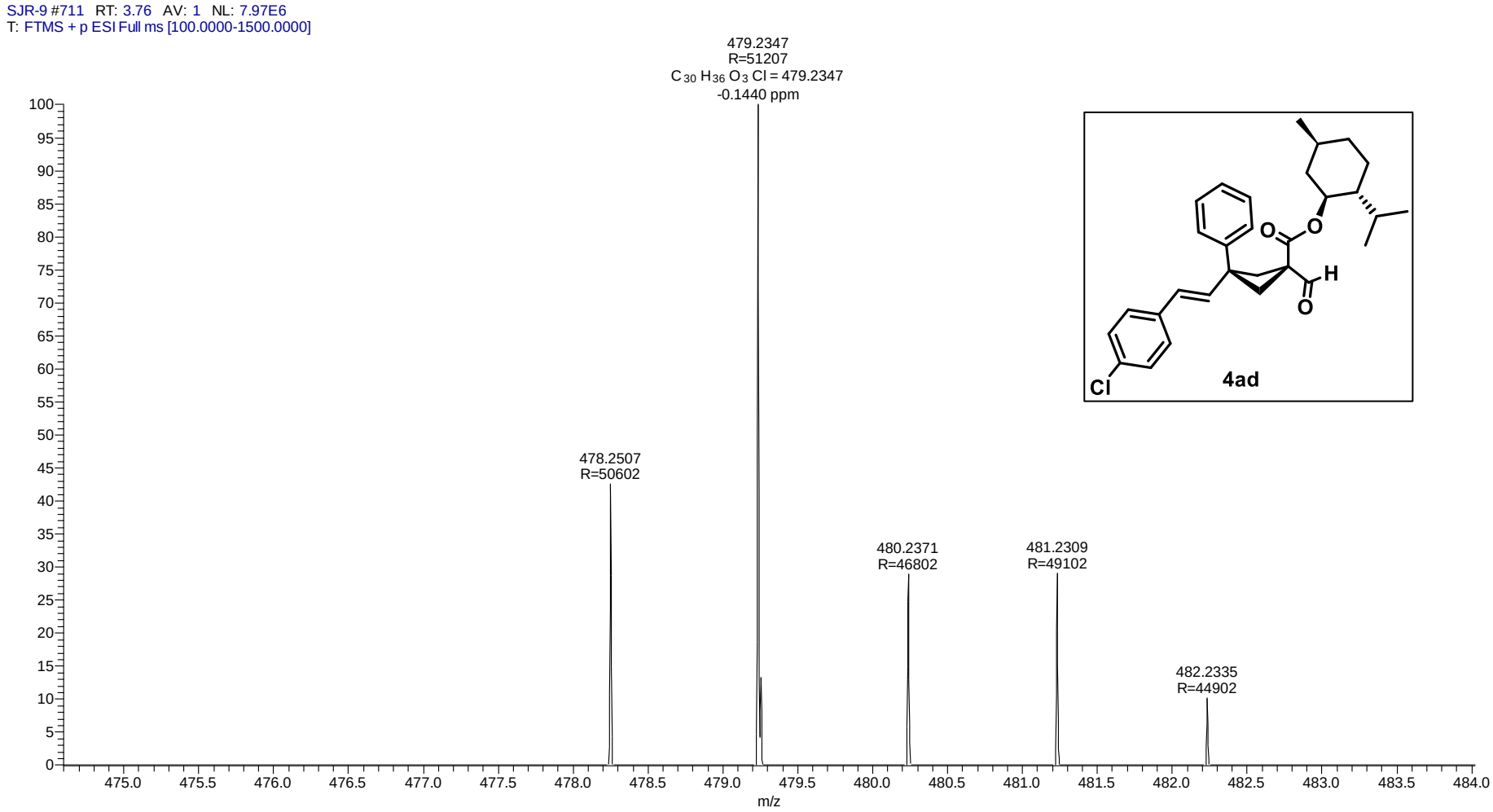
^{1}H NMRs (400 MHz, $CDCl_3$) spectrum of ((1S,2R,5S)-2-isopropyl-5-methylcyclohexyl (1s,3R)-3-((E)-4-chlorostyryl)-1-formyl-3-phenylcyclobutane-1-carboxylate (4ad)



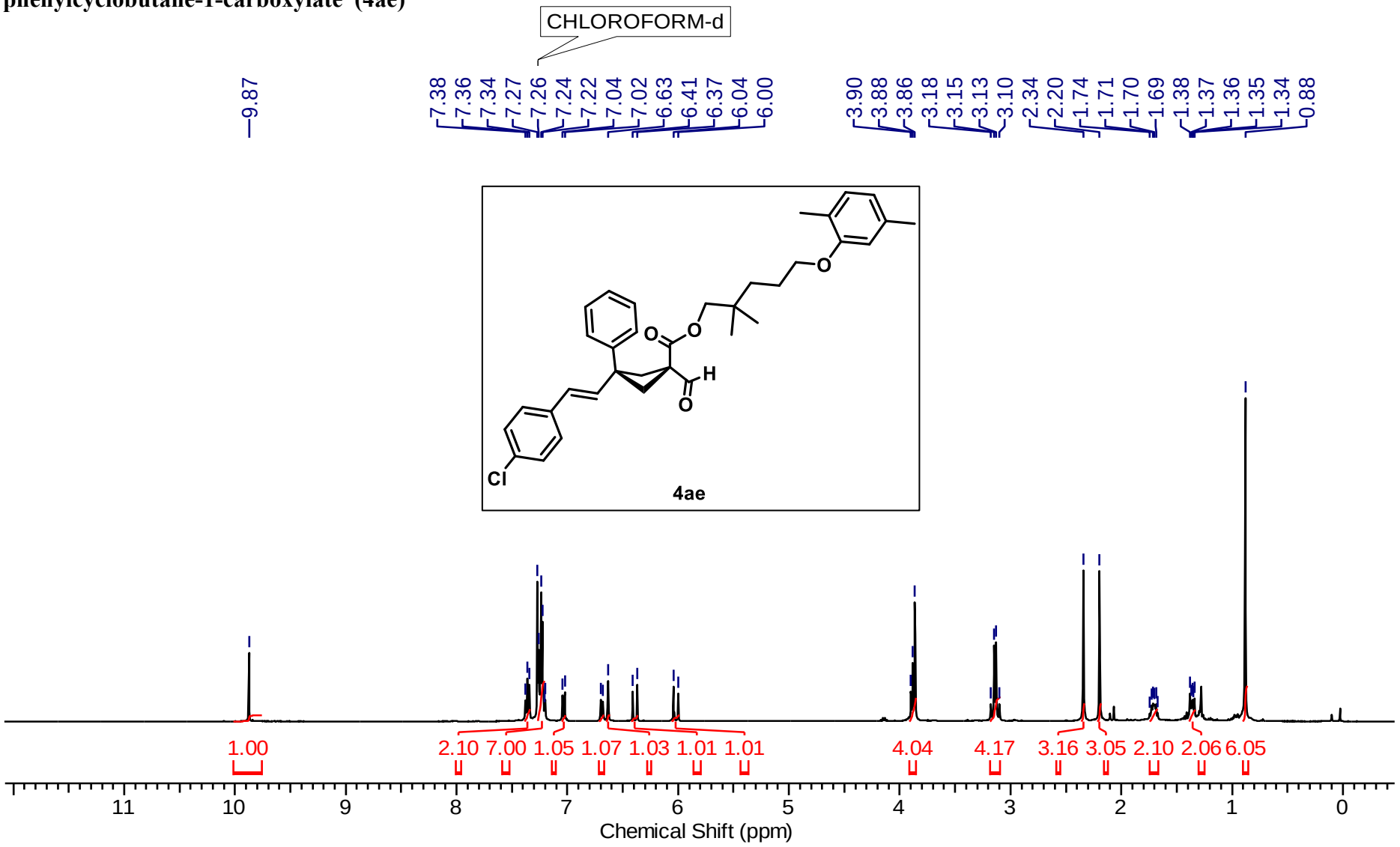
$^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) spectrum of (1S,2R,5S)-2-isopropyl-5-methylcyclohexyl (1s,3R)-3-((E)-4-chlorostyryl)-1-formyl-3-phenylcyclobutane-1-carboxylate (4ad)



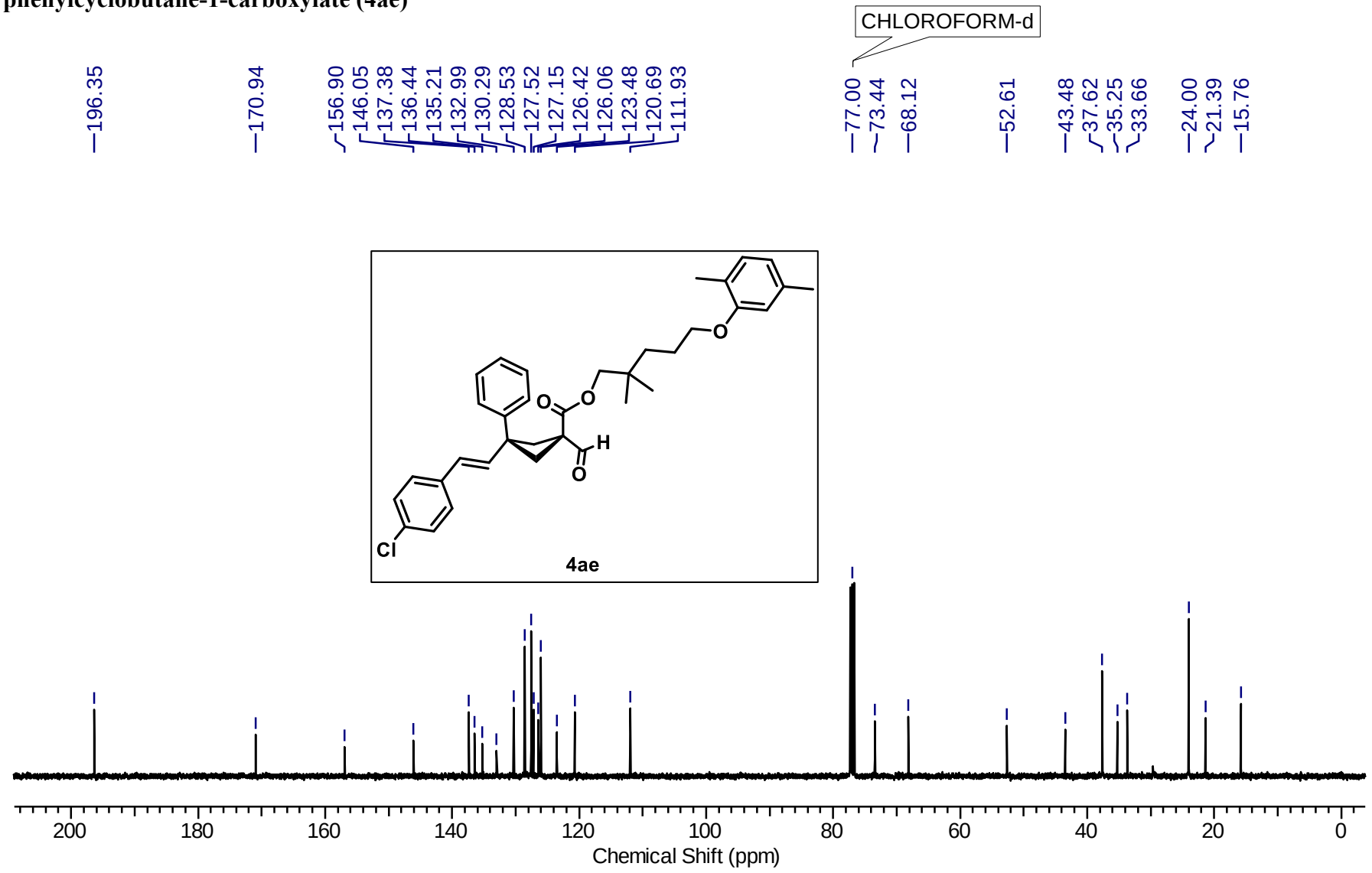
HRMS spectrum of (1S,2R,5S)-2-isopropyl-5-methylcyclohexyl (1s,3R)-3-((E)-4-chlorostyryl)-1-formyl-3-phenylcyclobutane-1-carboxylate (4ad)



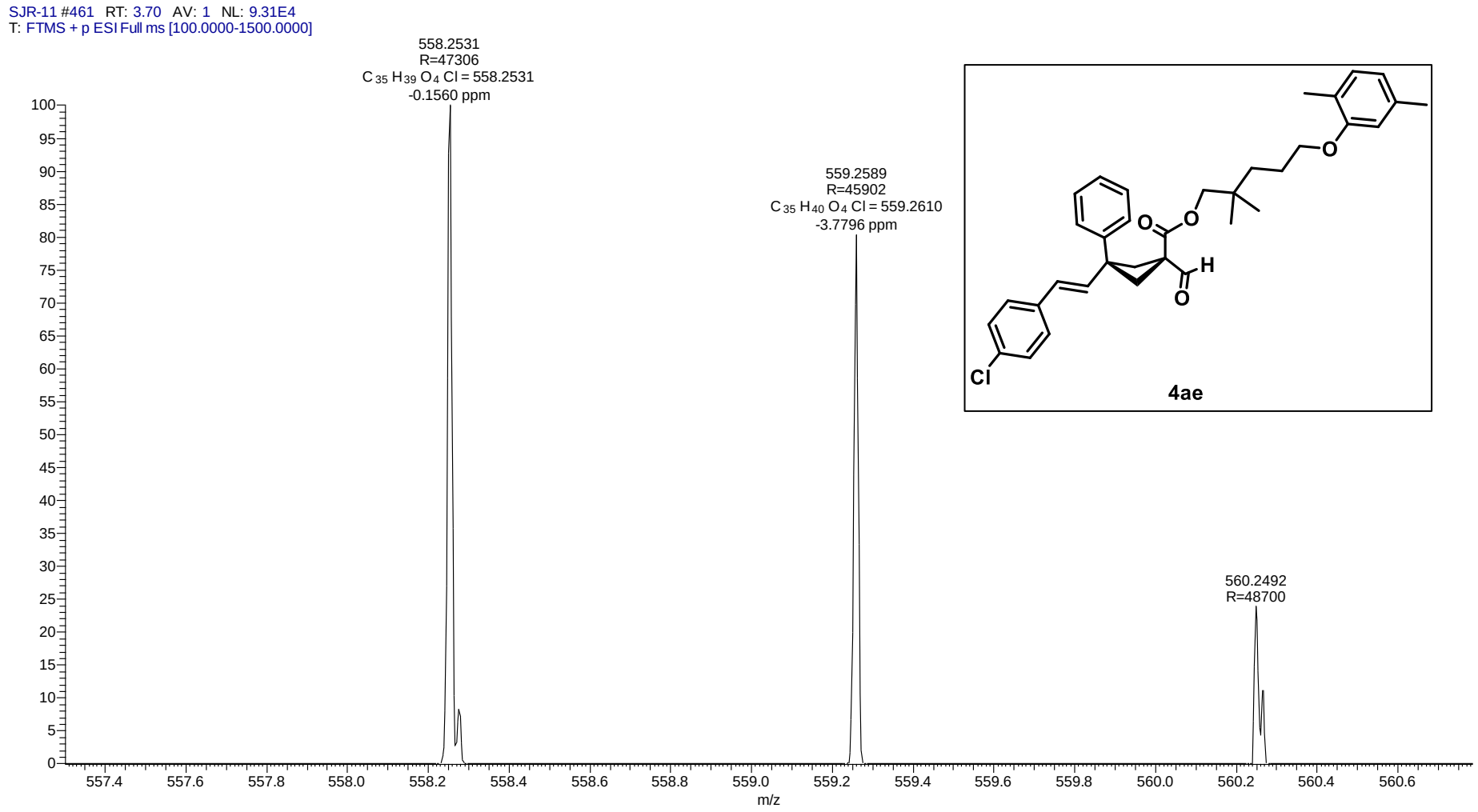
^{1}H NMR (400 MHz, $CDCl_3$) spectrum of 5-(2,5-dimethylphenoxy)-2,2-dimethylpentyl (1s,3s)-3-((E)-4-chlorostyryl)-1-formyl-3-phenylcyclobutane-1-carboxylate (4ae)



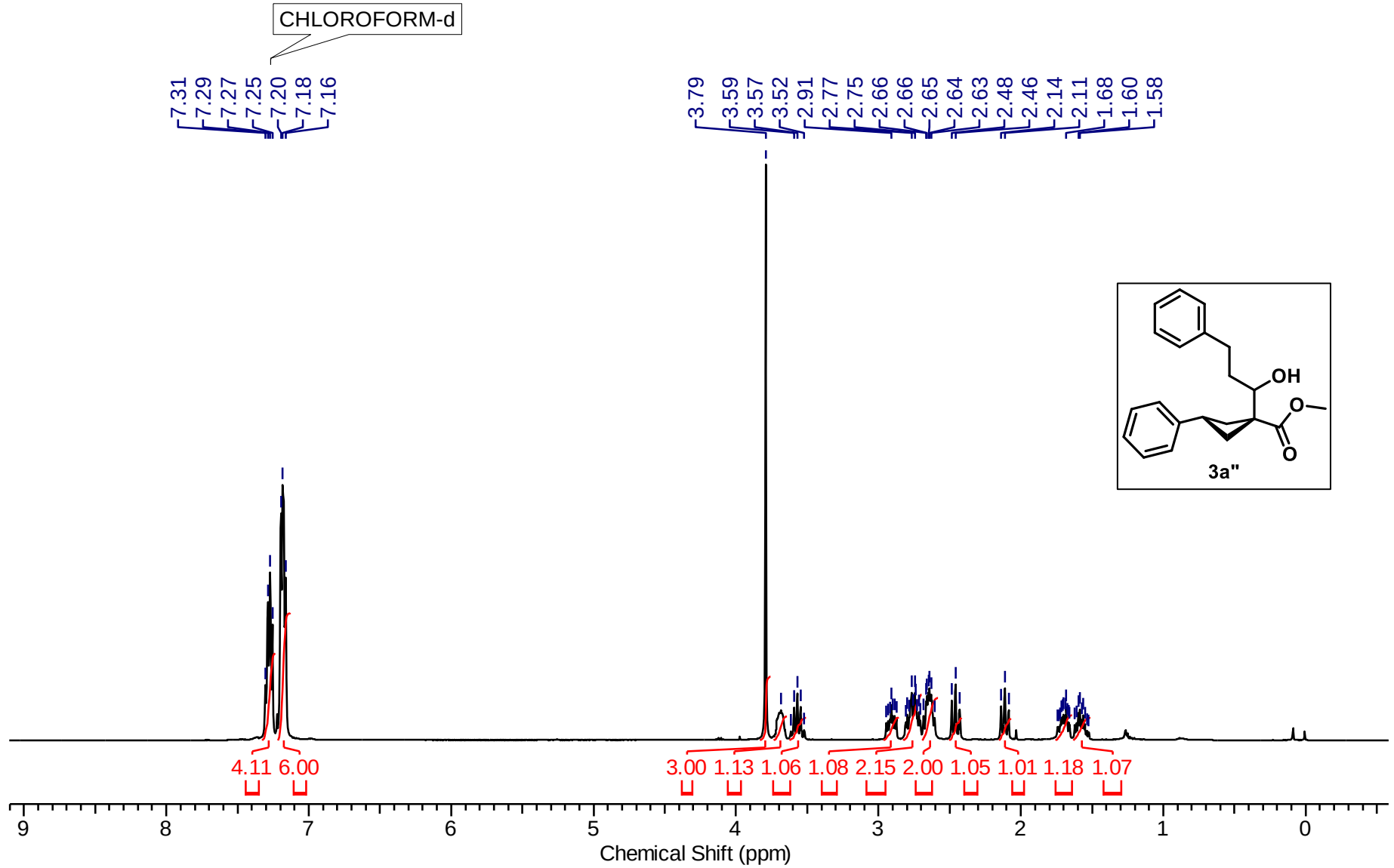
$^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) spectrum of 5-(2,5-dimethylphenoxy)-2,2-dimethylpentyl (1s,3s)-3-((E)-4-chlorostyryl)-1-formyl-3-phenylcyclobutane-1-carboxylate (4ae)



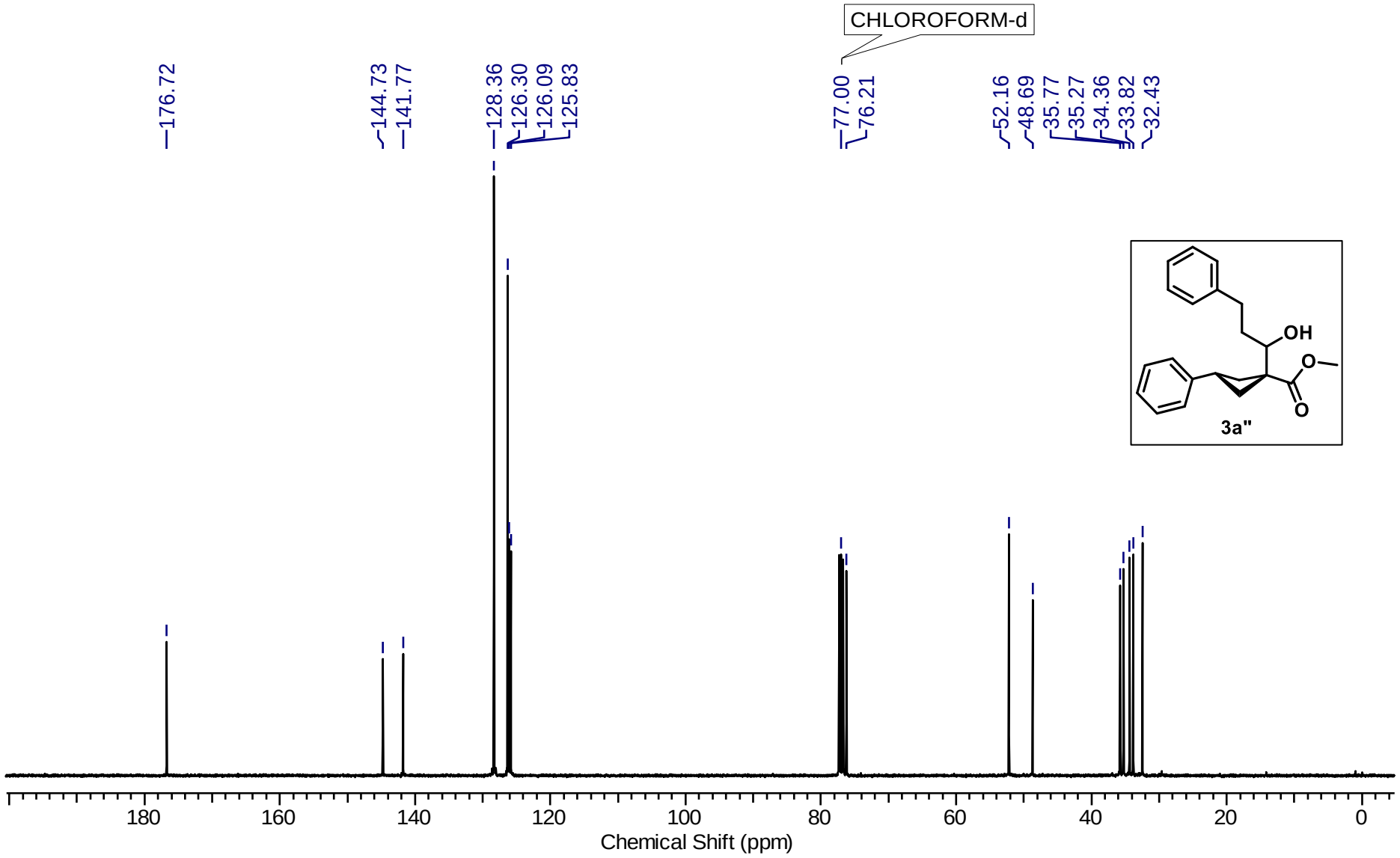
HRMS spectrum of 5-(2,5-dimethylphenoxy)-2,2-dimethylpentyl (1s,3s)-3-((E)-4-chlorostyryl)-1-formyl-3-phenylcyclobutane-1-carboxylate (4ae)



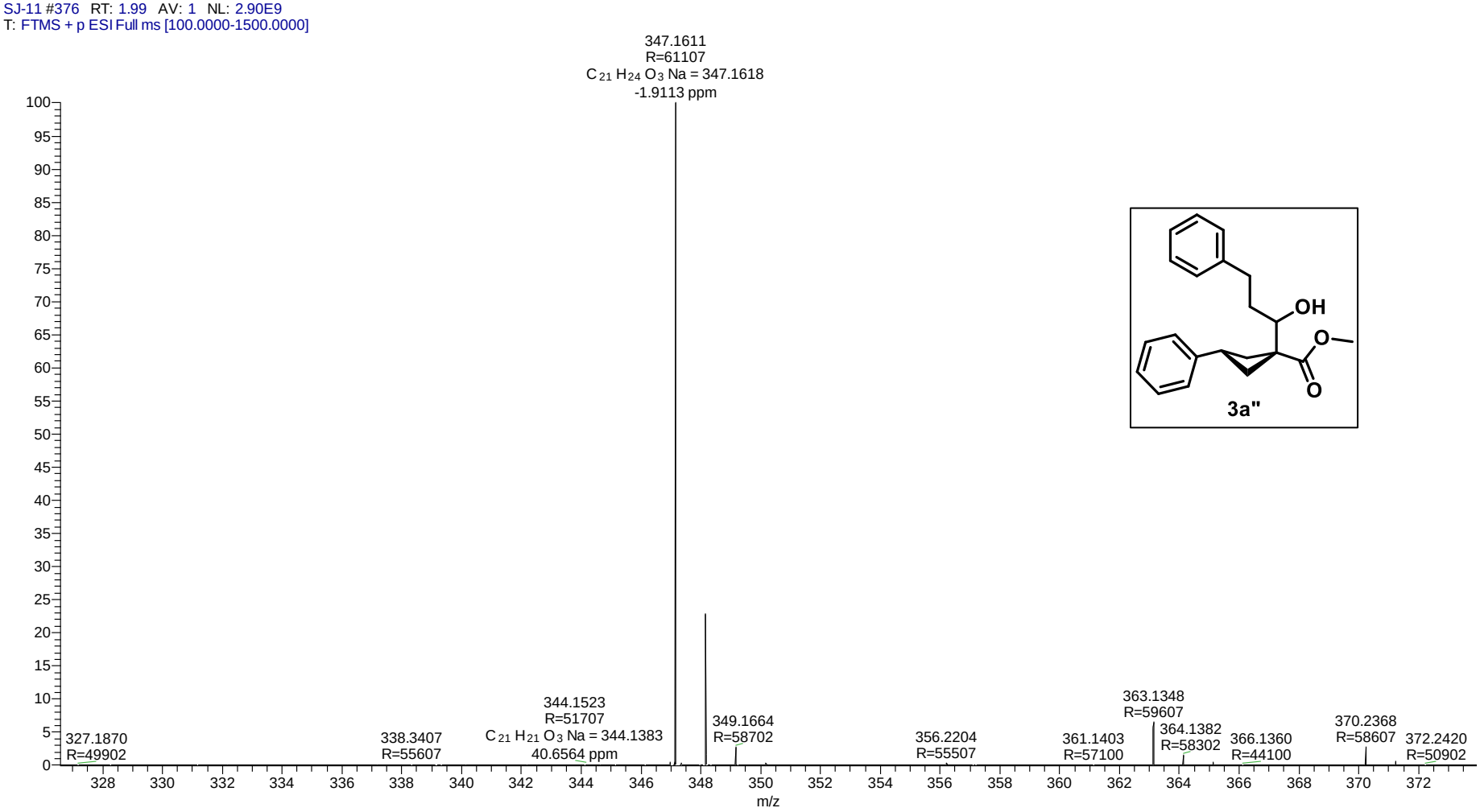
^{1}H NMR (400 MHz, $CDCl_3$) spectrum of Methyl (1s,3s)-1-(1-hydroxy-3-phenylpropyl)-3-phenylcyclobutane-1-carboxylate (3a")



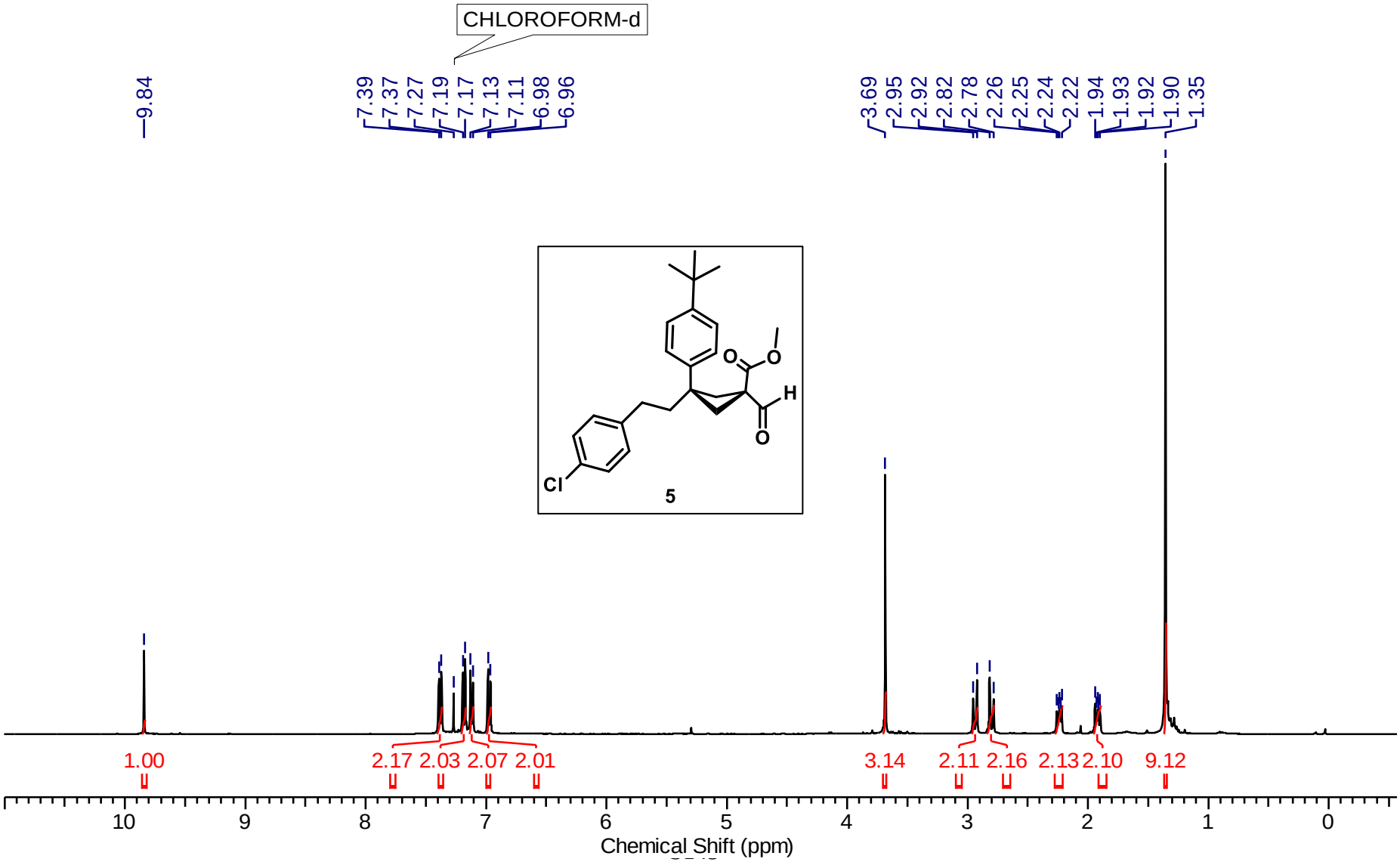
$^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) spectrum of Methyl (1s,3s)-1-(1-hydroxy-3-phenylpropyl)-3-phenylcyclobutane-1-carboxylate (3a")



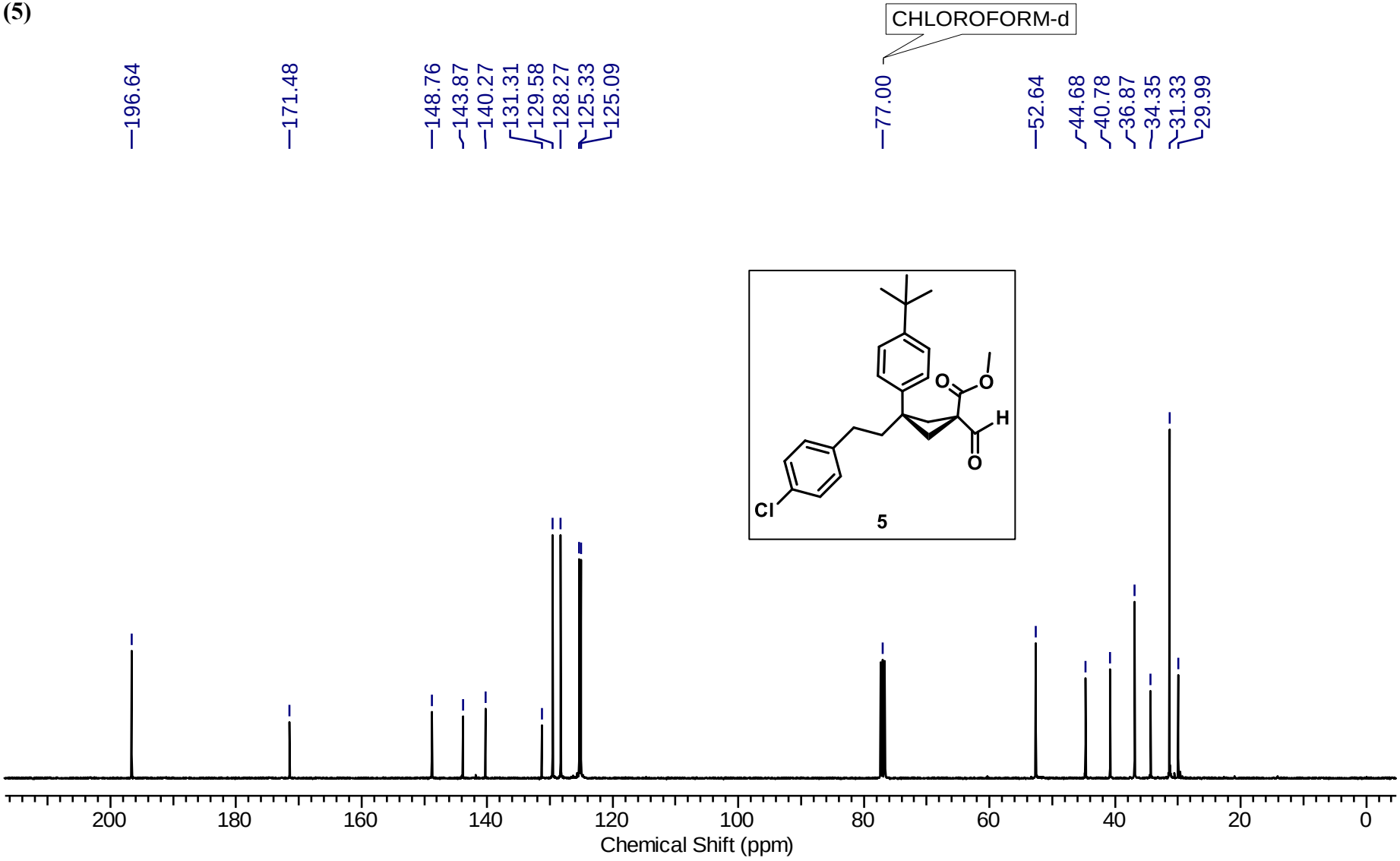
HRMS spectrum of Methyl (1s,3s)-1-(1-hydroxy-3-phenylpropyl)-3-phenylcyclobutane-1-carboxylate (3a")



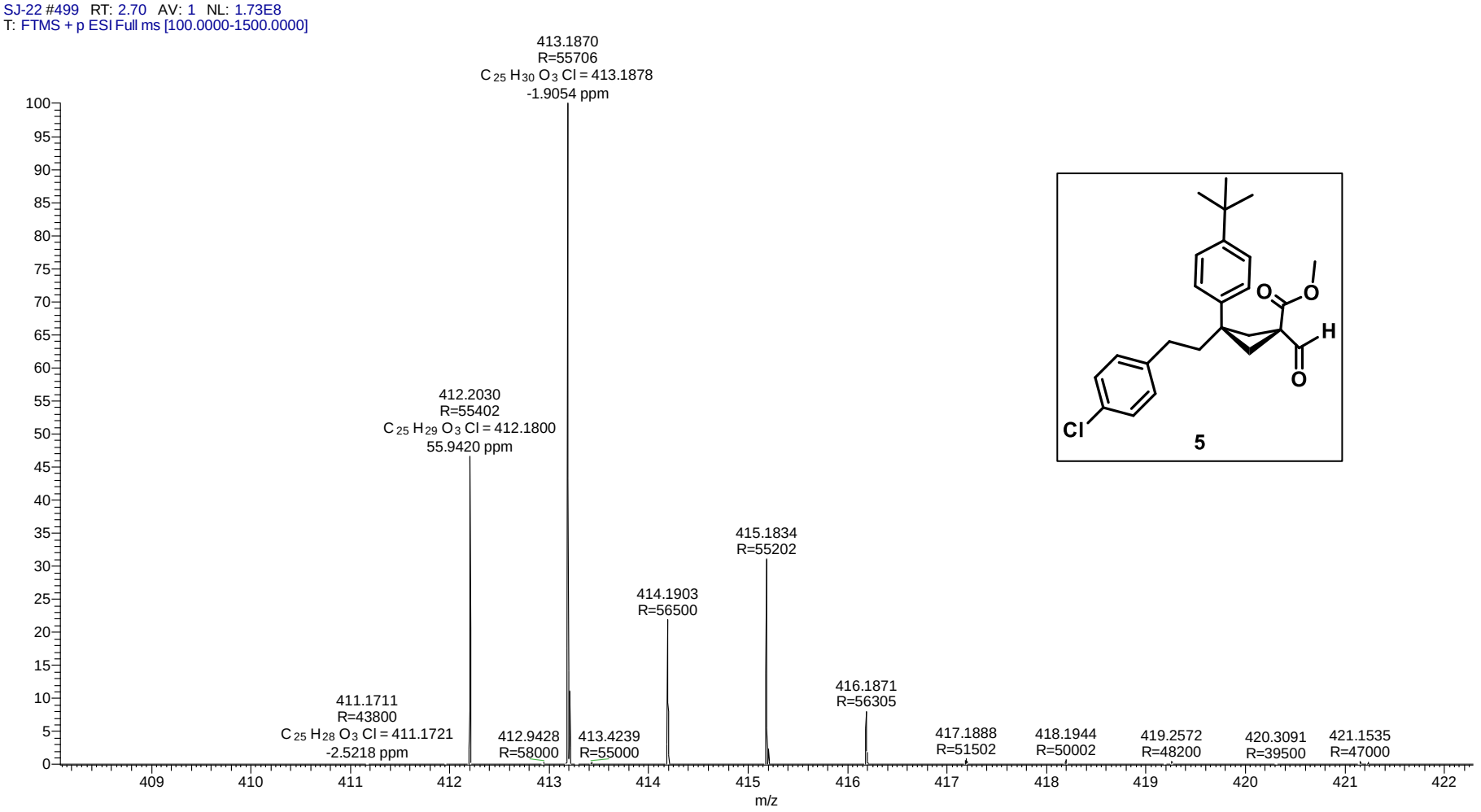
^{1}H NMR (400 MHz, $CDCl_3$) spectrum of (1r,3s)-3-(4-(*tert*-butyl)phenyl)-3-(4-chlorophenethyl)-1-formylcyclobutane-1-carboxylate (5)



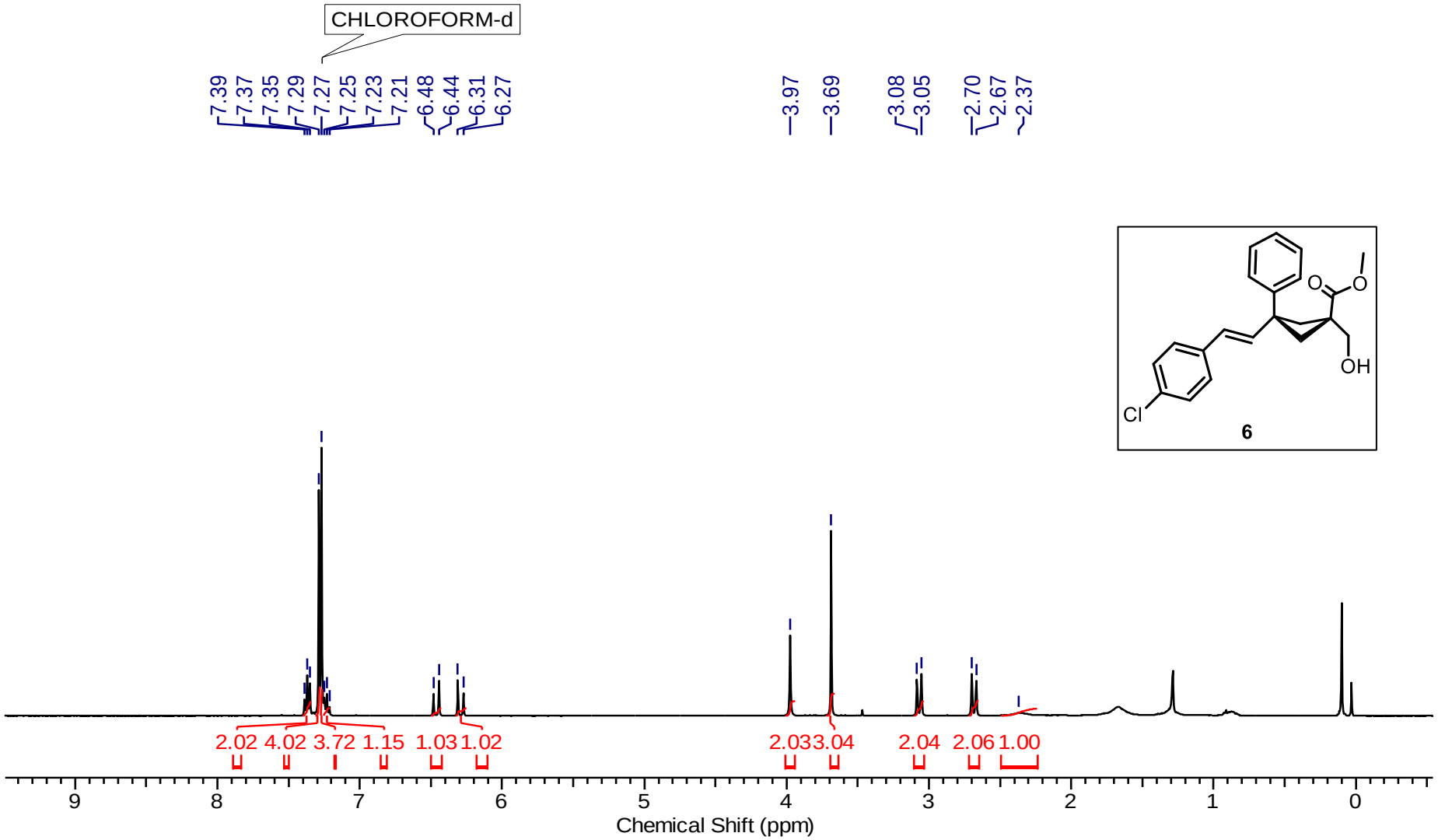
$^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) spectrum of (1r,3s)-3-(4-(*tert*-butyl)phenyl)-3-(4-chlorophenethyl)-1-formylcyclobutane-1-carboxylate (5)



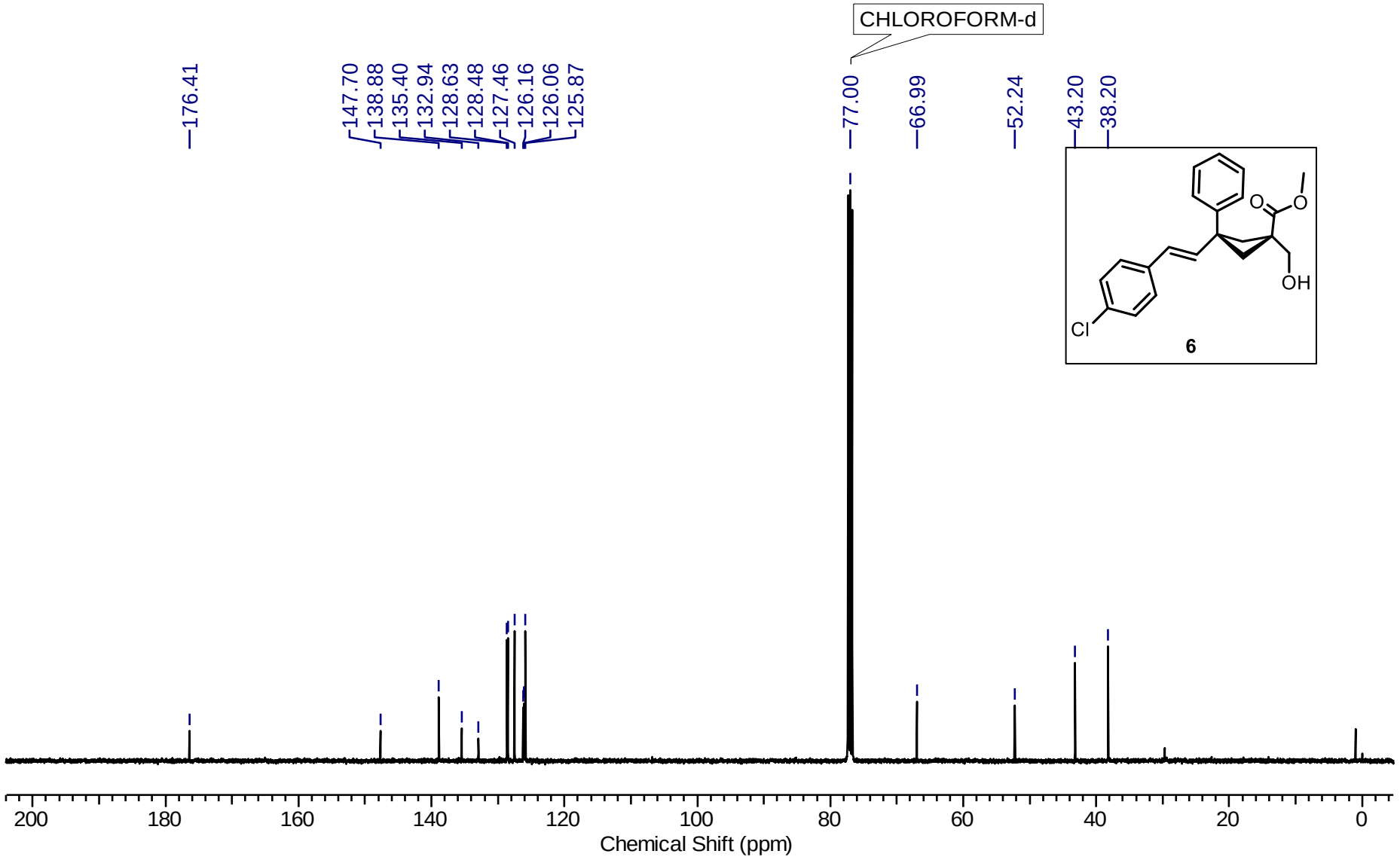
HRMS spectrum of (1r,3s)-3-(4-(*tert*-butyl)phenyl)-3-(4-chlorophenethyl)-1-formylcyclobutane-1-carboxylate (5)



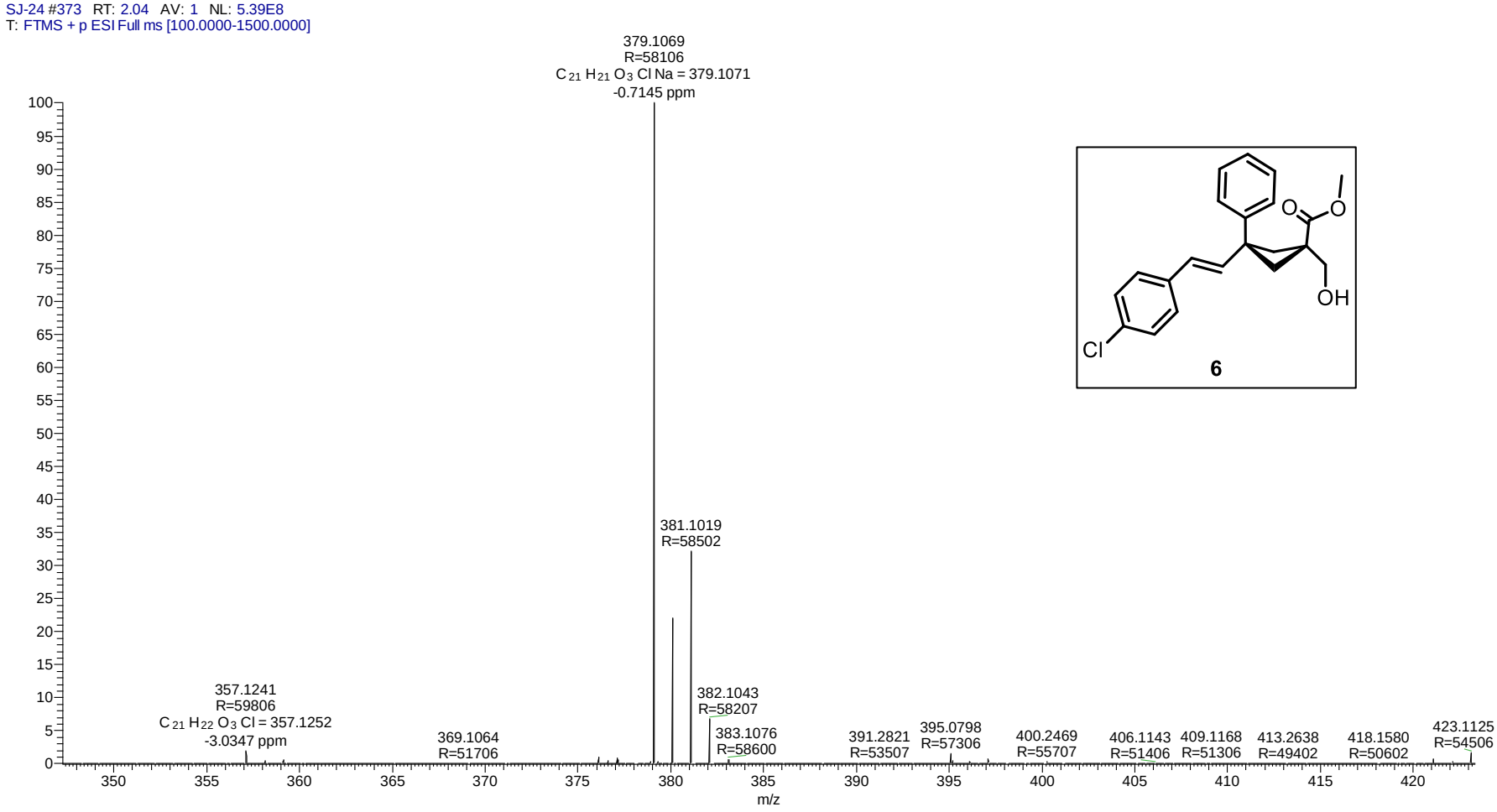
^{1}H NMR (400 MHz, $CDCl_3$) spectrum of Methyl (1s,3s)-3-((*E*)-4-chlorostyryl)-1-(hydroxymethyl)-3-phenylcyclobutane-1-carboxylate (6)



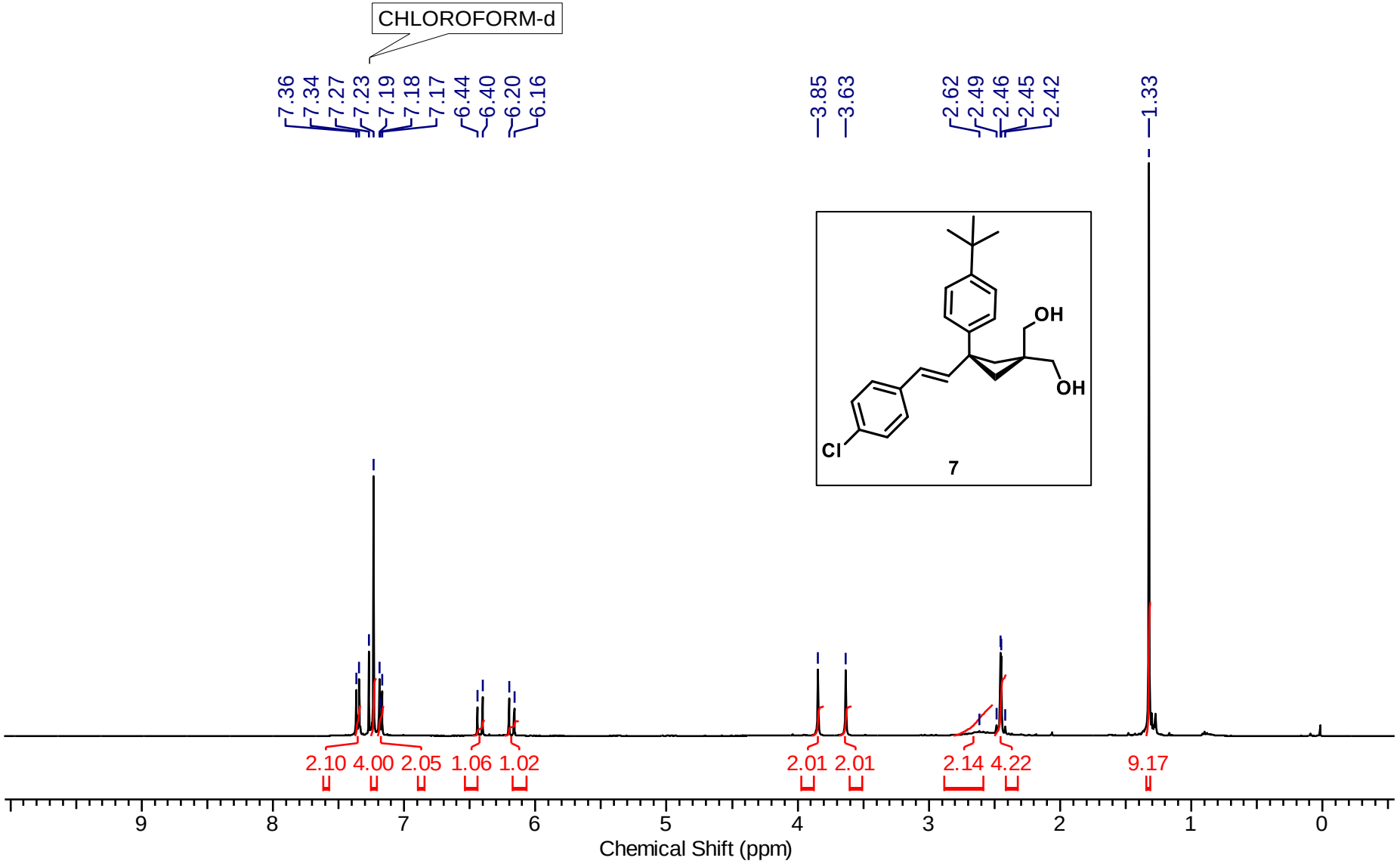
$^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) spectrum of Methyl (1s,3s)-3-((*E*)-4-chlorostyryl)-1-(hydroxymethyl)-3-phenylcyclobutane-1-carboxylate (6)



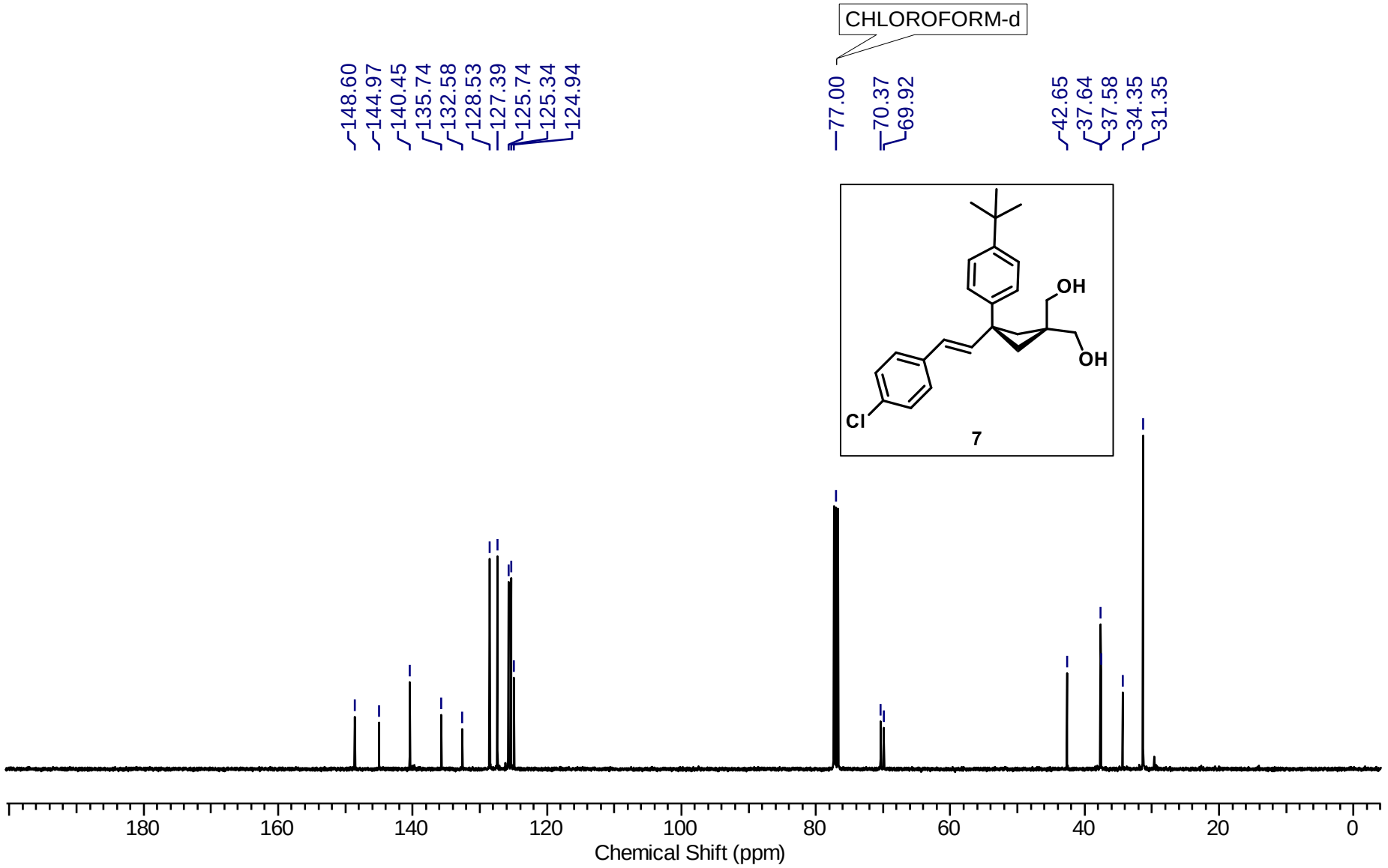
HRMS spectrum of Methyl (1s,3s)-3-((*E*)-4-chlorostyryl)-1-(hydroxymethyl)-3-phenylcyclobutane-1-carboxylate (6)



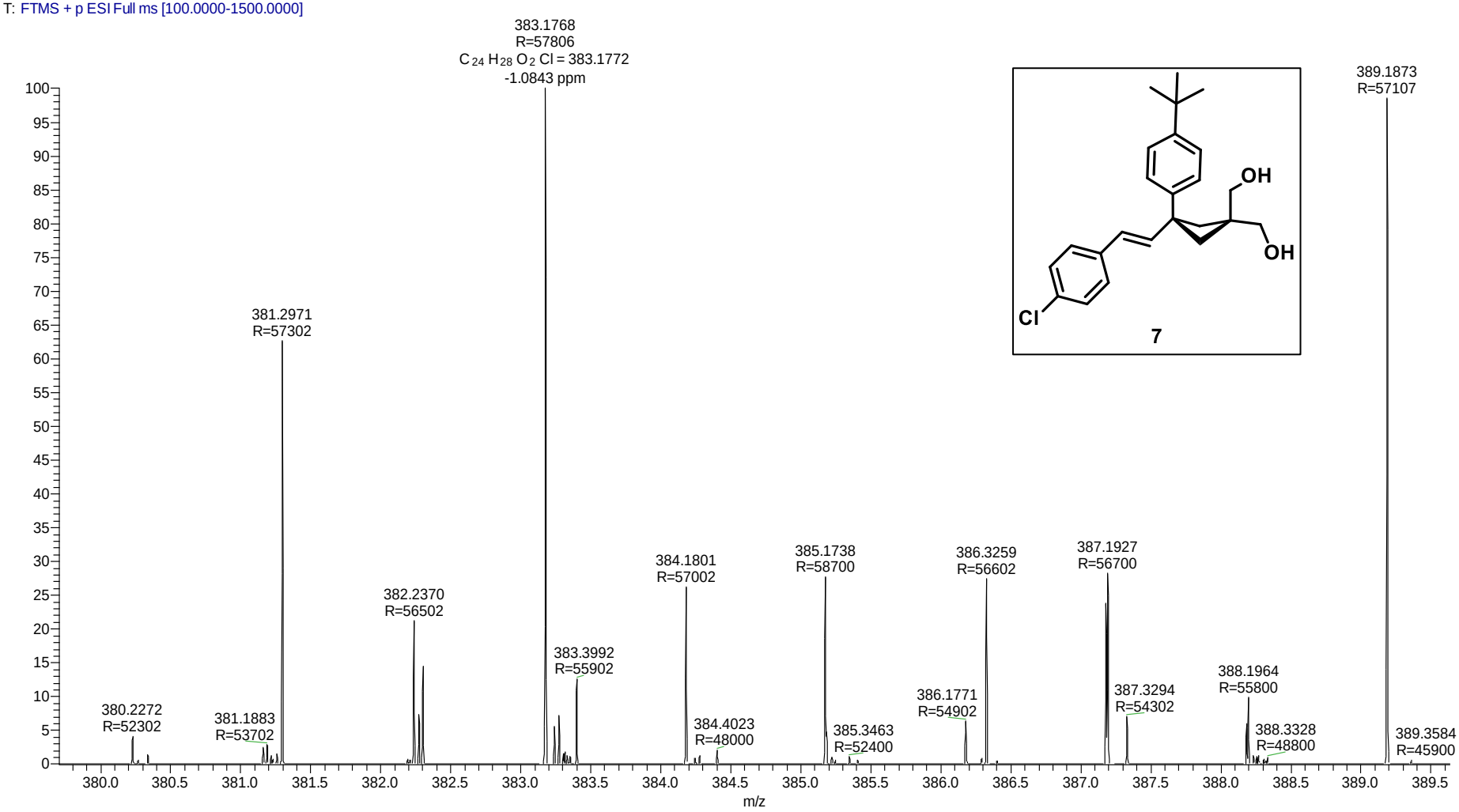
^{1}H fNMR (400 MHz, $CDCl_3$) spectrum of (*E*)-(3-(4-(*tert*-butyl)phenyl)-3-(4-chlorostyryl)cyclobutane-1,1-diyl)dimethanol (7)



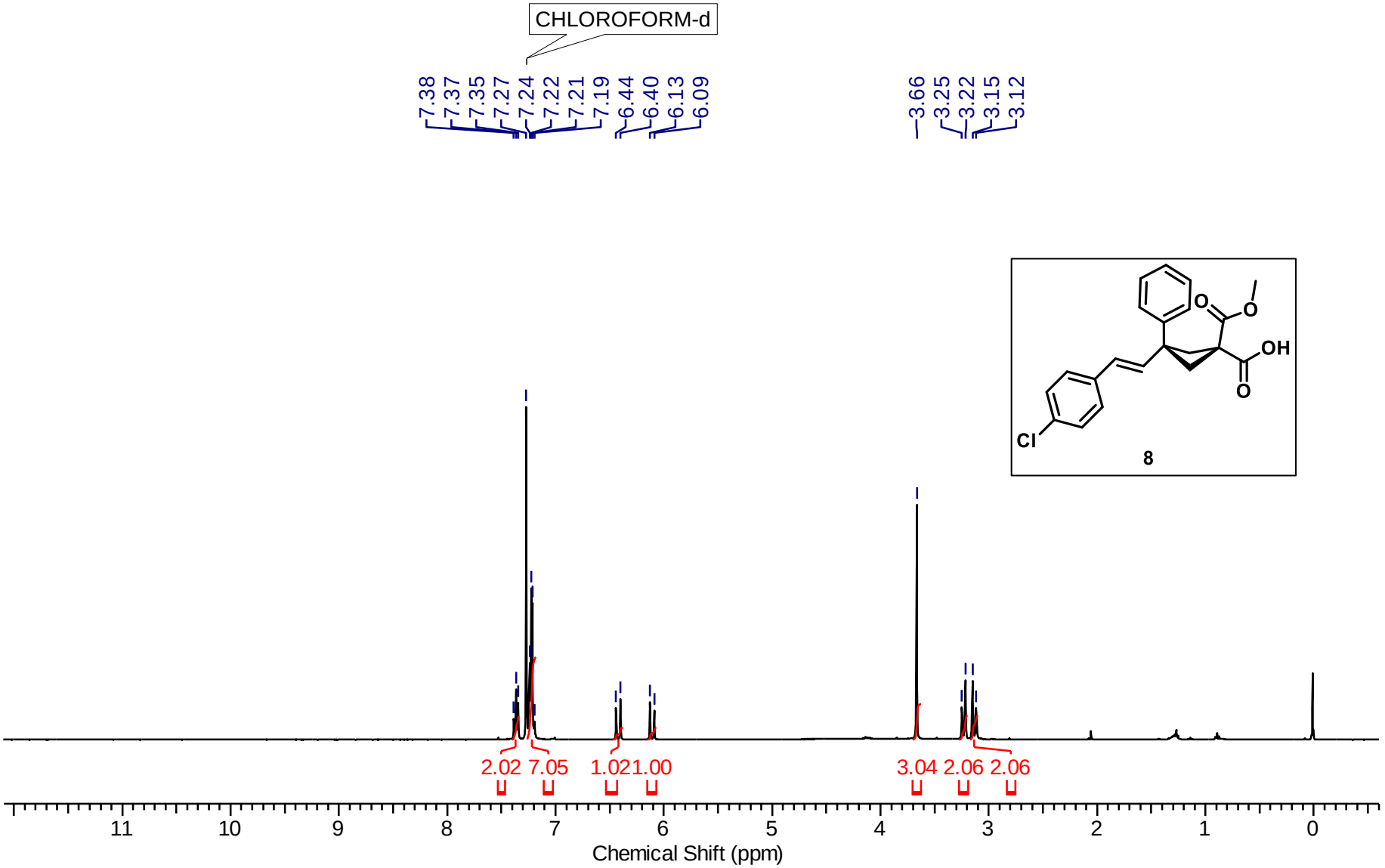
$^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) spectrum of (*E*)-(3-(4-(*tert*-butyl)phenyl)-3-(4-chlorostyryl)cyclobutane-1,1-diyl)dimethanol (7)



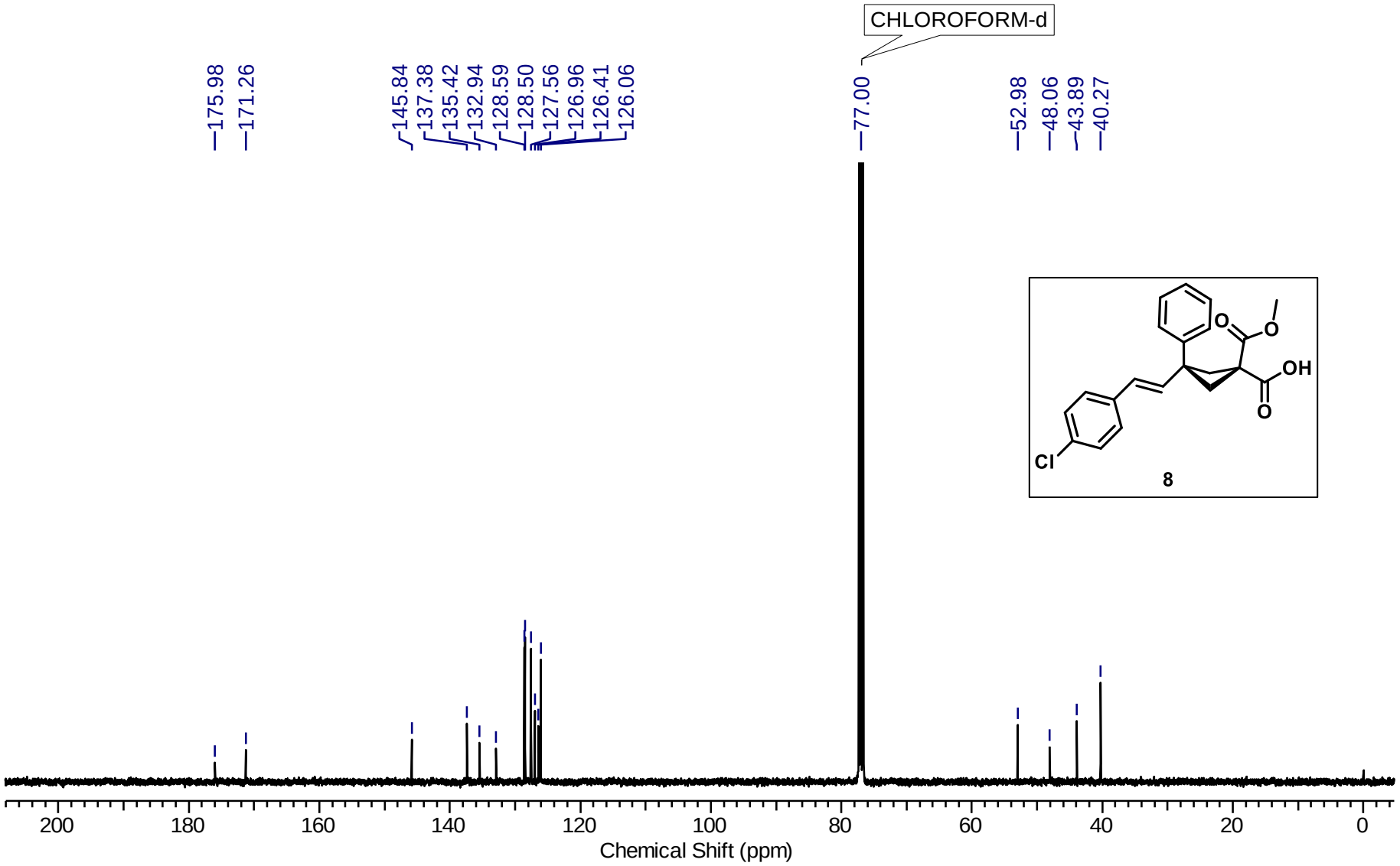
HRMS spectrum of (*E*)-(3-(4-(*tert*-butyl)phenyl)-3-(4-chlorostyryl)cyclobutane-1,1-diyl)dimethanol (7)



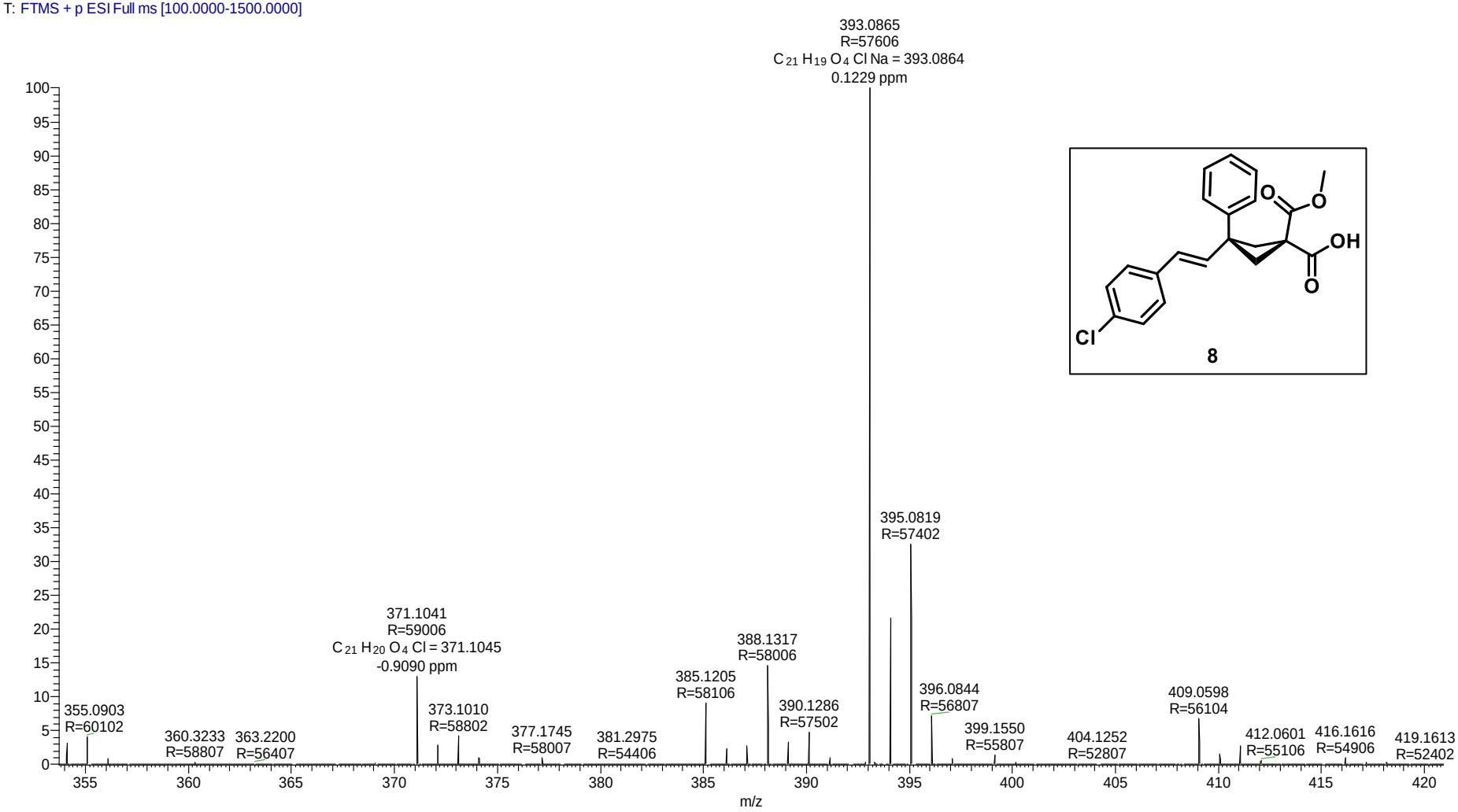
^{1}H NMR (400 MHz, $CDCl_3$) spectrum of (1s,3s)-3-((*E*)-4-chlorostyryl)-1-(methoxycarbonyl)-3-phenylcyclobutane-1-carboxylic acid (8)



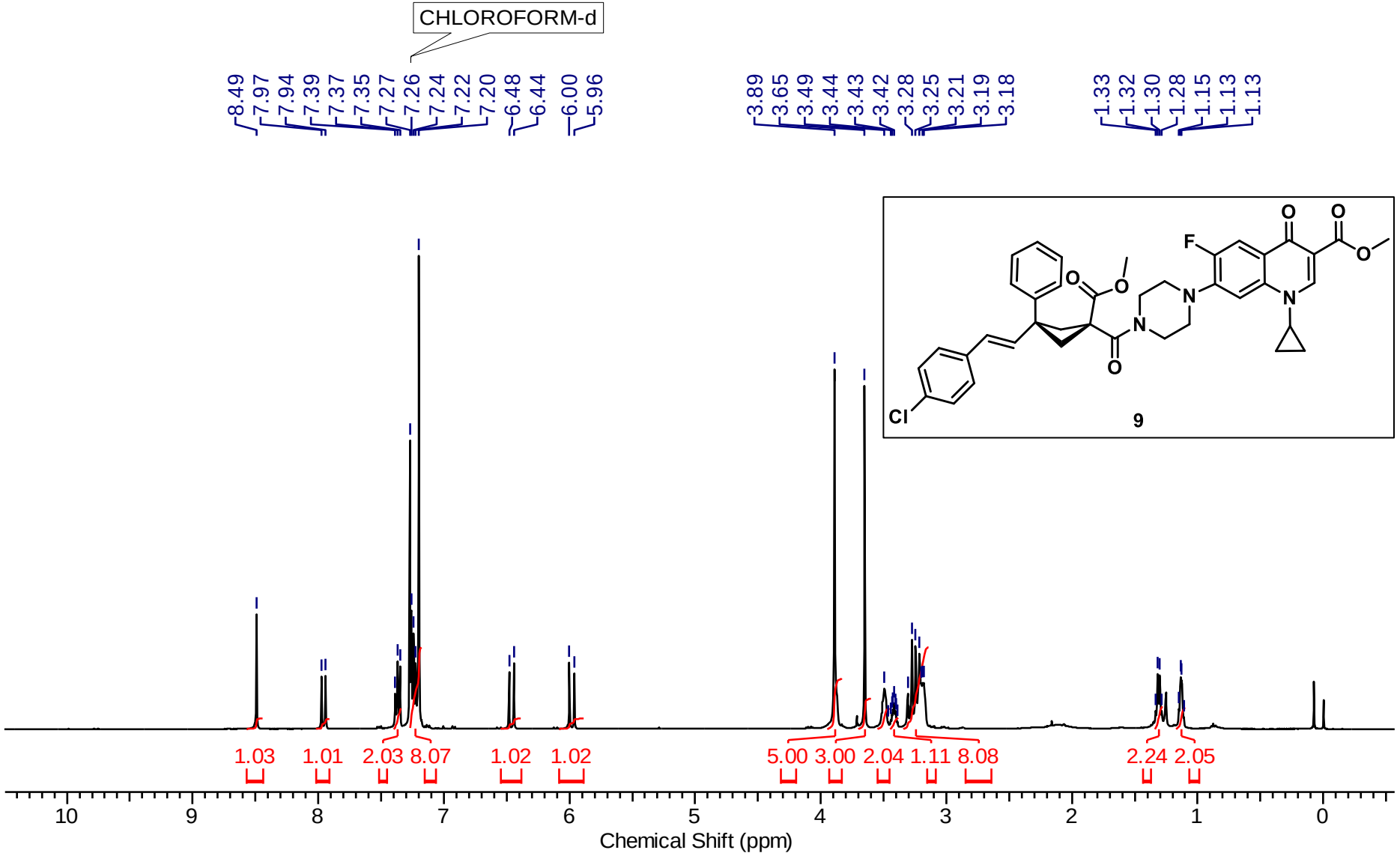
$^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) spectrum of (1s,3s)-3-((*E*)-4-chlorostyryl)-1-(methoxycarbonyl)-3-phenylcyclobutane-1-carboxylic acid (8)



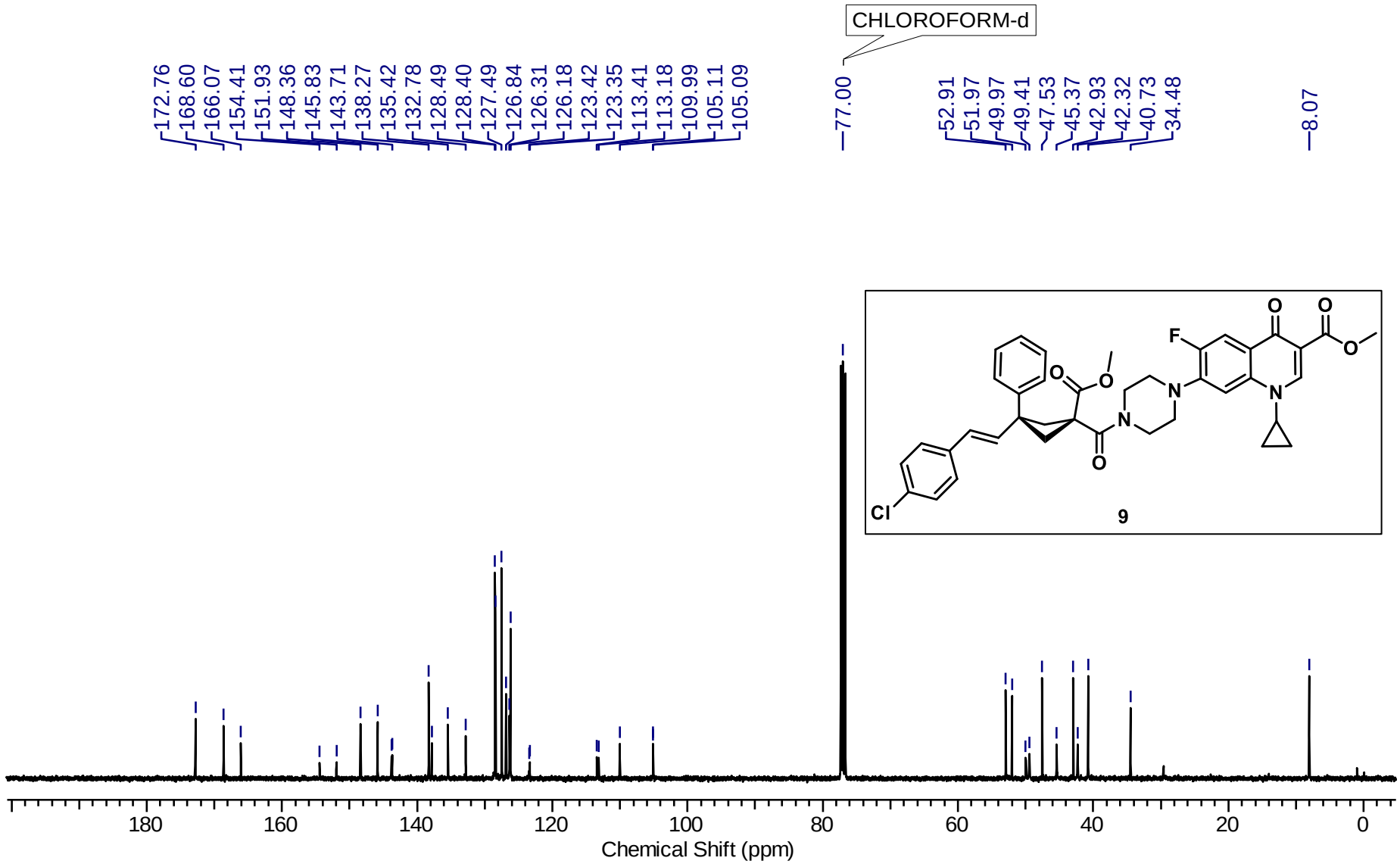
HRMS spectrum of (1s,3s)-3-((*E*)-4-chlorostyryl)-1-(methoxycarbonyl)-3-phenylcyclobutane-1-carboxylic acid (8)



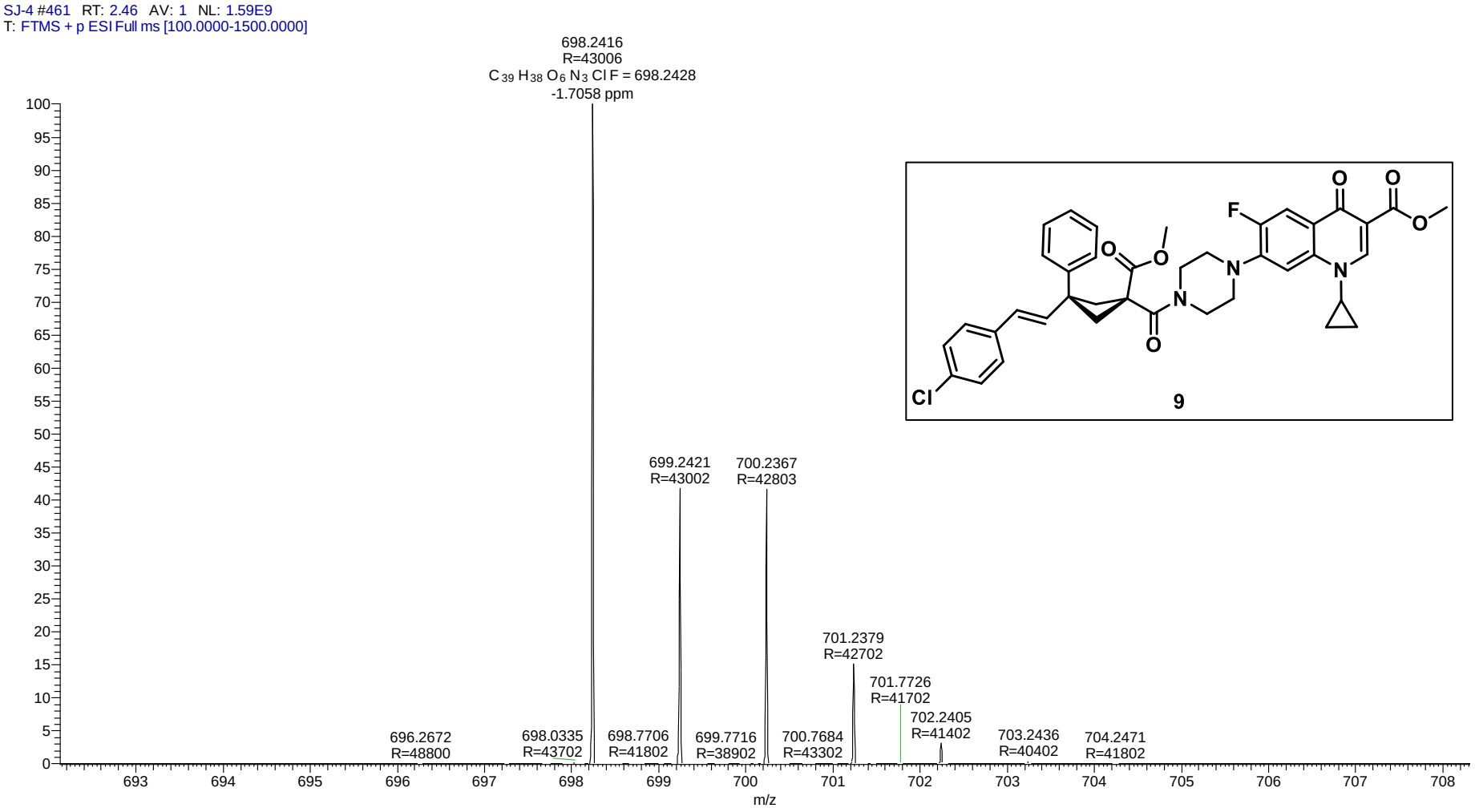
^{1}H NMR (400 MHz, $CDCl_3$) spectrum of Methyl 7-(4-((1s,3s)-3-((E)-4-chlorostyryl)-1-(methoxycarbonyl)-3-phenylcyclobutane-1-carbonyl)piperazin-1-yl)-1-cyclopropyl-6-fluoro-4-oxo-1,4-dihydroquinoline-3-carboxylate (9)



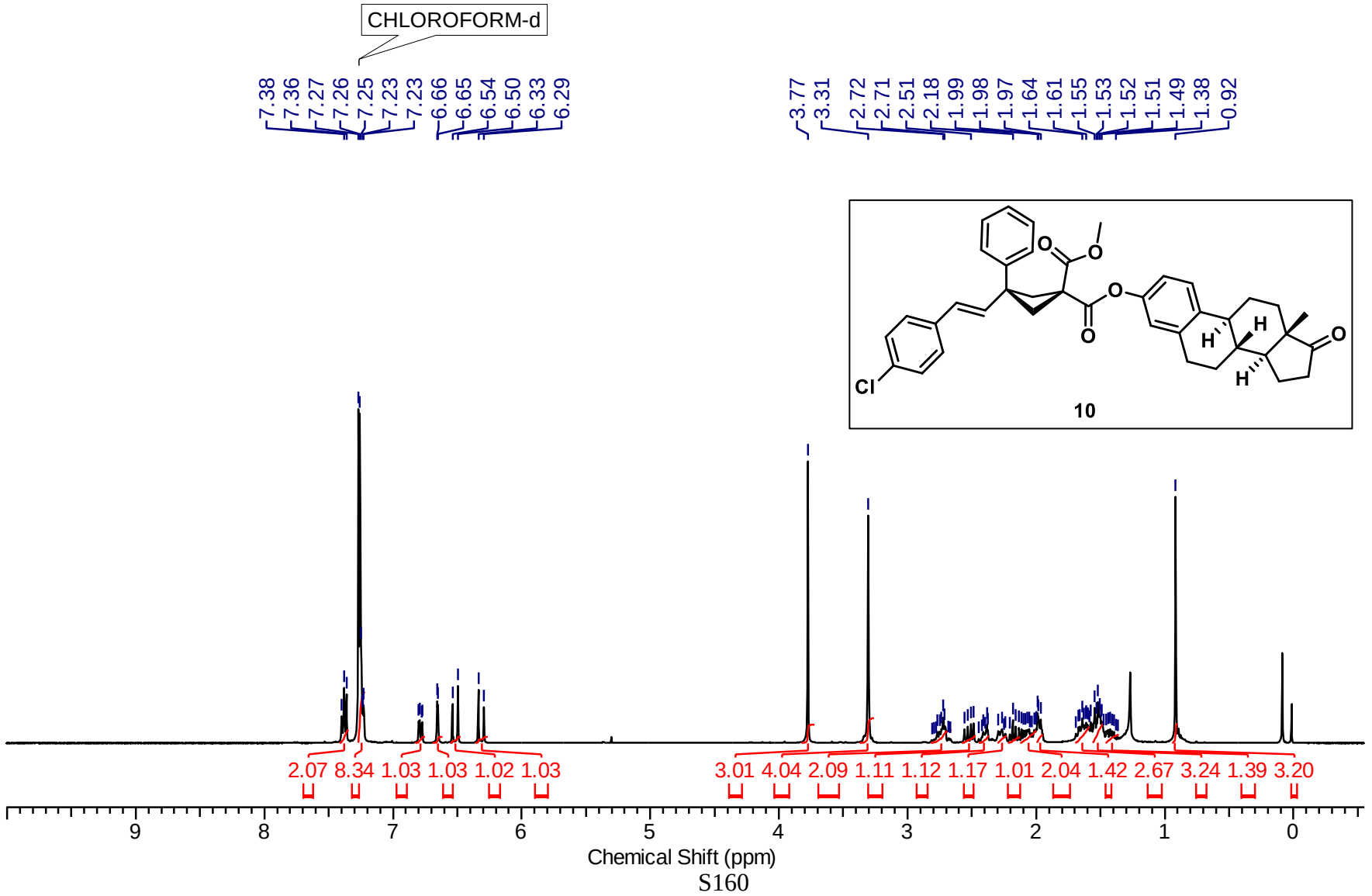
$^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) spectrum of Methyl 7-(4-((1s,3s)-3-((E)-4-chlorostyryl)-1-(methoxycarbonyl)-3-phenylcyclobutane-1-carbonyl)piperazin-1-yl)-1-cyclopropyl-6-fluoro-4-oxo-1,4-dihydroquinoline-3-carboxylate (9)



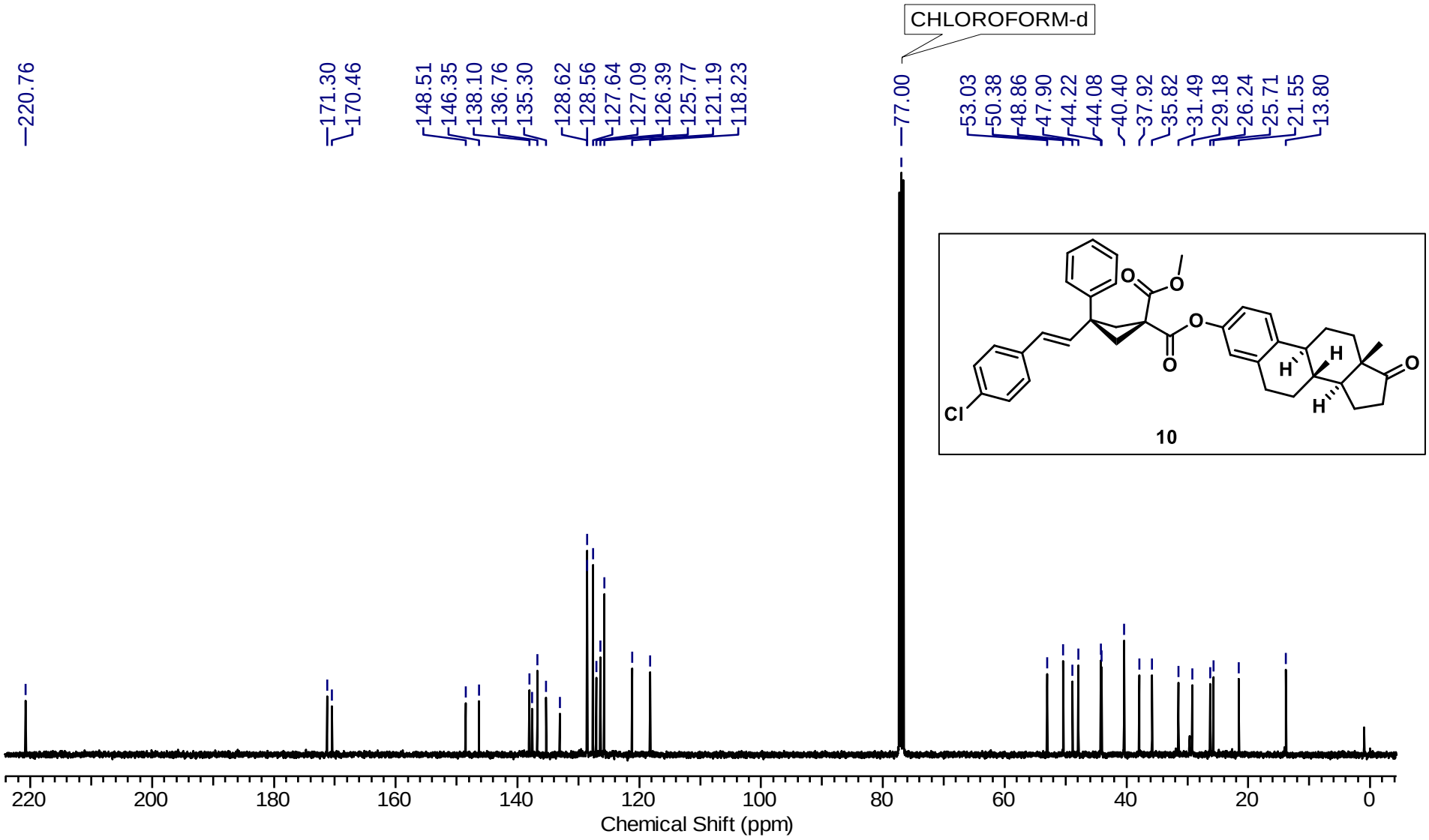
HRMS spectrum of Methyl 7-(4-((1s,3s)-3-((E)-4-chlorostyryl)-1-(methoxycarbonyl)-3-phenylcyclobutane-1-carbonyl)piperazin-1-yl)-1-cyclopropyl-6-fluoro-4-oxo-1,4-dihydroquinoline-3-carboxylate (9)



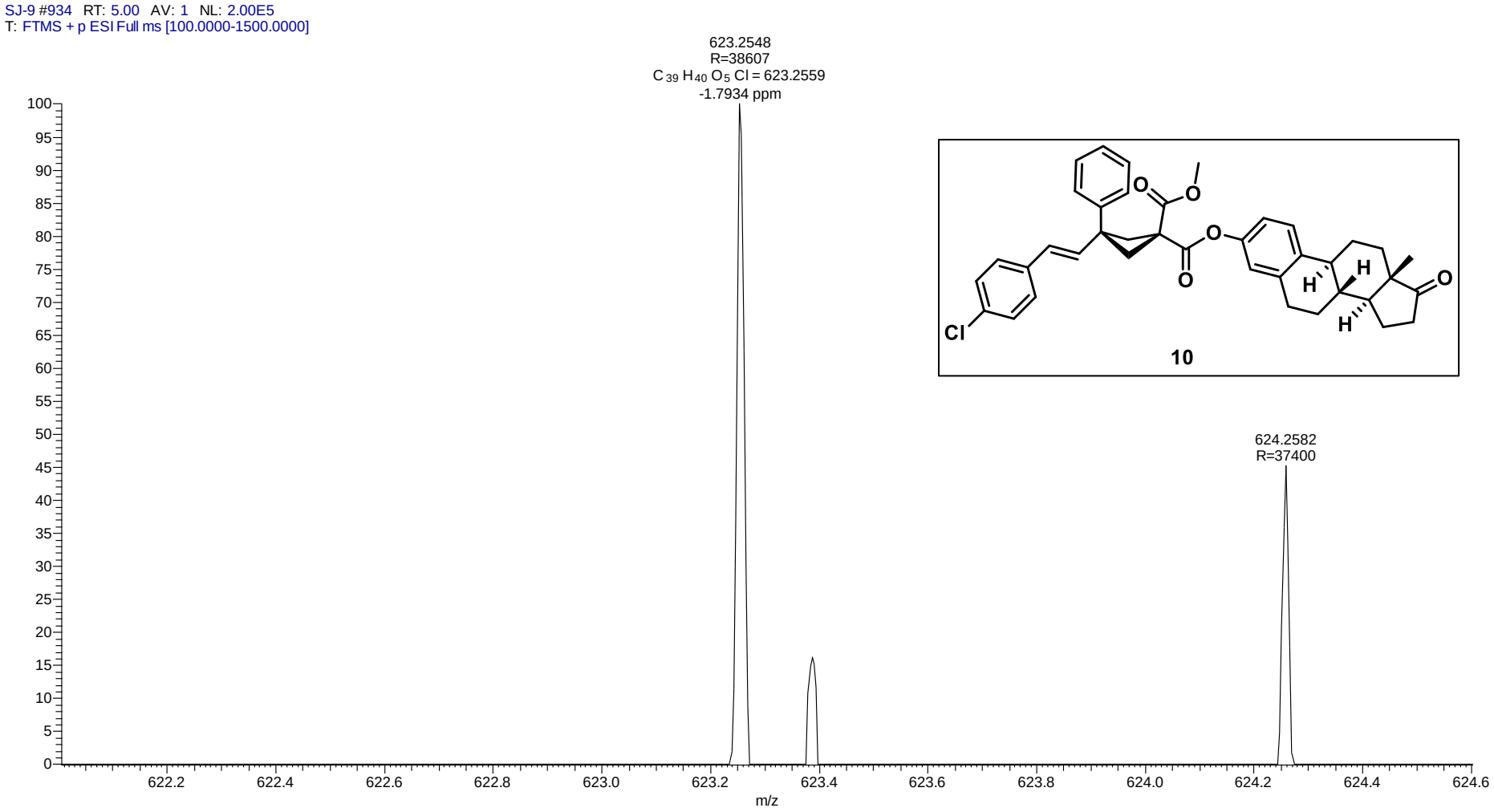
^{1}H NMR (400 MHz, $CDCl_3$) spectrum of 1-Methyl 1-((8R,9S,13S,14S)-13-methyl-17-oxo-7,8,9,11,12,13,14,15,16,17-decahydro-6H-cyclopenta[a]phenanthren-3-yl) (1r,3S)-3-((E)-4-chlorostyryl)-3-phenylcyclobutane-1,1-dicarboxylate (10)



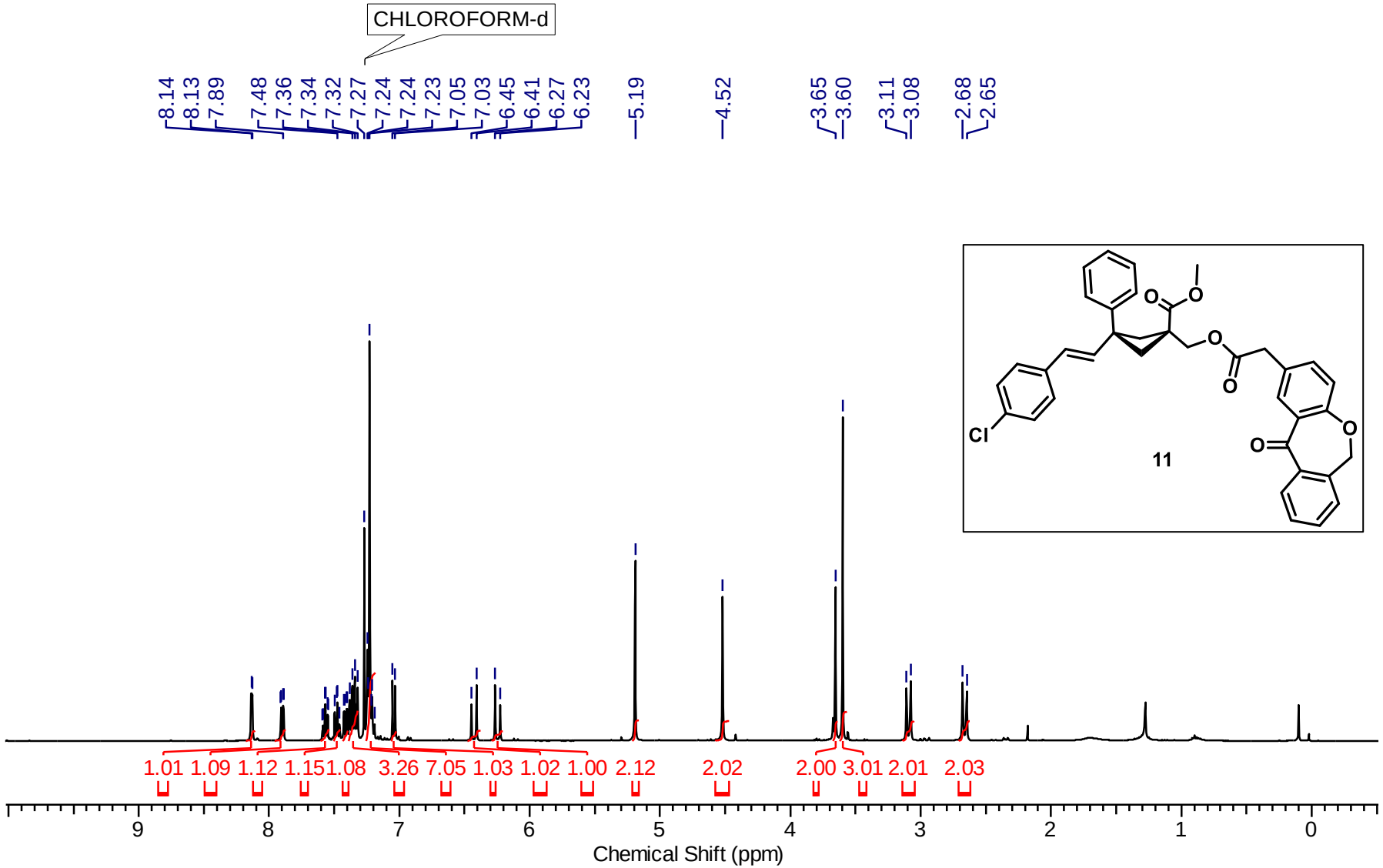
$^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) spectrum of 1-Methyl 1-((8R,9S,13S,14S)-13-methyl-17-oxo-7,8,9,11,12,13,14,15,16,17-decahydro-6H-cyclopenta[a]phenanthren-3-yl) (1r,3S)-3-((E)-4-chlorostyryl)-3-phenylcyclobutane-1,1-dicarboxylate (10)



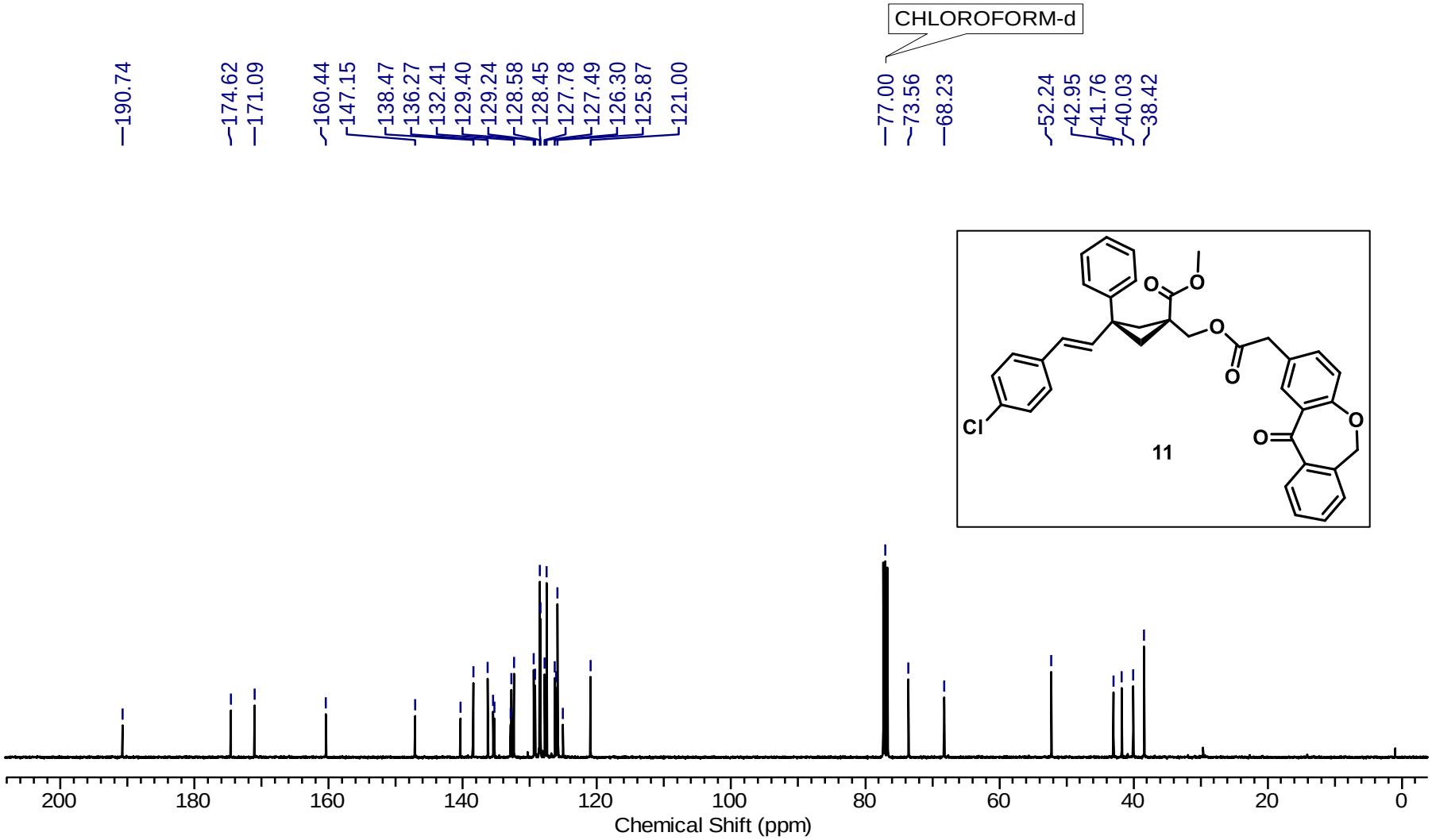
HRMS spectrum of 1-Methyl 1-((8R,9S,13S,14S)-13-methyl-17-oxo-7,8,9,11,12,13,14,15,16,17-decahydro-6H-cyclopenta[a]phenanthren-3-yl) (1r,3S)-3-((E)-4-chlorostyryl)-3-phenylcyclobutane-1,1-dicarboxylate (10)



^{1}H NMR (400 MHz, $CDCl_3$) spectrum of Methyl (1s,3s)-3-((E)-4-chlorostyryl)-1-((2-(11-oxo-6,11-dihydrodibenzo[b,e]oxepin-2-yl) acetoxy)methyl)-3-phenylcyclobutane-1-carboxylate (11)



$^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) spectrum of Methyl (1s,3s)-3-((E)-4-chlorostyryl)-1-((2-(11-oxo-6,11-dihydrodibenzo[b,e]oxepin-2-yl) acetoxy)methyl)-3-phenylcyclobutane-1-carboxylate (11)



HRMS spectrum of Methyl (1s,3s)-3-((E)-4-chlorostyryl)-1-((2-(11-oxo-6,11-dihydrodibenzo[b,e]oxepin-2-yl)acetoxy)methyl)-3-phenylcyclobutane-1-carboxylate (11)

