# Tandem $\alpha$-Arylation/Cyclization of 4-Haloacetoacetates with Arynes: A Metal-Free Approach towards 4-Aryl-3-(2*H*)-Furanones

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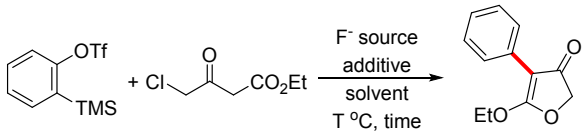
## 1. Synthesis of 4-aryl-3(2*H*)-furanones

### 1.1. Optimization of 4-aryl-3(2*H*)-furanone synthesis

Our optimization studies with **1a** and **2a** commenced with the screening of $F^-$ sources such as CsF, KF/18C-6 and TBAF; the combination of KF/18C-6 afforded 4-phenyl-3(2*H*)-furanone in the highest yield (entries 1-3). We then checked the efficacy of different additives such as $K_2CO_3$, $Na_2CO_3$ and $NaHCO_3$ (entries 4-6). These reactions were performed with 3 equivalents of KF/18C-6 and 2 equivalents of the additive. Disappointingly, none of the reactions with additives resulted in yield improvement. Next, we screened different solvents such as $CH_3CN$, THF, DMF, DME and 1,4-dioxane. From the solvent optimization, $CH_3CN$ was found afford **3** in the best yield (entries 2, 7-10). A slight improvement in the yield of 4-phenyl-3-(2*H*)-furanone was observed by increasing the amount of benzyne precursor **2a** to 1.25 equivalents (entry 11). Finally we studied the effect of temperature on the outcome of the reaction. For this we started the reaction at 0 $^oC$ and allowed the reaction mixture to attain ambient temperature gradually; from this reaction the expected furanone **3** was isolated in 70 % yield (entry 12). Thus the optimized conditions for the reaction was found to be a combination of 1.25 equivalents of benzyne precursor, 1.0 equivalent of 4-haloacetoacetate, 5.0 equivalents of KF/18C-6 in $CH_3CN$ at 0 $^oC$, and subsequent stirring at room temperature for 5 h.




**1a** **2a** **3**

| Entry | $F^-$ source | Additive | Solvent | Yield of **3** (%)[a] |
|---|---|---|---|---|
| 1 | CsF | - | $CH_3CN$ | 27 |
| 2 | KF/18C-6 | - | $CH_3CN$ | 51 |
| 3 | TBAF | - | $CH_3CN$ | 46 |
| 4 | KF/18C-6 | $K_2CO_3$ | $CH_3CN$ | 43[b] |
| 5 | KF/18C-6 | $Na_2CO_3$ | $CH_3CN$ | 32[b] |
| 6 | KF/18C-6 | $NaHCO_3$ | $CH_3CN$ | 21[b] |
| 7 | KF/18C-6 | - | THF | 36 |
| 8 | KF/18C-6 | - | DMF | 16 |
| 9 | KF/18C-6 | - | DME | 43 |
| 10 | KF/18C-6 | - | 1,4-dioxane | 46 |
| 11 | KF/18C-6 | - | $CH_3CN$ | 61[c] |
| **12** | **KF/18C-6** | **-** | **$CH_3CN$** | **70[d]** |

[a]Reaction conditions: **1a** (1.0 equiv., 0.6 mmol), **2a** (1.0 equiv., 0.6 mmol), $F^-$ source (5.0 equiv.), solvent (4.0 mL), rt, 4 h, isolated yield. [b] $F^-$ source (3.0 equiv.), additive (2.0 equiv.). [c] **1a** (1.25 equiv.), **2a** (1.0equiv.). [d] 0 °C - rt, 5 h.

## 1.2. Optimized procedure for synthesis of 4-aryl-3(2*H*)-furanones

Potassium fluoride (KF) (5.0 equiv) and 18-crown-6 (5.0 equiv) were weighed into a dry Schlenk tube. The tube was degassed and purged three times with $N_2$. Anhydrous $CH_3CN$ (4.0 mL) was added under $N_2$, after which the reaction mixture was cooled to 0 °C. Then, the benzyne precursor (1.25 equiv.) followed by 4-haloacetoacetate (1.0 equiv.) were added to the reaction mixture and stirred at 0 °C, after which the mixture was allowed to warm to RT. Upon completion of the reaction (5 h), the solvent was removed and the

residue was subjected to column chromatography on silica gel (100-200 mesh), using mixtures of hexanes/ethyl acetate as eluents, affording 4-aryl-3(2*H*)-furanones.

### 1.3. Procedure for the gram scale preparation of 4-aryl-3(2*H*)-furanone 4

Following the general experimental procedure, 2-(trimethylsilyl) phenyl trifluoromethanesulfonate **1a** (3.72 g, 1.25 equiv.), methyl-4-chloroacetoacetate **2b** (1.5 g, 9.9 mmol), KF (2.88 g, 5.0 equiv.), 18C-6 (13.08 g, 5.0 equiv.) in $CH_3CN$ (60 mL) at 0 $^oC$ and subsequent stirring at room temperature for 5 h. The crude product was purified over silica gel (100-200 mesh) column chromatography (30% ethyl acetate in hexanes) to afford the desired product **4** as an off-white solid (1.29 g, 69%).

## 2. DFT Calculations

The geometry optimizations were done at M06L/SMD/6-311G(d,p) level density functional theory.[1-3] M06L stands for the Minnesota 2006 local exchange−correlation functional[1] while SMD describes the self-consistent reaction field method to simulate the implicit solvation effect.[2] The selected solvent is acetonitrile. M06L functional is regarded as one of the most accurate local functionals currently available for describing energy barriers and non-covalent interactions.[1,3] All the transition states were characterized by a single imaginary frequency along the reaction coordinate, whereas all the intermediates were confirmed to be a minimum by locating zero imaginary frequency in the vibrational frequency analysis. All the calculations were done with the *Gaussian 16* suite of programmes.[4]

**Coordinates of Optimized Geometries in Å followed by energy parameters in au.**

**a**

| | | | |
|---|---|---|---|
| C | -1.593890000 | -0.127224000 | 0.101975000 |
| C | -0.581852000 | 0.137841000 | -0.962809000 |
| H | -0.376662000 | 1.247359000 | -0.912828000 |
| C | 0.771946000 | -0.485861000 | -0.721238000 |
| C | 1.489898000 | 0.173143000 | 0.418541000 |
| H | 0.944648000 | -0.002661000 | 1.347886000 |
| H | 1.446337000 | 1.263860000 | 0.214119000 |

| | | | |
|---|---|---|---|
| O | 1.245190000 | -1.336250000 | -1.443298000 |
| O | -1.383679000 | -0.213910000 | 1.292974000 |
| O | -2.826582000 | -0.223197000 | -0.431265000 |
| C | -3.885937000 | -0.407522000 | 0.518457000 |
| H | -3.745730000 | -1.332313000 | 1.081382000 |
| H | -3.933736000 | 0.432335000 | 1.214372000 |
| H | -4.801562000 | -0.461030000 | -0.066552000 |
| Cl | 3.176598000 | -0.393199000 | 0.636547000 |
| H | -0.960776000 | -0.160495000 | -1.940061000 |
| F | 0.438321000 | 2.682436000 | -0.359606000 |

Zero-point correction= 0.118756
Thermal correction to Energy= 0.130596
Thermal correction to Enthalpy= 0.13154
Thermal correction to Gibbs Free Energy= 0.078494
Sum of electronic and zero-point Energies= -980.562306
Sum of electronic and thermal Energies= -980.550466
Sum of electronic and thermal Enthalpies= -980.549522
Sum of electronic and thermal Free Energies= -980.602567
SCF Energy -980.681062

**TS1**

| | | | |
|---|---|---|---|
| C | 1.521127000 | -0.245636000 | 0.080157000 |
| C | 0.538094000 | 0.650126000 | 0.693713000 |
| H | 0.399851000 | 1.507957000 | -0.243638000 |
| C | -0.864180000 | 0.230683000 | 0.828139000 |
| C | -1.430586000 | -0.428809000 | -0.417631000 |
| H | -0.979106000 | -1.404356000 | -0.591329000 |
| H | -1.194576000 | 0.216116000 | -1.267560000 |
| O | -1.556676000 | 0.513349000 | 1.790759000 |
| O | 1.327488000 | -1.109913000 | -0.755919000 |
| O | 2.772114000 | 0.054099000 | 0.520517000 |
| C | 3.822195000 | -0.699352000 | -0.089181000 |
| H | 3.708246000 | -1.767750000 | 0.109042000 |

| | | | |
|---|---|---|---|
| H | 3.844973000 | -0.541096000 | -1.169990000 |
| H | 4.746934000 | -0.337723000 | 0.357200000 |
| Cl | -3.209931000 | -0.648930000 | -0.351805000 |
| H | 0.904641000 | 1.126395000 | 1.601738000 |
| F | 0.141618000 | 2.169989000 | -1.314314000 |

Zero-point correction= 0.114119
Thermal correction to Energy= 0.125659
Thermal correction to Enthalpy= 0.126603
Thermal correction to Gibbs Free Energy= 0.074483
Sum of electronic and zero-point Energies= -980.564001
Sum of electronic and thermal Energies= -980.552462
Sum of electronic and thermal Enthalpies= -980.551518
Sum of electronic and thermal Free Energies= -980.603638
SCF Energy -980.67812

**b**

| | | | |
|---|---|---|---|
| C | 1.472268000 | -0.273536000 | 0.204679000 |
| C | 0.513762000 | 0.597759000 | 0.805066000 |
| H | 0.456291000 | 1.587032000 | -0.751356000 |
| C | -0.900009000 | 0.413025000 | 0.776080000 |
| C | -1.408736000 | -0.645856000 | -0.211657000 |
| H | -1.088913000 | -1.648185000 | 0.071983000 |
| H | -1.039350000 | -0.458170000 | -1.219161000 |
| O | -1.696152000 | 1.072180000 | 1.450543000 |
| O | 1.284100000 | -1.210558000 | -0.566642000 |
| O | 2.754529000 | 0.080687000 | 0.569675000 |
| C | 3.780642000 | -0.700891000 | -0.027915000 |
| H | 3.696448000 | -1.756801000 | 0.245394000 |
| H | 3.762638000 | -0.624417000 | -1.119108000 |
| H | 4.722269000 | -0.302339000 | 0.349154000 |
| Cl | -3.209394000 | -0.684629000 | -0.314343000 |
| H | 0.881828000 | 1.307663000 | 1.540164000 |

| | | | |
|---|---|---|---|
| F | 0.409011000 | 1.961382000 | -1.631039000 |

| | |
|---|---|
| Zero-point correction= | 0.117572 |
| Thermal correction to Energy= | 0.129591 |
| Thermal correction to Enthalpy= | 0.130535 |
| Thermal correction to Gibbs Free Energy= | 0.077321 |
| Sum of electronic and zero-point Energies= | -980.571639 |
| Sum of electronic and thermal Energies= | -980.55962 |
| Sum of electronic and thermal Enthalpies= | -980.558676 |
| Sum of electronic and thermal Free Energies= | -980.61189 |
| SCF Energy | -980.689211 |

**c**

| | | | |
|---|---|---|---|
| C | 0.404752000 | -1.783775000 | -0.016596000 |
| C | 0.089601000 | -0.559602000 | 0.796686000 |
| H | 0.341797000 | -0.750004000 | 1.840283000 |
| C | -1.370104000 | -0.133751000 | 0.788466000 |
| C | -2.045328000 | -0.047582000 | -0.563697000 |
| H | -2.264726000 | -1.052177000 | -0.926529000 |
| H | -1.403947000 | 0.438010000 | -1.299283000 |
| O | -1.930978000 | 0.170234000 | 1.816132000 |
| O | -0.114894000 | -2.113797000 | -1.061454000 |
| O | 1.404006000 | -2.472267000 | 0.556571000 |
| C | 1.848098000 | -3.626482000 | -0.172961000 |
| H | 1.036709000 | -4.347826000 | -0.285668000 |
| H | 2.215978000 | -3.339719000 | -1.159952000 |
| H | 2.653607000 | -4.057111000 | 0.417506000 |
| Cl | -3.590396000 | 0.856184000 | -0.505796000 |
| C | 1.210581000 | 0.825599000 | -1.010432000 |
| C | 0.956186000 | 0.651102000 | 0.357887000 |
| C | 1.978056000 | 1.905802000 | -1.437473000 |
| H | 2.188398000 | 2.044467000 | -2.494558000 |
| C | 1.418830000 | 1.512772000 | 1.378627000 |
| C | 2.470980000 | 2.795538000 | -0.486227000 |

| | | | |
|---|---|---|---|
| H | 3.074231000 | 3.645619000 | -0.803613000 |
| C | 2.187851000 | 2.585138000 | 0.866670000 |
| H | 2.604955000 | 3.318323000 | 1.565440000 |
| H | 0.827657000 | 0.123384000 | -1.750783000 |

Zero-point correction= 0.18531
Thermal correction to Energy= 0.199931
Thermal correction to Enthalpy= 0.200875
Thermal correction to Gibbs Free Energy= 0.140973
Sum of electronic and zero-point Energies= -1111.028798
Sum of electronic and thermal Energies= -1111.014176
Sum of electronic and thermal Enthalpies= -1111.013232
Sum of electronic and thermal Free Energies= -1111.073135
SCF Energy -1111.214108

**d**

| | | | |
|---|---|---|---|
| C | 0.042018000 | -1.835640000 | 0.058438000 |
| C | -0.061191000 | -0.353039000 | 0.282062000 |
| H | -0.350532000 | -0.186109000 | 1.344090000 |
| C | -1.237987000 | 0.186385000 | -0.549395000 |
| C | -2.477444000 | 0.276984000 | 0.282838000 |
| H | -2.207936000 | 0.822658000 | 1.211099000 |
| H | -2.773732000 | -0.732308000 | 0.585506000 |
| O | -1.135469000 | 0.533212000 | -1.701370000 |
| O | -0.838489000 | -2.527019000 | -0.407268000 |
| O | 1.212518000 | -2.322684000 | 0.496489000 |
| C | 1.369251000 | -3.743454000 | 0.366479000 |
| H | 0.608931000 | -4.271122000 | 0.945269000 |
| H | 1.299251000 | -4.044963000 | -0.680345000 |
| H | 2.359847000 | -3.968300000 | 0.755491000 |
| Cl | -3.867254000 | 1.031515000 | -0.556219000 |
| C | 2.014522000 | 0.227339000 | -1.066903000 |
| C | 1.185859000 | 0.453345000 | 0.034697000 |
| C | 3.129581000 | 1.030467000 | -1.281557000 |

| | | | |
|---|---|---|---|
| H | 3.772218000 | 0.844467000 | -2.136915000 |
| C | 1.476594000 | 1.505359000 | 0.906794000 |
| C | 3.423064000 | 2.071899000 | -0.403126000 |
| H | 4.295167000 | 2.696176000 | -0.572201000 |
| C | 2.592958000 | 2.308053000 | 0.689444000 |
| H | 2.815877000 | 3.120575000 | 1.374928000 |
| H | 1.789588000 | -0.582979000 | -1.755539000 |
| H | 0.792769000 | 1.659009000 | 1.742368000 |
| F | -1.034440000 | 0.985875000 | 2.624504000 |

Zero-point correction= 0.199829
Thermal correction to Energy= 0.216331
Thermal correction to Enthalpy= 0.217275
Thermal correction to Gibbs Free Energy= 0.153265
Sum of electronic and zero-point Energies= -1211.56347
Sum of electronic and thermal Energies= -1211.546968
Sum of electronic and thermal Enthalpies= -1211.546024
Sum of electronic and thermal Free Energies= -1211.610034
SCF Energy -1211.763299

**TS2**

| | | | |
|---|---|---|---|
| C | 0.215880000 | 1.671105000 | -0.116729000 |
| C | 0.117252000 | 0.227042000 | 0.174202000 |
| H | 0.341707000 | 0.211661000 | 1.418312000 |
| C | 1.233147000 | -0.647659000 | -0.265485000 |
| C | 2.628487000 | -0.043733000 | -0.199913000 |
| H | 2.788941000 | 0.461355000 | 0.752634000 |
| H | 2.778138000 | 0.685596000 | -0.994334000 |
| O | 1.065210000 | -1.818046000 | -0.558474000 |
| O | 1.234951000 | 2.314478000 | -0.293276000 |
| O | -1.001978000 | 2.265108000 | -0.082016000 |
| C | -0.988827000 | 3.683468000 | -0.263931000 |
| H | -0.412152000 | 4.175089000 | 0.522805000 |
| H | -0.565938000 | 3.951915000 | -1.234538000 |

| | | | |
|---|---|---|---|
| H | -2.029505000 | 3.998484000 | -0.213339000 |
| Cl | 3.916491000 | -1.287894000 | -0.369828000 |
| C | -1.859338000 | -0.462102000 | -1.252911000 |
| C | -1.233193000 | -0.411581000 | -0.003726000 |
| C | -3.094609000 | -1.080899000 | -1.405842000 |
| H | -3.568281000 | -1.110353000 | -2.382893000 |
| C | -1.871120000 | -1.003710000 | 1.087868000 |
| C | -3.724938000 | -1.665863000 | -0.308304000 |
| H | -4.689618000 | -2.149746000 | -0.427411000 |
| C | -3.108554000 | -1.625695000 | 0.938325000 |
| H | -3.591930000 | -2.079645000 | 1.798653000 |
| H | -1.370340000 | -0.008299000 | -2.111815000 |
| H | -1.372087000 | -0.958258000 | 2.052074000 |
| F | 0.537794000 | 0.086872000 | 2.697304000 |

Zero-point correction= 0.19447
Thermal correction to Energy= 0.210743
Thermal correction to Enthalpy= 0.211687
Thermal correction to Gibbs Free Energy= 0.147699
Sum of electronic and zero-point Energies= -1211.562583
Sum of electronic and thermal Energies= -1211.54631
Sum of electronic and thermal Enthalpies= -1211.545365
Sum of electronic and thermal Free Energies= -1211.609354
SCF Energy -1211.757053

**e**

| | | | |
|---|---|---|---|
| C | 0.227869000 | 1.630294000 | -0.193315000 |
| C | 0.072144000 | 0.198533000 | -0.160333000 |
| H | 0.459527000 | 0.229934000 | 1.688317000 |
| C | 1.199392000 | -0.683477000 | -0.338535000 |
| C | 2.591015000 | -0.038225000 | -0.366901000 |
| H | 2.769658000 | 0.584431000 | 0.508331000 |
| H | 2.737208000 | 0.582576000 | -1.249022000 |
| O | 1.101871000 | -1.909607000 | -0.433462000 |

| | | | |
|---|---|---|---|
| O | 1.261740000 | 2.271232000 | -0.362947000 |
| O | -0.950380000 | 2.291878000 | 0.061197000 |
| C | -0.848006000 | 3.710858000 | 0.071643000 |
| H | -0.169529000 | 4.058645000 | 0.855558000 |
| H | -0.495159000 | 4.096561000 | -0.888809000 |
| H | -1.853627000 | 4.081857000 | 0.267621000 |
| Cl | 3.906574000 | -1.278641000 | -0.390618000 |
| C | -2.301818000 | 0.004309000 | -1.009835000 |
| C | -1.275630000 | -0.423168000 | -0.153033000 |
| C | -3.552884000 | -0.603320000 | -1.005463000 |
| H | -4.324501000 | -0.247447000 | -1.682594000 |
| C | -1.561881000 | -1.499843000 | 0.701904000 |
| C | -3.816400000 | -1.668147000 | -0.147179000 |
| H | -4.792002000 | -2.144524000 | -0.143968000 |
| C | -2.809739000 | -2.113241000 | 0.706494000 |
| H | -2.998862000 | -2.940167000 | 1.385395000 |
| H | -2.111789000 | 0.829411000 | -1.689063000 |
| H | -0.786997000 | -1.853433000 | 1.374340000 |
| F | 0.700454000 | 0.238177000 | 2.607047000 |

Zero-point correction= 0.198142
Thermal correction to Energy= 0.214833
Thermal correction to Enthalpy= 0.215777
Thermal correction to Gibbs Free Energy= 0.151544
Sum of electronic and zero-point Energies= -1211.571905
Sum of electronic and thermal Energies= -1211.555214
Sum of electronic and thermal Enthalpies= -1211.55427
Sum of electronic and thermal Free Energies= -1211.618503
SCF Energy -1211.770047

**f**

| | | | |
|---|---|---|---|
| C | -0.275563000 | 1.632398000 | 0.065567000 |
| C | -0.124660000 | 0.210076000 | -0.004131000 |
| H | 2.064349000 | 0.906571000 | -1.484824000 |

| | | | |
|---|---|---|---|
| C | -1.265365000 | -0.654208000 | -0.070010000 |
| C | -2.651457000 | 0.011354000 | -0.079398000 |
| H | -2.802418000 | 0.645821000 | -0.950875000 |
| H | -2.827893000 | 0.623906000 | 0.802926000 |
| O | -1.201499000 | -1.889994000 | -0.131881000 |
| O | -1.315707000 | 2.289478000 | 0.001872000 |
| O | 0.922259000 | 2.292307000 | 0.264586000 |
| C | 0.818049000 | 3.706228000 | 0.338600000 |
| H | 0.399884000 | 4.131781000 | -0.578500000 |
| H | 0.194888000 | 4.024072000 | 1.179811000 |
| H | 1.834088000 | 4.075312000 | 0.479996000 |
| Cl | -3.987347000 | -1.215172000 | -0.116240000 |
| C | 1.504575000 | -1.535221000 | 0.786325000 |
| C | 1.214645000 | -0.415730000 | -0.014631000 |
| C | 2.755600000 | -2.142443000 | 0.769539000 |
| H | 2.942957000 | -3.000100000 | 1.410374000 |
| C | 2.250788000 | 0.051309000 | -0.843385000 |
| C | 3.768054000 | -1.656024000 | -0.054471000 |
| H | 4.744919000 | -2.129735000 | -0.068782000 |
| C | 3.503462000 | -0.551552000 | -0.861456000 |
| H | 4.276157000 | -0.160751000 | -1.518230000 |
| H | 0.728779000 | -1.930406000 | 1.432283000 |

Zero-point correction= 0.186277
Thermal correction to Energy= 0.200438
Thermal correction to Enthalpy= 0.201382
Thermal correction to Gibbs Free Energy= 0.143943
Sum of electronic and zero-point Energies= -1111.10857
Sum of electronic and thermal Energies= -1111.094409
Sum of electronic and thermal Enthalpies= -1111.093465
Sum of electronic and thermal Free Energies= -1111.150904
SCF Energy -1111.294847

**TS3**

| | | | |
|---|---|---|---|
| C | -0.262519000 | 1.565002000 | 0.056651000 |
| C | 0.018260000 | 0.185361000 | -0.010316000 |
| H | 2.308282000 | 1.189598000 | -1.116652000 |
| C | -1.164350000 | -0.620548000 | -0.099360000 |
| C | -2.456805000 | 0.202821000 | -0.065453000 |
| H | -2.895041000 | 0.593065000 | -0.970941000 |
| H | -2.876881000 | 0.546862000 | 0.866489000 |
| O | -1.192386000 | -1.846821000 | -0.209041000 |
| O | -1.439886000 | 1.999657000 | 0.014666000 |
| O | 0.760595000 | 2.429466000 | 0.201315000 |
| Cl | -4.168933000 | -1.381840000 | -0.075855000 |
| C | 1.607185000 | -1.651219000 | 0.590579000 |
| C | 1.361720000 | -0.402874000 | -0.013719000 |
| C | 2.874825000 | -2.220770000 | 0.589720000 |
| H | 3.027394000 | -3.182231000 | 1.072490000 |
| C | 2.457324000 | 0.234552000 | -0.626581000 |
| C | 3.946697000 | -1.568620000 | -0.015008000 |
| H | 4.936548000 | -2.014302000 | -0.014572000 |
| C | 3.725109000 | -0.335280000 | -0.622546000 |
| H | 4.545288000 | 0.186486000 | -1.107918000 |
| H | 0.785179000 | -2.174511000 | 1.062716000 |
| C | 0.398673000 | 3.810932000 | 0.295757000 |
| H | -0.228629000 | 3.995046000 | 1.170694000 |
| H | 1.336913000 | 4.354061000 | 0.393521000 |
| H | -0.130480000 | 4.142648000 | -0.600166000 |

| | |
|---|---|
| Zero-point correction= | 0.185017 |
| Thermal correction to Energy= | 0.19893 |
| Thermal correction to Enthalpy= | 0.199874 |
| Thermal correction to Gibbs Free Energy= | 0.142648 |
| Sum of electronic and zero-point Energies= | -1111.088938 |
| Sum of electronic and thermal Energies= | -1111.075024 |
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| Sum of electronic and thermal Free Energies= | -1111.131306 |

SCF Energy -1111.273955

**g**

| | | | |
|---|---|---|---|
| C | 0.219145000 | 1.564592000 | -0.023116000 |
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| H | 2.948326000 | 1.154733000 | 0.376008000 |
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| H | -2.521581000 | 0.834003000 | -0.871645000 |
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| O | -1.313303000 | -1.528033000 | 0.037865000 |
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| Cl | -5.793427000 | -1.190918000 | 0.042487000 |
| C | 1.661086000 | -1.936446000 | -0.188436000 |
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| H | 2.812580000 | -3.735757000 | -0.342967000 |
| C | 2.905361000 | 0.085458000 | 0.211741000 |
| C | 4.068026000 | -2.024624000 | 0.011131000 |
| H | 4.992585000 | -2.593056000 | 0.011262000 |
| C | 4.085890000 | -0.646899000 | 0.210975000 |
| H | 5.029276000 | -0.133401000 | 0.371717000 |
| H | 0.713295000 | -2.439552000 | -0.334715000 |
| C | 0.735482000 | 3.867522000 | -0.103158000 |
| H | 0.162054000 | 4.120404000 | 0.788747000 |
| H | 1.660353000 | 4.437013000 | -0.130562000 |
| H | 0.146399000 | 4.059350000 | -1.000051000 |

Zero-point correction= 0.188225
Thermal correction to Energy= 0.202649
Thermal correction to Enthalpy= 0.203593
Thermal correction to Gibbs Free Energy= 0.142966
Sum of electronic and zero-point Energies= -1111.134179

Sum of electronic and thermal Energies= -1111.119755
Sum of electronic and thermal Enthalpies= -1111.118811
Sum of electronic and thermal Free Energies= -1111.179438
SCF Energy -1111.322404

## 3. References


1. Zhao, Y.; Truhlar, D. G. *J. Chem. Phys.* **2006**, *125* 194101.
2. Marenich, A. V.; Cramer, C. J.; Truhlar, D. G. *J. Phys. Chem. B,* **2009**, *113*, 6378.
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4. Gaussian 16, Revision A.03, Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Scalmani, G.; Barone, V.; Petersson, G. A.; Nakatsuji, H.; Li, X.; Caricato, M.; Marenich, A. V.; Bloino, J.; Janesko, B. G.; Gomperts, R.; Mennucci, B.; Hratchian, H. P.; Ortiz, J. V.; Izmaylov, A. F.; Sonnenberg, J. L.; Williams-Young, D.; Ding, F.; Lipparini, F.; Egidi, F.; Goings, J.; Peng, B.; Petrone, A.; Henderson, T.; Ranasinghe, D.; Zakrzewski, V. G.; Gao, J.; Rega, N.; Zheng, G.; Liang, W.; Hada, M.; Ehara, M.; Toyota, K.; Fukuda, R.; Hasegawa, J.; Ishida, M.; Nakajima, T.; Honda, Y.; Kitao, O.; Nakai, H.; Vreven, T.; Throssell, K.; Montgomery, J. A., Jr.; Peralta, J. E.; Ogliaro, F.; Bearpark, M. J.; Heyd, J. J.; Brothers, E. N.; Kudin, K. N.; Staroverov, V. N.; Keith, T. A.; Kobayashi, R.; Normand, J.; Raghavachari, K.; Rendell, A. P.; Burant, J. C.; Iyengar, S. S.; Tomasi, J.; Cossi, M.; Millam, J. M.; Klene, M.; Adamo, C.; Cammi, R.; Ochterski, J. W.; Martin, R. L.; Morokuma, K.; Farkas, O.; Foresman, J. B.; Fox, D. J. Gaussian, Inc., Wallingford CT, 2016.


## 4. X-Ray Structure Determination of Compound 3

*Crystal data*: $C_{12}H_{12}O_3$, $M_r$ = 204.22, monoclinic, space group *C*2/*c*, *a* = 15.6759, *b* = 7.2560(2), *c* = 19.3615(5) Å, β = 111.935(4)°, *V* = 2042.82 Å$^3$, *Z* = 8, *T* = 100 K, $D_x$ = 1.328 Mg m$^{-3}$, μ = 0.095 mm$^{-1}$, *F*(000) = 864. *Data collection*: A colourless block 0.4 × 0.25 × 0.15 mm was mounted on a glass fibre in inert oil and transferred to the cold gas stream of an Oxford Diffraction Xcalibur E diffractometer. Measurements were performed using monochromated Mo *K*α radiation (λ = 0.71073 Å). A total of 47291 intensities were registered to $2\theta_{max}$ = 61.7°, of which 3099 were independent ($R_{int}$ = 0.024). No absorption correction was applied, but appropriate frame scaling was performed. *Structure refinement*: The structure was refined anisotropically using the program

SHELXL-97 (G. M. Sheldrick, University of Göttingen, Germany). Hydrogen atoms were included using a rigid methyl group allowed to rotate but not tip, and a riding model for all other hydrogens. The final *wR*2 value was 0.099 for all reflections and 137 parameters, with a corresponding *R*1 of 0.036 for reflections with $F > 4\sigma(F)$. The GOOF was 1.05; residual electron density was 0.40 e Å$^{-3}$.

Complete crystallographic data have been deposited at the Cambridge Crystallographic Data Centre as CCDC-1891729. These can be obtained free of charge from www.ccdc.cam.ac.uk/data_request/cif.

The molecular structure is shown in Fig. S1. The two rings subtend an interplanar angle of 9.26(4)°. The ethoxy group is essentially coplanar with the five-membered ring; C6 lies 0.060(2) and C7 0.073(2) Å out of the plane. The packing features a "weak" but short hydrogen bond H2A···O2 (2.30 Å, 170°; operator –*x*, 1–*y*, 1–*z*) and an H···π contact H6B···$\text{Cent}_{\text{phenyl}}$ 2.65 Å, 149°, operator 0.5–*x*, 1.5–*y*, 1–*z*).

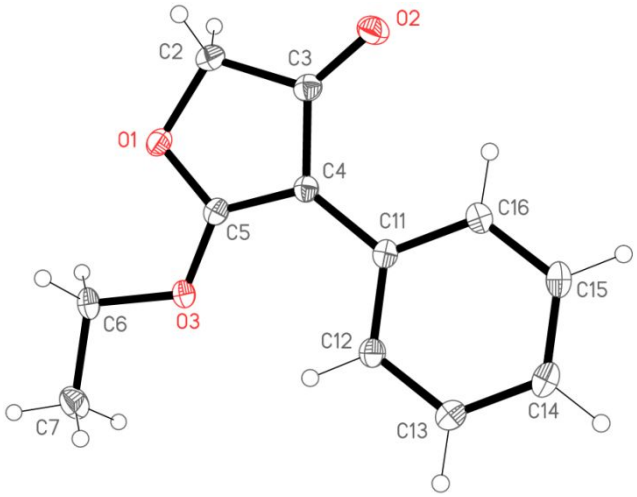
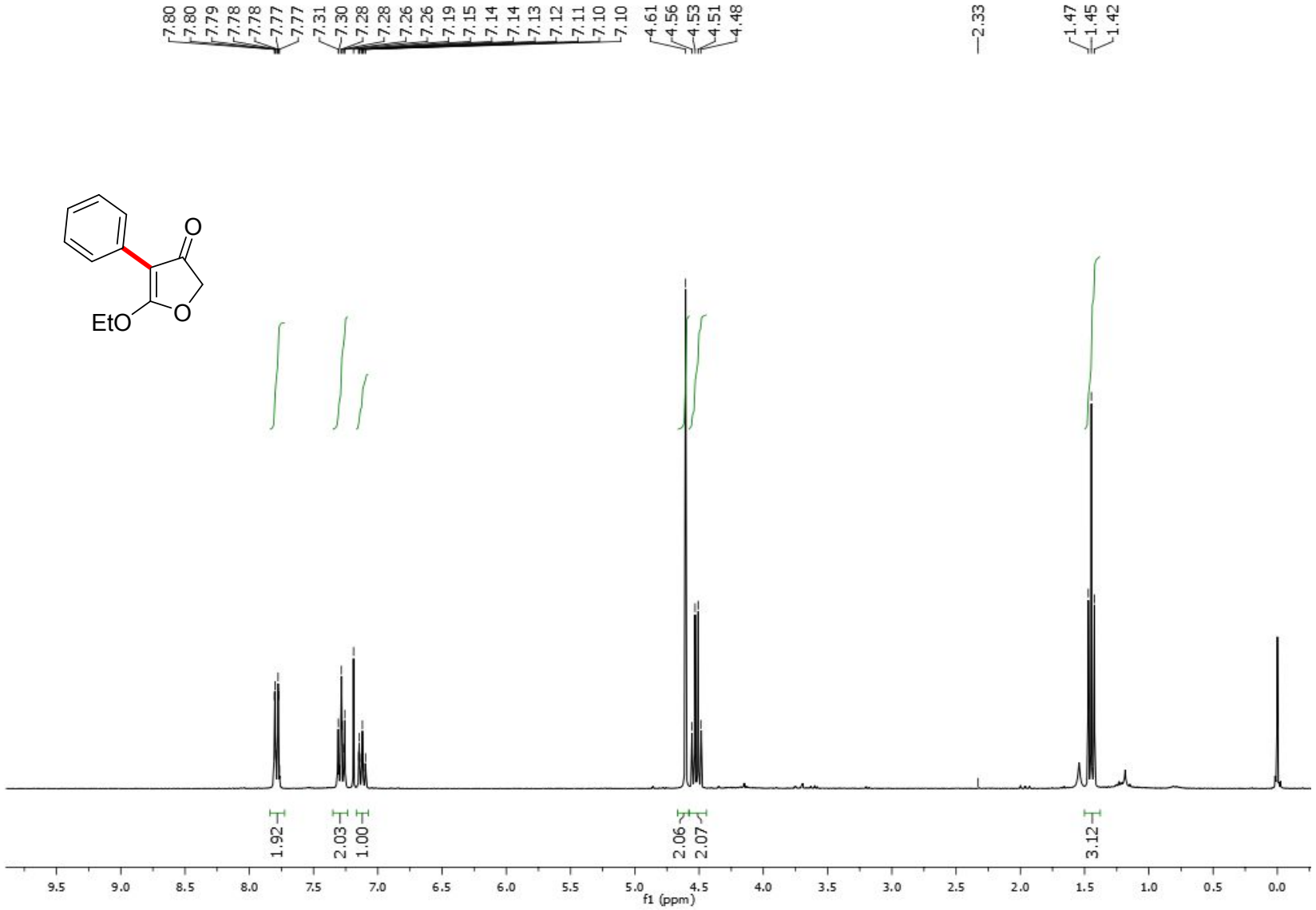


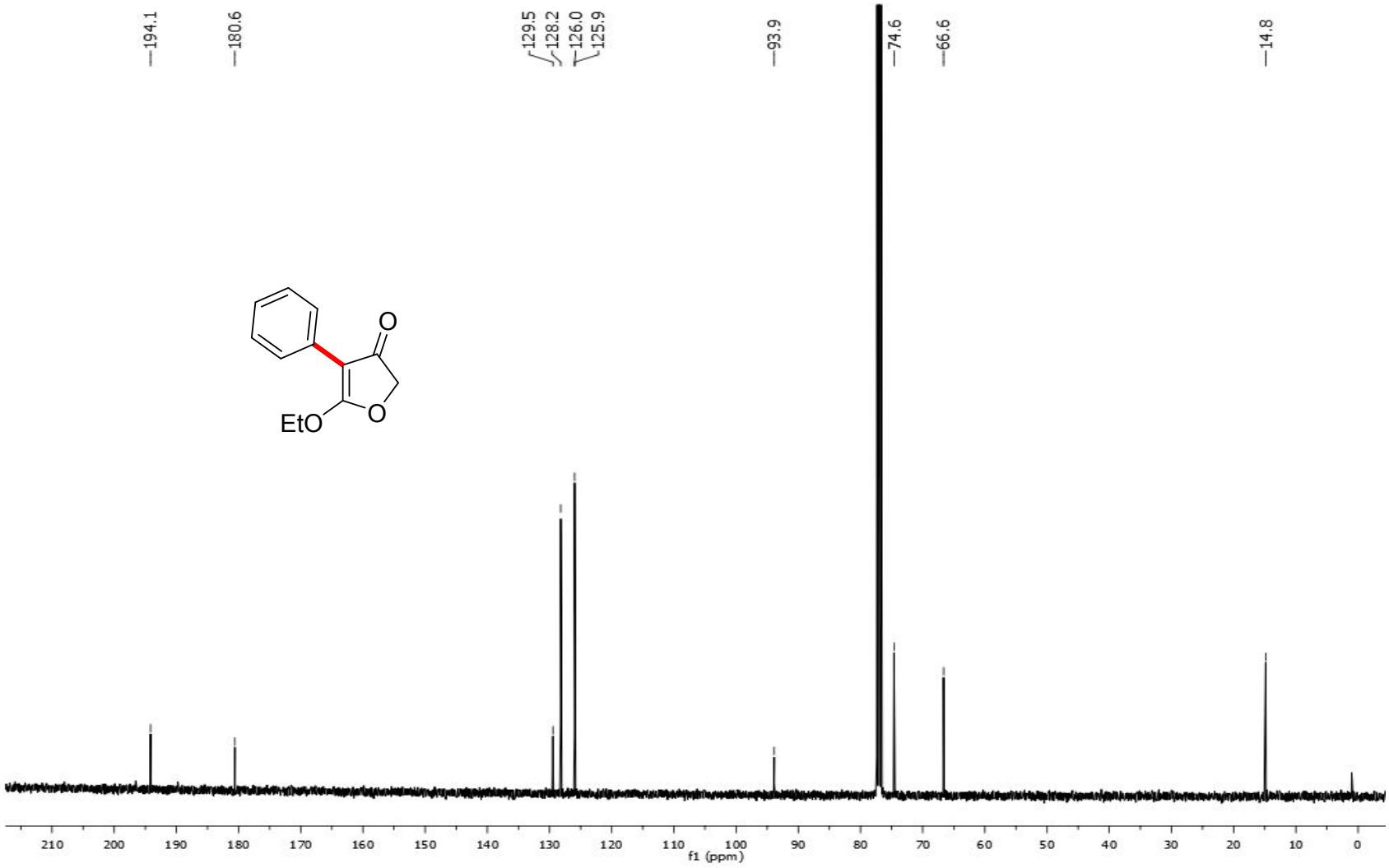

Figure S1. The molecule of compound **3** in the crystal. Ellipsoids correspond to 50% probability levels.

## 5. $^{1}H$ & $^{13}C\{^{1}H\}$ NMR spectra of compounds

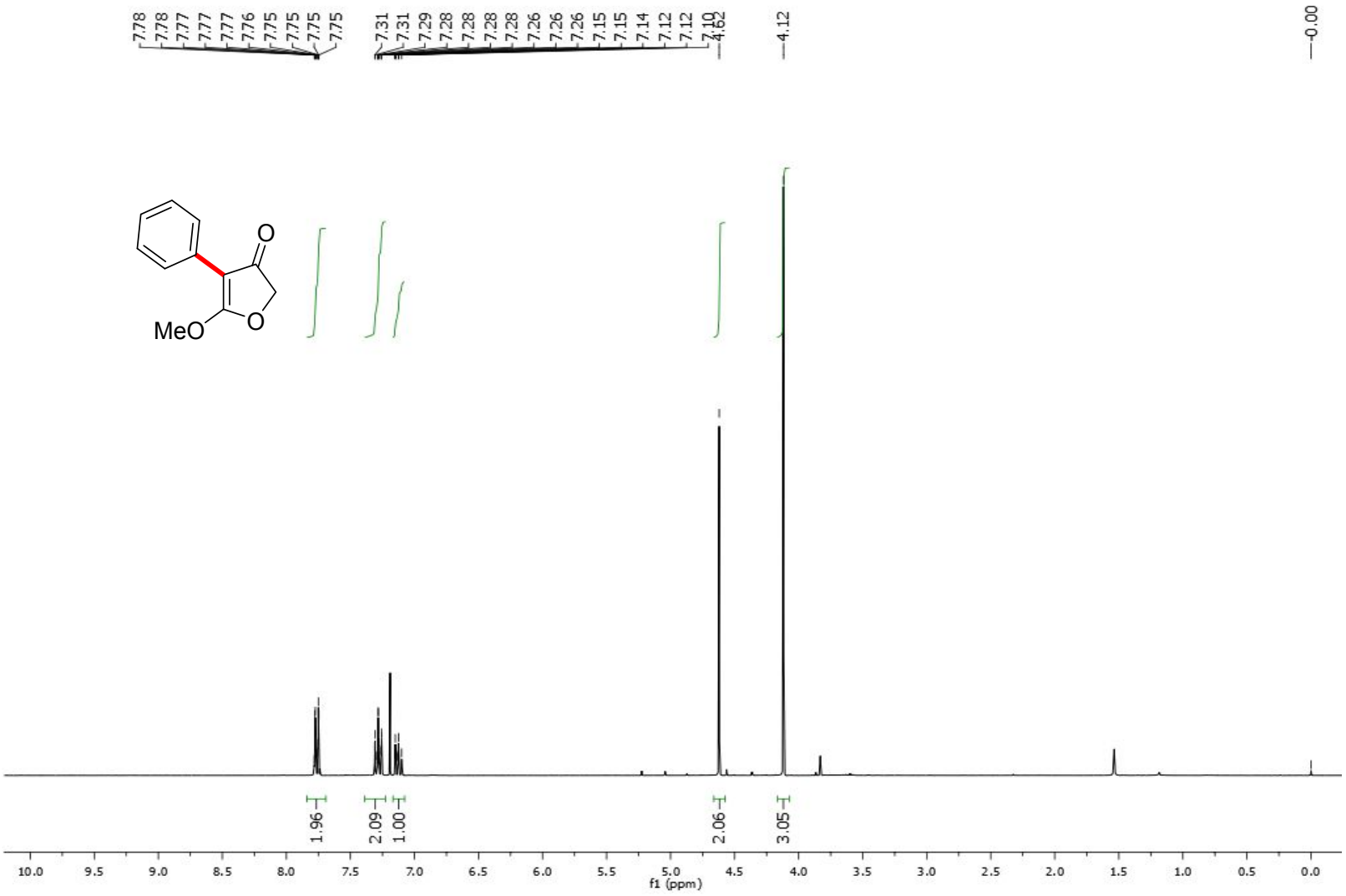
$^{1}H$ NMR (300 MHz) Spectra of **3**



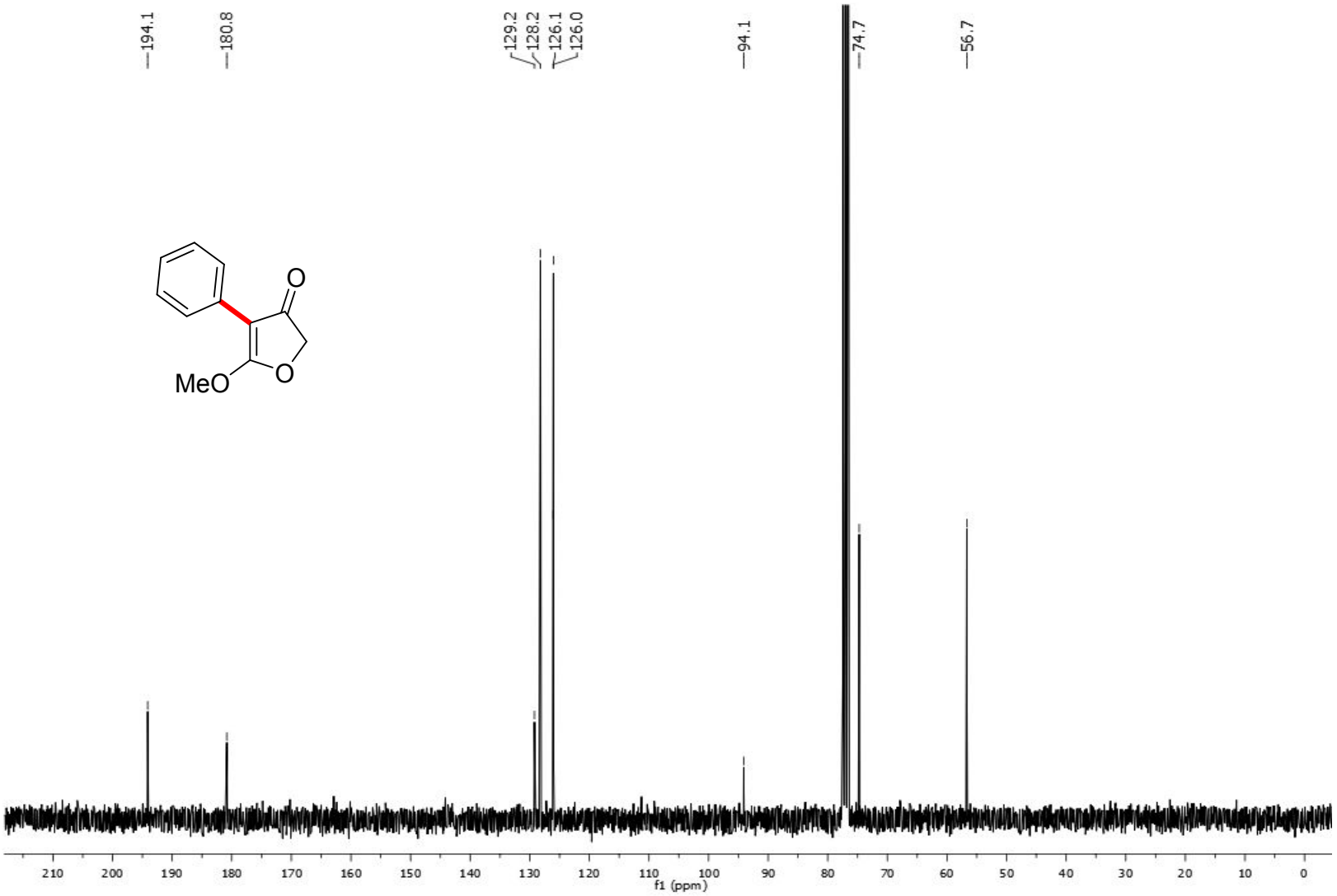
$^{13}C\{^{1}H\}$NMR (100 MHz) Spectra of **3**



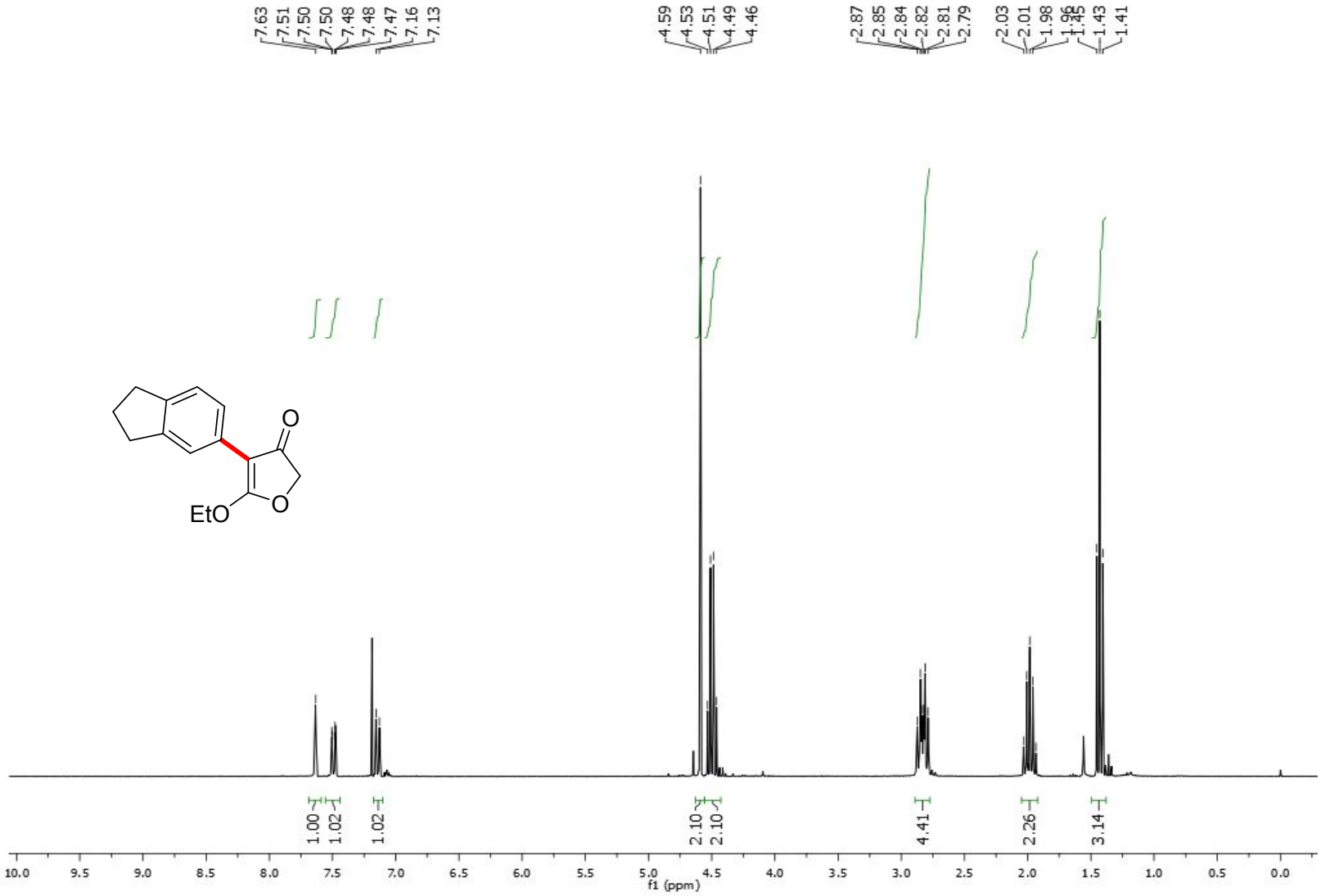
[1]H NMR (300 MHz) Spectra of **4**



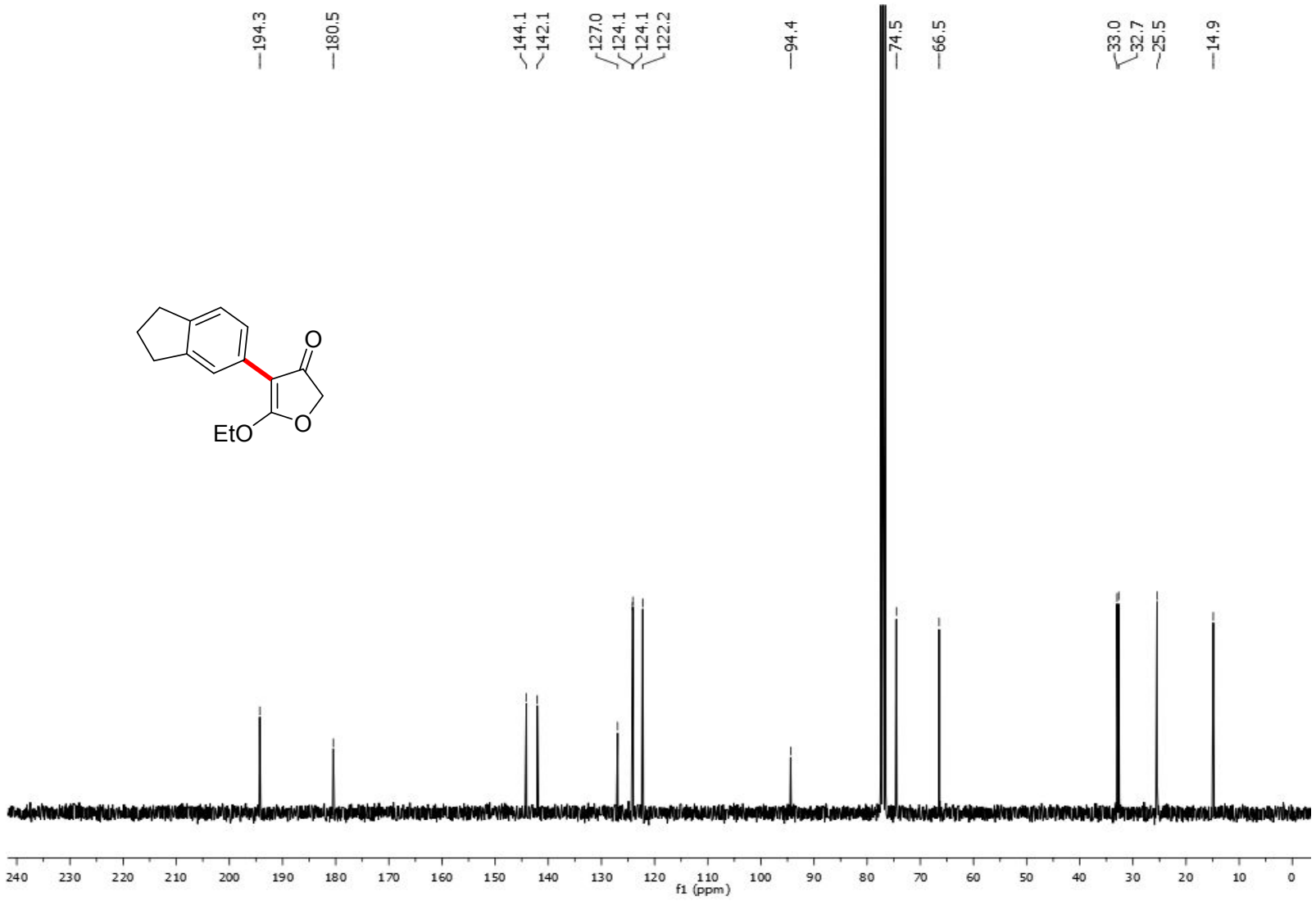
$^{13}C\{^{1}H\}$ NMR (75 MHz) Spectra of **4**



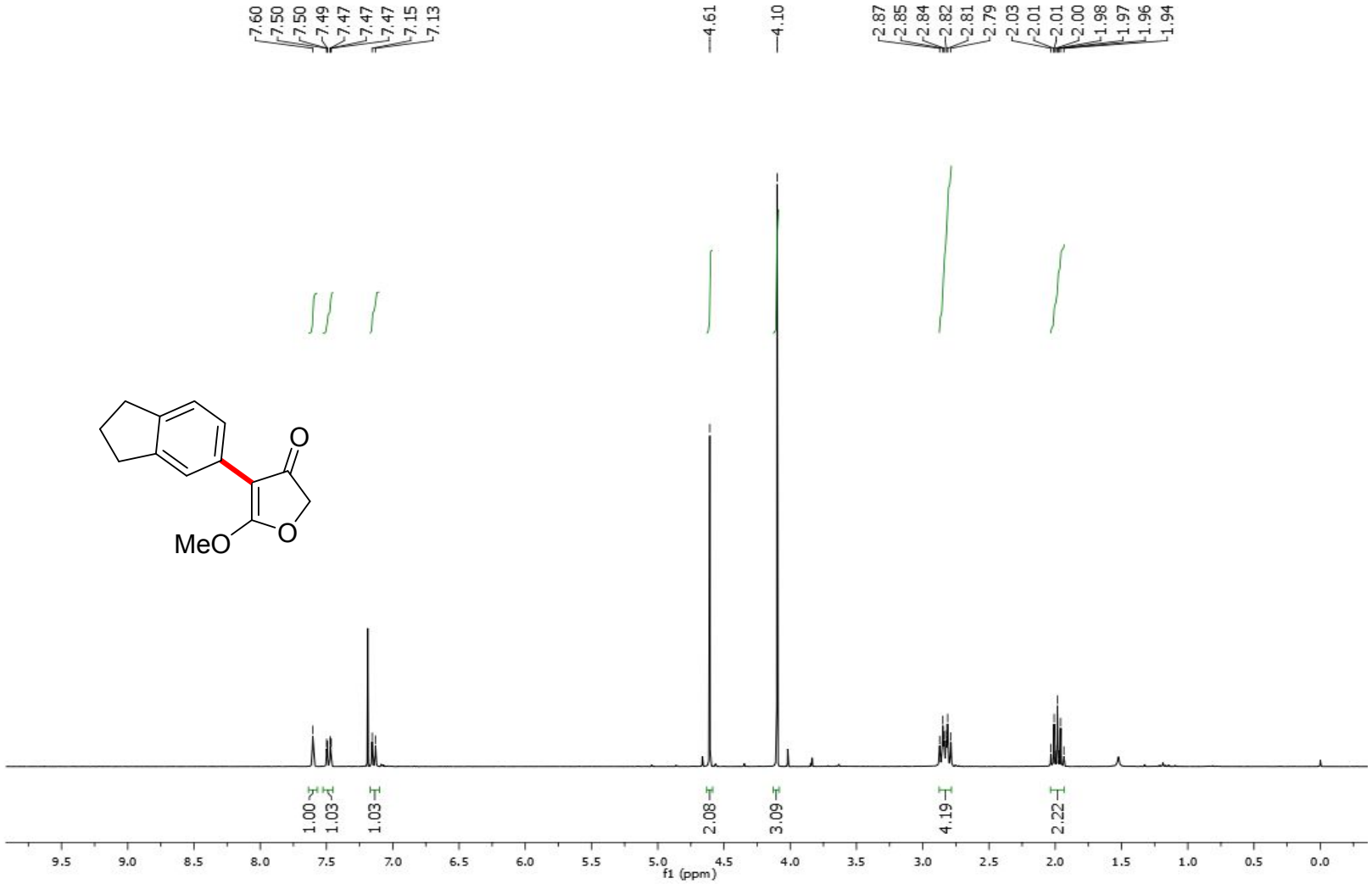
[1]H NMR (300 MHz) Spectra of **5**



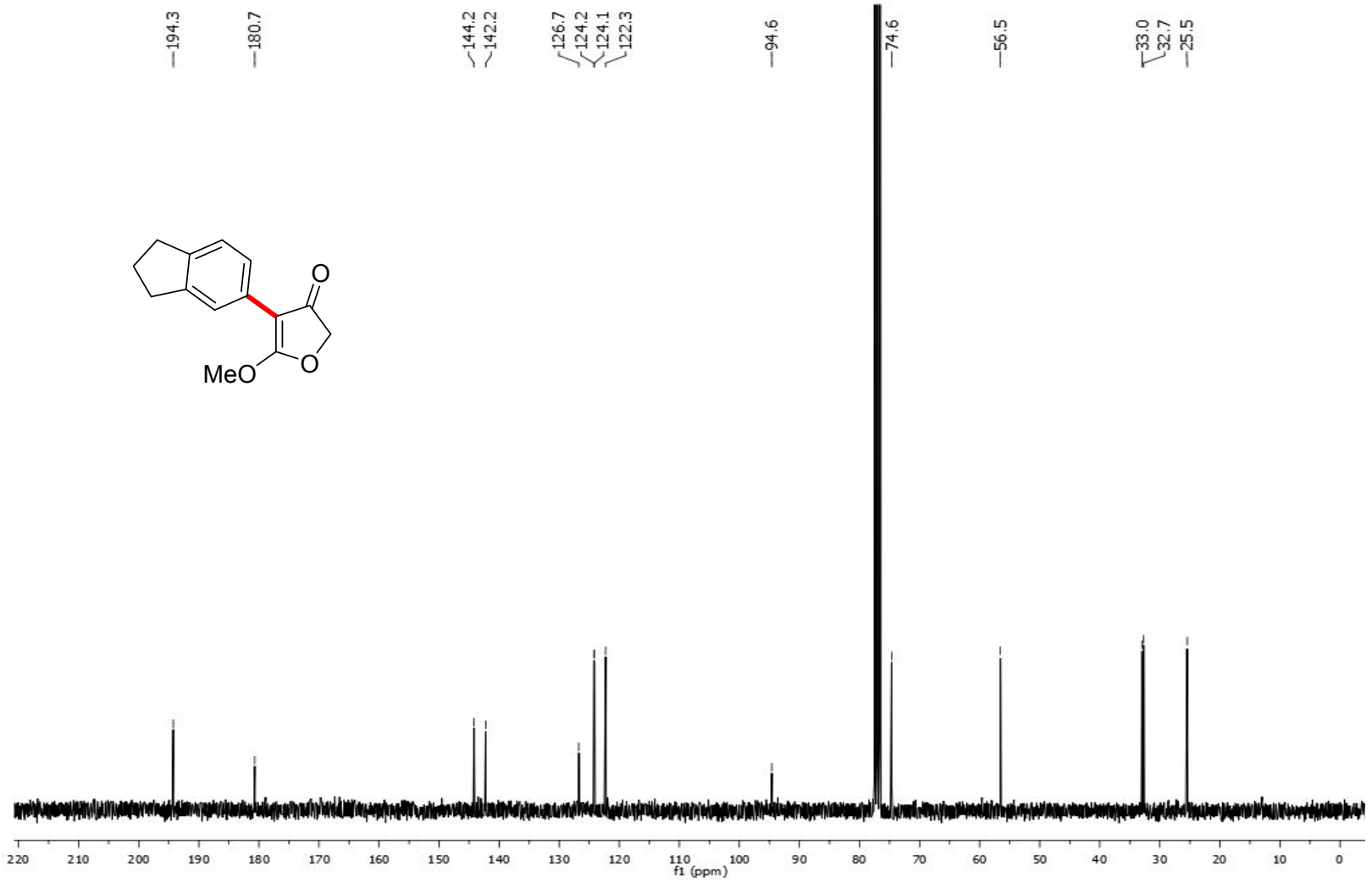
$^{13}C\{^{1}H\}$ NMR (75 MHz) Spectra of **5**



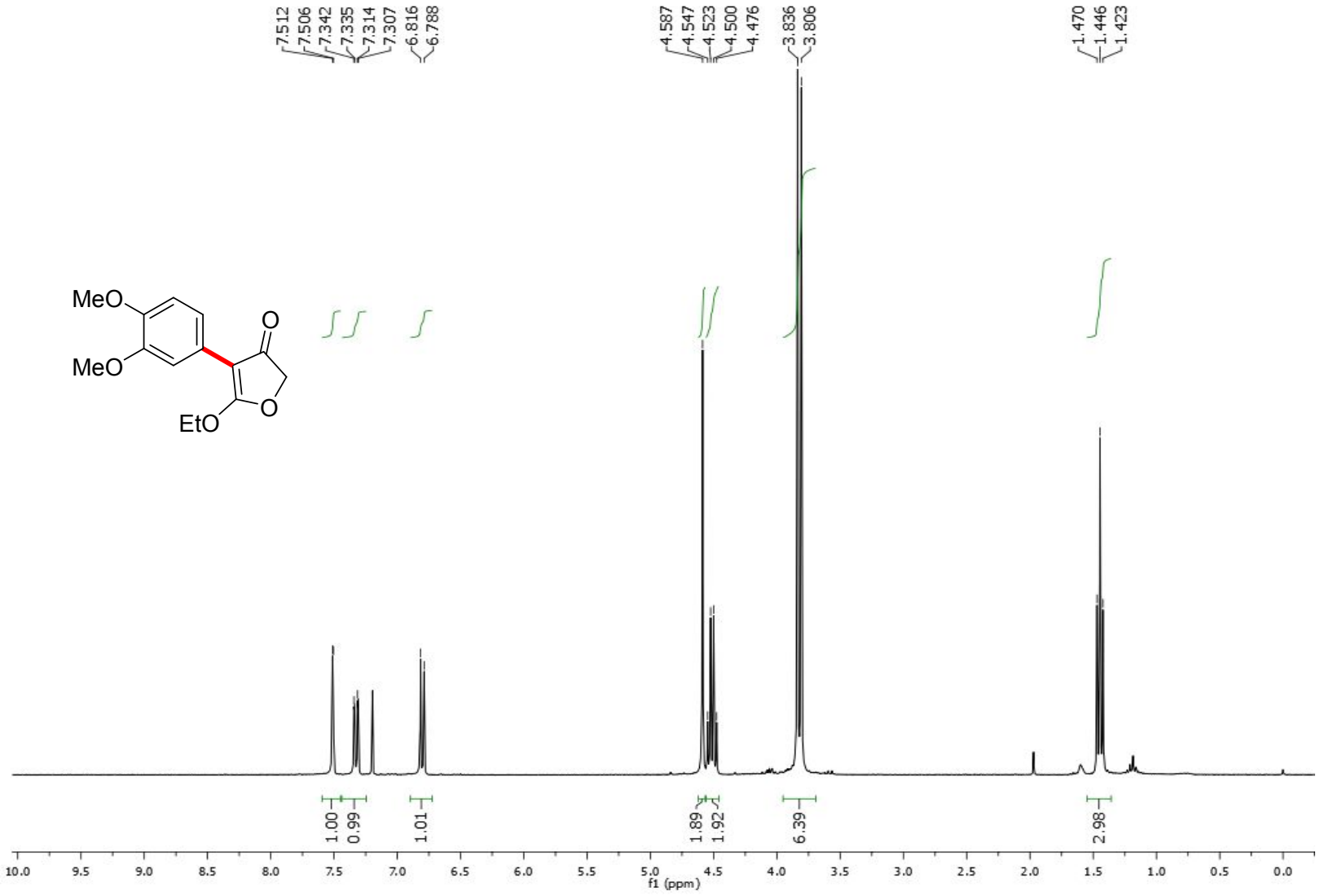
[1]H NMR (300 MHz) Spectra of **6**



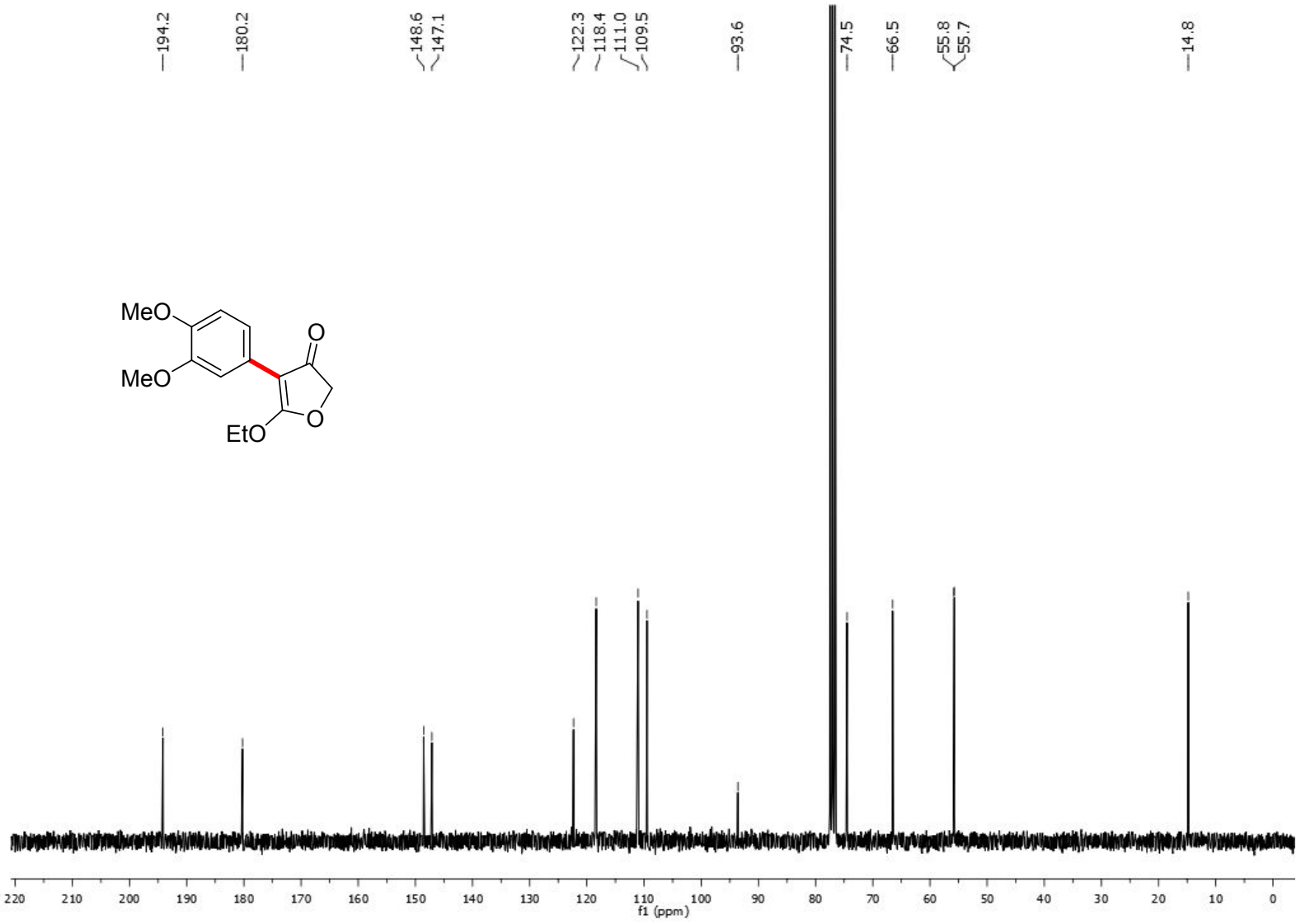
$^{13}C\{^{1}H\}$ NMR (75 MHz) Spectra of **6**



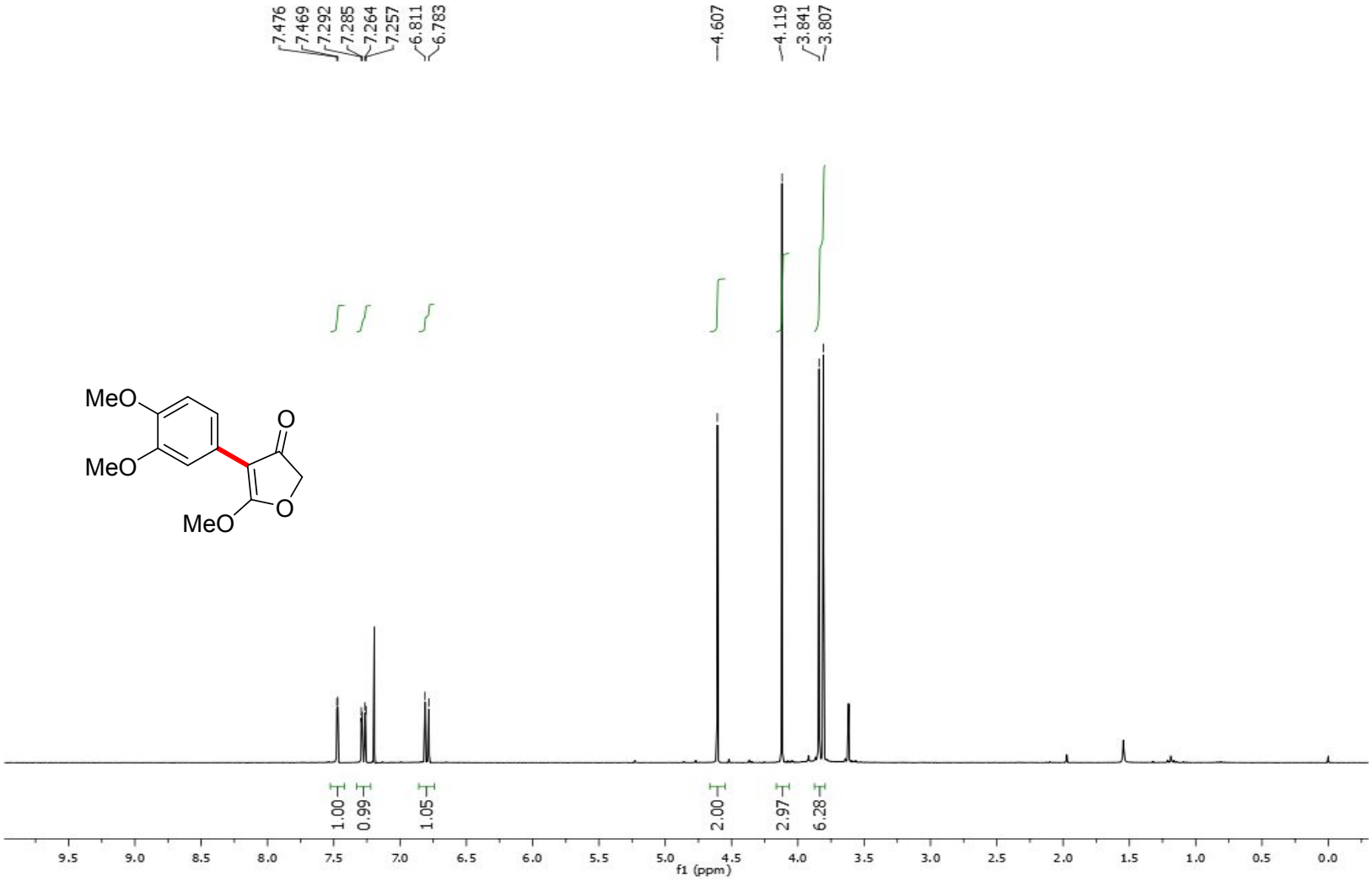
$^{1}$H NMR (300 MHz) Spectra of **7**



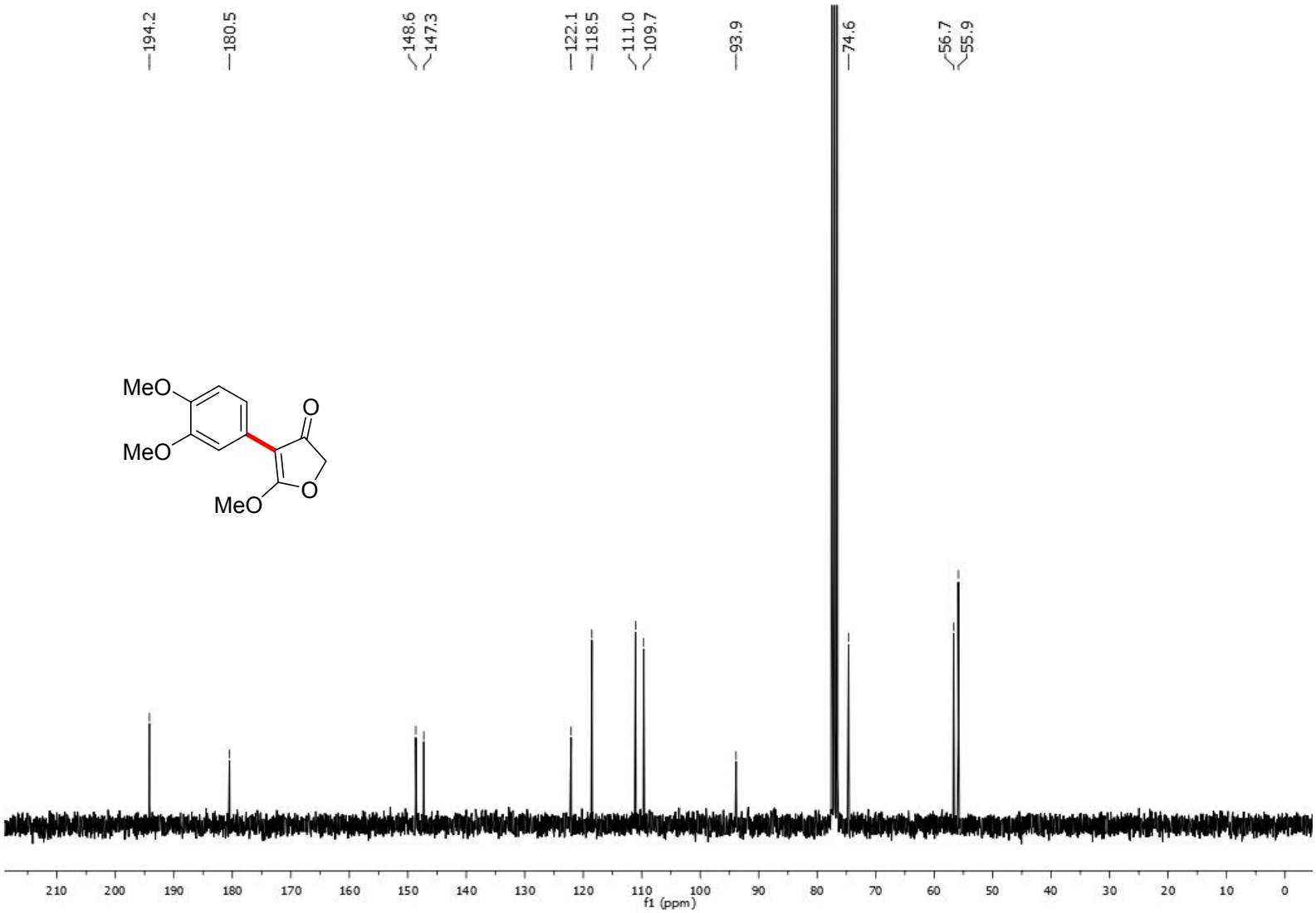
$^{13}C\{^{1}H\}$ NMR (75 MHz) Spectra of **7**



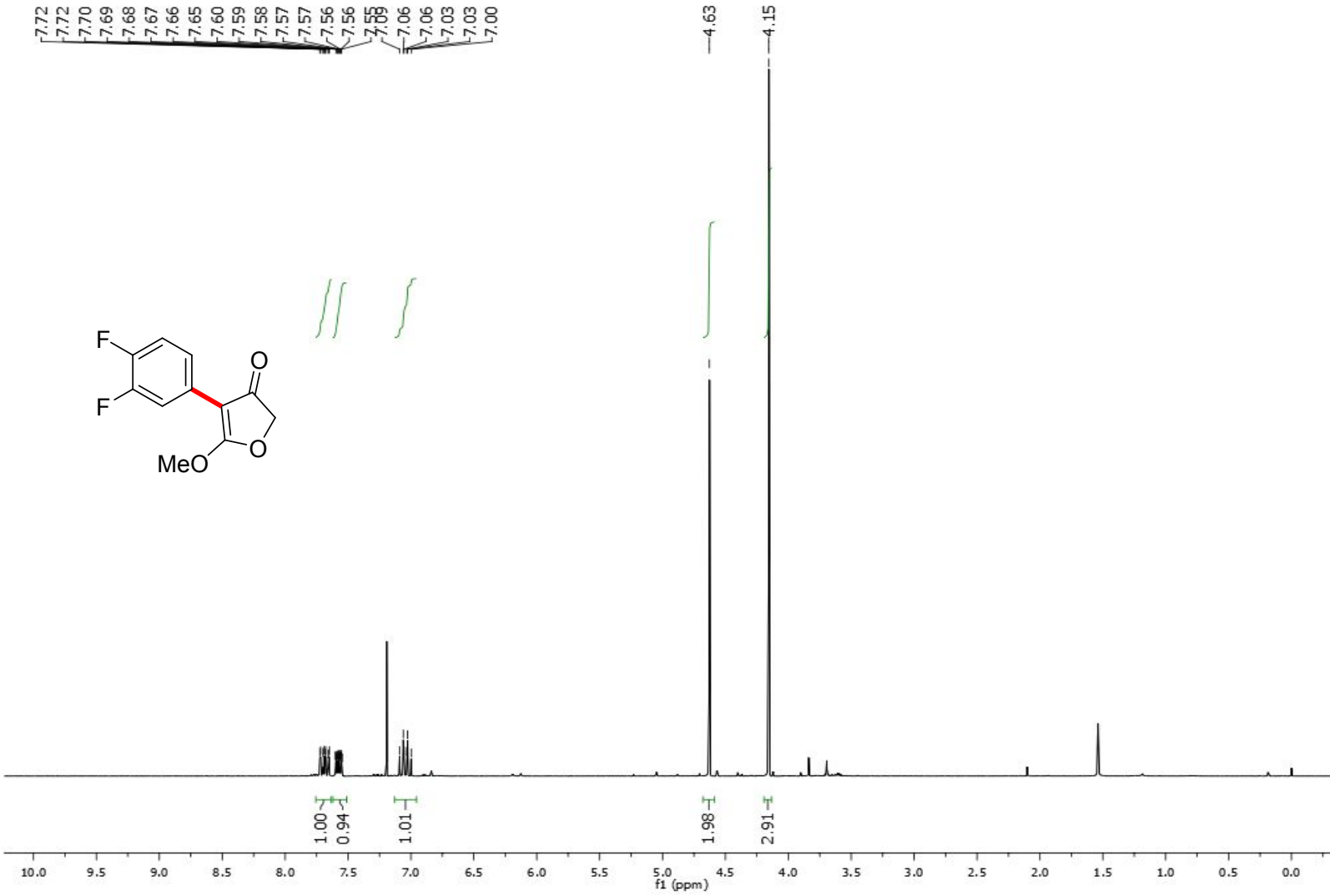
[1]H NMR (300 MHz) Spectra of **8**



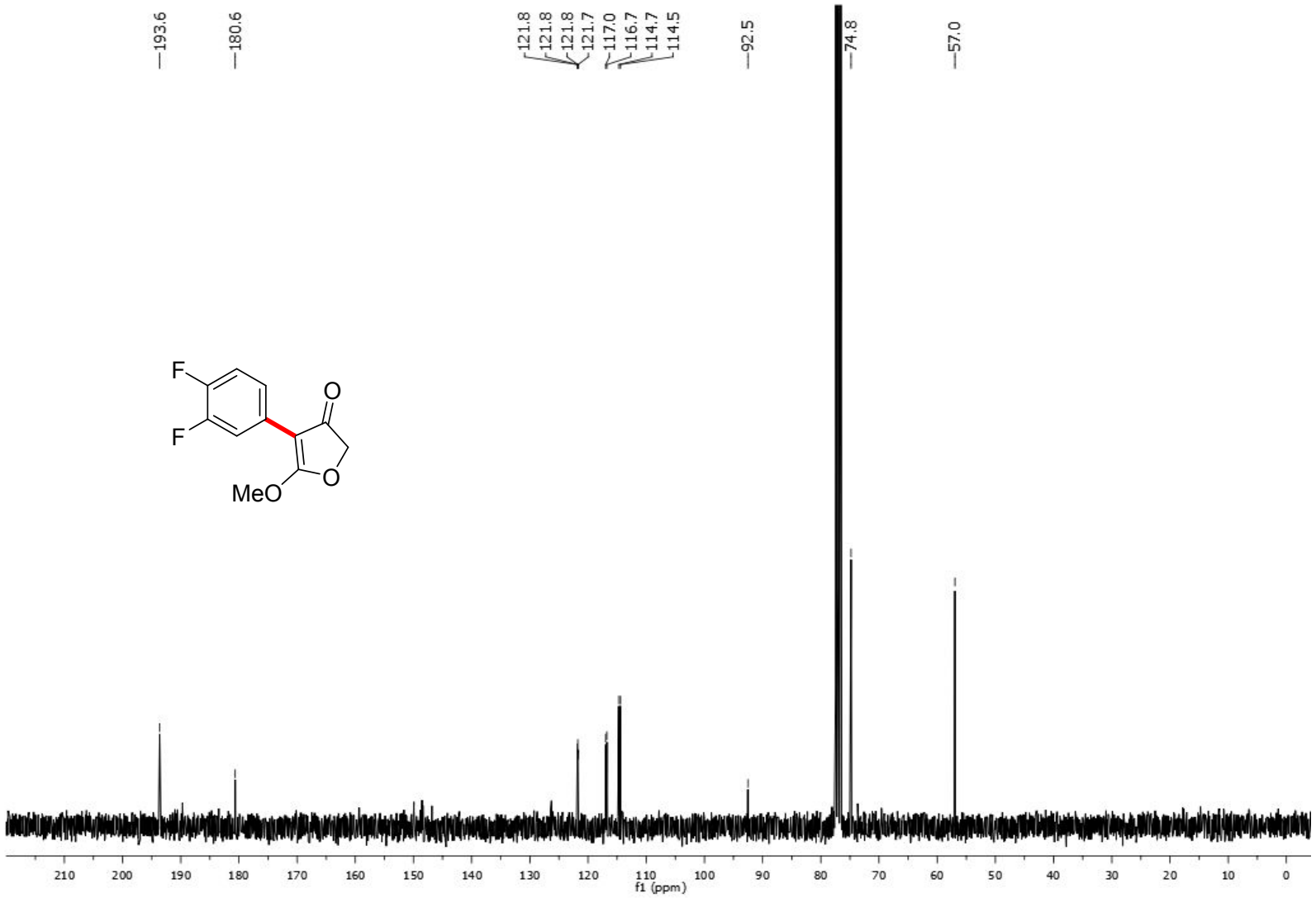
$^{13}C\{^{1}H\}$ NMR (75 MHz) Spectra of **8**



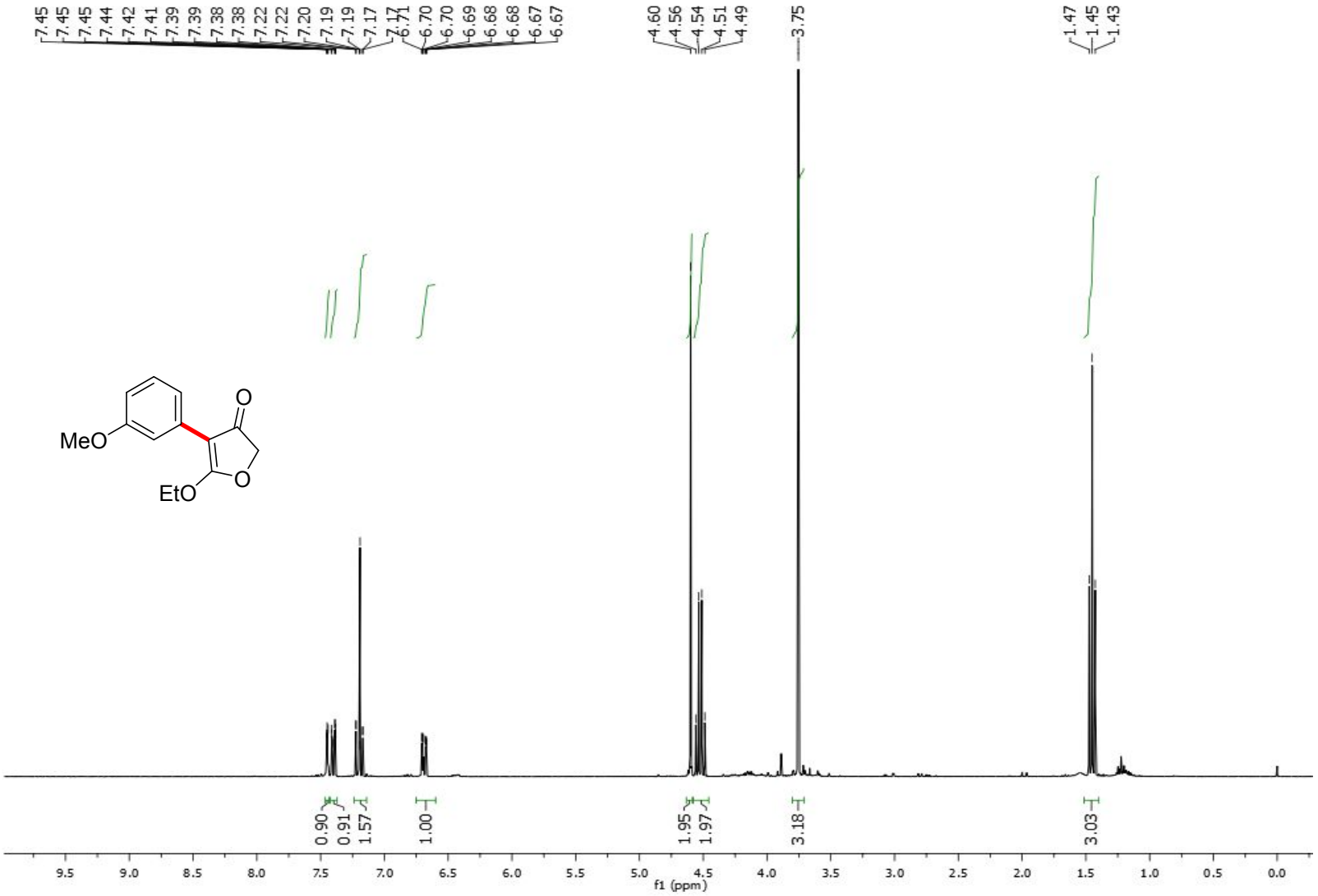
$^{1}$H NMR (300 MHz) Spectra of **9**



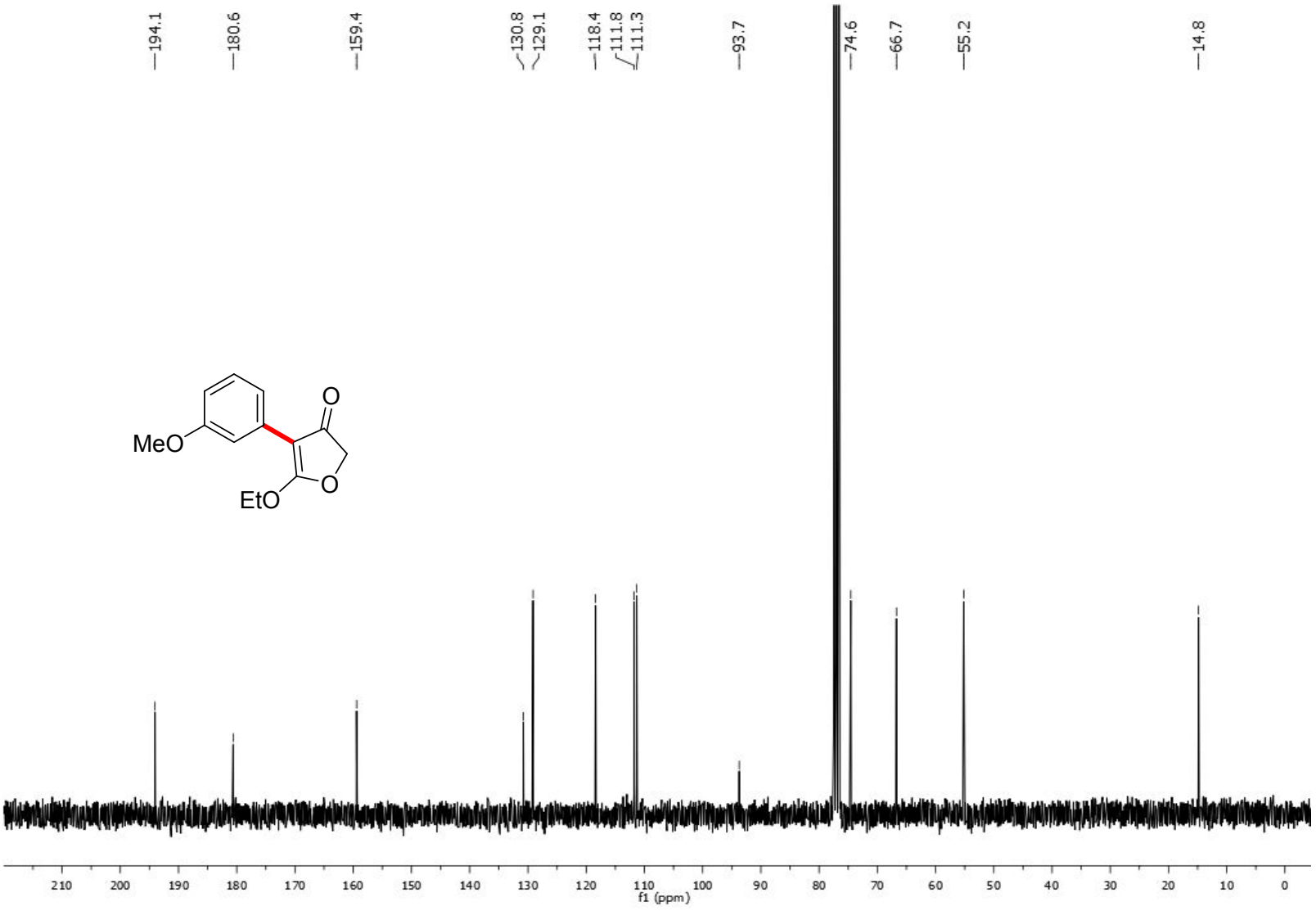
$^{13}C\{^{1}H\}$ NMR (75 MHz) Spectra of **9**



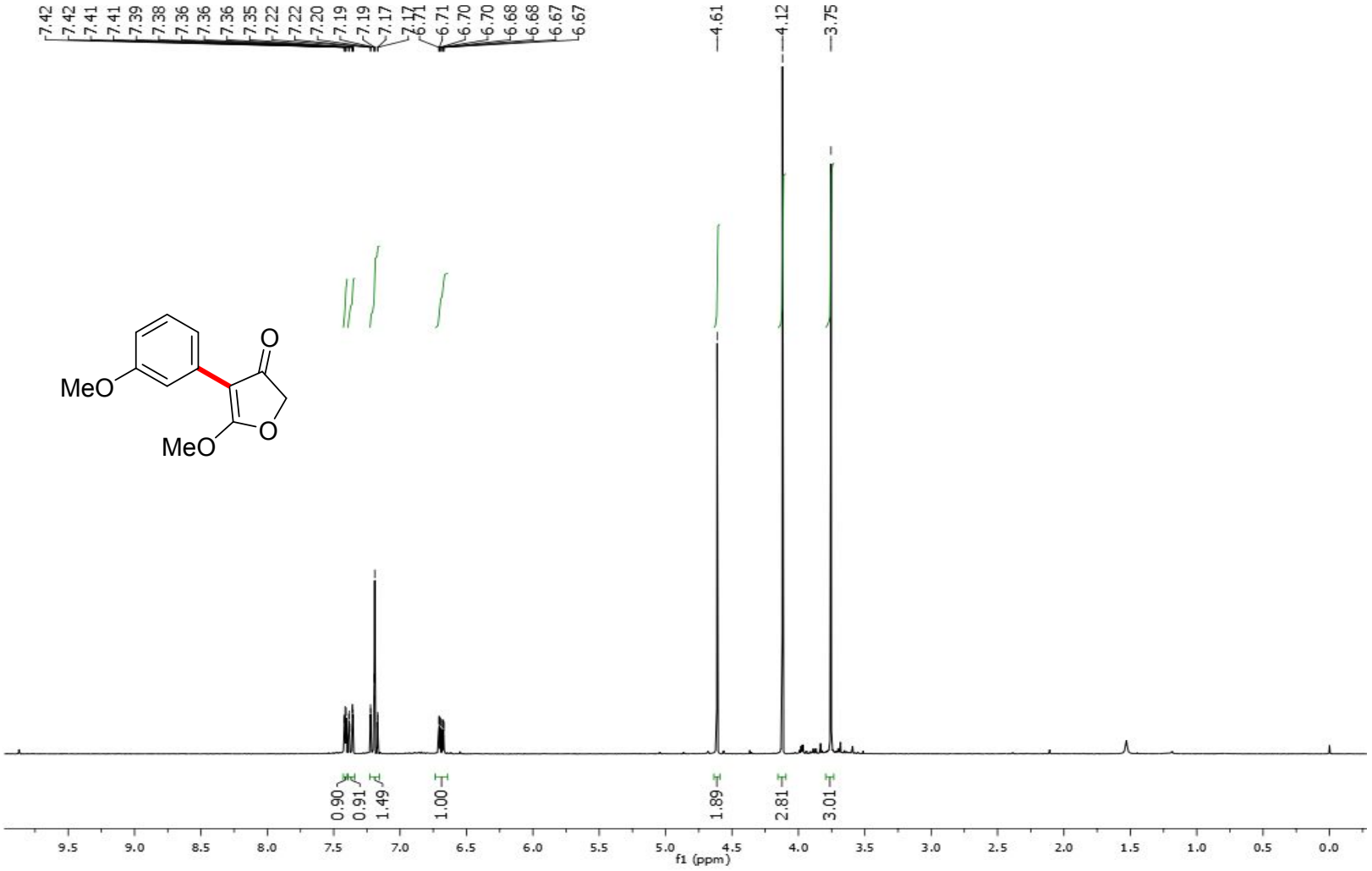
[1]H NMR (300 MHz) Spectra of **10**



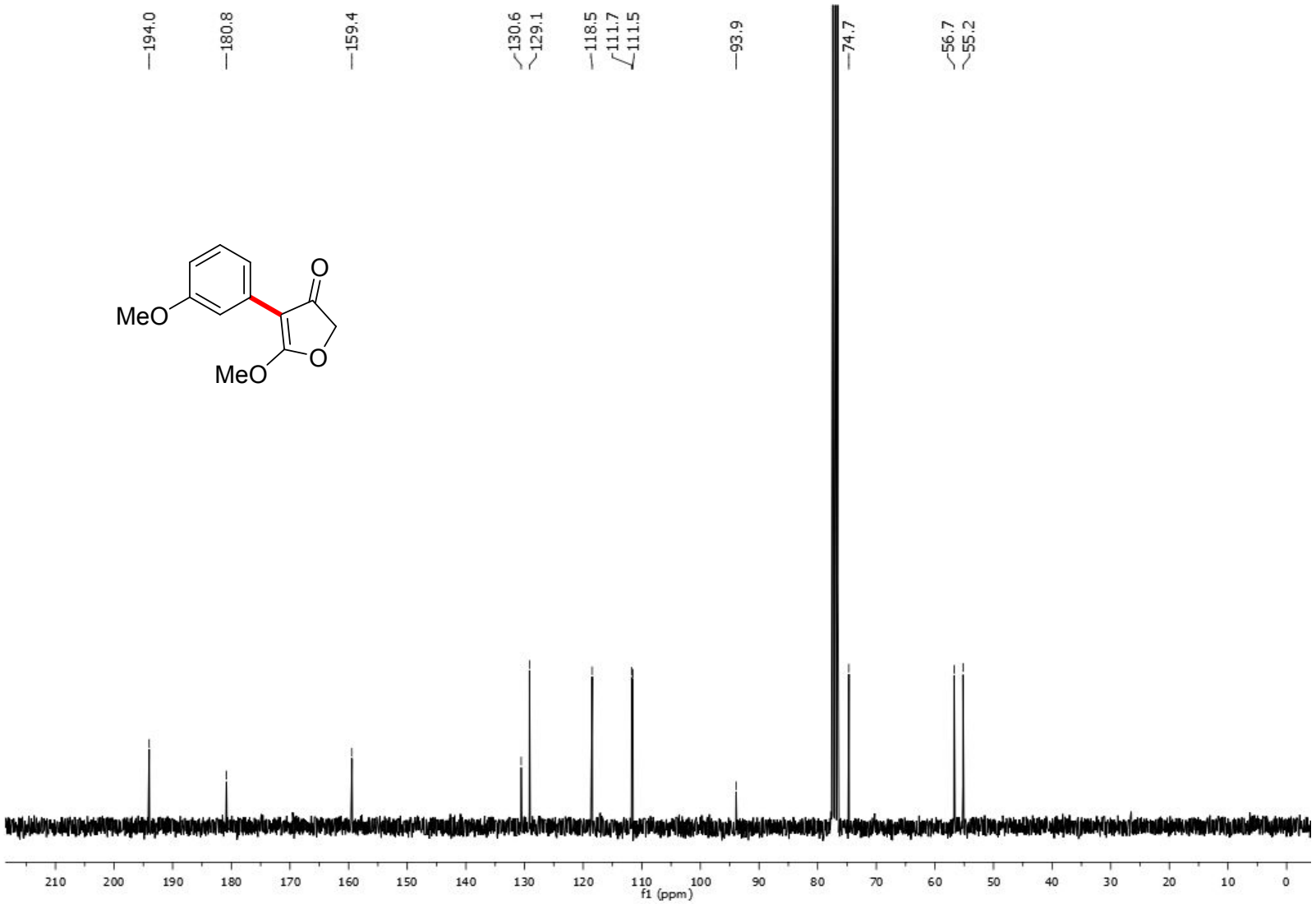
$^{13}C\{^{1}H\}$ NMR (75 MHz) Spectra of **10**



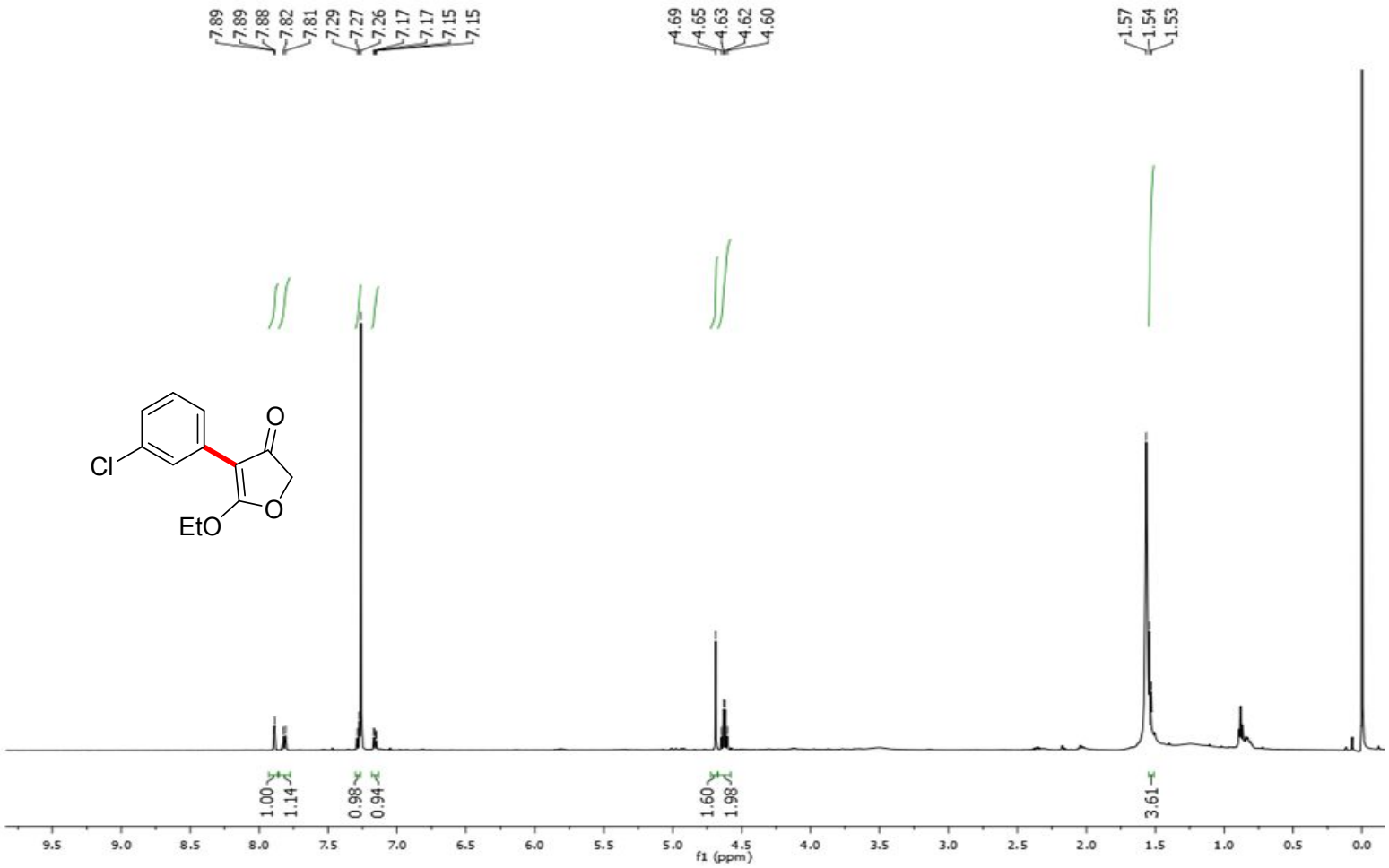
$^{1}$H NMR (300 MHz) Spectra of **11**



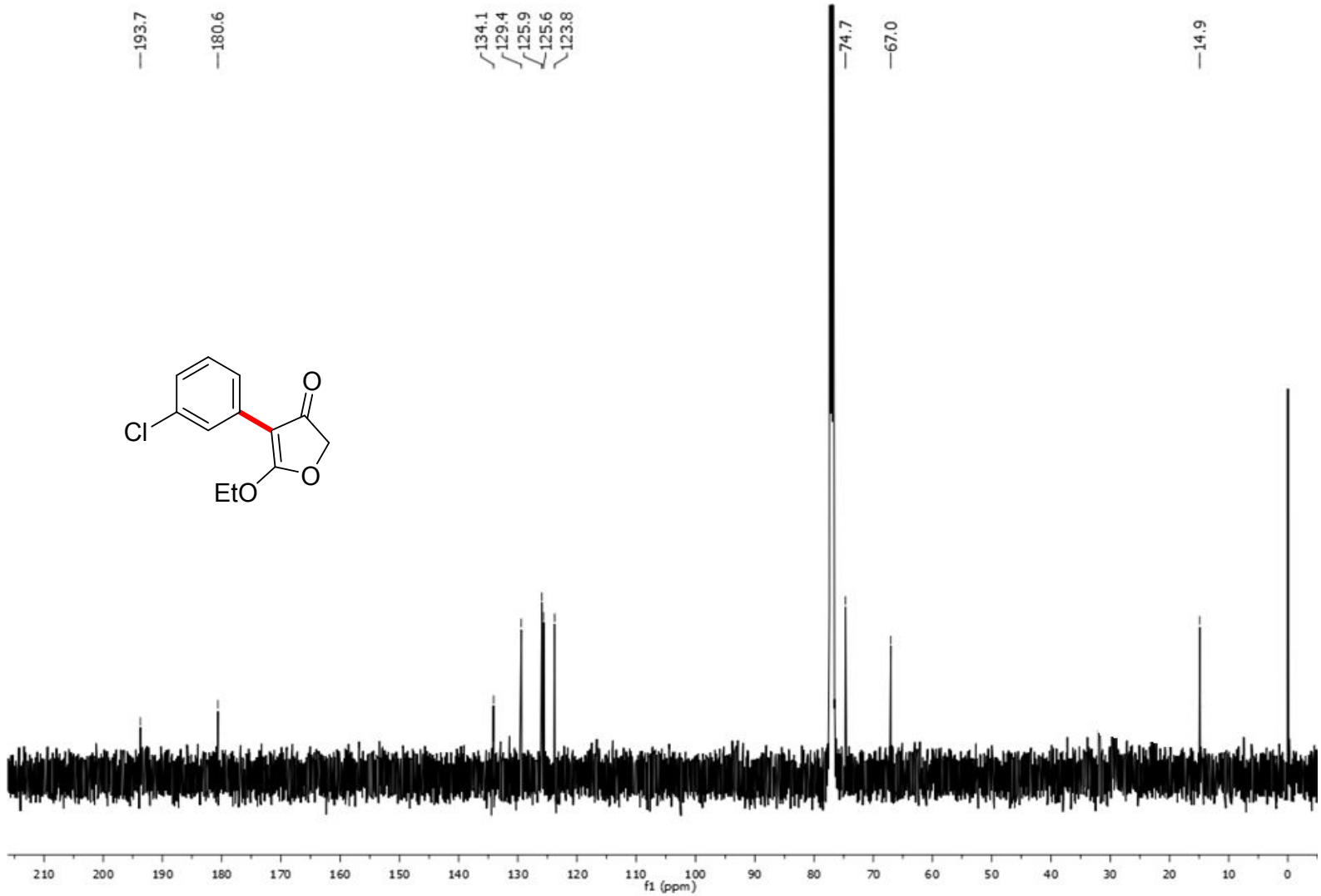
$^{13}C\{^{1}H\}$ NMR (75 MHz) Spectra of **11**



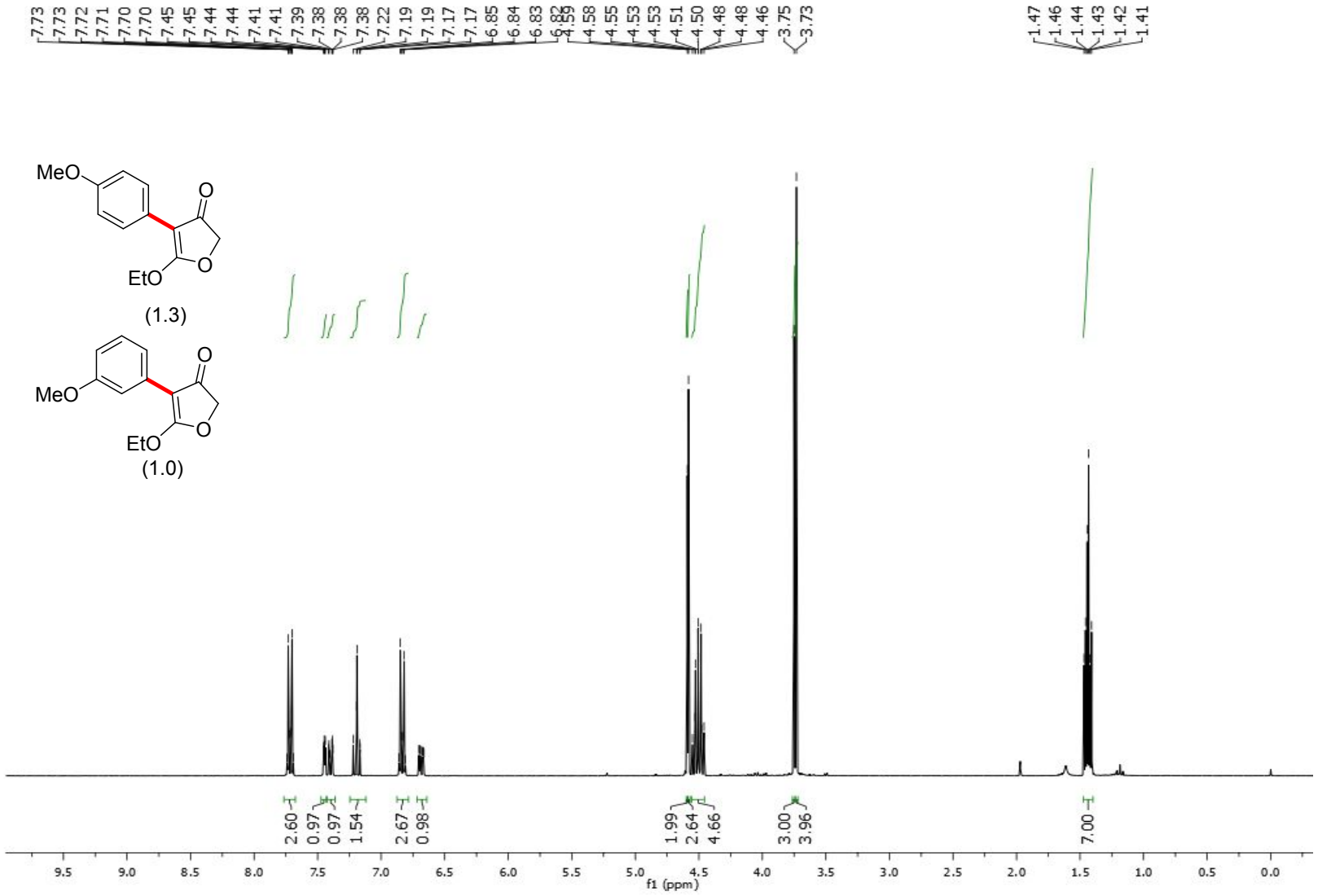
$^{1}$H NMR (500 MHz) Spectra of **12**



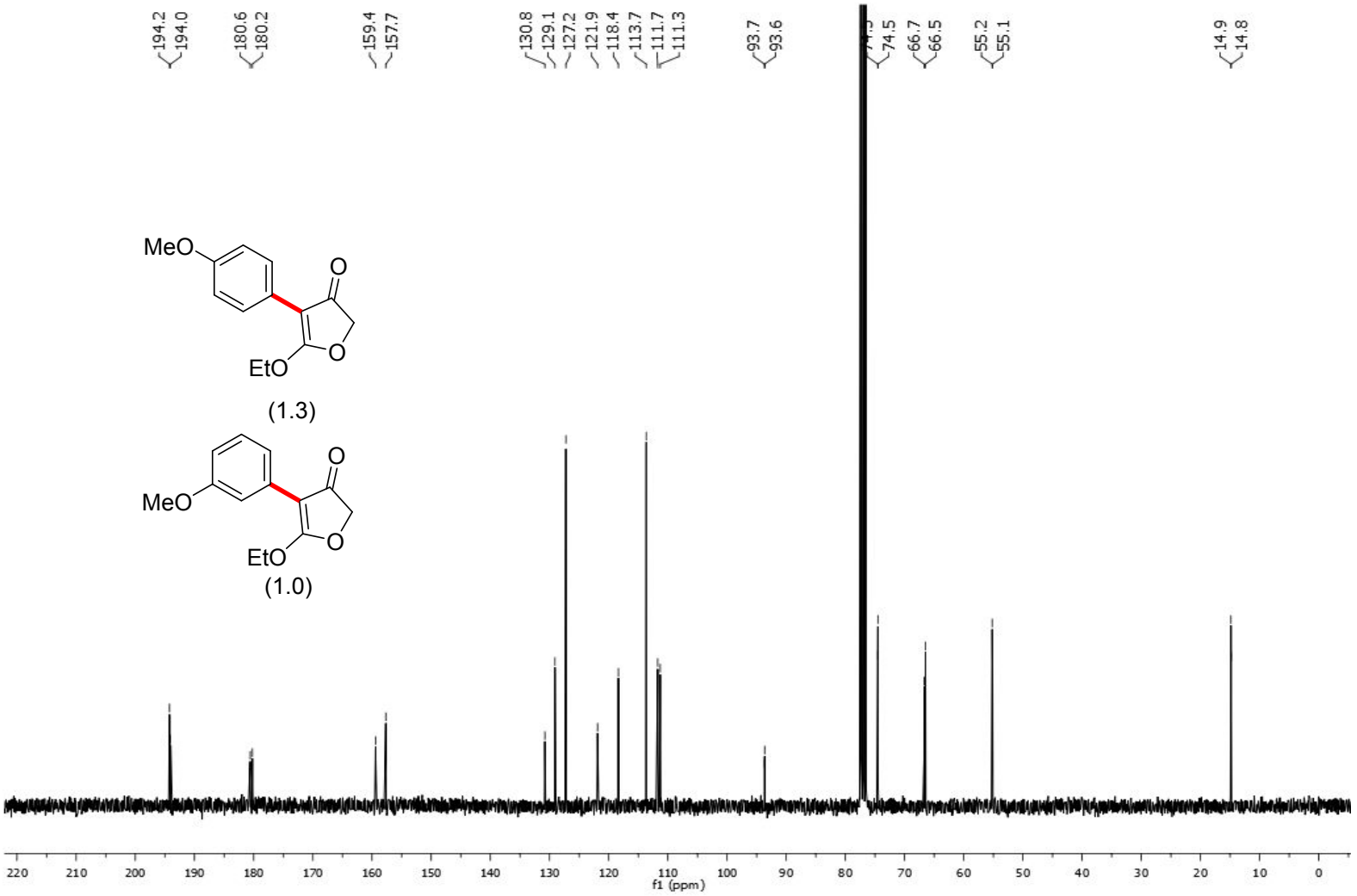
$^{13}C\{^{1}H\}$ NMR (125 MHz) Spectra of **12**



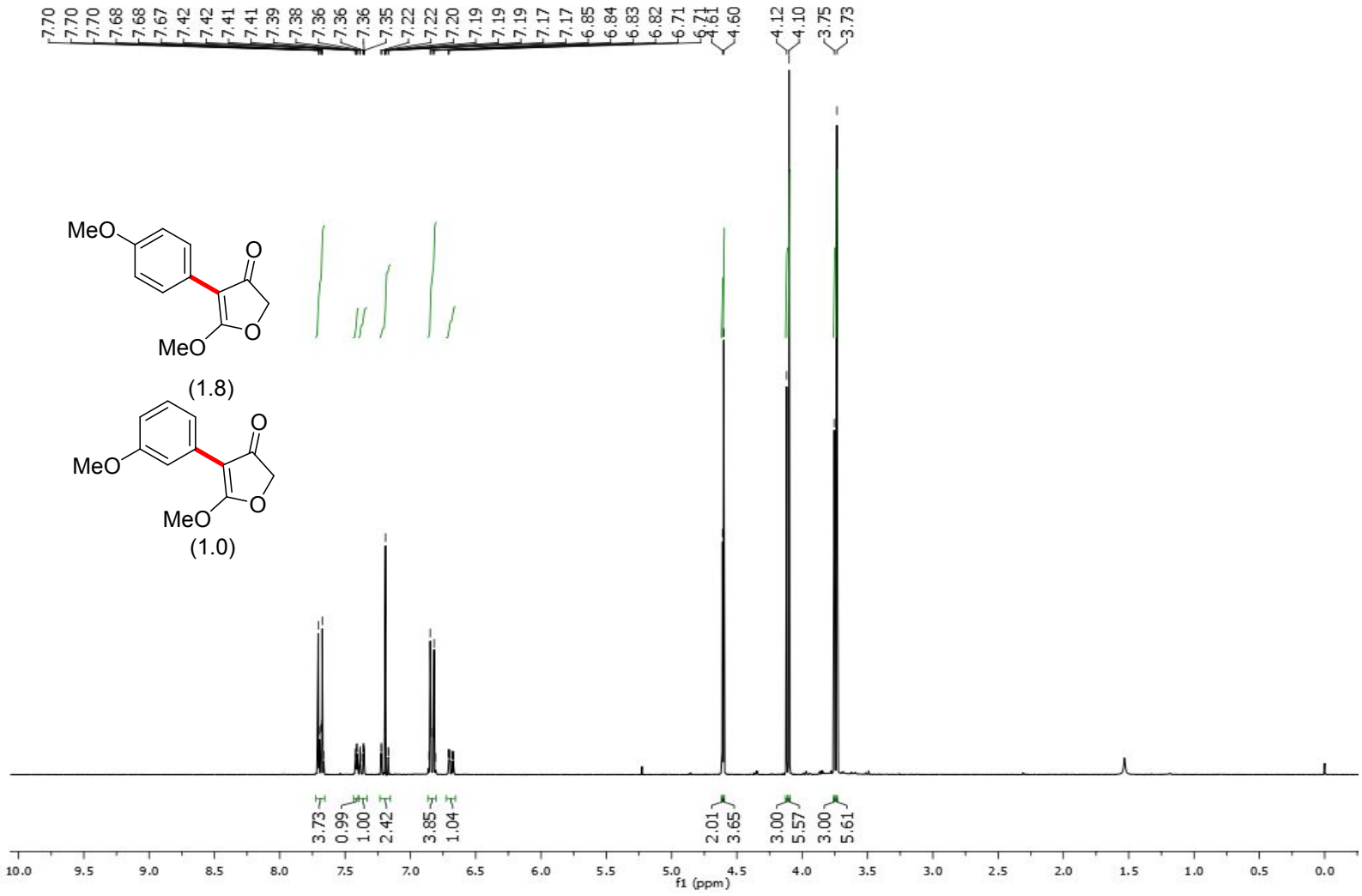
$^{1}$H NMR (300 MHz) Spectra of **13**



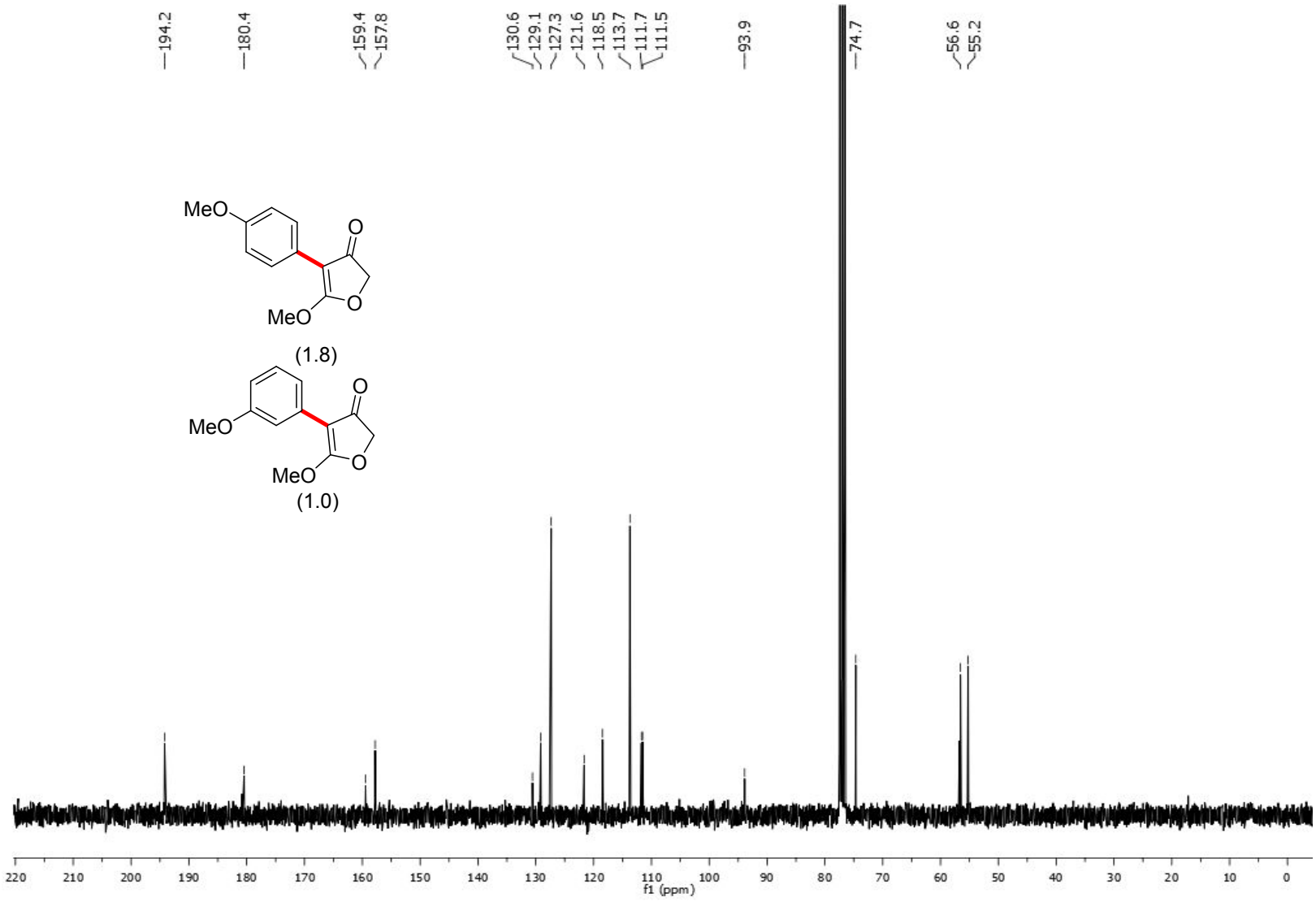
$^{13}C\{^{1}H\}$ NMR (75 MHz) Spectra of **13**



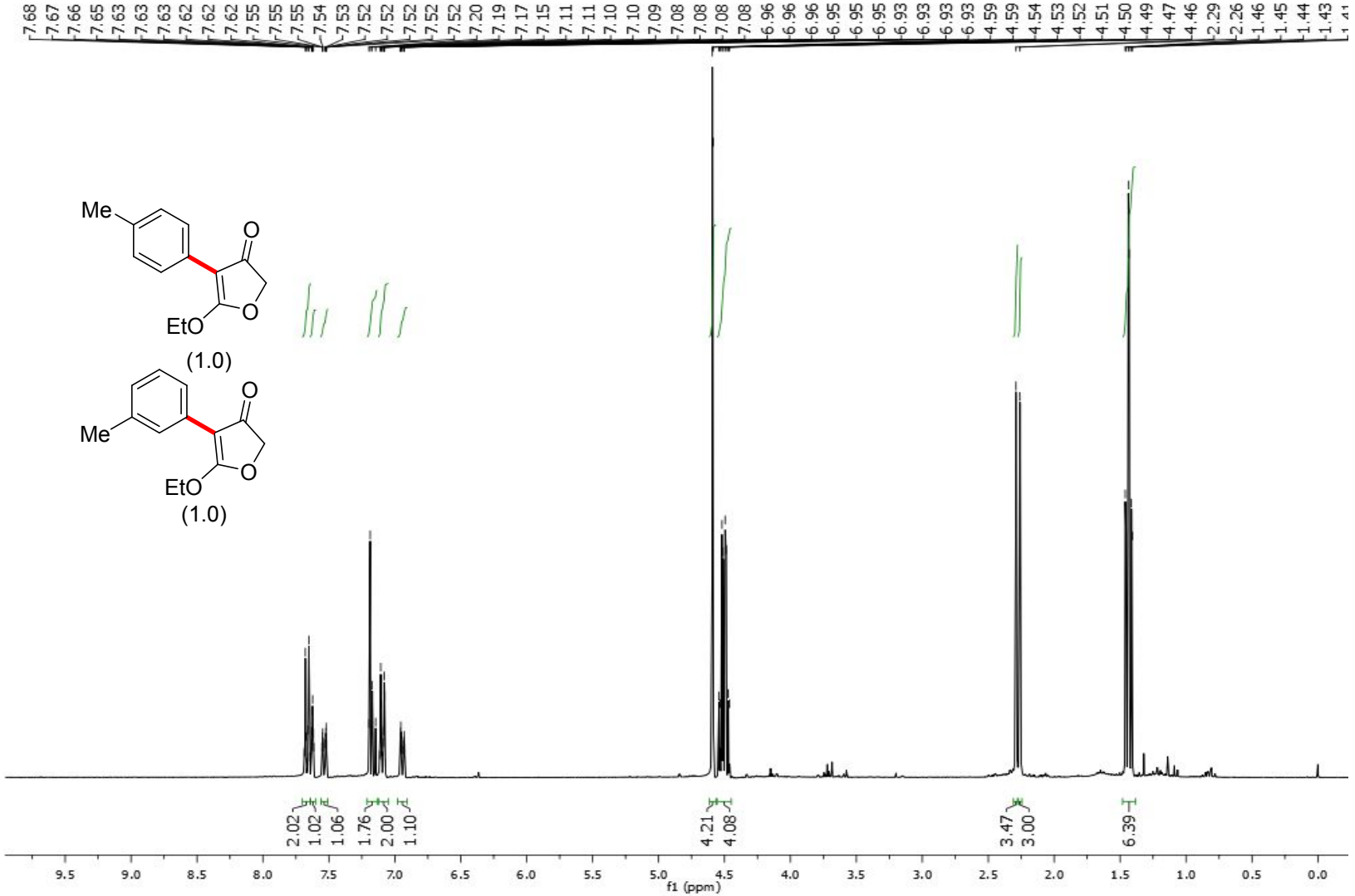
$^{1}$H NMR (300 MHz) Spectra of **14**



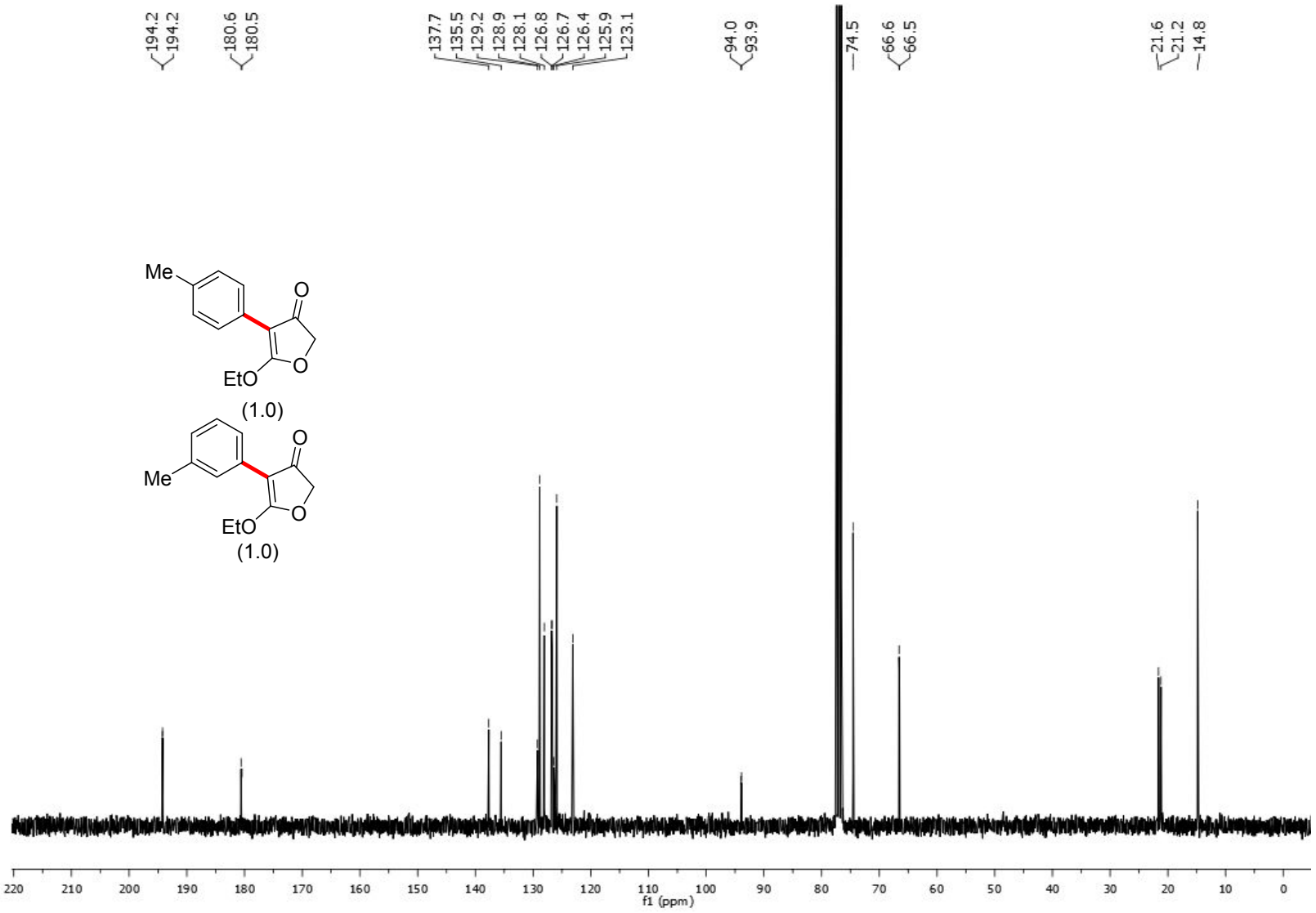
$^{13}C\{^{1}H\}$ NMR (75 MHz) Spectra of **14**



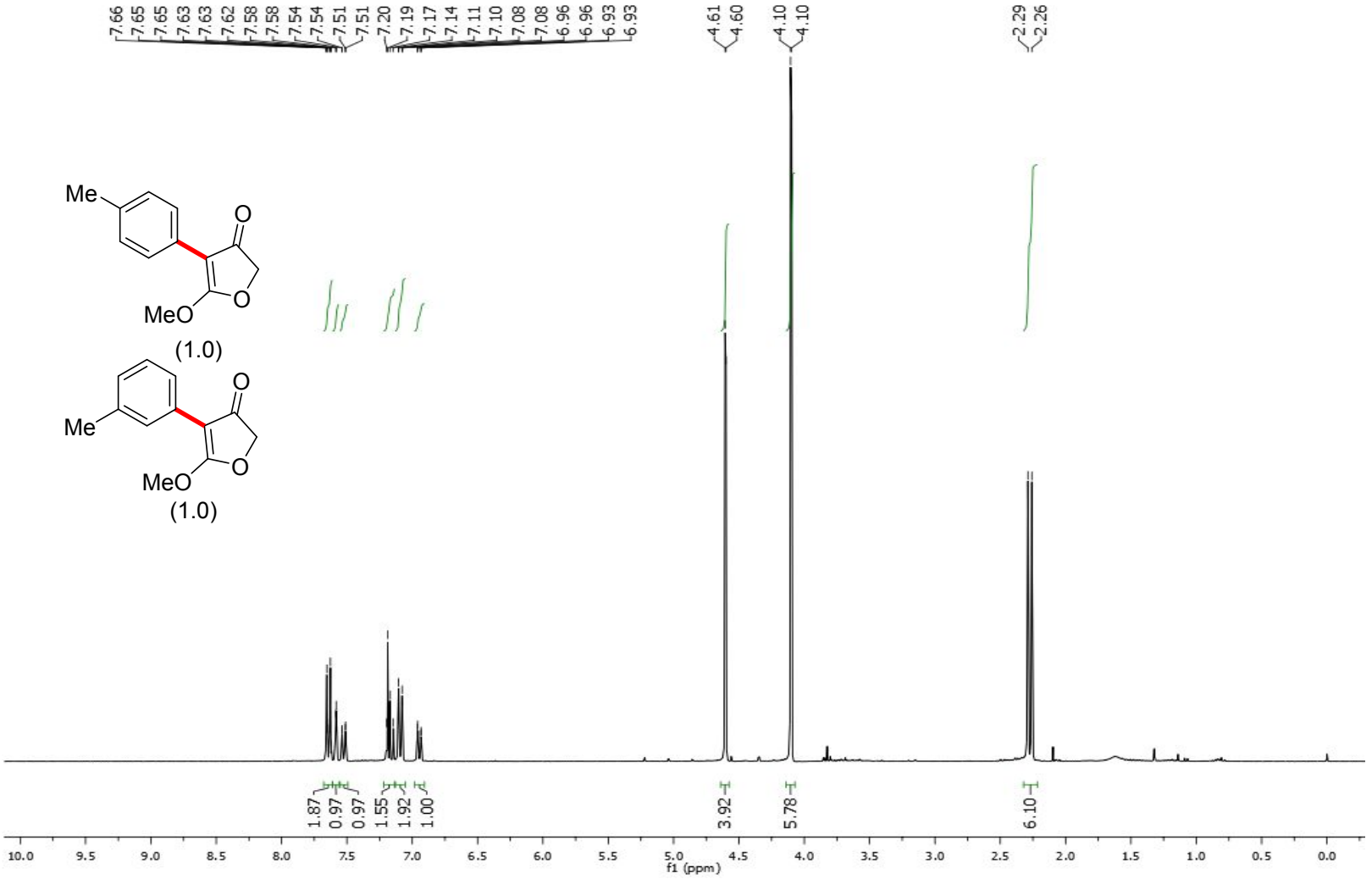
[1]H NMR (300 MHz) Spectra of **15**



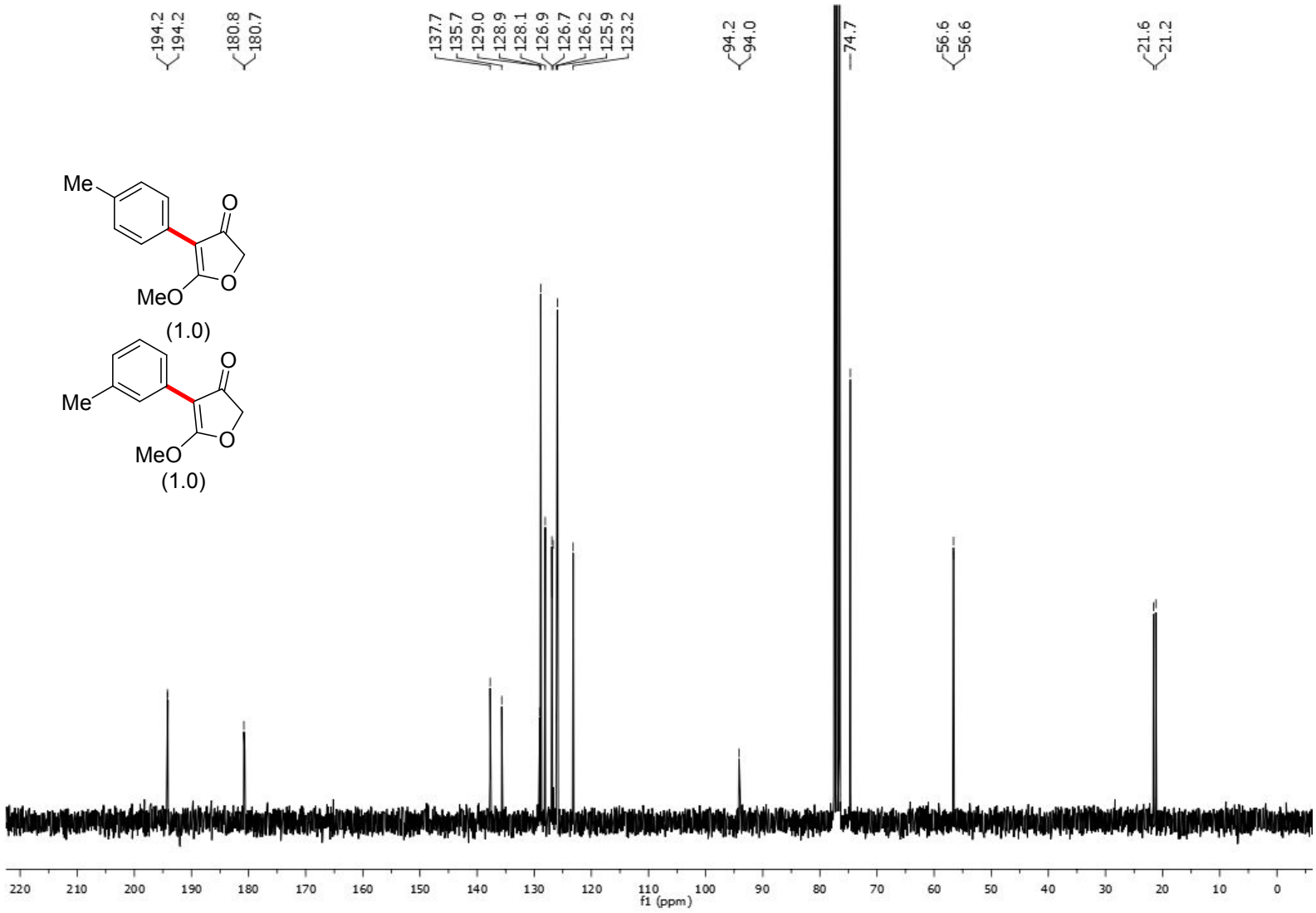
$^{13}C\{^{1}H\}$ NMR (75 MHz) Spectra of **15**



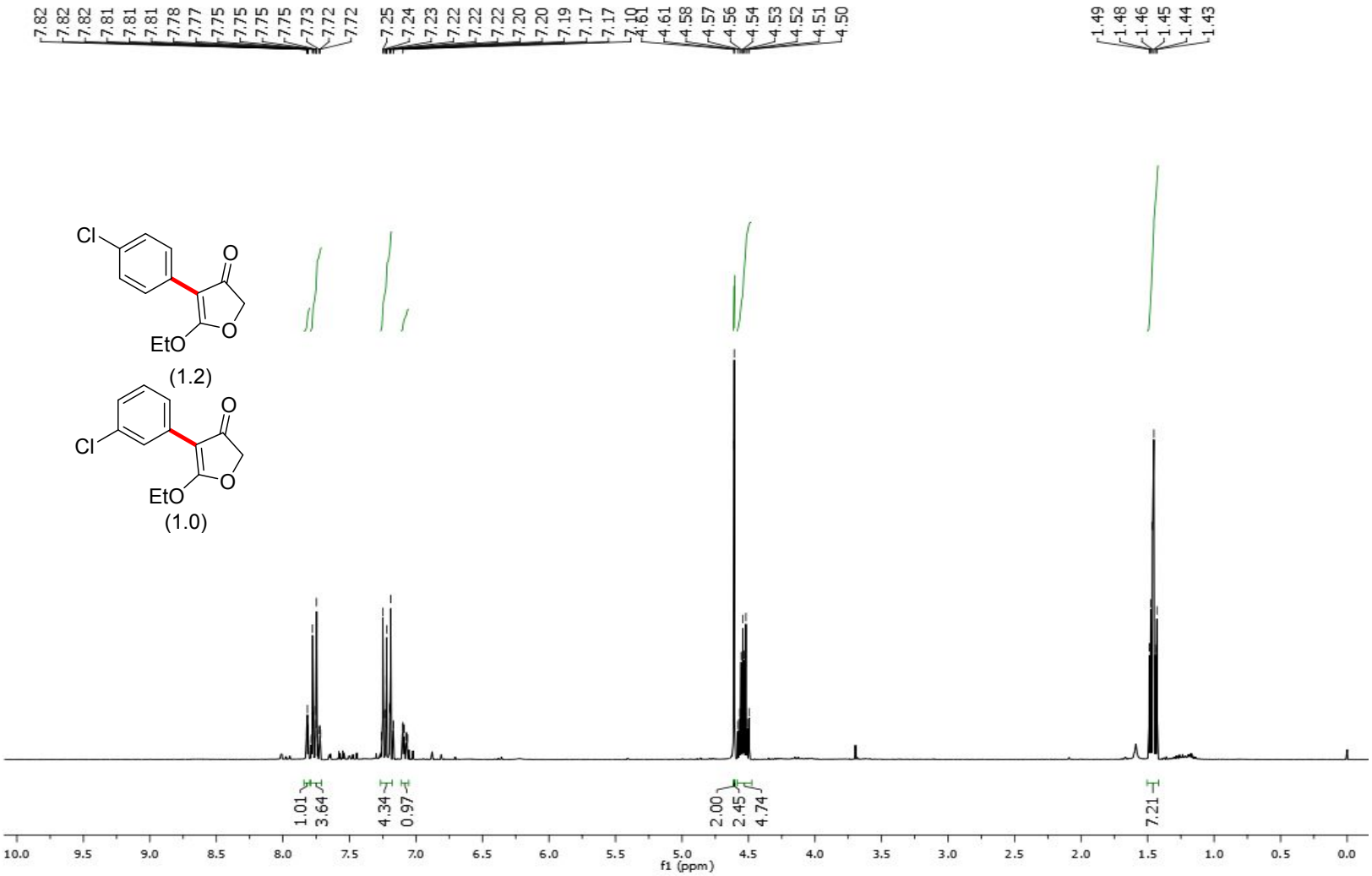
[1]H NMR (300 MHz) Spectra of **16**



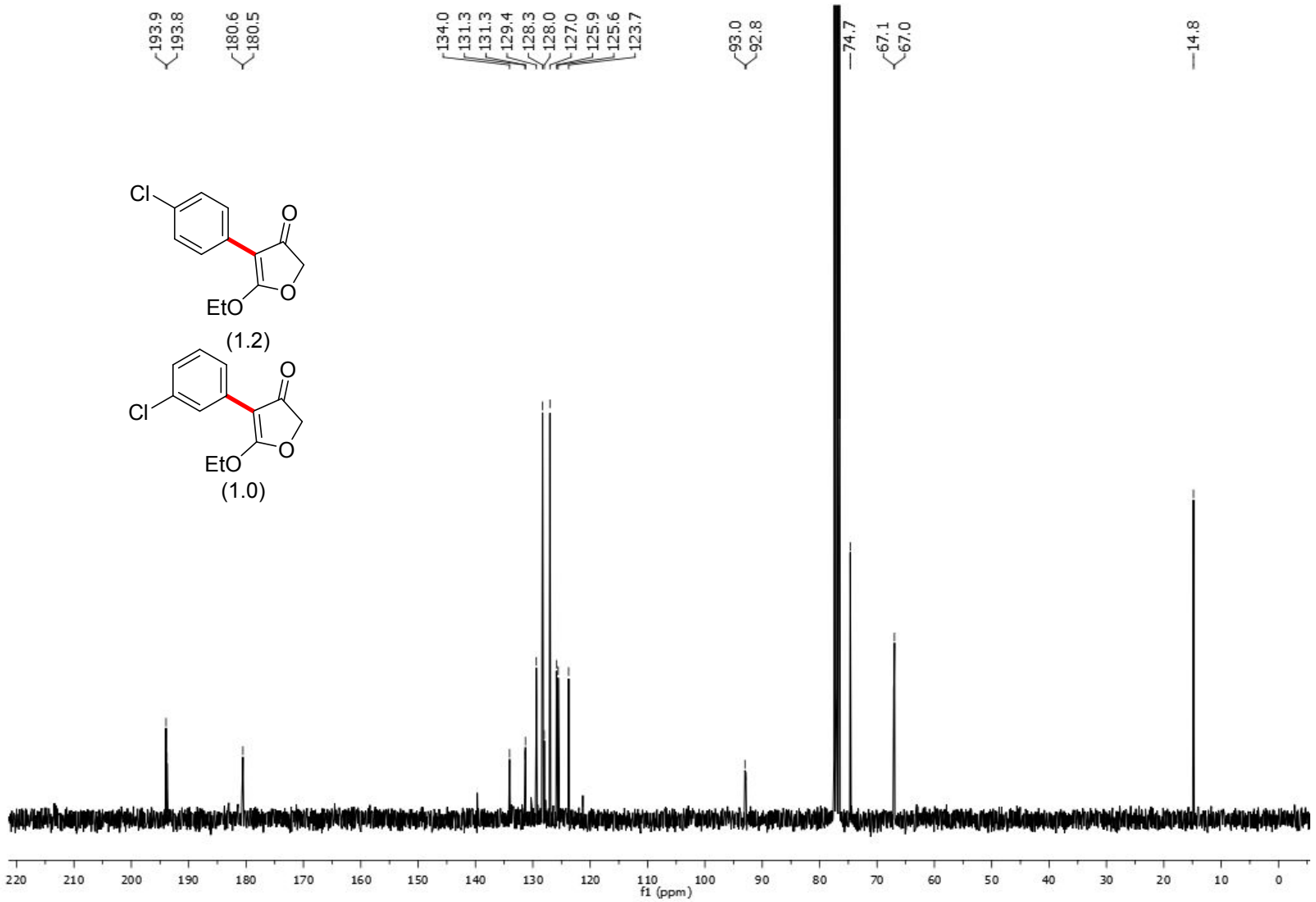
$^{13}C\{^{1}H\}$ NMR (75 MHz) Spectra of **16**



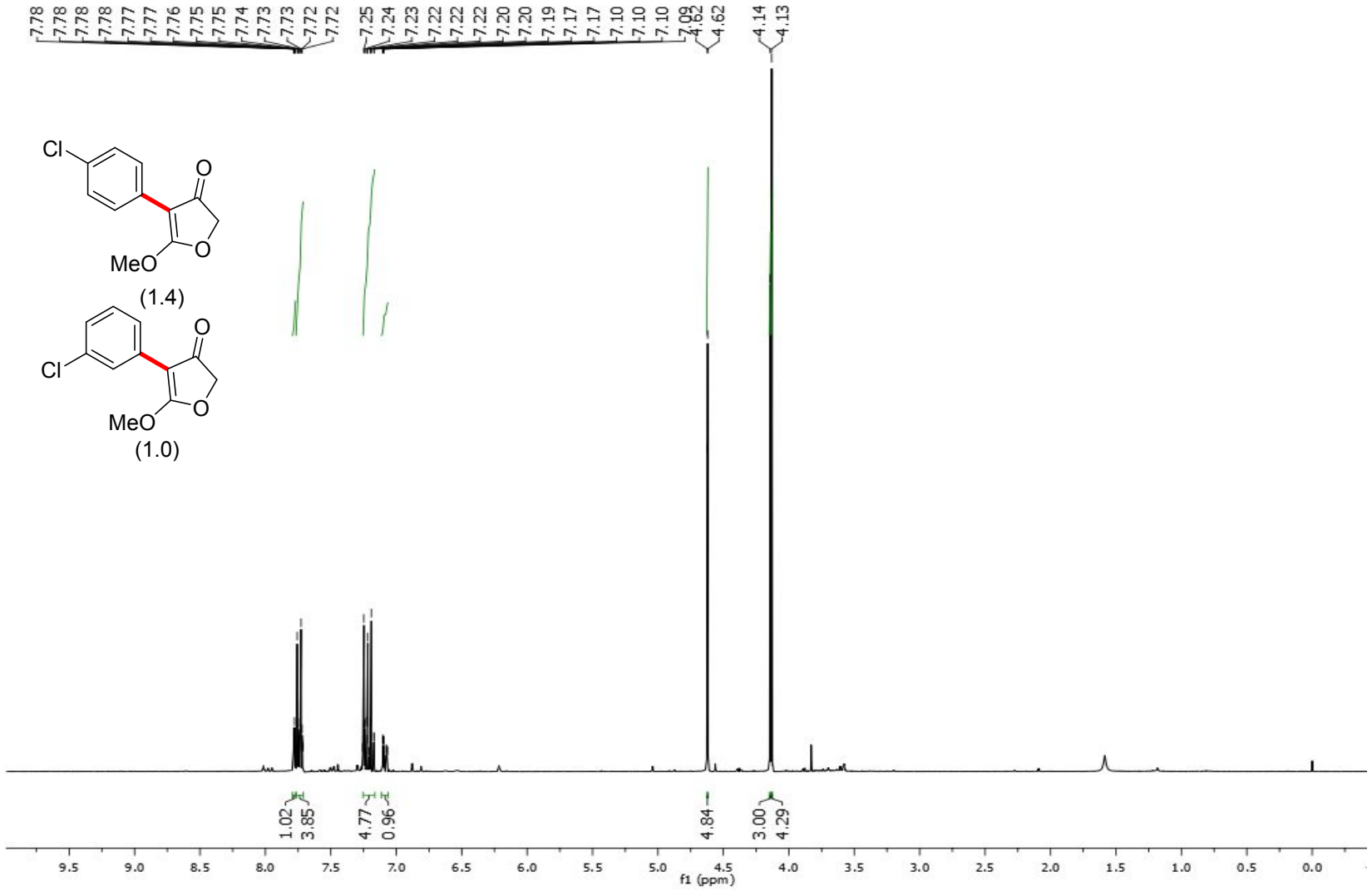
[1]H NMR (300 MHz) Spectra of **17**



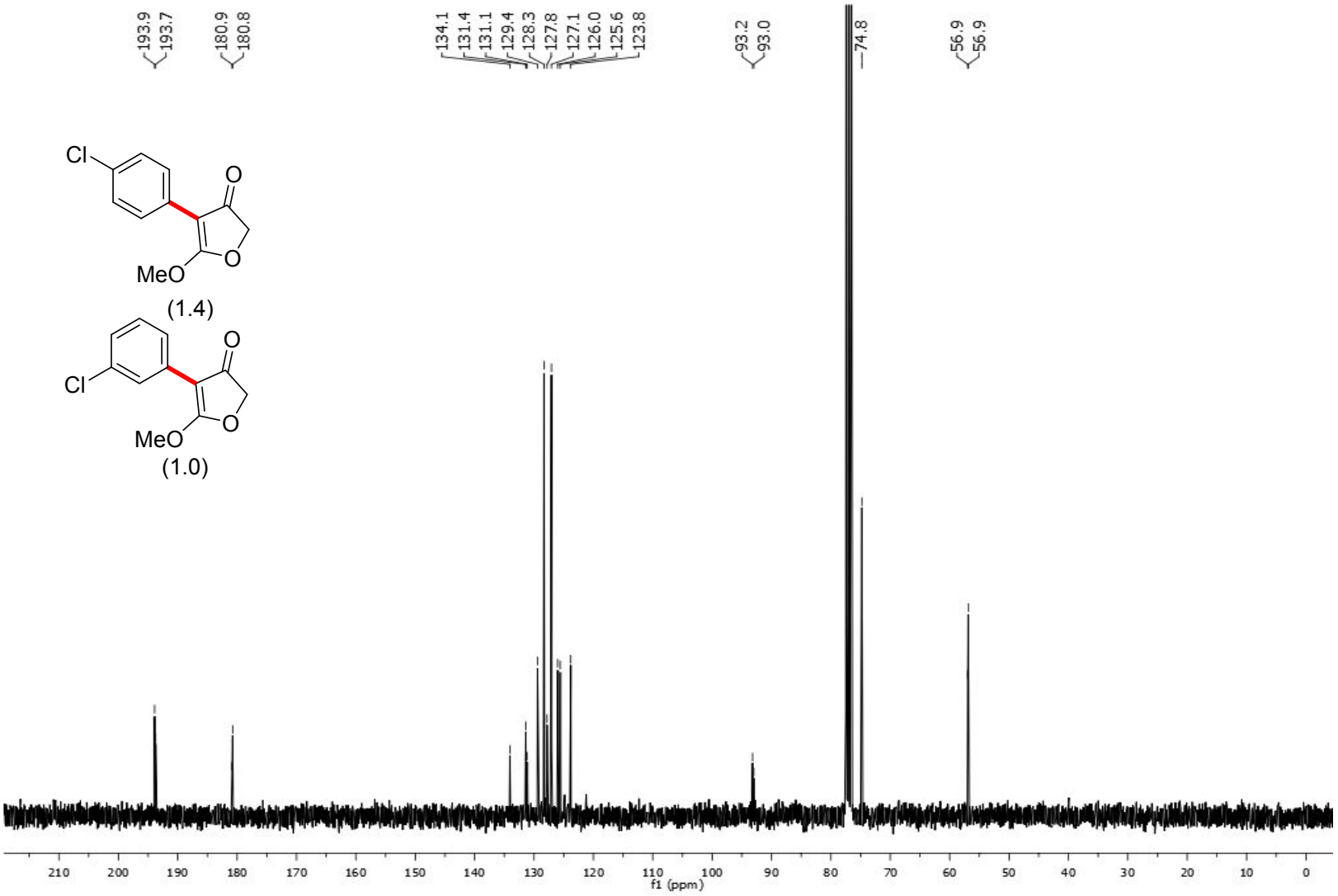
$^{13}C\{^{1}H\}$ NMR (75 MHz) Spectra of **17**



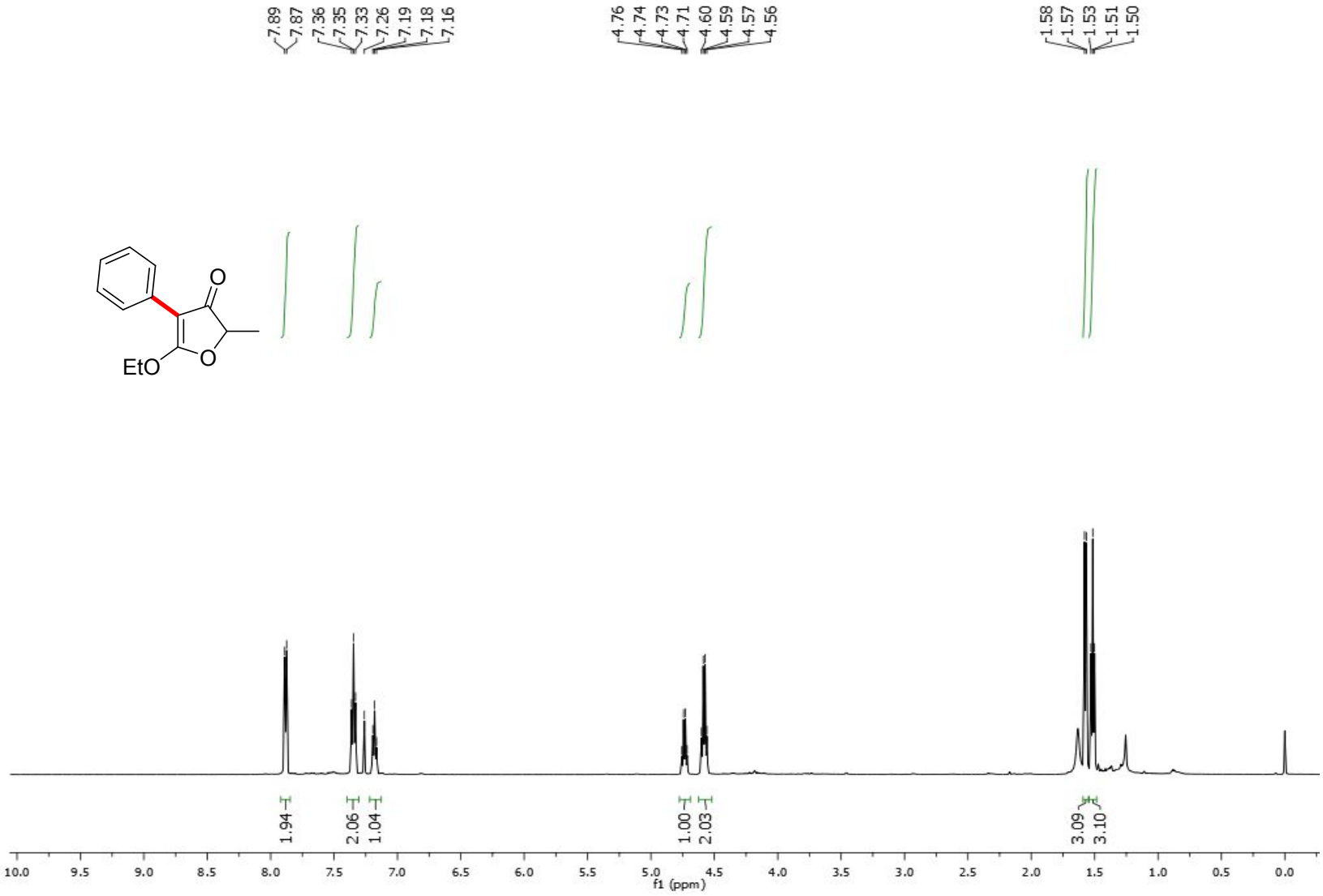
$^{1}$H NMR (300 MHz) Spectra of **18**



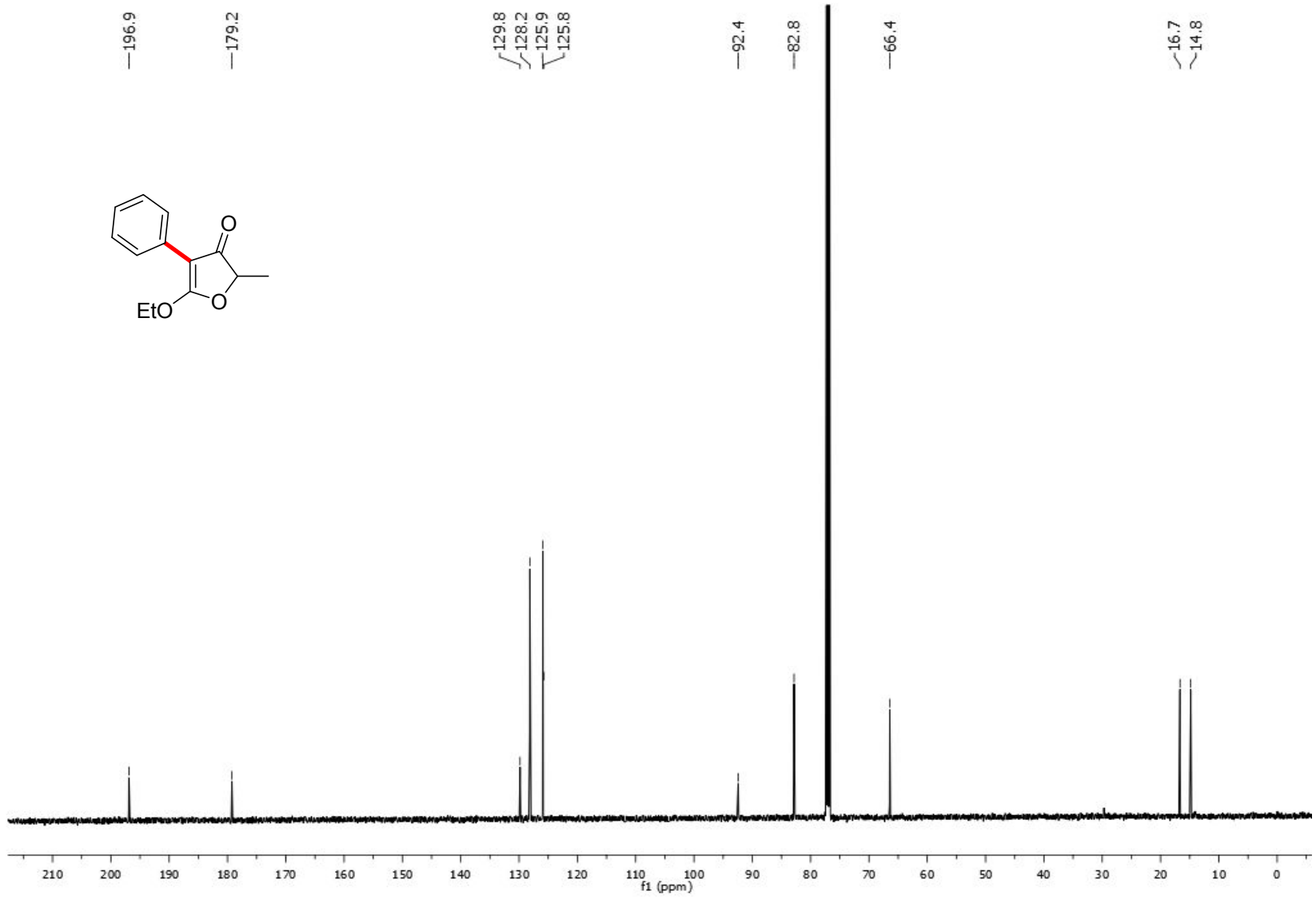
$^{13}C\{^{1}H\}$ NMR (75 MHz) Spectra of **18**



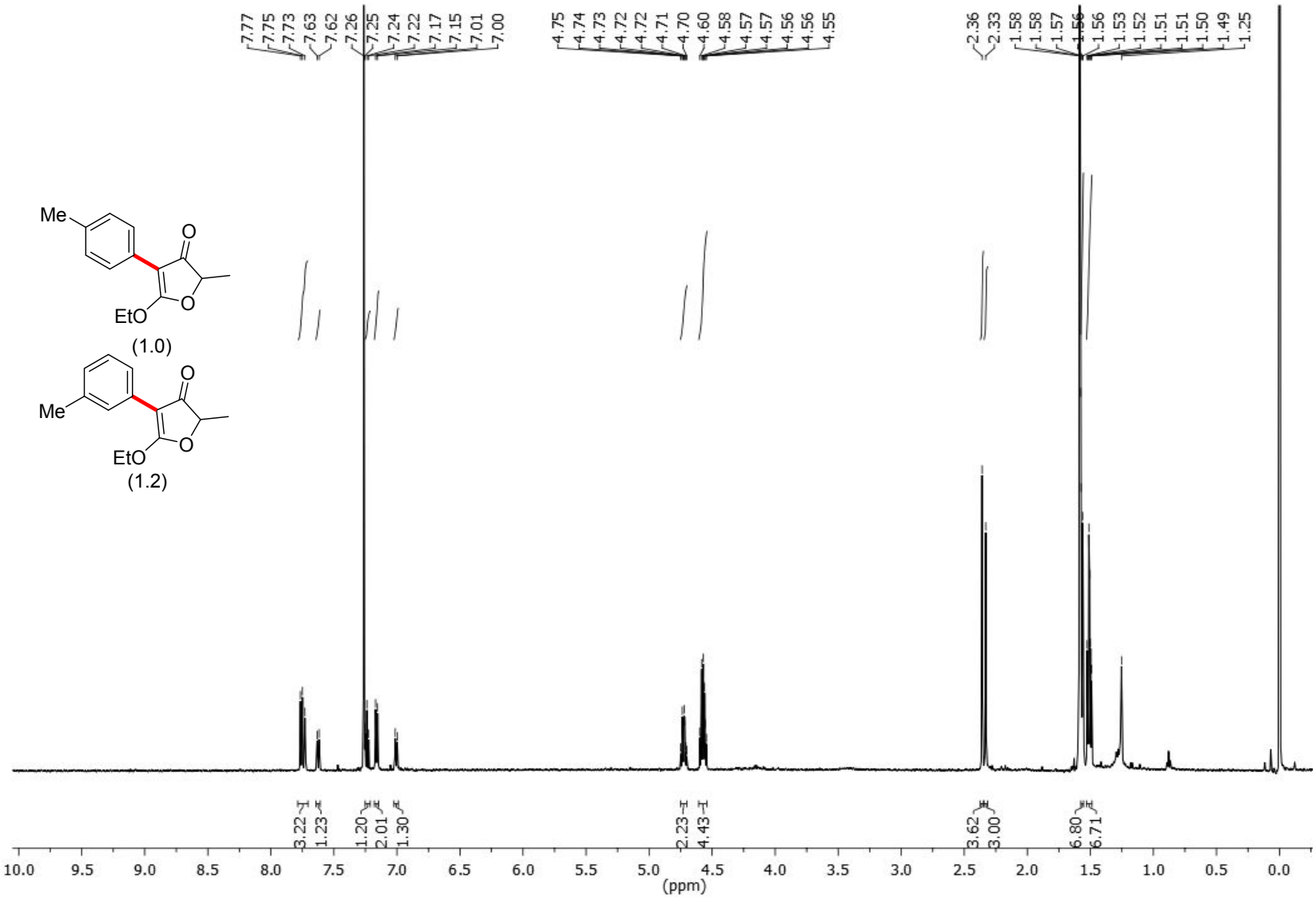
$^{1}$H NMR (500 MHz) Spectra of **19**



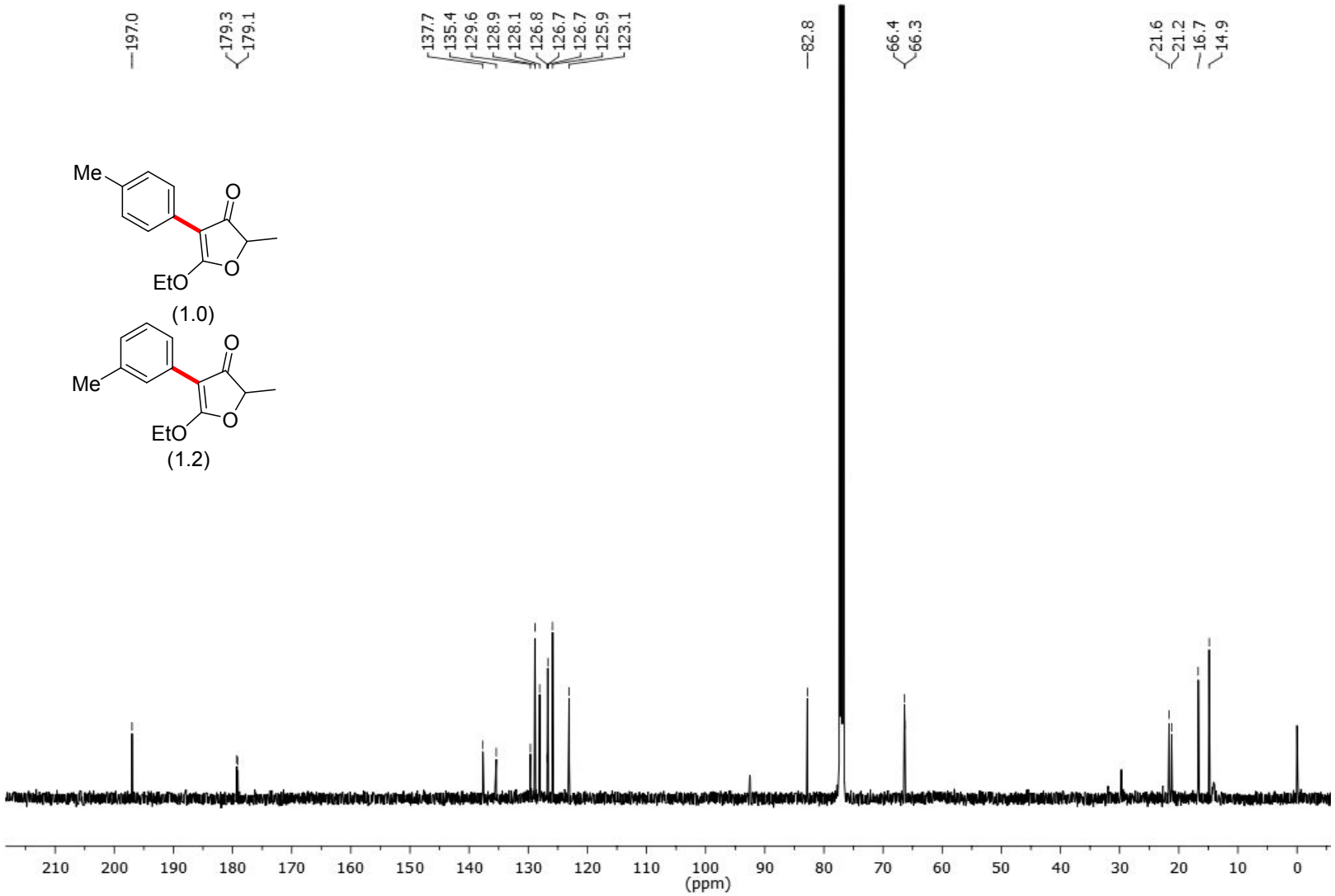
$^{13}C\{^{1}H\}$ NMR (125 MHz) Spectra of **19**



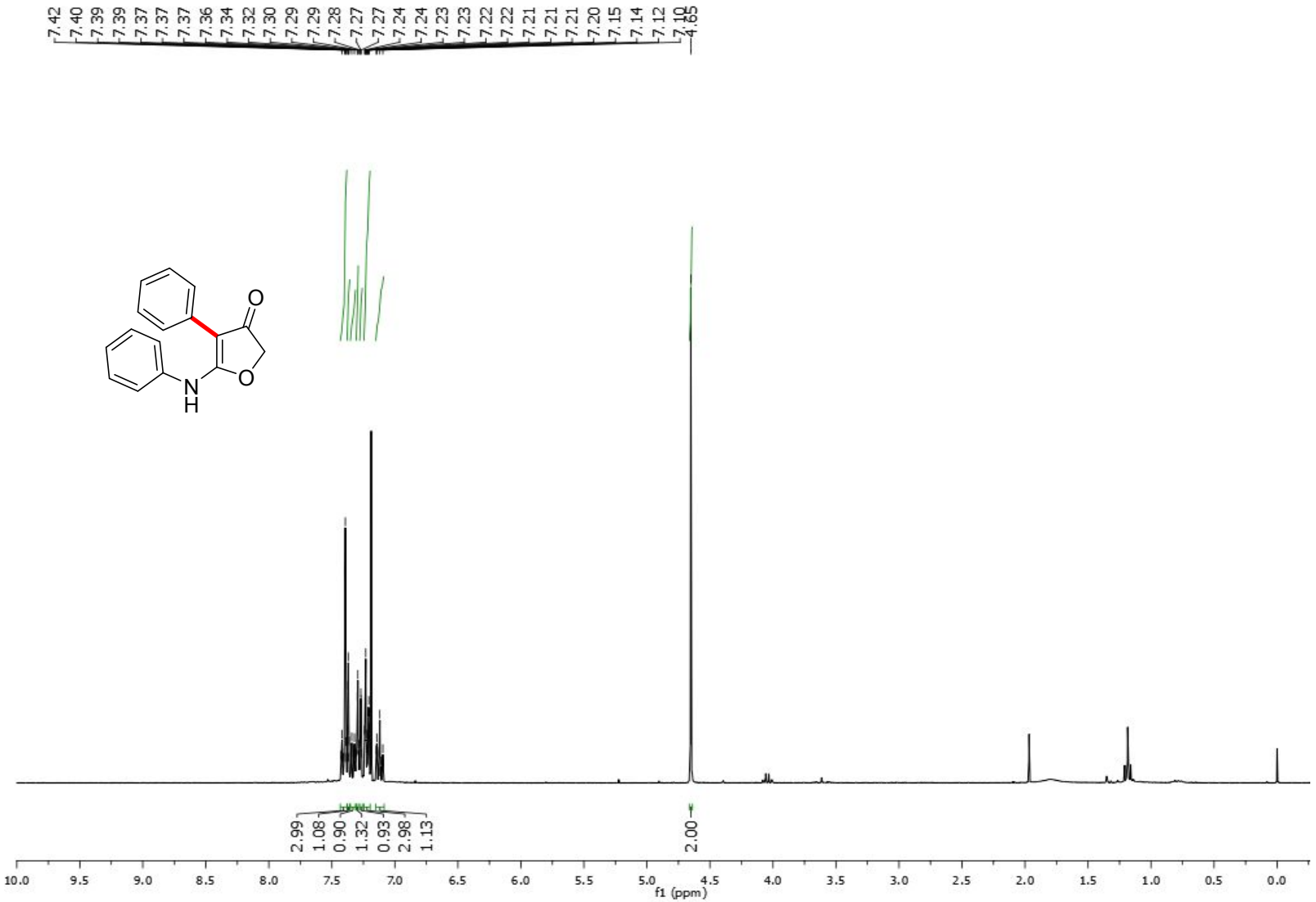
[1]H NMR (500 MHz) Spectra of **20**



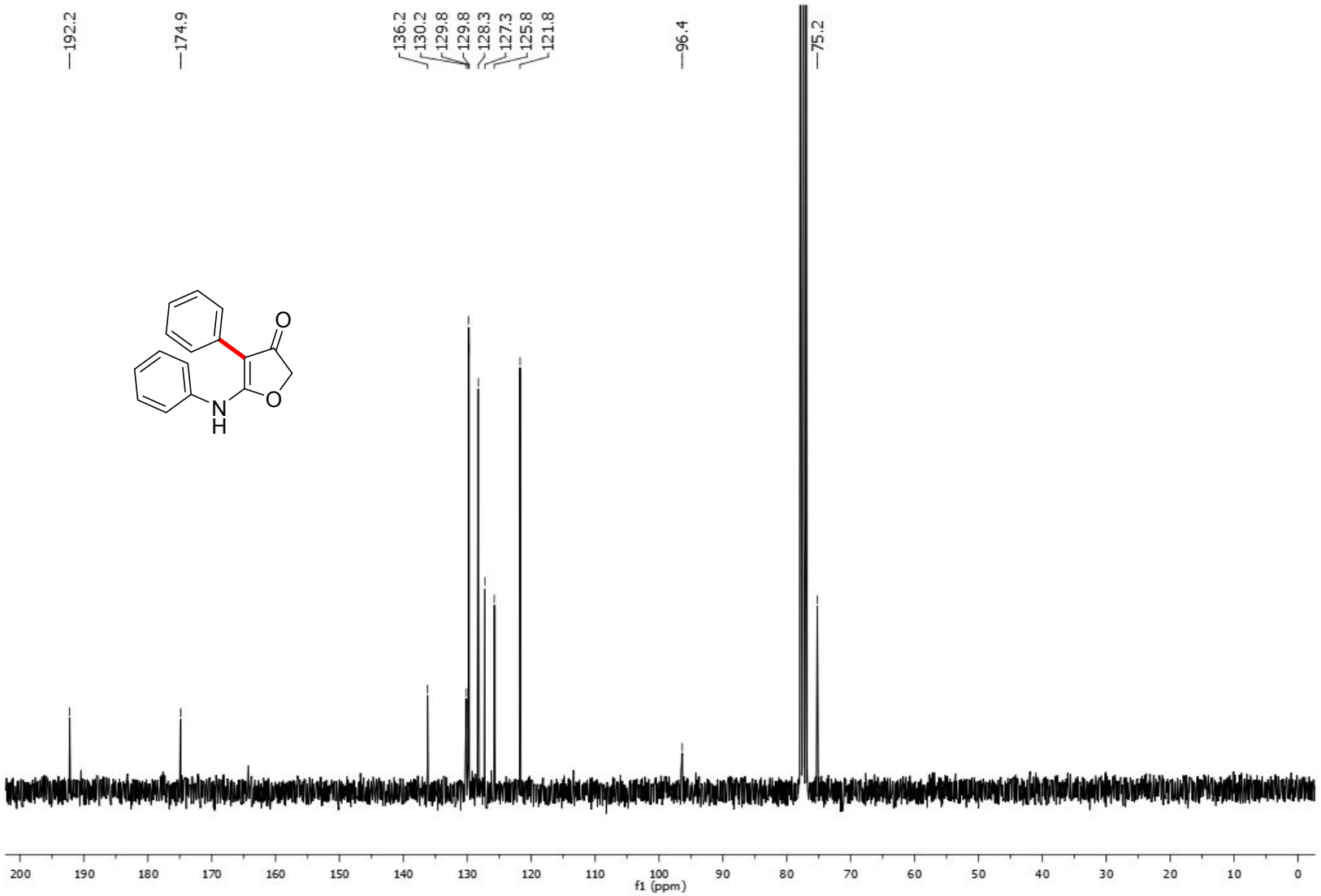
$^{13}C\{^{1}H\}$ NMR (125 MHz) Spectra of **20**



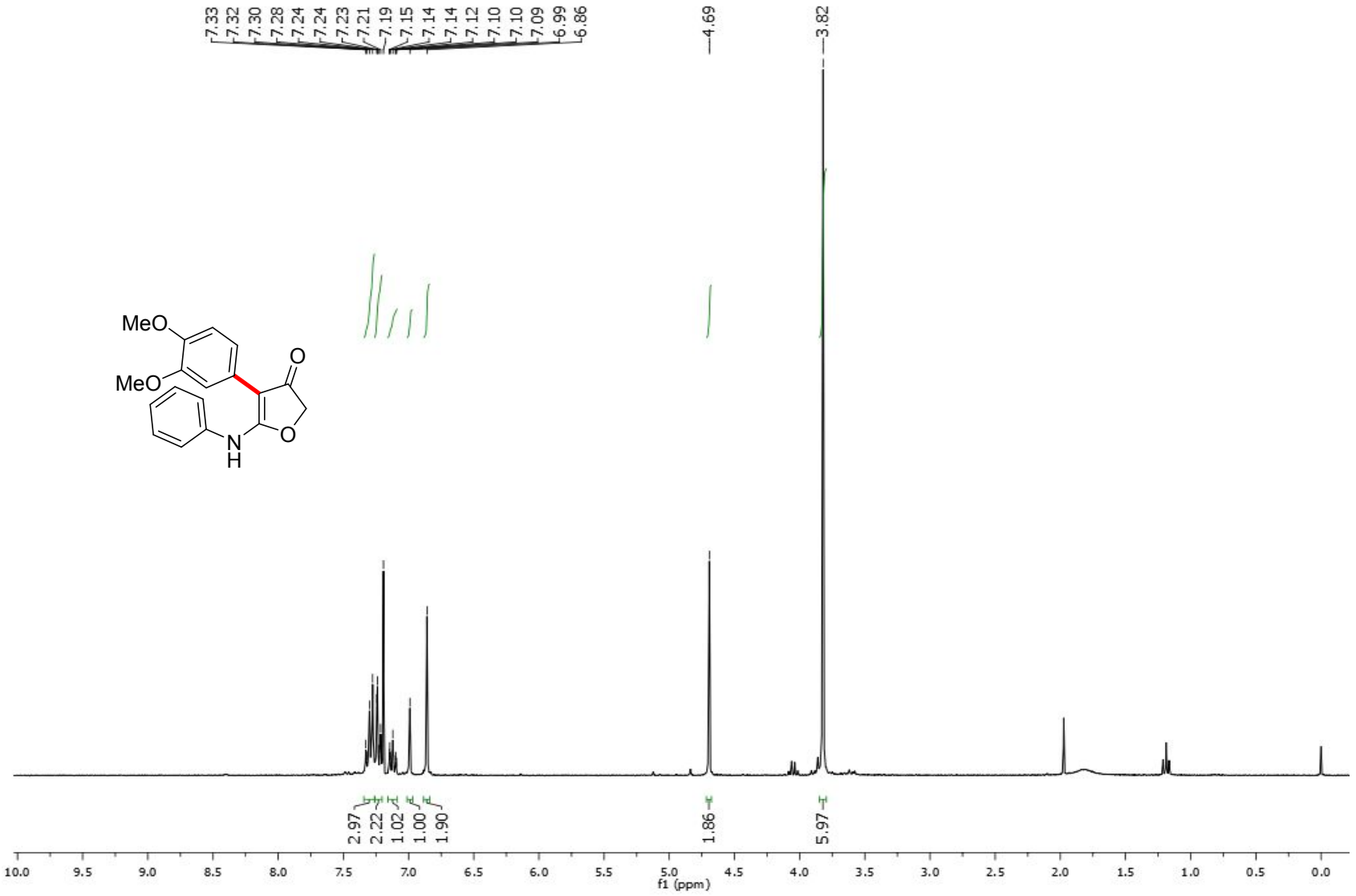
$^{1}$H NMR (300 MHz) Spectra of **22**



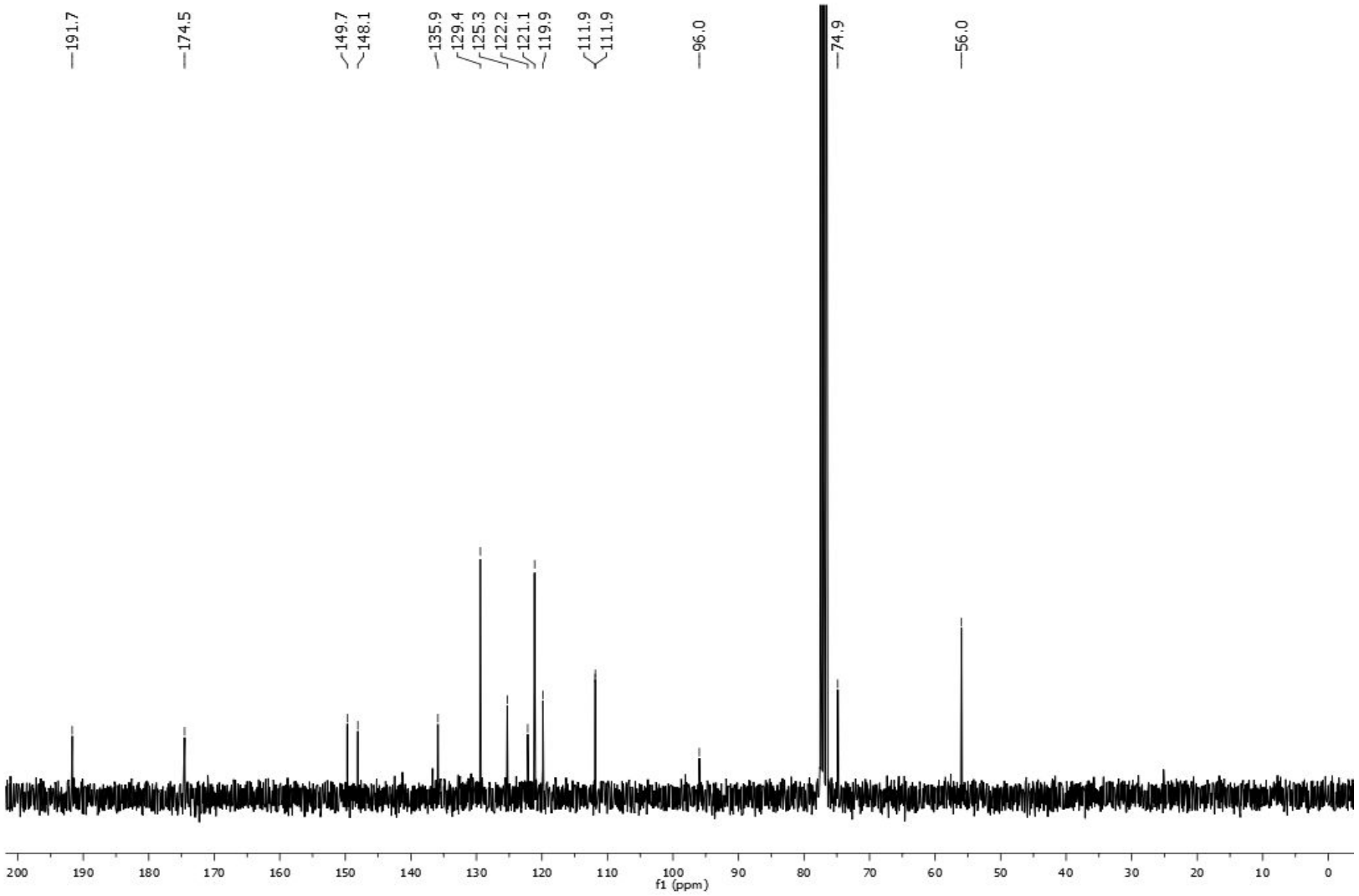
$^{13}C\{^{1}H\}$ NMR (75 MHz) Spectra of **22**



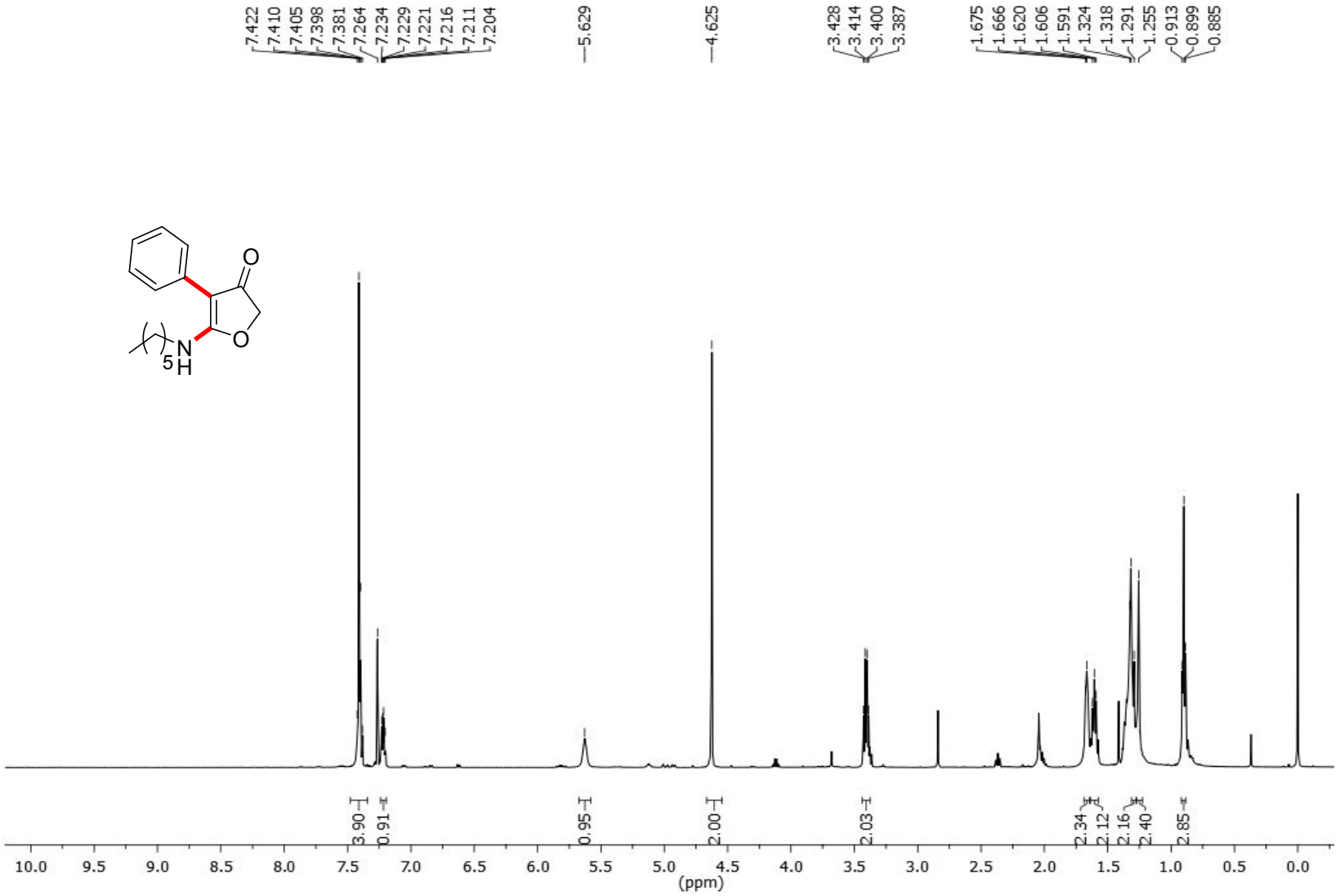
$^{1}$H NMR (500 MHz) Spectra of **23**



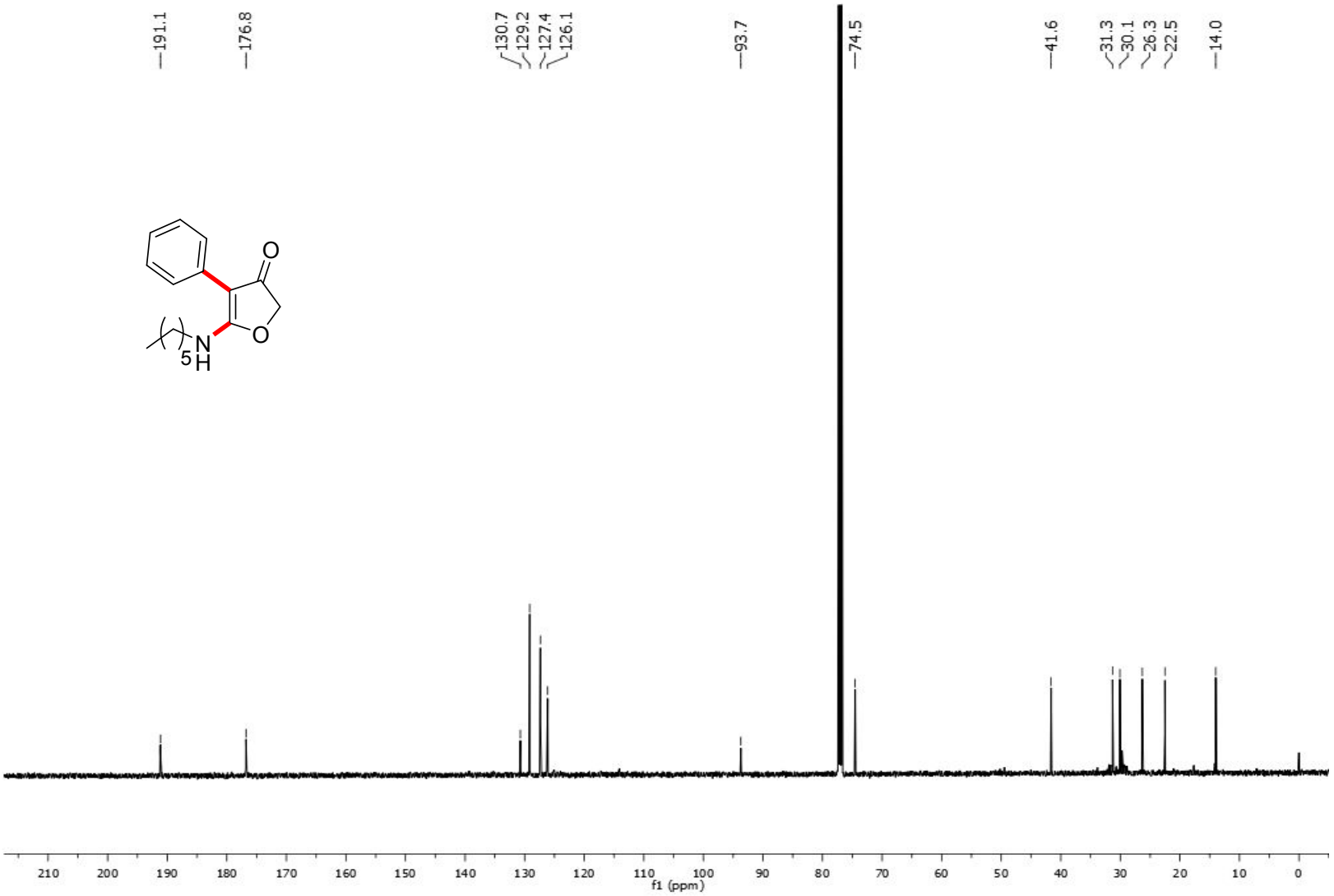
$^{13}C\{^{1}H\}$ NMR (75 MHz) Spectra of **23**



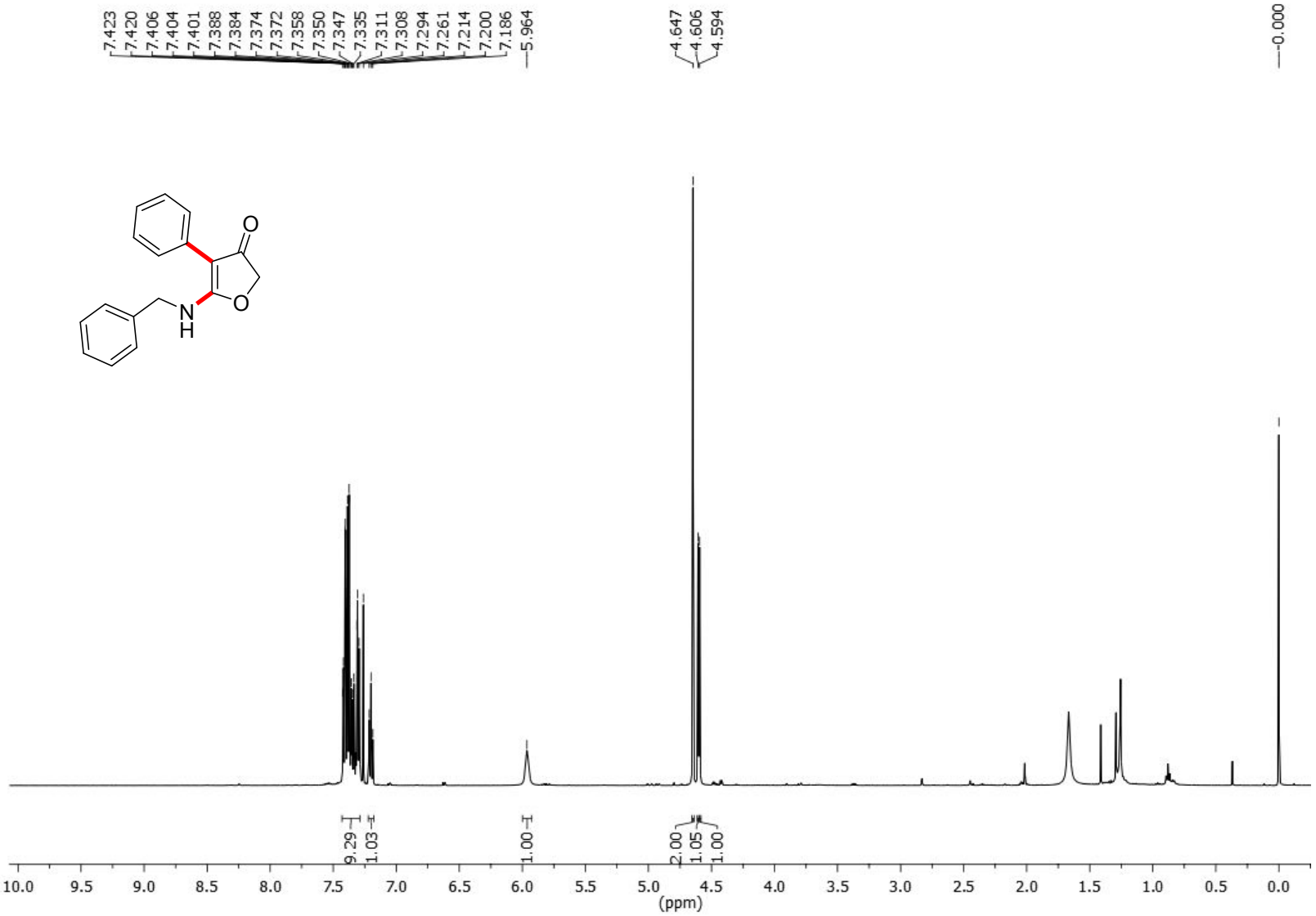
$^{1}$H NMR (500 MHz) Spectra of **26**



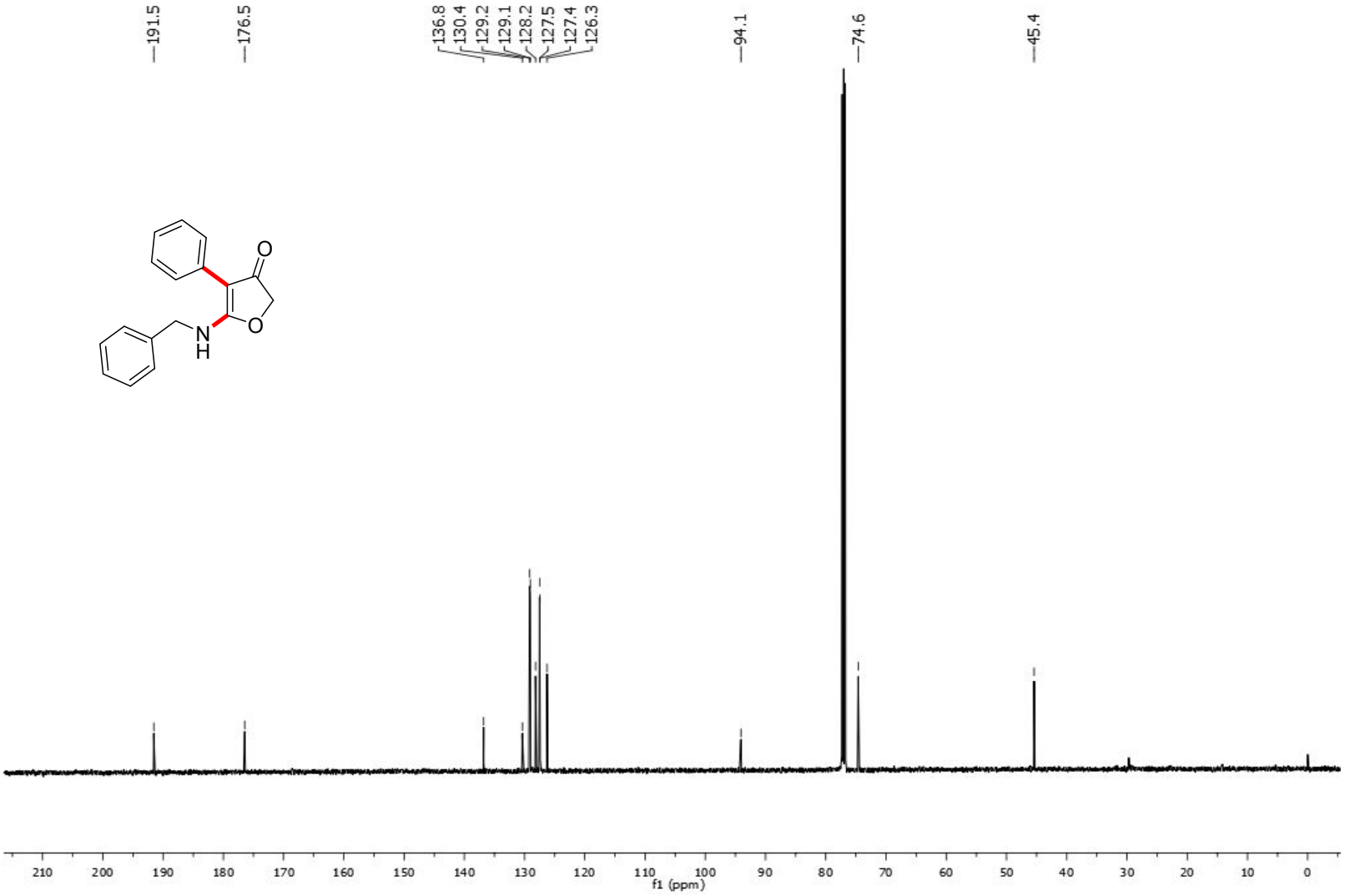
$^{13}C\{^{1}H\}$ NMR (125 MHz) Spectra of **26**



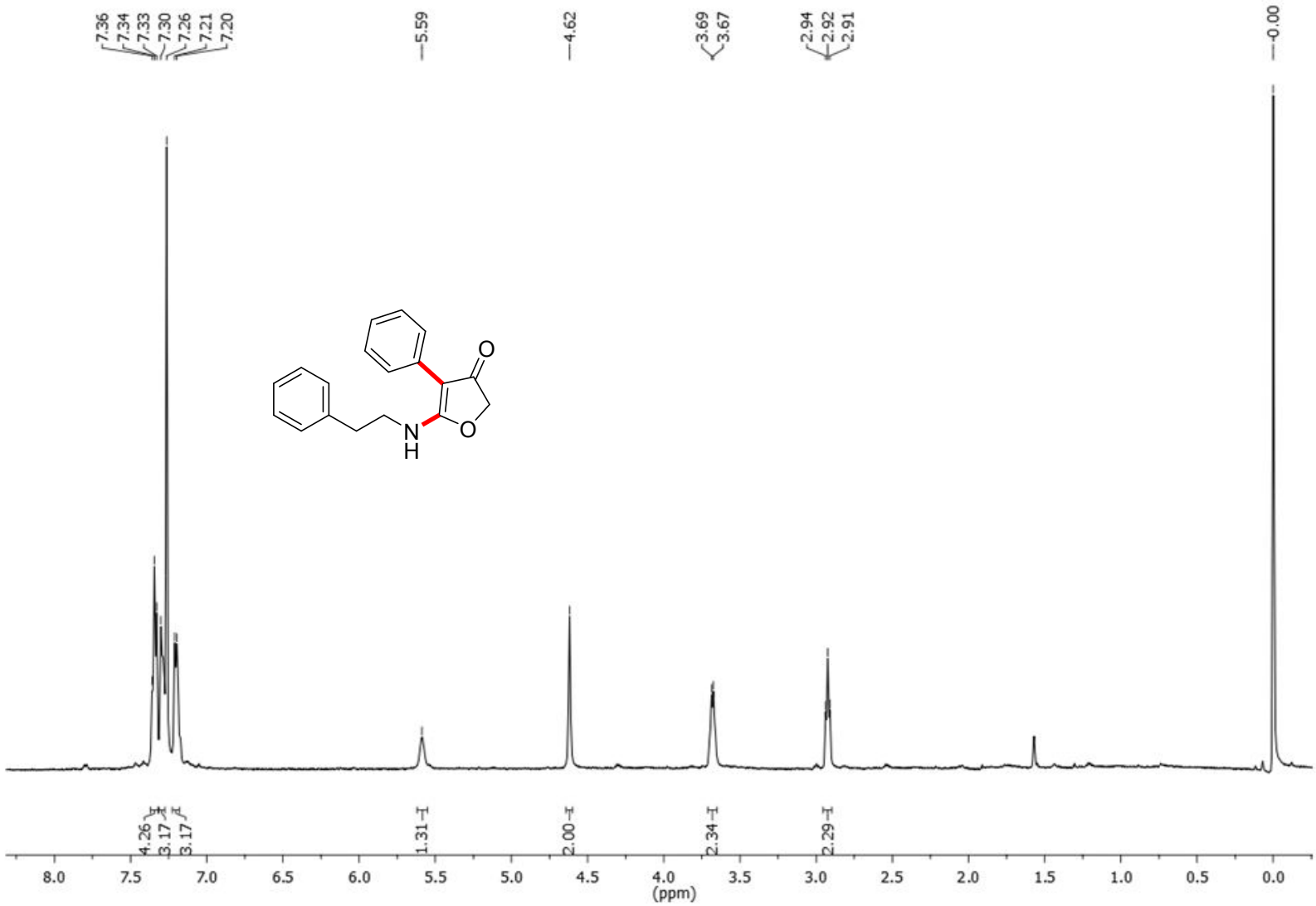
$^{1}$H NMR (500 MHz) Spectra of **27**



$^{13}C\{^{1}H\}$ NMR (125 MHz) Spectra of **27**



$^{1}$H NMR (500 MHz) Spectra of **28**



$^{13}C\{^{1}H\}$ NMR (125 MHz) Spectra of **28**