

*Supporting Information*

**Preparation of Cycloheptane Ring by Nucleophilic Cyclopropanation of  
1,2-Diketones with Bis(iodozincio)methane**

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- S-2**      **Preparation of Diketone**
- S-4**      **Optimization of Microflow Reaction**
- S-6**      **<sup>1</sup>H and <sup>13</sup>C NMR of Substrates and Products**

## Instrumentation and Chemicals

Nuclear magnetic resonance spectra were taken on Varian UNITY INOVA 500 ( $^1\text{H}$ , 500 MHz;  $^{13}\text{C}$ , 125 MHz) spectrometer using tetramethylsilane for  $^1\text{H}$  NMR as an internal standard ( $\delta = 0$  ppm),  $\text{CDCl}_3$  for  $^{13}\text{C}$  NMR as an internal standard ( $\delta = 77.0$  ppm).  $^1\text{H}$  NMR data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, quint = quintet, sext = sextet, sept = septet, br = broad, m = multiplet), coupling constants (Hz), and integration. High-resolution mass spectra were obtained with a JEOL JMS-700 spectrometer by electron ionization at 70 eV. Elemental analyses were carried out with a YANAKO MT2 CHN CORDER machine at Kyoto University Elemental Analysis Center. Infrared (IR) spectra were determined on a SHIMADZU FTIR-8200PC spectrometer. Melting points were determined using a YANAKO MP-500D. TLC analyses were performed by means of Merck Kieselgel 60 F254 (0.25 mm) Plates. Visualization was accomplished with UV light (254 nm) and an aqueous vanillin solution followed by heating. Flash column chromatography was carried out using Kanto Chemical silica gel (spherical, 40–100  $\mu\text{m}$ ).

Unless otherwise noted, commercially available reagents were used without purification. Tetrahydrofuran, Dehydrated stabilizer free —Super— was purchased from Kanto Chemical Co., stored under argon, and used as it is. Zinc powder was used after washing with 10% HCl according to the reported procedure.<sup>1</sup>

### Preparation of (*1E,5E*)-1,6-diphenylhexa-1,5-diene-3,4-dione (**2a**)

To a solution of dimethyl oxalate (47 mmol) in ether (100 ml), *N,N'*-dimethylethylene-1,2-diamine (47 mmol) was added. The resulting mixture was stirred for 12 h at 25 °C. The formed white powder was separated by filtration through glass filter G3. The residue was washed with ice-cooled ether. The obtained white powder was dried *in vacuo*. Without further purification, 1,4-dimethylpiperazine-2,3-dione (**11**, 42 mmol) was obtained in 90% yield. To a dispersion of **11** (5.0 mmol) in THF (7 ml), *E*-2-phenylethenylmagnesium bromide (15 mmol, 0.7 M in THF) was added dropwise at 0 °C under Ar. The mixture was stirred for 30 min at 25 °C and for 2 h under THF reflux. The resulting mixture was poured into 3 M HCl(aq) and extracted with ethyl acetate. The combined organic layers were washed with brine, dried over sodium sulfate, and concentrated. Purification by silica gel column chromatography (hexane / ethyl acetate) gave pure **2a** in 90% yield (1.17 g). 1,2-Diketones, **2b,c,d,e,g,h** were prepared in the same way.

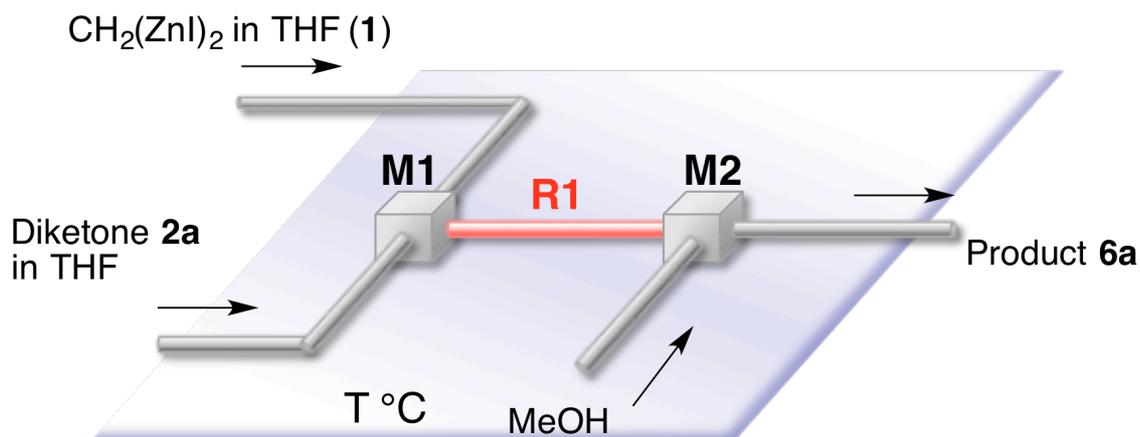
### Preparation of (*1E,5E*)-1,6-difurylhexa-1,5-diene-3,4-dione (**2f**)

To a solution of 2-furancarboxaldehyde (60.0 mmol) and 2,3-butanedione (15.0 mmol) in MeOH (20 ml), piperidine (3.0 mmol) and glacial acetic acid (3.0 mmol) were added sequentially. After the mixture was stirred under MeOH reflux for 6.5 h, methanol was moved by distillation. After the resulting mixture was cooled to 0 °C, it was filtered through glass filter G3. The residue was washed with ice-cold methanol. The title compound (**2f**) was obtained as brown powder in 44% yield (1.40 g).

### Preparation of (*1E,5E*)-1-phenylhepta-1,5-diene-3,4-dione (**2j**)

To a dispersion of 1,4-dimethylpiperazine-2,3-dione (**11**, 10.0 mmol) in THF (15 ml), *E*-2-phenylethenylmagnesium bromide (7.5 mmol, 0.7 M in THF) was added dropwise at 0 °C under Ar. After the mixture was stirred for 1.5 h at 25 °C, 1-propenylmagnesium bromide (15 mmol, 0.8 M in THF) was added at 0 °C under Ar. The resulting mixture was stirred for 0.5 h at 25 °C, and for 8 h under THF refluxing condition. and for 2 h under THF reflux. The resulting mixture was poured into 3 M HCl(aq) and extracted with ethyl acetate. The combined organic layers were washed with brine, dried over sodium sulfate, and concentrated. The crude product was a mixture of **2a**, **2h**, and **2j**. Purification by silica gel column chromatography (hexane/ethyl acetate and toluene/ether) gave pure **2j** in 25% yield (0.25 g). 1,2-Diketones, **2i,k** were prepared and isolated via separation in the same way.

## Optimization of Microflow Reaction



The reaction was performed using the microflow system shown above: T-shaped SUS micromixer: **M1** (inner diameter: 0.5 mm) and **M2** (inner diameter: 0.5 mm), SUS microtube reactor: **R1** ( $\phi = 1.0$  mm, length =  $x$  m), a solution of **1**: 3.92 mL/min, 0.16 and 0.11 M; a solution of **2a** in thf: 3.92 mL/min, 0.09 M; methanol: 7.25 mL/min. The flow rate was fixed and the residence time in **R1** was varied and optimized by changing its length. Residence time ( $t$ ) was calculated from the inner volume and the flow rates. After a steady state was reached, the product solution was collected for 90 sec. The resulting mixture was poured into 1M HCl<sub>aq</sub>. The product was extracted with ethyl acetate. The combined organic layers were washed with brine and dried over sodium sulfate. Purification by silica gel column chromatography (hexane/ethyl acetate) gave the cycloheptane derivatives **6a**, which gave the yield. In Tables S1, the yields of **6a**, under various temperature and various residence time using 1.8 equiv of **1** (0.16 M), are shown. In Table S2, those using 1.2 equiv of **1** (0.11 M) are shown. Among them the best yield of **6a** was 85% ( $t = 6$  s,  $x = 1$  m, 20 °C, **1/2a** = 1.8). When dichloromethane solution of **2a** was used instead of THF solution under the same condition, the yield of **6a** was improved to over 99% yield.

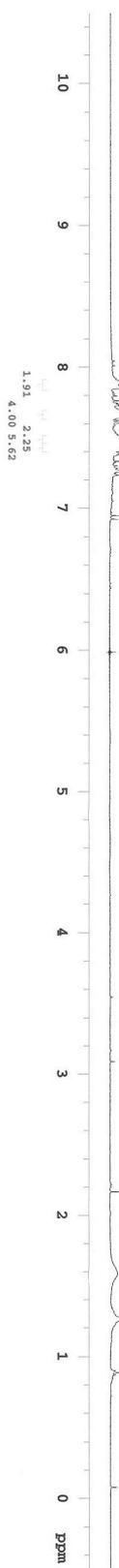
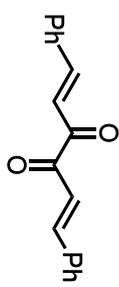
**Table S1.** Yields of **6a** under various residence time ( $t$  s) and temperature ( $T$  °C) using 0.16 M of **1** ( $1/2a = 1.8$ ).

$T$ °C \ $t$	4 s	6 s	8 s
40	77%	81%	83%
20	84%	<b>85%</b>	80%
0	71%	62%	55%

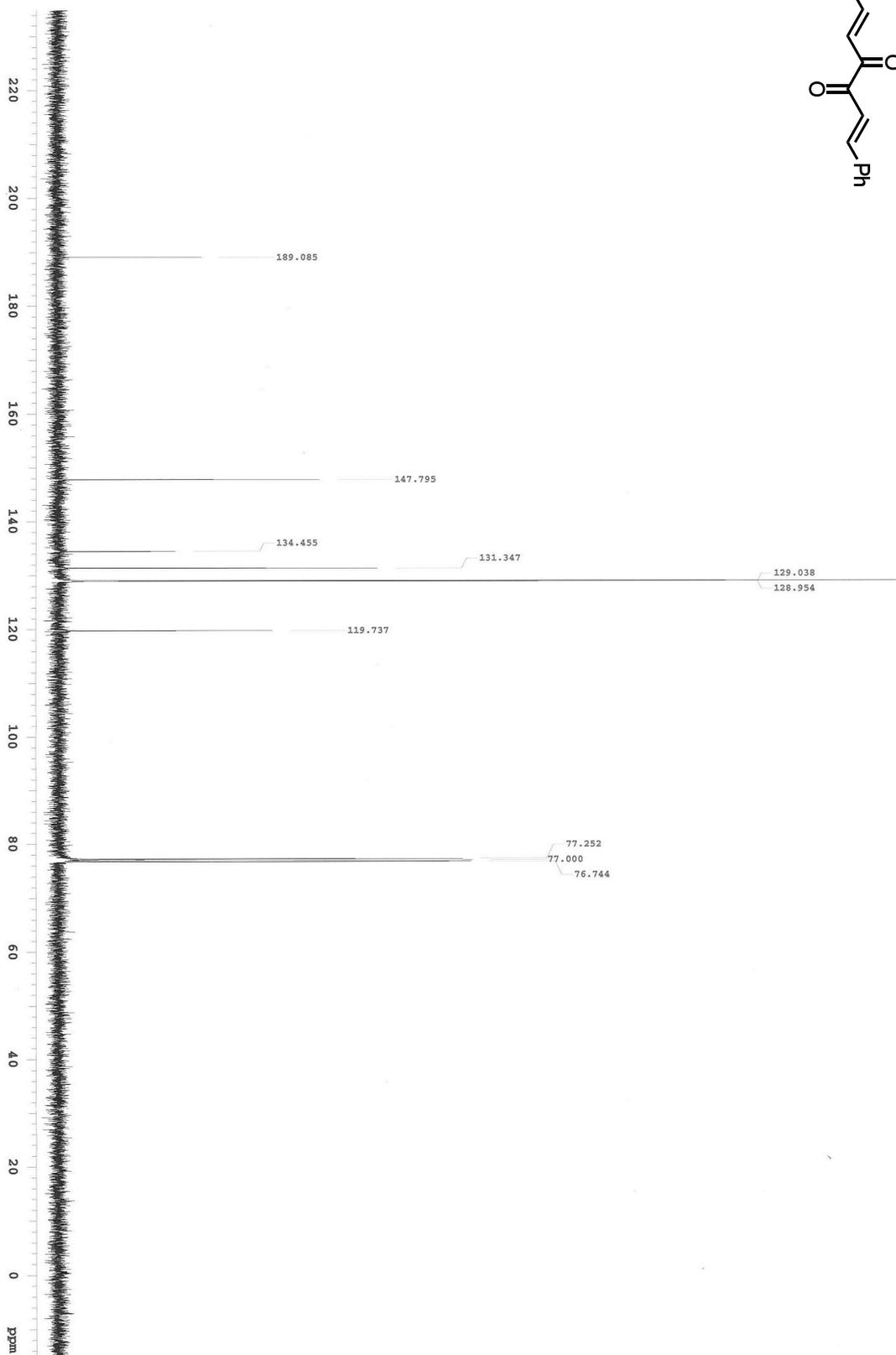
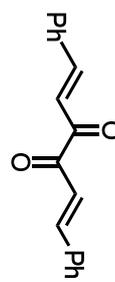
**Table S1.** Yields of **6a** under various residence time ( $t$  s) and temperature ( $T$  °C) using 0.11M of **1** ( $1/2a = 1.2$ ).

$T$ °C \ $t$	4 s	6 s	8 s
40	62%	60%	59%
20	41%	58%	57%
0	37%	53%	57%

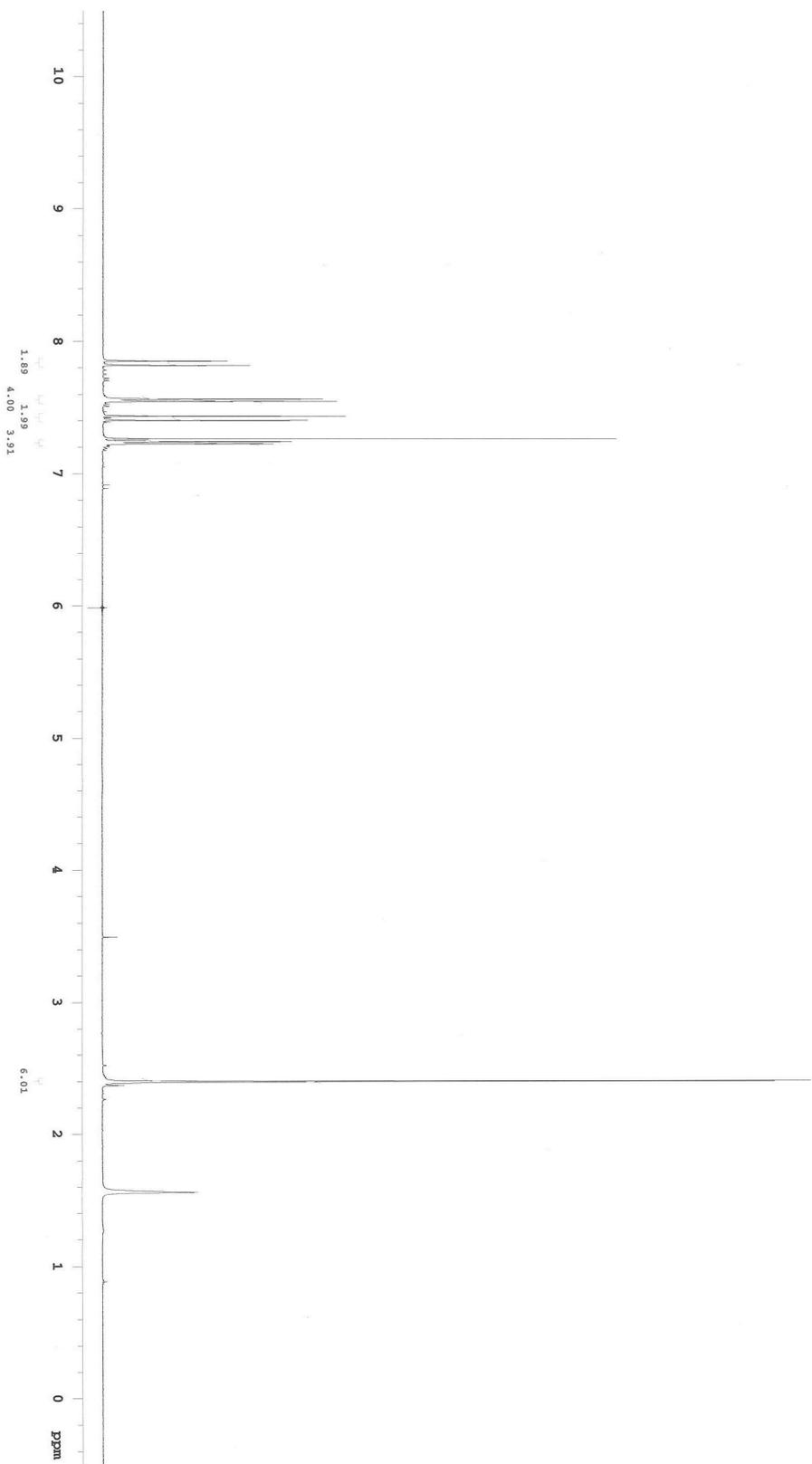
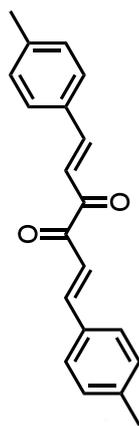
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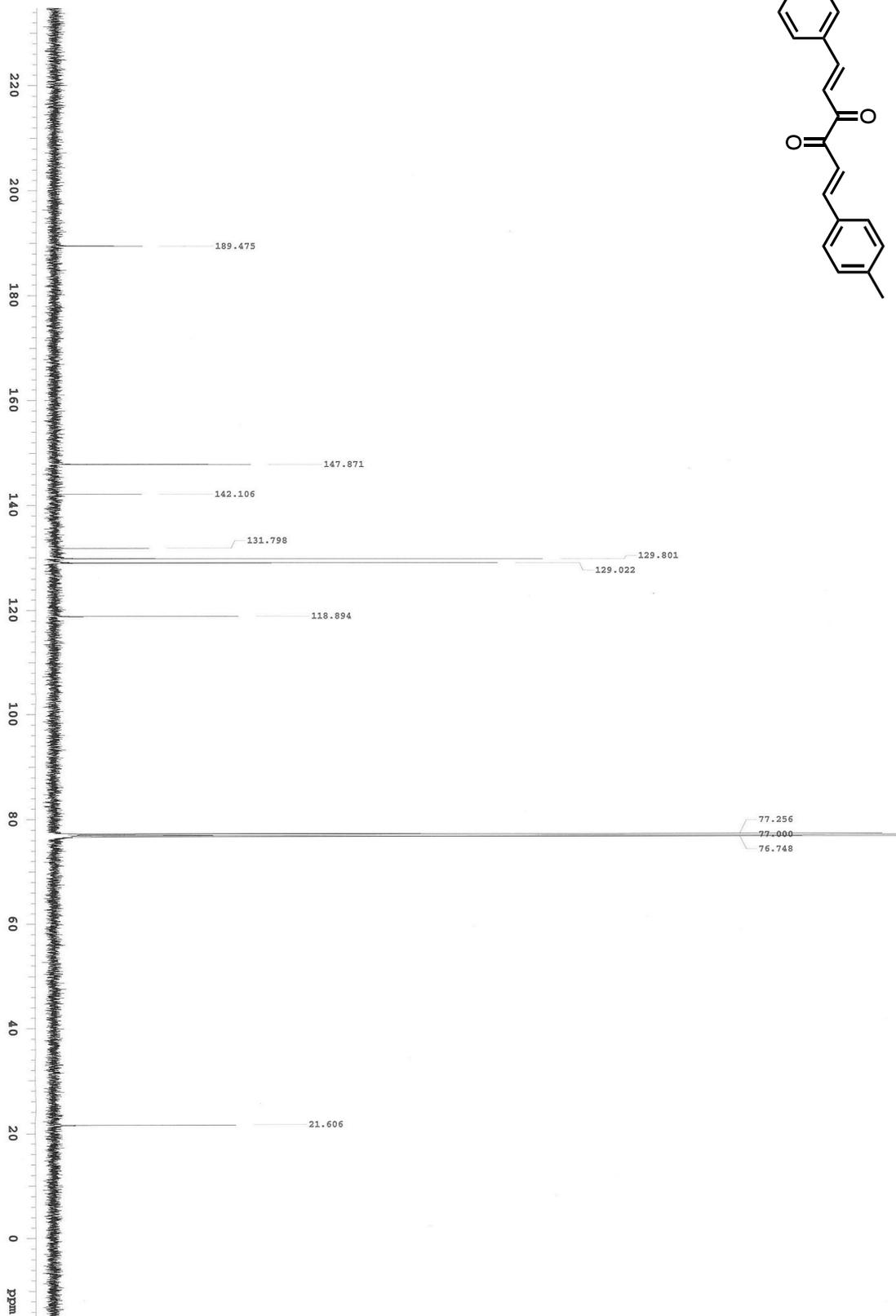
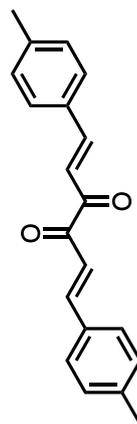
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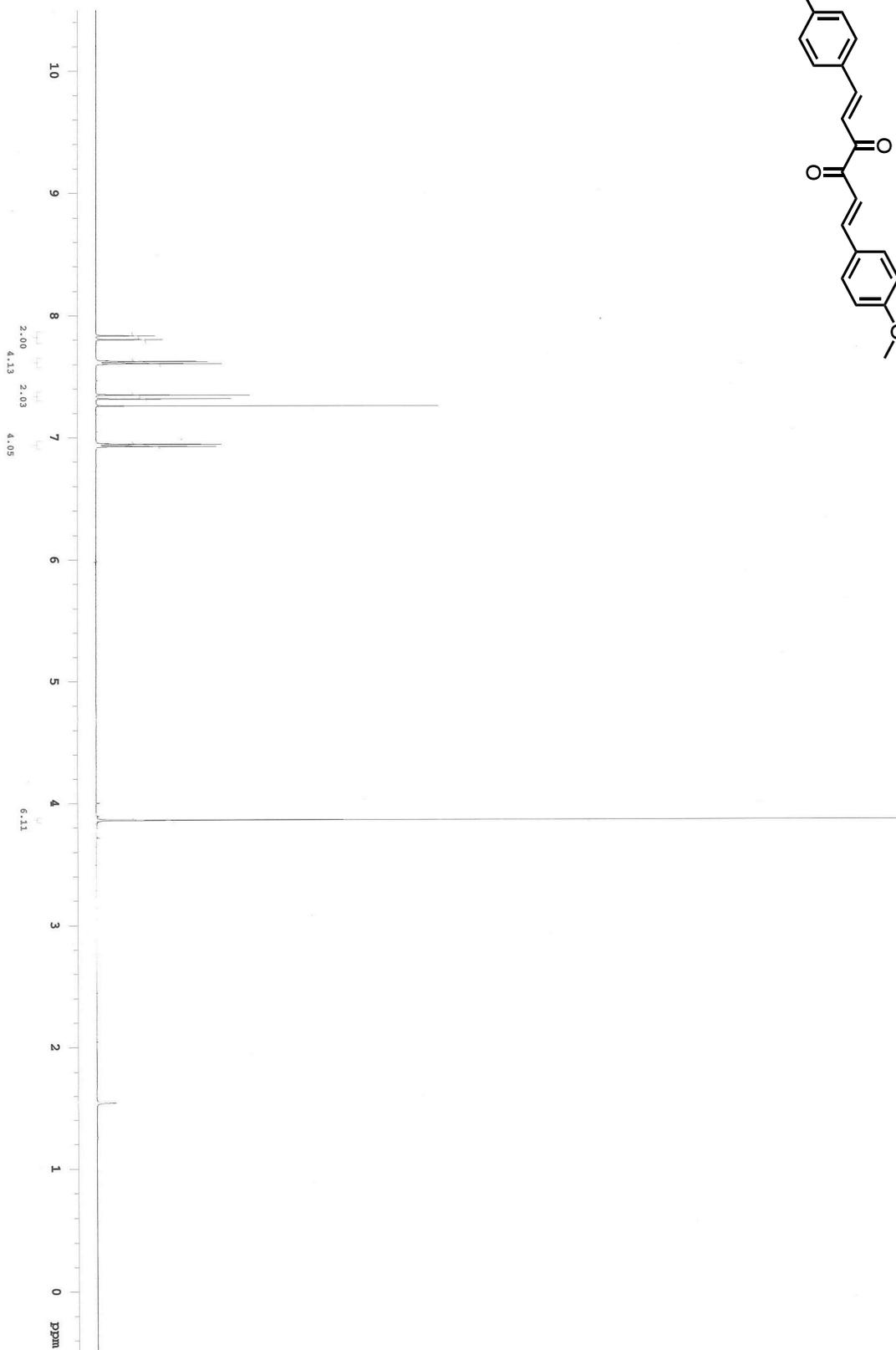
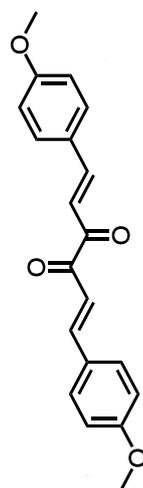
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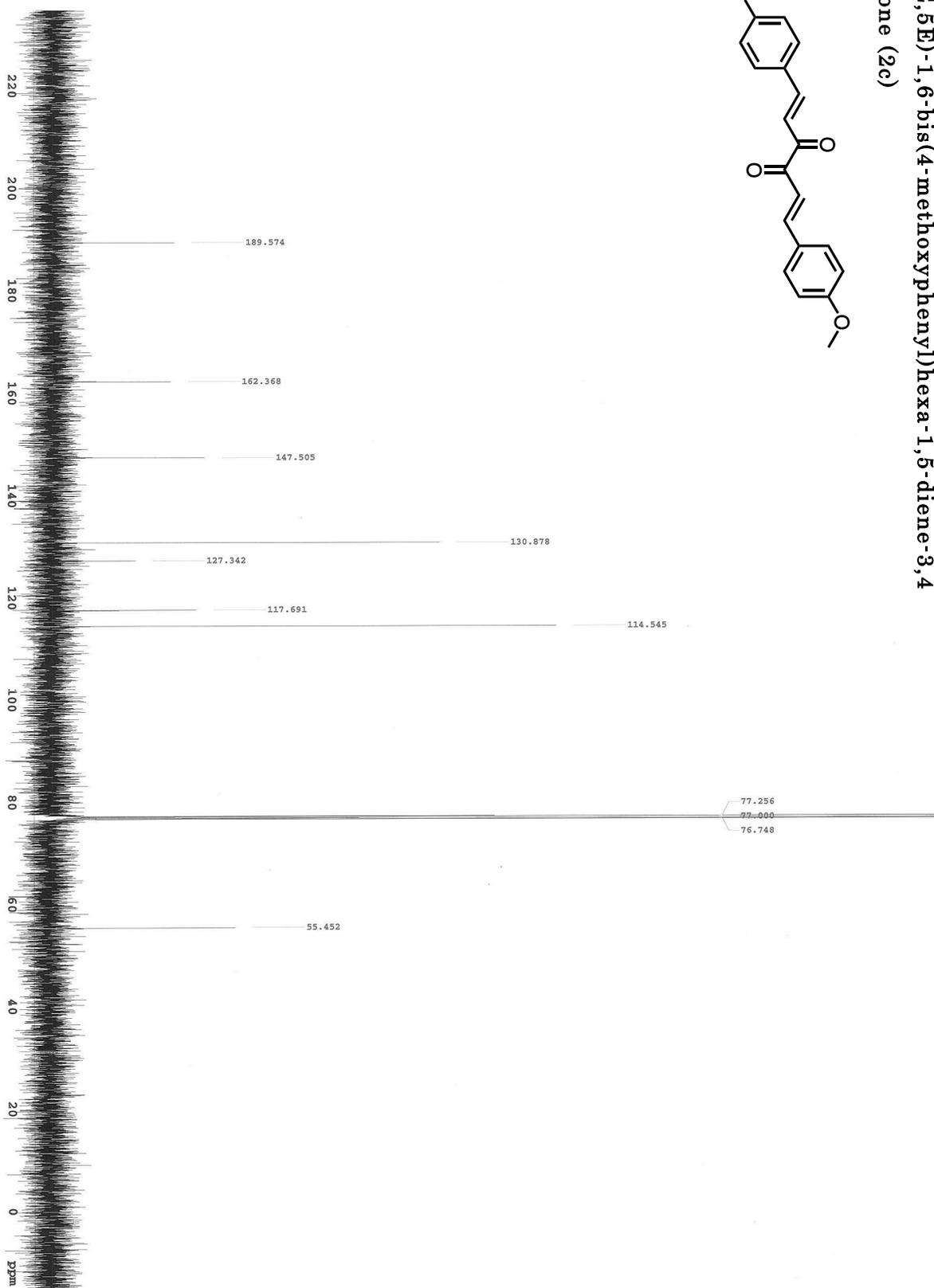
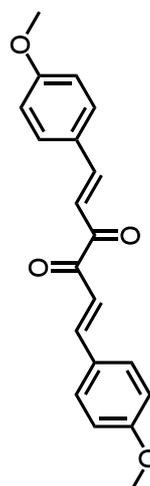
(1E,5E)-1,6-di-*p*-tolylhexa-1,5-diene-3,4-dione (2b)



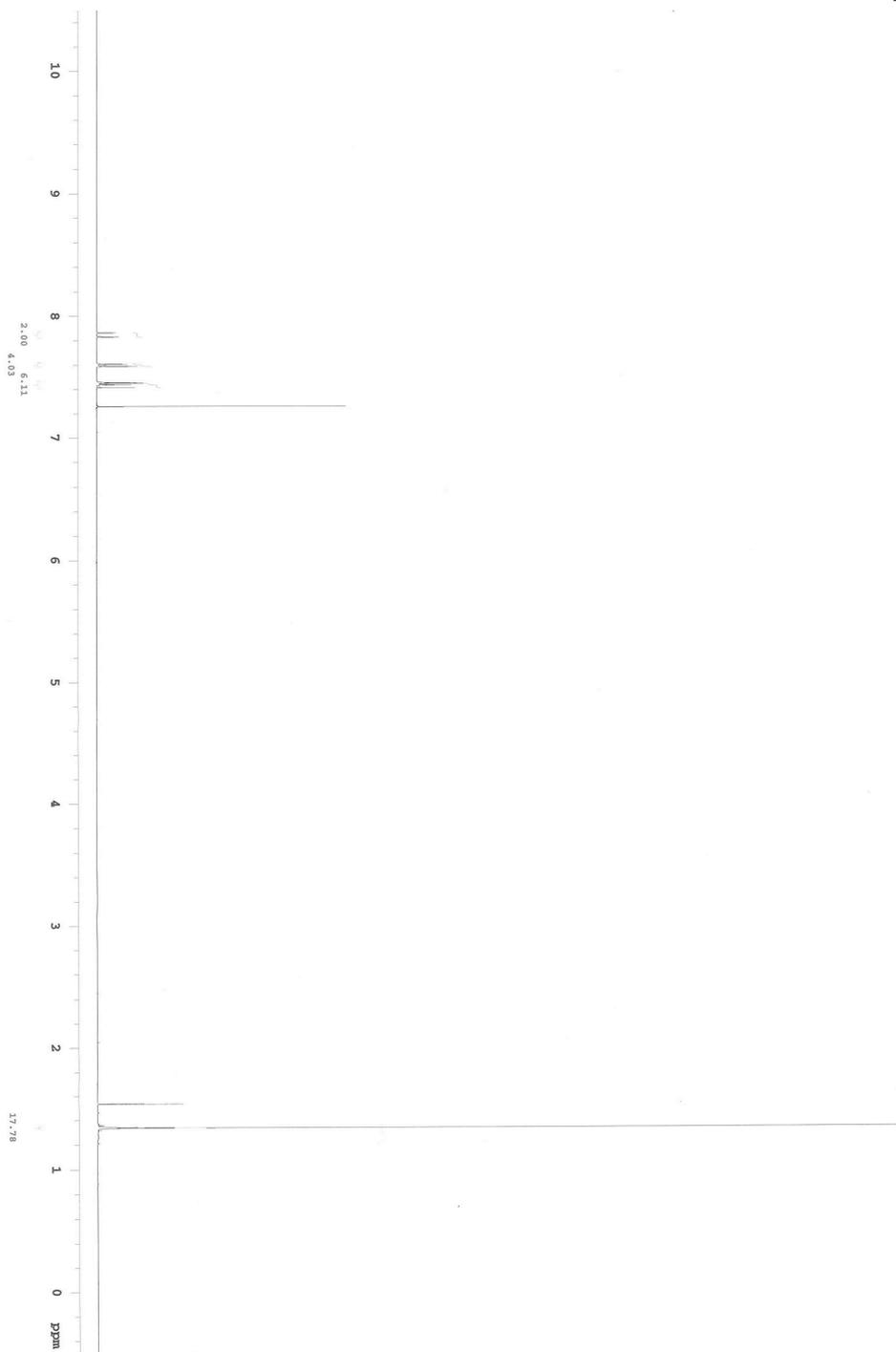
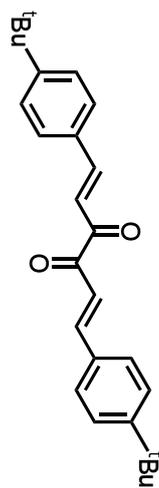
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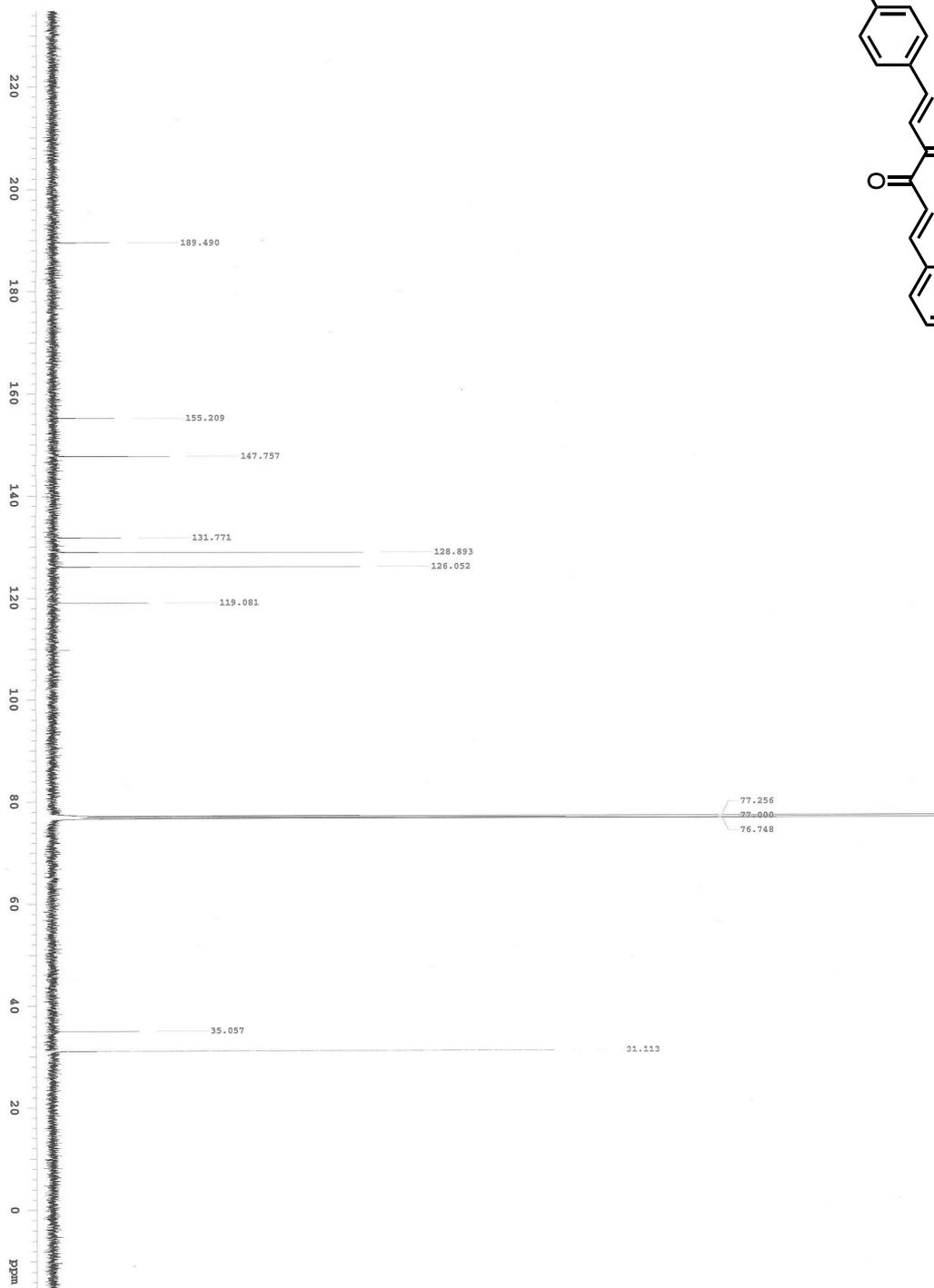
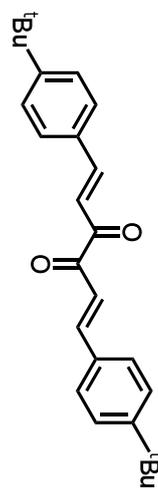
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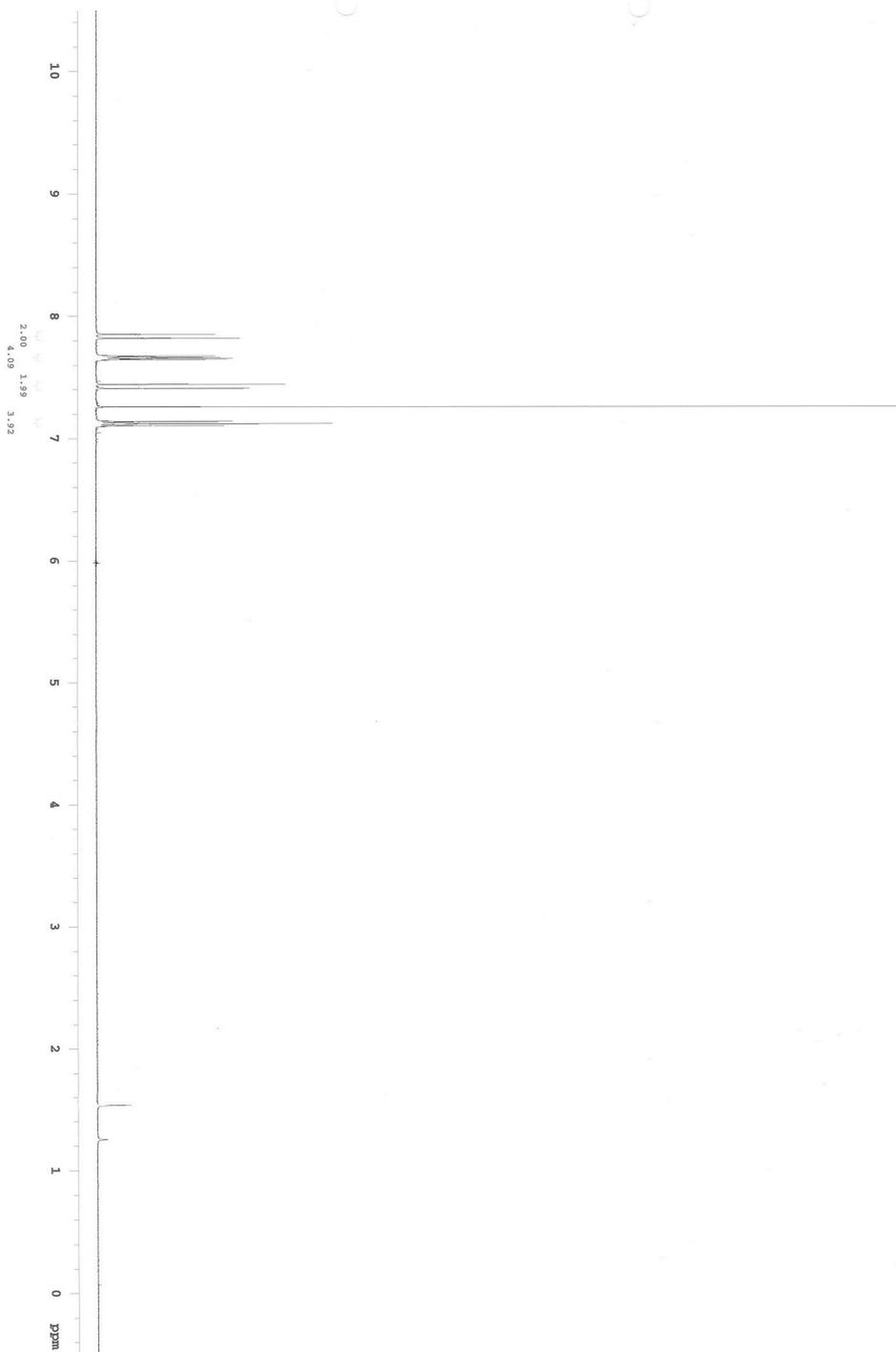
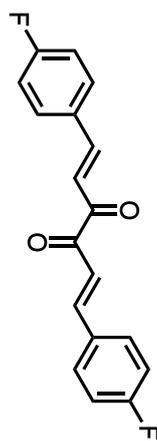
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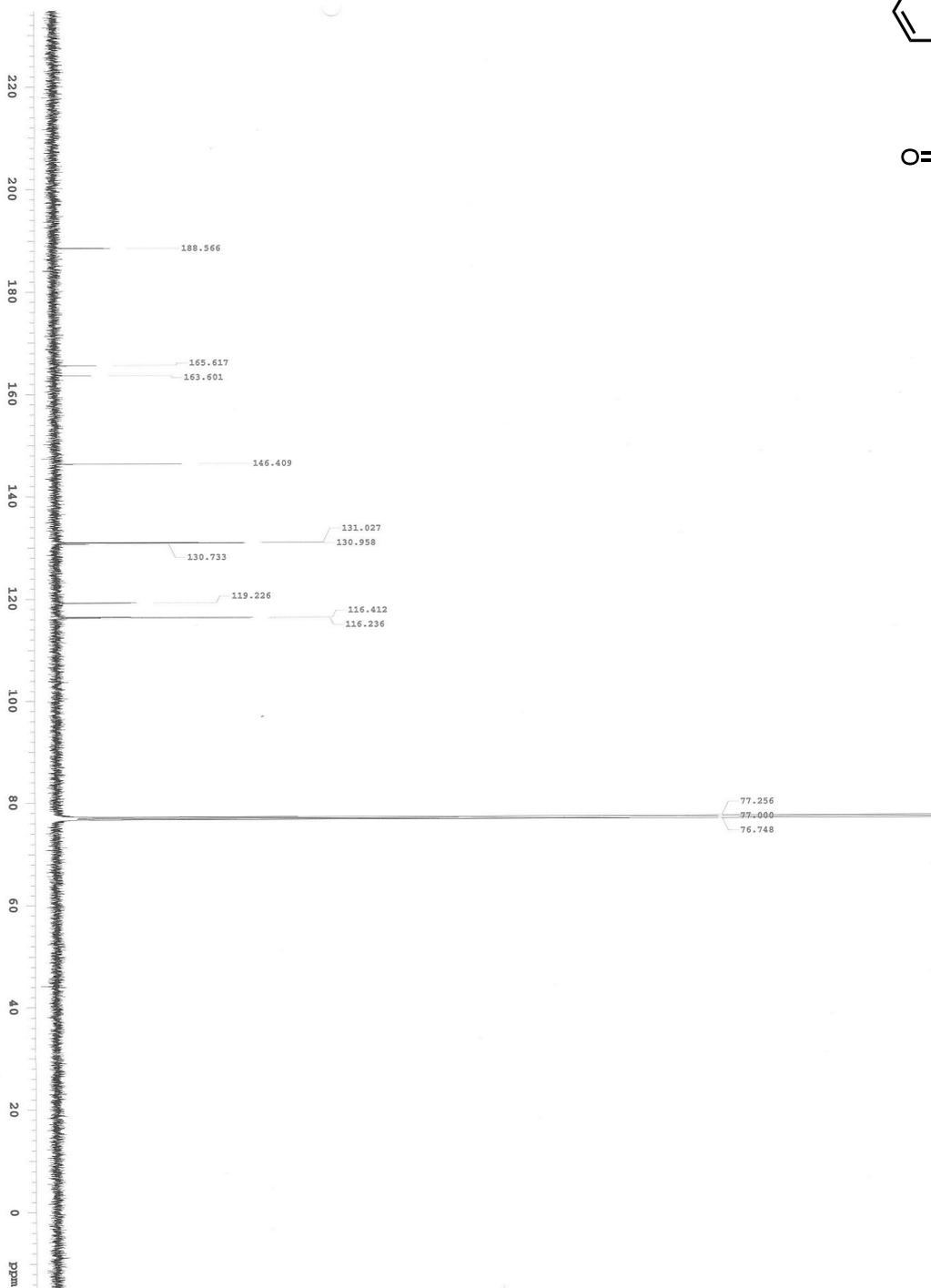
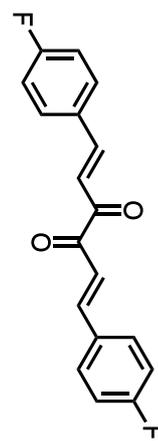
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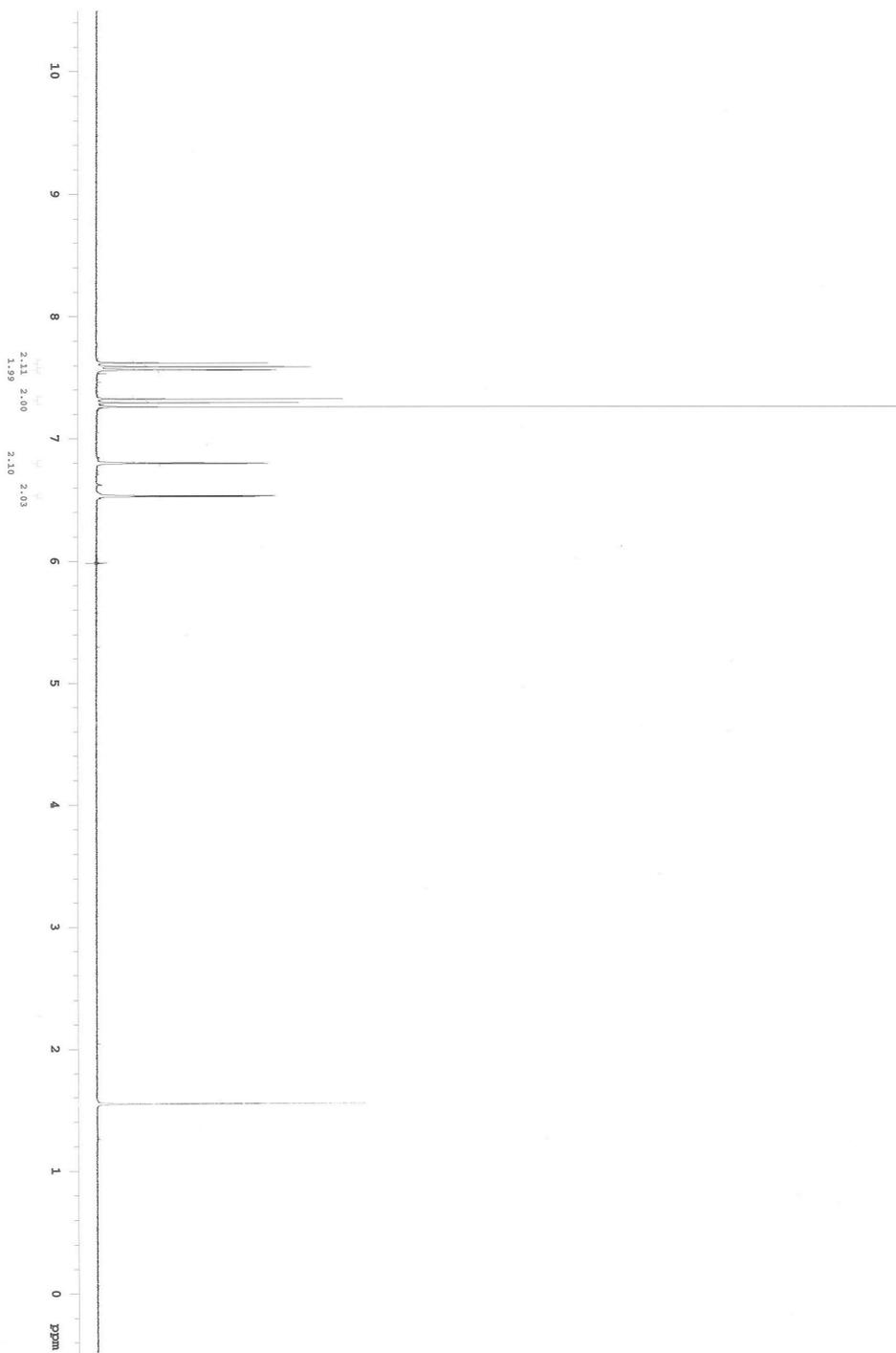
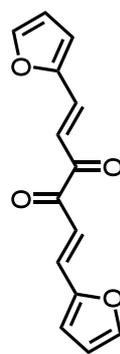
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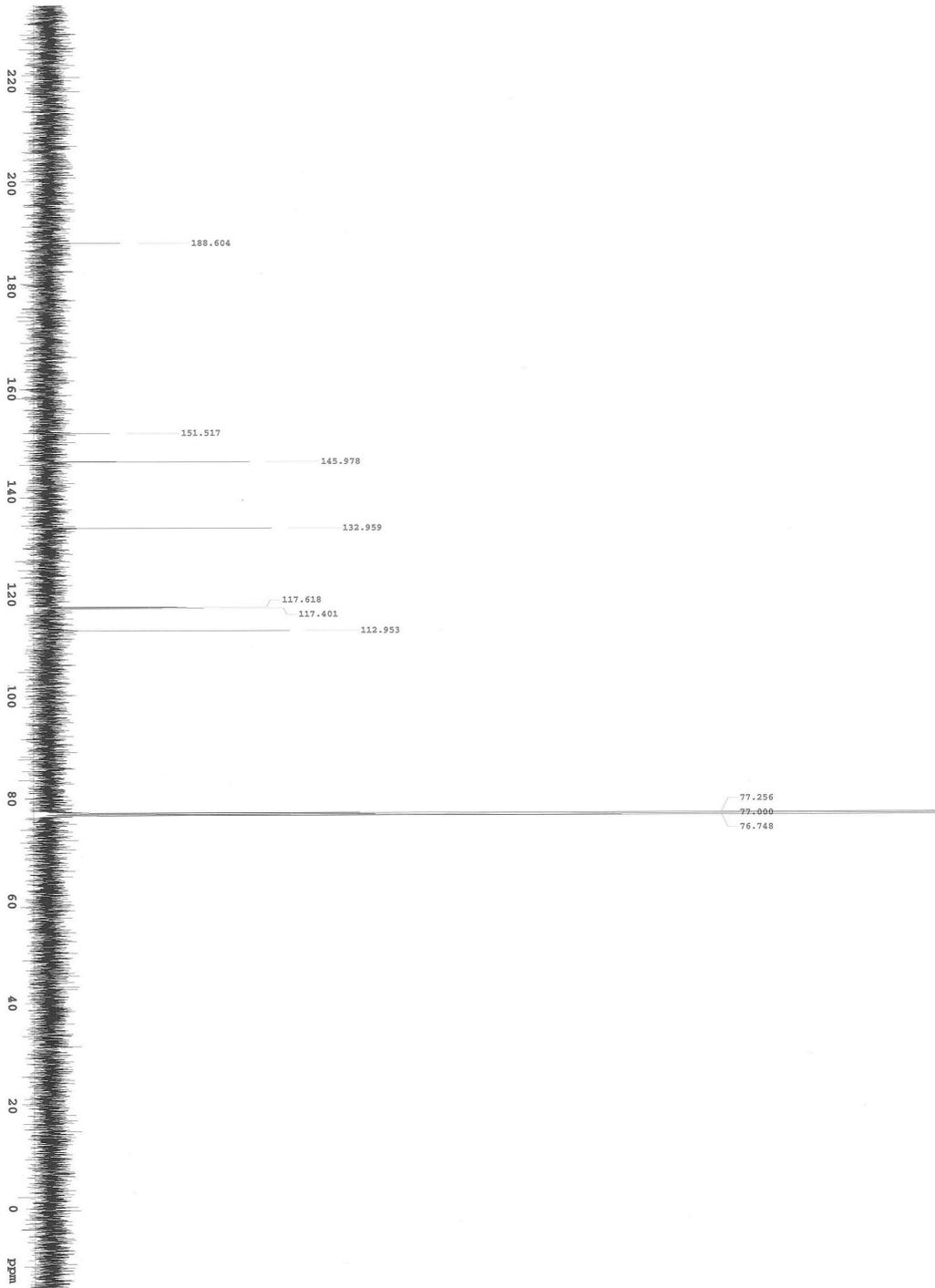
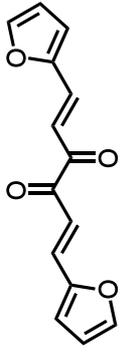
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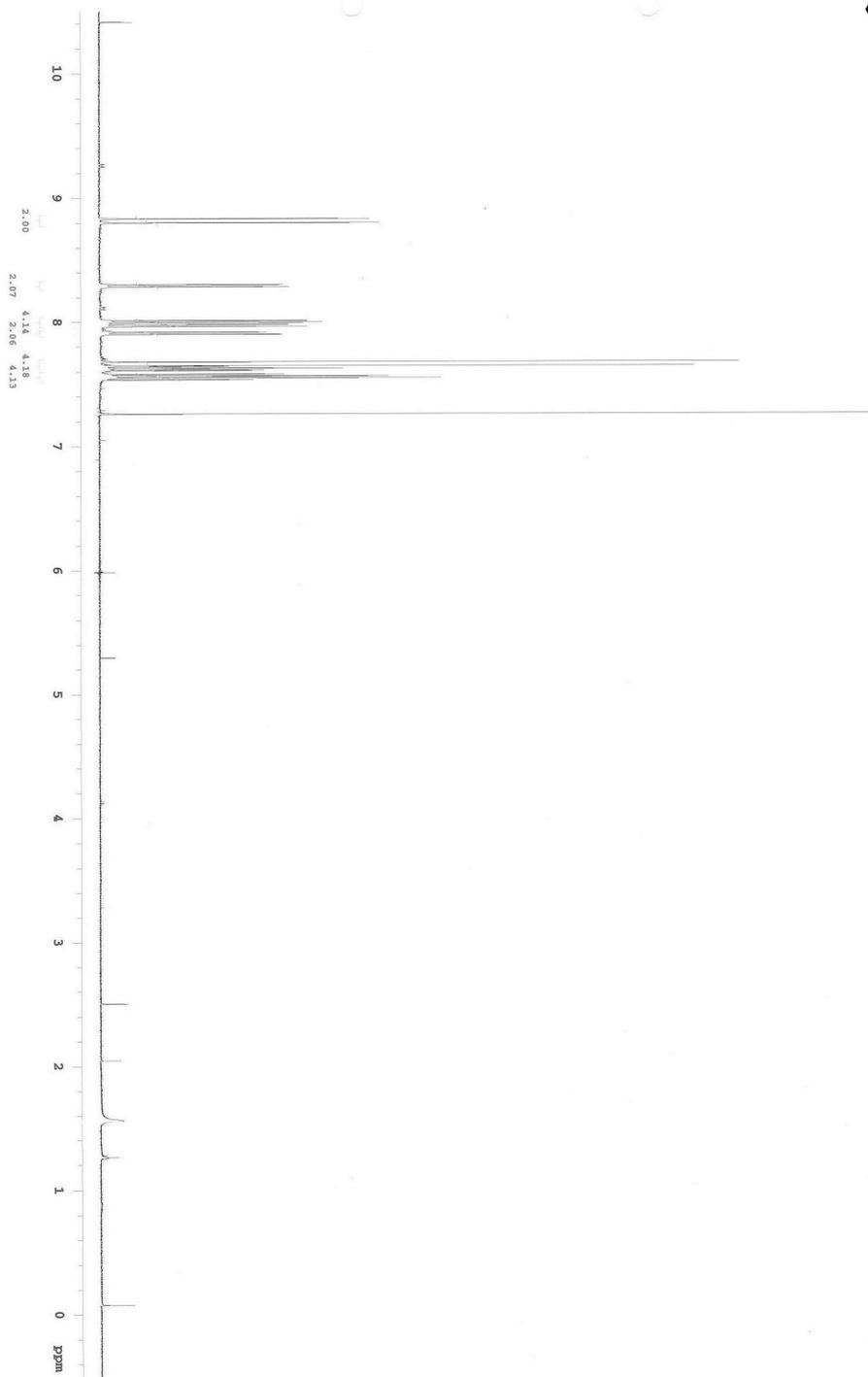
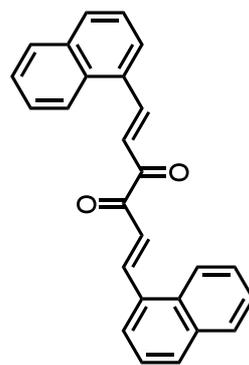
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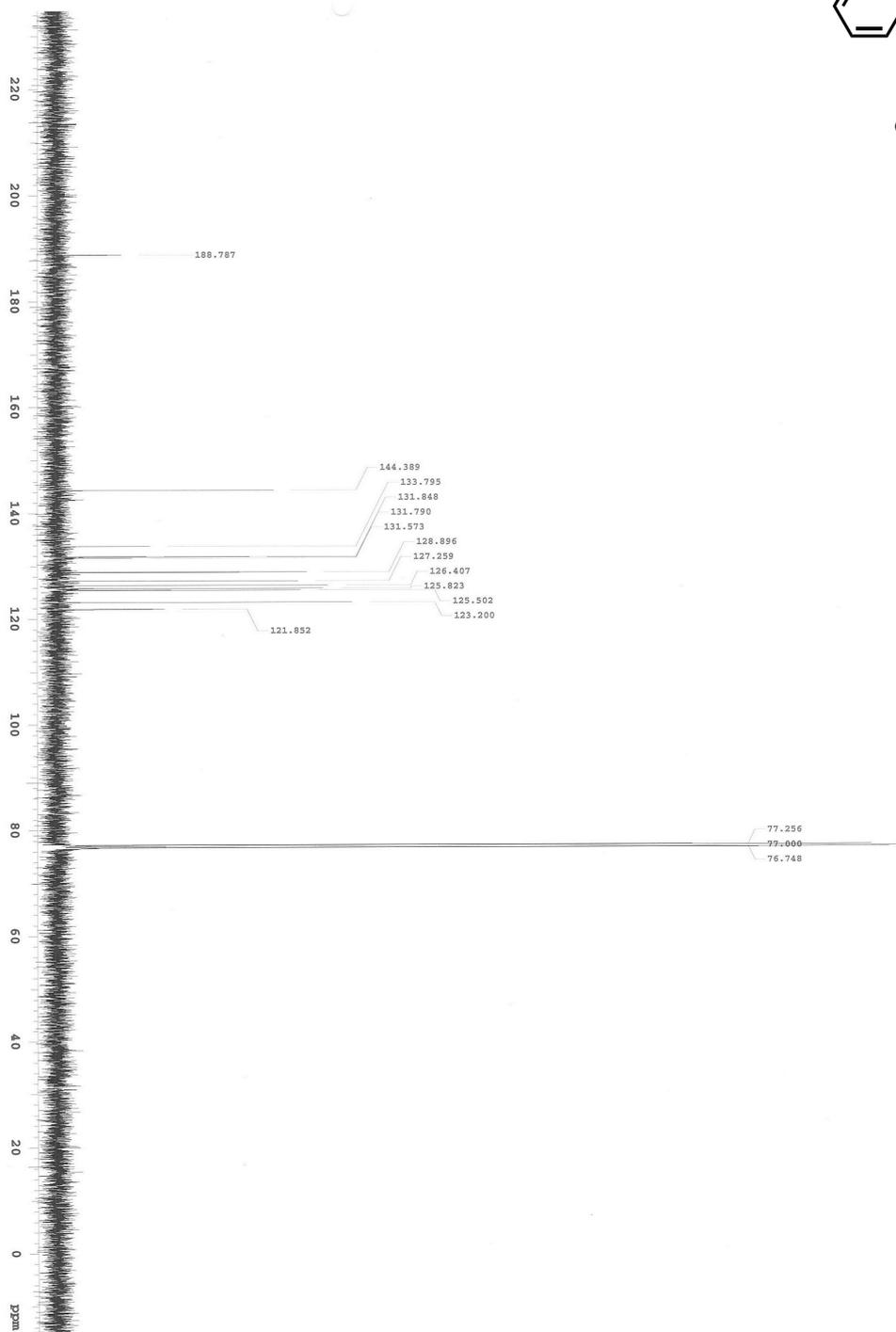
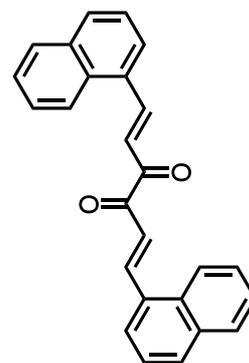
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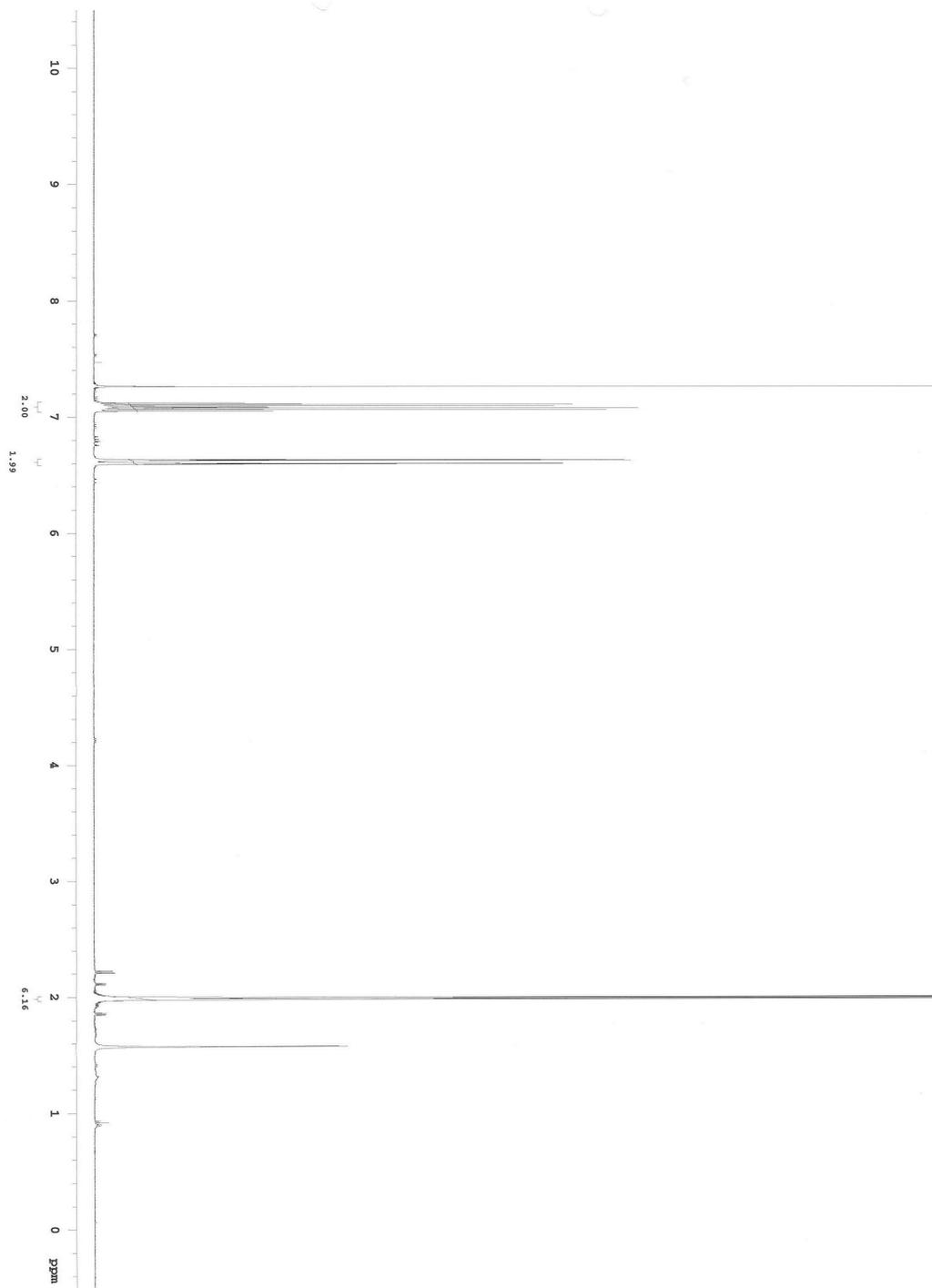
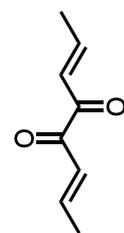
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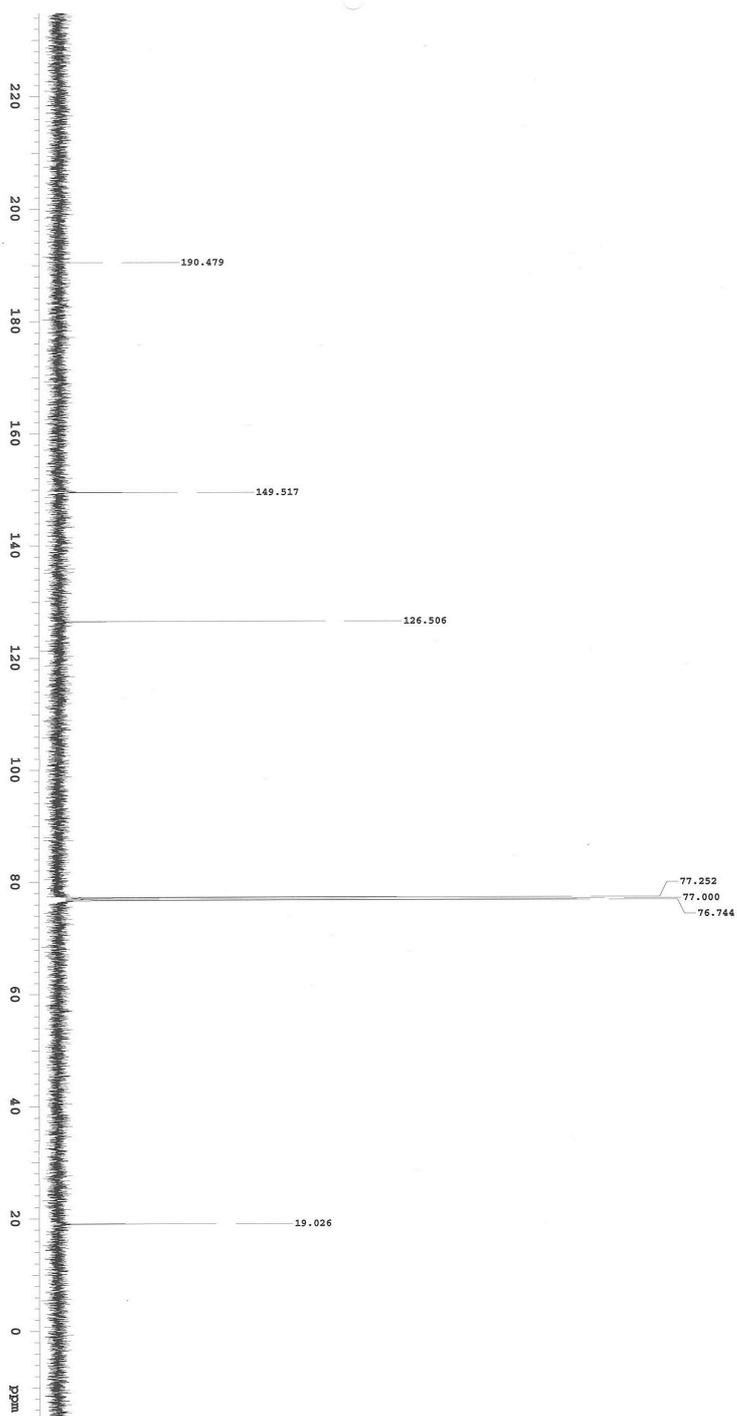
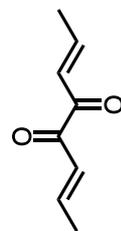
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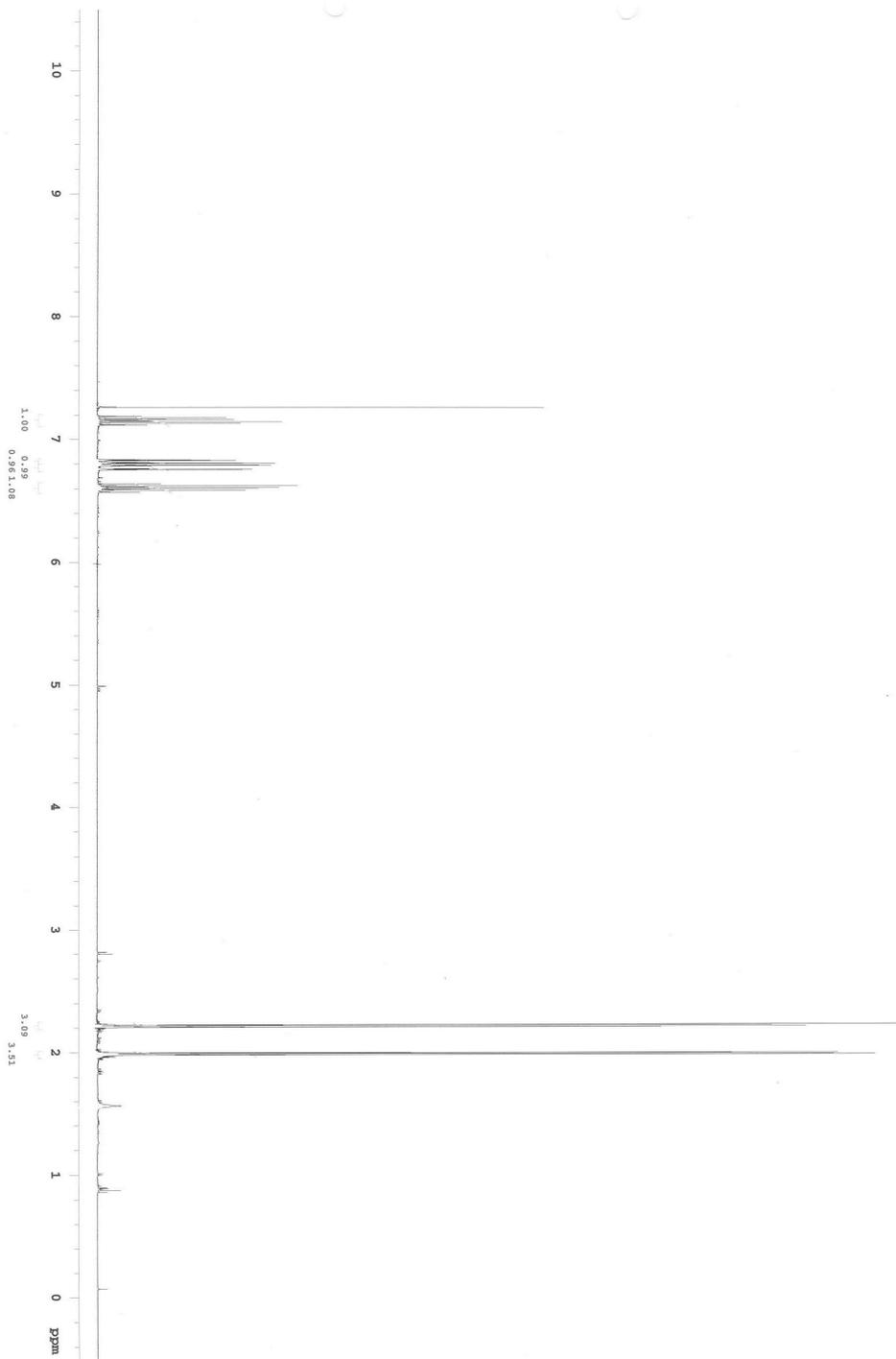
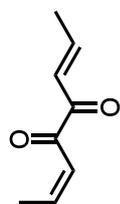
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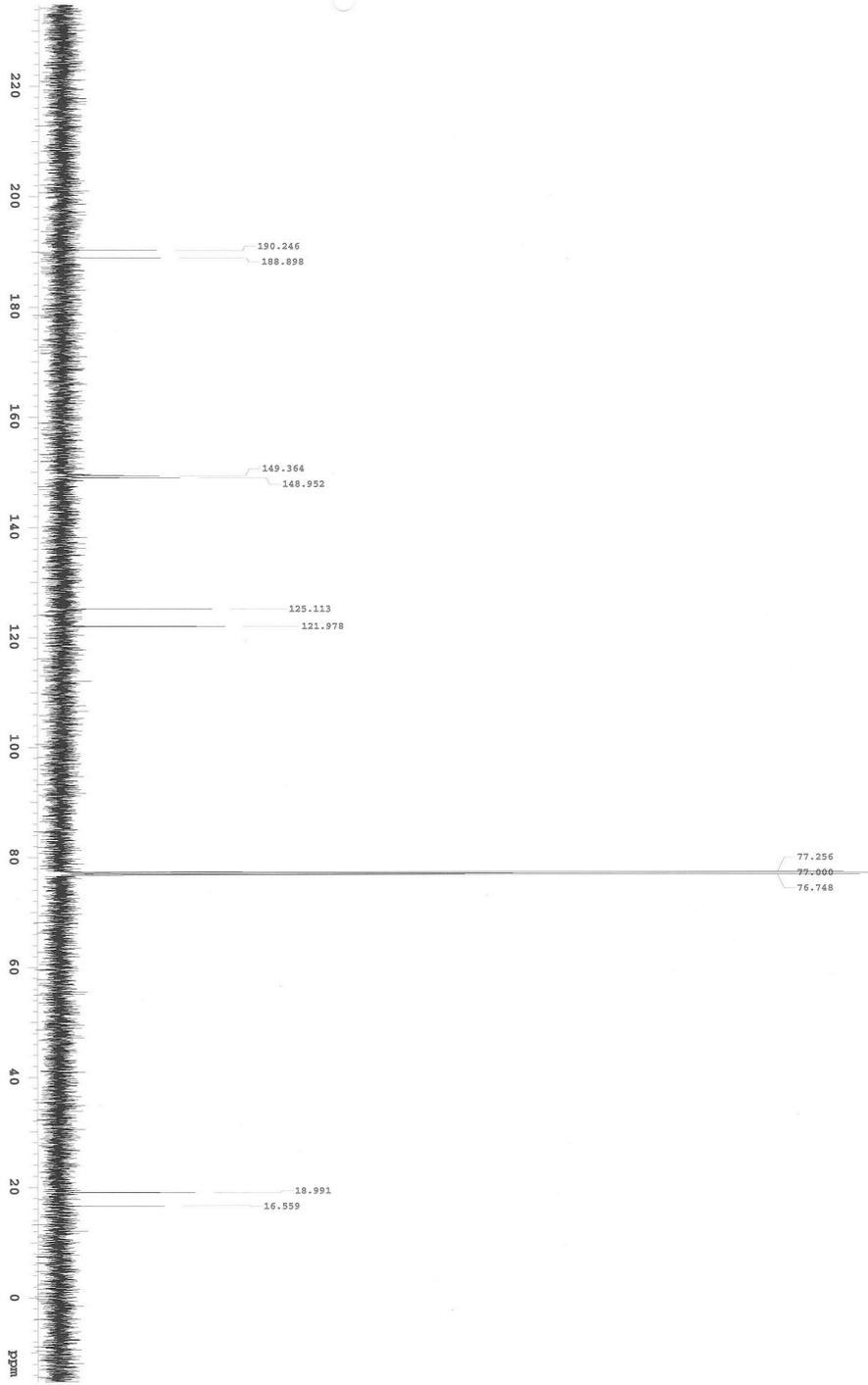
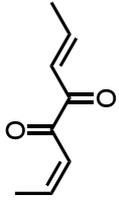
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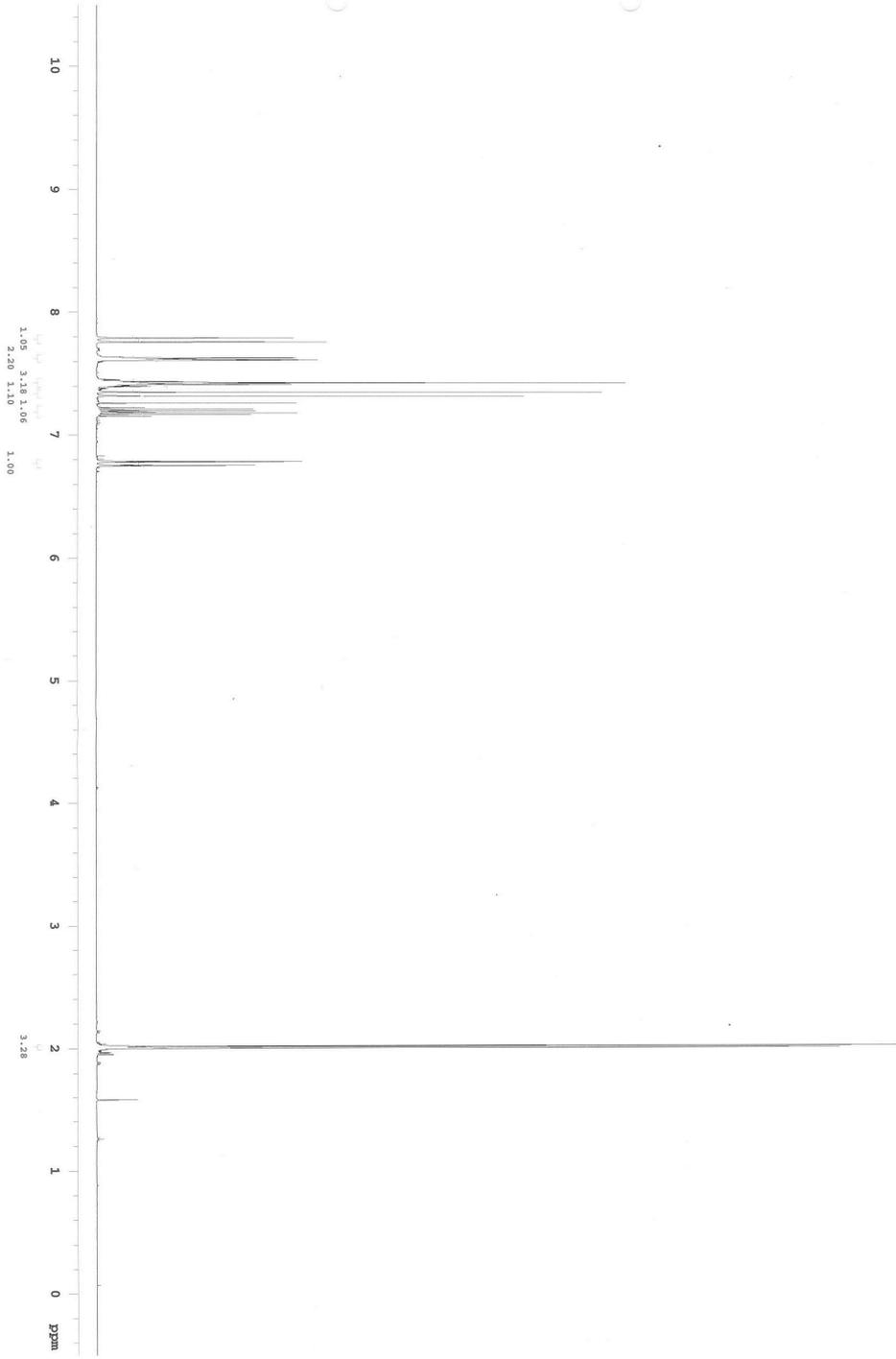
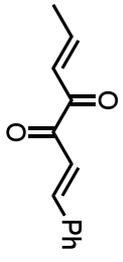
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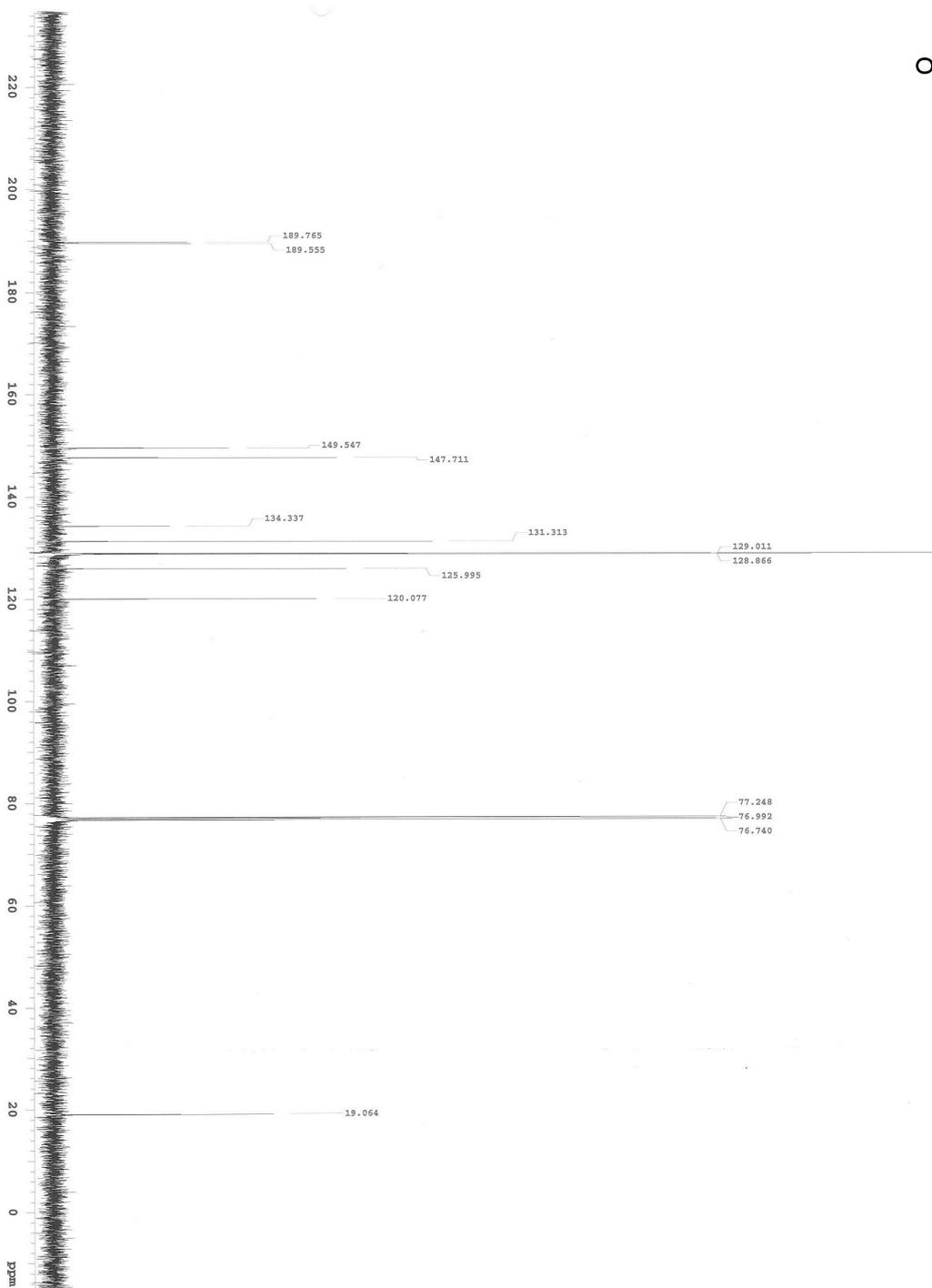
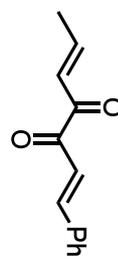
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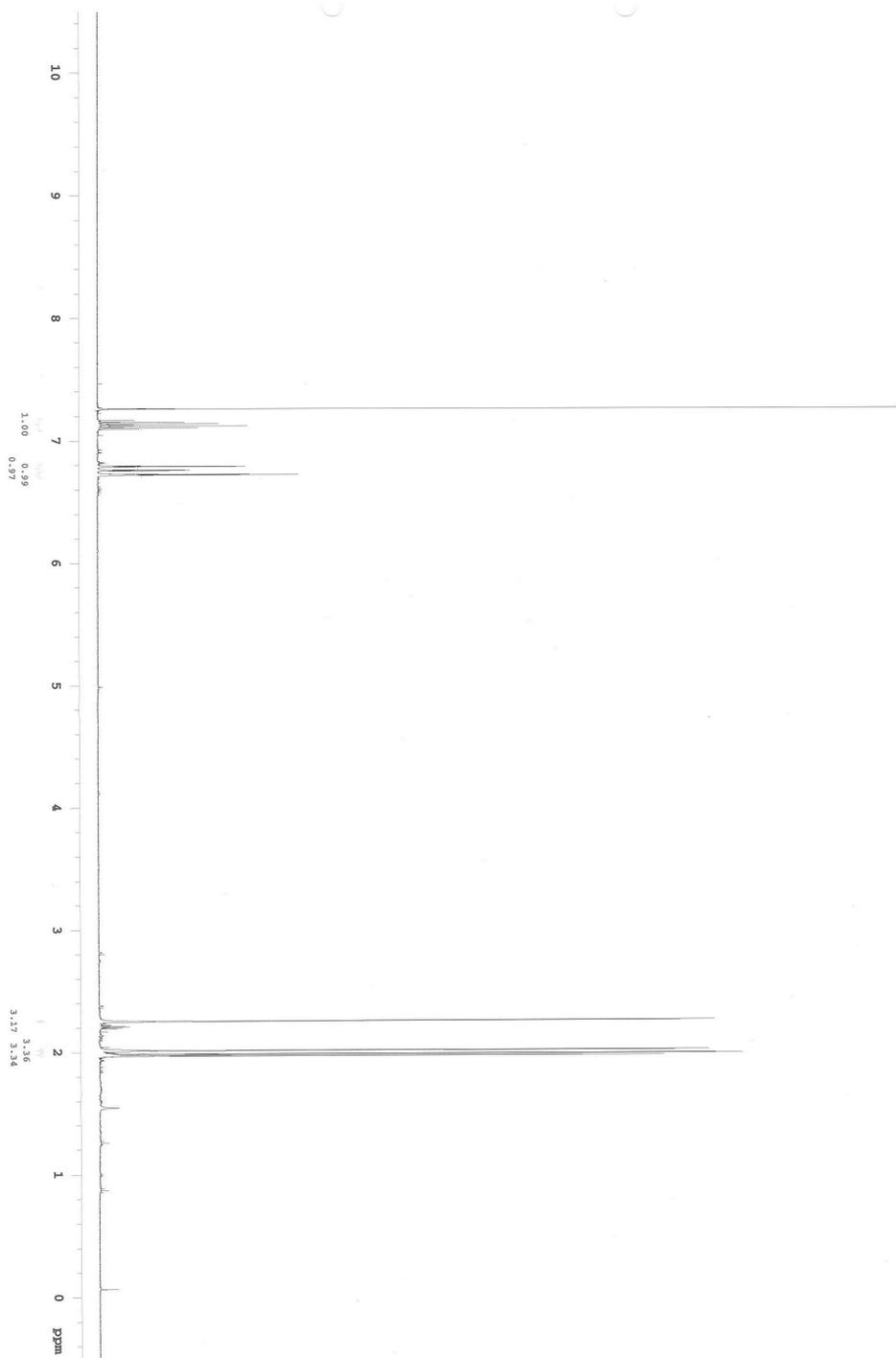
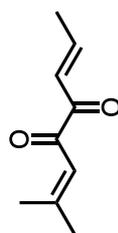
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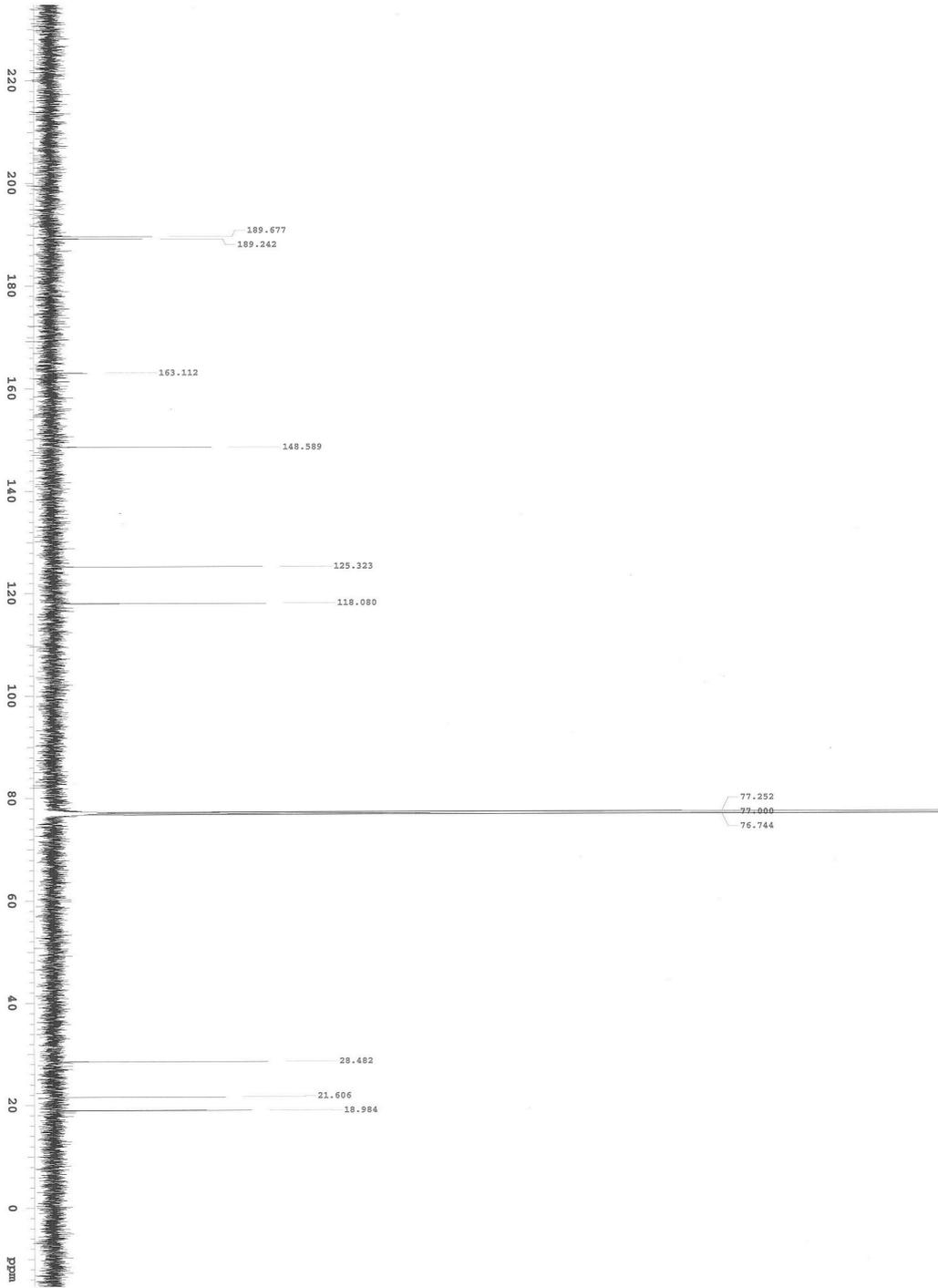
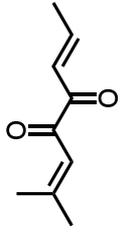
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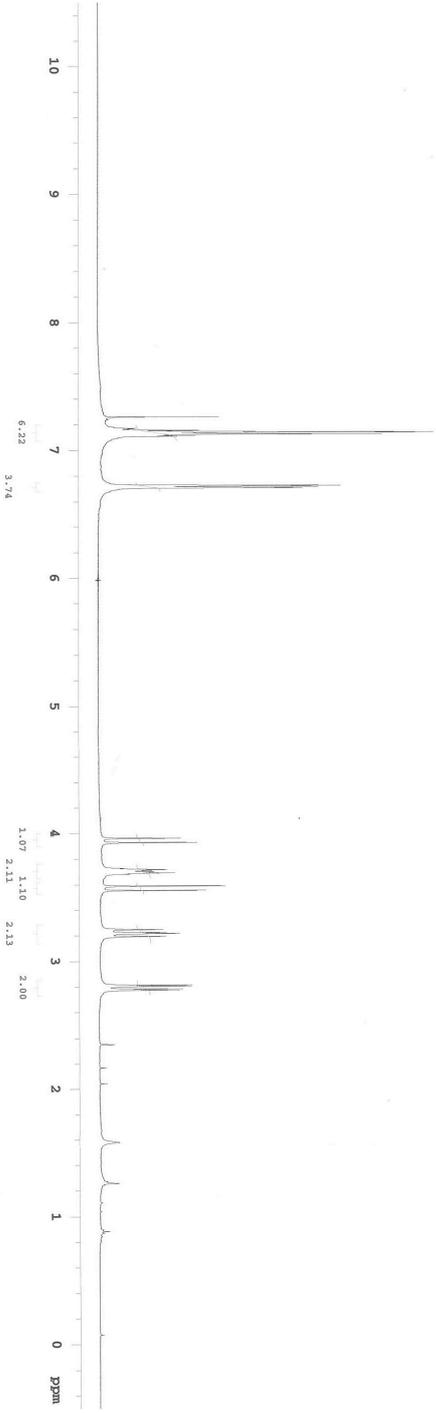
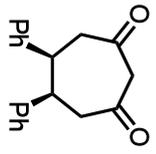
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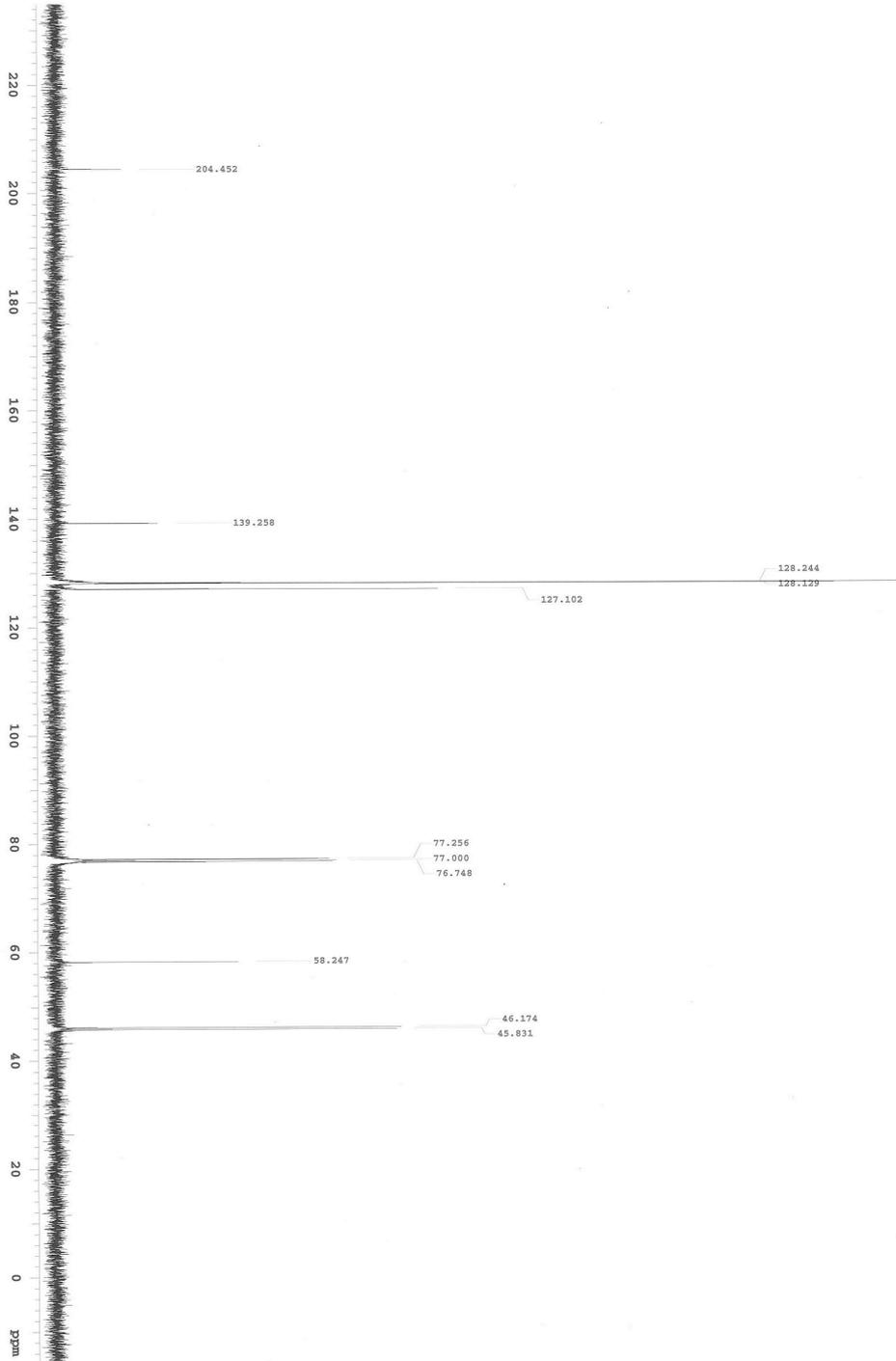
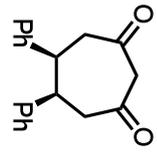
(E)-2-methylocta-2,6-diene-4,5-dione (2k)



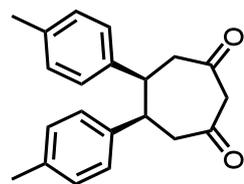
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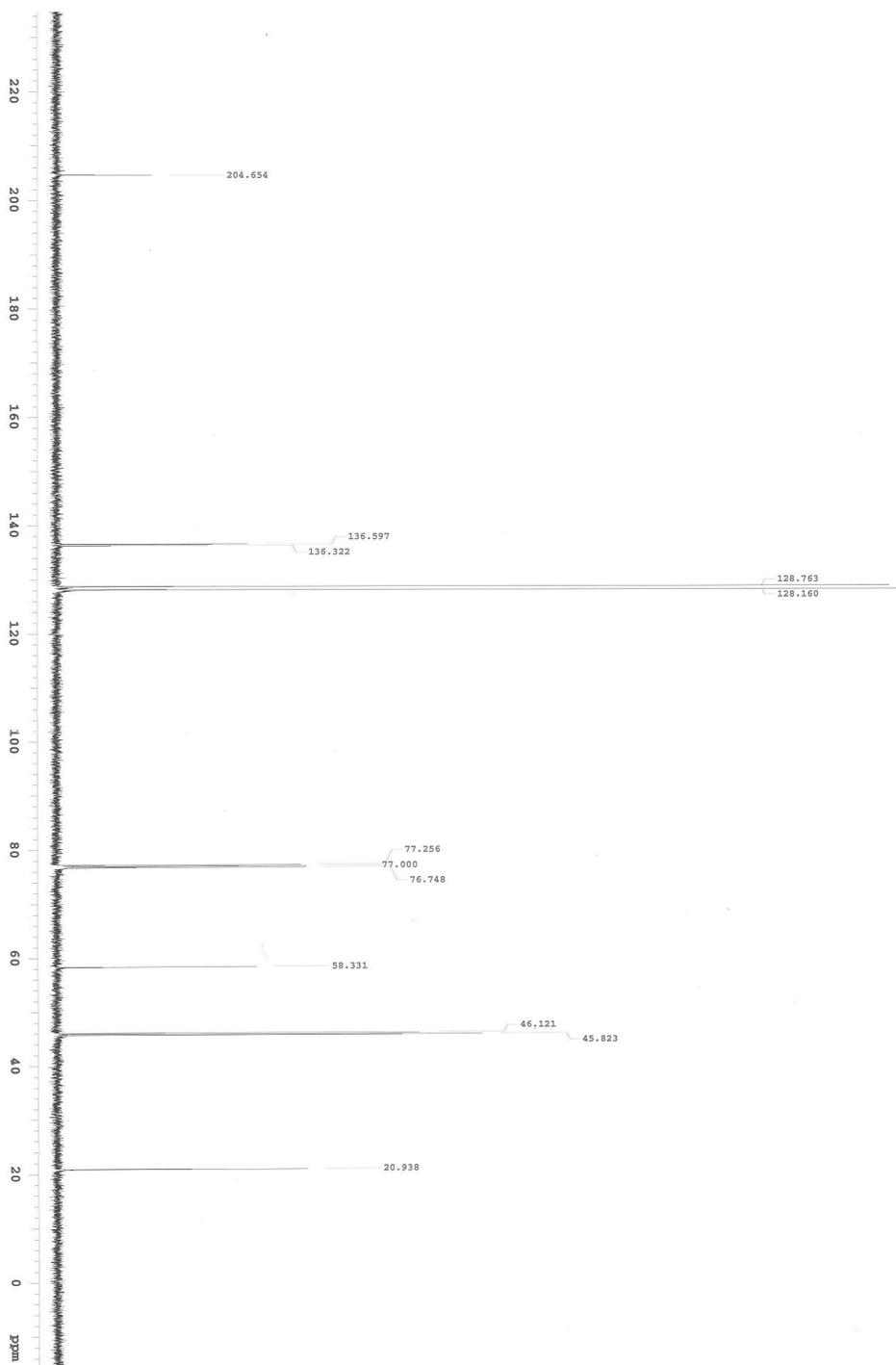
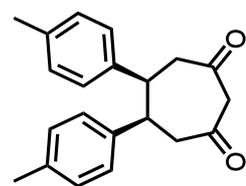
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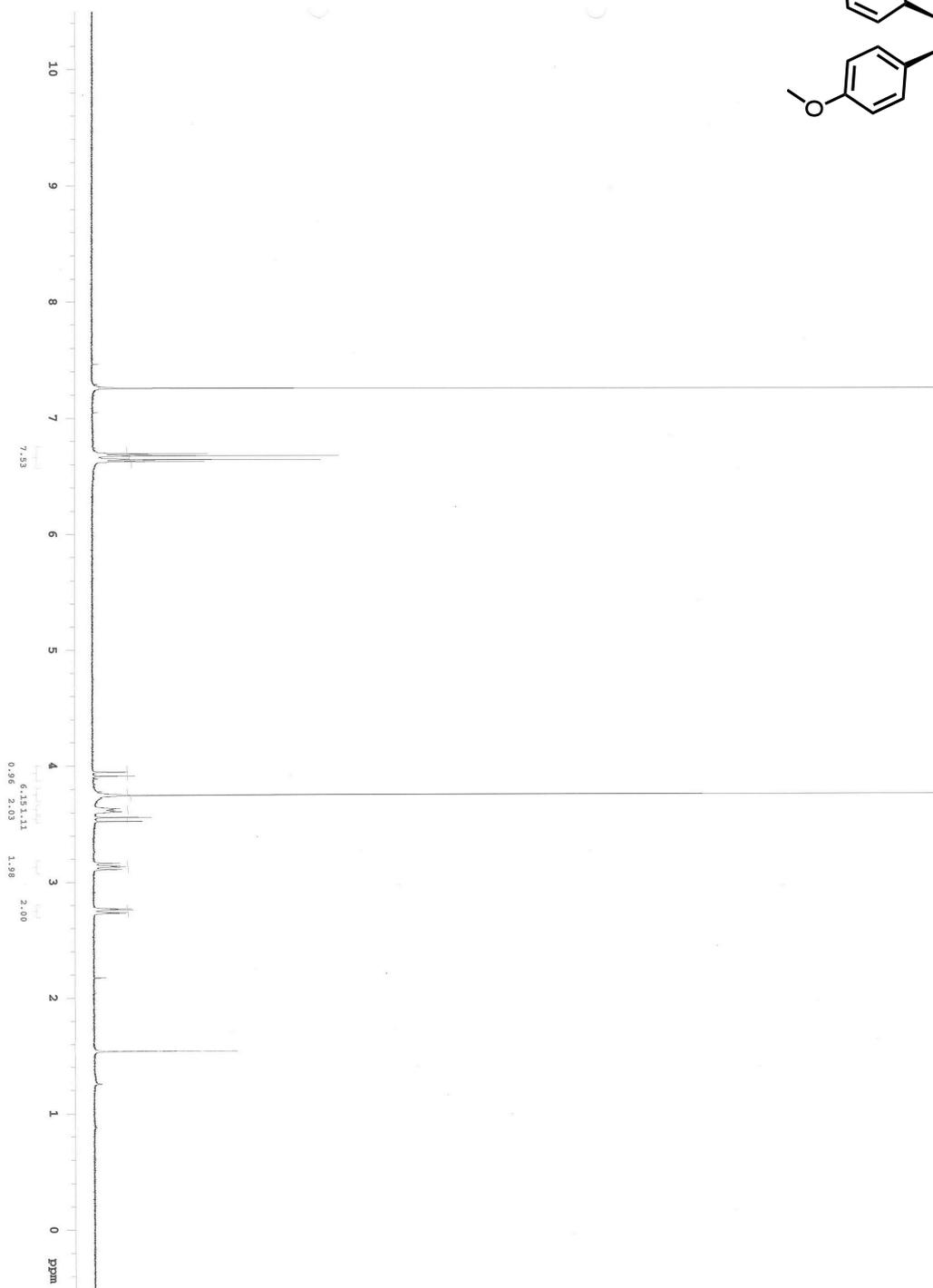
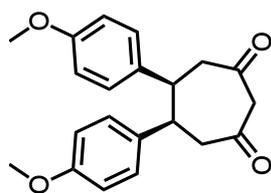
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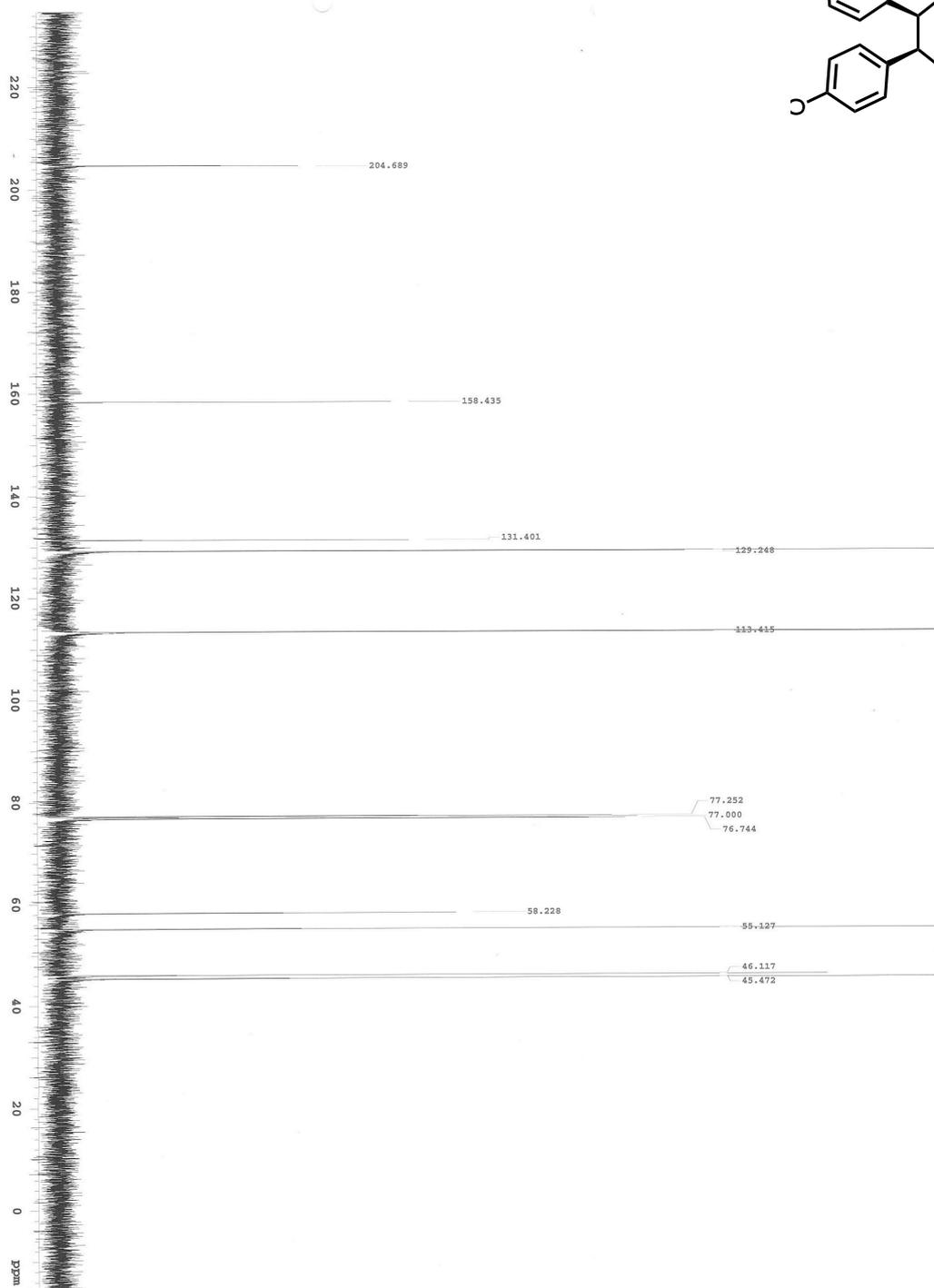
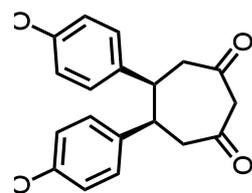
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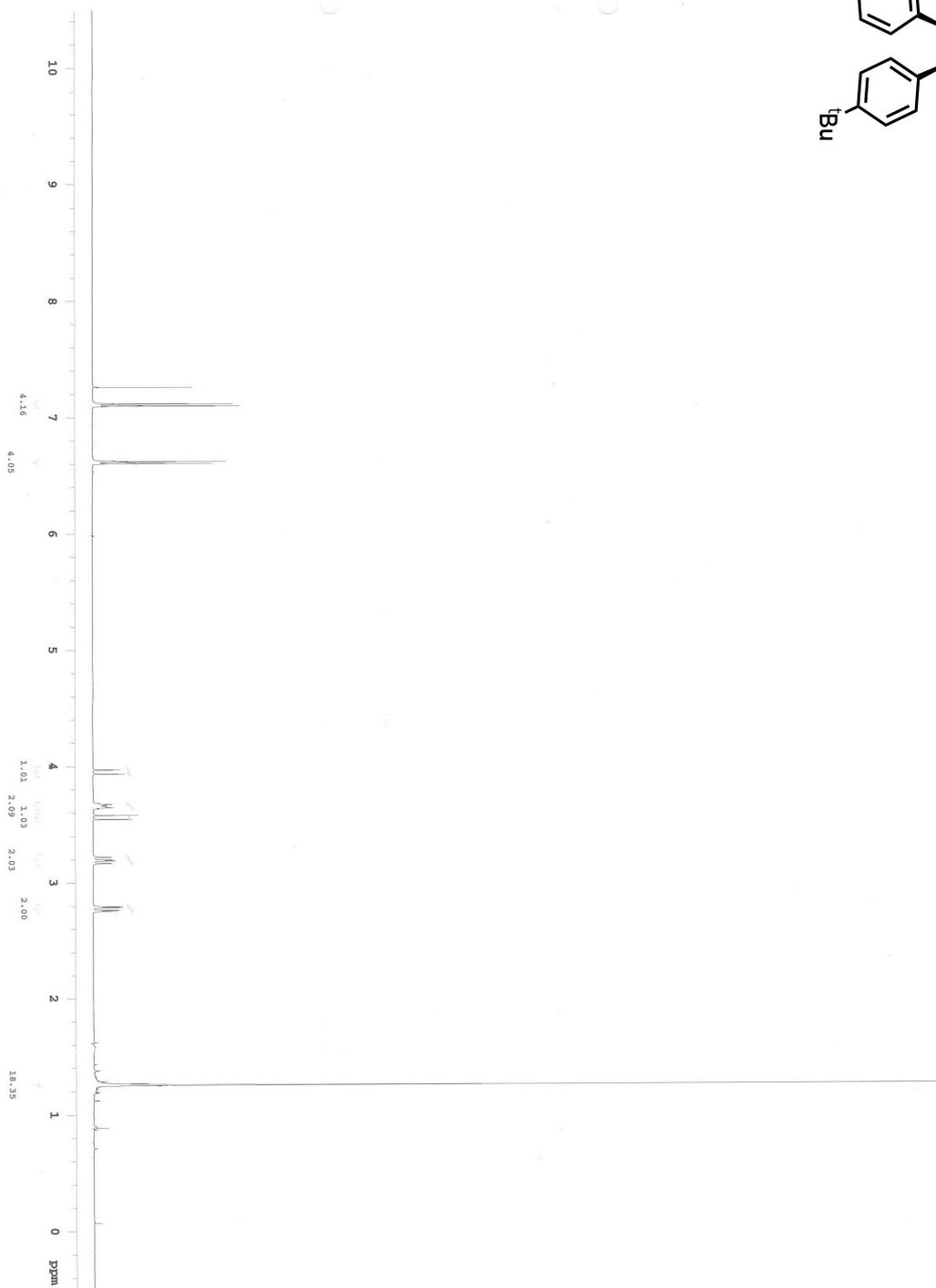
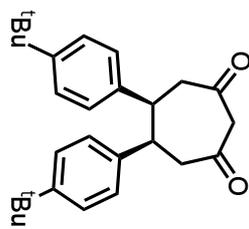
(5*R*\*, 6*S*\*)-5,6-bis(4-methoxyphenyl)cycloheptane-1,3-dione (**6c**)



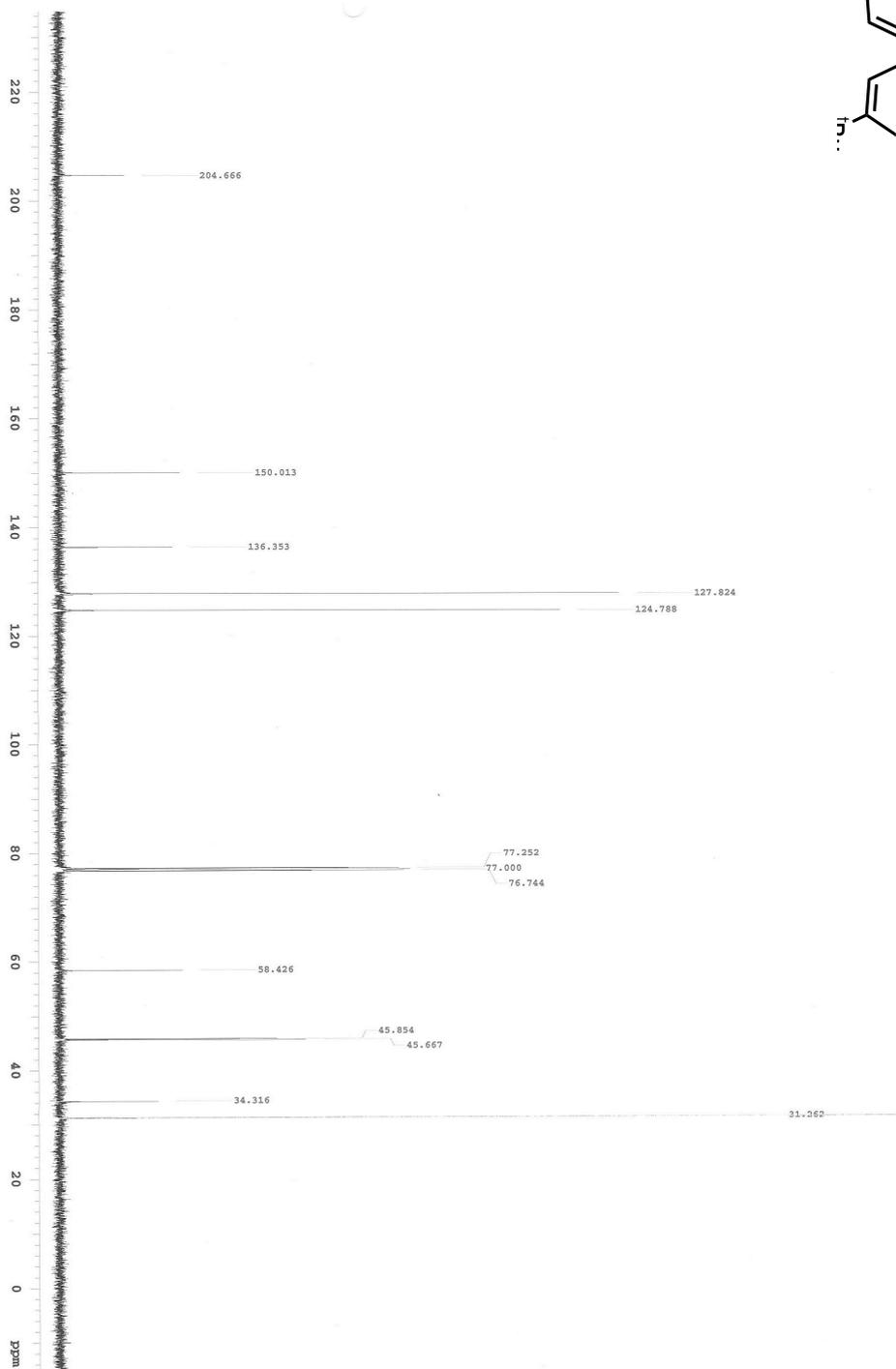
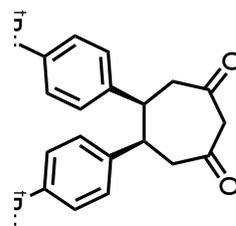
(5R\*, 6S\*)-5,6-bis(4-methoxyphenyl)cycloheptane-1,3-dione (6c)



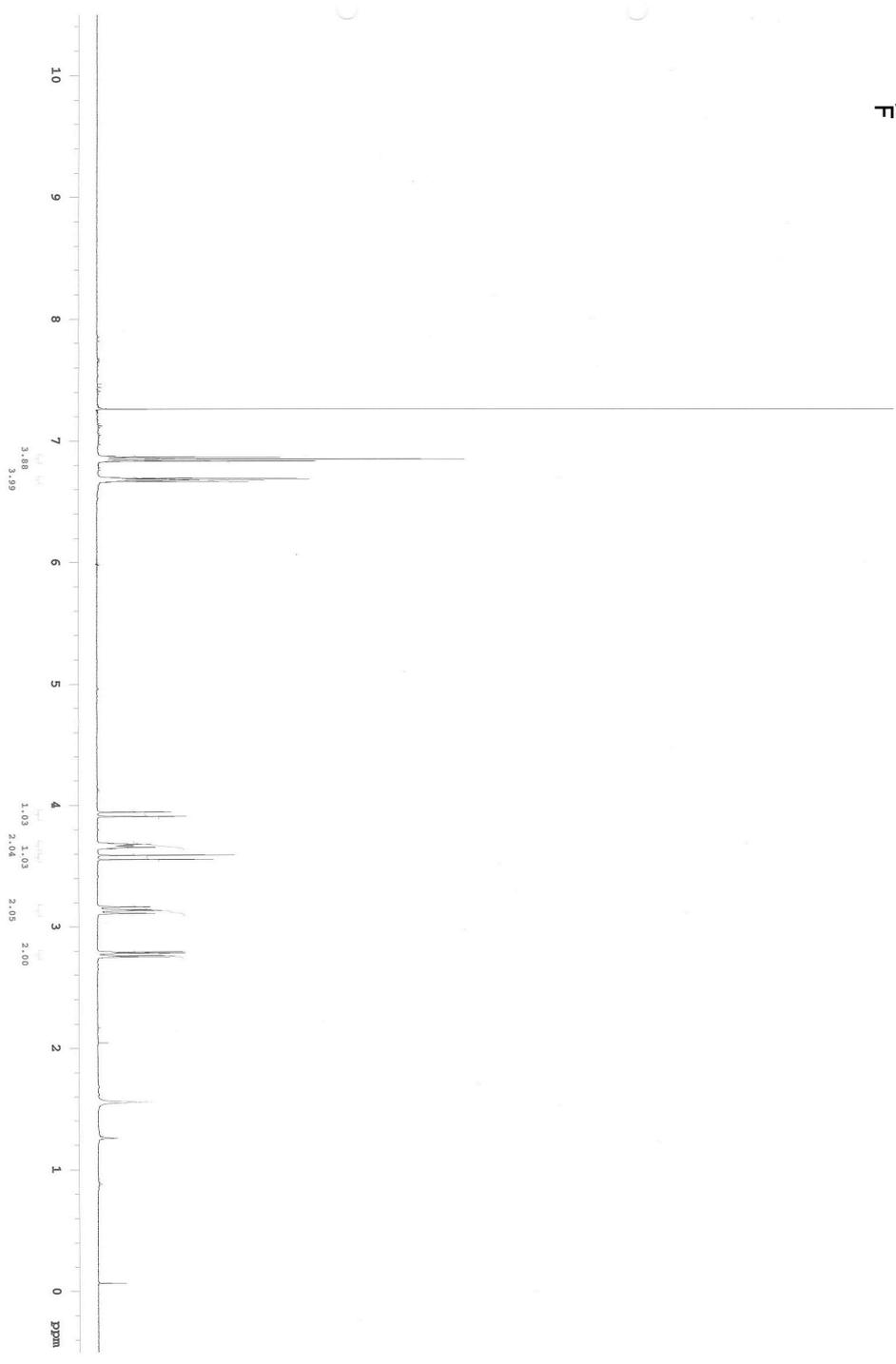
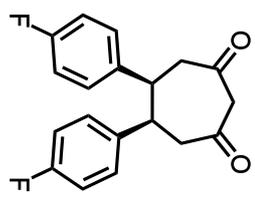
(5*R*\*, 6*S*\*)-5,6-bis(4-*tert*-butylphenyl)cycloheptane-1,3-dione (**6d**)



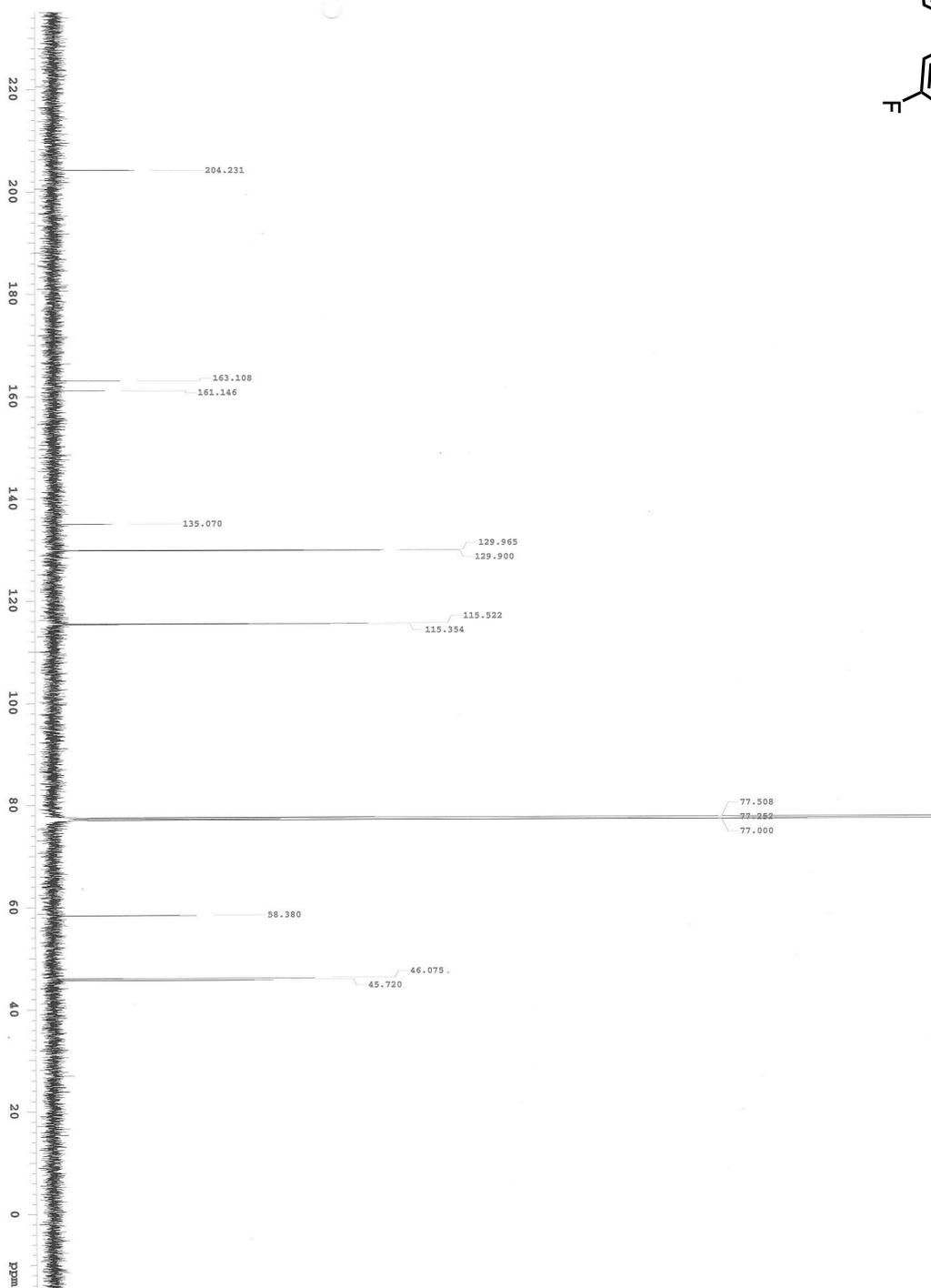
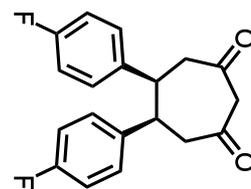
(5*R*\*, 6*S*\*)-5,6-bis(4-*tert*-butylphenyl)cycloheptane-1,3-dione (**6d**)



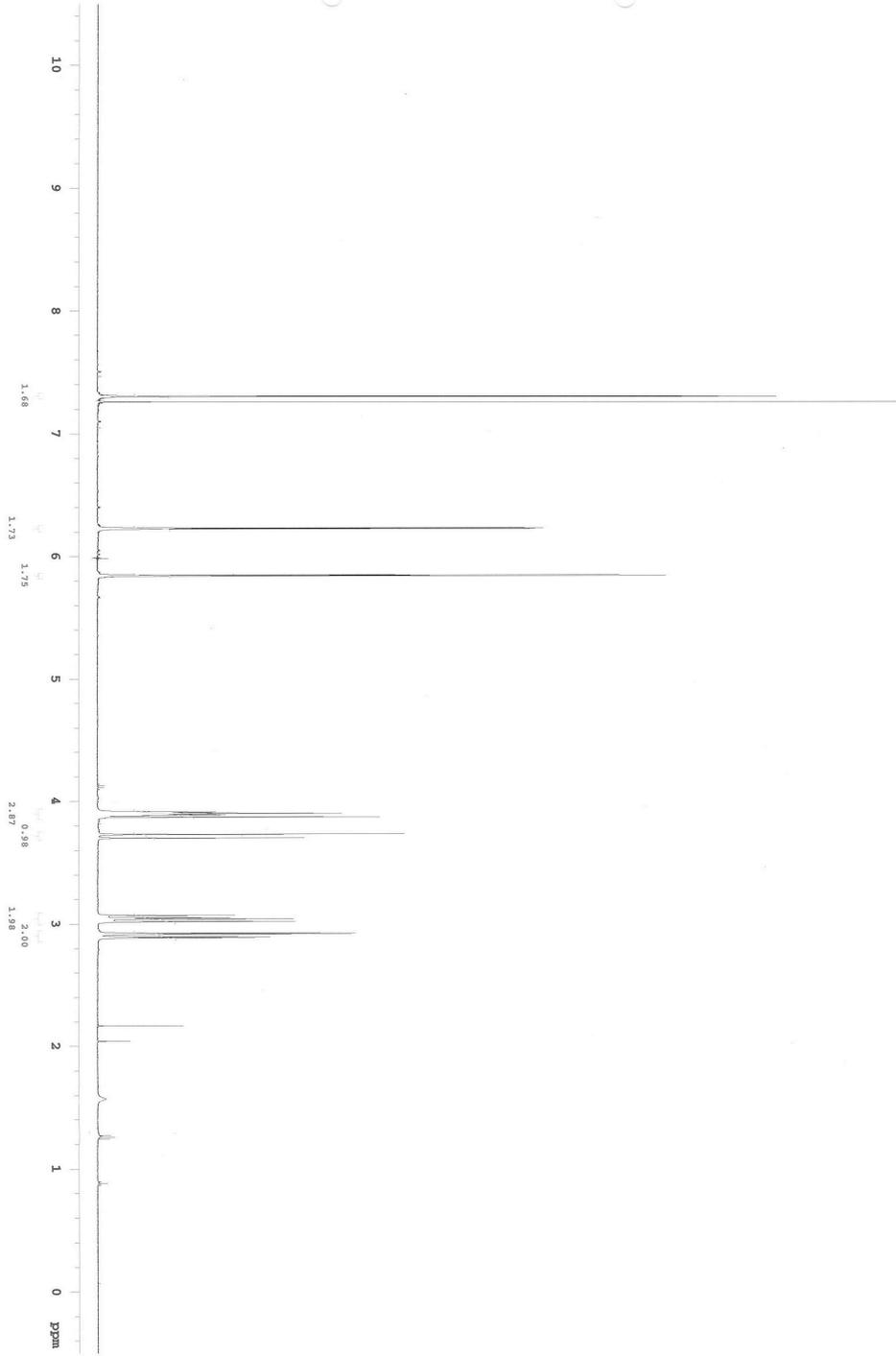
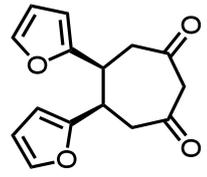
(5*R*\*, 6*S*\*)-5,6-bis(4-fluorophenyl)cycloheptane-1,3-dione (**6e**)



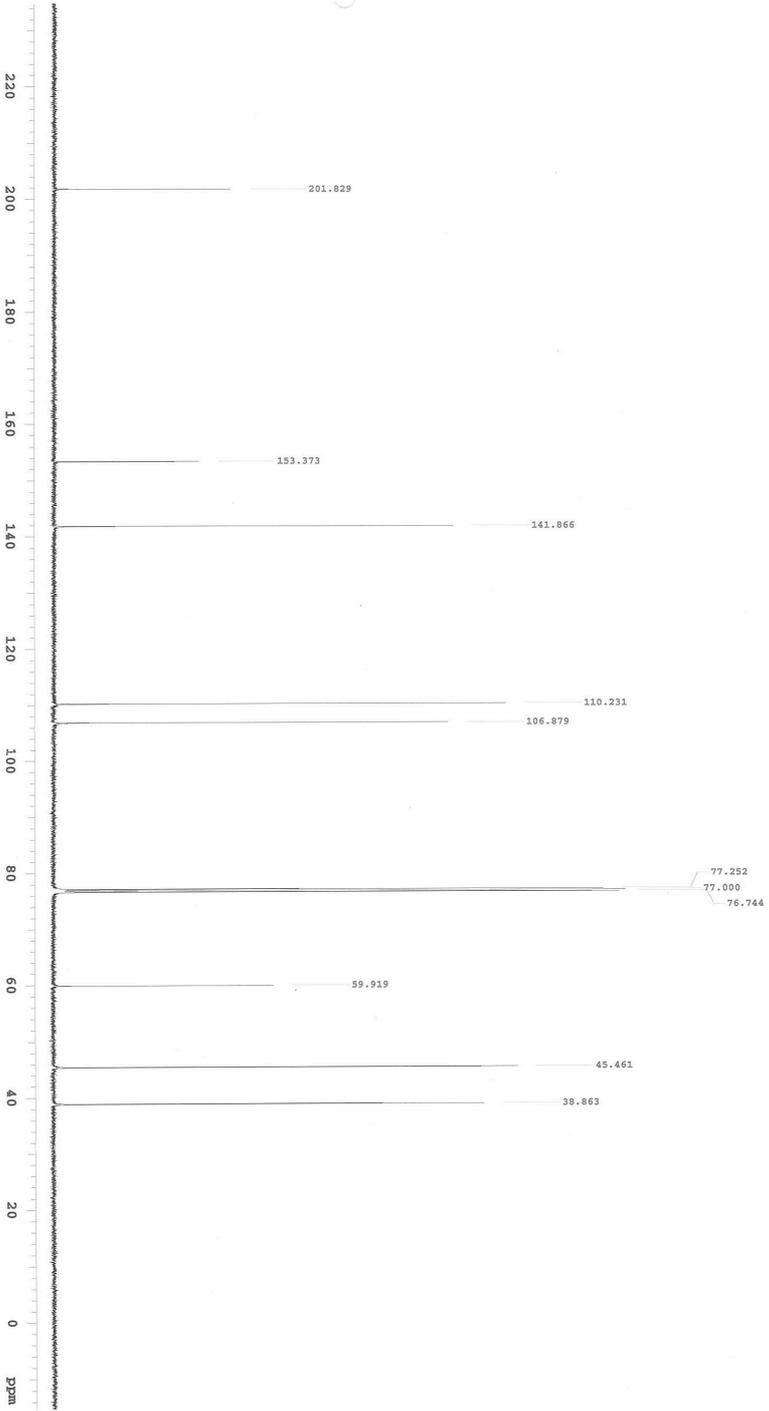
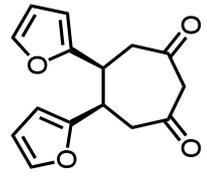
(5*R*\*, 6*S*\*)-5,6-bis(4-fluorophenyl)cycloheptane-1,3-dione (6e)



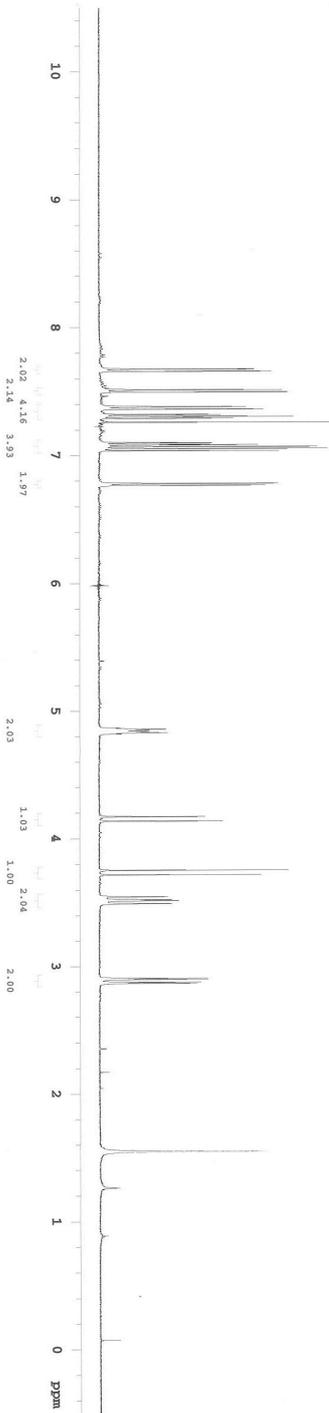
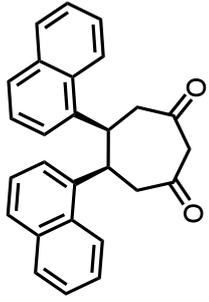
(5*R*\*, 6*S*\*)-5,6-di(furan-2-yl)cycloheptane-1,3-dione (**6f**)



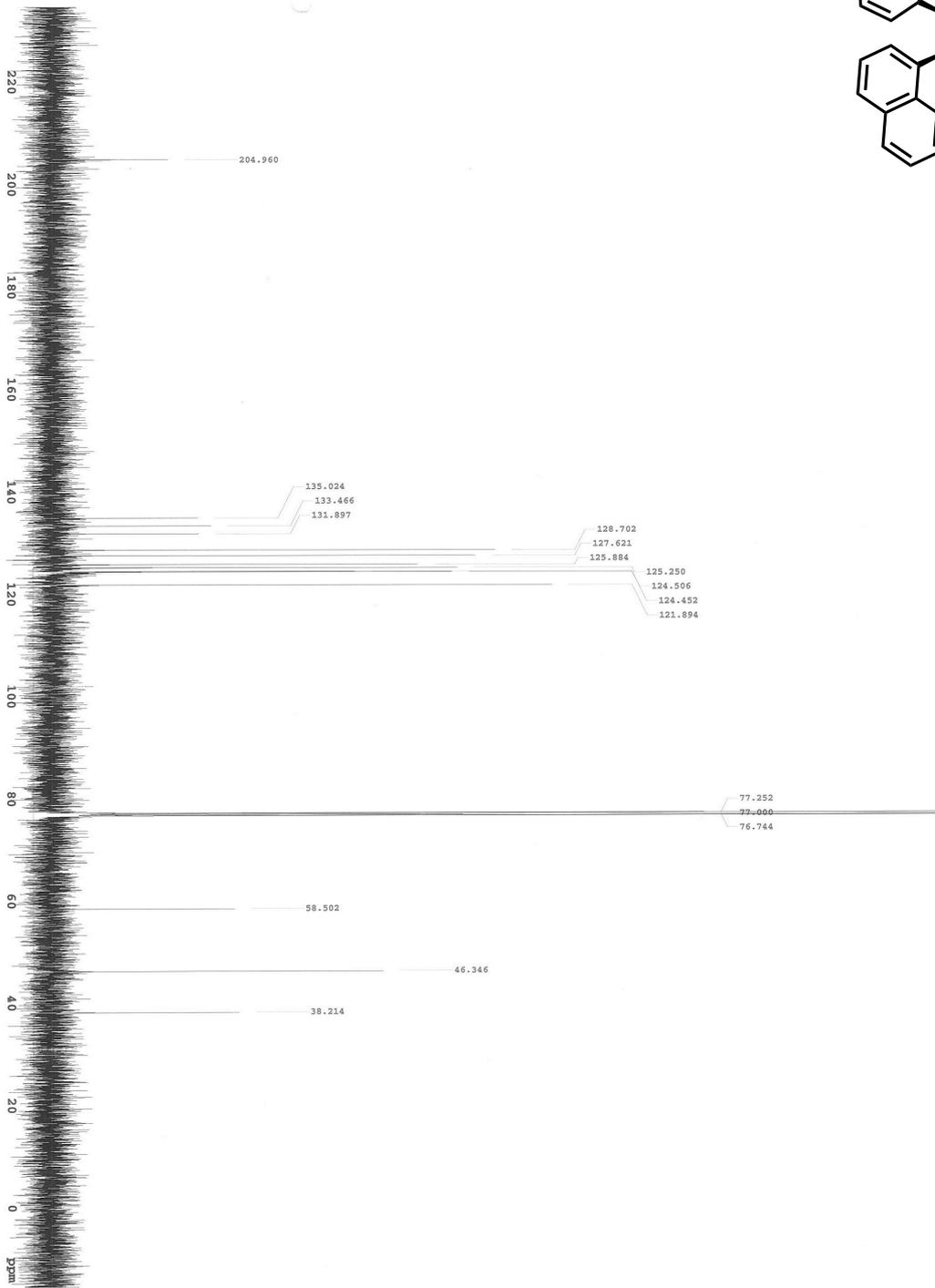
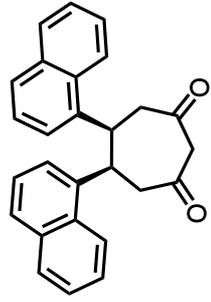
(5*R*\*, 6*S*\*)-5,6-di(furan-2-yl)cycloheptane-1,3-dione (**6f**)



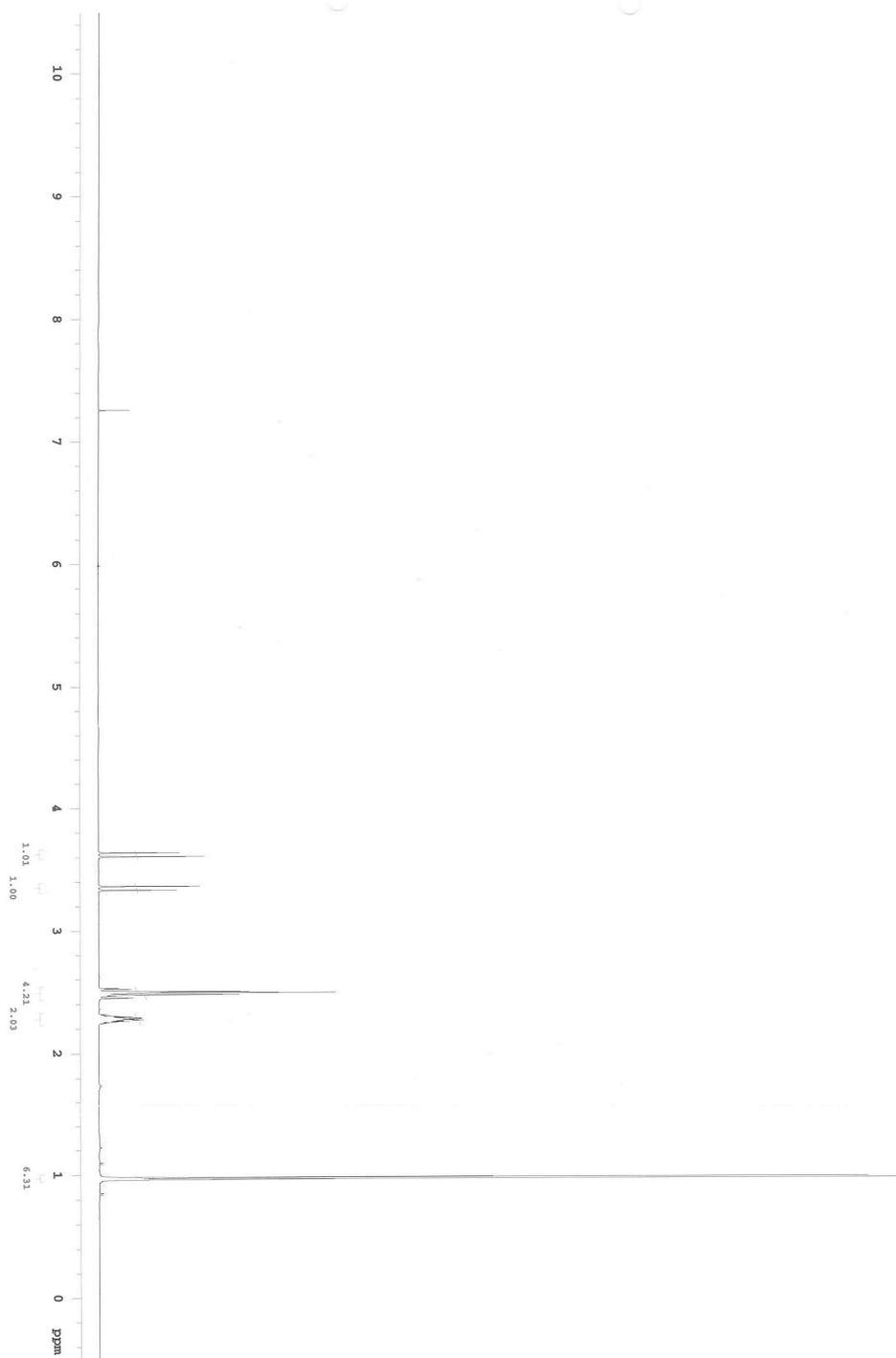
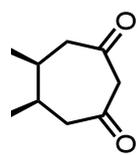
(5R\*, 6S\*)-5,6-di(naphthalen-1-yl)cycloheptane-1,3-dione (6g)



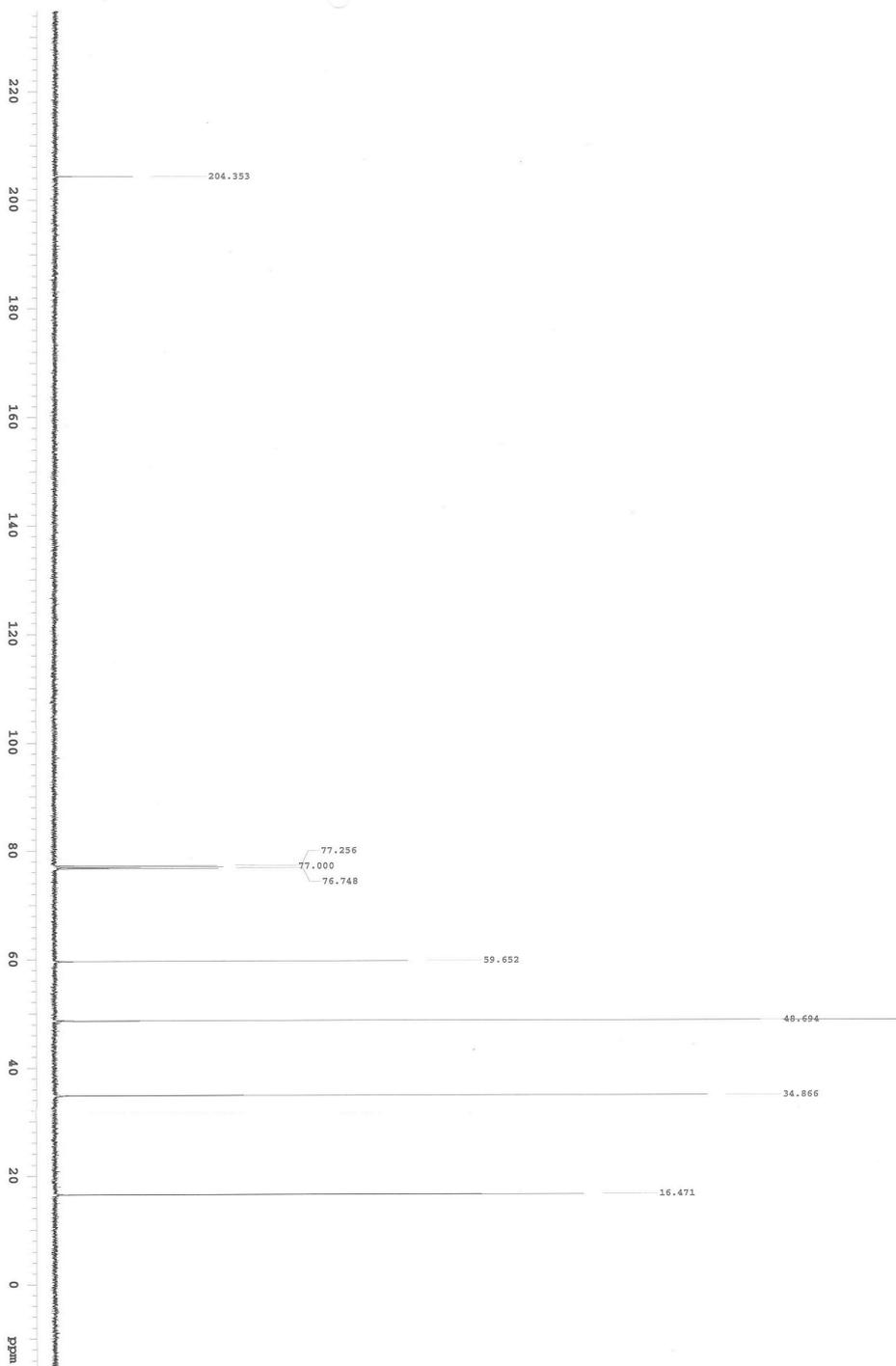
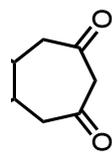
(5R\*,6S\*)-5,6-di(naphthalen-1-yl)cycloheptane-1,3-dione (6g)



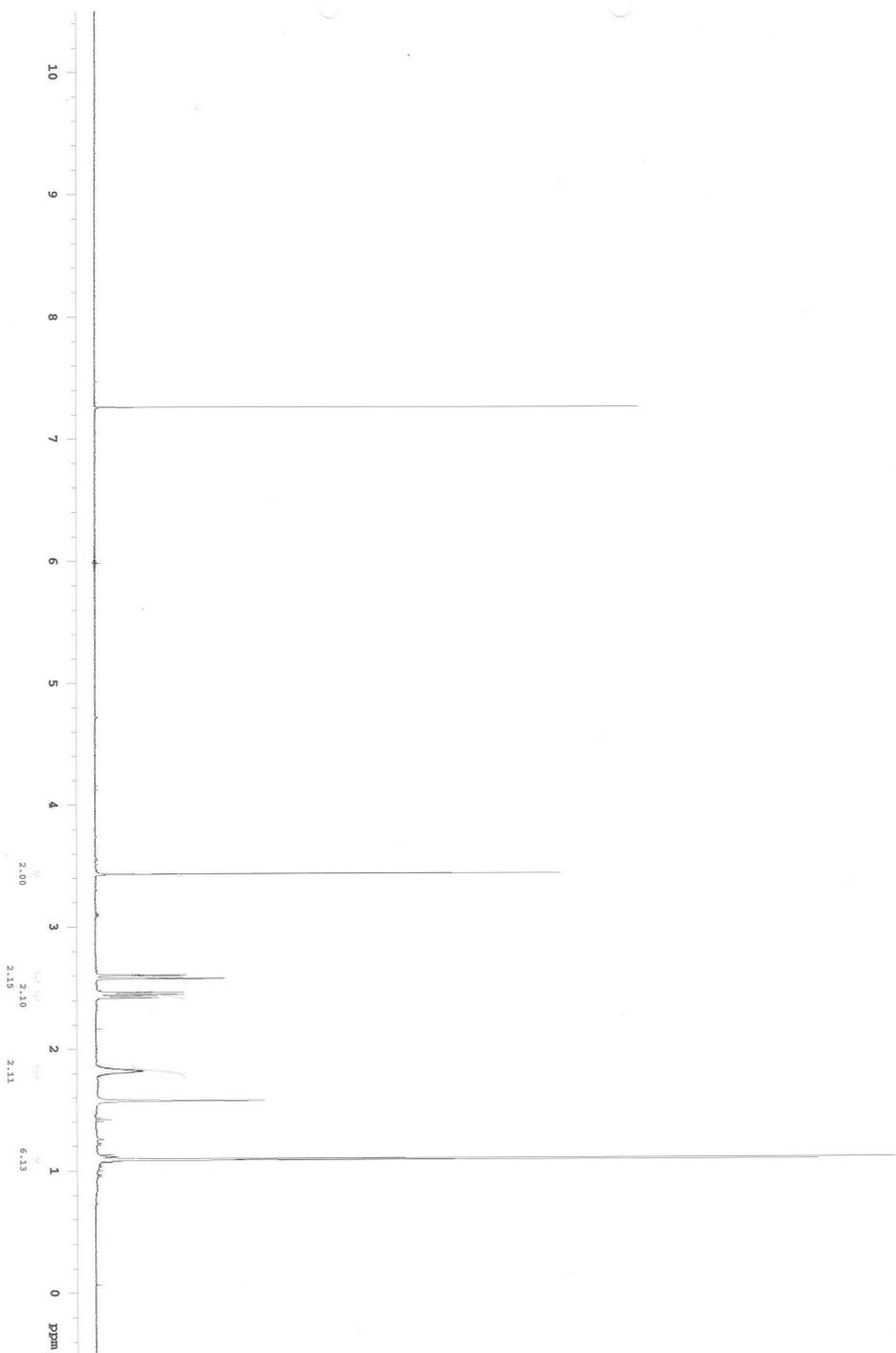
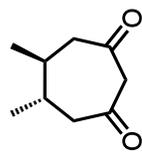
(5R\*,6S\*)-5,6-dimethylcycloheptane-1,3-dione (6h)



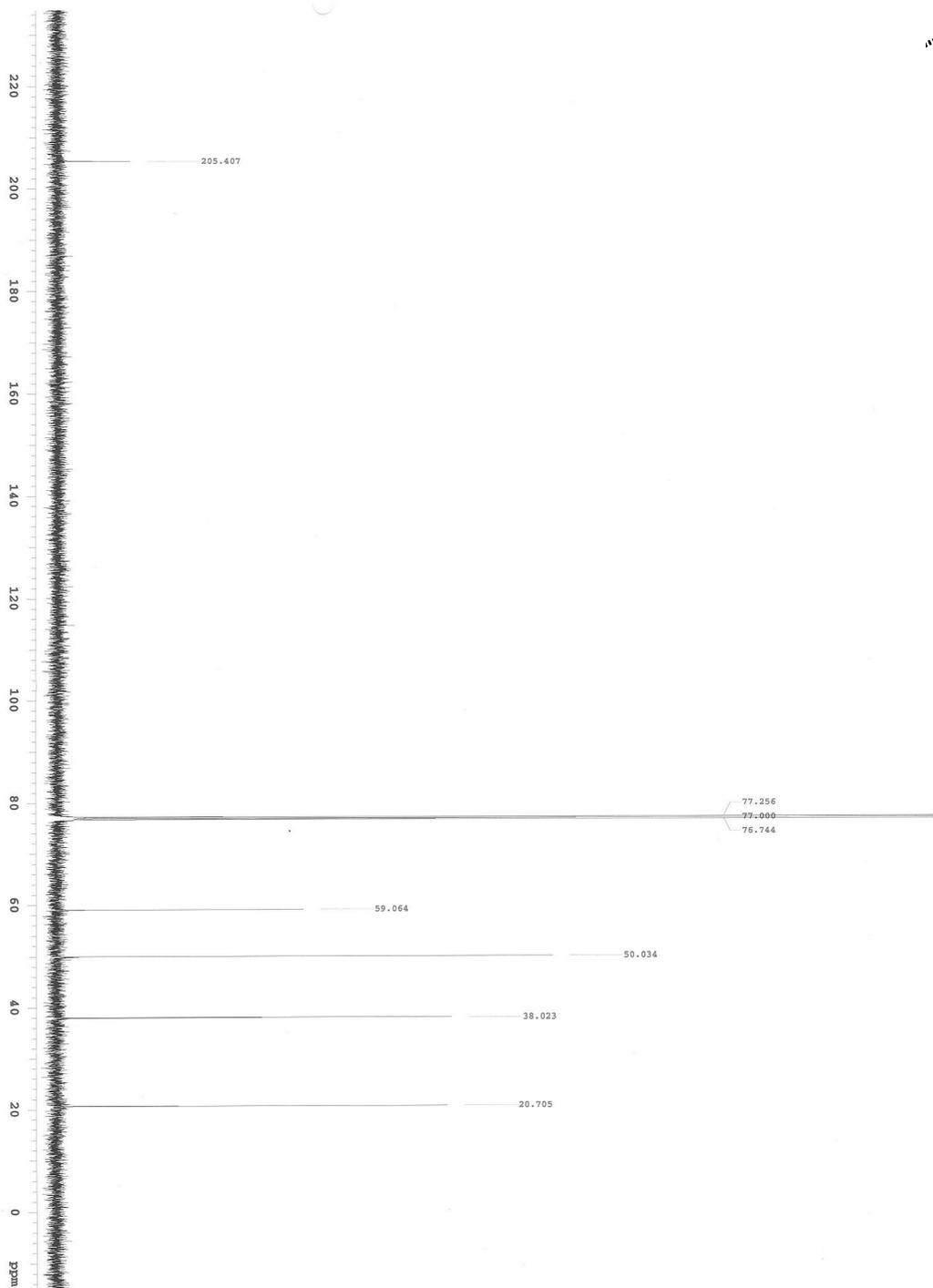
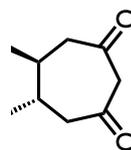
(5R\*,6S\*)-5,6-dimethylcycloheptane-1,3-dione (6h)



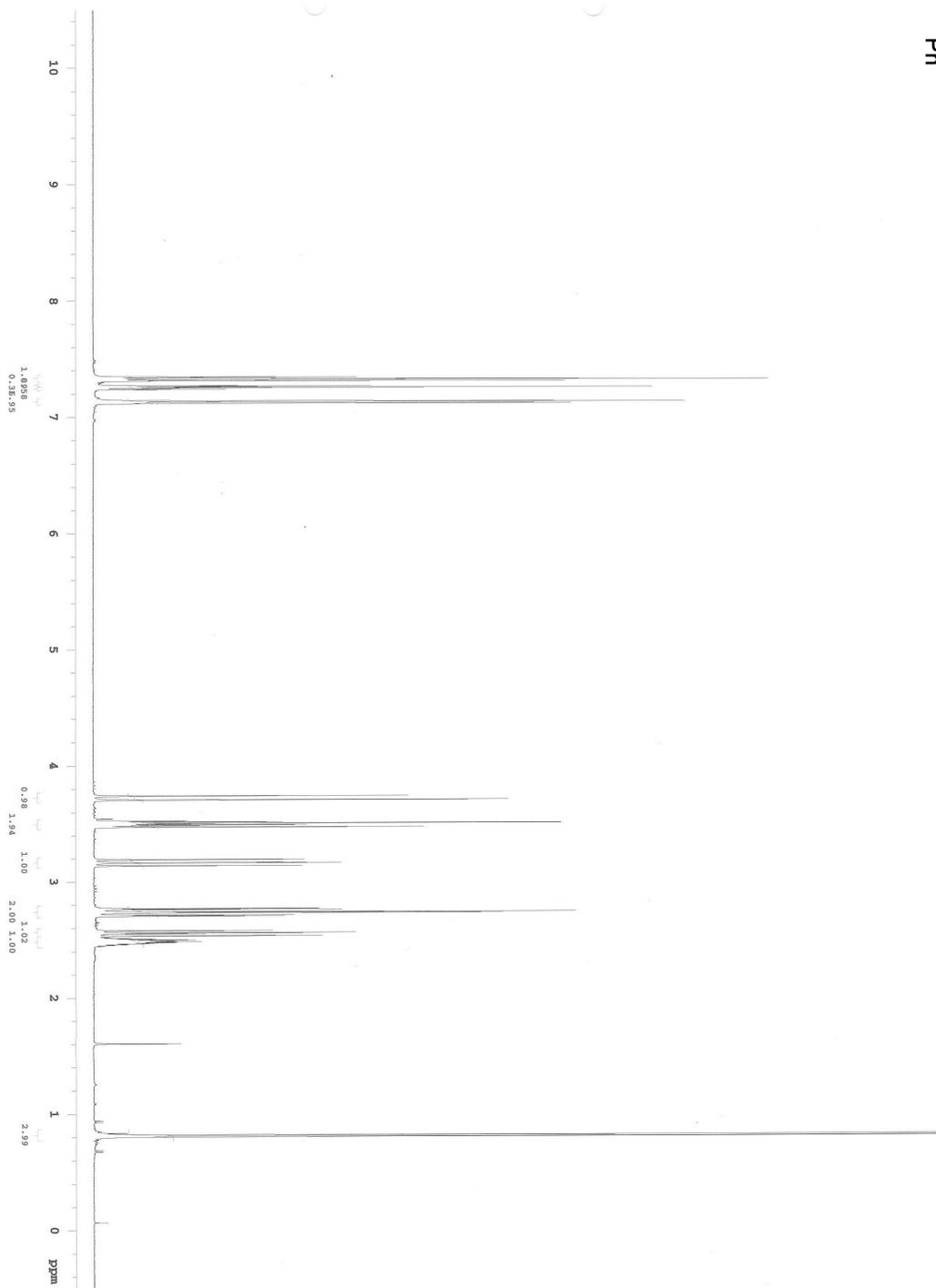
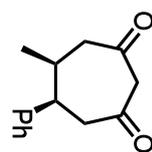
(5*S*,6*S*\*)-5,6-dimethylcycloheptane-1,3-dione (6i)



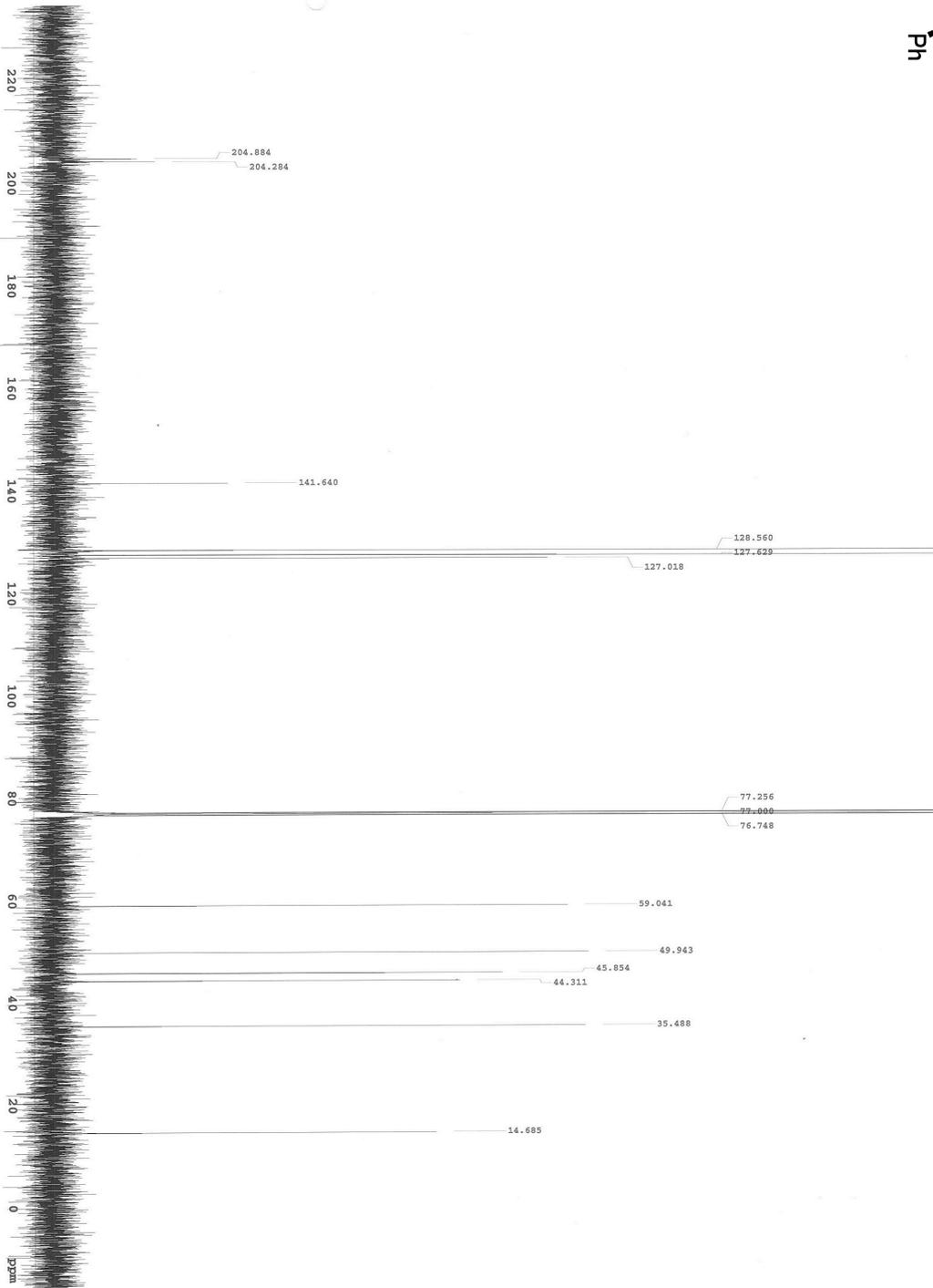
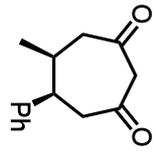
(5*S*\*,6*S*\*)-5,6-dimethylcycloheptane-1,3-dione (6i)



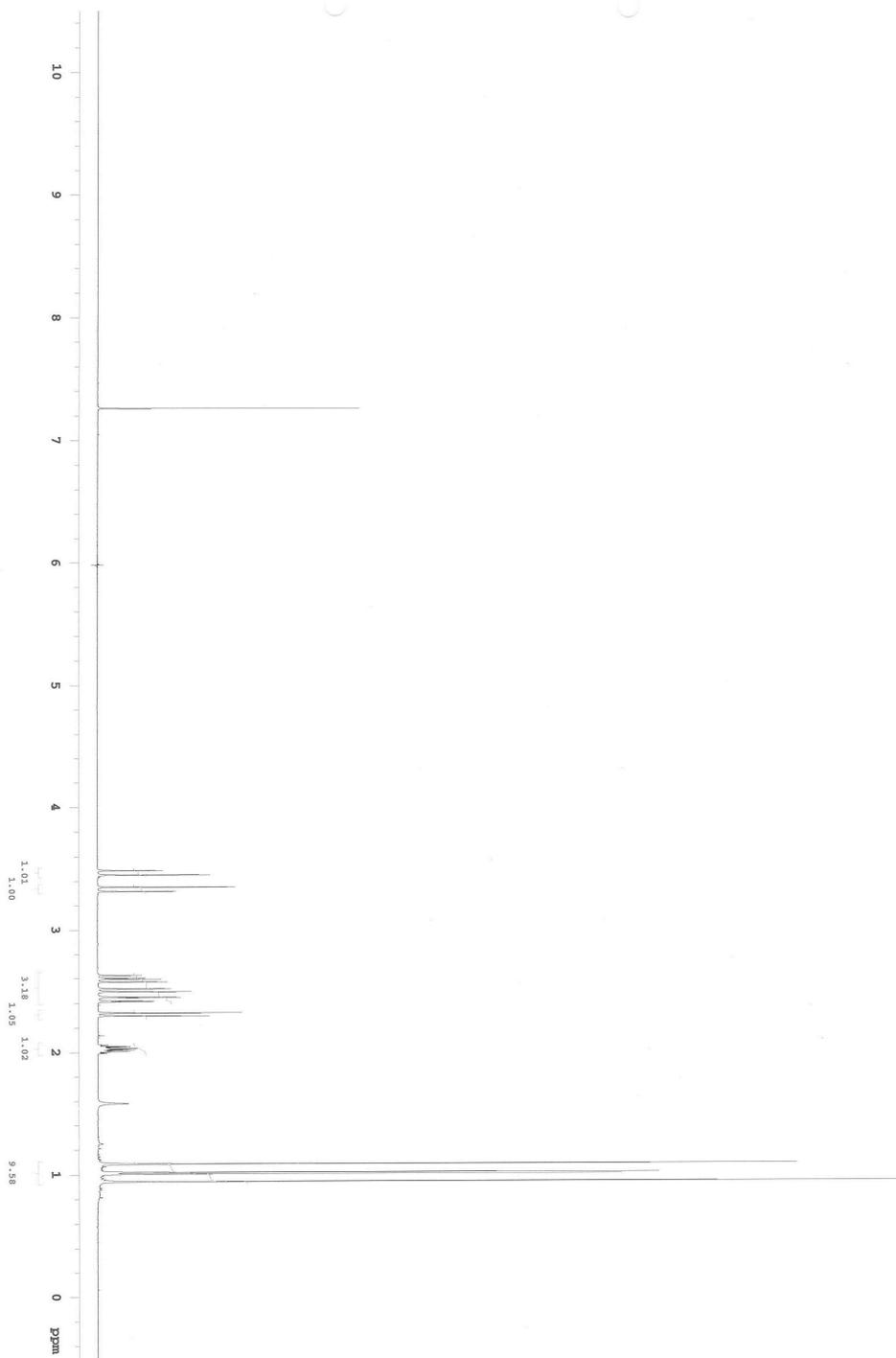
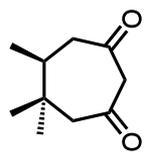
(5*S*\*,6*R*\*)-5-methyl-6-phenylcycloheptane-1,3-dione (6j)



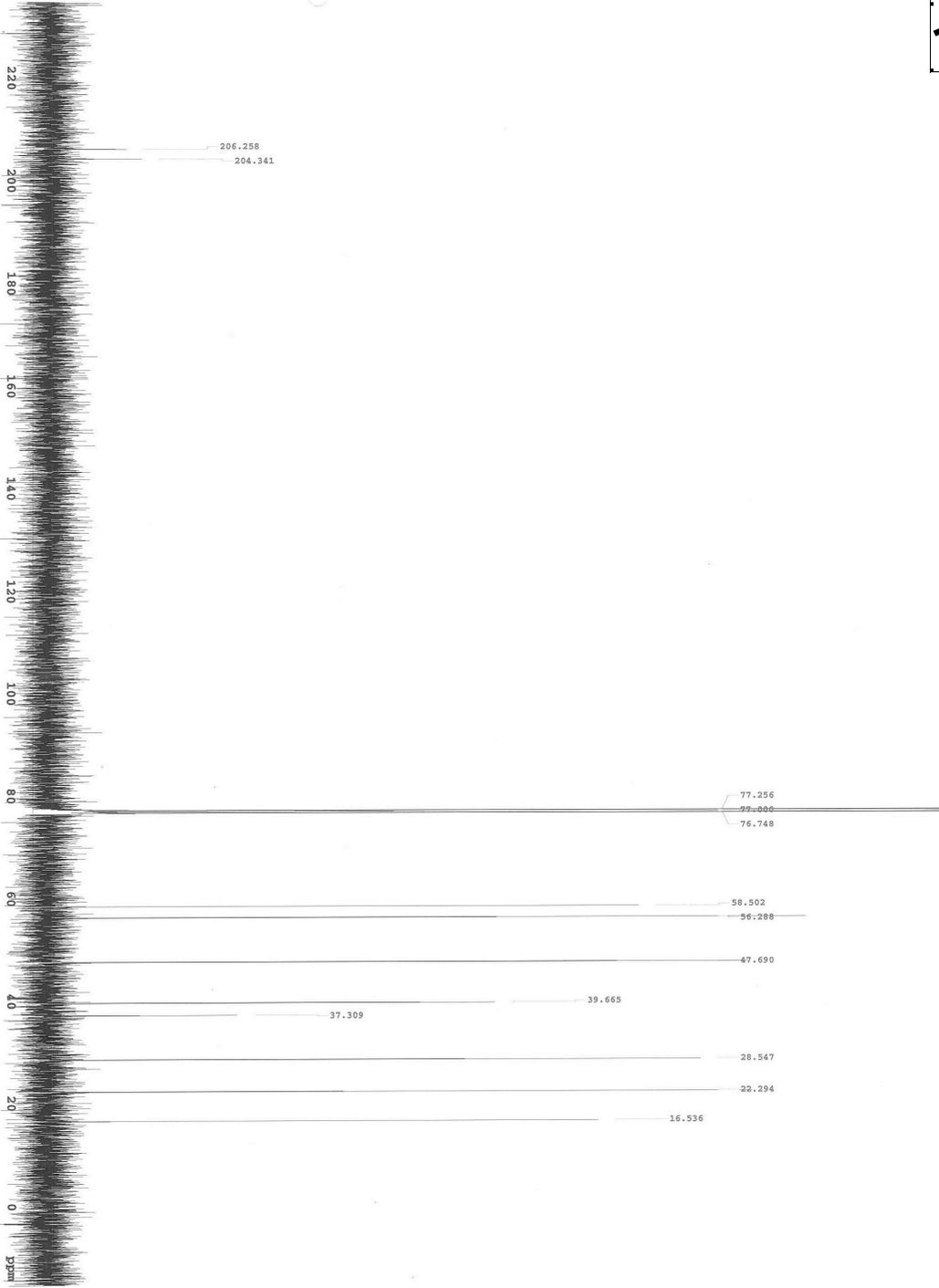
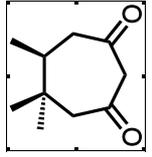
(5*S*\*, 6*R*\*)-5-methyl-6-phenylcycloheptane-1,3-dione (6j)



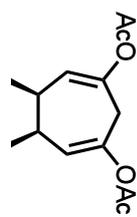
(S)-5,5,6-trimethylcycloheptane-1,3-dione (6k)



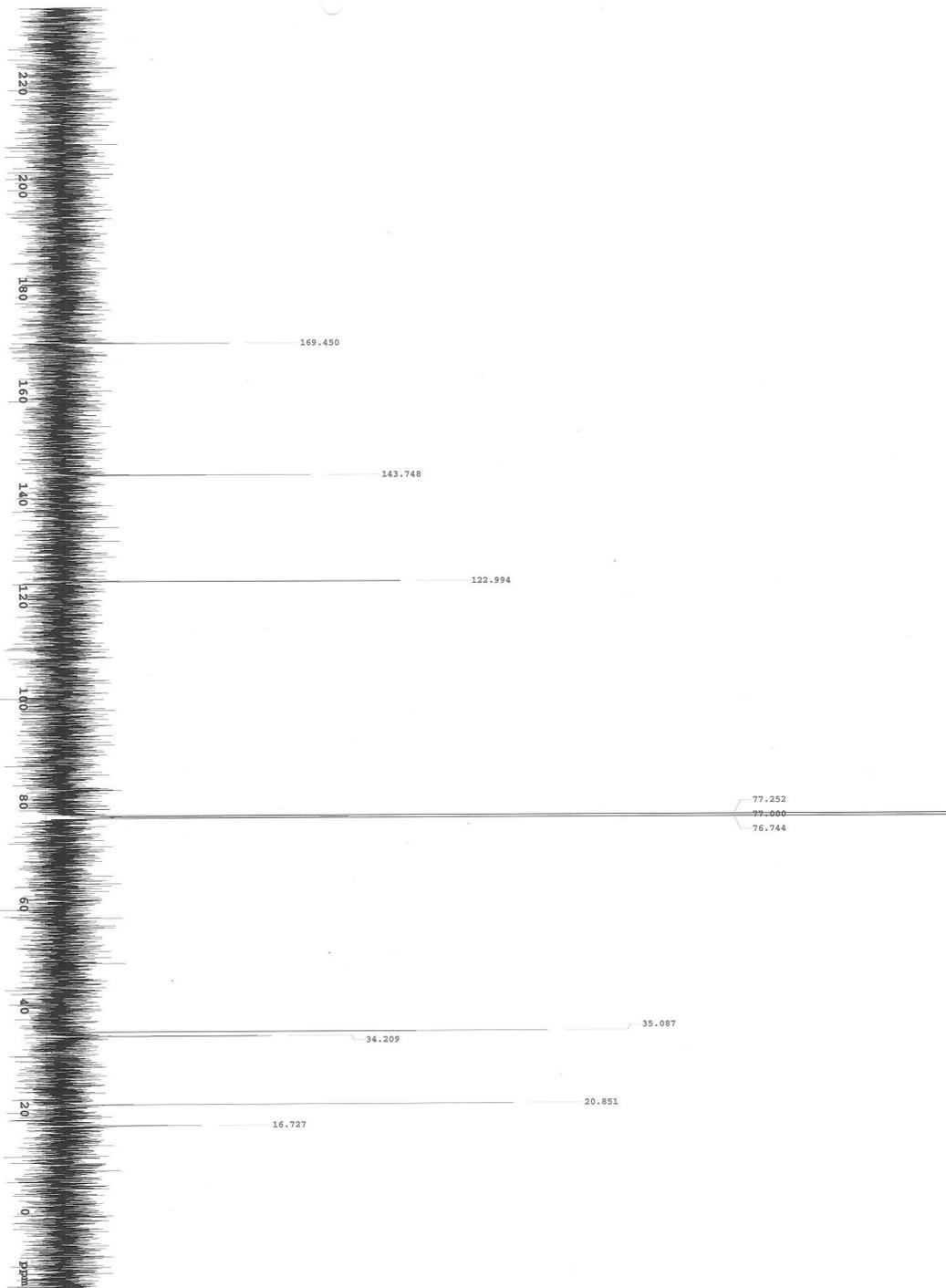
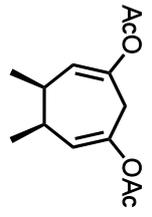
(S)-5,5,6-trimethylcycloheptane-1,3-dione (6k)



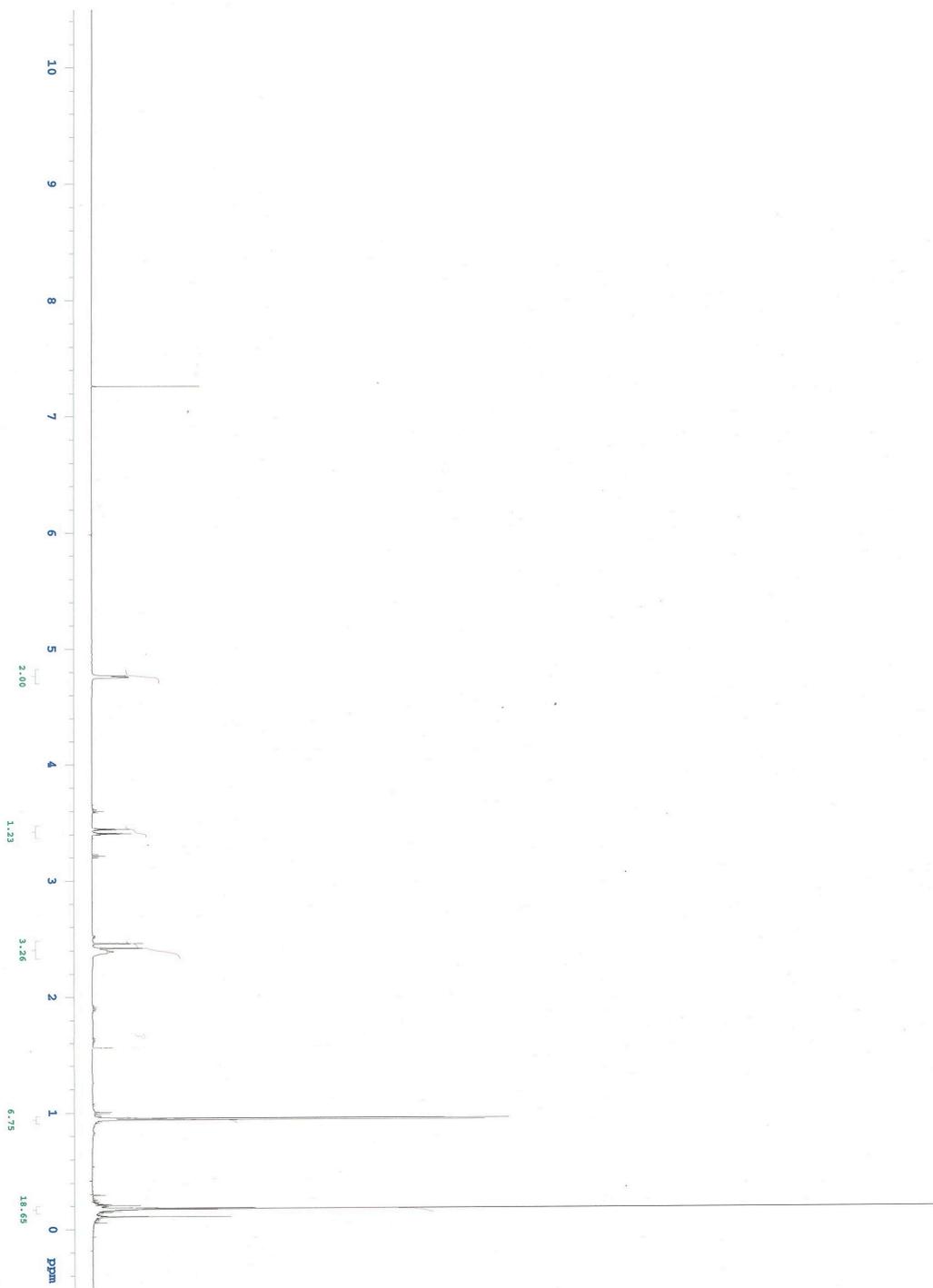
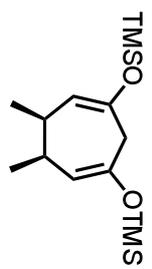
(5*R*\*, 6*S*\*)-5,6-dimethylcyclohepta-3,7-diene-1,3-diyl diacetate (7)



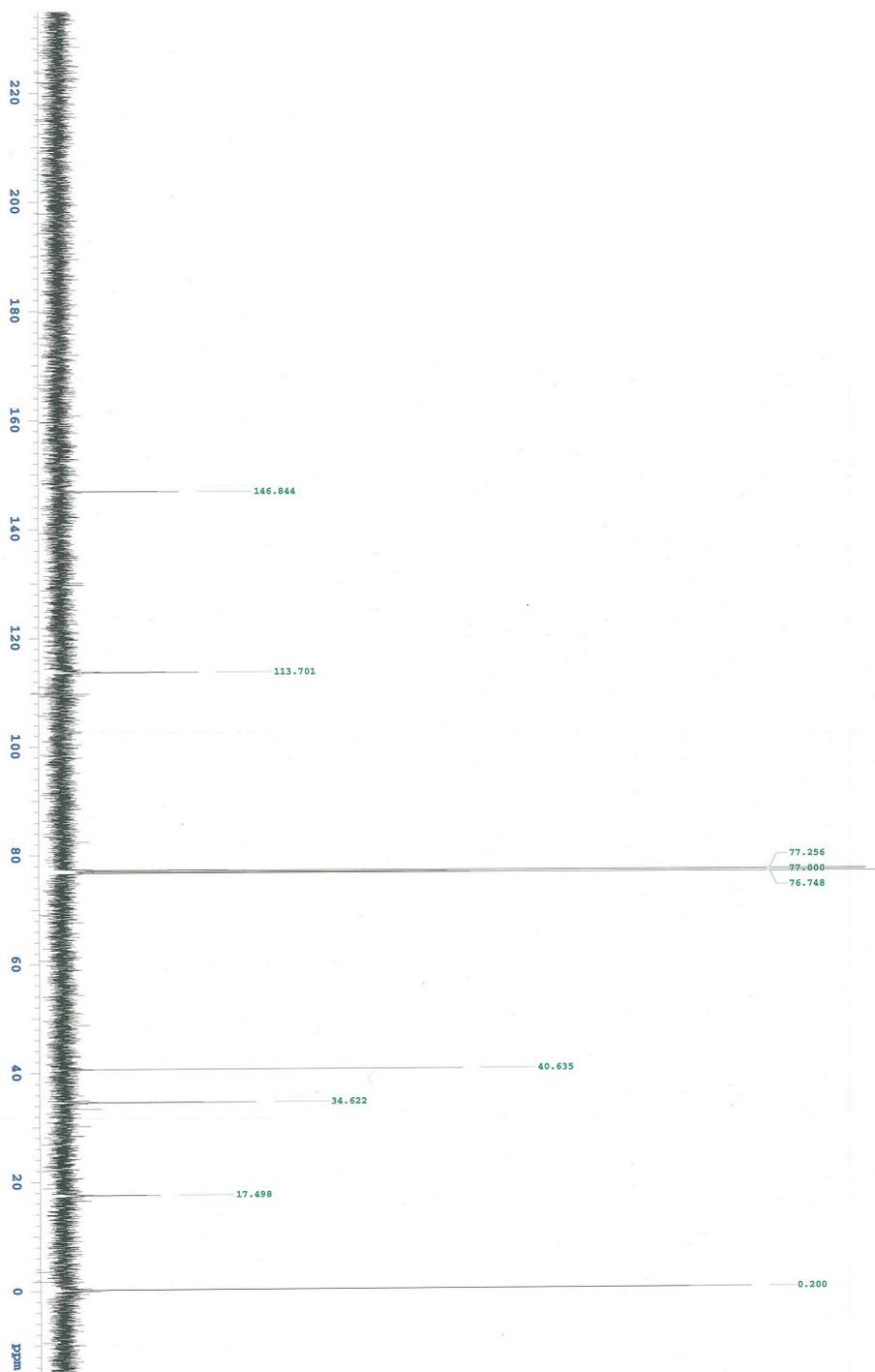
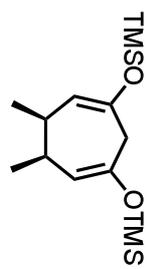
(5*R*\*, 6*S*\*)-5,6-dimethylcyclohepta-3,7-diene-1,3-diyl diacetate (7)



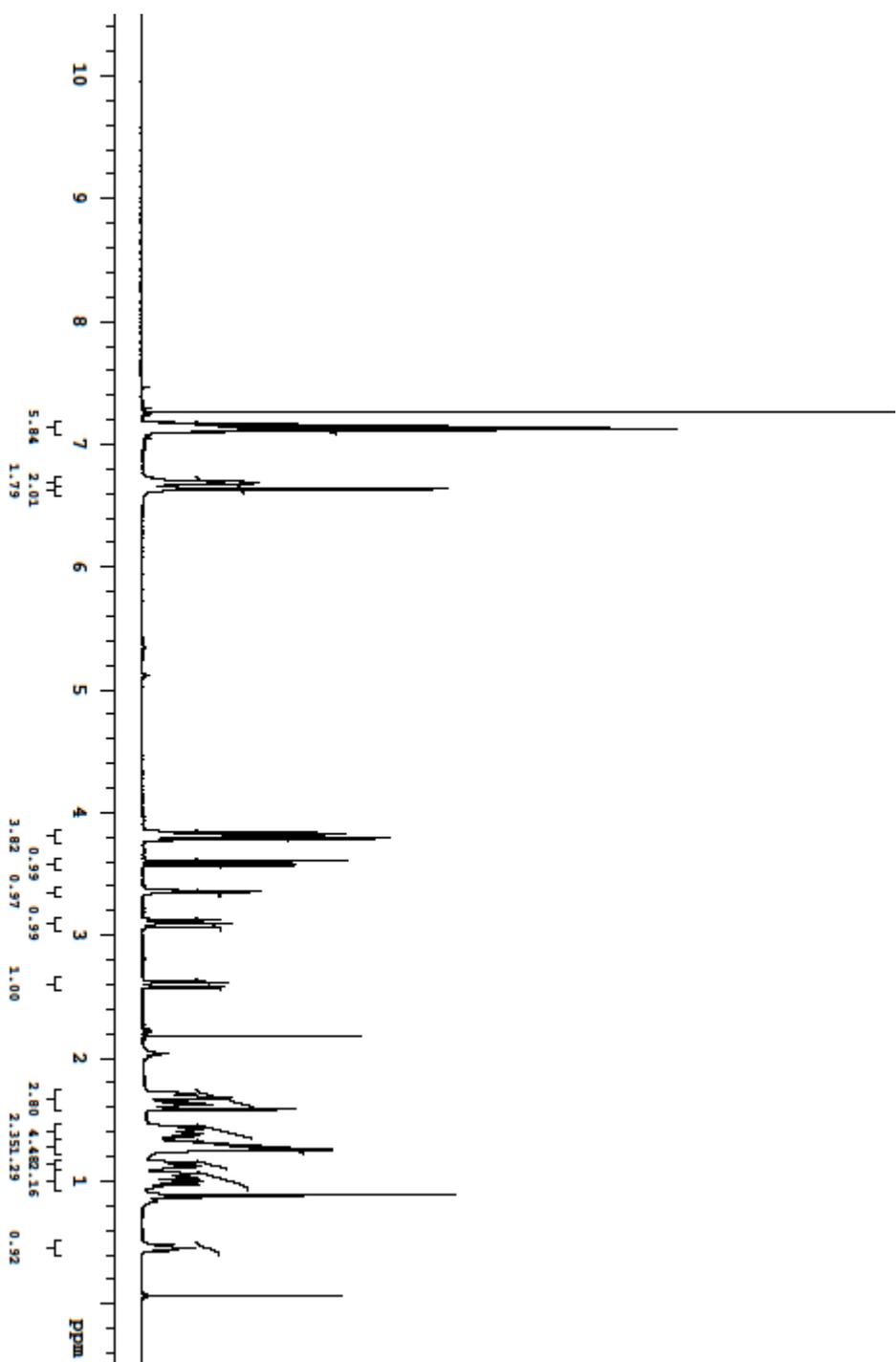
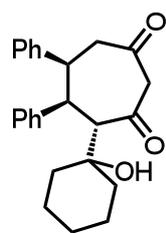
**((5*R*\*, 6*S*\*)-5,6-dimethylcyclohepta-3,7-diene-1,3-diyl)bis(oxy)bis(trimethylsilane) (8)**



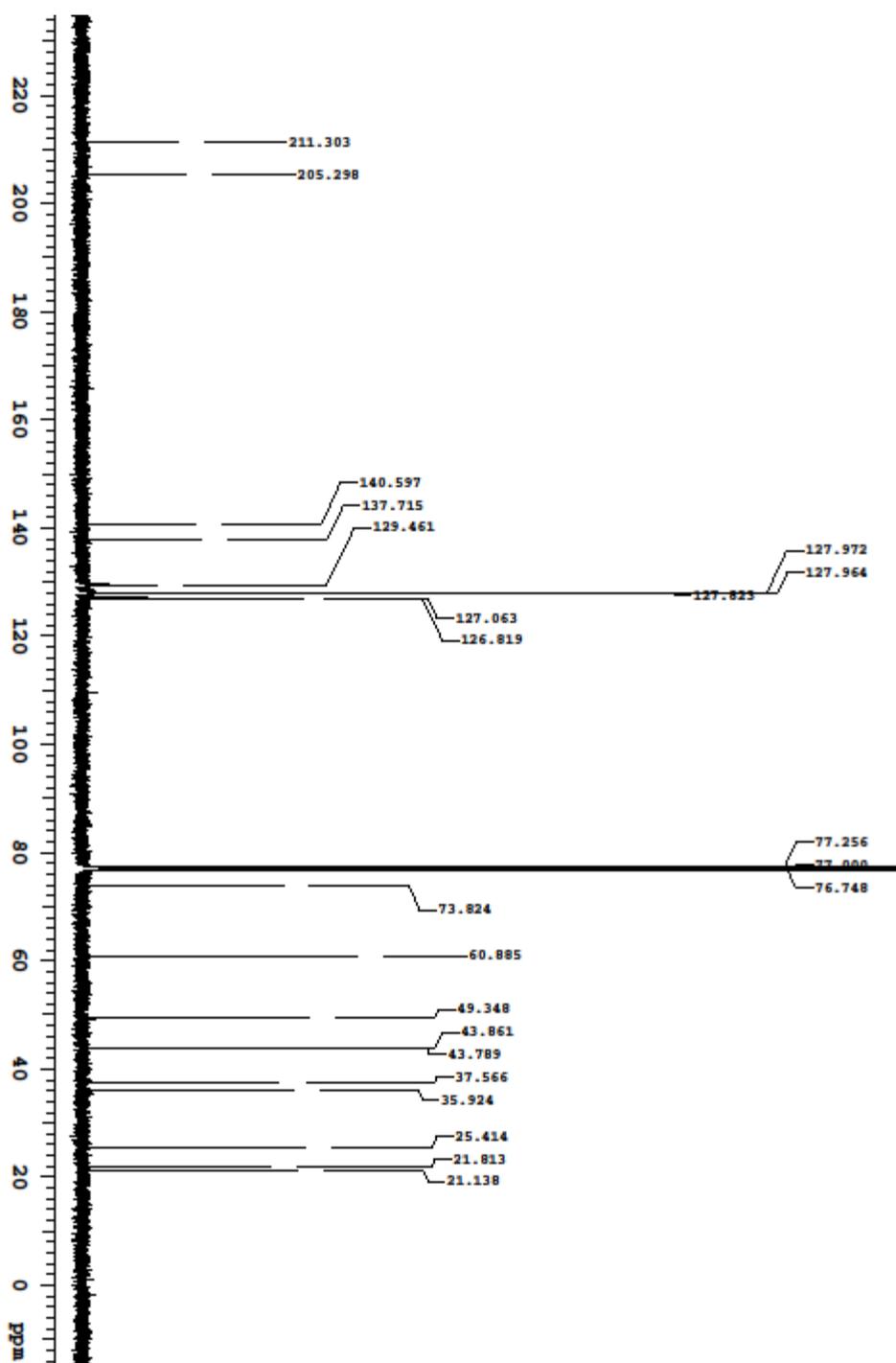
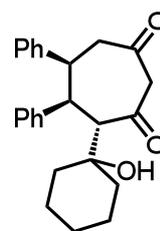
((5*R*\*, 6*S*\*)-5,6-dimethylcyclohepta-3,7-diene-1,3-diyl)bis(oxy)bis(trimethylsilane) (8)



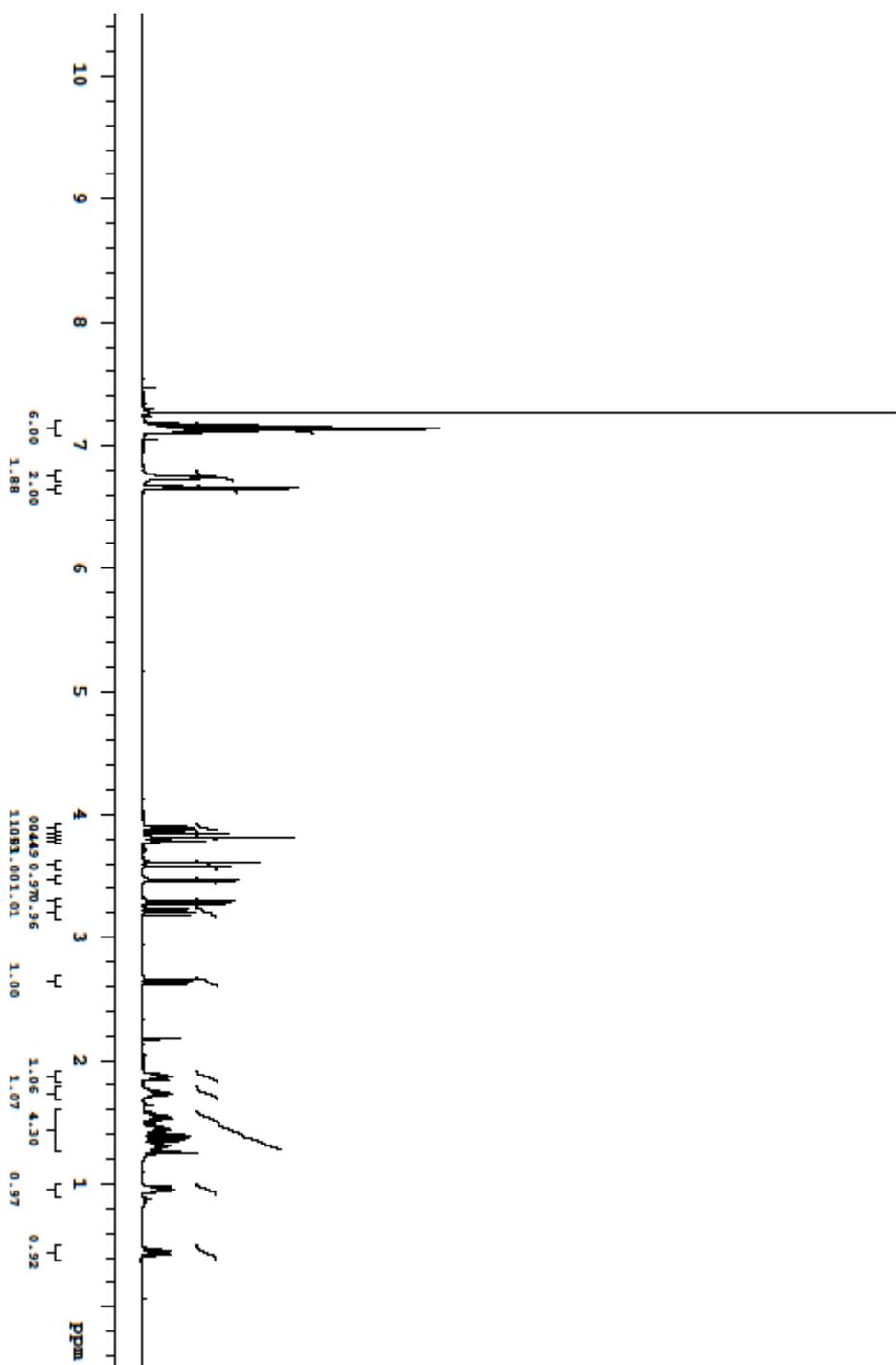
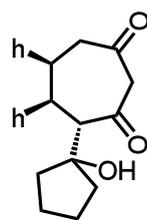
(4*S*,5*S*,6*S*)-4-(1-hydroxycyclohexyl)-5,6-diphenylcycloheptane-1,3-dione (10a)



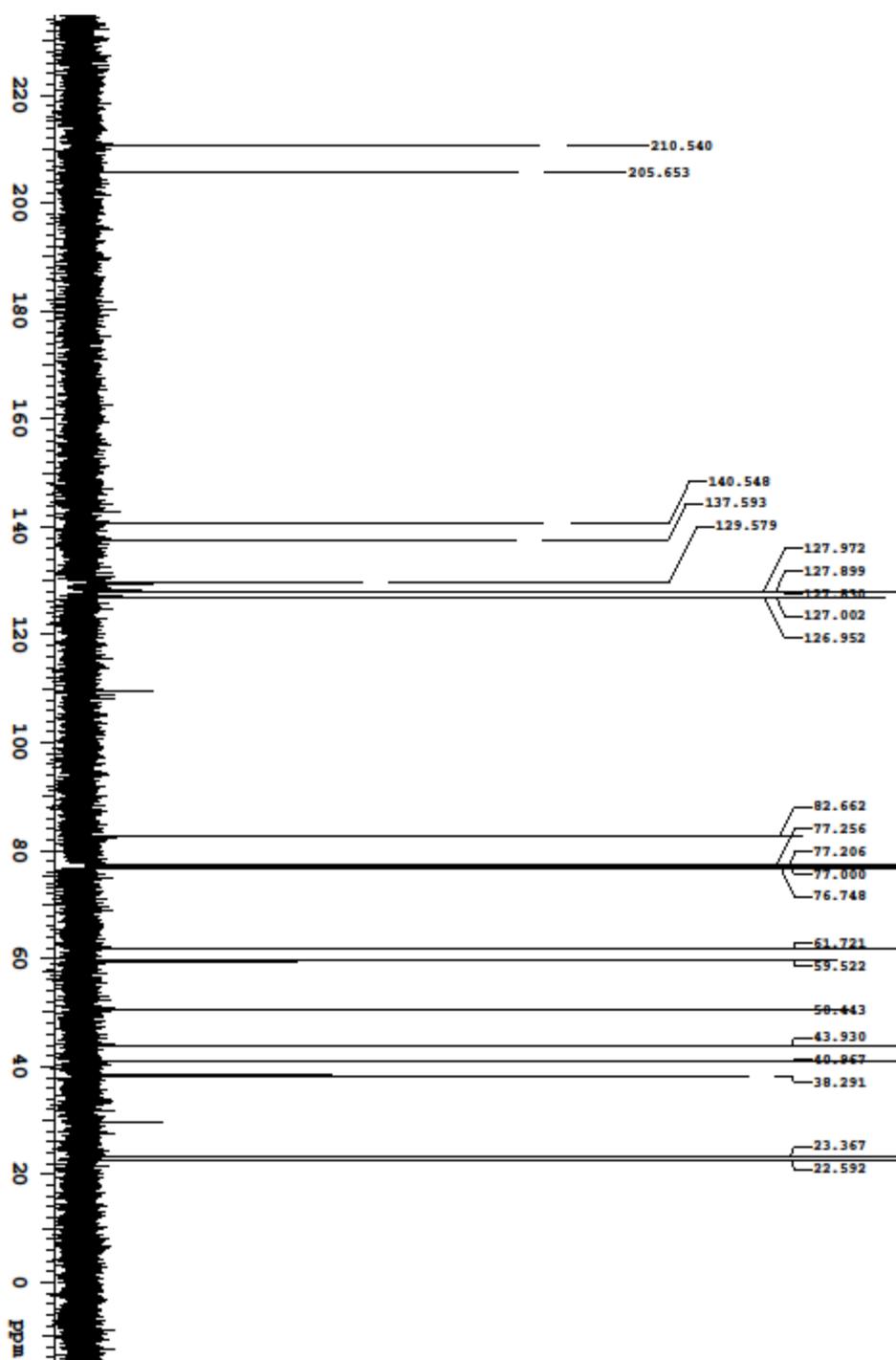
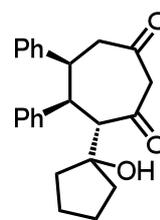
(4*S*,5*S*,6*S*)-4-(1-hydroxycyclohexyl)-5,6-diphenylcycloheptane-1,3-dione (10a)



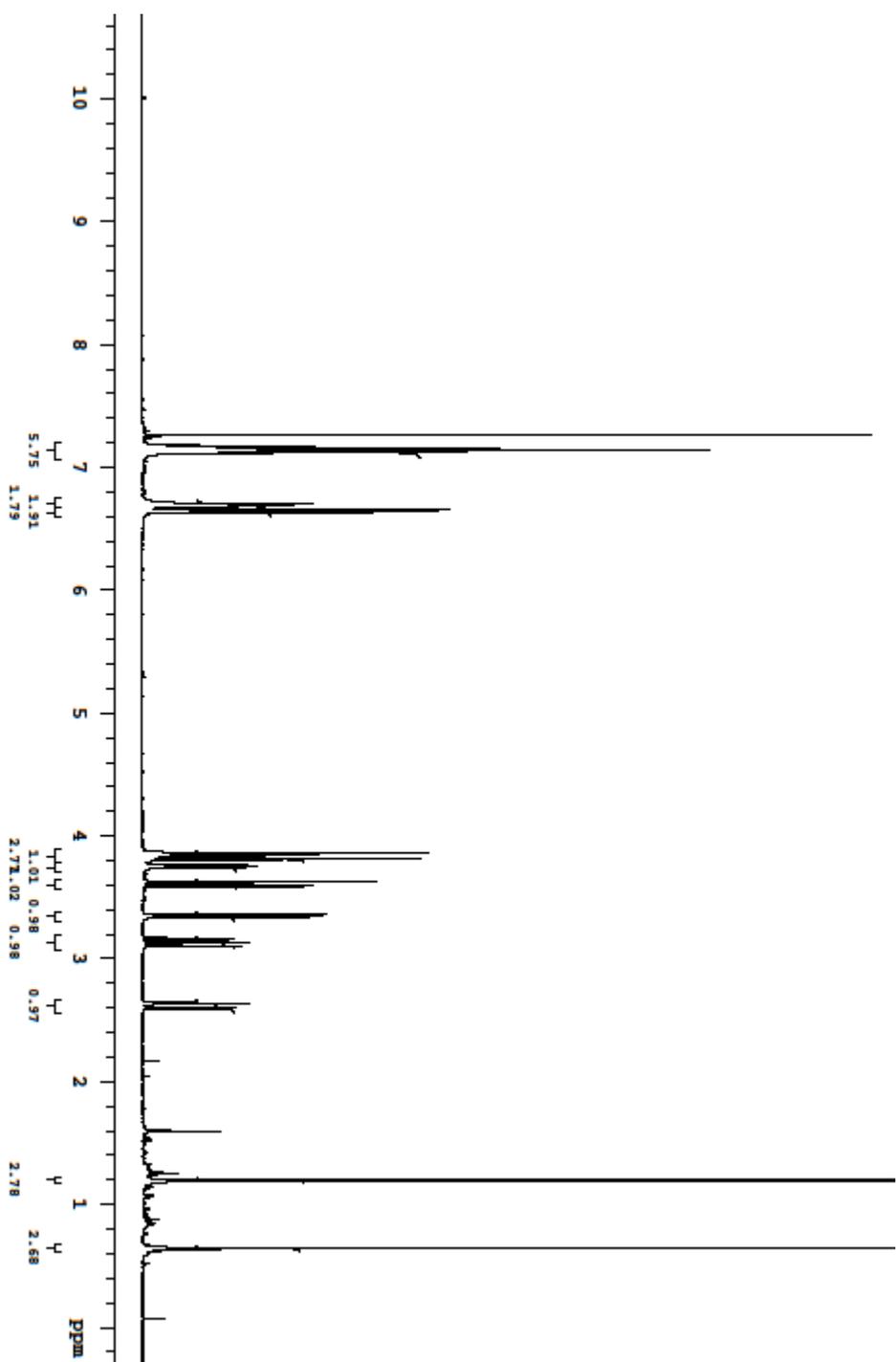
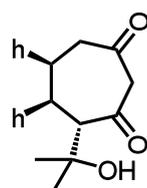
(4*S*,5*S*,6*S*)-4-(1-hydroxycyclopentyl)-5,6-diphenylcycloheptane-1,3-dione (10b)



(4*S*,5*S*,6*S*)-4-(1-hydroxycyclopentyl)-5,6-diphenylcycloheptane-1,3-dione (10b)



(4*S*,5*S*,6*S*)-4-(2-hydroxypropan-2-yl)-5,6-diphenylcycloheptane-1,3-dione (10c)



(4*S*,5*S*,6*S*)-4-(2-hydroxypropan-2-yl)-5,6-diphenylcycloheptane-1,3-dione (10c)

