

## Electronic Supporting Information

### Improved synthesis of (E)-12-nitrooctadec-12-enoic acid, a potent PPAR $\gamma$ receptor activator.

#### Development of a “buffer-free” enzymatic method for hydrolysis of methyl esters

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## General

All solvents were of commercial quality and were purified by distillation over the drying agents indicated: THF (Na/benzophenone),  $\text{CH}_2\text{Cl}_2$ , hexane,  $\text{Et}_3\text{N}$  ( $\text{CaH}_2$ ), toluene (Na/K). All other reagents were used as supplied. All moisture-sensitive reactions were carried out under a positive static atmosphere of Ar in flame-dried glassware. Syringes and needles for the transfer of reagents were dried at 140 °C and allowed to cool in a desiccator over  $\text{P}_2\text{O}_5$  before use. Routine monitoring of reactions was performed using silica gel 60 (0.25 mm), aluminum-supported TLC plates. Compounds were visualized by UV irradiation at a wavelength of 254 nm, or stained by exposure to a 0.5% soln. of vanillin in  $\text{H}_2\text{SO}_4$ /EtOH, followed by charring. Flash column chromatography was performed on silica gel (40–63  $\mu\text{m}$ ). 2-Nitrocyclododecanone was purchased from Sigma-Aldrich and used as received. CAL-B Lipase immobilized from *Candida antarctica*, beads, slightly brown, >2 units/mg IUBMB 3.1.1.3, EC number 232-619-9, batch 1241096 41708197, was purchased from Sigma-Aldrich.

$^1\text{H}$  and  $^{13}\text{C}$  NMR spectra were recorded at 300 MHz and 75 MHz, respectively, in the solvents indicated; chemical shifts ( $\delta$ ) are given in ppm relative to TMS, coupling constants ( $J$ ) in Hz. The solvent signals were used as references and the chemical shifts converted to the TMS scale ( $\text{CDCl}_3$ :  $\delta_{\text{C}}$  77.16; residual  $\text{CHCl}_3$  in  $\text{CDCl}_3$ :  $\delta_{\text{H}}$  7.26;  $\text{CD}_2\text{Cl}_2$ :  $\delta_{\text{C}}$  53.8; residual  $^1\text{H}$ :  $\delta_{\text{H}}$  5.32 ppm. The number of H-atoms attached to each C-atom (s = 0H, d = 1H, t = 2H, q = 3H) was determined by DEPT experiments. Optical rotations were recorded at 589 nm, concentration ( $c$ ) in g/100 mL.

## Synthesis of (*E*)-10-nitrooleic acid

### Step 1: synthesis of methyl 9-hydroxy-10-nitrooctadecanoate<sup>1</sup>

Methyl 9-oxononanoate<sup>2</sup> (300 mg, 1.611mmol) and the 1-nitro nonane (279 mg, 1.611 mmol) were stirred under Ar without solvent in a dry bottom flask. To this mixture was added DBU (0.161 mmol) and the mixture was stirred for 24h at room temperature. The reaction was diluted with EtOAc and was quenched with HCl 1N (8 ml). The layers were separated and the aq layer was extracted with Et<sub>2</sub>O. The organic layers reunited were dried on Na<sub>2</sub>SO<sub>4</sub>, filtered and concentrated under vacuum. The residue was purified on silica gel using hexane/EtOAc 9:1 as eluent (*R*<sub>f</sub> = 0.30): methyl 9-hydroxy-10-nitrooctadecanoate, 423 mg (yield=73%).

<sup>1</sup>H NMR (300MHz, CDCl<sub>3</sub>): δ 0.85 (t, *J*=6.8 Hz, 3H), 1.2-1.6 (m, 25H), 1.75 (m, 1H), 2.10 (m, 1H), 2.30 (t, *J*=7.5 Hz, 2H), 3.70 (s, 3H), 3.85 (bm, 0.5) 4.05 (bm, 0.5H), 4.45 (m, 1H).

<sup>13</sup>C NMR (75MHz, CDCl<sub>3</sub>): δ 174.26 (C), 92.92 (CH), 92.38 (CH), 72.30 (CH), 71.98 (CH), 51.40 (CH<sub>3</sub>), 33.96 (CH<sub>2</sub>), 33.45 (CH<sub>2</sub>), 33.11 (CH<sub>2</sub>), 31.70 (CH<sub>2</sub>), 30.37 (CH<sub>2</sub>), 29.13 (CH<sub>2</sub>), 29.03 (CH<sub>2</sub>), 28.96 (CH<sub>2</sub>), 28.88 (CH<sub>2</sub>), 28.04 (CH<sub>2</sub>), 25. 92 (CH<sub>2</sub>), 25.63 (CH<sub>2</sub>), 25.44 (CH<sub>2</sub>), 25.10 (CH<sub>2</sub>), 24.76 (CH<sub>2</sub>), 22.54 (CH<sub>2</sub>), 13.99 (CH<sub>3</sub>).

IR (CH<sub>2</sub>Cl<sub>2</sub>): 3474.2, 2925.2, 2854.9, 1736.9, 1555.9, 1438.2, 1365.7, 1200.6, 1107.9, 854.1, 724.1 cm<sup>-1</sup>.

HRMS-ESI, *m/z* for C<sub>19</sub>H<sub>37</sub>NO<sub>5</sub> [M+H]<sup>+</sup> calcd 360.2750, found 360.2775.

## Step 2: synthesis of (E)-methyl 10-nitrooctadec-9-enoate<sup>1</sup>

To a magnetically-stirred solution of methyl 9-hydroxy-10-nitrooctadecanoate (75 mg, 0.209 mmol) in dry  $\text{CH}_2\text{Cl}_2$  (0.3 ml) under Ar was added trifluoroacetic anhydride (0.219 mmol) and triethylamine (0.439 mmol) was added dropwise at 0°C. The reaction was allowed to reach room temperature and after 3-4 hours was quenched with aq  $\text{NH}_4\text{Cl}$ . The mixture was diluted with  $\text{CH}_2\text{Cl}_2$  and the two layers were separated. The aqueous layer was extracted with  $\text{CH}_2\text{Cl}_2$  and the organic layers reunited were washed with Brine, dried on  $\text{Na}_2\text{SO}_4$ , filtered, and concentrated under vacuum. The residue was purified on silica gel using hexane /EtOAc 95:5 as eluent ( $R_f = 0.28$ ) . (E)-methyl 10-nitrooctadec-9-enoate was thus obtained in 65% yield, 47 mg.

<sup>1</sup>H NMR (300MHz,  $\text{CDCl}_3$ ):  $\delta$  0.90 (t,  $J=6.4$  Hz, 3H), 1.25-1.40 (m, 16H), 1.55 (m, 4H), 1.65 (m, 2H), 2.25 (dt,  $J_1=7.7$  Hz,  $J_2=7.3$  Hz, 2H), 2.35 (t,  $J=7.4$  Hz, 2H), 2.60 (t,  $J=7.3$  Hz, 2H), 3.65 (s, 3H), 7.08 (t,  $J=7.9$  Hz, 1H).

<sup>13</sup>C NMR (75MHz,  $\text{CDCl}_3$ ):  $\delta$  174.15 (C), 151.95 (C), 136.17 (CH), 51.45 ( $\text{CH}_3$ ), 33.99 ( $\text{CH}_2$ ), 31.79 ( $\text{CH}_2$ ), 29.22 ( $\text{CH}_2$ ), 29.14 ( $\text{CH}_2$ ), 28.96 ( $\text{CH}_2$ ), 28.45 ( $\text{CH}_2$ ), 27.94 ( $\text{CH}_2$ ), 27.89 ( $\text{CH}_2$ ), 26.34 ( $\text{CH}_2$ ), 24.83 ( $\text{CH}_2$ ), 22.61 ( $\text{CH}_2$ ), 14.06 ( $\text{CH}_3$ ).

IR ( $\text{CH}_2\text{Cl}_2$ ) : 2928.0, 2855.7, 1740.4, 1522.8, 1458.6, 1436.9, 1336.5, 1198.0, 1171.2, 1112.9, 852.7, 724.2  $\text{cm}^{-1}$ .

HRMS-ESI,  $m/z$  for  $\text{C}_{19}\text{H}_{35}\text{NO}_4$  [M+H]<sup>+</sup> calcd 342.2644, found 342.2670

### Step 3: synthesis of (*E*)-10-nitrooleic acids<sup>1</sup>

To a magnetically-stirred solution of (*E*)-methyl 10-nitrooctadec-9-enoate (17 mg, 0.050 mmol) in tert-butyl methyl ether (0.4ml) were added water (2.5 mmol, 50 equiv.) and lipasi immobilized from *Candida Antarctica* B. The solution was stirred at room temperature. The reaction was filtered and concentrated under vacuum. The residue was purified on silica gel using hexane/EtOAc 7:3 as eluent ( $R_f$  = 0.25) : (*E*)-10-nitrooleic acids, 16 mg (yield 98%).

<sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>):  $\delta$  0.90 (t,  $J$ =6.9 Hz, 3H), 1.25-1.40 (m, 16H), 1.55 (m, 4H), 1.65 (m, 2H), 2.25 (dt,  $J_1$ =7.7 Hz,  $J_2$ =7.4 Hz, 2H), 2.40 (t,  $J$ =7.4 Hz, 2H), 2.60 (t,  $J$ =7.3 Hz, 2H), 7.08 (t,  $J$ =7.9 Hz, 1H).

<sup>13</sup>C NMR (75MHz, CDCl<sub>3</sub>):  $\delta$  179.27 (C), 151.98 (C), 136.15 (CH), 33.81 (CH<sub>2</sub>), 31.79 (CH<sub>2</sub>), 29.21 (CH<sub>2</sub>), 29.14 (CH<sub>2</sub>), 28.95 (CH<sub>2</sub>), 28.85 (CH<sub>2</sub>), 28.44 (CH<sub>2</sub>), 27.90 (CH<sub>2</sub>), 26.34 (CH<sub>2</sub>), 24.55 (CH<sub>2</sub>), 22.61 (CH<sub>2</sub>), 14.05 (CH<sub>3</sub>).

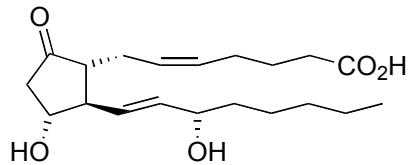
IR (CH<sub>2</sub>Cl<sub>2</sub>) : 2927.8, 2855.6, 1712.0, 1519.0, 1462.8, 1336.6, 1112.9, 937.5, 724.2 cm<sup>-1</sup>

HRMS-ESI, *m/z* for C<sub>18</sub>H<sub>33</sub>NO<sub>4</sub> [M+H]<sup>+</sup> calcd 328.2488, found 328.2512.

## Enzymatic Hydrolysis

Following the general procedure described in the manuscript, methyl esters afforded the corresponding acids, the  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra which were in agreement with those reported in literature have been reported.

### (-)Prostaglandin-E<sub>2</sub> (**10**)



Prostaglandin-E<sub>2</sub> methyl ester,<sup>4</sup> 8.2 mg (22.4  $\mu\text{mol}$ ) afforded (-)-prostaglandin-E<sub>2</sub> (**10**), 7.5 mg, yield 95% (3% MeOH in EtOAc,  $R_f$  = 0.2).

$^1\text{H}$  NMR (300MHz, CD<sub>3</sub>CN):  $\delta$  5.59 (dd,  $J_1$ =3.7,  $J_2$ =2.6 Hz, 2H), 5.48-5.04 (m, 2H), 4.04 (q,  $J$  = 9.0 Hz, 2H), 2.63 (dd,  $J_1$ =18.3,  $J_2$ =7.4 Hz, 1H), 2.41 - 2.19 (m, 5H), 2.18 - 1.87 (m, 5H), 1.70 - 1.56 (m, 2H), 1.54 - 1.19 (m, 7H), 1.04 - 0.77 (m, 3H). .

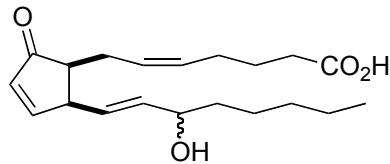
$^{13}\text{C}$  NMR (75MHz, CD<sub>3</sub>CN):  $\delta$  215.7 (C), 175.0 (C), 137.5 (CH), 131.4 (CH), 131.0 (CH), 128.0 (CH), 72.9 (CH), 72.6 (CH), 55.0 (CH), 53.9 (CH), 47.3 (CH<sub>2</sub>), 38.3 (CH<sub>2</sub>), 33.6 (CH<sub>2</sub>), 32.5 (CH<sub>2</sub>), 27.2 (CH<sub>2</sub>), 26.0 (CH<sub>2</sub>), 25.6 (CH<sub>2</sub>), 25.5 (CH<sub>2</sub>), 23.4 (CH<sub>2</sub>), 14.3 (CH<sub>3</sub>).

IR (CH<sub>2</sub>Cl<sub>2</sub>) : 3379, 2931, 2856, 1732, 1709, 1398, 1204, 1158, 1120, 1084, 1033, 973 cm<sup>-1</sup>

HRMS-ESI,  $m/z$  for C<sub>20</sub>H<sub>32</sub>O<sub>5</sub> [M+H]<sup>+</sup> calcd 353.2328, found 353.2353.

$[\alpha]^{20}_{\text{D}} = -71.4$  (*c* 0.7 EtOH).

**rac-Isoprostan-A<sub>2</sub> (11)**



**Isoprostan-A<sub>2</sub> methyl ester**

To a stirred solution of rac-isoprostan-A<sub>2</sub> 35 mg (0.105 mmol) in ether (5 ml) cooled at -20 °C, was added a saturated ethereal solution of CH<sub>2</sub>N<sub>2</sub> until persistent light yellow colour. Evaporation in vacuo at rt followed by silica gel purification (5g, hexane:EtOAc 7:3,  $R_f$  = 0.27) afforded 35 mg of the corresponding methyl ester in 97% yield.

<sup>1</sup>H NMR (300MHz, CD<sub>2</sub>Cl<sub>2</sub>):  $\delta$  0.9 (t,  $J$  = 6.62 Hz, 3H); 1.3 (bs, 6H); 1.48-1.62 (m, 2H); 1.70 (m, 3H); 2.1 (q,  $J$  = 7.4 Hz, 3H); 2.25-2.3 (t,  $J$  = 7.44 Hz, 2H); 2.50 (m, 2H); 3.65 (s, 3H); 3.72 (m, 1H); 4.14 (q,  $J$  = 6.48 Hz, 1H); 5.3-5.7 (m, 4H); 6.21-6.27 (dd,  $J_1$  = 1.83 Hz,  $J_2$  = 5.75 Hz, 1H); 7.50-7.56 (dd,  $J_1$  = 2.84 Hz,  $J_2$  = 5.69 Hz, 1H).

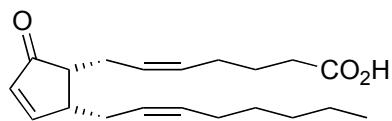
<sup>13</sup>C NMR (75MHz, CD<sub>2</sub>Cl<sub>2</sub>):  $\delta$  210.71 (C), 174.74 (C), 165.65 (CH), 138.15 (CH), 133.45 (CH), 130.54 (CH), 129.21 (CH), 128.51 (CH), 73.11 (CH), 52.11 (CH<sub>3</sub>), 50.44 (CH), 48.09 (CH), 38.07 (CH<sub>2</sub>), 34.10 (CH<sub>2</sub>), 32.51 (CH<sub>2</sub>), 27.53 (CH<sub>2</sub>) 25.88 (CH<sub>2</sub>), 25.39 (CH<sub>2</sub>), 23.38 (CH<sub>2</sub>), 14.56 (CH<sub>3</sub>).

IR (CH<sub>2</sub>Cl<sub>2</sub>) : 3445, 2929, 1738, 1713, 1699, 1694, 1559, 1456 cm<sup>-1</sup>

HRMS-ESI, *m/z* for C<sub>21</sub>H<sub>32</sub>O<sub>4</sub> [M+H]<sup>+</sup> calcd 349.2379 found 349.2403.

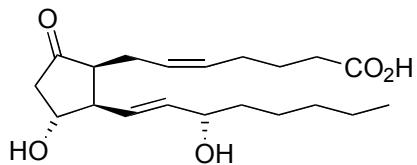
**Hydrolysis:** 30.8 mg (88.4  $\mu$ mol) of methyl ester afforded isoprostan-A<sub>2</sub> (11), 27.2 mg, yield 92% (eluent: hexane/EtOAc 1:1,  $R_f$  = 0.27). The NMR data of compound 11 were in perfect agreement with those reported in the literature<sup>3</sup>

(-)Preclavulone-A (**12**)



Preclavulone-A methyl ester,<sup>5</sup> 10.1 mg (30.3  $\mu$ mol), afforded preclavulone-A (**12**), 9 mg, yield 93% (eluent: hexane/EtOAc 4:1,  $R_f$  = 0.23). The NMR data of compound **12** were in perfect agreement with those reported in the literature.<sup>5</sup>

(+)-Isoprostane-E<sub>2t</sub> (**13**)



Isoprostane-E<sub>2t</sub> methyl ester,<sup>6</sup> 5.6 mg (15.3  $\mu$ mol), afforded isoprostane-E<sub>2t</sub> (**13**), 4.9 mg, yield 92% (3% MeOH in EtOAc,  $R_f$  = 0.2).

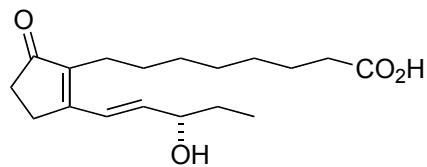
<sup>1</sup>H NMR (300MHz, CD<sub>3</sub>OD):  $\delta$  5.7-5.6 (dd,  $J_1$ =15.3 Hz,  $J_2$ =6.6 Hz, 1H), 5.5-5.3 (m, 2H), 5.3 (dd,  $J_1$ =15.3,  $J_2$ =9.9 Hz, 1H), 4.3-4.2 (m, 1H), 4.0 (m, 1H), 3.0 (m, 1H), 2.7-2.6 (m, 1H), 2.6-2.5 (dd,  $J_1$ =19.2,  $J_2$ =5.7 Hz, 1H), 2.5-2.3 (m, 1H), 2.3-2.2 (t,  $J$ =7.5Hz, 2H), 2.3-2.2 (m, 1H), 2.1-1.9 (m, 3H), 1.7-1.6 (quint.,  $J$ =7.5Hz, 2H), 1.6-1.2 (m, 8H), 0.9 (t,  $J$ =6.6Hz, 3H).

<sup>13</sup>C NMR (75MHz, CD<sub>3</sub>OD):  $\delta$  219.70 (C), 177.49 (C), 138.66 (CH), 131.12 (CH), 129.11 (CH), 128.23 (CH), 73.32 (CH), 72.85 (CH), 52.45 (CH), 51.74 (CH), 45.49 (CH<sub>2</sub>), 38.40 (CH<sub>2</sub>), 34.34 (CH<sub>2</sub>), 32.91 (CH<sub>2</sub>), 27.76 (CH<sub>2</sub>), 26.17 (CH<sub>2</sub>), 25.93 (CH<sub>2</sub>), 24.22 (CH<sub>2</sub>), 23.64 (CH<sub>2</sub>), 14.29 (CH<sub>3</sub>).

$[\alpha]^{25}_{\text{D}} = +87$  (c 0.057, MeOH).

HRMS-ESI,  $m/z$  for  $\text{C}_{20}\text{H}_{32}\text{O}_5$   $[\text{M}+\text{H}]^+$  calcd 353.2328, found 353.2349.

Phytoprostane-B<sub>1</sub> Type I (**14**)



Phytoprostane-B<sub>1</sub> Type I methyl ester,<sup>7</sup> 12.1 mg (37.5  $\mu\text{mol}$ ), afforded phytoprostane-B<sub>1</sub> Type I (**14**), 10.4 mg, yield 90% (eluent: hexane/EtOAc 1:1,  $R_f = 0.25$ ).

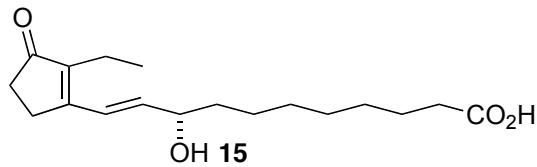
<sup>1</sup>H NMR (300MHz,  $\text{CDCl}_3$ ):  $\delta$  1.00 (t,  $J=7.4$  Hz, 3H), 1.25-1.46 (m, 8H), 1.57-1.73 (m, 4H), 2.25-2.47 (m, 6H), 2.66 (bt, 2H), 4.28-4.35 (q,  $J= 5.8$  Hz, 1H), 6.26 (dd,  $J_1=5.8$  Hz,  $J_2=15.8$  Hz, 1H), 6.82 (d,  $J=15.8$  Hz, 1H).

<sup>13</sup>C NMR (75MHz,  $\text{CDCl}_3$ ):  $\delta$  209.77 (C), 178.12 (C), 163.21 (C), 141.45 (C), 139.64 (CH), 124.11 (CH), 73.64 (CH), 33.80 (CH<sub>2</sub>), 30.06 (CH<sub>2</sub>), 28.96 (CH<sub>2</sub>), 28.80 (CH<sub>2</sub>), 28.53 (CH<sub>2</sub>), 28.50 (CH<sub>2</sub>), 28.39 (CH<sub>2</sub>), 25.61 (CH<sub>2</sub>), 24.52 (CH<sub>2</sub>), 22.77 (CH<sub>2</sub>), 9.63 (CH<sub>3</sub>).

IR ( $\text{CH}_2\text{Cl}_2$ ): 3400, 1695, 1645, 1600, 970  $\text{cm}^{-1}$ .

HRMS-ESI,  $m/z$  for  $\text{C}_{18}\text{H}_{28}\text{O}_4$   $[\text{M}+\text{H}]^+$  calcd 309.2066, found 309.2093.

(+)-Phytoprostane-B<sub>1</sub> Type II (**15**)



Phytoprostane-B<sub>1</sub> Type II methyl ester,<sup>7</sup> 10.3 mg (32  $\mu$ mol), afforded phytoprostane-B<sub>1</sub> Type II (**15**), 8.6 mg, yield 87% (eluent: hexane/EtOAc 1:1,  $R_f$  = 0.25).

<sup>1</sup>H NMR (300MHz, CDCl<sub>3</sub>):  $\delta$  1.01 (t,  $J$ =7.6 Hz, 3H), 1.28-1.55 (m, 9H), 1.60-1.74 (m, 4H), 2.27-2.40 (m, 4H), 2.42-2.50 (m, 2H), 2.65-2.71 (m, 2H), 4.32 (q,  $J$ =6.1 Hz, 1H), 6.26 (dd,  $J_1$ =5.98 Hz,  $J_2$ =15.8 Hz, 1H), 6.80 (d,  $J$ =15.7 Hz, 1H).

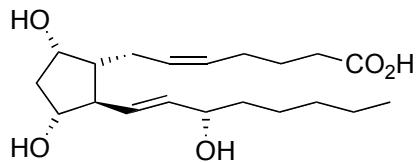
<sup>13</sup>C NMR (75MHz, CDCl<sub>3</sub>):  $\delta$  209.41 (C), 178.36 (C), 162.49 (C), 142.61 (C), 139.80 (CH), 123.62 (CH), 72.20 (CH), 36.97 (CH<sub>2</sub>), 33.64 (CH<sub>2</sub>), 33.58 (CH<sub>2</sub>), 29.01 (CH<sub>2</sub>), 28.86 (CH<sub>2</sub>), 28.68 (CH<sub>2</sub>), 25.39 (CH<sub>2</sub>), 25.02 (CH<sub>2</sub>), 24.39 (CH<sub>2</sub>), 16.10 (CH<sub>2</sub>), 13.29 (CH<sub>3</sub>).

IR (CH<sub>2</sub>Cl<sub>2</sub>): 3400, 1691, 1644, 1601, 969 cm<sup>-1</sup>.

HRMS-ESI, *m/z* for C<sub>18</sub>H<sub>28</sub>O<sub>4</sub> [M+H]<sup>+</sup> calcd 309.2066, found 309.2092.

$[\alpha]^{25}_D$ =+16.7 (c 0.054, EtOAc).

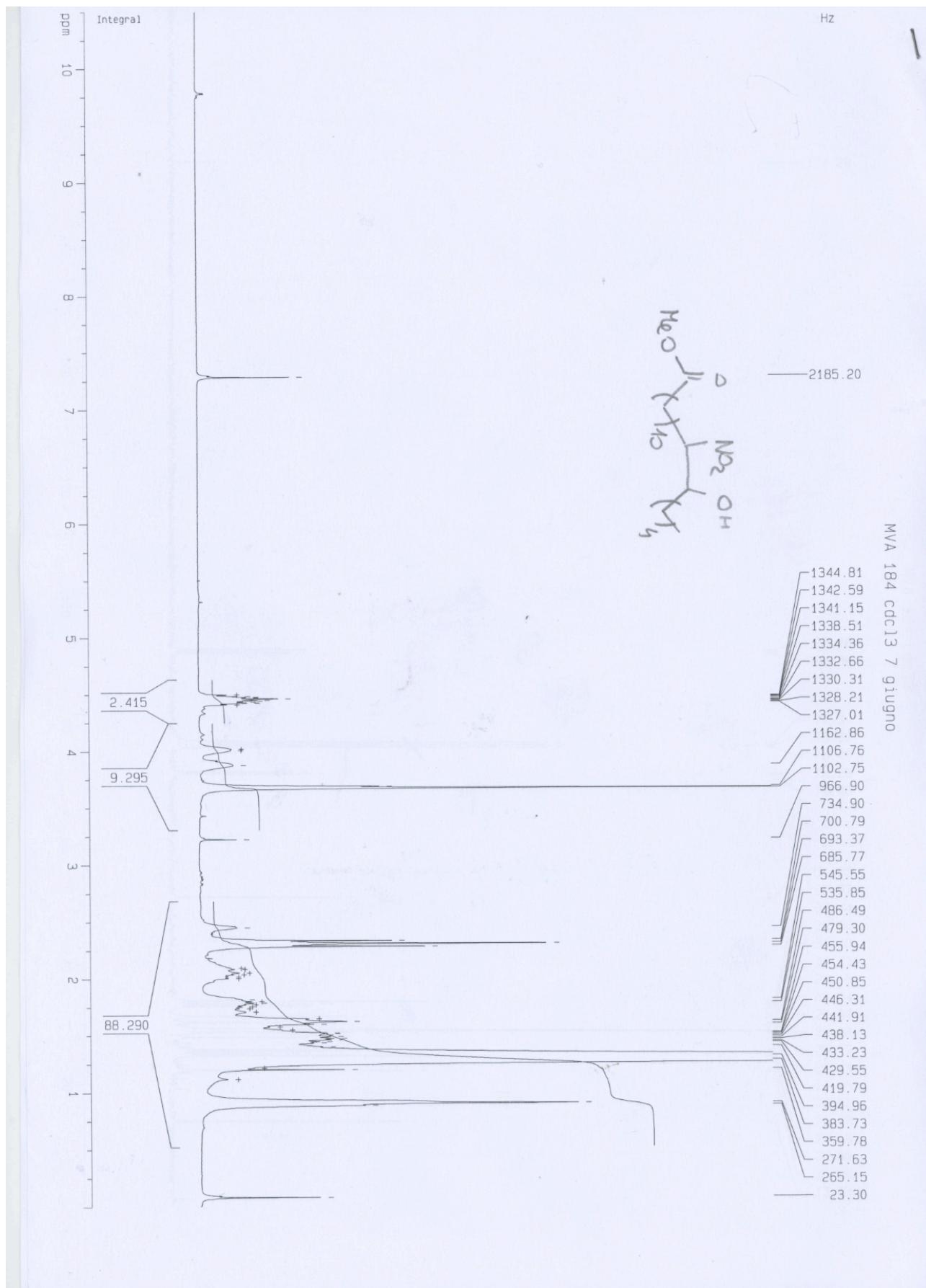
(+)-Prostaglandin-F<sub>2 $\alpha$</sub>  (**16**)

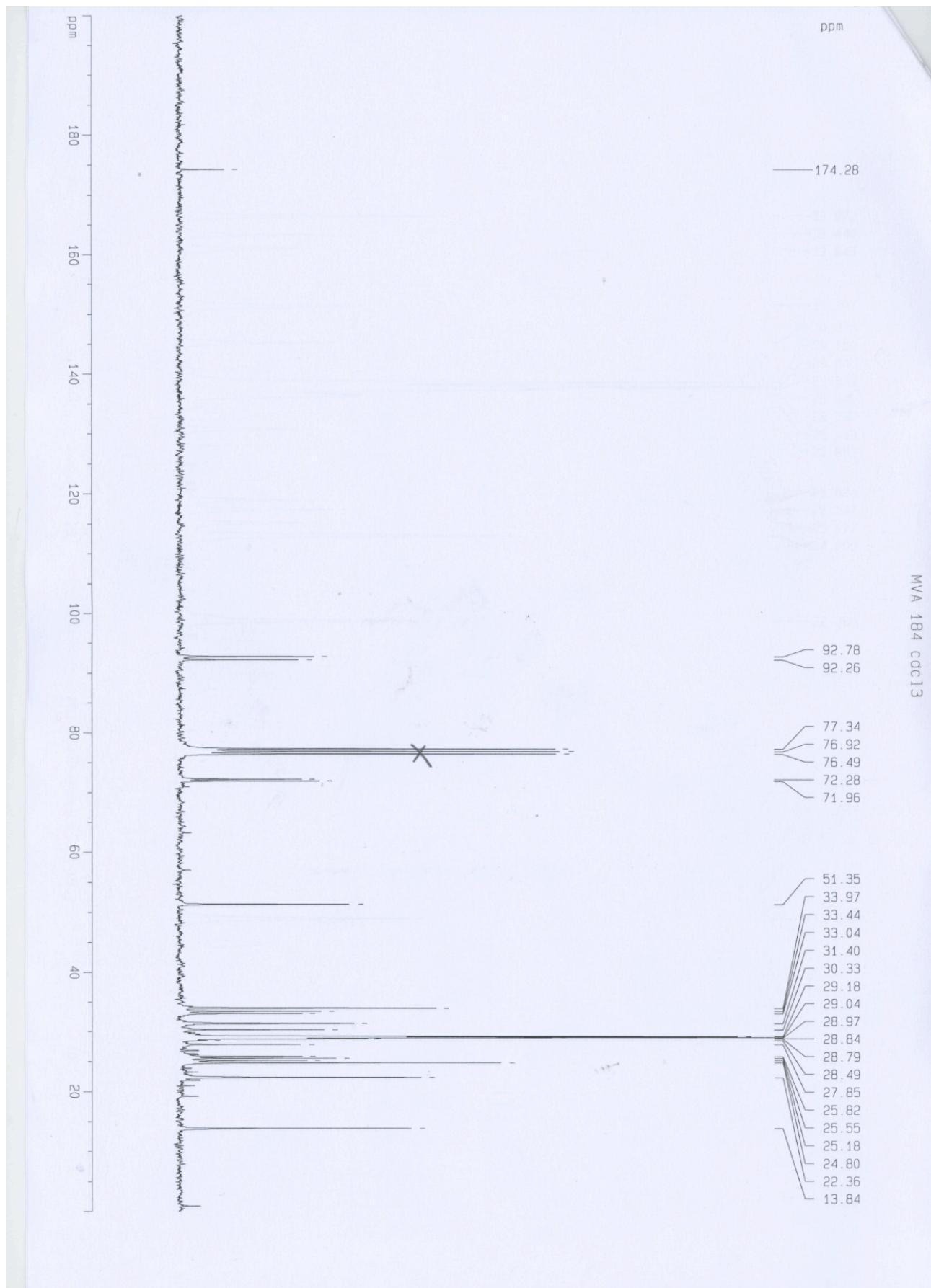


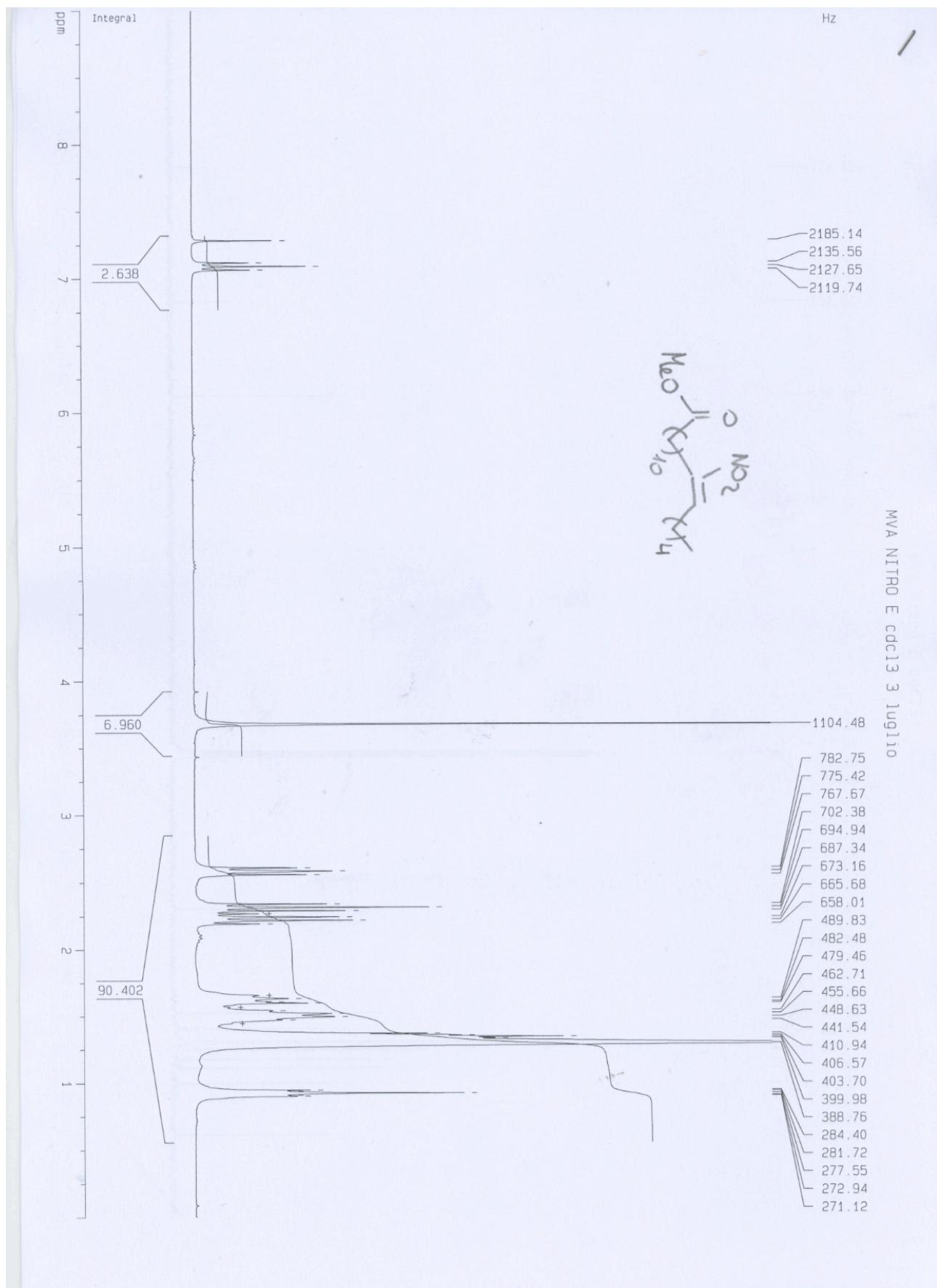
Prostaglandin-F<sub>2 $\alpha$</sub>  methyl ester,<sup>8</sup> 2.5 mg (6.8  $\mu$ mol), afforded prostaglandin-F<sub>2 $\alpha$</sub>  (**16**), 2.2 mg, yield 90% (3% MeOH in EtOAc,  $R_f$  = 0.2). The NMR data of compound **16** were in perfect agreement with those reported in the literature.<sup>9</sup>

## References

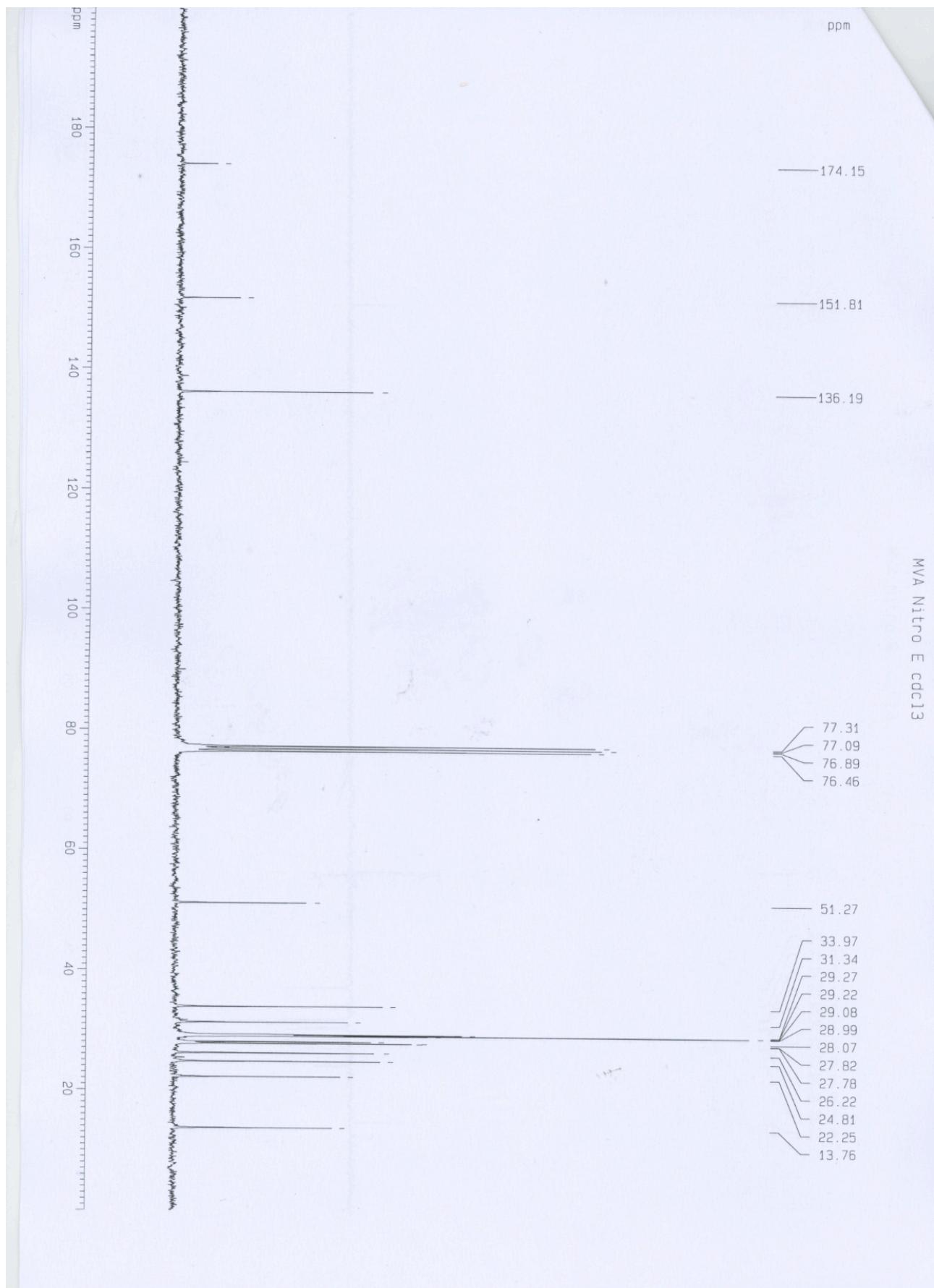
- (1) Gorczynski, M. J.; Huang, J.; King, B. S. *Org. Lett.* **2006**, *8*, 2305.
- (2) Zhang, W.; Sun, M.; Salomon, R. G. *J. Org. Chem.* **2006**, *71*, 5607.
- (3) Zanoni, G.; Porta, A.; Vidari, G. *J. Org. Chem.* **2002**, *67*, 4346.
- (4) Sih, C. J.; Heather, J. B.; Sod, R.; Price, P.; Peruzzotti, G.; Lee, H. L. F.; Lee, S. S. *J. Am. Chem. Soc.* **1975**, *97*, 865.
- (5) Porta, A.; Re, S.; Zanoni, G.; Vidari, G. *Tetrahedron* **2007**, *67*, 3989.
- (6) Rodríguez, A. R.; Spur, B., W. *Tetrahedron Lett.* **2002**, *43*, 9249.
- (7) El Fangour, S.; Guy, A.; Vidal, J-P.; Rossi, J-C.; Durand, T. *J. Org. Chem.* **2005**, *70*, 989.
- (8) Suzuki, M.; Yanagisawa, A.; Noyori, R. *J. Am. Chem. Soc.* **1988**, *110*, 4718.
- (9) Zanoni, G.; D'Alfonso, A.; Porta, A.; Feliciani, L.; Nolan, S. P.; Vidari, G. *Tetrahedron* **2010**, *66*, 7472.

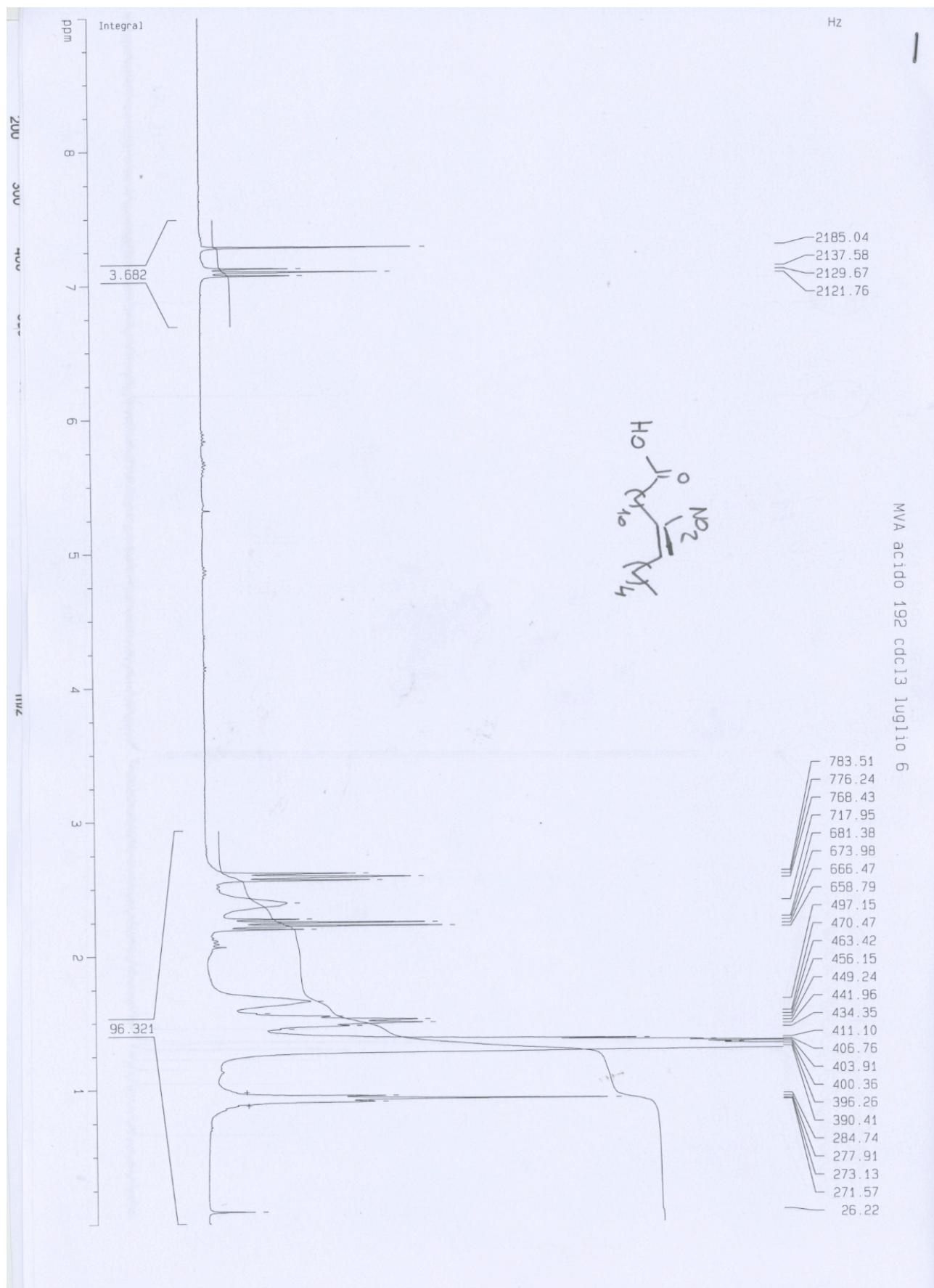


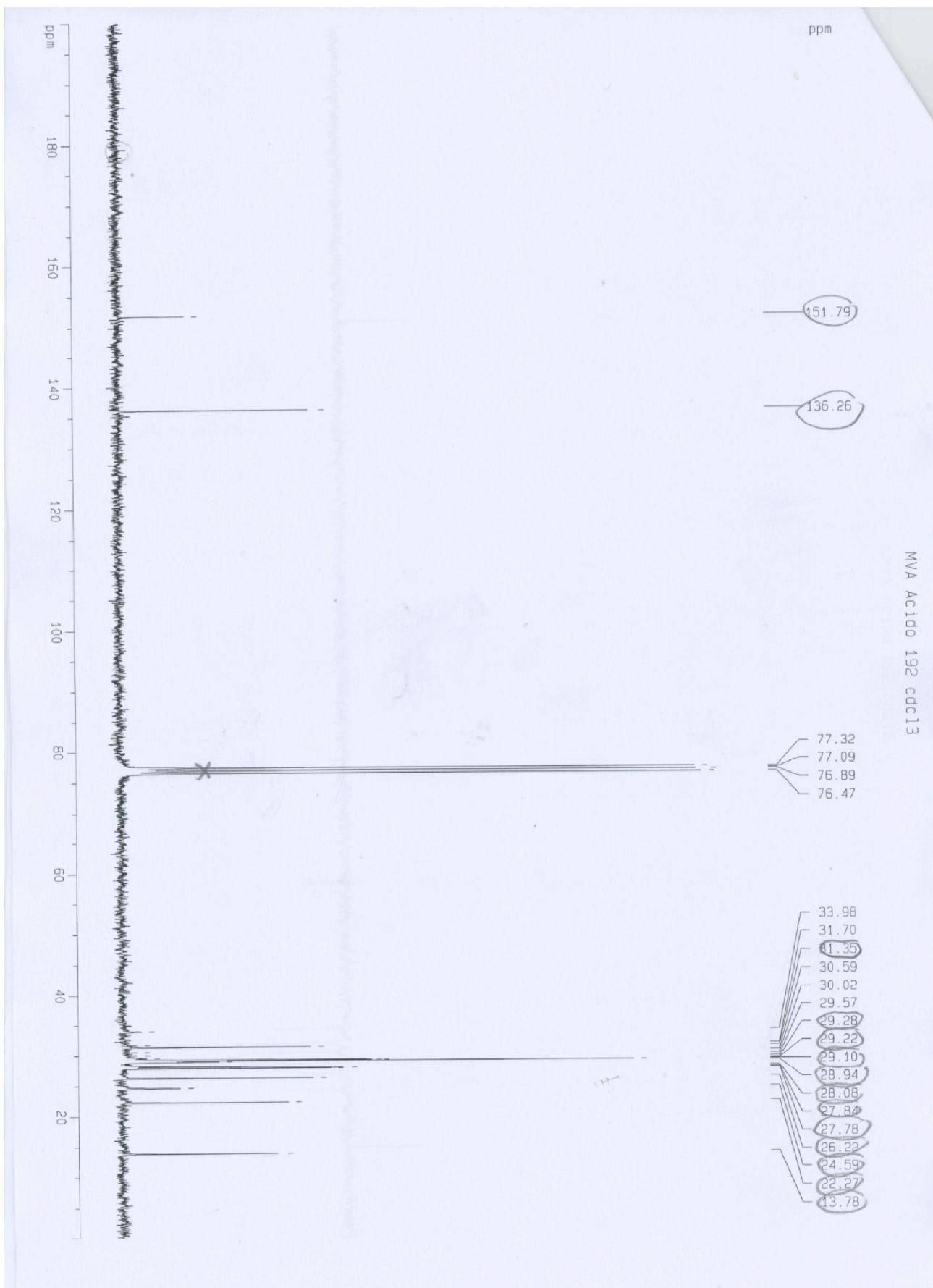


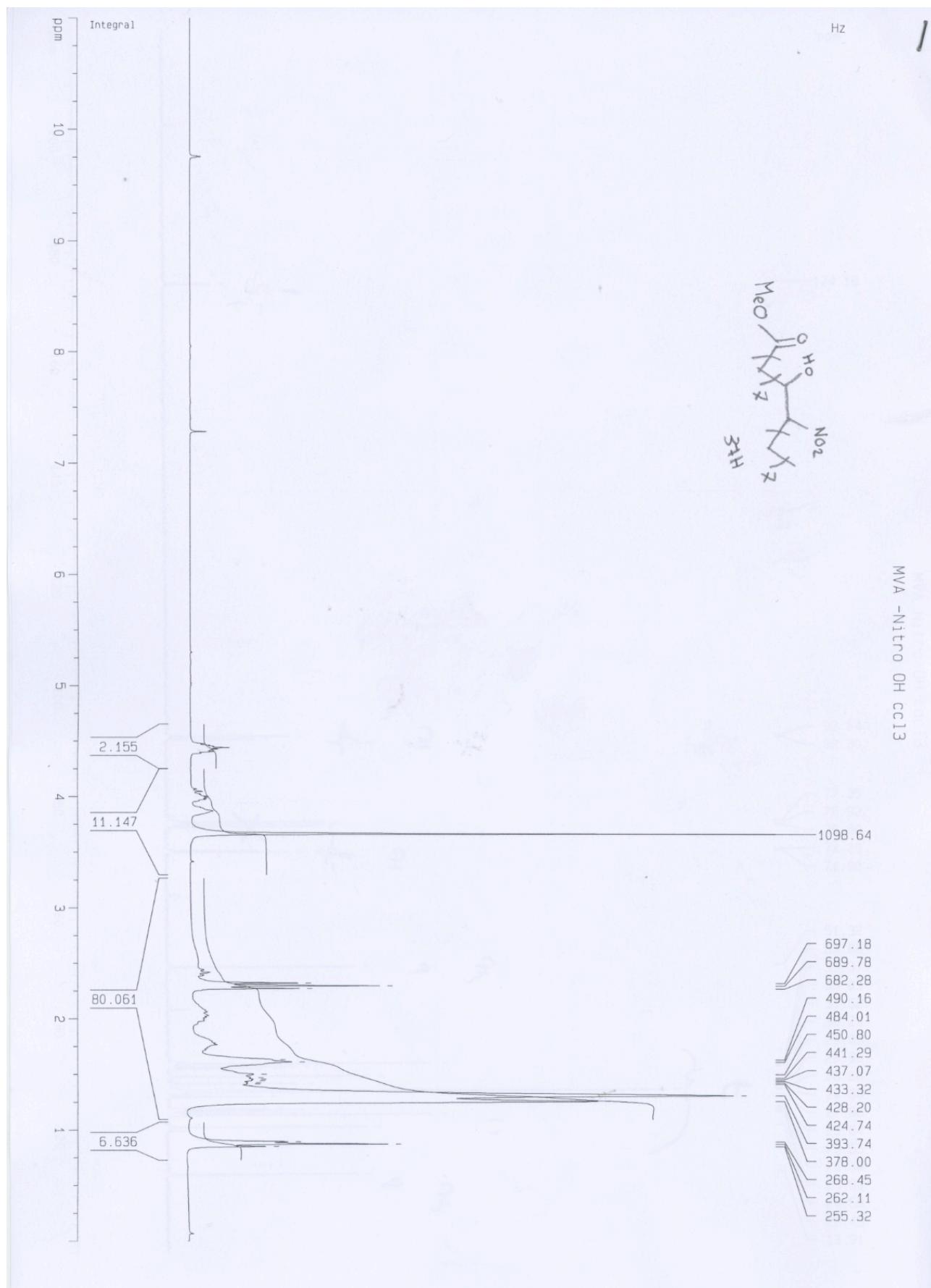


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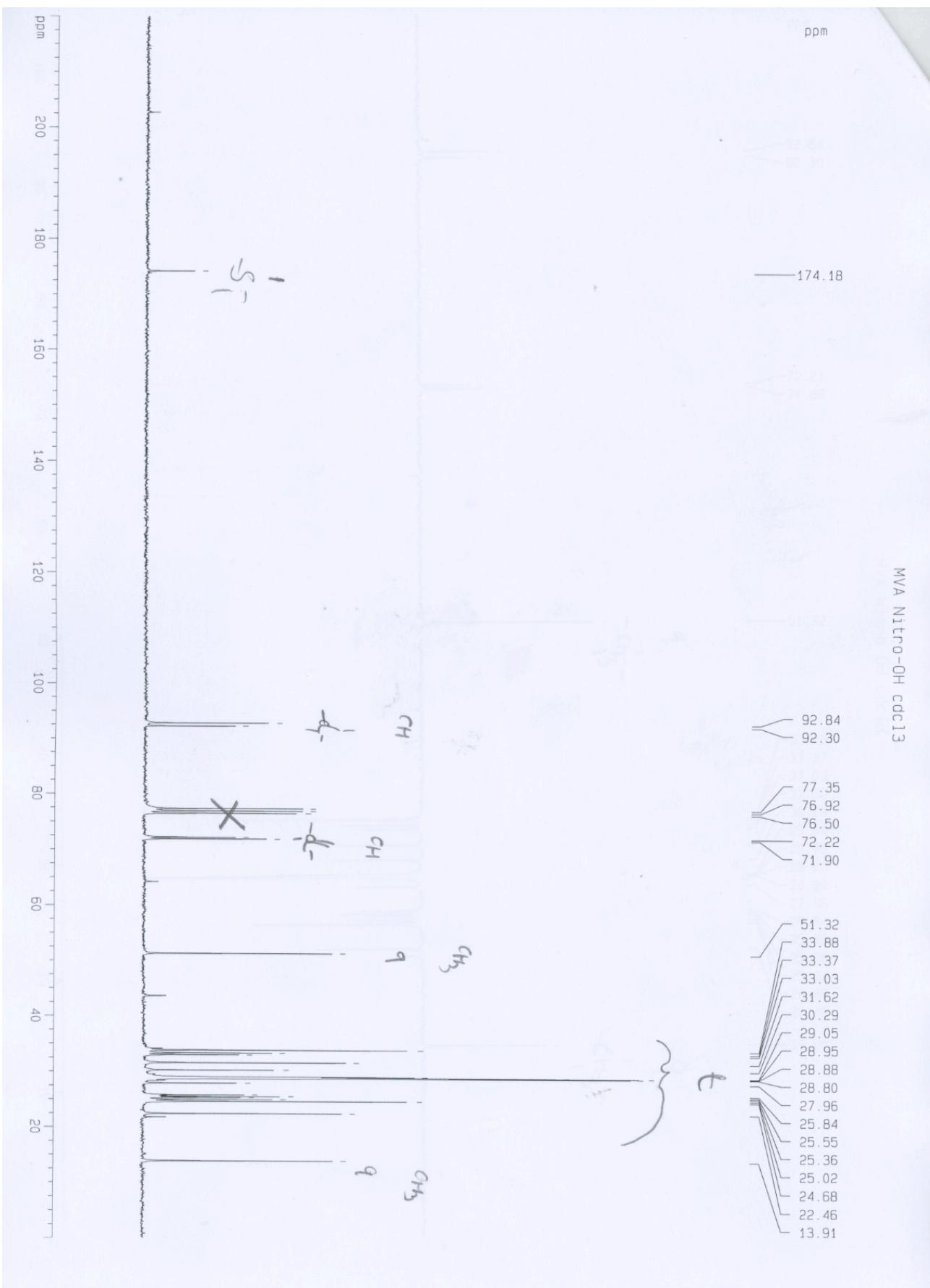


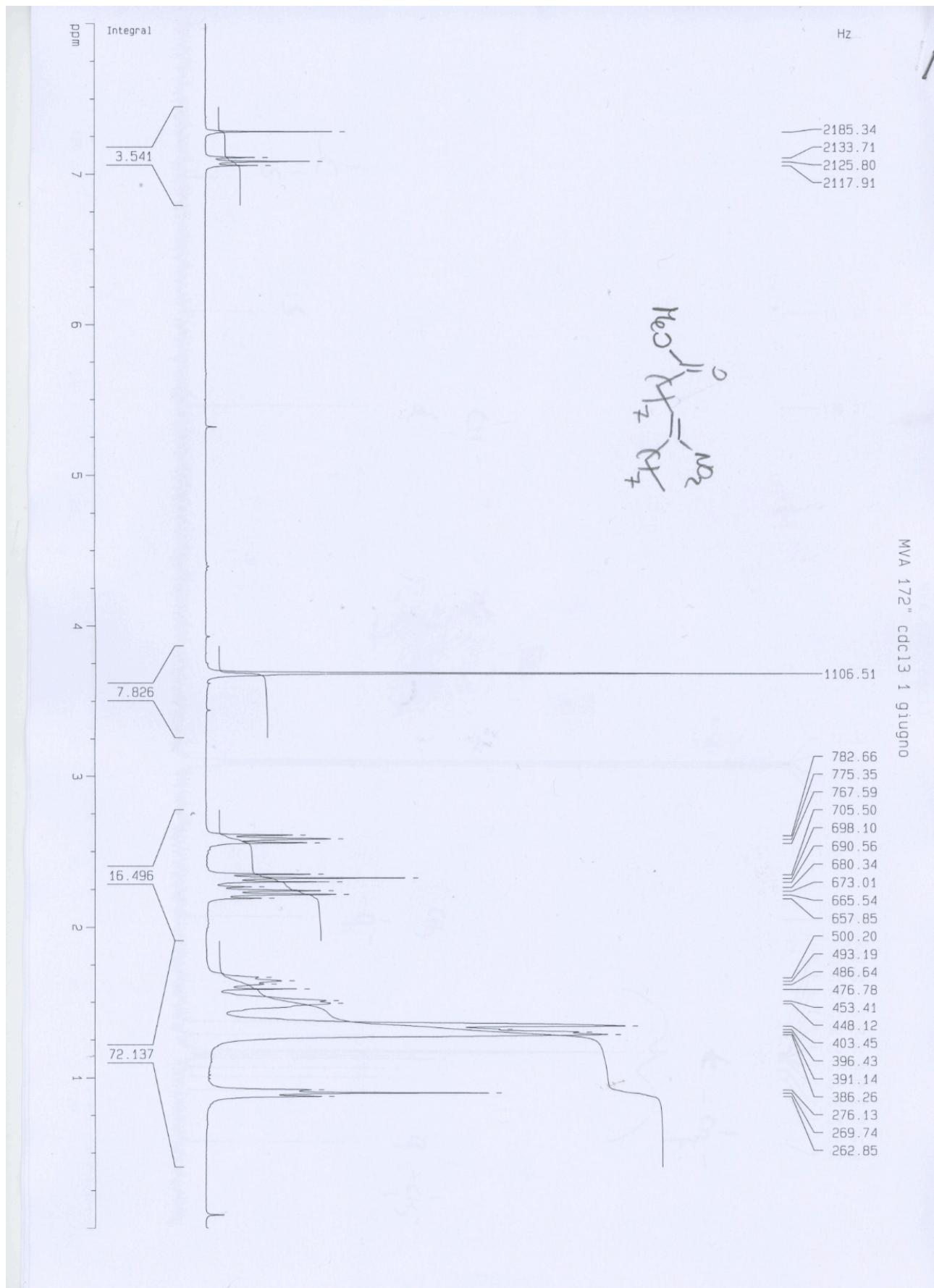


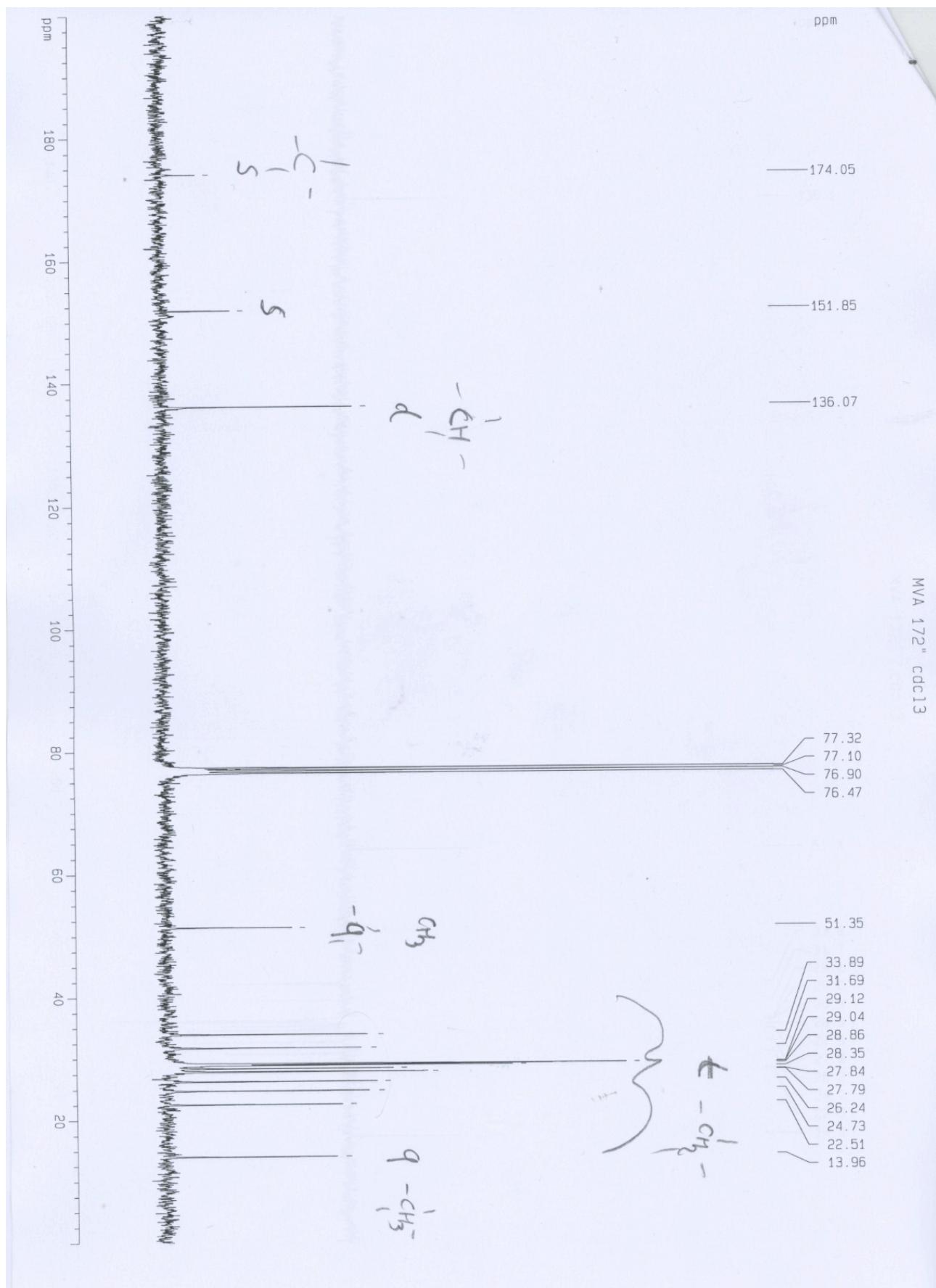


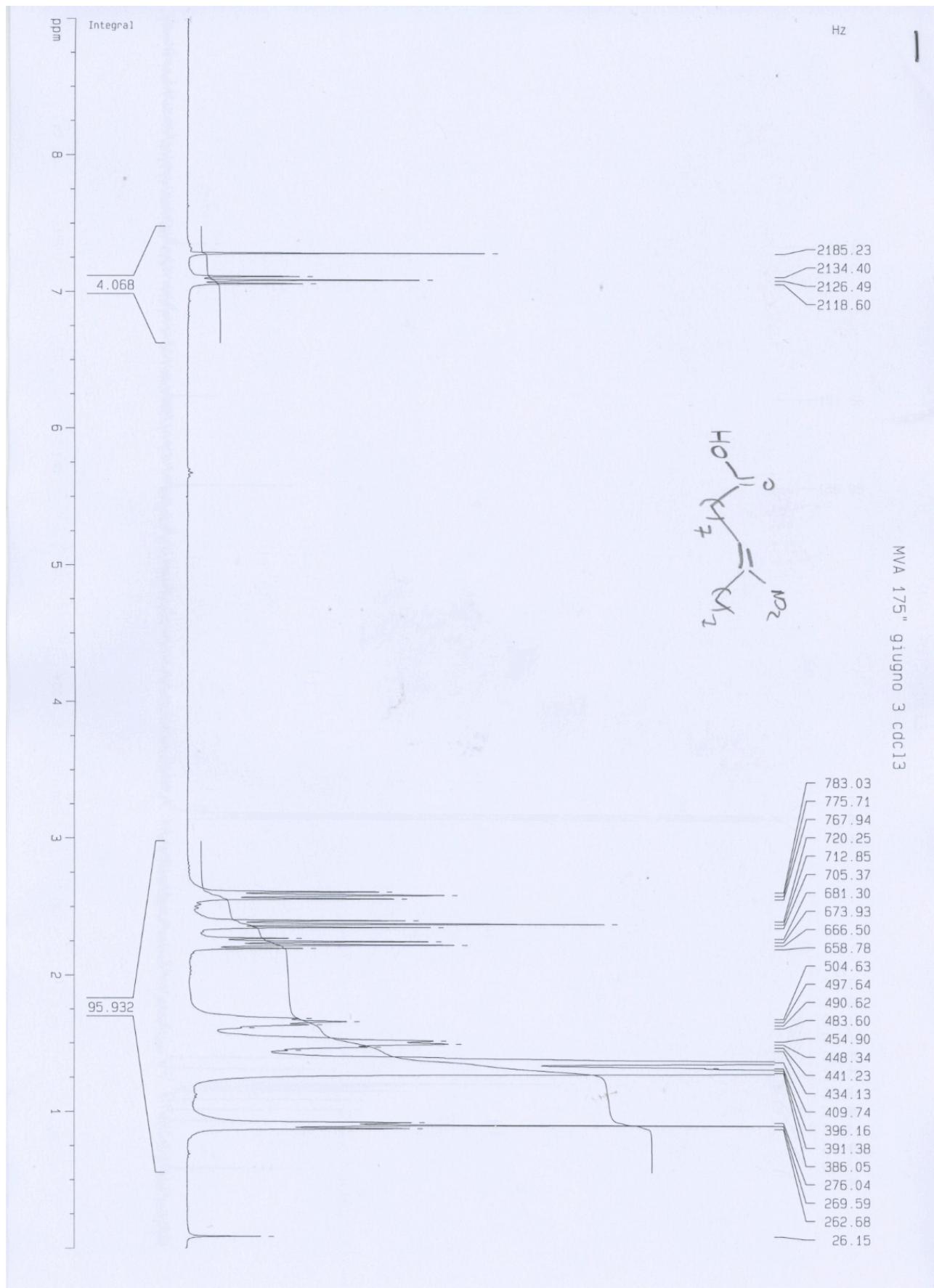


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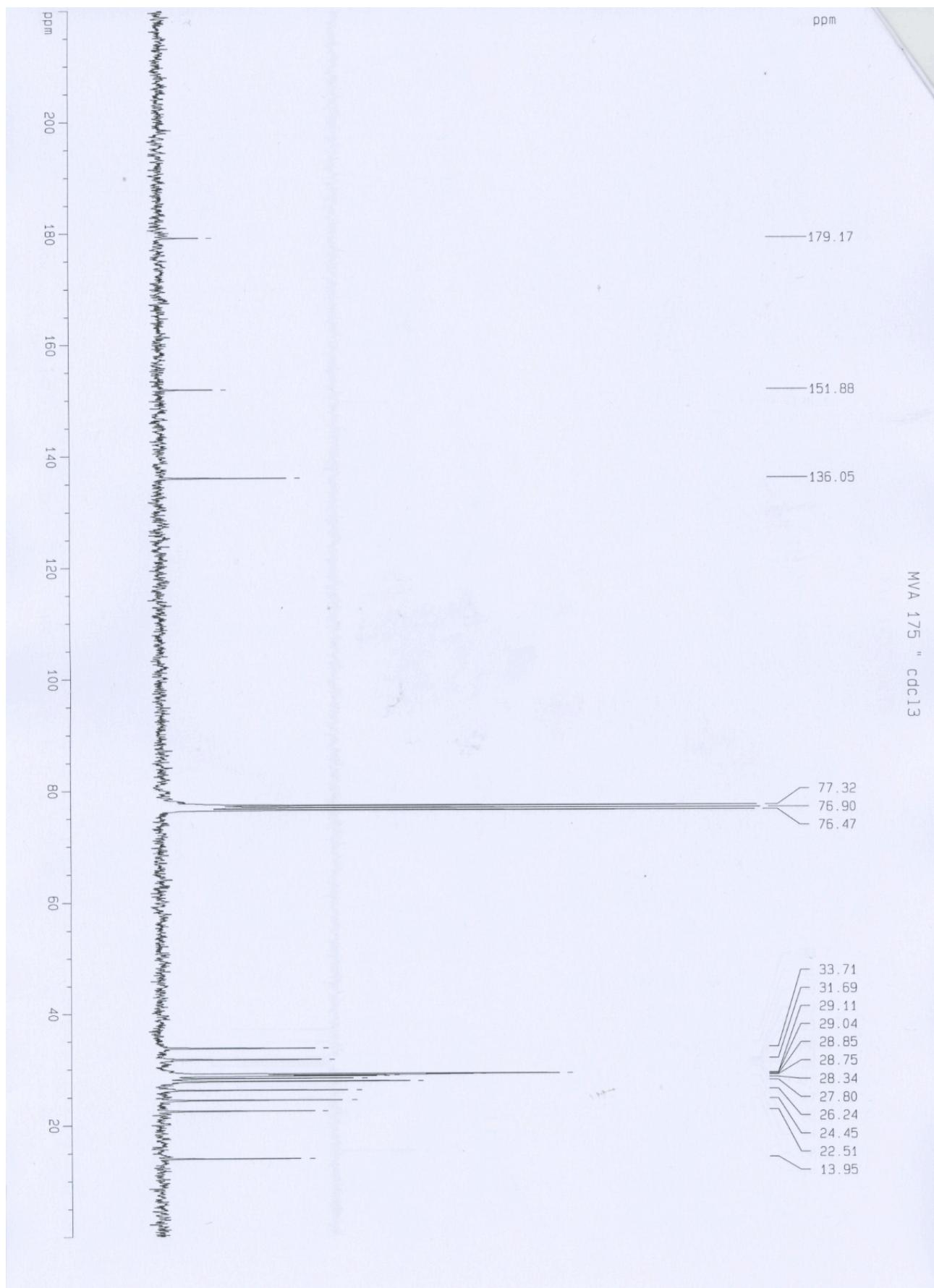




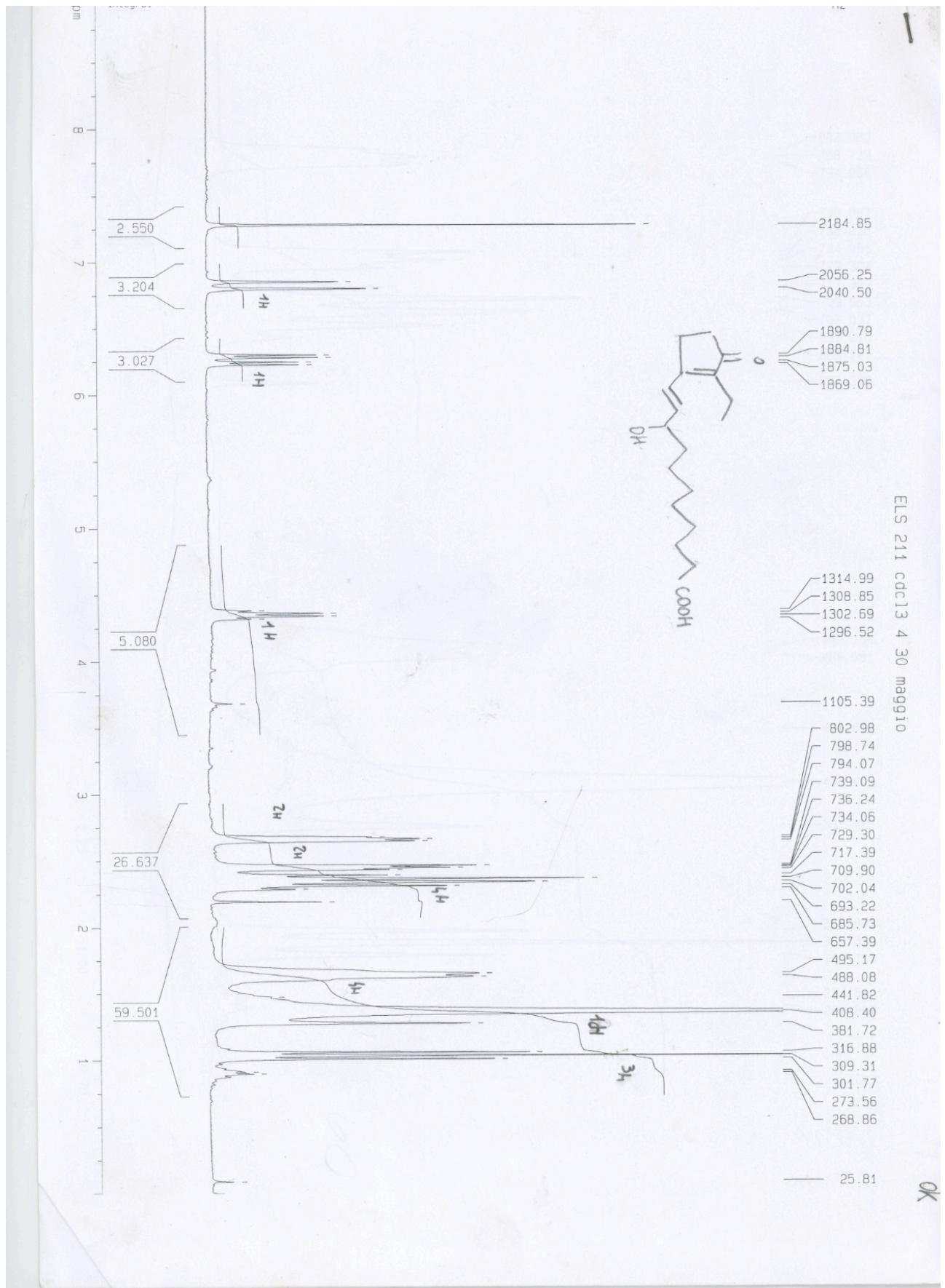


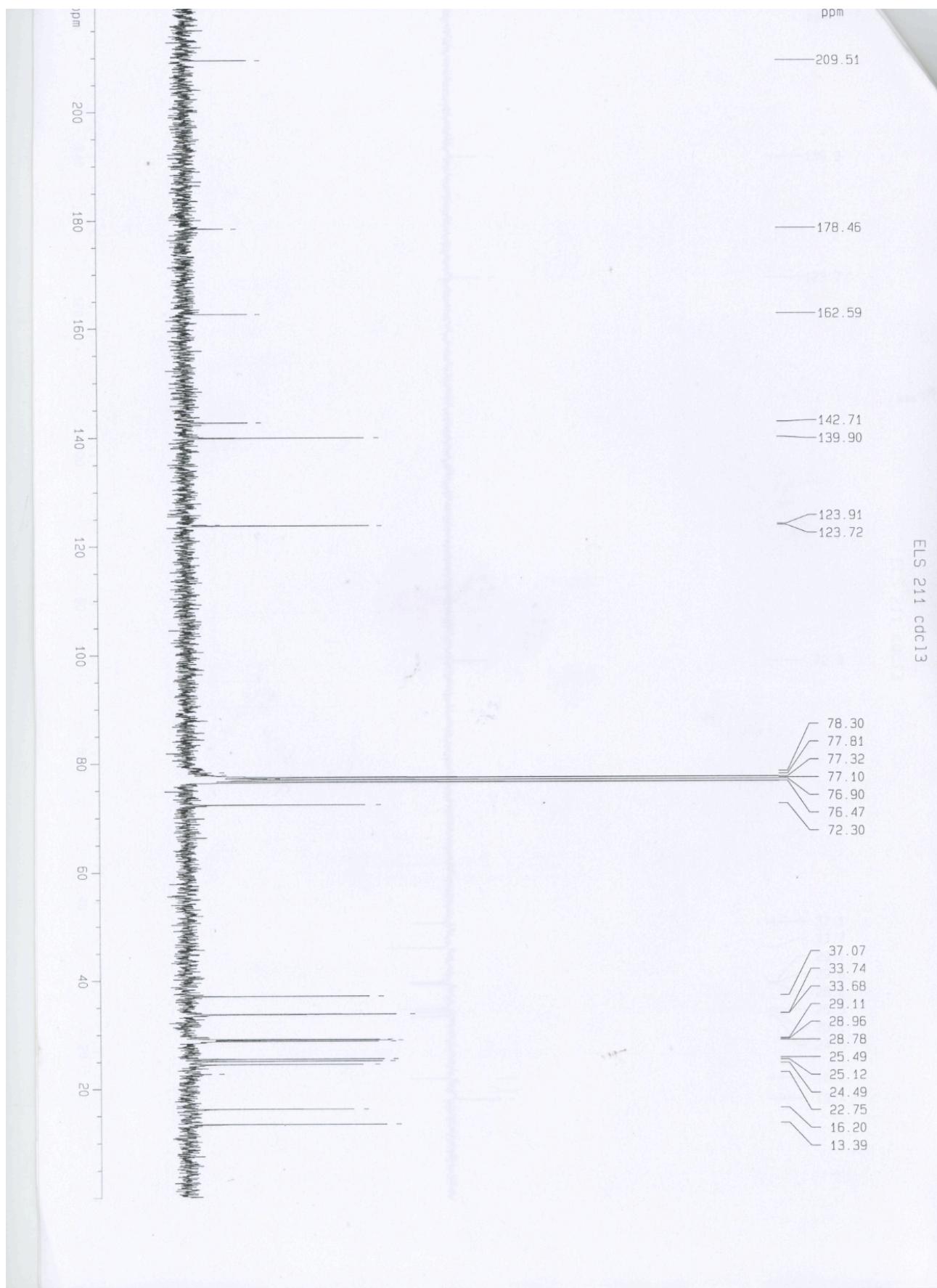


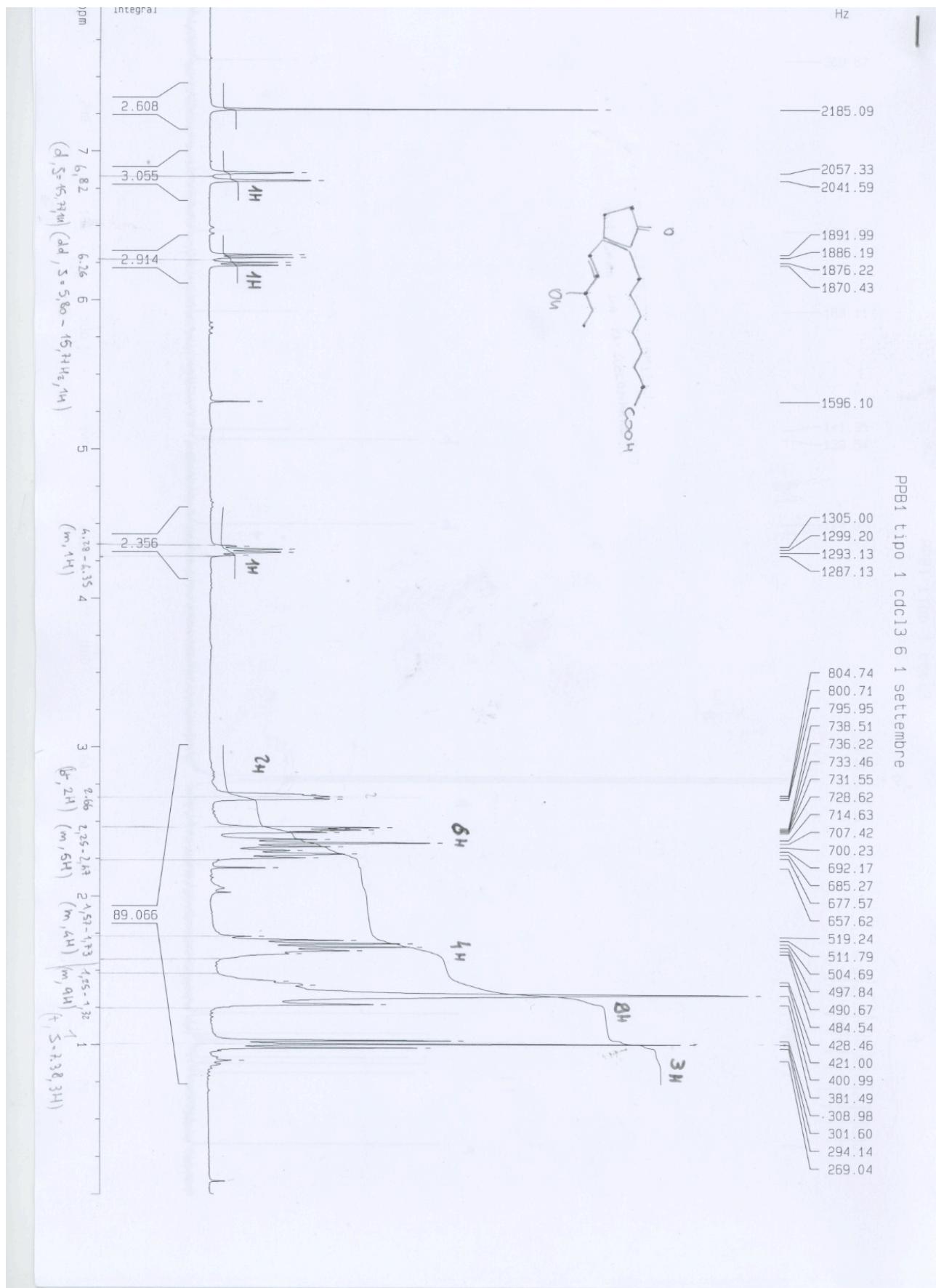
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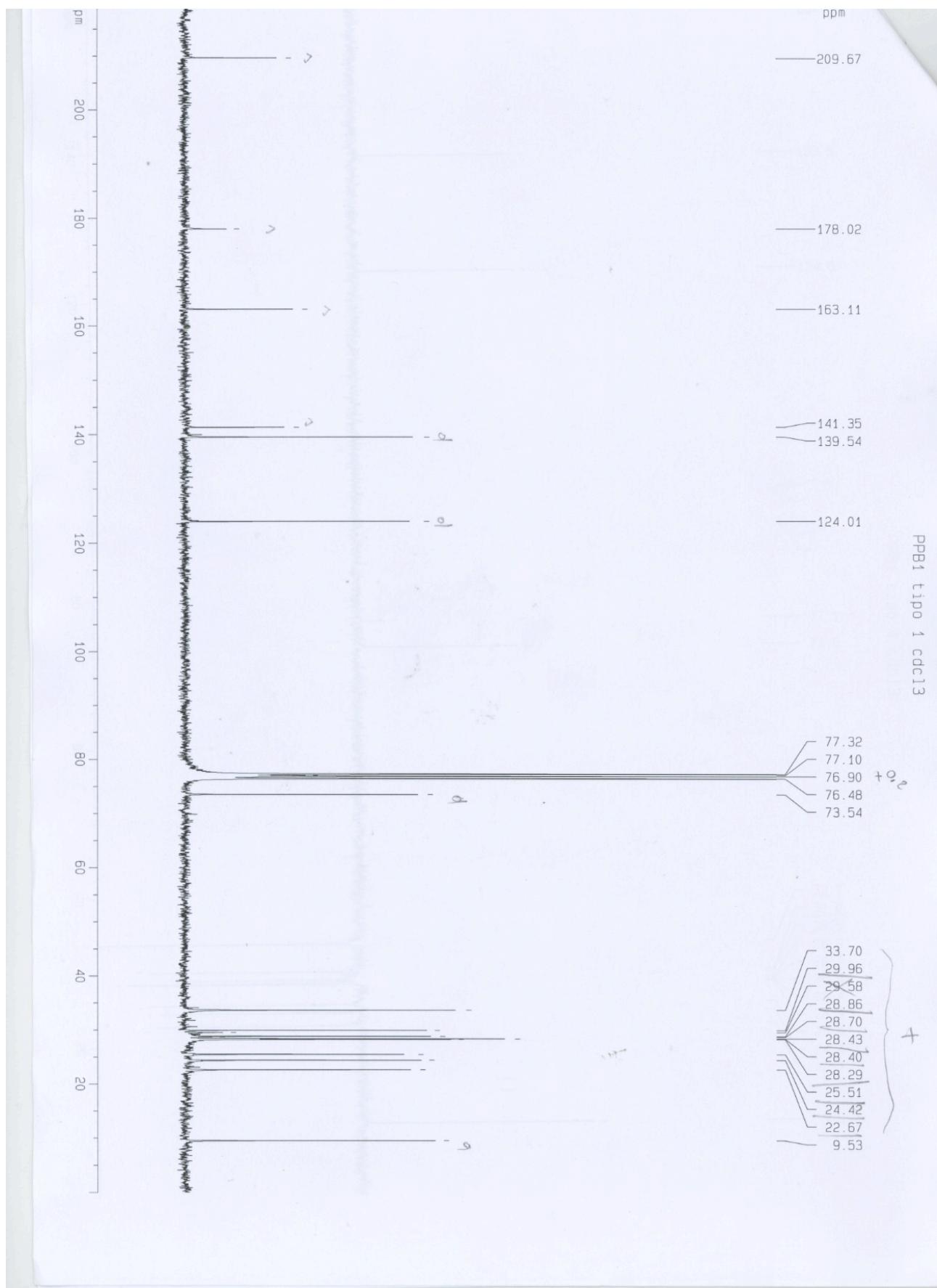
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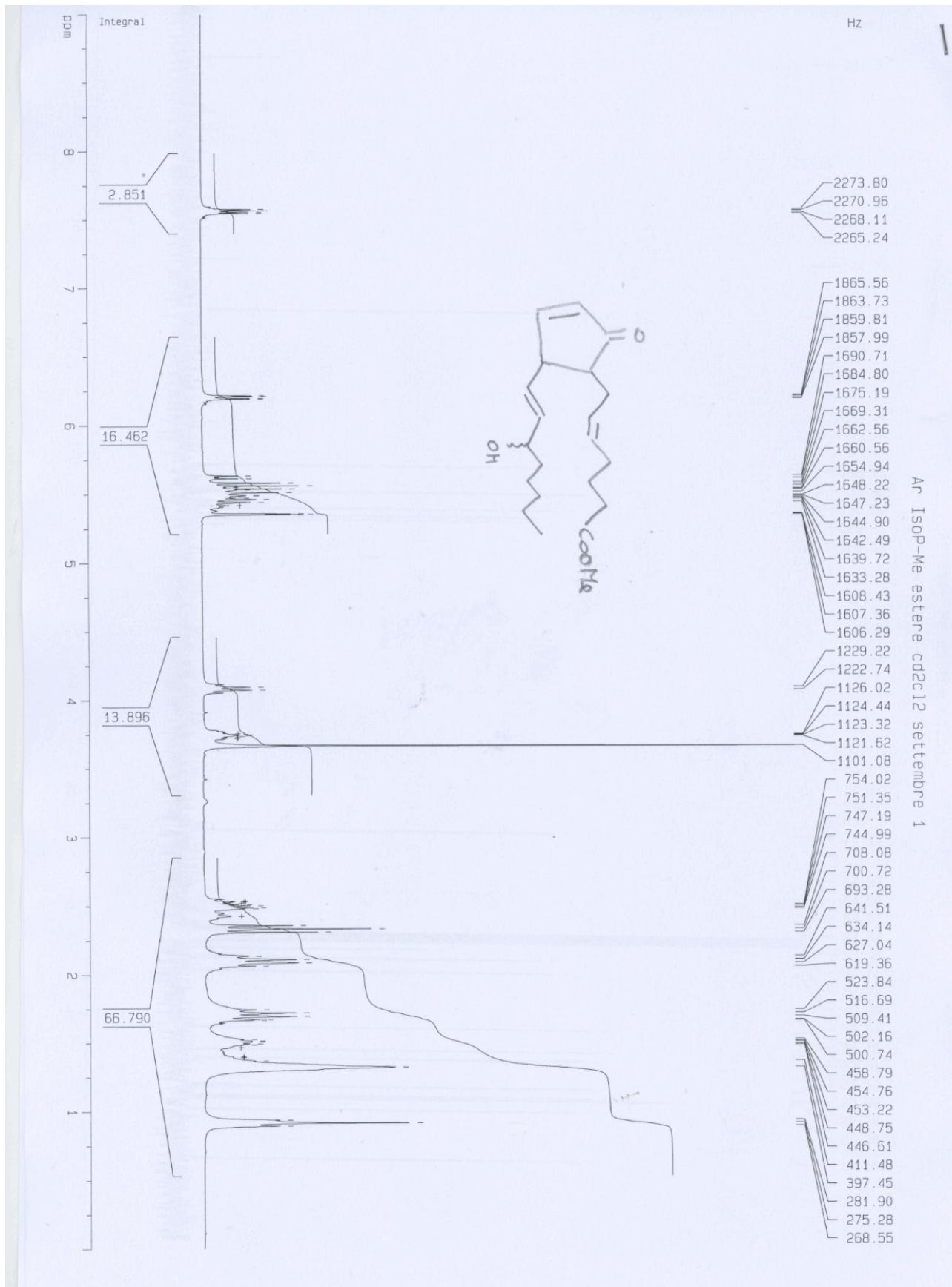






PPB1 tipo 1 cdc13





Ar-Isop-Me estere cd2c12

