Electronic supplementary materials *Mendeleev Commun.*, 2018, **28**, 505–507

Dimethylmalonoyl peroxide – the neglected lowest homologue: simple synthesis and high reactivity

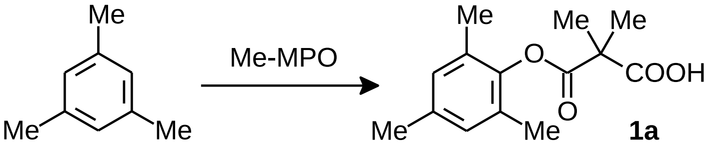
Margarita A. Lapitskaya, Vera A. Vil’, Elena D. Daeva, Alexander O. Terent’ev and Kasimir K. Pivnitsky

General

The numbers of the compounds are the same as those used in the main text. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker AM instruments at 25°C. In all solvents Me_4Si was used as an internal standard with δ 0.000 ppm.

Abbreviations used: RT: room temperature, 20-22°C; Me-MPO: dimethylmalonoyl peroxide; CP-MPO: spirocyclopropylmalonoyl peroxide; HFIP: 1,1,1,3,3,3-hexafluoroisopropanol; TFA: trifluoroacetic acid.

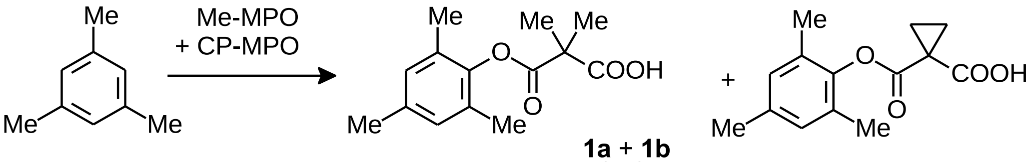
Oxidation of mesitylene.



1a

A solution of mesitylene (13.9 μl, 12 mg, 0.10 mmol) and Me-MPO (19.5 mg, 0.15 mmol) in HFIP (200 μl) was stored for 24 h at RT. The mixture was evaporated in a vacuum of <1 Torr and the residue was kept in a vacuum dessicator over NaOH. The residue is adduct **1a**, white crystals, yield 25 mg (100%), m.p. 123-125°C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.66 (s, 6H, Me_2), 2.10 (s, 6H, 2 o-ArMe), 2.25 (s, 3H, p-ArMe), 6.84 (s, 2H, 2 ArH). ^{13}C NMR (75 MHz, $CDCl_3$) δ 16.2, 20.8, 23.1, 50.2, 129.4, 129.8, 135.6, 145.6, 170.3, 178.8.

Competitive oxidation of mesitylene.



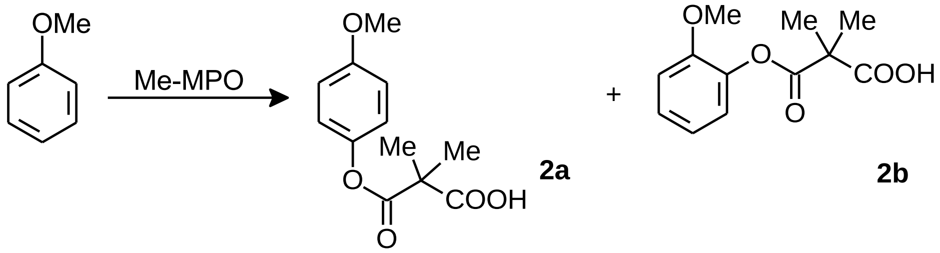
1a + 1b
1 : 2

A solution of mesitylene (27.8 μl, 24 mg, 0.20 mmol), Me-MPO (39 mg, 0.30 mmol) and CP-MPO (38.4 mg, 0.30 mmol) in $CDCl_3$ (1.0 ml) was divided equally into two ampoules for NMR spectra. TFA (23 µl, 34 mg, 0.30 mmol) was added in one of the ampoules, and both ampoules were stored at RT with periodical registration of ^{1}H NMR spectra. The values of mesitylene conversion and the product ratio were calculated from the integral intensities of singlet signals of aromatic ring protons at δ 6.80 (3H in mesitylene), 6.85 (2H in **1a**, product from Me-MPO) and 6.89 (2H in **1b**, product from CP-MPO). The results are shown in Table S1.

Table S1. Competitive oxidations of mesitylene in $CDCl_3$.

Catalyst	Reaction time, h	Conversion of mesitylene, %	1a : 1b ratio
None	10	5.9	1.00 : 2.00
None	98	29	1.00 : 2.39
TFA	10	64	1.00 : 1.89
TFA	98	100	1.00 : 1.90
		Average	**1.00 : 2.04**

Oxidation of anisole.

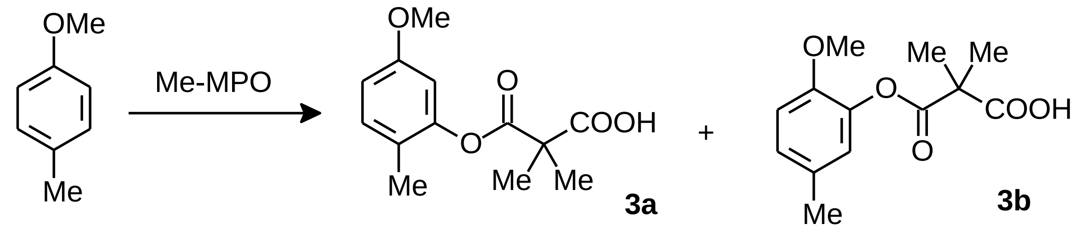


2a **2b**

A solution of anisole (43.3 µl, 43.3 mg, 0.40 mmol), Me-MPO (78.1 mg, 0.60 mmol) and TFA (138 µl, 205 mg, 1.8 mmol) in dichloromethane (800 µl) was kept at 33°C for 20 hours, then diluted with dichloromethane (3-4 ml) and washed with water (3 x 1 ml). The dried ($MgSO_4$) solution was evaporated to dryness and subjected to chromatography on silica gel to afford a 1.6:1 (NMR) mixture of products **2a,b** as a light yellow oil, yield 75 mg (79%), R_f 0.53 (CH_2Cl_2 + 2% HCOOH). ^{1}H NMR (300 MHz, $CDCl_3$) δ **2a** 1.61 (s, 6H, Me_2), 3.795 (s, 3H, OMe), 6.88 and 7.01 (2 d, 2 x 2H, *J* 9.0 Hz, ArH); **2b** 1.64 (s, 6H, Me_2), 3.800 (s, 3H, OMe), 6.88-7.00 (m, 2H, ArH), 7.05 (dd, 1H, *J* 1.6, 7.5 Hz, ArH), 7.20 (ddd, 1H, *J* 1.6, 7.5, 8.7 Hz, ArH). ^{13}C NMR (75 MHz, $CDCl_3$) δ **2a** 22.7, 50.1 (part of), 55.6, 114.4, 122.0, 144.1, 157.4, 171.4, 178.4; **2b** 22.8, 50.1 (part of), 55.9, 112.6, 120.7, 122.5, 127.1, 139.6, 151.1, 170.7, 178.3. HRMS (ESI) calculated for $[C_{12}H_{14}O_5$+H /

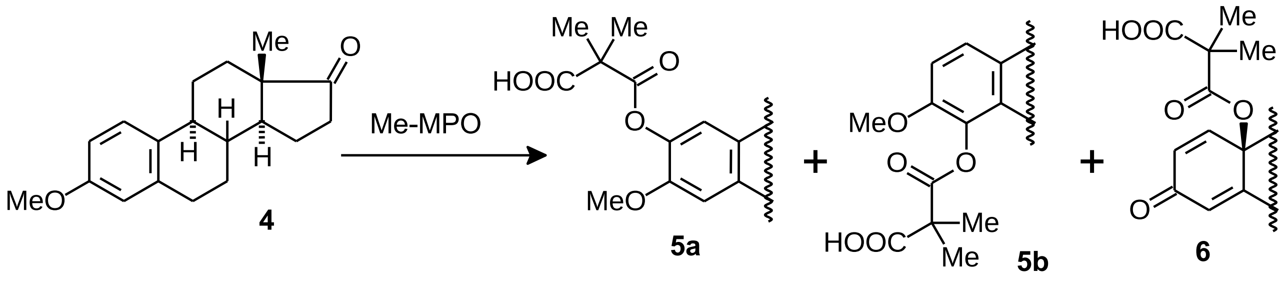
NH_4 / Na / K]$^+$ 239.0914 / 256.1179 / 261.0733 / 277.0473, found 239.0921 / 256.1183 / 261.0736 / 277.0472, corr.

Oxidation of *p*-methylanisole.



A solution of para-methylanisole (25.2 µl, 24.4 mg, 0.20 mmol), Me-MPO (33.8 mg, 0.26 mmol) and TFA (46 µl, 68 mg, 0.60 mmol) in chloroform (400 µl) was held for 24 hours at 32°C, evaporated to dryness, diluted with methylene chloride (2-3 ml) and washed with water (4 x 1 ml). The dried ($MgSO_4$) solution was evaporated to dryness and the residue was stored in vacuum dessicator over NaOH up to a constant weight. A brownish oil was obtained containing 94% of the product mixture **3a,b**, yield 39 mg (77%), the ratio **3a**: **3b** = 1.6 : 1, R_f 0.52 (CH_2Cl_2 + 2% HCOOH). ^{1}H NMR (300 MHz, $CDCl_3$) δ **3a** 1.63 (part of s, 6H, Me_2), 2.27 (s, 3H, ArMe), 3.76 (part of s, 3H, OMe), 6.85-6.87 (m, 1H, ArH), 6.84 (d, 1H, *J* 8.5 Hz, ArH), 6.99 (br.d, 1H, *J* 8.5 Hz, ArH); **3b** 1.63 (part of s, 6H, Me_2), 2.10 (s, 3H, ArMe), 3.76 (part of s, 3H, OMe), 6.57 (d, 1H, *J* 2.4 Hz, ArH), 6.72 (dd, 1H, *J* 2.7, 8.4 Hz, ArH), 7.10 (d, 1H, *J* 8.4 Hz, ArH). HRMS (ESI) calculated for [$C_{13}H_{16}O_5$+H / NH_4 / Na / K]$^+$ 253.1071 / 270.1336 / 275.0809 / 291.0603, found 253.1065 / 270.1328 / 275.0879, corr.

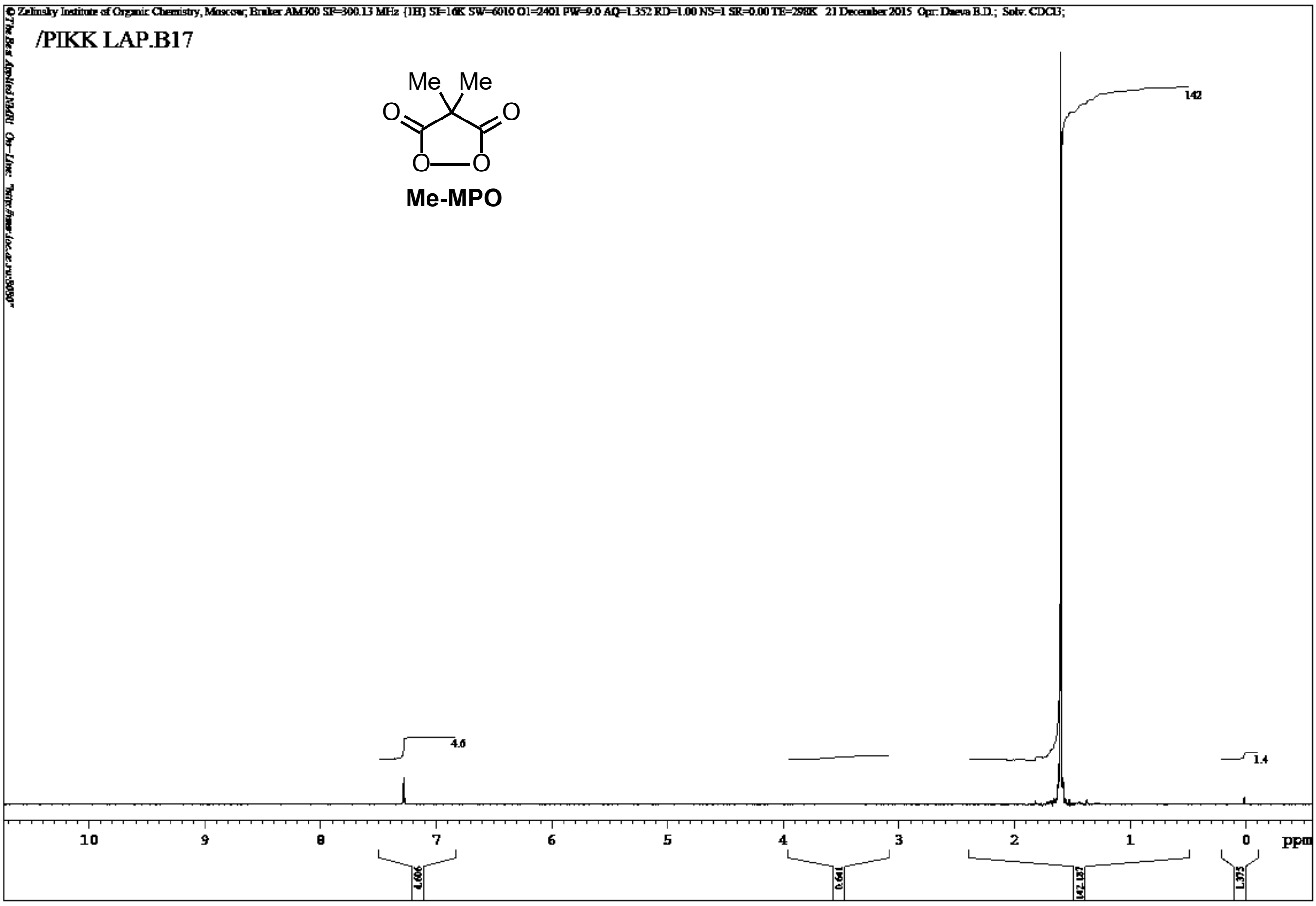
Oxidation of estrone methyl ether (4).



In each of four parallel experiments A-D estrone methyl ether **4** (56.9 mg, 0.20 mmol) and Me-MPO (33.8 mg, 0.26 mmol) were dissolved in (A) solution of TFA (46 µl, 68 mg, 0.60 mmol) in chloroform (400 µl); (B) HFIP (400 µl, 3.8 mmol); (C) solution of TFA (46 µl, 68 mg, 0.60 mmol) in HFIP (400 µl); (D) TFA (460 µl, 6 mmol). All the solutions A-D were kept at 30-35°C for 24 hours and evaporated in vacuum <1 Torr to dryness. From ^{1}H NMR spectra of product mixtures the conversions of **4** in (A) 86%, (B) 72%, (C) 84%, (D) 81%, and similar compositions of product mixtures were established. These mixtures were combined and chromatographed on silica gel (elution from CH_2Cl_2 to MeOBu^t), isolating the starting estrone ether **4** (41 mg, recovery 18%), a mixture of isomeric products **5a,b** (128 mg, 39%) and an abnormal product **6** (126 mg, 39%).

5a,b: white foam, isomer ratio 1.1 : 1.0, R_f 0.36 (hexane-EtOAc-HCOOH, 6:4:0.3). ^{1}H NMR (300 MHz, $CDCl_3$) δ **5a** 0.90 (s, 3H, 18-Me), 1.63 (s, 6H, Me_2), 3.76 (s, 3H, OMe), 6.66 (s, 1H, ArH), 6.93 (s, 1H, ArH); **5b** 0.89 (s, 3H, 18-Me), 1.645 + 1.649 (each s, 3H, diastereotopic Me_2), 3.77 (s, 3H, OMe), 6.77 (d, 1H, *J* 8.4 Hz, ArH), 6.93 (d, 1H, *J* 8.4 Hz, ArH). **5a,b** ^{13}C NMR (75 MHz, $CDCl_3$) δ 13.8, 13.9, 21.6, 22.8, 23.0, 23.3, 25.9, 26.5, 27.1, 29.4, 31.5, 35.9, 37.6, 38.0, 43.8, 43.9, 48.1, 48.2, 50.08, 50.12, 50.3, 56.1, 109.7, 113.0, 119.4, 123.4, 130.3, 132.3, 133.1, 135.2, 137.5, 137.6, 148.9, 150.0, 170.4, 171.1, 177.9, 221.92. HRMS (ESI) calculated for $[C_{24}H_{30}O_6+H / NH_4 / Na / K]^+$ 415.2115 / 432.2381 / 437.1935 / 453.1674, found 415.2110 / 432.2377 / 437.1930 / 453.1675, corr.

6: white crystals, m.p. 242-245°C (EtOAc), R_f 0.16 (hexane-EtOAc-HCOOH, 6:4:0.3). ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.93 (s, 3H, 18-Me), 1.51 + 1.52 (each s, 3H, diastereotopic Me_2), 6.20 (br.s, 1H, 4-H), 6.38 (dd, 1H, *J* 1.8, 10.2 Hz, 2-H), 6.93 (d, 1H, *J* 10.2 Hz, 1-H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 13.6, 22.0, 22.8, 30.9, 31.7, 32.9, 35.2, 35.6, 47.8, 49.8, 50.2, 56.7, 77.9, 124.3, 130.0, 147.3, 162.3, 170.1, 176.2, 185.6, 220.4. HRMS (ESI) calculated for $[C_{24}H_{30}O_6+H / Na / K]^+$ 401.1959 / 423.1778 / 439.1517, found 401.1949 / 423.1767 / 439.1507, corr.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Me
Me
O
O
O
O
Me-MPO
142
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1.4
10
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8
7
6
5
4
3
2
1
0
ppm
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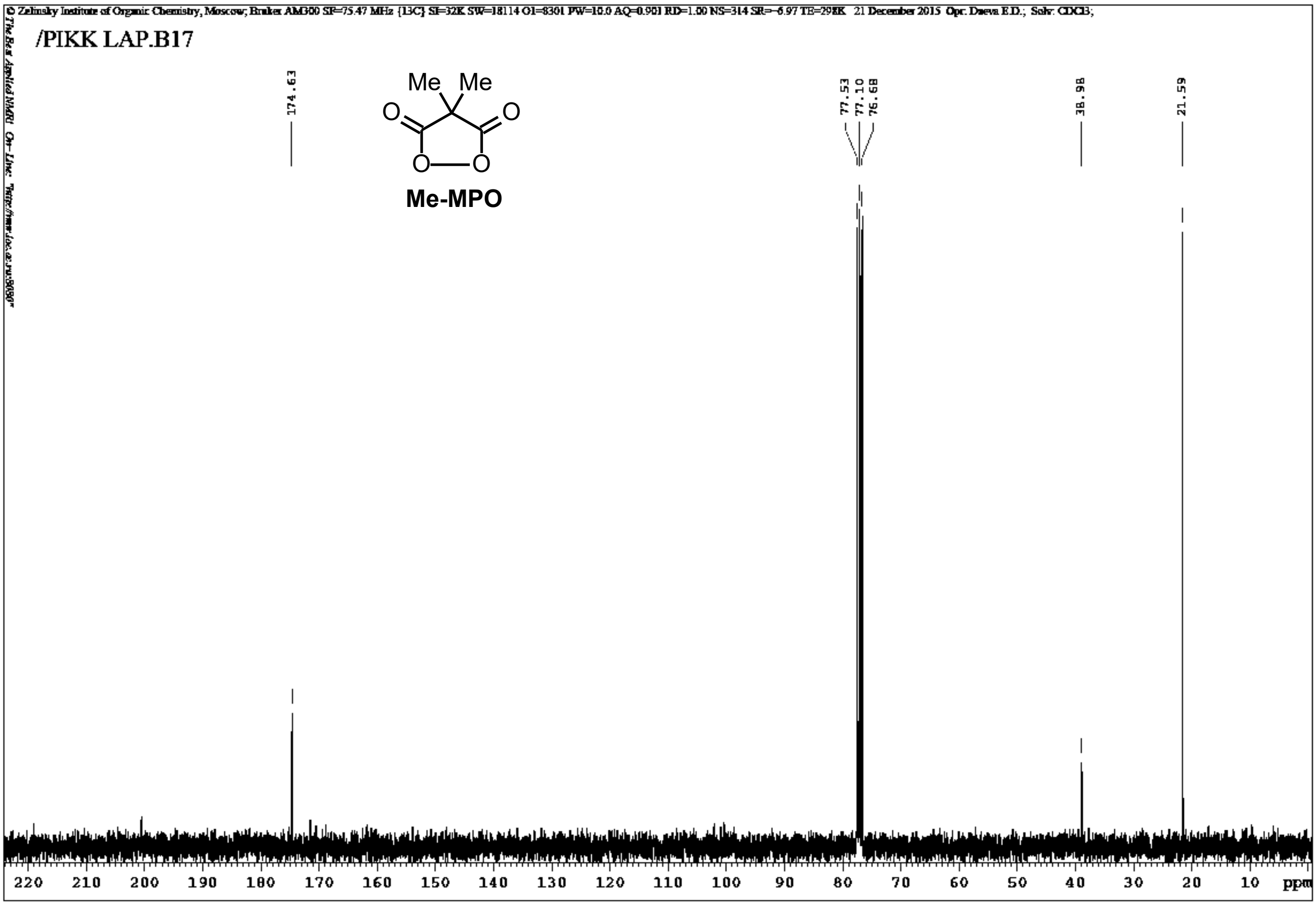
1.375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Me
Me
O
O
O
O
Me-MPO
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76.68
38.98
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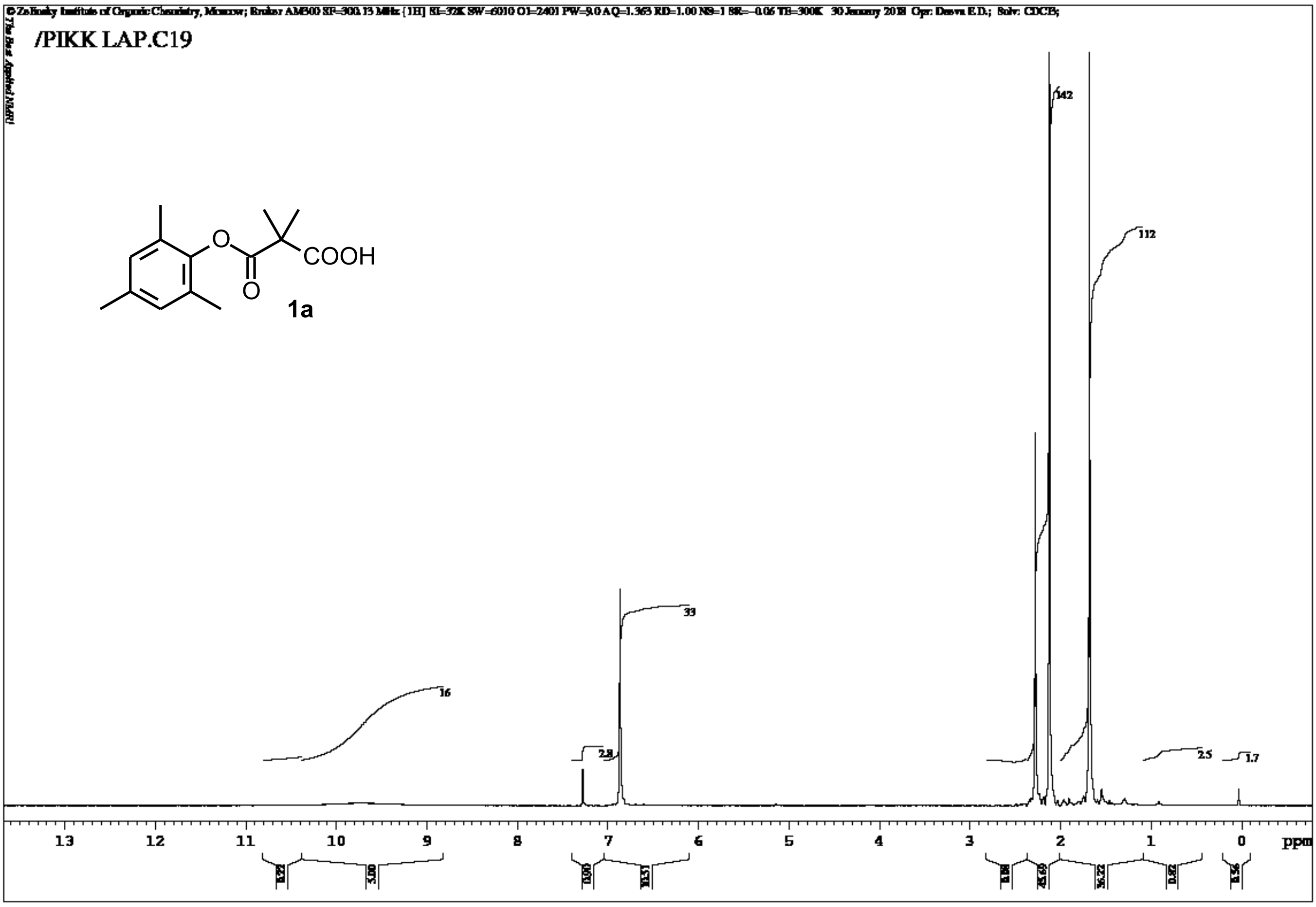
ppm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2.5
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10
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6
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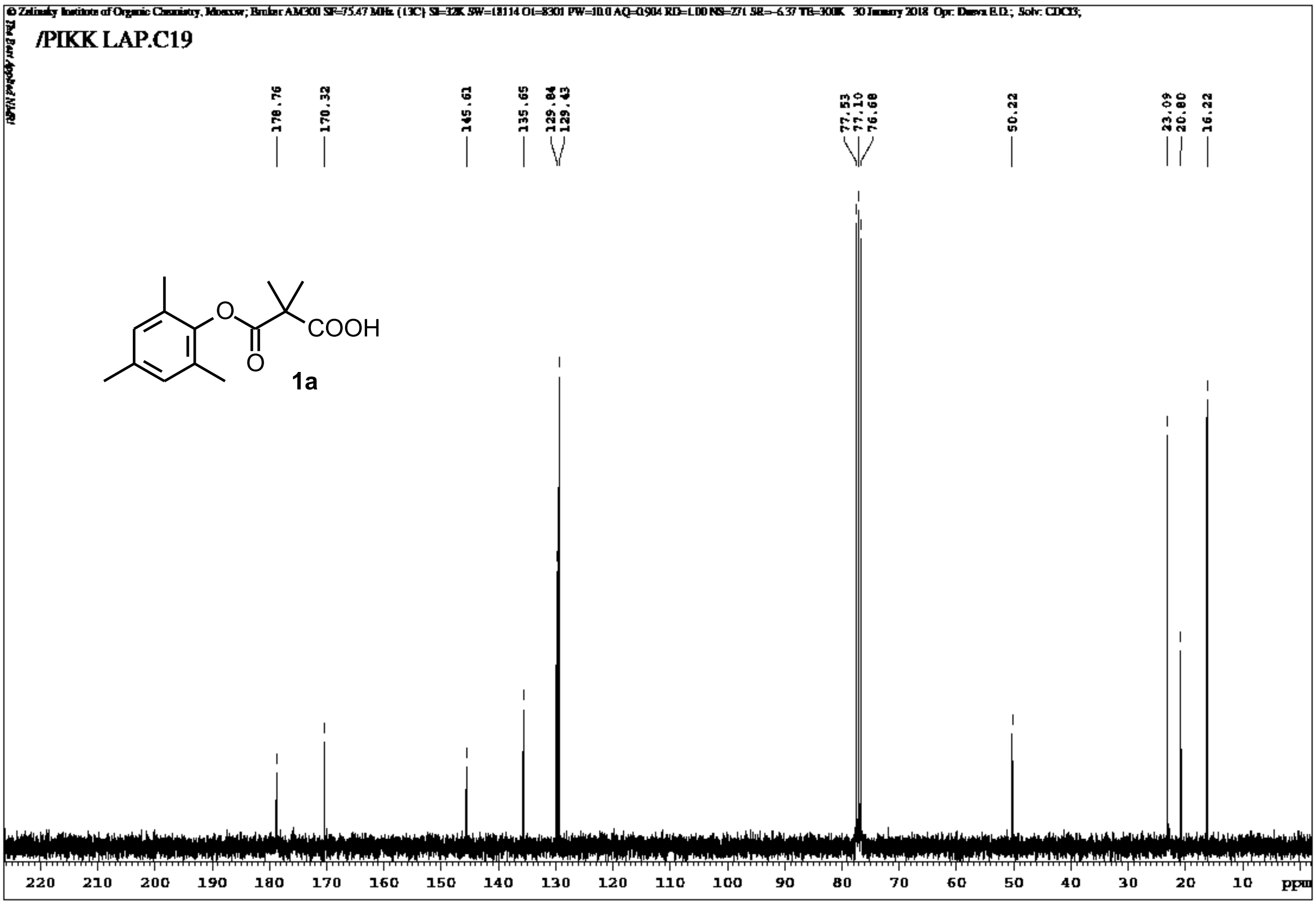
0
ppm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170.32
145.61
135.65
129.84
129.43
77.53
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76.68
50.22
23.09
20.80
16.22
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O
O
1a
220
210
200
190
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150
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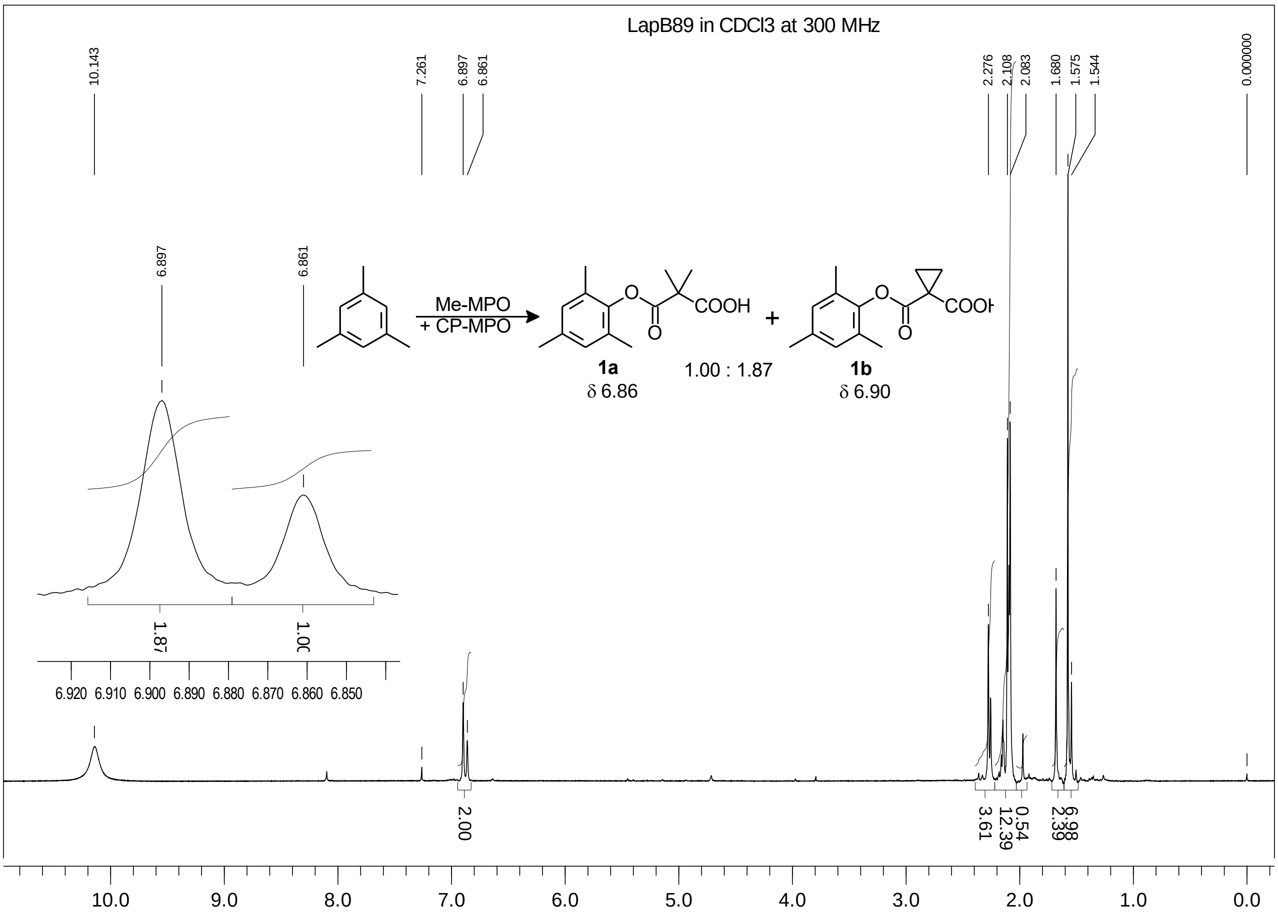
10
ppm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6.861
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2.108
2.083
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1.575
1.544
0.000000
Me-MPO
+ CP-MPO
O
COOH
+
COOH
1a
δ 6.86
1.00 : 1.87
1b
δ 6.90
1.87
1.00
6.920 6.910 6.900 6.890 6.880 6.870 6.860 6.850
2.00
3.61
12.39
0.54
2.39
6.98
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9.0
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7.0
6.0
5.0
4.0
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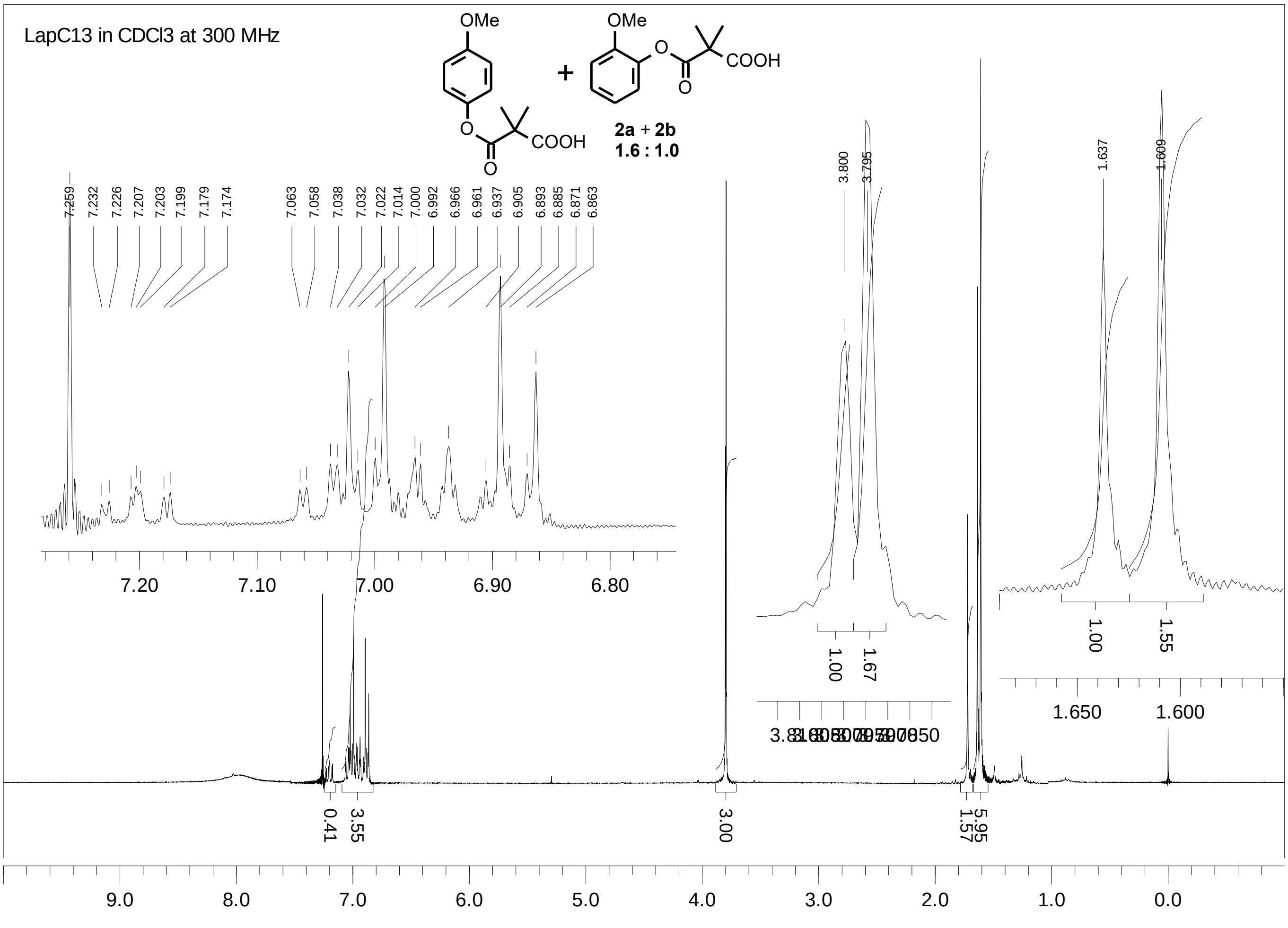
2.0
1.0
0.0


LapC13 in CDCl3 at 300 MHz
OMe
O
COOH
+
2a + 2b
1.6 : 1.0
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7.232
7.226
7.207
7.203
7.199
7.179
7.174
7.063
7.058
7.038
7.032
7.022
7.014
7.000
6.992
6.966
6.961
6.937
6.905
6.893
6.885
6.871
6.863
7.20
7.10
7.00
6.90
6.80
3.800
3.795
1.00
1.67
1.637
1.609
1.00
1.55
1.650
1.600
0.41
3.55
3.00
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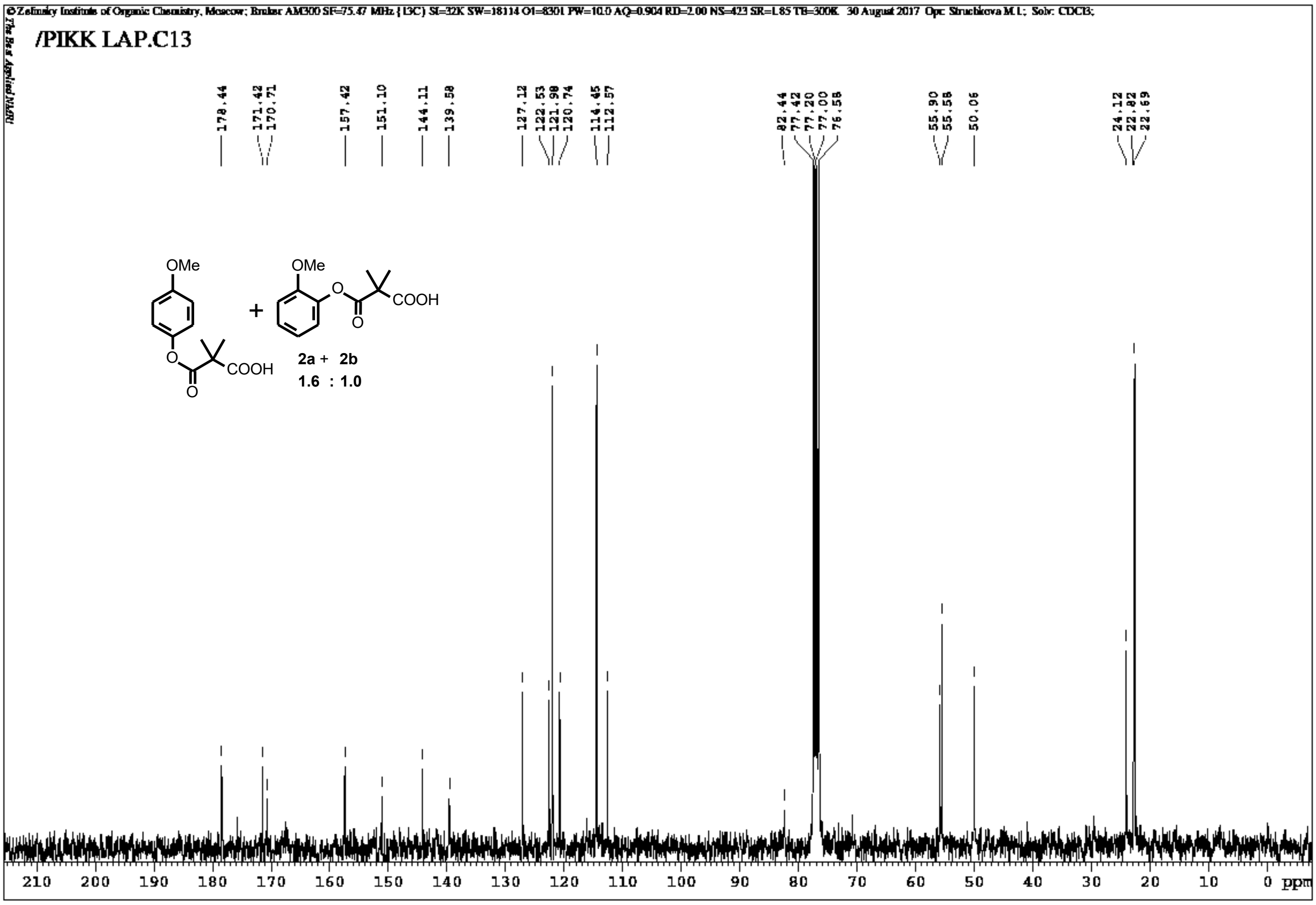
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139.58
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122.53
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120.74
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112.57
82.44
77.42
77.20
77.00
76.58
55.90
55.58
50.06
24.12
22.82
22.69
OMe
O
COOH
O
+
OMe
O
COOH
O
2a + 2b
1.6 : 1.0
210
200
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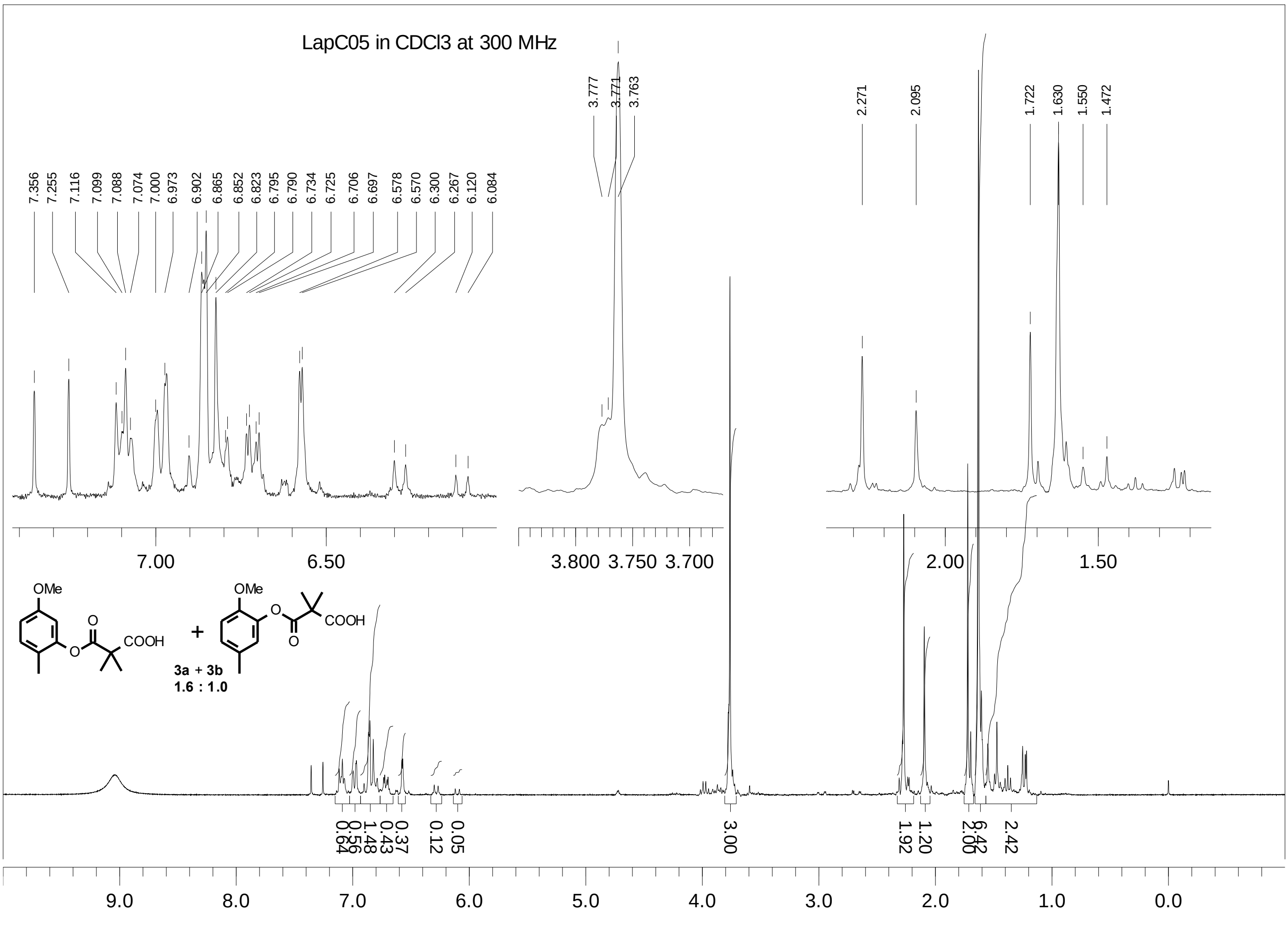
LapC05 in CDCl3 at 300 MHz
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7.255
7.116
7.099
7.088
7.074
7.000
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6.852
6.823
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6.790
6.734
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2.00
1.50
OMe
O
O
COOH
+
OMe
O
COOH
O
3a + 3b
1.6 : 1.0
0.64
0.56
1.48
0.43
0.37
0.12
0.05
3.00
1.92
1.20
2.00
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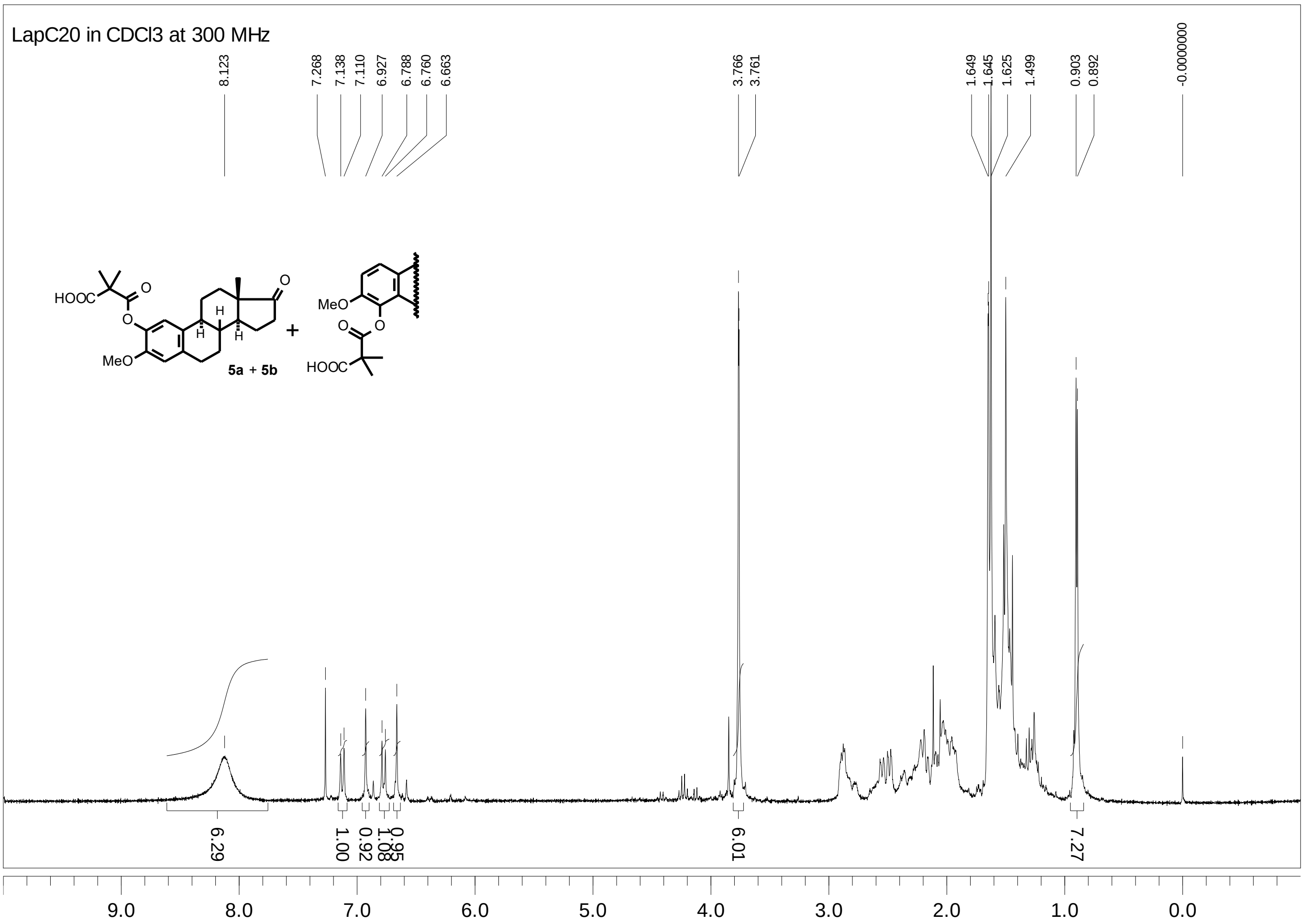
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7.138
7.110
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6.788
6.760
6.663
3.766
3.761
1.649
1.645
1.625
1.499
0.903
0.892
-0.0000000
HOOC
O
O
MeO
H
H
H
O
+
MeO
O
O
HOOC
5a + 5b
6.29
1.00
0.92
1.08
0.95
6.01
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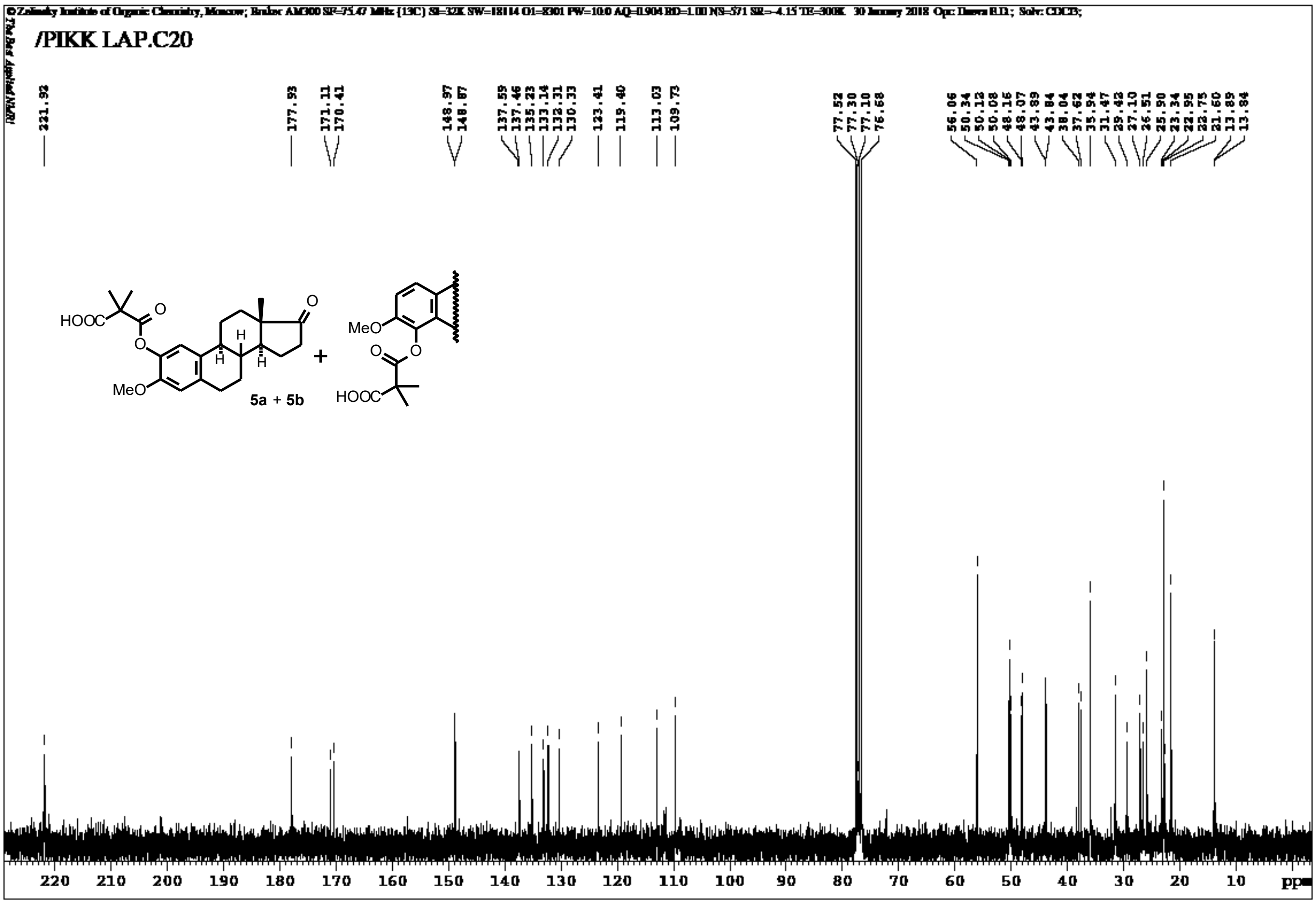
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77.30
77.10
76.68
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50.12
50.08
48.16
48.07
43.89
43.84
38.04
37.62
35.94
31.47
29.42
27.10
26.51
25.90
23.34
22.95
22.75
21.60
13.89
13.84
HOOC
O
O
MeO
H
H
H
O
+
MeO
O
O
HOOC
5a + 5b
220
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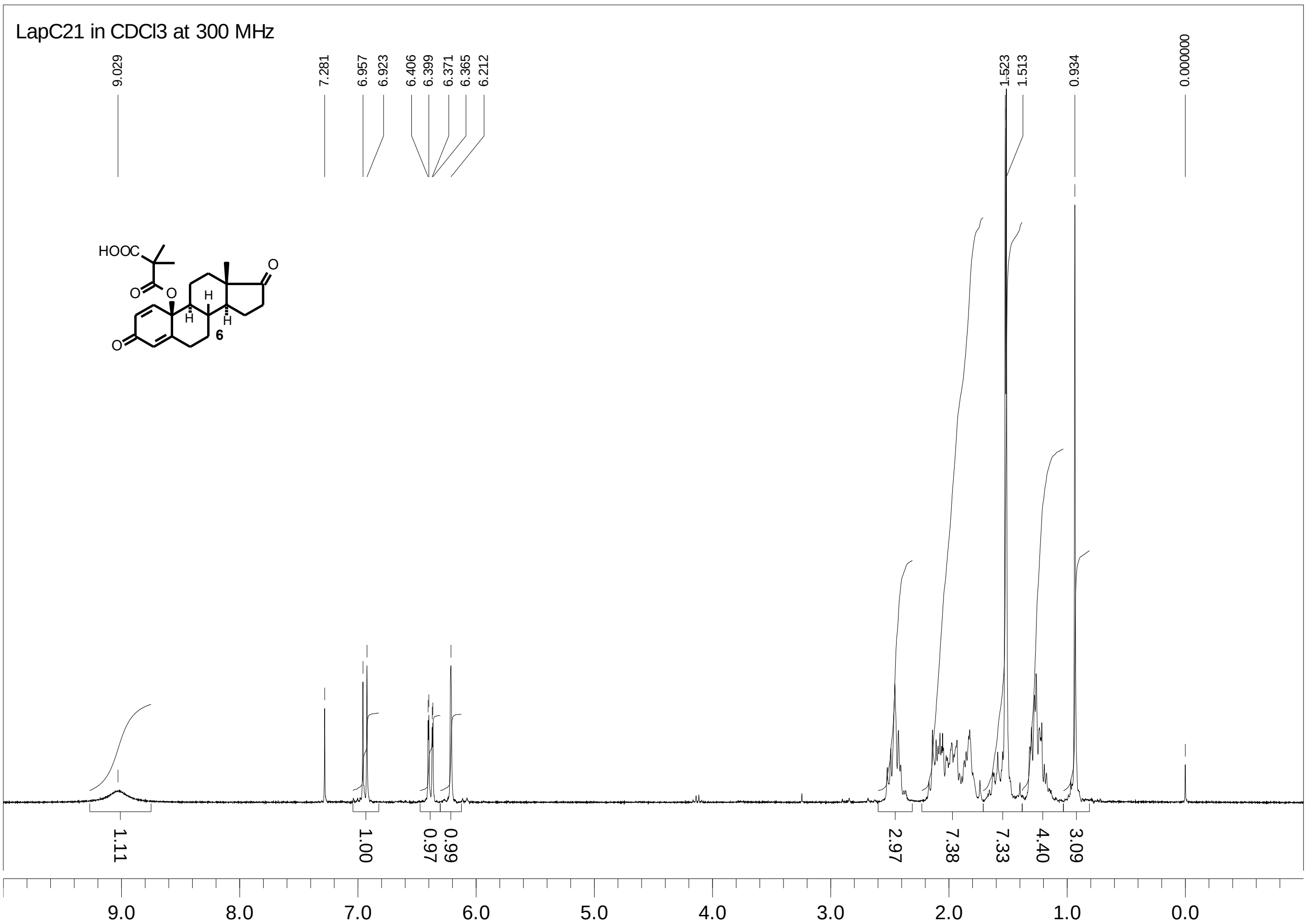
LapC21 in CDCl3 at 300 MHz
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0.000000
HOOC
O
O
O
H
H
H
O
6
1.11
1.00
0.97
0.99
2.97
7.38
7.33
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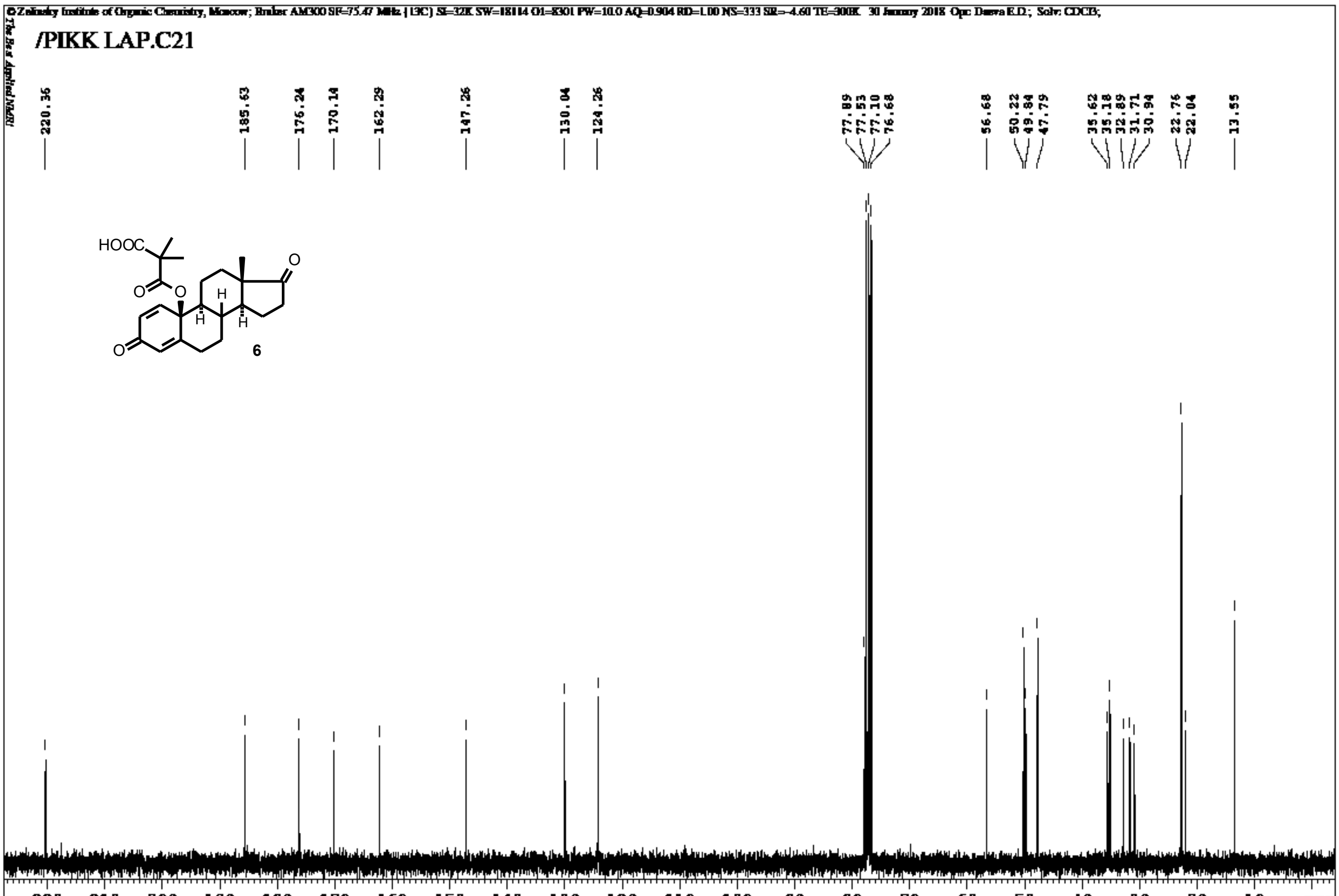
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130.04
124.26
77.89
77.53
77.10
76.68
56.68
50.22
49.84
47.79
35.62
35.18
32.89
31.71
30.94
22.76
22.04
13.55
HOOC
O
O
O
H
H
O
6
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm