Electronic Supplementary Material (ESI) for ChemComm.

Ozonolysis of α-angelica lactone: a renewable route to malonates

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Supporting Information

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1. General information

Reagents: α-angelica lactone (98%, Sigma Aldrich), hydrogen peroxide (30% aqueous solution, Sigma Aldrich), dimethyl sulfide (>99%, Sigma Aldrich), sodium borohydride (98%, ABCR), palladium on activated charcoal (10% Pd, Fluka) and all the solvents (>99%, Walter) were used as received.

NMR Spectroscopy: ^{1}H-NMR and ^{13}C-NMR were recorded at ambient temperature on 300 MHz spectrometers (Avance 300 or Fourier 300) or a 400 MHz spectrometer (Avance 400) from Bruker. The chemical shifts δ are given in ppm and referenced to the residual proton signal of the deuterated solvent used.

Mass spectroscopy: measurements were recorded on an Agilent 6210 time-of-flight LC/MS (ESI) or on a Thermo Electron MAT 95-XP (EI, 70 eV). Peaks as listed correspond to the highest abundant peak and are of the expected isotope pattern.

Ozonolysis: reactions were performed with a Sander model 301.19 ozonizer employing dry compressed air (Figure S1).

Figure S1. Typical set-up for ozonolysis reactions.

2. Synthetic procedures

Malonic acid (MA): α-AL (2.50 g, 25.5 mmol) was dissolved in 50 mL of the required solvent (see Table 1 in the main text). The solution was cooled down to the desired temperature (dry ice-acetone or ice-water) and ozone was bubbled through the solution (2 g*h^{-1}) until titration with KI showed an excess of ozone. Argon was bubbled through the reaction mixture for 30 minutes, the contents were carefully poured into hydrogen peroxide cooled at 0 °C (25 mL, 30% aq. solution, 255 mmol, 10 eq) and the resulting solution was stirred for further 20 hours at room temperature. After negative peroxide test, the aqueous layer was extracted with ethyl acetate (4x50 mL), the organic layer was concentrated under reduced pressure and dried *in vacuo* for 6 h. **MA** was obtained as a fine white powder in up to 91% isolated yield (see Tables 1 and 2 in the main text).

^{1}H NMR (300 MHz, Acetone-*d6*) δ 10.71 (s, 2H), 3.39 (s, 2H). ^{13}C NMR (300 MHz, Acetone-*d6*) δ 168.6, 41.3.[1]

ESI-MS (ES$^-$): calculated for $C_3H_4O_4$: 104.01; found: 103.00 [M-H]$^-$.

Methyl 3,3-dimethoxypropanoate (MOP Acetal): **α-AL** (2.50 g, 25.5 mmol) was dissolved in 50 mL of methanol (see Table 1 in the main text). The solution was cooled down to the desired temperature (dry ice-acetone or ice-water) and ozone was bubbled through the solution (2 g*h^{-1}) until titration with KI showed an excess of ozone. Argon was bubbled through the reaction mixture for 30 minutes, the contents were carefully poured into 19 mL of dimethyl sulfide (255 mmol, 10 eq) and stirred for a further 20 hours. The crude was concentrated to about half of the initial volume, then partitioned between water and ethyl acetate and the water phase extracted (4x50 mL EtOAc). The collected organic phases were washed with saturated aqueous $NaHCO_3$ (100 mL) and brine to remove the residual acetic acid, the volatiles concentrated under reduced pressure affording pure **MOP acetal** as a colourless liquid in up to 46% isolated yield (see Tables 1 and 2 in the main text).

^{1}H NMR (300 MHz, Chloroform-*d*) δ 4.82 (t, *J* = 5.6 Hz, 1H), 3.68 (s, 3H), 3.35 (s, 6H), 2.64 (d, *J* = 5.9 Hz, 2H). ^{13}C NMR (300 MHz, $CDCl_3$) δ 170.4, 101.4, 53.6, 51.9, 38.8.[2]

ESI-MS (ES$^-$): calculated for $C_6H_{12}O_4$: 148.07; found: 147.05 [M-H]$^-$.

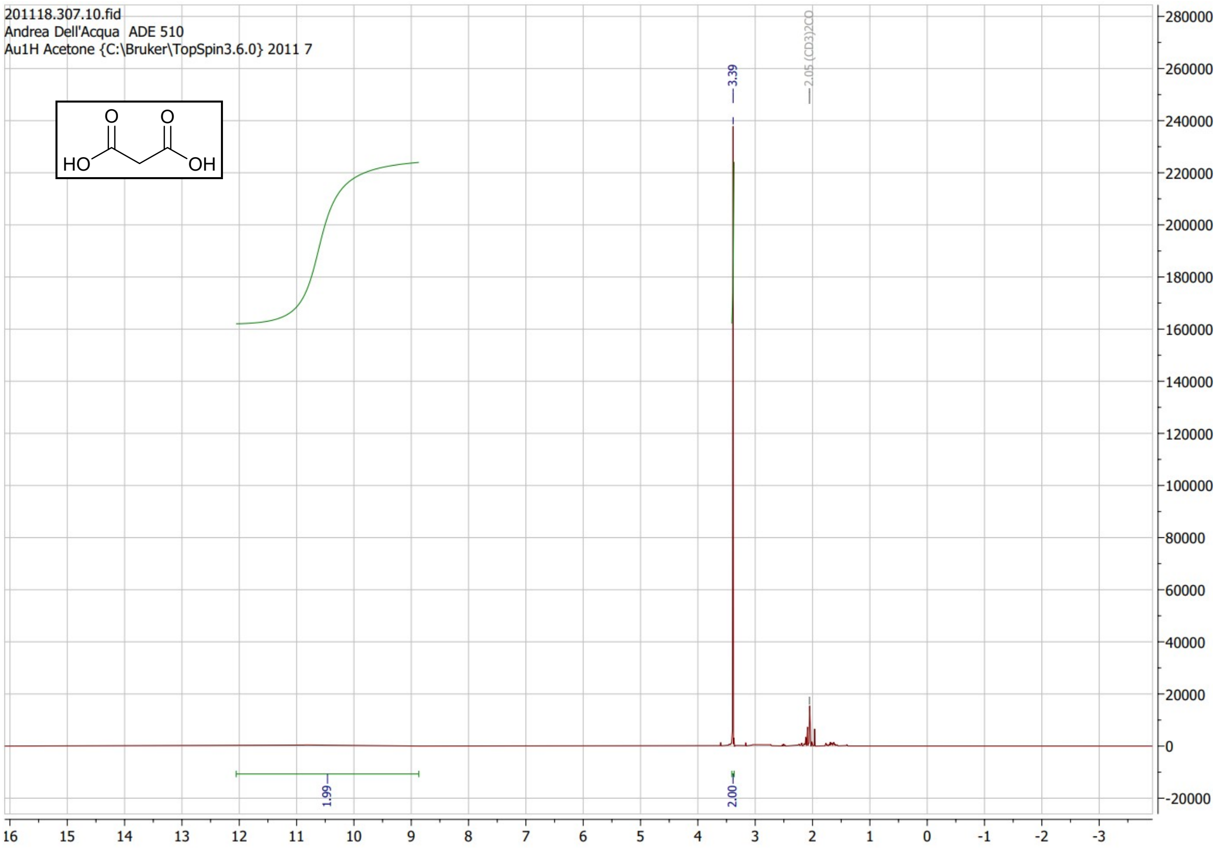
Monomethyl malonate (mMM): The general procedure described for the synthesis of **MA** was repeated using methanol as solvent. **mMM** was obtained after extraction with ethyl acetate and concentration in vacuum as colourless liquid (1.58 g, 52% yield).

^{1}H NMR (300 MHz, Chloroform-*d*) δ 3.78 (s, 3H), 3.45 (s, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.7, 167.4, 53.1, 41.3.[1]

ESI-MS (ES$^-$): calculated for $C_4H_6O_4$: 118.03; found: 117.05 [M-H]$^-$.

Scaled-up synthesis of MA: The procedure described for MA synthesis was repeated using 25 g (0.26 mol) of aAL in 500 mL of ethyl acetate. The organic phase was concentrated after negative peroxide test, affording a colourless liquid. **MA** (22.71 g, 86% yield) was obtained as a white solid after extensive drying in vacuum.

MA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O
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OH
3.39
2.05 (CD3)2CO
1.99
2.00
280000
260000
240000
220000
200000
180000
160000
140000
120000
100000
80000
60000
40000
20000
0
-20000
16
15
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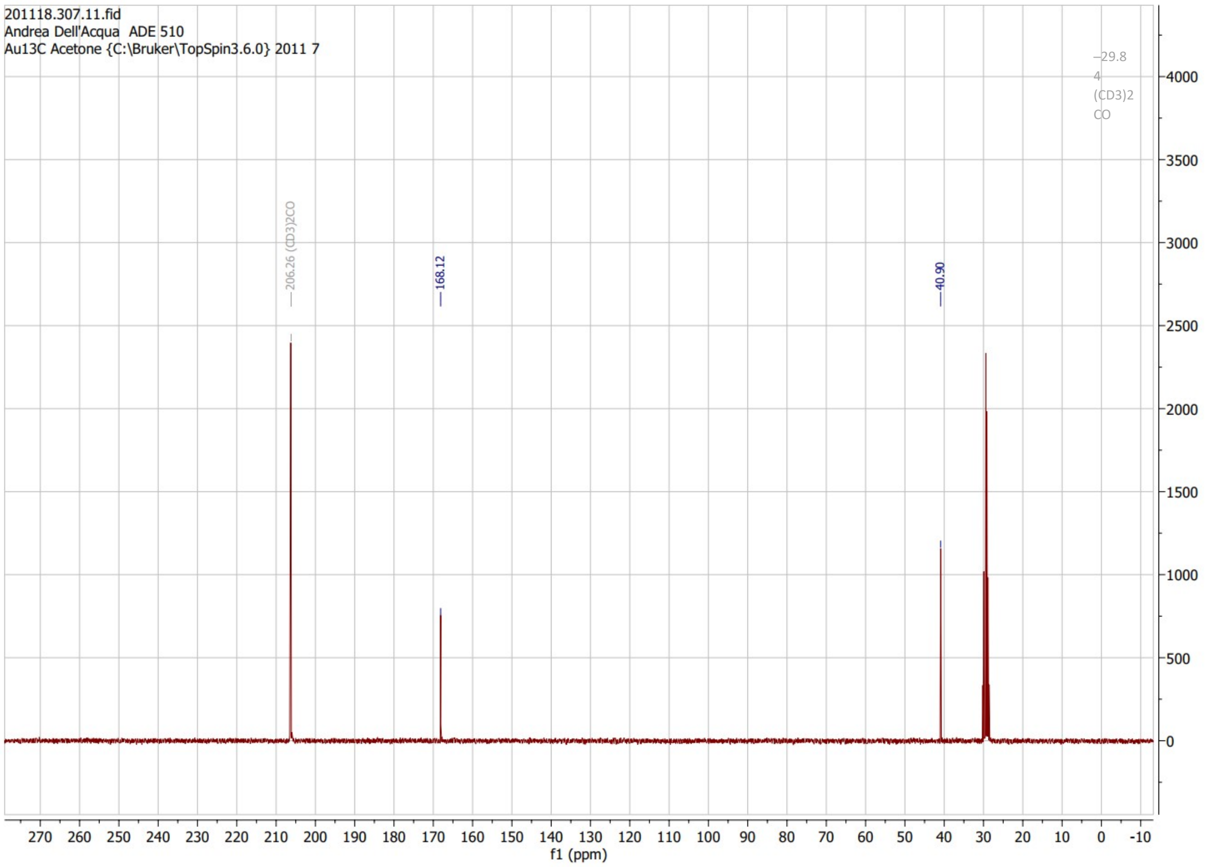
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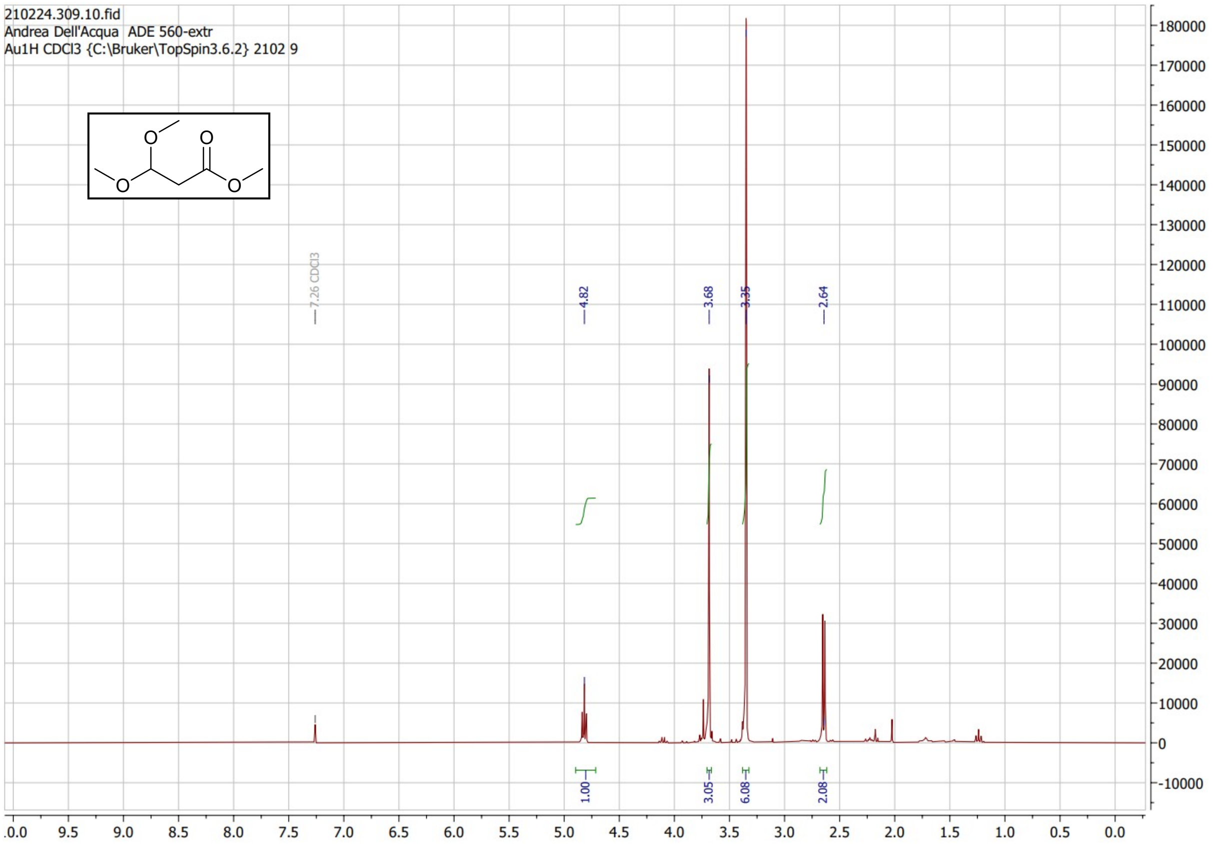
168.12
40.90
29.84 (CD3)2CO
4000
3500
3000
2500
2000
1500
1000
500
0
270
260
250
240
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

MOP-acetal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O
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3.68
3.35
2.64
1.00
3.05
6.08
2.08
180000
170000
160000
150000
140000
130000
120000
110000
100000
90000
80000
70000
60000
50000
40000
30000
20000
10000
0
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9.5
9.0
8.5
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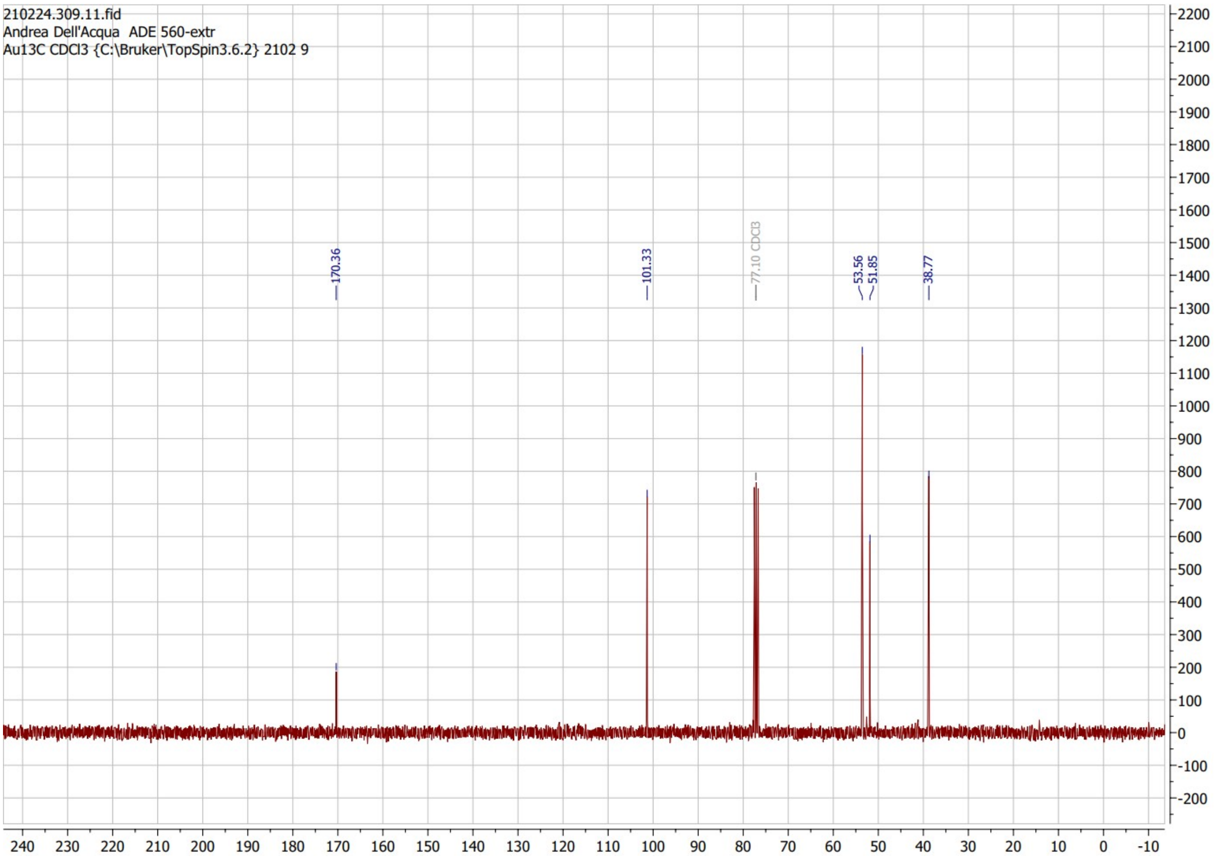
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77.10 CDCl3
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51.85
38.77
2200
2100
2000
1900
1800
1700
1600
1500
1400
1300
1200
1100
1000
900
800
700
600
500
400
300
200
100
0
-100
-200
240
230
220
210
200
190
180
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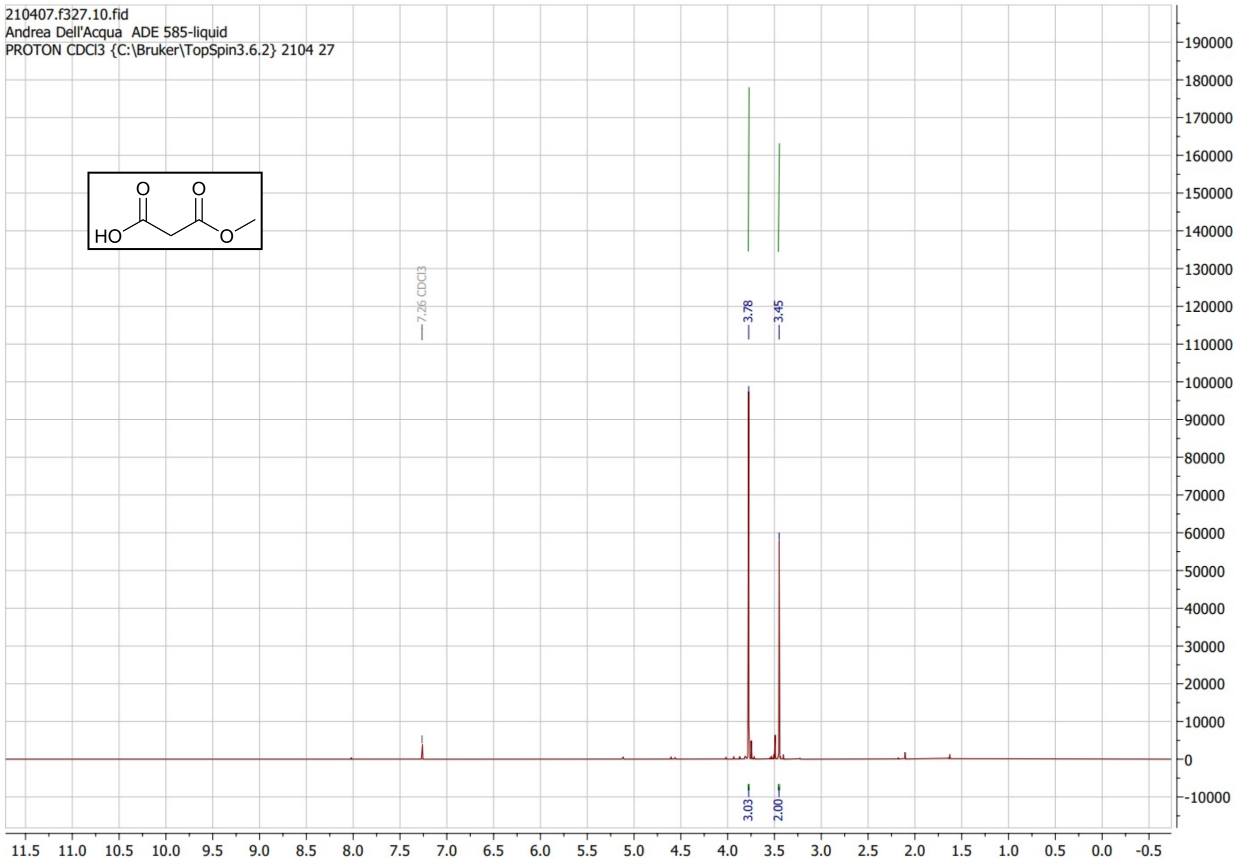
20
10
0
-10

mMM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3.45
3.03
2.00
11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
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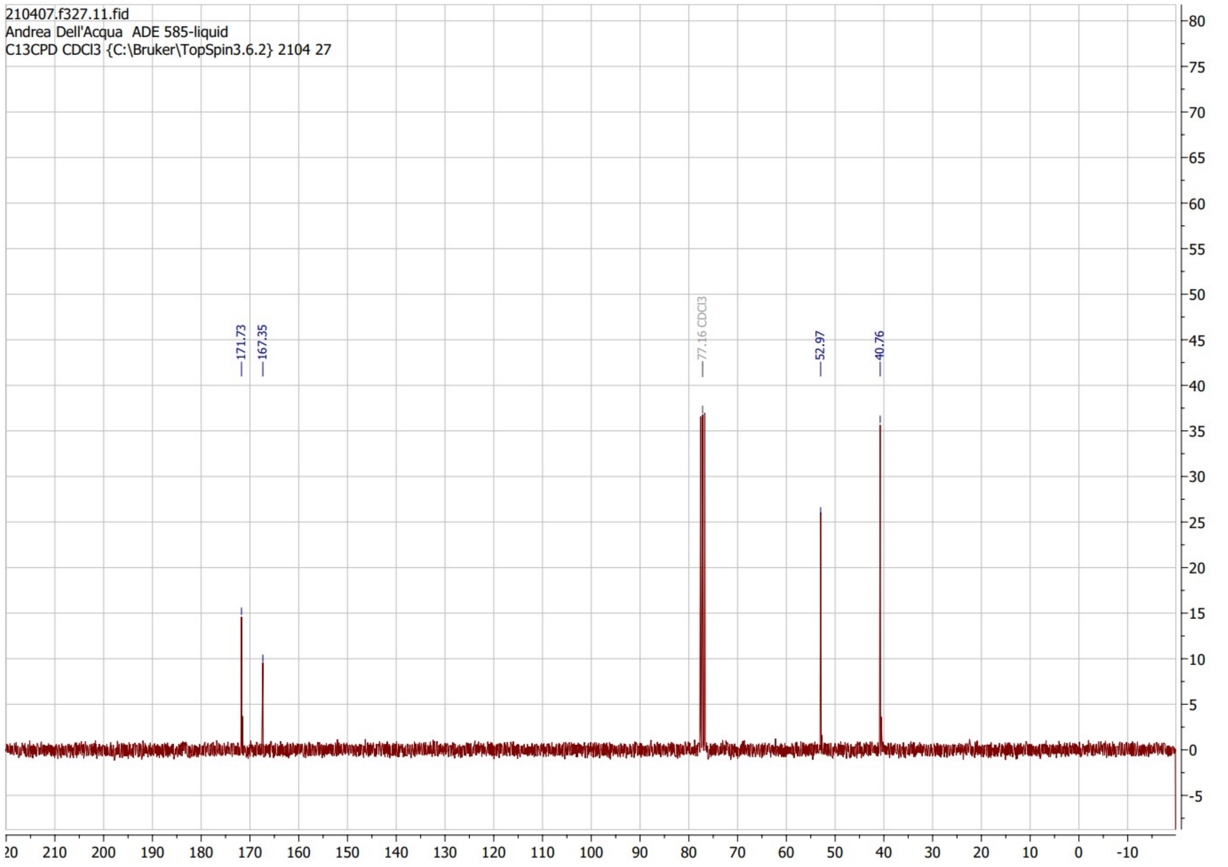
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167.35
77.16 CDCl3
52.97
40.76
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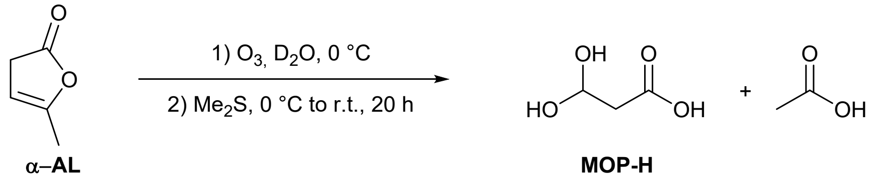
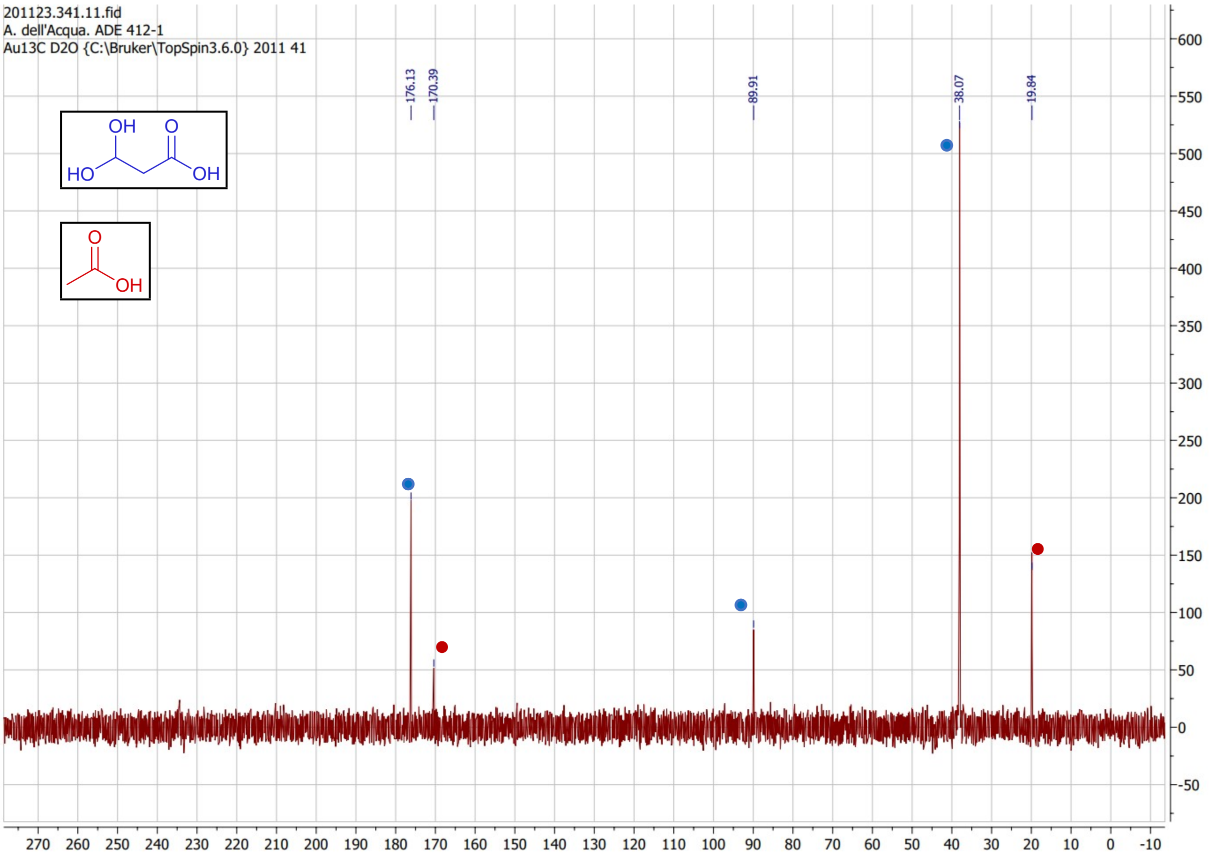
3. Aldehyde trapping experiments

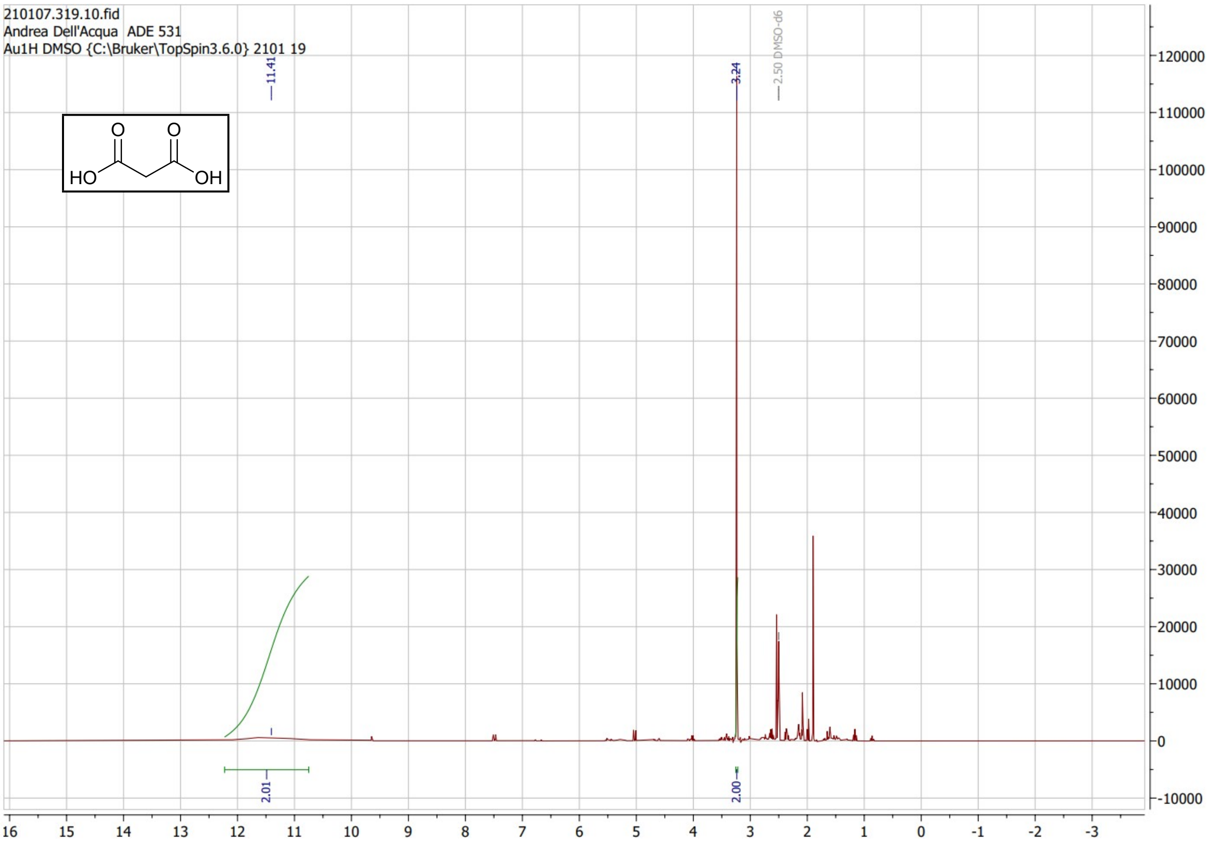


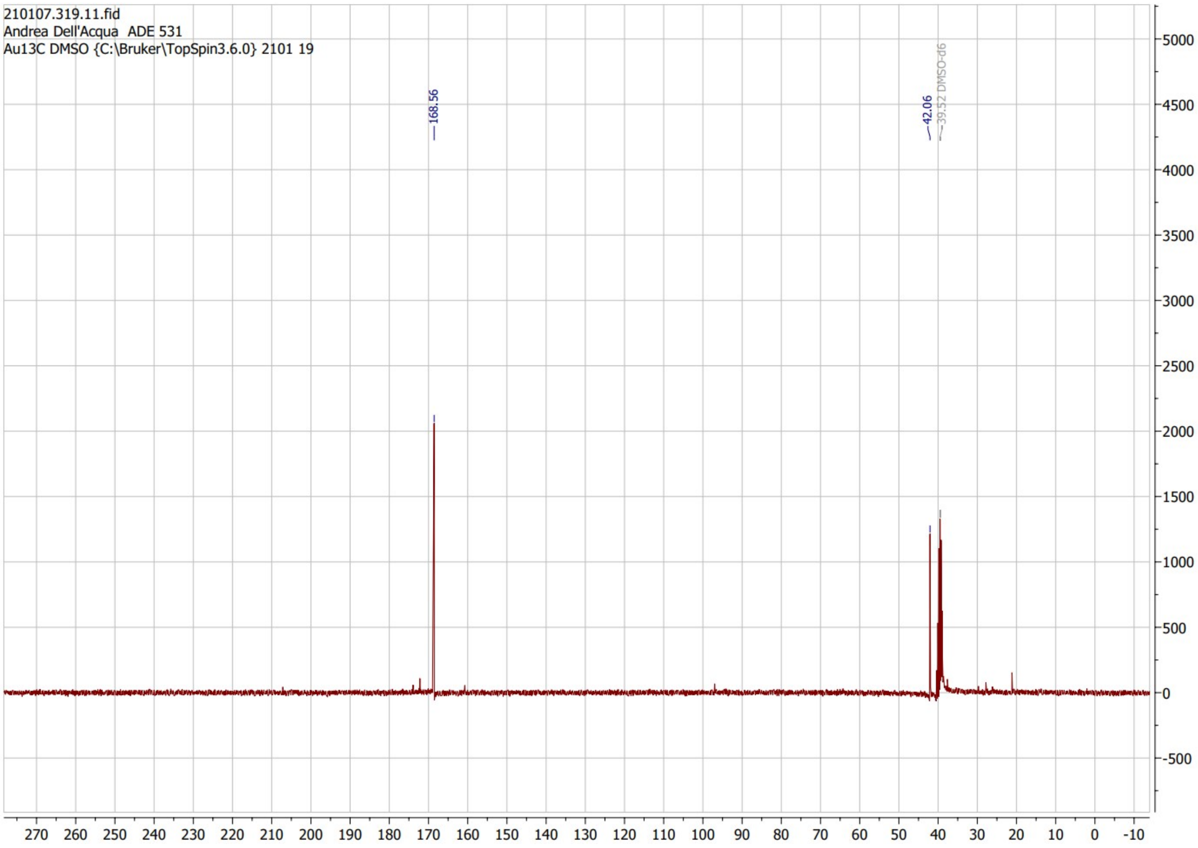
The general procedure described in 2. was repeated, performing the reaction in D_2O (250 mg of α–**AL** in 5.0 mL of D_2O). A ^{13}C NMR sample was measured after purging the reaction mixture with argon for 20 minutes, and the remaining solution worked-up following the procedure described above (1.0 mL Me_2S as quenching agent, followed by water-acetate extraction).

Before quenching (^{13}C in D_2O)

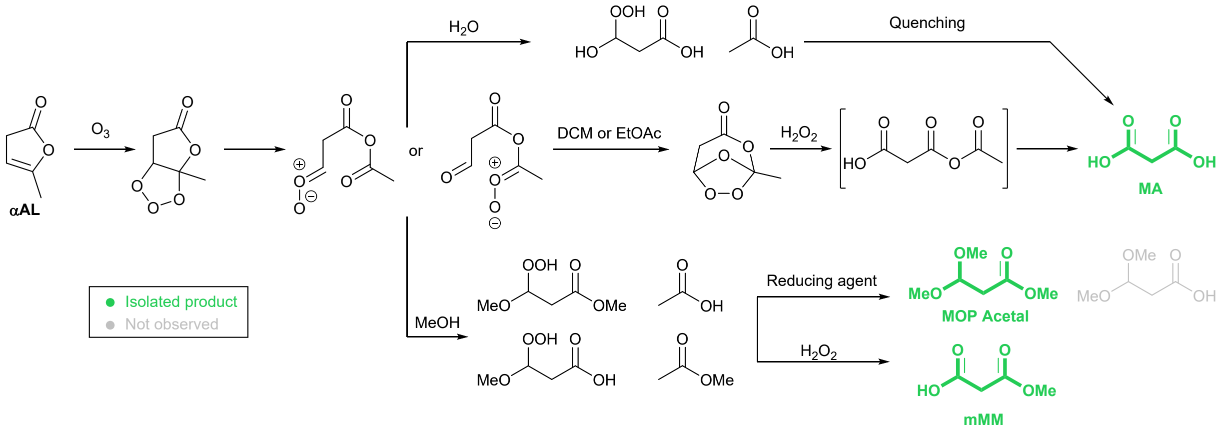


After quenching with Me_2S and extraction





5. Proposed mechanism[3, 4]



4. References

1. F. Rajabi, C. Wilhelm and W. R. Thiel, *Green Chem.*, 2020, **22**, 4438-4444.
2. M. Limbach, S. Dalai and A. de Meijere, *Advanced Synthesis & Catalysis*, 2004, **346**, 760-766.
3. R. Criegee, *Angew. Chem. Int. Ed.*, 1975, **14**, 745-752.
4. R. L. Kuczkowski, *Chem. Soc. Rev.*, 1992, **21**, 79-83.