

Supplementary information

Selective Aerobic Oxidation of Aliphatic Aldehydes: the Critical Role of Percarboxylate Anion on the Selectivity

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1. Safety

It is worth mentioning that in the case of oxidation reactions, fuel, oxidant, and energy are present simultaneously; thus, the process's safety should receive explicit attention. Liquid-phase aerobic oxidation innately poses the risk of fire and the formation of explosive vapor space, particularly when flammable organic solvents are used. As such, intensification of this reaction by increasing the reaction volume, the concentration of reactant(s) and catalyst, and the temperature **should not be** considered with classical glassware.

All liquid wastes must also be treated with an excess of aqueous sodium sulfide solution. The absence of remaining peracids in the liquid waste was checked using Quantofix® peracetic acid 500 test strips (Macherey-Nagel).

2. General information

Acetonitrile, heptane, 2-ethylhexanal **1**, 2-ethylhexanoic acid **6**, 2-methylpentanal **13**, octanal **14**, 3,5,5-trimethylhexanal **15**, cyclohexanecarboxaldehyde **16**, hexanoic acid (I.S.), manganese(III) acetylacetonate, methyl *p*-tolyl sulfide, methyl *p*-tolyl sulfoxide, N-hydroxyphthalimide (NHPI) and N-methylimidazole (NMI) **9** were used as obtained from the suppliers. Aldehydes were stored at 4°C with protection from light. Oxygen (99.9999%) was supplied from Air Liquide.

The gas pump was an RS PRO diaphragm positive displacement pump with a maximum flow rate of 380mL/min and a maximum working pressure of 11 psi (Ref N° RS 702-6898).

GC-FID was performed using a Shimadzu NEXIS GC-2030 gas chromatograph instrument with an FID detector and a DB-FFAP column (10 m x 0.1 mm x 0.1 µm). GC-MS was performed using a Shimadzu GC-MS-QP2010 SE instrument equipped with a DB-FFAP column (10 m x 0.1 mm x 0.1 µm).

The products and main by-products were identified by comparing them with authentic samples or using GC-MS for enoic acids **25**. Calibration curves of the products and main by-products were performed using hexanoic acid as an internal standard.

3. Experimental setup

Since the oxidation reaction occurs in the liquid phase, an adequate mass of oxygen is critical.^{1,2} It has already been shown that aerobic oxidations are often carried out in a mass transfer-limited regime, *i.e.*, the reaction rate is limited by the oxygen mass transfer.^{2,3} Since the oxygen solubility in common solvents is low and decreases with temperature,⁴ a gas pump was used in our experiments. The small gas pump (RS PRO diaphragm positive displacement pump) continuously pumps the oxygen atmosphere above the reaction mixture and re-injected it into the organic phase via a frit (Figure S 1). For aerobic oxidation, acetonitrile is a first choice, suitable aprotic polar solvent⁵ even if better selectivity are obtained using heptane.²

The temperature of the solution is also critical since highly temperature-sensitive intermediates (*i.e.*, peracid **10**) are formed. To minimize unwanted decomposition of **10**, the temperature of the reaction mixture of the different experiments should be comparable. The reaction is sluggish at a low temperature (<10°C);⁶ thus, the water bath temperature was set at 20°C. Despite the relatively low aldehyde concentration (< 1M), without a water bath, a raise of about 5 to 7°C could be observed for specific conditions, leading to a significant variation in selectivity. Using a water bath, the temperature variation was below 2°C, ensuring good reproducibility.

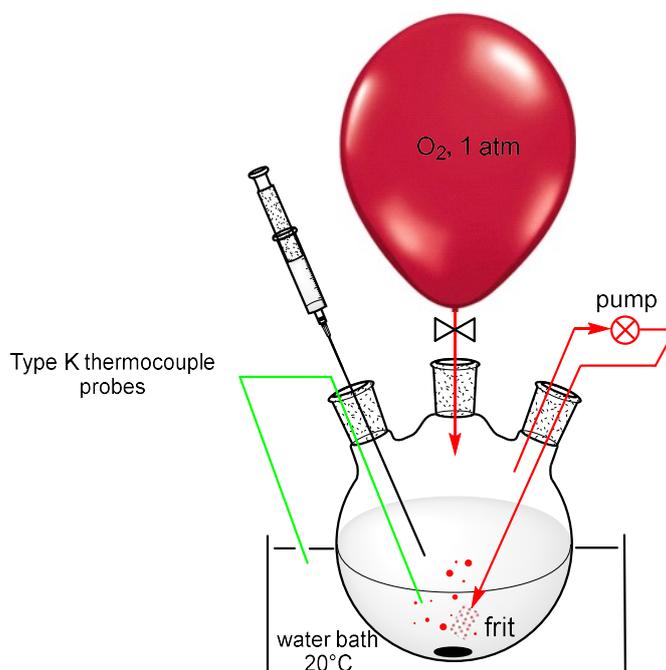


Figure S 1 Experimental setup for the aerobic oxidation of the 2-ethylhexanal **1**

4. Uncatalyzed aerobic oxidation of 2-ethylhexanal 1 in acetonitrile as the function of time

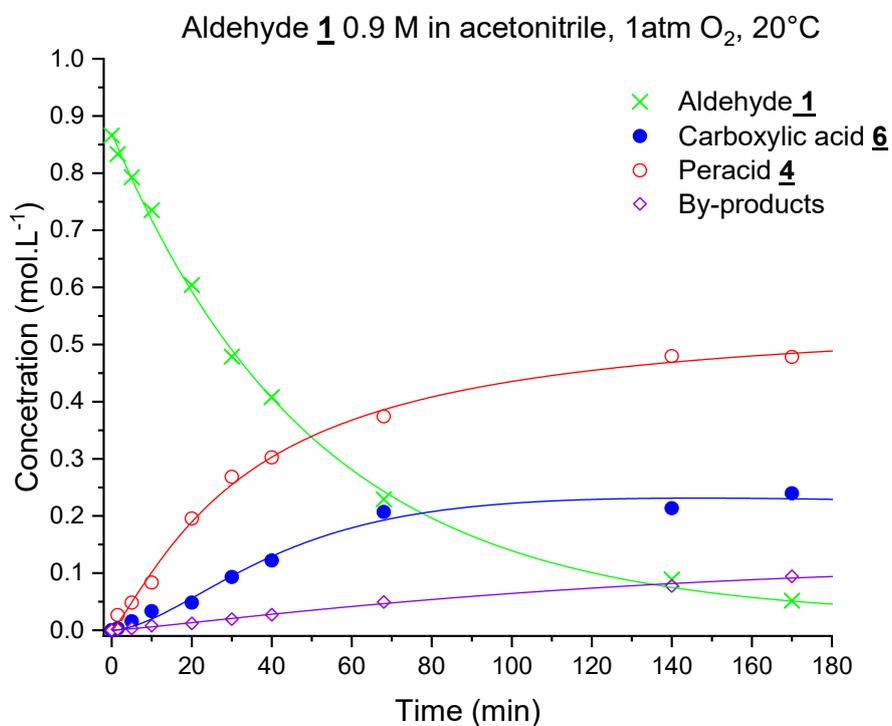


Figure S 2. Concentrations as a function of time during uncatalyzed aerobic oxidation of 2-ethylhexanal 1. Reactions conditions: 1 0.9M in acetonitrile, O₂ (1 atm), 20°C. The concentration of peracid 4 was determined on an aliquot using methyl *p*-tolyl sulfide in 1M in EtOH (1:1 vol.). Lines were added to guide the eye.

5. Uncatalyzed aerobic oxidation of 2-ethylhexanal 1 in heptane as the function of time

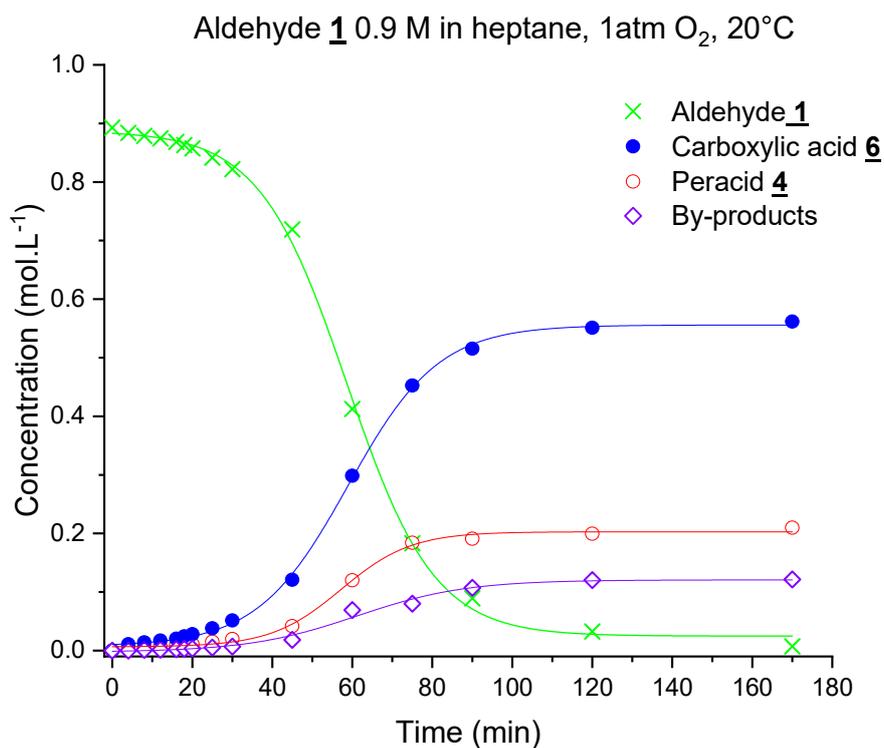


Figure S 3. Concentrations as a function of time during uncatalyzed aerobic oxidation of 2-ethylhexanal 1 in heptane. Reactions conditions: 1 0.9M in **heptane**, O₂ (1 atm), 20°C. The concentration of peracid 4 was determined on an aliquot using methyl p-tolyl sulfide in 1M in EtOH (1:1 vol.). Lines were added to guide the eye.

6. Structure and distribution of the by-products observed during the aerobic oxidation of 2-ethylhexanal 1

The products and the formation of by-products during the aerobic oxidation of 2-ethylhexanal 1 have been studied in detail in a previous publication.⁷ Formate SA is produced by the rearrangement of the Criegee intermediate 5 (Scheme 1). The formation of compounds SB to SE depends highly on the reaction conditions during the decomposition of the peracid 4. In particular, dissolved oxygen favored the formation of SC over SB. Temperature, presence of water, and MgSO₄ also impact the distribution of the by-products SB to SE. However, the selectivity toward the carboxylic acid 6 was directly related to the amount of peracid 4 in the crude reaction mixture at the total conversion of the aldehyde 1.

For safety reasons, we found that a pulse of Mn(II) catalyst (100 ppm, 0.01 mol%) at the end of the reaction allow the total transformation of peracid 4 into the corresponding carboxylic acid 6 with a selectivity of 50%. This procedure is effective and safe and gives reproducible results (\pm 5%). The peracid-free solution obtained could be further concentrated and purified.

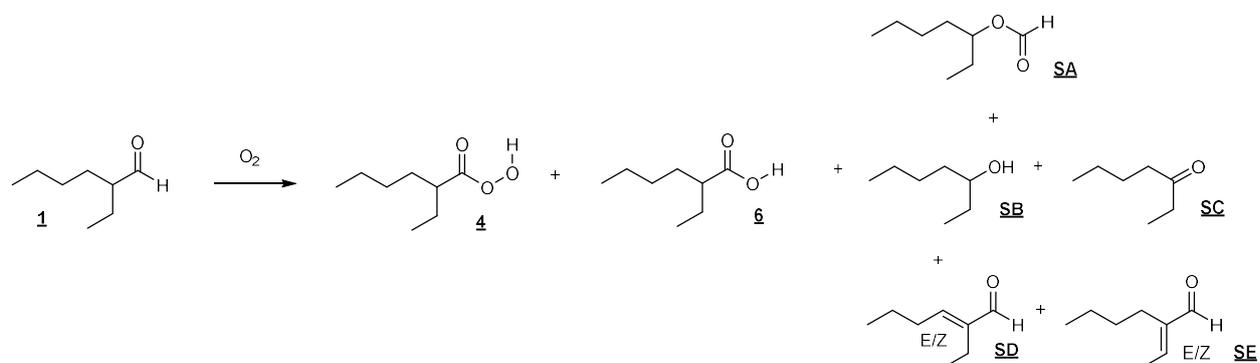


Figure S 4. Structure of the by-products observed during the aerobic oxidation of 2-ethylhexanal 1

7. Catalytic aerobic oxidation of 2-ethylhexanal **1** in acetonitrile as the function of time

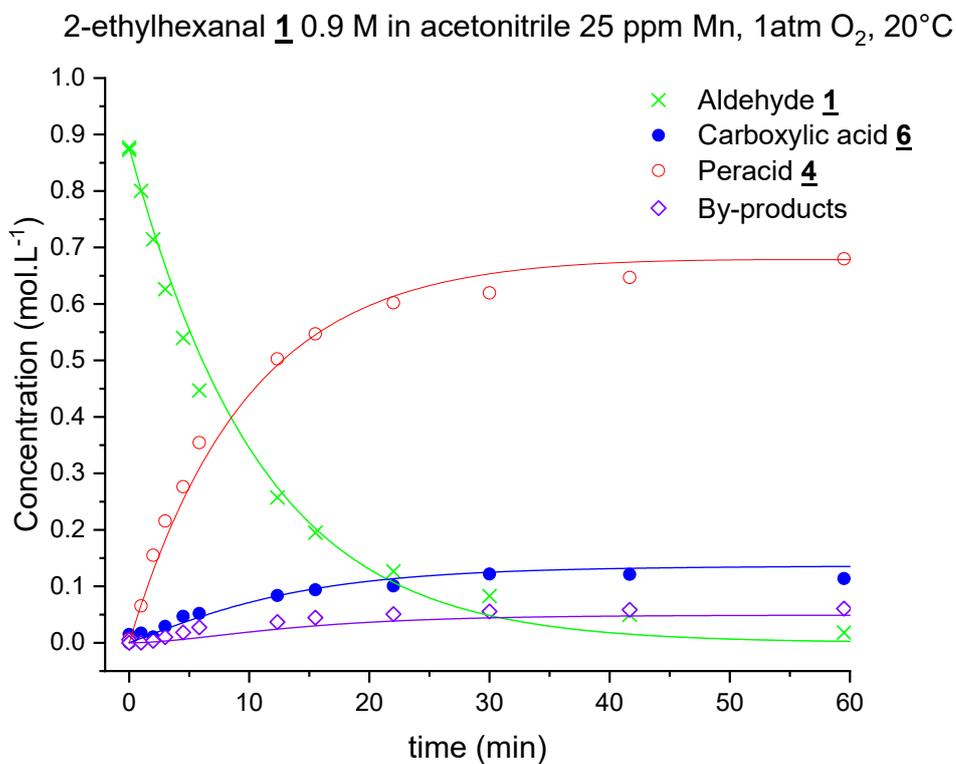


Figure S 5. Aerobic oxidation of 2-ethylhexanal **1** using Mn as the catalyst as the function of time using ex-situ G.C. monitoring. Reaction conditions: **1** 0.9 M in acetonitrile, O₂ (1 atm), Mn(II) 25 ppm (0.0025 mol %), room temperature. The concentration of peracid **4** was determined on an aliquot using methyl p-tolyl sulfide in 1M in EtOH (1:1 vol.). Lines were added to guide the eye.

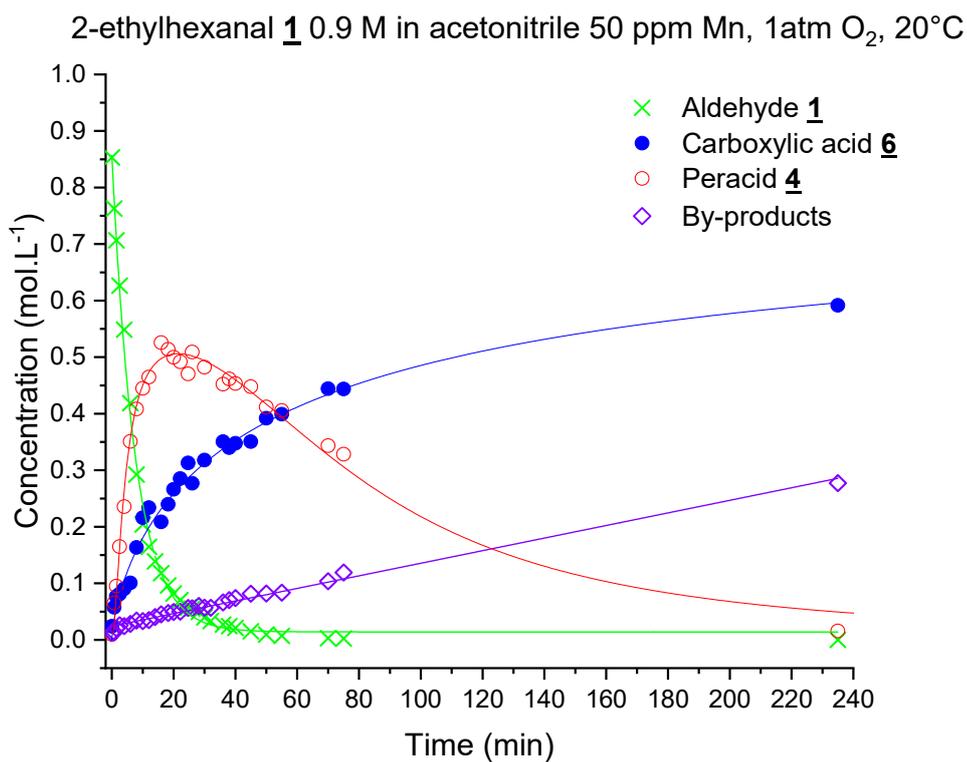


Figure S 6. Aerobic oxidation of 2-ethylhexanal **1** using Mn as the catalyst as the function of time using ex-situ G.C. monitoring. Reaction conditions: **1** 0.9 M in acetonitrile, O₂ (1 atm), Mn(II) 50 ppm (0.005 mol %), room temperature. The concentration of peracid **4** was determined on an aliquot using methyl p-tolyl sulfide in 1M in EtOH (1:1 vol.). Lines were added to guide the eye.

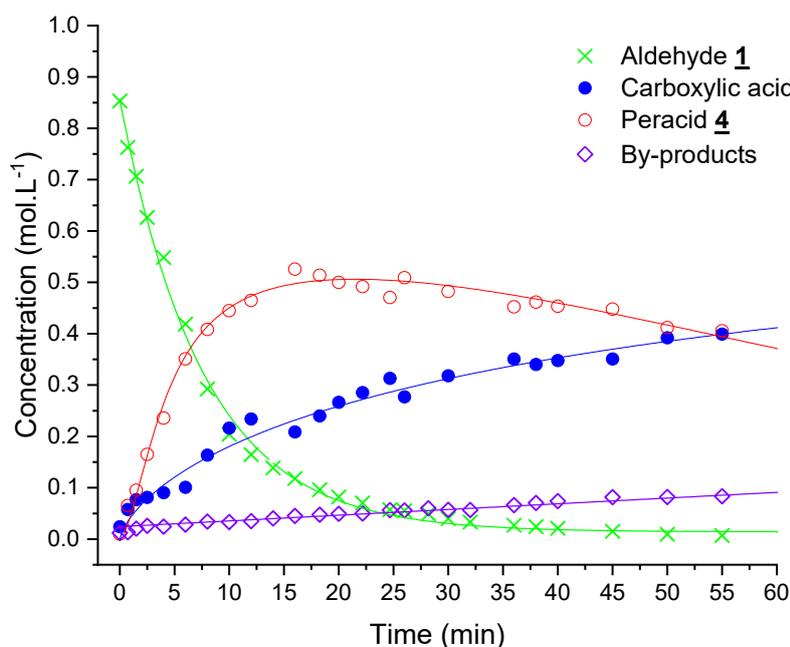


Figure S 7. Zoom of the Figure S 6

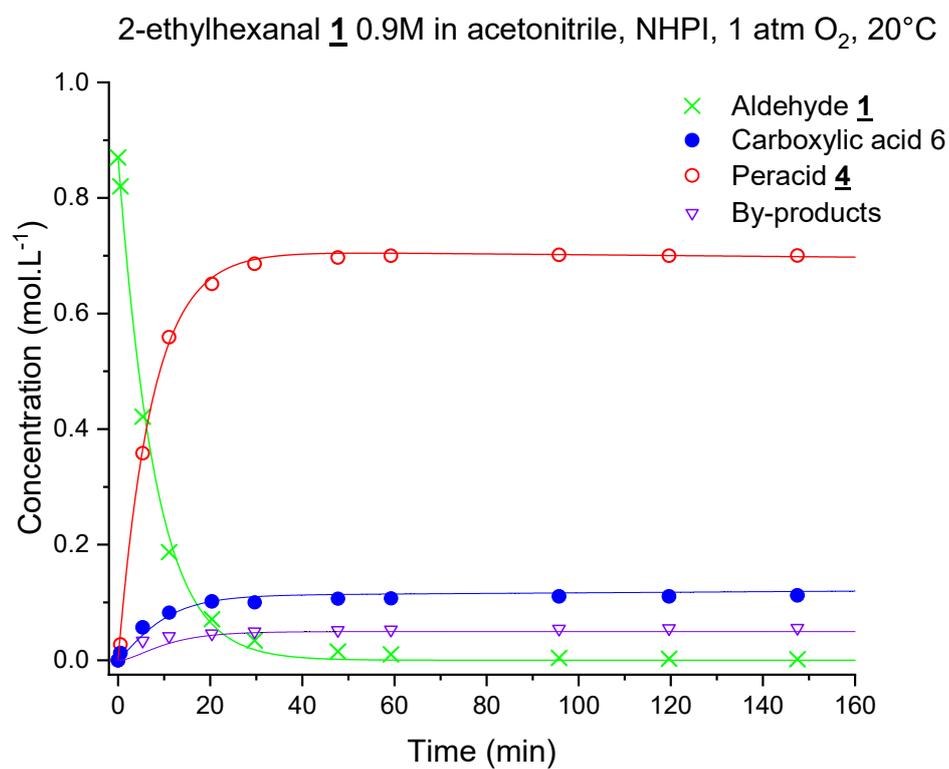


Figure S 8. Aerobic oxidation of 2-ethylhexanal **1** catalyzed by NHPI. Reactions conditions: Aldehyde **1** 0.9M in acetonitrile, O₂ (1 atm), 20°C, NHPI 4 mol%. The concentration of peracid **4** was determined on an aliquot using methyl p-tolyl sulfide in 1M in EtOH (1:1 vol.). Lines were added to guide the eye.

8. Catalytic aerobic oxidation of 2-ethylhexanal 1 in heptane as the function of time

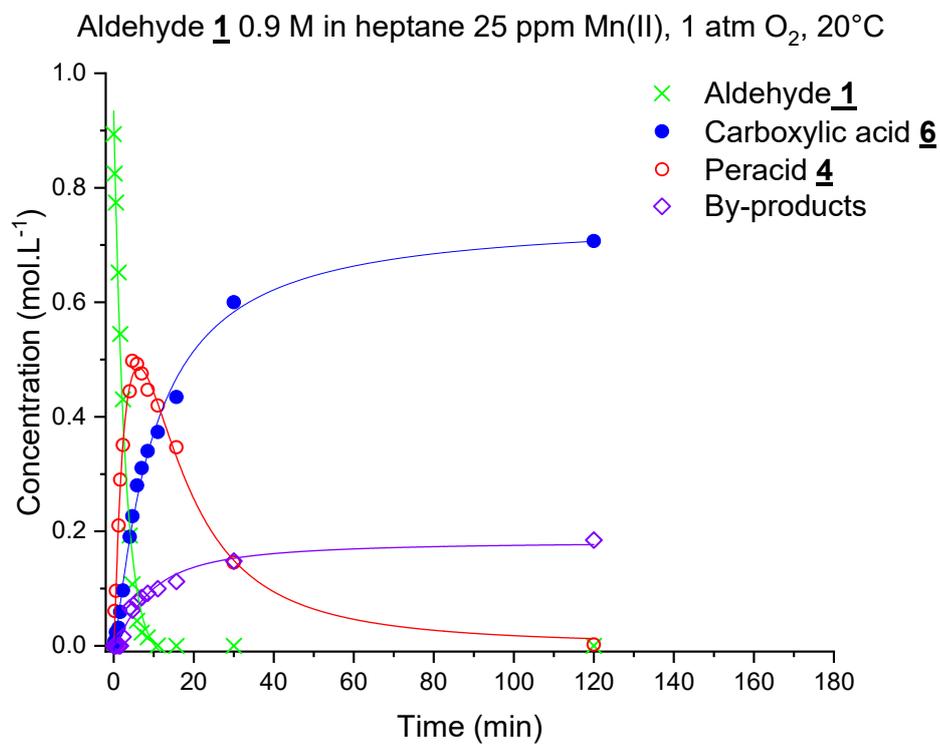


Figure S 9. Concentrations as a function of time during catalyzed aerobic oxidation of 2-ethylhexanal 1. Reactions conditions: 1 0.9M in heptane, 25 ppm Mn(II), O₂ (1 atm), 20°C. The concentration of peracid 4 was determined on an aliquot using methyl p-tolyl sulfide in 1M in EtOH (1:1 vol.). Lines were added to guide the eye.

9. Aerobic oxidation of 2-ethylhexanal **1** catalyzed by NHPI with a pulse of NMI at 4 min

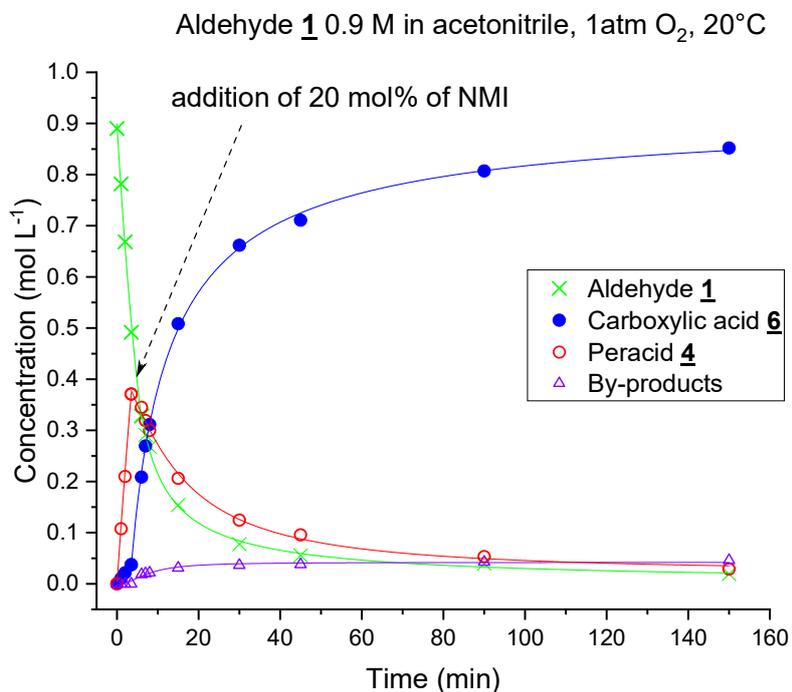


Figure S 10 Reactions conditions: Aldehyde **1** 0.9M in heptane, O₂ (1 atm), 20°C, NHPI 4 mol%. After 4 min, a pulse of NMI (2 wt%) was added. The concentration of peracid **4** was determined on an aliquot using methyl p-tolyl sulfide in 1M in EtOH (1:1 vol.). Lines were added to guide the eye.

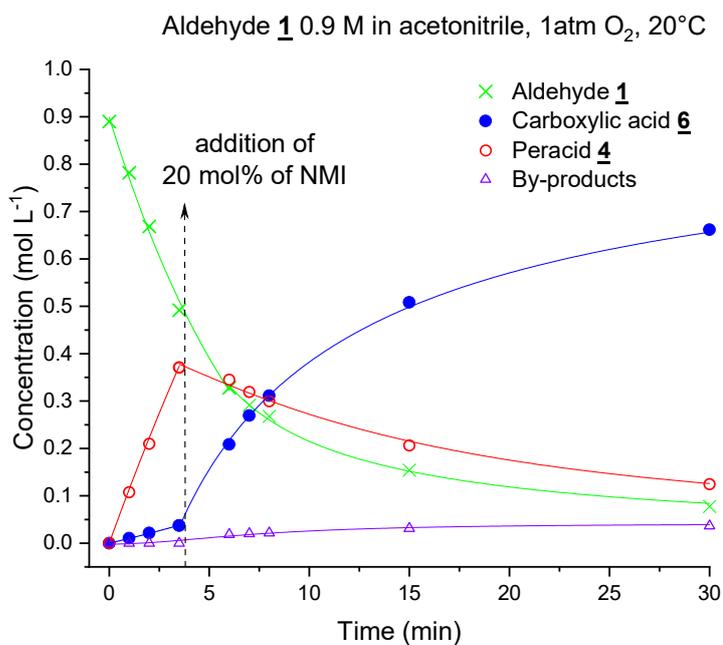


Figure S 11: Zoom of the Figure S9.

10. Aerobic oxidation of 2-ethylhexanal **1** in heptane as the function of time using 25 ppm of Mn as catalyst and 20mol% of NMI as an additive

Aldehyde **1** 0.9 M in acetonitrile, 50 ppm Mn(III), 20 mol% NMI, 1atm O₂, 20°C

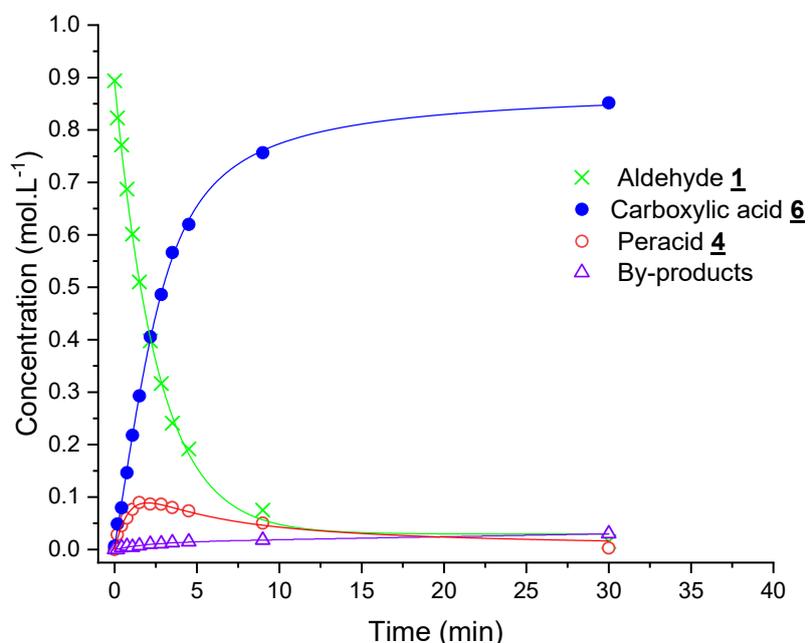


Figure S 12. Aerobic oxidation of 2-ethylhexanal **1** in heptane using 25 ppm of Mn(II) and 20 mol% of NMI. Reactions conditions: **1** 0.9M in heptane, O₂ (1 atm), 20°C, 0.0025 mol% Mn(II), 20 mol% of NMI. The concentration of peracid **4** was determined on an aliquot using methyl *p*-tolyl sulfide in 1M in EtOH (1:1 vol.). Lines were added to guide the eye.

11. References

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