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

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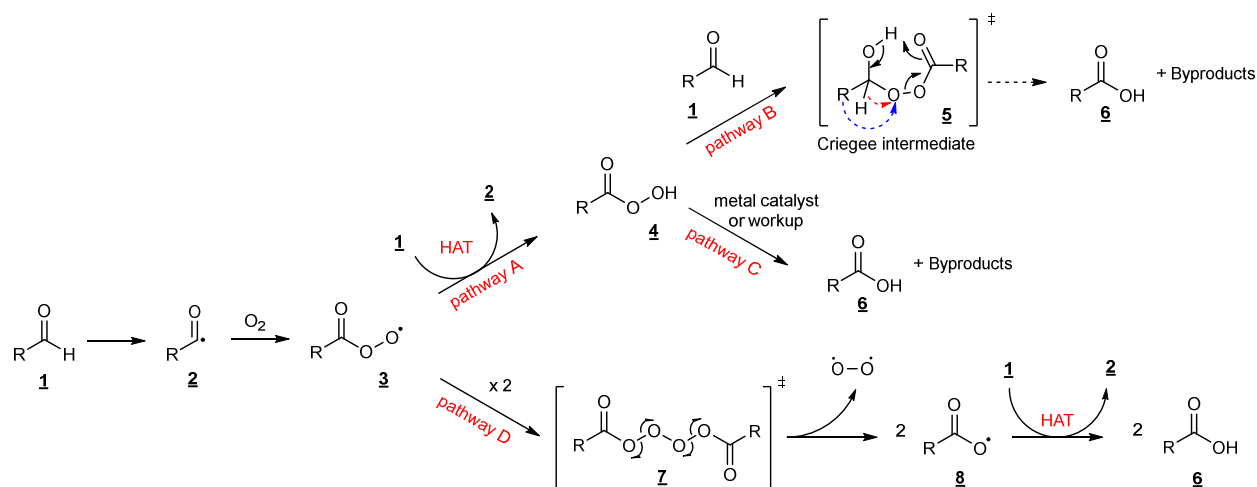
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During the aerobic oxidation of aldehydes, peracids accumulate in the reaction mixture. From a safety and selectivity perspective, the quantification and transformation of the peracids into the corresponding carboxylic acids are of vital importance in both laboratory and industrial applications. The presence of peracids in the crude reaction mixture is directly correlated with the selectivity of the oxidation, especially for β -substituted aliphatic aldehydes. We show that 20 mol% of carboxylate salts, added at the beginning of the reaction or generated *in situ*, catalyzed the selective transformation of the peracids into carboxylic acids and strongly increased the selectivity towards carboxylic acid without decreasing the chemical rate. This methodology increased the safety of the process by preventing the build-up of peracids in the course of the reaction. Otherwise, for aliphatic aldehydes, peracids are non-selectively decomposed during the course of the experiment or workup. We proposed that the presence of carboxylate salt in the reaction mixture improves aerobic oxidation's selectivity by forming a percarboxylate anion. The latter leads to the selective conversion of peracid into the corresponding carboxylic acid.

1. Introduction

It was recognized more than 190 years ago that aldehydes are prone to aerobic oxidation.^{1,2} In 1900, Bayer and Villiger³ hypothesized that the reaction was not a single-step process and that the first intermediate is peracid **4**. In 1927, Bäckstrom⁴ suggested the currently accepted free radical chain mechanism (autoxidation) for the formation of peracid **4** from acyl radical **2**. **2** reacts with triplet oxygen (³O₂) to form acylperoxy radical **3** (Scheme 1).^{5,6} Peracid **4** is formed by H-abstraction on remaining aldehyde **1**, regenerating the acyl radical **2** (Scheme 1, pathway A). To explain the formation of carboxylic acid **6** from peracid **4** and the formation of by-products, a mechanism similar to the Baeyer-Villiger oxidation of ketones was proposed via a Criegee intermediate **5** (Scheme 1,

pathway B).⁷ Recently, we have challenged this general mechanism. We have shown that pathway B, via the Criegee intermediate, could be neglected for aliphatic and aromatic aldehydes.⁸ In particular, we^{8,9} and others^{10,11} have shown that the peracid **4** accumulated in the reaction mixture. Peracid **4** is converted into carboxylic acid **6** during workup (Scheme 1, pathway C) or using a metal catalyst. We have also demonstrated that without high loading of metal catalyst, the carboxylic acid **6** does not only originate from the decomposition of the peracid **4** (Scheme 1, pathway B), but by dimerisation of **3** leading to the formation of the intermediate **7** (Scheme 1, pathway D). Rearrangement of **7** lead to the formation of two acyloxy radical **8** and oxygen triplet (³O₂). Carboxylic acid **6** is then formed by H-abstraction on remaining aldehyde **1**, generating the acyl radical **2** and carboxylic acid **6**.⁸



Scheme 1. General pathway of autoxidation of aldehydes **1** into carboxylic acid **6**

Recently, the presence of peracids in the reaction medium at complete conversion has been addressed in different ways:

- an excess of metal catalyst (> 1mol%) was added to the reaction mixture to decompose the peracid **4** into the corresponding carboxylic acid **6**.⁸
- the reaction mixture was heated to 100°C under O₂ pressure with a residence time of 20 min.¹⁰ Under those conditions, as the dissociation energy of the peroxy bond of peracids is low (*ca.* 50 kcal mol⁻¹),¹² the peracid **4** formed *in situ* is decomposed. This procedure is only possible in a continuous flow reactor for safety reasons.
- Kokotos et al. used acetone as a solvent.¹¹ They showed that acetone reacted with peracid **4** to form the corresponding acid **6** and dioxirane, which serves as a co-oxidant.

Nevertheless, the problem of selectivity for aliphatic aldehydes, particularly for β -substituted aliphatic aldehydes remains.^{8,10,11,13-17} A carboxylic acid selectivity between 70% and 90% without additives was

observed for 2-ethylhexanal **1**, an industrially important chemical intermediate.¹⁸ It has already been shown that the selectivity towards 2-ethylhexanoic acid **6** was also dependent on the solvent.^{8, 10, 13, 14, 17} On the other hand, the oxidation of aromatic aldehydes and linear aliphatic aldehydes are highly selective (> 95%), even if high concentrations of peracids are found during the reaction.⁹ It should be mentioned that selectivities were determined after workup or by GC analysis of the crude. Under those conditions, peracid **4** was decomposed more or less selectively into the carboxylic acid **6**, which could explain the yield fluctuation observed.¹⁵ Thus, the aerobic oxidation of 2-ethylhexanal **1**, an aldehyde of industrial importance with one of the lowest selectivity toward carboxylic acid,^{14, 15} was further studied at 20°C and under 1 atm of O₂ with different solvents, i.e., acetonitrile and heptane.

2. Experimental

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.

Furthermore, a relatively high concentration of peracids is formed during the aerobic oxidation of aldehydes. The bond dissociation energy of the peroxy bond of peracids is low (ca. 50 kcal.mol⁻¹).¹² As a consequence, peracids can decompose spontaneously and explosively under thermal or mechanical stress (shock, sparks, ...). As such, the concentration of aldehyde should be low (< 1M), and strict control of the reaction mixture's temperature and the reaction's local environment should be set up. Aerobic oxidation could be performed at higher temperatures and concentrations but require specific experimental setups and skills (*i.e.*, microreactors¹⁹⁻²¹).

Typical procedure

Aldehyde (90 mmol) was weighed in a 250 mL round bottom flask equipped with a stirring bar. A solution of hexanoic acid (internal standard, 0.1 M) in the solvent (100 mL) was added. Frit (Interchim 821760), type K thermocouple probes were adapted to the round bottom flask (Figure S1). A solution of catalyst and N-methylimidazole (NMI) **9** could be added at this point. A sample was taken for *ex-situ* analysis, and the air atmosphere was replaced by oxygen. A constant oxygen pressure was then ensured by using a balloon. The stirring and the gas pump were turned on, and 500 µL samples

(Hamilton Syringes Microlite series 700) were taken regularly and diluted with 500 μL of 1 M methyl *p*-tolyl sulfide in ethanol, mixed and analyzed by GC-FID and GC-MS.

3. Results and discussion

3.1. Influence of the solvent on the distribution of the products and by-products

The reactions were performed with an efficient mass transfer of O_2 (see supporting information) to avoid the formation of by-products via decarboxylation and decarbonylation processes.²² The evolution of the concentration as the function of time for acetonitrile and heptane can be found in the supporting information (Figure S2 and Figure S3). A ternary plot could be used to compare better the solvent's effect on selectivity (Figure 1), but the concentration of by-products must be neglected in this representation. Nevertheless, it should be noticed that the concentration of by-products is lower than 10% for conversions lower than 75%, and the formation of by-products was taken into account using circles, the circle radius being proportional (%) to the concentration of by-products.

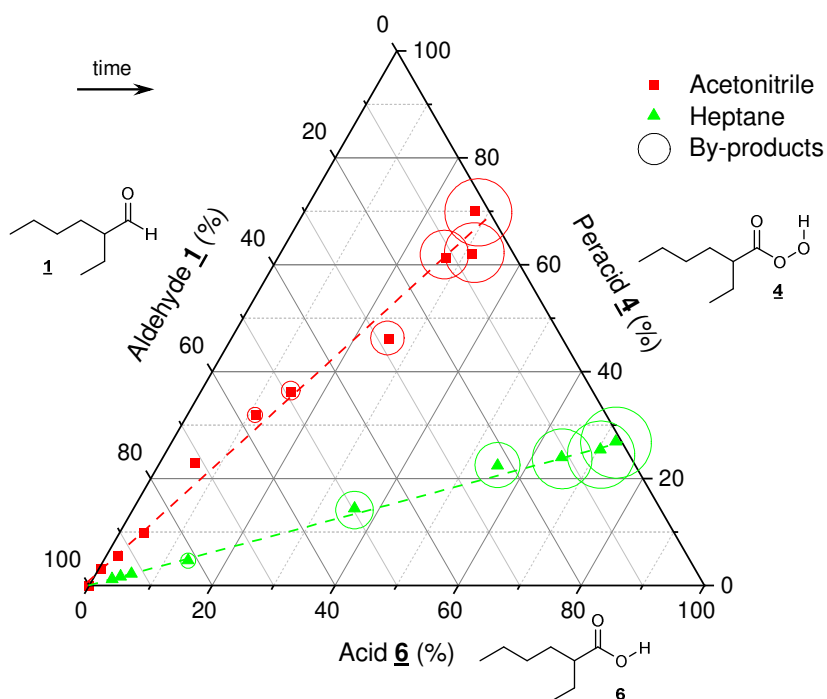


Figure 1. Ternary plot of the uncatalyzed aerobic oxidation of 2-ethylhexanal **1** as the function of solvent. Reactions conditions: **1** 0.9M in acetonitrile or heptane, O_2 (1 atm), 20°C. The concentration of peracid **4** was determined on an aliquot using methyl *p*-tolyl sulfide in 1M in EtOH (1:1 vol.). The radius of the circle is proportional to the percentage of by-products. The experimental error is $\pm 2\%$. The concentration of **1**, **4**, **6**, and by-products as the function of time and solvent could be found in the supporting information (Figure S2 and Figure S3).

Without a catalyst, dark aerobic oxidation of **1** occurs in less than 3 hours (Figure S2 and Figure S3) regardless of the solvent. However, the composition of the reaction mixture as the function of time (Figure 1) was influenced by the solvent. A higher amount of peracid **4** was obtained in acetonitrile, i.e., ~75% of the aldehyde **1** is oxidized into peracid **4**, whereas only ~25% of the aldehyde **1** is oxidized into peracid **4** in heptane (Figure S2 and Figure S3). For both solvents, a straight line could be drawn in the ternary plot (Figure 1), indicating that a constant ratio of acid/peracid was formed as the function of the conversion. The products, and among them the peracid **4**, are relatively stable as a function of time (Figure S2 and Figure S3). Such results highlighted that, as expected,⁸ acid **6** and peracid **4** are formed simultaneously (Scheme 1, pathway A and D), i.e., acid is not a product of the rearrangement of peracid **4** via Criegee intermediate **5** (Scheme 1, pathway B) or a decomposition product of the peracid **4** (Scheme 1, pathway C).

As already mentioned, the crude reaction mixture's composition highly depends on the solvent (Figure 1 and Figure 2). For aldehyde **1** conversion > 98%, the concentration of by-products in both solvents are similar, i.e., ~15%, but the amount of peracid **4** in acetonitrile is very high compared to heptane, i.e., 62 and 24 % respectively (Figure 2). For safety reasons, a workup procedure should be used to eliminate the peracid **4**. We tried several different workups for the selective decomposition of the peracid **4** into the corresponding carboxylic acid **6**. This step's outcome depended on the experimental conditions (solvent, removal of dissolved oxygen, temperature control, addition of catalyst, or use of stoichiometric reductant). The structure of the main by-products can be found in the supplementary information (Figure S4). However, the variability of these processes is high and induces waste generation. We found that a pulse of Mn(III) 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** (Figure 2). This procedure is effective, safe, and gives reproducible results.⁸

Thus, using a pulse of Mn(III) catalyst, the selectivity of the catalytic conversion of peracid **4** into the carboxylic acid **6** was also dependent on the solvent, i.e., 47% and 86% in acetonitrile and heptane, respectively. Under those conditions, a selectivity of 82% for the carboxylic acid **6** in heptane was obtained following previous results.^{15, 23}

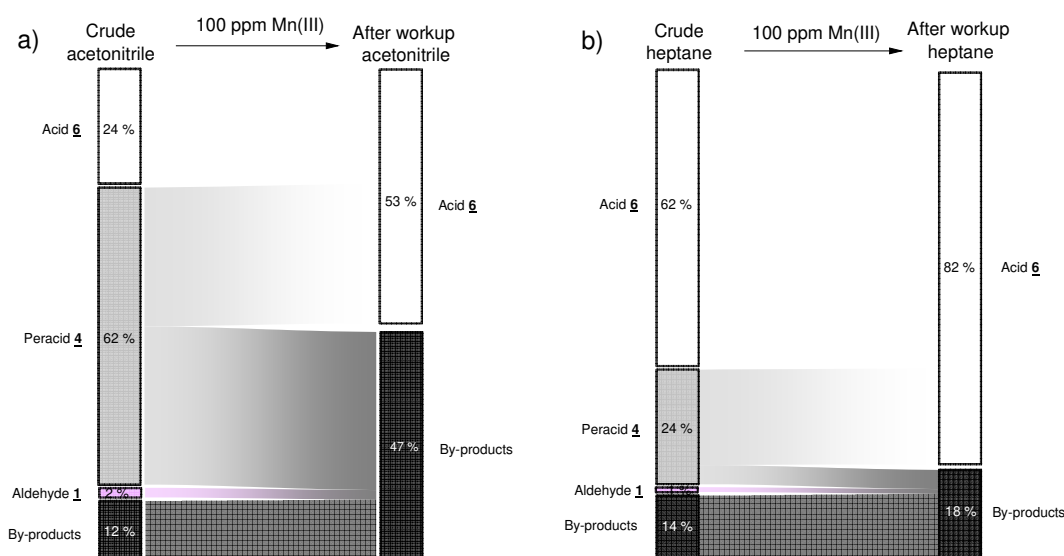


Figure 2. Composition of the crude reaction mixture at 180 min (**1** conversion ~ 98%) and after the addition of a pulse of 100 ppm of Mn(III) (0.01%) for each solvent. Reactions conditions: **1** 0.9M in acetonitrile or heptane, O₂ (1 atm), 20°C. The concentration of peracid **4** was determined on an aliquot using methyl *p*-tolyl sulfide in 1M in EtOH (1:1 vol.). The following assumptions are made to construct the graph: **6** and by-products do not react under these experimental conditions; **4** can only lead to the formation of **6** and by-products; **1** is only transformed into by-products. The experimental error is ±2%.

From these experiments, one can conclude that the conversion of peracid **4** into carboxylic acid **6** is a substantial source of by-products (Figure 2). This step could be improved, but we thought that minimizing the amount of peracid **4** during the aerobic oxidation of aldehyde **1** is critical to increasing the selectivity towards carboxylic acid **6**. As such, the solvent and catalyst's influence on the reaction's selectivity was further studied.

3.2. Influence of catalyst and solvent on the selectivity of the reaction

We have already shown the effect of catalyst on the concentration of the products in acetonitrile.⁸ We further study the catalyst's influence in heptane and acetonitrile (Figures S5 to S9). However, as previously mentioned,^{8, 14, 15} these different conditions did not significantly improve selectivity towards the carboxylic acid **6**. The best results were obtained in heptane (0.9 M) using 25 ppm of Mn(III) (Figure S9). After 60 min, total conversion was obtained, and a selectivity of 80 % in carboxylic acid **6** was obtained. This selectivity is comparable to metal-free aerobic oxidation after the addition of a pulse of 100 ppm of Mn(III) (*i.e.*, 82%, see Figure 2b). In acetonitrile, using NHPI as a catalyst, up to 70 % of peracid **4** are formed with less than 10% of carboxylic acid **6** (Figure S8). The selectivity towards carboxylic acid **6** was 72% using 50 ppm of Mn(III) in acetonitrile (Figure S 6). The selectivity was much higher than the selectivity observed with metal-free aerobic oxidation after the addition of a pulse of

100 ppm of Mn(III) (*i.e.*, 53%, see Figure 2a). The selectivity of decomposition of the peracid **4** under those conditions is linked with the initial concentration of the latter. From these results, one can conclude that the presence of a catalyst influences the concentration of peracid **4**, but the impact on selectivity toward carboxylic acid **6** was weak.

3.3. Influence of carboxylate on the aerobic oxidation of the aldehyde **1**

The influence of alkali metal salts or carboxylate on the selectivity of aerobic oxidation of aliphatic aldehydes has been claimed in patents²⁴⁻²⁶ and was recently studied using macroporous alkaline resins.¹⁶ Such salts are supposed to inhibit undesired reactions.²⁵ Even if a publication has questioned the influence of salts,¹³ we have reproduced these results in solution¹⁵ or neat using microreactors.²⁷ A selectivity higher than 98% towards acid **6** was obtained using 2 wt% of sodium 2-ethylhexanoate.¹⁵ ²⁷ Despite our efforts, we could not understand the "inhibition" of the formation of by-products by the sodium salts. The selectivity was increased, up to 98%,¹⁵ but we have no mechanistic hypothesis. However, we had not yet demonstrated the formation of large amounts of peracid during this reaction.^{8,9} We aimed to study more precisely the influence of salts on the composition of the reaction medium and, in particular, the peracid at the function of time. Sodium 2-ethylhexanoate is a powder soluble in aldehyde²⁷ but hardly soluble in a dilute aldehyde solution in heptane or acetonitrile. N-methylimidazole **9** (NMI) is an organic base soluble in most solvents. In the presence of a carboxylic acid, like **6**, a carboxylate salt **12** will be formed.

To test our hypothesis, NHPI was used as a catalyst to eliminate the catalytic degradation of the peracid as far as possible.^{8,9} Under those conditions, up to 72 % of peracid **4** are formed and 12% of by-products (Figure S8). As expected (Figure 3), the concentration of peracid **4** increased strongly in the first min of the reaction, much more than the acid concentration. After 4 min, the conversion of **1** was close to 50%, with selectivity for peracid **4** of 90% and 10 % for acid **6** (Figure 3 and Figure S11). Only traces amount of by-products could be detected in the reaction mixture. Then, a pulse of 20 mol% of NMI **9** was added to the reaction mixture. The concentration of peracid **4** suddenly drops, whereas the concentration of carboxylic acid **6** increases. After less than 3h (Figure S10), the total conversion of aldehyde was achieved. We were pleased to see that using 20 mol% of NMI **9**, the amount of peracid **4** and by-products was below 5%. A selectivity to carboxylic acid up to 90% could be obtained under those conditions.

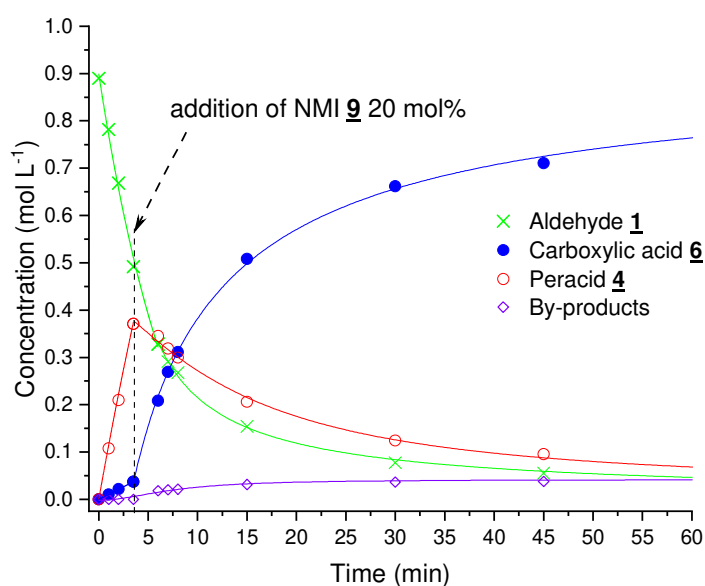
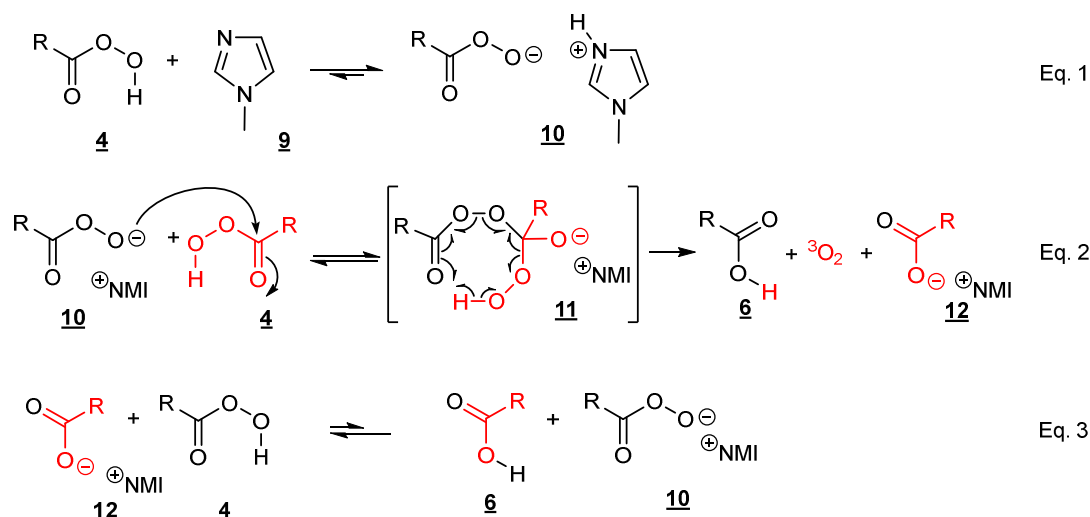


Figure 3. Concentrations as a function of time during sequential aerobic oxidation of 2-ethylhexanal **1** catalyzed by NHPI. Reactions conditions: Aldehyde **1** 0.9M in heptane, O₂ (1 atm), 20°C, NHPI 4 mol%. After 4 min, a pulse of NMI **9** (20 mol%) was added. The concentration of peracid **4** was determined on an aliquot using methyl *p*-tolyl sulfide in 1M in EtOH (1:1 vol.). The experimental error is $\pm 2\%$. The concentration of **1**, **4**, **6**, and by-products as the function of time for longer reaction time could be found in the supporting information (Figure S10 and Figure S11) and the comparison of the reaction without NMI **9** (Figure S8). Lines were added to guide the eye.

Such a result could be explained by a mechanism studied in the 1960s for the spontaneous decomposition of peracids in an aqueous solution.²⁸⁻³⁰ Experiments using a mixture of doubly labeled ¹⁸O peracid and unlabelled peracid have made it possible to propose a predominant pathway.²⁹ An adaptation of the mechanism is presented in Scheme 2.



Scheme 2. Percarboxylate anion **10** formation and selective decomposition of peracid **4** adapted from E. Koubek et al. ^{28, 29} Another pathway that accounts for ~15% was also described (see text).

In the presence of NMI **9**, peracid **4** will form percarboxylate anion **10** (Eq. 1). Nucleophilic attack of **10** upon the carbonyl group of the peracid **4** lead to the formation of intermediate **11**. Rearrangement of the latter led to the formation of carboxylic acid **6**, carboxylate salt **12**, and triplet oxygen ($^3\text{O}_2$) (Eq. 2).^{28, 29} Another pathway was also described.²⁹ Percarboxylate anion **10** could also attack the outer peroxidic oxygen of **4**. For peracetic acid, the second pathway counted for about 15%, and these pathways were strongly dependent on the steric effect.²⁹ However, the products are the same, *i.e.*, carboxylic acid **6**, carboxylate salt **12**, and triplet oxygen ($^3\text{O}_2$). Regeneration of percarboxylate salt **10** and carboxylic acid **6** could be performed according to Eq. 3. However, the equation is strongly shifted to the left ($\text{pK}_a \mathbf{4} \approx 8$ vs. $\text{pK}_a \mathbf{6} \approx 5$ in water), and thus it could explain why relatively high amount (20 mol%) of NMI **9** or carboxylate **12**^{15, 27} are necessary.

To further probe this pathway, the aerobic oxidation of **1** was performed under the best condition, *i.e.*, 0.9 M in heptane, 25 ppm of Mn(III) as the catalyst, but 20 mol% of NMI **9** was added in the solution of aldehyde **1** (Figure S12). The evolution of the composition of the reaction mixture in the presence of NMI **9** is shown in Figure 4.

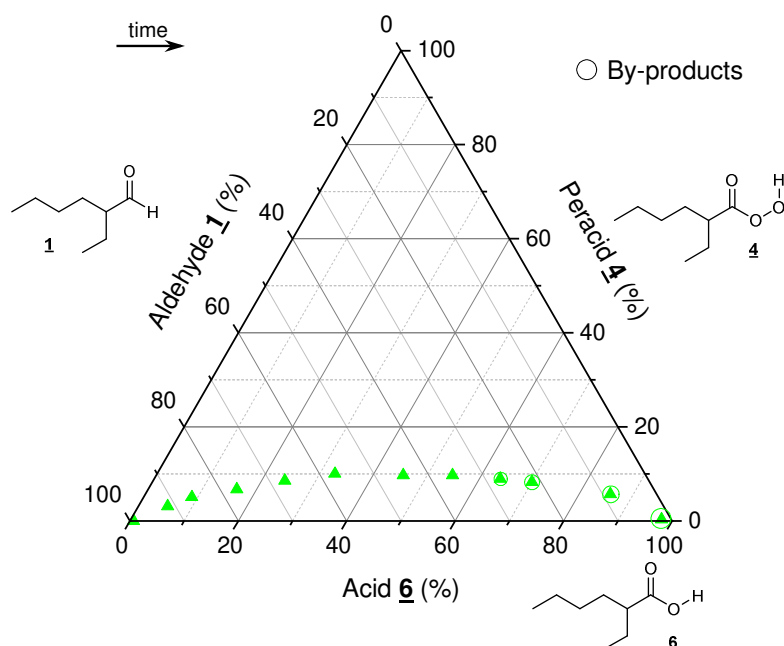


Figure 4. Ternary plot of the aerobic oxidation of 2-ethylhexanal **1** in heptane using 25 ppm of Mn(III) and 20 mol% of NMI **9**. Reaction conditions: **1** 0.9M in heptane, O₂ (1 atm), 20°C, 0.0025 mol% Mn(III), 0.2 eq of NMI **9**. The concentration of peracid **4** was determined on an aliquot using methyl *p*-tolyl sulfide in 1M in EtOH (1:1 vol.). The radius of the circle is proportional to the percentage of by-products. The experimental error is ±2%. The concentration of **1**, **4**, **6**, and by-products as the function of time and solvent could be found in the supporting information (Figure S12).

The composition of the reaction mixture as the function of conversion of aldehyde **1** is strongly impacted by the presence of NMI **9** and catalyst (Figure 1 vs. Figure 4). The maximum concentration of peracid **4** was below 10% (Figure 4 and Figure S14), whereas in the absence of NMI **9**, it was up to 50% (Figure 1, Figure S2, and Figure S6). Nevertheless, the most significant effect is shown in the concentration of by-products. Up to 25% of by-products could be observed in the absence of NMI **9** (figure S5), whereas using NMI **9**, the amount of by-products was below 3%. It should also be noticed that NMI **9** or carboxylate salt **12** does not influence the chemical rate of oxidation (See Figure S6 and Figure S12).

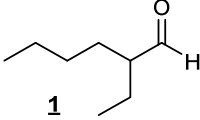
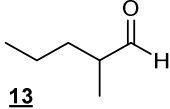
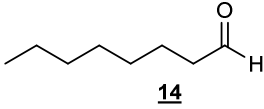
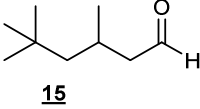
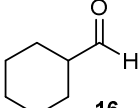
3.4. Scope and limitations

Selectivity problems in aldehyde autoxidation are limited to substituted aliphatic aldehydes. In the case of aromatic aldehydes, peracids are formed,⁹ but their decomposition is selective, unlike the aliphatic aldehydes. Acetonitrile was selected because of the low selectivity obtained compared to other solvents like heptane. NMI **9** is incompatible with NHPI and induces the formation of a red

complex which inhibits oxidation. Thus, 50 ppm Mn(III) was used as the catalyst. Under those conditions, the selectivity in acetonitrile obtained with 2-ethylhexanal **1** was low, i.e., 72% (Table 1, entry 1), compared to 82 % in heptane (Figure S9). It should be noticed that the selectivity observed in Figure 2 using a pulse of 100 ppm of Mn(III) is determined by the build-up of peracid **4** in the reaction mixture. The relatively low amount of Mn(III) (25 ppm) slowly decomposed the peracid **4** into the corresponding carboxylic acid **6** with a higher selectivity (Figure S9).

Using 20 mol% of NMI, the selectivity toward carboxylic acid was up to 95% for 2-ethylhexanoic acid **6** (Table 1, entry 1). This improvement is not observed for all carboxylic acids but remains noticeable (Table 1). The lowest improvement of the selectivity was obtained with 1-octanal **14** (Table 1, entry 3), since this oxidation was already selective without NMI **9** (94%). For the aliphatic aldehydes evaluated, the in situ formation of carboxylate **12** using NMI **9** improved the selectivity toward carboxylic acids. It should be noticed that the selectivity could be optimized further using different solvents, catalysts, and salts.

Table 1 Comparison of the selectivity obtained during the aerobic oxidation of aldehydes in acetonitrile with or without NMI ^{a)}

Entry	Aldehyde	Selectivity ^{b)}	Selectivity with NMI ^{b),c)}
1		72 %	97 %
2		71 %	84 %
3		94 %	96 %
4		88 %	97 %
5		83 %	96 %

^{a)} Reactions conditions: Aldehyde 0.9M in CH₃CN, O₂ (1 atm), 20°C, 0.0025 mol% Mn(III).

^{b)} Selectivity was determined by GC-FID at conversion > 98%. The experimental error is ±2%.

^{c)} 20 mol% of NMI **9** was added to the reaction mixture.

4. Conclusion

Thanks to efficient methods of monitoring the composition of the reaction medium as a function of time and, more particularly, the concentration of peracids, we were able to highlight the effect of percarboxylate anion on the selectivity of the aerobic oxidation of aliphatic aldehydes. The selective *in situ* decomposition of the formed peracid catalyzed by the percarboxylate anion makes it possible to obtain very high selectivities towards the acid, i.e., 97% vs. 72% without salts in less than 30 min. The conditions used (50 ppm (0.0050%) of Mn(III), room temperature, 20 mol% of carboxylate salts) are mild, and the safety is improved thanks to the elimination of the peracid **4**, which is continuously formed during this reaction. This methodology thus increased the safety of the process by preventing the build-up of peracids during the aerobic oxidation of both aliphatic and aromatic aldehydes. Furthermore, these results allow us to explain the salt effect described and claimed in publications and patents. The generality of this method offers the potential for safe and selective aerobic oxidation of aldehydes.

Conflicts of interest

There are no conflicts to declare.

Acknowledgments

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References

1. P. J. Robiquet and A. F. Boutron-Charlard, Nouvelles expériences sur les amandes amères et sur l'huile volatile qu'elles fournissent., *Ann. Chim. Phys.*, 1830, **44**, 352-382.
2. F. Wöhler and J. Liebig, Untersuchungen über das Radikal der Benzoesäure, *Justus Liebigs Ann. Chim.*, 1832, **3**, 249–282.
3. A. Baeyer and V. Villiger, Benzoylwasserstoffsperoxyd und die Oxydation des Benzaldehyds an der Luft, *Ber. Dtsch. Chem. Ges.*, 1900, **33**, 1569-1585.
4. H. L. J. Bäckström, The chain-reaction theory of negative catalysis, *J. Am. Chem. Soc.*, 1927, **49**, 1460-1472.
5. J. R. McNesby and C. A. Heller, Oxidation of Liquid Aldehydes by Molecular Oxygen, *Chem. Rev.*, 1954, **54**, 325-346.
6. P. A. A. van der Beek, The autoxidation of benzaldehyde, *Recl. Trav. Chim. Pays-Bas*, 1928, **47**, 286-300.
7. L. Sajus and I. Séré De Roch, in *Liquid-Phase Oxidation*, eds. C. H. Boamford and C. F. H. Tipper, Elsevier, Amsterdam, 1980, vol. 16, ch. 2, pp. 89-124.
8. L. Vanoye and A. Favre-Réguillon, Mechanistic Insights into the Aerobic Oxidation of Aldehydes: Evidence of Multiple Reaction Pathways during the Liquid Phase Oxidation of 2-Ethylhexanal, *Org. Process Res. Dev.*, 2022, **26**, 335-346.
9. L. Vanoye, M. Abdelaal, K. Grundhauser, B. Guicheret, P. Fongarland, C. De Bellefon and A. Favre-Réguillon, Reinvestigation of the Organocatalyzed Aerobic Oxidation of Aldehydes to Acids, *Org. Lett.*, 2019, **21**, 10134-10138.
10. B. S. Nagy, C. O. Kappe and S. B. Ötvös, N-Hydroxyphthalimide Catalyzed Aerobic Oxidation of Aldehydes under Continuous Flow Conditions, *Adv. Synth. Catal.*, 2022, **364**, 1998-2008.
11. C. S. Batsika, C. Koutsilieris, G. S. Koutoulogenis, M. G. Kokotou, C. G. Kokotos and G. Kokotos, Light-promoted oxidation of aldehydes to carboxylic acids under aerobic and photocatalyst-free conditions, *Green Chem.*, 2022, **24**, 6224-6231.
12. R. D. Bach and H. B. Schlegel, Bond Dissociation Energy of Peroxides Revisited, *J Phys Chem A*, 2020, **124**, 4742-4751.
13. C. Lehtinen and G. Brunow, Factors Affecting the Selectivity of Air Oxidation Of 2-Ethylhexanal, an α -Branched Aliphatic Aldehyde, *Org. Process Res. Dev.*, 2000, **4**, 544-549.
14. L. Vanoye, A. Favre-Reguillon, A. Aloui, R. Philippe and C. de Bellefon, Insights in the aerobic oxidation of aldehydes, *RSC Adv.*, 2013, **3**, 18931-18937.
15. L. Vanoye, M. Pablos, N. Smith, C. de Bellefon and A. Favre-Reguillon, Aerobic oxidation of aldehydes: selectivity improvement using sequential pulse experimentation in continuous flow microreactor, *RSC Adv.*, 2014, **4**, 57159-57163.
16. X. Fu, Y. Han, R. Chen, Q. Han, R. Zhang and J. Li, Selective oxidation of aldehydes by oxygen over macroporous alkaline resin, *React. Chem. Eng.*, 2022, **7**, 2427-2432.
17. Z. Wang, Y. Qin, H. Huang, G. Li, Y. Xu, P. Jin, B. Peng and Y. Zhao, Solvent Effect on Product Distribution in the Aerobic Autoxidation of 2-Ethylhexanal: Critical Role of Polarity, *Front. Chem.*, 2022, **10**, 855843.
18. R. Raju and K. Prasad, Synthetic applications of 2-ethylhexanoic acid derived reagents, *Tetrahedron*, 2012, **68**, 1341-1349.
19. A. Gavriilidis, A. Constantinou, K. Hellgardt, K. K. Hii, G. J. Hutchings, G. L. Brett, S. Kuhn and S. P. Marsden, Aerobic oxidations in flow: opportunities for the fine chemicals and pharmaceuticals industries, *React. Chem. Eng.*, 2016, **1**, 595-612.
20. C. A. Hone and C. O. Kappe, The Use of Molecular Oxygen for Liquid Phase Aerobic Oxidations in Continuous Flow, *Top. Curr. Chem.*, 2019, **377**, 1-44.
21. L. Wan, M. Jiang, D. Cheng, M. Liu and F. Chen, Continuous flow technology-a tool for safer oxidation chemistry, *React. Chem. Eng.*, 2022, **7**, 490-550.

22. B. B. Wentzel, P. L. Alsters, M. C. Feiters and R. J. M. Nolte, Mechanistic studies on the Mukaiyama epoxidation, *J. Org. Chem.*, 2004, **69**, 3453-3464.
23. L. Vanoye, A. Aloui, M. Pablos, R. Philippe, A. Percheron, A. Favre-Réguillon and C. de Bellefon, A safe and efficient flow oxidation of aldehydes with O₂, *Org. Lett.*, 2013, **15**, 5978-5981.
24. K. Fisher and G. Fritz, Synthesis of aliphatic C₂-C₂₂ carboxylic acids, US Patent N°5,504,229, BASF (Germany), (1996).
25. H. F. Koch and R. P. Reed, Oxidation process, Patent WO 01/46111, Celanese Int. Corp. (US), (2001).
26. D.-H. Ko, S.-G. Lee, O.-H. Kwon, J.-J. Moon, D.-C. Kim, J.-H. Choi, B.-K. Hong and S.-S. Eom, Preparation of organic acids from aldehyde compounds by means of liquid phase oxidation reaction US Patent 2007/0010688, LG CHEM, LTD., (2007).
27. L. Vanoye, J. Wang, M. Pablos, R. Philippe, C. de Bellefon and A. Favre-Réguillon, Continuous, fast, and safe aerobic oxidation of 2-ethylhexanal: pushing the limits of the simple tube reactor for a gas/liquid reaction, *Org. Process Res. Dev.*, 2016, **20**, 90-94.
28. E. Koubek, M. L. Haggett, C. J. Battaglia, K. M. Ibne-Rasa, H. Y. Pyun and J. O. Edwards, Kinetics and Mechanism of the Spontaneous Decompositions of Some Peroxoacids, Hydrogen Peroxide and t-Butyl Hydroperoxide, *J. Am. Chem. Soc.*, 1963, **85**, 2263-2268.
29. E. Koubek and J. E. Welsch, Base-catalyzed decomposition of peroxyphthalic acid in aqueous solution, *J. Org. Chem.*, 1968, **33**, 445-446.
30. R. E. Ball, J. O. Edwards, M. L. Haggett and P. Jones, A kinetic and isotopic study of the decomposition of monoperoxyphthalic acid, *J. Am. Chem. Soc.*, 1967, **89**, 2331-2333.