Origin of Byproducts during the Catalytic Autoxidation of Cyclohexane

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The formation of byproducts during the $Co(acac)_2$ and $Cr(acac)_3$-catalyzed cyclohexane autoxidation is compared with the noncatalyzed thermal process. Co^{II} ions seem to cause only a moderate perturbation of the reaction mechanism, causing a fast conversion of the cyclohexyl hydroperoxide via a redox cycle, rather than via abstraction of the αH-atom by chain carrying peroxyl radicals. Nevertheless, both the radical propagation and the Co^{II}-induced decomposition of the hydroperoxide cause the formation of cyclohexoxy radicals that are partially transformed to 6-hydroxyhexanoic acid, the major primary byproduct for these systems. However, during the Co^{II}-catalyzed reaction, the concentration of cyclohexanone increases much faster than that of the hydroperoxide, causing the ketone to take over the role of dominant byproduct source. A mechanism for the conversion of cyclohexanone to ring-opened byproducts is put forward. $Cr(acac)_3$ seems to catalyze additional reactions, some of them probably leading directly to byproducts. Indeed, the evolution of (by)products is significantly different from the Co^{II}-catalyzed and the thermal systems, in the sense that they all seem to be primary in origin.

Introduction

The liquid-phase oxidation of cyclohexane with molecular oxygen is an important process in the chemical industry.[1,2] The cyclohexanone and cyclohexanol product mixture (KA-oil, 6×10^6 Tons/y) is used for the synthesis of caprolactam and adipic acid, building blocks of nylon-6 and nylon-6,6, respectively. To maintain a good selectivity, the cyclohexane conversion is limited to less than 5%. At higher conversion, (ring-opened) byproducts, such as adipic acid and glutaric acid, appear from overoxidation of the desired products, cyclohexyl hydroperoxide (CyOOH), cyclohexanone (Q═O) and cyclohexanol (CyOH). The autoxidation is carried out without, or in presence of a transition metal ion catalyst (mostly soluble cobalt(II) salts) and is followed by a separate deperoxidation step, converting the remaining CyOOH to additional CyOH and Q═O.[1−4] During the autoxidation process, CyOOH is formed in the reaction of chain-carrying peroxyl radicals ($CyOO^\bullet$) with the substrate (reaction 1).[4,5] The reaction of the cyclohexyl radicals with O_2 is diffusion controlled and regenerates the peroxyl radicals (reaction 2). This sequence of propagation reactions is repeated many times before the $CyOO^\bullet$ radicals are destroyed in a mutual chain-termination reaction (3), hitherto considered to be the exclusive source of Q═O and the dominant source of CyOH.[1−4] The remaining CyOH was thought to originate from the fast H-abstraction by cyclohexoxy radicals ($CyO^\bullet$, reaction 4),[6] formed in the chain initiation (reaction 5).[7] However, given the ratio of the rates of propagation and termination (the so-called chain length) ≥50,[8] the less important termination reaction can obviously produce only a minor amount of products.

$$CyOO^\bullet + CyH \rightarrow CyOOH + Cy^\bullet \quad (1)$$

$$Cy^\bullet + O_2 \rightarrow CyOO^\bullet \quad (2)$$

$$CyOO^\bullet + CyOO^\bullet \rightarrow CyOH + Q{=}O + O_2 \quad (3)$$

$$CyO^\bullet + CyH \rightarrow CyOH + Cy^\bullet \quad (4)$$

$$CyOOH + Q{=}O \rightarrow CyO^\bullet + H_2O + Q_{-\alpha H}{}^\bullet{=}O \quad (5)$$

Recently, we demonstrated that the peroxyl radicals also abstract the αH-atom of the CyOOH product with a rate constant that is significantly higher than that of the main propagation reaction (1): $k^{CyOOH}/k^{CyH} \approx 55$ at 418 K.[8,9] Reaction 6 directly produces Q═O, because the initial product radical, $Cy_{-\alpha H}{}^\bullet OOH$, is unstable and decomposes spontaneously to Q═O and $^\bullet OH$.[10] The $^\bullet OH$ radical rapidly abstracts an H-atom from a CyH molecule constituting the wall of the solvent cage surrounding the nascent products (reaction 7), putting the energy released by reactions 6 and 7 at about 50 kcal/mol.[8,9]

$$CyOO^\bullet + CyOOH \rightarrow \{CyOOH + Q{=}O + {}^\bullet OH\}^{cage} \quad (6)$$

$$\{CyOOH + Q{=}O + {}^\bullet OH\}^{cage} + CyH^{cage-wall} \rightarrow \{CyOOH + Cy^\bullet + Q{=}O + H_2O\}^{cage} \quad (7)$$

This amount of energy, produced very rapidly, causes the formation of a nanosized hot-spot, activating the local environment for 10−100 ps. For liquid-phase reactions, the nascent products benefiting from such activation, may react with one another before diffusing away from each other, out of their solvent cage. In this case, the $Cy^\bullet$ radical can abstract the OH group of the nascent CyOOH molecule, still present in the solvent cage (reaction 8). This reaction faces a significant energy

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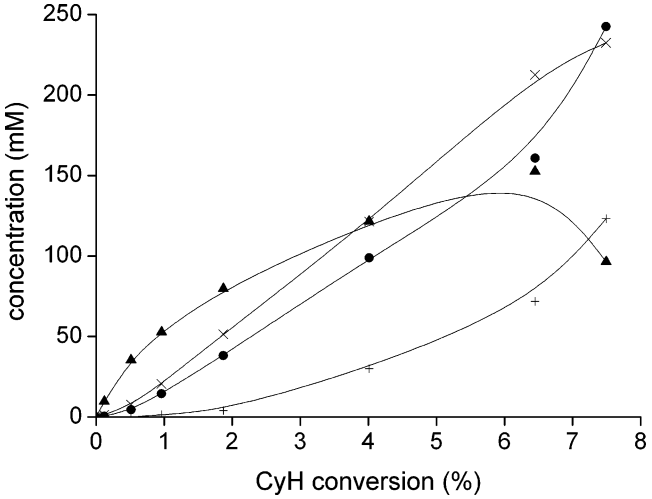


Figure 1. Product distribution during the 418 K autoxidation of pure cyclohexane; CyOOH (▲), CyOH (×), Q═O (●), and byproducts (+).

barrier, in contrast with the diffusive separation (reaction 9), but the substantially raised hot-spot temperature renders it competitive with the out-diffusion.[8,9]

$$\{\mathrm{CyOOH} + \mathrm{Cy}^{\bullet} + \mathrm{Q{=}O} + \mathrm{H_2O}\}^{\mathrm{cage}} \rightarrow \{\mathrm{CyO}^{\bullet} + \mathrm{CyOH} + \mathrm{Q{=}O} + \mathrm{H_2O}\}^{\mathrm{cage}} \quad (8)$$

$$\{\mathrm{CyOOH} + \mathrm{Cy}^{\bullet} + \mathrm{Q{=}O} + \mathrm{H_2O}\}^{\mathrm{cage}} \rightarrow \mathrm{CyOOH} + \mathrm{Cy}^{\bullet} + \mathrm{Q{=}O} + \mathrm{H_2O} \quad (9)$$

Kinetic and stoechiometric analyses of experimental data at a bulk temperature of 418 K show that cage-reaction (8) contributes about 70% of the reactive flux.[9] This reaction channel not only produces the majority of CyOH but also causes a net removal of CyOOH, explaining why this product features a maximum as a function of the CyH conversion (Figure 1). It is important to emphasize that a similar mechanism was also identified as the source of alcohol and ketone/aldehyde during the autoxidations of ethylbenzene[11] and toluene,[12] although the efficiencies of the cage reactions are only 20 and 55%, respectively. These differences could be ascribed to the relative stabilities of the corresponding alkyl radicals formed in generic reaction (7), controlling the energy barrier of the OH-abstraction step (cf. generic reaction 8).

Recently, we also discovered that this overlooked fast propagation of the hydroperoxide product is the predominant source (≥80%) of ring-opened byproducts in the thermal CyH autoxidation,[13] rather than the overoxidation of Q═O as assumed earlier.[1−3] Indeed, the $\mathrm{CyO}^{\bullet}$ radicals co-produced in reaction 8 not only react with the substrate (reaction 4) but also ring-open via β C−C cleavage (reaction 10).[6]

$$\mathrm{CyO}^{\bullet} \rightarrow {}^{\bullet}\mathrm{CH_2{-}(CH_2)_4{-}CHO} \quad (10)$$

Fast addition of O_2 to the resulting C-centered radical (reaction 11) produces a peroxyl radical, which will mainly react by internal H-abstraction of its weakly bonded aldehyde H-atom, i.e., by a 1,8-H-shift (reaction 12).[13] The resulting $\mathrm{HOOCH_2{-}(CH_2)_4{-}C^{\bullet}(=O)}$ acyl radical can rearrange via a 1,7-OH-shift (reaction 13), further transforming to 6-hydroxyhexanoic acid (HHA) after a fast H-abstraction from the substrate (reaction 14).[13]

HHA was experimentally identified as the primary byproduct from which nearly all other byproducts originate via subsequent

$$^{\bullet}\mathrm{CH_2{-}(CH_2)_4{-}CHO} + \mathrm{O_2} \rightarrow {}^{\bullet}\mathrm{OOCH_2{-}(CH_2)_4{-}CHO} \quad (11)$$

$$^{\bullet}\mathrm{OOCH_2{-}(CH_2)_4{-}CHO} \rightarrow \mathrm{HOOCH_2{-}(CH_2)_4{-}C^{\bullet}(O)} \quad (12)$$

$$\mathrm{HOOCH_2{-}(CH_2)_4{-}C^{\bullet}(O)} \rightarrow {}^{\bullet}\mathrm{OCH_2{-}(CH_2)_4{-}C(O)OH} \quad (13)$$

$$^{\bullet}\mathrm{OCH_2{-}(CH_2)_4{-}C(O)OH} + \mathrm{CyH} \rightarrow \mathrm{HOCH_2{-}(CH_2)_4{-}C(O)OH} + \mathrm{Cy}^{\bullet} \quad (14)$$

oxidation of the alcohol group (see initial finite slope and negative second derivative of the HHA contribution in Figure 2). The oxidation of HHA (reactions 15−24) produces mainly adipic acid (reaction 19), but also radical decarboxylation takes place via decomposition of the $^{\bullet}\mathrm{OC(O){-}(CH_2)_4{-}C(O)OH}$ acyloxy radical (reaction 24).[13]

$$\mathrm{HOCH_2{-}(CH_2)_4{-}C(O)OH} + \mathrm{CyOO}^{\bullet} \rightarrow {}^{\bullet}\mathrm{C(OH)H{-}(CH_2)_4{-}C(O)OH} + \mathrm{CyOOH} \quad (15)$$

$$^{\bullet}\mathrm{C(OH)H{-}(CH_2)_4{-}C(O)OH} + \mathrm{O_2} \rightarrow {}^{\bullet}\mathrm{OOC(OH)H{-}(CH_2)_4{-}C(O)OH} \quad (16)$$

$$^{\bullet}\mathrm{OOC(OH)H{-}(CH_2)_4{-}C(O)OH} \rightarrow \mathrm{OCH{-}(CH_2)_4{-}\,C(O)OH} + \mathrm{HO_2}^{\bullet} \quad (17)$$

$$\mathrm{CyOO}^{\bullet} + \mathrm{OCH{-}(CH_2)_4{-}C(O)OH} \rightarrow \{\mathrm{CyOOH} + \mathrm{OC}^{\bullet}\mathrm{{-}(CH_2)_4{-}C(O)OH}\}^{\mathrm{cage}} \quad (18)$$

$$\{\mathrm{CyOOH} + \mathrm{OC}^{\bullet}\mathrm{{-}(CH_2)_4{-}C(O)OH}\}^{\mathrm{cage}} \rightarrow \{\mathrm{CyO}^{\bullet} + \mathrm{HOC(O){-}(CH_2)_4{-}C(O)OH}\}^{\mathrm{cage}} \quad (19)$$

$$\{\mathrm{CyOOH} + \mathrm{OC}^{\bullet}\mathrm{{-}(CH_2)_4{-}C(O)OH}\}^{\mathrm{cage}} \rightarrow \mathrm{CyOOH} + \mathrm{OC}^{\bullet}\mathrm{{-}(CH_2)_4{-}C(O)OH} \quad (20)$$

$$\mathrm{OC}^{\bullet}\mathrm{{-}(CH_2)_4{-}C(O)OH} + \mathrm{O_2} \rightarrow {}^{\bullet}\mathrm{OOC(O){-}(CH_2)_4{-}\,C(O)OH} \quad (21)$$

$$^{\bullet}\mathrm{OOC(O){-}(CH_2)_4{-}C(O)OH} + \mathrm{CyH} \rightarrow \{\mathrm{HOOC(O){-}(CH_2)_4{-}C(O)OH} + \mathrm{Cy}^{\bullet}\}^{\mathrm{cage}} \quad (22)$$

$$\{\mathrm{HOOC(O){-}(CH_2)_4{-}C(O)OH} + \mathrm{Cy}^{\bullet}\}^{\mathrm{cage}} \rightarrow \{{}^{\bullet}\mathrm{OC(O){-}(CH_2)_4{-}C(O)OH} + \mathrm{CyOH}\}^{\mathrm{cage}} \quad (23)$$

$$^{\bullet}\mathrm{OC(O){-}(CH_2)_4{-}C(O)OH} \rightarrow \mathrm{CO_2} + {}^{\bullet}\mathrm{CH_2{-}(CH_2)_3{-}\,C(O)OH} \quad (24)$$

However, a detailed analysis of the experimental data reveals that still some 20% of the byproducts originate from overoxidation of the Q═O product.[13] Important to emphasize is the fact that no sound mechanism can be put forward that converts Q═O to HHA. Overoxidation of Q═O will probably immediately yield AA (see Scheme 1), along with other decarboxylated byproducts. It is our aim to assess the contribution of both sources of byproducts during cyclohexane autoxidation catalyzed by transition metal ions. Knowing the origin of

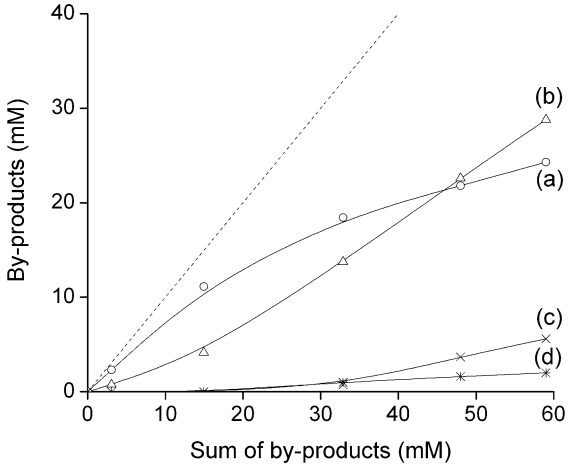
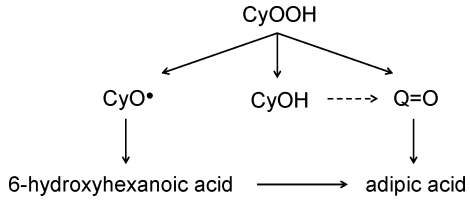


Figure 2. Evolution of the most important byproducts as a function of their sum during the 418 K autoxidation of cyclohexane: 6-hydroxyhexanoic acid (HHA, a), adipic acid (AA, b), glutaric acid (GA, c), and ϵ-caprolactone (d). Traces of other (decarboxylated) byproducts were not taken into account. Formation of the most important byproducts, 6-hydroxyhexanoic acid (HHA) and adipic acid (AA), starting directly from the primary CyOOH product, or via the secondary Q═O product.

SCHEME 1: Formation of the Most Important Byproducts, 6-Hydroxyhexanoic Acid (HHA) and Adipic Acid (AA), Starting Directly from the Primary CyOOH Product, or via the Secondary Q═O Product



byproducts under various conditions not only will contribute to the optimization of the process but also could guide rational catalyst design.

Experimental and Computational Methods

The autoxidation of cyclohexane (50 mL, HPLC-grade) was studied experimentally in a stirred (500 rpm) stainless steel high-pressure Parr reactor (100 mL) at an initial room-temperature pressure of 2.76 MPa of pure oxygen. Prior to each experiment, the reactor wall was passivated by means of a saturated sodium pyrophosphate solution.[5,8] Acetone was added to the reaction mixture to dissolve all products. The reaction products were quantified by GC-FID, after the addition of an external standard (1-heptanol, 99.9%) and the silylating agent *N*-methyl-*N*-(trimethylsilyl)trifluoroacetamide (MSTFA); the injection temperature was set to 150 °C. Peak areas were corrected for sensitivity differences by calibration. Quantum-chemical calculations were carried out with the GAUSSIAN03 program.[14] At the DFT level, the Becke three-parameter hybrid exchange functional was used, combined with the Lee−Yang−Parr nonlocal correlation functional B3LYP-DFT.[15] Unless stated in the text, the UB3LYP/6-31++G(df,pd)//UB3LYP/6-31G(d,p) method was applied, known to give reliable results for peroxyl radical chemistry.[8,9]

Results and Discussion

Cyclohexanone and Byproducts. It was previously observed that the addition of 1 mol % of Q═O causes a significant increase in byproducts at low conversions, but only a negligible increase at higher conversions.[13] For instance, at 1.5% conversion, the total amount of byproducts increased by a factor of 3, whereas only 18% more byproducts were detected at 4.5% conversion. This experiment demonstrates unequivocally not only that oxidation of Q═O indeed produce byproducts but also that there is another source that is far more important once the autoxidation is well underway. The latter mechanism was identified as the co-propagation of CyOOH and subsequent chemistry, described above. The addition of Q═O was also found to cause a significant decrease in the initial HHA/AA ratio, pointing to a direct source of AA, bypassing the stage of HHA (Figure 3). This supports the view that HHA does not (mainly) originate from Q═O. As the conversion increases, the HHA/AA acid ratio gradually levels off to the value for the pure thermal autoxidation. Indeed, as the conversion increases, CyOOH gradually builds up and resumes its role as dominant byproduct source.

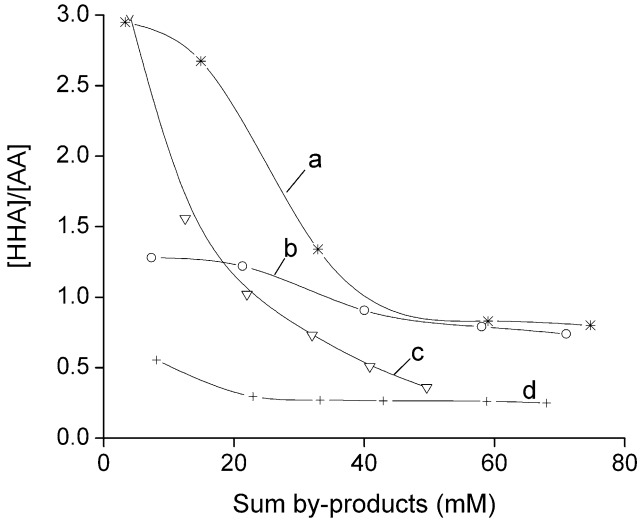


Figure 3. Ratio of 6-hydroxyhexanoic acid (HHA) over adipic acid (AA) versus the sum of byproducts: (a) for the pure thermal autoxidation at 418 K, (b) for the 418 K thermal autoxidation with 1 mol % initially added Q═O, (c) during the 403 K autoxidation catalyzed by 5 ppm of $Co(acac)_2$, and (d) during the 403 K autoxidation catalyzed by 5 ppm of $Cr(acac)_3$.

The ratio of byproduct stemming from Q═O and CyOOH is given by eq A, where the factor E stands for the efficiency of the activated cage-reaction (8), multiplied by the fraction of CyO• radicals that ring-open (reaction 10). Recently, we estimated $k^{CyOOH}E \approx 12k^{CyH}$ and $k^{Q=O} \approx 5k^{CyH}$.[8,9,13] It is obvious that initially added Q═O must dominate the formation of byproducts at low conversions when little hydroperoxide is yet formed and the ratio Q═O/CyOOH ratio is still very high (Figure 4).

$$\frac{[\text{byproduct}]^{Q=O}(t)}{[\text{byproduct}]^{CyOOH}(t)} = \frac{k^{Q=O}}{k^{CyOOH}E} \times \frac{\int [Q=O](t)\,[CyOO^{\bullet}](t)\,dt}{\int [CyOOH](t)\,[CyOO^{\bullet}](t)\,dt} \quad \text{(A)}$$

This analysis demonstrates that previous studies aiming to identify the origin of byproducts via addition of Q═O to ^{14}C labeled CyH,[16] or of ^{14}C labeled Q═O to regular CyH,[17] should be interpreted with due care. Indeed, even as little as 1 mol % of Q═O can at low conversions completely alter the relative

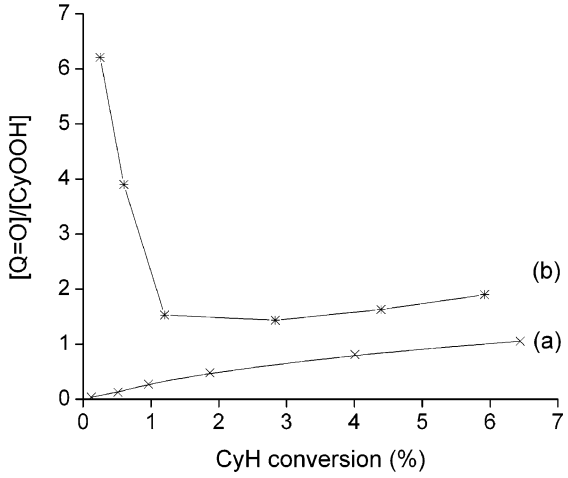


Figure 4. [Q=O]/[CyOOH] ratio as a function of the alkane conversion during the 418 K thermal autoxidation of CyH (a) and after initial addition of 1 mol % Q=O (b).

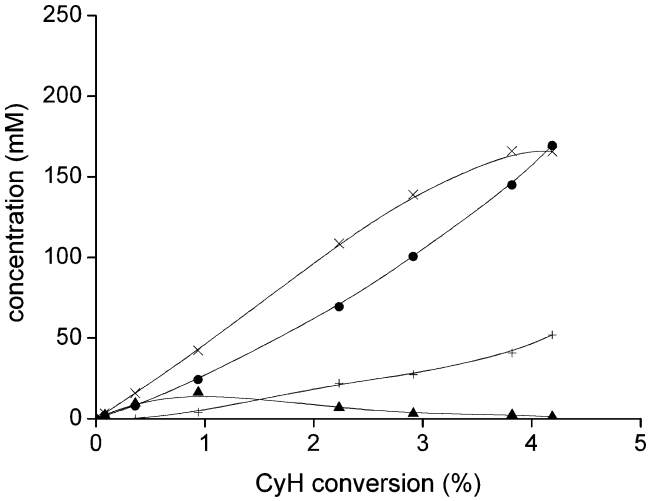


Figure 5. Product distribution during the 403 K autoxidation of cyclohexane in the presence of 5 ppm $Co(acac)_2$: CyOOH (▲), CyOH (×), Q=O (●), and byproducts (+).

importance of the different sources, leading to conclusions that are not relevant for the practical autoxidation process.

Transition Metal Ion Catalysis. Co^{II} ions are known to catalyze the rate-determining initiation step of autoxidations via a fast redox reaction with CyOOH,[1−4,18−23] producing $CyO^{\bullet}$ radicals (reaction 25). This so-called Haber−Weiss catalytic cycle is assumed to close via the reaction of $Co^{III}OH$ with an additional CyOOH molecule, regenerating Co^{II} (reaction 26). As demonstrated by the much lower CyOOH concentrations

$$Co^{II} + CyOOH \rightarrow Co^{III}OH + CyO^{\bullet} \quad (25)$$

$$Co^{III}OH + CyOOH \rightarrow Co^{II} + CyOO^{\bullet} + H_2O \quad (26)$$

than in the thermal autoxidation, this catalytic mechanism is highly efficient in removing the primary oxidation product, converting much of it into $CyO^{\bullet}$ radicals (see Figures 1 and 5). In fact, reactions 25 and 26 take over the role of the "thermal" reaction sequence (6)−(9) as major CyOOH sink, and at the same time of reaction 5 as chain-initiation step, and that with a much higher rate. Nevertheless, albeit through differing pathways, a major fraction of the oxidation reaction flux still goes through $CyO^{\bullet}$ radicals as in the thermal process. A fraction of the $CyO^{\bullet}$ radicals are converted to byproducts via the intermediate stage of HHA (reactions 10−24). This also rationalizes why the HHA/AA ratio in the cobalt-catalyzed autoxidation starts at a high value (Figure 3c), similar to the thermal value. The fast subsequent drop of this ratio to below the value observed in the thermal system, can be ascribed to the 50% higher yield of Q=O in the co-catalyzed reaction (see Figures 1 and 5). Nevertheless, the overall shape of the major-product distribution (Figure 5) and byproduct distribution (Figure 6) remains analogous to the situation in absence of any catalyst (cf. Figures 1 and 2), suggesting that the basic chemistry is more or less the same, apart from reactions 25 and 26.

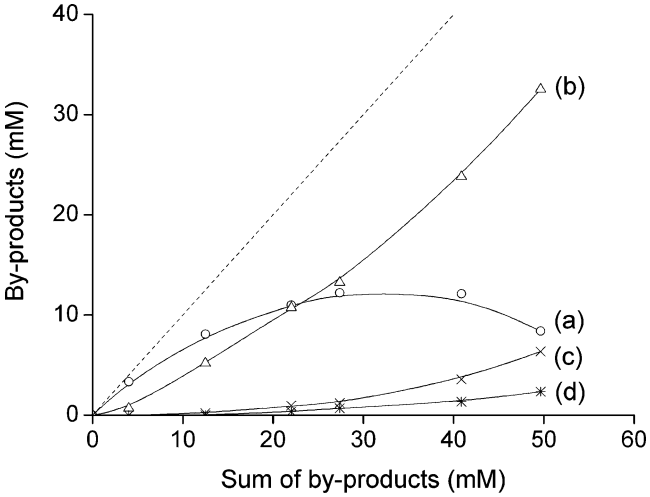


Figure 6. Evolution of the most important byproducts as a function of their sum during the 403 K autoxidation of cyclohexane in presence of 5 ppm $Co(acac)_2$: 6-hydroxyhexanoic acid (HHA, a), adipic acid (AA, b), glutaric acid (GA, c), and ϵ-caprolactone (d). Traces of other (decarboxylated) byproducts were not taken into account.

Also of interest is the relative increase and earlier appearance of the decarboxylated byproduct glutaric acid (GA) upon the addition of $Co(acac)_2$ catalyst (Figure 6 versus Figure 2). Above, it was explained how decarboxylation can take place via subsequent oxidation of HHA, consistent with its appearance as a secondary byproduct in the thermal autoxidation (see Figure 2). However, below we show that a similar decarboxylation mechanism is operative during the co-oxidation of cyclohexanone. Therefore, the increased and earlier decarboxylation contribution observed in Figure 6 is most likely due to the relatively lower HHA yields. Indeed, during the thermal autoxidation, HHA represents a major fraction of byproducts and decarboxylation must take place mainly in the fairly slow subsequent oxidation of this HHA. During the cobalt-catalyzed autoxidation, GA still originates largely from HHA oxidation, as attested by its secondary behavior illustrated in Figure 6.

In addition to their effect on the chain initiation, chromium ions are also able to catalyze the dehydration of CyOOH to Q=O.[1,2,24] This explains why the $Cr(acac)_3$-catalyzed CyH autoxidation exhibits such a high yield of Q=O (Figure 7) while the CyOOH concentration remains very low throughout the reaction. Clearly, the evolution of products, as well as the byproducts (Figure 8) is very different from those observed with $Co(acac)_2$ or without catalyst (vide supra). Indeed, all products as well as byproducts appear to be primary in origin, suggesting strongly that Cr^{III} ions are also involved in side-reactions. Similar (by)product distributions obtained with a recently immobilized Cr^{III} colloid catalyst point to a similar (catalytic) mechanism.[25,26]

From these observations it can be concluded that the catalytic mechanisms of $Co(acac)_2$ and $Cr(acac)_3$ exhibit fundamental differences. The Co^{II}-catalyzed system resembles the thermal

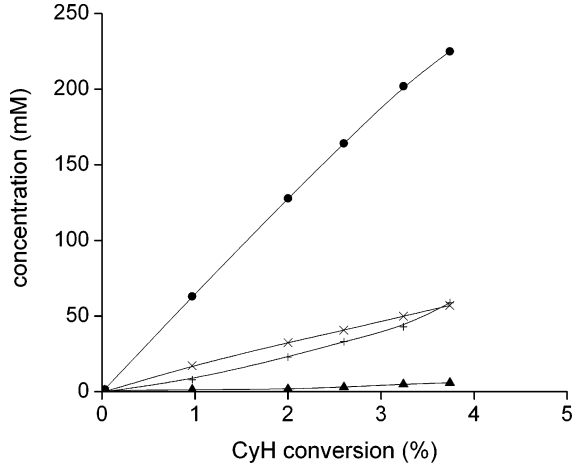


Figure 7. Product distribution during the 403 K autoxidation of cyclohexane in the presence of 5 ppm $Cr(acac)_3$: CyOOH (▲), CyOH (×), Q═O (●), and byproducts (+).

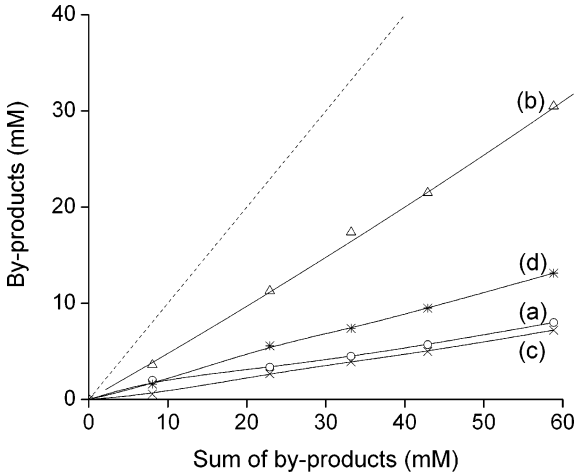


Figure 8. Evolution of the most important byproducts as a function of their sum during the 403 K autoxidation of cyclohexane in presence of 5 ppm $Cr(acac)_3$: 6-hydroxyhexanoic acid (HHA, a), adipic acid (AA, b), glutaric acid (GA, c), and ϵ-caprolactone (d). Traces of other (decarboxylated) byproducts were not taken into account.

autoxidation system in the overall shape of the (by)product distribution, even though cobalt is causing a faster removal of CyOOH than peroxyl radicals do. Nevertheless, both the peroxyl- and Co^{II}-induced CyOOH-removal paths lead to the formation of HHA as the first important byproduct via $CyO^{\bullet}$ radicals. Overoxidation of this HHA results in other byproducts, but in the case of Co^{II}-catalyzed oxidations, the co-oxidation of Q═O also becomes an important source of byproducts, immediately yielding AA and decarboxylated side-products.

In contrast, during the $Cr(acac)_3$-catalyzed reaction, all products and byproducts appear to be primary in origin. This suggests that chromium ions are also involved in additional reactions. This fundamental difference in reaction mechanisms, as evidenced by the present study, should be investigated in detail in the future.

From Cyclohexanone to Ring-Opened Byproducts. In the thermal and the Co^{II}-catalyzed autoxidation of cyclohexane, radical-initiated co-oxidation of cyclohexanone could be identified as a minor and important source of byproducts, respectively (vide supra). The Cr^{III} system appears to yield byproducts also by more direct catalytic reactions and should therefore be considered as a special case.

From previous studies it is known that $CyOO^{\bullet}$ radicals abstract the αH-atoms of Q═O significantly faster than those of CyH ($k^{Q=O}/k^{CyH} \approx 5$, reaction 27).[8,9] Resonance stabilization

$$CyOO^{\bullet} + Q{=}O \rightarrow \{CyOOH + Q_{-\alpha H}{}^{\bullet}{=}O\}^{cage} \quad (27)$$

of the $Q_{-\alpha H}{}^{\bullet}$═O ketonyl radical and the nearly thermoneutrality of reaction 27 hampers a fast subsequent cage reaction (reaction 28, barrier 8.8 kcal/mol at the UB3LYP/6-31G(d,p) level), favoring instead the formation of 2-oxocyclohexylperoxy radicals (reactions 29 and 30). It should, however, be noted that

$$\{CyOOH + Q_{-\alpha H}{}^{\bullet}{=}O\}^{cage} \rightarrow \{CyO^{\bullet} + Q_{-\alpha H}(=O)(OH)_{\alpha}\}^{cage} \quad (28)$$

$$\{CyOOH + Q_{-\alpha H}{}^{\bullet}{=}O\}^{cage} \rightarrow CyOOH + Q_{-\alpha H}{}^{\bullet}{=}O \quad (29)$$

$$Q_{-\alpha H}{}^{\bullet}{=}O + O_2 \rightarrow Q_{-\alpha H}(=O)(OO^{\bullet})_{\alpha} \quad (30)$$

2-hydroxycyclohexanone (reaction 28) is observed as a trace byproduct. In the literature, it has been suggested that the 2-oxocyclohexylperoxyl radicals can react with $CyOO^{\bullet}$ radicals, producing 2-oxocyclohexoxy radicals (reaction 31).[4] These

$$Q_{-\alpha H}(=O)(OO^{\bullet})_{\alpha} + CyOO^{\bullet} \rightarrow Q_{-\alpha H}(=O)(O^{\bullet})_{\alpha} + CyO^{\bullet} + O_2 \quad (31)$$

$Q_{-\alpha H}(=O)(O^{\bullet})_{\alpha}$ radicals are known to ring-open (reaction 32) much faster than $CyO^{\bullet}$ radicals (reaction 10), facing a barrier of only about 5 kcal/mol,[27] far outrunning H-abstraction. However, given the low $CyOO^{\bullet}$/CyH concentration ratio, reaction 31 seems less likely, the more that such a nonterminating cross reaction between two $CyOO^{\bullet}$ radicals (reaction 33) was never reported to occur in the liquid phase, although known to happen in the gas phase. Indeed, in the gas phase the ratio of

$$Q_{-\alpha H}(=O)(O^{\bullet})_{\alpha} \rightarrow OCH{-}(CH_2)_4{-}C^{\bullet}(=O) \quad (32)$$

$$CyOO^{\bullet} + CyOO^{\bullet} \rightarrow CyO^{\bullet} + CyO^{\bullet} + O_2 \quad (33)$$

rates of the nonterminating channel (viz. reaction 33) and the terminating channel (viz. reaction 3) ranges mostly between 1:3 and 3:1 between 300 and 400 K.[28] At the moment it is not yet clear whether or why reaction (33) would be unimportant in the liquid phase. Nevertheless, it is more likely that the 2-oxocyclohexylperoxyl radicals will abstract H-atoms from the substrate (reaction 34), producing nascent 2-oxocyclohexyl hydroperoxide ($Q_{-\alpha H}(=O)(OOH)_{\alpha}$). This abstraction reaction

$$Q_{-\alpha H}(=O)(OO^{\bullet})_{\alpha} + CyH \rightarrow \{Q_{-\alpha H}(=O)(OOH)_{\alpha} + Cy^{\bullet}\}^{cage} \quad (34)$$

can however be followed by a cage reaction in which the OH group of the nascent 2-oxocyclohexyl hydroperoxide molecule is abstracted by $Cy^{\bullet}$ radicals, producing 2-oxocyclohexoxy radicals (reaction 35). Indeed, the UB3LYP/6-31G(d,p) barrier

$$\{Q_{-\alpha H}(=O)(OOH)_{\alpha} + Cy^{\bullet}\}^{cage} \rightarrow \{Q_{-\alpha H}(=O)(O^{\bullet})_{\alpha} + CyOH\}^{cage} \quad (35)$$

of this cage reaction equals only 4.6 kcal/mol, compared to the out-of-cage diffusion, i.e., diffusive separation, which would require ca. 2.5 kcal/mol, due to the large dipole moment of the carbonyl group. On the basis of the pre-exponential rate-factors

of ca. 10^{12} s^{-1} for the cage reaction and ca. 5×10^{10} s^{-1} for the diffusive separation,[8] one can conclude that cage-reaction (35) will be the most likely fate under our experimental conditions.[29] Experimental evidence for the efficiency of cage-reaction (35) is found in 2-oxocyclohexyl hydroperoxide and 1,2-cyclohexadione being only minor trace byproducts. Indeed, if diffusive separation (reaction 36) would be important, significant amounts of both compounds would be observed as the main fate of the $Q_{-\alpha H}(=O)(OOH)_\alpha$ molecule would be the reaction with CyOO$^\bullet$, abstracting the doubly activated (remaining) αH-atom (reaction 37), resulting in $Q_{-2\alpha H}(=O)(=O)_\alpha$ (i.e., 1,2-cyclohexadione). Note that overoxidation of this 1,2-

$$\{Q_{-\alpha H}(=O)(OOH)_\alpha + Cy^\bullet\}^{cage} \rightarrow Q_{-\alpha H}(=O)(OOH)_\alpha + Cy^\bullet \quad (36)$$

$$Q_{-\alpha H}(=O)(OOH)_\alpha + CyOO^\bullet \rightarrow Q_{-2\alpha H}(=O)(=O)_\alpha + {}^\bullet OH + CyOOH \quad (37)$$

cyclohexadione cannot yield AA, as one would end up with three out of six carbon atoms being functionalized, rather than only two, as is the case in AA. Although elimination of CO is in principle possible from $CHO-(CH_2)_4-C^\bullet(=O)$ under conditions of O_2 starvation, the main fate of this acyl radical will, under our experimental conditions of a high oxygen concentration, be the addition of O_2, resulting in a acylperoxyl radical (reaction 38). Intramolecular abstraction of the aldehyde H-atom

$$CHO-(CH_2)_4-C^\bullet(=O) + O_2 \rightarrow CHO-(CH_2)_4-C(=O)OO^\bullet \quad (38)$$

(reaction 39) will be favored over a bimolecular reaction with the CyH substrate, given the barrier of only 9.6 kcal/mol for the former 1,8-H-shift (UB3LYP/6-311++G(df,pd)//UB3LYP/6-31G(d,p) level of theory). The 1,7-OH-shift (40), analogous

$$CHO-(CH_2)_4-C(=O)OO^\bullet \rightarrow {}^\bullet C(=O)-(CH_2)_4-C(O)OOH \quad (39)$$

to reaction (13) was found to face a barrier of about 13 kcal/mol, i.e., too large to compete with the diffusion controlled addition of O_2 (reaction 41). This acyl peroxyl radical will

$$^\bullet C(=O)-(CH_2)_4-C(O)OOH \rightarrow HOC(O)-(CH_2)_4-C(O)O^\bullet \quad (40)$$

$$^\bullet C(=O)-(CH_2)_4-C(O)OOH + O_2 \rightarrow {}^\bullet OOC(O)-(CH_2)_4-C(O)OOH \quad (41)$$

mainly react with the substrate (reaction 42), producing a nascent acyloxy radical after a fast subsequent cage-reaction (43), facing a barrier of only 2.4 kcal/mol. Rather than diffusing away from

$$^\bullet OOC(O)-(CH_2)_4-C(O)OOH + CyH \rightarrow \{HOOC(O)-(CH_2)_4-C(O)OOH + Cy^\bullet\}^{cage} \quad (42)$$

$$\{HOOC(O)-(CH_2)_4-C(O)OOH + Cy^\bullet\}^{cage} \rightarrow \{{}^\bullet OC(=O)-(CH_2)_4-C(O)OOH + CyOH\}^{cage} \quad (43)$$

its CyOH co-product, which requires breaking of a 1.8 kcal/mol strong H-bond, this nascent acyloxy radical can (partially) abstract the weakly bonded αH-atom of its cage-partner, producing $HOC(O)-(CH_2)_4-C(O)OOH$ (reaction 44). This cage reaction proceeds indeed via a so-called submerged TS; i.e., the computed barrier is smaller than the energy of the H-bonding between the caged $\{^\bullet OC(=O)-(CH_2)_4-C(O)OOH + CyOH\}$ pair.[30] Under the reaction conditions, the $HOC(=O)-(CH_2)_4-$

$$\{^\bullet OC(=O)-(CH_2)_4-C(O)OOH + CyOH\}^{cage} \rightarrow \{HOC(=O)-(CH_2)_4-C(O)OOH + Cy_{-\alpha H}{}^\bullet OH\}^{cage} \quad (44)$$

C(O)OOH peracid produced in reaction (44) is presumably able to oxidize substrate molecules, or even more likely Q=O, eventually catalyzed by the acidic proton at the other end of the molecule (viz. intramolecular acid-catalyzed Baeyer−Villiger oxidation). The latter mechanism could indeed also explain the increase in the ϵ-caprolactone byproduct upon initial addition of cyclohexanone. The fraction of $^\bullet OC(=O)-(CH_2)_4-C(O)OOH$ radicals that will not react with CyOH according to cage-reaction (44), but instead diffuse away from this cage-partner (reaction 45), will eliminate CO_2 (reaction 46) and produce decarboxylated byproducts.

$$\{^\bullet OC(=O)-(CH_2)_4-C(O)OOH + CyOH\}^{cage} \rightarrow {}^\bullet OC(=O)-(CH_2)_4-C(O)OOH + CyOH \quad (45)$$

$$^\bullet OC(=O)-(CH_2)_4-C(O)OOH \rightarrow {}^\bullet CH_2-(CH_2)_3-C(O)OOH + CO_2 \quad (46)$$

Conclusions

During the thermal autoxidation of cyclohexane, the majority of byproducts originates from cyclohexoxy radicals, formed in the co-propagation of the primary hydroperoxide product. Indeed, the high reactivity of CyOOH toward the CyOO$^\bullet$ chain carriers, relative to Q=O, and the high CyOOH/Q=O ratio causes the Q=O product to be only a minor precursor of side products. Initial addition of a small amount of Q=O can, however, alter the situation completely in the early stages of the oxidation. Trying to identify the origin of byproducts upon the addition of cyclohexanone can therefore be misleading, as it significantly disturbs the chemistry at issue. The cyclohexoxy radicals from the hydroperoxide propagation are rapidly transformed to 6-hydroxyhexanoic acid, which slowly co-oxidizes to other (decarboxylated) byproducts. Catalysis by Co^{II} ions also causes the formation of large quantities of cyclohexoxy radicals, as witnessed by the fairly high yield of 6-hydroxyhexanoic acid. In this system, the CyO$^\bullet$ radicals do not originate from the reaction of the CyOOH product with peroxyl radicals, but with Co^{II}. However, as the reaction proceeds, the ketone yield increases very rapidly, causing it to take over the role of byproduct source. Not only do Cr^{III} ions seem to catalyze the chain initiation and CyOOH destruction as $Co(acac)_2$ does, but also they seem to catalyze several other reactions, probably leading directly to byproducts. This complex mechanism should be investigated in detail in the future to unravel the elementary steps involved in this catalysis.

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Supporting Information Available: Geometries, vibration frequencies, and rotation constants of discussed transition states are available free of charge via the Internet at http://pubs.acs.org.

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(29) At $T = 418$ K, the ratio between the rate of cage-reaction (35) and the diffusive separation can be estimated at ≈ 2. However, at $T = 350$ K, this ratio drops to ≈ 1. This prediction is in agreement with the experimental observation that at lower temperatures, 2-oxocyclohexyl hydroperoxide is the dominant product whereas at higher temperatures, predominantly adipic acid is produced.[17]

(30) See Supporting Information.