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Selective Oxidation of Alkanes with Molecular Oxygen and Acetaldehyde in Compressed (Supercritical) Carbon Dioxide as Reaction Medium

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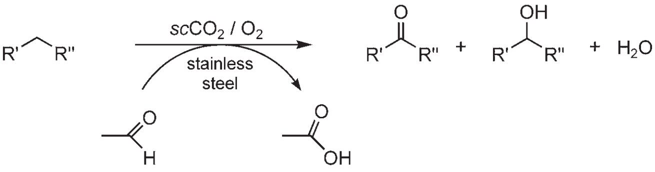
Abstract: The oxidation of cycloalkanes or alkylarenes with molecular oxygen and acetaldehyde as sacrificial co-reductant occurs efficiently in compressed (supercritical) carbon dioxide ($scCO_2$) under mild multiphase conditions. No catalyst is required and high-pressure ATR-FTIR online measurements show that a radical reaction pathway is heterogeneously initiated by the stainless steel of the reactor walls. For secondary carbon atoms, high ketone to alcohol ratios are observed (3.5–7.9), most probably due to fast consecutive oxidation of alcoholic intermediates. Since C−C scission reactions are detected only to a very small extent, tertiary carbon atoms are transformed into the corresponding alcohols with high selectivity. Detailed analysis of the product distributions and other mechanistic evidence suggest that acetaldehyde acts not only as the sacrificial oxygen acceptor, but also as an efficient H-atom donor for peroxo and oxo radicals and as a crucial reductant for hydroperoxo intermediates. In comparison to other inert gases such as compressed N_2 or Ar, the use of carbon dioxide was shown to increase the yields of alkane oxygenates under identical reaction conditions.

Keywords: heterogeneous catalysis • IR spectroscopy • oxidation • radical reactions • supercritical fluids

Introduction

The chemical composition of the worldwide oil and gas reservoirs and the limited spectrum of olefinic raw materials available from petrochemical refinery processes stimulate ever-growing interest in using alkanes directly as starting materials for chemical production. Partial and selective oxidation of alkanes with molecular oxygen to generate reactive basic chemicals for further conversion along the value chain is one of the most attractive strategies in this field.[1]

Compressed (supercritical) carbon dioxide ($scCO_2$)[2] is a very attractive reaction medium for oxidation reactions of hydrocarbons, because it combines a maximum availability of molecular oxygen with the additional safety of a totally inert environment.[3,4] Moreover it has been reported that the presence of CO_2 can improve yields, reaction rates, and/or selectivities in several selective alkane and alkene oxidation processes.[5,6] One of the most prominent examples is the industrial oxidation of ethylene to ethylene oxide, where addition of CO_2 to the reactor feed leads to improved selectivities.[7] As part of our ongoing interest in using $scCO_2$ for selective oxidation processes[8–10] we recently reported that cyclooctane is oxidized efficiently in $scCO_2$ by molecular oxygen as terminal oxidant and acetaldehyde (**1**) as sacrificial co-reductant.[11] Here we give a full account of the oxidation of simple hydrocarbons such as cycloalkanes and alkylarenes (Scheme 1) in this system.



1 **2**

Scheme 1. Steel-promoted oxidation of hydrocarbons with acetaldehyde as co-reductant and $scCO_2$ as reaction medium.

The use of molecular oxygen as a primary oxidant in selective alkane oxidation processes requires activation of at least one of the reaction partners. Possibilities to overcome the symmetry barrier in reactivity by spin adjustment include thermal, metal-catalyzed, photocatalytic, electrochem-

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ical and enzymatic activation. Due to the triplet ground state of molecular oxygen, its incorporation in chemical products is often realized by radical addition reactions even in biochemical systems. Therefore, effective and selective autoxidation processes provide a promising approach to functionalise the stable C–H bonds of alkanes.[1,12–14]

Radical oxidation pathways can be initiated by mixtures of molecular oxygen and aldehydes in the presence of stainless steel (e.g., from metal equipment) or even simple iron powder under mild reaction conditions.[8,10,15] In the present study, we chose acetaldehyde (**1**) as effective, cheap and CO_2-soluble oxygen activator that leads to acetic acid (**2**) as the co-product (Scheme 1). High-pressure ATR-FTIR online measurements provide strong evidence that the stainless steel of the reactor walls initiates the reaction in a heterogeneous manner.[16] The activating effect of aldehydes results from the low C–H dissociation energy of the acyl H atom, especially in the liquid phase, and relatively high stability of the peroxo radicals which are formed immediately in the presence of molecular oxygen.[14] These peroxo radicals can act as initiators and terminators for radical chains and thereby control the activity and selectivity of the overall pathway. For the oxidation of alkanes, the aldehyde can influence the selectivity also by chemical interaction with intermediates of the free-radical pathway, as will be described in detail for the present system. The optimum conditions were found to involve multiphase reaction systems, and CO_2 proved superior to other compressed gases that were tested as safe reaction media under identical conditions.

Results and Discussion

Substrate scope and optimization of the reaction conditions: Oxidation reactions were carried out in a window-equipped stainless steel reactor ($V=200$ mL) that could be coupled to a commercial online ATR-FTIR probe (ReactIR 1000) through a special home-built lid if required. In addition, a small dosing unit for aldehyde **1** was connected to the reactor via a needle valve. The reactor was loaded with substrate, CO_2 and O_2 in the given order and heated to the desired reaction temperature, and then the needle valve to the dosing unit was opened to start the reaction. An important fixed parameter in this study was the stoichiometry of hydrocarbon (1.0), **1** (2.0), and molecular oxygen (2.1). Thus, it is possible to identify the influence of the reaction parameters on the relative efficacy of productive alkane oxidative and nonproductive autoxidation of the co-reductant. Results for the oxidation of selected alkanes and alkylarenes are presented in Table 1.

Table 1. Oxidation of alkanes and alkylarenes with O_2/**1** in the presence of $scCO_2$.[a]

Entry	Hydrocarbon	Phases	Conv. [%][b]	Products (GC-FID response factors)	Sel. [%][c]	Yield [%][d]	ROOH[e] [$mmol^{-1}$]	Total GC recovery [%][f]
1	adamantane (**5**)	s/sc	3	2-adamantone (**6**)	11	0.3	0.53	n.d.
				1-adamantol (**7**)	49	1.5		
				1,3-adamantanediol (**8**)	40	1.3		
2	*n*-butane (**9**)	hom.	ca. 1	2-butanone (**10**)	ca. 40	ca. 0.4	n.d.	n.d.
3	cyclohexane (**11**)	l/sc	10	cyclohexanone (**12**) (1.43)	42	4.2	0.17	84
				cyclohexanol (**13**) (1.33)	12	1.2		
				ε-caprolactone (**14**) (1.32[g])	18	1.8		
				others (1.40[g])	28	2.8		
4	cyclooctane (**15**)	l/sc	28	cyclooctanone (**16**) (1.236)	67	18.4	1.31	87
				cyclooctanol (**17**) (1.240)	8.5	2.3		
				9-oxabicyclo(3.3.1)nonan-1-ol (**18**) (1.32[g])	3.5	1.0		
				cyclooctane-1,4-dione (**19**) (1.40[g])	7.8	2.2		
				others (1.40[g])	13	3.6		
5	cyclododecane (**22**)	l/sc	14	cyclododecanone (**23**) (1.15)	70	9.5	0.42	99
				cyclododecanol (**24**) (1.14)	17	2.4		
				others (1.30[g])	13	1.7		
6	cumene (**25**)	l/sc	34	acetophenone (**26**) (1.10)	17	5.8	>1.90	98
				2-phenyl-propan-2-ol (**27**) (1.15)	66	22.2		
				1-methyl-1-phenylethyl acetate (**28**) (1.40[g])	8.5	2.9		
				others (1.40[g])	8.5	2.9		
7	ethylbenzene (**29**)	l/sc	17	acetophenone (**26**) (1.10)	89	15.5	0.87	103
				1-phenylethanol (**30**) (1.14)	3.8	0.7		
				others (1.30[g])	6.9	1.2		

[a] $n(\text{hydrocarbon}):O_2:\mathbf{1}:CO_2=1:2.1:2.0:16$; $n(\text{hydrocarbon})=50$ mmol, $V(\text{reactor})=205$ mL; $T=52\,°C$; $t=27$ h; for further description of reaction conditions, see Experimental Section. Analysis by GC and GC/MS with suitable *n*-alkanes as internal standard. [b] Conversion $=\Sigma n(\text{product, GC})/n(\text{hydrocarbon, loaded})$. [c] Selectivity $=n(\text{product, GC})/\Sigma n(\text{products, GC})$. [d] Yield $=n(\text{product, GC})/n(\text{hydrocarbon, loaded})$. [e] Determined by iodometric analysis.[22] [f] Total GC recovery $=\Sigma n(\text{hydrocarbon}+\text{product, GC})/n(\text{hydrocarbon, loaded})$. [g] Estimated values.

The oxidation methodology used in this study is based on coupled autoxidation processes of the sacrificial co-reductant **1** and the hydrocarbon substrate. In a radical chain process, autoxidation of **1** is energetically favored over that of the hydrocarbon substrate. Therefore, the steady-state concentration of **1** in the reactive phase must be kept as low as possible to achieve high hydrocarbon conversion. In the present set-up, this was realized by slow diffusion of the desired amount of **1** into the reactor from the dosing unit, which was kept at room temperature. The effect is strongly amplified by carrying out the reactions under liquid/supercritical (l/sc) multiphase conditions, which were found to be most effective for hydrocarbon conversion in accordance with results obtained previously in a 3-D-Simplex optimization of the reaction conditions.[11,17] This observation argues for the liquid phase being the predominant reactive phase, which is consistent with findings under multiphase conditions from other groups[4b,c]

The partition coefficient of **1** and the hydrocarbon substrate are expected to differ significantly for most substrates in the multiphase system. Acetaldehyde (**1**) is highly volatile and "CO_2-philic" and therefore shows a preference for the $scCO_2$ phase under the reaction conditions, whereas substrates which are significantly less volatile are partitioned preferentially into the liquid phase. Thus, the concentration of substrate relative to **1** is high in the liquid phase, and this favors hydrocarbon conversion under multiphase conditions. This rationale is supported by the fact that the conversion of *n*-butane (**9**), which is more volatile than **1**, was found to be higher under single-phase conditions (Table 1, entry 2). Under multiphase conditions *n*-butane can be expected to participate preferentially in the gas phase and is therefore less available for the autoxidation process. However, the conversion of low-volatility linear simple alkanes was very low in this system in general, and was not investigated further.

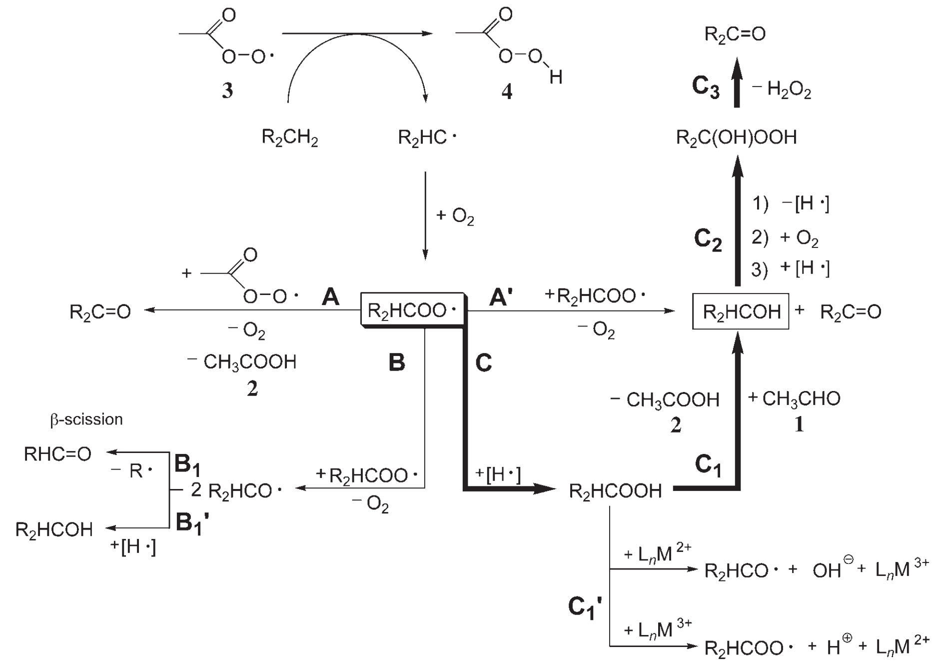
An additional important advantage of operating in the multiphase regime is the possibility of using high substrate concentrations (typically CO_2/hydrocarbon 16/1) and working at relatively low pressures (<100 bar). The amount of CO_2 was, however, never reduced below a density of $d = 0.18\,\mathrm{g\,mL^{-1}}$ in order to ensure safe reaction conditions with a oxygen content below the lower explosive limit reported for related mixtures ($c(O_2) < 14$ mol%).[18] High conversions and selectivities which are competitive with the best results reported in the open literature so far[13f] were obtained for cyclic alkanes (Table 1, entries 3–5) and alkylarenes (Table 1, entries 6 and 7) under these optimized conditions.

Interestingly, the compressed CO_2 atmosphere depresses the melting point of the substrates by dissolution of CO_2 in the substrates.[19] This broadens the range of potential substrates that can be used in the beneficial multiphase oxidation regime, as demonstrated for the oxidation of cyclododecane (**22**; Table 1, entry 5), which could be oxidized efficiently under liquid/supercritical conditions already at 45 °C, although its regular melting point is higher than the reaction temperature (m.p. 60.4 °C[20]). In contrast, adamantane (**5**), which remained solid under the reaction conditions, was oxidized with only 3% conversion (Table 1, entry 1).

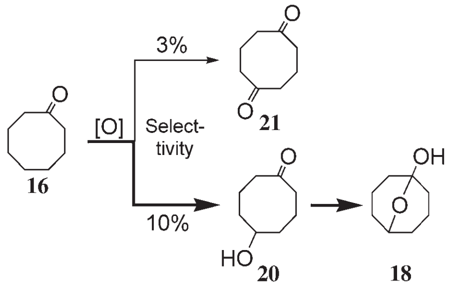
The presence of **1** is decisive for high conversion of the alkanes, as shown for the example of ethylbenzene (**29**). In the absence of **1**, conversion was reduced from 17% (Table 1, entry 7) to less than 4%. Comparing different substrates, their conversion can be correlated in first approximation with the number of oxidisable C–H bonds and their C–H bond-dissociation energies. In general, the oxidation processes proceeded with fair to high selectivities, and little if any total oxidation occurred, as seen from the mass balance. High ketone to alcohol ratios ranging from 3.5 to 7.9 were obtained in the oxidation of CH_2 units (Table 1, entries 3–5, 7). Oxidation of the benzylic CH group of cumene (**25**) led to the corresponding alcohol in good yield (Table 1, entry 6). Methyl groups remained largely unreactive. Although the overall conversion of adamantane (**5**) was low, the ratio of oxidation in tertiary versus secondary positions could be analyzed and showed a statistically corrected high value of 35:1. This finding supports a reaction pathway involving homolytic C–H cleavage by a selectively acting radical, most probably by the peroxy acyl radical **3** (vide infra).[21]

Mechanistic aspects of the radical oxidation pathways: A number of possible oxidation pathways may account for the formation of oxygenates under the present reaction conditions (Scheme 2). A detailed analysis of the product spectrum and a series of control experiments with potential intermediates were carried out for cyclooctane as model substrate to gain more insight into the reaction pathway in this system and in particular to rationalize the high ketone to alcohol selectivity.

The oxidation is initiated by formation of peroxy acyl radical **3**. This species can abstract a hydrogen radical from the alkane to give an alkyl radical and peracid **4**, which is detectable by on-line IR spectroscopy (vide infra). In the presence of O_2, the alkylperoxy radical is formed as the crucial intermediate. This can react further directly (pathways **A**/**A′** and **B**) or via formation of an alkyl hydroperoxide intermediate (pathway **C**). Pathways **A** and **A′** are based on bimolecular chain-termination reactions of peroxy radical intermediates, and products are generated by pericyclic elimination reactions from the radical-termination products (Scheme 2, **A** and **A′**).[14,23] This so-called Russel mechanism was proposed on the basis of a recent kinetic study on metal-free alkane oxidations using propionaldehyde.[24] This pathway is consistent with a high ketone to alcohol selectivity if the concentration of the peroxyacyl radical **3** is higher than that of the alkylperoxy radical. Under conventional reaction conditions, this is usually the case owing to the higher stability of **3**. Under the conditions used in the present study, the concentration of **1** and consequently **3** was kept very low in the reactive phase, and this border condition may therefore not be attained. To get more direct evidence, we subjected cyclooctanone (**16**) as a probe molecule to our oxidation conditions (Scheme 3).



Scheme 2. Overview of potential reaction pathways in oxygenate formation. The route which is believed to predominate in the present system is accentuated by bold arrows.



Scheme 3. Cyclooctanone (**16**) as substrate: Observed one/ol selectivities in the 5-position.

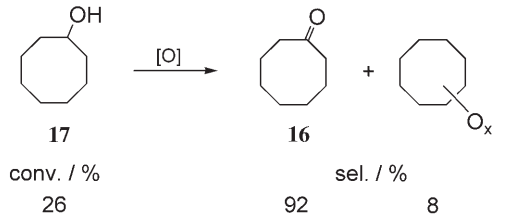
If the Russel mechanism (**A**/**A**′) is the dominant pathway in the present system and controls the high ketone selectivity, diketone **21** would be expected as the major product of oxidation at the 5-position of **16**. However, the bicyclic hemiketal **18** (9-oxabicyclo(3.3.1)nonan-1-ol, Scheme 3) was observed as the predominant doubly oxygenated product. Compound **18** is formed from hydroxylated ketone **20** in an intramolecular cyclization reaction.[25] As **18** is relatively inert against further oxidation, this product serves as a resting state for alcoholic intermediate **20**. Under the conditions of our study, **18** is largely preferred over the cyclooctane-1,5-dione **21** by a factor of more than three. Therefore, domination of the oxidation pathway by the Russel mechanism can be excluded, as the alcohol/ketone ratio would reach a maximum of 1/1 in this case (hypothetical termination via **A**′ only, Scheme 2).

The product distribution of the doubly oxygenated products arising from cyclooctane (**15**; Table 1, entry 4) is fully in line with these considerations. For the doubly oxygenated products, selectivity towards products arising from oxidation in 1,4- and 1,5-positions is remarkably high. This can be ascribed to the structure of the peroxycyclooctyl radical intermediate, in which the 4-position[26] and the 5-position are kinetically favored for intramolecular H abstraction. For oxidation in 1,5-positions, the bicyclic hemiketal **18** is formed as the major product (overall selectivity 3.5 %), as expected from the control experiment shown in Scheme 3. Stabilization in form of the intramolecular hemiketal is sterically unfavorable for the 1,4-oxidation product, and consequently cyclooctane-1,4-dione (**19**) is obtained as the main product in this case (7.8 %).

If we exclude the Russel mechanism as the major initial oxidation step, two alternative pathways for the formation of alcohols can be considered. On the one hand, two alkylperoxy radicals can recombine under loss of O_2 to form alkoxy radicals (Scheme 2, **B**). Secondary and in particular tertiary alkoxy radicals tend to undergo β-scission reactions accompanied by C–C bond cleavage (Scheme 2, $\mathbf{B_1}$) rather than H-atom abstractions to form the corresponding alcohols (Scheme 2, $\mathbf{B_1'}$).[14,23c] However, the β-scission reaction is observed only as a minor reaction channel in the present system. Even in the oxidation of cumene (**25**; Table 1, entry 6) the corresponding product acetophenone (**26**) is formed with only 17 % selectivity, as compared to the high selectivity of 66 % for the alcoholic product 2-phenylpropan-2-ol (**27**).

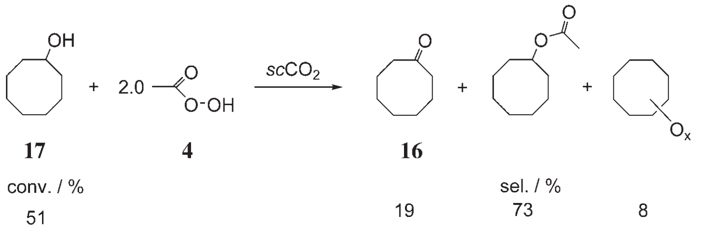
The remaining productive oxidation pathway is based on the formation of hydroperoxide intermediates owing to the high H-atom abstraction potential of alkylperoxy radicals (Scheme 2, **C**). These hydroperoxide intermediates could react further to peroxy and alkoxy radicals according to the Haber–Weiss mechanism (Scheme 2, $\mathbf{C_1'}$) in the presence of transition metal ions dissolved by corrosion from the stainless steel reactor walls (vide infra*)*. However, this pathway does not seem to play an important role, as indicated by the selectivity observed with cumene as substrate (**25**) (see above). Instead, the alkyl hydroperoxides can be expected to be effectively transformed into alcohols in a nonradical manner under the reaction conditions, most probably by the present co-reductant **1** (Scheme 2, $\mathbf{C_1}$). In accordance with these considerations, small amounts of hydoperoxides could be detected by iodometric titration in the product mixtures.

Further radical oxidation of the secondary alcohols to the ketones is favored by their highly activated geminal H atom for homolytic cleavage, which nicely explains the observed high ketone to alcohol selectivity (Scheme 2, $\mathbf{C_2}\rightarrow\mathbf{C_3}$). To check this hypothesis the oxidation of cyclooctanol (**17**) as a starting material was carried out under analogous reaction conditions as in Table 1 (Scheme 4). The observed conversion (26 %) and selectivity for **16** (92 %) are fully in line with the proposed pathway. The moderate conversion of pure **17** may be explained by the fact that secondary alcohols in high concentrations have the potential to form hydroperoxo radicals under autoxidation conditions, which are known to be effective radical scavengers.[14,23c]



Scheme 4. Selective transformation of cyclooctanol (**17**) into cyclooctanone (**16**) under analogous reaction conditions as in Table 1.

We also considered an ionic pathway for alcohol oxidation, which might result from high intermediate concentrations of peracetic acid (**4**) in the presence of transition metal ions from the reactor walls. The fact that peracid **4** can participate in oxidation processes under the present reaction conditions is evident from the results with cyclohexane (**11**), for which formation of small amounts of ε-caprolactone (**14**) by Baeyer–Villiger oxidation of the main product cyclohexanone (**12**) is most likely accomplished by **4** (Table 1, entry 3).[9] To check the possibility of similar oxidation of the alcohol intermediates, **17** was treated with two equivalents of **4** (as a 1/1 mixture with **2**) under comparable reaction conditions (Scheme 5). However, ketone **16** was formed with only 19 % selectivity. The main product of this reaction was cyclooctyl acetate (73 % selectivity), a species that was never observed under standard alkane oxidation conditions. These results argue strongly against a significant contribution of **4** to alcohol oxidation for product formation.



Scheme 5. Reaction of cyclooctanol (**17**) with peracetic acid (**4**) under otherwise comparable reaction conditions as in Table 1.

In summary, the substrate scope and product distribution summarized in Table 1 together with the control experiments for cyclooctane derivatives **16**–**18** strongly suggest that the formation of oxygenates occurs via hydroperoxide intermediates under the present conditions (Scheme 2, pathway **C**) which are converted to alcohols as the primary products (pathway $\mathbf{C_1}$). For tertiary C–H units, the reaction stops at this stage, whereas secondary alcohols are converted with high selectivity further to the corresponding ketones in a radical process (**C2**→**C3**).

Initiating effect of the reactor walls: As shown previously, the initiation of radical oxidation pathways with O_2/aldehyde mixtures is facilitated by the presence of steel or other metal surfaces.[8,27] To gain more insight into the initiating role of the stainless steel reactor under the present reaction conditions, we investigated the course of the reaction by time-resolved high-pressure ATR-FTIR online spectroscopy.[16,28] Two reactor types were compared: a standard reactor as used in the preparative runs (Figure 1 A) and a modified reactor in which the contact of the reaction mixture with the steel surface was greatly reduced by insertion of a glass liner (Figure 1 B). Experiments were carried out under identical conditions of reaction temperature, concentration of all reactants, and stirring speed. To avoid mass-transfer

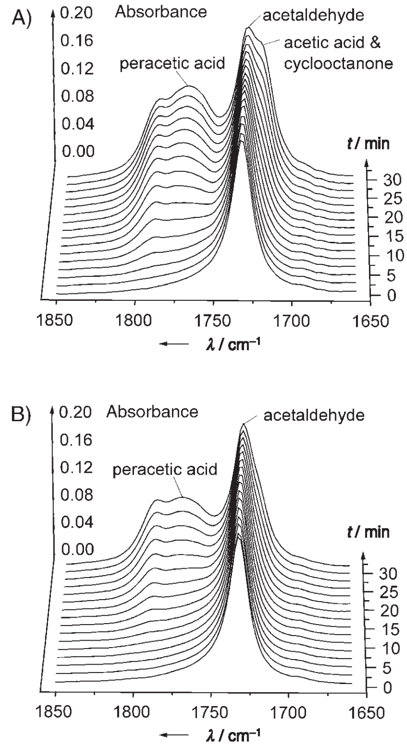


Figure 1. Time-resolved high-pressure ATR-FTIR online spectra in the carbonyl stretching region in the initial stage of comparable experiments (c, T, rpm = const.; oxygen addition at t_0 over 30 s). A) Standard reactor, B) reactor with glass liner.

limitations, oxygen was introduced at t_0 as the last component in these experiments within 30 s into the loaded and heated reactor at the temperature-equilibrium stage. At constant intervals of two minutes, an IR spectrum of the multiphase reaction mixture was recorded. The course of the reaction was followed by conversion of the bands assigned to **1** ($\tilde{\nu}_{C=O}=1735\,cm^{-1}$) to those of **4** ($\tilde{\nu}_{C=O}=1765\,cm^{-1}$), **2** ($\tilde{\nu}_{C=O}=1720\,cm^{-1}$) and **16** ($\tilde{\nu}_{C=O}=1710\,cm^{-1}$).

The time-resolved IR spectra of two representative experiments are shown in Figure 1. In both spectra the formation of **4** is clearly indicated as the corresponding band grows in, but it appears much later in the set-up with the glass liner. After 30 min the bands of acetic acid (**2**) and **16** can only be identified in the standard reactor, but are not yet significant in the glass-lined reactor. The peak area containing **2** and **16** shows the absorption maximum at the final stage of the reaction and was therefore chosen for analysis of the reaction profiles. Two independent experiments were carried out for all conditions and indicated very good reproducibility of the induction period and reaction rates under various conditions.

The resulting reaction profiles of standardized average absorbance at 1720 cm^{-1} together with the time-resolved standard deviation are depicted for the initial phase of the reaction in Figure 2. A shorter induction period was observed for the experiments in the standard reactor than in the glass-lined reactor. The probability for significant differences was found to be 90 % for each average value by interpolation of tabulated probabilities as a function of calculated integration limits of the t-distribution.[29] This result is a reliable proof for initiation of the radical pathway by the reactor walls.

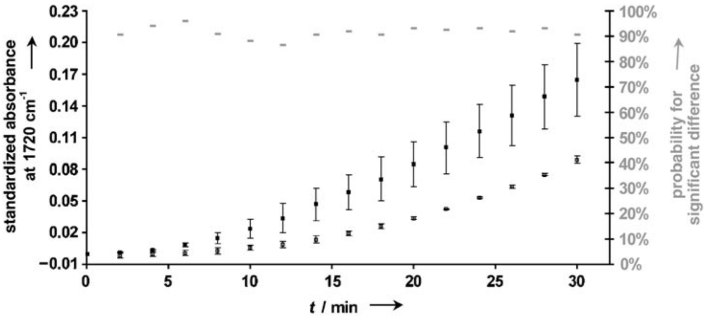


Figure 2. Initiating effect of the stainless steel reactor walls: Comparison of induction periods of the standard reactor with the reactor with a glass liner. ■ = standard reactor: average values including standard deviation; □ = reactor with glass liner: average values including standard deviation.

In a further experiment stainless steel shavings (V4A, reactor material) were added to the standard reactor before starting oxidation. The overall reaction profiles for all three conditions are summarized in Figure 3. The induction period was not significantly shortened further by the addition of steel shavings. However, the reaction rate was significantly faster with a higher maximum and, in particular, average rate. This indicates that the available steel surface initiates not only the formation, but probably also influences the concentration of the chain-starting radicals. The conversion of **15** and the selectivity for the various oxygenates was not significantly different under the three different conditions. Experiments in a high-pressure reactor made of titanium rather than stainless steel led also to comparable conversions and selectivities with **15**, that is, the initiation effect seems to be largely independent of the reactor material.

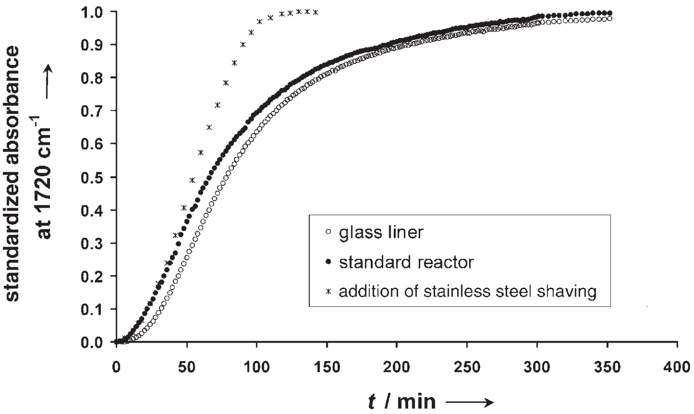


Figure 3. Reaction profiles with variation of the accessible stainless steel surface.

The initiation effect of the reactor wall could be a heterogeneous surface process or result from small amounts of metal ions that leach out of the reactor walls into the reaction mixture. Although the conditions of the reaction are very mild and noncorrosive in the beginning, the acetic acid formed during the reaction does indeed induce some corrosion, and in typical experiment leaching of 100 ppm of steel (composition: 44 % Fe, 31 % Ni, 16 % Mo, 8 % Cr) was observed. This value includes also the fraction of mobile metal ions that could be elutriated with hydrochloric acid (15 %, Suprapur, 5 min, room temperature) from the reactor walls after the reaction. However, a filtered crude fraction of such a colored acetic acid/metal-rich phase showed no initiation effect in the reactor with glass liner under standard reaction conditions (Figure 4, 3 versus 1 and 2). Product inhibition effects can be excluded in this experiment as conversion restarted with almost identical rate and conversion when fresh substrate was added at the end of a standard reaction (Figure 4, 2 versus 1). These results provide strong evidence for heterogeneous initiation at the metal surface rather than initiation by leached metal ions.

In summary, the results described in this section support a reaction mechanism in which surface metal species with the capability of one-electron transfer initiate the free-radical chain process via the formation of acyl radicals from acetaldehyde (**1**). In the presence of oxygen, peroxyacyl radicals **3** are generated rapidly, which are known to be potential H-atom abstracting agents even for unactivated C–H bonds.[14] The results indicate that the stainless steel surface acts not only as the initiator for the radical chain, but can also function as a catalyst, probably by influencing the concentration

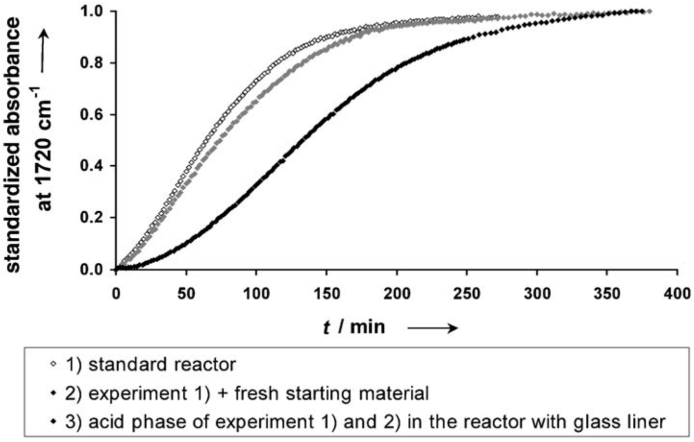


Figure 4. Proof for heterogeneous initiation.

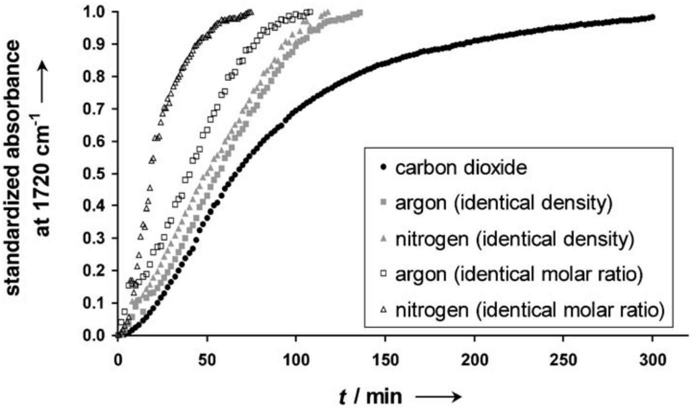


Figure 6. Reaction profiles in different inert gases with the use of either identical molar ratios or identical densities as with CO_2.

of the initiating radicals. However, the length and the relative rates of the radical chains seem to be largely independent of the metal surface, which further supports the mechanism discussed in the previous section involving **1** as the crucial controlling reagent for the overall reaction.

Comparison of carbon dioxide with nitrogen and argon as reaction media: Finally, the use of CO_2 as reaction medium was compared to other compressed gas phases. N_2 and Ar were chosen because of their inert character in radical reactions under mild conditions. Nitrogen is widely used as diluting gas in industrial oxidation processes using molecular oxygen. Reaction conditions such as temperature, oxygen/aldehyde/substrate ratio, stirring and so on were kept identical, and the two gases were compared under identical molar ratios (gas:**15** = 68:1) and fluid densities (0.17 gmL^{-1}) as used with CO_2. All three gases have very low dielectric constants and similar dielectric polarisabilities at 50 °C, with a marginally higher polarity of carbon dioxide as compared to the other two gases [$\varepsilon(CO_2) = 1.054$ (50 bar), $\varepsilon(Ar) = 1.034$ and $\varepsilon(N_2) = 1.033$ (both 70 bar)].[30] Dew-point measurements on **1** in the pure inert gases also indicated a largely identical solubility of **1** in the compressed gas phases at identical fluid densities (Figure 5).

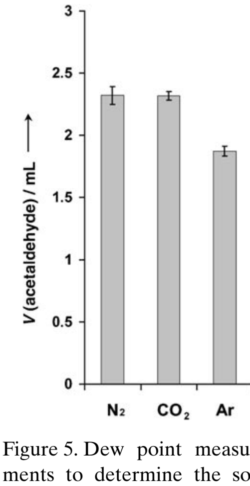


Figure 5. Dew point measurements to determine the solubility of **1** in compressed N_2, CO_2 and Ar. Conditions: V(autoclave) = 225 mL, d(gas) = 0.17 gmL^{-1}, T = 42 °C; observed pressures: $p(CO_2) = 63$ bar, $p(N_2) = 164$ bar, $p(Ar) = 111$ bar.

The reaction profiles in N_2 and Ar showed significantly shorter induction periods and higher reaction rates as compared with CO_2 (Figure 6). Independent of whether the comparison is made at identical fluid densities or molar ratios of the compressed gas phase, the time to reach the final state of the reaction corresponding to full conversion of **1** to **2** was longer by a factor of two and more for compressed CO_2. In sharp contrast, however, significantly higher conversion of cyclooctane (**15**) and higher yields of cyclooctanone (**16**) were observed with CO_2 as compared to the other two gases under otherwise identical reaction conditions (Figure 7). In a first approximation, the reaction time is in fact inversely proportional to the cyclooctane conversion, and this makes CO_2 the medium of choice under preparative conditions.

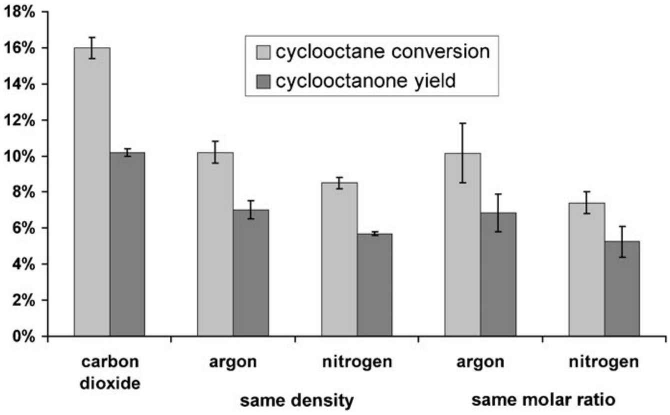


Figure 7. Comparison of conversions of cyclooctane (**15**) and yields cyclooctanone (**16**) in CO_2, Ar and N_2 under similar reaction conditions.

Although the beneficial influence of CO_2 on the conversion and yield of the oxidation process may result from a combination of various factors, it seems to be of particular relevance that only CO_2 effected a noticeable expansion of the liquid phase under the reaction conditions. Therefore, the higher oxygen availability in the CO_2-expanded liquid phase[6] may result in a more favorable conversion of the alkane relative to the autoxidation of aldehyde **1**.

Conclusion

The results of the present study demonstrate that compressed carbon dioxide provides an effective reaction medium for oxidation of saturated hydrocarbons in coupled processes using molecular oxygen as the terminal oxidant and acetaldehyde as sacrificial co-reductant. High conversions and good yields of oxygenates were obtained for cycloalkanes and alkylarenes under liquid/supercritical multiphase conditions. Ketones were formed as predominant products with high selectivity from secondary carbon centers, whereas alcohols were produced in good yields from tertiary carbon atoms. A common reaction pathway involving radical formation of hydroperoxide intermediates was proposed on basis of mechanistic evidence, and the co-reductant **1** was shown to play a decisive role not only in initiating but also in controlling this reaction network.

High-pressure ATR-FTIR on-line spectroscopy proved to be an excellent tool for reliable determination of reaction profiles in these multiphase systems and provided strong evidence for the heterogeneous initiation effect of the stainless steel reactor walls on the radical process. In comparison with N_2 and Ar, conversions and yields were significantly higher with CO_2 as the reaction medium under otherwise identical conditions. This may be due at least partly to the different swelling behavior of the substrate phase in the presence of these three compressed gases.

In conclusion, this study provides detailed insight into a complex radical oxidation process using $scCO_2$ as reaction medium. It provides guidelines to how the unique physicochemical properties of this medium can be utilized to influence a molecular transformation. This information may be useful also for other oxidation processes, including catalytic reactions. Further efforts to evaluate $scCO_2$ as potentially safe and efficient reaction medium for oxidation processes therefore seem promising.

Experimental Section

Safety warning: The use of compressed gases and especially O_2 in the presence of organic substrates requires appropriate safety precautions and must be carried out only in suitable equipment.

Reagents: All liquid starting materials were destilled under argon prior to use. The gases dioxygen (Messer Griesheim, 4.8), CO_2 (Messer Griesheim, 4.5 or technical quality) and *n*-butane (Messer Griesheim, 2.5) were used as recieved.

Reactor: Stainless steel reactor ($V = 205$ mL, austenitic steel No. 1.4571, Teflon O-seals) equipped with thick-walled glass windows, valves for addition and removal of samples, a dosing unit for acetaldehyde and a high pressure ATR-FTIR element (attenuated total reflection, ReactIR 1000, Mettler Toledo), which was introduced into the reactor through a specially designed and home-built lid. The ATR probe was situated in the middle of the reactor in the compressed gas phase, where constant wetting and exchange of the liquid film was ensured by vigorous stirring (2000 rpm).

Procedure for preparative experiments (Table 1): The reactor was filled with the alkane (50 mmol), carbon dioxide (35 g) and molecular oxygen (105 mmol) in that order. The amount of CO_2 was weighed into the reactor to achieve the desired density. Defined amounts of oxygen were added by a pressure difference of at least 30 bar (resolution 1 bar) from a storage vessel with known volume. The required pressure difference was calculated from the virial equation including the second virial coefficient and the temperature of the storage vessel. Then the reactor was heated to 52 °C (inner temperature) and the IR background was taken. Simultaneously with the beginning of acetaldehyde addition by diffusion from a completely filled dosing unit, IR monitoring was started (t_0). No temperature rise (resolution 1 °C) was detected inside the autoclave under these conditions.

When the absorbance at 1720 cm^{-1} (including carbonyl stretching frequencies of acetic acid and hydrocarbon oxygenates) achieved a constant value, monitoring was stopped and the reactor was cooled to room temperature and slowly depressurized (ca. 5 h) from the bottom through a needle valve into a cold trap kept at −50 °C. The two-phase mixture remaining in the cold trap (acetic acid-rich and hydrocarbon-rich phases) was homogenized by addition of diethyl ether. Three independent samples were analyzed by GC-MS with *n*-alkanes having suitable retention times as internal standard.

Procedure for monitoring reaction profiles: The reactor was filled with cyclooctane (11.6 mmol, glass-lined: 9.1 mmol) and different inert gases as described above. Then the reactor was heated to an inner temperature of 42 °C and the IR background was taken. IR monitoring was started with the beginning of acetaldehyde addition (23 mmol, glass-lined: 18 mmol) from a balanced dosing unit by diffusion (partially accelerated by moderate heating). After a constant intensity of the carbonyl stretching frequency of the acetaldehyde ($\tilde{\nu}_{C=O} = 1735\,cm^{-1}$) was reached, 25 mmol of molecular oxygen (glass-lined: 19 mmol) were added over 30 s as described above (t_0). At no time of the reaction could a temperature rise (resolution 1 °C) be detected inside the autoclave. Monitoring was stopped when the absorbance A at 1720 cm^{-1} achieved a constant value. Further workup was performed in a similar manner as described above. Standardized absorbances (SA) at 1720 cm^{-1} were calculated by Equation (1).

$$SA = \frac{A(t_i) - A(t_0)}{A_{max} - A(t_0)} \qquad (1)$$

Procedure for dew-point measurements: A continuously stirred (2000 rpm) window-equipped reactor ($V = 225$ mL) was filled with 40 g of inert gas and heated to an inner temperature of 42 °C. Then defined amounts of acetaldehyde were added in 0.06 mL aliquots by using a 5 mL burette (resolution 0.01 mL) connected to the reactor with a HPLC pump (flow rate 0.3 mL min^{-1}). Once condensation of small droplets of aldehyde was observed on the window, addition was stopped and the solubility determined from the amount added from the burette.

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compressed and heated at pressures and temperatures beyond the critical values of pure CO_2 ($T_c = 31.0\,°C$, $p_c = 74.75$ bar). For simplicity, this notation is used independently of the phase behavior of the complex multicomponent reaction mixture, which is currently not known exactly. Homogeneous or multiphase reaction conditions, as identified by visual inspection during the experiments, are indicated in the text.

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