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Selective oxidation of cyclooctane to cyclootanone with molecular oxygen in the presence of compressed carbon dioxide

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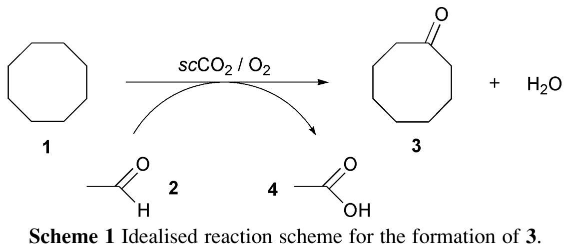
The oxidation of cyclooctane (1) to cyclooctanone (3) with molecular oxygen and acetaldehyde (2) as a co-reductant occurs efficiently in the presence of compressed CO_2. Up to 20% yields of 3 are obtained under optimised multiphase conditions.

The selective oxidation of hydrocarbons with molecular oxygen is one of the great challenges for synthetic chemistry from an economic as well as an ecological point of view.[1] Compressed carbon dioxide is a very attractive reaction medium for oxidation reactions, because it allows the combination of high concentrations of substrates and oxygen with the additional safety of a totally inert environment. There are, however, surprisingly few examples for selective oxidation reactions in carbon dioxide media.[2]

Recently we reported the steel-promoted epoxidation of olefins under Mukaiyama-type reaction conditions in supercritical carbon dioxide.[3] In the absence of an extra catalyst good to excellent yields were observed for substrates with internal double bonds and for long chain terminal olefins. Here, we describe the application of a similar methodology to alkane oxidation (Scheme 1).

The use of aldehydes as co-reductants is a very well established methodology in oxidation chemistry. Acetaldehyde was used in the present study as the cheapest suitable co-reductant. Cyclooctane was chosen as a model substrate because all reactive positions are identical and the main oxidation product, cyclooctanone, was proven to be inert towards Baeyer–Villiger-oxidation under these reaction conditions.[4] The reactions were monitored by online time-resolved high pressure IR-spectroscopy. † Fig. 1 shows the carbonyl region of a typical experiment in the initial stage.



Scheme 1 Idealised reaction scheme for the formation of **3**.

At t_0, **2** ($\tilde{\nu}_{C=O}$ = 1735 cm^{-1}) starts to diffuse into the reactor where it is converted to peracetic acid ($\tilde{\nu}_{C=O}$ = 1765 cm^{-1}) and acetic acid **4** ($\tilde{\nu}_{C=O}$ = 1720 cm^{-1}) during the course of the reaction. The C=O stretching frequency of **3** is obscured by these strong bands. Reactions were allowed to proceed until a constant intensity of the acetic acid band was reached. With this new system very high conversions and selectivities of **3** could be obtained in the absence of a catalyst with a maximum yield of **3** up to 20% (Table 1).

The yield of ketone **3** obtained in the presence of carbon dioxide compares favourably to the best values under conventional conditions with related oxidation systems (11%).[5,6] Conversion and especially selectivity are also significantly higher than those reported for the oxidation of cyclohexane in $scCO_2$. Only 3% of cyclohexanone was achieved with an iron porphyrin catalyst at 70 °C using 0.25 equivalents of acetaldehyde[7] or by autoxidation in the absence of aldehyde at 160 °C.[8]

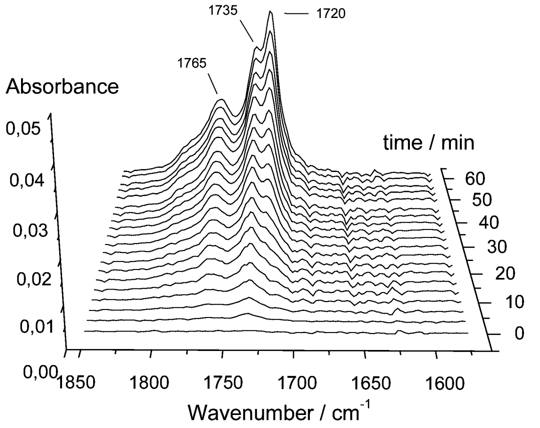


Fig. 1 Time resolved ATR-IR spectra of cyclooctane oxidation in compressed carbon dioxide showing the region of carbonyl stretching frequencies (conditions as in entry 4).

Table 1 Oxidation of cyclooctane **1** with molecular oxygen in the presence of acetaldehyde **2**[a]

Entry	ρ (CO_2)/g ml^{-1}	T/°C	Time/h	Cyclooctane **1** Conversion[b] (%)	Cyclooctanone **3** Selectivity[b] (%)	Yield[b] (%)	Cyclooctanol Selectivity[b] (%)	Cyclooctane-1,4-dione Selectivity[b] (%)
1	0.62	42	36	9.3	61.5	5.7	2.1	23.5
2	0.58	52	24	10.4	64.5	6.7	2.9	18.2
3	0.18	42	46	23.8	66.0	15.7	7.1	8.0
4	0.18	52	26	27.6	66.9	18.4	8.5	7.8
5	0.18	70	10	30.9	62.1	19.2	6.2	10.9
6	0.18	90	1.4	33.7	57.6	19.5	5.9	11.9
7[c]	0.18	70	10	37.3	59.6	22.3	4.1	14.2

[a] N (**1**:O_2:**2**) = 1:2.1:2.0; for standard reaction conditions see note †. [b] Determined by GC analysis. Selectivities were calculated from the mole fractions of the products. Total recoveries varied between 85 and 100%. Other typical by-products were 9-oxabicyclo(3.3.1)nonan-1-ol (isolated by preparative GC and identified by ^{13}C-NMRspectroscopy),[9] cyclooctyl hydroperoxide and adipic acid. [c] N (**1**:O_2:**2**) = 1:3.1:4.0.

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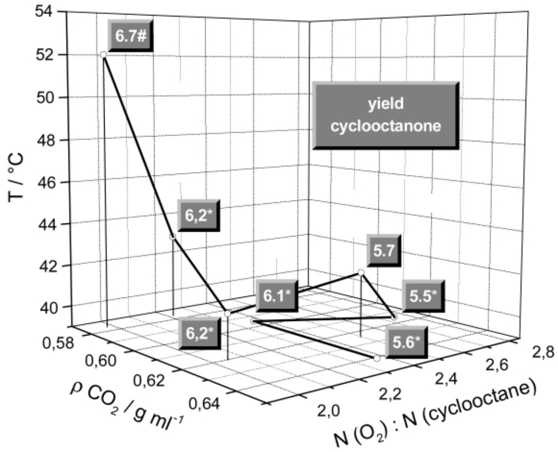

Fig. 2 3-D-Simplex-optimisation in the high density regime. * Reaction became heterogeneous during the reaction. # Experiment is not part of the statistical algorithm.

Notably, other gases were considerably less efficient as inert diluting agents as compared to CO_2. Using largely identical molar ratios of inert gas, oxygen and reagents, the yields of **3** were 10.7% for N_2, 7.1% for SF_6 and 4.3% for Ar under the conditions of entry 3. Furthermore, our results indicate that the density of carbon dioxide is instrumental to control the reactivity and selectivity of the catalyst-free oxidation.

Fig. 2 shows a 3-D-Simplex-Optimisation[10] of the relevant reaction parameters temperature, oxygen-to-substrate ratio and CO_2 density. The 3-D-Simplex-optimisation shows a trend to improved yields with lower CO_2-densities, lower oxygen to substrate ratio and higher reaction temperatures.

Further optimisation over a wider range of reaction conditions indicated a particularly pronounced effect of the carbon dioxide density (Table 1). Reducing the carbon dioxide density from around 0.60 g cm^{-3} to 0.18 g cm^{-3} results in a two-phase reaction system in all cases from the beginning.[11] This emerged as quite effective since the yield of **3** increased by a factor of 2.7 under otherwise identical reaction conditions (*cf.* Table 1, entries 1/3 and 2/4). The conversion of **2** was complete, however, in all cases. This indicates that the higher yield of **3** can be mainly attributed to a more efficient oxygen transfer relative to the autoxidation of **2**. This pronounced density effect can be related to a more efficient interception of free radicals in the liquid phase.[8]

The presence of a free radical pathway is strongly supported by two observations. First of all the exclusive formation of cyclooctane-1,4-dione as side product with two keto functions is best ascribed to the intramolecular attack of a cyclooctyl peroxo radical intermediate on the kinetically favoured 4-position. Secondly the observed 1-adamantol to 2-adamantone ratio of 4.5 : 1 for adamantane as substrate clearly indicates the operation of a radical rather than a metaloxo pathway[6] (conditions similar to those of entry 4).

The radical chain is believed to be initiated by steel-promoted formation of the peroxo acyl radical.[3] H-Abstraction from **1** followed by addition of molecular oxygen leads to the formation of the cyclooctyl peroxo radical. This species can either react with another cyclooctyl peroxo radical to give an equimolar amount of cyclooctanol and **3** or react with a peroxo acyl radical to give **3** and peracetic acid. We favour the latter pathway on basis of the high ketone to alcohol ratio[12] and the observed influence of the reaction parameters.[13]

In summary, compressed carbon dioxide provides an inert reaction medium for efficient and selective oxidation of cyclooctane using O_2–aldehyde mixtures. It is more effective than other inert diluting gases under identical conditions and up to 20% yield of cyclooctanone were obtained under optimised multiphase conditions.

Notes and references

† **Safety warning**: The use of compressed gases and especially O_2 in the presence of organic substrates requires appropriate safety precautions and must only be carried out using suitable equipment. In a typical experiment the stainless steel reactor (V = 205 ml, austenitic steel No. 1.4571, teflon O-seals) equipped with thick walled glass windows and an IR-ATR element (Attenuated Total Reflection, ReactIR, Mettler Toledo) was filled with cyclooctane (50 mmol), carbon dioxide and molecular oxygen 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 bars (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. Acetaldehyde (100 mmol) was added last by diffusion ($\dot{n}$ ~ 1 mmol min^{-1}) from a completely filled dosing unit into the reactor at the desired reaction temperature. When the absorbance at 1720 cm^{-1} (including carbonyl stretching frequencies of acetic acid and cyclooctyl compounds) achieved constant values the reaction was stopped by cooling to rt followed by slow depressurisation (~ 5 h) from the bottom of the reactor through a cold trap of −50 °C. The two-phase mixture remaining in the cold trap was homogenized by adding diethyl ether and analysed by GC-MS using n-decane as internal standard. The FID-signals of cycloctanone (f = 1.230 ± 0.009) and cyclooctanol (f = 1.246 ± 0.015) were corrected according to their exact response factors. The correction factors for 9-oxabicyclo-(3.3.1)nonan-1-ol (f = 1.32), cyclooctane-1,4-dione (f = 1.40) and all other found products (f = 1.40) were estimated. The contents of peroxides was < 4% in all experiments according to iodometric analysis;[14] the exact values showed no correlation with conversion or reaction temperature.

1 (*a*) A. E. Shilov and G. B. Shul'pin, *Activation and Catalytic Reactions of Saturated Hydrocarbons in the Presence of Metal Complexes*, Kluwer Academic Publishers, 2000; (*b*) J. M. Thomas, R. Raja, G. Sankar and R. G. Bell, *Nature*, 1999, **398**, 227; (*c*) A. K. Suresh and T. Sridhar, *Ind. Eng. Chem. Res.*, 2000, **39**, 3589; (*d*) I. W. C. E. Arends and R. A. Sheldon, *Applied Catalysis A: General*, 2001, **212**, 175–187; (*e*) U. Schuchardt, D. Cardoso, R. Sercheli, R. Pereira, R. S. da Cruz, M. C. Guerreiro, D. Mandelli, E. V. Spinacé and E. L. Pires, *Applied Catalysis A: General*, 2001, **211**, 1.
2 (*a*) *Chemical Synthesis Using Supercritical Fluids*, eds. P. G. Jessop and W. Leitner, Wiley-VCH, 1999; (*b*) D. A. Morgenstern, R. M. LeLacheur, D. K. Morita, S. L. Borkowsky, S. Feng, G. H. Brown, L. Luan, M. F. Gross, M. J. Burk and W. Tumas, in *Green Chemistry, ACS Symp. Ser. 626*, eds. P. T. Anastas and T. C. Williamson, American Chemical Society, Washington DC, 1996, 132; (*c*) A. Martin and B. Kerler, *Chem. Ing. Tech.*, 2000, **72**, 382.
3 W. Leitner and F. Loeker, *Chem. Eur. J.*, 2000, **6**, 2011.
4 C. Palazzi, C. Bolm, G. Franciò and W. Leitner, manuscript in preparation.
5 S.-I. Murahashi, Y. Oda and T. Naota, *J. Am. Chem. Soc.*, 1992, **114**, 7913.
6 A. M. Khenkin, A. Rosenberger and R. Neumann, *J. Cat.*, 1999, **182**, 82.
7 X.-W. Wu, Y. Oshima and S. Koda, *Chem. Lett.*, 1997, 1045.
8 P. Srinivas and M. Mukhopadhyay, *Ind. Eng. Chem. Res.*, 1997, **36**, 2066.
9 A. J. Bloodworth, J. A. Khan and M. E. Loveitt, *J. Chem. Soc., Perkin. Trans. 1*, 1981, 621.
10 M. Otto, *Chemometrie—Statistik und Computereinsatz in der Analytik*, Wiley-VCH, 1997, 127.
11 Although the exact explosion limits of the system under scrutiny are not known, the large amount of carbon dioxide can be expected to allow for safe operation even in the low density regime. See for example B. Lewis and G. von Elbe, *Combustion, Flames and Explosions of Gases*, Academic Press, New York, 1951.
12 Oxidation of cyclooctanol to **3** by intermediate high concentrations of peracetic acid can not be ruled out completely.
13 V. I. Timokhin, M. T. Lisovska and A. P. Pokutsa, *Kinet. Catal. (Engl. Transl.)*, 2000, **41**, 159.
14 R. Alcantara, L. Canoira, P. G. Joao, J.-M. Santos and I. Vázquez, *Applied Catalysis A: General*, 2000, **203**, 259.