New routes for the selective C–H hydroxylation of linear n-alkanes with molecular oxygen

Michiel Janssen,[a] **Lisa Van Emelen,**[a] **Dirk E. De Vos**[a,*]
[a]*Centre for Surface Chemistry and Catalysis, Department of Microbial and Molecular Systems, KU Leuven – University of Leuven, Leuven Chem&Tech, Celestijnenlaan 200F, Post Box 2461, 3001 Heverlee, Belgium*
**E-mail address: dirk.devos@biw.kuleuven.be*

Abstract: In this work, the use of a Shilov-inspired Pt(II) catalyst has been evaluated for the selective oxidation of linear n-alkanes to (primary) alcohols with molecular oxygen in aqueous solutions. To ensure reactant compatibility and solvent stability, perfluorinated micro-emulsions were introduced as innovative system. Although conversions remained low for heptane as model substrate, improved alcohol selectivities (> 15%) were achieved with selective formation of 1-heptanol (> 50%). Transfer of this concept to acetic acid resulted in a thirtyfold increase in conversion, while maintaining similar selectivities. For both systems, the ability of Pt to selectively activate long linear n-alkanes was unambiguously proven.

Keywords: Selective alkane hydroxylation, Shilov-inspired Pt catalyst, molecular oxygen.

1. Introduction

Alkanes are major inexpensive constituents of both natural gas and crude oil reserves, making them an ideal feedstock for the manufacture of valuable chemicals. Nevertheless, high C–H bond dissociation energies (BDE, > 380 kJ/mol), inherent to alkanes, render them chemically inert. The selective hydroxylation of linear n-alkanes therefore remains a largely unresolved challenge. More specifically, under the harsh conditions needed for C–H activation, radical-mediated pathways often predominate and decide upon the selectivity pattern, creating two important drawbacks: a low chemo- and regioselectivity.[1] As a result, the chemical industry uses energy-intensive multi-stage technologies rather than liquid-phase alkane autoxidation processes for the synthesis of (primary) alcohols.[2] The design of selective, low-temperature alkane hydroxylation processes is thus highly desired. Among the various (bio)catalytic routes under investigation, the electrophilic alkane activation stands out as it holds the intrinsic promise of both alcohol and terminal selectivity within the aliphatic chain. Accordingly, this research concentrates on using the environment-friendly Shilov system, which employs an electrophilic Pt(II) catalyst with molecular oxygen (O_2) in aqueous media (Figure 1).[3] Despite its broad applicability, linear n-alkanes are largely excluded from the substrate scope because of their negligible water solubility. We therefore aimed to overcome this limitation by introducing Shilov's concepts into more compatible solvents that still exhibit sufficient oxidative stability.

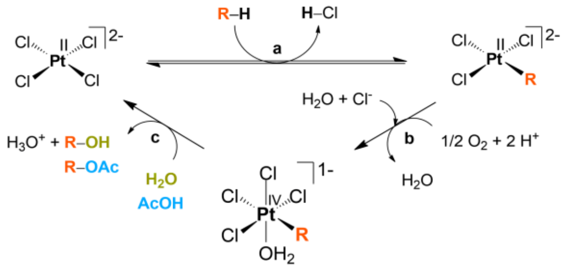

Figure 1. Catalytic cycle for the Shilov system in water vs. acetic acid as solvent.[3]

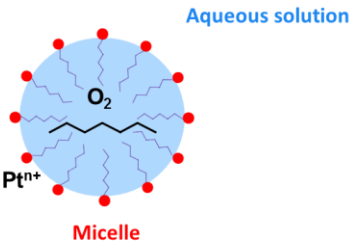

Figure 2. Pt-based perfluorinated micro-emulsion of heptane with perfluorooctanoic acid (●〰) as surfactant.

2. Experimental

All reactions were performed in a glass reaction vial, which was placed inside a high-pressure stainless steel reactor. In a typical reaction, the glass vial was loaded with heptane, a surfactant, a homogeneous Pt catalyst and an acidic aqueous solution. In contrast, equimolar amounts of a certain anhydride were added instead of the surfactant when similar reactions were conducted in acetic acid. Next, the reactor was sealed, pressurized with O_2 at room temperature and stirred for 1 h at 130-150 °C. Finally, the reactor was allowed to cool down, after which the product mixture was analyzed via GC and NMR.

3. Results and discussion

Perfluorooctanoic acid was selected as surfactant because of its high oxidative stability ($BDE_{C–F}$ = 485 kJ/mol) and its capacity to dissolve significant amounts of hydrocarbons and O_2.[4,5] In addition, we presumed that the carboxylic acid groups could immobilize and position the homogeneous Pt catalyst in close proximity of the substrate (heptane) and oxidant (Figure 2). Although low conversions (< 2%) were obtained, initial results revealed superior selectivities over those typically achieved during autoxidation (Table 1).[6]

Table 1. C–H oxidation of alkanes in a Pt-based perfluorinated emulsion vs. classical autoxidation.
S_{OH} = Alcohol selectivity, $S_{1\text{-}OH}$ = Positional selectivity for primary alcohol, C(–OH)/C(=O) = Alcohol-to-ketone ratio.

	Conversion (%)	S_{OH} (%)	$S_{1\text{-}OH}$ (%)	C(–OH)/C_7(=O)
Classical autoxidation	< 6	< 4	< 2	< 0.30
Pt-based perfluorinated emulsion	0.57	16	22	1.23

Moreover, a combined optimization of the acid concentration and catalyst loading allowed us to raise the amount of active Pt, coordinated to a carboxylate group, leading to a significant improvement in selectivity for 1-heptanol to > 50%. These results strongly point towards the functioning of Shilov's chemistry inside perfluorinated micro-emulsions.

In analogy with the system reported by Hanotier *et al*. (1972),[7] we successfully hypothesized that replacing water with acetic acid might improve the solubility and therefore reactivity of the substrate. Furthermore, the Shilov chemistry dictates that the aqueous solvent, instead of O_2, is required to form the desired alcohol product during functionalization (Figure 1, **c**). As displayed in Figure 1, in situ acetylation might thus occur when performing identical reactions in acetic acid, which could protect the resulting alcohols from overoxidation. In this way, we believed that enhanced selectivities could be maintained at higher conversions. In particular, a thirtyfold increase in conversion took place after a certain induction period, while a positional selectivity of 18% remained for the primary alcohol. Although overoxidation still occurred to some extent, selective functionalization was achieved with *tert*-butylbenzene as substrate. In addition, deviating selectivities were observed in the presence of Co(II)OAc, a well-known radically accelerating catalyst, displaying the inability of Pt to induce autoxidation. Both experiments explicitly demonstrate the role of Pt in achieving improved selectivities during the hydroxylation of linear n-alkanes. Finally, we identified that equimolar amounts of a certain anhydride are necessary to ensure Pt activity.

4. Conclusions

To our knowledge, we have proven for the first time that the one-step hydroxylation of linear n-alkanes with molecular oxygen becomes feasible by introducing a homogeneous Pt catalyst in perfluorinated micro-emulsions. In the presence of perfluorooctanoic acid as surfactant, superior (positional) selectivities were attained over those achieved during autoxidation. Changing the solvent to acetic acid allowed us to significantly improve the conversion without sacrificing these selectivities. Finally, we were able to clearly correlate our findings with the activity of the Pt catalyst.

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