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Regioselective C–H hydroxylation of *n*-alkanes using Shilov-type Pt catalysis in perfluorinated micro-emulsions†Michiel Janssen and Dirk E. De Vos *

Shilov-chemistry inspired catalysis has remained largely overlooked as a tool for establishing the remote hydroxylation of non-polar compounds, such as long linear alkanes, due to the need for an acidic aqueous solution. To circumvent the solubility issue, the concept of micellar catalysis is introduced, using Pt^{II} in perfluorinated micro-emulsions. Notably, the terminal C–H activation of *n*-heptane is demonstrated under an oxygen atmosphere using perfluorooctanoic acid (PFOA) as a surfactant, along with the intrinsic ability of Pt^{II} to convert the highly inert primary C–H bonds. Coordination of Pt^{II} to the carboxylate groups of PFOA proved to be particularly important for achieving maximum catalyst activity towards the hydrocarbon substrate solubilized inside the micelle interior. Based on these insights, optimization of the reaction parameters allowed a positional selectivity of 60% for 1-heptanol, among the C₇ alcohols, to be achieved, using low catalyst and surfactant loadings under acid-free conditions.

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Introduction

The one-step oxidation of linear saturated hydrocarbons is a valuable approach to obtain useful oxygenated organics with high atom economy and favorable thermodynamics.^{1,2} Herein, selective hydroxylation of the remote methyl group is of particular interest to the chemical and pharmaceutical industries for providing an economic route towards primary alcohols.³ Nonetheless, the intrinsic chemical inertness of aliphatic C–H bonds has hitherto impeded the development of appropriate methods. In general, current C–H activation systems still rely on radical-mediated pathways, induced by exposure to high temperatures or highly reactive compounds, *e.g.* peroxides, which are incompatible with high chemo- and regioselectivity. Accordingly, the reactivity in such processes is dictated by the homolytic C–H bond dissociation energy (BDE), which decreases upon the introduction of a neighboring hydroxyl group;^{2,4,5} the alcohol product is therefore considerably more reactive than the alkane substrate, causing the formation of more advanced oxidation products. Moreover, terminal C–H bonds are typically the least reactive within the aliphatic chain as they possess the highest BDEs.⁶

To our knowledge, terminal hydroxylation of long linear alkanes has exclusively been accomplished with high selectivity (>90%) by means of biocatalytic systems, in particular heme-containing (cytochrome P450)^{7,8} and non-heme membrane-bound (alkane hydroxylase AlkB)⁹ hydroxylases. However, the inherently low reaction rates, stoichiometric supply of expensive cofactors and high feed dilution have greatly hindered industrial applications.¹⁰ To overcome these limitations while maintaining the morphology induced shape selectivity, biomimetic alternatives with sterically constrained metal centers have been designed, including Mn-based porphyrins, metal-exchanged (alumino)silicates and metal-substituted aluminophosphates.^{11–14} For example, Thomas and co-workers reported the remote oxidation of *n*-hexane with MnALPO-18, resulting in a positional selectivity of 54% for 1-hexanol within the C₆ alcohol fraction.¹³ However, numerous shortcomings still need to be overcome, such as (i) the predominant formation of the corresponding aldehyde and carboxylic acid,¹³ (ii) the lack of confirmation by other independent studies,^{12,13,15} (iii) the use of complex organic ligands and expensive oxidants¹⁴ and (iv) the need for operation at very low conversion (<0.05%).¹⁴

Apart from imposing steric hindrance, the use of fundamentally different activation modes has been recognized as a promising strategy.¹⁶ Much attention has been directed towards electrophilic C–H activation with late transition metals. Notably, by combining a homogeneous Pt^{II} catalyst with H₂PtCl₆ as a stoichiometric oxidant, Shilov and co-workers succeeded in conducting the hydroxylation of

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Scheme 1 Catalytic cycle for a typical Shilov system (left) and for Shilov-type Pt catalysis in a perfluorinated micro-emulsion system (right), using a) Pt^{IV} and b) molecular oxygen (O_2) as the terminal oxidant ($\text{X} = \text{Cl}^-$ or HSO_4^-).¹

aliphatic compounds (Scheme 1).^{17–19} More importantly, the electrophilic nature of this Pt^{II} catalyst allows one to discriminate between non-equivalent C–H bonds in a very different manner than radicals do. Selectivity patterns in Pt-mediated Shilov-type reactions therefore show an enhanced reactivity of the remote C–H bonds, together with a reduced degree of overoxidation.^{19,20} Nevertheless, such Pt chemistry is almost exclusively performed in acidic aqueous solutions, thereby restricting the substrate scope to water-soluble substrates, *e.g.* alkyl ammonium salts, as well as lower carboxylic, sulfonic and phosphonic acids.^{21,22} Hence, Shilov-inspired Pt catalysis has hitherto not been applied for the selective oxidation of non-polar aliphatic compounds. While we demonstrated the potential of implementing acetic acid as a solvent in converting *n*-heptane to 1-heptanol,²³ the use of an aqueous solution would be highly desirable from an ecological perspective.

Like in the well-studied hydroformylation of long-chain olefins,²⁴ the concept of micellar catalysis is evaluated in this work as a viable approach to achieve terminal hydroxylation of *n*-alkanes (Scheme 1). Perfluorocarboxylic acids, notably perfluorooctanoic acid (PFOA), were selected as surfactants in order to simultaneously ensure (i) substrate compatibility with *n*-alkanes at elevated temperatures²⁵ and (ii) stability under oxidative conditions. In addition, the oxygen solubility is much higher in perfluorinated solvents (4200 ppm at 25 °C and 1 atm)²⁶ than in water (9 ppm at 20 °C and 1 atm);²⁷ this could allow the costly Pt^{IV} salt to be replaced with O_2 as a more economic, readily available and environmentally benign oxidant.

Experimental

Materials

All chemicals were used as received: *n*-heptane (Sigma-Aldrich, $\geq 99\%$), cyclohexane (Sigma-Aldrich, $\geq 99.8\%$),

2,2,3,3-tetramethylbutane (Sigma-Aldrich, $\geq 94\%$), potassium tetrachloroplatinate, K_2PtCl_4 (Acros Organics, 46–47% Pt), cobalt(II) acetate tetrahydrate, $\text{Co}(\text{OAc})_2 \cdot 4\text{H}_2\text{O}$ (Acros Organics, 97%), perfluorooctanoic acid (J&K Scientific, 98%), sulfuric acid, H_2SO_4 (Acros Organics, $\geq 95\%$), dioxygen, O_2 (Air Liquide, N25), D_2O (Sigma-Aldrich, 99.9% D), benzyl alcohol (Sigma-Aldrich, $\geq 99\%$), *n*-decane (Carl Roth, $\geq 99\%$), sodium hydroxide, NaOH (Acros Organics, $\geq 99\%$), chloroform (Acros Organics, 99.97%) and *N,O*-bis(trimethylsilyl)trifluoroacetamide (Sigma-Aldrich, BSTFA + TCMS 99:1).

Catalytic reaction

In a typical reaction, a glass vial (5.5 mL) was charged with the substrate (0.67 M), a noble metal catalyst (1 mol%), sulfuric acid (H_2SO_4 ; 0.33 M), a surfactant (0.48 M), deionized water (1.5 mL) and a magnetic stirring bar. By means of a pierced Teflon-lined stopper, the vial was partially closed and positioned inside a stainless steel reactor (11 mL). At room temperature, the latter was then sealed, flushed with pure O_2 for 5 s and subsequently pressurized to 20 bar O_2 . Next, the reaction was initiated by heating the reactor to 150 °C, while stirring at 500 rpm, upon which time recording was started. After 6 h, the reaction was discontinued by cooling of the reactor on ice. The aqueous product mixture, including any precipitated surfactant, was then transferred to a separate vial (11 mL), together with 1.5 mL of chloroform (CHCl_3) that was used to rinse the glass reaction vial. Ultimately, the resulting biphasic mixture was prepared for qualitative and quantitative analysis.

Product analysis and identification

After neutralization of the aqueous solution with NaOH (4 M), the biphasic mixture was first agitated on a vortex mixer (20 s) and subsequently subjected to centrifugation for 10 min (3200

rpm). To determine the product yields of the non-polar high molecular weight compounds, as well as of the higher aliphatic carboxylic acids, the CHCl_3 -phase was analyzed by gas chromatography (GC) before and after silylation with *N,O*-bis(trimethylsilyl)trifluoroacetamide (BSTFA), respectively. Non-derivatized samples were prepared by combining 300 μL of the CHCl_3 -phase with 300 μL of a 0.2 M solution of benzyl alcohol in CHCl_3 , after which analysis was carried out on a Shimadzu GC-2010 instrument with a 60 m DB-FFAP column and FID. At the same time, derivatization was conducted by transferring 54 μL of BSTFA to 300 μL of the CHCl_3 -phase, with subsequent heating of the solution for 90 min at 60 °C while stirring at 500 rpm. After heating was stopped, samples were produced by adding 300 μL of CHCl_3 containing an external standard (*n*-decane, 0.2 M) and analyzed on a similar Shimadzu GC-2010 instrument equipped with a 60 m CP-Sil 5 CB column and FID. Representative chromatograms with annotated peaks are shown in Fig. S1–S3.† The identity of each compound was unambiguously confirmed by comparing the observed retention time with that of a commercial or synthesized sample, along with analysis of the reaction samples on an Agilent 6890 GC instrument, equipped with an HP-1 MS column and coupled to an Agilent 5973 MSD mass spectrometer. In addition, to quantify the product yields of the polar low molecular weight by-products, the aqueous phase was analyzed by proton nuclear magnetic resonance (^1H NMR) spectroscopy. Sample preparation was performed by diluting 300 μL of the aqueous product solution with 300 μL of a 0.05 M solution of benzyl alcohol in D_2O , after which respective ^1H NMR spectra were recorded on a Bruker Ascend 400 MHz spectrometer containing a 5 mm PABBO BB/ ^{19}F - ^1H /D probe and autosampler. During measurements, the broad water signal was suppressed by applying a zgpr pulse program (p1 9.75 μs ; ns 32; d1 5 s; aq 2.55 s; plw1 15 W; plw9 5.7 $\times 10^{-5}$ W; o1P) on the resonance signal of water, determined and selected automatically. An overview of the identified products is given in the ESI.† Furthermore, a Gasmet DX4000 FTIR gas analyzer was used to elucidate the composition of the vapor phase after the reaction. Prior to each measurement, part of the vapor phase was transferred from the reactor into a plastic syringe (5 mL) and, as such, injected into a N_2 stream (75 mL min^{-1}). Next, the volume concentrations of the various gaseous compounds were measured at the detector level and subsequently processed using the Calcmeter Standard software version 12.161. Finally, since lower degradation by-products were formed through C–C splitting of the primary reaction products, quantitative yields were calculated as follows: the amount of each compound in mmoles was determined (i) by comparing the normalized peak area with that obtained for benzyl alcohol in ^1H NMR measurements and (ii) by applying the effective carbon number (ECN) during GC analysis, after which the corresponding carbon yields were obtained by dividing the number of mmoles of C in the respective product by the total number of mmoles of C initially supplied in *n*-heptane (7 mmol).

Catalyst characterization

Electrospray ionization mass spectrometry (ESI-MS) measurements were conducted in positive-ion mode with a Thermo Finnigan LCQ Advantage mass spectrometer. Samples were prepared by diluting the reaction mixture in Milli-Q water to obtain a catalyst concentration of approximately 0.1 mg mL^{-1} . Next, 5 mL of the resulting solution was injected into a water stream (0.2 mL min^{-1}) containing 0.1% of formic acid, directed towards the mass spectrometer without prior chromatographic separation and analyzed in full scan mode over an m/z range of 800 to 1000. To reduce the number of cations present in solution, aqueous product mixtures were neutralized with KOH (4 M), instead of NaOH, during work-up.

Results and discussion

Pt-mediated alkane oxidation in perfluorinated micro-emulsions

To assess the activity of Pt^{II} towards selective C–H oxidation with O_2 in a perfluorinated micro-emulsion, perfluorooctanoic acid (PFOA) was added to an acidic aqueous solution (0.33 M H_2SO_4) in concentrations above its critical micelle concentration (CMC; 11 mM at 25 °C and 1 atm),²⁸ together with 1 mol% of K_2PtCl_4 ; next, the conversion of *n*-heptane (standard deviation (SD) = 0.026%) was examined in a standard reaction for 1 h at 150 °C under 20 bar O_2 . As shown in Table 1, considerable reaction only occurred in the presence of a Pt-containing micro-emulsion. In particular, comprehensive qualitative analysis revealed eight distinct product categories, including C_7 alcohols ($\text{C}_7(\text{OH})$), C_7 ketones ($\text{C}_7(\text{O})$), C_7 aldehyde ($\text{C}_7\text{H}(\text{O})$), C_7 acid ($\text{C}_6(\text{COOH})$), lower alcohols ($\leq \text{C}_6(\text{OH})$), lower ketones ($\leq \text{C}_6(\text{O})$), lower aldehydes ($\leq \text{C}_6\text{H}(\text{O})$) and lower carboxylic acids ($\leq \text{C}_5(\text{COOH})$); a complete overview with molecular structures is given in Fig. S4.† Both the C_7 alcohols and the lower primary alcohols were also present as perfluorooctanoate esters due to *in situ* esterification with the PFOA carboxylic acid. Moreover, quantitative Fourier transform spectroscopy (FTIR) allowed identification of certain compounds in the vapor phase, primarily lower alkanes and a small amount of CO. Hence, overoxidation took place to some extent under the applied reaction conditions.

Nonetheless, a significant degree of hydroxylation was observed as well, along with a noteworthy positional selectivity of 21% for 1-heptanol (SD = 2.2%) within the fraction of C_7 alcohols (Table 1). These products seem to originate from a Pt^{II} -catalyzed reaction, rather than from a non-selective radical-mediated autoxidation process. In this regard, the reaction most likely starts with the Pt^{II} -catalyzed hydroxylation of *n*-heptane, after which the primary products, *viz.* the alcohols, are converted or degraded by consecutive side reactions, leading to a decline in alcohol selectivity. Furthermore, as evidenced by the much lower conversion upon omission of the surfactant (Table 1), it also appears

Table 1 Carbon yields in the Pt^{II}-catalyzed oxidation of *n*-heptane in a perfluorinated micro-emulsion^a

Catalyst	Surfactant	C (%)	Carbon yield ^b (%)								GP
			C ₇ (OH) ^c (1:-2:-3:-4) ^d	C ₇ (O)	C ₇ H(O)	C ₆ (COOH)	≤C ₆ (OH) ^c	≤C ₆ (O)	≤C ₆ H(O)	≤C ₅ (COOH)	
—	—	0.11	0	0.01	0	0	0.02	0.01	0	0.07	0
K ₂ PtCl ₄	—	0.11	0.01 (51:26:16:7)	0.01	0	0	0.01	0.01	0	0.07	0
—	PFOA	0.98	0.15 (9:44:33:14)	0.14	0.01	0	0.16	0.07	0.02	0.39	0.04
K ₂ PtCl ₄	PFOA	0.62	0.10 (21:39:27:13)	0.08	0	0	0.08	0.02	0.01	0.29	0.04

^a Conditions: *n*-heptane (0.67 M), K₂PtCl₄ (0–1 mol%), H₂SO₄ (0.33 M), perfluorooctanoic acid (PFOA; 0–0.48 M), H₂O (1.5 mL), 1 h, 150 °C, 20 bar O₂. Abbreviations: C₇(OH), C₇ alcohols; C₇(O), C₇ ketones; C₇H(O), C₇ aldehyde; C₆(COOH), C₇ acid; ≤C₆(OH), lower alcohols; ≤C₆(O), lower ketones; ≤C₆H(O), lower aldehydes; ≤C₅(COOH), lower carboxylic acids; GP, gaseous products. ^b Number of millimoles of C in the respective product divided by the total number of millimoles of C initially supplied in *n*-heptane (7 mmol). ^c Present in free form and as ester with PFOA.

^d Positional selectivities within the fraction of C₇ alcohols – 1-heptanol:2-heptanol:3-heptanol:4-heptanol.

that the Pt^{II} catalyst is only sufficiently active towards alkane C–H oxidation when incorporated into a micro-emulsion. Thus, solubilization of *n*-heptane into the micellar interior seems essential to ensure a close interaction between the substrate, the oxidant and Pt^{II}. Analogous results were obtained for the well-known oxidation of cyclohexane (see the ESI†, Table S1).²⁹

Remarkably, a substantial increase in the reaction rate was also noticed under metal-free conditions, when comparing oxidation in coarse *n*-heptane droplets to oxidation in a perfluorinated micro-emulsion containing solubilized *n*-heptane (Table 1). Since no CO₂ could be detected by FTIR-analysis of the vapor phase after the reaction, one cannot attribute this rate enhancement to a thermally induced decarboxylation of PFOA and ensuing formation of reactive radicals. Rather, the radical chemistry involved in these metal-free emulsions seems the same as that observed in a classic autoxidation, as no selectivity differences were found when comparing the oxidation process in pure *n*-heptane vs. perfluorooctane at a similar conversion (Fig. S5†). A more likely reason for the enhanced rate in the perfluorinated emulsion is the significantly higher solubility of O₂ in perfluoroalkanes, compared to their hydrocarbon counterparts,²⁶ which could favor the O₂-mediated H-abstraction from *n*-heptane inside the micelle interior and, as such, could accelerate initiation of the non-selective oxidation reactions.

Insight into the catalytic role of Pt^{II}

To prove the role of Pt^{II} in the enhanced terminal C–H hydroxylation observed for *n*-heptane (Table 1), its activity was compared with that of Co(OAc)₂, for which a slightly lower catalyst loading was adopted to avoid deactivation by clustering.³⁰ Co^{III/II} is in fact known to accelerate the initiation of hydrocarbon autoxidation, in particular *via* the one-electron decomposition of intermediate alkyl hydroperoxides according to the Haber–Weiss cycle [eqn (1) and (2)].³¹ It is therefore expected to elicit a selectivity pattern that is representative of reactions that are only mediated by radicals.

Under identical conditions as applied for K₂PtCl₄, a notable increase in conversion took place for the Co-catalyzed reaction, reflecting a faster oxidation (Fig. 1). More importantly, for reactions at a similar conversion, a lower alcohol selectivity was observed with Co(OAc)₂ in addition to a significantly reduced reactivity of the terminal C–H bonds (8% vs. 28% for Pt). These findings suggest that Pt^{II} is much less involved in accelerating radical-mediated reactions than Co^{II} yet, at the same time, is to a large extent responsible for the formation of 1-heptanol in the micro-emulsion system.

The question arises whether Pt^{II} is truly capable of activating the highly inert primary C–H bonds. Therefore, the activity of K₂PtCl₄ towards the oxidation of 2,2,3,3-tetramethylbutane (TMB) was investigated, given that TMB exclusively contains primary C–H bonds with very high C–H

Fig. 1 Comparison between the Pt^{II}- and Co^{II}-catalyzed oxidation of *n*-heptane in a perfluorinated micro-emulsion. Conditions: *n*-heptane (0.67 M), K₂PtCl₄ (1 mol%)/Co(OAc)₂·4H₂O (0.5 mol%), H₂SO₄ (0.33 M), PFOA (0.48 M), H₂O (1.5 mL), 1–2 h, 150 °C, 20 bar O₂.

Fig. 2 Time profiles for (a) the Pt^{II} -mediated and (b) the metal-free oxidation of *n*-heptane in a perfluorinated micro-emulsion. Conditions: *n*-heptane (0.67 M), K_2PtCl_4 (0–1 mol%), H_2SO_4 (0.33 M), PFOA (0.48 M), H_2O (1.5 mL), 0.25–4 h, 150 °C, 20 bar O_2 .

BDEs ($>400 \text{ kJ mol}^{-1}$).³² In this way, the radicals that are present during autoxidation are expected to be insufficiently active to induce homolytic C–H cleavage.⁴ Consequently, transformations can only be achieved under the influence of an appropriate catalyst. Notably, after reaction for 2 h at 150 °C under 20 bar O_2 , a distinct peak emerged from the chromatogram after analyzing the product mixture by GC-MS (Fig. S6†). Close examination of the corresponding mass spectrum (Fig. S7†) revealed the formation of 2,2,3,3-tetramethyl-1-butyl perfluorooctanoate as the product of the Pt^{II} -mediated reaction. Hence, this specific hydroxylation at $-\text{CH}_3$ can only be attributed to the presence of a functioning Pt^{II} catalyst in solution, confirming the crucial role of K_2PtCl_4 in synthesizing 1-heptanol directly from *n*-heptane.

With O_2 as the terminal oxidant, deactivation of Pt^{II} *via* reduction to metallic platinum (Pt^0) generally takes place over time in Shilov-type reactions.¹⁸ More insight into the catalyst lifetime was obtained by measuring time-dependent changes in catalyst activity. To this end, a time profile was constructed at 150 °C under 20 bar O_2 . The resulting graph (Fig. 2a) shows that catalyst deactivation became highly prominent between reaction times of 2 h and 4 h, as reflected by the significant formation of a black precipitate and by the decline in positional selectivity for 1-heptanol to the level observed for a metal-free micro-emulsion. This deactivation most likely results from (i) the disproportionation of Pt^{II} to Pt^0 and Pt^{IV} [eqn (3)] or (ii) the functioning of Pt^{II} as the terminal oxidant in the oxidation of the Pt^{II} -R complex [eqn (4)].¹⁸

When these reactions occur at a faster rate than the reoxidation of Pt^0 by O_2 , the amount of Pt^{II} that is available for C–H

activation strongly diminishes, thereby reducing the impact of the catalytic system on the overall selectivity pattern.

Structure of the active Pt^{II} catalyst

Remarkably, Fig. 2a also shows that the positional preference for alcohol formation at C1 increases over the first 2 h of the reaction, from 10% to 28%. This suggests that the catalytic system only assumes full activity after a certain induction period. Moreover, in the absence of K_2PtCl_4 , a less pronounced raise in primary alcohol selectivity was observed, giving rise to a lower value of 13% after 2 h (Fig. 2b). This confirms that the enhanced positional selectivities for 1-heptanol with Pt do not result from a difference in stability of the four positional isomers towards overoxidation, but instead are to be ascribed to the involvement of an active Pt^{II} catalyst. Given these findings, a pre-activation step was included in the catalytic procedure, during which Pt^{II} was allowed to equilibrate in a micro-emulsion environment, lacking the hydrocarbon substrate, at 150 °C and under 20 bar O_2 . Such catalyst pre-activation was performed for 10–40 min, after which 1 mmol of *n*-heptane was added and converted under standard reaction conditions for 30 min. A positive relation was found between the duration of this pre-activation step and the positional selectivity for 1-heptanol; by prolonging the pre-activation time to 40 min, an increase from 9% to 39% was observed (Fig. 3). This observation suggests that not K_2PtCl_4 itself, but an *in situ* formed Pt^{II} complex functions as the active catalyst in the perfluorinated micro-emulsion.

Accordingly, attention was devoted to unravelling the structure of this active Pt^{II} complex; ESI-MS was used to analyze a sample taken after converting *n*-heptane for 1 h with K_2PtCl_4 . The recorded spectrum in positive-ion mode clearly evidenced a Pt-based complex (Fig. 4), as indicated by the distinct peak pattern that is caused by the isotopic

Fig. 3 Influence of the catalyst pre-activation time on the Pt^{II} -mediated oxidation of *n*-heptane in a perfluorinated micro-emulsion. Conditions: K_2PtCl_4 (1 mol%), H_2SO_4 (0.33 M), PFOA (0.48 M), H_2O (1.5 mL), 150 °C; pre-activation – 0–40 min, 20 bar O_2 ; reaction – *n*-heptane (0.67 M), 30 min, 20 bar O_2 .

distribution of Pt (^{194}Pt , ^{195}Pt , ^{196}Pt , ^{198}Pt). Considering the m/z ratio of 874.6, as well as the different reagents present in solution, this complex was found to correspond to $[\text{Pt}(\text{C}_7\text{F}_{15}\text{COO})(\text{Cl})(\text{OSO}_3\text{H})_2(\text{H}_2\text{O})_2]$. It should be noted that, in addition to the solvent and homogeneous acid, perfluorooctanoate also seems to coordinate as an anionic ligand to the Pt^{II} center, revealing the essential role of PFOA in generating the active catalyst *in situ*. At the same time, the previously observed induction period (Fig. 2a) completely disappeared when sulfuric acid was omitted from the solution during kinetic experiments (Fig. S8†). Whether PFOA coordinates to Pt can indeed depend on the acidity of the aqueous solution, according to the acid dissociation equilibrium of PFOA [eqn (5)]:

An increase in proton concentration, caused by the addition of sulfuric acid ($\text{pK}_a = -2$ vs. 2.5 for PFOA),^{33,34} will drive the equilibrium towards the non-dissociated form, thereby suppressing coordination by the carboxylate groups of PFOA. From that perspective, acid-free conditions would indeed be more favorable for accelerating the *in situ* formation of the active Pt^{II} complex and for increasing its concentration in solution. On top of that, significant *n*-heptane conversion was only achieved in aqueous reaction mixtures containing a perfluorinated surfactant (Table 1). Moreover, a substantially reduced reaction rate was observed at surfactant concentrations well below the CMC of PFOA (11 mM at 25 °C and 1 atm; Fig. S9†).²⁸ Altogether, these observations strongly support the hypothesis that the positioning of Pt^{II} at the micellar surface is crucial for providing an active Shilov-catalyst that is capable of the terminal hydroxylation of *n*-heptane, solubilized inside the micelle interior.

Enhancing the catalytic activity of Pt^{II}

Considering the Pt^{II} (0.01 mmol) and surfactant (0.725 mmol) concentrations used so far, as well as the average aggregation number of PFOA (18 at 25 °C and 1 atm),³⁵ the number of Pt^{II} atoms per spherical micelle was calculated to be only 0.25. Consequently, the catalyst loading was raised under standard reaction conditions (1 h, 150 °C, 20 bar O_2) to increase the fraction of *n*-heptane that is exposed to Pt^{II} and, in this way, increase the impact of the catalyst over the background autoxidation reactions (Fig. 5). Moreover, the experiment was performed in the presence and absence of sulfuric acid to confirm the ligating role of PFOA in the active Pt^{II} catalyst (Fig. 4) and its dependency on the acidity of the aqueous solution (Fig. S8†). With sulfuric acid, doubling the amount

Fig. 4 Positive-ion mode ESI-MS spectrum of the aqueous solution obtained after the Pt^{II} -catalyzed oxidation of *n*-heptane in a perfluorinated micro-emulsion. Conditions: *n*-heptane (0.67 M), K_2PtCl_4 (0.0067 M, or 1 mol%), H_2SO_4 (0.33 M), PFOA (0.48 M), H_2O (1.5 mL), 1 h, 150 °C, 20 bar O_2 . ESI-MS: calcd. for $[\text{Pt}(\text{C}_7\text{F}_{15}\text{COO})(\text{Cl})(\text{OSO}_3\text{H})_2(\text{H}_2\text{O})_2]$ $[M]$: $m/z = 874.7$ ($[M + H]^+$), found: $m/z = 874.6$ ($[M + H]^+$).

Fig. 5 Pt^{II} -catalyzed oxidation of *n*-heptane in a perfluorinated micro-emulsion with varying catalyst loading, in the presence and absence of sulfuric acid (H_2SO_4). Conditions: *n*-heptane (0.67 M), K_2PtCl_4 (1–5 mol%), H_2SO_4 (0–0.33 M), PFOA (0.48 M), H_2O (1.5 mL), 1 h, 150 °C, 20 bar O_2 .

Fig. 6 Pt^{II} -catalyzed oxidation of *n*-heptane in a perfluorinated micro-emulsion with varying surfactant concentration. Conditions: *n*-heptane (0.67 M), K_2PtCl_4 (1 mol%), H_2SO_4 (0.33 M), PFOA (0.05–0.48 M), H_2O (1.5 mL), 1 h, 150 °C, 20 bar O_2 .

of Pt^{II} led to an increase in the positional selectivity for 1-heptanol (28%), though higher catalyst loadings did not have any additional influence. It therefore appeared that a

maximum cooperation between the micelles and Pt could be reached using 2 mol% of K_2PtCl_4 . In contrast, when sulfuric acid-free substrate mixtures were applied for *n*-heptane conversion, a steadily growing preference for the terminal C–H bonds was observed upon raising the catalyst loading to 5 mol%, thereby uncovering an exceptional positional selectivity for 1-heptanol of 52%. These results are thus in good agreement with previous findings concerning the need for acid-free conditions to ensure close proximity between the reactants.

Since low catalyst loadings are more attractive from an economic perspective, the effect of varying the surfactant concentration was studied for establishing similarly enhanced catalyst–substrate interactions using only 1 mol% of K_2PtCl_4 . When the positional selectivity for 1-heptanol was plotted against the amount of PFOA initially added, a volcano-type relation emerged, revealing an optimum Pt^{II} activity at 0.3 M PFOA (Fig. 6). As we previously found that perfluorooctanoate needs to be coordinated to form the active Pt complex *in situ* (Fig. 4), the corresponding positional selectivity of 45% could even be increased to 60% using 2 mol% of K_2PtCl_4 under acid-free conditions (Fig. S10†). Ultimately, it is worth noting that these positional selectivities are comparable to, or even substantially higher than those reported with most state-of-the-art systems (Table 2).

Table 2 Comparison of the present catalytic system with relevant state-of-the-art systems

Catalyst	Oxidant	<i>C</i> (%)	<i>S</i> _{OH} (%) ^e	<i>S</i> _{1-OH} (%) ^f	Ref.
$\text{K}_2\text{PtCl}_4^a$	O_2	0.97	13	60	This work
Cytochrome P450 (CYP153A) ^b	NADH/putidaredoxin (CamA)/putidaredoxin reductase (CamB)	10.3	95	95	8
MnAlPO-18^c	Compressed air	8.7	18	54	13
MnTTPPP(OAc)^d	Iodosobenzene	0.02	100	26	14

^a *n*-Heptane (0.67 M), K_2PtCl_4 (2 mol%), PFOA (0.3 M), H_2O (1.5 mL), 1 h, 150 °C, 20 bar O_2 . ^b *n*-Heptane (1 mM), potassium phosphate buffer (50 mM, pH 7.5), CYP153A (3 mM), CamA (15 mM), CamB (30 mM), NADH (1 mM), H_2O /ethanol (0.5 mL), 4 h, 30 °C. ^c *n*-Hexane (0.58 mol), MnAlPO-18 (0.5 g), 24 h, 100 °C, compressed air (15 bar). ^d *n*-Heptane (6.8 M), iodosobenzene (90 mM), (5,10,15,20-tetrakis(20,40,60-triphenylphenyl)porphyrinato)manganese(III) acetate (MnTTPPP(OAc) ; 0.8 mM), benzene (0.5 mL), 7 h, 25 °C. ^e Selectivity for alcohol products.

^f Positional selectivity for primary alcohol within the alcohol fraction.

Conclusions

By introducing a Shilov-type Pt^{II} catalyst in perfluorinated micro-emulsions, based on perfluorooctanoic acid (PFOA), we have successfully demonstrated the potential of using micellar catalysis for synthesizing primary alcohols directly from long linear alkanes, such as *n*-heptane, in an aqueous reaction medium. Comparative experiments with $\text{Co}(\text{OAc})_2$ as the catalyst or 2,2,3,3-tetramethylbutane as the reactant revealed the intrinsic role of Pt^{II} in achieving selective oxidation at the highly inert primary C–H bonds. While overoxidation of the alcohol products cannot be suppressed at the high temperatures required for Pt activity, the positional selectivity patterns among the heptanols are very different from those produced by radical-mediated reactions. Furthermore, characterization, *via* i.a. ESI-MS, disclosed the need for coordination of Pt^{II} to the accessible carboxylate groups of PFOA in order to ensure catalyst activity towards the hydrocarbon substrate. Catalyst–substrate interaction could therefore substantially be improved by changing the reactant concentrations under acid-free conditions, giving rise to an exceptional positional selectivity of 60% for 1-heptanol, among the C_7 alcohols, using only 2 mol% of K_2PtCl_4 and O_2 as the terminal oxidant.

Conflicts of interest

There are no conflicts to declare.

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